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THE JOURNAL OF Organic Chemistry®

VOLUME 37, NUMBER 6

MARCH 24, 1972

Thermal and Base-Induced Transformations of Epoxy-*N*-nitrosocarbamates[1]

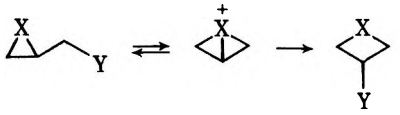
ALBERT PADWA,*[2] PAUL CIMILUCA, AND DAVID EASTMAN

Department of Chemistry, State University of New York at Buffalo, Buffalo, New York 14214

Received September 13, 1971

The thermal and base-catalyzed behavior of several *N*-nitrosoepoxycarbamates has been examined in mechanistic detail. Reaction of the *N*-nitrosocarbamates with base gave products resulting from both epoxide ring opening and collapse of intimate diazonium–hydroxide ion pairs. Thermal decomposition of methyl *trans*-*N*-nitroso(1,3-diaryl-2,3-epoxypropyl)carbamates gave the corresponding carbonates as the major products. Thermolysis of the related monophenyl epoxycarbamate proceeded *via* a different path. The thermal decomposition involves rearrangement of the nitrosocarbamate to a diazo ester which rapidly decomposes. For the diarylnitrosocarbamates, the decomposition involves dissociation into an ion pair, whereas a diazoalkane intermediate is formed with the monophenyl carbamate system.

Considerable attention has been focused in recent years on the conjugative properties of small rings when joined directly to an unsaturated grouping.[3] Among these studies have been many concerned with the conjugative interaction of small rings with adjacent carbonium ions.[4] Cyclopropylcarbinyl derivatives solvolyze with markedly enhanced rates to give rearranged and position-scrambled products of the allylcarbinyl, cyclobutyl, and cyclopropylcarbinyl types. There appears to be extensive charge delocalization from the carbinyl carbon of the cyclopropyl carbonium ion to the cyclopropane ring. Increased emphasis has also been given during the past few years to the solvolytic behavior of three-ring heterocyclic compounds.[5-10] The formal relationship of eq 1 to the cyclopropyl-



(1)

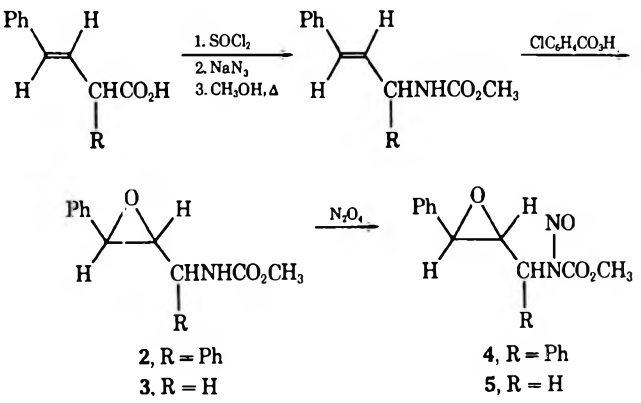
carbinyl–cyclobutyl nonclassical cation system has stimulated investigations with aziridinyl carbinyl derivatives,[5,6] as well as thirane[7-9] and oxirane analogs.[10] Replacement of a methylene group in cyclopropane by a heteroatom has been found to severely dampen the ability of the three ring to delocalize the charge.[5-10]

As part of a program designed to delineate the interaction of small ring heterocycles with adjacent reaction centers, we sought to define the reactivity of a carbenoid center adjacent to a three-membered heterocyclic ring. We felt that this would be a particularly interesting species, since its chemical properties would probably be different from the related carbocyclic system[11,12] (as was noted for the above carbonium ion system) by virtue of the interaction of the carbenoid center with the electron pair on the adjacent heteroatom. Of the variety of methods that have been developed to generate carbenes,[13] the thermal decomposition of an α-diazo epoxide seemed most appropriate. A standard method used for generating diazoalkanes and, hence, potential carbenes is the reaction of the appropriate *N*-nitrosocarbamate with base.[14] The purpose of this paper is to report the synthesis of several potential epoxycarbene progenitors and the novel reactions they undergo upon thermolysis or by treatment with base.

Methyl *trans*-*N*-(1,3-diphenyl-2,3-epoxypropyl)carbamate (2) was synthesized from *trans*-2,4-diphenyl-3-butenoic acid *via* the acid chloride, the acid azide, the isocyanate, and peracid epoxidation of the *N*-alkenylcarbamate. The *N*-nitrosocarbamate 4, mp 95–96°, was prepared by nitrosation of carbamate 2 with dinitrogen tetroxide by established procedures.[15]

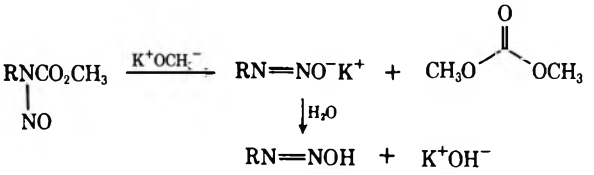
(1) For a preliminary report, see A. Padwa, N. C. Das, and D. Eastman, *J. Amer. Chem. Soc.*, **91**, 5178 (1969).
(2) Alfred P. Sloan Foundation Research Fellow, 1968–1972.
(3) For a review, see M. Y. Lukina, *Russ. Chem. Rev.*, 419 (1962).
(4) For a review, see R. Breslow in "Molecular Rearrangements," Vol. I, P. de Mayo, Ed., Interscience, New York, N. Y., 1963, Chapter 4.
(5) V. R. Gaertner, *Tetrahedron Lett.*, 5919 (1969); *J. Org. Chem.*, **35**, 3952 (1970).
(6) J. A. Deyrup and C. L. Moyer, *Tetrahedron Lett.*, 6179 (1969).
(7) J. C. Martin and D. J. Anderson, Abstracts, 139th National Meeting of the American Chemical Society, St. Louis, Mo., March 1961, p O-31.
(8) M. Sander, *Monatsh. Chem.*, **96**, 896 (1965).
(9) E. P. Adams, K. N. Ayad, F. P. Doyle, D. O. Holland, W. H. Hunter, J. H. C. Nayler, and A. Queen, *J. Chem. Soc.*, 2665 (1960).
(10) H. G. Richey, *Tetrahedron Lett.*, 5919 (1968).
(11) K. B. Wiberg and J. M. Lavanish, *J. Amer. Chem. Soc.*, **88**, 365 (1966).
(12) F. Cook, H. Shechter, J. Bayless, L. Friedman, R. L. Foltz, and R. Randall, *ibid.*, **88**, 3870 (1966).
(13) W. Kirmse, "Carbene Chemistry," Academic Press, New York, N. Y., 1964.
(14) H. Zollinger, "Azo and Diazo Chemistry," Interscience, New York, N. Y., 1961, pp 21–23.
(15) E. H. White, *J. Amer. Chem. Soc.*, **77**, 6008 (1955).

SCHEME I

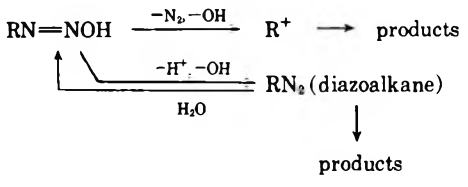


Methyl *trans*-*N*-nitroso-*N*-(3-phenyl-2,3-epoxypropyl)carbamate (**5**), mp 61–62°, was prepared in an analogous fashion from *trans*-4-phenyl-3-butenoic acid[16] (see Scheme I). The spectral data (infrared, ultraviolet, nmr) and elemental analysis of carbamates **2**–**5** were consistent with their assignments and are summarized in the Experimental Section.

Alkyl nitrosocarbamates are known to react with base in protic solvents to give diazoalkanes as well as solvolysis products that may be attributed to carbonium-like intermediates.[17–22] The observations of a number of investigators indicate that the reaction occurs by attack of base on the carbonyl carbon, with the formation of an alkyl diazotate and dialkyl carbonate.[23–28] Attack of the base at the acyl C or nitroso N has been shown to depend on the type of substrate, base, and solvent used.[29] The diazotates can, in the absence of protic solvents, be isolated as salts.[23–28] Addition of water to the diazotate salt involves a rapid proton transfer to produce a diazotic acid.

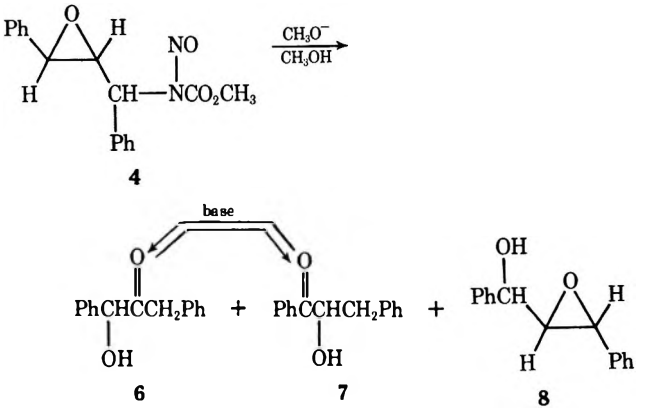


Two modes of decomposition are available to the diazotic acid in basic media.



The partition between carbonium ion derived products and products resulting from diazoalkanes is dependent upon the structure of the alkyl groups and the nature of the reaction medium. In general, secondary alkyl diazotates seem to decompose in aqueous solution to give carbonium ion products unless some structural feature is present to stabilize the diazoalkane.[30] Diazo compounds are favored in methanol compared with water. Since carbamate **4** bears a phenyl group in the α position whereas **5** does not, it was reasonable to assume that the epoxy diazotic acids derived from **4** and **5** would partition in different directions.

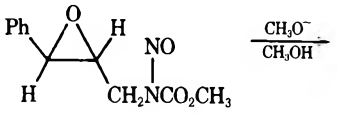
Treatment of an anhydrous methanolic solution of epoxy-*N*-nitrosocarbamate **4** with sodium methoxide resulted in the rapid and near-quantitative evolution of nitrogen. Conventional isolation procedures afforded 1,3-diphenyl-1-hydroxypropan-2-one (**6**), 1,3-diphenyl-2-hydroxypropan-1-one (**7**) (combined yield of **6** + **7** 40%) and 1,3-diphenyl-1-hydroxy-2,3-epoxypropane (**8**, 30%). These products were identified



by comparison of infrared and mixture melting points with those of authentic samples.[31–33] Dimethyl carbonate (isolated in over 90% yield) was produced by attack of methoxide ion on the carbonyl carbon of the *N*-nitrosocarbamate and is a coproduct of the reaction. Attack of the base at the carbonyl group was expected, since the reaction was carried out under conditions which favor acyl attack.[29] The relative amounts of **6** and **7** seemed to vary as a function of the experimental conditions and the work-up procedure employed. This variation could be attributed to the facile interconversion of the two ketones under the basic reaction conditions.[32] When the reaction was effected in absolute ethanol using sodium carbonate as the base, only negligible quantities of **7** were detected. This result implies that **7** is a secondary reaction product derived from enolization of **6**.

Similar treatment of carbamate **5** gave comparable results, except that in this case small amounts of 1-phenyl-1,2-propanedione (2%) (**11**) and a mixture of epoxy alcohols **12** and **13** were formed. The identity of the products derived from **5** was established by comparison with authentic samples (see Experimental Section). Again the relative amounts of hydroxy ketones **9** and **10** varied as a function of experimental conditions and can be attributed to their facile inter-

(16) R. P. Linstead and L. T. D. Williams, *J. Chem. Soc.*, 2735 (1926).
(17) H. V. Pechmann, *Ber.*, **28**, 855 (1895).
(18) R. Huisgen and J. Reinsertshofer, *Justus Liebigs Ann. Chem.*, **575**, 174 (1952).
(19) C. D. Gutshe and H. E. Johnson, *J. Amer. Chem. Soc.*, **77**, 109 (1955).
(20) D. E. Applequist and D. E. McGreer, *ibid.*, **82**, 1965 (1960).
(21) R. A. Moss, *J. Org. Chem.*, **31**, 1082 (1966).
(22) R. A. Moss and G. H. Temme, *Tetrahedron Lett.*, 3219 (1968).
(23) A. Hantzsch and M. Lehman, *Ber.*, **35**, 897 (1902).
(24) E. Muller, H. Haiss, and W. Rundel, *ibid.*, **93**, 1541 (1960).
(25) E. K. Tandy and W. M. Jones, *J. Org. Chem.*, **30**, 4257 (1965).
(26) R. A. Moss and F. C. Shulman, *Tetrahedron*, **24**, 2881 (1968).
(27) R. A. Moss, F. C. Shulman, and E. Emery, *J. Amer. Chem. Soc.*, **90**, 2731 (1968).
(28) W. M. Jones and D. L. Muck, *ibid.*, **88**, 68 (1966).
(29) W. M. Jones and D. L. Muck, *ibid.*, **88**, 3798 (1966).
(30) E. H. White and D. J. Woodcock in "The Chemistry of the Amino Group," S. Patai, Ed., Interscience, New York, N. Y., 1968, p 462.
(31) E. P. Kohler and R. H. Kimball, *J. Amer. Chem. Soc.*, **56**, 729 (1934).
(32) H. Burton and C. W. Shoppe, *J. Chem. Soc.*, 546 (1937).
(33) S. W. Chaikin and W. G. Brown, *J. Amer. Chem. Soc.*, **71**, 122 (1949).



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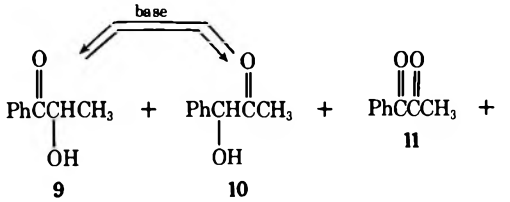

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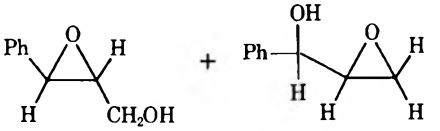
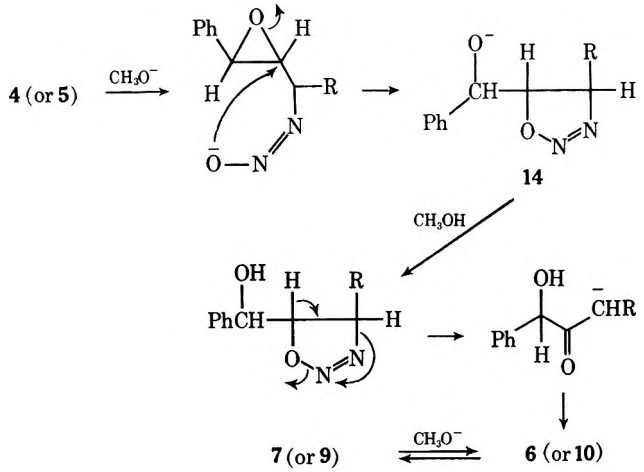


12 13

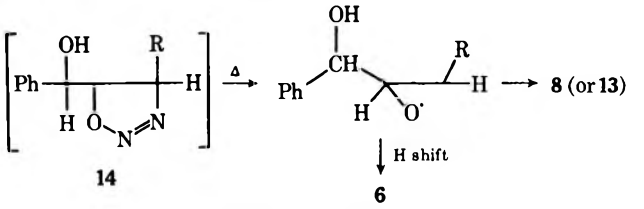
conversion under the reaction conditions.[32] The small amount of **11** formed is presumably due to the air oxidation of **9** or **10**.

These results are surprising, since the base-induced decomposition of nitrosocarbamates in anhydrous methanol should lead to methyl ethers rather than alcohols. The observation that nitrogen evolution occurred during the basic cleavage of nitrosocarbamates **4** and **5** suggests that products **6**–**13** were formed before the hydrolysis step. This suggestion is supported by the fact that similar yields of alcohols **6**–**13** were obtained from the reaction mixture prior to the addition of water.

The formation of hydroxy ketones **6** and **7** or **9** and **10** from the reaction of the epoxy-*N*-nitrosocarbamates in methanol may be rationalized by a nucleophilic attack of the diazotate on the epoxide ring to generate intermediate **14**. A related internal ring cyclization of an allenyl diazotate has been reported by Jones and Northington[34] and provides reasonable chemical precedent for the cyclization step.

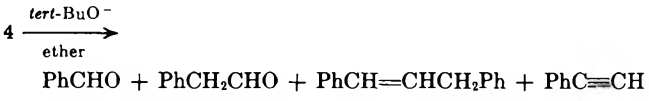


Alternatively, the opening of the three-membered ring may be synchronous with attack of the base on the carbonyl carbon. Protonation of intermediate **14** followed by extrusion of nitrogen and loss of a proton could give the enolate anion of ketone **6** (or **10**). These ketones could then interconvert under the reaction conditions. The conversion (**6** → **7**) would depend on the reaction conditions and the manner in which the products were separated from the reaction mixture. Another possibility would involve thermal loss of nitrogen from protonated **14** and formation of a diradical which could close to give an epoxy alcohol or undergo hydrogen migration to give ketone **6** (or **10**).

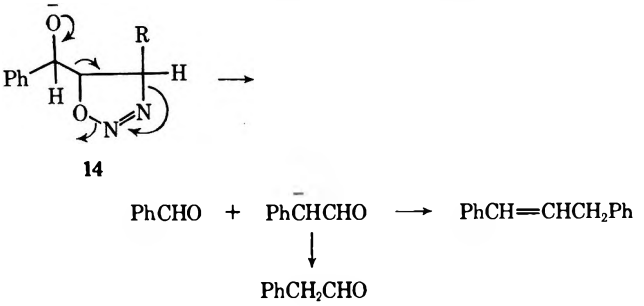


This latter sequence is reminiscent of the type of path involved in the photochemistry of α,β-epoxy ketones.[35] Whether hydroxy ketone **6** arises from the reaction of **14** with base or by thermal nitrogen extrusion remains an open question.[36]

Although we have not been successful in obtaining direct evidence for this mechanism, it appears attractive for several reasons. First, it readily accounts for the presence of hydroxy ketones in an anhydrous methanolic solution. Secondly, it accounts for the negligible quantities of **7** (or **9**) when sodium carbonate was used as the base. This is readily attributed to the low rate of enolization of **6** (or **10**) with a weak base. A third factor that makes this mechanism intuitively attractive is our finding that the reaction of epoxycarbamate **4** follows a different course in an aprotic medium. Thus, treatment of **4** with potassium *tert*-butoxide in ether resulted in the formation of benzaldehyde, phenylacetaldehyde, 1,3-diphenyl-1-propene, 80% of a carbonate mixture consisting mainly of di-*tert*-butyl carbonate and some methyl *tert*-butyl carbonate, and small quantities of phenylacetylene. In this case, intermediate **14** is poorly



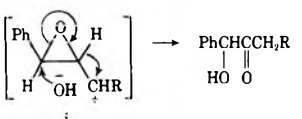
solvated and since it cannot undergo ready proton exchange it fragments to benzaldehyde and phenylacetaldehyde. The latter is known to undergo self-condensation to produce 1,3-diphenyl-1-propene.[37]



(34) D. J. Northington and W. M. Jones, *Tetrahedron Lett.*, 317 (1971).

(35) A. Padwa in "Organic Photochemistry," Vol. I. O. L. Chapman, Ed., Marcel Dekker, New York, N. Y., 1967, p 92.

(36) Still another possibility involves collapse of a tight ion pair such as i to keto alcohol **6** (or **10**). This would require a very tight and transient ion

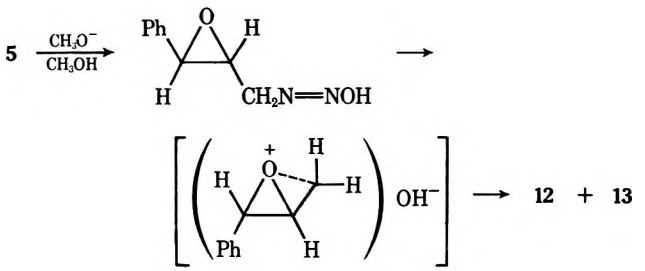


i

pair; otherwise it would be very difficult to explain the absence of methoxy products.

(37) E. K. Raunio and W. A. Bonner, *J. Org. Chem.*, **31**, 396 (1966).

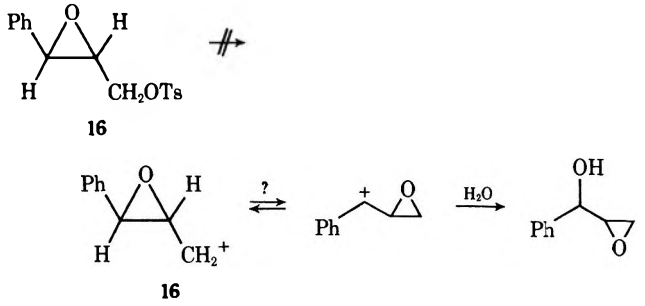
The mechanism of the epoxy alcohol formation is somewhat unclear. One possible explanation to account for the results would be that the epoxy diazotic acid decomposes with hydroxide return *via* an intimate diazonium–hydroxide ion pair. The rearranged epoxy alcohol **13** would then arise from an ion-pair intermediate such as **15**. This result is reasonable in



15

view of the observation by Moss and coworkers that the *N*-nitroso-2-octylurethan system gives considerable net inversion,[38] as well as the results from Hart's group wherein grossly different isomeric mixtures of ethers were obtained from isomeric allyl nitrosocarbamates.[39]

It is noteworthy that 2-phenyl-3-oxetanol was not detected as a by-product in the above reaction. Richey and Kinsman[10] have reported that the solvolysis of esters of several 2,3-epoxy-1-propanols led to the formation of 3-oxetanol derivatives by way of 1-oxabicyclobutonium cations. These workers did not dectect any epoxide rearrangement in the series investigated. It should be pointed out, however, that the epoxides examined in that study were so substituted as to minimize such a rearrangement. In an attempt to determine whether epoxy–carbinyl cations undergo epoxide scrambling, we have investigated the solvolytic behavior of tosylate **16**. After refluxing **16** for

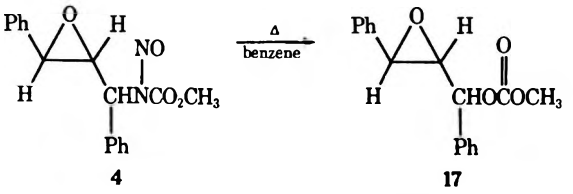


16

2 days in aqueous dioxane, there was no evidence of reaction and consequently we have not been able to reach a satisfactory conclusion in this regard.

The thermal decomposition of *N*-alkyl-*N*-nitrosoamides and *N*-alkyl-*N*-nitrosocarbamates has been well studied by White[40] and others.[41,42] The first step involves rearrangement of the nitroso compound to a diazo ester, which then rapidly decomposes to esters and olefins; the exact mechanism for this decomposition depends upon solvent polarity and the type of amine. For nitrosocarbamates of secondary amines, the decomposition involves dissociation of the initially formed diazo ester into an ion pair, extrusion of nitrogen to form a second ion pair, and the formation of either esters or olefins from the latter ion pair. In order to obtain additional data on the behavior of epoxy–carbinyl cation ion pairs, we have investigated the thermolysis of several *N*-nitrosocarbamates.

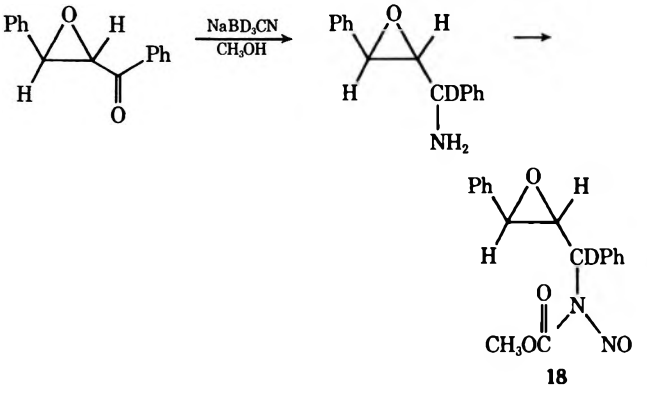
Thermal decomposition of **4** at 80° in benzene gave methyl 1(1,3-diphenyl-2,3-epoxypropyl)carbonate (**17**)



4 **17**

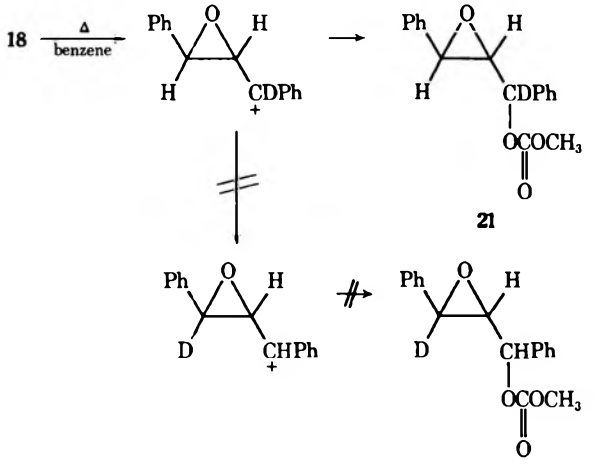
as the sole product (90%). The structure of the product was established by its spectral data and by hydrolysis to the corresponding alcohol followed by Sarett oxidation to *trans*-chalcone oxide.

In order to test for possible epoxide scrambling, we investigated the thermolysis of epoxycarbamates **18**, **19**, and **20**. The synthesis of epoxycarbamate



18

18, containing 85% deuterium at the 1 position, was carried out by sodium cyanodeuterioborate reduction[43] of *trans*-chalcone oxide, followed by reaction with methyl chloroformate and dinitrogen tetroxide. Thermal rearrangement of **18** at 80° in benzene gave a 93% yield of **21**. Nmr analysis of carbonate **21** indicated that no deuterium scrambling had occurred. Simi-



21

(38) R. A. Moss and S. M. Lane, *J. Amer. Chem. Soc.*, **89**, 5655 (1967).

(39) H. Hart and J. L. Brewbaker, *ibid.*, **91**, 716 (1969).

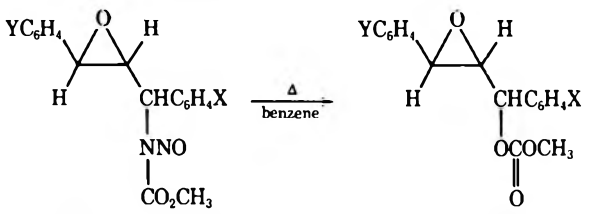
(40) E. H. White, *J. Amer. Chem. Soc.*, **77**, 6011 (1955); **77**, 6014 (1955); **83**, 1174 (1961); **83**, 1179 (1961).

(41) R. Huisgen and H. Reimlinger, *Justus Liebigs Ann. Chem.*, **599**, 183 (1956).

(42) A. Streitweiser and W. D. Schaffer, *J. Amer. Chem. Soc.*, **79**, 2893 (1957).

(43) R. F. Borch and H. D. Durst, *ibid.*, **91**, 3996 (1969).

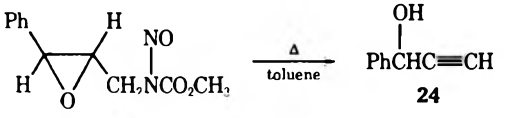
larly, thermolysis of carbamates **19** and **20** gave unscrambled carbonates **22** and **23**.



19, X = H; Y = Cl
20, X = Cl; Y = H

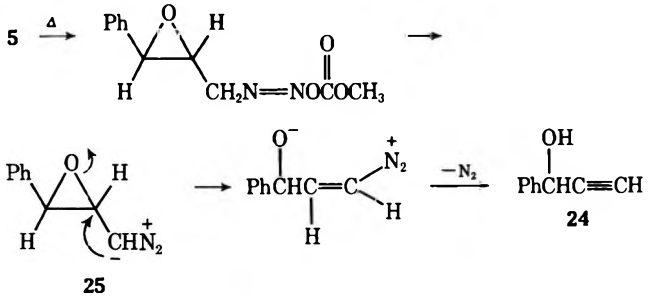
22, X = H; Y = Cl
23, X = Cl; Y = H

Since collapse of the ion pair in nonpolar solvents to form esters should be very fast, epoxide scrambling would have to proceed at a very rapid rate in order to compete. The results indicate that this is not the case. Epoxycarbamates **17**, **19**, and **20** were also treated with base and the epoxy alcohols isolated from the crude reaction mixture were found to be unrearranged. The absence of any significant scrambling of the aryl groups implies that either the collapse of the tight ion pair is very rapid when compared to the rearrangement, or that participation of the epoxide ring is only significant in those cases where a primary carbonium ion is generated adjacent to the epoxide ring. In order to test the latter possibility, we investigated the thermal behavior of epoxycarbamate **5**. The thermolysis of **5** was first attempted using conditions comparable to those used for the diaryl epoxycarbamates. Under this set of conditions only recovered starting material was obtained. However, when **5** was heated at reflux in toluene for 24 hr, a nearly quantitative yield of 3-phenyl-3-hydroxypropyne (**24**) was obtained. The results indicate that the



5 **24**

decomposition paths for carbamates **4** and **5** are substantially different. The carbonium ion pathway, found to operate in the decomposition of nitrosocarbamates of secondary carbinamines[30] (such as **4**) is not followed with **5**, presumably because of the relatively high energy of a primary carbonium ion. One intermediate which should be considered as a possible precursor for compound **24** is diazoalkane **25**. *N*-nitrosocarbamates of primary carbinamines are known to decompose to give the corresponding esters *via* a reaction series involving diazoalkane intermediates.[30] This diazo compound would readily account for product **24** by the route shown below. The elevated temperature required for the decomposition of **5** may result in the further decomposition of methyl bicarbonate, thereby precluding its recombination with diazoalkane **25**. The detection of carbon dioxide and methanol from the decomposition of **5** provides support for this suggestion.



25

An alternate path that could also explain the formation of acetylene **24** would involve decomposition of **25** to a carbene followed by bond reorganization. Attempts to trap such a carbene were unsuccessful. The absence of an adduct, however, cannot be taken as definitive evidence against a carbene because bond reorganization may be so fast as to preclude trapping. Unfortunately, the thermal behavior of carbamate **5** does not provide sufficient data to distinguish between these two possibilities, nor do the thermal results aid in understanding the mode of formation of epoxide **13**. Further experiments are underway to clarify this point.

Experimental Section[44]

Methyl *trans*-*N*-(1,3-Diphenyl-2,3-epoxypropyl)carbamate (2).—To a solution of 30 g of *trans*-1,3-diphenylpropene in 30 ml of anhydrous tetrahydrofuran at 0° was added 60 ml of a 1.6 *M* solution of *n*-butyllithium in hexane. After stirring for 5 min, 3 ml of hexamethylphosphorotriamide was added and the mixture was allowed to stir for an additional 2 hr. At the end of this time, an ethereal carbon dioxide mixture was introduced into the reaction flask until the red color disappeared. The resultant solid was hydrolyzed with 600 ml of a 2 *N* sodium carbonate solution followed by 200 ml of dilute ammonium hydroxide. The aqueous layer was extracted with ether and then acidified with concentrated hydrochloric acid. The solid that formed was filtered and crystallized from hexane to give 18 g (56%) of *trans*-2,4-diphenyl-3-butenoic acid, mp 124–126° (lit.[45] 128–129°).

To a solution of 18 g of the above acid in 200 ml of ether at 0° was added 20 ml of thionyl chloride. The mixture was stirred at 0° until all of the acid had reacted (*ca.* 1 hr). The solvent was removed under reduced pressure and the crude acid chloride was used without further purification. To a solution of the acid chloride in 150 ml of anhydrous acetone at −15° was added 14.4 g of sodium azide in 72 ml of water at such a rate so as to maintain the temperature of the reaction between −10 and −15°. The reaction solution was stirred for an additional 30 min at 0° and then poured onto 500 g of cracked ice. The water layer was extracted with ether and the ethereal layer was dried over magnesium sulfate. Anhydrous methanol (200 ml) was then added to the solution and the ether was removed by distillation. The solution was then heated at reflux for 2 hr, cooled, and allowed to stand overnight. The solvent was removed under reduced pressure and the resulting oil solidified upon standing. Crystallization from hexane gave 19.5 g (62%) of methyl *trans*-*N*-(1,3-diphenyl-2-propenyl)carbamate, mp 108–110°.

Anal. Calcd for $C_{17}H_{17}O_2N$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.19; H, 6.34; N, 5.01.

The infrared spectrum exhibited bands at 3.05, 5.91, 6.62, and 10.35 μ.

To a solution of 10.5 g of the above carbamate in 200 ml of methylene chloride at 0° was slowly added 15.7 g of 85% *m*-chloroperbenzoic acid. The mixture was stirred for an additional 2 hr at 0° and was then allowed to warm to room temperature. The *m*-chlorobenzoic acid was filtered and the solution was washed with water and 5% sodium bicarbonate and dried over magnesium sulfate. The solvent was removed under

(44) All melting points are corrected and boiling points are uncorrected. Elemental analyses were performed by Scandinavian Microanalytical Laboratory, Herlev, Denmark, and Alfred Bernhardt Laboratories, Hohenweg, Germany. The infrared absorption spectra were determined on a Perkin-Elmer Infracord spectrophotometer, Model 137. The ultraviolet absorption spectra were measured with a Cary recording spectrophotometer, using 1-cm matched cells. The nuclear magnetic resonance spectra were determined at 60 MHz with the Varian Associates high-resolution spectrometer. Tetramethylsilane was used as an internal standard.

(45) T. L. Jacobs and M. H. Goodrow, *J. Org. Chem.*, **23**, 1653 (1958).

reduced pressure to give a solid which was crystallized from hexane–ether to give 6.9 g (64%) of methyl *trans*-*N*-(1,3-diphenyl-2,3-epoxypropyl)carbamate (2), mp 101–102°.

Anal. Calcd for $C_{17}H_{17}O_3N$: C, 72.06; H, 6.05; N, 4.94. Found: C, 72.31; H, 6.32; N, 4.66.

The infrared spectrum exhibited bands at 3.05, 5.91, and 6.45 μ. The nmr spectrum ($CDCl_3$) was characterized by multiplets at τ 6.72 (1 H), 6.30 (1 H), and 5.16 (1 H), a singlet at τ 6.35 (3 H), a broad doublet at τ 4.80 (1 H), and a doublet at τ 2.70 (10 H).

Methyl *trans*-*N*-Nitroso-*N*-(1,3-diphenyl-2,3-epoxypropyl)carbamate (4).—To 4.1 g of the above epoxycarbamate in 50 ml of methylene chloride was added 1.2 g of anhydrous sodium acetate. The resulting mixture was cooled to −25°, a solution of 7.0 g of dinitrogen tetroxide in 50 ml of anhydrous ether was added, and the mixture was allowed to stir at −20 to −25° for 2 hr. At the end of this time the reaction mixture was poured into a cold 5% sodium bicarbonate solution and then extracted with ether. The ethereal extracts were dried over magnesium sulfate and the solvent was removed under reduced pressure to give a yellow solid (4.0 g). Crystallization from methanol gave yellow prisms of methyl *trans*-*N*-nitroso-*N*-(1,3-diphenyl-2,3-epoxypropyl)carbamate (4) (78%), mp 95–96°.

Anal. Calcd for $C_{17}H_{16}O_4N_2$: C, 65.37; H, 5.15; N, 8.97. Found: C, 65.29; H, 5.19; N, 8.99.

The infrared spectrum (KBr) exhibited bands at 5.70, 6.57, 6.92, and 9.91 μ. The nmr spectrum ($CDCl_3$) showed a doublet at τ 6.37 (1 H, J = 2.0 Hz), a doublet of doublets at τ 6.07 (1 H, J = 7.0 and 2.0 Hz), a singlet at τ 6.05 (3 H), a doublet at τ 4.36 (1 H, J = 7.0 Hz), and a multiplet at τ 2.71 (10 H).

Methyl *trans*-*N*-(3-Phenyl-2,3-epoxypropyl)carbamate (3).—To a solution of 10 g of 4-phenyl-3-butenoic acid in 100 ml of methylene chloride was slowly added 15 ml of thionyl chloride. The solution was stirred for 2 hr and the solvent and excess thionyl chloride were removed under reduced pressure. The crude acid chloride was dissolved in 100 ml of anhydrous acetone and the solution was cooled to −15°. A solution of 12 g of sodium azide in 50 ml of water was slowly added and the temperature was maintained at −10 to −15°. The reaction solution was stirred for an additional 15 min and then poured into ice water and extracted with ether. The ethereal layer was dried over sodium sulfate. Anhydrous methanol (200 ml) was added to the solution and the ether was removed by distillation. After the ether was removed the methanolic solution was heated at reflux for 1 hr. The methanol was removed under reduced pressure and the residue solidified upon cooling. Crystallization from hexane gave methyl *trans*-*N*-(3-phenyl-2-propenyl)carbamate, 6.2 g (30%), mp 51–52°. The infrared spectrum exhibited bands at 3.02, 5.81, 8.05, and 10.35 μ. The nmr spectrum showed a singlet at τ 6.47 (3 H), a triplet at τ 6.18 (2 H), a broad singlet a τ 4.42 (1 H), a multiplet centered at τ 3.8 (2 H), and a singlet at τ 2.82 (5 H).

To an ice-cooled solution of the above carbamate (0.56 g) in 10 ml of methylene chloride was slowly added 0.65 g of *m*-chloroperbenzoic acid (85%). The mixture was stirred for 1 hr at 0° and the solution was slowly allowed to reach room temperature. The solid precipitate that formed was removed by filtration and the methylene chloride solution was diluted with ether. The ethereal solution was washed with water and 5% sodium bicarbonate solution, and then dried over sodium sulfate. The solvent was removed under reduced pressure and the residue was crystallized from hexane to give 0.48 g (81%) of methyl *trans*-*N*-(3-phenyl-2,3-epoxypropyl)carbamate (3), mp 51–52°.

Anal. Calcd for $C_{11}H_{13}NO_3$: C, 63.75; H, 6.32; N, 6.76. Found: C, 63.43; H, 6.38; N, 6.81.

The infrared spectrum (CCl_4) showed bands at 3.01, 5.81, and 6.62 μ. The nmr spectrum ($CDCl_3$) showed a multiplet at τ 6.88 (1 H), a multiplet centered at τ 6.42 (3 H), a singlet at τ 6.37 (3 H), a broad singlet at τ 4.33 (1 H), and a singlet at τ 2.77 (5 H).

Methyl *trans*-*N*-Nitroso-*N*-(3-phenyl-2,3-epoxypropyl)carbamate (5).—To a solution of the above carbamate (0.621 g) in 20 ml of anhydrous ether at −78° was added 0.25 g of anhydrous sodium acetate and 0.5 g of dinitrogen tetroxide in 10 ml of ether. The mixture was stirred at −78° for 2 hr and then poured into an ice-cold 10% sodium bicarbonate solution. The aqueous layer was extracted with ether and the etheral extracts were dried over sodium sulfate. The solvent was removed under reduced pressure to give an oil which solidified on standing. Crystallization of the solid from ether–hexane gave 0.54 g of yellow crystals of methyl *trans*-*N*-nitroso-*N*-(3-phenyl-2,3-epoxypropyl)carbamate (5), mp 61–62°.

Anal. Calcd for $C_{11}H_{12}N_2O_4$: C, 55.98; H, 5.12; N, 11.86. Found: C, 56.18; H, 5.22; N, 11.81.

The infrared spectrum exhibited bands at 5.68 and 5.92 μ and a doublet at 8.62 and 8.82 μ. The nmr spectrum contained a multiplet at τ 6.38 (1 H, J = 1.8 Hz), a complex multiplet centered at τ 5.96 (2 H), and singlets at τ 5.94 (3 H) and 2.77 (5 H).

Methyl *trans*-*N*-Nitroso-*N*-(1-phenyl-3-*p*-chlorophenyl-2,3-epoxypropyl)carbamate (19).—To a solution of ammonium nitrate (30.4 g) and lithium cyanohydridoborate[43] (1.88 g) in 300 ml of anhydrous methanol was added 5.2 g of *trans*-1-phenyl-3-*p*-chlorophenyl-2,3-epoxypropan-1-one.[46] The solution was stirred for 46 hr at room temperature and then poured into dilute acetic acid. The acidic solution was washed with several portions of ether and was then made strongly basic with ammonium hydroxide. The basic solution was extracted with ether and the ethereal extracts were dried over magnesium sulfate. The solvent was removed under reduced pressure and the crude amine (2.3 g) that was obtained was used without further purification.

To a solution of 2.3 g of the above amine in 50 ml of anhydrous ether was added 0.36 g of sodium hydroxide and 0.86 g of methyl chloroformate. The reaction mixture was stirred for 45 min, then poured into water and extracted with ether. The ethereal layer was washed with dilute hydrochloric acid and water, and then dried over magnesium sulfate. The solvent was removed under reduced pressure to give a crude oil (1.6 g). The oil was crystallized from hexane–ether to give 0.96 g of epoxy carbamate. The infrared spectrum exhibited bands at 3.05, 5.91, 6.51, 8.01, 9.15, 9.65, and 9.85 μ. The epoxycarbamate was used without further purification.

A solution of the above epoxycarbamate (0.95 g) in 20 ml of methylene chloride was cooled to −25° and 0.25 g of anhydrous sodium acetate was added. A solution of 1.0 g of dinitrogen tetroxide in 30 ml of anhydrous ether was cooled to −78° and added to the above solution. The mixture was stirred for 2 hr, poured into a cold 5% sodium bicarbonate solution, and extracted with ether. The ethereal extracts were dried over magnesium sulfate and the solvent was removed under reduced pressure. Crystallization of the resulting oil from methanol–water gave yellow crystals of methyl *trans*-*N*-nitroso-*N*-(1-phenyl-3-*p*-chlorophenyl-2,3-epoxypropyl)carbamate (19), mp 95–96°.

Anal. Calcd for $C_{17}H_{15}O_4N_2Cl$: C, 58.88; H, 4.36; N, 8.07. Found: C, 59.09; H, 4.22; N, 8.23.

The infrared spectrum exhibited bands at 5.68, 6.58, 6.93, and 9.81 μ. The nmr spectrum consisted of a multiplet at τ 2.65 (9 H), a doublet at τ 4.44 (1 H, J = 7 Hz), a singlet at τ 5.98 (3 H), a multiplet at τ 6.20 (1 H), and a doublet at τ 6.44 (1 H).

Methyl *trans*-*N*-Nitroso-*N*-(1-*p*-chlorophenyl-3-phenyl-2,3-epoxypropyl)carbamate (20).—*trans*-1-*p*-Chlorophenyl-3-phenyl-2,3-epoxypropan-1-one[46] (5.0 g) was subjected to the same reductive amination conditions as described above and yielded 2.3 g of crude amine. To a solution of 2.3 g of the amine in anhydrous ether (30 ml) was added 0.8 g of methyl chloroformate and 0.36 g of sodium hydroxide in 1 ml of water. The reaction solution was stirred for 45 min and then poured into water. The ethereal layer was removed, washed with dilute hydrochloric acid and water, and then dried over magnesium sulfate. The solvent was removed under reduced pressure to give 2.4 g of a white solid. This material was crystallized from hexane–benzene to give 1.7 g of white crystals, mp 141–143°. Recrystallization from hexane–benzene gave analytically pure methyl *trans*-*N*-(1-*p*-chlorophenyl-3-phenyl-2,3-epoxypropyl)carbamate, mp 144–145°.

Anal. Calcd for $C_{17}H_{16}O_3NCl$: C, 64.25; H, 5.08; N, 4.40. Found: C, 64.11; H, 5.03; N, 4.38.

The infrared spectrum exhibited bands at 3.08, 5.91, 6.51, 7.82, 9.13, 9.61, and 9.83 μ. The nmr spectrum consisted of a multiplet at τ 6.7 (1 H), a singlet at τ 6.30 (3 H), a doublet at τ 6.27 (1 H, J = 8 Hz), a multiplet centered at τ 5.08 (1 H), a broad doublet at τ 4.35 (1 H, J = 8 Hz), and a multiplet at τ 2.63 (9 H).

A solution of the above carbamate (2.1 g) in methylene chloride (20 ml) was cooled to −25° and 0.25 g of anhydrous sodium acetate and 2.0 g of dinitrogen tetroxide in 20 ml of ether were added. The reaction mixture was stirred at −20° for 2 hr and

(46) H. O. House and G. D. Ryerson, *J. Amer. Chem. Soc.*, **83**, 979 (1961).

then poured into a cold 5% sodium bicarbonate solution which was extracted with ether. The ethereal extracts were dried over magnesium sulfate and the solvent was removed under reduced pressure to give 0.82 g of white crystals, mp 103–104.5°. The solid was recrystallized from methanol to give pure methyl *trans*-*N*-nitroso-*N*-(1-*p*-chlorophenyl-3-phenyl-2,3-epoxypropyl)-carbamate (**20**), mp 104–105° dec.

Anal. Calcd for $C_{17}H_{15}O_4N_2Cl$: C, 58.88; H, 4.36; N, 8.07. Found: C, 58.80; H, 4.17; N, 8.15.

The infrared spectrum (KBr) exhibited bands at 5.37, 6.53, 6.92, and 7.31 μ and a doublet at 9.75 and 9.85 μ. The nmr spectrum ($CDCl_3$) consisted of a doublet at τ 6.32 (1 H, J = 1.8 Hz), a multiplet at τ 6.08 (1 H), a singlet at τ 6.0 (3 H), a doublet at τ 4.37 (1 H, J = Hz), and a singlet at τ 2.63 (9 H).

Methyl *trans*-*N*-Nitroso-(1,3-diphenyl-1-deuterio-2,3-epoxypropyl)carbamate (18).—To a solution of 13.6 g of ammonium nitrate and 1.18 g of sodium cyanodeuterioborate[47] in 150 ml of absolute methanol was added 2.0 g of chalcone epoxide. The solution was stirred for 72 hr at room temperature and then poured into dilute acetic acid. The acidic solution was washed with several portions of ether and then made basic by the addition of ammonium hydroxide. The basic solution was extracted with ether and the ethereal extracts were dried over magnesium sulfate. The solvent was evaporated under reduced pressure and the crude amine obtained (0.96 g) was dissolved in 50 ml of anhydrous ether. To this solution was added 0.26 g of sodium hydroxide and 0.3 g of methyl chloroformate. The reaction mixture was stirred for 4 hr, then poured into water and extracted with ether. The ethereal layer was washed with dilute hydrochloric acid and water, and then dried over magnesium sulfate. The solvent was removed under reduced pressure and the residual oil was recrystallized from ether–hexane to give 0.41 g of methyl *trans*-*N*-(1,3-diphenyl-1-deuterio-2,3-epoxypropyl)-carbamate, mp 100–101°. The above carbamate was converted with dinitrogen tetroxide to the corresponding *N*-nitrosocarbamate by the procedure described above. The deuterium content was determined as 85% by mass spectral analysis, which showed the parent ion at *m/e* 313.

Reaction of Methyl *trans*-*N*-Nitroso-*N*-(1,3-diphenyl-2,3-epoxypropyl)carbamate (4) with Sodium Methoxide in Methanol.—A solution of 1.0 g of nitrosocarbamate **4** in 10 ml of methanol was added to an ice-cooled solution of sodium methoxide prepared by dissolving 0.37 g of sodium in 50 ml of anhydrous methanol. Nitrogen evolution (50 ml) was immediate and quantitative. The mixture was stirred for an additional 30 min and then poured into water (500 ml) and extracted with ether (300 ml). The ethereal layer was dried over magnesium sulfate and the solvent was removed under reduced pressure. The aqueous layer was acidified with dilute hydrochloric acid and then extracted with ether to give benzoic acid (0.12 g, 30%). The crude oil obtained from the ethereal layer was analyzed by vapor phase chromatography on a DEGS (5% on Chromosorb W, 5 ft × 0.25 in.) or a FS 1265 (6% on Anachrom ABS, 5 ft × 0.25 in.) column. The products were separated by preparative vapor phase chromatography. The products were identified as dimethyl carbonate (90%), benzaldehyde (4%), phenylacetaldehyde (2%), *trans*-1,3-diphenyl-1-hydroxy-2,3-epoxypropane (**8**)[48] (15%), 1,3-diphenyl-1-hydroxypropan-2-one (**6**), mp 113–114°,[49] and 1,3-diphenyl-2-hydroxypropan-1-one (**7**), mp 65–66°[49] (combined yield of **6** and **7**, 40%) by comparison with authentic samples. Keto alcohols **6** and **7** were found to equilibrate and partially decompose to benzoic acid under simulated work-up procedures. Similar treatment of nitrosocarbamate **4** with potassium carbonate in anhydrous ethanol gave mostly **6** and **8**. Under these conditions, negligible (2%) quantities of 1,3-diphenyl-2-hydroxypropan-1-one were detected.

Reaction of Methyl *trans*-*N*-Nitroso-*N*-(1,3-diphenyl-2,3-epoxypropyl)carbamate (4) with Potassium *tert*-Butoxide in Ether.—To a suspension of potassium *tert*-butoxide (0.17 g) in 50 ml of anhydrous ether was added 1.0 g of *N*-nitrosocarbamate (**4**) in 15 ml of ether. Nitrogen evolution was immediate. The mixture was stirred for an additional 30 min and then poured into 500 ml of water and extracted with ether. The ethereal layer was dried over magnesium sulfate. Analysis of the solution by gas chromatography indicated the presence of a mixture of methyl-*tert*-butyl carbonate and di-*tert*-butyl carbonate (80%). The solvent was removed under reduced pressure and the crude oil was analyzed by vpc (5% DEGS on Chromosorb W, 5 ft × 0.25 in.). The isolated products were identified as phenylacetylene (4%), benzaldehyde (8%), phenylacetaldehyde (18%), and a small amount (1%) of 1,3-diphenyl-1-propene. The aqueous layer contained a mixture of benzoic and phenylacetic acid. When benzene was employed as the solvent, the major product was 1,3-diphenyl-1-propene (20%), together with a small amount of benzaldehyde. The identity of all the products was confirmed by comparison with authentic samples.

Reaction of Methyl *trans*-*N*-Nitroso-*N*-(3-phenyl-2,3-epoxypropyl)carbamate (5) with Sodium Methoxide in Methanol.—The reaction conditions used for the decomposition of *N*-nitrosocarbamate (**4**) were used for carbamate **5**. The crude product obtained was analyzed by nmr and the products were isolated by liquid–liquid partition chromatography.[50] The yield of nitrogen was immediate and quantitative. The products were identified as 1-phenyl-2-hydroxypropan-1-one (**9**),[51] 1-phenyl-1-hydroxypropan-2-one (**10**)[51] (combined yield 35%), *trans*-1-hydroxy-3-phenyl-2,3-epoxypropane (**12**)[52] (16%), 1-hydroxy-1-phenyl-2,3-epoxypropane (**13**) (19%), and 1-phenyl-1,2-propanedione (2%). The identity of all compounds was established by spectral data and by comparison with authentic samples.[51,52] Epoxy alcohol **13**, prepared by the sodium borohydride reduction of the known epoxy ketone,[53] showed bands at 2.95 and 9.31 μ in the infrared. Its nmr spectrum consisted of multiplets at τ 7.3 (2 H), 6.9 (1 H), 6.5 (1 H), and 5.5 (1 H) and a singlet at τ 2.72 (5 H).

Thermal Decomposition of Methyl *trans*-*N*-Nitroso-*N*-(1,3-diphenyl-2,3-epoxypropyl)carbamate (5).—Epoxycarbamate **5** (0.3 g) was dissolved in benzene and the solution was heated at reflux for 26 hr. The solvent was removed under reduced pressure and the single product obtained was purified by preparative thick-layer chromatography (3% ethyl acetate–benzene). The structure of the clear oil was established as methyl 1-(1,3-diphenyl-2,3-epoxypropyl)carbonate (**17**). The infrared spectrum contained bonds at 5.71 and 7.93 μ. The nmr spectrum consisted of a multiplet at τ 6.67 (1 H), a singlet at τ 7.27 (3 H), a multiplet centered at τ 6.2 (1 H), a double doublet at τ 4.3 (1 H, J = 6 Hz), and a multiplet at τ 2.7 (10 H). Chemical confirmation of this structure was accomplished by hydrolysis of **17** with sodium hydroxide in aqueous ethanol followed by oxidation to *trans*-chalcone oxide. Compound **17** was independently synthesized by treating *trans*-1,3-diphenyl-1-hydroxy-2,3-epoxypropane with methyl chloroformate.

Thermal Decomposition of Methyl *trans*-*N*-Nitroso-*N*-(3-phenyl-2,3-epoxypropyl)carbamate (5).—Epoxycarbamate **5** (0.5 g) was heated at reflux in 70 ml of toluene for 24 hr. The solvent was removed under reduced pressure and the resulting oil was purified by preparative thick layer chromatography. The major product (>90% by nmr) was identified as 1-phenyl-1-hydroxypropyne (**24**) by comparison with an authentic sample prepared by the method of Jones and McCombie.[54] The infrared spectrum showed bands at 3.04 (exchanges with deuterium oxide), 3.12, 4.71, 9.82, and 10.51 μ. The nmr spectrum ($CDCl_3$) exhibited a doublet at τ 4.62 (1 H, J = 2.3 Hz) and a multiplet centered at τ 2.63 (5 H).

Thermal Decomposition of Chlorophenyl Epoxycarbamates 19 and 20.—Carbamates **19** and **20** were heated separately at reflux in benzene for 24 hr. The solvent was removed under reduced pressure and the crude mixture was chromatographed on a thick layer plate using ether–hexane as the eluent. The carbonates isolated in each instance were found to be at least 95% unrearranged. This was demonstrated by nmr spectroscopy and by comparison with authentic samples obtained from the reaction of the corresponding epoxy alcohols with methyl chloroformate.

The infrared spectrum of the carbonate (**22**) derived from **19** showed absorption at 5.72 and 7.91 μ. The nmr (CCl_4) consisted of multiplets at τ 6.8 (1 H), and 6.15 (4 H), a doublet at τ 6.3 (1 H), and a multiplet at τ 2.6 (9 H). The infrared spec-

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trum of carbonate **23** derived from epoxycarbamate **20** showed absorption at 5.71 and 7.91 μ. The nmr ($CDCl_3$) exhibited a multiplet at τ 6.67 (1 H), a singlet at τ 6.17 (3 H), a multiplet at τ 6.15 (1 H), a doublet at τ 4.21 (1 H), and a multiplet at τ 2.61 (9 H).

Registry No.—**2**, 33143-41-8; **3**, 33143-42-9; **4**, 24312-28-5; **5**, 24276-26-4; **13**, 33143-44-1; **17**, 33143-45-2; **19**, 33143-46-3; **20**, 33143-47-4; **22**, 33143-48-5; **23**, 33143-49-6; **24**, 4187-87-5; methyl *trans*-*N*-(1,3-diphenyl-2-propinyl)carbamate, 33143-50-9; methyl *trans*-*N*-(3-phenyl-2-propinyl)carbamate, 33143-51-0; methyl *trans*-*N*-(1-*p*-chlorophenyl-3-phenyl-2,3-epoxypropyl)carbamate, 33213-40-0; methyl *trans*-*N*-(1,3-diphenyl-1-deuterio-2,3-epoxypropyl)carbamate, 33143-53-2; sodium methoxide, 124-41-4; potassium *tert*-butoxide, 865-47-4.

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Intermediates in Nucleophilic Aromatic Substitution. XII.[1,2] Interaction of Alkoxide Ions with 3,5-Dinitrobenzonitrile[3]

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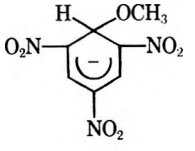
Addition of methanolic methoxide ions to 3,5-dinitrobenzonitrile (**3**) results in the immediate development of an absorption (λ_{max} 490 nm), assigned to the methoxyl σ complex of **3** (**4**), which subsequently decreases rapidly in intensity. The equilibrium constant for the formation of **4** in methanol at 25.00°, K = 1.9 l. mol^{-1}, has been obtained from kinetic treatment of the rate of decrease in the absorbance of **4** as a function of methoxide ion concentration. Using the Benesi–Hildebrand equation a value of 1.3 l. mol^{-1} has been obtained for this equilibrium constant under the same conditions. DMSO as a cosolvent increases the stability of **4**. The structure of **4** has been established from the pmr spectra of both the *in situ* generated and isolated complexes. Decomposition of **4** gave 1-methoxy-3-cyano-5-nitrobenzene. Pmr evidence is presented for the *in situ* formation of an analogous complex from 3-cyano-5-nitrobenzonitrile in DMSO-d_6 in the presence of methanolic potassium methoxide. The formation of low concentrations (<1%) of 3,5-dinitrobenzonitrile anion radicals, generated from alkoxide ions and **3** in several dipolar aprotic solvents, has been established using esr spectroscopy. The obtained results are compared to those for related σ, or Meisenheimer, complexes.

1,3,5-Trinitrobenzene has been shown to react extremely rapidly with methoxide ions in methanolic solution to give complex **1**,[6] which subsequently decomposes to produce 3,5-dinitroanisole.[7] The equilibrium constant for the formation of **1** in methanol at 28.0° has been determined to be 15 l. mol^{-1},[7] a value three orders of magnitude smaller than that obtained for the analogous formation of 1,1-dimethoxy-2,4,6-trinitrocyclohexadienylide ion (**2**).[8] We have demonstrated recently that substitution of one or two nitro groups by cyano groups in 2,4,6-trinitroanisole profoundly affects the kinetic and thermodynamic parameters for Meisenheimer complex formation.[8,9] More importantly, the unsymmetrical nature of 2-cyano-4,6-dinitroanisole allowed the observation of the preferential initial formation of a 1,3-dimethoxy-2-cyano-4,6-dinitrocyclohexadienylide ion over its 1,5-dimethoxy-2-cyano-4,6-dinitrocyclohexadienylide isomer.[8] As a continuation of our work on the stabilities and structures of Meisenheimer complexes we have, therefore, examined the kinetics for the interaction of methanolic sodium methoxide with 3,5-dinitrobenzonitrile (**3**), isolated crystalline potassium 1-methoxy-2-cyano-4,6-dinitrocyclohexadienylide (**4**) and established its structure together with those of its decomposition products under different conditions. We also wish to report the esr observation of radical anions formed from **3** and alkoxide ions. Pmr parameters for **4** formed *in situ* along with an unspecified amount of 1-hydroxy-2-cyano-4,6-dinitrocyclohexadienylide have been reported recently.[10] However, these authors could not isolate solid salts of **4**.[10]



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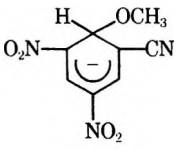

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Experimental Section

The solvents and reagents were prepared, purified, and standardized as previously described.[11] 3,5-Dinitrobenzonitrile (**3**) (Aldrich), mp 129–130°, was checked for purity and used without further purification.

3-Cyano-5-nitrobenzonitrile (**5**) was prepared in good yield from 5-nitroisophthalic acid (J. T. Baker) *via* 5-nitroisophthaloyl chloride and 5-nitroisophthalamide according to the procedure described previously for 1-bromo-2,4,6-tricyanobenzene[1] and 1-bromo-2,4- and -2,6-dicyanobenzenes.[9] After recrystallization from benzene, the white crystals of **5** melted at 209–210°.

Potassium 1-methoxy-2-cyano-4,6-dinitrocyclohexadienylide (**4**) was prepared by the addition of 1.88 ml (9.5 mmol) of 5.05 *M* potassium methoxide in methanol to a solution of 1.931 g (10 mmol) of **3** in *ca.* 5 ml of dry dioxane. The dark red solution was flushed with dry nitrogen and then allowed to stand overnight at 0°. After evaporation of some of the solvent with dry nitrogen, the dark purple crystals were removed by filtration under dry nitrogen and were washed four times with dry benzene and anhydrous ether. Pulverization of the dark purple crystals in a drybox resulted in a change in their color to dark red. After drying *in vacuo* over phosphorus pentoxide, **4** decomposed at *ca.* 180°. The structures of the purple and red crystals were shown to be identical from their pmr spectra and to contain 1 mol of dioxane of crystallization (by pmr integration of dioxane singlet, τ 6.43 ppm[11]). In addition the pmr spectrum of **4** in DMSO-d_6 (Table III) was essentially identical with that reported for the *in situ* formation of **4**.[10]

Anal.[12] Calcd for $C_8H_6N_3O_5K \cdot C_4H_8O_2$: C, 40.2; H, 4.05; N, 12.1; K, 11.3. Found: C, 39.9; H, 3.78; N, 12.1; K, 11.1.

The pmr samples of isolated (in methanol, DMSO-d_6, or CD_3CN) or *in situ* generated (in DMSO-d_6 or CD_3CN) **4** were decomposed by pouring the sample into *ca.* 10 ml of water and acidifying the solution to *ca.* pH 2 with 0.1 *M* HCl. The precipitate was then centrifuged, washed two times with water, and dried *in vacuo* over phosphorus pentoxide. The solutions were tested for the presence of cyanide ion using an Orion cyanide ion selective electrode and for nitrite ion using the method of Rider and Mellon[13] and were found to contain nitrite ion but not cyanide ion. In solutions of **3** in the same solvents in the absence of methoxide ion, no nitrite or cyanide ions could be detected. The structure of the precipitated 1-methoxy-3-cyano-5-nitrobenzene (**6**) was established by pmr and mass spectroscopy and by degradation studies (see Discussion); however, attempted syntheses of **6** by alternate routes were unsuccessful.

The absorption spectra of the transient from **3** and its rate of decay were observed in the thermostated cell compartment of a Beckman DU-2 spectrophotometer, using Teflon stoppered 1-cm cells. An energy recording adaptor (ERA) was used in conjunction with a Hewlett-Packard recorder. The cell compartment was equipped with a set of dual thermospacers; the temperature was measured inside the cells and was maintained within ±0.02°. Runs were started by injecting the appropriate methanolic solution of **3** into a cell containing the sodium methoxide solution in methanol or in methanolic DMSO. A Hamilton syringe was used and the solution was injected through a small bore in the Teflon stopper.

The decomposition of solid **4** was initiated by injecting a freshly prepared concentrated solution of the complex (50–100 μl in DMSO) into the thermostated methanolic DMSO contained in the cell compartment of the spectrophotometer, and the rate of color disappearance was followed at 490 mμ.

Rapid mixing techniques were used to determine the absorbance due to complex **4** at the various methoxide ion concentrations in methanol and in methanolic DMSO. The blank in each case contained the same concentration of methoxide ion in the corresponding solvent.

Pmr (60-MHz) spectra were obtained with a Varian Associates A-60 spectrometer at ambient probe temperature (34°) or at 25° (probe temperature maintained with a V-6040 variable-temperature controller). Unless otherwise noted, all spectra were determined on solutions in DMSO-d_6 using tetramethylsilane (TMS) as an internal standard; chemical shifts are given on the τ scale in parts per million relative to TMS (τ 10.00 ppm) and are accurate to ±0.03 ppm. Chemical shift data were taken from spectra determined at a sweep width of 500 Hz. The reported coupling constants are the average of three determinations at 50-Hz sweep widths and are accurate to ±0.2 Hz. The *in situ* reactions of methoxide ion with **3** and with **5** were followed by examining the pmr spectra of solutions resulting from the dropwise addition of 5.73 *M* potassium methoxide in methanol to *ca.* 20% solutions of **3** or **5** in DMSO-d_6. The spectrum of each solution was determined immediately after the addition of methoxide ion and the spectrum was scanned repeatedly until no further changes were observed. The process was repeated until sufficient methoxide ion had been added to consume all of the starting **3** or **5**. The 100-MHz spectrum of 3-cyano-5-nitroanisole (**6**) was obtained with a JEOLCO JMN-4H-100 spectrometer. Experimental line frequencies used in the analysis of this spectrum were the averages of four measurements obtained at 50-Hz sweep widths. The general procedure used in analysis has been reported previously;[14] the final fit was made on an LBM 360-44 computer, using the iterative program LAOCN-3.[15]

Esr experiments were performed with an X-band spectrometer constructed in the Radiation Research Laboratories (10-KHz field modulation frequency, Philco L-4154 detector), utilizing a Varian V-4102-3B 12-in. magnet. Magnetic field measurements were made by a field following nmr unit similar to that described by Fessenden and Schuler,[16] with nmr and microwave frequencies measured by a Hewlett-Packard 5246L frequency converter. Phase detection at the second harmonic of the modulation frequency was used to obtain second-derivative spectra. All experiments were done at room temperature using a flat quartz cell, thickness 0.5 mm, and a Varian V-4531 multipurpose cavity. Hyperfine coupling constants were determined by taking appropriate differences in the proton resonance frequency for pairs of lines. Proton resonance frequencies were converted to magnetic field values (gauss) using the factor 0.23487 G/KHz. Values of the coupling constants are estimated to be accurate to ±0.03 G. Estimates of the radical concentrations were made by comparing the spectra of the radical and standard solutions of galvinoxyl at the same instrument settings and in the same solvents and are considered to have a ±50% error.

The radicals were generated by mixing carefully degassed solutions of **3** with methoxide or *tert*-butoxide ions dissolved in the appropriate solvent mixtures in a cell similar to that described by Russell.[17] In some experiments paramagnetic species were obtained by mixing solid **4** placed in one side of the cell with the appropriate alkoxide solution or solvent (see Table II) contained in the other side.

Results

Addition of a *ca.* 10^{-5} *M* solution of **3** in methanol to a sodium methoxide solution [(3.6–360) × 10^{-4} *M*], either in methanol or in methanolic DMSO, results in the immediate formation of a red color which rapidly fades. The absorption spectra of the colored adduct (Figure 1) have been obtained, therefore, by linear extrapolation of the absorbance to zero time of mixing. Spectra were recorded at 5-mμ intervals throughout the wavelength region scanned. The absorption maxima at 390 and 490 mμ are assigned to complex **4**, since the spectra of the isolated complex in methanolic DMSO solutions have the same maxima. The formation and subsequent decay of **4** can be described by

$$\mathbf{3} + OCH_3^- \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \mathbf{4} \xrightarrow{k_3} \text{product(s)} \qquad (1)$$

and we define the formation constant, K, for **4** as

$$K = \frac{[\mathbf{4}]}{[\mathbf{3}][OCH_3^-]} \qquad (2)$$

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TABLE I
INTERACTION OF 3,5-DINITROBENZONITRILE (3) WITH SODIUM METHOXIDE IN METHANOL AND IN METHANOLIC DIMETHYL SULFOXIDE AT 25.00°

[DMSO], M	10^3[NaOCH$_3$], M	Absorbance at 490 mμ[a,b]	$10^2 k_{obsd}$,[b] sec^{-1}	K,[c] l. mol^{-1}	K,[d] l. mol^{-1}	$10^3 k_1$,[d] sec^{-1}
0[e]	5.25	0.034	3.17	1.3	1.9	32.4
	10.5	0.065	6.21			
	21.0	0.112	12.8			
	31.5	0.171	18.0			
	42.0	0.237	24.6			
	52.5	0.283	30.2			
	105	0.568	54.2			
	208		95.5			
	312		130			
	416		143.3			
	520		158			
1.41[f]	4.62	0.059	3.37	4.4	5.7	12.6
	9.25	0.126	15.9			
	18.5	0.194	12.4			
	27.8	0.356	18.2			
	37.0	0.403	24.0			
	46.2	0.530	27.4			
	46.8		26.2			
	93.6		48.3			
	140.4		62.1			
	187.2		67.8			
	234.0		81.7			
	280.8		78.2			
	329.6		82.8			
2.82[g]	1.26	0.023		15	21	4.55
	2.52	0.051				
	3.36	0.061	3.06			
	4.20	0.105	3.58			
	8.40	0.158	7.20			
	12.6	0.225	10.12			
	16.8	0.276	12.65			
	21.0	0.366	14.95			
	25.2	0.410	17.7			
	29.4	0.420	18.0			
	33.6	0.488	19.1			
	37.8	0.510	20.2			
	42.0		21.9			
	84.0		25.0			
	126		34.0			
	210		35.9			
	252		35.9			
	336		40.5			
	420		41.0			
4.23[h]	0.368	0.023		60	75	1.55
	0.735	0.032				
	1.025	0.051				
	1.47	0.056	1.75			
	1.84	0.058	1.97			
	2.21	0.069	2.49			
	2.57	0.076	2.64			
	3.68	0.092	3.30			
	7.35	0.194	6.05			
	11.02	0.244	7.82			
	14.7	0.286	9.09			
	22.1	0.337	9.60			
	25.7	0.338	10.1			
	36.8		12.0			

[a] Using a 1.00-cm cell. [b] Mean of three runs (each with a ±3% error). [c] Calculated from Benesi–Hildebrand plots (eq 3). [d] Calculated using eq 8. [e] [3] = 2.82×10^{-4} M. [f] [3] = 1.66×10^{-4} M. [g] [3] = 7.04×10^{-5} M. [h] [3] = 2.49×10^{-5} M.

Using the zero time absorption maxima at 490 mμ, (Table I) and the Benesi–Hildebrand equation[18] form

$$\frac{[3]}{A} = \frac{1}{\epsilon} + \frac{1}{K[OCH_3^-]} \quad (3)$$

where A is the zero time absorbance in a 1.00-cm cell, ϵ is the molar extinction coefficient, and K is the equilibrium constant for the complex, a good linear relationship was obtained on plotting $[3]/A$ *vs.* $[1]/[OCH_3^-]$, indicating that a simple 1:1 equilibrium prevails. Since the intercept of the Benesi–Hildebrand plot

(18) H. A. Benesi and J. H. Hildebrand, *J. Amer. Chem. Soc.*, **71**, 2703 (1949).

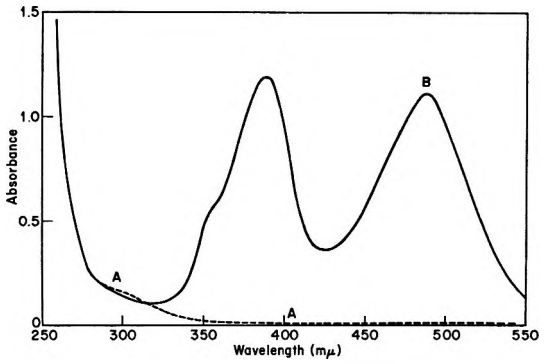


Figure 1.—Absorption spectra of **3** (6.5×10^{-5} *M*) in methanol (A) and in 0.29 *M* $NaOCH_3$ in MeOH at zero time (B), using a pair of matched 1.00-cm cells.

(*i.e.*, $1/\epsilon$) is susceptible to large errors, ϵ was determined independently by dissolving known amounts of **4** in DMSO and in DMSO–methanol mixtures and measuring the zero-time absorbances (using the appropriate blank solutions) at 490 mμ. A value of $\epsilon_{490\ m\mu} = (1.8 \pm 0.1) \times 10^4\ cm^{-1}\ mol^{-1}$ represents the mean of five independent measurements and was used in conjunction with eq 3 to obtain the *K* values in methanol and in methanolic DMSO (Table I).

Since the concentration of **3** is considerably smaller than that of $NaOCH_3$, good pseudo-first-order plots were obtained for the rate of absorbance decrease due to the decay of **4**. Figure 2 illustrates such first-order plots together with that observed when solid **4** was dissolved in methanolic sodium methoxide. The good agreement between k_{obsd} for absorbance decay for the *in situ* generated complex (line A) with that of the decay of solid **4** in the same concentration of methoxide ion (line B) is self-evident. The observed pseudo-first-order rate constant k_{obsd} represents a change in the concentration of **4**.

$$k_{obsd} = -\frac{d(\ln[4])}{dt} \quad (4)$$

The formation of products in eq 1 can be defined by

$$\frac{d([product])}{dt} = k_3[4] \quad (5)$$

and also by eq 6, if **3** and **4** are rapidly interconvertible.

$$\frac{d([products])}{dt} = \frac{d([3 + 4])}{dt} \quad (6)$$

Combination of eq 2, 4, 5, and 6 leads to

$$k_{obsd} = \frac{Kk_3[OCH_3^-]}{1 + K[OCH_3^-]} \quad (7)$$

and rearrangement of eq 7 gives

$$\frac{[OCH_3^-]}{k_{obsd}} = \frac{1}{Kk_3} + \frac{[OCH_3^-]}{k_3} \quad (8)$$

which suggests that plots of $[OCH_3^-]/k_{obsd}$ *vs.* $[OCH_3^-]$ should give straight lines whose slopes are $1/k_3$ and whose intercepts are $1/Kk_3$. Figure 3 illustrates such plots of eq 8 for reaction 1 in methanol and methanolic dimethyl sulfoxide solutions containing, respectively, 1.41 and 2.82 *M* DMSO in methanol. Values for *K* and k_3 are given in Table I. Considering the uncertainties involved in obtaining the equilibrium constants from eq 3 and 8, the agreement between the two sets of independently obtained values is considered to be good (Table I).

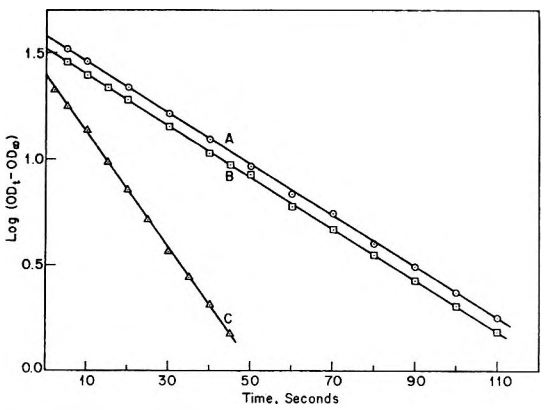


Figure 2.—Plots of log ($OD_t - OD_\infty$) against time for the fading of **4** at 25.00°. (A) [**3**] = 2.81×10^{-4} *M*, [$NaOCH_3$] = 5.25×10^{-2} *M*, solvent = MeOH. (B) Solid **4** dissolved in 5.25×10^{-2} *M* methanolic sodium methoxide. (C) [**3**] = 4.0×10^{-5} *M*, [$NaOCH_3$] = 0.187 *M*, solvent = MeOH–DMSO, 10:90 (v/v).

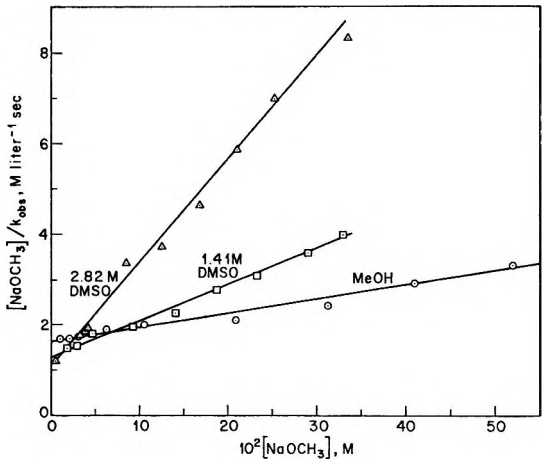


Figure 3.—Plots of [$NaOCH_3$], M/k_{obsd} against [$NaOCH_3$], *M*, in MeOH and in 1.42 *M* and 2.84 *M* DMSO in MeOH.

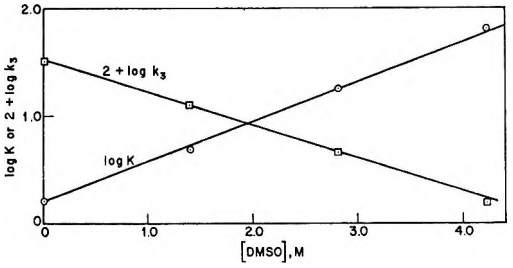


Figure 4.—Plot of log *K* and 2 + log k_3 against [DMSO], *M*.

Solid **4** decomposed instantaneously in methanol and all attempts to follow the kinetics for this process have failed. Good linear relationships between log *K* and log k_3 *vs.* [DMSO], *M*, are illustrated in Figure 4.

Anion radicals were formed from **3** in several base–solvent systems. In each case the esr spectrum could be observed 3 min after mixing and was generally found to increase slowly in intensity for a period of between 30 and 90 min before decaying. A summary of the conditions leading to the production of radicals, their estimated concentrations, and the hyperfine coupling constants of their esr spectra are given in Table II. Additional lines of weaker intensity were observed in the spectra from systems A, B, and C, and in B the coupling constants for this second species were deduced and are also given in Table II.

TABLE II

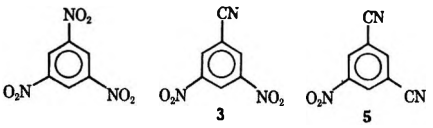
ESR PARAMETERS FOR RADICAL ANIONS DERIVED FROM 3 AND ALKOXIDE IONS[a]

System	[3], M	[Alkoxide], M	Solvent	Coupling constants, G			
A	0.085	2.5[b]	MeOH	$a_N^{NO_2} = 9.76$	$a_H(2) = 4.13$	$a_H = 3.36$	
B	0.085	2.5[b]	75% MeOH–25% DMSO[e]	$a_N^{NO_2} = 9.12$	$a_H(2) = 4.24$	$a_H = 3.31$	
				$a_N^{NO_2} = 10.92$[f]	$a_H(2) = 3.75$[f]	$a_H = 3.06$[f]	
C	0.024	0.094[c]	20% MeOH–80% DMSO[e]	$a_N^{NO_2} = 9.62$	$a_H(2) = 3.84$	$a_H = 2.98$	
D	0.042	0.027[d]	*tert*-BuOH	$a_N^{NO_2} = 9.71$	$a_H(2) = 3.43$	$a_H = 4.71$	
E	0.041	0.029[d]	20% *tert*-BuOH–80% DMF[e]	$a_N^{NO_2}(2) = 3.41$	$a_H(2) = 3.43$	$a_H = 4.74$	$a_N^{CN} < 0.3$
	0.005	Electrochemical[g] reduction	DMF	$a_N^{NO_2}(2) = 3.00$	$a_H(2) = 2.84$	$a_H = 5.00$	$a_N^{CN} < 0.3$

[a] The concentration of paramagnetic species in all cases was estimated to be (2.0–4.0) × 10^{-4} M. [b] CH_3OK. [c] CH_3ONa. [d] *tert*-BuOK. [e] Volume per cent. [f] Secondary species. [g] Taken from ref 36.

TABLE III

PMR SPECTRA OF 1,3,5-TRINITRO-, CYANODINITRO-, AND DICYANONITROBENZENES AND THEIR METHOXYL COMPLEXES[a]



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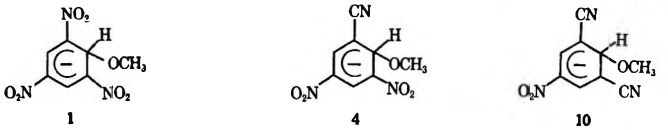

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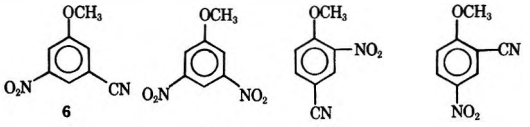
τ_2	0.80	0.84	1.14	3.86,[b] 3.78,[c] 3.88[d]	4.40	
	0.79[b]			(4.05)	(4.53) (4.6, broad)[e]	(5.74)
τ_4	0.80	0.92	1.29	1.58,[b,d] 1.48[c]	1.52	
	0.79[b]			(1.72)	(1.72) (1.92)[e]	(3.13)
τ_6	0.80	0.84	1.14	1.58,[b,d] 1.48[c]	2.23	
	0.79[b]			(1.72)	(2.41) (2.65)[e]	(3.13)
τOCH_3				6.90,[b] 6.78[d]	6.92	
				(6.88)	(6.95)	(7.20)
J_{24}		1.8	1.5	~1,[c] 1.5[f]	1.2	
				(1.2)	(1.2) (2)[e]	
J_{46}					2.2	
					(2.2	

[a] Values in parentheses have been obtained from formation of the complex *in situ* by the dropwise addition of 5.73 M potassium methoxide in methanol to a solution of the parent substituted benzene in DMSO-d_6. [b] Values taken from ref 6. [c] Values taken from R. Foster and C. A. Fyfe, *Tetrahedron*, 21, 3363 (1965). [d] Values taken from K. L. Servis, *J. Amer. Chem. Soc.*, 89, 1508 (1967). [e] Values taken from ref 9. [f] Values taken from M. R. Crampton in ref 2.

Pmr parameters for 1,3,5-trinitrobenzene, **3**, **5**, and their methoxyl complexes in DMSO-d_6 solutions are given in Table III and those for the decomposition product (**6**) of **4** and certain reference compounds in dioxane are collected in Table IV.

TABLE IV

PMR SPECTRA OF DINITRO- AND CYANONITROANISOLES IN DIOXANE[a]



6

τ_2	2.57	1.93		
τ_3			1.71	1.39
τ_4	2.40	1.47		
τ_5			2.12	1.56
τ_6	2.55	1.93	2.72	2.77
J_{24}	1.91	2.0		
J_{26}	2.37			
J_{35}			2.1	2.8
J_{56}			8.9	9.3
J_{36}				0.5
J_{46}	1.84			

[a] The spectrum of 6 was recorded at 100 MHz; other spectra were recorded at 60 MHz.

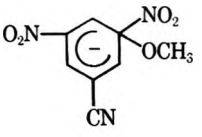
Discussion

The interaction of methoxide ions with 3,5-dinitrobenzonitrile (**3**) resembles, at least qualitatively, the formation of the methoxyl complex (**7**) of 2-cyano-4,6-dinitroanisole. Both complexes **4** and **7** have a shorter (380 mμ for **7**,[8] 390 mμ for **4**) and a longer (470 mμ for **7**,[8] 490 mμ for **4**) wavelength absorption maximum which is absent in their parent aromatic compounds. The structures of the isolated complexes **4** and **7** are also similar in that they both involve sp^2–sp^3 rehybridization of the carbon atom at the point of attack with respect to their parent aromatic compounds. Considerable quantitative differences exist, however, between the rates and equilibrium constants for the formation of complexes **4** and **7**. The attainment of the equilibrium for **7** was measurable and allowed the calculation of the equilibrium constant. Its value in methanol at 25.00° was found to be 2600 l. mol^{-1},[8] a value more than three orders of magnitude greater than that obtained for **4**. The instantaneous formation of **4** implies that k_1 for this process is considerably faster than that for the formation of **7**. Essentially similar kinetic behavior has been observed in the interaction of 1,3,5-trinitrobenzene with methanolic sodium methoxide.[7] The equilibrium constant for the formation of **1** in methanol has been reported to be 15.4 l. mol^{-1},[7] a value also three orders of magnitude smaller than that for the formation of 1,1-dimethoxy-2,4,6-trinitrocyclohexadienylide ion (**2**).[8] It is reassuring to observe that replacing an *o*-nitro group by a cyano group in trinitrobenzene causes an almost identical decrease in the equilibrium constant for complex formation as that ob-

served in comparing K_2 with K_7 (K_1/K_4 = 9.6 and K_2/K_7 = 6.6). The differences between the stabilities of trinitro and cyanodinitro Meisenheimer complexes reflect, of course, the smaller electron-withdrawing power of the cyano group.

The greater stability of the 1,1-dimethoxycyclohexadienylides (2 and 7) over the 1-methoxycyclohexadienylides (1 and 4) is largely explicable in terms of steric considerations. The methoxyl group in both 2,4,6-trinitroanisole and 2-cyano-4,6-dinitroanisole is sterically compressed by the neighboring nitro and cyano groups. The formation of the methoxyl complexes of these anisoles (2 and 5) results in structures in which both methoxyl groups lie out of the plane of the aromatic ring,[19-21] thereby relieving the crowding present in the parent ethers. No comparable steric compression exists for either 3,5-dinitrobenzonitrile (3) or 3-cyano-5-nitrobenzonitrile (5).

The formation of 3-cyano-5-nitroanisole (6) from solutions containing 4 must involve a species such as 8 either as a short-lived intermediate or as a transition state. A structure similar to 8 has been considered in



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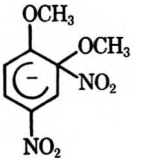
the interaction of methoxide ion with 1,3,5-trinitrobenzene[7] and with *N-tert*-butyl-2,4,6-trinitrobenzamide.[22] The lifetimes of 4 and 8 depend on the magnitude of the equilibrium constants for their formation (k_1/k_2 and K for 4 $\rightleftharpoons$ 8). In this sense either 4 or 8 or both can be transition states or intermediates of finite stability. The isolation of complexes on a preparative scale does not constitute an unambiguous proof that the same complexes are intermediates in the kinetic solutions involving generally 10^{-4}–10^{-5} M substrates. Proof for intermediates must be substantiated by obtaining thermodynamic parameters for the rates and hence for the equilibrium constants for their formation. We have provided such measurements and coupled them with structural analysis of the isolated complexes for several aromatic ethers.[8,23] The instantaneous formation of 4 did not allow, under our experimental conditions, meaningful kinetic determinations of the free energies of activation for its formation and decomposition. In spite of our isolation of solid 4 (under preparative conditions) we cannot, therefore, ascertain 4 to be an intermediate in reaction 1. Indeed, it is more likely that the product is formed *via* path A (rather than *via* path B as indicated in eq 1) through 8 as a transition state or as an intermediate which is undetectable under our experimental conditions. If 3 and methoxide ion are in rapid equilibrium with 4, as in the present case, formation of the product *via* path A is kinetically indistinguishable from that *via* path B.[24] It is apparent from our investigations[8,23] that the electron-withdrawing power of the substituents on the parent aromatic compounds, specific ground- and transition-state steric and solvation requirements, and the nucleophilic and basic strength of the attacking alkoxide ion all influence these equilibria. The stability of the 1,1-dimethoxy-2,4,6-trinitrocyclohexadienylide (2) is so great (K = 17,000 l. mol^{-1})[8] that any subsequent rearrangement of it is extremely unlikely. On the other hand, the instability of 1,1-dimethoxy-2,4-dinitrocyclohexadienylide (K = 2.5 × 10^{-5} l. mol^{-1})[25] allowed us to study its rearrangement, by pmr spectroscopy, to a relatively more stable 1,2-dimethoxy-2,4-dinitrocyclohexadienylide (9).[26]



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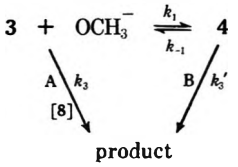
Since the stability of 4 (K = 1.6 l. mol^{-1}) is several orders of magnitude greater than that of 1,1-dimethoxy-2,4-dinitrocyclohexadienylide, one would expect its decomposition involving 8 to be extremely rapid. This is indeed the case, since all our attempts to follow the rates of this process in dilute solution have been unsuccessful.

It has been demonstrated previously that dipolar aprotic solvents enhance the stability of Meisenheimer complexes,[1,9,27] and we had hoped that a DMSO-rich methanolic solvent system might stabilize 4 to such an extent that the rate for its equilibrium attainment could be determined. Although the equilibrium constant for the formation of 4 was found to be some 40 times greater in 4.23 M DMSO (DMSO:MeOH = 30:70, v/v) than in pure methanol (Table I), its rate of equilibrium attainment was still unmeasurably fast by our technique. The increase in the equilibrium constant for the formation of the methoxyl complex of 2,4-dicyano-6-nitroanisole with increasing DMSO concentration was demonstrated to be a composite effect of an increase in k_1 and a decrease in k_2.[9] It is likely that the increase in K_4 with increasing DMSO concentration is also a composite effect and originates from changes in the activity coefficients of the reactants and of the transition states as a function of solvent composition.[9,28] In view of the numerous parameters involved in the solvent effects,[28,29] undue mechanistic significance cannot be attributed to the obtained linear correlation be-



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(28) J. H. Fendler and J. W. Larsen, *J. Org. Chem.*, in press.

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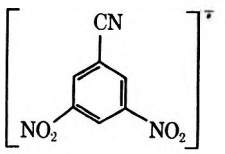
tween the logarithm of the rate and equilibrium constants for **4** and the molar DMSO concentration (Figure 4).

Pmr spectroscopy has been utilized both to establish the structures of the methoxyl complexes of **3** and **5** and their decomposition products and to detect any relatively long-lived transients involved in complex formation or decomposition. The pmr parameters for the isolated and *in situ* generated complexes (**1** and **4**) and their parent aromatics (1,3,5-trinitrobenzene and **3**) as well as for 1-methoxy-2,6-dicyano-4-nitrocyclohexadienylide (**10**) and its parent aromatic (**5**) are summarized in Table III. The spectra (*i.e.*, the chemical shift, multiplicities, coupling constants, and relative intensities) of both the *in situ* generated and isolated **4** are completely consistent with the postulated structures and the parameters are in good accord with those reported by Foreman and Foster[10] (Table III) considering the "water impurity" and the absence of methanol in their medium.[30,31] In addition, the chemical shifts and the absence of discernible coupling constants in the spectra obtained from the *in situ* reaction of **5** with methanolic potassium methoxide (Table III) are consistent with the postulated structure of the complex,[33] *i.e.*, **10**. These spectra unambiguously eliminate, particularly through the upfield shift for H-2, alternative formulations, *e.g.*, **8**, for complexes **4** and **10**. The pmr criteria for the structures have been discussed and reviewed[34] extensively elsewhere and will not be reiterated here. The chemical shifts and coupling constants observed for **4** are unremarkable, with the exception of the coupling of the methine proton, H-2, to H-4 (J_{24} = 1.2 Hz) but not to H-6 ($J_{24} < 0.4$ Hz). We have observed similar behavior in the case of the 1,3-dimethoxy-4-cyano-2,6-dinitro- and 2-cyano-4,6-dinitrocyclohexadienylides for which the methine proton ortho to a cyano and a nitro group is coupled to a meta aromatic proton ortho to two nitro groups but not to that ortho to a cyano and a nitro group.[8] These observations are also consistent with the postulated structure for the methoxyl complex of **5** (**10**) since coupling of the methine proton to H-4,6 is undiscernible.

The pmr parameters in dioxane solution for 3-cyano-5-nitroanisole (**6**) obtained from the decomposition of **4** and dinitro- and cyanonitroanisoles are given in Table IV. A tightly coupled ABC spectrum was observed for **6** at both 60 and 100 MHz, but a satisfactory fit of the observed transitions was obtained by an interative program.[15] The calculated coupling constants are of the expected order for meta J_{HH}. However, the marked shielding of all three ring protons relative to the shifts observed for 3,5-dinitroanisole (Table IV), and the accidental equivalence of τ_2 and τ_6 were unexpected. Presumably, the shielding effect is a reflection of the replacement of a nitro by a less strongly electron-withdrawing cyano group. This effect is apparent in other cyanonitroanisoles, but is most marked in the case of **6**. Similar accidental chemical shift equivalences for ring protons have been observed in other cyanonitroanisoles, *e.g.*, 2-cyano-4,6-dinitroanisole.[8,35]

A linear relationship between the chemical shifts of the H-3,5 protons of the complex in DMSO-d_6 and the equilibrium constant, K, for its formation in methanol has been found for **1**, **4**, the cyano complex of 1,3,5-trinitrobenzene, and the methoxyl complex of *N-tert*-butyl-2,4,6-trinitrobenzamide. An analogous relationship has been observed for the isomeric 2,4,6-substituted nitro- and cyanoanisoles.[1] Indeed, the sensitivity of the equilibrium constants to the chemical shifts (or vice versa) appears to be identical within experimental error. By extrapolation from this relationship an equilibrium constant for the formation of **10** of 1.4×10^{-3} l. mol^{-1} has been estimated. This value can only be considered to be accurate within an order of magnitude; however, the ratio of the equilibrium constants for the dicyanonitroanisoles to this value obtained for **10** is the same order of magnitude as the corresponding ratios for **1** and **4** ($K_2/K_1 \sim K_7/K_4 \sim 10^3$).

Paramagnetic species have been observed in the interaction of alkoxide ions with solutions of **3** in several solvent systems (Table II). The esr spectrum from system E, consisting of 27 lines, analyzes for two equivalent nitrogens, two equivalent protons, and a third proton (Figure 5), and is attributed to the 3,5-dinitrobenzonitrile radical anion (**11**). The similarity of the



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observed splitting constants to those of **11** produced by electrolysis of **3** in DMF[36] (Table II) allows the following assignments: $A_3^N = A_5^N = 3.41$, $A_2^H = A_6^H = 3.43$, $A_4^H = 4.74$. The larger value of $A_{NO_2}^N$ found in this work is due to the *tert*-BuOH cosolvent. Differential solvation of the nitro group has been shown to alter its spin density and hence $A_{NO_2}^N$.[36]

The esr spectra generated in A, B, C, and D show only one nitrogen hyperfine interaction. The radical anions of *m*-dinitrobenzene,[37-39] 2,6-dinitrotoluene,[40] and 3,5-dinitroanisole also give spectra of this type. However, high-resolution studies of the *m*-dinitroben-

(30) These authors observed, in addition to the methoxyl complex **4**, a species in "smaller abundance" (τ_2 = 4.5, τ_4 = 1.79, and τ_6 = 2.48 ppm), assigned as the hydroxyl complex, in the *in situ* reaction of **3** in DMSO with solid sodium methoxide. We, therefore, examined the pmr parameters for the *in situ* reaction of 5.00 *M* potassium hydroxide with **3** in DMSO-d_6. The parameters obtained for the hydroxyl complex (τ_2 = 4.52, τ_4 = 1.73, τ_6 = 2.48 ppm; $J_{24} < 0.5$ Hz, and J_{46} = 2.2 Hz) confirm the structure of this species.

(31) Subsequent to submission of this manuscript, Terrier and coworkers[32] reported the observation of **4** in 100-MHz pmr spectra obtained by the addition of potassium methoxide to a solution of **3** in DMSO-d_6. Resonances for a species in 5% abundance also were observed and were ascribed to the methoxyl complex resulting from attack of methoxide ion at the 4 position of **3**.

(32) F. Terrier, F. Millot, and M.-P Simonnin, *Tetrahedron Lett.*, 2933 (1971).

(33) In this case, however, coincidence of the resonance frequencies for the H-3 and H-5 protons of 1-methoxy-2,4-dicyano-6-nitrocyclohexadienylide would result in a similar spectrum.

(34) See ref 1 and 2 and references cited therein.

(35) In order to provide an unambiguous assignment of the structure of **6**, the compound was reduced with lithium aluminum hydride and converted *via* diazotization to 3-hydroxy-5-methoxybenzyl alcohol (i). Methylation of i gave 3,5-dimethoxybenzyl alcohol (ii). Pmr spectra provided an unambiguous demonstration of the 1,3,5 relationship of the substituents in i and ii. These data, coupled with the mass spectrum of **6** (appropriate M peak), conclusively establish the structure of **6**.

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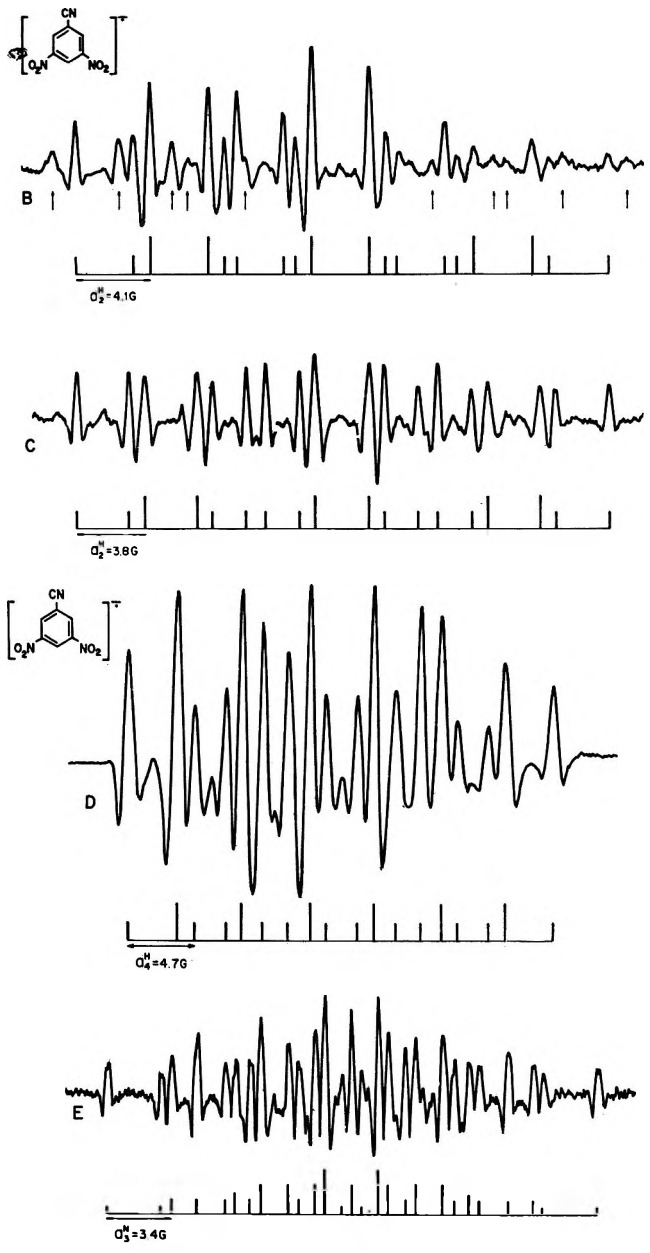

Figure 5.—Esr spectra of radical anions derived from **3** and alkoxide ions in systems B, C, D, and E.

zene radical anion, prepared by alkali metal reduction in ethanol, suggested the presence of a very small interaction with the second nitrogen.[41] The large difference between A_3^N and A_5^N was ascribed to a strong ion-pair type of interaction between one of the nitro groups and an alkali metal cation. Freed and Fraenkel have proposed a more general explanation of these one-nitrogen spectra in terms of an alternating line-width effect.[42] The spectrum from two equivalent nitrogen nuclei consists of five lines with intensities in the ratio 1:2:3:2:1 corresponding to M_N = 2, 1, 0, −1, −2, where M_N is the sum of the Z components of the spin angular momenta of the two nuclei. Any time-dependent process which results in a momentary inequality of the two nitrogen couplings can lead to broadening of the lines corresponding to $M_N = \pm 1$ and two components of the line corresponding to $M_N = 0$. In the limit, these lines would no longer be observed, leaving the lines corresponding to $M_N = \pm 2$ and 0 of equal intensity. Freed and Fraenkel regard their model as providing a basis for representing Ward's long-lived anion radical–alkali metal complex. The spectra due to **11** formed in systems A, B, C, and D which show only one nitrogen hyperfine splitting are considered to be examples of this type.[42] They show pronounced line-width variations, the high field lines being wider than those at low field. This is due to anisotropic g tensor and dipolar interactions resulting from the very viscous solvent. This phenomenon has been observed previously in nitro-substituted aromatic radical anions.[42,43]

The observed esr spectra in systems A, B, C, and D could alternatively represent 3-cyano-5-nitrophenol or 3-cyano-5-nitroanisole radical anions produced by nucleophilic replacement of the nitro group by alkoxyl or hydroxyl groups. The significant differences in coupling constants between the methoxyl- and hydroxyl-[44] substituted nitroarenes and those of **11** (Table II), however, renders this interpretation unlikely. The second radical species detected in these systems may indicate the presence of radicals formed from the "solvolysis" of **3** or possibly from other species present in reaction 1.

Absence of free radicals in solutions of 1,3,5-trinitrobenzene or 2,4,6-trinitroanisole in methanolic sodium methoxide or in ethanolic sodium ethoxide[7] reflects the greater stability of Meisenheimer complexes **1** and **2** as compared to **4**. Since the estimated concentration of the paramagnetic species in reaction 1 is less than 1% of that of **3**, radical processes constitute only a minor part of the overall reaction. The inherent complexity of the system[2,17] does not allow a distinction among the alkoxide ion, the methylsulfinyl carbanion (present in the DMSO–BuO$^-$K$^+$–*tert*-BuOH system), or **4** as the possible electron donor. Indeed all of these species can concurrently or consecutively transfer their charges to **3**. The fact that the radical concentration increases as a function of time and that identical radicals were observed in the *in situ* generation of **4** and in the decomposition of solid **4** in methanolic sodium methoxide solutions tend to suggest that **4** is, at least partially, involved in the radical formation.

Registry No.—**1**, 12244-65-4; **3**, 4110-35-4; **4**, 29661-06-1; **5**, 33224-18-9; **6**, 33224-19-0; **10**, 33293-81-1; sodium methoxide, 124-41-4; methanol, 67-56-1; DMSO, 67-68-5; potassium methoxide, 865-33-8; *tert*-BuOK, 865-47-4; 3,5-dinitroanisole, 5327-44-6; 4-cyano-2-nitroanisole, 33224-23-6; 2-cyano-4-nitroanisole, 10496-75-0.

(41) R. L. Ward, *J. Chem. Phys.*, **36**, 1405 (1962).
(42) G. H. Freed and G. K. Fraenkel, *ibid.*, **41**, 699 (1964).
(43) G. H. Freed and G. K. Fraenkel, *ibid.*, **40**, 1815 (1964).
(44) L. H. Pietter, P. Ludwig, and R. N. Adams, *J. Amer. Chem. Soc.*, **84**, 4212 (1962).

Ring Size Effects in the Neophyl Rearrangement. VIII. The Synthesis and Solvolysis of 1-Methyl-2,3-benzocycloalkenylcarbinyl Tosylates[1,2]

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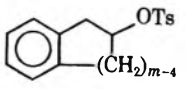
1-Methyl-2,3-benzocycloalkenylcarbinyl tosylates **5** were synthesized and their solvolytic reactivity was determined. Neither in acetolysis nor in hydrolysis in 60% acetone was a ring size effect of any significance evidenced. The reactivities mirrored those of the unmethylated analogs **3**. Products from **5** were totally rearranged *via* aryl ring migration indicating that aryl participation was essentially the only solvolysis pathway. The opposing factors in **3** of strain in the phenonium ion intermediate *vs.* conformational effects are discussed together with a reactant strain effect in **5**. The conclusion is drawn that the three effects are balanced to produce the similarity in behavior between the two sets of tosylates.

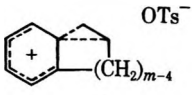
Some years ago Huisgen and coworkers[4] observed that the formolysis of tosylates **1** exhibited a ring size effect, as indicated in 1. Inspection of molecular



1

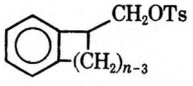
m (ring size)	6	7	8	9	(1)
$10^5 k_1$ (35°, sec^{-1})	27.3	152	2250	741	

models suggested that this rate effect was caused by strain energy differences existing in the phenonium ion intermediates **2** produced in the reaction, with maximum stability being accorded **2**, $m = 8$. The



2

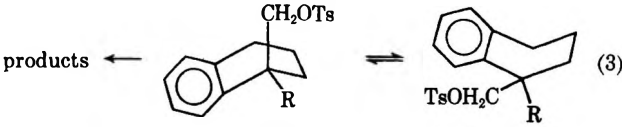
formolysis of tosylates **3**, which utilize the same phenonium ion intermediates, failed to exhibit as pronounced an effect, however (2), with the tetralyl analog (**3**,



3

n (ring size)	5	6	7	8	(2)
$10^5 k_1$ (35°, sec^{-1})	2.51	6.80	1.80	0.180	

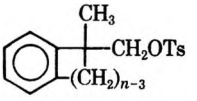
$n = 6$) exhibiting a weakly maximum reactivity.[5] To account for this decreased spread in reactivity, Huisgen and coworkers proposed that two counteracting effects were operative with **3**, the *strain effect* in **2** which increased reactivity with increasing ring size (at least to a point) and a *conformational effect* which decreased reactivity similarly. For example, with **3**, $n = 6$, only axial conformer **4a** (R = H) in eq 3 is sterically able to form **2** ($m = 7$) *via* phenyl participation. From relative rate comparisons, a "conformational hindrance effect" was calculated for **3**, with decelerating rate factors of 0, 2, 115, and 380 fold for $n = 5$, 6, 7, and 8,



4a, R = H, CH$_3$ **4e**, R = H, CH$_3$ (3)

respectively. These factors measured the decreased ability to achieve the proper axial conformation for formolysis with phenyl participation as the ring size increased. The two effects mentioned apparently were in best balance for reactivity for the tetralyl compound. The effects understandably became less important in acetolysis and ethanolysis where phenyl participation is not so strongly evident.

Because of our interest in conformational effects in the neophyl rearrangement[6] we decided to study the related neophyllike tosylates **5**. Both a poorly ion-

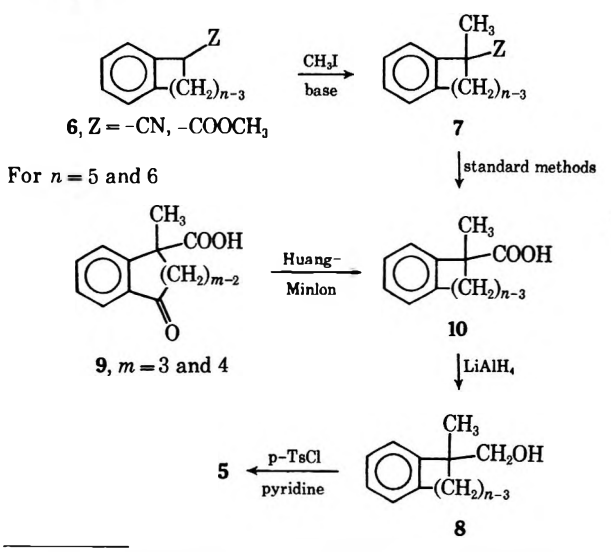


5

$n = 4, 5, 6, 7$

izing medium, acetic acid ($Y^7 = -1.65$), and a better one, 60% acetone–40% water ($Y^7 = +0.796$), were chosen as solvents for the study.

The tosylate syntheses were straightforward and warrant little discussion. Two general routes (4) were



(4)

(1) Paper VII: J. W. Wilt, L. L. Maravetz, and J. F. Zawadzki, *J. Org. Chem.*, **31**, 3018 (1966).

(2) Taken from portions of the dissertation of W. W. P., Jr., Loyola University of Chicago, 1970, and the M.S. thesis of J. J. W., Loyola University of Chicago, 1966.

(3) National Science Foundation Trainee, 1968–1969.

(4) R. Huisgen, E. Rauenbusch, G. Seidl, and I. Wimmer, *Justus Liebigs Ann. Chem.*, **671**, 41 (1954). See also R. Huisgen and G. Seidl, *Chem. Ber.*, **96**, 2730 (1963).

(5) R. Huisgen, G. Seidl, and I. Wimmer, *Tetrahedron*, **20**, 623 (1964).

(6) J. W. Wilt and D. D. Roberts, *J. Org. Chem.*, **27**, 3434 (1962).

(7) A. H. Fainberg and S. Winstein, *J. Amer. Chem. Soc.*, **78**, 2770 (1956).

TABLE I

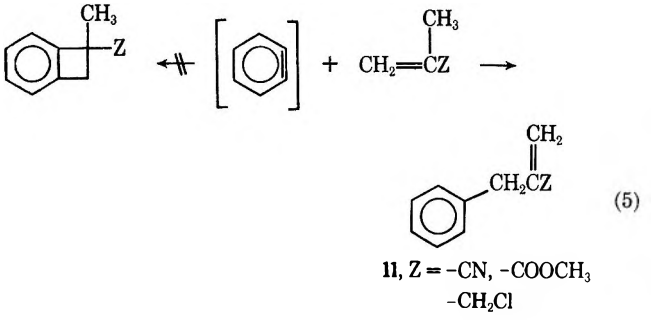
TITRIMETRIC RATE DATA

Tosylate 5, n	Temp, °C	$10^5 k_1$, sec^{-1} (HOAc[a])	$10^5 k_1$, sec^{-1} (Me_2CO–H_2O[b])
4	(25.0)	(0.128)[c]	(0.390)
	44.9	1.64 ± 0.01[d]	4.06 ± 0.08
	44.9	1.34 ± 0.06[e]	
	55.0		10.2 ± 0.31
	64.7	13.7 ± 0.20	26.0 ± 0.20
	76.8	50.1 ± 0.9	99.8 ± 0.30
	81.8	89.1 ± 0.9	
5	(25.0)	(0.034)	(0.128)
	44.9	0.601 ± 0.06	1.58 ± 0.11
	44.9	0.509 ± 0.02[e]	
	56.5		5.11 ± 0.32
	64.7	6.93 ± 0.14	12.10 ± 0.12
	76.8	24.6 ± 0.20	43.1 ± 0.60
	81.8	44.5 ± 0.30	
6	(25.0)	(0.059)	(0.157)
	44.9	0.873 ± 0.02	2.04 ± 0.02
	44.9	0.678 ± 0.02[e]	
	55.1		5.25 ± 0.12
	64.7	9.40 ± 0.32	15.6 ± 0.50
	76.8	25.7 ± 0.80	53.8 ± 0.70
	81.8	58.7 ± 0.24	
7	(25.0)	(0.036)	(0.999)
	56.5		4.63 ± 0.09
	64.7	6.47 ± 0.10	10.63 ± 0.26
	76.8	23.1 ± 0.40	35.5 ± 0.70
	81.8	40.7 ± 0.50	

[a] Redistilled glacial acid, containing 0.3% acetic acid anhydride and sodium acetate (0.050 *M* for 0.025 *M* tosylate). [b] Acetone distilled from potassium permanganate and distilled water (60:40, v/v) with 2,6-lutidine present (0.035 *M* for 0.030 *M* tosylate). [c] All values in parenthesis were extrapolated from data at other temperatures. [d] Errors are average deviations from the mean rate constant. [e] Initial rate constants when sodium acetate was absent.

used and the details may be found in the Experimental Section.

As a note of passing interest, attempts to obtain **5**, $n = 4$, *via* cycloaddition instead gave "ene" products at the initial stage (eq 5).



(5)

11, Z = -CN, -$COOCH_3$, -CH_2Cl

Table I contains the titrimetric rate data obtained for these tosylates and Table II lists the activation parameters.

Determination of products indicated complete ring expansion by aromatic ring migration in every case. The products are summarized in Table III.

The quantitative formation of ring-expanded products in both solvents indicates that very likely $k_\Delta \gg k_s$ in these systems. Such was not the case for **3** in 70% dioxane–water (Y[7] = +0.013). Huisgen and Seidl reported[8] considerable nucleophilic solvolysis to unrearranged product (11–26%), increasing as base was

(8) R. Huisgen and G. Seidl, *Chem. Ber.*, **96**, 2740 (1963).

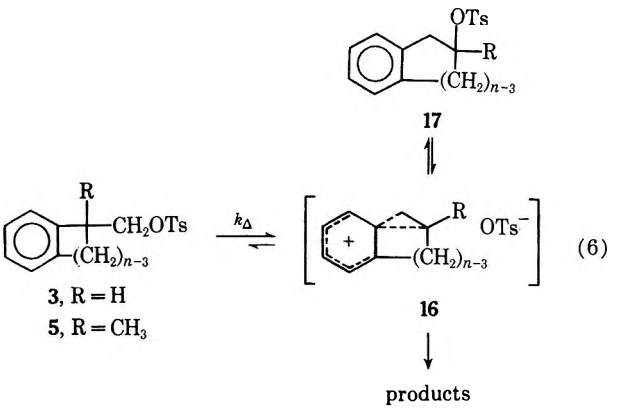
TABLE II

ACTIVATION PARAMETERS[a]

Tosylate 5, n	ΔH^*, kcal mol^{-1}	ΔS^*, eu
	Acetolysis	
4	23.5 ± 0.1	−6.6 ± 0.3
5	25.0 ± 0.1	−3.9 ± 0.4
6	24.8 ± 0.3	−3.7 ± 0.9
7	25.4 ± 0.3	−2.8 ± 0.8
	Hydrolysis	
4	21.4 ± 0.2	−11.6 ± 0.7
5	22.8 ± 0.2	−8.9 ± 0.5
6	22.7 ± 0.3	−8.8 ± 0.7
7	22.9 ± 0.3	−9.0 ± 0.9

[a] Calculated from an Eyring equation plot of log k_1/T *vs.* $1/T$.

added to the solvent. Moreover, acetolyses of the tosylates **5** showed good first-order kinetics throughout, unlike **3** (n = 5, 6)[5] which showed initial nonlinear kinetic behavior due to ion pair return with rearrangement. It is likely in our cases that the sequence shown in eq 6 (R = CH_3) occurs. From steric and reactivity



(6)

3, R = H
5, R = CH_3

12 from capture by solvent

13–15 from proton elimination

considerations, ion pair return from **16** (R = CH_3) either back to inital reactant **5** or to rearranged **17** would be less probable than such return from **16** (R = H). Because ion pair return (mostly to **17**, R = H) complicated Huisgen's acetolysis data,[5] it is unwise for us to compare the ratio of acetolysis rates of **3** and **5** for each value of n. Succinctly, our rates for **5** are very probably determined by k_Δ alone,[9] whereas Huisgen's rates for **3** reflect k_Δ very likely complicated by rates of rearrangement to **17**, R = H instead. Nonetheless, the *relative* rates in each series may be more meaningful because differences in k_Δ are undoubtedly involved in the trends observed.

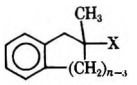
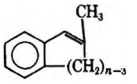
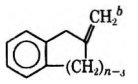
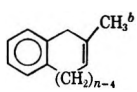
A comparison of relative formolysis rates for **3** and relative hydrolysis rates for **5** would seem even less faulty. Formolysis of **3** was smoothly first order and essentially totally limiting in nature,[5] and ring-expanded products formed over 90% of the products.[8] Such also was found in this study for the hydrolysis of **5**. The solvents each possess a $+Y$ value, though no claim is made for any other similarity. Nevertheless,

(9) Product formation *via* total rearrangement by aromatic ring migration, the lack of nonlinear kinetic behavior,[5] and analogy to neophyl tosylate itself (which is governed totally by k_Δ in solvolysis[10]) all point to the equality of the titrimetric rate constant k_1 with k_Δ in **5**.

(10) *Cf.* A. Diaz, I. Lazdins, and S. Winstein, *J. Amer. Chem. Soc.*, **90**, 6546 (1968).

TABLE III

PRODUCTS OF SOLVOLYSIS[a]

Tosylate 5, n	 12	 13	 14	 15
		Acetolysis		
4	15 (X = OAc)	74	11	
5	9	52	6	33
6	32	26	21	21
7	92	Trace	Trace	Trace
		Hydrolysis		
4	26 (X = OH)	61	13	
5	89	———	11[c] ———	
6	85	10	2	3
7	96	Trace	Trace	Trace

[a] The yields of products were essentially quantitative. [b] From nmr and glpc analyses only. Hydrogenation of the total olefins led to 2-methylbenzocyclenes only. [c] Obtained as 2-methylnaphthalene, presumably *via* air oxidation of the hydroaromatic olefinic products.

TABLE IV

RELATIVE RATES

Tosylate	Solvent	Temp, °C	k_{rel}, ring size 4	5	6	7
1[a]	HCOOH	35			1.0	5.6
3	HCOOH[b]	35[c]		1.0	2.7	0.7
		70		1.0	3.4	1.1
	70% Dioxane[b]	70			3.0	1.0
	60% Acetone[d,e]	82	1.4	1.0	2.9	0.67
	HOAc	70[b]		1.0	2.4	0.95
		82[d,e]	0.9	1.0	1.7	1.1
5	60% Acetone[d]	35[f]	2.6	1.0	1.2	0.81
		70[f]	2.0	1.0	1.2	0.82
		77	2.3	1.0	1.3	0.82
	HOAc[d]	35[f]	3.0	1.0	1.5	0.90
		70[f]	2.3	1.0	1.5	0.97
		82	2.0	1.0	1.3	0.91

[a] Reference 4. For ring size 8 and 9, k_{rel} = 82 and 27, respectively. [b] Reference 5. [c] For ring size 8, k_{rel} = 0.07. [d] This work. [e] The preparation of these tosylates was achieved as reported for n = 5–7[8] and n = 4 [M. R. Cava and M. J. Mitchell, *J. Org. Chem.*, 27, 631 (1962); J. A. Skorcz and J. E. Robertson, *J. Med. Chem.*, 8, 255 (1965)]. The details of these solvolyses may be found in the dissertation of W. W. P., Jr. [f] Calculated from data in Table II.

in such solvents the process in question should be essentially determined by k_Δ and one could examine the rates to look for "conformational hindrance effects" on k_Δ. These rate comparisons made from literature data and the results of the present study are collected in Table IV.

One sees immediately that the reduced spread in reactivity with the partial rate order of ring size = 6 > 7 was maintained in **5** comparably to **3**, regardless of the variety of solvents and temperatures listed. This is unexpected because the 1-methyl substituent should render axial and equatorial conformers in the six- and seven-membered ring cases more equivalent, *e.g.*, **4a** and **4e** (R = CH_3) in 3, and essentially cancel Huisgen and coworkers' conformational effect,[5] allowing a relative rate series more like that of 1 where the strain effect predominates, *i.e.*, a partial rate order of ring size 6 < 7.

We conclude that another factor, reactant internal energy, becomes important with tosylates **5**. The 1-methyl substituent would not in all likelihood add to the strain in **16** (R = CH_3) very much, but the quaternary carbon at C-1 in **5** would undoubtedly increase the torsional strain due to bond eclipsing and thus raise the internal energy of the tosylates in the order n = 4 > 5 > 6 > 7, *i.e.*, an effect that would decrease with ring size. Thus, for either **3** or **5**, n = 4, the strain in **16** would be considerable but so would be the reactant internal energy in **5**, n = 4, and the balance of these factors could be such as to give this ring size the modest maximum in reactivity noted in Table IV. For the other ring sizes these effects could be in balance such that the low spread in reactivity again occurs, even without the missing conformational hindrance effect of Huisgen.

In summary, the solvolytic reactivity of the neophyl-like tosylates **5** shows essentially no real change from the nonquaternary analogs **3**. The neophyl rearrangement therefore fails to demonstrate a noteworthy ring size effect in these instances.

Experimental Section

Melting points (Fisher-John block) and boiling points are uncorrected. Microanalyses were performed by Micro-Tech Laboratories, Skokie, Ill., and by the analytical department of G. D. Searle and Co., Skokie, Ill. Infrared data (λ in microns) were obtained on Beckman IR-5A and Perkin-Elmer Model 21 instruments. Only partial spectral assignments are given. Nuclear magnetic resonance spectra (δ) in parts per million were determined on a Varian A-60A spectrometer using TMS as an internal standard. Peak integrals were in agreement with the assignments given. The usual splitting abbreviations are used. Centers of complex multiplets are given unless a range is specified. AB patterns, however, have been assigned true chemical shifts.

Gas–liquid partition chromatography (glpc) was performed on a Varian Aerograph A-90P instrument with helium as the carrier gas. Columns and other details are given where appropriate. Peak areas were integrated with a disc integrator. General synthetic procedures are described with specific properties relegated to summaries, unless obviously otherwise.

Methylation Reactions. A. To Form 7 (Z = CN).—A solution of freshly prepared potassium *tert*-butoxide (0.23 mol) in dry *tert*-butyl alcohol was added to dimethyl sulfoxide (30 ml). The appropriate nitrile **6**, $n = 4$[11,12] or **7**,[11,12] Z = CN (0.054 mol), was then added at 50°. After being stirred for 30 min, the solution was cooled and methyl iodide (0.23 mol) was added dropwise over 30 min with additional cooling to moderate the reaction. Reaction was continued for 1 hr. Excess hydrochloric acid was then added cautiously and most of the solvent was removed by vacuum distillation. The residue was taken up in ether and washed with sodium thiosulfate solution and water. The dried (Na_2SO_4) ether solution was then distilled to obtain the product **7**.

1-Methylbenzocyclobutene-1-carbonitrile (**7**, $n = 4$, Z = CN): 67.7%; bp 95–99° (3.5 mm); $n^{25}D$ 1.5256; d^{27}_4 0.970; λ (neat) 4.5 (CN), 7.25 (CH_3); δ ($CDCl_3$) 7.37 m (ArH), 3.80 d, 3.10 d (CH_2, AB, J = 14 Hz), 1.75 s (CH_3).

Anal. Calcd for $C_{10}H_9N$: C, 83.88; H, 6.33. Found: C, 83.90; H, 6.37.

1-Methylbenzosuberene-1-carbonitrile (**7**, $n = 7$, Z = CN): 71.2%; bp 105–106° (0.25 mm); $n^{26}D$ 1.5428; d^{26}_4 0.992; λ (neat) 4.5 (CN), 7.21 (CH_3); δ ($CDCl_3$) 7.5–7.0 m (ArH), 3.7–2.9 m (4-CH_2), 2.9–1.2 m (other ring H's), 1.80 s (CH_3).

Anal. Calcd for $C_{13}H_{15}N$: C, 84.28; H, 8.16. Found: 84.46; H, 8.20.

B. To Form 7 (Z = $COOCH_3$).—The appropriate methyl ester **6**, $n = 4$[13] or **7**,[14] Z = $COOCH_3$ (0.086 mol) in ether (25 ml) was added to liquid ammonia (300 ml) containing sodium amide (0.09 mol). The solution was stirred at −55° for 1 hr. Methyl iodide (0.18 mol) in ether (25 ml) was then added dropwise over 30 min. The reaction warmed to −37°, at which temperature stirring was continued for 3 hr. Ammonium chloride (0.2 mol) was added and the ammonia was allowed to evaporate as it was replaced by ether. Subsequent operations were the same as described in A.

Methyl 1-methylcyclobutene-1-carboxylate (**7**, $n = 4$, Z = $COOCH_3$): 69%; bp 84° (1.4 mm); $n^{27}D$ 1.5130; λ (neat) 5.80 (CO), 7.28 (1-CH_3); δ ($CDCl_3$) 7.23 m (ArH), 3.73 d, 3.03 d (CH_2, AB, J = 14 Hz), 3.67 s (OCH_3), 1.67 s (CH_3).

Anal. Calcd for $C_{11}H_{12}O_2$: C, 74.97; H, 6.87. Found: C, 75.10; H, 6.94.

Methyl 1-methylbenzosuberene-1-carboxylate (**7**, $n = 7$, Z = $COOCH_3$): 19%;[15] bp 134° (1.5 mm); $n^{26}D$ 1.5350; d^{26}_4 1.117; λ(neat) 5.80 (CO), 7.25 (1-CH_3); δ ($CDCl_3$) 7.1 m (ArH), 3.62 s (OCH_3), 2.80–2.52 m (4-CH_2), 2.50–1.2 m (other ring H's), 1.62 s (CH_3).

Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 77.21; H, 8.14.

Conversion of 7 to 10.—Saponification of the methyl esters **7** with aqueous sodium hydroxide containing 20% ethanol produced the following compounds.

1-Methylbenzocyclobutene-1-carboxylic acid (**10**, $n = 4$): 84.4%; bp 134° (1.6 mm); $n^{28}D$ 1.5315; λ (neat) 3.0–4.5, 5.9 (COOH); δ ($CDCl_3$) 12.2 s (COOH), 7.23 s (ArH), 3.78 d, 3.02 d (ring CH_2, AB, J = 14 Hz), 1.70 s (CH_3).

Anal. Calcd for $C_{10}H_{10}O_2$: C, 74.05; H, 6.22. Found: C, 73.97; H, 6.31.

1-Methylbenzosuberene-1-carboxylic acid (**10**, $n = 7$): 45%; mp 161–162°; λ (KBr) 3.0–4.5, 6.0 (COOH); δ ($CDCl_3$) 10.3 br s (COOH), 7.38 m (ArH), 2.80 m (4-CH_2), 2.6–1.0 m (other ring H's), 1.73 s (CH_3).

Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.60; H, 7.95.

These acids were also obtained by various hydrolysis methods from the nitriles **7**. The tertiary nature of the latter hindered such hydrolyses, however, and only poor to modest yields could be obtained.[16]

Huang-Minlon Reduction of 9 to 10.—To a solution of potassium hydroxide (1.0 mol) in diethylene glycol (700 ml) was added the appropriate acid **9** (0.25 mol), $m = 3$[17] or 4,[18] together with hydrazine hydrate (90%, 50 ml). The solution was heated to reflux and the distillate was removed until the pot temperature rose to 220°. Heating at this temperature was continued under reflux for 12 hr. The cooled solution was then acidified with hydrochloric acid. Recrystallization of the precipitated material from benzene–hexane gave the following compounds.

1-Methylindan-1-carboxylic acid (**10**, $n = 5$): 94%; mp 71.5–72.5° (occasionally samples had mp 57–59°); λ (KBr) 3.0–4.5, 6.05 (COOH), 7.21 (CH_3); δ ($CDCl_3$) 10.49 br s (COOH), 7.20 m (ArH), 3.15 m and 1.63 m (centers of ABX_2 pattern for ring CH_2's), 1.55 s (CH_3).

Anal. Calcd for $C_{11}H_{12}O_2$: C, 74.98; H, 6.86. Found: C, 75.13; H, 7.05.

1-Methyltetralin-1-carboxylic acid (**10**, $n = 6$): 94%; mp 118–119° (lit.[20] mp 81°); λ (KBr) 3.0–4.5, 6.0 (COOH), 7.29 (CH_3); δ ($CDCl_3$) 11.25 br s (COOH), 7.00–7.34 (ArH), 2.79, 2.24, 1.83 all m (4-, 5-, 6-CH_2, respectively), 1.57 s (CH_3).

Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.51; H, 7.39.

Reduction of 7 and 10 to the Carbinols 8.—Reduction of the methyl esters (see B above) or the carboxylic acids **10** was achieved with lithium aluminum hydride in ether in standard fashion.[16]

1-Methylbenzocyclobutenyl-1-carbinol (**8**, $n = 4$): 95%; bp 78° (0.3 mm); $n^{26}D$ 1.5366; λ (neat) 3.0 (OH), 7.3 (CH_3), 9.7 (1° CO); δ ($CDCl_3$) 7.20 m (ArH), 3.67 br s (-CH_2OH, probably center of AB pattern), 3.08 d, 2.82 d (ring CH_2, AB, J = 14 Hz), 2.8 br s (OH), 1.40 s (CH_3).

Anal. Calcd for $C_{10}H_{12}O$: C, 81.04; H, 8.16. Found: C, 81.34; H, 8.07.

1-Methylindanyl-1-carbinol (**8**, $n = 5$): 92%; bp 90° (1.0 mm); $n^{26}D$ 1.5392; λ 3.03 (OH), 7.30 (CH_3), 9.7 (1° CO); δ ($CDCl_3$) 7.20 s (ArH), 3.50 s (CH_2OH), 2.90 m (4-CH_2), 2.4–1.6 sharp series of peaks (5-CH_2, probably AB portion of ABX_2 pattern, and OH), 1.23 s (CH_3).

Anal. Calcd for $C_{11}H_{14}O$: C, 80.99; H, 8.65. Found: C, 81.12; H, 8.88.

1-Methyltetralyl-1-carbinol (**8**, $n = 6$): 82%; bp 112° (1.25 mm); $n^{26}D$ 1.5530; λ (neat) 3.05 (OH), 7.3 (CH_3), 9.75 (1° CO); δ ($CDCl_3$) 7.18 m (ArH), 3.77 d, 3.51 d (CH_2OH, AB because of adjacent asymmetry,[21] J = 11 Hz), 2.80 m (4-CH_2), 2.2–1.4 m (other ring H's), 1.90 s (OH), 1.25 s (CH_3).

Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.65; H, 9.24.

1-Methylbenzosuberenyl-1-carbinol (**8**, $n = 7$): 100%; bp 105° (0.1 mm); $n^{26}D$ 1.5560; d^{26}_4 1.120; λ (neat) 3.05 (OH), 7.25 (CH_3), 9.8 (1° CO); δ ($CDCl_3$) 7.4–7.0 m (ArH), 3.72 sharp m (-CH_2OH, probably close AB pattern), 2.86 broad envelope (4-CH_2), 2.1–1.3 m (other ring H's), 1.55 s (OH), 1.32 s (CH_3).

Anal. Calcd for $C_{13}H_{18}O$: C, 82.05; H, 9.54. Found: C, 82.12; H, 9.38.

Preparation of Tosylates 5.—All tosylates were prepared from the alcohol in pyridine using *p*-toluenesulfonyl chloride in customary fashion.[22]

1-Methylbenzocyclobutenyl-1-carbinyl tosylate (**5**, $n = 4$): 89%; mp 55–56°; consonant spectra.

(11) J. F. Bunnett and J. A. Skorcz, *J. Org. Chem.*, **27**, 3836 (1962).

(12) We thank Dr. Skorcz for detailed information on the preparation of these nitriles.

(13) L. Horner, W. Kirmse, and K. Muth, *Chem. Ber.*, **91**, 430 (1958).

(14) Prepared from the acid[11] and diazomethane, 86%, bp 118° (0.5 mm). *Anal.* Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.31; H, 7.88.

(15) The principal product was unchanged starting ester. Various other methylation procedures gave no better results.

(16) Details of these and related experimental procedures are omitted for reasons of space. Full descriptions may be found elsewhere.[2]

(17) G. F. Woods, T. L. Heying, L. H. Schwartzman, S. M. Grenell, W. F. Gasser, E. W. Rowe, and N. C. Bolgiano, *J. Org. Chem.*, **19**, 1290 (1954).

(18) Prepared by ring closure of α-methyl-α-phenylglutaric acid[19] (0.1 mol) in concentrated sulfuric acid (150 g) at 100° for 1 hr. The hot mixture was poured over cracked ice (300 g) and the precipitated acid was collected and recrystallized from benzene–hexane, 66%, mp 128–129°, spectra consonant with structure. *Anal.* Calcd for $C_{12}H_{12}O_3$: C, 70.57; H, 5.92. Found: C, 70.57; H, 5.84.

(19) F. S. Legagneur and C. Neveu, *Bull. Soc. Chim. Fr.*, 70 (1953).

(20) M. Protiva, J. O. Jílek, Z. J. Vejdělek, and P. Finglová, *Chem. Listy* **47**, 584 (1953), report mp 81°. We have no explanation for the discrepancy, although it would be unusual to have such a quaternary acid with the same melting point as the parent (unmethylated) acid (81°).

(21) The expected AB character for the methylene protons in the -CH_2OH group of the alcohols **8** was clear only in this case.

(22) R. S. Tipson, *J. Org. Chem.*, **9**, 235 (1944).

Anal. Calcd for $C_{17}H_{18}O_3S$: C, 67.52; H, 5.99. Found: C, 67.59; H, 6.00.

1-Methylindanyl-1-carbinyl tosylate (**5**, n = 5): 53%; mp 38–39°; consonant spectra.

Anal. Calcd for $C_{18}H_{20}O_3S$: C, 68.32; H, 6.37. Found: C, 68.71; H, 6.28.

1-Methyltetralyl-1-carbinyl tosylate (**5**, n = 6): 83%; mp 53–53.5°; consonant spectra.

Anal. Calcd for $C_{19}H_{22}O_3S$: C, 69.06; H, 6.71. Found: C, 68.95; H, 6.76.

1-Methylbenzosuberenyl-1-carbinyl tosylate (**5**, n = 7): 87%; mp 65–66°; consonant spectra.

Anal. Calcd for $C_{20}H_{24}O_3S$: C, 69.73; H, 7.02. Found: C, 69.68; H, 7.03.

"Ene" Reactions to Form 11.—*o*-Benzenediazonium carboxylate was prepared as follows.[23] *Caution must be exercised. Use of a safety shield is advised. The compound when dry is treacherously explosive.* Anthranilic acid (15 g, 0.11 mol) and a catalytic amount of trifluoroacetic acid (*ca.* 0.1–0.2 g) were dissolved in dry tetrahydrofuran (250 ml). Isoamyl nitrite (25 g, 0.21 mol) was added dropwise to the solution as it was stirred in a cooling bath at 20°. The initial red precipitate slowly became cream-colored. After 30 min the solid was collected on a *plastic* funnel using a *rubber* spatula for transfer. The clinging tetrahydrofuran was washed away with 1,2-dichloroethane. *The solid must be kept moist with solvent.* The moist solid was washed into a large flask with more 1,2-dichloroethane (total volume ~500 ml) and the appropriate olefin (see below, 0.45–0.50 mol) was added to the suspension. Under efficient reflux condensers, the material was warmed to ~83°, whereupon a rapid evolution of nitrogen occurred with considerable foaming. After this brisk reaction was completed, the solvent and excess olefin were removed by rotary evaporation. The residual oil was then distilled and refractionated to give the products listed.[24]

From methacrylonitrile resulted **α-benzylacrylonitrile** (**11**, Z = –CN): 41%; bp 85–89° (1.5 mm); n^{26}D 1.5210; λ (neat) 4.58 (CN), 10.65 (=CH_2 conjugated with –CN); δ (CCl_4) 7.23 m (ArH), 5.75 slightly broadened s (terminal methylene H cis to CN), 5.57 t (terminal methylene H trans to CN, J = 1.5 Hz), 3.45 d (benzylic CH_2, J = 1.5 Hz).

Anal. Calcd for $C_{10}H_9N$: C, 83.88; H, 6.33. Found: C, 83.72; H, 6.54.

From methyl methacrylate resulted **methyl α-benzylacrylate**[25] (**11**, Z = –$COOCH_3$): 48%; bp 73° (0.6 mm); n^{28}D 1.5063; λ (neat) 5.81 (CO), 10.5 (=CH_2 conjugated with –$COOCH_3$); the nmr spectra corresponded to that reported.[25]

From methallyl chloride resulted two "ene" chlorides in 51% yield, bp 74–75° (5 mm), roughly corresponding to statistical attack by benzyne at the methyl and chloromethyl groups. **α-Benzylallyl chloride** (**11**, Z = CH_2Cl), 65% upon separation on an Reoplex 400 column at 150° and by nmr analysis: n^{24}D 1.5316; λ (neat) 10.95 (=CH_2); δ ($CDCl_3$) 7.45 s (ArH), 5.33 m and 5.08 m (=CH_2), 4.08 sharp m (–CH_2Cl) and 3.63 m (benzylic CH_2). **1-Chloro-2-benzylpropene**, a 78:22 mixture of stereoisomers by nmr analysis, probably richer in the trans-CH_3, Cl isomer: n^{24}D 1.5330; λ (neat) 7.23 (CH_3); δ ($CDCl_3$) 7.40 s (ArH), 6.05 m (=CH), 3.65 s (benzylic CH_2 in principal isomer), 3.42 m (benzylic CH_2 in minor isomer), 1.70 m (CH_3).

Anal. (of mixture). Calcd for $C_{10}H_{11}Cl$: C, 72.06; H, 6.67. Found: C, 71.75; H, 6.72.

The nitrile **11** and the ester **11** above could be hydrolyzed in refluxing ethyl Cellosolve or 20% aqueous alcohol, respectively, using potassium hydroxide for *ca.* 2 hr. Acidification and recrystallization from hexane gave **α-benzylacrylic acid**: 100%; mp 66–67°; λ (KBr) 3.0–4.5, 6.0 (–COOH), 6.2, 10.9 (=CH_2); δ ($CDCl_3$) 11.3 br s (COOH), 7.30 s (ArH), 6.43 s (terminal methylene H cis to –COOH), 5.60 narrow t (terminal methylene H trans to –COOH), 3.67 s (benzylic CH_3).

Anal. Calcd for $C_{10}H_{10}O_2$: C, 74.06; H, 6.21. Found: C, 74.19; H, 6.26.

Syntheses of Reference Compounds. 2-Methylbenzocyclen-2-ols.[25a]—Under nitrogen, the appropriate ketone (see below, 0.32 mol) was added to methylmagnesium iodide (0.32 mol) in ether (200 ml) at a rate sufficient to maintain reflux. After 8 hr reaction under reflux, cold aqueous ammonium chloride (200 ml of 0.3 *M* solution) was added to the cooled reaction material. The ether layer was separated, washed and dried. Distillation then gave the alcohols listed.

From 2-indanone[26b] was obtained **2-methyl-2-indanol** (**12**, n = 4, X = OH): 80%; mp 49–50°; bp 91° (1.75 mm); λ (neat melt) 3.03 (OH), 8.9 (3° CO); δ ($CDCl_3$) 7.23 s (ArH), 3.0 s (CH_2's), 2.30 s (OH), 1.47 s (CH_3).

Anal. Calcd for $C_{10}H_{12}O$: C, 81.04; H, 8.16. Found: C, 81.44; H, 7.95.

From 2-tetralone[27] was formed **2-methyl-2-tetralol** (**12**, n = 5, X = OH): 74%; bp 99° (1 mm); n^{28}D 1.5442; λ (neat) 3.03 (OH), 9.04 (3° CO); δ ($CDCl_3$) 7.22 s (ArH), 2.92 m (1- and 4-CH_2), 2.0–1.5 m (OH and 3-CH_2), 1.32 s (CH_3).

Anal. Calcd for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 81.35; H, 8.55.

From benzosuberen-2-one[4] was produced **2-methylbenzosuberen-2-ol** (**12**, n = 6, X = OH): 72%; bp 86–87° (0.25 mm); n^{25}D 1.5460; λ (neat) 2.98 (OH), 8.8–9.06 (3° CO); δ ($CDCl_3$) 7.22 s (ArH), 3.0 s (1-CH_2), 2.82 m (5-CH_2), 2.23 br s (OH), 2.08–1.42 m (3, 4-CH_2's), 1.17 s (CH_3).

Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.89; H, 9.44.

From benzocyclocten-2-one[28] was made **2-methylbenzocycloocten-2-ol** (**12**, n = 7, X = OH): 75%; bp 122° (2.25 mm); n^{26}D 1.5497; λ (neat) 3.0 (OH), 9.1 (3° CO); δ ($CDCl_3$) 7.13 s (ArH), 2.82 s (1-CH_2), 2.75 m (6-CH_2), 1.85–1.1 m (other CH_2's), 1.68 s (OH), 1.27 s (CH_3).

Anal. Calcd for $C_{13}H_{18}O$: C, 82.05; H, 9.54. Found C, 81.51; H, 9.63.

Conversion of these alcohols to their corresponding acetates by a variety of techniques gave varying amounts of olefin by dehydration.[16] Consequently, the acetate products **12**, Z = OAc, formed in the acetolysis study were characterized by saponification to **12**, Z = OH, or by pyrolysis to the following olefins: **2-methylindene**[29] (**13**, n = 4); **2-methyl-3,4-dihydronaphthalene**[30] (**13**, n = 5); **4-methylbenzo[1.2]cyclohepta-1,3-diene**[31] (**13**, n = 6); and **4-methylbenzo[1.2]cyclocta-1,3-diene** (**13**, n = 7). This last olefin was prepared from alcohol **12**, n = 7, X = OH, by dehydration in hot benzene containing a little iodine: 100%; bp 82–83° (1 mm); n^{27}D 1.5594; d^{27}_4 0.946; λ (neat) 7.22 (CH_3); δ ($CDCl_3$) 7.03 s (ArH), 6.23 m (=CH), 2.62 m (benzylic CH_2), 2.2–1.2 m (all other CH_2's), 1.87 d (CH_3, J = 2 Hz).

Anal. Calcd for $C_{13}H_{16}$: C, 90.64; H, 9.36. Found: C, 90.71; H, 9.31.

Products **14** and **15** were characterized by instrumental methods only. Hydrogenation of them over Pd/C at 25° gave the following benzocyclenes: **2-methylindan**[32] from **14**, n = 4; **2-methyltetralin**[33] from **14**, n = 5; and **2-methylbenzosuberene**: bp 100° (1 mm); n^{25}D 1.5282; d^{25}_4 0.940; λ (neat) 7.28 (CH_3); δ ($CDCl_3$) 7.05 s (ArH), 2.70 m (benzylic CH_2's), 2.03–1.12 m (all other rings H's), 0.95 distorted d (CH_3, J ~ 6 Hz).

Anal. Calcd for $C_{12}H_{16}$: C, 89.93; H, 10.07. Found: C, 89.97; H, 9.94.

The solvolysis products **14** and **15** from tosylate **5**, n = 7, were obtained in too small amounts for even characterization. Their structures are assumed.

In all cases, the 1-methyl analogs of the above alcohols and hydrocarbons were also prepared.[16] They were totally absent in the solvolysis reaction products.

Solvolysis Studies. Kinetic Runs. Acetolysis.—The procedure used was that of Winstein and coworkers.[34] The acetic

(23) We thank Dr. L. Friedman of Case Western Reserve University for this procedure.

(24) All glassware used to prepare the diazonium salt must be quickly rinsed with water and flushed into wide drains. The distillation residue must be taken up in 1,2-dichloroethane to prevent solidification to refractory tars.

(25) I. Tabushi, K. Okazaki, and R. Oda, *Tetrahedron*, **25**, 4401 (1969).

(26) (a) Except for **13**, these reference compounds have been numbered with the benzylic position as 1, according to usual practice, and thence around the alicyclic portion of the molecule *away* from the benzo moiety. (b) J. E. Horan and R. W. Schuessler, *Org. Syn.*, **41**, 53 (1961).

(27) M. D. Soffer, M. D. Beilis, E. Gellerson, and R. A. Stewart, "Organic Syntheses," Collect. Vol. IV, Wiley, New York, N. Y., 1963, p 902.

(28) W. Rapp, *Justus Liebigs Ann. Chem.*, **586**, 1 (1954).

(29) E. R. Alexander and A. Mudrak, *J. Amer. Chem. Soc.*, **73**, 59 (1951).

(30) W. Hückel, R. Cramer, and S. Laufer, *Justus Liebigs Ann. Chem.*, **630**, 89 (1960).

(31) P. Rona, *J. Chem. Soc.*, 3629 (1962).

(32) A. A. Khalaf and R. M. Roberts, *J. Org. Chem.*, **31**, 89 (1966).

(33) J. W. Wilt and C. A. Schneider, *ibid.*, **26**, 4196 (1961).

(34) S. Winstein, B. K. Morse, E. Grunwald, K. C. Schreiber, and J. Corse *J. Amer. Chem. Soc.*, **74**, 1113 (1952).

acid was redistilled and contained 0.3% acetic anhydride. Ampoules containing the reactants were sealed under nitrogen. The tables contain further information.

Hydrolysis.—Rate studies in 60% acetone were conducted as earlier described.[35] The acetone was freshly distilled from potassium permanganate. Again, ampoules were sealed under nitrogen. Further details may be found in the tables and ref 2.

Product Runs. Acetolysis.—Tosylate solutions (0.025 *M*) were prepared as for the acetolysis rate studies but in larger volume (50 ml). The solutions were heated under nitrogen in a pressure bottle at 95° for 25 hr. The material was added to water (1 l.) and thoroughly extracted with 1:1 ether–pentane. The organic extracts were washed and dried. Removal of solvent left an oil in each case. This oil was analyzed by spectral methods and by glpc to give the product data in Table III. Most glpc work was done on Flexol 8N8 columns, 6 ft × 0.25 in. at 175°. Acetate esters **12**, X = OAc, were characterized by λ 5.75, δ ≅ 2 s (-OCOCH$_3$). Olefins **13** have been described above. Olefins **14** were signified by λ 11, δ ≅ 5 (=CH$_2$). Olefins **15** were best evidenced by δ 5.5 (=CH), an upfield resonance relative to the vinyl proton in **13** (δ 6.3). Proper composition was better obtained prior to glpc because considerable acetate pyrolysis accompanied elution, enriching the vinyl products and decreasing the acetate esters. The olefin materials eluted at half the time of the esters and were easily distinguished. The olefin mixture could subsequently be simplified in composition by hydrogenation. Spectral and glpc data then indicated only the benzocyclenes mentioned above. Saponification of the crude product gave alcohols **12** (X = OH) which were correlated with the hydrolysis study (see below).

(35) J. W. Wilt, C. T. Parsons, C. A. Schneider, D. G. Schultenover, S. J. Wagner, and W. J. Wagner, *J. Org. Chem.*, **33**, 694 (1968).

Hydrolysis.—The product runs were performed upon tosylate solutions (0.030 *M*) made as for the hydrolysis rate studies and as described for acetolysis. Alcohols **12** and the olefin products have been described above and the spectral properties there reported were used to establish their presence in the product. Columns of Reoplex 400, Apiezon L and SE-30 at 175° caused extensive dehydration of **12** upon glpc. A column using Flexol 8N8 allowed less such dehydration, but again proper composition data was better obtained prior to glpc. In the instance of tosylate **5**, *n* = 5, the dihydronaphthalene olefin products were adventitiously oxidized to 2-methylnaphthalene. No olefins **13–15** were observed in this case.

Registry No.—**5**, *n* = 4, 33223-64-2; **5**, *n* = 5, 33223-65-3; **5**, *n* = 6, 33223-66-5; **5**, *n* = 7, 33223-67-5; **6**, *n* = 7, Z = COOCH$_3$, 33223-70-0; **7**, *n* = 4, Z = CN, 33223-68-6; **7**, *n* = 7, Z = CN, 33223-69-7; **7**, *n* = 4, Z = COOCH$_3$, 33223-71-1; **7**, *n* = 7, Z = COOCH$_3$, 33223-72-2; **8**, *n* = 4, 33223-73-3; **8**, *n* = 5, 33223-74-4; **8**, *n* = 6, 25634-94-0; **8**, *n* = 7, 33223-76-6; **10**, *n* = 4, 33223-77-7; **10**, *n* = 5, 33223-78-8; **10**, *n* = 6, 26516-28-9; **10**, *n* = 7, 33223-80-2; **11**, Z = CN, 28769-48-4; **11**, Z = COOCH$_3$, 3070-71-1; **11**, Z = CH$_2$Cl, 32223-83-5; **12**, *n* = 4, X = OH, 32223-84-6; **12**, *n* = 5, X = OH, 33223-85-7; **12**, *n* = 6, X = OH, 33223-86-8; **12**, *n* = 7, X = OH, 33223-87-9; **13**, *n* = 7, 33303-93-4; 1-chloro-2-benzylpropene, 33223-88-0; *cis*-α-benzylacrylic acid, 5669-19-2; 2-methylbenzosuberene, 22851-69-0.

Aryl Participation in the Solvolysis of Some *gem*-Dimethyl-Substituted 4-Aryl-1-alkyl *p*-Bromobenzenesulfonates[1]

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A series of 4-phenyl and 4-anisyl-1-butyl *p*-bromobenzenesulfates with 3,3- and 4,4-dimethyl groups was prepared, and acetolysis and formolysis rates were measured. The *gem*-dimethyl group can appreciably increase the tendency for aryl participation to occur in the solvolysis of these derivatives. Participation by both the 1- and 2(6)-carbon atoms of the aromatic ring is observed depending upon the substituents present. The formolysis of 4-(*m*-anisyl)-4-methyl-1-pentyl *p*-bromobenzenesulfonate produces mainly a mixture of 1,1-dimethyl-7- and 1,1-dimethyl-5-methoxytetralins formed by participation of carbons 2 and 6, respectively, in the solvolysis. With the related *p*-methoxy derivative, formolysis and acetolysis produce an appreciable amount (48% in formolysis) of 1,1-dimethyl-7-methoxytetralin, a rearranged product arising from participation of carbon atom 1 of the *p*-anisyl group producing a spirocationic intermediate which then undergoes a 1:2 shift of the tertiary group in preference to the primary one. In acetolysis, a significant amount (17%) of 1:4 shift of the *p*-anisyl group is also observed. Formolysis rate constants are divided into aryl-assisted and -unassisted fractions and yields of cyclized products were calculated assuming participation resulted in the exclusive formation of cyclized products. Those values were in reasonable agreement with the observed yields.

Participation of remote aryl groups in solvolysis reactions was clearly demonstrated in the previous papers in this series[3,4] with ω-aryl-1-alkyl *p*-bromobenzenesulfonates. Either carbon atom 1 or 2 of the ω-aryl group could assist solvolysis depending upon which was the more susceptible to electrophilic attack and depending upon the distance between the aryl and *p*-bromobenzenesulfonate groups. Participation by either aromatic carbon led exclusively to cyclization. Five- and six-membered rings were preferred. In this paper are reported results on some *gem*-dimethyl substituted aryl-1-alkyl *p*-bromobenzenesulfonates which show the rate-enhancing effect of the *gem*-dimethyl group and the rearrangement of appropriately substituted derivatives during solvolysis.

The compounds prepared and the kinetic data obtained from them are given in Table I. The addition of the 2,2-*gem*-dimethyl group to 2-phenylethyl *p*-bromobenzenesulfonate increases the rate of acetolysis by a factor of about 70,[5] while in the 3-phenyl-1-propyl system the 3,3-*gem*-dimethyl group actually decreases the rate by a factor of 0.7.[3] The *gem*-dimethyl group is apparently sterically inhibiting solvolysis in the last reaction. In the previous study[3,4] addition of methoxyl groups to the aromatic ring enhanced the solvolysis rates when participation was occurring. Since the

(1) Part of the work described in this paper was reported in preliminary form by S. Winstein, R. Heck, S. Lapporte, and R. Baird, *Experientia*, **12**, 138 (1956), and by S. Winstein, E. Allred, R. Heck, and R. Glick, *Tetrahedron*, **3**, 1 (1958).

(2) University of Delaware, Newark, Del. 19711.

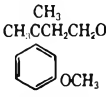
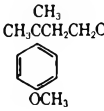
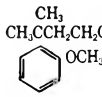
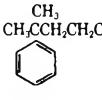
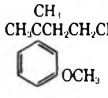
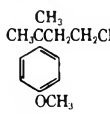
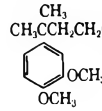
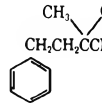
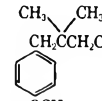
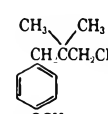
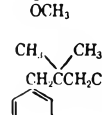
(3) R. Heck and S. Winstein, *J. Amer. Chem. Soc.*, **79**, 3105 (1957).

(4) R. Heck and S. Winstein, *ibid.*, **79**, 3114 (1957).

(5) S. Winstein and R. Heck, *ibid.*, **78**, 4801 (1956).

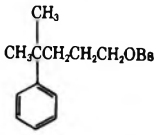
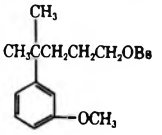
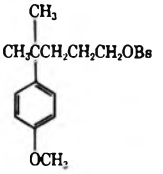
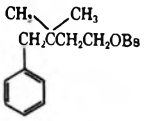
TABLE I

SUMMARY OF SOLVOLYSIS RATE CONSTANTS

Compd	Registry no.	Solvent	Concn, M[a]	Temp, °C	Added salt	k, sec^{-1}	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu
	33214-50-5	HOAc	0.0290	75.00		$(3.04 \pm 0.01) \times 10^{-7}$	24.5	−18.5
		HOAc	0.0268	100.00		$(3.47 \pm 0.05) \times 10^{-6}$		
	33214-51-6	HOAc	0.0269	75.00		$(3.02 \pm 0.09) \times 10^{-7}$		
	33214-52-7[c]							
	33214-53-8	HOAc	0.0282	75.00		$(3.15 \pm 0.03) \times 10^{-7}$		
	33214-54-9[c]							
	33289-90-6	EtOH	0.0274	75.00		$(1.52 \pm 0.04) \times 10^{-4}$ (100)[b]		
	33214-55-0[c]	HOAc	0.0313	50.00		4.5×10^{-5} (31)[b]		
		HOAc	0.0313	75.00		5.6×10^{-4} (34)[b]		
		HOAc	0.0283	75.00	0.0030 M $LiClO_4$	4.6×10^{-4} (42)[b]		
		HOAc	0.0308	75.00	0.0300 M $LiClO_4$	4.2×10^{-5} (92)[b]		
		HOAc	0.0450	75.00	0.0300 M LiOTs	5.2×10^{-4} (25)[b]		
		HOAc	0.0294	75.00	0.0310 M NaOAc	$(5.81 \pm 0.05) \times 10^{-4}$ (93)[b]		
		HOAc	0.0281	50.00	0.0300 M LiOAc	$(4.51 \pm 0.08) \times 10^{-5}$ (91)[b]		
		HOAc	0.0281	75.00	0.0300 M LiOAc	$(6.07 \pm 0.14) \times 14^{-4}$ (90)[b]		
		HCOOH	0.0306	25.00	0.0291 M NaOCHO	$(2.20 \pm 0.05) \times 10^{-4}$ (96)[b]		
	33214-56-1	HOAc	0.02651	75.00		$(1.90 \pm 0.02) \times 10^{-6}$	24.4	−14.9
	33214-57-2[c]	HOAc	0.02670	100.05		$(2.17 \pm 0.03) \times 10^{-5}$		
		HCOOH	0.02921	50.00	0.0315 M NaOCHO	$(4.56 \pm 0.12) \times 10^{-6}$		
		HCOOH	0.02682	75.00	0.0315 M NaOCHO	$(5.93 \pm 0.03) \times 10^{-5}$	22.3	−14.3
	33214-58-3	HCOOH	0.02445	50.00	0.0315 M NaOCHO	$(1.25 \pm 0.01) \times 10^{-5}$		
	33325-79-0[c]	HCOOH	0.02323	75.00	0.0291 M NaOCHO	$(1.58 \pm 0.03) \times 10^{-4}$	22.0	−13.1
	29510-28-9	HOAc	0.02225	75.00		$(2.86 \pm 0.02) \times 10^{-6}$	25.0	−12.4
	26315-95-7[c]	HOAc	0.02225	99.92		$(3.42 \pm 0.03) \times 10^{-5}$		
		HCOOH	0.02527	50.00	0.0315 M NaOCHO	$(9.43 \pm 0.07) \times 10^{-6}$		
		HCOOH	0.02546	75.00	0.0291 M NaOCHO	$(1.24 \pm 0.04) \times 10^{-4}$	23.0	−12.5
	33214-61-8	HCOOH	0.02590	50.0	0.0315 M NaOCHO	$(2.06 \pm 0.12) \times 10^{-5}$		
	33214-62-9[c]	HCOOH	0.02590	75.00	0.0315 M NaOCHO	$(2.54 \pm 0.03) \times 10^{-4}$	21.8	−12.8
	33214-63-0	HOAc	0.02896	75.00		$(2.46 \pm 0.02) \times 10^{-6}$		
	15732-85-1[c]	HCOOH	0.02796	50.00	0.0315 M NaOCHO	$(1.70 \pm 0.04) \times 10^{-5}$		
		HCOOH	0.02640	75.00	0.0291 M NaOCHO	$(2.21 \pm 0.04) \times 10^{-4}$	22.3	−11.7
	33289-91-7	HCOOH	0.02724	50.00	0.0315 M NaOCHO	$(1.03 \pm 0.04) \times 10^{-4}$		
	33214-65-2[c]	HCOOH	0.02580	75.00	0.0315 M NaOCHO	$(1.11 \pm 0.03) \times 10^{-3}$	20.8	−13.3
	33214-66-3	HOAc	0.01850	75.00		$(7.94 \pm 0.52) \times 10^{-6}$		
		HCOOH	0.02504	50.00	0.0291 M NaOCHO	$(4.98 \pm 0.18) \times 10^{-5}$		
		HCOOH	0.02504	75.00	0.0291 M NaOCHO	$(6.43 \pm 0.12) \times 10^{-4}$	22.2	−9.8
	33214-67-4	HCOOH	0.02866	50.0	0.0315 M NaOCHO	$(2.60 \pm 0.04) \times 10^{-6}$		
	33214-68-5[c]	HCOOH	0.02866	75.00	0.0315 M NaOCHO	$(5.20 \pm 0.03) \times 10^{-5}$	26.1	−3.5

[a] Calculated from the infinity titers observed. [b] Per cent of the starting ester which solvolyzed based on the "infinity titer" assuming that the ethanol value (95%) indicated purity of sample. [c] Free alcohol.

TABLE II
SUMMARY OF SOLVOLYSIS PRODUCTS

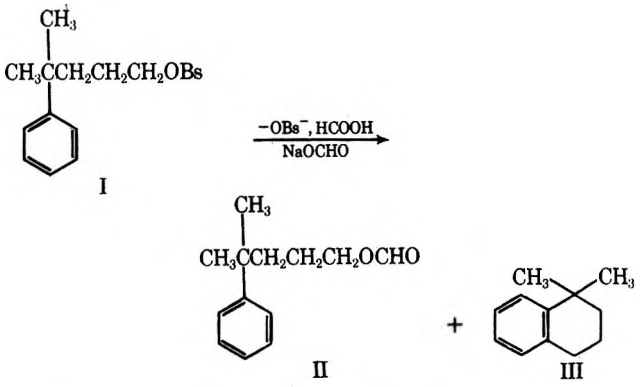
Compd	Solvent	Temp, °C	Total yield, %	Unrearranged products: % Alcohol	Unrearranged products: % Tetralin	Unrearranged products: % Olefin	Rearranged products: % Alcohol	Rearranged products: % Tetralin	Rearranged products: % Olefin
	HOAc	100	94.5	86.5	12.7	0.8			
	HCOOH	75	93.5	61.4	38.6				
	HCOOH	75	87.7	20.8	79.2 (51.5 VI, 27.7 VII)				
	HOAc	100	97.0	57.7	15.5		1.0	9.3	16.5
	HOAc(HOBs)[a]	100	95.0	57.0	15.0			22.0	
	HCOOH	75	86.0	29.0	22.7			48.3	
	HCOOH	75	95.0	5.0	95.0				

[a] HOBs not neutralized in this solvolysis.

m- and *p*-methoxyl derivatives of the 3-methyl-3-phenyl-1-propyl *p*-bromobenzenesulfonate have the same acetolysis rates as the phenyl compound within 5%, participation by either the 1- or 2-aryl carbon atoms in this system must be negligible. The *o*-methoxy derivative, on the other hand, is initially about 5000 times more reactive than the para compound. Only 31% of the expected quantity of sulfonic acid is produced, however, because of concurrent formation of methyl *p*-bromobenzenesulfonate, which is inert under our solvolysis conditions. Similar effects in other *o*-methoxy derivatives have been noted previously and an investigation of salt effects upon this compound demonstrated conclusively that it was another example of a compound showing participation by oxygen of the methoxyl group. A more complete discussion of methoxyl participation has been published elsewhere.[1b,6]

In the 4,4-*gem*-dimethyl-4-aryl-1-butyl derivatives some remote participation becomes detectable from kinetic data. In contrast to the propyl system, where the ω-*gem*-dimethyl group decreased the solvolysis rate of the phenyl derivative, the butyl case showed an increase by a factor of 1.3 in acetic acid and 1.7 in formic acid solvolysis. Here, *m*- and *p*-methoxyl substitution increased the solvolysis rates further; the *m*-methoxyl ω-*gem*-dimethyl compound reacted about 2.7 times faster and the para compound 2.1 times faster than the phenyl derivative in formolysis at 50°.

Convincing evidence that the relatively small rate increases observed in the above compounds were the result of aryl participation was found in an analysis of the formolysis products produced in the three cases. The results are summarized in Table II. Formolysis of 4-methyl-4-phenyl-1-pentyl *p*-bromobenzenesulfonate (I) at 75° produced a mixture of 57.4% 4-methyl-4-phenyl-1-pentyl formate (II, isolated as the alcohol) and 36.1% 1,1-dimethyltetralin (III). Control experiments with the more reactive 4-(*p*-anisyl)-4-methyl-1-pentyl formate show that it does not cyclize under formolysis conditions; therefore, the tetralin must be a product of formolysis, presumably formed from the part of the reaction which was promoted by aryl participation. Whether participation is localized at the 1- or 2-carbon of the phenyl group cannot be determined but more information on this point was obtained from a study of the methoxyl derivatives.



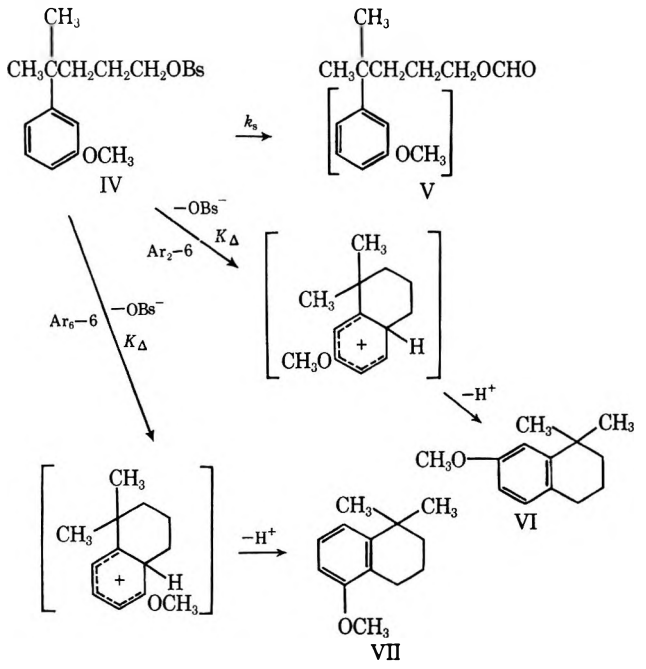
I II III

Formolysis of 4-(*m*-anisyl)-4-methyl-1-pentyl *p*-bromobenzenesulfonate (IV) gave 18.2% 4-(*m*-anisyl)-4-methyl-1-pentyl formate (V, isolated as the alcohol) and 69.5% of a mixture of two tetralins, 65% of which was 1,1-dimethyl-7-methoxytetralin (VI) and 35% 1,1-dimethyl-5-methoxytetralin (VII). There could not have been more than 1% of another possible product, 1,1-dimethyl-6-methoxytetralin (X), judging from infrared spectra. Thus, participation appears to be of the Ar_2-6 type[1] and both carbons 2 and 6 take part in the reaction.

The structure of 1,1-dimethyl-5-methoxytetralin was supported by an independent synthesis by the acid-catalyzed cyclization of 5-(*o*-anisyl)-2-methyl-2-pentanol and converison of the tetralin into 4,4-dimethyl-8-hydroxy-1-tetralone. The last compound

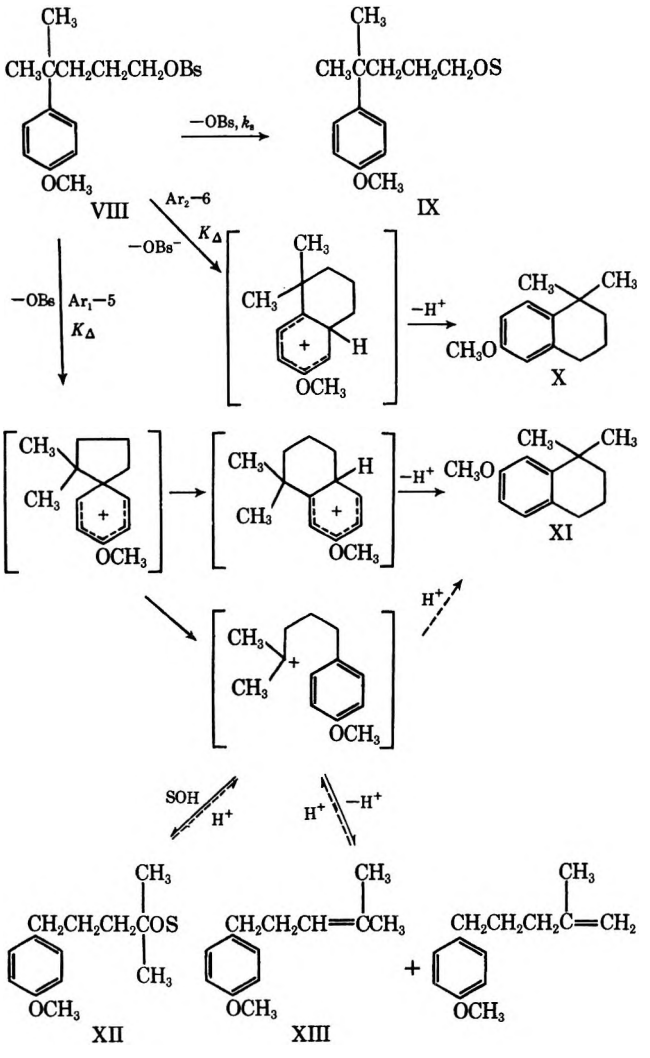
(6) R. Heck, J. Corse, E. Grunwald, and S. Winstein, *J. Amer. Chem. Soc.*, **79**, 3278 (1957).

showed the strong intramolecular hydrogen bonding expected from that structure.



The solvolysis of 4-(*p*-anisyl)-4-methyl-1-pentyl *p*-bromobenzenesulfonate (VIII), is more complicated. In formic acid at 75°, a 25% yield of 4-(*p*-anisyl)-4-methyl-1-pentyl formate (IX, S = CHO), isolated as the alcohol, and a 61% yield of a tetralin mixture was obtained. The mixture consisted of 32% 1,1-dimethyl-6-methoxytetralin (X) and 68% 1,1-dimethyl-7-methoxytetralin (XI). The major tetralin product is a rearranged one explicable in terms of an Ar_1-5 intermediate, a spirocarbonium ion, in which the tertiary carbon migrates to the ortho position. The minor tetralin could arise from the Ar_1-5 intermediate also if the primary carbon moved, but it more likely is the result of Ar_2-6 participation, which should still be a competitive reaction. We shall return to the point later.

Another complication of this solvolysis is the possible opening of the spirocationic intermediate to the tertiary carbonium ion which eventually yields the rearranged tetralin. Control experiments showed that under the formolysis conditions the same tertiary carbonium ion formed from the tertiary alcohol, 5-(*p*-anisyl)-2-methyl-2-pentanol (XII, S = H), cyclized exclusively to the "rearranged" tetralin, XI. Information on the spirocarbonium ion opening was obtained by an analysis of acetolysis products (in the presence of a slight excess of lithium acetate), since under basic acetolysis conditions (100°) the tertiary alcohol (XII, S = H) was relatively stable to cyclization and it gave only 6% tetralin along with 33% unrearranged olefin and 58% tertiary acetate ester (XII, S = $COCH_3$). The basic acetolysis of the 4-(*p*-anisyl)-4-methyl-1-pentyl *p*-bromobenzenesulfonate (VIII), at 100° gave 57 ± 1% acetate esters and 40 ± 1% of an olefin–tetralin mixture. The acetate esters consisted of about 98% 4-(*p*-anisyl)-4-methyl-1-pentyl acetate (IX, S = $COCH_3$) (56% of total solvolysis product) and 2 ± 1% of the rearranged tertiary ester, 5-(*p*-anisyl)-2-methyl-2-pentyl acetate (XII, S = $COCH_3$) (1% of total). Quantitative hydrogenation showed the olefin–tetralin mixture to be about 41% olefin (16% of total) presumably the rearranged olefins XIII, since the acetolysis of primary benzenesulfonates generally does not give appreciable amounts of olefinic products. Analyses of the tetralin product showed it to be a mixture of 37 ± 1% 1,1-dimethyl-7-methoxytetralin (XI) (9% of total) and 63 ± 1% 1,1-dimethyl-6-methoxytetralin (X) (15% of total). Acetolysis in the absence of acetate ion gave 57 ± 1% unrearranged acetate ester IX and 38 ± 1% tetralins. The latter product was a mixture of 40 ± 5% of the 6-methoxy isomer X (15% of total) and 60 ± 5% of the 7-methoxy compound XI (22% of total). The olefins and tertiary acetate ester apparently cyclized under the acidic acetolysis conditions, since the sum of the 16% olefin, 9% rearranged tetralin XI, and 1% tertiary acetate from the acetolysis of VIII under basic conditions roughly equals the amount of rearranged tetralin XI formed under acidic acetolysis conditions (22%). Three competing reactions are probably occurring in the basic acetolysis (and formolysis also): an unassisted solvolysis producing unrearranged acetate IX (59% of the reaction); Ar_2-6 type participation producing unrearranged tetralin X (15% of the reaction); Ar_1-5 participation producing rearranged tetralin XI, rearranged acetate XII, and rearranged olefins XIII (26% of the reaction). If this analysis is correct, then the Ar_1-5 intermediate in acetolysis opens to tertiary carbonium ion to the extent of 65%, which is equiva-

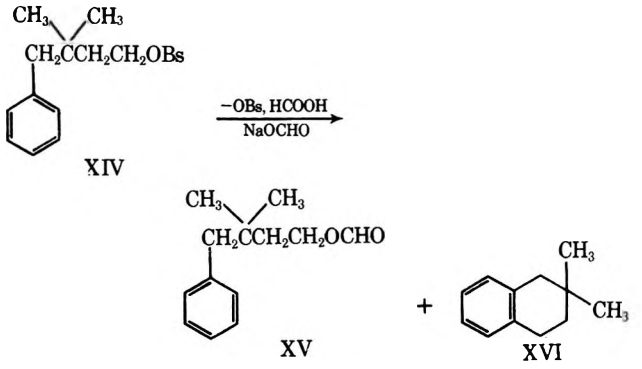


lent to 17% of the total product resulting from a 1:4 shift of the *p*-anisyl group.

For comparison we also investigated the acetolysis products of the parent compound 4-methyl-4-phenyl-1-pentyl *p*-bromobenzenesulfonate (I), under the same basic conditions. Here we obtained 81.5% "unrearranged acetate ester," 1–2% olefin, and 12 ± 1% 1,1-dimethyltetralin. The olefin appeared to be at least 98% unrearranged, suggesting that the participation probably is mainly of the Ar_2-6 type.

The formolysis rate of 4-(3-4-dimethoxyphenyl)-4-methyl-1-pentyl *p*-bromobenzenesulfonate was measured to see if the effects of two methoxyl groups were more than expected on the basis of the monomethoxyl derivatives. A significantly higher rate would suggest a general π-orbital participation rather than a more localized effect on one carbon of the aromatic ring. It is clear that any such effect must be small if it exists since the formolysis rate is only slightly faster than either of the monomethoxy compounds. A more quantitative analysis can be made on the basis of the fractions of the rates resulting from participation. This will be considered below.

The position of the *gem*-dimethyl group on the 4-aryl-1-butyl *p*-bromobenzenesulfonate side chain has a significant effect upon the solvolysis rates. The 3,3-dimethyl-4-phenyl-1-butyl *p*-bromobenzenesulfonate (XIV), reacted 1.3 times faster in acetolysis at 75° and 3.7 times faster in formolysis than the related 4,4-dimethyl compound. The formolysis products from the 3,3-dimethyl compound consisted of 5% 3,3-dimethyl-4-phenyl-1-butyl formate (XV), isolated as the alcohol, and 90% 2,2-dimethyltetralin (XVI). Again Ar_2-6 participation is suspected to be the major mechanism of tetralin formation.



The addition of methoxyl groups to the 3,3-*gem*-dimethyl system caused rate enhancements similar to those in the 4,4-*gem*-dimethyl system. The 3-methoxy derivative is six times and the 4-methoxy derivative is two times more reactive in formolysis at 50° than the 3,3-dimethyl-4-phenyl compound. Clearly Ar_2-6 is more favorable than Ar_1-5 participation.

The final compound in Table I is 2,2-dimethyl-4-phenyl-1-butyl *p*-bromobenzenesulfonate. This compound undergoes formolysis at only half the rate of the 4,4-dimethyl compound. Some Ar_1-5 or Ar_2-6 participation could still be possible here, but the similarity of the rate constant and the entropy of activation (*ca.* 6–10 eu higher than others that show Ar_1-5 or Ar_2-6 participation) to the corresponding values from neopentyl *p*-bromobenzenesulfonate suggest that β-alkyl participation must be the dominant reaction occurring.

The relative reactivities of various 4-aryl-1-butyl derivatives can be assessed more accurately if the rate constants are divided into the component parts resulting from solvent reaction, k_S, and aryl participation, k_Δ. The k_S values of various compounds with the same side chains studied here should be approximately the same, since changes in the aromatic ring are too far away to influence the solvent reaction appreciably. The k_S values are found simply by multiplying the fraction of unrearranged formate ester in the total product by the rate constant measured under the same conditions. The k_Δ values are similarly calculated by multiplying the fraction of tetralin found by the rate constant. Internal consistencies can then be measured and more meaningful comparisons can be made. Measured and calculated k_S and k_Δ values are given in Table III. The k_S values for the first four compounds in the table should have been the same. In the three cases where there were enough data, two agreed very well and the third rather poorly; the k_S of the 4-(*m*-anisyl)-4-methyl-1-pentyl *p*-bromobenzenesulfonate (IV) for formolysis was about 39% too large compared to the compound without the methoxyl group. Some support for the assumption that the k_Δ for 4-methyl-4-phenyl-1-pentyl *p*-bromobenzenesulfonate (I) arises nearly exclusively from Ar_2-6 participation can be obtained by using the value as a k_Δ for the Ar_2-6 part of the reaction of the related *p*-methoxy compound, VIII, and calcualting the yield of the unrearranged tetralin expected (1,1-dimethyl-6-methoxytetralin, X). The calculated value is 18.5% and 22.7% was found. In the 3,4-dimethoxy compound it can be seen that the k_Δ of 21.76×10^{-5} sec^{-1} is only slightly larger than the sum of the k_Δ's of the *m*- and *p*-methoxy derivatives (19.56) and therefore there can be little effect of one methoxyl group upon the other in this reaction.

In both the 4,4- and 3,3-*gem*-dimethyl systems Ar_2-6 ring closure is significantly better than the Ar_1-5 closure. The methoxyl groups in either the meta or para positions, however, are very much less effective in favoring aryl participation in the 4-aryl-1-butyl compounds than they are in the 2-arylethyl system, where factors of 100 are common *vs.* only ~5 in the above samples.

Experimental Section

***p*-Bromobenzenesulfonates.**—These compounds were all prepared by the method described previously.[5]

Kinetic Measurements.—Acetolysis rates[7] and formolysis rates[5] were measured in the usual way.

3-Methyl-3-phenyl-1-butanol.—The reduction of 3-methyl-3-phenylbutyric acid[8,9] with lithium aluminum hydride in ether gave a 93% yield of 3-methyl-3-phenyl-1-butanol, bp 81–82° (0.3 mm), $n^{25}D$ 1.5206 [lit.[10] bp 137–138° (16 mm)].[10]

The *p*-bromobenzenesulfonate had mp 51.5–53.5°. *Anal.* Calcd for $C_{17}H_{19}O_3SBr$: C, 53.27; H, 5.00. Found: C, 53.19; H, 5.14.

3-(4-Acetamidophenyl)-3-methylbutyric Acid.—The acetylation of 244 g of 3-(4-aminophenyl)-3-methylbutyric acid[10] with

(7) S. Winstein, E. Grunwald, and L. Ingraham, *J. Amer. Chem. Soc.*, **70**, 826 (1948).

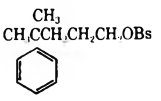
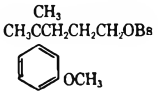
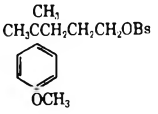
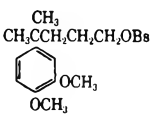
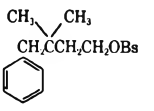
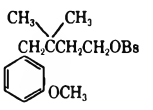
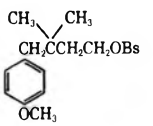
(8) F. Whitmore, C. Weisgerber, and A. Shabica, Jr., *ibid.*, **65**, 1469 (1943).

(9) F. Prout, E. Huang, R. Hartman, and C. Korpics, *ibid.*, **76**, 1911 (1954).

(10) J. Corse and E. Rohrmann, *ibid.*, **70**, 370 (1948).

TABLE III

DISSECTIONS OF RATE CONSTANTS INTO k_S AND k_Δ

Compd	Rel rates HOAc (75°)	Rel rates HCOOH (75°)	HOAc 75.00° 10^5k_S	HOAc 75.00° 10^5k_Δ	HOAc 75.00° k_Δ/k_S	HOAc 75.00° Rel k_Δ	HCOOH 75.00° 10^5k_S	HCOOH 75.00° 10^5k_Δ	HCOOH 75.00° k_Δ/k_S	HCOOH 75.00° Rel k_Δ
	1.0	1.0	1.64[a]	0.26[a]	0.15	1.0	3.64	2.29	0.6	1.0
		2.7					5.05	10.75	2.1	4.7
	1.5	2.1	1.66[a]	1.20[a]	0.72	4.6	3.59	8.81	2.5	3.8
		4.3					(3.64)[b]	(21.76)[b]	6.0	9.5
	1.3	3.7					1.10	21.0	19.1	9.2
		18.7					(1.10)[b]	(110)[b]	100.0	48
	4.2	10.8					(1.10)[b]	(63.2)[b]	57.5	28.

[a] Assuming product composition is the same at 75.00° as was found at 100°. [b] Calculated assuming k_S value is the same as in the compound without the methoxyl group.

155 g of acetic anhydride and 10 g of pyridine at 100° for 1.5 hr gave 263 g of product, mp 138–141°, after crystallization from a mixture of ethyl acetate and pentane. *Anal.* Calcd for $C_{13}H_{17}O_3N$: C, 66.36; H, 7.28. Found: C, 66.58; H, 7.46.

3-(4-Acetamido-3-nitrophenyl)-3-methylbutyric Acid.—A solution of 30 ml of concentrated nitric acid and 40 ml of concentrated sulfuric acid was added dropwise with stirring to 100 g of 3-(4-acetamidophenyl)-3-methylbutyric acid dissolved in 400 ml of concentrated sulfuric acid. The mixture was kept in an ice bath during the addition, and for 20 min afterward. After stirring for another 1 hr without cooling, the solution was poured onto ice. The product soon crystallized, and it was filtered and crystallized from a mixture of ethyl acetate and petroleum ether (bp 30–60°). The yield of bright yellow needles was 64 g. A small sample was recrystallized again for analysis. The material did not melt sharply, but decomposed at about 150°. *Anal.* Calcd for $C_{13}H_{16}O_5N_2$: C, 55.71; H, 5.75. Found: C, 55.83; H, 5.68.

3-Methyl-3-(3-nitrophenyl)butyric Acid.—3-(4-Acetamido-3-nitrophenyl)-3-methylbutyric acid (56 g) was boiled for 2 hr with a solution of 45 ml of concentrated hydrochloric acid and 90 ml of water. This mixture was treated with 50 ml more concentrated hydrochloric acid and cooled to 0° while a solution of 14.5 g of sodium nitrite in 35 ml of water was added during 1.5 hr. Then 104 ml of 50% hypophosphorus acid, cooled to 0°, was added over a period of 30 min. After standing overnight at 0°, the orange solid was filtered and air dried. The yield was 37 g. A small sample, after two recrystallizations from aqueous methanol, melted at 109–110°. *Anal.* Calcd for $C_{11}H_{13}O_4N$: C, 59.18; H, 5.87. Found: C, 59.20; H, 5.85.

3-(*m*-Anisyl)-3-methylbutyric Acid. Method A.—A solution of 80 g of 3-methyl-3-(3-nitrophenyl)butyric acid in 1200 ml of methanol was hydrogenated at 30 psig using 1 g of platinum oxide as catalyst. After filtering, the methanol was evaporated. A dark oil remained which could be crystallized, with great loss, from a mixture of ether and carbon tetrachloride. *Anal.* Calcd for $C_{11}H_{15}O_2N$: C, 68.37; H, 7.82. Found: C, 67.72; H, 7.32). For the conversion of this compound to 3-(*m*-anisyl)-3-methylbutyric acid, purification was not necessary. The crude dark oil was dissolved in ether and the amino acid was extracted with a solution of 35 g of sulfuric acid in 550 ml of water. The extract was cooled to 0° and diazotized with 27.5 g of sodium nitrite in 50 ml of water. After standing for 10 min at 0°, 5 g of urea was added and the solution was added as rapidly as possible to a refluxing solution of 275 ml of water and 70 ml of concentrated sulfuric acid. After a further 10 min of refluxing, the dark mixture was cooled and extracted twice with ether. The extracts were washed with water and the phenol was extracted from the ether phase with a solution of 30 g of potassium hydroxide in 100 ml of water. The aqueous solution was treated with methyl sulfate at 70–90° and the product from acidification of the basic reaction mixture was recrystallized twice from petroleum ether (bp 60–80°). The red-colored product weighed 5.9 g and was sufficiently pure to be used in the next step. A small sample was distilled under reduced pressure, mp 77–78.5°. *Anal.* Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.75. Found: C, 68.94; H, 7.76.

Method B.—To the Grignard reagent prepared from 75 g of *m*-bromoanisole and 10 g of magnesium in ether, 61 g of isopropylidenecyanoacetic ester was added with stirring. The resulting solution was boiled for 1 hr and poured onto ice and hydrochloric acid. The ether phase was separated and the aqueous phase was extracted again with ether. The combined extracts were washed with water and the solvent was evaporated. The dark residue was boiled for 7 hr with 180 g of potassium hydroxide in 600 ml of ethylene glycol. The cooled solution was diluted with 2 l. of water, and a small amount of a black oil was extracted with three portions of chloroform. On acidification, the aqueous solution precipitated a dark oil which was extracted with two portions of ether. The extracts were washed with water and dried and the solvent was evaporated. The dark oil re-

maining was dissolved in hot hexane and decolorized with Norit. The solution deposited 38 g of crystals on cooling, mp 75–77.5°.

3-(*m*-Anisyl)-3-methyl-1-butanol.—This alcohol, 33 g, bp 135–137° (2.5 mm), $n^{25}D$ 1.5258, was prepared by the reduction of the above acid (38 g) with lithium aluminum hydride. *Anal.* Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.18; H, 9.52.

The alcohol yielded a liquid *p*-bromobenzenesulfonate, $n^{25}D$ 1.5660, which was 97% pure by equivalent weight measurements in acetic acid.

3-(*p*-Anisyl)-3-methylbutyric Acid.—This acid has been prepared by two methods: by the methylation of the hydroxy acid prepared by Corse and Rohrman[10] and by a Friedel–Crafts reaction. Although the Friedel–Crafts reaction gave a poor yield, it was more convenient. A mixture of 220 g of anisole, 540 g of anhydrous aluminum chloride, and 100 g of 3-methylcrotonic acid in 1 l. of tetrachloroethane, was heated to 50–70° for 2 hr. The cooled reaction mixture was poured onto ice and hydrochloric acid. The aqueous phase was extracted with chloroform. The combined organic phases were extracted with water and with 210 g of sodium bicarbonate in 2 l. of water. The bicarbonate solution was extracted with ether and acidified. The liberated acid was extracted with ether. Evaporation of the ether left an oil which was crystallized twice from hexane. There was obtained 23 g of colorless solid, mp 85–87° (lit.[10] mp 89.6–91°).

3-(*p*-Anisyl)-3-methyl-1-butanol.—The above acid was reduced in 79% yield with lithium aluminum hydride. The alcohol had bp 130–133° (2.5 mm), $n^{25}D$ 1.5260. *Anal.* Calcd for $C_{18}H_{21}O_4SBr$: C, 52.30; H, 5.12. Found: C, 52.43; H, 4.86.

3-(*o*-Anisyl)-3-methylbutyric Acid.—A Grignard reagent was prepared in ether solution from 230 g of "*o*-methoxyneophyl chloride"[6] and 24 g of magnesium. The reaction was initiated with methyl iodide and 5–6 hr of refluxing was necessary to complete the reaction. A stream of carbon dioxide was then passed into the solution until the solution became cold. Hydrolysis with acid followed by extraction of acidic product into aqueous bicarbonate solution and reacidification gave the crude acid. Several recrystallizations from hexane gave 14 g of product, mp 70.5–71°. Some of the para isomer, mp 83–85°, crystallized initially from the hexane solution. *Anal.* Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.75. Found: C, 69.35; H, 7.94.

3-(*o*-Anisyl)-3-methyl-1-butanol.—Reduction of 14 g of the above acid with 3 g of lithium aluminum hydride in 300 ml of ether gave, after the usual isolation procedure, 12.5 g of alcohol, bp 109–112° (1.5 mm), $n^{25}D$ 1.5272. *Anal.* Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 73.96; H, 9.26.

This alcohol gave a viscous liquid *p*-toluenesulfonate which was 91% pure by equivalent weight measurements in formic acid.

1-Bromo-3-methyl-3-phenylbutane.—A cooled mixture of 74 g of 3-methyl-3-phenyl-1-butanol and 36 g of pyridine was treated with 125 g of phosphorus tribromide and heated on a steam bath for 2 hr. After cooling, the mixture was poured onto ice and an orange solid was filtered off and discarded. The filtrate was extracted with ether. The extract was washed with water and a sodium bicarbonate solution. After drying, the ether was evaporated and the bromide was fractionated. The yield of colorless product, bp 125–127° (11 mm), $n^{25}D$ 1.5370, was 59 g. *Anal.* Calcd for $C_{11}H_{15}Br$: C, 58.16; H, 6.66. Found: C, 58.20; H, 6.44.

4-Methyl-4-phenylpentanoic Acid. Method A.—The Grignard reagent was prepared from 34 g of 1-bromo-3-methyl-3-phenylbutane bromide and 3.7 g of magnesium. The reaction was initiated with 1 g of methyl iodide and the reaction mixture was heated with stirring for 1.5 hr. A stream of dry carbon dioxide was bubbled in until the ether became cold. The reaction mixture was treated with cold dilute sulfuric acid and the ether phase was separated and washed with water. The acid product was extracted from the ether with 25 g of sodium carbonate in 200 ml of water. After washing the carbonate extract with ether, it was acidified and the product was extracted with ether. After drying and evaporation of the solvent, an oil was obtained which could be crystallized from pentane at −30°. The yield of acid, mp 29–31°, was 11.5 g. *Anal.* Calcd for $C_{12}H_{16}O_2$: C, 74.96; H, 8.39. Found: C, 74.99; H, 8.16.

Method B.—This acid was produced in 40% yield by the Willgerodt reaction from 4-methyl-4-phenyl-2-pentanone as described by Campbell and Cromwell.[11]

(11) P. Campbell and N. Cromwell, *J. Amer. Chem. Soc.*, **77**, 5169 (1955).

4-Methyl-4-phenyl-1-pentanol.—The lithium aluminum hydride reduction of 4-methyl-4-phenylpentanoic acid afforded the alcohol, bp 110–111° (3 mm), $n^{25}D$ 1.5168, in 94% yield. *Anal.* Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.84; H, 10.41.

The *p*-bromobenzenesulfonate melted at 38–40°. *Anal.* Calcd for $C_{18}H_{21}O_3SBr$: C, 54.41; H, 5.33. Found: C, 54.46; H, 5.19.

4-(*m*-Anisyl)-4-methylpentanoic Acid.—The crude liquid *p*-bromobenzenesulfonate prepared from 33 g of 3-(*m*-anisyl)-3-methyl-1-butanol was added to a hot mixture of 75 g of potassium cyanide and 1.5 l. of absolute methanol. The mixture was boiled overnight and half of the solvent was distilled off. The remainder of the solution was poured into 4 l. of water. The nitrile which separated was extracted with three portions of ether and the extracts were washed with water. After removing the solvent, the crude nitrile was boiled for 3 hr with a solution of 150 g of potassium hydroxide in 500 ml of ethylene glycol. The cooled reaction mixture was diluted with 3 l. of water and a small amount of oil was extracted with three portions of chloroform. The aqueous phase was then acidified and the crude acid was extracted with two portions of ether. The extracts were washed with water and dried. After the solvent had been evaporated, the oil remaining was crystallized (with seeding) from pentane. The yield of light tan product, mp 47–50°, was 20 g. Another crystallization from pentane gave shiny, colorless needles, mp 48–50°. *Anal.* Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.06; H, 8.21.

4-(*m*-Anisyl)-4-methyl-1-pentanol.—The reduction of 10 g of 4-(*m*-anisyl)-4-methylpentanoic acid with 2 g of lithium aluminum hydride gave 9.35 g of alcohol, bp 145–148° (3 mm), $n^{25}D$ 1.5222. *Anal.* Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 74.92; H, 9.81.

The *p*-bromobenzenesulfonate was obtained as a colorless, viscous liquid, $n^{25}D$ 1.5588, which was shown to be 88% pure by equivalent weight measurements in acetic and formic acid. Purification of the *p*-bromobenzenesulfonate was achieved by chromatography on alumina. A pentane eluate was discarded and the sulfonate was eluted with 30% benzene–70% pentane. The chromatographed material, though still not crystalline ($n^{25}D$ 1.5228), was shown to be 97 ± 1% pure by an equivalent weight measurement in formic acid.

3-(*p*-Anisyl)-1-bromo-3-methylbutane.—A mixture of 20 g of 3-(*p*-anisyl)-3-methyl-1-butanol and 8 g of pyridine was treated with 28 g of phosphorus tribromide. The hot mixture was stirred for 30 min and poured onto ice. The product was extracted with ether and the extract was washed with water, dried, and distilled. The bromide, bp 126–128° (4 mm), $n^{25}D$ 1.5380, weighed 10 g.

4-(*p*-Anisyl)-4-methylpentanoic Acid. A.—A Grignard reagent was prepared in ether from 6 g of methyl iodide, 2 g of magnesium, and 10 g of 3-*p*-anisyl-1-bromo-3-methylbutane. After refluxing for 2 hr, the mixture was cooled and poured onto an excess of dry carbon dioxide. The mixture was decomposed with cold dilute hydrochloric acid. The ether phase was separated and washed with water and with 100 ml of a 10% sodium bicarbonate solution. Acidification of the bicarbonate extract gave the crude acid. After air-drying, the acid was recrystallized from pentane, giving 1.5 g of product, mp 65.5–67°. *Anal.* Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.17; H, 7.92.

4-Methyl-4-pentanolactone.—Methyl Grignard reagent was prepared from 200 g of methyl iodide and 33.8 g of magnesium in 1 l. of ether and added during 2.5 hr to a well stirred solution of 200 g of ethyl levulinate in 2.5 l. of ether at −80°. After the addition, the mixture was allowed to stand at room temperature overnight. Then 38 ml of concentrated sulfuric acid was diluted with ice and water to 300 ml and added to the reaction mixture. The precipitated solid dissolved slowly and it was necessary to cool the flask to keep the hydrolysis under control. After the solid had dissolved, the ether phase was separated and the aqueous phase was extracted again with ether. The combined extracts were washed with water, aqueous sodium bisulfite, water, and finally with aqueous sodium bicarbonate. After drying, the solvent was removed and the lactone was distilled. The product, bp 50–60° (1.5 mm), $n^{25}D$ 1.4300, weighed 100 g. The material was purified by hydrolysis. For this purpose, 100 g of the crude lactone was boiled for 1 hr with 60 g of sodium hydroxide in 250 ml of water. The cooled solution was extracted twice with ether and acidified carefully with cold

dilute hydrochloric acid. The lactone was extracted with three portions of ether, dried, and distilled. The purified product, bp 87–90° (16 mm), n^{25}D 1.4310, weighed 71.5 g (45%).

4-(*p*-Anisyl)-4-methylpentanoic Acid. Method B.—To a solution of 60 g of anhydrous aluminum chloride in 200 ml of tetrachloroethane, cooled in ice water, was added dropwise with stirring a mixture of 30 g of anisole and 23 g of crude 4-methyl-4-pentanolactone. After the addition the mixture was warmed to 50° for 30 min and poured onto ice and hydrochloric acid. The organic phase was separated and the aqueous solution was extracted with chloroform. The combined organic extracts were washed with water and the acid product was extracted with aqueous sodium bicarbonate. Acidification of the bicarbonate extract gave an oil which soon crystallized. The colorless solid obtained was recrystallized from hexane, giving 2.3 g of material, mp 65–67°.

4-(*p*-Anisyl)-4-methyl-1-pentanol.—The reduction of 5.3 g of 4-(*p*-anisyl)-4-methylpentanoic acid with 1 g of lithium aluminum hydride produced 4.5 g of the alcohol, bp 147–148° (4 mm), n^{25}D 1.5213. *Anal.* Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 74.74; H, 9.64. The *p*-bromobenzenesulfonate melted at 58–59°. *Anal.* Calcd for $C_{19}H_{23}O_4SBr$: C, 53.40; H, 5.42. Found: C, 53.26; H, 5.34.

3-(3,4-Dimethoxyphenyl)-3-methylbutyric Acid.—A solution of 50 g of 3-methylcrotonic acid and 70 g of veratrole in 500 ml of tetrachloroethane was stirred and cooled in ice while 270 g of powdered anhydrous aluminum chloride was added. The mixture was heated at 50° with stirring for 2 hr. After cooling and pouring onto ice and hydrochloric acid, the organic phase was steam-distilled in the presence of 100 g of sodium bicarbonate in 500 ml of water. After the solvents were removed, the residue was cooled and filtered from some dark tar. The filtrate was acidified and extracted with ether. The extract yielded an oil which was methylated with 80 g of sodium hydroxide in 150 ml of water and 130 g of dimethyl sulfate. The product from the methylation was crystallized from a mixture of benzene and petroleum ether. The light tan crystals obtained weighed 25 g. A small sample, crystallized again, consisted of long, colorless needles, mp 94–94.5°. *Anal.* Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.82; H, 7.87.

3-(3,4-Dimethoxyphenyl)-3-methyl-1-butanol.—A solution of 17 g of 3-(3,4-dimethoxyphenyl)-3-methylbutyric acid in 50 ml of ether was added to 3 g of lithium aluminum hydride in 500 ml of ether and boiled for 8 hr. The alcohol, bp 144–148° (3 mm), n^{25}D 1.5299, weighed 10 g. *Anal.* Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.42; H, 9.08.

1-Bromo-3-(3,4-dimethoxyphenyl)-3-methylbutane.—The *p*-toluenesulfonate was prepared from 10 g of 3-(3,4-dimethoxyphenyl)-3-methyl-1-butanol and 20 g of *p*-toluenesulfonyl chloride by the usual method. The liquid product was dissolved in 400 ml of dry acetone containing 20 g of lithium bromide and the solution was boiled for 3 days. The acetone was removed by distillation and the residue was treated with water. The bromide was extracted with ether and distilled. There was obtained a pale yellow liquid, bp 131–133° (2 mm), n^{25}D 1.5431, weighing 10.2 g. *Anal.* Calcd for $C_{13}H_{19}O_2Br$: C, 54.36; H, 6.67. Found: C, 54.31; H, 6.59.

4-(3,4-Dimethoxyphenyl)-4-methylpentanoic Acid. Method A.—Carbonation of the Grignard reagent prepared from 10 g of 1-bromo-3-(3,4-dimethoxyphenyl)-3-methylbutane with gaseous carbon dioxide yielded a small sodium bicarbonate soluble fraction. This material crystallized after being distilled and standing for 2 months. Once seeds were available, it was recrystallized from a mixture of ether and pentane. The yield was only 0.3 g. A small sample was recrystallized for analysis, mp 41–42°. *Anal.* Calcd for $C_{14}H_{20}O_4$: C, 66.64; H, 7.99. Found: C, 66.46; H, 7.47.

Method B.—To 100 ml of tetrachloroethane, cooled with ice and stirred, was added 20 g of anhydrous aluminum chloride followed by a mixture of 12 g of 4-methyl-4-pentanolactone and 25 g of veratrole. After the addition, the solution was stirred at 50° for 1 hr. The resulting solution was cooled and poured onto ice and hydrochloric acid. The aqueous phase was extracted twice with chloroform and the combined organic phases were washed twice with water. The product was extracted with a solution of 15 g of sodium bicarbonate in 200 ml of water in three portions. The bicarbonate extracts were washed twice with chloroform and acidified. The acid was extracted with three portions of chloroform. After drying, the solvent was removed and the acid was distilled. After *ca.* 1 g of unreacted lactone, the acid distilled, bp 170° (0.7 mm). The distillate (1.5 g) was crystallized from ether–pentane twice. There was obtained 0.5 g of acid, mp 42.5–44°. The mother liquors gave an additional 0.5 g of less pure acid, mp 41–42°. *Anal.* Calcd for $C_{14}H_{20}O_4$: C, 66.64; H, 7.99. Found: C, 66.67; H, 8.25.

4-(3,4-Dimethoxyphenyl)-4-methyl-1-pentanol.—Heating 1.0 g of the above acid with 0.5 g of lithium aluminum hydride in 200 ml of ether for 24 hr gave, after the usual purification, 0.85 g of alcohol, bp *ca.* 140° (0.8 mm), n^{25}D 1.5259. *Anal.* Calcd for $C_{14}H_{22}O_3$: C, 70.55; H, 9.31. Found: C, 70.35; H, 9.45. This alcohol also gave a liquid *p*-bromobenzenesulfonate which was quite pure by equivalent weight measurements in formic acid.

3,3-Dimethyl-4-phenylbutyric Acid.—This material, bp 140–145° (5 mm), n^{25}D 1.5130, was prepared from benzylmagnesium bromide and isopropylidenecyanoacetic ester by the method of Prout, *et al.*[9]

3,3-Dimethyl-4-phenyl-1-butanol.—Reduction of 20 g of the above acid with 4 g of lithium aluminum hydride afforded 17.5 g of the alcohol, bp 112–116° (4 mm), n^{25}D 1.5164. *Anal.* Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.05; H, 10.03.

The *p*-bromobenzenesulfonate of this alcohol, mp 29.5–30.5°, was crystallized from a mixture of pentane and ether. *Anal.* Calcd for $C_{18}H_{21}O_3SBr$: C, 54.41; H, 5.33. Found: C, 54.28; H, 5.58.

4-(*m*-Anisyl)-3,3-dimethylbutanoic Acid.—The Grignard reagent was prepared by a high dilution technique from 34 g of *m*-methoxybenzyl bromide,[12] n^{25}D 1.5733, bp 86–88° (2.0 mm). To the stirred Grignard reagent (obtained in 65% yield) was added 18 g of isopropylidenecyanoacetic ester. The solution was stirred and boiled for 2 hr more after the addition was complete. Then cold dilute hydrochloric acid was added with external cooling. The aqueous phase was separated and extracted with ether. The combined ether extracts were washed with water and with aqueous sodium bicarbonate. The solvent was removed and the residue was boiled 15 hours with a solution of 50 g of potassium hydroxide in 200 ml of ethylene glycol. After cooling, the hydrolysis solution was poured into 500 ml of water and extracted twice with ether. Acidification of the aqueous phase liberated the acid. The acid was extracted three times with ether. A considerable amount of material was accidentally lost during the extraction. The combined ether extracts were washed twice with water and dried. Removal of the ether left a dark oil which was distilled, bp 150–155° (1.0 mm), n^{25}D 1.5204, to give a viscous pale yellow oil weighing 7.7 g which could not be induced to crystallize. *Anal.* Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.41; H, 7.98.

4-(*m*-Anisyl)-3,3-dimethyl-1-butanol.—The reduction of 7.5 g of 4-(*m*-anisyl)-3,3-dimethylbutanoic acid with 1.5 g of lithium aluminum hydride in ether gave 6.5 g of the alcohol, bp 125–130° (0.8 mm), n^{25}D 1.5230, as a viscous pale yellow liquid. *Anal.* Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 75.18; H, 9.60.

The *p*-bromobenzenesulfonate of this alcohol could not be crystallized. The crude ester, n^{25}D 1.5569, was 93% pure by equivalent weight measurements in formic acid.

3,3-Dimethyl-4-(*p*-nitrophenyl)butyric Acid.—3,3-Dimethyl-4-phenylbutyric acid (14 g) was added to 25 ml of fuming nitric acid at −30° over a period of 10 min. The stirred mixture was allowed to warm up to 5° over a period of 3 hr and poured onto ice. After scratching and standing for about 1 hr at 0°, the yellow solid was filtered, washed, dried, and recrystallized from a mixture of ether and pentane and then twice from ether. There was obtained 1.6 g, mp 101–103°. *Anal.* Calcd for $C_{12}H_{15}O_4N$: C, 60.55; H, 6.37. Found: C, 60.91; H, 6.56.

The mother liquors gave 5 g of less pure acid, mp 95–100°, which was suitable for the hydrogenation described below.

4-(*p*-Aminophenyl)-3,3-dimethylbutyric Acid.—A solution of 11.5 g of 3,3-dimethyl-4-(*p*-nitrophenyl)butyric acid in 100 ml of methanol was hydrogenated at 15 psig in the presence of 0.3 g of platinum oxide until no more hydrogen was absorbed (*ca.* 15 min). The resulting hot solution was cooled and filtered through Celite and concentrated to *ca.* 40 ml. After cooling, the crude acid was filtered and recrystallized from methanol. There was obtained 4.5 g of the amino acid, mp 155–157°. *Anal.* Calcd for $C_{12}H_{17}O_2N$: C, 69.53; H, 8.27. Found: C, 69.70; H, 8.19.

(12) R. B. Woodward, *J. Amer. Chem. Soc.*, **62**, 1481 (1940).

3,3-Dimethyl-4-(*p*-hydroxyphenyl)butyric Acid.—A mixture of 4.5 g of the above amino acid and 50 ml of water containing 2 ml of concentrated sulfuric acid was cooled to 0° and treated with a solution of 2.5 g of sodium nitrite in 10 ml of water. The solution was filtered from a small amount of insoluble material, treated with 3 g of urea, and slowly added to 20 ml of boiling water containing 5 ml of sulfuric acid. After 10 min of boiling the mixture was cooled and the product was extracted with two portions of ether. The extracts were washed with water and dried. After removing the ether, a dark oil remained which solidified on scratching. The material was recrystallized from a mixture of carbon tetrachloride and hexane to give 1.6 g of an orange solid, mp 104–106°. The entire crude product was recovered and used in the methylation described below.

4-(*p*-Anisyl)-3,3-dimethylbutyric Acid.—The above crude hydroxy acid was dissolved in a solution of 12 g of sodium hydroxide in 50 ml of water and treated with 15 g of dimethyl sulfate. The reaction mixture was stirred and warmed until the methyl sulfate had reacted. The resulting solution was cooled, washed with ether, and acidified. The precipitated oil was extracted with ether. After washing the extracts with water and drying, the solvent was removed and the residue was crystallized in poor yield from hexane. The product, mp 64–66.5°, however, was still not pure. Since the substance was difficult to purify, the crude product was reduced in the following step.

4-(*p*-Anisyl)-3,3-dimethyl-1-butanol.—The above crude acid was reduced with 1 g of lithium aluminum hydride. The product, bp 137–140° (1.5 mm), $n^{25}D$ 1.5234, weighed 1.8 g. *Anal.* Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 74.71; H, 9.49.

The *p*-bromobenzenesulfonate of this alcohol was a viscous liquid, $n^{25}D$ 1.5602, which was 84% pure by equivalent weight measurements in acetic and formic acid.

2,2-Dimethyl-4-phenyl-1-butanol.—The reduction of 8.3 g of 3-benzoyl-2,2-dimethylpropionic acid by the Clemmensen method[13] gave 2.6 g of 2,2-dimethyl-4-phenylbutyric acid, mp 92–95°. The latter acid was reduced with 1 g of lithium aluminum hydride in ether by the usual method. The desired alcohol, bp 93–95° (0.8 mm), $n^{25}D$ 1.5109, weighed 2.3 g and had a strong rose-like odor. *Anal.* Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.78; H, 10.16.

This alcohol gave a *p*-bromobenzenesulfonate, mp 64–65.5°. *Anal.* Calcd for $C_{18}H_{21}O_3SBr$: C, 54.41; H, 5.33. Found: C, 54.45; H, 5.48.

4,4-Dimethyl-6-methoxy-1-tetralone.—To a solution of 10 g of 4-(*m*-anisyl)-4-methylpentanoic acid in 40 ml of benzene was added 12 g of phosphorus pentachloride in small portions. After standing for 1 hr, the solution was cooled and a cold solution of 8 g of stannic chloride in 20 ml of benzene was added all at once. The solution became green and a viscous green oil separated which soon crystallized. After being cooled and shaken for 15 min, the mixture was poured onto ice and hydrochloric acid. The benzene phase was separated and the aqueous solution was extracted with ether. The extracts were washed twice with cold dilute hydrochloric acid and then with water and aqueous sodium bicarbonate. After drying, the solvent was evaporated and the residue was crystallized from pentane. There was obtained 7.6 g of light tan crystals. Another crystallization from pentane gave a colorless sample, mp 51–53°. *Anal.* Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.20; H, 7.70.

1,1-Dimethyl-7-methoxytetralin.—The above tetralone (7 g) was boiled with 50 g of amalgamated zinc, 25 ml of water, and 55 ml of concentrated hydrochloric acid. The solution was refluxed for 2 days, and 10 ml of concentrated hydrochloric acid was added every 12 hr. The pale yellow product was extracted with two portions of ether and the extracts were washed with water and aqueous sodium bicarbonate. After drying, the extracts were concentrated and distilled over sodium hydride. The product, bp 105–106° (3.5 mm), $n^{25}D$ 1.5291, weighed 4.2 g. *Anal.* Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.53. Found: C, 82.20; H, 9.42.

1,2-Dimethyl-7-methoxynaphthalene.—A solution of 0.5 g of 1,1-dimethyl-7-methoxytetralin and 2 g of tetrachloro-1,2-quinone in 5 ml of benzene was refluxed for 20 hr according to the general method reported by Linstead.[14] The reaction mixture was diluted with 25 ml of hexane and chromatographed on 20 g of alumina using hexane as eluent. The first 500 ml of solvent was evaporated and the residue was dissolved in a few milliliters of ether, filtered, and treated with 1 g of picric acid in ether. The solution was concentrated to 40 ml and cooled. The picrate of 1,2-dimethyl-7-methoxynaphthalene crystallized as long orange needles. The product, after recrystallization from methanol, had mp 134.5–135.5° and weighed 0.55 g. *Anal.* Calcd for $C_{19}H_{17}O_8N_3$: C, 54.94; H, 4.13. Found: C, 54.88; H, 4.36.

4,4-Dimethyl-1-tetralone.[11]—The acid chloride was prepared from 100 g of crude 4-phenyl-4-methylpentanoic acid and 90 g of thionyl chloride. The reaction mixture was heated on the steam bath for 30 min and the excess thionyl chloride was distilled under reduced pressure at 100°. The crude acid chloride was then added dropwise to a cold, stirred solution of 80 g of anhydrous powdered aluminum chloride in 450 ml of carbon disulfide. After the addition was complete, the solution was heated to boiling for 10 min and poured onto ice and hydrochloric acid. The organic phase was separated and the aqueous phase was extracted with ether. The combined organic phases were washed with water and with aqueous sodium bicarbonate. The solution was dried and the solvent was distilled. The oil remaining after the removal of the solvent was chromatographed on 1200 g of alumina with pentane. The liquid product obtained, bp 109–110° (3.5 mm), mp 12–13°, $n^{25}D$ 1.5492, weighed 63 g.

4,4-Dimethyl-7-nitro-1-tetralone.—The above tetralone (16 g) was added with stirring to 50 ml of ice cold concentrated sulfuric acid. Then a cold solution of 5 ml of concentrated nitric acid and 10 ml of concentrated sulfuric acid was added with stirring and ice cooling during 5–10 min. The mixture was stirred at 0° for 30 min and then allowed to warm up to room temperature during 30 more min. The reaction mixture was poured onto ice and the pale yellow solid formed was filtered, washed with water, and recrystallized twice from ethanol to give 12.5 g of product, mp 160–161°. *Anal.* Calcd for $C_{12}H_{13}O_3N$: C, 65.74; H, 5.97. Found: C, 65.74; H, 6.08.

4,4-Dimethyl-7-hydroxy-1-tetralone.—A suspension of 36 g of 4,4-dimethyl-7-nitro-1-tetralone in 200 ml of methanol was hydrogenated at 20 psig using 0.2 g of platinum oxide as catalyst. Several hours were required before the uptake of hydrogen stopped. The catalyst was filtered using a filter aid and the filtrate was concentrated on the steam bath under reduced pressure. The amine was obtained as a brown oil which could not be crystallized. This crude amine was treated with a cold solution of 20 ml of concentrated sulfuric acid in 200 ml of water. The amine sulfate immediately crystallized from the solution. The solution was kept at 0° while a saturated aqueous solution of sodium nitrite was added with stirring until there was a positive starch–iodide test, 30 min after the last nitrite addition. A few grams of urea were added and a small insoluble residue was removed by filtration. The cold diazonium salt solution was added as rapidly as possible to a boiling solution of 100 ml of concentrated sulfuric acid and 900 ml of water. The solution was boiled for 1 hr after the addition and cooled. The brown solid so obtained was filtered, air-dried, and recrystallized twice from benzene. The yellow hydroxy tetralone, mp 135–136° weighed 15 g. A colorless sample was obtained by sublimation, mp 135–136°. *Anal.* Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.65; H, 7.39.

4,4-Dimethyl-7-methoxy-1-tetralone.—The above phenol (14.5 g) was dissolved in a solution of 12 g of sodium hydroxide in 50 ml of water and methylated with 30 g of dimethyl sulfate. The product was distilled, bp 120–122° (1.5 mm), and recrystallized twice from pentane, mp 53–54°. *Anal.* Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.45; H, 7.96.

1,1-Dimethyl-6-methoxytetralin.—The Clemmensen reduction of the preceding tetralone (7 g) was carried out at reflux temperature for 48 hr with 50 g of amalgamated zinc, 25 ml of water, 30 ml of toluene, and 55 ml of concentrated hydrochloric acid, adding 10 ml more acid every 12 hr. The tetralin, distilled from sodium hydride, bp 89–91° (1.0 mm), $n^{25}D$ 1.5311, weighed 4.0 g. *Anal.* Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.53. Found: C, 81.88; H, 9.71.

1,2-Dimethyl-6-methoxynaphthalene.—The above tetralin (0.5 g) was boiled with 2 g of tetrachloro-1,2-quinone in 5 ml of benzene for 20 hr. The product was isolated by chromatography as in the 1,1-dimethyl-7-methoxytetralin case. Recrystallization of the picrate from absolute ethanol gave 0.05 g of product, mp 131–132°, as orange clusters of needles. The mixture melting point with 1,2-dimethyl-6-methoxynaphthalene

(13) G. Clemo and H. Dickenson, *J. Chem. Soc.*, 256 (1937).

(14) R. Linstead, E. Braude, L. Jackman, and A. Beams, *Chem. Ind. (London)*, 1174 (1954).

picrate (mp 134.5–135.5°) was 114–125°. *Anal.* Calcd for $C_{19}H_{17}O_8N_3$: C, 54.94; H, 4.13. Found: C, 54.39; H, 4.66.

4-*o*-Anisylbutyric Acid.—To a solution of 15 g of sodium metal in 700 ml of dry ethanol was added 100 g of diethyl malonate. Then 100 g of β-*o*-anisylethyl *p*-toluenesulfonate[15] was added. The solution was heated and shaken until the tosylate had dissolved and then boiled overnight. The reaction mixture was cooled and poured into water. After acidification, the product was extracted with three portions of ether. Evaporation of the ether left an oil which was boiled with 140 g of potassium hydroxide in 400 ml of ethylene glycol for 2 hr. After cooling and diluting with water, oily by-products were extracted with two portions of ether and discarded. The clear aqueous solution was acidified with 300 ml of concentrated hydrochloric acid and the organic acid was extracted with three portions of ether. After drying, the solvent was removed and the solid malonic acid so obtained was distilled. The acid lost carbon dioxide at about 190° and the 4-*o*-anisylbutyric acid formed distilled at 155–160° (2.5 mm). The product, 39 g (64%), crystallized on cooling to a colorless solid, mp 39–40.5° (lit.[16] mp 39–39.5°).

The ethyl ester of this acid was prepared by boiling 30 g of the acid with 60 ml of dry ethanol and 0.5 ml of sulfuric acid overnight. The ester, 32 g, bp 115–117° (1.5 mm), $n^{25}D$ 1.5010, was a colorless, nearly odorless liquid. *Anal.* Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.14; H, 8.25.

5-(*o*-Anisyl)-2-methyl-2-pentanol.—To the Grignard reagent prepared from 9 g of magnesium and 52 g of methyl iodide in 500 ml of ether was added dropwise with stirring 40 g of ethyl 4-*o*-anisylbutyrate. After the addition, the solution was boiled for 2 hr and hydrolyzed with saturated aqueous ammonium chloride. The alcohol, bp 108–110° (0.8 mm), $n^{25}D$ 1.5142, was obtained as a colorless, viscous liquid weighing 44.5 g. *Anal.* Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 74.75; H, 9.86.

1,1-Dimethyl-5-methoxytetralin.—To 50 ml of 85% (by weight) aqueous sulfuric acid, cooled to 0°, was added dropwise with stirring 10 g of 5-(*o*-anisyl)-2-methyl-2-pentanol. The alcohol dissolved at first and then an oil separated. The addition funnel was rinsed with an additional 10 ml of cold 85% sulfuric acid which was added to the main reaction mixture. The pale pink solution was allowed to stir without cooling for 30 min and poured onto ice and water. The tetralin was extracted with three 100-ml portions of pure pentane. The combined extracts were washed with water twice and with aqueous sodium bicarbonate. After drying, the solvent was removed through a short Vigreux column and the colorless product was distilled. The yield of product, bp 90–93° (1.5 mm), $n^{25}D$ 1.5352, was 8.45 g. Three recrystallizations from pentane at −80° and redistillation gave a purer sample, $n^{25}D$ 1.5353, mp 21–22°. *Anal.* Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.53. Found: C, 82.24; H, 9.35.

4,4-Dimethyl-8-methoxy-1-tetralone.—A solution of 5 g of 1,1-dimethyl-5-methoxytetralin in 25 ml of acetic acid was cooled to 0° and stirred while a cold solution of 4.2 g of chromic acid in 12 ml of acetic acid and 2 ml of water was added dropwise, according to a method described by Linstead.[14] After the addition (*ca.* 15 min) the solution was stirred at room temperature for 4 hr. The reaction mixture was poured into 500 ml of water extracted four times with pentane. The extracts were washed with water twice and with aqueous sodium bicarbonate. The pentane solution was dried and distilled. Unreacted tetralin, bp 90–100° (1.5 mm), weighing 1 g, distilled first. The ketone, bp 100–135° (1.5 mm), weighed 3 g. Crystallization from hexane gave 1.1 g of ketone, mp 86–87°. A second crystallization gave material of mp 86.5–87.5°. *Anal.* Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.51; H, 7.89.

4,4-Dimethyl-8-hydroxy-1-tetralone.—The preceding methyl ether (1 g) was boiled for 4 hr with 10 ml of 48% aqueous hydrobromic acid and 2 ml of acetic acid. The reaction mixture was poured into cold water and the product was extracted with three portions of ether. The extracts were washed with water and then with cold dilute sodium hydroxide. A precipitate immediately appeared. The greenish solid was filtered, washed well with ether and water, and then treated with cold dilute hydrochloric acid. The oil which separated was extracted with two portions of ether, washed with water, dried, and distilled. The product, 0.4 g, was a pale yellow liquid which readily crystallized on cooling, mp 28–29°. The substance gave a strong violet color with ferric chloride in methanol and a positive carbonyl test with 2,4-dinitrophenylhydrazine in sulfuric acid and ethanol. The infrared spectrum showed a broad band at 3500–2200 cm^{-1} resulting from strong intramolecular hydrogen bonding. *Anal.* Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.76; H, 7.34.

1,2-Dimethyl-5-methoxynaphthalene.—A solution of 0.5 g of 1,1-dimethyl-5-methoxytetralin, 2 g of tetrachloro-1,2-quinone, and 5 ml of benzene was boiled for 20 hr. After cooling and diluting with 25 ml of hexane the products were chromatographed. The naphthalene was eluted with 700 ml of hexane. The product was dissolved in 20 ml of methanol, filtered from an insoluble crystalline material, and treated with 0.4 g of picric acid in 5 ml of methanol. On cooling, the picrate separated as red needles weighing 0.4 g. Recrystallization from methanol gave 0.25 g, mp 143–144°. *Anal.* Calcd for $C_{19}H_{17}O_8N_3$: C, 54.94; H, 4.13. Found: C, 55.16; H, 4.42.

Formolysis Products of 4-Methyl-4-phenyl-1-pentyl *p*-Bromobenzenesulfonate.—A solution of 5.40 g of dry sodium formate in 1 l. of formic acid (0.37% water) was heated to 75° and 27.7 g of the pure *p*-bromobenzenesulfonate was added. The solution was shaken until the sulfonate had dissolved and then kept at 75° for 43 hr. The cooled formolysis solution was poured into 3 l. of water and the products were extracted with five 500-ml portions of pure pentane. The combined extracts were washed with water and aqueous sodium bicarbonate and dried. The pentane was distilled through an 18-in. Vigreux column and the oil remaining was reduced with 2. 5 g of lithium aluminum hydride in 800 ml of ether. The reduced products were chromatographed on 300 g of alumina. The tetralin product was eluted with 1 l. of pentane. Evaporation of the solvent through a short Vigreux column and distillation gave the tetralin, 4.05 g (36.1%), bp 60–62° (1.5 mm), $n^{25}D$ 1.5256. This material did not react with potassium permanganate in acetone and had an infrared spectrum essentially identical with that of authentic 1,1-dimethyltetralin. Dehydrogenation of this tetralin (0.5 g) with 2 g of tetrachloro-1,2-quinone in 5 ml of boiling benzene for 20 hr gave 0.25 g of crude 1,2-dimethylnaphthalene, $n^{25}D$ 1.5616, which in turn gave 0.15 g of picrate, mp 129–131°. The mixture melting point with the authentic material described below was 129–131°.

The dehydrogenation of authentic 1,1-dimethyltetralin (0.5 g) with 2 g of tetrachloro-1,2-quinone as described above gave 0.3 g of crude naphthalene, $n^{25}D$ 1.5654, which also gave only 0.15 g of picrate, mp 129–131°. Thus, in our hands this dehydrogenation gave only a 12% yield of 1,2-dimethylnaphthalene instead of the quantitative yield reported by Linstead.[14]

Elution of the alcohol products of the formolysis was accomplished with 1500 ml of ether. The alcohol, bp 100–105° (1.5 mm), $n^{25}D$ 1.5168, weighed 7.15 g (57.4%). The infrared spectrum of the alcohol was identical with that of authentic 4-methyl-4-phenyl-1-pentanol.

Formolysis Products of 4-(*m*-Anisyl)-4-methyl-1-pentyl *p*-Bromobenzenesulfonate.—To a solution of 1.4 g of sodium formate in 350 ml of formic acid (0.31% water) heated to 75° was added 6.8 g of the liquid *p*-bromobenzenesulfonate (97 ± 1% pure). The solution was mixed well and left at 75° for 15.5 hr. The resulting formolysis solution was poured into 2 l. of water and the products were isolated exactly as in the case of the 4-(*p*-anisyl)-4-methyl-1-pentyl *p*-bromobenzenesulfonate formolysis described above.

The tetralin product, 2.1 g (69.5%), bp 95–100° (1.5 mm), $n^{25}D$ 1.5314 (distilled from sodium hydride under nitrogen), had exactly the same refractive index and infrared spectrum as a mixture of 65% 1,1-dimethyl-7-methoxytetralin and 35% 1,1-dimethyl-5-methoxytetralin. Dehydrogenation of 0.5 g of the tetralin product with 2 g of tetachloro-1,2-quinone as described above gave 0.20 g of the picrate of 1,2-dimethyl-7-methoxynaphthalene, mp 131–133°, mmp 131.5–134°.

The alcohol product from the formolysis was eluted with 1 l. of ether. The product, bp *ca.* 125° (2 mm), $n^{25}D$ 1.5216, weighed 0.60 g (18.2%). The infrared spectrum of this material was nearly identical with the spectrum of pure 4-(*m*-anisyl)-4-methyl-1-pentanol.

Formolysis Products of 4-(*p*-Anisyl)-4-methyl-1-pentyl *p*-Bromobenzenesulfonate.—To a solution of 1.40 g of sodium formate in 330 ml of formic acid (0.33% water), heated to 75°,

(15) S. Winstein, C. R. Lindegren, H. Marshall, and L. L. Ingraham, *J. Amer. Chem. Soc.*, **75**, 154 (1953).

(16) J. Lockett and W. Short, *J. Chem. Soc.*, 789 (1939).

was added 7.0 g of pure *p*-bromobenzenesulfonate. The solution was mixed well and kept at 75° for 16.5 hr and then poured into 2 l. of water. The products were extracted with four 300-ml portions of pure pentane and one of ether. The combined extracts were washed, reduced with 1.5 g of lithium aluminum hydride, and chromatographed as in the above examples. The pentane eluate (600 ml) contained 1.90 g of tetralin. This material, distilled over sodium hydride under nitrogen, had bp 90–92° (1.5 mm), $n^{25}D$ 1.5299. *Anal.* Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.53. Found: C, 81.86; H, 9.70. The refractive index and infrared spectrum of this product agreed exactly with those of a mixture of 68% 1,1-dimethyl-7-methoxytetralin and 32% 1,1-dimethyl-6-methoxytetralin. The dehydrogenation of 0.75 g of the tetralin product with 3 g of tetrachloro-1,2-quinone in 7 ml of benzene for 17 hr, as described above, gave 0.40 g of the picrate of 1,2-dimethyl-7-methoxynaphthalene, mp 131–133.5°, mmp 131–134.5°.

The alcohol product from the formolysis, eluted from the alumina with 1.5 l. of ether, weighed 0.85 g (25%) and had bp 130–132° (1.5 mm), $n^{25}D$ 1.5223.

A second formolysis with 1.50 g of sodium formate, 350 ml of formic acid, and 7.3 g of the *p*-bromobenzenesulfonate was carried out exactly as above. The products were 1.90 g of tetralins (58.8%) of $n^{25}D$ 1.5292 and 0.95 g (28.5%) of alcohol, $n^{25}D$ 1.5211. This alcohol fraction had an infrared spectrum essentially identical with the spectrum of pure 4-(*p*-anisyl)-4-methyl-1-pentanol.

Formolysis Products of 3,3-Dimethyl-4-phenyl-1-butyl *p*-Bromobenzenesulfonate.—To a solution of 2.6 g of sodium formate in 750 ml of formic acid (0.37% water) heated to 75° was added 14.0 g of the *p*-bromobenzenesulfonate. The solution was mixed well and left at 75° for 12 hr. It was then poured into 3 l. of water and the products were extracted with five 500-ml portions of pure pentane. The extracts were washed with water and the products were isolated as above. The tetralin product, eluted with 1 l. of pentane, weighed 5.05 g (89.7%) and had bp 109–110° (23 mm), $n^{25}D$ 1.5174. Dehydrogenation of this material (0.5 g) was accomplished with 2 g of tetrachloro-1,2-quinone in 5 ml of purified dioxane by boiling for 20 hr. Isolating the product by chromatography and distillation gave 0.35 g of the crude naphthalene, which yielded 0.15 g of the pure picrate of 1,2-dimethylnaphthalene.

The alcohol from the formolysis, 0.30 g (4.8%), was eluted with 500 ml of ether and 500 ml of methanol, bp *ca.* 110° (3 mm), $n^{25}D$ 1.5160. The infrared spectrum showed the product to be 3,3-dimethyl-4-phenyl-1-butanol.

Ethyl 4-*p*-Anisylbutyrate.—A mixture of 27 g of 4-*p*-anisylbutyric acid,[17,18] 50 ml of absolute ethanol, and 0.1 ml of concentrated sulfuric acid was boiled for 2 hr. There was obtained from this reaction mixture 25.4 g of colorless ester, bp 125–130° (1.5 mm), $n^{25}D$ 1.4994. *Anal.* Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.21; H, 8.06.

5-(*p*-Anisyl)-2-methyl-1-pentanol.—The Grignard reagent was prepared from 40 g of method iodide and 6 g of magnesium in 200 ml of ether. To this was added 25 g of ethyl 4-*p*-anisylbutyrate with stirring. The resulting solution was boiled for 1 hr and cooled while 200 ml of cold saturated aqueous ammonium chloride was added. Isolation gave 20.5 g of the alcohol, bp 120–122° (1.0 mm), $n^{25}D$ 1.5123. *Anal.* Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 74.54; H, 9.58.

The Reaction of 5-(Anisyl)-2-methyl-2-pentanol with Formic Acid.—A solution of 0.13 g of sodium formate and 2.0 g of the tertiary alcohol in 200 ml of formic acid was heated to 75° for 16 hr. After cooling, the reaction mixture was poured into water and the products were extracted with four portions of pentane. The extracts were washed with water and aqueous bicarbonate and dried. The solvent was distilled and the product was treated with 0.4 g of lithium aluminum hydride. Cold water was added cautiously and the ether solution was separated. The insoluble salts were extracted several times with ether and added to the main ether phase. The combined ether extracts were washed with water and aqueous sodium bicarbonate, dried, and concentrated. The product was chromatographed on 100 g of alumina. Pentane eluted 1.7 g, bp 87–90° (1.5 mm), $n^{25}D$ 1.5299. The infrared spectrum was identical with that of 1,1-dimethyl-7-methoxytetralin. The absence of bands at 1260, 1140, and 835 cm^{-1} limits the amount of the 1,1-dimethyl-6-methoxytetralin possibly present to less than 1%. Dehydrogenation of the product (0.5 g) with 2 g of tetrachloro-1,2-quinone in benzene gave 0.4 g of the picrate of 1,2-dimethyl-7-methoxynaphthalene, mp 130–132°.

Elution of the alumina column with ether gave only a trace (less than 0.1 g) of alcohol.

The Reaction of 5-(*p*-Anisyl)-2-methyl-2-pentanol with Acetic Acid.—A solution of 5.0 g of the alcohol in 100 ml of 0.0310 *M* sodium acetate in dry acetic acid, 500 ml of dry acetic acid, and 3 ml of acetic anhydride was heated at 100.0° for 66 hr. The reaction mixture was cooled, poured into water, and extracted as usual and the products were reduced with 1.0 g of lithium aluminum hydride and chromatographed as in the formic acid reaction described above. The chromatography gave two fractions. The first fraction, eluted with pentane, bp 85–90° (1.5 mm), $n^{25}D$ 1.5122, weighed 1.7 g (37.2%). The second fraction, 2.9 g (58.0%), bp 125–127° (1.5 mm), $n^{25}D$ 1.5123, was eluted with ether. The infrared spectrum was identical with that of pure 5-(*p*-anisyl)-2-methyl-2-pentanol.

A 0.1117-g sample of the first fraction absorbed 14.7 ml of hydrogen at 26° and 750 mm when hydrogenated in acetic acid with 10% Pd/C. A 1.0-g sample of the olefin was also oxidized with 1.5 g of osmium tetroxide and the products were chromatographed. Less than 0.1 g of inert material was eluted with pentane.

Stability of 1,1-Dimethyl-6-methoxytetralin in Formic Acid.—A solution of 0.5 g of the pure tetralin in 50.0 ml of dry formic acid was heated to 75.0° for 17 hr. The solution was cooled and poured into water and the product was extracted with three portions of pentane. The extracts were washed with water and aqueous sodium bicarbonate. The solution was dried and concentrated. Distillation of the product from sodium hydride gave 0.40 g (80%) of a colorless liquid, bp 93° (1.5 mm), $n^{25}D$ 1.5304. The infrared spectrum was identical with that of the starting tetralin. The absence of bands at 1075, 1045, 795, and 700 cm^{-1} indicated that less than 1% of 1,1-dimethyl-7-methoxytetralin could have been present.

The Acetolysis Products of 4-(*p*-Anisyl)-4-methyl-1-pentyl *p*-Bromobenzenesulfonate with Lithium Acetate.—A solution of 10.0 ml of 1.00 *M* lithium acetate in dry acetic acid was added to 1500 ml of dry acetic acid and the resulting solution was heated to 100.0°. Then 9.5 g of the *p*-bromobenzenesulfonate was added. After 1 hr at 100.0°, a titration showed the solution to be 0.0051 *M* in acetate ion, and 5.0 ml of 1.00 *M* lithium acetate was added. In 1.5 hr the solution was 0.0057 *M* in acetate ion and another 5.0 ml of 1 *M* lithium acetate was added. A third portion of 10.0 ml of 1 *M* lithium acetate was added after another 2 hr and 15 min when the solution was 0.0064 *M* in acetate ion. After a total of 56 hr at 100.0°, the solvolysis solution was cooled and poured into water. The products were extracted with five portions of pentane, washed, etc., reduced with 1.5 g of lithium aluminum hydride, and chromatographed on 200 g of alumina exactly as described in the examples above. The first fraction, 1.7 g, bp 85–90° (1.5 mm), $n^{25}D$ 1.5233, was eluted with pentane. The second fraction, 2.65 g, bp 125–130° (1.5 mm), $n^{25}D$ 1.5220, was eluted with ether.

The first fraction reacted slowly with potassium permanganate in acetone. Quantitative hydrogenation of a 0.2221-g sample with 10% Pd/C in acetic acid at 26° and 750 mm required 12.2 ml of hydrogen, hydrogenation being complete in 15 min (41.0% olefin). The infrared spectrum of the olefin mixture showed strong absorption at 825 cm^{-1}, probably indicating trisubstituted olefins. (This band is not present in the possible tetralin products.) The olefins were removed from a 1.00-g sample of the mixture by oxidation with 2 g of osmium tetroxide in ether with a trace of pyridine. Decomposition of the osmic esters with mannitol and aqueous potassium hydroxide gave a mixture of tetralines and glycols. Chromatography on alumina gave 0.65 g (65%) of tetralins, bp 100° (2.5 mm), $n^{25}D$ 1.5300. An infrared analysis of this material showed it to contain 37 ± 1% of 1,1-dimethyl-7-methoxytetralin and 63 ± 1% of 1,1-dimethyl-6-methoxytetralin ($n^{25}D$ 1.5303 calculated).

An infrared analysis of the second chromatographic fraction from the acetolysis products showed it to be 98 ± 1% 4-(*p*-anisyl)-4-methyl-1-pentanol and 2 ± 1% 5-(*p*-anisyl)-2-methyl-2-pentanol.

In the second solvolysis carried out with the same quantity, exactly as above, a 32.0% yield of olefins and tetralins ($n^{25}D$ 1.5229) was obtained and a 60.6% yield of alcohols, $n^{25}D$ 1.5219. The pure tetralins were isolated as above, $n^{25}D$

(17) E. Martin, *J. Amer. Chem. Soc.*, **58**, 1440 (1936).
(18) L. Gieser and V. Desreux, *ibid.*, **60**, 2255 (1938).

1.5297, and shown by infrared to contain 35 ± 2% of 1,1-dimethyl-7-methoxytetralin and 65 ± 2% of the 6-methoxy isomer. Similarly, the alcohol fraction was shown by infrared to contain 2 ± 1% of 5-(*p*-anisyl)-2-methyl-2-pentanol in 4-*p*-anisyl-4-methyl-1-pentanol.

The Acidic Acetolysis of 4-(*p*-Anisyl)-4-methyl-1-pentyl *p*-Bromobenzenesulfonate.—To 1000 ml of dry acetic acid at 100.0° was added 10.0 g of the bromobenzenesulfonate. After 47 hr at 100.0° the solvolysis solution was poured into water and the products were extracted, reduced, and chromatographed as described above. The first fraction, eluted with pentane, 1.7 g, bp 105–107° (2.5 mm), n^{25}D 1.5288, was pale yellow. The infrared analysis of the mixture indicated it to be 40 ± 5% 1,1-dimethyl-6-methoxytetralin and 60 ± 5% of the 7-methoxy isomer.

The second fraction was eluted with ether. This product, 2.75 g, bp 135–138° (1.5 mm), n^{25}D 1.5227, had an infrared spectrum identical with that of the starting alcohol, 4-(*p*-anisyl)-4-methyl-1-pentanol.

The Acetolysis Products from 4-Methyl-4-phenyl-1-butyl *p*-Bromobenzenesulfonate.—A solution of 15 ml of 1.00 *M* lithium acetate in dry acetic acid and 1500 ml of dry acetic acid was heated to 100.0° and 12.0 g of the bromobenzenesulfonate was added. In 5 hr another 20 ml of 1 *M* lithium acetate in acetic acid was added and after 90 more hr at 100.0° the solvolysis solution was cooled and poured into water. The products were extracted with five portions of pentane and isolated as in the above examples. Pentane elution of the products from alumina gave 0.70 g of hydrocarbons, bp 60° (1.5 mm), n^{25}D 1.5217, and elution with ether gave 4.40 g of alcohols, bp 112–115° (2 mm), n^{25}D 1.5162.

The hydrocarbon fraction reacted slowly with potassium permanganate in acetone. Quantitative hydrogenation of a 0.3121-g sample at 27° and 750 mm in acetic acid with 10% Pd/C took up 4.7 ml of hydrogen. A second sample, 0.2350 g, at 30° and 747 mm, took up 3.2 ml of hydrogen (9.4% and 8.4% olefin, respectively).

The infrared spectrum of the hydrogenated hydrocarbons, n^{25}D 1.5195, was generally very similar to that of 1,1-dimethyltetralin except for a band of medium intensity at 695 cm^{-1} and a small increase in intensity of absorption in the 1075–1300-cm^{-1} region. The 695-cm^{-1} band is present in both possible hydrogenated olefins, 2-methyl-2-phenylpentane and 4-methyl-1-phenylpentane. However, the absence of any appreciable absorption at 740 cm^{-1} indicates that there is less than *ca.* 2% of the second isomer present. A 20% solution of 2-methyl-2-phenylpentane in 1,1-dimethyltetralin will account for the 695-cm^{-1} band but not the 1075–1300 cm^{-1} discrepancy. Considering both the hydrogenation data and the infrared data, the mixture probably contains *ca.* 80% of 1,1-dimethyltetralin, *ca.* 10% of 2-methyl-2-phenylpentane, and *ca.* 10% of some other unknown product.

Registry No.—VI, 33214-69-6; VII, 33214-70-9; X, 33214-69-6; 3-(4-acetamidophenyl)-3-methylbutyric acid, 33214-72-1; 3-(4-acetamido-3-nitrophenyl)-3-methylbutyric acid, 33214-73-2; 3-methyl-3-(3-nitrophenyl)butyric acid, 33214-35-6; 3-(*m*-anisyl)-3-methylbutyric acid, 33214-36-7; 3-(*p*-anisyl)-3-methylbutyric acid, 1136-01-2; 3-(*o*-anisyl)-3-methylbutyric acid, 33214-38-9; 4-(*m*-anisyl)-4-methylpentanoic acid, 33214-39-0; 3-(*p*-anisyl)-1-bromo-3-methylbutane, 33214-40-3; 4-(*p*-anisyl)-4-methylpentanoic acid, 23203-48-7; 4-methyl-4-pentanolacetone, 3123-97-5; 1-bromo-3-methyl-3-phenylbutane, 1197-97-3; 4-methyl-4-phenylpentanoic acid, 4408-55-3; 3-(3,4-dimethoxyphenyl)-3-methylbutyric acid, 33214-44-7; 3-(3,4-dimethoxyphenyl)-3-methyl-1-butanol, 33214-45-8; 1-bromo-3-(3,4-dimethoxyphenyl)-3-methylbutane, 33214-46-9; 4-(3,4-dimethoxyphenyl)-4-methylpentanoic acid, 3754-68-5; 4-(*m*-anisyl)-3,3-dimethylbutanoic acid, 25380-95-4; 4-(*m*-anisyl)-3,3-dimethyl-1-butanol, 33214-48-1, 33214-49-2 (Br); 3,3-dimethyl-4-(*p*-nitrophenyl)butyric acid, 33209-64-2; 4-(*p*-aminophenyl)-3,3-dimethylbutyric acid, 33209-65-3; 4,3-dimethyl-4-(*p*-hydroxyphenyl)butyric acid, 33209-66-4; 4-(*p*-anisyl)-3,3-dimethylbutyric acid, 33209-67-5; 4,4-dimethyl-6-methoxy-1-tetralone, 23203-51-2; 1,2-dimethyl-7-methoxynaphthalene picrate, 33209-69-7; 4,4-dimethyl-1-tetralone, 2979-69-3; 4,4-dimethyl-7-nitro-1-tetralone, 33209-71-1; 4,4-dimethyl-7-hydroxy-1-tetralone, 33209-72-2; 4,4-dimethyl-7-methoxy-1-tetralone, 23203-49-8; 1,2-dimethyl-6-methoxynaphthalene picrate, 33209-74-4; 4-*o*-anisylbutyric acid, 33209-75-5, 33209-76-6 (Et ester); 5-(*o*-anisyl)-2-methyl-2-pentanol, 33209-77-7; 4,4-dimethyl-8-methoxynaphthalene, 33209-78-8; 4,4-dimethyl-8-hydroxy-1-tetralone, 33209-79-9; 1,2-dimethyl-5-methoxynaphthalene picrate, 33209-80-2; ethyl 4-*p*-anisylbuyrate, 4586-89-4; 5-(*p*-anisyl)-2-methyl-1-pentanol, 33209-82-4; 5-(*p*-anisyl)-2-methyl-2-pentanol, 4586-90-7.

Photoaddition Reactions. II.[1] Photoaddition of Dimethyl Acetylenedicarboxylate to Cyclic Ethers

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The photoinitiated free-radical addition of tetrahydrofuran, 2-methyltetrahydrofuran, 1,4-dioxane, and tetrahydropyran to dimethyl acetylenedicarboxylate is found to give cis and trans 1:1 adducts. The products were isolated and characterized. The reaction has been found to be specific in that the trans adducts predominate over the cis.

Dimethyl acetylenedicarboxylate (DMAD, 2), one of the most versatile acetylenes, has played an important role in organic synthesis because it undergoes a wide variety of thermal cycloaddition and conjugate addition reactions.[4] Very little is, however, known about its photochemical reactions. Photoaddition of 2 to benzene has been reported to give dimethyl cyclooctatetraene-1,2-dicarboxylate,[5,6] and norbornene and pyrrole have been reported to give 1:1 photoadducts with DMAD.[7,8] Recently, the photoaddition of DMAD to two molecules of ethylene has also been re-

(1) Paper I: P. Singh, *J. Org. Chem.*, **36**, 3334 (1971).

(2) Syva Research Institute, 3221 Porter Drive, Palo Alto, Calif. 94304.

(3) Part of this work was carried out at the Department of Chemistry, The University, Southampton, England.

(4) R. Fuks and H. G. Viehe in "Chemistry of Acetylenes," H. G. Viehe, Ed., Marcel Dekker, New York, N. Y., 1969, Chapter 8, pp 466–520, 550–567, and 574–575.

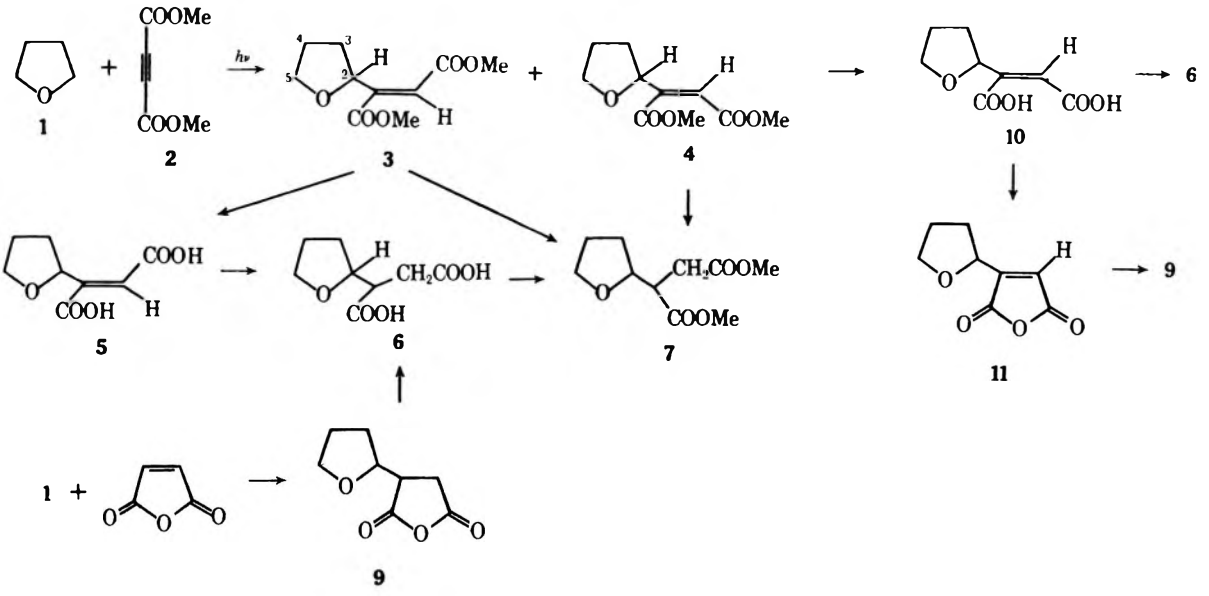
(5) E. Grovenstein, Jr., and D. V. Rao, *Tetrahedron Lett.*, 148 (1961).

(6) D. Bryce-Smith and J. E. Lodge, *J. Chem. Soc.*, 695 (1963).

(7) M. Hara, Y. Odaira, and S. Tsutsumi, *Tetrahedron*, **22**, 95 (1966).

(8) R. P. Gandhi and V. K. Chadha, *Indian J. Chem.*, **9**, 305 (1971).

SCHEME I



ported.[9] Jacobs and Ecke reported free radical initiated addition of cyclic ethers to maleic anhydride but failed to get any adduct with DMAD.[10] Ether free radicals have been reported to be relatively unstable at elevated temperatures and tend to disproportionate, which in the case of cyclic ethers results in ring opening of the ether ring.[11] Ring opening of cyclic ethers seldom takes place at room temperature, thus giving an excellent chance of addition of 2 to cyclic ether free radicals generated by ultraviolet light at room temperature.[12,13] In fact, efficient addition of cyclic ether free radicals generated photochemically to both alkenes and alkynes have been reported.[14-16] We wish now to report that dimethyl acetylenedicarboxylate also undergoes efficient addition with cyclic ethers under the influence of ultraviolet light.[17]

Results

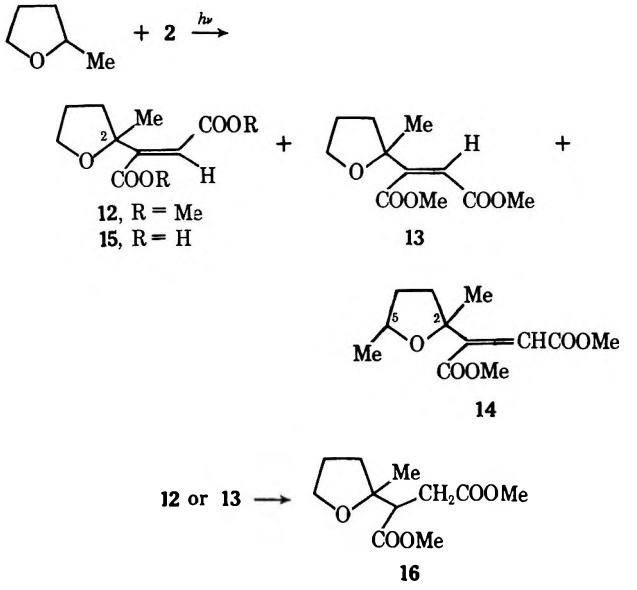
Reported below are the 1:1 addition reactions of DMAD (2) to tetrahydrofuran, 2-methyltetrahydrofuran, 1,4-dioxane, and tetrahydropyran. Unless stated otherwise, the reactions were carried out by ultraviolet irradiation, through a Pyrex filter, with a 450-W Hanovia lamp.

Irradiation of DMAD for 20 hr in tetrahydrofuran with a 250-W Hanovia lamp gave 1:1 adducts **3** and **4** in *ca.* 60% yield. The photoadducts were separated by preparative glpc, and their structures are based on analytical and spectral data. The nmr spectrum of **3** showed its vinylic proton as a doublet at δ 6.42 with a coupling constant of 0.5 Hz. The splitting of this proton is due to its long-range coupling with the tetrahydrofuryl methine proton, as was evident by its collapse to a sharp singlet when decoupled from the C-2 methine proton at δ 5.12. The vinylic proton of **4** appeared as a doublet at δ 6.07, showing its long-range coupling with the C-2 methine proton as 2.0 Hz. The large allylic coupling constant observed in **4** indicated a cisoid relationship of the C-2 methine protons as shown, while the small allylic coupling constant in **3** is in agreement with their transoid relationship.[18-20] The low-field chemical shift of the vinylic proton in **3** as compared to that of its isomer **4** is due to deshielding by methyl ester groups on the adjacent carbon atom.[21,22] The structures **3** and **4** were secured by hydrogenation of these photoadducts to dimethyl tetrahydro-2-furylsuccinate (**7**). Both the diesters **3** and **4** gave on saponification their corresponding diacids **5** and **10**, respectively. The diacid **10**, on being heated at 110° for 30 min, was quantitatively dehydrated to tetrahydro-2-furylsuccinic anhydride (**9**)[10] (Scheme I). The diacid **10**, therefore, is tetrahydro-2-furylmaleic acid, and the stereochemistry of the ester groups in **4** must be cis as shown. The diacid **5**, obtained by saponification of **3**, was recovered unchanged under similar conditions; the trans relationship of the acid groups in **5**, and hence the ester groups in **3**, is therefore assigned. It is interesting to point out that prolonged heating of the trans diacid **5** at 180° resulted in considerable charring and afforded the anhydride **11** in a poor yield (10%),[23] in agreement with the ob-

(9) D. C. Owsley and J. J. Bloomfield, *J. Amer. Chem. Soc.*, **93**, 182 (1971).
(10) R. L. Jacobs and G. G. Ecke, *J. Org. Chem.*, **28**, 3036 (1963).
(11) T. J. Wallace and R. J. Gritter, *ibid.*, **27**, 3037 (1962).
(12) D. Elad in "Organic Photochemistry," Vol. 2, O. L. Chapman, Ed., Marcel Dekker, New York, N. Y., 1969, pp 202–208.
(13) S. Jerumanis and A. Martel, *Can. J. Chem.*, **48**, 1716 (1970).
(14) R. C. Cookson, I. D. R. Stevens, and C. T. Watts, *Chem. Commun.*, 259 (1965).
(15) I. Rosenthal and D. Elad, *Tetrahedron*, **23**, 3193 (1967), and references cited therein.
(16) R. Srinivasan and E. H. Carlough, *Can. J. Chem.*, **45**, 3209 (1967).
(17) For a preliminary note, see P. Singh, *Tetrahedron Lett.*, 2155 (1970).
(18) J. W. Emsley, J. Feeney, and L. H. Sutcliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy," Vol. 2, Pergamon Press, Oxford, 1966, pp 726–741.
(19) A. A. Bothner-By, C. Naar-Colin, and H. Günther, *J. Amer. Chem. Soc.*, **84**, 2748 (1962).
(20) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, Oxford, 1969, p 323.
(21) L. M. Jackman and R. H. Wiley, *J. Chem. Soc.*, 2881, 2886 (1960).
(22) "Varian NMR Spectra Catalogue," Spectra No. 212 and 213.
(23) Based on this evidence and the presence of a strong fragment at M − 18 in the mass spectrum of **5** the major adduct **3** was tentatively considered in our preliminary communication to be a derivative of maleic acid. However, comparative studies on both the isomers **5** and **10** have revealed that our earlier assignment of cis stereochemistry to the adduct **3** is in error and it should now be considered as trans.

servation that fumaric acid on being heated at elevated temperature gives maleic anhydride.[24]

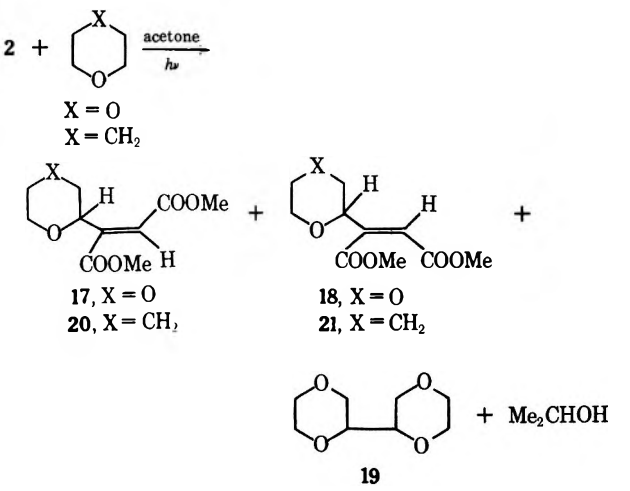
To determine the effect of an alkyl-substituted ether ring on the mode of addition, a solution of 2 in tetrahydro-2-methylfuran was irradiated. After 6 hr 1:1 adducts **12–14**, in a relative ratio of 7:2:1, respectively, were obtained in *ca.* 40% yield. The photolysis mixture was resolved by preparative glpc. The minor adduct **13**, obtained in a relative yield of 10%, could also be obtained by further irradiation of the major adduct **12**. Both the adducts **12** and **13** consumed 1 mol of hydrogen to give the same saturated diester **16**,



suggesting that these adducts are stereochemically related to each other. The nmr spectrum of **12** showed its vinylic proton as a singlet at δ 6.62 while the same proton in **13** appeared as a singlet at δ 5.98. A considerable downfield shift of the vinylic proton in **12** as compared to the same proton in its isomer **13** requires the cis relationship of the vinylic proton with the ester group (and hence, the trans relationship between the methyl ester groups).[21] The low-field chemical shift of the C-2 methyl group at δ 1.42 in **12** as compared to that of its isomer **13** at δ 1.39 is also in agreement with its cisoid relationship with the ester group.[25] The dicarboxylic acid **15**, obtained by saponification of the diester **12**, could not be dehydrated to its anhydride. Based on these arguments, and by analogy with the photoaddition of tetrahydrofuran to DMAD, the major and the minor isomers are assigned structures **12** and **13**, respectively.

The third compound, formed in a relative yield of 20% (nmr analysis), could not be obtained in pure form and is tentatively assigned structure **14** on the basis of its spectral data.

The photoaddition of DMAD (2) to six-membered cyclic ethers, 1,4-dioxane and tetrahydropyran, was also investigated. Ultraviolet irradiation of 1,4-dioxane in DMAD in the presence of acetone afforded the 1:1 photoadducts **17** and **18** (18% yield) in a relative ratio of 4:1, respectively, in addition to substantial amounts of 2-propanol and dehydro-1,4-dioxane



dimer **19**.[26] Similarly, 1:1 adducts **20** and **21** were obtained (36% yield) in a relative ratio of 3.5:1 when a solution of 2 in tetrahydropyran was irradiated in the presence of acetone. A substantial amount of 2-propanol was also obtained as a by-product. The structures of the photoadducts **17**, **18**, **20**, and **21** are in excellent agreement with their spectral data (see Experimental Section).

Discussion

The photoaddition of cyclic ethers to DMAD, induced directly or initiated with acetone by ultraviolet light, to give 1:1 adducts has been found to be quite a general reaction. The possibility that the primary step involved excitation of DMAD, followed by addition of the excited diester molecule to cyclic ethers to give the products observed, though tempting, is ruled out on the basis of its nonreactivity with 1,4-dioxane and tetrahydropyran in the absence of acetone. The formation of dehydro-1,4-dioxane dimer **19** and 2-propanol during the photolysis of 1,4-dioxane in DMAD (2) in the presence of acetone strongly suggests that the reactions in this system (and probably in all the other systems studied here) are free-radical reactions. The possibility that ether free radicals are produced by hydrogen expulsion from excited ether molecules is highly improbable.[15,27] The formation of ether free radicals **22**, as a result of hydrogen atom abstraction from ethers by other radicals formed during irradiation, is considered to be the key step in the photoaddition reactions (Scheme II).

The addition of tetrahydrofuran as well as of 2-methyltetrahydrofuran to DMAD could be affected without a photoinitiator, using ultraviolet light filtered through Pyrex. This is attributed to impurities present in commercial ethers which could act as photoinitiator.[15] Indeed, photoaddition of purer tetrahydrofuran (refluxed over lithium aluminum hydride) to DMAD was slow and gave the 1:1 adducts **3** and **4** in a poor yield (10%).

The radical addition of ethers to DMAD could occur both cis and trans, giving the cis and trans products, respectively. The photoaddition of ethers to DMAD

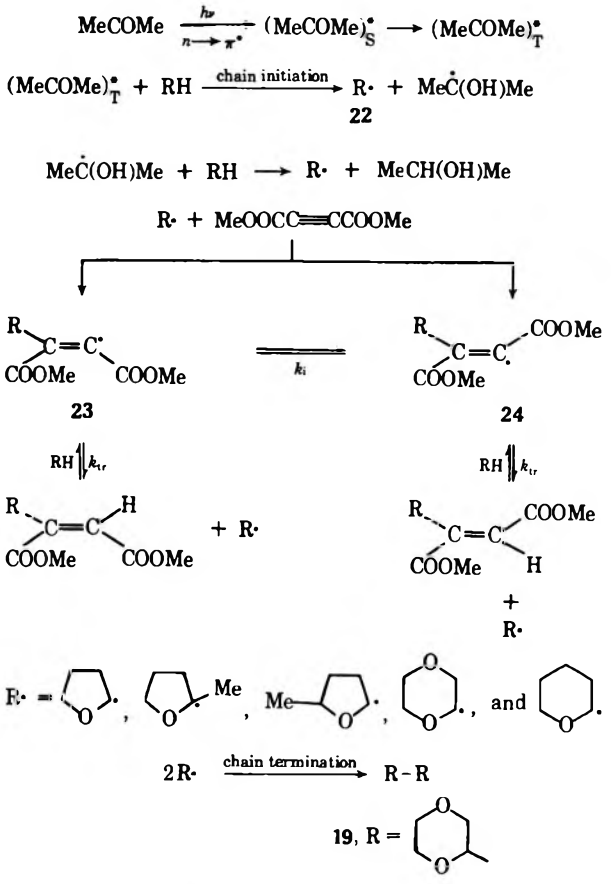
(24) "The Merck Index," P. G. Stecher, Ed., Merck and Co., Inc., N. J., 1968, pp 474 and 639.

(25) M. Cais in "The Chemistry of Alkenes," S. Patai, Ed., Interscience, London, 1964, pp 988–992.

(26) A white, fluffy solid, mp 103–110°, was also obtained which could not be identified. Based on spectral data the solid is tentatively considered to be a telomer of 1,4-dioxane and DMAD.

(27) G. Porter, "XIII-e Counseil de Chimie Solvay Report," Bruxelles, Oct 1965, p 29.

SCHEME II



has been found to be stereoselective in that the trans adducts predominate as a result of a preferential trans addition mechanism.[28-30] The preferential formation of the trans adducts does not necessarily mean that the stereochemistry of the intermediate radicals is trans, as the rate of invertion, K_i, of radicals **23** and **24** is much faster than their chain transfer, K_{tr}, steps.[31] The stereoselective trans addition of DMAD to cyclic ethers is probably due to a substantial difference in free energies of the transition states for the conversion of the intermediate radicals **23** and **24** to the products.[29] The formation of considerable amount of the cis adduct **13** after prolonged irradiation of DMAD in tetrahydrofuran is attributed to further isomerization of the trans adduct **12** under experimental conditions.[32,33] Indeed, the compound **13** could be obtained by ultraviolet irradiation of **12**.

Experimental Section

Melting points and boiling points are uncorrected. Ir spectra were recorded on a Unicam SP 200 spectrometer. Unless stated otherwise, nmr spectra were recorded on a Varian A-60 spectrometer; the values are given in δ units downfield from tetramethylsilane as internal standard. Mass spectra were recorded on an MS-12 instrument and tlc separations were accomplished on silica plates. Unless mentioned otherwise, gas chromatographic separations were achieved using a 6 ft × 0.25 in., 10% Carbowax on Chromosorb W column. For photochemical reactions, the reaction mixtures were thoroughly flushed with nitrogen before ultraviolet irradiations.

Solutions in organic solvents were dried over anhydrous magnesium sulfate.

Photolysis of Dimethyl Acetylenedicarboxylate (DMAD, 2) in Tetrahydrofuran. Formation of Dimethyl Tetrahydro-2-furylfumarate (3) and Dimethyl Tetrahydro-2-furylmaleate (4).—A solution of DMAD (2) (8.2 g, 0.058 mol) in tetrahydrofuran (200 ml) was irradiated with a 250-W Hanovia lamp contained in a water-cooled Pyrex well immersed in the solution. Glpc analysis (304 column[34] at 105°) of the reaction mixture after 1.5 hr irradiation showed the formation of adducts **3** and **4** in a relative ratio of 6:1, respectively. The relative ratio of **3** and **4** after 3-hr irradiation was 4:1 and their ratio changed to *ca.* 2:1 after further photolysis for 2 hr. The irradiation was stopped after 20 hr and removal of the excess of reactants under reduced pressure gave compounds **3** and **4** as a light yellow oil (7.5 g, 60%) in a relative ratio of 1:1. The mixture could not be distilled without extensive decomposition and was separated by preparative glpc.[35]

The diester **3**, a colorless, mobile liquid, showed the following spectral data: ir (CCl_4) 1730 (C=O), 1650 (C=C), 1065 (COC), and 1020 cm^{-1}; mass spectrum (70 eV) *m/e* (rel intensity) 214 (2, M^+), 183 (30), 182 (100, base peak), 155 (25), 154 (50), 124 (34), 113 (40), 71 (26), 59 (37), 53 (35), and 41 (40); nmr (CCl_4) δ 1.7–2.3 (m, 4 H, C-3 and C-4 ring methylenes), 3.68 (s, COO**Me**), 3.73 (s, COO**Me**), 3.6–4.0 (m, C-5 ring methylene) (total 8 H), 5.12 br (t, 1 H, J = 7 Hz, C-2 methine proton), and 6.42 (d, 1 H, J = 0.5 Hz, vinylic proton). The triplet at δ 5.12 was reduced to a broad singlet when decoupled from the protons at δ 3.6–4.0 and the doublet at δ 6.42 was a sharp singlet when irradiated at the C-2 methine proton (at δ 5.12).

Anal. Calcd for $C_{10}H_{14}O_5$: C, 56.07; H, 6.59. Found: C, 55.83; H, 6.85.

The diester **4**, with longer retention time, was a colorless oil: ir (CCl_4) 1735 (C=O), 1655 (C=C), and 1065 cm^{-1} (ether); nmr (CCl_4) δ 1.9–2.2 (m, 4 H, C-3 and C-4 ring methylenes), 3.73 (s, COO**Me**), 3.87 (s, COO**Me**), 3.6–4.0 (m, $-CH_2O-$) (total 8 H), 4.60 (triplet of doublets, 1 H, J_1 = 7.5, J_2 = 2.0 Hz, ring methine), and 6.07 (d, 1 H, J = 2.0 Hz, vinylic proton). The doublet at δ 6.07 was reduced to a sharp singlet when decoupled from the methine proton at δ 4.60.

The analytical sample was purified by preparative glpc.

Anal. Calcd for $C_{10}H_{14}O_5$: C, 56.07; H, 6.59; mol wt, 214. Found: C, 56.35; H, 6.47; mol wt, 214 (mass spectrum).

When pure tetrahydrofuran, refluxed over lithium aluminum hydride for 2 days, was used the reaction was very slow and afforded the adducts **3** and **4** in 10% yield after 30 hr irradiation.

Tetrahydro-2-furylfumaric Acid (5).—The dimethyl tetrahydro-2-furylfumarate (**3**) (450 mg) in methanol (20 ml) was refluxed with 5% aqueous sodium hydroxide (4 ml) on a steam bath. After 5 hr the reaction mixture was cooled and stripped of methanol under reduced pressure. The residue was diluted with water (35 ml) and extracted with chloroform. The aqueous layer was cooled in ice and acidified (pH 4) with 5% aqueous, cold hydrochloric acid. The solution was saturated with ammonium chloride and extracted with ethyl acetate. Removal of the solvent from the dried extract gave diacid **5** as a thick oil (380 mg) which solidified when set aside at 5°. The solid was crystallized twice from chloroform–petroleum ether (bp 30–60°) to give colorless crystals of **5**: mp 112–114°; ir ($CHCl_3$) 3600–2500 br (COOH), 1705 (C=O), 1645 (C=C), and 1050 cm^{-1} (ether); uv max (95% EtOH) 206 nm (log ϵ 3.96); nmr ($CDCl_3$) δ 1.9–2.3 (m, 4 H), 3.8–4.3 (m, 2 H), 5.3–5.7 (m, 1 H, C-2 ring methine), 7.08 br (s, 1 H, vinylic proton), and 9.6 br (s, 2 H, absent when washed with D_2O, acid protons); mass spectrum (70 eV) *m/e* (rel intensity) 168 (85, $M^+ - H_2O$), 140 (90), 128 (11), 122 (18), 112 (24), 99 (100, base peak), 95 (90), 71 (61), 55 (46), 43 (40), 42 (77), and 41 (90).

(28) A. A. Oswald, K. Griesbaum, B. E. Hudson, Jr., and J. M. Bregman, *J. Amer. Chem. Soc.*, **86**, 2877 (1964).

(29) J. A. Kampmeier and G. Chen, *ibid.*, **87**, 2608 (1965).

(30) W. E. Truce and G. C. Wolf, *J. Org. Chem.*, **36**, 1727 (1971).

(31) L. A. Singer and J. Chen, *Tetrahedron Lett.*, 4849 (1969), and references cited therein; for a review on stereochemical features of vinyl free radicals see L. A. Singer, *Intra-Sci. Chem. Rep.*, **4**, 139 (1970).

(32) G. S. Hammond, J. Saltiel, A. A. Lamola, N. J. Turro, J. S. Bradshaw, D. O. Cowan, R. C. Counsell, V. Vogt, and C. Dalton, *J. Amer. Chem. Soc.*, **86**, 3197 (1964).

(33) C. S. Angadiyavar and M. V. George, *J. Org. Chem.*, **36**, 1589 (1971).

(34) Perkin-Elmer 5 ft × 0.125 in. silicon gum rubber SE-30 on Chromosorb W.

(35) A partial separation of the mixture could, however, be achieved by its quick distillation under reduced pressure. The earlier fractions were rich in the trans isomer **3** while the later fractions were mostly the cis isomer **4**. In addition, a considerable amount of a nondistillable polymer was left behind in the distillation pot.

Anal. Calcd for $C_8H_{10}O_5$: C, 51.61; H, 5.41. Found: C, 51.89; H, 5.49.

Tetrahydro-2-furylmaleic Acid (10).—The dimethyl tetrahydro-2-furylmaleate (4) was saponified as above and diacid 10 was obtained as colorless crystals (crystallized from chloroform–30–60° petroleum ether): mp 84–86°; ir ($CHCl_3$) 3600–2500 br, 1700, 1645, and 1065 cm^{-1}; nmr ($CDCl_3$) δ 1.8–2.2 (m, 4 H), 3.7–4.2 (m, 2 H), 5.4–5.8 (m, 1 H), 6.65 (d, 1 H, J = 1.5 Hz, vinylic proton), and 9.3 br (s, 2 H, absent when washed with D_2O). The 70-eV mass spectrum of 10 was very similar to that of its isomer 5 and demonstrated its base peak at m/e 168 ($M^+ - H_2O$).

Anal. Calcd for $C_8H_{10}O_5$: C, 51.61; H, 5.41. Found: C, 51.75; H, 5.68.

Hydrogenation of Diacid 5 (and Diacid 10). Formation of Tetrahydro-2-furylsuccinic Acid (6).—The unsaturated diacid 5 (60 mg, 0.3 mmol) in ethanol was hydrogenated over 5% Pd on charcoal. The uptake of hydrogen was complete in 45 min. The solution was filtered, and removal of ethanol gave 6 as a thick liquid (55 mg, 90%) which crystallized when set aside. Recrystallization from methanol–chloroform afforded white crystals of 6, mp and mmp with authentic tetrahydro-2-furylsuccinic acid (see below) 142–144° (lit.[15] mp 142–144°).

Hydrogenation of the diacid 10 also afforded acid 6 in 80% yield.

Tetrahydro-2-furylsuccinic Anhydride (9).—The title compound 9 was obtained as a colorless, mobile liquid in 50% yield by peroxide-initiated free-radical addition of maleic anhydride to tetrahydrofuran according to the method of Jacobs and Ecke.[10] The adduct 9, bp 107–111° (0.1 mm), had the following spectral data: ir (neat) 1865, 1792, 1225, 1070, and 925 cm^{-1}; nmr ($CDCl_3$) δ 1.8–2.4 (m, 4 H, methylenes of the furyl ring), 2.8–3.5 (m, 3 H, anhydride ring protons), 2.6–4.0 (m, 2 H, $-CH_2O-$), and 4.1–4.5 (m, 1 H, $-CH_2OCH-$).

Tetrahydro-2-furylsuccinic Acid (6).—Tetrahydro-2-furylsuccinic anhydride (9) (2.0 g) in methanol (10 ml) was stirred at room temperature with 5% aqueous sodium bicarbonate (50 ml). After 3 hr the unreacted anhydride was extracted with chloroform. The aqueous layer was cooled and acidified with 2% hydrochloric acid. The solution was saturated with ammonium chloride and extracted with ethyl acetate. Removal of the solvent from the dried extract gave a thick liquid (800 mg) which solidified when set aside. Recrystallization from methanol–chloroform gave microcrystals of tetrahydro-2-furylsuccinic acid (6), mp 142–144°.

Anal. Calcd for $C_8H_{12}O_5$: C, 51.06; H, 6.43. Found: C, 50.95; H, 6.68.

Dimethyl Tetrahydro-2-furylsuccinate (7).—The mixture of adducts 3 and 4 was hydrogenated over 5% Pd on charcoal. Usual work-up afforded 7 as a colorless liquid, which was identified as dimethyl tetrahydro-2-furylsuccinate by spectral, tlc, and glpc comparison with an authentic sample (obtained by esterification of authentic diacid 6). The diester 7 showed the following spectral data: ir (neat) 1740 and 1070 cm^{-1}; nmr (CCl_4) δ 1.6–1.9 (m, 4 H), 2.4–3.0 (m, 3 H), 3.68 (s), 3.72 (s), 3.5–4.1 (m) (total 9 H).

The analytical sample was purified by preparative glpc.

Anal. Calcd for $C_{10}H_{16}O_5$: C, 55.54; H, 7.46. Found: C, 55.82; H, 7.71.

Tetrahydro-2-furylmaleic Anhydride (11).—The tetrahydro-2-furylmaleic acid (10) (40 mg) was heated at 110° in a drying pistol containing phosphorus pentoxide. After 30 min the reaction mixture was cooled and purification by tlc gave anhydride 11 as an oil (25 mg), ir (neat) 1815 and 1770 cm^{-1}.

The analytical sample was purified by preparative glpc.

Anal. Calcd for $C_8H_8O_4$: C, 57.14; H, 4.80. Found: C, 57.41; H, 5.07.

The anhydride 11 obtained above was hydrogenated over 5% Pd on charcoal and there was obtained tetrahydro-2-furylsuccinic anhydride (90%), identical in all respects to an authentic sample of 9 (spectral and glpc comparison).

Action of Heat on Tetrahydro-2-furylfumaric Acid (5).—The diacid 5 (50 mg) was heated for 4 hr at 180° under an atmosphere of nitrogen. There was considerable charring and the reaction mixture had turned dark brown. Analysis of the product by tlc (benzene–ether, 1:1) showed it to be a complex mixture. Preparative tlc of the mixture afforded tetrahydro-2-furylmaleic anhydride (11, 5 mg, *ca.* 10%) along with unreacted 5 (10 mg, 20%).

The diacid 5 was quantitatively recovered when heated for 30 min at 110° in the presence of phosphorus pentoxide.

Photolysis of DMAD in 2-Methyltetrahydrofuran. Formation of Dimethyl Tetrahydro-2-(2-methylfuryl)fumarate (12), Dimethyl Tetrahydro-2-(2-methylfuryl)maleate (13), and the Diester 14.—A solution of DMAD (1.5 g, 0.01 mol) in 2-methyltetrahydrofuran (10 ml) was irradiated in a Pyrex tube with a 450-W Hanovia lamp. Glpc analysis of the reaction mixture after 4-hr irradiation showed the formation of only one product, 12. The contents were further irradiated for 18 hr, and analysis by glpc showed an additional broad peak with longer retention time. The relative area under these glpc peaks was 5:2. Removal of the reactants under reduced pressure afforded a pale yellow oil (1.5 g). The oil was chromatographed on a silica column, and elution with benzene–ether (9:1) afforded adducts 12–14 (950 mg, 39%) as a colorless liquid. The mixture of the adducts was further separated by preparative glpc (column temperature 190°).

The major fraction 12 (shorter glpc retention time) was obtained as a colorless, mobile liquid: ir ($CHCl_3$) 1720 (C=O), 1645 (C=C), 1055 (ether), and 1018 cm^{-1}; nmr (CCl_4) δ 1.47 (s, 3 H, C-2 Me), 1.7–2.1 (m, 4 H, C-3 and C-4 ring methylenes), 3.70 and 3.77 (singlets, ester groups), 3.5–3.9 (m, C-5 methylene) (total 8 H), and 6.62 (s, 1 H, vinylic proton); mass spectrum (70 eV) m/e (rel intensity) 228 (2.7, M^+), 213 (25, $M^+ - Me$), 196 (23), 181 (24), 137 (12), 113 (21), 109 (14), 85 (50), 59 (31), 53 (22), and 43 (100, base peak).

Further purification of 12 by preparative glpc furnished an analytical sample.

Anal. Calcd for $C_{11}H_{16}O_5$: C, 57.88; H, 7.07. Found: C, 58.13; H, 7.25.

The minor fraction (longer glpc retention time) was also a colorless liquid and was assigned structure 14: ir ($CHCl_3$) 1725, 1645, 1435, 1065, and 1020 cm^{-1}; nmr (CCl_4) δ 1.20 (d, J = 6 Hz, C-5 Me), 1.7–2.3 (m, C-3 and C-4 methylenes), 3.72 (s, COOMe), 3.77 (s, COOMe), 3.5–4.0 (m, ring methine), and 6.35 br (s, vinylic proton).

The nmr spectrum of the minor adduct also showed singlets at δ 1.39 and 5.98 in a relative ratio of 3:1, assigned to the methyl and vinyl protons of 13 (see below), the cis stereoisomer of 12.

Anal. (mixture of 13 and 14). Calcd for $C_{11}H_{16}O_5$: C, 57.88; H, 7.07; mol wt, 228. Found: C, 57.75; H, 7.34; mol wt, 228 (mass spectrum).

The relative ratio of the photoadducts 12, 13, and 14, determined by areas under their vinylic signals at δ 6.62, 5.98, and 6.35 in the nmr spectrum of the crude reaction mixture, was 15:4:2, respectively.

Photoisomerization of the Photoadduct 12 to the Diester 13.—A solution of adduct 12 (100 mg) and acetone (0.5 ml) was irradiated in a Pyrex tube. After 15 hr the ratio of 12:13 as found by glpc was 1:4. The solvent was evaporated and the mixture was resolved by preparative glpc. The compound 13, a colorless liquid, showed the following spectral data: ir ($CHCl_3$) 1724, 1650, 1055, and 1020 cm^{-1}; nmr (CCl_4) δ 1.39 (s, 3 H), 1.7–2.2 (m, 4 H), 3.68 and 3.74 (s), 3.6–3.9 (m) (total 8 H), and 5.98 (s, 1 H, vinylic proton).

Anal. Calcd for $C_{11}H_{16}O_5$: C, 57.88; H, 7.07. Found: C, 58.14; H, 7.29.

Tetrahydro-2-(2-methylfuryl)fumaric Acid (15).—The diester 12 (114 mg) was hydrolyzed with 5% aqueous sodium hydroxide as outlined above and there was obtained diacid 15 (78 mg) as a thick liquid which solidified after prolonged standing. Two crystallizations from chloroform–30–60° petroleum ether afforded microcrystals of 15: mp 105–107°; ir ($CHCl_3$) 3600–2400, 1703, 1650, 1400, 1260, and 1040 cm^{-1}; nmr ($CDCl_3$) δ 1.60 (s, 3 H), 1.8–2.4 (m, 4 H), 3.7–4.1 (m, 2 H), 6.97 (s, 1 H, vinylic proton), and 9.7 br (s, 2 H, absent when washed with D_2O).

Anal. Calcd for $C_9H_{12}O_5$: C, 54.00; H, 6.00. Found: C, 54.28; H, 5.95.

The diacid 15 was recovered unchanged when heated at 110° for 60 min in a drying pistol containing phosphorus pentoxide. No anhydride was formed when the diacid 15 was treated with trifluoroacetic anhydride in the presence of pyridine according to Duckworth's method.[36]

Photoaddition of DMAD to 1,4-Dioxane. Formation of 2-

(36) A. C. Duckworth, *J. Org. Chem.*, **27**, 3146 (1962).

Propanol, Dehydro-1,4-dioxane Dimer 19, and the Diesters 17 and 18.—A solution of DMAD (2.0 g, 15.3 mmol) and 1,4-dioxane (10 ml) in acetone (10 ml) was irradiated in a Pyrex tube with a 450-W Hanovia lamp. After 6 hr the photolysis was stopped and the solution was distilled on a steam bath. Glpc analysis of the distillate on both polar and nonpolar columns showed, in addition to acetone and dioxane, the presence of 2-propanol. The residue was chromatographed on a silica column. Earlier eluents with benzene gave white crystals of meso and *dl* forms, mp 155–157° and 131–133°, of dioxane dimer 19[37] (560 mg) followed by a colorless, fluffy solid, mp 103–110°. The solid could not be crystallized from a host of solvents and is tentatively considered to be a telomer of 1,4-dioxane and DMAD from its spectral data: ir (Nujol) 1725 cm^{-1}; the nmr spectrum in $CDCl_3$ showed a broad singlet at δ 3.7 superimposed on a multiplet at δ 3.6–4.1 and a multiplet at δ 4.6–5.4. Further elution with benzene–ether (4:1) gave a mixture of adducts **17** and **18** as a pale yellow, mobile liquid (550 mg, 18%). The mixture was resolved by preparative glpc.

The major glpc fraction was a colorless liquid and is assigned structure **17**: ir (neat) 1730 (C=O), 1658 (C=C), and 1060 cm^{-1} (ether); nmr (CCl_4, 100 MHz) δ 3.72 and 3.80 (singlets, methyl esters), 3.5–3.9 (m, ring methylenes) (total 12 H), 4.1–4.4 (m, 1 H, ring methine), and 6.20 (s, 1 H, vinylic proton).

Anal. Calcd for $C_{10}H_{14}O_6$: C, 52.17; H, 6.13; mol wt, 230. Found: C, 52.41, H, 5.97; mol wt, 230 (mass spectrum).

The minor product **18**, which had spectral data similar to those of its isomer **17**, showed in its nmr the vinylic proton as a doublet at δ 6.32 (J = 1.5 Hz). The relative ratio of **17** and **18** in the mixture as determined by areas under its nmr signals at δ 6.2 and 6.32 was 4:1, respectively.

The analytical sample of **18** was obtained by further purification by preparative glpc.

Anal. Calcd for $C_{10}H_{14}O_6$: C, 52.17; H, 6.13. Found: C, 51.98; H, 6.33.

When DMAD in 1,4-dioxane was irradiated in the absence of acetone for 20 hr only the starting material could be recovered quantitatively.

Photoaddition of DMAD to Tetrahydropyran. Formation of Dimethyl Tetrahydro-2-pyrylfumarate (20) and Dimethyl Tetrahydro-2-pyrylmaleate (21).—A solution of DMAD (2.0 g, 15.3 mmol) and tetrahydropyran (10 ml) in acetone (10 ml) was irradiated with a 450-W Hanovia lamp. Usual work-up after 15 hr gave, in addition to 2-propanol, a mixture of adducts **20** and **21** in a relative ratio of 3.5:1, respectively, as a colorless liquid (1.2 g, 36%). The mixture was separated by preparative glpc.

The major fraction **20** with shorter retention time showed the following spectral data: ir (neat) 1725, 1645, 1070, and 1015 cm^{-1}; nmr ($CDCl_3$) δ 1.3–2.1 (m, 6 H), 3.71 (s), 3.75 (s), and 3.6–4.1 (m) (total 8 H), 5.20 br (t, 1 H, J = 6.0 Hz, C-2 methine proton), and 6.41 br (s, 1 H, vinylic proton).

Anal. Calcd for $C_{11}H_{16}O_5$: C, 57.88; H, 7.07. Found: C, 58.11; H, 7.35.

The minor adduct **21** (longer retention time) had the following spectral data: ir (neat) 1730, 1658, 1040, and 1025 cm^{-1}; nmr ($CDCl_3$) δ 1.4–2.1 (m, 6 H), 3.68 (s), 3.72 (s), and 3.5–4.0 (m) (total 8 H), 5.1–5.3 (m, 1 H, C-2 methine proton), and 6.10 (d, 1 H, J = 1.5 Hz, vinyl proton).

Anal. Calcd for $C_{11}H_{16}O_5$: C, 57.88; H, 7.07. Found: C, 57.69; H, 7.40.

Registry No.—**2**, 762-42-5; **3**, 33536-59-3; **4**, 28864-83-7; **5**, 33536-61-7; **6**, 10486-63-2; **7**, 33522-10-0; **9**, 7370-72-1; **10**, 28864-84-8; **11**, 33522-12-2; **12**, 33536-63-9; **13**, 33536-64-0; **14**, 33522-13-3; **15**, 33536-65-1; **17**, 33536-66-2; **18**, 33536-67-3; *dl*-**19**, 3333-27-5; *meso*-**19**, 3443-36-5; **20**, 33531-70-3; **21**, 33531-71-4.

Acknowledgments.—The author is thankful to Professor Gurbakhsh Singh, Banaras Hindu University, and Professor R. C. Cookson, Southampton University, for providing necessary facilities.

(37) G. Sosnovsky, *J. Org. Chem.*, **28**, 2934 (1963).

The Influence of Structure on the Rate of Thermal Rearrangement of Aryl Propargyl Ethers to the Chromenes. The *gem*-Dimethyl Effect

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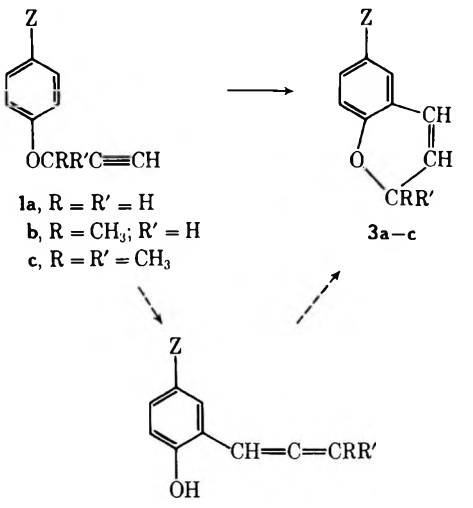
The rates of first-order thermal cyclizations of a group of para-substituted aryl propargyl ethers *p*-Z-C_6H_4-OCRR'C≡CH with R, R' = H or CH_3 were determined in *o*-dichlorobenzene as a function of Z (OCH_3, NHAc, H, Cl, CN, NO_2) and of the number of CH_3 groups. Where R and R' are both H (k values extrapolated to 189.8°) or where R was CH_3 and R' was H (k values extrapolated to 161.6°), the points followed an adequate Hammett relationship using σ^+ (ρ = −0.43) although the NO_2 and CN did not give a good fit for R = R' = H, and *p*-Cl was faster than *p*-H for R = H, R' = CH_3. The attempted Hammett plot for the *gem*-dimethyl analogs, R = R' = CH_3, had a paraboloid shape, *e.g.*, X = NHAc and X = NO_2 had about the same rate, with X = H at a minimum (k values extrapolated to 161.6°). The $\Delta S^{\ddagger}$ and $\Delta H^{\ddagger}$ followed no obvious order. The results are best explained by assuming that the "*gem*-dimethyl effect" results from an increase in the proportion of the rotamer with the ethnyl group positioned near the benzene ring, *i.e.*, the rotamer best positioned for reaction, when no hydrogen is available to rotate to that position, and that activation of the position meta to the substituent Z, at least by the electron-withdrawing groups, exists. Preparative runs showed that an essentially quantitative yield of 2-methyl- or 2,2-dimethyl-3-chromenes could be obtained in *o*-dichlorobenzene, and this solvent is preferred to *N*,*N*-diethylaniline at least for cyclization of 4-nitrophenyl propargyl ether.

Initial reports[1] of desirable analgetic and related activities of *p*-acetamidophenyl *tert*-butyl ether led us to prepare 3-(4-acetamidophenoxy)-3-methylbutyne [**1c**, Z = $NHC(O)CH_3$]. The method used involved reduction of the corresponding 3-(4-nitrophenoxy) compound **1c**, Z = NO_2, to the amino compound (iron and a trace of acid, with initial purification by steam distillation) and acetylation of that under mild conditions. Although the nitro compound gave the theoretical titer for acetylenic hydrogen, the amino compound produced by this procedure gave a low and variable acetylenic hydrogen titer. Acetylation and purification of the resulting acetylamino compound gave us as a major product in several preparations one or the other of the two isomeric products, one giving the theoretical titer for acetylenic hydrogen, the other giving none. The

(1) See M. Harfenist and E. Thom, *J. Org. Chem.*, **36**, 1171 (1971), for references.

literature available at that time[2] stated that propargyl ethers did not undergo the Claisen rearrangement, but we postulated that a portion of our aminophenyl ether had undergone a Claisen-like cyclization to the chromene **3c**, Z = NH_2, during the steam distillation. The



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acetamido product was shown to be the chromene, *i.e.*, the result of terminal addition to the ethynyl group, by synthesis by an alternative route of the chroman also made by catalytic reduction and later by nmr. Ionic addition of the nucleophilic benzene ring would have been expected to give the coumaran (five-membered ring) by addition to the internal ethynyl carbon.

After this work had been started, our attention was called to a study of yields in this same reaction.[3] Iwai and Ide concluded from yield data for the pure compound isolated (maximum yield 48% for rearrangement of propargyl ethers) that electron-releasing groups increased the yield, while electron-withdrawing groups gave much lower yields for a relatively constant time. Both statements referred to groups meta to the ethereal linkage, and these authors state that para substituents had no effect on the yield. We studied only para-substituted ethers to avoid any possibility of mixtures of cyclization products. While our studies were under way, other applications of this cyclization were reported.[4]

Our results are based on the rates of loss of acetylenic H. This does not show whether the chromenes **3** are produced directly or the *o*-allenylphenols **2** are produced by a Claisen rearrangement which is rate determining and followed by a rapid ring closure. Gaertner, who first reported[5] the preparation of *o*-allenylphenol **2**, Z = H, found that this compound cyclized readily by a base-catalyzed reaction to give 2-methylbenzofuran when in dilute solution and that it polymerized on attempted isolation. Zsindely and Schmid have shown recently[6] that in the absence of base, *e.g.*, in dilute refluxing benzene solution, *o*-allenylphenol cyclizes rapidly to the chromene. Since our loss of acetylenic hydrogen occurred at a reasonable speed only at temperatures over 100°, this cyclization is several orders of magnitude faster than our measured overall reactions, as would be required for a second step which does not affect the kinetics. Further, thermal rearrangement of di-ortho-substituted phenyl propargyl ethers has given products best formulated as derived from allenic intermediates.

It is stated[7] that the rate of Claisen rearrangements of substituted phenyl allyl ethers follows a Hammett σ^+ relationship. A similar kinetic relationship in our propargyl series would explain the nonrearrangement of the nitro compound during purification by distillation at a distillation temperature comparable to the steam distillation temperature leading to rearrangement of the amino analog. The other factor favoring ready thermal cyclization would be the presence in **1c** of the *gem*-methyl groups.

The existence of a *gem*-dimethyl effect,[8] which increases the rate of cyclization and stabilizes the cyclized products with respect to noncyclic precursors for appropriately-functionalized *gem*-dialkyl compounds as compared with the otherwise identical but unalkylated homologs, is unquestionable. No explanation, however, is universally accepted. Arguments[8b] against one explanation[9] based on bond angle changes seem convincing, at least for *gem*-dimethyl groups. Our own preference is for an explanation based on the relative proportion of rotamers being shifted in favor of rotamers best suited for cyclization, because of the geminal large groups (*vide infra*). However, a third possible explanation is particularly pertinent to our cyclization studies. This[8a,10] postulates that most of the increase of rate due to the *gem*-dimethyl effect is due to an effect on $\Delta F^{\ddagger}$ made up in part of an effect on $\Delta H^{\ddagger}$ due to the increase in gauche interactions on going from the open-chain precursor to the cyclic transition state which more closely resembles product. The increase in $\Delta H^{\ddagger}$ would be less for the *gem*-dimethyl compound which has large ground-state hindrance. In addition, an effect on $\Delta S^{\ddagger}$ is postulated, due to a smaller loss in internal rotations for the *gem*-dimethyl compounds in going to the cyclic form. In the case of our aryl propargyl ethers, the α-methylene group is flanked on one side by an oxygen whose electron pairs are known to offer low nonbonded repulsion[11] and on the other side by the ethynyl group, which at least in the ground state is essentially cylindrical, hence offering a constant, presumably low steric interference to rotation. The influence of the types of nonbonded interactions which Allinger and Zalkow discussed should be minimal in our cyclizations. This should lead to a small if not negligible *gem*-dimethyl effect. Conversely, a *gem*-dimethyl effect caused by increased concentration of the rotamer

(2) D. S. Tarbell, *Org. React.*, **2**, 4 (1944). However, C. D. Hurd and F. L. Cohen, *J. Amer. Chem. Soc.*, **53**, 1068 (1931), indicated that cyclic products formed, among others, on attempted Claisen rearrangement of phenyl propargyl ethers.

(3) I. Iwai and J. Ide, *Chem. Pharm. Bull.*, **11**, 1042 (1963).

(4) (a) B. S. Thyagarajan, K. K. Balasubramanian, and R. B. Rao, *Tetrahedron Lett.*, **21**, 1393 (1963); *Tetrahedron*, **23**, 1893 (1967); (b) J. Hlubucek, E. Ritchie, and W. C. Taylor, *Tetrahedron Lett.*, **17**, 1369, (1969), report excellent yields of *gem*-dimethyl chromenes; (c) Y. Basace and I. Marszak, *Bull. Soc. Chim. Fr.*, 2275 (1971).

(5) R. Gaertner, *J. Amer. Chem. Soc.*, **73**, 4400 (1951).

(6) J. Zsindely and H. Schmid, *Helv. Chim. Acta*, **51**, 1510 (1968).

(7) (a) W. N. White, D. Gwynn, R. Schlitt, C. Girard, and W. Fife, *J. Amer. Chem. Soc.*, **80**, 3271 (1958); (b) H. L. Goering and R. R. Jacobson, *ibid.*, **80**, 3277 (1958).

(8) For leading references, see (a) N. L. Allinger and V. Zalkow, *J. Org. Chem.*, **25**, 701 (1960); (b) F. G. Bordwell, C. E. Osborne, and R. D. Chapman, *J. Amer. Chem. Soc.*, **81**, 2698 (1959).

(9) Summarized by G. S. Hammond, "Steric Effects in Organic Chemistry," M. S. Newman, Ed., Wiley, New York, N. Y., 1956, p 425, *et seq.*

(10) This summarizes only that part of ref 8a of direct concern here.

(11) See E. L. Eliel, *Accounts Chem. Res.*, **3**, 1 (1970), in which the axial electron pair on oxygen shows a smaller nonbonded repulsion than does axial hydrogen on carbon.

favoring cyclization when the methyl groups are present, would still be important for our propargyl ether cyclizations.

We therefore studied the rates of thermal cyclization of a variety of para-substituted phenyl propargyl ethers in *o*-dichlorobenzene to determine first whether the effect of substituent on rate followed a Hammett relationship and second whether any connection could be found between rates, the number of methyl groups on the saturated carbon of the propargyl group, and the values of $\Delta S^{\ddagger}$ and $\Delta H^{\ddagger}$.

The propargyl ethers required were made by the procedures listed in Table III, which also lists properties of the new ethers. All were purified by base extraction to remove any phenols, followed by distillation or recrystallization, and then gave correct elemental analyses. Those which still had less than 95% of theoretical titer for acetylenic hydrogen, as well as all of the dimethyl propargyl ethers made from the phenol salts and 3-methyl-3-chlorobutyne, were purified by way of the silver salt. This was done lest allenic impurities rearrange to acetylenes during the kinetic runs; although normally the kinetic form of a first-order reaction would not be affected by impurities, formation of acetylenes from any allenes present during kinetic runs would have distorted our kinetics. All compounds gave clean first-order kinetics.

Results of Preparative Significance.—Because yields below those required for meaningful kinetics have been reported[3,4] for related reactions recently, it is important that our kinetic data is validated by yields obtained by preparative runs essentially under the conditions of the kinetic runs. Table I shows yields determined by glpc,

TABLE I
YIELDS OF CYCLIZED CHROMENE BY GLPC AND ISOLATED YIELDS[a]

Substituent			Per cent of theoretical by glpc[a]			
Para	R	R′	Product	Starting material	Glpc corrected yield, %	Isolated[a] yield, %
H	H	H	45.5	20.5	66	66
CN	H	H	75	27	102	
Cl	H	H	78	21.4	99.4	36[b]
OCH_3	H	H	71.3			76[b]
NO_2	H	H				46[c]
H	H	CH_3	91	9.0	99	53.5
Cl	H	CH_3	100		100	
OCH_3	H	CH_3	100		100	56[b]
CN	H	CH_3				99[d]
NHAc	H	CH_3				70
NO_2	H	CH_3				84
H	CH_3	CH_3	90		90	
OCH_3	CH_3	CH_3	100		100	83
NO_2	CH_3	CH_3	90		90	75
NHAc	CH_3	CH_3				96
CN	CH_3	CH_3				100[b]

[a] Blanks represent data not determined. [b] Isolated yield by distillation from *o*-dichlorobenzene. [c] Reference 3 reported that none of the chromene resulted from attempted cyclization in diethylaniline under reflux. [d] Sublimed.

and yields of chromene isolated analytically pure, from the cyclization of representative aryl propargyl ethers. While the yields of isolated pure chromene vary with the ease of separation from *o*-dichlorobenzene of the different chromenes, all yields of chromenes determined by glpc were over 90% both for cyclization of the monomethylpropargyl ethers **1b** and for the cyclization of the dimethylpropargyl ethers **1c**. The nonmethylated propargyl ethers **1a** gave lower yields of chromene in two of the four cases studied, together with much resinous material. However, reheating the isolated chromenes for further periods gave tar formation at a sufficiently fast rate to account for the deviation from near-quantitative yield in the cases studied, indicating that the rate of loss of acetylenic hydrogen which was measured in the kinetic runs corresponded in all probability to formation of the chromene and that tar formation was a subsequent reaction of the chromene.[12] Representative chromenes appeared as pure single substances to glpc and tlc and gave the expected pmr after the thermal cyclizations.

An interesting result, which might be of preparative significance but which we did not investigate further, is that we isolated a 46% yield of pure 6-nitrochromene from cyclization of its acetylenic precursor in *o*-dichlorobenzene, whereas Iwai and Ide[3] report only decomposition on attempted cyclization of 3-(4-nitrophenoxy)propyne in refluxing *N*,*N*-diethylaniline. Since *N*,*N*-dialkylanilines are preferred solvents in the true Claisen rearrangement because they diminish the amount of resinification, this result, if it can be confirmed and generalized, would represent a preparatively important difference between the propargyllic ether rearrangement and the true Claisen rearrangement.

Cyclization Rates and Derived Data.—The rates of cyclizations were determined in *o*-dichlorobenzene by titimetric loss of acetylenic hydrogen. This was followed in all cases (except the two indicated) through at least six and generally eight half-lives. In a few cases, the less precise nmr rates were used to check particular points, by determining the ratio at timed intervals of the pmr integral for the *C*-methyl hydrogens of the propargyl ethers (downfield) to the sum of that plus the integral of the *C*-methyl hydrogens of the chromenes produced. Excellent first-order kinetics was found in all cases.

Although it seemed unlikely that first-order kinetics was found fortuitously, this was checked. One cyclization, that of 3-(4-acetamidophenoxy)propyne, was run at three dilutions differing by a factor of 5. All of these gave k values within 2% of the mean. Two runs of the corresponding 4-nitrophenoxy compound differing in concentration by a factor of 2.5 also agreed in k to $\pm 1\%$. Three runs each with 3-(4-acetamidophenoxy)-3-methylbutyne and the corresponding nitro compound with concentrations differing fivefold had k values differing by 3.8 and 2.6%, respectively, from the mean.

The titimetric rate constants are tabulated in the Experimental Section for the temperatures used, which were three or more temperatures over a range of 30° or more. For rate intercomparisons, it was desirable to compare rates under identical conditions. Therefore, the rate constants found for the cyclization of the nonmethylated ethers **1a** in Table II were extrapolated to 161.6° by the usual linear plot of log k *vs.* $1/T_{abs}$ to facilitate the comparison with the rates of cyclization of the methylated homologs given later. A Hammett plot for the rates of these same cyclizations is shown in

(12) R. Hug, G. Frater, H.-J. Hansen, and H. Schmid, *Helv. Chim. Acta*, **54**, 306 (1971).

TABLE II

RATE CONSTANTS AND ACTIVATION PARAMETERS FOR THERMAL CYCLIZATION OF COMPOUNDS 1, EXTRAPOLATED TO STANDARD TEMPERATURES

R	R′	Z	$k \times 10^6$, sec^{-1} at 161.6°	Relative rate	$k \times 10^6$, sec^{-1}, at 189.8°	$\Delta H^{\ddagger}$, cal/mol	$\Delta S^{\ddagger}$, eu/mol
H	H	OCH_3	1.15	4.6	18.7	38,700	2.6
H	H	$CH_3C(O)NH$	1.14	4.5	13.4	34,100	−8.0
H	H	H	0.962	3.8	8.71	30,400	−17
H	H	Cl	0.722	2.9	6.74	30,800	−17
H	H	NO_2	0.252	1	5.38	42,600	8.4
H	H	CN	0.245	1	3.25	35,800	−7.2
CH_3	H	OCH_3	9.98	40		33,600	−5.0
CH_3	H	$CH_3C(O)NH$	7.57	30		32,100	−9.0
CH_3	H	H	3.49	14		35,900	−1.7
CH_3	H	Cl	3.79	18		36,100	−1.0
CH_3	H	NO_2	2.27	9.1		38,300	3.1
CH_3	H	CN	2.59	10		33,100	−8.7
CH_3	H	NH_2	50[a]	200[a]			
CH_3	CH_3	OCH_3	628	2500		34,700	5.8
CH_3	CH_3	$NHC(O)CH_3$	402	1600		25,700	−16
CH_3	CH_3	H	203	810		30,000	−7.2
CH_3	CH_3	NO_2	350	1400		34,000	3.1
CH_3	CH_3	CN	250	1000		34,000	2.5
CH_3	CH_3	NH_2[b]					

[a] Crude nmr rate in dimethylaniline. [b] Crude nmr rate in dimethylaniline at 130° was 80×10^{-6}; in trimethylene glycol at 130°, a crude rate determination by nmr gave $k = 250 \times 10^{-6}$.

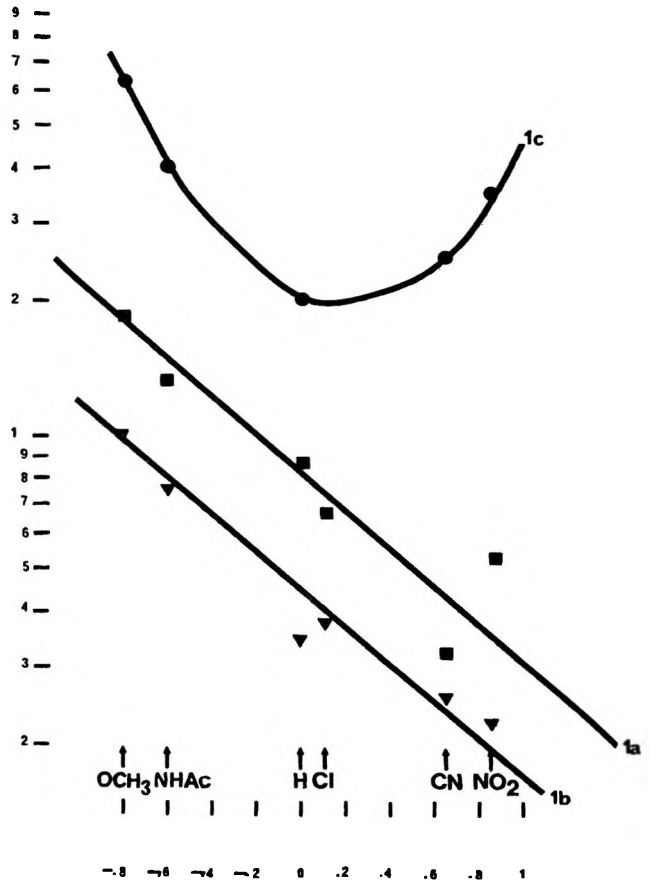


Figure 1.

Figure 1, using k values extrapolated to 189.8°, which is within the range of temperatures actually used for these cyclizations, to preclude significant distortions due to extrapolation. It is evident that σ^+ values[13] give an excellent fit for the electropositive methoxy and acetamido functions, for para hydrogen and for the weakly electron-attracting *p*-chloro substituents, and a poor but perhaps adequate fit for the strongly electronegative *p*-cyano and *p*-nitro groups. Neither the σ_m nor the σ_p values give an adequate fit for these values. This corresponds to the results reported for the Claisen rearrangement[7] both with respect to the magnitude of ρ (−0.43 here *vs.* −0.61 or −0.51) and in the better fit of the Hammett σ^+ relationship shown for electron-releasing substituents than for electronegative substituents here and in the Claisen case.

This Hammett relationship is also satisfactory when the rates of thermal cyclization of the monomethylpropargyl ethers **1b** are examined. Table II shows these rates extrapolated to 161.6°, which for these compounds is within the actual temperature range used for their cyclization. It is apparent, however, that, while the electropositive *p*-methoxy substituent again confers the highest rate of cyclization in this group, the rate of cyclization of the monomethylpropargyl ether with the electron-withdrawing *p*-chloro function is now slightly *faster* than that of the para-unsubstituted analog. A Hammett plot (Figure 1, curve **1b**) can still be drawn to give an excellent straight line, but a line holding all of the other data nicely has the *p*-H and *p*-Cl substituted points below it. This effect is even more marked for the *gem*-dimethylpropargyl ethers **1c**, where the *p*-methoxy leads to the highest rate, but the rates of the *p*-nitro and the *p*-acetamido ethers are nearly the same, both nearly twice as fast as the rate of cyclization of the unsubstituted **1c**, and even the *p*-cyano ether cyclizes faster than the unsubstituted analog, all again extrapolated to 161.6°.

Table II also gives the values found for the energies and entropies of activation.[14] No correlation of either $\Delta H^{\ddagger}$ or $\Delta S^{\ddagger}$ values with the degree of methylation at the propargyllic carbon is evident.

Discussion of Rate Results.—The relative rate in-

(13) H. C. Brown and Y. Okamoto, *J. Amer. Chem. Soc.*, **80**, 4979 (1958); **80**, 1913 (1958); Y. Okamoto, T. Inukai, and H. C. Brown, *ibid.*, **80**, 4969 (1958); G. Illuminati, *ibid.*, **80**, 4941 (1958).

(14) Values of constants, etc., from J. F. Bunnett, *Tech. Org. Chem.*, **8**, 200 (1961). Note that eq 6 is subject to misinterpretation as type set.

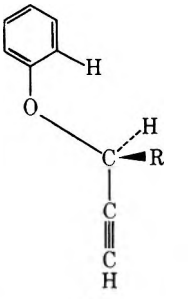
crease going from a given para-substituted monomethylpropargyl ether **1b** to the corresponding *gem*-dimethyl homolog **1c** is greater in all cases than the increase going from any unmethylated ether **1a** to the corresponding **1b**. Further, the increase in rate due to methyl substitution at the propargyl carbon outweighs that of profound change in the "electronic" character of the para substituent. These data are taken to show that this effect of methyl groups is steric, rather than being to any appreciable extent due to stabilization of positive charge on the ethereal oxygen. The low Hammett ρ value found for the undistorted (see below) cyclization of the unmethylated propargyl ethers also shows the small effect of electronic factors.

The obedience to a Hammett relationship and the similarity to the Claisen rearrangement make it likely that the cyclizations of the unmethylated propargyl ethers **1a** represent a valid model of the unperturbed reaction. It then is necessary to explain the deviations from this behavior in the methylated cases. Examination of space-filling models shows appreciable interference between the propargyllic methyl groups and the ortho hydrogen of the benzene ring, although the models can be rotated, more easily for the monomethyl compound models, to positions where the interference appears negligible. The obvious explanation of the relative increase in rate found for the dimethylated ethers **1c**, when Z is electron withdrawing, involves steric hindrance to the coplanarity required at the oxygen for electron withdrawal. The data do not allow a choice between interference with coplanarity due to twisting about the bonds to oxygen and that due to bending of these bonds. The para electron-withdrawing groups should shorten the aryl-to-oxygen bond,[15] but it is uncertain whether this would occur to an extent sufficient to significantly increase the *C*-methyl hindrance. If this steric interference were the only factor, the rates of cyclizations for **1c** when Z is electron withdrawing would approach rather than exceed the rate of the para-unsubstituted analog with the same number of methyls. The fact that the rates of these reactions are *faster* than the Z = H reactions requires that activation of the aryl position ortho to oxygen, which is meta to the electron-withdrawing groups, is also present. This could be electrostatic[16a] in origin and so not subject to steric hindrance effects para to the Z groups. Being an inherently small effect, this meta activation would not be noticeable, except in those cases where the para electromeric effect was minimized, *i.e.*, especially for the *gem*-dimethyl ethers **1c**. It is obvious that the formation of positive charge at the ethereal aryl carbon in the transition state (as shown by the obedience of cyclization rates to a σ^+ relationship) requires development of corresponding negative charge elsewhere in the molecule, for a unimolecular reaction. The electrostatic activation of the carbon meta to the substituent would then suggest that much of this negative charge is present at that carbon in the transition state. Alternatively, this meta activation effect could be present with all of the substituents, but only noticeable for the electron-withdrawing ones. This would be the case if it were due to stabilization of a "free-radical-like" transition state.[17] It is well known[16b] that free-radical-type reagents preferentially substitute in the ortho and para positions to the existing substituent in monosubstituted benzenes. This is attributed to the stabilization of the odd electron in the meta position by delocalization into the substituent. Application of this reasoning to the Claisen rearrangement has been presented.[17] A third alternative, that the electron-withdrawing substituents cause a change in mechanism in the dimethyl cases only, is considered less likely.

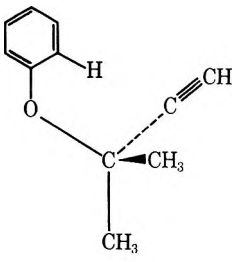
No definite reason is offered as to why our activation parameters, in particular the $\Delta S^{\pm}$ values, vary over such a wide range. Variation of ± 4–6 cal/mol would be expected, due to experimental error. It is likely that these reactions are not wholly "adiabatic,"[18] *i.e.*, that more than a single potential energy surface is involved in progress along the reaction coordinate.[19] It is conceivable that the structural differences would affect the crossing over, or lead to a different proportion of "free-radical" character in the transition state. Either of these might lead to a different factoring of $\Delta G^{\pm}$ into $\Delta H^{\pm}$ and $T\Delta S^{\pm}$ terms even for compounds with similar rates.

gem-**Dimethyl Effect.**—Our data show a large increase in the rate of cyclization caused by replacement of the geminal hydrogens by methyl groups. This of course is contrary to predictions based on the model for the *gem*-dimethyl effect in ref 8a, provided the flanking oxygen and ethynyl groups show the anticipated low steric interference.

Our suggestion as to the origin of the *gem*-dimethyl effect is that it is largely conformational. Thus **1a–c** would exist largely as the one of the three possible rotamers (ignoring degeneracy) with the lowest energy. If one (in **1b**) or both (in **1a**) R groups are hydrogen, the rotamer with that H nearer the benzene ring's ortho H (**4a**) would predominate, and the ethynyl group would not be situated in appreciable concentration in a position to react, without overcoming a substantial energy barrier to rotation. However, **1c**, with R = R′ = CH_3, would have the rotamer with the ethynyl group in a better position to react (**4b**), since the methyl groups



4a



4b

(15) V. Schomaker and D. P. Stevenson, *J. Amer. Chem. Soc.*, **63**, 37 (1941); T. F. Lai and R. E. Marsh, *Acta Crystallogr.*, **22**, 885 (1967).

(16) J. Hine, "Physical Organic Chemistry," 2nd ed, McGraw-Hill, New York, N. Y., 1962: (a) p 92; (b) p 471.

(17) (a) D. K. Black and S. R. Landor, *J. Chem Soc.*, 6784 (1965); (b) R. B. Woodward and R. Hoffman, *J. Amer. Chem. Soc.*, **87**, 2511 (1965); (c) W. N. White, C. D. Slater, and W. K. Fife, *J. Org. Chem.*, **26**, 627 (1961).

(18) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," 2nd ed, Wiley, New York, N. Y., 1961, p 78.

(19) That a low-lying excited state is available which has the transoid acetylenic bond required sterically for a Claisen-like rearrangement was shown by C. K. Ingold and G. W. King, *J. Chem. Soc.*, 2702, 2704, 2708, 2725, 2745 (1953). That the potential energy surface for this state intersects the ground state potential energy surface and that perturbations due to reagent attack can allow radiationless transition between them which otherwise would be quantum mechanically forbidden was shown by calculations of L. Burnelle, *Tetrahedron*, **20**, 2403 (1963).

would be more bulky at least than the ground-state ethynyl group and therefore would be away from the benzene ring. Other factors must be important to individual examples of the *gem*-dimethyl effect, but it seems obvious that this rotational factor is the most important one at least here.

Other Results.—In addition to the rates of cyclization of the *p*-aminophenyl ethers discussed earlier, data obtained by integration of pmr absorptions of the propargyl *C*-methyls as a function of time were used to get other preliminary results. Thus, to investigate the possibility that traces of impurities might disproportionately effect our cyclization rates, the rate of cyclization of **1c**, with Z = NO_2, was checked in dried *N,N*-dimethylaniline (DMA) and in DMA saturated with water, in DMA containing 12 or 24% (of the weight of **1c** taken) of α-pyridone or in the stronger base (at least in aqueous solution) *N,N*-dimethylbenzylamine. All of these rates were essentially identical. Solvent effects were not studied in any detail, but it was observed that the ratio of rate constants for **1c**, Z = NO_2, at 151° for DMA/*o*-dichlorobenzene (DCB) was 1.2,[20] while that for **1c**, Z = NHAc, was 1.6. The former is probably within the limit of error for the preliminary nmr results, while the latter is not. The ratio of rate constants for **1c**, Z = NH_2, at 130° comparing 1,3-propylene glycol/DCB as solvent was 3. This glycol reacted with the acetamido function and the nitro group at the high temperatures required for cyclization, so no further studies were done with it, but it might be useful in special circumstances.

A single preliminary study of the thermal cyclization of the sulfur analog of **1c**, Z = $NHC(O)CH_3$, gave a compound with no acetylenic hydrogen and the correct elemental analysis, presumably the thiochromene. Since this reaction is being studied by others,[21] we contemplate no further work along these lines.

Having relative data, we looked for evidence of uncyclized phenol in our fastest reactions, those of the amino compounds. We have found that a substance that reduces silver nitrate is present in the partial cyclization products of the 4-aminophenyl ethers. Cyclizations of monomethylpropargyl 4-aminophenyl ether (**1b**), Z = NH_2, followed by uv absorption, showed production and eventual disappearance of a strong absorption band at 335 nm (95% ethanol). We have not succeeded in isolating the intermediate, or an acetylated derivative of it, as yet.[22] Work designed to elucidate the mechanism of these cyclizations is continuing.

Experimental Section

Materials and Preparations.—The *o*-dichlorobenzene used as a solvent was commercial material which was distilled twice, taking a center cut arbitrarily. The propargyl ethers were made by the procedures outlined in Table III. Examples of the preparative methods for these propargyl ethers are given. Table IV gives physical properties of the new chromenes.

Method A. Phenol Potassium Salt plus Propargyl Bromide. 3-(4-Chlorophenoxy)butyne.—A solution of 64.3 g (0.5 mol) of *p*-chlorophenol in 400 ml of dried (CaH_2) *tert*-butyl alcohol was treated under N_2 with 56.5 g (0.505 mol) of potassium *tert*-butoxide and then in two equal portions with external cooling between them, with a total of 70 g (0.59 mol) of propargyl bromide, swirling occasionally. The reaction was allowed to stay for 6 hr and then heated under reflux for 0.5 hr and left overnight. It was then filtered, and the filtrate was distilled down, the residue combined with the ether-insoluble water-insoluble oil from the solids, and the resulting ethereal solution was extracted with 250-ml portions of 1 *N* aqueous NaOH and then with water.

(20) J. F. Kincaid and D. S. Tarbell, *J. Amer. Chem. Soc.*, **61**, 3085, (1939), reported that 10% of DMA had no effect on the rate of Claisen rearrangement in phenyl ether; more polar solvents are stated to increase Claisen rearrangement rates, but rather small solvent effects are the rule.

(21) Professor H. Kwart, private communication.

(22) The uv absorption maxima for what is labeled *o*-allenylphenoxide (anion) were reported in ref 5 to be about 250 and 280 nm, while *p*-aminophenol has uv maxima at about 233 and 300 nm in 95% ethanol.

TABLE III

PREPARATION OF PROPARGYL ETHERS AND PROPERTIES OF NOVEL ONES[a]

R	R′	X	Prepn[b]	Mp (c) or bp (mm), °C
H	H	OCH_3	A[d]	
H	H	$NHC(O)CH_3$	A, B	117.5–119 (B–H)
H	H	H	A, B[d]	
H	H	Cl	A[d]	
H	H	NO_2	A[d]	
H	H	CN	A	113–114 (A)
H	H	NH_2	E	102–104 (0.2)
CH_3	H	OCH_3	A + C, B + C	45 (1)
CH_3	H	$NHC(O)CH_3$	F	120.5–121.4 (A–W)
CH_3	H	H	B	43 (0.25)
CH_3	H	Cl	A	56–57 (H)
CH_3	H	NO_2	D	96–97 (A–W)
CH_3	H	CN	B	99–100 (A)
CH_3	H	NH_2	E	213.5–214[e] (A–E)
CH_3	CH_3	OCH_3	B + C	58–60 (0.1)
CH_3	CH_3	$NHC(O)CH_3$	F	82–83 (H–E)
CH_3	CH_3	H	B[f]	
CH_3	CH_3	NO_2	D	88–90 (0.05)
CH_3	CH_3	CN	B	29–30.5 (H)
CH_3	CH_3	NH_2	E	78–88[g] (0.06) 189–190.5[e] (A–E)

[a] Satisfactory analyses (±0.4 for C, H) were reported for all compounds except as footnoted. [b] See text for experimental details and examples. A = the phenol potassium salt plus the propargyl halide; B = the phenol plus the propargyl halide plus potassium carbonate in acetone; C = purification *via* the silver acetylide; D = 4-fluoronitrobenzene plus the potassium salt of the propargyl alcohol; E = reduction of the nitro compound by iron in acidic ethanol; F = acetylation with acetic anhydride in ethanol. [c] Recrystallization solvents: A = ethanol; B = benzene; E = anhydrous ether; H = hexane; W = water. [d] I. Iwai and J. Ide, *Chem. Pharm. Bull.*, **11**, 1042 (1963). [e] Hydrochloride; melting point with visible decomposition. [f] J. Hlubucek, E. Ritchie, and W. C. Taylor, *Tetrahedron Lett.*, **17**, 1369 (1969). [g] Base.

TABLE IV

PROPERTIES OF NEW[a] 3-CHROMENES[b]

R	R′	X	Mp (c) or bp (mm), °C
H	H	$NHC(O)CH_3$	63–64 (E–H)
H	H	CN	87–110 (0.1)[d]
H	H	NO_2	74.8–76 (A–W)
CH_3	H	OCH_3	70 (0.075)
CH_3	H	$NHC(O)CH_3$	94.5–96 (A–W)
CH_3	H	Cl	140–141 (26)
CH_3	H	NO_2	66–66.5 (E–H)
CH_3	H	CN	55.5–56 (E–H)
CH_3	CH_3	$NHC(O)CH_3$	126–126.8 (A–W)
CH_3	CH_3	NO_2	71–72 (E–H)
CH_3	CH_3	CN	36–37 (H)

[a] For **3a**, X = OCH_3, Cl, H: see I. Iwai and J. Ide, *Chem. Pharm. Bull.*, **11**, 1042 (1963). For **3b**, X = H: see E. E. Schweizer and R. Schepers, *Tetrahedron Lett.*, **15**, 979 (1963). For **3c**, X = $NHC(O)CH_3$: see British Patent 1,121,307. For **3c**, X = OCH_3: see J. Hlubucek, E. Ritchie, and W. C. Taylor, *Tetrahedron Lett.*, **17**, 1369 (1969). For **3c**, X = H: see *Beilstein*, 4th ed, **17**, 64 (1933). [b] Satisfactory analyses for C, H (±0.4) were reported for all new compounds tabulated. [c] Solvents: A = ethanol; E = anhydrous ether; H = hexane; W = water. [d] Solidified after some time, mp 48–50°. Not recrystallized.

TABLE V

R	R′	Z	Temp, °C	$k \times 10^6$, sec^{-1}
H	H	OCH_3	190.15	17.2
			190.55	22.3
			201.7	56.7
			210.3	114
H	H	NHAc[a]	170.6	2.46
			190.53	18.1, 16.85, 17.45[b]
			190.45	14.65
			200.9	29.9
H	H	H	180.6	4.49
			190.53	9.35
			200.9	17.6
			201.7	18.9
			210.3	41.1
H	H	Cl	190.15	7.18
			200.55	13.6
			210.3	30.3
H	H	NO_2	180.6	2.00
			190.52	6.17[c]
			200.55	15.2
H	H	CN	180.6	1.47
			190.05	2.94
			200.55	9.01
			200.9	9.22
			210.3	15.7
H	CH_3	OCH_3	150.13	3.36
			151.3	3.91
			160.3	8.40
			169.88	21.5
H	CH_3	NHAc	130.25	0.441
			138.9	0.987
			150.0	2.13
			150.12	2.58
			170.4	15.6
			190.05	86.7
H	CH_3	H	138.9	0.299
			150.13	1.30
			151.13	1.14
			160.6	3.45
			169.87	7.62
			190.05	45.2
H	CH_3	Cl	150.13	1.25
			151.3	1.05
			160.2	3.75
			169.88	10.2
			190.05	46.4
H	CH_3	NO_2[a]	149.95	0.565
			150.3	0.760
			160.1	1.91
			170.17	14.18
H	CH_3	CN	150.3	1.05
			160.6	2.03
			192.3	30.0
			200.3	75.3
CH_3	CH_3	OCH_3	140.65	72.1
			149.87	221
			151.7	256
			160.6	528
			170.55	1440
CH_3	CH_3	NHAc[a]	130.25	36.6
			130.75	41.8
			140.15	74.2[d]
			150.25	167
			160.9	408
CH_3	CH_3	H	140.65	33.6
			141.2	27.2
			149.9	78.7
			151.7	120
			160.9	203
			170.25	344
CH_3	CH_3	NO_2	130.25	15.1
			140.15	45.5[d]
			149.9	105
			160.6	333
			170.5	759
CH_3	CH_3	CN	141.2	34.6
			151.7	95.3
			160.6	231

[a] A very high temperature point omitted. [b] Done at 1:2, 1:5, and 1:10 dilutions, respectively. [c] Dilutions of 1:2 and 1:5 differed by 0.16. [d] Multiple dilutions used. See last paragraph of text.

Drying the ethereal solution ($MgSO_4$) and distillation gave 55 g (66%), bp 67° (0.5 mm) and 49° (0.1 mm). This had 99.8–100.3% of the theoretical titer for C≡CH. It crystallized after some time.

Anal. Calcd for $C_{10}H_9ClO$: C, 66.48; H, 4.94. Found: C, 66.64; H, 5.36.

Method B. Phenol plus the Propargyl Halide and Potassium Carbonate. 3-(4-Methoxyphenoxy)butyne.—A mixture of 45 g (0.36 mol) of *p*-methoxyphenol, 71 g of freshly ignited K_2CO_3, and 500 ml of dried acetone was stirred under N_2 while 40.4 g of 3-bromobutyne was added and under reflux for 20 hr more. It was then filtered and solvent was removed *in vacuo*, taken up in ether, washed with 1 *N* NaOH and then with water, dried ($MgSO_4$), and concentrated *in vacuo*, with bath temperatures in this and the preceding acetone removal not permitted to go over 50°. The residue was 37 g of an oil, with acetylenic H titer under 50%. Since rapid thermal cyclization was anticipated for this compound, it was not distilled at this point but instead purified by silver salt precipitation followed by rapid flash distillation.

Anal. Calcd for $C_{11}H_{12}O_2$: C, 75.00; H, 6.83. Found: C, 75.69; H, 6.95.

Method C. Purification by Silver Salt Precipitation. 3-(4-Methoxyphenoxy)-3-methylbutyne.—A 24-g sample of this ether made by procedure B with 61% of the theoretical acetylenic H titer wss dissolved in 150 ml of 95% ethanol and treated with a saturated aqueous solution of 15 g of silver nitrate. The resulting precipitate[23] was filtered with suction and washed with three small portions of ethanol. It was suspended in 150 ml of water and treated with stirring with 5 ml of HCl and extracted into ether. The ethereal solution was washed with water, dried ($MgSO_4$), and flash distilled *in vacuo* giving 9.5 g with a 97% titer for C≡CH.

Method D. 4-Fluoronitrobenzene plus the Potassium Salt of the Propargyl Alcohol. 3-(4-Nitrophenoxy)-3-methylbutyne.—A 25% suspension of potassium hydride (100 g) in oil was washed with dry toluene, using a fritted glass dip tube and N_2 pressure.

(23) If no precipitate forms, it is necessary to add ammonia to pH 9 (indicator paper).

Then 300 ml of 3-methylbutyn-3-ol was added with vigorous stirring under N_2 during 0.5 hr. The resulting solution was treated with 125 g of *p*-fluoronitrobenzene, added dropwise, and stirred at room temperature until 95% of the base had been consumed (3 days). It was then added to water and extracted with ether. The ethereal extract was washed with 1 *N* aqueous NaOH and then with water and dried ($MgSO_4$). Distillation gave recovered *p*-fluoronitrobenzene, bp 80–92° (10–20 mm), and 37 g of product of bp 80–90° (0.01 mm), a 35% yield.

Anal. Calcd for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40. Found: C, 64.78; H, 4.99.

Method E. Reduction of the Nitrophenyl Ether by Iron in Ethanol. 3-(4-Aminophenoxy)-3-methylbutyne.—The nitrophenoxy compound, 0.1 mol, was dissolved in 120 ml of 95% ethanol containing 4 ml of concentrated HCl, and 50 g (0.86 mol) of electrolytic iron powder was added in portions with stirring, starting immediately to minimize acid-catalyzed destruction of ether. After addition of the iron had been completed (*ca.* 15 min), the mixture was stirred another hour, 4 g of sodium acetate was added, and stirring was continued another hour. The precipitate was removed by filtration with a filtering aid and washed with ethanol. The combined filtrate and washings were concentrated *in vacuo* (aspirator and hot water bath) to ~60-ml volume and partitioned between water (1 l.) and ether (three 200-ml portions), and the ether was rapidly extracted with three 150-ml portions of 1 *N* aqueous HCl. The acidic solutions were basified with NaOH as each portion was separated and then extracted back into ether. The dried ($MgSO_4$) ethereal solutions were stripped of ether using a water bath (never over 80° for the dimethyl propargyl ether) and aspirator.

Typically with these precautions, the 3-(4-aminophenoxy)-3-methylbutyne was produced in 35% of the theoretical yield, with 96% of the theoretical acetylenic H.

Anal. Calcd for $C_{11}H_{13}NO$ (base): C, 75.43; H, 7.43; N, 8.00. Found: C, 75.43; H, 7.60; N, 8.04.

The hydrochloride was prepared in, and recrystallized from, anhydrous ethanol–ether and gave satisfactory elemental analyses.

Anal. Calcd for $C_{11}H_{14}ClNO$: C, 62.41; H, 6.67; N, 6.62. Found: C, 62.00; H, 6.65; N, 6.38.

2,2-Dimethyl-6-acetamidochroman.—Detailed preparations of this both by catalytic reduction of the chromene and by acid-catalyzed cyclization of 2-(3-methyl-2-buten-1-yl)-4-acetamidophenol will be found in British Patent 1,121,307 (1968).

Kinetics.—In general, 2.0-g samples of the ether were dissolved in 10 ml of *o*-dichlorobenzene, and the mixtures were heated when necessary in a steam bath until a homogeneous solution was formed. Then 0.2-ml aliquots were pipetted into ampoules which were flushed with N_2 for several minutes and sealed. Six to eight ampoules were placed in a Haake constant temperature bath, Model FT, containing silicone oil preheated to the selected temperature, and withdrawn singly through 6–8 half-lives, cooled to room temperature, and titrated for acetylenic hydrogen.[24] Total times of at least 4 hr and generally 1–5 days were used to minimize errors in time of cooling. Thermometers graduated to 0.2° (Brooklyn Thermometer Co.) were calibrated with Fisher triple-point standards, assuming the melting point to be identical with the triple point within the accuracy required.

Rate constants were calculated after discarding aberrant points found by manual (semilog paper) plots of log titer *vs.* $1/T_{abs}$ but never more than one point was discarded per run. The *k* was determined from a least-squares program, LINREG, available from the Program Library, General Electric Computer Time Sharing System, by substituting log titer for *Y*. All points of ln titer *vs.* time were weighted equally. Correlation coefficients better than 0.95 were regularly obtained.

The rates of thermal cyclization of the compounds **1** to give **3** directly determined are given in Table V, where R, R′, and Z refer to compound **1** structure.

Registry No.—**1a** (X = OCH_3), 17061-86-8; **1a** (X = NHAc), 26557-77-7; **1a** (X = H), 13610-02-1; **1a** (X = Cl), 19130-39-3; **1a** (X = NO_2), 17061-85-7; **1a** (X = CN), 33143-80-5; **1a** (X = NH_2), 26557-78-8; **1b** (X = OCH_3), 33146-82-7; **1b** (X = NHAc), 33143-83-8; **1b** (X = H), 1596-40-3; **1b** (X = Cl), 33143-85-0; **1b** (X = NO_2), 33143-86-1; **1b** (X = CN), 33143-87-2; **1b** (X = NH_2), 33143-88-3; **1c** (X = OCH_3), 33143-89-4; **1c** (X = NHAc), 2109-83-3; **1c** (X = H), 30504-61-1; **1c** (X = NO_2), 2109-84-4; **1c** (X = CN), 33143-92-9; **1c** (X = NH_2), 33143-93-0; **1c** HCl (X = NH_2), 33213-36-4; **3a** (X = NHAc), 33143-94-1; **3a** (X = CN), 33143-95-2; **3a** (X = NO_2), 16336-26-8; **3b** (X = OCH_3), 33143-98-5; **3b** (X = NHAc), 33143-99-6; **3b** (X = Cl), 33143-97-4; **3b** (X = NO_2), 33144-00-2; **3b** (X = CN), 33144-01-3; **3c** (X = NHAc), 19849-34-4; **3c** (X = NO_2), 33143-28-1; **3c** (X = CN), 33143-29-2.

(24) S. Siggia, "Quantitative Organic Analysis *via* Functional Groups," 3rd ed, Wiley, New York, N. Y., 1963, p 389.

Structure–Basicity Relationships of Sulfonium Ylides

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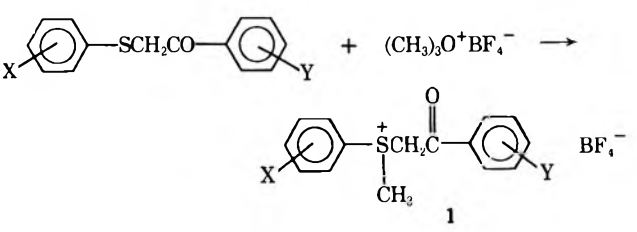
The substituent effect on basicity for a series of arylmethylphenacylsulfonium salts was determined. For the aryl substituents $\rho = +1.13$–1.23 and for the aroyl groups $\rho = +2.63$–2.68. The pK_a values for a series of dialkyl 4-bromophenacylsulfonium salts are directly related to the predicted effect of the S-attached groups on the degree of positive charge on sulfur. The results are interpreted in terms of the effect of various substituents on (1) carbanion delocalization and (2) inductive stabilization *via* the positively charged sulfur group.

The basicity of P ylides is significantly related to their nucleophilicity. A linear correlation between basicity and nucleophilicity has been observed in at least one case.[1] S ylides, however, exhibit no such correlation.[2] To outline fully the factors important to ylide basicity, an understanding of substituent effects is necessary. The purpose of this work is to define the above relationships for S ylides.

A series of methylarylphenacylsulfonium tetrafluoroborates (**1**) was prepared by alkylation of the corresponding sulfides (Table I) with trimethyloxonium tetrafluoroborate.



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The salts and their pK_a's are listed in Table II. A

(1) S. Fliszar, R. F. Hudson, and G. Salvadori, *Helv. Chim. Acta*, **46**, 1580 (1963).

(2) K. W. Ratts and A. N. Yao, *J. Org. Chem.*, **31**, 1185 (1966).

TABLE I

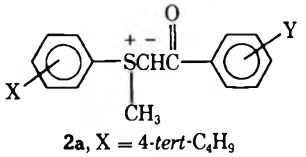
ARYL PHENACYL SULFIDES $XC_6H_4SCH_2COC_6H_4Y$

X	Y	Registry no.	Mp, °C	Yield, %	Calcd, % S	Calcd, % Hal	Calcd, % N	Found, % S	Found, % Hal	Found, % N
4-*tert*-C_4H_9	H	33191-96-7		84[a]						
4-CH_3	H	33046-45-6	36–37	75	13.23			13.30		
3-CH_3	H	27047-18-3	38–39		13.22			13.19		
H	H	16222-10-9	51–53	92	12.21	13.49		11.89	13.60	
4-Cl	H	30168-33-3	76–78	60	12.20	13.50		12.09	13.32	
4-Br	H	7312-06-3	77–78	90	10.44	26.02		10.51	25.96	
4-NO_2	H	33046-48-9	111–113	97	11.73		5.07	11.70		5.08
4-*tert*-C_4H_9	4-Cl	33191-98-9	89–90	77	10.06	11.12		9.78	11.12	
4-*tert*-C_4H_9	3-OCH_3	33191-99-0		95[a]						
4-*tert*-C_4H_9	4-OCH_3	33046-49-0	70–71	86	10.19			10.45		
H	4-Cl	33192-00-6	58.5–59.0	67	12.21	13.49		11.89	13.60	
4-Cl	4-Cl	33046-50-3	103–105	95	10.79	23.86		10.93	24.03	
4-Cl	3-OCH_3	33046-51-4		100[a]						
4-Cl	4-OCH_3	33046-52-5	72–74	92	10.96	12.11		11.38	12.68	
4-NO_2	4-Cl	33046-53-6	131–132	37	11.52	4.55		10.13[b]	5.15[b]	

[a] The crude undistilled oil obtained in these reactions was used directly in the preparation of the corresponding sulfonium salts. [b] This compound, though analyzing incorrectly for the sulfide, gave a sulfonium salt which analyzed correctly; see Table II.

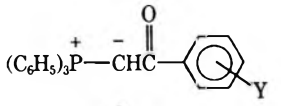
summary of $\sigma\rho$ treatment of the pK_a's is given in Table III. The pK_a values were determined by the titrimetric methods.[3]

The stabilization of the S ylides (2) by phenacyl-attached electron-withdrawing groups is indicated by the ρ values 2.63–2.68. This compares with values of



2a, X = 4-*tert*-C_4H_9
b, X = 4-Cl

2.3 for triphenylphosphonium phenacylides (**3**)[1], 2.1 for dimethylsulfonium phenacylides (**4**),[2] and 2.2–2.3 for pyridinium phenacylides (**5**) with Y varied.[4] Direct resonance interaction of the carbanion carbon increases the ρ value significantly, as illustrated by triphenylphosphonium fluorenylides (**6**) with Y varied (ρ = 5.0).[5]



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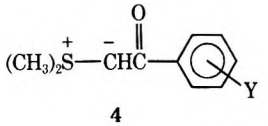

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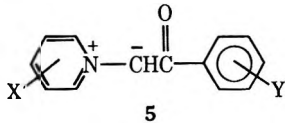

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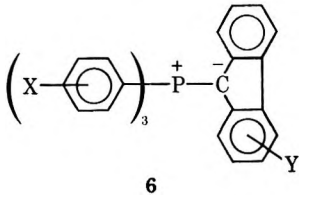

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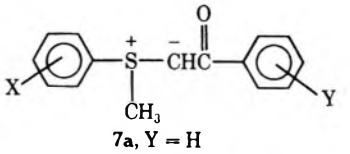
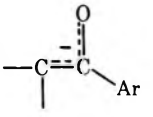
Stabilization of *S*-arylsulfonium ylides (**7**) by electron-withdrawing aryl substituents is indicated by the ρ values 1.13-1.23. The smaller ρ value indicates, however, less dependence of basicity upon a substituent in the *S*-aryl ring than in the phenacyl group,



7a, Y = H
b, Y = 4-Cl

i.e., the I effect of a substituted aryl ring is greater when attached to the pπ–pπ delocalization system i



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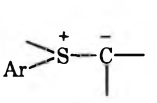


ii

than when attached to the dπ–pπ delocalization system ii. The same is observed in triphenylphosphonium fluorenylides (**6**) with X varied, where the ρ value is 1.7.[5] Pyridinium phenacylides[4] with X varied show a greater dependence (ρ = 2.6–3.1), but in that instance the positive heteroatom, nitrogen, is part of the resonance system directly affected by the attached group.[5] This type of stabilization is markedly dependent upon the type of carbanionic ylide considered, since $(XC_6H_5)_3P{=}NAr$ has a ρ value of 3.1.[6]

The p*K*a's of a series of *S*-alkyl substituted ylides were determined (Table IV).

Groups which stabilize the positive charge on sulfur increase the basicity of the corresponding ylide. This is evidenced by the higher values for **8** (7.4) and **13** (8.13). The stabilization involves delocalization of the positive charge by methyl[7] and transannular ring effects.[8] Such delocalization increases the extent of adjacent negative charge by reducing inductive electron withdrawal and decreasing pπ-dπ overlap with positive sulfur. Consequently, replacing *S*-methyl groups (**8**) with *S*-ethyl groups (**9**) results in a lower pK_a (7.4 → 6.46).[9] Similarly a ring compound such

(3) A. J. Speziale and K. W. Ratts, *J. Amer. Chem. Soc.*, **85**, 2790 (1963). Linear regression analysis was done by computer where r = multiple correlation coefficient and s = standard error of estimate.

(4) W. G. Phillips and K. W. Ratts, *J. Org. Chem.*, **35**, 3144 (1970).

(5) A. W. Johnson, S. Y. Lee, R. A. Swor, and L. D. Ryder, *J. Amer. Chem. Soc.*, **88**, 1953 (1966).

(6) A. W. Johnson and S. C. K. Wong, *Can. J. Chem.*, **44**, 2793 (1966).

(7) M. J. S. Dewar, "Hyperconjugation," Ronald Press, New York, N. Y., 1962.

(8) N. J. Leonard, T. W. Milligan, and T. L. Brown, *J. Amer. Chem. Soc.*, **82**, 4075 (1960).

(9) A. W. Johnson and R. T. Amel report a similar lowering of pK_a values when methyl groups are replaced by butyl groups; see ref 10.

(10) A. W. Johnson and R. T. Amel, *Can. J. Chem.*, **46**, 461 (1968).

TABLE II

X	Y	Registry no.	Mp, °C	Yield, %	Calcd, % C	Calcd, % H	Calcd, % S	Calcd, % Hal	Calcd, % N	Found, % C	Found, % H	Found, % S	Found, % Hal	Found, % N	Nmr, τ CH_3S^+	Nmr, τ SCH_2CO	pK_a
4-*tert*-C_4H_9	H	33043-69-5	138–139	95	59.08	6.00	8.30			59.27	6.10	8.54			6.56	4.45	7.19
4-CH_3	H	33043-70-8	130–135	40	55.83	4.99	9.32			55.96	5.06	9.66			6.58	4.45	7.16
3-CH_3	H	33043-71-9	115–116	93	55.83	4.99	9.32			55.73	4.99	9.44			6.58	4.44	7.09
H	H																(7.06)
4-Cl	H	33192-02-8	123–124	93	49.42	3.87	8.79	9.72		49.69	3.89	8.93	9.74		6.52	4.39	6.58
4-Br	H	33043-72-0	111–112	91	44.04	3.45	7.84	19.53		44.02	3.42	8.04	19.43		6.54	4.36	6.58
4-NO_2	H	33043-73-1	133–134	48	48.02	3.76	8.69		3.73	48.48	3.81	8.69		3.77	6.42	4.16	6.05
4-*tert*-C_4H_9	4-Cl	33043-74-2	158–159	35	54.24	5.27				54.41	5.30				6.59	4.50	6.62
										54.23					6.59	4.49	7.11
4-*tert*-C_4H_9	3-OCH_3	33043-75-3	91–94	49			7.7					7.45			6.63	4.56	8.01
4-*tert*-C_4H_9	4-OCH_3	33043-76-4	137–139	14			7.7					7.61			6.56	4.44	6.44
H	4-Cl	33043-77-5	155–157	94	49.41	3.87	8.79	9.72		49.85	3.61	3.73	9.80		6.56	4.46	6.07
4-Cl	4-Cl	33043-78-6	147–149	9			8.04					8.50			6.56	4.41	6.61
4-Cl	3-OCH_3	33043-79-9	94–100	13	48.7	4.09	8.13	8.98		49.02	4.13	8.37	9.22				
										49.18	4.26						
4-Cl	4-OCH_3	33043-80-0	143–144	75	48.7	4.09	8.13	8.98		49.63	4.21	8.30	9.21		6.59	4.48	7.46
4-NO_2	4-Cl	33043-81-1	170–174	76	43.98	3.2		8.66		44.22	3.01		8.37		6.46	4.23	5.54

TABLE III

$\sigma\rho$ TREATMENT OF pK_a VALUES FOR SALTS 1

Substituents	Equation	r	s
Vary X, Y = H	$pK_a = 6.96 - 1.23\sigma$	0.98	0.08
Vary X, Y = 4-Cl	$pK_a = 6.40 - 1.13\sigma$	0.99	0.06
Vary Y, X = 4-*tert*-C_4H_9	$pK_a = 7.28 - 2.68\sigma$	0.98	0.12
Vary Y, X = 4-Cl	$pK_a = 6.73 - 2.63\sigma$	0.97	0.17

TABLE IV

pK_a VALUES FOR SULFONIUM 4-BROMOPHENACYLIDES

Compd	Registry no.	M⁺	pK_a
8	7380-85-0	$(CH_3)_2\overset{+}{S}-$	7.4[a]
9	33046-55-8	$(C_2H_5)_2\overset{+}{S}-$	6.46
10	33046-56-9		7.54
11	33046-57-0		7.00
12	33046-58-1		6.63
13	33046-59-2		8.13

[a] Reference 4. [b] Kindly supplied by Professor N. J. Leonard; see J. Kleiner, Ph.D. Thesis, University of Illinois.

as **12**, where the sulfur atom is not positioned to stabilize the positive sulfur atom as it is in **13**, exhibits a lower pK_a (8.13 → 6.63).

Tieing the *S*-alkyl group into a ring tends to increase pK_a; *e.g.*, compare **9**, pK_a = 6.46, and **10**, pK_a = 7.54. Increasing the ring size lowers the pK_a value: **10**, 7.54; **11**, 7.00. Strain in the five-membered ring **10** conceivably results in increased p character in the ring C–S bonds and increased s character in the exo C–S bond, which decreases the acidity of protons attached to the exo carbon atom. Consequently, ylide **10** is more basic than ylide **9** or **11**.

The above results form a consistent picture of the structure–basicity relationships in S ylides. Electron delocalization by an attached group at any point in the molecule leads to decreased basicity. Such action by S-attached groups is related to the expected amount of sulfur positive charge. An increase in positive charge results in a stronger inductive effect, *via* increased electronegativity at sulfur, and stronger $d\pi$–$p\pi$ overlap, *via* decreased size of d orbitals to correspond more closely to p orbitals (**10**).

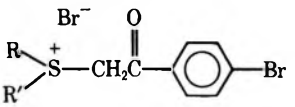
It is now possible to prepare S ylides of closely predicted basicities to determine the contribution of basicity to resulting nucleophilicities and finally reactivity.

Experimental Section

Preparation of Aryl Phenacyl Sulfides.—The procedure used is illustrated by 4′-*tert*-butylphenyl-4′-chlorophenacyl sulfide. Sodium (11.5 g, 0.5 g-atom) was dissolved in 350 ml of absolute ethanol. 4′-*tert*-butylthiophenol (83.2 g, 0.5 mol) was then added to the sodium ethoxide solution, followed by portionwise addition of 2-bromo-4′-chloroacetophenone (116.8 g, 0.5 mol). The mixture was heated at reflux for 10 min and poured onto 2 l. of ice. Filtration of the suspension gave a gummy brown solid which upon recrystallization from methanol yielded 123.3 g (77%) of 4′-*tert*-butylphenyl-4′-chlorophenacyl sulfide, mp 89–90°. The remaining sulfides prepared are listed in Table I.

Preparation of Arylmethylphenacylsulfonium Tetrafluoro-

TABLE V[a]



R	R′	Registry no.	Mp, °C	pK	Calcd, % C	Calcd, % H	Calcd, % Br	Calcd, % S	Found, % C	Found, % H	Found, % Br	Found, % S
C_2H_5	C_2H_5	6320-83-8	122–123	6.46	39.15	4.38	43.41	8.71	39.22	4.33	43.46	8.76
$-CH_2(CH_2)_2CH_2-$		19158-69-1	123–125	7.54	39.37	3.85	43.65	8.76	40.18	3.93		
$-CH_2(CH_2)_3CH_2-$		33046-62-7	141–142	7.00	41.07	4.24	42.04	8.43	40.47	4.07	42.43	8.56
$-CH_2(CH_2)_4CH_2-$		33046-63-8	149–150		42.66	4.60	40.55	8.13	42.66	4.96	40.17	7.99

[a] R = R′ = CH_3, reference 4; R, R′ = $-CH_2CH_2SCH_2CH_2-$ and $-(CH_2)_3S(CH_2)_3-$ supplied by Professor N. J. Leonard.

borates.—The procedure used is illustrated by methylphenyl-4′-chlorophenacylsulfonium tetrafluoroborate. Phenyl-4-chlorophenacyl sulfide (26.2 g, 0.1 mol) was added to trimethyloxonium tetrafluoroborate (14.8 g, 0.1 mol) in 200 ml of methylene chloride at room temperature. The mixture, after standing for 10 days, was diluted with ether and filtered. The methylphenyl-4-chlorophenacylsulfonium tetrafluoroborate was obtained as a white solid which after washing with ether and drying gave 34.2 g (94%), mp 155–157°. The salts prepared are listed in Table II.

Preparation of Dialkyl-4′-bromophenacylsulfonium Bromides.—The procedure used is illustrated with 4′-bromophenacyltetramethylenesulfonium bromide. Tetrahydrothiophene (17.6 g, 0.2 mol) and 2,4′-dibromoacetophenone (55.6 g, 0.2 mol) were mixed in 200 ml of benzene and heated to effect solution. After allowing the mixture to stand for 5 days the solid was removed by filtration. It was washed with benzene and dried in air to give 54.5 g (75%) of product, mp 123–125°. The sulfonium bromides prepared are listed in Table V.

Silver(I)-Catalyzed Oxidative Cleavage Reactions of Cyclic 1,2-Diols by Peroxydisulfate[1]

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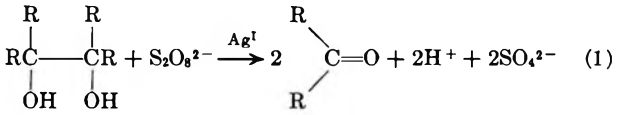
The oxidative cleavage rates of *cis*- and *trans*-1,2-cycloalkanediols by peroxydisulfate ($S_2O_8^{2-}$) in Ag^I-catalyzed reactions have been measured. The mechanistic implications of the observed reaction rates are discussed in terms of two mechanistic paths for the oxidative cleavage reactions. Path I proceeds by interaction of Ag^{III} with the diol. The kinetic data suggest the possible formation of a dsp^2 square planar complex as a reaction intermediate in oxidative cleavage by path I. The more rapid oxidative cleavage by path II is a free-radical chain reaction involving attack of the diol by Ag^{II} and apparently does not require formation of a cyclic complex between Ag^{II} and the diol.

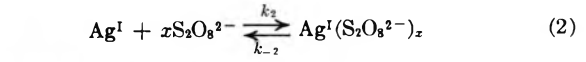
The oxidative cleavage reactions of glycols by peroxydisulfate in silver(I)-catalyzed reactions reported by Greenspan and Woodburn[2] have been the object of several mechanistic investigations.[3-8] Recently we



(1)

reported, on the basis of the kinetics of the reactions, that these oxidative cleavages were accomplished by two paths.[9] One route (path I) involves Ag^{III}, formed by oxidation of an $Ag^I(S_2O_8^{2-})_x$ complex, as the cleaving agent. The other route (path II) is a chain sequence of free-radical reactions involving Ag^{II} as the oxidative cleaving agent. Initiation of the chain sequence 6–8 is accomplished by reaction of Ag^{III} with Ag^I (reaction 5) yielding the chain-carrying Ag^{II} radical. Formation of Ag^{III} is the rate-determining factor for reaction by path I, whereas the rate of oxidative cleavage by path II, which is generally more rapid than reaction by path I, may depend on a variety of factors. Most significant of these is the partitioning of the Ag^{III} formed in reaction 3 between the substrate, resulting in cleavage by path I, and Ag^I which initiates the more rapid oxidation *via* the chain sequence. The relative amounts of cleavage by paths I and II depend on both the concentration of the substrate and its ability to interact with Ag^{III}. Thus, at lower substrate concentrations the overall rates of oxidative cleavage are faster, since more of the reaction is occurring by the more rapid free-radical chain sequence. On the other hand, if the substrate is capable of reacting readily with Ag^{III}, cleavage by the slower path I will be more prevalent than with substrates that react less readily with Ag^{III}. The latter situation allows for more extensive reaction of Ag^{III} with Ag^I, thereby initiating the faster oxidative cleavage by the free-radical chain reaction.

Path I



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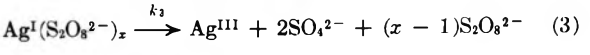
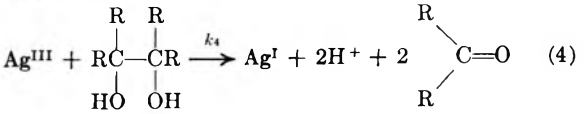


(3)



(4)

(1) This work was supported by a grant (AM-08517) from the U. S. Public Health Service.

(2) P. Greenspan and M. Woodburn, *J. Amer. Chem. Soc.*, **76**, 6345 (1954).

(3) D. D. Mishra and S. Ghosh, *J. Indian Chem. Soc.*, **41**, 397 (1964).

(4) M. M. Mhala and R. V. Iyer, *Indian J. Chem.*, **3**, 568 (1965).

(5) N. Venkatasubramanian and A. Sabesan, *Curr. Sci.*, 632 (1967).

(6) N. Venkatasubramanian and A. Sabesan, *Tetrahedron Lett.*, No. 40, 4919 (1966).

(7) G. V. Bakore and S. N. Joshi, *Z. Phys. Chem. (Leipzig)*, 250 (1965).

(8) G. D. Manghani and G. V. Bakore, *Bull. Chem. Soc. Jap.*, **41**, 2574 (1967).

(9) E. S. Huyser and L. G. Rose, *J. Org. Chem.*, **37**, 649 (1972).

Path II

$$Ag^{III} + Ag^{I} \xrightarrow{k_5} 2Ag^{II} \quad (5)$$

$$Ag^{II} + RC(OH)-CR(OH) \xrightarrow{k_6} Ag^{I} + R_2C{=}O + {\cdot}COH \quad (6)$$

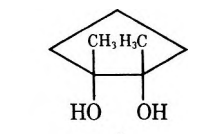
$$R_2{\cdot}COH + S_2O_8^{2-} \xrightarrow{k_7} R_2C{=}O + H^+ + SO_4^{2-} + SO_4{\cdot}^- \quad (7)$$

$$SO_4{\cdot}^- + Ag^{I} \xrightarrow{k_8} SO_4^{2-} + Ag^{II} \quad (8)$$

$$R_2\dot{C}OH + SO_4{\cdot}^- \xrightarrow{k_9} SO_4^{2-} + H^+ + R_2C{=}O \text{ (termination reaction)} \quad (9)$$

Both Ag^{II} and Ag^{III} form dsp^2 square planar complexes with bifunctional species such as glycols.[10] If the Ag^{I}-catalyzed peroxydisulfate oxidative cleavages of diols proceed *via* such intermediates, the reactions would be expected to have stereochemical requirements of the hydroxy groups similar to those encountered in periodic acid[11] and lead tetraacetate[12] cleavage reactions which proceed by decomposition of cyclic intermediates formed from the diol and the oxidative cleavage agent. Cyclic intermediates capable of decomposition in this manner are formed more readily from cis 1,2-diols than from the corresponding trans isomers, as evidenced by the more rapid rates of cleavage of cis diols.[13]

To determine if the dsp^2 square planar cyclic complexes are intermediates in the Ag^{I}-catalyzed peroxydisulfate reactions, we have examined oxidative cleavages of *cis*- and *trans*-1,2-dimethylcyclopentane-1,2-diols (**1** and **2**, respectively) and *cis*- and *trans*-1,2-dimethylcyclohexane-1,2-diols (**3** and **4**, respectively) with



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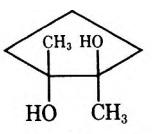

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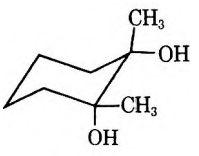

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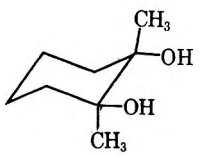


4

these reagents. The cleavage products from **1** and **2** and from **3** and **4** are the expected diketones 2,6-heptadione (**5**) and 2,7-octadione (**6**), respectively. Table I lists the initial rates of oxidative cleavage of these

(10) J. A. McMillan, *Chem. Rev.*, **62**, 65 (1962).

(11) C. C. Price and H. Kroll, *J. Amer. Chem. Soc.*, **60**, 2726 (1938); C. C. Price and M. Knell, *ibid.*, **64**, 552 (1942); G. J. Buist and C. A. Burton, *J. Chem. Soc.*, 1406 (1954).

(12) R. Criegee, L. Kraft, and R. Bank, *Justus Liebigs Ann. Chem.*, **507**, 159 (1933); R. Criegee, E. Buchner, and W. Walther, *Ber.*, **73**, 571 (1940); R. Criegee, E. Hager, G. Huber, P. Kruck, R. Marktscheffel, and H. Schellenberger, *Justus Liebigs Ann. Chem.*, **599**, 81 (1956).

(13) Evidence is available, however, that indicates that *trans*-1,2-diols not capable of forming cyclic intermediates can be cleavaged by lead tetraacetate but at slower rates than encountered for those diols that are able to form cyclic intermediates. See C. A. Grob and P. W. Schiess, *Helv. Chim. Acta*, **43**, 1546 (1960).

TABLE I

INITIAL OXIDATIVE CLEAVAGE RATES[a] OF CYCLIC 1,2-DIOLS BY PEROXYDISULFATE AT 30° [c]

Diol	$[Ag^{I}] \times 10^3$	[Diol] 0.0375	[Diol] 0.00938
1	5.12	0.565	
1	2.56	0.296 (0.040)[b]	0.355
2	5.12	0.879	
2	2.56	0.457 (0.079)[b]	0.516
3	5.12	0.299	
3	2.56	0.160 (0.113)[b]	0.225
4	5.12	0.916	
4	2.56	0.488 (0.120)[b]	0.597

[a] Rate expressed in mol $l.^{-1}$ $min^{-1} \times 10^4$ and measured over the first 10% of the reaction. [b] Rate of oxidative cleavage in presence of 0.1 *M* allyl acetate. [c] pH = 1.7, $[S_2O_8^{2-}] = 0.01$ *M*.

$$1 \text{ (or } 2) + S_2O_8^{2-} \xrightarrow{Ag^{I}} 2SO_4^{2-} + CH_3C(=O)(CH_2)_3C(=O)CH_3 + 2H^+ \quad (10)$$

5

$$3 \text{ (or } 4) + S_2O_8^{2-} \xrightarrow{Ag^{I}} 2SO_4^{2-} + CH_3C(=O)(CH_2)_4C(=O)CH_3 + 2H^+ \quad (11)$$

6

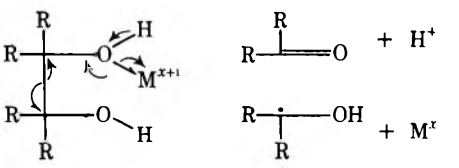
diols by peroxydisulfate in silver(I)-catalyzed reactions. The reaction rates follow the rate law

$$\text{rate} = \frac{k_2k_3[Ag^{I}][S_2O_8^{2-}]^{x+1}}{k_3[S_2O_8^{2-}] + k_{-2}} + \left(\frac{k_2k_3k_7k_8}{k_9(k_3[S_2O_8^{2-}] + k_{-2})}\right)[Ag^{I}][S_2O_8^{2-}]^{(x+1)^1/_2+1} \quad (12)$$

where the first term is the rate of cleavage by path I and the second term that for path II provided chain termination occurs only by reaction 9, the most likely termination route under these conditions.[9]

The reactions are very nearly first order in $[Ag^{I}]$. However, changes in the diol concentration have an inverse effect on the oxidative rate, which is indicative of more reaction of Ag^{III} with Ag^{I} at the lower diol concentration, thereby initiating the more rapid cleavage by the free-radical chain mechanism (path II). That some cleavage occurs by path II in each case is also evidenced by the effect of allyl acetate, a free-radical chain inhibitor, on decreasing the overall reaction rate.

Assuming that the observed oxidative cleavage rates at the lower diol concentrations reflect mainly reaction by path II, then the similarities of the rates of oxidative cleavage of the trans diols relative to the corresponding cis diols obviate the necessity of formation of a cyclic intermediate of the diol with Ag^{II} for cleavage *via* the free radical chain mechanism. The necessity of cyclic complexes as reaction intermediates has been disposed of in oxidative cleavage reactions effected by Ce^{IV} and V^{V}.[14] These species also effect one-electron oxidations generating a free radical from the glycol in a manner

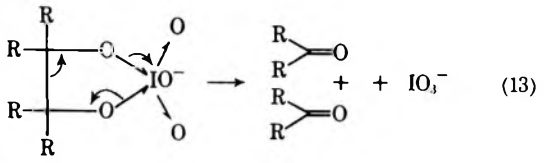


$(M^{x+1} = Ag^{II}, Ce^{IV}, V^{V})$

(14) J. S. Littler and W. A. Waters, *J. Chem. Soc.*, 2767 (1960); H. L. Hintz and D. C. Johnson, *J. Org. Chem.*, **32**, 556 (1967).

similar to the reactions of Ag^{II}. Involvement of both oxygens of the diol is not required in these processes.

Cyclic intermediates have been suggested to be necessary only in oxidative cleavage reactions that involve two-electron oxidants [*e.g.*, IO_4^-, $Pb(OAc)_4$]. In such oxidations, the electron movement involves all of the atoms of the rings and apparently is more facile if the participating atoms are coplanar (or very nearly so). Oxidative cleavage by path I involving Ag^{III}, a two-



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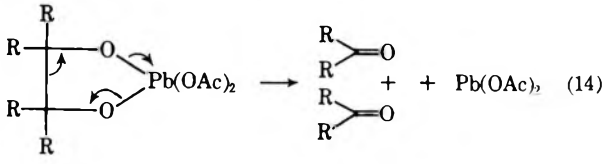
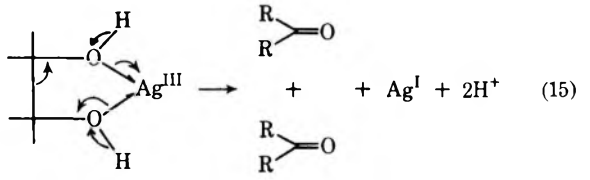


(14)

electron oxidant, may require the formation of a cyclic intermediate. By analogy with the periodic acid and lead tetraacetate reactions, cyclic complexes that decompose yielding the oxidative cleavage products should be formed more readily between Ag^{III} and the cis diols than with the trans isomers.[15] Although



(15)

there is no direct evidence for a cyclic intermediate in the oxidative cleavages by path I, the formation and participation of such a species can be inferred from the kinetic data in Table I. Since the cis diols would be expected to undergo cleavage by path I more readily than the trans isomers, less Ag^{III} would react with Ag^I to initiate oxidative cleavage by the more rapid free-radical chain sequence of path II. Initiation of the chain reaction could be expected to occur more readily in the reactions of the trans isomers because the Ag^{III} is not so efficiently consumed by the trans diols as it is by the corresponding cis diols, which can form the cyclic intermediates that decompose by path I. The somewhat faster rates of cleavage of the trans isomers with respect to the corresponding cis isomers may reflect, therefore, a greater amount of cleavage by the more rapid path II.

In the case of *cis*-1,2-dimethylcyclohexane-1,2-diol (**3**), not only is the oxidative cleavage rate decidedly slower than that of the trans isomer under similar conditions, but allyl acetate is considerably less effective in inhibiting the reaction rate of the cis isomer. Both factors suggest that a significant amount of the oxidative cleavage of **3** occurs by path I because Ag^{III} complexes readily with this diol. The more effective retardation of the overall cleavage rate of **1**, **2**, and **4** reflects a larger proportion of the available Ag^{III} being partitioned in the reaction with Ag^I to initiate cleavage by path II.

(15) A cyclic complex having essentially the same strain as that obtained from the *cis*-cyclohexane-1,2-diol (**3**) should be formed from the *trans*-diequatorial cyclohexane-1,2-diol (**4**). However, a low-energy transition state for the decomposition of the trans isomers complex cannot be attained owing to the conformational aspects of the cyclohexane ring that prevent 1,2-diequatorial substituents from becoming coplanar.

Experimental Section

Materials.—1,2-Dimethylcyclohexene, bp 129–135°, $n^{20}D$ 1.4601, was prepared by dehydration of 1,2-dimethylcyclohexan-1-ol, which in turn was obtained by reaction of methylmagnesium iodide with 2-methylcyclohexanone (Aldrich Chemical Co.). ***trans*-1,2-Dimethylcyclohexane-1,2-diol**, mp 92–93° (lit.[16] 93°), was obtained in 22% yield from the performic acid hydroxylation[17] of 1,2-dimethylcyclohexene. ***cis*-1,2-Dimethylcyclohexane-1,2-diol**, mp 51° (lit.[18] 50°), was obtained in about 2% conversion from the reaction of 1,2-dimethylcyclohexene with osmium tetroxide and hydrogen peroxide.[19] ***trans*-1,2-Dimethylcyclopentane-1,2-diol**, mp 104–105° (lit.[20] 105–107°), was prepared in 16% conversion by performic acid hydroxylation[17] of 1,2-dimethylcyclopentane (K and K Laboratories, Inc.). ***cis*-1,2-Dimethylcyclopentane-1,2-diol**, mp 23° (lit.[21] 24°), was obtained in about 7% conversion from the osmium tetroxide catalyzed hydroxylation of 1,2-dimethylcyclopentene with hydrogen peroxide.[18]

Oxidative Cleavage of *cis*- and *trans*-1,2-Dimethylcyclopentane-1,2-diol.—A reaction mixture consisting of *cis*-1,2-dimethylcyclopentane-1,2-diol (0.130 g, 1 mmol), potassium peroxydisulfate (0.270 g, 1 mmol), and silver nitrate (0.0136 g, 0.08 mmol) in 20 ml of water was allowed to stand at room temperature under a nitrogen atmosphere for 2 days. A saturated solution of 2,4-dinitrophenylhydrazine in 2 *N* HCl (120 ml) was added to the reaction mixture. 2,6-Heptadione bis-2,4-dinitrophenylhydrazone, mp 184–185° (lit.[21] 183–185°), was isolated in 79% yield (0.387 g). In a similar experiment the 2,6-heptadione bis-2,4-dinitrophenylhydrazone, mp 184°, was obtained from *trans*-1,2-dimethylcyclopentane-1,2-diol (0.466 g, 95% of theory).

Oxidative Cleavage of *cis*- and *trans*-1,2-Dimethylcyclohexane-1,2-diols.—A solution of *cis*-1,2-dimethylcyclohexane-1,2-diol (0.144 g, 1 mmol), potassium peroxydisulfate (0.270 g, 1 mmol), and silver nitrate (0.135 g, 0.08 mmol) was allowed to react under a nitrogen atmosphere for 2 days. Addition of 120 ml of a 2 *N* HCl solution saturated with 2,4-dinitrophenylhydrazine resulted in formation of 0.242 g (48% of theory) of 2,7-octanedione bis-2,4-dinitrophenylhydrazone, mp 218–219° (lit.[22] 219°). In a similar experiment employing 1.5 mmol of potassium peroxydisulfate, the 2,7-octanedione bis-2,4-dinitrophenylhydrazone was obtained in 71% yield. Oxidative cleavage of 0.144 g (1 mmol) of *trans*-1,2-dimethylcyclohexane-1,2-diol with 0.27 g (1 mmol) of potassium peroxydisulfate and 0.0136 g (0.08 mmol) of silver nitrate yielded 0.492 g (96% of theory) of 2,7-octanedione bis-2,4-dinitrophenylhydrazone which melted at 218–218.5°.

Kinetic Measurements.—The reactions were performed in distilled water buffered to a pH of 1.7 by 0.25 *M* sodium sulfate and 0.25 *M* sodium bisulfate. The organic substrate and potassium peroxydisulfate were dissolved in the buffered solution and placed in a painted three-neck 500-ml flask. The flask was placed in a water bath maintained at 30 ± 0.1° and nitrogen was bubbled through the solution for 1 hr to remove any dissolved oxygen. An appropriate amount of 0.4 *M* silver nitrate was added and immediate reaction ensured. Aliquots of the reaction mixture were removed at appropriate time intervals and the unreacted peroxydisulfate was determined by the iodometric method described by Bartlett and Cotman.[23]

Registry No.—**1**, 33046-19-4; **2**, 33046-20-7; **3**, 33046-21-8; **4**, 33046-22-9; silver(I) ion, 14701-21-4; peroxydisulfate, 15092-81-6; 2,7-octanedione bis-2,4-DNP, 33046-95-6.

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Chemistry of the Sulfur–Nitrogen Bond. II.[1] A Mechanistic Study of the Rearrangement of 2-Nitrobenzenesulfenanilides to 2-Aminobenzenesulfonanilides

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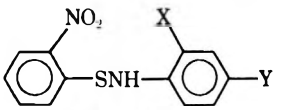
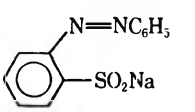
2-Nitrobenzenesulfenanilides thermally rearranged to give, among other products, 2-aminobenzenesulfonanilides. A mechanistic scheme is proposed which involves homolytic cleavage of the sulfur–nitrogen bond and transfer of a hydrogen atom from the solvent.

The ability of an *o*-nitro group to transfer its oxygens to an adjacent group is well known and has been reviewed.[3] There are a number of examples in the literature in which an *o*-nitro group transfers its oxygens to an adjacent sulfur. In this oxidation–reduction the sulfur is oxidized and the nitro group reduced. For example, *o*-nitrothiophenol, when heated in the presence of base, gave 2-azobenzenesulfinic acid;[4] methyl 2,4-dinitrobenzenesulfenate in hydrochloric acid gave 2-amino-4-nitrobenzenesulfonic acid;[5] 2-nitrobenzenesulfenyl chloride in hydrofluoric acid gave bis(2,2′-fluorosulfonyl)azobenzene;[6] and 2-nitrobenzenesulfenanilide (**1a**) with sodium hydroxide gave 2-azobenzenesulfenate (**2**).[7] More recently, the pyrolysis of *tert*-butyl 2-nitrobenzenesulfenate gave, among other products, aniline.[8] Photolysis of 2,4-dinitrobenzenesulfen-*N*-methylanilide gave 2-amino-4-nitrobenzenesulfon-*N*-methylanilide[9] and the photolysis of 2-nitrodiphenyl sulfoxide gave 2-nitrosodiphenyl sulfone.[10] With the exception of Brown's detailed investigation of the mechanism of rearrangement of sulfenamide **1a** to 2-azobenzenesulfenate (**2**),[11] no attempt has been made to elucidate the mechanism of these unusual oxidation–reduction reactions.

In the course of an investigation of the chemistry of the sulfur–nitrogen bond we observed that when 2-nitrobenzenesulfenanilide (**1a**) and 2-nitrobenzenesulfen-*p*-toluide (**1b**) were heated in their corresponding amine solvents they rearranged to give aminonitrodiphenyl sulfides **3a–c**, phenothiazine **4a,b**, and the major products, 2-aminobenzenesulfonanilide (**5a**) and 2-aminobenzenesulfon-*p*-toluide (**5b**).[1] We report here the results of our investigation into the mechanism of rearrangement of 2-nitrobenzenesulfenanilides to 2-aminobenzenesulfonanilides.



1a, X = Y = H
b, X = H; Y = CH_3
c, X = H; Y = CH_3O
d, X = Y = Cl
e, X = C_6H_5; Y = H



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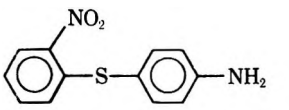
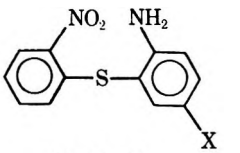
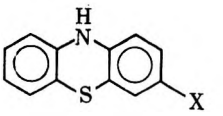


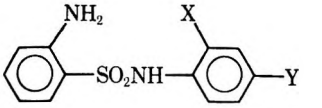
3a



3b, X = H
c, X = CH_3



4a, X = H
b, X = CH_3



5a, X = Y = H
b, X = H; Y = CH_3
c, X = H; Y = CH_3O
d, X = Y = Cl
e, X = C_6H_5; Y = H

Results

To determine the scope of the rearrangement we investigated the thermal rearrangements of 2-nitrobenzenesulfen-*p*-anisidine (**1c**),[12] 2-nitrobenzenesulfen-2,4-dichloroanilide (**1d**),[13] 2-nitrobenzenesulfen (2-phenyl)anilide (**1e**),[13] and 2-nitrobenzenesulfen-*N*-methylanilide (**6**).[12] The general rearrangement procedure involved heating the sulfenamide in a sealed tube with an excess of the corresponding amine solvent at 195° for 15.5 hr. The excess solvent was removed, and the dark residue was dissolved in methylene chloride, filtered, and chromatographed on Florisil. Products were identified when possible with authentic samples. These results are summarized in Table I.

Sulfenamide **1c** in *p*-anisidine gave two products: *p*-methoxyazobenzene (**7**)[14] and 2-aminobenzenesulfon-*p*-anisidine (**5c**). Structural proof of **5c** is supported by elemental analysis, infrared spectrum, and nmr spectrum. Sulfonamide **5c** was prepared independently by condensation of 2-nitrobenzenesulfonyl chloride with 2-aminobiphenyl. Reduction of the resulting 2-nitrobenzenesulfon-*p*-anisidine gave **5c** in greater than 70% yield.

(1) Part I: F. A. Davis, R. B. Wetzel, T. J. Devon, and J. F. Stackhouse, *J. Org. Chem.*, **36**, 799 (1971).
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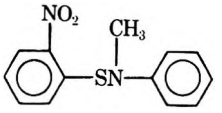
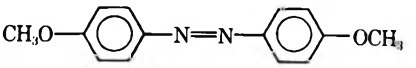
TABLE I
THERMAL REACTIONS OF 2-NITROBENZENESULFENANILIDES AT 195° FOR 15.5 HR

Sulfenamide	Solvent	Products (yield, %)
1a	Aniline[a]	1a (34), 3a (12), 3b (5), 4a (3), 5a (37)
	Anisole	3a (4), 3b (6), 4a (trace), 5a (22), 15 (12)
	Decalin	3a (5), 3b (4), 4a (trace), 5a (20), 15 (21)
	Neat	3a (3), 3b (4), 5a (21), 15 (10)
1b	*p*-Toluidine[a]	3c (18), 4b (14), 5b (55)
1c	*p*-Anisidine	7 (27)[b], 5c (56)
	p-Anisidine[c]	7 (24)[b], 5c (57)
	Decalin	5c (17), 15 (37)
1d	2,4-Dichloroaniline	3d (61), 5d (28)
1e	2-Aminobiphenyl	1e (61), 8 (18),[b] 5e (25)
6	*N*-Methylaniline	9 (1), 10a (5), 10b (5), 11 (57)
	Decalin	9 (10), 10a (16), 10b (30), 11 (8)

[a] Reference 1. [b] Yield calculated assuming that 1 mol of sulfenamide yields 0.5 mol of azobenzene. [c] Degassed.

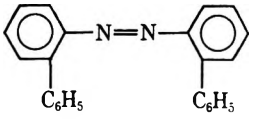


6



7

Sulfenamide **1d** in 2,4-dichloroaniline gave 2-amino-3,5-dichloro-2′-nitrodiphenyl sulfide (**3d**)[15] and 2-aminobenzenesulfon-2,4-dichloroaniline (**5d**).[16]



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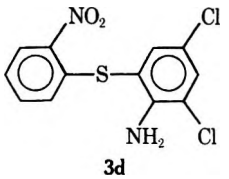
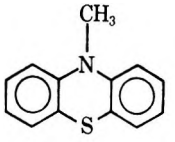


3d

Sulfenamide **1e** in 2-aminobiphenyl gave two products, 2-azobiphenyl (**8**)[17] and 2-aminobenzenesulfon(2-phenyl)anilide (**5e**). Structural proof of sulfonamide **5e** was based upon elemental analysis, infrared spectrum, proton nmr spectrum, and independent synthesis. The proton nmr spectrum of **5e** showed absorption at δ 4.8 (amine) and at δ 6.5 and 7.2 (relatively areas 2:2:12) in agreement with the proposed structure.

Sulfonamide **5e** was prepared independently by condensation of 2-nitrobenzenesulfonyl chloride with 2-aminobiphenyl. Reduction of the 2-nitrobenzenesulfon(2-phenyl)anilide gave **5e** in 7% overall yield.

Sulfenamide **6** in *N*-methylaniline gave four products, *N*-methylphenothiazine (**9**),[18] 2-nitro-2′-(*N*-methyl)-aminodiphenyl sulfide (**10a**),[19] 2-nitro-4′-(*N*-methyl)-aminodiphenyl sulfide (**10b**), and 2-aminobenzenesulfon(*N*-methyl)anilide (**11**).[20] The structure of sulfide **10b** is supported by elemental analysis, infrared spectrum, nmr spectrum, and independent synthesis. The proton nmr spectrum showed absorption at δ 3.80 (broad singlet, amine) and complex absorption at δ 7.05 and 8.24 (relative areas 3:1:7:1) in agreement with the proposed structure. Diphenyl sulfide **10b** was prepared by methylation of sulfide **3b** using *p*-toluenesulfonyl chloride and dimethyl sulfate.



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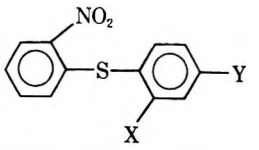
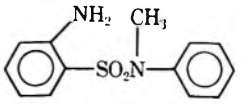


10a, X = $NHCH_3$; Y = H
b, X = H; Y = $NHCH_3$



11

Ullmann and Gross reported that sulfonamide **11** was a white solid, mp 63°.[21] The product that we isolated from the thermal rearrangement of sulfenamide **6** in *N*-methylaniline was an oil which failed to solidify after purification by column chromatography, sublimation, or preparative glc. We prepared sulfonamide **11** according to the method of Ullmann and Gross and isolated an oil which was identical in all aspects with **11**. The structure of sulfonamide **11** is supported by elemental analysis, infrared spectrum, and proton nmr spectrum. The proton nmr spectrum showed absorption at δ 6.62, 7.26, and 7.33 (relative areas 3:2:2:5:2) in agreement with the proposed structure.

Discussion

Previously we reported that 3-nitrobenzenesulfenanilide gave none of the corresponding sulfonamide when treated under the reaction conditions and that the presence or absence of oxygen had little effect on the formation of the 2-aminobenzenesulfonanilides[1] (*i.e.*, **1a,c** in degassed solutions gave nearly the same yields of sulfonamides **5a,c**, respectively). Brown has recently shown using ^{18}O that the oxygens of the nitro group are transferred intramolecularly in the rearrangement of **1a** to **2**.[11] These results suggest that the oxygens of the nitro group in 2-nitrobenzenesulfenanilides are transferred intramolecularly to the sulfur in the formation of the 2-aminobenzenesulfonanilides. The reported close proximity of the oxygens of the nitro group to the sulfur in 2-nitrobenzenesulfenic acid further supports this conclusion.[21]

Questions as yet unanswered are what is the origin of the hydrogen of the amino group, and does anything happen to the S–N bond during the rearrangement?

The hydrogen of the amino group may be transferred either from the solvent or by some intramolecular process from the sulfenamide nitrogen. This latter process may be ruled out as a major pathway for the

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(16) A. A. Patchett and S. A. Harris, French Patent 1,348,006 (1964); *Chem. Abstr.*, **60**, P10695*e* (1964).
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(18) H. I. Berstein and L. R. Rothstein, *ibid.*, **66**, 188 (1944).
(19) W. J. Evans and S. Smiles, *J. Chem. Soc.*, 181 (1935).
(20) F. Ullman and G. Gross, *Chem. Ber.*, **43**, 2694 (1910).
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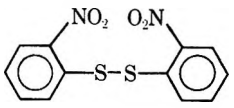
formation of the sulfonamide by a consideration of the rearrangement of sulfenamide **6**. Sulfenamide **6**, which has no sulfenamide hydrogen, gave a greater than 57% yield of sulfonamide **11**. In this example the hydrogen must be transferred from the solvent.

Sulfenamide **1a** in anisole, decalin, or in the absence of solvent gave 20–22% of sulfonamide **5a**, and **1c** in decalin gave 17% of **5c**. The hydrogen is therefore transferred from the sulfenamide nitrogen because the reaction proceeded to the same extent without solvent as in anisole or decalin. The transfer of the hydrogen is probably not intramolecular, since sulfenamide **6** in decalin gave 8% sulfonamide **11**. In all probability the hydrogen is transferred after cleavage of the S–N bond, since in all cases bis(2-nitrophenyl) disulfide (**12**) was isolated in substantial amounts (Table I).



12

There is compelling evidence that the sulfur–nitrogen bond in sulfenamides is labile under thermal conditions. At 109° aryl sulfenanilides undergo a facile exchange with aryl amines.[1,22] Homolytic cleavage of the S–N bond in benzothiazole-2-alkylsulfenamides to give thiyl and amino radicals has been suggested to account for their activity as accelerators in the vulcanization of rubber.[23] Heating *N*-cyclohexylbenzothiazole-2-sulfenamide at 143° gave strong esr signals.[24]

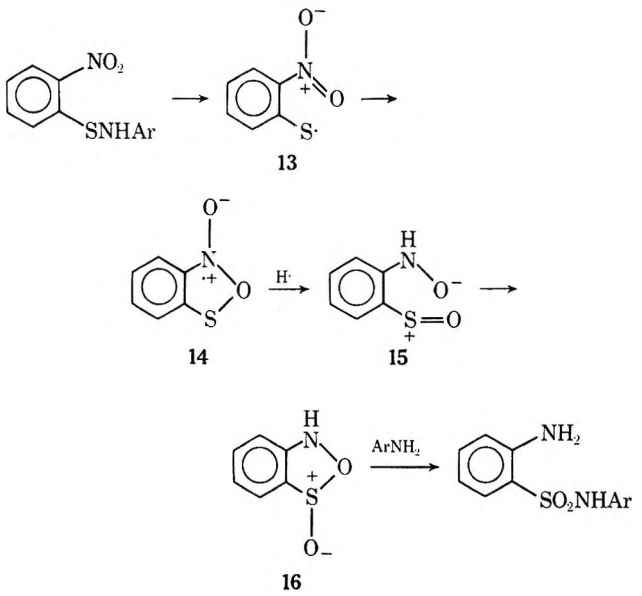
Heterolytic cleavage of the sulfur–nitrogen bond must also be considered. Heating *tert*-butyl 2-nitrobenzenesulfonate is reported to give sulfenium ions,[8] and alkyl sulfenyl esters thermally decompose by a cyclic mechanism.[25] Field and coworkers have shown that unsymmetrical disulfides, at moderate temperatures (*ca.* 68–89°), cleave heterolytically.[26,27]

Scheme I suggests a mechanistic pathway for the formation of the 2-aminobenzenesulfonanilides and involves cleavage of the S–N bond prior to transfer of the hydrogen. This scheme involves homolytic cleavage of the S–N bond to give the 2-nitrobenzenesulfenyl radical (**13**), which may be stabilized by interaction with the oxygens of the nitro group (**14**). Structures similar to **13** have been suggested to account for the "abnormal" chlorination of 2-nitrobenzenesulfenyl chloride[28] and the stabilization of the 2,4-dinitrobenzenesulfenium ion.[29]

Addition of a hydrogen atom from the amine solvent gave **15**, which cyclizes to **16**. Attack of the amine solvent on **16** gave the sulfonamides.

Although mechanistic schemes involving heterolytic cleavage of the sulfur–nitrogen bond have been considered,[30] the present data are most in agreement with a mechanistic scheme which involves homolytic cleavage of the S–N bond to produce a sulfenyl radical **13** and an aryl amino radical (ArNH·). Support for this interpretation is obtained from the reactions of bis(2-nitrophenyl) disulfide (**12**) and aryl amines, substituent electronic effects, the isolation of bis(2-nitrophenyl) disulfide (**12**), and the formation of azobenzenes **7** and **8**.

SCHEME I



13 **14** **15** **16**

Support for the formation of sulfenyl radical **13** is obtained from the reactions of disulfide **12** and aryl amines. When treated under the reaction conditions with aryl amines, **12** gave high yields (51–81%) of the corresponding 2-aminobenzenesulfonanilides (**5**).[31]

Neglecting possible steric effects and assuming that the rate-determining step is either cleavage of the S–N bond or transfer of the hydrogen atom from the solvent, then the substituent electronic effects of groups attached to the aryl amine support the formation of an amino radical. Increased formation of the sulfonamides were observed in the order $2,4\text{-}Cl_2 \leq 2\text{-}C_6H_5 < H < 4\text{-}CH_3 \leq 4\text{-}CH_3O \leq NCH_3$. The formation of the sulfonamides is not very sensitive to the substituents as expected for a radical. However, electron-donating groups stabilize the radical, and electron-withdrawing groups destabilize the radical. These substituent effects are in approximate agreement with those reported for homolytic cleavage of unsymmetrical disulfides[26] and the thermal decomposition of bis(*N*-arylimidoyl) disulfides.[32]

When the rearrangement of sulfenamides **1a,c** and **6** was carried out in solvents less likely to transfer a hydrogen atom than aryl amines, bis(2-nitrophenyl) disulfide (**12**) was isolated. Disulfide **12** is presumably formed by dimerization of two sulfenyl radicals, **13**.

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(30) A detailed discussion of the various mechanistic possibilities for the rearrangement of *o*-nitrobenzenesulfonanilides to 2-aminobenzenesulfonanilides 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 author, title of article, volume, and page number. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche.

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This result further supports homolytic cleavage of the S–N bond and transfer of a hydrogen atom from the aryl amine solvent.

Finally, the formation of azobenzenes **7** and **8** support homolytic cleavage of the sulfur–nitrogen bond.

Azobenzenes.—A rationalization for the formation of azobenzenes **7** and **8** is derived from thermal dismutation of the corresponding hydrazobenzenes. Hydrazobenzenes are known to thermally rearrange to give azobenzenes and aryl amines.[33,34] Hydrazobenzenes would be formed by dimerization of two aryl amino radicals formed by cleavage of the S–N bond or by

$$2ArNH\cdot \longrightarrow ArNHNHAr \longrightarrow ArN{=}NAr + ArNH_2$$

transfer of a hydrogen atom from the amine solvent. The yields of **6** and **8** are calculated based on this assumption (Table I).

Azobenzenes were isolated in only two cases: the rearrangements of sulfenamides **1c** and **1e**. In each of these examples a phenyl amino radical may be substantially stabilized by resonance with the substituent group. A fairly long lifetime for the amino radical may be necessary for two aryl amino radicals to dimerize to form the hydrazobenzenes. A more reactive radical may react with the solvent to give the tars that were isolated in all of these reactions.

Conclusions

A radical mechanism appears to be consistent with the present experimental data for the rearrangement of 2-nitrobenzenesulfenanilides to 2-aminobenzenesulfonanilides. Attempts to isolate or trap intermediates or to inhibit the rearrangement by use of radical scavengers have thus far proved disappointing. Undoubtedly, this is in part due to the temperature and solvent which is necessary for the rearrangement. Mass spectral and esr studies may shed further light on the mechanism.

Experimental Section

Sulfenamides **1c**,[12] **1d**,[13] **1e**,[13] and **6**[12] were prepared according to procedures given in the literature. Melting points were obtained on a Fisher-John apparatus. Proton nmr spectra were measured on a Varian A-60A instrument. Infrared spectra were measured on a Perkin-Elmer 457 spectrometer. Solvents were purified according to literature procedures.

General Procedure for Thermal Rearrangement of Sulfenamides.—Sulfenamides were heated in an oil bath with an excess of solvent in a sealed tube for 15.5 hr. Excess solvent was removed either by distillation (vacuum pump) or sublimation and the dark residue was dissolved in methylene chloride and filtered. The filtrate was chromatographed on Florisil unless otherwise noted. Samples isolated from the column were washed with pentane or methanol and dried under high vacuum for at least 12 hr.

2-Nitrobenzenesulfenanilide (1a).—Sulfenamide **1a** (0.234 g, 0.00095 mol) in anisole gave, on elution with pentane–benzene (4:1), 0.01 g (1%) of a white solid, mp 183° (lit.[35] mp 192°), identified as **phenothiazine (4a)** by comparison of its properties with those of an authentic sample. Elution with pentane–benzene (1:1) gave 0.018 g (12%) of a yellow solid, mp 193–194° (lit.[36] mp 192°), identified as **bis(2-nitrophenyl) disulfide (12)** by comparison of its properties with those of an authentic sample. Elution with pentane–benzene (1:2) gave 0.013 g (6%) of a yellow solid, mp 86° (lit.[37] mp 85°), identified as **2-amino-2′-nitrodiphenyl sulfide (3b)** by comparison of its properties with those of an authentic sample. Further elution with pentane–benzene (1:2) gave 0.01 g (4%) of a yellow-brown solid, mp 102° (lit.[38] mp 102–103°), identified as **4′-amino-2-nitrodiphenyl sulfide (3a)** by comparison of its properties with those of an authentic sample. Elution with chloroform gave a brown oil which was alternately washed with 5% sodium hydroxide solution and water (three 50-ml portions). The aqueous washings were carefully neutralized with 5% hydrochloric acid solution and on cooling overnight gave 0.051 g (22%) of white crystals, mp 119–120° (lit.[20] mp 119°), identified as **2-aminobenzenesulfonanilide (5a)** by comparison of its properties with those of an authentic sample.

Sulfenamide **1a** (0.204 g, 0.00084 mol) in decalin gave, on elution with pentane–benzene (1:1), 0.027 g (21%) of **12**; elution with pentane–benzene (1:2) gave 0.0082 g (4%) of **3b** and 0.01 g (5%) of **3a**; elution with chloroform gave an oil which, when treated with 5% sodium hydroxide solution followed by neutralization and cooling, gave 0.041 g (20%) of **5a**.

Sulfenamide **1a** (0.222 g, 0.0009 mol) in the absence of solvent gave, on elution with pentane–benzene (1:1), 0.01 g (7%) of **12**; elution with pentane–benzene (1:2) gave 0.007 g (3%) of **3b** and 0.0087 g (4%) of **3a**; elution with chloroform gave an oil which when treated with sodium hydroxide followed by neutralization and cooling gave 0.047 g (21%) of **5a**.

2-Nitrobenzenesulfen-*p*-anisidine (1c).[12]—Sulfenamide **1c** had the following properties: infrared (KBr) 3325 (s), 3070–2830 (w), 1590 (s), 1565 (s), 1500 (vs), 1460 (s), 1445 (s), 1385 (w), 1340 (s), 1305 (s), 1285 (s), 1260 (m), 1225 (vs), 1175 (m), 1120 (m), 1095 (m), 1035 (s), 900 (s), 850 (m), 820 (s), 790 (m), 780 (s), 730 (s), 710 (m), 565 (m), and 515 cm^{-1} (m); nmr ($CDCl_3$) δ 3.75 (s, 3 H), 5.02 (s, 1 H), 6.87 (m, 4 H), 7.34 (d, 1 H), 7.60 (d, 1 H). Sulfenamide **1c** (0.150 g, 0.00054 mol) in *p*-anisidine gave, on elution with pentane–benzene (3:2), 0.017 g (27%) of a yellow solid, mp 164–165° (lit.[14] mp 165°), identified as **4,4′-dimethoxyazobenzene (7)** by comparison of its properties with those of an authentic sample. Compound **7** had the following properties: infrared (KBr) 3020 (s), 2840 (s), 1600 (s), 1580 (s), 1495 (s), 1455 (m), 1440 (m), 1420 (m), 1315 (m), 1290 (m), 1240 (s), 1180 (m), 1140 (s), 1100 (m), 1020 (s), 840 (s), 820 (w), 745 (m), 640 (w), 550 (m), 540 (m), 505 (w), and 405 cm^{-1} (w); nmr ($CDCl_3$) δ 3.75 (s, 6 H), 7.39 (q, 8 H). Elution with chloroform gave a brown oil which was alternately washed with 20% potassium hydroxide solution and water (three 50-ml portions); the aqueous washings were carefully neutralized with 5% hydrochloric acid solution and on cooling overnight gave 0.087 g (56%) of white crystals, mp 123–124°, identified as **2-aminobenzenesulfon-*p*-anisidide (5c)** by comparison of its properties with those of an authentic sample.

Sulfenamide **1c** (0.184 g, 0.00067 mol) in decalin gave, on elution with pentane–benzene (3:2), 0.038 g (37%) of **12**. Elution with chloroform gave an oil which, when treated with 20% potassium hydroxide solution followed by neutralization and cooling, gave 0.032 g (17%) of **5c**.

2-Aminobenzenesulfon-*p*-anisidide (5c).—2-Nitrobenzenesulfon-*p*-anisidide was prepared by condensation of 2-nitrobenzenesulfonyl chloride with *p*-anisidine in ether.[39] The crude sulfonamide, 0.5 g, in 100 ml of acetic acid at 35 psi of hydrogen over 25 mg of 10% palladium on charcoal for 14 hr gave, after solvent removal, a green oil. The oil was dissolved in 20% potassium hydroxide solution and neutralized with 5% hydrochloric acid solution and, on cooling overnight, gave a brown solid which was crystallized from ethanol to give 0.38 g (72%) of colorless crystals, mp 123–124°.

Anal. Calcd for $C_{13}H_{14}N_2O_3S$: C, 56.09; H, 5.08. Found: C, 56.05; H, 5.22.

Sulfonamide **5c** had the following properties: infrared (KBr) 3480 (s), 3380 (s), 3210 (s), 1630 (s), 1595 (m), 1500 (s), 1480 (s), 1325 (s), 1300 (s), 1240–1220 (s), 1140 (s), 1020 (s), 930 (s), 825 (m), 745 (s), 695 (m), 635 (m), 595–580 (s), and 540–510 cm^{-1} (m); nmr ($CDCl_3$) δ 3.74 (s, 3 H), 4.63 (s, 2 H), 6.66–7.53 (m, 9 H).

2-Nitrobenzenesulfen-2,4-dichloroanilide (1d).[13]—Sulfenamide **1d** had the following properties: infrared (KBr) 3380 (m), 3100 (w), 1595 (m), 1570 (m), 1505 (s), 1480 (s), 1380 (w), 1365 (w), 1340 (s), 1315 (m), 1290 (s), 1170 (w), 1155 (w), 1105 (m), 1050 (doublet, m), 910 (m), 875 (m), 820 (s), 790 (m), 740 (s), 720

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(m-s), 700 (w), 682 (w), 655 (m-w), 560 cm^{-1} (m-w); nmr ($CDCl_3$) δ 5.8 (s, 1 H), 7.2–7.6 (m, 6 H), and 8.3 (d, 1 H). Sulfenamide **1d** (0.153 g, 0.000486 mol) in 2,4-dichloraniline was chromatographed on acidic alumina and on elution with pentane–benzene (1:1) gave 0.093 g (61%) of yellow plates which on sublimation (140°, 0.05 mm), mp 198° (lit.[15] mp 175°), was identified as **2-amino-3,5-dichloro-2′-nitrodiphenyl sulfide (3d)** by comparison of its properties with those of an authentic sample.[40]

Anal. Calcd for $C_{12}H_8Cl_2N_2O_2S$: C, 45.86; H, 2.55. Found: C, 45.92; H, 2.54.

Diphenyl sulfide **3d** had the following properties: infrared (KBr) 3480 (m-w), 3390 (m), 1610 (m), 1590 (m), 1565 (m), 1506 (s), 1450 (s), 1335 (s), 1310 (m), 1280 (w), 1255 (m), 1210 (w-m), 1045 (w), 875 (m), 855 (m), 790 (m), 740 (s), 715 (w), and 655 cm^{-1} (w); nmr ($CDCl_3$) δ 4.8 (s, 2 H), 6.9 (d, 1 H), 7.5 (m, 4 H), and 8.4 (d, 1 H). Elution with chloroform gave a brown oil which was subblimed (120°, 0.1 mm) to give a white, crystalline solid which was crystallized from ether–pentane to give 0.042 g (28%) of white needles, mp 105–106° (lit.[16] mp 108°), identified as **2-aminobenzenesulfon-2,4-dichloroanilide (5d)** by comparison of its properties with those of an authentic sample.

Sulfonamide **5d** had the following properties: infrared (KBr) 3460 (m), 3380 (m), 3280 (m), 1620 (m), 1600 (w-m), 1570 (w), 1475 (s), 1415 (m), 1380 (m), 1335 (s), 1280 (w), 1220 (w), 1170 (s-m), 1150 (s-m), 1150 (s), 1100 (w-m), 1050 (w-m), 910 (m), 865 (w-m), 840 (m), 815 (w-m), 765 (m), 750 (m), 730 (w), 700 (m), 655 (w), 600 (s), and 580 cm^{-1} (s); nmr ($CDCl_3$) δ 5.0 (s, 2 H), 6.75 (m, 2 H), 7.25 (m, 4 H), and 7.55 (m, 2 H).

2-Nitrobenzenesulfen(2-phenyl)anilide (1e).[13]—Sulfenamide **1e** had the following properties: infrared (KBr) 3380 (s), 1590 (m), 1570 (m), 1500 (s), 1480 (s), 1450 (m), 1440 (m), 1382 (m), 1340 (s), 1310 (s), 1270 (s), 1215 (w), 1160 (w), 1112 (w), 1100 (m), 1055 (w), 1010 (w), 900 (m), 860 (m), 790 (m), 755 (s), 740 (s), 705 (s), 655 (w), and 520 cm^{-1} (m); nmr ($CDCl_3$) δ 5.4 (s, 1 H), 7.2 (m, 4 H), 7.5 (s, 8 H), and 8.3 (d, 1 H). Sulfenamide **1e** (0.181 g, 0.00056 mol) in 2-aminobiphenyl was chromatographed on neutral alumina, and elution with *n*-pentane gave 0.016 g (18%) of a red solid which on sublimation (80°, 0.1 mm), mp 137–138° (lit.[18] mp 136–139°), was identified as **2-phenylazobenzene (8)** by comparison of its properties with those of an authentic sample. Compound **8** had the following properties: infrared (KBr) 3070 (w), 1475 (m), 1460 (w-m), 1435 (w-m), 1280 (w-m), 1280 (w), 1250 (w), 1330 (w), 1195 (w), 1160 (w), 1120 (w), 1080 (w), 1050 (w), 1015 (w), 990 (w), 960 (w), 910 (w), 840 (w), 775 (s), 740 (s), 730 (m-s), 700 (s), 620 (w), 590 (m), 550 (m), 540 (m), and 480 cm^{-1} (m); nmr ($CDCl_3$) δ 7.48 (s, 18 H). Elution with chloroform gave a brown oil which was alternately washed with 10% sodium hydroxide solution and water (three 50-ml potions). The aqueous washings were carefully neutralized with 5% hydrochloric acid solution and on cooling overnight gave an oil which was extracted into ether. The ether solution was dried over $MgSO_4$ and on removal gave 0.045 g (25%) of an oil which was identified as **2-aminobenzenesulfon(2-phenyl)anilide (5e)** by comparison of its properties with those of an authentic sample.

2-Aminobenzenesulfon(2-phenyl)anilide (5e).—2-Nitrobenzenesulfon(2-phenyl)anilide was prepared by condensation of 2-nitrobenzenesulfonyl chloride with 2-aminobiphenyl in tetrahydrofuran.[39] The crude sulfonamide, 10.0 g, in 50 ml of ethanol at 40 psi over 100 mg of 10% palladium on charcoal for 24 hr gave 0.64 g (70%) of an oil which was purified by molecular distillation (120°, 0.1 mm).

Anal. Calcd for $C_{18}H_{16}N_2O_2S$: C, 66.67; H, 5.56. Found: C, 66.55; H, 5.41.

Sulfonamide **5e** had the following properties: infrared (thin film) 3485 (s), 3380 (s), 3060 (w), 1620 (s), 1570 (m), 1480 (s), 1455 (m), 1440 (w), 1395 (m-s), 1330 (s), 1260 (m), 1205 (m-w), 1150 (s), 1110 (m), 1055 (m-w), 1030 (w), 1010 (s), 900 (s), 840 (m), 820 (w), 750 (s), 700 (s), 700 (s), and 635 cm^{-1} (m-s); nmr ($CDCl_3$) δ 4.7 (s, 2 H), 6.6 (m, 2 H), and 7.3 (m, 12 H).

2-Nitrobenzenesulfen-*N*-methylanilide (6).[12]—Sulfenamide **6** had the following properties: infrared (KBr) 3070–2820 (w), 1600 (s), 1570 (m), 1500 (s), 1450 (m), 1345 (s), 1315 (s), 1290 (s), 1195 (w), 1170 (w), 1100 (m), 1090 (m), 1070 (m), 1040 (m), 1030 (m), 995 (w), 870 (s), 820 (m), 785 (m), 760 (s), 735 (s), 695 (m), 520 (w), 490 (w), and 435 cm^{-1} (w), nmr ($CDCl_3$) δ 3.46 (s, 3 H), 7.3 (m, 8 H), and 8.3 (d, 1 H). Sulfenamide **6** (0.852 g, 0.00325 mol) in *N*-methylphenothiazine was chromatographed on basic alumina. Elution with cyclohexane gave 0.005 g (1%) of white needles, mp 97–99° (lit.[18] mp 99–100°), identified as **3-methylphenothiazine (9)** by comparison of its properties with those of an authentic sample. Phenothiazine **9** had the following properties: infrared (KBr) 1590 (w), 1565 (w), 1460 (s), 1335 (s), 1290 (m), 1260 (s), 1140 (m), 1040 (m), 860 (w), 760 (s), 750 (s), and 730 cm^{-1} (w); nmr ($CDCl_3$) δ 3.3 (s, 3 H) and 6.7–7.2 (m, 8 H). Elution with cyclohexane–benzene (4:1) gave a yellow solid which was crystallized from ethanol to give 0.046 g (5%) of yellow-orange plates, mp 105–106° (lit.[19] mp 110°), identified as **2-nitro-2′-(*N*-methyl)aminodiphenyl sulfide (10a)** by comparison of its properties with those of an authentic sample. Compound **10a** had the following properties: infrared (KBr) 3380 (s), 3070 (w), 2810 (w), 1595 (s), 1570 (s), 1500 (s), 1450 (m), 1340 (s), 1300 (s), 1170 (m), 1100 (m), 1040 (m), 860 (m), 785 (m), 740 (s), and 715 cm^{-1} (m); nmr ($CDCl_3$) δ 2.8 (s, 3 H), 4.8 (s, 1 H), 6.8 (m, 3 H), 7.4 (m, 4 H), and 8.3 (m, 1 H). Elution with cyclohexane–benzene (4:1) gave a red solid which was recrystallized from 95% ethanol to give 0.041 g (5%) of orange crystals, mp 84.5–85.5°, identified as **2-nitro-4′-(*N*-methyl)aminodiphenyl sulfide (10b)** by comparison of its properties with those of an authentic sample (*vide infra*). Elution with chloroform gave a pale brown oil which was purified by molecular distillation at 0.05 mm (50°) to give 0.491 g (57%) of a colorless oil identified as **2-aminobenzenesulfon-*N*-methylanilide (11)** by comparison of its properties with those of an authentic sample (*vide infra*).

2-Nitro-4′-(*N*-methyl)aminodiphenyl Sulfide (10b).—Diphenyl sulfide **3b** (7.0 g, 0.0285 mol) was dissolved in 11.7 ml of pyridine in a 100-ml flask fitted with a reflux condenser and the flask was cooled to 0°. *p*-Toluenesulfonyl chloride (Matheson Coleman and Bell) (5.41 g, 0.0284 mol) was dissolved separately in 11.7 ml of pyridine, cooled, and added slowly to the reaction flask through the condenser with constant swirling and cooling. When the exothermic reaction had subsided the reaction mixture was heated on the steam bath for 3 hr, cooled, and washed into a 100-ml separatory funnel with 10% hydrochloric acid solution (300 ml) and chloroform (300 ml). The aqueous layer was discarded and the organic layer was washed with 10% hydrochloric acid solution (two 200-ml portions) and water (two 200-ml portions) and dried over $MgSO_4$. Solvent removal under vacuum gave 10.5 g of an orange solid, which was added without further purification to a 250-ml flask containing 6.6 ml of 4 *N* sodium hydroxide. The reaction mixture was heated to reflux and cooled to 0°, and 6.6 ml of 4 *N* sodium hydroxide and 2.4 ml of dimethyl sulfate were added. The dark residue was heated in 200 ml of 0.75 *N* sodium hydroxide for 15 min, the reaction mixture was cooled, and the aqueous portion was decanted. The residue was dissolved in 200 ml of chloroform, washed with 3% sodium hydroxide solution and water, and dried over $MgSO_4$. Removal of the solvent gave a yellow solid. The solid was added to 10.0 g of phenol and 75 ml of 48% hydrobromic acid and the reaction mixture was heated at reflux for 1.5 hr. To the cooled solution 150 ml of water was added and the aqueous solution was extracted with ether. The aqueous solution was neutralized with 20% sodium hydroxide to pH 6 and then extracted with chloroform (three 100-ml portions). The chloroform extracts were dried over anhydrous magnesium sulfate and the solvent was removed under vacuum to give an orange solid, which on crystallization from 95% ethanol gave 1.74 g (23%) of orange needles, mp 84.5–85.5°.

Anal. Calcd for $C_{13}H_{12}N_2O_2S$: C, 59.96; H, 4.65. Found: C, 59.86; H, 4.74.

Diphenyl sulfide **10b** had the following properties: infrared (KBr) 3420 (m), 3100–2820 (w), 1595 (s), 1565 (m), 1500 (s), 1450 (m), 1335 (s), 1310 (s), 1265 (w), 1250 (w), 1185 (s), 1155 (w), 1110 (m), 1060 (w), 1055 (w), 850 (w), 820 (m), 785 (w), and 740 cm^{-1} (m); proton nmr ($CDCl_3$) δ 2.9 (s, 3 H), 3.8 (s, 1 H), 7.1 (m, 7 H), and 8.3 (m, 1 H).

2-Aminobenzenesulfon-*N*-methylanilide (11).—The compound was prepared according to the method of Ullmann and Gross[20] and purified by molecular distillation (50°, 0.05 mm) to yield a colorless oil.

Anal. Calcd for $C_{13}H_{14}N_2O_2S$: C, 59.50; H, 5.39. Found: C, 59.46; H, 5.48.

Sulfonamide **11** had the following properties: infared (thin film) 3500 (s), 3390 (s), 3070–2880 (w), 1620 (s), 1600 (s), 1565 (m), 1490 (s), 1455 (s), 1350 (s), 1325 (s), 1260 (m), 1175 (s),

(40) An authentic sample of **3d** was prepared by the method of Farrington and Warburton[16] and on sublimation had a melting point and mixture melting point identical with those of **3d**.

1145 (s), 1070 (s), 1030 (s), 920 (w), 870 (s), 760 (s), 735 (s), 700 (s) and 680 cm^{-1} (m); nmr ($CDCl_3$) δ 3.3 (s, 3 H), 4.5 (s, 2 H), 6.6 (m, 2 H), 7.3 (s, 5 H), and 7.3 (m, 2 H).

Sulfenamide 6 (0.2183 g, 0.00084 mol) in decalin gave on elution with pentane–benzene (4:1) 0.017 g (10%) of 9; elution with pentane–benzene (3:2) gave 0.035 g (16%) of **10a**; elution with benzene–methylene chloride (2:3) gave 0.018 g (8%) of **11**.

Registry No.—**1a**, 4837-33-6; **1b**, 4837-32-5; **1c**, 4997-95-9; **1d**, 33224-41-8; **1e**, 33224-42-9; **3d**, 33224-43-0; **5c**, 33224-44-1; **5d**, 33224-45-2; **5e**, 33224-46-3; **6**, 33224-04-3; **7**, 501-58-6; **8**, 13701-27-5; **9**, 1207-72-3; **10a**, 33224-08-7; **10b**, 33224-09-8; **11**, 33224-10-1.

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Chemistry of the Sulfur–Nitrogen Bond. III.[1] The Reactions of Bis(2-nitrophenyl) Disulfide with Amines

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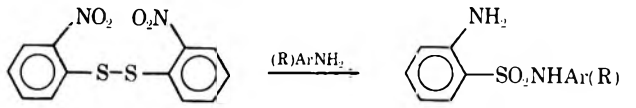
The thermal rearrangement of bis(2-nitrophenyl) disulfide with primary or secondary alkyl or aryl amines to give the corresponding 2-aminobenzenesulfonamides is described. A radical mechanism is proposed.

We wish to report a new and facile synthesis of 2-aminobenzenesulfonamides (**1**) from bis(2-nitrophenyl) disulfide (**2**) and primary or secondary alkyl



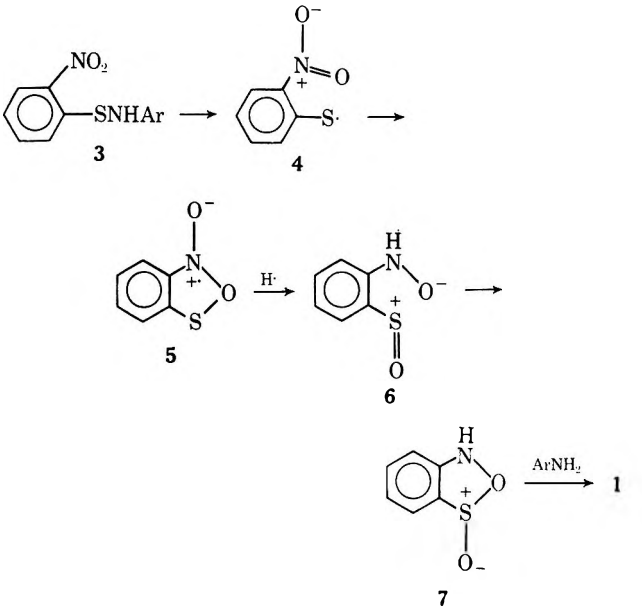
2

1a, Ar = C_6H_5
b, Ar = 4-$CH_3C_6H_4$
c, Ar = 4-$CH_3OC_6H_4$
d, Ar = 2,4-$Cl_2C_6H_3$
e, Ar = 2-$C_6H_5C_6H_4$
f, R = $CH_3(CH_2)_8CH_2$

or aryl amines. This reaction lends support to the mechanism recently proposed for the thermal rearrangement of 2-nitrobenzenesulfenanilides (**3**) to 2-aminobenzenesulfonanilides **1**.[1] The mechanism involved homolytic cleavage of the sulfur–nitrogen bond in **3** to give the 2-nitrobenzenesulfenyl radical **4**, which was stabilized by interaction with one of the *o*-nitro group oxygens (**5**). Transfer of a hydrogen atom from the amine solvent gave **6**, which cyclized to **7**. Attack of the amine solvent on **7** gave **1** (Scheme I). This mechanistic sequence was supported by several results, including the substantial amount of disulfide **2**, isolated when the thermal rearrangements of the sulfenamides were carried out in solvents less likely to transfer a hydrogen atom than the amine solvent. Disulfide **2** is presumably formed by dimerization of two sulfenyl radicals (**4**).

There appears to be a considerable amount of evidence which suggests that disulfides dissociate homolytically at elevated temperatures.[3–5] Therefore, to test whether or not sulfenyl radical **4** was an intermediate in the rearrangement of **3** to **1** we investigated the reactions of disulfide **2** with the primary aryl amines, aniline,

SCHEME I



p-toluidine, *p*-anisidine, 2,4-dichloroaniline, and 2-aminobiphenyl, and with a secondary aryl amine, *N*-methylaniline. With the exception of 2,4-dichloroaniline, yields of the corresponding 2-aminobenzenesulfonamides **1a–c**, **1e**, and **8a** were 51–81% (1 mol of **2** yields 2 mol of **1**).

The reaction also works with primary and secondary alkyl amines; *N*-decylamine gave 63% **1f** and diisobutylamine gave 74% **8b**.

In addition to the sulfonamides, several other products were isolated. Disulfide **2** with *p*-anisidine and 2-aminobiphenyl gave azobenzenes **9** and **10**, respectively. Disulfide **2** with aniline gave diphenyl sulfides **11a,b**; in *p*-toluidine **2** gave 3-methylphenothiazine (**12**) and diphenyl sulfide **13a**; and in 2,4-dichloroaniline **2** gave diphenyl sulfide **13b**.

Several minor fractions were isolated as oils from the reaction of **2** with *n*-decylamine and diisobutylamine. They were not identified. In both reactions a small amount (*ca.* 10–30 mg) of a white solid, insoluble in organic solvents but soluble in water, was

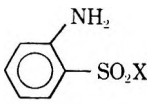
(1) Part II: F. A. Davis and R. P. Johnston II, *J. Org. Chem.*, **37**, 854 (1972).

(2) Taken in part from the M.S. thesis of R. P. Johnston II, Drexel University, 1971.

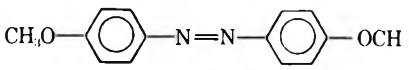
(3) W. A. Pryor, "Mechanisms of Sulfur Reactions," McGraw-Hill, New York, N. Y., 1962, pp 42–45.

(4) U. Schmidt, *Angew. Chem., Int. Ed. Engl.*, **3**, 602 (1964).

(5) R. E. Davis and C. Perrin, *J. Amer. Chem. Soc.*, **82**, 1590 (1960).



8a, X = $N(CH_3)C_6H_5$
c, X = $N[CH_2CH(CH_3)_2]_2$



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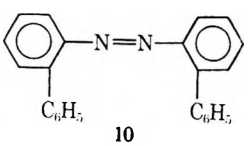

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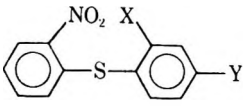
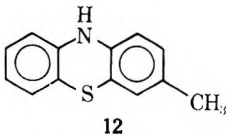


11a, X = NH_2; Y = H
b, X = H; Y = NH_2



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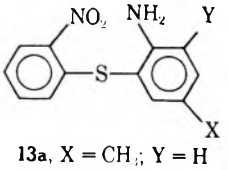

13a, X = CH_3; Y = H
b, X = Y = Cl

isolated. The solid is presumably the hydrosulfate of the amine, since the infrared of both samples showed strong absorption at 1100 cm^{-1} [6] and precipitated barium sulfate from barium chloride solution.

The rearrangement conditions involved heating disulfide **2** with an excess of amine in a sealed tube for 15.5 hr at 195°. The solvent was removed and the dark residue was chromatographed. Products were identified by comparison with authentic samples. These results are summarized in Table I.

TABLE I

REARRANGEMENT OF BIS(2-NITROPHENYL) DISULFIDE IN AMINE SOLVENTS AT 195° FOR 15.5 HR

Solvent	Registry no.	Products (yield, %)
Aniline	62-53-3	**11a** (3),[a] **11b** (7),[a] **1a** (65)[b]
p-Toluidine	106-49-0	**12** (5),[a] **13a** (6),[a] **1b** (77)[b]
p-Anisidine	104-94-9	**9** (21),[c] **1c** (81)[b]
2,4-Dichloroaniline	554-00-7	**13b** (6),[a] **1d** (23),[b] **2** (67)
2-Aminobiphenyl	90-41-5	**10** (16),[c] **1e** (51),[b] **2** (22)
n-Decylamine	2016-57-1	**1f** (63)[b]
N-Methylaniline	100-61-8	**8a** (78)[b]
Diisobutylamine	110-96-3	**8b** (74)[b]

[a] One mole of disulfide yields 1 mol of diphenyl sulfide. [b] One mole of disulfide yields 2 mol of sulfonamide. [c] One mole of disulfide yields 0.5 mol of azobenzene.

The high yields of sulfonamides formed in the reactions of disulfide **2** with amines is consistent with homolytic cleavage of the S–N bond to form two sulfenyl radicals **4**, both of which can rearrange to the sulfonamide. The isolation of azobenzenes **9** and **10** further supports the radical mechanism and the transfer of a hydrogen atom from the amine solvent with the formation of an amino radical.

Disproportionation of hydrazobenzenes (ArNHNHAr) to give amine and azobenzene[7-9] was previously suggested to account for the formation of **9** and **10** in the thermal rearrangement of the corresponding 2-nitrobenzensulfenanilides.[1] The hydrazobenzenes would be formed by dimerization of two aryl amino radicals (ArNH·) formed in the transfer of a hydrogen atom from the amine solvent to **5** (Scheme I). If it is assumed that 1 mol of disulfide **2** results in 0.5 mol of azobenzene, then the yield of **9** (21%) and **10** (16%) are, within experimental error, similar to the yields of **9** and **10** isolated in the rearrangement of the corresponding sulfenamides (*i.e.*, 27 and 18%, respectively[1]).[10]

Displacements at sulfenyl sulfur are well known,[11] and displacements on alkyl sulfenylthiocyanates[12] and disulfides[13] to give sulfenamides have been reported.

$$ArS\text{–}SAr + Ar'NH_2 \longrightarrow ArS\text{–}NHAr' + ArSH$$

Unboubtedly some displacement by the amine solvent on the S–S bond to form the corresponding sulfenamide does take place, since the only plausible way to rationalize the formation of diphenyl sulfides **11a,b** and **13a,b** is *via* the sulfenamide. Phenothiazine **12** is formed by a Smiles rearrangement of **13a**.[14]

However, it is unlikely that the major pathway for the formation of the sulfonamides is *via* the sulfenamide. This becomes quite clear when the ratio of the yields of phenothiazine and nitroaminodiphenyl sulfides to sulfonamide are compared for the rearrangement of disulfide **2** and the corresponding sulfenamide. These results are summarized in Table II. As can be seen from this table, the ratios for the disulfide rearrangement are much less than those obtained for the corresponding sulfenamide.[1] These results indicate that the major pathway for formation of the sulfonamides is not *via* the sulfenamides.

TABLE II

RATIOS OF THE YIELDS OF PHENOTHIAZINE AND NITROAMINODIPHENYL SULFIDES TO SULFONAMIDES

Solvent	Sulfenamide[a]	Disulfide
Aniline	0.54	0.15 (**11a** + **11b**/**1a**)
p-Toluidine	0.58	0.14 (**12** + **13a**/**1b**)
2,4-Dichloroaniline	2.18	0.26
N-Methylaniline	0.19	*b*

[a] From ref 1. [b] Phenothiazine and nitroaminodiphenyl sulfide not isolated.

Finally, the rearrangement of **2** with alkyl and aryl primary and secondary amines to give high yields of 2-aminobenzenesulfonamides appears to have some synthetic utility. The alternate route to these sulfonamides is *via* a two-step synthesis: condensation of 2-nitrobenzenesulfonyl chloride with the amine to give the nitrobenzenesulfonamide followed by reduction of the nitro group.

(6) R. T. Conley, "Infrared Spectroscopy," Allyn and Bacon, Boston, Mass., 1966, Chapter 5.

(7) P. Walker and W. A. Waters, *J. Chem. Soc.*, 1632 (1962).
(8) L. G. Korlik and V. O. Lukashevic, *Dokl. Chem.*, 649 (1961).
(9) H. Wieland and E. Schamberg, *Ber.*, **53**, 1329 (1920).
(10) The sulfenamide may form aryl amino radicals in two ways: (i) homolytic cleavage of the S–N bond; (ii) transfer of a hydrogen atom from the amine solvent to **5**.
(11) For a review see E. Ciuffarin and A. Fava, *Progr. Phys. Org. Chem.*, **6**, 81 (1968).
(12) R. T. Major and L. H. Peterson, *J. Amer. Chem. Soc.*, **78**, 6181 (1956).
(13) M. Busch, *Ber.*, **29**, 2127 (1896).
(14) F. A. Davis and R. B. Wetzel, *Tetrahedron Lett.*, 4483 (1969).

The yields are often low *via* the latter synthetic route. For example, the synthesis of sulfonamide **1e** *via* this route was only 7%.[1] The reaction of **2** with 2-aminobiphenyl, however, gave **1e** in greater than 51% yield.

Experimental Section

Solvents were purified according to procedures given in the literature. Melting points were obtained on a Fisher-Johns melting point apparatus. Proton nmr spectra were measured on a Varian A-60A instrument. Infared spectra were measured on a Perkin-Elmer 457 spectrometer.

General Procedure for Thermal Rearrangement of Bis(2-nitrophenyl) Disulfide (2) with Amines.—Disulfide **2** was heated with an excess of the primary or secondary alkyl or aryl amine in a sealed tube at 195° in an oil bath for 15.5 hr. Excess solvent was removed either by distillation (vacuum pump) or sublimation and the resulting dark residue was dissolved in chloroform and filtered. The filtrate was chromatographed on Florisil unless otherwise noted. Samples isolated from the column were washed with pentane or methanol and dried for at least 12 hr at high vacuum. Products were identified by comparison of their properties with those of authentic samples.

Aniline.—Disulfide **2** (0.174 g, 0.000565 mol) in aniline gave on elution with pentane–benzene (3:2) 0.004 g (3%) of a yellow solid, mp 86° (lit.[15] mp 85°), identified as **2-amino-2′-nitrodiphenyl sulfide (11a)**. Further elution with pentane–benzene (3:2) gave 0.01 g (7%) of a yellow solid, mp 102° (lit.[16] mp 102–103°), identified as **4-amino-2′-nitrodiphenyl sulfide (11b)**. Elution with chloroform gave a brown oil which was alternately washed with 5% sodium hydroxide solution and water (three 50-ml portions). The aqueous washings were carefully neutralized with 5% hydrochloric acid solution and on cooling overnight gave 0.181 g (65%) of white crystals, mp 119° (lit.[17] mp 119°), identified as **2-aminobenzenesulfonanilide (1a)**.

***p*-Toluidine.**—Disulfide **2** (0.174 g, 0.000654 mol) in *p*-toluidine gave on elution with pentane–benzene (3:2) 0.007 g (6%) of a white solid, mp 167–168° (lit.[18] mp 168°), identified as **3-methylphenothiazine (12)**. Further elution with pentane–benzene (3:2) gave 0.008 g (5%) of red crystals, mp 87° (lit.[1] mp 87°), identified as **2-amino-5-methyldipenyl sulfide (13a)**. Elution with chloroform gave a brown oil which, when treated with sodium hydroxide solution followed by neutralization and cooling, gave 0.227 (77%) of white crystals, mp 124–125° (lit.[19] mp 124°), identified as **2-aminobenzenesulfon-*p*-toluidide (1b)**.

***p*-Anidisine.**—Disulfide **2** (0.205 g, 0.000664 mol) in *p*-anisidine gave on elution with pentane–benzene (3:2) 0.017 g (21%) of a yellow solid, mp 164–165° (lit.[20] mp 164°), identified as ***p*-methoxyazobenzene (9)**. Elution with chloroform gave a brown oil, which was treated with potassium hydroxide solution and water, and the aqueous solution was extracted with ether. The aqueous washings were carefully neutralized with 5% hydrochloric acid solution and on cooling overnight gave 0.297 g (81%) of white crystals, mp 123–124° (lit.[1] mp 123°), identified as **2-aminobenzenesulfon-*p*-anisidine (1c)**.

2,4-Dichloroaniline.—Disulfide **2** (0.168 g, 0.00054 mol) in 2,4-dichloroaniline gave on elution with pentane–benzene (1:1) 0.1122 g (67%) of a yellow solid, mp 193° (lit.[21] mp 193°), identified as **bis(2-nitrophenyl) disulfide (2)**. Elution with pentane–benzene (1:1) gave 0.01 g (6%) of a yellow solid, mp 198° (lit.[1,22] mp 198°), identified as **2-amino-3,5-dichloro-2′-nitrodiphenyl sulfide (13b)**. Elution with chloroform gave a brown oil which was sublimed at 120° (0.1 mm) to give 0.0785 g (23%) of white needles, mp 106° (lit.[23] mp 108°), identified as **2-aminobenzenesulfon-2,4-dichloroanilide (1d)**.

2-Aminobiphenyl.—Disulfide **2** (0.2258 g, 0.000733 mol) in 2-aminobiphenyl was chromatographed on neutral alumina. Elution with pentane gave an orange solid which was sublimed (80° 0.1 mm) to give 0.020 g (16%) of an orange-red solid, mp 137–138° (lit.[24] mp 136–139°), identified as **2-phenylazobenzene (10)**. Elution with pentane–benzene (1:1) gave 0.05 g (27%) of a yellow solid, mp 193 (lit.[21] mp 198°), identified as disulfide **2**. Elution with chloroform gave a brown oil which was alternately washed with 10% sodium hydroxide solution and water (three 50-ml portions). The aqueous washings were carefully neutralized with 5% hydrochloric acid solution and on cooling overnight gave an oil which was extracted into ether. The ether solution was dried over $MgSO_4$ and on removal gave 0.240 g (51%) of an oil which was identified as **2-aminobenzenesulfon(2-phenyl)anilide (1e)**.[1]

***n*-Decylamine.**—Disulfide **2** (0.218 g, 0.00071 mol) in *n*-decylamine gave on elution with pentane–benzene two minor fractions isolated as an oil which were not identified. Elution with chloroform gave a brown oil which was sublimed at 120° (0.1 mm) to give white crystals, mp 48–49°, identified as **2-aminobenzenesulfon-*n*-decylamide (1f)**.

2-Aminobenzenesulfon-*n*-decylamide (1f).—Compound **1f** was prepared by reduction of the corresponding 2-nitrobenzenesulfonamide as previously described.[1] The crude sulfonamide (5.0 g, 0.0146 mol) in ethanol gave 4.1 g (90%) of a white solid which was crystallized from pentane–ether to give white needles, mp 48°.

Anal. Calcd for $C_{16}H_{28}N_2O_2S$: C, 61.54; H, 8.97. Found: C, 61.77; H, 9.12.

Sulfonamide **1f** has the following properties: infrared (KBr) 3500 (m), 3400 (m), 3290 (s), 2930 (s), 2860 (m), 1615 (s), 1540 (w), 1480 (s), 1430 (m-w), 1380 (w), 1320 (s), 1145 (s), 1070 (s), 1020 (m-w), 890 (m), 860 (w), 845 (w), 755 (s), 720 (w), 700 (m), 610 (m), 575 (w), and 525 cm^{-1} (m); nmr ($CDCl_3$) δ 0.9 (m, 3 H), 1.2 (s, 16 H), 2.9 (q, 2 H), 4.7 (broad s, 2 H), 6.7–7.5 (m, 4 H), and 7.7 (m, 1 H).

***N*-Methylaniline.**—Disulfide **2** (0.50 g 0.00163 mol) in *N*-methylaniline was chromatographed on basic alumina. Elution with chloroform gave a pale brown oil which was purified by molecular distillation at 50° (0.05 mm) to give 0.670 g (78%) of a colorless oil identified as **2-aminobenzenesulfon-*N*-methylanilide (8a)**.

Diisobutylamine.—Disulfide **2** (0.350 g, 0.0011 mol) in diisobutylamine gave on elution with pentane–benzene two minor fractions isolated as oils which were not identified. Elution with chloroform gave a brown oil which was purified by molecular distillation at 110° (0.5 mm) to give 0.48 g (74%) of a colorless oil identified as **2-aminobenzenesulfondiisobutylamide (8b)**.

2-Aminobenzenesulfondiisobutylamide (8b).—Compound **8b** was prepared as previously described by reduction of the corresponding 2-nitrobenzenesulfonamide.[1] The crude sulfonamide (5.0 g, 0.016 mol) in ethanol gave an oil which was purified by molecular distillation at 110° (0.5 mm).

Anal. Calcd for $C_{14}H_{24}N_2O_2S$: C, 59.15; H, 8.45. Found: C, 58.97; H, 8.33.

Sulfonamide **8b** had the following properties: infrared (thin film) 3480 (s), 3380 (s), 3200 (w), 2960 (s), 1610 (s), 1470 (s), 1390 (m), 1320 (s), 1140 (s), 1090 (m), 1005 (s), 960 (w), 940 (w), 920 (w), 870 (m), 840 (m), 815 (w), 750 (s), and 690 cm^{-1} (m); nmr ($CDCl_3$) δ 0.9 (d, 12 H), 1.9 (m, 2 H), 3.0 (d, 4 H), 5.1 (broad s, 2 H), and 6.6 to 7.7 (m, 4 H).

Registry No.—**1f**, 33214-32-3; **2**, 1155-00-6; **8b**, 33214-34-5.

Acknowledgment.—We thank Mr. E. W. Kluger for the synthesis of **8b**.

(15) A. Levi, L. A. Warren, and S. Smiles, *J. Chem. Soc.*, 1492 (1933).
(16) H. H. Hodgson and W. Rosenberg, *ibid.*, 181 (1930).
(17) F. Ullmann and G. Gross, *Chem. Ber.*, **43**, 2694 (1910).
(18) H. Gilman and D. A. Shirley, *J. Amer. Chem. Soc.*, **66**, 888 (1944).
(19) J. H. Freeman and E. C. Wagner, *J. Org. Chem.*, **16**, 815 (1951).
(20) R. Walter, *Chem. Ber.*, **58**, 2306 (1925).
(21) M. T. Bogert and A. Stall, "Organic Syntheses," Collect. Vol. I, Wiley, New York, N. Y., 1941, p 220.
(22) K. J. Farrington and W. K. Warburton, *Aust. J. Chem.*, **9**, 480 (1956).
(23) A. A. Patchett and S. A. Harris, French Patent 13,480,006 (1964); *Chem. Abstr.*, **63**, P10695*e* (1964).
(24) E. Wenkert and B. F. Barnett, *J. Amer. Chem. Soc.*, **82**, 4671 (1960).

Mobile Keto Allyl Systems. XII.[1a] The Reaction of 2-(α-Bromobenzyl)-1,4-dihydro-4,4-dimethyl-1-ketonaphthalene with Amines[1b]

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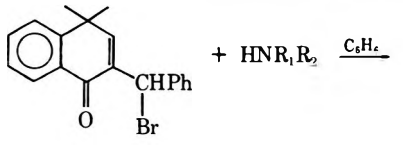
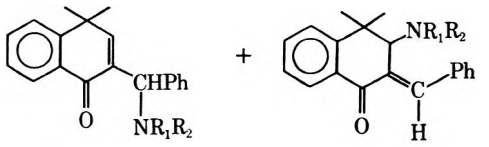
The title compound **1a** was found to react in benzene with 2 equiv of the following amines to yield the abnormal product of rearrangement–substitution, *trans*-2-benzal-3-amino-4,4-dimethyl-1-tetralone (**3**): isopropylamine, cyclohexylamine, morpholine, piperidine, and *sec*-butylamine. In the presence of an excess of amine, these first-formed amino ketones underwent an amine exchange reaction to yield the thermodynamically more stable amino ketones 2-[α-(amino)benzyl]-1,4-dihydro-4,4-dimethyl-1-ketonaphthalene (**2**). The bromo ketone **1a** reacts with more space-demanding amines, such as *tert*-butylamine, to yield both the normal product of direct substitution **2d** and the abnormal product of rearrangement–substitution **3d** by parallel pathways.

Hassner and Cromwell[2] were the first to report the reaction of 2-(α-bromobenzyl)-1,4-dihydro-4,4-dimethyl-1-ketonaphthalene (**1a**) with amines. Using 2.32 molar equiv of piperidine and 2.13 molar equiv of morpholine in benzene solution, they obtained only the corresponding normal products **2a** and **2b**, respectively. Cromwell and Wu[3] extended these studies and found that **1a** gave normal products with an excess of piperidine and methylamine. Only with *tert*-butylamine did they observe an abnormal product, **3d**.



1a



2a, R_1R_2 = piperidine
b, R_1R_2 = morpholine
c, R_1 = H; R_2 = methyl
d, R_1 = H; R_2 = *tert*-butyl
e, R_1 = H; R_2 = isopropyl
f, R_1 = H; R_2 = cyclohexyl
g, R_1 = H; R_2 = *sec*-butyl

3a–g

It was decided, therefore, to treat **1a** with different amines at room temperature in benzene to attempt to determine the steric requirements of the reaction. An nmr spectrum of the crude reaction mixture was taken to determine if two products were obtained. The region between 250 and 300 Hz where the methine proton absorbances appear for **2d** and **3d** was carefully scanned at high amplitude. One signal indicated that one product was obtained. By this method, only products amounting to at least 10% of the total were observed.

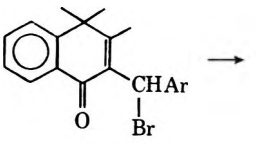
Results

Steric Requirements.—The reaction of **1a** with 10 molar equiv of isopropylamine, cyclohexylamine,[4] and *sec*-butylamine gave only the normal isomers **2e**, **2f**, and **2g**, respectively.

Adamantylamine and *tert*-octylamine (1,1,3,3-tetramethylbutylamine) reacted very slowly at room temperature with **1a** to give both the normal substitution product and the abnormal isomer, as observed by the nmr spectrum of the crude product mixture. The yields of crude oil were approximately 10–15% after several weeks. The two products could not be separated by column chromatography or tlc; so the products were not isolated or characterized. Diisopropylamine appeared to give no reaction after a week.

The procedure was repeated using slightly less than 2 molar equiv of piperidine, morpholine, isopropylamine, cyclohexylamine, and *sec*-butylamine in benzene. In each case, the only product was the abnormal amino ketone **3**, except in the reactions of piperidine and morpholine, in which cases the normal product **2** was also observed. When 1 molar equiv of piperidine or morpholine was added slowly to the stirred bromo ketone solution, the crude reaction mixture was shown by nmr analysis to consist entirely of abnormal amino ketone **3**.

It appeared that, if the amine was not very space-demanding, the first formed product was the abnormal isomer **3**, but the amine exchange reaction **3** to **2** was very fast. It was felt that by blocking the 2a position with an ortho methyl group on the benzyl ring, the rate of the amine exchange reaction could be reduced. As previously reported[4] 2-[α-bromo-*o*-methylbenzyl]-1,4-dihydro-4,4-dimethyl-1-ketonaphthalene (**4**) reacted with 10 molar equiv of isopropylamine, cyclohexylamine, and *tert*-butylamine to yield both normal product **5** and abnormal product **6**. Using 2 molar equiv



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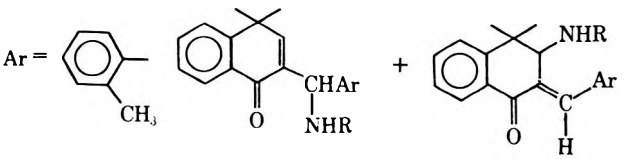


5a, R = isopropyl
b, R = cyclohexyl
c, R = *tert*-butyl

6a–c

(1) (a) For paper XI in this series, see A. D. George, E. Doomes, and N. H. Cromwell, *J. Org. Chem.*, **36**, 3918 (1971); (b) presented at the 162nd National Meeting of the American Chemical Society, Washington, D. C., Sept 1971.

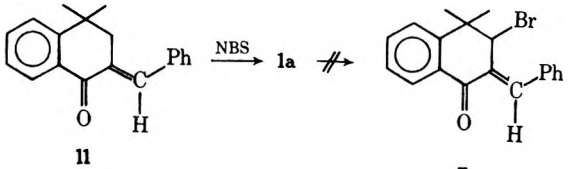
(2) A. Hassner and N. H. Cromwell, *J. Amer. Chem. Soc.*, **80**, 901 (1958).

(3) N. H. Cromwell and E. M. Wu, *J. Org. Chem.*, **33**, 1895 (1968).

(4) G. Glaros and N. H. Cromwell, *ibid.*, **36**, 3033 (1971).

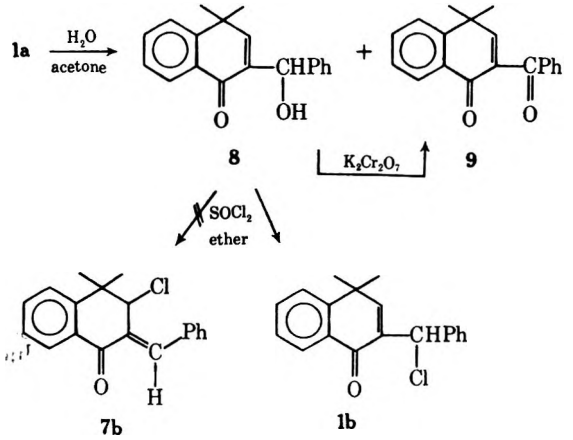
of isopropylamine and cyclohexylamine only the abnormal isomers **6a** and **6b**, respectively, were obtained.

Stability of Compounds.—Following the suggestion of DeWolfe and Young[5] the stability of all compounds was examined. The bromo ketone **1a** was stable under reaction conditions, with only slight decomposition taking place when stored in sunlight. There was no formation of the isomeric 2-benzal-3-bromo-4,4-dimethyl-1-tetralone (**7a**). This is not surprising, since the allylic system rearranges to the endocyclic structure during bromination.[3] It is known[6] that in the 4,4-dimethyl-1-tetralone system the endocyclic 2-benzyl isomer is thermodynamically more stable than the exocyclic 2-benzal isomer. In addition, if the reaction of **1a** with amines is stopped before completion, no evidence for **7a** is found.



11 **7a**

Attempts were made to prepare exocyclic chloro ketone **7b**. Bromo ketone **1a** was solvolyzed in aqueous acetone to 2-[α-hydroxybenzyl]-1,4-dihydro-4,4-dimethyl-1-ketonaphthalene (**9**). This latter compound was identified by dichromate oxidation[7] of **8** to **9** and presumably arises during the solvolysis of **1a** by air oxidation of **8**.



7b **1b**

The allylic alcohol **8** was treated with thionyl chloride under conditions which are favorable for the SNi′ reaction[8] in hopes of obtaining 2-benzal-3-chloro-4,4-dimethyl-1-tetralone (**7b**). The only product observed was the previously reported[3] chloro ketone **1b**.

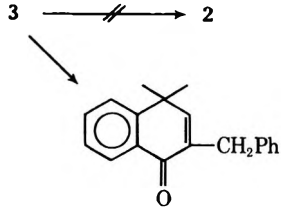
The normal products **2** were all stable under reaction conditions and with an excess of the corresponding amine present. Thus, the thermodynamically more stable isomers did not rearrange to the exocyclic unsaturated amino ketones **3**.

The exocyclic unsaturated amino ketones **3** are thermodynamically unstable relative to the endocyclic isomers **2**. All amino ketones **3** were stable, without added amine, to rearrangement to endocyclic unsaturated amino ketones **2** in $CDCl_3$ solution for periods up to 30 days. These amino ketones **3** having a hydrogen atom α to the nitrogen in the amino moiety decomposed slightly at room temperature to 2-benzyl-1,4-dihydro-4,4-dimethyl-1-ketonaphthalene (**10**). This decomposition was quantitative at elevated temperatures.[4]

TABLE I
INFRARED AND ULTRAVIOLET DATA

Compd	Ir,[a] cm⁻¹ C=O	C=C	C=C Ar	Uv[b] λmax, nm	ε × 10⁻³
2e	1660	1648	1600	257	7.95
				300 sh	2.2
2g	1660	1645	1601	257	10.55
				300 sh	2.8
3a	1660	1610	1600	287 sh	11.25
				303	11.9
3b	1670	1610	1600	285 sh	12.8
				302	13.85
3e	1670	1615	1600	280 sh	12.8
				298	14.2
3f	1660	1610	1595	280 sh	12.78
				298	13.93
3g	1675	1620	1600	282 sh	10.6
				294	11.4
8[c]	1655	1635	1600	254	10.65
				300 sh	2.45
9	1655		1600	257	18.27
				350	0.28
14	1670	1620	1600	237	13.2
				260 sh	11.6
				305	9.95
15	1675		1600	268	11.3
				302	7.7

[a] CCl_4 solution. [b] 95% ethanol. [c] Also OH 3620/84, 3600/87, and 3500/81 broad.



10

All amino ketones **3** except **3d** reacted in a period of 1 week with added amine to yield the corresponding endocyclic unsaturated amino ketones **2**. In the case of the *tert*-butylamino ketone **3d**, the rearrangement was very slow. With a large excess of *tert*-butylamine in either C_6D_6, $CDCl_3$, or CD_3CN, only a trace of **2d** could be observed after 2 weeks at 40°.

During periodic nmr analysis of the reaction of **1a** with *tert*-butylamine in benzene, chloroform, and acetonitrile the ratio of amino ketone **2d** to **3d** did not change with time.[9] Thus, the presence of *tert*-butylamine hydrobromide did not appreciably alter the rate of the slow rearrangement of **3d** to **2d**.

$$3 + HNR_1R_2 \xrightarrow{C_6D_6} 2 + HNR_1R_2$$

While morpholine was found[10] to add to the exocyclic unsaturated ketone **11**, to an extent of 10%, it did not add to the endocyclic unsaturated ketone **10**. The ketone **10** prepared by the reaction scheme described previously[10] was allowed to react with *tert*-

(5) R. H. DeWolfe and W. G. Young, *Chem. Rev.*, **56**, 753 (1956).
(6) N. H. Cromwell, R. P. Ayer, and P. W. Foster, *J. Amer. Chem. Soc.*, **82**, 130 (1960).
(7) L. T. Sandborn, "Organic Syntheses," Collect. Vol. I, H. Gilman, Ed., Wiley, New York, N. Y., 1941, p 340.
(8) F. F. Caserio, G. E. Dennis, R. H. DeWolfe, and W. G. Young, *J. Amer. Chem. Soc.*, **77**, 4182 (1955).
(9) G. Glaros and N. H. Cromwell, *J. Org. Chem.*, **37**, 867 (1972).
(10) A. Hassner and N. H. Cromwell, *J. Amer. Chem. Soc.*, **80**, 893 (1958).

TABLE II
ELEMENTAL ANALYSES

Compd	Calcd, % C	H	N	X	Found, % C	H	N	X
2e[a]	74.24	7.36	3.95	10.19[b]	74.27	7.42	4.08	10.48[b]
2g	82.84	8.16	4.20		82.71	8.16	4.34	
3a[c]	62.71	5.26	9.75		62.93	5.27	9.74	
3b	79.50	7.25	4.03		79.59	7.37	4.04	
3e	82.72	7.89	4.38		82.64	7.86	4.31	
3f	83.52	8.13	3.90		83.51	8.19	3.81	
3g[a]	74.67	7.62	3.78	9.58[b]	74.71	7.65	3.59	9.64[a]
8	81.98	6.52			81.78	6.56		
9	82.84	5.84			82.05	5.65		
14	82.84	8.16	4.20		82.63	8.16	4.11	
15[a]	76.16	7.87	3.42	8.65[b]	76.27	8.05	3.39	8.63[b]

[a] Hydrochloride salt. [b] Chlorine. [c] Picrate.

TABLE III
NMR SPECTRA[a,b]

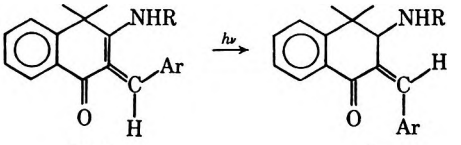
Compd	$(CH_3)_2C$	Methine	Vinyl	Amino
2e	86, 88	305	?[c]	d 65, J = 7 Hz, $(CH_3)_2CH$[d]–; s 95 NH; m 165 $(CH_3)_2CH$–
2g	82, 85	310	?[c]	m 40–95 $CH_3CH_2CHCH_3$; s 102 NH; m 150 $CH_3CH_2CHCH_3$
3a	81, 95	245	491	m 65–160 piperidino
3b	82, 95	246	496	m 125 $-(CH_2)_2=N$; m 202 $=(CH_2)_2=O$
3e	85, 96	245	480	d 29, J = 6 Hz; d 43, J = 6 Hz, $(CH_3)_2CH$;[d] s 48 NH; m 150, J = 6 Hz, $(CH_3)_2CH$–
3f	85, 96	247	482	m 30–140 cyclohexyl plus NH
3g	84, 97	249	482	m 15–75 CH_3CH_2–$CHCH_3$ plus NH; m 115–150 $CH_3CH_2CHCH_3$
8[e]	85	d 344 (J = 4 Hz)	d 408 (J = 1 Hz)	
9[f]	95	427		
14	84, 86	213	400	s 57 NH; s 65 *tert*-butyl
15[g]	84, 89	206	398	m 140–170 cyclohexyl plus NH

[a] All nmr spectra were taken in $CDCl_3$ and chemical shifts are reported in hertz, relative to internal TMS. [b] All compounds exhibited a multiplet downfield of the aromatic region assigned to the ring proton β to the carbonyl (483–504 Hz) and aromatic protons in the region 400–465 Hz. [c] Buried under the aromatic protons. [d] Nonequivalent methyls. [e] This compound also exhibited a signal which was lost upon addition of D_2O, d 238 Hz, J = 4 Hz, OH. [f] This compound exhibited a doublet of doublets at 460–475 Hz assigned to the ortho protons of the benzoyl group. [g] s 136 Hz, CH_3CH_3Ar–.

butylamine either alone or with sufficient benzene to dissolve all the ketone. No reaction took place after 2 weeks.

Structure of Compounds.—In this series of compounds, the position of the double bond, exocyclic or endocyclic, has been thoroughly studied by ir,[10] uv,[10] and nmr.[11,12] (See Tables I–III.) In general, the exocyclic unsaturated ketones have an intense long wavelength band, which is to be expected for the extended conjugation. Nmr has been found[11,12] to be definitive in determining both the position of the double bond and the stereochemistry about it. The diamagnetic anisotropy of the carbonyl group deshields the ring proton β to the carbonyl. This proton appears as a complex multiplet near 480 Hz.[11–13]

In *trans*-2-benzal-4,4-dimethyl-1-tetralones, the vinyl proton is in the same position relative to the carbonyl group as the β ring proton. Thus a downfield shift of this proton is observed, at approximately 460 Hz as predicted.[11] The cis isomer has its vinyl proton outside the deshielding cone of the carbonyl group and appears upfield at approximately 400 Hz.[14] All of the 2-benzal-4,4-dimethyl-1-tetralones studied have the vinyl proton absorbance downfield of the aromatic region. This includes the amino ketones **3** and **6**. Two of these trans compounds, **3d** and **6b**, were irradiated by the previously published procedure[11] to the corresponding *cis*-2-(substituted benzal)-3-amino-4,4-dimethyl-1-tetralones **14** and **15**, respectively. An upfield shift of the vinyl proton to approximately 400 Hz was observed, confirming the trans stereochemistry of the exocyclic double bond in **3d** and **6b**.



trans *cis*

3d, R = *tert*-butyl; Ar = Ph **14**
6b, R = cyclohexyl; Ar = o-CH_3Ph **15**

Discussion

There are two possible pathways for the reaction of **1a** with amines. With the less space-demanding amines, the first formed product is **3**. In the presence of an excess of amine, there is an amine exchange reaction with **3** to yield the amino ketones **2**. Thus, these normal substitution products arise *via* two rearrangement reactions rather than by direct substitution.

With the more space-demanding *tert*-butylamine, the rearrangement–substitution reaction is slowed

(11) D. N. Kevill, E. D. Weiler, and N. H. Cromwell, *J. Org. Chem.*, **29**, 1276 (1964).
(12) J.-L. Imbach, A. E. Pohland, E. D. Weiler, and N. H. Cromwell, *Tetrahedron*, **23**, 3931 (1967).
(13) For published spectra see G. Glaros and N. H. Cromwell, *J. Chem. Educ.*, **46**, 854 (1969).
(14) G. Glaros and N. H. Cromwell, *ibid.*, **48**, 204 (1971).

down to where direct substitution is competitive, and the rate of the amine exchange reaction is immeasurably slow. Thus, while small amines yield normal products *via* two consecutive rearrangement–substitution reactions, *tert*-butylamine reacts with bromo ketone **1a** *via* parallel direct substitution and rearrangement–substitution reactions, as had previously been suggested[3] (Scheme I).

The stability of **3d** in the presence of *tert*-butylamine when it is known to react with the less space-demanding amine piperidine[3] may be explained in terms of steric hindrance. The SN2′ reaction has been shown[15] to proceed with a cis orientation of entering and leaving group. If a cis orientation is a requirement for this reaction as well, two *tert*-butylamine groups entering and leaving cis to each other would present a very crowded transition state.[16] The facile aminotropic rearrangement with the less space-demanding piperidine[3] demonstrates that such a reaction is possible, but prevented with bulky amines.

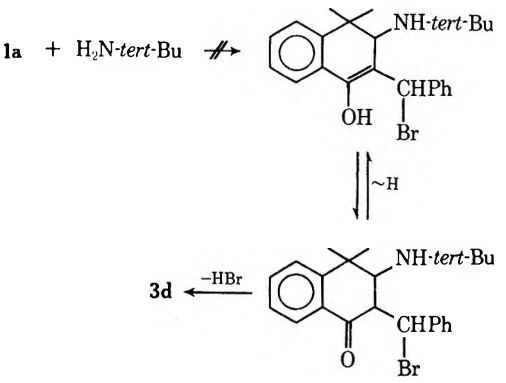
The stability of the bromo ketone **1a** under reaction conditions, toward rearrangement to the exocyclic structure **7a** precludes an SNi′–SN2 reaction sequence to explain the appearance of rearranged isomers **3**. That amino ketones **2** are thermodynamically more stable than amino ketones **3** and do not rearrange to **3** also precludes an SN2–SNi′ reaction sequence to explain the appearance of amino ketones **3**. That amines did not add in a 1,4 manner to the s-trans enone system present in the endocyclic unsaturated ketone **10** is not surprising and argues against a "1,4-addition–loss of amine and HBr" sequence to explain the appearance of amino ketones **3**.

Thus, the appearance of abnormal substitution products **3** is best explained in terms of a variant of an SN2′-type reaction. The nature of the transition state involved in this rearrangement reaction is discussed in the accompanying paper.[9]

Experimental Section[19,20]

Reaction of 1a with Amines (10 equiv).—The general procedure followed was that of Cromwell and Wu.[3] A solution of **1a**, mp 117–117.5° (lit.[2] mp 116.5–117.5°), and 10 molar equiv of amine in benzene was allowed to react at room temperature for periods of 3–14 days. The amine hydrobromide was recovered by filtration and the solvent was evaporated under reduced pressure to yield an oil. The oil was dissolved in ether and dry HCl gas was bubbled through the ethereal solution to precipitate the amino ketone hydrochloride. The amino ketone hydrochloride was filtered from the ether and dissolved in 95% ethanol.[21] The ethanolic solution was made basic with Na_2CO_3 solution and extracted with benzene. The benzene layer was separated, dried over $MgSO_4$, filtered free from drying agent, and evaporated under reduced pressure to yield an oil. This oil was analyzed by nmr and tlc and the pure amino ketones were isolated as described below.

SCHEME I
MICHAEL ADDITION–ELIMINATION SEQUENCE



A. With Isopropylamine.—The crude oil obtained in 38% yield showed two spots on tlc, but nmr analysis showed only 2-[α-(isopropylamino)benzyl]-1,4-dihydro-4,4-dimethyl-1-ketonaphthalene (**2e**) to be present. Repeated attempts to crystallize this compound failed, and it was analyzed as its hydrochloride salt, mp 232–233°.

B. With *sec*-Butylamine.—The crude oil obtained in 92% yield exhibited two spots on tlc, but nmr analysis showed it to consist of 2-[α-(*sec*-butylamino)benzyl]-1,4-dihydro-4,4-dimethylketonaphthalene (**2g**). The product crystallized slowly and was recrystallized from 95% ethanol to yield 47% of pale yellow needles, mp 66–68°.

C. With Diisopropylamine.—The reaction of **1a** with diisopropylamine was very slow. After 1 week, using 2 g (0.006 mol) of **1a** and 4.25 ml of amine in 20 ml of benzene, there was insufficient product for an nmr analysis.

D. With Adamantylamine.—Adamantylamine is a high-melting solid which was found to be only partially soluble in benzene, chloroform, and acetonitrile. To 1.7 g (0.005 mol) of bromo ketone **1a** is 25 ml of benzene was added 3 g (0.02 mol) of adamantylamine. Most of the amine did not go into solution, but the reaction was stirred at room temperature and worked up in the usual manner. Nmr analysis of the crude oil showed it to contain two products. From integrating the assumed methine signals, the ratio of nonrearranged product to rearranged product was found to be 21:79. Tlc showed two poorly resolved spots and column chromatography was unsuccessful in separating the two isomers.

E. With *tert*-Octylamine.—The reaction of bromo ketone **1a** with *tert*-octylamine was similar to that with adamantylamine. The reaction was slow, 18% crude oil was obtained after 2 weeks, and the products could not be separated on tlc or by column chromatography. Nmr analysis of the crude oil showed it to contain the nonrearranged product and the rearranged product in a ratio of 78:22.

Reaction of 1a with Amines (2 equiv).—The general procedure followed was the same as that described above, except that 2 equiv of amine were used.

A. With Isopropylamine.—From 1.7 g (0.005 mol) of **1a** and 0.6 g (0.01 mol) of isopropylamine in 25 ml of benzene, there was obtained 0.517 g (85%) of isopropylamine hydrobromide and 1.39 g (87%) of crude product. Nmr analysis of the crude product showed it to consist of *trans*-2-benzal-3-(isopropylamino)-4,4-dimethyl-1-tetralone (**3e**) with only a trace of nonrearranged product **2e**. The crude oil crystallized readily and was recrystallized from 95% ethanol to yield 0.798 g (50%) of pure **3e** as yellow crystals, mp 88–89°.

B. With Cyclohexylamine.—From 1.7 g (0.005 mol) of **1a** and 0.99 g (0.01 mol) of cyclohexylamine in 25 ml of benzene, there was obtained 0.68 g (76%) of cyclohexylamine hydrobromide. Nmr analysis of the crude solid which formed after removal of solvent showed it to consist entirely of *trans*-2-benzal-3-(cyclohexylamino)-4,4-dimethyl-1-tetralone (**3f**). The crude solid was recrystallized from 95% ethanol to yield 1.1 g (61%) of pure **3f** as yellow crystals, mp 94–95°.

(15) G. Stork and W. N. White, *J. Amer. Chem. Soc.*, **75**, 4119 (1953).

(16) A sensitivity to the steric requirements of the amine in similar aminotropic rearrangements has been observed in the indanone system[17] as well as in the chalcone system.[18]

(17) G. Maury, E. M. Wu, and N. H. Cromwell, *J. Org. Chem.*, **33**, 1907 (1968).

(18) N. H. Cromwell, K. Matsumoto, and A. D. George, *ibid.*, **36**, 272 (1971).

(19) Melting points were taken by the capillary method in a Mel-Temp melting point apparatus and are uncorrected. Infrared spectra were obtained as CCl_4 solutions using a Perkin-Elmer Model 237 spectrophotometer. Ultraviolet spectra were taken on a Cary Model 14 recording spectrophotometer. Proton magnetic resonance spectra were obtained on a Varian A-60 or A-60D spectrometer employing $CDCl_3$ solutions and are reported in Hertz relative to internal TMS (0.0 Hz). Elemental analyses were performed by Micro-Tech Laboratories, Skokie, Ill.

(20) All physical data on new compounds are presented in Tables I–III.

(21) If the hydrochloride was hygroscopic and formed a gummy mass, the ether was decanted off and the hydrochloride was washed with fresh ether.

C. **With *sec*-Butylamine.**—From 1.7 g (0.005 mol) of **1a** and 0.73 g (0.01 mol) of *sec*-butylamine in 25 ml of benzene, there was obtained 0.54 g (75%) of *sec*-butylamine hydrobromide. Nmr analysis of the crude product showed it to consist of *trans*-2-benzal-3-(*sec*-butylamino)-4,4-dimethyl-1-tetralone (**3g**). This crude oil could not be crystallized when triturated with petroleum ether (bp 30–60°) or ethanol. The oil was analyzed as its hydrochloride salt, mp 176–177°.

D. **With Morpholine.**—From 1.7 g (0.005 mol) of **1a** and 0.87 g (0.01 mol) of morpholine in 25 ml of benzene, there was obtained 0.856 g (102% wet) of morpholine hydrobromide. Nmr analysis of the crude product showed it to consist of *trans*-2-benzal-3-morpholino-4,4-dimethyl-1-tetralone (**3b**) and 2-[α-(morpholino)-benzyl]-1,4-dihydro-4,4-dimethyl-1-ketonaphthalene (**2b**) in a ratio of 50:50. Tlc showed two spots of similar R_f value. Chromatography of the mixture on a Florisil column eluting with benzene gave a first fraction enriched in **3b**. Recrystallization of this enriched fraction yielded 0.218 g (12.5%) of pure **3b** as yellow crystals, mp 147–149°.

E. **With Piperidine.**—From 1.7 g (0.005 mol) of **1a** and 0.85 g (0.01 mol) of piperidine in 25 ml of benzene, there was obtained 0.74 g (89%) of piperidine hydrobromide. Nmr analyses of the crude product showed it to consist of *trans*-2-benzal-3-piperidino-4,4-dimethyl-1-tetralone (**3a**) and 2-[α-(piperidino)benzyl]-1,4-dihydro-4,4-dimethyl-1-ketonaphthalene (**2a**) in a ratio of 50:50. Chromatography on a column of Florisil eluting with benzene afforded **3a** as a yellow oil, analyzed as its picrate salt, mp 184–185° dec.

Further elution with ethyl acetate yielded **2a** as a yellow solid. Recrystallization from 95% ethanol yielded pure **2a**, mp 103–104° (lit.[2] mp 102–103°).

Reaction of 1a with Amines (1 equiv).—The general procedure followed is described above, except that only 1 equiv of amine was used. The amine was added as a solution in 10 ml of benzene over a period of 1 hr. The reaction was worked up after stirring for an additional 1 hr at room temperature.

A. **With Morpholine.**—From 1.7 g (0.005 mol) of **1a** and 0.49 g (0.0056 mol) of morpholine in 25 ml of benzene, there was obtained 0.218 g (52%) of morpholine hydrobromide. Nmr analysis of the crude product showed it to consist entirely of the rearrangement–substitution product *trans*-2-benzal-3-(morpholino)-4,4-dimethyl-1-tetralone (**3b**), which was recrystallized from 95% ethanol to yield pure **3b**, mp 148–150°.

B. **With Piperidine.**—From 1.7 g (0.005 mol) of **1a** and 0.424 g (0.005 mol) of piperidine in 25 ml of benzene, there was obtained 0.252 g (60%) of piperidine hydrobromide. Nmr analysis showed the yellow oil to consist entirely of *trans*-2-benzal-3-(piperidino)-4,4-dimethyl-1-tetralone (**3a**).

Reaction of 4 with Amines (2 equiv).—The general procedure followed is described above, except that 2 equiv of amine were used.

A. **With Isopropylamine.**—From 1.72 g (0.005 mol) of **4** and 0.59 g (0.0098 mol) of isopropylamine in 25 ml of benzene, there was obtained 0.443 g (63%) of isopropylamine hydrobromide. Nmr analysis of the crude product showed it to consist entirely of *trans*-2-*o*-methylbenzal-3-(isopropylamino)-4,4-dimethyl-1-tetralone (**6a**). The product was recrystallized from 95% ethanol to yield 0.78 g (47%) of pure **6a**, mp 95–96° (lit.[4] mp 96–97°).

B. **With Cyclohexylamine.**—From 1.7 g (0.005 mol) of **4** and 0.987 g (0.01 mol) of cyclohexylamine in 25 ml of benzene there was obtained 0.64 g (71%) of cyclohexylamine hydrobromide. Nmr analysis of the crude product showed it to consist entirely of *trans*-2-*o*-methylbenzal-3-(cyclohexylamino)-4,4-dimethyl-1-tetralone (**6b**). The crude product was recrystallized from 95% ethanol to yield 1.133 g (61%) of pure **6b** as yellow crystals, mp 116–117° (lit.[4] mp 116–117.5°).

Reactions of Abnormal Substitution Products (3) with Amines.—The general procedure involved weighing approximately 100 mg of the amino ketone **3** into an nmr tube and adding 0.25 ml of C_6D_6 and approximately 1 equiv of the corresponding amine. The nmr spectrum was then recorded and the region between 200 and 350 Hz was scanned periodically. For compounds **3** having the amino moiety isopropyl, cyclohexyl, morpholino, piperidino, and *sec*-butyl the rearrangement to amino ketone **2** was essentially quantitative in 1 week. There was only a trace of **2d** observed with **3d** and *tert*-butylamine in CD_3CN at 45° after 2 weeks.

Solvolysis of 1a.—A 3.41-g (0.01 mol) sample of **1a** was dissolved in 50 ml of reagent grade acetone and 15 ml of deionized water. The mixture was stirred at room temperature for 3 days, the solvent was removed under reduced pressure, and the residue was extracted with ether. The ether layer was separated, dried over $MgSO_4$, filtered, and evaporated to yield a colorless oil which crystallized upon trituration with petroleum ether, yielding 2.1 g (75%) of a white solid. Nmr analysis showed this crude product to contain two compounds identified as 2-[α-(hydroxy)benzyl]-1,4-dihydro-4,4-dimethyl-1-ketonaphthalene (**8**) and 2-benzoyl-1,4-dihydro-4,4-dimethyl-1-ketonaphthalene (**9**) in a ratio of 79:21. Recrystallization from ether or petroleum ether gave a mixture enriched in the diketone **9**. Column chromatography on alumina (Woelm activity I) eluting with benzene gave a first fraction also enriched in **9**. The enriched fraction was recrystallized until nmr and melting point showed it to be pure **9**, mp 153–154°.

Further elution with benzene yielded alcohol **8** as colorless plates, mp 116–118°.

Oxidation of Alcohol 8.—The procedure followed was essentially that recorded in the literature.[7] To a stirred mixture of 0.34 g of concentrated H_2SO_4, 0.406 g of $K_2Cr_2O_7$, and 2.5 ml of water was added 0.5514 g (0.00198 mol) of the alcohol **8**. Acetone (4 ml) was then added to dissolve all the alcohol and the mixture was stirred for 15 min. The reaction mixture was extracted with ether; the ether was washed with water, NaOH solution, and water and dried over $MgSO_4$. After filtering the dried ether solution, the ether was evaporated and the solid which remained was recrystallized from ether to yield 0.188 g (34%) of the diketone **9**, mp 153–154°, with an nmr spectrum superimposable on that of the product obtained previously from the solvolysis of **1a**.

Reaction of 8 with Thionyl Chloride. Attempted Synthesis of 2-Benzal-3-chloro-4,4-dimethyl-1-tetralone (7b). A.—Thionyl chloride (1.33 g, 0.007 mol) was added dropwise to 2.0 g (0.0060 mol) of alcohol **8** in 20 ml of chloroform. The mixture was stirred for 4 hr and the solvent was removed under reduced pressure. Cooling the residue in an ice bath yielded 0.8 g (39%) of a colorless compound, mp 108–109°, which had an nmr spectrum superimposable with that of 2-(α-chlorobenzyl)-1,4-dihydro-4,4-dimethyl-1-ketonaphthalene (**1b**) prepared as previously described,[3] mp 108–109° (lit.[3] mp 107–108°).

B.—The procedure followed was that recorded in the literature.[8] When 0.12 g (0.001 mol) of thionyl chloride was added dropwise to an ice bath cooled solution of 0.278 g (0.001 mol) of alcohol **8** in 25 ml of dried ether, only the previously prepared chloro ketone **1b** was again observed.

Irradiation of Trans Exocyclic Amino Ketones.—The procedure followed has been previously published.[11] Irradiation of a methanolic solution of *trans*-amino ketone using a B-100A Blakray source, followed by evaporation of the solvent under reduced pressure, yielded the corresponding *cis*-amino ketones.

***cis*-2-Benzal-3-(*tert*-butylamino)-4,4-dimethyl-1-tetralone (14).**—Irradiation of a 0.5-g sample of **3d**[3] in chloroform, followed by evaporation of the solvent, yielded 0.22 g (44%) of **14** as deep yellow crystals, mp 140–142°.

***cis*-2-(*o*-Methylbenzal)-3-(cyclohexylamino)-4,4-dimethyl-1-tetralone (15).**—Irradiation of 0.374 g of **6b**[4] yielded 42% of **15** as a yellow oil. This oil could not be crystallized and was analyzed as its hydrochloride salt, mp 187–188°.

Control Experiments. Stability of Compounds. A. Bromo Ketone 1a.—Approximately 100 mg of **1a** was dissolved in 0.25–0.30 ml of C_6D_6, $CDCl_3$, or CD_3CN in nmr sample tubes. The nmr tubes were sealed and placed in a constant-temperature bath at 45°. The nmr spectrum was recorded periodically and no change was observed for periods up to 2 weeks.

B. **Nonrearranged Products 2.**—The amino ketones **2** were found to be stable when kept in the pure state or in solution. Amino ketone **2** was stable when dissolved in benzene and heated to 135° for 4 hr.[4]

C. **Abnormal Substitution Products 3.**—In a typical experiment, approximately 100 mg of amino ketone **3** was dissolved in 0.25 ml of $CDCl_3$ and the nmr spectrum was recorded periodically. In each case except for **3d** there was some decomposition to 2-benzyl-1,4-dihydro-4,4-dimethyl-1-ketonaphthalene (**10**), but no evidence was obtained for rearrangement to the corresponding amino ketones **2**. These control experiments were conducted at room temperature for 30 days.

D. **Endocyclic Double Bond.**—A 0.66-g (0.0025 mol) sample of 2-benzyl-1,4-dihydro-4,4-dimethyl-1-ketonaphthalene (**10**) was placed in a test tube and 1.4 g of *tert*-butylamine was added. The test tube was sealed and allowed to stand at room temperature for 2 weeks. The tube was opened, the amine was removed

under reduced pressure, and the contents were analyzed. Nmr and tlc showed no compounds present except **10**.

In another experiment, 0.66 g (0.0025 mol) of **10**, 1.4 g of *tert*-butylamine, and enough benzene to dissolve all the ketone were placed in a test tube and the tube was sealed. After 2 weeks at room temperature, nmr and tlc analysis showed that no reaction had taken place.

Registry No.—**1a**, 33224-47-4; **2a**, 33224-50-9; **2b**, 33224-51-0; **2e**, 33224-52-1; **2e** HCl, 33224-53-2; **2g**, 33224-54-3; **3a**, 33224-55-4; **3a** picrate, 33224-56-5; **3b**, 33224-57-6; **3e**, 33240-01-6; **3f**, 33240-02-7; **3g**, 33240-03-8; **3g** HCl, 33303-98-9; **6a**, 30765-51-6; **6b**, 30765-50-5; **8**, 33240-06-1; **9**, 33240-07-2; **14**, 33240-08-3; **15**, 33240-09-4; **15** HCl, 33240-10-7.

Acknowledgments.—This work was supported in part by a Special Departmental Science Development Award to the Department of Chemistry from the National Science Foundation, No. GU-2054, and in part by a grant from the Nebraska Research Council. One of us (G. G.) wishes to acknowledge financial assistance received in the form of an NSF traineeship and a Monsanto summer fellowship.

Mobile Keto Allyl Systems. XIII.[1] The Kinetics and Mechanism of the Reaction of 2-(α-Halobenzyl)-1,4-dihydro-4,4-dimethyl-1-ketonaphthalene with *tert*-Butylamine[2]

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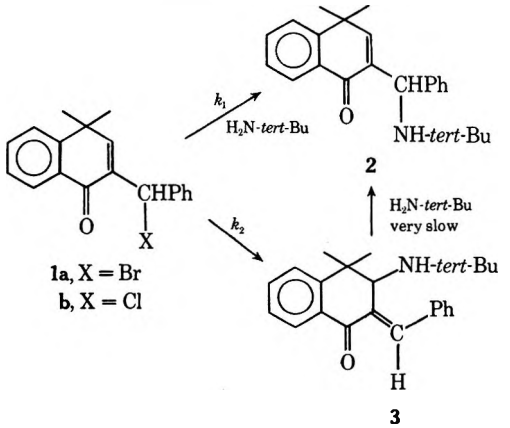
The title compound **1** was found to react with *tert*-butylamine by parallel reactions which obeyed second-order kinetics, first order in **1** and amine. The reaction yielding direct substitution product **2** is characterized by a large solvent effect ($k_{CH_3CN}/k_{C_6H_6}$ = 124), large leaving group effect (k_{Br}/k_{Cl} = 110), and an activation energy of 15–17 kcal/mol. These data are consistent with a normal SN2 displacement reaction. The reaction yielding abnormal substitution product is characterized by a small solvent effect ($k_{CH_3CN}/k_{C_6H_6}$ = 11), a small leaving group effect (k_{Br}/k_{Cl} = 5.5), and an activation energy of 12–13 kcal/mol. Although not ruling out the possibility of a dipolar intermediate being involved, the data are best interpreted in terms of a variant of an SN2′-type reaction in which the entering of the amino group and the departure of the halogen ion are concerted, but the carbon to nitrogen bond making is running ahead of carbon to halogen bond breaking, and the carbonyl group serves to disperse some of the developing negative charge.

In earlier papers[1,3] in this series it was shown that the halo ketone **1** reacts with *tert*-butylamine to yield two products **2** and **3** by parallel pathways. Compounds **1**, **2**, and **3** were shown to be stable under reaction conditions to rearrangement or decomposition. Because of the stability of these compounds, and because the rearrangement–substitution reaction could be compared with the direct substitution process, it was decided to study the kinetics of the reaction of halo ketone **1** with *tert*-butylamine.



Method.—Compounds **1** and **2** have very similar ir and uv spectra;[3] so both of these methods are unsatisfactory to follow the kinetics of the reaction. Halide titration would give only the overall rate constants $(k_1 + k_2) = k$; so this method is unsatisfactory also. Since the methine proton absorbance of **1** appears near 400 Hz, the methine proton absorbance of **2** appears near 300 Hz, and the methine proton absorbance of **3** appears near 250 Hz[3], it was decided to use nmr to follow the rate of the reaction. The assumption was made that the sum of the concentrations of **1**, **2**, and **3** at any time was a constant and equal to the initial concentration of **1**. Thus, $[1]_0 = [1]_t + [2]_t + [3]_t$ and the individual rate constants k_1 and k_2 could be obtained.

The use of nmr to follow kinetics places certain restrictions on the system. First, large quantities of reactants must be used to get strong enough signals for accurate measurements. Secondly, the method is relatively insensitive; consequently greater errors are introduced when one species is present to a much greater extent than another, as occurs in the beginning and end of a reaction. Lastly, although good correlation may be obtained for the overall rate constant k, the error involved in determining the ratio of **2** to **3** causes a greater error to be introduced in determining the individual rate constants k_1 and k_2. With these restrictions in mind we determined the kinetics of the reaction of **1** with *tert*-butylamine under various conditions. Because of the inaccuracy of the method we have been very cautious about comparing a rate constant we obtained with one obtained by other workers. Instead, we have tried to make comparisons in our system as various factors governing the rate of reaction are changed, such as temperature, solvent, and leaving group.

(1) For paper XII in this series, see G. Glaros and N. H. Cromwell, *J. Org. Chem.*, **37**, 862 (1972).

(2) Presented at the 162nd National Meeting of the American Chemical Society, Washington, D. C., Sept 1971.

(3) N. H. Cromwell and E. M. Wu, *J. Org. Chem.*, **33**, 1895 (1968).

TABLE I

SECOND-ORDER RATE CONSTANTS FOR THE REACTION OF 2-(α-BROMOBENZYL)-1,4-DIHYDRO-4,4-DIMETHYL-1-KETONAPHTHALENE (1a) WITH *tert*-BUTYLAMINE IN BENZENE

Temp, °C	[Bromo ketone], mol/l.	[*tert*-Butylamine], mol/l.	k, l. mol^{-1} min^{-1}	k_1, l. mol^{-1} min^{-1}	k_2, l. mol^{-1} min^{-1}
15.0	0.169	0.886	2.3×10^{-5}	4.0×10^{-6}	1.9×10^{-5}
15.0	0.179	0.632	2.3×10^{-5}	4.9×10^{-6}	1.8×10^{-5}
15.0	0.177	0.760	2.0×10^{-5}	3.6×10^{-6}	1.6×10^{-5}
30.0	0.386	1.930	1.0×10^{-4}	2.3×10^{-5}	7.7×10^{-5}
30.0	0.456	2.373	1.0×10^{-4}	1.9×10^{-5}	8.1×10^{-5}
30.0	0.295	1.599	8.1×10^{-5}	2.0×10^{-5}	6.1×10^{-5}
35.0	0.297	1.069	1.1×10^{-4}	3.5×10^{-5}	7.5×10^{-5}
35.0	0.334	1.249	1.2×10^{-4}	3.7×10^{-5}	8.3×10^{-5}
35.0	0.376	1.487	1.1×10^{-4}	3.2×10^{-5}	7.8×10^{-5}
45.5	0.183	0.880	2.2×10^{-4}	7.1×10^{-5}	1.5×10^{-4}
45.5	0.193	0.609	2.2×10^{-4}	7.0×10^{-5}	1.5×10^{-4}
45.5	0.148	0.816	2.4×10^{-4}	8.2×10^{-5}	1.6×10^{-4}
			E_a, kcal/mol	17	13

TABLE II

SECOND-ORDER RATE CONSTANTS FOR THE REACTION OF 2-(α-BROMOBENZYL)-1,4-DIHYDRO-4,4-DIMETHYL-1-KETONAPHTHALENE (1a) WITH *tert*-BUTYLAMINE IN CHLOROFORM

Temp, °C	[Bromo ketone], mol/l.	[*tert*-Butylamine], mol/l.	k, l. mol^{-1} min^{-1}	k_1, l. mol^{-1} min^{-1}	k_2, l. mol^{-1} min^{-1}
15.0	0.162	0.924	6.1×10^{-5}	4.1×10^{-5}	2.0×10^{-5}
15.0	0.0837	0.0965	7.1×10^{-5}	5.1×10^{-5}	2.0×10^{-5}
15.0	0.181	1.654	7.2×10^{-5}	4.2×10^{-5}	3.0×10^{-5}
25.0	0.369	1.604	2.0×10^{-4}	1.3×10^{-4}	7.1×10^{-5}
25.0	0.369	2.406	2.6×10^{-4}	1.5×10^{-4}	1.1×10^{-4}
25.0	0.407	2.406	2.5×10^{-4}	1.4×10^{-4}	1.1×10^{-4}
30.0	0.358	0.855	2.7×10^{-4}	1.2×10^{-4}	9.4×10^{-5}
30.0	0.508	1.079	2.8×10^{-4}	1.8×10^{-4}	9.8×10^{-5}
30.0	0.265	1.238	2.4×10^{-4}	1.5×10^{-4}	8.6×10^{-5}
35.0	0.230	1.234	3.6×10^{-4}	2.3×10^{-4}	1.2×10^{-4}
35.0	0.350	1.443	3.7×10^{-4}	2.5×10^{-4}	1.2×10^{-4}
35.0	0.441	1.802	4.2×10^{-4}	2.7×10^{-4}	1.5×10^{-4}
45.5	0.137	0.594	8.2×10^{-4}	6.6×10^{-4}	1.6×10^{-4}
45.5	0.143	0.904	7.6×10^{-4}	5.8×10^{-4}	1.8×10^{-4}
			E_a, kcal/mol	15	12

TABLE III

SECOND-ORDER RATE CONSTANTS FOR THE REACTION OF 2-(α-BROMOBENZYL)-1,4-DIHYDRO-4,4-DIMETHYL-1-KETONAPHTHALENE (1a) WITH *tert*-BUTYLAMINE IN ACETONITRILE

Temp, °C	[Bromo ketone], mol/l.	[*tert*-Butylamine], mol/l.	k, l. mol^{-1} min^{-1}	k_1, l. mol^{-1} min^{-1}	k_2, l. mol^{-1} min^{-1}
15.0	0.157	0.642	9.9×10^{-4}	7.4×10^{-4}	2.5×10^{-4}
15.0	0.159	0.812	9.5×10^{-4}	7.1×10^{-4}	2.4×10^{-4}
30.0	0.154	0.690	3.4×10^{-3}	2.5×10^{-3}	8.5×10^{-4}
30.0	0.110	0.638	2.6×10^{-3}	2.0×10^{-3}	6.2×10^{-4}
30.0	0.156	0.647	3.7×10^{-3}	2.8×10^{-3}	8.9×10^{-4}
35.0	0.156	0.607	5.9×10^{-3}	4.7×10^{-3}	1.2×10^{-3}
45.5	0.148	0.580	1.3×10^{-2}	1.1×10^{-2}	2.2×10^{-3}
45.5	0.149	0.740	1.2×10^{-2}	9.7×10^{-3}	2.4×10^{-3}
			E_a, kcal/mol	16	13

Results and Discussion

The kinetics were found to be overall second order, first order in halo ketone **1** and first order in amine. The data best fits an equation involving two equivalents of amine, which is consistent with the overall scheme shown below. The second molecule of amine

$$R'X + RNH_2 \longrightarrow \overset{+}{R}NH_2R'X^- \xrightarrow{RNH_2} RNHR' + \overset{+}{R}NH_3X^-$$

acts as a base to free the amino ketone from its hydrobromide salt.

The activation energy for the reaction yielding direct substitution product was found to be 15–17 kcal/mol, while that for the rearrangement–substitution reaction was found to be 12–13 kcal/mol (Tables I–IV). The lower activation energy for the rearrangement–substitution reaction is consistent with the results of the study of the steric requirements of the reaction.[1] The carbonyl group is probably responsible for the lowering of the activation energy of the rearrangement reaction, relative to direct displacement. The carbonyl group can be expected to lower the activation energy of the abnormal substitution reaction in two ways. First, it can reduce the electron density at the γ carbon atom by the normal ground-state resonance effect. Secondly, it can act as an electron sink during the transition state to help disperse the developing charge.

Leaving Group Effect.—In Table V are listed the average rate constants obtained for the reaction of *tert*-butylamine with bromo ketone **1a** and chloro

TABLE IV

SECOND-ORDER RATE CONSTANTS FOR THE REACTION OF 2-(α-CHLOROBENZYL)-1,4-DIHYDRO-4,4-DIMETHYL-1-KETONAPHTHALENE (1b) WITH *tert*-BUTYLAMINE IN ACETONITRILE

Temp, °C	[Chloro ketone], mol/l.	[*tert*-Butylamine], mol/l.	k, l. mol^{-1} min^{-1}	k_1, l. mol^{-1} min^{-1}	k_2, l. mol^{-1} min^{-1}
30.0	0.152	0.582	1.7×10^{-4}	2.3×10^{-5}	1.5×10^{-4}
30.0	0.198	0.660	1.8×10^{-4}	2.3×10^{-5}	1.6×10^{-4}

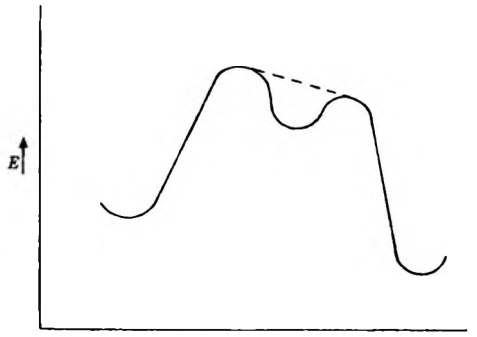
TABLE V

LEAVING GROUP EFFECT IN ACETONITRILE

Halo ketone	k, l. mol^{-1} min^{-1}	k_1, l. mol^{-1} min^{-1}	k_2, l. mol^{-1} min^{-1}	Relative rates k_1	Relative rates k_2
1a	3.2×10^{-3}	2.4×10^{-3}	8.2×10^{-4}	110	5.5
1b	1.8×10^{-4}	2.3×10^{-5}	1.5×10^{-4}	1	1

ketone **1b** at 30° in acetonitrile. It can be seen from the table that the bromo ketone **1a** reacts 110 times faster than the chloro ketone **1b** to yield the direct substitution product, but reacts only 5.5 times faster to yield the rearranged substitution product. The large "element effect" in the reaction yielding direct substitution product is consistent with a concerted SN2 reaction in which bond breaking has made significant progress in the rate-determining transition state. The smaller "element effect" for the reaction yielding rearrangement–substitution product is less easily interpreted.

If a stable dipolar intermediate were involved, and if addition of amine occurred in the rate-determining step, then a Br:Cl rate ratio of one would be predicted. That is, the carbon to halogen bond breaking occurs well after the rate-determining transition state, and an energy profile as in A, might best illustrate the reaction.



reaction coordinate

A

Small Br:Cl rate ratios have been observed in both aromatic nucleophilic substitution reactions ($k_{Br}/k_{Cl} \approx$ 1–2)[4] as well as in nucleophilic vinyl substitution reactions ($k_{Br}/k_{Cl} \approx$ 2–3).[5] In both cases the small leaving group effect has been cited in support of the addition–elimination mechanism. Bunnett and coworkers[6] have concluded that, while the small "element effect" in aromatic substitution reactions supports the presence of an intermediate and indicates that the breaking of the C–X bond has not made significant progress in the rate-determining transition state, it does not rule out the possibility of a synchronous reaction represented by the dotted line in the energy profile shown above. Thus a small Br:Cl rate ratio is in itself not rigorous evidence for an intermediate.

It should be recognized that the leaving group effect is probably solvent dependent. Indeed, in the reaction of *p*-nitrobenzene halides with piperidine the Br:Cl rate ratio varies from 1.16 in acetonitrile to 1.69 in benzene.[7] This is to be expected, since the more polar solvent would stabilize the dipolar intermediate more, leading to a smaller leaving group effect. Bordwell[8] has also observed a variation in leaving group effect with solvent. He has interpreted this to indicate that in the nonpolar solvent benzene (k_{Br}/k_{Cl} = 16) there is a dipolar transition state involved, but in the polar solvent ethanol (k_{Br}/k_{Cl} = 1.4) there is a dipolar intermediate involved.

The leaving group effect observed in this study is too large to support postulating an intermediate and, while small, it is significant, especially in as polar a solvent as acetonitrile. The leaving group effect is best interpreted as indicating that carbon–halogen bond breaking occurs late in the transition state. Another way of putting this is to say that the transition state of the reaction yielding abnormal substitution products is "reactantlike."

Solvent Effects.—Table VI contains a summary of the rate constants for the reaction of bromo ketone **1a** with *tert*-butylamine at 30° in the solvents benzene, chloroform, and acetonitrile. In the reaction yielding direct substitution product the rate enhancement in going from benzene to acetonitrile is 124. This is in accord with predictions based upon principles set forth by Ingold.[9] The more polar solvent stabilizes the charged transition state of the SN2 reaction involving neutral reactants, thereby substantially increasing the rate. By way of comparison, the relative rates of the reaction of trimethylamine with *p*-nitrobenzyl chloride in benzene, chloroform, and acetonitrile are 1:10.7:170.[10,11] It was concluded[11] that the charge separation in the transition state was small, although the degree of charge separation may vary from solvent to solvent.

TABLE VI

SOLVENT EFFECT ON THE RATE OF REACTION OF *tert*-BUTYLAMINE WITH BROMO KETONE **1b**

Solvent	k_1, l. mol^{-1} min^{-1}	Relative rate	k_2, l. mol^{-1} min^{-1}	Relative rate
C_6H_6	2.1×10^{-5}	1	7.3×10^{-5}	1
$CHCl_3$	1.5×10^{-4}	7.1	9.3×10^{-5}	1.3
CH_3CN	2.6×10^{-3}	124	7.9×10^{-4}	11

The relative rates for the reaction yielding abnormal

(4) (a) J. Miller, "Aromatic Nucleophilic Substitution," Elsevier, New York, N. Y., 1968, p 114; (b) J. F. Bunnett in "Theoretical Organic Chemistry," Kekule Symposium, Butterworths, London, 1959, p 144.

(5) (a) Z. Rappoport, *Advan. Phys. Org. Chem.*, **7**, 1 (1971); (b) G. Modena, *Accounts Chem. Res.*, **4**, 73 (1971); (c) A. Campagni, G. Modena, and P. E. Todesco, *Gazz. Chim. Ital.*, **90**, 694 (1960).

(6) J. F. Bunnett, E. W. Garbisch, Jr., and K. M. Pruitt, *J. Amer. Chem. Soc.*, **79**, 385 (1957).

(7) H. Suhr, *Chem. Ber.*, **97**, 3277 (1964).

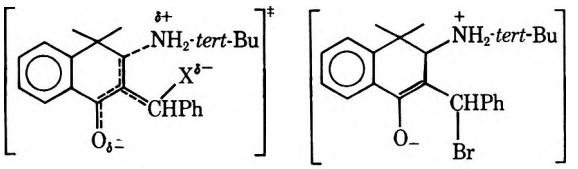
(8) F. G. Bordwell and D. A. Schexnayder, *J. Org. Chem.*, **33**, 3236 (1968).

(9) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," 2nd ed, Cornell University Press, Ithaca, N. Y., 1969, p 457.

(10) H. v. Halban, *Z. Phys. Chem.*, **84**, 129 (1913).

(11) (a) M. H. Abraham, *Chem. Commun.*, 1307 (1969); (b) M. H. Abraham, *J. Chem. Soc. B*, 299 (1971).

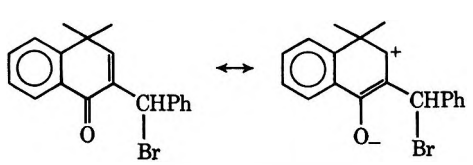
substitution product in benzene, chloroform, and acetonitrile are 1:1.3:11. This reaction also involves neutral reactants going to a charged transition state as in the classical Menschutkin reaction and should, therefore, be very sensitive to solvent polarity. One possible explanation for the small solvent effect observed in this reaction is that the developing charge is dispersed over several nuclei. It is not unreasonable to assume that some of the developing charge is located on the carbonyl group, as well as on the halogen ion, which has been shown by the leaving group effect to be involved in the transition state. A "picture" of the transition state emerges from this discussion and may be postulated as in B. The intermediate B has fully



A B

developed charges which would be expected to be stabilized by the more polar solvent, perhaps to a greater degree than is observed. Nucleophilic aromatic substitution reactions in which a dipolar intermediate is postulated exhibit solvent effects of the order $k_{CH_3CN}/k_{C_6H_6}$ = 24–35,[7] while addition of amines to α,β-unsaturated carbonyl compounds which may also involve dipolar intermediates exhibit small solvent effects.[12] Thus, while the solvent effect observed does not rigorously rule out a dipolar intermediate such as B, a charge dispersed transition state, as in A, accommodates all the data.

Proposed Mechanism.—The halo ketones 1 may react by direct displacement at the 2α position or by rearrangement–substitution *via* attack at the 3 position. Although the 3 position would appear to be sterically hindered by the geminal methyl groups on the 4 carbon, attack takes place at the 3 position to the exclusion of direct displacement with small amines.[1] The lower activation energy of the rearrangement–substitution reaction is probably brought about by the carbonyl group, which reduces the electron density at the 3 position by the normal resonance effect in the ground state of the molecule as shown below. With more space-demanding amines, such as *tert*-butylamine, the rearrangement–substitution reaction is made sterically more difficult, and the direct displacement at the 2-α position becomes competitive with rearrangement–



substitution.[1] The rearrangement–substitution reaction, however, is still a lower energy process than direct displacement. These first formed products, being thermodynamically less stable than the normal substitution products, then may react with a second molecule of amine to yield the final thermodynamically stable isomers.[1] It is likely that this second aminotropic rearrangement–substitution occurs with a cis configuration of entering and leaving amine, since this reaction is quite sensitive to the steric requirements of the amines.

Bromo ketone **1a** reacts with *tert*-butylamine by two parallel paths: direct SN2 displacement of halide to yield amino ketone 2 and an SN2′-type displacement to yield amino ketone **3**. The direct displacement reaction is characterized by a large leaving group effect k_{Br}/k_{Cl} = 110, as well as by a large solvent effect $k_{CH_3CN}/k_{C_6H_6}$ = 124, both fairly typical of Menschutkin-type reactions.

The rearrangement–substitution reaction does not appear to proceed *via* Michael 1,4 addition of amine to the s-trans enone system. Thus, an SN2′-type reaction is most likely. The relatively small solvent effect ($k_{CH_3CN}/k_{C_6H_6}$ = 11) and the small leaving group effect (k_{Br}/k_{Cl} = 5.5), while not ruling out the possibility of a dipolar intermediate, argue against such an intermediate.

Therefore, with no strong evidence to support an intermediate, we feel that all the data is best interpreted in the following manner. In a concerted process, the amine attacks the 3 position which is polarized by resonance with the carbonyl. Before the complete development of the negative charge on the carbonyl oxygen, the carbon–halogen bond begins to break. Thus, this mechanism may best be considered to be a variant of an SN2′-type reaction in which the entering of the amino group and the departure of the halogen ion are concerted, but the carbon to nitrogen bond making is running ahead of carbon to halogen bond breaking, and the carbonyl group serves to disperse some of the developing negative charge.

Experimental Section[13]

Preparation of Materials. Halo Ketones.—All halo ketones were prepared by the previously published procedure[2] and the physical data compared favorably with published values. The halo ketones were recrystallized from CCl_4 or isopropyl ether twice, powdered in a mortar and pestle, and dried in a desiccator. Nmr and tlc showed the halo ketones to be pure.

tert-**Butylamine.**—Commercially available *tert*-butylamine, of reagent grade or better, was dried over BaO and distilled twice using a Vigreux column. The constant-boiling fraction was stored in a glass-stoppered flask covered with aluminum foil to exclude light.

Solvents.—Reagent grade solvents were used in all cases. The benzene was dried over sodium, acetonitrile was dried over P_2O_5, and the chloroform was passed through a column of alumina (Woelm activity I) to remove water and ethanol. After drying, the solvents were distilled using a Vigreux column and stored in a glass-stoppered flask. The chloroform was used within a week to prevent interference from phosgene.

General Procedure.—The dry halo ketone was weighed by difference into a volumetric flask (25, 50, or 100 ml) with the aid of a small funnel. The halo ketone was then dissolved in the appropriate solvent and the funnel was washed well with solvent. The amine was then weighed by addition into a glass-stoppered weighing bottle. After an initial rough weighing, the stopper was replaced, a fine weighing was made, and the flask was placed in an ice bath. The amine was then added to the solution of the halo ketone with a pipet, the weighing bottle was rinsed several

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(13) All nmr spectra were obtained on a Varian A-60 or A-60D spectrometer. Eastman silica gel chromagram sheet 6060 with fluorescent indicator was used in a solvent system consisting of *n*-hexane, ethyl acetate, and benzene in a ratio of 1:1:8 for all tlc. Rate constants and activation energies were calculated on an IBM 360 computer by the least-squares method.

times with solvent, and the volume was made up (to 25, 50, or 100 ml) with additional solvent. After mixing well, the solvent was delivered by means of a pipet into test tubes having a constriction. The test tubes were placed in a Dry Ice–acetone bath and then sealed. The sealed tubes were then placed in a constant-temperature bath and removed at appropriate intervals for analysis. Because the reaction was slow, it was not found necessary to either cool the volumetric flask below room temperature when aliquots were being removed or to take an initial reading at time = 0 min. At appropriate intervals, a sealed tube was removed from the bath, opened, and filtered into a 50-ml flask. The tube was washed several times with solvent and these washings were added to the flask. The combined filtrate and washings were evaporated under vacuum without heating. The oily residue was dissolved in $CDCl_3$ (0.3 ml) and filtered into an nmr tube. This final filtering was necessary to remove the amine hydrobromide which was dissolved in the original solvent.

For each run 8–10 points were obtained for up to 80% completion. The ratio of **2** to **3** remained constant, within experimental error, over the course of the reaction.

Analysis.—The general appearance of the spectrum was observed at a sweep width of 500 Hz, scanning from approximately 400 to 200 Hz. This was necessary so that spinning side bands, which might be near the methine absorption of the halo ketone, could be shifted away be varying the sample spin rate. The methine absorptions of the halo ketone and both amino ketones were recorded at a sweep width of 50 Hz and at a sweep time of 250 or 500 sec. Saturation of absorbances did not occur during integration which was performed at a sweep time of 50 sec. Each of the absorbances was electronically integrated 8 to 12 times, depending upon reproducibility.

The assumption was made that the sum of the concentrations of halo ketone and both amino ketones was a constant and was equal to the initial concentration of halo ketone. In this way, a quantitative internal standard was unnecessary. Furthermore, the actual size of the aliquot taken and the volume to which the sample was made up were not important. The overall rate constants were calculated assuming that 2 equiv of amine are consumed. The following equation was used in these calculations where a_0 = initial concentration of amine, b_0 = initial concentration of halo ketone, and x = amount of reaction or concentration of both products.

$$\frac{1}{(a_0 - 2b_0)} \ln \frac{b_0(a_0 - 2x)}{a_0(b_0 - x)} = (k_1 + k_2)t$$

The individual rate constants k_1 and k_2 were then determined by multiplying the observed rate constant by the fraction of each product obtained.

Registry No.—**1a**, 33224-47-4; **1b**, 15982-14-6; *tert*-butylamine, 75-64-9.

Acknowledgments.—This work was supported in part by a Special Departmental Science Development Award to the Department of Chemistry from the National Science Foundation, No GU-2054, and in part by a grant from the Nebraska Research Council. One of us (G. G.) wishes to acknowledge financial assistance received in the form of an NSF traineeship and a Monsanto summer fellowship. The authors also wish to thank Mr. Russ Pennelly for the computer programs.

Secondary Valence Force Catalysis. XIII. Kinetics of the Alkaline Fading of Crystal Violet in the Presence of Cationic Surfactants[1]

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The alkaline fading of crystal violet in aqueous solution at 30° is subject to catalysis by dilute solutions of *n*-alkyltrimethylammonium bromides. Catalytic effectiveness of these surfactants increases markedly with increasing alkyl chain length as judged both by the maximal rate increase elicited and by the surfactant concentration required to elicit the maximum catalysis. The best catalyst studied, octadecyltrimethylammonium bromide, increases the rate constant for the fading reaction 30-fold at a concentration of 0.0003 *M*. The surfactant-dependent reactions are subject to marked inhibition by anions and by the nonionic surfactant dodecyldimethyl phosphine oxide. The effectiveness of the anions as inhibitors increases in the order $F^- < Cl^- < Br^- < N_3^- < NO_3^-$.

During the last several years there have appeared a substantial number of publications dealing with the kinetics of organic reactions in the presence of micelle-forming surfactants. These studies have been recently reviewed.[2,3] Among them, one of the more notable investigations is that of Duynstee and Grunwald concerning the kinetics of fading of triphenylmethyl dyes.[4] These workers observed catalysis of the attack of hydroxide ion on these cationic dyes by cationic surfactants and marked inhibition for the same reaction by anionic surfactants. The attack of water on these dyes was found subject to inhibition by both cationic and anionic dyes. In many respects, this seminal study provided the basis for later ones concerning other reactions. A subsequent study by Ritchie and coworkers, employing surfactant-free media, has extended study of the uncatalyzed reaction to include additional nucleophiles and has clarified some mechanistic details, including the possible importance of solvent reorientation in the activation process for these reactions.[5] Both in light of this new work and in view of gaps in our information concerning the kinetics of the surfactant-catalyzed reactions, additional study seems warranted. Specifically, there is no available information concerning the effects of surfactant concentration, of surfactant structure, or of salts on the reaction kinetics. To provide this information, we have examined the kinetics of attack of hydroxide ion on crystal violet [tris(*p*-dimethylaminophenyl)methyl cation] in the presence of a series of *n*-alkyltrimethylammonium bromides.

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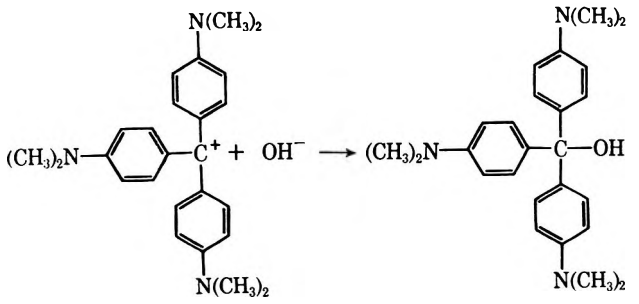

Experimental Section

Materials.—Crystal violet was obtained commercially. *n*-Alkyltrimethylammonium bromides were prepared from carefully redistilled alkyl bromides and trimethylamine according to the method of Scott and Tarter.[6] The surfactants were repeatedly recrystallized prior to use. Dodecyldimethyl phosphine oxide was a gift from the Miami Valley Laboratories of Procter and Gamble, Inc. Reagent grade inorganic salts were obtained commercially. Glass-distilled water was used throughout.

Kinetics.—All rate constants were measured spectrophotometrically employing a Zeiss PMQ II spectrophotometer equipped with a thermostated cell holder. The fading of crystal violet was followed at 590 nm with an initial dye concentration of 2×10^{-6} *M*. First-order rate constants were evaluated from plots of log (OD − OD_∞) *vs.* time in the usual way. Excellent first-order behavior was observed in all cases. The reaction proceeded to completion, as judged from the essentially complete fading of the dye at the conclusion of the reaction. All reactions were carried out in aqueous solution at 30° at a concentration of sodium hydroxide of 0.003 *M*.

Results

In the absence of surfactants, the first-order rate constant for fading of crystal violet in 0.003 *M* sodium hydroxide at 30° is 0.040 min^{-1}. This value accords with one calculated from the data of Duynstee and Grunwald at the same base concentration but at 25° of 0.031 min^{-1}.[4] At this base concentration, the fading reaction is almost completely the consequence of attack of hydroxide on the cationic dyes.[4]

In dilute solution of cationic surfactants, the rate of fading of crystal violet is much increased, in accord with the earlier results.[4] First-order rate constants for this reaction in 0.003 *M* sodium hydroxide were measured as a function of the concentration of decyl-, dodecyl-, tetradecyl-, hexadecyl-, and octadecyltrimethylammonium bromides. A portion of the results, those obtained at surfactant concentrations up to 0.01 *M*, are collected in Figure 1. From this data alone, two points are clear: the extent of catalysis increases with increasing chain length and the concentration at which maximal catalysis is observed decreases with increasing chain length. At higher concentrations, catalysis is observed with the decyl and dodecyl surfactants, although the former is only slightly effective. Each rate–concentration profile is qualitatively similar: as the surfactant concentration is increased, the rate constants increase, level off, and then begin to decrease slowly. The rate constant in the presence of 0.01 *M* hexadecyltrimethylammonium bromide and 0.003 *M* hydroxide, 1.1 min^{-1}, is in agreement with one of 0.43 min^{-1} measured under the same conditions except at 25°.[4]

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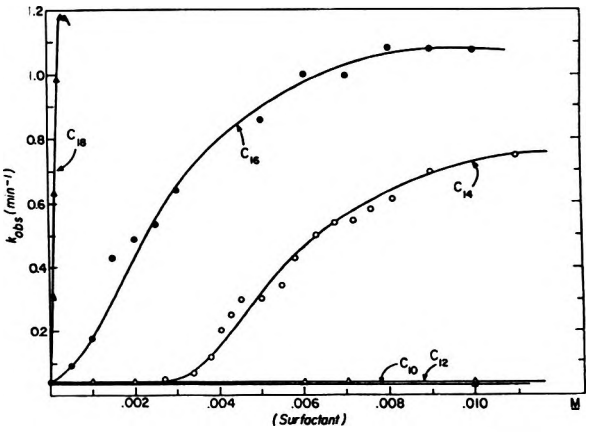

Figure 1.—First-order rate constants for the attack of hydroxide ion on crystal violet in aqueous solution at 30°, (OH^-) = 0.003 *M*, plotted as a function of the concentration of several *n*-alkyltrimethylammonium bromides.

TABLE I

KINETICS OF FADING OF CRYSTAL VIOLET IN 0.003 *M* SODIUM HYDROXIDE IN THE PRESENCE OF A SERIES OF ALKYLTRIMETHYLAMMONIUM BROMIDES AT 30°

Surfactant	Registry no.	k_{max},[a] min^{-1}	k_{max}/k_0,[b]	c_{max},[c] *M*
n-Decyl	2082-84-0	0.075	1.9	0.10
n-Dodecyl	1119-94-4	0.29	5.8	0.028
n-Tetradecyl	1119-97-7	0.75	19	0.011
n-Hexadecyl	57-09-0	1.1	27.5	0.008
n-Octadecyl	1120-02-1	1.2	30	0.0003

[a] Maximum first-order rate constants. [b] Ratio of maximum rate constant to that observed in the absence of catalysts. [c] Concentration of surfactant at which maximal catalysis is observed.

In Table I, the maximal rate increases and the surfactant concentrations necessary to elicit maximal catalysis, taken from the complete set of data, are collected. This data corroborates our conclusions reached above. In Figure 2, the maximal first-order rate constants and the surfactant concentrations required to reach half-maximal catalysis, $(k_{max} - k_0)/2$, an approximate measure of the dissociation constant for the dye–micelle complex, are plotted as a function of the number of carbon atoms in the alkyl chain of the surfactant.

A preliminary study of the fading of malachite green in the presence of the same surfactants gave a pattern of results similar to that just described. The attack of hydroxide ion on this dye, however, is less susceptible to catalysis than is that on crystal violet.

The cationic surfactant-dependent attack of hydroxide ion on crystal violet is sensitive to inhibition by salts. In Figure 3, first-order rate constants for this reaction in the presence of 0.003 *M* sodium hydroxide and 0.01 *M* hexadecyltrimethylammonium bromide are plotted as a function of the concentration of several anions. All are inhibitors. The effectiveness of the anions as inhibitors increases in the order $F^- < Cl^- < Br^- < N_3^- < NO_3^-$. Only the behavior of sulfate is unusual. This ion is an excellent inhibitor at low concentrations but the effect does not increase with increasing concentration above 0.07 *M*. At 0.20 *M* nitrate and azide, the rate constants closely approach those that would have been observed were no surfactant present.

In Figure 4, first-order rate constants for fading of

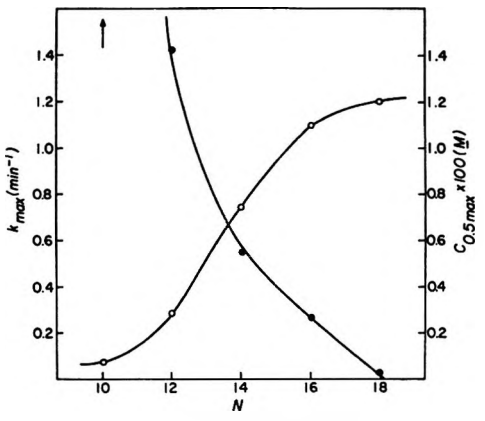

Figure 2.—Plots of the maximal first-order rate constants (left scale, open circles) and the surfactant concentrations required to reach half-maximal catalysis (right scale, closed circles) for the fading of crystal violet as a function of the chain length of *n*-alkyltrimethylammonium bromides.

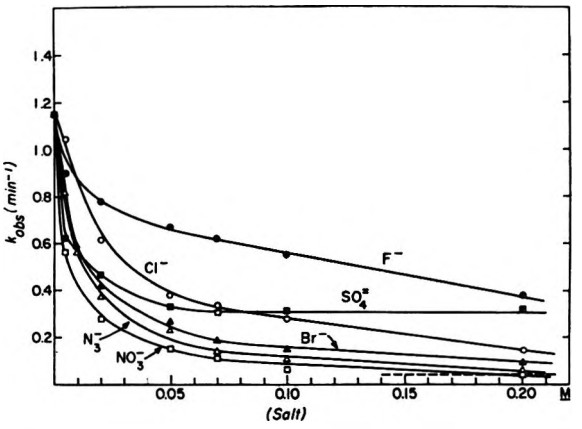

Figure 3.—First-order rate constants for the fading of crystal violet in aqueous solution containing 0.003 *M* sodium hydroxide and 0.01 *M* hexadecyltrimethylammonium bromide at 30° plotted as a function of the concentration of several anions. The dotted line in the lower right of the figure is the rate constant under these conditions in the absence of surfactant.

crystal violet in 0.003 *M* sodium hydroxide and 0.01 *M* hexadecyltrimethylammonium bromide are plotted as a function of the concentration of dodecyldimethyl phosphine oxide. This nonionic surfactant is a potent inhibitor; a concentration of 0.01 *M* nearly suffices to halve the observed catalysis.

Discussion

The catalysis of attack of hydroxide ion on crystal violet and other cationic dyes by cationic surfactants is almost certainly partially the result of electrostatic factors: one expects less electrostatic destabilization for the zwitterionic transition state than for the cationic ground state by the cationic micellar surface. In addition both medium effects and changes in hydrophobic interactions between substrate and micelle as the geometry of the dye changes in approaching the transition state may make significant contributions to the observed rate effects.

Perhaps the most striking aspect of the catalysis of the attack of hydroxide ion on crystal violet by *n*-alkyltrimethylammonium ions is the dependence of the catalysis on the length of the alkyl chain (Figures 1, 2; Table I). Increasingly effective catalysis with increasing surfactant hydrophobicity has been observed several times previously: for the attack of hydroxide ion on *p*-nitrophenyl hexanoate catalyzed by cationic surfactants,[7] the addition of cyanide ion to pyridinium ions catalyzed by cationic surfactants,[8] the hydrolysis of methyl orthobenzoate catalyzed by anionic surfactants,[9] the acid-catalyzed hydrolysis of alkyl sulfates,[10] and the attack of *N*-alkylhistidines on phenyl esters,[11] among other examples. The chain length dependence noted in the present case is perhaps the most striking yet observed.

The concentration of surfactant required to elicit maximal catalysis must principally reflect two things: the cmc for the surfactant and the equilibrium constants for absorption of the substrate onto the micelle. The values for the cmc of some of the surfactants used in this study follow:[2] C-12, 1.5×10^{-2} *M*; C-14, 3.5×10^{-3} *M*; C-16, 9.2×10^{-4} *M*. Clearly, these values partially account for the observed results. For example, catalysis by the C-18 surfactant is maximal at a concentration below the cmc of the other surfactants. Even when one corrects for the differences in cmc, however, it is quite clear that the equilibrium constant for absorption of crystal violet onto the micelles increases rapidly with increasing chain length.

Moreover, it appears that the crystal violet itself induces micelle formation. In each case, catalysis of the reaction is observed at concentrations of the surfactants below the critical micelle concentration. For example, catalysis by the C-12 surfactant is half-maximal by the time that the cmc is reached.

Not only is the special catalytic efficiency of the long-chain surfactants manifested in terms of the concentration of surfactant required to elicit maximum catalysis, but in terms of the maximal rate attained (Table I). Thus, even when the substrate is essentially completely associated with micelles, it is more reactive when the micelles are formed from more hydrophobic surfactants. However, the effect appears to be reaching the point of saturation (Figure 2). Similar observations have been observed in two previous cases.[8,11] This behavior may reflect an increasing electrostatic field at the micellar surface, a change in the medium effects at the micellar surface, or direct contributions of hydrophobic interactions to the activation energy.[11] It is difficult to distinguish between those possibilities in the present case. However, the rate effects appear to approach saturation under conditions in which the hydrophobic interactions, as judged by the shape of the rate–concentration profiles, are still increasing substantially. This suggests that the last of these possibilities may not be very important.

The surfactant-dependent fading of crystal violet is strongly inhibited by anions (Figure 3). The order of effectiveness of anions as inhibitors parallels the expected affinity of the anions for the micellar surface as judged from their relative abilities to lower the cmc and increase the aggregation numbers for these

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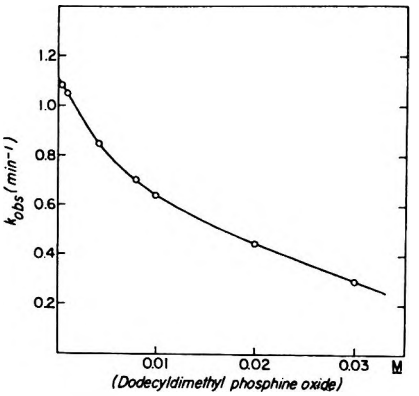

Figure 4.—First-order rate constants for the fading of crystal violet in aqueous solution containing 0.003 *M* sodium hydroxide and 0.01 *M* hexadecyltrimethylammonium bromide at 30° plotted as a function of the concentration of dodecyldimethyl phosphine oxide.

surfactants,[12-14] cause phase separation in solutions of cationic surfactants,[15] associate with strong base anion exchange resins,[16] ion pair with tetraalkylammonium ions in water,[17-19] inhibit carbonic anhydrase,[20] and associate with bilayers containing hexadecyltrimethylammonium bromide.[21] Consequently, this behavior must principally reflect a diminution in the electrostatic field at the micellar surface and, perhaps, specific competition with hydroxide ions for binding sites within the Stern layer. The salt effects observed almost exactly parallel those previously observed for the hydrolysis of *p*-nitrophenyl hexanoate in the presence of the same surfactants,[7] and are related to those observed for the addition of hydroxide ion to 2,4-dinitrochlorobenzene.[22]

The nonionic surfactant dodecyldimethyl phosphine oxide is also an excellent inhibitor for the surfactant-dependent reaction (Figure 4). A similar effect has been noted upon the addition of nonionic species to systems composed of methyl orthobenzoate and sodium dodecyl sulfate.[23] While a number of explanations are possible, the most obvious one is a diminution in the strength of the electrostatic field at the micelle surface due to dilution of the number of charged groups there.

Among earlier studies of surfactant-dependent reactions, this one is most closely associated with catalysis of addition of cyanide ion to pyridinium ions.[8,24] Both reactions involve addition of anions to positively charged substrates and both are subject to catalysis by cationic surfactants. Qualitatively the systems behave in quite a similar way. Quantitatively, however, some differences do appear. The addition of cyanide ion to pyridinium ions is more susceptible to catalysis, less susceptible to inhibition by salts, and more sensitive to the hydrophobicity of the surfactant in terms of maximal rate constants than is addition of hydroxide ion to crystal violet. These observations indicate that the two reactions are differentially influenced by the variety of forces that contribute to relative rates of reactions in purely aqueous solution and in aqueous solutions containing ionic surfactants.

Registry No.—Crystal violet, 14426-25-6; dodecyldimethyl phosphine oxide, 871-95-4.

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Secondary Valence Force Catalysis. XIV. The Effect of Several Surfactants on the Kinetics of Hydrolysis of a Series of 2-(Substituted phenoxy)tetrahydropyrans[1]

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Received August 12, 1971

Dilute aqueous solutions of sodium dodecyl sulfate and sodium hexadecyloxyethyl sulfate catalyze the hydrolysis of a series of 2-(substituted phenoxy)tetrahydropyrans. Rate increases from 15- to 50-fold are observed, depending on the nature of surfactant and substrate. Introduction of a methyl group at the 1 position of the hexadecyloxyethyl sulfate markedly reduces its catalytic effectiveness. Activation parameters for the surfactant-dependent reactions vary nonsystematically from those for the same reactions in 50% dioxane–water or in water. In contrast to the behavior of the anionic surfactants, dodecyltrimethylammonium propanesulfonate and dodecyldimethyl phosphine oxide inhibit the hydrolysis of these substrates.

A growing number of investigations during the last several years have established that a variety of organic reactions are subject to catalysis or inhibition in the presence of dilute aqueous solutions of surfactants.[3,4] Among these reactions are the hydrolysis of acetals and ortho esters[5-9] These studies have established that hydrolysis of acetals derived from benzaldehyde is subject to catalysis by sodium dodecyl sulfate and other anionic surfactants. A variety of aspects of the surfactant-catalyzed reactions have been probed. Because of the importance of acetal hydrolysis or, more exactly, glycoside hydrolysis, in biochemistry, it appears worthwhile to pursue these studies in more detail employing substrates which more closely resemble those found in living systems. For this purpose, we have chosen a series of phenoxytetrahydropyrans. Fife and his coworkers have examined the hydrolysis of these substrates in some detail in the absence of surfactants, providing the basis for an examination of the effect of surfactants.[10,11] The results of this investigation are detailed herein.

Experimental Section

Materials.—Sodium dodecyl sulfate was obtained commercially in a highly purified form. Sodium hexadecyloxyethyl sulfate and sodium hexadecyloxy-1-methylethyl sulfate were generously provided by the Eastern Regional Research Laboratory, Department of Agriculture, Philadelphia, Pa. Dodecyldimethylammonium propanesulfonate and dodecyldimethyl phosphine oxide are the generous gifts of the Miami Valley Laboratories of Procter and Gamble, Inc. 2-(Para-substituted phenoxy)tetrahydropyrans were prepared by simple modifications of the general method of Woods and Kramer.[10,12,13]

Kinetic measurements were made spectrophotometrically employing a Zeiss PMQ II spectrophotometer through which water from a thermostated bath was continuously circulated.[5-9] Except for the measurement of activation parameters, all rate constants were measured at 30°. First- and second-order rate constants were evaluated in the usual way. Excellent pseudo-first-order kinetics were observed throughout. Each first-order rate constant is the average of three determinations. Hydrogen ion activity was calculated from the known amount of added hydrochloric acid. Activation parameters were evaluated from the dependence of second-order rate constants on temperature employing the customary equations.

Results and Discussion

The results of Fife and his coworkers have established some of the basic aspects of the hydrolysis of 2-(para-substituted phenoxy)tetrahydropyrans.[10,11] The hydrolysis of each is subject to specific acid catalysis: the second-order rate constants in 50% dioxane–water are correlated by the Hammett σ constants with a value of ρ of -0.92. The *p*-nitro derivative also exhibits a pH-independent reaction, important above pH 4, and hydrolysis of this substrate is subject to general acid catalysis, $\alpha = 0.5$. Since our studies employing surfactants are best carried out in aqueous solution containing a minimum of organic solvent, we have repeated certain aspects of these studies using water as solvent at a temperature of 30°.

In accord with the earlier results, we observe that hydrolysis of each acetal is subject to specific acid catalysis in the pH range 1–3. Second-order rate constants for these reactions were evaluated at a minimum of five values of pH; the results are collected in Table I. Throughout, the pH was maintained with hydrochloric acid and no inorganic salts were added to maintain constant ionic strength since salts inhibit the surfactant-dependent reactions. The rate constants measured in water are about tenfold greater than those observed by Fife and Jao in 50% dioxane–water at the same temperature.[10] This difference agrees with that found for the same solvent change at 50° by Fife and Brod[11] and for related changes in solvent for hydrolysis of simple acetals.[14] The rate constants are well correlated by the σ constants with a value of ρ of -0.99, nearly the same as that observed in the partially organic solvent.

Hydrolysis of 2-(*p*-nitrophenoxy)tetrahydropyran in aqueous solution at 30° is subject to general acid cataly-

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(2) Career Development Awardee of the National Institutes of Health, Grant K03 GM 10248. To whom correspondence should be addressed at Indiana University.

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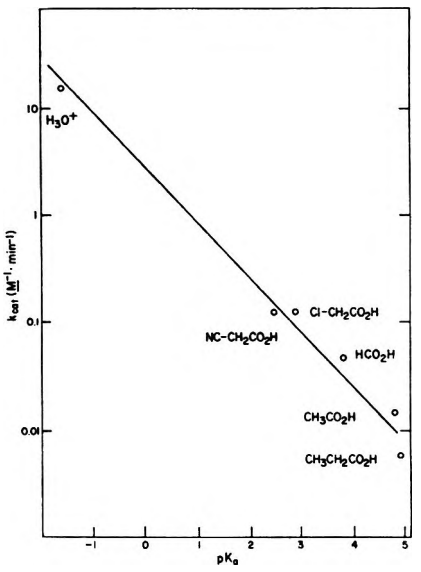

Figure 1.—Catalytic constants of several acids for the hydrolysis of 2-(*p*-nitrophenoxy)tetrahydropyran in aqueous solution at 30° plotted against the values of pK_a of the acids. The slope of the indicated line is −0.50.

TABLE I

KINETICS OF HYDROLYSIS OF 2-(PARA-SUBSTITUTED PHENOXY)TETRAHYDROPYRANS IN THE PRESENCE OF AQUEOUS SOLUTIONS OF SODIUM DODECYL SULFATE AT 30°

Substituent	k_0,[a] M^{-1} min^{-1}	k_{max},[b] M^{-1} min^{-1}	k_{max}/k_0	(SDS)$_{max}$,[c] M
p-NO_2	15.1	261	17	0.020
p-Cl	45	2100	47	0.015
H	87	2400	32	0.025
p-CH_3	138	2900	21	0.015
p-OCH_3	159	2400	15	0.020

[a] Second-order rate constant in aqueous solution in the absence of surfactant. [b] Second-order rate constants in the presence of the optimal concentration of sodium dodecyl sulfate. [c] Concentration of sodium dodecyl sulfate at which maximal catalysis is observed.

sis by carboxylic acids. Catalytic constants were evaluated for five such acids over a total buffer concentration range of 0.1–1.0 *M*. In Figure 1, these catalytic constants, and that for the hydrated proton, are plotted against the appropriate values of pK_a. A satisfactory straight line is obtained, $\alpha = 0.5$, in agreement with the value obtained in 50% dioxane–water.[11] These results establish that the course of hydrolysis of 2-(substituted phenoxy)tetrahydropyrans in water and 50% dioxane–water is similar. The observation of a similar value of ρ and α, for the hydrolysis of the *p*-nitro derivative, serves to support this point of view.[10,11]

Hydrolysis of each of the substituted acetals is subject to catalysis by dilute aqueous solutions of sodium dodecyl sulfate. In Figure 2, second-order rate constants for these reactions are plotted against the concentration of this surfactant. Although the curves differ in detail, each exhibits the same general features: catalysis up to some optimal concentration followed by inhibition at increasing surfactant concentrations. A similar behavior has previously been observed for catalysis of the hydrolysis of benzaldehyde diethyl acetals and ethyl orthobenzoates by this surfactant.[5–8] Catalysis observed in the present case is not surprising,

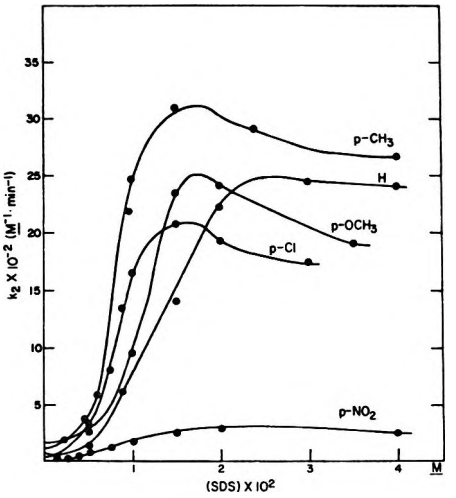

Figure 2.—Second-order rate constants for the hydrolysis of a series of 2-(para-substituted phenoxy)tetrahydropyrans in water at 30° plotted against the concentration of sodium dodecyl sulfate.

since the studies of Fife and coworkers have established that these substrates hydrolyze *via* a transition state in which carbonium ion formation occurs.[10,11] Consequently, it would appear that the major part of the catalysis is the result of electrostatic stabilization of the cationic transition state compared to the ground state, the uncharged acetals associated with the micelles and the hydrated proton in the bulk phase. Medium effects and hydrophobic interactions may, of course, contribute to the overall rate of the catalyzed reaction. The maximal rate constant for each substrate and the corresponding concentration of sodium dodecyl sulfate are included in Table I. The maximal rate constants are largely independent of the nature of the polar substituent, except in the case of the *p*-nitro derivative, which is much less reactive than the others.

Hydrolysis of the 2-(substituted phenoxy)tetrahydropyrans is also subject to catalysis by the anionic surfactant sodium hexadecyloxyethyl sulfate; the pertinent data are collected in Table II. The degree

TABLE II

RATE CONSTANTS FOR THE HYDROLYSIS OF 2-(PARA-SUBSTITUTED PHENOXY)TETRAHYDROPYRANS IN THE PRESENCE OF AQUEOUS SOLUTIONS OF HEXADECYLOXYETHYL SULFATE AT 30°

Substituent	k_0,[a] M^{-1} min^{-1}	k_{max},[b] M^{-1} min^{-1}	k_{max}/k_0	(Sur)$_{max}$,[c] M
p-nitro	15.1	562	37	0.005
p-chloro	45	1870	42	0.01
p-methoxy	159	2650	17	0.01

[a] Second-order rate constant in the absence of surfactant. [b] Second-order rate constant at the optimal concentration of surfactant. [c] Surfactant concentration at which optimal catalysis is observed.

of catalysis observed is about the same as that elicited by sodium dodecyl sulfate except in the case of the *p*-nitro substrate, which is more sensitive to catalysis by hexadecyloxyethyl sulfate. Note that the latter surfactant is maximally effective at significantly lower concentrations than is sodium dodecyl sulfate.

Analysis of the data in Tables I and II suggests some regularity in terms of a relation between sub-

strate structure and sensitivity to catalysis. In the case of both sodium dodecyl sulfate and hexadecyloxyethyl sulfate, the extent of catalysis, as judged by the ratio of rate constants in the presence and in the absence of surfactant, increases with increasing electron withdrawal in the polar substituent. This conclusion must be regarded as tentative, since (i) it depends on the use of k_{max}/k_0 values as a measure of sensitivity to catalysis which, although the most reasonable measure, is not the only possible one; and (ii) the correlation for catalysis by hexadecyloxyethyl sulfate is derived from just two points. Moreover, the *p*-nitro substrate does not follow this pattern, being less susceptible to catalysis than would be expected on the basis of the behavior of the other substrates. This may reflect one of two possible causes. First, it has been established that, of the substrates studied here, only that derived from *p*-nitrophenol exhibits a large pH-independent reaction in the absence of surfactant and, moreover, the hydrolysis of only this substrate is markedly subject to general acid catalysis.[10,11] Hence, a mechanistic distinction can be drawn between the hydrolysis of the *p*-nitro substrate and the others: substrate protonation is more important in determining the overall rate of acetal hydrolysis for the *p*-nitro compound than for the other acetals. In light of past studies of acetal and ortho ester hydrolysis,[13,14] this is a reasonable interpretation. Specifically, simple acetals hydrolyze *via* rate-determining carbonium ion formation preceded by rapid and reversible substrate protonation, whereas hydrolysis of the less basic ortho esters occurs with concerted proton transfer and carbonium ion formation in the transition state. Clearly, with less basic acetals, one expects their behavior to eventually change to that of ortho esters. The *p*-nitro substrate is, of course, the least basic one studied here and its behavior does appear to be most nearly like that of an ortho ester. The other possibility for the apparent aberrant behavior of the *p*-nitro compound lies in the disposition of the substrate with respect to the micellar surface. Should this substrate occupy a position distinct from that for the other acetals, one would expect its rate of hydrolysis to be altered. While this explanation is certainly possible, it is difficult to examine experimentally. In any event, let us analyze the results assuming that, for whatever reason, the *p*-nitro compound does behave unusually.

Previous work with both benzaldehyde diethyl acetals and ethyl orthobenzoates has established that substrate sensitivity to catalysis by anionic surfactants increases with increasing electron *donation* of polar substituents.[7,8] This result is apparently the opposite of that observed here. However, all these observations are, in fact, nicely concordant. Recent studies of secondary deuterium isotope effects for acetal hydrolysis reveal that the transition state is reached progressively earlier with increasing electron *donation* from polar substituents for hydrolysis of benzaldehyde acetals and with increasing electron *withdrawal* by polar substituents for hydrolysis of tetrahydropyran acetals.[13] Hence, the important factor in determining susceptibility to electrostatic catalysis appears to be the extent of progress along the reaction coordinate at the time that the transition state is reached. This is reasonable, since increasing progress leads to increasing dispersal of charge and a lessened necessity for electrostatic stabilization.

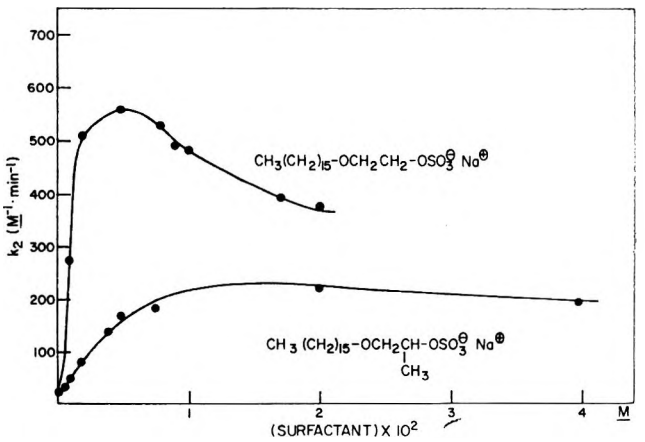

Figure 3.—Second-order rate constants for the hydrolysis of 2-(*p*-nitrophenoxy)tetrahydropyran in water at 30° plotted against the concentration of the indicated anionic surfactants.

Catalysis of hydrolysis of the tetrahydropyran acetals by anionic surfactants is sensitive to the structure of the surfactant. In Figure 3, second-order rate constants for hydrolysis of 2-(*p*-nitrophenoxy)tetrahydropyran are plotted as a function of the concentration of hexadecyloxyethyl sulfate and 2-hexadecyloxy-1-methylethyl sulfate. Clearly, the minor structural modification has substantially changed the catalytic effectiveness of the surfactant, both in terms of the concentration necessary to elicit optimal catalysis and the maximal rate constant obtained.

A small change in surfactant structure can introduce changes in the surface properties of the micelle which are markedly reflected in the reactivity of adsorbed molecules, in agreement with results of an extensive earlier survey.[7] A comparison between sodium dodecyl sulfate and hexadecyloxyethyl sulfate as catalysts for hydrolysis of the tetrahydropyran acetals reveals that the maximal rate increases achieved are not very different. On the other hand, these maximal changes are attained at much lower concentrations in the case of the latter surfactant compared to the former. This must reflect a difference in equilibrium constant for formation of micelle–substrate complexes in the two cases.

Activation parameters for hydrolysis of the 2-(para-substituted phenoxy)tetrahydropyrans in the presence and absence of anionic surfactants were evaluated from second-order rate constants measured at four temperatures in the range 30–60°. In all cases, the data generated excellent Arrhenius plots. The activation parameters, together with some taken from the work of Fife and Brod,[11] are collected in Table III. The results generate a curious pattern; note, for example, the discordant effects between water and 50% aqueous dioxane for the hydrogen and nitro derivatives. Parts of the observed differences may, of course, be attributed to experimental error. The effects of the anionic surfactants fall into two categories: (i) modest change in enthalpy and entropy of activation making it difficult to judge the source of the surfactant catalysis (methoxy and hydrogen substrates); and (ii) sharply reduced enthalpy of activation coupled with a substantially more negative entropy of activation (chloro and nitro substrates). The latter type of

TABLE III

ACTIVATION PARAMETERS FOR HYDROLYSIS OF 2-(PARA-SUBSTITUTED PHENOXY)TETRAHYDROPYRANS IN THE ABSENCE AND PRESENCE OF ANIONIC SURFACTANTS

Substituent	Solvent	ΔH, kcal/mol	ΔS, eu
Methoxy	Water	12.8	−15.1
	0.02 *M* SDS[a]	11.7	−12.8
Hydrogen	Water	14.3	−11.0
	0.025 *M* SDS[a]	12.1	−11.7
	50% Aqueous dioxane[b]	17.9	−3.0
Chloro	Water	17.3	−2.5
	0.015 *M* SDS[a]	12.1	−12.0
Nitro	Water	17.8	−2.0
	0.02 *M* SDS[a]	13.9	−9.4
	0.005 *M* HDOS[c]	13.4	−9.8
	50% Aqueous dioxane[b]	17.7	−7.6

[a] Sodium dodecyl sulfate, present in the concentration necessary to elicit optimal catalysis. [b] Data from ref 11. [c] Hexadecyloxyethyl sulfate.

TABLE IV

RATE CONSTANTS FOR THE HYDROLYSIS OF A SERIES OF 2-(SUBSTITUTED PHENOXY)TETRAHYDROPYRANS IN THE PRESENCE OF 0.02 *M* SOLUTIONS OF A ZWITTERIONIC AND A NONIONIC SURFACTANT AT 30°

Surfactant	Substituent	k,[a] M^{-1} min^{-1}	k_0/k[b]
Dodecyldimethylammonium propanesulfonate	*p*-NO_2	3.0	5.0
	p-Cl	6.0	7.5
	H	27	3.2
	p-CH_3	37	3.8
	p-OCH_3	49	3.2
Dodecyldimethyl phosphine oxide	*p*-NO_2	2.5	
	H	20	

[a] Second-order rate constant in the presence of 0.02 *M* of the indicated surfactant. [b] Ratio of second-order rate constants for the reaction in the absence and presence of 0.02 *M* surfactant.

result has earlier been observed for benzaldehyde diethyl acetal hydrolysis in the presence of sodium dodecyl sulfate for which a very large favorable enthalpic change is largely compensated by a large unfavorable enthalpic change is largely compensated by a large unfavorable entropic one.[6] It seems likely that even more complex results would be obtained by examining the activation parameters as a function of surfactant concentration.

In contrast with the results observed in the presence of anionic surfactants, both a zwitterionic surfactant and a nonionic surfactant inhibit hydrolysis of the acetals. In Table IV, rate constants for hydrolysis of the series of acetals are collected as a function of the concentration of dimethyldodecylammonium propanesulfonate and dodecyldimethyl phosphine oxide. The two surfactants are approximately equally effective as inhibitors for these reactions.

Zwitterionic surfactants have been little studied in the past, although the one used here has been demonstrated to be an excellent catalyst for the addition of cyanide ion to pyridinium ions.[15] Whatever the source of the rate effects is, they have quite different consequences in the case of these two reactions. There have been several studies of reaction kinetics in the presence of nonionic surfactants. A related study involving hydrolysis of methyl orthobenzoate also revealed, as in the present case, inhibition by nonionic surfactants.[7] These results most likely reflect a medium effect on the hydrolysis rate. Several studies have established that hydrolysis of acetals and ortho esters is retarded in partially organic solvents.[14] However, there have been various examples of catalysis by nonionic surfactants as well. For example, the hydrolysis of certain sulfate esters.[16,17] is subject to substantial catalysis by such surfactants, as are some aromatic nucleophilic addition reactions,[9,18] These results must reflect a complicated pattern of medium effects for the various reactions.

Registry No.—2-(*p*-NO_2 phenoxy)tetrahydropyran, 20443-91-8; 2-(*p*-Cl phenoxy)tetrahydropyran, 20443-90-7; 2-phenoxytetrahydropyran, 4203-50-3; 2-(*p*-CH_3 phenoxy)tetrahydropyran, 13481-09-9; 2-(*p*-OCH_3 phenoxy)tetrahydropyran, 20443-88-3; SDS, 33143-35-0; HDOS, 14858-54-9.

(15) J. Baumrucker, M. Calzadilla, M. Centeno, G. Lehrmann, P. Lindquist, M. Price, B. Sears, D. Dunham, and E. H. Cordes, *J. Phys. Chem.*, **74**, 1152 (1970).

(16) T. H. Baxter and H. B. Kostenbauder, *J. Pharm. Sci.*, **58**, 33 (1969).

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(18) C. A. Bunton and L. Robinson, *J. Amer. Chem. Soc.*, **92**, 356 (1970).

Synthesis, Structure, and Reactions of a Benziodolium Cation

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The 3-butyl-2-phenylbenziodolium cation has been synthesized by the low-temperature reaction of *trans*-chlorovinyliodoso dichloride and *trans*-1-lithio-2-*o*-lithiophenyl-1-phenyl-1-hexene. The iodonium ion underwent attack by nucleophiles (Cl^-, I^-, and CH_3O^-) exclusively at the 2 position to give a mixture of *cis*- and *trans*-stilbenes. Reaction of the iodonium ion with water in the absence of oxygen gave 2-*o*-iodophenyl-1-phenyl-1-hexanone, which has been independently synthesized by hydrolysis of *trans*-1-iodo-2-*o*-iodophenyl-1-phenyl-1-hexene. Reaction of the iodonium ion with oxygen in water gave 2-hydroperoxy-2-*o*-iodophenyl-1-phenyl-1-hexanone, which was thermally cleaved to benzoic acid and 1-*o*-iodophenyl-1-pentanone. The latter compound has been independently synthesized by addition of butylmagnesium chloride to *o*-iodobenzaldehyde followed by oxidation of the resulting alcohol with the Jones reagent. The α-hydroperoxy ketone was reduced by sodium borohydride or sodium iodide to 2-hydroxy-2-*o*-iodophenyl-1-phenyl-1-hexanone, which was oxidatively cleaved with lead tetraacetate in benzene to benzoic acid and 1-*o*-iodophenyl-1-pentanone. Mechanisms of some of these transformations are discussed. The crystal structures of 3-butyl-2-phenylbenziodolium chloride and dibenziodolium tetrafluoroborate are reported. Correlations between structure and reactivity of these compounds are discussed. Numerous attempts to form an iodolium cation finally gave, by the reaction of 1,4-dilithio-1,2,3,4-tetraphenyl-1,3-butadiene with *trans*-chlorovinyliodoso dichloride, a low yield of 2,3,4,5-tetraphenyliodolium chloride.

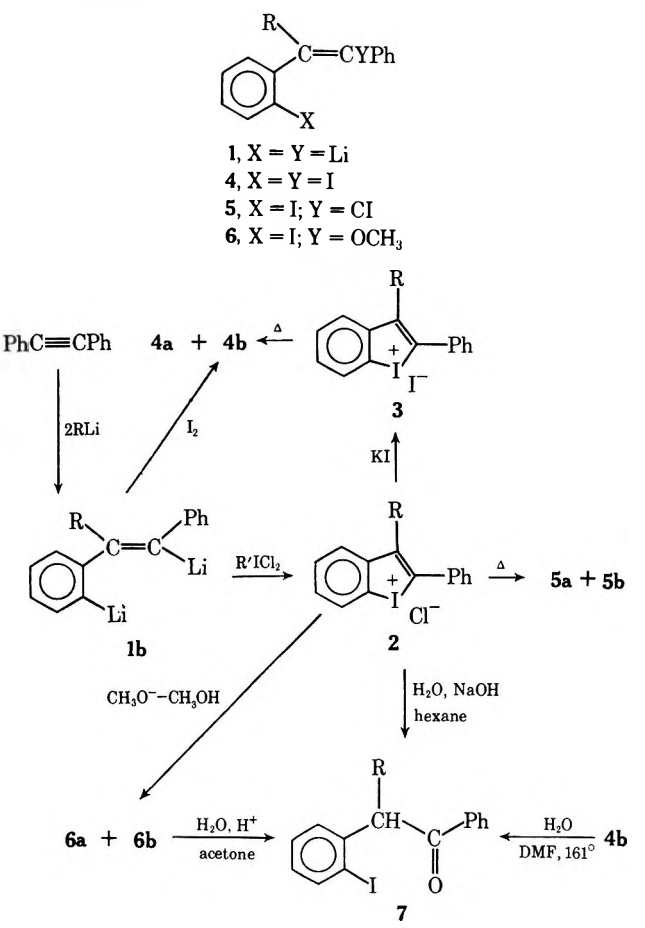
In previous papers[4] there has been reported a new route to symmetrical diaryliodonium salts *via* the low-temperature reaction of *trans*-chlorovinyliodoso dichloride with 2 equiv of aryllithium reagent. Fair to excellent yields of the diphenyl-, di-*p*-tolyl-, di-1-naphthyl-, di-2-naphthyl-, di-9-anthryl-, 2,2′-biphenylene-, di-2-thienyl-, and di-2-furanyliodonium salts were obtained. Attempts to form iodonium salts with one or two bonds to sp^3 carbon were unsuccessful. We have now extended the synthesis to yield an interesting heterocyclic arylvinyliodonium salt and have studied its ring-opening reactions. We have determined its crystal structure and also, for comparison, that of dibenziodolium (2,2′-biphenyleneiodonium) tetrafluoroborate.

Results

Mulvaney and coworkers[5] have reported the addition to and metalation of diphenylacetylene with *n*-butyllithium in ether to give *trans*-1-lithio-2-*o*-lithiophenyl-1-phenyl-1-hexene (**1b**). The low-temperature reaction of **1b** with *trans*-chlorovinyliodoso dichloride in ether gave in 26% yield 3-butyl-2-phenylbenziodolium chloride (**2**), converted by metathesis to 3-butyl-2-phenylbenziodolium iodide (**3**) (Scheme I). The nmr spectrum of **2** in CD_2Cl_2 shows a downfield shift of the 8 proton expected of protons ortho to the iodonium group.[6] This proton appears as a doublet at τ 1.05, with further splitting evident. By comparison, the proton ortho to uncharged iodine in *trans*-1-iodo-2-*o*-iodophenyl-1-phenyl-1-hexene (**4b**), synthesized by reaction of **1b** with iodine, appears at τ 2.14. The C=C ir stretching bands in both **2** and **3** are very weak or absent as expected for tetrasubstituted olefins.[7]

SCHEME I

SYNTHESIS AND REACTIONS OF BENZIODOLIUM SALTS[a]



R = *n*-butyl

R′ = *trans*-2-chlorovinyl

[a] In text, cis isomers are a and trans isomers are b.

Reactions of Salts 2 and 3.—Decomposition of **2** at its melting point gave an equimolar mixture of *cis*- and *trans*-stilbenes. Decomposition of **3** gave 42% of the *cis*- and 58% of the *trans*-stilbene. The mass spectrum of the melt from **3** was identical with that from **4b**, apparently indicating equilibrium of the *cis*- and *trans*-stilbenes upon electron impact. These

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(3) Taken in part from the dissertation of H. Jaffe, submitted to the Faculty of the Polytechnic Institute of Brooklyn, in partial fulfillment of the requirements for the degree of Ph.D., 1971; NDEA Fellow, 1966–1969.

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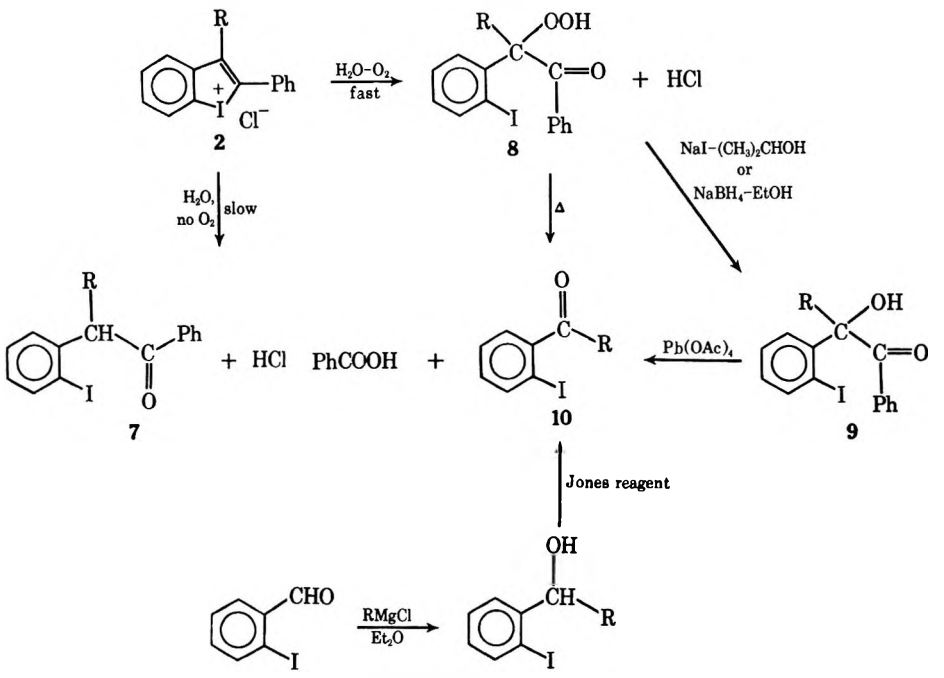
SCHEME II

OXIDATIVE HYDROLYSIS OF A BENZIODOLIUM SALT



R = *n*-butyl

halogenated stilbenes display M and M − halogen peaks.

Reaction of **2** with sodium methoxide in anhydrous methanol gave an equimolar mixture of *cis*- and *trans*-2-iodophenyl-1-methoxy-1-phenyl-1-hexene (**6a** and **6b**), which was separated by glpc. (The mass spectra of these isomers are identical and display molecular ions.) The mixture of vinyl ethers undergoes acid-catalyzed hydrolysis to 2-*o*-iodophenyl-1-phenyl-1-hexanone (**7**), independently synthesized by high-temperature hydrolysis of diiodo compound **4b**. Reaction of **2** with sodium hydroxide gives ketone **7**, apparently by tautomerization of the first-formed enols.

Reaction of Iodonium Salt 2 with Water and Oxygen.—When a suspension of **2** is stirred in distilled water at room temperature in the presence of oxygen, a novel oxidative hydrolysis occurs rapidly (*ca.* 1–2 hr) to give 2-hydroxyperoxy-2-*o*-iodophenyl-1-phenyl-1-hexanone (**8**). The uptake of oxygen is almost quantitative as measured by the Warburg respirometer. Under the same conditions but in the absence of oxygen a very slow (*ca.* 1 month) hydrolysis to ketone **7** occurs in almost quantitative yield. The structure of α-hydroperoxy ketone **8** is based on microanalysis, ir and nmr spectroscopy, reduction to 2-hydroxy-2-*o*-iodophenyl-1-phenyl-1-hexanone (**9**), and thermal cleavage to benzoic acid and 1-iodophenyl-1-pentanone (**10**) (Scheme II). The ir spectrum of **8** displays on OH band at 3300 and a C=O band at 1668 cm^{-1}. The nmr of **8** in acetone-d_6 displays a one-proton singlet (D_2O exchangeable) at τ −1.13 for the strongly deshielded hydroperoxy proton.[8]

Brief exposure to sodium borohydride in ethanol at room temperature reduced **8** to hydroxy ketone **9**. Neither the carbonyl group nor the iodine[9] was affected under these conditions. Treatment of **8** with solium iodide in acetone also gave **9**.

Hydroxy ketone **9** is oxidatively cleaved with lead tetraacetate to benzoic acid and ketone **10**. The ir spectrum of **9** is almost identical with that of **8** except for a slight shift of the C=O band to 1662 cm^{-1} and a larger shift of the OH band to 3450 cm^{-1}. The nmr spectrum in $CDCl_3$ is similar to that of **8** except for a dramatic upfield shift of the OH peak to a one-proton, D_2O-exchangeable, singlet at τ 5.17. The mass spectrum displays major peaks at *m/e* 289, 231, 203, 105, 77, and 76. The molecular ion at 394 was not observed. We propose α cleavage as the major fragmentation pathway to account for these peaks. By comparison, the mass spectrum of benzoin displays major peaks at *m/e* 107 ($PhCHOH^+$, α cleavage), 105 ($PhC{=}O^+$, α cleavage), and 77 (Ph^+).

Ketone **9** is cleaved by lead tetraacetate in refluxing benzene to benzoic acid and ketone **10**, synthesized independently by Jones reagent oxidation of the alcohol resulting from addition of *n*-butylmagnesium chloride to *o*-iodobenzaldehyde.

Crystal Structures of the Dibenziodolium and Benziodolium Salts.—In Figure 1 the molecular parameters of dibenziodolium tetrafluoroborate are reported. The standard deviations of the bond lengths and angles are 0.015 Å and 0.2°, respectively. The molecule is planar; deviations from the mean molecular plane are less than 0.03 Å. The molecule has an almost exact C_2 symmetry; this symmetry is even extended to the mode of thermal vibrations of the atoms (see Figure 1a). The bond angle C–I–C of 83° is appreciably smaller than the corresponding angle in the structure of di-

(8) Hydroperoxy protons characteristically show low-field nmr absorption: S. Fujiwara, M. Katayama, and S. Kamio, *Bull. Chem. Soc. Jap.*, **32**, 657 (1959).

(9) The reduction of aryl iodides by lithium aluminum hydride and sodium borohydride has recently been reported: H. C. Brown and S. Krishnamurthy, *J. Org. Chem.*, **34**, 3918 (1969); H. M. Bell, C. W. Vanderslice, and A. Spehar, *ibid.*, **34**, 3923 (1969).

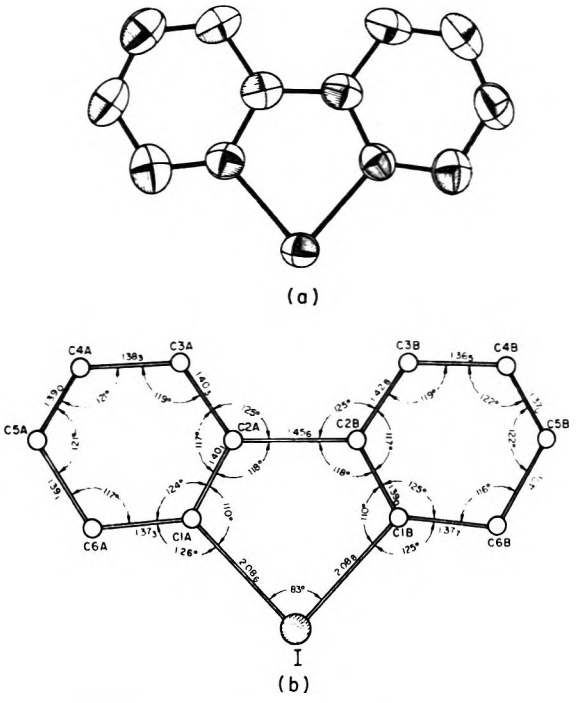
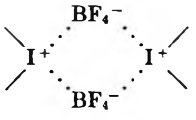


Figure 1.—The dibenziodolium ion: (a) modes of thermal atomic vibrations; (b) molecular conformational parameters.

phenyliodonium chloride[10] (93°). The bond lengths C–I^+ are almost the same as the normal C–I bonds (2.10–2.15 Å). Relevant are the distortions from 120° of some bond angles of the phenyl rings (up 5–6°). Dibenziodolium ions are held together pairwise by two BF_4^- ions. Groups with almost identical distances $I^+\cdots BF_4^-$ (3.65 Å) are formed in this way around inversion centers.[11]



In Figure 2 the molecular parameters of 3-butyl-2-phenylbenziodolium chloride (2) are reported. The standard deviations of these parameters are the same as in 11. Except for the phenyl group and the butyl group the molecule is planar within the standard deviations. The phenyl group bonded to C7 forms an angle of 52° with the plane of the benziodolium moiety. Also the butyl group has a nearly planar full-extended conformation and its mean plane forms an angle of 76° with the plane of the benziodololium moiety. The bond length C7–C8 (1.34 Å) shows the olefinic character of this bond. In spite of the different environment on the two sides of I^+ in 2 the two C1 bond lengths are identical within the standard deviations.

In 3-butyl-2-phenylbenziodolium chloride the two nonequivalent $I^+\cdots Cl^-$ distances are quite different (3.22 and 2.95 Å) as in the case of diphenyliodonium

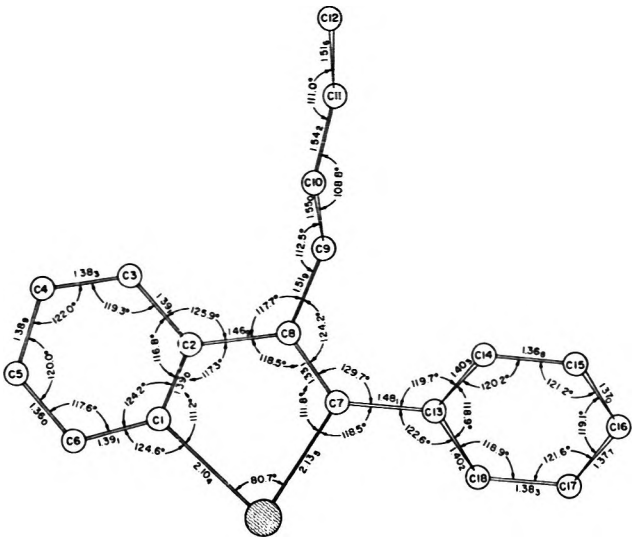


Figure 2.—Molecular conformation parameters of the 3-butyl-2-phenylbenziodolium ion.

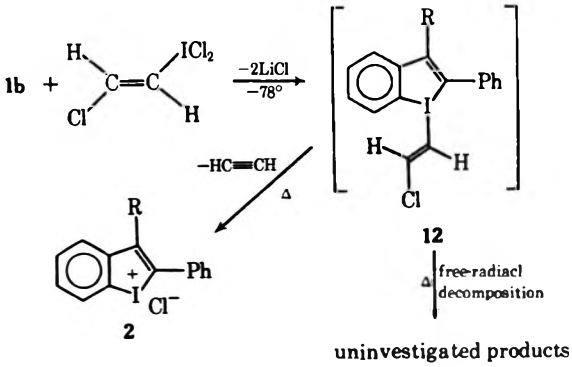
chloride,[10] indicating a different character of the bonds.[11] These are the first crystal structures of heterocyclic aryliodolium salts reported so far.

Discussion

The synthesis of 2 from the reaction of *trans*-chlorovinyliodoso dichloride and dilithium compound 1b probably proceeds *via* the trivalent organoiodine intermediate 12. Analogous intermediates have been proposed in the synthesis of diaryliodonium salts from the reaction of *trans*-chlorovinyliodoso dichloride and aryllithium reagents.[4] Upon warming to room temperature 12 is believed to undergo two modes of decomposition.[4] Ionic elimination gives acetylene and the desired product, iodonium salt 2. The major mode of decomposition is apparently a free-radical cleavage of the bonds to iodine yielding a complex mixture of products (Scheme III).

SCHEME III

DECOMPOSITION OF INTERMEDIATE 12



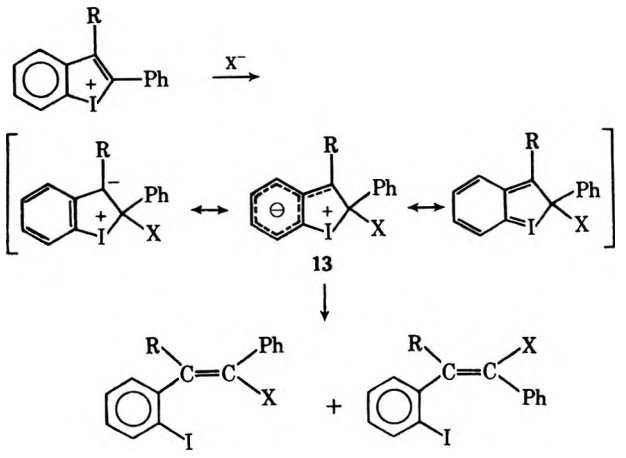
We have seen that 3-butyl-2-phenylbenziodolium cation undergoes attack by nucleophiles exclusively at the 2 position to give almost equal amounts of *cis*- and *trans*-stilbenes. In no case was any product of attack at the 9 position observed. The following mechanism (Scheme IV) might best account for these results. Attack of the nucleophile at the 2 position from above or below the plane of the ring can occur with

(10) T. L. Khotsyanova, *Dokl. Akad. Nauk SSSR*, **110**, 7 (1956) [*Chem. Abstr.*, **52**, 4282*h* (1958)]; T. L. Khatsyanova and Yu. T. Struckhov, *Zh. Fiz. Khim.*, **26**, 644, 669 (1952) [*Chem. Abstr.*, **49**, 6684*e* (1952)].

(11) The tables of observed and calculated structure factors, the positional and thermal parameters and crystallographic projections of compounds **2** and **11** will appear immediately following this article in the microfilm edition of this volume of the journal. Single copies may be obtained from the Reprint Department, ACS Publications, 1155 Sixteenth St., N.W., Washington, D. C. 20036, by referring to author, title of article, volume, and page number. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche.

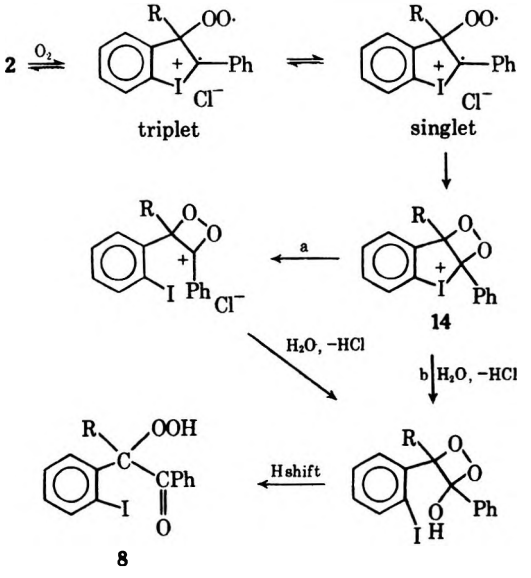
SCHEME IV

REACTION OF THE 3-BUTYL-2-PHENYLBENZIODOLIUM ION WITH NUCLEOPHILES



SCHEME V

REACTION OF THE BENZIODOLIUM ION WITH OXYGEN



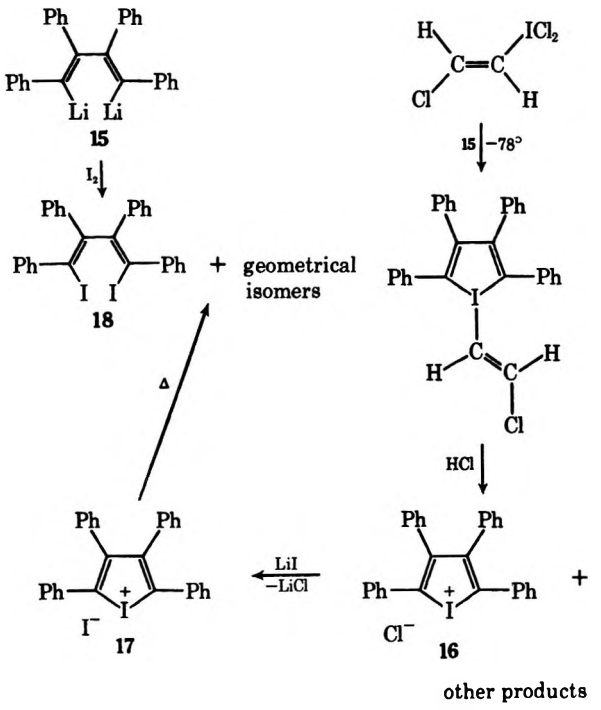
equal probability to give a dipolar intermediate (**13**). Delocalization of the negative charge into the aromatic ring and into the d or f orbitals of iodine might help stabilize the intermediate. E1 elimination of the $-I^{+}-$ group would give equal amounts of the cis and trans isomers. By contrast, attack at the 9 position would involve disruption of the aromatic system, while backside displacement of the $-I^{+}-$ group would be expected to give only the *cis*-stilbene. The proposed mechanism is in accord with the X-ray results which show no electronic interaction between the α-vinyl group and any of the aromatic groups.

The formation of α-hydroperoxy ketone **8** from **2** might involve addition of triplet oxygen to the double bond to give a cyclic peroxide intermediate (**14**, Scheme V). In this addition, the iodine might facilitate conversion of an initially formed 1,4 diradical with spins unpaired to one with spins paired[12] which then closes

(12) Transitions between the singlet and triplet states are facilitated by a heavy atom, especially if the electron is located in an orbital close to the heavy atom: N. J. Turro, "Molecular Photochemistry," W. A. Benjamin, New York, N. Y., 1967, p 50.

SCHEME VI

SYNTHESIS AND REACTIONS OF TETRAPHENYLIODOLIUM SALTS



to **14**. The latter, which contains a sp^3 carbon bonded to a positive iodine,[13] would be expected to undergo SN1-like heterolysis (pathway a) or, less likely, SN2-like displacement of the $-I^{+}-$ group by water (pathway b) to give intermediates which rearrange to the observed product. The very slow rate of formation of ketone **7** in the absence of oxygen excludes any mechanism for the formation of **8** involving addition of oxygen to an intermediate enol.[14]

The thermal decomposition of **8** to benzoic acid and ketone **10** is characteristic of α-hydroperoxy ketones.[15] Pritzkow[16a] has proposed that such cleavages are acid catalyzed and proceed by a mechanism similar to that involved in the conversion of cumyl hydroperoxide to phenol and acetone.[16b]

Tetraphenyliodolium Salts.—The procedure used to form the benziodolium chloride (**2**) has been adapted, by the use of 1,4-dilithio-1,2,3,4-tetraphenyl-1,3-butadiene (**15**) as the dilithio reagent, to give in low yield 2,3,4,5-tetraphenyliodolium chloride (**16**), the first salt having an iodolium cation without a fused ring (Scheme VI). The tetraphenyliodolium chloride and iodide reacted at the melting point to give 1-halo-4-iodo-1,2,3,4-tetraphenyl-1,3-butadienes, whose mass spectra showed peaks at M^+, $M^+ - X$, $M^+ - I$, $M^+ - X - I$, and ions related to 1,2,3-triphenylnaphthalene and 1,2-diphenylnaphthalene.

(13) The only aliphatic iodonium salt to be isolated, dimethyliodonium hexafluoroantimonate, undergoes immediate hydrolysis when exposed to moisture: G. A. Olah and J. R. Demember, *J. Amer. Chem. Soc.*, **92**, 718 (1970).

(14) Addition of oxygen to stabilized enols is known to give α-hydroperoxy ketones: for example, R. C. Fuson and H. L. Jackson, *ibid.*, **72**, 1637 (1950).

(15) For example, D. B. Sharp, L. W. Patton, and S. E. Whitcomb, *ibid.*, **73**, 5600 (1951); E. P. Kohler, M. Tishler, and H. Potter, *ibid.*, **57**, 2517 (1935).

(16) (a) W. Pritzkow, *Chem. Ber.*, **88**, 572 (1954). (b) J. D. Roberts and M. C. Caserio, "Basic Principles of Organic Chemistry," W. A. Benjamin, New York, N. Y., 1964, p 432.

A comparison between the molecular structures of **11** and **2** shows that the nature of the groups bonded to the iodolium ring do not affect to an appreciable extent the conformation of the iodonium group C–I^+–C. The different reactivity of the bonds C1–I and C7–I in 3-butyl-2-phenylbenziodolium ion appears to be due simply to the different chemical environments on the two sides of I^+.

Experimental Section

Analyses were performed by Galbraith Laboratories, Knoxville, Tenn., or by Chermalytics, Inc., Tempe, Ariz. Gas chromatography was done on 6- or 10-ft columns packed respectively with 20% OV1 or 4% SE-30 on Chromosorb W with an Aerograph 1520 gas chromatograph or on 2-m columns packed with 1.5% SE-30 on Chromosorb W with a Perkin-Elmer 154 vapor fractometer. Peak areas were measured by planimetry. Melting points were taken in capillary tubes on a Thomas-Hoover apparatus. Melting and boiling points are uncorrected. Infrared spectra were taken on Perkin-Elmer 521 and 337 grating infrared spectrophotometers. Nmr spectra were taken on a Varian Associates Model A-60 instrument. Chemical shifts are reported in parts per million (τ) downfield from tetramethylsilane. Mass spectra were taken at 80 eV on a Hitachi Perkin-Elmer RMU-6E instrument. Oxygen absorption was measured by a mercury-calibrated Warburg respirometer corrected with a thermobarometer.

Starting Materials.—Iodine trichloride was purchased from City Chemical Co. or Alpha Inorganics, Inc. Organolithium compounds were purchased from Alpha Inorganics, Inc., and standardized before use by the method of Gilman and Cartledge.[17] *n*-Butylmagnesium chloride in THF was purchased from Alpha Inorganics, Inc. Lithium wire was purchased from Lithium Corp. of America. Diphenylacetylene was synthesized by the method of Cope, Smith, and Cotter[18] or purchased from Aldrich Chemical Co. Acetylene and prepurified argon were supplied by Matheson. The anhydrous ether was analytical grade as supplied by Mallinchrodt; only cans opened immediately before use and sealed with a septum were used. Methanol was dried by distillation from magnesium and stored over molecular sieves. Benzene and toluene were dried by distillation and stored over molecular sieves.

***trans*-Chlorovinyliodoso Dichloride.**—The procedure of Beringer and Nathan[4] was modified as follows. Through a solution of 100 g (0.427 mol) of ICl_3 in 160 ml of HCl, diluted to three times its original volume with ice and contained in an ice water bath, acetylene was bubbled. After 1.0–1.5 hr the bright yellow crystals were collected by vacuum filtration; the filtrate was returned for further treatment with acetylene. The yellow solid was washed with water until the filtrate was colorless, pressed on the filter to remove excess water, and air-dried on the filter for 30–45 min to give dry *trans*-chlorovinyliodoso dichloride. The cycle was repeated one or two times to give a total yield of 37.5 g (34%). The dried solid was used immediately or was stored in amber bottles in a Dry Ice box. *Caution: trans*-Chlorovinyliodoso dichloride is a hazardous material subject to spontaneous decomposition with the evolution of noxious vapors, especially if it appears reddish in places. Such material is to be discarded immediately. The compound should not be handled with metal spatulas. Several sealed bottles have exploded upon warming to room temperature. Not more than *ca.* 10 g of the compound should be stored in a 1-oz bottle. Sealed cold bottles should be warmed to room temperature behind a safety shield under the hood and opened with caution.

***trans*-1-Lithio-2-*o*-lithiophenyl-1-phenyl-1-hexene (1b).**—The procedure of Mulvaney, *et al.*,[5] was modified as follows. To 332[19] ml of anhydrous ether there was added 143 ml of 2.23 M *n*-butyllithium (0.320 mol) in hexane and then a solution of 25.0 g (0.140 mol) of diphenylacetylene in 100 ml of anhydrous ether. The resulting solution was stirred for 24 hr[20] under argon to give an orange-red solution of *trans*-1-lithio-2-*o*-lithiophenyl-1-phenyl-1-hexene (**1b**).

3-Butyl-2-phenylbenziodolium Chloride (2).—The above solution was added dropwise over 1 hr to a stirred solution of 47.5 g (.183 mol) of *trans*-chlorovinyliodoso dichloride in 300 ml of anhydrous ether under argon cooled in a Dry Ice–acetone bath. The resulting yellow suspension was kept cold for an additional 3 hr and then allowed to warm to room temperature overnight.

The reaction mixture was filtered, washed with ether, suspended in water, filtered, and dried on the filter to give 11.5 g of an off-white powder.[21] Recrystallization from 300 ml of benzene[22] (heated funnel) gave 8.10 g (14.6,[23] 26.2%[24]) of yellow crystals of 3-butyl-2-phenylbenziodolium chloride (**2**): mp 151.5–152.5° dec; ir (KBr) 3054, 2960, 2928, 2867, 1570, 1483, 1460, 1439, 1429, 1375, 1108, 1073, 1028, 1000, 850, 772, 762, 750, 715, 692, 652, 648, 635, 552, and 418 cm^{-1}; nmr (CD_2Cl_2) τ 1.05 (d with further splitting evident, 1, proton ortho to –I^+–), 2.15–2.69 (m, 8, other aromatic H), 7.32 (broad t, 2, $CH_2CH_2CH_2CH_3$), and 8.10–9.47 (m, 7, other aliphatic H).

Anal. Calcd for $C_{18}H_{18}ICl$: C, 54.49; H, 4.58; Cl, 8.94; I, 31.98. Found: C, 54.76; H, 4.57; Cl, 8.72; I, 32.04.

When 41.6 g (.160 mol) of *trans*-chlorovinyliodoso dichloride was used, the yield of **2** was only 1.74 g (3.1,[23] 5.7%[24]).

When 400 ml of dry toluene were used instead of the 300 ml of ether, the yield of **2** was 7.71 g (13.9,[23] 25.0%[24]).

3-Butyl-2-phenylbenziodolium Iodide (3).—To a solution of 30.0 g of NaI in 75 ml of 50% aqueous acetone (v:v) cooled to room temperature there was added .75 g (1.9 mmol) of 3-butyl-2-phenylbenziodolium chloride (**2**). The reaction flask was stoppered and vigorously stirred in the dark for 15 hr. Filtration followed by washing with water gave an orange-yellow solid. Recrystallization from 30 ml of acetone gave 0.43 g (three crops, 46%) of 3-butyl-2-phenylbenziodolium iodide (**3**). The iodide was not indefinitely stable at room temperature and was stored in the cold to retard decomposition: mp 121–122° dec (tube in at 120° and heated at 1–2°/min); ir (KBr) essentially the same as for **2**.

Anal. Calcd for $C_{18}H_{18}I_2$: C, 44.28; H, 3.72; I, 51.99. Found: C, 44.37; H, 3.78; I, 51.86.

Decomposition of 3-Butyl-2-phenylbenziodolium Chloride (2).—A small amount of **2** was heated at its melting point until the entire sample had decomposed to a pale yellow oil. Analysis by glpc (4% SE-30, 10 ft × 0.25 in., 190°, 84 ml/min He) indicated 51.0% isomer A, with shorter retention time, and 49.0% isomer B, with longer retention time. By comparison with the glpc data for **4a** and **4b** (see below), isomer B is probably the *trans*-1-chloro-2-*o*-iodophenyl-1-phenyl-1-hexene (**5b**) and isomer A the cis isomer. Data for this mixture follows: ir (neat) 3055, 2956, 2928, 2870, 2858, 1485, 1458, 1438, 1424, 1373, 1225, 1069, 1010, 890, 752, 736, 722, 691, 676, 638, 592, 583, 560, and 521 cm^{-1}; mass spectrum (decomposition in the instrument) *m/e* 398 (M^+ for ^{37}Cl), 396 (M^+ for ^{35}Cl), 361 ($M^+ - Cl$), 355 ($M^+ - CH_3CH_2CH_2$ for ^{37}Cl), 353 ($M^+ - CH_3CH_2CH_2$ for ^{35}Cl), 317, 234 ($M^+ - Cl - I$), 213, 192, 191, ($M^+ - Cl - I - CH_3CH_2CH_2$), 190, 189, 178, 91, 77 (Ph^+), and 57.

Anal. Calcd for $C_{18}H_{18}ICl$: C, 54.49; H, 4.58; Cl, 8.94; I, 31.98. Found: C, 54.64; H, 4.52; Cl, 8.99; I, 32.22.

Decomposition of 3-Butyl-2-phenylbenziodolium Iodide (3).—A small amount of **3** was heated at its melting point until the entire sample had decomposed to a reddish oil. Analysis by glpc (4% SE-30, 10 ft × 0.25 in., 190°, 84 ml/min He) indicated 57.9% of *trans*-1-iodo-2-*o*-iodophenyl-1-phenyl-1-hexene (**4b**) with longer retention time and 42.1% of the cis isomer **4a** (*vide infra*) with shorter retention time: ir (neat) 3058, 2959, 2929, 2871, 2861, 1485, 1461, 1442, 1429, 1378, 1218, 1120, 1109, 1073, 1059, 1031, 1013, 1001, 868, 852, 759, 749, 731, 723, 698, 662, 648, 640, 580, 549, 522, and 442 cm^{-1}; mass spectrum (decomposition in the instrument) identical with that of **4b**.

(17) H. Gilman and F. K. Cartledge, *J. Organometal. Chem.*, **2**, 447 (1964).

(18) A. J. Cope, D. S. Smith, and R. J. Cotter, "Organic Syntheses," Collect. Vol. IV, Wiley, New York, N. Y., 1963, p 377.

(19) The volume of ether is enough to dilute the hexane threefold in the final solution.

(20) The yield of **1b** was determined by quenching an aliquot of the reaction mixture with water and analyzing for the resulting *trans*-α-*n*-butylstilbene by glpc (1.5% SE-30, 2 m × 0.25 in., 190°) with triphenylmethane as an internal standard. An average yield of 55.6% was found after 24 hr. Analysis after 45 hr showed no significant change in the yield. *trans*-α-*n*-Butylstilbene was prepared by the method Mulvaney, *et al.*[5]

(21) *Caution:* this powder is an irritant to the nose and throat. It should be handled under the hood.

(22) Alternately, this material can be recrystallized from acetone.

(23) Yield based on diphenylacetylene.

(24) Yield based on **1b**.

trans-1-Iodo-2-*o*-iodophenyl-1-phenyl-1-hexene (4b).—A solution of 1b was prepared as described above from 25.0 g (140 mmol) of diphenylacetylene in 100 ml of anhydrous ether, 142 ml of 2.24 *M* (320 mmol) of *n*-butyllithium in hexane, and 325 ml of anhydrous ether. To the solution at 0–5° a solution of iodine in anhydrous ether was added dropwise with stirring until the purple color of iodine persisted (30 min); *ca.* 56 g (0.22 mol) of iodine in 300 ml of anhydrous ether was required. After warming to room temperature the reaction mixture was poured into an equal volume of water. The ether layer was separated, washed with water, dried ($MgSO_4$), and evaporated to give 52.7 g of a dark oil which was distilled with a short path apparatus at 0.07 mm. To prevent decomposition a pot temperature of 210° was not exceeded. Purity of fractions (*ca.* 4 ml) was monitored by glpc (1.5% SE-30, 2 m × 0.25 in., 230°). Fractions 1–4, bp 25–154° (15.6 g), were mainly unreacted diphenylacetylene. Fraction 5, bp 154–156° (5.9 g), was largely 4b. Fractions 6–8, bp 156–163° (20.9 g, *ca.* 30.6%), were 4b (95% purity) as viscous pale yellow oils. Recrystallization of fractions 6–8 from methanol afforded white crystals of *trans*-1-iodo-2-*o*-iodophenyl-1-phenyl-1-hexene (4b). Attempted crystallization of fraction 5 gave an oil which partially solidified upon slow evaporation of the solvent at room temperature and standing for several months. Absorption of the excess oil with paper towels followed by recrystallization of the crude solid from methanol gave additional pure crystals of 4b: mp 59–61°; ir (KBr) 3053, 2953, 2926, 2867, 1482, 1457, 1437, 1424, 1228, 1210, 1115, 1105, 1067, 1029, 1010, 936, 839, 756, 732, 723, 702, 671, 655, 633, 572, and 438 cm^{-1}; nmr (CCl_4) τ 2.14 (d with further splitting evident, 1, proton ortho to iodine), 2.42–3.28 (m, 8, other aromatic H), 7.23–8.11 (m, 2, $CH_2CH_2CH_2CH_3$), and 8.40–9.61 (m, 7, other aliphatic H); mass spectrum *m/e* 488 (M^+), 361 ($M^+ - I$), 318 ($M^+ - I - CH_3CH_2CH_2$), 234 ($M^+ - 2I$), 205 ($M^+ - 2I - CH_3CH_2$), 192, 191 ($M^+ - 2I - CH_3CH_2CH_2$), 189, 131, 130, 91, and 77 (Ph^+).

Anal. Calcd for $C_{18}H_{18}I_2$: C, 44.28; H, 3.72; I, 51.99. Found: C, 44.29; H, 3.74; I, 52.02.

Reaction of 2 with Sodium Methoxide in Anhydrous Methanol.—To a solution of 0.130 g (2.41 mmol) of sodium methoxide in 20 ml of anhydrous methanol, 2 (0.400 g, 1.01 mmol) was added. The resulting yellow solution was stirred in the dark for 75 min to give a nearly colorless solution. Ether and water were added to form two layers which were separated. The ether layer was washed twice with saturated $NaHCO_3$ solution, dried ($MgSO_4$), and evaporated to give 0.370 g of a yellow oil. The aqueous phase, which was neutral to pH paper, was combined with the $NaHCO_3$ washings, acidified with HCl, and extracted with ether. The ether extract was dried ($MgSO_4$) and evaporated to give 6.3 mg (5.1%) of benzoic acid.[25] Analysis of the yellow oil by glpc (20% OV1, 6 ft × 0.25 in., 195°, 100 ml/min He) indicated 92% of a mixture of *cis*- and *trans*-2-*o*-iodophenyl-1-methoxy-1-phenyl-1-hexene (6a and 6b), 4% 1-*o*-iodophenyl-1-pentanone (10),[25] and 4% of unidentified materials. The mixture of isomers consisted of 48.7% isomer A, with shorter retention time, and 51.3% isomer B, with longer retention time. Samples of the isomer mixture were collected by preparative glpc (same conditions) for microanalysis and nmr. Samples of each isomer were collected for ir and mass spectroscopy. All samples were highly viscous pale yellow oils: ir (isomer A, neat) 3051, 2957, 2930, 2870, 2858, 2830, 1638, 1595, 1486, 1459, 1440, 1425, 1263, 1252, 1234, 1124, 1104, 1072, 1054, 1025, 1012, 773, 758, 742, 730, 697, and 648 cm^{-1}; ir (isomer B, neat) 3054, 2958, 2932, 2871, 2858, 2834, 1650, 1595, 1486, 1458, 1440, 1424, 1287, 1266, 1245, 1127, 1102, 1070, 1058, 1010, 758, 742, 731, 700, 644, and 629 cm^{-1}; mass spectrum (isomer A) *m/e* 392 (M^+), 349 ($M^+ - CH_3CH_2CH_2$), 222, 207, 192, 191, 179, 178, 121, 165, 161, 121, 115, 105, 91, 89, 77 (Ph^+), and 51; mass spectrum (isomer B) identical with that of isomer A; nmr (both isomers) (CCl_4) τ 2.02–3.48 (m, 9, aromatic H), 6.60 (s, 1.5, OCH_3), 6.86 (s, 1.5, OCH_3), 7.46–8.11 (m, 2, $CH_2CH_2CH_2CH_3$), and 8.20–9.52 (m, 7, other aliphatic H).

Anal. Calcd for $C_{19}H_{21}IO$: C, 58.17; H, 5.40. Found: C, 58.10; H, 5.39.

Hydrolysis of 6a and 6b to 7.—To a solution in 10 ml of acetone of 0.100 g of the crude yellow oil mentioned in the previous reaction there was added 1.5 ml of 35% $HClO_4$, and the resulting solution was refluxed for 1 hr. After the mixture was cooled to room temperature, ether and water were added to form two layers which were separated. The aqueous layer was extracted with ether, and the combined organic phase was washed with saturated $NaHCO_3$ solution, dried ($MgSO_4$), and evaporated to give 91 mg of a pale yellow brown oil. Analysis by glpc (20% OV1, 6 ft × 0.25 in., 210°, 108 ml/min He) indicated 92% 2-*o*-iodophenyl-1-phenyl-1-hexanone (7), 6% 1-*o*-iodophenyl-1-pentanone (10),[25] and 2% unidentified materials. Ketone 7, collected by preparative glpc (same conditions), was identical (mass spectroscopy) with an authentic sample.

Reaction of 2 with NaOH.—A flask was charged with 0.397 g (1.00 mmol) of 2, 0.100 g (2.50 mmol) of NaOH, 7 ml of water, and 7 ml of hexane. After 30 min of reflux all the solid had reacted to give a yellow hexane solution and a cloudy water phase. To the cooled reaction mixture were added ether and water, and the layers were separated. The organic layer was washed with water containing 1 drop of HCl, dried ($MgSO_4$), and evaporated to give 0.356 g of a viscous yellow oil. Analysis by glpc (20% OV1, 6 ft × 0.25 in., 220°, 104 ml/min He) indicated 74% 2-*o*-iodophenyl-1-phenyl-1-hexanone (7), 0.6% 1-*o*-iodophenyl-1-pentanone (10),[25] 3.3% of *ca.* an equal mixture of *cis*- and *trans*-1-chloro-2-*o*-iodophenyl-1-phenyl-1-hexene (5a and 5b), and 22.3% of various unidentified products. Ketone 7 was collected by preparative glpc (same conditions) and found to be identical (ir and mass spectroscopy) with an authentic sample.

Reaction of 2 with H_2O in the Absence of Oxygen.—A Carius tube was charged with 150 mg (3.78 mmol) of 2 and 4 ml of water. The tube was degassed *via* four freeze–thaw cycles (0.07 mm), sealed, and shaken in the dark for 30 days after which time all the solid had changed to an oil. The ethereal extract was washed with saturated $NaHCO_3$ solution, dried ($MgSO_4$), and concentrated to give 0.127 g of a colorless oil. Analysis by glpc (20% OV1, 6 ft × 0.25 in., 210°, 108 ml/min He) indicated 97% 2-*o*-iodophenyl-1-phenyl-1-hexanone (7), 1% 1-*o*-iodophenyl-1-pentanone (10),[25] and 2% unidentified materials. Preparative glpc (same conditions) gave a sample of ketone 7 identical (ir and mass spectroscopy) with an authentic sample.

2-Hydroperoxy-2-*o*-iodophenyl-1-phenyl-1-hexanone (8). Method A.—A suspension of 100 mg (0.252 mmol) of 2 in 12 ml of water was vigorously stirred in the dark under a balloon of oxygen for 17 hr. After ether was added to the resulting white suspension to give two clear layers, these were filtered to remove a small amount (*ca.* 1 mg) of unreacted starting material. The layers were separated, and the aqueous phase was extracted with ether. The aqueous phase was strongly acid (HCl). The combined ether phase was washed with saturated $NaHCO_3$ solution, dried ($MgSO_4$), and evaporated at reduced pressure to give 0.097 g (94%) of a white solid. Recrystallization from 15 ml of ether–hexane (1:3) gave 58.6 mg (57%) of 2-hydroperoxy-2-*o*-iodophenyl-1-phenyl-1-hexanone (8) as white crystals (two crops). The crystals were stored in the freezer, since decomposition was evident after several days at room temperature: mp 93–94.5° dec; ir (KBr) 3300 (OH) 3063, 2950, 3917, 2867, 1668 (C=O), 1592, 1575, 1462, 1441, 1424, 1321, 1302, 1292, 1267, 1250, 1230, 1181, 1097, 1022, 1009, 968, 861, 858, 761, 732, 708, 698, 683, 656, 643, 619, 568, 535, and 449 cm^{-1}; nmr (acetone-d_6) τ −1.13 (s, 1, OOH, exchangeable with D_2O), 1.94–3.22 (m, 9, aromatic H), 7.18–7.45 (m, 2, $CH_2CH_2CH_2CH_3$), and 8.28–9.55 (m, 7, other aliphatic H).

Anal. Calcd for $C_{18}H_{19}IO_3$: C, 52.70; H, 4.67; I, 30.92. Found: C, 52.73; H, 4.65; I, 30.67.

Method B.—A flask was charged with 2.25 g (5.68 mmol) of 2, 75 ml of water, 125 ml of hexane, and 5 drops of concentrated HCl. The reaction mixture was refluxed for 30 min with vigorous stirring, filtered hot to remove any unreacted starting material, and cooled to room temperature. Ether was added until the precipitated solid dissolved, and two clear layers resulted. Work-up as before (method A) gave a waxy solid that was triturated with a minimum amount of hexane to give 1.72 g (74%) of a white solid. Recrystallization from 180 ml of ether–hexane (1:3) gave 1.25 g of (54%) of 8 (two crops).

2-*o*-Iodophenyl-1-phenyl-1-hexanone (7).[26]—A sealed tube containing 200 mg (0.505 mmol) of 4b and 2.00 ml of 30% aqueous DMF and protected from light was heated in an oil bath at 161 ± 2° for 308 hr. The tube was cooled to room temperature and opened. Ether and water were added to form two layers which

(25) These products probably arise from decomposition of α-hydroperoxy ketone 8 which is formed by reaction of 2 with water and oxygen present.

(26) This procedure is similar to those described in L. L. Miller and D. A. Kaufman, *J. Amer. Chem. Soc.*, **90**, 7282 (1968).

were separated. The aqueous layer was extracted with ether and the combined organic phase was extracted several times with water. The dried organic phase ($MgSO_4$) was evaporated to give 0.161 g of an oil. Analysis by glpc (20% OV1, 6 ft × 0.25 in., 205°, 88 ml/min He) indicated 47.5% 2-*o*-iodophenyl-1-phenyl-1-hexanone (**7**), 46.2% unreacted diiodo compound **4b**, and 6.3% of various unidentified materials. Preparative glpc (same conditions) gave pure 2-*o*-iodophenyl-1-phenyl-1-hexanone (**7**) as a viscous colorless oil: ir (neat) 3059, 2958, 2930, 2870, 2860, 1680 (C=O), 1591, 1575, 1555, 1460, 1444, 1430, 1342, 1280, 1253, 1230, 1200, 1176, 1008, 968, 984, 934, 750, 715, 699, 683, 652, 582, and 545 cm^{-1}; nmr (CCl_4) τ 1.89–3.42 (m, 9, aromatic H), 5.07–5.40 (m, 1, tertiary H), and 7.59–9.38 (m, 9, $CH_2CH_2CH_2CH_3$); mass spectrum *m/e* 378 (M^+), 322, 251 ($M^+ - I$), 217, 165, 115, 106, 105 ($PhC{=}O^+$), 91, 90, 77 (Ph^+), and 51.

Anal. Calcd for $C_{18}H_{19}IO$: C, 57.16; H, 5.07. Found: C, 57.06; H, 5.22.

1-*o*-Iodophenyl-1-pentanone (10).—To a solution of 4.84 g (19.0 mmol) of *o*-iodobenzaldehyde in 50 ml of dry ether there was added dropwise over a period of 40 min 7.00 ml (21.0 mmol) of 3.00 *M* *n*-butylmagnesium chloride in tetrahydrofuran. After the reaction mixture had been refluxed for 2 hr, the cooled white suspension was poured into water. Acidification with H_2SO_4 followed by addition of ether and water gave two layers which were separated. The aqueous layer was extracted with ether and the combined ether phase was washed with water, dried ($MgSO_4$), and evaporated to give 5.49 g of an oil. Infrared spectroscopy indicated the absence of carbonyl bands and the presence of an OH band at 3338 cm^{-1}. To the oil dissolved in 40 ml of acetone, the Jones reagent[27a] was added dropwise with stirring until the brown color persisted. After excess reagent had been destroyed with $NaHSO_3$ solution and the reaction mixture had been filtered, the green residue was washed with several portions of acetone. To the combined filtrate, ether and water were added, forming two layers, which were separated. The aqueous layer was extracted with ether, and the combined ether phase was washed with water, saturated $NaHCO_3$ solution, and again water, then dried ($MgSO_4$), and evaporated to give 4.41 g of a yellow oil. Analysis by glpc (20% OV1, 6 ft × 0.25 in., 160°, 88 ml/min He) indicated 47% 1-*o*-iodophenyl-1-pentanone (**10**), 34% o-iodobenzaldehyde, and 20% of various unidentified materials. Ketone **10** was purified by preparative glpc (same conditions) to give an analytical sample as a pale yellow oil: ir (neat) 3059, 2960, 2935, 2873, 1696 (C=O), 1588, 1556, 1459, 1426, 1399, 1377, 1351, 1341, 1275, 1245, 1205, 1049, 1020, 1013, 1004, 978, 969, 756, 728, 666, and 636 cm^{-1}; nmr (CCl_4) τ 2.18 (d with further splitting evident, 1, proton ortho to iodine), 2.46–3.20 (m, 3, other aromatic H), 7.18 (t, 2, $CH_2C{=}O$), and 8.01–9.33 (m, 7, other aliphatic H); mass spectrum *m/e* 288 (M^+), 246, 231 ($M^+ - CH_2CH_2CH_2CH_3$), 203 ($M^+ - C{=}O - CH_2CH_2CH_3CH_3$), 161 ($M^+ - I$), 105, 104, 91, 77, 76, 75, 74, 57, 51, and 50.

Anal. Calcd for $C_{11}H_{13}IO$: C, 45.85; H, 4.55. Found: C, 45.89; H, 4.48.

The formation of *o*-iodobenzaldehyde in 34% yield apparently reflects substantial reduction[28] of the starting material by the Grignard reagent followed by subsequent oxidation by the Jones reagent.

Thermal Decomposition of 8 in Heptane.—A suspension of 1.26 g (3.07 mmol) of **8** in 50 ml of heptane was refluxed for 20 min. Solvent removal gave an oil which partially solidified on standing. The semisolid was taken up in ether and extracted several times with saturated $NaHCO_3$ solution. The ether phase was dried ($MgSO_4$) and evaporated to give 0.91 g of a yellow oil. The $NaHCO_3$ extracts were acidified and extracted twice with ether. The extracts were dried ($MgSO_4$) and evaporated to give 230 mg (62%) of a white solid identified as benzoic acid. Recrystallization from hexane gave white crystals whose ir spectrum (KBr) was identical with that of an authentic sample of benzoic acid, mp and mmp 121–122° (lit.[29a] mp 121°).

The yellow oil was distilled with a short-path apparatus to give 530 mg (60%) of a pale yellow oil, bp 85° (0.07 mm). Preparative glpc (20% OV1, 6 ft × 0.25 in., 160°, 104 ml/min He) gave analytically pure 1-*o*-iodophenyl-1-pentanone (**10**) identical (ir and mass spectroscopy) with an authentic sample.

Analysis of 8 by Iodometry.[30]—A weighed sample of *ca.* 40–50 mg of **8** was dissolved in 25 ml of 2-propanol in an iodine flask. Several small pieces of Dry Ice were added, followed by 10 drops of glacial acetic acid and several drops of saturated KI solution. The stopper was set in place and sealed with 2-propanol. The flask was gently heated on a steam bath for 15 min to give a dark brown solution of iodine. To the hot solution were added 25 ml of water and several small pieces of Dry Ice. Immediate titration with 0.025 *N* $Na_2S_2O_3$ to the disappearance of the iodine color allowed calculation of the molecular weight of **8**, calcd 410, found 425 (average of three determinations).

Reduction of 8. Method A.—To a solution of 388 mg (0.946 mmol) of **8** in 20 ml of absolute ethanol was added 71.1 mg (1.88 mmol) of $NaBH_4$. After the reaction mixture had been stirred at room temperature for 5 min, the excess $NaBH_4$ was decomposed by several drops of acetic acid. Ether and water were added to form two layers which were separated. The aqueous layer was extracted with ether. The combined ether phase was extracted with saturated $NaHCO_3$ solution, washed with water, dried ($MgSO_4$), and evaporated to give 310 mg of a semisolid. Trituration with a minimum of hexane gave 250 mg (67%) of 2-hydroxy-2-*o*-iodophenyl-1-phenyl-1-hexanone (**9**). Recrystallization from hexane gave an analytical sample: mp 102–103°; ir 3450 (OH), 3062, 2936, 2924, 2865, 1661 (C=O), 1591, 1570, 1457, 1443, 1430, 1418, 1378, 1370, 1287, 1261, 1240, 1217, 1178, 1162, 1139, 1021, 1010, 978, 971, 965, 841, 792, 758, 730, 716, 702, 689, 659, 640, 620, 535, and 441 cm^{-1}; nmr ($CDCl_3$) τ 2.02–3.18 (m, 9, aromatic H), 5.17 (s, 1, OH, exchangeable with D_2O), 7.64 (broad t with further splitting evident, 2, $CH_2CH_2CH_2CH_3$), and 8.37–9.47 (m, 7, other aliphatic H); mass spectrum *m/e* 289 ($M^+ - PhCO$), 233, 231 ($C_6H_4ICO^+$), 203 ($C_6H_4I^+$), 143, 133, 120, 91, 78, 77 (Ph^+), 76 ($C_6H_4\cdot^+$), 71, and 57.

Anal. Calcd for $C_{18}H_{19}IO_2$: C, 54.84; H, 4.86; I, 32.19. Found: C, 54.88; H, 4.81; I, 32.02.

Method B.—To a solution of 646 mg (1.58 mmol) of **8** in 50 ml of acetone there were added 3 drops of acetic acid and 1 ml of a saturated acetone solution of NaI. The solution was refluxed gently on a steam bath for 15 min, cooled to room temperature, and treated with $Na_2S_2O_3$ solution to destroy the liberated iodine. Water and ether were added to form two layers which were separated. The aqueous layer was extracted with ether, and the combined ether phase was extracted with saturated $NaHCO_3$ solution, dried ($MgSO_4$), and evaporated to give 590 mg of a yellow oil. Trituration with a minimum amount of pentane and cooling gave 280 mg (45%) of **9**. Recrystallization from hexane gave analytically pure **9**, identical (ir and mass and nmr spectroscopy) with a sample prepared by method A, mp and mmp 102–103°.

Anal. Calcd for $C_{18}H_{19}IO_2$: C, 54.84; H, 4.86; I, 32.19. Found: C, 54.57; H, 4.87; I, 32.19.

Oxidative Cleavage of 9 with Lead Tetraacetate.—To a solution of 78.4 mg (0.119 mmol) of **9** in 5 ml of dry benzene was added 133 mg (0.300 mmol) of $Pb(OAc)_4$. After 1 hr of reflux the off-white suspension was cooled to room temperature and several drops of ethylene glycol were added to destroy any excess reagent. The reaction mixture was filtered, and the residual salts were washed with several portions of benzene. To the combined benzene filtrate were added ether and water to form two layers which were separated. The organic layer was extracted twice with saturated $NaHCO_3$ solution, washed with water, dried ($MgSO_4$), and evaporated to give 51.4 mg of a yellow oil. The $NaHCO_3$ extracts were acidified and extracted twice with ether. The ether extracts were dried ($MgSO_4$) and evaporated to give 8.1 mg (33%) of benzoic acid. Recrystallization from hexane gave white crystals identical (ir) with an authentic sample, mp and mmp 119.5–120° (lit.[29a] mp 121°). Reduction of the reflux time to 0.5 hr increased the yield of benzoic acid to 50%.

The yellow oil was purified by preparative glpc (20% OV1, 6 ft × 0.25 in., 160°, 104 ml/min He) to give 24.6 mg (43%) of analytically pure 1-*o*-iodophenyl-1-pentanone (**10**) identical (ir and mass spectroscopy) with an authentic sample.

(27) L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," Vol. 1, Wiley, New York, N. Y., 1967: (a) p 142; (b) p 817.

(28) Reduction by the Grignard reagent accompanies its addition to hindered carbonyl compounds: D. J. Cram and G. S. Hammond, "Organic Chemistry," McGraw-Hill, New York, N. Y., 1964, p 316.

(29) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," Wiley, New York, N. Y., 1964: (a) p 313; (b) p 147.

(30) Based on procedures in A. V. Tobolsky and R. B. Mesrobian, "Organic Peroxides," Interscience, New York, N. Y., 1954, p 52.

Attempted cleavage of 9 with periodic acid in THF[27b] was unsuccessful, possibly because of steric hindrance to the formation of the intermediate ester.[29b]

Measurement of the Absorption of Oxygen by 2.[31]—A sample of *ca.* 4–5 mg of 2 was accurately weighed to ±0.1 mg and added to the Warburg flask containing 4.00 ml of water, pH 2.00 buffer or 0.05 *M* KCl solution, previously equilibrated at 24.7 ± 0.10°. The apparatus was quickly assembled, the stirrer was started, and readings were taken and corrected with the thermobarometer. Typical results follow.

Fluid	% reaction	Approximate time of reaction, hr
Water	96	1.5–2.5
pH 2.00	95	5–6
0.05 *M* KCl	95	6

Determination of the Crystal Structures of 3-Butyl-2-phenylbenziodolium Chloride (2) and Dibenziodolium Tetrafluoroborate (11) by X-Ray Analysis.—Dibenziodolium tetrafluoroborate (11) was prepared according to the method of Beringer and Chang,[32] by metathesis of the iodonium chloride with silver tetrafluoroborate in 20% H_2O–80% MeOH followed by recrystallization from water. Single crystals (needles) of 11 and 2 were chosen with dimensions 0.15 × 0.30 × 0.10 mm and 0.10 × 0.30 × 0.10 mm, respectively. A Picker four-circle automated diffractometer was used for the collection of 1527 independent reflections in the case of 11 and 2175 in the case of 2 to a 2θ angle at 45°. A 2θ–θ scan mode was used. Mo Kα radiation was used. From Weissenberg photographs the space groups $P\bar{1}$ and $C2/c$ (later confirmed) have been assigned to compounds 11 and 2, respectively. The unit cell parameters have been determined by least-squares refinement of the setting angles of 12 reflections. The resulting crystal data are reported in Table I. The structures have been solved by Patterson method and refined by least-squares calculations to R values of 0.036 and 0.031 for 11 and 2, respectively. $R = \Sigma w|\Delta F|/\Sigma wF_o$, $w = 1/(A + BF_o + CF_o^2)$, with $A = 0.11111$, $B = 1/18F_{o(min)}$, $C = 2(18\text{-}F_{o(min)}\cdot F_{o(max)})$.[33] The refinement was performed using anisotropic thermal parameters for all the nonhydrogen atoms. The hydrogens were included assuming their geometrically calculated positions. Absorption corrections have been done assuming the crystals are cylinders. We used the atomic scattering factors of Moore.[34] The tables of observed and calculated structure factors are available."

Tetraphenyliodolium Chloride (16).—A suspension of 1,4-dilithiotetraphenyl-1,3-butadiene (15)[35] was prepared under argon rom 26.7 g (150 mmol) of diphenylacetylene, 1.05 g (150 mg-atoms) of lithium wire in 75 ml of anhydrous ether. The suspension was transferred *via* a syringe (equipped with an 18-gauge needle) to an addition funnel and added dropwise over a period of 45 min to a stirred solution of 20.8 g (80.0 mmol) of *trans*-chlorovinyliodoso dichloride in 350 ml of anhydrous ether under argon at −78°. Small portions of ether were used to facilitate the transfers. After the resulting yellow suspension had been stirred for 15 min, excess ether–HCl complex was added dropwise. The greenish suspension that resulted was warmed to room temperature, filtered, washed with ether, suspended in water, filtered, dried, suspended in ether, filtered, and dried. The yellow solid was stirred in 50 ml of methylene chloride for 15 min to give a fine white powder suspended in a brownish green solution. Vacuum filtration through two layers of filter paper and a fine sintered-glass funnel gave 862 mg of a white powder. Slow dilution of the clear methylene chloride filtrate with a large volume of hexane caused precipitation of 963 mg (2.5%) of crude tetraphenyliodolium chloride as a pale yellow solid. Addition of ether dropwise to a solution of the crude salt in a minimum of tetrahydrofuran precipitated an analytically pure sample as an off-white solid. If insufficient ether were added to cause immediate precipitation, the pure salt could be obtained as off-white fluffy crystals by cooling the solution overnight: mp 140.5–141.5° dec (tube in at 135° and heated at *ca.* 1–2°/min); ir 3076, 3062, 3032, 1594, 1570, 1480, 1439, 1277, 1172, 1152, 1068, 1024 998, 952, 913, 872, 791, 779, 753, 726, 700, 690, 628, 622, 561, and 552 cm^{-1}; nmr (CD_2Cl_2) 2.62–3.18 (m, Ar H).

Anal. Calcd for $C_{28}H_{20}ICl$: C, 64.82; H, 3.89; I, 24.46. Found: C, 64.71; H, 3.96; I, 24.64.

Tetraphenyliodolium Iodide.—To a solution of 57 mg (0.11 mmol) of crude tetraphenyliodolium chloride in a minimum amount of acetone there was added a solution of excess anhydrous lithium iodide in acetone. Tetraphenyliodolium iodide precipitated as an orange powder: mp 133.0–133.5° dec to red liquid (tube in at 125° and heated at *ca.* 1–2°/min); ir essentially identical with that of tetraphenyliodolium chloride.

Anal. Calcd for $C_{28}H_{20}I_2$: C, 55.10; H, 3.30; I, 41.59. Found: C, 55.18; H, 3.27; I, 41.67.

Decomposition of the Tetraphenyliodolium Salts.—Tetraphenyliodolium chloride was decomposed in the mass spectrometer: *m/e* 520 (M^+ for ^{37}Cl), 518 (M^+ for ^{35}Cl), 483 ($M^+ - Cl$), 393 ($M^+ - 1$ for ^{37}Cl), 391 ($M^+ - 1$ for ^{35}Cl), 356 ($M^+ - I - Cl$), 355 ($C_{27}H_{19}^+$), 279 ($M^+ - I - Cl - Ph$), 278 ($C_{21}H_{14}\cdot^+$), 178 ($PhC{\equiv}CPh\cdot^+$), 77 (Ph^+).

Tetraphenyliodolium iodide was similarly decomposed in the mass spectrometer yielding the following mass spectrum which is identical with that obtained from 1,4-diiodo-1,2,3,4-tetraphenyl-1,3-butadiene:[36] *m/e* 610 (M^+), 483 ($M^+ - I$), 356 ($M^+ - 21$), 355 ($C_{27}H_{19}^+$), 279 ($M^+ - 21 - Ph$), 278 ($C_{21}H_{14}\cdot^+$), 178 ($PhC{\equiv}CPh\cdot^+$), and 77 (Ph^+).

Registry No.—**2**, 32730-78-2; **3**, 32730-79-3; **4a**, 32721-29-2; **4b**, 32721-30-5; **5a**, 32721-31-6; **5b**, 32721-32-7; **6a**, 32721-33-8; **6b**, 32721-34-9; **7**, 32730-80-6; **8**, 32730-81-7; **9**, 32730-82-8; **10**, 32730-83-9; **11**, 18116-06-8; **16**, 34143-18-5; **17**, 34143-19-6.

TABLE I
CRYSTAL DATA FOR 11 AND 2

Dibenziodolium Tetrafluoroborate

a = 10.168 ± 0.004 Å	Space group $P\bar{1}$
b = 10.081 ± 0.004 Å	Z = 2
c = 7.238 ± 0.003 Å	V = 610.9 Å^3
α = 110° 46 ± 3 min	D_x = 2.00 g cm^{-3}
β = 105° 11 ± 2 min	D_{obsd} = 1.97 g cm^{-3}
γ = 106° 2 ± 2 min	μ = 26.8 cm^{-1} (Mo Kα)

3-Butyl-2-phenylbenziodolium Chloride

a = 28.310 ± 0.019 Å	Space group $C2/c$
b = 7.646 ± 0.005 Å	Z = 8
c = 17.547 ± 0.014 Å	V = 3227.0 Å^3
β = 121° 50 ± 3 min	D_x = 1.64 g cm^{-3}
	D_{obsd} = 1.63 gm^{-3}
	μ = 21.6 cm^{-1} (Mo Kα)

(31) Based on procedures in W. W. Umbrieit, R. H. Burris, and J. F. Stauffer, "Manometric Techniques," 4th ed, Burgess Publishing Co., Minneapolis, Minn., 1964.

(32) L. L. Chang, Ph.D. Dissertation, Polytechnic Institute of Brooklyn, 1971.

(33) D. N. J. Cruickshank, *Acta Crystallogr.*, **2**, 1965 (1949).

(34) F. H. Moore, *ibid.*, **16**, 1169 (1963).

(35) L. I. Smith and H. H. Hoehn, *J. Amer. Chem. Soc.*, **63**, 1184 (1941).

(36) E. M. Braye, W. Hübel, and I. Caplier, *ibid.*, **84**, 4406 (1961).

The Synthesis of 2-Carbonyl-1,3-dithiolanes from the Reaction of 1,2-Disulfenyl Chlorides with Aldehydes and Active Methylene Compounds

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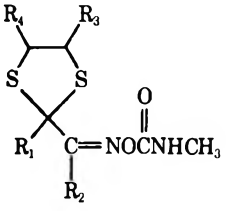
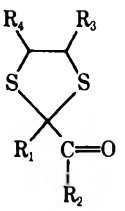
A new reaction of 1,2-disulfenyl chlorides with aldehydes to give substituted 1,3-dithiolanes is reported. Treatment of 1,2-ethane- or 1,2-propanedisulfenyl chloride with propionaldehyde, butyraldehyde, isovaleraldehyde, and phenylacetaldehyde provided 2-substituted 1,3-dithiolone-2-carboxaldehydes **4a–h**. Ethyl acetoacetate and the disulfenyl chlorides gave keto ester dithiolanes **5a** and **6a**, which afforded 2-acetyl-1,3-dithiolanes **5b** and **6b** on hydrolysis and decarboxylation.

As part of our continued interest in 2-substituted 1,3-dithiolane-2-carboxyaldehyde *O*-(methylcarbamoyl)oximes of structure **1** as potential insecticides and nematicides,[2] a convenient method for the preparation of dithiolane aldehyde and ketone precursors **2** was necessary.



1



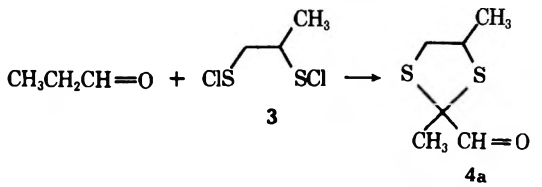
2

Presently, compounds of type **2** in which $R_1 = R_2 = CH_3$ (**2a**) and $R_1 = CH_3$, $R_2 = H$ (**2b**) are readily prepared from the reaction of 2,3-butanedione or of aqueous pyruvaldehyde with a variety of vicinal dithiols.[3]

Additional examples in which R_1 is a group other than methyl have not been readily available by this method, however, either owing to inaccessibility of the starting α-dicarbonyl compounds or to the complex mixture of products obtained from the reactions.

As a possible alternative route to such compounds of interest, the reaction of vicinal disulfenyl chlorides with suitable carbonyl compounds was investigated. Some precedence in the literature gave an indication of the feasibility of such a scheme. For example, the reaction of certain aryl sulfenyl chlorides with ketones to provide β-keto sulfides is well documented;[4] however, only one example of a similar reaction of simple aliphatic sulfenyl chlorides with an active methylene compound has been reported.[5]

Initial attempts to prepare 2,4-dimethyl-1,3-dithiolane-2-carboxaldehyde (**4a**) from 1,2-propanedisulfenyl chloride (**3**) and propionaldehyde in benzene solution were unsuccessful, resulting in extensive tar formation and no detectable amount of desired material. However, in methylene chloride solution, a 30% yield of **4a** was obtained. A variety of other solvents and reaction conditions were tested, with best results being realized in cold (0°), dilute ethyl acetate solution, which provided the dithiolane aldehyde **4a** in 50–55% yields.

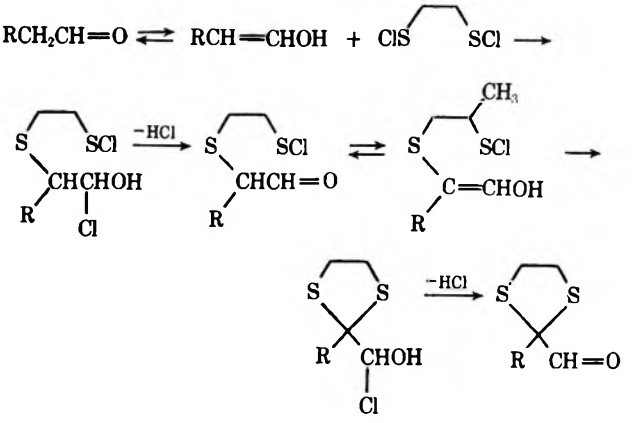


3 **4a**

Several other 2-substituted 1,3-dithiolane-2-carboxaldehydes were prepared in this manner from various aldehydes and disulfenyl chlorides, and results are listed in Table I. In these experiments, no attempts were made to determine optimum conditions.

The reaction most likely proceeds by the stepwise addition of the disulfenyl chloride to the enol form of the aldehyde, possibly as outlined in Scheme I.[6]

SCHEME I



Under the highly acidic conditions encountered during the course of this reaction, it is very likely that a major competing reaction involves the aldol condensation of the aldehydes. The usual products in this event (aldols, α,β-unsaturated aldehydes, and water) can all serve to destroy the highly reactive disulfenyl chlorides.[7] Attempts to minimize these undesirable reactions through the use of dilute solutions and by keeping the temperatures low were only partially successful, as evidenced by the often rather low yields of dithiolanes obtained, especially in those cases using ethanedisulfenyl chloride (Table I). Nevertheless, the simplicity of the method and ready availability of the starting materials make the route an attractive one, since most

(1) Contribution No. 643.

(2) T. L. Fridinger, E. L. Mutsch, J. W. Bushong, and J. W. Matteson, *J. Agr. Food Chem.*, **19**, 422 (1971).

(3) T. L. Fridinger and K. R. Henery-Logan, *J. Hetrocycl. Chem.*, **8**, 469 (1971).

(4) C. Rappe and R. Gustafsson, *Acta Chem. Scand.*, **22**, 2927 (1968), and references cited therein.

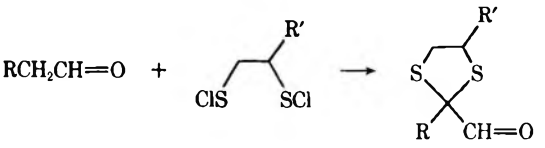
(5) I. F. Kay, D. J. Lovejoy, and S. Glue, *J. Chem. Soc. C*, 445 (1970).

(6) (a) N. Kharasch in "Organic Sulfur Compounds," Vol. I, N. Kharasch, Ed., Pergamon Press, Oxford, 1961, p 375; (b) R. Gustafsson, C. Rappe, and J. O. Levin, *Acta Chem. Scand.*, **23**, 1843 (1969).

(7) M. L. Kee and I. B. Douglass, *Org. Prep. Proced.*, **2**, 235 (1970), and references cited therein.

TABLE I

DITHIOLANE ALDEHYDES



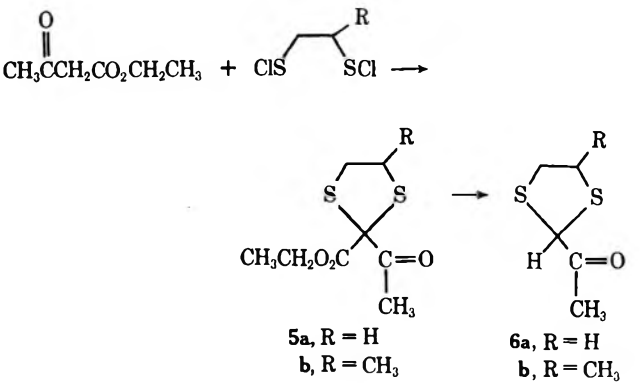
Compd	R	R′	Yield, %	Bp, °C (mm)	Ir (neat), cm⁻¹ (-CH=O)	Nmr (CDCl₃), δ	Calcd, % C	Calcd, % H	Found, % C	Found, % H
4a	CH_3	CH_3	55[a]	70–73 (0.1)	1725	1.50 (m, 3, >CHCH₃) 1.78 (s, 3, -CCH₃) 3.30 (m, 2, -CH₂CH<) 4.05 (m, 1, -CH₂CH<) 9.55 (d, 1, -CH=O)[e]	44.5	6.2	44.5	6.1
4b	CH_3CH_2	CH_3	47[b]	89–95 (0.1)	1720	1.15 (t, 3, J = 7.45 Hz) 1.44 (d, 3) 2.16 (q, 2, J = 7.45 Hz) 3.24 (m, 2) 4.00 (m, 1) 9.25 (d, 1)	47.7	6.8	47.9	6.9
4c	$(CH_3)_2CH$	CH_3	60[a,c]	90–95 (0.2)	1725	1.15 (m, 6) 1.43 (d, 3) 2.38 (m, 1) 3.00 (m, 2) 3.80 (m, 1) 9.45 (d, 1)	50.5	7.4	50.4	7.1
4d	C_6H_5	CH_3	49[a,d]	137–140 (0.1)	1725	1.48 (d, 3) 3.20 (m, 2) 9.98 (m, 1) 7.42 (m, 5) 9.40 (s, 1)	58.9	5.4	59.1	5.4
4e	CH_3	H	19[a]	71–84 (0.4)	1715	1.85 (s, 3, -CCH₃) 3.38 (s, 4, -CH₂CH₂-) 9.42 (s, 1, -CH=O)	40.5	5.4	40.5	5.5
4f	CH_3CH_2	H	30[b]	71–75 (0.1)	1720	1.11 (t, 3, J = 7.45 Hz) 2.10 (q, 2, J = 7.45 Hz) 3.34 (s, 4) 9.50 (s, 1)	44.5	6.2	44.7	6.2
4g	$(CH_3)_2CH$	H	29[a]	62–70 (0.1)	1730	1.16 (d, 6) 2.50 (m, 1) 3.30 (s, 4) 9.60 (s, 1)	47.7	6.8	47.3	6.5
4h	C_6H_5	H	25[a]	150–160 (0.5)	1730	3.32 (m, 4) 7.37 (m, 5) 9.58 (s, 1)	57.2	4.8	57.5	4.8

[a] Ethyl acetate as solvent. [b] Methylene chloride as solvent. [c] 0.2 mol scale. [d] 0.1 mol scale. [e] In most cases in which R′ = CH_3 the product is an isomeric mixture, which is reflected in the appearance of the aldehyde proton as a doublet.

of the compounds are not available by any other means.[8]

Attempts to prepare compounds of type 2 in which $R_1 = R_2 = H$ from the reaction of disulfenyl chlorides with acetaldehyde were unsuccessful, with only polymeric materials being obtained. In addition, acetone and acetophenone gave no detectable amounts of dithiolane ketones under the conditions investigated. However, compounds of type 2 where $R_1 = H$ and $R_2 = CH_3$ could be prepared by a convenient two-step procedure. Ethyl acetoacetate and 1,2-ethanedisulfenyl chloride gave 2-carbethoxy-2-acetyl-1,3-dithiolane (**5a**).

Hydrolysis and decarboxylation of the material provided 2-acetyl-1,3-dithiolane (**6a**). The 4-methyl derivatives **5b** and **6b** were prepared similarly from



5a, R = H
b, R = CH_3

6a, R = H
b, R = CH_3

ethyl acetoacetate and 1,2-propanedisulfenyl chloride (**3**).

(8) A very brief attempt to prepare 2,4-dimethyl-1,3-dithiolane-2-carboxaldehyde (**4a**) by a modification of the method of Corey and Seebach[9] starting with 2,4-dimethyl-1,3-dithiolane and n-butyllithium failed completely, probably because the resulting dithiolane carbanion was much more unstable than the corresponding 1,3-dithiane carbanions more commonly employed.

(9) (a) D. Seebach, *Synthesis*, **1**, 17 (1969); (b) E. J. Corey and D. Seebach, *Angew. Chem., Int. Ed. Engl.*, **4**, 1075, 1077 (1966).

Experimental Section

Boiling points are uncorrected. Vapor phase chromatographic (vpc) analyses were performed on a Varian Aerograph 1720 instrument using a 5-ft 20% SE-30 on Chrom W column. The following spectrometers were used: nmr, Varian A-60D (TMS as internal standard); ir, Perkin-Elmer Model 137B. Microanalyses were performed by Paul Olson and the microanalytical group of these laboratories. The starting aldehydes (used to prepare the compounds listed in parentheses) were freshly distilled prior to use: propionaldehyde (**4a** and **4e**), butyraldehyde (**4b** and **4f**), isovaleraldehyde (**4c** and **4g**), and phenylacetaldehyde (**4d** and **4h**). The preparations were run on a 0.5-mol scale, unless otherwise noted.[10]

Dithiolane Aldehydes. General Procedure.—To a solution of 0.5 mol of 1,2-dithiol in 500 ml of either ethyl acetate or methylene chloride[10] cooled to −20 to −10° was added dropwise with mechanical stirring 135.0 g (1.0 mol) of sulfuryl chloride over a 0.5-hr period. A white precipitate of polymeric disulfide[11] which formed initially slowly dissolved to give a red solution of disulfenyl chloride.[12] The solution was allowed to warm to 0° and stirred at this temperature for 0.5 hr. The aldehyde (0.52 mol) dissolved in 50 ml of the appropriate solvent was added dropwise with stirring at 0° over a 1-hr period from a dropping funnel equipped with a pressure-equalizing side arm. A slow stream of dry nitrogen was passed through the funnel into the vented reaction vessel to prevent the resulting HCl fumes from contacting the acid-labile aldehyde. After addition was complete, the reaction was stirred at 0° for 4–8 hr, and then allowed to warm to room temperature overnight. The black solution was filtered if necessary and washed with water and saturated sodium bicarbonate solution until neutral, the organic phase was dried ($MgSO_4$), and the solvent was evaporated to give a black oil which was distilled under high vacuum. During the distillation, especially of the higher-boiling aldehydes, impurities present in the mixture often decomposed as the pot temperature reached ~100°, giving off HCl fumes which made maintaining a good vacuum difficult during this brief period. Nevertheless, after the decomposition was completed, high vacuum was regained and examination by vpc of the products obtained revealed them to be consistently of 97–99% purity.

2-Carbethoxy-2-acetyl-1,3-dithiolane (5a).—The procedure was essentially the same as for the aldehydes above. To a solution of 1,2-ethanedisulfenyl chloride prepared from 47.1 g (0.50 mol) of 1,2-ethanedithiol and 135.0 g (1.0 mol) of sulfuryl chloride in 300 ml of methylene chloride was added 65.1 g (0.50 mol) of ethyl acetoacetate dropwise with stirring at 0–5° over a 1-hr period. After addition was complete, the reaction mixture was stirred for 2 hr at 0–5° and at room temperature for an additional 2 hr. The golden yellow solution was filtered to remove a small amount of white polymer, the solvent was evaporated, and the crude brown oil was distilled under high vacuum. All material distilling from 140–160° (0.1–0.5 mm) (HCl evolution) was collected and redistilled. The fraction boiling at 119–125° (0.1 mm) was collected to give 53.6 g (49%) of **5a** as a light yellow oil: ir (neat) 1720, 1750 cm^{-1}; nmr ($CDCl_3$) δ 1.32 (t, 3, J = 7.45 Hz), 2.40 (s, 3), 3.40 (s, 4), 4.28 (q, 2, J = 7.45 Hz).

Anal. Calcd for $C_8H_{12}O_3S_2$: C, 43.6; H, 5.5. Found: C, 43.4; H, 5.4.

2-Carbethoxy-2-acetyl-4-methyl-1,3-dithiolane (5b).—The procedure was identical with that for the preparation of **5a** except that ethyl acetate was used as solvent and 54.1 g (0.50 mol) of 1,2-propanedithiol was used in place of ethanedithiol. Work-up and distillation provided the crude product, bp 136–156° (0.1–1.0 mm), which was redistilled to afford 42.3 g (36%) of **5b**: bp 118–122° (0.1 mm); ir (neat) 1720, 1750 cm^{-1}; nmr ($CDCl_3$) δ 1.35 (m, 6), 2.38 (s, 3), 3.23 (m, 2), 3.84 (m, 1), 4.26 (q, 2).

Anal. Calcd for $C_9H_{14}O_3S_2$: C, 46.1; H, 6.0. Found: C, 46.0; H, 5.9.

2-Acetyl-1,3-dithiolane (6a).—A mixture of 47.5 g (0.21 mol) of **5a**, 80 ml of water, 10 ml of glacial acetic acid, and 20 ml of concentrated H_2SO_4 was stirred and heated under reflux for 24 hr. A vpc of an aliquot revealed the complete disappearance of the starting material. The mixture was cooled to room temperature and the product was extracted with two 100-ml portions of methylene chloride. The combined extracts were dried ($MgSO_4$) and evaporated to give a brown oil. Distillation afforded 27.5 g (86%) of **6a**: bp 70–73° (0.05 mm); ir (neat) 1740 cm^{-1}; nmr ($CDCl_3$) δ 2.32 (s, 3), 3.35 (s, 4), 4.86 (s, 1).

Anal. Calcd for $C_5H_8OS_2$: C, 40.50 H, 5.4. Found: C, 40.6; H, 5.3.

2-Acetyl-4-methyl-1,3-dithiolane (6b).—The procedure was identical with that for the preparation of **6a** above except that 48 hr were required for complete hydrolysis and decarboxylation of the keto ester. From 41.8 g (0.18 mol) of **5b** there was obtained 24.7 g (84%) of **6b**: bp 63–69° (0.05 mm); ir (neat) 1740 cm^{-1}; nmr ($CDCl_3$) δ 1.45 (m, 3), 2.30 (d, 3), 3.22 (m, 2), 3.90 (m, 1), 4.85 (d, 1).

Anal. Calcd for $C_6H_{10}OS_2$: C, 44.5; H, 6.2. Found: C, 44.4; H, 6.2.

Registry No.—**4a**, 33177-96-7; **4b**, 33406-16-5; **4c**, 33406-17-6; **4d**, 33406-18-7; **4e**, 26419-66-9; **4f**, 33406-20-1; **4g**, 33406-21-2; **4h**, 33406-22-3; **5a**, 33406-23-4; **5b**, 33406-24-5; **6a**, 33406-25-6; **6b**, 33406-26-7.

Acknowledgment.—The author wishes to express his sincere appreciation to Mr. Roy T. Knafla for his competent technical assistance, to Dr. Edward L. Mutsch for his interest and many helpful discussions during the course of this work, and to P. E. Olson and the members of the Analytical Research and Services Laboratory of the 3M Company for microanalytical analyses.

(10) See Table I.

(11) W. H. Mueller and M. Dines, *J. Heterocycl. Chem.*, **6**, 627 (1969).

(12) When 1,2-propanedisulfenyl chloride was prepared in methylene chloride solution, this polymer was evidently soluble, since no precipitate was observed throughout the addition.

The Reactions of Medium-Membered-Ring Unsaturated Compounds with Iodine Azide[1]

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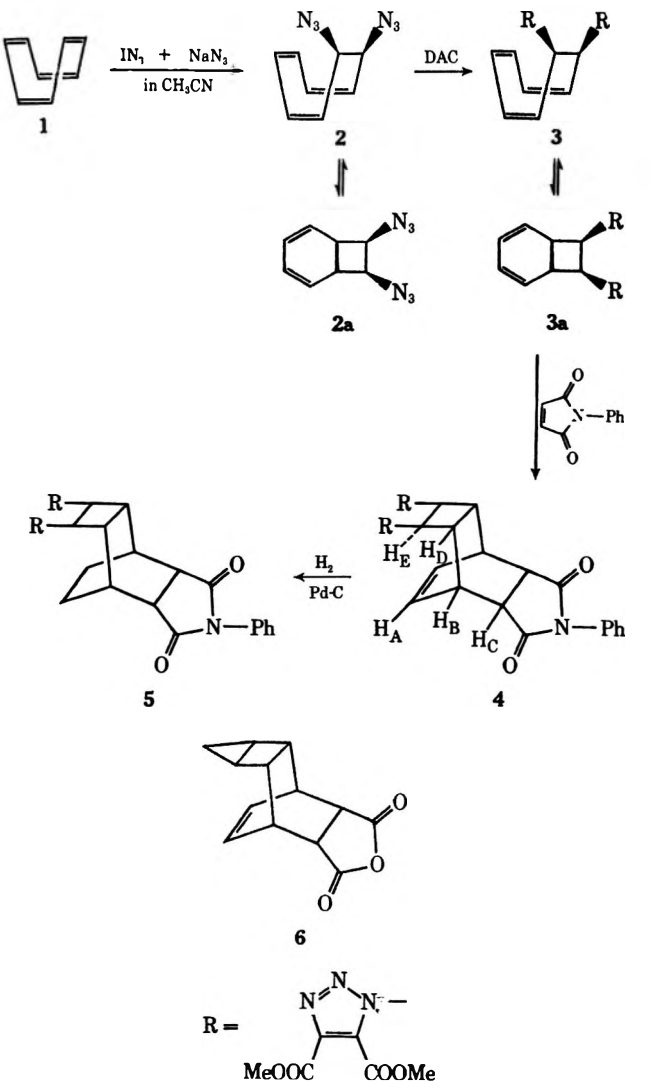
Reaction of some medium-membered-ring unsaturated compounds such as cyclooctatetraene, 1-ethoxycarbonyl-1(1*H*)-azepine, and tropone ethylene ketal with the IN_3 solution, a mixture of iodine azide and sodium azide, gave the bisazides. However, in the case of the reactions of cycloocta-1,3- and -1,5-dienes with the same mixture under the same conditions, only normal monoazides were obtained which were convertible to the corresponding bisazides with NaN_3 in DMF at 35–40°. The formation of these adducts was confirmed by spectral evidence of their triazolo derivatives prepared by the reactions of the adducts with dimethyl acetylenedicarboxylate.

The addition reactions of halogen azides to olefins provide a useful general method for the stereospecific and regiospecific introduction of an iodo azide function into organic molecules.[2] Although the reactions of numerous olefins with iodine azide (IN_3) have been examined, little is known about the similar reactions of cyclic conjugated polyolefins with the exception of cycloocta-1,3-diene.[3] In this paper we report the reactions of cyclooctatetraene (COT), 1-ethoxycarbonyl-1(1*H*)-azepine, and tropone ethylene ketal with IN_3 to give the bisazides **2**, **15**, and **18**, respectively.

Results and Discussion

Formation of the Bisazides. –The reaction of COT (**1**) with an IN_3 solution prepared *in situ* from excess sodium azide and iodine monochloride in acetonitrile[2] afforded an oily compound **2**. When an excess of NaN_3 was removed in the reaction, considerable amounts of tarry compounds were obtained, presumably because of unstable 1:1 IN_3 adduct initially formed (*cf.* Experimental Section, method B). Compound **2** showed a strong azide absorption at 2100 cm^{-1} in the ir spectrum and is negative to the Beilstein halogen test. Since the azide is quite explosive at room temperature, the structure determination was based on that of 1,3-dipolar cycloadduct; treatment of **2** with dimethyl acetylenedicarboxylate (DAC) gave a crystalline compound **3**. From the analytical data, the adduct **3** was determined to be a bistriazolo derivative. The nmr spectrum of **3** showed signals at τ 3.30 (2 H, dd, J = 4.0 and 2.5 Hz), 3.68 (2 H, dd, J = 8.2 and 4.0 Hz), 4.75 (4 H, complex multiplets), 6.05 (3 H, s, $COOCH_3$), and 6.10 (3 H, s, $COOCH_3$). From the spectrum, however, it is difficult to determine the positions of the triazolo groups whether at 1,2 or 1,4, because of the complexity of the signals centered at τ 4.75. Thus, the cycloaddition reaction of **3** with *N*-phenylmaleimide was attempted, which afforded a 1:1 adduct **4**; the nmr spectrum exhibited signals at τ 2.50–3.00 (m, C_6H_5), 4.00 (H_A, dd, J = 3.4 and 4.2 Hz), 6.05 (s, 4 $COOCH_3$), 6.45 (H_B, m), 6.87 (H_C, t, J = 1.5 Hz), 7.38 (H_E, m), and 8.26 (H_D, m). Double resonance experiments verified the assignments of H_A and H_B; on irradiation at τ 6.45 the double

SCHEME I



doublet signals at τ 4.00 were collapsed into a singlet. Furthermore, the spectrum pattern of **4** is quite similar to that of an endo cycloadduct (**6**)[4] of tricyclo[4.3.0.0^{7,9}]nona-2,4-diene to maleic anhydride. The signals at both τ 4.00 and 6.45 disappeared by the catalytic hydrogenation and new ones appeared at τ 8.2–8.6 (m, 6 H). These results indicate that the signal at τ 4.0 is due to the olefinic protons (H_A), and that at τ 6.45 is attributable to the methine proton (H_B) ad-

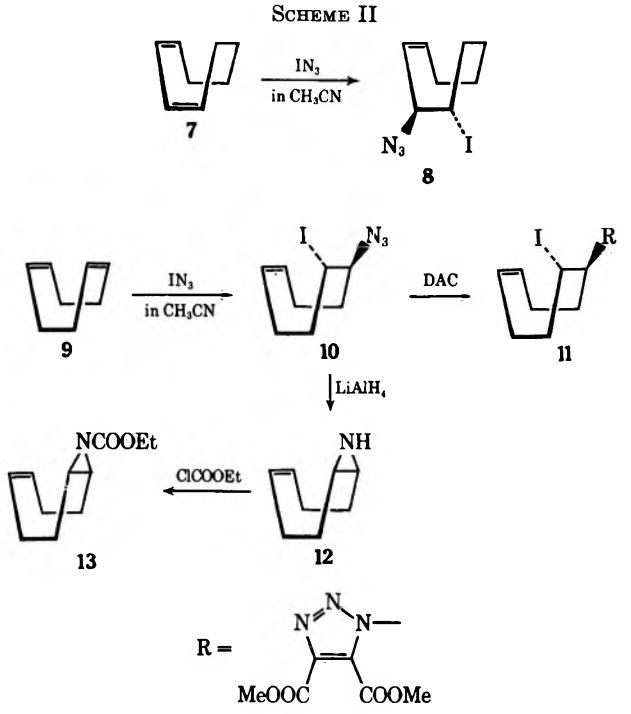
(1) Studies of Heteroaromaticity. Part LX. For Part LIX of this series, see T. Sasaki, K. Kanematsu, and K. Hayakawa, *J. Chem. Soc. C.* in press.

(2) A. Hassner, *Accounts Chem. Res.* **4**, 9 (1971).

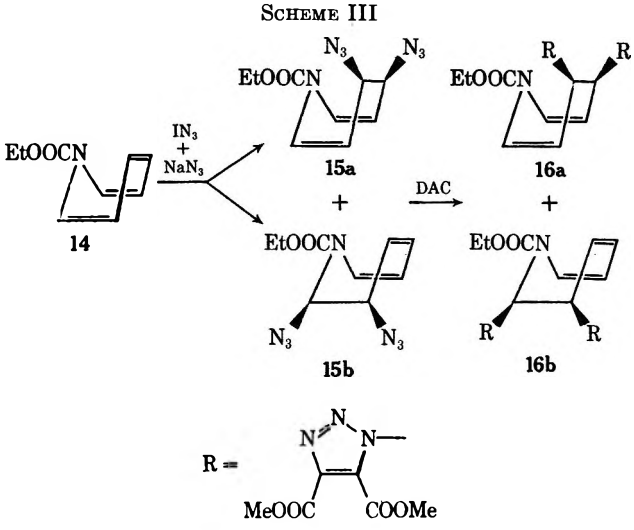
(3) F. W. Fowler, A. Hassner, and L. A. Levy, *J. Amer. Chem. Soc.*, **89**, 2077 (1967).

(4) W. H. Okamura and T. W. Osborn, *J. Amer. Chem. Soc.*, **92**, 1061 (1967).

SCHEME II



SCHEME III



jacent to the double bond. Thus, the adduct (**4**) is assigned as a (4 + 2) π cycloadduct of *N*-phenylmaleimide to 7,8-bistriazolobicyclo[4.2.0]octa-2,4-diene.

From these results, compound **3** could be assigned as 7,8-bistriazolobicyclo[4.2.0]octa-2,4-diene (**3a**) as depicted in Scheme I. Further structural confirmation of the adduct will be described below.

The reaction of cycloocta-1,3-diene (**7**) with IN_3 has been reported to give a normal 1:1 adduct (**8**).[2] We reinvestigated similar reactions of cycloocta-1,3- and -1,5-dienes with the IN_3 solution under the same conditions as described above to give 1:1 IN_3 adducts **8** and **10**. Compound **10** exhibited a strong azide absorption at 2100 cm^{-1} and is positive to the Beilstein halogen test. For the structural elucidation, the 1,3-dipolar cycloaddition reaction of **10** with DAC was also carried out and gave the cycloadduct **11** in 40% yield. Compound **10** was converted to the aziridine derivative **12** by lithium aluminium hydride.[5] Treatment of **12** with ethyl chloroformate afforded **13**, which was

(5) This reaction was studied in detail for the proof of anti addition of IN_3 to the olefin providing by $LiAlH_4$ reduction of the adducts; see ref 2.

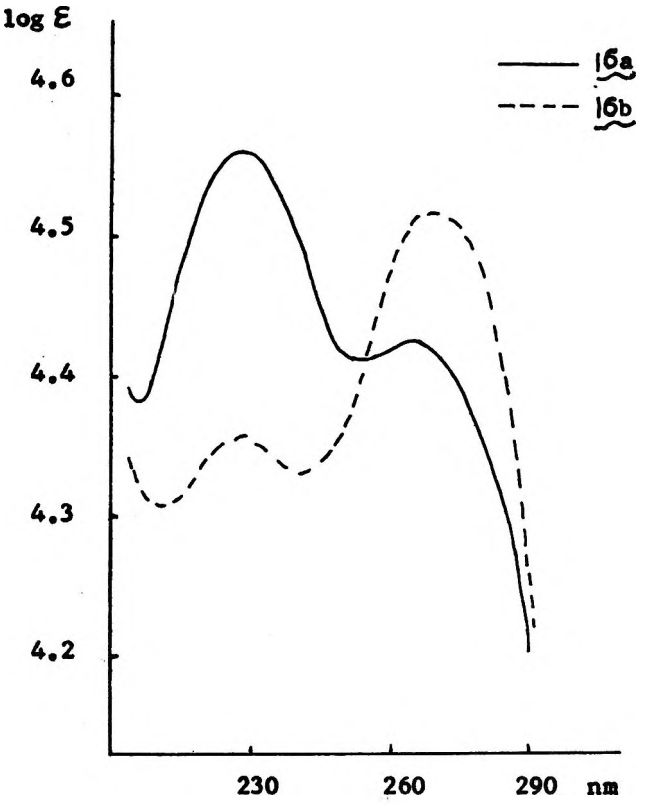


Figure 1.—Ultraviolet spectra of compounds **16a** and **16b** in MeOH.

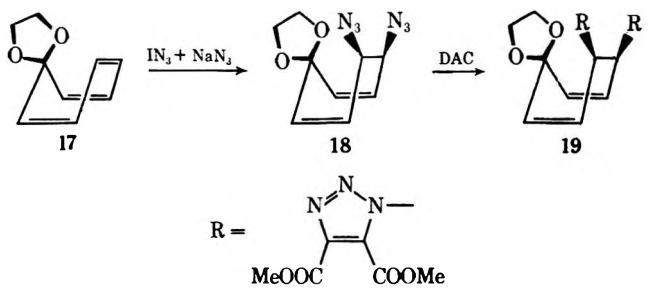
identical with an authentic sample prepared from the photochemical reaction of cycloocta-1,5-diene and ethyl azidoformate[6] (Scheme II).

Similar treatment of 1-ethoxycarbonyl-1(1*H*)-azepine (**14**) with the IN_3 solution gave a mixture of **15a** and **15b**, which was readily converted to the cycloadducts to DAC. The isomeric mixture was separated by column chromatography and recrystallized into **16a** and **16b** in the ratio of 10:1. The isomeric adducts were assigned on the basis of the spectral inspection. The ir and uv spectra (*cf.* Figure 1) of **16a** were quite similar to those of the 4,5-homoazepine derivative,[7] and the spectra of **16b** were similar to those of the 2,3-homoazepine isomer.[7]

The nmr spectrum of **16a** shows symmetrical patterns at τ 2.79 (H_A, d, J_{AB} = 9.0 Hz), 3.61 (H_C, d, J_{CB} = 6.0 Hz), 4.63 (H_B, dd, J = 9.0 and 6.0 Hz), the two methoxycarbonyl signals at τ 6.06 and 6.15, and the ethoxycarbonyl signals at τ 5.65 (OCH_2, q, J = 7.0 Hz) and 8.60 (CH_3, t, J = 7.0 Hz). The spectrum of **16b** exhibited the 1,3-diene ring proton signals at τ 3.10 (1 H, t, J = 6.0 Hz), 3.12 (1 H, d, J = 9.0 Hz), 3.85 (1H, d, J = 6.0 Hz), and 4.65 (1 H, dd, J = 6.0 and 9.0 Hz), the methine proton signals at τ 2.50 (1 H, d, J = 4.3 Hz) and 3.92 (1 H, d, J = 4.3 Hz), the two methoxycarbonyl signals at τ 6.06 and 6.15, and the ethoxycarbonyl signals at τ 5.65 (OCH_2, q, J = 7.0 Hz) and 8.60 (CH_3, t, J = 7.0 Hz). From the results, the structures of **16a** and **16b** were characterized as the 1-ethoxycarbonyl-4,5-*cis*-bistriazolo-4,5-dihydro-1(1*H*)-azepine derivative and the 2,3 isomer, respectively (Scheme III).

(6) S. Fujita, T. Hiyama, and H. Nozaki, *Tetrahedron*, **26**, 4347 (1970).
(7) W. H. Okamura and W. H. Snider, *Tetrahedron Lett.*, 3367 (1968).

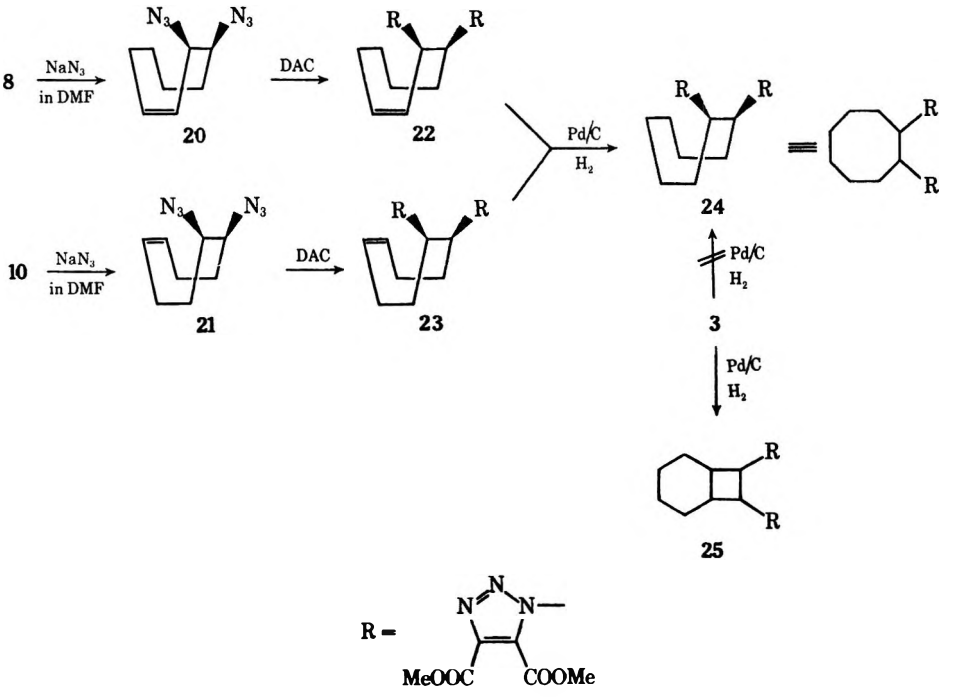
SCHEME IV



7.25. It should be mentioned that the reaction of the tropone ketal with the IN_3 solution is entirely similar to that of the azepine with the polyolefinic characters, although the tropone ethylene ketal is classified as a spiro-conjugated aromatic system from the calculated stabilization energy by Simmons and Fukunaga.[8]

Stereochemistry of the Bisazides.—For further structural elucidation, the stereochemistry of the bisazides was studied. The 1:1 adducts **8** and **10** to cycloocta-1,3- and -1,5-dienes were treated with NaN_3 in DMF at 30–40° for 10 hr to give the bisazides **20** and **21**, respectively, whose structual determinations were based on that of the corresponding 1,3-dipolar cycloadducts **22** and **23** to DAC. Catalytic hydrogenation of the cycloadducts **22** and **23** in ethanol over palladium on charcoal gave **24** (uptake 1 g-atom of H_2) in quantitative yield. However, the cycloadducts **3** absorbed only 2 g-atoms of hydrogen and afforded **25** (no olefinic protons by nmr) in quantitative yield (Scheme V). The difference in the nmr spectra of **24** and **25** suggested that **25** was not the trans isomer of **24** but a bicyclo[4.2.0]octane derivative. Compound **25** can be assigned the cis configuration because of the symmetrical pattern by nmr (*cf.* Figure 2).

SCHEME V



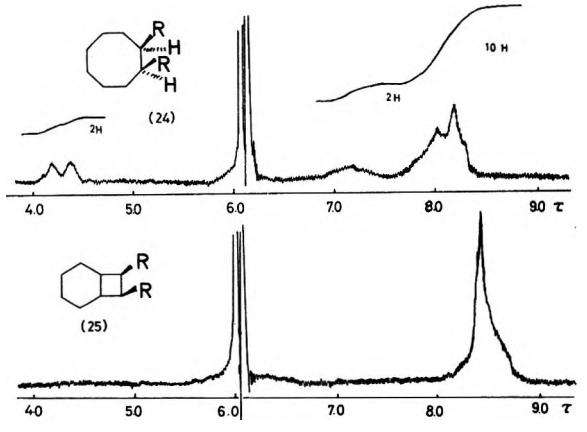


Figure 2.—Nmr spectra of compounds **24** and **25**.

Similar reaction of tropone ethylene ketal (**17**) with the IN_3 solution gave an oily compound (**18**), which was converted to the cycloadduct **19** with DAC (Scheme IV). The adduct **19** was also assigned as the *cis*-bistriazolo derviative from a completely symmetrical pattern of the nmr spectrum: it displayed four equivalent vinyl protons as a singlet at τ 3.75, two methine protons as a singlet at τ 3.80, two methyl protons of two methoxycarbonyl groups as two singlet patterns at τ 6.00 and 6.07, and two equivalent pairs of methylene protons ($-OCH_2CH_2-O-$) as doublets (J = 6.0 Hz) centered at τ 6.95 and

Mechanisms for the Formation of the Bisazides.—As described above, the reactions of the conjugated cyclotetraene and trienes with the IN_3 solution gave readily the 1,2-cis bisazides, and those of the conjugated and nonconjugated cyclic dienes afforded only the 1:1 adducts. Further treatment of the 1:1 adduct with NaN_3 under the conditions as described above gave the bis adduct.

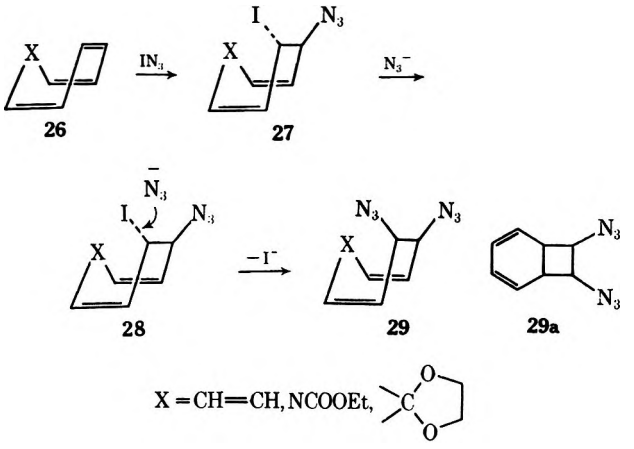
Based on these facts, we suggested that the adduct **27** where

$$X = NCOOEt, \overline{COCH_2CH_2OC}$$

(8) H. E. Simmons and T. Fukunaga, *J. Amer. Chem. Soc.*, **89**, 5208 (1967).

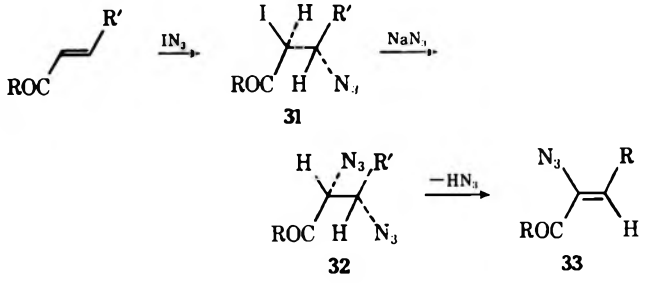
was initially formed in the reaction of **26** with IN_3, followed by the SN2 attack of the azide ion to give **29**, since the iodine group in **27** might be activated by the vinyl function rather than by the alicyclic group. In the case of COT (**25**, X = CH=CH), the monocyclic adducts were not isolated, which readily gave the bicyclic adduct **29a** through valence tautomerization (Scheme VI).

SCHEME VI



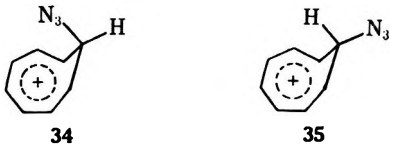
In these connections, Hassner, *et al.*,[9] recently suggested that the bisazides **32** might be formed by the SN2 attack of the azide ion on the iodine-bearing carbon of **31**, as shown in Scheme VII.

SCHEME VII



An alternative mechanism involving homotropylium ions **34** and **35** could be considered;[10,11] the former should lead to the cis azide, whereas the latter might be a precursor to the trans isomer (Scheme VIII).

SCHEME VIII



However, neither the 1,2-trans bisazide nor the 1,4 bisazide could be obtained in these reactions. Consequently, this mechanism might be deleted.

(9) G. Lábbé and A. Hassner, *J. Org. Chem.*, **36**, 258 (1971).

(10) We are grateful to a referee for a valuable suggestion.

(11) In these connections, the 1,4 cycloadduct rather than the 1,2 cycloadduct of COT to chlorosulfonyl isocyanate has been rationalized by the intervention of a dipolar homotropylium cation, followed by collapse of two intermediates *via* either one of two equivalent six-centered transition states; see L. A. Paquette, J. A. Malpass, and T. J. Barton, *J. Amer. Chem. Soc.*, **91**, 4714 (1969).

Experimental Section[12]

General Procedure for Iodine Azide Addition Reactions. A.—To 3.9 g (0.06 mol) of sodium azide in 25 ml of acetonitrile at −20° was added slowly 3.6 g (0.022 mol) of iodine monochloride over a period of 5–10 min. The reaction mixture was then stirred for an additional 5 min. After 0.02 mol of the unsaturated compound was added to the solution, the reaction mixture was allowed to stand at room temperature overnight. The red-brown slurry was poured into 50 ml of water, and the mixture was extracted with ether. The extract was washed with 40 ml of 5% aqueous sodium thiosulfate and then with water and dried over magnesium sulfate. Removal of the solvent under reduced pressure at room temperature produced yellow oily compounds **2**, **15**, and **18** in 80–90% yields, respectively. These compounds were used in the following reactions without further purification, since the azido functions in the adducts are quite explosive even under the reduced distillation.

B.—To a stirred slurry of 0.01 mol of sodium azide in 20 ml of acetonitrile in a methanol–ice cold bath was added slowly 0.011 mol of iodine monochloride over a period of 10–20 min. The reaction mixture was stirred for an additional 5 min. After excess insoluble sodium azide was removed by filtration, the filtered IN_3 solution was added to 0.01 mol of the olefin using a cooled addition funnel.[10] However, when treated with IN_3 and COT, considerable amounts of black tarry compounds were obtained.

1,3-Dipolar Cycloaddition of the Bisazides with DAC.—A solution of the bisazides **2**, **15**, and **18** (0.01 mol) and DAC (0.02 mol) in acetonitrile (40 ml) was refluxed for 12 hr. The solvent was removed under reduced pressure to give the cycloadducts as follows.

7,8-*cis*-Bis(4,5-dimethoxycarbonyl-1,2,3-triazolo)bicyclo[4.2.0]octa-2,4-diene (3a) was obtained as a crude colorless solid and recrystallized from methanol in 70% yield: mp 137–139°; ν_{max}^{KBr} 1720 (C=O) and 1570 cm^{-1} (C=C); τ ($CDCl_3$, both at 40 and 52°) 3.30 (2 H, dd, J = 4.0 and 2.5 Hz), 3.68 (2 H, dd, J = 8.2 and 4.0 Hz), 4.75 (4 H, m), 6.05 (3 H, s, COOMe), 6.10 (3 H, s, COOMe).

Anal. Calcd for $C_{20}H_{20}N_6O_8$: C, 50.85; H, 4.28; N, 17.79. Found: C, 51.01; H, 4.40; N, 17.59.

1-Ethoxycarbonyl-4,5-*cis*-bis(4,5-dimethoxycarbonyl-1,2,3-triazolo)-4,5- and -2,3-dihydro-1(1H)-azepines 16a and **16b** were obtained as a mixture in 80% yield. The mixture was purified by silica gel chromatography with methanol–benzene (3%) as an eluent to give **16a**, mp 149–151°, and **16b**, mp 152–155° (recrystallization from methanol).

16a: ν_{max}^{KBr} 1720 (C=O) and 1675 cm^{-1} (C=C); λ_{max}^{MeOH} 225 nm (log ϵ 4.57), 265 (ϵ 4.43); τ ($CDCl_3$) 2.79 (1 H), d, J = 9.0 Hz), 3.61 (1 H, d, J = 6.0 Hz), 4.63 (1 H, dd, J = 9.0 and 6.0 Hz), 6.06 (3 H, s, $COOCH_3$), 6.15 (3 H, s, $COOCH_3$), 5.65 (2 H, q, J = 7.0 Hz), 8.60 (3 H, t, J = 7.0 Hz).

16b: ν_{max}^{KBr} 1745 (shoulder), 1720 (C=O), 1650, 1615 cm^{-1} (C=C); λ_{max}^{MeOH} 225 nm (log ϵ 4.36), 268 (ϵ 4.52); τ ($CDCl_3$) 3.10 (1 H, t, J = 6.0 Hz), 3.12 (1 H, d, J = 9.0 Hz), 3.85 (1 H, d, J = 6.0 Hz), 4.65 (1 H, dd, J = 6.0 and 9.0 Hz), 2.50 (1 H, d, J = 4.3 Hz), 3.92 (1 H, d, J = 4.3 Hz), 6.06 (3 H, s, $COOCH_3$), 6.15 (3 H, s, $COOCH_3$), 5.65 (2 H, q, J = 7.0 Hz, OCH_2), 8.60 (3 H, t, J = 7.0 Hz, OCH_2CH_3).

Anal. Calcd for $C_{21}H_{23}N_7O_{10}$: C, 47.28; H, 4.35; N, 18.38. Found for **16a**: C, 47.16; H, 4.36; N, 18.21. Found for **16b**: C, 47.55; H, 4.41; N, 18.24.

4,5-*cis*-Bis(4,5-dimethoxycarbonyl-1,2,3-triazolo)-4,5-dihydrotropone ethylene ketal (19) was obtained as colorless prisms in 40% yield: mp 206–209°; ν_{max}^{KBr} 1730 (C=O) and 1565 cm^{-1} (C=C); τ ($CDCl_3$) 3.75 (4 H, s), 3.80 (2 H, s), 6.00 (3 H, s, $COOCH_3$), 6.07 (3 H, s, $COOCH_3$), 6.95 (2 H, t, J = 6.0 Hz), 7.25 (2 H, t, J = 6.0 Hz).

Anal. Calcd for $C_{21}H_{22}N_6O_{10}$ C, 48.65; H, 4.28; N, 16.21. Found: C, 48.63; H, 4.29; N, 16.19.

Cycloaddition of 3 with *N*-Phenylmaleimide.—A solution of **3** (2.4 g, 0.05 mol) and *N*-phenylmaleimide (1.7 g, 0.01 mol) in

(12) The melting points were measured with a Yanagimoto micromelting 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 Model C-60-XL nmr spectrometer and with a Varian A-60 recording spectrometer with tetramethylsilane as an internal standard. The chemical shifts are expressed in τ values. The ir spectra were taken with a JASCO Model IR-S spectrophotometer.

toluene (100 ml) was refluxed for 3 days. The solvent was then removed under reduced pressure and the residue was recrystallized from benzene to give colorless needles of **4** (80%), mp 243–245°, ν_{max}^{KBr} 1730 and 1705 cm^{-1}.

Anal. Calcd for $C_{30}H_{27}N_7O_{10}$: C, 55.81; H, 4.22; N, 15.19. Found: C, 55.86; H, 4.25; N, 14.90.

Hydrogenation of 4.—A solution of **10** (1.0 g, 0.0015 mol) in 50 ml of acetone was hydrogenated over 10% Pd/C (0.1 g) for 12 hr at room temperature. The catalyst was then separated by filtration and the solvent was removed under reduced pressure. The residue was recrystallized from methanol to give colorless needles of **5** in a quantitative yield: mp 240–241°; ν_{max}^{KBr} 1730 and 1710 cm^{-1}; τ ($CDCl_3$) 2.5–3.0 (m, C_6H_5), 6.90 (m, 2 H), 7.32 (m, 2 H), and 8.2–8.6 (m, 8 H).

Anal. Calcd for $C_{30}H_{29}N_7O_{10}$: C, 55.64; H, 4.51; N, 15.14. Found: C, 55.63; H, 4.56; N, 14.91.

5-Azido-6-iodocyclooctene (10) was prepared from cycloocta-1,5-diene and the IN_3 solution as described in method A. This compound was obtained in 80% yield and was used in the following reactions without further purification.

1-(2-Iodocyclooct-5-enyl)-4,5-dimethoxycarbonyl-1,2,3-triazole (11) was prepared from **10** (2.77 g, 0.01 mol) and DAC (1.42 g, 0.01 mol) in 40% yield: mp 98–99.5° (from methanol); ν_{max}^{KBr} 1745 and 1720 cm^{-1}; τ ($CDCl_3$) 4.32 (m, 2 H), 4.40–4.92 (m, 2 H), 6.02 (s, OCH_3), 6.05 (s, OCH_3), 7.0–8.0 (m, 8 H).

Anal. Calcd for $C_{14}H_{18}N_3O_4I$: C, 40.11; H, 4.33; N, 10.02. Found: C, 40.37; H, 4.35; N, 10.28.

9-Azabicyclo[6.1.0]nona-4-ene (12).—To a stirred solution of 2.0 g of lithium aluminium hydride in 50 ml of anhydrous ether was added the iodo azide adduct **10** (5.5 g, 0.02 mol) in 15 ml of ether. The solution was stirred at room temperature and added with excess $LiAlH_4$ (1 g). The reaction mixture was then treated with 20% sodium hydroxide solution and extracted with ether. The extract was removed under reduced pressure to give **12** (50%) as a pale yellow oil, picrate mp 173–175° (from methanol).

Anal. Calcd for $C_{14}H_{16}N_4O_7$ (picrate): C, 47.73; H, 4.58; N, 1590. Found: C, 47.61; H, 4.51; N, 15.94.

9-Ethoxycarbonyl-9-azabicyclo[6.1.0]non-4-ene (13).—To 1.23 g (0.01 mol) of the aziridine **12** and 5 g of triethylamine in 70 ml of benzene was added 1.1 g (0.01 mol) of ethyl chloroformate at 0°. The reaction mixture was stirred for 5 hr at room temperature. The salts were filtered and the solution was removed under reduced pressure to give a pale yellow oil (**13**) (80%). Compound **13** shows identical spectroscopic properties with those of an authentic sample prepared from the photochemical reaction of ethyl azidoformate and cycloocta-1,5-diene.[6]

Reaction of the Iodine Azide Adducts with Sodium Azide.—The corresponding IN_3 adducts **8** and/or **10** were allowed to react with sodium azide (0.02 mol) in DMF (60 ml) at 30–40° for 15 hr. The solution was then poured into water and extracted with ether. The extract was washed with water and dried ($MgSO_4$). Removal of the solvent under reduced pressure at room temperature produced the corresponding bizazides **20** and/or **21** as a yellow oil in 30–40% yields. However, these compounds were explosive at room temperature and were used in the following reactions without further purification.

3,4-*cis*-Bis(4,5-dimethoxycarbonyl-1,2,3-triazolo)-1-cyclooctene (22) was obtained by the reaction of DAC and **20** as described above: mp 179–181°; colorless prisms; yield 50%; ν_{max}^{KBr} 1730 (C=O), cm^{-1} 1570 (C=C); τ ($CDCl_3$) 3.3–3.9 (3 H, m), 4.2–4.7 (1 H, m), 6.00 (3 H, s, $COOCH_3$), 6.10 (3 H, s, $COOCH_3$), 6.13 (3 H, s, $COOCH_3$), 6.30 (3 H, s, $COOCH_3$), 7.2–8.7 (8 H, m).

Anal. Calcd for $C_{20}H_{24}N_6O_8$: C, 50.42; H, 5.08; N, 17.64. Found: C, 50.50; H, 5.10; N, 17.60.

5,6-*cis*-Bis(4,5-dimethoxycarbonyl-1,2,3-triazolo)-1-cyclooctene (23) was obtained by the reaction of DAC and **21** as described above: mp 141–142°; colorless prisms; yield 20%; ν_{max}^{KBr} 1740 (C=O) and 1560 cm^{-1} (C=C); τ ($CDCl_3$) 4.0–4.5 (4 H, m), 6.10 (3 H, s, COOMe), 6.18 (3 H, s, COOMe), 6.5–8.5 (8 H, H, m).

Anal. Calcd for $C_{20}H_{24}N_6O_8$: C, 50.42; H, 5.08; N, 17.64. Found: C, 50.39; H, 5.03; N, 17.65.

Hydrogenation of 22 and 23.—A solution of **22** or **23** (0.1 g) in acetone (20 ml) was hydrogenated over 10% Pd/C (0.02 g) for 2 hr at room temperature. The catalyst was then separated by filtration and the solvent was removed under reduced pressure. The residue was recrystallized from methanol to give colorless needles (**24**) in quantitative yield: mp 158–160°; ν_{max}^{KBr} 1735 (C=O) and 1660 cm^{-1} (C=C); τ ($CDCl_3$) 4.28 (2 H, br d, J = 10.0 Hz), 7.15 (2 H, m), 7.5–8.3 (10 H, m).

Anal. Calcd for $C_{20}H_{26}N_6O_8$: C, 50.20; H, 5.48; N, 17.57. Found: C, 50.18; H, 5.50; N, 17.51.

Hydrogenation of 3.—A solution of **3** (0.94 g, 0.002 mol) in acetone (50 ml) was hydrogenated over 10% Pd/C (0.1 g) at room temperature. Uptake of hydrogen was complete after 2 hr and amounted to a total of 90 ml (0.004 mol). The catalyst was then separated by filtration and the solvent was removed under reduced pressure. The residue was recrystallized from methanol to give colorless needles (**25**) in quantitative yield: mp 145–147°; ν_{max}^{KBr} 1730 (C=O) and 1765 cm^{-1} (C=C); τ ($CDCl_3$) 6.00 (3 H, s, COOMe), 6.10 (3 H, s, COOMe), 8.1–8.8 (12 H, m).

Anal. Calcd for $C_{20}H_{24}N_6O_8$: C, 50.42; H, 5.08; N, 17.64. Found: C, 50.45; H, 5.10; N, 17.60.

Registry No.—**2**, 33224-25-8; **3a**, 33224-26-9; **4**, 33303-95-6; **5**, 33224-27-0; **11**, 33224-28-1; **12** picrate, 33224-29-2; **15a**, 33224-30-5; **15b**, 33224-31-6; **16a**, 33224-32-7; **16b**, 33264-04-9; **18**, 33224-33-8; **19**, 33224-34-9; **22**, 33303-96-7; **23**, 33224-35-0; **24**, 33224-36-1; **25**, 33224-37-2; cyclooctatetraene, 629-20-9; 1-ethoxycarbonyl-1(1*H*)-azepine, 2955-79-5; tropone ethylene ketal, 17637-62-6; cycloocta-1,3-diene (*Z*,*Z*), 3806-59-5; cycloocta-1,5-diene (*Z*,*Z*), 1552-12-1; iodine azide, 14696-82-3.

The Reaction of Benzenediazonium-2-carboxylate with 1,1-Dimethyl-2,5-diphenyl-1-silacyclopentadiene[1]

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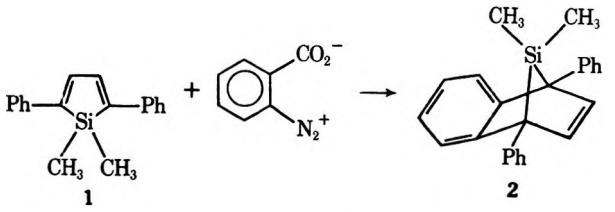
The attempted addition of benzyne, produced thermally from benzenediazonium-2-carboxylate, to 1,1-dimethyl-2,5-diphenyl-1-silacyclopentadiene (1) did not yield the expected Diels–Alder product, 2,3-benzo-7,7-dimethyl-1,4-diphenyl-7-silanorbornadiene (2). Instead, further reaction with benzenediazonium-2-carboxylate afforded an adduct (8) which had resulted from silicon–carbon bond cleavage concomitant with silicon–oxygen bond formation. While this reaction formally amounted to addition of the often proposed 1,4-dipolar species 3 to the silanorbornadiene, it was conclusively established that benzenediazonium-2-carboxylate is itself the attacking species. The driving force for this reaction is attributed to the great strength of the silicon–oxygen bond. The structure of 8 was determined by X-ray diffraction.

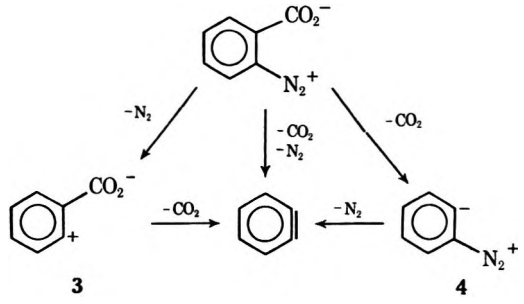
As part of a program which involves the preparation of silicon-bridged hydrocarbons, we undertook the synthesis of 2,3-benzo-7,7-dimethyl-1,4-diphenyl-7-silanorbornadiene (2) from 1,1-dimethyl-2,5-diphenyl-1-silacyclopentadiene (1) and benzyne. No particular difficulties were foreseen, as a similar addition between benzyne and 1,1-dimethyl-2,3,4,5-tetraphenyl-1-silacyclopentadiene had been reported[3] to proceed in yields up to 60%. However, when an equimolar solution of the hydrochloride salt of benzenediazonium-2-carboxylate, propylene oxide (to remove the hydrogen chloride),[4] and 1 were refluxed in 1,2-dichloroethane, much of the silacyclopentadiene was recovered unreacted, along with a small amount of a colorless adduct. Use of a threefold molar excess of the benzyne precursor afforded, after chromatography on silica gel, a 77% yield of the same colorless, crystalline solid, mp 278–279°, as the sole isolable product derived from the silacyclopentadiene.

The mass spectrum (base and parent ion *m/e* 458) and combustion analysis clearly indicated that the adduct was composed of the elements of one molecule of 1, one molecule of benzyne, and a molecule of benzenediazonium-2-carboxylate less a molecule of nitrogen. For an explanation of this type of adduct formation we turned to the mechanism of benzyne formation.



1 2

While it has been known for the last decade that benzenediazonium-2-carboxylate will thermally decompose to benzyne,[5] the detailed mechanism of this decomposition in solution has not been fully elucidated. Three possibilities must be considered: (a) concerted loss of carbon dioxide and nitrogen; (b) loss of nitrogen to afford the dipolar species 3 followed by loss of carbon dioxide or attack on some trapping agent before loss of carbon dioxide; and (c) initial loss of carbon dioxide to provide 4, which may either lose nitrogen or react directly with the trapping molecule.



3 4

Intermediate 4 has never been seriously implicated in this decomposition, but 3 has several times been suggested as a possible intermediate. Both Knorr[6] and Yaroslavsky[7] have isolated phthalimides from the reaction of isocyanides with benzenediazonium-2-carboxylate, and 3 has been postulated as the reactive intermediate which adds across the carbon–nitrogen multiple bond. The formation of phthalic anhydride from the reaction of nickel tetracarbonyl and benzenediazonium-2-carboxylate may also proceed through 3.[6] A search of the literature reveals that the only situation where 3, although in these cases generated from the pyrolysis of diphenyliodonium-2-carboxylate[8] or potassium 2-halogenobenzoates,[9] might be involved in an addition to a carbon–carbon multiple bond is in the reaction with benzyne itself to produce 3,4-benzocoumarins and xanthones. In each of these cases, the products could also be explained by a series of substitution reactions in which benzyne attacks benzenediazonium-2-carboxylate. However, benzocoumarin has never been observed during the decomposition of benzenediazonium-2-carboxylate.[10] Other evidence for the existence of 3 comes from trapping by nucleo-

(1) (a) Heterocyclopentadienes. II. For the previous paper in this series, see T. J. Barton and A. J. Nelson, *Tetrahedron Lett.*, 5037 (1939). (b) Presented in part at the 160th National Meeting of the American Chemical Society, Chicago, Ill., Sept 1970, ORGN 29.

(2) NASA Predoctoral Fellow, 1969–present.

(3) H. Gilman, S. G. Cottis, and W. H. Atwell, *J. Amer. Chem. Soc.*, **86**, 1596 (1964).

(4) For an example of the use of this particular technique in the synthesis of triptycene, see R. M. Roberts, J. C. Gilbert, L. B. Rodewald, and A. S. Wingrove, "An Introduction to Modern Experimental Organic Chemistry," Holt, Rinehart and Winston, New York, N. Y., 1969, pp 196–201.

(5) (a) M. Stiles and R. G. Miller, *J. Amer. Chem. Soc.*, **82**, 3802 (1960); (b) R. S. Berry, G. N. Spokes, and R. M. Stiles, *ibid.*, **82**, 5240 (1960); (c) M. Stiles, R. G. Miller, and U. Burckhardt, *ibid.*, **85**, 1792 (1963); (d) R. G. Miller and M. Stiles, *ibid.*, **85**, 1798 (1963); (e) L. Friedman and F. M. Logullo, *ibid.*, **85**, 1549 (1963).

(6) R. Knorr, *Chem. Ber.*, **98**, 4038 (1965).

(7) S. Yaroslavsky, *Chem. Ind. (London)*, 765 (1965).

(8) F. M. Beringer and S. J. Huang, *J. Org. Chem.*, **29**, 445 (1964).

(9) E. McNelis, *ibid.*, **28**, 3188 (1963).

(10) R. W. Hoffmann, "Dehydrobenzene and Cycloalkynes," Academic Press, New York, N. Y., 1967, p 77.

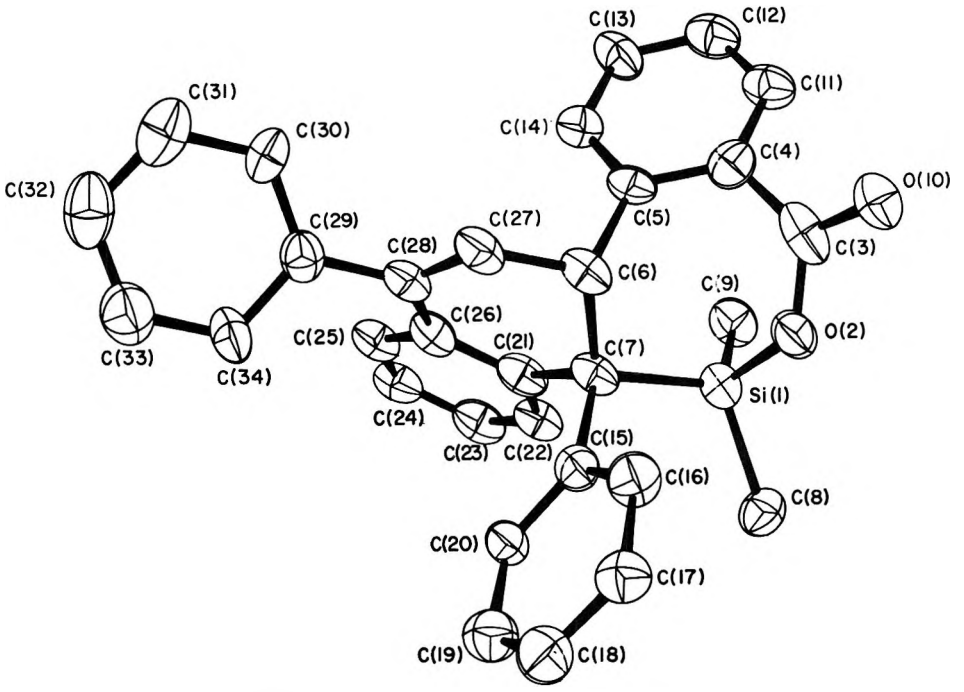
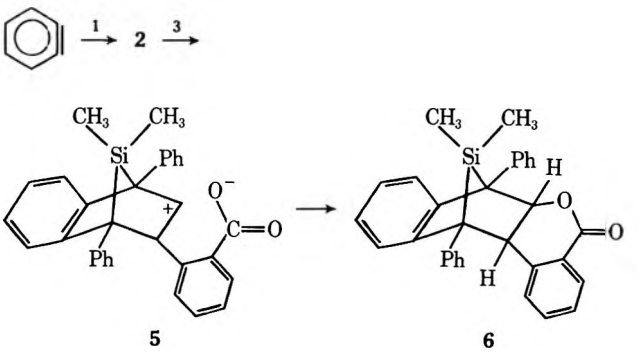


Figure 1.—The molecular structure of adduct 8.

philic solvents, *e.g.*, in water to provide salicyclic acid in 88% yield,[5a,11] and observed greater than unity ratios of nitrogen to carbon dioxide evolution upon decomposition of benzenediazonium-2-carboxylate in a variety of solvents in the absence of suitable trapping agents.[5a,c] Perhaps the most frequently quoted work which has been offered as evidence for the intermediacy of **3** (or some isomer of **3**) is that of Gompper.[12] When benzenediazonium-2-carboxylate was decomposed in acetonitrile–water–furan mixtures the ratio of products derived from water (salicylic acid) and furan (1,4-epoxy-1,4-dihydronaphthalene, from a Diels–Alder reaction with benzyne) was found to be dependent upon the water concentration but independent of the furan concentration. These results were interpreted as being consistent with the formation of both products from a common intermediate, namely **3** or some isomer of **3**.

In view of this information it was tempting to assign a structure such as **6** [ir 1729 (lactone carbonyl) and 1327 cm^{-1} (lactone C–O stretch)] as it is mechanistically simple to account for the inclusion of the elements of **3** in the product. However, although the striking upfield position of one of the *Si*-methyl groups (δ −0.33) in the nmr spectrum was in keeping with this assignment, a one-proton doublet at δ 5.78 (J = 6.8 Hz) was difficult to assign to anything other than an olefinic proton. Also this addition would represent the only suggested example of the trapping of intermediate **3** by a simple olefinic system. Current evidence has characterized 1,4-dipolar cycloaddition[13] as a two-step process proceeding through a zwitterionic intermediate such as **5**. However, it has been generalized that only dipolarophiles possessing strong nucleophilic or electrophilic reactivity will combine with 1,4 dipoles.[13] It would be quite difficult to rationalize these observations with the formation of **6**, as no pronounced reactivity of this type would be expected from either **1** or **2**. Lastly, and most importantly, there was no loss of CO_2 from the parent ion observed in the mass spectrum, as would be expected from **6**. Consequently it was deemed necessary to determine the structure of the reaction product by X-ray diffraction techniques.



5 **6**

Single crystals of the adduct from **1** and benzenediazonium-2-carboxylate suitable for X-ray analysis were grown from diisopropyl ether. The course of the analysis was routine and the details are given in the Experimental Section. A computer drawing of the final X-ray model is given in Figure 1.[14] The bond distances and angles (Tables I and II) agree satisfactorily with generally accepted values.[15] The seven-membered ring containing silicon and oxygen (atoms 1–7) is in a boat conformation. The silicon atom is tetrahedrally coordinated and the four atom fragments of the carboxyl group [O(2), C(3), C(4), and O(10)] and C(3), C(4), C(5), and C(6) are all planar. C(6) and C(7) are tetrahedral. The bond distances to C(7) all seem slightly long. The six-membered ring [C(6), C(7),

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(14) C. K. Johnson, ORTEP, Oak Ridge National Laboratory Report No. 3794, Oak Ridge, Tenn. (1965).

(15) "Tables of Interatomic Distances and Configurations in Molecules and Ions," The Chemical Society, London, 1958.

TABLE I

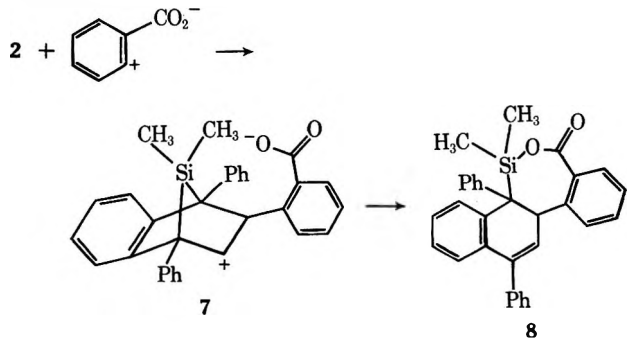
BOND DISTANCES, Å[a]

Si(1)-O(2)	1.685(4)	C(17)-C(18)	1.388(8)
Si(1)-C(8)	1.848(6)	C(18)-C(19)	1.394(9)
Si(1)-C(9)	1.862(6)	C(19)-C(20)	1.392(8)
Si(1)-C(7)	1.901(6)	C(20)-C(15)	1.391(6)
C(7)-C(15)	1.580(7)	C(21)-C(22)	1.384(7)
C(7)-C(21)	1.545(7)	C(22)-C(23)	1.433(8)
C(7)-C(6)	1.576(8)	C(23)-C(24)	1.400(9)
C(6)-C(5)	1.538(7)	C(24)-C(25)	1.370(8)
C(6)-C(27)	1.489(8)	C(25)-C(26)	1.395(7)
C(5)-C(4)	1.411(7)	C(21)-C(26)	1.415(8)
C(5)-C(14)	1.384(7)	C(26)-C(28)	1.467(7)
C(14)-C(13)	1.377(7)	C(27)-C(28)	1.348(7)
C(13)-C(12)	1.419(8)	C(28)-C(29)	1.476(8)
C(12)-C(11)	1.378(8)	C(29)-C(30)	1.398(8)
C(11)-C(4)	1.373(7)	C(30)-C(31)	1.375(8)
C(4)-C(3)	1.509(8)	C(31)-C(32)	1.385(9)
C(3)-O(10)	1.221(6)	C(32)-C(33)	1.414(10)
C(3)-O(2)	1.357(7)	C(33)-C(34)	1.383(9)
C(15)-C(16)	1.390(7)	C(34)-C(29)	1.405(7)
C(16)-C(17)	1.414(7)		

[a] The estimated standard deviation, as computed by the inverse least-squares matrix, is given in parentheses.

C(21), C(26), C(28), and C(27)] is fused to the seven-membered heterocyclic ring in a cis diequatorial manner. The hydrogen of C(6) is axial as is the phenyl ring [C(15) through C(20)]. The conformation about the double bond [C(27)-C(28)] is cis relative to the C(6)-C(28) ring. All four aromatic rings are planar within experimental error.

Therefore the adduct resulting from **1** and benzenediazonium-2-carboxylate is the siloxapinone **8**. In view of the previously mentioned proposals for the mechanism of thermal decomposition of benzenediazonium-2-carboxylate it appeared that a logical mechanism for the formation of **8** would involve attack on the olefinic bond of **2** by **3**, to generate **7**, followed by carboxylate anion attack upon the silicon atom. Given this mechanism, it is apparent from the stereochemistry of **8** that attack by the benzenium cation must be exo, as only this mode would result in the proper orientation for carboxylate attack upon the silicon atom. It would of course be possible for the reaction to proceed in a concerted fashion.



The isolation of this unique adduct (**8**) by a process which the similar reaction between cyclopentadiene and benzyne generated from benzenediazonium-2-carboxylate does not undergo[16] appears to indicate that a likely driving force is the formation of the silicon–oxygen bond, which is well established to be far stronger than the carbon–oxygen bond.[17] Upon consideration of the fact that the mechanism presented above for the formation of **8** does not depend upon the

TABLE II

BOND ANGLES[a]

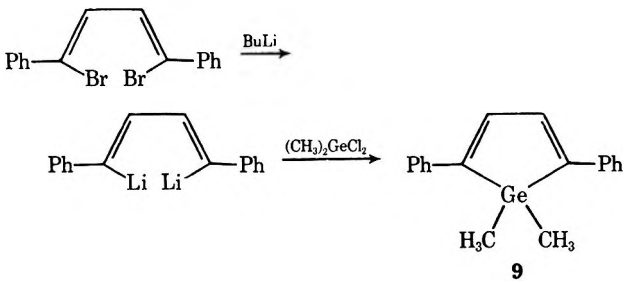
C(7)-S(1)-C(8)	113.3(3)
C(7)-Si(1)-O(2)	103.9(2)
C(7)-Si(1)-C(9)	114.0(2)
C(9)-Si(1)-O(2)	110.0(2)
C(9)-Si(1)-C(8)	110.8(3)
O(2)-Si(1)-C(8)	103.8(2)
Si(1)-O(2)-C(3)	127.4(4)
O(2)-C(3)-O(10)	118.4(6)
O(10)-C(3)-C(4)	123.4(5)
O(2)-C(3)-C(4)	118.0(4)
C(3)-C(4)-C(5)	121.4(5)
C(3)-C(4)-C(11)	116.7(5)
C(11)-C(4)-C(5)	121.6(5)
C(4)-C(11)-C(12)	120.2(5)
C(11)-C(12)-C(13)	119.1(5)
C(12)-C(13)-C(14)	119.5(6)
C(13)-C(14)-C(5)	121.8(5)
C(14)-C(5)-C(4)	117.3(5)
C(14)-C(5)-C(6)	122.4(5)
C(4)-C(5)-C(6)	120.0(5)
C(5)-C(6)-C(7)	113.1(4)
C(5)-C(6)-C(27)	112.6(5)
C(27)-C(6)-C(7)	110.0(4)
C(6)-C(7)-Si(1)	108.0(3)
C(6)-C(7)-C(15)	108.9(4)
C(6)-C(7)-C(21)	109.2(5)
Si(1)-C(7)-C(15)	107.3(3)
Si(1)-C(7)-C(15)	114.3(3)
C(15)-C(7)-C(21)	108.7(3)
C(7)-C(15)-C(16)	118.5(4)
C(7)-C(15)-C(20)	122.0(4)
C(16)-C(15)-C(20)	119.3(5)
C(15)-C(16)-C(17)	120.3(5)
C(16)-C(17)-C(18)	118.9(6)
C(17)-C(18)-C(19)	120.8(6)
C(18)-C(19)-C(20)	119.2(5)
C(19)-C(20)-C(15)	120.9(5)
C(6)-C(27)-C(28)	123.2(5)
C(27)-C(28)-C(29)	120.8(5)
C(27)-C(28)-C(26)	119.9(5)
C(29)-C(28)-C(26)	119.2(5)
C(28)-C(26)-C(25)	123.2(5)
C(28)-C(26)-C(21)	119.0(5)
C(21)-C(26)-C(25)	117.6(5)
C(26)-C(25)-C(24)	123.3(6)
C(25)-C(24)-C(23)	119.8(6)
C(24)-C(23)-C(22)	117.7(6)
C(22)-C(21)-C(26)	119.7(5)
C(22)-C(21)-C(7)	120.6(5)
C(7)-C(21)-C(26)	119.4(5)
C(28)-C(29)-C(34)	119.5(5)
C(28)-C(29)-C(30)	122.5(5)
C(34)-C(29)-C(30)	117.8(6)
C(29)-C(34)-C(33)	119.3(6)
C(34)-C(33)-C(32)	122.8(6)
C(33)-C(32)-C(31)	116.4(6)
C(32)-C(31)-C(30)	121.5(7)
C(31)-C(30)-C(29)	121.9(6)

[a] The estimated standard deviation, as estimated from the inverse least-squares matrix, is given in parentheses.

(16) This reaction provides the normal Diels–Alder adduct in 78% yield: F. M. Logullo, A. Seitz, and L. Friedman, personal communication quoted in ref 10, p 210.

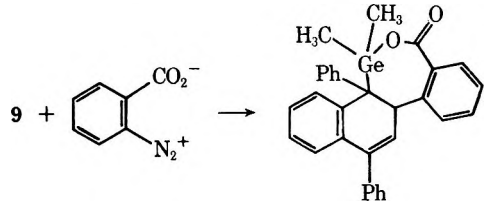
(17) The observed bond energy of a Si–O bond is *ca.* 112 kcal/mol as compared with a value of 85.5 kcal/mol for a C–O bond: E. A. V. Ebsworth in "Organometallic Compounds of the Group IV Elements," A. G. MacDiarmid, Ed., Marcel Dekker, New York, N. Y., 1968, p 51.

silicon–oxygen bond formation for a driving force, it was decided to put that point to a test. The intermediate strength of a germanium–oxygen bond[17] compared with the carbon–oxygen and silicon–oxygen bonds made the prospect of performing this reaction with a system where silicon had been replaced by germanium especially intriguing. For this purpose we prepared 1,1-dimethyl-2,5-diphenyl-1-germacyclopentadiene (**9**)[18] by a route exactly analogous to that used by Atwell and Weyenberg[19] for the synthesis of 1,1-dimethyl-2,5-diphenyl-1-stannacyclopentadiene.



9

If the thermodynamics of this bond formation were really the controlling factor in the trapping of **3**, we might expect not to obtain any products resulting from addition of **3**. However, when the reaction between benzenediazonium-2-carboxylate and **9** was run under exactly the same conditions as for **1**, a single isolable product was obtained whose spectra and elemental analysis corresponded to **10**. The nmr spectrum of **10** virtually identical with that of **8** [δ *ca.* 7.75–7.1 (complex aromatic multiplet, 18 H), 5.85 (olefin doublet, J = 6.8 Hz, 1 H), 4.84 (methine doublet, J = 6.8 Hz), 0.33 (methyl singlet, 3 H), and −0.12 (methyl singlet, 3 H)]. The mass spectrum showed a strong parent ion and a *very* small fragment ion resulting from loss of carbon dioxide, in keeping with structure **10**.



10

Although the use of **3** was mechanistically convenient, the very inability of this mechanism to account for the driving force derived from Si–O or Ge–O bond formation argued against its operation. Therefore it appeared wise to reevaluate the reported evidence for the two-step decomposition of benzenediazonium-2-carboxylate. In most instances it appears that **3** is invoked simply as a matter of convenience and to be in step with the contemporary thought regarding the reactions of aryldiazonium cations. Indeed, if we center our attention upon the work of Gompper[12] (*vide supra*), it may be easily shown that his results can be equally well explained by a combination of bimolecular displacement of nitrogen by water to afford salicylic acid and simultaneous loss of nitrogen and carbon dioxide to give benzyne, which then reacts solely with furan. Why displacement of nitrogen by water through a one-step process was not considered may be understood only when one examines the history of the mechanism of denitrogenation of benzenediazonium salts in solution.

In 1942, Waters[20] first proposed that the benzenediazonium cation reacted through the unstable phenyl cation intermediate with no participation of the adding nucleophile in the rate-determining step. This two-step mechanism was generally accepted because of its ability to explain the lack of anion or acidity dependence and because of the observed first-order kinetics of the reaction.[21] However, in 1969 Lewis reported that in the reaction of diazonium salts with nucleophiles rate accelerations could be observed from a variety of added salts.[22] These results were therefore interpreted as a result of a bimolecular displacement reaction which consequently did not involve any intermediate such as the phenyl cation. Since Lewis found the relative reactivities of the different nucleophiles toward the diazonium ion to vary only slightly, it was pointed out that the general unselectivity led to an inherent difficulty in distinguishing between a single-step reaction and a two-step reaction which proceeded through a reactive intermediate. Interestingly, Swain has recently presented rather convincing evidence that this reaction proceeds by rate-determining unimolecular cleavage to a singlet phenyl cation.[23] This conclusion was reached on the basis of results which showed only unrearranged products, first-order rate constants which varied less than tenfold with anion change, and large secondary kinetic hydrogen isotope effects for each ortho position. The situation therefore appears to be somewhat in a state of flux but it is now obvious why, in light of the then-accepted Waters' mechanism, Gompper did not consider a nitrogen displacement reaction in the production of salicylic acid from benzenediazonium-2-carboxylate.

In order to determine whether the 7-silanorbornadiene (**2**) was reacting directly with benzenediazonium-2-carboxylate or with some intermediate (*e.g.*, **3**) derived from benzenediazonium-2-carboxylate, it would be desirable to prepare **2** and attempt to react it with benzenediazonium-2-carboxylate under conditions where the inner salt does not decompose. To achieve this purpose the method of benzyne generation chosen was the lead tetraacetate oxidation of 1-aminobenzotriazole (**11**).[24] However, reaction of the silole **1** with benzyne generated in this fashion yielded only 1,4-diphenylnaphthalene (**12**) upon normal work-up. While this represents a drastic difference in thermal stability between **2** and the tetraphenyl adduct reported by Gilman,[3] we have often noted that the Diels–Alder adducts of **1** and acetylenes were far less stable than the analogous adducts resulting from 1,1-dimethyl-2,3,4,5-tetraphenyl-1-silacyclopentadiene.[25] We

(18) The photochemical properties, but not the synthesis, of this "germole" were briefly reported in ref 1 and A. J. Nelson, J. C. Clardy, and T. J. Barton, 159th National Meeting of the American Chemical Society, Houston, Texas, Feb 1970, ORGN-92.

(19) W. H. Atwell, D. R. Weyenberg, and H. Gilman, *J. Org. Chem.*, **32**, 885 (1967).

(20) W. A. Waters, *J. Chem. Soc.*, 266 (1942).

(21) D. F. DeTar and A. R. Ballentine, *J. Amer. Chem. Soc.*, **78**, 3916 (1956).

(22) E. S. Lewis, L. D. Hartung, and B. M. McKay, *ibid.*, **91**, 419 (1969).

(23) C. G. Swain, J. E. Sheats, K. G. Harbison, and D. G. Gorenstein, 160th National Meeting of the American Chemical Society, Chicago, Ill., Sept 1970, ORGN 34.

(24) C. D. Campbell and C. W. Rees, *Proc. Chem. Soc.*, 296 (1964).

(25) T. J. Barton, unpublished observations.

have attributed this to the fact that with phenyls only at the bridgeheads of the silanorbornadiene, as in **2**, these rings are much less restricted with regard to their ability to properly orient themselves to stabilize cleavage of the bridge. When the reaction of **1** and benzyne, generated from 1-aminobenzotriazole, was performed at −78° and the reaction mixture was examined by nmr (at *ca.* −50°), it was revealed that *ca.* one-half of the silole **1** was consumed and two new singlets of equal intensity appeared slightly upfield, therefore presumably corresponding to the two methyl groups in **2** (Figure 2). After establishing that the relative concentrations of **1** and **2** did not noticeably change after several hours at −50°, a slight excess of benzenediazonium-2-carboxylate was added to the reaction mixture and the mixtrue was allowed to stand at 0° overnight. Work-up of the reaction afforded both **12** and **8** in *ca.* a 2:1 ratio. As the solubility of benzenediazonium-2-carboxylate in the solvent used, dichloromethane, was probably not high at these temperatures, it is likely that there was an insufficient amount of this reagent to react with **2** before the thermal decomposition of **2** to **12**. The key point is that **2** apparently reacts with benzenediazonium-2-carboxylate to form the siloxapinone **8** *at temperatures where benzenediazonium-2-carboxylate is quite stable.* Possibly more conclusive evidence that **8** arises solely from reaction between **2** and benzenediazonium-2-carboxylate comes from experiments where **2** was first formed from **1** and the benzotriazole **11** at low temperatures, benzenediazonium-2-carboxylate was added, and the reaction mixture was allowed to warm slightly below room temperature. After only 10 min at 20° gas evolution from this sample was essentially quantitative for loss of only nitrogen. At the same time and under identical thermal conditions, solutions containing benzenediazonium-2-carboxylate and (a) only solvent (dichloroethane), (b) lead diacetate, (c) lead tetraacetate and lead diacetate, or (d) **1** evolved either no gas or only a *very* small fraction of the amount obtained from the sample containing preformed **2**. Therefore, it can be conclusively stated that **8** is the result of reaction between **2** and benzenediazonium-2-carboxylate with *no* involvement of any intermediate derived from prior decomposition of the latter named compound.

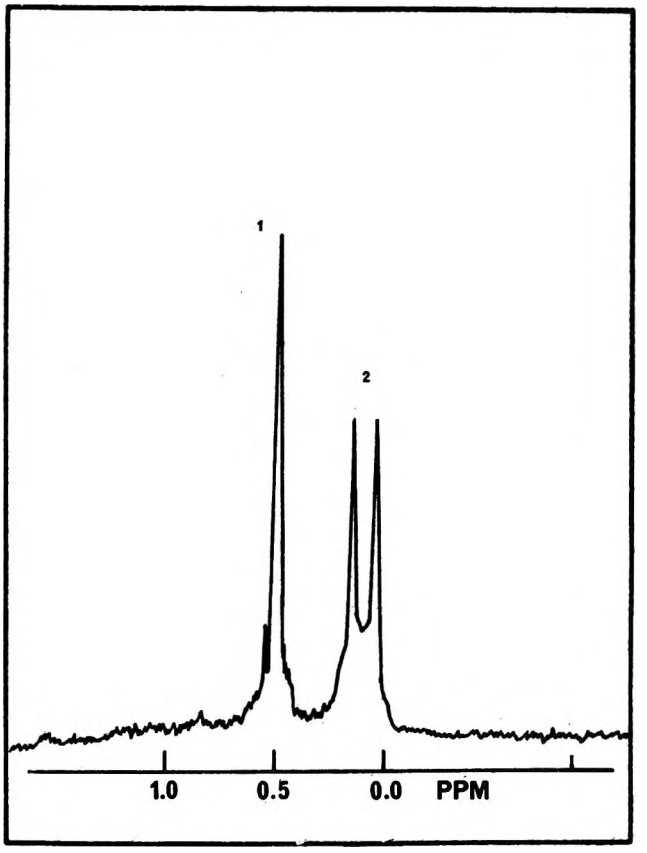
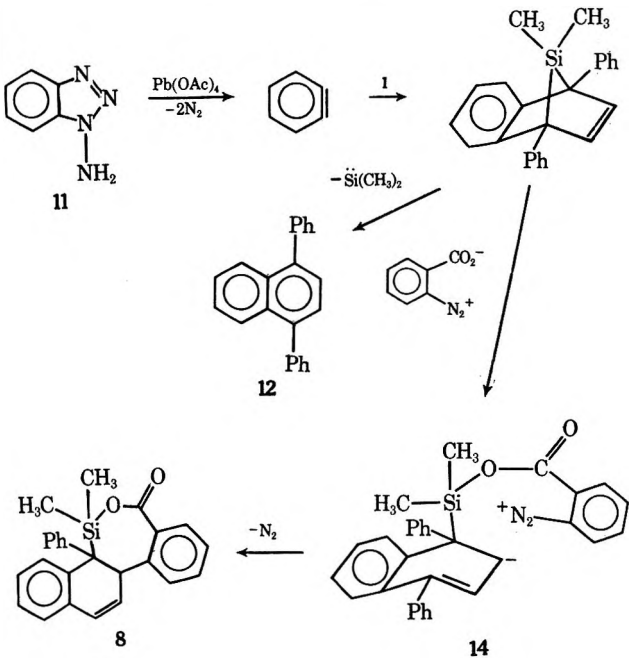
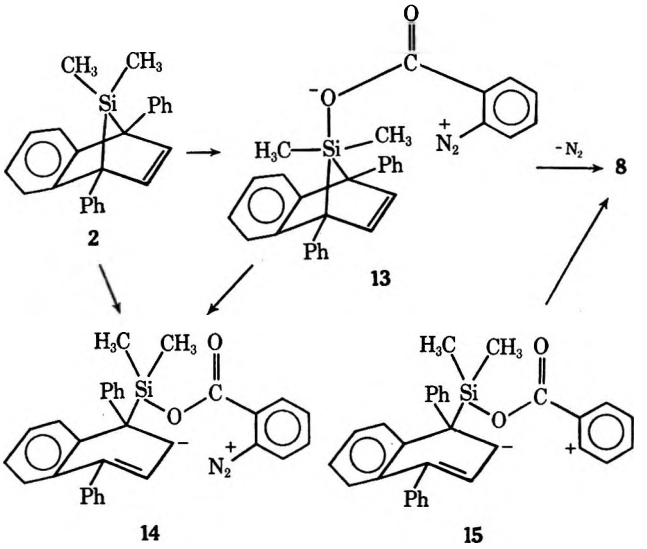


Figure 2.—60-Hz nmr spectrum of a mixture of **1** and **2** at *ca.* −50°.

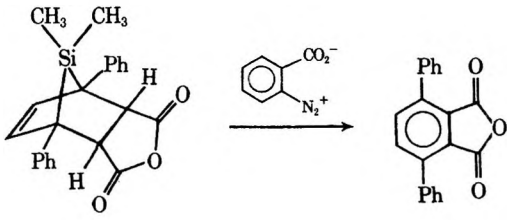
After attack of **2** by the carboxylate anion of benzenediazonium-2-carboxylate we cannot know the intimate details of this reaction. Several courses are available: (a) formation of a pentavalent silicon anion (**13**) which may either go directly to **8** or collapse to the allylic anion (**14**); (b) going directly by carbon displacement to **14** followed either by nitrogen loss to **15**, and then final bond formation to give **8**, or displacement of nitrogen by the anionic portion to provide **8** directly; or (c) an essentially concerted process leading





to **8**. No decision can be made at this time as to which terminal route this reaction follows.

The discovery of a high-yield reaction with benzenediazonium-2-carboxylate which could easily have been explained in mechanistic terms involving the intermediate **3**, but instead has been shown to involve only benzenediazonium-2-carboxylate itself, casts serious doubt upon the evidence which has been offered for the existence of **3** in the thermal decomposition of this useful benzyne precursor. However, it should be noted that this work has no bearing upon the mechanism of benzyne formation from benzenediazonium-2-carboxylate, since the reaction of **2** → **8** and the corresponding reaction leading to **10** do not involve decomposed benzenediazonium carboxylate. We seem to have accidentally hit upon an optimum system for this type reaction which depends not only on the presence of a bridged silicon or germanium but also on the particular substitution of the bicyclic system. As mentioned previously,[3] 1,1-dimethyl-2,3,4,5-tetraphenyl-1-silacyclopentadiene does not undergo this reaction—presumably for steric reasons. The same is true for 1,1,2,3,4,5-hexaphenyl-1-silacyclopentadiene.[26] Also, the maleic anhydride adduct of **1**, **16**, gives no isolable products resulting either from the addition of benzyne or benzenediazonium-2-carboxylate; indeed the reaction of **16** and benzenediazonium-2-carboxylate afforded reasonable yields of 1,4-diphenylphthalic anhydride under conditions where **16** is quite stable alone. The nature of this reaction, including the dehydrogenation step, is under investigation.



16

Experimental Section[27]

X-Ray Data Collection.—Single crystals of **8** can be grown from isopropyl ether as long needles with square cross sections. Cubes roughly 0.08 mm on an edge were cut from the needles for diffraction work. No crystal decomposition was noticed during the course of the study.

Weissenberg photographs displayed $2/m$ reciprocal lattice symmetry. The systematic absence $0k0$ for k odd and $h0l$ for $h+l$ odd establish the space group as $P2_1/n$. The goniometer head was then transferred to a fully atutomated Hilger–Watts four circle diffractometer. Lattice constants were determined using Cu Kα radiation (1.5418 Å). The unit cell dimension are a = 10.725 ± 0.003 Å, b = 10.775 ± 0.003 Å, c = 20.888 ± 0.005 Å, and β = 87.76 ± 0.08°. The calculated density is 1.26 g/cm³ for Z = 4 and molecular formula $C_{31}H_{26}O_2Si$. The measured density (flotation) was 1.24 g/cm³.

The intensity data were collected using the stationary-crystal stationary-counter technique with two 5-sec backgrounds and a 10-sec peak height count. Ni-filtered Cu Kα radiation was employed. Two hundred reflections were measured with the θ–2θ scan mode and these were used to convert the peak height intensities to integrated intensities. The net intensity of each reflection was assigned an eror, $\sigma(I)$ = [total count + background + 5% (total count)² + 5% (background)²]$^{1/2}$. Reflections for which $\sigma(I)/I \geq 0.33$, or for which a negative net count was observed, were omitted from refinement. These omitted reflections constituted roughly one-third of the total reflections measured. Periodically monitored check reflections showed no decomposition. Since μ = 10 cm^{-1} no absorption corrections were made. The 2136 observed reflections were corrected for Lorentz and polarization factors to give F_o^2.

Solution and Refinement.—A three-dimensional Patterson synthesis gave the Si coordinates unambiguously. The 33 remaining nonhydrogen atoms were located in subsequent electron density syntheses. Several cycles of full-matrix least-squares refinement in which all atomic coordinates were varied and all atoms had anisotropic thermal parameters (307 total parameters of which 200 could be varied in each cycle) reduced the conventional discrepancy index, $R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$ to 0.089 for the 2136 independent reflections.[28] Hydrogen atoms were not included in these calculations.

The weighted discrepancy index, $wR = (\Sigma w||F_o| - |F_c||^2/\Sigma w|F_o|^2)^{1/2}$, was 0.113. The w's were calculated from $\sigma(F_o) = (F_o^2 + \sigma(I)/Lp)^{1/2} - |F|_o$. A final electron density difference map showed no peaks greater than 0.8 e/Å.³ Some of these were attributed to hydrogens but a detailed analysis was not attempted. The final atomic parameters are given in Table III[29] along with the least squares estimated standard deviations. The anisotropic thermal parameters are listed in Table IV.[29] Bond distances and angles are given in Tables I and II.

Reaction of Benzenediazonium-2-carboxylate with 1.—A mixture of 2.02 g (7.7 mmol) of 1,1-dimethyl-2,5-diphenyl-1-silacyclopentadiene,[19] 4.26 g (23.2 mmol) of benzenediazonium-2-carboxylate hydrochloride, and 2.24 g (38.6 mmol) of propylene oxide in 1,2-dichloroethane (40 ml) was stirred at reflux for 2 hr.[4] The solvent was removed *in vacuo* and the resultant solid was redissolved with difficulty in the minimum amount of chloroform. The solution was put on a 30-in. (1.15-in. i.d.) chromatographic column of silica gel packed in hexane. The column was first flushed with hexane to remove any hydrocarbon byproducts and then eluted with methylene chloride. Continuous monitoring by tlc revealed the complete absence of starting material and only one product. The methylene chloride fractions were combined and the solvent was removed *in vacuo* to afford 2.72 g (77%) of yellow-brown product which was shown to be at least 90% pure by nmr. A single recrystallization from acetone yielded 1.52 g (43%) of white, crystalline **8**, mp 275–276°. Repeated recrystallization from acetone gave analytically pure material, mp 278–279°.

Anal. Calcd for $C_{31}H_{26}SiO_2$: C, 81.18; H, 5.71; Si, 6.13. Found: C, 81.04; H, 5.67; Si, 6.27.

1,1-Dimethyl-2,5-diphenyl-1-germacyclopentadiene (9).[18]—*n*-Butyllithium, 13.0 ml of a 1.6 *M* solution in hexane, was added dropwise under argon to a stirred, ice-bath cooled solution of 1,4-dibromo-1,4-diphenylbutadiene,[19] 3.62 g (10 mmol), in 40 ml of ether freshly distilled from lithium aluminum hydride. All glassware was previously flame dried under argon. After the addition was complete, the reaction mixture was allowed to warm to room temperature and then added dropwise to a stirred solution of dimethylgermanium dichloride, 1.77 g (10 mmol), in 80 ml of dry ether also under an argon atmosphere. The resulting yellow solution was percolated through a short column packed with neutral alumina to remove the lithium chloride. The residue was crystallized from ether–hexane to afford yellow, crystalline **9**: yield 2.35 g (65%); mp 128°; nmr ($CDCl_3$) δ 0.68 (methyl singlet, 6 H), 7.15–7.40 (complex multiplet for both aromatic and olefinic protons, 12 H); mass spectrum[30] (16 eV) m/e

(26) H. Gilman, S. G. Cottis, and W. H. Atwell, *J. Amer. Chem. Soc.*, **86**, 5584 (1964). We have confirmed this result by attempting to react the Diels–Alder adduct of 1,1,2,3,4,5-hexaphenyl-1-silacyclopentadiene and benzyne with benzenediazonium-2-carboxylate. No reaction took place.

(27) Melting points are uncorrected. The analyses were performed by Ilse Beetz, Mikroanalytisches Laboratorium, 8640 Kronach, Postfach 460, West Germany.

(28) W. R. Busing, K. O. Martin, and A. A. Levy, ORFLS, A Fortran Crystallographic Least-Squares Program, ORNL-TM-305 (The Oak Ridge National Laboratory, Oak Ridge, Tenn.), 1962.

(29) Listings of structure factors and atomic and thermal parameters (Tables III and IV) 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 author, title of article, volume, and page number. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche.

(30) We thank the National Science Foundation for funds contributed toward the purchase of an Atlas CH-4 mass spectrometer.

310 (17%, parent ion, Ge^{76}), 308 (100%, Ge^{74}), 307 (17%, Ge^{73}), 306 (75%, Ge^{72}), 304 (50%, Ge^{70}), 206 (100%).

Anal. Calcd for $C_{18}H_{18}Ge$: C, 70.44; H, 5.91. Found: C, 70.61; H, 6.12.

Reaction of Benzenediazonium-2-carboxylate with 9.—A solution consisting of 0.731 g (2.1 mmol) of **9**, 1.44 g (7.8 mmol) of benzenediazonium-2-carboxylate hydrochloride, and 1.2 ml of propylene oxide in 30 ml of 1,2-dichloroethane was refluxed for 2 hr. The dark reaction product was filtered through silica gel, the solvent was removed *in vacuo*, and the residue was crystallized from acetone to afford 0.155 g of white, crystalline **10**, mp 254–262°. A second crop of 0.108 g was obtained from addition of pentane to the filtrate, yield 0.263 g (0.48 mmol, 23%). Repeated recrystallization from acetone gave analytically pure material: mp 267.5–269.5°; ir absorption 1682 (C=O), 1274 (CO), 1118 cm (GeO?).

Anal. Calcd for $C_{31}H_{26}GeO_2$: C, 74.00; H, 5.21; Ge, 14.43. Found: C, 74.05; H, 5.34; Ge, 14.35.

Preparation of 2 from 1-Aminobenzotriazole (11)[31] and 1.—A solution containing 0.444 g (3.7 mmol) of 1-aminobenzotriazole (**11**) in 10 ml of dry dichloromethane was added dropwise to a stirred solution of 1.64 g (3.7 mmol) of lead tetraacetate, 0.96 g (3.7 mmol) of **1**, and *ca.* 15 ml of dry dichloromethane under nitrogen at −78°. After 40 min the addition was complete and an aliquot was removed for low-temperature nmr investigation. Two new singlets at δ 0.04 and 0.14 corresponding to the nonequivalent methyls in **2** (Figure 2) were observed. The reaction mixture was then warmed to 0° while simultaneously adding 0.39 g (2.6 mmol) of benzenediazonium-2-carboxylate.[5c] The mixture was heterogeneous and stirring was difficult. After allowing the reaction mixture to stand under N_2 at 0° for 8 hr, the mixture was worked up by immediate filtration through silica gel, evaporation of solvent *in vacuo*, and chromatography on a 2.3 × 45 cm column packed with silica gel in hexane: fraction A, hexane eluent, 0.320 g (1.22 mmol, 33%) of **1**; fraction B, 5% ether–hexane, 0.306 g (1.1 mmol, 49%) of **13**; fraction C, 20% ether–hexane, 0.122 g (15%) of **8**, mp 277–279°.

Reaction of 11 and 1 with Room Temperature Work-Up.—A solution containing 0.350 g (2.89 mmol) of 1-aminobenzotriazole (**11**) in 30 ml of dry dichloromethane was added dropwise to a stirred solution of 1.512 g (2.93 mmol) of lead tetraacetate and 0.757 g (2.89 mmol) of **1** in 50 ml of dry dichloromethane at 0°. After *ca.* 40 min, the addition was complete and gas evolution had ceased. The reaction mixture was immediately filtered through silica gel and the solvent was removed *in vacuo*. Chromatography of the residue on a 2.2 × 30 cm silica gel column packed in hexane afforded two fractions: 0.14 g (18.5%) of yellow, crystalline **1**, mp 131–133° (lit.[19] mp 130–133°), and 0.297 g (36.8%) of white, crystalline **12**, mp 132–134° (lit.[32] mp 134–135°, *m/e* 280).

Reaction of 2 with Benzenediazonium-2-carboxylate.—A solution containing 0.195 g (1.5 mmol) of **11** in 10 ml of dry 1,2-dichloroethane was added dropwise to a stirred solution of 0.390 g (1.5 mmol) of **1** and 0.626 g (1.41 mmol) of lead tetraacetate in 10 ml of dry 1,2-dichloroethane held at −50° under nitrogen. After completion of addition the reaction vessel (flask A) was removed from the Dry Ice bath and placed in a 20° water bath. At the same time two flasks (flasks B and C), each containing 20 ml of dry 1,2-dichloroethane, were lowered into the same water bath. To each of the three flasks was then added 0.170 g (1.15 mmol) of dry benzenediazonium-2-carboxylate and to flask B was added 0.400 g (1.5 mmol) of lead diacetate. The three flasks were immediately capped with a condenser and a gas outlet tube which led in each case to a 50-ml gas burette filled with water and having a leveling bulb. Each of the mixtures was stirred magnetically. The evolution of gas from flask A was essentially complete after 10 min, during which time 11.9 ml (0.484 mmol) of gas was collected. Assuming that a maximum of 50% **2** had been formed, this represented 65% of the theoretical volume of nitrogen to be expected with no correction being made for solubility. During the same time period flasks B and C gave off *no* gas. After stirring the three solutions for 40 min at 20°, 0.176 g (0.67 mmol) of **1** was added to flask C and a catalytic amount of lead tetraacetate was added to flask B. No evolution of gas from new flask C was observed over a 5-hr period. Slow gas evolution from new flask B was, however, observed—15.6 ml (0.64 mmol) after 4.2 hr but only 0.9 ml (0.037 mmol) after 10 min. Isolation of **8** from flask A by filtration through silica gel, evaporation of the solvent *in vacuo*, and crystallization of the residue from hexane–methanol afforded 0.251 g (0.55 mmol) of **8**, mp 275–277°). Therefore, based on isolated **8**, the 11.9 ml (0.484 mmol) of nitrogen collected represented 88% of theoretical. Thin layer chromatography of the solid revealed the absence of **12**. This is probably due to the homogeneity of the reaction mixture at this higher temperature and the resultant more efficient stirring.

Reaction of 1 with Maleic Anhydride.—A mixture of 1.31 g (5 mmol) of **1** and 0.49 g (5 mmol) of maleic anhydride was refluxed for several minutes in benzene (*ca.* 15 ml). The solution was cooled and filtered to afford 1.80 g (5 mmol, 100%) of white, crystalline **16**: mp 179–181°; nmr ($DCCl_3$) δ 0.12 (methyl singlet, 3 H), 0.18 (methyl singlet, 3 H), 4.38 (singlet methine α to carbonyl, 2 H), 6.62 (vinyl singlet, 2 H), 7.33 (singlet, aromatic, 10 H); ir (KBr) 5.40 and 5.65 (anhydride carbonyl), 8.20 μ (anhydride C–O stretch). In the mass spectrometer **16** apparently undergoes a retrograde Diels–Alder reaction, as the spectrum observed is essentially that of **1**. The highest *m/e* observed is 300, corresponding to 1,4-diphenylphthalic anhydride, but this peak has an intensity of *ca.* 0.07% of the base peak at *m/e* 262 (**1**).

Reaction of 16 and Benzenediazonium-2-carboxylate.—A solution containing 0.525 g (1.46 mmol) of 7,7-dimethyl-1,4-diphenyl-2,3-dicarboxy-7-sila-5-norbornene anhydride (**16**) and 0.22 g (1.49 mmol) of dry benzenediazonium-2-carboxylate in *ca.* 25 ml of dry 1,2-dichloroethane was stirred at 15–20° for 2.7 hr. Gas evolution from the reaction was measured using a gas burette and leveling bulb filled with water. During a period of 8 min, 7.3 ml (0.297 mmol) of gas were evolved. The evolution ceased after 62 min, giving a total gas volume of 24.2 ml (1 mmol). The mixture was then filtered through silica gel using ether, the solvent was evaporated *in vacuo*, and three fractions were separated by chromatography on a 2.8 × 25 cm column of silica gel packed in hexane: fraction A, 25% ether–hexane, 0.162 g (0.54 mmol, 37%) of 1,4-diphenylphthalic anhydride, mp 223–225°, recrystallized to 227° (lit.[33] mp 228–230°), *m/e* 300; fraction B, 10% acetone–ether; fraction C, methanol. B and C gave only uncharacterizable tars.

Registry No. **1**, 7688-03-1; **8**, 33069-00-0; **9**, 28124-19-8; **10**, 33070-29-0; **16**, 33122-21-3; benzenediazonium carboxylate, 1608-42-0.

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Revision of Azoxy Assignments in LL-BH872α and Elaiomycin Based on Circular Dichroism Studies on Synthetic Azoxy Compounds

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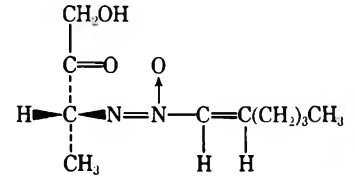
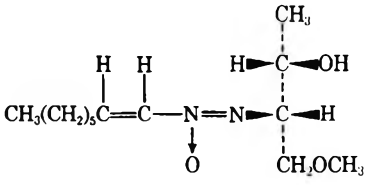
The previous cis and trans assignments of the azoxy chromophores in elaiomycin and LL-BH872α, respectively, have been shown to be in error. Both optical antipodes of *ONN*-1-cyclohexylazoxyethane have been prepared and the synthetic compounds have the same configuration of the azoxy chromophore as the two natural products as shown by CD curves. The optical antipodes of *ONN*-1-phenylazoxyethane have also been prepared. The CD curves of these materials are complex; nevertheless an assignment of the azoxy Cotton effect has been made. The rotational strength of this Cotton effect is greatly enhanced due to coupling between the azoxy and homoconjugated phenyl systems.

The antibiotics LL-BH872α and elaiomycin have been described[1] as (3*R*)-1-hydroxy-3-(1′-*cis*-hexenyl-*trans*-azoxy)-2-butanone and (2*S*,3*S*)-4-methoxy-3-(1′-*cis*-octenyl-*cis*-azoxy)-2-butanol, respectively.

The configurational assignments of the azoxy chromophores in these natural products were based on the notion that the configuration of the adjacent asymmetric carbon atoms in each material was the same (D). In fact, the carbon atoms in question are of opposite configuration. The original correlations of these asymmetric centers were made with the amino acids D-alanine[2] and D-threonine,[3] respectively, but different rather than corresponding substituents were related with the amino acid carboxyl groups. Specifically, the hydroxy methyl ketone substituent of LL-BH872α, I (which corresponds to the ethanolic substituent of elaiomycin II), was related to the carboxyl group of D-alanine while the methyl methyl ether of substituent of II (corresponding to the methyl substituent of I) was related to the carboxyl group of D-



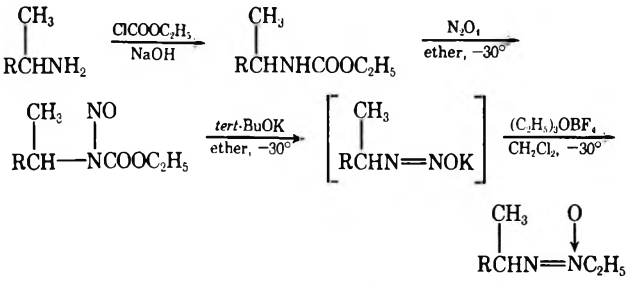
I



II

threonine. This pitfall, although overlooked in the original assignments of configuration in LL-BH872α and elaiomycin, is well known,[4] and Neuberger[5] suggested a simple method to avoid it, namely, that in correlations with amino acids the substituent of the higher state of oxidation should be deemed to have been formed by replacing the carboxyl group of the amino acid. Since the asymmetric carbon atoms adjacent to the azoxy chromophores in I and II are of opposite absolute configuration, the observed opposite Cotton effects of azoxy chromophores in these compounds are normal and the invocation of opposite configurations of these chromophores was in error.

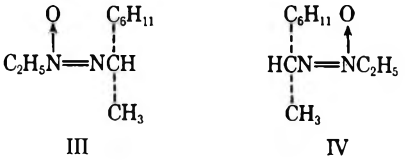
Recently Moss and Landon[6] described useful methods which are outlined below for the preparation of azoxy compounds. With the idea in mind of examining the



azoxy assignments in the antibiotics I and II, we prepared both optical antipodes of the azoxy compounds where the R substituents were cyclohexyl and phenyl groups, respectively.

As was anticipated, we had more trouble with the isolation and purification of the cyclohexyl compound than with those of the phenyl series. The urethanes of both series were low-melting solids which yielded readily to purification by adsorption chromatography. The phenyl nitrosourethanes could be obtained analytically pure by partition chromatography over diatomaceous earth using the system heptane saturated with acetonitrile followed by low-pressure, short-path distillation. The corresponding cyclohexyl compounds were not amenable to either low pressure distillation or glc because of their instability and consequently we could not obtain analytically pure samples of these intermediates. Fortunately, the azoxy compounds of the cyclohexyl series are stable compounds and may be purified by glc.

The compounds (*S*)-*ONN*-1-cyclohexylazoxyethane[7] and its R enantiomorph are represented by the Fisher projections III and IV. The CD curves of compounds



III IV

(1) W. J. McGahren and M. P. Kunstmann, *J. Amer. Chem. Soc.*, **92**, 1587 (1970).

(2) W. J. McGahren and M. P. Kunstmann, *ibid.*, **91**, 2808 (1969).

(3) C. L. Stevens, B. T. Gillis, and T. H. Haskell, *ibid.*, **81**, 1435 (1959).

(4) D. W. Slocum, D. Sugarman, and S. P. Tucker, *J. Chem. Educ.*, **48**, 597 (1971).

(5) A. Neuberger, *Advan. Protein Chem.*, **4**, 297 (1948).

(6) R. A. Moss and M. J. Landon, *Tetrahedron Lett.*, 3869 (1969).

(7) NNO denotes that the group attached to NO is unprimed whereas ONN would denote that this group would be primed.[8]

(8) Former Chemical Abstracts practice as stated in the introduction to Vol. 56 (1961) defined the unprimed group as always being attached to NO.

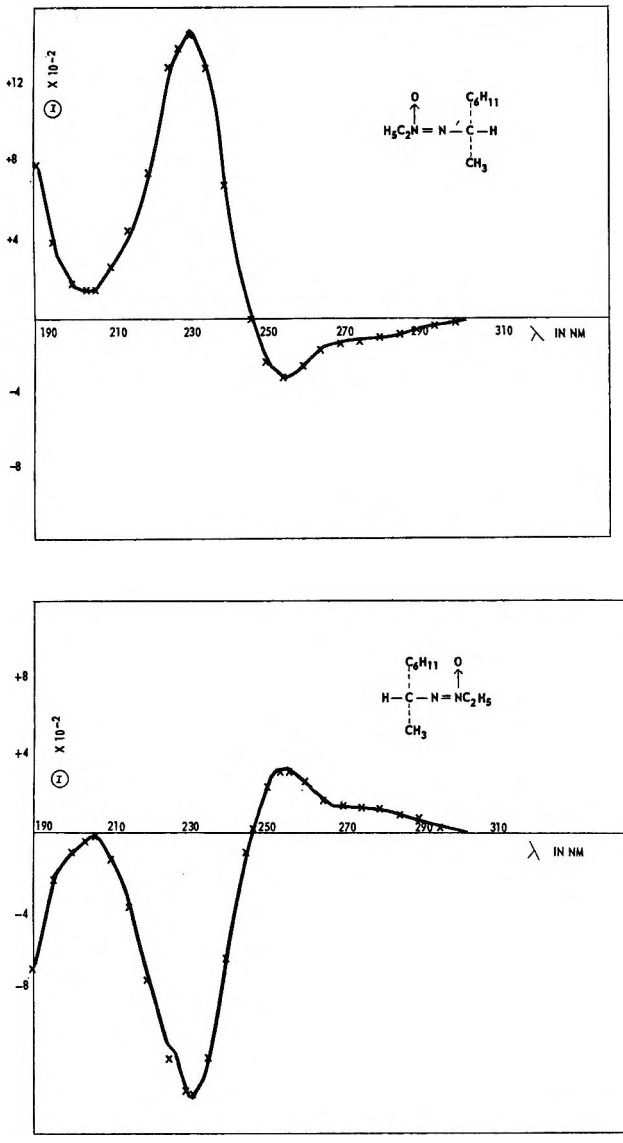
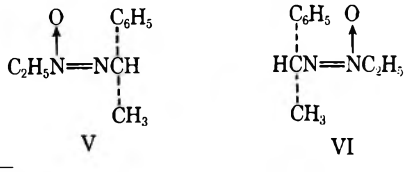


Figure 1.—CD curves of (*S*)-*ONN*-1-cyclohexylazoxyethane (above) and (*R*)-*ONN*-1-cyclohexylazoxyethane (below) in cyclohexane.

III and IV are shown in Figure 1. The S compound III has a Cotton effect $[\theta]_{232}$ +1.47 × 10^3, which matches in sign, location, and magnitude that of II.[1] The antipodal IV has a Cotton effect $[\theta]_{232}$ −1.36 × 10^3, which corresponds in location and sign with that of I. This agreement between the signs and locations of the Cotton effects of the two natural products with those of the corresponding synthetic antipodal azoxy compounds establishes beyond reasonable doubt the same configuration for all four azoxy chromophores. As indicated by Freeman,[9] this configuration is most likely to be the trans form.

The compound (*S*)-*ONN*-1-phenylazoxyethane and its R antipode are given by projections V and VI, respectively, and the CD curves of these materials are illustrated in Figure 2. The uv curve of V or VI



V VI

(9) J. P. Freeman, *J. Org. Chem.*, **28**, 2508 (1963).

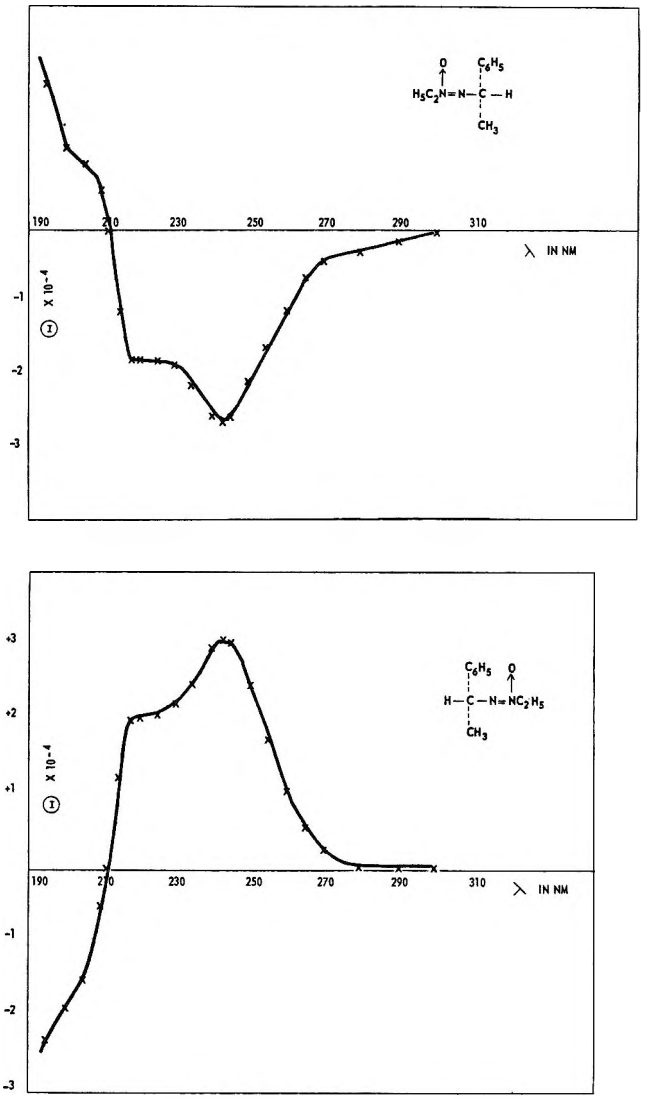
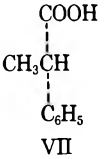


Figure 2.—CD curves of (*S*)-*ONN*-1-phenylazoxyethane (above) and (*R*)-*ONN*-1-phenylazoxyethane (below) in cyclohexane.

shows a strong band at about 210 nm due to the phenyl chromophore which swamps out the azoxy band normally observed around 220 nm. The CD curves are complicated by the presence of Cotton effects due to both chromophores. Similar difficulties have been encountered with regard to the observed Cotton effects in the 200–220 nm region of α-substituted phenylactic acids.[10,11]

Recently, definite assignments[12] have been made for the observed Cotton effects in the CD curve of (*S*)-(+)-hydratropic acid (VII). The strongly positive band at 223 nm is attributed to the n → π* transition of the carboxyl group, while the Cotton effect at 205 nm is said to be due to a π → π* phenyl transition.



VII

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(11) M. Sakota, K. Okita, and Y. Matsui, *Bull. Chem. Soc. Jap.*, **43**, 1138 (1970).

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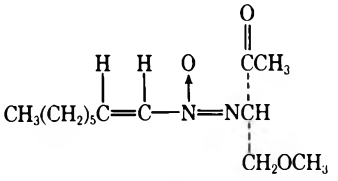
Two strong positive Cotton effects are clearly visible in the CD curve of VI and possibly two strong negative bands are at least partially visible. We assign the $[\theta]_{220}$ +2.05 × 10^4 effect to the $\pi \rightarrow \pi^*$ transition of the azoxy chromophore. In the more polar trifluoroethanol solvent this Cotton effect moves to $[\theta]_{213}$ +2.09 × 10^4. A blue shift such as this is normally diagnostic of an $n \rightarrow \pi^*$ transition[13] except in the case of certain heteropolar systems.[14]

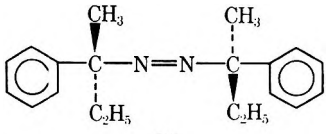
The shift observed here exactly parallels that of the azoxy chromophore of VIII,[1] which moved from 237



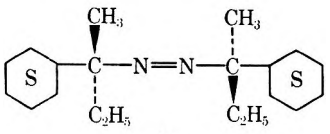
VIII

nm in cyclohexane to 230 nm in trifluoroethanol. Hence, the assignment of the 220 nm Cotton effect in the curve of VI to the azoxy chromophore is reasonable and it follows that the large effect $[\theta]_{243}$ +3.14 × 10^4 belongs to the phenyl chromophore. In the more polar solvent this band appears at $[\theta]_{242}$ +2.97 × 10^4 and it may be assigned to the phenyl ^1L_b[15] band, since this weak $\pi \rightarrow \pi^*$ transition is normally insensitive to solvent change or blue shifted in more polar solvents.[13]

The azoxy Cotton effects of V and VI are about an order of magnitude greater than those exhibited by the same chromophore in II, III, and IV and about the same size as that of I. The enhanced Cotton effect of I[1] was shown to be due to coupling between the azoxy and carbonyl systems. In a similar manner, it can be argued that the enhanced effects in V and VI are due to coupling between the azoxy and homoconjugated phenyl systems. Severn and Kosower[16] prepared and studied the CD curves of the two optically active *trans*-dialkyldiazenes IX and X. The Cotton effects due

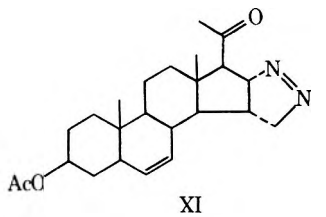


IX



X

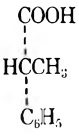
to the azochromophores of IX and X are approximately given by $[\theta]_{382}$ +2700 and $[\theta]_{379}$ +4200, respectively. Hence, there is no effective coupling between the $n \rightarrow \pi^*$ transition and the homoconjugated π system, probably because of the large energy difference between the systems. On the other hand, the pyrazoline steroid XI shows unusual rotational strength[17]



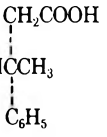
XI

due to interaction between the azo and carbonyl systems where the energy differences are not so great. In comparing the CD curves of V and VI with those of III and IV and the natural products I and II it is evident that the presence of a phenyl substituent on the asymmetric center inverts the sign of the azoxy Cotton effect. It is well known that the concept which claims that structurally similar compounds of the same absolute configuration give Cotton effects of the same sign[18] is not so clear-cut when one of the substituents is a phenyl group. Brewster and Buta[19] observed that configurationally related 1-substituted indans and α-substituted phenylethyl compounds have ORD curves of mirror image shape.

Verbit, *et al.*,[20] have shown that the configurationally related acids XII and XIII have Cotton effects in the

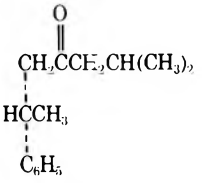


XII

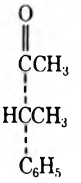


XIII

230 nm region which are virtually mirror images of each other. The same authors have examined the $n \rightarrow \pi^*$ carbonyl Cotton effect of XIV and found it to be of opposite sign to that of carbonyl Cotton effect of XV. On the other hand, Verbit and Heffron[10]



XIV



XV

found that both (*S*)-(+)-α-hydroxyphenylacetic acid and (*S*)-(−)-α-hydroxy-4-methylpentanoic acid have Cotton effects of the same sign in the 220 nm region. It is also evident from the CD curve of VI that the Cotton effect attributed to the ^1L_b band of the phenyl chromophore is inverted while the effect due to the ^1L_a band of the same chromophore is not in comparison with the Cotton effects of the corresponding transitions in (*R*)-α-phenylethylamine (Figure 3).

The cyclohexylazoxy compounds III and IV each give double-humped CD curves as did the natural compounds I and II. An equilibrium involving solvated and unsolvated forms[1,21] reasonably accounted for the appearance of the two oppositely signed CD absorptions of I and II. The CD reversals observed for III and IV do not fit this pattern so well, as the separation of the reverse effects in each curve is about

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(14) J. W. Sidman, *Chem. Rev.*, 689 (1958).
(15) P. E. Stevenson, *J. Chem. Educ.*, **41**, 234 (1964).
(16) D. J. Severn and E. M. Kosower, *J. Amer. Chem. Soc.*, **91**, 1710 (1969).
(17) G. Snatzke and J. Himmelreich, *Tetrahedron*, **23**, 4337 (1967).
(18) W. Schlenk Jr., *Angew. Chem., Int. Ed. Engl.*, **4**, 139 (1965).
(19) J. H. Brewster and J. G. Buta, *J. Amer. Chem. Soc.*, **88**, 2233 (1966).
(20) L. Verbit, A. S. Rao, and J. W. Clark-Lewis, *Tetrahedron*, **24**, 5839 (1968).
(21) K. M. Wellman, P. H. A. Laur, W. S. Briggs, A. Moscowitz, and C. Djerassi, *J. Amer. Chem. Soc.*, **87**, 66 (1965).

24 nm instead of the expected 28–32 nm. Severn and Kosower[16] have put forward another explanation of CD reversal based on the assumption that transition from low-energy ground state to low-energy excited state has opposite polarizability to the transition from low-energy ground state to high-level excited state. The argument is developed in connection with an $n \rightarrow \pi^*$ transition but presumably should apply equally well to a $\pi \rightarrow \pi^*$ transition except that in such a case the reverse effect would be observed on the long wavelength side.

Experimental Section[22]

Tlc was carried out on 0.25 mm silica gel plates from Brinkmann Instruments. Developing solutions varied from 5 to 40% ethyl acetate in hexane. Organic solutions were dried over anhydrous $MgSO_4$ and distillation of small quantities of oils was carried out on a Kugelrohr. CD data were obtained on a Cary 60 spectropolarimeter with CD attachment. Pertinent data are given in Table I.

TABLE I

Compd	Concn, mg/ml	Sensitivity	Cell width, mm	Solvent
XVI	1.29	0.1	0.1	Cyclohexane
XVII	1.13	0.1	0.1	Cyclohexane
XVI	1.14	0.1	0.1	Trifluoroethanol
XV	8.40	0.1 and 0.2	0.1	Cyclohexane
XIV	8.00	0.1 and 0.2	0.1	Cyclohexane
(*R*)-α-Phenylethylamine	4.96	0.1	0.5	Cyclohexane
(*R*)-α-Phenylethylamine	1.24	0.04	0.1	Cyclohexane

Urethans from α-Phenylethylamines.[24]—The literature procedure was followed using 6.4 ml (50 mmol) of (*R*)-α-phenylethylamine to get 6.5 g of crude product which was purified by passage over Davison 62 grade silica gel using 10% ethyl acetate in hexane as eluting solvent. The analytical sample was obtained by distillation at 100° under 80 μ pressure to get a colorless oil which solidified at room temperature: $[\alpha]^{25}D$ +82.5 ± 0.19° (c 1.032, MeOH); λ_{max}^{MeOH} 209 nm (ε 1600) and 257 (57); nmr (CCl_4) δ 1.18 (3 H, triplet, J = 7 Hz, $-OCH_2CH_3$), 1.45 (3 H, doublet, J = 7 Hz, α-CH_3), 4.08 (2 H, quartet, J = 7 Hz, $-OCH_2CH_3$), 4.88 (1 H, quartet, J = 7 Hz, benzylic proton), 5.03 (1 H, broad exchangeable signal, NH), and 7.30 (5 H, singlet, aromatic protons).

Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.24; H, 7.85; N, 7.18.

The urethan from (*S*)-α-phenylethylamine had $[\alpha]^{25}D$ −82.0 ± 0.34° (c 0.587, MeOH).

Nitroso-α-phenylurethans.—The procedure of Moss[25] and White[26] was followed using 4.0 g (just under 21 mmol) of (*S*)-α-phenylethylurethan. The crude reaction product was partially purified by silica gel chromatography using 5% ethyl acetate in hexane as eluting solvent. About 500 mg of the partially purified product was subjected to partition chromatography over 200 g of acid-washed diatomaceous earth using the system heptane saturated with CH_3CN. The nitroso carbamate was recovered from the second holdback volume as a yellow oil which could be distilled at 75° under 70 μ pressure: $[\alpha]^{25}D$ −310 ± 0.18° (c 1.115, MeOH); nmr (CCl_4) δ 1.37 (3 H, triplet, J = 7 Hz, $-OCH_2CH_3$), 1.62 (3 H, doublet, J = 7 Hz, α-CH_3), 4.60 (2 H, quartet, J = 7 Hz, $-OCH_2CH_3$), 5.95 (1 H, quartet, J = 7 Hz, benzylic proton), and 7.12 (5 Hz, singlet, aromatic protons).

Anal. Calcd for $C_{11}H_{14}N_2O_3$: C, 59.45; H, 6.35; N, 12.00. Found: C, 59.74; H, 6.30; N, 12.20.

***ONN*-1-Phenylazoxyethanes.**—About 2.6 g of *tert*-BuOK were stirred in 30 ml of ether and cooled to −30° under positive nitrogen pressure. About 2.8 g (13 mmol) of (*R*)-nitroso-α-phenylethylurethan was added through a septum using a syringe. The ether was evaporated off by increasing the nitrogen flow and then 50 ml of dry CH_2Cl_2 was added. About five or six 1-g aliquots of $(C_2H_5)_3OBF_4$ were added from an ether suspension (reagent is supplied by Baker as a solid under ether). Stirring was continued for 2 hr. The organic layer was extracted with H_2O, dried, and evaporated to 1.2 g of faintly yellow oil. Passage over silica gel and elution with 10% ethyl acetate in hexane gave 970 mg of nearly colorless oil. Further purification was effected by partition chromatography over 180 g of acid-washed diatomaceous earth using the heptane–CH_3CN system, yield 600 mg. For analytical and CD purposes, a small sample was distilled at 65° under 70 μ pressure to get a colorless, mobile liquid which spectral data showed to be (*R*)-*ONN*-1-phenylazoxyethane (VI): mass spectrum m/e 178; $[\alpha]^{25}D$ +139.5 ± 0.19° (c 1.049, MeOH); λ_{max}^{MeOH} 210 nm (ε 11,700); nmr (CCl_4) 1.48 (6 H, distorted triplet, J = 7 Hz, $-N(\rightarrow O)CH_2CH_3$ and α-CH_3), 4.10 (2 H, quartet, J = 7 Hz, $-N(\rightarrow O)CH_2CH_3$), 5.01 (1 H, quartet, J = 7 Hz, benzylic proton), and 7.17 (5 H, singlet, aromatic protons).

Anal. Calcd for $C_{10}H_{14}N_2O$: C, 67.38; H, 7.92; N, 15.72. Found: C, 67.15; H, 8.13; N, 16.14.

The other isomer, (*S*)-*ONN*-1-phenylazoxyethane (V), had $[\alpha]^{25}D$ −141.4 ± 0.3° (c 0.654, MeOH).

Reduction of α-Phenylethylamines.—Some methods recommended for the reduction of the aromatic ring in compounds of this type in our hands gave only partial reduction.[27,28] A slight modification of Leithe's procedure gave the best results. About 12.8 ml of (*R*)-α-phenylethylamine in 50 ml of acetic

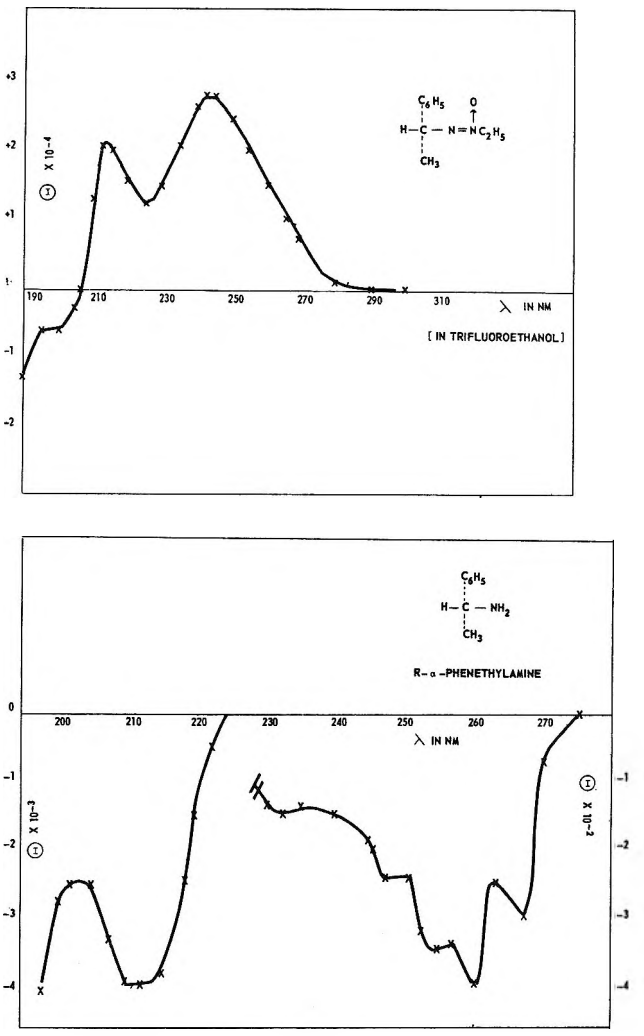

Figure 3.—CD curves of (*R*)-*ONN*-1-phenylazoxyethane (above) in trifluoroethanol and (*R*)-α-phenylethylamine (below) in cyclohexane.

(22) The optically active amines were purchased from Aldrich. Isomer *l*(−)-α-methylbenzylamine, which we call (*S*)-α-phenylethylamine, had $[\alpha]^{26}D$ −39.65 ±0.002° (neat). The other isomer, *d*(+)-α-methylbenzylamine, had $[\alpha]^{26}D$ +38.7 ±0.002° (neat) [lit.[23] $[\alpha]^{25}D$ +40.7° (neat)].

(23) W. Leithe, *Ber.*, **65**, 660 (1932).

(24) A. H. Blatt, Ed., "Organic Syntheses," Collect. Vol. II, Wiley, New York, N. Y., 1963, p 278.

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(26) E. H. White, *J. Amer. Chem. Soc.*, **77**, 6008 (1955).

(27) R. L. Augustine, "Catalytic Hydrogenation," Marcel Dekker, New York, N. Y., 1965, p 72.

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acid together with 2.5 g of PtO_2 catalyst were hydrogenated in a Parr shaker for 12 hr to get about 98% of theoretical hydrogen uptake. The acetic acid filtrate was diluted with ether and then with 4 *N* NaOH until the system was alkaline. The ether phase was recovered, dried, and evaporated to 12.0 g of faintly yellow oil. On exposure of this oil for any length of time in the laboratory, fine white crystals began to form on the surface of the container. An oxalate of the material prepared as described by Leithe[23] gave white crystals, mp 136° (lit.[23] 132°). A sample of the oxalate was added to water–ether (50:50) and 4 *N* NaOH was added until the system was strongly basic. The ether layer was processed to give a colorless oil. About 0.5 g of this oil was added to 20 ml of 5% NaOH solution and 2 ml of benzoyl chloride were added wtih stirring. The precipitate was recovered, taken up in ethyl acetate, dried, and worked up to give 500 mg of crystals: mp 158.5° (lit.[23] 162°); $[\alpha]^{25}D$ −21.3 ± 0.06° (*c* 3.49, MeOH) (lit.[23] 19.2° for the other isomer).

Anal. Calcd for $C_{15}H_{21}NO$: C, 77.88; H, 9.15; N, 6.05. Found: C, 77.92; H, 9.09; N, 5.92.

(*S*)-α-Cyclohexylethylamine was obtained in the same way. The *N*-benzoyl derivative melted at 159° and had $[\alpha]^{25}D$ +20.9 ± 0.07° (c 2.57, MeOH).

α-Cyclohexylethylurethans.—These materials were prepared in the same fashion as the α-phenylethylurethans. The following physical data were obtained on the material (*R*)-α-cyclohexylethylurethan: mp 49–50°; $[\alpha]^{25}D$ +13.8 ± 0.2° (*c* 1.043, MeOH); nmr (CCl_4) δ 1.09 (3 H, doublet, *J* = 7 Hz, α-CH_3), 1.23 (3 H, triplet, *J* = 7 Hz, -OCH_2CH_3) (the doublet and triplet appear as five lines on a broad base signal which integrates for 12 protons, that is, two CH_3 and six axial protons), 1.75 (5 H, broad signal for equatorial protons), 3.53 (1 H, broad signal for α-H), 4.08 (2 H, quartet, *J* = 7 Hz, -OCH_2CH_3), and 4.53 (1 H, broad exchangeable signal for NH).

Anal. Calcd for $C_{11}H_{21}NO_2$: C, 66.29; H, 7.03; N, 10.62. Found: C, 66.47; H, 7.07; N, 10.85.

The (*S*)-α-cyclohexylurethan had mp 51–52° and $[\alpha]^{25}D$ −14.32 ± 0.09° (*c* 2.192, MeOH).

Nitroso-α-cyclohexylethylurethans.—The methods described for the syntheses of nitroso-α-phenylurethans were used. The corresponding cyclohexyl compounds could be passed over silica gel to get golden oils which appeared as single spots by tlc using 10% ethyl acetate in hexane developer. At this stage data on (*R*)-nitroso-α-cyclohexylethylurethan were as follows: $[\alpha]^{25}D$ +51.0 ± 0.35° (c 0.56, MeOH); nmr (CCl_4) δ 1.00 (3 H, doublet, *J* = 7 Hz, α-CH_3), 1.45 (3 H, triplet, *J* = 7 Hz, -OCH_2CH_3) (these five lines appeared on broad base signals integrating for 21 protons which includes the axial and equatorial protons plus impurity), 4.18 (1 H, multiplet, α-H) and 4.47 (2 H, quartet, *J* = 7 Hz, -OCH_2CH_3).

Anal. Calcd for $C_{11}H_{20}N_2O_3$: C, 57.89; H, 8.77; N, 12.28. Found: C, 59.58; H, 9.24; N, 11.40.

These nitroso compounds could not be purified by partition chromatography since, because of their low polarity, they moved at the solvent front. Attempts to purify them by glc resulted in decomposition; consequently no analytically pure samples were obtained.

***ONN*-1-cyclohexylazoxyethanes.**—These materials were prepared as described for the corresponding phenyl compounds. Some purification was effected by silica gel chromatography but the ir spectrum of the material off the silica gel column had a carbonyl peak at 1730 cm^{-1} in addition to a strong azoxy peak at 1495 cm^{-1}. Glc using a 10-in. 10% SF-96 column gave the pure isomers.

For the material (*R*)-*ONN*-1-cyclohexylazoxyethane (III) the following physical data were obtained: mass spectrum *m/e* 184; $[\alpha]^{25}D$ −38.24 ± 0.19° (*c* 1.025, MeOH); λ_{max}^{MeOH} 223 nm (ε 8200); nmr (CCl_4) δ 0.97 (3 H, doublet *J* = 7 Hz, α-CH_3) (this doublet appeared as two lines on a broad base signal accounting for the six axial protons), 1.47 (3 H, triplet, *J* = 7 Hz, $-N(\rightarrow O)CH_2CH_3$) (this triplet appeared as three lines on a broad base signal accounting for five equatorial protons), 3.80 (1 H, broad multiplet, α-H), and 4.08 (2 H, quartet, *J* = 7 Hz, $-N(\rightarrow O)CH_2CH_3$).

Anal. Calcd for $C_{10}H_{20}N_2O$: C, 65.17; H, 10.94; N, 15.20. Found: C, 64.81; H, 10.94; N, 14.77.

The material (*S*)-*ONN*-1-cyclohexylazoxyethane had *m/e* 184 in the mass spectrum and $[\alpha]^{25}D$ +36.00 ± 0.55° (c 0.358, MeOH).

Registry No.—I, 24397-77-1; II, 23315-05-1; III, 33290-09-4; V, 33325-77-8; VI, 33290-10-7; urethan of (*R*)-α-phenylethylamine, 14185-43-4; urethan of (*S*)-α-phenylethylamine, 33290-12-9; nitroso-α-phenylurethans, 33290-13-0; (*S*)-α-cyclohexylethylamine *N*-benzoyl derivative, 33325-78-9; (*R*)-α-cyclohexylethylurethan, 33290-14-1; (*S*)-α-cyclohexylethylurethan, 33290-15-2; (*R*)-nitroso-α-cyclohexylethylurethan, 33364-43-1; (*S*)-*ONN*-1-cyclohexylazoxyethane, 33290-16-3.

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Woodhousin, a New Germacranolide from *Bahia woodhousei* (Gray) Gray[1]

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The isolation and structure determination of a new complex germacranolide, woodhousin (1), from *Bahia woodhousei* (Gray) Gray is reported. Jaceidin (4′,5,7-trihydroxy-3,3′,6-trimethoxyflavone) was also found. No homogeneous lactone component could be isolated from *Bahia dissecta* (Gray) Britton.

Earlier investigations of representatives of the genus *Bahia* (tribe Helenieae, Compositae) resulted in the isolation of several closely related guaianolides.[2,3] We now report isolation and structure determination of a new relatively complex germacranolide woodhousin from *Bahia woodhousei* (Gray) Gray,[4] which also contains the flavone jaceidin (4′,5,7-trihydroxy-3,3′,6-trimethoxyflavone).[5-7]

Woodhousin, $C_{21}H_{28}O_8$, mp 183–184.5°, $[\alpha]D$ −206.3°, was a conjugated γ-lactone (ir bands at 1765 and 1662 cm^{-1}; strong uv end absorption). The nmr spectrum (Table I) exhibited the typical two doublets of H_a and H_b in partial structure A. Spin decoupling experiments involving H_a and H_b established the loca-

(1) Supported in part by grants from the U. S. Public Health Service (GM 05814) and Hoffmann-La Roche, Inc.

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TABLE I

NMR SPECTRA OF WOODHOUSIN AND DERIVATIVES[a]

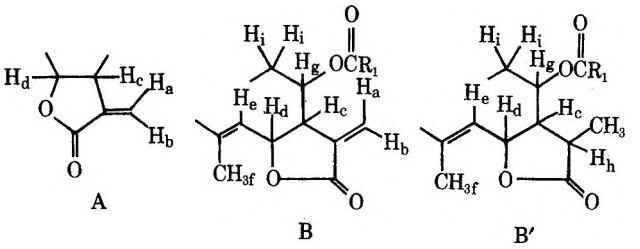
Compd	H-2	H-5	H-6	H-7	H-8	H-13	H-14[b]	H-15[b]	Ac[b]	H-3'[b]	Misc
1	5.36 d br (5.0)	5.60 c[c]	5.50 c[c]	4.06 m	5.50 c[c]	6.23 d (2.4) 5.60 d (2.0)	1.77 t (1.5)	1.50	2.12	1.07 d (7) 1.05 d (7)	3.23 (OH)[d]
2[d]	5.36 dd ($J_{1a,2}$ = 2.8) ($J_{1b,2}$ = 6.5)	5.76 dq ($J_{5,6}$ = 5.0) ($J_{5,14}$ = 1.5)	5.59 qm ($J_{6,7}$ = 2.0) ($J_{6,14}$ = 1.5)	3.56 dt ($J_{7,11}$ = 10.6) ($J_{7,8}$ = 2.4)	5.22 td ($J_{8,9a}$ = 6.4) ($J_{8,9}$ = 6.4)	1.10 d[b] ($J_{11,13}$ = 7.2)	1.78 t (1.5)	1.43	2.08	1.12 d (7) 1.12 d (7)	3.07 (OH)[d] 2.80 m (H-11)
3	5.38 d br (5.3)	3.34 ($J_{5,6}$ = 0)	5.23 d ($J_{6,7}$ = 4.5)	4.30 m	5.50 m[e] ($J_{7,8}$ = 4.5) ($J_{8,9a}$ = 10.2) ($J_{8,9b}$ = 4.8)	6.28 d (2.7) 5.63 d (2.3)	1.35	1.46	2.18	1.05 d (7) 1.04 d (7)	3.12 (OH)[d]
4	5.42 dd (3.2, 7.4)	[f]	4.80 dd br (12.5, 6)	[f]	5.20 dd br (9.5, 4)	1.30 d[b,g] (6.8)	1.10 d[g] (7.0)	1.48	2.15	1.10 d (7) 1.10 d (7)	
5	[f]	[f]	4.05[c]	4.15[c]	5.33 ddd (10, 6, 1.8)	1.04 d[b,g] (7.0)	0.86 d[g] (7)	1.25		1.04 d (7) 1.04 d (7)	4.75 dt (11.0, 3.0, H-3)
6	5.47 dd ($J_{1a,2}$ = 4.8) ($J_{1b,2}$ = 3.2)	[f]	4.27 td ($J_{5a,6}$ = 10.2) ($J_{5b,6}$ = 3.3) ($J_{6,7}$ = 10.2)	2.7 m	5.90 dd ($J_{7,8}$ = 6.5) ($J_{8,9}$ = 11.0)	1.42 d[b,g] (7.0)	1.26 d[g] (6.8)	1.88 d ($J_{9,15}$ = 1.0)	2.14	1.15 d (7) 1.15 d (7)	3.52 dd (15.4, 4.8, H-1a) 2.33 dd (15.4, 3.2, H-1b) 5.43 d br (11.0, 1.0, H-9)[h]
7	5.2[c]	[f]	4.59 dd br (4.5, 12.3)	[f]	5.2[c]	1.29 d[b,g]	1.08 d[g] (7.0) 5.37 br[i]	5.07 br[i]	2.09	1.08 d 1.08 d	
8a	4.69q[j]	[f]	3.88 td (10, 3.0)	[f]	5.96 dd[h] (11.0, 6.0)	1.37 d[b,g] (7.0)	1.17 d[g] (6.8)	1.87 d (1)		1.15 d (7) 1.15 d (7)	5.24 d br (11, 1, H-9)[h] 3.63 d (4.2, OH)
8b	4.73 q[j] (4)	[f]	4.19 td (10.5, 3.5)	[f]	5.91 dd[h] (11.5, 6.5)	1.44 d[b,g] (7.0)	1.18 d[g] (6.8)	1.86 d (1)		1.15 d (7) 1.15 d (7)	5.39 d br (11, 1, H-9)[h] 3.59 d (4.2, OH)
9a	4.69 q[j] (3.5)	[f]	3.67 td (10, 3.0)	[f]	5.28 dd[c,h] (11.0, 7)	1.38 d[b,g] (6.8)	1.13 d[g] (7)	1.83 d (1)			5.07 d br[c,h] (11.0, 1, H-9)
9b	5.46 dd (5.5, 2.5)	[f]	4.99 td (10, 3.0)	[f]	5.30[c]	1.39 d[b,g] (7)	1.32 d[g] (7)	1.89 br	2.13 2.06		3.25 dd (18, 2.5, H-1a) 5.25[c] (H-9)
10		[f]	3.93[c]	[f]	5.41 d[h] (11)	1.18 d[b,g] (6.8)	1.40 d[g] (7)	1.98 br		1.15 d (7) 1.15 d (7)	3.17 d (17.8, H-1a) 3.80 d br (17.8, H-1b) 5.50 d br[c] (11, H-9)[h]
11		[f]	4.54 dd br (12.0, 3.8)	[f]	5.07 td (7, 2)	1.13 d[b,g] (6.0)	1.07 d[g] (7)	1.90 d (1)	2.22	1.05 d (7) 1.05 d (7)	6.2 br (H-1) 5.10 d (0.8, H-3)
12		[f]	4.33 dd br (12.0, 3.0)	[f]	5.07 ddd (11, 7.2)	1.23 d[b,g] (6.0)	1.08 d[g] (7)	1.93 d (1)		1.04 d (7) 1.04 d (7)	6.23 br (H-1) 4.10 br (H-3) 3.66 br (OH) 3.21 dd (11.0, 12.5, H-9a)
13	5.32 dd (9.5, 7.5)	[f]	4.80[c]	[f]	4.75 td[c] (12.0, 3.5)	1.06 d[b] (7)	1.34 d[j] (7.0)	1.06 d (7)	2.06	1.06 d (7) 1.06 d (7)	
14	5.30 dd (9.8, 6.5)	[f]	4.35 ddd (11.5, 4.5, 2.5)	[f]	[f]	1.13 d[b] (6.3)	1.30 d[j] (6.8)	1.0 d (6.0)	2.07		
17	[k]	5.38 dq (11, 1.2)	5.05 dd (11, 1.7)	3.05 quint (1.7)	5.19 m	6.37 d (2.0) 5.83 d (2.0)	1.98 d (1.2)	1.40		1.89 t (1.2) 6.06 br[i] 5.62 br[i]	
18	[k]		4.48 dd (12.0, 3)	[f]	5.23 t br (3.5)	1.18[b,l]	1.12 d[l] (7)	1.39		1.14 d (7)[l] 1.13 d (7)[l]	

[a] Run at 90 MHz on a Bruker nmr spectrometer in $CDCl_3$ using TMS as internal standard. Chemical shifts are in parts per million. Signals are denoted in the usual way: d, doublet; t, triplet, q, quartet; m, multiplet; c, complex signal whose center is given; br, broadened singlet. Unmarked signals are singlets. Figures in parentheses are line separations or coupling constants in hertz. [b] Three-proton signal. [c] Overlapping signals. [d] Disappeared on addition of D_2O. [e] Outerpart of signal under H-2 and H-13b. [f] Obscured in methylene and methinyl envelope. [g] Tentative assignment on assumption that H-13 is generally at lower field. [h] Part of AB system. [i] One-proton signal. [j] On addition of D_2O H-2 signal collapsed to triplet. [k] Part of ABC multiplet, centered at 3.2. [l] Arbitrary assignment.

tion of the H_c multiplet at the unusually low frequency of 4.06 ppm. H_d was obscured in a multiplet near 5.5 ppm. The presence of partial structure A was further confirmed by formation of a dihydro derivative 2 on sodium borohydride reduction. In the nmr spectrum of 2 the signals of H_a and H_b were replaced by a new methyl doublet and the multiplet of H_c was converted to a doublet of triplets at 3.56 ppm.

A narrowly split three-proton triplet at 1.77 ppm in the nmr spectrum of woodhousin indicated the presence of a vinyl methyl group which was apparently coupled to a vinyl proton responsible for a multiplet component

of a relatively complex signal near 5.6 ppm and to one other proton. The presence of a second, unconjugated double bond indicated by this observation was confirmed by an ir band at 1665 cm^{-1} and by conversion of **1** to an epoxide **3**. In the nmr spectrum of **3**, the signals at 1.77 and 5.6 ppm were replaced by singlets at 1.35 and 3.34 ppm.[8]



A B B′

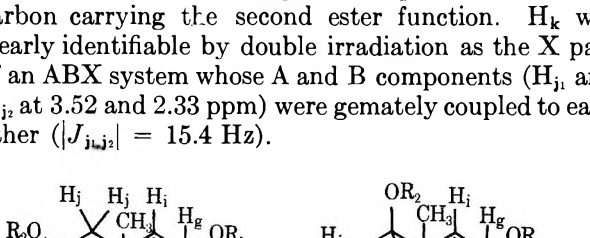
Spin decoupling experiments on **2** allowed expansion of partial structure A for woodhousin to B (modified to B′ in **2**).[9] Irradiation at the frequency of the vinyl methyl triplet (H_f) converted a doublet of quartets at 5.76 ppm (H_e) into a doublet and simplified a complex signal at 5.59 ppm (H_d) into a doublet of doublets. Irradiation at the frequency of H_c (4.3 ppm) sharpened a broadened triplet at 5.2 ppm (H_g) and created changes in the signals corresponding to H_d and H_h. The chemical shifts of H_d and H_g were characteristic of protons on carbon carrying ester or lactone functions; the multiplicity of H_g indicated that it was adjacent to a methylene group (H_i). Irradiation at the frequency of H_h collapsed the methyl doublet to a singlet and simplified H_c to a triplet. Conversely, irradiation at the frequencies of H_d or H_g collapsed the H_c signal to a doublet of doublets.

The ir spectrum of woodhousin also indicated the presence of a hydroxyl group and two ester functions (ir bands at 3470, 3440, 1750, and 1730 cm^{-1}).[10] One of the ester functions was an acetate (nmr signal at 2.12 ppm). In view of the molecular formula, the second ester side chain was therefore that of a four-carbon acid. Since **1** was recovered after treatment with acetic anhydride–pyridine, the hydroxyl group was tertiary and not located in the four-carbon side chain because of the presence of two methyl doublets in the nmr spectrum of woodhousin and its derivatives. Hence, the side chain was isobutyric acid. This was corroborated by the mass spectrum which, in addition to the molecular ion (408.1772), exhibited significant peaks at 390.1684 (0.5%, M − H_2O), 384.1603 (4.4%, M − $C_2H_4O_2$), 320.1230 (M − $C_4H_8O_2$), 302.1122 (M − H_2O − $C_4H_8O_2$), 278.1159 (22.5%, M − $C_4H_8O_2$ − C_2H_2O), 277.1048 (M − $C_4H_8O_2$ − C_2H_3O), 261.1104 (7.0%, M − $C_4H_8O_2$ − $C_2H_3O_2$), 260.1043 (38.2%, M − $C_4H_8O_2$ − $C_2H_4O_2$), 242.0918 (10.3%, M − $C_4H_8O_2$ − $C_2H_4O_2$ − H_2O), and 71.0501 (base peak, C_4H_7O).

Catalytic hydrogenation of woodhousin ($Pd/BaSO_4$) resulted in the uptake of 2 mol equiv of hydrogen and the formation of a saturated ketol **4** (ir bands at 3432, 1775, 1735, 1728, and 1710 cm^{-1}; CD curve λ_{max} 288 nm, θ +8050). Hydrogenation had obviously resulted not only in reduction of the two double bonds but was accompanied by an isomerization which was responsible for creation of a keto group. It could be rationalized by postulating the presence in woodhousin of a hemiacetal linkage which is cleaved when saturation of the unconjugated double bond forces the ketone and hydroxyl groups out of close proximity. Presence of a hemiacetal grouping would also account for the eighth oxygen atom of the molecular formula.

Occurrence in the nmr spectra of **1**, **2**, **3**, and **4** of a three-proton singlet near 1.45 ppm suggested that the carbon atom carrying the methyl group responsible for this singlet was one terminus of the hemiacetal linkage. This suggestion was confirmed by dehydrating **4** to a mixture of **6** and **7** which were separated by preparative tlc. In the nmr spectrum of **6**, the methyl singlet of **4** at 1.48 ppm had been replaced by a narrowly split vinyl methyl signal at 1.88 ppm; simultaneously, a new vinyl proton resonance at 5.34 ppm (broadened doublet) had made its appearance (Chart I).

Spin decoupling experiments on **6** permitted expansion of B′ to D or E. Irradiation at the frequency of the vinyl methyl doublet sharpened the broad vinyl doublet of H_i. Conversely, irradiation of H_i collapsed the methyl doublet to a singlet and converted a doublet of doublets of 5.90 (H_g, now allylic and hence shifted to lower field) to a doublet. Irradiation at the frequency of H_g collapsed the H_i doublet and caused some changes at 2.70 ppm (H_c). Irradiation of H_c collapsed H_g to a doublet and converted a triplet of doublets at 4.27 ppm (H_d, no longer allylic, hence displaced toward higher field in comparison with **1** and probably also shielded by the new double bond) to a doublet of doublets. The remaining low-field signal at 5.47 ppm could be assigned to a proton (H_k) under carbon carrying the second ester function. H_k was clearly identifiable by double irradiation as the X part of an ABX system whose A and B components (H_{j_1} and H_{j_2} at 3.52 and 2.33 ppm) were gemately coupled to each other ($|J_{j_1j_2}|$ = 15.4 Hz).

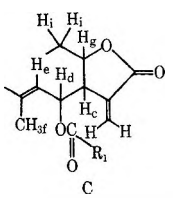


D E

Controlled hydrolysis of **6** yielded two isomeric monohydroxy ester lactones $C_{19}H_{26}O_6$ (**8a** and **8b**) and a small amount of a diol $C_{15}H_{22}O_5$ (**9a**). The nmr spectrum of **8b** indicated disappearance of the acetyl function; simultaneously the signal corresponding to H_k had moved upfield. On the other hand, the two superimposed methyl doublets of the isobutyryl group were still in evidence and the chemical shifts of H_d and H_g had remained unaltered. Acetyla-

(8) In **3**, $J_{5,6}$ = 0, thus giving rise to a singlet for H-5.

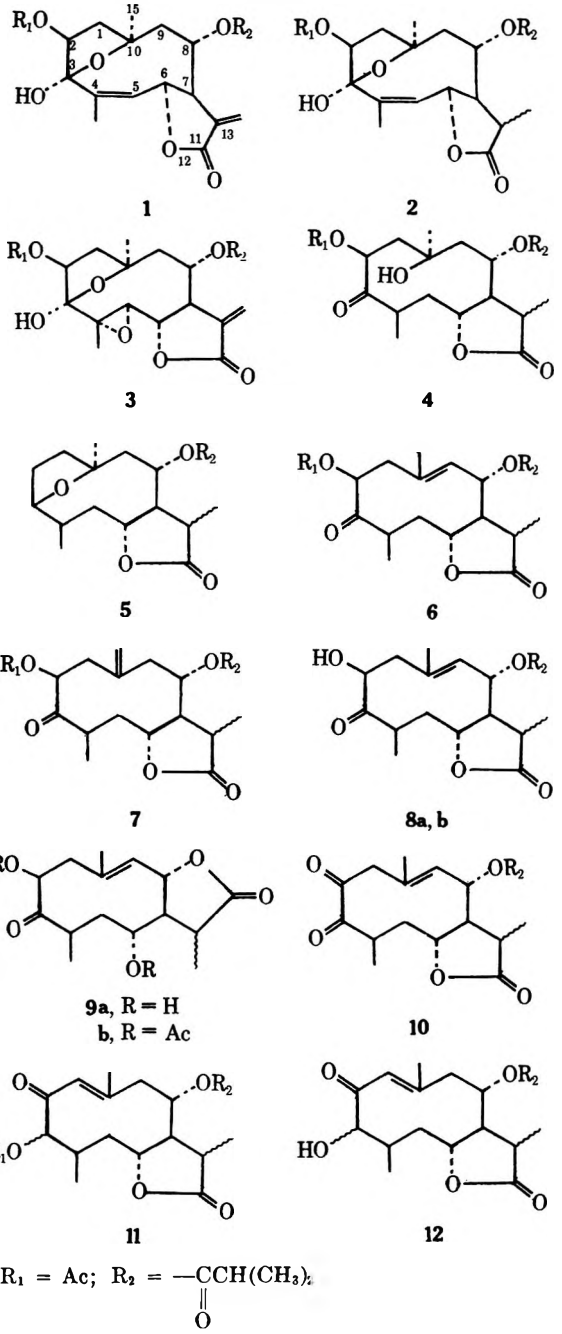
(9) In the interest of clarity, the results are discussed in terms of structure B, although at this point the alternative partial structure C could not yet be excluded.



C

(10) The possibility that ketone functions were responsible for the two carbonyl bands was excluded by the lack of appropriate n,π^* transitions in the uv and CD curves.

CHART I[a]



[a] R_1 = Ac; R_2 = $-\overset{\overset{O}{\|}}{C}CH(CH_3)_2$

tion of **8b** regenerated **6**[11a] thus ruling out the absence of a rearrangement during the partial hydrolysis of **6** to **8b**. Hence R_1 is isobutyryl and R_2 is acetyl.

Compound **8b** gave a positive α-ketol test with Benedict's reagent and could be oxidized to an unconjugated α diketone **10**. Since **6** was recovered unchanged or prolonged treatment with basic alumina,[11b] formula E for **6** was ruled out and formula D for **6** (R_1 = isobutyryl; R_2 = acetyl) and hence **1** for woodhousin was established, pending definition of the lactone ring orientation[9] (*vide infra*). This formula also explains the observation that catalytic hydrogenation of **1** with platinum oxide–acetic acid–perchloric acid is accompanied by hydrogenolysis of the acetate function to **5**.

The nmr spectrum of the isomeric anhydro derivative **7** contained no vinyl methyl resonance but had two additional signals in the low-field region characteristic of an exocyclic methylene group (see Table I). Treatment of **7** with basic alumina gave an α,β-unsaturated ketone **11** [λ_{max} 235 nm (ϵ 9850)] whose nmr spectrum (Table I) had signals consonant with the proposed formula. The formation of this compound requires migration of the acetate function from C-2 to C-3 under basic conditions.[12] Controlled hydrolysis of **7** afforded, again with rearrangement, an α,β-unsaturated ketol **12** [λ_{max} 243 nm (ϵ 6300)] which gave a positive Benedict's test and retained the isobutyryl function at C-8 (nmr spectrum).

We now turn to the question of lactone ring orientation.[13] This was settled by studying the catalytic hydrogenation of **6**. Use of platinum oxide in acetic acid–perchloric acid resulted not only in the production of **13** by saturation of the double bond but was also accompanied by hydrogenolysis and formation of **14**. Disappearance of the isobutyrate function under these conditions showed that it was attached to C-8 and that the lactone ring of woodhousin had to be closed to C-6. Hence woodhousin is correctly represented as **1** (exclusive of stereochemistry).

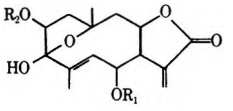
The ir spectrum of diol **9a** displayed only two carbonyl bands at 1764 and 1708 cm^{-1}, indicating loss of both side chains. This was confirmed by the nmr spectrum. Acetylation of **9a** gave a diacetate **9b**; comparison of the nmr spectra of **9a** and **9b** (Table I) indicated that a doublet of doublets at 5.28 ppm had to be associated with the proton under the lactone ether oxygen. Multiplicity and chemical shift required that this be assigned to H-8, *i.e.*, that complete hydrolysis of **6** to **9a** was accompanied by lactone ring reorientation from C-6 to C-8. The implications of this finding will be considered subsequently.

Lastly we consider the stereochemistry of woodhousin. In the nmr spectra of **1**, **2**, and **3**, the signal corresponding to H-7 has an abnormally low chemical shift (4.06 ppm) which indicated that H-7 is close to the oxygen of the tetrahydrofuran ring. If the usual assumption is made that the C-7 side chain is β and equatorial as in all sesquiterpene lactones of authenticated stereochemistry, this proximity requires, as is seen by construction of Dreiding models, α-oriented

(11) (a) Because of the similarity of the nmr spectra, we assume that **8a** and **8b** are C-11 epimers. The only significant difference in the nmr spectra is the chemical shift of H-9 (see Table I). (b) Under these conditions a β-acyloxy ketone is generally transformed to an α,β-unsaturated ketone.

(12) For analogous isomerizations of steroidal and triterpenoid α-acetoxy ketones, see L. F. Fieser and R. Stevenson, *J. Amer. Chem. Soc.*, **76**, 1728 (1954); N. S. Leeds, D. K. Fukushima, and T. F. Gallagher, *ibid.*, **76**, 2943 (1954); H. Henbest, D. N. Jones, and G. P. Slater, *J. Chem. Soc.*, 4442 (1961); D. Lavie, E. Glotter, and Y. Shvo, *Tetrahedron*, **19**, 1377 (1963); A. Lablache-Combier, B. Lacoume, and J. Levisalles, *Bull. Soc. Chim. Fr.*, 897 (1966); A. D. Boul, P. M. Fairweather, J. M. Hall, and G. D. Meakins, *J. Chem. Soc. C*, 1199 (1971).

(13) On the basis of our experience with germacranolides, it seemed logical to associate the signal near 4–4.5 ppm in the nmr spectra of **6**, **7**, **8b**, **10**, **11**, and **12** with the proton under the lactone function (H_d) rather than with H_g, the latter being associated with the doublet of doublets or broad triplet at lower field. This would lead to formula **1** for woodhousin in preference to **1a**. Extensive decoupling experiments on **12** and related compounds



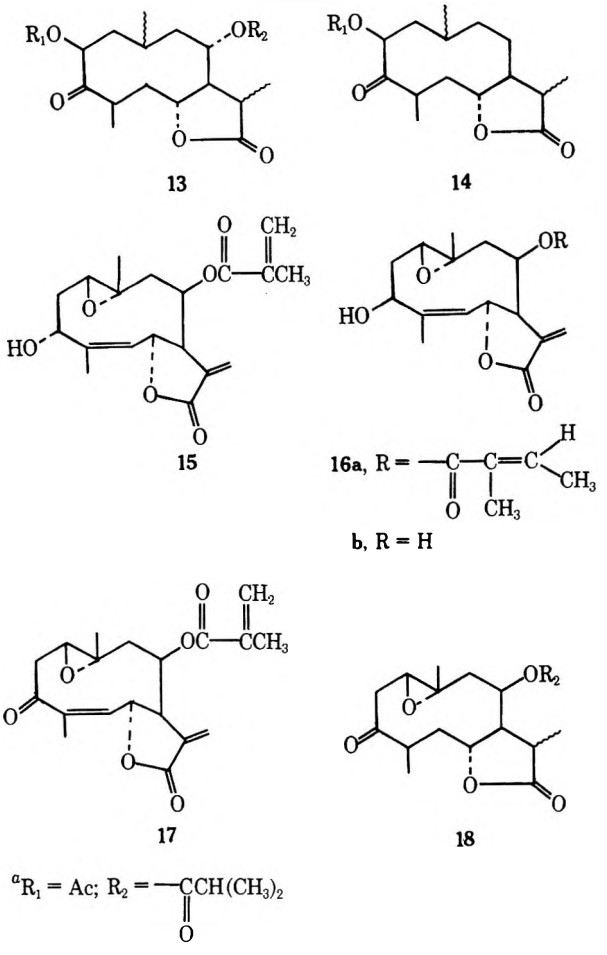
1a

provided confirmation for this view but will not be detailed here because the formation of **14** from **6** furnished decisive chemical evidence in favor of **1**.

3-hydroxyl and C-10 methyl groups and incorporation of a cisoid C-4–C-5 double bond.[14] An attempt to provide more positive evidence for the latter point by means of showing the existence of a nuclear Overhauser effect in **1** or **2** failed because H-5 was not sufficiently differentiated from the other low-field protons.[15]

Values of $J_{4,5}$, $J_{5,6}$, $J_{6,7}$, and $J_{8,9}$ given in Table I did not permit a unique assignment of stereochemistry to the centers at C-6 and C-8. However, a comparison of **12** with a substance **18** prepared from erioflorin (**15**)[17] *via* **17** (Chart II) proved instructive.

CHART II[a]

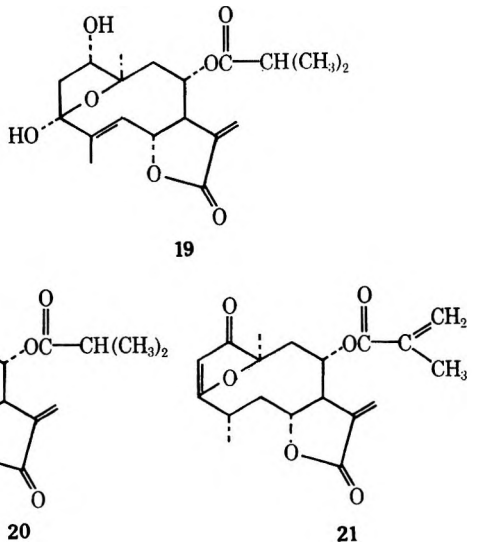


[a] R_1 = Ac; R_2 = —CCH(CH$_3$)$_2$ (O)

Inspection of models indicated that, if the configurations of **12** and **18** at C-6 were identical, the conformations of **12** and **18** should be almost the same. In fact, coupling constants and chemical shifts of H-6 in **12** and **18** were very similar, thus leading to the conclusion that H-6 in **12** and in woodhousin is also β. On the other hand, $J_{7,8}$ and $J_{8,9}$ in **12** and **18** differed considerably, an observation which suggested that H-8 of woodhousin was β instead of α as in erioflorin. This deduction is substantiated by the formation of **9a** during the hydrolysis of **6** since it has been shown[18] that germacranolides containing α-oriented lactonizable groups at C-6 and C-8 preferentially lactonize toward C-8.[19]

A clue to the stereochemistry at C-2 is furnished by the nmr spectrum of **3** which exhibits the H-2 resonance as a slightly broadened doublet ($J_{1a,2}$ = 5.3 Hz, $J_{1b,2}$ < 1 Hz). This is only possible if H-2 is α or pseudoaxial (model). Our failure to effect facile elimination of the β-oriented oxygen function at C-2 is in accord with this inference.

The complete structure and stereochemistry deduced for woodhousin (Figure 1) is identical at the relevant centers C-1, C-4, C-6, C-7, C-8, and C-10, with that recently proposed for orizabin (**19**)[20] by correlation through ciliarin (**20**)[21] with zexbrevin (most probable structure[22] **21**). The correspondence in all significant



detail between the nmr spectra of woodhousin and orizabin[20] provides additional support for the proposed identical stereochemistry as do the CD curves (Figure 2) which are very similar.[23,25] The correspondence of physical properties also requires that orizabin and ciliarin be reformulated as Δ^4-*cis*-germacranolides if our

(14) Construction of a Dreiding model containing a trans C-4–C-5 double bond proved impossible.

(15) Woodhousin would not be the first germacranolide with a cis C-4–C-5 double bond. Professor D. Rogers of Imperial College, London, has drawn our attention to the fact that the constitutional formula (C-4–C-5 bond trans) given for heliangine by N. Nishikawa, K. Kamiya, A. Takabatake, H. Oshio, Y. Tomiie, and I. Nitta, *Tetrahedron*, **22**, 3601 (1966), is in error since the pictorial representation and the coordinate list in the paper by the Japanese authors indicate the presence of a cis C-4–C-5 bond. Hence, erioflorin[16] (**15**), which has been correlated with heliangin (now written as **16a**) without saturating the double bonds also possesses a cis C-4–C-5 double bond.

(16) S. J. Torrance, T. A. Geissman, and M. R. Chedekel, *Phytochemistry*, **8**, 2381 (1969).

(17) We wish to thank Professor T. A. Geissman for a generous sample of erioflorin.

(18) H. Yoshioka, W. Renold, and T. J. Mabry, *Chem. Commun.*, 148 (1970).

(19) The nmr spectrum of **17** also provides convincing evidence for the cis arrangement of the C-4–C-5 double bond in erioflorin. In the Dreiding model of **17** with a trans Δ^4 bond, the H-6–H-7 dihedral angle is approximately 160°, which is much too large for the observed value (1.7 Hz) of $J_{6,7}$. By contrast, the H-6–H-7 dihedral angle in the model with a cis Δ^4 bond is ~100°, which is in excellent agreement with the observed coupling constant.

(20) A. Ortega, C. Guerrero, A. R. de Vivar, J. Romo, and A. Palafox, *Rev. Latinoamer. Quim.*, **2**, 38 (1971).

(21) A. Ortega, A. Romo de Vivar, E. Diaz, and J. Romo, *ibid.*, **1**, 81 (1970).

(22) A. Romo de Vivar, C. Guerrero, E. Diaz, and A. Ortega, *Tetrahedron*, **26**, 1657 (1970).

(23) The observed positive Cotton effect due to the lactone n,π^* transition is at variance with the negative Cotton effect predicted on the basis of a recently formulated rule[24] for germacranolides whose lactone ring is transfused and closed toward C-6. However, it should be noted that heliangenol (**16b**, stereochemistry authenticated by X-ray analysis) also exhibits[24] a positive Cotton effect. Obviously, dissymmetry effects are altered by introduction of a cis C-4–C-5 double bond.

(24) W. Stöcklin, T. G. Waddell, and T. A. Geissman, *Tetrahedron*, **26**, 2397 (1970).

(25) We are grateful to Dr. A. Romo de Vivar for a sample of orizabin.

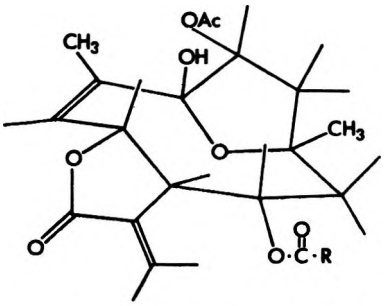


Figure 1.—Model of woodhousin.

conclusions concerning the Δ^4 double bond of woodhousin are correct.

Extraction of *Bahia dissecta* (Gray) Britton followed by extensive chromatography did not result in isolation of homogeneous sesquiterpene lactone fractions.

Experimental Section[26]

Isolation of Woodhousin and Jaceidin.—Finely ground *Bahia woodhousei* (Gray) Gray, wt 1.2 kg, collected by Mr. R. Barr on Sept 16, 1963, along U. S. 60 near Vernon, Apache Co., Arizona (Barr No. 63-467, on deposit in herbarium of Florida State University), was extracted with chloroform and worked up in the usual manner.[27] The crude gum, wt 14 g, was chromatographed over 200 g of silicic acid (Mallinckrodt, 100 mesh), 300-ml fractions being collected in the following order: 1–10 (benzene), 11–20 (benzene–$CHCl_3$, 3:1), 21–30 (benzene–$CHCl_3$, 1:1), 31–40 (benzene–$CHCl_3$, 1:3), 41–50 ($CHCl_3$), 51–59 ($CHCl_3$–CH_3OH, 97:3), 60–69 ($CHCl_3$–CH_3OH, 19:1), 70–75 ($CHCl_3$–CH_3OH, 9:1). All fractions were monitored by tlc. Fractions 21–26 which showed a major spot on tlc were combined and recrystallized from ethyl acetate–hexane to give pure woodhousin, wt 1.98 g, which melted at 183–184.5°: $[\alpha]D$ −206.3° (*c* 4.26); uv end absorption 207 nm (ϵ 19,000); ir bands at 3570, 3440, 1765, 1750, 1730, 1662, and 1665 cm^{-1}.

Anal. Calcd for $C_{21}H_{28}O_8$: C, 61.75; H, 6.91; O, 31.34; mol wt, 408.1784. Found: C, 62.18; H, 6.91; O, 31.29; mol wt (mass spectrum), 408.1772.

Fractions 28–29 gave jaceidin which was recrystallized from methanol and then melted at 127–135° (lit.[5] 127–133°): wt 0.26 g; nmr spectrum identical with reported[7] spectrum; ir and uv (ethanol, ethanol–sodium acetate, aluminum chloride, sodium methoxide) superimposable on spectra of an authentic specimen;[28] mixture melting point undepressed.

Anal. Calcd for $C_{18}H_{16}O_8 \cdot H_2O$: C, 57.14; H, 4.80; O, 38.06. Found: C, 57.23; H, 4.71; O, 38.07.

Dihydrowoodhousin (2).—To a solution of 0.115 g of 1 in 8 ml of methanol was added with stirring 0.080 g of $NaBH_4$ in 2 ml of methanol at 0°. Stirring was continued for 1 hr at 0°. The solution was acidified, evaporated at reduced pressure, diluted with 10 ml of water, and extracted with chloroform. The washed and dried extract was evaporated and the residue (2) was recrystallized from ethyl acetate–hexane: yield 75 mg; mp 156–159°; ir bands at 3578, 3450, 1765, 1750, and 1728 cm^{-1}.

Anal. Calcd for $C_{21}H_{30}O_8$: C, 61.45; H, 7.37; O, 31.18. Found: C, 61.21; H, 7.43; O, 30.57.

Epoxywoodhousin (3).—A solution of 88 mg of 1 in 4 ml of dry chloroform was allowed to stand with 44 mg of *m*-chloroperbenzoic acid overnight at 0°. The reaction mixture was diluted with chloroform, washed, dried, and evaporated. The residue was recrystallized from ethyl acetate–hexane: yield 58 mg; mp 198–201°; ir bands at 3560, 3440, 1775, 1755, 1730, and 1660 cm^{-1}.

Anal. Calcd for $C_{21}H_{28}O_9$: C, 59.43; H, 6.65; O, 33.92. Found: C, 59.31; H, 6.68; O, 34.38.

Tetrahydrowoodhousin (4).—A solution of 0.586 g of 1 in 40 ml of ethyl acetate was reduced at atmospheric pressure with 0.76 g of prereduced 5% Pd/$BaSO_4$ for 5 hr. The filtered solution was evaporated and the residue purified by preparative tlc. The product was recrystallized from ethyl acetate: yield 0.430 g; mp 181–183°; $[\alpha]^{27}D$ −35.5° (*c* 1.417); CD curve λ_{max} 288 nm (θ +8051); ir bands (KBr) at 3432, 1775, 1735, 1728, and 1710 cm^{-1}.

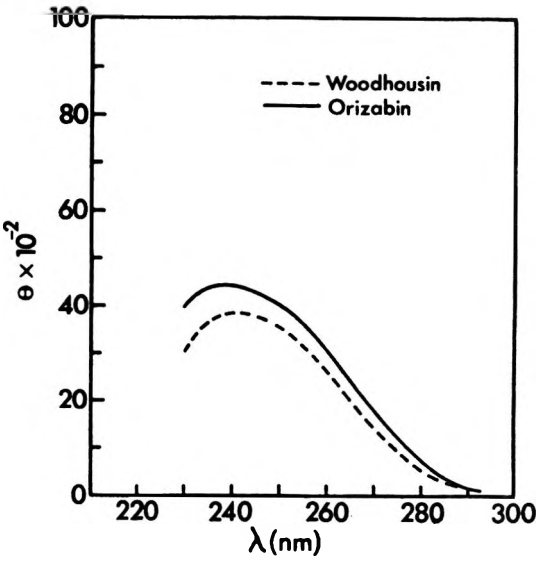


Figure 2.—CD curves.

Anal. Calcd for $C_{21}H_{32}O_8$: C, 61.15; H, 7.82; O, 31.03. Found: C, 61.53; H, 7.86; O, 30.81.

2-Deacetoxy-3-dehydroxytetrahydrowoodhousin (5).—A solution of 0.13 g of 1 in 5 ml of acetic acid containing 2 drops of perchloric acid was stirred with 40 mg of platinum oxide in a hydrogen atmosphere for 4 hr, filtered, and evaporated. The residue was subjected to preparative tlc. The major fraction was recrystallized from ethyl acetate–hexane: yield 80 mg; mp 99–101°; ir bands at 1770 and 1725 cm^{-1}; no CD absorption.

Anal. Calcd for $C_{19}H_{30}O_5$: C, 67.43; H, 8.93; O, 23.64. Found: C, 67.18; H, 8.92; O, 23.69.

Anhydrotetrahydrowoodhousin (6 and 7).—To a solution of 0.374 g of 4 in 5 ml of pyridine was added with stirring 0.8 ml of thionyl chloride at 0°. Stirring was continued at this temperature for 15 min. Excess thionyl chloride was decomposed with ice water and the mixture was extracted with chloroform. The washed and dried extract was evaporated and the residue was purified by preparative tlc. Fraction 1 gave 0.126 g of 6 and fraction 2 gave 0.120 g of 7; 0.096 g of starting material was recovered. Recrystallization of 6 from ethyl acetate–hexane afforded material which melted at 164–166°: $[\alpha]^{24}D$ +206.8 (*c* 2.05); CD curve λ_{max} 284 nm (θ +11660); ir bands at 1770, 1750, 1728 (double intensity), and 1656 cm^{-1}.

Anal. Calcd for $C_{21}H_{30}O_7$: C, 63.94; H, 7.69; O, 28.39. Found: C, 64.26; H, 7.58; O, 28.31.

7 was a gum and had ir bands at 1770, 1763, 1740, 1722, and 1639 cm^{-1}; CD curve λ_{max} 290 nm (θ +11030).

Anal. Calcd for $C_{21}H_{30}O_7$: C, 63.94; H, 7.69; O, 28.30. Found: C, 64.04; H, 7.85; O, 28.43.

Hydrolysis of 6. A.—A solution of 100 mg of 6 in 4 ml of 80% aqueous methanol containing 40 mg of potassium carbonate was stirred at room temperature for 40 min (nitrogen atmosphere). The solvents were removed, water was added, and the mixture was thoroughly extracted with chloroform. The washed and dried extract was evaporated and the residue was subjected to preparative tlc. The least polar fraction (8a) was recrystallized from ethyl acetate–hexane and melted at 165–169°: yield 8 mg; ir bands at 3470, 1770, 1723, 1709, and 1653 cm^{-1}; positive Benedict's test.

Anal. Calcd for $C_{19}H_{28}O_6$: C, 64.75; H, 8.01; O, 27.24. Found: C, 64.91; H, 8.21; O, 27.09.

A second fraction (8b) was recrystallized from ethyl acetate–hexane and melted at 124–126°: yield 8 mg; ir bands at 3470, 1770, 1723, 1710, and 1656 cm^{-1}; positive Benedict's test.

Anal. Calcd for $C_{19}H_{28}O_6$: C, 64.75; H, 8.01; O, 27.24. Found: C, 64.97; H, 7.88; O, 26.89.

The most polar fraction 9a was recrystallized from ethyl acetate–hexane and melted at 201–204°: yield 5 mg; ir bands at 3470, 1764, 1708, and 1660 cm^{-1}; positive Benedict's test; mol

(26) Experimental conditions specified by W. Herz, S. V. Bhat, and A. L. Hall, *J. Org. Chem.*, **35**, 1110 (1970), apply. High-resolution mass spectra were run at 70 MeV on a MS-9 high-resolution mass spectrometer.

(27) W. Herz and G. Högenauer, *ibid.*, **27**, 905 (1962).

(28) We wish to thank Professor H. Wagner for a sample of jaceidin.

wt (mass spectrometry), 282.1462 (calcd for $C_{15}H_{22}O_5$, 282.1466). There was insufficient material for an elementary analysis. Acidification of the aqueous layer, from the original extraction, followed by extraction with chloroform and the usual work-up gave an additional 20 mg of **8b**, mp 118–120°.

B.—A solution of 50 mg of **6**, 30 mg of sodium bicarbonate, and 10 ml of 80% aqueous methanol was stirred at room temperature for 8 hr. The solvent was removed at reduced pressure and the residue was subjected to preparative tlc after the usual work-up. The major fraction was recrystallized from ethyl acetate–hexane, melted at 124–126°, yield 15 mg, and was identified as **8b**.

Acetylation of 8b.—A solution of 15 mg of **8b** in 1 ml of pyridine and 0.5 ml of acetic anhydride was left overnight at room temperature and then worked up in the usual way. Recrystallization from ethyl acetate–hexane gave 10 mg of **6**: mp 164–166°; mixture melting point undepressed; nmr and ir spectra superimposable on that of an authentic sample.

Acetylation of 9a.—**9a** (4 mg), 0.1 ml of acetic anhydride, and 0.15 ml of pyridine was allowed to stand overnight and worked up in the usual manner. The residue was a gum (**9b**): wt 4 mg; nmr spectrum (see Table I); mol wt (mass spectrum), 366.1668 (calcd for $C_{19}H_{26}O_7$, 366.1677).

Oxidation of 8b.—A solution of 20 mg of **8b** in acetone containing a few drops of Jones reagent was stirred at 0° for 0.5 hr. Excess reagent was destroyed by addition of methanol and solvents were removed at reduced pressure. The residue **10** was purified by preparative tlc but remained a gum and had ir bands at 1775, 1724, 1708, and 1658 cm^{-1}.

Anal. Calcd for $C_{19}H_{26}O_6$: C, 65.13; H, 7.48; O, 27.40. Found: C, 64.48; H, 7.46; O, 27.61.

Isomerization of 7.—A solution of 0.5 g of **7** in benzene was placed on a column of 5 g of basic alumina and left overnight. Elution with chloroform gave 0.35 g of gum (**11**) which had ir bands at 1770, 1735, 1728, 1700, and 1633 cm^{-1}; λ_{max} 235 nm (ϵ 9850); mol wt (mass spectrum), 394.2006 (calcd for $C_{21}H_{30}O_7$, 394.1990).

Hydrolysis of 7.—A solution of 99 mg of **7** in 4 ml of 80% aqueous methanol was hydrolyzed in the same manner as **6**. The crude product was purified by preparative tlc. Fraction 1, 20 mg, was a gum which had ir bands at 1775, 1725, 1638, and 1629 cm^{-1}; λ_{max} 237 nm (ϵ 7700). Fraction 2 was a solid (**12**) and was recrystallized from ethyl acetate–hexane: mp 169–172°; yield 35 mg; ir bands at 3480, 1768, 1728, 1680, and 1637 cm^{-1}; λ_{max} 243 nm (ϵ 6300).

Anal. Calcd for $C_{19}H_{28}O_6$: C, 64.75; H, 8.01; O, 27.24; mol wt, 352.1884. Found: C, 64.42; H, 7.98; O, 27.31; mol wt, 352.1896.

Preparation of 13 and 14.—A solution of 80 mg of **6** in 7 ml of acetic acid containing 2 drops of perchloric acid was stirred with 40 mg of platinum oxide for 5 hr. Work-up as described for **5** and preparative tlc gave two fractions. Fraction 1 (**14**) was recrystallized from ethyl acetate–hexane: yield 8 mg; mp 172–175°; ir bands at 1762 and 1723 cm^{-1}.

Anal. Calcd for $C_{17}H_{26}O_5$: C, 65.78; H, 8.44; O, 25.77; mol wt, 310.1779. Found: C, 64.96; H, 8.12; O, 26.20; mol wt (mass spectrum), 310.1824.

Fraction 2 (**13**) was recrystallized from ethyl acetate–hexane: yield 41 mg; mp 196–198°; ir bands at 1765 and 1723 cm^{-1} (double intensity).

Anal. Calcd for $C_{21}H_{32}O_7$: C, 63.62; H, 8.14; O, 28.25. Found: C, 63.78; H, 8.52; O, 28.02.

Oxidation of Eriofloriin.—A solution of 0.190 g of eriofloriin (**15**) in 10 ml of acetone was mixed with 0.2 ml of Jones reagent and stirred at room temperature for 10 min. Excess reagent was destroyed by addition of methanol, the solvent removed *in vacuo*, the residue diluted with water and extracted with chloroform. The washed and dried chloroform extract was evaporated and the residue was recrystallized from ethyl acetate–hexane. The yield of **17** was 0.165 g: mp 169–172°; ir bands at 1763, 1718, 1705, 1662, and 1630 cm^{-1}. The analysis was not satisfactory, mol wt (mass spectrum), 346.1548 (calcd for $C_{19}H_{22}O_6$, 346.1530).

Hydrogenation of 17.—A solution of 0.052 g of **17** in 25 ml of ethyl acetate was hydrogenated with 0.54 g of 5% Pd/$BaSO_4$ for 4 hr at atmospheric pressure. Filtration and evaporation gave a solid (**18**) which was recrystallized from ethyl acetate–hexane: yield 0.039 g; mp 183–186°; ir bands at 1770, 1775, and 1720 cm^{-1}; CD curve λ_{max} 285 nm (θ +6390) (c 0.29 mg/ml).

Anal. Calcd for $C_{19}H_{28}O_6$: C, 64.75; H, 8.01; O, 27.24. Found: C, 64.88; H, 7.87; O, 27.48.

Extraction of *Bahia dissecta*.—Finely ground *Bahia dissecta* (Gray) Britton, wt 0.75 kg, collected by Mr. R. Barr on Sept 17, 1963, at Big Lake 10 miles south of Eager, Apache Co., Arizona (Barr No. 63-477, on deposit in herbarium of Florida State University), was extracted with chloroform and worked up in the usual way. The crude gum, wt 12 g, was chromatographed over 200 g of silicic acid as described for the extract of *B. woodhousei*, the eluate being monitored by tlc. All fractions showed several spots on tlc.

Registry No.—**1**, 33143-54-3; **2**, 33143-55-4; **3**, 33143-56-5; **4**, 33143-57-6; **5**, 33143-58-7; **6**, 33143-59-8; **7**, 33143-60-1; **8a**, 33143-61-2; **8b**, 33143-62-3; **9a**, 33143-63-4; **9b**, 33143-64-5; **10**, 33143-65-6; **11**, 33143-66-7; **12**, 33143-67-8; **13**, 33143-68-9; **14**, 33143-69-0; **17**, 33143-70-3; **18**, 33143-71-4.

Notes

A New Etherification Method

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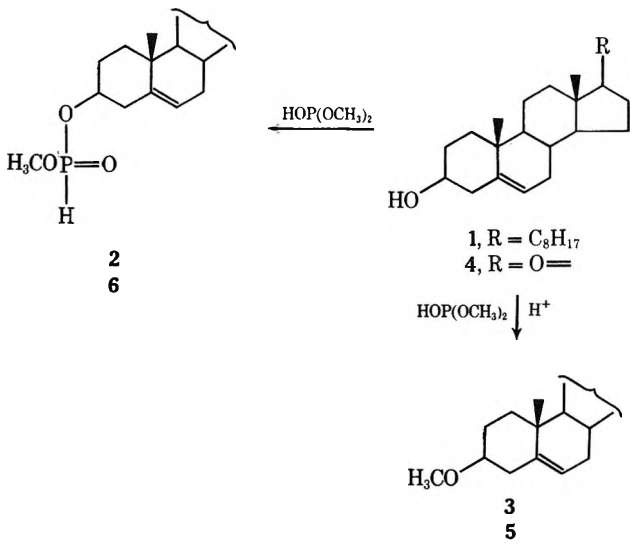
While carrying out research on phosphorus-bearing steroids,[1] we found that the presence of catalytic amounts of acid, in a solution of a steroidal alcohol in dialkyl phosphite, caused the unexpected formation of the corresponding ether. In the absence of acid, the mixed steroidal alkyl phosphite, whose formation can be easily explained, is the main product. Thus, if cholesterol (**1**) is heated for several hours in $HOP(OCH_3)_2$, cholesteryl methyl phosphite (**2**) is the main product. The structure of compound **2** is unequivocally deduced from its nmr spectrum [δ 3.74 d, J = 12 Hz, $P(O)(OCH_3)$; 6.81 d, J = 696 Hz, P(O)H; and 4.24 m, C-3α H]; mass spectrum [m/e 386 (100%), $M^{\cdot+} - P(O)(OCH_3)$; 368 (57%), $M^{\cdot+} - HOP(O)(OCH_3)H$ ("McLafferty" rearrangement); and 353 (29%), $M^{\cdot+} - 96 - CH_3\cdot$], ir, and elemental analysis (see Experimental Section). If, on the other hand, *p*-TsOH (or some other acid) is present in the dimethyl phosphite solution, 3β-methoxycholest-5-ene (**3**)[2] is the

(1) Y. Kashman and M. Sprecher, *Tetrahedron*, **27**, 1331 (1971).

(2) E. Müller and I. Page, *J. Biol. Chem.*, **101**, 127 (1933).



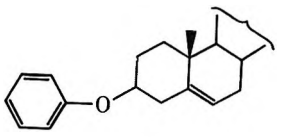
2
6

3
5

main product (*ca.* 60% yield). Hindered or α,β-unsaturated ketones which do not react with $HOP(OCH_3)_2$[1,3] do not interfere with the etherification process. Thus 17-ketoandrost-5-en-3β-ol (**4**) yielded upon heating in $HOP(OCH_3)_2$ containing *p*-TsOH the 3β-methoxy derivative **5**,[4] while in the absence of the acidic catalyst, as in the case of compound **1**, the mixed phosphonate **6** was obtained: nmr δ 3.76 [d, J = 12 Hz, P(O)(OCH_3)], 6.81 [d, J = 694 Hz, P(O)H]; mass spectrum *m/e* 366 (0.15%), $M\cdot^+$, 288 (1.5%), $M\cdot^+ - P(O)(OCH_3)$, 270 (100%), $M\cdot^+ - HOP(O)(OCH_3)H$, and 255 (20%), $M\cdot^+ - 96 - CH_3\cdot$.

The potential utility of phosphites, like compounds **2** and **6**, as intermediates in the preparation of mixed phosphates is now further examined.

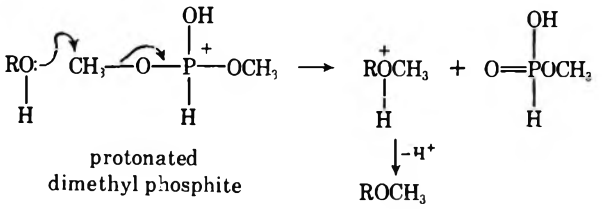
An interesting, although limited, application of this etherification method is the possibility of preparing phenyl ethers, which under other methods are obtained with great difficulty. Heating of cholesterol in diphenyl phosphite in the presence of *p*-TsOH yielded the hitherto unknown 3β-phenoxycholest-5-ene (**7**)



7

[$(C_{33}H_{48}O$; nmr δ 4.10 (m, C-3α H), 7.25 (m, 2 H), and 6.88 (m, 3 H, phenyl group)]. However, this O-arylation is limited to Δ^5-3-hydroxy steroids which can produce a homoallylic cation. When, for example, cholestanol was submitted to these reaction conditions no ether was obtained (Δ^2-cholestane, the elimination product, was the only product isolated).[5]

The most appealing explanation for the mechanism of this O-arylation is firstly the formation of a homoallylic cation[6,7] which then attacks the phosphonate phenoxy group. This in turn gives rise to the 3β ether, known to be the most stable alkoxy isomer obtained from such homoallylic cations, under strong acidic reaction conditions.[7,8] As cholestanol (**8**) does undergo O-methylation with $HOP(OCH_3)_2$ + *p*-TsOH to give the 3β-methoxycholestane[9] (**9**) (60–70% yield) another possible mechanism must exist in the case of the O-alkylation.



From preliminary studies we have found that, in the case of molecules containing more than one alcoholic group, selective etherification phosphorylation occurs, *i.e.*, submitting 3β,17β-androst-5-enediol to the acidic $HOP(OCH_3)_2$ conditions yielded among other products its 3β-methoxy-17β-methylphosphonate derivative [nmr δ 3.32 (s, OCH_3), 3.05 (m, C-3α H), 4.2 (m, C-17α H), and 3.75 (d, J = 12 Hz, P(O)(OCH_3)]. The potential applications of this reaction are being further investigated.

Experimental Section

Melting points were taken on a Unimelt Thomas-Hoover capillary melting point apparatus and are uncorrected. Nmr spectra were taken on a Varian HA-100 spectrometer on 5–10% solutions in $CDCl_3$ containg TMS as an internal standard. Mass spectra were determined with a Hitachi Perkin-Elmer RMU-6 instrument. Ir spectra were recorded on a Perkin-Elmer Model 337. Optical rotations were determined on a Perkin-Elmer Model 141 automatic polarimeter in $CHCl_3$ solution.

The following general procedure was used for the etherification process.

General Procedure.—A steroidal alcohol (1.0 g) dissolved in a minimum amount of dialkyl phosphite (2–10 ml) was left overnight at 90–100°, in the presence of catalytic amounts of *p*-TsOH. The cooled solution was poured into water and the steroid was etherified. The ethereal solution was washed several times with water, aqueous $NaHCO_3$, and again with water and then dried (Na_2SO_4). The solvent was evaporated and the residue was chromatographed through a short silica gel column from which the ether was eluted by hexane.

3β-Methoxycholest-5-ene (3), 3β-Methoxy-17-oxoandrost-5-ene (5), and 3β-Methoxycholestane (9).—These ethers, prepared according to the above procedure, were identical in all respects ($[\alpha]^{25}D$, melting point, ir and nmr) with the known ones.[2,4,9]

3β-Phenoxycholest-5-ene (7).—Compound **7** was prepared according to the general procedure, using diphenyl phosphite, in 50% yield: mp 149° (ethanol); $[\alpha]^{25}D$ −25° (*c*, 0.05, $CHCl_3$); ir (KBr) 1600, 1500, 1240, 1080, 1050, 810, 770, 700 cm^{-1}; nmr ($CDCl_3$) 0.71 (s, C-18 CH_3), 1.08 (s, C-19 CH_3), 4.10 (m, C-3α H), 2.45 (m, C-4 protons), 5.38 (m, C-6 H), 6.88 [*m*-Ph (2 H)], and 7.25 [m, Ph (3 H)]. *Anal.* Calcd for $C_{33}H_{50}O$: C, 86.03; H, 10.50. Found: C, 85.89; H, 10.70.

3β-Cholesteryl Methyl Phosphite (2).—Heating of cholesterol (1.0 g) in dimethyl phosphite (3 ml) for 4 hr, followed by the same work-up as described above for the ethers, yielded compound **2**: low-melting crystals; $[\alpha]^{25}D$ −31° (*c* 0.05, $CHCl_3$); ir (neat) 2400, 1240, 1180, 1050, 1030, 970, 820, 750 cm^{-1}; nmr ($CDCl_3$) 0.68 (s, C-18 CH_3), 1.02 (s, C-19 CH_3), 3.74 [d, J = 12 Hz, P(O)(OCH_3)], 6.81 [d, J = 696 Hz, P(O)H], 4.24 (m, C-3 H), 2.43 (double m, C-4 protons), 5.37 (m, C-6 H), and 1.90 (m, C-7 protons). *Anal.* Calcd for $C_{28}H_{49}O_3P$: C, 72.37; H, 10.63; P, 6.66. Found: C, 72.00; H, 10.29; P, 6.41.

3β-(17-Ketoandrost-5-enyl) Methyl Phosphite (6).—Following the same procedure described for compound **2**, compound **4** yielded compound **6** (50% yield): mp 136–138° (hexane); $[\alpha]^{25}D$

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+5° (c 0.05, $CHCl_3$); ir (KBr) 2400, 1760, 1270, 1190, 1030, 990, 820, 540 cm^{-1}; nmr ($CDCl_3$); 0.89 (s, C-18 CH_3), 1.05 (s, C-19 CH_3), 3.76 [d, J = 12 Hz, P(O)(OCH_3)], 6.81 [d, J = 694 Hz, P(O)H)], 4.30 (m, C-3α H), 2.48 (double m, C-4 protons), and 5.42 (m, C-6 H). *Anal.* Calcd for $C_{20}H_{31}O_4P$: C, 65.56; H, 8.52; P, 8.45. Found: C, 65.90; H, 8.32; P, 8.36.

Registry No.—2, 33066-23-8; 6, 33066-24-9; 7, 13913-60-5.

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The Kinetics and Mechanism of the Decomposition of Potassium Cyanide in Aqueous Alkaline Medium. Hydrolysis of the Simplest Nitrile, HCN

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Cyanide ion is known to decompose slowly in aqueous alkaline solution to yield formate ion and ammonia.[2] In acidic medium the products are formic acid and ammonium ion.[3] In connection with some earlier studies[4] involving aqueous cyanide solutions, we sought to determine the extent and pathway by which this decomposition competed with the reactions under investigation.

$$CN^- + 2H_2O \xrightarrow{OH^-} HCO_2^- + NH_3$$

Krieble[3,5,6] studied the rate of decomposition of hydrogen cyanide in various strongly acidic media. Noting that aqueous cyanide solutions used in electroplating lost strength with "an apparent regularity" upon standing, Leftin[7] found that solutions about 0.25 N in cyanide lost about 0.000240 N/day in cyanide concentration at room temperature. This loss was nearly constant over a period of 180 days. Other workers[8,9] also have discussed the loss of cyanide from electroplating solutions.

In a more definitive study Ricca and D'Amore determined the rate of the decomposition in aqueous solutions through which a stream of CO_2-free air was passed to remove HCN, formed in the hydrolysis of cyanide ion, and the ammonia resulting from the decomposition itself.[2,10] The first-order rate constants for the disappearance of cyanide ion at 30, 50, and 80° were found to be 0.122×10^{-6}, 0.366×10^{-6}, and 2.72×10^{-6} sec^{-1}, respectively. Addition of a 30-fold excess of NaCl was found to retard the rate of the reaction.

More recently, several studies have dealt with the hydrolysis and polymerization of HCN in aqueous solution as a means for removal of HCN from crude coal gas[11] and as a possible means of formation of purine precursors under primitive earth conditions.[12,13]

We present here the results of a more extensive kinetic study of this decomposition and the mechanistic implications of these results.

Results

Experimental procedure differed from that of Ricca and D'Amore in that no air was passed through the solutions during the course of the reaction. Instead, the reaction was carried out under a nitrogen atmosphere in tightly stoppered flasks. Potassium hydroxide was added to suppress the polymerization of HCN, the pH being adjusted to a value of 11 or greater for all runs.[14]

The overall decomposition was found to be cleanly first order with respect to the cyanide ion concentration throughout the range of temperatures and concentrations studied. That the rate was independent of the concentration of hydroxide ion was shown by comparison of the volume of titrant used in simultaneous runs at 33.1 and 49.5° in which the concentration of hydroxide ion was varied. At 49.5°, for example, simultaneous runs 0.0680 and 0.0340 M in KOH required the same volume of titrant, within experimental error, over more than 60% of the reaction.

Effects of added salt and of changes in solvent polarity were also observed. Addition of a tenfold excess of KNO_3 resulted in a small but significant decrease in the overall rate. This effect is the same as was observed earlier for added NaCl.[10] A marked increase in rate was observed when the solvent polarity was diminished by the addition of small amounts of ethanol. The overall rate constants for the decomposition under various conditions are presented in Table I.

Discussion

The kinetic data clearly preclude a reaction mechanism involving direct attack of hydroxide ion upon cyanide ion in the rate-determining step, or one in which two or more hydroxide ions are consumed before the slow step in the reaction. Two reaction pathways are consistent with these data, one involving the direct attack of water upon cyanide ion in the rate-determining step (eq 1), and the other the rapid hydrolysis of

$$CN^- + H_2O \underset{\text{slow}}{\xrightarrow{k_b}} [\text{activated complex}] \underset{\text{fast}}{\xrightarrow{\text{rel}}} \text{products} \quad (1)$$

cyanide ion to HCN (eq 2), with subsequent attack of

$$CN^- + H_2O \overset{K_h}{\rightleftharpoons} HCN + OH^- \quad (2)$$

hydroxide ion upon the HCN in the rate-determining step (eq 3).

$$HCN + OH^- \underset{\text{slow}}{\xrightarrow{k_s}} \begin{bmatrix}\text{activated}\\ \text{complex}\end{bmatrix} \underset{\text{fast}}{\xrightarrow{\text{rel}}} \text{products} \quad (3)$$

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(14) Below pH 10 polymerization of HCN competes with hydrolysis, and at high cyanide concentrations and low pH becomes the predominant reaction pathway.[11,13]

TABLE I
FIRST-ORDER RATE CONSTANTS FOR THE DECOMPOSITION OF POTASSIUM CYANIDE[a]

Temp, °C	Reaction conditions	$k \times 10^7$, sec^{-1}	Standard deviation
33.1	0.181 *M* KOH	0.274	0.020
49.5	0.0680 *M* KOH	1.97	0.09
60.0	0.0680 *M* KOH	5.86	0.09
	0.0667 *M* KOH	5.38	0.17
	4.9% in KNO_3		
	No added KOH	6.09	0.12
65.0	0.0680 *M* KOH	10.07	0.16
	0.0616 *M* KOH, 8.05% in ethanol	14.61	0.15
	0.0551 *M* KOH, 16.4% in ethanol	16.76	0.25

[a] Initial concentration of KCN was 0.05 *M* in all cases.

The rate expression for this process can be derived as follows.[15]

$$\frac{d[\text{activated complex}]}{dt} = k_s[HCN][OH^-] \quad (4)$$

$$[HCN] = K_h[CN^-]/[OH^-] \quad (5)$$

$$\frac{d[\text{activated complex}]}{dt} = -\frac{d[CN^-]}{dt} \quad (6)$$

$$-\frac{d[CN^-]}{dt} = k_s K_h[CN^-] \quad (7)$$

Qualitatively, it can be seen that, in the initial rapid hydrolysis (eq 2), an increase in $[OH^-]$ results in a corresponding decrease in [HCN]. Since the overall rate is actually dependent upon the product, $[HCN][OH^-]$, no change in rate should occur as $[OH^-]$ is varied.

If the former mechanism, in which cyanide ion and water participate directly in the rate-determining step (eq 1), were operative, the overall rate constants, k, would be pseudo first order, since water would be in large excess. The second-order rate constants, k_b, therefore can be obtained by dividing the values of k by the concentrations of water at the respective temperatures.

In the case of the second pathway in which there is attack of hydroxide ion upon HCN, the overall rate constants, k, would in effect be the product, $k_s K_h$. The second-order rate constants, k_s, can be found by dividing each of the overall rate constants by the appropriate hydrolysis constant, K_h. The values of K_h for cyanide ion at different temperatures were obtained by use of the empirical relationship, $\log K_h$ (mol/l.) $= -2.274 - 757.2/T$ (°K), obtained by Marshall and Moelwyn-Hughes.[16] Calculated values of k_b, K_h, and k_s are presented in Table II.

A comparison of the values of k_b and k_s indicates clearly that the reaction pathway involves attack of hydroxide ion upon HCN in the rate-determining step, since k_s is on the order of $10^6 k_b$. Using the tabulated values of k_s the average activation energy, E_a, was found to be 19.7 kcal/mol (standard deviation 0.6). Similarly, values of k_b yielded a value of 23.3 kcal/mol (standard deviation 0.7). It should be noted that the former value, obtained from k_s, is consistent with those for a host of other reactions in which an ion and a neutral molecule are involved in the rate-determining step, whereas the higher value from k_b is not.[17]

(15) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," 2nd ed, Wiley, New York, N. Y., 1961, pp 193–196.

(16) B. W. Marshall and E. A. Moelwyn-Hughes, *J. Chem. Soc.*, 7119 (1965).

TABLE II
CALCULATED VALUES OF k_b, K_h, AND k_s

Temp, °C	33.1[a]	49.5[b]	60.0[b]	65.0[b]
$K_h \times 10^5$, mol/l.[c]	1.79	2.39	2.84	3.07
$k_b \times 10^{10}$, M^{-1} sec^{-1}	4.96	35.9	107	185
$k_s \times 10^3$, M^{-1} sec^{-1}	1.53	8.24	20.6	32.8

[a] Run in 0.181 *M* KOH. [b] Run in 0.0680 *M* KOH. [c] Calculated from $\log K_h$ (mol/l.) $= 2.274 - 757.2/T$ (°K), ref 16.

Effects of added salt upon reactions involving an ion and a neutral molecule participating in the rate-determining step are usually small.[18,19] The small, negative salt effect of both added KNO_3 and NaCl on the overall rate of the decomposition, then, is not inconsistent with either mechanism. The more marked increase in rate which occurs as the solvent polarity is reduced is also consistent with the two mechanisms.[20]

The exact reaction pathway following k_s, is, of course, subject to speculation, although it is likely that formamide is an intermediate. Amides are known to be rapidly hydrolyzed intermediates in the alkaline hydrolysis of nitriles, the initial attack upon the nitrile being the slower step.[23] That formamide is an intermediate is feasible, since the rate constant for the alkaline hydrolysis of formamide[24] at 17° is 1.24×10^{-3} M^{-1} sec^{-1}, whereas k_s calculated at 17° is 8.18×10^{-4} M^{-1} sec^{-1}.

Summary

The spontaneous decomposition of cyanide ion in alkaline medium is believed to follow the reaction pathway

$$CN^- + H_2O \underset{\text{rapid}}{\overset{K_h}{\rightleftharpoons}} HCN + OH^-$$

$$HCN + OH^- \xrightarrow[\text{slow}]{k_s} [\text{activated complex}] \longrightarrow$$

$$HCONH_2 \xrightarrow[\text{fast}]{\text{rel}} HCO_2^- + NH_3$$

(17) Reference 15, p 148.

(18) Reference 15, pp 151–152.

(19) E. S. Gould, "Mechanism and Structure in Organic Chemistry," Holt, Rinehart and Winston, New York, N. Y., 1959, p 186.

(20) However, if the effect of added salt upon k_s in the second pathway is to be determined, the effect upon K_h must be known. Unfortunately, little is known about the latter, although it is known that added NaCl increases K_h slightly, and KNO_3 "salts in" KCN, which would have the same effect. Sodium chloride also "salts in" HCN.[21] An increase in K_h, since the overall rate, k, is decreased, would result in an even larger decrease in k_s than is indicated by the small decrease in k. Since the activated complex would exhibit charge dispersal, solvation of the activated complex, as compared to that of the reactants (HCN and OH^-), would be less in a medium of greater ionic strength.

It is also necessary to determine how a reduction in solvent polarity would affect K_h in the second pathway. Since the hydrolysis of cyanide ion is isoelectric, and the change in solvent polarity is small, the effect should be negligible.[22] The increased overall rate, therefore, would be primarily the result of an increase in k_s.

(21) H. S. Harned and B. B. Owen, "The Physical Chemistry of Electrolyte Solutions," 2nd ed, Reinhold, New York, N. Y., 1950, p. 403.

(22) I. M. Kolthoff and P. J. Elving, "Treatise on Analytical Chemistry," Vol. 1, Part 1, The Interscience Encyclopedia, New York, N. Y., 1959, p 437.

(23) S. Kilpi, *Z. Phys. Chem. (Leipzig)*, **86**, 740; *Chem. Abstr.*, **8**, 2293 (1914).

(24) E. Calvet, *J. Chim. Phys.*, **30**, 140 (1933); *Chem. Abstr.*, **27**, 2868 (1933).

At lower temperatures the decomposition is very slow, the rate increasing by a factor of about three for each 10° rise in temperature. This decomposition can become important, especially at higher temperatures in systems in which cyanide ion is undergoing another reaction, particularly if this reaction is itself fairly slow. There is at least one instance in the literature in which only approximations as the kinetics could be made owing to the lack of rate data on the decomposition of cyanide.[16] Also, there are undoubtedly instances in which this reaction was ignored as being insignificant in kinetic studies.

Experimental Section

General.—J. T. Baker "Analyzed" Reagent KCN was used in the experiments without further purification.

Kinetics.—The progress of the reaction was followed by titration of aliquots of the reaction mixture with standard $AgNO_3$ solution, KI being used as the indicator.[25] The presence of KNO_3 or ethanol in the reaction mixture did not interfere with this method of analysis.

Solutions were prepared using CO_2-free distilled water, stored under nitrogen, and protected from atmospheric CO_2 by trapping the vent with Ascarite. Stock solutions of KOH were prepared in large quantities and standardized; the KCN solutions were prepared from these KOH stock solutions immediately prior to each run.

Runs were made in triplicate under a nitrogen atmosphere in tightly stoppered 125-ml flasks. An initial volume of 100 ml of reaction mixture 0.05 *M* in KCN was used in each instance. The mixtures were prepared from stock solutions kept in the thermostated bath and were reimmersed in the bath immediately after preparation. After 1 hr, and at suitable intervals thereafter, 10-ml aliquots were withdrawn and titrated, the nitrogen in the flasks being replenished each time. The first point obtained after mixing was taken as $t = 0$ in the calculation of the rate constants. Determinations were made until the reactions were 55–80% complete, except for the runs at 33.1°, which were followed to only 16% completion. Runs of different mixture compositions made at the same temperature were carried out simultaneously in order that comparison of differences in rate could be made without regard to small variations in temperature over the course of the experiments.

Errors.—Titrations were read to ±0.02 ml (initial volume of titrant consumed was about 5 ml) and the average volumes of titrant, having a standard deviation of 0.03 ml or less, were used in calculation of the point-by-point rate constants. Each value of k reported in Table I is the average of all of the individual rate constants obtained in a given run. Individual rate constants obtained early in the reaction showed more scatter than those obtained later on, proably because of the very small differences in titre observed initially. The large standard deviation in k obtained at 33.1° is no doubt a reflection of this, since the reaction at this temperature was so slow. Since the accuracy of the values of K_h is uncertain, errors in k_s have not been reported.

Although it was possible to control temperatures to ±0.05°, it is doubtful that this value was realized because of the long duration of the kinetic runs. A value of ±0.1° would probably be a better estimate.

Registry No.—Potassium cyanide, 151-50-8; hydrocyanic acid, 74-90-8; potassium hydroxide, 1310-58-3.

Acknowledgments.—We wish to thank Professor G. Myron Arcand for many helpful discussions. Partial support of this project from the National Science Foundation and the Idaho State University Research Programs Committee is also gratefully acknowledged.

(25) R. A. Day and A. L. Underwood, "Quantitative Analysis," Prentice-Hall, Englewood Cliffs, N. J., 1965, p 106.

A Simple, Comprehensive Correlation of Organic Oxidation and Ionization Potentials

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We have been interested in developing new and useful organic electrooxidations. The sublime goal of this work is of course the ability to predict the products and rates of reactions for any oxidation. The most fundamental data needed for such predictions are the oxidation potentials of the reactants and possible products. One must know if the reactant will give up one or more electrons in the accessible potential range and if the possible products will survive the potential necessary to oxidize the reactant. It would, therefore, be useful to have an equation to predict oxidation

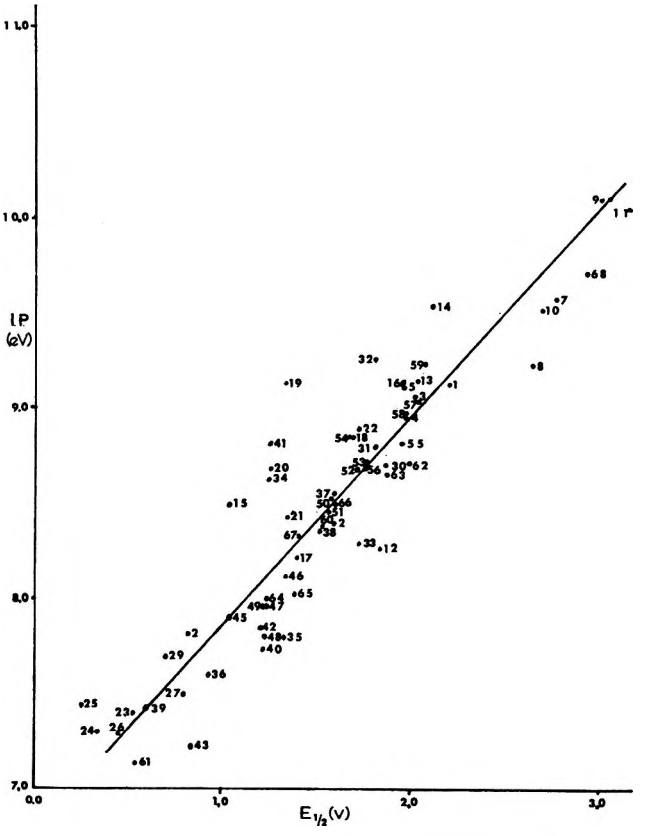

Figure 1.—Plot of vertical IP *vs.* $E_{1/2}$. Numbers refer to Table I.

potentials. This equation should be simple, use readily accessible input data, and provide oxidation potentials for a wide variety of species. We describe such an equation using ionization potentials (IP) as the only input data. Extensive tabulations of IP are available,[1-3] and photoelectron spectroscopy should provide a burgeoning source of data.[4]

(1) R. W. Kiser, "Introduction to Mass Spectrometry and Its Applications," Prentice-Hall, Englewood Cliffs, N. J., 1965, p 308.

(2) M. J. S. Dewar and S. D. Worley, *J. Chem. Phys.*, **50**, 654 (1969).

(3) J. L. Franklin, *et al.*, "Ionization Potentials, Appearance Potentials and Heats of Formation of Gaseous Positive Ions," U. S. Department of Commerce, 1969.

(4) D. W. Turner, C. Baker, A. O. Baker, and C. R. Brundle, "Molecular Photoelectron Spectroscopy," Wiley-Interscience, New York, N. Y., 1970.

TABLE I
OXIDATION AND IONIZATION POTENTIALS

	Compd	IP, eV[a]	$E_{1/2}$, V[b]		Compd	IP, eV[a]	$E_{1/2}$, V[b]
1	2-Butene	9.13	2.21	35	Triphenylene	7.80	1.35
2	1,4-Cyclohexadiene	8.40	1.60	36	Coronene	7.60	0.93
3	1,3-Butadiene	9.07	2.03	37	*m*-Xylene	8.56	1.60
4	Cyclohexene	8.95	1.98	38	Mesitylene	8.39	1.53
5	2-Methyl-1-butene	9.12	1.97	39	Azulene	7.43[f]	0.61
6	Ethylene	10.51	2.90	40	Chrysene	7.75	1.22
7	1-Butene	9.58	2.78	41	Indene	8.81	1.25
8	2-Methylpropene	9.23	2.65	42	Hexamethylbenzene	7.85	1.20
9	2-Methylpentane	10.11	3.01	43	Anthracene	7.23	0.84
10	1-Octene	9.52	2.70	44	Tetracene	6.88	0.53
11	2,2-Dimethylbutane	10.05	3.28	45	1,4-Dimethoxybenzene	7.90[g]	1.04
12	2,3-Dimethyl-1,3-butadiene	8.27	1.84	46	Naphthalene	8.12	1.34
13	2-Iodopropane	9.17	2.04	47	1-Methylnaphthalene	7.96	1.24
14	Methyl iodide	9.54	2.12	48	Phenanthrene	7.80	1.23
15	Phenol	8.50	1.04	49	2-Methylnaphthalene	7.96	1.22
16	1,4-Dioxane	9.13	1.97[c]	50	*o*-Xylene	8.56	1.58
17	Anisole	8.22	1.40	51	*p*-Xylene	8.45	1.54
18	Thiophene	8.86	1.70	52	*p*-Bromotoluene	8.67	1.72
19	*n*-Butyl mercaptan	9.14	1.34	53	Iodobenzene	8.73	1.77
20	Dimethyl sulfide	8.69	1.26	54	Anisaldehyde	8.86[g]	1.64
21	Diethyl sulfide	8.43	1.35	55	Toluene	8.82	1.96
22	Dimethyl sulfoxide	8.84	1.73[c]	56	*p*-Chlorotoluene	8.69	1.76
23	Diphenylamine	7.40	0.53	57	Chlorobenzene	9.07	2.07
24	1-Naphthylamine	7.30	0.34	58	Bromobenzene	8.89	1.98
25	2-Naphthylamine	7.25	0.44	59	Benzene	9.24	2.04
26	Dimethylaniline	7.14	0.45	60	Biphenyl	8.27	1.48
27	Triethylamine	7.50	0.79[c]	61	Perylene	7.15	0.55
28	Trimethylamine	7.82	0.82	62	1-Propylbenzene	8.72	1.97
29	Aniline	7.70	0.70[d]	63	2-Propylbenzene	8.69	1.88
30	*n*-Butylamine	8.71	1.87[c]	64	Pentamethylbenzene	7.92	1.28
31	*N,N*-Dimethylacetamide	8.81	1.82[c]	65	1,2,4,5-Tetramethylbenzene	8.03	1.29
32	Pyridine	9.27	1.82	66	1,2,3-Trimethylbenzene	8.48	1.58
33	Quinoline	8.30	1.73[e]	67	1,2,4-Trimethylbenzene	8.27	1.41
34	Fluorene	8.63	1.25	68	*tert*-Butyl alcohol	9.71	2.94[c]

[a] Photoionization or spectroscopic values compiled by Kiser[1] except where noted. [b] Measured in acetonitrile at platinum. Reported *vs.* $Ag|AgNO_3$. Values from the compilation of C. K. Mann and K. K. Barnes, "Electrochemical Reactions in Nonaqueous Systems," Marcel Dekker, New York, N. Y., 1970, except where noted. [c] Measured by E. A. Mayeda. [d] C. Parkanyi and R. Zahradnik, *Collect. Czech. Chem. Commun.*, **30**, 4287 (1965). [e] R. N. Adams, "Electrochemistry at Solid Electrodes," Marcel Dekker, New York, N. Y., 1969, p. 320. [f] Reference 2. [g] A. D. Baker, D. P. May, and D. W. Turner, *J. Chem. Soc. B*, 22 (1968).

Previous workers have correlated the IP and oxidation potentials ($E_{1/2}$) of aromatic hydrocarbons and alkenes and discussed the reasons underlying such a correlation.[5,6] In particular, the relatively small solvation energy changes and the probable monotonic variation of solvation energy with the size of the hydrocarbon and therefore its IP were mentioned.

Expansion of this idea to include all sorts of organic molecules is possible as illustrated by Figure 1. This plot includes all the reliable data that we could collect from the literature and several values determined in our laboratory. The electrochemical data all refer to acetonitrile solvent and a smooth platinum anode. The reference electrode is $Ag|AgNO_3$ in acetonitrile. Data reported *vs.* sce were corrected by adding -0.30 V. The numbers used are simple averages of all reports. Both half-wave and peak potentials are reported in the literature. We have corrected the latter by adding -0.15 V. This value is approximate but reasonable for these irreversible oxidations. Several literature values were checked and a few not on the line were not reproduced. These points were rerun several times including a determination by an independent investigator.[7] The revised values were used and several closely related points (same papers, similar structures) which appeared to need revision were excluded.[8] Only vertical IP were used (Table I).

The plot in Figure 1 fits the equation $E_{1/2} = 0.92(\text{IP}) - 6.20$. As expected, the slope is less than unity. Because there are a disproportionate number of aromatic hydrocarbons included in Figure 1, we have made a more representative plot in Figure 2. The least-squares line has the equation $E_{1/2} = 0.89(\text{IP}) - 6.04$. The correlation coefficient for the plot in Figure 1 is 0.92 and in Figure 2 is 0.95. Since the data came from many different sources and we know there is often considerable error in the $E_{1/2}$ values, this seems quite acceptable.

It should be realized that since the initially formed

(5) W. C. Neikam, G. R. Dimeler, and M. M. Desmond, *J. Electrochem. Soc.*, **111**, 1190 (1964).

(6) E. S. Psych and N. C. Yang, *J. Amer. Chem. Soc.*, **85**, 2124 (1963).

(7) We thank Dr. Lloyd Jones for these measurements.

(8) The point for ethylene is not on the plot but was included in the least-squares calculation. Points 30 and 31 are revised values. $E_{1/2}$ data for several substituted anilines[9] and amides and primary amines[10] were excluded. Different sets of values for the latter are given in the original literature and in a book by the same author. Our values differ from both.

(9) S. Wawzonek and T. W. McIntyre, *J. Electrochem. Soc.*, **114**, 1025 (1967).

(10) C. K. Mann and K. K. Barnes, "Electrochemical Reactions in Nonaqueous Systems," Marcel Dekker, New York, N. Y., 1970, Chapter 9.

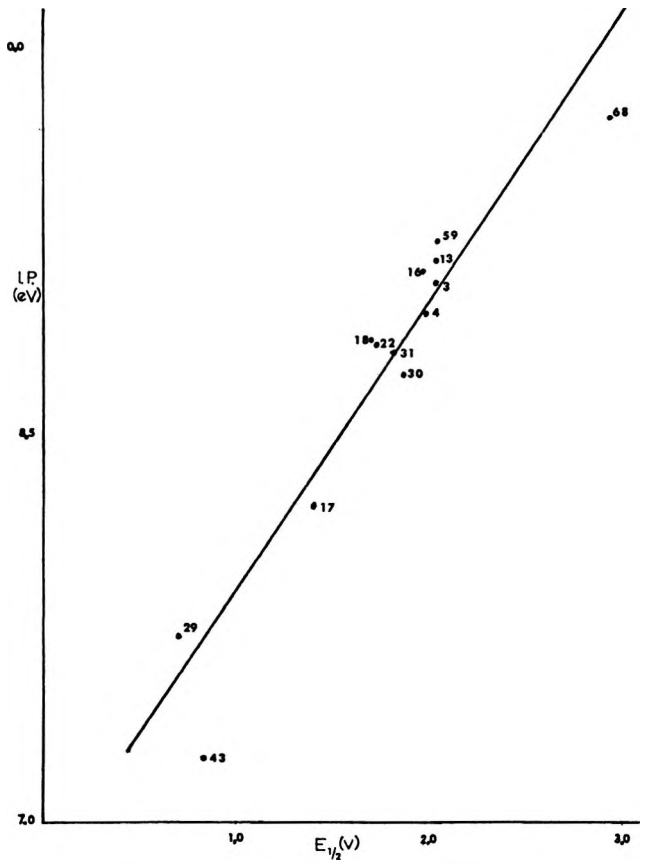

Figure 2.—Plot of selected vertical IP *vs.* $E_{1/2}$. Numbers refer to Table I.

cation radical decays much more rapidly than the time required for the measurement $E_{1/2}$ is a kinetic parameter for the overall oxidation process. If one considers this fact in addition to the possible incursion of specific surface effects and differential solvation, this simple correlation is fascinatingly accurate. The correlation results because the energy of the highest occupied molecular orbital (HOMO) primarily determines both potentials. Several groups have described correlations of IP or $E_{1/2}$ with the HOMO energy[2,11] and it is clear that either potential should be calculable. It does appear that phenol and butyl mercaptan have abnormally low $E_{1/2}$ values because of special solvation. The cation radicals of these species will be strong acids stabilized by hydrogen bonding to the basic solvent, acetonitrile. This will, of course, lower the $E_{1/2}$. Other solvation effects and specific surface effects might be uncovered by a careful study of $E_{1/2}$ variations as a function of solvent and electrode material.

This correlation should have interesting ramifications in organic electrochemistry. As indicated, decisions about synthetic feasibility can be made with some confidence based upon oxidation potential predictions for reactants and products. In a similar manner, electrooxidation can be applied selectively to the most easily oxidized functionality of a complex molecule. Photoelectron spectroscopy is of interest in this regard since it not only provides IP data but reveals the nature of the HOMO.[4] Finally, it is noted that homogeneous electron-transfer oxidation rates and the $E_{1/2}$ of radicals[12] and inorganic complexes may be amenable to a similar treatment.

Acknowledgment.—We thank the Petroleum Research Fund and the National Science Foundation for support.

(11) An extensive and modern treatment with references is M. J. S. Dewar, J. A. Hashmall, and N. Trinajstic, *J. Amer. Chem. Soc.*, **92**, 5555 (1970).

(12) H. Volz and W. Lotsch, *Tetrahedron Lett.*, 2275 (1969) report −0.47 V for the reduction $E_{1/2}$ of tropylium perchlorate on mercury. Since this couple is probably fully reversible and therefore independent of electrode, we would calculate the IP as 6.25. The reported[1] spectroscopic IP is 6.24!

Oxidative Coupling of Aldehydes and the Rearrangement of Dioxa-1,5-hexadienes

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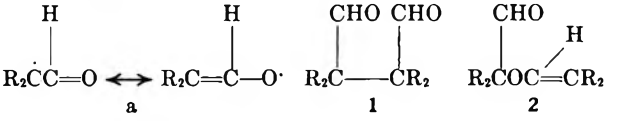
The oxidation[2] of aldehydes of the form R_2CHCHO by active manganese dioxide gives products which can be formulated as dimers of the free radical a. These are **1** and **2**. The other symmetrical coupling product, the divinyl peroxide, $R_2C{=}C(H)OOC(H){=}CR_2$, **3**, has not been observed. We have been interested in dioxa-1,5-hexadienes and their rearrangements in connection with our studies[3] of allylic carboxylates, which are 1,3-dioxa-1,5-hexadienes. Compounds **1**, **2**, and **3** are respectively substituted 1,6-, 1,4-, and 3,4-dioxa-1,5-hexadienes.



The Cope rearrangement would lead to the rearrangements **2** ⇄ **2** and **1** ⇄ **3**. The first is a degenerate rearrangement which could be revealed by labeling as has been done in one cyclic case;[4] in the open-chain case the completely methylated compound **2a** does not show any nmr line broadening at 150°,[2] showing by this method no degenerate rearrangement. In this note we present evidence supporting in some detail the free-radical coupling mechanism and observe some of the proposed rearrangements.

There was a possibility that the active manganese dioxide oxidation could be exploited to give products allowing a study of the rearrangement whether or not the radical coupling mechanism is correct. If the mechanism is incorrect, then oxidation of optically active α-methylbutylraldehyde might give an optically active form of the oxidation product in either of the geometrically isomeric form **2b** or **2c**. On the other hand, if the mechanism is correct, **2b** and **2c** will be optically inactive, but cross products **2d**, **2e**, and **2f** might result from the oxidation of a mixture of isobutyraldehyde and α-methylbutyraldehyde. The Cope rearrangement would be expected to be accom-

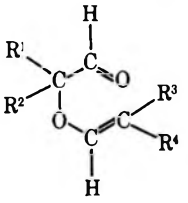
(1) National Science Foundation Predoctoral Fellow, 1968–1971.

(2) J. C. Leffingwell, *Chem. Commun.*, 357 (1970).

(3) E. S. Lewis, J. T. Hill, and E. R. Newman, *J. Amer. Chem. Soc.*, **90**, 662 (1968).

(4) J. D. Roberts and R. P. Lutz, *ibid.*, **83**, 2198 (1961).

panied by the racemization of optically active **2b** or **2c**, and by the interconversions **2b** ⇄ **2c**, **2f** ⇄ **2e**, and **2f** ⇄ **2d**.



2a, $R^1 = R^2 = R^3 = R^4 = CH_3$
b, $R^1 = R^3 = CH_3$; $R^2 = R^4 = C_2H_5$
c, $R^1 = R^4 = CH_3$; $R^2 = R^3 = C_2H_5$
d, $R^1 = R^2 = R^3 = CH_3$; $R^4 = C_2H_5$
e, $R^1 = R^2 = R^4 = CH_3$; $R^3 = C_2H_5$
f, $R^1 = R^3 = R^4 = CH_3$; $R^2 = C_2H_5$

We find that the manganese dioxide oxidation of optically active α-methylbutyraldehyde (from the oxidation of *sec*-butylcarbinol from fusel oil) gave in agreement with the previous report a mixture of **2b** and **2c**, as shown by the nmr,[5] with no detectable rotation (<0.01° neat in a 1-dm tube). The oxidation of a mixture of isobutyraldehyde and α-methylbutyraldehyde gave a complex mixture. After steam distillation, the volatile fraction showed upon gas chromatographic analysis peaks of retention time corresponding to **2a**, the mixture of **2d**, **2e**, and **2f**, and the mixture of **2b** and **2c**. It was possible by preparative gas chromatography to further isolate and characterize **2f** and the mixture of olefinic stereoisomers **2d** and **2e**. All of these results are consistent with the proposed free-radical mechanism.

It did prove possible to separate partially the cis and trans isomers, **2b** and **2c**, by gas chromatography. From the roughly 1:1 mixture given by oxidation, a fraction containing a 3.8:1 ratio was obtained. This fraction on heating to 200° in a capillary tube for 95 min was converted to a mixture of 1.8:1 ratio, together with a good deal of polymer. If we assume an equilibrium constant of unity and equal rates of polymerization, this gives a rate constant for **2b** → **2c** (or the reverse) of roughly 6×10^{-5} sec^{-1}. Assuming an *A* factor of 10^{11} sec^{-1}, we calculate an activation energy of roughly 33 kcal/mol. Furthermore, we have observed that **2f** → **2d** and **2e** at 200° at about the same rate as the cis–trans isomerization.

A simple estimate of ΔH for the **3** → **1** process using average bond energies shows it to be exothermic by more than 100 kcal/mol. The activation energy for this reaction would be probably no more than half that for the symmetric **2** → **2** process. This low an activation energy would make the reaction **3** → **1** very fast and account for the failure to observe **3** even if formed, and the slower rate of the **2** → **2** process accounts for the temperature-independent nmr spectrum of **2a**.

Registry No.—**2d**, 33066-03-4; **2e**, 33066-04-5; **2f**, 33061-15-3; isobutyraldehyde, 78-84-2; α-methylbutyraldehyde, 96-17-3.

Acknowledgment.—We acknowledge gratefully the support of this research by a grant from the National Science Foundation. We also thank Dr. J. C. Leffingwell for telling us of an improved technique for the oxidation.

(5) J. C. Leffingwell, French Patent 1,544,604 (1968).

Reduction of Sulfoxides with Sodium Hydrogen Sulfite[1]

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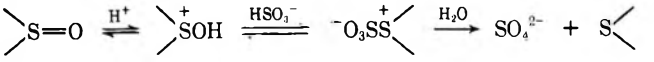
Received September 8, 1971

Sulfoxides can be reduced to sulfides under a variety of conditions.[2] The sulfoxide group is capable of oxidizing a carbon atom, but more typical are reactions in which heteroatoms are oxidized. Thiols are oxidized to disulfides,[3] phosphines to phosphine oxides,[4] phosphorus thioacids to phosphorus oxyacids,[5] halide ions to halogens,[6] and silanes to silicon–oxygen derivatives[7] with the concomitant reduction of a sulfoxide to the corresponding sulfide.

The sulfoxides of *dl*-methionine and α-ethyl thioglucoside were reported in 1939 to be reduced by aqueous sulfite.[8] More recently, aqueous solutions of sodium "metabisulfite" have been employed in the selective reduction of the sulfoxide group in α-methylsulfinylacetophenone and derived compounds.[9] Our interest in this method of reduction of sulfoxides was fostered by a fortuitous observation that brief treatment of a mixture of *cis*- and *trans*-2-methylthiolane 1-oxide[10] with aqueous sodium hydrogen sulfite results in the preferential destruction of the cis isomer. This experiment provided an easy method for the preparation of pure *trans*-2-methylthiolane 1-oxide. The more rapid consumption of the cis isomer immediately suggests to us that this reduction reaction involves a nucleophilic attack at sulfur. The "back-side" of the sulfoxide group is less sterically encumbered in the cis diastereomer. Similarly, we find that the *cis*-4-*tert*-butylthiane 1-oxide[11] is reduced somewhat faster than *trans*-4-*tert*-butylthiane 1-oxide. As a working hypothesis we propose the following mechanistic scheme



Analysis of reaction of thiolane 1-oxide and sodium hydrogen sulfite revealed that sulfate was formed in amounts equimolar with the consumption of the sulfoxide. As predicted from the scheme, aqueous sodium sulfite is not an effective reducing reagent for sulfoxides; the pH of the solution is not low enough to result in a significant concentration of protonated sulfoxide. On the other hand, aqueous solutions of

(1) Part XXXVII in the series "Chemistry of Sulfoxides and Related Compounds." We gratefully acknowledge support by the National Science Foundation (GP 8648).

(2) For recent leading references see D. W. Chasar, *J. Org. Chem.*, **36**, 613 (1971).

(3) T. J. Wallace and H. A. Weiss, *Chem. Ind. (London)*, 1558 (1966).

(4) H. H. Szmant and O. Cox, *J. Org. Chem.*, **31**, 1595 (1966); I. Granoth, A. Kalic, and Z. Pelak, *J. Chem. Soc. C*, 2424 (1969).

(5) M. Mikolajczyk and M. Para, *Chem. Commun.*, 1192 (1969).

(6) D. Landini, F. Montanari, H. Hogevein, and G. Maccagnani, *Tetrahedron Lett.*, 2691 (1964).

(7) T. H. Chan, A. Milnyk, and D. N. Harpp, *ibid.*, 201 (1969).

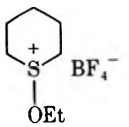
(8) F. Michael and H. Schmitz, *Chem. Ber.*, **72**, 992 (1939).

(9) G. A. Russell and E. T. Sabourin, *J. Org. Chem.*, **34**, 2336 (1969).

(10) J. J. Rigau, C. C. Bacon, and C. R. Johnson, *ibid.*, **35**, 3655 (1970).

(11) C. R. Johnson and D. McCants, Jr., *J. Amer. Chem. Soc.*, **87**, 1109 (1965).

sulfur dioxide (which is acidic) readily reduced sulfoxides to sulfides.[12] Compared to the free sulfoxide, the protonated sulfoxide has a more electrophilic sulfur and a better leaving group on sulfur (^{-}OH *vs.* O^{2-}). Similar advantages should also be available in O-alkylated sulfoxides. It was found that alkoxysulfonium salts were rapidly and quantitatively reduced to sulfides by saturated aqueous solutions of either sodium hydrogen sulfite or sodium sulfite. The reactions of alkoxysulfonium salts are much faster than the direct reductions of sulfoxides by hydrogen sulfite; *e.g.*, the reduction of **1** is complete



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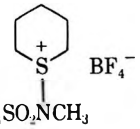


2

in a few minutes at room temperature, whereas reduction of thiane 1-oxide is only 27% complete after 135 min. Other leaving groups on sulfur also facilitate the reaction. The aminosulfonium salt **2**[13] was quickly and cleanly converted to thiane by sulfite solutions.

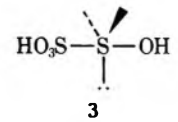
The relative rates of reduction of a series of sulfoxides under standardized conditions were examined in a semiquantitative fashion; partial data which reflect the trends found are summarized in Table I. These

TABLE I
REDUCTION BY SATURATED AQUEOUS SODIUM HYDROGEN SULFITE

Sulfoxide	% Reduction after 60 min
Diethyl sulfoxide	45
Isopropyl methyl sulfoxide	8
Thietane 1-oxide	18
Thiolane 1-oxide	100[a]
Thiane 1-oxide	16
Thiepane 1-oxide	52

[a] Reduction complete at 10 min.

data appear to indicate that the reduction proceeds *via* a pathway involving substitution at the sulfoxide sulfur, which occurs in, or prior to, the rate-determining step. Branching at the carbon α to the sulfoxide has a retarding effect on the reaction. In the cyclic sulfoxides, the rate reaches a maximum in the case of the five-membered ring. In reactions which involve rehybridization from sp^3 to sp^2 of a carbon reaction center, five-membered rings react faster than four- or six-membered ones, and branching is known to retard rates.[14] Whether **3** represents a transition state



3

or an energetically contiguous intermediate, the response to substitution pattern and ring size should follow along the same general trends as observed for SN2 reactions at carbon. It appears to be typical of the thiolane ring system to display increased reactivity. In the case of thermally induced pyramidal inversion of cyclic sulfonium salts, the five-membered rings were found to invert slightly faster than a six-membered one.[15] In the hydrogen chloride catalyzed stereomutation of sulfoxides, the thiolane 1-oxides react some 300 times faster than thiane 1-oxides.[15] In periodate oxidations of sulfides to sulfoxides, thiolane reacts faster than either thietane or thiane.[16]

For preparative purposes, especially when stereoselectivity is not a consideration, the bisulfite reductions are conveniently run on a steam bath. A cosolvent such as dioxane or methanol may be added in the case of poorly soluble sulfoxides.

Experimental Section

Reduction of *n*-Butyl Sulfoxide.—*n*-Butyl sulfoxide (4 g) was added to a solution of 16 g of sodium hydrogen sulfite in 40 ml of water. The mixture was heated on a steam bath with stirring for 40 hr. The mixture was cooled and extracted several times with chloroform. Vpc analysis showed the extract to contain no sulfoxide. Distillation provided 2.5 g (70 %) of pure *n*-butyl sulfide.

***trans*-2-Methylthiolane 1-Oxide.**—Mixtures[10] enriched in the trans sulfoxide were treated briefly (10 to 20 min) with aqueous sodium hydrogen sulfite at room temperature. The reactions were followed by vpc analysis. The 2-methylthiolane was extracted with pentane. Pure *trans*-2-methylthiolane 1-oxide was obtained by extraction with chloroform.

Reaction of *trans*-2-methylthiolane 1-oxide with trimethyloxonium fluoroborate in methylene chloride gave *trans*-2-methyl-1-methoxythioniacyclopentane fluoroborate, mp 82–83°.

Anal. Calcd for $C_6H_{13}BF_4OS$: C, 32.75; H, 5.95. Found: C, 33.01; H, 6.24.

***cis*-2-Methylthiolane 1-Oxide.**—Hydrolysis of the above salt with aqueous sodium hydroxide gave pure cis sulfoxide, which was converted to *cis*-2-methyl-1-methoxythioiacyclopentane fluoroborate, mp 53–54°.

Anal. Calcd for $C_6H_{13}BF_4OS$: C, 32.25; H, 5.95. Found: C, 32.63; H, 5.96.

Basic hydrolysis of this salt gave 100% of the trans sulfoxide.

1-Ethoxythioniacyclohexane fluoroborate (2) was prepared by reaction of thiane 1-oxide with triethyloxonium fluoroborate in methylene chloride. The very hygroscopic salt had mp 35–37°.

Anal. Calcd for $C_7H_{15}BF_4OS$: C, 35.92; H, 6.46. Found: C, 36.20; H, 6.59.

Registry No.—**2**, 33143-36-1; sodium hydrogen sulfite, 7631-90-5; *n*-butyl sulfoxide, 2168-93-6; *trans*-2-methylthiolane 1-oxide, 25859-45-4; *trans*-2-methyl-1-methoxythioniacyclopentane fluoroborate, 33213-38-6; *cis*-2-methylthiolane 1-oxide, 25859-44-3; *cis*-2-methyl-1-methoxythioniacyclopentane fluoroborate, 33143-40-7.

(12) Sulfurdioxide in ethanol or chloroform failed to reduce sulfoxides.

(13) For method of preparation see C. R. Johnson, J. J. Rigau, M. Haake, D. McCants, Jr., J. E. Keiser, and A. Gertsema, *Tetrahedron Lett.*, 3719 (1968).

(14) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, New York, N. Y., 1962, p 268.

(15) A. Garbesi, N. Corsi, and A. Fava, *Helv. Chim. Acta*, 1499 (1970).

(16) C. R. Johnson and P. E. Rogers, unpublished results.

Cyclization of Dimethyl-1,6-octadienes

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Received August 9, 1971

In this paper, we describe the cyclization of 5,7-dimethyl-1,6-octadiene (**1**) and 3,7-dimethyl-1,6-octa-

diene (2) with formic acid in the presence of BF_3 etherate or a strong mineral acid as a catalyst.

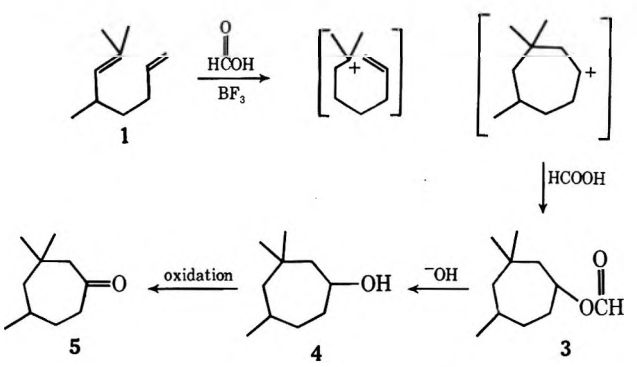
Diene **1**, when treated with excess of formic acid in the presence of a catalytic amount of BF_3 or mineral acid at 50° for 6 hr gave a mixture of 3,3,5-trimethylcycloheptanyl formates **3a,b** in about 50% conversion (two peaks by glc[1] analysis). The formates **3a,b** were hydrolyzed with aqueous methanolic sodium hydroxide to yield a mixture of alcohols **4a,b** (two peaks by glc[1]) which were oxidized with chromic acid at 30° to give 3,3,5-trimethylcycloheptanone (**5**) (single peak by glc[1]). The semicarbazone of **5** gave mp 196–198° (lit.[2] 196–197°).

Diene **2** when treated with formic acid in the presence of a catalytic amount of BF_3 etherate at 50–60° for 4 hr, gave in 45% conversion a mixture of formates **6** and **7** which appeared as a single major peak on glc.[1] Hydrolysis of the mixture with 25% methanolic sodium hydroxide gave the corresponding alcohols **8** and **9**, which were shown to be in 4:1 ratio respectively by glc (10% Apeizon column, 20 ft × 1/4 in.).

The mixture of alcohols **8** and **9** was oxidized with chromic acid at 30° to give the corresponding ketones **10** and **11**, which were separated by preparative glc (10% Apeizon column). The structure of the major component, 3,3-dimethylcyclohexyl methyl ketone (**10**) was supported by the spectral data (see Experimental Section). The nmr spectrum of **11** was superimposable with that of tetrahydroeucarvone[3] prepared by the hydrogenation of eucarvone. The DNP derivative had mp 135–137° (lit.[4] 137–138°).

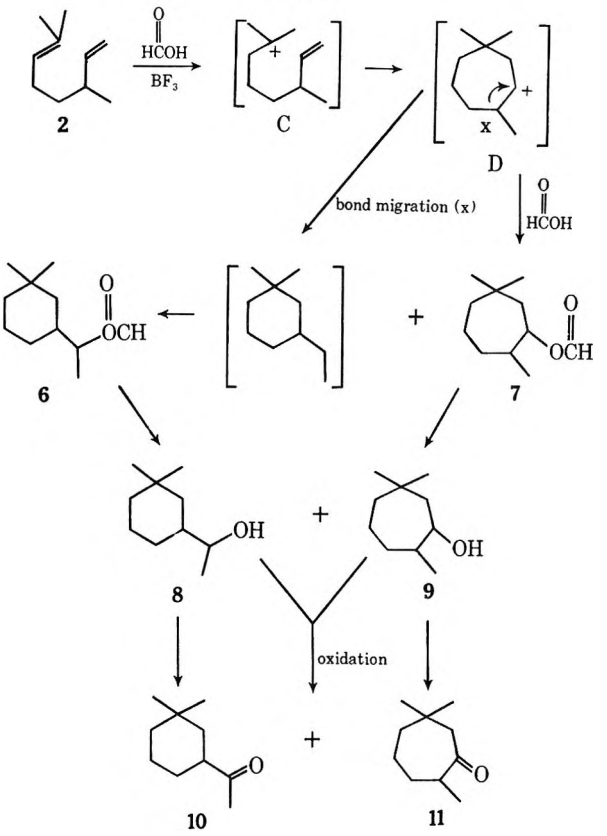
Mechanism.—The products obtained in treating 5,7-dimethyl-1,6-octadiene (**1**) and 3,7-dimethyl-1,6-octadiene (**2**) with formic acid and BF_3 etherate could be accounted for by the mechanism shown in Schemes I and II, respectively.

SCHEME I



In connection with this work, it was of interest to see if the solvolysis of tetrahydroeucarvanyl tosylate **12** would yield the rearranged product **6**. Tetrahydroeucarvanol, which was obtained by the reduction of tetrahydroeucarvone with lithium aluminum hydride, on treatment with *p*-toluenesulfonyl chloride and pyridine gave the corresponding tosylate **12**, which when treated with sodium formate and formic acid under nitrogen atmosphere at 75° for 6 hr gave a mixture of formates along with a mixture of olefins. The formates were hydrolyzed with methanolic sodium hydroxide and then oxidized with chromic acid to give a mixture of ketones which were separated by preparative vpc and were identified as **10** and **11**.

SCHEME II



Experimental Section

All the nmr spectra were run on a Varian HA-100 spectrometer. All chemical shifts are reported in parts per million (δ) relative to TMS. The C and H analyses were run by Schwarzkopf Microanalytical Laboratory.

Cyclization of 5,7-Dimethyl-1,6-octadiene (**1**).—In a three-necked flask fitted with a condenser, stirrer, thermometer, and dropping funnel 26 g of BF_3 etherate was added slowly at room temperature to a mixture of 211 g of formic acid (90%) and 290 g of 5,7-dimethyl-1,6-octadiene. The mixture was stirred for 6 hr at 50–60°. After this period, 150 g of sodium acetate was added and the mixture was stirred for 10 min. After separating the oil layer, the acid layer was diluted with an equal volume of water and extracted with benzene. The combined organic layers were washed once with water and the solvent was removed *in vacuo*. After distilling the hydrocarbons the product was fractionated to give 1749 g (45% conversion) of the pure formates (**3a,b**): bp 80° (5 mm); $n^{20}D$ 1.4490; ir (film) 5.78 and 8.5 μ; nmr 0.92, 1.01 [6 H, 2 singlets, $-C(CH_3)_2$], 0.88 (3 H, doublet, $CHCH_3$), 1.2–2.1 (8 H, multiplet, CH_2), 4.81 [1 H, multiplet, HCO(C=O)H], 7.9 [1 H, O(C=O)H].

Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.75; H, 10.89. Found: C, 71.55; H, 10.91.

3,3,5-Trimethylcycloheptanone (**5**).—To 55.0 g of alcohols (**4a,b**) obtained by hydrolysis of the corresponding formates with methanolic sodium hydroxide was added a solution of 43.2 g of chromic acid, 43.2 g of glacial acetic acid, and 43.2 g of water over a period of 1 hr, maintaining the temperature of 25–30°. The reaction mixture was further stirred at 30° for 3 hr. After

(1) Glc 5% SE-30 column, 20 ft × 1/4 in. at 150°.
(2) G. Buchi and E. M. Burgess, *J. Amer. Chem. Soc.*, **82**, 4333 (1960).
(3) E. J. Corey and H. J. Burke, *ibid.*, **78**, 174 (1956).
(4) J. R. B. Campbell, A. M. Islam, and R. A. Raphael, *J. Chem. Soc.*, 4097 (1956).

this period, 60 ml of water was added and the mixture was steam distilled to give 42.1 g of the crude product, which was fractionated to give 36 g of pure ketone 5 (65% yield), $n^{20}D$ 1.4578, semicarbazone mp 196–198° (lit.[4] 196–197°). The infrared spectrum was superimposable on the spectrum of 3,3,5-trimethylcycloheptanone kindly supplied by Professor Buchi. The mass spectrum showed a parent peak with *m/e* 154, and fragmentation ions with *m/e* 139, 126, 83, 69, 55, 41.

Cyclization of 3,7-Dimethyl-1,6-octadiene (2).—In a three-necked flask fitted with stirrer, thermometer, and reflux condenser was added 44 g of BF_3 etherate to a stirred mixture of 422 g of 3,7-dimethyl-1,6-octadiene and 307 g of formic acid (90%) over a period of 10 min at room temperature (slightly exothermic). The mixture was then heated to 50–60° and stirred at this temperature for 4 hr. Heating was discontinued and the mixture was stirred for another 30 min. An equal volume of water was added and the oil layer was separated. The water layer was extracted twice with benzene. The combined organic layer was washed neutral with sodium bicarbonate solution, and benzene was removed *in vacuo*. After distilling off hydrocarbons the product was fractionated to give 270 g of the formates 6 and 7 (50% conversion). The mixture of formates (6, 7) showed a single peak by glc analysis (20 ft ×, 1/4 in., SE-30, 5%, packed column). The infrared spectrum (film) showed absorption bands at 5.78 and 8.5 μ. The mass spectrum exhibited a peak at *m/e* 138 (M − 46).

Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.75; H, 10.89. Found: C, 71.50; H, 11.04.

Hydrolysis of Formates 6 and 7 to Alcohols 8 and 9.—The mixture of formates (11.0 g) was refluxed with 25.0 g of sodium hydroxide and 75 ml of 50% aqueous methanol for 2 hr. After recovering methanol, the crude mixture was acidified with 2% acetic acid and extracted with ether. The ether extract was washed once with sodium carbonate solution and once with water and then dried ($MgSO_4$). The solvent was removed *in vacuo* and the residue was distilled to give a mixture of alcohols (8, 9) in 75% yield. Glc analysis indicated two components in an approximate ratio of 4:1. The major peak, isolated by preparative vpc (10% Apeizon, 20 ft × 1/4 in.), was shown to be alcohol 8: ir (film) hydroxyl band at 2.93 μ; nmr ($CDCl_3$) 0.89, 0.92 [6 H, 2 singlets, $C(CH_3)_2$], 1.08 (3 H, doublet, $CHCH_3$), 1.55 (1 H, broad singlet, for OH), 1.12–1.86 (8 H, multiplet, $-CH_2-$). The mass spectrum showed a parent peak at *m/e* 156.

Anal. Calcd for $C_{10}H_{20}O$: C, 76.95; H, 12.81. Found: C, 76.82; H, 12.77.

Oxidation of Alcohols 8 and 9 to Ketones 10 and 11.—To 52.0 g of mixture of alcohols (8, 9) was added a solution of 40.0 g of chromic acid, 40.0 g of acetic acid, and 40.0 g of water at 25–30° over a period of 1 hr. The reaction mixture was stirred further for 3 hr at 30°. The mixture was then diluted with 60 ml of water and steam distilled to give 43.0 g of the crude product which was distilled to give a mixture of ketones (10, 11), bp 89° (14 mm). Glc analysis using an Apeizon column (10%) 20 ft × 1/4 in. showed two peaks in a ratio of 4:1, respectively. The infrared spectrum (film) of the major compound, obtained by preparative vpc, exhibited a carbonyl band (5.86 μ); nmr (CCl_4) 0.92, 0.95 [6 H, two singlets, $C(CH_3)_2$], 1.12–1.86 (8 H, multiplet, $-CH_2-$), 2.02 [3 H, singlet, $(C{=}O)CH_3$], 2.17–2.55 (1 H, multiplet, $CH(C{=}O)CH_3$]. The mass spectrum showed a peak at *m/e* 154.

Anal. Calcd for $C_{10}H_{18}O$: C, 78.00; H, 11.78. Found: C, 77.82; H, 12.01.

The 2,4-dinitrophenylhydrazone had mp 102–103°.

The infrared spectrum (film) of 11, the minor component isolated by preparative vpc, exhibited a carbonyl band at 5.84 μ. The nmr spectrum ($CDCl_3$) indicated signals at 0.91, 0.96 [6 H, two singlets, $C(CH_3)_2$], 1.02 (3 H, doublet $CHCH_3$), 2.28 (2 H, AB quartet, J_{AB} = 11.5 Hz, $=OCHCH$), 2.28 (1 H, multiplet, $CHCH_3$), 1.2–1.7 (6 H, multiplet, $-CH_2-$). The 2,4-dinitrophenylhydrazone had mp 136–139° (lit.[3] 137–138°).

Registry No.—1, 33515-77-4; 2, 33515-78-5; *cis*-3a, 33511-45-4; *trans*-3b, 33511-46-5; 6, 25225-08-5; 7, 33515-80-9; 8, 25225-09-6; 9, 33515-82-1; 10, 25304-14-7; 10 2,4-DNPH, 25412-05-9; 11, 4436-59-3.

Acknowledgment.—The authors thank Professor G. Stork for helpful discussions with regard to the mechanism of the reaction.

Preparation of Difluoramino-Substituted Vinyl *N*-Fluorimines[1]

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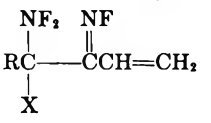
Received November 5, 1970

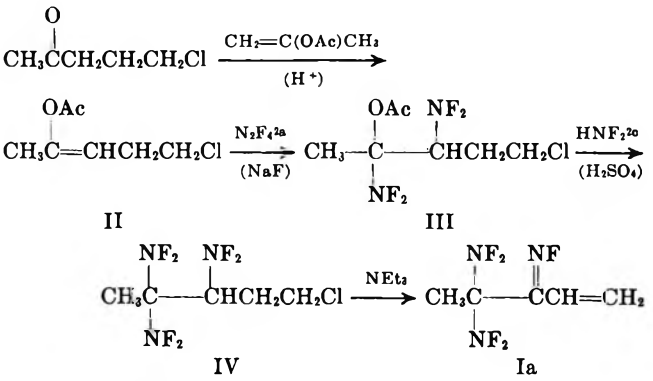
As part of our synthetic studies on poly(difluoramino) compounds,[2] materials polymerizable by way of the vinyl fluorimine function were prepared. The synthesis and characterization of the difluoramino-substituted vinyl fluorimines Ia–e are described here.[3]



Ia, R = CH_3; X = NF_2
b, R = CH_3; X = Cl
c, R = C_6H_5; X = NF_2
d, R = C_6H_5; X = Cl
e, R = C_6H_5; X = $-OP(O)(OC_2H_5)_2$

The sequence of reactions by which Ia was prepared from 5-chloro-2-pentanone is shown in Scheme I. The

SCHEME I



2-acetoxy-5-chloro-1-pentene accompanying the mixture of *cis*- and *trans*-2-acetoxy-5-chloro-2-pentene (II) produced in the first step could be converted selectively to 5-chloro-2-pentanone and acetic anhydride with an acid catalyst; distillation then removed these contaminants.

The cis and trans isomers of II were identified by proton nmr on the basis of relative shifts of vinyl and acetoxy methyl protons compared with data from the literature for other enol acetate isomers.[4]

The low yields encountered in the conversion of III to IV are undoubtedly due to fragmentation reactions

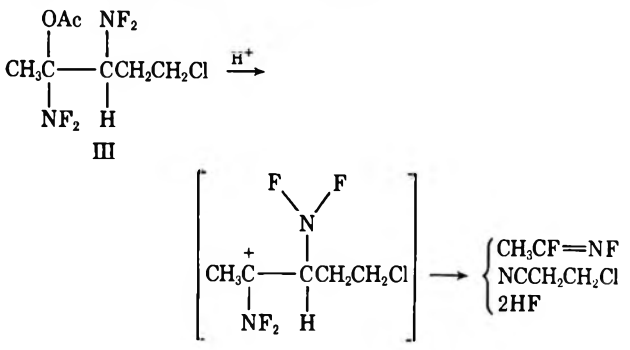
(1) This research was supported by the Advanced Research Projects Agency under U. S. Army Missile Command, Redstone Arsenal, Ala., Contract DA-01-021-11909.

(2) (a) R. C. Petry and J. P. Freeman, *J. Org. Chem.*, **32**, 4034 (1967); (b) W. H. Graham and J. P. Freeman, *ibid.*, **34**, 2589 (1969); (c) J. P. Freeman, R. C. Petry, and T. E. Stevens, *J. Amer. Chem. Soc.*, **91**, 4778 (1969); (d) T. E. Stevens, *J. Org. Chem.*, **34**, 2451 (1969).

(3) The polymerization studies are unpublished results of Dr. Mart Baldwin. In summary, these vinyl fluorimines could not be homopolymerized using AIBN initiator but Va, Vb, and Vd copolymerized with methyl methacrylate and with styrene. A 1:5 Ia–MMA comonomer mixture formed a 1:8 copolymer and a 3:1 Vb–styrene comonomer mixture gave a 1:1 copolymer. Vd copolymerized sluggishly with methyl methacrylate.

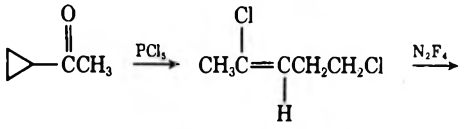
(4) H. O. House and V. Kramer, *J. Org. Chem.*, **28**, 3362 (1963).

of the type illustrated; such fragmentations have been observed earlier.[2c] An expected product of this process, β-chloropropionitrile, accompanied IV.

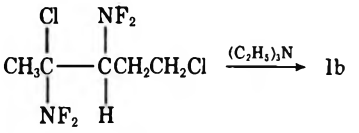


Another route devised for the synthesis of Ia is shown in Scheme II. The intermediate 2,3-bis(difluoramino)-

SCHEME II



V, *cis* and *trans* isomers



2,5-dichloropentane failed to undergo any detectable replacement of chlorine in the 2 position by difluoramine,[5] and consequently this route did not afford any alternative synthesis of Ia. However, the vinyl fluorimine Ib was obtained by dehydrohalogenation of 2,3-bis(difluoramino)-2,5-dichloropentane.

The preparation of fluorimines Ic, Id, and Ie, carried out by closely related procedures, is outlined in the Experimental Section.

Experimental Section

Melting points and boling points are uncorrected. The ^{19}F nmr spectra were run in CCl_4 or $CDCl_3$ at 40 MHz on a Varian 4300B spectrometer; ϕ values are in parts per million from internal CCl_3F. Proton nmr spectra were recorded on a Varian A-60 spectrometer.

The reaction mixtures and products, including difluoramino compounds, reported below must be considered explosive hazards. Adequate shielding must be employed at all times. Accurate elemental analyses are difficult to obtain on polydifluoramino compounds; many samples, including Ia, have exploded in the combustion furnace. Thus, nmr spectral data was used extensively for characterization purposes.

2-Acetoxy-5-chloro-2-pentene.—A mixture of 100 g (1.0 mol) of isopropenyl acetate, 60 g (0.5 mol) of 5-chloro-2-pentanone, and 1.4 g (0.0074 mol) of *p*-toluenesulfonic acid was heated under a distilling column removing 39 ml (*ca.* 0.5 mol) of acetone during 5.5 hr (some acetyl chloride was present in the acetone). The mixture was cooled, treated with 2 g of anhydrous sodium acetate, stirred for 0.5 hr, filtered, and distilled rapidly under reduced pressure without fractionating, giving 33 g of volatiles (condensed in a CO_2 trap), 67 g of crude product, and 7 g of residue. The volatiles consisted mainly of isopropenyl acetate with a little acetone. The crude product fraction, by glc,[6] consisted of isopropenyl acetate (1.3%), acetic anhydride (4%), 5-chloro-2-pentanone (22%), *trans*[7]-2-acetoxy-5-chloro-2-pentene (34%), *cis*-2-acetoxy-5-chloro-2-pentene (11%), and 2-acetoxy-5-chloro-1-pentene (28%).

Separation of the three isomeric acetoxychloropentenes from one another could not be effected by fractional distillation. However, the 2-acetoxy-5-chloro-1-pentene was selectively destroyed (converted to ketone, pentene-2 isomers, and acetic anhydride) by stirring for several hours over 10–20% by weight of Amberlyst[8]-15 or additional toluenesulfonic acid. This treatment was applied to crude reaction mixture, to distilled crude mixtures (as above), and to distilled mixtures of product isomers from which ketone had been removed in forefractions and succeeded in all cases.

For example, to 88.5 g of a crude, distilled reaction product mixture which was stirred at room temperature was added three 5-g portions of Amberlyst-15 resin over 24 hr. At the end of this time, glc assay of the mixture showed that all of the pentene-1 component had disappeared. The mixture was distilled through a 36-in. spinning-band column, collecting a forerun which was principally ketone, bp 34° (3 mm). When this fraction was finished, the pot residue was cooled, removed, and distilled rapidly through a short-path apparatus, collecting 23.4 g of mixed *trans*- and *cis*-2-acetoxy-5-chloro-2-pentene isomers, bp 50° (3 mm).

Anal. Calcd for $C_7H_{11}O_2Cl$: C, 51.69; H, 6.77. Found: C, 51.59; H, 6.99.

The isomers were identified from proton nmr spectra of glc fractions trapped separately. These data are summarized in Table I.

TABLE I

CCl_4 soln	trans (AcO–H), δ	cis (AcO–H), δ
5-CH_2Cl	t, 3.41	3.5
4-CH_2	q, 2.3	2.45
3-=CH	t, 5.02	5.1
2-OAc	s, 2.08	2.01
1-CH_3	s, 1.85	1.85

2,3-Bis(difluoramino)-2-acetoxy-5-chloropentane (III).—A solution of 18 g (0.111 mol) of 2-acetoxy-5-chloro-2-pentene in 25 ml of CCl_4 containing 3.5 g of NaF was stirred in a 90-ml Fisher-Porter tube under 200–300 psi of N_2F_4; the temperature of 115° was maintained for 5 hr. The mixture was allowed to cool, the apparatus was vented and flushed with nitrogen, and the product was isolated from the filtrate after evaporation of solvent. This material was used directly in the next step. A sample of 2,3-bis(difluoramino)-2-acetoxy-5-chloropentane was isolated from an earlier run, bp 50° (0.1 mm).

Anal. Calcd for $C_7H_{11}N_2O_2ClF_4$: C, 31.52; H, 4.14; N, 10.51; F, 28.52. Found: C, 31.82; H, 4.27; N, 11.99; F, 27.2.

The proton and fluorine nmr spectra were attributable to an isomer mixture. The proton spectrum had two $CH_3(C{=}O)O$ singlets at δ 2.12 and 2.15. The ^{19}F spectrum had two tertiary $-NF_2$ singlets, nearly superimposed at ϕ −23.2. The secondary $-NF_2$ group appeared as a superposition of two AB quartets near −1800 Hz.

3,4,4-Tris(difluoramino)-1-chloropentane (IV).—The solution of 18 g (0.111 mol) of *trans*-2-acetoxy-5-chloro-2-pentene in 25 ml of CCl_4, saturated with N_2F_4 as above, was added dropwise onto 0.425 mol of HNF_2 refluxing from a CO_2 cold finger over a stirred mixture of 10 ml of 30% fuming H_2SO_4 and 7 ml of CCl_4 at −10 to 16°. The mixture was kept at 14–16° for 90 min after the addition. Layers were separated; the acid layer was quenched and extracted with CCl_4; and the extracts were combined, washed with water, $NaHCO_3$ solution, and water, and dried with $MgSO_4$. Solvent was distilled at atmospheric pressure and the residue at 2.7–2.9 mm to give a β-chloropropionitrile mixture comprising 1.5 g, bp 39–42°, 0.6 g, bp 42–45°, and 6.2 g, bp 45° (IV).

Anal. Calcd for $C_5H_8ClN_3F_6$: C, 23.12; H, 3.08; N, 16.18; Cl, 13.68; F, 43.93. Found: C, 23.34; H, 3.09; N, 16.46; Cl, 13.2; F, 45.0.

The ^{19}F nmr spectrum had a geminal NF_2 singlet at ϕ −28.5; the secondary $-NF_2$ group was an AB quartet near −1740 Hz.

(5) Conversion of $ClCNF_2$ to NF_2CNF_2 has been reported by K. Baum, *J. Org. Chem.*, **34**, 2046 (1969), and by K. Johnson, Rohm and Haas Co., Redstone Research Laboratories, unpublished results.

(6) Determined by using a 10-ft Carbowax 20M on firebrick 60–80 column.

(7) The acetoxy and hydrogen atom trans.

(8) Trademark of Rohm and Haas Co., Philadelphia, Pa.

4,4-Bis(difluoramino)-3-fluorimino-1-pentene (Ia).—A solution of 6.7 g (0.026 mol) of the tris(NF_2)chloropentane IV in 40 ml of CH_2Cl_2 was stirred in an ice bath while a solution of 5.2 g (0.052 mol) of triethylamine in 5 ml of CH_2Cl_2 was added dropwise holding the temperature at 5–7°. The addition required 40 min, after which stirring at 0° was continued for 30 min and, after reaching room temperature, for 1 hr. The mixture (which had not darkened) was filtered and the CH_2Cl_2 solution was extracted with 5% aqueous HCl and two portions of water and dried with $MgSO_4$. Solvent was distilled off through a Holtzman column at atmospheric pressure and the product at 50° (50 mm). The yield was 2.2 g, 42% of theoretical.

Anal. Calcd for $C_5H_6N_3F_5$: C, 29.56; H, 2.96; N, 20.69; F, 46.8. Found: C, 29.17; H, 3.66; N, 21.42; F, 48.8.

2,5-Dichloropentene-2.—A suspension of 118 g (0.565 mol) of PCl_5 in CH_2Cl_2 was stirred in a three-neck flask equipped with a condenser and drying tube while 48 g (0.565 mol) of methyl cyclopropyl ketone was added to it slowly dropwise controlling the temperature at 15–18° by external cooling. When the suspended PCl_5 had all reacted (clear solution) the condenser was replaced by a Vigreux column and solvent was distilled until the pot temperature reached 95°. The pot was cooled, the pressure was reduced to 90–100 mm, and $POCl_3$ was distilled at 38–52° head temperature. The pot residue was cooled again, poured into ice and water, and stirred for 1–2 hr. One volume of CH_2Cl_2 was added, and the lower layer was separated, washed with water and $NaHCO_3$ solution, and dried with $MgSO_4$. Since the dried solution still gave an acid reaction when shaken with water, some anhydrous Na_2CO_3 was added and the solution was stirred for 2 hr. Solids were filtered, solvent was evaporated, and the product was distilled away from the residue at 48–52° (14 mm), giving 29 g of distillate. This proved to be a mixture of *cis*- (Me–H) and *trans*- (Me–H) 2,5-dichloropentene-2, which, for synthetic purposes, was used directly. It was separated by fractional distillation through a 24-in. spinning band column collecting pure fractions (by glc assay): (1) 14.4 g, bp 44° (10.0 mm), $n^{20}D$ 1.4681; (2) 2.8 g, bp 54° (9.8 mm), $n^{20}D$ 1.4744.

Anal. Calcd for $C_5H_8Cl_2$: C, 43.17; H, 5.76. Found: (1) C, 42.59; H, 5.93; (2) C, 43.52; H, 6.11.

2,3-Bis(difluoramino)-2,5-dichloropentane.—A solution of 13.5 g (0.1 mol) of 2,5-dichloropentene-2 ($n^{20}D$ 1.4681) in 30 ml of CH_2Cl_2 was saturated with N_2F_4 at 95° (300 psi) during 7 hr and was left under pressure overnight. The product solution was evaporated and the residue was distilled through a Holtzman column, collecting 19.1 g of distillate in fractions, bp 40–47° (<1 mm), $n^{20}D$ 1.4293–1.4297. The ^{19}F nmr spectrum had peaks at ϕ −33.4 ($ClCNF_2$) and two NF_2 AB quartets near −1760 Hz.

Reaction of 2,3-Bis(difluoramino)-2,5-dichloropentane with HNF_2–H_2SO_4.—A solution of 11.3 g of the above pentane in 23 ml of CH_2Cl_2 was added dropwise onto 0.4 mol of HNF_2 refluxing from a CO_2 cold finger condenser over a stirred mixture of 10 ml of 30% fuming H_2SO_4 and 7 ml of CH_2Cl_2. The addition was finished in 10 min at −10 to 21°. Stirring was continued for 5 hr at 10°. Work-up of the product resulted in recovery of 63% of the bisdifluoramino dichloropentane, identified by its ^{19}F nmr spectrum. No evidence of the presence of any 3,4,4-tris(difluoramino)-1-chloropentane was detected.

4-Difluoramino-4-chloro-3-fluoriminopentene-1 (Ib).—A solution of 4.1 g (0.041 mol) of triethylamine in 5 ml of CH_2Cl_2 was added dropwise to a stirred solution of 5 g (0.02 mol) of 2,3-bis(difluoramino)-2,5-dichloropentane in 40 ml of CH_2Cl_2 at 0°, controlling the exotherm by external cooling. The mixture was stirred at 0° for 30 min after addition and at room temperature for another hour. Solids were filtered and the filtrate was washed with cold 5% aqueous HCl and water and dried. Solvent was distilled at atmospheric pressure and the residue was distilled under reduced pressure, giving a forerun (0.15 g) and 2.1 g of product, bp 55° (50 mm).

Anal. Calcd for $C_5H_6N_2F_3Cl$: C, 32.17; H, 3.22; N, 15.01; F, 30.56. Found: C, 32.13; H, 3.43; N, 15.88; F, 30.9.

The ^{19}F nmr spectrum had peaks at ϕ −21.1 (C=NF) and an AB quartet near −4500 Hz.

Preparation of 1-Phenyl-1-chloro-1-difluoramino-2-fluorimino-3-butene (Id).—1,4-Dichloro-1-phenyl-1-butene, bp 103° (0.8 mm), prepared from phosphorus pentachloride and γ-chlorobutyrophenone, was exposed to tetrafluorohydrazine in the usual fashion (Freon 113–methylene chloride solvent).[2a] The crude adduct from 6.0 g (30 mmol) of olefin was dissolved in 50 ml of *tert*-butyl alcohol and at 20° 50 ml of 1.10 *N* potassium *tert*-butoxide in *tert*-butyl alcohol was added. After 30 min the mixture was poured into H_2O, and the organic product was extracted into methylene chloride. The residue was chromatogaphed on silica gel to give, in the 10:1 pentane–methylene chloride eluate, 5.5 g of a mixture of the desired product and material that had not been dehydrochlorinated. This was taken up in *tert*-butyl alcohol (25 ml) and 7 ml of 1.10 N potassium *tert*-butoxide was added. The usual work-up of this reaction (chromatography on silica gel) gave 1-phenyl-1-chloro-1-difluoramino-2-fluorimino-3-butene, 2.35 g, a colorless liquid.

Anal. Calcd for $C_{10}H_8ClF_3N_2$: C, 48.30; H, 3.24; N, 11.27; F, 23.0. Found: C, 48.12; H, 3.51; N, 11.16; F, 21.7.

The ^{19}F nmr spectrum had peaks at ϕ −26.4 (C=NF) and an AB quartet with ϕ_A near −43.9 and ϕ_B near −37.2 (J_{FF} = 552 Hz).

Preparation of 1-Phenyl-1,1-bis(difluoramino)-2-fluorimino-3-butene (Ic).—1-Phenyl-1,1,2-tris(difluoramino)-4-chlorobutane was prepared in the usual way[2c] from 1-phenyl-1-(diethylphosphoryloxy)-1,2-bis(difluoramino)-4-chlorobutane and was isolated as a colorless liquid.

Anal. Calcd for $C_{10}H_{10}ClN_3F_6$: C, 37.34; H, 3.13; N, 13.06; F, 35.4. Found: C, 37.32; H, 3.18; N, 13.18; F, 34.5.

The ^{19}F nmr spectrum exhibited $C(NF_2)_2$ at ϕ −26.5 and HC-NF_2 as a quartet of doublets, center members at −2110 and −1604 Hz.

Dehydrofluorination of the trisdifluoramino chlorobutane (3.50 g) in 25 ml of methanol and 10 ml of methylene chloride at 0° with 7.8 ml of 1.40 *N* sodium methoxide in methanol gave 3.2 g of product that had undergone some dehydrochlorination (proton nmr). Therefore, the 3.2 g of product was dehydrochlorinated in 25 ml of *tert*-butyl alcohol with 10 ml of 1.02 *N* potassium *tert*-butoxide in *tert*-butyl alcohol. The product, 2.9 g, was chromatographed on silica gel. 1-Phenyl-1,1-bis(difluoramino)-2-fluorimino-3-butene was obtained in the pentane–methylene chloride (10:1) eluate, 2.16 g, a colorless liquid.

Anal. Calcd for $C_{10}H_8N_3F_5$: C, 45.29; H, 3.04; N, 15.85; F, 35.8. Found: C, 44.30; H, 3.62; N, 16.18; F, 34.6.

The ^{19}F nmr spectrum showed $C(NF_2)_2$ at ϕ −31.9 and >C=NF at ϕ −37.7.

Reaction of 1-Phenyl-1,2-bis(difluoramino)-1-(*O,O*-diethylphosphoryloxy)-4-chlorobutane and Potassium *tert*-Butoxide.—A solution of 53 g (125 mmol) of the above N_2F_4 adduct[2c] in 100 ml of methylene chloride and 150 ml of *tert*-butyl alcohol was stirred at 10° while 116 ml of 1.08 *N* potassium *tert*-butoxide in *tert*-butyl alcohol was added dropwise. The solution was neutral at this time, and a ^{19}F nmr spectrum of a portion of the organic product indicated that a considerable portion of unreacted starting material was still present. Addition of the *tert*-butoxide solution was continued until the solution remained basic; an additional 151 ml of the standard base was required. The reaction mixture was processed as usual. The solid product was recrystallized from hexane–chloroform to give 1-phenyl-1-difluoramino-1-(*O,O*-diethylphosphoryloxy)-2-fluorimino-3-butene (24 g), mp 64–66°.

Anal. Calcd for $C_{14}H_{18}N_2O_4PF_3$: C, 45.91; H, 4.95; N, 7.65. Found: C, 45.61; H, 5.27; N, 7.45.

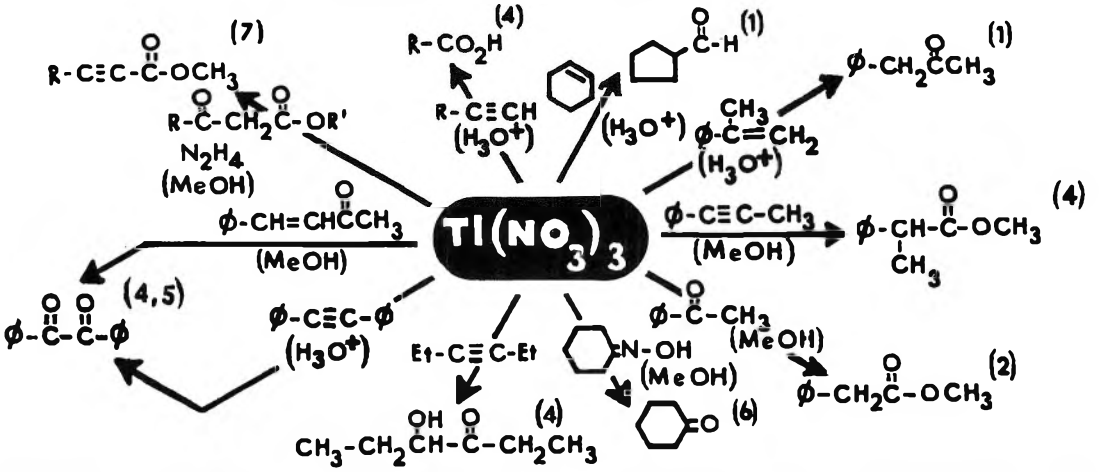
The ^{19}F nmr spectrum had peaks for –C=NF at ϕ −27.6 and for –CNF_2, AB quartet with ϕ_A near −31 and ϕ_B near −27.2, J_{FF} = 552 Hz.

Registry No.—Ia, 33364-51-1; Ib, 33364-52-2; Ic, 33364-53-3; Id, 33364-54-4; *cis*-II, 33364-55-5; *trans*-II, 33364-56-6; III, 33364-57-7; IV, 33364-58-8; *cis*-V, 5680-46-6; *trans*-V, 5680-47-7; 2,3-bis(difluoramino)-2,5-dichloropentane, 33364-60-2; 1-phenyl-1-difluoramino-1-(*O,O*-diethylphosphoryloxy)-2-fluorimino-3-butene, 33364-61-3.

TTN

[Thallium (III) Nitrate]

For the syntheses of aldehydes, ketones, esters, etc., *via* organothallium intermediates



Analogous to oxymercuration, an olefin readily undergoes oxythallation[1] with TTN in methanol but gives a highly unstable thallium compound. The transition state in heterolysis of the C-Tl bond apparently approaches that of a carbonium ion for cyclic olefins and olefins bearing substituents with good migrating properties. The products are ketals and acetals, formed by a Wagner-Meerwein type rearrangement. Acidic workup gives **carbonyl compounds** in high yields. In straight chain olefins, such as 1-decene, participation by solvent in heterolysis increases and substituted glycols predominate. These reactions are completed within minutes at room temperature.

Acetophenones with TTN in acidic methanol undergo oxidative rearrangement[2] to methyl phenylacetates, products which can be obtained only tediously by the conventional Willgerodt-Kindler reaction. In contrast, this TTN reaction can be extended[3] to alkyl aryl ketones for the synthesis of **α-alkyl arylacetates.** The latter can also be prepared **in high yield** by the oxidative rearrangement[4] of arylalkylacetylenes with TTN in methanol.

TTN **oxidizes**[4] acetylenes and the product depends upon the structure of the acetylenes. Thus, monoalkylacetylenes with two equivalents of TTN in aqueous acid glyme medium are oxidized to **carboxylic acids containing one carbon less** than the starting material. Dialkylacetylenes under acidic conditions with one equivalent of TTN give **acyloins** in good yield and diarylacetylenes with two equivalents of TTN give **benzils** in high yield. **Symmetrical** and **unsymmetrical benzils** can also be prepared[5] in good yield by the action of TTN on chalcones under acidic conditions.

TTN is also a highly efficient reagent for the **regeneration**[6] of aldehydes and ketones from oximes, semicarbazones and phenylhydrazones and for the conversion[7] of β-ketoesters into **α,β-acetylenic esters.**

Thallium (III) nitrate is available as the crystalline trihydrate and is soluble in alcohols, glyme and dilute mineral acids.

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