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THE JOURNAL OF Organic Chemistry®

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OCTOBER 6, 1972

Synthesis and Chemistry of Hexamethyl-*trans*-15,16-dihydropyrene[1a]

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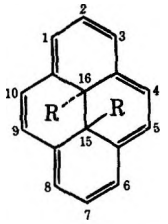
Received May 1, 1972[1b]

A seven-step synthesis of hexamethyl-*trans*-15,16-dihydropyrene is described. The dark green hydrocarbon possesses spectra and physical properties characteristic of this 14-π-electron system. It easily undergoes electrophilic substitution reactions yielding 2- and 4-mono- and 2,7-disubstituted derivatives, with which further transformations have been accomplished.

The syntheses of *trans*-15,16-dimethyl-[2] and *trans*-15,16-diethyldihydropyrene[3] by Boekelheide,[2,3] Phillips,[2] and Miyasaka[3] constitute a very interesting test of the Hückel theory of aromaticity. These unique molecules (**1**, R = CH_3 or C_2H_5) bear substituents



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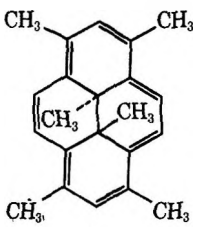
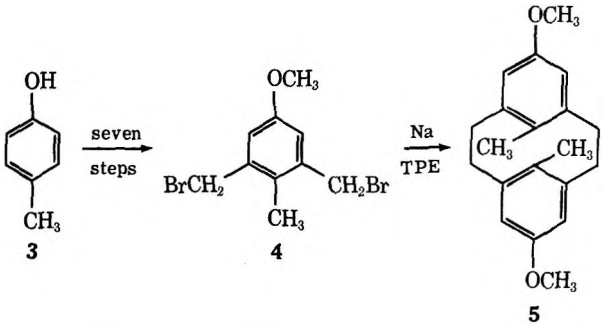


2

which are contained completely within the cavity generated by the planar 14-π-electron periphery. The physical and chemical properties of these molecules provide strong support for the Hückel theory, which predicts that $(4n \pm 2)$ π electrons of an aromatic ring form a doughnut-shaped cloud above and below the plane of the ring. The center of such a π cloud then might be empty space, and these molecules present a special opportunity to examine the effect of substituent groups within a π-electron system on the π cloud, and vice versa.

An investigation conducted in our laboratory has produced 1,3,6,8,15,16-hexamethyl-*trans*-15,16-dihydropyrene (**2**), the synthesis, physical properties, and chemistry of which we would now like to record.

The synthesis of *trans*-15,16-dimethyldihydropyrene began with *p*-cresol (**3**) and required seven steps to effect the placement of bromomethyl groups adjacent to the methyl group of **4**, a necessary precursor for the Wurtz cyclization to the corresponding [2.2]metacyclophane (**5**).[2] Although this route is necessary for the



construction of the desired metacyclophane, and consequently for dimethyldihydropyrene, shorter approaches for the preparation of other dihydropyrenes could be foreseen. In this laboratory the need for a hexaalkyldihydropyrene prompted the use of mesitol (**6**, Chart I) as starting material for the synthesis of **2**. From a synthetic viewpoint, the presence of alkyl groups adjacent to the more strongly orienting hydroxyl function of **6** fortunately allowed direct introduction of halomethyl substituents, *e.g.*, *via* a chloromethylation procedure. Accordingly, our synthesis of the resultant hexamethyl-*trans*-15,16-dihydropyrene is shown in Chart I.

Mesitol (**6**) was converted to methoxymesitylene (**7**) which was chloromethylated[4] to the bis(chloromethyl) compound **8** in good yield. Transformation of **8** into hexamethyl 5,13-dimethoxy[2.2]metacyclo-

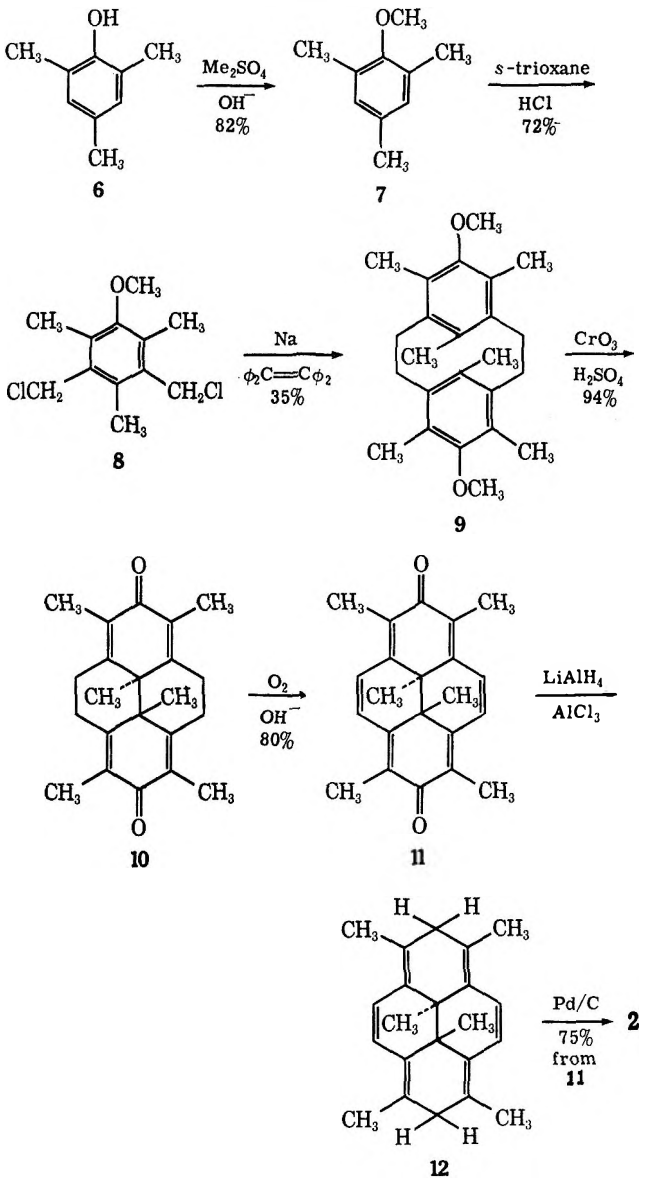
(1) (a) Presented in part at the 153rd National Meeting of the American Chemical Society, Miami Beach, Fla., April 1967, Paper O-184. (b) Original manuscript received February 26, 1968.

(2) V. Boekelheide and Joseph B. Phillips, *J. Amer. Chem. Soc.*, **89**, 1695 (1967).

(3) V. Boekelheide and T. Miyasaka, *ibid.*, **89**, 1709 (1967).

(4) J. von Braun and J. Nelles, *Chem. Ber.*, **67**, 1094 (1934).

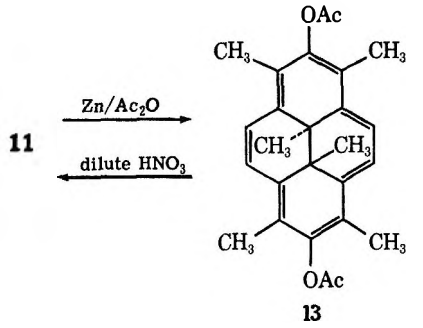
CHART I



phane[5] (**9**) was accomplished *via* a modified Wurtz procedure using a very fine sodium sand and tetraphenylethylene[6,7] as catalyst. The average yield for this step was 35%, which is higher than that reported previously for 8,16-substituted [2.2]metacyclophanes formed in a double bridge closure.[7] When the corresponding bis(iodomethyl)methoxymesitylene, prepared from **8** by halide exchange, was subjected to the same cyclization conditions, **9** was obtained only in 17% yield. Thus the use of the chloromethyl intermediate not only eliminates the necessity for a halide exchange step but also leads to a considerable improvement in the yield of metacyclophane. The nmr spectrum of this compound shows a six-proton singlet at τ 9.50, characteristic of the 8,16 internal methyl groups of [2.2]metacyclophanes.[7]

Oxidation of **9** gave the pale yellow hexamethylbis(dienone) (**10**),[8] the internal methyls of which appear in its nmr spectrum at τ 8.87. The downfield shift from τ 9.50 to 8.87 of the internal methyls is indicative of the change from the stepped *trans*-[2.2]metacyclophane structure to the more planar bis(dienone), where the internal methyl groups of **10** no longer protrude over the shielding face of the opposing aromatic ring.

Air oxidation of hexamethylbis(dienone) in ethanolic potassium hydroxide produces the stable bright orange hexamethyldihydropyrene-2,7-quinone (**11**) which is a true quinone as shown by its ready reduction to its dark green hydroquinone diacetate, 2,7-diacetoxyhexamethyldihydropyrene (**13**), which could be reoxidized



to the quinone by dilute nitric acid. The nmr spectrum of **13** is indicative of the strong ring current of the 15,16-dihydropyrenes,[2,3] whereas the lateral 4, 5, 9, and 10 protons are deshielded and appear as a singlet at τ 1.34 (as do the 1-, 3-, 6-, and 8-methyls which appear at τ 7.00); the internal 15- and 16-methyls are strongly shielded by the 14 π system which surrounds them and appear at τ 13.88.

The reduction of the quinone to the bis(triene) **12** at room temperature yields a 3:2 mixture of the desired hexamethyldihydropyrene **2** and the bis(triene) **12**. The ready formation of some hexamethyldihydropyrene directly in this reduction is a striking illustration of the driving force directed toward the formation of this stable 14-π-electron system. No attempt was made to separate the two products, but from the nmr spectrum of such a mixture (see Experimental Section) the resonances and therefore the relative amount of **12** could easily be determined.

Dehydrogenation of this mixture produced hexamethyl-*trans*-15,16-dihydropyrene (**2**); the overall yield in seven steps was 11%. The ultraviolet–visible absorption spectrum of the hydrocarbon, which crystallizes from heptane in large black-green prisms, mp 185–186°, is shown in Figure 1. The nmr spectrum of **2** shows dramatically the effect of a strong induced ring current. Whereas the internal methyl resonances are shifted to abnormally high field and appear as a singlet at τ 14.04, the peripheral methyl resonances appear at τ 6.84, and proton resonances appear at τ 2.20 for the 2 and 7 protons and at τ 1.44 for four lateral protons. The signals for these peripheral methyls and protons are significantly downfield from the usual regions for aromatic methyl and proton resonances.

(5) The numbering of [2.2]metacyclophanes used here is that suggested by B. H. Smith in "Bridged Aromatic Compounds," Academic Press, New York, N. Y., 1964, Chapter 1.

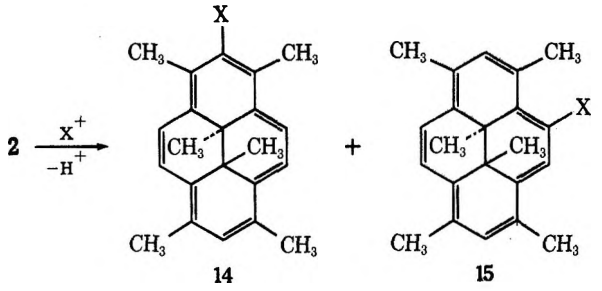
(6) E. Muller and G. Roscheisen, *Chem. Ber.*, **90**, 543 (1957).

(7) W. S. Lindsay, Peter Stokes, Leslie G. Humber, and V. Boekelheide, *J. Amer. Chem. Soc.*, **83**, 943 (1961).

(8) The transformation **9** → **10** was accomplished also with anhydrous ferric chloride in 10–15% yields.

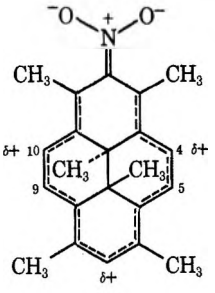
In addition to the strong ring current demonstrated by 15,16-dimethyldihydropyrene,[2] chemical evidence[9] for its aromatic character was indicated by its ease of electrophilic substitution to give numerous derivatives. Hexamethyldihydropyrene, similarly, will undergo such reactions.[10]

The electrophilic substitution of hexamethyldihydropyrene usually resulted in the formation of a mixture of 2- and 4-monosubstituted products, **14** and **15**, when 1 mol of the electrophile was employed.



14 **15**

Nitration of **2** with cupric nitrate in acetic anhydride[9,11] produces a 2:1 mixture of 2-nitro- (**14**) and 4-nitrohexamethyldihydropyrene (**15**). The 2-nitro isomer shows singlet resonances in its nmr spectrum at τ 1.24 for the 4, 5, 9, and 10 protons, τ 2.06 for the 7 proton, τ 6.83 and 6.92 for the 1,3- and 6,8-methyls, and two singlets separated by 30 Hz centered at τ 13.88 for the internal 15,16-methyls. It is of interest to observe the chemical equivalence of the 4 and 10 protons to the 5 and 9 protons. If the nitro group of **14** were conjugated to a great extent with the dihydropyrene ring, a resulting resonance hybrid like **16** would require the 4 and 10 protons to be equivalent and distinct from the equivalent 5 and 9 protons;



16

consequently an AB-type spin system would be expected. That only a singlet is observed for these protons suggests that the nitro group is not interacting with the π system, but is in fact forced out of the plane of the ring by the flanking 1- and 3-methyls. Since **14** (X = NO_2) easily undergoes more extensive nitration to give polynitro products, there is no evidence of diminished reactivity toward further electrophilic attack, also indicative of a nonconjugated nitro group. This observation is in marked contrast to the formylation experiment described below.

(9) J. B. Phillips, R. J. Molyneux, E. Sturm, and V. Boekelheide, *J. Amer. Chem. Soc.*, **89**, 1704 (1967).

(10) Another measure of aromaticity is diamagnetic susceptibility. The diamagnetic anisotropy of **2** has been reported. See H. J. Dauben, J. D. Wilson, and John L. Laity, *J. Amer. Chem. Soc.*, **91**, 1991 (1969).

(11) A. G. Anderson, Jr., J. A. Nelson, and J. J. Tazuma, *ibid.*, **75**, 4980 (1953).

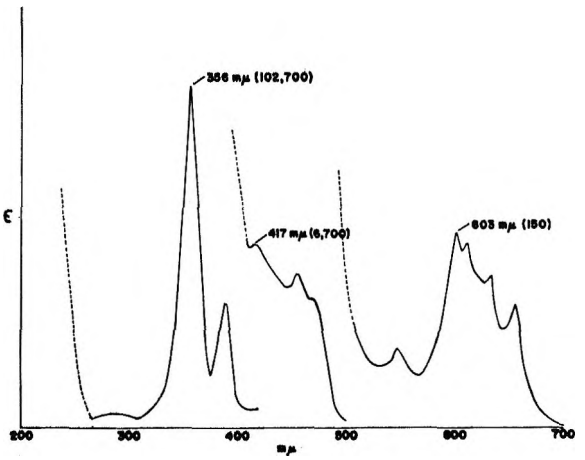
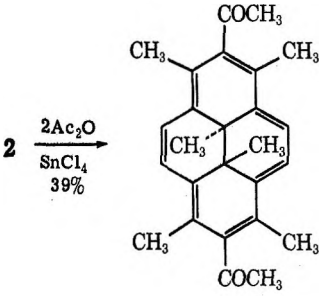


Figure 1.—Ultraviolet-visible absorption spectrum of hexamethyl-*trans*-15,16-dihydropyrene in hexane.

X-ray analysis of a dimethyldihydropyrene[12] has shown that the aromatic bond distances and bond angles are quite close to those of benzene. Therefore it should be expected that the effect of flanking 1,3-methyls in **16** would simulate that of 2,6-methyls on the steric inhibition of resonance in 1-substituted benzenes.[13]

Likewise, the nmr spectrum of the 4-nitro isomer indicates a lack of conjugation with the aromatic ring. A singlet resonance at τ 1.44 is assigned to the 9 and 10 protons in **15** (X = NO_2), which appear to be chemically equivalent. The internal methyls appear as two singlets centered at τ 13.68.

Acylation of **2** gives several products, depending upon the particular reaction. Acetylation[11] produced 2:1 mixtures from which the 2-acetyl isomer (**14**), what is believed to be the 4-acetyl isomer (**15**) that eluded exact characterization, and a trace of the 2,7-diacetylhexamethyldihydropyrene (**17**) could be isolated. All prod-



17

ucts retain the dark green dihydropyrene color. With two equivalents of acetic anhydride, **17** is the chief product. The infrared spectra of **14** (X = $COCH_3$) and **17** possess carbonyl bands at 1705 cm^{-1}, suggesting lack of conjugation of these acetyl groups with the aromatic ring. This is fully confirmed by the nmr spectrum of the 2-acetyl compound, which shows a singlet at τ 1.36, assigned to the nondifferentiated 4, 5, 9, and 10 protons. Also, the chemical reactivity of these compounds is undiminished toward further acetylation, indicating the lack of transmission by the acetyl group of

(12) A. W. Hanson, *Acta Crystallogr., Sect. B*, **18**, 599 (1965).

(13) Such steric effects in the aromatic substitution of benzenes are well documented. See, for example, G. S. Hammond and M. F. Hawthorne in "Steric Effects in Organic Chemistry," Melvin S. Newman, Ed., Wiley, New York, N. Y., 1956, Chapter 3.

any deactivating effect to the ring. As with the nitro compounds, this is due to its noncoplanar arrangement with the ring caused by the 1- and 3-methyl groups.

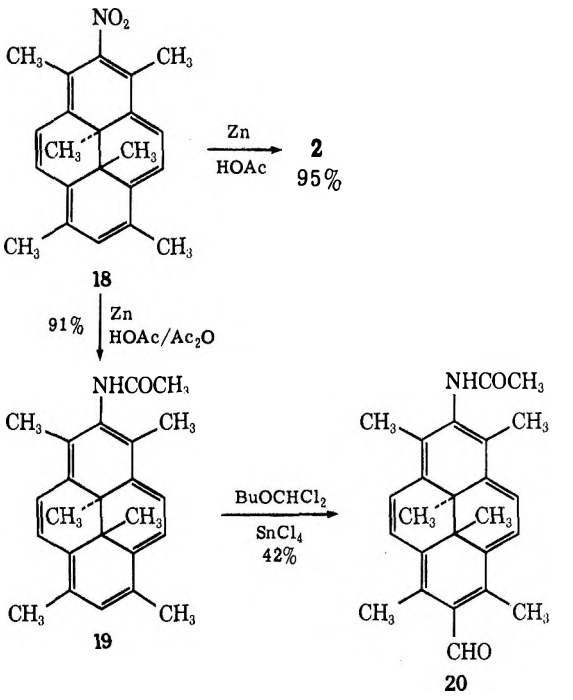
Formylation of **2** was accomplished smoothly and in excellent yield by means of the Rieche[9,14] procedure.

A mixture of 2-formyl- (**14**, X = CHO) and 4-formylhexamethyldihydropyrene (**15**, X = CHO) was obtained in 81 and 9% yields, respectively. Infrared spectra of these black-red substances show carbonyl frequencies at 1675 and 1656 cm^{-1}, respectively, indicating a strong conjugation of the formyl carbonyls with the dihydropyrene ring, a conclusion which is in complete agreement with the nmr spectra of these products, and the fact that they are inert toward further formylation under the same conditions in the presence of excess reagent. The nmr spectrum of the 2-formyl isomer shows two sharp singlets at τ 13.68 and 13.63 (the two internal methyls), singlets at τ 6.90 (the methyls at 6 and 8) and 6.65 (the methyls at 1 and 3), a singlet at τ 2.18 (the 7 hydrogen), a singlet at τ −1.36 (the formyl hydrogen), and an AB quartet, J = 8 Hz, centered at τ 1.33, clearly indicating strong coupling of the 4,10 protons with the 5,9 protons. The formyl group is apparently small enough to assume a coplanar arrangement with the dihydropyrene ring, in spite of the flanking 1,3-methyls.

The nmr spectrum of the 4-formyl isomer indicates the same degree of conjugation: two singlets at τ 2.26 and 2.18 are assigned to the 2 and 7 protons, and an AB quartet centered at τ 1.53 (J = 8 Hz) shows the coupling of the 9 and 10 protons. The proton at C-5 experiences additional deshielding due to its location adjacent to the formyl and appears at τ 0.82.

Halogenation of **2** using bromine occurred readily, yielding polybrominated products. With *N*-bromosuccinimide the reaction is much cleaner; mixtures of 2-bromo and 2,7-dibromo products result in good crude yields. The nmr spectrum of the 2-bromo compound (**14**, X = Br) shows singlet resonances at τ 13.88 for internal methyls, and an AB-type quartet centered at τ 1.32 (J = 8 Hz) for the 4, 5, 9, and 10 protons. However, the components of these mixtures are sufficiently similar in properties that their complete separation and rigorous identification have not been possible.

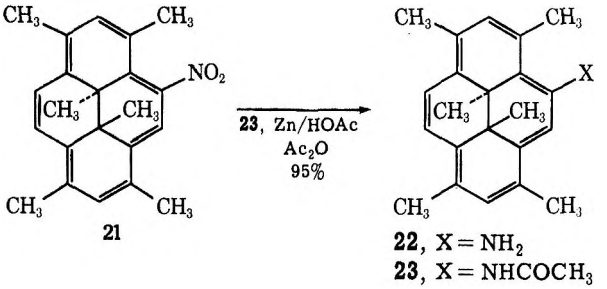
Various transformations of these electrophilically introduced substituents have been carried out. Reduction studies of the 2- and 4-nitrohexamethyldihydropyrenes were the first to be considered. Attempts to prepare 2-aminodimethyldihydropyrene[9] by reduction of the 2-nitro compound appeared to give the corresponding ammonium salt, but liberation of the free base resulted in its decomposition. It seems that strong electron-releasing substituents on the dihydropyrene ring produce an unstable or highly reactive molecule,[15] but in the hexamethyl series we anticipated that the amino group might be forced by the adjacent methyls into a more noncoplanar arrangement with the aromatic ring, with a resultant increase in stability of the molecule. However when **18** was treated with zinc in acetic acid, a rapid clean reduction to the parent hydrocarbon **2** occurred in 95% yield. This unusual reductive cleavage of an aromatic nitro group is apparently



an effect of the dihydropyrene ring and not a purely steric effect of the 1- and 3-methyls. Reduction of 2-nitromesitylene under the same conditions does not give mesitylene, while reduction in the presence of acetic anhydride gives a 70% yield of the expected 2-acetomesidide. Since, in the presence of acetic anhydride, the 2-acetamido derivative **19** is obtained in 91% yield, it would appear that 2-aminohexamethyldihydropyrene is present in some form in the course of the reduction.

An unsymmetrical disubstituted dihydropyrene **20** was prepared by formylation of **19** using the Rieche procedure.

Reduction of the 4-nitro isomer **21** appears to form the 4-amino compound **22**, but the rapidity of its decomposition prevented its isolation; the reductive removal of the nitro group to give **2** does not occur in this case. In the presence of acetic anhydride the corresponding 4-acetamido compound **23** is obtained in high yield.

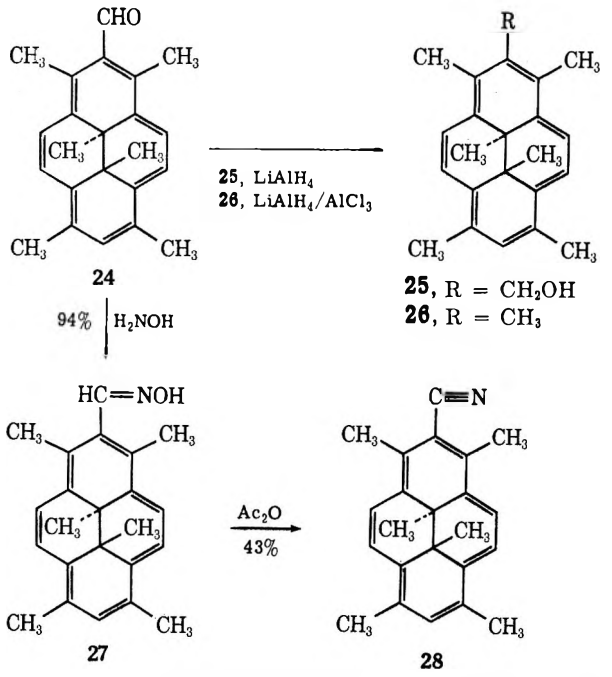


The 2-formyl derivative **24** could easily be reduced to the hydroxymethyl compound **25**, which in turn could be oxidized back to the aldehyde with manganese dioxide[16a] in quantitative yield. When the mixed hydride reducing reagent was employed, a quantitative reduction of **24** to the heptamethyldihydropyrene **26** resulted.

(14) A. Reiche, H. Gross, and E. Hoft, *Chem. Ber.*, **93**, 88 (1960).

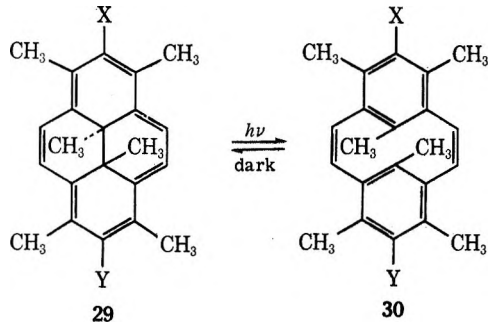
(15) Likewise, 2-ethoxydimethyldihydropyrene is an unstable oil; *cf.* ref 2.

(16) (a) R. M. Evans, *Quart. Rev. Chem. Soc.*, **13**, 61 (1959); (b) H. R. Blattman and W. Schmidt, *Tetrahedron*, **26**, 5885 (1970).



The 2-formyl compound could also be converted to the oxime **27** which, on dehydration, formed the 2-cyano derivative **28**. Both the oximino and cyano groups are conjugated with the π system, as judged by infrared and nmr spectra. The cyano group of course has linear geometry and should experience little steric hindrance by the adjacent methyl groups.

The unique phototautomerization **29** $\rightleftarrows$ **30** which has



been reported for 15,16-dihydropyrenes[2,3,9] occurs as well with the hexamethyl derivatives which have been studied. The rate of the dark reaction was found to be greatly influenced by the nature of substituents X and Y. A detailed study of this phenomenon has been reported.[16b]

For an estimation of its resonance energy, a sample of hexamethyl-15,16-dihydropyrene was submitted to Professor J. L. Margrave for combustion studies. The stabilization energy was evaluated as 68.6 kcal mol^{-1}; these studies will be reported elsewhere.

Experimental Section

General.—All melting points were observed in open-end soft glass capillaries with a Thomas–Hoover apparatus and are uncorrected. Column chromatographies were run on silica gel, mesh size 200 × 235, supplied by the Davidson Division, Grace Chemical Corp.; thin-layer chromatograms were developed on silica gel GF, containing phosphor, supplied by Brinkmann Instruments, and were observed visually and by short and long wavelength ultraviolet light. Organic extracts were washed with a concentrated sodium chloride solution, dried over anhydrous magnesium sulfate, and concentrated under water aspirator vacuum in a rotary evaporator. Nuclear magnetic resonance spectra were recorded with a Varian A-60, in deuteriochloroform unless specified, and infrared spectra were taken with a Perkin-Elmer 21 instrument. All ultraviolet–visible absorption spectra were determined with a Cary 14 recording spectrophotometer; solutions of hexamethyldihydropyrane derivatives were prepared in a darkened room and allowed to stand 48 hr in the dark before spectra were recorded.

Methoxymesitylene (**7**).—To 272.4 g (2.0 mol) of 2,4,6-trimethylphenol was added a solution of 80 g (2.0 mol) of sodium hydroxide in 800 ml of water. After being stirred 45 min at room temperature, the solution was cooled to 15–20° in an ice bath, and 188 ml (252 g, 2.0 mol) of dimethyl sulfate was added over 1 hr. The resulting suspension was heated at 85–95° for *ca.* 2 hr, after which time a second mole of sodium hydroxide was added and the suspension was heated at 95° for 12 hr. An additional 0.5 mol of sodium hydroxide and 0.5 mol of dimethyl sulfate were added, and heating at 95° was continued for 3 hr. After cooling, the two-phase suspension was extracted with ether. The combined ether extracts were shaken with 25% sodium hydroxide solution. The organic layer yielded 273.5 g of a clear pale-gold liquid. Distillation at 32° (0.3 mm) gave 248.2 g (82%) of product, n^{20}D 1.5041 (lit.[17] 1.5040).

4,6-Bis(chloromethyl)methoxymesitylene (**8**).—To 198 g (1.32 mol) of 2-methoxymesitylene were added 1400 ml of concentrated hydrochloric acid and 78.4 g (0.87 mol) of s-trioxane. Hydrogen chloride was then passed through the stirred suspension, which was warmed at 80–90° for 12–15 hr. The reaction slurry was cooled and the crude product was collected by filtration. The solid obtained was washed with water several times, dissolved in methylene chloride, and washed with sodium bicarbonate solution.

The organic layer was dried and concentrated; the residue, after slurrying with heptane, yielded the product as white needles, 234.2 g (72%), mp 138–139°. The analytical sample was prepared by recrystallization from heptane: nmr singlets at 2.39 (6, methyls), 2.45 (3, methyl), 3.68 (3, *o*-methyl), and 4.67 (4, $-CH_2Cl$).

Anal. Calcd for $C_{12}H_{16}OCl_2$: C, 58.31; H, 6.53. Found: C, 58.33; H, 6.39.

Hexamethyl-5,13-dimethoxy[2.2]metacyclophane (**9**).—A three-necked flask equipped with a Vibromixer[18] and condenser was flame-dried, while a stream of prepurified nitrogen purged the system, and the flask was allowed to cool under a positive pressure of nitrogen, controlled by a mercury bubbler. To the flask was added 200 ml of dry toluene, 20 g of freshly cut sodium pieces, and *ca.* ten drops of oleic acid. A fine sodium sand was prepared according to the procedure of Whaley.[19] The oil bath temperature was raised to 130–140° and, when all the sodium had melted (the sodium pieces, on melting, usually float to the surface of the toluene, encapsulated in sodium oleate), agitation provided by the Vibromixer was carried out for 15 min. At the end of this time agitation was stopped, and the sodium sand was allowed to cool *without stirring*.

To this mixture was added a solution of 750 mg of tetraphenylethylene in 300 ml of tetrahydrofuran (distilled from lithium aluminum hydride and stored over sodium); a deep red color forms immediately.

A 1-l. Hershberg dropping funnel[20] was attached to the flask, under the same nitrogen pressure, and a solution of 30 g of 4,6-bis(chloromethyl)methoxymesitylene in 700 ml of tetrahydrofuran was added at a rate of 20–25 drops/min. Throughout the addition, slow agitation was provided by the Vibromixer.

Addition of the first charge was complete in 15 hr. A second 30-g charge was added over 15 hr. A few drops of ethanol were then added to destroy the red color and, after standing for several minutes to allow the unreacted sodium to settle, the suspension was decanted from most of the unreacted sodium. The reaction flask and Supercel pad were washed with additional tetrahydrofuran, and the clear colorless filtrate was concentrated, yielding a crystalline residue.

This residue was dissolved in 600 ml of methylene chloride–ether (1:1), filtered, and washed with 6 *N* hydrochloric acid, and the organic layer was concentrated to a volume of 300 ml and

(17) K. von Auwers, *Ann.*, **415**, 156 (1914).
(18) Available from Chemapec, Inc., One Newark Street, Hoboken, N. J.
(19) T. P. Whaley, *Inorg. Syn.*, **5**, 6 (1956).
(20) For a description see K. B. Wiberg, "Laboratory Techniques in Organic Chemistry," McGraw-Hill, New York, N. Y., 1960, pp 206–208.

applied to a 1.5 in. × 24 in. column of dry-packed Florisil (60–200 mesh). Of six 300-ml fractions collected, fractions 2, 3, and 4 contained 17.28 g (35%) of white crystals, mp 220–230°, which contained 86% metacyclophane (*via* nmr). Two recrystallizations from ethanol–heptane yielded clear colorless prisms: mp 234–235°; nmr τ 3.58 (s, 2 $-OCH_3$), 7.5 (A_2B_2 m, 2 $-CH_2PH_2-$), 7.69 (s, 4 CH_3), and 9.50 (s, 8,16-methyls).

Anal. Calcd for $C_{24}H_{32}O_2$: C, 81.77; H, 9.15. Found: C, 81.71; H, 8.89.

The crude product was suitable for conversion to the hexamethyl bis(dienone). Two runs using the 4,6-bis(iodomethyl) compound gave yields of only 17%.

Continued elution of the column produced the corresponding [2.2.2.2]metacyclophane (*ca.* 5%), mp 275–280°, the nmr spectrum of which showed signals at τ 6.32 (s, 4 $-OCH_3$), 7.34 (s, 8 $-CH_2-$), 7.70 (s, 8 external $-CH_3$), and 8.75 (s, 4 internal $-CH_3$).

Hexamethylbis(dienone) 10.—A chromic acid solution was prepared by treating 8.0 g of chromium trioxide with 3–4 ml of water, followed by 6.4 ml of sulfuric acid and dilution with water to a total volume of 30 ml.

To a stirred suspension of 6.7 g (0.019 mol) of **9**, mp 230–235°, in 500 ml of acetone were added dropwise 15 ml of this solution over 15–20 min. Near completion of the addition, a green pasty precipitate formed which became more solid after 1.5 hr of stirring.

This was extracted with water–methylene chloride (1.5–1.0). The organic extract yielded a light yellow residue which was washed with acetone, leaving a very pale cream-colored crystalline solid, wt 5.77 g (94%), mp 341–343°. Recrystallization from chloroform raised the melting point to 345–347°; λ_{max}^{MeOH} 270 mμ (ε 31,000); ir ν_{max}^{KBr} 1660 cm^{-1} (s) and 1620 cm^{-1} (s); nmr τ 7.15 (m, 8 H), 7.92 (s, 4 CH_3), and 8.87 (s, internal CH_3's).

Anal. Calcd for $C_{22}H_{26}O_2$: C, 81.95; H, 8.13. Found: C, 81.71; H, 8.07.

Hexamethyldihydropyrene-2,7-quinone (11).—Hexamethylbis(dienone) (11.6 g, 0.036 ml) was added to a solution of potassium hydroxide (5 g) and dissolved in 1500 ml of warm absolute ethanol, and the slurry was maintained at 55° for 17 hr, while a slow stream of oxygen was passed over the reaction mixture. The dark red solution was cooled to room temperature and acidified slowly with concentrated hydrochloric acid. The red-orange mixture was filtered and the filtrate was concentrated. The residue was dissolved in 300–500 ml of chloroform, washed with brine, dried, concentrated to a volume of *ca.* 300 ml, and chromatograped over 800 g of silica gel. A dark maroon band was collected and yielded a bright red solid. Drying at 40° for 12 hr gave 9.10 g (79.5%) of a bright orange solid, mp 282–284°. The analytical sample was prepared by sublimation at 180–185° (0.01 mm): mp 284–285°; λ_{max}^{MeOH} 225 mμ (ε 23,000), 286 (54,000), 295 (58,450), and 348 (15,000); ir ν_{max}^{KBr} 1640 cm^{-1} (sh, s) and 1625 cm^{-1} (s); nmr τ 3.45 (s, 4 H), 7.98 (s, 2 internal methyls), and 8.05 (s, 4 external methyls).

Anal. Calcd for $C_{22}H_{22}O_2$: C, 82.98; H, 6.96. Found: C, 82.91; H, 6.84.

In many runs a sediment remained in the ethanol after oxidation which was the [2.2.2.2]metacyclophane impurity in the bis-dienone; this was the best point at which to collect this side product.

1,3,6,8,15,16-Hexamethyl-*trans*-15,16-dihydropyrene (2). A. Reduction of 2,7-Quinone.—A reducing solution was prepared by heating at reflux 40 g of aluminum chloride and 12 g of lithium aluminum hydride in 500 ml of dry ether.

After cooling, the clear supernatant solution was carefully decanted into a 3-l. reaction flask. Six grams of hexamethyldihydropyrene-2,7-quinone was dissolved in 100 ml of dry tetrahydrofuran and diluted to *ca.* 500 ml with ether. This red solution was added dropwise over 2 hr to the reducing solution at room temperature, which gained a deep green color; the suspension was then heated at reflux temperature for 1 hr.

After cooling, 30–50 ml of ethyl acetate was added, followed by water, with vigorous stirring until the reaction mixture formed two clear phases. The organic layer, after work-up, gave a dark green residue which was dried for 12–15 hr at 40° in a vacuum oven. The nmr spectrum of this material indicated that it was a 3:2 mixture of **2** and **12**; those resonances assigned to **12** are τ 3.62 (s, 4 H, 4, 5, 9, and 10 protons), 7.16 (broad s, 2- and 7-methylenes), 8.12 (s, external methyls), and 9.14 (s, internal methyls). This mixture was subjected directly to the following dehydrogenation.

B. Dehydrogenation of Hexamethylbis(triene) (12).—The dark green residue from above was dissolved in 250 ml of dry toluene and heated to reflux temperature with 4 g of 10% palladium on charcoal for 15–18 hr. The progress of the reaction was followed by thin-layer chromatography (hexane); no dehydrogenations proceeded to 100% completion. Filtration and concentration of the dark mixture yielded 4.55 g of solid, mp 180–185°, which was boiled in methanol for several minutes and collected, wt −4.06 g (75% from quinone), mp 182–185°. The analytical sample was prepared from heptane: dark blue-green prisms; mp 184–186°; $\lambda_{max}^{CH_2Cl_2}$ 274 mμ (ε 10,650), 358 (97,850), 390 (37,400), 417 (6250), 446 (5200), 474 (4450), 548 (70), 602 (150), 610 (150), 637 (100), 656 (150); nmr τ 1.44 (s, 4 H), 2.20 (s, 2 H), 6.84 (s, external methyls), and 14.04 (s, internal methyls).

Anal. Calcd for $C_{22}H_{24}$: C, 91.61; H, 8.39. Found: C, 91.50; H, 8.22.

Mass spectral analysis of **2** shows, in addition to ions at *m/e* 318 ($M^+ + 2CH_3$, 0.5% base peak), 303 ($M^+ + CH_3$, 5%), 288 ($M^+ + CH_3$, 5%), 288 (M^+, 3%), 273 ($M^+ - CH_3$, 25%), essentially one intense fragment at 258 ($M^+ - 2CH_3$), corresponding to the stable tetramethylpyrene cation.[21]

2,7-Diacetoxyhexamethyldihydropyrene (13).—To a mixture of 500 mg of **11** in 50 ml of acetic anhydride and six drops of triethylamine at room temperature was added portionwise over 5 min 1.0 g of zinc dust; a color change from red to green became apparent in about 2 min. The mixture was stirred for 4 hr and quenched by pouring the dark green mixture into ice and water. The aqueous suspension, after 2 hr, was then extracted with methylene chloride–ether. The organic layer, after work-up, gave a dark green residue which smelled strongly of acetic acid. The residue, after slurrying in methanol, gave 500 mg (78%), mp 238–239°, of crude product which was recrystallized from methylene chloride–heptane, and sublimed at 180° (0.01 mm) producing a dark green solid: mp 239–240°; $\lambda_{max}^{CH_2Cl_2}$ 357 mμ (ε 109,000), 385 (39,600), 413 (7300), 451 (6200), 468 (6200), 541 (100), 608 (150), 642 (250), and 647 (250); ir ν_{max}^{KBr} 1755 cm^{-1} (s), 1370 (s), 1215 (vs), 1175 (vs), and 1080 (vs); nmr τ 1.34 (s, 4 H), 7.00 (s, external methyls), 7.46 (s, acetoxy methyls), and 13.88 (s, internal methyls).

Anal. Calcd for $C_{26}H_{28}O_4$: C, 77.20; H, 6.98. Found: C, 77.48; H, 7.08.

2-Acetylhexamethyldihydropyrene (14, X = Ac).—To a solution of 500 mg of hexamethyldihydropyrene in 25 ml of methylene chloride was added dropwise over 45 min a solution of 0.17 ml of acetic anhydride and 0.10 ml of stannic chloride in 25 ml of methylene chloride. After several hours thin layer chromatography (heptane–ethyl acetate, 90:10) indicated a mixture of isomeric acetylhexamethyldihydropyrenes and an appreciable amount of starting material. After 18 hr the reaction was poured into ice water and this mixture was stirred for 2 hr and extracted with methylene chloride–ether. The residue from the organic extract was chromatographed on silica gel with methylene chloride. A green band was eluted rapidly, which was identified as starting material, 243 mg. Slowly a second green band was eluted with methylene chloride, 145 mg (49%), mp 202–203°, which was 2-acetylhexamethyldihydropyrene [sublimation at 120–130° (0.01 mm) raised the melting point to 205–206°]: $\lambda_{max}^{CH_2Cl_2}$ 361 mμ (ε 106,000), 392 (39,900), 457 (5600), 478 (5800), 549 (100), 603 (200), and 659 (150); ir ν_{max}^{KBr} 1710 cm^{-1} (s); nmr τ 1.36 (s, 4 H), 2.20 (s, 1 H), 6.85 and 6.95 (2 s, external methyls), 7.20 (s, acetyl methyl), and 13.84 (s, internal methyls).

Anal. Calcd for $C_{24}H_{26}O$: C, 87.23; H, 7.93. Found: 87.02; H, 7.67.

2,7-Diacetylhexamethyldihydropyrene (17).—To a solution of hexamethyldihydropyrene (490 mg) in 25 ml of methylene chloride was added all at once a solution of 0.2 ml of acetic anhydride and 0.1 ml of stannic chloride in 25 ml of methylene chloride. Thin-layer chromatography (methylene chloride–heptane, 75:25) indicated the presence of both mono- and diacetyl products after 2 min. After 1.5 hr, 15 ml of 2 *N* hydrochloric acid was added. The organic layer was dried, concentrated to a volume of 25 ml, and applied to a silica gel column. A small green band of hexamethyldihydropyrene (25 mg) was eluted rapidly. This was followed by 2-acetylhexamethyldihydropyrene (55 mg). Continued elution with methylene chloride and methylene chloride–3% ether produced 46 mg of an oil which was identical to a

(21) Mass spectra were determined by Dr. Paul C. Nicolson of these laboratories on a C.E.C. model 21-103C instrument using a heated inlet operating at 220°.

similar fraction obtained in the monoacetylation experiment, and is probably the 4-acetyl isomer.

A dark olive-gold fraction was then eluted which contained 240 mg (39%) of crude 2,7-diacetylhexamethyldihydropyrene. This material, after recrystallization from methylene chloride–methanol, yielded 103 mg of long green prisms: mp 226–227°; $\lambda_{max}^{CH_2Cl_2}$ 363 mμ (ε 101,750), 395 (32,900), 482 (6600), 552 (100), 608 (200), and 665 (200); ir ν_{max}^{KBr} 1705 cm^{-1} (s) and 1205 cm^{-1} (s); nmr singlet resonances at τ 1.32 (4 H), 6.95 (external methyls), 7.22 (acetyl methyls), and 13.78 (internal methyls).

Anal. Calcd for $C_{28}H_{28}O_2$: C, 83.83; H, 7.58. Found: 83.74; H, 7.58.

Nitration of Hexamethyldihydropyrene.—Hexamethyldihydropyrene (1.40 g, 4.85 mol) was slurried in 100 ml of acetic anhydride, and 590 mg (4.85 mol) of powdered cupric nitrate (trihydrate) was added over 5 min. After 15 min the green color had changed to a dark olive-gold. Thin layer chromatography (methylene chloride–heptane, 50:50) indicated the presence of two new components. After 1.5 hr the dark solution was poured into ice water and stirred until the acetic anhydride had reacted. The resulting mixture was extracted with methylene chloride–ether.

The crude residue from the organic extract, after reconcentration twice from toluene to remove acetic acid, was dissolved in 100 ml of 30% methylene chloride in heptane and chromatographed on 400 g of silica gel. A green band of unreacted starting material (139 mg) was eluted rapidly with 5% methylene chloride–heptane. Two large dark bands then moved slowly down the column; 20% methylene chloride–heptane eluted the 2-nitro compound cleanly, followed by clean elution of the 4-nitro isomer with 40% methylene chloride–heptane.

The first fraction yielded 706 mg (49%), mp 223–224°, of 2-nitrohexamethyldihydropyrene (**14**, X = NO_2), and the second fraction yielded 375 mg (26%), mp 203–205°, of 4-nitrohexamethyldihydropyrene (**15**, X = NO_2). Both fractions were homogenous on thin-layer chromatography.

2-Nitrohexamethyldihydropyrene could be recrystallized from methylene chloride–methanol, which yielded purple-black needles, mp 224–226°. The analytical sample was sublimed at 130–140° (0.01 mm): $\lambda_{max}^{CH_2Cl_2}$ 359 mμ (ε 81,850), 388 (30,600), 480 (5100), 593 (500), and 658 (350); ir ν_{max}^{KBr} 1521 cm^{-1} (vs), 1460 (s), 1333 (s); nmr singlet resonances at τ 1.24 (4 H), 2.06 (1 H), 6.83 and 6.92 (external methyls), and 13.88 [2, $(\nu_1 - \nu_2)$ = 3 Hz, internal methyls].

Anal. Calcd for $C_{22}H_{23}NO_2$: C, 79.25; H, 6.95; N, 4.20. Found: C, 79.19; H, 6.99; N, 4.40.

4-Nitrohexamethyldihydropyrene was recrystallized from methylene chloride–methanol, yielding purple-black needles, mp 207–209°. The analytical sample was sublimed at 130° (0.01 mm): $\lambda_{max}^{CH_2Cl_2}$ 354 mμ (ε 14,200), 392 (9700), 6.08 (500), and 671 (600); ir ν_{max}^{KBr} 1524 cm^{-1} (vs) and 1328 cm^{-1} (s); nmr singlets at τ 1.18 (C_5 proton), 1.44 (2 H, 9 and 10 protons), 2.18 [2 s, $(\nu_1 - \nu_2)$ = 0.5 Hz, 2 H], 6.90 (1-, 6-, 8-methyls), 7.18 (3-methyl), and 13.68 [2 s, $(\nu_1 - \nu_2)$ = 3 Hz, internal methyls].

Anal. Calcd for $C_{22}H_{23}NO_2$: C, 79.25; H, 6.95; N, 4.20. Found: C, 79.42; H, 7.02; N, 4.39.

2-Formylhexamethyldihydropyrene (14, X = CHO).—To a solution of hexamethyldihydropyrene (956 mg) in 50 ml of dry methylene chloride was added at room temperature 0.5 ml of stannic chloride and 1.0 ml of dichloromethylbutyl ether (3 mol equiv). The dark green solution was stirred at room temperature for 17 hr, during which time starting material was completely consumed as indicated by thin-layer chromatography (heptane–ethyl acetate, 90:10), and poured into water. The aqueous burgundy-red suspension was stirred for 15 min and extracted with methylene chloride–ether. The organic residue in methylene chloride was applied to a silica gel column. A dark maroon band was eluted with 3% ethyl acetate–methylene chloride. Toward the end of the elution the color changed from burgundy to red-brown, and a second fraction was taken. The main fraction yielded 850 mg (81%) of the 2-formyl isomer, mp 213–215°, and the red-brown fraction yielded 95 mg (9%) of the 4-formyl isomer (**15**, X = CHO), mp 203–205°. Thin layer chromatography indicated both fractions to be homogenous.

The 2-formyl compound was recrystallized from methanol in black-red needles: mp 214–216°; $\lambda_{max}^{CH_2Cl_2}$ 243 mμ (ε 12,300), 369 (77,100), 412 (21,200), 518 (8750); 631 (600), and 698 (1300); ν_{max}^{KBr} 1675 cm^{-1}; nmr τ −1.36 (s, –CHO), 1.33 [center of AB quartet (*J* = 8 Hz), 4 H], 2.18 (broad s, 1 H), 6.65 and 6.90 (2 s, external methyls), and 13.68 [2 s, $(\nu_1 - \nu_2)$ = 3 Hz, internal methyls].

Anal. Calcd for $C_{23}H_{24}O$: C, 87.30; H, 7.65. Found: C, 87.22; H, 7.74.

The 4-formyl isomer was also recrystallized from methanol, giving essentially black prisms: mp 204–205°; $\lambda_{max}^{CH_2Cl_2}$ 280 mμ (ε 8000), 395 (42,500), 447 (5400), 503 (6000), 616 (700), and 680 (1700); ir ν_{max}^{KBr} 1681 cm^{-1} (sh, s) and 1656 cm^{-1} (vs); nmr τ 1.38 (s, –CHO), 0.82 (s, C_5 proton), 153 [center of AB quartet (*J* = 8 Hz, 2 H], 2.12 (s, 1 H), 2.20 (s, 1 H), 6.70 and 6.90 (3, 4 external methyls), 13.58 and 13.66 (2 s, internal methyls).

Anal. Found: C, 87.14; H, 7.43.

2-Acetamidohexamethyldihydropyrene (19).—To a suspension of 20 ml of acetic anhydride, 20 ml of acetic acid, 200 mg of 2-nitrohexamethyldihydropyrene, and 200 mg of sodium acetate was added portionwise over 10 min 500 mg of zinc dust. The mixture was stirred at 20° for 15 hr. The color changed slowly from a dark brown-gold to a dark green over 5 hr. The mixture was poured into ice water and extracted with methylene chloride–ether. The organic layer, after concentration, yielded 188 mg (91%) of 2-acetamidohexamethyldihydropyrene: mp 214–216° (recrystallization from methylene chloride–heptane raised the melting point to 215–217°); ir ν_{max}^{KBr} 3250 cm^{-1} (w, 1660 cm^{-1} (vs), 1525 cm^{-1} (m); nmr (DMSO-d_6) τ 0.00 (broad s, NH), 1.40 (s, 4 H), 2.14 (s, 1 H), 6.94 and 7.02 (equiv s, external methyls), 7.72 (s, –$COCH_3$), and 14.06 (s, internal methyls).

Anal. Calcd for $C_{24}H_{27}NO$: C, 83.44; H, 7.88; N, 4.05. Found: C, 83.56; H, 7.93; N, 4.02.

2-Acetamido-7-formylhexamethyldihydropyrene (20).—To a stirred solution of 400 mg of **19** in 50 ml of methylene chloride was added 0.2 ml of stannic chloride followed by 0.4 ml of dichloromethylbutyl ether (twofold excess). After 3 hr the reaction solution was poured into water. The deep burgundy-red suspension was extracted with methylene chloride–ether and the organic extract was concentrated and reconcentrated from toluene to remove traces of acetic acid. Chromatography of the dark maroon residue (426 mg) on silica gel using 50% ethyl acetate–heptane as eluting solvent yielded 182 mg (42%) of 2-acetamido-7-formylhexamethyldihydropyrene, together with a lesser component, which is probably the 2-acetamido-4-formyl compound. Recrystallization of this material from methylene chloride–heptane yielded a dark maroon solid: mp 216–218°; ir ν_{max}^{KBr} 3300 cm^{-1} (m), 1675 cm^{-1} (vs), and 1575 cm^{-1} (m); nmr τ −1.32 (s, –CHO), 1.35 [center of AB quartet, (*J* = 8 Hz), 4 H], 2.30 (broad s, NH), 6.70 (s, 2 CH_3) 7.00 (broad s, 2 CH_3), 7.60 (broad s, –$COCH_3$), and 13.58 [2 s, $(\nu_1 - \nu_2)$ = 5 Hz, internal methyls].

Anal. Calcd for $C_{25}H_{27}NO_2$: C, 80.39; H, 7.29; N, 3.75. Found: C, 80.31; H, 7.25; N, 3.79.

4-Acetamidohexamethyldihydropyrene (23).—To a mixture of 200 mg of 4-nitrohexamethyldihydropyrene in 20 ml of acetic acid and 20 ml of acetic anhydride was added 200 mg of sodium acetate, followed by the portionwise addition of 500 mg of zinc dust over 10 min at 20°. The dark olive-gold mixture changed rapidly over 0.5 hr in color to a dark green. After 2.5 hr, thin layer chromatography (ethyl acetate–heptane, 75:25) indicated complete consumption of starting material. The reaction mixture was poured into ice water and resulting suspension was extracted with chloroform–ether. The organic layer yielded 197 mg (95%) of a dark green solid. Recrystallization from chloroform–heptane gave dark green microprisms: mp 229–231°; ir ν_{max}^{KBr} 3550 cm^{-1} (m), 1680 cm^{-1} (sh s), 1660 cm^{-1} (v s), and 1555 cm^{-1} (s); nmr τ 1.40 (broad s, 3 H), 2.00 (broad s, NH), 2.20 (s, 2 H), 6.80 (2 nonequiv overlapping s, external methyls), 7.80 (s, –$COCH_3$), and 13.78 [2 s, $(\nu_1 - \nu_2)$ = 3 Hz, internal methyls].

Anal. Calcd for $C_{24}H_{27}NO$: C, 83.44; H, 7.88; N, 4.05. Found: C, 83.64; H, 7.58; N, 4.01.

2-Hydroxymethylhexamethyldihydropyrene (25, R = CH_2OH).—To 75 ml of absolute ether in a 200-ml three-necked flask was added carefully 400 mg of lithium aluminum hydride, and to this slurry was added, over 45 min, a solution of 300 mg of 2-formylhexamethyldihydropyrene in 50 ml of tetrahydrofuran. Immediately a dark green color formed. After addition was complete the reaction was stopped by addition of 30 ml of ethyl acetate, followed by 30 ml of water. The organic layer after work-up yielded a dark green solid, wt 295 mg (98%), mp 210–212°; ir spectra showed no carbonyl band. The analytical sample was recrystallized from methanol: mp 212–214°; nmr τ 1.38 [center of AB quartet, (*J* = 9 Hz), 4 H], 2.30 (s, 1 H), 4.58 (s, –CH_2–),

6.72 and 6.85 (equiv s, external methyls), and 13.83 [s, ($\nu_1 - \nu_2$) = 2 Hz, internal methyls].

Anal. Calcd for $C_{23}H_{26}O$: C, 86.74; H, 8.23. Found: C, 86.75; H, 8.23.

When the product was treated in refluxing chloroform with manganese dioxide, a near quantitative recovery of 2-formylhexamethyldihydropyrene resulted.

Heptamethyldihydropyrene (26, R = CH_3).—Into a 300-ml three-necked flask was decanted 50 ml of a hydride solution described in the reduction of **11** to **2**. To this was added dropwise over 0.5 hr a deep red solution of 400 mg of 2-formyl-hexamethyldihydropyrene in 20 ml of tetrahydrofuran and 50 ml of ether. A dark green solution immediately resulted. This slurry was heated at reflux temperature for 1 hr and, after cooling, the excess reductant was destroyed by addition of 30 ml of ethyl acetate, followed by 30 ml of water. The organic layer yielded 387 mg (99%) of a dark green solid. Recrystallization from methylene chloride–heptane gave the analytical sample: mp 213–214°; ir spectra (Nujol) showed the absence of carbonyl or hydroxy bands; nmr τ 1.40 (s, 4 H), 2.27 (s, 1 H), 6.86 (s, 1-, 3-, 6-, and 8-methyls), 7.08 (s, 2-methyl), 13.95 and 13.98 (s, internal methyls).

Anal. Calcd for $C_{23}H_{26}$: C, 91.33; H, 8.67. Found: C, 91.32; H, 8.65.

2-Hexamethyldihydropyrene Aldoxime (27).—To a slurry of 514 mg of the 2-formyl derivative **24** in 50 ml of ethanol were added 5 ml of an aqueous hydroxylamine hydrochloride solution which had been neutralized to pH 7 with sodium carbonate. This was warmed on a steam bath for 15 min, after which time thin layer chromatography showed complete conversion of starting material. Careful addition of water to the dark solution while hot resulted in a crystallization of the oxime on cooling, wt 508 mg (94%), mp 205–207°. Recrystallization from ethanol yielded olive-brown platelets: mp 210–211°; $\lambda_{max}^{CH_2Cl_2}$ 245 mμ (ϵ 12,200), 363 (106,300), 396 (32,300), 486 (8000), 610 (200), and 666 (350); ir $\nu_{max}^{CH_2Cl_2}$ 3600 cm^{-1} (s), 3300 (m), 1625 (w), and 1450 (s); nmr (DMSO-d_6) τ −1.42 (s, C=NOH), 0.96 (s, -CH=N-), 1.36 [AB quartet (J = 8 Hz), 4 H], 2.16 (s, 1 H), 6.90 (two equiv s, external methyls), and 13.94 (s, internal methyls).

Anal. Calcd for $C_{23}H_{25}NO$: C, 83.34; H, 7.60; N, 4.23. Found: C, 83.14; H, 7.49; N, 4.09.

2-Cyanohexamethyldihydropyrene (28).—Acetic anhydride (20 ml) and 244 mg of **27** were mixed and heated at reflux temperature for 15 min. After cooling, the dark solution was poured into water. When all solvent had reacted, the mixture was extracted with a mixture of methylene chloride and ether. The residue from the organic extract was twice recovered from toluene to remove traces of acetic acid, and was chromatographed on silica gel with methylene chloride–heptane (50:50). A dark bronze band was eluted to give 99 mg (43%) of **28**, mp 218–219°. Recrystallization from methanol produced fine, olive-brown needles: mp 215–216°; $\lambda_{max}^{CH_2Cl_2}$ 365 mμ (ϵ 91,000), 402 (39,800), 505 (9700), 611 (800), and 678 (1800); ir $\nu_{max}^{CHCl_3}$ 2210 cm^{-1} (vs) and 1445 cm^{-1} (s); nmr τ 1.33 [AB quartet, (J = 8 Hz), 4 H], 2.08 (s, 1 H), 6.60 and 6.84 (equiv s, external methyls), and 13.87 (s, internal methyls).

Anal. Calcd for $C_{23}H_{23}N$: C, 88.13; H, 7.40; N, 4.47. Found: C, 87.93; H, 7.39; N, 4.51.

Registry No.—**2**, 20349-16-0; **7**, 4028-66-4; **8**, 16927-60-9; **9**, 20518-37-0; **10**, 21654-31-9; **11**, 21654-32-0; **13**, 35051-08-2; **14** (X = Ac), 32347-25-4; **14** (X = NO_2), 32347-21-0; **14** (X = CHO), 32347-27-6; **15** (X = NO_2), 33872-82-1; **15** (X = CHO), 32347-29-8; **17**, 32347-24-3; **19**, 35051-15-1; **20**, 35051-16-2; **23**, 35051-17-3; **25**, 35051-18-4; **26**, 32500-00-8; **27**, 32347-26-5; **28**, 32347-28-7.

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The Retentive Nucleophilic Displacements of α-Substituted Alkylferrocenes[1]

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Ferrocenylethane derivatives with suitable leaving groups [chloro, acetate (**9**), trimethylammonium (**2**)] in the α position generally undergo nucleophilic substitutions with complete retention of configuration and are useful for the preparation of a variety of chiral ferrocene derivatives. Stereochemical and kinetic evidence indicates an SN1 mechanism *via* a configurationally stable α-ferrocenylethyl carbonium ion intermediate. Departure of the leaving group and entry of the substituting nucleophile involve analogous conformations of the α-ferrocenylalkyl system. Winstein–Grunwald *m*Y analysis of ammonium compound **2** indicates only a very slight solvent effect for solvolysis in this stable carbonium ion system.

Chiral ferrocene derivatives[3] with the general formula **5** and analogous compounds may serve as asymmetrically inducing amine components[4] in stereoselective peptide synthesis by four-component condensations,[5] *i.e.*, **3** → **4**, because primary amines related to **3** are not only effective steric templates without excessive steric bulk, but their condensation products (**4**) may also be readily cleaved, **4** → **5** + **6**, under mild conditions.[5] The use of **3** as an asymmetrically inducing amine component in four-component condensations offers further advantages. Model reactions[5-7] indicate that the cleavage products can be used to resynthesize the amines. Both antipodes of optically active **1** are easy to obtain and can be effectively converted into compounds of type **1** with a sub-

(1) Stereoselective Syntheses. VIII.

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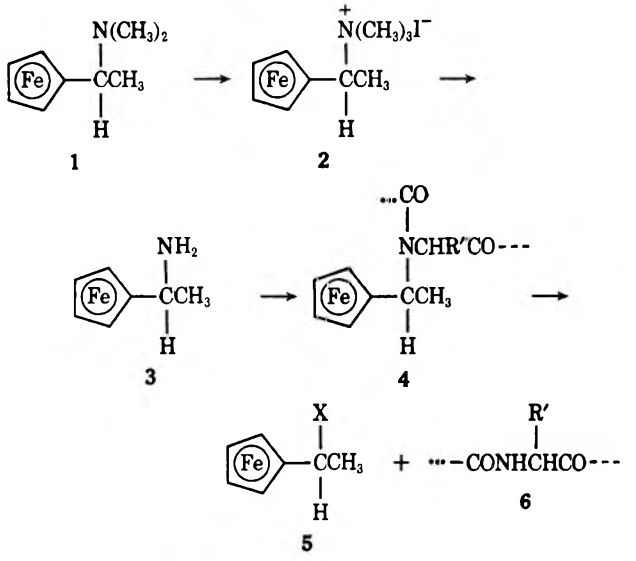
stituent in the 2 position,[8,9] and, since the ammonium group of 2 and its analogs can be replaced by a primary amino group, 3 and derivatives can be obtained conveniently and in good overall yield from readily accessible precursors (Scheme I).

SCHEME I

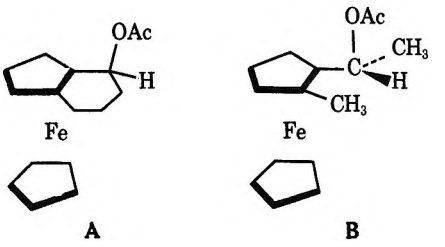


Reactions 2 → 3, 4 → 5 + 6, and 5 → 3 involve nucleophilic substitutions at a tetracoordinate (sp^3) center of chirality carrying a ferrocenyl ligand. Knowledge of the mechanism and stereochemical course of the latter reactions would allow full use of the potentially favorable properties of 3 and its 2-organyl derivatives.

Nucleophilic substitutions at a center of chirality with a tetrahedral skeleton proceed either with retention or with inversion of the configuration of the central chiroid. If the substitution product is homochiral[10] to its precursor, the substitution is called retentive; the substitution is considered to occur with inversion if the product is heterochiral to the initial chiral species. The product of nucleophilic substitution is called homochiral to its starting material if it is configurationally similar to the latter and not to its antipode. In this context, the entering and leaving groups are considered to be sequentially equivalent.

Retentive substitution is observed if either an SNi reaction[11] takes place or if a limiting SN1 process[12] takes place in such a manner that departure of the leaving group to give a carbonium ion and addition of the substituting nucleophile occur from the same side of the intermediate sp^2 tricoordinate skeleton of the carbonium ion.

Recent investigations of the solvolytic behavior of the α-ferrocenylalkyl systems have demonstrated the pronounced stabilization of ferrocenylalkyl cations.[13-21] This has been explained by assuming metal participation[13,15-18] or iron hyperconjugation.[16,19,20] Both interpretations imply retentive nucleophilic substitution of the SN1 type for the α-ferrocenylalkyl compounds, and there is some previous evidence[21] for the retentive nature of the above reactions. The elegant work of Richards and Hill[13] and Trifan and Bacskai[14] on cyclic and 2-substituted ferrocenyl acetates foreshadows the present results. A subtle though very important difference should be noted. The previously examined cases (see **A** and **B** below) involved systems with a ring or neighboring substituent.



To our knowledge, prior to our preliminary reports[6,7] of this phenomenon, in this context, retentive nucleophilic substitution at an acyclic chiral center without adjacent substituents had not been demonstrated. A confirmatory report has recently appeared.[22]

We have observed complete retention of the configuration of the chiral center during most of the nucleophilic substitution reactions presented in Scheme II. This is further evidence for the remarkable influence of an α-ferrocenyl group upon the stereochemistry of nucleophilic substitution.

There is a remarkable variety in the stereospecific interconversions of the α-ferrocenylethyl carbonium ions. The cycle 1 → 2 → 10 → 3 → 1 which involves transformations A, B, C, and D contains only one reaction at carbon (reaction C). Since the optical rotations of 1 were the same before and after the cycle, reaction C must occur with retention of configuration.[6] This transformation cycle defines the stereochemistry of compounds 2, 3, and 10 relative to 1. The absolute configuration of 1 has been established by X-ray methods[9] and the absolute configuration of 3 has been determined independently by chemical methods.[23]

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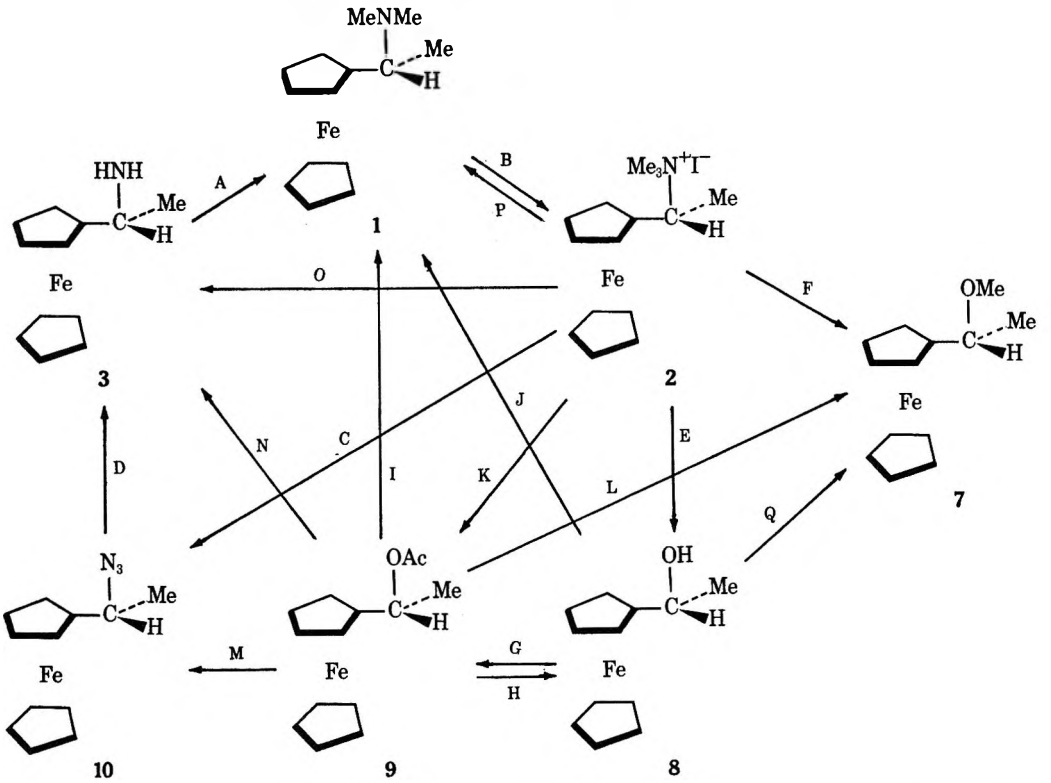
SCHEME II

STEREOSPECIFIC INTERCONVERSIONS IN THE α-FERROCENYLALKYL SYSTEM[a]



[a] A, See ref 6; B, CH_3I in acetone; C, NaN_3 in aqueous THF; D, $NaH_2Al(OCH_2CH_2OCH_3)_2$ in ether (see Experimental Section) or ref 6; E, 1:1 water–THF; F, 1:1 MeOH–MeCN; G, Ac_2O in C_5H_5N; H, aqueous THF, acetone, ethanol, etc.; I, $HNMe_2$ in aqueous MeOH; J, $COCl_2$ then $HNMe_2$; $AlCl_3$ then $HNMe_2$;[22] K, NaOAc in anhydrous DMF (partial racemization, see text); L, NaOMe in MeOH; M, NaN_3 in aqueous THF; N, aqueous NH_3 in MeOH; O, aqueous NH_3 in MeCN; P, $HNMe_2$ in MeCN; Q, *n*-BuLi then Me_2SO_4.

The degree of retention of the reactions was determined by a comparison of optical rotations before and after the cycle (Table I). Within the error of our method,

TABLE I

OPTICAL ROTATIONS FOR α-FERROCENYLETHANE DERIVATIVES[a,b]

Compd	Rotation, deg	Solvent used
1	+14.2	Ethanol
2	+43.0	2-Methoxyethanol
2	+32.5	Acetonitrile
3	−21.0	Ethanol
7	+27.5	Ethanol
8	−30.5	Benzene
9	−28.5	Ethanol
10	−69.8	Benzene

[a] Recorded at the 589-nm (D) line of Na at 25.0°. [b] For the *R* configuration.

each reaction (except K) was found to proceed with essentially complete retention (see Experimental Section for exact data). Kinetic evidence is presented below which indicates that reaction C is first order. These observations imply a configurationally stable carbonium ion intermediate. Other reactions which clearly take place at carbon and therefore involve the α-ferrocenylethyl cation are E, F, I, J, K, L, M, N, O, and P. It is less obvious that H is a retentive SN1 reaction, which also involves the carbonium ion rather than a normal type of hydrolysis. That this is so was demonstrated by Richards and Hill a decade ago.[13] Dixneuf[22] has recently confirmed the stereochemistry assigned in our preliminary report[7] for **8** and the retention of reaction J, albeit by an entirely different method.

Reaction G in this cycle is normal acylation with acetic anhydride in pyridine solution. 1-Ferrocenylethanol has also been converted into 1-ferrocenylethyl acetate by refluxing the alcohol in benzene solution with an excess of glacial acetic acid and concomitant removal of water.[7,24] This reaction probably involves protonation of the alcohol and elimination of water, followed by ion-pair collapse to give the ester. A carbonium ion mechanism is believed to occur rather than a normal esterification mechanism[25] because of the stability of the carbonium ion.[21] The early work of Richards and Hill[13] indicated that the ethanolyses of α-ferrocenylcarbinyl acetates afford the ethyl ethers, and Hammond and Rudesill[26] observed that esterification of benzoic acid with triphenylcarbinol (a precursor to a stable carbonium ion) involves the trityl cation. Stephens and coworkers[27] have shown that hydroxymethyl ferrocene will esterify on heating in an acetic acid solution (greater than 60 mol of acetic acid per mole of alcohol). It is their belief that the α-ferrocenylmethyl carbonium is involved here also. In later work by this same group, hydroxymethylferrocene was converted directly into a sulfide by the action of a thiol under acetic acid catalysis. Without acetic acid to

(24) G. W. Gokel and I. K. Ugi, *J. Chem. Educ.*, **49**, 294 (1972).
(25) M. L. Bender, *Chem. Rev.*, **60**, 53 (1960).
(26) G. S. Hammond and J. T. Rudesill, *J. Amer. Chem. Soc.*, **72**, 2769 (1950).
(27) C. S. Combs, C. I. Ashmore, A. F. Bridges, C. R. Swanson, and W. D. Stephens, *J. Org. Chem.*, **33**, 4301 (1968).

protonate the alcohol and provide a good leaving group, water-insoluble mercaptans failed to react.[28]

$$FcCH_2OH \xrightarrow[1:1\ n\text{-BuSH–}H_2O]{HOAc} FcCH_2Sn\text{-}Bu$$

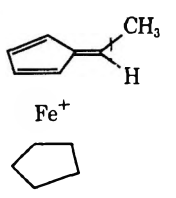
The collapse of the ion pair appears to be slow since treatment of the optically active alcohol (**8**) under these conditions results in racemic acetate.

It is possible that the racemization is due to the presence of vinylferrocene as an intermediate in this reaction. The ease of elimination of α-ferrocenylethanol to vinylferrocene[29] and the documented ease of addition of acetic acid to this molecule[15] seem to support this hypothesis.

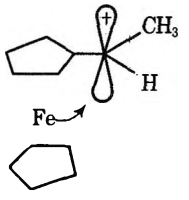
This racemization phenomenon also discounts a normal esterification mechanism because, if nucleophilic attack by the alcohol occurred at the acetic acid carbonyl, the stereochemistry of the resulting compound should be unaffected.

We have found that reaction K proceeds to give acetate (**9**) with partial racemization. The optical rotation of **9** produced from reaction G is 28.5° and, when produced by reaction K, it is 21° or only 73.5% optically pure. One possible explanation for this behavior is that, in the case of weak nucleophiles, the ion pairs collapse more slowly and partial racemization occurs in the interim.

We have interpreted the observed stereospecificity of the α-ferrocenylethyl cation in terms of a structure like **11** in our preliminary report.[6] This structure



11



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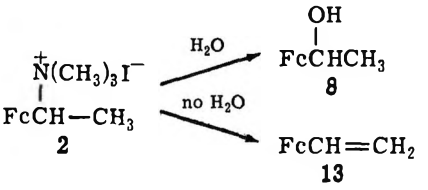
seemed best able to explain the stereochemical retention. After this work was submitted, the report of the stereospecific hydrolysis of optically active β-ferrocenylpropyl tosylate appeared.[30] Clearly, a structure like **11** cannot account for β stereospecificity, whereas some iron lone pair overlap might. On the other hand, structure **12** does not reasonably account for the ability of the dimethylferrocenyl carbinyl cation to undergo cycloaddition.[31] Although the exact nature of the carbonium ion stabilization is still not completely elucidated, recent work by several groups bears on this point.[32-34]

Our interest in this system led us to measure the kinetic dependence of some of the reactions shown in Scheme II. We have determined kinetic parameters for reactions C, E, and H in that scheme. In addition, we have determined Winstein–Grunwald "*m*" values for reactions E and H. The reaction which often competes with SN1 reactions in this system is the E1 reaction of **2** to give vinylferrocene (**13**). We have also



measured the kinetics of this reaction. Results for the reactions illustrated above are given in Table II. All

TABLE II

RATES OF DISPLACEMENT AND ELIMINATION REACTIONS OF **2**[a]

Reaction[b]	Solvent[c]	Temp, °C	k, sec^{-1} [d]
2 + H_2O ⟶ 8	50% THF	30.0	$9.92 \pm 0.95 \times 10^{-5}$
2 + H_2O ⟶ 8	50% THF	40.0	$3.62 \pm 0.01 \times 10^{-4}$
2 + H_2O ⟶ 8	50% THF	50.0	$1.61 \pm 0.13 \times 10^{-3}$
2 + NaN_3 ⟶ 10[e]	50% THF	50.0	$2.26 \pm 0.01 \times 10^{-3}$
2 + NaN_3 ⟶ 10[f]	50% THF	50.0	$2.17 \pm 0.07 \times 10^{-3}$
2 ⟶ 13	MeCN	40.0	$3.44 \pm 0.16 \times 10^{-4}$
2 ⟶ 13	MeCN	45.0	$8.16 \pm 0.23 \times 10^{-4}$
2 ⟶ 13	MeCN	50.0	$2.04 \pm 0.15 \times 10^{-3}$

[a] Determined polarimetrically at the 589-nm line of Na. [b] Concentration of **2** is *ca.* 0.05 *M* unless otherwise noted. [c] Solvent mixtures are vol./vol. [d] Average of two or more runs. [e] Concentration of **2** is 0.013 *M*; concentration of NaN_3 is 0.026 *M*. [f] Concentration of **2** is 0.013 *M*; concentration of NaN_3 is 0.048 *M*.

rates were determined by performing the reaction on the appropriate optically active substrate in a thermostated polarimeter tube, where the time dependence of the optical rotation was used as a measure of the extent of reaction.

We have confirmed that, in the concentration range examined, reaction C in Scheme II is first order. The *m* value obtained from reaction H indicates that in this case a carbonium ion mechanism is also operative. The hydrolysis of **2** follows first-order kinetics, although the possibility that it is pseudo-first order cannot be rigorously excluded. The implication that all of the substitution reactions in Scheme II are SN1 is clear, but this was not specifically confirmed for each case.

We have determined activation parameters for the hydrolysis of **2** in 50% aqueous THF and for the E1 reaction of **2** in anhydrous acetonitrile. The hydrolysis of **2** (Scheme II, reaction E) had E_a = 27.2 kcal/mol and ΔS is 5.2 eu. The elimination of **2** to vinylferrocene had E_a = 35.6 kcal/mol and ΔS = −31.6 eu. In our efforts to determine Arrhenius parameters for the latter reaction, it was found that the reactivity of the carbonium ion formed from **2** is sufficiently high toward water that any traces of water in the solvent caused formation of the alcohol, detected by a slight negative rotation at infinity. In the solvolysis of **2**, on the other hand, no vinylferrocene was detected in the product when nmr analysis was applied to crude alcohol obtained from a small-scale preparation.

It has been recognized for some time,[35] if not specifically stated, that the Winstein–Grunwald *m*Y cor-

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TABLE III

SOLVENT DEPENDENCE OF THE HYDROLYSES OF 2 AND 5[a]

Expt no.	Solvolysis of compd no.	Solvent[b]	Y[c]	Substrate concn M[d]	K, sec^{-1} [e]
1	2	90% acetone	−1.856	0.050	2.56 ± 0.16 × 10^{-3}
2	2	80% acetone	−0.673	0.052	2.02 ± 0.03 × 10^{-3}
3	2	70% acetone	0.130	0.051	2.16 ± 0.19 × 10^{-3}
4	2	60% acetone	0.796	0.026	2.28 ± 0.22 × 10^{-3}
5	2	90% ethanol	−0.747	0.064	5.77 ± 0.23 × 10^{-3}
6	2	80% ethanol	0.000	0.054	4.90 ± 0.27 × 10^{-3}
7	2	70% ethanol	0.595	0.036	3.88 ± 0.21 × 10^{-3}
8	2	60% ethanol	1.124	0.038	3.45 ± 0.20 × 10^{-3}
9	9	90% acetone	−1.856	0.056	1.58 ± 0.17 × 10^{-4}
10	9	80% acetone	−0.673	0.054	1.65 ± 0.02 × 10^{-3}
11	9	75% acetone	−0.250[f]	0.054	3.28 ± 0.03 × 10^{-3}
12	9	70% acetone	0.130	0.053	6.17 ± 0.29 × 10^{-3}

[a] Determined polarimetrically at the Na 589-nm line (expt 1–8) or at the Hg 546-nm line (expt 9–12). [b] Solvent mixtures are vol./vol. [c] Y values from A. H. Fainberg and S. Winstein, *J. Amer. Chem. Soc.*, **78**, 2770 (1956). [d] Average of several runs. [e] At 50.0 ± 0.1°, average of at least two runs. [f] Determined graphically from data taken from footnote *c*.

relation[36] is not generally applicable to charged substrates like sulfonium salts and therefore presumably also to ammonium salts. The extensive investigations of Hyne and coworkers in this field[37-41] have established clearly an increase in rate of solvolysis of sulfonium salts with decrease in solvent dielectric constant. This corresponds to a negative *m* value in the Winstein–Grunwald treatment. That this should be so is not surprising and indeed was predicted by Hughes and Ingold many years ago.[42]

We have now observed this phenomenon in α-ferrocenylethyl ammonium compounds. The data are summarized in Table III, and show that solvolyses of **2** and **9** give remarkably different *m* values. The *m* value for **2** in aqueous acetone at 50° (expt no. 1–4) is −0.008, and in aqueous ethanol at 50° (expt no. 5–8) it is −0.131. The *m* value determined for **9** in aqueous acetone (expt no. 9–12) is 0.807, the value anticipated for an SN1 reaction with charge separation and in excellent agreement with the titrimetrically determined value of 0.8 determined by Hill and Richards.[13]

The retentive nucleophilic substitutions of the α-ferrocenyl cation in combination with the facile synthesis and resolution of **1**[7,24,43] and the stereorelating syntheses demonstrated for the ferrocene series[8] give a general entry into a great variety of ferrocenes which may be both central and planar chiroids. The recent X-ray configuration determination[9] of a 1,2-disubstituted derivative of optically active **1** solidifies the stereochemical assignments presented herein and may serve as a foundation for other configuration determinations.

Experimental Section

General.—Optical rotations were determined at the 589-nm (D) line of Na in a 10-cm microcell, thermostated at 25° unless otherwise indicated, using a Perkin-Elmer 141 digital polarimeter. Solvents were AR grade. Melting points were determined using a Thomas–Hoover capillary melting apparatus, and are uncorrected. Infrared spectra were recorded on a P.E. 457, and nmr spectra were recorded on either a Varian A-60 or Varian T-60, using TMS as internal standard.

Kinetic Procedure.—All kinetic runs were done using a Perkin-Elmer 141 digital polarimeter. The cell used is a jacketed 1-dl microcell heated by a Bronwill Scientific circulating thermostat calibrated and maintained at each temperature to t ± 0.1°. All runs utilized the 589-nm (D) line of sodium except the solvolyses of **9** (expt. no. 9–12), which utilized the 546-nm line of Hg. In each case, the substrate was weighed in an erlenmeyer flask; then the appropriate solvent (preheated to the required temperature) was pipetted into the flask containing substrate; the timer was started simultaneously. The flask was stoppered and swirled vigorously for 25 sec; then the solution was transferred to the preheated cell; and the readout was switched on. The first reading was generally taken at 100-sec elapsed time; this allowed about 50 sec for instrumental equilibration. Solvent mixtures were prepared by mixing the specified volume of each at 25°. Water was aspirated and then distilled. Acetone and ethanol (AR grade) were redistilled. Acetonitrile (MCB-AR) was refluxed over excess P_2O_5 and then distilled through a 50-cm vacuum jacketed column packed with Raschig rings. The dry acetonitrile was stored under dry N_2 in a serum bottle and transferred by syringe.

The data utilized were taken for a minimum of three half-lives and the infinity point was experimentally determined. The best fit of the data was obtained by least-squares analysis carried out on an IBM 360 computer.

All compounds are known; physical and spectral properties agree with literature values.

***N,N*-Dimethyl-1-ferrocenylethylamine (1).**—Preparation was as described in ref 43. For resolution data see ref 24.

(*R*)-(+)-*N,N,N*-Trimethyl-1-ferrocenylethylammonium Iodide (2) (Scheme II, Reaction B). (*R*)-(+)-1 [26 g, 0.1 mol; $[\alpha]^{25}D$ 14.2 (*c* 2.0, ethanol)] is dissolved in 50 ml of dry acetone and cooled to 0°. Iodomethane (64 g, 0.45 mol, 28 ml) is added in a thin stream with stirring. The flask is stoppered and stirred at 0° for 30 min. The solution is diluted with 200 ml of ether; the product separates as an oil which solidifies quickly to a yellow solid and is isolated by filtration: yield 39 g (97%); mp 132–133° (dec); $[\alpha]^{25}D$ +43° (*c* 0.6, 2-methoxyethanol; rotation diminishes on standing in solution); $[\alpha]^{25}D$ +32.5° (*c* 1.4, acetonitrile).

(*R*)-(−)-1-Ferrocenylethylazide (10) (Scheme II, Reaction C).—The solution of (*R*)-(+)-2 [4.0 g, 0.01 mol; $[\alpha]^{25}D$ +32.5° (*c* 1.4, MeCN)] and NaN_3 (3.9 g, 0.06 mol) in 50% THF is refluxed for 2 hr, diluted with 100 ml of ether, and the phases are separated. The organic phase is washed with three 100-ml portions of water and dried over $MgSO_4$, and the solvent is removed *in vacuo:* yield 2.12 g (82%) of a red-brown oil; bp 80° (0.02 Torr); $[\alpha]^{25}D$ −69.8° (*c* 1.1, benzene). *Caution: This compound is known to explode on distillation.*

(*R*)-(−)-1-Ferrocenylethylamine (3) (Scheme II, Reaction D).—For reduction of **10** with $K_2[Sn(OH)_4]$, see ref 6.

(*R*)-(−)-10 [2.6 g, 0.01 mol; $[\alpha]^{25}D$ −69.8° (*c* 1.1, benzene)] is dissolved in 50 ml of ether and sodium bis(methoxyethoxy)alu-

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minum hydride (SDMEA)[44] (2.8 ml, 0.02 mol) in 10 ml of ether is added dropwise. The solution is refluxed for 1 hr and then poured into water. The layers are separated, the ether layer is dried (K_2CO_3), and the solvent is removed *in vacuo* [yield, 2.0 g (87%) of an amber oil]. This material is dissolved in ether, gaseous HCl is added, and the yellow HCl salt is collected by filtration. The salt is washed quickly with ether, added to 20% NaOH, and extracted with CH_2Cl_2. The solvent is removed *in vacuo*, leaving material with $[\alpha]^{25}D$ −21.0° (*c* 2, ethanol). If the amine is allowed to stand open to the air even for a brief time, the oil converts to a yellow solid, presumably the hydroxylamine.[45] The rotation of this solid is *ca.* 30–35° in EtOH, depending on purity.

(*R*)-(−)-1-Ferrocenylethanol (8) (Scheme II, Reaction E).—A solution of (*R*)-(+)-**2** [10 g, 0.025 mol; $[\alpha]^{25}D$ +32.5° (*c* 1.4, MeCN)] in 200 ml of 50% THF is refluxed for 2 hr. Water (200 ml) is added and the phases are separated. The aqueous layer is extracted with ether; the organic material is combined, washed with water and brine, and dried ($MgSO_4$). Evaporation of the solvent gives an orange solid, 5.3 g (77%), which is recrystallized from *n*-heptane (10 ml/g of solute). The bright yellow product has mp 72–73°; $[\alpha]^{25}D$ −30.5° (*c* 1.1, benzene).

(*R*)-(+)-1-Ferrocenyl-1-methoxyethane (7) (Scheme II, Reaction F).—A solution of (*R*)-(+)-**2** [2.0 g, 0.05 mol; $[\alpha]^{25}D$ +32.4 (*c* 1.0, MeCN)] in 50 ml of 1:1 methanol–acetonitrile is stirred at ambient temperature for 20 hr. The solution is diluted with 100 ml of ether and 100 ml of water and the phases are separated. The organic phase is washed with brine and dried ($MgSO_4$), and the solvent is removed *in vacuo* [yield is 1.0 g (83%), of a dark brown oil which partially solidifies on standing, $[\alpha]^{25}D$ 27.5° (*c* 2, EtOH)].

(*R*)-(−)-1-Ferrocenylethyl Acetate (9) (Scheme II, Reaction G).—A solution of (*R*)-(−)-**8** [1.15 g, 0.005 mol; $[\alpha]^{25}D$ −30.5° (*c* 1.1, benzene)] is dissolved in 5 ml of pyridine; Ac_2O (2 ml) is added; and the flask is stoppered and allowed to stand at ambient temperature overnight. The solution is then reduced *in vacuo* to minimum volume and the residue is dissolved in ether. The resulting solution is washed with ice water (3 × 100 ml) and brine (1 × 100 ml) and dried over 3A molecular sieves. Evaporation of the solvent gives 1.18 g (87%) of a yellow solid which is recrystallized from Skelly A (30 ml) at −60°: mp 70–71°; $[\alpha]^{25}D$ −27.8° (*c* 1.15, EtOH). Sublimation of the recrystallized acetate (45°, 0.4 Torr) raises the rotation, $[\alpha]^{25}D$ −28.5 (*c* 1.4, EtOH). The same experiment performed on (*S*)-(+)-**8** gave (*S*)-(+)-**9** with $[\alpha]^{25}D$ +28.7° (*c* 1.5, EtOH). (Rotation diminishes on standing in solution.)

(*S*)-(+)-1-Ferrocenylethanol (8) (Scheme II, Reaction H).—A solution of (*S*)-(+)-**9** [0.5 g, 0.00218 mol; $[\alpha]^{25}D$ +28.7 (*c* 1.5, EtOH)] in 25 ml of 50% acetone is allowed to stand for 20 hr at ambient temperature. The solution is diluted with water (25 ml), extracted with ether (3 × 25 ml), and dried over K_2CO_3, and the solvent is removed *in vacuo* [yield 0.39 g (78%)]. Recrystallization from *n*-heptane (4 ml) affords (*S*)-(+)-**8** as a yellow powder: $[\alpha]^{25}D$ +30.1° (*c* 1.2, benzene).

(*R*)-(+)-*N*,*N*-Dimethyl-1-ferrocenylethylamine (1) (Scheme II, Reaction I).—A solution of (*R*)-(−)-**9** [1.0 g, 3.68 mmol; $[\alpha]^{25}D$ −29.4° (*c* 1.3, ethanol), optical purity 96.5%], 25% aqueous dimethylamine (3.5 ml, 20 mmol), and methanol (20 ml) is allowed to stand for 2 days. Ice (50 g) is added and the product is extracted with ether (50 ml), then extracted into 8.5% H_3PO_4, washed with ether (50 ml), neutralized with 20% NaOH, and returned to ether. Evaporation of the solvent yields 943 mg (94%) of (*R*)-(+)-**1**: $[\alpha]^{25}D$ 13.6° (*c* 1.2, EtOH) (optical purity 96%).

(*S*)-(−)-*N*,*N*-Dimethyl-1-ferrocenylethylamine (1) (Scheme II, Reaction J).—Phosgene (3.0 g, 0.03 mol) is dissolved in 50 ml of dry ether in a 250-ml three-necked flask equipped with overhead stirrer, nitrogen inlet, and dropping funnel. The phosgene solution is cooled in a Dry Ice–ethanol bath to −20°. The solution of (*S*)-(+)-**8** [4.6 g, 0.02 mol; $[\alpha]^{25}D$ +27.6° (*c* 1.6, benzene) (optical purity 91%)] in 50 ml of ether is added dropwise with stirring. Stirring is continued at −20° for 15 min, and then at ambient temperature for 15 min. The solution is then transferred to a dropping funnel and added in a thin stream to a stirred solution of anhydrous $HNMe_2$ (4.5 g, 0.1 mol) in 100 ml of *i*-PrOH at −20°. When the solution reaches ambient temperature, it is filtered to remove $HNMe_2 \cdot HCl$ and evaporated. The residue is dissolved in 100 ml of ether, extracted into 8.5% H_3PO_4 (3 × 75 ml), washed with ether (100 ml), made basic with solid Na_2CO_3, and returned to ether. The solution is dried (K_2CO_3) and evaporated to yield, after distillation [bp 110° (0.5 Torr), 3.0 g (58%)], a brown oil: $[\alpha]^{25}D$ −12.9° (*c* 1.3, EtOH) (optical purity 91.5%)].

(*R*)-(−)-1-Ferrocenylethyl Acetate (9) (Scheme II, Reaction K).—A solution of (*R*)-(+)-**2** [2.0 g, 0.005 mol; $[\alpha]^{25}D$ +32.4° (*c* 1.4, MeCN)] and anhydrous NaOAc (2.05 g, 0.025 mol) in 50 ml of anhydrous DMF is allowed to stand for 24 hr at ambient temperature, and then diluted with ether (100 ml) and water (100 ml). The ether solution is washed repeatedly with water to remove DMF, dried over $MgSO_4$, and the solvent is removed *in vacuo* to leave a yellow-orange oil (solidifies on standing). The crude material is sublimed (50°, 0.5 Torr) to give 100 mg (7.4%) of pure **9**: $[\alpha]^{25}D$ −21.0° (*c* 0.6, EtOH) (optical purity 73.5%).

(*S*)-(−)-1-Ferrocenyl-1-methoxyethane (7) (Scheme II, Reaction L).—A solution of (*S*)-(+)-**9** [0.50 g, 0.0025 mol; $[\alpha]^{25}D$ +28.7° (*c* 1.5, EtOH)] in 25 ml of dry MeOH is allowed to stand for 24 hr at ambient temperature. Evaporation of the solvent *in vacuo* leaves **7** as a light brown oil: yield 390 mg (63%); $[\alpha]^{25}D$ −27.0° (*c* 1.9, EtOH).

(*R*)-(−)-1-Ferrocenylethyl Azide (10) (Scheme II, Reaction M).—A solution of (*R*)-(−)-**9** [3.0 g, 0.011 mol; $[\alpha]^{25}D$ −20.1° (*c* 1.4, EtOH) (optical purity 70.5%)] and sodium azide (4.0 g, 0.061 mol) in 300 ml of 25% MeOH is stirred overnight at ambient temperature. Most of the MeOH is removed *in vacuo*, saturated salt solution (75 ml) is added, and the product is extracted with three 50-ml portions of CH_2Cl_2. The combined extracts are dried over $MgSO_4$ and the solvent is removed *in vacuo* to give 2.0 g (70%) of a brown oil: ir 2100 cm^{-1}; $[\alpha]^{25}D$ −47.5° (*c* 2.5, benzene) (optical purity 68%). *Caution*: product is explosive.

(*R*)-(−)-1-Ferrocenylethylamine (3) (Scheme II, Reaction N).—A solution of (*R*)-(−)-**9** [3.0 g, 0.011 mol; $[\alpha]^{25}D$ −20.1° (*c* 1.4, EtOH) (optical purity 70.5%)] in 10 ml of concentrated aqueous NH_3 solution and 150 ml of MeOH is stirred for 10 hr at ambient temperature. The MeOH is then removed *in vacuo* and the residue is treated with 8.5% H_3PO_4 and ether. The acid solution is washed with ether and made basic with 20% NaOH, and the product is extracted with CH_2Cl_2. The solution is dried (K_2CO_3) and the solvent is removed *in vacuo*. The residue (1 g, 40%) has $[\alpha]^{25}D$ −14.5° (*c* 1.3, EtOH) (optical purity 69%). {Vacuum sublimation [40° (1 Torr)] affords a yellow solid, probably the hydroxylamine.[45]}

(*R*)-(−)-1-Ferrocenylethylamine (3) (Scheme II, Reaction O).—A solution of (*R*)-(+)-**2** [4.0 g, 0.01 mol; $[\alpha]^{25}D$ +32.4° (*c* 1.0, MeCN)] in 25 ml of concentrated aqueous NH_3 solution and 25 ml of acetonitrile is stirred for 20 hr at ambient temperature. Work-up is the same as for reaction N above. Yield was 1.58 g (69%) of a red-brown oil: $[\alpha]^{25}D$ −20.7 (*c* 1.2, EtOH)

(*R*)-(+)-*N*,*N*-Dimethyl-1-ferrocenylethylamine (1) (Scheme II, Reaction P).—A solution of (*R*)-(+)-**2** [4.0 g, 0.01 mol; $[\alpha]^{25}D$ +32.4° (*c* 2, MeCN)] in 100 ml of MeCN saturated with anhydrous $HNMe_2$ is allowed to react overnight at ambient temperature. The mixture is diluted with water (150 ml) and extracted with ether. The ether solution is extracted with 8.5% H_3PO_4, washed with ether, and made basic with solid Na_2CO_3, and the amine is returned to ether. The ether solution is dried (K_2CO_3) and the solvent is removed *in vacuo* to give (*R*)-(+)-**1**: yield 1.8 g (70%); $[\alpha]^{25}D$ +13.9° (*c* 1.1, ethanol).

(*R*)-(+)-1-Ferrocenyl-1-methyldimethyl Ether (7) (Scheme II, Reaction Q).—A solution of *n*-butyllithium in hexane (15 ml, 2 *M*) is added dropwise to an ether solution of (*R*)-(−)-**8** [4.6 g, 0.02 mol; $[\alpha]^{25}D$ −18.5 (*c* 2.3, benzene) (optical purity 60.6%)] and refluxed for 1 hr. Me_2SO_4 (2.8 g, 0.022 mol) in ether (25 ml) is added dropwise at reflux and heating is continued for 2 hr. The mixture is then poured into ice water (100 ml); the organic phase is washed with water (3 × 100 ml) and brine (100 ml) and dried ($MgSO_4$). Removal of the solvent *in vacuo* gives a viscous amber oil (4.8 g). Chromatography over silica gel (5.5 × 50 cm, J. T. Baker, no. 3405, 60–200 mesh) gives the following fractions: Skelly B, 90 mg (2.1%) of vinylferrocene; 1:5 acetone–Skelly B, 1.1 g (22.5%) of (*R*)-(+)-**7** {$[\alpha]^{25}D$ +16.2° (*c* 0.9, EtOH) (optical purity 59%)}; 1:3 acetone–Skelly B, 3.3 g of a mixture of **7** and **8**.

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Reaction of (S)-(+)-1-Ferrocenylethanol (8) with Acetic Acid in Benzene.—A solution of glacial HOAc (6 g, 0.1 mol) and (S)-(+)-8 [4.6 g, 0.02 mol, $[\alpha]^{25}D$ +29.3° (c 1.7, benzene)] in 130 ml of dry benzene is refluxed for 4 hr while water separates (Dean-Stark trap). The solvent is removed *in vacuo* and the crude acetate (9) (4.9 g, 90%) is purified by chromatography (activated alumina, 5.5 × 20 cm, MCB, 80–325 mesh, eluent-Skelly B). The resulting yellow solid is sublimed: 35° (1 Torr), $[\alpha]^{25}D$ 0 (ethanol).

Registry No.—2, 11136-56-4; 9, 11136-55-3.

Nucleophilic Substitutions Initiated by Electrochemical Oxidation. I. Intramolecular Nucleophilic Substitutions

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The overcrowded 8-*tert*-butyl-1-(2-pyridyl)naphthalenes **1a–c** have been anodically oxidized to give the zwitterions **2a–c** after treatment of the initial reaction mixtures with aqueous base. The initial product of the two-electron oxidation of **1a** was the isolable perchlorate **3**, which slowly eliminates the *tert*-butyl group. The overall mechanism of the formation of zwitterions **2a–c** can be viewed as an electrochemically initiated intramolecular nucleophilic substitution reaction.

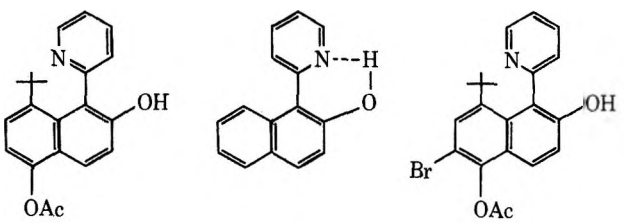
Anodic substitution reactions have been the subject of research for many years, with numerous investigations being described in the literature and summarized in review articles.[1–4] There has been much discussion of the mechanism of these reactions; recent studies have been concerned mainly with the pyridination of substituted anthracenes. Mechanisms proposed for these reactions include (a) the initial formation of a dication and subsequent attack by the nucleophile;[5–7] (b) the formation of a radical cation, attack of this species by the nucleophile, and further electron transfer (ECE mechanism);[8] and (c) disproportionation of the initial radical cation and attack of the resulting dication by the nucleophile.[9]

In all these mechanisms the proton can be considered as the leaving group. Reports of anodic substitution reactions with leaving groups other than the proton are scarce, but such reactions might prove more tractable and thereby offer useful mechanistic insight. The anodic nucleophilic displacement of bromine has been reported for 9,10-dibromoanthracene.[10] However, the authors did not elaborate on the chemical nature of the leaving group. Other communications have dealt with the replacement of a *tert*-butyl group during the course of the anodic oxidation of 2,4,5-tri-*tert*-butylphenol[11] and of 2,4,6-tri-*tert*-butylaniline[12] in acetonitrile solution.

We have investigated intramolecular nucleophilic substitution reactions of highly sterically hindered 8-*tert*-butyl-1-(2-pyridyl)naphthalenes[13] initiated *via* electrochemical oxidation. The leaving group in this case is also the *tert*-butyl group. However, when the oxidations are carried out under suitable reaction conditions, the intermediate cationic species, which still incorporate the *tert*-butyl group, can be isolated as their perchlorate salts. Decomposition of these salts yields isobutylene and zwitterions as the final products. One of these novel zwitterions was observed earlier[13] when 2-hydroxy-5-acetoxy-8-*tert*-butyl-1-(2-pyridyl)-naphthalene was treated with cupric chloride in refluxing ethanol. Although a two-electron oxidation product was obtained from this reaction, the polarographic oxidation was then described as a one-electron exchange. The suggested mechanism included the hitherto unprecedented oxidative coupling of a pyridyl radical through nitrogen rather than carbon. Our own studies on the anodic substitution of a *tert*-butyl group of 2,4,6-tri-*tert*-butylphenol by pyridine, which we shall describe in another paper, led us to the assumption that this intramolecular reaction may also proceed *via* a nucleophilic substitution. Therefore, the objective of this work was to explore the scope and mechanism of the oxidative formation of the zwitterions from their pyridyl naphthol precursors.

Results and Discussion

Cyclic Voltammetric Studies.—Upon scanning anodically from 0.0 V, compounds **1a–c**, all of which have



1a **1b** **1c**

a free hydroxyl group, show three "irreversible" responses A, B, and C, the peak potentials of which are given in Table I. Response C, which is near the solvent cutoff, is often ill-defined; therefore, no effort was made to elucidate its nature.

Compounds **1a–c** do not show a cathodic response between 0 and −2.0 V if the scan is started at 0 V.

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TABLE I

PEAK POTENTIALS OF CYCLIC VOLTAMMETRIC RESPONSES[a]

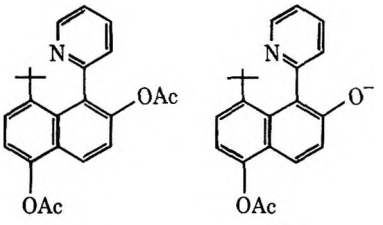
Compound	Response A	B	C	D	E
1a	0.98	1.60	1.9	−0.55	−1.35
1b	1.05	1.75	2.1	−0.52	−1.45
1c	1.00	1.70	2.1	−0.47	−1.25

[a] Scan rate, 0.1 V/sec; Pt electrode; 0.1 *M* TBAP in CH_3CN; potential *vs.* ssce.

However, if the scan is started at potentials corresponding to the diffusion plateau of the first oxidation response A, two reductive responses D and E (Table I) can be observed. Preoxidation at potentials corresponding to the diffusion plateau of response B produces only responses D and E.

Both acetylation of the hydroxyl group of **1a** and removal of the hydroxyl proton of **1a** change the cyclic voltammetric behavior drastically.

The first oxidative response of the diacetylated compound **1d** occurs at +1.48 V and a second response is



1d **1e**

observed at +1.80 V. Reduction responses, which are again present only after preoxidation at potentials corresponding to the diffusion plateau of the first oxidation wave, occur at −0.50 and −0.95 V.

Compared with the parent naphthol, the anion **1e**, which can be generated *in situ* from **1a** with tetramethylguanidine, is oxidized much more easily. At slow scan rates (~0.05 V/sec) only one broad oxidation response can be observed with a peak potential of approximately +0.24 V. If the scan rate is increased, this broad response becomes better defined and, at a scan rate of 0.5 V/sec, two separate responses at the potentials +0.17 and +0.43 V can be clearly distinguished. A further increase in scan rate does not increase the definition of these two responses appreciably. A current maximum at +0.35 V in the reverse scan, which could indicate some reversibility of the second response, also shows no improvement in definition at scan rates greater than 0.5 V/sec.

If cyclic voltammetric studies are performed in the presence of perchloric acid, response A decreases with increasing concentration of the acid, whereas response B increases. The addition of pyridine reconstitutes response A to its original height. Furthermore, cyclic voltammetric scans of the salt **1c** $HClO_4$ in the presence of equimolar amounts of **1c** show clearly that responses B and D are the result of oxidation and reduction, respectively, of protonated starting material.

Scan-rate studies reveal no basic difference in the voltammetric behavior of the compounds with hydroxyl groups and their diacetylated derivatives. Plots of $i_pA/V^{1/2}$ *vs.* log *V* of compounds **1a**, **1b**, and **1d** give horizontal straight lines over a scan rate of three decades.

Coulometric Data.—Coulometry (on a time scale of approximately 15 min) at potentials corresponding to the diffusion plateau of response A resulted in an exchange of one electron per molecule of starting material for compounds **1a–d**. If the oxidation is performed at potentials corresponding to the diffusion plateau of response B, the number of electrons exchanged per molecule of starting material is two.

Addition of pyridine to the coulometry solution changes the apparent one-electron process of response A to a two-electron process.

The results of coulometric studies of the anion **1e** are dependent on potential. A voltammogram of a stirred solution of **1e** exhibits a broad wave with a diffusion plateau attained at +0.5 V. Coulometry at this potential results in an exchange of two electrons per molecule of starting material. If the oxidation is performed at +0.2 V, 1.54 F are exchanged per mole of starting material and at +0.1 V a one-electron process is observed.

The results of the coulometric studies are summarized in Table II.

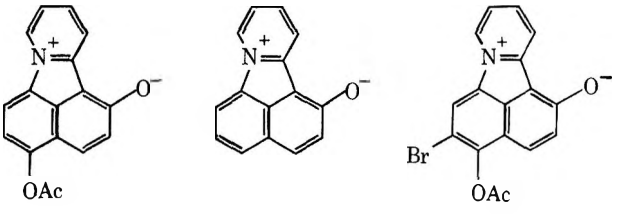
TABLE II

RESULTS OF COULOMETRY AT CONTROLLED POTENTIALS

	Electrons/molecule					
				1e		
	1a	1b	1c	+0.5 V	+0.2 V	+0.1 V
Response A	1	1	1	2.0	1.54	1.0
Response B	2	2	2			
1a + 5% pyridine	2					

Macroelectrolyses.—Macroelectrolyses have been performed on a gram scale at potentials corresponding to the diffusion plateau of the first oxidation response in an acetonitrile–sodium perchlorate medium.

The oxidation of **1a** was carried out at +1.15 V until the current had decayed to 5% of its original value. Starting material and the zwitterion **2a** were isolated



2a **2b** **2c**

from the reaction mixture in approximately 50 and 40% yields, respectively. The current yield of **2a** was 80%. The characteristic data of **2a** are shown in Table III. Oxidation of **1b** was performed at +1.15 V until the current had decayed to 5% of its original value. Besides 50% starting material, zwitterion **2b** was isolated in 4% yield from the reaction mixture. A second product of the formula $C_{30}H_{20}N_2O_2$ was obtained in 40% yield. The current yield for **2b** and the second product was approximately 4 and 40%, respectively. The mass spectrum of the unknown compound displayed a parent peak at *m/e* 440, and the fragmentation pattern suggested an unsymmetrical dimer of **1b** having a C–O–C bridge and a hydroxyl group. These results were supported by ^1H nmr spectroscopy. How-

TABLE III
CHARACTERISTIC DATA OF ZWITTERIONS 2a–c

Compd	Mp, °C	Mass spectrum	Uv spectrum, nm (ϵ 10^{-3})	C_v peak pot in CH_3CN–TBAP, 0.1 V/sec
2a[a]	211	277 m^+	489 (11.1) (2)[b]	E_{p1} = +1.20 V
		235 m − CH_2CO	451 (8.6)	(irreversible)
			430 (4.0)	
			405	
			335 (4.7)	E_{p2} = −1.43 V
			270 (6.65)	(reversible)
			262 (9.8)	
			242 (21.4)	
2b	135	219 m^+	498 (4.95) (1)	E_{p1} = +1.10 V
		191 m − CO	459 (4.30)	(irreversible)
		190 m − HCO	433 (2.20)	
			418 (0.85)	E_{p2} = −1.47 V
			335 (2.95)	(reversible)
			265 (19.0)	
			243 (17.1)	
			227	
2c[a]	235–240 dec	355 m^+	491 (9.4) (1)	E_{p1} = +1.22 V
		315 m − CH_2CO	462 (7.25)	(irreversible)
			437 (3.19)	
			410 (sh)	E_{p2} = −1.32 V
			333 (3.77)	(reversible)
			278 (11.6)	
			268 (11.6)	
			246 (17.0)	

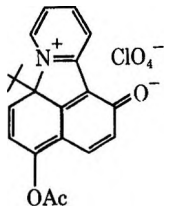
[a] Prepared also through oxidation with $CuCl_2$ by D. L. Fields. [b] (1) In acetonitrile; (2) in methanol.

ever, a conclusion about the exact position of the C–O–C linkage could not be reached. The characteristic data of zwitterion 2b are presented in Table III.

Compound 1c was similarly oxidized at +1.1 V, giving unchanged starting material (50% yield) and the zwitterion 2c in approximately 45% yield. The current yield of 2c was 90% and its characteristic data can be found in Table III.

When compound 1a was electrolyzed at +1.3 V in acetonitrile–sodium perchlorate in the presence of pyridine (6% by volume) at 0°, two electrons were exchanged per molecule of starting material and an orange solution was obtained. From this solution a red-brown compound was isolated which decomposed at 160° with the evolution of gas. ^1H nuclear magnetic resonance spectra in DMSO-d_6 together with mass spectral data showed that the compound still contained a *tert*-butyl group. The ^1H nmr spectrum exhibited broad absorptions for aromatic protons in the region of τ 1.8–3.0. A relatively broad signal at τ 9.02 (area 9) was assigned to a *tert*-butyl group, and two sharp absorptions of equal intensity at τ 8.08 (area 0.5) and at τ 7.92 (area 0.5) were attributed to acetyl groups on the assumption of the existence of two isomers. Mass spectra, recorded as a function of increasing probe temperature, showed that the compound thermally decomposed to form isobutylene, the zwitterion 2a, and, probably because of reducing conditions in the spectrometer, 1-(2-pyridyl)-2-hydroxy-5-acetoxynaphthalene. The zwitterion 2a was also isolated as the main product of both the thermal decomposition at 160° and the photolytic decomposition of an acetonitrile solution of this red-brown material in the beam of a xenon high-pressure lamp.

The ir spectrum in a KBr pellet exhibited, among others, absorptions at 1100 (attributable to ClO_4^-), 1650 (possible quinoid carbonyl group), and 1740 cm^{-1} (acetyl group). This combined information suggests that the isolated oxidation product has the structure 3



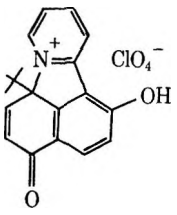
3

which was further supported by elemental analysis.

A uv–visible spectrum of 3 in acetonitrile showed maxima at 540 nm (ϵ 1000), 454 (8500), 430 (9000), and 350 (8900).

When a solution of 3 in acetonitrile was treated with 5% aqueous potassium hydroxide, a deep-red solution was formed. Immediate dropwise addition of 35% perchloric acid solution yielded a brownish red precipitate, which decomposed at 170° with the evolution of gas. As for compound 3, this composite proved to be a perchlorate salt (ir absorption in KBr at 1100 cm^{-1}), the cation of which contained a *tert*-butyl group (broad absorption in the ^1H nmr spectrum at τ 9.08 and the appearance of abundant isobutylene in the mass spectrum). Probes for the presence of an acetyl group by ^1H nmr, ir, and mass spectroscopy were negative. A band at 1640 cm^{-1} in the infrared spectrum indicated the presence of a quinoid carbonyl group. The following structure (4) was accordingly assigned to the compound.

A uv–visible spectrum of 4 in acetonitrile showed maxima at 540 nm (ϵ 3000), 478 (260), 445 (5700), and 365 (6600). When 4 was thermally decomposed, the uv–visible spectrum of the major reaction product was



4

identical with that of the hydrolysis product of zwitterion **2a**.

Both **3** and **4** also decomposed on standing at room temperature, with the formation of the same products. Cyclic voltammetric scans of **3** in an acetonitrile–sodium perchlorate medium show that response E (see Table I) is the result of the reduction of **3**.

The oxidation of the diacetylated compound **1d** at +1.7 V led to a yellow solution, which yielded a brown residue when the solvent was evaporated. Treatment of this residue with aqueous sodium bicarbonate gave a bright-red fluorescent solution and an insoluble yellow material. The yellow material was identified after chromatography as unchanged starting material (~50% of the initial amount). On standing, the bright-red aqueous solutions turned yellow and exhibited a green fluorescence. The major component of these solutions was the zwitterion **2a**. However, all attempts to elucidate the structure of the red fluorescent intermediate failed.

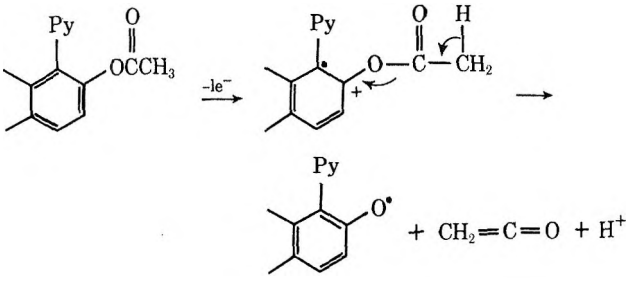
Cyclic voltammetric studies together with coulometric experiments and product characterization of macroelectrolyses show that in aprotic media the apparently one-electron process under response A is, in reality, a two-electron oxidation. The electrolysis product is, for example, the cyclic perchlorate **3** when **1a** is oxidized at potentials corresponding to the diffusion plateau of response A. The formation of this material requires the loss of two electrons and one proton from the starting material. The protons generated in this oxidation are accepted by starting material, thus giving rise to response B in the cyclic voltammograms of **1a–c**. The isolation of the perchlorate **3** after exhaustive electrolysis demonstrates furthermore that ring closure occurs prior to the ejection of the *tert*-butyl group. Thus, the formation of the zwitterions **2a–c** can be formally considered as an electrochemically initiated nucleophilic substitution reaction.

More detailed aspects of the electrochemical oxidation mechanism are less clearly defined and need some further discussion. The question of whether or not the naphthols are oxidized and the resulting radical cations deprotonate or a dissociation of the naphthols occurs before electron transfer cannot be answered on the basis of the collected data. Deprotonation of both the radical cation and the naphthol are expected to be very fast reactions[14] and would therefore be of no major consequence in determining the pathway of the overall reaction. The product in either case is an uncharged radical, which may be oxidized further to a cation or undergo chemical reactions.

Cyclic voltammetric and coulometric studies of the anion **1e** shed some light on the reactions of the uncharged radical. At potentials of approximately +0.1 V, **1e** is oxidized in a one-electron process, which appears to be irreversible even when studied by fast-sweep cyclic voltammetry. Thus, a rapid chemical reaction seems to come into play after one electron has been removed from the anion. Among the reactions which can be expected are an intermolecular dimerization or an intramolecular attack of the pyridine nitrogen atom on carbon-8 of the naphthalene moiety. The isolation of the dimer from the oxidation of **1b** and the observation that the yield of zwitterion increases when **1e** is oxidized at potentials increasing from +0.1 to +0.5 V support the idea of dimerization of the intermediate radical. The intermediate radical from the oxidation of **1b** appears to be much more reactive toward dimerization than the comparable radicals from **1a** and **1c**. Therefore, dimerization can compete effectively with the transfer of the second electron and, as a result, zwitterion **2b** is obtained only in low yield.

The data for the oxidation of the diacetylated compound **1d** reveal that there is no basic mechanistic difference between the oxidation of it and that of the hydroxyl derivatives. Exhaustive electrolysis of **1d** at potentials corresponding to the diffusion plateau of the first oxidation response in aprotic solvent leaves 50% starting material, and the second oxidative response corresponds to electron transfer from protonated starting material. In addition, ^{1}H nmr studies show that acetic acid is produced during the electrolysis and the zwitterion **2a** was isolated as the final product of the reaction.

In view of these observations, a reasonable mechanistic picture for this oxidation process can be visualized through the loss of ketene from the initial radical cation.



The remaining reaction steps are analogous to those for the oxidation of the hydroxyl derivatives. Since the plot of $i_p/V^{1/2}$ *vs.* log V is a horizontal straight line, the loss of ketene appears also to be a very fast reaction. Deketenization of acetyl compounds is a common fragmentation process in mass spectrometry[15–17] and can therefore also be expected from an electrochemically generated cation radical of a short enough lifetime to exclude solution chemistry.

Since the mechanistic studies have been performed mainly with compound **1a**, a mechanism for the electrochemical oxidation of this compound is outlined in Scheme I.

Experimental Section

Chemicals.—Acetonitrile (Eastman X488) was used after drying for several days over a molecular sieve.

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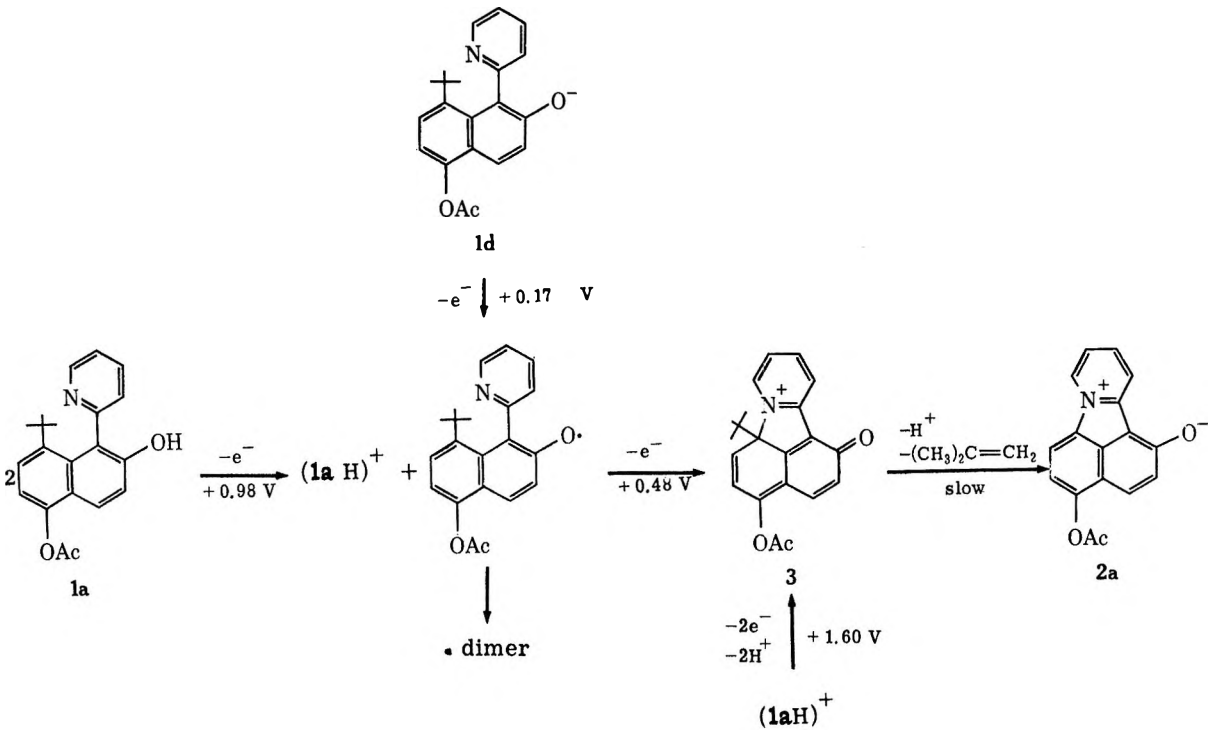
(16) D. Becker, C. Djerassi, R. E. Moore, H. Singh, and P. J. Scheurer, *J. Org. Chem.*, **31**, 3650 (1966).

(17) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, San Francisco, Calif., 1967.

SCHEME I



Tetrabutylammonium perchlorate (TBAP) (Southwestern Analytical Chemicals) was dried under vacuum before use. For macroelectrolyses, sodium perchlorate (G. Fredrick Smith Chemical Co., recrystallized from acetone–methylene chloride) was used as supporting electrolyte.

Apparatus.—Cyclic voltammetric experiments were performed in a conventional three-electrode cell (design after that marketed by Brinkmann) with an Electrochemistry System Model 170 from the Princeton Applied Research Corp. All potentials are referred to an aqueous saturated sodium chloride calomel reference electrode (ssce).

Controlled potential coulometry and preparative oxidations were carried out in conventional two-compartment cells at platinum-working electrodes. The potentiostat was either the Model 170 from Princeton Applied Research Corp. or a Model AS100 from Tacussel Electronique.

^1H nuclear magnetic resonance spectroscopy was performed with a Varian A-60 instrument, mass spectroscopy was performed with the Hitachi RMS-4 spectrometer, and uv–visible and ir spectra were obtained with the Cary Model 14 and Perkin-Elmer Model 137 instruments, respectively.

Preparations. Zwitterions 2a–c.—After the acetonitrile solutions of the starting materials had been electrolyzed exhaustively at the proper potentials, the reaction mixture was filtered and acetonitrile was evaporated under reduced pressure. The residue was treated with 5% aqueous sodium bicarbonate solution, the resulting mixture was extracted with dichloromethane, and the organic phase was dried over anhydrous sodium sulfate. After evaporation of the dichloromethane, the oxidation products were separated on a Florisil column with acetone–methanol mixtures as eluents.

Compounds 3 and 4.—Solutions of **1a** at 2–5 m*M* concentration in acetonitrile–sodium perchlorate were oxidized exhaustively at 0° in the presence of 6% pyridine. The orange solution was filtered and evaporated to approximately $^1/_{10}$ of the original volume. The remaining solution was diluted with distilled water and a red-brown precipitate was collected on a filter. After repeated washings with cold water the precipitate was dried at room temperature under high vacuum. Reprecipitation from acetone–hexane and drying under high vacuum yielded a red-brown powder, which decomposed at 160°. Yields were 60–70% of **3**.

Anal. Calcd for: C, 58.2; H, 4.64; N, 3.57; Cl, 8.18. Found: C, 57.6; H, 4.5; N, 3.7; Cl, 8.0.

When a solution of **3** in acetonitrile was treated with 5% aqueous potassium hydroxide solution, a deep-red solution was formed. Immediate dropwise addition of 35% perchloric acid yielded a brownish red precipitate, which was collected by filtration. After several washings with cold water, this precipitate was dried under high vacuum at room temperature. After reprecipitation from acetone–hexane and drying under high vacuum, brown-red **4** was obtained, which decomposed at 170°.

Registry No.—**1a**, 30310-07-7; **1b**, 23825-09-4; **1c**, 35026-49-4; **2a**, 30310-10-2; **2b**, 35026-51-8; **2c**, 35026-52-9; **3**, 35026-53-0; **4**, 35026-54-1.

Acknowledgment.—I am indebted to Dr. D. L. Fields for supplying the starting materials and for many helpful discussions. I also wish to thank Mr. D. P. Maier for his patience in recording and interpreting the mass spectra and Mr. R. L. Young for supplying the ^1H nmr spectral data. Discussions with Drs. J. Chang and R. F. Large are gratefully acknowledged.

Kinetic Study of the Acid-Catalyzed Chromium(VI) Oxidation of the Methyl Group. Oxidation of 3-Picoline 1-Oxide and 4-Nitro-3-picoline 1-Oxide

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The acid-catalyzed Cr^{VI} oxidation of 3-picoline 1-oxide (PNO) and 4-nitro-3-picoline 1-oxide (NPNO) has been studied kinetically in aqueous sulfuric acid solution. The rate law is first order with respect to both Cr^{VI} and the substrate; the logarithm of the experimental second-order rate constant increases linearly with the H_0 function up to a sulfuric acid concentration of 10 M and becomes acidity independent at higher acid concentrations. The observed kinetics are consistent with a rate-limiting attack by the chromacidium ion, $H_3CrO_4^+$. The constant for the protolytic equilibrium $H_3CrO_4^+ \rightleftharpoons H_3CrO_4 + H^+$ amounts to $K_1 = 2.4 \times 10^6$ M; the second-order rate constants for the oxidation by the chromacidium ion are $k_2 = 1.75 \times 10^{-2}$ M^{-1} sec^{-1} for PNO and $k_2 = 4.9 \times 10^{-3}$ M^{-1} sec^{-1} for NPNO at 45°. The activation parameters measured at a sulfuric acid concentration of 10.6 M are $\Delta H^{\pm} = 11.7$ kcal/mol and $\Delta S^{\pm} = -33.1$ eu for PNO and $\Delta H^{\pm} = 13.5$ kcal/mol and $\Delta S^{\pm} = -30.2$ eu for NPNO.

The acid-catalyzed Cr^{VI} oxidation of methyl arenes yields the corresponding aryl carboxylic acids.[1] In spite of its synthetic significance this reaction has been studied kinetically to a lesser extent than the Cr^{VI} oxidation of other functional groups for which the kinetics are well established.[2] Moreover, most of the previous work has been carried out with acetic acid as a solvent, due to the fact that most arenes are only weakly soluble in aqueous systems. In the similar case of diphenylmethane, a substrate which has been studied extensively, the rate law $v = kh_0[Cr^{VI}][\text{diphenylmethane}]$ has been reported for the acetic acid system.[3] This study is concerned with the kinetics of the Cr^{VI} oxidation of a methyl group in the α position to a heterocyclic ring with aqueous sulfuric acid as a solvent. The title compounds are particularly suitable as substrates since they exhibit excellent solubilities in aqueous sulfuric acid and do not decompose even at high acid concentrations. The oxidation leads almost exclusively to the corresponding nicotinic acid N-oxides without major complications by side reactions. Furthermore, the use of two substrates of similar structure but with different reactivities toward Cr^{VI} should allow one to discriminate between the effects which are caused by the oxidant and those which are specific for the respective substrate.

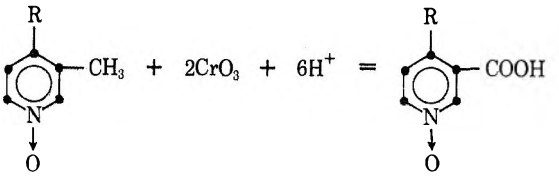
Experimental Section

Chemicals.—Sulfuric acid (Baker) and chromium trioxide (Matheson) were both reagent grade. PNO was synthesized by oxidation of 3-picoline with hydrogen peroxide in acetic acid solution. The product had mp 31–35°. NPNO was obtained by nitration of PNO and purified by recrystallization from toluene. The pure material had mp 137–138°. Nicotinic acid 1-oxide (Aldrich) had mp 258–259° and was used without further purification.

Kinetic Procedure.—The kinetic runs were carried out in a thermostat with a temperature constancy of ±0.1°. Fifty milliliters of a solution of picoline oxide in sulfuric acid of known acidity was mixed with an equal volume of a solution of chromium trioxide in sulfuric acid. In order to minimize heat effects during the mixing, both solutions always had identical acidities. Suitable aliquots were withdrawn at different times and the Cr^{VI} concentration was determined by iodometric titration. If possible, the reaction was monitored to more than 90% completion.

Results

The stoichiometry of the reaction is given by eq 1.



$$+ 2Cr^{3+} + 4H_2O \qquad (1)$$

RPNO = R = H: PNO (3-picoline 1-oxide); R = NO_2: NPNO (4-nitro-3-picoline 1-oxide)

Oxidation of the aromatic ring is expected to be slow compared to the attack on the methyl group. This is verified by the observation that, with identical reaction conditions, nicotinic acid 1-oxide is oxidized at a rate which is negligible in comparison with the oxidation rate of 3-picoline 1-oxide. It is therefore possible to follow the reaction by the decay of the analytical Cr^{VI} concentration. In order to simplify the kinetic analysis the reaction conditions are always chosen so that $[H^+] \gg [RPNO] \gg [Cr^{VI}]_0$. For $[H_2SO_4] \leq 14$ M the kinetics are pseudo first order with respect to Cr^{VI}. The rate constants obtained from the slopes of log $[Cr^{VI}]$ *vs.* time plots are summarized in Table I.

TABLE I[a]
EFFECT OF REACTANT CONCENTRATION ON THE PSEUDO-FIRST-ORDER RATE CONSTANTS

Substrate	$[Cr^{VI}]_0 \times 10^2$ M	[RPNO] $\times 10^1$ M	$k_I \times 10^3$ sec^{-1}	$k_{II} \times 10^2$ M^{-1} sec^{-1}
PNO	0.41	2.50	4.32	1.73
	1.25	2.50	4.15	1.66
	2.50	2.50	3.92	1.57
	2.50	5.00	8.90	1.78
	2.50	1.00	1.58	1.58
	2.50	0.60	0.98	1.63
NPNO	0.40	2.50	1.12	0.448
	1.26	2.50	1.17	0.469
	2.50	2.50	1.21	0.484
	2.50	4.00	1.90	0.475
	2.50	1.00	0.48	0.48
	2.50	0.50	0.23	0.46

[a] $[H_2SO_4] = 10.6$ M; $T = 45°$.

(1) D. G. Lee, "Oxidation, Techniques and Applications in Organic Synthesis," Vol. I, R. L. Augustine, Ed., Marcel Dekker, New York, N. Y., 1969.

(2) K. B. Wiberg, "Oxidation in Organic Chemistry," Part A, K. B. Wiberg, Ed., Academic Press, New York and London, 1965.

(3) K. B. Wiberg and R. J. Evans, *Tetrahedron*, **8**, 313 (1960).

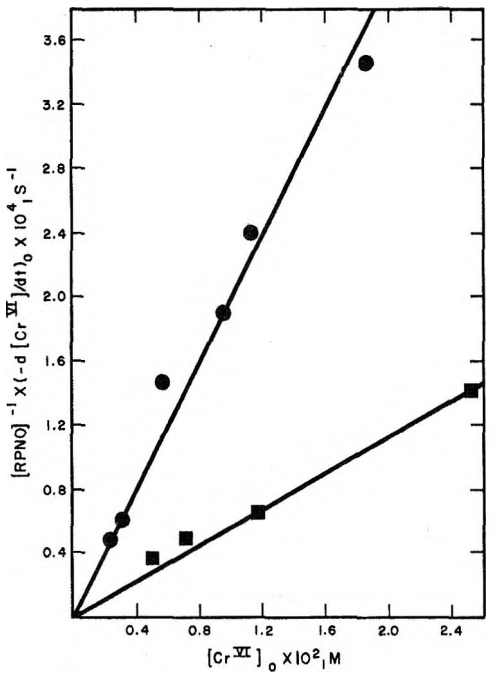


Figure 1.—Estimation of k_{II} from the initial reaction rates: $[H_2SO_4] = 17.7\ M$, $T = 45°$; ●, PNO; ■, NPNO.

Table I shows that for identical reaction conditions PNO is oxidized faster than NPNO. No effect of the initial $[Cr^{VI}]$ on the rate constants is apparent for $4 \times 10^{-3}\ M < [Cr^{VI}]_0 < 2.5 \times 10^{-2}\ M$, indicating that the formation of dimeric Cr^{VI} species is kinetically not important. For $5 \times 10^{-2}\ M <$ [RPNO] $< 5 \times 10^{-1}\ M$ the relation $k_{II} = k_I/$[RPNO] is obeyed. Therefore, the experimental rate law for $[H_2SO_4] \leq 14\ M$ and constant acidity is given by eq 2.

$$\text{Rate} = k_{II}[Cr^{VI}][\text{RPNO}] \quad (2)$$

For $[H_2SO_4] > 14\ M$ the log $[Cr^{VI}]$ *vs.* time plots are no longer linear. However, evaluation of the reaction order from the initial slopes of the concentration–time curves yields again an order of unity for both Cr^{VI} and the substrate. This indicates that the rate law given by eq 2 is obeyed throughout the entire acidity range examined; however, for $[H_2SO_4] > 14\ M$ its validity is restricted to the initial stage of the reaction. Since a deviation from the uncomplicated pseudo-first-order kinetics occurs only at high acidity, it is probably caused by a species which becomes protonated at $[H_2SO_4] > 14\ M$. Figure 1 shows plots of the reduced initial rates, $[\text{RPNO}]^{-1} \times (-d[Cr^{VI}]/dt)_0$, *vs.* $[Cr^{VI}]_0$ for $[H_2SO_4] = 17.7\ M$. The slopes of the straight lines yield second-order rate constants of $2.0 \times 10^{-2}\ M^{-1}$ sec^{-1} for PNO and $0.57 \times 10^{-2}\ M^{-1}$ sec^{-1} for NPNO. Table II shows the effect of acidity on the rate constants. Up to $[H_2SO_4] = 10\ M$ a strong increase of the rate constants with increasing acid concentration is observed; at acid concentrations higher than that the rate constants become acidity independent.

In Figure 2, log k_{II} is plotted *vs.* the H_0 acidity function.[4] For acidities lower than $H_0 = -5$ these plots are linear with slopes close to unity. At $H_0 = -5.5$ the rate constants for both PNO and NPNO level off; the average plateau values amount to $k_{II} = 1.75 \times 10^{-2}\ M^{-1}$ sec^{-1} for PNO and to $k_{II} = 4.9 \times 10^{-3}\ M^{-1}$ sec^{-1} for NPNO.

(4) M. A. Paul and F. A. Long, *Chem. Rev.*, **57**, 1 (1957).

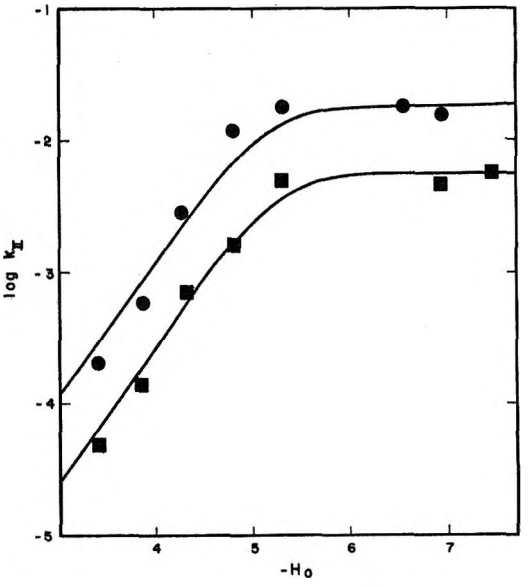


Figure 2.—Acidity dependence of k_{II}. Plot of k_{II} *vs.* H_0: ●, PNO; ■, NPNO.

TABLE II[a]
EFFECT OF ACIDITY ON THE SECOND-ORDER RATE CONSTANTS

$[H_2SO_4]$, M	k_{II}, M^{-1} sec^{-1} PNO	k_{II}, M^{-1} sec^{-1} NPNO
7.1	1.95×10^{-4}	4.95×10^{-5}
8.0	5.80×10^{-4}	1.51×10^{-4}
8.9	2.75×10^{-3}	7.05×10^{-4}
9.7	1.16×10^{-2}	1.59×10^{-3}
10.6	1.70×10^{-2}	4.69×10^{-3}
12.4	1.75×10^{-2}	
13.3	1.61×10^{-2}	4.40×10^{-3}
14.2		5.70×10^{-3}
17.7[b]	2.0×10^{-3}	5.7×10^{-3}

[a] $[Cr^{VI}]_0 = 1.25 \times 10^{-3}\ M$; [RPNO] $= 0.250\ M$; $T = 45°$. [b] The rate constants for this acidity are obtained from the initial reaction rates.

The temperature dependence of the rate constants follows the Arrhenius equation. The rate constants measured at different temperatures are listed in Table III together with the graphically determined activation energies and frequency factors. From these the apparent activation enthalpies and entropies are calculated. For PNO the values $\Delta H^{\pm} = 11.7$ kcal/mol and $\Delta S^{\pm} = -33.1$ eu are obtained; the corresponding values for NPNO are $\Delta H^{\pm} = 13.5$ kcal/mol and $\Delta S^{\pm} = -30.2$ eu.

TABLE III[a]
EFFECT OF TEMPERATURE ON THE PSEUDO-FIRST-ORDER RATE CONSTANTS

Temp, °C	k_I, sec^{-1} PNO	k_I, sec^{-1} NPNO
25	1.03×10^{-3}	
35	2.11×10^{-3}	4.48×10^{-4}
45	3.92×10^{-3}	1.21×10^{-3}
55	7.12×10^{-3}	1.77×10^{-3}
65		3.46×10^{-3}
E	12.3 kcal/mol	14.1 kcal/mol
log A	6.08, sec^{-1}	6.66, sec^{-1}

[a] $[Cr^{VI}]_0 = 2.5 \times 10^{-2}\ M$; [RPNO] $= 0.250\ M$; $[H_2SO_4] = 10.6\ M$.

Discussion

The reaction is first order with respect to Cr^{VI}, which suggests that the oxidizing agent is a monomeric Cr^{VI} species. Since the rate constants are independent of the total Cr^{VI} concentration, the equilibrium concentration of dimeric Cr^{VI} has to be very small. This may be accounted for by the high sulfuric acid concentration present, which favors the formation of sulfatochromate instead of dichromate species.[5]

The shape of the acidity profile shown in Figure 2 indicates the existence of a kinetically important protolytic equilibrium with a pK within the acidity range examined. Alternatively, this may involve the ionization of either a Cr^{VI} species or the substrates. For PNO pK = 1.08 has been reported[6] and a comparable value should be reasonable for NPNO, which means that both substrates are completely protonated throughout the entire acidity range. Since a further protonation of the picoline 1-oxides appears to be unlikely, the shape of the observed acidity profile is probably caused by the protonation of a Cr^{VI} species. This is also supported by the fact that the plateau values of the rate constants are attained at the same acidity regardless whether PNO or NPNO is the substrate which is oxidized.

The acid chromate ion, $HCrO_4^-$, has been reported to oxidize the side chain of alkyl benzenes at elevated temperatures and $5.4 < pH < 7.0$.[7] However, within the acidity range of this study, oxidation by the acid chromate ion can be ruled out, since with $K = 1.68$ for the dissociation of chromic acid at 45° as extrapolated from the data of Tong and Johnson,[8] the equilibrium concentration of the acid chromate ion is negligible. Therefore, the protolytic equilibrium, which is kinetically important, is evidently established between chromic acid, H_2CrO_4, and the chromacidium ion, $H_3CrO_4^+$, with both species probably existing as complexes with sulfuric acid. If the equilibrium constant is defined by eq 3, the analytical Cr^{VI} concentration may be expressed according to eq 4, provided that chromic acid and the chromacidium ion are the only species present.

$$K_1 = [H_2CrO_4]h_0/[H_3CrO_4^+] \quad (3)$$

$$[Cr^{VI}] = [H_3CrO_4^+](1 + K_1/h_0) \quad (4)$$

With $H_3CrO_4^+$ as the oxidizing agent, the true rate law is given by eq 5. From eq 4 one obtains the rate law in terms of the analytical $[Cr^{VI}]$ according to eq 6.

$$\text{Rate} = k_2[H_3CrO_4^+][\text{RPNO}] \quad (5)$$

$$\text{Rate} = k_2[Cr^{VI}][\text{RPNO}]/(1 + K_1/h_0) \quad (6)$$

From eq 2 and 6 the acidity dependence of the experimental rate constants, k_{II}, is obtained. By means of eq 7 the true rate constants k_2 and the equilibrium constant K_1 may be graphically evaluated.

$$1/k_{II} = 1/k_2 + K_1/k_2h_0 \quad (7)$$

The plot of eq 7 using the k_{II} values from Table II is shown in Figure 3. Straight lines are obtained with slopes of 1.27×10^7 M^2 sec for PNO and of 5.1×10^7 M^2 sec for NPNO. The ordinate intercepts are too small to be evaluated with any degree of accuracy. However, since, for $K_1/h_0 \ll 1$, the experimental rate constants k_{II} become identical with the true rate constants k_2, one may use the plateau values of k_{II} from Figure 2 to obtain an estimate for K_1. Multiplying the plateau values $k_{II} = 1.75 \times 10^{-2}$ M^{-1} sec^{-1} for PNO and $k_{II} = 4.9 \times 10^{-3}$ M^{-1} sec^{-1} for NPNO by the respective slopes of the Figure 3 plots gives $K_1 = 2.2 \times 10^5$ M in the case of PNO and $K_1 = 2.5 \times 10^5$ M in the case of NPNO. The fact that, for both substrates, the equilibrium constants are virtually identical confirms the validity of the proposed mechanism. Independent evidence for the oxidation by a protonated Cr^{VI} species may be derived from the acidity profile obtained with 2-propanol as a substrate.[9] In this case a maximum, rather than a plateau, is observed which is attributed to the existence of two different protolytic equilibria with constants of 2.16×10^5 and 1.51×10^4 M, respectively. The first value agrees with the results of this study and therefore represents the ionization of the Cr^{VI} species; consequently, the second one should be ascribed to the protonation of 2-propanol.

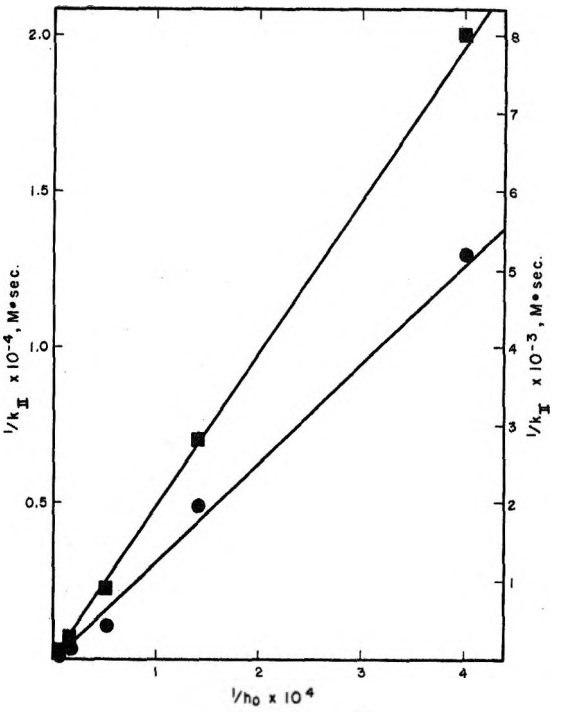


Figure 3.—Acidity dependence of k_{II}. Plot of $1/k_{II}$ *vs.* $1/h_0$: ●, right-hand scale, PNO; ■, left-hand scale, NPNO.

It should be mentioned that, in the case of the Cr^{VI} oxidation of a series of aliphatic dicarboxylic acids in acetic acid, the plateau values of the individual rate constants are attained at acidities which differ with each substrate, suggesting a kinetic effect caused by the protonation of the substrate rather than the Cr^{VI}.[10] However, it has been shown earlier that in sulfuric acid solution, at very high acidities, the rate constants decrease from these plateau values, again indicating that two independent protolytic equilibria are operative.[11] For $K_1/h_0 \gg 1$, *i.e.*, for low acidities, the rate ex-

(5) D. G. Lee and R. Stewart, *J. Amer. Chem. Soc.*, **86**, 3051 (1964).
(6) H. H. Jaffé and G. O. Doak, *ibid.*, **77**, 4441 (1955).
(7) D. G. Lee and U. A. Spitzer, *Can. J. Chem.*, **49**, 2763 (1971).
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pression, eq 6, may be written as $v = (k_2/K_1)h_0[Cr^{VI}][RPNO]$, which agrees with the rate law reported for the oxidation of diphenylmethane in acetic acid.[3] This indicates that the kinetic behavior is essentially the same in both the aqueous sulfuric and the acetic acid system. However, since the value of K_1 presumably depends on the nature of the anions present,[5] the equilibrium constants are not expected to be identical for the two solvent systems.

Registry No.—Cr^{VI}, 18540-29-9; PNO, 2398-81-4; NPNO, 1078-05-3.

The Effect of Solvent and Cation on the Reaction of Organometallic Derivatives of Indole with Methyl Iodide[1]

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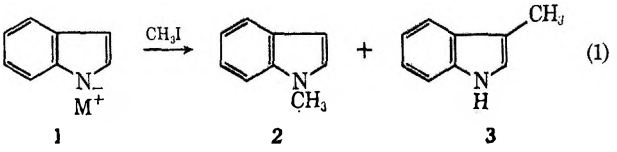
The alkali metal salts of indole behave as typical ambident anions in their reactions with methyl iodide. Indolylmagnesium halides reveal their ambident character only in HMPT which breaks up the tight N–Mg association *via* a 2:1 complex. This observation can be used to reveal structural effects on the reactions of indole Grignard reagents as illustrated by the variation of the C- to N-methylation ratio with the halogen atom of the Grignard reagent.

The rate and position of reaction of ambident anions is markedly affected by a variety of structural and experimental variables.[3,4] Among heterocyclic compounds this phenomenon is most obvious in the chemistry of alkali metal and Grignard derivatives of pyrrole[5] and indole[6] which may react with electrophiles at either carbon or nitrogen. As part of the study of the structure of these derivatives by nmr,[7-9] detailed information on their reactivity as ambident anions was desired. Since such data was already available in the pyrrole series,[5] an examination of the related indole derivatives was undertaken.[1]

The reaction selected for investigation, the methylation of indole salts (eq 1), was known for both the so-



1 2 3 (1)

dium[10] and Grignard[11] derivatives, which yield primarily the N- and C-methylated products **2** and **3**, respectively. A methyl halide was chosen rather than an allyl or benzyl halide, since the latter reagents increase the tendency toward reaction at the less electronegative atom of an ambident system[4,12] thereby leading, particularly with the Grignard derivatives, to essentially exclusive C-alkylation.[13,14] By using methyl iodide, however, some reaction on nitrogen was anticipated with the Grignard reagent,[11] thus permitting an examination of C- *vs.* N-alkylation as a function of structural and media effects for both the Grignard and alkali metal derivatives of indole. The results of this study, as summarized in Tables I–III,

TABLE I

EFFECT OF CATION AND SOLVENT ON THE REACTION OF INDOLE SALTS WITH METHYL IODIDE (EQ 1)

	Per cent of methylation on carbon[a]		
Cation	THF	Et_2O	Toluene
K	2		13
Na	12	35	60
Li	44	85	91
MgBr	100		100

[a] ±4% calculated as [3/(2 + 3)] × 100; in several experiments traces (<4%) of 1,3-dimethylindole were also found and counted as C-methylation product **3**.

TABLE II

EFFECT OF SOLVENT COMPOSITION ON REACTION OF INDOLYLMAGNESIUM BROMIDE WITH METHYL IODIDE

Equiv of HMPT / InMgBr	Vol % HMPT in THF	Per cent of methylation on carbon[a]
0	0	100
1	12.5	100
2	25	97
2.5	22	62
2.8	22	36
3.1	24	30
3.4	22	9
3.9	30	5
4.4	33	0
6.4	50	0
10.3	100	0

[a] See footnote to Table I.

(1) Taken in part from the Ph.D. Dissertation of J. F. Sebastian, University of California, Riverside, 1965.

(2) To whom inquiries should be directed at the first address.

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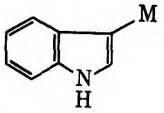
TABLE III
HALIDE EFFECT IN THE REACTION OF INDOLYLMAGNESIUM HALIDES WITH METHYL IODIDE IN THF–HMPT[a]

Halide	Per cent methylation on carbon[b]
Cl	11
Br	37
I	79

[a] 2.8 equiv of HMPT per InMgX. [b] See footnote to Table I.

complement and extend those of Lerner[13] and Cardillo[14] obtained primarily with allyl halides.

For the alkali metals increasing ionic radius or electropositivity leads to less carbon and more nitrogen methylation in the three solvents studied (Table I). This observation is consistent with generalizations from other ambident ion systems,[3-5] including the reactions of indole metal derivatives with allyl halides in THF[13,14] and dioxane,[13] and has been rationalized by assuming that the smaller, less positive cations are more tightly associated with the electronegative end of the ambident ion system, thereby hindering attack at that position. Support for this explanation in the case of indole salts comes from a study of their nmr spectra,[7,9,15] which clearly show these to be nitrogen (**1**) and not carbon (**4**, **5**) derivatives. The magnesium



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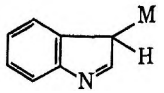

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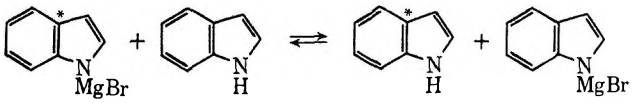
of the indole Grignard reagent must be the most tightly associated of all, since no N-alkylated product is found. The results also indicate that indolyllithium is more associated than the sodium and potassium derivatives. This does not contradict the nmr studies,[9] which indicate that the former is a solvent-separated ion pair in THF while the latter are contact ion pairs, since solvent-separated lithium ion pairs may still be strongly associated in THF.[16]

The increasing percentage of C- *vs.* N-methylation of a particular salt as the polarity and cation-solvating ability of the solvent decreases (Table I) again finds analogy in other ambident ion systems,[3-5] including the reactions of indolylpotassium with allyl bromide in THF, dioxane, toluene, and heptane[13] as well as indolylsodium in THF and dimethylformamide.[17] Presumably the more polar solvents are better able to break up the association of the cation with the nitrogen atom, thereby permitting reaction at that site. Once again the magnesium atom of the indole Grignard reagent apparently is held so tightly that N-alkylation is not obtained in either the above reaction solvents or in diethyl ether[13,14] and dibutyl ether.[14] In hexamethylphosphortriamide (HMPT), however, a solvent with a remarkable ability to dissociate organometallic compounds,[18,19] indolylmagnesium bromide gives exclusive N-methylation (Table II). Similar observations have been made[20] for the reaction of the indole and pyrrole Grignard reagents with allyl bromide and in the former case for isoamyl bromide as well.[14] The exchange reaction between the indole Grignard reagent and indole (eq 2) has also been shown to be markedly



(2)

accelerated in the presence of HMPT.[9] None of these results indicate whether HMPT simply modifies the bulk solvent properties of the media[14] or forms a complex with the Grignard reagent.

The existence of 2:1 complexes of HMPT and Grignard reagents has been proposed,[21-23] as has one between indolylmagnesium iodide and D_2O.[24] However, Cardillo found that with 2 equiv of HPMT per Grignard reagent (solvent composition unspecified) both isoamyl and allyl bromide still gave predominantly C-alkylation.[14]

The nature of the interaction between HMPT and indolylmagnesium bromide is revealed from a study of the methylation reaction in mixed THF–HMPT solvent systems (Table II). The ratio of C- to N-methylation is clearly related to the equivalents of HMPT per Grignard reagent present and not the bulk composition of the solvent. Below 2 and above 4 equiv of HMPT the position of alkylation is independent of solvent composition, occurring predominantly on carbon in the former situation and on nitrogen in the latter. The region of transition is relatively narrow and suggests the existence of a 2:1 complex of indolylmagnesium bromide and HMPT in which the magnesium is still tightly associated with the nitrogen atom. Additional HMPT dissociates this complex until at 4 equiv no effective hindrance to attack by methyl iodide at the nitrogen atom remains.

In the intermediate solvent composition range (2–4 equiv of HMPT) the C- to N-alkylation ratio should display maximum sensitivity to structural variations in the reactants, thus permitting an examination of these factors. This hypothesis was verified from a study (Table III) which reveals a strong halide effect in the reaction of indolylmagnesium halides with methyl iodide. Significant halide effects have been observed previously[25] but are by no means common. The present results indicate that the magnesium and nitrogen are most tightly associated in the iodide and least in the chloride. This trend could be explained by the increased electronegativity of the latter halogen imparting more ionic character (polarity) to the N–MgX bond, thereby leading to more extensive dissociation

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by the solvent. Alternatively, the nature of the halogen may also effect the Schlenk equilibrium, intermolecular aggregation, or solvent complexation in such a manner as to alter the degree of N–Mg association. A further possibility, suggested by a referee, is that the indolylmagnesium halides and methyl iodide undergo halogen exchange to give indolylmagnesium iodide and methyl halides, which might display a leaving group effect in the observed direction.[12,26] Additional studies are obviously required to determine the cause of this halogen effect as well as other structural effects which may be revealed in mixed HMPT–ether solvent systems.

Experimental Section

Nmr spectra were measured on a Varian A-60 or A-60A spectrometer and the infrared spectra on a Perkin Elmer 137 instrument. Gas chromatographic analyses were carried out on an Aerograph Autoprep A-700 using a 5 ft × 0.25 in. column of 20% Carbowax 20M on firebrick at 220°.

Chemicals.—THF and ether were distilled from lithium aluminum hydride immediately before use. Toluene was distilled from sodium and HMPT was dried over BaO powder, decanted, and distilled under a nitrogen atmosphere at 84° (2 mm). The magnesium (99.99%) was purchased from A. D. Mackay, Inc., New York, N. Y. Indole (mp 52–53°), 2-methylindole (mp 59–61°), and 3-methylindole (mp 94–96°) were purchased from the Aldrich Chemical Co. and were used without further purification. 1-Methylindole was prepared by the method of Potts and Saxton[27] and purified by elution from a neutral alumina column with petroleum ether (bp 60–90°). 1,3-Dimethylindole was prepared from 3-methylindolyllithium and methyl iodide in HMPT as described below.

General Procedure for the Preparation and Methylation of Indolylmetal Derivatives. A. In THF.—Observing the usual precautions[9] against H_2O and CO_2, a solution of indole in THF was added to a 10% excess of potassium metal, NaH, LiH, or EtMgBr in THF and the mixture was heated to reflux until reaction was complete. A solution of methyl iodide (10% excess) in THF was slowly added and the reaction was allowed to proceed at room temperature until complete as determined from preliminary experiments (from 30 min for the potassium compound to 48 hr for the Grignard reagent).

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B. In Ether.—The same procedure as above was followed except that the ether was used in place of THF and MeLi in place of LiH.

C. In Toluene.—With the exception of indolylpotassium, which was synthesized directly in toluene from metallic potassium and indole, the indole derivatives were first prepared in THF as above, dry toluene was added, and the THF was removed by distillation. Methyl iodide in toluene was added to the heterogeneous mixtures and the reaction was allowed to proceed for 6–8 days.

D. In HMPT.—Indolylmagnesium bromide and 3-methylindolyllithium were prepared in ether as described in B, HMPT was added, and the ether was removed by distillation up to 90° at 30 mm. Methyl iodide in HMPT was added and the reaction was carried out for 15 hr at room temperature.

E. In THF–HMPT Mixtures.—*n*-Butylmagnesium chloride, ethylmagnesium bromide, or methylmagnesium iodide were prepared in THF and a solution of indole in THF–HMPT was added so that the desired final solvent composition was obtained. A solution of methyl iodide in THF–HMPT of the same composition was added and the reaction was allowed to proceed at room temperature for 3–45 hr (the more HMPT the faster the reaction). To a first approximation the C- to N-methylation ratio was found to be independant of reaction time, as is also the case with indolylsodium.[17]

F. Work-Up and Analysis.—The reaction mixtures were treated with water (alkali metals) or 5% NH_4Cl (Grignards) and then extracted with ether. After the mixtures were dried and ether was evaporated, the products were collected by preparative glc and identified by a comparison of their nmr and infrared spectra with those of authentic samples. Quantitative analyses were carried out by glc and nmr spectroscopy of the crude reaction mixtures utilizing in the latter case the relative areas of the aromatic (τ 2.3–3.7), 1-methyl (τ 6.3–6.4), and 3-methyl (τ 7.7) resonances. The 1-methyl resonances of 1-methylindole and 1,3-dimethylindole could be cleanly detected in one another's presence. No evidence for the presence of any 2-methylindole was obtained in any of these reactions.

Registry No.—Indole (K salt), 31163-74-3; indole (Na salt), 16982-67-5; indole (Li salt), 18344-49-5; indolylmagnesium bromide, 20356-50-7; methyl iodide, 74-88-4; indolylmagnesium chloride, 35099-77-5; indolylmagnesium iodide, 13884-15-6.

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Aminomercuration of Olefins

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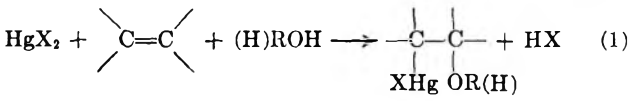
Olefins containing carbonyl, alcohol, or ether groups in the γ position to the double bond undergo facile addition of amine and HgCl residues (aminomercuration). The mechanism is thought to involve a cyclic transition state, wherein the mercury atom is held in position over the double bond to facilitate reaction.

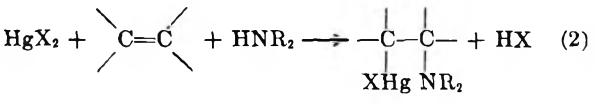
The reaction of mercuric salts with olefins has been studied widely.[1-3] The majority of these studies center around oxymercuration in which either an alkoxy, carboxylate, or a hydroxyl group is added across a double bond along with a mercuric salt (eq 1). These



(1)

reactions are usually carried out in aqueous or alcoholic media and the solvent participates in the addition.

However, much less attention has been devoted to aminomercuration in which the elements of an amine (usually secondary) and a mercuric salt are added to a double bond (eq 2).



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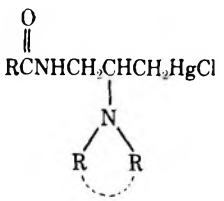
I

A few reports of this type of reaction in the literature[4-8] have centered around the reactions of the olefins ethylene and styrene.

In 1957, Wendt and coworkers[9] showed that various substituted allylureas would undergo aminomercuration to form derivatives possessing the general structure II.



II

Only a few organomercurials possessing the structure of I and II have been reported; so we felt that more investigation in this area was necessary. Since the compounds reported by Wendt were formed quite well and were structurally more complicated than ethylene, we were led to believe that perhaps aminomercuration may be assisted by olefins which possess internal coordinating groups.

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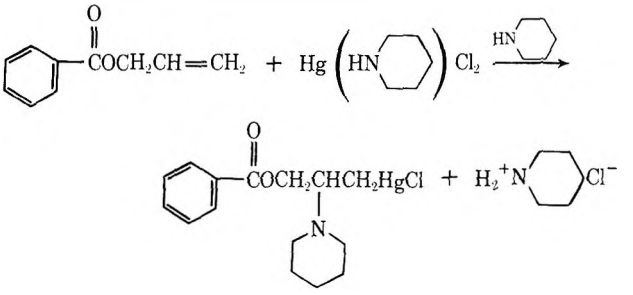
Results

Allylic Esters.—We have found that functionally substituted allyl derivatives react very well in aminomercuration. For example, allyl benzoate was found to react with a mercuric chloride–piperidine complex to give an addition product in 65% yield. Other addi-

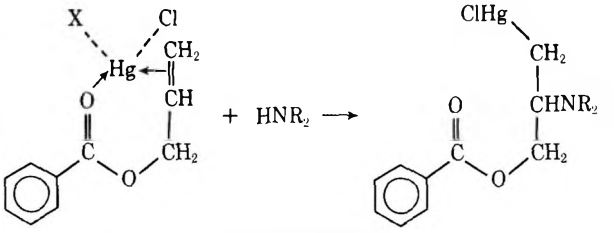


tion products of carbonyl-containing olefins with piperidine are summarized in Table I.

Typically, the addition is achieved by stirring equimolar amounts of the olefin and the mercuric chloride–amine complex in excess amine (solvent) for 1–3 days. The amine hydrochloride is filtered and the solvent is removed under vacuum. The addition product is then crystallized from ethanol. Stirring mercuric chloride and the olefin in piperidine worked equally well, but the reaction times were much longer due to difficulties in stirring heavy precipitates of mercuric chloride–amine complexes.

Aminomercuration is not limited to piperidine; other amines were found to yield addition products. The reaction products with allyl benzoate are listed in Table II. It is interesting to note that from the 2:1 complexes of amine with mercuric chloride, we were unable to form addition products with allyl benzoate.

We have found some restraints as to the structure of carbonyl-containing olefins which will undergo the aminomercuration reaction. The most favorable geometry involves mercuric ion and six other atoms which may form a seven-membered ring in the transition state.



X = Cl^- or HNR_2

The importance of carbonyl coordination is supported by the fact that electron-donating para-substituted

TABLE I
AMINOMERCURATION ADDUCTS FROM CARBONYL-CONTAINING OLEFINS WITH PIPERIDINE

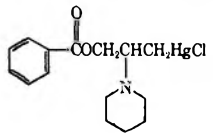
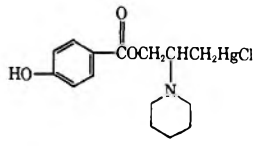
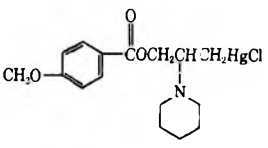
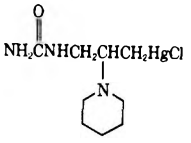
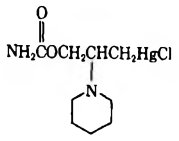
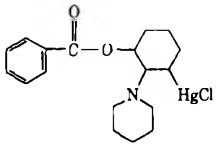
Olefin	$HgCl_2$–piperidine adduct	No.	Yield, %	Mp, °C	Recrystn solvent	Nmr, δ	Ir, cm^{-1}	Anal.
Allyl		1	65	115–116	Absolute ethanol	($CDCl_3$) 8.0–8.2 (doublet, 2 H, J = 8 Hz, phenyl) and 7.4–7.6 (multiplet, 3 H, phenyl), 4.2–4.6 (octet, 2 H, J = 4 Hz, CH_2O), 3.1–3.4 (multiplet, 1 H, CHN), 2.5–3.0 (multiplet, 4 H, CH_2N), 2.2–2.3 (doublet, 2 H, J = 8 Hz, CH_2Hg), 1.4–1.8 (multiplet, 6 H, CH_2)	(KBr) 2900 (CH), 1680 (C=O), 1260 (CO), 1120, 1030, 970, 710	Calcd for $C_{16}H_{20}NO_2HgCl$: C, 37.42; H, 4.16; N, 2.90; Cl, 7.40. Found: C, 37.37; H, 4.25; N, 2.80; Cl, 7.60.
Allyl *p*-hydroxybenzoate		2	14	122–123	Methanol	(DMSO-d_6) 7.8–7.9 (doublet, 2 H, J = 8 Hz, phenyl) and 6.8–6.9 (doublet, 2 H, J = 8 Hz, phenyl), 4.1–4.5 (octet, 2 H, J = 4 Hz, CH_2O), 3.1–3.3 (multiplet, 1 H, CHN), 2.4–2.8 (multiplet, 4 H, CH_2N), 1.9–2.1 (doublet, 2 H, J = 8 Hz, CH_2Hg), 1.4–1.7 (multiplet, 6 H, CH_2)	(KBr) 3350 (OH), 2930 (CH), 1680 (C=O), 1260 (CO), 1165, 850, 770	Calcd for $C_{16}H_{20}NO_3HgCl$: C, 36.21; H, 4.02; N, 2.89; Hg, 40.24; Cl, 7.05. Found: C, 35.99; H, 4.08; N, 3.06; Hg, 40.01; Cl, 7.12.
Allyl *p*-methoxybenzoate		3	40	97–98	Absolute ethanol	($CDCl_3$) 7.9–8.1 (doublet, 2 H, J = 8 Hz, phenyl) and 6.8–7.0 (doublet, 2 H, J = 8 Hz, phenyl), 4.1–4.6 (octet, 2 H, J = 4 Hz, CH_2O), 3.8 (singlet, 3 H, OCH_3), 3.1–3.4 (multiplet, 1 H, CHN), 2.5–2.9 (multiplet, 4 H, CH_2N), 2.3–2.4 (doublet, 2 H, J = 8 Hz, CH_2Hg), 1.4–1.7 (multiplet, 6 H, CH_2)	(KBr) 2900 (CH), 1695 (C=O), 1250 (CO), 1100, 1025, 840, 770	Calcd for $C_{18}H_{22}NO_3HgCl$: C, 37.57; H, 4.30; N, 2.74; Hg, 39.13; Cl, 6.85. Found: C, 37.32; H, 4.26; N, 2.71; Hg, 38.93; Cl, 6.59.
Allylurea		4	50	115–116	Ethyl acetate–isopropyl alcohol	(DMSO-d_6) 6.1–6.4 (multiplet, 1 H, NH), 5.8–6.0 (multiplet, 2 H, NH_2), 3.7–3.9 multiplet, 2 H, CH_2-NH), 3.2–3.6 (multiplet, 1 H, CHN), 2.8–3.0 (multiplet, 4 H, CH_2N), 2.2–2.4 (doublet, 2 H, J = 8 Hz, CH_2Hg), 1.7–2.0 (multiplet, 6 H, CH_2)	(KBr) 3350 (NH), 3100 (NH), 1600 (C=O), 1270, 1190, 1070, 880, 855	Calcd for $C_9H_{18}N_3OHgCl$: C, 23.96; H, 4.40; N, 10.26; Hg, 48.90; Cl, 8.90. Found: C, 24.22; H, 4.19; N, 9.97; Hg, 48.75; Cl, 9.05.
Allyl carbanate		5	42	92–93	Isopropyl alcohol	(DMSO-d_6) 6.3–6.5 (singlet, 2 H, NH_2), 2.9–3.2 (multiplet, 1 H, CHN), 2.5–2.8 (multiplet, 4 H, CH_2N), 1.9–2.0 (doublet, 2 H, J = 8 Hz, CH_2Hg), 1.3–1.6 (multiplet, 6 H, CH_2)	(KBr) 3300 (NH_2), 2900 (CH), 1650 (C=O), 1440, 1100, 1050, 860, 750	Calcd for $C_9H_{17}N_2O_2HgCl$: C, 23.90; H, 4.14; N, 6.83; Hg, 48.78; Cl, 8.53. Found: C, 23.73; H, 4.01; N, 6.45; Hg, 48.89; Cl, 8.02.
3-Cyclohexenyl benzoate		6	6	133	Absolute ethanol	($CDCl_3$) 8.0–8.2 (doublet, 2 H, J = 8 Hz, phenyl) and 7.4–7.6 (multiplet, 3 H, phenyl), 5.6–5.7 (multiplet, 1 H, CHO), 2.9–3.1 (multiplet, 1 H, CHN), 2.6–2.8 (multiplet, 2 H, CH_2N), 2.0–2.2 (doublet, 2 H, J = 12 Hz, CH_2Hg), 1.4–1.8 (multiplet, 12 H, CH_2)	(KBr) 2920 (CH), 1690 (C=O), 1440, 1275 (C—O), 1110, 880, 715	Calcd for $C_{18}H_{24}NO_2HgCl$: C, 41.45; H, 4.60; N, 2.68; Hg, 38.38; Cl, 6.71. Found: C, 41.25; H, 4.66; N, 2.66; Hg, 38.36; Cl, 6.50.

TABLE I

(*Continued*)

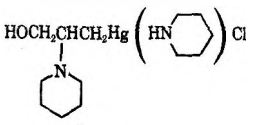
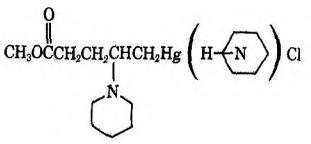
Olefin	$HgCl_2$–piperidine adduct	No.	Yield, %	Mp, °C	Recrystn solvent	Nmr, δ	Ir, cm^{-1}	Anal.
Allyl acetate		7	74	67–68		Same as that obtained from allyl alcohol		
Methyl allylacetate		8	73	Oil		($CDCl_3$) 5.0 (singlet, 1 H, N–H), 3.6 (singlet, 3 H, OCH_3), 2.8–3.2 (multiplet, 5 H, CH_2–NHHg), 2.4–2.6 (multiplet, 4 H, CH_2N), 2.3–2.4 (multiplet, 2H, $CH_2C{=}O$), 2.1–2.3 (doublet, 2 H, J = 8 Hz, CH_2Hg), 1.3–1.9 (multiplet, 12 H, CH_2)		

TABLE II

AMINOMERCURATION ADDUCTS FROM ALLYL BENZOATE WITH VARIOUS AMINES[a]

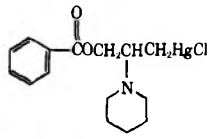
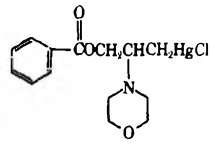
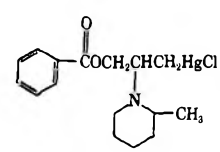
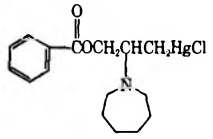
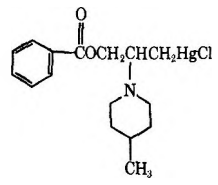
Amine	$HgCl_2$–allyl benzoate adduct	No.	Yield, %	Mp, °C	Recrystn solvent	Nmr, δ	Ir, cm^{-1}	Anal.
Piperidine		1	65	115–116	Absolute ethanol	($CDCl_3$) 8.0–8.2 (doublet, 2 H, J = 8 Hz, phenyl) and 7.4–7.6 (multiplet, 3 H, phenyl), 4.2–4.6 (octet, 2 H, J = 4 Hz, CH_2O), 3.1–3.4 (multiplet, 1 H, CHN), 2.5–3.0 (multiplet, 4 H, CH_2N), 2.2–2.3 (doublet, 2 H, J = 8 Hz, CH_2Hg), 1.4–1.8 (multiplet, 6 H, CH_2)	(KBr) 2900 (CH), 1680 (C=O) 1260 (CO), 1120, 1030, 970, 710	Calcd for $C_{15}H_{20}NO_2HgCl$: C, 37.42; H, 4.16; N, 2.90; Cl, 7.40. Found: C, 37.37; H, 4.25; N, 2.80; Cl, 7.60.
Morpholine		9	45	104	Absolute ethanol	($CDCl_3$) 8.0–8.2 (doublet, 2 H, J = 8 Hz, phenyl) and 7.4–7.6 (multiplet, 3 H, phenyl), 4.2–4.6 (octet, 2 H, J = 4 Hz, CH_2O), 3.6–3.9 (triplet, 4 H, J = 4 Hz, CH_2O), 3.1–3.4 (multiplet, 1 H, CHN), 2.6–2.9 (quartet, 4 H, J = 4 Hz, CH_2N), 2.2–2.3 (doublet, 2 H, J = 8 Hz, CH_2Hg)	(KBr) 2940 (CH), 2840 (CH), 1700 (C=O), 1440, 1250 (C–O), 1110, 850, 710	Calcd for $C_{14}H_{18}NO_3HgCl$: C, 34.78; H, 3.72; N, 2.90; Hg, 41.40; Cl, 7.24. Found: C, 34.56; H, 3.75; N, 2.84; Hg, 41.21; Cl, 7.28.
Hexamethyleneimine		10	26	108	Absolute ethanol	($CDCl_3$) 7.9–8.1 (doublet, 2 H, J = 8 Hz, phenyl), 7.4–7.6 (multiplet, 3 H, phenyl), 4.1–4.6 (octet, 2 H, J = 8 Hz, CH_2O), 3.1–3.4 (multiplet, 1 H, CHN), 2.7–3.0 (multiplet, 4 H, CH_2N), 2.2–2.4 (doublet, 2 H, J = 8 Hz, CH_2Hg), 1.5–1.8 (multiplet, 8 H, CH_2)	(KBr) 2920 (CH), 1700 (C=O), 1450, 1280 (CO), 1130, 1070, 1030, 710	Calcd for $C_{16}H_{22}NO_2HgCl$: C, 38.78; H, 4.44; N, 2.82; Hg, 40.40; Cl, 7.07. Found: C, 38.69; H, 4.30; N, 2.70; Hg, 40.10; Cl, 7.00.

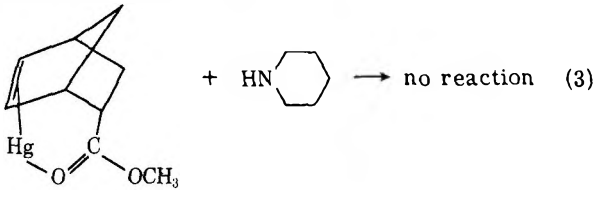
TABLE II
(*Continued*)

Amine	$HgCl_2$–allyl benzoate adduct	No.	Yield, %	Mp, °C	Recrystn solvent	Nmr, δ	Ir, cm^{-1}	Anal.
4-Methyl-piperidine		11	27	104	Absolute ethanol	($CDCl_3$) 8.0–8.2 (doublet, 2 H, J = 8 Hz, phenyl) and 7.3–7.6 (multiplet, 3 H, phenyl), 4.2–4.6 (octet, 2 H, J = 4 Hz, CH_2O), 3.2–3.4 (multiplet, 1 H, CHN), 2.2–2.4 (doublet, 2 H, J = 8 Hz, CH_2-Hg), 1.1–1.8 (multiplet, 5 H, CH_2CH), 0.8–1.0 (doublet, 3 H, J = 6 Hz, CH_3)	(KBr) 2900 (CH), 1700 (C=O), 1430, 1250 (CO), 1080, 710	Calcd for $C_{16}H_{22}NO_2HgCl$: C, 38.78; H, 4.44; N, 2.82; Hg, 40.40; Cl, 7.07. Found: C, 39.38; H, 4.60; N, 2.87; Hg, 41.25; Cl, 7.08.
2-Methyl-piperidine		12	6	127	Absolute ethanol	($CDCl_3$) 8.0–8.1 (doublet, 2 H, J = 8 Hz, phenyl) and 7.3–7.6 (multiplet, 3 H, phenyl), 4.1–4.6 (octet, 2 H, J = 4 Hz, CH_2O), 2.8–3.1 (multiplet, 1 H, CHN), 2.3–2.5 (doublet, 2 H, J = 8 Hz, CH_2-Hg), 1.4–1.9 (multiplet, 6 H, CH_2), 1.2–1.3 (doublet, 3 H, J = 5 Hz, CH_3)	(KBr) 2950 and 2920 (CH), 1710 (C=O), 1450, 1270 (C—O), 1170, 1120, 710	Calcd for $C_{16}H_{22}NO_2HgCl$: C, 38.78; H, 4.44; N, 2.82; Hg, 40.40; Cl, 7.07. Found: C, 38.55; H, 4.47; N, 2.76; Hg, 40.10; Cl, 6.82.

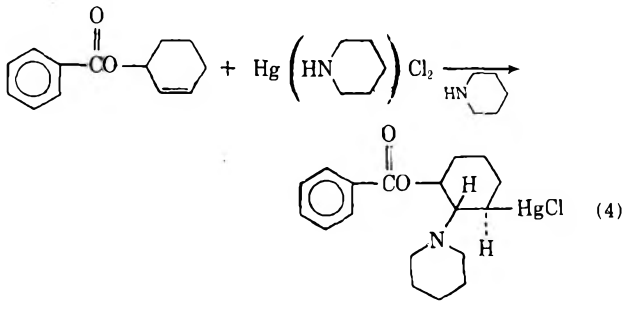
[a] Amines which gave no addition products under these conditions were pyrrolidine, 4-methylpiperazine, 3-methylpiperidine, heptamethyleneimine, and diethylamine.

allyl benzoates (–OH, $-OCH_3$) formed addition products whereas allyl *p*-nitrobenzoate failed to react.

No additions were observed in the allylcarbinyl benzoate system (eight-membered ring), the 4-pentenyl acetate system (nine-membered ring), or in the methyl vinyl acetate system (six-membered ring). Compounds with very rigid structures, such as the bicyclo[2.2.1]-5-heptenes, failed to yield addition products even though they would conform to a seven-membered ring intermediate (eq 3).



The stereochemistry of the addition can be observed in the case of the product **6** from 3-cyclohexen-1-yl benzoate. The large coupling constant for axial protons (J = 10 cps) in the nmr indicates that the $-NR_2$ and –HgCl groups are trans to each other (eq 4). This



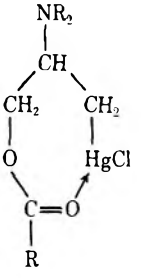
is in agreement with what is observed in oxymercuration (trans addition) in the cases of nonsterically hindered olefins.[1-3]

The infrared carbonyl absorption frequencies of the aminomercuration products were shifted to lower frequencies (Table III). This indicates a weakening of

TABLE III

Compd	Normal, cm^{-1}	Aminomercuration product, cm^{-1}	$\Delta_{C=O}$, cm^{-1}
Aryl esters	1750–1735	1710–1680	~50
Urea	~1660	1600	~60
Urethane	1740–1690	1650	~40

the carbonyl bond, perhaps by coordination to the chloromercuri substituent.

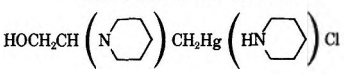
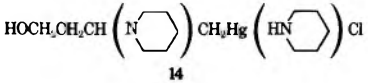
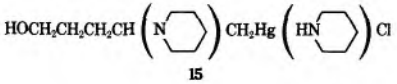
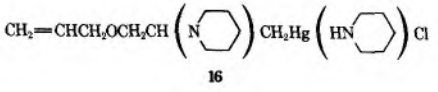
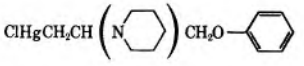


This would be one explanation for the observed magnetic nonequivalence of the two hydrogens adjacent to oxygen.[10] Alternatively, this nonequivalence could be ascribed to the presence of the adjacent asymmetric carbon carrying the amino group.

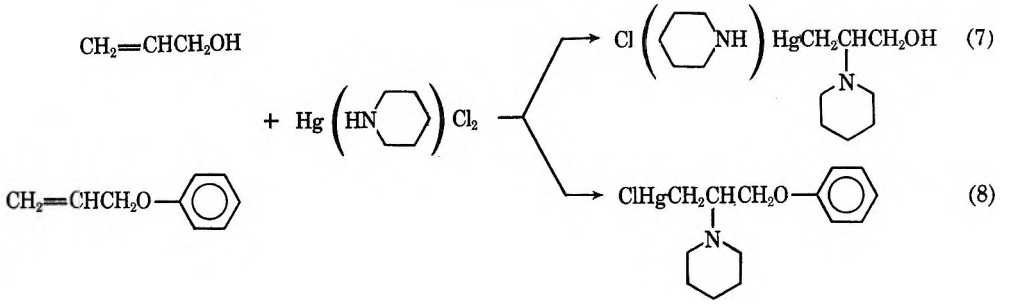
(10) We are indebted to Dr. G. Noren for pointing this out.

TABLE IV

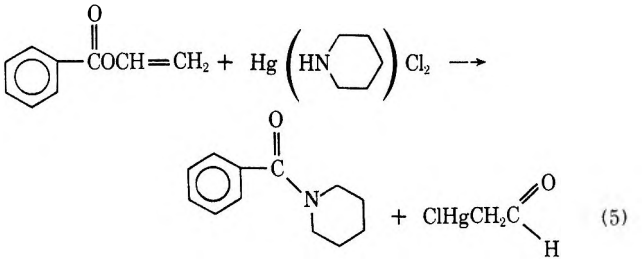
AMINOMERCURATION ADDUCTS FROM OLEFINIC ALCOHOLS AND ETHERS WITH PIPERIDINE

Olefin	$HgCl_2$–piperidine adducts	No.	Yield, %	Mp, °C	Recrystn solvent	Nmr, δ	Ir, cm^{-1}	Anal.
Allyl alcohol		13	74	67–68		($CDCl_3$) 4.5 (singlet, 2H, NH, OH), 3.4–3.6 (doublet, 2 H, J = 8 Hz, CH_2O), 2.9–3.3 (multiplet, 4 H, CH_2NHg), 2.5–2.7 (multiplet, 4 H, CH_2N), 1.9–2.1 (doublet, 2 H, J = 8 Hz, CH_2Hg), 1.4–1.9 (multiplet, 12 H, CH_2)	(KBr) 3300 (NH, OH), 2920 (CH), 1410, 1110, 1095, 1025 (CO), 860, 760, 735	Calcd for $C_{13}H_{27}N_2OHgCl$: C, 33.76; H, 5.84; N, 6.06; Hg, 43.29; Cl, 7.57. Found: C, 33.76; H, 5.92; N, 6.07; Hg, 42.90; Cl, 7.44.
3-Buten-1-ol	 14	14	53	68		($CDCl_3$) 5.3 (singlet, 2 H, NH and OH), 3.6–3.9 (multiplet, 2 H, CH_2O), 2.9–3.2 (multiplet, 5 H, CH_2NH and CHN), 2.5–2.8 (multiplet, 4 H, CH_2N), 1.9–2.1 (doublet, 2 H, J = 8 Hz, CH_2Hg), 1.4–1.8 (multiplet, 14 H, CH_2)	(KBr) 3160 (OH), 2900 (CH), 1445, 1110, 1090, 1040, 950, 880, 870	Calcd for $C_{14}H_{29}N_2OHgCl$: C, 35.29; H, 6.09; N, 5.88; Hg, 42.01; Cl, 7.35. Found: C, 35.04, H, 6.16; N, 5.62; Hg, 41.77; Cl, 7.30.
4-Penten-1-ol	 15	15	88	Oil		($CDCl_3$) 5.1 (singlet, 2 H, NH and OH), 3.6–3.7 (multiplet, 2 H, CH_2O), 3.0–3.3 (multiplet, 5 H, CH_2NHg and CHN), 2.6–2.8 (multiplet, 4 H, CH_2N), 2.1–2.3 (doublet, 2 H, J = 8 Hz, CH_2Hg), 1.5–1.9 (multiplet, 16 H, CH_2)	(neat) 3400–3200 (OH, NH), 2950 (CH), 1650 (CN), 1480, 1100, 1050 (CO), 870, 810, 750	
Diallyl ether	 16	16	40	Oil		($CDCl_3$) 5.6–5.9 (multiplet, 1 H, CH=), 5.4 (singlet, 1 H, NH), 5.0–5.3 (doublet, 2 H, J = 12 Hz, CH_2=), 3.8–4.0 (doublet, 2 H, J = 6 Hz, CH_2O), 3.3–3.7 (octet, 2 H, J = 4 Hz, CH_2O), 2.7–3.1 (multiplet, 4 H, CH_2NH), 2.3–2.7 (multiplet, 4 H, CH_2N), 1.9–2.1 (doublet, 2 H, J = 8 Hz, CH_2Hg), 1.3–1.8 (multiplet, 12 H, CH_2)	(neat) 3030 (CH=), 2910 (CH), 1645 (C=C), 1450, 1110, 1000, 930, 870, 760	
Allyl phenyl ether		17	46	75	Absolute ethanol	($CDCl_3$) 6.8–7.4 (multiplet, 5 H, phenyl), 3.7–4.3 (octet, 2 H, J = 4 Hz, CH_2O), 2.9–3.3 (multiplet 1 H, CHN), 2.5–2.7 (multiplet, 4 H, CH_2N), 2.1–2.2 (doublet, 2 H, J = 8 Hz, CH_2Hg), 1.4–1.7 (multiplet, 6 H, CH_2)	(KBr) 3050, 2910 (CH), 1580, 1490, 1460, 1240 (CO), 1170, 1100, 1040, 885, 755, 690	Calcd for $C_{14}H_{20}NOHgCl$: C, 37.08; H, 4.41; N, 3.09; Hg, 44.15; Cl, 7.72. Found: C, 36.89; H, 4.48; N, 2.90; Hg, 43.85; Cl, 7.36.

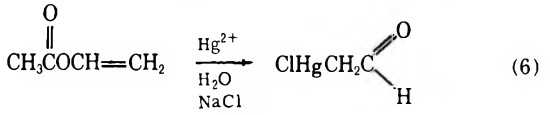
SCHEME I



Vinyl Esters.—Vinyl benzoate and vinyl acetate undergo an aminolysis–oxidation reaction under the aminomercuration conditions to produce *N*-benzoylpiperidine and chloromercuriacetaldehyde (eq 5).



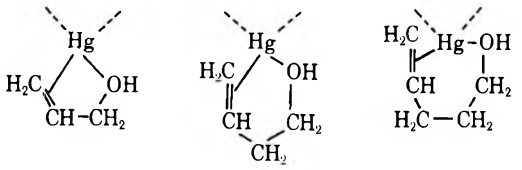
This is in agreement with the work of Nesmeyanov, *et al.*,[11] who found that vinyl acetate yielded chloromercuriacetaldehyde under oxymercuration conditions (eq 6). It is not necessary, however, for carbonyl coordination to occur in these examples since vinyl ethers also produce chloromercuriacetaldehyde.[11]



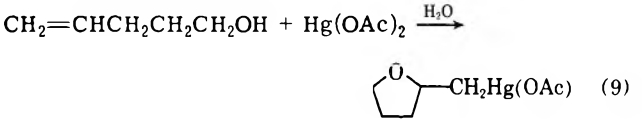
Allylic Alcohols and Ethers.—We also found that unsaturated alcohols and ethers will undergo the aminomercuration reaction (Scheme I). The olefinic compounds listed in Table IV were found to yield addition products. In some cases, the addition product could only be obtained crystalline from the piperidine solvent and a molecule of the amine was found in the mercuric ion coordination sphere (eq 7).

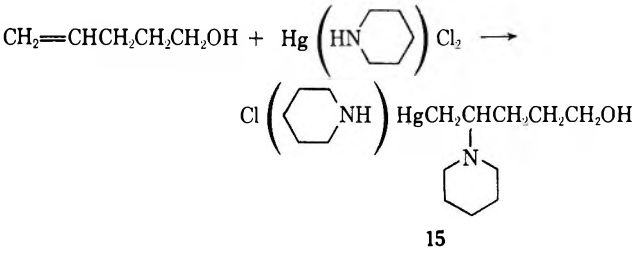
(It is interesting to note that the addition product obtained from allyl alcohol was identical with that obtained from allyl acetate. This indicates that aminolysis is a competing reaction in the case of allyl esters.)

The saturated alcohol systems appear to be much more flexible than the carbonyl-containing olefins in that the geometry requirements are less stringent. Allyl alcohol, 3-buten-1-ol, and 4-penten-1-ol, which could form intermediates consisting of five-, six-, and seven-membered rings, were all found to give addition products.



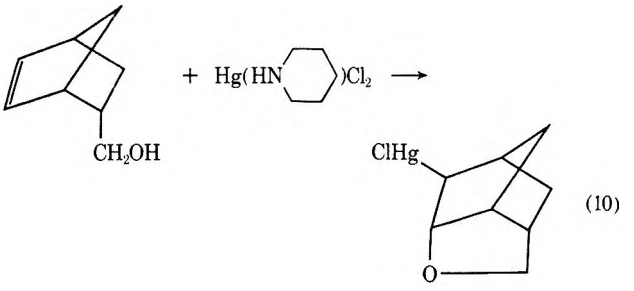
In the oxymercuration of 4-penten-1-ol, the hydroxyl group in the substrate is able to participate in the reaction and a tetrahydrofuran derivative is formed[12] (eq 9). This reaction does not compete under aminomercuration conditions since only an aminomercurial product is observed.





15

Bicyclo[2.2.1]-5-hepten-2-methanol,[11] however, undergoes internal oxymercuration even in the presence of an amine solvent to produce the known tricyclic ether (eq 10).



Conclusion

Aminomercuration is not so general a reaction as oxymercuration. However, aminomercuration reactions can be carried out with olefins which possess internal coordinating groups. The effects of structural changes in both the olefin and the amine have been explored.

Experimental Section

All melting points are uncorrected. Nuclear magnetic resonance spectra were taken on Varian HA-100 and T-60 spec-

(11) A. Nesmeyanov, I. Lutsenko, and R. Tumanova, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 601 (1949).

(12) M. Lora-Tamayo, F. Martín-Panizo, and F. Bonnet, *An. Real Soc. Espan. Fis. Quím, Ser. B*, **51**, 711 (1955); *Chem. Abstr.*, **50**, 11246 (1956).

TABLE V
ADDUCTS OF AMINES WITH MERCURIC CHLORIDE

Registry no.	1:1 Complex $HgCl_2$–Amine	Mp, °C	Anal, % Calcd C	H	N	Hg	Cl	Found C	H	N	Hg	Cl
34805-71-5	Piperidine	142	16.85	3.09	3.93	56.52	20.00			3.77	55.92	19.74
34805-72-6	4-Pipecoline	159	19.64	3.51	3.78	54.05	19.19	19.42	3.53	3.74	54.24	18.87
34805-73-7	3-Pipecoline	149	19.64	3.51	3.78	54.05	19.19	19.75	3.56	3.88	54.27	18.95
34805-74-8	2-Pipecoline	106	19.64	3.51	3.78	54.05	19.19	19.07	3.44	3.76	54.41	18.92
34805-75-9	Hexamethyleneimine	141										
34805-76-0	Ethylamine	179	7.94	2.21	4.43	63.29	22.46	7.70	2.12	4.62	64.30	20.56
34805-77-1	Morpholine	151	13.40	2.51	3.91	55.86	19.83	13.26	2.44	3.93	55.93	19.57

trometers. Infrared spectra were taken on Perkin-Elmer 337 and Infracord spectrometers. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn.

A typical preparation of a amine–mercuric chloride complex was as follows.

Mercuric Chloride–Piperidine Complex.—To a solution of 8.1 g (0.03 mol) of mercuric chloride in 120 ml of hot water was added a solution of 2.5 g (0.03 mol) of piperidine (Aldrich) in 10 ml of water while stirring vigorously with a magnetic stir bar. A yellow precipitate separated out of solution immediately. The precipitate was filtered, washed with water, and air dried overnight. The light yellow solid (10.2 g, 100%) melted at 142–143°.

Other 1:1 mercuric chloride–amine complexes were formed in an analogous manner and are summarized in Table V. A typical aminomercuration reaction was as follows.

3-Chloromercuric-2-piperidinopropyl Benzoate (1).—To a solution of 5.0 g (0.030 mol) of allyl benzoate (K & K Laboratories) in 35 ml of piperidine (Aldrich) was added 6.0 g (0.016, mol) of mercuric chloride–piperidine complex. The suspension was stirred with a magnetic stir bar. After 1 hr, the solution was homogeneous, and after 36 hr, piperidine hydrochloride began to precipitate from the solution. Stirring was continued for another 36 hr. The solution was filtered and the excess piperidine was removed with the aid of a vacuum pump. The resulting yellow oil was dissolved in absolute ethanol and allowed to crystallize. The product was filtered, yielding 5.0 g (65%), mp 115–116°.

Esters.—Methyl allylacetate, bp 120–122° (lit.[12] bp 125–126°), was prepared by reaction of allylacetyl chloride with methanol. 2-Cyclohexen-1-ol benzoate was prepared from 2-cyclohexen-1-ol (Aldrich) and benzoyl chloride in pyridine, bp 97° (0.2 mm) [lit.[13] bp 160–165° (15 mm)]. *endo*-Bicyclo[2.2.1]hepten-2-yl benzoate was prepared from the reaction of cyclopentadiene with vinyl benzoate for 20 hr at 200° (autoclave), bp 98° (0.2 mm).

Anal. Calcd for $C_{14}H_{14}O_2$: C, 78.50; H, 6.54; O, 14.95. Found: C, 78.62; H, 6.69; O, 15.66.

(13) Koetz and Richter, *J. Prakt. Chem.*, [2] **111**, 385.

4-Chloromercuri-6-oxatricyclo[3.2.1.2^{3,8}]nonane.—To a solution of 3.0 g (0.024 mol) of *endo*-bicyclo[2.2.1]-5-hepten-2-methanol (K & K Laboratories) in 40 ml of piperidine was added 6.0 g (0.016 mol) of mercuric chloride–piperidine complex. The solution was stirred with the aid of a magnetic stir bar for 4 days. Piperidine hydrochloride was filtered from the reaction mixture and the filtrate was evaporated to an oil with the aid of a vacuum pump. The resulting oil was dissolved in absolute alcohol, and ether was added until cloudy. After standing overnight, the crystals were filtered, yielding 4.2 g (60%) of product: mp 205° (lit.[14] mp 227° from benzene–petroleum ether); nmr spectrum (DMSO-d_6) 4.6–4.7 (doublet, 1 H, J = 4 Hz, CHO), 3.4–3.6 (multiplet, 2 H, CH_2O), 3.2–3.3 (multiplet, 1 H, CH bridgehead), 3.0–3.1 (multiplet, 1 H, CH bridgehead), 2.2–2.4 (multiplet, 2 H, 9-CH and 1-CH), 2.0–2.1 (multiplet, 1 H, CHHg), 1.4–1.7 (quartet, 2 H, J = 12 Hz, 2-CH_2), 0.9–1.1 ppm (doublet, 1 H, J = 12 Hz, 9-CH); ir spectrum (KBr) 2950, 2900, 2850 (CH), 1295, 1240, 1140, 1050, 1030, 1015, 950, 900 cm^{-1}.

Anal. Calcd for $C_8H_{11}OHgCl$: C, 26.88; H, 3.07; Hg, 55.86; Cl, 9.93. Found: C, 26.80; H, 3.45; Hg, 55.05; Cl, 10.10.

Registry No.—**1**, 34792-29-5; **2**, 34792-30-8; **3**, 34805-78-2; **4**, 34805-79-3; **5**, 34805-80-6; **6**, 34805-81-7; **7**, 34805-82-8; **8**, 34805-83-9; **9**, 34805-84-0; **10**, 34805-85-1; **11**, 34805-86-2; **12**, 34805-87-3; **14**, 34805-88-4; **15**, 34805-89-5; **16**, 34805-90-8; **17**, 34805-91-9; *endo*-bicyclo[2.2.1]hepten-2-yl benzoate, 34805-92-0; 4-chloromercuri-6-oxatricyclo[3.2.1.2^{3,8}]-nonane, 34805-93-1.

Acknowledgment.—We wish to thank the National Science Foundation and the Hercules Company for the support of this work.

(14) H. Henbest and B. Nicholls, *J. Chem. Soc.*, 227 (1959). We have no explanation for this discrepancy in melting points.

π and σ Interactions of Electron-Deficient Aromatics with Amines. Addition to the Ring and to a Ring Substituent

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Received March 24, 1972

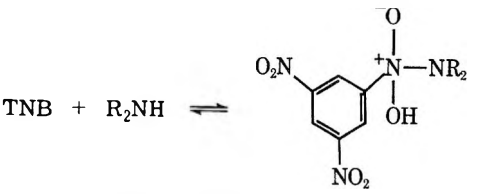
The addition of phenylhydrazine to the ring and to a nitro group in 1,3,5-trinitrobenzene has been observed. Only addition to the nitro group occurs with 2,4,6-trinitrotoluene. This is the first confirmed observation of concurrent substituent and ring addition, and confirms earlier proposals. The nature of the interactions is discussed.

Reactions of electron-deficient aromatics with amines have been of interest for a number of years, and a variety of different types of interactions have been identified.[1-12] With aromatic amines, the most commonly observed product is a donor–acceptor or π complex.[1,2] There is some evidence in one instance for formation of an aromatic amine σ complex, but it was not isolated.[13] Tertiary aliphatic amines also form donor acceptor complexes with electron-deficient aromatics if the solvent in which the precursors are mixed is aprotic.[4,7] With primary and secondary amines, there is substantial evidence for addition to the aromatic ring, resulting in stable covalently bonded σ complexes.[7,13] In addition to these more commonly observed interactions, anion radicals and aromatic anions have been proposed to arise from the reaction of amines and 1,3,5-trinitrobenzene.[11,12] A proposal of amine addition to a nitro group in this latter aromatic has recently been published.[6]

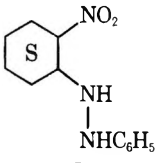
We report here a study of the reaction of 1,3,5-trinitrobenzene (TNB) and 2,4,6-trinitrotoluene (TNT) with phenylhydrazine. This latter amine is of interest for several reasons. It possesses both aromatic and aliphatic amine character, and was expected to easily form both π and σ complexes. In addition, attack of phenylhydrazine on a nitro group in TNB or TNT could lead to isolable triazene oxides or diazohydroxyamino compounds. Similar reactions occur upon addition of phenylhydrazine to nitrosobenzenes,[14] and the reducing action of phenylhydrazines on aromatic nitro compounds to yield anilines[15] suggests that a similar addition might occur to the nitro group.

$$ArNO + ArNHNH_2 \longrightarrow ArN^{+}(O^{-})-NHNAr \rightleftharpoons ArNN(OH)=NAr$$

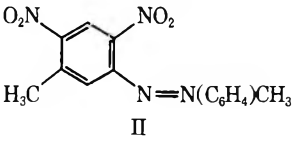
In fact, an oxyhydroxylamine intermediate was recently proposed to result from the interaction of TNB and amines, but the product was quite unstable and could not be isolated.[6]



It has been reported that phenylhydrazine adds to 1-nitrocyclohexene to give the adduct I,[16] and that *p*-methylphenylhydrazine displaces a nitro group in 2,4,6-trinitrotoluene to give the rearranged substitution product II.[17] A mixture of trinitrobenzene and phenylhydrazine was reported to yield a 1:1 adduct,[18] but the nature of this interaction is unclear as the authors did not state which isomer of trinitrobenzene was used.



I



II

It is well known that ortho dinitro substituted benzenes are prone to lose NO_2^- when attacked by nucleophiles[19-21] whereas polynitrobenzenes without ortho nitro groups can form reasonably stable charge transfer or σ complexes under similar conditions.[5]

Addition of 0.02 equiv (2.2 g) of phenylhydrazine in 50 ml of benzene to 0.01 equiv (2.1 g) of TNB in 100 ml of benzene produces a yellow solution which absorbs strongly below 400 mμ. This absorption develops instantaneously and probably results from a charge transfer interaction as depicted in III.[22] It is difficult to determine λ_{max} as absorptions from uncomplexed phenylhydrazine and *sym*-trinitrobenzene overlap the charge transfer band.[23] Upon standing 3 days

(1) R. Foster, "Organic Charge Transfer Complexes," Academic Press, New York, N. Y., 1969.

(2) L. J. Andrews and R. M. Keefer, "Molecular Complexes in Organic Chemistry," Holden-Day, San Francisco, Calif., 1964.

(3) E. Buncel, A. R. Norris, and K. E. Russell, *Quart. Rev. Chem. Soc.*, **22**, 123 (1968).

(4) M. J. Strauss, *Chem. Rev.*, **667**, 70 (1970).

(5) R. Foster and C. A. Fyfe, *Rev. Pure Appl. Chem.*, **16**, 61 (1966).

(6) C. F. Bernasconi, *J. Amer. Chem. Soc.*, **92**, 129 (1970).

(7) M. R. Crampton and V. Gold, *J. Chem. Soc., B*, 23 (1967).

(8) K. L. Servis, *J. Amer. Chem. Soc.*, **89**, 1508 (1967).

(9) G. Briegleb, W. Liptay, and M. Canter, *Z. Phys. Chem. (Frankfurt am Main)*, **26**, 55 (1960).

(10) G. N. Lewis and G. T. Seaburg, *J. Amer. Chem. Soc.*, **62**, 2122 (1940).

(11) R. E. Miller and W. F. K. Wynne Jones, *Nature (London)*, **186**, 149 (1960).

(12) V. Balish and V. R. Krishnan, *Recl. Trav. Chim. Pays-Bas*, **78**, 783 (1959).

(13) E. Buncel and J. Webb, *Can. J. Chem.*, **50**, 129 (1972).

(14) Bamberger and Billeter, *Helv. Chim. Acta*, **14**, 219 (1931).

(15) L. Fieser and M. Fieser, "Reagents for Organic Synthesis," Wiley, New York, N. Y., 1967.

(16) A. V. Topchiev and E. L. Fantalova, *Dokl. Akad. Nauk SSSR*, **132**, 628 (1960).

(17) M. Giva and A. Angeletti, *Gazz. Chim. Ital.*, **51**, 318 (1921).

(18) K. A. Hoffmann and H. Kirmrenther, *Ber.*, **43**, 1746 (1910).

(19) A. Holleman and F. v. Haeften, *Recl. Trav. Chim. Pays-Bas*, **40**, 67–98 (1921).

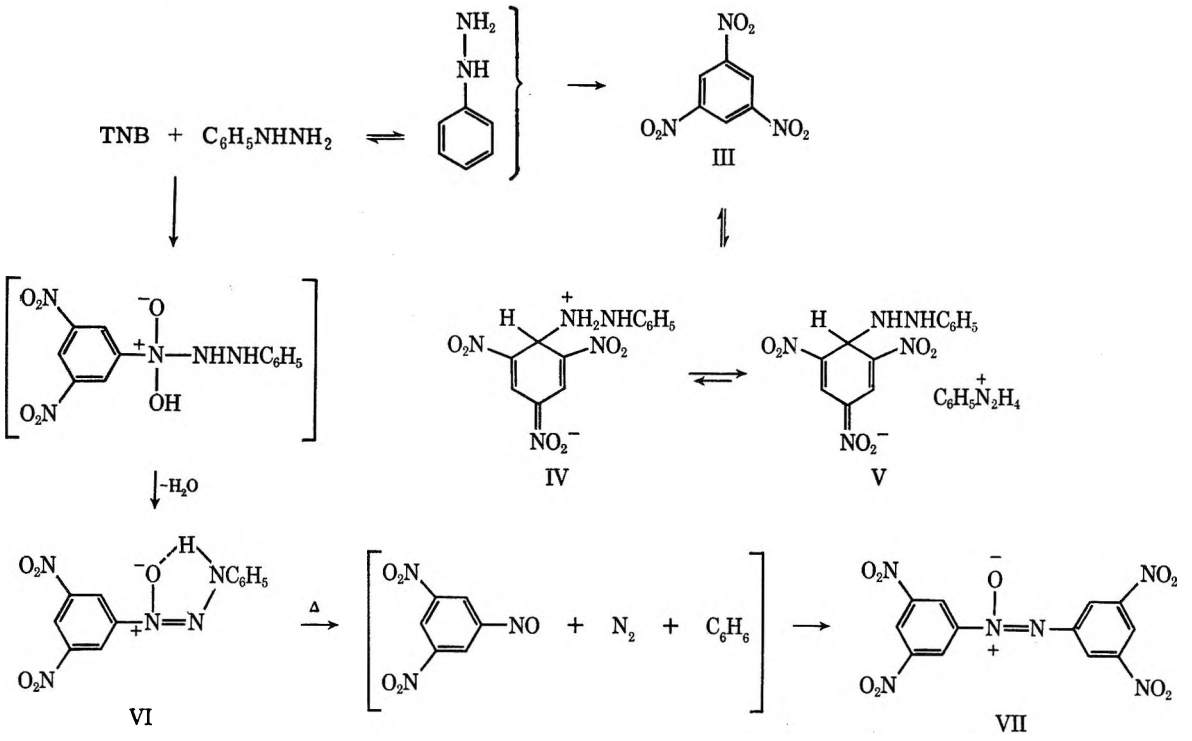
(20) R. E. Parker and T. O. Read, *J. Chem. Soc.*, 3149 (1962).

(21) D. C. Morrison, *J. Org. Chem.*, **27**, 296 (1962).

(22) The type of coordination (*n* donation or π donation) is not specified.

(23) Charge transfer bands arising from solvent interaction with both *sym*-trinitrobenzene and phenylhydrazine may also obscure the absorption of interest. Since alkoxide forms to some extent in alcoholic solutions of phenylhydrazine and since halogenated hydrocarbons react with amines, these other solvents were excluded. Hydrocarbons and ethers did not dissolve sufficient *sym*-trinitrobenzene for the subsequent reactions to occur.

SCHEME I



the solution turns red and a small quantity of purple crystals (<0.2 g) forms on the bottom of the reaction flask. These melt at 109–111° and observation of this material with a Bausch and Lomb stereomicroscope for 6 hr showed decomposition occurring at room temperature. The nmr spectrum in DMSO-d_6 (Figure 1) and the two absorption maxima in methanol at 462 and 561 mμ are consistent with a σ complex salt like V. A σ complex in which nitrogen adjacent to the ring in the phenylhydrazine moiety is bonded to the cyclohexadienide ring is not precluded by the data presented here. However, aniline forms a π complex with *sym*-trinitrobenzene,[24] presumably because the nonbonding pair on nitrogen is delocalized into the aromatic ring and is not available for covalent bond formation. Similar considerations in the system under investigation here lead us to conclude that the σ complex between *sym*-trinitrobenzene and phenylhydrazine is best represented as V (Scheme I).

The nmr spectrum (Figure 1) deserves comment. The cyclohexadienide protons appear as a singlet at δ 8.3 (2 H) and the tertiary ring proton as a singlet at δ 5.5 (1 H). This latter absorption is not split as the adjacent NH proton is rapidly exchanged. The aromatic protons of both phenyl rings (in the cation and anion) appear as a multiplet from δ 7.4 to δ 6.4 and the NH protons as a broad absorption centered at δ 4.7. Both these absorptions integrate to slightly more than the expected relative area (10 H and 6 H, respectively) owing to slow decomposition to starting materials and other products (*vide infra*).

Formation of V might proceed through a preliminary equilibrium between the charge transfer complex III and the zwitterionic structure IV (Scheme I). Abstraction of an NH^+ proton in IV by phenylhydrazine would yield V. Similar processes, in which zwitterionic σ complexes of primary or secondary amines and

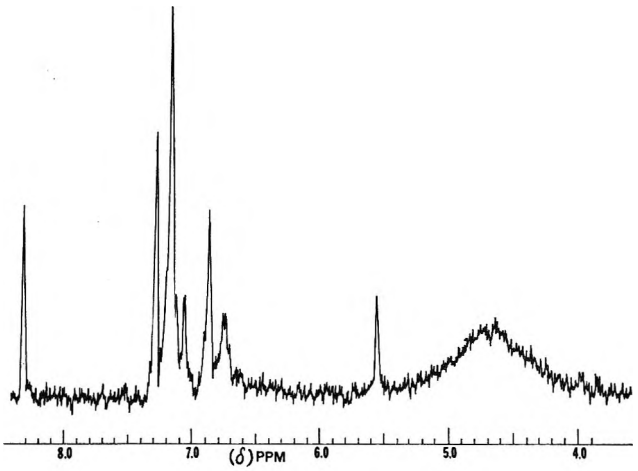


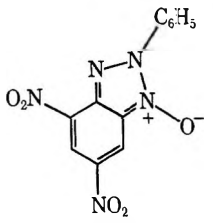
Figure 1.

sym-trinitrobenzene are converted to σ complex salts, are known to occur.[13]

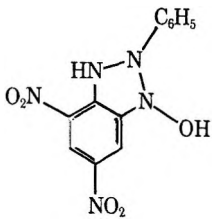
When the reaction solution is allowed to stand for extended periods of time (about 2 weeks), yellow needles of another product precipitate. This material violently decomposes at 139.5° with extensive gaseous evolution, and analyzes correctly for $C_{12}H_9N_5O_5$ (see Experimental Section). The infrared spectrum (KBr) shows N—O (N=O) absorptions at 1530, 1505, and 1337 cm^{-1}. The nmr spectrum (DMSO-d_6) was poorly resolved and consisted of two aromatic absorptions and a broad absorption for NH (see Experimental Section). The compound is extremely unstable in a variety of common nmr solvents (DMSO, DMF, pyridine-d_5, etc). It reacts violently with DMSO on warming and explodes when rapidly heated. It is insoluble in, and unreactive toward, sulfuric acid (6 *N*), but is very sensitive to base, yielding red solutions which turn black upon standing. We initially supposed that the yellow product might have arisen by cyclization–

(24) S. D. Ross and M. M. Labes, *J. Amer. Chem. Soc.*, **79**, 76 (1957).

dehydration of V to yield a 5,7-dinitrobenzotriazole derivative, VIII, but such benzotriazoles, including VIIIa which we prepared by a published method,[25] are not temperature sensitive and do not decompose



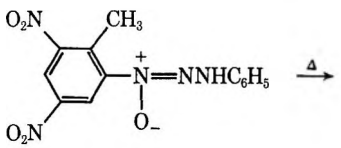
VIIIa



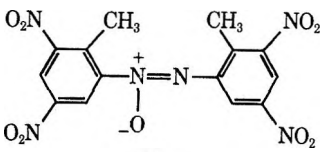
VIIIb

in solution. In addition, their infrared spectra are markedly different from that of the yellow product formed from phenylhydrazine and TNB. The thermal instability of this latter material is similar to that of triazene oxides,[26] and suggests that the structure could be VI. Aromatic triazenes readily liberate nitrogen on heating.[26] In the case of VI, benzene and 3,5-dinitronitrosobenzene might then be formed. This latter aromatic has never been isolated, as its readily formed dimer is rapidly converted to 3,3′,5,5′-tetranitroazoxybenzene,[27] VII. In fact, boiling a benzene solution of TNB–phenylhydrazine condensation product for 12 hr gives a high yield of VII (see Experimental Section). In addition, when the decomposition is carried out in dioxane, benzene can be distilled from the reaction solution. These results, coupled with the elemental analysis, chemical properties, and infrared and pmr spectra, are substantial evidence for structure VI.

The reaction of TNT with phenylhydrazine results in a compound analogous to IX, which analyzes correctly for $C_{13}H_{12}N_5O_5$ and explodes at 143.5°. In this case, there is no evidence at all for σ complex formation. The visible spectrum of the reaction solution immediately after mixing, and during the reaction, shows no double maximum characteristic of the 2,4,6-trinitrocyclohexadienate function. Instead, a spectrum similar to that of VI is observed. Although anionic σ complexes are formed from TNT and a variety of organic bases, they are considerably less stable than those formed from TNB.[4] The product of phenylhydrazine addition to TNT is thus IX. Addition to the nitro group ortho to methyl is confirmed by the pmr spectrum of IX. This compound is more



IX



X

soluble and stable in common nmr solvents than VI (see Experimental Section). Thermal decomposition of IX gives good yields of X.

The formation of V and VI by attack of phenylhydrazine on TNB is the first confirmed observation of concurrent nitro group and ring attack on this electron deficient aromatic, and supports Bernasconi's earlier proposals.[6] It is clear that ring substitution strongly affects the mode of reaction, since only addition to a nitro group is observed with TNT and phenylhydrazine. With other organic bases, ring addition to TNT becomes predominant however.[4,28]

Addition to the nitro group is a further type of interaction, besides charge transfer and σ complexation, radical ion formation, and proton transfers, which is likely to occur when electron-deficient aromatics are treated with base. Many such addition products probably revert rapidly back to starting materials,[6] and thus are difficult to detect. Phenylhydrazine may be unique in that stable nitro group addition products cannot be isolated by treating alkyl hydrazines or alkyl amines with TNB.[4,28]

Experimental Section

All melting points are uncorrected. Ir and uv spectra were recorded with Perkin-Elmer Model 21 and Model 402 spectrophotometers, respectively. Pmr spectra were recorded with JEOL C-60HL and MH-100 spectrometers, and chemical shifts are reported with respect to internal tetramethylsilane.

Reaction of TNB and Phenylhydrazine.—Addition of phenylhydrazine (2.16 g, 0.02 mol) to a benzene solution of TNB (2.13 g, 0.01 mol, in 100 ml of solvent) resulted in a bright yellow solution. After 72 hr purple crystals of V (~0.2 g) were deposited on the bottom of the flask. After filtering and washing with ether, these melted at 109–111°. Slow decomposition at room temperature precluded a satisfactory elemental analysis. Spectra were taken on freshly washed and dried crystals: visible λ_{max} 452, 561 nm; nmr shown in Figure 1.

If V was not filtered from the initial reaction mixture, and the solution was allowed to stand for 10 days, a yellow precipitate formed. After filtration, a methanol wash, and recrystallization from benzene, yellow needles were obtained (~1.0 g) which exploded at 139.5° and analyzed correctly for VI. *Anal.* Calcd for $C_{12}H_9N_5O_5$: C, 47.54; H, 2.99; N, 23.09. Found: C, 47.58; H, 3.17; N, 22.96.

The nmr spectrum (DMSO-d_6), which was poorly resolved owing to decomposition, showed absorptions at δ 9.1 (~2.5 H, m), δ 7.4 (~5 H, s), and δ 3.5 (NH, br). The uv (MeOH) and ir (KBr) spectra showed absorptions at 217 and 388 nm and 1337, 1505, and 1530 cm^{-1}, respectively.

When a 10-equiv excess of phenylhydrazine was used, V could not be isolated, even though the reaction solution showed strong absorptions at 452 and 561 nm. A yellow precipitate of VI was formed within 6 hr. If the reaction was carried out in phenylhydrazine, VI precipitated within a few minutes (caution, exothermic).

Reaction of TNT and Phenylhydrazine.—When a 2-equiv excess of phenylhydrazine was added to a benzene solution of TNT, a yellow precipitate was formed after 12 hr. There was no evidence for formation of a σ complex, even immediately after mixing the reactants, as the visible spectrum of the solution showed no double maxima. Recrystallization of the yellow precipitate from benzene yielded yellow needles which exploded at 143.5°, and analyzed correctly for IX. *Anal.* Calcd for $C_{13}H_{11}N_5O_5$: C, 49.23; H, 3.49; N, 22.08. Found: C, 49.52, H, 3.53; N, 22.09.

The nmr spectrum (dioxane) showed absorptions at δ 8.1 (~1 H, s), δ 7.9 (~1 H, s), δ 6.7 (~5 H, m), and δ 2.5 (~3 H, s). This latter absorption could only be seen in DMSO-d_6. On the basis of the nonequivalence of the protons on the tetrasubstituted ring, the triazene oxide function has been assigned ortho to the

(25) S. Joshi and D. Deorha, *J. Indian Chem. Soc.*, **34**, 77 (1957).

(26) E. H. Rodd, "Chemistry of Carbon Compounds," Vol. IIIA, Elsevier, New York, N. Y., 1954, p 307.

(27) C. Moberg and O. Wennerstrom, *Acta Chem. Scand.*, **25**, 2355 (1971).

(28) M. J. Strauss and S. P. B. Taylor, unpublished work.

methyl group. The uv spectrum of IX (MeOH) showed maximum absorptions at 227 and 378 nm.

Thermal Decomposition of VI in Benzene.—When a suspension of VI (1.0 g) in benzene (200 ml) was refluxed for 48 hr, a clear yellow solution resulted. Concentration of this solution to 25 ml resulted in a white crystalline precipitate (0.25 g), which when recrystallized three times from a benzene–cyclohexane mixture yielded white needles of VII, mp 186°, lit.[27] mp 180–186°. The uv and pmr spectra of VII are identical with those previously reported.[29,30]

Thermal Decomposition of VI in Dioxane.—When a suspension of VI was refluxed in dioxane, a clear yellow solution was obtained. When this solution was distilled, the first 10-ml fraction had a uv spectrum identical with that of benzene in dioxane. When the reaction solution was further concentrated, VII was obtained.

Thermal Decomposition of IX in Benzene.—When a suspension of IX (1.4 g) in benzene (350 ml) was refluxed for 48 hr, a clear yellow solution resulted. Concentration of this solution to 25 ml resulted in a white powder which when recrystallized three times from a benzene–cyclohexane mixture yielded white needles, mp 211–212°, which analyzed correctly for X. *Anal.* Calcd for $C_{14}H_{10}N_6O_9$: C, 41.38; H, 2.47; N, 20.67. Found: C, 41.31; H, 2.41; N, 20.41.

The uv spectrum of X is almost identical with that of VII.[29] The former exhibits maxima (MeOH) at 243, 248, 254, 260, and 326 nm. The pmr spectrum ($CDCl_3$) showed absorptions at δ 8.8 (2 H, s), δ 8.7 (2 H, s), δ 2.65 (3 H, s), and δ 2.60 (3 H, s). The ir spectrum (KBr) showed absorptions at 1620, 1550, 1490, 1355, 908, 811, 725 cm^{-1}.

Registry No.—V, 35211-98-4; VI, 35211-99-5; IX, 35212-00-1; X, 35212-01-2; TNB, 99-35-4; TNT, 118-96-7; phenylhydrazine, 100-63-0.

Acknowledgments. This research was supported by the Army Research Office at Durham, Grant No. DAHCO4 69 C 0064, and the Research Corporation.

(29) P. H. Gore and O. H. Wheeler, *J. Amer. Chem. Soc.*, **78**, 2160 (1956).
(30) V. I. Steinberg and D. J. Holter, *J. Org. Chem.*, **29**, 3420 (1964).

Thermal Rearrangement of β-Nitro Nitrates to Dinitro Alcohols

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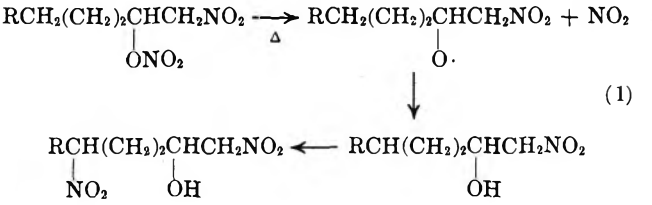
The decomposition of β-nitroalkyl nitrates in dilute hydrocarbon or halocarbon solution follows first-order kinetics (ΔH_a = 38–40 kcal mol^{-1}) to give dinitro or bromonitro alcohols derived from a 1,5 intramolecular hydrogen shift. For instance, 1-nitro-2-methyl-2-pentyl nitrate (**5**) rearranges at 130° in chlorobenzene to 1,5-dinitro-2-methyl-2-pentanol (**13**) in 86% yield; in refluxing $CBrCl_3$, **5** is converted to 1-nitro-5-bromo-2-methyl-2-pentanol (**13a**) in 72% yield. Products from a cyclohexyl β-nitro nitrate **19** indicate partial decay of the intermediate alkoxyl radical by β scission. The β-nitro nitrates are less thermally stable than are simple alkyl nitrates. Product structures were established by alternate syntheses or by base-catalyzed cleavage of β-nitro alcohols to the expected nitroalkane and carbonyl compound; *e.g.*, treatment of **13** with base yields 5-nitro-2-pentanone (**25**) and nitromethane. In addition to cleaving, bromonitro alcohols cyclized when treated with base; *e.g.*, **13a** gave a mixture of 5-bromo-2-pentanone (**32**), nitromethane, and the tetrahydrofuran **30**.

The low-pressure gas phase pyrolyses of ethyl,[1,2] *n*-propyl,[3,4] and *tert*-butyl[4] nitrates proceed by homolytic decomposition to give NO_2 and an alkoxyl radical intermediate. It has been established in these cases that the nitrate decomposition follows at least initial first-order kinetics, and, if the cleavage is made irreversible, first-order kinetics are obeyed over the entire decomposition range. These decompositions are difficult to study, however, because the intermediates undergo subsequent reactions to give a wide range of products. For instance, *tert*-butyl nitrate gives, besides nitrogen dioxide, *tert*-butyl nitrite, acetone, nitromethane, methyl nitrite, and nitric oxide.[4,5]

Our studies have shown that the complexity of nitrate decompositions may be markedly reduced if one chooses a vicinal nitro nitrate with a carbon chain of sufficient length to accommodate intramolecular hydrogen abstraction by the intermediate alkoxyl radical; molecules of this structure decompose at lower temperatures than do simple nitrates. Moreover, intramolecular abstraction by a 1,5 hydrogen shift appears to be the preferred reaction of the alkoxyl radicals so generated. Such a rearrangement (eq 1) appears to be a general



(1)

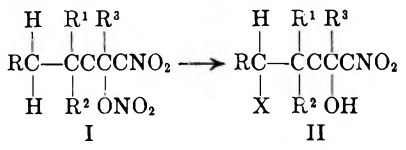
reaction of alkoxyl radicals having a hydrogen atom at the correct distance in the molecule.[6] In addition, such substituted nitrates, readily prepared from the reaction of nitrogen dioxide and oxygen with olefins,[7] allow the effect of the vicinal nitro group on homolytic cleavage to be evaluated.

Decomposition of β-Nitro Nitrates in Inert Solvents.—When β-nitro nitrates are heated neat or in concentrated solution, nitro olefins are major products.[8] Nitro olefin formation became insignificant, however, when dilute solutions of nitro nitrates were heated in inert solvents. Suitable inert solvents were chlorobenzene, *o*-dichlorobenzene, or Fluorolube.[10] Intra-

(1) J. B. Levy, *J. Amer. Chem. Soc.*, **76**, 3790 (1954); J. B. Levy, Navy Ordnance Report 2897, (1953).
(2) L. Phillips, *Nature (London)*, **160**, 753 (1947); **165**, 564 (1950).
(3) L. Phillips, Thesis, University of London, 1949.
(4) J. B. Levy and F. J. Adrian, Navy Ordnance Report 2608, Dec 22, 1952.
(5) R. Boschan, R. T. Merrow, and R. W. Van Dolah, *Chem. Rev.*, **55**, 485 (1955).
(6) R. S. Davidson, *Quart. Rev. Chem. Soc.*, **21**, 249 (1967); O. L. Chapman, *Advan. Photochem.*, **1**, 399 (1963); D. H. R. Barton, G. C. Ramsay, and D. Wege, *J. Chem. Soc. C*, 1915 (1967); K. Heusler and J. Kalvoda, *Angew. Chem., Int. Ed. Engl.*, **3**, 525 (1964).
(7) (a) D. R. Lachowicz and K. L. Kreuz, *J. Org. Chem.*, **32**, 3885 (1967). (b) D. R. Lachowicz, J. M. Larkin, and K. L. Kreuz, paper in preparation; D. R. Lachowicz and K. L. Kreuz, U. S. Patent 3,282,983 (Nov 1, 1966).
(8) *E.g.*, 1-nitro-2,4,4-trimethyl-2-pentyl nitrate (**1**), when heated neat at 138° for 1.5 hr, gives 1-nitro-2,4,4-trimethyl-1-pentene as the major product.[9]
(9) W. S. Pelton, Texaco Research Center, private communication.
(10) Fluorolube, grade S-30, Hooker Chemical Corp., is a perhalogenated alkane (with repeating $-CF_2CFCl-$ units) of 775 average mol wt.

molecular hydrogen abstraction occurred according to eq 1 above; nitrogen dioxide produced in the homolysis step apparently combined with the resultant alkyl radical to give the dinitro alcohol as the final product. 1-Nitro-2,4,4-trimethyl-2-pentyl nitrate (**1**), 1-nitro-2-pentyl nitrate (**2**), 1-nitro-2-hexyl nitrate (**3**), 1-nitro-4-methyl-2-pentyl nitrate (**4**), 1-nitro-2-methyl-2-pentyl nitrate (**5**), 1-nitro-4-acetoxy-2-hexyl nitrate (**6**), and 1-nitro-2-methyl-2-hexyl nitrate (**7**) all underwent smooth rearrangement to give the corresponding dinitro alcohols in moderate to good yields (see Table I).

TABLE I
CONVERSION OF NITRO NITRATES TO DINITRO AND BROMONITRO ALCOHOLS



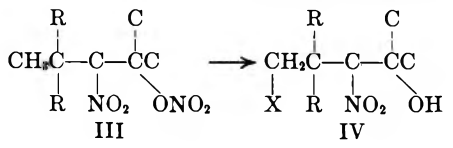
Nitro nitrate (I)	R	R¹	R²	R³	X	Product II	Yield, %
2	H	H	H	H	NO_2	10	80
3	CH_3	H	H	H	NO_2	11	72
4	H	CH_3	H	H	NO_2	12	83
5	H	H	H	CH_3	NO_2	13	86
5	H	H	H	CH_3	Br	13a	72
6	CH_3	OA_c	H	H	NO_2	14	58
7	CH_3	H	H	CH_3	NO_2	15	75
1	H	CH_3	CH_3	CH_3	NO_2	16	*a*
1	H	CH_3	CH_3	CH_3	Br	16a	74

[a] Yield could not be calculated because of a large amount of impurities.

It was necessary to heat the β-nitro *tert*-nitrates to above 100° and the β-nitro *sec*-nitrates to above 140° to effect rearrangement. Improved yields of dinitro alcohols could be realized from the β-nitro *sec*-nitrates by conducting the rearrangement at high temperatures for short periods of time (above 170° for less than 30 min). When heated for extended periods, even at lower temperatures, the dinitro alcohols themselves decomposed to give black resinous solids.

The rearrangement also occurred with the nitrate esters **8** and **9** (*cf.* Table II) where the vicinal nitro

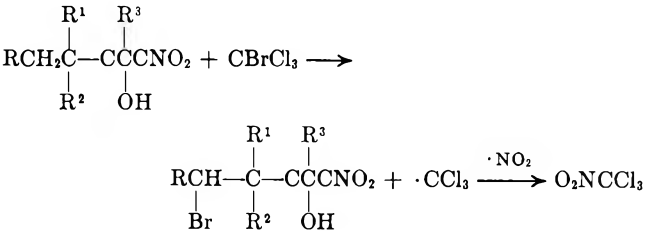
TABLE II
PRODUCTS FROM INTERNAL NITRO NITRATES



Nitro nitrate (III)	R	X	Product IV	Yield, %
8	H	NO_2	17	64
9	CH_3	NO_2	18	77
9	CH_3	Br	18a	75

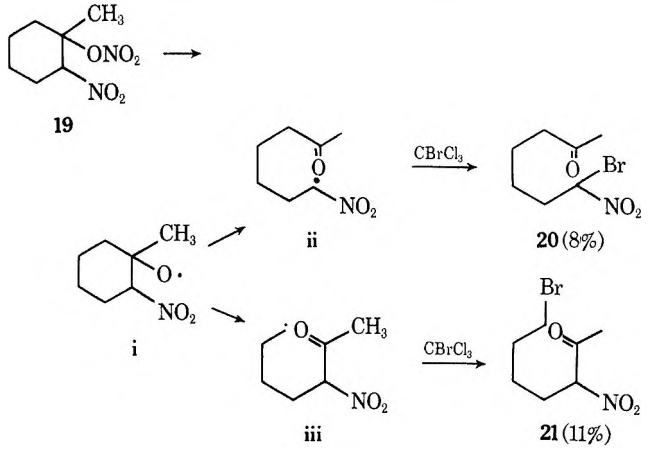
substituent was on an internal carbon atom. In no instance were nitro nitrito alcohols isolated. On the basis of products isolated and identified, there is an exclusive preference for the six-membered ring transition state (*i.e.*, a 1,5 hydrogen shift) in the intramolecular hydrogen abstraction.

Decomposition of β-Nitrates in the Presence of Radical Trapping Agents.—By conducting the decomposition of **1**, **5**, or 3-nitro-2,4,4-trimethyl-2-pentyl nitrate (**9**) in refluxing bromotrichloromethane, it was possible to trap the intermediate alkyl radical to give the corresponding bromonitro alcohols **16a**, **13a**, and **22a**, respectively (*cf.* Tables I and II).[11] During the



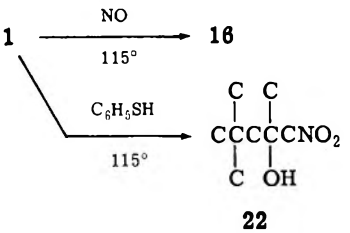
reactions conducted in bromotrichloromethane, an infrared peak at 6.19 μ attributable to chloropicrin (CCl_3NO_2) increases as the nitrate peaks decrease. Although their proximate boiling points precluded separation, a synthetic mixture of $CBrCl_3$ and CCl_3NO_2 give an ir spectrum identical to that of the solvent from the reaction mixtures.

1-Methyl-2-nitrocyclohexyl nitrate (**24**) should decompose to give an alkoxy radical (i) incapable of abstracting hydrogen by a 1,5 shift. The radical should decay (at least partially) by β scission to give either of the ring-opened radicals (ii or iii) which, on interception by Br, would give the bromonitroheptanones **20** and **21**. These compounds were produced in *iso-*



lated yields of 8 and 11% when **19** was heated in $CBrCl_3$ at reflux. The remainder of the products were unidentified.

When the decomposition of 1-nitro-2-pentyl nitrate (**2**) or of 1-nitro-2,4,4-trimethyl-2-pentyl nitrate (**1**) was conducted in an atmosphere of nitric oxide, only dinitro alcohols (**10** and **16**, respectively) were found.



(11) For similar trapping of alkyl radicals (after intramolecular hydrogen abstraction by alkoxy radicals from nitrite photolyses) by bromotrichloromethane, see M. Akhtar, D. H. R. Barton, and P. G. Sammes, *J. Amer. Chem. Soc.*, **87**, 4601 (1965).

This result is somewhat surprising because nitric oxide is ordinarily an efficacious radical-trapping agent.[12] In the presence of thiophenol, nitro nitrate **1** was converted to 1-nitro-2,4,4-trimethyl-2-pentanol (**22**). This observation parallels those of Barton, *et al.*,[13] who used thiophenol as a hydrogen source to trap alkyl radicals derived from alkoxyl radical intramolecular abstraction.[11,12]

While this work was in progress, Mills reported the thermal rearrangement of a steroidal β-chloro nitrate to a chloronitro alcohol in 15% yield,[14] and a corresponding photochemical rearrangement in somewhat lower yield.[15] These rearrangements were also shown to occur by cleavage to an alkoxyl radical followed by intramolecular hydrogen abstraction in a six-membered ring transition state.[14,15] Mills also found no nitrite products, indicating that under rearrangement conditions NO_2 combines with the alkyl radical through nitrogen rather than oxygen.

Kinetics of Nitro Nitrate Decompositions.—The rate of decomposition (See Experimental Section) was measured for several nitro nitrates in dilute (1.0–3.7%) solutions of Fluorolube,[10] *n*-alkanes, or bromotrichloromethane, as listed in Table III. In addition, observed rates of decomposition for 2-octyl nitrate (**24**) and the reported rate for ethyl nitrate[1] are included for comparison.

First-order kinetics are obeyed for all decompositions listed in Table III over a range of at least two half-lives. Previous workers have reported the energies of activation for the homolysis of ethyl nitrate in the range of 36 to 41.3 kcal/mol, with the latter figure obtained by Levy[1] probably being the most nearly accurate.[5] An Arrhenius treatment of the rate data for 1-nitro-2,4,4-trimethyl-2-pentyl nitrate (**1**) in Fluorolube gives an energy of activation of 40.0 kcal mol^{-1}, a value which is in reasonable agreement with the reported values for homolysis of ethyl nitrate.[5] The activation energies for **1** and 1-nitro-2-octyl nitrate (**23**) in saturated hydrocarbons, 38.0 and 39.7 kcal mol^{-1}, respectively, are also indicative of homolytic cleavage. The kinetic data then is in accord with the mechanism postulated for production of dinitro alcohols *via* an alkoxyl radical intermediate.

There is an important difference concerning the relative thermal stability of the β-nitro nitrates and simple alkyl nitrates toward homolytic cleavage. The simple nitrates, as exemplified by ethyl nitrate and 2-octyl nitrate, require temperatures in excess of 170° to achieve reasonably rapid (half-lives of less than 35 min) homolytic decomposition, whereas the β-nitro *sec*-nitrate **23** is noticeably unstable above 150° and it was qualitatively observed (*cf.* Table I) that other β-nitro *sec*-nitrates decomposed at about the same rate as nitro nitrate **23**. The β-nitro *tert*-nitrate **1** undergoes rapid decomposition above 120°, and the other β-nitro *tert*-nitrates listed in Table III (**5** and **19**) are also unstable to prolonged heating at relatively low temperatures (105°). Because the measured activation energies are about equivalent for all three types of nitrates, the entropies of activation must decrease in the order β-nitro *tert*-nitrates > β-nitro *sec*-nitrates > unsubstituted alkyl nitrates. The Arrhenius parameters for the decomposition of **1** in Fluorolube are given by $k = 10^{18.5} \times e^{-40,000/RT}$ sec^{-1}. The very high frequency factor indicates that the transition from reactant to transition state (in this case, emerging alkoxy radical) requires little molecular reorientation. It is not clear whether this could be due to an electronic or steric interaction between the nitrate function and the adjacent nitro group. It may be significant that the radical decomposition temperatures for a vicinal dinitrate (60–90°)[16] and of a vicinal chloro nitrate (130°)[14] (two other types of β-substituted nitrates) lie below the decomposition temperature of simple alkyl nitrates.

Table III
Rates of Vicinal Nitro Nitrate Decomposition in Dilute Solutions

Nitro nitrates	Solvent	Concentration, vol. %	Av temp, °C	$k \times 10^{5}$[a] (min^{-1})	Method[b]
1	Fluorolube[c]	2.5	100	1.5	A
	Fluorolube	2.5	110	6.5	A
	Fluorolube	2.5	114.5	11	A
	Fluorolube	2.5	120	21	A
	Fluorolube	2.5	130	84	A
	n-Dodecane	1.0	110	12	A
	n-Dodecane	2.5	120	34	A
	n-Octane	2.5	123.5	70	B
	n-Dodecane	2.5	130	120	A
	n-Dodecane[d]	2.4	128	160	B
23	*n*-Dodecane	2.5	142	4.3	B
	n-Dodecane	2.5	151	14	B
	n-Dodecane	2.5	160.5	37	B
	n-Dodecane[f]	2.0	139.4	3.4	B
5	$CBrCl_3$	1.8	105.3[g]	1.0	B[h]
19	$CBrCl_3$	3.7	*ca.* 105[g]	1.3	B[h]
Alkyl nitrate					
24	*n*-Dodecane	2.5	171.5[i]	13[i]	B
	n-Dodecane	2.5	178.5[i]	32[i]	B
Ethyl nitrate[j] (gas phase) 20-mm initial pressure			171	21.8	Ref 1

[a] First-order rate constant. [b] Method A: decomposition conducted in AgCl infrared cell. Method B: decomposition conducted in Pyrex glassware, and $CHCl_3$ added to aliquots prior to ir determination. [c] Fluorolube is described in ref 10. [d] 1% of 1-nitro-2-octanone[7a] added.[e] [e] These compounds were added to assess the effects of these possible reaction products on the reaction rate. [f] 2% of 1-nitro-2-octanol added.[e] [g] Temperature of refluxing solution. [h] $CHCl_3$ not added to aliquots prior to ir determination. [i] Temperature control was poor above 170° (±1.5°) and these data are considered less accurate. [j] NO and CH_3CHO added.[1]

Characterization and Reactions of Homolysis Products.—Structural assignments of products were made on the basis of alternate methods of synthesis, degradation to known compounds, or in some instances spectral analysis only.[17] All dinitro alcohols had ir peaks (singlets) at about 2.8 (–OH), 6.4, and 7.3 μ ($-NO_2$).

(12) See M. Akhtar, *Advan. Photochem.*, **2**, 263 (1964).

(13) Barton[11] has established, by use of deuterium labeling, that the alkyl radical and not the alkoxyl radical is trapped by thiophenol.

(14) J. S. Mills, *J. Chem. Soc. C*, 2261 (1966).

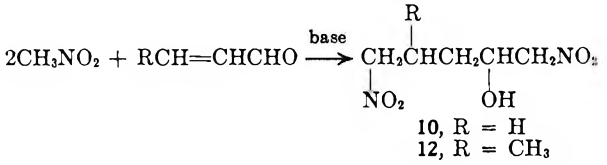
(15) B. W. Finucane, J. B. Thomson, and J. S. Mills, *Chem. Ind. (London)*, 1747 (1967).

(16) J. A. Hicks, *Trans. Faraday Soc.*, **52**, 1526 (1956).

(17) Because the products were all high-boiling liquids, unstable at high temperatures, no method of separation and purification other than elution chromatography was found. Consequently, elemental analyses were often not in strict agreement with calculated molecular formulae, and heavy reliance was placed on ir and nmr spectra for identification.

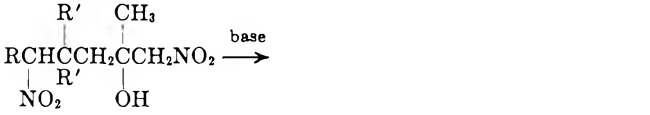
The 60-MHz nmr spectra of the dinitro *sec*-alcohols (**10**, **11**, **12**, and **14**) showed a multiplet (sometimes poorly resolved) at τ 5.4–5.78 attributable to the protons on both the carbon atoms bearing the nitro groups and to the proton adjacent to the hydroxy group. In simple β-nitro alcohols, there is a near coincidence of the position of the proton signals from the hydrogens on the carbon atoms bearing the nitro and hydroxy groups.[18] In the dinitro alcohols, the second nitro group apparently causes a downfield shift of the proton adjacent to the hydroxy group, so that overlap is complete.

Alternate syntheses of 1,5-dinitro-2-pentanol (**10**) and 1,5-dinitro-4-methyl-2-pentanol (**12**) were achieved by the reaction of acrolein and crotonaldehyde, respectively, with excess nitromethane according to published procedures.[19]

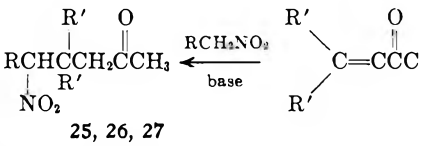


10, R = H
12, R = CH_3

1,5-Dinitro-2-methyl-2-pentanol (**13**), 1,5-dinitro-2-methyl-2-hexanol (**15**), and 1,5-dinitro-2,4,4-trimethyl-2-pentanol (**16**) reacted with weak bases (Al_2O_3, Na_2CO_3, or NaOAc) to give the 5-nitro-2-pentanones, **25**, **26** and **27**, respectively, by loss of nitromethane (a reverse Henry[20] reaction). 3,5-Dinitro-2-methyl-2-pentanol (**17**) and 3,5-dinitro-2,4,4-trimethyl-2-pentanol (**18**), when treated with benzyltrimethylammonium hydroxide in refluxing methanol, reacted similarly to give acetone and 1,3-dinitropropanes (**28** and **29**, respectively). Authentic nitro ketones (**25**, **26**, and **27**) and 1,3-dinitro-2,2-dimethylpropane (**29**) were prepared for comparison purposes. Positive identification of 1,3-dinitropropane (**28**) was made on the basis of its ir and nmr spectra, and acetone was characterized as its 2,4-dinitrophenylhydrazone.

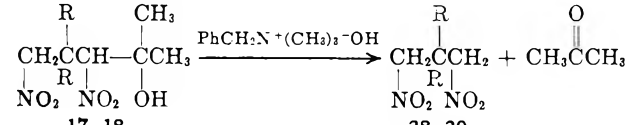


13, **15**, **16**



25, **26**, **27**

13, **25**, R = R′ = H
15, **26**, R = CH_3; R′ = H
16, **27**, R = H; R′ = CH_3

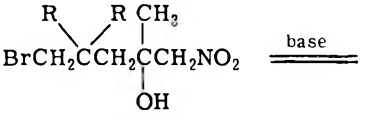


17, **18** **28**, **29**

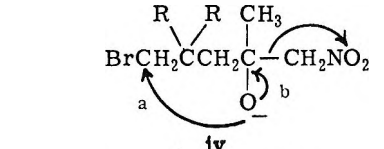
17, **28**, R = H
18, **29**, R = CH_3

7-Bromo-7-nitro-2-heptanone (**20**) was analyzed as its semicarbazone, and reliance on the ir and nmr spectra was made for the structure elucidation of 3-nitro-7-bromo-2-heptanone (**21**). The latter compound (**21**) has an infrared carbonyl peak at 5.75 μ (a hypsochromic shift of 0.05 μ from a normal carbonyl) as do other α-nitro ketones.[21] The nmr shows two triplets [τ 4.75 (1 proton) and 6.56 (2 protons)] for the hydrogens adjacent to the nitro and bromine, a singlet [τ 7.70 (3 protons)] for the methyl ketone, and a six-proton multiplet centered at τ 8.03 for the normal alkyl protons. 7-Bromo-7-nitro-2-heptanone (**20**), on the other hand, showed normal ir carbonyl absorption at 5.80 μ. The nmr showed the three-proton singlet for the methyl ketone at τ 7.90, poorly resolved multiplets (4 protons each) at about τ 7.6 and 8.5 attributable to the alkyl hydrogens, and a triplet at τ 4.11 (1 proton) for the proton adjacent to both the nitro and bromo groups. 1,3-Dinitropropane (**28**) had ir absorption at 6.4 μ; its nmr spectrum consisted of a triplet at τ 5.41 and a quintet at τ 7.32 in a respective ratio of 2:1.

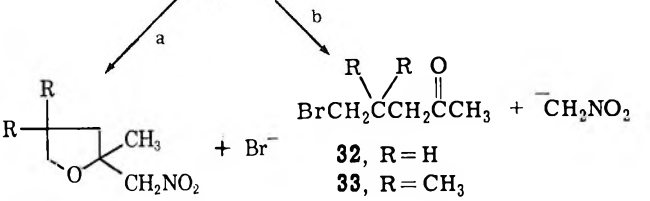
The bromonitro alcohols **13a** and **16a** were characterized by their reaction with weak bases (Al_2O_3 or NaOAc). The possibility arises that the alkoxide intermediate **iv**, once formed, may give stable products in either of two ways. It may eliminate nitromethyl anion (reverse Henry[20] reaction) to give a bromo ketone, or it may displace bromide ion to give a cyclic ether.[22]



13a, R = H
16a, R = CH_3



iv



30, R = H
31, R = CH_3

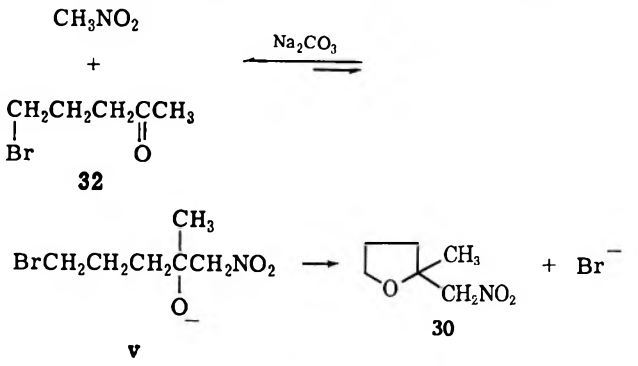
32, R = H
33, R = CH_3

Actually, both reactions occur. Treatment of 1-nitro-2-methyl-5-bromo-2-pentanol (**13a**) with alumina in benzene for 28 hr results in formation in high yield of a mixture of 2-methyl-2-(nitromethyl)tetrahydrofuran (**30**) and 5-bromo-2-pentanone (**32**) in respective ratios of between 4:1 and 7:1. 1-Nitro-2,4,4-trimethyl-5-bromo-2-pentanol (**16a**) under similar conditions gives 2,4,4-trimethyl-2-(nitromethyl)tetrahydrofuran (**31**) and 4,4-dimethyl-5-bromo-2-pentanone (**33**) in a 3:2 ratio. When methanolic sodium acetate is used, bromonitro alcohol **16a** gives **31** and **33** in a respective ratio of 1:3. The product ratios were determined by nmr integration.

The 7:1 mixture of 2-methyl-2-(nitromethyl)tetrahydrofuran (**30**) and 5-bromo-2-pentanone (**32**) was

(18) A. I. Meyers and J. C. Sicar, *J. Org. Chem.*, **32**, 4134 (1967).
(19) O. Wulff, German Patent 860,795 (Dec 22, 1952).
(20) L. Henry, *C. R. Acad. Sci.*, **120**, 1265 (1895).
(21) T. Simmons, R. F. Love, and K. L. Kreuz, *J. Org. Chem.*, **31**, 2400 (1966).
(22) C. Walling and A. Padwa, *J. Amer. Chem. Soc.*, **85**, 1597 (1963).

converted entirely to the cyclic ether **30** by treatment with excess nitromethane and sodium carbonate. In this case, the unfavorable thermodynamic equilibrium in the Henry reaction[20] of **32** with nitromethane was



apparently overcome by providing an irreversible step for the alkoxide ion intermediate **v**, namely cyclic ether formation.[23]

It has been shown that the presence of a β-nitro substituent fosters the controlled decomposition of the alkyl nitrate function along a relatively clean reaction path. Furthermore, such reactions provide ready access to a variety of interesting trifunctional compounds. It is likely that nitrate ester pyrolysis will assume an increasingly important role in functionalization of unactivated alkyl groups. The nature of the effect of the vicinal nitro substituent, which markedly changes the kinetics of nitrate decomposition, is presently being investigated in these laboratories.

Experimental Section

The vicinal nitro nitrates were prepared and purified as previously described.[7] 2-Octyl nitrate (**24**) was prepared (91% yield) by the reaction at −5° of 2-octanol with acetyl nitrate.[24,25] The reaction solvents were the best quality commercially available and generally were used without further purification. Alumina was Fisher adsorption alumina, 80–200 mesh. Chromatographic grade silica gel (28–200 mesh) was from W. R. Grace and Co. Chromatography solvents were dried and distilled prior to use. Infrared spectra were obtained with a Beckman IR-4 or a Perkin-Elmer Model 137 spectrophotometer. Nmr spectra were obtained in $CDCl_3$ with a Varian Associates Model V-4311 spectrometer operated at 60 MHz using tetramethylsilane as an internal standard. Gas–liquid chromatography was performed on an Aerograph A-90-P2 instrument using a 10 ft × 1/4 in. column of 12% XF-1150 Cyanosilicon oil on 44/60 mesh Embosel. Melting points, determined on a Fisher–Johns apparatus, are uncorrected. Elemental analyses were performed by the Analytical Research Section of Texaco Inc., Beacon, N. Y.

Unless otherwise stated, products obtained were high-boiling liquids.

Kinetic Procedure.—Nitrate ester decomposition was followed by measuring the decrease of the infrared absorption at 6.05–6.10 or 7.8 μ by one of two methods. In method A, a solution of the nitro nitrate was heated in a variable temperature infrared cell (Limit Model V-LTJ) in the optical beam of a Beckman IR-4 or a Perkin-Elmer 21 recording spectrophotometer. A variable thickness cell containing the same solvent as the sample cell was placed in the reference beam, and the thickness was adjusted for optimum optical balance. The electrically heated cell was controlled with a variable resistor, and temperature was monitored with an iron–constantan thermocouple. The temperature was maintained constant to within ±5–9°, and spectra were scanned at timed intervals.

In method B, a solution of the nitro nitrate was heated in Pyrex glassware. The solution temperatures were maintained constant to ±1° by use of a thermostated oil bath or by refluxing the solution at its boiling point. In some instances, dry nitrogen was slowly conducted through the hot solutions. Measured aliquots were withdrawn at timed intervals and were rapidly cooled by contact with cool vessels. Each aliquot was diluted with a given amount of chloroform (to effect homogeneity in the cold samples), and the spectra were recorded differentially on a Perkin-Elmer Model 137 Infracord. Chloroform was not added to bromotrichloromethane solutions prior to infrared determinations.

The absorbances at 6.05–6.10 or 7.8 μ were obtained by determining the difference between maximum deflection and base line absorption. (Similar techniques are described by Morgan, *et al.*[26]) The rate constants were obtained from straight-line plots of log absorbance *vs.* time. Beer's law was found to hold for nitro nitrates **1** and **23** over the concentration range studied.

1,5-Dinitro-2-pentanol (10).—A solution of 8.00 g of 1-nitro-2-pentyl nitrate (**2**) in 80 ml of *o*-dichlorobenzene was heated at reflux (175°) in a nitrogen atmosphere for 19 min. The solvent was removed by vacuum distillation [67° (15 mm)]. The yellow oil **10** remaining (6.41 g) is identical spectrally to authentic[19] **10**: ir (neat) 2.8 (OH), 6.4, 7.25 μ ($-NO_2$); nmr ($CDCl_3$) δ 1.7, 2.2 (m, 4), 4.5 (m, 5), 5.94 (s, 1, exchanges with D_2O).

1,5-Dinitro-2-hexanol (11).—A solution of 6.00 g of 1-nitro-2-hexyl nitrate (**3**) in 100 ml of *o*-dichlorobenzene was refluxed under nitrogen for 18 min. The solvent was distilled [108–117° (80–85 mm)] and the brown liquid remaining was chromatographed on 100 g of silica gel. There was eluted (80:20 CH_2Cl_2–hexane) 0.22 g of starting material (**14**) and (92–80:8–20 CH_2Cl_2–Et_2O) 4.17 g (72%) of dinitro alcohol **11**: ir (neat) 2.8 (–OH), 6.4, 7.25 μ ($-NO_2$); nmr (acetone-d_6–$CDCl_3$) δ 1.56 [d, J = 7 Hz, $CH_3CH(NO_2)$] superimposed on 1.3–2.9 [m, 7 total, $CH_3CH(NO_2)CH_2CH_2$–], 4.3–4.9 (m, 4), 6.34 (s, 1 –OH).

1,5,-Dinitro-4-methyl-2-pentanol (12).—A solution of 2.00 g of 1-nitro-4-methyl-2-pentyl nitrate (**4**) in 90 ml of *o*-dichlorobenzene was refluxed (179–180°) in a nitrogen atmosphere for 10 min. The solvent was concentrated by vacuum distillation [67° (15 mm)] to about 4 ml. This liquid was washed with pentane (3 × 10 ml) and air dried. The product (1.53 g) is dinitro alcohol **12**. From the pentane extract there was obtained an additional 0.03 g of **12** and 0.10 g of starting material **4**. Total yield of **12** (based on unrecovered **4**) is 83%. It is spectrally identical with **12** prepared according to Wulff:[19] ir (neat) 2.8 (–OH), 6.4, 7.25 μ ($-NO_2$); nmr ($CDCl_3$) δ 1.11 (dd, 3, J = 7 Hz, $-CHCH_3$), 1.6 (m, 2, $-CHCH_2CH(OH)$–], 2.5 [m, 1, $O_2NCH_2CH(CH_3)$–], 3.86 (s, 1, –OH), 4.48 [m, 5, $O_2NCH_2CH(OH)CH$, $(CH_3)CH_2NO_2$].

1,5-Dinitro-2-methyl-2-pentanol (13).—A solution of 7.34 g of 1-nitro-2-methyl-2-pentyl nitrate (**5**) in 150 ml of chlorobenzene was refluxed (130–132°) in a nitrogen atmosphere for 25 min. After cooling, the solvent was removed by distillation [38° (20 mm)]. There remained 6.28 g (86%) of **13**: ir (neat) 2.8 (–OH), 6.4, 7.25 μ ($-NO_2$); nmr ($CDCl_3$) δ 1.35 (s, 3, CH_3–), 1.7, 2.1 (m, 4, $-CH_2CH_2$–), 3.69 (s, 1, –OH), 4.50 (m, 4, O_2NCH_2–).

1-Nitro-2-methyl-5-bromo-2-pentanol (13a).—A solution of 1.35 g of 1-nitro-2-methyl-2-pentyl nitrate (**5**) in 75 ml of $CBrCl_3$ was heated at reflux (105.3°) for 31 hr. During heating, the infrared nitrate absorbances (6.1, 7.8 μ) decreased, and a band at 6.19 μ (CCl_3NO_2) appeared. The solvent from 73 ml of the solution was removed *in vacuo* at 35°. (The recovered solvent contained CCl_3NO_2.) A yellow-brown liquid (1.23 g) remained. It was chromatographed on silica gel. There was eluted (70:30 CH_2Cl_2–hexane) 0.26 g of nitro nitrate **5** and (80:20 CH_2Cl_2–Et_2O) 0.88 g of 1-nitro-2-methyl-5-bromo-2-pentanol (**13a**). The yield of **13a** is 72%, based on unrecovered starting material: ir (neat) 2.8 (–OH), 6.43, 7.27 μ ($-NO_2$); nmr ($CDCl_3$–D_2O) δ 1.34 (s, 3), 1.96 (m, 4), 3.47 (t, 2), 4.45 (s, 2).

1,5-Dinitro-4-acetoxy-2-hexanol (14).—A solution of 2.00 g of 1-nitro-2-nitrato-4-acetoxyhexane (**6**) in 75 ml of *o*-dichlorobenzene was heated at reflux (179–180°) in a nitrogen atmosphere for 22 min. The solvent was removed by distillation at reduced pressure, and the residue was chromatographed on 28 g of silica

(23) *Cf.* H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, New York, N. Y., 1965, pp 234–242, for examples of other types of condensation reactions made irreversible by internal cyclizations.

(24) F. G. Bordwell and E. W. Garbisch, Jr., *J. Amer. Chem. Soc.*, **82**, 3588 (1960).

(25) F. Hodosan, I. Jude, N. Serban, and A. Balogh, *Chem. Ber.*, **95**, 1094 (1962).

(26) H. Morgan, R. M. Sherwood, and T. A. Washall, *Anal. Chem.*, **38**, 1009 (1966).

gel. There was eluted (5–50:95–50 ether–CH_2Cl_2) 1.17 g (58%) 1,5-dinitro-4-acetoxy-2-hexanol (14): ir (neat) 2.8 (–OH), 5.72, 8.1 [OC(=O)CH_3], 6.41, 7.30 μ (–NO_2); nmr ($CDCl_3$) δ 1.58 (d, 3, 8 Hz), 1.86 (m, 2), 2.12 (s, 3), 3.50 (s, 1, exchanges with D_2O), 4.44 [m, 3, –$CH(OH)CH_2NO_2$], 4.78 (m, 1), 5.58 (m, 1).

Anal. Calcd for $C_8H_{14}N_2O_7$: C, 38.4; H, 5.6; N, 11.2. Found: C, 39.2; H, 6.1; N, 10.5.

1,5-Dinitro-2-methyl-2-hexanol (15).—A solution of 2.75 g of 1-nitro-2-methyl-2-hexyl nitrate (7) in 80 ml of Fluorolube[10] was heated at 128 ± 3° for 2.5 hr. When cool, the mixture was extracted with methanol (3 × 25 ml). The solvent from the methanol extract was evaporated *in vacuo*. The two-phase liquid which remained was chromatographed on 50 g of silica gel. There was obtained 0.48 g of starting material (7) and 1.70 g (75%) of 1,5-dinitro-2-methyl-2-hexanol (15): ir (neat) 2.8 (–OH), 6.42, 7.25, 7.35 μ (–NO_2); nmr ($CDCl_3$) δ 1.34 (s, 3), 1.55 [d, 3, J = 6 Hz, $CH_3CH(NO_2)$], 1.68–2.3 (m, 4), 3.85 (s, 1, exchanges with D_2O), 4.47 (s, 2), 4.67 [m, 1, $CH_3CH(NO_2)CH_2$–].

1,5-Dinitro-2,4,4-trimethyl-2-pentanol (16).—A solution of 2.00 g of 1-nitro-2,4,4-trimethyl-2-pentyl nitrate (1) in 50 ml of Fluorolube[10] was heated at 112° for 17 hr. The solution was cooled and extracted with methanol (4 × 25 ml). The methanol was evaporated from the extract, and the two-phase liquid was chromatographed on 16 g of silica gel. Excess Fluorolube[10] was eluted with 25:75 CH_2Cl_2–hexane. With 100% CH_2Cl_2 there was eluted 0.467 g of a yellow liquid which showed ir –NO_2, –OH, and –C=CNO_2 bands. With 20:80 ether–CH_2Cl_2 there was eluted 0.977 g of crude 1,5-dinitro-2,4,4-trimethyl-2-pentanol (16). This material contained some carbonyl impurity, tentatively identified as 2,2,4-trimethyl-4-hydroxy-5-nitropentanoic acid lactone.[27] When vacuum distilled [110° (0.05 mm)], the carbonyl impurity codistilled. When rechromatographed on silica gel, there was obtained relatively uncontaminated dinitro alcohol 16: ir (neat) 2.8 (–OH), 6.4, 7.3 μ (–NO_2); nmr ($CDCl_3$) δ 1.22, 1.25 [2 s, 6, –$C(CH_3)_2$–], 1.47 [s, 3, –$C(CH_3)(OH)CH_2NO_2$], 1.73 (s, 2 –CH_2–), 3.30 (s, 1, exchanges with D_2O), 4.42, 4.44 (2 s, 2, –CH_2NO_2), 4.57, 4.60 (2 s, 2, –CH_2NO_2).

Anal. Calcd for $C_8H_{16}N_2O_5$: N, 12.7 (mol wt 220). Found: N, 12.3 [mol wt (osmometry) 229].

1-Nitro-5-bromo-2,4,4-trimethyl-2-pentanol (16a).—A solution of 2.80 g of 1-nitro-2,4,4-trimethyl-2-pentyl nitrate (1) in 50 ml of $CBrCl_3$ was heated at reflux for 17 hr. The solvent was stripped at reduced pressure at 45°. The yellow oil which remained was chromatographed on 20 g of silica gel. There was eluted (with CH_2Cl_2 and 80:20 CH_2Cl_2–Et_2O) 2.39 g (74%) of 1-nitro-5-bromo-2,4,4-trimethyl-2-pentanol: ir (neat) 2.8 (–OH), 6.40, 7.25 μ (–NO_2); nmr ($CDCl_3$) δ 1.08, 1.16 [2 s, 6, –$C(CH_3)_2$–], 1.43 [s, 3, –$C(CH_3)OHCH_2NO_2$], 1.70 (s, 2), 3.42 (s, 1, exchanges with D_2O), 3.52 (s, 2, –CH_2Br), 4.55, 4.57 (2 s, 2, –CH_2NO_2).

Anal. Calcd for $C_8H_{16}NO_3Br$: C, 37.8; H, 6.3; N, 5.5; Br, 31.5. Found: C, 38.7; H, 6.9; N, 5.5; Br, 31.9.

3,5-Dinitro-2-methyl-2-pentanol (17).—A solution of 4.55 g of 2-methyl-3-nitro-2-pentyl nitrate (8) in 175 ml of chlorobenzene was heated at reflux (130°) in a nitrogen atmosphere for 3 hr. The solvent was distilled at reduced pressure [31–34°, (15 mm)]. The residue remaining (2.89 g, 64%) was 3,5-dinitro-2-methyl-2-pentanol (17): ir (neat) 2.85 (–OH), 6.4, 7.25 μ (–NO_2); nmr ($CDCl_3$) δ 1.32, 1.36 [2 s, 6, –$C(CH_3)_2$–], 2.7, (m, 2), 3.78 (s, 1, exchanges with D_2O), 4.53 (m, 3, O_2NCH_2–, –$CHNO_2$–).

3,5-Dinitro-2,4,4-trimethyl-2-pentanol (18).—A solution of 6.00 g of crude 3-nitro-2,4,4-trimethyl-2-pentyl nitrate[7b] (9) in 125 ml of chlorobenzene was heated at 120–123° for 1 hr and at 113–120° for 0.5 hr. The solvent was removed at 13 mm. The liquid which remained (4.65 g) was 3,5-dinitro-2,4,4-trimethyl-2-pentanol (18): ir (neat) 2.8 (–OH), 6.42, 7.25 μ (–NO_2).

3-Nitro-5-bromo-2,4,4-trimethyl-2-pentanol (18a).—A solution of 2.20 g of 3-nitro-2,4,4-trimethyl-2-pentyl nitrate (9) in 75 ml of $CBrCl_3$ was heated at reflux (103–104°) for 10 hr. The solution was cooled and decanted from some black residue (0.2 g), and the solvent was distilled under reduced pressure at 38°. The residual yellow oil was chromatographed on silica gel. By elution with 80:20 CH_2Cl_2–hexane, 100% CH_2Cl_2, 20:80 Et_2O–CH_2CH_2, and 100% Et_2O, there was obtained 1.91 g of liquid 3-nitro-2,4,4-trimethyl-2-pentanol (18a): ir (neat) 2.8 (–OH), 6.4, 7.25 μ (–NO_2); nmr ($CDCl_3$) δ 1.25 (s, 3), 1.40 (s, 6), 1.48 (s, 3), 2.87 (s, 1, exchanges with D_2O), 3.24, 3.84 (dd, 2, J = 10 Hz), 4.73 (s, 1).

7-Bromo-7-nitro-2-heptanone (20) and 7-Bromo-3-nitro-2-heptanone (21).—A solution of 1.85 g of 1-methyl-2-nitrocyclohexyl nitrate (19) in 50 ml of $CBrCl_3$ was heated at reflux for 28 hr. (During heating, a total of 1.5 ml of solution was removed for kinetic measurements.) The solvent was removed under reduced pressure at 40–45°. The residual yellow liquid (1.76 g) was chromatographed on 32 g of silica gel. From 80:20 CH_2Cl_2–hexane eluent there was obtained a yellow liquid which was rechromatographed on silica gel. There was obtained 222 mg (11%) of liquid 7-bromo-3-nitro-2-heptanone (21): ir (neat) 5.75 (C=O), 6.4, 7.3 μ (–NO_2); nmr ($CDCl_3$) δ 1.97 (m, 6), 2.30 (s, 3), 3.44 (t, 2, J = 6 Hz), 5.25 (t, 1, J = 7 Hz).

From 90:10 CH_2Cl_2–hexane eluent there was obtained a yellow liquid which, after rechromatography on silica gel, yielded (with 100% CH_2Cl_2 eluent) 162 mg (8%) of 7-bromo-7-nitro-2-heptanone (20): ir (neat) 5.8 (C=O), 6.4, 7.3 μ (–NO_2); nmr ($CDCl_3$) δ 1.50 (m, 4), 2.10 (s, 3), 2.32 (m, 4), 5.89 (t, 1, J = 7 Hz).

From 20 there was prepared a semicarbazone, mp 124–126°.

Anal. Calcd for $C_8H_{15}N_4O_3Br$: C, 32.6; H, 5.1; N, 19.0. Found: C, 33.2; H, 5.3; N, 19.1, 19.2.

5-Nitro-2-pentanone (25).—A mixture of 2.29 g of 1,5-dinitro-2-methyl-2-pentanol (13), 50 ml of methanol, and 4 g of Na_2CO_3 was allowed to stand overnight. Insolubles were removed by filtration, and the solvent was evaporated *in vacuo*. The pasty residue was dissolved in 50 ml of water and extracted with 50 ml of ether. Evaporation of the ether left 0.94 g of liquid 5-nitro-2-pentanone (25). From the H_2O, there was obtained an additional 0.50 g of 25 (by acidification with 1.2 *N* HCl and extraction into ether, followed by drying and evaporation of the ether). Total yield of 25 was 1.44 g (92%); it is identical to 25 (by ir and nmr) prepared by reaction of nitromethane with methylvinyl ketone, and forms a 2,4-dinitrophenylhydrazine (mp 130–132°) which has an undepressed melting point when mixed with the 2,4-dinitrophenylhydrazone of authentic 25.[29]

5-Nitro-2-hexanone (26).—Alumina (4.2 g) was added to a solution of 0.91 g of 1,5-dinitro-2-methyl-2-hexanol (15) in 25 ml of benzene. The slurry was stirred at room temperature for 24 hr. The alumina was filtered off and washed with benzene, and the filtrate was evaporated. 5-Nitro-2-hexanone (26) (0.29 g) remained. It has ir and nmr spectra identical to 26 prepared from methylvinyl ketone and nitroethane:[29] nmr ($CDCl_3$) δ 1.56 (d, 3, J = 7 Hz, CH_3CHNO_2–), 2.17 (s, 3 superimposed on m, 2), 2.57 (m, 2), 4.63 [m, 1, $CH_3CH(NO_2)CH_2$–].

Degradation of 3,5-Dinitro-2-alkanols. I. 3,5-Dinitro-2-methyl-2-pentanol. A solution of 2.85 g of 3,5-dinitro-2-methyl-2-pentanol (17), 1 ml of 40% methanolic benzyltrimethylammonium hydroxide, and 225 ml of methanol was slowly distilled for 6 hr. The distillate was delivered into a receiver containing 2.0 g of 2,4-dinitrophenylhydrazone, 10 ml of concentrated H_2SO_4, and 15 ml of H_2O. A total of 0.81 g of orange crystals was recovered (by filtration) from the distillate. A portion was recrystallized from 95% ethanol to give acetone 2,4-dinitrophenylhydrazone, mp 123–125°, undepressed when mixed with authentic acetone 2,4-dinitrophenylhydrazone.

The pot residue was concentrated by vacuum evaporation at 40°. Water (100 ml) was added, and the heterogeneous mixture was extracted with 150 ml of ether. The extract was washed (saturated NaCl solution), dried ($MgSO_4$), and evaporated. The residue (0.99 g) was crude 1,3-dinitropropane (28). It was chromatographed on silica gel and was eluted with CH_2Cl_2. There was obtained 0.24 g of (28): $n^{20}D$ 1.4669; ir (neat) 6.4, 7.2, 7.35 μ (–NO_2); nmr ($CDCl_3$) δ 2.68 (p, 2, J = 6 Hz), 4.59 (t, 4, J = 7 Hz).

II. 3,5-Dinitro-2,4,4-trimethyl-2-pentanol.—A solution of 2.50 g of 3,5-dinitro-2,4,4-trimethyl-2-pentanol (18), 1 ml of 40% methanolic benzyltrimethylammonium hydroxide, and 75 ml of methanol was slowly distilled, and the distillate was delivered to a receiver containing 2,4-dinitrophenylhydrazine solution as in the preceding experiment. Total yield of acetone 2,4-dinitrophenylhydrazone from the distillate was 0.90 g (33%). The melting point (127–129°) is undepressed when mixed with authentic acetone 2,4-dinitrophenylhydrazone.

(27) 2,2,4-Trimethyl-4-hydroxy-5-nitropentanoic acid lactone has been synthesized by an alternate route.[28]

(28) D. R. Lachowicz and K. L. Kreuz, unpublished results.

(29) H. Schechter, D. E. Ley, and L. Zeldin, *J. Amer. Chem. Soc.*, **74**, 3664 (1952).

The pot residue was concentrated by vacuum evaporation at 35°. Water (50 ml) was added and the mixture was extracted with ether (2 × 50 ml). The extract was dried ($MgSO_4$) and evaporated. The orange liquid residue (1.59 g) was chromatographed on silica gel. With CH_2Cl_2 there was eluted 0.19 g of 1,3-dinitro-2,2-dimethylpropane (**29**). Its ir and nmr spectra are identical to those of **29** prepared by the procedure of Lambert and Lowe:[30] nmr ($CDCl_3$) δ 1.20 (s, 6), 4.58 (s, 4).

5-Nitro-4,4-dimethyl-2-pentanone (27).—A solution of 1.00 g of crude 1,5-dinitro-2,4,4-trimethyl-2-pentanol (**16**) in 20 ml of benzene was allowed to stand at room temperature for 20 hr over 3.0 g of alumina. After filtration and evaporation of the filtrate, 0.56 g (72%) of 5-nitro-4,4-dimethyl-2-pentanone (**27**) remained. It is identical spectrally (ir and nmr) to authentic[31] **27** and forms a semicarbazone (mp 163.5–165.5°), the melting point of which is undepressed when mixed with the semicarbazone of authentic **27** (lit.[31] mp 164–165°).

1-Nitro-2,4,4-trimethyl-2-pentanol (22).—A solution of 2.63 g of 1-nitro-2,4,4-trimethyl-2-pentyl nitrate (**1**) in 150 ml of benzenethiol was heated in a nitrogen atmosphere at 115–118° for 3.5 hr. Then most of the benzenethiol was removed by vacuum distillation. The residue was dissolved in 10 ml of 20:80 CH_2Cl_2–hexane and chromatographed on silica gel. Unidentified material was eluted with mixtures of hexane and CH_2Cl_2 and with 100% CH_2Cl_2. With 95:5 CH_2Cl_2–ether there was eluted 0.38 g of 1-nitro-2,4,4-trimethyl-2-pentanol (**22**):[32] ir (neat) 2.8 (–OH), 6.41, 7.25 μ ($-NO_2$); nmr ($CDCl_3$) δ 1.05 [s, 9, $-C(CH_3)_3$], 1.39 (s, 3, CH_3COH), 1.57 (s, 2, $>CCH_2C<$), 3.10 (s, 1, exchanges with D_2O), 4.43 (s, 2, $-CH_2NO_2$).

2-Methyl-2-(nitromethyl)tetrahydrofuran (30) and 5-Bromo-2-pentanone (32).—A solution of 0.80 g of 1-nitro-2-methyl-5-bromo-2-pentanol (**15a**) in 50 ml of benzene was allowed to stand over 3.6 g of alumina for 27 hr. The solution was filtered and the filtrate was evaporated. A yellow oil (0.48 g) composed of **30** and **32** remained: ir (neat) 5.80 (C=O), 6.42, 7.22 ($-NO_2$), 9.55 μ (five-membered cyclic ether); nmr ($CDCl_3$) δ 1.36 (s, CH_3– of **30**), 2.00 (m, $-CH_2-$ of **30** and **32**), 2.15 (s, $-COCH_3-$ of **32**), 3.39 (m, $-CH_2Br$ of **32**), 3.88 (m, $-CH_2O-$ of **30**), 4.41 (s, $-CH_2NO_2$ of **32**). The ratio of peak areas δ 1.36:2.15 is 4:1.

In a repeat experiment with 4.00 g of **13a**, 18 g of alumina, and 200 ml of benzene, and with a reaction time of 28 hr, there was obtained 2.61 g of the mixture of **30** and **32**. The ratio of peak areas of δ 1.34:2.19 is 7:1.

A solution composed of 1.83 g of 7:1 mixture of **30** and **32** (from the preceding experiment), 50 ml of 95% ethanol, 5.0 ml of nitromethane, and 0.5 g of sodium carbonate was allowed to stand for 66 hr. The filtrate was concentrated to about 3 ml by vacuum evaporation at 45–50°. The pasty residue was dissolved in 25 ml of H_2O, and the solution was extracted with ether (2 × 50 ml). The extract was dried ($MgSO_4$) and evaporated. The residue consisting of 2-methyl-2-(nitromethyl)-tetrahydrofuran (**30**) only weighed 0.96 g. A portion was chromatographed on silica gel: nmr ($CDCl_3$) δ 1.34 (s, 3), 1.99 (m, 4, $-CH_2CH_2-$), 3.88 (m, 2, $-CH_2O-$), 4.40 (s, 2).

Anal. Calcd for $C_6H_{11}NO_3$: C, 49.7; H, 7.7; N, 9.7. Found: C, 50.5; H, 7.6; N, 9.0.

2,4,4-Trimethyl-2-(nitromethyl)tetrahydrofuran (31) and 5-Bromo-4,4-dimethyl-2-pentanone (36). A. From Bromonitro Alcohol 16a and Alumina.—A solution of 0.30 g of 1-nitro-5-bromo-2,4,4-trimethyl-2-pentanol (**16a**) and 15 ml of benzene was allowed to stand over alumina (2.3 g) for 25 hr. After filtration and evaporation of the solvent there was obtained 152 mg of a clear liquid composed of **31** and **33**: ir (neat) 5.80 (C=O), 6.43, 7.23 ($-NO_2$), 9.58 μ (five-membered cyclic ether); nmr ($CDCl_3$) δ 1.11, 1.17 [s, $-C(CH_3)_2-$], 1.46 [s, $-C(CH_3)CH_2NO_2-$ of **31**], 1.77, 1.90 (s, $>CCH_2C<$ of **31**), 2.14 (s, CH_3CO- of **33**), 2.54 (s, $-CH_2CO-$ of **33**), 3.52 (s, $-CH_2Br$ of **33**), 3.58 (s, $-CH_2O$ of **31**), 4.44 (s, CH_2NO_2 of **31**). There is a 3:2 ratio of the following peak areas: δ 1.46:2.14; 1.77, 1.90:2.54; 3.58:3.52; 4.44:3.52.

The reaction was repeated with a reaction time of 92 hr. The same ratio of **31** and **33** was obtained. Glpc of the mixture on a preparative scale (175°, He flow = 120 cm^3 min^{-1}) resulted in isolation of 2,4,4-trimethyl-2-(nitromethyl)tetrahydrofuran (**31**) (retention time, 6 min); 5-bromo-4,4-dimethyl-2-pentanone (**33**) was not recovered from the column.

B. From Bromonitro Alcohol 16a and Sodium Acetate.—A solution of 1.05 g of 1-nitro-5-bromo-2,4,4-trimethyl-2-pentanol (**16a**) and 0.75 g of $NaOAc \cdot 3H_2O$ in 25 ml of methanol stood at room temperature for 22 hr. The solvent was removed *in vacuo*, and the wet solid residue was stirred with ether The solids were removed by filtration. (An aqueous solution of the solids gives precipitate with $AgNO_3$.) The solvent was evaporated from the filtrate, and a brown liquid (0.51 g) remained. It is composed of **31** and **33** in a 1:3 ratio, as determined by nmr peak ratios.

Registry No.—**1**, 32778-22-6; **5**, 35223-51-9; **10**, 35223-52-0; **11**, 35223-53-1; **12**, 35223-54-2; **13**, 35223-55-3; **13a**, 32774-58-6; **14**, 35223-57-5; **15**, 35223-58-6; **16**, 31710-59-5; **16a**, 32774-56-4; **17**, 35223-61-1; **18**, 35223-62-2; **18a**, 32774-57-5; **19**, 35262-02-3; **20**, 35223-64-4; **20** semicarbazone, 35223-65-5; **21**, 35223-66-6; **22**, 35223-67-7; **23**, 13434-64-5; **24**, 7214-64-4; **25**, 22020-87-7; **26**, 35223-72-4; **27**, 35223-73-5; **28**, 6125-21-9; **29**, 762-98-1; **30**, 35223-76-8; **31**, 35262-01-2.

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(30) A. Lambert and A. Lowe, *J. Chem. Soc.*, 1517 (1947).

(31) M. C. Kloetzel, *J. Amer. Chem. Soc.*, **69**, 2271 (1947).

(32) Compound **22** has an ir spectrum identical to that prepared by the method of Bordwell and Garbisch[24,33] (addition of acetyl nitrate to 2,4,4-trimethyl-1-pentene followed by hydrolysis).

(33) Private communication, R. F. Love.

The Nonstereospecific Addition of 2,4-Dinitrobenzenesulfenyl Chloride to *cis*- and *trans*-Anethole[1]

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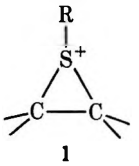
The addition of 2,4-dinitrobenzenesulfenyl chloride to *cis*-anethole in 1,1,2,2-tetrachloroethane (TCE) at 30° gives 30% of the erythro (**2**) and 70% of the threo (**3**) Markovnikov adduct, while addition to *trans*-anethole forms **2** and **3** in 95 and 5% yields, respectively, under the same reaction conditions. The products in TCE at 30° slowly rearrange to an equilibrium mixture containing 51.8% **2** and 48.2% **3**. The nonstereospecific addition to *cis*-anethole must involve an open carbonium ion prior to the product-determining step. This result is in contrast to the usual trans addition of aryl and alkylsulfenyl chlorides to olefins. The addition to *trans*-anethole is highly stereoselective and it is not clear to what extent an open ion is involved in the reaction.

The reaction of aryl and alkylsulfenyl chlorides to olefins has been found to be a stereospecific trans addition by numerous workers.[2-4] Based upon this observation as well as other evidence, a mechanism involving an episulfonium ion (**1**) has been postulated for this reaction.[5]



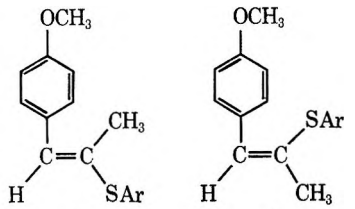
1

We wish to report the first case of a nonstereospecific addition of an arylsulfenyl chloride to an olefin and discuss its mechanistic implications.

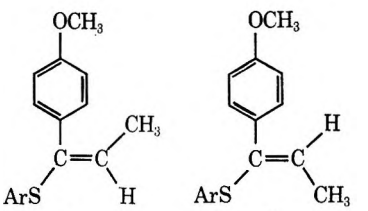
Results

The addition of 2,4-dinitrobenzenesulfenyl chloride to *cis*-anethole at 30° in 1,1,2,2-tetrachloroethane (TCE) gives two products, **2** and **3**, in 30 and 70% yields, respectively, while addition to *trans*-anethole forms **2** and **3** in 95 and 5% yields, respectively, under the same reaction conditions. No difference in products was observed in the presence of added oxygen or in the presence or absence of light. It was found that the reaction products in TCE slowly rearrange to an equilibrium mixture which contains 51.8% **2** and 48.2% **3** at 30.92 ± 0.02°, in TCE. Compound **2** was obtained pure by fractional crystallization of the initial reaction mixture obtained from *trans*-anethole. Despite numerous attempts, **3** could not be obtained free of **2**. Compounds **2** and **3** are the erythro Markovnikov and the threo Markovikov adducts, respectively. Their structures were deduced from the following chemical and spectral information.

A mixture containing 64% **2** and 36% **3** was dehydrochlorinated by reaction with diazabicyclononene to produce a 50:50 mixture of cis and trans olefins in 85% yield. Four structures, **4**–**7**, are possible for these olefins. The structures assigned to the olefins are based on the coupling constants between the vinyl and methyl protons. For structures **4** and **5**, J should be approximately 2 Hz, while for structures **6** and **7**, J should be approximately 7 Hz. Since the observed



4 **5**

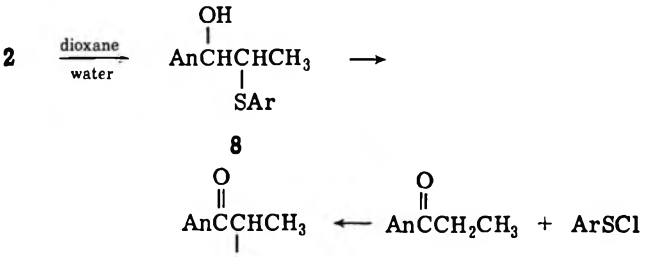


6 **7**

Ar = 2,4-dinitrophenyl

coupling constants are J = 2.0 and 1.0 Hz, **4** and **5** were assigned the structures of the olefins. These results indicate that the adducts **2** and **3** both have a structure with the chlorine in the 1 position and the ArS group in the 2 position.

Additional information regarding the structure of **2** is provided by the following experiment. A pure sample of **2** was solvolyzed in dioxane–water. The resulting alcohol **8** was oxidized to the ketone **9** using



8

9

Ar = *p*-methoxyphenyl

An = 2,4-dinitrophenyl

the Jones reagent. This ketone proved to be identical with the α-keto sulfide obtained from the reaction of 2,4-dinitrobenzenesulfenyl chloride and 4-methoxypropiophenone.

Final confirmation that **2** and **3** are configurational isomers is based on a comparison of the nmr spectra of **2** and **3** with the nmr spectra of the addition products of 4-chloro- and 2,4-dinitrobenzenesulfenyl chloride to *cis*- and *trans*-1-phenylpropene. The data are

(1) Reactions of Sulfenyl Chlorides and their Derivatives. VII. Part VI: G. H. Schmid and V. M. Csizmadia, *Can. J. Chem.*, **50**, 2465 (1972).
(2) G. H. Schmid and V. M. Csizmadia, *Can. J. Chem.*, **44**, 1338 (1966).
(3) W. H. Mueller and P. E. Butler, *J. Amer. Chem. Soc.*, **88**, 2866 (1966).
(4) G. M. Beverly and D. R. Hogg, *Chem. Commun.*, 138 (1966).
(5) W. H. Mueller, *Angew. Chem., Int. Ed. Engl.*, **8**, 482 (1969).

TABLE I

NMR DATA OF 2 AND 3 AND THE ADDUCTS OF 4-CHLORO- AND 2,4-DINITROBENZENESULFENYL CHLORIDE TO *cis*- AND *trans*-1-PHENYLPROPENE

Compd	Ar	Configuration	δ_a	δ_b	δ_c
$PhCH^aCH^bCH_3{}^c$	**10a**, 4-Chloro	Threo	4.97 (d)	3.66 (m)	1.23 (d)
Cl SAr	**11a**, 4-Chloro	Erythro	4.82 (d)	3.49 (m)	1.38 (d)
	10b, 2,4-Dinitro	Threo	5.12 (d)	4.10 (m)	1.44 (d)
	11b, 2,4-Dinitro	Erythro	5.05 (d)	4.00 (m)	1.63 (d)
$PhCH^aCH^bCH_3{}^c$	**12a**, 4-Chloro	Threo	4.34 (d)	4.34 (m)	1.44 (d)
SAr Cl	**13a**, 4-Chloro	Erythro	4.22 (d)	4.22 (m)	1.54 (d)
	12b, 2,4-Dinitro	Threo	4.73 (d)	4.46 (m)	1.56 (d)
	13b, 2,4-Dinitro	Erythro	Unknown		
2			4.92 (d)	3.96 (m)	1.65 (d)
3			5.07 (d)	3.96 (m)	1.43 (d)

given in Table I. The nmr spectra of **2** and **3** are almost identical with those of **11b** and **10b**, respectively. The isomerization of **2** and **3** is particularly revealing, since it serves to establish their relative configurations. When **2** isomerizes to **3** the nmr signal of the methyl group (H_c) is shifted to higher field, while the doublet of the methine hydrogen (H_a) is shifted to lower field. If this were a Markovnikov to anti-Markovnikov isomerization, as found in the case of the adducts of 4-chlorobenzenesulfenyl chloride to 1-phenylpropene,[1] the signals for the methine proton (H_a) would be shifted to higher field, since protons next to chlorine are known to be deshielded relative to protons next to sulfur. Also the methyl protons (H_c) would be shifted to lower field. These relationships are evident from a comparison of the chemical shifts of H_c and H_a in the transformations **10a** → **12a**, **11a** → **13a**, and **10b** → **12b** in Table I.

These observed changes in chemical shifts upon isomerization of **2** to **3** as well as the chemical data are compatible with the assignment of their configuration as a pair of erythro–threo Markovnikov isomers. From an examination of the nmr spectra of a series of racemic erythro and threo isomers, it has been found that the methyl protons of the erythro isomer always appears at lower field than those of the threo isomer.[6] On this basis, **2** is the erythro Markovnikov while **3** is the threo Markovnikov adduct. The fact that the same two products result from the addition of 2,4-dinitrobenzenesulfenyl chloride to *cis*- and trans-anethole strongly supports this structural assignment.

The kinetics of the addition were carried out at 30.92 ± 0.02° in TCE as solvent. The change in concentration of 2,4-dinitrobenzenesulfenyl chloride with time was determined by a modification of the usual titration technique used to determine the concentration of sulfenyl chlorides.[7]

The data gave good straight lines for a second-order reaction, first order in both anethole and 2,4-dinitrobenzenesulfenyl chloride. Attempts to fit the data to a first- or third-order kinetic rate law produced curved plots. The second-order rate constants obtained by a least squares fit are listed in Table II.

The isomerization of **2** and **3** to an equilibrium mixture was followed by measuring the change in the area of their methyl signals in the nmr with time. The rate constants obtained by treating the data according to the method of Frost and Pearson[8] are listed in Table III.

TABLE II

SPECIFIC RATE CONSTANTS FOR THE ADDITION OF 2,4-DINITROBENZENESULFENYL CHLORIDE TO *cis*- AND *trans*-1-ANETHOLE

trans-Anethole

$[ArSCl]_0 \times 10^3$, mol/l.	$[Olefin]_0 \times 10^3$, mol/l.	$k \times 10^2$, M^{-1} sec^{-1}
8.06	10.91	2.04
7.26	11.63	2.13
7.63	10.68	1.89
9.86	6.05	1.94
7.00	13.50	1.89
5.72	8.45	1.93
		Av 1.97 ± 0.09

cis-Anethole

$[ArSCl]_0 \times 10^3$, mol/l.	$[Olefin]_0 \times 10^3$, mol/l.	$k \times 10^3$
5.79	8.29	3.82
5.07	9.46	3.87
5.54	7.19	3.90
		Av 3.86 ± 0.04

TABLE III

RATE OF ISOMERIZATION OF ERYTHRO- AND THREO MIXTURES

$$2 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} 3$$

From excess **2**	$k_1 + k_{-1} = 7.3 \pm 0.5 \times 10^{-6}$ sec^{-1}
From excess **3**	$k_1 + k_{-1} = 6.9 \pm 0.2 \times 10^{-6}$ sec^{-1}
	$K = 1.07$
	$k_{-1} = 3.5 \times 10^{-6}$ sec^{-1}
	$k_1 = 3.8 \times 10^{-6}$ sec^{-1}

Discussion

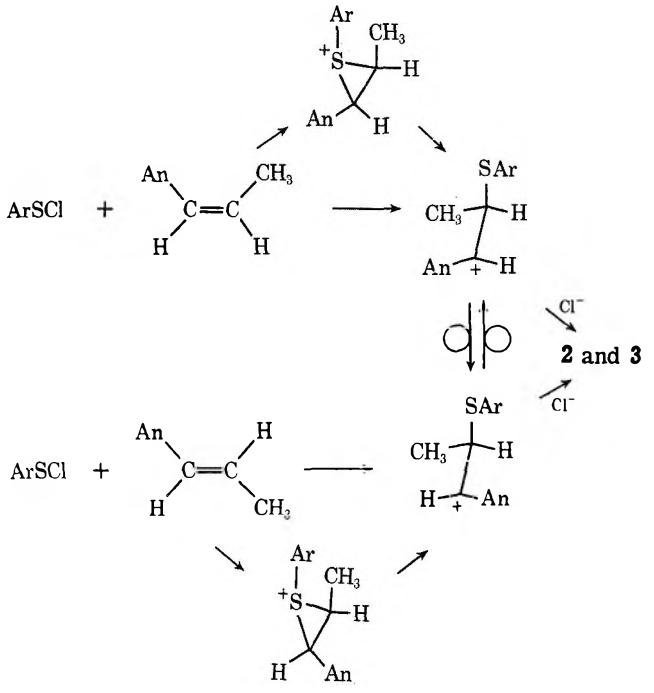
From the data presented it is clear that the addition of 2,4-dinitrobenzenesulfenyl chloride to *cis*-anethole is nonstereospecific. The addition to *trans*-anethole is highly stereoselective and may be stereospecific. We cannot rule out the possibility that the formation of the small amount of **3**, the threo isomer, is due to subsequent isomerization of the initially formed product

(6) G. H. Schmid, *Can. J. Chem.*, **46**, 3415 (1968).
(7) N. Kharasch and M. M. Wald, *Anal. Chem.*, **27**, 996 (1955).
(8) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," Wiley, New York, N. Y., 1953, p 113.

2. These results are in contrast to the stereospecific trans addition observed for the reaction of 4-chloro- and 2,4-dinitrobenzenesulfenyl chloride to both *cis*- and *trans*-1-phenylpropene.[9] Despite this change in the stereochemistry of the products, the rate of the addition follows second-order kinetics, first order in olefin and first order in sulfenyl chloride, which is identical with that found for additions to simple olefins,[10] styrenes,[11] and acetylenes.[12]

These results indicate that adding a methoxy group to the 4 position of the phenyl group of *cis*-1-phenylpropene has caused a change in mechanism of the reaction. Clearly an open carbonium ion rather than a bridged ion is involved as an intermediate prior to the product determining step. However, it is not clear whether the open carbonium ion is the first-formed intermediate. Consequently there are two possible mechanisms consistent with the facts. The first involves a bridged transition state in the rate determining step leading to an episulfonium ion intermediate which then opens to an open carbonium ion intermediate. This open carbonium ion is now able to rotate to its isomeric carbonium ion, which upon reaction with chloride ion leads to nonstereospecific products. In this mechanism only the product determining transition states resemble the open carbonium ion intermediate. A second mechanism involves only one intermediate, an open carbonium ion. In this mechanism both the rate and product determining transition states resemble the open carbonium ion. These two mechanisms are illustrated in Scheme I.

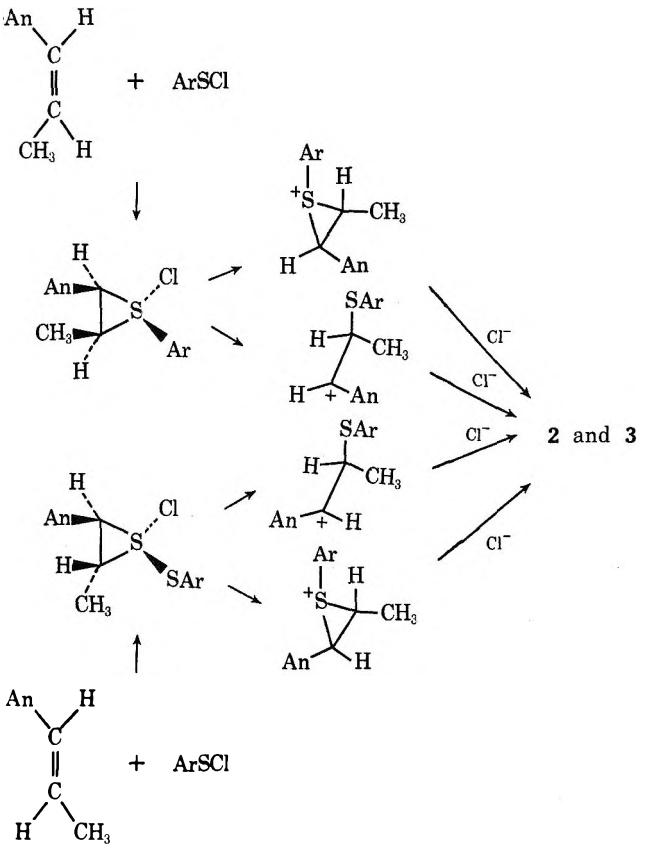
SCHEME I



Ar = 2,4-dinitrophenyl
An = 4-methoxyphenyl

A variant of the first mechanism involving the tetracoordinate covalently bonded sulfur intermediate proposed by Helmkamp[13] is also consistent with our data. In this mechanism the tetracoordinate sulfur intermediate can ionize to either an open carbonium ion or to an episulfonium ion as illustrated in Scheme II.

SCHEME II

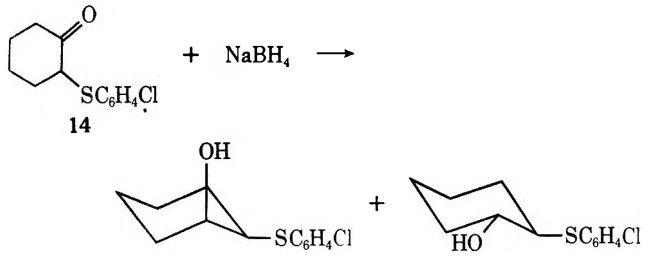


The rate data tends to support some type of bridged structure in the rate-determining step. The rate of addition to *trans*-anethole is faster than to the cis isomer even though the trans isomer is the more stable. Similar results were obtained in the addition of arylsulfenyl chlorides to *cis*- and *trans*-1-phenylpropene and were explained on the basis of increased steric strain in the rate-determining bridged transition state of the addition to the *cis* isomer. In the addition to *cis*-anethole this steric crowding in the bridged or the tetracovalent sulfur intermediate can be relieved by opening to the carbonium ion, whose stability seems to be comparable to that of the episulfonium ion. The highly stereoselective addition to the trans isomer is consistent with this idea, since less opening of the intermediate bridged ion would occur because there is less steric crowding in this intermediate.

The argument that addition to both isomers occurs by an open ion as the first intermediate and that the difference in product composition is due to a difference in the rate of rotation of the open carbonium ions cannot be entirely ruled out. Rotation of the open carbonium ion is not necessary to give nonstereospecific products. It has been found[14] that the $NaBH_4$ reduc-

(9) G. H. Schmid and V. M. Csizmadia, *Chem. Ind. (London)*, 1811 (1968).
(10) G. M. Beverly and D. R. Hogg, *J. Chem. Soc B*, 175 (1971).
(11) W. L. Orr and N. Kharasch, *J. Amer. Chem. Soc.*, **75**, 6030 (1953).
(12) G. H. Schmid and M. Heinola, *ibid.*, **90**, 3466 (1968).
(13) D. C. Owsley, G. K. Helmkamp, and M. F. Retting, *ibid.*, **91**, 5239 (1969).
(14) G. H. Schmid and P. H. Fitzgerald, unpublished results.

tion of **14** gives 75% cis and 25% trans alcohol. If the reduction of the ketone is a good model for chloride attack on the open ion, then it is a bit surprising that addition to the trans isomer is so stereoselective.



14

We conclude on the basis of the data available that the experimental results for addition to *cis*-anethole are consistent with the formation of an open carbonium ion intermediate prior to the product determining step. For the addition to *trans*-anethole, it is not clear to what extent an open ion is involved in the reaction.

Experimental Section

All melting and boiling points are uncorrected. Nuclear magnetic resonance spectra were recorded on Varian A-60 and HA-100 spectrophotometers using tetramethylsilane as internal reference. Microanalysis was carried out by A. B. Gygli Microanalysis Laboratories, Toronto, Ontario. *trans*-Anethole was obtained commercially from Eastman Organic Chemicals and purified by distillation, bp 76.5–77° (1.5 mm) [lit.[15] bp 81–81.5 (2.3 mm)]. *cis*-Anethole was obtained by photochemical isomerization and purified by preparative glc on a 25-ft. UCON column.

2,4-Dinitrobenzenesulfenyl chloride was prepared by the method of Kharasch and Lawson,[16] mp 96–97° (lit.[16] mp 97–98°).

erythro-1-*p*-**Anisyl-1-chloro-2-(2',4'-dinitrophenylthio)propane** (**2**) was isolated from the reaction mixture and purified by recrystallization from carbon tetrachloride, mp 134–135°.

Anal. Calcd for $C_{16}H_{15}O_5N_2ClS$: C, 50.20; H, 3.94; N, 7.31; Cl, 9.26; S, 8.37. Found: C, 50.58; H, 3.84; N, 7.36; Cl, 9.98; S, 8.39.

Dehydrochlorination of 2 and 3.—The erythro adduct **2** (2.0 g, 5.2 mmol) was heated under reflux in benzene until a mixture of 64% **2** and 36% **3** was obtained. This mixture was dehydrochlorinated by the method of Eiter and Oediger[17] using 1,5-diazabicyclo[4.3.0]nonene to give an 85% yield of a 50:50 mixture of two olefins: nmr ($CDCl_3$) 2.27 (d, 3 H), J = 1 Hz, 2.31 (d, 3 H, J = 2 Hz), 3.80 (s, 3 H), 3.91 (s, 3 H), 6.7–8.9 (14 H).

Solvolysis of 2 and Oxidation of the Ketone. A solution of 2.00 g (5.22 mmol) of **2** in 100 ml of 60% dioxane–water was kept at 65° overnight. The reaction mixture was diluted with 100 ml of water, then extracted with three 75 ml portions of ether. The combined ether extracts were washed with water and dried over $MgSO_4$. Removal of the ether left a dark oil which was recrystallized from methylene chloride–pentane to 1.35 g of crude alcohol (71% yield), mp 105–110°, nmr 1.38 (d, 3 H), 4.83 (d, 1 H, J = 4 Hz), 6.65–8.8 (7 H).

A solution of 1.30 g of alcohol in 25 ml of acetone was titrated with the Jones reagent.[18] The solid Cr(III) salts were removed by filtration and 50 ml of water was added to the filtrate, which was then extracted with two 50-ml portions of ether. Removal of the ether left a yellow solid which was recrystallized from 95% ethanol to give 0.96 g of product, mp 150.5–151° (74% yield), identical with the α-keto sulfide isolated from the reaction of 2,4-dinitrobenzenesulfenyl chloride with 4-methoxypropiophenone, nmr ($CDCl_3$) 1.78 (d, 3 H), 3.92 (s, 3 H), 5.02 (g, 1 H), 7.0–8.4 (m, 7).

Anal. Calcd for $C_{16}H_{14}N_2SO_6$: C, 53.03; H, 3.89; N, 7.73; S, 8.85. Found: C, 53.20; H, 3.89; N, 7.79; S, 8.85.

1,1,2,2-Tetrachloroethane was purified by washing with concentrated H_2SO_4 until the acid wash remained colorless. The solvent was then washed with water until neutral, dried over K_2CO_3, and distilled from K_2CO_3 through a Vigreux column, bp 146° (lit.[18] bp 146°).

Kinetics of Addition of 2,4-Dinitrobenzenesulfenyl Chloride to *cis*- and *trans*-Anethole at 30.92 ± 0.02°.—Solutions of ArSCl and olefin in 1,1,2,2-tetrachloroethane (TCE) were equilibrated to bath temperatures, then mixed. Zero time was taken at half mixing. The change in concentration of ArSCl with time was followed by an aliquot technique. A 5 ml aliquot of the reacting mixture was added to 0.5 g NaI in a 125 ml separatory funnel. After the mixture was shaken vigorously for 3 min, 10 ml of water was added followed by 5 ml of 0.01 N $Na_2S_2O_3$ solution. The mixture was then shaken for 3 min. After the lower layer was drawn off (TCE), the excess thiosulfate was titrated with 0.005 N iodine solution. Second-order rate constants were obtained by a least squares fitting program.

Registry No.—**2**, 35031-15-3; **3**, 35031-16-4; **4**, 35031-17-5; **5**, 35031-18-6; **8**, 35031-19-7; **9**, 35031-20-0; **10a**, 22556-38-3; **10b**, 35031-22-2; **11a**, 22556-40-7; **11b**, 35031-24-4; **12a**, 22556-39-4; **12b**, 35031-26-6; **13a**, 22556-41-8; **13b**, 35031-28-8; 2,4-dinitrobenzenesulfenyl chloride, 528-76-7; *cis*-anethole, 25679-28-1; *trans*-anethole, 4180-23-8.

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On the Additive-Constitutive Character of Partition Coefficients[1]

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The addition of a CH_2 or CH_3 group to a parent structure normally increases the logarithm of the octanol–water or ether–water partition coefficient (P) by about 0.5. This fact has proved to be widely useful in the calculation of partition coefficients when the value of a parent compound is known. However, it has now been discovered that, when such groups are attached to certain electron-withdrawing functions, little or no increase in log P is observed. This knowledge is important for the study of the additive–constitutive character of log P. It is also important in understanding the nature of the "hydrophobic forces" between water molecules and apolar portions of organic compounds.

In this report we continue our study[2] of the additive–constitutive nature of the partition coefficients of organic compounds between a water and an apolar phase. Additive–constitutive relationships break down sooner or later and further refinements must be introduced. It is now apparent that such a break often occurs between H–X and CH_3X when X is a very strong electron-withdrawing function. The main driving force for such study comes from the use of partition coefficients as systems for modeling "hydrophobic bonding" of organic compounds in biochemical systems.[3] We wish to consider hydrophobic character from the point of view of Frank and Evans.[4] Their view has been extended by Kauzmann,[5] especially in connection with biochemical systems. Hydrophobic forces are still poorly understood and the term hydrophobic bonding is a controversial one, the use of which has been criticized by Hildebrand.[6] His criticism has been answered by Némethy, *et al.*[7] Since a completely satisfactory term to describe the forces which tend to stabilize or destabilize nonpolar molecules in an aqueous environment has not been formulated, we shall refer to these collective properties as hydrophobic. In the present discussion we are interested in the forces which determine the equilibrium position of organic compounds when they are partitioned between an aqueous phase and an apolar solvent such as 1-octanol, ether, or benzene.

It has been pointed out that, when an apolar molecule is placed in water, the water tends to form a flickering cluster[7] or sweater[8] about the apolar molecule. When the apolar molecules leave the aqueous phase during partitioning, this flickering cluster of water is lost. The increase in entropy in the removal of the loosely held water molecules is one of the main forces causing the apolar molecules to leave an aqueous phase to partition into an apolar phase, such as an organic solvent, or macromolecular phase, such as a protein or membrane. Many linear relationships between the binding of organic compounds by apolar phases and the octanol–water partition coefficients are now known.[9] These same hydrophobic forces also play an important role in determining the solubility of organic compounds in water.[10] The partitioning might be partially illustrated as in Figure 1, where x represents a water molecule. These loosely structured water molecules are more or less lost, depending on the nature of the apolar phase when the compound is partitioned out of aqueous phase.

One of the interesting and important features of the partition coefficient is that it is an additive–constitutive property of organic compounds.[2] It is now possible to calculate the partition coefficients of complex compounds from suitable reference molecules with considerable confidence.[2] The ability to calculate partition coefficients is very important in drug design,[11] and it is for this reason among others that we have become very interested in the additive–constitutive character of the partition coefficient P. For convenience, the discussion will be cast in terms of log P and π, where π is defined as $\pi_X = \log P_X - \log P_H$. In this symbolism, P_X refers to the partition coefficient of a derivative and P_H refers to that of a parent compound. π_X is the logarithm of the partition coefficient of a molecular fragment such as CH_3, Cl, NO_2, etc. Our main concern in this paper is with electron-withdrawing effects of substituents on π for CH_2 and CH_3 functions.

The π values for CH_2 and CH_3 groups in a given solvent system such as octanol–water or ether–water are usually constant. This is apparent in Table I. Many such examples in homologous series are known.[2] The average π_{CH_2} for 15 different examples[2] where CH_2 is attached to a benzene ring is 0.50 ± 0.04.

We have now uncovered enough examples to make it quite apparent that π of about 0.5 per CH_2 or CH_3 does not hold when a strong electron-attracting group is adjacent to the alkyl moiety. This can be seen in Table I, where acetic and formic acid have almost the same value for log P in the ether–water system. Other cases support this example so that this constitutive property can be utilized in more refined calculations of log P. The examples of Table II illustrate the generality of this phenomenon.

In seven out of the ten examples of Table II, π is reduced from its usual value of about 0.5 to about 0.1. In three of the examples the value of π is about one-half the normal value.

A more extreme example is the following: for I, $CH_3(CH_2)_9N^+(CH_3)_3Br^-$, the log P of octanol–water is -0.16, and, for II, $CH_3(CH_2)_9N^+H_3Cl^-$, it is 0.85,

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TABLE I
ADDITIVITY OF LOG P

Octanol-water system					Ether-water system			
Compound	Registry no.	Log P	π	π/CH₂	Compd	Registry no.	Log P	π/CH₂
CH_3OH	67-56-1	−0.66			HCOOH	64-18-6	−0.44	
			1.00	0.50				0.10
C_3H_7OH	71-23-8	0.34			CH_3COOH	64-19-7	−0.34	
			0.54	0.54				0.56
C_4H_9OH	71-36-3	0.88			C_2H_5COOH	79-09-4	0.22	
			0.52	0.52				0.48
$C_5H_{11}OH$	71-41-0	1.40			C_3H_7COOH	107-92-6	0.70	
			0.63	0.63				0.56
$C_6H_{13}OH$	111-27-3	2.03			C_4H_9COOH	109-52-4	1.26	
			3.10	0.51				0.67
$C_{12}H_{25}OH$	112-53-8	5.13			$C_5H_{11}COOH$	142-62-1	1.93	
Benzene	71-43-2	2.13						
			0.56	0.56				
Toluene	108-88-3	2.69						
			0.46	0.46				
Ethylbenzene	100-41-4	3.15						
			0.53	0.53				
Propylbenzene	103-65-1	3.68						

TABLE II
COMPARATIVE PARTITION COEFFICIENTS

Solvent system	Compound	Registry no.	Log P[a]	Δ log P
Ether–water	$HCONH_2$	75-12-7	−2.85	0.25
	CH_3CONH_2	60-35-5	−2.60	
Ether–water	CH_3CHO	75-07-0	−0.48	0.27
	CH_3COCH_3	67-64-1	−0.21	
Ether–water	C_6H_5CHO	100-52-7	1.74	0.01
	$C_6H_5COCH_3$	98-86-2	1.75	
Benzene–water	C_6H_5CHO		2.10	0.10
	$C_6H_5COCH_3$		2.20	
Octanol–water	C_6H_5CHO		1.48	0.10
	$C_6H_5COCH_3$		1.58	
Octanol–water	C_6H_5NHCHO	103-70-8	1.15	0.01
	$C_6H_5NHCOCH_3$	103-84-4	1.16	
Octanol–water	CH_3CONH_2		−1.21[b]	0.16
	$CH_3CONHCH_3$	79-16-3	−1.05	
Octanol–water	HCOOH		−0.54	0.23
	CH_3COOH		−0.31	
Ether–water	HCOOH		−0.44	0.10
	CH_3COOH		−0.34	
Ether–water	$(COOH)_2$	144-62-7	−0.90	−0.07
	$CH_2(COOH)_2$	141-82-2	−0.97	
Octanol–water	$HCON(CH_3)_2$		−1.01	0.24
	$CH_3CON(CH_3)_2$		−0.77	
Octanol–water	$HCONH_2$		−1.46	0.25
	CH_3CONH_2		−1.21[b]	

[a] The log P values are from ref 2 or were experimentally determined. [b] Calculated from butyramide.

calculated from the dodecyl derivative. Despite the fact that compound I contains three more CH_3 groups, it is more hydrophilic than compound II. In view of the preceding and following discussion, it is not surprising that the three methyl groups attached to the nitrogen atom are not "seen" in hydrophobic terms. Recent calculations by Pullman, *et al.*,[12] make this understandable. They have shown that the positive charge "on nitrogen" in acetylcholine $CH_3COOCH_2CH_2N^+(CH_3)_3$ is almost entirely dispersed onto the 11 hydrogen atoms on the adjacent four carbon atoms.

(12) B. Pullman, P. H. Courriére, and J. L. Coubeils, *Mol. Pharmacol.*, **7**, 397 (1971).

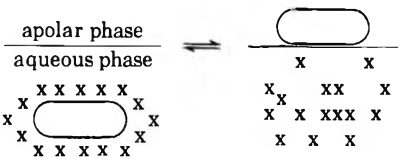


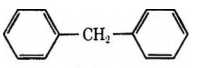
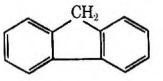
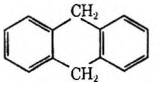
Figure 1.

The charge calculated for N is only +0.06, while most of the hydrogens carry charges of +0.07.

After discounting the methyl groups of compound I, it is seen that compound II is still more lipophilic than I in the octanol–water system. This may be related to the fact that the more concentrated positive charge on the nitrogen in II is able to interact with oxygen in octanol more effectively. Octanol is more basic than water.

A similar effect appears when a methylene group is placed between two benzene rings (Table III). It

TABLE III

	Registry no.	Log P Obsd	Log P Two benzene rings	Log P Calcd
	101-81-5	4.14	4.26	4.76
	86-73-7	4.18	4.26	4.76
	613-31-0	4.25	4.26	5.26

would appear in the three examples from Table III that the normal flickering cluster of water molecules does not form around the methylene groups; that is, log P for the whole molecule is simply that for the sum of two benzene rings.

Another set of examples in which π_{CH_2} is much less than 0.5 is that of the following benzyl derivatives (Table IV). In the set from Table IV, the calculated

TABLE IV

Compound	Registry no.	Log P Obsd	Log P Calcd	Δ log P
$C_6H_5CH_2CN$	140-29-4	1.56	1.79	−0.23
$C_6H_5CH_2OH$	100-51-6	1.10	1.47	−0.36
$C_6H_5CH_2CONH_2$	103-81-1	0.45	0.92	−0.47
$C_6H_5CH_2NH_2$	100-46-9	1.09	1.51	−0.42
$C_6H_5CH_2COCH_3$	103-79-7	1.44	1.84	−0.40
$C_6H_5CH_2COOCH_3$	101-41-7	1.83	2.46	−0.63

values are the sum of log $P_{benzene}$ − log P_{CH_3X}. For example, log $P_{C_6H_5CH_2OH}$ = log $P_{benzene}$ + log P_{CH_3OH} = 2.13 + (−0.66) = 1.47. In every one of the above instances, log P falls short of the calculated value and, except for the CN function, it is about one CH_2 short of the expected value.

A single function operating only through the inductive effect does not appear to have as profound an effect on log P. For example, log P_{I_2} = 2.49 ∴ log P_{EtI} = π_{Et} + $^1/_2$ log P_{I_2} = 1.00 + 1.24 = 2.24. The experimental value for EtI is 2.00. Again the observed value is lower than the calculated value. The agreement is closer in iodobenzene where the electronic effect of the benzene ring is present: log $P_{C_6H_5I}$ = log $P_{C_6H_6}$ + $^1/_2$ log P_{I_2} = 3.37. The observed log $P_{C_6H_5I}$ = 3.25. Of course, the validity of taking $^1/_2$ log P_{I_2} for the value of a covalently bound I is open to question and needs further study.

There is no reason to predict *a priori* that the effect upon the partition coefficient of replacing H by CH_3 would reside primarily in the structure of the solvent around those two groups. One must also consider the possibility that those two groups will affect the solvation of the polar group, and that the polar solvation effect can explain the lack of a normal increase in hydrophobicity produced when CH_3 replaces H. However, it will be seen that such a postulate leads to a predicted effect exactly the reverse of that observed.

First of all, the methyl group releases electrons more readily than does a hydrogen. Since it more effectively satisfies the demands of the electron-seeking substituent, it reduces its total polarity and thus decreases its affinity for the highly polar aqueous phase. Furthermore, the methyl group is bulkier and might be expected to shield some of the polar group's charge from the polar surroundings. Both these effects would tend to make the log P increment for the first methyl group greater than for subsequent ones, rather than smaller as is observed, and thus one concludes that they are of minor importance compared to that of the reduction in electron density in the methyl group. The greater positive charge on the methyl group's hydrogen atoms may reduce the electron correlation with the atoms of the water molecules and in turn reduce the structured nature of the aqueous envelope surrounding this first methyl group.

Electron withdrawal makes the alkyl group more positive. One could argue that this positive character provides the hydrogen atoms with some hydrogen-bonding character so that they have more affinity for the aqueous phase. This effect could simply offset the normal hydrophobic character of the CH_3 or CH_2 function.

Another and more interesting possibility is that, when a CH_3 or CH_2 group attains a certain degree of positive character, water molecules do not form as stable a flickering cluster around the group. Consequently, there is less or no desolvation when such a group moves from the aqueous to the apolar phase. If this is true, one must ask what are the predominant forces holding the envelope of water molecules about a hydrocarbon moiety. Since carbon atoms in alkyl groups are covered by hydrogens, it seems likely that it is the interaction of these hydrogens with the water molecules which produces the loose envelope of water. Assuming that the lack of hydrophobic character means the envelope of water does not form, this could be attributed to lack of electron correlation between the alkyl hydrogens and the atoms of the water molecule.

The above observations, when taken with other information,[2] indicate that the partition coefficient can be a useful tool to the physical–organic chemist for the study of electronic influence on the interaction of solutes with solvents.

Registry No.—I, 2082-84-0; II, 143-09-9.

Enthalpies of Solvent Transfer of Reactants and Transition States in the Diels–Alder Reaction

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The cause of the solvent effect on the activation enthalpies of four Diels–Alder reactions has been examined. Calorimetric determinations of the relative enthalpies of the reactants in electron-donor solvents (dioxane, *o*-xylene) *vs.* more electronegative solvents (chloroform, chlorobenzene) reveals that, whereas electron-donor solvents stabilize the reactants, the more electronegative solvents stabilize the transition state. The solvent effect on the enthalpy of activation is a consequence of these two effects. The transition state in the Diels–Alder reaction behaves like an electron-rich system.

The enthalpy of transfer of a transition state from one solvent to another can provide valuable information concerning the geometry and electronic constitution of the transition state and thus give one a greater insight into the mechanism of a reaction.[1] In particular, if the transfer is from a solvent which is an electron donor to one which is an electron acceptor, then the transfer enthalpy should be a measure of the degree of electron deficiency (or the lack of it) of the transition state.

The Diels–Alder reaction is distinguished by having a mechanism which is believed to involve no production or loss of charges along the path from reactants to products.[2] Neutral reactants produce a neutral product in a single, usually symmetrical step. Although the dienophile in this reaction generally is a molecule having a considerable dipole, this dipole is incorporated unchanged into the product and there is no *a priori* reason to believe that it increases or decreases greatly along the reaction path. In harmony with the above is the observation that this reaction usually has little or no solvent effect on its rate or on its enthalpy of activation.[3]

One objection that can be raised against this picture of a thoroughly "nonpolar" reaction mechanism is the fact that many of the dienes and dienophiles which undergo the Diels–Alder reaction also form charge-transfer complexes with each other.[4] It is not clear whether these complexes are along the reaction path and whether the transition state in any way resembles a charge-transfer complex. The fact that changes in exo/endo adduct ratios have been observed as a function of solvent[5] suggests that there can be sufficient *differences* in the polarities of Diels–Alder transition states. The importance of ionic contributors to the resonance hybrid of the transition state has been invoked to explain differences in reactivity in the Diels–Alder reaction.[6] Recent studies of the pressure dependence of the rate of this reaction has led to the suggestion that the dipole moment of the transition state is much greater than that of the dienophile.[7] Finally, there are some examples of substantial solvent effects on the activation enthalpy of Diels–Alder reactions.[8]

Determination of the enthalpies of transfer of Diels–Alder transition states from one solvent to another may shed some light on some of the questions raised by the above facts.

Results and Discussion

Table I contains four Diels–Alder reactions which exhibit a solvent effect on their activation enthalpies.[9] (See Charts I and II). In Table II are listed the results

TABLE I
SOLVENT EFFECT ON THE ENTHALPIES OF ACTIVATION OF DIELS–ALDER REACTIONS

Reactants	Solvent	$\Delta H^{\pm}$, kcal/mol	$\delta\Delta H^{\pm}$, kcal/mol
Anthracene and maleic anhydride	Dioxane	15.7[a]	
			−3.2
Anthracene and maleic anhydride	Chloroform	12.5[b]	
Dimethylanthracene and maleic anhydride	Dioxane	10.3[a]	
			−2.9
Dimethylanthracene and maleic anhydride	Chloroform	7.4[b]	
Anthracene and tetracyanoethylene	*o*-Xylene	12.3[c]	
			−4.8
Anthracene and tetracyanoethylene	Chlorobenzene	7.5[c]	
Norbornadiene and tetracyanoethylene	*o*-Xylene	17.5[c]	
			−4.0
Norbornadiene and tetracyanoethylene	Chlorobenzene	13.5[c]	

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(7) R. A. Grieger and C. A. Eckert, *Trans. Faraday Soc.*, **66**, 2579 (1970), calculated the dipole moments of the reactants, transition state, and product from their partial molal volumes and the pressure derivative of the dielectric constant factor of the solvent. For the reaction of maleic anhydride with isoprene this yielded dipole moments of 2.5 D for maleic anhydride (actual value = 3.95 D), 4.1 D for the transition state, and 4.0 D for the product (actual value = 4.46 D).

(8) P. Brown and R. C. Cookson, *Tetrahedron*, **21**, 1977 (1965).

(9) The reported uncertainty in the activation enthalpies of the four tetracyanoethylene reactions was ±0.5 kcal/mol or about one-tenth as large as the solvent effect. The same authors[8] also reported similar solvent trends in a more complete series of solvents, namely *o*-xylene, toluene, benzene, bromobenzene, and chlorobenzene ($\Delta H^{\pm}$ = 12.3, 11.0, 9.2, 7.5, and 7.4 kcal/mol, respectively, for the reaction with anthracene, and $\Delta H^{\pm}$ = 17.5, 16.0, 15.0, 13.5, and 13.8 kcal/mol, respectively, for the reaction with norbornadiene). There can therefore be little doubt that a solvent effect on $\Delta H^{\pm}$ is operative here and that the donor–acceptor quality of the solvent seems to be the principal variable.

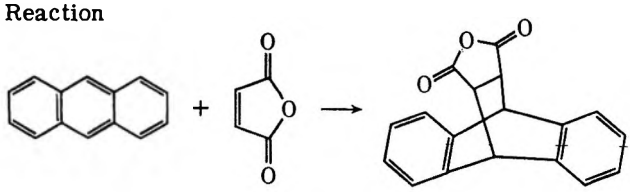
TABLE II
HEATS OF SOLUTION

Solute	Registry no.	Solvent	Registry no.	ΔH_s, kcal/mol[a]
Anthracene	120-12-7	Dioxane	123-91-1	5.34
Anthracene		Chloroform	67-66-3	5.22
Dimethylanthracene	781-43-1	Dioxane		5.52
Dimethylanthracene		Chloroform		4.85
Maleic anhydride	108-31-6	Dioxane		2.52
Maleic anhydride		Chloroform		3.77
Anthracene		*o*-Xylene	95-47-6	5.68
Anthracene		Chlorobenzene	108-90-7	5.88
Norbornadiene	121-46-0	*o*-Xylene		0.00
Norbornadiene		Chlorobenzene		0.00
Tetracyanoethylene	670-54-2	*o*-Xylene		0.33
Tetracyanoethylene		Chlorobenzene		5.29

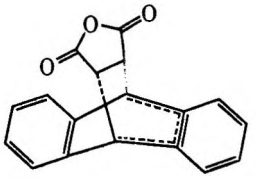
[a] Concentrations ranged from 0.01 to 0.1 *M*. No changes in molar heat of solution with concentration were observed in this range. The standard deviations for the ΔH_s values ranged from 0.04 to 0.23 kcal/mol.

CHART I

Reaction



Transition state



Solvents

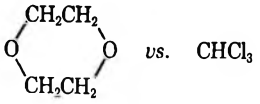
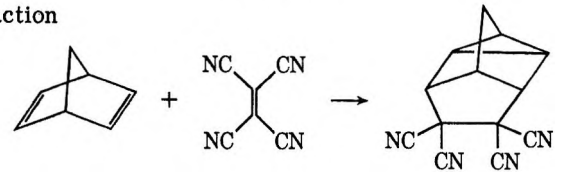
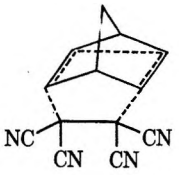


CHART II

Reaction



Transition state



Solvents

of our calorimetric measurements of the heats of solution, ΔH_s, in the appropriate solvents, of the reactants in these four reactions. The enthalpy of transfer of a transition state, δH^t, is obtained from the relations $\delta H^t = \delta\Delta H_s^r + \delta\Delta H^{\ddagger}$, where $\delta\Delta H_s^r$ is the enthalpy of transfer of the reactants from one solvent to another, and $\delta\Delta H^{\ddagger}$ is the difference in the enthalpies of activation of the reaction in the two solvents. The enthalpies of transfer of the reactants, $\delta\Delta H_s^r$, and of the transition states, δH^t, for the above four Diels–Alder reactions are listed in Table III.

TABLE III
ENTHALPIES OF SOLVENT TRANSFER OF REACTANTS, $\delta\Delta H_s^r$, AND TRANSITION STATES, δH^t (KCAL/MOL)

Reaction	Solvent	$\delta\Delta H_s^r$	δH^t
Anthracene + maleic anhydride	Dioxane ⟶ Chloroform	1.1	−2.1
Dimethylanthracene + maleic anhydride	Dioxane ⟶ Chloroform	0.6	−2.3
Anthracene + tetracyanoethylene	*o*-Xylene ⟶ Chlorobenzene	5.2	0.4
Norbornadiene + tetracyanoethylene	*o*-Xylene ⟶ Chlorobenzene	5.0	1.0

As can be seen, the solvent effect on the activation enthalpies in the reaction of maleic anhydride with anthracene and with dimethylanthracene in dioxane and chloroform is caused by desolvation of the reactants (actually only the dienophile) and by superior solvation of the transition state in chloroform.[10] Since it is unreasonable to view the inferior solvation of maleic anhydride by $CHCl_3$ as being due to the greater polarity of $CHCl_3$, the principal solvent property determining the solvation enthalpy in this system must be the electron donating–releasing capacity of the solvent. Viewing the solvation enthalpy diagram (Chart III) of this reaction in this light we see that, while the reactant dienophile is an electron-deficient system (having an endothermic transfer enthalpy from dioxane to chloroform), the transition state behaves like an electron-rich system, having 2.1–2.3 kcal/mol more solvation energy in the more electronegative solvent, chloroform, than in the electron-donating solvent, dioxane.[11]

Turning to the second pair of reactions (Chart IV), that of tetracyanoethylene with anthracene and with norbornadiene, we see that the same general conclusions

(10) It has been suggested by S. Seltzer (ref 2, p 17) that this solvent effect is not explicable in terms of a solvent–dienophile interaction only. Our results bear out this prediction.

(11) While it would not be surprising to find the transition state *less* electron deficient than the dienophile (because of electron delocalization in the transition state), it is remarkable that there is a *net effect* indicating that the transition state behaves as an electron donor toward the solvent. This property of the transition state cannot be mainly due to the diene because (1) the transfer enthalpy of the diene itself into the more electronegative solvent, though exothermic, is quite small, and (2) the exothermic transfer enthalpy of the dimethylanthracene transition state is only slightly greater than that of the anthracene transition state.

CHART III

RELATIVE ENTHALPIES (KCAL/MOL) OF REACTANTS AND TRANSITION STATES IN THE DIELS–ALDER REACTION OF MALEIC ANHYDRIDE WITH ANTHRACENE AND WITH DIMETHYLANTHRACENE IN DIOXANE AND IN CHLOROFORM

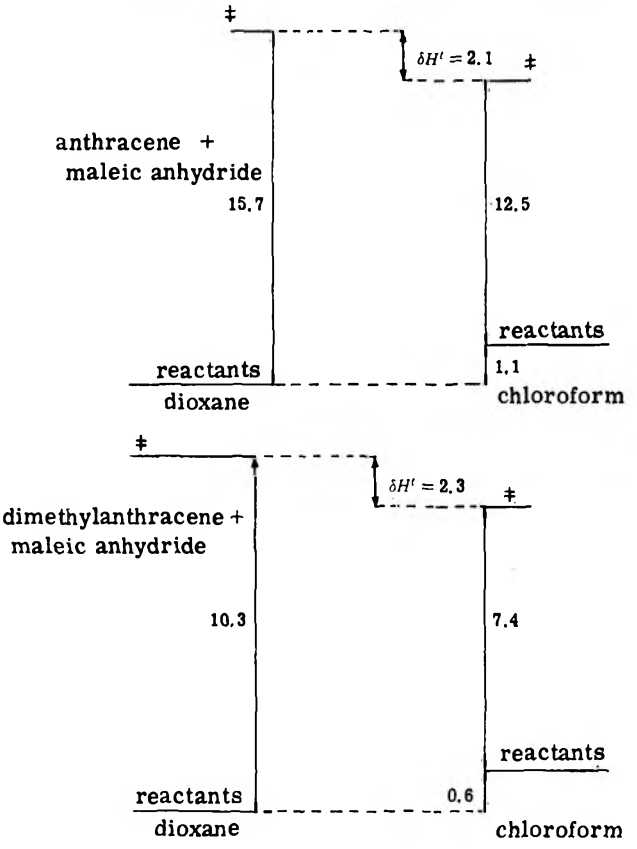
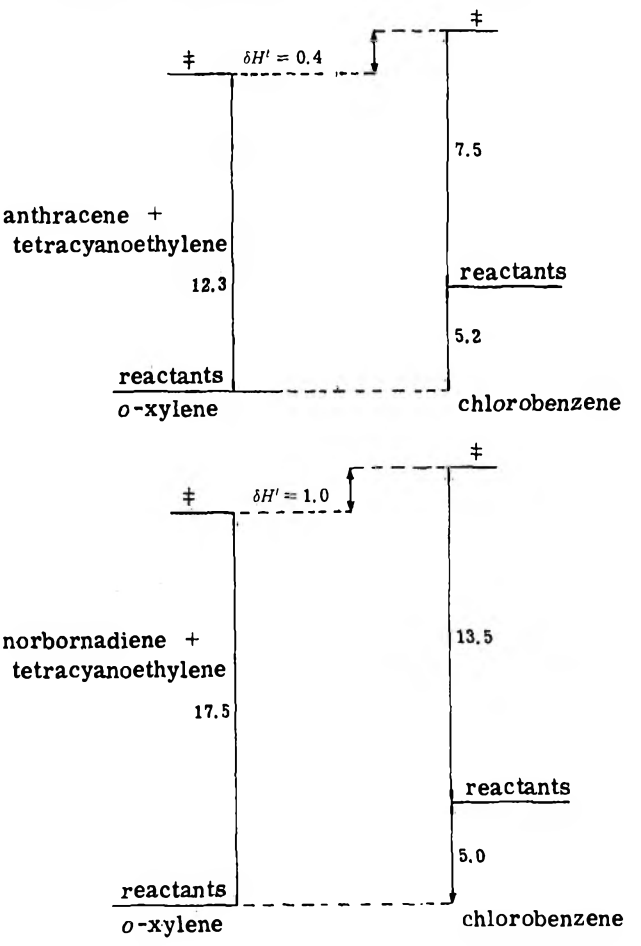


CHART IV

RELATIVE ENTHALPIES (KCAL/MOL) OF REACTANTS AND TRANSITION STATES IN THE DIELS–ALDER REACTION OF TETRACYANOETHYLENE WITH ANTHRACENE AND WITH NORBORNADIENE IN *o*-XYLENE AND IN CHLOROBENZENE



hold. Here the dienophile (tetracyanoethylene) is far more electron deficient than is the case for maleic anhydride and therefore its transfer enthalpy from an electron-donor solvent (*o*-xylene) to an electron-acceptor solvent (chlorobenzene) is even more highly endothermic (5.0 kcal/mol). Because of the extreme, intrinsic electron-withdrawing power of tetracyanoethylene, even the transition state containing the tetracyanoethylene moiety has an endothermic transfer enthalpy into the more electronegative solvent (0.4–1.0 kcal/mol). Thus in this case, because of the extreme nature of the dienophile, the net effect is that the Diels–Alder transition state behaves like an electron-poor system. However, here too the transition state behaves as a far more electron-rich entity than the diene plus the dienophile (by 4.0–4.8 kcal/mol).[12]

It therefore appears that solvent effects on the activation enthalpies of these Diels–Alder reactions are not to be understood in terms of solvent polarity (dielectric constant, dipole moment)[13] but rather in terms of the electron donor–acceptor property of the solvent and the different influence of this property on the reactants and on the transition state. (Some relevant solvent properties are shown in Table IV.) An electron-donor solvent lowers the energy of the dienophile while an electron-acceptor solvent lowers the energy of the transition state.

TABLE IV

SOLVENT PROPERTIES

	Dioxane	Chloroform	*o*-Xylene	Chlorobenzene
Dielectric constant	2.2[a]	4.9[b]	2.4[a]	5.5[a]
Dipole moment, Debye	0.3[c]	1.1[c]	0.5[c]	1.5[c]
E_T, kcal/mol	36.0[d]	39.1[d]		
Ionization potential, eV	9.5[e]	11.4[e]	8.6[e]	9.1[e]

[a] C. Marsden and S. Mann, "Solvents Guide," Interscience, New York, N. Y., 1963. [b] L. Scheflan and M. B. Jacobs, "Handbook of Solvents," Van Nostrand, New York, N. Y., 1953. [c] A. L. McClelan, "Tables of Experimental Dipole Moments", W. H. Freeman and Co., San Francisco, Calif., 1963. [d] C. Reichardt, *Angew. Chem., Int. Ed. Engl.*, 4, 29 (1965). [e] V. I. Vedeneyev, L. V. Gurvich, V. N. Kondratyev, V. A. Medvedev, and Y. L. Frankevich, "Bond Energies, Ionization Potentials and Electron Affinities," St. Martin's Press, New York, N. Y., 1966.

(12) The suggestion that the Diels–Alder transition state, while structurally similar to products, is electronically similar to reactants (C. K. Ingold in "The Transition State," Special Publication No. 16, The Chemical Society, London, 1962, p 119; see also R. A. Grieger and C. A. Eckert, ref 2d) is not supported by our observation of a large difference between the transfer enthalpy of the transition state and the transfer enthalpy of the reactants.

(13) The lack of correlation of the solvent effect with the dielectric constant has been pointed out by Dewar (ref 3) and others.

Experimental Section

Materials.—**Anthracene** (Aldrich) was recrystallized twice from benzene and then sublimed, mp 215.0–215.5°. **Maleic anhydride** (Fisher) was recrystallized twice from chloroform and sublimed, mp 53.0–53.5°. **Norbornadiene** (Eastman) was refluxed over $LiAlH_4$ and then fractionated, the fraction of bp 89–90° being used. **Tetracyanoethylene** (Aldrich) was recrystallized from dry chlorobenzene and sublimed, mp 198–199° (sealed tube). **9,10-Dimethylanthracene** was prepared according to the method of Phillips and Cason.[14] After two recrystallizations from benzene and sublimation it had mp 182–183°. **1,4-Dioxane** (Matheson Coleman and Bell, scintillation grade) was distilled from $LiAlH_4$, bp 101°. **Chloroform** (Matheson Coleman and Bell, Spectroquality) was dried over anhydrous $CaCl_2$ and distilled, bp 61°. **Chlorobenzene** (Aldrich) was passed through a column of Linde Molecular Sieves, 4A, and fractionated, the fraction boiling at 131° being used. ***o*-Xylene** (Eastman) was passed through a column of molecular sieves, 4A, and fractionated, the fraction distilling at 143° being used.

Heats of Solution.—The calorimeter and the procedure employed have been described previously.[1e]

(14) D. D. Phillips and J. Cason, *J. Amer. Chem. Soc.*, **74**, 2934 (1952).

10-Ethoxy-9-phenanthroxyl Radical and Dimer

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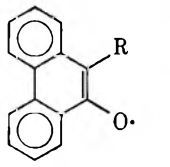
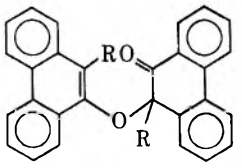
Received April 14, 1972

The dimer of the title radical **1b** is assigned a structure **3** different from that of the dimer **2** of the analogous chloro-substituted radical **1a**. The pmr spectrum of **3** is quite sensitive to temperature effects on the line widths and the epr spectrum of the radical **1b** is affected by solvent as well as by temperature. The spectra of **1a** and **2** are insensitive to solvent and temperature changes. The extent of dissociation of **3** has been measured in several solvents at several temperatures, and is found to increase with increasing solvent internal pressure. The chloro dimer **2** is more than an order of magnitude less dissociated than **3**. The rate constant for the disproportionation of **1b** to 10-ethoxy-9-phenanthrol, phenanthrenequinone, and ethylene is 19 M^{-1} sec^{-1} at 67°.

The dimers of 10-substituted 9-phenanthroxyl radicals, at one time believed to be peroxides, are now known to be keto ethers.[1] In the case of the 10-chloro dimer, the point of attachment of the ether linkage is at the 10 position, as shown in structure **2**. This structure



1a, R = Cl
b, R = CH_3CH_2O



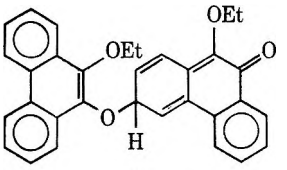
2

is supported by chemical evidence (only one of the two chlorine atoms is labile),[1,2] by the infrared spectrum,[1,2] and by the 90-MHz proton magnetic resonance spectrum,[2] which shows only aromatic protons.

The properties of the 10-ethoxy-9-phenanthroxyl radical **1b** and its dimer were different enough from those of the chloro radical and dimer to warrant further investigation. Thus the ethoxy dimer is more dissociated and the line widths of its proton magnetic resonance spectrum are strongly temperature dependent, unlike those of the chloro dimer. Although the latter phenomenon proved not to be suitable for the measurement of dissociation rates[3] in this case, the equilibrium constant for the dissociation has been determined in a series of solvents by means of epr. The decomposition of **1b** into 10-ethoxy-9-phenanthrol, phenanthrenequinone, and ethylene was also studied.

Results and Discussion

Structure of the Ethoxy Dimer.—Although the infrared spectrum of the dimer of **1b** is that of a keto ether, the 90-MHz pmr spectrum has peaks in the vinyl region (doublet at δ 6.4, distorted triplet at δ 7.0), indicating a keto ether structure different from that of **2**. On the basis of the position of the uv absorption maximum (340 nm in CCl_4, ϵ 4.10 × 10^3) **3** appears to be the most probable structure.[4]



3

The Temperature-Dependent Pmr Spectrum.—The 90-MHz proton magnetic resonance spectrum of the ethoxy dimer in $CDCl_3$ solution at 0, 25, and 40° is shown in Figure 1. The line broadening and narrowing effects shown in the figure are reversible, although samples heated for extended periods show peaks due to the decomposition product, 10-ethoxy-9-phenanthrol. The small triplet at δ 1.6 is assigned to the latter compound (Figure 1). Complete resolution of the spectrum for quantitative line width studies of the rate of dissociation is prevented by the presence of extra sets of peaks assigned to different conformers of the dimer.[5] These include three different and only partly resolved methyl group triplets centered at δ 0.6, 0.8, and 1.3, and overlapping quartets in the region of δ 2.8–3.7.

(1) E. Müller, K. Schurr, and K. Scheffler, *Justus Liebigs Ann. Chem.*, **627**, 132 (1954).

(2) R. E. Schwerzel, Dissertation, Florida State University, 1970.

(3) D. J. Williams and R. Kreilick, *J. Amer. Chem. Soc.*, **90**, 2775 (1968).

(4) Better evidence for **3** was sought by attempting to tautomerize the dimer to the totally aromatic ether by means of acidic and basic catalysts. Unfortunately, the prevailing reaction in all of these experiments was decomposition to phenanthrenequinone, for which polar as well as radical mechanisms can be envisioned.

(5) Molecular models indicate two possible isomeric folded structures for the dimer. Both structures are more compact than an extended structure and might be favored by the internal pressure of the solvent if not by π complexing between the ring systems of the two moieties. In one of the folded structures, each ethoxy group of one moiety is in the shielding region of an aromatic ring of the other moiety; the signal from these groups may be the large triplet at δ 0.6. In the other folded structure, the ethoxy groups are shielded less and to different extents, giving the triplets at δ 0.8 and 1.3.

Epr Spectra and Extent of Dissociation.—Both dimers give multiline epr spectra in degassed 0.10 *M* solution.[2] The spectra are centered about $g = 2.0038$.

The spectrum of **1a**, from the chloro dimer in C_6H_5Cl at 120°, consists of at least 36 apparent lines, most of them showing signs of incipient further resolution. However, the appearance of this spectrum is not noticeably affected by changes either in solvent or temperature, except for its intensity. The width is about 18 G.

The spectrum of **1b**, from the ethoxy dimer, has even more peaks, and in this case additional hyperfine splitting appears at low temperatures and in certain solvents. The width of these spectra is about 16 G. Splittings of about 0.1 G are resolved in tetrahydrofuran (THF) at 23.5°, but not at 52.5°. The spectrum in CCl_4 at 23.5° is also less resolved, resembling that seen in THF at 52.5°.[6]

Extents of dissociation were determined by double integration of overmodulated first-derivative spectra, using galvinoxyl as a standard. The dissociation constants at 25° (by interpolation of van't Hoff plots) are given in Table I. Because of the limited solubility of

TABLE I
DISSOCIATION EQUILIBRIUM CONSTANTS[a]

Solvent	$10^3 K_{298}$[b]	$\Delta\bar{H}^0$, kcal/mol, ±2	$\Delta\bar{S}^0$, cal/mol deg, ±7
CCl_4	1.2	21[c]	29
THF	2.9	19[c]	25
C_6H_6	3.3	16[d]	16
$CHCl_3$	4.1	17[c]	19
$(C_6H_5Cl)^f$	$(0.10)^f$	$(8.5)^{e,f}$	$(-17)^f$

[a] The ethoxy dimer **3** unless otherwise noted. [b] Interpolated from the van't Hoff plots. [c] Temperature range, 255–313°K. [d] Temperature range, 293–313°K. [e] Temperature range, 298–392°K. [f] The chloro dimer **2**.

the chloro dimer, its dissociation constant was determined in only one solvent. The dissociation constant of the ethoxy dimer appears to increase with increasing internal pressure of the solvent, in contrast to that of N_2O_4, which decreases.[7] Solvent effects on the enthalpies and entropies of dissociation are small relative to the experimental error, but both quantities appear to be significantly lower for the chloro dimer than for the ethoxy dimer.

The rate of dissociation of the ethoxy dimer is fast compared with the time of mixing with a radical trapping agent. Thus the dimer is instantly reduced to the phenanthrol by 2,5-di-*tert*-butylhydroquinone. Stopped flow measurements of the rate were not attempted because of overlap of the absorption spectrum of the dimer with that of 2,5-di-*tert*-butyl-1,4-benzoquinone.

The Decomposition of the Ethoxy Dimer 3.—Degassed solutions of the ethoxy dimer slowly decompose

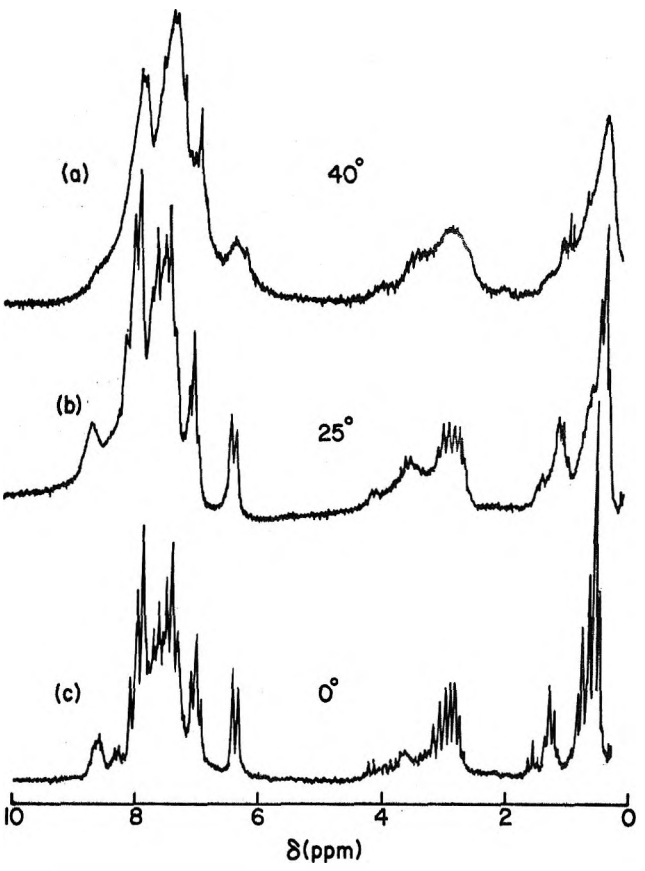
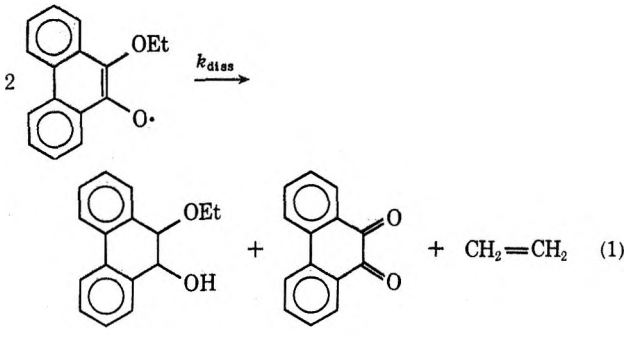


Figure 1.—90-MHz pmr spectrum of the ethoxy dimer in $CDCl_3$.

to the phenanthrol, phenanthrenequinone, and ethylene, as indicated in eq 1. Phenanthrenequinone has been



identified as a product in a previous study.[1] If the product mixture is exposed to air, the yield of phenanthrenequinone is greater than the theoretical value because of oxidation of the phenanthrol.

Assuming that the dissociation equilibrium is fast and that the mechanism of the decomposition reaction is a disproportionation of the radicals, the rate of disappearance of the radicals will be a first-order process with rate constant $0.5k_{diss}K$. Using the epr signal to monitor the concentration of radicals, $0.5k_{diss}K$ for a 0.02 *M* solution of the dimer in CCl_4 at 67° was found to be 0.65×10^{-6} sec^{-1} and k_{diss} 19 M^{-1} sec^{-1}. A rate constant of about 12 M^{-1} sec^{-1} is estimated for the disproportionation of 2,6-di-*tert*-butyl-4-isopropylphenoxy radicals in cyclohexane at 67°.[8]

(6) It is not known what process is responsible for the line broadening and loss of resolution, but we note that the dissociation constant (Table I) is higher in THF than in CCl_4, which may imply a lower recombination rate and less lifetime broadening in THF. A more likely explanation has to do with the rate of intramolecular rotation of the ethoxy substituent. THF has a higher internal pressure than CCl_4, and using a cavity model for the rotation, it should be faster in the latter solvent.

(7) R. J. Ouellette and S. H. Williams, *J. Amer. Chem. Soc.*, **93**, 466 (1971).

(8) C. D. Cook and B. E. Norcross, *J. Amer. Chem. Soc.*, **81**, 1176 (1959).

Experimental Section

10-Chloro-9-phenanthrol and the chloro dimer **2** were prepared by the method of Müller, *et al.*[1]

10-Ethoxy-9-phenanthrol was prepared by a modification of the procedure of Forneau and Matti.[9]

A slurry of 45 g (0.217 mol) of phenanthrenequinone in a mixture of 375 ml of 95% ethanol and 45 ml of H_2O was stirred and heated to reflux. Then, with *vigorous* stirring and refluxing, SO_2 was passed into the reaction mixture for 8 hr, and the dark reddish-brown solution was filtered and cooled to −20° for several hours to crystallize the product. Additional material can be obtained by diluting the filtrate with 10–20 ml of H_2O and cooling overnight at −20°. It is essential to protect the product from air, as it is very easily oxidized, especially when impurities are present. It is best purified by several recrystallizations from warm 95% ethanol with rapid cooling to −20°, followed by crystallization from hexane and then again from ethanol. The product is colorless, mp 76–77°. The yield (of pure material) is 8–10 g.

Anal. Calcd for $C_{16}H_{14}O_2$: C, 80.68; H, 5.88. Found: C, 80.62; H, 5.88.

(9) E. Forneau and J. Matti, *Bull. Soc. Chim. Fr.*, **9**, 633 (1942).

The ethoxy dimer **3** was prepared using both Müller's procedure[1] and that of Goldschmidt,[10] the properties of the product being the same. Recrystallization from a mixture of chloroform and ethanol gave material melting at 137–138° and with less included solvent of crystallization than recrystallization from the solvent recommended previously.[1,10]

Equilibrium Studies.—All epr spectra were measured in degassed solutions in the same quartz sample tube. The output from the overmodulated first derivative signal was digitized using a Dymec digital voltmeter and a Hewlett-Packard digital recorder. The data were then transferred to punch cards and doubly integrated by means of DINGRT,[11] a program which includes automatic base-line correction after the first integration. The integrated absorptions were then converted to concentrations using a calibration curve based on galvinoxyl.

Registry No.—3, 35099-79-7; 10-ethoxy-9-phenanthrol, 35099-80-0.

Acknowledgment.—The authors wish to acknowledge support of this research by the Army Research Office (Durham) and by the National Science Foundation.

(10) S. Goldschmidt and C. Steigerwald, *Chem. Ber.*, **55**, 3197 (1922).
(11) Supplied by Dr. R. H. Johnsen, Florida State University.

The Induced Decomposition of *tert*-Butyl Peroxide by Ether Radicals. A Nuclear Magnetic Resonance Study

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An examination of the products of the decomposition of *tert*-butyl peroxide in 4-chlorobenzyl ethyl ether and 3,4-dichlorobenzyl phenyl ether shows that the formed mixed acetals of the type ArCH(OR)O-*t*-Bu partially decomposed. The formation of the mixed acetal PhCH(OMe)O-*t*-Bu in the decomposition of *tert*-butyl peroxide in benzyl methyl ether was found to be promoted in the presence of added chlorinated solvents. *o*-Dichlorobenzene was found to promote the induced decomposition of the peroxide by several ether radicals; the mixed acetal $CH_3CH(OEt)O$-*t*-Bu was also isolated from a reaction in diethyl ether.

Although for a long time it was commonly believed that *tert*-butyl peroxide is inert to radical-induced decomposition, a property which has made it superior to other organic peroxides, evidence recently obtained indicates that in a number of solvents induced decomposition does in fact occur.[1] In certain primary and secondary alcohols and amines Huyser[2,3] has reported that induced decomposition of the peroxide occurs by hydrogen transfer. In alkyl benzyl ethers $ArCH_2OR$, however, a direct attack of the ether radical on the peroxo linkage has been postulated.[4]

The present paper reports a further study of the reaction products of these systems by nmr spectroscopy and discusses the nature of the induced decomposition reaction.

Results and Discussion

α-Alkoxybenzyl radicals $ArĊHOR$, generated by the decomposition of *tert*-butyl peroxide in alkyl benzyl ethers, are known to undergo the following reactions (eq 1–4). Earlier work[1] has shown that for the series

$$2ArĊHOR \longrightarrow (ArĊHOR)_2 \quad (1)$$

$$ArĊHOR \longrightarrow ArCHO + R\cdot \quad (2)$$

$$ArĊHOR + t\text{-}Bu_2O_2 \longrightarrow ArCH(OR)O\text{-}t\text{-}Bu + t\text{-}BuO\cdot \quad (3)$$

$$ArĊHOR + t\text{-}BuO\cdot \longrightarrow ArCH(OR)O\text{-}t\text{-}Bu \quad (4)$$

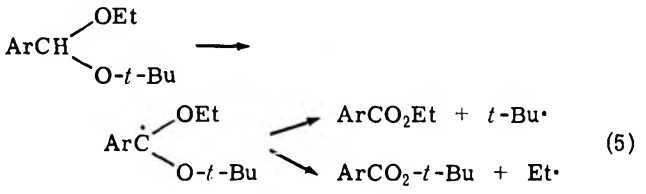
of ethers $PhCH_2OR$ (R = Me, Et, *i*-Pr, *t*-Bu, and Ph) the radical PhĊHOR only undergoes dimerization and fragmentation reactions (eq 1 and 2). However in chloro substituted benzyl ethers, $ClC_6H_4CH_2OR$ and $3,4\text{-}Cl_2C_6H_3CH_2OR$, kinetic results and the isolation of mixed acetals ArCH(OR)O-*t*-Bu have provided evidence for the induced decomposition and cross-dimerization pathways (eq 3 and 4).[4,5]

4-Chlorobenzyl Ethyl Ether.—In the decomposition of *tert*-butyl peroxide in several alkyl 3,4-dichlorobenzyl ethers it was found that 3,4-dichlorobenzaldehyde was produced in surprisingly high yields (44–88%).[1] Since this is much greater than that expected from simple radical fragmentation (*e.g.*, PhĊHOMe gives only 10% benzaldehyde), it was suspected that the aldehyde must have originated from another source.

An examination of the reaction products from the decomposition of *tert*-butyl peroxide in 4-chlorobenzyl ethyl ether by nmr spectroscopy revealed that in addition to the expected products, *viz.*, 4-chlorobenzaldehyde, the dimer $(4\text{-}ClC_6H_4ĊHOEt)_2$ and the mixed acetal $4\text{-}ClC_6H_4CH(OEt)O$-*t*-Bu, smaller quantities of 4-chlorobenzaldehyde diethyl acetal $4\text{-}ClC_6H_4CH$-

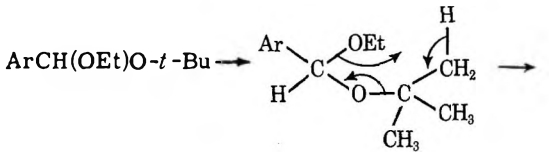
(1) S. H. Goh, R. L. Huang, S. H. Ong, and I. Sieh, *J. Chem. Soc., C*, 2282 (1971).
(2) E. S. Huyser and A. A. Kahl, *Chem. Commun.*, 1238 (1969).
(3) E. S. Huyser, C. J. Bredeweg, and R. M. Vanscoy, *J. Amer. Chem. Soc.*, **86**, 4148 (1964).
(4) R. L. Huang, T.-W. Lee, and S. H. Ong, *J. Chem. Soc., C*, 2522 (1969).
(5) S. H. Goh and S. H. Ong, *J. Chem. Soc., B*, 870 (1970).

$(OEt)_2$, ethyl 4-chlorobenzoate, *tert*-butyl 4-chlorobenzoate, and isobutylene were also formed. The esters are probably derived from the hydrogen abstraction of the mixed acetal[6] as shown. Isobutylene and 4-



(5)

chlorobenzaldehyde diethyl acetal were found to arise *via* the thermal decomposition of the mixed acetal probably by the following mechanism (eq 6 and 7). Since



$$ArCHO + EtOH + CH_2{=}C(CH_3)_2 \quad (6)$$

$$ArCH(OEt)O\text{-}t\text{-}Bu + EtOH \longrightarrow ArCH(OEt)_2 + t\text{-}BuOH \quad (7)$$

aldehyde is produced by these reactions, its formation in high yields can be accounted for in cases where the mixed acetals are thermally unstable.

3,4-Dichlorobenzyl Phenyl Ether.—The reaction of *tert*-butyl peroxide with this ether gave mainly 3,4-dichlorobenzaldehyde but none of the mixed acetal. This is rather surprising for two reasons. Firstly, it is unlikely that the radical ArĊHOPh generated would undergo fragmentation to give the highly unstable phenyl radical.[1,7] Secondly, the relative rate of decomposition of *tert*-butyl peroxide in this ether is very rapid and indicates that induced decomposition of the peroxide has occurred.[1] An examination of the products by nmr spectroscopy however revealed that the formation of aldehyde was accompanied by an approximately similar quantity of isobutylene. This observation could be accounted for as being due to the thermal decomposition of an initially formed mixed acetal product (analogous to eq 6). These findings indicate that the induced decomposition of the peroxide occurs readily in alkyl 3,4-dichlorobenzyl ethers; changes in the alkyl group (Me, Et, *i*-Pr, and Ph) do not significantly affect the extent of induced decomposition.

Effect of *o*-Dichlorobenzene.—An examination of the previous results[1,4] of the decomposition of *tert*-butyl peroxide in a number of alkyl benzyl ethers $ArCH_2OR$ reveals the fact that the chloro substituted ethers are the most significant in causing induced decomposition of the peroxide. This suggests that the medium, *i.e.* the chloro-substituted benzyl ethers, may at least in part be responsible for the induced decomposition pathway. Experiments to verify this possibility were conducted with benzyl methyl ether and an added solvent, and the results are given in Table I. The formation of the mixed acetal PhCH(OMe)O-*t*-Bu product was found to be dependent on the solvent used; the

(6) E. S. Huyser and D. T. Wang, *J. Org. Chem.*, **29**, 2720 (1964).
(7) M. S. Kharasch, A. Fono, and W. Nudenberg, *ibid.*, **16**, 113 (1951).

Table I
Decomposition of *tert*-Butyl Peroxide in Benzyl Methyl Ether with Added Solvent[a]

Solvent	% PhCH(OMe)O-*t*-Bu	% PhCHO
None[b]	3	10
o-Dichlorobenzene[c]	19	8
o-Dichlorobenzene	42	13
Chlorobenzene	16	7
p-Dichlorobenzene	13	6
1,2,3-Trichlorobenzene	39	12
m-Bromochlorobenzene	26	10
Dichloromethane	21	5
Benzonitrile	0	1
Others[d]	0	1

[a] Reactions of benzyl methyl ether (10 mmol), *tert*-butyl peroxide (2.5 mmol), and the solvent (6 mmol) at 110° for 72 hr. Percentage yields are based on *tert*-butyl peroxide. [b] Reference 1. [c] Only 3 mmol of solvent was used. [d] Includes acetonitrile, dimethylformamide, diphenyl ether, and bromobenzene.

chloro substituted benzene solvents in particular show a dramatic effect in promoting induced decomposition but other solvents including dimethylformamide, acetonitrile, benzonitrile, and diphenyl ether fail to do so.

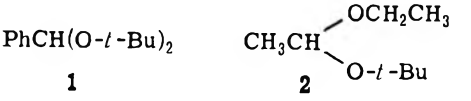
The effect of added *o*-dichlorobenzene in promoting the induced decomposition of *tert*-butyl peroxide was also examined for the series of benzyl alkyl ethers $ArCH_2OR$ and the results are summarized in Table II.

Table II
Decomposition of *tert*-Butyl Peroxide in Benzyl Alkyl Ethers in the Presence of *o*-Dichlorobenzene[a]

$ArCH_2OR$	Registry no.	% ArCH(OR)O-*t*-Bu (δ)[b]	ArCHO
4-$ClC_6H_4CH_2OMe$		45 (5.67)	10
4-$ClC_6H_4CH_2OMe$	1195-44-4	36[c]	11
$PhCH_2OMe$		42 (5.73)	12
$PhCH_2OMe$	538-86-3	40 (5.69)	9
$PhCH_2O$-*i*-Pr	937-54-2	25 (5.70)	10
$PhCH_2O$-*t*-Bu	3459-80-1	40 (5.69)	12
$PhCH_2O$-c-C_6H_{11}	16224-09-2	32 (5.68)	7
p-$MeC_6H_4CH_2OMe$	3395-88-8	50 (5.71)	12

[a] Reactions of the ether $ArCH_2OR$ (10 mmol), *tert*-butyl peroxide (2.5 mmol), and *o*-dichlorobenzene (6 mmol) at 110° for 72 hr. Percentage yields are based on *tert*-butyl peroxide. [b] Chemical shift of the benzylic proton in ppm downfield from TMS in the reaction mixture. [c] Without *o*-dichlorobenzene (ref 4); the other ethers yield no or negligible amounts of mixed acetal without added dichlorobenzene.

Mixed acetals ArCH(OR)O-*t*-Bu, estimated by their characteristic absorptions at δ ~5.7, were obtained in all cases. In the case of 4-chlorobenzyl methyl ether, which gives the mixed acetal without added dichlorobenzene, the yield of the mixed acetal was increased by the solvent added. Interestingly, despite the high tendency of α-*tert*-butoxybenzyl radical PhĊHO-*t*-Bu to undergo fragmentation[1] and the steric restriction imposed by the *tert*-butoxy group, a 40% yield of benzaldehyde di-*tert*-butyl acetal (**1**) could be isolated.



Further, it was found that the reaction could be extended to diethyl ether which gave 43% of the mixed acetal (2). It may be noted that decomposition of the peroxide in the pure ether does not give this product.[3]

Mechanism of the Induced Decomposition Reaction.—The mechanism of the induced decomposition of *tert*-butyl peroxide by ether radicals may be discussed in the light of the new findings. It may be noted that other cases of radical-induced decomposition of the peroxide occurs by hydrogen transfer.[3,8] In the decomposition of *tert*-butyl peroxide in 1-butanol, for example, a kinetic deuterium isotope effect has been observed. In the case of ether radicals induced decomposition can take place by electron transfer or by direct attack on the peroxo linkage. The former mechanism has been suggested to be a key step in many induced decomposition reactions of acyl peroxides.[9] This mechanism is probably important for the induced decomposition of benzoyl peroxide by ether radicals.[10,11] Although *tert*-butyl peroxide may be expected to be a much poorer electron acceptor compared to benzoyl peroxide, recent evidence has shown the possibility of a *tert*-butyl peroxide radical anion species.[12]

The present results show that chlorinated solvents play an important role in promoting the formation of mixed acetals; medium polarity[13] or a simple dilution effect of the added solvent does not appear to be important. Further, chloride ion was not detectable in the reaction products by silver nitrate solution and only a negligible amount of *o*-dichlorobenzene was consumed at the end of each reaction. These results may be attributed to a complexing of the ether radical to *o*-dichlorobenzene (**3**), which should be favorable in view

$$\underset{}{\text{PhĊHOR}}\ C_6H_4Cl_2 \rightleftarrows \underset{\mathbf{3}}{\overset{+}{\text{PhĊHOR}}}\ C_6H_4Cl_2\cdot^-$$

of the donor property of the radical.[14] (This, however, may not be the complete explanation since in the case of dichloromethane it is difficult to see how complexing could occur.) The direct effect of complexing would be the inhibition, by polar and steric effects, of radical dimerization (which is the major reaction of PhĊHOR radicals in the absence of dichlorobenzene) and thus allowing pathways leading to mixed acetal formation to compete favorably. Since the preliminary kinetic data indicate that the formation of mixed acetal is accompanied by enhanced rate of decomposition of the peroxide, the induced decomposition reaction must be important. This can occur by direct interaction of the peroxide with **3** but the possibility of electron transfer as important step(s) in the mechanism, however, cannot be excluded; such electron transfers through chlorine atom as bridges are better known in inorganic systems.[15]

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(12) T. Shida, *J. Phys. Chem.*, **72**, 723 (1968).

(13) E. S. Huyser in "Advances in Free-Radical Chemistry," Vol. 1, G. H. Williams, Ed., Logos, 1965, Chapter 3.

(14) R. L. Huang, T.-W. Lee, and S. H. Ong, *J. Chem. Soc., C*, 40 (1969).

(15) H. Taube, "Electron Transfer Reactions of Complex Ions in Solution," Academic Press, New York, N. Y., 1970.

Experimental Section

Nmr spectra were obtained with a Hitachi Perkin-Elmer R20B spectrometer (60 MHz) and are given in δ (ppm) with TMS as internal standard. Gas chromatography (glc) was performed on a Varian-Aerograph 1520 instrument using 6-ft QF-1 or 6-ft SE-30 columns.

tert-Butyl peroxide was purified by distillation under reduced pressure before use. Benzyl alkyl ethers were prepared and purified as reported previously.[1,4] Other solvents were redistilled and dried over 4-Å molecular sieves.

4-Chlorobenzyl Ethyl Ether.—A mixture of the ether (17.1 g, 100 mmol) and *tert*-butyl peroxide (2.92 g, 20 mmol) was heated in a sealed Carius tube at 110° for 96 hr. The reaction mixture was fractionally distilled under reduced pressure to give three fractions: mainly unreacted ether (12 g), impure mixed acetal (2.5 g), and a residue (2.5 g). Preparative glc afforded the following products (yields are based on ether consumed): (a) **the mixed acetal** 4-$ClC_6H_4CH(OEt)O$-*t*-Bu (33%), δ (CCl_4) 7.25 (4 H, broad s), 5.66 (1 H, s), 2.9–3.6 (2 H, m), 1.30 (9 H, s), and 1.07 (3 H, t, 7 Hz), hydrolysis by dilute H_2SO_4 gave 4-ClC_6H_4-CHO, EtOH, and *t*-BuOH; (b) **4-chlorobenzaldehyde diethyl acetal** (14%), δ (CCl_4) 7.28 (4 H, broad s), 5.41 (1 H, s), 3.46 (4 H, q, 7 Hz), and 1.19 (6 H, t, 7 Hz), hydrolysis by dilute H_2SO_4 gave 4-chlorobenzaldehyde and ethanol; (c) **ethyl 4-chlorobenzoate** (2%), δ (CCl_4) 7.93 (2 H, d, 9 Hz), 7.33 (2 H, d, 9 Hz), 4.33 (2 H, q, 7 Hz), and 1.40 (3 H, t, 7 Hz); (d) ***tert*-butyl 4-chlorobenzoate** (1%), δ (CCl_4) 7.86 (2 H, d, 9 Hz), 7.29 (2 H, d, 9 Hz), and 1.57 (9 H, s); and (e) **4-chlorobenzaldehyde** (10%). *meso*-α,α'-Diethoxy-4,4'-dichlorobibenzyl (10%), δ (CCl_4) 7.17 (2 × 4 H, s), 4.10 (2 × 1 H, s), 2.9–3.5 (2 × 2 H, m), and 1.10 (2 × 3 H, t, 7 Hz), crystallized out from the residue.

A pure sample of the mixed acetal (50 mg) on heating in a sealed tube at 110° for 96 hr gave 4-chlorobenzaldehyde diethyl acetal, 4-chlorobenzaldehyde, and isobutylene.

3,4-Dichlorobenzyl Phenyl Ether.—The reaction of the ether (4.4 mmol) with *tert*-butyl peroxide (1.8 mmol) at 130° for 48 hr gave upon distillation and glc the following products (yields are based on ether consumed): (a) 3,4-dichlorobenzaldehyde (41%), (b) phenol (3%), and (c) a mixture of *o*-*tert*-butoxy- and *p*-*tert*-butoxyphenols (4%), δ (CCl_4) 6.5–7.2 (total 9 H, both s, O-*t*-Bu), ν_{OH}(CCl_4) 3600 and 3200 cm^{-1}. Isobutylene (50%) could also be detected in the crude reaction mixture.

Reaction of Benzyl Methyl Ether with *tert*-Butyl Peroxide in Different Solvents.—Reactions were carried out using the ether (10 mmol), *tert*-butyl peroxide (2.5 mmol), and the solvent (6 mmol) in tubes (sealed under nitrogen) heated at 110° for 72 hr. The following reaction products PhCH(OMe)O-*t*-Bu, $PhCH(OMe)_2$, PhCOOMe, and PhCHO can be estimated by nmr after an addition of known quantity of trichloroethylene or tetrachloroethane as standard to the reaction mixture (Table I). Using authentic samples in *o*-dichlorobenzene solvent the characteristic chemical shifts 5.73, 3.04, and 1.19 ppm for the mixed acetal PhCH(OMe)O-*t*-Bu, 5.23 and 3.21 ppm for the acetal $PhCH(OMe)_2$, 3.72 ppm for methyl benzoate, and 9.77 ppm for benzaldehyde can be distinguished. When shaken with 1 drop of 0.5 *M* sulfuric acid the absorptions of the mixed acetal PhCH(OMe)O-*t*-Bu immediately vanish, those of the acetal $PhCH(OMe)_2$ also disappear after a few minutes, and corresponding increases in the aldehyde absorption were observed.

Mixed acetals can be isolated as described previously by fractional distillation under reduced pressure.[4] Benzaldehyde di-*tert*-butyl acetal was isolated and purified by glc, δ (CCl_4) 7.1–7.3 (5 H, m), 5.62 (1 H, s), and 1.17 (18 H, s); hydrolysis by water gave benzaldehyde and *tert*-butyl alcohol.

In all the reactions using *o*-dichlorobenzene and dichloromethane as solvents no free chloride ion in the products was detectable by silver nitrate solution. Glc showed that only a negligible amount of *o*-dichlorobenzene was consumed after the reaction.

Reactions of Benzyl Alkyl Ethers with *tert*-Butyl Peroxide in the Presence of *o*-Dichlorobenzene.—Reactions were carried out as described above using the ether (10 mmol), *tert*-butyl peroxide (2.5 mmol), and *o*-dichlorobenzene (6 mmol), and the reaction products, *viz.*, ArCH(OR)O-*t*-Bu, $ArCH(OR)_2$, and ArCHO, were estimated by their characteristic nmr absorption peaks; the mixed acetal when shaken with 1 drop of dilute acid gave the aldehyde. The results are given in Table II. In cases where the

mixed acetals were relatively unstable, isobutylene could be detected from its characteristic nmr signals, *i.e.*, δ 4.63 (septet, 1.1 Hz) and 1.64 (t, 1.1 Hz).

Diethyl Ether.—The reaction of ether under the same conditions as above gave a 43% yield of the mixed acetal MeCH(OEt)O-*t*-Bu. The crude product was short path distilled at 100° (bath) and 150-mm pressure and purified by preparative glc, δ (CCl_4) 1.11 (3 H, t, 7 Hz), 1.17 (3 H, d, 5 Hz), 1.19 (9 H, s), 3.43 (2 H, q, 7 Hz), and 4.84 (1 H, q, 5 Hz). Hydrolysis by dilute sulfuric acid gave acetaldehyde, ethanol, and *tert*-butyl alcohol.

Registry No.—3,4-Dichlorobenzyl phenyl ether, 33598-40-2; *tert*-butyl peroxide, 75-91-2.

Acknowledgments.—I thank Yap Chuan Hoe, Ong Lam Eng, and Miss Tan Chear Eng for some preliminary experiments.

Naphthyridine Chemistry. XIV. The Meisenheimer Reaction of the 1,X-Naphthyridine 1-Oxides

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The treatment of the 1,X-naphthyridine 1-oxides with phosphorus oxychloride affords the 2-, 3-, and 4-chloro-1,X-naphthyridines in varying amounts depending upon the position of the nonoxidized nitrogen atom. The 2-chloro compounds formed decrease from 0.60 to 0.13 mol ratio in the sequence 1,7-, 1,5-, 1,8-, 1,6-naphthyridine 1-oxide, while, in the same sequence, the 3-chloro isomers increases from 0.03 to 0.02 and the 4-chloro isomers from 0.37 to 0.67 mol ratio. Possible mechanisms to account for these changes are discussed.

Several recent papers[1-3] have described the results of studies of the Meisenheimer reaction on various naphthyridine *N*-oxides. In order to further delineate the effect that the position of the nonoxidized nitrogen atom has upon the product distribution in the naphthyridine 1-oxides when they are treated with phosphorus oxychloride, we have examined the behavior of the 1-oxides of 1,7- (**1**) and 1,8-naphthyridine (**2**).

When 1,7-naphthyridine 1-oxide (**1**) is treated with phosphorus oxychloride, a four-component mixture (as established by tlc and vpc) is obtained. Preparative scale vpc allows the separation of this mixture into three components. The compound with the shortest retention time is 1,7-naphthyridine (4% of the total reaction mixture); the second component (35% of the total reaction mixture) has a molecular formula of $C_8H_5N_2Cl$. The melting point of this material, as collected from the gas chromatograph, is 108–110°. Since the melting point for this compound, whose nmr spectrum is that expected for 4-chloro-1,7-naphthyridine, is 121–122°,[4] it appeared that we were dealing with a mixture. When this substance was twice sublimed and finally recrystallized from cyclohexane, its melting point was raised to that reported for the 4-chloro-1,7-naphthyridine (**3**). Thus, the material collected from the gas chromatograph is a mixture. In order to identify the component which "contaminated" the vpc peak, a sample of the crude reaction products was hydrolyzed with aqueous base in the anticipation that any 2- or 4-chloro-1,7-naphthyridine would be converted to the corresponding dihydro-oxo compounds, while any 3-chloro-1,7-naphthyridine that might be present would not be affected by these conditions.

In this fashion we obtained a two-component mixture consisting of 1,7-naphthyridine and 3-chloro-1,7-naphthyridine (**5**). The identity of these two products was established by comparison with authentic samples. It is of interest to note that the 3-chloro- and the 4-chloro-1,7-naphthyridines have the same retention times on several vpc columns and, consequently, the very minor amount of 3-chloro-1,7-naphthyridines formed in this reaction is not detectable in the presence of the substantial amounts of 4-chloro-1,7-naphthyridine formed. The amount of 3-chloro-1,7-naphthyridine obtained from this reaction could, consequently, not be directly calculated by an analysis of the vpc traces alone. The data presented in Table I are those obtained by taking this fact into account.

The third component (56% of the total reaction mixture) has a molecular formula of $C_8H_5N_2Cl$ and is identified as 2-chloro-1,7-naphthyridine (**4**) by an analysis of its nmr spectrum. This spectrum (Table II) shows the presence of one deshielded singlet (τ 0.61) and two AB patterns. The sizes of the coupling constants of the AB patterns (9.0 and 6.0 Hz, respectively) require that both of the systems involve coupling of protons on vicinal carbon atoms, thus establishing structure **4** as the correct one.

The fourth component, which appears as a very minor shoulder on the trailing edge of the peak due to the 2-chloro-1,7-naphthyridine, is estimated to correspond to 2% of the total reaction mixture. This material is neither 5-chloro-[5] nor 8-chloro-1,7-naphthyridine[6] by gc comparisons of these compounds with the unknown, and has not yet been identified.

In order to assure ourselves that neither the 2-chloro- (**4**) nor the 4-chloro-1,7-naphthyridine (**3**) is hydrolyzed during the aqueous work-up, we modified the usual procedure by utilizing methanol in place of water. When this was done, and the methanolic solution was heated with sodium methoxide until tlc no longer showed the presence of either the 2-chloro- or 4-chloro-1,7-naphthyridine (a total of 12 hr), we isolated a mixture of the 2- (**6**) and 4-methoxy-1,7-naphthyridines (**7**). An analysis of the nmr spectrum of this mixture showed that the ratio of 2- to 4-methoxy derivatives is

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(6) H. Rapoport and A. D. Batcho, *J. Org. Chem.*, **28**, 1753 (1963).

TABLE I
RELATIVE PROPORTIONS OF THE MEISENHEIMER REACTION PRODUCTS OF THE 1-OXIDES OF 1,7- AND 1,8-NAPHTHYRIDINES

	Substituent					
Reactant	Nil	2-Chloro	3-Chloro	4-Chloro	2-Methoxy	4-Methoxy
1,7-Naphthyridine 1-oxide (1)	4[a]	56[a]	3[a]	35[a]	63[b]	37[b]
1,8-Naphthyridine 1-oxide (2)		36	7	57	40[b]	60[b]

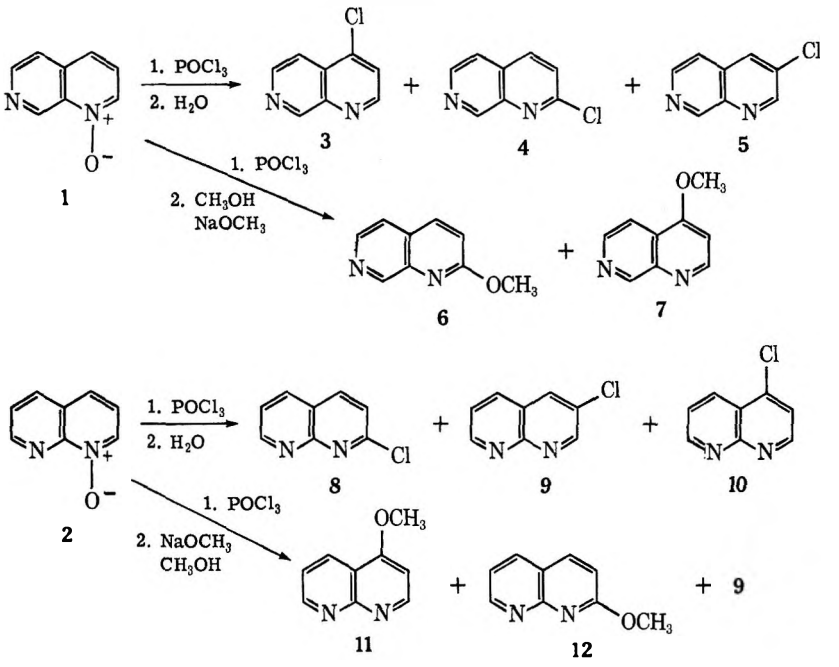
[a] These values were obtained by means of gc analysis. [b] These values were obtained from an analysis of the nmr spectrum of the reaction mixture and do not include the parent and 3-chloro isomers formed.

TABLE II
NMR SPECTRAL DATA OF SOME SUBSTITUTED 1,X-NAPHTHYRIDINES

	Chemical shifts, τ							Coupling constants, Hz					
Compound[a]	H_2	H_3	H_4	H_5	H_6	H_7	H_8	J_{23}	J_{24}	J_{34}	J_{56}	J_{57}	J_{67}
2-Chloro-1,7-naphthyridine (4)		2.48	1.94	2.40	1.39		0.61			9.0	6.0		
3-Chloro-1,7-naphthyridine (5)	1.14		1.93	2.46	1.41		0.56		2.0		5.5		
4-Chloro-1,7-naphthyridine (3)	1.12	2.34		2.02	1.28		0.46	5.0			6.0		
2-Methoxy-1,7-naphthyridine[b] (6)		2.98	2.11	2.51	1.55		0.78			8.8	5.5		
4-Methoxy-1,7-naphthyridine[c] (7)	1.21	3.17		2.11	1.44		0.57	5.0			6.0		
2-Chloro-1,8-naphthyridine (8)		2.53	1.84	1.78	2.49	0.89				8.5	8.0	2.0	4.4
3-Chloro-1,8-naphthyridine (9)	1.00		1.84	1.86	2.48	0.90			2.5		8.0	1.9	4.2
4-Chloro-1,8-naphthyridine (10)	0.98	2.42		1.41	2.40	0.82		4.8			8.5	2.0	4.2
2-Methoxy-1,8-naphthyridine[d] (11)		3.03	2.04	1.93	2.67	1.05				8.8	8.0	2.0	4.0
4-Methoxy-1,8-naphthyridine[e] (12)	1.10	3.24		1.48	2.59	0.95		5.0			8.0	2.0	4.0

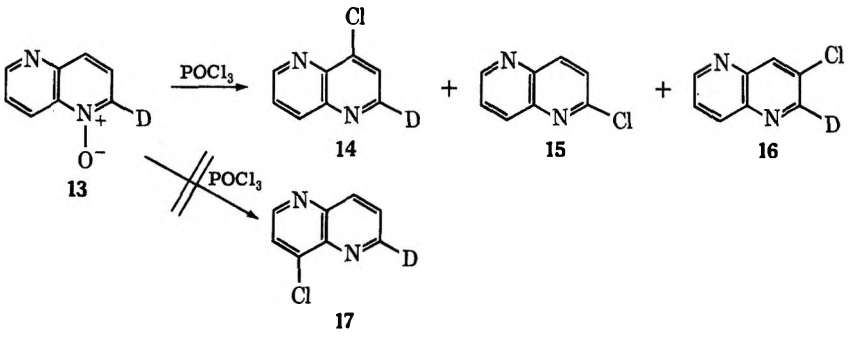
[a] Dilute solutions in $CDCl_3$. [b] $-OCH_3$, 5.96. [c] $-OCH_3$, 5.99. [d] $-OCH_3$, 6.01. [e] $-OCH_3$, 5.84.

SCHEME I



63:37%. Column chromatography afforded the 2-methoxy- (6) and the 4-methoxy-1,7-naphthyridines (7) in pure form. Thus, the results of the aqueous and the methanolic work-up procedures are identical, and none of the chloro compounds are hydrolyzed during the aqueous isolation procedure.

The treatment of 1,8-naphthyridine 1-oxide (2) and separation of the resulting mixture by column chromatography affords three pure components. In order of their elution they are 2-chloro- (8), 3-chloro- (9), and 4-chloro-1,8-naphthyridine (10) (36, 7, and 57%, respectively). The 2-chloro-1,8-naphthyridine (8) was identified by comparison with a sample obtained by an unequivocal synthesis (see Experimental Section). The 3-chloro-1,8-naphthyridine (9) was identified by its nmr spectrum (see Table I) and its stability to base. The 4-chloro-1,8-naphthyridine (10) was identified by an analysis of its nmr spectrum. The spectrum of the 4-chloro-1,8-naphthyridine (10) is typical of that expected for a 4-chloro-1,X-naphthyridine in that H_5 is considerably more deshielded (0.37 ppm) than the same proton in the corresponding naphthyridine itself. Furthermore, the 4-chloro- (10) as well as the 2-chloro-1,8-naphthyridine (8) are readily converted to their corresponding methoxy derivatives (11 and 12) by treatment with methanolic sodium methoxide (see Scheme I). In order to, again, make certain that none of the chloro compounds were hydrolyzed during the aqueous work-up, the isolation was modified, as described for the 1,7-naphthyridine instance, by replacing the water with methanol. Again, no change in the 2- (8) to 4-chloro-1,8-naphthyridine (10) product ratio was detected.



Discussion and Results

A comparison of the product distribution of the various 1,X-naphthyridine 1-oxides, upon treatment with phosphorus oxychloride, demonstrates that the location of the nonoxidized nitrogen atom has a ratio-reversing influence only in the case of the 1,7-naphthyridine, where the amount of 2 isomer (56%) formed predominates over that of the 4 isomer (35%).

The presence of a 6-nitrogen atom drastically increases the amount of 4-chloro (66%) with respect to the amount of 2-chloro (12%) isomer formed.[1] This decrease in the amount of 2-chloro isomer is counteracted by the formation of a substantial amount of 3-chloro-1,6-naphthyridine (20%). Since we have already shown[7] that electrophilic substitution of 1,6-naphthyridine affords 18% of the 3-substituted along with 23% of the 8-substituted isomer, and because no 8-chloro-1,6-naphthyridine is obtained in the Meisenheimer reaction of the 1,6-naphthyridine 1-oxide,[2] the generation of the 3-chloro-1,6-naphthyridine cannot be as a result of electrophilic substitution on some deoxygenated 1,6-naphthyridine 1-oxide in this reaction.

It is also highly improbable that electrophilic substitution would occur at the 3 position of 1,6-naphthyridine 1-oxide[8] or any phosphorylated derivative thereof. Thus, one is left with having to invoke either a free radical or a nucleophilic substitution process.[9]

In considering 1,5-naphthyridine 1-oxide, there exists the possibility that some of the 4-chloro-1,5-naphthyridine might be formed by substitution at C_8 in the 1,5-naphthyridine 1-oxide. In order to test this, we examined the Meisenheimer reaction on 2-deuterio-1,5-naphthyridine 1-oxide (**13**).

An analysis of the reaction products, in the manner described earlier,[1] established that the chlorine atoms in all of the monochloro-1,5-naphthyridines reside in the originally *N*-oxidized ring. Consequently, the 4:2 chloro-1,5-naphthyridine ratio is not artificially increased by halogenation at C_8 of the 1,5-naphthyridine 1-oxide (to form compound **17**).

A reasonable way to examine the various changes in isomer distribution is a comparison of the molar isomer ratios obtained in the different cases (see Table III).

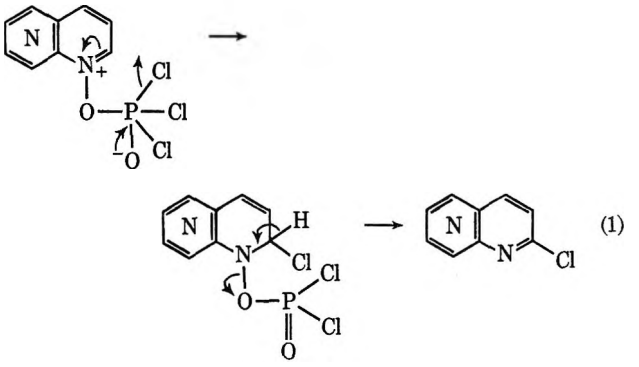
TABLE III
RELATIVE ISOMER RATIOS OF THE VARIOUS CHLORONAPHTHYRIDINES OBTAINED FROM THE MEISENHEIMER REACTION ON 1,X-NAPHTHYRIDINE 1-OXIDES

Compound	2-Chloro isomer	3-Chloro isomer	4-Chloro isomer
1,7-Naphthyridine	0.60	0.03	0.37
1,5-Naphthyridine[a,b]	0.42	0.03	0.55
1,8-Naphthyridine	0.36	0.07	0.57
1,6-Naphthyridine[a]	0.13	0.20	0.67

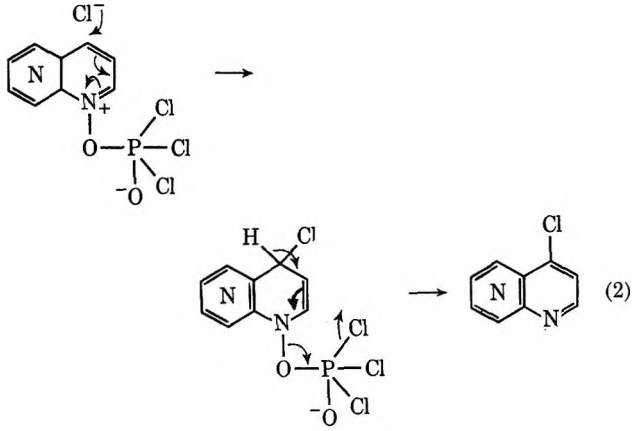
[a] See ref 1. [b] See ref 2.

These data clearly show that in the sequence 1,7-, 1,5-, 1,8-, 1,6-naphthyridine 1-oxides, decreasing amounts of the 2-chloro isomers are formed with concurrently increasing amounts of the 3-chloro and 4-chloro isomers.

The formation of the 2-chloro compounds is envisioned to occur *via* an *intramolecular* process, as exemplified by sequence 1.



On the other hand, the 4-chloro isomers are probably formed by an *intermolecular* process as delineated in sequence 2.[10]



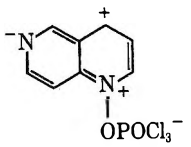
(7) W. W. Paudler and T. J. Kress, *J. Org. Chem.*, **33**, 1384 (1968).

(8) In some, as yet unpublished work, we have found, for example, that bromination, under Eisch conditions, of 1,5-naphthyridine 1-oxide affords 7-bromo-1,5-naphthyridine 1-oxide.

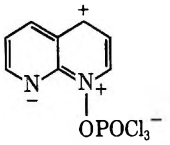
(9) R. A. Abramovitch and G. M. Singer, *J. Amer. Chem. Soc.*, **91**, 5672 (1969), have suggested that the small amounts of 3-chloropyridine that are formed when pyridine *N*-oxide is treated with imidoyl chloride arise *via* the intermediacy of a 2,3-dihydropyridine derivative. This process cannot be significantly responsible for the differing amounts of 3-chloro-1,X-naphthyridines that are formed, since one would anticipate that the 3-chloro-1,5- and 3-chloro-1,7-naphthyridines should be formed in larger amounts than the 3-chloro isomers of the 1,6- and 1,8-naphthyridines.

(10) Similar mechanisms have been proposed for the reaction of pyridine *N*-oxide with phosphorus pentachloride: J. Eisch and H. Gilman, *Chem. Rev.*, **57**, 561 (1957); R. A. Abramovitch and J. G. Saha, *Advan. Heterocycl. Chem.*, **6**, 229 (1966).

If we consider that the intermolecular process is readily facilitated by the presence of a nitrogen atom at either the 6 or 8 position because of some involvement of resonance contributors to the ground state such as **18** and **19**, we can account for the increased formation of

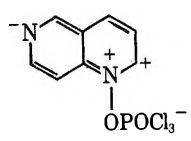


18



19

the 4-chloro isomers in these cases. The corresponding 2 isomer would not be formed by a similar involvement of the 2 position in light of the charge repulsions in the ground state resonance contributors such as exemplified by structures **20** and **21** that would be utilized in these instances.



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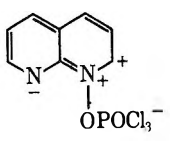

21

The relatively high 4- to 2-chloro ratio in the 1,5-naphthyridine as compared to the 1,7-naphthyridine case may well be a matter of the inductive effect that the α-situated nonoxidized nitrogen atom has upon the C_4 position. This inductive effect certainly would be considerably less in evidence in the 1,7-naphthyridine, where the nonoxidized nitrogen atom is situated in a γ position with respect to C_4.

While these arguments, which involve the classical resonance and inductive considerations, account qualitatively for the observed changes in the isomer distribution in the Meisenheimer reaction of the 1,X-naphthyridine 1-oxides, it is not yet clear how these effects might be employed to explain the changes in the 3-chloro isomers that are formed. One is tempted, however, to suggest that, since the 3-chloro isomer amounts increase along with the 4-chloro isomers, there may well be a mechanistic relationship involved.

Experimental Section

The gas chromatograph used in these studies was an Aerograph Model A-90P-3 equipped with a Disc integrator. The pmr spectra were obtained with a Varian HA-100 instrument and are dilute (8%) solutions in $CDCl_3$ with TMS as internal standard. All column chromatography was done with Bio-Rad Laboratories neutral alumina grade III (Brockmann).

Preparation of 1,7-Naphthyridine 1,7-Dioxide.[11]—A solution containing 1,7-naphthyridine (1.3 g, 10 mmol), $NaWO_4 \cdot 2H_2O$ (0.1 g), and 30% H_2O_2 (10 ml) was heated at 55° for 6 hr. The excess peroxide was decomposed by the addition of activated MnO_2 (0.2 g) in portions to the ice-cold reaction mixture. After 2 hr the peroxide-free solution was filtered to remove MnO_2 and was evaporated to dryness under vacuum. The remaining solid was recrystallized, with clarification by charcoal, from absolute ethanol to afford yellow needles of 1,7-naphthyridine 1,7-dioxide: 1.3 g, 8.0 mmol, 80%; mp 273–275 dec, lit.[11] 275° dec.

Preparation of 1,7-Naphthyridine 1-Oxide from 1,7-Naphthyridine 1,7-Dioxide.[11]—A sample of 1,7-naphthyridine 1,7-dioxide (0.88 g, 5.4 mmol) was dissolved in hot methanol (400 ml). The cooled solution was transferred to a hydrogenation flask and nickel catalyst (0.9 g of Raney Nickel alloy treated with 50 ml of 20% NaOH for 2 hr at 100°) was added. The reduction was conducted at atmospheric pressure and was halted after an uptake of 160 ml (uncorrected) of hydrogen. The catalyst was removed by filtration and washed with methanol. The combined filtrate and washings were evaporated onto 5 g of alumina and placed on a chromatographic column (30 g of alumina) which had been prepared with anhydrous ether. The column was eluted with 700 ml of ether to afford 1,7-naphthyridine (0.18 g) followed by elution with 400 ml of chloroform to afford crude 1,7-naphthyridine 1-oxide (1), which was further purified by sublimation [100° (0.01 mm)] to give a white powder: 0.211 g, 1.4 mmol, 26%; mp 190–191°, lit.[11] 190–191°.

Meisenheimer Reaction of 1,7-Naphthyridine 1-Oxide (1).—The 1,7-naphthyridine 1-oxide (100 mg, 0.68 mmol) was added in portions to well-stirred, ice-cold, freshly distilled $POCl_3$ (10 ml). After 5 min at ice-bath temperature, the mixture was refluxed at 120° for 1 hr. The excess $POCl_3$ was removed *in vacuo*. A mixture of 20 g of ice and 20 ml of saturated $NaHCO_3$ solution was added to the ice-cold residue and the clear solution was extracted with 5 × 10 ml of cold methylene chloride. The dried (anhydrous Na_2CO_3) combined extracts were filtered and evaporated to dryness *in vacuo* to afford 38 mg of a pale yellow oil. Tlc (alumina–ether) revealed the presence of at least three components (visualized with I_2 vapor). Gas chromatography (20 ft × $^3/_8$ in. aluminum column, packed with 20% SE-30 on Chromosorb W, column temperature 220°, flow rate 200 ml/min) showed the presence of 1,7-naphthyridine (10.2 min), 4-chloro- (13.6 min), 2-chloro- (15.1 min), and a shoulder (16.6 min). Preparative gc (same conditions as for analytical data) afforded samples of 4-chloro- (**3**) and 2-chloro-1,7-naphthyridine (**4**) as pure compounds, mp 122°, after two sublimations and a recrystallization from cyclohexane (lit.[4] 122°), mp 134–135°, respectively. The compounds in decreasing R_f value on neutral alumina with ether were **4**, **5**, **3**, and parent. The relative proportions of each compound as determined by integration of the gc traces and compared with artificial mixtures are shown in Table I.

Anal. Calcd for $C_8H_5N_2Cl$ (**4**): C, 58.37; H, 3.06; N, 17.02. Found: C, 58.22; H, 3.02; N, 16.93.

Identification of 3-Chloro-1,7-naphthyridine (**5**).—The Meisenheimer reaction of 1,7-naphthyridine 1-oxide (120 mg, 0.82 mmol) as described in the previous section was repeated and, after removal of the excess $POCl_3$, 20 ml of 10% NaOH solution was added to the residue and the mixture was refluxed for 12 hr. Continuous extraction of the resulting solution with CH_2Cl_2 for 12 hr and evaporation of the dried (anhydrous $MgSO_4$) extract afforded 3.3 mg of a mixture of 1,7-naphthyridine and 3-chloro-1,7-naphthyridine, as established by comparisons with authentic samples on tlc and vpc. Analysis of the vpc traces established that the mixture consisted of 61% 1,7-naphthyridine and 39% 3-chloro-1,7-naphthyridine, which corresponds to 4 and 3%, respectively.

Preparation of 4-Methoxy-1,7-naphthyridine (**7**).—A solution of 4-chloro-1,7-naphthyridine[4] (140 mg, 0.85 mmol) in 50 ml of methanol containing sodium methoxide (0.5 g) was refluxed for 8 hr. Evaporation of the methanol afforded a residue which was dissolved in water and continuously extracted with chloroform. The chloroform extract was dried (anhydrous $MgSO_4$), filtered, and evaporated to dryness. The remaining oil was sublimed [70° (0.1 mm)] to afford white crystalline **7** (34.2 mg, 0.21 mmol, 25%; mp 92–94°).

Anal. Calcd for $C_9H_8N_2O$: C, 67.48; H, 5.03; N, 17.49. Found: C, 67.19; H, 5.28; N, 17.27.

Formation of 2-Methoxy- and 4-Methoxy-1,7-naphthyridine.—A sample of compound **1** (200 mg, 1.37 mmol) was treated with $POCl_3$ and worked up, as above, with the exception that sodium methoxide (0.1 g) in methanol (50 ml) was added to the residue in place of the ice and $NaHCO_3$ solution. The solution thus obtained was refluxed for 12 hr and evaporated to dryness. The residue was dissolved in water and continuously extracted with chloroform. The chloroform extract was dried with anhydrous $MgSO_4$, filtered, and evaporated to dryness to afford 132 mg of a pale orange oil. Tlc (alumina–ether) shows the presence of two components. Integration of the nmr spectrum of the oil as a solution in $CDCl_3$ revealed the composition of the mixture (Table I). The chloroform solution of the product mixture was evaporated onto 3 g of alumina and the residue was placed on top of an alumina-packed (60 g) chromatographic column using anhydrous distilled hexane. Elution with 1:1 ether–hex-

(11) This procedure affords higher yields than the previously reported one: W. W. Paudler, D. J. Pokorny, and S. J. Cornrich, *J. Heterocycl. Chem.*, **7**, 291 (1970).

ane (300 ml) afforded, after evaporation and sublimation of the residue [70° (0.1 mm)], 2-methoxy-1,7-naphthyridine (6): 42 mg; mp 52–54°. Further elution with pure ether gave 4-methoxy-1,7-naphthyridine (7) (28 mg; mp 92–94°) after evaporation and sublimation [70° (0.1 mm)] of the residue.

Anal. Calcd for $C_9H_8N_2O$ (6): C, 67.48; H, 5.03; N, 27.49. Found: C, 67.30; H, 5.17; N, 17.45.

Preparation of 2-Chloro-1,8-naphthyridine (8).—To a Carius tube was added 1-methyl-2-keto-1,2-dihydro-1,8-naphthyridine[12] (0.3 g, 1.87 mmol) and $POCl_3$ (25 ml). The tube was sealed and heated in an oven at 180° for 24 hr. The reaction mixture was treated in the same fashion as that described for the Meisenheimer reaction of **2**. The solid (0.1 g) that was obtained was sublimed twice [85° (0.10 mm)], affording white crystals (86 mg, 28%, mp 135–136°).

Anal. Calcd for $C_8H_5N_2Cl$: C, 58.37; H, 3.06; N, 17.02. Found: C, 58.25; H, 3.17; N, 17.32.

Meisenheimer Reaction of 1,8-Naphthyridine 1-Oxide (2).—This reaction was carried out in the same manner as that of compound **1** with $POCl_3$. In this reaction 1,8-naphthyridine 1-oxide[1] (500 mg, 3.42 mmol) yielded a semisolid material (471 mg). Tlc (alumina–ether) indicates the presence of three components. The integration of the pmr spectrum of the crude reaction mixture permits the determination of the relative amounts of 2-chloro- (**8**) and 4-chloro-1,8-naphthyridine (**10**) (see Table I). The mixture of chloro compounds was evaporated onto alumina (5 g) and placed onto a chromatographic column (30 g of alumina) prepared with ether. Elution with ether afforded 2-chloro-1,8-naphthyridine (**8**) which melted at 135–136° after sublimation [85° (0.10 mm)]. Further elution with 1:1 chloroform–ether afforded a small amount of the 3-chloro isomer contaminated with the 4-chloro isomer. Finally, elution with chloroform afforded 4-chloro-1,8-naphthyridine (**10**). Recrystallization from cyclohexane gave white needles (mp 62–64°).

The amount of 3-chloro-1,8-naphthyridine (**9**) formed in the reaction was determined in the following manner. The reaction mixture from 500 mg of compound **2**, after removal of excess $POCl_3$, was refluxed with 50 ml of 10% NaOH solution for 6 hr. The resulting solution was continuously extracted with chloroform and the chloroform extracts were dried with anhydrous $MgSO_4$, filtered, and evaporated to dryness affording crude **9**. Sublimation [80° (0.10 mm)] afforded pure 3-chloro-1,8-naphthyridine (33 mg, mp 143–144°). This amount represents 7% of the total products formed.

Anal. Calcd for $C_8H_5N_2Cl$: C, 58.37; H, 3.06; N, 17.02. Found for **9**: C, 58.35; H, 3.11; N, 17.27. Found for **8**: C, 58.10; H, 3.27; N, 16.80.

Formation of 2-Methoxy- (12) and 4-Methoxy-1,8-naphthyridine (11).—In order to ascertain that hydrolysis of neither the 2-chloro- nor the 4-chloro-1,8-naphthyridine occurred during the work-up, the procedure was modified in the following manner. The crude product mixture from compound **2** obtained by removal of the excess $POCl_3$ was refluxed with 70 ml of methanol containing 1 g of CH_3ONa. After removal of the methanol and addition of water, the solution was continuously extracted with chloroform. The extracts were dried, filtered, and evaporated to dryness. The pmr spectrum of the product mixture was employed to obtain the relative percentages of the 2-methoxy and 4-methoxy isomers. Tlc (alumina, 7 drops; 3 ml of NeOH–EtOAc) shows three components. These compounds in order of their decreasing R_f values are **12**, **9**, and **11**. Column chromatography of the mixture afforded 2-methoxy-1,8-naphthyridine (**12**) (53–55°, sublimed) and 4-methoxy-1,8-naphthyridine (**11**) (oil; picrate 183–185°).

Anal. Calcd for $C_9H_8N_2O$: C, 67.48; H, 5.03; N, 17.49. Found: C, 67.40; H, 5.31; N, 17.69. Calcd for $C_{15}H_{11}N_5O_8$: C, 46.28; H, 2.85; N, 17.99. Found: C, 46.00; H, 3.08; N, 17.71.

Preparation of 2-Deuterio-1,5-naphthyridine 1-Oxide (13).—A sample of 1,5-naphthyridine 1-oxide[1] (0.5 g) was dissolved in 5 ml of 2.4 *N* NaOD in D_2O. After being stirred at room temperature for 12 hr, the solution was continuously extracted with chloroform, evaporated to dryness, and dried under vacuum, affording a sample (0.49 g) of compound **13**. The nmr spectrum revealed that H_2 had been completely replaced by deuterium. This material was used without further purification in the Meisenheimer reaction.[1]

3-Chloro-4-hydroxy-1,7-naphthyridine Hydrochloride (22).—To a solution of 292 mg (2.0 mmol) of 4-hydroxy-1,7-naphthyridine[4] in 0.4 ml of acetic anhydride and 2.4 ml of acetic acid was added 0.2 ml of SO_2Cl_2.[13] The mixture containing a yellow precipitate was heated on a steam bath for 30 min. To the cooled solution was added 15 ml of dry ether and the precipitated solid was collected and washed with ether. The sample was dried under vacuum at 100° for 1 hr to afford the hydrochloride salt of 3-chloro-4-hydroxy-1,7-naphthyridine (400 mg, 1.85 mmol, 93%). A sample was recrystallized from acetic acid to afford the pure compound: mp 271–272 dec; nmr (in deuteriotrifluoroacetic acid) τ 1.32 (H_2, s), 1.27 (H_5, d), 1.05 (H_6, d), 0.20 (H_8, s, J_{56} = 6.0 Hz).

Anal. Calcd for $C_8H_6N_2OCl_2$: C, 44.24; H, 2.79; N, 12.91. Found: C, 43.97; H, 2.93; N, 13.20.

3,4-Dichloro-1,7-naphthyridine (23).—A solution of 375 mg (1.73 mmol) of compound **22** in 20 ml of freshly distilled $POCl_3$ was heated under reflux for 2 hr. The excess $POCl_3$ was removed *in vacuo* and an ice-cold saturated aqueous solution of $NaHCO_3$ (50 ml) was added to the chilled residue. The white precipitate that formed was extracted with $CHCl_3$ (3 × 75 ml). The dried combined extracts were evaporated to dryness to yield orange crystals (250 mg). A solution of this material in $CHCl_3$ was passed through a column of alumina and the eluate was evaporated to dryness. The remaining solid was sublimed to afford **23**: 210 mg, 1.06 mmol, 61%; mp 125–127°; nmr ($CDCl_3$) τ 1.20 (H-2, s), 2.17 (H-5, d), 1.35 (H-6, d), 0.60 (H-8, s, J_{56} = 6.0 Hz).

Anal. Calcd for $C_8H_4N_2Cl_2$: C, 48.27; H, 2.03; N, 14.08. Found: C, 48.01; H, 2.27; N, 13.97.

3-Chloro-1,7-naphthyridine (45).—To a solution of 3,4-dichloro-1,7-naphthyridine (200 mg, 1.0 mmol) in 45 ml of ethanol was added 0.8 ml of 95% hydrazine and the solution was stirred for 18 hr. The precipitated analytically pure hydrochloride salt of 3-chloro-4-hydrazino-1,7-naphthyridine (80 mg, mp 200° dec) was removed by filtration and washed with a small amount of cold ethanol. Tlc (alumina; 1:1 hexane–ether) indicated that all of the starting material had been consumed. The filtrate was evaporated to dryness and the residue was dried under vacuum [100° (0.1 mm), 30 min], affording an additional sample of product: 125 mg, mp 190°, total yield 89%; nmr (in deuteriotrifluoroacetic acid) τ 1.20 (H_2, 5), −0.92 (H_2, d), 1.17 (H_6, d), 0.06 (H_8, s, J_{56} = 7 Hz).

Anal. Calcd for $C_8H_8N_4Cl_2$: C, 41.58; H, 3.49; N, 24.25. Found: C, 42.67; H, 3.30; N, 24.26.

The above sample (200 mg, 0.86 mmol) was dissolved in 40 ml of water containing 2 ml of acetic acid and heated to its boiling point. To this boiling solution was added in portions a hot solution of 1 g of $CuSO_4 \cdot 5H_2O$ in 10 ml of water. The resulting mixture was then heated at the boiling point for 5 min, cooled, and made basic with 50% aqueous NaOH. The mixture was then continuously extracted (8 hr) with $CHCl_3$ and the extracts were concentrated to a small volume (2 ml). This solution was used for preparative gas chromatography (some conditions as above) to separate the 3-chloro-1,7-naphthyridine from traces of 1,7-naphthyridine. In this fashion 38 mg of product was isolated and sublimed [100° (0.10 mm)] to afford pure 3-chloro-1,7-naphthyridine (35 mg, 24%, mp 88–89°).

Anal. Calcd for $C_8H_5N_2Cl$: C, 58.37; H, 3.06; N, 17.02. Found: C, 58.14; H, 2.95; N, 16.80.

Registry No.—**1**, 27305-52-8; **2**, 27284-59-9; **3**, 16287-97-1; **4**, 35192-05-3; **5**, 35170-89-9; **6**, 35170-90-2; **7**, 35170-91-3; **8**, 15936-10-4; **9**, 35170-93-5; **10**, 35170-94-6; **11**, 35171-00-7; **11** picrate, 35170-95-7; **12**, 15936-12-6; **22**, 35170-97-9; **23**, 35170-98-0; 3-chloro-4-hydrazino-1,7-naphthyridine hydrochloride, 35170-99-1.

(12) W. W. Paudler and T. L. Kress, *J. Heterocycl. Chem.*, **5**, 561 (1968).

(13) A. R. Surrey and R. A. Cutler, *J. Amer. Chem. Soc.*, **68**, 2570 (1946).

Synthesis and Characterization of *N*-Vinyliminopyridinium Ylides.[1] Evidences for 1,5-Dipolar Cyclizations

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N-Vinyliminopyridinium ylides (**13**–**22**) were prepared from pyridinium *N*-imine hydriodides (**3**–**12**) and dimethyl 1-chlorofumarate or -maleate in the presence of potassium carbonate. The N ylides cyclized in various solvents at room temperature to afford primary dihydro-type cycloadducts (**23**–**34**) in moderate yields. The dihydro-type cycloadducts (**23**–**33**) were stable in the crystalline state but aromatized readily with dehydrogenating agents to give the corresponding pyrazolo[1,5-*a*]pyridine derivatives (**35**–**45**) in good yields. Structural elucidation of the N ylides, dihydro cycloadducts, and the pyrazolo[1,5-*a*]pyridine derivatives was accomplished by physical and spectral means. The structures of the pyrazolo[1,5-*a*]pyridine derivatives were also established by independent syntheses. Orientations and modes of these cycloadducts are also discussed.

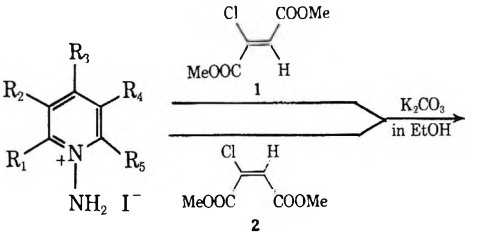
Although intermolecular cycloaddition reactions of pyridinium ylides with various reagents have been extensively studied,[2] intramolecular cyclizations of *N*-vinyliminopyridinium ylides have not been well investigated.

Recently, Tamura and coworkers[3] have reported the cyclization reactions of *N*-(1-oxocyclohexen-2-yl)iminopyridinium ylides and the reactions of pyridinium *N*-imines with ethyl β-chloroisocrotonate in the presence of potassium carbonate to give the corresponding pyrazolopyridine derivatives. In particular, they have suggested that the latter reactions might proceed *via* 1,3-dipolar cycloaddition rather than 1,5-dipolar cyclization, since attempts to obtain the possible intermediates of *N*-vinyliminopyridinium ylides were unsuccessful. In this paper, we wish to report the isolation of *N*-vinyliminopyridinium ylides and their cyclization products.

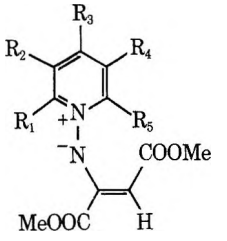
Results and Discussion

Isolations of the *N*-Vinyliminopyridinium Ylides.—A mixture of pyridinium *N*-imine hydriodides, **3**–**12**, prepared by the Gösl method,[2] and dimethyl 1-chlorofumarate (**1**) were treated with an excess potassium carbonate in ethanol at room temperature within 1 hr to afford the corresponding *N*-vinyliminopyridinium ylides, **13**–**22**, in over 75% yields. Interestingly, similar reactions of the N imines with dimethyl 1-chloromaleate (**2**) gave the same N ylides. These results are shown in Scheme I.

SCHEME I



3, $R_1=R_2=R_3=R_4=R_5=H$
4, $R_1=H$; $R_2=Me$; $R_3=R_4=R_5=H$
5, $R_1=R_2=H$; $R_3=Me$; $R_4=R_5=H$
6, $R_1=H$; $R_2=R_3=Me$; $R_4=R_5=H$
7, $R_1=H$; $R_2=R_4=Me$; $R_3=R_5=H$
8, $R_1=Me$; $R_2=R_3=R_4=R_5=H$
9, $R_1=R_2=Me$; $R_3=R_4=R_5=H$
10, $R_1=R_3=Me$; $R_2=R_4=R_5=H$
11, $R_1=R_4=Me$; $R_2=R_3=R_5=H$
12, $R_1=R_5=Me$; $R_2=R_3=R_4=H$



13, $R_1=R_2=R_3=R_4=R_5=H$
14, $R_1=H$; $R_2=Me$; $R_3=R_4=R_5=H$
15, $R_1=R_2=H$; $R_3=Me$, $R_4=R_5=H$
16, $R_1=H$; $R_2=R_3=Me$; $R_4=R_5=H$
17, $R_1=R_3=R_5=H$; $R_2=R_4=Me$
18, $R_1=Me$; $R_2=R_3=R_4=R_5=H$
19, $R_1=R_2=Me$; $R_3=R_4=R_5=H$
20, $R_1=R_3=Me$; $R_2=R_4=R_5=H$
21, $R_1=R_4=Me$; $R_2=R_3=R_5=H$
22, $R_1=R_5=Me$; $R_2=R_3=R_4=H$

Isomerization of the N Ylides.—The N ylides, **13**–**22**, were comparatively stable in the crystalline state but in solvent such as chloroform, methylene chloride and carbon tetrachloride they isomerized intramolecularly to afford the corresponding cycloadducts, **23**–**34**. These cyclizations were influenced by the substituents on the pyridine ring: (a) α-unsubstituted N ylides **13**–**17** cyclized quantitatively in chloroform at room temperature within 24 hr to yield the cycloadducts **23**–**29**, respectively (Scheme II); (b) with unsymmetrical substituted N ylides **14** and **16**, cyclization was observed to take place at two sites, and the cyclization of the more sterically hindered site on a pyridine ring was always predominant to the alternate less substituted site [the ratio of **24** to **25** (or **27** to **28**) as determined by nmr spectroscopy was 1:12 (or 1:8), respectively]; and (c) in α-substituted N ylides **18**–**22** similar isomerizations were observed, but the rates were slower than those of α-unsubstituted N ylides (below 30% after 24 hr), and in these cases only cyclization to the less hindered α′ position was observed (Scheme III).

Photochemical Behavior of the N Ylides.—With a view to obtaining mechanistic information on the

(1) Studies of Heteroaromaticity. Part LXII. Part LXI of this series: T. Sasaki, K. Kanematsu, and M. Murata, *Tetrahedron*, **28**, 2383 (1972).

(2) T. Sasaki, K. Kanematsu, and A. Kakehi, *J. Org. Chem.*, **36**, 2978 (1971).

(3) (a) Y. Tamura, N. Tsujimoto, and M. Ikeda, *Chem. Commun.*, 310 (1971); (b) Y. Tamura, A. Yamagami, and M. Ikeda, *Yakugaku Zasshi*, **91**, 1154 (1971).

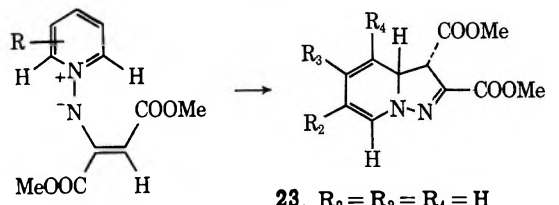
TABLE I

NMR SPECTRA OF N YLIDES IN $CDCl_3$ (τ VALUE)[a]

Compd	R_1	R_2	R_3	R_4	R_5	Vinyl H	$COOCH_3$	Coupling constant (J, Hz)
13	1.51 (br d)		1.9–2.4 (m)		1.51 (br d)	6.34 (s)	6.10 (s), 6.51 (s)	$J_{1,2} = J_{4,5} = 6.0$
14	1.73 (s)	7.42 (s)	2.11 (br d)	2.33 (q)	1.68 (br d)	6.46 (s)	7.12 (s), 6.53 (s)	$J_{3,4} = 7.5$, $J_{4,5} = 6.0$
15	1.63 (d)	2.43 (d)	7.40 (s)	2.43 (d)	1.69 (d)	7.43 (s)	6.09 (s), 6.50 (s)	$J_{1,2} = J_{4,5} = 7.0$
16	1.92 (s)	7.47 (s)	7.57 (s)	2.51 (d)	1.88 (d)	6.47 (s)	6.09 (s), 6.50 (s)	$J_{4,5} = 7.0$
17	1.95 (s)	7.53 (s)	2.30 (br s)	7.53 (s)	1.95 (s)	6.46 (s)	6.10 (s), 6.50 (s)	
18	7.30 (s)	2.29 (br d)	2.00 (m)	2.35 (m)	1.60 (d d)	6.75 (s)	6.09 (s), 6.51 (s)	$J_{4,5} = 6.5$, $J_{3,5} = 2.0$, $J_{2,3} = 6.5$
19	7.38 (s)	8.48 (s)	2.14 (br d)	2.52 (q)	1.73 (br d)	6.76 (s)	6.07 (s), 6.49 (s)	$J_{3,4} = 7.5$, $J_{4,5} = 6.5$
20	7.37 (s)	2.60 (s)	7.43 (s)	2.65 (d)	1.92 (d)	6.77 (s)	6.11 (s), 6.53 (s)	$J_{4,5} = 6.0$
21	7.34 (s)	2.38 (d)	2.16 (d)	7.53 (s)	1.80 (br s)	6.75 (s)	6.09 (s), 6.49 (s)	$J_{2,3} = 9.0$, $J_{3,5} = 2.0$
22	7.28 (s)	2.50 (d)	2.13 (q)	2.52 (d)	7.28 (s)	6.81 (s)	6.06 (s), 6.49 (s)	$J_{2,3} = 6.5$, $J_{3,4} = 9.0$

[a] Multiplicity is indicated as follows: s, singlet; d, doublet; q, quartet; br, broad.

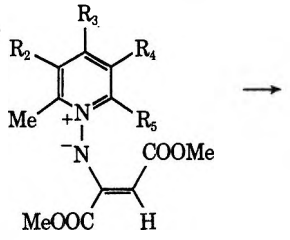
SCHEME II



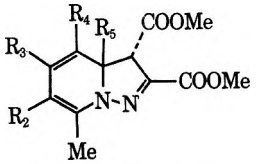
13–17

23, $R_2 = R_3 = R_4 = H$
24, $R_2 = Me$, $R_3 = R_4 = H$
25, $R_2 = R_3 = H$; $R_4 = Me$
26, $R_2 = H$; $R_3 = Me$; $R_4 = H$
27, $R_2 = R_3 = Me$; $R_4 = H$
28, $R_2 = H$; $R_3 = R_4 = Me$
29, $R_2 = R_4 = Me$; $R_3 = H$

SCHEME III



18, $R_2 = R_3 = R_4 = R_5 = H$
19, $R_2 = Me$; $R_3 = R_4 = R_5 = H$
20, $R_2 = H$; $R_3 = Me$; $R_4 = R_5 = H$
21, $R_2 = R_3 = H$; $R_4 = Me$; $R_5 = H$
22, $R_2 = R_3 = R_4 = H$; $R_5 = Me$



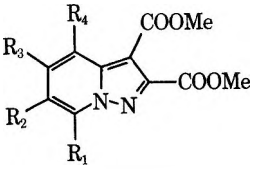
30, $R_2 = R_3 = R_4 = R_5 = H$
(**31**, $R_2 = Me$; $R_3 = R_4 = R_5 = H$)
32, $R_2 = H$; $R_3 = Me$; $R_4 = R_5 = H$
33, $R_2 = R_3 = H$; $R_4 = Me$; $R_5 = H$
34, $R_2 = R_3 = R_4 = H$; $R_5 = Me$

above-mentioned reactions, the photochemical reactions of unsubstituted and α,α'-disubstituted *N*-vinyliminopyridinium ylides were investigated, since the photochemical intramolecular 1,3-dipolar cyclization of substituted 1-ethoxycarbonyliminopyridinium ylides produced 1*H*,1,2-diazepines.[4]

(4) T. Sasaki, K. Kanematsu, A. Kakehi, K. Hayakawa, and I. Ichikawa, *J. Org. Chem.*, **36**, 426 (1970).

Irradiation of **13** in acetone at 0° for 45 min gave a 60% yield of a mixture of **23** and **35** (2,3-dimethoxycarbonylpyrazolo[1,5-*a*]pyridine) in the ratio of 1:1 (by nmr analysis) instead of the seven-membered product. The same reaction at 25° for 2 hr gave only **35** in 50% yield. Isolated **23** was converted rapidly on irradiation to **35** in 80% yield. These results appear to involve a photoinduced process, since the formation of **23** and **35** occurs thermally to the extent of only few per cent. Compound **22**, whose α and α' positions of the pyridine ring were occupied, was irradiated in acetone at room temperature to give the bicyclic product **34** in 20% yield, and no isomeric dihydro compound could be detected.

Dehydrogenation of the Cycloadducts.—The cycloadducts **23–34** are generally stable in the crystalline state. The dehydrogenation reactions of these adducts (**23–33**) except **34** were carried out by treating them with dehydrogenation agents such as palladium on carbon or tetracyanoethylene to afford the corresponding pyrazolopyridine derivatives, **35–45**, in high yields. The dehydrogenation was also observed under irradiation of the cycloadduct as described above. Compounds **27–33**, in particular, were dehydrogenated smoothly without such reagents even at room temperature. Compound **34** which has a methyl substituent on a bridged carbon was too stable in carbon tetrachloride even at 100° in a sealed tube to be aromatized to **42** with a loss of methane.



35, $R_1 = R_2 = R_3 = R_4 = H$
36, $R_2 = Me$; $R_1 = R_3 = R_4 = H$
37, $R_4 = Me$; $R_1 = R_2 = R_3 = H$
38, $R_3 = Me$; $R_1 = R_2 = R_4 = H$
39, $R_2 = R_3 = Me$; $R_1 = R_4 = H$
40, $R_3 = R_4 = Me$; $R_1 = R_2 = H$
41, $R_2 = R_4 = Me$; $R_1 = R_3 = H$
42, $R_1 = Me$; $R_2 = R_3 = R_4 = H$
43, $R_1 = R_2 = Me$; $R_3 = R_4 = H$
44, $R_1 = R_3 = Me$; $R_2 = R_4 = H$
45, $R_1 = R_4 = Me$; $R_2 = R_3 = H$

Structural Elucidation of the N Ylides.—The structures of N ylides **13–22** were determined by elemental and spectral analyses (Table I) and by chemical re-

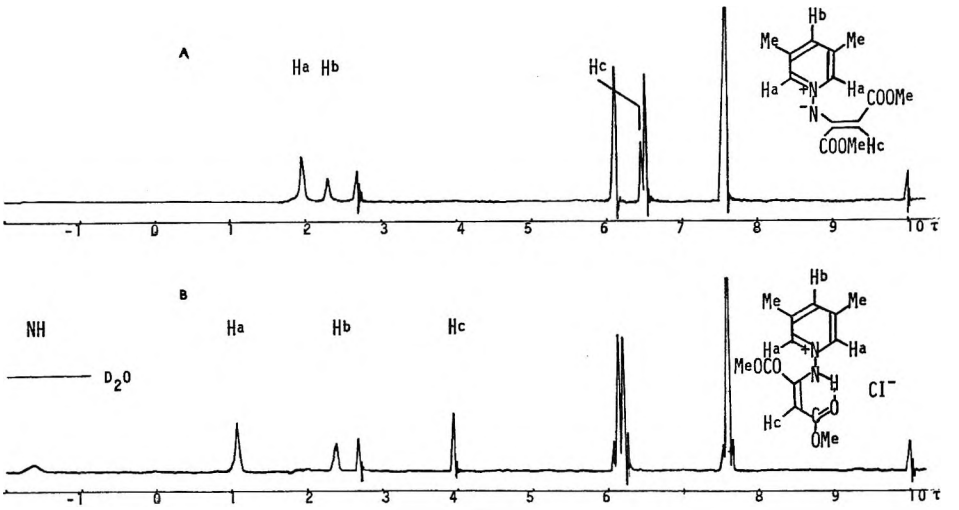


Figure 1.—A, observed nmr spectrum of 17 in $CDCl_3$; B, nmr spectra of 17 added HCl in $CDCl_3$.

actions. The elemental analyses were in good accord with the proposed structures. The configuration of the *N*-vinylimino group in all the N ylides was assigned as trans. This was based on the nmr inspection of the salt of the N ylide. In the nmr spectra, they show each singlet at higher region due to the vinyl proton (τ 6.34–6.81) suggesting strongly the delocalization of the vinyl proton with ester carbonyl group. Interestingly, the nmr of hydrochloride of the N ylide was considerable changed. For example, when the nmr of **17** was taken in deuteriochloroform at room temperature, the signals appeared at τ 1.95 (H_a), 2.30 (H_b), and 6.46 (H_c). By contrast, when **17** was added with a small amount of hydrochloric acid in deuteriochloroform, the signals were exhibited at τ −1.63 (NH, exchanged by D_2O), 1.07 (H_a), 2.40 (H_b), and 3.96 (H_c). The signal of τ −1.63 indicated obviously the presence of a hydrogen bonding with carbonyl group, which was possible only in the trans configuration as shown in Figure 1.

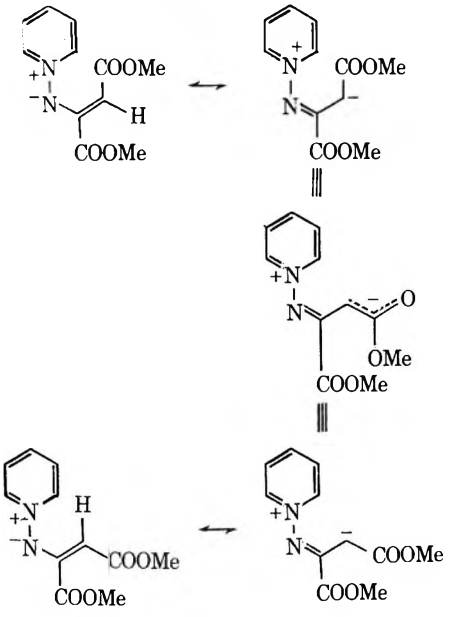
Further deviation of chemical shifts between the vinyl proton in α-unsubstituted N ylides **13**–**17** (τ 6.34–6.47) and α-substituted N ylides **18**–**22** (τ 6.75–6.81) (Table I) might be caused from the effect of the diamagnetic ring current on the pyridine ring, since the steric hindrance of free rotation of the N substituent by the α-methyl group could favor a conformation in which the vinyl proton is less influenced by the pyridine ring than in the α-unsubstituted N ylides. As observed experimentally, such an effect obviously leads to retardation of the isomerization of α-substituted N ylides **18**–**22** to the corresponding cycloadducts, **30**–**34**.

Formation of the same N ylides from both **1** and **2** indicates rapid cis–trans isomerization of the vinyl moiety as indicated in Scheme IV.

Structural Elucidation of the Cycloadducts.—Based mainly on nmr analysis, these cycloadducts, **23**–**30** and **32**–**34**, were assigned as the cis rather than the trans configurations at the C-3 and C-3a positions. The nmr spectral patterns of the cycloadducts are grossly similar to each other, as shown in Table II.

The nmr signals of **23** at τ 3.14, 4.00, 4.54, 4.78, and 5.35 with the relative intensities of 1:1:1:1:1 are attributable to five protons of the six-membered ring, at 6.03 to one proton of C-3 position, and at 6.24 to two methyl protons. In particular, signals at τ 5.35 and 6.03 coupling each other with the coupling constant of

SCHEME IV

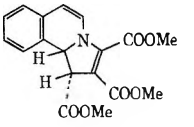


17.0 Hz[5] attributable to the protons attached at C-3a and C-3 positions indicate clearly its cis configuration[6] which is supported by Dreiding models of these structures. Similarly, the singlet signal (1 H) at τ 6.30 of compound **34** is assigned to the C-3 position.

Structural Elucidation of the Aromatics.—Structures of the aromatics, **35**–**45**, were determined as pyrazolo-

(5) The 100-MHz nmr spectrum of **23** taken in CCl_4 shows the same coupling constant: τ 3.06 (br, d, $J_{1,2}$ = 7.0 Hz, H_1), 4.71 (br t, $J_{1,2}$ = 7.0, $J_{2,3}$ = 6.0 Hz, H_2), 3.93 (m, H_3), 4.45 (br d, $J_{3,4}$ = 9.0 Hz, H_4), 5.29 (br d, $J_{5,6}$ = 17.0 Hz, H_5), 5.96 (d, $J_{6,5}$ = 17.0 Hz, H_6).

(6) In general, such a large coupling constant is not assignable to trans, since, so far, vicinal trans coupling constants are usually smaller than cis, and cis coupling constants are 13.0–14.0 Hz in a similar compound (shown below) as reported by Kobayashi, *et al.*; see Y. Kobayashi, T. Kuzuma, Y. Sekine, and K. Fujiyama, Abstracts of Papers in Symposium of the Chemistry of Heteroaromatic Compounds, p 93, 1970, Tokyo.



τ 4.67 (d)
τ 5.51 (d)
J = 13.3 Hz

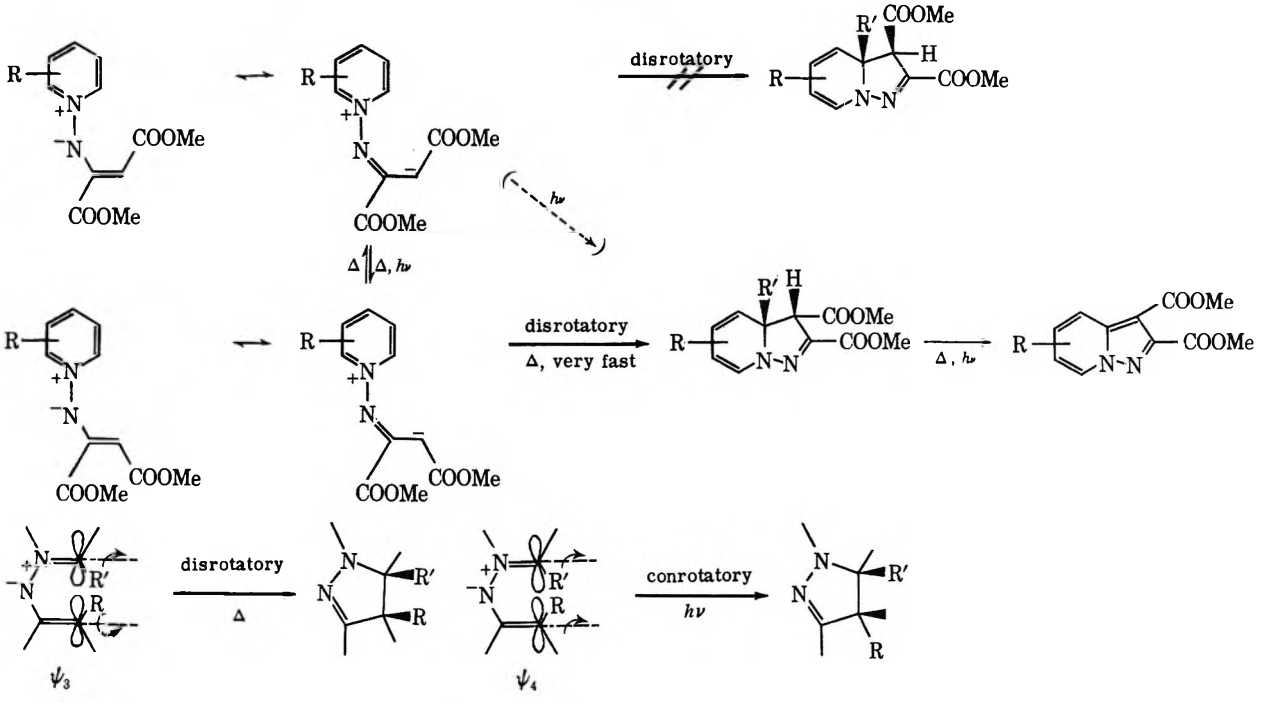
TABLE II

NMR SPECTRA OF DIHYDROPYRAZOLOPYRIDINES IN CCl_4 (τ VALUE)

Compd[a]	R_1	R_2	R_3	R_4	R_5	C_3H	Coupling constant (J, Hz)
23	3.14 (br d)	4.78 (br t)	4.00 (m)	4.54 (br d)	5.35 (br d)	6.03 (d)	$J_{1,2} = 7.0$, $J_{2,3} = 7.0$, $J_{3,4} = 9.0$, $J_{5,C_3H} = 17.0$
25[b]	3.29 (br d)	4.91 (q)	4.33 (br d)	8.15 (d)	5.10 (br d)	5.82 (d)	$J_{1,2} = 7.0$, $J_{2,3} = 6.0$, $J_{3,4} = 1.5$, $J_{5,C_3H} = 17.0$
26	3.16 (d)	4.90 (d d)	8.21 (t)	4.76 (m)	5.38 (br d)	6.07 (d)	$J_{1,2} = 7.5$, $J_{2,4} = 1.5$, $J_{5,C_3H} = 17.0$
28[c]	3.33 (d)	4.96 (d)	8.24[d] (m, 2 H)		5.13 (br d)	5.83 (d)	$J_{1,2} = 7.5$, $J_{5,C_3H} = 17.0$
29	3.46	8.22	4.40	8.14	5.15	5.85	$J_{1,2} = 1.0$, $J_{4,5} = 1.5$, $J_{5,C_3H} = 17.0$
31	7.85 (s)	4.95 (br d)	4.08 (m)	4.55 (br d)	5.45 (br d)	6.08 (d)	$J_{2,3} = 6.0$, $J_{3,4} = 9.0$, $J_{5,C_3H} = 17.0$
32	7.90 (s)	5.06 (br s)	8.25 (d)	4.80 (br s)	5.44 (br d)	6.11 (d)	$J_{5,C_3H} = 17.0$
33	7.95 (s)	5.13 (br s)	4.46 (br d)	8.21 (s)	5.29 (br d)	5.90 (d)	$J_{2,3} = 6.0$, $J_{5,C_3H} = 17.0$
34	7.83 (s)	5.05 (br s)	6.15 (q)	4.68 (br d)	8.88 (s)	6.30 (s)	$J_{2,3} = 6.0$, $J_{3,4} = 9.0$

[a] Chemical shifts to the methyl protons of dimethoxycarbonyl groups appeared in the regions of τ 6.06–6.53 as each a singlet. [b] Chemical shifts of isomeric product **24** appeared at τ 8.18 (R_2) and 4.80 (R_4). [c] Chemical shifts of isomeric product **27** appeared at τ 3.34 (br s, R_1), 4.63 (br s, R_4), and 5.68 (d, C_3H). [d] Overlapping with 2 H.

SCHEME V



[1,5-*a*]pyridine derivatives by physical and spectral comparison with authentic samples prepared by independent syntheses.[2]

Reaction Mechanism.—From the above results, it is concluded that the pyrazolo[1,5-*a*]pyridine derivatives are produced by 1,5-dipolar cyclization of the *N*-vinyliminopyridinium ylides. However, as described above, the isolated trans N ylides **13**–**22** seem not to be precursors of the corresponding cycloadducts, **23**–**34**. Thermal intramolecular concerted electrocyclic reactions of the N ylides should give rise to the trans cycloadducts but the disrotatory cyclization of the trans N ylide is unfavorable owing to steric hindrance of the substituents. Actually, the cycloadducts were obtained as cis isomers, suggesting that such precursors are cis N ylides and not trans isomers. Thus thermal or photochemical trans–cis isomerization of the N ylide must occur prior to ring closure, followed by thermal cyclization and dehydrogenation. The photochemical preparation of **23** or **34** from N ylide **13** or **22** is seen as a result of photochemical trans–cis isomerization, followed by the thermal disrotatory cyclization[7] rather than photochemical conrotatory process as shown in Scheme V.

(7) For an analogous disrotatory ring closure in a heterocyclic reaction, see J. Elguero, *Bull. Soc. Chim. Fr.*, 1925 (1971).

Experimental Section[8]

Reaction of N Imine and Olefin.—A mixture of dimethyl 1-chlorofumarate (**1**) or -maleate (**2**) (0.36 g, 2 mmol) and a small excess of pyridinium *N*-imine hydriodide in ethanol was stirred with excess potassium carbonate (~6 g) at room temperature for 0.5–1 hr. The insoluble substances were removed by filtration. The filtrate was evaporated *in vacuo*. The results are summarized in Table III.

Isomerizations of N Ylides 13–22 and Aromatizations of Their Cycloadducts, 23–33. General Procedure.—A mixture of N ylide (0.2–0.4 g) and chloroform (50 ml) was kept at room temperature for 1 day and then the solvent was removed *in*

(8) Melting points were measured with a Yanagimoto micro melting point apparatus and are uncorrected. Microanalyses were performed on a Perkin-Elmer 240 elemental analyzer. The uv spectra were determined with a JASCO Model ORD/UV-5 recorder. The nmr spectra were taken with a Japan Electric Optics, Model C-60-XL, nmr spectrometer and with a Varian A-60 recording spectrometer with tetramethylsilane as an internal standard. Chemical shifts are expressed in τ values. The ir spectra were taken with a JASCO Model IR-S spectrophotometer. The glpc was done isothermally on a Hitachi K-23 gas chromatograph with a 3-ft, 5 wt % SE-30 (Chromosorb G-NAW) column (flame-isomerization detector). A Varian Aerograph Model 7000 (hydrogen flame-ionization detector, nitrogen carrier gas, fitted with a 5 ft × 1/8 in. column containing 12% Dow Corning silicone oil 550 on 80–100 Chromosorb W) was used for preparative separation.

TABLE III

N Imine	Olefin	N Ylide[a]	Yield, %	Mp, °C	Ir (KBr), cm^{-1} (C=O)	Uv λ_{max} (MeOH), nm (ϵ)
3	**1**	**13**	87	103–105	1649, 1732	416 (1.28×10^2)
3	**2**		85			280 (1.72×10^4)
						238 (6.39×10^3)
4	**1**	**14**	88	85–86	1649, 1734	408 (1.93×10^2)
4	**2**		80			280 (1.75×10^4)
						238 (5.68×10^3)
5	**1**	**15**	88	112–113	1652, 1737	400 (1.99×10^2)
5	**2**		90			281 (1.75×10^4)
						238 (8.52×10^3)
6	**1**	**16**	95	113–114	1655, 1721	410 (1.58×10^2)
						281 (1.39×10^4)
						238 (5.35×10^3)
7	**1**	**17**	93	96–98	1650, 1735	410 (1.68×10^2)
						279 (1.68×10^4)
						238 (4.86×10^3)
8	**1**	**18**	78	107–108	1658, 1738	400 (0.78×10^2)
						280 (1.46×10^4)
						236 (3.65×10^3)
9	**1**	**19**	95	160–162	1659, 1730	405 (1.22×10^2)
						278 (2.23×10^4)
						234 (7.39×10^3)
10	**1**	**20**	91	119–122	1645, 1743	390 (0.66×10^2)
						282 (1.53×10^4)
						236 (5.45×10^3)
11	**1**	**21**	87	113–115	1651, 1733	404 (0.99×10^2)
						283 (2.04×10^4)
						236 (5.50×10^3)
12	**1**	**22**	95	130–133	1660, 1731	400 (1.32×10^2)
						279 (2.15×10^4)
						235 (5.90×10^3)

[a] Satisfactory analytical data (±0.2% for C, H, N) were reported for ylides **13**–**22**: Ed.

vacuo without heating. When unreacted N ylide still remained, the cycloadduct was separated by column chromatography (alumina) using ether as eluent. Furthermore, these phenomena were observed in time-interval measurements of its uv and nmr spectra. The cycloadducts in benzene were aromatized by heating or treatment with palladium on carbon or tetracyanoethylene to give the corresponding 2,3-dimethoxycarbonylpyrazolo[1,5-a]pyridine derivatives (**35**–**45**) in high yields.

Isomerization of 13.—From **13** (0.20 g) in chloroform (50 ml) 2,3-dimethoxycarbonyl-*cis*-3,3a-dihydropyrazolo[1,5-*a*]pyridine (**23**) was obtained in quantitative yield as orange needles (from *n*-hexane): mp 83–86°; ν (KBr) 1685, 1725 cm^{-1} (C=O); λ_{max} (MeOH) 379 nm (ϵ 8.68×10^3), 305 (sh), 252 (5.73×10^3).

Anal. Calcd for $C_{11}H_{12}N_2O_4$: C, 55.93; H, 5.12; N, 11.86. Found: C, 55.97; H, 5.11; N, 11.81.

A solution of **23** (0.20 g) in dry benzene (30 ml) was treated with palladium on carbon (0.20 g) at 60–80° for 6 hr to give **35** (0.16 g, 80%) as pale yellow needles (from *n*-hexane), mp 71–73°, identical with an authentic sample.[2]

Isomerization of 14.—From **14** (0.3 g) in chloroform (50 ml) **25** and **24** were obtained in quantitative yield as orange needles (from *n*-hexane).

Anal. Calcd for $C_{12}H_{14}N_2O_4$ (a mixture of **24** and **25**): C, 57.59; H, 5.64; N, 11.20. Found: C, 57.77; H, 5.58; N, 11.30.

The isomer ratio of **24** to **25** was 1:12 by nmr inspection (Table II). A mixture of **24** and **25** (0.20 g) was treated with palladium on carbon (0.20 g) in benzene (30 ml) at 60–80° for 6 hr to give **37** and **36** (0.17 g, 85%) as colorless needles (from methanol), identical nmr with that of authentic samples.[2]

Isomerization of 15.—From **15** (0.20 g) in chloroform (50 ml) there was obtained **26** in quantitative yield as orange needles (from ether–*n*-hexane): mp 86–89°; ν (KBr) 1690, 1728 cm^{-1} (C=O), λ_{max} (MeOH) 379 nm (ϵ 1.00×10^4), 310 (sh), 259 (7.15×10^3).

Anal. Calcd for $C_{12}H_{14}N_2O_4$: C, 57.59; H, 5.64; N, 11.20. Found: C, 57.65; H, 5.68; N, 11.16.

Cycloadduct **26** (0.20 g) was treated with palladium on carbon (0.20 g) in benzene (30 ml) at room temperature overnight to give **38** (0.18 g, 90%) as colorless needles (from methanol), mp 119–121°, identical with an authentic sample.[2]

Isomerization of 16.—From **16** (0.30 g) in chloroform (50 ml) there was obtained **28** and **27** in quantitative yield as orange needles (from *n*-hexane). The ratio of **27** to **28** was 1:8 by nmr (Table II). The mixture (0.2 g) was heated at reflux benzene for 8 hr to give a mixture of **40** and **39** (0.16 g, 80%) as colorless needles (from methanol), identical with authentic samples (by nmr inspection).[2]

Isomerization of 17.—From **17** (0.20 g) in chloroform (50 ml) there was obtained **29** in quantitative yield as orange needles (from ether–*n*-hexane): mp 95–100°; ν (KBr) 1683, 1730 cm^{-1} (C=O); λ_{max} (MeOH) 398 nm (ϵ 9.42×10^3), 320 (sh), 252 (6.78×10^3).

Anal. Calcd for $C_{13}H_{16}N_2O_4$: C, 59.08; H, 6.10; N, 10.60. Found: C, 59.10; H, 6.12; H, 10.65.

Cycloadduct **29** (0.20 g) was treated in benzene (30 ml) at reflux temperature for 8 hr to give **41** (0.18 g, 90%) as colorless needles (from methanol): mp 95–96°; ν (KBr) 1684, 1727 cm^{-1} (C=O); λ_{max} (EtOH) 300 nm (ϵ 8.5×10^3), 224 (2.85×10^4).

Anal. Calcd for $C_{13}H_{14}N_2O_4$: C, 59.53; H, 5.38; N, 10.68. Found: C, 59.44; H, 5.41; N, 10.88.

Isomerization of 18.—From **18** (0.4 g) in chloroform (50 ml) there was obtained **30** together with the dehydrogenated compound (**42**) in 30% yield as orange crystals. The mixture was heated in benzene (20 ml) to give **42** (80%), identical with an authentic sample.[2]

Isomerization of 19.—From **19** (0.40 g) in chloroform (50 ml) there was obtained **43** (0.02 g, 5%) as colorless needles (from methanol): mp 115–118°; ν (KBr) 1695, 1728 cm^{-1} (C=O); λ_{max} (EtOH) 309 nm (ϵ 9.50×10^3), 225 (2.66×10^4).

Anal. Calcd for $C_{13}H_{14}N_2O_4$: C, 59.53; H, 5.38; N, 10.68. Found: C, 59.53; H, 5.22; N, 10.50.

In this case, **31** was not detected.

Isomerization of 20.—From **20** (0.40 g) in chloroform (50 ml) there was obtained **32** together with **44** in ~10% yield. The mixture was heated in benzene (30 ml) at reflux temperature for 4 hr to give **44** in 85% yield, mp 118–120°, identical with an authentic sample.[2]

Isomerization of 21.—From **21** (0.40 g) in chloroform (50 ml) there was obtained **33** together with **45** in 25% yield as orange crystals. The mixture was heated in benzene (20 ml) at reflux temperature overnight to give **45** in 75% yield as colorless needles: mp 107–110°; ν (KBr) 1703, 1733 cm^{-1} (C=O); λ_{max} (EtOH) 300 nm (ϵ 8.51×10^3), 224 (2.82×10^4).

Anal. Calcd for $C_{13}H_{14}O_4N_2$: C, 59.53; H, 5.38; N, 10.68. Found: C, 59.37; H, 5.53; N, 10.61.

Isomerization of 22.—From **22** (0.40 g) in chloroform (50 ml) there was obtained **34** (0.02 g, 5%) as orange needles (from *n*-hexane): mp 81–83°; ν (KBr) 1717, 1730 cm^{-1} (C=O); λ_{max} (MeOH) 392 nm (ϵ 7.84×10^3), 303 (2.15×10^3).

Anal. Calcd for $C_{13}H_{16}N_2O_4$: C, 59.08; H, 6.10; N, 10.60. Found: C, 59.10; H, 6.17; N, 10.65.

This compound in carbon tetrachloride did not convert to **42** under heating at 100°.

Irradiation of 13.—A mixture of **13** (0.2 g) and acetone (100 ml) was irradiated at 0° for 45 min. Reaction mixture was concentrated *in vacuo*. A mixture of **23** and **35** was obtained in 60% yield in the ratio of 1:1 (by nmr inspection).

When compound **13** was irradiated under above condition for 2 hr at room temperature, only **35** was obtained in 50% yield.

Irradiation of 22.—A mixture of **22** (0.40 g) and acetone (100 ml) was irradiated at room temperature for 1 hr. The solution was concentrated *in vacuo* and the residual oil was separated by column chromatography (silica gel) using benzene. Recrystallization from *n*-hexane gave **34** (0.08 g, 20%).

Irradiation of 23.—A mixture of **23** (0.20 g) and acetone (100 ml) was irradiated at room temperature for 2 hr. Work-up as above gave **35** (0.16 g, 80%).

Compounds **24**–**33** were also observed to undergo dehydrogenation under irradiation and gave the pyrazolo[1,5-*a*]pyridine derivatives together with considerable amounts of tar.

Registry No.—**13**, 35116-54-2; **14**, 35116-55-3; **15**, 35116-56-4; **16**, 35116-57-5; **17**, 35116-58-6; **18**, 35116-59-7; **19**, 35116-60-0; **20**, 35116-61-1; **21**, 35116-62-2; **22**, 35116-63-3; **23**, 35116-64-4; **24**, 35116-65-5; **25**, 36116-66-6; **26**, 35116-67-7; **27**, 35116-68-8; **28**, 35116-69-9; **29**, 35116-70-2; **30**, 35116-71-3; **32**, 35116-72-4; **33**, 35116-73-5; **34**, 35116-74-6; **38**, 30689-98-6; **41**, 35116-76-8; **43**, 35116-77-9; **44**, 30758-71-5; **45**, 35116-79-1.

Synthesis of Ring-Fused Pyrroles. I. 1,3-Dipolar Cycloaddition Reactions of Munchnone Derivatives Obtained from Tetrahydro-β-carboline-3- and -1-carboxylic Acids

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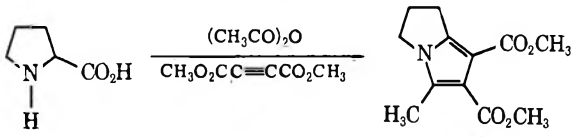
The reaction of various tetrahydro-β-carboline-3-carboxylic acids, **2a–c**, with dimethyl acetylenedicarboxylate in acetic anhydride directly afforded the corresponding indolizino[6,7-*b*]indoles **4a–c**, in moderate yields. Likewise, treatment of 1,2,3,4-tetrahydro-β-carboline-1-carboxylic acid, **5**, in acetic anhydride, with a variety of acetylenic dipolarophiles and less successfully with olefinic dipolarophiles furnished the corresponding indolizino-[8,7-*b*]indole derivatives. These reactions involve a 1,3-dipolar cycloaddition of the respective munchnone intermediates (**3** and **6**), respectively, formed *in situ*, with the dipolarophilic substrates.

Huisgen and coworkers have recently reported a general synthesis of pyrroles[1] and pyrrolines[2] using mesoionic Δ^2-oxazolium-5-olates (munchnones). These reactions involved a 1,3-dipolar cycloaddition of the munchnone, behaving like a cyclic azomethine ylide,[3] to the corresponding acetylenic or olefinic dipolarophile, followed by CO_2 evolution, and aromatization or tautomerization.[4] Most examples of the application of this reaction, to date, have involved the use of acyclic, *N*-acyl α-amino acids as the starting material,[5-8] although Huisgen has converted L-proline to the pyrrolizine derivative, **1**, in 76% yield by reaction with dimethyl acetylenedicarboxylate in acetic anhydride.[1]



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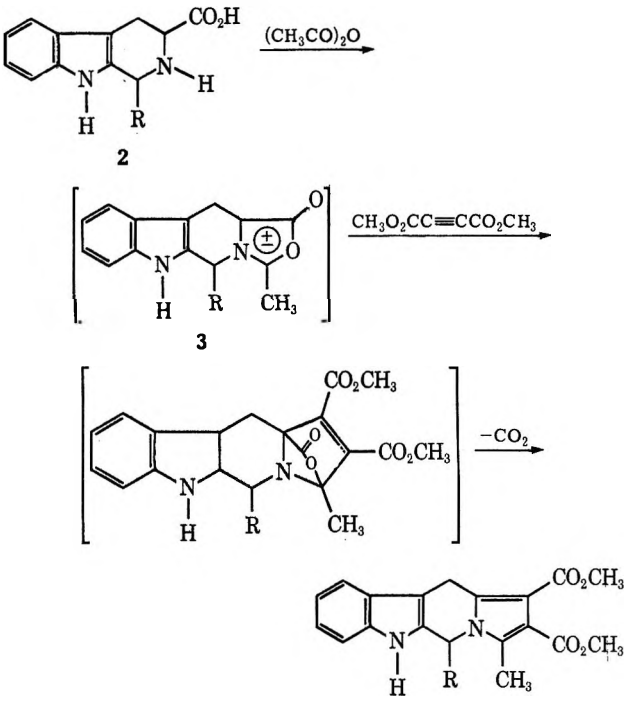
This paper will describe the transformation of another group of "cyclic" α-amino acids, namely, the tetrahydro-β-carboline-3- and -1-carboxylic acids (**2** and **5**), respectively, into the corresponding pyrrole derivatives *via* munchnone intermediates.

The conversion of the three tetrahydro-β-carboline-3-carboxylic acids **2a–c**, to the 5,6-dihydro-11*H*-indolizino[6,7-*b*]indoles, **4a–c**, involved treatment with dimethyl acetylenedicarboxylate in acetic anhydride at 70–120° (Scheme I). No attempt was made to isolate the intermediate munchnones (**3a–c**), since Huisgen has shown the oxazolium-5-olate system to be extremely reactive.[9] The progress of these reactions, and those described below, was monitored by CO_2 evolution. Work-up procedures generally involved the simple evaporation of solvents (acetic acid and acetic anhydride) *in vacuo* and subsequent recrystallization of the product. Only **4b** required the use of column chromatography in the work-up.

SCHEME I



4a, R = H
b, R = $C_6H_5CH_2$
c, R = *p*-$CH_3OC_6H_4$

The facility by which three steps, namely, acetylation, 1,3-dipolar cycloaddition, and aromatization, could be achieved in a single operation, prompted the examination of this reaction with the isomeric tetrahydro-β-carboline-1-carboxylic acid, **5**.

Whereas attempts to nitrosate **5** with sodium nitrite in cold concentrated hydrochloric acid, followed by formation of the sydnone derivative with acetic anhydride, failed,[10] the reaction of **5** with dimethyl acetylenedicarboxylate in acetic anhydride at 115° furnished methyl 3-methyl-5,6-dihydro-11*H*-indolizino[8,7-*b*]indole-1,2-dicarboxylate (**7a**) in 75% yield (Scheme II). Once again, no attempt was made to isolate the intermediate munchnone **6**. Compound **5** reacted in similar manner with propionic anhydride and dimethyl acetylenedicarboxylate, yielding the 3-ethylindolizino-[8,7-*b*]indole derivative **7b**; however, attempts to

(1) R. Huisgen, H. Gotthardt, H. O. Bayer, and F. C. Schaefer, *Chem. Ber.*, **103**, 2611 (1970).

(2) H. Gotthardt and R. Huisgen, *ibid.*, **103**, 2625 (1970).

(3) For a classification of 1,3 dipoles, see R. Huisgen, *Angew. Chem., Int. Ed. Engl.*, **2**, 565 (1963).

(4) H. Gotthardt, R. Huisgen, and H. O. Bayer, *J. Amer. Chem. Soc.*, **92**, 4340 (1970).

(5) A. Padwa and L. Hamilton, *J. Heterocycl. Chem.*, **4**, 118 (1967).

(6) K. T. Potts and U. P. Singh, *Chem. Commun.*, 66 (1969).

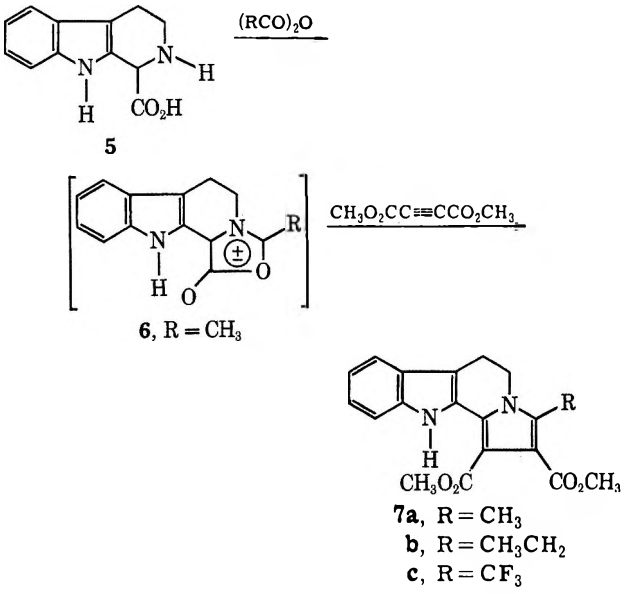
(7) H. W. Heine, A. B. Smith, and J. D. Bower, *J. Org. Chem.*, **33**, 1097 (1968).

(8) D. F. McLean, *Org. Prep. Proc.*, **2**, 145 (1970).

(9) Isolation of munchnones have been possible when aromatic substituents are present at the 2 and 4 positions of the oxazolium-5-olate ring, *i.e.*, 2,4-diphenyl- and 2-(*p*-nitrophenyl)-4-phenyloxazolium-5-olates: ref 4; G. Kille and J. P. Fleury, *Bull. Soc. Chim. Fr.*, 4636 (1968); H. O. Bayer, R. Huisgen, R. Knorr, and F. C. Schaefer, *Chem. Ber.*, **103**, 2581 (1970).

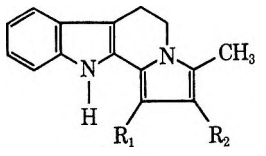
(10) H. A. Wagner, G. D. Searle & Co., personal communication.

SCHEME II

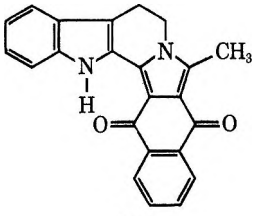


employ trifluoroacetic anhydride failed to provide the desired trifluoromethyl analog, **7c**. Instead, decarboxylation of **5** in the presence of the strong acid, trifluoroacetic acid, occurred prior to munchnone formation.[11,12]

In addition to using dimethyl acetylenedicarboxylate, several other acetylenic and olefinic dipolarophiles were employed. Ethyl propiolate provided the two isomeric monoesters, **8** and **9**, in 51 and 11% yields,



8, $R_1 = CO_2CH_2CH_3$; $R_2 = H$
9, $R_1 = H$; $R_2 = CO_2CH_2CH_3$
10, $R_1 = C_6H_5$; $R_2 = H$
11, $R_1 = H$; $R_2 = C_6H_5$
12, $R_1 = R_2 = H$



13

respectively. The isomers were easily separated by fractional crystallization and identification of each isomer was made on the basis of their respective nmr spectra. Particular attention was given to the chemical shifts and coupling constants of the pyrrole ring protons. In **8**, the pyrrole ring proton appeared as a quartet at δ 6.31 with long-range coupling to the adjacent ring methyl group (J_{H,CH_3} = 1.0 Hz). The ring proton in **9**, however, appeared as a singlet at δ 6.73. This deshielding of H-1 in **9** *vs.* H-2 in **8** is undoubtedly due to the anisotropic effect of the indole ring.

Treatment of **5** with phenylacetylene in acetic anhydride at 115° furnished a single product, **10**, in 34% yield. Careful examination of the reaction mixture failed to provide any evidence for the formation of the isomeric product, **11**. The nmr spectrum of **10**, once again, showed the pyrrole ring proton to be a quartet at δ 6.00 with long-range coupling to the adjacent ring methyl protons (J_{H,CH_3} = 0.8 Hz). The apparent regiospecificity of the reaction of phenylacetylene with munchnones has been reported,[1] and the isolation of **10** as the only product here is consistent with the arguments previously presented.

The reaction of **5** with olefinic dipolarophiles in acetic anhydride was generally less successful. While vinyl acetate or excess 1,4-naphthoquinone afforded the corresponding pyrrole derivatives **12** and **13**, reactions involving the use of acenaphthylene, isopropenyl acetate, *N*-*p*-methoxyphenylmaleimide, 2-cyclohexen-1-one, or methyl acrylate furnished complex, inseparable mixtures of products. These mixtures generally consisted of pyrrolines and dimeric products.[2]

Experimental Section[13]

Methyl 3-Methyl-5,6-dihydro-11*H*-indolizino[6,7-*b*]indole-1,2-dicarboxylate (4a).—A mixture consisting of 1,2,3,4-tetrahydro-β-carboline-3-carboxylic acid[14] (**2a**, 7.0 g, 0.03 mol), dimethyl acetylenedicarboxylate (6.4 g, 0.045 mol), and acetic anhydride (100 ml) was stirred and heated to 80°. Carbon dioxide evolution ensued and the reaction mixture warmed to 115°. This temperature was maintained until the CO_2 evolution had ceased (~15 min). The brown solution that remained was then cooled and a light yellow powder (6.50 g, 64% yield), mp 255–260°, was collected: ir (KBr disk) NH at 3360, C=O at 1725 and 1690 cm^{-1}; nmr (DMSO-d_6) CH_3 at δ 2.41 (s), two OCH_3 at 3.75 (s), CH_2 at 4.08 (m), CH_2 at 5.15 (m).

Anal. Calcd for $C_{19}H_{18}N_2O_4$: C, 67.44; H, 5.36; N, 8.28. Found: C, 67.08; H, 5.37; N, 8.03.

Methyl 3-Methyl-5-benzyl-5,6-dihydro-11*H*-indolizino[6,7-*b*]-indole-1,2-dicarboxylate (4b).—A mixture of 1-benzyl-1,2,3,4-tetrahydro-β-carboline-3-carboxylic acid[15] (**2b**, 9.2 g, 0.03 mol), dimethyl acetylenedicarboxylate (6.4 g, 0.045 mol), and acetic anhydride (100 ml) was stirred and heated to 80–90° for 45 min. The reaction mixture was then cooled to room temperature and evaporated to dryness *in vacuo*. The brown gum that remained was washed several times with petroleum ether, 60–90°, and the resultant brown, amorphous solid that formed was dissolved in benzene and chromatographed on a column of silica gel (800 g) in benzene. Elution with 10% ethyl acetate–90% benzene afforded a light brown solid (5.6 g). Recrystallization from ethanol yielded a yellow crystalline solid (3.5 g, 27% yield): mp 199–200.5°; ir ($CHCl_3$) NH at 3465, C=O at 1705 and 1695 cm^{-1}; nmr ($CDCl_3$) CH_3 at δ 2.54 (s), CH_2 at 3.15 (m), CH at 3.20 (d of d), OCH_3 at 3.80 (s), OCH_3 at 3.85 (s), CH at 4.13 (d of d), CH at 5.52 (m).

Anal. Calcd for $C_{28}H_{24}N_2O_4$: C, 72.88; H, 5.65; N, 6.54. Found: C, 72.72; H, 5.90; N, 6.18.

Methyl 3-Methyl-5-(*p*-methoxyphenyl)-5,6-dihydro-11*H*-indolizino[6,7-*b*]indole-1,2-dicarboxylate (4c).—Dimethyl acetylenedicarboxylate (6.4 g, 0.045 mol) was added to a stirred suspension of 1-(*p*-methoxyphenyl)-1,2,3,4-tetrahydro-β-carboline-3-carboxylic acid[16] (**2c**, 9.65 g, 0.03 mol) in acetic anhydride (150 ml), and the reaction mixture was heated to 100° for 1 hr. After cooling and evaporation to dryness *in vacuo*, the residual oil was triturated with warm cyclohexane. The cyclohexane supernatant was decanted and the syrupy residue dissolved in warm ethanol. The ethanolic solution was cooled and an orange solid

(11) G. Hahn and K. Stiehl, *Chem. Ber.*, **69**, 2627 (1936).

(12) R. A. Abramovitch and I. D. Spenser, *Advan. Heterocycl. Chem.*, **3**, 79 (1964).

(13) Melting points were determined in capillary tubes with a Thomas-Hoover melting point apparatus and are uncorrected. The author wishes to thank Dr. J. W. Ahlberg and staff for the analyses and spectra reported. Ir spectra were obtained in a 3% $CHCl_3$ solution or in KBr disks on an IR-12 spectrometer, Beckman Instruments, and are reported in reciprocal centimeters. Nmr spectra were determined in $CDCl_3$ or DMSO-d_6 solutions on a Model A-60 or HA-100 spectrometer, Varian Associates, Inc., using tetramethylsilane as an internal standard. Chemical shifts for aliphatic and aromatic pyrrole protons are reported in parts per million (δ). Aromatic (benzenoid) protons, in all cases studied, appeared as multiplets in the region of δ 6.66–8.33.

(14) D. G. Harvey, E. J. Miller, and W. Robson, *J. Chem. Soc.*, 153 (1941).

(15) H. R. Snyder, C. H. Hansch, L. Katz, S. M. Parmerter, and E. C. Spaeth, *J. Amer. Chem. Soc.*, **70**, 219 (1948).

(10.15 g, 75%), mp 202–205°, collected. Recrystallization from 2-propanol furnished a light yellow powder (6.55 g, 49%): mp 207–208°; ir (KBr) NH at 3320 C=O at 1725 and 1695 cm^{-1}; nmr (DMSO-d_6) CH_3 at δ 2.49 (s), CH_2 at 3.67 (m), OCH_3 at 4.00, 4.03, and 4.11 (s), CH at 4.68 (m).

Anal. Calcd for $C_{26}H_{24}N_2O_5$: C, 70.25; H, 5.44; N, 6.30. Found: C, 69.96; H, 5.69; N, 5.80.

Methyl 3-Methyl-5,6-dihydro-11*H*-indolizino[8,7-*b*]indole-1,2-dicarboxylate (7a).—A stirred mixture consisting of 1,2,3,4-tetrahydro-β-carboline-1-carboxylic acid[16] (**5**, 14.0 g, 0.065 mol), dimethyl acetylenedicarboxylate (12.8 g, 0.09 mol), and acetic anhydride (150 ml) was heated to 115° for 45 min. The reaction mixture was cooled, filtered, and evaporated to dryness *in vacuo*. The amorphous residue was triturated with cold methanol and then recrystallized from methanol yielding light tan prisms (16.50 g, 75%): mp 172–174°; ir ($CHCl_3$) NH at 3400, C=O at 1720 and 1695 cm^{-1}; nmr ($CDCl_3$) CH_3 at δ 2.35 (s), CH_2 at 3.10 (t), two OCH_3 at 3.86 (s), CH_2 at 3.93 (t).

Anal. Calcd for $C_{19}H_{18}N_2O_4$: C, 67.74; H, 5.36; N, 8.28. Found: C, 67.34; H, 5.55; N, 8.06.

Methyl 3-Ethyl-5,6-dihydro-11*H*-indolizino[8,7-*b*]indole-1,2-dicarboxylate (7b).—A similar reaction as described above for **7a** was carried out using propionic anhydride (150 ml) in place of acetic anhydride. Recrystallization of the crude product from methanol furnished a light yellow crystalline solid in 69% yield: mp 168–169°; ir ($CHCl_3$) NH at 3370, C=O at 1705 and 1685 cm^{-1}; nmr ($CDCl_3$) CH_3 at δ 1.21 (t), CH_2 at 2.81 (q), CH_2 at 3.13 (t), two OCH_3 at 3.88 (s), CH_2 at 4.03 (t).

Anal. Calcd for $C_{20}H_{20}N_2O_4$: C, 68.17; H, 5.72; N, 7.95. Found: C, 68.07; H, 5.85; N, 7.86.

Reaction of 5 with Ethyl Propiolate in Acetic Anhydride.—Ethyl propiolate (4.4 g, 0.045 mol) was added to a mixture of **5** (6.5 g, 0.03 mol) in acetic anhydride (100 ml). After heating to 110° for 1 hr, the reaction mixture was cooled to room temperature and filtered. The solid collected was washed with cold methanol leaving a light beige powder (0.95 g, 11%), mp 285–289°, which was identified as **ethyl 3-methyl-5,6-dihydro-11*H*-indolizino[8,7-*b*]indole-2-carboxylate (9)**: ir (KBr) NH at 3320, C=O at 1665 cm^{-1}; nmr (DMSO-d_6) CH_3 at δ 1.30 (t), CH_3 at 2.55 (s), CH_2 at 3.06 (t), CH_2 at 4.10 (t), CH_2 at 4.21 (q), pyrrole CH at 6.73 (s).

Anal. Calcd for $C_{18}H_{18}N_2O_2$: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.24; H, 6.35; N, 9.37.

The acetic anhydride filtrate of **9** was evaporated to dryness *in vacuo* and the residue was recrystallized from methanol. **Ethyl 3-methyl-5,6-dihydro-11*H*-indolizino[8,7-*b*]indole-1-carboxylate (8**, 4.5 g, 51%), mp 104–105°, was thus obtained as light tan plates: ir ($CHCl_3$) NH at 3370, C=O at 1680 cm^{-1}; nmr (DMSO-d_6) CH_3 at δ 1.33 (t), CH_3 at 2.25 (d), CH_2 at 3.11 (t), CH_2 at 4.08 (t), CH_2 at 4.33 (q), pyrrole CH at 6.31 (q).

Anal. Calcd for $C_{18}H_{18}N_2O_2$: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.21; H, 6.15; N, 9.45.

1-Phenyl-3-methyl-5,6-dihydro-11*H*-indolizino[8,7-*b*]indole (10).—A stirred mixture consisting of **5** (6.5 g, 0.03 mol), phenylacetylene (4.6 g, 0.045 mol), and acetic anhydride (100 ml) was heated to 115° for 30 min, then cooled to room temperature, and evaporated to dryness *in vacuo*. The residue was washed, first with petroleum ether (bp 60–90°) and then with cold methanol. Recrystallization of the remaining residue from methanol furnished a light tan crystalline solid (3.10 g, 34%): mp 156–158°; ir ($CHCl_3$) NH at 3470 cm^{-1}; nmr ($CDCl_3$) CH_3 at δ 2.30 (d), CH_2 at 3.11 (t), CH_2 at 4.00 (t), pyrrole CH at 6.00 (q).

Anal. Calcd for $C_{21}H_{18}N_2$: C, 84.53; H, 6.03; N, 9.39. Found: C, 84.67; H, 6.46; N, 9.17.

Combination of the mother liquor and washings of **10**, followed by evaporation, and column chromatographic work-up of the residue failed to provide the isomeric indolizino[8,7-*b*]indole (**11**).

3-Methyl-5,6-dihydro-11*H*-indolizino[8,7-*b*]indole (12).—A mixture of **5** (6.5 g, 0.03 mol), vinyl acetate (3.9 g, 0.045 mol), and acetic anhydride (150 ml) was heated to 110° for 1 hr. The reaction mixture was cooled and evaporated to dryness *in vacuo*, and the residue was recrystallized from ethanol, yielding a light tan powder (3.55 g, 53%): mp 209.5–212°; ir ($CHCl_3$) NH at 3480 cm^{-1}; nmr ($CDCl_3$) CH_3 at δ 2.26 (d), CH_2 at 3.06 (t), CH_2 at 3.98 (t), pyrrole CH (H-2) at 5.93 (d of d), pyrrole CH (H-1) at 6.18 (d).

Anal. Calcd for $C_{15}H_{14}N_2$: C, 81.05; H, 6.35; N, 12.60. Found: C, 81.10, H, 6.27; N, 12.46.

5,14-Dioxo-13-methyl-5,11,12,14-tetrahydro-6*H*-naphth[2′,3′:1,2]indolizino[8,7-*b*]indole (13).—A similar reaction as described above for **12** was carried out using 1,4-naphthoquinone (9.5 g, 0.06 mol) in place of vinyl acetate. The reaction mixture, on cooling to room temperature, furnished **13**, as a red-brown solid (9.0 g, 85%), mp 241–244°. Recrystallization from DMF yielded a red-brown solid: mp 244–245°; ir ($CHCl_3$) NH 3330, C=O at 1660 cm^{-1}; nmr ($CDCl_3$) CH_3 at δ 2.60 (s), CH_2 at 3.21 (t), CH_2 at 4.08 (t).

Anal. Calcd for $C_{23}H_{16}N_2O_2$: C, 78.39; H, 4.58; N, 7.95. Found: C, 78.28; H, 4.55; N, 7.82.

Registry No.—**4a**, 35105-58-9; **4b**, 35105-59-0; **4c**, 35105-60-3; **7a**, 35105-61-4; **7b**, 35105-62-5; **8**, 35105-63-6; **9**, 35105-64-7; **10**, 35105-65-8; **12**, 35105-66-9; **13**, 35105-67-0.

Acknowledgments.—The author wishes to thank Dr. Hans A. Wagner for many valuable discussions and Mr. Paul Langerman for technical assistance.

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Formation and Mass Spectral Fragmentation of Ritter Products from Some Monoenic Fatty Acids. Location of Double-Bond Position in Unsaturated Acids

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By modification of the known Ritter conditions for making N-substituted amides by addition of acrylonitrile to olefinic compounds, it is possible to apply this reaction to new monoenic fatty acids. Procedures are presented for the addition of acrylonitrile to oleic acid (**2a**), methyl *cis*-5-eicosenoate (**3**), erucic (**4**), and brassidinic (**5**) acids, and the addition of acetonitrile to brassidinic acid. Yields of 54 to 80–84% of the respective monoacrylamides (**10–12**) and acetoamide (**8**) were obtained in crystalline form from the monoenic fatty acids by applying the proper ratio of reactants and by the mode of addition. Evidence is adduced, showing that it is possible to determine the addition sites in the Ritter products by mass spectrometry, and also that mass spectral analysis of Ritter products from olefinic compounds could be of general utility for the assignment of double bond position in the carbon chain.

The formation of acylamino fatty acids of structure $CH_3[CH_2]_xCH(NHCOR)[CH_2]_yCOOR'$ by interaction of nitriles and monoenic acids in the presence of strong acids (designated the Ritter reaction) is well documented.[1-6]

Earlier investigators in the fatty acid field have noted that the C_{18}-monoenic acids, oleic (**2a**)[2b] and petroselinic (**1**),[2c] lend themselves to smooth Ritter reaction with a variety of saturated and unsaturated aliphatic nitriles, dinitriles,[3] and hydrogen cyanide, but in no case was the position of the addition determined.

With the exception of **1** → **6** and **2** → **7** conversions, reactions of acrylonitrile with some other monoenic fatty acids do not appear to have been studied. Our interest in such a study emerged from a research project aimed at exploring the ability of Ritter-type products (**6–7**, **10–12**) from acrylonitrile to undergo the Diels–Alder reaction.[7]

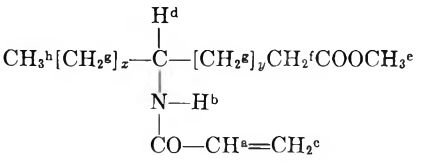
We have presented here the application of the Ritter reaction to a variety of pure homologs of long-chain unsaturated acids in the C_{18} to C_{22} range (see Scheme I) and results of a mass spectral study of the Ritter products **7–12**.

Results of the Ritter Reaction.—The procedures and results of the Ritter reaction between acrylonitrile and a series of monoenic fatty acids described here relate to the following substrates: oleic (**2a**), *cis*-5-eicosenoic (**3**), *cis*-13-docosenoic (erucic **4**), and *trans*-13-docosenoic (brassidinic, **5**) acids. We also included in this study the reaction between acetonitrile and **2b**, and the catalytic reduction of methyl acrylamidostearate (**9**) into methyl propionamidostearate (**10**).

The experimental part describes the series of experiments which give the optimum yields of once-recrystallized material obtained from a series of reactions in which variations in the ratio of reactants and in the mode of addition were studied. Other features were determined after three or more recrystallizations from acetone.

Satisfactory yields of methyl *N*-acrylamidostearate (**9**) were obtained when concentrated sulfuric acid was added to a mixture comprised of oleic acid–acrylonitrile–H_2SO_4 in a ratio of 1:3:3, with a reaction time of 45–60 min at 27–30°. Reasonable yields of the respective acrylamide, methyl acrylamidobehenate (**12b**), and methyl acetamidobehenate (**8**) were obtained in the cases of *cis*- and *trans*-13-docosenoic acids (erucic and brassidinic acid, **4** and **5**, respectively) when a ratio of fatty acid–nitrile–H_2SO_4 of 1:1.2:6 was employed under similar reaction conditions. The highest yield (80%) of an acrylamide (**11**) was obtained from the reaction of acrylonitrile with methyl *cis*-5-eicosenoate (**3**), the double bond of which appears to be relatively highly reactive towards the Ritter reaction.

The ir spectra of the Ritter products showed strong absorption at 3250–3300 and 1610–1625 cm^{-1}, corresponding to the amide group. In addition, these compounds also exhibited bands at 1650–1660, 972–987, and 947–965 cm^{-1} due to the vinyl group conjugated with a carbonyl.



The nmr spectral parameters of **7**, **9**, **11**, and **12** in $CDCl_3$ are essentially the same. As expected, the protons attached to the long carbon chain resonate between τ 6.0 and 9.12 [τ 6.05 (1 H, m, H^d), 6.35 (3 H, s, H^e), 7.70 (2 H, t, J = 7 Hz, H^f), 8.2–9.0 (H^g), and 9.12 (3 H, t, J = 5 Hz, H^h)], whereas the resonances of protons attached to the acrylamido group are only slightly affected by the environment, as follows: 3.75 τ (1 H, d, H^a), 4.38–4.50 (2 H, d, H^c), and 4.05–3.48 (1 H, d, J = 9 Hz, H^b).

Experimental Section

Materials and Sources.—The sources for the purchased chemicals are given in parentheses. Oleic acid (**2a**) (Nutritional Biochemicals Corp.), methyl oleate (**2b**) (British Drug House), *trans*-13-docosenoic (brassidinic acid, **5**) (Fluka, A.G.), *cis*-13-docosenoic (erucic acid, **4**) (Fluka), ethyl linoleate (**7b**) (Fluka), and acrylonitrile (British Drug House) were of "chemically pure" grade. Acrylonitrile, bp 72–73° (690 mm), was distilled under nitrogen atmosphere before use. Silicic acid (100 mesh) for chromatography (Mallinckrodt) was of analytical grade.

Isolation of *cis*-5-Eicosenoic and *cis,cis*-5,13-Docosadienoic Acids from *Limnanthes douglasii* Seed Oil.—The major compo-

(1) Deceased.

(2) (a) L. I. Krimen and D. J. Cota, *Org. React.*, **17**, 213 (1969); (b) E. T. Roe and D. Swern, *J. Amer. Chem. Soc.*, **75**, 5479 (1953); (c) *ibid.*, **77**, 5408 (1955).

(3) A. E. Kulikova, S. B. Meiman, and E. N. Zilberman, *Chem. Abstr.*, **59**, 11240e (1963).

(4) R. L. Holmes, J. P. Moreau, and G. Sumrell, *J. Amer. Oil Chem. Soc.*, **42**, 922 (1965).

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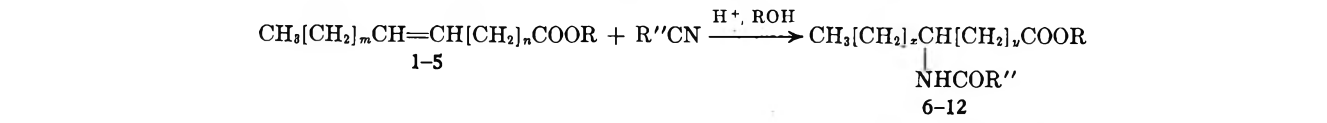
(7) S. Blum, S. Gertler, S. Sarel, and D. Sinnreich, submitted for publication.

SCHEME I



1–5 6–12

1, R = H; $m = 10$; $n = 4$
2a, R = H; $m = n = 7$
2b, R = CH_3; $m = n = 7$
3, R = CH_3; $m = 13$; $n = 3$
4, R = H; CH=CH (cis); $m = 7$; $n = 11$
5, R = H; CH=CH (trans); $m = 7$; $n = 11$

6, R = H; R'' = $CH=CH_2$; $(x + y) = 15$
7, R = H; R'' = $CH=CH_2$; $(x + y) = 15$
8, R = R'' = CH_3; $(x + y) = 15$
9, R = CH_3; R'' = $CH=CH_2$; $(x + y) = 15$
10, R = CH_3; R'' = C_2H_5; $(x + y) = 15$
11, R = CH_3; R'' = $CH=CH_2$; $(x + y) = 17$
12, R = CH_3; R'' = $CH=CH_2$; $(x + y) = 19$

nents of the seed oil are: *cis*-5-eicosenoic acid ($C_{20}H_{38}O_2$, 65%), *cis*-13-docosenoic (erucic) acid ($C_{22}H_{42}O_2$, 13%), *cis*-5-docosenoic acid ($C_{22}H_{42}O_2$, 7%), and *cis,cis*-5,13-docosadienoic acid ($C_{22}H_{40}O_2$, 11%).[8] The predominant C_{20}-monoenic and the minor C_{22}-dienoic acids were obtained by way of fractional crystallization at −60° followed by separation between the mercuric acetate adducts, according to the procedure of Fore, *et al.*[9] The separation between the two C_{22}-monoenic acids was troublesome. In the vpc a mixture of these acids exhibits a single peak.

Methyl *cis*-5-eicosenoate (5) had bp 185–187° at 2 mm (lit.[9] bp 180–182° at 1 mm), was of 90–95% purity (vpc analysis with a 10-ft by 0.25-in. width column filled with 20% stabilized DEGS on 60–80 Chromosorb W, at 245°), and was obtained in 40–45% yield.

Acrylamido Fatty Acids and Derivatives. Application of the Ritter Reaction.—Procedure and **Results** are given for additions of acrylonitrile to oleic (2a), *cis*-13-docosenoic (erucic) (4), *trans*-13-docosenoic (brassidinic) (5), and *cis*-5-eicosenoic (3) acids. The reaction in sulfuric acid was generally started at or below 0°, according to the tendency of the unsaturated compound to undergo the Ritter reaction, and then was allowed to warm up. The reaction was completed at 27–30° for *ca.* 1 hr, followed by addition of methanol or ice water.

Methyl Acrylamidostearate (9).—The procedure described below represents the optimal conditions for generation of the title compound from oleic acid.

A mixture of 28.2 g (0.1 mol) of 2a and 15.9 g (0.3 mol) of freshly distilled acrylonitrile was well stirred and cooled to −20° (ice–salt) while 33.8 g of H_2SO_4 (95%) was added dropwise in such a rate as to maintain the internal temperature around 27° (about 20 min). This was then stirred for 1 hr at room temperature, and then poured into 200 ml of cold methanol and allowed to stand overnight. The esterification was completed by refluxing the mixture for 2.5 hr and the excess methanol was removed at reduced pressure. The residue was extracted by ether, thoroughly washed with water, 5% aqueous sodium bicarbonate, and saturated sodium chloride solution, and dried. Removal of ether furnished 31.5 g of an oily residue which, on trituration with petroleum–ether (40–60°), yielded 22.7 g (62%) of crystalline methyl acrylamidostearate of mp 37–42°. Successive recrystallizations of the product from ethanol at −70° raised the melting point to 72–77°. Its ir spectrum exhibited peaks at 3255 (NH), 1736 (CO ester), 1622 (amide), 1652, 982, and 945 cm^{-1} ($CH=CH_2$).

Acrylamidostearic Acid (7).—In a typical experiment, 0.4 mol of concentrated sulfuric acid (98%) was added dropwise to a well-stirred mixture of 2a (0.1 mol) and freshly distilled acrylonitrile (0.11 mol) at 0° during 30 min. The mixture was allowed to warm to 27–30° for 30 min and then was carefully poured with stirring into ice water. Stirring was continued for 16 hr, resulting in a homogeneous viscous mass which was then extracted with ether. The extract was washed with 5% sodium bicarbonate and dried ($MgSO_4$), and solvent was removed. The brown oily residue (7.1 g, 20%) was chromatographed on a silica column (350 g), using ether as eluting solvent, providing a colorless low-melting solid product. Recrystallization from acetone at −70° yielded microcrystals of 7 [mp 35–40° (lit.[2a] viscous oil); ir (KBr) 3250, 1705, 1620, 1650, 983, and 950 cm^{-1}], which analyzed as a $C_{21}H_{39}NO_3$ product.

Acrylamidostear-*p*-toluidide.—A mixture of 7 (0.52 g) and *p*-toluidine (1 g) was heated to 190–210° for 2 hr, and then was cooled. The mixture was extracted by ether, washed with 10% hydrochloric acid and water, and dried, and the solvent was removed. Recrystallization from aqueous ethanol provided 0.12 g (18%) of colorless crystals of the *p*-toluidide, mp 125–135°.

Anal. Calcd for $C_{28}H_{46}N_2O_2$: C, 76.0; H, 10.5; N, 6.3. Found: C, 76.0; H, 10.6; N, 6.4.

Acrylamidostearanilide, mp 63–65°, was similarly prepared from 7 (1.1 g) and aniline (1 g) in 16% yield.

Methyl Acrylamidobehenate (12b). i. **From *trans*-13-Docosenoic (Brassidinic) (5) Acid.**—In a manner described above, a mixture of 13.5 g of 5 and 6.36 g of acrylonitrile was well stirred and cooled in an ice–salt bath, while 13.5 ml of 98% H_2SO_4 was added dropwise during 30 min. The mixture was then allowed to warm up for 30 min and finally was poured into cold methanol with continual stirring. After the work-up, as described above, 15.4 g of an oily product (12b) was obtained. It was eluted with petroleum ether (60–80°) and finally recrystallized from ethanol at −60°, mp 55–70°. An analytial sample of methyl acrylamidobehenate (12b) of mp 73–77°, which analyzed as a $C_{26}H_{49}NO_3$ product, could be obtained after several recrystallizations.

ii. **From *cis*-13-Docosenoic (Erucic) Acid (4).**—The reaction of erucic acid (0.1 mol) and acrylonitrile (0.25 mol) in the presence of 98% H_2SO_4 (27 ml) in a fashion described above afforded methyl acrylamidobehenate (53%): mp 73–77°; ir 3254, 1737, 1622, 1653, 982, and 947 cm^{-1}.

Acrylamidobehenic Acid (12a). **From *trans*-Docosenoic (Brassidinic) Acid.**—To a mixture of 5 (20 mmol) and acrylonitrile (24 mmol) was added dropwise 98% H_2SO_4 (120 mmol) during 30 min, at −20°. The mixture was treated in a manner described above. Column chromatography (silica gel) followed by successive recrystallizations from acetone at low temperature furnished colorless crystals (42–45%) of acrylamidobehenic acid (12a) (mp 55–70°; ir 3250, 1711, 1622, 1655, 985, and 954 cm^{-1}), which gave the correct elemental analysis for $C_{25}H_{47}NO_3$.

Methyl Acrylamidoeicosanoate (11). The Ritter Reaction of Methyl *cis*-5-Eicosenoate (3).—A well-stirred mixture of methyl *cis*-5-eicosenoate (3) (6.5 g, 0.02 mol) and acrylonitrile (3.2 g, 0.06 mol) was cooled to 0°, 6.3 ml of 98% H_2SO_4 being added dropwise during 30 min, finally poured into 20 ml of cold methanol, and left to stand for 16 hr at room temperature. It was then poured onto ice, extracted with ether, washed, and dried, and the solvent was removed. The crude methyl acrylamidoeicosanoate (11) was obtained in 80% yield. The pure product was obtained by vapor phase chromatography on a 2-ft column packed with silica gum rubber SE-30 on Chromosorb W 60–80 mesh reg, followed by recrystallization from acetone: mp 71–74°; R_f 0.39–0.42 [tlc, on Kieselgel, chloroform–methanol (24:1) as eluent]; ir 3300, 1740, 1620, 1650, 9.72, and 960 cm^{-1}. It gave the correct elemental analysis for $C_{25}H_{47}NO_3$.

Methyl Acetamidobehenate (8).—In the fashion described above, a mixture of 2.7 g of 5 and 1 g of acetonitrile was treated with 2.7 ml of 98% H_2SO_4 at 0° during 30 min, and, before the reaction mixture was quenched in cold methanol, it was allowed to warm up for 30 min. After the usual work-up the Ritter product 8 was obtained in crystalline form (51%), mp 69–74° (from ethanol).

Anal.. Calcd for $C_{25}H_{49}NO_3$: C, 73.0; H, 11.9; N, 3.31. Found: C, 72.7; H, 11.8; N, 3.0.

Preparation of Methyl Propioamidostearate (10). The Catalytic Reduction of 9.—Into a Parr instrument bottle was placed a solution of 0.8 g of methyl acrylamidostearate (9) [mol wt 367 (mass spectra)] in 50 ml of ethanol and 50 mg of 5% Pd/C, shaken with hydrogen for 2 hr. After the usual work-up, crystals (85%) of methyl propionamidostearate (10) were obtained. Recrystallization from ethanol afforded white crystals of mp 57–61°, mol wt 369 (mass spectra), analyzed as $C_{22}H_{43}NO_3$ product,

(8) M. O. Ragby, C. R. Smith, T. K. Miwa, R. L. Lohmer, and I. A. Wolff, *J. Org. Chem.*, **26**, 1261 (1961).

(9) S. P. Fore, F. G. Dollear, and G. Sumrell, *Lipids*, **1**, 73 (1966).

displaying the characteristic bands at 3230 (NH), 1680 (C=O ester), and 1580 cm^{-1} (C=O amide), the disappearance of the vinyl stretching vibration at 1652 cm^{-1}, and the deformation vibrations at 982 and 945 cm^{-1}, in ir spectrum.

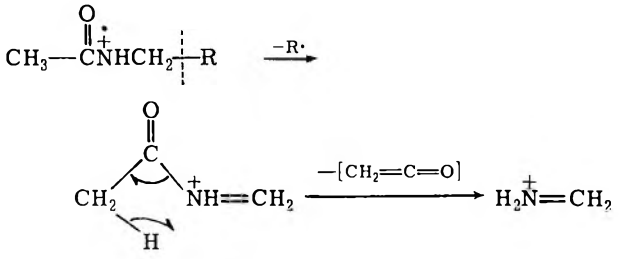
Determination of Addition Positions in Ritter Products by Mass Spectrometry

The physical properties of the Ritter product from acrylonitrile and oleic acid have been discussed earlier[2a] in terms of the formation of an isomeric mixture. To establish isomeric distribution in Ritter products from 1-octadecene and a variety of nitriles, Clarke, *et al.*,[10] applied the vapor phase chromatographic technique (vpc) to the amines obtained after alkaline hydrolysis. They have encountered increasing difficulty in separating the isomers by vpc as the amino group becomes more remote from the terminal position.

In order to determine the addition positions in Ritter products from acrylonitrile and the monoenic fatty acids described above, a mass spectral study of these products was undertaken.

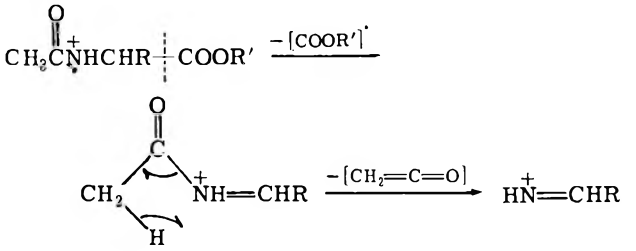
The mass spectral analysis was based on the well-known observation evidenced in a thorough mass spectral study of *N*-butylacetamide[11] that the principal electron-induced fragmentation of secondary amides involves rupture of the C–C bond α to the amido function, with charge retention on the latter. This fragment then loses a methylene ketene molecule by cleavage of the CO–N bond with hydrogen rearrangement to give iminium ions[12] (see Scheme II).

SCHEME II



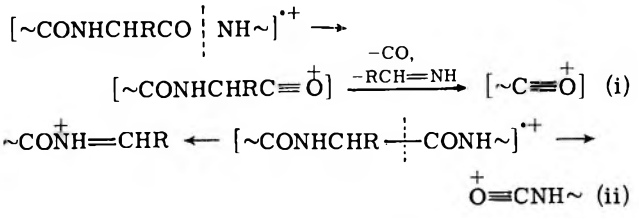
The mass spectra of *N*-acetylamino acids[13] and their alkyl esters[14] all show an intense acetyl ion (*m/e* 43), and the chief common feature is loss of the carboxyl (or alkoxycarbonyl) group to give an acyliminium ion, which then ejects methyleneketene with formation of an amine fragment (Scheme III). Ionized peptide chains, on the other hand, rupture at the amide bonds in two main modes:[15] (i) cleavage of the CO–N bond giving

SCHEME III



acylium ions which then lose carbon monoxide and a neutral imine fragment, and (ii) cleavage of the C–CO bond with retention of charge by either moiety (Scheme IV).

SCHEME IV



On the basis of this knowledge one might expect that, upon electron impact, the fragmentation of N-substituted fatty acrylamides of structures **9** and **11**–**12** would be very characteristic, which would permit the deduction of addition site in the Ritter products from the respective unsaturated fatty acids **2**, **3**, and **4**–**5**.

The mass spectra were measured on the Atlas MAT CH4 mass spectrometer using the direct inlet system. The electron energy was maintained at 70 eV and the ionization current was maintained at 20 μA. The abundances of ions from primary fragmentations are given in percentages relative to the *m/e* 55 peak ion (CH_2=$CHCO^+$) and assembled in Tables I–V.

In the mass spectra of all unsaturated Ritter products (**9**, **11**, and **12**) the ion of highest mass-to-charge ratio is the acryl ion, CH_2=CHC^+≡O (*m/e* 55) (see Tables I, III, and V), whereas in methyl propionamidostearate (**10**), resulting from **9** → **10** conversion, and also in methyl acetamidostearate (**8**), the most intense peak is *m/e* 74 (see Tables II and IV). This corresponds to the $C_5H_6O_2^+$ fragment, which is the predominant peak in the mass spectra of methyl stearate,[16] and to which the structure CH_2=$C(OH)OCH_3$ was assigned. It probably results from McLafferty rearrangement as depicted in Scheme V.

In analogy to secondary aliphatic amides and to esters of fatty acids, the most prominent peaks in the mass spectra of **8**–**12** correspond to ions of structures **13**–**17**, resulting from α cleavages at both sides of the C–N bond (fragmentations of type A and B),[17] which upon expulsion of either a C_3H_2O unit (conversions of **14** to **16** and of **13** to **15**) or alcohol from the acid moiety (rupture of **14** to **17**) give rise to the iminium ions **15** and **16** and the acylium ion **17** (Scheme VI).

(10) T. Clarke, J. Devine, and D. W. Dicker, *J. Amer. Oil Chem. Soc.*, **41**, 78 (1964).

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(14) C. O. Andersson, R. Ryhage, and E. Stenhagen, *Ark. Kemi*, **19**, 417 (1962).

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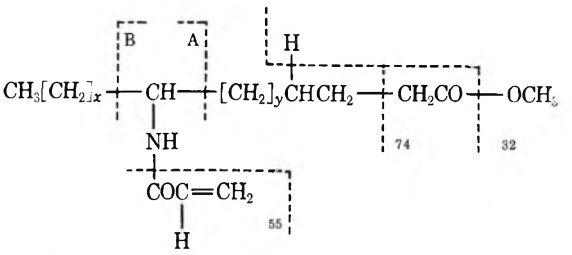
(16) (a) Ng. Dinh-Nguyen, R. Ryhage, S. Stallberg-Stenhagen, and E. Stenhagen, *Ark. Kemi*, **18**, 393 (1961); (b) K. K. Sun and R. T. Holman, *J. Amer. Oil Chem. Soc.*, **45**, 810 (1968).

(17) (a) W. Vetter, P. Longevialle, F. Khuong-Huu-Laine, Q. Khuong-Huu, and R. Goutarel, *Bull. Soc. Chim. Fr.*, 1324 (1963); (b) L. Dolejs, V. Hanus, V. Cerny, and F. Sorm, *Collect. Czech. Chem. Commun.*, **28**, 1584 (1963); (c) see ref 11a.

TABLE I

RELATIVE ABUNDANCE OF AMINE (A-54), AMIDE (A, B-32), AND ESTER PEAKS (B, B-54) IN THE MASS SPECTRUM OF METHYL ACRYLAMIDOSTEARATE (9)

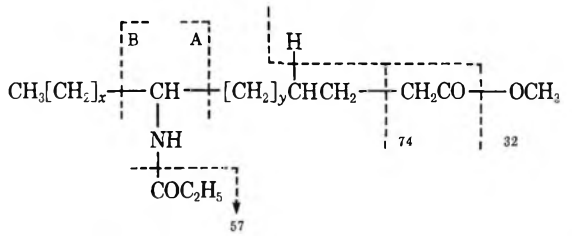


mol peak (m/e 366) = 3%; base peak (m/e 55) = 100%; ester peak (m/e 74) = 10%

Position of attachment	Peak A		A-54		B		B-32		B-54	
	m/e	Rel abund, %	m/e	Rel abund, %	m/e	Rel abund, %	m/e	Rel abund, %	m/e	Rel abund, %
C-7	238	6	184	4	212	7	180	5	158	2
C-8	224	19	170	13	226	19	194	13	172	4
C-9	210	65	156	32	240	50	208	30	186	9
C-10	196	66	142	33	254	50	222	31	200	9
C-11	182	15	128	9	268	6	236	5	214	2

TABLE II

RELATIVE ABUNDANCE OF AMINE (A-56), AMIDE (A, B-32), AND ESTER PEAKS (B, B-56) IN THE MASS SPECTRUM OF METHYL PROPIONAMIDOSTEARATE (10)

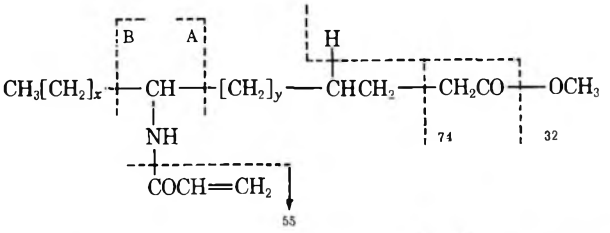


mol peak (m/e 369) = 14%; base peak (m/e 74) = 100%; peak (m/e 57) = 55%

Position of attachment	Peak A		A-56		B-32		B		B-56	
	m/e	Rel abund, %	m/e	Rel abund, %	m/e	Rel abund, %	m/e	Rel abund, %	m/e	Rel abund, %
C-7	240	6			182	5	214	15	158	6
C-8	226	22	170	43	196	6	228	32	172	24
C-9	212	48	156	80	210	18	242	57	186	52
C-10	198	50	142	80	224	18	256	50	200	52
C-11	184	22	128	13	238	3	270	7	214	15

TABLE III

RELATIVE ABUNDANCE OF AMINE (A-54), AMIDE (A, B-32), AND ESTER PEAKS (B, B-54) IN THE MASS SPECTRUM OF METHYL ACRYLAMIDOBEHENATE (12)

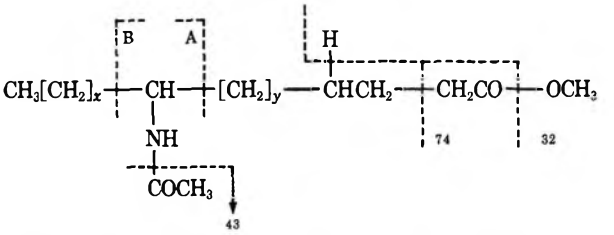


mol peak (m/e 423) = 22%; base peak (m/e 55) = 100%; peak (m/e 74) = 10%

Position of attachment	Peak A		A-54		B-32		B		B-54	
	m/e	Rel abund, %	m/e	Rel abund, %	m/e	Rel abund, %	m/e	Rel abund, %	m/e	Rel abund, %
C-11	238	6	184	1.5	236	3	268	1	214	1.5
C-12	224	16	170	3	250	3	282	4	228	1.5
C-13	210	98	156	63	264	31	296	74	242	9
C-14	196	95	142	65	278	32	310	75	256	9
C-15	182	8	128	1.5	292	1.5	324	5	270	1.5

TABLE IV

RELATIVE ABUNDANCE OF AMINE (A-42), AMIDE (A, B-32), AND ESTER PEAKS (B, B-42) IN THE MASS SPECTRUM OF METHYL ACETAMIDOBEHENATE (8)

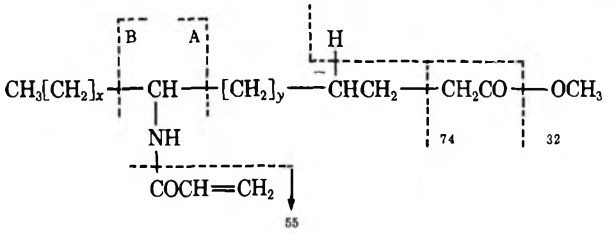


mol peak (*m/e* 411) = 9%; base peaks (*m/e* 74) = 100%, (*m/e* 43) = 98%

Position of attachment	Peak A *m/e*	Peak A Rel abund, %	A-42 *m/e*	A-42 Rel abund, %	B-32 *m/e*	B-32 Rel abund, %	B *m/e*	B Rel abund, %	B-42 *m/e*	B-42 Rel abund, %
C-11	226	20			224	10	256	30	214	12
C-12	212	33			238	11	270	35	228	18
C-13	198	99	156	22	252	14	284	97	242	28
C-14	184	99	142	19	266	12	298	81	256	30
C-15	170	30	128	11	280	6	312	26		

TABLE V

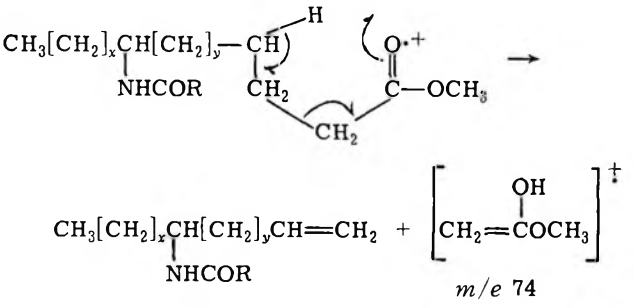
RELATIVE ABUNDANCE OF AMINE (A-54), AMIDE (A, B-32), AND ESTER PEAKS (B, B-54) IN THE MASS SPECTRUM OF METHYL ACRYLAMIDOEICOSENOATE (11)



mol peak (*m/e* 395) = 57%; base peak (*m/e* 55) = 100%; peak (*m/e* 74) = 13%

Position of attachment	Peak A *m/e*	Peak A Rel abund, %	A-54 *m/e*	A-54 Rel abund, %	B-32 *m/e*	B-32 Rel abund, %	B *m/e*	B Rel abund, %	B-54 *m/e*	B-54 Rel abund, %
C-5	294	14	240	27	152	4	184	30	130	1
C-6	280	81	226	85	166	20	198	95	144	29
C-7	266	84	212	100	180	24	212	100	158	39
C-8	252	58	198	95	194	15	226	85	172	19
C-9	238	14	184	30	208	2	240	27	186	3

SCHEME V



8, R = CH_3; $(x + y) = 12$
10, R = C_2H_5; $(x + y) = 12$

This suggest that loss of a C_3H_2O unit from fragment **18**, where R″ equals CH_2=CH– (from ionized **9**, **11**, and **12**), should involve rearrangement of an inner vinylic hydrogen as formulated in Scheme VII.

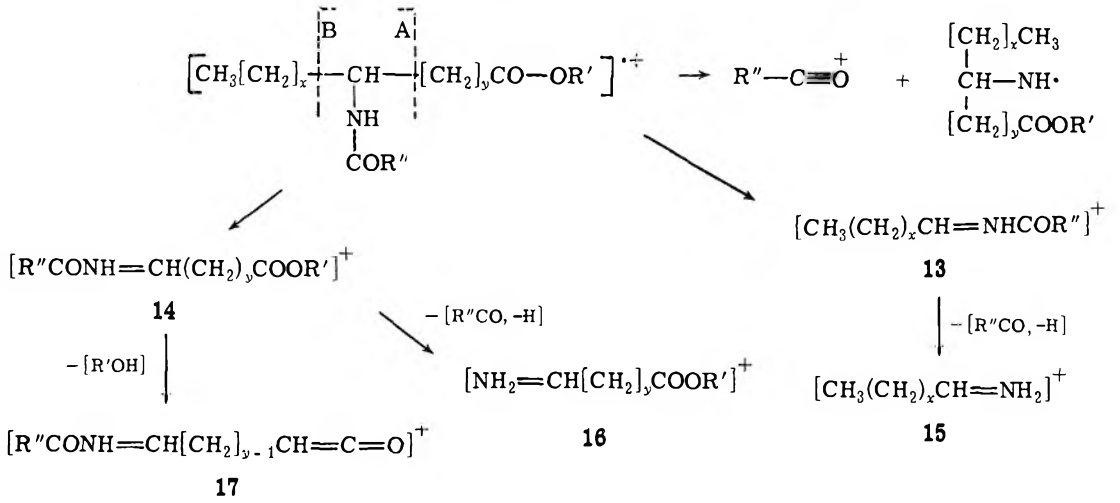
Like the pure homologs of long-chain acid esters,[16,18] the relative abundance of molecular ions in the mass spectra of **9**–**12** remarkably increases as the fatty carbon chain increases (compare Tables I, III, and V).

Examination of mass spectral data assembled in Tables I–V reveals that the most prominent peaks in the fragmentation of **8**–**10** and **12** are characterized by their appearance in pairs of equal intensity which are 14 mass units apart. Thus, in the mass spectra of **12** (Table III), they are *m/e* 156–142, 210–196, 242–256, 264–278, and 296–310, corresponding to fragments resulting from the primary reaction (cleavages A and B, in Scheme VI) and the secondary reactions involving losses of a C_3H_2O unit as depicted in Scheme VII (fragments A-54 and B-54) or the expulsion of methanol to yield B-32. Simple analysis shows that these fragments could originate from a mixture of ionized molecules of structure **12**, where the acrylamido nitrogen is equally and predominantly attached to carbons 13 ($x = 8$; $y = 11$) and 14 ($x = 7$; $y = 12$) of the fatty acid carbon chain.

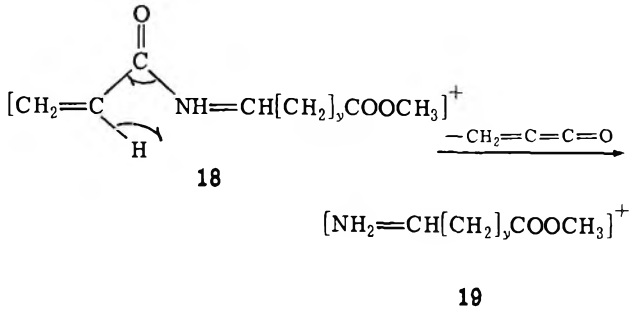
This suggest that the most favored carbonium ions from protonation of **4** or **5**, occurring in the course of Ritter reaction, are the secondary ones on C-13 and C-14, the isomerization of which to the C-12 and C-15

(18) (a) R. Ryhage and E. Stenhagen, *Ark. Kemi*, **13**, 523 (1959); (b) R. Ryhage, *ibid.*, **13**, 475 (1959).

SCHEME VI



SCHEME VII

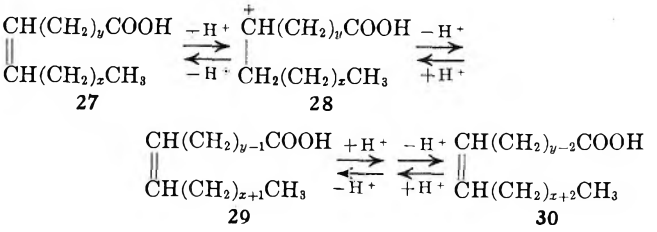


carbonium ions (which presumably generate products **12** where $x = 9$, $y = 10$, or $x = 6$, $y = 13$, respectively) is very small indeed.

The case is similar for the Ritter product **9** which emerges from the reaction of oleic acid with acrylonitrile. Its mass spectral analysis reveals that the entering acrylamido group favors an attachment either to C-9 or to C-10 (see Table I) and to a much lesser extent also to C-8, probably through equilibria between the various carbonium ion species.

Mass spectral analysis of **11** (Table V) shows that the isomeric distribution in the latter is relatively much broader. Under strong acidic conditions *cis*-5-eicosenoic acid (**3**) undergoes attack by acrylonitrile at carbons 6, 7, and 8 (at the carbonium ions **24**, **25**, and **26**, respectively; see Scheme VIII) rather than at the expected ones, 5 and 6 (**20** and **21**, respectively). An entrance of the acrylamido group has not been observed at carbons 2, 3, or 4. This can be explained, at least partly, in terms of formation of a γ-lactone intermediate[9] (**23**) which hinders isomerization of **20**, the first protonated species of **3**, toward the carboxyl group. Thus, the Ritter product **11** comprises an isomeric mixture mainly of **11ii**, **11iii**, and **11iv**, and to a much smaller extent of **11i** and **11v** (**11**, $x = 10$, $y = 7$).

The variation in isomeric distribution between the Ritter products from the various monoenic acids may be related to the reactivity of the specific carbonium ion species toward the acrylonitrile. Thus, the greater the reactivity of the carbonium ion species, the less is isomerization of the double bond of the type **27** → **30**, as shown in the following series of equations.



Hence, the additions in such cases should occur essentially on either carbon of the original double bond to yield 1:1 mixtures of the corresponding positional isomers. However, in the presence of a less reactive nitrile (acetonitrile), the initial protonated species of a monoenic acid appear to undergo isomerization prior to fruitful reaction with the nitrile. Indeed, mass spectral analysis of Ritter product **8** from the reaction of **5** with acetonitrile shows that **8** comprises a more complex mixture of the respective positional isomers relative to **12** (compare data in Tables III and IV).

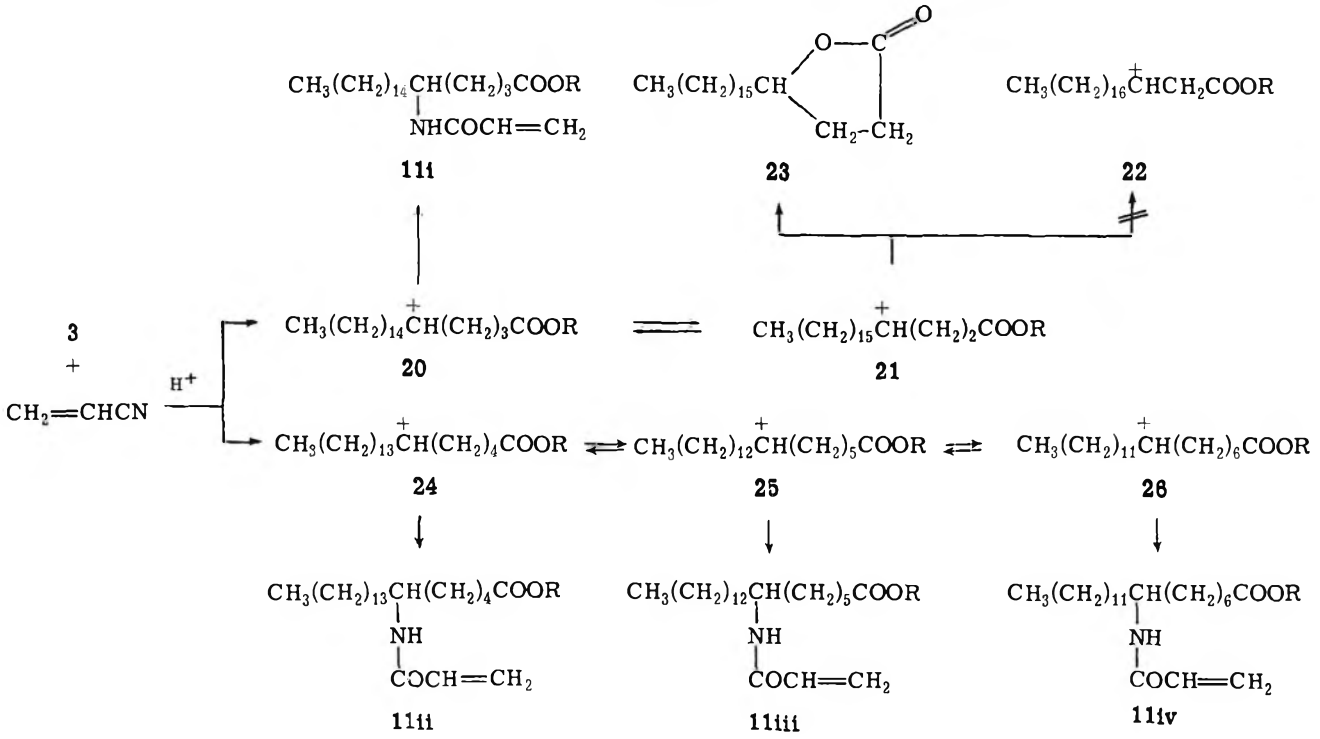
The differences in isomeric composition between the various Ritter products (**8**–**12**) suggest that their protonations give rise to highly reactive carbonium ions which collapse as soon as they are formed.

Following the evidence presented above we deemed it of interest to compare our data with that reported by Audier and coworkers,[19] who have shown that it is possible to locate the double bond position in a long-chain unsaturated compound by mass spectrometry.[20] This entailed first an epoxidation of the double bond and then treatment of the resulting epoxide with dimethylamine to afford the respective isomeric mixture of dimethylamino alcohols. Upon bombardment by high energy electrons the dimethylamino alcohols fragment to give, in addition to the base peak, two prominent peaks of similar intensity and 50% abundance relative to the predominant peak. Most significantly, the results obtained through application of Audier and coworkers' method for dimethyloleamide (**31**) compare remarkably well with those produced in this study for the oleic acid **2a** case (see Table II), as delineated in Scheme IX.

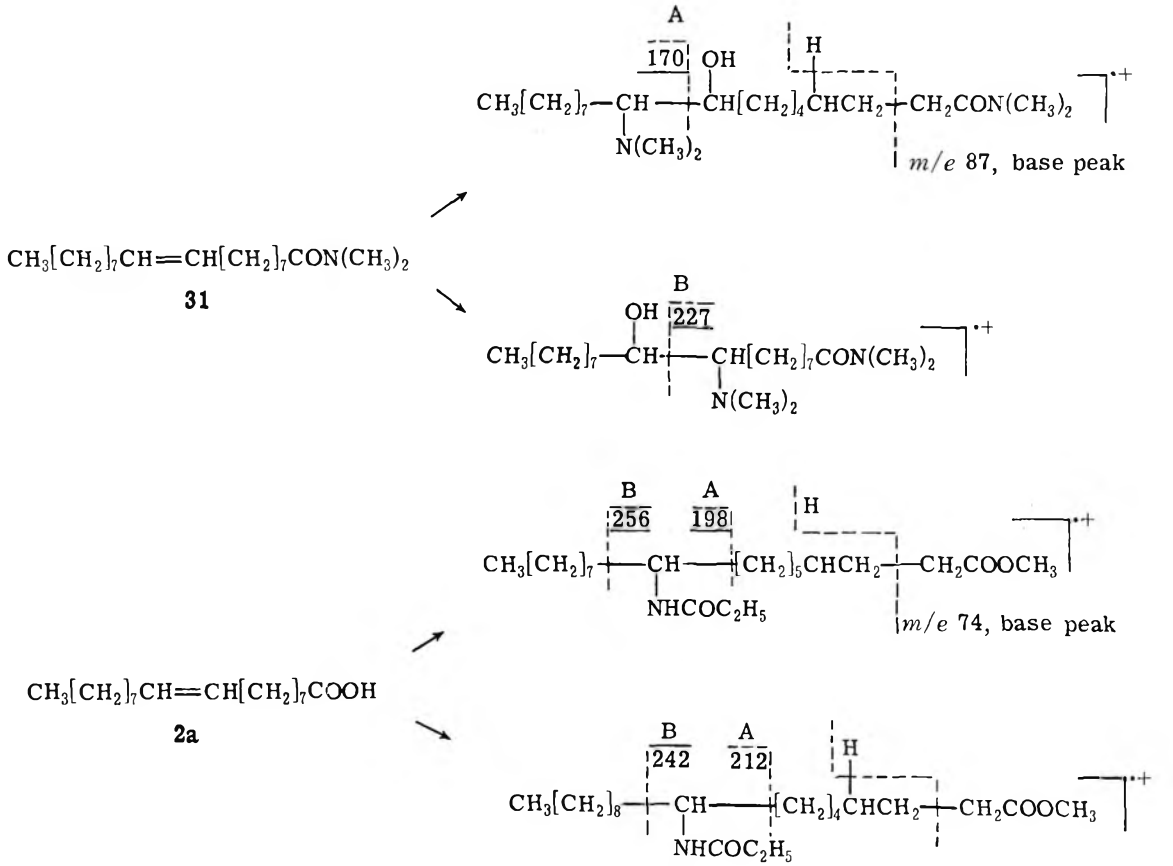
(19) H. Audier, S. Bory, M. Fetizon, P. Longevialle, and R. Toubiana, *Bull. Soc. Chim. Fr.*, 3034 (1964).

(20) See also (a) R. Ryhage and E. Stenhagen, *Ark. Kemi*, **15**, 545 (1960); (b) G. W. Kenner and E. Stenhagen, *Acta Chem. Scand.*, **18**, 1551 (1964).

SCHEME VIII



SCHEME IX



From the evidence presented here it follows that mass spectral analysis of Ritter products could be utilized conveniently as a tool in assigning the double bond position in a long-chain unsaturated compound.

Registry No.—2a, 112-80-1; 3, 35053-79-3; 4, 112-86-7; 5, 506-33-2; 7, 30995-39-2; 8, 35025-51-5; 9, 35025-52-6; 10, 35025-53-7; 11, 35025-54-8; 12a, 35025-55-9; 12b, 35025-56-0; acrylonitrile, 107-13-1; acrylamidostear-*p*-toluide, 35025-57-1; acrylamidostearanilide, 35025-58-2.

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Synthetic and Mass Spectral Study of Bis Ritter Adducts from Some Dienoic Fatty Acids

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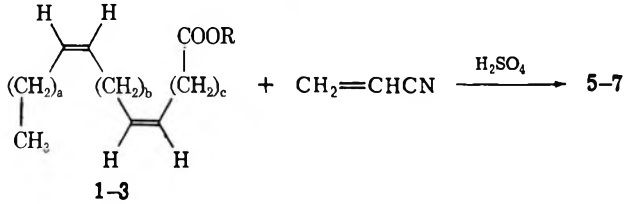
Received March 20, 1972

The Ritter reactions of some long-chain dienoic and hydroxymonoenic acids with acrylonitrile were investigated. The low temperature reactions of linoleic and 5,13-docosadienoic acid derivatives gave good yields of the respective bisacryloamides. In analogy to monoacrylamido fatty acid derivatives, it was possible to determine the addition sites in the Ritter products from the former dienoic fatty acids by mass spectrometry. For comparison, the synthesis and mass spectral study of 1,8-dipropionamido-*p*-menthane are also included.

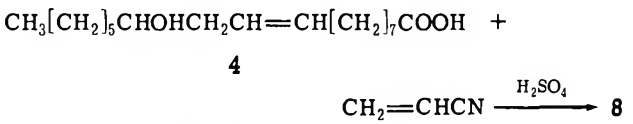
In a preceding paper[1] we described the preparation and the mass spectral cracking patterns of some new Ritter adducts emerging from the reaction between acrylonitrile and long-chain monoenic fatty acids or their esters. It was shown that the assignment of the addition sites in the Ritter products is now possible by mass spectrometry.

The present investigation consists of extending the synthetic studies of the Ritter reaction to some dienoic (**1**–**3**) and hydroxymonoenic fatty acids and their esters (see Scheme I) and presenting a study of the behavior of bis Ritter adducts under electron impact. Evidence is adduced, showing that mass spectral analysis can also be applied for the assignment of the double bond positions in dienoic fatty acids.

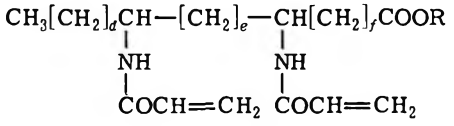
Scheme I



1–3



4

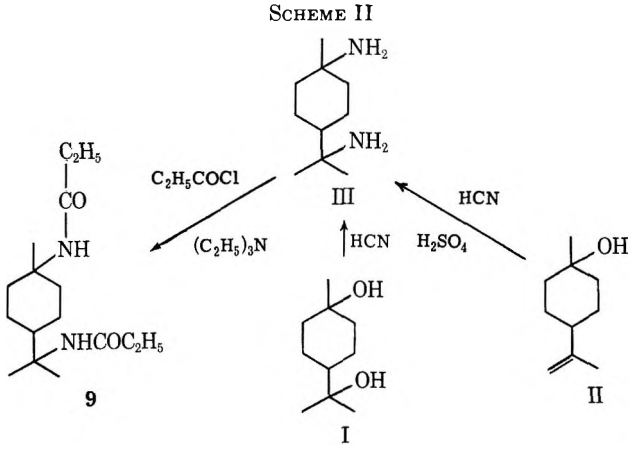


5–8

1, $a=4$; $b=1$; $c=7$; $R=CH_3$
2, $a=4$; $b=1$; $c=7$; $R=C_2H_5$
3, $a=7$; $b=6$; $c=3$; $R=CH_3$
5, $(d+e+f)=14$; $R=CH_3$
6, $(d+e+f)=14$; $R=C_2H_5$
7, $(d+e+f)=18$; $R=CH_3$
8, $(d+e+f)=14$; $R=CH_3$

To shed light on molecular environment influences on the primary reaction in the mass spectra of diamides structurally related to Ritter bis adducts (rupture of the C–C bond α to the amido group), we included in this study the preparation and the mass spectral fragmentation of the hitherto unknown 1,8-dipropionamido-*p*-menthane (**9**). As delineated in Scheme II, **9** was prepared by exposing the known 1,8-diamino-*p*-

Scheme II



menthane (III) to the action of propionyl chloride in the presence of triethylamine. The terpenic diamine (III) could be obtained in good yields from the Ritter reaction of either 1,8-terpin (I) or β-terpineol (II) with hydrogen cyanide in the presence of concentrated sulfuric acid.[2]

Earlier workers have noted that, unlike the long-chain C_{18}-monoenic acids, the Ritter reaction of linoleic acid with hydrogen cyanide resulted in poor yields of an unidentified product.[3] By contrast, the similar reaction between ricinoleic acid (**4**) and hydrogen cyanide afforded the monoadduct $CH_3[CH_2]_5CHOH$-$[CH_2]_2CH(NHCHO)[CH_2]_zCOOH$ in 80% yield.[3]

It is significant to note that the Ritter reaction of **4** seems to involve essentially the double bond, leaving the hydroxyl function intact.

This study provides the first report on the successful preparation of methyl and ethyl bis(acrylamido)stearate (**5** and **6**, respectively) in 25–32% yield from the Ritter reaction of acrylonitrile with linoleic acid, followed by treatment with the appropriate alcohols, and of methyl bis(acrylamido)docosanoate (**7**) from **3** in remarkably good yield (55%). This entailed the exposure of the appropriate substrates (**1**–**4**) to the action of acrylonitrile in the presence of concentrated sulfuric acid first at $-50°$ and then up to $-10°$. Finally, it was kept at 20–27° for 45 min before being processed in the usual fashion.

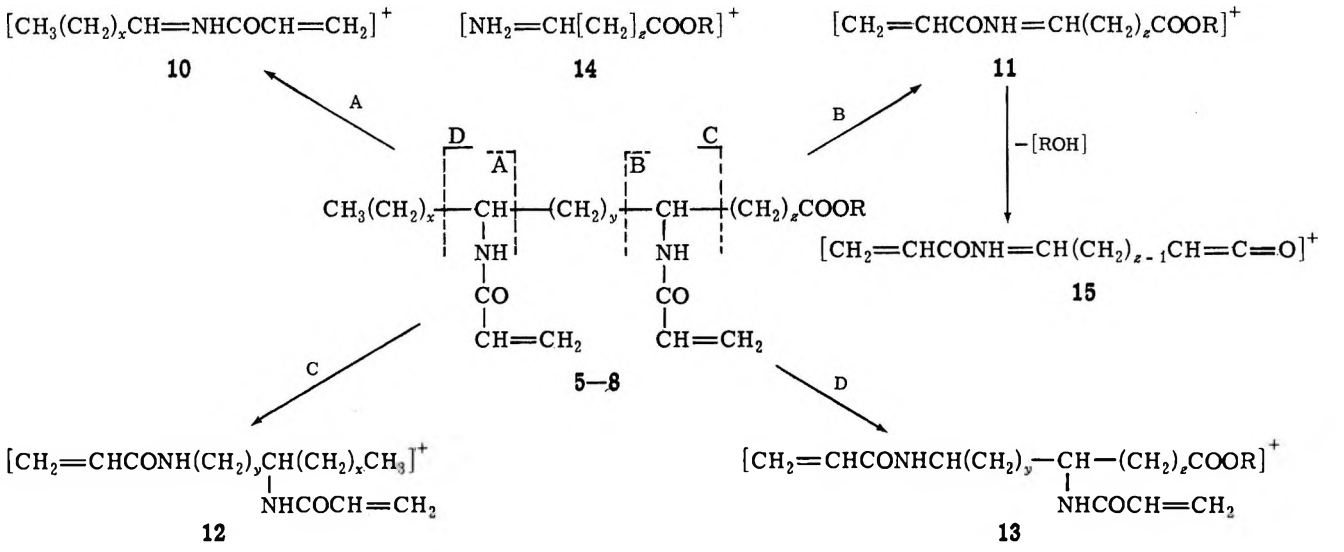
In the reaction of **1** with acrylonitrile we were able to detect the formation of some isomeric monoadducts in

(1) S. Blum, S. Gertler, S. Sarel, and D. Sinnreich, *J. Org. Chem.*, **37**, 3114 (1972).

(2) N. M. Bortnick, British Patent 681,688; U. S. Patent 2,632,022; *Chem. Abstr.*, **48**, 727f, 4003h (1954).

(3) E. T. Roe and D. Swern, *J. Amer. Chem. Soc.*, **77**, 5408 (1955).

SCHEME III



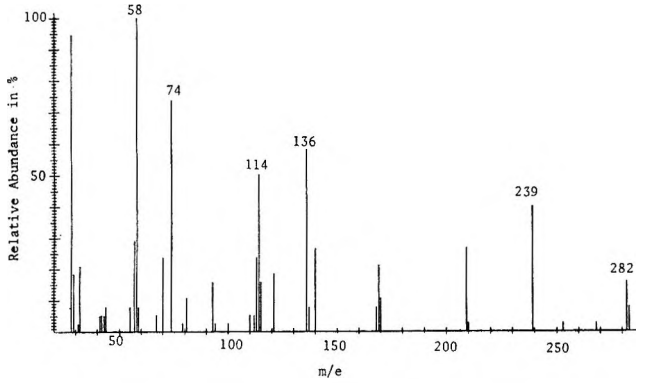


Figure 1.—Mass spectrum of 1,8-dipropionamido-*p*-mehthane.

very small yields. In the case of **3**, where the two double bonds are separated by a chain of six methylene groups, no appreciable amounts of the respective monoadducts could be observed under similar reaction conditions. The two double bonds in **3** do not appear to exhibit differences in reactivity toward acrylonitrile.

Mass Spectra.—On the basis of the electron-induced fragmentation of monoacrylamides of fatty acid esters described in a preceding paper,[1] it is expected that under electron impact each of the bisacrylamido fatty acid esters presented here (**5–8**) would generate four characteristic imidium ions (**10–13**) (see Scheme III) associated with four α cleavages (A, B, C, and D in Scheme III). It is plausible to assume that the recognition of these fragmentation products could ultimately lead to the determination of the addition sites in the Ritter reaction of long-chain dienoic acids and derivatives.

In parallel to mono Ritter adducts from monoenic fatty acid esters, the ion of highest mass-to-charge ratio in the mass spectra of fatty bisacrylamido acid esters (**5–8**) is again the acrylium ion, $CH_2{=}CH{-}{}^+C{\equiv}O$ (*m/e* 55) (see Tables I–IV). As expected, the most prominent peaks in the mass spectra of **5–8** correspond to ions of structures **10–13**, resulting from α cleavages at both sides of the C–N bond (fragmentation routes A to D in Scheme III). However, the intensities of iminium ions of structure **14**, resulting from expulsion of a ketene molecule from **11** or of acrylium ions of structure **15** (from ejection of an alcohol molecule from **11**) in the mass spectra of **5–8**, are relatively weak in comparison to corresponding peaks in the Ritter products from monoenic fatty acids. Most significantly, in the mass spectra of **5–8**, the intensities of peaks corresponding to ions of structure **13**, which contain all of the functional groups of the parent molecule (fragmentation type D), are notably weaker than those corresponding to ions of structure **12**, resulting from an expulsion of an ester radical $\cdot CH_2(CH_2)_{z-1}COOR$ (fragmentation type C). However, the relative abundance of ions of structure **13** in the mass spectra of **6** and **8** increases, by one order of magnitude, as the carbon chain on either moiety of the fatty acid ester increases (compare Tables I, II, and IV).

Simple analysis shows that the prominent ions in the mass spectra of **5**, **6**, and **8** could originate from mixtures of ionized molecules of structures as formulated, where the acrylamido nitrogens are preferably attached to carbons 9, 12, or 13 of the fatty acid carbon chain.

Mass spectral analysis of **7** (Table IV) suggests that this Ritter product comprises a complex mixture of positional isomers in which the site of attachment of the entering amido groups stretches from carbons 6 to 15, clustering around carbons 8 and 12 of the fatty acid long chain.

In analogy to tetramethylated lysine ethyl ester,[4] to alicyclic amines,[5] and to propionamido fatty acid derivatives,[1] the predominant peak in the mass spectra of **9** (Figure 1) corresponds to ions of structures **18** and **19**, resulting from rupture of the C–C bond α to the amido group (**9** → **18** conversion), which upon expulsion of methylketene[5a] gives rise to the iminium ion **19** (base peak). Other prominent peaks in the mass spectrum of

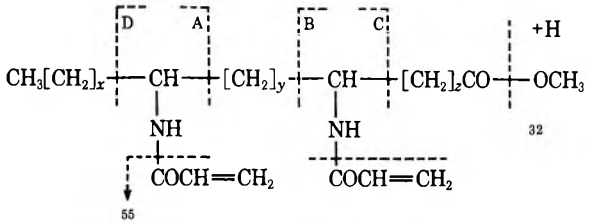
(4) K. Biemann, "Mass Spectrometry of Organic Chemical Applications," McGraw-Hill, 1962, Chapter 7B, pp 278–280.

(5) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, San Francisco, Calif., 1967, Chapter 8, pp 304–322.

(5a) NOTE ADDED IN PROOF.—J. A. Ballantine and R. G. Fenwick [*Org. Mass Spectrom.*, **2**, 1145 (1969)] have noted that the [M − 68] ion in the mass spectra of griseofulvin analogs results from an elimination of C_4H_4O unit ($CH_3CH{=}C{=}C{=}O$) from ring C and is often accompanied by a metastable ion.

TABLE I

RELATIVE ABUNDANCE (PER CENT) OF PROMINENT IONS (A, B, B-32, B-54, C, AND D) IN THE MASS SPECTRA OF METHYL BIS(ACRYLAMIDO)STEARATE (5)

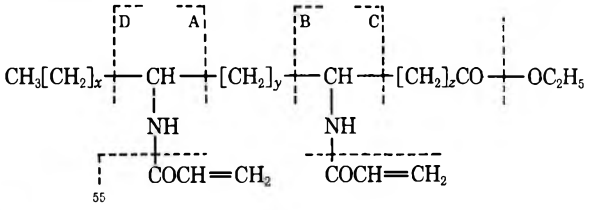


base peak (m/e 55) = 100%

Site of attachment	A		D		Site of attachment	B		B-32		B-54		C	
	m/e	Rel abund	m/e	Rel abund		m/e	Rel abund	m/e	Rel abund	m/e	Rel abund	m/e	Rel abund
C-10	196	13	323	1.6	C-5	184	3	152	12	130	2.5	335	3
C-11	182	17	337	1.6	C-6	198	9	166	12	144	5	321	8
C-12	168	29	351	0.4	C-7	212	15	180	13	158	8	307	14
C-13	154	44	365	2.9	C-8	226	20	194	14	172	8	293	19
C-14	140	27	379	3.8	C-9	240	24	208	27	183	13	279	20
					C-10	254	10	222	14	200	4	265	12

TABLE II

RELATIVE ABUNDANCE (PER CENT) OF PROMINENT PEAKS IN THE MASS SPECTRA OF ETHYL BIS(ACRYLAMIDO)STEARATE (6)

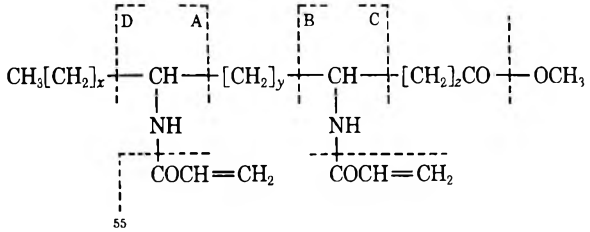


base peak (m/e 55) = 100%

Site of attachment	A		D		Site of attachment	B		B-46		B-54		C	
	m/e	Rel abund	m/e	Rel abund		m/e	Rel abund	m/e	Rel abund	m/e	Rel abund	m/e	Rel abund
C 10	196		337	1	C-5	198	3	152	2	144	0.8	335	2
C-11	182	14	351	2	C-6	212	5	166	3	158	1.4	321	5
C 12	168	20	365	3	C-7	226	18	180	4	172	2.2	307	19
C-13	154	27	379	8	C-8	240	22	194	0	186	4.0	293	25
C-14	140	15	393	8	C-9	254	53	208	13	200	8.4	279	26
					C-10	268	16	222	10	214	3.8	265	13

TABLE III

RELATIVE ABUNDANCE (PER CENT) OF PROMINENT IONS IN THE MASS SPECTRA OF RITTER PRODUCT (8) FROM METHYL RICINOLEATE AND ACRYLONITRILE

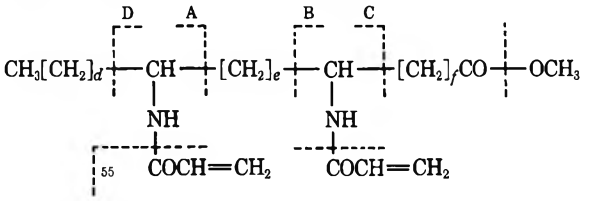


base peak (m/e 55) = 100%

Site of attachment	A		D		Site of attachment	B		B-32		B-54		C	
	m/e	Rel abund	m/e	Rel abund		m/e	Rel abund	m/e	Rel abund	m/e	Rel abund	m/e	Rel abund
C-10	196	6	323	2	C-5	184	5	152	1	130	0.5	335	6
C-11	182	11	337	1	C-6	198	6	166	2	144	1.0	321	6
C-12	168	24	351	2.5	C-7	212	12	180	4	158	2.5	307	17
C-13	154	26	365	5	C-8	226	15	194	5	172	3.0	293	21
C-14	140	21	379		C-9	240	19	208	7	186	3.5	279	23
					C-10	254	10	222	5	200	1.5	265	8

TABLE IV

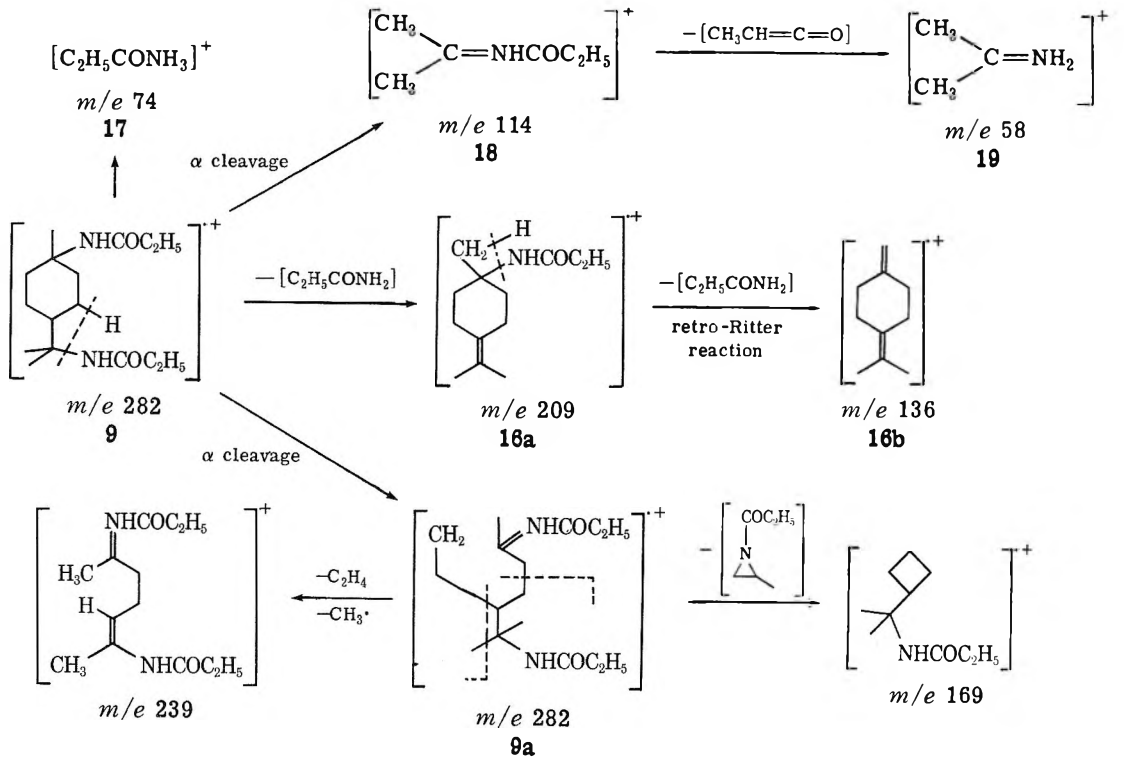
RELATIVE ABUNDANCE OF PROMINENT PEAKS (A, B, C, D, B-54, AND B-32) IN THE MASS SPECTRA OF METHYL BIS(ACRYLAMIDO)DOCOSANOATE (7)



base peak (m/e 55) = 100%; $(d + e + f) = 18$

Site of attachment	A		D		Site of attachment	B		B-54		B-32		C	
	m/e	Rel abund	m/e	Rel abund		m/e	Rel abund	m/e	Rel abund	m/e	Rel abund	m/e	Rel abund
C-15	182	31	337	9	C-6	198	19	144	23	166	15	377	9
C-14	196	35	351	10	C-7	212	21	158	37	180	16	363	16
C-13	210	38	365	11	C-8	226	25	172	50	194	18	349	27
C-12	224	42	379	15	C-9	240	24	186	46	208	16	335	37
C-11	238	30	393	14	C-10	254	20	200	26	222	15	321	8
C-10	252	20	407	12	C-11	268	15	214	11	236	12	307	6

SCHEME IV



9 correspond to ions of masses 239 and 169, resulting from α cleavage (**9** → **9a**) followed by either the successive losses of methyl and ethylene or the loss of propionamidomethylaziridine, and to ions of structure **16a–16b** and **17**, which probably emerge from the successive retrograde Ritter reactions involving the McLafferty rearrangement (**9** → **16**, **9** → **16a** → **16b**, and **9** → **17** conversions) with retention of charge by either moiety (Scheme IV). It is clear from the above discussion that the rupture of the C–C bond α to the amido groups in the diacrylamido fatty acid esters **1–3** occurs at a considerably faster rate than the elimination of fragment m/e 74 which involves the breakage of one C–C and one C–H bond (McLafferty rearrangement). Qualitatively, the situation in **9** is similar to that in **1–3** in the sense that the McLafferty rearrangements (**9** → **16**, **9** → **17** conversions) occur somewhat slower than the α cleavage processes, **9** → **18** → **19** and **9** → **9a** → m/e 239.[6]

Experimental Section

Melting points were taken in a Thomas-Hoover capillary melting point apparatus and are uncorrected. Nuclear magnetic resonance spectra were taken on a Jeol C-60H spectrometer, using Me_4Si as internal standard.

Materials and Sources.—The sources for the purchased chemicals are given in parentheses. They were of "chemically pure" grade and employed as received: ethyl linoleate (2) (Fluka); 1,8-diamino-*p*-menthane (Fluka); and acrylonitrile (British Drug House) (bp 72–73°, 690 mm). Silicic acid (100 mesh) for chromatography (Mallinckrodt) was of analytical grade.

(6) On the other hand, according to ref 5, p 337, the energy requirements for the McLafferty rearrangement in *n*-butyramide are considerably lower than those for α cleavage.

Methyl linoleate, (1), bp 164–169° (1 mm), was prepared from safflower oil by the method described.[7]

Methyl ricinoleate (4) was prepared from castor oil according to the literature.[8]

Methyl *cis,cis*-5,13-docosenoate (3), bp 180–184° (1 mm) [lit.[9] bp 153–156° (0.005 mm)], was obtained according to the literature[9] in 3–4% yield.

Methyl Bis(acrylamido)docosanoate (7). **The Ritter Reaction of Methyl *cis,cis*-5,13-Docosadienoate.**—To a stirred solution of 3 g of methyl *cis,cis*-5,13-docosadienoate (3) and 14 g of acrylonitrile at −50° there was added rapidly (during 3–4 min) 9 ml of concentrated sulfuric acid. The external cooling must be as efficient as to keep the internal temperature below −10° during the addition of the acid. The cooling bath was removed and the mixture was allowed to warm up to 27°. Stirring was continued for 45 min at 27°; the mixture was then cooled to 0°, 10 ml of methanol being added, and left to stand overnight at ambient temperature. The mixture was poured onto crushed ice and the resulting oil was taken up in chloroform. Upon the usual work-up, the residue was chromatographed on a column packed with a mixture of 90 g of Florisil (200–300 mesh) and 45 g of Celite, which was successively eluted by cyclohexane, benzene, ether, and methanol. The ether eluate was rechromatographed on a column packed with a mixture of 90 g of silicic acid and 45 g of Celite, using cyclohexane, benzene, benzene–ether (2:1), ether, and methanol as eluents. The first eluted fraction (benzene–ether) consisted of monoacrylamido esters, mainly of methyl 5-eicosenoate arising from contaminants present in the starting ester, and small amounts (3–5%) of the normal monoaddition of the nitrile to the dienic ester (shown by mass spectroscopy). Later fractions eluted by the benzene–ether mixture comprised the isomeric methyl bis(acrylamido)docosanoate (2.35 g, 44%) in oil form: ir 3300 (NH), 1730 (C=O ester), 1610 (C=O amide), 1650, 980, 965 cm^{-1} (vinyl); nmr ($CDCl_3$) τ 3.78 (2 H, d), 3.42 (2 H, m), 4.43 (4 H, d), 6.08 (2 H, m), 6.35 (3 H, s), 7.70 (2 H, t), 8.0–9.0 (36 H, s), 9.12 (3 H, t, J = 5 Hz). The content of the fractions was analyzed by tlc, on Kieselgel G, using chloroform–methanol (48:2) as eluent. Saturated cupric sulfate solutions containing 0.5% of potassium permangante were used as spray reagents. On tlc, methyl bis(acrylamido)docosanoate (13) gives an elongated green spot (the background is violet) in the range of R_f 0.19 to 0.26, suggesting that the product comprises an isomeric mixture.

Anal. Calcd for $C_{25}H_{52}N_2O_4$: C, 70.7; H, 10.5; N, 5.5. Found: C, 70.9; H, 10.8; N, 5.6.

The Ritter Reaction of Methyl and Ethyl Linoleate.—Methyl linoleate does not appear to lend itself to straightforward Ritter reaction. When it is exposed to the action of acrylonitrile in the presence of concentrated sulfuric acid at about 15°, the reaction leads to a complex product mixture. It consists of (i) Ritter adducts of mono- and bis(acrylamido)stearates, (ii) isomerization products, (iii) unidentified polymeric substances, and (iv) unchanged starting material. The formation of polymeric substances could not be subdued even at much lower reaction temperatures.

Low Temperature Ritter Reaction of Methyl Linoleate.—A well-stirred mixture of methyl linoleate (1) (2 g) and acrylonitrile (1 g) was cooled in solid carbon dioxide–acetone bath (*ca.* −50°) while 4.2 ml of 98% H_2SO_4 was added dropwise during 40 min. The mixture was then processed in a way described for the 3 → 7 conversion. The crude reaction product was a dark-colored oil which could be purified by three successive chromatographies on a column packed with a mixture of Florisil (50 g) and Celite (25 g), using cyclohexane, benzene, ether, and methanol as eluting solvents, in the order described above. From the ether eluted fraction, 0.55 g of a colorless powder was isolated. The main reaction product consisted of polymeric materials which did not migrate on preparative thin-layer chromatographic plates.

(7) W. E. Parker, R. E. Roos, and D. Swern, *Biochem. Prep.*, **4**, 86 (1955).

(8) D. Swern and E. F. Jordan, *ibid.*, **2**, 104 (1953).

(9) S. P. Fore, F. G. Dollear, and G. Sumrell, *Lipids*, **1**, 73 (1966).

The Ritter Reaction of Ethyl Linoleate and Acrylonitrile.—Ethyl linoleate (2) (3.08 g, 0.01 mol) was exposed to the action of acrylonitrile (0.03 mol) and 98% H_2SO_4 (12 g) during 40 min, below 18°, and processed as described for the 1 → 5 conversion. Column chromatography yielded the respective monooctadec-12-enoate, together with the desired ethyl bis(acrylamido)stearate (6), in oil forms (25% yield total). After several successive chromatographies (10:1 silica gel–Celite), it was possible to induce both 6 and the monooctadec-12-enoate to recrystallize from acetone at low temperature, with great losses of material. The bisamide (6) was obtained as colorless crystals of mp 107–110°; ir (KBr) 3255, 1737, 1625, 1660, 978, and 95 cm^{-1}; nmr ($CDCl_3$) τ 3.78 (2 H, α), 4.05 (2 H, m), 4.40 (4 H, d), 5.98 (2 H, m), 6.33 (3 H, s), 7.70 (2 H, t, J = 7.0 Hz), 8.2–9.0 (28 H), 9.12 (3 H, t, J = 5.0 Hz). The monoamide consisted of a wax-like material (no melting point). On tlc 6 appears at the lower region of the chromatogram, R_f 0.2–0.27, whereas the monoadduct had a higher R_f value, between 0.4 and 0.44, as expected.

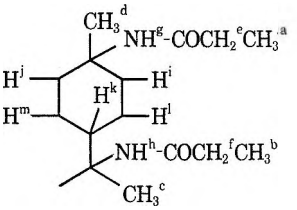
The Reaction of Methyl Ricinoleate (4) **with Acrylonitrile.**—A mixture of 4 (2 g) and acrylonitrile (1 g) was cooled to −50° and treated with 4.2 ml of sulfuric acid in the manner described above. The colorless reaction mixture thus obtained was subjected to chromatography, using a column packed with a mixture of 50 g of Florisil and 25 g of Celite and the same eluting solvents. The ether eluted 1.10 g of methyl bis(acrylamido)stearate (8) as semisolid material, ir (KBr) 3300, 1730, 1610, 1650, 980, and 965 cm^{-1}, and 0.18 g of 4, but no monoacrylamide could be isolated.

Anal. Calcd for $C_{25}H_{44}N_2O_4$: C, 68.9; H, 10.1; N, 6.4. Found: C, 68.5; H, 10.6; N, 6.3.

Nmr ($CDCl_3$): τ 9.12 (3 H, t, J = 5 Hz), 9.0–8.2 (28 H, m), 7.70 (2 H, t, J = 7 Hz), 6.33 (3 H, m, methoxyl), 5.98 (1 H, m), 4.40–3.78 (6 H, vinylic protons), 4.05 (2 H, m, NH).

Preparation of 1,8-Dipropionamido-*p*-menthane (9).—To a cooled (ice) mixture of 1,8-diamino-*p*-menthane (3.4 g, 20 mmol) and 5 g (50 mmol) of triethylamine in 20 ml of dry ether was added with stirring a solution of 4.6 g (50 mmol) of propionyl chloride in 15 ml of ether. An immediate precipitate of [$Et_3N \cdot HCl$] is formed. The resulting mixture is allowed to stand overnight, filtered, and then washed with water, leaving on the funnel the crude diamide. Tlc analysis shows that the diamide thus obtained is chemically pure. An analytical sample of 9, mp 124–126°, was obtained by preparative tlc (silica plates, chloroform as developing solvent) followed by trituration with ether.

Anal. Calcd for $C_{13}H_{30}N_2O_2$: C, 68.1; H, 10.6. Found: C, 67.9; H, 10.5.



Nmr ($CDCl_3$): τ 4.73 (1 H, broad s, $H^{g/h}$), 4.86 (1 H, broad s, $H^{g/h}$), 7.84 (2 H, q, $H^{e/f}$), J = 7.5 Hz), 7.87 (2 H, q, $H^{e/f}$), J = 7.5 Hz), 8.2–7.4 (9 H, m, H^{i-m}), 8.65 (3 H, s, H^{d}), 8.73 (6 H, s, H^{c}), 8.87 (6 H, t, $H^{a/b}$), and 8.89 (3 H, t, $H^{a/b}$).

Registry No.—**1**, 112-63-0; **2**, 544-35-4; **3**, 2566-96-3; **4**, 141-24-2; **5** or **8**, 35039-28-2; **6**, 35039-29-3; **7** or **13**, 35039-30-6; **9**, 35046-17-4; acrylonitrile, 107-13-1.

Acknowledgment.—The authors wish to thank the U. S. Department of Agriculture, Foreign Research and Technical Program Division (Grant FG-IS-191), for generous support of this work and also Dr. Joseph Deutsch of this laboratory for his valuable help and advice.

9-Azabicyclo[4.2.1]nona-2,4,7-triene and Derivatives[1]

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Received January 21, 1972

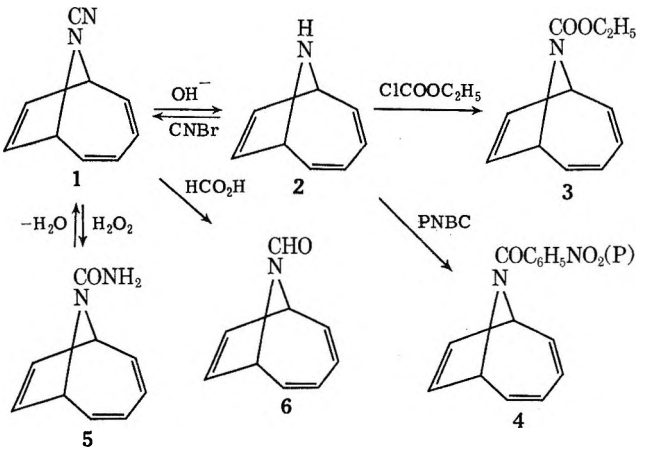
The preparation of parent 9-azabicyclo[4.2.1]nona-2,4,7-triene and certain N-substituted derivatives is described. Selective saturation of the general [4.2.1]-triene system through catalytic hydrogenation and epoxidation is also detailed.

In recent years we recorded our active interest in C_8H_8X heterobicyclics in terms of their response to heat and light[2,3] as well as their unique potential as heteronin progenitors.[4] Our participation in this area dates to a report describing the reaction of cyanonitrene with cyclooctatetraene to yield two isomeric C_8H_8NCN bicyclic substances, one of which was shown to possess the novel skeleton shown in **1**.[2] We now wish to record additional chemical information relating to this general system. Specifically, we report on a number of select chemical transformations of **1**, including its conversion to the parent amine **2**. For the most part our interest in the compounds described herein derives from their obvious potential as appropriate models for studying the stereoelectronic factors controlling possible reorganization and cheletropic[5] processes.

Functionalization on Nitrogen.—The chief emphasis in our earlier description of **1** was mechanistic rather than synthetic, so that no effort was exerted at optimizing the yield. In the present report we describe a modified work-up procedure whereby as many as 4 g of **1** become routinely available from single runs (see Experimental Section).[6]

Conversion of **1** to the parent substance **2** was accomplished in good yield (*ca.* 71%) on heating the nitrile with 10% sodium hydroxide in aqueous acetone (Scheme I).[7] The bicyclic amine is a thermally stable, air-sensitive, colorless liquid displaying the following spectral characteristics: mass spectrum *m/e* (rel intensity) 119 (P^+, 60), 91 (100); ν_{neat}^{NH} 3250 cm^{-1}; $\lambda_{max}^{C_6H_{12}}$ 245 nm (ϵ 2300); nmr (60 MHz, $CDCl_3$) τ 3.50–4.20 (4 H, m), 4.69 (2 H, s), 5.70 (2 H, d, J = 5 Hz), 8.45 (1 H, s, exchanges with D_2O). Secure chemical evidence for structure **2** derives from its ready reversal to **1** (nmr, ir, melting point) on treatment with cyanogen bromide and its conversion to the N-substituted derivatives shown in **3** and **4** on exposure to ethyl chloroformate and *p*-nitrobenzoyl chloride, respectively.

SCHEME I



While **2** undoubtedly represents the ideal progenitor to a variety of N-substituted derivatives, introduction of an N substituent may in some cases be forced directly on **1**. This is properly exemplified by the ready conversion of this cyanamide to urea **5** on treatment with H_2O_2 in acetone and to formamide **6** on exposure to hot formic acid in the presence of BF_3.[10] It is interesting to note that the two bridgehead hydrogens of **6** are magnetically distinct, each appearing as a doublet, τ 4.85 (J = 5.5 Hz) and 5.22 (J = 5.5 Hz), in the nmr spectrum. This induced asymmetry in the neighborhood of the bridgehead positions is no doubt introduced by the *N*-formyl substituent and is best reasoned in terms of restricted rotation about the amide linkage. Of course the operation of such a process would necessarily constrain the formyl group within the plane defined by the C–N–C bridge so that its hydrogen would be exposed to the same chemical environment. This notion is fully substantiated by the appearance of the aldehydic resonance (τ 2.02) in singlet form. It is also perhaps interesting to note that within the present line of reasoning the carboethoxyl and carbamoyl analogs of **6** must possess N substituents that are freely rotating at ambient temperature, since the bridgehead protons of either **3** or **5**

(1) Work submitted (July 1970) by R. P. C. in partial fulfillment of the requirements for the Ph.D. degree in Chemistry.

(2) (a) A. G. Anastassiou, *J. Amer. Chem. Soc.*, **87**, 5512 (1965); (b) A. G. Anastassiou, *ibid.*, **90**, 1527 (1968).

(3) A. G. Anastassiou and R. P. Cellura, *Chem. Commun.*, 762 (1967).

(4) A. G. Anastassiou, S. W. Eachus, R. P. Cellura, and J. H. Gebrian, *ibid.*, 1133 (1970), and references cited therein.

(5) R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry," Academic Press, New York, N. Y., 1970.

(6) We thank Dr. R. M. Lazarus for his contribution at optimizing the yield of **1**.

(7) The various substances depicted in Scheme I are obviously of interest as potential models for studying the effect that substituent electronegativity may have on the course of the thermal and photochemical bond-relocation processes available to this general system. Further, parent amine **2** is clearly well suited structurally for a study of the general stereoelectronic factors controlling heteroatom extrusion, which ought to be readily triggered on generation of the corresponding diazene, *i.e.*, in the manner described earlier for a dimeric counterpart of **2**.[8] In fact, **2** may well prove to be an ideal model for assessing the relative merits of linear *vs.* nonlinear cheletropy *within the same molecule*, since the two isolated π segments of the molecule are expected to oppose one another in this connection.[9] Specifically, while the influence of the ethylene portion of the molecule ought to manifest itself in such a way as to induce a *linear* extrusion of N_2, analogous participation by the butadiene segment should promote the process in a nonlinear fashion.[9]

(8) A. G. Anastassiou and R. M. Lazarus, *Chem. Commun.*, 373 (1970).

(9) This conclusion was arrived at on employing the method of analysis described earlier by D. M. Lemal and S. D. McGregor, *J. Amer. Chem. Soc.*, **88**, 1335 (1966).

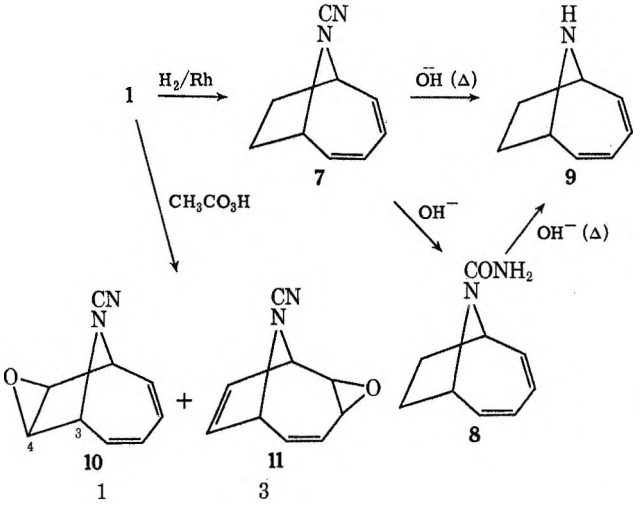
(10) Mechanistically, the overall conversion of **1** to **6** is best viewed as a reduction–hydrolysis process whereby initial hydride transfer from formic acid to **1** produces the corresponding imino (–CH=NH) derivative, which is in turn converted to **6** on hydrolysis. For related instances see H. Kauffman and P. Rannwitz, *Ber.*, **45**, 766 (1912); A. Kovache, *Ann. Chim. (Paris)*, **10**, 184 (1918).

are magnetically equivalent, the pair in each case appearing as a clean 2 H doublet ($J \cong 4.5$–5.0 Hz).

Selective Double-Bond Saturation.—Attention in this project was next directed at modifying the general π system of **1** through selective saturation of one of its olefinic centers in the hope of obtaining additional models for studying the constraints imposed on this rigid system by orbital symmetry. In particular, the various dienes that are formally accessible in this manner might prove useful in assessing the degree to which linear or nonlinear cheletropy might be "forbidden" in the triene counterpart **2**.

Careful partial hydrogenation of **1** over 5% rhodium on charcoal produced a single dihydro derivative displaying the following spectral characteristics: mass spectrum m/e (rel intensity) 146 (P^+, 10); ν_{KBr}^{CN} 2245 cm^{-1}; $\nu_{max}^{CH_3CN}$ 257 nm (ϵ 4630); nmr (60 MHz, $CDCl_3$) τ 3.98 (4 H, narrow m), 5.71 (2 H), and 7.75 (4 H). The nmr spectrum demands that the substance be symmetrical and that it possess four olefinic, two allylic, and four paraffinic protons, while the uv characteristics establish the presence of the same diene chromophore as in **1**. This information effectively singles out structure **7** for the product of partial hydrogenation. Mild hydrolysis (10% aqueous NaOH) of **7** led to the corresponding carbamoyl derivative **8** (Scheme II), which was characterized

SCHEME II



on the basis of entirely consistent spectral and microanalytical data. Under more vigorous hydrolytic conditions (*ca.* 40% methanolic KOH) **7** produced, in good yield, the corresponding amine **9**, which was isolated as an air-sensitive, colorless liquid and formulated on the basis of its spectral and microanalytical characteristics. Further, in order to establish that the various transformations described for the dihydro system occur without skeletal rearrangement, we effected the conversion of **9** to **7** on treatment with cyanogen bromide and that of **8** to **9** on hydrolysis with methanolic KOH.

Epoxidation provided yet another means of selectively saturating **1**. Thus, treatment of this substance with peracetic acid produced a mixture of two monoepoxides in a ratio of *ca.* 3:1. The two were separated pure by column chromatography and are characterized by the following spectral data: **minor isomer**, mass spectrum m/e (rel intensity) 160 (P^+, 5); ν_{KBr}^{CN} 2250 cm^{-1}; $\lambda_{max}^{CH_3CN}$ 247 nm (ϵ 4250); nmr (60 MHz, $CDCl_3$) τ 3.91 (4 H, broad s), 5.56 (2 H, d, $J = 3.5$ Hz), 6.31 (2 H, s); **major isomer**, mass spectrum m/e (rel intensity) 160 (P^+, 48); ν_{KBr}^{CN} 2250 cm^{-1}; $\lambda_{max}^{CH_3OH}$ 212 nm (ϵ ~3700); nmr (60 MHz, $CDCl_3$) τ 3.8–4.0 (4 H, m), 5.1 (1 H, m), 5.30 (1 H, d, $J = 5.0$ Hz), 6.40 (1 H, dd, $J = 4.0$, 2.5 Hz), 6.78 (1 H, t, $J = 4.0$ Hz). This information clearly requires that the minor component be symmetrical (nmr) and that it possess a conjugated diene chromophore (uv) and that the major isomer be, by contrast, devoid of both molecular symmetry (nmr) and diene chromophore (uv). Hence, one's choice is effectively limited to structures **10** and **11** for the minor and major isomeric epoxides, respectively. Further, the nmr spectrum of **10** provides some useful clues regarding stereochemistry. Thus, the appearance of the epoxide protons as a sharp singlet in this case is no doubt suggestive of an exo disposition for the epoxide function, as examination of Dreiding molecular models reveals the H_8–H_4 dihedral angle to be *ca.* 80° for the exo arrangement and *ca.* 20° for the endo disposition.

Finally, brief comparison of the nmr chemical shifts of the butadiene moieties of **1** and **2** to those of their dihydro analogs **7** and **9** reveals a shift, 18 and 12 Hz, respectively, to higher field in the case of the latter. It is tempting to interpret this difference to the occurrence of an intramolecular Diels–Alder ($_\pi 4_s + {}_\pi 2_s$) interaction between the two olefinic entities in **1** and **2** with the $_\pi 4_s$ segment behaving in its normal *donor* capacity, *i.e.*, to a situation where there occurs net transfer of electron density from butadiene to ethylene.

Presently, we are actively examining the various substances described herein in terms of molecular reorganization, cheletropy, and response to certain choice reagents.

Experimental Section[11]

Preparation of *N*-Cyano-9-azabicyclo[4.2.1]nona-2,4,7-triene (1).[6]—To a rapidly stirring solution of cyclooctatetraene (50 ml) in ethyl acetate (3800 ml) maintained at the reflux temperature (*ca.* 80°) was added a fresh solution of cyanogen azide[12] (*ca.* 25 g) in ethyl acetate (220 ml) over a period of 4 hr. After stirring for an additional 30 min (total nitrogen evolution *ca.* 75% theory) the reaction mixture was cooled and suction filtered through a bed of Merck anhydrous neutral alumina (*ca.* 900 g). Evaporation of the filtrates at the water aspirator at *ca.* 45° gave an orange oil, from which cyclooctatetraene was removed at 30° and *ca.* 0.5 mm. The residue was dissolved in methylene chloride (*ca.* 50 ml) and the resulting solution was applied onto a column of Woelm activity IV *acidic* alumina (200 g). Elution with benzene (*ca.* 500 ml) gave a yellow solution which was concentrated to *ca.* 30 ml and added dropwise to rapidly stirring petroleum ether (bp 30–60°, *ca.* 500 ml) to yield **1** (2.5–4.0 g) as a white, crystalline solid, mp 101–103°.[2]

Preparation of 9-Azabicyclo[4.2.1]nona-2,4,7-triene (2).—A solution of *N*-cyano-9-azabicyclo[4.2.1]nona-2,4,7-triene (**1**) (1.2 g, 0.0083 mol) in 10% (w/v) aqueous sodium hydroxide

(11) All melting points were obtained with a Thomas-Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 137 infrared spectrophotometer. Ultraviolet spectra were determined with either a Perkin-Elmer, Model 202, or a Cary 14 spectrophotometer. Proton nuclear magnetic resonance spectra were obtained with a Varian Model A-60 spectrometer; tetramethylsilane was employed as the internal standard throughout. Mass spectra were recorded with a Hitachi Model RMU-6E single focusing spectrometer. Microanalyses were performed at Galbraith Laboratories, Knoxville, Tenn.

(12) See ref 2b.

solution (40 ml) and acetone (5 ml) was maintained at reflux (*ca.* 100°), under nitrogen and with constant stirring, for a period of 16 hr. After cooling to room temperature the acetone was drawn off at the water aspirator and to the remaining solution were added sodium hydroxide pellets (*ca.* 6 g). The mixture was stirred until all the sodium hydroxide dissolved and then extracted with chloroform (6 × 20 ml). The combined extracts were washed with water (2 × 20 ml), dried over calcium sulfate, and concentrated, first at water aspirator pressure and then at *ca.* 0.5 mm, to a yellow oil (0.8 g). Short-path distillation under reduced pressure gave 9-azabicyclo[4.2.1]nona-2,4,7-triene (**2**) (0.69 g, 71%) as a colorless liquid: bp 58–59° (0.25 mm); ir (neat) 3250 (NH), 1395, 1110, 955, 880, and 765 cm^{-1}; uv (C_6H_{12}) 245 nm (ϵ 2300); nmr (100 mg/0.3 ml $CDCl_3$) τ 3.50–4.20 (4 H, m), 4.69 (2 H, s), 5.70 (2 H, d, J = 5 Hz), 8.45 (1 H, s, exchanges with D_2O); mass spectrum (20 eV), parent ion at m/e 119, base peak at m/e 91.

Reaction of 9-Azabicyclo[4.2.1]nona-2,4,7-triene (2) with Cyanogen Bromide. Formation of 1.—To a solution of 9-azabicyclo[4.2.1]nona-2,4,7-triene (**2**) (80 mg, 0.68 mmol) and triethylamine (0.2 ml) in methylene chloride (3 ml) was added at *ca.* 0°, under nitrogen and with constant stirring, a solution of cyanogen bromide (78 mg, 0.74 mmol) in methylene chloride (5 ml). After the addition was completed (1 hr), the mixture was allowed to warm to room temperature and stirred at this temperature for an additional 23 hr. The resulting suspension was then filtered and the filtrate was concentrated at water aspirator pressure to a white solid (120 mg). Elution of this material with benzene on a column packed with silica gel and benzene gave *N*-cyano-9-azabicyclo[4.2.1]nona-2,4,7-triene (**1**) (97 mg, 98%) identical in all respects (melting point, ir, nmr) with authentic material.

Reaction of *N*-Cyano-9-azabicyclo[4.2.1]nona-2,4,7-triene (1) with 88% Formic Acid. Formation of 6.—A mixture of *N*-cyano-9-azabicyclo[4.2.1]nona-2,4,7-triene (**1**) (144 mg, 1 mmol), 88% formic acid (0.085 ml, ~1 mmol), and one drop of boron trifluoride etherate was maintained at the reflux temperature for a period of 1 hr. The solution was then diluted with 2 ml of water and extracted with methylene chloride (3 × 5 ml). The combined organic extracts were then washed successively with 10% (w/v) sodium carbonate solution (2 × 5 ml) and water (2 × 5 ml). The solution was dried over calcium sulfate, filtered, and concentrated, first at water aspirator pressure and then at *ca.* 0.5 mm. The crude orange oil obtained (120 mg) was purified by distillation under reduced pressure into a micro cup. The distillate solidified on standing to give *N*-formyl-9-azabicyclo-[4.2.1]nona-2,4,7-triene (**6**) (100 mg, 64%) as white crystals: mp 45–46°; ir (KBr) 1690 (C=O), 1450, 1410, 1005, 930, and 760 cm^{-1}; uv (CH_3CN) max 252 nm (ϵ 2700); nmr ($CDCl_3$) τ 2.02 (1 H, br s), 3.50–4.15 (4 H, m), 4.55 (2 H, s), 4.85 (1 H, d, J = 5.50 Hz), 5.22 (1 H, d, J = 5.50 Hz); mass spectrum (20 eV), parent ion at m/e 147, base peak at m/e 118.

Anal. Calcd for C_9H_9NO: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.45; H, 6.06; N, 9.54.

Preparation of *N*-Carboethoxy-9-azabicyclo[4.2.1]nona-2,4,7-triene (3).—To a solution of 9-azabicyclo[4.2.1]nona-2,4,7-triene (**2**) (457 mg, 3.8 mmol) and triethylamine (0.53 ml, 385 mg, 3.8 mmol) in ethyl ether (15 ml) was added, at 0°, under nitrogen and with constant stirring, a solution of ethyl chloroformate (415 mg, 3.8 mmol) in ethyl ether (5 ml). After the addition was completed (1 hr) the solution was allowed to warm to room temperature and then stirred for an additional 8 hr. The mixture was filtered free of precipitate and the filtrate was washed first with 10% sodium carbonate solution (2 × 10 ml) and then water (5 × 10 ml). The solution was dried over calcium sulfate, filtered, and concentrated, first at water aspirator pressure and then at *ca.* 0.5 mm, to a crude yellow oil (700 mg). Distillation under reduced pressure (bath temp *ca.* 90°, 0.25 mm) into a micro cup gave *N*-carboethoxy-9-azabicyclo[4.2.1]nona-2,4,7-triene (**3**) (600 mg, 81%) as a colorless liquid: ir (neat) 1750 (C=O), 1450, 1410, 1360, 1310, 1280, 1125, 905, 870, and 775 cm^{-1}; uv (C_6H_{12}) max 252 nm (ϵ 2200); nmr (CCl_4) τ 3.60–4.33 (4 H, m), 4.69 (2 H, d, J ~ 1 Hz), 5.24 (2 H, d, J = 4.5 Hz), 6.05 (2 H, q), 8.88 (3 H, t); mass spectrum, parent ion at m/e 191, base peak at m/e 162.

Preparation of *N*-Carbamoyl-9-azabicyclo[4.2.1]nona-2,4,7-triene (5).—To a solution of *N*-cyano-9-azabicyclo[4.2.1]nona-2,4,7-triene (**1**) (392 mg, 3.0 mmol) and 30% hydrogen peroxide (7 ml) in acetone (8 ml) was added, under nitrogen and with constant stirring, an aqueous solution of sodium carbonate (2 g/15 ml) over a temperature range of 5–10°. Upon completion of the addition (3 hr) the suspension was allowed to warm slowly to room temperature and was stirred for an additional 18 hr. The mixture was then filtered to remove the precipitate which formed during the reaction and the filtrate was extracted with methylene chloride (5 × 20 ml). The combined extracts were in turn washed with water (2 × 10 ml), dried over calcium sulfate, filtered, and concentrated at water aspirator pressure to a cream-colored solid (300 mg). Recrystallization from ethyl acetate gave pure *N*-carbamoyl-9-azabicyclo[4.2.1]nona-2,4,7-triene[13] (250 mg, 52%) as white crystals: mp 182–183°; ir (KBr) 3380 and 3180 (NH), 1650 and 1620 (C=O), 1445, 1140, 1090, 895, 855, 763, and 740 cm^{-1}; uv (CH_3OH) max 255 nm (ϵ 1980); nmr (33 mg/0.3 ml DMSO-d_6) τ 3.55–4.50 (6 H, m, 2 H exchangeable with CD_3COOD), 4.55 (2 H, s), 5.18 (2 H, d, J = 5.0 Hz); mass spectrum, parent ion at m/e 162, base peak at m/e 118.

Anal. Calcd for $C_9H_{10}N_2O$: C, 66.65; H, 6.21; N, 17.27. Found: C, 66.34; H, 6.23; N, 17.17.

Dehydration of *N*-Carbamoyl-9-azabicyclo[4.2.1]nona-2,4,7-triene (5). Formation of 1.—A mixture of *N*-carbamoyl-9-azabicyclo[4.2.1]nona-2,4,7-triene (**5**) (40 mg, 0.24 mmol) and *p*-toluenesulfonyl chloride (138 mg, 0.72 mmol) in pyridine (5 ml) was heated with constant stirring over a steam bath for 1.5 hr. The solution was poured onto ice water (100 ml) and then extracted with methylene chloride (3 × 20 ml). The combined organic extracts were dried over calcium sulfate, filtered, and concentrated at water aspirator pressure to a white solid (35 mg, 100%) identified as *N*-cyanoazabicyclo[4.2.1]nona-2,4,7-triene (**1**) (melting point, ir, nmr).

Reaction of *N*-Cyano-9-azabicyclo[4.2.1]nona-2,4,7-triene (1) with Commercial Peracetic Acid. Formation of 10 and 11.—To a solution of *N*-cyano-9-azabicyclo[4.2.1]nona-2,4,7-triene (**1**) (1 g, 7 mmol) in methylene chloride (20 ml) was added, with constant stirring at *ca.* 20°, a solution of commercial peracetic acid (1.5 ml, 0.85 g, 11 mmol) in methylene chloride (5 ml). After the addition was completed (30 min) the solution was maintained at *ca.* 30° for 44 hr and then concentrated to a red liquid at water aspirator pressure. The liquid was dissolved in benzene (50 ml) and the resulting solution was washed with 10% sodium hydroxide solution (5 × 10 ml) and water (2 × 10 ml), dried over calcium sulfate, filtered, and concentrated to an oil which solidified on standing. The nmr spectrum ($CDCl_3$) of this substance displays, besides a signal characteristic of **1**, new absorptions at τ 3.58–4.00, 5.12, 5.21, 5.56, 6.31, 6.42, and 6.70.

The mixture was dissolved in benzene and placed on a column (350 × 20 mm) packed with silica gel–benzene. Elution with benzene afforded a white, crystalline compound (0.375 g) characterized as **1** (melting point, ir, nmr). Elution with benzene was continued until all of **1** was removed (200 ml). Continued elution with petroleum ether–ethyl ether (1.5:1.0, v/v) afforded two distinct fractions. The first (40 ml) contained pure 7,8-epoxy-*N*-cyano-9-azabicyclo[4.2.1]nona-2,4-diene (**10**) (0.125 g, 11%) as white crystals: mp 98–99°; ir (KBr) 2250 (C≡N), 1235 and 1215 (▷O), 1180, 928, 855, 792, 730, and 704 cm^{-1}; uv (CH_3CN) max 247 nm (ϵ 4250); nmr ($CDCl_3$) τ 3.91 (4 H, br s), 5.56 (2 H, d, J = 3.5 Hz), 6.31 (2 H, s); mass spectrum, parent ion at m/e 160, base peak at m/e 131.

Anal. Calcd for $C_9H_8N_2O$: C, 67.49; H, 5.03; N, 17.49. Found: C, 67.27; H, 4.94; N, 17.36.

The second fraction (150 ml) contained pure 2,3-epoxy-*N*-cyano-9-azabicyclo[4.2.1]nona-4,7-diene (**11**) (0.370 g, 31%) as white crystals: mp 101–102°; ir (KBr) 2250 (C≡N), 1230 (▷O), 975, 920, 895, 885, 795, 775, and 715 cm^{-1}; uv (MeOH) max 212 nm (ϵ 3650); nmr ($CDCl_3$) τ 3.8–4.0 (4 H,m), 5.1 (1 H, m), 5.30 (1 H, d, J = 5.0 Hz), 6.40 (1 H, dd, J = 4.0, 2.5 Hz), 6.78 (1 H, t, J = 4.0 Hz); mass spectrum, parent ion at m/e 160, base peak at m/e 68.

Anal. Calcd for $C_9H_8N_2O$: C, 67.49; H, 5.03; N, 17.49. Found: C, 67.06; H, 5.04; N, 17.49.

Similar results were obtained when the peracid employed was either *m*-chloroperbenzoic acid or perphthalic acid.

Preparation of *N*-Cyano-9-azabicyclo[4.2.1]nona-2,4-diene (7).—A solution of *N*-cyano-9-azabicyclo[4.2.1]nona-2,4,7-triene (**1**) (0.75 g, 0.0052 mol) in tetrahydrofuran (25 ml) and 5% rhodium on charcoal catalyst (0.75 g) was treated with hydrogen

(13) This compound was also isolated in good yield from the low-temperature (~70°) alkaline hydrolysis of **1**. However, the exact experimental details for this process have not been worked out.

at room temperature and atmospheric pressure. Uptake was stopped after a total of 235 ml (60% theory) of hydrogen had been absorbed.[14] The mixture was filtered free of catalyst and the filtrate was concentrated under water aspirator pressure to a white solid (0.75 g). The nmr spectrum ($CDCl_3$) of this material displayed signals at τ 3.98, 5.75, and 7.85 and no absorptions characteristic of **1**. The solid was dissolved in benzene and placed on a column (350 × 20 mm) packed with silica gel–benzene. Elution with (7:3 v/v) petroleum ether–ethyl ether (20 ml) afforded pure *N*-cyano-9-azabicyclo[4.2.1]nona-2,4-diene (0.62 g, 82%) as white crystals: mp 70–71.5°; ir (KBr) 2245 (C≡N), 1350, 1220, 1105, 920, 895, 870, and 715 cm^{-1}; uv (CH_3CN) max 257 nm (ϵ 4630); nmr ($CDCl_3$) τ 3.98 (4 H, m), 5.71 (2 H, m), 7.5–7.9 (4 H, m); mass spectrum, parent ion at *m/e* 146, base peak at *m/e* 58.

Anal. Calcd for $C_9H_{10}N_2$: C, 73.94; H, 6.89; N, 19.16. Found: C, 74.06; H, 6.94; N, 19.20.

Preparation of *N*-Carbamoyl-9-azabicyclo[4.2.1]nona-2,4-diene (8).—A solution of *N*-cyano-9-azabicyclo[4.2.1]nona-2,4-diene (**7**) (146 mg, 1 mmol) in 10% (w/v) aqueous sodium hydroxide solution (10 ml) and acetone (2 ml) was maintained at reflux (*ca.* 100°) under nitrogen and with constant stirring for 8 hr. Upon cooling to room temperature the acetone was removed under aspirator pressure and to the remaining solution was added solid sodium hydroxide (1.5 g). The mixture was stirred until all the sodium hydroxide had dissolved and was then extracted with chloroform (4 × 20 ml), and the organic layer was dried over calcium sulfate. Concentration at water aspirator pressure gave a white solid, which on recrystallization from ethyl acetate produced pure *N*-carbamoyl-9-azabicyclo[4.2.1]nona-2,4-diene (**8**) as white crystals: mp 169–170°; ir (KBr) 3350 and 3180 (NH), 1650 and 1620 (C=O), 1440, 1160, 1085, 925, 895, 855, 763, and 685 cm^{-1}; uv (CH_3CN) max 255 nm (ϵ 1600); nmr (DMSO-d_6, 53 mg/0.3 ml) τ 3.7–4.6 (6 H, m, 2 H exchangeable with D_2O/CDCOOD), 5.5–5.7 (2 H, m), 7.7–8.2 (4 H, m); mass spectrum, parent ion at *m/e* 164, base peak at *m/e* 73.

Anal. Calcd for $C_9H_{12}N_2O$: C, 65.83; H, 7.37; N, 17.06. Found: C, 65.93; H, 7.25; N, 16.80.

Preparation of 9-Azabicyclo[4.2.1]nona-2,4-diene (9) from *N*-Cyano-9-azabicyclo[4.2.1]nona-2,4-diene (7).—A solution of *N*-cyano-9-azabicyclo[4.2.1]nona-2,4-diene (**7**) (1.0 g, 0.0068 mol) and potassium hydroxide (25 g) in methanol (60 ml) was maintained at reflux (*ca.* 100°) under nitrogen and with constant stirring for 8 hr. The solution was then concentrated at water aspirator pressure to a semisolid, which in turn was suspended in petroleum ether (150 ml). The suspension was boiled under nitrogen with constant stirring for 2 hr. The petroleum ether layer was separated, extracted with water (2 × 25 ml), and dried over calcium sulfate. Concentration of the solution at water aspirator pressure gave a crude yellow oil (0.68 g). Short-path distillation under reduced pressure gave pure 9-azabicyclo[4.2.1]-nona-2,4-diene (**9**) (0.55 g, 66%) as an air-sensitive, colorless oil: bp 118–119° (0.1 mm); ir (neat) 3250 (NH), 3000, 1440, 1420, 1100, 1040, 948, 875, 847, 755, and 708 cm^{-1}; uv (CH_3CN) max 248 nm (ϵ 2200); nmr ($CDCl_3$, 100 mg/0.3 ml) τ 3.6–4.5 (4 H, m), 6.0–6.5 (2 H, m), 7.8–8.0 (4 H, m), 8.07 (1 H, s, exchangeable with D_2O/CD_3COOD); mass spectrum, parent ion at *m/e* 121, base peak at *m/e* 91.

(14) Before filtration, a 1-ml sample aliquot was worked up separately and analyzed by nmr. If any **1** was present the solution was further hydrogenated until none of this substance remained.

Preparation of 9-Azabicyclo[4.2.1]nona-2,4-diene (9) from *N*-Carbamoyl-9-azabicyclo[4.2.1]nona-2,4-diene (8).—A solution of *N*-carbamoyl-9-azabicyclo[4.2.1]nona-2,4-diene (**8**) (164 mg, 1 mmol) and potassium hydroxide (2.5 g) in methanol (6 ml) was maintained at reflux (*ca.* 80°) under nitrogen and with constant stirring for 8 hr. The solution was then concentrated at water aspirator pressure to a semisolid, which was in turn suspended in petroleum ether (150 ml) and the suspension was maintained at reflux under nitrogen with constant stirring for 2 hr. The organic layer was separated, extracted with water (2 × 25 ml), and dried over calcium sulfate. Concentration of the solution at water aspirator pressure gave a crude yellow oil (90 mg, 73%) with spectral properties (ir, nmr) identical with those of authentic 9-azabicyclo[4.2.1]nona-2,4-diene (**9**) prepared from the hydrolysis of *N*-cyano-9-azabicyclo[4.2.1]nona-2,4-diene.

Reaction of 9-Azabicyclo[4.2.1]nona-2,4-diene (9) with Cyanogen Bromide. Formation of 7.—To a solution of 9-azabicyclo[4.2.1]nona-2,4-diene (**9**) (121 mg, 1 mmol) and triethylamine (101 mg, 1 mmol) in methylene chloride (10 ml), maintained at *ca.* 0°, was added, under nitrogen and with constant stirring, a solution of cyanogen bromide (105 mg, 1 mmol) in methylene chloride (5 ml). After the addition had been completed (1 hr) the solution was allowed to warm to room temperature and stirred at this temperature for an additional 23 hr. The solution was then filtered and the filtrate was concentrated at water aspirator pressure to a white solid (130 mg). Recrystallization from carbon tetrachloride gave a crystalline white compound (120 mg, 82%) with melting point and spectral characteristics (ir, nmr) identical with those of authentic *N*-cyano-9-azabicyclo[4.2.1]nona-2,4-diene (**7**).

Preparation of *N*-(*p*-Nitro)benzoyl-9-azabicyclo[4.2.1]nona-2,-4,7-triene (4).—To a solution of 9-azabicyclo[4.2.1]nona-2,4,7-triene (**2**) (119 mg, 1 mmol) and triethylamine (101 mg, 1 mmol) in dry benzene (5 ml), maintained at a gentle reflux temperature, was added under nitrogen and with constant stirring a solution of *p*-nitrobenzoyl chloride (185 mg, 1 mmol) in dry benzene (10 ml). After the addition was completed (30 min) the solution was filtered to remove precipitated solid. Concentration of the filtrate at the water aspirator gave a crude yellow solid, which on recrystallization from boiling carbon tetrachloride gave pure *N*-(*p*-nitro)benzoyl-9-azabicyclo[4.2.1]nona-2,4,7-triene (**4**) (250 mg, 82%) as yellow crystals: mp 112–114°; ir 1650 (C=O), 1525, 1430, 1345, 870, 845, and 720 cm^{-1}; nmr ($CDCl_3$) τ 1.6–1.8 (2 H, m), 2.4–2.5 (2 H, m), 3.6–4.0 (4 H, m), 4.50 (2 H, s), 5.3–5.4 (2 H, m); mass spectrum (20 eV) parent (base) ion at *m/e* 268.

Anal. Calcd for $C_{16}H_{12}N_2O_3$: C, 67.16; H, 4.51; N, 10.44. Found: C, 67.05; H, 3.96; N, 10.55.

Registry No.—**2**, 6789-38-4; **3**, 35105-34-1; **4**, 35105-35-2; **5**, 35105-36-3; **6**, 35105-37-4; **7**, 35105-38-5; **8**, 35105-39-6; **9**, 7129-31-9; **10**, 35105-41-0; **11**, 35105-42-1.

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Epoxyamines. III. Synthesis and Reactions of 2-(1-Aziridinyl)-2-phenyl-3,3-dimethyloxirane and 2-(1-Aziridinyl)-2-phenyl-1-oxaspiro[2.4]heptane[1,2]

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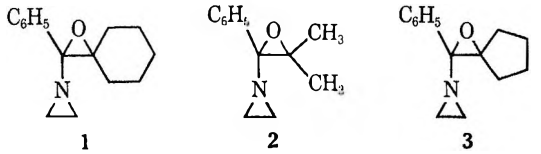
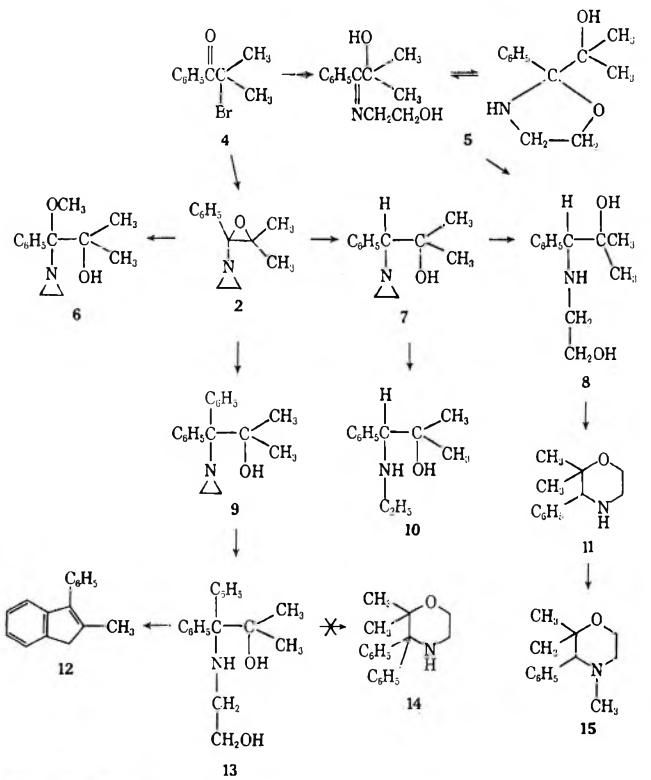
Two new epoxyamines, 2-(1-aziridinyl)-2-phenyl-3,3-dimethyloxirane (**2**) and 2-(1-aziridinyl)-2-phenyl-1-oxaspiro[2.4]heptane (**3**), are synthesized. Reactions of **2** with sodium borohydride, methanol, and phenyllithium are discussed. Hydrolysis of 1-(1-aziridinyl)-1,1-diphenyl-2-methyl-2-propanol (**9**) with 1 *N* perchloric acid followed by treatment with concentrated sulfuric acid yielded 2-methyl-3-phenylindene (**12**) and not the expected morpholine derivative, **14**. The structure of **12** was confirmed by an independent synthesis, and the previous data on **12** are corrected. Epoxyamine **3** was rearranged to give 2-(1-aziridinyl)-2-phenylcyclohexanone (**21**), which on reduction with sodium borohydride gave the *trans*-aziridinyl alcohol, **22**. The formation of various other derivatives is discussed.

After the isolation and characterization of 2-(1-aziridinyl)-2-phenyl-1-oxaspiro[2.5]octane (**1**), the first



1 **2** **3**

stable epoxyamine reported,[1a] attempts were made to synthesize other epoxyamines by similar methods. We now report the preparation, reactions, and rearrangement of two new epoxyamines, 2-(1-aziridinyl)-2-phenyl-3,3-dimethyloxirane (**2**) and 2-(1-aziridinyl)-2-phenyl-1-oxaspiro[2.4]heptane (**3**).



Treatment of α-bromoisobutyrophenone (**4**) with the lithium salt of ethylenimine yielded 83% of epoxyamine **2** as a clear, colorless liquid. Reactions of **2** were analogous to those reported for epoxyamine **1**.[1b] Thus reduction of **2** with sodium borohydride in methanol yielded the aziridinyl alcohol **7**, which on hydrogenation in the presence of palladium on carbon as catalyst gave the known amino alcohol[4] **10** characterized as its hydrochloride. Compound **7** was further characterized by its reaction with 1 *N* perchloric acid to give the amino diol **8** (74%), which was also formed in 64% yield by the reduction of **5** with sodium borohydride. Compound **5**, which was formed by the action of ethanolamine on **4**, has been assigned the oxazolidine structure, as the crystalline material did not show an imine absorption in an infrared spectrum on a potassium bromide pellet. However, as it can be reduced with sodium borohydride, a part of **5** may be existing as the imine in solution. In fact, an infrared spectrum of **5** in chloroform did show a weak imine absorption at 1650 cm^{-1}. Treatment of epoxyamine **2** with methanol without any catalyst opened the epoxide ring to yield 60% of 1-(1-aziridinyl)-1-methoxy-1-phenyl-2-methyl-2-propanol (**6**). Opening of the epoxide without rupturing the aziridine ring was also accomplished by treating **2** with phenyllithium. 1-(1-(Aziridinyl)-1,1-diphenyl-2-methyl-2-propanol (**9**) thus obtained was converted to the amino diol **13** by treatment with 1 *N* perchloric acid.

As amino diols like **8** and **13** have been used for the synthesis of substituted morpholines[5] and since 3-phenylmorpholines are rather uncommon, the conversion of these amino diols to morpholines was attempted. Thus **8** on treatment with concentrated sulfuric acid gave 50% of 2,2-dimethyl-3-phenylmorpholine (**11**) characterized as its hydrogen *p*-toluenesulfonate. Methylation of **11** with formaldehyde and formic acid afforded the *N*-methyl derivative **15**, characterized as its hydrochloride.

Treatment of amino diol **13** with concentrated sulfuric acid did not yield the expected 2,2-dimethyl-3,3-diphenylmorpholine (**14**) but gave 51% of a neutral, crystalline material which was subsequently shown to be 2-methyl-3-phenylindene (**12**). Although elemental

(1) Previous papers in this series: (a) C. L. Stevens and P. M. Pillai, *J. Amer. Chem. Soc.*, **89**, 3084 (1967); (b) C. L. Stevens and P. M. Pillai, *J. Org. Chem.*, **37**, 173 (1972).

(2) A preliminary account of a part of this work has been reported: C. L. Stevens, T. R. Potts, and P. M. Pillai, Abstracts, 154th National Meeting of the American Chemical Society, Chicago, Ill., Sept 1967, No. S-92.

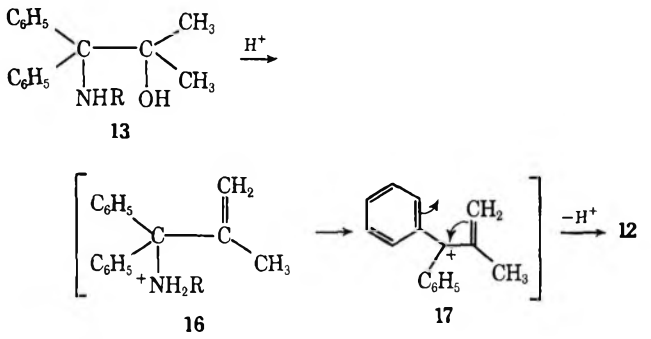
(3) Abstracted in part from the Ph.D. Dissertation of J. M. Cahoon; Frank Knoller Predoctoral Fellow, 1970–1971.

(4) C. L. Stevens, P. Blumbergs, and M. Munk, *J. Org. Chem.*, **28**, 331 (1963).

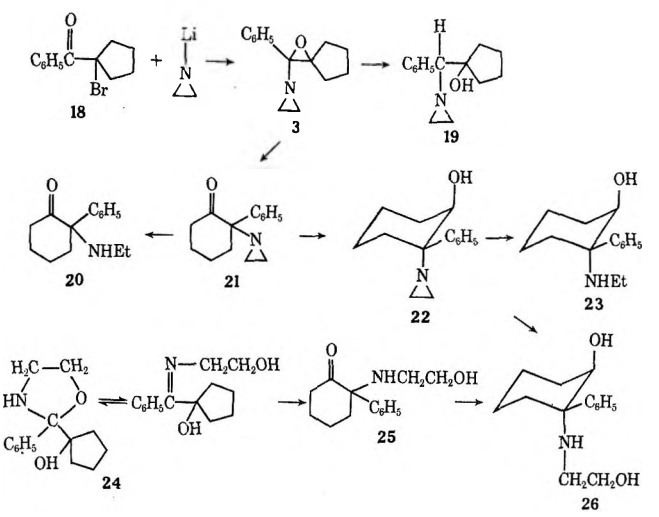
(5) C. L. Stevens, M. E. Munk, C. H. Chang, K. G. Taylor, and A. L. Schy, *ibid.*, **29**, 3146 (1964).

analysis and nmr spectrum were consistent with the structure, the reported characteristics[6] of 2-methyl-3-phenylindene [liquid, uv λ_{max}^{alc} 263 nm (log ϵ 3.87)] were substantially different from our findings [crystals, mp 58–59°, uv λ_{max}^{EtOH} 254 nm (log ϵ 4.01)]. This compound was therefore synthesized by essentially the same route used by Christol and coworkers[6] and the crystalline product obtained in 58% yield from 2-methyl-1-indanone was shown to be identical with our sample **12** in all respects.

The formation of **12** from **13** can be brought about by the ionization of both the hydroxyl and amine functions by the strong sulfuric acid medium. If a carbonium ion was formed on the benzilic position first, the product would have been 2,2-diphenyl-3-butanone, as obtained from the pinacol rearrangement of 1,1-diphenyl-2-methyl-1,2-propanediol.[7] In order to form **12**, the tertiary hydroxyl group in **13** should be eliminated first to give the olefin intermediate **16**. The ionization of the protonated amine group from **16** can be envisaged as taking place in a strong acid medium to give an extremely stable cation, **17**, which can then close with the loss of a proton to form the indene derivative **12**.



Treatment of α-bromocyclopentyl phenyl ketone[8] (**18**) with the lithium salt of ethylenimine in ether at room temperature gave 2-(1-aziridinyl)-2-phenyl-1-oxaspiro[2.4]heptane (**3**) in 78% yield. Further characterization of **3** was achieved by its reduction with sodium borohydride in methanol to give 85% of the aziridinyl alcohol **19**. Rerrangement of **3** in *o*-dichlorobenzene at 185° for 15 hr gave 2-(1-aziridinyl)-2-phenylcyclohexanone (**21**) in 80% yield. The direction of this rearrangement is in complete agreement with previous findings.[1] Upon catalytic hydrogenation in ethyl acetate in the presence of 10% palladium on carbon as catalyst, **21** was selectively reduced to the known 2-*N*-ethylamino-2-phenylcyclohexanone[9] (**20**) characterized as its hydrochloride. Reduction of **21** with sodium borohydride in methanol gave *trans*[10]-2-(1-aziridinyl)-2-phenylcyclohexanol[11] (**22**) in 75% yield. Catalytic hydrogenation of **22** in ethyl acetate in the presence of 10% palladium on carbon afforded



the known *trans*-2-*N*-ethylamino-2-phenylcyclohexanol[12] (**23**) characterized as its hydrochloride. Treatment of **22** with 1 *N* perchloric acid gave the *trans*-β-hydroxyethylamino alcohol **26**. Compound **26** was also obtained by sodium borohydride reduction of the amino ketone **25**, which in turn was obtained by the thermal rearrangement[13] of **24**. Compound **24**, which was prepared by the general method[4] involving the action of ethanolamine on the α-bromo ketone **18**, did not show an imine absorption in an infrared spectrum on a potassium bromide pellet and therefore has been assigned the oxazolidine structure.

Attempted rearrangement of epoxyamine **2** did not yield any clean products; when a solution of **2** in *o*-dichlorobenzene was heated at 185° for several hours, it decomposed into many products, none of which could be characterized.

Experimental Section

Melting points were taken on a Thomas-Hoover melting point apparatus using capillary tubes and are uncorrected. Nmr spectra were obtained on a Varian A-60 or T-60 spectrometer using tetramethylsilane as internal standard. The ultraviolet spectra were recorded on a Cary 14 spectrophotometer. Infrared spectra were obtained on a Perkin-Elmer (Model 237B) grating spectrophotometer. Elemental analyses were performed by Midwest Microlab, Inc., Indianapolis, Ind.

2-(1-Aziridinyl)-2-phenyl-3,3-dimethyloxirane (2).—A solution of 9.05 g (39.9 mmol) of α-bromoisobutyrophenone (**4**) in ether was treated with a suspension of the lithium salt of ethylenimine[1b] in ether according to the procedure of Stevens and Pillai.[1b] The product after distillation yielded 6.25 g (83%) of **2** as a colorless liquid: bp 55–57° (0.1 mm); nmr (CCl_4) δ 7.1–7.6 (m, 5 H, phenyl), 1.5 (s, 6 H, methyl), 0.9 (s, 4 H, methylene).

Anal. Calcd for $C_{12}H_{15}NO$: C, 76.16; H, 7.99; N, 7.40. Found: C, 76.31; H, 8.19; N, 7.67.

2-(2-Hydroxy-2-propyl)-2-phenyloxazolidine (5).—A mixture of 22.7 g (0.1 mol) of bromo ketone **4** was stirred with 50 ml of 2-aminoethanol for 46 hr. The product was extracted with ether, and the ether layer was washed with water, dried (K_2CO_3), and evaporated to dryness. The crude product was crystallized from ether–hexane to give **5**: mp 93–95°; ir (KBr) 3475 cm^{-1} (OH); ir ($CHCl_3$) 1650 cm^{-1} (weak, C=N); uv λ_{max}^{EtOH} 207 nm (log ϵ 3.78). The mother liquor was recycled with more 2-aminoethanol to obtain a total yield of 13.3 g (64.4%).

Anal. Calcd for $C_{12}H_{17}NO_2$: C, 69.53; H, 8.27; N, 6.76. Found: C, 69.77; H, 8.32; N, 6.98.

(6) H. Christol, C. Martin, and M. Mousseron, *Bull. Soc. Chim. Fr.*, 1696 (1960).

(7) T. E. Zalesskaya and I. K. Lavrova, *Zh. Org. Khim.*, **4**, 2070 (1968); *Chem. Abstr.*, **70**, 67788b (1969).

(8) C. L. Stevens, R. D. Elliot, and B. L. Winch, *J. Amer. Chem. Soc.*, **85**, 1464 (1963).

(9) C. L. Stevens, A. B. Ash, A. Thuillier, J. H. Amin, A. Balys, W. E. Dennis, J. P. Dickerson, R. P. Glinski, H. T. Hanson, M. D. Pillai, and J. W. Stoddard, *J. Org. Chem.*, **31**, 2593 (1966).

(10) Trans heteroatom substituents.

(11) The authors thank Mr. Kenneth J. TerBeek for establishing the stereochemistry of this reduction.

(12) C. L. Stevens, H. T. Hanson, and K. G. Taylor, *J. Amer. Chem. Soc.*, **88**, 2769 (1966).

(13) For a review on amino ketone and hydroxyimine rearrangements, see C. L. Stevens, P. M. Pillai, M. E. Munk, and K. G. Taylor in "Mechanisms of Molecular Migrations," B. S. Thyagarajan, Ed., Wiley, New York, N. Y., 1971, p 271.

1-(1-Aziridinyl)-1-methoxy-1-phenyl-2-methyl-2-propanol (6).—Epoxyamine **2** (3.38 g, 17.9 mmol) was dissolved in 25 ml of absolute methanol and after the solution had been left at room temperature for 3 hr it was evaporated to dryness. The residue was recrystallized from hexane to give 2.05 g (60%) of **6**: mp 63–65°; nmr (CCl_4) δ 7.2–7.7 (m, 5 H, phenyl) 3.2 (s, 3 H, OCH_3), 2.4 (s, 1 H, OH), 2.0 and 1.8 (m, 4 H, aziridinyl), 1.2 (s, 3 H, CH_3), 1.0 (s, 3 H, CH_3).

Anal. Calcd for $C_{13}H_{19}NO_2$: C, 70.56; H, 8.65; N, 6.33. Found: C, 70.45; H, 8.81; N, 6.48.

1-(1-Aziridinyl)-1-phenyl-2-methyl-2-propanol (7).—A solution of 4.51 g (23.9 mmol) of **2** in 5 ml of ether was added to a solution of 5.6 g of $NaBH_4$ in 130 ml of CH_3OH at 0°. After 2 hr at 0° and 16 hr at room temperature, most of the CH_3OH was evaporated. The solution was diluted with water, extracted with ether, and dried (K_2CO_3) and solvent was expelled. The residue was recrystallized from ether–pentane to give 3.326 g (73.8%) of **7**, mp 52–53°, ir (KBr) 3340 cm^{-1}.

Anal. Calcd for $C_{12}H_{17}NO$: C, 75.35; H, 8.96; N, 7.32. Found: C, 75.44; H, 8.92; N, 7.22.

A small portion of **7** dissolved in ether was treated with a saturated solution of HCl in ethyl acetate to give 1-(2-chloroethylamino)-1-phenyl-2-methyl-2-propanol hydrochloride, mp 198–200° after recrystallization from methanol–ether.

Anal. Calcd for $C_{12}H_{19}Cl_2NO$: C, 54.55; H, 7.25; Cl, 26.84; N, 5.30. Found: C, 54.77; H, 7.45; Cl, 26.56; N, 5.37.

Catalytic hydrogenation of 300 mg (1.7 mmol) of **7** in ethyl acetate in the presence of 50 mg of 10% Pd/C for 3 hr gave 302 mg (83.5%) of 1-*N*-ethylamino-1-phenyl-2-methyl-2-propanol (**10**) hydrochloride, mp 199–200°, identical with an authentic sample.[4]

1-(2-Hydroxyethylamino)-1-phenyl-2-methyl-2-propanol (8).

A. By the Hydrolysis of 7.—A solution of 200 mg (1.04 mmol) of **7** in 50 ml of 1 *N* $HClO_4$ was heated on a steam bath for 12 hr. The mixture was cooled and extracted with ether. The aqueous layer was basified with NaOH, extracted with chloroform, dried (K_2CO_3), and evaporated to dryness. The residue was recrystallized from methanol–ether to give 163 mg (74.5%) of **8**, mp 102–104°.

Anal. Calcd for $C_{12}H_{19}NO_2$: C, 68.87; H, 9.15; N, 6.69. Found: C, 68.93; H, 9.16; N, 6.79.

B. From the Reduction of 5.—A solution of 10.2 g (49.3 mmol) of **5** in 150 ml of CH_3OH was reduced with 7.9 g of $NaBH_4$ with stirring. The reaction was worked up after standing overnight to give 7.93 g (76.9%) of **8**, mp 104–106°. A mixture melting point with a sample from A above was undepressed.

1-(1-Aziridinyl)-1,1-diphenyl-2-methyl-2-propanol (9).—A solution of 4.65 g (24.6 mmol) of **2** in 60 ml of pure dry ether was cooled to 0° and 23 ml of a 2.11 *M* solution of phenyllithium in ether was added slowly with stirring. Another 20 ml of ether was added and the mixture was stirred overnight. It was poured into water and extracted with $CHCl_3$. The crude product was distilled under reduced pressure to give 6.33 g (96.2%) of **9** as a pale yellow liquid, bp 120–130° (0.2 mm).

A solution of 507 mg of **9** in ether was treated with an excess of HCl in ethyl acetate and the product was recrystallized from methanol–ether to give 419 mg (65%) of 1-(2-chloroethylamino)-1,1-diphenyl-2-methyl-2-propanol hydrochloride, mp 214–215° dec.

Anal. Calcd for $C_{18}H_{23}Cl_2NO$: C, 63.53; H, 6.81; Cl, 20.84; N, 4.12. Found: C, 63.32; H, 6.88; Cl, 20.79; N, 4.16.

2,2-Dimethyl-3-phenylmorpholine (11).—A mixture of 3.25 g (15.5 mmol) of **8** and 100 ml of cold concentrated H_2SO_4 was stirred at 0° for 3 hr. The solution was poured into ice, the neutrals were extracted with ether, and the aqueous layer was basified with NaOH. The product was extracted with ether, the ether solution was dried (K_2CO_3), and the solvent was evaporated. The residue was redissolved in ether and treated with anhydrous *p*-toluenesulfonic acid to give 2.86 g (51%) of **11** as the hydrogen *p*-toluenesulfonate. Recrystallization from acetone gave an analytical sample: mp 200–202°; nmr ($CDCl_3$) of free base, δ 7.2–7.6 (m, 5 H, aromatic), 3.5–4.3 (m, 3 H, benzilic and OCH_2), 2.9–3.2 (m, 2 H, NCH_2), 1.8 (s, 1 H, NH), 1.2 (s, 3 H, CH_3), 1.1 (s, 3 H, CH_3).

Anal. Calcd for $C_{19}H_{25}NO_4S$: C, 62.78; H, 6.93; N, 3.85; S, 8.82. Found: C, 62.53; H, 6.85; N, 4.08; S, 8.96.

Methylation of 1.106 g (5.79 mmol) of **11** with formaldehyde and formic acid[5] gave 1.19 g (84.2%) of 2,2,4-trimethyl-3-phenylmorpholine (**15**) hydrochloride: mp 246–247° dec after recrystallization from methanol–ether; nmr (CCl_4) of free base, δ 7.2–7.3 (s, 5 H, aromatic), 3.8 (m, 2 H, OCH_2), 2.8 (s, 1 H, benzylic), 2.4 (m, 2 H, NCH_2), 2.0 (s, 3 H, NCH_3), 1.2 (s, 3 H, CH_3), 1.0 (s, 3 H, CH_3).

Anal. Calcd for $C_{13}H_{20}ClNO$: C, 64.58; H, 8.34; Cl, 14.67; N, 5.79. Found: C, 64.50; H, 8.53; Cl, 14.59; N, 5.78.

1-(2-Hydroxyethylamino)-1,1-diphenyl-2-methyl-2-propanol (13).—A solution of 5.33 g (20 mmol) of **9** in 25 ml of acetone was added to a mechanically stirred solution of 533 ml of 1 *N* $HClO_4$ which was heated on a steam bath. After heating for 10 hr, the solution was cooled and extracted with ether. The aqueous layer was made basic with NaOH, extracted with $CHCl_3$, dried (K_2CO_3), and evaporated to dryness. The residue was dissolved in 150 ml of dry ether and treated with a saturated solution of HCl in isopropyl alcohol. The product was filtered and recrystallized from methanol–ether to give 4.13 g (64%) of **13** as the hydrochloride, mp 202–203° dec.

Anal. Calcd for $C_{18}H_{24}ClNO_2$: C, 67.17; H, 7.52; Cl, 11.02; N, 4.35. Found: C, 66.92; H, 7.39; Cl, 11.16; N, 4.36.

2-Methyl-3-phenylindene (12).—Compound **13** (HCl) (1.0 g, 3.2 mmol) was added in small portions with stirring to 25 ml of concentrated H_2SO_4 at room temperature. After stirring for 3 hr, the reaction mixture was poured into ice and the neutral material was extracted with ether. The ether solution was washed with water and dried (Na_2SO_4), and the solvent was evaporated. The oily residue was crystallized from ether–pentane to give 326 mg (51%) of **12**: mp 59.5–60.5°; nmr (CCl_4) δ 7.0–7.5 (m, 9 H, aromatic), 3.4 (s, 2 H, methylene), 2.1 (s, 3 H, CH_3); uv λ_{max}^{EtOH} 254 nm (log ε 4.01). Practically no basic material was isolated from this reaction.

Anal. Calcd for $C_{16}H_{14}$: C, 93.16; H, 6.84. Found: C, 93.19; H, 6.93.

2-Methyl-3-phenylindene (**12**) was also prepared in 57.6% yield from 2-methyl-1-indanone[14] by the addition of phenyllithium followed by mild dehydration.[6] A mixture melting point with the two samples was not depressed and the ir spectra were superimposable.

2-(1-Aziridinyl)-2-phenyl-1-oxaspiro[2.4]heptane (3).—A solution of 9.5 g (37 mmol) of α-bromocyclopentyl phenyl ketone (**18**) in ether was treated with 2 equiv of the lithium salt of ethylenimine according to the previously published procedure.[1b] The product after work-up was crystallized from pentane by cooling in a Dry Ice–acetone bath to give 6.2 g (78%) of **3**, mp 34–35°.

Anal. Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96; N, 6.51. Found: C, 78.34; H, 8.02; N, 6.65.

1α-(1-Aziridinyl)benzylcyclopentanol (19).—A solution of 1.5 g (6.97 mmol) of epoxyamine **3** was reduced with $NaBH_4$ as described previously.[1b] The product was recrystallized from pentane to yield 1.3 g (86%) of **19**, mp 85–88°.

Anal. Calcd for $C_{14}H_{19}NO$: C, 77.38; H, 8.81; N, 6.44. Found: C, 77.43; H, 9.03; N, 6.48.

2-(1-Aziridinyl)-2-phenylcyclohexanone (21).—A solution of 4.0 g of **3** in 25 ml of o-dichlorobenzene was refluxed under a N_2 atmosphere on a metal bath at 190–195° for 15 hr. The mixture was cooled and the solvent was removed under vacuum. The residue was crystallized from hexane to give 3.23 g (80.7%) of **21**, mp 95–97°, ir ($CHCl_3$) 1710 cm^{-1} (C=O). A small portion of **21** was dissolved in ether and treated with excess HCl in isopropyl alcohol to give 2-(2-chloroethylamino)-2-phenylcyclohexanone hydrochloride, mp 197–201° dec, ir (KBr) 1720 cm^{-1} (C=O).

Anal. Calcd for $C_{14}H_{19}Cl_2NO$: C, 58.33; H, 6.64; N, 4.86. Found: C, 58.04; H, 6.82; N, 5.02.

Hydrogenation of 50 mg (0.23 mmol) of **21** in ethyl acetate in the presence of 20 mg of 10% Pd/C followed by treatment with HCl in isopropyl alcohol gave 51 mg (85%) of 2-*N*-ethylamino-2-phenylcyclohexanone (**20**) hydrochloride,[11] mp 239–240°. A mixture melting point with an authentic sample was undepressed.

***trans*-2-(1-Aziridinyl)-2-phenylcyclohexanol (22).**—A solution of 100 mg (0.46 mmol) of **21** in methanol was reduced with $NaBH_4$ according to the previously reported procedure[1b] to give 76 mg (75%) of **22**, mp 111–112° after recrystallization from hexane.

Anal. Calcd for $C_{14}H_{19}NO$: C, 77.38; H, 8.81; N, 6.44. Found: C, 77.21; H, 8.60; N, 6.32.

(14) G. Baddeley, J. W. Rasburn, and R. Rose, *J. Chem. Soc.*, 3168 (1958).

A solution of 11.8 mg (0.054 mmol) of **22** in ethyl acetate was hydrogenated in the presence of 10% Pd/C and the product was treated with HCl in isopropyl alcohol to give 11.2 mg (81%) of *trans*-2-*N*-ethylamino-2-phenylcyclohexanol (**23**) hydrochloride,[12] mp 207–209°, identical with an authentic sample.

2-(1-Hydroxycyclopentyl)-2-phenyloxazolidine (24).—Treatment of 15.0 g (59.3 mmol) of bromo ketone **18** with 100 ml of 2-aminoethanol as in the preparation of **5** gave 11.5 g (83.6%) of **24** after recrystallization from hexane: mp 94–95°; ir (KBr) 3475 cm^{-1} (OH); ir ($CHCl_3$) 1650 cm^{-1} (weak, C=N); uv λ_{max}^{EtOH} 208 nm (log ϵ 3.80).

Anal. Calcd for $C_{14}H_{19}NO_2$: C, 72.07; H, 8.21; N, 6.01. Found: C, 71.81; H, 8.23; N, 6.03.

2-(2-Hydroxyethylamino)-2-phenylcyclohexanone (25).—A solution of 3.04 g (13 mmol) of **24** in 60 ml of freshly distilled *o*-dichlorobenzene was heated at 175° under a N_2 atmosphere for 6 hr. After cooling, the mixture was diluted with ether and extracted with 1 *N* HCl. The aqueous layer was separated, basified with NaOH, and reextracted with ether. The product crystallized from ether on concentration to give 1.06 g (35%) of **25**, mp 97–99°, ir (KBr) 1710 cm^{-1} (C=O).

Anal. Calcd for $C_{14}H_{19}NO_2$: C, 72.07; H, 8.21; N, 6.01. Found: C, 72.27; H, 8.40; N, 6.23.

Treatment of the mother liquor with picric acid yielded 1.18 g (19.3%) more of **25** as the picrate, mp 185–187° dec.

Anal. Calcd for $C_{20}H_{22}N_4O_9$: C, 51.95; H, 4.80; N, 12.12. Found: C, 51.89; H, 5.03; N, 12.29.

A small sample of **25** was converted to the HCl salt, mp 183–185° dec after recrystallization from methanol–ether.

Anal. Calcd for $C_{14}H_{20}ClNO_2$: C, 62.33; H, 7.47; Cl, 13.14; N, 5.19. Found: C, 62.24; H, 7.69; Cl, 12.95; N, 4.93.

trans-**2-(2-Hydroxyethylamino)-2-phenylcyclohexanol (26).**—Aziridinyl alcohol **22** (407 mg, 1.9 mmol) was hydrolyzed with 150 ml of 1 *N* $HClO_4$ as for the preparation of **8** to give 232 mg (52.7%) of **26**, mp 130–132° after recrystallization from ether–pentane.

Anal. Calcd for $C_{14}H_{21}NO_2$: C, 71.45; H, 9.00; N, 5.95. Found: C, 71.21; H, 8.81; N, 5.79.

Reduction of 504 mg (1.1 mmol) of **25** picrate with $NaBH_4$ also provided 217 mg (84.8%) of **26**, mp 130–132°. A mixture melting point with the two samples was undepressed.

Registry No.—**2**, 35099-50-4; **3**, 35099-51-5; **5**, 35099-52-6; **5** imine form, 35099-53-7; **6**, 35099-54-8; **7**, 35099-55-9; **8**, 35099-56-0; **9**, 35099-57-1; **11**, 35099-58-2; **11** hydrogen *p*-toluenesulfonate, 35099-59-3; **12**, 35099-60-6; **13** HCl, 35099-61-7; **15**, 35099-62-8; **15** HCl, 35099-63-9; **19**, 35099-64-0; **21**, 35099-65-1; **22**, 35099-66-2; **24**, 35099-67-3; **25**, 35099-68-4; **25** picrate, 35099-69-5; **25** HCl, 35099-70-8; **26**, 35099-71-9; 1-(2-chloroethylamino)-1-phenyl-2-methyl-2-propanol HCl, 35099-72-0; 1-(2-chloroethylamino)-1,1-diphenyl-2-methyl-2-propanol HCl, 35099-73-1.

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The Catalytic and Photolytic Decomposition of 1-Chloro-4-diazoalkenes

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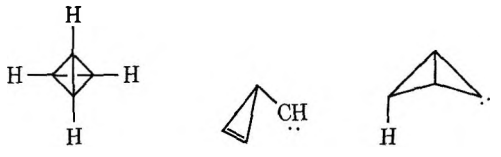
The synthesis of 1-chloro-4-diazo-2,3-dimethyl-1-pentene from 3-methyl-3-penten-2-one and of 1-chloro-4-diazo-2,3-dimethyl-1-butene from methyl acetoacetate is described. The catalytic decomposition of the diazoalkenes was studied; the decomposition of the latter with mercuric iodide gave 1-chloro-2,3-dimethyl-1,3-butadiene, 1-chloro-2-methyl-1,3-pentadiene, and 3-chloro-1,4-dimethylcyclobutene as major products. The mechanism of formation of these products is discussed in terms of the rearrangement of either a metal complexed carbenoid species or a metal complexed bicyclobutane.

The synthesis of tetrahedranes represents a fascinating challenge to the organic chemist.[3] The



availability of such a molecular system would represent a significant development in furthering our understanding of the correlation between chemical bonding and chemical reactivity. Most of the previous unsuccessful approaches evolved around intramolecular insertion of a carbene into a proximate cyclopropene double bond.[3a-c] A more attractive alternative involves intramolecular C–H insertion of a carbene in a suitable bicyclo[1.1.0]butane. Such an intermediate is presumed to be generated in the photodecomposition of carbon suboxide in the presence of cyclopropenes.[3d,e] The subsequent products allow an interpretation of a tetrahedrane intermediate. In an attempt to generate this carbene (or carbenoid) at low temperature in its ground state, we became interested in the synthesis of 2-halobicyclo[1.1.0]butanes.[4] Among the various approaches to such compounds, the catalytic decomposition of diazobutenes appeared particularly suitable.[5,6] We therefore undertook a study of the synthesis and decomposition of 1-chloro-4-diazo-2,3-dimethyl-1-pentene (**1**) and 1-chloro-4-diazo-2,3-dimethyl-1-butene (**2**) as a route to the 2-chlorobicyclo[1.1.0]butanes **3** and **4**. The fascinating rearrangement products obtained relate to the mechanism of decomposition of bicyclobutanes by transition metal catalysis.

Synthesis.—The envisioned precursor of bicyclobutane **3**, 1-chloro-4-diazo-2,3-dimethyl-1-pentene (**1**), was prepared as outlined in Scheme I. Addition of cyanide ion to 3-methyl-3-penten-2-one, saponification of the crude product, and esterification gave the keto ester **5**. Introduction of the chloromethylene group

(1) National Institutes of Health Predoctoral Fellow.

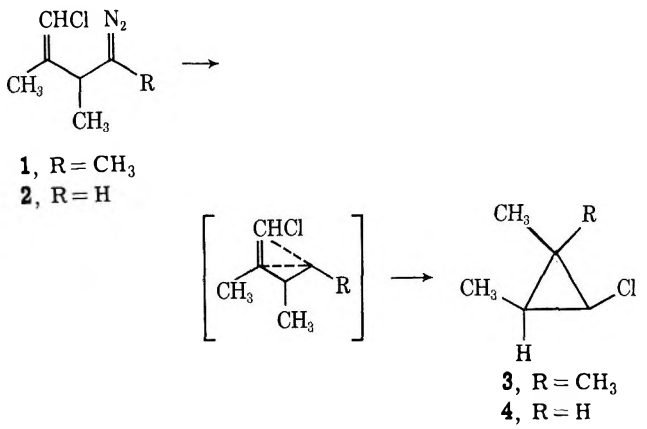
(2) Camille and Henry Dreyfus Teacher–Scholar Grant Recipient.

(3) (a) H. Ona, H. Yamaguchi, and S. Masamune, *J. Amer. Chem. Soc.*, **92**, 7495 (1970); S. Masamune and M. Kato, *ibid.*, **87**, 4190 (1965), and **88**, 610 (1966); (b) E. H. White, G. E. Maier, R. Graeve, V. Zingible, and E. W. Friend, *ibid.*, **88**, 611 (1966); (c) G. L. Closs and V. N. M. Rao, *ibid.*, **88**, 4116 (1966); (d) P. B. Shevlin and A. P. Wolf, *ibid.*, **92**, 406 (1970); (e) R. F. Peterson, R. T. K. Baker, and R. L. Wolfgang, *Tetrahedron Lett.*, 4749 (1969).

(4) B. M. Trost and R. C. Atkins, *Chem. Commun.*, 1254 (1971).

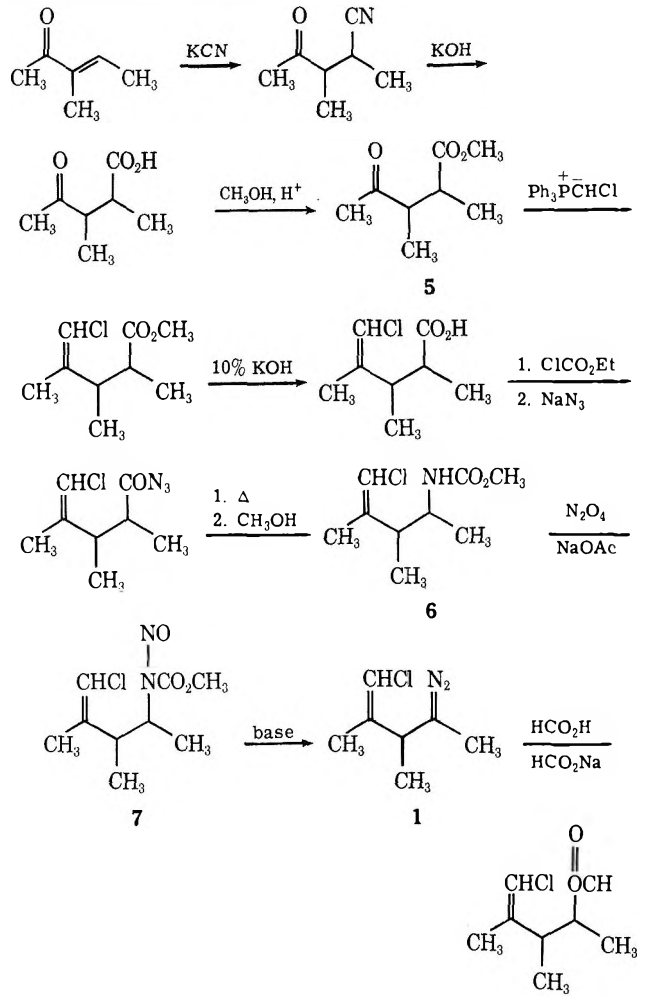
(5) K. B. Wiberg, *Advan. Alicycl. Chem.*, **2**, 185 (1968).

(6) G. L. Closs and P. F. Pfeffer, *J. Amer. Chem. Soc.*, **90**, 2452 (1968).

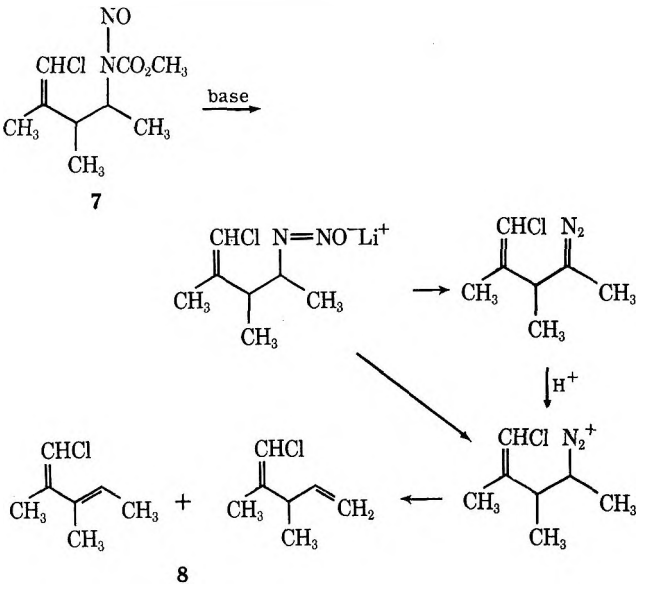


SCHEME I

SYNTHESIS OF 1-CHLORO-4-DIAZO-2,3-DIMETHYL-1-PENTENE (1)



by the Wittig reaction,[7] saponification, and use of the modified[8] Curtius reaction afforded the chloromethylene carbamate **6** in 37% overall yield from **5**. Compound **6** exhibited the expected carbamate ir absorption at 3450, 3400, and 1705 cm^{-1}. The base peak in the mass spectrum was at *m/e* 102 ($CH_3CHNHCO_2$-CH_3^+). Nitrosation with dinitrogen tetroxide gave, after rapid chromatography through neutral alumina, an 87% yield of the nitrosocarbamate **7** as an unstable yellow liquid which exhibited no N–H band and a shifted carbonyl band (to 1740 cm^{-1}) in its ir spectrum. Treatment of **7** with base (lithium ethoxide)[9] yielded a pink solution exhibiting strong ir absorption at 2040 cm^{-1}. Characterization of the diazoalkene **1** was achieved through analysis of the formate esters obtained when the solution was quenched with anhydrous formic acid containing sodium formate. The yield of **1** (based on nitrosocarbamate) was found to be only 17%, the major products being the various isomers of 1-chloro-2,3-dimethyl-1,3- and -1,4-pentadienes (**8**,



vide infra). The predominance of products derived from a carbonium ion intermediate in the reaction of nitrosocarbamate **7** with base is in agreement with other studies[10] related to the generation of a secondary diazoalkene.

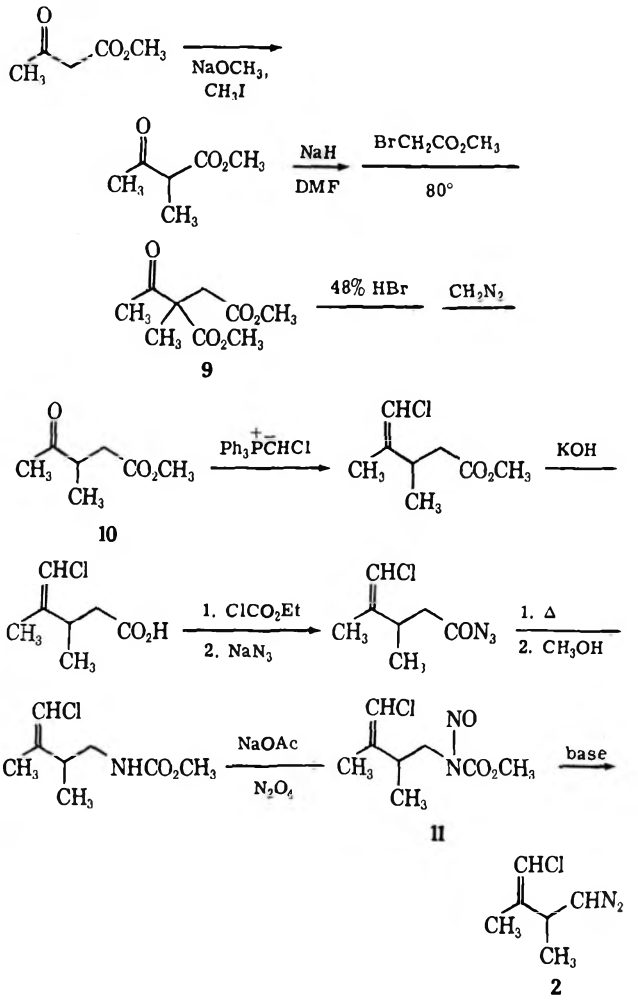
It is known[11] that primary diazo systems are more readily generated, and with this consideration in mind the synthesis of 1-chloro-4-diazo-2,3-dimethyl-1-butene (**2**), a precursor to the bicyclobutane **4**, was undertaken (Scheme II). Alkylation of methyl α-methylacetoacetate with methyl bromoacetate yielded the keto diester **9** which, after hydrobromic acid decarboxylation and esterification, gave methyl 3-methyllevulinate (**10**). The *N*-nitrosocarbamate **11**, obtained from **10** in a manner similar to that described in Scheme I, gave on treatment with lithium ethoxide an orange solution of the diazoalkene **2**, ir 2060 cm^{-1}, visible 400–500 nm ($\epsilon \sim 17$). Quenching of the diazo solution with acetic acid–sodium acetate allowed full characterization of **2** as the acetate. Gas chromatography revealed that elimination products were absent in the formation of **2**.

Decomposition Results.—A detailed analysis of the catalytic decomposition of the secondary diazopentene **1** was precluded by the facile formation of carbonium ion derived products (**8**). Attempts to purify **1** met with failure, and it became necessary to examine the decomposition of **1** in the presence of the previously formed dienes **8**. A variety of catalysts (*vide infra* the study of **2**) were found to yield only the dienes **8**. In view of the difficulties inherent in the secondary

(7) G. Köbrich, H. Trapp, K. Flory, and W. Drischel, *Chem. Ber.*, **99**, 689 (1966).
(8) J. Weinstock, *J. Org. Chem.*, **26**, 3511 (1961).
(9) W. M. Jones and D. L. Muck, *J. Amer. Chem. Soc.*, **88**, 3798 (1966).
(10) J. Meinwald and T. N. Wheeler, *ibid.*, **92**, 1009 (1970).
(11) R. A. Moss, *J. Org. Chem.*, **31**, 1082 (1966).

SCHEME II

SYNTHESIS OF 1-CHLORO-4-DIAZO-2,3-DIMETHYL-1-BUTENE (2)



diazo system, attention was focused on the study of the decomposition of the primary diazobutene **2**.

The catalytic decomposition of **2** was investigated under a variety of conditions (see Table I), all of which

TABLE I

PRODUCT DISTRIBUTION FROM DECOMPOSITION OF DIAZOALKANE **2**

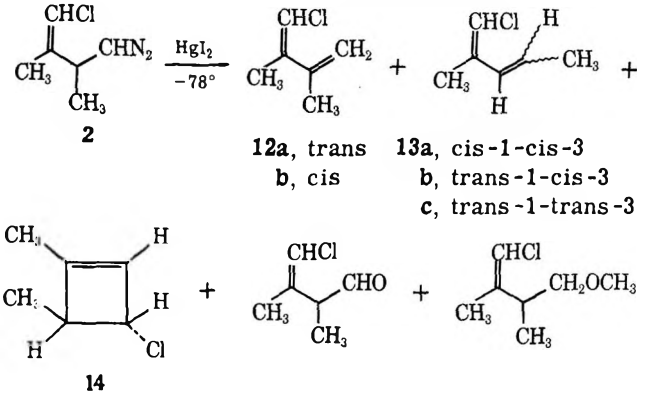
Catalyst	12a	12b	13a	13b + 13c	14	15
HgI_2[a]	12	37	3	20	3	
CuCN[b]	25	47	4	6	9	
$CuBF_4$	35	63			2.5	
LiBr[c]	25	50	3	10	5	
$ZnCl_2$[d]	20	60		15	5	
$h\nu$	17	31				52

[a] Reference 12. [b] Reference 6. [c] Reference 13. [d] Reference 14.

failed to produce detectable quantities of any bicyclobutane.[12-14] As a representative example, the addition of a pentane solution of **2** to a dimethyl ether solution of mercuric iodide[12] at −78° led to a disappearance of the 2060-cm^{-1} ir band. Gas chromatography of the resulting mixture allowed identification of the products shown in Scheme III.[15]

SCHEME III

REACTION OF **2** WITH MERCURIC IODIDE



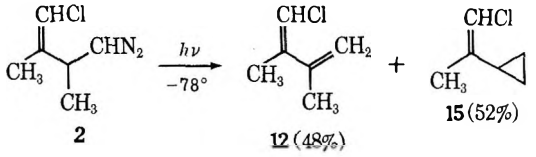
The major product of the reaction, the 1,3-butadiene **12**, exhibited nmr absorption at δ 5.1, 4.9 (br s, CH_2), 5.86, 6.23 (m, =CHCl, anti and syn chlorine, respectively), and ir absorption at 890 cm^{-1} ($R_2C{=}CH_2$). The 1,3-pentadiene structure of **13** was evident from the spectral data: nmr δ 1.81 (d, J = 6 Hz, $=CHCH_3$), 5.8–6.2 (m, *cis*-methyl isomer **13a**), 6.68 (d, J = 15 Hz, *trans*-methyl isomer **13b**). The assignment of the cyclobutene structure rests on the spectroscopic data and its precursor structure. The high resolution mass spectrum established a formula of C_6H_9Cl. The nmr spectrum indicated a vinylic methyl group (δ 1.72, finely coupled singlet) and a secondary saturated methyl group (δ 1.19, d, J = 7 Hz). The methine proton coupled to the methyl group is also allylic (2.9, bm). A single vinylic proton (δ 5.76, br s) and a saturated methine proton geminate to a chlorine (δ 4.22, br s) complete the spectrum. Lack of observable coupling between the vicinal protons is common in trans-3,4-disubstituted cyclobutenes. Two minor products also isolated, 2,3-dimethyl-4-chloro-3-butenal and 2,3-dimethyl-4-methoxy-1-butene, arise as by-products in the preparation of the diazo compound.

The available data failed to suggest the presence of any bicyclobutanes in the reaction mixture. Careful gas chromatography, including variation of injector, detector, and column temperatures, did not alter the number or relative amounts of the products obtained. In an effort to explore the possible existence of bicyclobutanes in the reaction prior to gas chromatography, a solution of diazobutene **2** was prepared in fluorotrichloromethane (Freon 11) and reacted with mercuric iodide in dimethyl ether at −78°. After removal of the majority of solvent under reduced pressure at −20° and filtration, a −25° nmr spectrum was recorded. Only the presence of dienes (absorption due to allylic methyl groups) was noted.[16] A further indication that bicyclobutanes were absent from the reaction mixture (at least at −20°) arises from consideration of the rapid rearrangement of bicyclobutanes when exposed to acidic media.[17] Stirring an aliquot of the reaction solution with glacial acetic acid followed by gas chroma-

(12) E. J. Corey and K. Achiwa, *Tetrahedron Lett.*, 2245 (1970).
(13) G. L. Closs and R. B. Larrabee, *ibid.*, 287 (1965).
(14) S. H. Goh, L. E. Closs, and G. L. Closs, *J. Org. Chem.*, **34**, 25 (1969).
(15) The molecular formula of all products was confirmed by high resolution mass spectrometry—see Experimental Section.
(16) An estimated limit of detection of bicyclobutane was 5%.
(17) K. B. Wiberg and G. Szeimies, *J. Amer. Chem. Soc.*, **92**, 571 (1970).

tography yielded a chromatogram which was identical with that obtained from the solution which had not been exposed to acid.

The photolytic decomposition of diazobutene **2** was studied in a further attempt to generate the bicyclobutane **4**. Known[18] to be an efficient method of generating carbenes from diazoalkanes, direct photolysis of **2** led to formation of the butadiene **12** and, as the major product, the vinyl cyclopropane **15**.



2 **12** (48%) **15** (52%)

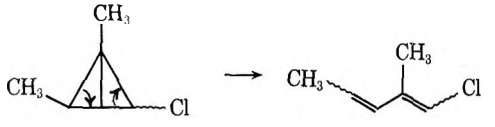
The vinyl cyclopropane structure of **15** was evident from the nmr [(CCl_4) δ 0.8–0.4 (br m), 1.66 (allylic methyl), 5.80 and 5.95 (=CHCl, mixture of isomers)] and ir (3130, 3050, 920 cm^{-1}) spectra. Insertion of the singlet carbene into the neighboring methyl group (to yield **15**) is not unexpected in view of the work by Kirmse[18b] on the reactions of α-methyl-substituted carbenes. Attempts to generate the triplet carbene *via* sensitized photolysis failed owing to the low solubility of the sensitizers under the photolysis conditions (pentane, −78°). In all cases singlet carbene products (*i.e.*, **15**) were observed.

Discussion

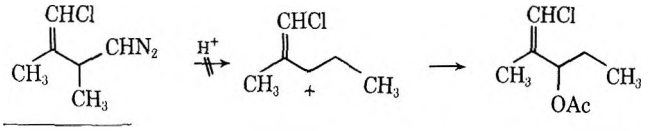
The products obtained in the catalytic decomposition of diazobutene **2** allow a discussion of the mechanistic possibilities related to their formation. The terminal butadiene **12** is the product to be expected from either hydrogen migration of a carbenoid species or elimination of a diazonium cation.

Of greater interest is the mechanism of formation of the dienes **13** and the cyclobutene **14**. Possible considerations of the origin of **13** include: (a) thermal ring opening of a bicyclobutane (in what would formally be a retro [$2_s + 2_a$] process); (b) metal catalyzed ring opening of a bicyclobutane; (c) migration in a cationic diazonium species; (d) migration in a metal complexed carbenoid species.

Thermal ring opening (mechanism a) of a bicyclobutane generally requires temperatures on the order of 200°. The experimental data require that any pathway involving such intermediate be capable of taking place at below −25°. Thus, such a course is rendered unlikely. Migration in a cationic species (mechanism c)



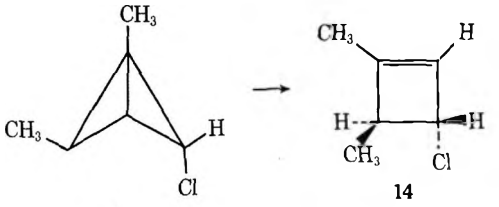
is equally unlikely. Thus, carbonium ion products resulting from treatment of **2** with acid do not possess such rearranged structures. In this case, methyl



migration in the homoallylic cation is at least slower than solvent capture, whereas significant methyl migration occurs in the acetolysis of isobutyldiazonium cation.[19] This discrepancy may relate to partial stabilization of the primary cation center by the proximate double bond.

The data available do not allow a clear distinction between the two remaining mechanistic possibilities—metal catalyzed rearrangement of a bicyclobutane (mechanism b) and migration in a metal complexed carbenoid (mechanism d). Recent studies[20] involving the rearrangement of bicyclobutanes to butadienes with silver, palladium, or rhodium catalysts have all involved temperatures of 25° or above. As noted above, the low temperature product analysis precludes the presence of bicyclobutanes at temperatures above −20°. Alternatively, it has been shown that migration of a metal complexed carbenoid is rapid at low temperature.[20a-c] These observations have led to the interpretation that such metal complexed carbenes are intermediates in the bicyclobutane rearrangement.[20a-c] Alternatively, organosilver cations have been invoked to rationalize rate data in the silver perchlorate catalyzed rearrangement.[20a]

In the present experiments, two types of rearrangement products **13** and **14** must be reconciled. The cyclobutene **14** most simply arises from thermal re-



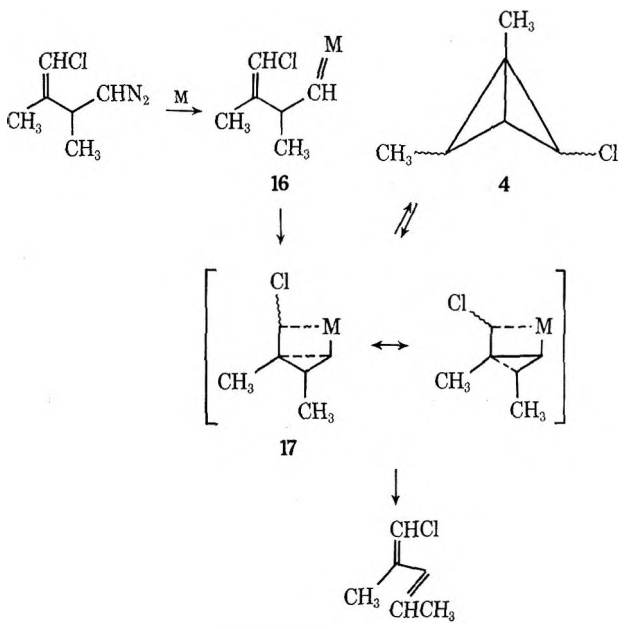
4 **14**

arrangement of the desired bicyclobutane system (**4**) with an endo chlorine. We have previously shown that 2,2-dichloro-1,3,4-trimethylbicyclo[1.1.0]butane rearranges to the corresponding cyclobutene even at −70°. The dienes **13** may be rationalized by either a methyl shift or a vinyl shift. If the latter, the same bicyclobutane (**4** chlorine endo or exo) may be invoked; however, the higher temperatures usually required for metal catalyzed rearrangement make this pathway unattractive also. A partitioning most likely occurs earlier in the sequence. To differentiate between the Gassman and Paquette views of the reaction is exceedingly difficult since they clearly merge. Vinyl migration in the metal complexed carbene **16** is undoubtedly preceded by interaction of the π electrons with the carbenoid center. The question factors to whether the species **17** is an intermediate or a transition state. Such an important but fine distinction is not allowed at the present time. Assuming that cyclobutene **14** has its origin in **4**, the low yields of bicyclobutane products may be attributed to (1) diminished double-bond participation as envisioned in species **17**

(18) (a) D. M. Lemal and K. S. Shim, *Tetrahedron Lett.*, 3231 (1964); (b) W. Kirmse and D. Groszmass, *Chem. Ber.*, **99**, 1746 (1966).

(19) J. H. Bayless, A. T. Jurewicz, and L. Friedman, *J. Amer. Chem. Soc.*, **90**, 4466 (1968).

(20) (a) P. G. Gassman, T. J. Akins, and F. J. Williams, *ibid.*, **93**, 1812 (1971); (b) P. G. Gassman and F. J. Williams, *Tetrahedron Lett.*, **No. 18**, 1409 (1971); (c) M. Sakai, H. Yamaguchi, and S. Masamune, *Chem. Commun.*, 486 (1971); (d) M. Sakai, H. H. Westberg, H. Yamaguchi, and S. Masamune, *J. Amer. Chem. Soc.*, **93**, 4611 (1971), and references therein; (e) L. A. Paquette and S. E. Wilson, *ibid.*, **93**, 5934 (1971), and references therein.



due to the negative inductive effect of the chloride and (2) diminished metal–C_1 interaction in species **17** due to the ability of chlorine to stabilize adjacent positive charge. The important role of the metal cation in both processes is demonstrated by the absence of both types of rearrangement products in the photolysis experiments.

Experimental Section[21]

Preparation of Methyl 2,3-Dimethyl-4-ketopentanoate (5).—Following the procedure of Haworth, *et al.*,[22] 20.0 g (0.20 mol) 3-methyl-3-penten-2-one was dissolved in 500 ml of 95% ethanol. Potassium cyanide (14.3 g, 0.22 mol) in 50 ml water was added over 5 min. The cloudy mixture was heated to 75° with stirring for 18 hr. After cooling to 0°, ether and saturated brine were added and the reaction was extracted. Drying over magnesium sulfate and solvent removal gave 17 g of a viscous yellow oil, which exhibited the spectral characteristics expected for an amide:[23] ir ($CHCl_3$) 3650, 3450, 3200, 1660 cm^{-1}.

Saponification of 12.68 g (0.089 mol) of the crude product in 250 g of refluxing 20% potassium hydroxide for 26 hr, followed by hydrochloric acid acidification, extraction with ether, and drying over magnesium sulfate, gave 7.06 g (55%) of crude 2,3-dimethyl-4-ketopentanoic acid: ir ($CHCl_3$) 3000 (br), 1750, 1700 cm^{-1}; nmr ($CDCl_3$) δ 9.2 (br, 1 H). Heating the total product on a steam bath overnight in 500 ml of methanol containing 3 ml of concentrated sulfuric acid, followed by extraction with ether and washing with sodium bicarbonate, afforded 6.7 g (86%) of crude ester. Distillation gave 5.20 g (67%) of clear, colorless product: bp 30° (0.05 mm); ir (CCl_4) 1740, 1710 cm^{-1}; nmr (CCl_4) δ 3.62 (s, 3 H), 2.72 (m, 2 H), 2.12 (s, 3 H), 1.10 (m, 6 H); mass spectrum m/e (rel intensity) 158 (4), 143 (5), 127 (21). *Anal.* Calcd for $C_8H_{14}O_3$: 158.09429. Found: 158.09089.

Preparation of Chloromethyltriphenylphosphonium Chloride.—Chloromethyltriphenylphosphonium chloride was prepared according to the procedure of Kobrich.[7] The material obtained (36.0 g, 44%) exhibited hydroxyl absorption in the ir, indicating the presence of either water or hydroxymethyltriphenylphosphonium salt. Purification attempts met with failure, and the salt was used in an impure state.

Preparation of Methyl 5-Chloro-2,3,4-trimethyl-4-pentenoate.—To 300 ml of freshly distilled ether was added 19.1 g (0.055 mol) of chloromethyltriphenylphosphonium chloride and 4.42 g (0.052 mol) of *n*-butyllithium was added over 15 min to yield a dark orange suspension. After this mixture stirred for 15 min at 0°, 3.50 g (0.022 mol) of keto ester **5** was added dropwise. After stirring 0.5 hr at room temperature, the reaction mixture was quenched with 25 ml of water and extracted with ether. Evaporation of solvent, dissolving the residue in hexane, and filtration enabled removal of the triphenylphosphine oxide. The filtrate was washed with 5% hydrochloric acid, dried over magnesium sulfate, and evaporated. Distillation (short path) yielded 2.078 g (50%) of a clear colorless liquid: ir (CCl_4) 1740, 1630 cm^{-1}; nmr (CCl_4) δ 5.74 (m, 1 H), 3.58 (s, 3 H), 2.4 (m, 2 H), 1.70 (finely coupled s, J = 1.5 Hz, 3 H), 1.0–1.2 (complex m, 6 H).

Anal. Calcd for $C_9H_{15}O_2Cl$: C, 56.69; H, 7.93; Cl, 18.59. Found: C, 56.96; H, 7.80; Cl, 18.79.

Preparation of Methyl *N*-4-(1-Chloro-2,3-dimethyl-1-pentenyl)-carbamate (6).—Saponification of 0.445 g (2.34 mmol) of methyl 5-chloro-2,3,4-trimethyl-4-pentenoate in 20 ml of 10% aqueous potassium hydroxide containing 2 ml of ethanol by refluxing for 1 hr yielded, after work-up, 0.383 g (93%) of the corresponding acid: ir ($CHCl_3$) 3000, 1700 cm^{-1}; nmr ($CDCl_3$) δ 10.5 (br m, 1 H).

Subjecting the acid to the modified Curtius reaction[8] enabled the desired carbamate to be prepared as follows. To a solution of 1.65 g (9.40 mmol) of the acid prepared above in 25 ml of acetone containing 5 ml of water in a 100-ml three-neck flask was added 1.10 g (10.9 mmol) triethylamine in 5 ml of acetone at 0°. Ethyl chloroformate (1.32 g, 12.2 mmol in 5 ml of acetone) was added dropwise from a syringe over 10 min. After the mixture stirred for 0.5 hr at 0°, sodium azide (0.925 g, 14.2 mmol in 8 ml of water) was added dropwise from a funnel over 15 min. The reaction mixture was then stirred at 0° for 1 hr, poured onto ice, and extracted with ether. After drying (magnesium sulfate) and evaporation (without heating), an oil was obtained which exhibited strong azide ir absorption at 2140 cm^{-1}.

The oil was dissolved in 25 ml of dry toluene and heated to 90–100° for 1 hr. After gas evolution had ceased, 20 ml of dry methanol was added and the solution was refluxed for 3 hr. Distillation over a short path (bath temperature 125°, 0.05 mm) yielded 1.55 g (80%) of a pale yellow liquid exhibiting the following spectral characteristics: ir ($CHCl_3$) 3450, 3400, 1705, 1630 cm^{-1}; nmr ($CDCl_3$) δ 5.9 (m, 1 H), 4.5 (br s, 1 H), 3.65 (s, 3 H), 2.2 (m, 2 H), 1.75 (finely coupled m, 3 H), 1.2 (complex m, 6 H); mass spectrum m/e (rel intensity) 102 (100, $CH_3CHNHCO_2CH_3^+$).

Anal. Calcd for $C_9H_{16}NO_2Cl$: C, 52.55; H, 7.84; N, 6.81; Cl, 17.24. Found: C, 52.85; H, 7.85; N, 6.83; Cl, 17.06.

Preparation of Methyl *N*-Nitroso-*N*-4-(1-chloro-2,3-dimethyl-1-pentenyl)carbamate (7).—Nitrosation[24] was effected by filtration of a solution of 1.042 g (5.1 mmol) of distilled carbamate **6** in 20 ml of dry ether through sodium sulfate into a 50-ml side-arm flask, addition of 1.64 g (20 mmoles) anhydrous sodium acetate, and cooling to −20°. Dinitrogen tetroxide was distilled into the flask for 1 hr, during which time the color became green. After an additional 2 hr at −20°, the mixture was carefully poured onto 250 ml of ice-cold 10% sodium bicarbonate, causing vigorous bubbling and the elution of a brown vapor. Extraction with cold ether, washing with water, and drying over magnesium sulfate yielded a yellow solution which was stored at −20°. The absence of any N–H band in the ir (at 3400 cm^{-1}) was noted in the crude material. Chromatography of the crude product (1.35 g, 100%) through neutral alumina (Woelm, activity III) using hexane as the eluent afforded 1.036 g (87%) of the pure nitrosocarbamate: ir ($CHCl_3$) 1740, 1630 cm^{-1}; nmr ($CDCl_3$) δ 5.8 (m, 1 H), 4.05 (s, 3 H), 0.80–1.80 (complex m, 9 H); tlc (alumina, 6% ether–hexane) R_f 0.52. The product was stored in ether solution at −20°. Attempts to obtain an analytically pure sample met with failure.

Preparation of 1-Chloro-4-diazo-2,3-dimethyl-1-pentene (1).—Lithium ethoxide[25] (195 mg, 3.8 mmol) was added to a solution of

(21) All ir spectra were recorded on a Beckman IR-8 spectrophotometer, all uv spectra on a Cary Model 15 spectrophotometer, and all nmr spectra on a Varian Model A-60A spectrometer fitted with a variable-temperature probe. Chemical shifts are reported in parts per million downfield from TMS as an internal standard. Mass spectra were obtained on an AEI MS-902 double focusing instrument at an ionizing voltage of 70 eV. Elemental analyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Michigan. Vpc analyses were performed on an Aerograph Model A90-P3 gas chromatograph using a 15-ft 20% SE-30 on Chromasorb W column.

(22) R. D. Haworth, B. G. Hutley, R. G. Leach, and G. Rodgers, *J. Chem. Soc.*, 2720 (1962); A. Bowers, *J. Org. Chem.*, **26**, 2043 (1961).

(23) Haworth[22] found that extended reflux times resulted in partial saponification of the cyano group to an amide.

(24) E. H. White, *J. Amer. Chem. Soc.*, **77**, 600 (1955).

(25) T. L. Brown, D. W. Dickerhoof, and D. A. Bafus, *ibid.*, **84**, 1371 (1962).

173 mg (3.3 mmol) N nitrosocarbamate 7 in 6 ml of anhydrous ethanol cooled to −20°. After stirring for 1 hr at −20°, the orange solution was diluted with 50 ml of pentane and washed with three portions of dilute aqueous potassium hydroxide. Drying the organic phase over potassium hydroxide pellets yielded a pink solution having strong ir absorption at 2040 cm^{-1}.

Characterization of the diazo solution was achieved by addition of an aliquot to a rapidly stirring mixture of 1.5 g of sodium formate in 5 ml anhydrous formic acid (prepared by refluxing 90% formic acid over phthalic anhydride and distilling[26]). The pink color was immediately discharged. After extraction of ether, washing with sodium bicarbonate, and drying over potassium carbonate, vpc analysis allowed isolation and characterization of the formate ester of 1, 4-(1-chloro-2,3-dimethyl-1-pentenyl)-formate: ir (CCl_4) 3100, 1730, 1630, 1180 cm^{-1}; nmr (CCl_4) δ 7.90 (br s, 1 H), 5.80 (br s, 1 H), 1.72 (finely coupled s, J = 1.5 Hz, 3 H), 1.1 (complex m, 6 H); mass spectrum m/e (rel intensity) 178, 175 (weak, ratio 1:3, M^+ for $C_8H_{13}ClO_2$), 132 (10), 130 (30), 95 (30). The yield was determined to be 17%.

Anal. Calcd for $C_8H_{13}ClO_2$: C, 54.39; H, 7.42; Cl, 20.07. Found: C, 54.56; H, 7.44; Cl, 20.30.

The major products from the reaction were shown to be the various isomers of 1-chloro-2,3-dimethyl-1,4-pentadiene and 1-chloro-2,3-dimethyl-1,3-pentadiene (8, 30% yield): ir (CCl_4) 3100, 1630, 1370, 1100, 910 cm^{-1}; nmr (CCl_4) δ 5.5–6.0 (m, 2 H), 5.14, 4.92 (br m, 2 H), 1.5–1.9 (complex m, 6 H), 1.13 (two overlapping doublets, J = 7 Hz, 3 H); mass spectrum m/e (rel intensity) 132 (6), 130 (17), 115 (4), 95 (100).

Anal. Calcd for $C_7H_{11}Cl$: C, 64.36; H, 8.49; Cl, 27.15. Found: C, 64.49; H, 8.53; Cl, 27.09.

Two additional products were shown to have arisen from reaction with solvent (ethanol) and by air oxidation. In an effort to eliminate the former, freshly distilled hexamethylphosphoramide was employed as the solvent for generating the diazo compound. It was found, however, that the yield of formate esters dropped to 14%, and the yield of dienes rose to 56%.

Preparation of Methyl 3-Carbomethoxy-4-keto-3-methylpentanoate (9).—Into a 250-ml three-neck flask fitted with a reflux condenser and dropping funnel was put 3.93 g (0.090 mol) sodium hydride–mineral oil dispersion which was washed with hexane. Freshly distilled dimethylformamide (90 ml) was added and stirred. Methyl α-methylacetoacetate (12.00 g, 0.0925 mol), prepared according to the procedure of Marvel[27] from methyl acetoacetate, was added dropwise over 20 min. After the mixture stirred at room temperature for 0.5 hr, 15.30 g (0.10 mol) methyl bromoacetate (diluted in DMF) was added dropwise over 1 hr. After the reaction was heated to 80° for 3 hr an aliquot was found to be neutral to moist litmus. After cooling, water was added and the reaction mixture was concentrated on a rotary evaporator fitted with a vacuum pump. Extraction with ether, washing with water, and drying over magnesium sulfate gave, after concentration, 15.98 g (89%) crude product. Distillation afforded 12.24 g (68%) of pure product as a clear, colorless liquid, bp 61–70° (0.05 mm). A vpc-collected sample had the following spectral properties: ir ($CHCl_3$) 1725, 1710 cm^{-1}; nmr ($CDCl_3$) δ 3.76 (s, 3 H), 3.66 (s, 3 H), 2.90 (s, 2 H), 2.25 (s, 3 H), 1.50 (s, 3 H); mass spectrum m/e (rel intensity) 202 (1), 171 (45), 160 (55), 128 (100).

Anal. Calcd for $C_9H_{14}O_5$: C, 53.45; H, 6.97. Found: C, 53.42; H, 6.84.

Preparation of Methyl 4-Keto-3-methylpentanoate (Methyl 3-Methyllevulinate, 10).—To 50 ml of hydrobromic acid (48%) was added 12.24 g (0.60 mol) keto diester 9 (neat). After refluxing for 3 hr, the mixture was cooled, extracted with ether, then sodium bicarbonate, and ether again, following acidification. After drying (magnesium sulfate), solvent was removed to give a colorless oil: ir ($CHCl_3$) 3000, 1700 cm^{-1}; nmr ($CDCl_3$) δ 10.1 (br s, 1 H).

To an ethereal solution of the crude acid cooled to 0° was added an excess of diazomethane (prepared from EXR-101 in ether). The usual work-up gave 2.97 g (35%) of a clear, pale yellow liquid. Analytical samples, collected on the vpc, exhibited the following spectral properties: ir (CCl_4) 1730, 1700, 1350 cm^{-1}; nmr (CCl_4) δ 3.60 (s, 3 H), 2.2–3.0 (complex m, 3 H), 2.14 (s, 3 H), 1.12 (d, J = 7 Hz, 3 H); mass spectrum m/e (rel intensity) 144 (4), 129 (10), 113 (44), 102 (40), 87 (67).

Anal. Calcd for $C_7H_{12}O_3$: C, 58.31; H, 8.39. Found: C, 58.21; H, 8.40.

Preparation of Methyl *N*-Nitroso-*N*-4-(1-chloro-2,3-dimethyl-1-butenyl)carbamate (11).—The remainder of the synthesis was identical with that described above for the synthesis of the N nitrosocarbamate 7. Reaction of 2.93 g (20.4 mmol) of the keto ester 10 with triphenylphosphonium chloromethylide gave the chloro olefin ester, which, after saponification, yielded 1.83 g (56%) of the corresponding acid. The ester exhibited the following spectral data: ir (CCl_4) 3100, 1740, 1630 cm^{-1}; nmr (CCl_4) δ 5.75, 5.90 (br s, 1 H), 3.60 (s, 3 H), 2.3 (m, 3 H), 1.7 (two finely coupled s, J = 1.5 Hz, 3 H), 1.10 (two overlapping d, J = 7 Hz, 3 H); mass spectrum m/e (rel intensity) 178, 176 (weak, ratio 1:3), 161 (1), 141 (50), 105 (23), 103 (70).

Anal. Calcd for $C_8H_{13}ClO_2$: C, 54.39; H, 7.42; Cl, 20.07. Found: C, 54.64; H, 7.39; Cl, 19.99.

Curtius rearrangement of the acid (1.83 g, 11.3 mmol) yielded, after distillation, 1.736 g (80%) of the desired carbamate: ir ($CHCl_3$) 3450, 3400, 3100, 1700, 1630, 1500 cm^{-1}; nmr ($CDCl_3$) δ 5.90 (br s, 1 H), 4.7 (br m, 1 H), 3.66 (s, 3 H), 3.12 ("triplet," J = 7 Hz, 2 H), 2.4 (complex m, 1 H), 1.75 and 1.69 (two finely coupled s, J = 1.5 Hz, 3 H), 1.05 (two overlapping d, J = 7 Hz, 3 H); mass spectrum m/e (rel intensity) 88 (100, CH_2NHCO_2-CH_3^+).

Anal. Calcd for $C_8H_{14}N_2OCl$: C, 50.13; H, 7.36; N, 7.31; Cl, 18.50. Found: C, 50.29; H, 7.33; N, 7.27; Cl, 18.42.

Reaction of 0.960 g (5.00 mmol) of the carbamate with dinitrogen tetroxide, followed by alumina chromatography as before, yielded 0.880 g (80%) yellow N nitrosocarbamate 11: ir ($CHCl_3$) 1750, 1630 cm^{-1}; uv (EtOH) λ_{max} 238 nm (ε 1830), 401 (55), 421 (52). An attempt to obtain an analytically pure sample failed.

Preparation of 1-Chloro-4-diazo-2,3-dimethyl-1-butene (2).—Following the procedure previously described, 39.3 mg (0.18 mmol) of the nitrosocarbamate 11 was treated with 85 mg (1.6 mmol) lithium ethoxide in ethanol. Extraction into pentane, washing with dilute potassium hydroxide, and drying over potassium hydroxide pellets afforded a yellow solution exhibiting strong ir absorption at 2060 cm^{-1} and visible absorption from 400 to 500 nm (ε ~17). Addition of an aliquot to a mixture of anhydrous sodium acetate in glacial acetic acid, followed by extraction with ether, washing with sodium bicarbonate, and drying over potassium carbonate, allowed isolation of the acetate adduct of 2. Vpc analysis enabled the adducts to be identified as *cis*-4-acetoxy-1-chloro-2,3-dimethyl-1-butene (22.5% yield) and *trans*-4-acetoxy-1-chloro-2,3-dimethyl-1-butene (19.5% yield). The spectral properties were as follows.

Cis isomer: ir (CCl_4) 3050, 1740, 1630, 1240, 950 cm^{-1}; nmr (CCl_4) δ 5.93 (br s, 1 H), 2.3 (m, 1 H), 2.00 (s, 3 H), 1.84 (d, J = 1.5 Hz, 3 H), 1.22 (d, J = 7 Hz, 3 H); mass spectrum m/e (rel intensity) 141 (4), 118 (32), 116 (100).

Anal. Calcd for $C_8H_{13}O_2Cl$: C, 54.39; H, 7.41; Cl, 20.07. Found: C, 54.21; H, 7.59; Cl, 20.38.

Trans isomer: ir (CCl_4) 3050, 1740, 1630, 1230 cm^{-1}; nmr (CCl_4) δ 5.89 (br d, J = 7.5 Hz, 2 H), 2.4 (broad m, 1 H), 1.98 (s, 3 H), 1.75 (d, J = 1.5 Hz, 3 H), 1.08 (d, J = 7 Hz, 3 H); mass spectrum m/e (rel intensity) 141 (4) 118 (32), 116 (100).

Anal. Calcd for $C_8H_{13}O_2Cl$: C, 54.39; H, 7.41; Cl, 20.07. Found: C, 54.19; H, 7.48; Cl, 20.35.

Decomposition of 1-Chloro-4-diazo-2,3-dimethyl-1-pentene (1).—The decomposition of the diazopentane 1 by cuprous cyanide, cuprous chloride, tri-*n*-butylphosphinecopper(I) iodide, and photolysis was studied. In a typical experiment, 110 mg (1.2 mmol) cuprous cyanide was added to a solution of diazoalkane 1 [prepared from 84 mg (0.36 mmol) nitrosocarbamate 7 and 70 mg (1.8 mmol) lithium ethoxide] in 40 ml of ether cooled to −78°. After warming to −20° and stirring for 2 hr, the reaction mixture was analyzed by vpc. The only identifiable products were the diene mixture 8.

Decomposition of 1-Chloro-4-diazo-2,3-dimethyl-1-butene (2).—The previously described pentane solution of diazobutene 12 [prepared from 304 mg (1.38 mmol) nitrosocarbamate 11] was added over 0.5 hr dropwise from a temperature-controlled dropping funnel (cooled to −78°) to a solution of 420 mg (0.97 mmol) of mercuric iodide dissolved in 75 ml of dimethyl ether and cooled to −78°. The diazobutene solution was deaerated in the dropping funnel by the bubbling of nitrogen through the

(26) D. D. Perrin, W. L. F. Armarego, and D. R. Perrin, "Purification of Laboratory Chemicals," Pergamon Press, Oxford, 1966, p 170.

(27) C. S. Marvel and F. D. Hager, "Organic Syntheses," Collect. Vol. I, Wiley, New York, N. Y., 1941, p 248.

solution. After the solution stirred for 1.5 hr at −78°, an ir spectrum was taken of the now colorless solution; the absorption at 2060 cm^{-1} was absent.

After the solution was warmed to −20° and the dimethyl ether was allowed to distil from the reaction, the residue was filtered and concentrated by careful distillation under reduced pressure into a flask cooled to −78°. The distillate was concentrated in a similar manner (the residue flask was kept at or below −10°, and the combined residues were analyzed by gas chromatography (the residue solution was kept at the storage temperature of −20°). After initial separation of the complex mixture into two major fractions, the individual components were isolated and identified by preparative gas chromatography. The products isolated were as follows.

trans-1-Chloro-2,3-dimethyl-1,3-butadiene (**12a**, 12.7% rel yield): ir (CCl_4) 3130, 1630, 1375, 890 cm^{-1}; nmr (CCl_4) δ 5.86 (br s, 1 H), 5.09, 4.95 (br s, 2 H), 1.9 (complex m, 6 H); mass spectrum *m/e* (rel intensity) 118 (25), 116 (80), 81 (100). *Anal.* Calcd for C_6H_9Cl: 116.03927. Found: 116.03888.

cis-1-Chloro-2,3-dimethyl-1,3-butadiene (**12b**, 37.2%): ir (CCl_4) 3130, 1630, 1375, 890 cm^{-1}; nmr (CCl_4) δ 6.23 (br s, 1 H), 5.10, 4.98 (br s, 2 H), 1.9 (complex m, 6 H); mass spectrum *m/e* (rel intensity) 118 (24), 116 (64), 81 (100). *Anal.* Calcd for C_6H_9Cl: 116.03927. Found: 116.03915.

cis-1-Chloro-2-methyl-*cis*-1,3-pentadiene (**13a**, 22.6% total **14a** and **14b**): nmr (CCl_4) δ 5.97 (br s, 1 H), 5.8–5.2 (m, 2 H), 1.90 (finely coupled s, 3 H), 1.81 (d, J = 6 Hz, 3 H); mass spectrum *m/e* (rel intensity) 118 (16), 116 (46), 81 (100). *Anal.* Calcd for C_6H_9Cl: 116.03927. Found: 116.03840.

trans-1-Chloro-2-methyl-*cis*-1,3-pentadiene (**13b**): ir (CCl_4) 3080, 3030, 1600, 1440, 950, 850 cm^{-1}; nmr (CCl_4) δ 6.2–5.5 (complex m with br s at 5.92, 3 H), 1.85 (finely coupled s, 3 H), 1.79 (d, J = 5 Hz, 3 H); mass spectrum *m/e* (rel intensity) 118 (13), 116 (40), 81 (100). *Anal.* Calcd for C_6H_9Cl: 116.03927. Found: 116.03930.

1-Chloro-2-methyl-*trans*-1,3-pentadiene (**13c**): ir (CCl_4) 3080, 3030, 1630, 1440, 960, 850 cm^{-1}; nmr (CCl_4) δ 6.68 (d, J = 15 Hz, 1 H), 6.1–5.6 (m, 2 H), 1.8 (complex m, 6 H); mass spectrum *m/e* (rel intensity) 118 (15), 116 (45), 81 (100). *Anal.* Calcd for C_6H_9Cl: 116.03927. Found: 116.03915.

3-Chloro-1,4-dimethylcyclobutene (**14**): nmr (CCl_4) δ 5.76 (br s, 1 H), 4.22 (br s, 1 H), 2.9 (br m, 1 H), 1.72 (finely coupled s, 3 H), 1.19 (d, J = 7 Hz, 3 H); mass spectrum *m/e* (rel intensity) 118 (12), 116 (36), 81 (100). *Anal.* Calcd for C_6H_9Cl: 116.03927. Found: 116.03915.

The remaining products were identified as having arisen from reaction with solvent (methanol) and air during generation of the diazobutene.

4-Chloro-2,3-dimethyl-3-butenal (6.5%): ir (CCl_4) 2820, 2750, 1730, 1630 cm^{-1}; nmr (CCl_4) δ 9.61 (s, 1 H), 6.12 (br s, 1 H), 3.87 (q, J = 7 Hz, 1 H), 1.69 (finely coupled s, 3 H), 1.20 (d, J = 7 Hz, 3 H); mass spectrum *m/e* (rel intensity) 134 (1), 132 (4), 105 (13), 103 (40), 97 (52). *Anal.* Calcd for C_6H_9ClO: 132.03419. Found: 132.03065.

1-Chloro-2,3-dimethyl-4-methoxy-1-butene (8.1%): ir (CCl_4) 3050, 1630, 1120 cm^{-1}; nmr (CCl_4) δ 5.82 (br s, 1 H), 3.25 (s, 3 H), 2.2 (m, 3 H), 1.79 (finely coupled s, 3 H), 1.09 (d, J = 7 Hz, 3 H); mass spectrum *m/e* (rel intensity) 150 (1), 148 (4), 113 (3), 81 (9). *Anal.* Calcd for $C_7H_{13}ClO$: 148.06548. Found: 148.06533.

Four additional minor components (total 7.9%) were not identified. Nmr spectra of each indicated they were probably decomposition products.

Stirring an aliquot of the reaction mixture (prior to gas chromatography) for 0.5 hr with glacial acetic at room temperature, followed by vpc analysis, did not alter the chromatogram obtained with respect to the number or relative yields of the products present. Generation of the diazobutene in methanol followed by extraction into fluorotrichloromethane (Freon 11) allowed nmr analysis to be performed on the crude reaction mixture after reaction with mercuric iodide at −78° and warming to −25° to remove the dimethyl ether present. Only absorption due to allylic methyl groups (δ 1.7–2.0) was noted at −25°. An estimated limit of detection of bicyclobutane was 10%.

Photochemical Decomposition of Diazobutene 2.—A pentane solution (~0.1%) of the diazobutene **2**, prepared from the reaction of 36 mg (0.16 mmol) of nitrosocarbamate **11** with 90 mg (1.7 mmol) of lithium ethoxide, was deaerated with nitrogen in a Pyrex photolysis tube and cooled to −78°. The solution was photolyzed 1.5 hr at −78° (methanol heat exchanger and recirculating pump using Dry Ice as coolant) with a Hanovia 450-W high pressure mercury vapor lamp. The ir spectrum of the now colorless solution lacked absorption at 2060 cm^{-1}. Concentration of the solution (at −10° as described above) afforded a colorless solution which was analyzed by vpc.

In addition to a 48% relative yield of the 1,3-butadiene **12**, the major product of the reaction was found to be 1-chloro-2-cyclopropylpropene (**15**, 52%): ir (CCl_4) 3130, 3050, 920 cm^{-1}; nmr (CCl_4) δ 5.95, 5.80 (br s, 1 H), 1.9 (m, 1 H), 1.66 (d, J = 1.5 Hz, 3 H), 0.8–0.4 (m, 4 H); mass spectrum *m/e* (rel intensity) 118 (15), 116 (46), 81 (100). *Anal.* Calcd for C_6H_9Cl: 116.03927. Found: 116.04120.

The attempted triplet sensitized photolysis of the diazoalkane in pentane containing benzophenone and in 1:1 pentane–acetone gave identical product mixtures as did the direct photolysis above. It was found, however, that both acetone and benzophenone are insoluble in pentane at −78°.

Registry No.—**1**, 35147-19-4; **2**, 35191-78-7; **5**, 35140-52-4; **6**, 35140-53-5; **7**, 35191-79-8; **8** (1,3-diene), 35140-54-6; **8** (1,4-diene), 35191-80-1; **9**, 35140-55-7; **10**, 25234-83-7; **11**, 35191-81-2; **12a**, 35140-57-9; **12b**, 35140-58-0; **13a**, 35140-59-1; **13b**, 35140-60-4; **13c**, 35140-61-5; **14**, 35140-62-6; **15**, 5296-54-8; methyl 5-chloro-2,3,4-trimethyl-4-pentenoate, 35140-64-8; 5-chloro-2,3,4-trimethyl-4-pentenoic acid, 35140-65-9; 4-(1-chloro-2,3-dimethyl-1-pentenyl) formate, 35140-66-0, methyl 5-chloro-3,4-dimethyl-4-pentenoate, 35191-82-3; methyl *N*-4-(1-chloro-2,3-dimethyl-1-butenyl)carbamate, 35140-67-1; *cis*-4-acetoxy-1-chloro-2,3-dimethyl-1-butene, 35140-68-2; *trans*-4-acetoxy-1-chloro-2,3-dimethyl-1-butene, 35140-69-3; 4-chloro-2,3-dimethyl-3-butenal, 35140-70-6; 1-chloro-2,3-dimethyl-4-methoxy-1-butene, 35140-71-7.

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Synthesis and Reactions of Some Highly Chlorinated Azobenzenes

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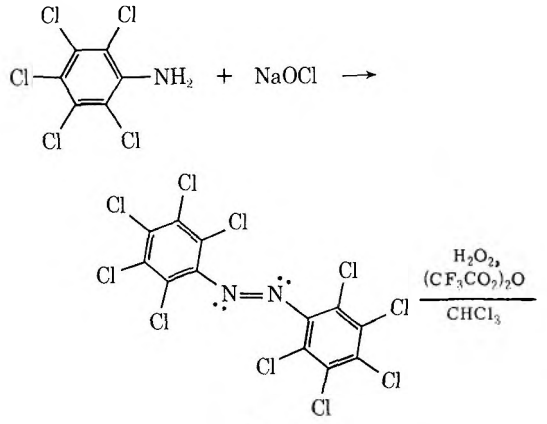
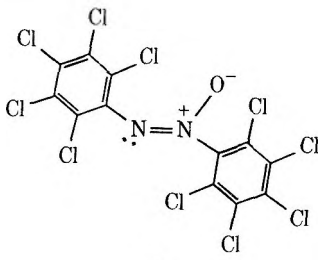
Decachloroazobenzene (1) was synthesized in 56% yield directly from pentachloroaniline. 1 was oxidized to decachloroazoxybenzene (2) in 97% yield and also reduced to pentachloroaniline along with minor amounts of decachlorohydrazobenzene. A series of pentachloroazo- and -azoxybenzenes were also prepared and their nmr spectra determined. The nmr spectra of a series of pentadeuterioazo- and -azoxybenzenes indicated that in the pentachloroazoxy series the α isomer had been formed exclusively. This was confirmed by mass spectroscopy.

Decachloroazobenzene (1) was first prepared in 1922 by refluxing heptachloroaniline in toluene.[2] More recently 1 was synthesized *via* oxidation of pentachloroaniline,[3] but yields were not given in either case. We now report the preparation of 1 in 56% yield by the reaction of pentachloroaniline with 5% aqueous sodium hypochlorite. This reaction appears to have some degree of generality at least when applied to highly halogenated aromatic amines.[4]



1



2

As expected, 1 is more sterically crowded than its fluoro analog. This was confirmed by their uv spectra, in which the extinction coefficient of decafluoroazobenzene was calculated as ϵ 20,000 (λ_{max}^{EtOH} 308 nm),[4] while that of 1 was only 8600 (301). Decafluoroazobenzene was first reported[4] to be inert toward a number of peracids; however, we readily obtained a 97% yield of decachloroazoxybenzene (2) by refluxing 1 in a mixture of trifluoroacetic anhydride, 98% hydrogen peroxide, and chloroform.[5,6] Peracetic and performic acids had no effect on 1.

Exhaustive catalytic hydrogenation of both 1 and 2 gave pentachloroaniline. When the hydrogenation of 1 was stopped before completion, decachlorohydrazobenzene (3) was obtained, but was always contaminated with amine. This suggests that the reductions of 1 and 3 do not have widely different rates, a marked contrast with highly fluorinated analogs, which gave pure hydrazobenzenes from this reaction.[4] The reduction of 2 to 1 was never accomplished under these conditions. However, 3 did disproportionate on heating to give 1 and pentachloroaniline, although at a higher temperature than was necessary in the analogous reaction of hydrazobenzene.

Performic acid oxidation of pentachloroaniline gave pentachloronitrosobenzene[7] (4), in 30% conversion (~100% yield). This enabled a series of stable reddish orange pentachloroazobenzenes (Table I) to be prepared by the condensation of 4 with aniline, and four para-substituted anilines, in glacial acetic acid. Similar condensations could not be achieved with pentachloro- or pentafluoroaniline.

The 2,3,4,5,6-pentachloroazobenzenes were oxidized rapidly and almost quantitatively to their corresponding pale yellow azoxy derivatives by peroxytrifluoroacetic acid (Table I). Oxidation of these azobenzenes using the more common peracids (acetic, benzoic, etc.) was difficult and incomplete even after several days of reflux.

In addition to cis–trans isomerism[8] unsymmetrically substituted azoxy compounds, such as those in Table I, may also exist in two other isomeric forms, often designated α and β, depending on the position of the oxygen in the azoxy group.[9] The nmr spectra (Table II) of the para-substituted azo- and azoxybenzenes exhibited simple A_2B_2 quartets which indicated that only one of these isomers had been obtained. The ortho protons of the azoxybenzenes were shifted downfield, com-

(1) Allied Chemical Corp. Research Fellow, 1963–1966.

(2) S. Goldschmidt and L. Strohmenger, *Ber.*, **55**, 2450 (1922).

(3) M. Hedayatullah, C. Ollé, and L. Denivelle, *C. R. Acad. Sci., Paris, Ser. C.*, **264**, 106 (1967).

(4) J. Burdon, C. J. Morton, and D. F. Thomas, *J. Chem. Soc.*, 2621 (1965).

(5) Under the proper conditions decafluoroazobenzene can also be oxidized with these reagents: J. M. Birchall, R. N. Haszeldine, and J. E. Kemp, *J. Chem. Soc. C*, 1519 (1970).

(6) Hedayatullah reported[3] that 1 was unreactive with trifluoroperacetic acid at 75°.

(7) D. Berry, I. Collins, S. Roberts, H. Suschitzky, and B. Wakefield, *J. Chem. Soc. C*, 1285 (1969).

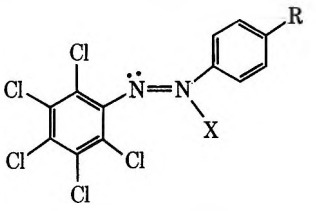
(8) All of our azo and azoxy compounds were assumed to exist in the more stable trans configuration. Their mode of preparation makes this a reasonable assumption: H. Zollinger "Azo and Diazo Chemistry Aliphatic and Aromatic Compounds," Interscience Publishers, Inc., New York, N. Y., 1961, pp 59, 267.

(9) Although the α and β designations can be confusing, they are used in this paper to simplify the discussion. The α isomer has been defined as the one with the N–O function adjacent to the smaller or less highly substituted aryl group.[10] Consequently, in this paper the α-azoxy isomer (where R = Br) will be the one named 4′-bromo-2,3,4,5,6-pentachloro-*ONN*-azoxybenzene.

(10) G. G. Spence, E. C. Taylor, and O. Buchardt, *Chem. Rev.*, **70**, 231 (1970).

TABLE I

2,3,4,5,6-PENTACHLOROAZO- AND -AZOXYBENZENES[a]

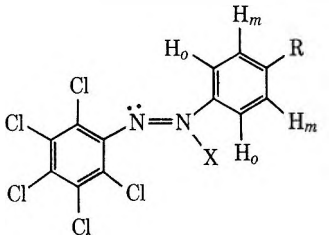


R	X	Mp, °C	% yield	% calcd C	% calcd H	% calcd Cl	% found C	% found H	% found Cl
H		117–118	85	40.64	1.41	50.09	40.93	1.58	50.20
H	O	148–150	>95	38.88	1.35	47.88	38.52	1.19	47.07
Br		179–181	40	33.23	0.92	6.46[c]	32.99	0.82	6.34[c]
Br	O	192–193	>95	32.05	0.89	6.24[c]	31.92	1.00	6.34[c]
CH_3		234–237	41	42.35	1.90	48.14	42.06	2.17	48.64
CH_3	O	159–161	>95	40.59	1.82	46.13	40.58	1.89	46.25
Cl		168–170	53	37.03	1.03	54.73	36.84	1.19	55.13
Cl	O	169–171	>95	35.37	0.98	52.56	35.25	0.99	51.98
OCH_3		136–138	35	40.59	1.82	46.13	40.83	1.49	45.80
OCH_3	O	158–159	>95	38.97	1.75	44.29	38.74	2.03	44.03

[a] We define the azoxybenzenes in this table as the α isomers. [b] Registry numbers are, respectively, 35159-10-5, 35159-11-6, 35191-76-5, 35159-12-7, 35159-13-8, 35159-14-9, 35159-15-0, 35159-16-1, 35159-17-2, 35159-18-3. [c] % N was analyzed for in this compound instead of % Cl.

TABLE II

NMR SPECTRAL DATA FOR THE 2,3,4,5,6-PENTACHLOROAZO- AND -AZOXYBENZENES IN $CDCl_3$



R	X	Chemical shift,[a] Hz H_o	H_m	H_{CH_3}	$J(H_o-H_m)$,	$\Delta_{azoxy-azo}$ H_o	$\Delta_{azoxy-azo}$ H_m
H		478[b]	454[b]			22	2
H	O	500[b]	456[b]				
Cl		476	453			20	−2
Cl	O	496	451		9		
Br		469	463		9	22	−2
Br	O	491	461		9		
OCH_3		477	422	233[c]	9	21	−3
OCH_3	O	498	419	233[d]	9		
CH_3		474	443	148[e]	8.5	20	0
CH_3	O	494	443	148[f]	8.5		

[a] The chemical shifts were found to be relatively insensitive to concentration. [b] Values given are the approximate centers of complex multiplets. [c] This singlet appears at 200 Hz in benzene. [d] This singlet appears at 195 Hz in benzene. [e] This singlet appears at 127 Hz in benzene. [f] This singlet appears at 122 Hz in benzene.

pared with the corresponding azobenzenes, by a constant 21 ± 1 Hz.

Surprisingly few methods existed at the beginning of this work for distinguishing between α and β isomers.[11] Consequently, model azo- and azoxybenzenes, which had one completely deuterated phenyl ring, were synthesized for further nmr studies. The α- and β-azoxy isomers were then separated by column chromatography and identified by comparison of their melting points (Table III) with those of the known hydrogen analogs.[12]

Nmr spectral data for these deuterated compounds are also given in Table III. Once again the ortho hydrogens of the α-azoxybenzenes were shifted downfield by 21 ± 1 Hz, while the corresponding deshielding in the β-azoxybenzenes varied from 16 to 24 Hz. In addition, the methyl protons of the β-azoxybenzene were shifted by a slightly larger amount than the methyl protons of the α-azoxybenzene.[13]

We had hoped that these differences in the nmr spectra of the α- and β-azoxy isomers would be somewhat larger and more definitive; fortunately, however, mass spectroscopy provided complete confirmation of the assignments. The pertinent mass spectral data for the pentachloroazoxybenzenes is given in Table IV. It is known that the base peaks in the mass spectra of azoxybenzenes are produced by C–N cleavage α to the *N*-oxide group.[14] As is evident from Table IV, the base ion[15] ($C_6H_4R\cdot^+$) in every spectra resulted from the type of fragmentation expected for the α isomer.

In addition, while no $(M - Cl)\cdot^+$ ions were observed in the mass spectra of the pentachloroazobenzenes, with only one exception, this ion was the second most abundant peak in the spectra of the corresponding azoxy compounds (Table IV). It has been established that the formation of five-membered cyclic structures involving the oxygen of the N–O group is an important rearrangement in the mass spectra

(11) (a) G. M. Badger and G. E. Lewis, *J. Chem. Soc.*, 2151 (1953); (b) L. C. Behr, *J. Amer. Chem. Soc.*, **76**, 3672 (1954), and references therein; (c) L. C. Behr, E. G. Alley, and O. Levand, *J. Org. Chem.*, **27**, 65 (1962).

(12) Assignments were also confirmed by mass spectroscopy.

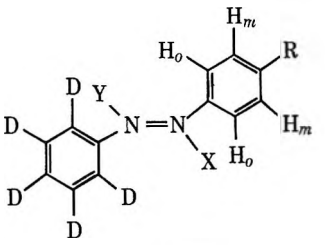
(13) The methyl and methoxy protons of the *α-azoxybenzenes* are apparently shifted upfield more from their corresponding azobenzenes when benzene is used as the solvent for determining the nmr spectra. For examples see footnotes *c–f* in Table II and D. Webb and H. Jaffé. *J. Amer. Chem. Soc.*, **86**, 2419 (1964).

(14) J. H. Bowie, R. G. Cooks, and G. E. Lewis, *Aust. J. Chem.*, **20**, 1601 (1967).

(15) Additional facile fragmentations due to the presence of the *p*-methoxy group led to other ions, such as $C_8H_4O\cdot^+$, which were observed in greater abundance in the mass spectra of this compound. For simplicity these low *m/e* ions were ignored in preparing Table IV.

Table III

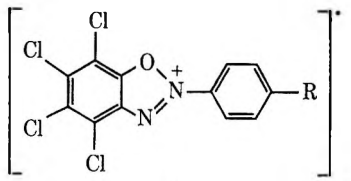
Melting Points and Nmr Spectral Data for the Pentadeuterioazo- and -azoxybenzenes in CCl_4



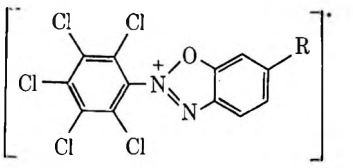
				Chemical shift, Hz				$\Delta_{azoxy-azo}$	
R	X	Y	Mp, °C[b]	H_o	H_m	H_{CH_3}	$J(H_o-H_m)$, Hz	H_o	H_m
CH_3			68–70 (71–72)[c]	469	433	143	8.5		
OCH_3			55–55.5 (54–56)[c]	472[d]	417[d]	229[d]	9.0		
Br			88–89.5 (89)[c]	467	458		9.0		
CH_3	O		64.5–66 (65)[e]	489	430	139	8.5	20	−3
OCH_3	O		50–51.5 (42–43)[e]	494[d]	414	232[d]	9.0	22	−3
Br	O		91.5–93 (92–92.5)[e]	489	452		9.0	22	−6
CH_3		O	45–47 (46–48)[e]	489	428	137	8.5	20	−5
OCH_3		O	74–75 (66.5–67.5)[e]	496[d]	415[d]	232[d]	9.0	24	−2
Br		O	71–72 (73–73.5)[e]	483	451		9.0	16	−7

[a] Registry numbers, are, respectively, 35159-19-4, 35261-92-8, 35159-20-7, 35159-21-8, 35159-22-9, 35159-23-0, 35159-24-1, 35159-25-2, 35159-26-3, 35159-27-4, 35159-28-5. [b] Melting points of the corresponding nondeuterated azo- and -azoxybenzenes are given in parentheses. [c] "Dictionary of Organic Compounds," J. R. A. Pollack and R. Stevens, Ltd., Oxford University Press, New York, N. Y., 1965: Vol. 1, p 419; Vol. 3, p 1647; Vol 5, pp 2130 and 2429. [d] The chemical shift is dependent somewhat on concentration, and the value given is that calculated for infinite dilution. The remaining chemical shifts are relatively insensitive to concentration. [e] H. Jaffé and C. S. Hahn, *J. Amer. Chem. Soc.*, **84**, 949 (1962).

of azoxybenzenes.[14,16] With the α isomer this rearrangement leads to an (M − Cl) ion such as **5** while the β isomer would yield an (M − H) ion such as **6**.



5



6

These two major mass spectral arguments, together with nmr and the remaining mass spectroscopy data, leave little doubt that only the α isomers of the pentachloroazoxybenzenes were formed.

Experimental Section[18]

Decachloroazobenzene (1).—To a magnetically stirred slurry of 5 g of pentachloroaniline in 100 ml of 95% ethanol, 400 ml of 5% aqueous sodium hypochlorite was added. The heterogeneous mixture turned yellow immediately after addition. After 3 hr of stirring at room temperature, the reaction mixture turned red and tended to coagulate. Stirring was continued for a further 10 hr. Then the mixture was filtered and the red solid washed with water and crystallized from toluene to give 2.8 g (56%) of dimorphic crystals of decachloroazobenzene: mp 314–316° (lit.[2] mp 316–318°); uv max (dioxane) 233 nm (ϵ 30,800), 301 (8600), 270 (sh, 10,800); ir (mull) 6.60 (w), 7.38 (s), 7.58 (m), 8.16 (w), 13.18 (m), 13.55 (s), 13.68 (s), 14.22 μ (s).

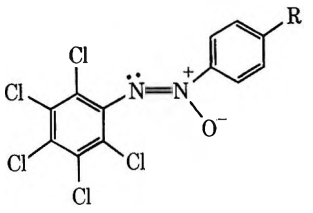
Anal. Calcd for $C_{12}Cl_{10}N_2$: C, 27.38; Cl, 67.33. Found: C, 27.43; Cl, 67.00.

Decachloroazoxybenzene (2).—To a stirred mixture of 1.0 g (1.9 mmol) of 1, 15 ml of trifluoroacetic anhydride, and 100 ml of chloroform, 6 ml of 98% hydrogen peroxide (Columbia Organic Chemicals Co.) was added rapidly. After refluxing for 5 hr, the solvent was evaporated to give 1.0 g (97% yield) of 2 which recrystallized from chloroform–hexane as shiny, yellow flakes: mp 257–258°; uv max (dioxane) 231 nm (ϵ 33,000), 302 (3700); ir (mull) 6.60 (s), 6.88 (s), 7.45 (s), 7.68 (m), 8.18 (w), 12.98 (m), 13.10 (m), 13.95 (br s), 14.15 (s), 14.82 μ (w).

Anal. Calcd for $C_{12}Cl_{10}N_2O$: C, 26.54; Cl, 65.35. Found: C, 26.16; Cl, 65.53.

Table IV

Mass Spectra[a] of the 2,3,4,5,6-Pentachloroazoxybenzenes



	R				
Ion	H	^{79}Br	CH_3	^{35}Cl	OCH_3
M·+	368 (4.0)	446 (6.8)	382 (2.1)	402 (3.5)	398 (2.7)
M − Cl	333 (82)	411 (32)	347 (33)	367 (74)	363 (7.3)
M − N_2Cl_2	270 (56)	348[b]	284 (28)	304 (38)	300 (9.1)
C_6Cl_5	247 (3.2)	247 (28)	247 (4.8)	247 (4.0)	247 (31)
C_6Cl_4N	226 (22)	226 (29)	226 (13)	226 (29)	226 (63)
ONC_6H_4R	107 (8.6)	185 (9.4)	121 (19)	141 (8)	137 (45)
C_6H_4R	77 (100)	155 (100)	91 (100)	111 (100)	107 (100)[c]

[a] Spectral data is given as *m/e* (% of base ion). [b] This particular ion appeared at very low abundance; however, this compound had a very prevalent (M − N_2BrCl) ion at *m/e* 304 (32). [c] See ref 15.

(16) Azoxybenzenes have been reported to form similar cyclic structures under other conditions.[10,17]

(17) A. I. Feinstein and E. K. Fields, *J. Org. Chem.*, **36**, 3878 (1971).

(18) All melting points are uncorrected. Elemental analysis were determined by Dr. C. S. Yeh, Purdue University. Ir spectra were obtained on a Beckman IR-8 spectrophotometer. Uv spectra were obtained on a Bausch and Lomb Spectronic 505 spectrophotometer. Nmr spectra were measured using a Varian A-60 spectrometer, with tetramethylsilane as an internal standard. Mass spectra were recorded on a Hitachi Perkin-Elmer RMU-6A high resolution mass spectrometer.

Reduction of 1.—Stirred together in 100 ml of toluene and in an atmosphere of hydrogen was 0.3 g (0.6 mmol) of **1** and 0.7 g of 5% palladium on charcoal. After only 18.2 ml (0.81 mmol) of H_2 had been taken up, the reaction was stopped, the mixture was filtered, and the filtrate was evaporated to an orange mass which was chromatographed on acid-washed alumina. Three bands were eluted with toluene which were, in order of elution, **1** (trace); 0.1 g of decachlorohydrazobenzene (**3**); and 0.15 g of pentachloroaniline. **3** recrystallized from toluene as light yellow needles which darkened to a copper color at 150° and at 195° began to disproportionate to pentachloroaniline (identified by ir and melting point) and to a red liquid (**1**). Spectral data for **3**: ir (mull) 2.92 (w), 6.28 (m), 7.08 (m), 7.28 (w), 7.45 (br m), 7.58 (m), 13.16 (br), 13.60 μ (br, w).

Anal. Calcd for $C_{12}H_2Cl_{10}N_2$: C, 27.23; H, 0.38. Found: C, 27.13; H, 0.19.

Reduction of 2.—A solution of 0.5 g (0.9 mmol) of **2** dissolved in 80 ml of benzene and 40 ml of toluene was stirred with 1 g of 5% palladium on charcoal in an atmosphere of H_2. Hydrogen uptake was very slow and, after 26 hr, the reaction was worked up as described above to yield 0.45 g of a white solid, melting between 160 and 240° and containing only a small amount of **3**. The solid was mainly pentachloroaniline as determined by ir spectroscopy.

Pentachloronitrosobenzene (4).—A two-phase liquid system containing 5.0 g (19 mmol) of pentachloroaniline, 20 ml of 90% formic acid, 100 ml of chloroform, and 5 ml of 98% hydrogen peroxide was stirred under reflux for 6 hr. After the deep green mixture cooled, white granular crystals settled and were collected. The green filtrate was washed with water, dried, and evaporated to yield 3.4 g of crude pentachloroaniline. The filtered crystals, after recrystallization from toluene, afforded 1.5 g (30% conversion) of **4**: mp 168–170°; ir (mull) 6.70 (w), 7.41 (s), 7.75 (s), 8.19 (m), 8.85 (w), 10.40 (w), 12.60 (w), 13.92 μ (s).

Anal. Calcd for C_6Cl_5NO: C, 25.78; Cl, 63.48. Found: C, 26.09; Cl, 63.57.

A. Typical Condensation of 4 with an Amine.—A solution of 1.0 g (3.6 mmol) of **4**, 0.64 g (5.0 mmol) of 4-chloroaniline, and 70 ml of glacial acetic acid was refluxed for 3 hr. Water was added to the reaction mixture and the precipitated solid was collected *via* suction filtration. Elution of this material with benzene on a column (1 × 22 in.) of acid-washed alumina (110 g) produced 0.74 g (53%) of 2,3,4,4′,5,6-hexachloroazobenzene and 0.25 g (25%) of pentachloroaniline. The product was recrystallized from ethanol: mp 168–170°; uv max (EtOH) 212 nm (ϵ 31,300), 226 (sh, 23,000), 307 nm (14,300); ir (mull) 6.35 (w), 6.73 (m), 7.13 (m), 7.44 (s), 7.61 (m), 8.71 (m), 9.11 (m), 9.90 (m), 11.30 (m), 12.00 (s), 13.72 (m), 13.85 (m), 13.92 μ (s).

An Improved Condensation of 4 with Aniline.—Aniline (0.5 g, 5 mmol) was added rapidly to a solution of 1.0 g (3.6 mmol) of **4** and 50 ml of toluene–acetic acid solution (4% glacial acetic acid in toluene) maintained at 40°. After 18 hr the reaction temperature was increased slowly to 75° over an additional 12-hr period. Evaporation of the solvent gave a red solid, which was chromatographed twice (acid-washed alumina, benzene). Obtained was 1.08 g (85%) of 2,3,4,5,6-pentachloroazobenzene: mp 117–118°; uv max (EtOH) 215 nm (ϵ 24,000), 229 (23,000), 293 (12,600); ir (mull) 3.28 (w), 6.71 (m), 7.44 (s), 7.65 (m), 8.15 (m), 8.70 (s), 11.28 (m), 12.88 (m), 13.10 (s), 13.78 (m), 13.95 (m), 14.72 (s), 15.05 μ (vr).

A Typical Oxidation of the 2,3,4,5,6-Pentachloroazobenzenes.—A two-phase liquid system of 0.3 g (0.85 mmol) of 2,3,4,5,6-pentachloroazobenzene, 3 ml of trifluoroacetie anhydride, 2 ml of 98% hydrogen peroxide, and 20 ml of $CHCl_3$ was stirred at reflux for 2 hr. The red solution faded to a light yellow almost immediately. On cooling, the mixture was washed with water; the organic layer separated and was evaporated to give 0.3 g (96% yield) of crude 2,3,4,5,6-pentachloroazoxybenzene. The product was recrystallized three times from hexane as fine, yellow needles: mp 148–150°; uv max (EtOH) 214 nm (ϵ 50,000), 260 (11,900); ir (mull) 6.99 (s), 7.43 (s), 12.92 (s), 13.85 (s), 14.90 μ (s).

Pentadeuterioazo- and -azoxybenzenes.—Pentadeuteronitrosobenzene (obtained from Merck Sharp and Dohme of Canada Ltd.) was condensed with the appropriately substituted aniline in acetic acid–benzene solution. The resulting pentadeuterioazobenzenes were oxidized in chloroform with peracetic acid solution, prepared from glacial acetic acid and 98% hydrogen peroxide. The α and β isomers of each azoxy mixture were partially resolved by elution chromatography on alumina and brought to constant melting point by repeated recrystallizations (methanol) of the initial and final chromatographic fractions.

Registry No.—**1**, 35159-27-4; **2**, 35159-28-5; **3**, 35191-77-6; **4**, 13665-49-1; pentachloroaniline, 527-20-8.

Acknowledgment.—The authors are indebted to the Allied Chemical Corp. for financial support of the work and to R. G. Cooks for his assistance with the mass spectra interpretation.

Studies on 4-Quinazolinones. V.[1] Reductive Ring Cleavage by Metal Hydrides

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Metal hydride reductions of some substituted 4-quinazolinones have been studied under various conditions. Though the reduction was found to be facile in the *N*-methylated compounds under ordinary conditions irrespective of the substitution at position 2, the C=N function in those with a free NH group proved to be extremely resistant to the reducing agents and led to unusual products under forcing condition. 2,3-Disubstituted 4-quinazolinones and only the 3-phenyl derivative among the monosubstituted ones studied underwent ring cleavage at the bond between C_2 and the tertiary nitrogen. Reduction of the carbonyl group could only be brought about by lithium aluminum hydride in tetrahydrofuran under reflux in all cases.

While the carbonyl function of indoloquinazolinones is known[3] to be fully reduced by lithium aluminum hydride at room temperature, 1-methyl-2-benzyl-4-quinazolinone (**1**), a naturally occurring alkaloid[4] known as arborine, under the same condition afforded[5] only its 2,3-dihydro derivative **2**. We therefore investigated the metal hydride reduction of a series of variously substituted simple 4-quinazolinones under different conditions, and the results are summarized in Scheme I.

The reduction of 2-benzyl-3-methyl-4-quinazolinone (**3a**) with the same reagent at room temperature re-

(1) Paper IV: S. C. Pakrashi, J. Bhattacharyya, and A. K. Chakravarty, *Indian J. Chem.*, **9**, 1220 (1971).

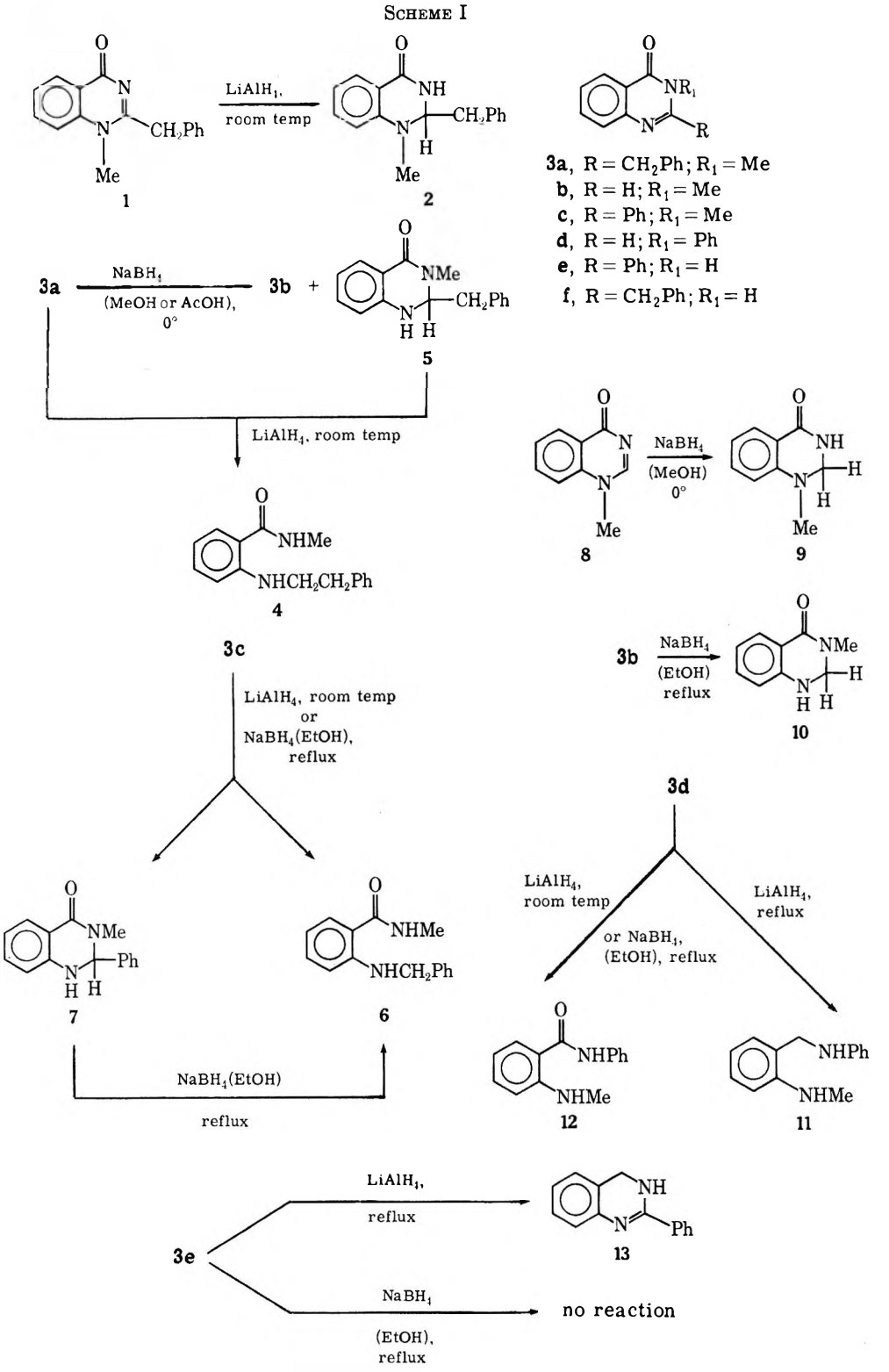
(2) Senior Research Fellow, CSIR, New Delhi.

(3) I. J. Pachter, R. F. Raffauf, C. E. Ullyot, and O. Ribeiro, *J. Amer. Chem. Soc.*, **82**, 5187 (1960).

(4) D. Chakravarti, R. N. Chakravarti, and S. C. Chakravarti, *J. Chem. Soc.*, 3337 (1953).

(5) A. Chatterjee and S. Ghosh Mazumdar, *J. Amer. Chem. Soc.*, **76**, 2459 (1954).

SCHEME I



sulted in the fission of the 2,3 bond with retention of the carbonyl function leading to *o*-(β-phenylethylamino)-*N*-methylbenzamide (**4**) in 55% yield. The same compound was, however, obtained with the same reagent in better yield in a shorter period from the 1,2-dihydro derivative **5** prepared by catalytic hydrogenation of **3a**. The structure of **4** was ascertained from its ir and nmr spectra and confirmed by its synthesis from *o*-amino-*N*-methylbenzamide and β-phenylethyl chloride in the presence of potassium carbonate.

The sodium borohydride reduction of **3a** in methanol at 0°, however, provided an interesting case of C_2-debenzylation leading to 3-methyl-4-quinazolinone (**3b**) in 15% yield. The mechanism of this unusual reaction has already been suggested by us[6] and recently corroborated by Finch and Gschwend.[7]

2-Phenyl-3-methyl-4-quinazolinone (**3c**) on lithium aluminum hydride reduction at room temperature afforded both 2,3-bond cleaved product, *viz.*, *o*-benzylamino-*N*-methylbenzamide (**6**, 60%), and the 1,2-dihydro derivative (**7**, 4%). The structure **6** was confirmed by its synthesis.

(6) S. C. Pakrashi and A. K. Chakravarty, *Chem. Commun.*, 1443 (1969).
(7) N. Finch and H. W. Gschwend, *J. Org. Chem.*, **36**, 1463 (1971).

On the other hand, the reduction of **3c** with sodium borohydride in ethanol under reflux afforded both **6** and **7** in 44 and 54% respective yields. The higher yield of compound **6** was, however, obtained when the dihydro derivative **7** itself was treated with sodium borohydride.

It was therefore apparent that the reduction with both the metal hydrides must involve similar mechanisms and that the ring cleavage proceeds *via* the intermediacy of the dihydro derivatives.

The reduction of 1-methyl-4-quinazolinone (**8**) and 3-methyl-4-quinazolinone (**3b**) with lithium aluminum hydride under reflux has been reported[8] to yield the corresponding 1,2,3,4-tetrahydroquinazolines. Sodium borohydride reduction, however, afforded the respective dihydro derivatives (**9** and **10**) even on refluxing in ethanol in the case of **3b**.

3-Phenyl-4-quinazolinone (**3d**) has recently been reported[9] to yield *o*-methylamino-*N*-phenylbenzylamine (**11**) by lithium aluminum hydride treatment under unspecified conditions. In our hands, it suffered very facile reductive cleavage of the 2,3 bond by the same reagent at room temperature, forming *o*-methylaminobenzanilide (**12**) in quantitative yield. Under refluxing condition, **11** was indeed obtained as the major product. Sodium borohydride reduction of **3d** in ethanol under reflux also afforded **12** in *ca.* 70% yield. Thus, we could also confirm the facile reductive ring cleavage of 3-aryl-4-quinazolinones reported by other workers.[9,10]

The results of metal hydride reduction of 4-quinazolinones with no substituent at either of the nitrogen atoms proved to be more interesting. Thus, while 2-phenyl-4-quinazolinone (**3e**) remained unaffected with sodium borohydride, lithium aluminum hydride under reflux led to the reduction of the carbonyl function to give 2-phenyl-3,4-dihydroquinazoline (**13**) in 46% yield rather than effecting ring rupture or reduction of 1,2 double bond. The structure **13** was supported by the nmr signals at δ 4.72 for a CH_2, at δ 5.67 (exchangeable with deuterium) for a NH, and a multiplet at δ 6.75–7.90 for nine aromatic protons and the disappearance of the ir bands at 1665 and 1680 cm^{-1}.

On the other hand, it has already been shown[1] by us that 4-quinazolinone itself and its 2-benzyl derivative (**3f**) remained unaffected under conditions in which 2-benzyl-3-methyl-4-quinazolinone (**3a**) readily yielded its 1,2-dihydro derivative **5** and the ring-cleaved product **4**, while under reflux with lithium aluminum hydride in tetrahydrofuran **3f** underwent an abnormal oxidation at the benzylic methylene group.

It is thus apparent from the foregoing data that, while its reduction was facile in *N*-methylated 4-quinazolinones, with or without substituents at position 2, C=N was extremely resistant to reducing agents in those with free NH. It therefore appeared likely that the reduction to dihydro derivative proceeds *via* a quinazolinium cation[11,12] (Scheme II) in analogy[13,14] to the reduction of *N*-alkylpyridinium salts by metal hydride to 1,2-dihydropyridines. In any case, however, the carbonyl group at position 4 could be reduced only by lithium aluminum hydride treatment under forcing conditions with or without concomitant cleavage of the hetero ring, depending on the substitution pattern. Thus, our results show that, with the exception of 3-phenyl compound **3d**, the other monosubstituted 4-quinazolinones (**3b**, **8**, or **3e**) did not suffer ring rupture, contrary to the claim by Gelling, *et al.*,[9] for the compound **3e**. On the other hand, the reductive cleavage of 2,3-disubstituted and 3-phenyl derivatives occurred at the bond between C_2 and the tertiary nitrogen atom. A similar observation was made by Larizza, *et al.*,[15] with secondary tertiary diamines.

Though the mechanism has already been suggested,[9] using different metal hydrides and by variation of reaction conditions, we could clearly show that the ring rupture (retaining the carbonyl function) of 2,3-disubstituted 4-quinazolinones requires the intermediacy of the dihydro derivative[16] by either lithium aluminum hydride at room temperature or sodium borohydride in ethanol under reflux. Nevertheless, the reason for difference in ring opening between mono- or disubstituted or 2-phenyl substituted derivatives is not clear. However, primary reduction of C=N and adequate stabilization of the anion at N-3, apparently necessary for the cleavage of the 2,3 bond of 2,3-disubstituted 4-quinazolinones, would also explain why only 3-phenyl-4-quinazolinone (**3d**) among the monosubstituted derivatives studied undergoes facile cleavage.

On the other hand, the formation of quinazolinium cation being not favored in compounds with a free NH group, the preferred site for hydride attack would be the amide carbonyl function leading to 3,4-dihydroquinazoline derivatives.

Experimental Section[17]

General Procedure for Lithium Aluminum Hydride Reductions.—Unless otherwise mentioned, solutions of 4-quinazolinones in dry and freshly distilled tetrahydrofuran (100 ml/g of quinazolinone) were added dropwise to a magnetically stirred slurry of powdered lithium aluminum hydride in the same solvent (100 ml/g of hydride). The reaction mixture was then stirred at room temperature or refluxed, as the case may be, for a specified period. The complex was decomposed with water and worked up in the usual way.

Reduction of 2-Benzyl-3-methyl-4-quinazolinone (3a). A. With Lithium Aluminum Hydride.—The compound **3a** (0.25 g) was treated with lithium aluminum hydride (0.5 g) at room temperature for 3 hr. The oily product (0.25 g) was chromatographed. The fractions eluted with benzene (200 ml) on crystallization yielded *o*-(β-phenylethylamino)-*N*-methylbenz-

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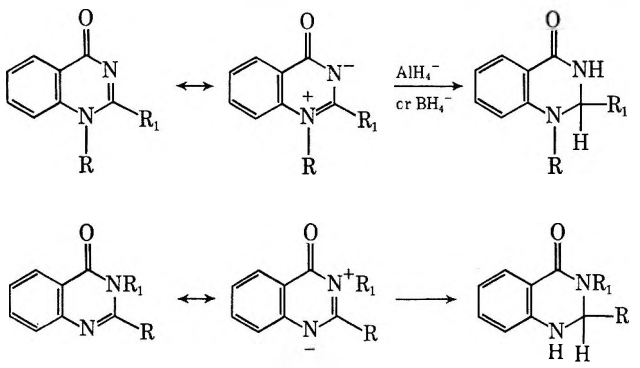
(16) The intermediacy of the dihydro derivative was also shown by Okumura, *et al.*,[10] who observed that the reductive cleavage of the 2,3 bond of 2-methyl-3-phenyl-4-quinazolinone by sodium borohydride is more facile in its 1,2-dihydro form.

(17) All melting points were recorded in open capillaries and are uncorrected. Silica gel was employed throughout for column chromatography and benzene–petroleum ether (bp 60–80°) was mostly used for crystallization. The nmr spectra were recorded on a 60-MHz Varian instrument in $CDCl_3$ and the chemical shifts are expressed in parts per million from TMS as internal standard. The infrared spectra were determined in Nujol mull on a Perkin-Elmer Infracord Model 137. The homogeneity of the compounds was ascertained by tlc on 0.3-mm silica gel G plates using chloroform–ethyl acetate–formic acid (5:4:1) and benzene–ethyl acetate–petroleum ether (5:3:2) as the solvent systems. The spots were located by exposing the dried plates to iodine vapor. Unless otherwise stated, the products were identified by direct comparison with authentic specimens.

SCHEME II



amide (4) as long needles (0.14 g, 55%): mp 113°; ir 3330 (NH), 1645, and 1635 cm^{-1} (C=O); nmr δ 2.9 (d, 3, $-NHCH_3$, J = 5 Hz), 2.93 and 3.38 (m, 2 H each, $-CH_2CH_2-$), 6.13 (br, 1, $-NHCH_2-$), 6.4–7.45 (m, 9, ArH).

Anal. Calcd for $C_{16}H_{18}N_2O$: C, 75.56; H, 7.14; N, 11.03. Found: C, 75.55; H, 7.20; N, 11.06.

Hydrogenation of 3a to 5.—The compound **3a** (0.2 g) in absolute alcohol (15 ml) was stirred in an atmosphere of hydrogen in the presence of Pd/C (10%) for 15 hr. The oily product on crystallization afforded 1,2-dihydro-2-benzyl-3-methyl-4-quinazolinone (5, 0.13 g), mp 140–141° in 65% yield: ir 3265 (NH), 1630 (C=O), 1610 cm^{-1}; nmr δ 2.98 (d, 2, $-CHCH_2-$, J = 7 Hz), 3.08 (s, 3, NCH_3), 4.63 (t, 1, $-CHCH_2-$, J = 7 Hz), 4.42 (br, 1, -NH), 7.87 (dd, 1, C_5 H, J = 8, 2 Hz), 6.4–7.4 (m, 8, ArH).

Anal. Calcd for $C_{16}H_{16}N_2O$: C, 76.16; H, 6.40; N, 11.12. Found: C, 76.41; H, 6.65; N, 11.03.

Lithium Aluminum Hydride Reduction of 5 to 4.—The dihydro derivative 5 (75 mg) was reduced with lithium aluminum hydride (0.15 g) at room temperature for 0.5 hr. The oily product on crystallization afforded 4 in 73% yield.

Preparation of *o*-(β-Phenylethylamino)-*N*-methylbenzamide (4).—*o*-Amino-*N*-methylbenzamide (0.75 g) was refluxed with β-phenyl ethyl chloride (1.5 ml) in 5% aqueous alcoholic potassium carbonate (20 ml) for 16 hr. The reaction mixture was cooled, diluted with water (50 ml), and extracted with chloroform. The chloroform extract was evaporated and the residue was taken up in ether (20 ml) and extracted with 2 *N* HCl (4 × 30 ml). The acid extract was basified (Na_2CO_3) and again extracted with chloroform. The crude product could not be induced to crystallize and purification by chromatography over silica gel yielded 4 (0.15 g, 12%), mp 112–113°, besides the starting material.

Reduction of 2-Phenyl-3-methyl-4-quinazolinone (3c). A. With Lithium Aluminum Hydride.—Compound **3c** (0.3 g) was treated with lithium aluminum hydride (0.6 g) at room temperature for 1.5 hr. The product (0.28 g) on crystallization yielded *o*-benzylamino-*N*-methylbenzamide (6) in shining flakes (0.1 g): mp 125–126°; ir 3305 (NH), 1632 (C=O), 1600 cm^{-1}; nmr δ 2.92 (d, 3, $-NHCH_3$, J = 5.2 Hz), 4.38 (s, 2, $-CH_2-$), 5.97 (br, 1, $-NHCH_2-$), 7.93 (br, 1, -CONH–), 6.35–7.4 (m, 9, ArH).

Anal. Calcd for $C_{15}H_{16}N_2O$: C, 74.97; H, 6.72; N, 11.67. Found: C, 74.60; H, 6.82; N, 11.16.

The mother liquor on chromatography afforded more of 6 (80 mg, total yield 60%) along with 1,2-dihydro derivative 7 (12 mg, 4%), mp 165–166°.

B. With Sodium Borohydride.—The metal hydride (1 g) was added to an ethanolic solution (15 ml) of **3c** (0.3 g) and refluxed for 5 hr. The oily product (0.3 g) was chromatographed. The fraction eluted with 50% benzene in petroleum ether (500 ml) on crystallization furnished 6 (44%), mp 125–126°.

Further elution (400 ml) with benzene–chloroform (1:1) afforded 7 crystallizing in needles (0.16 g, 54%): mp 165–166°; ir 3250 (NH), 1630 (C=O), 1610 cm^{-1} (sh); nmr δ 2.85 (s, 3, $-NCH_3$), 4.8 (br, 1, -NH), 5.67 (s, 1, C_2 H), 7.88 (dd, 1, C_5 H, J = 8, 2 Hz), 6.4–7.4 (m, 8, ArH).

Anal. Calcd for $C_{15}H_{14}N_2O$: C, 75.60; H, 5.93; N, 11.77. Found: C, 75.97; H, 6.25; N, 11.63.

Sodium Borohydride Reduction of 7 to 6.—The dihydro derivative 7 (50 mg) was treated with sodium borohydride (0.1 g) in ethanol (5 ml) under reflux for 3 hr. Usual work-up, chromatography, and crystallization of the product afforded 6 (30 mg) in 60% yield.

Preparation of *o*-Benzylamino-*N*-methylbenzamide (6).—*o*-Amino-*N*-methylbenzamide (0.65 g) was refluxed in 5% aqueous alcoholic KOH (20 ml) with benzyl chloride (1.5 ml) for 20 hr. It was cooled, diluted with water (50 ml), and extracted with chloroform, and the organic extract was evaporated. From the crude mixture, the amine was separated by extraction of ethereal solution with 2 *N* HCl. The base on regeneration was extracted with chloroform. The crude product on crystallization yielded 6 (0.45 g, 45%) in shining flakes, mp 125–126°, identical in all respects with the reduction product.

Sodium Borohydride Reduction of 1-Methyl-4-quinazolinone (8).—Reduction of 8 (0.1 g) with sodium borohydride (0.5 g) in dry methanol (5 ml) was carried out at 0° and the oily product (60 mg) was converted to its picrate, crystallizing out of alcohol in golden yellow flakes, mp 245° dec. The base, regenerated through IRA-400 ion-exchange resin, on repeated crystallizations afforded the 2,3-dihydro derivative 9 in prisms (40 mg, 40%): mp 112°; ir ($CHCl_3$) 3415 and 3200 (NH), 1680–1640 cm^{-1} (broad, C=O); nmr δ 2.83 (s, 3, $-NCH_3$), 4.41 (d, 2, $-CH_2-$, J = 3 Hz), 6.68 (d, 1, C_8 H, J = 8 Hz), 6.88 (dt, 1, C_6 H, J = 7, 1 Hz), 7.41 (octet, 1, C_7 H, J = 8, 7, 2 Hz), 7.93 (dd, 1, C_5 H, J = 8, 2 Hz), 8.15 (br, 1, -CONH–).

Anal. Calcd for $C_9H_{10}N_2O$: C, 66.64; H, 6.22; N, 17.29. Found: C, 66.34; H, 6.01; N, 17.40.

Sodium Borohydride Reduction of 3-Methyl-4-quinazolinone (3b).—The compound **3b** (0.2 g) was reduced in ethanol (15 ml) with sodium borohydride (0.5 g) under reflux for 3 hr. The oily product (0.185 g) on repeated crystallizations furnished 1,2-dihydro derivative 10 in long needles (0.156 g, 78%): mp 115° (lit.[18] mp 115°); ir 3230 (NH), 1660–1610 cm^{-1} (broad, C=O); nmr δ 3.03 (s, 3, $-NCH_3$), 4.57 (s, 2, $-CH_2-$), 4.77 (br, 1, NH), 7.85 (dd, 1, C_5 H, J = 7.5, 2 Hz), 6.5–7.4 (m, 3, ArH).

Anal. Calcd for $C_9H_{10}N_2O$: C, 66.64; H, 6.22; N, 17.29. Found C, 66.70; H, 6.26; N, 16.95.

Reduction of 3-Phenyl-4-quinazolinone (3d). A. With Lithium Aluminum Hydride.—Compound **3d** (0.25 g) was reduced with lithium aluminum hydride (0.5 g) at room temperature for 1 hr. The oily product (0.25 g) on crystallization afforded long needles (0.20 g, 80%) of *o*-methylaminobenzanilide (12): mp 125–126°; ir 3375 and 3200 (NH), 1640 (sh) and 1630 cm^{-1} (C=O); nmr δ 2.82 (s, 4, $-NHCH_3$), 7.82 (br, 1, -CONH–), 6.4–7.65 (m, 9, ArH).

Anal. Calcd for $C_{14}H_{14}N_2O$: C, 74.40; H, 6.24; N, 12.40. Found: C, 74.80; H, 6.28; N, 12.19.

Compound **3d** (0.3 g) was treated with the same reagent (1 g) under reflux for 6 hr. The oily product (0.29 g) on repeated chromatography yielded, besides 12 (0.05 g, 13%), a homogeneous oil (0.19 g, 63%) characterized as *o*-methylamino-*N*-phenylbenzylamine (11): ir (thin film) 3325 and 3000 (NH), 1595 cm^{-1}; nmr δ 2.85 (s, 3, $-NHCH_3$), 3.92 (br, 2, two NH–), 4.2 (s, 2, $-CH_2-$), 6.5–7.5 (m, 9, ArH); mass spectrum *m/e* (rel intensity) 212 (M^+, 100), 211 (14), 197 (21), 195 (36), 121 (73), 120 (95), 119 (77), 106 (50), 105 (21), 104 (45), 93 (71), 92 (57), 91 (60), 78 (50), 77 (54).

B. With Sodium Borohydride.—Reduction of **3d** (35 mg) was carried out with sodium borohydride (70 mg) in ethanol under reflux for 2.5 hr. Usual work-up and repeated crystallizations yielded 12 (27 mg) in 77% yield.

Reduction of 2-phenyl-4-quinazolinone (3e).—Compound **3e** (0.5 g) was reduced with lithium aluminum hydride (1.5 g) under reflux for 6 hr. The solid product (0.43 g) was boiled with benzene and filtered. The residue (0.1 g) was the unconverted starting material. The filtrate on chromatographic resolution afforded a further amount (25 mg) of **3e** and 0.23 g (46%) of 2-phenyl-3,4-dihydroquinazoline (13) crystallizing in fine needles: mp 139° (lit.[19] mp 142–143°); ir 3180 (NH), 1580 cm^{-1}; nmr δ 4.72 (s, 2, $-CH_2-$), 5.67 (s, 1, -NH), 6.75–7.9 (m, 9, ArH).

Anal. Calcd for $C_{14}H_{12}N_2$: C, 80.84; H, 5.82; N, 13.47. Found: C, 81.25; H, 6.08; N, 13.20.

Registry No.—**4**, 35042-12-7; **5**, 26750-20-9; **6**, 35042-14-9; **7**, 16285-32-8; **9**, 35042-16-1; **10**, 16353-

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02-9; **11**, 35042-18-3; **12**, 21258-59-3; **13**, 1904-73-0.

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Isomeric Diacetal and Dimethoxime Derivatives of Acenaphthenequinone

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The reactions of acenaphthenequinone (**1**) with ethylene glycol and methoxyamine were investigated. The acetalization reaction afforded the monoacetal (**2**), the normal diacetal (**3**), and the bisdioxane (**4**). The use of mass spectrometry to differentiate between structures **3** and **4** is outlined. The loss of $C_2H_4O_2$ from the molecular ion of **4** is diagnostic for the bisdioxane structure. The two isomeric methoximes were determined by nmr spectroscopy to have the symmetrical (**6**, *E,E*) and unsymmetrical (**8**, *E,Z*) structures.

In the course of some studies that required the protection of one or both carbonyl groups of acenaphthenequinone (**1**), we investigated the reaction of **1** with both ethylene glycol and methoxyamine, respectively. In each case, we were able to isolate and identify isomeric addition products, and these are the subject of this paper.

Ethylene Glycol Adducts.[1]—The condensation of an α diketone with ethylene glycol in the presence of acid, when investigated about 40 years ago, was found to give a mixture of two isomers. The structure of the products obtained with glyoxal sulfate[2] or *cis*- or *trans*-2,3-dichlorodioxane[3] and ethylene glycol was a matter of controversy until quite recently.[4,5] Of late, a renaissance of activity has taken place in this general area, both in the synthesis and the differentiation of the isomeric acetals.[6-10] We have directed our attention to the use of mass spectrometry[11] as a means of structural assignment.

The acid-catalyzed reaction of acenaphthenequinone (**1**) with an excess of ethylene glycol in benzene gave a tricomponent mixture that was separated by silica gel plate chromatography. The least polar component was identified as the monoacetal (**2**), on the basis of its ir spectrum (>C=O at 5.78 μ), elemental analysis, and mass spectrum. The low-resolution mass spectrum of **2** is shown in Figure 1. The composition of the M^+ at *m/e* 226 was confirmed by high-resolution techniques as $C_{14}H_{10}O_3$. The odd-electron ion at *m/e* 198, arising from the loss of the ketonic carbonyl as carbon monoxide, was ten times as abundant as the ion at *m/e* 198 resulting from the elimination of ethylene. The *m/e* 170 ion had the molecular composition $C_{11}H_6O_2$. The *m/e* 198 ion eliminated C_2H_4O to form the *m/e* 154 ion. Metastable-ion defocusing experiments[12,13] confirmed that the *m/e* 182 ion was also a precursor of the *m/e* 154 ion, although the precursor ion was present in only very small abundance. However, doubly charged ions at *m/e* 182, 154, and 126 were present. Although the elimination of carbon dioxide from the *m/e* 170 ion was expected, the double decarbonylation to form the *m/e* 142 and 114 ions was unexpected, especially since the loss of a nuclear carbon was involved. To explain this finding, we postulate that the ion resulting from the elimination of ethylene from the *m/e* 198 ion rearranged, in part, to 1,8-naphtholactone, which in turn decarbonylated in two steps to form the *m/e* 114 ion. Recently, Seibl described the fragmentation of 1,8-naphtholactone by a double decarbonylation in a similar manner.[14]

The material of intermediate polarity (mp 213.5-214°) and the most polar product (mp 147.5-148°) both analyzed satisfactorily for $C_{16}H_{14}O_4$. The mass spectrum of the low-melting isomer (**3**) is shown in Figure 2. Below *m/e* 200, the mass spectrum is very similar to that of the ketonic product (**2**). The doubly charged ions at *m/e* 182, 154, and 126 are, however, more prominent in the spectrum of **3**. As in **2**, it is believed that the *m/e* 170 ion exists as the 1,8-naphtholactone ion, from which two CO groups are eliminated successively. The *m/e* 198 ion may be formed in three different ways: (1) by loss of ethylene, followed by the elimination of carbon dioxide; (2) by loss of $C_3H_4O_2$;[15] and (3) by ring cleavage, with successive losses of $C_2H_3O\cdot$ and $CHO\cdot$. The chemical-ionization spectrum of the low-melting isomer (**3**) is shown in Figure 3. The base ion at *m/e* 183 was probably protonated acenaphthenequinone, which had been formed through the consecutive elimination of two C_2H_4O moieties from the protonated molecular ion (MH^+) at *m/e* 271. These data for the low-melting

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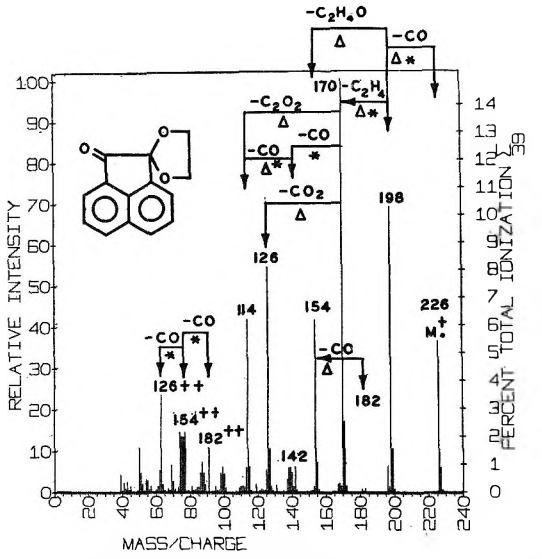


Figure 1.—Electron impact mass spectrum of **2**: *, metastable transition; Δ, defocused ion transition.

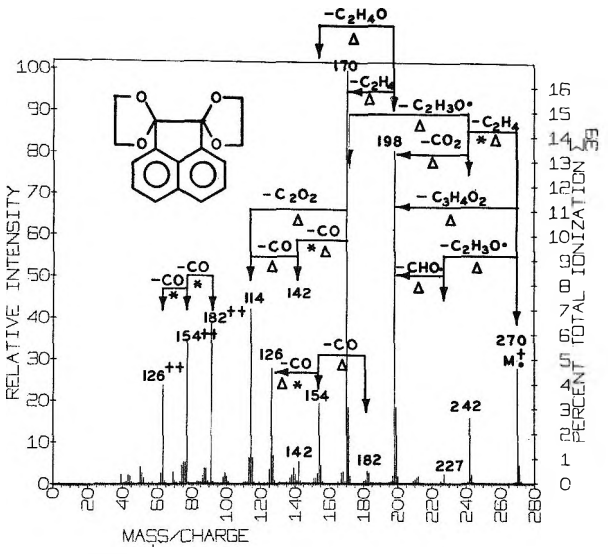
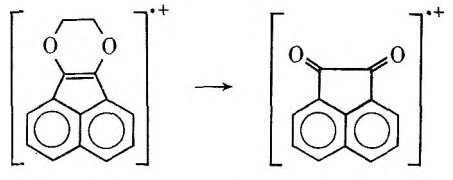


Figure 2.—Electron impact mass spectrum of **3**.

isomer are consistent with the normal diacetal structure (**3**).

The mass-spectral data for the high-melting isomer are consistent only with a bisdioxane of structure **4** (Figure 4). The base ion of the latter was 16 amu lower (*m/e* 154) than in the low-melting isomer (*m/e* 170), whereas a prominent *m/e* 182 ion was observed. The *m/e* 182 ion was formed either through the elimination first of $C_2H_4O_2$ and then of ethylene, or by the reverse process; like the acenaphthenequinone ion (*cf.* Figure 5), it lost carbon monoxide in two steps. The fragmentation pathway that demonstrated the bisdioxane structure, however, was the elimination of $C_2H_4O_2$ from the molecular ion to form the stabilized un-



m/e 210 *m/e* 182

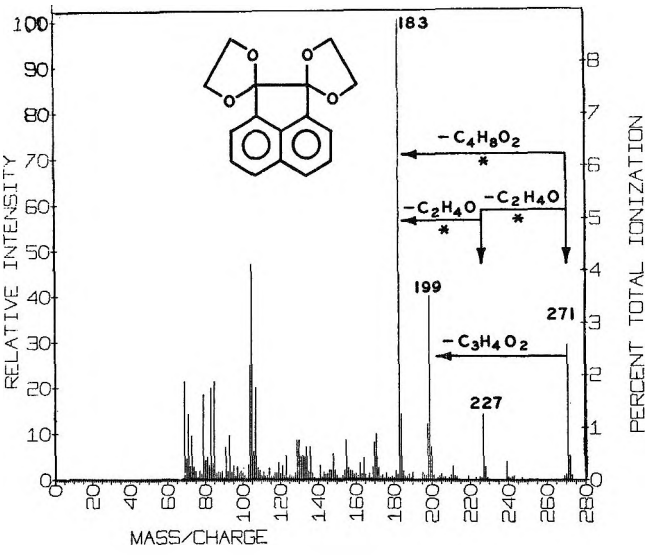


Figure 3.—Chemical ionization mass spectrum of **3**.

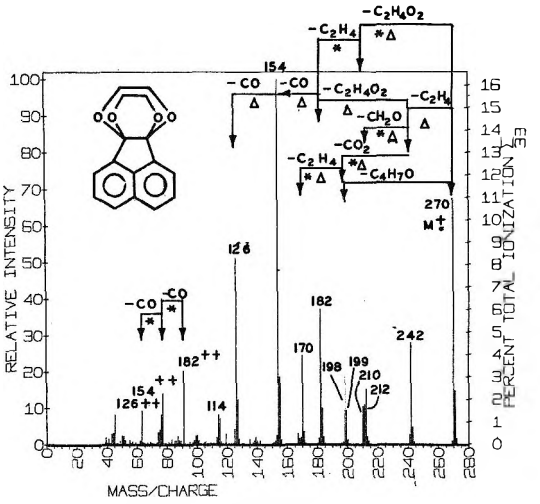


Figure 4.—Electron impact mass spectrum of **4**.

saturated ion of *m/e* 210, which further eliminated ethylene to form the *m/e* 182 ion.[16] The M − 58 ion was formed by the stepwise elimination of ethylene and formaldehyde from the M^+. The ions at *m/e* 198, 170, 142, and 114 were formed in the same manner as in the low-melting isomer, *i.e.*, by the elimination of carbon dioxide from the *m/e* 242 ion. The loss of formaldehyde and $C_2H_4O_2$ could occur from a *m/e* 242 ion that had been formed from the elimination of ethylene, whereas the loss of carbon dioxide from the *m/e* 242 ion would require rearrangement to the *m/e* 198 ion present in the low-melting isomer. Although no ion was found for the loss of C_4H_8O, there were two ions at *m/e* 199, one corresponding to the ^{13}C isotope peak of the *m/e* 198 ion and the other to the loss of C_4H_7O from the M^+. In contrast to the electron impact mass spectrum of the high-melting isomer, the chemical-ionization mass spectrum (*cf.* Figure 6) shows a very intense *m/e* 199 ion. No metastable ion was detected for its formation and, unfortunately, the exact mass for this ion was not measured, nor was it determined by metastable de-

(16) G. A. Russell and L. A. Ochrymowycz, *J. Org. Chem.*, **34**, 3618 (1969), reported that the mass spectrum of the diacetal of phenylglyoxal favors the normal product, although they found a small M − 60 ion whose presence would be consistent with the bisdioxane structure.

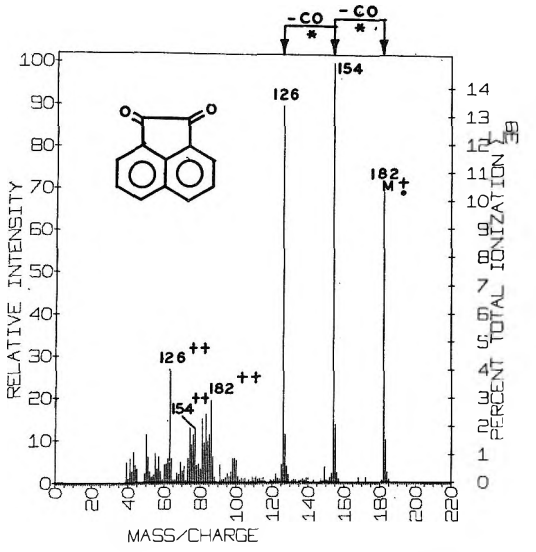


Figure 5.—Electron impact mass spectrum of **1**.

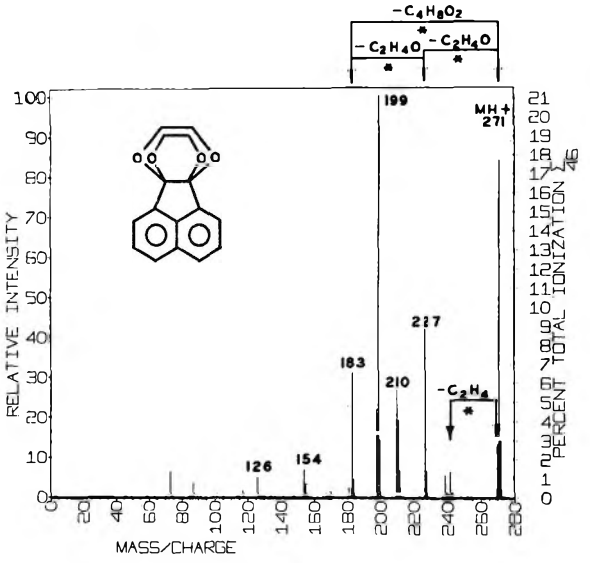


Figure 6.—Chemical ionization mass spectrum of **4**.

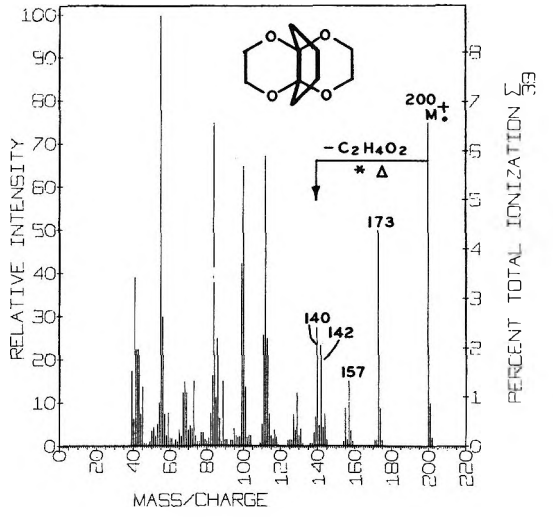
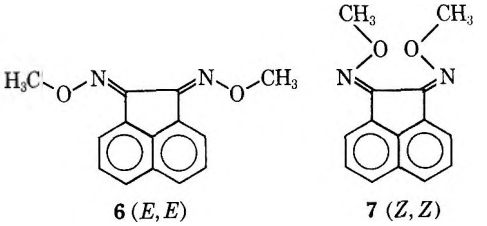


Figure 7.—Electron impact mass spectrum of **5**.

focusing experiments. Assuming that rearrangement is not favored in chemical ionization, C_4H_8O should be lost from the MH^+ ion to form the *m/e* 199 ion. Metastable ion transitions were observed for the consecutive losses of two C_2H_4O moieties from the MH^+. Finally, a *m/e* 210 ion was present, resulting from the elimination of $C_2H_4O_2$ and a proton to form the unsaturated ion; the ion corresponding to loss of the elements of ethylene and formaldehyde was not observed.

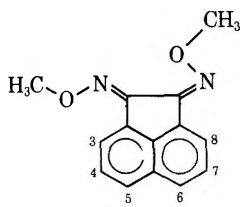
The reaction of cyclohexane-1,2-dione with ethylene glycol (*p*-TsOH catalysis) afforded only a small amount (~2%) of the tetraoxapropellane (**5**) along with the normal diacetal.[17] Further treatment of the normal diacetal under the same acetalization conditions did not convert it to **5**. These results are in sharp contrast to those obtained in the present case. Here, both **2** and **3** can be completely converted to **4** under further treatment, and **4** is initially formed in substantial yield. This preference for the formation of **4** is due, in part, to stabilization of a benzylic protonated intermediate. We have also examined the mass spectrum of **5** (Figure 7) and have observed the characteristic peak for the elimination of $C_2H_4O_2$ from the M^+, accompanied by both metastable and defocused ions.

Methoxyamine Adducts.—Geometrical isomerism was first observed in nitrogen compounds during the latter part of the nineteenth century, when the dioxime of benzil was shown to occur in three stereoisomeric forms. The historical aspects and chemistry of vicinal dioximes have been reviewed.[18] The dioxime of **1** has been prepared[19-22] and exists in only one form, presumably the anti[23] (*E*,*Z*).[24] After treatment of **1** with an excess of methoxyamine hydrochloride in pyridine, tlc and vpc of the crude crystalline product indicated the presence of two components [27% more polar isomer (A) and 73% less polar isomer (B)]. Separation of this mixture by preparative thick layer chromatography gave pure A (mp 153–153.5°) and pure B (mp 147–147.5°). There are three possible structures for the dimethoxime derivatives: two symmetrical forms [**6** (*E*,*E*) and **7** (*Z*,*Z*)] and the unsymmetrical form [**8** (*E*,*Z*)].



6 (*E*,*E*)

7 (*Z*,*Z*)



8 (*E*,*Z*)

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TABLE I

PROTON CHEMICAL SHIFTS AND COUPLING DATA OF THE DIMETHOXIMES IN DEUTERIOCHLOROFORM (HERTZ)

Compd	H-3	H-4	H-5	H-6	H-7	H-8	OCH_3
6	496.2 (q, 7.13, 0.91)	456.1 (q, 7.13, 8.01)	471.4 (q, 8.01, 0.91)	471.4 (q, 8.01, 0.91)	456.1 (q, 7.13, 8.01)	496.2 (q, 7.13, 0.91)	258.0
8	495.9 (q, 6.57, 0.72)	455.4 (q, 6.57, 7.95)	471.1 (q, 7.95, 0.72)	470.7 (q, 8.43, 0.53)	454.7 (q, 5.94, 8.43)	468.4 (q, 5.94, 0.53)	255.5, 259.2

Single methoxyl and ortho hydrogen signals were expected for **6** and **7**, owing to their symmetrical nature, whereas dual signals were expected for both the methoxyl and ortho hydrogen atoms in **8**. An inspection of the nmr data in Table I permitted the assignment of the unsymmetrical structure (**8**) to isomer A. The methoxyl signals appeared as singlets at δ 4.26 and 4.32, whereas the ortho hydrogens appeared as quartets centered at 8.26 and 7.81. It has been observed that, when an oximino oxygen atom is cis to an aromatic ring, the ortho hydrogen atom is deshielded and resonates further downfield;[24] thus, the signal at δ 8.26 was assigned to the ortho hydrogen on the side of the molecule having the methoximino group in the *E* configuration. The *E,E* configuration (**6**) was assigned to isomer B, since it exhibited a signal at δ 8.27 for both ortho hydrogens and a single methoxyl signal at 4.30. The *Z,Z* formula (**7**) was ruled out since, in this case, the signal for the ortho hydrogens would be expected to appear further upfield at about δ 7.8. The mass spectra of **6** and **8** were identical.

Experimental Section

The melting points were determined on a Thomas-Hoover capillary apparatus and are uncorrected. The mass spectra were obtained with an AEI MS-902 double-focusing mass spectrometer (70 eV) equipped with a manually operated accelerating voltage defocusing attachment and, for high-resolution data acquisition, a Honeywell 7600 frequency-modulated analog tape recorder. The ion-block temperature was maintained at 180°. In high-resolution mode, the dynamic resolution was one part in 13,000 and the spectra were scanned at a rate of 16 sec/decade. The analog tape was processed on an IBM 1800 computer, using Squibb programs. The accuracy of high-resolution mass measurements was better than 10 ppm whereas that of metastable ion defocusing was ±1 amu. Chemical ionization spectra were obtained by Dr. H. Fales on a modified AEI MS-902, with methane at 0.5-mm pressure, 220°. The nmr spectra were determined on a Varian Associates A-60 spectrometer operated at ambient temperatures, employing TMS as the internal standard. The chemical shifts and coupling constants were calculated by use of NMREN and NMRIT[25] programs. Computed spectra from the above data gave the best fit to the experimental spectra. Average deviations were <0.16 Hz in all cases. Plate chromatography was carried out on silica gel (Quantum Industries, PQ1F, 20 × 40 cm plates) and the compounds were visualized with ultraviolet light.

Reaction of Acenaphthenequinone (1) with Ethylene Glycol.—A mixture of **1** (1.0 g) and *p*-TsOH (50 mg) in benzene (50 ml) and ethylene glycol (5 ml) was stirred and refluxed overnight in a modified Dean–Stark trap containing a calcium carbide thimble. The mixture was cooled and the benzene layer separated. The aqueous layer was diluted with H_2O and extracted with benzene. The combined benzene fractions were washed with 8% salt solution, dried (Na_2SO_4), and evaporated. Plate chromatography of the residue, using $CHCl_3$ as the developing solvent, gave rise to three bands, which were eluted with EtOAc.

The least polar product was crystallized from chloroform–isopropyl ether to give **2** (115 mg, mp 93–94°).

Anal. Calcd for $C_{14}H_{10}O_3$: C, 74.33; H, 4.46. Found: C, 74.14; H, 4.45.

The product of intermediate polarity was crystallized from chloroform–isopropyl ether to give **4** (218 mg): mp 213.5–214°; nmr ($CDCl_3$) δ 5.69 (m, OCH_2CH_2O, $w_{1/2}$ = 3 Hz).

Anal. Calcd for $C_{16}H_{14}O_4$: C, 71.10; H, 5.22. Found: C, 70.85; H, 5.26.

The most polar product was crystallized from chloroform–isopropyl ether to give **3** (297 mg): mp 147.5–148°; nmr ($CDCl_3$) δ 6.03 (AA'BB' pattern, OCH_2CH_2O, w = 55 Hz).[6]

Anal. Calcd for $C_{16}H_{14}O_4$: C, 71.10; H, 5.22. Found: C, 71.23; H, 5.48.

Reaction of Acenaphthenequinone (1) with Methoxyamine.—A mixture of **1** (5.0 g) and methoxyamine hydrochloride (5.0 g) in pyridine (100 ml) was warmed to achieve solution and then left at room temperature overnight. The mixture was poured into H_2O, and the solid was collected by filtration. The solid was dissolved in $CHCl_3$, and this solution was washed with 2 *N* HCl and with 8% salt solution, then dried (Na_2SO_4), and evaporated to give the mixture of dimethoximes (4.1 g, mp 124–130°). Plate chromatography of the mixture, using chloroform–hexane (1:1) as the developing solvent, gave rise to two bands, which were eluted with EtOAc.

Crystallization of the less polar product from isopropyl ether gave **6** (mp 147–147.5°).

Anal. Calcd for $C_{14}H_{12}N_2O_2$: C, 69.99; H, 5.03; N, 11.66. Found: C, 69.70; H, 5.06; N, 11.60.

Crystallization of the more polar product from isopropyl ether gave **8** (mp 153–153.5°).

Anal. Calcd for $C_{14}H_{12}N_2O_2$: C, 69.99; H, 5.03; N, 11.66. Found: C, 70.13; H, 5.06; N, 11.67.

Registry No.—**1**, 82-86-0; **2**, 30339-97-0; **3**, 30339-98-1; **4**, 30384-15-7; **6**, 35171-04-1; **8**, 35171-05-2.

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The Photochemistry of Pyracyloquinone

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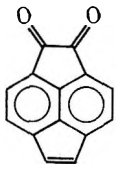
Irradiation of pyracyloquinone in methanol gave dimethyl 5,6-acenaphthenedicarboxylate in 30% yield. Photolysis of pyracyloquinone in ethanol and in 2-propanol gave the corresponding diesters, while photolysis in benzene containing *p*-anisidine yielded the diamide. These observations represented indirect evidence for the formation and reaction of a diketene intermediate, formed in a photoinitiated benzenoid–quinoid valence isomerism. A detailed study of the luminescence spectra of pyracyloquinone in protic media as well as kinetic studies of the reaction between pyracyloquinone and protic solvents leads to the conclusion that the initially formed excited state is a singlet species represented as a diketene. The dark reactions which led to the formation of diesters (when the photolysis took place in aliphatic alcohol solution) were postulated to occur by attack of alcohol on the diketene to give labile intermediates. Although no photochemical reaction between pyracyloquinone and cyclohexane was observed, irradiation (3500 Å) of a solution of the quinone in cyclohexene resulted in the formation of a mixture of bicyclohexenyl derivatives and 1,2-dihydroxypyracene. The major product isolated from this mixture was identified as 1,1′-dehydro-2,2′-bicyclohexenyl. The quantum efficiency for the disappearance of pyracyloquinone during photolysis in cyclohexene was found to be only 0.02, but the high yield of bicyclohexenyl derivatives was 20 times greater than for a 1:1 mole reaction. This indicated that a radical chain mechanism which involved abstraction of hydrogen from the solvent by the triplet state of pyracyloquinone was operative. Luminescence studies of the quinone in nonprotic media were consistent with this mechanism and indicated highly efficient intersystem crossing.

The objective of this work was the preparation and photochemical investigation of aromatic compounds expected to undergo light-induced benzenoid–quinoid valence isomerizations. Although valence isomerism involving benzenoid–nonbenzenoid systems has been well documented in the literature,[2-7] few examples of benzenoid–quinoid transformations have been reported.

Pyracyloquinone (**1**) was considered an excellent



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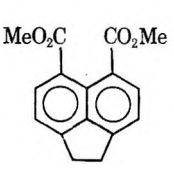
candidate for study, since it bears a formal resemblance to conjugated unsaturated ketones, a series of compounds the photochemistry of which has been extensively investigated over the past several years.[8-12] In addition, the compound could be prepared (albeit in low yield) from readily available acenaphthene by a three-step synthesis.[13,14] The discovery[15] that this compound reacted photochemically with protic substances prompted a detailed investigation of the photochemistry of pyracyloquinone in both protic and nonprotic solvents. The detailed mechanism by which these products are formed is the subject of the present paper. The results indicate that pyracyloquinone is an example of a compound which reacts from either a singlet or a triplet excited state depending upon the nature of the coreactant.

Photoreactions of Pyracyloquinone in Protic Solvents.—Irradiation of **1** in various solvents was initially carried out for periods in excess of 24 hr. When the isolation of intermediates was desired, however, shorter periods of irradiation were employed.

A. Prolonged Irradiation.—Irradiation of a methanolic solution of **1** under argon led to the formation of a yellow-orange photoproduct, which was conveniently isolated by chromatography as a colorless solid in 30% yield. Elemental and spectroscopic analysis identified the material as dimethyl 5,6-acenaphthenedicarboxylate (**2**). In addition, the physical and spectral properties of this material were identical with those of an authentic sample prepared from 1,2-diketopyracene (**3**) by peracid oxidation followed by Fischer



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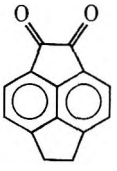

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esterification. In contrast to the behavior of **1**, no photoreaction of **3** was found.

That this reaction occurs with other protic substances was indicated by the photolysis of **1** in the presence of ethanol, 2-propanol, and *p*-anisidine, which resulted in the formation of diethyl 5,6-acenaphthenedicarboxylate (11% yield), diisopropyl 5,6-acenaphthenedicarboxylate (13% yield), and acenaphthene-5,6-di-

(1) (a) Taken from the dissertation submitted to the Faculty of the Polytechnic Institute of Brooklyn in partial fulfillment of the requirements of the degree of Doctor of Philosophy (Chemistry), June 1969. (b) To whom inquiries should be addressed.

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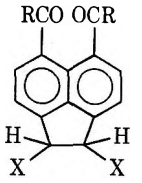
TABLE I

PRODUCTS DERIVED FROM PYRACYLOQUINONE PHOTOLYSIS IN POLAR SOLVENTS AT 25°



Solvent[a]	Other constituents	Time of irradiation, hr	Products R	X	Yield, %	Major *m/e* peaks in mass spectrum
Methanol		48	CH_3O	H	30	270, 239, 196, 180, 152
Methanol	H_2SO_4[e]	65	CH_3O	H	33	270, 239, 196, 180, 152
Methanol-*O-d*		48	CH_3O	D	30	272, 241, 198, 182, 154
Ethanol		40	C_2H_5O	H	11	224, 180, 152
2-Propanol[b]		40	*i*-C_3H_7O	H	13	224, 180, 152
Benzene[c]	*p*-Anisidine[d]	25	*p*-$CH_3OC_6H_4NH$	H	51 (crude)	329, 180, 123, 152, 108
Methanol	NaOMe[f]	42	**4**		90	268, 237, 194, 178, 150

[a] Concentration of **1** was 2.5×10^{-4} *M*. [b] Concentration of **1** was 1.25×10^{-4} *M*. [c] Concentration of **1** was 2.5×10^{-3} *M*. [d] Concentration of *p*-anisidine was 0.10 *M*. [e] pH of solution was 1.5. [f] pH of solution was 10.5.

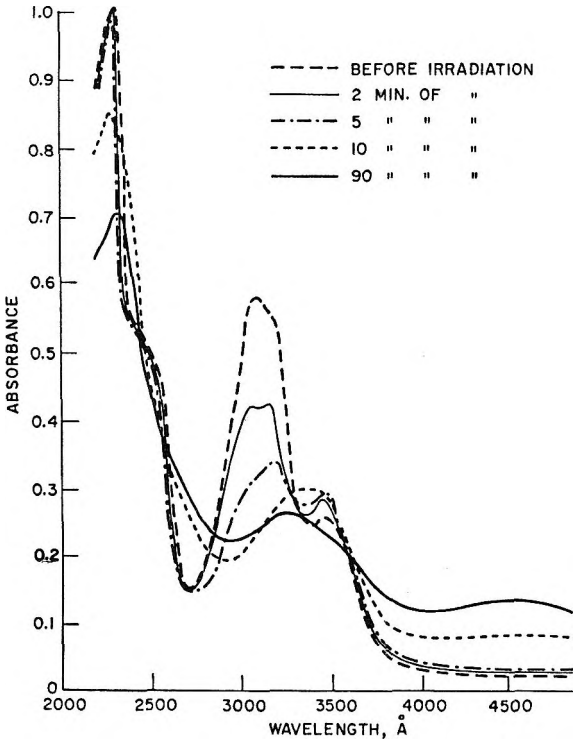


Figure 1.—Changes in the ultraviolet absorption spectrum of pyracyloquinone during photolysis in methanol.

carboxylic acid di-*p*-methoxyanilide (51% yield), respectively.

In an effort to determine the nature of proton transfer during the reaction of photoexcited **1** with protic substances, irradiation of **1** in methanol-*O-d* was carried out. The product, which was isolated in 30% yield, was characterized by infrared and mass spectral analysis as dimethyl 1,2-dideuterio-5,6-acenaphthenedicarboxylate. That only two deuterium atoms had been incorporated was indicated by the mass fragmentation pattern, which was identical with that of **2** with the exception that the mass/charge ratio of each fragment ion was increased by two units.

The effect of acid and base on the course of this photochemical reaction was also studied. Irradiation of a methanolic solution of **1** containing 4 mequiv of sulfuric acid (pH 1.5) gave a 33% yield of **2**. Thus, no dramatic change in the overall course of the reaction was observed in the presence of acid. In contrast, when photolysis of a methanol solution containing 4 mequiv of sodium methoxide (pH 10.5) was carried out for an extended period, separation and purification of the product in the usual manner led to the isolation of an ortho ester (**4**) in 90% yield. That this compound was not formed as a result of methoxide ion attack on **2** was established by a control experiment. A summary of the photoproduct study is presented in Table I.

B. Brief Irradiation.—In an effort to obtain a better understanding of the overall mechanism of the photoreactions of **1** in protic solvents, the spectral changes associated with the irradiation of **1** in methanol solution were monitored by both visible and ultraviolet spectrophotometry. In a typical run, a stirred solution of **1** in methanol was flushed with argon for 2 hr followed by short periods of irradiation. The ultraviolet absorption spectrum of **1** during photolysis (Figure 1) showed a rapid decrease in the absorption band at 3080 Å after only 5 min. Concomitant with this decrease in the concentration of **1** was an increasing coloration[16] (red) of the solution. The increase in the red color as a function of irradiation time was illustrated by the visible absorption spectrum changes associated with the photolysis. The rate of formation of the species with a long wavelength (~5000 Å) absorption band approximately corresponded to the rate of disappearance of **1**. As irradiation was continued, however, this species reacted slowly over a period of hours, during which time the diester **2** was formed. The formation of the latter was determined by isolation of **2** from the reaction mixture at various time intervals.

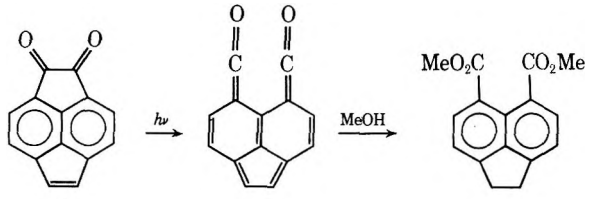
That the formation of the diester from the red species was not the result of a thermal reaction was established by the following experiments. A solution of **1** in methanol was irradiated for 30 min (at this time, essentially all of **1** is converted to the red intermediate) and subsequently refluxed for 24 hr. No changes in the absorption spectrum of the red solution were observed during this period. After evaporation of the solvent, the residue was chromatographed and a 15% yield

(16) This appeared green initially but changed to a deep red on standing.

of 2 (based on 1) was obtained with chloroform as the eluent. This was the expected yield for this period of irradiation. Further elution of the column with methanol led to the isolation of a red solid (80% of weight of 1). This material was redissolved in spectroquality methanol and the solution (10^{-4} M) was irradiated for 26 hr. Treatment of the reaction mixture in the usual way led to the isolation of an additional 17% yield of diester 2 (based on starting 1). These observations indicated that two photochemical reactions occurred during the photolysis of 1 and that an isolable intermediate was produced. In a related experiment, the red intermediate was converted to the ortho ester 4 on treatment with a methanolic solution of sodium methoxide in the dark.

The possibility of diketene formation in the initial stage of the photoreaction in protic solvents has already been mentioned. However, an attempt to observe this intermediate directly by infrared spectroscopy at −78° was unsuccessful. The concentration of diketene present (if it indeed forms) is apparently too low for detection by this technique.

Mechanism of Photoreactions in Protic Solvents.—The intermediate formation of diketenes in photochemical reactions of unsaturated diketones has previously been invoked and is supported by indirect evidence. Specific examples are the photolysis of 3-phenylcyclobutene-1,2-dione[17] and benzocyclobutenedione[18] in which simple mechanisms are postulated to account for the various products formed. A simplified mechanism was also presented in our preliminary report[15] on the photolysis of pyracyloquinone (1) in



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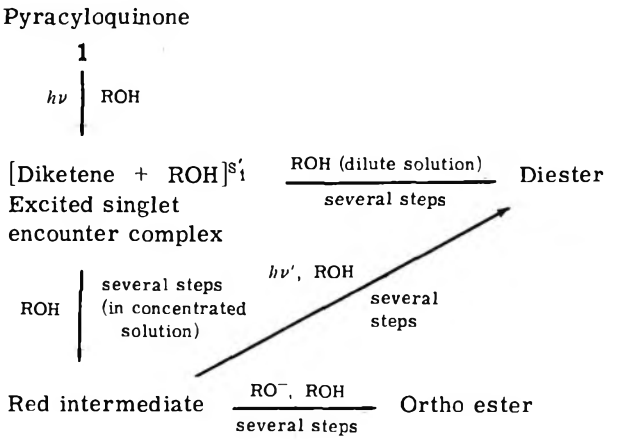
methanol. In that paper,[15] however, we suggested that the mechanism of the overall reaction was more complicated than that depicted above. This suggestion was based largely on the observation of a transient (thermally stable) species absorbing at long wavelength. A subsequent paper by Trost[14] on the photolysis of 1 in moist 1,2-dimethoxyethane also presented results which suggested the intermediate formation of the diketene from 1; 5,6-acenaphthenedicarboxylic anhydride was postulated to form by attack of water on the diketene. This diketene was also postulated to be responsible for a transient red color.

The present results confirm our earlier suggestion[15] that the mechanism of the photochemical reaction of pyracyloquinone with protic substances is complex. A schematic representation of the postulated overall mechanism of the photochemical reaction of 1 with aliphatic alcohols is illustrated below; a discussion of the individual steps in this mechanism follows.



A. Nature of the Excited State.—A determination of the nature of the initially formed excited species responsible for the processes involved was accomplished, in part, by a study of the luminescence spectra of 1 and 1,2-diketopyracene (3) in protic and aprotic solvents. All the studies were conducted with 1:4 mixtures of isopentane–methylcyclohexane (aprotic medium) and 1:4 mixtures of methanol–ethanol (protic medium); these gave clear, rigid glasses at the temperature of liquid nitrogen (77°K).[19] Since the absorption bands for both 1 and 3 occur in the region 3100–3700 Å, the excitation wavelength was varied within this range.

The O–O band for fluorescence of 3 occurs at 3679 Å and corresponds to an energy of 77.6 kcal/mol for the first excited singlet state of the n–π^* transition. The absorption spectrum shows more fine structure than the fluorescence spectrum, with the O–O band for absorption appearing at 3645 Å. The luminescence spectrum of 3 in the hydrocarbon glass at 77°K shows a strong, broad peak at 4200 Å due to fluorescence and weak phosphorescence peaks at 5400 (shoulder) and 5600 Å. The 5400 Å peak was taken as the O–O band of the phosphorescence, and an energy of 53 kcal/mol for the lowest triplet state was thus obtained. The lifetime of the triplet state ($\tau = 1.3 \times 10^{-2}$ sec) was determined by measurements of the exponential decay of the 5600-Å emission (greenish-yellow) as a function of time. The low intensity of phosphorescence, relative to fluorescence, indicates that intersystem crossing from the first excited singlet state of 3 to the first excited triplet state is less efficient than in most other aromatic carbonyl compounds. The large energy difference between the states is presumably responsible for this situation.[20]

In contrast to the behavior of 3, pyracyloquinone exhibits a higher singlet → triplet efficiency in aprotic solvents. The fluorescence spectrum exhibited emission from the first excited singlet state at 3660 Å (78 kcal/mol), which coincides with the corresponding O–O band for absorption. The phosphorescence spectrum showed strong peaks at 4600, 4700, and 4754 Å. The energy of emission from the first excited triplet state was, therefore, calculated to be 62 kcal/mol. The blue phosphorescence had a half-life τ of 5.9 sec.

The fluorescence spectrum of 3 in methanol–ethanol at 77°K showed weak but discrete fluorescence peaks

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TABLE II

ENERGIES AND LIFETIMES OF EXCITED STATES OF PYRACYLOQUINONE AND 1,2-DIKETOPYRACENE

Compd	Solvent system	E_{S_1}, kcal/mol	τ, sec	E_{T_1}, kcal/mol	τ, sec	Intersystem crossing efficiency
1,2-Diketopyracene	Aprotic[a]	77.6	$<10^{-5}$	53	1.3×10^{-2}	Low
	Protic[b]	75	$<10^{-5}$	57	2×10^{-2}	High
Pyracyloquinone	Aprotic[a]	78	$<10^{-5}$	62	5.9	High
	Protic[b]	48.5[c]	$<10^{-5}$			

[a] 1:4 mixture (by volume) of isopentane–methylcyclohexane. [b] 1:4 mixture (by volume) of methanol–ethanol. [c] Estimated energy of $S_1 \rightarrow S_0$ transition of complex.

at 3818, 4031, and 4256 Å. An energy of 75 kcal/mol was obtained for the $S_1 \rightarrow S_0$ transition assuming 3818 Å for the O–O band. In addition, there was a very strong phosphorescence with peaks at 5000 (57 kcal/mol), 5140, and 5420 Å and a half-life of 2×10^{-2} sec. Therefore, the differences in the energy levels of **3** in protic and aprotic solvents are not very large (Table II).

The behavior of pyracyloquinone in protic and aprotic solvents was found to be quite different. Since **1** reacted rapidly with protic substances, it was not possible to measure its luminescence spectrum in the polar solvent mixture at room temperature. However, at liquid nitrogen temperatures (77°K), no changes in the absorption spectrum of this solution were noted, even after prolonged irradiation with the full mercury vapor lamp. The luminescence spectrum at 77°K showed a weak, broad emission which peaked at 5885 Å (48.5 kcal/mol). The half-life τ of the orange luminescence was less than 5×10^{-5} sec, which was the limit of experimental observation. Since this decay was observed visually, the lifetime of the excited state was estimated to be $\sim 10^{-6}$ sec.

The results of these luminescence studies (summarized in Table II) indicate that the excited species which forms in solutions of **1** in alcoholic solvents is quite different from that which forms in aprotic solvents. The absence of emission from the 3500–4500-Å region indicated that the first excited singlet state of **1** was quenched by the solvent and that a new species, which emitted at 5885 Å, was formed. The short lifetime of this long-wavelength emission indicates that a singlet species is probably involved.

The formation of a new species with a characteristic emission has previously[20] been postulated to occur *via* a transient dimer ("excimer") or encounter complex. Since the concentration of **1** in the solutions used in the luminescence studies was 10^{-5} *M*, it is highly unlikely that "normal" excimer formation occurs. The formation of "mixed excimer,"[21] however, is possible. Thus, a second substance, S, can quench the fluorescence of $^1A^*$ by forming a mixed excimer (AS*), even if no energy-transfer process (in the usual sense) takes place. This effect has been studied with mixtures of pyrene (A) and substituted pyrenes (S) (where the singlet energies of each component are not far apart).

A mechanism for solvent quenching of fluorescence which specifically involves chemical interaction between the solvent and excited solute has been postulated[22,23] to lead to formation of an encounter complex. This complex may form through transfer of one electron from the solvent to an excited molecule of **1** (A) as illustrated below.

$$A^{S_0} \xrightarrow{h\nu} A^{S_1}$$

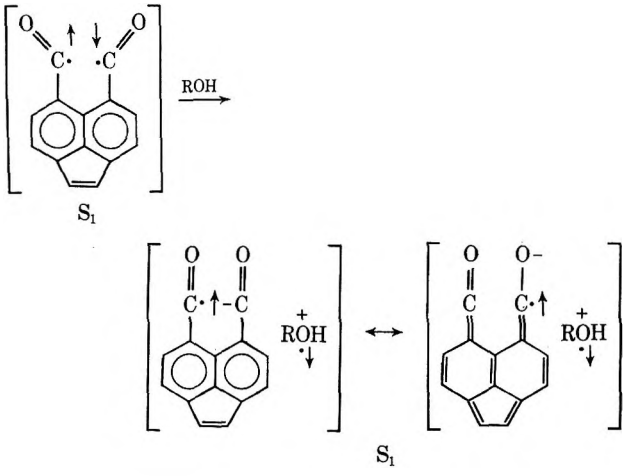
$$A^{S_1} \xrightarrow{-h\nu'} A^{S_0}$$

$$A^{S_1} + ROH \longrightarrow [A^- \dot{R}\dot{O}H]^{S_1'}$$

$$[A^- \dot{R}\dot{O}H]^{S_1'} \xrightarrow{-h\nu''} A^0 + ROH$$

The molecular form of **1** absorbs radiation to form its lowest excited singlet state, S_1, which can either emit its molecular fluorescence, $h\nu'$, or react with ROH to produce an excited-state ion pair, S_1'. If the latter reaction occurs in a time which is short compared to the lifetime of the excited singlet state, the excited ion pair S_1' can emit its own characteristic fluorescence $h\nu''$ as observed. The net outcome of this process is emission of fluorescence characteristic of an ionic species in a solution which does not contain ions in the ground state. A mechanism very similar to this was used to explain the luminescence spectrum of phenol.[20]

The structure of the excited singlet state, S_1', may



be represented as a diketene. The lifetime of this state ($\sim 10^{-6}$ sec) is sufficiently long to allow the two carbonyl groups to move apart (after the bond has been broken as in S_1) and to form the diketene–alcohol complex (vibrational processes occur in $\sim 10^{-8}$ sec). At liquid nitrogen temperatures, collisions between the excited complex (S_1') and other ground-state alcohol molecules are minimized. Thus, the excited diketene complex emits its excess energy as fluorescence and returns to the ground state. The resulting ground-state diketene, which is most likely higher in energy than the diketone, may be spontaneously converted (radiationless process) to ground-state diketone. An

(21) J. B. Birks and L. G. Christophorou, *Nature (London)*, **196**, 33 (1962).
(22) E. J. Bowen and R. J. Cook, *J. Chem. Soc.*, 3059 (1953).
(23) E. J. Bowen and K. West, *ibid.*, 4394 (1955).

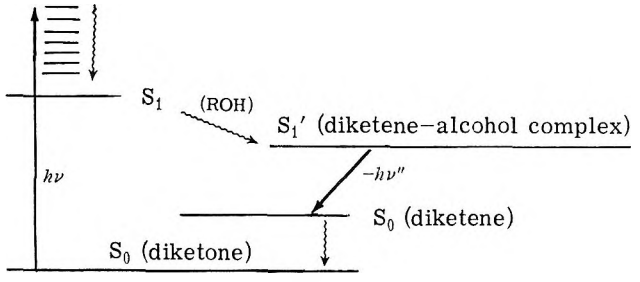
TABLE III

QUANTUM EFFICIENCIES FOR DISAPPEARANCE OF PYRACYLOQUINONE IN PROTIC SOLVENTS AT 25°

Solvent[a]	Other constituents	Concentration of other constituents	Φ	Mean deviation
Methanol	None		0.30	±0.01
Methanol	Air	Saturated (10^{-2} *M*)[b]	0.30	±0.01
Methanol	H_2SO_4	3×10^{-3} *N*	0.16	±0.01
Methanol	$NaOCH_3$	3×10^{-3} *M*	0.59	±0.02
Methanol	*trans*-1,3-Pentadiene (piperylene)	0.2 *M*	0.30	±0.01
Methanol	1,3-Cyclohexadiene	0.2 *M*	0.30	±0.01
Methanol-*O*-*d*			0.29	±0.01
Ethanol			0.27	±0.03
2-Propanol			0.23	±0.01
2-Butanol			0.20	±0.01

[a] Concentration of pyracyloquinone was 1.00×10^{-5} *M* for all solvents. [b] Solubility of oxygen in methanol at 20°: "International Critical Tables," Vol. III, McGraw-Hill, New York, N. Y., 1928, p 262. The actual value given is 175 cm³ of O_2/l of methanol, or 7.8×10^{-3} *M*.

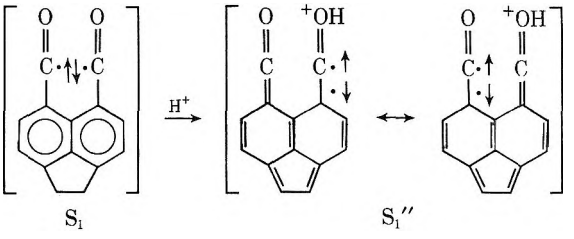
energy level diagram illustrating this situation is depicted below.



At room temperature, attack of alcohol on the excited complex S_1' (or ground-state diketene) leads to the formation of ground-state intermediates which undergo additional thermal and/or photochemical reactions.

Ferrioxalate actinometry[24] was used to determine the quantum efficiency for disappearance of **1** in protic solvents and the results of this study are summarized in Table III. The small decrease in quantum efficiency for disappearance of pyracyloquinone (or S_1') with increasing molecular weight of the attacking alcohol is related to two factors. An increase in basicity of the alcohol would be expected to increase the efficiency of electron transfer from the alcohol to S_1. Complexes (S_1') with methanol, ethanol, 2-propanol, and 2-methylpropanol would be required to have decreasing energies and hence increasing efficiencies of decay to the ground state. The picture is further complicated, however, by a second factor, the rates of diffusion of the various alcohols. Since the differences in the basicities of the alcohols are smaller than the differences in rates of diffusion, it would appear that the latter factor is more important in determining the efficiency of disappearance of S_1'. Since the lifetime of the excited singlet, S_1', is long ($\tau \cong 10^{-6}$ sec) compared with diffusion-controlled processes ($\sim 10^{-9}$ sec),[20] this concept appears valid. Thus, it is postulated that diffusion of solvent molecules into the "cage" containing the excited species, S_1', is the primary factor which controls the rate of disappearance of S_1'. That proton transfer does not take place (in neutral solution) during attack of ROH on S_1' was indicated by the absence of a deuterium isotope effect (see Table III).

Although profound changes in the quantum efficiency for disappearance of the quinone **1** in methanol were observed with large changes in pH, negligible changes in the absorption spectrum were noted. This phenomenon suggested a decrease in the acidity of **1** upon electronic excitation. Such changes have been observed for a variety of organic compounds.[20] In particular, aromatic ketones such as acridone[25] and acetophenone[26] exhibit a decrease in acidity in the first excited singlet state relative to the ground state. Thus, a change in the mechanism of the reaction may occur in the presence of strong acid. Transfer of a proton to the carbonyl oxygen (in the presence of acid) of the S_1 state of **1** might lead to a new excited singlet state S_1''. The efficiency of conversion of this less acidic



state to ground-state products by attack of ROH would therefore be considerably reduced. Conversely, at high pH the efficiency of conversion of S_1 and S_1' would be increased and would account for the higher quantum efficiency. The result at high pH, however, is further complicated by the fact that methoxide ion leads to a product different from that obtained in neutral or acidic media.

The results summarized above lead to the conclusion that the excited species responsible for the photochemical reaction between **1** and protic substances (specifically aliphatic alcohols) is a singlet encounter complex (or "mixed excimer") in a solvent "cage." The multiplicity (singlet) of the state was established by (1) the short lifetime of emission from the complex; (2) the lack of a change in the quantum efficiency for disappearance of **1** in the presence of triplet-state quenchers such as O_2, piperylene, and 1,3-cyclohexadiene[24] (see Table III); (3) absence of photoproducts arising from

(24) J. G. Calvert and J. N. Pitts, "Photochemistry," Wiley, New York, N. Y., 1966, p 783, presents an excellent description of the experimental details involved in this system.

(25) H. Kokubun, *Z. Electrochem.*, **62**, 599 (1958).

(26) A. Weller and W. Urban, *Angew. Chem.*, **66**, 336 (1954).

hydrogen abstraction processes, which are known[27] to occur through excited triplet states. In addition, no triplets could be detected by electron spin resonance measurements (77°K) when a 10^{-4} *M* solution of **1** in 1:4 methanol–ethanol was irradiated with the full emission from a mercury vapor lamp. On the other hand, irradiation of 1,2-diketopyracene (**3**) under identical conditions produced a strong esr spectrum characteristic of methyl radicals. This type of spectrum has been observed[28] upon irradiation of a number of other aromatic carbonyl compounds (triplet-state sensitizers) in alcohol glasses.

B. Nature of the Intermediates.—In an effort to further elucidate the mechanism of this reaction with regard to the steps following the formation of the excited singlet species, a detailed study was made of the photolysis of the quinone **1** in neutral methanol. These experiments resulted in the isolation of a red intermediate, **5**.

The photolysis of **5** under conditions identical with those used in the photolysis of the quinone led to the formation of the diester, dimethyl 5,6-acenaphthenedicarboxylate (**2**). That the photolysis of this intermediate was a less efficient process than that of the quinone **1** was indicated by a determination of the quantum efficiency for the disappearance of **5** in methanol. A value of 0.10 ± 0.01 was obtained by monitoring the disappearance of the absorption (shoulder) at 4820 Å during the photolysis. This compares with a value of 0.30 for disappearance of **1** in methanol (Table III).

The solutions used for the *product* study were sufficiently concentrated (10^{-3}–10^{-4} *M*) to allow dimerization of the initially formed ground-state intermediates to occur. Since the red intermediate had a molecular weight (determined by vapor osmometry in methylene chloride solution) in excess of 500 (537 ± 18), dimerization is indicated.

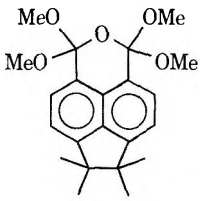
An attempt to elucidate the structure of this dimeric intermediate by a combination of chemical and spectroscopic techniques has not been successful to date. Further work will be required to establish the structure of this material.

Photolysis of the quinone **1** in a methanol solution containing methoxide ion resulted in formation of a new compound, **4**. This compound also formed when the red intermediate was treated with a solution of sodium methoxide in methanol. It was not found, however, on treatment of diester **2** with a similar solution.

The infrared spectrum of this compound did not exhibit hydroxyl or carbonyl absorptions but instead exhibited a strong ether absorption at ν 1250 cm^{-1}. The only peak observed in the nmr spectrum of **4** was a large singlet at τ 6.28 due to equivalent methoxyl protons. The ultraviolet spectrum exhibited bands with λ_{max}^{MeOH} at 225 and 310 mμ. Acenaphthylene derivatives generally have absorptions in the 320–350-mμ region (*i.e.*, acenaphthylene, 322 mμ; dimethyl 5,6-acenaphthylenedicarboxylate, 335 mμ), while acenaphthene compounds exhibit these absorptions at shorter wavelengths (*i.e.*, dimethyl 5,6-acenaphthenedicarboxylate, 315 mμ). Thus, it appears that the compound does not have unsaturation at the 1,2 position. Since the nmr spectrum could only be obtained in CD_3OD solution, where the undeuterated solvent has peaks in the τ 6.5 region, it was impossible to observe absorption due to the benzylic protons. The solubility of **4** in methylene chloride was insufficient to give an accurate molecular weight determination by vapor osmometry.

The mass fragmentation pattern of **4** exhibited strong peaks at *m/e* 268, 237 (base peak), 194, 178, 151, and 150. This spectrum was very similar to that of dimethyl 5,6-acenaphthylenedicarboxylate.[30] Since the other spectroscopic evidence indicates that **4** is not an unsaturated ester, we conclude that the molecular ion derived from **4** is very unstable and fragments with loss of oxygen and methanol to give the *m/e* 268 species. Fragmentation of this species then occurs by processes similar to those described for other pyracene derivatives.[29]

On the basis of the spectroscopic evidence, **4** is



4

postulated to be an ortho ester. Its formation may occur by attack of methoxide ion on the red intermediate followed by dissociation and solvolysis.

It is highly unlikely that a dimeric species was formed in the solutions used for the *kinetic* studies, since the concentration of quinone was only 10^{-5} *M*. Thus, our scheme (*vide supra*) indicates that at this concentration the diester was formed solely from the diketene.

Photoreactions in Aprotic Solvents.—The possibility of photocycloaddition of olefins to **1** prompted an investigation of the photochemistry of **1** in cyclohexene. This type of reaction has been reported to occur with 9,10-phenanthraquinone and various olefins.[30]

Irradiation of a cyclohexane solution of **1** was carried out for 24 hr with 3500-Å light. No changes in the absorption spectrum or the appearance of the solution were noted during this time. However, the photolysis of **1** in cyclohexene solution under identical conditions resulted in disappearance of the absorption at 3080 Å in the spectrum of **1**. In addition, the solution gradually became intensely fluorescent (blue). Column chromatography of the yellow oil formed in this reaction led to the isolation of a mobile liquid and a small amount of pale yellow solid.

Preparative gas–liquid chromatography of the liquid was carried out and two products were isolated. The minor product, a nonfluorescent liquid, was found to be a mixture of compounds with very similar retention times. The mass spectrum of this mixture showed a peak at *m/e* 162 (1.5%) and strong peaks at *m/e* 81 (54%) and 68 (100%) in addition to a number of other moderately strong peaks between *m/e* 98 and 27. The

(27) N. J. Turro, "Molecular Photochemistry," W. A. Benjamin, New York, N. Y., 1965, p 139.

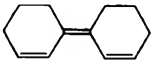
(28) A. Terenin, V. Rylkov, and V. Klolmagorov, *Photochem. Photobiol.*, **5**, 543 (1966), and references cited therein.

(29) J. A. Castellano, F. M. Beringer, and R. E. K. Winter, unpublished work.

(30) M. B. Rubin and R. A. Reith, *Chem. Commun.*, 431 (1966).

major peaks in the nmr spectrum consisted of a complex multiplet between τ 7.5 and 8.5 due to the saturated ring protons, a singlet at τ 6.3 (presumably due to protons on tertiary carbon atoms), and a multiplet at τ 4.25 due to olefinic protons. These results indicate that the mixture consists of bi-2-cyclohexen-1-yl (6) and 2-cyclohexenylcyclohexane (7). The strong peak at *m/e* 68 suggests the presence of 7. The formation of this fragment has been reported[39] to occur through loss of a methyl radical from various cycloalkyl derivatives.

The major product (8), a blue fluorescent liquid,



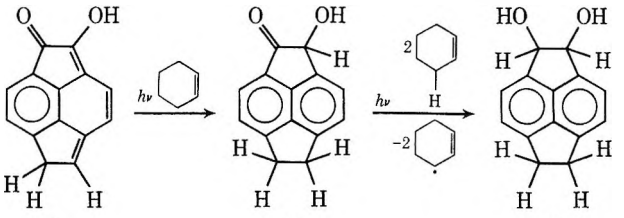
8

was initially believed to be 1,1′-bicyclohexenyl. However, the infrared, nmr, and mass spectrum and gas chromatographic retention time of an authentic sample of 1,1′-bicyclohexenyl did not coincide with those of 8.[31] The nmr spectrum of 8 exhibited two broad complex multiplets (12 H) in the τ 7.8–8.5 region due to saturated ring protons and a sharp multiplet (4 H) centered at τ 4.45 due to olefinic protons. The mass spectrum (70 eV) showed the molecular ion peak at *m/e* 160 (2%) and strong peaks at *m/e* 79 (33%), 80 (69%), and 81 (base peak).[32] Symmetrical cleavage of the molecular ion to give cyclohexenyl radical cation (*m/e* 80) suggested 1,1′-dehydro-2,2′-bicyclohexenyl as the structure for 8. The nmr spectrum confirms this assignment.

The pale yellow solid was chromatographed and two fractions were obtained. This first fraction had a mass spectrum which exhibited major peaks at *m/e* 212, 194, 152, 166, and 165. Since these peaks were also found in the spectrum of 1,2-dihydroxypyracene, it appeared that this compound formed from 1. The second fraction exhibited a mass spectrum with weak peaks at *m/e* 109, 97, 81, 79, and 67, which are characteristic of bicyclohexenyl derivatives. This material appeared to be polymeric.

Mechanism of Photoreactions in Aprotic Solvents. — The luminescence spectrum of pyracycloquinone (1) in aprotic solvents at 77°K shows a high intersystem crossing efficiency for transition from the first excited singlet state to the first excited triplet state. In addition, the triplet state was found to have a long lifetime. These facts present strong evidence that the species responsible for formation of the photoproducts in aprotic solvents was the first excited triplet state of 1. Since the excitation of 1 was achieved with 3500-Å light, it was presumed that n → π^* excitation was involved. The isolation of products which could only have been formed through hydrogen abstraction processes is consistent with this hypothesis.

The low quantum efficiency for disappearance of 1 concomitant with the relatively high yield of C_{12} hydrocarbons indicated that a radical chain process was involved. Thus, the initiation process is postulated to proceed through abstraction of allylic hydrogen atoms from cyclohexene by the n → π^* triplet state of pyracycloquinone. The triplet states of ketones 9 and 10 would, by appropriate hydrogen abstraction processes, give additional cyclohexenyl radicals and result in complete reduction of 1 to 1,2-dihydroxypyracene (11). Hydrocarbons are produced by chain



9 10 11

propagation steps through attack of the cyclohexenyl radical on cyclohexene. This would result in the formation of C_{12} hydrocarbons as well as oligomeric polycyclohexenes.

A process which competes with these reactions is dimerization of cyclohexenyl radicals to produce 6. As the concentration of C_{12} hydrocarbons (such as 6, cyclohexenylcyclohexane, cyclohexylcyclohexane) increases, they compete with cyclohexene in the initial allylic hydrogen abstraction reaction. Abstraction of the allylic hydrogens at the bridgehead carbon atoms of 6 should be more facile than those of cyclohexene (due to the intermediate formation of a tertiary radical) and would account for the formation of 8.

The by-product formation of 6 has been reported to occur in the photolysis of cyclohexene solutions of ethyl chloroformate,[33a] maleic anhydride,[33b] diethyl maleate,[33c] benzoyl diazomethane,[33d] biacetyl,[33e] and ethyl pyruvate.[33e] All of these reactions have been postulated to occur through allylic hydrogen abstraction by free radicals. In the last two cases, the n → π^* triplet of the carbonyl compound was postulated to be the initiating species. It is interesting to note, however, that 8 was not isolated as a product of any of these reactions.

Conclusions

The photolysis of pyracyloquinone in protic solvents proceeds through a singlet encounter complex which is attacked by the solvent to yield ground-state intermediates. These intermediates condense to form thermally stable quinoid species which are converted to diesters photochemically. Thus, overall benzenoid–quinoid valence isomerism occurs upon photoexcitation of pyracyloquinone in protic solvents.

The photolysis of pyracyloquinone in cyclohexene, however, yields bicyclohexenyl derivatives which are postulated to form through abstraction of hydrogen from the solvent by the first excited triplet state of pyracyloquinone, which is reduced in the process.

These results present an example of a compound which reacts from either a singlet or a triplet state depending upon the protic nature of the solvent medium.

(31) The nmr spectrum of 1,1′-bicyclohexenyl (CCl_4) exhibited similar intense multiplets (16 H) for the saturated ring protons at τ 7.85 and 8.38 but the resonance at τ 4.30 due to olefin protons (2 H) was half the intensity of the corresponding peak in the spectrum of 8. The mass spectrum exhibited base peaks at *m/e* 162 (molecular ion) and 79 with moderately strong peaks at *m/e* 81 and 80.

(32) In the low voltage (14 eV) mass spectrum, however, the base peak was found at *m/e* 80.

(33) (a) C. Pac and S. Tsutsumi, *Bull. Chem. Soc. Jap.*, **36**, 234 (1963); (b) J. A. Barltrop and R. Robson, *Tetrahedron Lett.*, 597 (1963); (c) P. de Mayo, S. T. Reid, and R. W. Yip, *Can. J. Chem.*, **42**, 2828 (1964); (d) G. S. Hammond, *J. Org. Chem.*, **29**, 1922 (1964); (e) P. W. Jolly and P. de Mayo, *Can. J. Chem.*, **42**, 170 (1964).

Experimental Section[34]

Materials.—The starting materials used for the preparation of the pyracene derivatives were either reagent grade compounds or were purified directly before use. Deuterated solvents were purchased from Merck Sharp and Dohme Co., Ltd., Montreal, Canada. *p*-Anisidine (Eastman Kodak) was recrystallized three times from water and three times from benzene to give colorless crystals, mp 57–58° (lit.[35] mp 57.2°). 1,1′-Bicyclohexenyl was purchased from Frinton Laboratories.

Elemental analyses were performed by B. L. Goydish and A. Murray of RCA Laboratories, Princeton, N. J.

Spectra.—Nmr spectra were recorded with a Varian Model A-60 spectrometer at 25°. The solvents used were deuteriochloroform, deuterioacetone, deuteriomethanol (CD_3OD), and carbon tetrachloride, with tetramethylsilane as internal standard. The mass spectra were recorded by Morgan-Schaffer Corp. with a Hitachi Perkin-Elmer RMU-6D spectrometer equipped with a heated direct inlet. Ionization was generally achieved with 70-eV electrons, but a lower voltage (12–14 eV) was used in an attempt to identify parent ions. Infrared spectra were recorded with a Perkin-Elmer Model 221 spectrophotometer (KBr disks) while the ultraviolet–visible spectra were recorded with a Cary 14R spectrophotometer.

Photochemical Equipment.—The preparative photochemical experiments with pyracyloquinone were carried out in Pyrex flasks and were conducted in a Rayonet reactor equipped with 16 8-W bulbs emitting at 3500 Å. The solutions were degassed by purging with argon for several hours directly prior to irradiation. The solvents used for all the photolysis studies were spectroquality reagents purchased from Matheson Coleman and Bell.

Pyracyloquinone.[13,14,36]—A solution of 17.60 g (0.114 mol) of acenaphthene in 1500 ml of carbon disulfide was prepared under nitrogen. After cooling in an ice–salt bath at −5°, 25.0 g (0.116 mol) of oxalyl bromide was added. The mixture was stirred vigorously and 62.50 g (0.234 mol) of fresh aluminum bromide was added over a period of 10–15 min. A black gum slowly formed and, after about 30–40 min, stirring became impossible and was discontinued. The mixture was allowed to warm to room temperature overnight. After the mixture was warmed to 35° for 30 min, the carbon disulfide was decanted. The black gum was treated with 1000 ml of cold 10% aqueous HCl and the mixture was stirred for 30 min. The dark brown solid was filtered and thoroughly washed with water before it was mixed with 7.5 g of Norit and 7.5 g of Celite filter aid. This mixture was suspended in 500 ml of 4% aqueous sodium bisulfite solution and the solution was heated for 30 min at 80°. The hot suspension was filtered and the filtrate was acidified to pH 1 with concentrated HCl. This solution was heated at 80° until a fluffy yellow solid formed. The mixture was allowed to stand for about 30 min, and the yellow solid was collected by filtration. The material was washed with water and anhydrous methanol and vacuum dried. The extraction process was repeated six times on the dark brown, Norit–Celite mixture to yield a total of 3.5 g (14.5% yield) of 1,2-diketopyracene, mp 288–290° dec. The material was recrystallized from dimethylformamide to give 2.0 g of yellow crystals, mp 303–305° dec (lit.[37] mp 309–311°).

A solution of 2.1 g (10 mmol) of 1,2-diketopyracene, 4.0 g (23 mmol) of *N*-bromosuccinimide, 150 ml of carbon tetrachloride, and a trace of benzoyl peroxide was refluxed for 8 hr. The solution was filtered hot to give 1.8 g (18 mmol, 91%) of succinimide. The filtrate was cooled, and the crystals which separated were collected to yield 2.0 g (5.5 mmol, 55%) of 5,6-dibromo-1,2-diketopyracene, mp 170–174° dec. This material was recrystallized from ethanol to give 1.0 g of pure product, mp 187–189° (lit.[13] mp 191°).

A solution of 1.0 g (2.8 mmol) of 5,6-dibromo-1,2-diketopyracene, 2.0 g (15 mmol) of potassium iodide, and 100 ml of acetone was refluxed for 24 hr. The solvent was removed *in vacuo*, and the residue was treated with a saturated aqueous solution of sodium thiosulfate. The orange solid was collected, washed with water, and vacuum dried. The solid was recrystallized from benzene to give 0.40 g (1.9 mmol, 71%) of pyracyloquinone (1), mp >350° (lit.[13] mp >350°). The ultraviolet, infrared (ν_{max}^{CO} 1680, 1730 cm^{-1}), nmr (CD_3COCD_3) [τ 1.60 (4 H), quartet (J_{AB} = 8 Hz), 2.38 (2 H) singlet] and mass spectrum were identical with those reported in the literature.[13,14]

Photolysis of Pyracyloquinone in Methanol. Prolonged Irradiation. A. Neutral Solution.—A degassed solution of 50 mg (0.25 mmol) of pyracyloquinone in 1000 ml of methanol was irradiated for 48 hr. After solvent removal, the residue was taken up in chloroform and chromatographed over 100 g of Florisil. Elution of the product with a large volume of chloroform was followed by its strong blue fluorescence. Evaporation of the solvent furnished 20 mg (0.074 mmol, 30%) of dimethyl 5,6-acenaphthenedicarboxylate (2), mp 170–175°. The nmr spectrum consisted of an AB quartet (aromatic protons) centered at τ 2.25 (4 H, $J_{AB} \leq 7$ Hz), a singlet at τ 6.12 (6 H) due to methyl protons, and a singlet due to bridge protons at τ 6.51 (4 H). The infrared, ultraviolet, and mass spectrum were identical with those of an authentic sample. In addition, a mixture of the photoproduct and the authentic sample melted at 170–175°.

B. Acid Solution.—A degassed solution of 25 mg (0.13 mmol) of pyracyloquinone, 4 mequiv of sodium methoxide, and 500 ml of methanol was irradiated for 65 hr. The solution was neutralized with 10 ml of a methanol solution containing 0.4 mequiv of sodium methoxide per 1 ml. The solvent was removed *in vacuo* and the residue was chromatographed as above to yield 11 mg (0.041 mmol, 33%) of dimethyl 5,6-acenaphthenedicarboxylate (2), mp 169–174°. The infrared and mass spectra were identical with those of the authentic sample.

C. Basic Solution.—A degassed solution of 25 mg (0.13 mmol) of pyracyloquinone, 4 mequiv of sodium methoxide, and 500 ml of methanol was irradiated for 42 hr. The solution was neutralized with 10 ml of a methanol solution containing 0.4 mequiv of sulfuric acid per 1 ml. After solvent removal, the residue was chromatographed as above. The fluorescence of the material eluted with chloroform, however, was very weak. Evaporation of the solvent produced 36 mg of white crystals, mp 205–206° dec. Characterization of this compound (4) by spectroscopic analysis is discussed in the text.

In order to establish that this compound was not formed as a result of methoxide ion atttack on the product diester, a solution of 8 mg of dimethyl 5,6-acenaphthenedicarboxylate in 2 ml of methanol was treated with several drops of methanolic sodium methoxide solution (0.4 mequiv/ml). The solution immediately became deeply colored (red). Neutralization of the solution with several drops of methanolic sulfuric acid solution (0.4 mequiv/ml) produced decolorization. The solvent was evaporated and the residue was taken up in a minimum amount of chloroform–methanol and filtered. The solvent was removed *in vacuo* to yield 6 mg (75%) of off-white solid. The infrared spectrum of this material was identical with that of the starting diester.

Photolysis of Pyracyloquinone in Methanol. Brief Irradiation.—A stirred, degassed solution of 50 mg (0.25 mmol) of pyracyloquinone in 1000 ml of methanol was irradiated for short periods of time. After each period of irradiation, an aliquot of the solution was transferred to a 0.100-cm quartz cell and the ultraviolet spectrum was recorded. The results of this analysis are shown in Figure 1. In a related experiment, a stirred, degassed solution of 80 mg (0.40 mmol) of pyracyloquinone in 1000 ml of methanol was also irradiated for short periods of time. An aliquot of the solution was removed after each period of irradiation and transferred to a 5.000-cm quartz cell. The visible spectral changes were recorded and it was established that pyracyloquinone was entirely converted to the red intermediate in about 30 min.

A series of experiments were conducted in order to establish the approximate rate of formation of dimethyl 5,6-acenaphthenedicarboxylate. This involved irradiation of degassed solutions of 50 mg of pyracyloquinone in 1000 ml of methanol for various time intervals and isolation of the diester by the procedure described above for long irradiation time. The results of this study are as follows [minutes of irradiation (% yield)]: 5 (3–5), 20 (8), 30 (16), 60 (21), 120 (26), 1440 (30).

The intermediacy of a red species was established by the following set of experiments. A stirred, degassed solution of 50 mg of pyracyloquinone in 1000 ml of methanol was irradiated for 30 min. The resulting deep green solution became deep red almost immediately after removal from the Rayonet reactor. This solution was refluxed for 24 hr under argon. The solution remained intensely colored during this period and no changes in the absorption spectrum were noted. At the end of this time, the solvent was removed *in vacuo* and the red residue was chro-

(34) All melting points are corrected.

(35) N. A. Lange, "Handbook of Chemistry," 10th ed, Handbook Publishers, Sandusky, Ohio, 1961.

(36) The assistance of Professor B. M. Trost, Department of Chemistry, University of Wisconsin, in providing this procedure is gratefully acknowledged.

(37) H. J. Richter and F. B. Stocker, *J. Org. Chem.*, **24**, 366 (1959).

matographed over 100 g of Florisil. Elution with a large volume of chloroform led to the isolation of 10 mg (15% yield) of dimethyl 5,6-acenaphthenedicarboxylate, mp 170–175°. Further elution with 500 ml of methanol gave 40 mg of a deep red, crystalline solid, mp >350° (turned black above 150°). This material was redissolved in 1000 ml of methanol and the resulting solution was degassed and irradiated for 26 hr. Work-up of the reaction mixture in the usual way led to the isolation of 13 mg (17% yield) of dimethyl 5,6-acenaphthenedicarboxylate.

In order to establish the course of the reaction in the presence of base, a stirred, degassed solution of 26.5 mg of pyracyloquinone in 500 ml of methanol was irradiated for 30 min, and the resulting red solution was treated with 10 ml of methanolic sodium methoxide (0.4 mequiv/ml). The very deep red solution was neutralized with 10 ml of methanolic sulfuric acid (0.4 mequiv/ml) and evaporated to dryness. The residue was chromatographed as above and 37 mg of a white, crystalline solid, mp 205–206° dec, was obtained. The infrared and mass spectra of this material were identical with those of the material obtained in the photolysis of pyracyloquinone in basic methanol. In addition, a 1:1 mixture of the two solids had a melting point of 205–206° dec.

A sample of the red intermediate was obtained by the following procedure. The photolysis of 50 mg of pyracyloquinone in 1000 ml of methanol was carried out in the usual way for 30 min. The solvent was removed *in vacuo* and the residue was chromatographed over Florisil. The diester was removed by elution with chloroform and the red band was eluted with methanol. The methanol was evaporated and the residue was chromatographed over Florisil with ethyl acetate as the eluent. Finally, the red solid was chormatographed over silica gel (Fischer), with ethyl acetate as the eluent. After a number of runs, about 30 mg of the red intermediate was obtained. Attempts at characterization of this compound by spectroscopic analysis were unsuccessful.

An attempt to monitor the reaction by infrared spectroscopy was made. A saturated solution of pyracyloquinone in methanol was prepared by stirring 10 mg of the diketene with 5 ml of methanol for several hours. The solution was filtered and the filtrate was introduced into a 1.00-mm infrared cell (sodium chloride windows). The cell was placed into a variable-temperature jacket (Beckman J-3), and cold (−78°) acetone was circulated through the unit. The cell was irradiated with an 8-W mercury vapor lamp (3500 Å) while the spectrum was scanned. Weak, broad absorptions in the 2000–2500-cm^{-1} range (due to a small amount of carbon dioxide) were observed but no sharp absorption indicative of ketene groups at 2100 cm^{-1}. Similar results were obtained whe a more viscous medium, polypropylene polyol (Union Carbide), was used as the solvent.

Photolysis of Pyracyloquinone in Methanol-*O*-*d*.—A degassed solution of 50 mg (0.25 mmol) of pyracyloquinone in 1000 ml of methanol-*O*-*d* was irradiated for 48 hr. The reaction mixture was worked up in exactly the same way as described above for the neutral methanol photolysis to yield 23 mg (0.075 mol, 30%) of dimethyl 1,2-dideuterio-5,6-acenaphthenedicarboxylate, mp 163–166°. This was recrystallized from methanol to give 9 mg of colorless solid: mp 167–170°; ν_{max}^{CO} 1725 cm^{-1}; mass spectrum (70 eV) *m/e* (rel intensity) 272 (40), 241 (100), 198 (10), 182 (30), 154 (30).

Photolysis of Pyracyloquinone in Ethanol.—A degassed solution of 25 mg (0.13 mmol) of pyracyloquinone in 1000 ml of ethanol was irradiated for 42 hr. The reaction mixture was worked up in exactly the same way as described above for the neutral methanol photolysis to yield 4.5 mg (0.015 mmol, 11%) of diethyl 5,6-acenaphthenedicarboxylate, mp 180–185°, ν_{max}^{CO} 1720 cm^{-1}. The mass spectrum showed the moderately intense peaks at *m/e* 152 and 180 which are observed in the spectrum of the dimethyl ester. However, the molecular ion of the diethyl ester is much less stable than that of 2 and fragmentation by a number of alternate pathways gives other peaks at *m/e* 268, 238, and 154.

Photolysis of Pyracyloquinone in 2-Propanol.—A degassed solution of 25 mg (0.13 mmol) of pyracyloquinone in 1000 ml of 2-propanol was irradiated for 40 hr. The reaction mixture was worked up in exactly the same way as described above for the neutral methanol photolysis to yield 5.3 mg (0.016 mmol, 13%) of diisopropyl 5,6-acenaphthenedicarboxylate, mp 143–146°, ν_{max}^{CO} 1710 cm^{-1}. The mass spectrum showed moderately intense peaks at *m/e* (rel intensity) 224 (15), 180 (23), and 152 (16) and a very low intensity peak for the molecular ion at *m/e* 326. Fragmentation processes characteristic of higher esters[38] were also observed in the spectrum (*m/e* 282, 240, and 238).

Photolysis of Pyracyloquinone in Benzene with *p*-Anisidine.—A degassed solution of 50 mg (0.25 mmol) of pyracyloquinone, 600 mg (4.9 mmol) of *p*-anisidine, and 50 ml of benzene was irradiated for 25 hr. The solvent was removed *in vacuo* and the residue was taken up in chloroform and filtered. The filtrate was evaporated to dryness to yield 57 mg (0.13 mmol, 51%) of crude 5,6-acenaphthenedicarboxylic acid di-*p*-methoxyanilide, mp 255–260° dec, ν_{max}^{CO} 1650 cm^{-1}. The mass spectrum did not exhibit a molecular ion peak (*m/e* 452) but a number of very weak peaks between *m/e* 451 and 330 were observed. The major fragments appeared at *m/e* (rel intensity) 329 (100), 180 (5), 152 (20), 123 (75), and 108 (92). The presence of species at *m/e* 180 (5) and 152 (20), which are characteristic of 5,6-disubstituted acenaphthene derivatives,[30] was again observed.

Photolysis of Pyracyloquinone in Cyclohexene.—A solution of 25 mg (0.13 mmol) of pyracyloquinone in 1000 ml of cyclohexene was degassed in the usual manner and irradiated for 24 hr. As the photolysis proceeded, the solution became intensely fluorescent (blue). The cyclohexene was removed *in vacuo* to yield 2.0 g of yellow, viscous oil. Chromatography of this material over Florisil with chloroform as the eluent led to the isolation of 1.93 g of a mobile, pale yellow liquid (A). Further elution of the column with methanol produced 60 mg of a pale yellow solid (B). Further separation of the liquid A into two fractions was accomplished by gas–liquid chromatography.[39] Under identical conditions, 1,1′-bicyclohexenyl had a retention time of 18.8 min. The major fraction, which had a retention time of 11.8 min, was characterized as 1,1′-dehydro-2,2′-bicyclohexenyl (8): ir 1690 cm^{-1} (C=C); nmr (CCl_4) τ 7.8–8.5 (12 H), 4.45 (4 H); mass spectrum (70 eV) *m/e* (rel intensity) 160 (2), 79 (33), 80 (69), 81 (100).

Anal. Calcd for $C_{12}H_{16}$: C, 89.94; H, 10.06. Found: C, 89.48; H, 10.51.

The minor fraction, which had a retention time of 2.4 min, was a nonfluorescent liquid. Gas chromatography of this liquid at a lower temperature showed it to be a mixture of products with very similar retention times. The mass spectrum of this mixture showed a molecular ion peak at *m/e* 162 and strong peaks at *m/e* 81 and 68 in addition to a number of other moderately strong peaks between *m/e* 98 and 27. The major peaks in the nmr spectrum (CCl_4) consisted of a complex multiplet between τ 7.5 and 8.5 due to the saturated ring protons, a singlet at τ 6.3 (presumably due to protons on tertiary carbon atoms), and a multiplet at τ 4.25 due to olefinic protons.

The solid B was chromatographed over Florisil and two fractions were obtained. The first fraction, which was isolated by elution with ether–methanol, had a mass spectrum which exhibited major peaks at *m/e* 212, 194, 152, 166, and 165. These peaks were also found in the spectrum of 1,2-dihydroxypyracene.[19] However, other peaks at low *m/e* values not present in this spectrum indicated that this material was impure.

The second fraction isolated from the chromatography of B had a very weak spectrum with peaks at *m/e* 109, 97, 81, 79, and 67.

Determination of Quantum Yields.[24]—All of the determinations were carried out with 10^{-5} *M* solutions of pyracyloquinone in the appropriate spectroquality solvents. The optical density of these solutions was high enough to absorb all incident light. A 14.00-ml aliquot of the solution was transferred to a 5.000-cm quartz cell. The cell was placed on an optical bench equipped with a Hanovia 150-W high-pressure mercury vapor lamp, 3650 Å filter (Oriel #6-572-3650), lens system, and mechanical shutter. The solution was degassed by a conventional[24] freeze–thaw technique under high vacuum. After each period of irradiation, the solution was agitated for several minutes, and the absorption spectrum was measured with the Cary 14R spectrometer. Measurements were made between 2 and 40% conversion of 1. Immediately before and after each run, a 6×10^{-3} *M* solution of potassium ferrioxalate was irradiated in the same cell for 60 sec. A 10.00-ml aliquot of this irradiated solution was withdrawn and transferred to a 25.00-ml volumetric flask. After the addition of 5.0 ml of a buffer solution and 2 ml of 1,10-phenanthroline solu-

(38) C. Djerassi, H. Budzikiewicz, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, San Francisco, Calif., 1967.

(39) Gas–liquid chromatography of A was carried out with an Aerograph Autoprep Model 700 equipped with a 6-ft column containing 10% silicone oil (SF96) on 60/80 firebrick. A column temperature of 110° and a flow rate of 100 ml of He per minute was used.

tion, the solution was made to volume and the absorbance at 5100 Å was measured. The number of ferrous ions produced per unit time was then determined from a standard calibration graph prepared by the reported procedure.[24]

Luminescence Studies.—The luminescence spectra were prepared with apparatus similar to that which was previously described.[24] The degassed solutions [conventional freeze (−78°)–thaw (25°) technique] were contained in 1.00-cm quartz cells which were sealed under vacuum.

Registry No.—**1**, 5253-87-2; **2**, 4599-96-6; **3**, 5254-01-3; **4**, 35191-44-7; **8**, 35140-90-0; dimethyl 1,2-dideuterio-5,6-acenaphthenedicarboxylate, 35140-91-1; diisopropyl 5,6-acenaphthenedicarboxylate, 35140-92-2; 5,6-acenaphthenedicarboxylic acid di-*p*-methoxyanilide, 35140-93-3; diethyl 5,6-acenaphthenedicarboxylate, 35140-94-4.

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The Photochemistry of Aryl Alkyl Carbonates. II. The Methoxyphenyl Ethyl Carbonates

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The photochemical reaction of the three methoxyphenol ethyl carbonates has been examined. Each of the compounds undergoes a photo-Fries type of reaction to produce methoxyhydroxybenzoates. A free-radical mechanism is proposed based on the substitution patterns observed in the products and on the quantum yields of the reactions. A minor reaction observed was the apparent free-radical displacement of the methoxy group by the carboethoxy radical to produce the corresponding hydroxybenzoate.

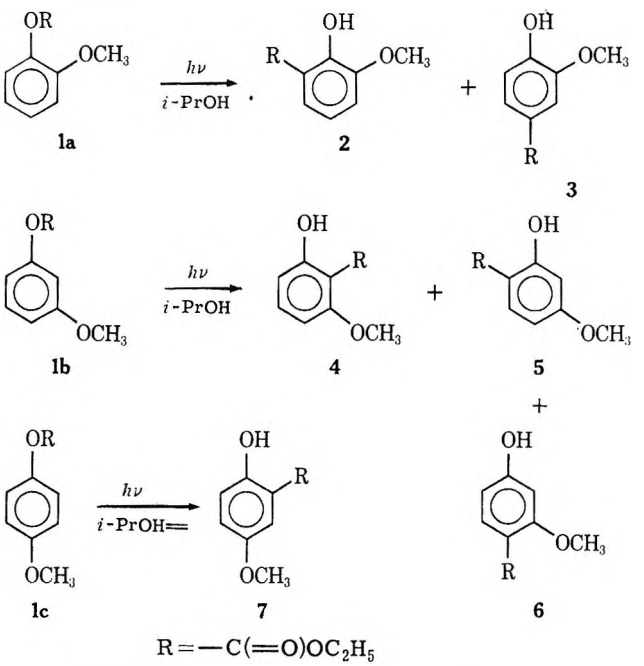
As part of our continuing study of the photochemistry of the aryl alkyl carbonates,[2] we would like to report our observations on the photolysis of the methoxyphenyl ethyl carbonates. Several investigators have shown that phenyl ethyl carbonate undergoes a photo-Fries type of reaction to give ethyl salicylate and ethyl *p*-hydroxybenzoate.[2,3] In contrast with this, we have shown that the chlorophenyl ethyl carbonates do not undergo the photo-Fries type of reaction, but instead undergo photodechlorination.[2] However, the methoxyphenyl ethyl carbonates do undergo a photo-Fries type of reaction and, in addition, an apparent free-radical displacement of the methoxyl group also occurs.

Results

o-, *m*-, and *p*-methoxyphenyl ethyl carbonate (**1a–c**) have been photolyzed in isopropyl alcohol, and the major reaction products are indicated as follows. In addition to the photo-Fries products obtained in this reaction, there is also obtained in each case a product that results from the substitution of the carboethoxy group ($-COOC_2H_5$) for the methoxyl group.

***o*-Methoxyphenyl Ethyl Carbonate (1a).**—Two photo-Fries-type products were isolated from the reaction mixture ethyl 2-hydroxy-3-methoxybenzoate (**2**), constituting about 10% of the reaction mixture, and ethyl 4-hydroxy-3-methoxybenzoate (**3**), constituting about 13% of the reaction mixture (see Table I). The remainder of the reaction mixture was mostly unreacted starting material.

Compound **2** was obtained by preparative gas–liquid partition chromatography (glpc) and its structure was ascertained through the use of nmr, ir, and mass spectroscopy (ms). The second photo-Fries-type product isolated was ethyl vanillate (**3**), a well-



characterized compound. A sample isolated from the reaction mixture by preparative glpc was identical in all respects to an authentic sample of ethyl vanillate. The presence of ethyl salicylate in the reaction mixture was shown by the identity of its mass spectrum with that of an authentic sample of ethyl salicylate.

(1) Abstracted from the Ph.D. Thesis of Ira Rosenberg, The George Washington University, 1969.

(2) Part I: E. Caress and I. Rosenberg, *J. Org. Chem.*, **36**, 769 (1971).

(3) C. Pac and S. Tsutsumi, *Bull. Chem. Soc. Jap.*, **37**, 1392 (1964); C. Pac, S. Tsutsumi, and H. Sakurai, *Kogyo Kagaku Zasshi*, **72** (1), 224 (1969).

TABLE I

PHOTOLYSIS OF *o*-METHOXYPHENYL ETHYL CARBONATE

Compound	Gc retention time, sec	Column temp, °C	%	Deviation, ±
Pinacol[a]	120	100	0.7	0.1
Phenol	52	150	0.3	0.1
o-Methoxyphenol	96	150	7.4	0.2
Ethyl salicylate	258	150	1.5	0.2
Unknown peak	288	150	0.5	0.1
o-Methoxyphenyl ethyl carbonate	520	150	66.2	0.7
Ethyl 2-hydroxy-3-methoxybenzoate	810	150	10.1	0.8
Ethyl 3-methoxy-4-hydroxybenzoate	1056	150	13.2	0.1

[a] Separate run.

***p*-Methoxyphenyl Ethyl Carbonate (1c) (see Table II).**—The photolysis of **1c** produced only one photo-Fries-type product; it was identified as ethyl 2-hydroxy-5-methoxybenzoate (**7**).

TABLE II

PHOTOLYSIS OF *p*-METHOXYPHENYL ETHYL CARBONATE

Compound	Gc retention time, sec	Column temp, °C	%	Deviation, ±
Pinacol	120	100	0.6	0.1
p-Methoxyphenol	210	150	12.9	0.5
p-Methoxyphenyl ethyl carbonate	684	150	49.1	0.6
Ethyl 2-hydroxy-5-methoxybenzoate	792	150	30.2	0.7
Ethyl *p*-hydroxybenzoate	960	160	7.2	0.5

One other compound was found in this reaction mixture and it was identified as ethyl *p*-hydroxybenzoate. The identification was made by comparing the reaction mixture compound's spectrum (obtained by glpc–ms) with that of a known sample of ethyl *p*-hydroxybenzoate.

***m*-Methoxyphenyl Ethyl Carbonate (1b).**—Three photo-Fries-type products were identified in the reaction mixture that resulted from the photolysis of **1b** (see Table III). Ethyl 4-hydroxy-2-methoxybenzoate (**6**) was identified on the basis of the following evidence. The nmr spectrum showed, in addition to the expected aromatic and aliphatic signals, a singlet at τ 2.2 (1 H), indicating that the compound is not a salicylate. That the compound is not a salicylate was also shown in the mass spectrum in that the base peak was found to be *m/e* 151 (M − C_2H_5O) rather than *m/e* 150 (M − C_2H_5-OH). If the material is not a salicylate, it must be either ethyl 4-hydroxy-2-methoxybenzoate (**6**) or ethyl 3-hydroxy-5-methoxybenzoate. The pattern of the reactions described in this paper (a point which will be developed later) strongly suggests that the compound must be **6**.

TABLE III

PHOTOLYSIS OF *m*-METHOXYPHENYL ETHYL CARBONATE

Compound	Gc retention time, sec	Column temp, °C	%
Pinacol	120	120	2.3
m-Methoxyphenol	180	150	4.7
Ethyl *m*-hydroxybenzoate	208	150	4.7
m-Methoxyphenyl ethyl carbonate	624	150	76.6
Ethyl 2-hydroxy-4-methoxybenzoate	684	150	2.1
Ethyl 2-methoxy-6-hydroxybenzoate	804	150	5.7
Ethyl 2-methoxy-4-hydroxybenzoate[a]		194	3.8

[a] Peak was eluted by programming the column temperature at 4°/min to 194° after the ethyl 2-methoxy-6-hydroxybenzoate had been eluted.

Ethyl 2-hydroxy-4-methoxybenzoate (**5**) and ethyl 2-hydroxy-6-methoxybenzoate (**4**) were identified in the reaction mixture as follows. Both materials were shown to be salicylates on the basis that their mass spectra show base peaks at *m/e* 150. A sample of the material comprising the larger peak in the chromatograph was obtained by preparative glpc. The nmr of this material has a singlet (1 H) at τ −0.8 (confirming the salicylate assignment) and expansion of the aromatic region of the spectrum does not show the doublet, doublet, triplet pattern found for **2**, thus indicating the absence of the 1,2,3 substitution pattern on the benzene ring. The smaller peak, identified as compound **4**, could not be successfully collected because of its small size and its closeness to the large, unreacted starting material peak. The above evidence clearly indicates that the larger peak is quite reasonably identified as compound **5** and the smaller peak must, therefore, be compound **4**.

There was also found in this reaction mixture a compound with a molecular ion at *m/e* 166 whose mass spectrum does not correspond to that of phenyl ethyl carbonate, ethyl salicylate, or ethyl *p*-hydroxybenzoate. On the basis of this nonidentity and its fragmentation pattern, this compound is identified as ethyl *m*-hydroxybenzoate.

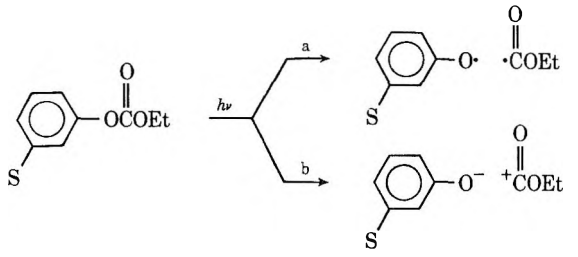
The quantum yields for the conversion of the aryl ethyl carbonates to the various products were determined and found to be 0.21 and 0.20 for the *o*- and *p*-methoxyphenyl compounds, respectively. The *m*-methoxy isomer, however, had a quantum yield of only 0.02.

Discussion

In our study of the photolysis of aryl alkyl carbonates we have been trying to examine the mechanism of the reaction by observing the effect of various ring substituents on the course of the reaction. Our hypothesis has been that, by changing from electron-donating to electron-attracting substituents, we could induce a change in mechanism. For example, Zimmerman[4] has shown that, in the case of meta-substituted benzyl acetates, a change from free-radical to ionic solvolysis occurs as you change from electron-attracting to electron-donating substituents. In his example, the electron-donating methoxyl substituent is able to stabilize in the excited state the developing carbonium ion. In our case, Zimmerman's approach would lead one to predict that an electron-withdraw-

(4) H. Zimmerman, in "Advances in Photochemistry," Vol I, W. Noyes, Jr., G. Hammond, and J. Pitts, Jr., Ed., Interscience, New York, N. Y., 1963, p 200.

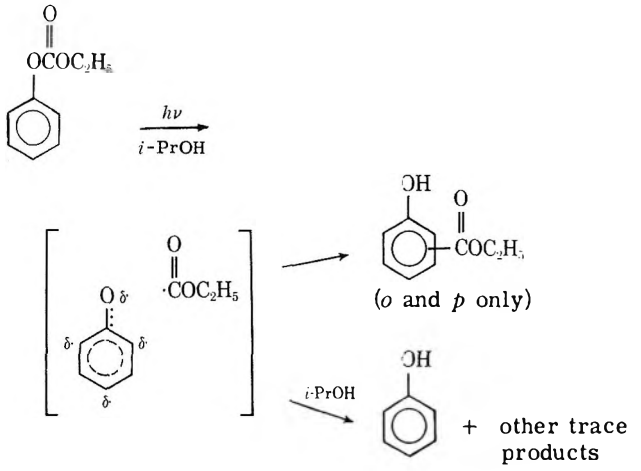
ing group will stabilize in the excited state a developing phenoxide anion. Therefore, pathway b would be



favored by electron withdrawal in the excited state by substituent S. Pathway a, which is analogous to the mechanism generally accepted for the related photo-Fries reaction, would then be the pathway expected for cases where S was electron-donating in the excited state. Thus, we would predict a change in mechanism from free radical to ionic as we move from electron-donating to electron-withdrawal substituents. The change in mechanism might be indicated in the trends of the quantum yields, shifts in the proportions of the various products, and/or in the nature of the products.

Recently, we reported our results on the chlorophenyl ethyl carbonate[2] series, which followed a non-photo-Fries reaction course, and now we are reporting our results on the methoxyphenyl ethyl carbonates. Our results for the methylphenyl ethyl carbonates will be reported in the near future.[5]

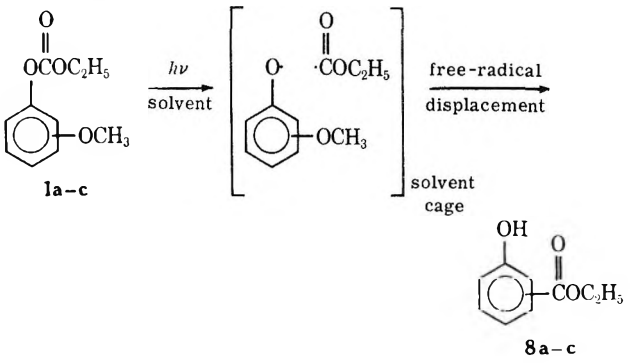
The three photoreactions in the present study each give products that result from carboethoxy substitution in all of the open ortho and para positions. These products are consistent with the mechanism proposed by Kobsa[6] for the photo-Fries reaction, which is outlined below for the phenyl ethyl carbonate case.



The observation that the quantum yield for the *m*-methoxyphenyl ethyl carbonate is an order of magnitude lower than for the ortho- and para-substituted compounds indicates that stabilization of an anionic excited state is not occurring. The greater quantum yield observed for the latter two compounds is attributed to the expected resonance stabilization of a phenoxy radical by *o*- and *p*-methoxy substitution, stabilization which cannot occur in meta-substituted phenoxy radicals.

(5) I. Rosenberg, *Diss. Abstr. B*, **31**, 1839 (1970).
(6) H. Kobsa, *J. Org. Chem.*, **27**, 2293 (1962).

The substitution of the carboethoxy group for the methoxy group can be explained as a radical displacement reaction, examples of which have been reported in the similar photo-Fries reaction.[6,7]



A molecular pathway for the photo-Fries reaction has been proposed[8] and could be written for the reactions presented in this paper. However, the recent report by Kalmus and Hercules[9] of their success in obtaining spectroscopic evidence for the presence of phenoxy radicals and substituted cyclohexadienones in the photo-Fries reaction seems to substantiate the mechanism proposed by Kobsa. On the basis of this spectroscopic evidence and our results, a molecular pathway does not appear to play an important part in these reactions.

The multiplicity of the photo-Fries reaction has been recently studied in the case of *p*-tolyl acetate[8] and phenyl benzoate.[10] Trecker and coworkers conclude from their results that for *p*-tolyl acetate the overall transformations occur from the singlet excited state or from a very short-lived triplet state. In the case of phenyl benzoate, Plank concludes that the triplet state is the reacting species. We are presently investigating the multiplicity of the reactive state in the photolysis of the aryl ethyl carbonates.

Experimental Section

The pmr spectra were obtained using a 60-MHz Hitachi Perkin-Elmer high-resolution nmr spectrometer, Model R-20. The spectra were obtained in carbon tetrachloride and perdeuterioacetone solution using tetramethylsilane as an internal reference. The chemical shift values are reported in ppm, using the τ scale. The mass spectra were obtained with an ionizing voltage of 70 eV, using a Perkin-Elmer Model 270 gc–ms, which is a medium-resolution, double-focusing mass spectrometer interfaced with a gas chromatograph. Gas chromatographic analyses and sample collections were carried out on a Hewlett-Packard Model 200 gas–liquid partition chromatograph equipped with a thermal conductivity detector, a Model 240 temperature programmer, and a Disc integrator equipped Honeywell recorder. The analytical work was performed using a 6 ft $\times$ $^1/_8$ in. column packed with 10% UC-W98 on Chromosorb A. Sample collections were made using a 3 ft $\times$ $^1/_4$ in. column packed with 20% SE-52 on Chromosorb A.

The methoxyphenyl ethyl carbonates, 1a–c, were prepared from ethyl chlorocarbonate and the appropriate phenol, using the method of Smith and Kosters.[11] It was found that, by allowing

(7) R. Finnigan and D. Knudson, *Chem. Ind. (London)*, 1837 (1965).
(8) M. Sandner, E. Hedaya, and D. Trecker, *J. Amer. Chem. Soc.*, **90**, 7249 (1968).
(9) C. E. Kalmus and D. M. Hercules, Abstracts, 163rd National Meeting of the American Chemical Society, Boston, Mass., April 9–14, 1972, ORGN No. 28.
(10) D. Plank, *Tetrahedron Lett.*, **No. 50**, 4365 (1969); **No. 52**, 5423 (1968).
(11) G. Smith and B. Kosters, *Chem. Ber.*, **93**, 2403 (1960).

the reaction mixtures to stand for 24–48 hr longer than indicated, the yields could be increased over those reported. The boiling points, yields, and uv maxima (in isopropyl alcohol solution) are as follows: **1a** (ortho) {bp 99–100° (0.5 Torr) [lit.[11] 106–107° (1.6 Torr)]; 82%; 270 mμ (ε 6.63 × 10³), 276 (ε 5.85 × 10³)}; **1b** (meta) {bp 171–172° (39 Torr) [lit.[11] 111–113° (2.5 Torr)]; 79%; 270 mμ (ε 2.06 × 10³), 276 (2.02 × 10³)}; **1c** (para) {bp 84° (0.01 Torr) [lit.[11] 111–113° (2.2 Torr)]; 69%; 276 mμ (ε 2.26 × 10³), 282 (ε 1.89 × 10³)}.

The photolyses of the methoxyphenyl ethyl carbonates were carried out as follows. The carbonate (5 ml, 5.3 g, 0.027 mol) was dissolved in 250 ml of Spectrograde isopropyl alcohol and the solution was placed in a standard immersion-well-type photochemical apparatus. The solution was stirred with a magnetic stirrer and purged with nitrogen for 15 min. The solution was then irradiated with a 450-W Hanovia[12] medium-pressure mercury lamp through a Corex filter sleeve. The photolyses were carried out under a positive nitrogen pressure for the following lengths of time: **1a**, 24 hr; **1b**, 45 hr; **1c**, 15.5 hr. The composition of the reaction mixtures can be found in Tables I–III.

A control reaction was carried out for each of the methoxyphenyl ethyl carbonates, and gc analysis showed that no dark reaction had occurred. The photolyses were monitored by gc and were stopped when it appeared that no new products were being formed. During the course of the reactions there was a smooth conversion of starting material to products. The product peaks increased in size throughout the photolysis period and did not plateau or diminish in size. This observation strongly suggests that the observed products were not labile under the conditions of the reaction. At the conclusion of the photolysis, the solvent was evaporated under reduced pressure and the remaining solution was analyzed by gc and gc–mass chromatography and were analyzed further by nuclear magnetic resonance and by infrared spectroscopy.

Product Identification.—The pinacol and the phenols that were formed in the reactions were identified by their retention times.

Ethyl Salicylate.—The retention time, infrared spectrum, and mass spectrum were identical with those obtained from an authentic sample.

Ethyl 2-Hydroxy-3-methoxybenzoate (2).—The nmr spectrum, the ir spectrum, and the mass spectrum obtained from a sample collected from the gc support this identification. The ir spectrum (liquid film) shows absorption at 3100 (O–H stretch) and 1660 cm^{-1} (C=O stretch), both of which are common for intramolecularly-hydrogen-bonding compounds.[13] The nmr spectrum shows the following signals: τ −0.8 (s, 1 H), 2.6–3.4 (m, 3 H), 5.6 (q, 2 H), 6.3 (s, 3 H), and 8.6 (t, 3 H). The intramolecular nature of the hydrogen bonding is also revealed by the position of the singlet (1 H) at τ −0.8. Dyer[14] states that, at ordinary concentrations, phenols absorb in the region of τ 2.3 to 4.0. *o*-Hydroxybenzoates, however, show very strong intramolecular hydrogen bonding and absorb in the region of τ −2.5 to −0.5. For example, methyl salicylate absorbs at τ −0.58. The value of τ −0.8 measured for **2** clearly establishes the relative positions of the hydroxyl and benzoate groups. The position of the methoxyl group relative to the hydroxyl group is fixed in the starting compound.

Expansion of the aromatic region of the nmr spectrum of **2** shows that there are two sets of doublets at 2113 and 2105 Hz and 2088 and 2808 Hz. A triplet appears at 2074, 2066, and 2058 Hz. When the absorption system was spin-decoupled by irradiating the 2066-Hz signal of the triplet, both of the doublets collapsed into singlets. These results are in accordance with the behavior expected for three aromatic protons on adjacent carbons, thus confirming the 1,2,3 substitution pattern on the aromatic ring.

The mass spectrum is as follows and confirms the structural assignment (*m/e*, % of base peak): 197, 4.1; 196, 28.5; 151, 26.0; 150, 61.0; and 122, 100. It is possible to use ms to distinguish between salicylates and *p*-hydroxybenzoates because the major mode of fragmentation for salicylates is the loss of alcohol from the molecular ion, while the major mode of fragmentation for *p*-hydroxybenzoates is the loss of the alkoxy group.[15] In the mass spectrum of **2** there is a major peak at *m/e* 150 (M − C_2H_5OH), while the peak at *m/e* 151 is relatively small.

Ethyl 3-Methoxy-4-hydroxybenzoate (Ethyl Vanillate) (3).—The nmr spectrum and the ir spectrum of this compound, as isolated by preparative gc from the reaction mixture, were identical with those obtained from an authentic sample.

Ethyl 2-Hydroxy-4-methoxybenzoate (5).—A sample was isolated from the reaction mixture and the nmr and mass spectral data obtained are nmr τ −0.8, (s, 1 H), 2.4 (d, 1 H), 3.7 (m, 2 H), 5.6 (q, 2 H), 6.2 (s, 3 H), and 8.6 (t, 3 H); mass spectrum *m/e* (% of base peak) 197 (4.1), 196 (27.5), 151 (36.0), 150 (100), and 122 (35).

Ethyl 2-Methoxy-6-hydroxybenoate (4).—The identification was made on the basis of the mass spectrum obtained by gc–ms, which is mass spectrum *m/e* (% of base peak) 197 (3.2,) 196 (23.5), 151 (27.0), 150 (100), and 122 (26.0).

Ethyl 2-Methoxy-4-hydroxybenzoate (7).—A sample was obtained by preparative gc and the identification was made on the basis of the following nmr and mass spectral data: nmr τ 2.27, (s, 1 H), 2.7–3.5 (m, 3 H), 5.65 (q, 2 H), 6.2 (3 H), and 8.6 (t, 3 H); mass spectrum *m/e* (% of the base peak) 197 (4.5), 196 (25.0), 151 (100), 150 (13.0), and 122 (7.0).

Ethyl 2-Hydroxy-5-methoxybenzoate.—A sample was isolated by preparative gc and the identification was made on the basis of the following spectral information: nmr τ −0.2, (s, 1 H), 3.0 (m, 3 H), 5.6 (q, 2 H), 6.2 (s, 3 H), and 8.6 (t, 3 H); ir (liquid film) 3110 and 1669 cm^{-1}; mass spectrum *m/e* (% of base peak) 197 (2.1), 196 (20.0), 151 (20.0), 150 (100), and 122 (17.0). The nmr spectrum shows a τ −0.2 singlet (1 H) and the ir has bonds at 3110 (O–H) and 1669 cm^{-1} (C=O). These are all indicative of strong intramolecular hydrogen bonding as found in *o*-hydroxybenzoates. The mass spectrum has a *m/e* 176 molecular ion and a base peak at *m/e* 150 (M − C_2H_5OH); the latter peak is indicative of a salicylate.

Ethyl *p*-Hydroxybenzoate.—The identification was made on the basis of the identity of the mass spectrum of an authentic sample with that obtained from the gc peak using gc–ms.

Ethyl *m*-Hydroxybenzoate.—The identification was made on the basis of the relative retention time of this material compared to that of ethyl salicylate and ethyl *p*-hydroxybenzoate, and on the mass spectrum obtained by gc–ms. The material showed a molecular ion at *m/e* 166 and has a fragmentation pattern similar to but not identical with ethyl salicylate and ethyl *p*-hydroxybenzoate.

Quantum Yields.—The quantum yields[16] for the conversion of the methoxyphenyl ethyl carbonates to products are as follows: **1a**, 0.21; **1b**, 0.02; **1c**, 0.20. The actinometer used was the benzophenone–benzohydrol type described by Beckett and Porter.[17] The apparatus used to determine the quantum yields was a Rayonet photochemical reactor equipped with a Merry-go-round (The Southern New England Ultraviolet Co., Middletown, Conn.).

Registry No.—**1a**, 1847-84-3; **1b**, 35030-97-8; **1c**, 22719-84-2; **2**, 35030-98-9; **4**, 35030-99-0; **5**, 35031-00-6; **6**, 35031-01-7; **7**, 22775-40-2.

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(12) Engelhard-Hanovia, Inc., Newark, N. J.

(13) L. Bellamy, "The Infrared Spectra of Complex Molecules," Wiley, New York, N. Y., 1959, pp 103 and 184.

(14) J. Dyer, "Applications of Absorption Spectroscopy of Organic Compounds," Prentice-Hall, Englewood Cliffs, N. J., 1965, p 90.

(15) H. Budzikiewicz, C. Djerassi, and D. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, San Francisco, Calif., 1967, pp 200–201.

(16) The determinations were made by Patricia Ann Tatem as part of her M.S. thesis at The George Washington University.

(17) A. Beckett and G. Porter, *Trans. Faraday Soc.*, **59**, 2038 (1963).

Photosensitized Monomerization of 1,3-Dimethyluracil Photodimers

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The photomonomerization of the four 1,3-dimethyluracil (DMU) photodimers in the presence of a variety of photosensitizers is described. The reactions lead to the recovery of DMU in yields of up to 100%. The syn dimers are monomerized faster than the anti ones. An excited charge-transfer complex (exciplex) is proposed as the intermediate in these reactions. Monomerization of the photodimers could also be achieved with $AlCl_3$.

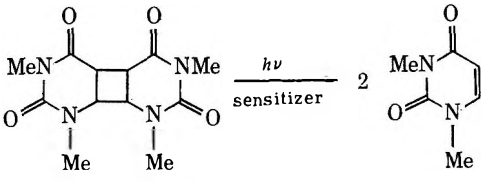
Irradiation of DNA or RNA with ultraviolet light has been reported to induce chemical and physical changes in these biopolymers.[2] These changes were found to be responsible for the damage caused to the living system, and the major known reaction was the formation of cyclobutane dimers between two adjacent pyrimidine moieties.[3] The lesion caused by ultraviolet light on the biological system is usually photoreactivable; that is, the effects caused by ultraviolet light are reversed in part by subsequent irradiation with light of wavelengths longer than 330 nm. For example, illumination of ultraviolet-inactivated transforming DNA in the presence of some enzyme extracts resulted in an increase in the transforming activity. Photoreactivating activity has been observed also in many living systems, such as bacteria, yeast, and fish.[4] It has been shown that during this photoreactivating process thymine dimers formed in irradiated DNA were cleaved to yield the thymine monomer moieties.[4]

The mechanism by which the enzymic photoreactivation process operates is still obscure.[5] Several attempts aiming at the clarification of this point have been made,[6-8] however, without any final conclusion. The aim of the present investigation is to study photochemical reactions which might be relevant to the photoreactivation process and shed light on its mechanism. We have chosen the DMU dimers and a variety of photosensitizers as suitable models for this study.[9] The availability of the four isomeric dimers enables also the study of the stereoselectivity of these photomonomerization reactions. The present publication includes details of some photosensitized monomerization reactions of DMU dimers, mainly with quinones, and a proposal for a mechanism for these reactions.

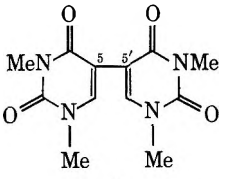
Results and Discussion

We have found that the four photodimers of DMU can be monomerized through irradiation of their solution with light of $\lambda > 290$ nm in the presence of a photosensitizer. The reactions can be represented as described in Scheme I.

SCHEME I



The trans,syn (dimer B)[10] and the cis,syn (dimer D) dimers were monomerized faster than the trans,anti (dimer A) and cis,anti (dimer C) dimers with the same photosensitizer under similar reaction conditions. The quantum yields of the monomerization sensitized by 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) of the trans,syn and cis,syn dimers were 0.77 and 0.7, respectively, while those of the trans,anti and cis,anti dimers were 0.22 and 0.26, respectively. It has been observed, with sensitizers of the same series, that the higher the electron affinity (EA) of the sensitizer the higher the efficiency of the monomerization. Comparison of the photosensitized monomerization of the four DMU dimers with some benzoquinones in benzene, acetone, and acetonitrile indicated that the process is fastest in acetonitrile. Bis-5,5′-(1,3-dimethyl)uracil (I) was formed as a by-product in some of the reactions of the syn dimers, while none of this product could be



I

observed in reactions of the anti dimers.[10] The reactions studied and the results obtained are summarized in Table I.

The progress of the reactions was followed through the increase in the absorption at the 265-nm region and by thin layer chromatography. Isolation of DMU and I, when formed, was achieved by column chromatography (silica gel). I was characterized by comparison with an authentic sample.[11] When chloranil was used as a photosensitizer, dihydrochloranil accompanied the formation of I (from the syn dimers), whereas none of the former could be detected in reactions where I was absent (with the anti dimers). Dihydrochloranil was isolated and characterized by comparison with an authentic sample. No reaction could be observed in the dark, even after heating of the reaction mixture to 50°; also light of $\lambda > 290$ nm failed to monomerize the dimers in the absence of a photosensitizer. Mono-

(1) In partial fulfillment of the requirements for a Ph.D. thesis submitted to the Feinberg Graduate School, 1971.

(2) For reviews see (a) K. C. Smith, *Radiat. Res. Suppl.*, **6**, 54 (1966); (b) R. B. Setlow, *Progr. Nucl. Acid Res. Mol. Biol.*, **8**, 257 (1968); (b) J. G. Burr, *Advan. Photochem.*, **6**, 193 (1968); (d) E. Fahr, *Angew. Chem., Int. Ed. Engl.*, **8**, 578 (1969).

(3) K. C. Smith and P. C. Hanawalt, "Molecular Photobiology," Academic Press, New York, N. Y., 1969, pp 62–68, and references cited therein.

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(7) A. Wacker, *et al.*, *Photochem. Photobiol.*, **3**, 369 (1964).

(8) C. Helene and M. Charlier, *Biochem. Biophys. Res. Commun.*, **43**, 252 (1971).

(9) Preliminary communication: I. Rosenthal and D. Elad, *ibid.*, **32**, 599 (1968).

(10) D. Elad, I. Rosenthal, and S. Sasson, *J. Chem. Soc. C*, 2053 (1971).

(11) H. Ishihara and S. Y. Wang, *Nature (London)*, **210**, 1222 (1966).

Table I
Photosensitized Monomerization of the Four 1,3-Dimethyluracil Photodimers

Photosensitizer	$E_{1/2}^{red}$,[a] eV	EA,[b] eV	E_T, kcal/mol	Solvent	Irradiation time, hr	Monomerization %[g] A	B	I	C	D	I
DDQ	−0.51	1.9	55.5[c]	Benzene	1[d]	0	60	0	34	50	0
				Acetone	1[d]	49	99	1	83	99	1
				Acetonitrile	1[d]	96	100	0	100	100	0
p-Chloranil	−0.01	1.37	57.2	Benzene	2[d]	0	26	29	0	22	10
				Acetone	2[d]	9	59	28	5	82	14
				Acetonitrile	2[d]	9	78	19	5	87	6
2,5-Dichloro-1,4-benzoquinone				Benzene	2[d]	0	3	31	0	1	0
				Acetone	2[d]	8	10	62	2	28	36
				Acetonitrile	2[d]	8	13	55	2	31	31
Tetracyanoethylene	−0.24	2.2		Acetonitrile	8[e]	44	59	0	59	76	0
o-Chloranil		1.5		Acetonitrile	8[e]	3	26	7	3	24	1
2,4,7-Trinitrofluorenone		1.1	64.4[c]	Acetonitrile	3[e]	5	41	27	2	64	11
				Acetone	18[d]	7	32	68	4	76	21
1,3,5-Trinitrobenzene		0.7		Acetonitrile	16[e]	25	13	9	1	14	6
				Acetone	18[d]	0	6	22	0	8	12
1,4-Benzoquinone	+0.51	0.7		Acetonitrile	8[e]	0	9	0	0.5	8	0
1,4-Naphthoquinone	+0.71	0.7	57	Acetonitrile	8[e]	10	35	40	1	31	3
2-Methyl-1,4-benzoquinone	+0.77	0.64		Acetonitrile	8[e]	0	12	8	0	12	4
				Acetone	18[d]	6	23	19	5	23	9
2-Bromo-1,4-naphthoquinone				Acetone	18[d]					32	33
2-Amino-1,4-naphthoquinone				Acetone	18[d]					4	0
9,10-Anthraquinone	+0.94	0.5	62	Acetonitrile	4[e]	3	58	23	3	56	11
				Acetone	18[d]	14	50	30	4	37	24
1,2,4-Tribromobenzene				Acetonitrile	22[e]	16	16	0	11	21	0
9-Fluorenone			53	Acetonitrile	16[e]	0	2	0	0	0.5	0
Hexachlorobenzene		0.5	70	Acetone	18[d]	3	20	0	0	18	0
Aluminum chloride				Acetonitrile	3[f]		60	0		34	0

[a] Half-wave reduction potential. See G. Briegleb, *Angew. Chem., Int. Ed. Engl.*, **3**, 617 (1964). [b] Electron affinity. [c] See Experimental Section. [d] Hanau Q81 high-pressure mercury vapor lamp (Pyrex filter). [e] Hanovia 200-W high-pressure mercury vapor lamp (Pyrex filter). [f] Hanovia 450-W high-pressure mercury vapor lamp (Pyrex filter). [g] A, trans,anti; B, trans,syn; C, cis,anti; D, cis,syn.

merization could be observed while leaving the reaction mixtures on the bench in the laboratory, due to the absorption of visible light by the appropriate sensitizer. It could also be achieved by exposure of powdered mixtures of the dimers with DDQ or *p*-chloranil to ultraviolet light or sunlight, resulting in good yields of DMU.

The reactions described operate through light absorption by the photosensitizer, as seen from the absorption spectra of the systems. The transfer of the excitation energy from the sensitizer to the dimer can be performed by several routes.

$$S \xrightarrow{h\nu} S^* \qquad (a)$$
$$S^* + MM \longrightarrow 2M$$

$$S + MM \longrightarrow \{S\text{-}MM\} \xrightarrow{h\nu} \{S\text{-}MM\}^* \qquad (b)$$
$$\{S\text{-}MM\}^* \longrightarrow 2M$$

$$S \xrightarrow{h\nu} S^*$$
$$S^* + MM \longrightarrow \{S\text{-}MM\}^* \qquad (c)$$
$$\{S\text{-}MM\}^* \longrightarrow 2M$$

S = photosensitizer; M = monomer; MM = dimer

The first route (a) involves an energy transfer process which may be of a singlet–singlet or a triplet–triplet nature. The singlet–singlet energy transfer process can be eliminated due to the absorption spectra of the dimers and the photosensitizers, the former absorbing at shorter wavelength than the latter.[12] The vertical triplet energy transfer process seems to be improbable, since sensitizers with high triplet energies, such as acetone, acetophenone, and benzene, did not lead to monomerization of any of the dimers. On the other hand, photosensitizers with relatively low triplet energies were effective in these reactions. The triplet energy of 5,6-dihydro-1,3-dimethyluracil has been used as the approximate triplet energies of the DMU dimers.[6,13] We derived the triplet energy of the former from its phosphorescence spectrum, and found it to be 67.5 kcal/mol. This number is higher by 10–12 kcal/mol than the triplet energies of the sensitizers (*p*-chloranil or DDQ) which were most efficient in the photomonomerization process. Therefore, we assume that a triplet–triplet energy transfer either vertical or nonvertical,[14] does not operate in these reactions, due to the large differences in the triplet energies of the reactants. The alternative mechanism (route b) involves the formation of a ground state complex between the quinone and the dimer. The ultraviolet, infrared, and nmr spectra of the reaction mixture do not indicate any formation of a ground state complex.[15] Similar results were obtained from an X-ray powder picture of the mixture of the quinone and the dimer. Further evidence against a ground state charge-transfer complex was derived from studies on the effect of temperature on the rate of the photomonomerization. We

(12) A. A. Lamola in "Technique of Organic Chemistry," Vol. 14, P. A. Leermakers and A. Weissberger, Ed., Interscience, New York, N. Y., 1969, pp 37–42, and references cited therein.

(13) The direct determination of the triplet energies of the dimers involved difficulties, due to the instability of the dimers to light in their absorption region (see ref 10).

(14) N. J. Turro, "Molecular Photochemistry," W. A. Benjamin, New York, N. Y., 1965, pp 182–183, and references cited therein.

(15) *Cf.* E. M. Kosower, *Progr. Org. Chem.*, **3**, 81 (1965).

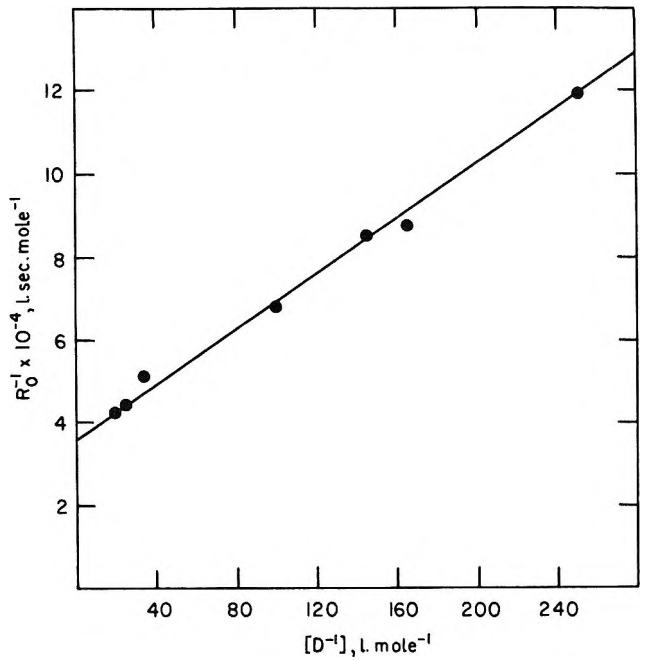

Figure 1.—Effect of initial concentration of dimer D on the rate of photomonomerization sensitized with DDQ.

have found that the latter increases with raise of temperature (temperature range 3–59°). This observation eliminates a mechanism involving a ground state charge-transfer complex, since the association constant of such a complex decreases with a rise in temperature.[16]

A plot of the reciprocal of the rate of photomonomerization (R_0, see Experimental Section) *vs.* the reciprocal of the concentration of the photodimer gave a straight line. An intercept at 3.57×10^4 and a slope of 3.37×10^2 were obtained with dimer D, while DDQ served as the photosensitizer (Figure 1). These results indicate that the photosensitized monomerization process involves an interaction of an excited species with a ground state molecule.[17] Since route a, which would involve such a process, is eliminated, it is most plausible that route c represents the mechanism of the monomerization, *i.e.*, that it proceeds through the formation of a complex between the excited photosensitizer and a ground state dimer molecule (exciplex).[18] Results obtained with the *p*-benzoquinones as sensitizers indicate that those sensitizers with higher electron affinities were more efficient in monomerizing the dimers (see Table I). Therefore, we assume that the process involves the transfer of an electron from the dimer to the excited quinones, so that the resultant complex is of a charge transfer nature. The enhancement in the monomerization with the increase in the polarity of the solvent presents additional evidence for such an intermediate, which is stabilized in polar solvents.[19,20] Further evidence for the trend of the DMU dimers to act as electron donors is given in our observation that aluminum chloride cleaves the DMU photodimers. We have found that the addition of aluminum chloride to a solution of dimer A or C resulted in the cleavage of the dimer into DMU. Monomerization of dimer B or D in the presence of aluminum chloride could also be achieved, however, only upon irradiation of the mixture. The addition of aluminum chloride to a solution of dimer B or D resulted in a downfield shift of the cyclobutane protons in the nmr spectrum, indicating the formation of a complex, which is concerned with the transfer of an electron from the dimer to aluminum chloride. Beresford, Lambert, and Ledwith[21] proposed a cation radical as an intermediate in the cleavage of *trans*-1,2-di(carbazol-9-yl)cyclobutane by tris(*p*-bromophenyl)amine cation or by cerium(IV). This intermediate results from the transfer of an electron from the cyclobutane compound to the amine cation or the cerium salt. A similar mechanism might fit very well for the reactions described.

The photosensitized monomerization reactions of the DMU dimers show some stereoselectivity,[22] as dimers B and D (syn type) are monomerized faster than dimers A and C (anti type). This results, most probably, from the steric factors involved in the complex formation between the dimer and the excited sensitizer. In the syn dimers the two carbonyl groups, which are near the cyclobutane ring, point to the same direction in space; this spatial arrangement might, perhaps, suit better for a sensitizer molecule to fit itself into a close contact with the dimer.[23] It is also noteworthy that *o*-chloranil, although possessing a higher electron affinity than *p*-chloranil, was less efficient than the latter in the photomonomerization process.

We feel that the present experiments shed some light on the possible mechanism of the photoreactivation process, in which a photosensitized monomerization of pyrimidine cyclobutane dimers occurs. It should be noted that various photosensitizers might cleave the dimers by different mechanisms, and that they do not necessarily follow the mechanism proposed by us for the photomonomerization with the *p*-benzoquinones. It appears that factors involving electron affinities and chemical structure play a role in determining the ability of a photosensitizer to cleave pyrimidine cyclobutane dimers; therefore, these should be evaluated in addition to triplet energy considerations.

Experimental Section

Kieselgel (0.05–0.20 mm, Merck) was used for chromatography. Petroleum ether refers to the fraction of bp 60–80°. Ascending thin layer chromatography was performed on Kieselgel G (Merck); a mixture of acetone–petroleum ether was used as eluent. Nmr spectra were determined with a Varian A-60 instrument as solutions in $CDCl_3$, unless otherwise stated.

Experiments in solution were carried out at room temperature in an immersion apparatus; Hanau Q81 or Hanovia 200-W and 450-W high-pressure mercury vapor lamps were used as the light source, and were cooled internally with running water. Pyrex filters were employed. Agitation was effected by bubbling oxygen-free nitrogen through the reaction mixtures as well as by magnetic stirring.

(16) R. Foster, "Organic Charge-Transfer Complexes," Academic Press, New York, N. Y., 1969, p 189.

(17) O. L. Chapman and R. D. Lura, *J. Amer. Chem. Soc.*, **92**, 6352 (1970).

(18) *Cf.* S. L. Murov, R. S. Cole, and G. S. Hammond, *J. Amer. Chem. Soc.*, **90**, 2957 (1968).

(19) T. Foerster, *Angew. Chem., Int. Ed. Engl.*, **8**, 341 (1969), and references cited therein.

(20) Dr. A. A. Lamola informed us that he has reached a similar conclusion regarding the mechanism of anthraquinone-sensitized monomerization of thymine dimer. We are grateful to Dr. Lamola for disclosure of his results prior to publication.

(21) P. Beresford, M. C. Lambert, and A. Ledwith, *J. Chem. Soc. C*, 2508 (1970).

(22) *Cf.* E. Ben-Hur and I. Rosenthal, *Photochem. Photobiol.*, **11**, 163 (1970).

(23) *Cf.* N. C. Yang and W. Eisenhardt, *J. Amer. Chem. Soc.*, **93**, 1277 (1971), and ref 16, pp 195–201.

Photosensitized Monomerization of Dimer A with DDQ in Acetone.—A solution of dimer A (0.3 g, 1.07 mmol) and DDQ (0.3 g, 1.32 mmol) in acetone (150 ml) was irradiated (Hanau Q81) for 1 hr. The monomerization was followed by the increase in absorption at 265 nm. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel (50 g). Acetone–petroleum ether (1:4) afforded 1,3-dimethyluracil (0.15 g) followed by the starting dimer (0.14 g, eluted with a 3:7 mixture).

Other reactions, described in Table I, were run under similar conditions in the appropriate solvent. I, when formed, was eluted after DMU with a 3:7 mixture of solvent, while dimer B, C, or D was eluted with 4:6, 1:1, or 3:7 mixtures, respectively.

Photosensitized Monomerization of Dimer A with DDQ on Silica Gel.—A solution of dimer A and DDQ (1:1 ratio) was spotted on a silica gel plate, dried, and irradiated (Mineralight lamp Model R-51) for 30 min. The product was eluted with a mixture of acetone–chloroform (2:1) and was found to be identical with DMU.

Similar results were obtained while employing dimer B, C, or D and DDQ or *p*-chloranil.

Photomonomerization of Dimer A with DDQ in the Solid State.—A powder mixture of dimer A (28 mg, 0.1 mmol) in DDQ (22.7 mg, 0.1 mmol) was irradiated (Westinghouse sun lamp, Pyrex filter, at a distance of 25 cm) for 90 hr. Work-up indicated 8% monomerization.

Similar experiments with dimer B, C, or D indicated 14, 9, and 22% monomerization, respectively. Irradiation under similar conditions in the absence of DDQ indicated 3% monomerization of dimer B or D and no monomerization of dimer A or C. Exposure of the mixture of dimer D and DDQ to sunlight afforded 55% monomerization after 4 hr. No monomerization was observed in the absence of DDQ.

Monomerization of Dimer A with Aluminum Chloride.—A solution of dimer A (28 mg, 0.1 mmol) and aluminum chloride (0.3 g, 2.26 mmol) in acetonitrile (10 ml) was left in the dark at room temperature. A maximum at 265 nm gradually appeared. Work-up after 22 hr indicated quantitative monomerization.

Similar results were obtained with dimer C.

Photomonomerization of Dimer B with Aluminum Chloride.—A solution of dimer B (28 mg, 0.1 mmol) and aluminum chloride (0.3 g, 2.26 mmol) in acetonitrile (10 ml) was irradiated externally (Hanovia 450-W lamp, Pyrex filter) under nitrogen for 3 hr. The solvent was removed under reduced pressure and the residue was treated with a saturated aqueous solution of sodium acetate and extracted with chloroform. Further work-up led to DMU (60% yield).

A similar experiment with dimer D led to 34% monomerization. No monomerization of either dimer B or D with $AlCl_3$ could be observed in the dark even after heating the mixture to 70° for 4 hr.

Quantum Yield Determination in Monomerization of Dimer A with DDQ.—A solution of dimer A (28 mg, 0.1 mmol) and DDQ (22.7 mg, 0.1 mmol) in acetonitrile (10 ml) was irradiated externally (Hanovia 200-W lamp, Pyrex filter). The intensity of the incident light was reduced by the use of a net (optical density of 0.7 was employed). The degree of monomerization was determined according to the increase in the 265-nm maximum. Actinometry measurements with ferrioxalate were taken before and after every run.[24] A quantum yield of 0.22 was observed for the monomerization of dimer A.

(24) C. A. Parker, *Proc. Roy. Soc., Ser. A*, **220**, 104 (1953).

Similar determinations with dimers B, C, and D led to quantum yields of 0.77, 0.26, and 0.7, respectively.

Determination of the Triplet Energy of 1,3-Dimethyl-5,6-dihydrouracil.—The phosphorescence spectrum of the compound was determined on an Aminco-Bowman spectrophotofluorometer equipped with a Hg-Xe 200-W lamp and a photomultiplier (S-20, EMI 9558 QV). A solution of 1,3-dimethyl-5,6-dihydrouracil (2×10^{-2} *M*) in ethanol–methanol (1:4 mixture) was irradiated (Sovirel tube, 3 mm, λ 313 nm) at 77°K. The triplet energy was calculated according to the maximum emission at 430 nm (single maximum) and was found to be 67.5 kcal/mol.

Determination of the Triplet Energy of DDQ.—The phosphorescence spectrum of DDQ was determined on the Aminco-Bowman spectrofluorometer equipped with a photomultiplier (IP28). A solution of DDQ (10^{-3} *M*) in EPA (ethyl ether:isopentane:ethyl alcohol, 2:5:5) was irradiated (λ 295 nm) at 77°K. The triplet energy was calculated according to the maximum emission at 515 nm (single maximum) and was found to be 55.5 kcal/mol.

Determination of the Triplet Energy of 2,4,7-Trinitrofluorenone.—The determination was carried out as described above at 77°K using a 5×10^{-3} *M* solution in EPA (2:5:5) and λ 295 nm. The shorest wavelength maximum of emission was at 445 nm, corresponding to a triplet energy of 64.3 kcal/mol.

Dependence of the Rate of Monomerization on the Initial Concentration of the Dimer.—Solutions of dimer D (varying concentrations) and DDQ (22.7 mg, 0.1 mmol) in acetonitrile (10 ml) were irradiated externally (Hanovia 200-W lamp, Pyrex filter) while using a net of optical density of 0.7. The absorption at 265 nm was determined periodically. R_0, the reaction rates at $t = 0$, were obtained by plotting the amount of monomerization *vs.* time and extrapolation to $t = 0$. Experimental results are summarized in Table II.

Table II

Photosensitized Monomerization of Dimer D with DDQ

Initial amount of dimer, mol × 10^{-5}	R_0, mol $l.^{-1}$ sec^{-1} × 10^{-5}
4	0.83
6	1.15
8	1.18
10	1.47
30	2.15
40	2.25
50	2.38

Effect of Temperature on the Rate of Photomonomerization of Dimer D with DDQ.—Solutions of the dimer (28 mg, 0.1 mmol) and DDQ (22.7 mg, 0.1 mmol) in acetonitrile (10 ml) were irradiated at different temperatures (3, 25, 36, and 59°). The amount of monomerization as well as R_0 were determined as described above. R_0 values for the various temperatures were plotted *vs.* $1/T$ (T = absolute temperature) to give a straight line (Figure 1).

Registry No.—Dimer A, 17237-77-3; dimer B, 17237-75-1; dimer C, 17237-76-2; dimer D, 17237-74-0; 1,3-dimethyl-5,6-dihydrouracil, 4874-13-9; DDQ, 84-58-2; 2,4,7-trinitrofluorenone, 129-79-3.

Sesquiterpene Lactones of Sagebrush. New Guaianolides from *Artemisia cana* ssp. *viscidula*[1]

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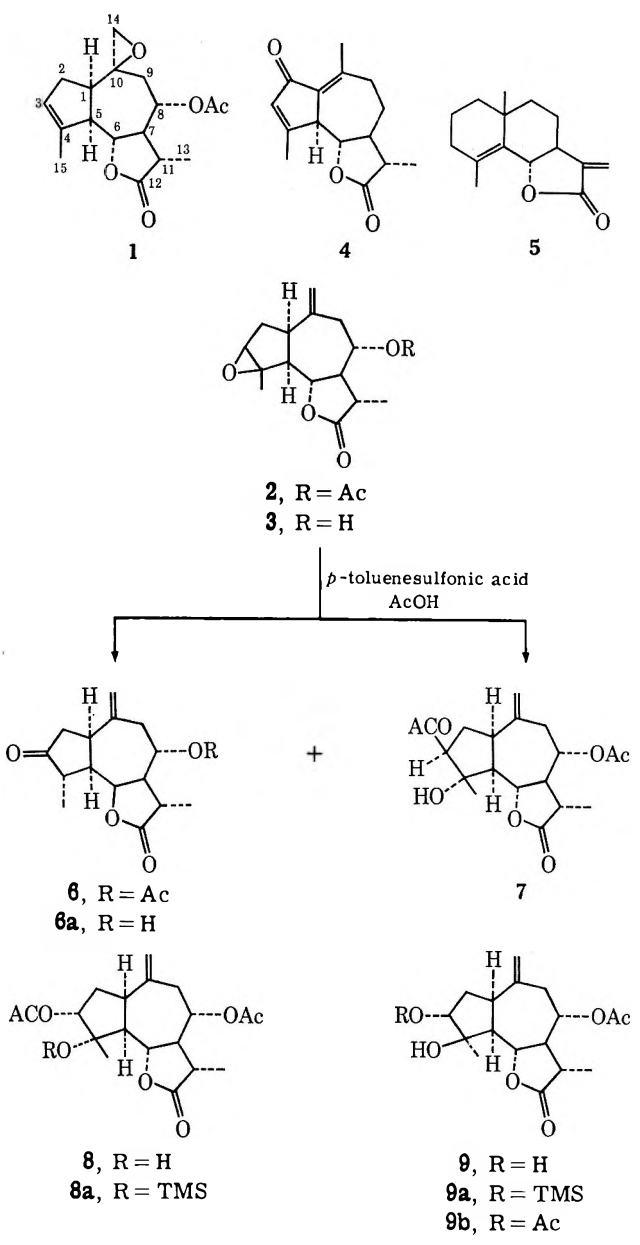
Four crystalline sesquiterpene lactones were isolated from samples of *Artemisia cana* Pursh ssp. *viscidula* (Osterhout) Beetle collected in Montana. Three of these lactones were found to be new guaianolides and were named viscidulin A (**1**), B (**2**) and C (**3**). The other compound was shown to be the known guaianolide deacetoxymatricarin (**4**). Structures of the new compounds were determined by their spectral properties and chemical reactions. Viscidulin B was related to known guaianolides by synthesis from cumambrin B (**10**) and conversion to isoamberboin (**6a**). The new guaianolides were correlated by acetylation of viscidulin C to viscidulin B and epoxidation of viscidulin B and viscidulin A to a common diepoxide (**18**).

The sesquiterpene lactones of *Artemisia cana* Pursh ssp. *viscidula* (Osterhout) Beetle were investigated as a part of this laboratory's program on chemical constituents of sagebrush in Montana.[3-6] Tlc of a sample of this subspecies (denoted by **ACV1**) collected near Eureka Basin, Mont., in August 1970, showed four distinct spots. One of these spots (second from top) corresponded with the known guaianolide deacetoxymatricarin (**4**). The other spots represented new guaianolides named viscidulin A (**1**), B (**2**), and C (**3**). Deacetoxymatricarin was absent in a sample (**ACV2**) collected the next August at Beaver Creek, Snowline Ranch, another Montana location. None of these samples, however, showed the presence of arbusculin B (**5**), reported for a sample of this subspecies collected in Wyoming.[7] These compounds were isolated from the plant materials by the established methods for separation of sesquiterpene lactones, and their structures were determined through spectroscopic studies and correlation with the known guaianolides isoamberboin[8] (**6a**) and cumambrin B (**10**).[9,10] See Chart I.

CHART I



Results and Discussion

Viscidulin B (2).—Elemental analysis and mass spectrum of viscidulin B showed the empirical formula of $C_{17}H_{22}O_5$ and a molecular weight of 306. The compound showed an ir band at 1779 cm^{-1} and a moderate uv end absorption indicative of a γ-lactone moiety. Further ir bands at 1735 and 1254 cm^{-1} coupled with C_{17} composition of the sesquiterpene lactone and mass spectral fagmentation peaks at *m/e* 264 (M − 42) and 246 (M − 60) suggested the presence of an acetate group. Aromatization of the molecule as discussed later gave chamazulene, showing the guaianolide carbon skeleton. Other features of the ir spectrum included a weak band at 1647 cm^{-1} and a medium band at 885 cm^{-1}, which suggested the presence of unsaturation. The lactone and the acetate groups accounted for four of the five oxygen atoms in the molecule, and the absence of any bands for hydroxyl or keto group in the ir and uv spectra suggested that the fifth oxygen is involved in the formation of a heterocyclic ring. This

(1) Part V in the series on "Chemical Constituents of Sagebrush;" for part IV, see *J. Org. Chem.*, **37**, 274 (1972).

(2) Established through a grant from Hoerner–Waldorf Corporation of Montana.

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(5) F. Shafizadeh, N. R. Bhadane, M. S. Morris, R. G. Kelsey, and S. N. Khanna, *ibid.*, **10**, 2745 (1971).

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(8) A. Corbella, P. Gariboldi, G. Jommi, Z. Samek, M. Holub, B. Drożdż, and E. Bloszyk, *Chem. Commun.*, 386 (1972).

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conclusion was supported by a positive epoxide test.[11,13]

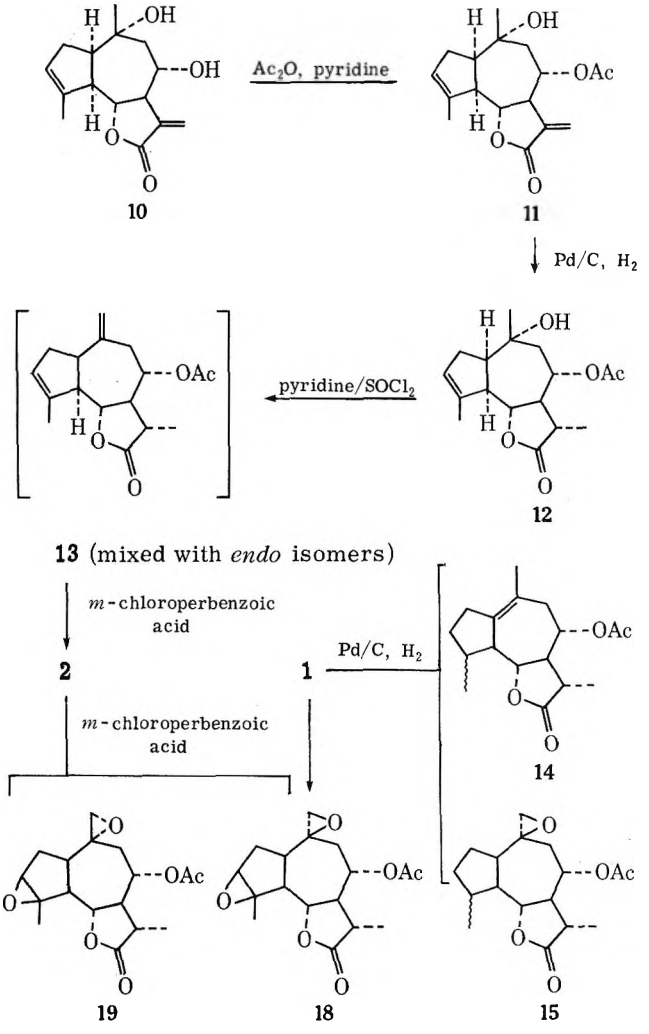
Presence of the above functions was confirmed by the nmr spectrum, which also indicated other structural features of the molecule. The C-6 lactone proton appeared as a triplet at 4.08 ppm (J = 10 Hz). The coupling of this proton indicated its trans-diaxial disposition to the hydrogens at C-5 and C-7.[13] A three-proton singlet at 2.03 ppm confirmed the presence of the acetate group, and the unsaturation of the molecule was signaled by two broad one-proton singlets at 4.88 and 5.03 ppm ($W_{1/2}$ = 4 Hz, characteristic of unconjugated *exo*-methylene protons).[5,14] The latter signals assigned to C-10 methylene protons were superimposed on a broad signal for the proton under the acetate group at C-8. Using benzene-d_6 or pyridine-d_5 as a solvent did not help to separate these signals. The C-3 proton of the C-3–C-4 epoxide function appeared as a singlet at 3.33 ppm. The position and nature of this signal was similar to the C-3 protons in cumambrin A epoxide[9] and arteglasin A.[13] A sharp three-proton singlet at 1.52 ppm and a three-proton doublet at 1.15 ppm (J = 6.5 Hz) were assigned to a methyl group attached to the C-4 of the epoxide ring and the C-11 secondary methyl group of the guaianolide structure, respectively. The first signal corresponded closely to the singlets for the C-4 CH_3 groups in cumambrin A epoxide[9] and arteglasin A[13] at 1.60 and 1.64 ppm, respectively. Assuming that the C-11 secondary methyl group is α oriented, as in many lactones of this genus like santonin and deacetoxymatricarin,[15] these data led to the structure 2 for viscidulin B.

Synthesis of Viscidulin B (2).—The principal features of structure 2 were confirmed by synthesis of viscidulin B from the known guaianolide, cumambrin B,[9,10] that was isolated in good yield from a Montana sample of *A. nova* Nels. This lactone (**10**) was acetylated to give the monoacetate cumambrin A (**11**) (Chart II). Controlled hydrogenation of cumambrin A gave crystalline dihydrocumambrin A[9] (**12**), which was dehydrated with pyridine and thionyl chloride. Tlc of the gummy product gave a single spot, but the nmr spectrum showed that it is a mixture of unsaturated lactones. Since the desired compound **13** could not be obtained in pure form, the mixture was used as such for the next reaction. Epoxidation of this gum with 1 mol equiv of *m*-chloroperbenzoic acid gave another complex mixture from which viscidulin B (**2**) was isolated as a crystalline product after extensive column chromatography.

Viscidulin B Derivatives.—The above synthesis does not establish the stereochemistry of the C-11 methyl and the C-3–C-4 epoxide groups. The α orientation of the methyl group was confirmed by conversion of viscidulin B (**2**) to the known guaianolide isoamberboin (**6a**)[8] through the opening of the epoxide ring.

Initial attempts for the opening of the epoxide ring by hydrogenation or treatment with acetic anhydride

CHART II



and *p*-toluenesulfonic acid[16] gave intractable mixtures. A dark-colored oil produced by the latter treatment, however, after chromatography on silica gel gave traces of a blue oil which presumably was an azulene. Finally, treatment of viscidulin B with *p*-toluenesulfonic acid in glacial acetic acid resulted in the opening of the epoxide function and gave a reaction mixture showing four major spots on tlc. Elaborate column chromatography of the mixture resulted in the separation of four components (**6**–**9**), three of which (**6**, **8**, and **9**) were obtained in crystalline form. Overheating of compound **7**, which could not be crystallized, gave chamazulene as a blue oil in sufficient quantity to be characterized as the crystalline trinitrobenzene adduct.[10,17]

The chemical structures of lactones **6**–**9** were determined through the following considerations.

Lactone **6** had the same empirical formula, $C_{17}H_{22}O_5$, as the parent compound and gave mass spectrum peaks at m/e 306 (M^+), 264 (M − 42), 246 (M − 60), and 218 (M − 60 − 28). Its ir spectrum showed γ-lactone (1769 cm^{-1}), cyclopentanone (1725 cm^{-1}), and acetate (1725, 1220 cm^{-1}) bands. The presence of the cyclopentanone ring was also confirmed by the uv absorp-

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(13) K. H. Lee, S. Matsueda, and T. A. Geissman, *Phytochemistry*, **10**, 405 (1971).
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(16) W. Herz, P. S. Subramaniam, P. S. Santhanam, K. Aota, and A. L. Hall, *J. Org. Chem.*, **35**, 1453 (1970).
(17) A. Meisels and A. Weizmann, *J. Amer. Chem. Soc.*, **75**, 3865 (1953).

tion at 294 nm (ε 24.14). Furthermore, the nmr data listed in Table I showed that the singlet at 3.33 ppm due to C-3 H in the parent compound (2) has disappeared and the singlet at 1.52 ppm due to C-4 CH_3 in the parent compound has been replaced by a doublet at 1.27 ppm (J = 6.5 Hz) as the only discernible changes after the reaction. These changes indicated that

i ii

group i in the original compound has been converted to ii in lactone 6. Deacetylation of this lactone gave the known guaianolide isoamberboin (6a),[8] confirming the spectroscopic structural deductions and the α orientation of the C-11 methyl group.

Lactone 7 could not be obtained in crystalline form, but it was purified chromatographically to give sharp ir and nmr spectra. The ir spectrum showed the presence of a hydroxyl group (3333 cm^{-1}) and unsaturation (1639 cm^{-1}) functions. In the nmr spectrum, the hydroxyl proton appeared as a broad singlet at 3.36 ppm which exchanged with D_2O. There were also two three-proton singlets at 2.07 and 1.97 ppm, indicating the presence of an additional acetate group. The new acetate group was evidently located at C-3 and the hydroxyl group at C-4 because the C-3 H gave a narrow triplet at 4.68 ppm (J = 5 Hz) instead of a singlet at 3.33 ppm in the parent lactone (2) and the C-4 CH_3 signal remained almost unchanged at 1.6 ppm. Other features of the nmr spectrum were closely similar to those of the starting material. These data indicated the diol–monoacetate opening of the epoxide group shown in structure 7. Presence of an additional acetate group was consistent with peaks at m/e 306 (M − 60), 246 (M − 60 − 60), and 231 (M − 60 − 60 − 15).

Lactone 8 was obtained as a crystalline compound. It had the empirical formula of $C_{19}H_{26}O_7$ and the same ir bands as lactone 7. It formed a monotrimethylsilyl derivative in which the hydroxyl band had disappeared. Attempted acetylation under normal conditions failed, indicating that the hydroxyl group must be tertiary. Presence of two acetate groups was suggested by the mass spectrum with peaks at m/e 366 (M^+), 324 (M − 42), 306 (M − 60), 264 (M − 60 − 42), and 246 (M − 60 − 60). These observations along with the nmr data (see Table I) indicated that lactone 8 is the C-3 epimer of lactone 7. The configuration of C-3 and C-4 substituents of these compounds was determined by the pyridine-induced chemical shift of the C-6 H and C-4 CH_3 nmr signals (Table I).

Lactone 9 gave the elemental analysis of $C_{17}H_{24}O_6$ and showed ir bands for hydroxyl (3483 and 3389 cm^{-1}), γ-lactone (1763 cm^{-1}), acetate (1742 and 1240 cm^{-1}), and unsaturation (892 cm^{-1}) groups. The mass spectrum with peaks at m/e 306 (M − 18), 264 (M − 60), and 246 (M − 60 − 18) also suggested the presence of hydroxyl and acetate groups. The lactone formed monotrimethylsilyl and monoacetyl derivatives under normal conditions. However, both of these compounds still showed ir bands for hydroxyl groups, suggesting the presence of a resistant tertiary hydroxyl group in the lactone. These observations, along with the nmr spectra of the lactone and its derivatives (Table I), supported the structure assigned to lactone 9, including configuration of C-3 and C-4 substituents determined from the pyridine-induced chemical shifts of C-6 H, C-4 CH_3, and C_3 H.

Viscidulin C (3).—Viscidulin C had the empirical formula of $C_{15}H_{20}O_4$ and gave a parent ion at m/e 264 in the mass spectrum. The ir spectrum showed the presence of hydroxyl (3496 cm^{-1}), γ-lactone (1745 cm^{-1}), and unsaturation (1639, 896 cm^{-1}) functions. The nmr spectral features (Table I) were similar to those of viscidulin B, except for a broad signal which appeared at 3.75 ppm instead of 4.7 to 5.0 ppm and the absence of the acetate singlet at 2.03 ppm. These differences suggested the presence of a hydroxyl group at C-8 instead of the acetate group. This conclusion was confirmed by acetylation of viscidulin C to viscidulin B.

Viscidulin A (1).—Viscidulin A had the empirical formula of $C_{17}H_{22}O_5$, a moderate uv end absorption, and an ir band at 1773 cm^{-1}, suggesting a γ-lactone structure as in viscidulin B and C. Other ir bands at 1733 and 1243 cm^{-1}, the C_{17} composition, and mass spectrum peaks at m/e 264 (M − 42) and 246 (M − 60) suggested the presence of an acetate group. A weak band at 1640 cm^{-1} indicated unsaturation of the molecule. As in 2, one oxygen atom appeared to form a heterocyclic ring, since no hydroxyl or carbonyl group was detected in the ir and uv spectra and viscidulin A gave a positive test for epoxide function.[11,12]

The nmr spectum of viscidulin A indicated the guaianolide structure 1. The lactone proton appeared as a triplet at 4.24 ppm (J = 9.5 Hz) and the proton under the acetate group gave a broad signal at 5.20 ppm (coupled with C-7 H and C-9 H_2) as in viscidulin B, indicating *trans*-lactone closure at C-6 and α orientation of the acetate group at C-8.[13] The secondary methyl group at C-11 gave a doublet at 1.27 ppm (J = 6.5 Hz). Comparison of the nmr spectrum of viscidulin A (1) with the spectra of viscidulin B (2) and C (3) showed the presence of an *exo*-epoxide group at C-10–C-14 in 1 instead of the *endo*-epoxide function at C-3–C-4 in 2 and 3. Conversely, the double bond in 1 appeared at C-3–C-4 instead of C-10–C-14 in 2 and 3.

Viscidulin A gave a two-proton singlet at 2.64 ppm for an $-OCH_2$ group instead of the one-proton singlet at 3.30 ppm due to the –OC-3 H group in 2 and 3. Also, there was a narrow one-proton multiplet at 5.47 ppm and a narrow three-proton doublet at 1.87 ppm (J = = 1 Hz) due to a $CH_3C{=}CH$ group instead of the two one-proton broad singlets at ~5.0 ppm due to the C-10 $=CH_2$ group and the three-proton singlet at ~1.50 ppm for the CH_3C-4 O in 2 and 3. The epoxide proton singlet at 2.64 ppm in viscidulin A corresponded closely to the singlet signal at 2.80 ppm for the $O^{14}CH_2$ in artefransin.[12] Furthermore, the olefinic proton in viscidulin A was coupled with the C-2 protons to give a narrow multiplet ($W_{1/2}$ = 5 Hz) as in cumamabrin B.[9,10] These data are only consistent with the mutual replacement of the epoxide and unsaturation functions in 2 and 3 to form 1.

Viscidulin A Derivatives.—Hydrogenation of viscidulin A gave a mixture of four products (14–17). One of these products was the expected dihydroviscidulin A

TABLE I

NMR DATA FOR VISCIDULIN GUAIANOLIDES AND RELATED COMPOUNDS

Compd	C-3 H	C-4 CH_3	C-6 H	C-8 H	C-10 $=CH_2$ C-10 CH_3	C-11 $=CH_2$ C-11 CH_3	C-14 H_2	Miscellaneous
1[a]	5.47 (nm, $W_{1/2}$ = 5)	1.87 (d, 1)	4.24 (t, 9.5)	5.20 (br)		1.27 (d, 6.5)	2.64 (s)	2.03 (s), OAc
2[a]	3.33 (s)	1.52 (s)	4.08 (t, 10)	(mx, with C-10 $=CH_2$ signals)	5.03, 4.88 (bs, $W_{1/2}$ = 4)	1.15 (d, 6.5)		2.03 (s), OAc
3[a]	3.30 (s)	1.48 (s)	3.95 (t, 9.5)	3.75 (br)	4.98, 4.90 (bs, $W_{1/2}$ = 5)	1.32 (d, 6.5)		2.12 (bs), OH
4[a]	6.18 (nm, $W_{1/2}$ = 4)	2.27 or 2.4	3.60 (t, 10)		2.27 or 2.4	1.23 (d, 6.5)		
6[a]		1.27 (d, 6.5)	4.01 (t, 9.5)	4.93 (br)	5.10, 4.78 (bs, $W_{1/2}$ = 2.5)	1.17 (d, 6.5)		2.05 (s), OAc
7[a]	4.68 (t, 5)	1.60 (s)	4.40 (t, 9.5)	(mx, with C-10 $=CH_2$ signals)	5.13, 5.02 (bs, $W_{1/2}$ = 4)	1.30 (d, 6.5)		2.07 (s), 1.97 (s), OAc 3.37 (bs), OH
7[b]	(mx, with C-10 $=CH_2$ signals)	1.85 (s)	4.50 (t, 9.5)	(mx, with C-10 $=CH_2$ signals)	5.02 (bs, $W_{1/2}$ = 8)	1.27 (d, 6.5)		1.98 (s), 1.93 (s),OAc
8[a]	(mx, with C-10 $=CH_2$ and C-8 H signals)	1.27 (s)	4.17 (t, 9.5)	(mx, with C-10 $=CH_2$ and C-3 H)	5.19, 5.10 (bs, $W_{1/2}$ = 4.5)	1.27 (d, 6.5)		2.07 (s), 2.09 (s), OAc
8[b]	(mx)	1.33 (s)	4.12 (t, 9.5)	(mx)	4.95 (bs, $W_{1/2}$ = 4)	1.25 (d, 6.5)		1.92 (s), 1.87 (s), AOc 5.75 (br), OH
8a[a]	(mx)	1.22 (s)	4.00 (t, 9.5)	(mx)	4.97 (bs, $W_{1/2}$ = 5)	1.15 (d, 6.5)		1.97 (s), strong, OAc 0.00 (s), OTMS
8a[b]	(mx)	1.25 (s)	4.03 (t, 9.5)	(mx)	4.95 (bs, $W_{1/2}$ = 5)	1.14 (d, 6.5)		1.96 (s), 1.92 (s), OAc
9[b]	4.10 (d, 3.4)	1.71 (s)	4.54 (t, 9.5)	(mx, with C-10 $=CH_2$ signals)	5.13, 5.02 (bs, $W_{1/2}$ = 4)	1.27 (d, 6.5)		1.97 (s), OAc 5.55 (bs), OH
9a[a]	3.79 (d, 3.5)	1.41 (s)	4.22 (t, 9.5)	4.78 (br)	5.07 (bs, $W_{1/2}$ = 4)	1.27 (d, 6.5)		2.05 (s), OAc 0.10 (s), OTMS
9a[b]	3.95 (d, 3.5)	1.57 (s)	4.52 (t, 9.5)	4.90 (br)	5.13, 5.03 (bs)	1.28 (d, 6.5)		1.93 (s), OAc
9b[a]	4.96 (d, 3.5)	1.38 (s)	4.21 (t, 9.5)	4.73 (br)	5.06 (bs, $W_{1/2}$ = 5)	1.30 (d, 6.5)		1.98, 1.94 (s), OAc
9b[b]	5.18 (d, 3.5)	1.49 (s)	4.53 (t, 9.5)	(mx)	5.08, 5.0 (bs, $W_{1/2}$ = 4)	1.27 (d, 6.5)		1.96 (s), strong, OAc
10[c]	5.48 (nm, $W_{1/2}$ = 5.5)	1.88 (s)	3.98 (t, 9.5)	3.70 (br)	1.22 (s)	6.12 (dd, 3.5, 1.5) 6.02 (dd, 3.5, 1.5)		
11[c]	5.53 (mx)	1.82 (s)	3.97 (t, 9.5)	5.00 (br)	1.12 (s)	6.03 (d, 3.0) 5.53 (d, 3.0)		4.35 (s), OH 2.12 (s), OAc
12[a]	5.46 (nm, $W_{1/2}$ = 5.5)	1.82 (s)	4.05 (t, 9.5)	5.08 (br)	1.15 (s)	1.21 (d, 7)		2.05 (s), OAc
14[a]		0.87 (d, 6.5)	3.79 (t, 10)	4.87 (br)	1.70 (s)	1.26 (d, 6.5)		2.03 (s), OAc
15[a]		0.87 (d, 6.5)	4.35 (t, 9.5)	5.12 (br)		1.23 (d, 6.5)	2.47 (s)	2.02 (s), OAc
18[a]	3.31 (s)	1.53 (s)	4.13 (t, 9.5)	5.13 (br)		1.25 (d, 6.5)	2.70 (s)	2.02 (s), OAc
19[a]	3.30 (s)	1.52 (s)	4.04 (dd, 10, 9)	5.04 (br)		1.29 (d, 6.5)	2.50 (s)	2.02 (s), OAc

[a] $CHCl_3$-*d* was used as the general solvent for the spectra discussed in the text. [b] Pyridine-d_5 was used as the solvent. [c] DMSO-d_6 was used as the solvent. The nmr spectra were obtained with the Varian HA-60 nmr spectrometer. TMS was used as the general internal standard (lock) and chloroform was used for 8a[a] and 9a.[a] Chemical shifts are quoted in δ (parts per million) and the signals are denoted by s, singlet; d, doublet; dd, doublet of doublets; t, triplet; br, broad; bs, broad singlet; nm, narrow multiplet; mx, mixed signals. Figures in parentheses denote coupling constants in Hz. $W_{1/2}$ represents the width of the signal in Hz at the half-height.

(**15**), which was obtained in crystalline form and readily recognized by its spectral properties.

The following consideration indicated that lactone **14**, which was also obtained as a crystalline material, is formed through the saturation of the C-3–C-4 double bond and elimination of the epoxide ring to produce a new double bond at C-1–C-10. This compound gave the elemental analysis of $C_{17}H_{24}O_4$ and mass spectral

peaks at m/e 232 (M − 60) and 217 (M − 60 − 15). Saturation of C-3–C-4 double bond was evident from the absence of a signal for an olefinic proton and the appearance of a new doublet at 0.87 ppm (J = 6.5 Hz) in the nmr spectrum. Elimination of the epoxide group to form a double bond at C-1–C-10 was reflected by the replacement of the two-proton singlet at 2.64 ppm with a three-proton singlet at 1.70 ppm for the CH_3 at C-10. Other nmr features of this lactone were similar to those of the parent compound.

The remaining hydrogenation products could not be obtained in sufficient quantities to allow complete identification. However, their ir spectra suggested the opening of the epoxide function.

The structural relationship between viscidulin A (**1**) and B (**2**) was established by epoxidation of these compounds to a common diepoxy derivative (**18**). The exo double bond in **2** also produced another isomer (**19**). Comparing the nmr data of this isomer (**19**) with the spectra of **1** and **18** showed a downfield position of C-6 H and C-8 H in latter compounds suggesting β orientation of the C-10 O bond of the epoxy groups in **1** and **18**.[18]

The sesquiterpene components of other Montana species of sagebrush and their taxonomical significance will be discussed in subsequent reports.

Experimental Section[19]

Plant Materials.—Two separate samples of *Artemisia cana* Pursh ssp. *viscidula* (Osterhout) Beetle were collected in Montana.[20] One of these samples, denoted by **ACV1**, was collected from Eureka Basin (T. 12 S, R. 4 W, Section 36) in August 1970 and the other, denoted by **ACV2**, was collected from Beaver Creek in the Snowline Ranch (T. 15 S, R. 6 W, NE quarter of Section 31) in August of 1971.

Tlc of ACV1[5,19] gave four distinct spots corresponding to viscidulin A, deacetoxymatricarin, viscidulin B, and viscidulin C. Tlc of **ACV2** was similar, except for the deacetoxymatricarin spot that was missing.

Isolation of Viscidulin A.—A portion of the **ACV1** sample (300 g) containing dried twigs and foilage was extracted with chloroform and processed in the usual manner.[5,21] The resulting dark sirup (15 g) was dissolved in a small amount of benzene and chromatographed on a 4 × 45 cm column of silica gel using benzene and benzene–diethyl ether of increasing polarity as eluents. One-hundred-milliliter aliquots were collected. The first ten aliquots of benzene eluted gums smelling of camphor and menthol. The following two fractions of the mixed solvent (95:5) gave a transparent gum which crystallized from ether–petroleum ether to give 15 mg of needles of viscidulin A (**1**): mp 124°; $[\alpha]_D$ +77.0° (*c* 2.14, $CHCl_3$); ir bands at 1773, 1733, 1243, and 1640 cm^{-1}; moderate uv end absorption; mass spectrum peaks at m/e 264 and 246; nmr data listed in Table I.

Anal. Calcd for $C_{17}H_{22}O_5$: C, 66.67; H, 7.19. Found: C, 66.90; H, 7.03.

Viscidulin A was also obtained from the **ACV2** sample.

Isolation of Deactoxymatricarin.—The next two fractions (13 and 14) eluted from the above column with the same solvent mixture gave a transparent gum which crystallized from chloroform–ether and gave 40 mg of needles of deactoxymatricarin: mp 203–204° (alone or in admixture with an authetic sample);[21] ir bands at 1779 (γ-lactone), 1685 (cyclopentenone), 1639, and 1618 (unsaturation) cm^{-1}; nmr data listed in Table I.

Isolation of Viscidulin B.—The next few fractions (15 to 20) eluted with benzene–ether (9:1) showed a single purple spot on tlc and crystallized from chloroform–ether to give 140 mg of viscidulin B: mp 132–133°; $[\alpha]_D$ + 59.8° (c 2.3, $CHCl_3$); ir bands at 1779, 1735, 1254, 1647, and 885 cm^{-1}; λ_{max} 206 nm (ϵ 1050); mass spectrum peaks at m/e 306, 264, and 246; nmr data listed in Table I.

Anal. Calcd for $C_{17}H_{22}O_5$: C, 66.67; H, 7.19. Found: C, 66.49; H, 7.24.

The same compound was also isolated from **ACV2**. Further elution of the column with more polar benzene–ether solvent mixtures (8:2, 7:3, and 6:4) and methanol gave colored gummy materials which could not be crystallized.

Isolation of Viscidulin C.—Extraction and processing of the **ACV2** sample (2.2 kg) as before gave 90 g of a sirup. Chromagraphy of this sirup on a 5 × 100 cm column of silica gel gave 2 g of viscidulin A, mp 124–125°, and 7.5 g of viscidulin B, mp 132–133°. Further elution of the column with more polar solvent mixtures (benzene–ether, 8:2, 7:3) gave a colorless gum which was crystallized from ether–petroleum ether to give 1.5 g of viscidulin C: mp 147°; $[\alpha]_D$ + 49.0° (c 1.955, $CHCl_3$); ir bands at 3496, 1745, 1639, and 836 cm^{-1}; uv end absorption; mass spectrum peaks at m/e 264 and 246; nmr data listed in Table I.

Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.18; H, 7.57. Found: C, 68.39; H, 7.46.

The above compounds gave a positive color test for epoxide function.[11,12]

Hydrogenation of Viscidulin B.—A solution of 50 mg of viscidulin B in 15 ml of ethanol was stirred with 5% Pd/C catalyst in a hydrogen atmosphere for 2 hr, when it had absorbed 1.2 mol of hydrogen. The catalyst was then filtered and the filtrate was concentrated to a gummy product which showed four close tlc spots, but could not be resolved to separate compounds. The mixture had ir bands at 3510 (hydroxyl), 1779 (γ-lactone), 1735, and 1240 (acetate) cm^{-1}.

Reaction of Viscidulin B with Acetic Anhydride and *p*-Toluenesulfonic Acid.[16]—A solution of 40 mg of viscidulin B in 5 ml of acetic anhydride was refluxed with 30 mg of *p*-toluenesulfonic acid for 1.5 hr. The reaction gave a colored oil, which was chromatographed on a silica gel column. Elution of the column gave traces of a blue oil and dark gummy materials.

Reaction of Viscidulin B with *p*-Toluenesulfonic Acid and Acetic Acid.[7]—A solution of 1.2 g of viscidulin B in 20 ml of glacial acetic acid was cooled and treated with 400 mg of *p*-toluenesulfonic acid. The reaction mixture was kept in the refrigerator for 3 hr. It was then poured on crushed ice and extracted with chloroform. The chloroform extract was washed with sodium bicarbonate solution and distilled water. Removal of solvent left a colorless gum which showed four spots on tlc. Column chromatography of this gum gave lactones **6**, **7**, **8**, and **9** in pure form.

Lactone **6** was crystallized from ether–petroleum ether: yield 250 mg; mp 132°; ir bands at 1769, 1725, and 1220 cm^{-1}; λ_{max} 294 nm (ϵ 24.14); mass spectrum peaks at m/e 306, 264, 246, and 218; nmr spectrum listed in Table I.

Anal. Calcd for $C_{17}H_{22}O_6$: C, 66.67; H, 7.19. Found: C, 66.25; H, 7.29.

Lactone **7** was obtained as a chromatographically pure gel: yield 180 mg; ir bands at 3333, 1769, 1730, 1639, and 1235 cm^{-1}; mass spectrum peaks at 306, 246, and 231; nmr data listed in Table I.

Heating of this lactone formed a blue oil which condensed on the wall of the flask. The crude product was extracted with petroleum ether and purified by chromatography to give 12 mg of chamazulene as a deep blue oil. The pure oil on treatment with trinitrobenzene gave purple fibrous needles of the adduct, mp 132–133° (lit.[10,17] 132–133°).

Lactone **8** was crystallized from methanol as fine flakes: yield 96 mg; mp 192°; ir bands at 3571, 1770, 1730, 1628, and 1250 cm^{-1}; mass spectrum peaks at m/e 366, 324, 306, 288, 264, and 246; nmr data listed in Table I.

Anal. Calcd for $C_{19}H_{26}O_7$: C, 62.29; H, 7.10. Found: C, 62.63; H, 6.97.

Lactone **8** (40 mg) was treated with 5 ml of Tri-sil reagent in the usual manner. The resulting trimethylsilyl derivative was obtained as a solid which showed a single spot on tlc; ir bands at 1769 (γ-lactone), 1739 and 1245 (acetate), and 1639 (unsaturation) cm^{-1}; nmr spectrum listed in Table I.

(18) K. Tori, Y. Hamashima, and K. Takamizawa, *Chem. Pharm. Bull.*, **12**, 924 (1964).

(19) All melting points are uncorrected. The uv and ir spectra were recorded on Coleman–Hitachi EPS-3T and Beckman IR-5 spectrophotometers in 95% ethanol and in Nujol mulls, respectively. Mass spectra were determined on a Varian-Mat 111 spectrometer at 80 eV, using direct insertion. Baker A. R. No. 3405 silica gel was used for column chromatography and silica gel G Woelm was used for tlc. The plates were visualized by spraying with concentrated H_2SO_4 and heating.

(20) The samples were identified and collected by Professor M. S. Morris, School of Forestry, University of Montana.

(21) T. A. Geissman, T. Stewart, and M. A. Irwin, *Phytochemistry*, **6**, 901 (1967).

Lactone 9 was crystallized from chloroform–methanol as fine needles: yield 80 mg; mp 185°; ir bands at 3483, 3389, 1763, 1742, 1240, and 892 cm^{-1}; mass spectrum peaks at *m/e* 306, 264, and 246; nmr data listed in Table I.

Anal. Calcd for $C_{17}H_{24}O_6$: C, 62.96; H, 7.40. Found: C, 63.12; H, 7.31.

The monotrimethylsilyl derivative of lactone 9 was obtained in the manner described above. It gave a single spot on tlc and ir bands at 3521 (hydroxyl), 1769 (γ-lactone), 1739 and 1242 (acetate), and 1639 (unsaturation) cm^{-1}. The nmr data are listed in Table I.

Lactone 9 (35 mg) was dissolved in 2 ml of pyridine and 2 ml of acetic anhydride, and the solution was kept overnight at room temperature. Removal of the solvent gave lactone 9 monoacetate as a gum which resisted crystallization; the product gave a single spot on tlc and was chromatographically different from lactone 7; ir spectrum showed a broad band in the carbonyl region (γ-lactone and acetates) and other bands at 3500 (hydroxyl) and 1639 (unsaturation) cm^{-1}; nmr data are listed in Table I.

Deacetylation of Lactone 6 to Isoamberboin.—A solution of 60 mg of lactone 6 in 5 ml of 2% methanolic KOH was refluxed for 0.5 hr, acidified, and extracted with chloroform. Removal of the solvent left a colorless gum which was recrystallized twice to give 16 mg of isoamberboin as granules: mp 179–181° (lit.[8] 183°); $[\alpha]D$ +132° (c 1.026, $CHCl_3$); ir bands at 3475, 1750, 1737, and 1645 cm^{-1}.

Isolation of Cumambrin B.—Cumambrin B (2.5 g) and its acetate cumambrin A (0.9 g) were isolated in the usual manner from *Artemisia nova* Nels (450 g), collected near Red Rock, Mont. (T. 11 S, R. 10 W, Section 8), in August 1970. Cumambrin B had mp 178–179° (lit.[10] mp 178–180°); ir bands at 3509, 3290 (hydroxyl), 1750 (γ-lactone), and 1660 (unsaturation) cm^{-1}; nmr data listed in Table I.

Cumambrin A.—Cumambrin B (1.5 g) was acetylated with pyridine and acetic anhydride at room temperature to give 1.25 g of the crystalline monoacetate, cumambrin A: mp 188–189°, alone or in admixture with the naturally occurring cumambrin A isolated in the previous experiment (lit.[10] mp 188–190°); ir bands at 3533 (hydroxyl), 1745 (γ-lactone and acetate), 1248 (acetate), and 1663 (unsaturation) cm^{-1}; nmr data listed in Table I.

Dihydrocumambrin A.—A solution of 1.125 g of cumambrin A in 30 ml of ethyl acetate was hydrogenated in the presence of 280 mg of 5% Pd/C catalyst. Hydrogenation was stopped after 1 hr, when approximately 1 mol of hydrogen was absorbed. The catalyst was filtered off and the filtrate was evaporated to dryness. Crystallization of the residue from chloroform–ether gave 850 mg of dihydrocumambrin A as prisms: mp 171–172° (lit.[9] 170–173°); ir bands at 3510 (hydroxyl), 1782 (γ-lactone), 1748, and 1253 (acetate), cm^{-1}; nmr data listed in Table I.

Dehydration of Dihydrocumambrin A.—An ice-cold solution of 800 mg of dihydrocumambrin A in 8 ml of pyridine was treated with 2 ml of thionyl chloride and kept cold for 15 min. The reaction mixture was then lyophilized to remove the solvents and the residue obtained was dissolved in chloroform. The chloroform solution was filtered through a short column of silica gel. Evaporation of the colorless filtrate gave 675 mg of a transparent gum, which resisted crystallization. The product gave a single spot on tlc but the nmr data showed a mixture of exo and endo unsaturated lactones. Ir spectrum of the mixture had a broad band at 1786 to 1725 (γ-lactone and acetate), a sharp band at 1639 (unsaturation), and a broad band around 1250 (acetate) cm^{-1}.

Epoxidation of the Unsaturated Lactones.—A solution of 580 mg of the above mixture in 20 ml of chloroform was cooled to 0° and treated with an ice-cold solution of 415 mg of *m*-chloroperbenzoic acid in 10 ml of chloroform, and the reaction mixture was kept in the refrigerator. Progress of the reaction was monitored by periodic tlc of the reaction mixture for 24 hr until only traces of the starting material was left. The reaction mixture was then washed with $NaHCO_3$ solution and water. Removal of chloroform gave 490 mg of a colorless gum which gave several spots on tlc, including a spot corresponding to viscidulin B. Extensive chromatography of this mixture on silica gel gave viscidulin B, which was crystallized from chloroform–ether (yield 35 mg; mp 132–133°) alone or in admixture with the natural product. The ir and nmr spectra of these materials were also identical. Attempted isolation of other products from the reaction mixture was not successful.

Acetylation of Viscidulin C to Viscidulin B.—Viscidulin C (100 mg) was acetylated with pyridine and acetic anhydride at room temperature. Crystallization of the product from chloroform–ether gave viscidulin B (yield 95 mg; mp 132–133°) alone or in admixture with the natural product. The nmr and ir spectra of these materials were also identical.

Hydrogenation of Viscidulin A.—A solution of 468 mg of viscidulin A in 30 ml of ethyl acetate was hydrogenated in the presence of 125 mg of 10% Pd/C catalyst for 4 hr. The reaction gave a colorless product which resisted crystallization and showed four spots on tlc. Extensive chromatography of this material resulted in the isolation of lactones **14**, **15**, **16**, and **17**.

Lactone **14** was crystallized from ether–petroleum ether as needles: yield 75 mg; mp 156–157°; ir bands at 1770 (γ-lactone), 1736, and 1226 (acetate) cm^{-1}; mass spectrum peaks at *m/e* 232 and 217; nmr data listed in Table I.

Anal. Calcd for $C_{17}H_{24}O_4$: C, 69.86; H, 8.22. Found: C, 70.07; H, 8.45.

Lactone **15** (dihydroviscidulin A) gave fine needles after crystallization from ether–petroleum ether: yield 190 mg; mp 155–156°; ir bands at 1773 (γ-lactone), 1724, and 1234 (acetate) cm^{-1}; mass spectrum peaks at *m/e* 308 (M^+) and 248 (M − 60); nmr data listed in Table I.

Anal. Calcd for $C_{17}H_{24}O_5$: C, 66.23; H, 7.14. Found: C, 66.50; H, 7.91.

Lactone **16** was crystallized from ether–petroleum ether as fine needles: yield 3 mg; mp 142–144°; ir bands at 3500 (hydroxyl), 1760 (γ-lactone), 1730, and 1250 (acetate) cm^{-1}; mass spectrum peaks at *m/e* 250 and 232.

Lactone **17** was obtained in a small amount as a gum which showed a single spot on tlc but resisted crystallization. It had ir bands at 3450 (hydroxyl), 1760 (γ-lactone), 1725, and 1240 (acetate) cm^{-1}.

Reaction of Viscidulin A with *p*-Toluenesulfonic Acid in Acetic Acid.—A cold solution of 500 mg of viscidulin A in 20 ml of glacial acetic acid was treated with 200 mg of *p*-toluenesulfonic acid as before. The reaction gave a colorless gum which showed several spots on tlc but could not be fractionated or crystallized to pure compounds. The mixture had a strong ir band in the hydroxyl region.

Epoxidation of Viscidulin A.—A solution of 60 mg of viscidulin A in 10 ml of chloroform was treated with 60 mg of *m*-chloroperbenzoic acid and the reaction mixture was kept at room temperature for 3 hr. The mixture was washed with $NaHCO_3$ solution and the solvent was removed under reduced pressure. The product crystallized to give 45 mg of **18**: mp 142–143°; ir bands at 1755 (γ-lactone), 1720, and 1245 (acetate) cm^{-1}; mass spectrum peaks at *m/e* 322, 280, and 262; nmr data listed in Table I.

Anal. Calcd for $C_{17}H_{22}O_6$: C, 63.35; H, 6.83. Found: C, 63.07; H, 6.67.

Epoxidation of Viscidulin B.—A solution of 200 mg of viscidulin B and 200 mg of *m*-chloroperbenzoic acid in 20 ml of chloroform was refluxed for 3 hr.[22] The gummy product showed two spots on tlc. Column chromatography of the mixture gave diepoxide **18** [yield 70 mg; mp 142–143° (alone or in admixture with the one obtained from viscidulin A)] and an epimeric diepoxide **19**: yield 41 mg; mp 148–149°; ir bands at 1760 (γ-lactone), 1710, and 1250 (acetate) cm^{-1}; mass spectrum peaks at *m/e* 322, 280, and 262; nmr data listed in Table I.

Anal. Calcd for $C_{17}H_{22}O_6$: C, 63.35; H, 6.83. Found: C, 63.19; H, 7.01.

Registry No.—**1**, 35144-09-3; **2**, 35144-10-6; **3**, 35191-38-9; **4**, 17946-87-1; **6**, 23516-00-9; **6a**, 30825-69-5; **7**, 35144-13-9; **8**, 35144-14-0; **9**, 35191-40-3; **9a**, 35144-15-1; **9b**, 35144-16-2; **10**, 21982-83-2; **11**, 20482-33-1; **12**, 20482-39-7; **14**, 35144-20-8; **15**, 35144-21-9; **18**, 35191-41-4; **19**, 35191-42-5.

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Asymmetric Synthesis with (S)-(−)-*n*-Butyl-*tert*-butylcarbinyl Benzoylformate[1]

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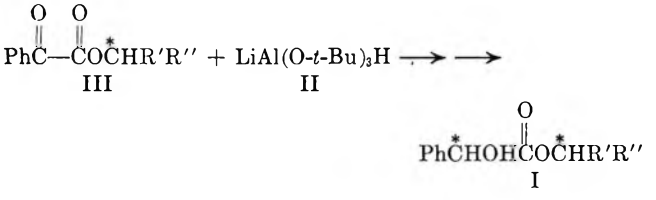
We have found that the reaction of methylmagnesium iodide in ether with (*S*)-(−)-*n*-butyl-*tert*-butylcarbinyl benzoylformate preferentially attacks the *re* face of the α-keto group to give a 7.5% excess of the (*S*)-atrolactate diastereomer. Based on the premise that *tert*-butyl acts as a larger group than *n*-butyl this result is in accord with Prelog's generalization concerning the course of this reaction. In tetrahydrofuran, however, the stereoselectivity was essentially zero. On the other hand, reduction of this same substrate by lithium tri-*tert*-butoxyaluminohydride in either tetrahydrofuran or ether resulted in preferential attack on the *si* face of the α-keto group to give the (*R*)-mandelate diastereomer in excess (13 and 8%, respectively). This reversal in stereoselectivities between the Grignard addition and lithium tri-*tert*-butoxyaluminohydride reductions emphasizes the caution necessary in extrapolating stereoselectivities from one seemingly closely related reaction to another, especially when the stereoselectivities are low and the nature of steric differences are not clearly evident. Stereochemical analysis of the reaction mixtures was greatly facilitated by the use of the nmr enantiomer reagent, α-methoxy-α-trifluoromethylphenylacetic acid, alone and in conjunction with europium nmr shift reagents.

Previous nuclear magnetic resonance (nmr) studies on a series of chiral esters (I) of mandelic acid[3] which were prepared by lithium tri-*tert*-butoxyaluminohydride (II) reduction[4] of the chiral benzoylformate esters (III) led to one or more of the following con-

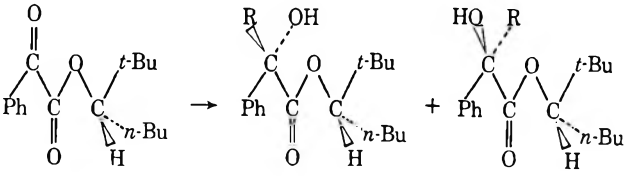


clusions: (a) that the stereochemical course of this reaction[5] did not follow Prelog's generalization[6] assuming that the *tert*-butyl group exerts greater steric nonbonded interactions than the *n*-butyl group (an assumption which had been found to satisfactorily rationalize our results in earlier asymmetric reduction studies[5]), (b) that our nmr configurational correlation model[3,7] did not hold in this case, (c) that the configurational assignment for (*S*)-(−)-*n*-butyl-*tert*-butylcarbinol is wrong. It thus became necessary to determine unequivocally which of these alternative conclusions was unreliable.

The stereochemistry of the acid moiety of the mandelate ester (IV, R = H) was established by lithium aluminum hydride reduction to the corresponding phenylethylene glycol of known configuration[8,9] and that of the atrolactate ester (IV, R = CH_3) by hydrolysis to atrolactic acid of known configuration. The (*S*)-(−)-*n*-butyl-*tert*-butylcarbinol was recovered unchanged. The stereoselectivities observed are given in Table I.

TABLE I

STEREOSELECTIVITIES IN THE LiAl(O-*t*-Bu)$_3$H AND MeMgI ADDITIONS TO (*S*)-(−)-*n*-BUTYL-*tert*-BUTYL BENZOYLFORMATE



R	Reagent	Solvent	Stereoselectivity	Yield, %
H	LiAl(O-*t*-Bu)$_3$H	Et_2O	8% excess *R,S*	92
H	LiAl(O-*t*-Bu)$_3$H	THF	13% excess *R,S*	99
CH_3	MeMgI	Et_2O	7.5% excess *S,S*	94
CH_3	MeMgBr	THF	*R,S* ≅ *S,S*	95

[a] Formula drawn according to Prelog model in ref 6b. An earlier model[6] which predicts the same stereochemistry has the small rather than large group eclipsing the C–O–C bond.

It is apparent that the stereoselectivities for the LiAl(O-*t*-Bu)$_3$H reduction and MeMgI addition in either solvent are reversed. Thus alternative (a) above is the root of the discrepancy but only for the reduction reaction since the methylmagnesium iodide reaction did follow the Prelog generalization based on the stated assumption. From these results it is seen that the stereoselectivities are not high. In fact in THF the reaction with methylmagnesium bromide[10] showed zero stereoselectivity within experimental limits.

It is reasonable to conclude that the steric interactions of *n*-butyl and *tert*-butyl might be effectively different in different reactions. The *tert*-butyl group could show greater steric hindrance to reactions which are centered near the attachment of the *tert*-butyl group, as for instance in the asymmetric reduction of alkyl or aryl *tert*-butyl ketones, while the *n*-butyl group might more effectively block one face of a carbonyl group which was further away as in the benzoylformate

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(2) On leave from Department of Chemistry, Tohoku University, Sendai, Japan.

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(4) (a) H. C. Brown and R. F. McFarlin, *J. Amer. Chem. Soc.*, **80**, 5372 (1958); (b) H. C. Brown and H. R. Deck, *ibid.*, **87**, 5620 (1965); (c) H. Haubenstock and E. L. Eliel, *ibid.*, **84**, 2363 (1962); (d) E. C. Ashby, J. P. Sevenair and F. R. Dobbs, *J. Org. Chem.*, **36**, 197 (1970).

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(7) James A. Dale and H. S. Mosher, *J. Amer. Chem. Soc.*, in press. This empirical correlation model predicted from the nmr spectrum alone that the *S,S* diastereomer with the upfield *tert*-butyl signal was produced in 10% excess over the *R,S* diastereomer.[3]

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(9) J. A. Dale and H. S. Mosher, *J. Org. Chem.*, **35**, 4002 (1970).

(10) Methylmagnesium iodide is not soluble as such in THF, giving a precipitate of MgI_2; we therefore used methylmagnesium bromide in the THF reaction. Similarly, the lithium tri-*tert*-butoxyaluminohydride reagent is not soluble in ether although it rapidly went into solution as the reaction progressed.

esters such as III. It is more difficult to rationalize the reversal of stereoselectivities observed when the same substrate is being acted on by two different reagents. Intimate details of the transition states of these reactions are not known and thus reasons for the observed reversal of stereoselectivities in these two cases cannot be carried much beyond these speculations. Differences in stereoselectivities of 7–13% at 35° represent $\Delta\Delta G^{\ddagger}$ values of only 75 to 150 cal/mol; our understanding of transition states is seldom good enough to account for such small differences even in closely comparable competitive reactions of the asymmetric synthesis type. Thus we feel that such results, taken together, are indicative of subtle interactions between solvent, reagent, and conformational factors, a greater knowledge of which are requisite to a more detailed understanding of transition states.

Another example of reversal of stereoselectivities has been reported[8] in the lithium aluminum hydride reduction of phenyldihydrothebainyl benzoylformate *vs.* the addition of methylmagnesium iodide to the same substrate. The reduction product upon hydrolysis gave (*S*)-(+)-phenylethylene glycol while the Grignard product on hydrolysis gave (*R*)-(−)-atrolactic acid; these two products have opposite configurational relationships. This was rationalized by assuming that in this substrate the ester carbonyl group was reduced faster than the α-keto group. Stereochemical control of the further reduction of the α-keto group once an intermediate hemiacetal was formed would be quite different from the initial reduction of the α-keto group.[11] The present example cannot be explained on this basis since even in the presence of substantial excess of lithium tri-*tert*-butoxyaluminohydride only mandelate ester was formed; no phenylethylene glycol could be detected.

An interesting analytical point is the use of Sievers europium reagent[12] Eu(fod)$_3$ to spread out and separate the signals of the diastereomeric atrolactates of *n*-butyl-*tert*-butylcarbinol. Whereas the uncomplexed atrolactate ester had coincident signals for the α-methyl groups of the *S,R* and *S,S* diastereomers, in the presence of 0.6 molar amount of Eu(fod)$_3$ these signals occurred almost completely separated at δ 6.33 (*S,S* diastereomer) and 6.43 (*R,S* diastereomer) ppm, respectively, so that they could be readily integrated and the percentage diastereomer composition ascertained. The use of lanthanide chemical shift reagents constitutes a valuable adjunct technique in stereochemical studies such as these.

Experimental Section[13]

(*S*)-(−)-*n*-Butyl-*tert*-butylcarbinyl Benzoylformate (III).—A solution of oxalyl chloride (4.4 g, 34.8 mmol) in carbon tetrachloride (6.7 ml) was added to the stirred, ice-cooled suspension of sodium benzoylformate (3.5 g, 20 mmol, thoroughly dried in a vacuum desiccator over P_2O_5) in carbon tetrachloride (10 ml) and pyridine (0.4 ml) according to a modification of the method of Stork and Clark.[14] After stirring for 12 hr, the reaction mixture was evaporated under reduced pressure below 40°, diluted with carbon tetrachloride (10 ml), and evaporated (1–2 mm) again to remove excess oxalyl chloride. The residue was diluted with carbon tetrachloride (10 ml); to the stirred suspension was added a solution of (*S*)-(−)-*n*-butyl-*tert*-butylcarbinol[5] [0.72 g, $[\alpha]^{22.5}$D −39.2° (*c* 23.3, cyclopentane)] in pyridine (2.5 ml) and carbon tetrachloride (2.5 ml) during a 5-min period while it was cooled with ice. After stirring for 12 hr at room temperature, the reaction mixture was poured onto ice and extracted with ether. The ether extract was successively treated with cold dilute HCl, dilute NaOH, and H_2O and dried (Na_2SO_4). The ether was removed under reduced pressure to give an oil, which was purified (silica gel column, benzene solvent). Obtained was 1.2 g (87%) of ester: $[\alpha]^{22.8}$D −30.3° (CCl_4, *c* 9.08); ir 1730 (ester C=O), 1694 cm^{-1} (α-keto), nmr δ 0.96 [s, C(CH$_3$)$_3$].

Anal. Calcd for $C_{17}H_{24}O_3$: C, 73.88; H, 8.75. Found: C, 73.98; H, 8.71.

Reaction of (*S*)-(−)-*n*-Butyl-*tert*-butylcarbinyl Benzoylformate with Methylmagnesium Iodide.—An aliquot of ethereal Grignard reagent (3.01 ml, 3.6 mmol), prepared from sublimed magnesium and methyl iodide and standardized by neutralization titration just before use, was added to (*S*)-(−)-*n*-butyl-*tert*-butylcarbinyl benzoylformate [III, 0.5 g, 1.8 mmol, $[\alpha]^{22.8}$D −30.3° (CCl_4)] in ether (2.0 ml) at 0° under N_2. After 14 hr, the reaction mixture was hydrolyzed (saturated NH_4Cl solution) and extracted with ether. The extracts were washed (dilute HCl, dilute NaOH, H_2O), dried (Na_2SO_4), and concentrated under reduced pressure to give 0.50 g of *n*-butyl-*tert*-butylcarbinyl atrolactate as a pale yellow oil, isolated yield 94%, $[\alpha]^{20.0}$D −23.4° (*c* 8.25, CCl_4). The spectra were taken on a sample of the ester which was purified (silica gel column, benzene solvent): ir 1725 cm^{-1}; nmr δ 0.60 (s, *t*-Bu, *S,S* diastereomer), 0.87 (s, *t*-Bu, *S,R* diastereomer), 1.72 ppm (s, α-CH$_3$), and complex multiplet for *n*-butyl group.

The higher field signal (δ 0.60, arising from the *tert*-butyl group of the *S,S* diastereomer) is stronger than that of the lower field signal (δ 0.87, arising from the *tert*-butyl group of the *S,R* diastereomer). However, overlapping signals from the *n*-butyl group made an accurate direct analysis of the diastereomeric composition of these esters by integration of these signals either at 60 or 100 MHz impossible. The addition of the chemical shift reagent[12] Eu(fod)$_3$ caused a shift of nmr resonances so that the previously unresolved α-methyl signals (δ 1.73 ppm) were removed to an uncomplicated region of the spectrum: δ 6.33 (*S,S* diastereomer), 6.43 ppm (*R,S* diastereomer). Although the signals were not completely resolved, the upfield resonance was clearly more intense and represented 7 ± 2% excess of the *S,S* diastereomer.

Hydrolysis of (*S*)-(−)-*n*-Butyl-*tert*-butylcarbinyl Atrolactates.—The above mixture of atrolactates (0.40 g, without further purification), methanol (4.5 ml), water (0.9 ml), and potassium hydroxide (0.27 g) was gently refluxed for 5 hr under nitrogen atmosphere.[6] The reaction mixture was poured onto ice and extracted three times with ether. The extracts were washed (dilute HCl, H_2O), dried (Na_2SO_4), and concentrated to give 0.18 g (91%) of *n*-butyl-*tert*-butylcarbonol, $[\alpha]^{23.4}$D −38.0° (*c* 8.80, cyclopentane). The aqueous basic solution was acidified (cold dilute HCl) and extracted three times with ether. These extracts were washed (H_2O), dried (Na_2SO_4), and concentrated to give 0.20 g (88%) atrolactic acid, $[\alpha]^{27.5}$D +2.8° (*c* 10.23, C_2H_5OH). Taking the value of $[\alpha]^{13.8}$D 37.7° (C_2H_5OH)[15] as enantiomerically pure atrolactic acid, this corresponds to 7.5% excess of the (*S*)-(+) isomer in accord with Prelog's rule where *tert*-butyl is acting as a larger group than *n*-butyl.

Reaction of *n*-Butyl-*t*-butylcarbinyl Benzoylformate with Methylmagnesium Bromide in THF.—To a cold stirred solution of (−)-*n*-butyl-*tert*-butylcarbinyl benzoylformate (III, 0.28 g, 1 mmol) in THF (1 ml) was added 4.3 ml (2 mmol) of methylmagnesium bromide reagent[10] under N_2. The reaction mixture was decomposed (saturated NH_4Cl) and processed as in the previous preparation in ether solvent to give 0.28 g (95%) of atrolactate ester (IV, R = CH$_3$) as a colorless oil. The nmr of this ester (41 mg in CCl_4) mixed with Eu(fod)$_3$ (Eu-Resolve II, 86 mg,

(11) This explanation has been questioned based upon subsequent experiments: J. A. Dale and H. S. Mosher, *J. Org. Chem.*, **35**, 4002 (1970).

(12) For leading reference on the use of lanthanide chemical shift reagents, see R. E. Rondeau and R. E. Sievers, *J. Amer. Chem. Soc.*, **93**, 1522 (1971); fod stands for the anion from 1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedione. This extension of the use of lanthanide shift reagents for the determination of enantiomeric composition as well as configuration by nmr is being studied further.

(13) Ir spectra were taken on a Perkin-Elmer Model 137B grating instrument; nmr spectra were taken either on a Varian T-60 or Varian HR-100 instrument as appropriate. Chemical shifts are reported in δ, parts per million, downfield from internal tetramethylsilane in carbon tetrachloride solvent. Optical rotations were taken on a Perkin-Elmer Model 141 electronic polarimeter in 1-dcm tubes with a reproducibility of ±0.002°.

(14) G. Stork and T. Clark, Jr., *J. Amer. Chem. Soc.*, **83**, 3114 (1961).

(15) A. McKenzie and G. W. Clough, *J. Chem. Soc.*, **97**, 1016 (1910).

molar ratio 1:0.6)[12] showed that the signal for the α-methyl group of the atrolactate moiety (δ 1.73 ppm unresolved) was shifted downfield and separated into two signals (δ 6.03 and 6.13 ppm) which within experimental limits (*ca.* ±2%) had the same integrated area, indicating essentially zero stereoselectivity for this reaction in THF solvent.

Reduction of (*S*)-(−)-*n*-Butyl-*tert*-butylcarbinyl Benzoylformate with Lithium Tri-*tert*-butoxyaluminohydride in THF.—A solution of (*S*)-(−)-*n*-butyl-*tert*-butylcarbinyl benzoylformate [III, 0.68 g, $[\alpha]^{22.8}D$ −30.3° (CCl_4)] in THF (2.5 ml, distilled from $LiAlH_4$) was added to a solution of $LiAlH(O\text{-}t\text{-}Bu)_3$[4] (1.36 g in 25 ml THF) over a 5-min period with ice cooling. After 2-hr stirring, 1 ml of water was added. Ether extracts of the acidified (dilute HCl) reaction mixture were washed (dilute NaOH, H_2O), dried (Na_2SO_4), and concentrated to give 0.63 g (92%) of *n*-butyl-*tert*-butylcarbinyl mandelate: mp 54–58°; $[\alpha]^{24}D$ −35.8° (*c* 10.18, $CHCl_3$); ir 1727 cm^{-1}; nmr δ 0.55 (s, *t*-Bu, *S,S* diastereomer), 0.87 (s, *t*-Bu, *S,R* diastereomer).

Anal. Calcd for $C_{17}H_{26}O_3$: C, 73.33; H, 9.41. Found: C, 73.44; H, 9.18.

In the nmr spectra of the mandelates the two *tert*-butyl signals are more clearly separated from the *n*-butyl resonances than in the atrolactates. The lower field signal by integration was 13% greater than the higher field signal, *i.e.*, 13% excess of *S,R* diastereomer. This nmr analysis was confirmed by the following experiment.

Reduction of (*S*)-(−)-*n*-Butyl-*tert*-butylcarbinyl Mandelate with Lithium Aluminum Hydride.—A solution of the above mandelates without further purification (0.57 g, in 3.0 ml of ether) was added dropwise with stirring to a solution of $LiAlH_4$ (0.76 g in 9.5 ml of ether) at 0°. After 1-hr reflux, excess $LiAlH_4$ was decomposed with water (3 ml) and the hydrolysis mixture was treated with dilute HCl and extracted with ether. The combined ether extracts were washed (dilute Na_2CO_3, H_2O), dried (Na_2SO_4), and concentrated under vacuum at 0° to give 0.49 g of colorless oil which was purified (silica gel column, CH_2Cl_2 followed by CH_3OH) to give a first fraction containing 0.26 g (88%) of (*S*)-(−)-*n*-butyl-*tert*-butylcarbinol [$[\alpha]^{20.4}D$ −39.0° (*c* 10.81, cyclopentane] and a second fraction containing 0.20 g (71%) of (−)-phenylethylene glycol which was further purified by sublimation: mp 68–71°; $[\alpha]^{21.5}D$ −7.7° (*c* 9.38, $CHCl_3$). Based on the reported maximum rotation of $[\alpha]^{25.6}D$ −63.7° (*c* 5.45, $CDCl_3$)[8,9] for (*R*)-(−)-phenylethylene glycol, this represents 12% excess of the (*S*)-*n*-butyl-*tert*-butylcarbinyl (*R*)-mandelate.

Reduction of (*S*)-(−)-*n*-Butyl-*tert*-butylcarbinyl Benzoylformate with $LiAl(O\text{-}tert\text{-}Bu)_3H$ in Ether.—An ether solution (2 ml) of (−)-*n*-butyl-*tert*-butylcarbinyl benzoylformate (III, 0.28 g) was added to an ice-cold suspension of lithium tri-*tert*-butoxyaluminohydride[4] (0.55 g) in ether (30 ml). After 10 min the reagent was dissolved and after 2 hr the reaction mixture was worked up as indicated in the previous reaction in THF to give 0.28 g (99%) of mandelate ester as colorless crystals. Integration of the nmr spectrum indicated an 8% excess of the *S,R* diastereomer (*tert*-butyl signal δ 0.7, *S,R* diastereomer). This compares to the 13% excess of the same stereoisomer observed during the reduction in THF.

Optical Rotation of *n*-Butyl-*tert*-butylcarbinol in Cyclopentane.—The original sample[5] of (*S*)-(−)-*n*-butyl-*tert*-butylcarbinol obtained by resolution [$[\alpha]^{27.0}D$ −32.46° (neat, *l* 1); $[\alpha]^{27.0}D$ −39.4° (neat)] was found to give rotations in cyclopentane which were nearly the same as that of the neat liquid and not strongly concentration dependent: $[\alpha]^{21.5}D$ −39.2° (*c* 49.14), $[\alpha]^{22.5}D$ −39.2° (*c* 23.3), $[\alpha]^{21.5}D$ −40.0° (*c* 10.16), $[\alpha]^{23.5}D$ −39.9° (*c* 8.92), $[\alpha]^{24}D$ −40.4° (*c* 4.46).

The (*R*)-(+)-α-methoxy-α-trifluoromethylphenyl esters [*R*-(+)-MTPA esters] prepared in the usual way[9] from racemic *n*-butyl-*tert*-butylcarbinol gave *tert*-butyl signals at δ 0.83 corresponding to the *S,R* diastereomer and at 0.92 corresponding to the *S,S* diastereomer. The nmr spectrum of the *R*-(+)-MTPA ester prepared from the above sample of (−)-*n*-butyl-*tert*-butylcarbinol [$[\alpha]^{27.0}D$ −32.46° (neat, *l* 1)] gave only one *tert*-butyl signal at δ 0.83 with no detectable signal from the diastereomer. The prior resolution[5] was therefore complete. The overlapping OCH_3 proton signals in the nmr spectrum of the diastereomeric mixture (*R,R*, δ 3.50; *R,S*, δ 3.55) were widely separated and their positions reversed upon the addition of 0.2 molar equivalents of $Eu(fod)_3$[12] (*R,R*, δ 5.57; *R,S*, δ 5.40).

Registry No.—(*S*)-III, 35147-13-8; (*S,S*)-IV (R = CH_3), 35147-12-7; (*R,S*)-IV (R = CH_3), 35147-14-9; (*S,S*)-III (R = H), 35147-15-0; (*R,S*)-IV (R = H), 35147-16-1; (*S*)-(−)-*n*-butyl-*tert*-butylcarbinol, 35147-17-2; (*R*)-(−)-phenylethylene glycol, 16355-00-3.

Photoreduction of Aromatic Esters with Some Electron-Withdrawing Substituents

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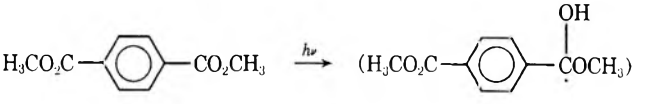
The photoreduction of aromatic esters, having an electron-withdrawing substituent such as an ester or cyano group, by aromatic hydrocarbons is described. The photoreduction of para- or meta-substituted aromatic esters led to the formation of the two possible types of pinacols and carbinols depending on the aromatic hydrocarbons employed. In the case of ortho-substituted aromatic esters, various benzo-γ-lactone derivatives were produced. It is demonstrated that steric effects play an important role in the hydrogen transfer step and that an excited charge-transfer complex between the aromatic ester and the aromatic hydrocarbon may be the photoreactive species.

Although many studies have been done on the photoreduction of aromatic ketones by a variety of hydrogen donors, such as alcohols,[1] ethers,[1a] hydrocarbons,[1a,2] and amines,[3] the photoreduction of aromatic esters has not yet been reported.

Recently, we reported[4] that dimethyl terephthalate (Ia) was readily photoreduced by various aromatic



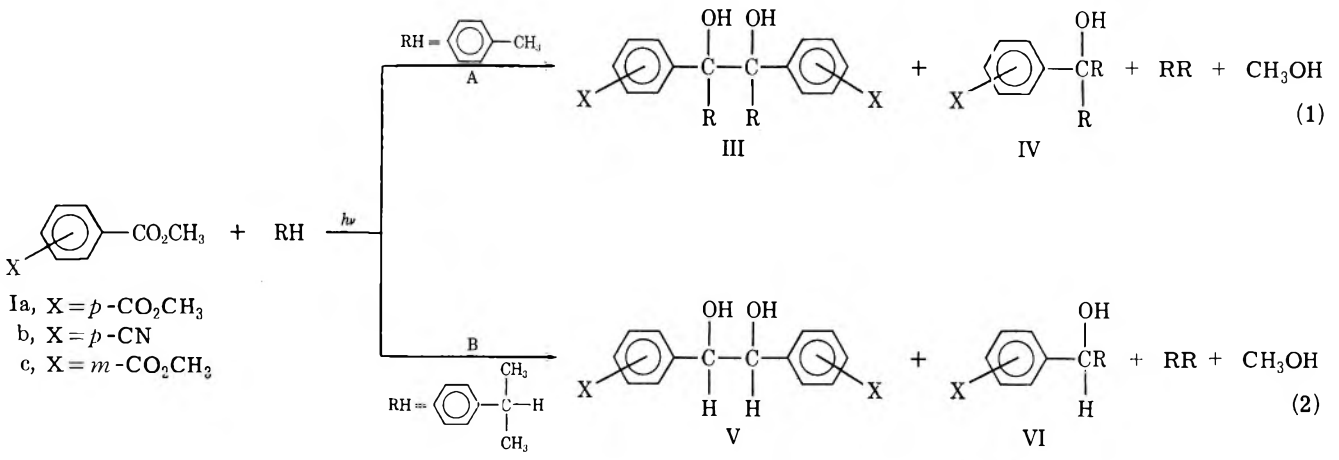
Ia II

(1) (a) D. C. Neckers, "Mechanistic Organic Photochemistry," Reinhold, New York, N. Y., 1967, p 163; (b) N. Fillipescu and F. L. Minn, *J. Amer. Chem. Soc.*, **90**, 1544 (1968); J. H. Stocker, R. M. Jenevein, and D. H. Kern, *J. Org. Chem.*, **34**, 2810 (1969).

(2) (a) D. Bellus and K. Schaffner, *Helv. Chim. Acta*, **52**, 1010 (1969); (b) P. J. Wagner and R. A. Leavitt, *J. Amer. Chem. Soc.*, **92**, 5806 (1970).

(3) S. G. Cohen and H. M. Chao, *ibid.*, **90**, 165 (1968); **91**, 3690 (1969); R. S. Davidson, *Chem. Commun.*, 575 (1966); R. S. Davidson and P. F. Lambeth, *ibid.*, 1098 (1969); C. Pac, H. Sakurai, and T. Tosa, *ibid.*, 1311 (1970); S. G. Cohen and J. I. Cohen, *J. Amer. Chem. Soc.*, **89**, 164 (1967); *J. Phys. Chem.*, **72**, 3782 (1968); R. S. Davidson, P. F. Lambeth, F. A. Younis, and R. Wilson, *J. Chem. Soc. C*, 2204 (1969); R. A. Caldwell, *Tetrahedron Lett.*, 2121 (1969); S. G. Cohen and J. B. Guttenplan, *ibid.*, 5353 (1968); 2125, 2129 (1969); G. A. Davis, P. A. Carapelluci, K. Szoc, and J. D. Gresser, *J. Amer. Chem. Soc.*, **91**, 2264 (1969); G. A. Davis and S. G. Cohen, *Chem. Commun.*, 622 (1970); S. G. Cohen and B. Green, *J. Amer. Chem. Soc.*, **91**, 6824 (1969); A. Padwa, W. Eisenhardt, R. Gruber, and D. Pashayan, *ibid.*, **91**, 1857 (1969).

(4) K. Fukui and Y. Odaira, *Tetrahedron Lett.*, 5255 (1969).



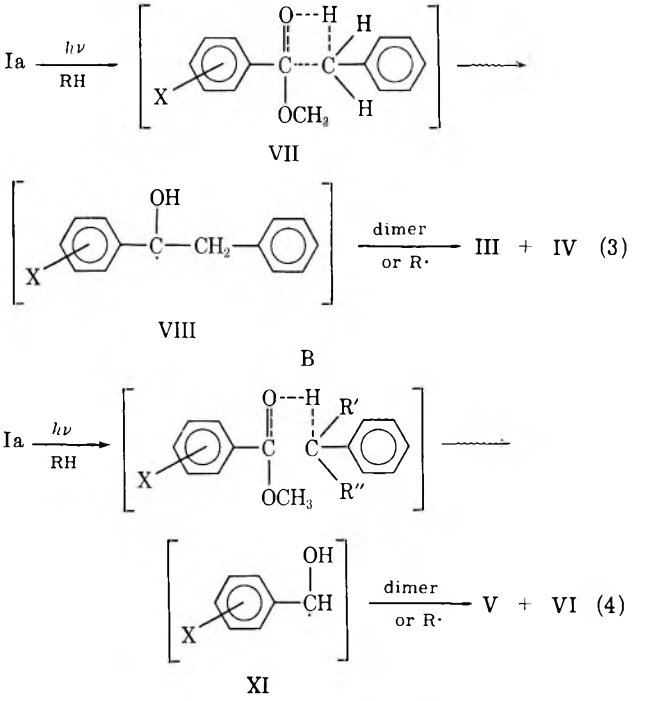
hydrocarbons having labile benzylic hydrogens to give pinacols, carbinols, and aromatic hydrocarbon dimers, along with a substantial amount of methanol. It was pointed out that the most significant characteristics of this photoreduction were the following. (1) No coupling products containing II were found at all, although it was assumed that the hemiketal radical II might be formed *via* hydrogen abstraction by Ia. This is probably due to the instability of II. (2) Varying the aromatic hydrocarbons as hydrogen donors had a definite influence on the photoreduction and two types of reactions occurred. We explained these results on the basis of steric effects affecting the hydrogen transfer step.

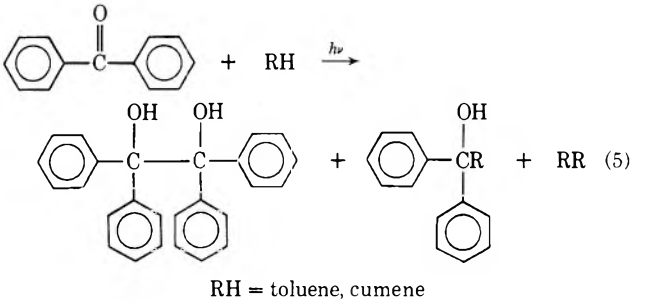
It is very interesting that the photoreactivity of Ia is much different from that of benzophenone.[5] Therefore, the photoreduction of other aromatic esters, such as methyl *p*-cyanobenzoate, dimethyl isophthalate, and tetramethyl pyromellitate, by aromatic hydrocarbons was studied. In addition, in order to obtain some information about the nature of the photoreactive species, photoreductions with cyclohexane were carried out. In this paper, the influence of steric factors on the hydrogen transfer step and the nature of the photoreactive species will be discussed.

Results and Discussion

As reported in the previous paper,[4] the photoreduction of dimethyl terephthalate (Ia) with toluene gave the pinacol IIIa, the carbinol IVa, and bibenzyl, whereas use of cumene gave the pinacol Va, the carbinol VIa, and bicumyl. In each case, an appreciable amount of methanol was always found. It was further reported that the reaction of Ia with *p*-xylene proceeded along path A, while path B was followed when α-substituted analogs (ethylbenzene, diphenylmethane) were employed. This suggests that a steric factor is involved in the hydrogen transfer step. It may be proposed that hydrogen abstraction and radical coupling take place concertedly through a cyclic transition state VII when steric hindrance is not prohibitive, and stepwise (eq 4) when it is. Subsequent steps then lead to the appropriate radicals VIII and IX.

It is remarkable that the photoreduction products of Ia depend on the aromatic hydrocarbon employed while these same hydrogen donors give rise to only one kind of photoreduction products from benzophenone.[5]





To ascertain the dependence of the photoreduction of aromatic esters on the nature of the aromatic hydrocarbon, the reactions of methyl *p*-cyanobenzoate (Ib) and dimethyl isophthalate (Ic) with toluene or cumene were studied. It was found that Ib and Ic were photoreduced in a manner similar to that of Ia. The results are summarized in Table I.

Walling[6] previously showed that cumene was more reactive then toluene toward hydrogen abstraction by photoexcited benzophenone in accordance with their

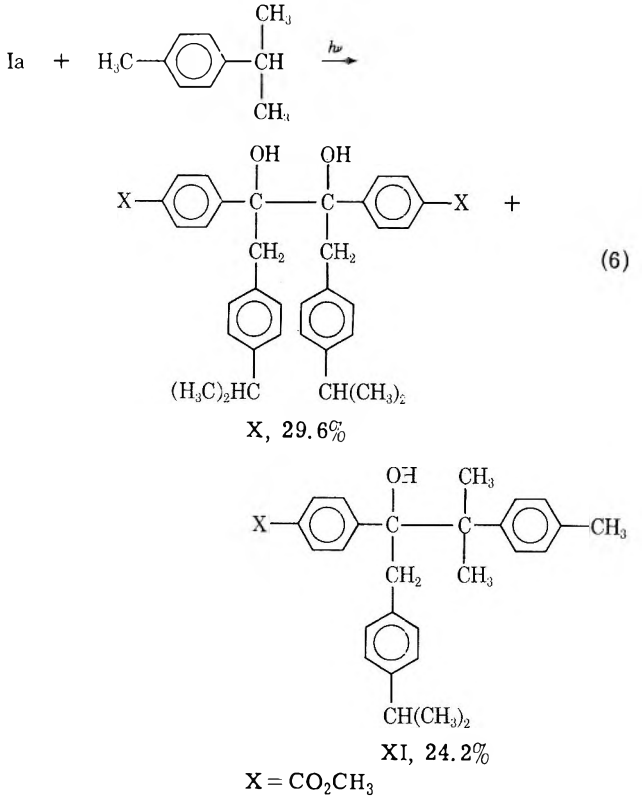
(5) G. S. Hammond, W. P. Baker, and W. M. Moore, *J. Amer. Chem. Soc.*, **83**, 2795 (1961).

(6) C. Walling and M. J. Gibian, *ibid.*, **86**, 3902 (1964); **87**, 3361 (1965).

TABLE I
PHOTOREDUCTION OF PARA- OR META-SUBSTITUTED AROMATIC ESTERS BY TOLUENE AND CUMENE

	Yield, %			
	Toluene		Cumene	
	III	IV	V	VI
X = *p*-CO_2CH_3 (Ia)	26	40	22	55
X = *p*-CN (Ib)	37	44		25
X = *m*-CO_2CH_3 (Ic)	Trace	57		

hydrogen-donating ability. In order to clarify the reactivity of aromatic esters toward methyl and isopropyl groups attached to an aromatic ring, we carried out the photoreduction of Ia with *p*-cymene and obtained two coupling products (X, XI) as the major products.



The relative yields show that in contrast to their hydrogen-donating abilities the methyl group of cymene is more easily photoreduced than the isopropyl group to give a radical species VIII rather than a radical species IX.

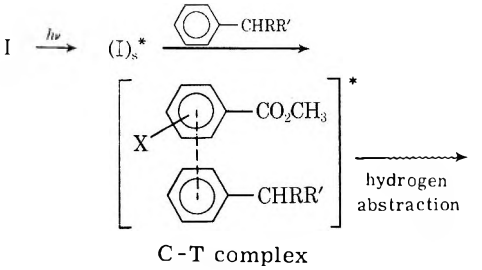
The photoreduction of dimethyl phthalate derivatives could conceivably be strongly influenced by the large steric hindrance exerted by the neighboring ester group. However, dimethyl phthalate itself was not a suitable substrate for such studies, since it exhibits an absorption maximum in almost the same ultraviolet region as the aromatic hydrocarbons employed for such reduction. Therefore, tetramethyl pyromellitate (Id) was in turn photoreduced with toluene[7] and cumene. With toluene, the benzo-γ-lactone derivative XII (60%), and, with cumene, XVI (49.5%) and XVII (41%) were obtained as major products. In addition, XIII, XIV, and XV were produced as minor products with toluene, and XVIII and XIX as minor products with cumene. It is assumed that they are derived from further reaction of XII, XVI, and XVII.

The results suggest the scheme shown in eq 9 for the photoreduction of Id.

An intermediate radical (XX), formed by hydrogen abstraction from Id, may give a radical species XXI by lactonization accompanied by elimination of methanol. Radical species XX and XXI are formed from Id, regardless of which aromatic hydrocarbon is employed, as shown in eq 9. In this case, it appears that the contribution of the steric factor in the aromatic hydrocarbons to the hydrogen transfer step is suppressed owing to the large intramolecular steric compression of Id and that, therefore, the photoreduction proceeds through a B-like path (see eq 4).

Although we assumed previously that the n–π* triplet of Ia was the chemically reactive intermediate, studies of the photoaddition of aromatic esters to olefins[8] suggested that this assumption might be incorrect. To obtain pertinent information, the photoreduction of Ia–c with cyclohexane, a good hydrogen donor to the n–π* excited benzophenone triplet, was attempted. Interestingly, no photoreduction occurred. Since excited Ia and benzophenone had already been shown to display different reactivities toward *p*-cymene, it is probable that the photoreactive species of Ia–d in the present studies is not a typical n–π* triplet.

More recently, Wagner suggested[2b] a charge-transfer mechanism for the photoreduction of α-trifluoroacetophenone by alkylbenzenes, because of the finding that toluene was more reactive than cumene, independent of the benzylic C–H bond strength of aromatic hydrocarbons. Thus, Ia–d and α-trifluoroacetophenone exhibit similar behavior in photoreduction by aromatic hydrocarbons. Furthermore, it has been reported[9] that Ia and Ic form an excited charge-transfer complex with *N*-vinylcarbazole to initiate photopolymerization. We would, therefore, like to propose that an excited charge-transfer complex between an excited state of I (acceptor) and an aromatic hydrocarbon (donor) may be the reactive species in the photoreduction of Ia–d by aromatic hydrocarbons. Accordingly, it is assumed that the hydrogen transfer occurs *via* a charge-transfer complex and that the steric factor controls the postreaction paths as mentioned before.

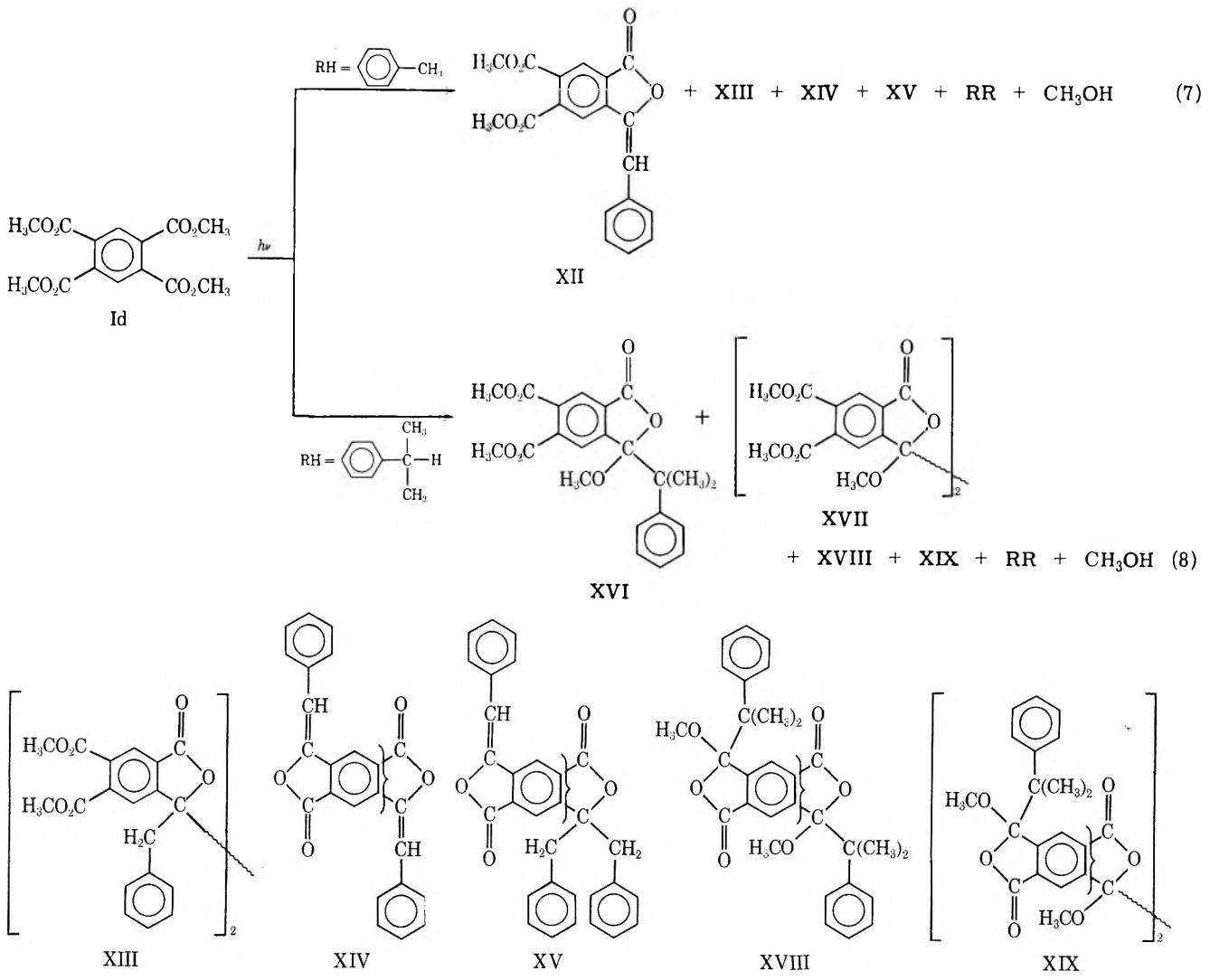


A more precise study of the excited charge-transfer complex postulated in the photoreduction of aromatic esters is now in progress and will be published shortly.

(7) The same reaction was done independently by T. Yonezawa, *et al.*, and XII and bibenzyl were obtained: A. Yoshino, M. Ohashi, and T. Yonezawa, *Chem. Commun.*, 97 (1971).

(8) In a series of the photoaddition reactions of aromatic esters to some olefins, we have found that an excited charge transfer complex may be a significant intermediate for the formation of oxetane: Y. Shigemitsu, Y. Katsuhara, and Y. Odaira, *Tetrahedron Lett.*, 2887 (1971).

(9) M. Yamamoto, T. Ohmichi, M. Ohoka, K. Tanaka, and Y. Nishijima, *Rep. Progr. Polym. Phys.*, **12**, 457 (1969).



Experimental Section

All melting points are uncorrected. Ir spectra were recorded with a Japan Spectroscopic Model IR-G spectrophotometer; nmr spectra with a Nippon Denshi Model JNM-3H60 spectrometer; and mass spectra with a Hitachi Model RMU-6E mass spectrometer. All irradiations were made with a 500-W high-pressure mercury arc through Pyrex under nitrogen at room temperature.

Materials.—Methyl *p*-cyanobenzoate (mp 62°) was prepared from methyl *p*-aminobenzoate by the Sandmeyer reaction. Dimethyl terephthalate (mp 142°) and dimethyl isophthalate (mp 72–73°) were commercially available and purified by recrystallization from methanol. Tetramethyl pyromellitate (mp 142.5–143.5°) was obtained by the esterification of the corresponding acid. Alkylbenzenes were purified by concentrated H_2SO_4, dried on sodium wire, and freshly distilled before use.

Reaction of Dimethyl Terephthalate (Ia) with Toluene.—A solution of Ia (0.97 g, 5×10^{-3} mol) in toluene (46 g, 5×10^{-1} mol) was irradiated for 300 hr. The reaction mixture was distilled to remove the solvent; by glpc analysis, the distillate (bp 62–108°) contained a small amount of methanol. The residual solid (3.5 g) was chromatographed on a silica gel column (60 g). Elution with petroleum ether (bp 30–60°) gave bibenzyl (0.27 g) which was recrystallized from ethanol, mp 51–53° (lit. mp 53–54°). Benzene–petroleum ether (1:1) gave a trace of unreacted Ia. The carbinol IVa (0.7 g, 40% based on reacted Ia) was eluted with benzene. Recrystallization from ethanol gave colorless needles: mp 113.5–114.5°; ir (KBr disk) 3570, 1690, 1600, 1495, 780, 750, 695 cm^{-1}; nmr (CCl_4) τ 2.12–3.00 (m, 14 H), 6.20 (s, 3 H), 6.80 and 6.99 (AB quartet, 4 H), 8.10 (s, 1 H); mass spectrum m/e 328 ($M - H_2O$), 91 (C_7H_7–).

Anal. Calcd for $C_{23}H_{22}O_3$: C, 79.74; H, 6.40. Found: C, 79.86; H, 6.46.

The pinacol IIIa (0.33 g, 26%) was eluted with ether. Recrystallization from dioxane gave colorless needles: mp 255–256°; ir (KBr disk) 3450, 1710, 1600, 1495, 745, 710, 695 cm^{-1}; nmr (DMSO-d_6) τ 2.20–3.10 (m, 18 H), 4.17 (broad s, 2 H), 6.23 (s, 6 H), 6.47 (broad, 4 H); mass spectrum m/e 255 (M/2), 224 ($M/2 - OCH_3$).

Anal. Calcd for $C_{32}H_{30}O_6$: C, 75.27; H, 5.92. Found: C, 75.30; H, 6.10.

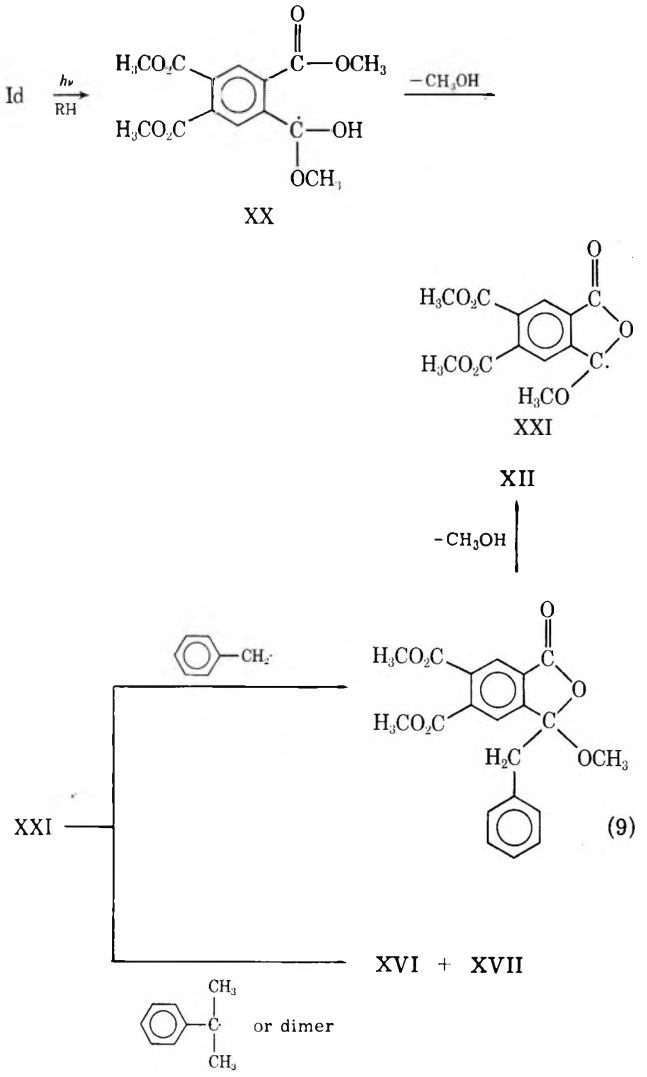
Reaction of Methyl *p*-Cyanobenzoate (Ib) with Toluene.—A solution of Ib (0.81 g, 5×10^{-3} mol) in toluene (92 g, 1 mol) was irradiated for 90 hr. The reaction mixture was treated as described above. In the distillate, a small amount of methanol was detected by glpc analysis. A trace of unreacted Ib was recovered. Bibenzyl (0.3 g), the carbinol IVb (0.65 g, 42%), white needles from ethanol, and the pinacol IIIb (0.44 g, 40%), white crystals from dioxane, were isolated. The carbinol IVb had mp 153–154°; ir (KBr disk) 3450, 2200, 1590, 1490, 740, 690 cm^{-1}; nmr (CCl_4) τ 2.38–3.28 (m, 14 H), 6.73 and 6.88 (AB quartet, 4 H), 8.70 (s, 1 H); mass spectrum m/e 313 (M^+), 295 ($M - H_2O$), 222 ($M - 91$), 91.

Anal. Calcd for $C_{22}H_{19}NO$: C, 84.31; H, 6.11; N, 4.47. Found: C, 84.61; H, 5.96; N, 4.50.

The pinacol IIIb had mp 240–241.5°; ir (KBr disk) 3480, 2200, 1600, 1490, 740, 700 cm^{-1}; nmr (DMSO-d_6) τ 2.45 (s, 8 H), 3.05 (s, 10 H), 4.50 (s, 2 H), 6.20 (broad, 4 H); mass spectrum m/e 222 (M/2), 204 ($M/2 - H_2O$).

Anal. Calcd for $C_{30}H_{24}N_2O_2$: C, 81.06; H, 5.44; N, 6.30. Found: C, 81.03; H, 5.33; N, 6.19.

Reaction of Dimethyl Isophthalate (Ic) with Toluene.—A solution of Ic (0.97 g, 5×10^{-3} mol) in toluene (92 g, 1 mol) was irradiated for 360 hr and unreacted Ic, 0.38 g, was recovered. The products were isolated as described above. A small amount of methanol was detected by glpc analysis. Bibenzyl (0.3 g) was obtained as white needles, mp 52–53°. The carbinol IVc



(0.6 g, 57%) was semisolid: ir (neat) 3460, 1720, 1605, 1495, 760, 730, 700 cm^{-1}; nmr (CCl_4) τ 2.00–3.20 (m, 14 H), 6.13 (s, 3 H), 6.69 and 6.92 (AB quartet, 4 H), 8.15 (s, 1 H); mass spectrum m/e 346 (M^+), 328 (M − H_2O), 91. IVc (0.1 g) was hydrolyzed with alkali to give the corresponding acid (0.05 g). The acid was obtained as colorless plates from benzene: mp 149–150°; ir (KBr disk) 3500, 3005, 3000, 2650, 2500, 1680, 1605, 1585, 1500, 760, 720 cm^{-1}; mass spectrum m/e 314 (M − H_2O), 91.

Anal. Calcd for $C_{22}H_{20}O_3$: C, 79.49; H, 6.06. Found: C, 79.52; H, 6.06.

A trace of white crystals, mp 228–230°, was obtained and assumed to be the pinacol IIIc by ir (3450, 1700, 1605, 1500, 745, 710 cm^{-1}) and mass spectra [m/e 255 (M/2), 224 (M/2 − OCH_3)], though further identification was impossible.

Reaction of Dimethyl Terephthalate (Ia) with Cumene.—A solution of Ia (0.97 g, 5 × 10^{-3} mol) in cumene (120 g, 1 mol) was irradiated for 150 hr. After removal of cumene and methanol, the residual solid was triturated with ether and allowed to stand overnight. The precipitate, which was identified as Ia, was collected by filtration (0.55 g, mp 138–140°). The filtrate was evaporated to leave solid (1.1 g), which was chromatographed on a silica gel column (40 g). Bicumyl (0.55 g) was eluted with petroleum ether and recrystallized from ethanol, mp 117–119° (lit.[6] mp 117–118°). The carbinol VIa (0.34 g, 55%) was eluted with benzene. Recrystallization from petroleum ether gave colorless needles: mp 94–95°; ir (KBr disk) 3500, 1690, 1610, 780, 690 cm^{-1}; nmr ($CDCl_3$) τ 2.10–3.00 (m, 9 H), 5.20 (s, 1 H), 6.15 (s, 3 H), 8.20 (s, 1 H), 8.66 (s, 3 H), 8.71 (s, 3 H); mass spectrum m/e 253 (M − OCH_3), 165 (M − 119), 119 [$C_6H_5C(CH_3)_2$].

Anal. Calcd for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 75.90; H, 7.06.

The pinacol Va (0.08 g, 22%) was eluted with ether. Recrystallization from dioxane gave colorless needles: mp 245–249°; ir (KBr disk) 3450, 1680, 1600, 770, 730, 700 cm^{-1}; nmr (DMSO-d_6) τ 2.10–3.00 (m, 8 H), 4.45 (broad, 2 H), 5.35 (broad, 2 H), 6.20 (s, 6 H); mass spectrum m/e 299 (M − OCH_3), 165 (M/2), 134 (M/2 − OCH_3).

Anal. Calcd for $C_{18}H_{18}O_6$: C, 65.44; H, 5.49. Found: C, 65.16; H, 5.58.

Reaction of *p*-Cyanobenzoate (Ib) with Cumene.—A solution of Ib (0.81 g, 5 × 10^{-3} mol) in cumene (120 g, 1 mol) was irradiated for 90 hr and unreacted Ib (0.05 g) was recovered. After removal of cumene and methanol by distillation, the products were isolated as described above. Bicumyl (0.84 g) was obtained as white crystals, mp 117–118°. The carbinol VIb (0.29 g, 25%) was obtained as colorless needles and recrystallized from benzene: mp 129–130.5°; ir (KBr disk) 3450, 2200, 1600, 1495, 770, 700 cm^{-1}; nmr (CCl_4:$CDCl_3$, 1:1) τ 2.50–3.05 (m, 9 H), 5.30 (s, 1 H), 8.00 (s, 1 H), 8.70 (s, 3 H), 8.76 (s, 3 H); mass spectrum m/e 251 (M^+), 132 (M − 119), 119.

Anal. Calcd for $C_{17}H_{17}NO$: C, 81.24; H, 6.82; N, 5.57. Found: C, 81.30; H, 6.86; N, 5.60.

Reaction of Dimethyl Terephthalate (Ia) with *p*-Cymene.—A solution of Ia (1.78 g, 0.92 × 10^{-2} mol) in *p*-cymene (430 g, 3.2 mol) was irradiated for 15 hr. After removal of *p*-cymene and methanol, the products were separated by silica gel column chromatography. Unreacted Ia (0.36 g) was recovered. The mixture of some aromatic hydrocarbons (0.88 g) was isolated and recrystallized from ethanol, mp 154–155° (lit.[10] mp 157°). The above compound was identified as 2,3-dimethyl-2,3-di-*p*-tolylbutane by its ir spectrum. The carbinol XI and two types of pinacol (X, Va) were isolated.

The carbinol XI (0.76 g, 24.2%) was obtained as colorless needles recrystallized from ligroin: mp 93–94.5°; ir (KBr disk) 3500, 1710, 1610, 1510, 770, 710 cm^{-1}; nmr (CCl_4) τ 2.15–3.50 (m, 12 H), 6.20 (s, 3 H), 6.62 and 6.96 (AB quartet, 2 H), 7.15–7.60 (m, 1 H), 7.70 (s, 3 H), 8.33 (s, 1 H), 8.60 (d, 6 H), 8.85 (d, 6 H); mass spectrum m/e 399 (M − OCH_3), 297 (M − 133), 133.

Anal. Calcd for $C_{29}H_{34}O_3$: C, 80.89; H, 7.96. Found: C, 81.03; H, 8.10.

The pinacol X (0.64 g, 29.6%) was obtained as white crystals from benzene: mp 212–220°; ir (KBr disk) 3510, 1730, 1610, 1510, 760, 715 cm^{-1}; nmr ($CDCl_3$) τ 2.07–3.60 (m, 16 H), 6.07 (s, 6 H), 6.33 and 7.16 (AB quartet, 4 H), 7.10–7.60 (m, 2 H), 7.70 (broad, 2 H), 8.88 (d, 12 H); mass spectrum m/e 563 (M − OCH_3), 297 (M/2), 133.

Anal. Calcd for $C_{38}H_{42}O_6$: C, 76.74; H, 7.12. Found: C, 76.67; H, 7.20.

The pinacol Va (0.01 g, 0.8%) was recrystallized from dioxane and identified by comparison with the pinacol from the reaction of Ia with cumene.

Reaction of Tetramethyl Pyromellitate (Id) with Toluene.—A solution of Id (3.1 g, 1 × 10^{-2} mol) in toluene (460 g, 5 mol) was irradiated for 15 hr. After removal of toluene and methanol by distillation, the residue (4.1 g) was chromatographed on a silica gel column (100 g). Bibenzyl (0.15 g) was eluted with petroleum ether. Elution with benzene–petroleum ether (1:1) gave the dilactone derivative XV (24 mg) along with a small amount of yellow crystals. To the mixture, benzene was added and a trace of insoluble precipitated material was separated by filtration, which was assumed to be the dibenzyliden phthalide derivative XIV by ir [1760, (carbonyl), 1650 (double bond), 740, 680 cm^{-1}] and mass spectra [m/e 366 (M^+), 91], though further identification was impossible. The filtrate was concentrated and then the pale yellow needles (XV) were precipitated: mp 265–267°; ir (KBr disk) 1785, 1760, 1660, 980, 795, 760, 700 cm^{-1}; mass spectrum m/e 458 (M^+), 367 (M − 91), 91.

Anal. Calcd for $C_{31}H_{22}O_4$: C, 81.20; H, 4.84. Found: C, 81.03; H, 4.82.

The benzylidene phthalide derivative XII (1.73 g, 60%) was eluted with benzene–petroleum ether (9:1). Recrystallization from benzene gave the pale yellow needles: mp 222–223°; ir (KBr disk) 1790, 1730, 1650, 1620, 1590, 970, 760, 690 cm^{-1}; nmr ($CDCl_3$) τ 1.70 (s, 1 H), 2.05 (s, 1 H), 2.10–2.70 (m, 5 H), 3.50 (s, 1 H), 6.02 (s, 3 H), 6.06 (s, 3 H); mass spectrum m/e 338 (M^+), 307 (M − OCH_3).

Anal. Calcd for $C_{19}H_{14}O_6$: C, 67.45; H, 4.17. Found: C, 67.64; H, 4.04.

Unreacted Id (0.47 g) was eluted with benzene. The lactone derivative XIII (0.26 g, 9.0%), eluted with chloroform, was

(10) A. H. Beckett and G. O. Jolliffe, *J. Chem. Soc.*, 1078 (1956).

recrystallized from benzene to give white crystals: mp 298–300°; ir (KBr disk) 1790, 1740, 1620, 770, 700 cm^{-1}; nmr ($CDCl_3$) τ 1.75 (s, 2 H), 2.00 (s, 2 H), 2.85–3.50 (m, 10 H), 5.85 (s, 6 H), 6.10 (s, 6 H), 6.75 (d, 2 H), 7.35 (d, 2 H); mass spectrum m/e 678 (M^+), 339 (M/2).

Anal. Calcd for $C_{38}H_{30}O_{12}$: C, 67.25; H, 4.46. Found: C, 67.43; H, 4.44.

Reaction of Tetramethyl Pyromellitate (Id) with Cumene.—A solution of Id (3.1 g, 1×10^{-2} mol) in cumene (600 g, 5 mol) was irradiated for 10 hr. After removal of cumene and methanol, benzene was added to the residual solid (5.8 g). The precipitate XVIIa was separated by filtration. XVIIa (0.92 g, 34.7%) was recrystallized from benzene to give white crystals: mp 258.5–260°; ir (KBr disk) 1795, 1730, 1620, 765, 695 cm^{-1}; nmr ($CDCl_3$) τ 1.52 (s, 1 H), 1.68 (s, 1 H), 2.46 (s, 1 H), 2.58 (s, 1 H), 5.93 (s, 12 H), 6.81 (s, 6 H); mass spectrum m/e 527 ($M - OCH_3$), 279 (M/2), 248 ($M/2 - OCH_3$).

Anal. Calcd for $C_{26}H_{22}O_{14}$: C, 55.92; H, 3.97. Found: C, 56.01; H, 3.77.

The filtrate was concentrated and the residual solid (4.8 g) was chromatographed on a silica gel column (120 g). Bicumyl (0.85 g) was eluted with petroleum ether as colorless needles, mp 117–118°. The benzo-γ-lactone derivative XVIII (20 mg) was eluted with benzene–petroleum ether (1:1). Recrystallization from benzene gave white crystals: mp 233–235°; ir (KBr disk) 1790, 1775, 1620, 1500, 785, 750, 700 cm^{-1}; nmr ($CDCl_3$) τ 2.11 (s, 1 H), 2.76 (m, 10 H), 3.46 (s, 1 H), 7.11 (s, 6 H), 8.48 (s, 6 H), 8.54 (s, 6 H); mass spectrum m/e 486 (M^+), 367 ($M - 119$), 119.

Anal. Calcd for $C_{30}H_{30}O_6$: C, 74.05; H, 6.22. Found: C, 73.84; H, 6.31.

The benzo-γ-lactone derivative XVI (1.87 g, 49.5%) was eluted with benzene–petroleum ether (9:1). Recrystallization from ether gave colorless plates: mp 88–90°; ir (KBr disk) 1780, 1730, 1620, 1500, 770, 760, 700 cm^{-1}; nmr (CCl_4) τ 2.03 (s, 1 H), 2.81 (broad, 5 H), 3.29 (s, 1 H), 6.12 (s, 3 H), 6.18 (s, 3 H), 7.00 (s, 3 H), 8.33 (s, 3 H), 8.66 (s, 3 H); mass spectrum m/e 398 (M^+), 367 ($M - OCH_3$), 279 ($M - 119$), 119.

Anal. Calcd for $C_{22}H_{22}O_7$: C, 66.32; H, 5.57. Found: C, 66.31; H, 5.35.

XIX (23 mg) was eluted with benzene as white crystals, which were insoluble in organic solvents: mp 341–343°; ir (KBr disk) 1785, 1630, 700 cm^{-1}; mass spectrum m/e 615 ($M - 119$), 119.

Anal. Calcd for $C_{42}H_{38}O_{12}$: C, 68.65; H, 5.21. Found: C, 68.83; H, 5.16.

Unreacted Id (0.14 g) was eluted with benzene. XVIIb (0.17 g, 6.4%) was eluted with ether. Recrystallization from benzene gave white crystals: mp 278–280°; ir (KBr disk) 1780, 1745, 1730, 1630, 775, 695 cm^{-1}; nmr ($CDCl_3$) τ 1.47 (s, 1 H), 1.67 (s, 1 H), 2.49 (s, 1 H), 2.57 (s, 1 H), 5.94 (s, 6 H), 5.97 (s, 6 H), 7.00 (s, 6 H); mass spectrum m/e 527 ($M - OCH_3$), 279 (M/2), 248 ($M/2 - OCH_3$).

Anal. Calcd for $C_{26}H_{22}O_{14}$: C, 55.92; H, 3.97. Found: C, 55.96; H, 3.60.

Reaction of I with Cyclohexane.—The solution of Ia (1.94 g, 1×10^{-2} mol), Ib (0.81 g, 5×10^{-3} mol), or Ic (0.97 g, 5×10^{-3} mole) in cyclohexane was irradiated for 270 hr and the reaction mixtures were treated in the same way as described in the reaction of Ia with toluene. However, neither methanol, bicyclohexyl, nor photoreductants was isolated.

Registry No.—Ia, 120-61-6; Ib, 1129-35-7; Ic, 1459-93-4; Id, 635-10-9; IIIa, 34566-34-2; IIIb, 34566-35-3; IIIc, 34566-36-4; IVa, 34566-37-5; IVb, 34566-38-6; IVc, 34599-29-6; Va, 34566-39-7; VIa, 34599-30-9; VIb, 34566-40-0; X, 34566-41-1; XI, 34566-42-2; XII, 34599-31-0; XIII, 34566-43-3; XV (1,7-dioxobenzofuran), 34566-44-4; XV (1,5-dioxobenzofuran), 34566-45-5; XVI, 34566-46-6; *meso*-XVII; 34599-32-1; (±)-XVII, 34599-33-2; XVIII (1,7-dioxobenzodifuran), 34566-47-7; XVIII (1,5-dioxobenzodifuran), 34566-48-8; XIX, (1,7-dioxobenzodifuran), 34599-34-3; XIX (1,5-dioxobenzodifuran), 34566-49-9; toluene, 108-88-3; cumene, 98-82-8; *p*-cymene, 99-87-6; cyclohexane, 110-82-7.

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Notes

A Stereochemical Study of the Ring Opening of Indene Oxide by Benzoic Acid[1]

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The stereochemistry of epoxide ring opening reactions has been extensively studied in recent years with the accrual of considerable information concerning the mechanisms of such reactions. The generally accepted mechanism is a bimolecular nucleophilic displacement (SN2) resulting in an inversion of configuration.[3] However, examples of ring opening reactions which gave retention of configuration have been reported.[4,5] In order to shed additional light on the mechanism of epoxide openings, we have examined the reaction of an unsymmetrical oxide with a carboxylic acid in an aprotic solvent.

The reaction of benzoic acid with indene oxide in anhydrous chloroform formed a hydroxy benzoate which, upon saponification, yielded exclusively *trans*-1,2-dihydroxyindan (**4**); no *cis*-1,2-dihydroxyindan (**5**) was detected (Scheme I). To substantiate the reaction products, known derivatives were synthesized by previously established routes.

The reaction of indene oxide with aqueous acid was reported[6] to yield a mixture of trans (**4**) and cis (**5**) isomers where the proportion of isomers formed was

(1) Taken in part from the Master's thesis of A. Gagis, at Fairleigh Dickinson University, 1971.

(2) Inmont Corp., Hawthorne, N. J. 07506.

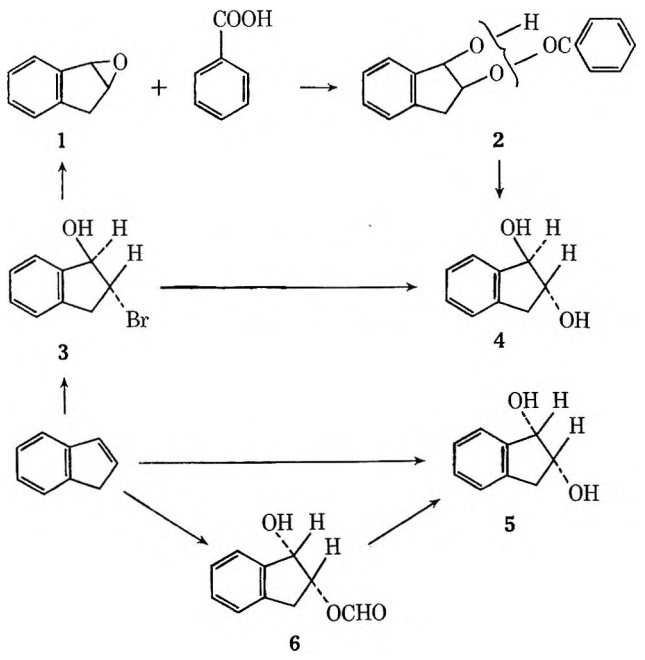
(3) (a) R. E. Parker and N. S. Isaacs, *Chem. Rev.*, **59**, 737 (1959); (b) S. Winstein and R. B. Henderson, "Hetrocyclic Compounds," Vol. 1, 27, R. C. Elderfield, Ed., Wiley, New York, N. Y.

(4) D. Y. Curtin, A. Bradley, and Y. Hendrickson, *J. Amer. Chem. Soc.*, **78**, 4064 (1956).

(5) J. H. Brewster, *ibid.*, **78**, 4061 (1956).

(6) J. Böeseken, *Recl. Trav. Chim. Pays-Bas*, **47**, 683 (1928).

SCHEME I



dependent on pH and temperature. Based on these results, Brewster[5] maintained the unfeasibility of the phenonium ion mechanism due to the geometry of indene oxide, instead postulating the "ion pair" mechanism. Berti and Bottari[7] supported the ion pair theory with their study of the cis addition of peracids to *trans*- and *cis*-stilbene to form hydroxy esters. The fact that the original work was performed in an aqueous rather than in a nonacidic, aprotic medium appears to have been overlooked.

In our work indene oxide was allowed to react with benzoic acid under the conditions recommended by Curtin[4] for the analogous reaction of *p*-methoxystilbene oxide. The latter proceeded through a cis addition (retention of configuration), while our product was the result of trans addition (inversion of configuration). Since the two reactions were performed under identical conditions, the only possible explanation for the pronounced stereochemical differences must be the position of the phenyl group. Unlike stilbene oxide, the structure of indene oxide does not permit the interaction of the phenyl group with the epoxide carbons to form the discrete phenonium ion intermediate. An ion pair mechanism proceeds with retention of configuration whether the phenyl group is free to migrate (as in stilbene oxide) or is held rigid (as in indene oxide). The possibility of an SN1 mechanism occurring is excluded on the basis of the bonds in a carbonium ion being coplanar, thus permitting attack from either side. This results in a mixture of cis and trans isomers.

The phenonium ion, "ion pair," or SN1 mechanisms are precluded by the absence of *cis* isomer (**5**). The results of our study therefore indicate that the ring opening of indene oxide by carboxylic acids in aprotic, nonacidic solvents proceeds with complete inversion of configuration. The reaction mechanism is of an SN2 order, which is considered the normal course for ring openings of epoxides.

(7) G. Berti and F. Bottari, *J. Org. Chem.*, **25**, 1286 (1960).

Experimental Section

All melting points were taken on a Fisher-Johns block apparatus and are uncorrected; boiling points are also uncorrected. Infrared spectra were recorded on a Beckman IR-5A spectrophotometer and were determined as Nujol mulls (unless otherwise stated). Nuclear magnetic resonance data were determined with a Varian T-60 using tetramethylsilane as an internal standard. Where "dried" is stated, magnesium sulfate was employed as the drying agent.

Reaction of Indene Oxide with Benzoic Acid in Chloroform (2).—A solution of 5.0 g of indene oxide in 60 ml of dried chloroform was allowed to stand for 3 days with benzoic acid. The solution was then washed with a 5% sodium carbonate solution and then with water, dried, and concentrated to yield 8.0 g (83%) of an oily liquid which proved difficult to crystallize: ir ($CHCl_3$) 3450 (OH), 1700 (C=O), 1265 (benzoate CO), 1050 (ether CO), 745 cm^{-1} (*o*-phenylene). This material was used directly without purification in the saponification step.

***trans*-1-Hydroxy-2-bromoindan (3).**—This bromo glycol was prepared in 60% yield according to the method of Suter and Milne:[8] mp on recrystallization from 95% ethanol, 129–130.5°; ir 725 cm^{-1} (*o*-phenylene); nmr ($CDCl_3$) δ 5.25 (m, 1, ArCH), 4.23 (m, 1, CHCH), 3.42 (q, 1, J = 15, 8.5 Hz, $ArCH_2$), 3.27 (q, 1, J = 16, 8 Hz, $ArCH_2$), 2.59 (s, 1, OH).

Indene Oxide (1).—To 400 ml of 13 *N* potassium hydroxide was added, with rapid agitation, 67.0 g of **3**. After stirring for 0.5 hr, a precipitate formed. The reaction mixture was poured into cold water, decanted, and extracted with ether. The ethereal extract was dried, concentrated, and distilled under reduced pressure to yield 22.4 g (53.8%) of epoxide **1**: bp 107–108° (8 mm); mp 30° (lit. mp 31°); ir ($CHCl_3$) 1240 cm^{-1} (epoxide); nmr ($CDCl_3$) δ 4.25 (d, 1, J = 3.5 Hz, ArCH), 4.02 (m, 1, CHCH), 3.10 (d, 1, J = 5 Hz, $ArCH_2$), 3.03 (d, 1, J = 3 Hz, $ArCH_2$).

***trans*-1,2-Dihydroxyindan (4).**—To a solution of 48.5 g of sodium carbonate in 725 ml of water was added 41.5 g of **3**, heated to reflux (102°) and held for 3.5 hr. The reaction solution was filtered and allowed to stand overnight at room temperature. The crystals that precipitated were filtered and dried *in vacuo* to yield 8.5 g (25%) of **4**. The crude product was stirred with toluene and then recrystallized twice from ethyl acetate: mp 157–159° (lit. mp 158.5–159.5°); ir 3300 (OH), 745 cm^{-1} (*o*-phenylene); nmr (pyridine) δ 5.52 (d, 1, J = 5 Hz, ArCH), 4.83 (m, 1, CHCH), 3.28 (q, 1, J = 16, 5 Hz, $ArCH_2$), 3.18 (q, 1, J = 16, 8 Hz, $ArCH_2$).

Osmium Tetraoxide Oxidation of Indene to *cis*-1,2-Dihydroxyindan (5).—A solution of 28.0 g of indene in 15 ml of ether and 1 ml of pyridine was added to a solution of 0.5 g of osmium tetraoxide in 15 ml of ether. The solution turned dark immediately; after 16 hr of stirring at room temperature, crystals were collected and washed with ether. They were dissolved in 20 ml of chloroform; the solution was stirred with 0.5 g of KOH in 40 ml of water containing 2.0 g of mannitol. Separation, decolorization with "Nuchar," and concentration yielded 0.29 g (67%) of **5**, mp 94–96°. Repeated recrystallizations did not raise the melting point above 98°: ir 3150 (OH), 745 cm^{-1} (*o*-phenylene); nmr (pyridine) δ 4.85 (d, 1, J = 5 Hz, ArCH), 4.59 (m, 1, CHCH), 3.09 (d, 1, J = 4 Hz, $ArCH_2$), 3.02 (d, 1, J = 5 Hz, $ArCH_2$).

Saponification of Glycol Ester (2).—To a solution of 25.0 g of 95% ethanol and 25.0 g of 6 *N* sodium hydroxide was added 6.0 g of **2**. The reaction mixture initially turned brown and then a deep violet. The solution was heated to reflux and held for 2.5 hr, cooled to 25°, and extracted with 5 × 50 ml portions of ether. The extract was washed with water, dried, and concentrated to yield 2.9 g (80%) of an oil which solidified on standing overnight. An ir spectrum of the oil prior to solidification was shown to be identical with that of authentic **4**. Addition of chloroform caused a precipitate to form which was filtered and dried *in vacuo*, mp 156–157°, ir spectrum identical with that of **4**. Recrystallization from ethyl acetate gave mp 156–157°. A mixture melting point with authentic **4** showed no depression.

Registry No.—**1**, 768-22-9; **3**, 10368-44-2; **4**, 4647-43-2; **5**, 4647-42-1; benzoic acid, 65-85-0.

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An Efficient Synthesis of 19-Nor-9β,10α Steroids

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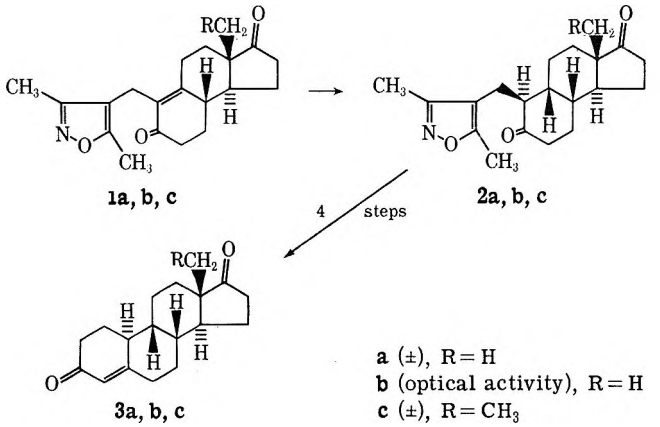
For a number of years, we have been interested in the biological properties of steroids having the abnormal 9β,10α configuration. As a logical extension of this work, we wished to prepare representative 19-nor-9β,-10α steroids. Previous syntheses of these compounds have involved hydrogenation of a de-A-Δ^9-5 ketone over an acidic palladium catalyst followed by closure of ring A,[1b] isomerization of 9α-11-oxoestranes with base followed by Birch reduction,[2] isomerization of a 5α,9α,-10α-11-oxo-19-norandrostane,[3,4] β-face hydrogenation of a $\Delta^{9(11)}$-estrane followed by Birch reduction,[3] hydrogenation of a 5β,10β-$\Delta^{9(11)}$-19-norandrostane followed by aromatization of ring A and Birch reduction,[5]



lithium–ammonia reduction of a Δ^8-estrane,[6] α-face epoxidation of a $\Delta^{9(11)}$-estrane followed by $LiAlH_4$ reduction and Birch reduction,[7] and hydrogenation of a 3-keto-$\Delta^{4,9}$-dienone followed by acid-catalyzed epimerization of C-10.[8] For a variety of reasons (low yield, lack of reduction specificity and/or unavailability of starting materials), these syntheses were not amenable to our purposes. We have, however, devised a stereoselective, high-yield preparation of (±)- and (+)-19-nor-9β,10α-androst-4-ene-3,17-dione (**3a,b**) and (±)-13β-ethyl-9β,10α-gon-4-ene-3,17-dione (**3c**), which were subsequently employed as starting materials for the desired derivatives.[9]

The isoxazole-substituted de-A 9-en-5-ones (**1**) were obtained[10,11] as intermediates in our syntheses of 19-nor steroids. In these syntheses the stereochemistry at C-9 was correctly established by hydrogenation of the enones **1** over palladium on carbon in an ethanol–triethylamine mixture. In order to obtain 19-nor-9β,-10α steroids, it was necessary to effect hydrogenation from the opposite, *i.e.*, β, face. In line with the observations of others,[1b,12] we hoped that a change in pH of the medium would reverse the direction of hydrogenation. In fact, hydrogenation of the enones **1** over palladium on barium sulfate in ethanolic HBr, conditions which were established after considerable experimentation with catalyst, solvent, and acid, gave mixtures containing high ratios (>7:1 by gc) of 9β:9α products. Despite relatively long hydrogenation times, no hydrogenolysis of the isoxazole ring occurred.[13] The 9β-diones **2a,b,c** were isolated by column filtration (to remove minor colored impurities) and crystallization in 75, 71, and 73% yield, respectively.[14] ORD measurements were in agreement with 9β configurations for these compounds;[15] this was confirmed by the obtention of known steroids from these materials.

Conversion of the diones **2** to the desired 19-nor-9β,-10α steroids **3** was carried out by an improved procedure developed earlier by us.[16] Thus, ketalization, hydrogenation in ethanolic NaOH solution, refluxing with aqueous base, and acidic deketalization and ring closure gave products **3a,b,c** in 61, 65, and 58% yield, respectively. These yields are somewhat lower than we have obtained in other similar conversions[10,16] due to the formation of small quantities of isomeric 19-nor-9β-androst-5(10)-ene-3,17-diones in the last step.[8] The completion of the synthesis of steroids **3** demonstrates the usefulness of the enones **1** as intermediates in high-yield syntheses of both 19-nor and 19-nor-9β,10α steroids.

Experimental Section[17]

(+)-19-(3,5-Dimethyl-4-isoxazolyl)-de-*A*-9β-androstane-5,17-dione (**2b**).—To a solution of 16.37 g (50 mmol) of enone **1b**[11] in 1 l. of absolute ethanol was added 5.0 g of 10% Pd/$BaSO_4$ catalyst (Fluka puriss) and the resulting mixture was stirred at 25° for 15 min. To the flask was added 25 ml (217 mmol) of 47% HBr and the mixture was then hydrogenated at atmospheric pressure and room temperature. After 16.0 hr, the uptake of

(1) (a) Correspondence concerning this communication should be addressed to this author at Hoffmann-La Roche, Inc., Nutley, New Jersey 07110; (b) L. Velluz, G. Nominé, R. Bucourt, A. Pierdet, and J. Tessier, *C. R. Acad. Sci., Ser. B*, **252**, 3903 (1963); Roussel-Uclaf S.A., French Patent 1,366,725 (1964).

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(9) The synthesis and testing results for these compounds will be reported separately.

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(11) J. W. Scott, R. Borer, and G. Saucy, *ibid.*, **37**, 1659 (1972).

(12) M. Uskoković, J. Iacobelli, R. Philion, and T. Williams, *J. Amer. Chem. Soc.*, **88**, 4538 (1966); R. A. Micheli, J. N. Gardner, R. Dubuis, and P. Buchschacher, *J. Org. Chem.*, **34**, 1457 (1969).

(13) The remarkable effect of pH on the hydrogenolytic lability of isoxazole rings has previously been noted: G. Stork, S. Danishefsky, and M. Ohashi, *J. Amer. Chem. Soc.*, **89**, 5459 (1967).

(14) A yield of 52% was reported[1b] for a similar hydrogenation.

(15) The products **2** were homogeneous at C-10 (nmr). It is assumed that the side chain, initially α, was isomerized to the stable equatorial (β) position under the reaction conditions.

(16) J. W. Scott, B. L. Banner, and G. Saucy, *J. Org. Chem.*, **37**, 1664 (1972).

(17) Melting points were determined on a Büchi melting point apparatus and are uncorrected. A Varian A-60 spectrometer was used to obtain the nmr spectra; tetramethylsilane was employed as internal standard. Infrared and ultraviolet spectra were recorded on Beckman IR-9 and Cary Model 14M spectrometers, respectively.

H_2 (1170 ml) had ceased. The catalyst was removed by filtration (Filter-Cel) and washed with fresh ethanol. The combined filtrates were cautiously neutralized with saturated $NaHCO_3$ and concentrated at reduced pressure to *ca.* 200 ml. This residue was diluted with benzene, washed with H_2O, and dried (Na_2SO_4). Solvent removal gave a light yellow solid which was filtered through silica gel with 7:3 benzene–ether to give 15.4 g of light tan solid. Crystallization from CH_2Cl_2–ether gave 11.72 g (71.3%) of dione **2b** as fine white needles, sintered at 171°, mp 173–175°. The analytical sample was prepared by a second crystallization from CH_2Cl_2–ether of similarly prepared material: mp 170.5–174°; uv max (C_2H_5OH) 222 nm (ϵ 4750); ir ($CHCl_3$) 1740 (C-17 C=O), 1714 (C-5 C=O), and 1638 cm^{-1} (isoxazole); $[\alpha]^{25}D$ +122.0° (c 0.895, $CHCl_3$); mass spectrum (70 eV) *m/e* 329 (M^+) and 110 (base peak); nmr ($CDCl_3$) δ 0.99 (s, 3, C-18 CH_3), 2.20 (s, 3), and 2.37 ppm (s, 3, 2 isoxazole CH_3); ORD (dioxane) $[\alpha]_{230}$ +560°, $[\alpha]_{232}$ ±0°, $[\alpha]_{244}$ −938° (sh), $[\alpha]_{276}$ −2276° (min), $[\alpha]_{295}$ ±0°, and $[\alpha]_{317}$ +2926° (max).

Anal. Calcd for $C_{20}H_{27}O_3N$: C, 72.95; H, 8.26; N, 4.25. Found: C, 72.80; H, 8.40; N, 4.14.

Following similar procedures, we prepared these respective compounds.

(±)-19-(3,5-Dimethyl-4-isoxazolyl)-de-*A*-9β-androstane-5,17-dione (2a).—Very fine white needles were obtained by crystallization from CH_2Cl_2–ether: mp 176–178.5°; nmr, ir, uv, and mass spectrum identical with those of (+) enantiomer **2b**.

Anal. Calcd for $C_{20}H_{27}O_3N$: C, 72.96; H, 8.26; N, 4.25. Found: C, 72.57; H, 8.26; N, 4.13.

(±)-19-(3,5-Dimethyl-4-isoxazolyl)-18-methyl-de-*A*-9β-androstane-5,17-dione (2c).—Fine white needles were obtained by crystallization from CH_2Cl_2–ether: sintered at 159–163°, mp 174–176°; uv max (C_2H_5OH) 221 nm (ϵ 4850); ir ($CHCl_3$) 1730 (C-17 C=O), 1707 (C-5 C=O), and 1634 cm^{-1} (isoxazole); mass spectrum (70 eV) *m/e* 343 (M^+) and 110 (base peak); nmr ($CDCl_3$) δ 0.83 (t, 3, J = 7 Hz, C-18 CH_3), 2.21 (s, 3), and 2.38 ppm (s, 3, 2 isoxazole CH_3).

Anal. Calcd for $C_{21}H_{29}O_3N$: C, 73.43; H, 8.51; N, 4.08. Found: C, 73.36; H, 8.52; N, 4.05.

19-Nor-9β,10α-androst-4-ene-3,17-diones (3).—The procedure previously described[10,16] for the conversion of an isoxazole group to the steroid ring A was employed. We obtained the following compounds.

(±)-9β,10α-Estr-4-ene-3,17-dione (3a).—Small white prisms from CH_2Cl_2–ether: mp 149.5–152° and 159–162° (lit.[6] mp 150–151° and 156–157°)[18]; uv max (C_2H_5OH) 241 nm (ϵ 16,800); ir ($CHCl_3$) 1740 (C-17 C=O), 1669 (C-3 C=O), and 1619 cm^{-1} (conjugated C=C); mass spectrum (70 eV) *m/e* 272 (M^+); nmr ($CDCl_3$) δ 0.97 (s, 3, C-18 CH_3) and 5.84 ppm (broad s, 1, C-4 *H*).

(−)-9β,10α-Estr-4-ene-3,17-dione (3b).—Fine white needles from acetone–isopropyl ether: mp 132–135.5° (lit.[19] mp 135°); ir, uv, mass spectrum, and nmr are identical with those of racemic material; $[\alpha]^{25}D$ −23.9° (c 1.055, $CHCl_3$).

(±)-13β-Ethyl-9β,10α-gon-4-ene-3,17-dione (3c).—Small colorless prisms from acetone: mp 203.5–207°; uv max (C_2H_5OH) 240 nm (ϵ 17,900); ir ($CHCl_3$) 1730 (C-17 C=O), 1662 (C-3 C=O), and 1615 cm^{-1} (conjugated C=C); mass spectrum (70 eV) *m/e* 286 (M^+) and 110 (base peak); nmr ($CDCl_3$) δ 0.81 (t, 3, J = 7 Hz, C-18 CH_3) and 5.89 ppm (broad s, 1, C-4 *H*).

Anal. Calcd for $C_{19}H_{26}O_2$: C, 79.68; H, 9.15. Found: C, 79.64; H, 9.12.

Registry No.—**2a**, 35085-36-0; **2b**, 35085-37-1; **2c**, 35085-38-2; **3a**, 35085-39-3; **3b**, 2645-92-3; **3c**, 35085-41-7.

Acknowledgments.—We would like to thank the members of our Physical Chemistry Section for their assistance during the course of this work.

(18) In many preparations this compound exhibited only a single mp of 149.5–152°.

(19) Roussel-Uclaf S.A., French Patent 1,453,221 (1966).

Tautomerism of Acid Derivatives[1a]

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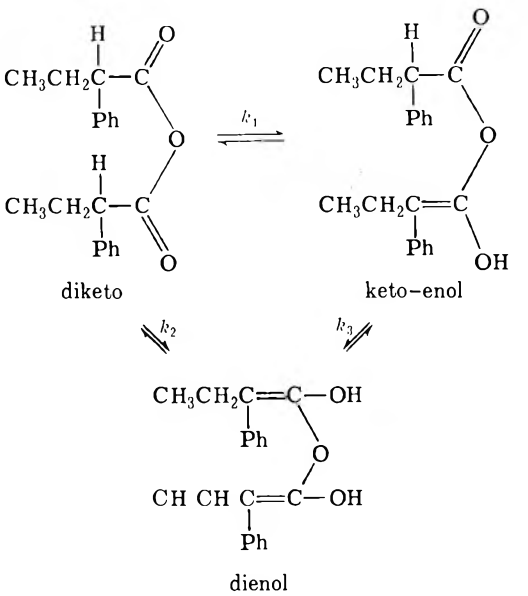
Optically active 2-phenylbutyric acid anhydride has been observed to undergo racemization on vacuum distillation[2,3] and to be thermochromic.[4,5,12] Distillation of the pure 2-phenylbutyric acid anhydride yields a distillate which is bright yellow. After a period of several hours, the yellow color of the distillate disappears. Repeated distillations of a sample of the anhydride give the same result. Nuclear magnetic resonance and infrared spectral studies of the freshly distilled anhydride indicate that diketo, keto-enol, and dienol forms are present.



An equilibrium between diketo and dienol tautomers can be established and maintained in carbon tetrachloride at room temperature. The dienol tautomer is believed to be responsible for the yellow color.

Thermochromism and tautomerism have also been observed during distillations of other acid derivatives

(1) (a) Supported in part by the Committee on Institutional Studies and Research, Murray State University, Murray, Ky. Presented in part at the Southeastern Regional Meeting of the American Chemical Society, Nashville, Tenn., Nov 1971. (b) Abstracted from the M.S. thesis of J. E. Hendon, Murray State University, 1971.

(2) A. Horeau, *Tetrahedron Lett.*, **No. 21**, 965 (1962).

(3) A. Horeau and R. Weidman, *Bull. Soc. Chim. Fr.*, 117 (1967).

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(5) A variety of organic compounds change color when heated and revert to the original color on cooling. This reversible dependence of color on temperature is known as thermochromism.[6] Thermochromism due to keto–enol equilibria has been observed for chromones, their derivatives, and chromone dimers.[7-9] Thermochromism of bindone has been explained on the basis of keto–enol tautomerism,[10] and the enolization of 1,3-diketo-2-phenyl-5-bromoindan has been used to explain its thermochromism.[11]

(6) J. H. Day, *Chem. Rev.*, **63**, 65 (1963).

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(9) A. Schoenberg and E. Singer, *ibid.* **94**, 254 (1961).

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such as 2-phenylpropionic and 2-phenylacetic acid anhydrides and 2-*p*-nitrophenylbutyric acid chloride.

Nmr Spectra.—The nmr spectrum of the colorless 2-phenylbutyric acid anhydride (diketo tautomer) gives the expected results: δ 7.05 (s, 10 H, phenyl), 3.3 (t, 2 H, methinyl), 1.8 (o, 4 H, methylene), 0.8 (t, 6 H, methyl). The results of the nmr spectra show that the rates of exchange among the tautomers were slow enough to observe each tautomer.

Spectra taken as a function of time indicate that the ratios of tautomers also change with time when the sample is maintained at the temperature of the instrument magnet (36°). If the freshly distilled anhydride is maintained at −80°, no change in tautomer composition is observed for at least 6 months, perhaps longer. Vacuum distillation of the anhydride and direct collection into an nmr tube containing carbon tetrachloride at −80° followed by warming and observing the nmr spectrum permitted the establishment of an equilibrium of approximately half and half diketo and dienol tautomers.

Chemical shift values for the various types of protons present in each tautomer are given in Table I.

TABLE I

CHEMICAL SHIFTS FOR 2-PHENYLBUTYRIC ACID ANHYDRIDE

	Type of proton (in CCl_4, ppm)			
Tautomer	Methyl	Methylene	Methinyl	Enol OH
Diketo	0.8	1.8	3.3	
Keto half of keto–enol	0.9	1.9	3.4	
Enol half of keto–enol	1.2	2.3		11.5
Dienol	1.2	2.3		11.5

Infrared Spectra.—In addition to the normal peaks observed in the infrared for the anhydride, the peaks described below underwent changes with time. Observations of infrared spectra of the freshly distilled anhydride as a function of time showed a broad peak at 3000 cm^{-1} that disappeared rapidly, a peak at 1700 cm^{-1} that disappeared more slowly than the one at 3000 cm^{-1}, and a strong, sharp peak at 2100 cm^{-1} that disappeared at the same rate as the one at 1700 cm^{-1}. The peak at 1700 cm^{-1} is due to the carbonyl in the keto half of the keto–enol tautomer. The broad peak at approximately 3000 cm^{-1} suggests intermolecular hydrogen bonding between dienol and diketo molecules. Perhaps the most interesting peak is the one at 2100 cm^{-1} because of its relative strength and position within the spectral region. At the present time no specific assignment can be made for this peak.

Experimental Section[13]

2-Phenylbutyric acid anhydride was prepared from the reaction of the sodium salt of 2-phenylbutyric acid with 2-phenylbutyryl chloride according to accepted procedures. Vacuum distillation [70° (0.02 mm)] of the anhydride was accomplished using a Nester-Faust Annular Teflon spinning band column. The collection apparatus permitted immediate sampling of the distillate and subsequent recording of nmr and ir spectra In some cases, collection was made directly into nmr tubes onto the solid solvent at −80°.

(13) Nmr spectra were taken on a Varian A-60A spectrometer in carbon tetrachloride with TMS as an internal standard. Infrared spectra were taken on Beckman IR-10 and Perkin-Elmer 137B spectrophotomers.

Registry No.—2-Phenylbutyric acid anhydride (diketo), 1519-21-7; 2-phenylbutyric acid anhydride (keto–enol), 35046-01-6; 2-phenylbutyric acid anhydride (dienol), 35046-02-7.

Magnetic Shielding of Acetylenic Protons in Ethynylarenes

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A number of studies of the nuclear magnetic resonance spectra of monosubstituted acetylenes, with particular emphasis on chemical shifts, have been reported in the literature.[1-4] These investigations mainly dealt with the effects of substituents,[1] the intermolecular interactions, and solvent anisotropy on the chemical shifts of acetylenic protons.[2,3] In general, alkyl substituents increase the shielding of the acetylenic protons while phenyl group largely decreases the shielding.[1] The decrease in shielding is attributed to the distortion of the π system of the acetylenic bond by the inductive effect,[4] or accounted for by the counteracting effect of the ring current by the phenyl moiety on the diamagnetic shielding of the cylindrical π-electron cloud of the triple bond.[5]

In the course of study on another problem, we have had occasion to prepare several ethynylarenes. In order to investigate further the effects of the aromatic nuclei on the diamagnetic shielding of the acetylenic proton, we have studied the nmr spectra of the acetylenic protons in ethynylarenes. The chemical shifts of the acetylenic protons of ethynylarenes are listed in Table I. These values were determined at a concentration of 0.015–0.020 mol fraction solute in CCl_4. The chemical shifts are reported in hertz and τ below TMS.

TABLE I

CHEMICAL SHIFTS OF THE ACETYLENIC PROTONS OF ETHYNYLARENES

		Chemical shift			
No.	Compd	Hz	τ	ΣR^{-3}	ΣIR^{-3}
1	Phenyl	183	6.95	0.02567	0.02567
2	2-Naphthyl	190	6.83	0.03144	0.03426
3	1-Naphthyl	201	6.65	0.03939	0.04293
4	1-Pyrenyl	214	6.43	0.04733	0.05612
5	9-Anthryl	220	6.32	0.05221	0.06157

The effects of substituents on the chemical shift of the acetylenic proton in phenylacetylene have been extensively investigated, and correlations between the

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(3) N. Nagakawa and S. Fujiwara, *Bull. Chem. Soc. Jap.*, **33**, 1634 (1960).

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(5) J. Dale, "Chemistry of Acetylenes," H. G. Viehe, Ed., Marcel Dekker, New York, N. Y., 1969, p 46.

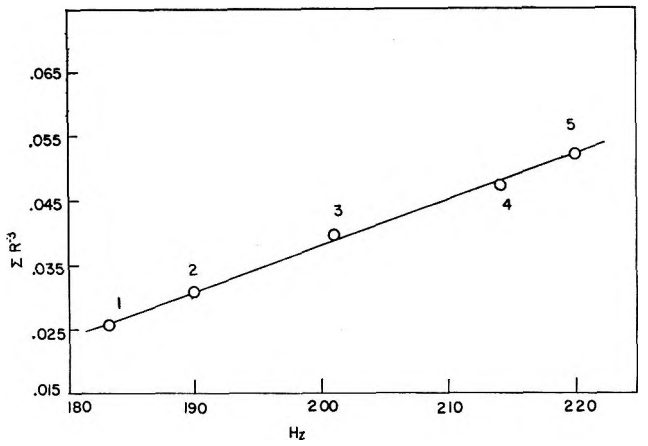

Figure 1.—Relationship between the chemical shift of acetylenic protons and ΣR^{-3}.

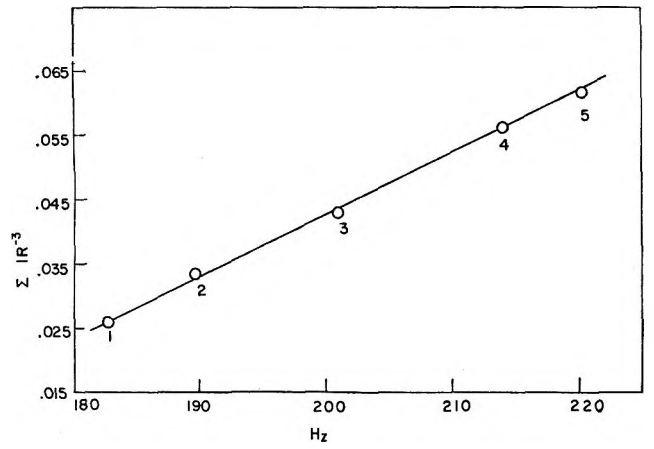

Figure 2.—Relationship between the chemical shift of acetylenic protons and ΣIR^{-3}.

chemical shifts and inductive (σ_I) and resonance (σ_R) parameters were empirically demonstrated. Strongly electron-donating substituents lead to an increase in shielding of the acetylenic proton, whereas electron-withdrawing substituents decrease the shielding. This phenomenon was simply explained by the changes of electron distribution in the ground state brought about by substituents transmitted to the acetylenic side chain.[6] Of the compounds studied in the present work, the electron density at the carbon to which the acetylene group is attached increases as shown by the following sequence.[7]

9-anthryl > 1-pyrenyl > 1-naphthyl > 2-naphthyl > phenyl

However, the shielding of the acetylenic proton in the above series was found to be in the reverse order. This observation suggests that the determinative factor in the chemical shifts of the ethynyl protons is the ring current of the different aromatic nuclei. The proton in phenylacetylene is located at a distance of 5.08 Å from the center of the phenyl ring. Our calculations based on Johnson and Bovey's[8] work showed a shift of 0.22 ppm due to the direct effect of ring current on the chemical shift of the acetylenic proton through space. This may be compared to the difference of 1.2 ppm observed between acetylene and phenylacetylene.

The magnitude of the chemical shift of the ring-bound protons in aromatic hydrocarbons is expressed by eq 1.[2] The term R is the distance from the center

$$\Delta\delta = \frac{-e^2a^2}{2mc^2R^3} \quad (1)$$

of the ring to the affected proton. Ouellette and van Leuwen have reported the chemical shifts of the methyl group of methyl arenes.[9] A good correlation was found between the chemical shifts of the methyl protons and the summation of the inverse cubes of the distances which separate the methyl groups and the centers of the aromatic rings.

A point dipole model for ethynylarenes was used to correlate the observed chemical shifts and the distance R separating the acetylenic bonds and the center of each aromatic ring. A half-bond distance (0.6 Å) of acetylenic bond was employed and all distances reported in this paper were determined by projections of Drieding models on paper. The data are shown in Table I, in which I is the ring current intensity,[10] which increases with the increase in number of rings and is a function of molecular structure. The chemical shift of the acetylenic protons plotted against ΣR^{-3} and ΣIR^{-3} are shown in Figures 1 and 2, respectively. Excellent correlations are obtained and slopes are given by eq 2 and 3 with the correlation coefficients $r = 0.991$ and 0.998, respectively.

$$\delta = 1408.3\Sigma R^{-3} + 136.4 \quad (2)$$

$$\delta = 1041.6\Sigma IR^{-3} + 155.7 \quad (3)$$

Butadi- and hexatriynyl derivatives of 1- and 2-naphthalenes and benzene were synthesized for further studies of the effects of the ring current on the acetylenic protons. The syntheses were carried out by the coupling reactions of the corresponding copper acetylides with bromoacetylene in dimethylformamide. The nmr spectra of these compounds with the reported data of the methyl di- and triynes are summarized in Table II.

TABLE II
CHEMICAL SHIFTS OF THE ACETYLENIC PROTONS OF POLYYNES

Compd	Chemical shifts, Hz (τ)[a] $n = 1$	$n = 2$	$n = 3$
$CH_3(-C\equiv C-)_nH$[b]	108 (8.20)	105 (8.25)	112 (8.13)
$C_6H_5(-C\equiv C-)_nH$	183 (6.95)	138 (7.70)	
$1\text{-}C_{10}C_9(-C\equiv C-)_nH$	201 (6.65)	150 (7.50)	145 (7.58)
$2\text{-}C_{10}H_9(-C\equiv C-)_nH$	190 (6.83)	141 (7.65)	

[a] In CCl_4 solution. [b] P. Jouve and M. P. Simonnin, *C. R. Acad. Sci.*, **257**, 121 (1963).

In the case of the methyl polyyne system, the spectra of the acetylenic protons are not affected by the chain length. However, aromatic polyynes show large differences in chemical shifts between mono- and diynes, whereas the chemical shift for the proton beyond diyne remains constant within experimental error. These observations support the explanation that the counter-

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TABLE III
PHYSICAL CONSTANTS AND MICROANALYTICAL DATA OF POLYYNES

Compd	Infrared absorption, cm^{-1} $\nu_{C\equiv CH}$	Infrared absorption, cm^{-1} $\nu_{C\equiv C\ Cu}$	Cu salt Dec pt, °C[a]	Cu salt Registry no.	Microanalytical data (Cu salts), % Found C	Found H	Calcd C	Calcd H
$C_6H_5(-C\equiv C-)_2H$	2110, 2190	2170 (broad)	170	34993-58-3	62.9	2.25	63.7	2.65
$1\text{-}C_{10}H_9(-C\equiv C-)_2H$	2195, 2210	2165	193	34993-59-4	69.0	3.50	69.8	3.74
$1\text{-}C_{10}H_9(-C\equiv C-)_3H$	2220, 2240	2180	165	34993-60-7	72.1	3.00	72.6	3.40
$2\text{-}C_{10}H_9(-C\equiv C-)_2H$	2220, 2180	2280	183	34993-61-8	69.2	3.44	69.8	3.74

[a] The decomposition temperatures were measured by a Du Pont 900 differential thermal analyzer.

acting effect of the ring current on the triple bond cloud in the ethynylarenes plays an important role for the deshielding in the acetylenic proton.

Experimental Section

Solvents and Reagents.—All solvents were dried over Drierite and distilled. 1,2-dibromoacetylene (Eastman Kodak Co.) and 1- and 2-acetylnaphthalenes (K and K Laboratories, Inc.) were purified by distillation.

Instrumental Analyses.—Nmr spectra were obtained on a Varian A-60 instrument. A Perkin-Elmer Model 237 infrared spectrophotometer was used for ir measurements. Mass spectra were obtained on a Hitachi Perkin-Elmer Model RMU 60.

Preparation of Ethynylarenes.—Ethynylbenzene purchased from Aldrich Chemical Co. was purified by distillation. 1- and 2-Ethynylnaphthalenes were prepared from 1- and 2-acetylnaphthalenes, respectively, by conversion to the α-chloroethenyl derivatives and then dehydrochlorination of the chloro derivatives with ethanolic potassium hydroxide: 1-ethynylnaphthalene, bp 135° (20 mm) [lit.[11] bp 143–144° (20 mm)], ir 3300 (C≡CH), 2100 cm^{-1} (C≡C); 2-ethynylnaphthalene, bp 110° (1 mm) [lit.[12] bp 104–107° (1 mm)], ir 3300 (C≡CH), 2100 cm^{-1} (C≡C). 1-Ethynylpyrene was supplied by Professor M. Nakagawa, Osaka University, Japan.

Preparation of 9-Ethynylanthracene.—9-Acetylanthracene was prepared from anthracene in 62% yield by Friedel–Crafts acetylation, mp 76°, ir 1690 cm^{-1} (C=O). A mixture of 110 g (0.50 mol) of 9-acetylanthracene and 228.8 g (1.10 mol) of phosphorous pentachloride in 600 ml of dried benzene was refluxed until the evolution of hydrogen chloride gas ceased (*ca.* 20 hr). The reaction mixture was then cooled and poured over crushed ice. The organic layer was then separated and washed twice with cold water. After drying over anhydrous magnesium sulfate, it was concentrated to about 100 ml and then treated with 600 ml of petroleum ether (bp 30–60°). After the solution was kept in an icebox overnight, the crystalline solid (32 g) separated was collected by filtration and recrystallized from benzene–petroleum ether to afford 9,10-dichloroanthracene, mp 217°, mass spectrum *m/e* 246 (M^+), no depression in mixture melting point with an authentic sample. From the filtrate, 9-(α-chloroethenyl)-anthracene was obtained: 30 g; mp 78° (after three recrystallizations from methanol); ir 1630, 1618 (C=C), 928, 900, 890 cm^{-1}; pmr ($CDCl_3$) τ 3.86 (d, 1H, J_{vic} = 1.6 Hz), 4.48 (d, 1 H, J_{vic} = 1.6 Hz), 2.54, 1.60 ppm (m, 9 H); mass spectrum *m/e* 238 (M^+), 202.

Anal. Calcd for $C_{16}H_{11}Cl$: C, 81.34 H, 4.68. Found: C, 81.45; H, 4.73.

9-(α-Chloroethenyl)anthracene (20 g) was then added portionwise with vigorous stirring to a solution of sodium *tert*-butoxide in *tert*-butyl alcohol, prepared from 18 g of sodium, at room temperature. After 3 hr of gentle reflux, the reaction mixture was left overnight at room temperature in the dark and treated with 200 ml of methanol, followed by the addition of 600 ml of ice–water. It was then extracted thoroughly with benzene. The benzene layer was washed with water and then dried over anhydrous magnesium sulfate. After the solvent was evaporated under vacuum at 30°, the residue was extracted with 1000 ml of petroleum ether. Evaporation of petroleum ether afforded 5 g of 9-ethynylanthracene. It was further purified by recrystallization from petroleum ether as orange-red crystals: mp 110–112°; ir 3250 (C≡CH), 2130 cm^{-1} (C≡C); mass spectrum *m/e* 202 (M^+).

Anal. Calcd for $C_{16}H_{10}$: C, 95.05; H, 4.95. Found: C, 95.17; H, 4.97.

Preparation of Di- and Triynes.—The syntheses were carried out by coupling reactions of the corresponding copper acetylides with bromoacetylene in DMF.[13] The di- and triynes obtained (Table III) were isolated, purified, and characterized as the copper salts. Free acetylenic compounds were isolated from the copper salts by treatment with aqueous hydrochloride. The following is a typical procedure for the reaction. Bromoacetylene was generated by the reaction of 1,2-dibromoacetylene with alcoholic potassium hydroxide and was dissolved in DMF. To this DMF solution of bromoacetylene, copper 1-naphthylacetylide was added and kept in an icebox for 24 hr. The reaction mixture was poured into water and the excess bromoacetylene was allowed to escape by constant stirring. 1-Naphthyldiyne obtained was extracted with ether. The ether extract was added to CuCl and NH_4OH solution under a nitrogen atmosphere. The copper salt was filtered, washed with alcohol and acetone, and dried.

Registry No.—**1**, 536-74-3; **2**, 2949-26-0; **3**, 15727-65-8; **4**, 34993-56-1; **5**, 13752-40-4; 9-(α-chloroethenyl)anthracene, 13752-41-5.

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An Improved Synthesis of Acylated 3-Amino-3-deoxy-D-ribofuranose[1]

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In the synthesis of puromycin a lengthy preparation of the modified sugar moiety is involved and the overall yield[2] from D-xylose to the acylated 3-amino-3-deoxy-D-ribofuranose (**1**) is 5%. We have been interested in the preparation of puromycin with sulfur replacing the oxygen of the sugar ring and in the course of our thinking envisioned a shorter route to the acylated **1** which would make possible a much easier route to the synthesis of natural puromycin. Our shorter procedure leads from D-glucose to the acylated **1** in an overall yield of 29%.

Earlier this laboratory reported the synthesis of 3-azido-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (**2**) from 1,2:5,6-di-*O*-isopropylidene-α-D-3-*O*-(*p*-tolysulfonyl)-α-D-glucofuranose.[3] When the azido compound **2** is selectively hydrolyzed at 25° with

(1) This work was supported by Public Health Service Research Grant No. CA12422 from the National Cancer Institute. Journal Paper No. 4660.
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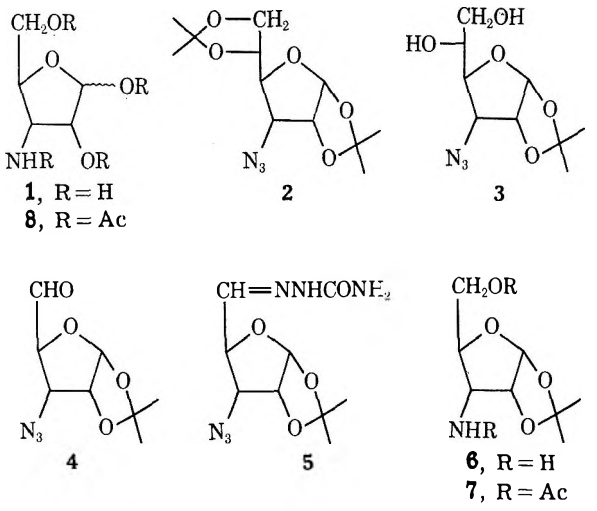

50% aqueous acetic acid, 3-azido-3-deoxy-1,2,*O*-isopropylidene-α-D-allofuranose (**3**) is obtained in 86% yield. The oxidation of **3** with sodium metaperiodate in water containing sodium bicarbonate affords 3-azido-3-deoxy-1,2-*O*-isopropylidene-5-*aldehydo*-α-D-ribopentadialdo-1,4-furanose (**4**) in 91% yield. The infrared spectrum of **4** shows strong absorptions at 2150 (N_3) and 1725 cm^{-1} (CHO) and none for the hydroxyl group. The aldehyde **4** gives a crystalline semicarbazone **5**. It is known that sodium borohydride reduces the azido group to the amino group in such solvent systems as 2-propanol[4] or *N*,*N*-dimethylformamide–methanol,[5] but we have found that, when the azido compound **4** is treated with sodium borohydride in water at 25°, the azido group is only partially reduced even after 16 hr, as indicated by the infrared spectrum which shows peaks at 3400 (OH), 2150 (N_3), and 1616 cm^{-1} (NH_2). However, the reduction becomes complete within 2 more hr when the reaction temperature is raised to 80° (bath). The initial lower temperature is desirable to prevent side reactions of the aldehyde group during reduction. The crude 3-amino-3-deoxy-1,2-*O*-isopropylidene-α-D-ribofuranose (**6**) reacts with acetic anhydride in pyridine to give crystalline 3-acetamido-3-deoxy-5-*O*-acetyl-1,2-*O*-isopropylidene-α-D-ribofuranose (**7**) in 98% yield based on aldehyde **4**. Acetolysis of **7** gives mainly the β anomer of 1,2,5-tri-*O*-acetyl-3-acetamido-3-deoxy-D-ribofuranose (**8**) isolable in 82% yield. The nmr spectrum of acetate **8** shows expected H-1 absorption occurring as a singlet at τ 3.85.

Predominant formation of the β-D anomer by acetolysis of 5,6-di-*O*-benzoyl-1,2-*O*-isopropylidene-3-deoxy-3-*C*-methyl-α-D-allofuranose has been reported.[6]

Experimental Section

Purity of products was determined by thin layer chromatography (tlc) on silica gel G[7] coated glass plates[8] irrigated with (a) benzene–ethyl acetate (6:1), (b) chloroform–acetone (9:2), and (c) chloroform–methanol (6:1). Solvent ratios were based on volumes. Melting points were determined on a Fisher-Johns apparatus and were corrected. Evaporations were done under reduced pressure with a bath temperature below 40°. Infrared spectra were obtained with a Perkin-Elmer Model 337 spectrometer and nmr spectra were determined with a Varian A-60 instrument. Optical rotations were measured on a Perkin-Elmer Model 141 polarimeter.

3-Azido-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (2).—D-Glucose gave 1,2:5,6-*O*-isopropylidene-α-D-glucofuranose in 90% yield on reaction with dry acetone in the presence of phosphoric acid and zinc chloride.[9] The diisopropylidene derivative reacted at 25° for 4 days with *p*-toluenesulfonyl chloride in pyridine to give 1,2:5,6-diisopropylidene-α-D-3-(*p*-tolylsulfonyl)-α-D-glucofuranose in 96% yield. The azido compound **2** was obtained from the tosyl compound in 53% yield by the literature procedure,[3] mp 38–39° (lit.[3,10] mp 38–39°).

3-Azido-3-deoxy-1,2-*O*-isopropylidene-α-D-allofuranose (3).—A solution of 0.8 g of **2** in 20 ml of 50% aqueous acetic acid was kept at 25° for 6 hr, after which acetic acid was neutralized with sodium bicarbonate and the mixture was extracted with chloroform (3 × 3 ml). The dried (Na_2SO_4) extract was evaporated to a syrup which crystallized on trituration with hexane. Recrystallization from ether–hexane gave the azido compound **3** (0.6 g, 86%): mp 76–77°; $[\alpha]^{25}D$ +111° (c 1.5, $CHCl_3$); ν_{max}^{Nujol} 3450 (OH) and 2150 cm^{-1} (N_3).

Anal. Calcd for $C_9H_{15}N_3O_5$: C, 44.03; H, 6.17; N, 17.13. Found: C, 44.23; H, 6.41; N, 17.07.

3-Azido-3-deoxy-1,2-*O*-isopropylidene-5-*aldehydo*-α-D-ribopentadialdo-1,4-furanose-5-semicarbazone (5).—The dihydroxy compound **3** (499 mg) was dissolved in 25 ml of water containing 200 mg of sodium bicarbonate. Sodium metaperiodate (950 mg) was then added in several portions with stirring. Progress of the reaction was monitored by tlc using the solvent system b. When the reaction was complete, the mixture was extracted with chloroform (3 × 25 ml). The dried (Na_2SO_4) extract was evaporated to give 3-azido-3-deoxy-1,2-*O*-isopropylidene-5-*aldehydo*-α-D-ribopentadialdo-1,4-furanose (**4**) (400 mg, 91%), which was homogeneous by tlc with the solvent system b: ν_{max} film 2150 (N_3), 1725 cm^{-1} (CHO).

A 100-mg portion of **4** was treated with a solution of 150 mg of semicarbazide hydrochloride and 220 mg of sodium acetate in 5 ml of water. On cooling crystals separated which were extracted with chloroform. The dried (Na_2SO_4) extract was evaporated to a crystalline residue which was recrystallized from chloroform–hexane to give 105 mg of the semicarbazone **5**, mp 170°, $[\alpha]^{25}D$ +187° (c 1.5, $CHCl_3$).

Anal. Calcd for $C_9H_{14}N_6O_4$: C, 39.99; H, 5.22; N, 31.10. Found: C, 40.09; H, 5.23; N, 30.97.

3-Acetamido-3-deoxy-5-*O*-acetyl-1,2-*O*-isopropylidene-α-D-ribofuranose (7).—The crude aldehyde **4** (300 mg) was taken up in 20 ml of water, 360 mg of sodium borohydride was added in several portions, and the mixture was stirred at 25° for 16 hr. A small portion was extracted with chloroform and an ir spectrum of the extract showed peaks at 3450 (OH), 2150 (N_3), and 1615 cm^{-1} (NH_2). The reaction temperature was then raised to 80° (bath) and 360 mg more of sodium borohydride was added. Within 2 hr the reaction was complete. The mixture was cooled, neutralized with acetic acid, and extracted with chloroform (3 × 25 ml). The dried extract was evaporated to give 3-amino-3-deoxy-1,2-*O*-isopropylidene-α-D-ribofuranose (**6**) (280 mg) as a syrup which was homogeneous by tlc with solvent b, ν_{max} film 3400 (OH) and 1615 cm^{-1} (NH_2) but none at 2150 cm^{-1}. The crude amino compound **6** (280 mg) was taken up in 3 ml of pyridine and 1.5 ml of acetic anhydride and kept at 25° for 16 hr. The mixture was poured into 20 g of ice and water and extracted with chloroform (3 × 15 ml). The extract was washed with sodium bicarbonate solution, dried (Na_2SO_4), and evaporated to a crystalline residue which was recrystallized from ether–hexane to give the acetyl derivative **7** (380 mg): mp 165°; ν_{max}^{Nujol} 3440 (NH), 1740 (OAc), and 1680 cm^{-1} (CONH); $[\alpha]^{25}D$ +101° (c 1.5, $CHCl_3$).

Anal. Calcd for $C_{12}H_{19}NO_6$: C, 52.72; H, 7.00; N, 5.12. Found: C, 52.92; H, 6.98; N, 5.04.

1,2,5-Tri-*O*-acetyl-3-acetamido-3-deoxy-β-D-ribofuranose (8).—A solution of 4.5 ml of acetic anhydride, 4.5 ml of acetic acid, and 0.25 ml of concentrated sulfuric acid was added at 0° to 400 mg of the isopropylidene derivative **7** and the resulting solution was kept at 0° for 3 days. The reaction mixture was

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then stirred with 5 g of sodium acetate, diluted with 30 ml of water, and extracted with chloroform. The extract was washed with saturated sodium bicarbonate solution, dried (Na_2SO_4), and evaporated to a syrup which was crystallized from ethyl acetate–heptane to give the acetyl derivative **8** (380 mg, 82%): mp 102–103°; ν_{max}^{Nujol} 3440 (NH), 1740 (OAc), and 1680 cm^{-1} (CONH); nmr ($CDCl_3$) τ 3.85 (s, due to H-1), 4.9 (d, H-2, $J_{2,3}$ = 5 Hz), 7.85, 7.90, 7.91, and 8.0 (due to 12 Ac protons); $[\alpha]^{25}D$ +44° (*c* 1.5, $CHCl_3$).

Anal. Calcd for $C_{13}H_{19}NO_8$: C, 49.18; H, 6.04; N, 4.41. Found: C, 49.39; H, 6.31; N, 4.42.

Registry No.—**3**, 35085-25-7; **4**, 35085-26-8; **5**, 35085-27-9; **6**, 14125-95-2; **7**, 29881-54-7; **8**, 35085-30-4.

4-Phenyl-1,2,3,6-tetrahydropyridines in the Prins Reaction. Examples of a Cis Steric Course

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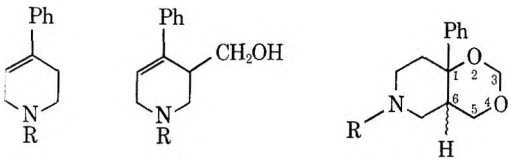
Schmidle and Mansfield[3] reported that the acid-catalyzed addition of formaldehyde to 1-substituted 4-phenyl-1,2,3,6-tetrahydropyridines (**1**) gave the corresponding 3-hydroxymethyltetrahydropyridines **2**. When this Prins reaction[4] is performed using a 10-fold or larger molar excess of formaldehyde, we find that the novel bicyclic 1,3-dioxanes **3** form in yields above 50%; they are isolated as crystalline hydrohalides. The 100-MHz pmr spectrum of **3a** in deuteriochloroform (Figure 1) shows a pair of doublets near δ 4.83 and 3.7, respectively each of two-proton intensity. The former is assigned to the 3-methylene group as the chemical shifts of the equatorial and axial protons are typical of protons flanked by oxygen atoms in 1,3-dioxanes[5] while the ^2J value is numerically low (~6 Hz), also characteristic of methylene in this environment.[6] The lower field half of the four-line signal near δ 3.7, assigned to the 5-methylene protons, shows clear evidence of vicinal coupling (^3J = 2.5 Hz) but the higher field doublet is merely broadened. The absence of a large



1 **2** **3**

a, R = Me; **b**, R = CH_2Ph; **c**, R = *t*-Bu

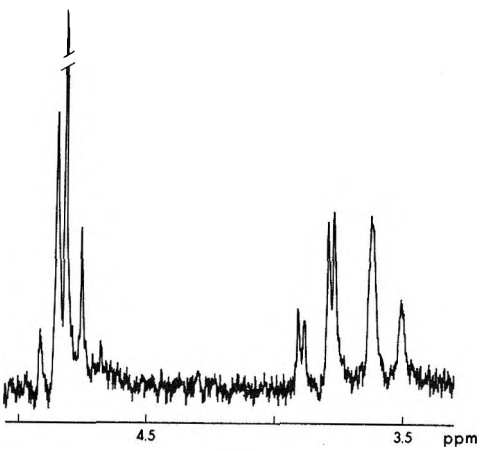
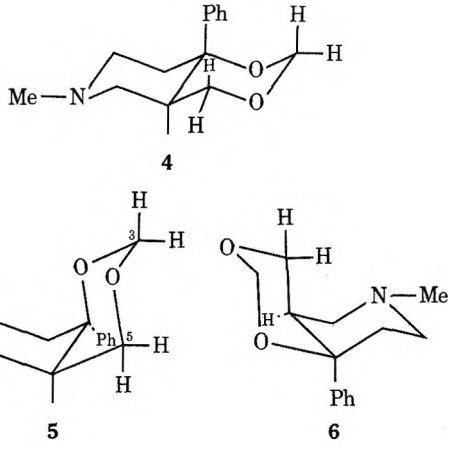


Figure 1.—Part of the 100-MHz pmr spectrum of the 1,3-dioxane **3a** in $CDCl_3$.

^3J value within this signal establishes that neither 5-methylene proton bears a 180° dihedral angle relationship to the 6-methine proton.[7] This conclusion excludes the trans isomer **4** and shows that **3a** is the cis form with the "O inside" (**5**) (opposed to axial hydrogens) rather than "O outside" (**6**)[8] preferred conformation. In **5** the 3 and 5 equatorial protons are linked by a near planar W pathway and their pmr signals display the anticipated long range coupling which broadens the doublets,[7] in support of this stereochemical assignment. Similar evidence was derived from the pmr spectra of **3b** and **3c** (Experimental Section).



4 **5** **6**

While both cis and trans products have been identified from the Prins reaction of acyclic alkenes,[9] the alicyclic derivatives cyclohexene[10] and *trans*-Δ^2-octalin[11] yield trans products exclusively in this procedure. Observation of a cis reaction pathway in the present alicyclic examples is probably a result of the steric demands of the bridgehead phenyl substituent; the same factor will similarly influence the conformation of the

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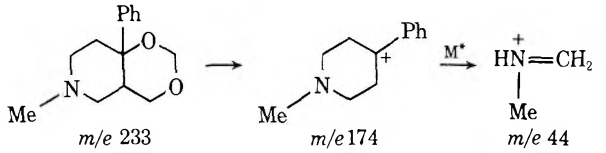
cis derivatives as will also that of the known preference for the "O inside" rather than "O outside" conformation in cis 1,3-dioxadecalanes.[8]

The mass spectral features of **3a** were consistent with the assigned structure; a molecular ion peak was present (*m/e* 233) and prominent lines at *m/e* 44 (base peak) and 174 plus a metastable peak at 11.1 showed the chief fragmentation pathway to be **7** → **8** → **9**.



7 8 9

Experimental Section[12]

Prins Reaction of 1-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine and Analogs.—A mixture of the tetrahydropyridine **1a** (112 g),[13] aqueous formaldehyde (500 ml, 37%), concentrated sulfuric acid (250 ml), and water (to 1-l. total volume) was heated under reflux for 5 hr. The cooled product was made alkaline with aqueous ammonia and extracted with ether which was dried (Na_2SO_4) and evaporated. The residue with excess of ethanolic hydrogen chloride gave the **1,3-dioxane 3a hydrochloride** (81 g): mp 323° dec from ethanol; pmr (base in $CDCl_3$) δ 4.87, 4.80 (2 d, 3-CH_2, ^2J = 6.5 Hz), 3.94, 3.45 (d d, d, 5-CH_2, ^2J = 11.5, ^3J = 2.5 Hz for lower field signal), 2.39 (s, NMe).

Anal. Calcd for $C_{14}H_{20}ClNO_2$: C, 62.32 H, 7.47 N, 5.19. Found: C, 62.05 H, 7.52; N, 5.14.

Similar treatment of **1b**[13] gave the *N*-benzyl analog **3b hydrochloride**: mp 282° dec from ethanol; pmr (base in $CDCl_3$) δ 4.87, 4.71 (2 d, 3-CH_2, ^2J = 6.5 Hz), ~3.78 (d d, one 5-CH_2 proton, ^2J = 11.5, ^3J = 2.0 Hz, higher field signal not resolved), 3.6 (s, NCH_2).

Anal. Calcd for $C_{21}H_{24}ClNO_2$: C, 69.45; H, 7.0; N, 4.0. Found: C, 68.95; H, 7.27; N, 3.93.

Reaction of **1c** gave the *N-tert*-**butyl analog 3c hydrobromide**: mp 297° dec; pmr (base in $CDCl_3$) δ 4.66, 4.58 (2 d, 3-CH_2, ^2J = 6.5 Hz), 3.81, 3.55 (dd, d, 5-CH_2, ^2J = 11.6 Hz, ^3J = 2.5 Hz for lower field signal), 1.12 (s, *t*-Bu).

Anal. Calcd for $C_{17}H_{26}BrNO_2$: C, 57.31; H, 7.36; N, 3.93. Found: C, 57.50; H, 7.38; N, 3.78.

The tetrahydropyridine **1c** was made by treating 1-*tert*-butyl-4-phenyl-4-piperidinol (see below) with a hot mixture of acetic and hydrochloric acids;[14] it formed a **hydrogen oxalate**, mp 224° from acetone–ether.

Anal. Calcd for $C_{17}H_{23}NO_4$: C, 66.8; H, 7.46; N, 4.5. Found: C, 66.8; H, 7.59; N, 4.6.

The 4-piperidinol, prepared from 1-*tert*-butyl-4-piperidone[15] and phenyllithium in the usual manner,[14] melted at 112–113° (from ether–ligroin).

Anal. Calcd for $C_{15}H_{23}NO$: C, 77.2; H, 9.93; N, 6.0. Found: C, 77.59; H, 9.93; N, 6.1.

It formed a **hydrogen oxalate**, mp 201–203°.

Anal. Calcd for $C_{17}H_{25}NO_5$: C, 63.14; H, 7.79; N, 4.3. Found: C, 62.98; H, 7.65; N, 4.3.

Registry No.—**1c** hydrogen oxalate, 35116-80-4; **3a** hydrochloride, 35116-81-5; **3b** hydrochloride, 35116-82-6; **3c** hydrobromide, 35116-83-7; 1-*tert*-butyl-4-phenyl-4-piperidinol, 35116-84-8; 1-*tert*-butyl-4-phenyl-4-piperidinol hydrogen oxalate, 35116-85-9.

(12) Melting points were determined in sealed capillary tubes (Gallenkampf apparatus) and are uncorrected. Pmr spectra were recorded in deuteriochloroform with tetramethylsilane as internal standard on a Varian HA-100 instrument.

(13) C. J. Schmidle and R. C. Mansfield, *J. Amer. Chem. Soc.*, **78**, 425 1702.

(14) A. F. Casy, A. H. Beckett, M. A. Iorio, and H. Z. Youssef, *Tetrahedron*, **21**, 3387 (1965).

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Reactions of 6-Acyl-5*H*-1-pyrindine-5,7(6*H*)-diones with Diamines

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As a continuation of our work on the preparation of 6-acyl-5*H*-1-pyrindine-5,7(6*H*)-diones (**1**) and on their reactions with hydrazine,[1] we now report the results of the reactions of compounds **1** with a variety of other diamines, with emphasis on a new pyridocyclopentadiazepine system.

We found that condensation of 6-acetyl-5*H*-1-pyrindine-5,7(6*H*)-dione (**1a**) with ethylenediamine yielded two different types of products depending upon the reaction conditions. Addition of **1a** (1 mol) to a refluxing ethanolic solution of ethylenediamine (1.5 mol) in the presence of formic acid gave 6-[1-(2-aminoethylimino)ethyl]-5*H*-1-pyrindine-5,7(6*H*)-dione (**2**) in good yields. Structure **2** is based on the elemental analyses, on the spectral data, and on the method of preparation which is analogous to that used by Mosher and Piesch to prepare 2-[1-(2-aminoethylimino)alkyl]-1,3-indandiones.[2]

Reverse addition of the reactants, ethylenediamine to a refluxing ethanolic solution of **1a**, and change of their molar ratio yielded the 1:2 product, 6,6′-[ethylenebis(nitriloethylidyne)]di-5*H*-1-pyrindine-5,7(6*H*)-dione (**6**), in very good yields.

When compound **2** was heated for 12 hr in refluxing 1-propanol and in the presence of formic acid, the expected ring closure took place with the formation of only one of the two possible isomers, 2,3-dihydro-5-methylpyrido[2′,3′:4,3]cyclopenta[2,1-*e*][1,4]diazepin-6(1*H*)-one (isomer **4**) or 2,3-dihydro-5-methylpyrido-[2′,3′:3,4]cyclopenta[2,1-*e*][1,4]diazepin-6(1*H*)-one (**3**). Structure **4** was assigned to the isolated isomer on the basis of elemental analyses, spectral data, and its reaction with ferrous ammonium sulfate. A 2:1 complex of pyridocyclopentadiazepinone **4** with ferrous iron as an intense blue-violet product was obtained. The ferrous iron complexes with the nitrogen of pyridine and the oxygen (enol form) of the cyclopentadiazepine moiety. The structurally related 2,3-dihydro-5-methyl-6*H*-indeno[1,2-*e*][1,4]diazepin-6-one[2] did not form a chelate with ferrous ammonium sulfate, indicating that it is not the diazepine ring which complexes with ferrous iron.

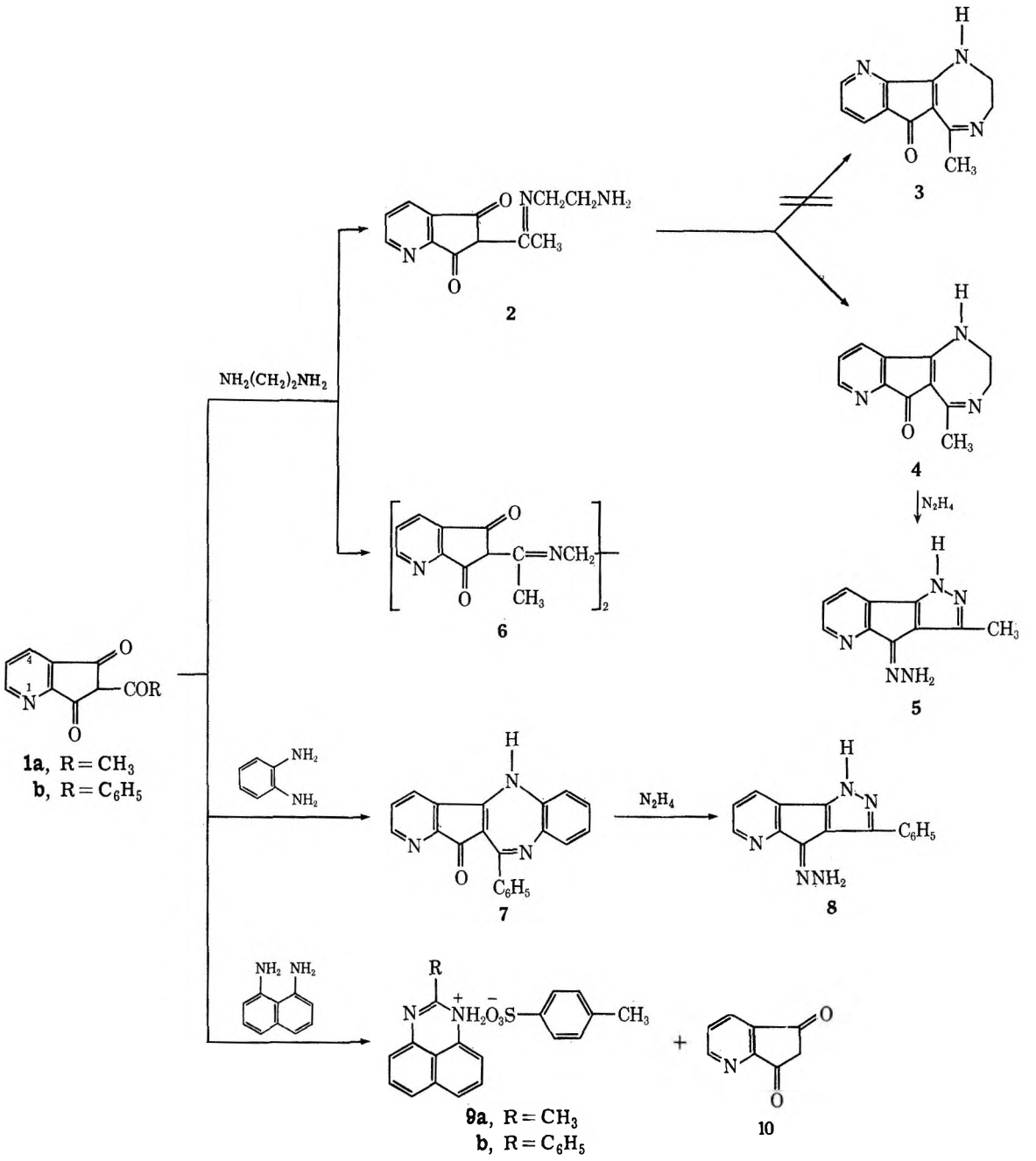
The ring closure of compound **2** to diazepinone **4** is similar to those previously observed in the reactions of 2-acetyl-1,3-indandione with ethylenediamine[2] and of 6-benzoyl-5*H*-1-pyrindine-5,7(6*H*)-dione with hydrazine.[1] Treatment of compound **4** with an excess of hydrazine in ethanolic solution gave the known hydrazone of 3-methylpyrazolo[3′,4′:3,4]cyclopenta[1,2-*b*]pyridin-4(1*H*)-one (**5**).[1]

Addition of 6-benzoyl-5*H*-1-pyrindine-5,7(6*H*)-dione (**1b**) to a refluxing solution of *o*-phenylenediamine in

* Deceased July 23, 1972.

(1) W. A. Mosher, T. El-Zimaity, and D. W. Lipp, *J. Org. Chem.*, **36**, 3890 (1971).

(2) W. A. Mosher and S. Piesch, *ibid.*, **35**, 1026 (1970).



2-propanol and in the presence of formic acid yielded directly 6-phenylbenzo[*b*]pyrido[2′,3′:4,3]cyclopenta-[2,1-*e*][1,4]diazepin-7(12*H*)-one (**7**). As in the above reported ring closure of compound **2** only one isomer was isolated and by analogy structure **7** was assigned. Treatment of compound **7** with excess hydrazine gave the known hydrazone of 3-phenylpyrazolo[3′,4′:3,4]-cyclopenta[1,2-*b*]pyridin-4(1*H*)-one (**8**).[1]

Like the 2-acyl-1,3-indandiones,[3] the acylpyrindine-diones **1a** and **1b** reacted with 1,8-naphthalenediamine in the presence of *p*-toluenesulfonic acid to give the known[3] *p*-toluenesulfonates of 2-methyl- and 2-phenyl-perimidines (**9a** and **9b**), respectively, in good yields. The expected by-product, 5*H*-1-pyrindine-5,7(6*H*)-dione (**10**), was isolated from the reaction mixture. The structure of the new compound **10** is based on elemental analyses and is consistent with the spectral data.

(3) W. A. Mosher and T. E. Banks, *J. Org. Chem.*, **36**, 1477 (1971).

Experimental Section[4]

6-Acetyl- and 6-benzoyl-5*H*-1-pyrindine-5,7-(6*H*)-diones were prepared as described in ref 1 from dimethyl 2,3-pyridinedicarboxylate and the appropriate methyl ketone.

6-[1-(2-Aminoethylimino)ethyl]-5*H*-1-pyrindine-5,7(6*H*)-dione (2).—A solution of 6-acetyl-5*H*-1-pyrindine-5,7(6*H*)-dione (1a, 1.89 g, 10 mmol) in ethanol (50 ml) was added dropwise over a 2-hr period to a refluxing mixture of formic acid (0.25 ml), ethanol (20 ml), and ethylenediamine (0.90 g, 15 mmol). The mixture was reduced to $^1/_4$th volume *in vacuo*. Water was added (5 ml) with stirring and the mixture was kept at room temperature overnight for complete crystallization. The solid was recrystallized from aqueous ethanol to give 1.36 g (59%) of **2**: mp 245–246°; ir 3340, 3150, 1690 cm^{-1}; mol wt 231 (mass spectrum).

(4) Melting points were determined with a Fisher-Johns melting point apparatus and are uncorrected. Ir spectra were recorded on Perkin-Elmer Infracord Models 137 and 237 spectrophotometers, using potassium bromide pellets. Nmr spectra were obtained on a Varian A-60A spectrometer using TMS as an internal standard and solvents as specified. Chemical shifts are reported as δ values (parts per million). Elemental analyses were performed by Dr. A. Bernhardt, Mikroanalytisches Laboratorium in Max Planck Institute für Kohlenforschung, Mülheim, Germany, and by Micro Analysis Inc., Marshallton, Del.

Anal. Calcd for $C_{12}H_{13}N_3O_2$: C, 62.34; H, 5.63; N, 18.18. Found: C, 62.32; H, 5.70; N, 18.06.

2,3-Dihydro-5-methylpyrido[2′,3′:4,3]cyclopenta[2,1-*e*][1,4]-diazepin-6(1*H*)-one (4).—A solution of **2** (1.15 g, 5 mmol) in 1-propanol (25 ml) and formic acid (1 ml) was heated at reflux for 12 hr. The solution was allowed to stand at room temperature. The formed orange plates of the formic acid salt of the ring-closed compound were treated with dilute NH_4OH in a water–ethanol mixture to yield 0.57 g (52%) of **4** as yellow needles, mp 264–266° (acetone), ir 3300 and 1640 cm^{-1}.

Anal. Calcd for $C_{12}H_{11}N_3O$: C, 67.61; H, 5.16; N, 19.72. Found: C, 67.58; H, 5.03; N, 19.84.

Reaction of Compound 4 with Ferrous Ammonium Sulfate.—A solution of compound **4** as the formate salt (2.4 g, 10 mmol) in water (5 ml) was added to a solution of $Fe(NH_4)_2(SO_4)_2 \cdot 6H_2O$ (1.5 g, 5 mmol) in water. An intense violet colored solution was formed. The dark blue residue obtained after evaporation of the water was crystallized from 1-propanol and dried at 100° in a drying pistol to give a 2:1 complex of pyridocyclopentadiazepinone **4** with ferrous iron, as a blue-violet product of mp 280–281° dec, ir 3300 cm^{-1}. The carbonyl band at 1640 cm^{-1}, observed in compound **4**, was absent.

Anal. Calcd for $C_{24}H_{20}N_8O_2Fe$: C, 59.75; H, 4.56; N, 17.43. Found: C, 59.34; H, 4.40; N, 17.11.

3-Methylpyrazolo[3′,4′:3,4]cyclopenta[1,2-*b*]pyridin-4(1*H*)-one Hydrazone (5).—A mixture of **4** (1.07 g, 5 mmol), 95% hydrazine (0.5 ml), and ethanol (25 ml) was heated at reflux for 24 hr. The solvent and excess hydrazine were evaporated under reduced pressure and the residue was crystallized from benzene to give 0.81 g (80%) of **5** as yellow crystals of mp 265°, alone and in mixture with an authentic sample synthesized by the literature procedure.[1]

6,6′-[Ethylenebis(nitriloethylidyne)]di-5*H*-1-pyrindine-5,7(6*H*)-dione (6).—A solution of ethylenediamine (0.6 g, 10 mmol) in ethanol (25 ml) was added dropwise to a refluxing solution of 6-acetylpyrindine-5,7-dione (**1a**, 3.80 g, 20 mmol) in ethanol (50 ml) over 1 hr while it stirred. The mixture was refluxed for 12 hr and cooled in an ice bath, and the resulting solid was collected by filtration, washed with cold ethanol, and recrystallized from ethanol to give **6** as yellow crystals (3.9 g, 95%), mp >300°.

Anal. Calcd for $C_{22}H_{18}N_4O_4$: C, 65.67; H, 4.47; N, 13.93. Found: C, 65.53; H, 4.49; N, 13.77.

6-Phenylbenzo[*b*]pyrido[2′,3′:4,3]cyclopenta[2,1-*e*][1,4]-diazepin-7(12*H*)-one (7).—A solution of 6-benzoyl-5*H*-1-pyrindine-5,7(6*H*)-dione (**1b**, 2.7 g, 10 mmol) in 2-propanol (25 ml) was added dropwise over a 1-hr period to a refluxing solution of formic acid (1 ml) and *o*-phenylenediamine (1.5 g, 15 mmol) in 2-propanol (25 ml). The mixture was refluxed for 24 hr and cooled. The dark green solid formed was recrystallized from ethanol to give **7** (47%) as dark green crystals: mp >300°; ir 3300, 1675–1640, 1600 cm^{-1}; mol wt 323 (mass spectrum).

Anal. Calcd for $C_{21}H_{13}N_3O$: C, 78.01; H, 4.01; N, 13.00. Found: C, 77.94; H, 4.00; N, 12.90.

Compound **7** when refluxed with excess hydrazine, as above described for the analogous methyl derivative **4**, gave compound **8**. The identity of this compound with an authentic sample of 3-phenylpyrazolo[3′,4′:3,4]cyclopenta[1,2-*b*]pyridin-4(1*H*)-one hydrazone[1] was established by mixture melting point determination and by comparison of the ir spectra.

Reaction of 6-Acyl-5*H*-1-pyrindine-5,7(6*H*)-diones with 1,8-Naphthalenediamine.—To a refluxing solution of 1,8-naphthalenediamine (9.0 g, 5.6 mmol), *p*-toluenesulfonic acid (0.8 g, 4 mmol), and anhydrous 2-propanol (50 ml), was added a solution of **1a** (0.76 g, 4 mmol) in anhydrous 2-propanol (70 ml) over 1 hr. The mixture was heated at reflux for an additional 24 hr, concentrated to 1/4th volume under reduced pressure and cooled. The precipitate was crystallized from 2-propanol to give a 77% yield of **9a**, mp 285–287°, identified by mixture melting point with an authentic sample.[3]

The mother liquor was evaporated to dryness and the residue (0.25 g) was dissolved in chloroform and chromatographed on neutral alumina (elution with chloroform). The compounds isolated from the column in order of elution were 1,8-naphthalenediamine, 5*H*-1-pyrindine-5,7(6*H*)-dione (**10**), and the starting material **1a**. Compound **10** recrystallized from ether–hexane gave yellow crystals: mp 150–151°; nmr ($CDCl_3$) 7.6, 8.0, 8.5 (m, 3 H), 3.2 (s, 2 H).

Anal. Calcd for $C_8H_5NO_2$: C, 65.31; H, 3.40; N, 9.52. Found: C, 65.30; H, 3.48; N, 9.47.

6-Benzoyl-5*H*-1-pyrindine-5,7(6*H*)-dione (**1b**) reacted with 1,8-naphthalenediamine as compound **1a** to give a 61% yield of 2-phenylperimidine *p*-toluenesulfonate (**9b**), identified (mixture melting point and ir) with an authentic sample,[3] and the above-cited 5*H*-1-pyrindine-5,7(6*H*)-dione (**10**).

Registry No.—**2**, 35092-40-1; **4**, 35129-61-4; 2:1 **4**–ferrous iron complex, 35085-14-4; **5**, 32111-70-9; **6**, 35092-42-3; **7**, 35092-43-4; **9a**, 28478-03-7; **10**, 35092-45-6.

The Chemistry of Cumulated Double-Bond Compounds. XI. The Reaction of Nitrones with Diphenylcarbodiimide

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The present paper reports a cycloaddition of nitrones to diphenylcarbodiimide, leading to oxadiazolidines. In these reactions, either oxadiazolidine **3** or triazolidinone **4**, which is a rearranged product from the oxadiazolidine **3**, was obtained and an amidine **5** was isolated in some cases. The formation of the amidine **5** may be due to the fragmentation of **3** or **4**. The results of the reactions and the analytical data of the products, **3** and **4**, are given in Tables I and II, respectively.

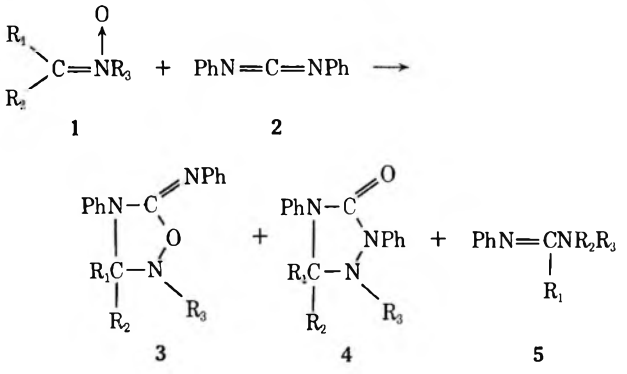


TABLE I

REACTION OF NITRONES WITH DIPHENYLCARBODIIMIDE

Compd	Nitrone R1	Nitrone R2	Nitrone R3	Reaction time, hr[a]	Yield, %[b] 3	Yield, %[b] 4	Yield, %[b] 5
1a	Ph	H	*t*-Bu	3	100	0	0
1b	Ph	H	Me	7	64	0	19
1c	Ph	H	Ph	34	0	28	43
1d	$-(CH_2)_5-$		Me	3.5	34	0	0

[a] An equimolar mixture of nitrone and diphenylcarbodiimide was refluxed in benzene under a nitrogen stream until the ir absorption of the N=C=N group disappeared. [b] After chromatography (aluminum oxide–benzene).

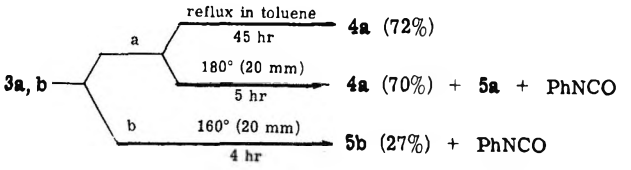
The ir spectra of **3a** and **4a** indicated peaks at 1685 and 1715 cm^{-1}, respectively. The former peak was assigned to a C=N stretching vibration and the latter to a C=O stretching vibration. Other spectral data were consistent with structures **3a** and **4a**.

TABLE II

PROPERTIES OF 3 AND 4[a]

Compd	Mp, °C	Ir (Nujol), cm⁻¹	Nmr (CDCl₃), τ	Mass spectrum (70 eV), m/e
3a	122–122.5	1685 (C=N)	2.4∼3.4 (m, 15, 3 Ph) 4.30 (s, 1, CH) 8.85 (s, 9, *t*-Bu)	371 (M^+) 252 (M^+ − PhNCO) 194 (PhNCNPh⁺) 180 (PhN=CPh⁺)
3b	108.5–109.5	1675 (C=N)	2.3∼3.2 (m, 15, 3 Ph) 4.44 (s, 1, CH) 7.02 (s, 3, CH_3)	329 (M^+) 210 (M^+ − PhNCO) 194 (PhNCNPh⁺)
3d	115–116	1675 (C=N)	2.5∼3.3 (m, 10, 2 Ph) 7.16 (s, 3, CH_3) 7.7∼9.1 (m, 10, $(CH_2)_5$)	321 (M^+) 202 (M^+ − PhNCO) 194 (PhNCNPh⁺)
4a	137–138.5	1715 (C=O)	2.4∼3.3 (m, 15, 3 Ph) 4.14 (s, 1, CH) 8.80 (s, 9, *t*-Bu)	371 (M^+) 314 (M^+ − *t*-Bu) 195 (314 − PhNCO)
4c	142–143.5	1710 (C=O)		391 (M^+) 271 (M^+ − PhNCO) 180 (PhN=CPh⁺)

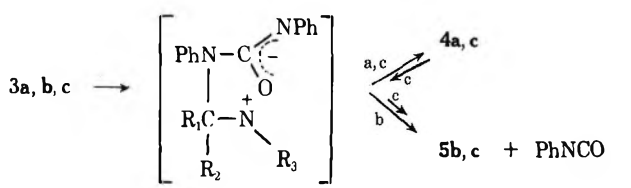
[a] Satisfactory analytical data (±0.2% for C, H, N) are reported for all compounds: Ed.



In the reaction of the nitrone **1a**, the oxadiazolidine **3a** was quantitatively obtained. The compound **3a** underwent thermal rearrangement to **4a** and fragmentation to the amidine **5a** and phenyl isocyanate under severe conditions. Although the reaction of the nitrone **1b** was carried out under mild conditions, the triazolidinone **4b** was not observed, but a considerable amount of the fragmentation product **5b** was isolated. The rearrangement of **3d** to **4d** was not observed under similar conditions. The low yield of **3d** may be ascribed to the hygroscopic property and instability of the nitrone **1d**.

The thermal rearrangement of **3a** to **4a** implies that a triazolidinone **4** is more stable than an oxadiazolidine **3**. The electron-donating ability of substituents, R_3, is considered to be the dominant effect on the stability of **3**. A steric effect of R_3 is inconsistent with the stability order **3a** > **3b** > **3c**.

The rearrangement and fragmentation of **3** can be accounted for by the assumption of the intermediate **6**.



6

Unless the positive nitrogen atom has an effective electron-donating substituent, hydride shift occurs immediately to give amidine **5** and phenyl isocyanate. Therefore, **4b** was not formed. The fact that a large amount of **5c** was obtained in the reaction of **1c** can be accounted for by the reverse reaction, **4c** to **6**, due to the instability of **4c**.

Experimental Section

Materials.—α-Phenyl-*N*-*tert*-butylnitrone (**1a**),[1,2] α-phenyl-*N*-methylnitrone (**1b**),[3] α,*N*-diphenylnitrone (**1c**),[4] and α,α-pentamethylene-*N*-methylnitrone (**1d**)[5] were prepared from 2-*tert*-butyl-3-phenyloxaziridine, benzaldehyde and *N*-methylhydroxylamine, benzaldehyde and *N*-phenylhydroxylamine, and cyclohexanone and *N*-methylhydroxylamine according to the reported procedures, respectively: **1a**, mp 74–75° (lit.[2] mp 75°); **1b**, mp 80–81° (lit.[3] mp 82°;) **1c**, mp 112–113.5° (lit.[4] mp 113–114°); **1d**, bp 101–106° (2 mm) [lit.[5] bp 96° (1 mm)].

Diphenylcarbodiimide was prepared from phenyl isocyanate according to the same procedure as reported previously:[6] bp 170° (7 mm).

Reaction of Nitrone 1a.—A solution of nitrone **1a** (0.026 mol) in benzene (20 ml) was added dropwise to diphenylcarbodiimide (0.026 mol), and the mixture was refluxed under nitrogen stream for 3 hr until the characteristic ir absorption of the N=C=N group (2140 cm^{-1}) disappeared. After the mixture cooled, 9.55 g (100%) of the crude product was filtered off and recrystallized (benzene–hexane) to give pure 2-*tert*-butyl-3,4-diphenyl-5-phenylimino-1,2,4-oxadiazolidine (**3a**), colorless granules.

Reaction of Nitrone 1b.—The reaction between 0.033 mol of nitrone **1b** and 0.033 mol of diphenylcarbodiimide was carried out by the same procedure as above. After refluxing for 7 hr, the reaction mixture was chromatographed (aluminum oxide–benzene) to give 7.0 g (64%) of 2-methyl-3,4-diphenyl-5-phenylimino-1,2,4-oxadiazolidine (**3b**), 1.3 g (19%) of N^1-methyl-N^2-phenylbenzamidine (**5b**), and 0.9 g of *N*,*N*′-diphenylurea.

Oxadiazolidine **3b** was recrystallized (benzene–hexane), colorless needles.

Amidine **5b** was recrystallized (benzene–hexane): colorless needles; mp 136.5–138°; ir (Nujol mull) 3240 (NH), 1605 cm^{-1} (C=N); mass spectrum (70 eV) *m/e* 210 (M^+, calcd 210), 180 (M^+ − $NHCH_3$), 133 (M^+ − Ph).

The ir spectrum of *N*,*N*′-diphenylurea was identical with that of an authentic sample.

Reaction of Nitrone 1c.—The reaction between 0.025 mol of nitrone **1c** and 0.025 mol of diphenylcarbodiimide was carried out by the same procedure as above. Ir spectra indicated the formation of product **4c** in the initial course of the reaction which slowly increased. After refluxing for 34 hr, the reaction mixture was chromatographed (aluminum oxide–benzene) to

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(6) Y. Ohshiro, Y. Mori, T. Minami, and T. Agawa, *J. Org. Chem.*, **35**, 2076 (1970).

give 2.7 g (28%) of 1,2,3,4-tetraphenyl-1,2,4-triazolidin-5-one (4c), 2.9 g (43%) of *N*,*N'*-diphenylbenzamidine (5c), and 2.8 g of *N*,*N'*-diphenylurea.

Triazolidinone 4c was recrystallized (benzene–hexane), colorless needles.

Amidine 5c was recrystallized (EtOH) to give colorless needles, whose spectral data and melting point were identical with those of the authentic sample:[7] mmp 148.5–149.5°.

Reaction of Nitrone 1d.—Nitrone 1d (0.088 mol) and diphenylcarbodiimide (0.084 mol) were treated by the same procedure as above to give 9.1 g (34%) of 2-methyl-3,3-pentamethylene-4-phenyl-5-phenylimino-1,2,4-oxadiazolidine (3d). Compound 3d was recrystallized (petroleum ether), colorless plates.

Thermal Treatment of Oxadiazolidine 3a. A.—A solution of oxadiazolidine 3a (0.50 g) in toluene (20 ml) was refluxed for 45 hr. The ir spectrum of the solution indicated that almost all of 3a had changed. The solvent was removed and then the residue was chromatographed (aluminum oxide–benzene) to give 0.36 g (72%) of 2-*tert*-butyl-1,3,4-triphenyl-1,2,4-triazolidin-5-one (4a), which was recrystallized (benzene–hexane) to afford colorless granules.

B.—Oxadiazolidine 3a (1.0 g) was heated at 180° for 5 hr under reduced pressure (20 mm), and a small amount of phenyl isocyanate was trapped (−70°). The residue was chromatographed (aluminum oxide–benzene) to give 0.70 g (70%) of triazolidinone 4a and a small amount of N^1-*tert*-butyl-N^2-phenylbenzamidine (5a): ir (Nujol mull) 3420 (NH), 1622 cm^{-1} (C=N). The oxadiazolidine was not recovered.

Thermal Treatment of Oxadiazoldine 3b.—Employing the same procedure as above, 0.60 g of 3b was heated at 160° for 4 hr (20 mm). Phenyl isocyanate (0.11 g, 52%) was trapped and the residue was chromatographed (aluminum oxide–benzene) to give 0.10 g (27%) of amidine 5b. Compounds 3b and 4b were not obtained.

Registry No.—3a, 35105-50-1; 3b, 35105-51-2; 3d, 35105-52-3; 4a, 35105-53-4; 4c, 35105-54-5; 5b, 2397-29-7; diphenylcarbodiimide, 622-16-2.

Acknowledgment.—The authors thank Mr. Tetsuya Taguchi and Mr. Akio Baba for their help in the experiments.

(7) A. C. Hontz, and E. C. Wagner, "Organic Syntheses," Collect. Vol. IV, Wiley, New York, N. Y., 1955, p 258.

3-Oxo-5-cyanopentanamide. A Novel β-Keto Amide from *meso*-Butadiene Diepoxide

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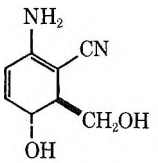
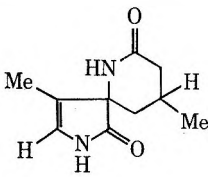
In 1964 Johnson and Heeschen[1] reported the isolation of compound I from the reaction of unbuffered sodium cyanide solution (pH 11.5–12.5) with epichlorohydrin. More recently Moppett, Johnson, and Dix[2] reported the analogous reaction of 2-methylepichlorohydrin which led to an entirely different structural type, namely compound II.



I

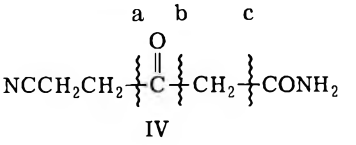


II

In continuation of these studies we now find that *meso*-butadiene diepoxide (III) on treatment with potassium cyanide in the presence of magnesium sulfate (pH ~9.5) leads to 3-oxo-5-cyanopentanamide (IV), and not *meso*-1,4-dicyano-2,3-dihydroxybutane (V). Under conditions of high pH IV not unexpectedly undergoes further transformation, and, when the reaction is conducted in the absence of magnesium sulfate (pH 11.5–12.5), little or none of the β-keto amide IV is obtained.

3-Oxo-5-cyanopentanamide (IV) is a water-soluble, white crystalline solid whose ir spectrum displayed characteristic bands at 3400 and 3170 (NH), 2245 (CN), 1720 (C=O), and 1650 ($CONH_2$) cm^{-1}. It gives with ferric chloride solution an intense violet coloration diagnostic for a β-dicarbonyl system. The nmr spectrum of IV possesses two diffuse singlets at δ 7.0 (one NH proton) and 7.4 (one NH proton) which are readily exchanged with deuterium oxide. The remaining six protons are present as a complex multiplet in the region of δ 2.2–3.2.

The most prominent peaks of the mass spectrum of IV arise from α cleavages. Cleavage at a, b, and c



IV

leads to the ions $C_3H_4NO_2$, C_4H_4NO, and C_5H_6NO, respectively. The parent ion and the fragment $C_3H_4NO_2$ eliminate ammonia.

Oxidation of IV by treatment with concentrated nitric acid followed by methylation of the acidic crystalline residue with diazomethane led to dimethyl oxalate and dimethyl succinate. Base-catalyzed hydrolysis of IV gave succinic acid, further identified as its dimethyl ester. The sodium salt of IV was generated by the use of dimsyl sodium.[3] On treatment with *meta*-chlorobenzyl bromide it afforded the mono-*meta*-chlorobenzyl derivative (VI) and the bis(*meta*-chlorobenzyl) derivative (VII).

We propose the reaction sequence of Scheme I for the mechansim of transformation of *meso*-butadiene diepoxide (III) into 3-oxo-5-cyanopentanamide (IV). The first step of our proposed scheme embraces nucleophilic substitution by cyanide ion on the primary carbon atoms of III leading us to V, whereupon interaction of one of the secondary hydroxyl groupings with a nitrile moiety (1,3 relationship) affords the cyclic intermediate VIII. Base-catalyzed rearrangement of VIII in the fashion indicated by Scheme I would then generate IX or X depending on which of its two diastereotopic protons are abstracted by base. The latter now has available to it by a series of conventional steps a mechanism for passage into IV by virtue of the cis relationship of its secondary hydroxyl and nitrile groupings.

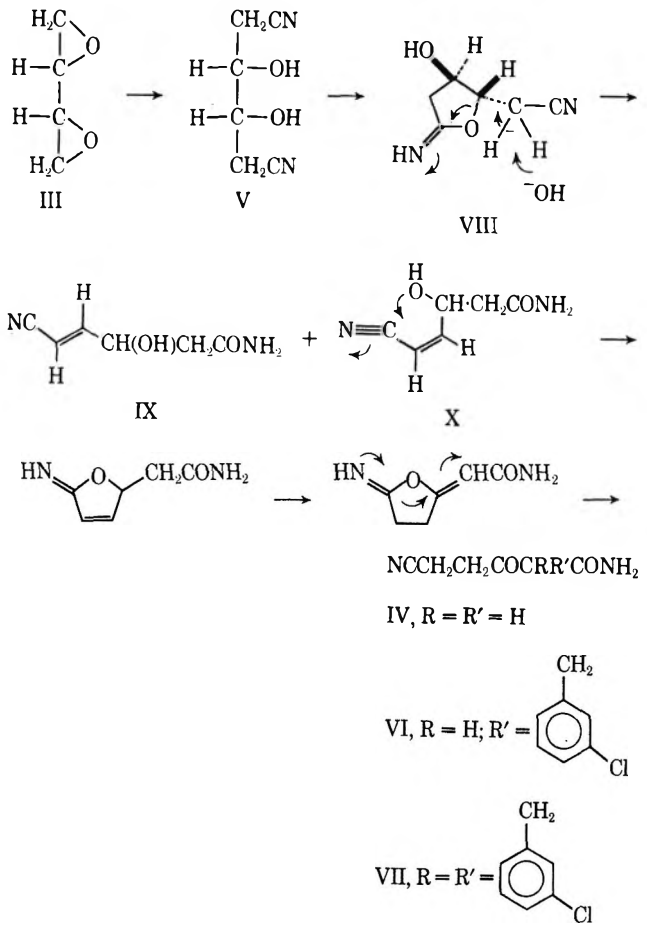
We were able to isolate from the mother liquors from the crystallization of IV a crystalline compound which we formulate as *trans*-3-hydroxy-5-cyanopent-4-enamide (IX). Its nmr spectrum is uniquely consistent

(1) F. Johnson and J. P. Heeschen, *J. Org. Chem.*, **29**, 3252 (1964).

(2) C. E. Moppett, F. Johnson, and D. T. Dix, *Chem. Commun.*, 1560 (1971).

(3) E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, **87**, 1345 (1965).

SCHEME I



with the assigned structure. The trans stereochemistry follows quite clearly from the magnitude of the couplings constants for the vinylic protons at C-4 (δ 6.8, doublet of doublets, J = 16 and 3.5 Hz) and C-5 (5.7, doublet of doublets, J = 16 and 1.5 Hz). The downfield position of the proton at C-4 reflects the deshielding characteristics[4,5] of the cyano grouping at C-5. The additional 3.5-Hz coupling for this proton arises from its spin-spin interaction with the proton at C-3. There are three exchangeable protons at δ 5.4, 6.8, and 7.3, respectively, and a two-proton doublet at 2.28 attributable to the methylene grouping at C-2, and the single proton at C-3 appears as a multiplet at 4.45.

We were unable to bring about the transformation of IX into V under the conditions of the reaction. Our inability to bring about this change is consistent with the mechanism outlined in Scheme I for the formation of IV and IX from *meso*-butadiene diepoxide (III) and cyanide ion.

Experimental Section

Melting points were taken on an Arthur H. Thomas hot stage apparatus and are uncorrected. Nmr spectra were taken at ambient temperature (31.5°) on a Varian A-56-60 spectrometer. Chemical shifts are expressed in parts per million downfield from internal tetramethylsilane. Ir spectra were taken as Nujol mulls on a Perkin-Elmer Model 337 spectrometer. Mass spectra were obtained on a CEC 21-110B mass spectrometer. Samples were admitted *via* a direct insertion probe at ion source temperatures of ~200°. Metastable transitions were determined by the defocussing technique. Microanalyses were performed by Scandinavian Microanalytical Laboratory, Denmark.

3-Oxo-5-cyanopentanamide (IV).—To an ice-cooled, vigorously stirred solution of 28 g (0.4 mol) of potassium cyanide and 48 g (0.4 mol) of magnesium sulfate in 150 ml of water was added dropwise over 30 min 17.2 g (0.2 mol) of *meso*-butadiene diepoxide. The reaction mixture was allowed to come to room temperature and then left to stand for 18 hr. Continuous extraction with ethyl acetate gave a gummy residue which on tritration with ethanol afforded 5.9 g (21%) of IV: mp 76–77°[6] (from ethanol); ir 3400, 3170, 2245, 1720, 1650 cm^{-1}; nmr (DMSO-d_6) δ 2.2–3.2 (m, 6), 7.0 (br s, NH), and 7.4 (br s, NH); high-resolution mass measurements [empirical formula, experimental (calculated)], $C_6H_8N_2O_2$, 140.0619 (140.0585), $C_6H_5NO_2$, 123.0336 (123.0320), C_5H_6NO, 96.0447 (96.0449), $C_3H_4NO_2$, 86.0250 (86.0242), C_4H_4NO, 82.0298 (82.0293), C_3HO_2, 68.9953 (68.9977); metastables $140^+ \rightarrow 96^+ + 44$, $140^+ \rightarrow 86^+ + 54$, $86^+ \rightarrow 69^+ + 17$.

Anal. Calcd for $C_6H_8N_2O_2$: C, 51.45; H, 5.76; N, 20.01. Found: C, 51.40; H, 5.87; N, 19.77.

It proved possible to isolate from the mother liquors from the crystallization of IV by chromatography on silica gel *trans*-3-hydroxy-5-cyanopent-4-enamide (IX) (12%): mp 122–123° (from methanol); ir 3500–2400 (NH and OH), 2230 (C≡N), 1670 ($CONH_2$), 1630 (C=C) cm^{-1}; nmr (DMSO-d_6) δ 2.28 (d, 2, J = 6 Hz, C-2), 4.45 (m, 1, C-3), 5.4 (s, 1), 5.7 (dd, 1, J = 16.0 and 1.5 Hz, C-5), 6.8 (dd, 1, J = 16.0 and 3.5 Hz, C-4), 6.8 (s, 1), and 7.3 (s, 1); high-resolution mass measurements [empirical formula, experimental (calculated)], $C_6H_8N_2O_2$, 140.0558 (140.0585); C_5H_6NO, 96.0440 (96.0449), $C_3H_6NO_2$ 88.0393, (88.0397); metastable $140^+ \rightarrow 96^+ + 44$.

Anal. Calcd for $C_6H_8N_2O_2$: C, 51.45; H, 5.76; N, 20.01. Found: C, 51.37; H, 5.82; N, 20.17.

Nitric Acid Oxidation of IV.—3-Oxo-5-cyanopentanamide (IV, 77 mg) and 1 ml of concentrated nitric acid were heated on the steam bath for 1 hr—vigorous evolution of brown fumes. The reaction mixture was evaporated *in vacuo* and the white, crystalline residue was treated with a small volume of water. This too was removed *in vacuo* and this procedure was repeated. A methanolic solution of the above was treated with an excess of an ethereal solution of diazomethane. Evaporation of the organic solvents left dimethyl oxalate and dimethyl succinate—identified by gas–liquid chromatography on a Hewlett-Packard 5750 instrument.[7]

Base-Catalyzed Hydrolysis of IV.—3-Oxo-5-cyanopentanamide (IV, 100 mg) and 5 ml of 25% aqueous potassium hydroxide were heated under reflux overnight—strong smell of ammonia. After cooling to room temperature the reaction mixture was acidified with concentrated hydrochloric acid and continuously extracted with ether to give succinic acid, mp 189–190°, mmp 189–190°.

A small portion was methylated with an ethereal solution of diazomethane to yield dimethyl succinate—identified by comparison with an authentic sample.

2-*meta*-Chlorobenzyl-3-oxo-5-cyanopentanamide (VI) and 2,2-Bis(*meta*-chlorobenzyl)-3-oxo-5-cyanopentanamide (VII).—A solution of 140 mg (0.001 mol) of IV in 2 ml of dimethyl sulfoxide (distilled from calcium hydride) was added to a vigorously stirred, ice-cold solution of dimsyl sodium (0.002 mol)—generated[3] from 94 mg (0.002 mol, 51.3% dispersion) of sodium hydride and 3 ml of dimethyl sulfoxide. After ~30 min a solution of 388 mg (0.002 mol) of *meta*-chlorobenzylbromide in 2 ml of dimethyl sulfoxide was added and the reaction mixture was left to stir overnight at room temperature.

Dilution with water was followed by extraction with methylene chloride to give after removal of the organic solvents *in vacuo* 381 mg of a gummy residue.

Examination of the latter by tlc (silica gel PF_{254}, 90:10% v/v CH_2Cl_2–MeOH) indicated the presence of two compounds which were successfully separated by preparative tlc (two 20 × 20 cm plates, silica gel PF_{254}, 95:5% v/v CH_2Cl_2–MeOH, two elutions).

(4) G. S. Reddy, J. H. Goldstein, and L. Mandell, *J. Amer. Chem. Soc.*, **83**, 1300 (1961).

(5) A. N. Kurtz, W. E. Billups, R. B. Greenlee, H. F. Hamil, and W. T. Pace, *J. Org. Chem.*, **30**, 3141 (1965).

(6) When first obtained this compound had mp 67–68°. All subsequent preparations, however, gave only the form of mp 76–77°. The two forms which were separately characterized had identical ir (in solution) and mass spectra and identical tlc behavior. The two forms had mmp 76–77°.

(7) Both dimethyl succinate and dimethyl oxalate were identified by comparison with authentic samples. Separation was achieved on an Hewlett-Packard 5750 instrument, injector 370°, detector 360°, column 150°, flow 85 ml/min. The column was 12 ft, 0.25 in., 10% QF-1 on 60/80 Chromosorb W.

The upper band afforded 144 mg of VII: mp 128–130° (from ethanol); ir 3400, 2250, 1710, 1690, and 1670 cm^{-1}; nmr ($CDCl_3$) δ 2.2–3.0 (m, 4), 3.19 (s, 2), 3.32 (s, 2), 6.7–7.3 (m, 8), and the two exchangeable NH protons; mass spectrum *m/e* 388 (M^+ $C_{20}H_{18}{}^{35}Cl_2N_2O_2$).

Anal. Calcd for $C_{20}H_{18}Cl_2N_2O_2$: C, 61.72; H, 4.66; Cl, 18.22; N, 7.20. Found: C, 61.51; H, 4.75; Cl, 18.36; N, 7.14.

From the lower band there was obtained 74 mg of VI: mp 121° (from ethanol); ir 3475, 3370, 2250, 1710, 1660, and 1605 cm^{-1}; mass spectrum *m/e* 264 (M^+ $C_{13}H_{13}{}^{35}ClN_2O_2$).

Anal. Calcd for $C_{13}H_{13}ClN_2O_2$: C, 58.99; H, 4.95; Cl, 13.4; N, 10.59. Found: C, 58.86; H, 4.98; Cl, 13.25; N, 10.52.

Registry No.—III, 564-00-1; IV, 35159-06-9; VI, 35159-07-0; VII, 35159-08-1; IX, 35159-09-2.

Acknowledgment.—We thank Dr. L. Shadoff for the high-resolution mass spectral measurements and Dr. F. Johnson and Mr. A. A. Carlson for the initial isolation of IX.

Synthesis and Reactivity of Adamantane-1-carbonitrile *N*-Oxide

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Received March 10, 1972

The functionalization of adamantane has received considerable attention in recent years and several 1-substituted and some 2-substituted derivatives have been prepared.[1] Although most of the available data pertains to the unusual properties of adamantanes in polar and free-radical reactions involving the bridged ring system,[1,2] considerable interest on the internal reactivity of functional groups linked to the adamantyl moiety has arisen.[3]

We wish to report the first preparation of an adamantylfulmide and to describe some typical reactions at the CNO function in this compound. The present work enlarges the number of adamantane derivatives and provides information on the reactions of nitrile oxides[4] in general. We are currently investigating the chemistry of nitrile oxides.[5]

Adamantane-1-carbonitrile *N*-oxide (**1**) was prepared in good yield from adamantane-1-carboxaldehyde oxime (**1a**) and *N*-bromosuccinimide as outlined by Grundmann[6] for other nitrile oxides. Nitrile oxide **1** was practically unchanged after several days at room temperature, but in carbon tetrachloride solution at 50° it readily dimerized to di[adamantyl-(1)]furazan *N*-oxide (**2**) (*ca.* 80% yield). The structure of **2** is supported by the mass spectrum. Compound **2** gives the parent peak at *m/e* 354 (M^+) and on electron impact behaves in the characteristic manner[7] of furazan *N*-oxides, giving $(M - O)^+$, $(M - N_2O_2)^+$, $(AdCN)^+$, and $(AdCNO)^+$ as the major fragments ions. The peaks at *m/e* 338, corresponding to the loss of one oxygen, and at *m/e* 294, from the loss of N_2O_2, and the absence of absorption corresponding to $(AdCO)^+$ at *m/e* 163 are compatible only with the furoxan structure **2** and rule out other possible five- or six-membered isomers.

When heated at reflux in carbon tetrachloride, nitrile oxide **1** yielded, in addition to dimer **2**, the isomer 1-adamantylisocyanate (**3**) in variable amounts depending on the time of heating. Typically, after 8 hr of reflux **3** was only present in small amounts with respect to furoxan **2**, but, when heating was prolonged to 10 days, the ratio **2**:**3** was *ca.* 1:2. In the latter experiment, the infrared spectrum of the reaction mixture, taken at intervals, showed that, after the complete disappearance of the 2285- (CN) and 1335-cm^{-1} (NO) bands[8] of **1**, the absorption of the NCO group[9] at 2255 cm^{-1} gradually increased. These facts suggest that on prolonged heating the isocyanate **3** was the major reaction product because a part of it could possibly form from the furazan *N*-oxide **2** *via* a retrocycloaddition to **1** (Scheme I). The formation of isocyanate **3** and trapping of the transient nitrile oxide **1** by cycloaddition with styrene from a sample of **2** heated at reflux in carbon tetrachloride indicate that this possibility is real. Therefore, in spite of the initial formation of **2**, the isomerization of **1** to **3** can still occur directly *via* the mechanism outlined by Grundmann and Kochs.[10] However, it must be noted that an alternative route from the furazan *N*-oxide **2**, in equilibrium with the nitrile oxide **1**, is also conceivable.[11]

(1) R. C. Fort, Jr., and P. v. R. Schleyer, *Chem. Rev.*, **64**, 277 (1964); *Advan. Alicycl. Chem.*, **1**, 283 (1966).

(2) Recent references include Z. Majerski, P. v. R. Schleyer, and A. P. Wolf, *J. Amer. Chem. Soc.*, **92**, 5731 (1970); I. Tabushi, Z. Yoshida, and N. Takahashi, *ibid.*, **92**, 6670 (1970); C. Rüchardt, *Angew. Chem., Int. Ed. Engl.*, **9**, 830 (1970); J. K. Chakrabarti and A. Todd, *Chem. Commun.*, 556 (1971); M. O. Luke and J. G.-Atkinson, *Tetrahedron Lett.*, 117 (1971).

(3) J. Strating, A. H. Alberts, and H. Wynberg, *Chem. Commun.*, 818 (1970); J. Scharp, H. Wynberg, and J. Strating, *Recl. Trav. Chim. Pays-Bas*, **89**, 18, 23 (1970); W. V. Curran and R. B. Angier, *J. Org. Chem.*, **34**, 3668 (1969); A. Kreutzberger and H.-H. Schroders, *Tetrahedron Lett.*, 4921 (1970); H. Stetter and E. Smulders, *Chem. Ber.*, **104**, 917 (1971).

(4) Reviews: (a) C. Grundmann, *Synthesis*, 344 (1970); (b) A. Quilico, *Chim. Ind. (Milan)*, **53**, 157 (1971); (c) C. Grundmann and P. Grünanger, "The Nitrile Oxides," Springer-Verlag, Berlin, Heidelberg, New York, 1971.

(5) G. Barbaro, A. Battaglia, and A. Dondoni, *J. Chem. Soc. B*, 588 (1970); A. Battaglia, A. Dondoni, and A. Mangini, *ibid.*, 554 (1971); A. Battaglia, A. Dondoni, G. Maccagnani, and G. Mazzanti, *ibid.*, 2096 (1971).

(6) C. Grundmann and R. Richter, *J. Org. Chem.*, **33**, 476 (1968).

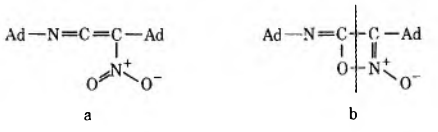
(7) (a) C. Grundmann, H.-D. Frommeld, K. Flory, and S. K. Datta, *ibid.*, **33**, 1464 (1968); (b) A. J. Boulton, P. Hadjimihalakis, A. R. Katritzky, and A. Majid Hamid, *J. Chem. Soc. C*, 1901 (1969).

(8) A. Battaglia, A. Dondoni, G. Galloni, and S. Ghersetti, *Spectrosc. Lett.*, **3**, 207 (1970).

(9) W. H. T. Davidson, *J. Chem. Soc.*, 3712 (1953). For the reliability of the 2290- and 2255-cm^{-1} bands to distinguish nitrile oxides from isocyanates, see also R. H. Wiley and B. J. Wakefield, *J. Org. Chem.*, **25**, 546 (1960).

(10) C. Grundmann and P. Kochs, *Angew. Chem., Int. Ed. Engl.*, **9**, 635 (1970).

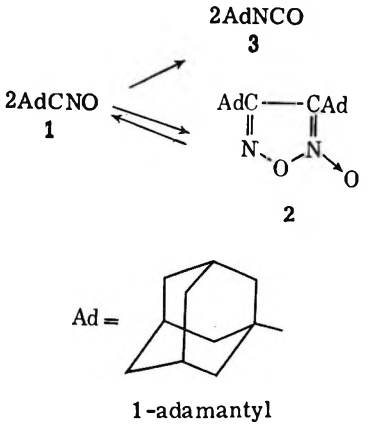
(11) A referee has drawn our attention to a variant of Scheme I, *i.e.*, **1** ⇆ **2** → **3** + **1**. The ring opening of **2** can take place *via* initial migration of the adamantyl group onto the imino nitrogen to give the open-chain intermediate **a** which in turn forms the four-membered ring compound **b** by



a b

an electrocyclic rearrangement of the butadiene–cyclobutene type. The latter product leads to **3** and **1** by ring opening as indicated. This route, which is also compatible with the data reported in ref 10, needs to be considered in a more extensive study.

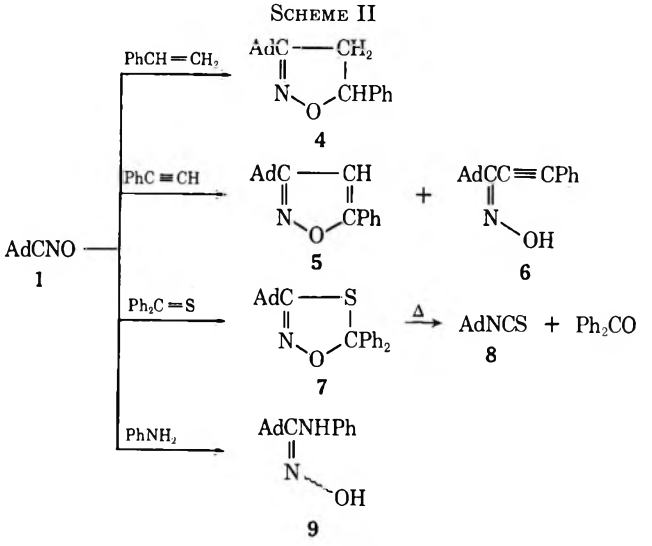
SCHEME I



These results indicate that, in the case of **1**, the formation of furazan *N*-oxide **2** and isocyanate **3** is governed by a kinetic and thermodynamic control, respectively. Of the several sterically hindered nitrile oxides which have been reported[10,12] to rearrange to the corresponding isocyanates, only in the case of mesitonitrile *N*-oxide have both dimerization and isomerization products been observed under controlled temperature conditions.[7a] In the other cases, on heating at reflux in an inert high-boiling solvent such as toluene or xylene, the transient formation of furazan *N*-oxide was not noticed or was neglected. With respect to the results reported here and in view of the large steric requirements of the adamantyl group, a reconsideration of the behavior of nitrile oxides with a bulky group around to the CNO function would be of interest.

Kinetic data[5,13] and a number of syntheses[4,12] with sterically hindered nitrile oxides have shown that the steric hindrance around the CNO function decreases the tendency of nitrile oxides to dimerize, but reduces the rate of 1,3-addition reactions to only a small extent. Thus, adamantane-1-carbonitrile *N*-oxide (**1**) was quite reactive toward typical reagents of the CNO function, yielding a number of compounds, some of which were hitherto unknown, containing the adamantyl moiety (Scheme II). 1,3-Dipolar cycloadditions of **1** with styrene, phenylacetylene, and thiobenzophenone occurred readily at room temperature to yield the corresponding five-membered heterocycles **4**, **5**, and **7**, while the 1,3 additions of aniline and phenylacetylene gave the oximes **9** and **6**, the latter being the by-product of the isoxazole **5**. According to previous reports,[14] the α-acetylenic oxime **6** is assigned the configuration in which the hydroxyl group is anti with respect to the adamantyl function, whereas for amidoxime **9** the assignment is currently being studied. The oxime **6** was stable under the reaction conditions of **1** with phenylacetylene,[15] thus excluding the formation of **5** *via* a partial rearrangement of **6**.

SCHEME II



Ad = 1-adamantyl

Experimental Section

All melting points are uncorrected. Reagents and solvents, commercially available unless otherwise stated, were purified by standard procedures. All tlc was done using silica gel plates, benzene as eluent, and an iodine chamber to develop the spots. Nmr spectra were recorded on a JNM-PS-100 instrument with TMS as internal reference (δ 0 ppm); ir spectra were determined with a Perkin-Elmer 257 grating spectrophotometer.

Adamantane-1-carboxaldehyde Oxime (**1a**).—A mixture of adamantane-1-carboxaldehyde[16] (from reduction of 9.0 g of adamantane-1-carboxylic acid chloride), hydroxylamine hydrochloride (10.5 g), and sodium hydroxide (7.2 g) in 80 ml of ethanol–water (1:2, v/v) was heated on a steam bath for 2 hr. Dilution of the reaction mixture with 100 ml of water produced a solid, which was collected and recrystallized from ethanol–water (1:1, v/v) to yield 4.8 g of **1a**: mp 144–145°; ir (CCl_4) 3600 and 3300 cm^{-1} (OH); nmr (CCl_4) δ 8.6 (s, 1, OH, disappeared on treatment with D_2O), 6.9 (s, 1, CH=N), 2.1–1.6 (m, 15, adamantyl protons).

Anal. Calcd for $C_{11}H_{17}NO$: C, 73.70; H, 9.56; N, 7.81. Found: C, 73.85; H, 9.42; N, 7.63.

This oxime appears to have a syn configuration on the basis of further nmr data[17] in Me_2SO, δ 9.93 (OH), 6.87 (CH=N).

Adamantane-1-carbonitrile *N*-Oxide (**1**).—To a stirred solution of 0.54 g (3 mmol) of oxime **1a** and 0.53 g (3 mmol) of *N*-bromosuccinimide in 15 ml of DMF was added dropwise a solution of 0.30 g (3 mmol) of triethylamine in 5 ml of DMF at *ca.* 10°. After the mixture had been stirred for 30 min at room temperature, dilution with 50 ml of ice water gave a white solid which was collected, washed with water, and recrystallized from ethanol to yield 0.32 g (66%) of **1**: mp 160–161°; ir (CCl_4–CS_2) 2285 (C≡N), 1335 cm^{-1} (NO); nmr (CCl_4) δ 2.1–1.4 (m, adamantyl protons).

Anal. Calcd for $C_{11}H_{15}NO$: C, 74.54; H, 8.53; N, 7.90. Found: C, 74.86; H, 8.38; N, 7.91.

The melting point of **1** was unchanged after 6 days at room temperature.

Thermal Dimerization and Isomerization of 1.—A solution of 1.35 g of nitrile oxide **1** in 120 ml of CCl_4 was heated at 50°. The ir spectrum of the solution showed that the 2285-cm^{-1} band of nitrile oxide had disappeared after 5 days. Removal of the solvent *in vacuo* gave a residue which was recrystallized twice from isopropyl alcohol to yield 1.06 g (78%) of di[adamantyl-

(12) C. Grundmann and J. M. Dean, *J. Org. Chem.*, **30**, 2809 (1965); C. Grundmann and S. K. Datta, *ibid.*, **34**, 2016 (1969); S. Ranganathan, B. B. Singh, and C. S. Panda, *Tetrahedron Lett.*, 1225 (1970).

(13) P. Beltrame and C. Vintani, *J. Chem. Soc. B*, 873 (1970).

(14) S. Morocchi, A. Ricca, A. Zanarotti, G. Bianchi, R. Gandolfi, and P. Grünanger, *Tetrahedron Lett.*, 3329 (1969); Z. Hamlet, M. Rampersad, and D. J. Shearing, *ibid.*, 2101 (1970); Z. Hamlet and M. Rampersad, *Chem. Commun.*, 1230 (1970).

(15) No appreciable isomerization of oxime **6** (0.004 *M* in CCl_4) to isoxazole **5** was noticed after 12 hr at 25°, whereas the reaction of **1** (0.01 *M*) with a tenfold excess of phenylacetylene has $t_{0.5}$ of 2.5 hr under the same conditions.

(16) The aldehyde was prepared as described [D. E. Applequist and L. Kaplan, *J. Amer. Chem. Soc.*, **87**, 2194 (1965)] from adamantane-1-carboxylic acid chloride and tri-*tert*-butoxyaluminum hydride, but was not purified because of its tendency to polymerize on handling [F. N. Stepanov and N. L. Dovgan, *Zh. Org. Khim.*, **4**, 277 (1968)]. The aldehyde was characterized as the 2,4-dinitrophenylhydrazone, mp 225–226° (from acetonitrile) [lit. mp 225°: H. Stetter and E. Rauscher, *Chem. Ber.*, **93**, 1161 (1960)].

(17) G. G. Kleinspehn, J. A. Jung, and S. A. Studniarz, *J. Org. Chem.*, **32**, 460 (1967).

(1)]furazan *N*-oxide (**2**): mp 179–180°; ir (CCl_4–C_2Cl_4) 1550 cm^{-1}; mass spectrum[18] *m/e* 354 (M^+), 338 ($M - 16$)$^+$, 294 ($M - 60$)$^+$, 177 ($AdCNO$)$^+$, 161 ($AdCN$)$^+$, 135 (Ad^+).

Anal. Calcd for $C_{22}H_{30}N_2O_2$: C, 74.54; H, 8.53; N, 7.90. Found: C, 74.75; H, 8.43; N, 8.05.

An identical reaction mixture of **1** in CCl_4 was heated at reflux for 8 hr. The ir spectrum of the solution showed an absorption at 2255 cm^{-1}. The solvent was removed at reduced pressure and the residue was subjected to vacuum sublimation in a cold finger apparatus. At 0.2 mm and 85–95° bath temperature, 0.12 g (9%) of 1-adamantyl isocyanate (**3**) collected on the condenser, mp 139–141°, ir (CCl_4) 2255 cm^{-1}. The specimen was identical with an authentic sample[19] by ir and mixture melting point. The residue of the sublimation, which contained a small quantity of **3**, was recrystallized from isopropyl alcohol, yielding 0.86 g (64%) of furazan *N*-oxide **2**.

In another experiment the same amounts of **1** and solvent were heated for 10 days. The reaction mixture, worked up as detailed above, gave 0.80 g (59%) of isocyanate **3** and 0.42 g (31%) of furoxan **2**.

Retro Cycloaddition of Di[adamantyl-(1)]furazan *N*-Oxide (2).—A solution of 0.50 g (1.4 mmol) of **2** in 50 ml of dry CCl_4 was heated at reflux and the transformations were monitored by ir analysis in the 2300–2200-cm^{-1} region. After 15 hr the ir spectrum showed a broad absorption with the maximum at 2280 cm^{-1}, but after 40 hr two overlapping bands at 2285 and 2255 cm^{-1} could be clearly distinguished. On heating for a total of 10 days, the ir spectrum showed a gradual increase of the isocyanate band at 2255 cm^{-1}. Removal of the solvent *in vacuo* and sublimation of the residue at 0.2 mm and 85–95° bath temperature gave 0.21 g (42%) of 1-adamantyl isocyanate (**3**), mp 138–140°, identical with an authentic sample.[19] The residue of the sublimation, 0.26 g (52%), was the unaltered furazan *N*-oxide **2**.

The same amount of furazan *N*-oxide **2** and 1.46 g (14 mmol) of styrene were heated to reflux in 50 ml of CCl_4 for 10 days. Removal of the solvent *in vacuo* gave an oil from which, on addition of petroleum ether (bp 30–60°) and chilling, fractionally separated 71 mg of unchanged **2**, mp 175–179°, and 0.28 g of a product, mp 66–67°, which upon recrystallization from ethanol–water melted at 72–73° and was identical by mixture melting point and ir with an authentic sample of 3-[adamantyl-(1)]-5-phenyl-4,5-dihydro-1,2-oxazole (**4**). The petroleum ether filtrate, after distillation of the solvent, gave an oil which chromatographed through a column of silica, benzene as eluent, yielded a fraction containing the isocyanate **3** with styrene as an impurity, and two fractions containing 65 mg of **2** and 0.17 g of **4**.

Addition Reactions to Nitrile *N*-Oxide 1.—To a stirred solution of **1** (0.62 g, 3.5 mmol) in 25 ml of dry CCl_4 was added dropwise 20–30 mmol of reactant in an equal volume of carbon tetrachloride at 25°. Only thiobenzophenone was used in a quantity equimolar to **1**. After overnight additional stirring, the solvent and the excess of reactant were removed *in vacuo* and the residue was worked up as detailed in each case. The following compounds were obtained.

3-[Adamantyl-(1)]-5-phenyl-4,5-dihydro-1,2-oxazole (4).—The residue was an oil which on treatment with petroleum ether and chilling yielded 0.87 g (89%) of **4**, mp 68–72°. After recrystallization from ethanol–water, **4** had mp 72.5–73.5°; nmr[20] (CCl_4) δ 7.0–6.8 (m, 5, aromatic protons), 5.15 (2 d, 1, CHPh), 3.15 and 2.65 (2 q, 2, CH_2 isoxazoline ring), 2.1–1.6 (m, 15, adamantyl protons).

Anal. Calcd for $C_{19}H_{23}NO$: C, 81.10; H, 8.24; N, 4.98. Found: C, 81.50; H, 8.30; N, 5.10.

1-[Adamantyl-(1)]-5-phenyl-1,2-oxazole (5) and 1-[Adamantyl-(1)]-3-phenylprop-2-ynone Oxime (6).—The residue was an oil which on tlc showed the presence of two main components at R_f 0.47 and 0.20. The residue was chromatographed on a silica gel column. Elution with benzene, after initial fractions containing unchanged phenylacetylene, gave 0.67 g (69%) of isoxazole **5**: mp 102–103° after recrystallization from ethanol–water; ir (CCl_4–C_2Cl_4) 1630 cm^{-1}; nmr[21] (CCl_4–$CDCl_3$) δ 7.5–6.9 (m, 5, aromatic protons), 6.0 (s, 1, CH isoxazole ring), 2.1–1.6 (m, 15, adamantyl protons). *Anal.* Calcd for $C_{19}H_{21}NO$: C, 81.68; H, 7.58; N, 5.01. Found: C, 81.95; H, 7.47; N, 5.21.

Subsequent elution with benzene–ether (8:2, v/v) gave 0.20 g (21%) of oxime **6**: mp 134–135° (benzene–petroleum ether); ir (CCl_4) 3580, 3250 (OH), 2220 cm^{-1} (C≡C); nmr (CCl_4–$CDCl_3$) δ 8.9 (s, 1, OH, disappeared on treatment with D_2O), 7.2–6.7 (m, 5, aromatic protons), 2.1–1.6 (m, 15, adamantyl protons). *Anal.* Calcd for $C_{19}H_{21}NO$: C, 81.68; H, 7.58; N, 5.01. Found: C, 81.48; H, 7.46; N, 5.20.

The α-acetylenic oxime **6** was satisfactorily stable at room temperature.[15] However, when the reaction solution of **1** with phenylacetylene, obtained as described, was kept at 50° for 5 days, the oxime **6** was not longer detectable on tlc. After evaporation of the solvent, the residue, dissolved in ethanol–water and kept at −10° overnight, gave 0.92 g of isoxazole **5**.

3-[Adamantyl-(1)]-5,5-diphenyl-1,4,2-oxathiazole (7).—After careful[22] evaporation of the solvent *in vacuo*, the residue was recrystallized from methanol to yield 0.97 g (75%) of **7**, mp 109–110°, ir (CCl_4–C_2Cl_4) 1660 cm^{-1} (C=N).

Anal. Calcd for $C_{24}H_{25}NOS$: C, 76.76; H, 6.71; N, 3.73; S, 8.54. Found: C, 76.68; H, 6.80; N, 3.94; S, 8.76.

The structure of **7** is supported by its thermal decomposition products (see below).

***N*-Phenyladamantane-1-carboxamide Oxime (9).**—The white solid precipitated from the reaction solution was collected and washed with two 5-ml portions of CCl_4. Recrystallization from ethanol gave 0.82 g (86%) of **9**: mp 216–217°; ir (Nujol) 3380 (NH), 3250 (br), 1660 cm^{-1} (C=N); nmr (DMSO-d_6) δ 9.75 (s, 1, OH, disappeared on treatment with D_2O), 7.20–6.50 (m, 6, NH and aromatic protons), 2.1–1.6 (m, 15, adamantyl protons).

Anal. Calcd for $C_{17}H_{22}N_2O$: C, 75.51; H, 8.20; N, 10.36. Found: C, 75.81; H, 8.39; N, 10.31.

Thermal Decomposition of 1,4,2-Oxathiazole (7).—The oxathiazole (0.6 g, 1.6 mmol) was heated at 185° for 1 hr as described.[22] Chromatography of the reaction mixture on a silica gel column using benzene as eluent afforded 0.28 g (96%) of benzophenone, mp 48–50°, and 0.24 g (78%) of 1-adamantyl isothiocyanate[19] (**8**), mp 166–167°. These products were identical with authentic samples by infrared spectra and mixture melting points.

Registry No.—**1**, 35105-43-2; **1a**, 35099-47-9; **2**, 35147-20-7; **3**, 4411-25-0; **4**, 35105-45-4; **5**, 35105-46-5; **6**, 35147-21-8; **7**, 35105-47-6; **9**, 35105-48-7.

(18) Determined with a low-resolution gas chromatograph–mass spectrometer, Perkin-Elmer 270, at 70 eV, chamber temperature 200°, through the courtesy of Dr. A. Giumanini of the University of Bologna.

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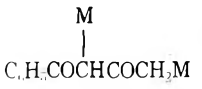
See Editorial, J. Org. Chem., 37, No. 19, 4A (1972).

Reaction of Dialkali Salts of Benzoylacetone with 2-Chloroquinoline. Evidence for an SRN1 Mechanism in Heteroaromatic Nucleophilic Substitution[1]

Summary: Dialkali metal salts of benzoylacetone have been found to react with 2-chloroquinoline in liquid ammonia to produce 1-phenyl-4-(2-quinolyl)-1,3-butanedione by a radical-chain mechanism.

Sir: In view of recent reports[2-4] concerning the newly discovered SRN1 mechanism for carboaromatic nucleophilic substitution, we wish to describe the present results, which provide strong evidence that a similar mechanism can operate in heteroaromatic substitution.

Recently,[5] we examined the reaction of disodiobenzoylacetone (**1**, M = Na) with 2-chloroquinoline in



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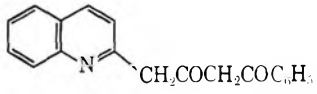

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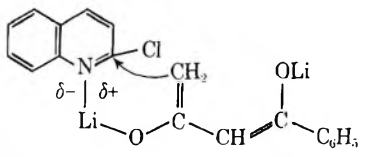
liquid ammonia as a route to β diketone **2** and as a previously unreported type of reaction involving 1,3 dianions such as **1**. However, exposure of 2-chloroquinoline to **1** (M = Na or K) at −33° afforded only modest yields of diketone **2** in spite of the established nucleophilicity of such dianions[6] and the propensity of 2-chloroquinoline toward halogen displacement by carbanionic species.[7] On the assumption that these reactions were proceeding by a classical SNAr2 mechanism,[8] we extended our study to include dilithiobenzoylacetone (**1**, M = Li), in the hope that the more effective coordinating power of lithium would lead to appreciable cationization[8] of the ring nitrogen. It seemed that the desired displacement reaction might then be facilitated by delivery of the terminal carbanion site of **1** to the electrophilic 2 position of the heterocyclic nucleus through a cyclic transition state such as **3**.[8,9] To assess this potential metallic cation effect,



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2-chloroquinoline was allowed to react with 2 mol equiv of dialkali salts **1** (M = K, Na, and Li) in liquid ammonia at −33° for 1 hr under a nitrogen atmosphere to afford ketone **2** in yields of 17, 30, and 71%, respectively.[10] The dramatic increase in the yield of **2** with **1** (M = Li) lent support to the hypothesis presented above.[11] However, on closer examination, it became evident that these reactions were markedly retarded by radical inhibitors. Thus, when 2-chloroquinoline was allowed to react with **1** (M = Li) for 1 hr in the presence of 0.1 equiv of tetraphenylhydrazine (TPH)[2] or *p*-dinitrobenzene (DNB),[12] yields of **2** dropped to 7 or 2%, respectively. Catalytic amounts of oxygen[12] decreased the yield of **2** to <1%. Yields of **2** obtained with **1** (M = Na or K) were also lowered to <1% by DNB.

The inhibitory action of TPH, DNB, and oxygen, coupled with the observation that catalytic amounts of DNB do not destroy **1** (M = K) in the absence of 2-chloroquinoline, indicates that the present reactions occur through a radical-chain mechanism in which inhibition takes place by a chain breaking process. On the basis of this evidence and precedents cited by other investigators,[2-4,13] we propose that the substitutions involving dialkali salts **1** occur *via* the mechanism shown in Scheme I. The enhanced reactivity

Scheme I[a]

$$\text{2-ClQ} + \text{BAc}^{2-} \longrightarrow \text{2-ClQ}\cdot^{-} + \text{BAc}\cdot^{-}$$

$$\text{2-ClQ}\cdot^{-} \longrightarrow \text{Q}\cdot + \text{Cl}^{-}$$

$$\text{Q}\cdot + \text{BAc}^{2-} \longrightarrow \text{QBAc}\cdot^{2-}$$

$$\text{QBAc}\cdot^{2-} + \text{2-ClQ} \longrightarrow \text{QBAc}^{-} + \text{2-ClQ}\cdot^{-}$$

[a] 2-ClQ = 2-chloroquinoline; BAc^{2-} = benzoylacetone dianion.

of **1** (M = Li) may indeed result from coordination of the lithium cation with the ring nitrogen, which

(1) (a) Supported by Grants GM-14340 and NS-10197 from the National Institutes of Health. (b) Abstracted from the Ph.D. dissertation of J. C. Greene, Virginia Polytechnic Institute and State University, Sept 1971. (c) Presented in part at the Southeastern Regional Meeting of the ACS, Nashville, Tenn., Nov 1971.

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(5) J. F. Wolfe and T. P. Murray, *J. Org. Chem.*, **36**, 354 (1971).

(6) For reviews of the chemistry of 1,3 dianions, see T. M. Harris and C. M. Harris, *Org. React.*, **17**, 155 (1969); H. Smith, "Organic Reactions in Liquid Ammonia," Interscience Publishers, New York–London, 1963, pp 55–89.

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(9) W. H. Puterbaugh and R. L. Readshaw [*J. Amer. Chem. Soc.*, **82**, 3635 (1960)] propose a related transition state in the reaction of lithium enolates with α-halo acids.

(10) Details for these and all other experiments described in this paper will appear following these pages in the microfilm edition of this volume of the journal. Single copies may be obtained from the Business Operations Office, Books and Journals Division, American Chemical Society, 1155 Sixteenth St., N.W., Washington, D. C. 20036, by referring to code number JOC-72-3199. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche.

(11) This effect is opposite that normally observed in alkylations of dianions such as **1** with primary halides, where dilithio salts are considerably less reactive than their disodio and dipotassio counterparts; see K. G. Hampton, T. M. Harris, and C. R. Hauser, *J. Org. Chem.*, **30**, 61 (1965).

(12) G. A. Russell and W. C. Danen, *J. Amer. Chem. Soc.*, **90**, 347 (1968).

(13) A. R. Buick, T. J. Kemp, G. T. Neal, and T. J. Stone, *J. Chem. Soc. A*, 666 (1969).

facilitates electron transfer[14] from dianion **1** and initiation of the radical-chain reaction. Apparently such complexation is less pronounced with **1** (M = Na or K).

(14) (a) Quaternization of aromatic azines markedly increases their ease of electrochemical reduction: K. B. Wilberg and T. P. Lewis, *J. Amer. Chem. Soc.*, **92**, 7154 (1970). (b) Although the electron-donor properties of 1,3 dianions have not been extensively investigated, electron transfer does occur with diaryliodonium salts; see K. G. Hampton, T. M. Harris, and C. R. Hauser, *J. Org. Chem.*, **29**, 3511 (1964).

Studies designed to test the generality of the present radical substitution mechanism with other halogenated heterocycles and carbanions are in progress.

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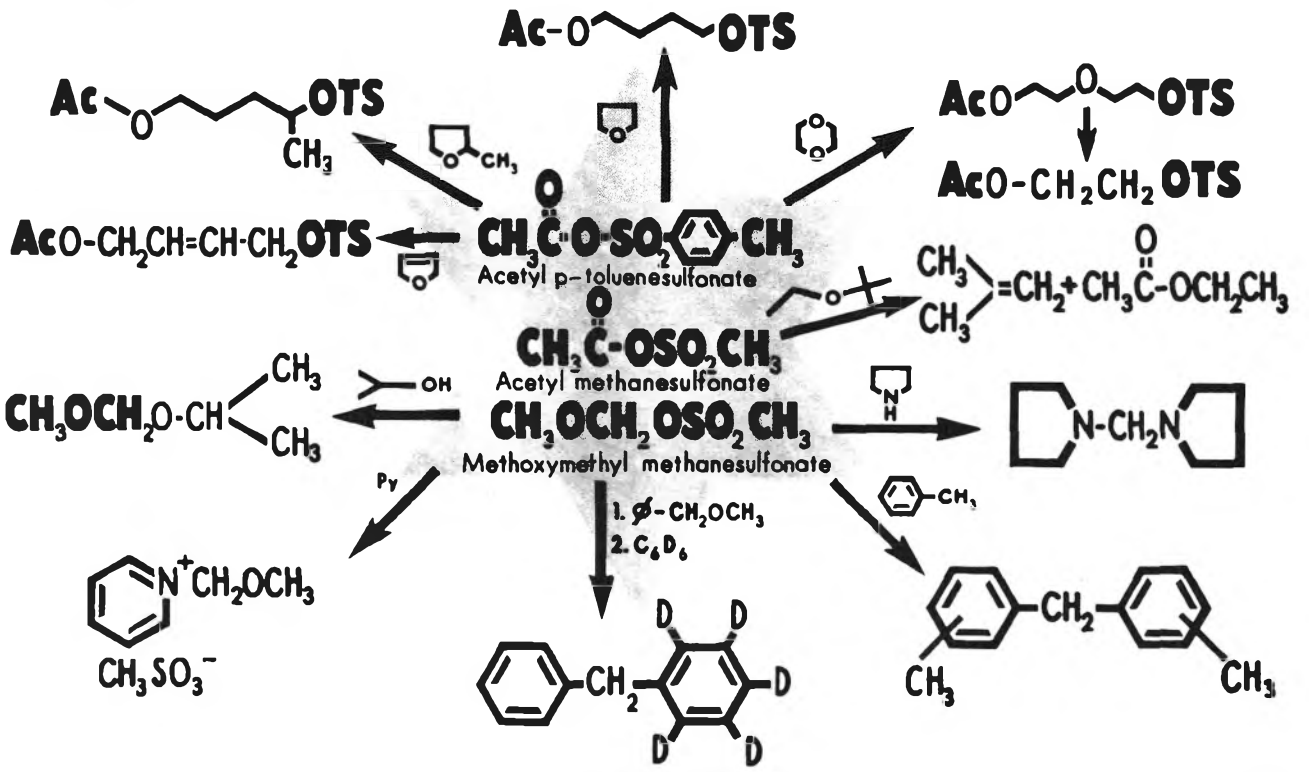
RECEIVED AUGUST 25, 1972

MORE ALDRICH FIRSTS

Recent publications by Karger and Mazur of the Weizmann Institute of Science have greatly extended the utility of the acetyl sulfonates and have introduced a *new* reagent, methoxymethyl methanesulfonate (MMM).



ACETYL p-TOLUENESULFONATE and ACETYL METHANESULFONATE are members of a class of mixed sulfonic-carboxylic anhydrides[1] which function as acylating agents. The aromatic carboxylic-sulfonic anhydrides were shown[2] to acylate phenols, anilines and alcohols and the acetyl sulfonates have been used[3] in the Friedel-Crafts reaction. The acetyl sulfonates are such *powerful acylating agents* that simple, mixed and cyclic *ethers are cleaved*[4] *in high yield* without Lewis acid catalysis at 25°C in most cases. THF has been cleaved[5] to butane-1,4-diol acetate with acetic anhydride-$ZnCl_2$ at 230°C over many hours but acetyl *p*-toluenesulfonate gives the diester[4] in just 3 hours at 25°C. Also *unsymmetrical ethers*[4] are cleaved with a high degree of *specificity* so that 2-methylTHF gives only a single product as a consequence of the SN1 nature of the cleavage step, further exemplified by the cleavage of *t*-butyl ethyl ether. Cleavage of 1,4-dioxane under stringent conditions[6] (acetyl chloride; $SnCl_4$; 30 hrs at 200°C) gave very poor results whereas acetyl *p*-toluenesulfonate gives 87% of the diester.[4] This diester at higher temperatures will give[4] ethylene glycol acetate tosylate as the only product, again a result of the SN1 nature of the reaction with neighboring group participation. Such mixed acetate sulfonate diesters should be useful alkylating agents.

METHOXYMETHYL METHANESULFONATE is a powerful *alkylating agent.*[7] Primary and secondary alcohols react with it within 5 min at 25°C to yield *mixed acetals*, and this reagent should find extensive use as a *protecting group* which can be removed by acid treatment. *tert*-Amines yield[7] *quaternary salts* quantitatively within 5 min at 0°C. *sec*-Amines yield[7] *aminals* which can be used in α-aminoalkylations as in the Mannich reaction.[8] Even ethers are cleaved, although in low yield (ethylene oxide at 0°C and THF after extended reflux), but this property accounts for methoxymethyl methanesulfonate's unique behavior[7] toward benzene derivatives. Alkylation first takes place to give readily the intermediate methyl benzyl ether which is further cleaved to a benzyl carbonium ion, which in turn reacts with the aromatic starting material to yield substituted diphenylmethanes.[7]

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