VOLUME 36 MAY 21, 1971 NUMBER 10 JOCEAH

# THE JOURNAL OF Organic Chemistry

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The two new reagents, $Eu(fod)_3$ and $Pr(fod)_3$ will be described in an important paper by Roger E. Rondeau and Robert E. Sievers, "New Superior Paramagnetic Shift Reagents for NMR Spectral Clarification", to appear in a forthcoming issue of *Journal of the American Chemical Society*. As the result of the extensive work required for this paper the authors have concluded that the Eu and Pr chelates of $H(fod)_3$ offer distinct advantages over all of the hundreds of other lanthanide chelates investigated. $Eu(fod)_3$ and $Pr(fod)_3$ have considerably better solubility than the currently popular tetramethylheptanedione (thd) chelates of Eu and Pr, thus enabling the use of sufficient molar ratios to produce spectra of essentially completely coordinated ligands. Another most important point: the electron withdrawing effect of the fluorines increases the residual acidity of the cation, offering an improved coordination site for weak donors.

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MAY 21, 1971

# Intermediates in Nucleophilic Aromatic Substitution. V.[1] Kinetic Study of Meisenheimer Complexes of 1,3,5-Trinitrobenzene with Hydroxide and Alkoxide Ions in Ethanol–Water and Methanol–Water Mixtures[2]

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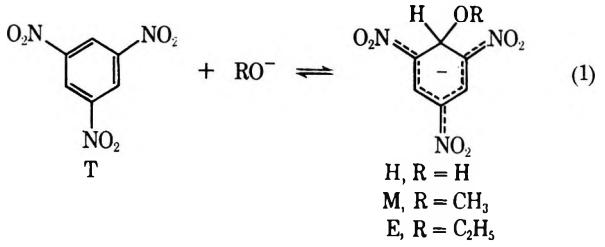
*Received October 16, 1970*

The kinetics of reversible Meisenheimer complex formation between 1,3,5-trinitrobenzene and the respective lyate ions in 19% ethanol–81% water (v/v) and in 22.5% methanol–77.5% water (v/v), respectively, has been studied by the temperature-jump and stopped-flow methods. These very aqueous mixed solvents approximate a "common" solvent for the three equilibrium reactions concerned. The rate coefficients for nucleophilic attack and for leaving group departure respectively are 7700 $M^{-1}$ sec$^{-1}$ and 32.0 sec$^{-1}$ for $EtO^-$ in ethanol–water, 2425 $M^{-1}$ sec$^{-1}$ and 254 sec$^{-1}$ for $MeO^-$ in methanol–water, 70.2 $M^{-1}$ sec$^{-1}$ and 6.8 sec$^{-1}$ for $HO^-$ in ethanol–water, and 17.1 $M^{-1}$ sec$^{-1}$ and 10.5 sec$^{-1}$ for $HO^-$ in methanol–water. A change from pure methanol and ethanol to the mainly aqueous solvents has an expected small retarding effect (three- or fourfold) on the rate of nucleophilic attack by $MeO^-$ and by $EtO^-$, whereas leaving group departure is practically unaffected.

Recently we reported a kinetic study on the Meisenheimer complex forming equilibria between 1,3,5-trinitrobenzene (T) and the lyate ions in water, methanol, and ethanol[1] (eq 1). One of our general objectives is to




T

H, R = H
M, R = $CH_3$
E, R = $C_2H_5$

(1)

study leaving group reactivities in nucleophilic aromatic substitutions.[3] The work reported[1] provided information about leaving group reactivities of $HO^-$, $MeO^-$, and $EtO^-$ with respect to the model reaction 1 in the solvents mentioned. Though interesting, this comparison of the three bases in three different solvents suffers from the fact that a solvent effect may account for at least part of the reported differences.

The aim of this and subsequent studies to be reported shortly is to provide data on reaction 1 in a "common" solvent. Because of the inherent nature of protic solvents such a "common" solvent can only be approximated. We have chosen predominantly aqueous alcohol–water mixtures with alcohol contents around 20%. The choice of the alcohol content was dictated by the need of a sufficient equilibrium concentration of $RO^-$ arising from equilibrium 2 on the one hand and

$$ROH + HO^- \overset{K'}{\rightleftharpoons} RO^- + H_2O \qquad (2)$$

the wish to keep the solvent as aqueous as possible on the other. For the lack of a better criterion, the content for the various alcohols was chosen so as to give mixtures of equal dielectric constants at 25°, $D$ = 67.5,[4] for all the solvents whenever possible. In this first account we report on our findings in 19% ethanol–81% water (v/v) and 22.5% methanol–77.5% water (v/v).

## Experimental Section

**Materials.**—1,3,5-Trinitrobenzene (Eastman White Label) was recrystallized twice from ethanol, mp 123°. Reagent grade methanol and ethanol were used without further purification.

**Rate and Equilibrium Measurements.**—Stopped-flow determinations were performed on a Durrum stopped-flow spectrometer. The relaxation times listed in Tables I and II represent average values of three or four oscilloscope pictures taken from two and frequently more independently prepared reactant solutions. The reproducibility of the $\tau_2$ values in methanol–water was less satisfactory than the others; these $\tau_2$ values represent the average of up to six independent determinations.

The temperature-jump experiments were carried out on a temperature-jump transient spectrometer from Messanlagen Gmbh. Temperature jumps of 1° were found to be adequate for the systems under study. Reported relaxation times represent the average of three or four oscilloscope pictures taken from two independently prepared reactant solutions.

(1) Part IV: C. F. Bernasconi, *J. Amer. Chem. Soc.*, **92**, 4682 (1970).

(2) Supported in part by a grant from the Petroleum Research Fund administered by the American Chemical Society. Grateful acknowledgment is made to the donors of this fund.

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

(4) H. S. Harned and B. B. Owen, "The Physical Chemistry of Electrolytic Solutions," Reinhold, New York, N. Y., 1950, p 118.

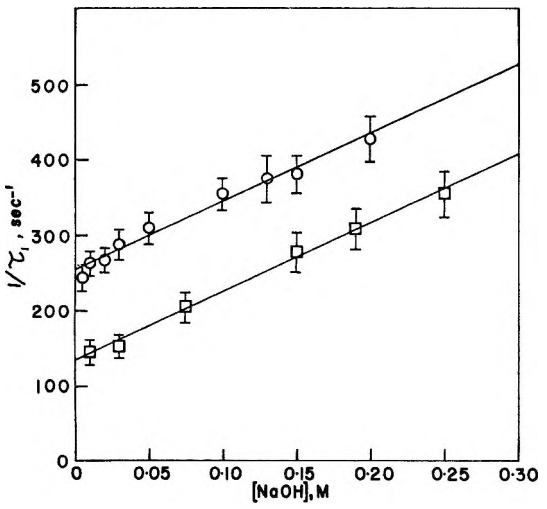



Figure 1.—$\tau_1$ in 22.5% methanol–77.5% water (v/v); ○ with 0.5 *M* NaCl, □ with 3 *M* NaCl.

TABLE I

REACTIONS OF $MeO^-$ AND $HO^-$ WITH 1,3,5-TRINITROBENZENE IN 22.5% METHANOL–77.5% WATER (V/V) AT 25°

| [NaOH]$_0$, *M* | [TNB]$_0$ × $10^5$ *M* | Electrolyte concn,[a] *M* | $1/\tau_1$,[b] $sec^{-1}$ | $1/\tau_2$,[c] $sec^{-1}$ |
|---|---|---|---|---|
| 0.005 | 40 | 0.5 | 244 ± 17 | |
| 0.01 | 30 | 0.5 | 263 ± 18 | |
| | 30 | 3.0 | 145 ± 15 | |
| | 2 | 0.5 | | 10.7 ± 0.9 |
| | 2 | 3.0 | | 9.2 ± 0.5 |
| 0.02 | 30 | 0.5 | 267 ± 18 | |
| | 2 | 3.0 | | 8.8 ± 0.5 |
| 0.03 | 30 | 0.5 | 287 ± 20 | |
| | 2 | 0.5 | | 10.6 ± 0.5 |
| | 30 | 3.0 | 152 ± 12 | |
| | 2 | 3.0 | | 9.0 ± 0.5 |
| 0.05 | 20 | 0.5 | 310 ± 20 | |
| | 2 | 0.5 | | 11.0 ± 0.5 |
| | 2 | 3.0 | | 9.0 ± 0.5 |
| 0.075 | 20 | 3.0 | 205 ± 20 | |
| | 2 | 0.5 | | 10.8 ± 0.5 |
| | 2 | 3.0 | | 8.8 ± 0.6 |
| 0.10 | 20 | 0.5 | 355 ± 20 | |
| 0.13 | 20 | 0.5 | 376 ± 30 | |
| 0.15 | 14 | 0.5 | 380 ± 25 | |
| | 14 | 3.0 | 277 ± 25 | |
| | 2 | 0.5 | | 11.4 ± 0.7 |
| | 2 | 3.0 | | 9.1 ± 1.0 |
| 0.19 | 14 | 3.0 | 308 ± 26 | |
| 0.20 | 12 | 0.5 | 427 ± 30 | |
| | 2 | 0.5 | | 12.1 ± 0.8 |
| | 2 | 3.0 | | 9.0 ± 1.0 |
| 0.25 | 12 | 3.0 | 354 ± 30 | |
| 0.30 | 1 | 0.5 | | 12.5 ± 1.2 |
| 0.35 | 1 | 0.5 | | 12.7 ± 1.5 |
| 0.40 | 1 | 0.5 | | 12.7 ± 1.2 |

[a] NaCl added as needed. [b] Observed at 535 nm by temperature-jump method. [c] Observed at 425 nm by stopped-flow method.

Absorbance measurements for equilibrium determinations were made on a Gilford spectrophotometer with thermostatted cuvettes.

## Results

Solutions of T in basic 19% aqueous ethanol and 22.5% aqueous methanol are characterized by several relaxational processes in the time range from a few milliseconds to about 20 sec. Depending on reaction conditions such as base concentration and electrolyte concentration, one observes at least four but possibly five or more relaxation processes, mostly well separated, which can be attributed to equilibrium reactions. Furthermore, there is at least one slow process with a half-life >15 min which is believed to be an irreversible decomposition of TNB.

TABLE II

REACTIONS OF $EtO^-$ AND $HO^-$ WITH 1,3,5-TRINITROBENZENE IN 19% ETHANOL–81% WATER (V/V) AT 25° [a]

| [NaOH]$_0$, *M* | [TNB]$_0$ × $10^5$ *M* | $1/\tau_1$, $sec^{-1}$ [b] | $1/\tau_2$, $sec^{-1}$ [c] |
|---|---|---|---|
| 0.005 | 2 | | 7.13 ± 0.35 |
| 0.010 | 2 | 36.3 ± 4.0[d] | |
| | 1.5 | | 7.40 ± 0.37 |
| 0.020 | 1.5 | | 8.05 ± 0.40 |
| 0.030 | 2 | 39.2 ± 4.0[d] | |
| | 1.5 | | 8.32 ± 0.41 |
| 0.040 | 1.5 | | 8.76 ± 0.44 |
| 0.050 | 2 | 55.7 ± 7.0[d] | |
| | 0.4 | | 9.11 ± 0.45 |
| 0.075 | 0.4 | | 9.64 ± 0.48 |
| 0.10 | 10 | 63 ± 5.0 | |
| | 0.4 | | 10.2 ± 0.5 |
| 0.13 | 10 | 74 ± 3.5 | |
| | 0.4 | | 10.5 ± 0.5 |
| 0.15 | 10 | 85 ± 4.0 | |
| | 0.3 | | 11.0 ± 0.5 |
| 0.17 | 10 | 89 ± 4.3 | |
| | 0.3 | | 11.3 ± 0.6 |
| 0.19 | 10 | 99 ± 4.5 | |
| | 0.3 | | 11.5 ± 0.6 |
| 0.22 | 10 | 112 ± 5 | |
| | 0.3 | | 11.7 ± 0.6 |
| 0.25 | 10 | 117 ± 6 | |
| | 0.3 | | 11.9 ± 0.6 |

[a] Total electrolyte concentration maintained at 0.5 *M* by addition of NaCl as needed. [b] Determined at 535 nm by the temperature-jump method. [c] Determined at 500 nm by the stopped-flow method. [d] Calculated by computer.

In this report we are concerned with only the two fastest processes (with relaxation times $\tau_1$ and $\tau_2$) which arise from the reactions of eq 1 leading to complexes H and E in ethanol–water and to H and M in methanol–water. In a subsequent paper we will deal with 1:2 complexes formed by the attack of two lyate ions on T which give rise to the longer relaxation times and necessitate an involved kinetic analysis.

In methanol–water the two relaxation times are well separated under all conditions, *i.e.*, $\tau_2 \gg \tau_1$.[5] $\tau_1$ was measured by the temperature-jump method.[6] The data which are summarized in Table I show a strong dependence on base concentration. When $\tau_1^{-1}$ is plotted *vs.* the stoichiometric base concentration $[NaOH]_0$, a straight line results. Figure 1 shows such plots at two different electrolyte concentrations.

$\tau_2$ was measured by the stopped-flow method. It is only very slightly concentration dependent; plots of $\tau_2^{-1}$ *vs.* $[NaOH]_0$ are shown in Figure 2.

In ethanol–water $\tau_1$ is appreciably longer than in methanol–water, whereas $\tau_2$ is about the same in both

(5) $\tau_2 \gg \tau_1$ means $\tau_2/\tau_1 \geq 10$.

(6) M. Eigen and L. DeMaeyer in "Technique of Organic Chemistry," Vol. VIII, Part 2, Interscience, New York, N. Y., 1963, p 895.

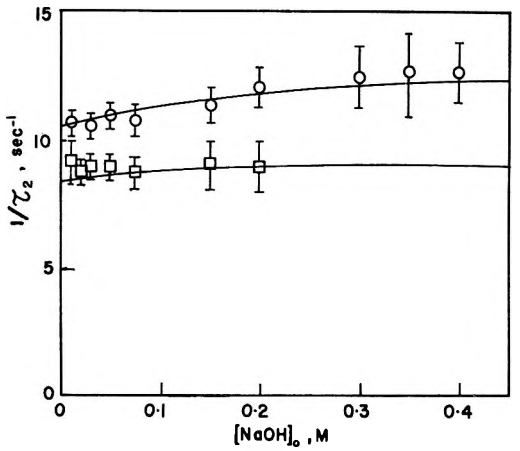



Figure 2.—$\tau_2$ in 22.5% methanol–77.5% water (v/v); ○ with 0.5 *M* NaCl, □ with 3 *M* NaCl.

solvents. As a consequence, the relation $\tau_2 \gg \tau_1$ is just barely fulfilled, $\tau_2/\tau_1 \approx 7$–10 for $[NaOH]_0 \leqslant 0.25$ *M*, $\tau_2/\tau_1 \geqslant 10$ for $[NaOH]_0 \geqslant 0.25$ *M*. Representative oscilloscope traces at low and at high base concentration are shown in Figure 3. It is noteworthy that $\tau_2$ interferes rather strongly with $\tau_1$ at low base concentrations (Figure 3A) but only insignificantly at high base concentrations (Figure 3B). This lesser interference is only to a small extent due to a larger separation of $\tau_1$ and $\tau_2$ at higher base concentration. The principal reason is a decrease in the amplitude (change in absorbance as a consequence of the temperature jump) of $\tau_2$ relative to the amplitude of $\tau_1$ when the base concentration is increased, which arises from a favorable interplay of the enthalpies of the various equilibria involved.[7]

Where the interference of $\tau_2$ with $\tau_1$ was appreciable, the relaxation times were evaluated with the help of a computer.[8] Otherwise it was possible to use standard graphical procedures.

The data for the ethanol–water reactions are reported in Table II; plots of $\tau_1^{-1}$ and $\tau_2^{-1}$ in Figure 4 and 5 show a strong concentration dependence for $\tau_1$ and weak dependence for $\tau_2$ just as in methanol–water.

As will be shown below, the concentration dependence of $\tau_1^{-1}$ and $\tau_2^{-1}$ in both solvent systems is consistent with two distinct 1:1 T–base interactions which, in the light of all known evidence,[1,10] can reasonably only be the Meisenheimer complexes M and H in aqueous methanol and E and H in aqueous ethanol, respectively. With reference to our previous study[1] on reaction 1 in pure methanol (M), pure ethanol (E), and pure water (H), where the relaxation times in both alcohols were found to be significantly shorter than in water, we further conclude that in our present study $\tau_1$ is associated with $MeO^-$ and $EtO^-$ attack, respectively, whereas $\tau_2$ is associated with $HO^-$ attack in both solvents. A full justification for this interpretation is given in the Discussion.

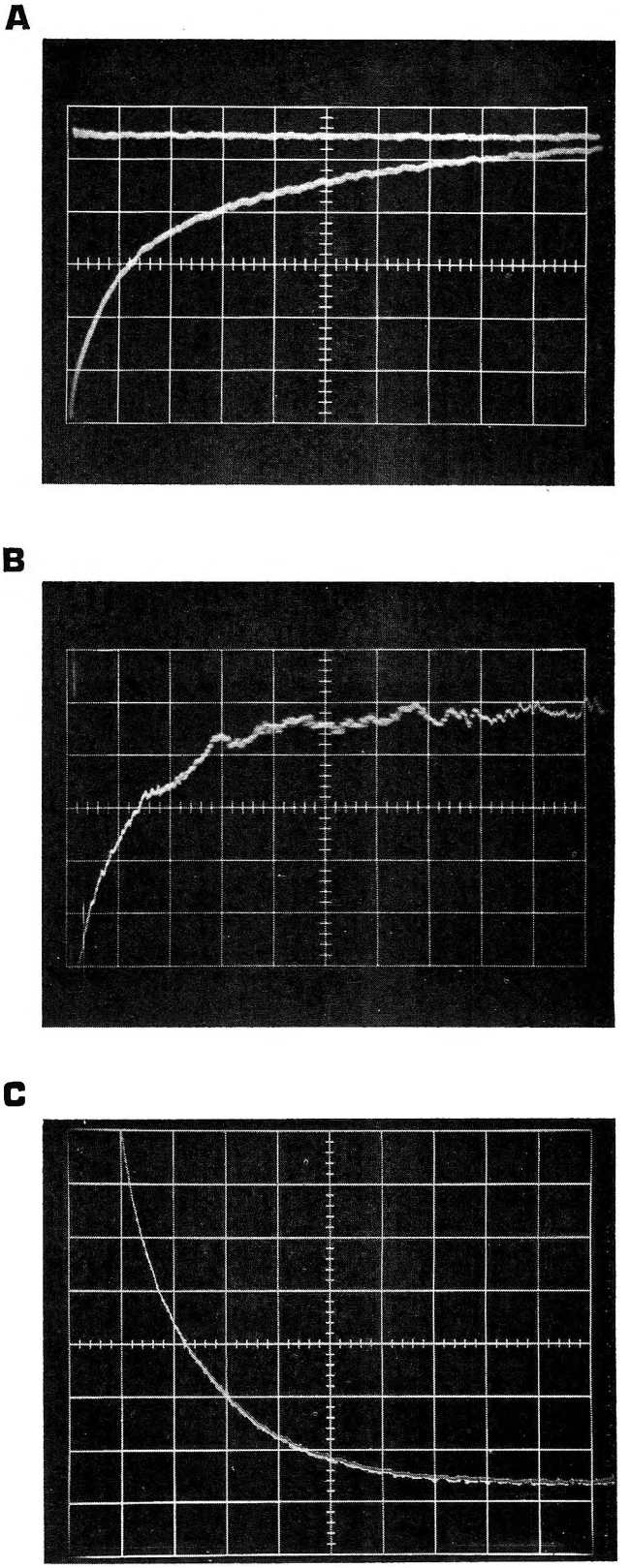



Figure 3.—Representative oscilloscope traces in 19% ethanol–81% water (v/v); A, $\tau_1$ and $\tau_2$ at $[NaOH]_0 = 0.03$ *M*, $\lambda = 535$ mμ, 20 msec/division, temperature-jump method; B, $\tau_1$ at $[NaOH]_0 = 0.19$ *M*, $\lambda = 535$ mμ, 5 msec/division, temperature-jump method; C, $\tau_2$ at $[NaOH]_0 = 0.19$ *M*, $\lambda = 425$ mμ, 50 msec/division, stopped-flow method.

(7) In the stopped-flow experiments, $\tau_2$ interferes more strongly with $\tau_1$ over the entire concentration range. It is for this reason that the temperature-jump rather than the stopped-flow technique was used for measuring $\tau_1$.

(8) A computer program proposed by Wiberg[9] for first-order rate calculations was modified to calculate the parameters $\Delta A_1/\Delta A_0$, $\tau_1$ and $\tau_2$ which give the best fit between experimental absorbance data (A), and the function

$$\frac{\Delta A}{\Delta A_0} = \frac{\Delta A_1}{\Delta A_0} e^{-t/\tau_1} + \left(1 - \frac{\Delta A_1}{\Delta A_0}\right) e^{-t/\tau_2}$$

(9) K. B. Wiberg, "Physical Organic Chemistry," Wiley, New York, N. Y., 1966, p 570.

(10) For recent reviews of this evidence, see (a) R. Foster and C. A. Fyfe, *Rev. Pure Appl. Chem.*, **16**, 61 (1966); (b) E. Buncel, A. R. Norris, and K. E. Russell, *Quart. Rev., Chem. Soc.*, **22**, 123 (1968); (c) M. R. Crampton, *Advan. Phys. Org. Chem.*, **7**, 211 (1969).

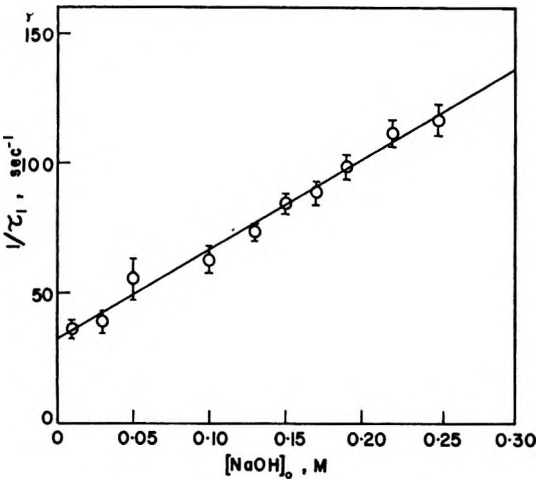



Figure 4.—$\tau_1$ in 19% ethanol–81% water (v/v).

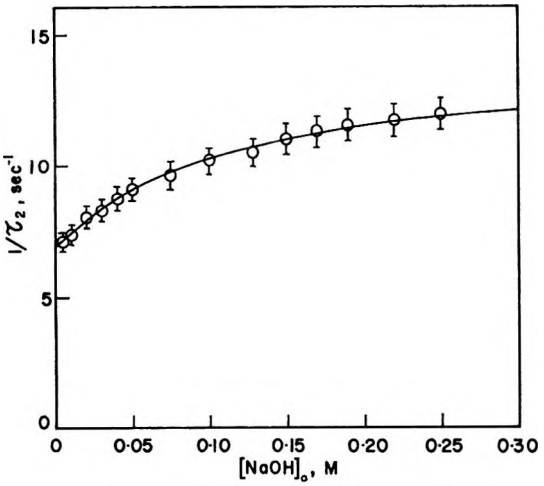



Figure 5.—$\tau_2$ in 19% ethanol–81% water (v/v).

We can describe our reaction systems by eq 3 which

$$H \underset{k_{-2}^H}{\overset{k_2^H}{\rightleftharpoons}} T + HO^- \overset{K}{\rightleftharpoons} RO^- + T \underset{k_{-1}^R}{\overset{k_1^R}{\rightleftharpoons}} M \text{ or } E \qquad (3)$$

$$R = CH_3 \text{ or } C_2H_5$$

includes the $RO^-/HO^-$ equilibrium 2, though the solvent species have been omitted for simplicity. Equilibrium 2 is established very fast; the relaxation time associated with it could not possibly be determined by our methods.

In the general case, eq 3 calls for complex expressions relating $\tau_1$ and $\tau_2$ to reactant concentrations. However, all our experiments were performed with $[NaOH]_0 \gg [T]_0$, so that we can write the simplified eq 4.

$$H \underset{k_{-2}^H}{\overset{k_2^H[HO^-]}{\rightleftharpoons}} T \underset{k_{-1}^R}{\overset{k_1^R[RO^-]}{\rightleftharpoons}} M \text{ or } E \qquad (4)$$

The $RO^-/HO^-$ equilibrium has to be considered only for the calculation of the equilibrium concentrations of $RO^-$ and $HO^-$ by means of eq 5 and 6, where $K$ is defined by eq 7, $\chi_{ROH}$ and $\chi_{H_2O}$ being mole fractions. For $K'$ we use Murto's[11] values, $K' = 4.5$ in methanol–water, $K' = 0.065$ in ethanol–water.

$$[RO^-] = \frac{K}{1+K}[NaOH]_0 \qquad (5)$$

$$[HO^-] = \frac{1}{1+K}[NaOH]_0 \qquad (6)$$

$$K = \frac{[RO^-]}{[HO^-]} = K' \frac{\chi_{ROH}}{\chi_{H_2O}} \qquad (7)$$

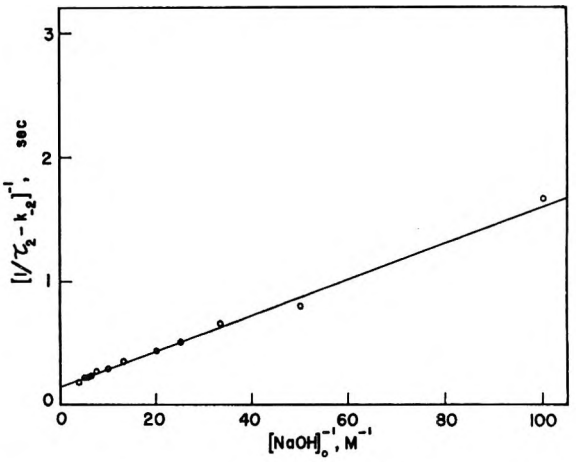



Figure 6.—Inversion plot of $\tau_2$ in 19% ethanol–81% water (v/v).

For $\tau_2 \gg \tau_1$ the relaxation times are straightforwardly derived according to well-established procedures[6] and can be written as eq 8 and 9, where $K_1^R = k_1^R/k_{-1}^R$. Taking into consideration eq 5 and 6, they become eq 10 and 11.

$$\frac{1}{\tau_1} = k_1^R[RO^-] + k_{-1}^R \qquad (8)$$

$$\frac{1}{\tau_2} = \frac{k_2^H[HO^-]}{1 + K_1^R[RO^-]} + k_{-2}^H \qquad (9)$$

$$\frac{1}{\tau_1} = \frac{k_1^R K}{1+K}[NaOH]_0 + k_{-1}^R \qquad (10)$$

$$\frac{1}{\tau_2} = \frac{k_2^H[NaOH]_0}{1 + K + KK_1^R[NaOH]_0} + k_{-2}^H \qquad (11)$$

In methanol–water eq 10 and 11 hold well under all conditions. In ethanol–water the separation of $\tau_1$ and $\tau_2$, though not very large, is nevertheless sufficient to warrant the use of eq 10 and 11; the small deviation introduced compared to a more rigorous treatment[6] is less than 5% and thus comparable with or less than the experimental error.

Equation 10 allows one to determine the various $k_1^R$ and $k_{-1}^R$ values from slopes and intercepts in Figures 1 and 4. They are reported in Table III as calculated from a least-squares analysis.[12] For the determination of $k_2^H$ and $k_{-2}^H$, eq 11 is rearranged to eq 12, where $k_{-2}^H$ is the intercept of a plot of $\tau_2^{-1}$ *vs.* $[NaOH]_0$. By plotting the left-hand side of eq 12 *vs.* $[NaOH]_0^{-1}$ ("inversion plot"), one should obtain a straight line. In principle this should allow $k_2^H$ to be calculated (from slope) as well as $K_1^R$ to be checked (from intercept) against its value derived from $\tau_1$.

$$\frac{1}{\tau_2^{-1} - k_{-2}^H} = \frac{1+K}{k_2^H[NaOH]_0} + \frac{KK_1^R}{k_2^H} \qquad (12)$$

In aqueous ethanol one indeed obtains a satisfactory linear inversion plot, Figure 6; $k_2^H$ and $K_1^R$ calculated by least-squares analysis[12] are reported in Table III. It is to be noted that the $K_1^R$ values derived by the two methods agree very well. The curve as drawn in

(11) J. Murto, *Ann. Acad. Sci. Fenn., Ser. A2*, 117 (1962).

(12) These calculations were performed by an electronic desk computer, the Olivetti Programma 101.

TABLE III
RATE AND EQUILIBRIUM CONSTANTS FOR MEISENHEIMER COMPLEXES BETWEEN 1,3,5-TRINITROBENZENE AND $EtO^-$, $MeO^-$, AND $OH^-$ IN VARIOUS SOLVENTS AT 25° [a]

| | 19% EtOH–81% $H_2O$ | | 22.5% MeOH–77.5% $H_2O$ | | | | |
|---|---|---|---|---|---|---|---|
| | $\tau_1$: E<br>$\tau_2$: H | $\tau_1$: H<br>$\tau_2$: E | $\tau_1$: M<br>$\tau_2$: H | $\tau_1$: H<br>$\tau_2$: M | EtOH[b] | MeOH[b] | $H_2O$[b] |
| $k_1^E$ ($M^{-1}$ sec$^{-1}$) | 7700 ± 300 | 1550 | | | 33400[d] | | |
| $k_{-1}^E$ (sec$^{-1}$) | 32.0 ± 3.0 | 68 | | | 27.5[d] | | |
| $K_1^E = k_1^E/k_{-1}^E$ ($M^{-1}$) | 241 ± 24<br>(248 ± 20)[c] | 228 | | | 1210[d] | | |
| $k_1^M$ ($M^{-1}$ sec$^{-1}$) | | | 2425 ± 125<br>(2460 ± 130)[e] | 29.5 | | 7050[d] | |
| $k_{-1}^M$ (sec$^{-1}$) | | | 254 ± 9<br>(134 ± 6)[e] | 10.5 | | 305[d] | |
| $K_1^M = k_1^M/k_{-1}^M$ ($M^{-1}$) | | | 9.55 ± 0.60<br>(18.3 ± 1.0)[e] | 2.81 | | 23.1[d] | |
| $k_2^H$ ($M^{-1}$ sec$^{-1}$) | 70.2 ± 3.5 | 362 | 17.1 ± 1.7[f]<br>(8.8 ± 0.9)[e,f] | 1410 | | | 37.5[g] |
| $k_{-2}^H$ (sec$^{-1}$) | 6.8 ± 0.4 | 32.0 | 10.5 ± 0.5<br>(8.5 ± 0.5)[e] | 254 | | | 9.8[g] |
| $K_2^H = k_2^H/k_{-2}^H$ ($M^{-1}$) | 10.3 ± 0.8 | 11.3 | 1.63 ± 0.08[f]<br>(1.03 ± 0.05)[e,f] | 5.67 | | | 3.73[g] |

[a] Unless otherwise stated total electrolyte concentration maintained at 0.5 $M$ by addition of NaCl as required. [b] Reference 1. [c] From $\tau_2$ by means of an inversion plot. [d] Electrolyte concn, 0.2 $M$ $NaClO_4$. [e] Electrolyte concn, 3 $M$ NaCl. [f] From equilibrium measurements. [g] Electrolyte concn, 1 $M$ NaCl.

Figure 5 has been calculated from eq 11 with the values of $k_2^H$ and $K_1^E$ as determined from the inversion plot.

In methanol–water an inversion plot is not practical because the differences $\tau_2^{-1} - k_{-2}^H$ are of the same order of magnitude as the experimental error. One can determine $k_2^H$ however from equilibrium measurements in the following way. The visible absorption of basic T solution is given by eq 13, where $\epsilon_M$ and $\epsilon_H$ are the extinction coefficients of the respective Meisenheimer complex.[13,14] The spectra of M and H in their respective pure solvents are known[15] to be similar and are likely to be even more so in a common solvent. Thus we do not introduce a large error by assuming $\epsilon_M = \epsilon_H = \epsilon$ at wavelengths between 450 and 490 mμ. With this assumption and by expressing [M] and [H] in terms of known or measurable quantities, one obtains eq 14; a derivation is given in the Appendix. In combination with $k_{-2}^H$, $k_2^H$ is then calculated. The values of $K_2^H$ and $k_2^H$ reported in Table III represent averages of two independent determinations each at 0.004 $M$ and 0.01 $M$ NaOH concentration, which gave virtually identical results.

$$A = \epsilon_M[M] + \epsilon_H[H] \quad (13)$$

$$K_2^H = \frac{A + \frac{KK_1^M}{1+K}(A - \epsilon[T]_0)[NaOH]_0}{(\epsilon[T]_0 - A)\frac{[NaOH]_0}{1+K}} \quad (14)$$

The curves in Figure 2 have been calculated with reference to eq 11 by using $k_2^H$ as determined from these equilibrium measurements. The fit with the experimental points is within the experimental error.

## Discussion

**Identification of $\tau_1$ and $\tau_2$.**—In Table III we have summarized the various rate coefficients which were determined under the assumption that $\tau_1$ is due to the formation of M or E, respectively, and that $\tau_2$ is due to H formation in both systems.

A different set of rate coefficients can be calculated by assuming that it is the formation of H which gives rise to $\tau_1$, and alkoxide ion attack which leads to $\tau_2$. Instead of eq 8 and 9 we use eq 15 and 16, which by virtue of eq 5 and 6 are converted to eq 17 and 18. This alternate set of rate coefficients derived by applying eq 17 and 18 to our experimental data is also included in Table III.

$$\frac{1}{\tau_1} = k_2^H[HO^-] + k_{-2}^H \quad (15)$$

$$\frac{1}{\tau_2} = \frac{k_1^R[RO^-]}{1 + K_2^H[HO^-]} + k_{-1}^R \quad (16)$$

$$\frac{1}{\tau_1} = \frac{k_2^H}{1+K}[NaOH]_0 + k_{-2}^H \quad (17)$$

$$\frac{1}{\tau_2} = \frac{k_1^R K[NaOH]_0}{1 + K + K_2^H[NaOH]_0} + k_{-1}^R \quad (18)$$

Finally the rate coefficients referring to equilibrium 1 in pure ethanol, methanol, and water are included for the purpose of comparison.

Let us compare the various rate coefficients in the mixed solvents with those in the pure solvents. In the "aqueous" solvent, $k_1^M$ is decreased by a factor of about 2.9, $k_1^E$ by a factor of about 4.3; $k_{-1}^M$ and $k_{-1}^E$ are almost unchanged except for $k_{-1}^M$ at 3 $M$ salt concentration, where it is about half as big as in methanol. Compared to pure water, $k_2^H$ increases by a factor of about 2 in ethanol–water but decreases by approximately the same factor in methanol–water; $k_{-2}^H$ only changes slightly in the mixed solvents. These small solvent effects are consistent with classical theory,[16] the only slight discrepancy being the low value of $k_2^H$ in methanol–water which will be discussed below.

(13) $\epsilon_T = 0$ at the wavelengths chosen.

(14) The base concentration has to be low to avoid appreciable 1:2 complex formation.

(15) (a) V. Gold and C. H. Rochester, *J. Chem. Soc.*, 1692 (1964); (b) F. Čuta and J. Písecký, *Chem. Listy*, **51**, 433 (1957); (c) T. Abe, *Bull. Chem. Soc. Jap.*, **33**, 41 (1960).

(16) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p 345.

In contrast, the alternate set of coefficients based on the assumption that $\tau_1$ is due to H, $\tau_2$ to M or E formation leads to solvent effects which are difficult to rationalize. According to this interpretation a change from methanol to 22.5% aqueous methanol would reduce $k_1^M$ by a factor of 240, $k_{-1}^M$ by a factor of 29; the similar change from ethanol to 19% aqueous ethanol would decrease $k_1^E$ by a factor of 22 and $k_{-1}^E$ by a factor of 4. Finally the addition of 22.5% methanol to water would raise $k_2^H$ by a factor of 38 and $k_{-2}^H$ by a factor of 26, whereas the addition of 19% ethanol to water would augment $k_2^H$ by nearly a factor of 10 and $k_{-2}^H$ by a factor of over 3. Hence there can be no doubt that our identification of $\tau_1$ with M and E and $\tau_2$ with H is the only acceptable one.

**Solvent Effects.**—As pointed out above, the reduction of $k_1^M$ and $k_1^E$ in the "aqueous" solvents compared to pure methanol and ethanol, respectively, and the increase of $k_2^H$ in ethanol–water are consistent with Ingold's[16] theory. It should be emphasized at this point that the $k_1^R$, $k_2^H$, $K_1^R$, and $K_2^H$ but not $k_{-1}^R$ and $k_{-2}^H$ depend on the values of $K$ estimated by Murto;[11] if Murto's values should be in error, the rate coefficients dependent on them will contain a systematic error in addition to the standard deviations indicated in Table III.[17] The magnitudes of $K$ are such that in methanol–water the concentrations of $MeO^-$ and $HO^-$ are comparable to each other so that $k_1^M$, $k_2^H$, $K_1^M$, and $K_2^H$ would be about equally affected by such a systematic error. In ethanol–water the equilibrium favors $HO^-$ greatly over $EtO^-$ so that only $k_1^E$ and $K_1^E$ but not $k_2^H$ and $K_2^H$ are very sensitive to errors in $K$.

Hence one should not attach too much importance to the *quantitative* aspect of the reported solvent effects on $k_1^M$, $k_1^E$, and $k_2^H$ in methanol–water. The small reduction of $k_2^H$ in this latter solvent compared to pure water might be partly due to such a systematic error in $K$, though interestingly Murto's[18] rate coefficients for the comparable $HO^-$ attack on 2,4-dinitrofluorobenzene in various methanol–water and ethanol–water mixtures which are based on the same $K$ values show an increase in both mixtures as the alcohol content increases.

(17) There is also a probability of error at high electrolyte concentrations where $K$ may be slightly different. For lack of more suitable data the same $K$ has been used in our calculations, independent of electrolyte concentration.

(18) J. Murto, *Acta Chem. Scand.*, **18**, 1029 (1964).

Thus another rationalization may be in terms of a special solvation effect due to enhanced water structure in water of low alcohol content[19] which is known to give rise to irregularities.[19,20]

It is noteworthy that all the rate coefficients for leaving group departure are barely affected by the solvent changes. Thus the interesting reactivity pattern of the three bases found in the pure solvents is essentially unchanged. The abnormally low value for $k_{-2}^H$ in relation to the equilibrium constant $K_2^H$ when compared to $k_{-1}^M$ and $k_{-1}^E$ has been attributed to intramolecular hydrogen bonding to an ortho nitro group in H.[1]

**Salt Effect.**—That the $k_1^M$ values in the presence of 0.5 *M* and of 3 *M* NaCl come out to be virtually identical is somewhat surprising. Our working hypothesis that $K$ is equal in both situations may be responsible for this result. $k_{-1}^M$ (which does not depend on $K$ for its evaluation) shows a significant salt effect which is similar to the one found for leaving group departure from the Meisenheimer complex between 2,4-dinitroanisole and $MeO^-$ in methanol.[21]

**Registry No.**—1,3,5-Trinitrobenzene, 99-35-4; $MeO^-$, 3315-60-4; $HO^-$, 14280-30-9; $EtO^-$, 16331-64-9.

**Acknowledgment.**—We wish to thank Professor J. F. Bunnett for reading the manuscript and for valuable suggestions.

## Appendix

**Derivation of Equation 14.**—If we express [M] and [H] in eq 13 as functions of $[T]_0$ and assume $\epsilon_M \approx \epsilon_H \approx \epsilon$, we obtain eq 19. We can solve for $K_2$ which

$$A = \epsilon \frac{(K_1^M[MeO^-] + K_2^H[HO^-])\,[T]_0}{1 + K_1^M[MeO^-] + K_2^H[HO^-]} \qquad (19)$$

leads to eq 20. In combination with 5 and 6 eq 14 is

$$K_2 = \frac{A + K_1^M[MeO^-]\,(A - \epsilon[T]_0)}{(\epsilon[T]_0 - A)\,[HO^-]} \qquad (20)$$

obtained.

(19) F. Franks and D. J. G. Ives, *Quart Rev., Chem. Soc.*, **20**, 1 (1966).

(20) R. G. Bates in "Hydrogen Bonded Solvent Systems," A. K. Covington and P. Jones, Ed., Taylor and Francis Ltd., London 1968, p 49.

(21) C. F. Bernasconi, *J. Amer. Chem. Soc.*, **90**, 4982 (1968).

# The Meisenheimer Reaction in the 1,5-Naphthyridine Series. II[1a]

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The action of phosphorus oxychloride on 1,5-naphthyridine 1,5-dioxide yields a mixture of isomeric dichloro-1,5-naphthyridines. The presence of 2,4-dichloro-1,5-naphthyridine and 3,8-dichloro-1,5-naphthyridine was verified by comparison with synthetic samples prepared *via* known procedures. 2,6-Dichloro-1,5-anphthyridine and 2,8-dichloro-1,5-naphthyridine were prepared by new unambiguous synthetic routes and also found to be present among the reaction products. The mass and nmr spectra indicate that the fifth major product of the mixture is 2,7-dichloro-1,5-naphthyridine. The expected 4,8-dichloro-1,5-naphthyridine isomer was not detected anywhere in the reaction products. The independent synthesis of this isomer and comparison of it with all of the products isolated from the reaction mixture substantiate its absence. The nmr and mass spectra of the dichloronaphthyridines are discussed.

The Meisenheimer reaction is the action of phosphorus oxychloride or sulfuryl chloride on the *N*-oxide function of pyridine or a polycyclic azine resulting in nucleophilic substitution by the chloride ion at a ring carbon and loss of oxygen.[2] This reaction usually gives mixtures of isomers and an extensive review of the literature has been made by Ochiai.[3]

Previously we have shown[4] that 1,5-naphthyridine 1-oxide yields a mixture of 2- and 4-chloro-1,5-naphthyridines from the Meisenheimer reaction rather than just 2-chloro-1,5-naphthyridine as had been previously reported by Hart.[5] In the same paper, Hart reported 2,6-dichloro-1,5-naphthyridine as the only product isolated from the Meisenheimer reaction on 1,5-naphthyridine 1,5-dioxide.[5] This result has recently been questioned[6] and we now wish to report our investigations as to the identity of the reaction products.

We have now repeated Hart's work using the same conditions he described.[5] Analysis of the mixture by gas chromatography shows six distinct peaks with peak 5 having a definite shoulder indicating that the peak consists of two components. The assignment of structures to the compounds giving peaks 3, 4, 5, and 6 was made from interpretation of the nmr and mass spectra for each and the results are in Table I.

Table I

Components of Meisenheimer Mixture

| Peak | Percentage[a] | Compd |
|---|---|---|
| 1 | 1.1 | |
| 2 | 0.3 | |
| 3 | 9.4 | 2,7-Dichloro-1,5-naphthyridine |
| 4 | 17.6 | 3,8-Dichloro-1,5-naphthyridine |
| 5 | 46.1 (37%)[b] | 2,6-Dichloro-1,5-naphthyridine |
| | (9%)[b] | 2,4-Dichloro-1,5-naphthyridine |
| 6 | 25.5 | 2,8-Dichloro-1,5-naphthyridine |

[a] These percentages are an average of two runs and the maximum deviation is 0.36%. [b] This value was obtained as an approximation from fractional sublimation of peak 5.

In addition, the two components of peak 5 and the identity of the components in peaks 4 and 6 were confirmed by comparison of their nmr spectra with those of synthetic samples made by unambiguous routes. The infrared spectra of the four synthetic isomers were identical with the components of peaks 4, 5, and 6. Mixture melting points with three of the components further confirmed their identity.

The preparative gas chromatogram of peak 1 indicates that it is a mixture of two compounds. The mass spectrum of peak 1 shows the molecular ion as *m/e* 198 indicating that at least one and probably both of the components are dichloro-1,5-naphthyridine isomers. However, insufficient material was obtained for further analysis.

No data are available to identify peak 2 due to insufficient material. The material from peaks 1 and 2 amounts to less than 1.5% of the reaction products. The five dichloro-1,5-naphthyridine isomers which have been identified comprise over 98% of the products.

The mass spectrum of peak 3 shows a molecular ion at *m/e* 198. This indicates the material is a dichloro-1,5-naphthyridine. The nmr spectrum consists of two different AB systems with two protons overlapped, one from each AB system. The chemical shifts of the protons indicate that the position para to the nitrogen is unsubstituted in both rings. The chemical shifts of the other two protons that indicate one meta and one ortho position also have hydrogens. The coupling constant of 1.4 cps is typical of ortho–para coupling indicating substitution at the meta or 3 position. The coupling constant of 8.6 cps is typical of 3–4 coupling, meaning the 2 position is substituted in the other ring. The isomer with the chlorine substituted at the ortho position in one ring and the meta position in the other ring would be 2,7-dichloro-1,5-naphthyridine.

The mass spectrum of peak 4 shows *m/e* 198 as the molecular ion. The nmr spectrum clearly shows the presence of two different AB systems and integrates for four protons. The coupling constant 2.1 cps indicates the $H_2$ and $H_4$ protons are coupled, meaning the ring is substituted with a chlorine in the 3 position. The AB pattern for the other ring is indicative of chlorine substitution para to the nitrogen or in the 8 position. The coupling constant of 4.3 cps must come from hydrogens ortho and meta to the nitrogen. Thus, peak 4 then could only be 3,8-dichloro-1,5-naphthyridine. The chemical shifts of the four protons are in full agreement with this assigned structure as can be seen from Table II. McCaustland

(1) (a) Presented in part at the combined Southeast and Southwest Regional Meeting of the American Chemical Society, New Orleans, La., Dec 2–4, 1970. (b) Taken in part from the Ph.D. Dissertation of A. C. Plasz, University of Kentucky, 1970.

(2) J. Meisenheimer, *Ber.*, **59**, 1848 (1926).

(3) E. Ochiai, "Aromatic Amine Oxides," Elsevier, New York, N. Y., 1967, pp 259–269.

(4) E. V. Brown and A. C. Plasz, *J. Org. Chem.*, **32**, 241 (1967).

(5) E. P. Hart, *J. Chem. Soc.*, 1879 (1954).

(6) W. W. Paudler and T. J. Kress, *Advan. Heterocycl. Chem.*, **11**, 168 (1970).

TABLE II

NMR SPECTRAL DATA OF SOME CHLORO-1,5-NAPHTHYRIDINES

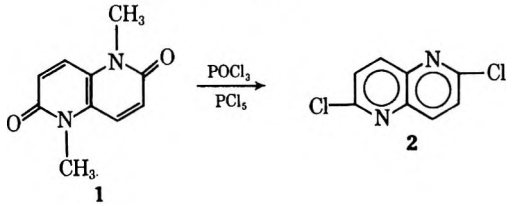
| Compd | Solvent | Chemical shifts[a] $H_2$ | $H_3$ | $H_4$ | $H_6$ | $H_7$ | $H_8$ | Coupling constants[b] $J_{2,3}$ | $J_{2,4}$ | $J_{3,4}$ | $J_{6,7}$ | $J_{6,8}$ | $J_{7,8}$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2-Chloro-1,5-naphthyridine[c] | $CCl_4$ | | 7.48 | 8.19 | 8.78 | 7.53 | 8.16 | | | 8.0 | 4.3 | 1.6 | 8.6 |
| 4-Chloro-1,5-naphthyridine[c] | $CCl_4$ | 8.66 | 7.45 | | 8.89 | 7.41 | 8.27 | 4.5 | | | 4.0 | 1.5 | 8.4 |
| 2,4-Dichloro-1,5-naphthyridine | $CDCl_3$ | | 7.75 | | 8.99 | 7.71 | 8.30 | | | | 4.1 | 1.9 | 8.4 |
| 2,6-Dichloro-1,5-naphthyridine | $CDCl_3$ | | 7.62 | 8.23 | | 7.62 | 8.23 | | | 8.4 | | | 8.4 |
| 2,7-Dichloro-1,5-naphthyridine | $CDCl_3$ | | 7.62 | 8.35 | 8.92 | | 8.32 | | | 8.6 | | 1.4 | |
| 2,8-Dichloro-1,5-naphthyridine | $CDCl_3$ | | 7.66 | 8.77 | 8.33 | 7.74 | | | | 8.5 | 4.5 | | |
| 3,8-Dichloro-1,5-naphthyridine | $CDCl_3$ | 8.98 | | 8.44 | 8.66 | 7.74 | | | 2.1 | | 4.3 | | |
| 4,8-Dichloro-1,5-naphthyridine | $CDCl_3$ | 8.95 | 7.82 | | 8.95 | 7.82 | | 4.4 | | | 4.4 | | |

[a] Chemical shifts ($\delta$) are recorded as parts per million downfield from TMS. [b] Coupling constants ($J$) are in cycles per second. [c] E. V. Brown and A. C. Plasz, *J. Heterocycl. Chem.*, **7**, 593 (1970).

and Cheng[7] have recently reported the synthesis of 3,8-dichloro-1,5-naphthyridine from 3-amino-5-chloropyridine *via* the diethyl ethoxymethylenemalonate (EMME) route. The 3,8-dichloro-1,5-naphthyridine we prepared by their method was identical with the material from peak 4.

Almost one-half of the reaction products are found in peak 5. There are two components in this fraction and they have been identified as 2,6-dichloro-1,5-naphthyridine and 2,4-dichloro-1,5-naphthyridine and are present in an approximate 4:1 ratio. This was determined by fractional sublimation which separated the two isomers. 2,4-Dichloro-1,5-naphthyridine was prepared according to Oakes and Rydon.[8] The synthetic 2,4-dichloro-1,5-naphthyridine was identical with that of the more volatile fraction of peak 5. The nmr spectrum of 2,4-dichloro-1,5-naphthyridine had the expected AMX system for the unsubstituted ring with the singlet peak for the $H_3$ proton superimposed on the quartet from the X proton of the AMX system. Coupling constants for all protons were typical for this system. A modification of Fargher and Farness'[9] synthesis of 2-chloropyridine applied to 1,5-dimethyl-1,5-naphthyridine-2,6(1*H*,5*H*)-dione[10] (1) afforded 2,6-dichloro-1,5-naphthyridine (2) in 14.4% yield (Scheme I). The synthetic 2,6-dichloro-1,5-naphthyridine was

SCHEME I




1 2

identical with the fraction which sublimed above 95° from peak 5. The nmr spectrum of 2,6-dichloro-1,5-naphthyridine was characterized by the expected $A_2B_2$ pattern and typical coupling constant and chemical shifts (see Tables II and III).

The identity of peak 6 has been confirmed by the synthesis of 2,8-dichloro-1,5-naphthyridine. Diethyl ethoxymethylenemalonate (EMME) and 5-amino-2-hydroxypyridine were refluxed in phenyl ether at 250° to afford 7-carbethoxy-2,8-dihydroxy-1,5-naphthyridine (3). Saponification gave 7-carboxy-2,8-dihydroxy-1,5-naphthyridine (4) followed by decarboxylation in mineral oil at 300° to yield 2,8-dihydroxy-1,5-naphthyridine (5). The 2,8-dihydroxy-1,5-naphthyridine was converted to 2,8-dichloro-1,5-naphthyridine (6) by refluxing with a phosphorus oxychloride–phosphorus pentachloride mixture (Scheme II). The synthetic 2,8-dichloro-1,5-naphthyridine was identical with the material isolated from the peak 6 in the Meisenheimer mixture. The nmr spectrum of 2,8-dichloro-1,5-naphthyridine was characterized by two different AB systems. Typical chemical shifts and coupling constants were observed for the AB system of the $H_3$ and $H_4$ protons and the AB system of the $H_6$ and $H_7$ protons. As would be expected, the $H_3$ and $H_7$ protons have similar chemical shifts; however, the splitting and slight difference in chemical shifts allow both peaks

TABLE III

MASS SPECTRA OF DICHLORO-1,5-NAPHTHYRIDINE

| m/e | Relative abundances 2,4 | 2,6 | 2,7 | 2,8 | 3,8 | 4,8 |
|---|---|---|---|---|---|---|
| 202 | 11 | 10 | 10 | 10 | 10 | 11 |
| 200 | 64 | 64 | 60 | 60 | 56 | 62 |
| 199 | 10 | 10 | 9 | 9 | 9 | 10 |
| 198 | 100 | 100 | 100 | 100 | 100 | 100 |
| 165 | 28 | 25 | 29 | 30 | 18 | 24 |
| 164 | 8 | 7 | 9 | 9 | 5 | 8 |
| 163 | 85 | 75 | 94 | 97 | 54 | 73 |
| 138 | 2 | 2 | 4 | 4 | 7 | 5 |
| 137 | 2 | 4 | 7 | 9 | 4 | 5 |
| 136 | 7 | 5 | 14 | 11 | 20 | 17 |
| 127 | 14 | 56 | 12 | 16 | 5 | 8 |
| 112 | 12 | 2 | 3 | 3 | 2 | 2 |
| 103 | 10 | 2 | 3 | 1 | 1 | 1 |
| 102 | 9 | 3 | 2 | 2 | 1 | 1 |
| 101 | 10 | 13 | 8 | 10 | 7 | 8 |
| 100 | 25 | 28 | 25 | 33 | 33 | 38 |
| 99 | 13 | 11 | 10 | 10 | 12 | 15 |
| 85 | 5 | 8 | 7 | 11 | 7 | 9 |
| 81 | 5 | 14 | 7 | 2 | 1 | 3 |
| 76 | 23 | 23 | 17 | 23 | 17 | 19 |
| 75 | 32 | 27 | 23 | 30 | 19 | 19 |
| 74 | 15 | 11 | 12 | 17 | 18 | 21 |
| 73 | 4 | 12 | 17 | 16 | 16 | 18 |
| 64 | 8 | 24 | 20 | 22 | 22 | 21 |
| 63 | 8 | 9 | 16 | 8 | 8 | 7 |
| 62 | 9 | 8 | 9 | 9 | 7 | 7 |
| 52 | 13 | 16 | 11 | 15 | 8 | 7 |
| 51 | 37 | 17 | 11 | 14 | 11 | 10 |
| 50 | 37 | 36 | 7 | 39 | 28 | 27 |
| 49 | 10 | 10 | 7 | 11 | 10 | 11 |
| Temp, °C | 170 | 170 | 200 | 185 | 185 | 180 |
| Trap | 10 | 10 | 70 | 10 | 10 | 10 |

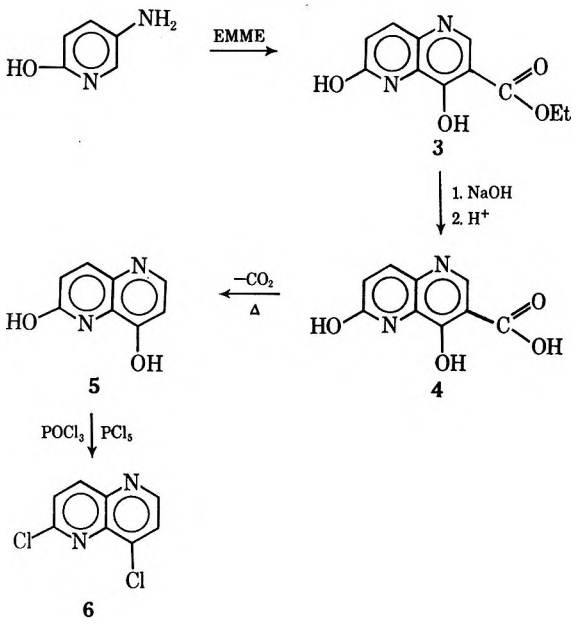
(7) D. J. McCaustland and C. C. Cheng, *J. Heterocycl. Chem.*, **7**, 467 (1970).

(8) V. Oakes and H. N. Rydon, *J. Chem. Soc.*, 204 (1958).

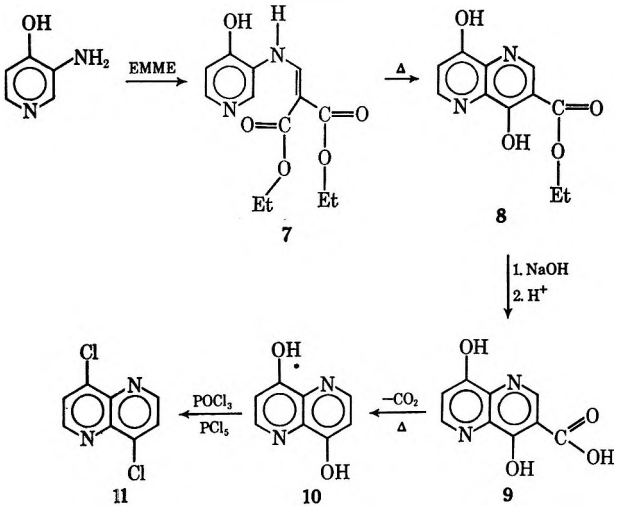
(9) R. G. Farcher and R. Farness, *ibid.*, **107**, 688 (1915).

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

Scheme II




Scheme III




of each doublet to be distinctly clear in the nmr spectrum.

One surprising feature in the analysis of the reaction products was the fact that no 4,8-dichloro-1,5-naphthyridine was formed. In all of the fractions of the Meisenheimer mixture analyzed by nmr, there was no indication that 4,8-dichloro-1,5-naphthyridine was present. The independent synthesis of 4,8-dichloro-1,5-naphthyridine was achieved using the diethyl ethoxymethylenemalonate route. Condensation of 4-hydroxy-3-aminopyridine with EMME in refluxing toluene gave the uncyclized ester **7**. An attempt to condense and cyclize in one step with phenyl ether was accompanied by vigorous frothing and foaming upon formation of the condensation product at 110–130°. Cyclization of purified **7** to 3-carbethoxy-4,8-dihydroxy-1,5-naphthyridine (**8**) in refluxing phenyl ether proceeded smoothly. Saponification of **8** gave crude 3-carboxy-4,8-dihydroxy-1,5-naphthyridine (**9**) which was directly decarboxylated and sublimed under vacuum at 250–300° to give 4,8-dihydroxy-1,5-naphthyridine (**10**). The conversion of **10** to 4,8-dichloro-1,5-naphthyridine (**11**) was done with a refluxing mixture of phosphorus oxychloride and phosphorus pentachloride (Scheme III). When this compound was injected into the gas chromatograph, its retention time was higher than any of the other isomers under exactly the same conditions. The nmr spectrum of 4,8-dichloro-1,5-naphthyridine had the expected $A_2B_2$ pattern and $J_{2,3}$ coupling constant.

The mass spectra for the dichloro-1,5-naphthyridines are shown in Table III. The major fragmentation from the molecular ion of the dichloro-1,5-naphthyridines is the loss of a chlorine atom to give the expected isotopic cluster at *m/e* 163 and 165 in a 3:1 ratio due to the one chlorine atom still attached (spectra in which metastables are observed which support these transitions are in Table IV). Metastable evidence (Table IV) supports two different fragmentations from the *m/e* 163 and 165 peaks. The loss of HCl as a neutral fragment gives rise to the peak *m/e* 127. The loss of HCN from *m/e* 163 and 165 to give the fragments at *m/e* 136 and 138 still in the approximate 3:1 ratio indicating the chlorine atom has not been lost yet. The fragments at *m/e* 138 and 136 expel HCl to give rise to a *m/e* 100 moiety. This *m/e* 100 moiety also results from the loss of HCN from the *m/e* 127 peak. Metastable evidence supports both fragmentations. Contributions to the peaks at *m/e* 101, 100, and 99 could also come from doubly charged ions.

Table IV

Metastables

| Parent ion | Daughter ion | Neutral fragment | Calcd met | Obsd 2,4 | 2,6 | 2,7 | 2,8 | 3,8 | 4,8 |
|---|---|---|---|---|---|---|---|---|---|
| 200 → | 165 | 35 | 136.13 | √ | √ | √ | √ | √ | √ |
| 200 → | 163 | 37 | 132.84 | √ | √ | √ | √ | √ | √ |
| 198 → | 163 | 35 | 134.19 | √ | √ | √ | √ | √ | √ |
| 163 → | 136 | 27 | 113.47 | √ | | √ | √ | √ | √ |
| 165 → | 138 | 27 | 115.42 | | | | √ | √ | √ |
| 163 → | 127 | 36 | 98.95 | √ | √ | √ | √ | √ | √ |
| 165 → | 127 | 38 | 97.75 | √ | √ | | √ | √ | √ |
| 127 → | 100 | 27 | 78.74 | √ | √ | | √ | | |
| 138 → | 100 | 38 | 72.83 | √ | | | √ | | |
| 136 → | 100 | 36 | 73.53 | √ | √ | | √ | √ | √ |
| 100 → | 73 | 27 | 53.29 | | | | | | |

Further fragmentation is quite similar to other naphthyridines recorded in the literature.[11,12] The peaks at *m/e* 76, 75, 74, 64, 63, 52, 51, and 50 are characteristic in naphthyridine spectra,[11,12] and the peaks at *m/e* 52, 51, 50, and 49 are characteristic of pyridine systems.[13]

## Experimental Section

Melting points were taken on a Fisher-Johns block and are corrected unless otherwise stated. Melting points of compounds which sublime easily were taken in a sealed tube and are uncorrected and noted in the text. Infrared spectra were taken on a Beckman IR-8 spectrometer using potassium bromide pellets. Nuclear magnetic resonance spectra were obtained with a Varian T-60 spectrometer using 25 mg of sample and 0.5 ml of solvent except for the 2,7-dichloro-1,5-naphthyridine where only 3 mg of compound was obtained pure. The internal standard was TMS (4%) and deuteriochloroform was the solvent unless otherwise

(11) E. V. Brown, A. C. Plasz, and S. R. Mitchell, *J. Heterocycl. Chem.*, **7**, 661 (1970).

(12) W. W. Paudler and T. J. Kress, *ibid.*, **4**, 547 (1967).

(13) American Petroleum Institute, Research Project 44, "Mass Spectral Data," Thermodynamics Research Center Publications, College Station, Texas, 1966, Spectra No. 617.

indicated. Mass spectra were obtained with either a Hitachi Perkin-Elmer RMU-6E or RMU-7 mass spectrometer with an ionizing potential of 70 eV. The direct inlet was used and the temperature and trap current for each compound are in Table III.

**3,8-Dichloro-1,5-naphthyridine** was prepared by the method of McCaustland and Cheng,[7] mp 176.5–177.5° (lit.[7] mp 176–179°).

**2,4-Dichloro-1,5-naphthyridine** was prepared by the method of Oakes and Rydon,[8] mp 138–139° (lit.[8] 140°).

**2,6-Dichloro-1,5-naphthyridine (2).**—1,5-Dimethyl-1,5-naphthryidine-2,6(1*H*,5*H*)-dione (1)[10] (1.20 g, 0.0063 mol), phosphorus pentachloride (2 g, 0.0096 mol), and phosphorus oxychloride (10 ml) were refluxed for 9 hr. The excess phosphorus oxychloride was removed under vacuum and ice was added. The mixture was basified with concentrated ammonium hydroxide and a solid precipitated. The purple solid was removed by filtration to yield 0.18 g (14.4%). This was sublimed twice under vacuum to give 0.11 g of yellow powder, mp 258–260° uncor (sealed tube), (lit.[5] 236°).

*Anal.* Calcd for $C_8H_4N_2Cl_2$: C, 48.24; H, 2.01; N, 14.07. Found: C, 48.40; H, 1.86; N, 14.22.

**7-Carbethoxy-2,8-dihydroxy-1,5-naphthyridine (3).**—2-Hydroxy-5-nitropyridine (20.0 g, 0.143 mol) was reduced with 10% palladium on carbon in ethanol on the low-pressure (3 atm) Parr apparatus. The catalyst was removed by filtration and the ethanol was evaporated. The 5-amino-2-hydroxypyridiue (15.0 g, 0.108 mol) was added to 475 ml of phenyl ether containing (31 g, 0.14 mol) of diethyl ethoxymethylenemalonate and refluxed at 250° for 1 hr. The solution was cooled, and the solids were removed by filtration and then slurried in hot Skellysolve B. Filtration gave 19.6 g of brown crude ester. The brown solid (18.95 g) was vacuum sublimed at 250–300° for 1 hr to give 5.1 g (20.2%) of yellow solid. This yellow solid was recrystallized twice from methanol to give a white fluffy solid, mp 293–295°.

*Anal.* Calcd for $C_{11}H_{10}N_2O_4$: C, 56.41; H, 4.27; N, 11.97. Found: C, 56.32; H, 4.48; N, 11.73.

**7-Carboxy-2,8-dihydroxy-1,5-naphthyridine (4).**—7-Carbethoxy-2,8-dihydroxy-1,5-naphthyridine (48 g, 0.21 mol) was refluxed in 400 ml of 6% sodium hydroxide for 15 hr. The mixture was treated with charcoal while hot and was filtered through a Celite bed. The cooled solution was neutralized with 50% hydrochloric acid added dropwise to pH 7. The solid was filtered and dried at 110° overnight. The yield was 34 g (80.5%), mp >350°.

**2,8-Dihydroxy-1,5-naphthyridine (5).**—7-Carboxy-2,8-dihydroxy-1,5-naphthyridine (11.6 g, 0.0565 mol) was slowly added to stirring mineral oil (500 ml) at 300°. After addition the mixture was kept at 300–310° for 45 min, and the mixture was cooled and filtered. The solids were washed with Skellysolve B to remove the mineral oil and dried overnight at 120°. The solid was then extracted with 500 ml of boiling water and the solution was filtered. The solution was concentrated to give a solid which was removed by filtration yielding 2.67 g (29.2%). Sublimation under vacuum at 280° separated the dihydroxy compound from the residue. The material was resublimed at 280° under vacuum and recrystallized from ethanol; another sublimation and final recrystallization from methanol gave a white powder, mp >360° (sublimes).

*Anal.* Calcd for $C_8H_6N_2O_2$: C, 59.26; H, 3.70; N, 17.28. Found: C, 59.02; H, 3.94; N, 17.09.

**2,8-Dichloro-1,5-naphthyridine (6).**—2,8-Dihydroxy-1,5-naphthyridine (2 g, 0.012 mol), phosphorus oxychloride (50 ml), and phosphorus pentachloride (10 g, 0.048 mol) were refluxed for 4 hr. The excess phosphorus oxychloride was removed *in vacuo* and the residue dissolved in 200 ml of ice water. Ammonium hydroxide was added and the yellow precipitate was removed by filtration. The yield, after drying, was 1.15 g, recrystallized from Skellysolve B, 1.06 g (43.4%). The material was sublimed at 120–155° at atmospheric pressure to give the analytical sample as white needles, mp 153.5–156° (sealed tube).

*Anal.* Calcd for $C_8H_4N_2Cl_2$: C, 48.24; H, 2.01; N, 14.07. Found: C, 48.43; H, 1.79; N, 14.03.

**Ethyl β-(4-Hydroxy-3-pyridylamino)-α-carbethoxyacrylate (7).**—3-Nitro-4-hydroxypyridine[14] was reduced with 10% palladium on carbon in ethanol on the low-pressure Parr apparatus (3 atm). The catalyst was removed by filtration and the ethanol was evaporated to give the crude amine which was used without further purification for the next step. To a 1-l. three-necked round-bottomed flask, fitted with a stirrer and condenser, was added 400 ml of toluene. Diethyl ethoxymethylenemalonate (20 g, 0.093 mol) and 3-amino-4-hydroxypyridine (5 g, 0.047 mol) were added, and the mixture was heated to reflux and kept there 8 hr. The solution was cooled, and the product was removed with suction filtration and recrystallized from methanol (charcoal) to give 7.7 g. (58.3%) of white plates, mp 243.5°–245.5°.

*Anal.* Calcd for $C_{13}H_{16}N_2O_5$: C, 55.01; H, 5.72; N, 10.00. Found: C, 55.21; H, 5.72; N, 9.85.

**3-Carbethoxy-4,8-dihydroxy-1,5-naphthyridine (8).**—Ethyl β-(4-hydroxy-3-pyridylamino)-α-carbethoxyacrylate (15 g, 0.054 mol) was added to 450 ml of phenyl ether and refluxed (250–255°) for 1 hr. The mixture was cooled and filtered. The solid was washed with large volumes of Skellysolve B until the washings were colorless and was then refluxed 1 hr in boiling benzene to remove the remaining phenyl ether, cooled, removed by filtration from the benzene, and dried to give 6.3 g (50.2%) of dirt-brown solid. This was sublimed under vacuum at 280° in 1-g amounts for 3 hr. The sublimer was rinsed clean with hot ethanol and the ethanol was evaporated to give a total yield of 0.44 g (3.5%) of yellow solid, mp >300° (sublimes). An additional sublimation and recrystallization from ethanol gave the analytical sample.

*Anal.* Calcd for $C_{11}H_{10}N_2O_4$: C, 56.41; H, 4.27. Found: C, 56.28; H, 4.26.

**3-Carboxy-4,8-dihydroxy-1,5-naphthyridine (9).**—3-Carbethoxy-4,8-dihydroxy-1,5-naphthyridine (1.0 g, 0.0043 mol) was refluxed with 50 ml of 4% sodium hydroxide for 4 hr. The solution was cooled overnight and then acidified with 3 *M* hydrochloric acid at pH 7. The precipitate was collected in a sintered glass funnel and the precipitation process repeated on the mother liquor three more times. The four crops were dried at 110° for 1 hr and gave 0.68 g (77.3%) of acid which decarboxylates and sublimes at >320°.

**4,8-Dihydroxy-1,5-naphthyridine (10).**—3-Carboxy-4,8-dihydroxy-1,5-naphthyridine (0.68 g, 0.0033 mol) was decarboxylated and sublimed under vacuum at 250–300° and the yellow solid was removed from the sublimer with boiling ethanol–water. The process was repeated two additional times and the solids were dried at 110° for 1 hr. The yield of yellow solids was 0.33 g (61.7%), mp >300° (sublimes).

*Anal.* Calcd for $C_8H_6N_2O_2$: C, 59.26; H, 3.70; N, 17.28. Found: C, 58.79; H, 3.77; N, 17.18.

**4,8-Dichloro-1,5-naphthyridine (11).**—4,8-Dihydroxy-1,5-naphthyridine (0.20 g, 0.0012 mol), phosphorus oxychloride (50 ml), and phosphorus pentachloride (5 g, 0.024 mol) were refluxed for 1 hr, after which time all of the solid dissolved. After an additional hour of reflux, the mixture was cooled and excess phosphorus oxychloride was removed under vacuum. The resulting purple, syrupy liquid was cooled in an ice bath and ice-cold dilute ammonium hydroxide was added with vigorous stirring until the syrup had dissolved and formed a gray suspension. The mixture was made strongly basic with additional ammonium hydroxide and filtered through a sintered-glass funnel, and the precipitate was washed with 10 ml of 1:1 ice-cold ethanol–water and air-dried overnight. The crude dichloro compound (0.22 g) was sublimed under vacuum at 150° to give 0.15 g (61.5%) of grayish white powder. Recrystallization from Skellysolve B and then benzene, followed by two sublimations at 200–220° and atmospheric pressure, gave white needles, mp 278–279°.

*Anal.* Calcd for $C_8H_4N_2Cl_2$: C, 48.24; H, 2.01; N, 14.07. Found: C, 48.38; H, 1.99; N, 14.14.

**1,5-Naphthyridine 1,5-Dioxide.**[5]—1,5-Naphthyridine (4.1 g, 0.032 mol), peracetic acid (15 ml), and glacial acetic acid (40 ml) were heated in a 100-ml round-bottomed flask in an oil bath. The temperature initially rose to 75° and dropped to 50° where it was kept for 20 hr. The mixture was cooled in ice, basified with solid potassium hydroxide, and extracted with 500 ml of chloroform, and the chloroform was evaporated. The solids were extracted with boiling ethanol. Upon cooling, 1.22 g (24.9%) of yellow needles were collected, mp 298–301° (lit.[5] 301°).

**Meisenheimer Reaction.**—1,5-Naphthyridine 1,5-dioxide (1.24 g, 0.00766 mol) and phosphorus oxychloride (40 ml) were mixed together while cooling in an ice bath. The mixture was brought to reflux and the dioxide went into solution and then was refluxed for 30 min. The excess phosphorus oxychloride was removed *in vacuo*, 100 ml of ice water and 20 ml of ammonium hydroxide were added, and the black gum turned into a gray-white solid. The solid was removed by filtration and air-dried to give 1.17 g of crude material which softened at 135°, darkened at 175°, and

(14) E. Koenigs and K. Freter, *Ber.*, **57**, 1187 (1924).

melted from 205 to 240° where some sublimation was noted. The mixture was dissolved in acetone and analyzed with a Hewlett-Packard Model 5750 gas chromatograph and Infotronics Digital Readout CRS-108 integrator using a 6 ft × 0.125 in. Carbowax 20M column at 180°. Six distinct peaks were obtained and the fifth peak had a definite shoulder indicating two components for that peak. The area percentages calculated for each peak appear in Table I.

**Separation and Identification of Isomers.**—The crude mixture from the Meisenheimer reaction was separated with a Hewlett-Packard Model 5750 gas chromatograph using a 20 ft × 0.375 in. o.d. aluminum column filled with 20% Carbowax 20M on Chromosorb W. The sample was dissolved in acetone and injected into the column at 230°. The components of the six individual peaks were collected and the two components of peak 5 were separated by fractional sublimation. The components were identified by their mass, infrared, and nmr spectra and by comparison with spectra of synthetic isomers where possible. Mixture melting points were used in three cases as additional proof of structure. In the cases where infrared and nmr spectra of synthetic isomers and separated isomers could be obtained, they were identical in all respects leaving no doubt as to the identity of the compound. The melting point of 3,8-dichloro-1,5-naphthyridine separated from the mixture was 177.5–178.5° and the mixture melting point with the synthetic sample occurred at 177–178.5°. The melting point of separated 2,4-dichloro-1,5-naphthyridine from peak 5 was 124.5–130°. The melting point of separated 2,6-dichloro-1,5-naphthyridine from peak 5 was 257–260° and the mixture melting point with synthetic 2,6-dichloro-1,5-naphthyridine occurred at 257–259°. The melting point of 2,8-dichloro-1,5-naphthyridine, separated as peak 6 from the Meisenheimer mixture, was 154.5–156° and the mixture melting point with synthetic 2,8-dichloro-1,5-naphthyridine occurred at 154–157°. All of these melting points in this section were taken in a sealed tube and are uncorrected.

**Registry No.**—**2**, 27017-66-9; **3**, 28252-73-5; **4**, 28252-74-6; **5**, 28252-75-7; **6**, 28252-76-8; **7**, 28252-77-9; **8**, 28252-78-0; **9**, 28252-79-1; **10**, 28312-61-0; **11**, 28252-80-4; 3,8-dichloro-1,5-naphthyridine, 28252-81-5; 2,4-dichloro-1,5-naphthyridine, 28252-82-6; 2-chloro-1,5-naphthyridine, 7689-62-5; 4-chloro-1,5-naphthyridine, 7689-63-6; 2,7-dichloro-1,5-naphthyridine, 28252-85-9.

# Permanganate Ion Oxidations. VI. Kinetics and Mechanism of the Oxidation of Alkanenitronate Anions[1]

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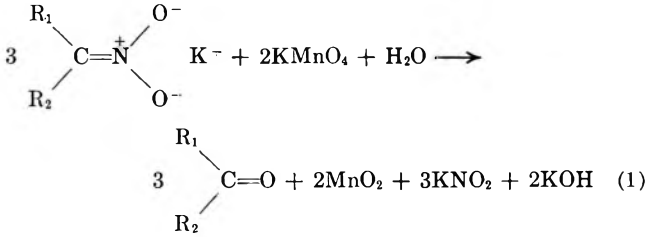
The kinetics of the permanganate ion oxidation of the alkanenitronate anions from nitromethane, nitroethane, 1- and 2-nitropropane, and 1- and 2-nitrobutane have been studied by spectrophotometric stopped-flow techniques. Between pH 11.6 and 13.7 the reaction follows the rate law $v = k$[alkanenitronate anion][$MnO_4^-$]. The reactions are characterized by low enthalpies of activation ($\Delta H^{\ddagger}$ = 6.00 to 8.84 kcal/mol) and large negative entropies of activation ($\Delta S^{\ddagger}$ = −16.0 to −23.0 eu). A positive salt effect is observed, and correlation of $\sigma^*$ substituent values and second-order rate constants gives a $\rho$ of 0.53 at 10°. The kinetic data suggest that the rate-determining step involves a stepwise addition of permanganate ion to the carbon of the carbon–nitrogen double bond in the alkanenitronate anion. Possible activated complexes for the permanganate ion oxidation of cyclohexanenitronate anion and phenylmethanenitronate anions are also discussed.

Although kinetic and mechanistic studies of the alkaline permanganate ion oxidation of the potassium salts of phenylmethanenitronate anions,[2,3] cyclopentanenitronate anion,[4] and cyclohexanenitronate anion[4] have been reported in recent years, not one of them has been concerned with the permanganate ion oxidation of simple alkanenitronate anions.[5] The permanganate ion oxidation of the potassium salts of aliphatic nitro compounds is an excellent preparative method[6,7] for the synthesis of aldehydes and ketones (eq 1).[6-10] These reactions are also of interest because of their extremely rapid rates of oxidation ($k_2$ larger than 100 l. mol$^{-1}$ sec$^{-1}$). It is the purpose of this work to point out some pertinent features of a reasonable mechanism proposed herein for the permanganate ion oxidation of alkanenitronate anions.



$$3\ R_1R_2C{=}\overset{+}{N}(O^-)_2 + K^- + 2KMnO_4 + H_2O \longrightarrow 3\ R_1R_2C{=}O + 2MnO_2 + 3KNO_2 + 2KOH \quad (1)$$

$R_1$ = H; $R_2$ = $(CH_3)_3C$ (69%)[7]
$R_1$ = H; $R_2$ = $(CH_3)_2CH$ (73%)[7]
$R_1$ = H; $R_2$ = $CH_3(CH_2)_2$ (97%)[7]
$R_1$ = $CH_3$; $R_2$ = $(CH_3)_3C$ (94%)[7]
$R_1$ = $R_2$ = $CH_3$ (96%)[7]

## Experimental Section

**Reagents.**—2-Nitropropane,[11,12] 1-nitropropane,[12] 1-nitrobutane,[13,14] 2-nitrobutane,[13,14] nitromethane,[12] and nitroethane[11] were distilled immediately before use. Distilled water, which was passed through an ion-exchange cartridge (Type R-2, Illinois Water Treatment Co., Rockford, Ill.), was used to prepare all solutions. Potassium chloride (Malinckrodt) was used to maintain 1.0 *M* ionic strength. Potassium permanganate stock solutions were prepared from Acculute standard volumetric concentrates. The pH, which was measured potentiometrically, was adjusted with Acculute standard volumetric potassium hydroxide ($CO_2$ free) concentrate.

(1) Previous paper in series: F. Freeman and M. A. H. Scott, *J. Org. Chem.*, **35**, 2989 (1970).
(2) F. Freeman and A. Yeramyan, *Tetrahedron Lett.*, 4783 (1968).
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(5) H. B. Hass and M. L. Bender [*J. Amer. Chem. Soc.*, **71**, 1767 (1949)] have suggested that alkali salts of nitroalkanes be named as metal alkanenitronates.
(6) H. Shechter and R. B. Kaplan, *ibid.*, **75**, 3980 (1953).
(7) H. Shechter and F. T. Williams, Jr., *J. Org. Chem.*, **27**, 3699 (1962).
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(9) S. Nametkin and O. Madaeff-Ssitscheff, *Chem. Ber.*, **52**, 370 (1926).
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(11) Commercial Solvents Corp.
(12) Aldrich Chemical Co., Inc.
(13) Sample from Professor H. Feuer, Department of Chemistry, Purdue University, Lafayette, Ind.
(14) Sample from Dr. A. T. Nielsen, U. S. Naval Ordnance Test Station, China Lake, Calif.

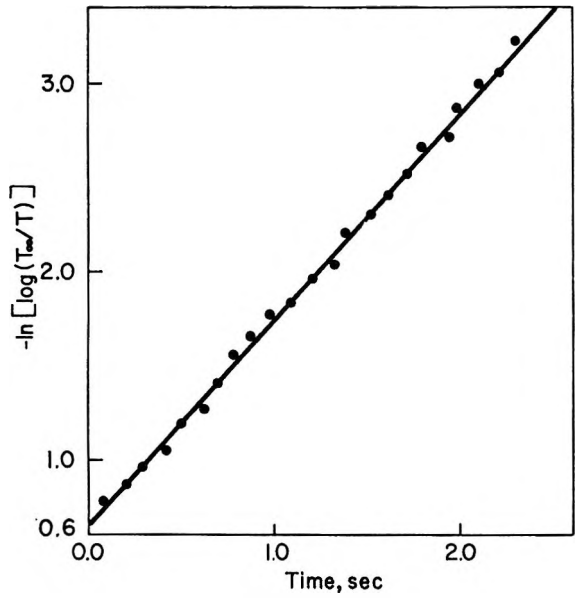



Figure 1.—A typical pseudo-first-order plot. The conditions are [2-propanenitronate anion] = $8 \times 10^{-3}$ $M$, [$OH^-$] = 0.20 $M$, [$MnO_4^-$] = $4.0 \times 10^{-4}$ $M$, $\mu$ = 1.0, $\lambda$ = 510 m$\mu$, $T$ = 0.0°.

**Rate Procedures.**—The rates were determined by observing the disappearance of permanganate ion at 510 and 522 m$\mu$, and the rate constant determinations were made using a specially designed stopped-flow reactor.[3,4] Pseudo-first-order rate constants ($k_\psi$) were calculated from the slopes of plots of $-\ln [\log (T_\infty/T)]$ against time (Figure 1) on a CDC 3300 computer.[15,16] The rate constants given in the tables are the average of two or more determinations.

Temperature in the stopped-flow cell was maintained (±0.02°) with a Forma Model 2095-2 refrigerated and heated bath and circulator. Dry air was blown around the cell to preclude condensation at low temperatures.

## Results

**Kinetic Data.**—The kinetic data for the permanganate ion oxidation of 2-propanenitronate anion (1) are summarized in Table I. The first-order dependence

TABLE I
PERMANGANATE ION OXIDATION OF 2-PROPANENITRONATE ANION AT pH 13.0[a]

| [2-Propanenitronate anion], $10^3$ $M$ | [$MnO_4^-$] × $10^4$ $M$ | $k_\psi$,[b] sec$^{-1}$ | $k_2$[c] × $10^{-2}$ $M^{-1}$ sec$^{-1}$ |
|---|---|---|---|
| 2.0 | 4.0 | 0.297 | 1.48 |
| 4.0 | 4.0 | 0.606 | 1.51 |
| 6.0 | 4.0 | 0.867 | 1.45 |
| 8.0 | 4.0 | 1.18 | 1.48 |
| 12.0[d] | 4.0 | 1.71 | 1.42 |
| 16.0[e] | 4.0 | 2.14 | 1.33 |
| 8.0 | 2.0 | 0.991 | 1.24 |
| 8.0 | 6.0 | 1.10 | 1.37 |
| 8.0 | 8.0 | 1.14 | 1.42 |
| 8.0[f] | 2.0 | 0.955 | 1.24 |
| 8.0[f] | 4.0 | 1.12 | 1.40 |
| 8.0[f] | 6.0 | 0.993 | 1.24 |
| 8.0[f] | 8.0 | 1.05 | 1.33 |

[a] [$OH^-$] = 0.1 $M$, $\mu$ = 1.0, $\lambda$ = 510 m$\mu$, $T$ = 0.0°. [b] Pseudo-first-order rate constant. [c] Second-order rate constant = $k_\psi$/[2-propanenitronate anion]. [d] One determination. [e] Rate almost too fast for the capability of the stopped-flow system. [f] $\lambda$ = 522 m$\mu$.

(15) K. B. Wiberg and R. D. Geer, *J. Amer. Chem. Soc.*, **87**, 5202 (1965); **88**, 5827 (1966).

(16) K. B. Wiberg, "Computer Programming for Chemists," W. A. Benjamin, New York, N. Y., 1965, p 168.

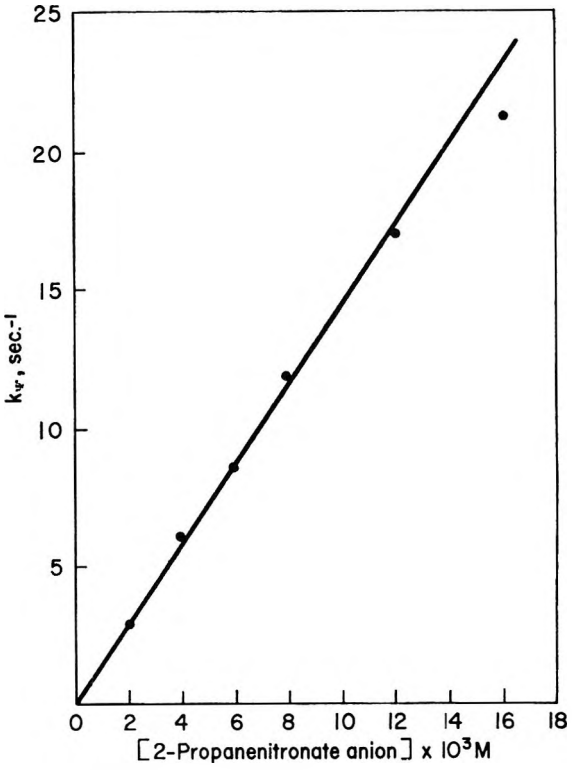



Figure 2.—Effect of potassium 2-propanenitronate on the pseudo-first-order rate constants for the permanganate ion oxidation of potassium 2-propanenitronate at 0.0°.

on the concentration of 1 is shown in the plot (Figure 2) of the pseudo-first-order rate constant ($k_\psi$) *vs.* an eightfold range of concentration of 1 which gives a straight line that goes through the origin. The constancy of the pseudo-first-order rate constant ($k_\psi$) at constant hydroxide ion and 1 concentrations and changing permanganate ion concentration indicates a first-order dependence on permanganate ion. Figure 1, which illustrates a typical linear pseudo-first-order plot, further confirms the first-order dependence on permanganate ion concentration. The effect of hydroxide ion concentration on the rate of oxidation is summarized in Table II.

TABLE II
KINETIC DEPENDENCE ON HYDROXIDE ION CONCENTRATION[a]

| [$OH^-$], $M$ | pH | $k_\psi$,[b] sec$^{-1}$ |
|---|---|---|
| $1.4 \times 10^{-5}$ | 9.14[c] | 0.64 |
| $1.3 \times 10^{-3}$ | 11.1[c] | 0.86 |
| $3.9 \times 10^{-3}$ | 11.6[c] | 0.93 |
| 0.02 | 12.3 | 0.95 |
| 0.085 | 12.9 | 0.90 |
| 0.10 | 13.0 | 1.14 |
| 0.17 | 13.2 | 1.00 |
| 0.32 | 13.5 | 1.00 |
| 0.50 | 13.7 | 1.14 |

[a] [2-Propanenitronate anion] = $8.0 \times 10^{-3}$ $M$, [$MnO_4^-$] = $4.0 \times 10^{-4}$ $M$, $\mu$ = 1.0, $\lambda$ = 510 m$\mu$, $T$ = 0.0°. [b] Pseudo-first-order rate constant. [c] Unbuffered solution.

It is seen at constant 1 concentration and constant permanganate ion concentration that the pseudo-first-order rate constant ($k_\psi$) does not change appreciably on a 125-fold range of hydroxyl ion concentration; this observation confirms a zero-order dependence

on hydroxide ion concentration. Consequently, the data are consistent with the following rate law.

$$v = k[\text{2-propanenitronate anion}][MnO_4^-] \quad (2)$$

**Effect of Added Salts on Rates.**—Table III shows that there is a positive salt effect in the permanganate ion oxidation of **1**.

TABLE III

EFFECT OF IONIC STRENGTH ON THE RATE OF OXIDATION OF 2-PROPANENITRONATE ANION AT pH 13.0[a]

| $\mu$ | $k_\psi$,[b] $sec^{-1}$ | $k_2$,[c] $M^{-1}$ $sec^{-1}$ |
|---|---|---|
| 0.1 | 0.46 | 57.3 |
| 0.25 | 0.63 | 79.4 |
| 0.50 | 0.81 | 101.6 |
| 0.75 | 0.95 | 118.6 |
| 1.0 | 1.09 | 136.0 |

[a] [2-Propanenitronate anion] = $8.0 \times 10^{-3}$ $M$, $[OH^-] = 0.1$ $M$, $[MnO_4^-] = 4.0 \times 10^{-4}$ $M$, $\lambda = 510$ m$\mu$, $T = 0.0°$. [b] Pseudo-first-order rate constant. [c] Second-order rate constant = $k_\psi/$[2-propanenitronate anion].

**Thermodynamic Parameters.**—The activation parameters for the permanganate ion oxidation of eight alkanenitronate anions are summarized in Table IV.

TABLE IV

ACTIVATION PARAMETERS FOR THE PERMANGANATE ION OXIDATION OF SOME ALKANENITRONATE ANIONS AT pH 13.0[a]

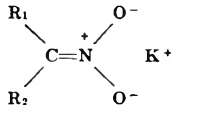
| Anion | $\Delta F^{\ddagger}$, kcal/mol | $\Delta H^{\ddagger}$, kcal/mol | $-\Delta S^{\ddagger}$, eu |
|---|---|---|---|
| Methanenitronate[b] | 13.1 | 8.51 | 16.6 |
| Ethanenitronate[b] | 13.0 | 8.40 | 16.4 |
| 1-Propanenitronate[b] | 12.9 | 6.00 | 24.7 |
| 2-Propanenitronate[b] | 13.3 | 8.84 | 16.0 |
| 1-Butanenitronate[b] | 13.0 | 7.72 | 18.9 |
| 2-Butanenitronate[b] | 13.3 | 6.86 | 23.0 |
| Cyclohexanenitronate[c] | 12.9 | 7.47 | 19.6 |
| Phenylmethanenitronate[d,e] | 13.1 | 6.58 | 23.5 |

[a] Calculated on a CDC 3300 computer. [b] This work. [c] Reference 4. [d] References 2 and 3. [e] pH 13.6.

**Linear Free-Energy Relationships.**—Table V summarizes the rate data for the permanganate ion oxidation of six alkanenitronate anions. Correlation of $\sigma^*$ substituent constants and second-order rate constants ($k_2$) (excluding the value for methanenitronate anion) gives a $\rho$ of 0.53, a correlation coefficient ($r$) of 0.963, and a standard deviation ($s$) of 0.045.

TABLE V

EFFECT OF SUBSTITUENTS ON THE RATE OF PERMANGANATE ION OXIDATION OF SOME ALKANENITRONATE ANIONS AT pH 13.3[a]



| | $k_\psi$,[b] $sec^{-1}$ | $k_2$,[c] $M^{-1}$ $sec^{-1}$ | $\Sigma\sigma^*$ [d] | Log $k_2$ |
|---|---|---|---|---|
| $R_1 = R_2 = H$ | 1.47 | 368 | 0.980 | 2.57 |
| $R_1 = H; R_2 = CH_3$ | 1.98 | 496 | 0.490 | 2.70 |
| $R_1 = H; R_2 = CH_2CH_3$ | 2.19 | 548 | 0.390 | 2.74 |
| $R_1 = H; R_2 = CH_2CH_2CH_3$ | 1.96 | 490 | 0.375 | 2.69 |
| $R_1 = R_2 = CH_3$ | 1.12 | 280 | 0.000 | 2.45 |
| $R_1 = CH_3; R_2 = CH_2CH_3$ | 1.11 | 277 | −0.100 | 2.44 |

[a] $[MnO_4^-] = 4.0 \times 10^{-4}$ $M$, $[OH^-] = 0.20$ $M$, $\mu = 1.0$, $\lambda = 510$ m$\mu$, $T = 10.0°$. [b] Pseudo-first-order rate constant. [c] Second-order rate constant = $k_\psi/$[alkanenitronate anion]. [d] R. W. Taft, Jr., in "Steric Effects in Organic Chemistry," M. S. Newman, Ed., Wiley, New York, N. Y., 1956, p 556.

TABLE VI

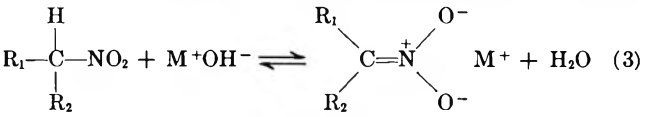
ACIDITY CONSTANTS OF SOME NITROALKANES

| Nitroalkane | $K_a$ | $pK_a$ |
|---|---|---|
| Nitromethane[a,b] | $6.1 \times 10^{-11}$ | 10.2 |
| Nitroethane[a,b] | $2.5 \times 10^{-9}$ | 8.6 |
| 1-Nitropropane[a,b] | $1.1 \times 10^{-9}$ | 8.98 |
| 2-Nitropropane[b,c] | $2.1 \times 10^{-8}$ | 7.7 |
| 1-Nitrobutane[c] | $2.5 \times 10^{-9}$ | 8.6 |
| 2-Nitrobutane[c] | $1.8 \times 10^{-8}$ | 7.8 |
| Phenylnitromethane[c] | $1.6 \times 10^{-7}$ | 6.8 |

[a] R. G. Pearson and R. L. Dillon, *J. Amer. Chem. Soc.*, **72**, 3574 (1950). [b] G. W. Wheland and J. Farr, *ibid.*, **65**, 1433 (1943). [c] W. Kemula and W. Turnowska-Rubaszewska, *Rocz. Chem.*, **37**, 1597 (1963).

## Discussion

Primary and secondary nitroalkanes yield alkali metal salts in sodium or potassium hydroxide solution (Table VI). Self-consistent molecular orbital calcula-



$R_1 = H$; $R_2$ = alkyl
$R_1 = R_2$ = alkyl
$M^+$ = potassium or sodium

tions[17,18] and ultraviolet,[18] infrared,[19] and Raman[19] spectra suggest that in alkanenitronate anions there is a delocalization of the six $\pi$ electrons which results in essentially a C=N and two equivalent N—O bonds with low double bond character.

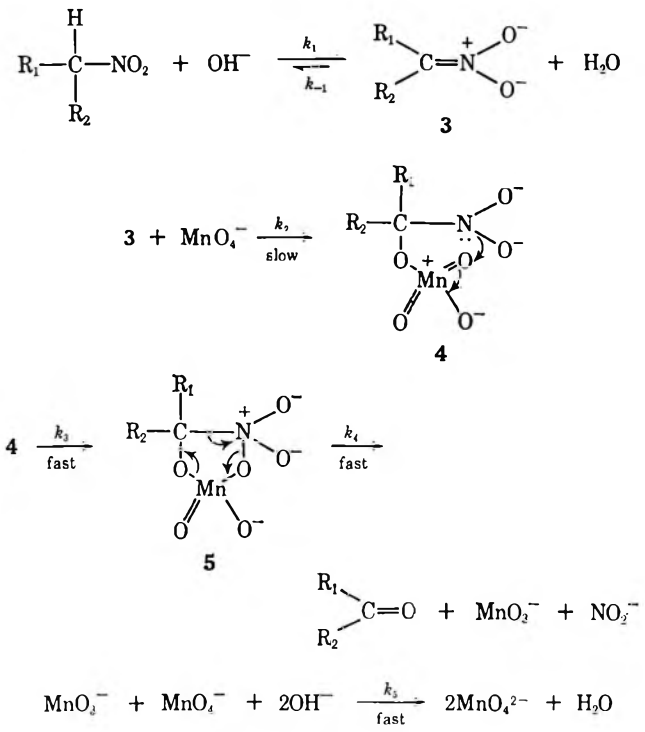
It is seen from the kinetic data that the permanganate ion oxidation of alkanenitronate anions is zero order in hydroxide ion concentration, first order in alkanenitronate anion concentration, and first order in permanganate ion concentration. The zero-order dependence on hydroxyl ion concentration is consistent with a mechanism involving the alkanenitronate anion and permanganate ion in the rate-controlling step (Scheme I). Although Scheme I depicts the formation of **4** as the slow step, the kinetic data do not exclude the formation of **5**, *via* a concerted cis cycloaddition, as the rate-limiting step (eq 4).

$$3 + MnO_4^- \xrightarrow{\text{slow}} 5 \quad (4)$$

The data on the effect of alkyl substituents (Table V) show that an increase in alkyl substitution on the carbon of the C=N causes only a slight change in the rate of oxidation. The observed small $\rho$ value (0.53) is similar to the small values obtained in the permanganate ion oxidation of phenylmethanenitronate anions (−0.67),[3] in the permanganate ion oxidation of salts of unsaturated carboxylate anions (≅0),[15] and in cis-1,3-dipolar cycloaddition reactions (+0.8 to +1.2).[20] Consequently, the activated complex in the permanganate ion oxidation of alkanenitronate

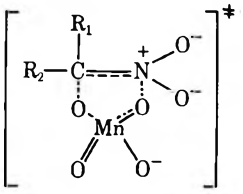
(17) N. Jonathan, *J. Mol. Spectrosc.*, **7**, 105 (1961).
(18) F. T. Williams, Jr., P. W. K. Flanagan, W. G. Taylor, and H. Shechter, *J. Org. Chem.*, **30**, 2674 (1965).
(19) M. J. Brookes and N. Jonathan, *Spectrochim. Acta, Part A*, **25**, 187 (1969).
(20) R. Huisgen, R. Grashey, and J. Sauer in "The Chemistry of Alkenes," S. Patai, Ed., Interscience, London, 1964, p 844.

SCHEME I



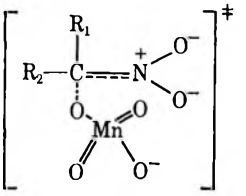
anions probably has a close resemblance to either structure **4** or **5**.

1,3-Dipolar cycloaddition reactions require strict orientation of the components in the activated complex. Consequently these reactions are characterized by small values for the enthalpy of activation and large negative values for the entropies of activation ($\Delta S^{\pm}$ = −25 to −45 eu). Permanganate ion presumably reacts with unsaturated systems *via* a concerted cis-cycloaddition mechanism.[3,15,21,22] These oxidations have $\Delta H^{\pm}$ values of 4.8 to 7.5 kcal/mol and $\Delta S^{\pm}$ values of −24 to −36 eu.[15] It is seen that the observed $\Delta S^{\pm}$ values (−16.0 to −23.0 eu) for the permanganate ion oxidation of alkanenitronate anions are not very similar to cis-1,3-dipolar cycloadditions[23,24] and permanganate ion cycloaddition reactions. Therefore, the activated complex for the permanganate ion oxidation of alkanenitronate anions probably cannot have a very close resemblance to **6**.[25]



**6**

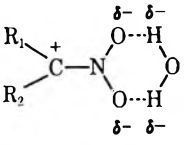
There is a remarkable similarity among the salt effects, $\Delta F^{\pm}$ values, $\Delta H^{\pm}$ values, and $\Delta S^{\pm}$ for the permanganate ion oxidation of alkanenitronate anions, cyclopentanenitronate anion,[4] cyclohexanenitronate anion,[4] phenylmethanenitronate anions,[2,3] and other anions.[2,26] Consequently the kinetic data for the permanganate ion oxidation of alkanenitronate anion, and probably for cycloalkylnitronate anions and phenylnitromethane nitronate anions, are consistent with a rate-determining attack of permanganate ion at the carbon of the C=N with a synchronous movement of a pair of electrons to the nitrogen atom to give the possible activated complex (**7**). Carbon–oxygen



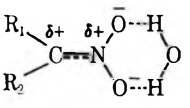
**7**

bond formation logically leads to the intermediate **4** which then rearranges to **5** according to Scheme I.

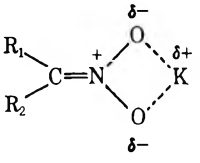
The argument against activated complex **6**, which is partly based on $\Delta S^{\pm}$ values, is an oversimplification[25] since the charge type of the reactants for the alkanenitronate anion oxidation is not the same as the model reactants. Also, values of $\Delta S^{\pm}$ are known to be determined by solvation effects in many reactions,[4] and a vast majority of permanganate ion oxidations generally have large negative entropies of activation.[1-4,15,26] Consequently, one must also consider structures such as **8**–**11**, which influence the charge density at the



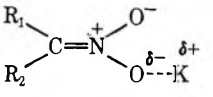
**8**



**9**



**10**



**11**

nitronate carbon and the carbon–nitrogen double bond character, in a discussion of the influence of electronic, steric, and solvation factors on the mechanism.[4,27]

**Registry No.**—Potassium methanenitronate, 28273-52-1; potassium ethanenitronate, 26241-08-7; potassium 1-propanenitronate, 28273-54-3; potassium 2-propanenitronate, 28273-55-4; potassium 1-butanenitronate, 28273-56-5; potassium 2-butanenitronate, 28273-57-6.

(21) K. B. Wiberg and K. A. Saegebarth, *J. Amer. Chem. Soc.*, **79**, 2822 (1957).

(22) V. Boeseken, *Recl. Trav. Chim. Pays-Bas*, **40**, 553 (1921).

(23) Reference 20, p 834.

(24) R. Huisgen, *Angew. Chem., Int. Ed. Engl.*, **2**, 633 (1963).

(25) Although bond formation begins simultaneously, cycloaddition does not require that the two new bonds be formed at identical rates. Bond formation at different rates could lead to charge separation in the transition state region.

(26) F. Freeman, J. B. Brant, N. B. Hester, A. A. Kamego, M. L. Kasner, T. G. McLaughlin, and E. W. Paull, *J. Org. Chem.*, **35**, 982 (1970); S. M. Taylor and J. Halpern, *J. Amer. Chem. Soc.*, **81**, 2933 (1959).

(27) M. Fukujama, P. W. K. Flanagan, F. T. Williams, Jr., L. Frainier, S. A. Miller, and H. Shechter, *ibid.*, **92**, 4689 (1970).

# Oxidations with Silver Carbonate/Celite. V.[1] Oxidations of Phenols and Related Compounds[2]

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*Received October 29, 1970*

Silver carbonate on Celite in neutral media effects selective oxidative coupling of hindered phenols giving the corresponding dipheno- and stilbenequinones in high yields. Bis phenols obtained by reduction of these quinones were also oxidized by silver carbonate. When coupling was not possible due to steric factors, the stable phenoxy radicals were isolated quantitatively. Hydroquinones and pyrocatechols gave the corresponding *p*- and *o*-quinones in excellent yields. Oxidation of *p*-hydroxydiphenylamine and *o*-aminophenol gave the corresponding monoanil and phenoxazone, respectively.

Phenol coupling is an important synthetic tool and an essential step in the biosynthesis of many alkaloids and other natural products.[3] The reagents most extensively employed to effect this coupling (ferricyanide, ferric chloride, metal oxides, *e.g.*, $MnO_2$, $PbO_2$, HgO, $Ag_2O$, etc.) often suffer from poor selectivity and usually give a mixture of quinones, dimers, and polymers, the product distribution varying widely with the nature of the reagent. Moreover, the alkaline or acidic media required for these oxidations limit their applicability when sensitive functional groups are present.

The recently reported oxidizing agents, vanadium tetrachloride[4] and vanadium oxychloride, are useful in the preparation of some diphenols and diamino phenols. The oxychloride has been used advantageously in the intramolecular oxidative coupling[5] of 1,3-bis(hydroxyphenyl)propane; however when applied to hindered phenols either they did not react or gave comparatively poor yields.

Manganic tris(acetylacetonate) (MTA),[6] another new reagent which acts in homogeneous solution, has been found to bring about coupling of phenols to diphenols in fair yields, and the reaction can be controlled to give diphenols rather than quinones, but neither the experimental details nor its scope has yet been published.

Isoamyl nitrite[7] oxidizes 2,6-disubstituted phenols to the diphenoquinones in 50–60% yield, but the yields are lowered when the substituents are bulky or deactivating. Furthermore, there is the complication of the possible oximination by the reagent.

An interesting modification of $PbO_2$ oxidation carried out in polar solvents[8] gives diphenoquinones or *p*-benzoquinones almost exclusively.

$MnO_2$–silica gel[9] has been employed for the biogenetic type oxidative coupling of reticuline to salutaridine in 4% yield. Despite the somewhat higher yield obtained with this reagent, it still falls short of being a useful synthetic tool.

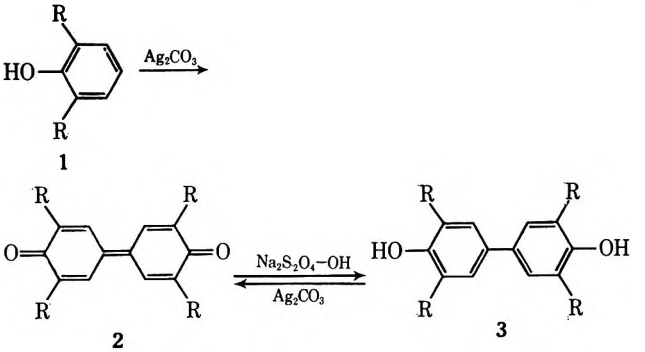
Some cobalt complexes of the salcomine type[10] have been reported to catalyze the autoxidation of phenols.

In spite of the obvious advantages, the anodic oxidation of phenols[11] has not been studied extensively since the early work by Fichter. None of the few recent examples[12,13] effects carbon–carbon coupling as the main feature.

We report here on the oxidation of phenols by silver carbonate/Celite a highly specific and selective oxidizing agent, the usefulness of which in the oxidation of a variety of aliphatic and alicyclic hydroxy compounds has already been demonstrated.[1] Oxidation of phenols by this reagent is superior to the existing reagents in the ease of operation and the homogenity and facile recovery of the products. The reaction is conducted in an inert organic solvent under mild conditions. Whenever coupling is observed, it is exclusively carbon–carbon.

## Results

**Selective Oxidative Coupling.**—Oxidation of 2,6-dimethyl-, 2,6-diisopropyl-, and 2,6-di-*tert*-butylphenol give the corresponding diphenoquinones **2a–c** resulting




**a**, R = $CH_3$
**b**, R = $CH(CH_3)_2$
**c**, R = $C(CH_3)_3$

from para–para C–C coupling and subsequent oxidation of the dimers **3a–c**. The redox potential of the reagent ($Ag^+ + e^- \rightarrow Ag$ ~0.80 V) is high enough to oxidize the dimers to extended quinones. The di-

(1) (a) Part I: M. Fétizon and M. Golfier, *C. R. H. Acad. Sci.*, **267**, 900 (1968). (b) Part II: V. Balogh, M. Fétizon, and M. Golfier, *Angew. Chem.*, **81**, 423 (1969); *ibid.*, *Int. Ed. Engl.*, **8**, 444 (1969). (c) Part III: M. Fétizon, M. Golfier, and J-M. Louis, *Chem. Commun.*, 1102 (1969). (d) Part IV: M. Fétizon, M. Golfier, and J-M. Louis, *ibid.*, 1118 (1969).

(2) For a preliminary communication on this subject, see ref 1b.

(3) W. I. Taylor and A. R. Battersby, "Oxidative Coupling of Phenols," Marcel Dekker, New York, N. Y., 1967, and papers cited therein.

(4) W. L. Carrick, G. L. Karapinka, and G. T. Kwiatkowski, *J. Org. Chem.*, **34**, 2388 (1969).

(5) M. A. Schwartz, R. A. Holton, and S. W. Scott, *J. Amer. Chem. Soc.*, **91**, 2800 (1969).

(6) M. J. S. Dewar and T. Nakaya, *ibid.*, **90**, 7134 (1968).

(7) R. A. Jerussi, *J. Org. Chem.*, **35**, 2105 (1970).

(8) C. R. H. I. de Jonge, H. M. van Dort, and L. Vollbracht, *Tetrahedron Lett.*, **22**, 1881 (1970).

(9) B. Frank, Z. Dunkelmann, and H. J. Lubs, *Angew. Chem., Int. Ed. Engl.*, **6**, 1075 (1967).

(10) L. H Vogt, Jr., J. G. Wirth, and H. L. Finkbeiner, *J. Org. Chem.*, **34**, 273 (1969).

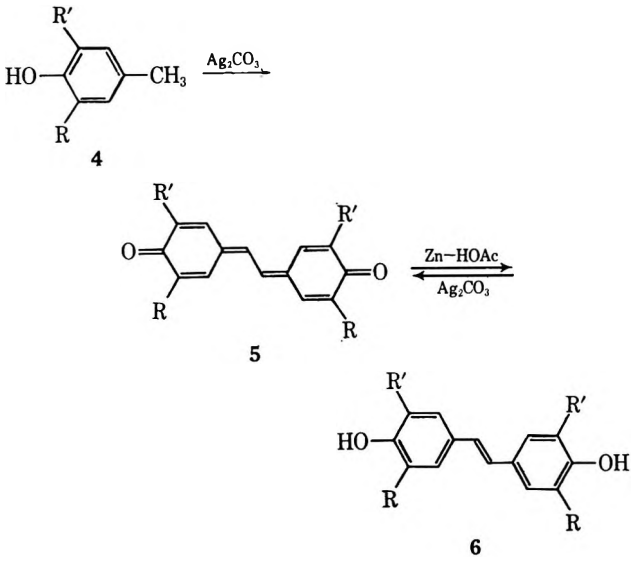
(11) A. I. Scott, *Quart. Rev., Chem. Soc.*, **19**, 1 (1965).

(12) F. W. Steuber and K. Dimroth, *Chem. Ber.*, **99**, 258 (1966).

(13) A. B. Suttie, *Tetrahedron Lett.*, **21**, 953 (1969), and papers cited therein.

phenoquinones **2a–c** were reduced by sodium hydrosulfite in weakly alkaline solutions. These diphenols could be readily reoxidized to the parent quinones by silver carbonate.

Oxidation of hindered phenols bearing a methyl group at the para position (**4a–c**) gives the corresponding stilbenequinones **5a–c** in high yields; dimerization probably occurs *via* the intermediate benzyl radicals. On reduction with zinc and acetic acid these quinones give the corresponding 4,4′-dihydroxystilbenes **6a–c** which are reconverted to the stilbenequinones by oxidation with silver carbonate (Tables I and II).




**a**, R = R′ = $CH_3$
**b**, R = R′ = $C(CH_3)_3$
**c**, R = $CH_3$; R′ = $C(CH_3)_3$

TABLE I

| Phenol | Mol of $Ag_2CO_3$ | Reaction time, hr | Product, % yield | Mp, °C Found | Mp, °C Lit. |
|---|---|---|---|---|---|
| 1a | 4.4 | 0.5 | 2a, 98 | 217–218 | 215[a] |
| 1b | 5.0 | 1.5 | 2b, 100 | 200–201 | 199–203[b] |
| 1c | 4.4 | 2.0 | 2c, 99 | 248 | 245–247[c] |
| 3a | 4.2 | 0.5 | 2a, 98 | 218–219 | |
| 3b | 4.3 | 1.5 | 2b, 97 | 198–200 | |
| 3c | 4.1 | 2.0 | 2c, 95 | 247 | |
| 4a | 4.4 | 2.0 | 5a, 93 | 227–228 | 220–230[d] |
| 4b | 4.2 | 1.0 | 5b, 90 | 313–314 | 316[e] |
| 4c | 4.5 | 2.0 | 5c, 97 | 225 | 225[f] |
| 6a | 32.0 | 0.5 | 5a, 83 | 228–229 | |
| 6b | 32.0 | 1.0 | 5b, 90 | 312–314 | |
| 6c | 37.0 | 2.0 | 5c, 83 | 249–250 | |
| 7 | 6.1 | 2.0 | 8, 100 | ~80 dec | ~80 dec[g] |
| 10 | 14.3 | 3.0 | 11, 98 | 154–155 | 157.5[h] |

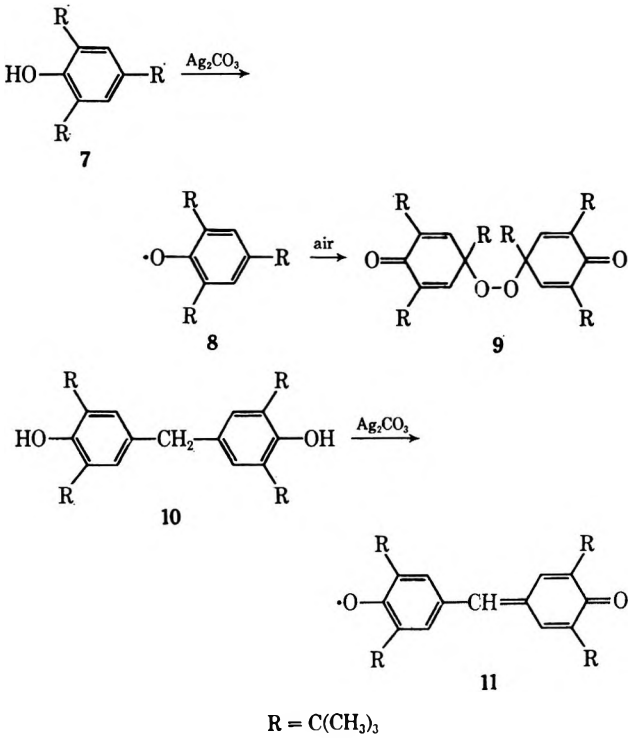
[a] R. G. R. Bacon and A. R. Izzat, *J. Chem. Soc. C*, 791 (1966). [b] W. B. Wheatley and C. T. Holdrege, *J. Org. Chem.*, **23**, 568 (1958). [c] H. Hart and F. A. Cassis, Jr., *J. Amer. Chem. Soc.*, **73**, 3179 (1951). [d] K. Fries and E. Brandes, *Justus Liebigs Ann. Chem.*, **542**, 48 (1939). [e] R. H. Bauer and G. M. Coppinger, *Tetrahedron*, **19**, 1201 (1963). [f] J. R. Dunn and W. A. Waters, *J. Chem. Soc.*, 2993 (1953). [g] C. D. Cook, D. A. Kuhn, and P. Fianu, *J. Amer. Chem. Soc.*, **78**, 2002 (1956). [h] M. S. Kharasch and P. S. Joshi, *J. Org. Chem.*, **22**, 1435 (1957).

**Stable Free Phenoxy Radicals.**—The formation of a stable free phenoxy radical by one-electron oxidation of a phenol becomes possible when all C–C coupling positions are protected by bulky groups. Thus oxidation of 2,4,6-tri-*tert*-butylphenol and 4,4′-dihydroxy-3,5,3′,5′-tetra-*tert*-butyldiphenylmethane in benzene solutions under argon atmosphere gives the free radicals **8** and **11** quantitatively. In the presence of air **8** gives the peroxide **9**. In contrast, **11** in benzene solution is quite stable toward molecular oxygen; however in methanol it decomposes to 2,6-di-*tert*-butyl-*p*-hydroxybenzaldehyde, 3,5,3′,5′-tetra-*tert*-butyldiphenoquinone, and a trace of an unidentified red oil.

TABLE II

| Quinone | Product, % yield | Mp, °C Found | Mp, °C Lit. |
|---|---|---|---|
| 2a | 3a, 85 | 228–229 | 226[a] |
| 2b | 3b, 89 | 118–119 | 115–117[b] |
| 2c | 3c, 95 | 184–185 | 185[c] |
| 5a | 6a, 81 | 237–240 | 239–240[d] |
| 5b | 6b, 80 | 244–246 | 240–241[e] |
| 5c | 6c, 89 | 167–168 | 171[f] |

[a] See footnote *a* in Table I. [b] *Chem. Abstr.*, **63**, 5561*f* (1965); Neth. Appl. 6,410,238 (Mar 4, 1965). [c] M. S. Kharasch and B. S. Joshi, *J. Org. Chem.*, **22**, 1439 (1957). [d] See footnote *d* in Table I. [e] C. D. Cook, *J. Org. Chem.*, **18**, 261 (1953). [f] *Chem. Abstr.*, **49**, 3263*a* (1955); British Patent 699,180 (Nov 4, 1953).




R = $C(CH_3)_3$

***o*-Quinones.**—Oxidation of catechols **12a–d** by silver carbonate affords highly pure *o*-quinones **13a–d** in essentially quantitative yields (Table III). Oxidations of this type using other reagents[14] in the few cases where yields were specified reportedly ranged from 12 to 81%.

***p*-Quinones.**—A large number of known oxidizing agents are able to transform hydroquinones to quinones in high yields.[15] Silver carbonate/Celite also converts hydroquinones to quinones quantitatively and is a

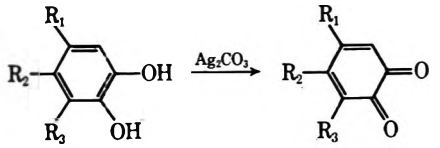
(14) See, for some of the examples, Table III, footnotes *a–d*.
(15) See Table III, footnote *a*.

TABLE III

| Phenol | Mol of $Ag_2CO_3$ | Reaction time, hr | Product, % yield | Mp, °C Found | Mp, °C Lit. |
|---|---|---|---|---|---|
| **12a** | 5.0 | 2.00 | **13a**, 98 | 60–70 | 60–70[a] |
| **12b** | 5.0 | 3.00 | **13b**, 100 | 76–80 | 75–84[b] |
| **12c** | 5.0 | 3.00 | **13c**, 98 | 66–67 | 68[c] |
| **12d** | 5.0 | 3.00 | **13d**, 99 | 114–115 | 113–114[d] |
| **14a** | 2.0 | 1.00 | **15a**, 97 | 116 | 116[e] |
| **14b** | 2.0 | 1.00 | **15b**, 98 | 65.5–66.5 | 68–69[f] |
| **14c** | 2.0 | 1.00 | **15c**, 100 | 139–141 | 145[g] |
| **14d** | 2.5 | 1.00 | **15d**, 98 | 44–45 | 46–47[h] |
| **14e** | 5.0 | 2.00 | **15e**, 98 | 152 | 152–153[i] |
| **14f** | 5.0 | 2.00 | **15f**, 99 | 290 | 290[a] |
| **16** | 2.5 | 1.25 | **17**, 100 | 123.5–124.5 | 124–125[j] |
| **18** | 2.0 | 0.16 | **19**, 97 | 102–103 | 100–101[k] |
| **20** | 4.0 | 0.25 | **21**, 33 | 255–256 | 249[l] |

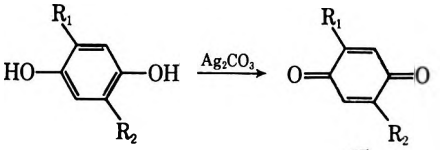
[a] Z. E. Jolles in "Chemistry of Carbon Compounds," Vol. IIIB, Elsevier, New York, N. Y., 1956, p 704, *et seq.* [b] J. Cason, *Org. React.*, **4**, 314 (1948). [c] *Chem. Abstr.*, **52**, 432*i* (1958); U. S. Patent 2,782,210 (Feb 10, 1957). [d] *Chem. Abstr.*, **57**, 8504*g* (1962); German Patent 1,126,852 (April 5, 1962). [e] F. Kehrman and E. Hoehn, *Helv. Chim. Acta*, **8**, 221 (1925). [f] P. T. T. Sah, *Recl. Trav. Chim. Pays-Bas*, **59**, 454 (1940). [g] L. I. Smith and W. B. Irwin, *J. Amer. Chem. Soc.*, **63**, 1036 (1941). [h] L. F. Fieser, *J. Amer. Chem. Soc.*, **70**, 3165 (1948). [i] S. G. Cohen, *ibid.*, **69**, 1057 (1947). [j] L. F. Fieser in "Organic Syntheses," Collect. Vol. I, 2nd ed, Wiley, New York, N. Y., 1941, p 383. [k] R. Willstätter and C. W. Moore, *Chem. Ber.*, **40**, 2665 (1907). [l] A. M. Osman and I. Bassioni, *J. Amer. Chem. Soc.*, **82**, 1607 (1960).

particularly useful reagent to prepare acid- or base-sensitive quinones. Thus to prepare **15c** from the hydroquinone **14c**, oxidation by 2 equiv of silver carbonate in methylene chloride is by far the best available method. Oxidation of 1,4-dihydroxynaphthalene (**16**) gives 1,4-naphthaquinone (**17**). (*Cf.* Table III.)



**12a**, $R_1 = R_2 = R_3 = H$
**b**, $R_1 = R_3 = H; R_2 = CH_3$
**c**, $R_1 = R_3 = H; R_2 = C(CH_3)_3$
**d**, $R_2 = H; R_1 = R_3 = C(CH_3)_3$

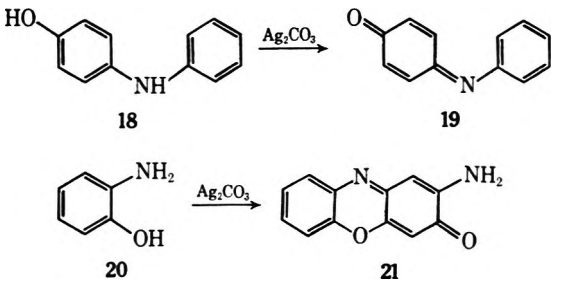
**13**



**14a**, $R_1 = R_2 = H$
**b**, $R_1 = H; R_2 = CH_3$
**c**, $R_1 = H; R_2 = OCH_3$
**d**, $R_1 = CH_3; R_2 = C(CH_3)_3$
**e**, $R_1 = R_2 = C(CH_3)_3$
**f**, tetrachlorohydroquinone

**15**

**Oxidation of Aminophenols.**—Silver carbonate oxidation of *p*-hydroxydiphenylamine (**18**) gives the quinone monoanil **19** in quantitative yield. *o*-Aminophenol gives the dimeric phenoxazone **21** (Table III), a product which has been obtained using other oxidants.[11]



**18** **19**

**20** **21**

## Experimental Section

**A. Preparation of the Reagent.**—The Celite support is purified by washing it successively with methanol containing 10% concentrated HCl and then with distilled water until neutral; it is finally dried at 120°.

Purified Celite (30 g) is added to a mechanically stirred solution of 34 g (200 mmol) of silver nitrate in 200 ml of distilled water. A solution of 30 g (105 mmol) of $Na_2CO_3 \cdot 10H_2O$ (or 21 g, 210 mmol of $KHCO_3$) in 300 ml of distilled water is then added slowly to the resulting homogeneous suspension. When the addition is complete, stirring is continued for a further 10 min. The yellow-green precipitate which is formed is then filtered off and finally dried in a rotary evaporator over a period of several hours. The silver carbonate/Celite reagent contains about 1 mmol of $Ag_2CO_3$, 0.57 g.

**B. Oxidations. General Procedure.**—Before use, the reagent is freed from the residual water azeotropically by distillation with benzene. The compound to be oxidized is then added and refluxed in benzene (*ca.* 200 ml for 0.5–2.0 g of compound). At the end of the reaction, determined by tlc monitoring, the solid phase is filtered off and the solvent evaporated. The product is usually highly pure and recrystallization is unnecessary. Reaction times and molar ratios are given in Tables I and III.

**Free radicals 8** and **11** forming reactions are conducted under argon atmosphere.

**Pyrocatechol** and its derivatives **12b–d** are oxidized at 0° and room temperature, respectively, under constant stirring.

**Hydroquinones 14a–c** and *o*-aminophenol (**20**) are oxidized in boiling methylene chloride. The oxidation of **18** is carried out in the same solvent but at room temperature.

**C. Reductions. General Procedures. 3,3′,5,5′-Tetramethyl-4,4′-dihydroxybiphenyl (3a).**—To a suspension of 0.65 g of the diphenoquinone **2a** in 35 ml of ether a solution of 6.5 g of sodium hydrosulfite in 70 ml of aqueous NaOH (1 *N*) is added. After shaking the mixture for about 30 min the colorless aqueous layer is acidified by concentrated HCl. Filtration gives 0.57 g of a white precipitate which is dried *in vacuo*: mp 228–229°; nmr ($D_3CCOCD_3$) δ 7.17 (s, 4), 3.12 (s, 2), 2.30 (s, 12).

*Anal.* Calcd for $C_{16}H_{18}O_2$: C, 79.3; H, 7.5; O, 13.2. Found: C, 79.4; H, 7.5; O, 13.4.

**3,3′,5,5′-Tetramethyl-4,4′-dihydroxystilbene (6a).**—A solution of 0.05 g of the stilbenequinone **5a** in 100 ml of acetic acid is shaken with 4 g of zinc dust for about 1 hr. The colorless mixture is filtered and the filtrate neutralized by sodium bicarbonate. Extraction by ether and evaporation of the solvent gives 0.04 g of yellow crystals: mp 237–240°; nmr ($D_3CCOCD_3$) δ 7.12 (s, 3.8), 6.87 (s, 1.9), 3.00 (s, 2.1), 2.24 (s, 12.1).

*Anal.* Calcd for $C_{18}H_{20}O_2$: C, 80.6; H, 7.5; O, 11.9. Found: C, 80.4; H, 7.5; O, 12.0.

Oxidation and reduction products were identified by their melting points[16] and elemental analyses.[17] The spectral measurements are all in agreement with the reported structures.

**Registry No.**—**3a**, 2417-04-1; **6a**, 25347-59-5, silver carbonate, 534-16-7.

(16) Melting points were determined on a Kofler hot stage and are uncorrected.

(17) Satisfactory combustion analytical data have been obtained on the following compounds—diphenoquinones **2a–c**, stilbenequinones **5a–c**, dihydroxybiphenyls **3a–c**, 4,4′-dihydroxystilbenes **6a–c**, peroxide **9**, radical **11**, *o*-quinones **12a–d**, *p*-quinones **15b–e**, quinone monoanil **19**, and phenoxazone **21**: Ed.

# Solvatochromic Shifts for Some 4-Nitroaniline and 4-Nitrophenol Derivatives as Measures of Relative Solvent Proton Affinities

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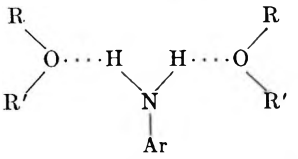
Enhanced red shifts ($-\Delta\Delta\nu_{max}$) of the [$^{+}R_2N{=}C_1{\rightarrow}C_4{=}NO_2^{-}$] band in the ultraviolet spectrum for 4-nitroaniline relative to *N,N*-diethyl-4-nitroaniline on going from cyclohexane to oxygen-base solvents are attributable primarily to the bathochromic influence of hydrogen bonding by 4-nitroaniline to these solvents and are considered to be measures of relative solvent–proton affinity. Such $\Delta\Delta\nu_{max}$ values show good correlation with $\sigma^*$ values of R in a series of ROH solvents which includes water. Good correlations between $-\Delta\Delta\nu_{max}$ and $\sigma^*$ values are also obtained from the following pairs: *N*-ethyl-4-nitroaniline/*N,N*-diethyl-4-nitroaniline and 4-nitrophenol/4-nitroanisole. These probes of relative solvent–proton affinity do not, however, show ethers to be better hydrogen-bond acceptors than alcohols, probably because of steric factors.

In terms of inductive effects, one would expect ethers to be better proton acceptors than alcohols which, in turn, should show stronger proton affinities than water. However, most indicator and titration studies represent water as being more basic than alcohols and ethers,[1] and among the simple alcohols the basicity order is often reported as antiinductive.[1,2] Indeed, Arnett has argued convincingly that any attempt to establish a single ordering for the oxygen bases toward differing classes of acidic species is likely to be doomed from the start;[1] it is difficult to disagree with this appraisal.

The complications arise from three factors which are liable to outweigh simple proton affinity effects: (a) significant solvent reorganization under the influence of the titrant or indicator; (b) differential solvation of conjugate anions or anionic ends of undissociated acid dipoles; and (c) steric effects. We wish now to report a reasonably sensitive method for the estimation of proton affinities of solvents wherein type a and b effects appear to be minimal.

This new method derives from the following observations, certain of which have been reported earlier.[3,4] The [$^{+}R_2N{=}C_1{\rightarrow}C_4{=}NO_2^{-}$] bands in the ultraviolet spectra of 4-nitroaniline and its *N*-alkyl and *N,N*-dialkyl derivatives[5] show significant red shifts ($-\Delta\nu_{max}$) in going from cyclohexane to more polar solvents. Where the more polar solvents are incapable of accepting a hydrogen bond, these spectral displacements are of closely comparable magnitudes for the primary, secondary, and tertiary nitroaromatic amines (*e.g.*, $-\Delta\nu_{max} = 0.72 \pm 0.03$ kK on going from cyclohexane to carbon tetrachloride, $-\Delta\nu_{max} = 2.57 \pm 0.10$ kK on going to 1,2-dichloroethane for the parent compound and a large variety of *N*-mono and *N,N*-dialkyl derivatives).

This suggests that the bathochromic influences of increased solvent polarity or polarizability are quite similar for the three classes of compounds. It is reasonable, then, that appreciably enhanced red shifts ($-\Delta\Delta\nu_{max}$) for 4-nitroaniline relative to an *N,N*-dialkyl-4-nitroaniline on going from cyclohexane to oxygen-base solvents should be a consequence primarily of the bathochromic influence[6] of hydrogen bonding by 4-nitroaniline to the solvent, *e.g.*,



which is excluded in the case of the *N,N*-dialkyl derivatives.[7]

A logical next step is that the enhanced red shift in a given solvent should be greater, the greater the strength of the hydrogen bonds by 4-nitroaniline to that solvent. Hence, the magnitudes of $-\Delta\Delta\nu_{max}$ values in a variety of solvents provide the basis for our estimating relative solvent proton affinities.

Positions of maximal absorption for the [$^{+}R_2N{=}C_1{\rightarrow}C_4{=}NO_2^{-}$] bands of 4-nitroaniline and *N,N*-diethyl-4-nitroaniline in cyclohexane, nine alcohols, and water are listed in Table I. Also tabulated are values of the red shifts from cyclohexane to each solvent ($-\Delta\nu_{max}$), the enhanced bathochromic shifts for the primary relative to the tertiary amine ($-\Delta\Delta\nu_{max}$), and the Taft $\sigma^*$ values[8] of R– in ROH. It is seen that the $-\Delta\Delta\nu_{max}$ values for the alcohols follow the inductive order, the greater the electron density on oxygen the higher being the $-\Delta\Delta\nu_{max}$ value. Very significantly, also, the $-\Delta\Delta\nu_{max}$ value for water is near that which would be expected on the basis of the $\sigma^*$ for R = H.

A plot of $-\Delta\Delta\nu_{max}$ *vs.* $\sigma^*$ is given in Figure 1. The data show good linear regression and fit the equation

$$-\Delta\Delta\nu_{max}\ (\text{in kK}) = 2.03 - 2.69\,\sigma^* \qquad (1)$$

with the correlation coefficient, $r = 0.98$, and the standard deviation, $s = 0.14$ kK. By Jaffé's criteria for $\rho$–$\sigma$ type relationships, these represent good correlation.[9]

We consider that the almost unique success of this method in arranging the alcohols and water in the

(1) E. M. Arnett, *Progr. Phys. Org. Chem.*, **1**, 283 (1963).

(2) *Inter alia*, L. S. Guss, and I. M. Kolthoff, *J. Amer. Chem. Soc.*, **62**, 1494 (1940); C. E. Newell and A. M. Eastham, *Can. J. Chem.*, **39**, 1752 (1961).

(3) M. J. Kamlet, *Israel J. Chem.*, **1**, 428 (1963).

(4) J. W. Eastes, M. H. Aldridge, and M. J. Kamlet, *J. Chem. Soc. B*, 922 (1969).

(5) M. J. Kamlet, H. G. Adolph, and J. C. Hoffsommer, *J. Amer. Chem. Soc.*, **86**, 4018 (1964).

(6) Such hydrogen bonding serves toward charge concentration on the amine nitrogen in the ground state and a strengthened hydrogen bond in the electronic excited state and hence tends toward lowered electronic transition energy; see ref 3, 4, and J. H. P. Utley, *J. Chem. Soc.*, 3252 (1963).

(7) In our previously used classification of solvation types,[3,4] this is referred to as type-B hydrogen bonding. Type-A hydrogen bonding involves the proton of the solvent and the nitrogen of the amine. For a discussion of spectral effects of type-A hydrogen bonding, see M. J. Kamlet, R. R. Minesinger, E. G. Kayser, M. H. Aldridge, and J. W. Eastes, *J. Org. Chem.*, in press.

(8) R. W. Taft, Jr., in "Steric Effects in Organic Chemistry," M. S. Newman, Ed., Wiley, New York, N. Y., 1965, Chapter 13.

(9) H. H. Jaffé, *Chem. Rev.*, **53**, 191 (1953).

TABLE I

SPECTRAL DISPLACEMENTS ($-\Delta\nu_{max}$ RELATIVE TO SPECTRA IN CYCLOHEXANE) FOR 4-NITROANILINE AND *N,N*-DIETHYL-4-NITROANILINE IN SOME WEAKLY BASIC SOLVENTS[a]

| Solvent, ROH, R = | $\sigma^*$ of R | 4-Nitroaniline | | | *N,N*-Diethyl-4-nitroaniline | | | $-\Delta\Delta\nu_{max}$, kK[c] |
|---|---|---|---|---|---|---|---|---|
| | | $\lambda_{max}$, nm | $\nu_{max}$, kK | $-\Delta\nu_{max}$, kK[b] | $\lambda_{max}$, nm | $\nu_{max}$, kK | $-\Delta\nu_{max}$, kK[b] | |
| $(CH_3)_3C$- | −0.30 | 377.5 | 26.49 | 4.52 | 390.5 | 25.61 | 1.79 | 2.73 |
| $(CH_3)_2CH$- | −0.19 | 378 | 26.46 | 4.55 | 392 | 25.51 | 1.89 | 2.66 |
| *n*-$C_4H_9$- | −0.13 | 375 | 26.67 | 4.34 | 392 | 25.51 | 1.89 | 2.45 |
| $C_2H_5$- | −0.10 | 372.5 | 26.85 | 4.16 | 392.5 | 25.48 | 1.92 | 2.24 |
| $CH_3$- | 0.00 | 371 | 26.95 | 4.06 | 397.5 | 25.16 | 2.24 | 1.82 |
| $C_6H_5CH_2CH_2$- | +0.08 | 375 | 26.67 | 4.34 | 401 | 24.94 | 2.46 | 1.88 |
| HO-$CH_2CH_2$- | +0.20 | 382.5 | 26.14 | 4.87 | 415 | 24.10 | 3.30 | 1.57 |
| $C_6H_5CH_2$- | +0.22 | 381 | 26.25 | 4.76 | 411 | 24.33 | 3.07 | 1.69 |
| Cl-$CH_2CH_2$- | +0.38 | 373.5 | 26.77 | 4.24 | 414 | 24.15 | 3.25 | 0.99 |
| H- | +0.49 | 380.5 | 26.28 | 4.73 | 430.5 | 23.23 | 4.17 | 0.56 |
| Cyclohexane | | 322.5 | 31.01 | | 365 | 27.40 | | |

[a] Precision in $\lambda_{max}$ *ca.* ±0.5 nm. [b] Red shift relative to spectrum in cyclohexane solvent. [c] Enhanced red shift for 4-nitroaniline as compared with its *N,N*-diethyl derivative; attributable to hydrogen bonding by 4-nitroaniline to weakly basic solvent.

"theoretical" order may arise from the following. Solute concentrations required for the spectrophotometric determinations are low, and 4-nitroaniline is about as weak an acid as can be used to test solvent proton affinities. Hence, solvent reorganization effects (factor a above) should be relatively minor. Factor b should also introduce only minimal complications because differential solvation effects at the anionic ends of the indicator dipoles (*i.e.*, solvation at the nitro group) should be relatively little influenced by N,N-dialkylation and should cancel out in the nitroaniline *vs.* dialkylnitroaniline comparisons.

We are on less firm ground as concerns factor c, steric effects on hydrogen bond strengths. The good fit of the *tert*-butyl alcohol result to the correlation equation suggests that steric effects are relatively unimportant in the ROH series. They may play a more significant part, however, in weakening hydrogen bonds by 4-nitroaniline to other ROR′ compounds. Proton affinities by this method do not arrange a series of ethers in the inductive order, nor do the ethers prove to be better hydrogen bond acceptors than the alcohols discussed above. Values of $-\Delta\Delta\nu_{max}$, determined as before, are for tetrahydrofuran, 1.67 kK; diethyl ether, 1.66 kK; 1,2-dimethoxyethane, 1.85 kK; dioxane, 1.13 kK. Sterically weakened hydrogen bonds by 4-nitroaniline to ROR′ compounds might result from ortho repulsions, which would be expected to be significantly greater where R′ is alkyl than where R′ is hydrogen.

An exercise similar to the above has also been carried out in obtaining $-\Delta\Delta\nu_{max}$ values for *N*-ethyl-4-nitroaniline relative to the *N,N*-diethyl derivative in the same series of solvents; the data are assembled in Table II. The trend of $-\Delta\Delta\nu_{max}$ again follows the inductive order and, with the exception of one out-of-line data point,[10] is near linear with $\sigma^*$ of R in ROH as is shown by the lower plot in Figure 1. The result fit the least-squares correlation equation

$$-\Delta\Delta\nu_{max} = 1.03 - 1.41\,\sigma^* \qquad (2)$$

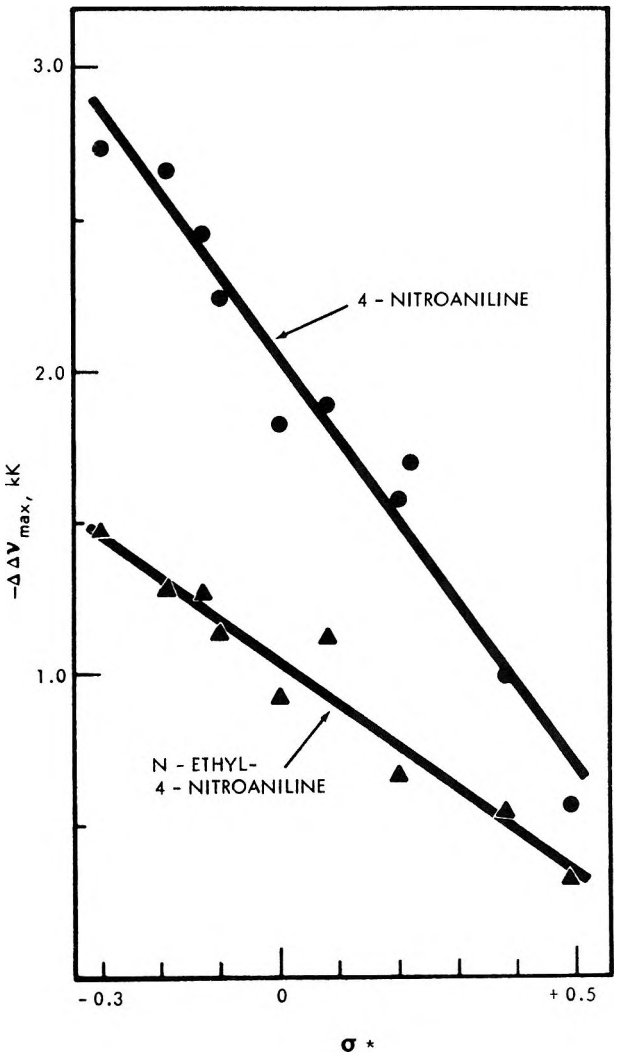



Figure 1.— $-\Delta\Delta\nu_{max}$ for 4-nitroaniline and *N*-ethyl-4-nitroaniline relative to *N,N*-diethyl-4-nitroaniline *vs.* $\sigma^*$ of R in ROH.

TABLE II

SPECTRAL DISPLACEMENTS FOR *N*-ETHYL-4-NITROANILINE

| Solvent, ROH, R = | $\sigma^*$ of R | $\lambda_{max}$, nm | $\nu_{max}$, kK | $-\Delta\nu_{max}$, kK | $-\Delta\Delta\nu_{max}$, kK |
|---|---|---|---|---|---|
| $(CH_3)_3C$- | −0.30 | 388 | 25.77 | 3.25 | 1.46 |
| $(CH_3)_2CH$- | −0.19 | 387 | 25.84 | 3.18 | 1.29 |
| *n*-$C_4H_9$- | −0.13 | 386.5 | 25.87 | 3.15 | 1.26 |
| $C_2H_5$- | −0.10 | 385 | 25.97 | 3.05 | 1.13 |
| $CH_3$- | 0.00 | 386.5 | 25.87 | 3.15 | 0.91 |
| $C_6H_5CH_2CH_2$- | +0.08 | 393 | 25.45 | 3.57 | 1.11 |
| HO-$CH_2CH_2$- | +0.20 | 399 | 25.06 | 3.96 | 0.66 |
| Cl-$CH_2CH_2$- | +0.38 | 398 | 25.13 | 3.89 | 0.54 |
| H- | +0.49 | 407.5 | 24.54 | 4.48 | 0.31 |

(10) If the point for 2-phenylethanol (in which solvent the absorption peak is very dissymmetric about the maximum) is excluded, the correlation equation becomes $-\Delta\Delta\nu_{max} = 1.01 - 1.43\,\sigma^*$, with $r = 0.99$ and $s = 0.06$ kK (excellent correlation).[9]

TABLE III

SPECTRAL DISPLACEMENTS FOR 4-NITROPHENOL AND 4-NITROANISOLE

| Solvent, ROH, R = | $\sigma^*$ of R | 4-Nitrophenol | | | 4-Nitroanisole | | | $-\Delta\Delta\nu_{max}$, kK |
|---|---|---|---|---|---|---|---|---|
| | | $\lambda_{max}$, nm | $\nu_{max}$, kK | $-\Delta\nu_{max}$, kK | $\lambda_{max}$, nm | $\nu_{max}$, kK | $-\Delta\nu_{max}$, kK | |
| $(CH_3)_3C-$ | −0.30 | 315 | 31.74 | 3.35 | 304 | 32.89 | 1.24 | 2.11 |
| $(CH_3)_2CH-$ | −0.19 | 312.5 | 32.00 | 3.09 | 303.5 | 32.94 | 1.19 | 1.90 |
| $n$-$C_4H_9-$ | −0.13 | 313 | 31.95 | 3.14 | 304 | 32.89 | 1.24 | 1.90 |
| $C_2H_5-$ | −0.10 | 311.5 | 32.10 | 2.99 | 304 | 32.89 | 1.24 | 1.75 |
| $CH_3-$ | 0.00 | 311.5 | 32.10 | 2.99 | 305 | 32.79 | 1.34 | 1.65 |
| $C_6H_5CH_2CH_2-$ | +0.08 | 317.5 | 31.50 | 3.59 | 311 | 32.15 | 1.98 | 1.61 |
| $HO\text{-}CH_2CH_2-$ | +0.20 | 317 | 31.55 | 3.54 | 313 | 31.95 | 2.18 | 1.36 |
| $ClCH_2CH_2-$ | +0.38 | 316.5 | 31.60 | 3.49 | 314 | 31.87 | 2.26 | 1.23 |
| H− | +0.49 | 317.5 | 31.50 | 3.59 | 317 | 31.55 | 2.58 | 1.01 |
| $CF_3CH_2-$ | +0.92 | 312 | 32.05 | 3.04 | 315 | 31.75 | 2.38 | 0.66 |
| Cyclohexane | | 285 | 35.09 | | 293 | 34.13 | | |
| $CCl_4$ | | 289 | 34.60 | (0.49) | 298 | 33.56 | (0.57) | |
| $ClCH_2CH_2Cl$ | | 301.5 | 33.17 | (1.92) | 309 | 32.36 | (1.77) | |

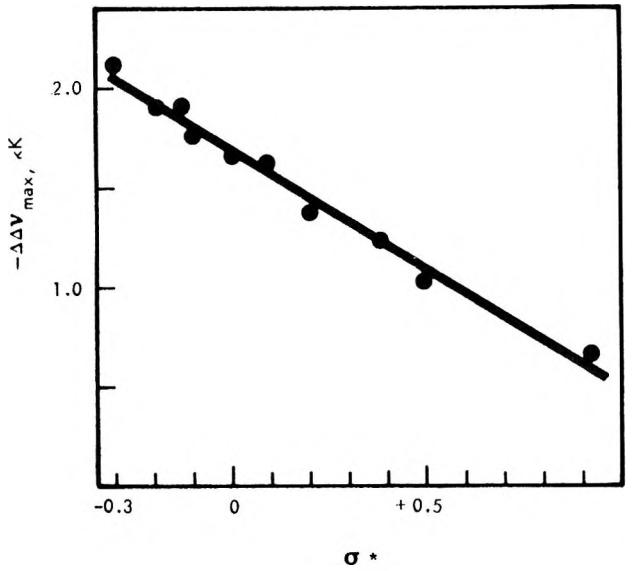



Figure 2.— $-\Delta\Delta\nu_{max}$ for 4-nitrophenol relative to 4-nitroanisole *vs.* $\sigma^*$ of R in ROH.

with $r = 0.97$ and $s = 0.09$ kK (good correlation).[9]

It is of some interest that both the slope and the intercept for 4-nitroaniline in eq 1 come very near to being twice the corresponding values for *N*-ethyl-4-nitroaniline in eq 2. This finding suggests to us that 4-nitroaniline forms *two* hydrogen bonds to the ROH solvents and that these hydrogen bonds are very nearly equal in strength to each other and to the single hydrogen bond in *N*-ethyl-4-nitroaniline.[11]

The above results also help to explain some seeming variations in the effects of *N*-alkyl groups on the spectra of nitroaromatic amines depending on the solvent. In cyclohexane the bathochromic displacement on N,N-diethylation of 4-nitroaniline is 42.5 nm; in methanol the shift amounts to 26.5 nm; and in *tert*-butyl alcohol 13 nm. This decreasing trend can now be rationalized on the basis that, on N,N-dialkylation, we are excluding progressively stronger bathochromic effects of hydrogen bonding in the more basic solvents. The fact that the solvent effect is almost as great as the substituent effect emphasizes the need to take such hydrogen bonding phenomena into account in spectra–structure correlations for compounds of the types discussed here.

Parallel effects on $[^+X{=}C_1{\rightarrow}C_4{=}NO_2^-]$ transition maxima as occur on N-alkylation of 4-nitroaniline should also take place on O-alkylation of 4-nitrophenol, *i.e.*, a bathochromic effect on replacing hydrogen by alkyl in nonpolar solvents,[12] partially or completely offset in alcoholic or aqueous media, by a hypsochromic displacement resulting from exclusion of a hydrogen bond to the solvent.

It would follow in a similar manner, then, that $-\Delta\Delta\nu_{max}$ values, obtained by comparing red shifts from cyclohexane to ROH solvents for 4-nitrophenol and 4-nitroanisole, should be measures of $ArOH\cdots O<\begin{matrix}H\\R\end{matrix}$ hydrogen bond strengths.[13] We have carried out such a comparison; the results, in terms of $\lambda_{max}$, $\nu_{max}$, $-\Delta\nu_{max}$, and $-\Delta\Delta\nu_{max}$, are given in Table III and a plot of $-\Delta\Delta\nu_{max}$ *vs.* $\sigma^*$ is shown in Figure 2. As was anticipated, the $-\Delta\Delta\nu_{max}$ values again arrange the alcohols and water in the inductive order and the trend with $\sigma^*$ is near linear. The least-squares correlation equation is

$$-\Delta\Delta\nu_{max} = 1.68 - 1.20\,\sigma^* \qquad (3)$$

with $r = 0.99$ and $s = 0.06$ kK (excellent correlation).[9]

It is of some interest that in this series the hypsochromic effect of excluding the hydrogen bond in some instances outweighs the "normal" bathochromic effect of O-alkylation. The consequence is that 4-nitroanisole absorbs at the longer wavelengths in cyclohexane, carbon tetrachloride, 1,2-dichloroethane, and trifluoroethanol, but 4-nitrophenol absorbs at the longer wavelengths in water and the more basic alcohols.

It should be noted in conclusion that we have represented these $-\Delta\Delta\nu_{max}$ values as being measures of relative solvent proton affinity, rather than intrinsic basicity. Hydrogen bond strength is only one of many possible criteria for proton acceptor ability and, as we have mentioned in earlier papers,[4,7,14] proton acceptor

(11) An alternative possibility, that 4-nitroaniline forms a single hydrogen bond to solvent and that this is somehow sterically weakened on N-ethylation to give about half the enhanced bathochromic effect, seems ruled out by the fact that $-\Delta\Delta\nu_{max}$ values in all ROH solvents are almost identical for *N*-methyl-, *N*-ethyl-, and *N*-isopropyl-4-nitroaniline.

(12) The red shift in cyclohexane on going from 4-nitroaniline to *N*-ethyl-4-nitroaniline ($\lambda_{max}$ 343 nm) is −1.86 kK; the corresponding shift for 4-nitroanisole relative to 4-nitrophenol is −0.97 kK.

(13) As was the case earlier, shifts on going from cyclohexane to carbon tetrachloride or 1,2-dichloroethane are reasonably similar for both compounds (Table III).

(14) J. W. Eastes, M. H. Aldridge, R. R. Minesinger, and M. J. Kamlet, *J. Org. Chem.*, in press.

ability is in turn only one of the many complex interacting factors influencing $pK_a$'s.

### Experimental Section

Ultraviolet absorption spectra were determined on a Cary Model 14 recording spectrophotometer with matched 1-cm silica cells. Concentrations were 3–5 $\times$ $10^{-5}$ $M$. The reported data represent the average of two determinations for each spectrum, with occasional checks that $\lambda_{max}$ did not vary with concentration. All solvents were Spectro Grade or the best grade commercially available and were checked by glpc to confirm the absence of significant impurities.

**Registry No.**—4-Nitroaniline, 100-01-6; *N*,*N*-diethyl-4-nitroaniline, 2216-15-1; *N*-ethyl-4-nitroaniline, 3665-80-3; 4-nitrophenol, 100-02-7; 4-nitroanisole, 100-17-4.

**Acknowledgment.**—We are grateful to Miss Mona Lisa Jones for determining some of the spectra. The work was done under U. S. Naval Ordnance Laboratory Independent Research Task IR-44.

## Substituent and Secondary Deuterium Isotope Effects for Hydrolysis of Schiff Bases[1]

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The inverse kinetic secondary deuterium isotope effect, $k_D/k_H$, for attack of hydroxide ion on the conjugate acids of substituted *N*-benzylidene-1,1-dimethylethylamines is near 1.22 and is independent of the nature of the polar substituent. The same isotope effect for the attack of water on the conjugate acid of *N*-4-methoxybenzylidene-1,1-dimethylethylamine is 1.20. Thus, transition states for these reactions resemble the adducts more closely than the substrates. Second-order rate constants for the attack of hydroxide ion on substituted *N*-(substituted)-benzylideneanilines are correlated by the Hammett $\sigma$ constants. Values of $\rho$ near 2.7 were obtained in all cases except for the Schiff bases derived from 4-nitrobenzaldehyde, for which a value of 1.9 was found. These large values are consistent with adduct-like transition states for Schiff base hydrolysis.

Previous studies of addition of nucleophilic reagents to Schiff bases derived from aromatic aldehydes have sufficed to establish a number of points pertinent to these reactions.[3] Some general conclusions include (i) the rate-determining step for hydrolysis changes from nucleophile attack to intermediate decomposition as the solution pH is lowered;[4-9] (ii) the conjugate acids of Schiff bases are very much more reactive toward nucleophilic attack than are the free bases;[6-10] (iii) the basicity of the departing amine has a marked influence on the kinetics of Schiff base hydrolysis—decreasing basicity decreases reactivity under basic but increases reactivity under acidic conditions;[6,8,9] and (iv) the addition of nucleophilic reagents to Schiff bases is subject to general acid–base catalysis.[5,8,9,11,12]

Having a general understanding of the course and kinetics of these reactions, it appears desirable to begin to probe the structure of the associated transition states and the variation in such structures with substrate reactivity in more detail. This manuscript reports the results of some efforts in this direction. Two approaches have been employed: kinetic secondary deuterium isotope effects and effects of polar substituents. The former have been studied employing *N*-benzylidene-1,1-dimethylethylamines deuterated at the aldehydic carbon as substrates and the latter using *N*-benzylideneanilines. In both cases the magnitude of the observed effects has been probed as a function of the nature of the polar substituent in the benzaldehyde moiety.

### Experimental Section

**Materials.**—Substituted *N*-(substituted)-benzylideneanilines were prepared by the direct condensation of the appropriate aldehydes and anilines. All such substrates were recrystallized to constant melting point or carefully redistilled prior to use. *N*-Benzylidene-1,1-dimethylethylamines were prepared as previously described.[8] Benzaldehyde-*1-d* was prepared by oxidation of benzoin-*1-d* in tetrahydrofuran at 17° by the slow addition of $D_5IO_6$, prepared by exchanging $H_5IO_6$ with $D_2O$. Following completion of the reaction, the solvent was removed on a rotary evaporator and the benzaldehyde-*1-d* was isolated as the bisulfite complex. The deuterated benzoin substrate was prepared by refluxing for 24 hr a solution of 0.43 mol of benzoin, 1.00 mol of $D_2O$, and 0.001 mol of NaOH in 450 ml of dioxane. The dioxane–water azeotrope was removed by distillation and the exchange process was repeated. 4-Methoxybenzaldehyde-*1-d* was prepared in the same way, beginning with 4,4′-dimethoxybenzoin. 3-Bromobenzaldehyde-*1-d* was prepared by the bromination of benzaldehyde-*1-d*.[13] Proton magnetic resonance spectra of neat benzaldehyde-*1-d* samples revealed that each had an isotopic purity of at least 98%. Reagent grade salts and distilled water were employed throughout.

**Kinetic Methods.**—All reactions were followed spectrophotometrically employing Zeiss PMQ II spectrophotometers equipped with cell holders through which water from a constant-temperature bath was continuously circulated. Reactions were ordinarily monitored at wavelengths near the absorption maximum of the Schiff base under study. Spectra recorded at the conclusion of the hydrolysis reactions corresponded to those of a mixture of the appropriate aldehyde and amine. For those reactions not involving determination of secondary isotope effects, first-order rate constants were obtained from semilogarithmic plots of the difference in optical density and infinite time optical density

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(2) Career Development Awardee of the National Institutes of Health.

(3) Two comprehensive reviews are available: W. P. Jencks, *Progr. Phys. Org. Chem.*, **2**, 63 (1964); "Catalysis in Chemistry and Enzymology," McGraw-Hill, New York, N. Y., 1969, Chapter 10.

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TABLE I

SECONDARY DEUTERIUM ISOTOPE EFFECTS FOR THE HYDROLYSIS OF *N*-(SUBSTITUTED)-BENZYLIDENE-1,1-DIMETHYLETHYLAMINES AT 25°

| Substituent | Registry no. | pH | Solvent[a] | $k_D/k_H$[b] | $\sigma_{mean}$ |
|---|---|---|---|---|---|
| 3-Bromo | 28405-57-4 | 0.1 *M* NaOH | 45.7% aqueous ethanol | 1.224 | ±0.004 |
| Unsubstituted | 6852-58-0 | 0.1 *M* NaOH | 58.2% aqueous ethanol | 1.222 | ±0.005 |
| 4-Methoxy | 15875-74-8 | 0.1 *M* NaOH | 64.2% aqueous ethanol | 1.224 | ±0.004 |
| 4-Methoxy | | 4.62 | Water | 1.199 | ±0.002 |

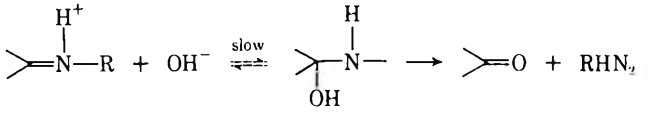
[a] Solvent composition was chosen so as to obtain reaction half-lives near 30 min. [b] Mean of five observations.

against time in the usual way. Second-order rate constants were calculated from slopes of plots of first-order rate constants against the concentration of hydroxide ion. In those cases involving determination of secondary deuterium isotope effects, first-order rate constants were obtained by linear regression analysis as previously described.[14] These rate constants were reproducible to within ±1%.

## Results and Discussion

Kinetic secondary deuterium isotope effects have been successfully employed in a number of cases, particularly solvolytic reactions, to define transition state structures.[15,16] This technique has been applied in relatively few cases for the study of reactions involving substrates at the carbonyl level of oxidation, and a conflicting pattern of results has emerged from these studies in some cases.[17-19] A recent study of secondary deuterium isotope effects for acetal hydrolysis has provided new insight into these reactions.[14] These findings have prompted our study of such effects for Schiff base hydrolysis.

It has been established that the rate-determining step for pH-independent hydrolysis of *N*-benzylidene-1,1-dimethylethylamines involves the attack of hydroxide ion on the conjugate acids of the substrates.[8]




In Table I, secondary deuterium isotope effects are collected for the attack of hydroxide ion on the protonated Schiff bases derived from 3-bromo, 4-methoxy, and unsubstituted benzaldehydes. As expected, the isotope effect is inverse; *i.e.*, the deuterio substrates react more rapidly than the protio ones. In each case the rate ratio is near 1.22. While the maximal isotope effect for the addition of oxygen nucleophiles to carbon–nitrogen double bonds has not been experimentally established, analogy to related systems suggests that the observed value is close to the maximal one.[16] Thus, the $sp^2$ carbon atom of the substrate has been largely converted to $sp^3$ geometry in the transition state; *i.e.*, carbon–oxygen bond formation is nearly complete in the transition state. The extent of carbon–oxygen bond formation, as measured by the isotope effect, is independent of the nature of the polar substituent. This result contrasts with the observation that the extent of carbon–oxygen bond cleavage in the hydrolysis of diethyl acetals of benzaldehydes changes markedly as a function of the nature of the polar substituent.[14]

Under more acidic conditions, the attack of water, rather than hydroxide ion, on the protonated Schiff bases becomes the predominant reaction pathway.[3,8] The secondary deuterium isotope effect for the hydrolysis of *N*-4-methoxybenzylidene-1,1-dimethylethylamine at pH 4.62 is included in Table I. Under these conditions the rate of carbinolamine decomposition contributes not more than 10% to the overall reaction rate. The magnitude of the isotope effect is similar to that for the attack of hydroxide ion, indicating that, in this case too, the carbon–oxygen bond is well-formed in the transition state. This is certainly the expected result based on the earlier observations. It would be hard to rationalize an observation suggesting that the transition state for the attack of water on the Schiff base occurred appreciably sooner along the reaction coordinate than that for attack of hydroxide ion.[20] A previous investigation has established that the attack of water on protonated *N*-benzylidene-1,1-dimethylethylamines is slightly more sensitive to the nature of polar substituents than is the attack of hydroxide ion.[8] This would suggest that the transition state for the former reaction is reached somewhat later along the reaction coordinate than is that for the former. However, the secondary deuterium isotope effects do not provide support for this suggestion. It is possible that factors other than degree of carbon–oxygen bond formation, particularly electrostatic factors, may account for the observed difference in $\rho$ values.

Within a series of closely related reactions, such as the attack of the same nucleophilic reagent on structurally related substrates, values of $\rho$ potentially yield useful information concerning transition state structures, and the variation in $\rho$ with substrate reactivity may indicate how these structures vary as a function of reactivity.[6] There have, in fact, been rather few studies of the effect of the variation in substrate reactivity on values of $\rho$. A model study of this type has been carried out by Kirsch, *et al.*, who have examined the alkaline hydrolysis of acyl- and aryl-substituted phenyl benzoates.[21] These workers observed that the values of $\rho$ for alkaline hydrolysis of aryl-substituted phenyl benzoates did not vary detectably as a function of the nature of the polar substituent in the acyl moiety. In efforts to more fully define the transition state for Schiff base hydrolysis, we have studied a related set of reactions: the alkaline hydrolysis of substituted *N*-(substituted)-benzylideneanilines.

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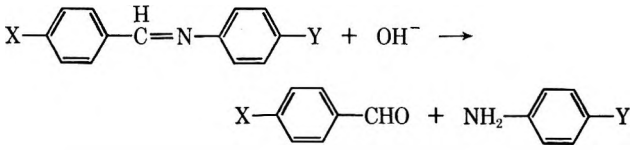
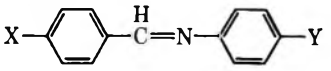


It has previously been established that hydrolysis of these substrates under alkaline conditions exhibits both pH-independent and base-catalyzed reaction routes.[6,8] The former reflects attack of hydroxide ion on the protonated substrates and the latter reflects the attack of this nucleophile on the corresponding free bases. In Table II second-order rate constants

TABLE II

RATE CONSTANTS FOR THE pH-INDEPENDENT AND BASE-CATALYZED HYDROLYSIS OF SUBSTITUTED BENZYLIDENEANILINES IN WATER AT 30° AND IONIC STRENGTH 0.50



| X | Y | $k_{OH}$,[a] $M^{-1}$ min$^{-1}$ | $k_0$,[b] min$^{-1}$ |
|---|---|---|---|
| $CH_3O$ | $CH_3O$ | | 0.029 |
| | $CH_3$ | | 0.033 |
| | H | 0.054 | 0.022 |
| | Cl | 0.088 | 0.023 |
| | $CH_3CO$ | 1.52 | 0.025 |
| | $NO_2$ | 5.8 | |
| $CH_3$ | $CH_3O$ | | 0.020 |
| | $CH_3$ | | 0.050 |
| | H | 0.09 | 0.013 |
| | $CH_3CO$ | 1.96 | |
| | $NO_2$ | 10.6 | |
| H | $CH_3$ | 0.045 | 0.023 |
| | H | 0.076 | 0.014 |
| | Cl | 0.25 | |
| | $CH_3CO$ | 3.75 | |
| | $NO_2$ | 9.5 | |
| Cl | $CH_3$ | 0.061 | 0.043 |
| | H | 0.185 | 0.010 |
| | COOH | 0.90 | 0.038 |
| | Cl | 1.07 | |
| | $CH_3CO$ | 5.3 | |
| | $NO_2$ | 17.3 | |
| $NO_2$ | $CH_3O$ | 0.37 | |
| | $CH_3$ | 0.57 | |
| | H | 1.03 | |
| | Cl | 3.0 | |
| | $NO_2$[c] | 26.0 | |

[a] Second-order rate constants for the attack of hydroxide ion on the Schiff bases. [b] First-order rate constants for the pH-independent hydrolysis reaction. [c] *m*-Nitro.

for the base-catalyzed reaction and first-order rate constants for the pH-independent hydrolysis for a series of substituted *N*-benzylideneanilines are collected. In each case, the rate constants have been calculated, respectively, from the slope and intercept of plots of first-order rate constants against hydroxide ion concentration. Base concentrations of 0.05, 0.10, 0.20, and 0.40 *M* were generally employed. For those Schiff bases possessing electron-donating substituents, the pH-independent reaction was frequently so great as to mask the basic reaction; for those possessing electron-withdrawing substituents, the converse was frequently true.

Note that the values of the pH-independent rate constants vary rather little with the nature of polar substituent in either the aldehyde or amine moiety, in accord with previous observations.[22] This finding reflects the opposing effects of polar substituents on substrate protonation and hydroxide ion attack. In contrast, second-order rate constants for hydroxide ion attack on the free bases increase rapidly with increasing electron withdrawal. Plots of the logarithm of these rate constants against $\sigma$ values for aniline-substituted Schiff bases yield fair (but not excellent) straight lines from which values of $\rho$ have been calculated. (Surprisingly, corresponding plots of rate constants for benzaldehyde-substituted Schiff bases did not yield satisfactory Hammett plots.) The following values of $\rho$ were obtained for the indicated benzaldehyde-substituted substrates: 4-methoxy, 2.6; 4-methyl, 2.7; unsubstituted, 2.6; 4-chloro, 2.7; and 4-nitro, 1.9. Two points are of note here. First, these are the largest values of $\rho$ observed for the attack of a nucleophile on Schiff bases. For example, rate constants for attack of water, hydroxylamine, and methoxyamine on protonated benzhydrylidenemethylamines yield values of $\rho^+$ near unity;[9] attack of water on protonated benzhydrylideneimines generates a $\rho$ value of 2.0;[23] and on protonated *N*-benzylidene-1,1-dimethylethylamines a value of $\rho^+$ of 1.7 is obtained.[8] Finally, rate constants for attack of hydroxide ion on protonated *N*-benzylidene-1,1-dimethylethylamines are correlated by a $\rho^+$ value of 1.26.[8] All of the above substrates, reacting as the conjugate acids, are substantially more reactive than those studied here; the variation in sensitivity to polar substituents may reflect a difference in extent of carbon–oxygen bond formation in the transition state, although other factors may be important as well. Additional studies of secondary deuterium isotope effects for the pertinent reactions would be of interest. At any event, the large values suggest a good deal of carbon–oxygen bond formation in the transition states.

Second, values of $\rho$ are, with the exception of those for the substrates derived from 4-nitrobenzaldehyde, independent of the nature of the polar substituent on the benzaldehyde moiety, a situation similar to that encountered by Kirsch, *et al.*[21] Only the slightly smaller value for the 4-nitro derivatives, the most reactive substrates, provides a suggestion of a detectable change in transition state structure with changing substrate reactivity.

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# The Mechanism of the Reaction of Phenylpropargylaldehyde with Aqueous Sodium Hydroxide to Give Phenylacetylene and Sodium Formate[1a]

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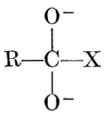
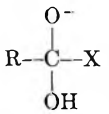
The rate of cleavage of phenylpropargylaldehyde in the presence of aqueous sodium hydroxide at 35.2° has been studied spectrophotometrically. The results were interpreted in terms of rate-controlling cleavage of the monoanion and the dianion of the aldehyde hydrate, with the latter being the principal reaction path at the base concentrations (>0.001 *M*) used. An approximate value was obtained for the equilibrium constant for hydration of the aldehyde and from it was obtained an approximate ionization constant for the aldehyde hydrate, which was found to fit a Taft equation correlation of the acidities of aldehyde hydrates.

Kinetic studies have shown that the cleavage of the carbanion $X^-$ from compounds of the type RCOX by the action of hydroxide ions involves, at least in part, two hydroxide ions in cases where X is trichloromethyl,[2,3] pyridinomethyl,[4] acetonyl,[5] 1-acetylethyl,[5] α-arylsulfonylmethyl,[6] and 2,6-dihalophenyl.[7] These observations may be explained by a mechanism involving rate-controlling loss of $X^-$ from the dianion **1**.



**1**

Of the compounds undergoing cleavage *via* the dianion, only in the cases where X was acetonyl or 1-acetylethyl was the reaction involving only one hydroxide ion also clearly detectable under the alkaline conditions used.[8] In these cases a significant fraction of the reaction presumably consists of the rate-controlling loss of $X^-$ from the monoanion **2**. Cleavage *via* the



**2**

monoanion appears to take place in cases in which X is a 1,1-bis(carbalkoxy)alkyl group[9] or a cyano group[10] in acidic solutions, where the concentration and rate of formation of the dianion must be very small, but in more basic solutions the rate-controlling step becomes attack on the carbonyl group. Kinetic studies show the participation of only one hydroxide ion in alkaline cleavages where X is 2-acetyl-2-propyl[5] and nitromethyl.[6] Although it is likely that loss of $X^-$ from anion **2** is rate-controlling in these cases (especially the former), this has not been established. The cleavage of the hydrate of a 2-acetylthiazolium ion involves rate-controlling cleavage of ion **2** in the pH range of 5–7, but the reaction became too fast to study in basic solutions.[11] In order to learn more about the factors that control the relative extent to which $X^-$ is lost from ions **1** and **2**, we have studied the kinetics of the cleavage of phenylpropargylaldehyde, which was found by Claisen to yield phenylacetylene and formate in the presence of dilute aqueous alkali.[12]

## Results and Discussion

The cleavage of phenylpropargylaldehyde in $6.5 \times 10^{-5}$ *M* aqueous solutions was studied kinetically in the presence of about 0.001–0.014 *M* sodium hydroxide by following the decrease in absorbance at the 285.5-nm aldehyde absorption maximum. The absorption spectrum of a reaction solution after about 11 half-lives was in good agreement with that of phenylacetylene formed in 96% yield. Although phenylacetylene and sodium formate do not absorb appreciably at 285.5 nm and at the time of measurement less than 0.05% of the aldehyde should be left, there was an "infinity" absorbance equal to 3.6% of the initial absorbance. Plots of $\ln (A_t - A_\infty)$ *vs.* time (where $A_t$ is the absorbance at time $t$ and $A_\infty$ that at infinite time) gave good straight lines from whose slopes first-order rate constants were calculated. These rate constants will be treated in terms of mechanism 1, where

$$\underset{\text{P}}{\text{PhC}\equiv\text{CCHO}} + \text{H}_2\text{O} \overset{K_H}{\rightleftharpoons} \underset{\text{POH}_2}{\text{PhC}\equiv\text{CCH(OH)}_2}$$

$$\text{PhC}\equiv\text{CCH(OH)}_2 + \text{OH}^- \overset{K_1}{\rightleftharpoons} \text{PhC}\equiv\text{CCH(OH)O}^-$$

$$\underset{\text{POH}^-}{\text{PhC}\equiv\text{CCH(OH)O}^-} + \text{OH}^- \overset{K_2}{\rightleftharpoons} \underset{\text{PO}^{2-}}{\text{PhC}\equiv\text{CCH(O}^-)_2} \qquad (1)$$

$$\text{PhC}\equiv\text{CCH(OH)O}^- \xrightarrow{k_1} \text{PhC}\equiv\text{C}^- + \text{HCO}_2\text{H} \xrightarrow{\text{fast}} \text{PhC}\equiv\text{CH} + \text{HCO}_2^-$$

$$\text{PhC}\equiv\text{CCH(O}^-)_2 \xrightarrow{k_2} \text{PhC}\equiv\text{C}^- + \text{HCO}_2^- \xrightarrow[\text{H}_2\text{O}]{\text{fast}} \text{PhC}\equiv\text{CH} + \text{HCO}_2^-$$

the abbreviations to be used for various species are written under their formulas. There is evidence that

(1) (a) This investigation was supported in part by Public Health Service Research Grant AM 10378 from the National Institute of Arthritis and Metabolic Diseases and by Grant DA-ARO-D-31-124-G648 from the Army Research Office, Durham. (b) Public Health Service Fellow under Award 6 FO2 CA39914-01A1 from the National Cancer Institute.

(2) C. Gustafsson and M. Johanson, *Acta Chem. Scand.*, **2**, 42 (1948).

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(8) A reaction involving only one hydroxide ion was reported in the case where X was trichloromethyl,[2] but under the conditions where this reaction is most important the formation of chloride ions becomes a major side reaction[3] that was not taken into account.

(9) G. E. Lienhard and W. P. Jencks, *J. Amer. Chem. Soc.*, **87**, 3855 (1965).

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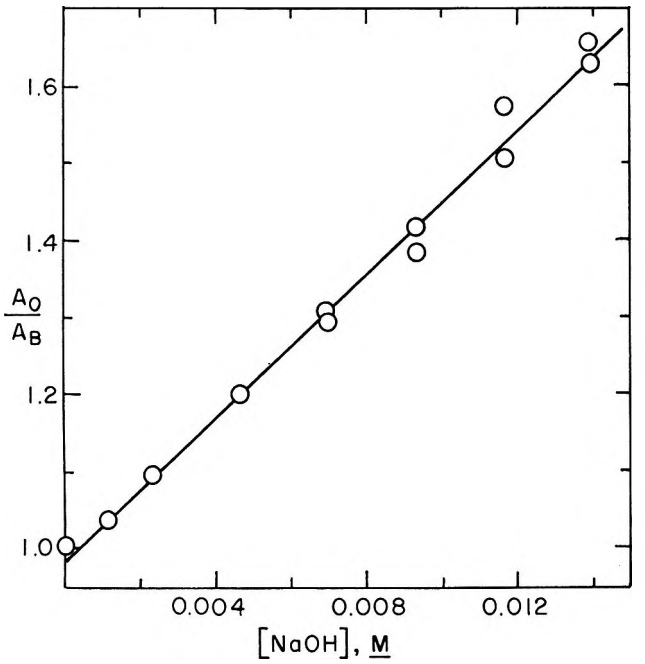


Figure 1.—Plot of ratio of absorbance in the absence of base to the absorbance in the presence of base *vs.* base concentration for phenylpropargylaldehyde in water at 35.2°.

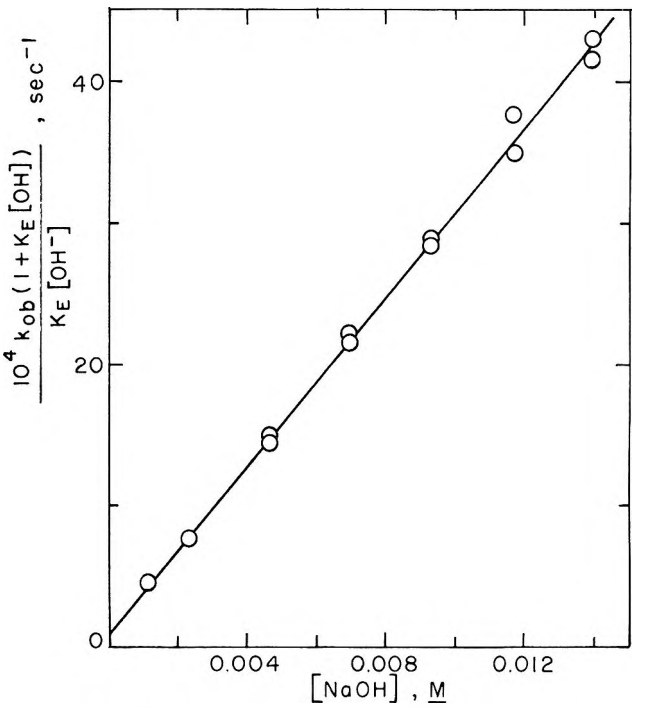


Figure 2.—Plot of the left-hand side of eq 4 *vs.* the sodium hydroxide concentration.

significant fractions of the aldehyde are present in each of the three forms, P, $POH_2$, and $POH^-$, but $K_2$ is believed to be so small that the concentration of $PO^{2-}$ is much lower. If this assumption is correct, and if the rate-controlling steps of the reaction are those governed by $k_1$ and $k_2$, the observed first-order rate constant for the reaction at a given hydroxide ion concentration may be expressed as shown in eq 2,

$$k_{obsd} = \frac{K_E[OH^-](k_1 + k_2K_2[OH^-])}{1 + K_E[OH^-]} \quad (2)$$

where $K_E$ is defined as $(K_1K_H)/(1 + K_H)$. The hydration equilibrium of the aldehyde was found to be established almost as rapidly as absorbance measurements could be made after preparation of a solution in neutral water. It therefore appears safe to assume that the equilibria governed by $K_H$ and $K_1$ are established before measurements can be made on mixtures of aqueous aldehyde and alkali solutions. This and the assumption that the aldehyde hydrate is too weakly acidic to ionize appreciably in neutral solution lead to eq 3, in which $A_0$ is the absorbance of a neutral

$$A_0/A_B = 1 + K_E[OH^-] \quad (3)$$

solution of aldehyde and $A_B$ is the absorbance, extrapolated to zero time, of a solution containing the same total amount of aldehyde and the indicated concentration of hydroxide ions. Values of $A_0$ and $A_B$ are listed with the kinetic data in Table I. A plot of $A_0/A_B$ *vs.* $[OH^-]$,[13] as shown in Figure 1, gives a satisfactory straight line with the intercept 0.98, in reasonable agreement with the value required by eq 3, and slope ($K_E$) 46.5 $M^{-1}$. Rearrangement of eq 2 gives eq 4. Using the value of $K_E$ obtained from

$$\frac{k_{obsd}(1 + K_E[OH^-])}{K_E[OH^-]} = k_1 + k_2K_2[OH^-] \quad (4)$$

(13) The hydroxide ion concentrations used in this plot were the initial values after establishment of equilibrium between P, $POH_2$, and $POH^-$ but before any cleavage occurred.

TABLE I

KINETICS OF ALKALINE CLEAVAGE OF PHENYLPROPARGYLALDEHYDE IN WATER AT 35.2° [a]

| $10^3$ [NaOH],[b] $M$ | $A_B$[c] | $10^5 k_{obsd}$, sec$^{-1}$ |
|---|---|---|
| 4.67 | 0.535[d] | 26.5 |
| 7.00 | 0.496[d] | 54.4 |
| 9.34 | 0.463[d] | 87.2 |
| 11.7 | 0.426[d] | 123.0 |
| 14.0 | 0.394[d] | 164.2 |
| 1.16 | 0.620 | 2.34 |
| 2.33 | 0.586 | 7.41 |
| 4.66 | 0.539 | 25.7 |
| 6.99 | 0.493 | 53.0 |
| 9.32 | 0.454 | 85.9 |
| 11.6 | 0.409 | 132.2 |
| 14.0 | 0.389 | 169.1 |
| 11.6[e] | 0.415 | 151.8 |
| 11.6[f] | 0.418 | 115.0 |

[a] The ionic strength was adjusted with sodium chloride and was 0.10 $M$ except where otherwise noted. The initial aldehyde concentration was 6.50 × $10^{-5}$ $M$ in the first five runs and 6.48 × $10^{-5}$ $M$ in the other runs. [b] Initial concentrations. The concentration of sodium hydroxide originally present has been corrected by about 0.2% for formation of $POH^-$, 0.3% for expansion on warming from room temperature to 35.2°, and 0.6% for dilution by added aldehyde solution. [c] Using a 1.00-cm cell; $A_0$ was 0.643 except where otherwise noted. [d] $A_0$ was taken to be 0.643(6.5/6.48). [e] Ionic strength 0.20 $M$. [f] Ionic strength 0.05 $M$.

eq 3, the left-hand side of eq 4 was plotted against the hydroxide ion concentration[14] (Figure 2), to give a satisfactory straight line whose intercept ($k_1$) is 9.3 × $10^{-5}$ sec$^{-1}$ and whose slope ($k_2/K_2$) is 0.299 $M^{-1}$ sec$^{-1}$. Since the intercept is fairly near the origin, the value of $k_1$ is probably much less reliable than that of $k_2K_2$. From these values it may be calculated that, even in the most favorable case, less than

(14) The hydroxide ion concentrations plotted were the average values present during the kinetic run which were smaller than the "initial" value by as much as 0.7%.

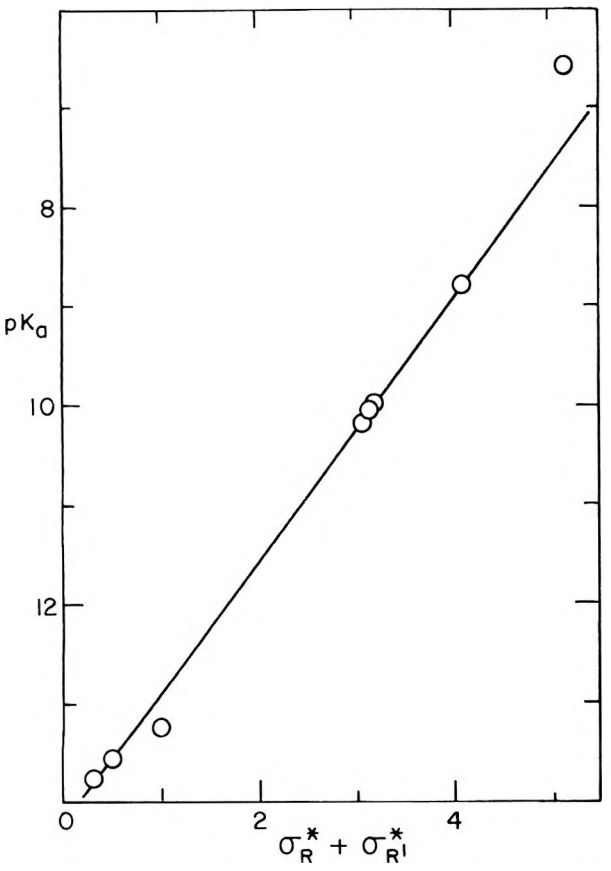


Figure 3.—Taft equation correlation of acidities of compounds of the type RR'C(OH)$_2$.

22% of the reaction took place by cleavage of the monoanion 2.

The three runs in Table I made at hydroxide ion concentrations of 0.0116 $M$ show that the reaction has a positive ionic strength effect. This is, of course, the result expected since the major part of the reaction involves the formation of a doubly charged transition state from singly charged and uncharged reactants.

Since $K_E$ is a function of $K_H$ and $K_1$, if either of the latter two constants is known the other may be calculated. We have made a rough measurement of $K_H$ by determining the relative extinction coefficients of phenylpropargylaldehyde in 0.10 $M$ aqueous sodium chloride and in 1,4-dioxane. Attributing the 29.6% decrease in the extinction coefficient at about 280 nm on going from dioxane to water entirely to hydration of the aldehyde and assuming that the aldehyde hydrate does not absorb at this wavelength gives a $K_H$ value of 0.296. The assumption that the aldehyde hydrate does not absorb is plausible since it has the same chromophoric groups as phenylacetylene, which does not absorb near 280 nm. The $K_H$ value obtained is uncertain, however, because of the implicit assumption that the true extinction coefficient of the aldehyde is the same in water and dioxane, in which the absorption maxima have somewhat different shapes and are at 285.5 and 278 nm, respectively. From this $K_H$ value and the $K_E$ obtained from spectral measurements, a value of 158 $M^{-1}$ may be calculated for $K_1$ at 35° and ionic strength 0.10 $M$. According to the Debye–Hückel limiting law, this value should be the same at infinite dilution. Combination with p$K_w$ gives a p$K_a$ value of 11.48 for the first ionization constant of phenylpropargylaldehyde hydrate at 35° and, if $K_1$ is assumed to have the same value at 25°, a p$K_a$ value of 11.80 at 25°. Available data on the ionization constants of the hydrates of aldehydes and ketones in water at 25° are listed in Table II. A

TABLE II
IONIZATION CONSTANTS OF HYDRATES OF ALDEHYDES AND KETONES IN WATER AT 25°

| Compd | p$K$ |
|---|---|
| $(CH_3)_2CHCH(OH)_2$ | 13.77[a] |
| $CH_3CH(OH)_2$ | 13.57[a] |
| $CH_2(OH)_2$ | 13.27[a] |
| $CF_3CH(OH)_2$ | 10.20[b] |
| $CCl_3CH(OH)_2$ | 10.04[a] |
| $C_6H_5C(OH)_2CF_3$ | 10.00[a] |
| $(F_2CH)_2C(OH)_2$ | 8.79[c] |
| $(CF_3)_2C(OH)_2$ | 6.58[c] |

[a] Reference 17. [b] R. Stewart and M. M. Mocek, *Can. J. Chem.*, 41, 1160 (1963). [c] W. J. Middleton and R. V. Lindsey, Jr., *J. Amer. Chem. Soc.*, 86, 4948 (1964).

plot of the p$K_a$ values for RR'C(OH)$_2$ compounds *vs.* $\sigma^*_R + \sigma^*_{R'}$ (Figure 3) gives a straight line from which the points for the hydrates of formaldehyde and hexafluoroacetone deviate somewhat.[15] A least-squares treatment, neglecting the two deviant points, gave eq 5 for this line. Bell obtained a similar value

$$pK_a = 14.19 - 1.315(\sigma^*_R + \sigma^*_{R'}) \quad (5)$$

(1.4) for $\rho^*$ using data on four compounds.[17] From eq 5 a p$K$ value of 11.77 may be calculated for phenylpropargylaldehyde hydrate, in reasonable agreement with the value we have obtained.

An approximate value for $k_2$ may be obtained by estimating $K_2$. From the value determined for p$K_1$, an acid-weakening factor of $10^{4.4}$ for a negative charge two atoms away calculated by the method of Branch and Calvin,[18] and a statistical factor of four, a p$K_2$ value of 2.8 may be calculated. This gives values of $1.58 \times 10^{-3}$ $M^{-1}$ and 190 sec$^{-1}$ for $K_2$ and $k_2$, respectively.

As an alternative to part of mechanism 1, it might be suggested that the part of the reaction involving two hydroxide ions has as its rate-controlling step attack of hydroxide ions on POH$^-$, either to give PO$^{2-}$, which is cleaved faster than it is reprotonated, or to give formate ions and phenylacetylide anions in a concerted $\beta$ elimination. Such mechanisms give a rate equation identical with eq 2, except the term $k_2K_2$ is replaced by $k_2'$, the rate constant for attack of hydroxide ions on POH$^-$. Hence, if either of these alternative mechanisms is correct, $k_2'$ has the value 0.299 $M^{-1}$ sec$^{-1}$. Since the equilibrium governed by $K_2$ is a proton transfer between oxygen atoms in which the equilibrium lies to the left, the work of Eigen and others[19] shows that the reverse rate constant must

(15) The value of $\sigma^*_{CF_3}$ used in this plot was $2.8\sigma^*_{CF_3CH_2}$, or 2.58. The other values were from Taft's collection.[16]

(16) R. W. Taft, Jr., "Steric Effects in Organic Chemistry," M. S. Newman, Ed., Wiley, New York, N. Y., 1956, Chapter 13.

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(19) M. Eigen, *Angew. Chem., Int. Ed. Engl.*, 3, 1 (1964).

be about $10^{10}$ $M^{-1}$ sec$^{-1}$. Therefore, the rate constant for the simple deprotonation of $POH^-$ by hydroxide ions must be about $10^{8.9}$ $M^{-1}$ sec$^{-1}$. This exceeds the value 0.299 $M^{-1}$ sec$^{-1}$ by an amount that is much larger than the uncertainty of the estimate. Hence the simple deprotonation of $POH^-$ by hydroxide ions cannot be the rate-controlling step of that part of the reaction involving two hydroxide ions.

## Experimental Section

**Phenylpropargylaldehyde Solutions.**—In order to prevent the formation of the yellow-to-red color that occurs with neat aldehyde at room temperature, the phenylpropargylaldehyde was distilled *in vacuo* into a receiver at −78° just before preparing stock solutions. About 0.01 $M$ standard solutions of aldehyde in freshly purified 1,4-dioxane were prepared gravimetrically shortly after the aldehyde warmed to room temperature. All the operations were carried out under nitrogen. No decomposition of the aldehyde in the dioxane solutions could be detected over a period of several days. In 99% water–1% dioxane the aldehyde was found to have absorption maxima at 285.5, 247.5, and 236.5 nm with extinction coefficients of 10,040, 9250, and 9530 $M^{-1}$ cm$^{-1}$, respectively.

**Kinetic Runs.**—In a typical run, 3 ml of a standard aqueous solution of sodium hydroxide containing enough sodium chloride to give an ionic strength of 0.10 $M$ was pipetted into both the sample and reference cells of a Cary spectrophotometer, Model 14. After the solutions had reached thermal equilibrium at 35.2 ± 0.3°, 14 μl (20 μl in some runs) of a standard solution of phenylpropargylaldehyde in dioxane was added at a recorded time. The cell was shaken and absorbance measurements at 288.5 nm were begun within ~30 sec. In a reaction that had proceeded to about 11 half-lives (about 99.95% reaction), the absorbance was found to be 0.023. This value was taken as $A_\infty$ for all the runs, and rate constants were calculated from the least-squares lines through plots of log $(A_t - A_\infty)$ *vs.* time. The slowest run was followed only to 24% reaction, but most of the other runs were followed to about 70% reaction. A typical kinetic plot is shown in Figure 4. The full uv spectrum of the solution that was run to 99.95% reaction showed maxima at 2343 and 2447 Å, with absorbances of 0.975 and 0.862, respectively, and shapes identical with those of authentic phenylacetylene, whose extinction coefficients were found to be 15,890 and 13,690 $M^{-1}$ cm$^{-1}$ at the respective wavelengths. These results correspond to a 95.9 ± 1.3% yield of phenylacetylene (assuming that sodium formate and any by-products absorb negligibly).

The kinetic runs were carried out under nitrogen. Concentrations used in the calculations were corrected for expansion from room temperature to 35.2°. In calculating $A_B$ by extrapolation to zero time, only the first few kinetic points were used.

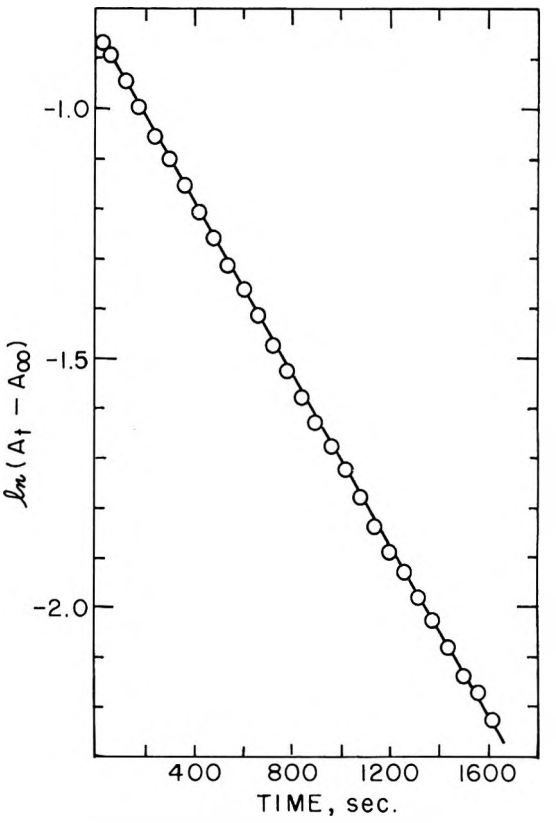


Figure 4.—Kinetic plot for cleavage of 6.48 × 10$^{-5}$ $M$ phenylpropargylaldehyde by 0.00932 $M$ sodium hydroxide in water at 35.2°.

**Rate of Hydration of Phenylpropargylaldehyde.**—When 15-μl samples of 6.72 × 10$^{-3}$ $M$ solutions of phenylpropargylaldehyde in dioxane were injected into 3.00 ml of 0.100 $M$ aqueous sodium chloride at 35° and ultraviolet measurements begun within 10 sec, the hydration reaction appeared to be essentially at equilibrium. The same technique at about 5° gave rate constants of 0.03 ± 0.01 sec$^{-1}$ that are unreliable because of condensation on the cells and other complications that also prevented a reliable determination of the extinction coefficient of the free aldehyde by extrapolation to zero time.

**Registry No.**—Phenylpropargylaldehyde, 2579-22-8; sodium hydroxide, 1310-73-2.

# The Effects of Aliphatic and Cycloalkyl Substituents on a Ring–Chain Tautomeric Equilibrium[1]

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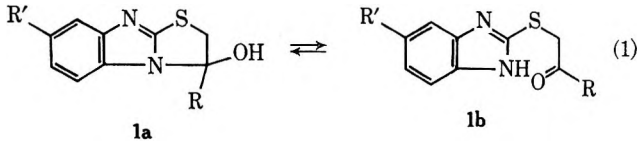
Reaction of 2-mercaptobenzimidazole with a variety of α-halo ketones ($RCOCH_2X$, where R = alkyl or cycloalkyl and X = bromine or chlorine) gave products capable of exhibiting carbinolamine–amino ketone ring–chain tautomerism. The tautomeric equilibrium, determined by infrared and nuclear magnetic resonance spectral measurements, is controlled by the inductive effect of the R group for all but the most bulky nonconjugative substituents. Only the chain tautomer exists in the solid state or solution when the substituent is capable of conjugating with the carbonyl group.

Jones,[4] in a review article published in 1963, noted that there were few examples of ring–chain tautomerism where both ring and chain tautomers were present in solution. The past 7 years, however, have witnessed the appearance of numerous publications describing systems exhibiting dynamic ring–chain tautomerism including: 1,3,4-thiadiazolidine-2-thiones,[5] oxazolidines,[6] 1,3-oxazines,[7,8] 1,2,5-oxadiazines,[9] 1,3,4-oxadiazines,[10,11] pyrimido[4,5-*d*]pyrimidines,[12] thiazolo[3,2-*a*]-benzimidazoles,[13] lactones,[14] and azidopurines.[15] Several of these papers have reported investigations of inductive and resonance effects of various aromatic substituents on the position of the tautomeric equilibrium.[6,7,12,14,15] In addition, Dorman[10] has shown that 2-alkyl-4,5-dimethyl-6-phenyltetrahydro-2*H*-1,3,4-oxadiazines exist in equilibrium with their γ-hydroxyhydrazone chain tautomers, the proportion of chain form increasing with an increase in the size of the 2-alkyl group. There have been no systematic studies, to our knowledge, of the effect of various simple aliphatic and cycloalkyl substituents on the position of a ring–chain tautomeric equilibrium. This paper reports on such a study our intention being to determine what factors (steric or inductive or both) control the equilibrium process.

The system chosen for investigation was 3-hydroxy-3-substituted 2,3-dihydrothiazolo[3,2-*a*]benzimidazole



**1a** ⇌ **1b** (1)

(**1a**, R′ = H) which can exist in equilibrium with its open-chain amino ketone tautomer **1b** (R′ = H). The nuclear magnetic resonance spectra (nmr) of most derivatives of this system are very simple with the signal for the methylene protons of **1b** appearing as a singlet while that given by **1a** is an AB quartet.[16] The infrared spectra (ir) are also generally easy to interpret (indicating presence or absence of C=O, N–H, O–H, and C–O stretching). The parent heterocycle (**1**, R = R′ = H) exists solely as the cyclic carbinolamine both in the solid state and in solution. Solid-state infrared studies have shown 3-hydroxy-3-methyl-2,3-dihydrothiazolo[3,2-*a*]benzimidazole to exist as the ring tautomer (**1a**, R = $CH_3$, R′ = H), but nmr spectra of dimethyl sulfoxide-$d_6$ (DMSO-$d_6$) solutions indicate a 1:2 mixture of **1a** and the chain tautomer **1b**, respectively.[13]

## Experimental Section

**General Comments.**—Melting points were determined on a Fisher-Johns or Gallenkamp apparatus and are uncorrected. Elemental analyses were carried out by A. Bernhardt, 5251 Elbach Uber Engelskirchen, Fritz-Pregl-Strasse, West Germany, and Galbraith Laboratories, Inc., Knoxville, Tenn. Infrared spectra were recorded on Perkin-Elmer 457 and 521 spectrophotometers; the wavelength readings were calibrated with a polystyrene film. Nmr spectra were determined on a Varian A-60 or HA-100 spectrophotometer. Tetramethylsilane was used as internal standard.

**α-Halo Ketones.**—Chloro-2-propanone, 1,3-dichloro-2-propanone, 1-adamantyl bromomethyl ketone, 1-bromo-3,3,3-trifluoro-2-propanone, and ethyl bromopyruvate were commercial products. We are grateful to Professor V. Rosnati of the Istituto di Chimica Industriale dell'Universita di Milano for a generous gift of 1-chloro-3-phenylmercapto-2-propanone.

1-Bromo-2-butanone was prepared by bromination of 2-butanone in aqueous solution in the presence of potassium chlorate.[17] 1-Bromo-3,3-dimethyl-2-butanone[18] was obtained by bromination of pinacolone at room temperature. Chlorination of methyl cyclopropyl ketone according to Kosower and coworkers[19] gave chloromethyl cyclopropyl ketone. In our hands, chlorination of methyl isopropyl ketone with sulfuryl chloride failed to give any 1-chloro-3-methyl-2-butanone.[20] The desired chloro ketone could be obtained, however, by reaction of isobutyryl chloride with diazomethane.[21] Also prepared by diazomethane treatment of acid chlorides were chloromethyl cyclohexyl ketone,[22] 1-chloro-

(1) For a preliminary communication of this work, see H. Alper, *Chem. Commun.*, 383 (1970).

(2) Author to whom inquiries should be addressed.

(3) Undergraduate Research Participant, State University of New York at Binghamton, 1970.

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4,4-dimethyl-2-pentanone,[23] 1,1,1,3-tetrachloro-2-propanone,[24] and 1-chloro-3,3-diphenyl-2-propanone.[25]

**General Procedure for Reaction of 2-Mercaptobenzimidazole with α-Halo Ketones.**—An equimolar mixture of 2-mercaptobenzimidazole (recrystallized from 95% ethanol) and α-halo ketone (8–30 mmol) in 2-butanone (40–200 ml) was refluxed with stirring for 2–8 hr. The reaction mixture was cooled and the precipitated hydrohalide salt of **1** isolated by suction filtration. The salt was then converted to the free base by (a) dissolving the salt in water and basifying with a saturated sodium bicarbonate solution, or by (b) suspending the salt in 95% ethanol, heating the mixture to reflux, adding triethylamine, and pouring the resulting basic solution into 4–6 vol of water. The latter procedure was used for those salts which were insoluble in water. Recrystallization from acetonitrile, aqueous ethanol, or acetone gave pure **1**. The melting points and analyses of these compounds are listed in Table I.

TABLE I

CONDENSATION PRODUCTS FROM REACTIONS OF 2-MERCAPTOBENZIMIDAZOLE AND 2-MERCAPTO-5-NITROBENZIMIDAZOLE WITH α-HALO KETONES

| 1a ⇄ 1b | | Registry no. | | | |
|---|---|---|---|---|---|
| R | R′ | 1a | 1b | Mp, °C | Molecular formula[a] |
| $CH_2CH_3$ | H | 27784-37-8 | 27784-38-9 | 94.0–96.0 | $C_{11}H_{12}N_2OS$ |
| $CH(CH_3)_2$ | H | 27784-39-0 | 27784-40-3 | 109.0–111.0 | $C_{12}H_{14}N_2OS$ |
| $C(CH_3)_3$ | H | 27784-41-4 | 26559-22-8 | 104.5–105.5 | $C_{13}H_{16}N_2OS$ |
| $CH_2C(CH_3)_3$ | H | 27784-43-6 | 27932-06-5 | 116.0–117.0 | $C_{14}H_{18}N_2OS$ |
| $CH_2SC_6H_5$ | H | 27784-44-7 | 27784-45-8 | 138.0–139.0 dec | $C_{16}H_{14}N_2OS_2$ |
| $CH_2Cl$ | H | 27784-46-9 | 27784-47-0 | 181.0–184.0 dec | $C_{10}H_9ClN_2OS$ |
| $CH(C_6H_5)_2$ | H | 27784-48-1 | 27784-49-2 | 150.0–152.0 | $C_{22}H_{18}N_2OS$ |
| $CF_3$ | H | 26559-21-7 | 27784-51-6 | 138.0–139.0 | $C_{10}H_7F_3N_2OS$ |
| $COOC_2H_5$ | H | 27784-52-7 | 27784-53-8 | 124.0–125.5 | $C_{12}H_{12}N_2O_3S$ |
| Cyclopropyl | H | 27784-54-9 | 27784-55-0 | 131.0–132.0 | $C_{12}H_{12}N_2OS$ |
| Cyclohexyl | H | 27784-56-1 | 27784-57-2 | 155.0–156.0 | $C_{15}H_{18}N_2OS$ |
| 1-Adamantyl | H | 27784-58-3 | 27932-07-6 | 188.5–190.5 | $C_{19}H_{22}N_2OS$ |
| $CH_3$ | $NO_2$ | 27784-59-4 | 27784-60-7 | 122.0–124.0 | $C_{10}H_9N_3O_3S$ |
| $CF_3$ | $NO_2$ | 27784-61-8 | 27784-62-9 | 206.5–208.5 | $C_{10}H_6F_3N_3O_3S$ |

[a] All compounds except one gave C, H, and N analysis within 0.4 of the calculated values and the analytical data were made available to the editors and referees. The exception is $C_{10}H_9N_3O_3S$. Calcd: C, 47.80; H, 3.62; N, 16.73. Found: C, 48.27; H, 3.99; N, 16.53.

The same general procedure was applied to the reaction of 2-mercapto-5-nitrobenzimidazole (recrystallized from 50% aqueous ethanol) with chloro-2-propanone and 1-bromo-3,3,3-trifluoro-2-propanone. The melting points and analyses of the products are given in Table I.

## Results and Discussion

Condensation of 2-mercaptobenzimidazole with a series of α-halo ketones in 2-butanone gave **1** (R′ = H; R groups listed in Table I). The position of condensation of 2-mercaptobenzimidazole and α-halocarbonyl compounds has been established as occurring at the mercapto group.[13,26] The infrared spectra were recorded as potassium bromide disks and in chloroform or dimethyl sulfoxide solutions (Table II). The spectra of the KBr disks indicate the presence of either tautomer **1a** or **1b** but not both as ring–chain tautomerism occurs only in solution or in the liquid or gaseous states. Tautomer **1a** shows broad absorption in the region of 3300–2500 $cm^{-1}$ due to the O–H stretch of the hydrogen-bonded hydroxyl group and a sharp, usually intense band in the region of 1182–1068 $cm^{-1}$ for the C–O stretch of a tertiary alcohol. The spectrum of the amino ketone tautomer **1b** also exhibits broad absorption in the region of 3200–2500 $cm^{-1}$ due to the hydrogen-bonded N–H stretch but in addition a strong band, due to carbonyl stretching, appears at 1747–1693 $cm^{-1}$. We have observed, in all instances, that the occurrence of tautomer **1b** in the solid state indicates that this will be the *only* tautomer present in solution. If the carbinolamine **1a** is the tautomer present in the solid state, then solution studies will show the presence of only tautomer **1a** or a mixture of ring and chain tautomers. Similar ir bands occur for **1a** and **1b** in both chloroform and dimethyl sulfoxide with the appearance of free N–H or O–H stretching absorptions in addition to, or in place of, the corresponding hydrogen-bonded stretch.

The nmr spectra were recorded for DMSO-$d_6$ solutions of **1**. Unfortunately, any study of solvent effects on the equilibrium **1a** ⇄ **1b** is generally limited by low solubility of **1** in less polar solvents [certain derivatives were sufficiently soluble in deuteriochloroform ($CDCl_3$) for nmr purposes]. The position of the singlet for the methylene protons of **1b** and the center of the AB quartet for the corresponding protons of **1a** are given in Table II ($J_{AB}$ = 11–13 cps). The relative amounts of ring and chain tautomers, where applicable, were evaluated by careful and repeated integration of the appropriate nmr signals of the two forms. The results obtained for the series, methyl, ethyl, isopropyl, and *tert*-butyl (Table II), indicate that the equilibrium shifts to the chain form with increasing steric bulk of R.[27] However, the data could also be interpreted as the chain tautomer being more favored as the electron-donating ability of the alkyl group increases. Alternatively, the equilibrium may be controlled by both inductive and steric effects. Results obtained with some of the other substituents demonstrate the importance of inductive effects in these systems.

The group, $CH_2SC_6H_5$, probably has a steric effect[28] similar to that of an isopropyl group.[29] Consequently, these should be approximately 90% **1b** (R = $CH_2S$-$C_6H_5$, R′ = H) present in DMSO-$d_6$ solution if the tautomerism is governed by steric effects. However, the $CH_2SC_6H_5$ group is electron attracting thus favoring an increased proportion of ring tautomer (41% observed). Similarly, the steric effect of a trifluoromethyl group is between that of the isopropyl and *tert*-butyl groups indicating that the chain form should be predominant for **1** (R = $CF_3$, R′ = H). The latter, in fact, exists only as the ring tautomer in the solid state and in chloroform or DMSO solution in agreement with its powerful electron-withdrawing ability. The cyclohexyl group, although sterically larger than the isopropyl group, shows a small amount of ring form **1a** in solution in agreement with the smaller electron-donating properties of a cyclohexyl compared to an isopropyl group. The chloromethyl group is sterically not much larger than a methyl substituent but has considerable electron-withdrawing character.[28] As another illustration of the extent of inductive control of the tautomeric equilib-

(23) F. Asinger and F. Gentz, *Monatsh. Chem.*, **96**, 1461 (1965).

(24) Ch. Grenacher, E. Usteri, and M. Geiger, *Helv. Chim. Acta*, **32**, 703 (1949).

(25) C. L. Stevens and A. E. Sherr, *J. Org. Chem.*, **17**, 1228 (1952).

(26) H. Ogura, T. Itoh, and K. Kikuchi, *J. Heterocycl. Chem.*, **6**, 797 (1969).

(27) The proportion of chain tautomer for **1** (R = $CH_3$, R′ = H) was redetermined and found to be slightly less than the originally reported value of 66.7%.[13] We had hoped to be able to study the compound **1** (R = $CD_3$, R′ = H) in order to determine deuterium isotope effects. Reaction of 1-chloro-3,3,3-trideuterio-2-propanone with 2-mercaptobenzimidazole gave the hydrochloride salt of **1**. However, basification with triethylamine in dry acetonitrile resulted in H–D exchange.

(28) R. W. Taft, Jr., "Steric Effects in Organic Chemistry," M. S. Newman, Ed., Wiley, New York, N. Y., 1956, Chapter 13.

(29) Based on a comparison of steric substituent constants for $CH_3OCH_2$, $CH_3SCH_2$, and $C_6H_5OCH_2$.[28]

TABLE II

PERTINENT IR AND NMR DATA AND RING–CHAIN TAUTOMERIC RATIOS FOR 1a ⇄ 1b

| 1a ⇄ 1b | | Ir[a] | | Nmr[d] | | | |
|---|---|---|---|---|---|---|---|
| R | R′ | KBr, $\nu$[b] | Solution,[c] $\nu$ | Solvent[e] | Chain, $SCH_2$ | Ring, $SCH_2$ ($J$)[f] | % chain |
| $CH_3$ | H | | | | | | 65[g] |
| $CH_2CH_3$ | H | 3200–2700 (OH), 1081 (CO) | C, 3660 (OH, free), 3545 (OH, bonded), 3454 (NH, free), 3300–3200 (NH, bonded), 1710 (C=O), 1110 (CO) | D | 4.33 | 3.92 (12) | 71 |
| $CH(CH_3)_2$ | H | 3300–2700 (OH), 1068 (CO) | D, 3200–2780 (OH, NH), 1705 (C=O) | D | 4.44 | 3.83 (12) | 90 |
| $C(CH_3)_3$ | H | 3100–2600 (OH), 1712 (C=O) | C, 3455 (NH, free), 3307 (NH, bonded), 1705 (C=O) | C | 4.45 | | 100 |
| | | | | D | 4.62 | | 100 |
| $CH_2C(CH_3)_3$ | H | 3100–2600 (NH), 1710 (C=O) | C, 3450 (NH, free), 3320–3160 (NH, bonded), 1712 (C=O) | D | 4.30 | | 100 |
| $CH_2SC_6H_5$ | H | 3100–2600 (OH), 1129 (CO) | C, 3670 (OH, free), 3561 (OH, bonded), 3456 (NH, free), 3300–3100 (NH, bonded), 1719 (C=O), 1126 (CO) | D | 4.52 | 4.08 (11) | 59 |
| $CH_2Cl$ | H | 3200–2600 (OH), 1132 (CO) | A, 3450 (NH, free), 3140–2780 (OH, NH, bonded), 1720 (C=O), 1138 (CO) | *h* | | | |
| $CH(C_6H_5)_2$ | H | 3300–2700 (NH), 1718 (C=O) | C, 3450 (NH, free), 3305 (NH, bonded), 1720 (C=O) | C | 4.15 | | 100 |
| | | | | D | 4.45 | | 100 |
| $CF_3$ | H | 3100–2550 (OH), 1182 (CO) | C, 3100–2600 (OH), 1188 (CO) | D | | 4.38 (13) | 0 |
| $COOC_2H_5$ | H | 3100–2600 (NH), 1747 (C=O) | C, 3480 (NH, free), 3300–3150 (NH, bonded), 1740 (C=O) | C | 4.09 | | 100 |
| | | | | D | 4.17 | | 100 |
| Cyclopropyl | H | 3100–2560 (NH), 1693 (C=O) | C, 3460 (NH, free), 3290 (NH, bonded), 1698 (C=O) | D | 4.47 | | 100 |
| Cyclohexyl | H | 3200–2700 (OH), 1071 (CO) | D, 3465 (NH, free), 3300–2800 (OH, NH, bonded), 1705 (C=O) | D | 4.42 | 3.86 (12) | 85 |
| 1-Adamantyl | H | 3100–2600 (NH), 1705 (C=O) | C, 3445, (NH, free), 3300–3160 (NH, bonded), 1685 (C=O) | C | 4.41 | | 100 |
| | | | | D | 4.56 | | 100 |
| $CH_3$ | $NO_2$ | 3200–2700 (OH), 1082 (CO) | D, 3420 (NH, free), 3200–2660 (OH, NH, bonded), 1710 (C=O) | D | 4.44 | 3.04 (12) | 79 |
| $CF_3$ | $NO_2$ | 3200–2600 (OH), 1193 (CO) | D, 3200–2600 (OH), 1198 (CO) | D | | 4.42 (12) | 0 |

[a] Data given in units of $cm^{-1}$. [b] Type of stretching vibration. [c] A = acetonitrile, C = chloroform, D = dimethyl sulfoxide. Reliable C–O stretching values could not be obtained in dimethyl sulfoxide due to background solvent absorption in the C–O stretching region. [d] Chemical shifts in ppm. Spectra measured within 10 min of preparing the solutions do not change when measured again 24 hr later [except for **1** (R = $CH_2Cl$, R′ = H)]. [e] C = chloroform-*d*, D = dimethyl sulfoxide-$d_6$. [f] Coupling constants in cycles per second. [g] Previously reported as 66.7% with identical ir and nmr data (ref 13). [h] In both DMSO-$d_6$ and acetonitrile-$d_3$, the signals for the protons of the $-SCH_2-$ group of the ring and chain tautomers and the $-CH_2Cl$ group of the chain tautomer appeared in the region of 4.0–4.5 ppm and could not be reliably assigned.

rium, infrared studies indicate the ring tautomer **1a** (R = $CH_2Cl$, R′ = H) to be the major tautomer in solution (acetonitrile). Unfortunately, proton magnetic resonance spectra did not afford a value for the ring–chain tautomer ratio for **1** (R = $CH_2Cl$, R′ = H) because the signals for the $-SCH_2-$ of the ring and chain tautomers and for the $-CH_2Cl$ of the chain tautomer were not well separated in either DMSO-$d_6$ or acetonitrile-$d_3$. Furthermore, the heterocycle reacted with DMSO-$d_6$.[30] Attempts to prepare **1** (R = $CCl_3$, R′ = H) by reaction of 1,1,1,3-tetrachloro-2-propanone with 2-mercaptobenzimidazole failed as reaction of the trichloromethyl group occurred on basification of the hydrochloride salt of **1** (R = $CCl_3$, R′ = H) with triethylamine in 95% ethanol.

An exception to the above results occurs for **1** [R = $CH_2C(CH_3)_3$, R′ = H]. The steric substituent constant of the neopentyl group is more negative than the value reported for the *tert*-butyl group while the electron-releasing ability of the latter is greater than that of the neopentyl group.[28] Hence, if inductive effects alone controlled the equilibrium, one would expect approximately 10–15% ring tautomer to be present in solution. The total absence of ring tautomer may be due to the steric effect becoming substantial for groups larger than *tert*-butyl. In this case, severe repulsion between one of the substituent methyl groups and a hydrogen of the $-SCH_2-$ group may occur in the ring form. This steric strain is relieved, of course, in the amino ketone tautomer. The diphenylmethyl group **1** [R = $CH(C_6H_5)_2$, R′ = H] is essentially the same size as the neopentyl group[28] and gives the same results as neopentyl although it has greater electron-withdrawing properties. Weber[31] has reported $\sigma^n$ values for *m*-1-adamantyl and *p*-1-adamantyl groups of −0.121 and −0.131, respectively, from which one can estimate the $\sigma^*$ value of 1-adamantyl to be roughly comparable to that of a methyl group. No steric substituent constant for 1-adamantyl has been published, but it is reasonable to assume that the steric effect of this group is substantial, and thus **1** (R = 1-adamantyl,

(30) The reaction of a number of α-halo ketones with DMSO to form α-keto aldehydes has been reported: N. Kornblum, J. W. Powers, G. J. Anderson, W. J. Jones, H. O. Larson, O. Levand, and W. M. Weaver, *J. Amer. Chem. Soc.*, **79**, 6562 (1957). The tautomer **1b** (R = $CH_2Cl$, R′ = H) also gives the keto aldehyde (a singlet at 9.67 ppm due to the aldehydic proton begins to appear within a few minutes after dissolving the heterocycle in DMSO-$d_6$).

(31) J. Weber, Dissertation, Aachen, Germany, 1965, p 51. We thank Professor P. v. R. Schleyer for informing us of these data.

R′ = H) exists solely as the chain tautomer in the solid state and in solution.

The results for the cyclopropyl substituent appear surprising on first inspection. Cyclopropyl is both sterically small and inductively slightly electron withdrawing,[32] and thus one would predict a ring–chain tautomer ratio similar to that for **1** (R = $CH_3$, R′ = H). However, the conjugative ability of a cyclopropyl group is well documented.[33] Cyclopropyl–carbonyl conjugation in the chain form is destroyed on forming the carbinolamine and thus **1** (R = cyclopropyl, R′ = H) exists solely as the chain tautomer both in the solid state and in solution, conjugation being the driving force for chain tautomer stabilization. Similarly, **1** (R = $COOC_2H_5$, R′ = H) exists only as the amino ketone in solution. These results are further supported by earlier work[34] on **1** [R = *p*-$XC_6H_4$– (where X = H, Cl, Br, $NO_2$, $OCH_3$), R′ = H] where, in all cases, **1b** was the only tautomer present in solution. Here, the aromatic ring can conjugate with the carbonyl group of the amino ketone.

The results previously obtained for **1** (R = R′ = H)[13] cannot be applied to the study reported herein since an aldehyde such as **1b** is substantially more susceptible to condensation with an amino group than a ketone, thus giving the ring tautomer **1a**.

It was also of interest to determine whether or not a strongly electron-attracting group on the benzene ring would have an effect on the ring–chain tautomeric equilibrium; *i.e.*, would a compound existing solely as the ring tautomer for **1** (R′ = H) be a mixture of tautomers when R′ = $NO_2$? 2-Mercapto-5-nitrobenzimidazole was treated with chloro-2-propanone and 1-bromo-3,3,3-trifluoro-2-propanone to give **1** (R = $CH_3$ or $CF_3$, R′ = $NO_2$). Consider **2a** and **2b** as resonance contributors to **1a**.[35] If **2b** makes an important contribution to **1a**, then the positive nitrogen of **2b** would favor opening of the thiazolidine ring. Table II shows that for **1** (R = $CH_3$, R′ = $NO_2$), the presence of the nitro group exerts a modest shift to the chain tautomer from **1** (R = $CH_3$, R′ = H). However, the presence of a nitro group on the benzene ring has no effect on the tautomeric equilibrium of the trifluoromethyl compound, thereby indicating the powerful inductive control by the substituent in the 3 position.

In summary, the results obtained from this investigation lead to the following conclusions: (a) for R groups of steric bulk up to *tert*-butyl, ring–chain tautomerism of **1** is controlled predominantly, if not exclusively, by the inductive effects of the substituent (*e.g.*, if R is electron releasing, the carbonyl carbon of **1b** becomes more negative thus making it less susceptible to ring formation by reaction with the amino group; the reverse argument applies when R is electron withdrawing); (b) for very bulky groups, *e.g.*, neopentyl and diphenylmethyl, steric effects become important; (c) any group having conjugative properties will result in the heterocyclo existing solely as **1b**.

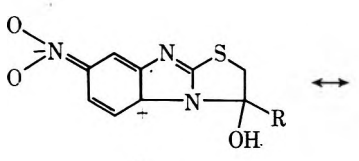
**Acknowledgment.**—Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

(32) Y. E. Rhodes, Fourteenth Annual Report on Research under Sponsorship of the Petroleum Research Fund, 1969, p 70.

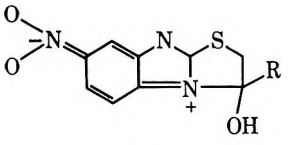
(33) (a) W. G. Dauben and G. H. Berezin, *J. Amer. Chem. Soc.*, **89**, 3449 (1967); (b) J. C. Bourmanne, G. Leroy, and J. Weiler, *Tetrahedron*, **26**, 2281 (1970).

(34) H. Alper and A. E. Alper, *J. Org. Chem.*, **35**, 835 (1970).

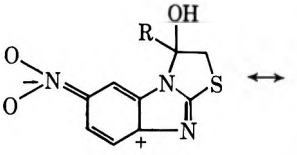
(35) The nitrogen on the carbon atom meta to the nitro group may also be involved in the tautomeric process but, in any case, the same arguments apply as per **2a** ↔ **2b**.



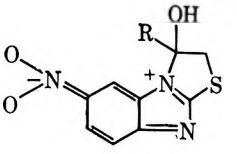
**2a**



**2b**



**3a**



**3b**

# On the Mechanism of 1-Phenylcyclobutene Formation in the Reaction of 1-Chloro-4-bromo-1-phenyl-1-butene with Magnesium[1]

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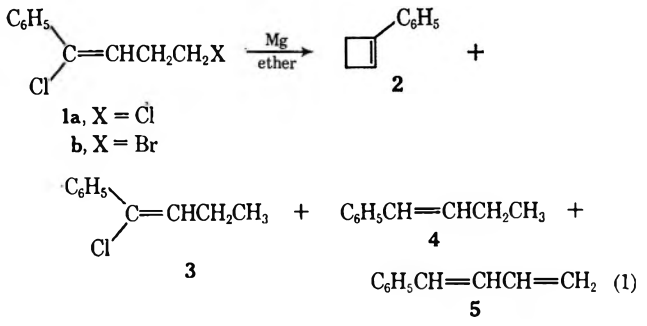
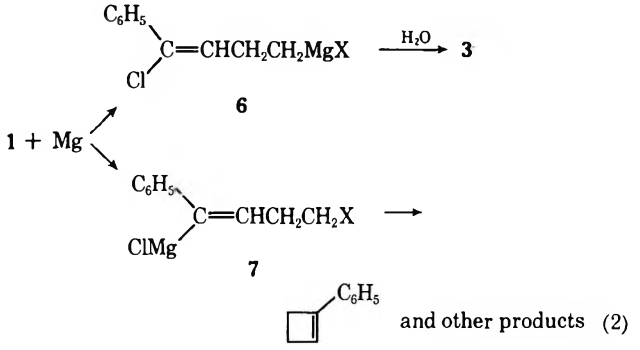
A mechanism previously proposed for formation of 1-phenylcyclobutene from the reaction of 1,4-dihalo-1-phenyl-1-butene is shown to be unacceptable, since a proposed intermediate Grignard reagent (6) is stable under the reaction conditions. Among several possibilities considered, a radical cyclization mechanism appears to be the most likely.

In 1965, Newman and Kaugars[2] reported that 1,4-dichloro-1-phenyl-1-butene (**1a**) reacts with magnesium in ether to produce a product mixture including 1-phenylcyclobutene (**2**), *trans*-1-chloro-1-phenyl-1-butene (**3**), *cis*- and *trans*-1-phenyl-1-butene (**4**), and 1-phenyl-1,3-butadiene (**5**) (eq 1). They proposed the

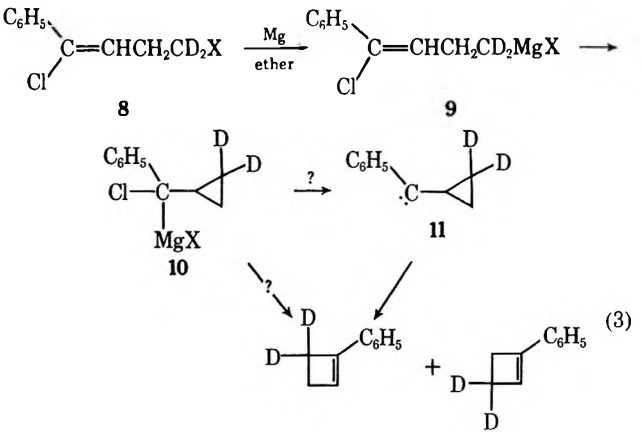


mechanism shown in eq 2. Largely because **2** did not



increase at the expense of **3** with longer reaction times, they concluded that, once formed, primary Grignard reagent **6** does not undergo any further reaction until hydrolysis. Then, other products were thought to be formed from a vinylic Grignard reagent **7**. The phenylcyclobutene may be explained by an internal nucleophilic displacement in **7**. From yields of products, the rather surprising conclusion was reached that the vinylic Grignard reagent **7** is formed more rapidly than primary Grignard **6**.

More recently, Fry and Moore[3] reinvestigated this reaction. They found by a deuterium labeling experiment that the phenylcyclobutene is formed by a pathway that results in scrambling of carbon atoms 3 and 4. A pathway including intermediate carbenoid **10** or carbene **11** was proposed (eq 3). Experiments in our



laboratories, to be published shortly, suggest a similar mechanism for cyclobutene formation from 1-chloro-4-bromo-1-butene. However, this mechanism again raises the question as to why the yield of **3** remains constant. Fry and Moore were forced to conclude that a portion of the primary Grignard reagent **6** must abstract a proton from some other species present in the reaction mixture, in competition with its cyclizing rearrangement.

## Results and Discussion

At the time that the report of Fry and Moore was published, we were also engaged in a reinvestigation of the Newman and Kaugars reaction. Since alkyl bromides form Grignard reagents more readily than alkyl chlorides, the use of **1b** should almost exclusively produce primary Grignard reagent **6**. Hence, by the Newman–Kaugars mechanism, little or no phenylcyclobutene should have formed. However, it remained a major product of the reaction. A deuterium labeling experiment with **1b** had also led to results similar to those of Fry and Moore, again requiring a product-determining precursor for **2** with essential equivalence of carbon atoms 3 and 4.

However, additional results also exclude the mechanism of Fry and Moore. Specifically, primary Grignard reagent **6**, *once formed*, does not rearrange readily to phenylcyclobutene (**2**), and most of the 1-chloro-1-phenyl-1-butene (**3**) is formed only upon final hydrolysis of the reaction solution. Hence, **6** cannot be an intermediate in the formation of **2**. This crucial point is demonstrated by the following experiments, which are reported in detail in the Experimental Section.

A solution prepared from **1b** and magnesium in ether was found by examination of the nmr spectrum to con-

(1) We gratefully acknowledge support of the research by the Petroleum Research Fund, administered by the American Chemical Society.

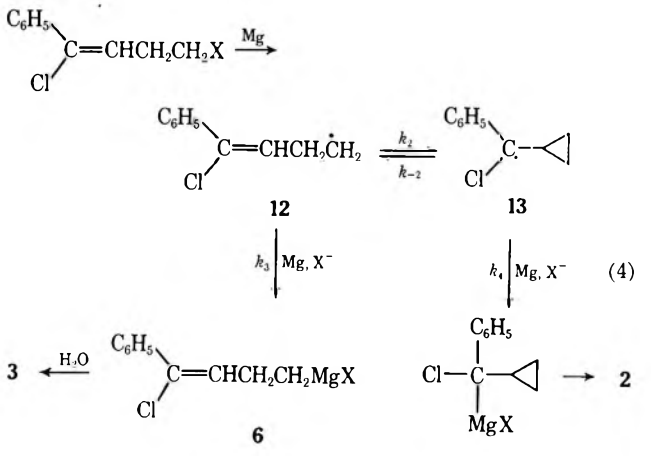
(2) M. S. Newman and G. Kaugars, *J. Org. Chem.*, **30**, 3295 (1965).

(3) A. J. Fry and R. H. Moore, *ibid.*, **33**, 425 (1968).

tain both phenylcyclobutene and a primary Grignard reagent. Extraction of the mixture with pentane removed the former but left the latter. Additional heating of the residual Grignard in ether solution produced more phenylcyclobutene, but only slowly at 115°. This is far too slow to account for its presence as a major product after only a few minutes' reflux in ether or tetrahydrofuran during preparation of the reagent. A portion of Grignard solution was hydrolyzed with deuterium oxide. The spectrum of 1-chloro-1-phenyl-1-butene isolated showed at least 75% (and probably nearly 95%) of one deuterium in the methyl group (smaller amounts of 1-phenyl-1-butene isolated from the same reaction were also largely monodeuterated in *both* 1 and 4 positions). Therefore, it may be safely concluded that the major Grignard reagent present was indeed **6**.

The present results, then, appear to exclude both the mechanisms of Newman and Kaugars[2] and of Fry and Moore.[3] Several previously unconsidered possibilities exist. First of all, it is possible that the mechanism is indeed a Grignard cyclization, as proposed by Fry and Moore, but that the cyclization involves an initially formed active Grignard reagent species, which is in part deactivated to ordinary Grignard. Bryce-Smith[4] notes that alkylation of aromatic rings by an initially formed, possibly unsolvated and monomeric, Grignard reagent occurs much more readily than with a pre-formed reagent in hydrocarbon solution. A similar species might be involved in the present instance. A related possibility is that a free carbanion, which might be an intermediate in Grignard formation, is the unstable, rearranging intermediate.

A second possibility is shown in eq 4. A free radical, likely an intermediate in the formation of Grignard reagent, may cyclize and subsequently be reduced by

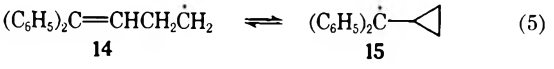



the magnesium. Similar mechanisms have been proposed for cyclizations from acetylenic halides upon reaction with magnesium[5] or alkyllithium[5,6] reagents. Reasonable routes to the other products reported by Newman and Kaugars, 1-phenyl-1-butene (**4**) and 1-phenyl-1,3-butadiene (**5**), might be hydrolysis of the di-Grignard from the dihalide and a dehydrohalogenation, respectively. The latter product was not identified in the present study.

(4) D. Bryce-Smith and B. J. Wakefield, *Tetrahedron Lett.*, 3295 (1964).
(5) J. L. Derocgue, U. Beisswenger, and M. Hanack, *ibid.*, 2149 (1969).
(6) H. R. Ward, *J. Amer. Chem. Soc.*, **89**, 5517 (1967).

In this mechanism, partition between the two pathways may occur at either of two stages. First, if equilibrium between radicals **12** and **13** is attained, then the relative yields of products by the two pathways will depend upon the equilibrium constant for their interconversion and the relative rates of further reduction of the two radicals ($k_3$ and $k_4$). On the other hand, if $k_4 \gg k_{-2}$, $k_2$ is effectively irreversible. Then the product-determining partition is between $k_2$ and $k_3$.

There is substantial precedent for rapid equilibrium cyclization of 3-buten-1-yl radicals. Roberts and coworkers have found that the rearrangement shown in eq 5 is extremely rapid.[7] The relative yields of the hydrogen-abstraction products of the two radicals at 125° are independent of the concentration of the very effective hydrogen atom donor, triethyltin hydride. Equilibration of the methylene groups of **14** also was complete. With triethyltin hydride at 125°, the ratio of products derived from **14** and **15** was about 14:1.



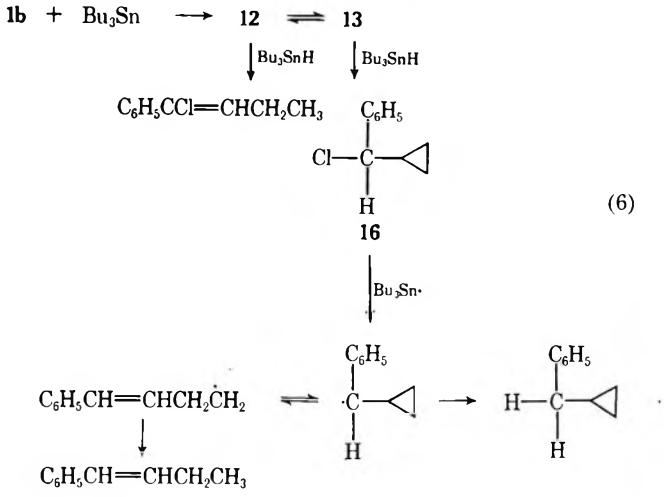

The Grignard reagent corresponding to **14** reacts with oxygen or cobaltous chloride, by mechanisms believed to involve free radicals, to yield 66 and 12% of cyclized products, respectively.[8] Since the new bond formed by **14** should be stronger than the one formed by **15**, it is probable that **14** reacts more rapidly than **15**. Therefore, though there is no quantitative basis for an estimate of the equilibrium constant, **15** is surely an important, if not the major, constituent. While the chlorine atom in radical **13** should not stabilize the radical as effectively as the second phenyl in **15**, it is still reasonable that substantial amounts of **13** may be present at equilibrium. It is also possible that electron transfer to **13** may be particularly enhanced by the conjugated $\pi$-orbital system. In other related studies, smaller amounts of cyclized products appear to be formed from substituted cyclopropylmethyl radicals lacking resonance stabilization.[9]

A consequence of rapid equilibration of radicals **12** and **13** is that the methylene groups in the labeled halide **8** should become scrambled in Grignard reagent **6**. The nmr spectrum of the solution formed from **8** with magnesium has a broadened singlet resonance at the position expected for the $CH_2Mg$ group, but it only accounts for 20% of two hydrogens. Therefore, we must conclude that radicals **12** and **13** do not attain equilibrium. Reduction of cyclized radical **13** occurs more rapidly than its ring opening, so that radical lifetimes during the Grignard formation stage must be quite short.

In order to learn more of the behavior of radical **12**, we have briefly studied the reaction of **1b** with tri-*n*-butyltin hydride. Cyclization of the radical before hydrogen abstraction from the hydride would lead to phenylcyclopropylmethyl chloride (**16**). This might

(7) T. A. Halgren, M. E. H. Howden, M. E. Medof, and J. D. Roberts, *ibid.*, **89**, 3051 (1967).
(8) M. E. Howden, A. Maercher, J. Burdon, and J. D. Roberts, *ibid.*, **88**, 1732 (1966).
(9) L. K. Montgomery and J. W. Matt, *ibid.*, **89**, 934 (1967).

be expected to undergo further reduction itself at a rate competitive with that of **1b** (eq 6). Evidence was

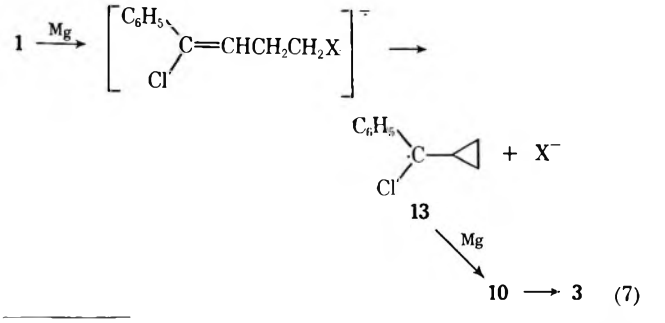


(6)

not found in the nmr spectrum for any cyclopropane products. However, 1-phenyl-1-butene was identified in quantities about 10–20% as much as the 1-chloro-1-phenyl-1-butene in a run with 1 *M* tri-*n*-butyltin hydride. Abstraction of a vinylic chlorine would not be expected to compete effectively with that of the primary bromine of **1b**; so we conclude that any 1-phenyl-1-butene present must have been formed by the route shown in eq 6. In control experiments, 1-phenyl-1-butene did not react at all under the conditions used, and 1-chloro-1-phenyl-1-butene appeared to produce some *n*-butylbenzene, by a route not presently understood, with very little 1-phenyl-1-butene.

Another reaction in which radical intermediates appear to be generated from alkyl halides is in the reaction with alkyllithium compounds.[10] When **1b** reacts with excess methyllithium in tetrahydrofuran, a vigorous reaction ensues, and 1-phenylcyclobutene is the only identified product. The same reaction with deuterated bromide produced 1-phenylcyclobutene with $C_3$ and $C_4$ scrambled. A mechanism may be proposed similar to that of eq 4, but with methyllithium rather than magnesium acting as the electron source. In a reaction between **1b** and butyllithium in hexane–ether, carried out in the probe of a T-60 nmr spectrometer, the CIDNP spectrum of 1-butene[10a] was detected. No enhanced absorption or emission attributable to phenylcyclobutene was observed, but the complexity of the product and the relatively small amount of phenylcyclobutene might be responsible for the lack of observation.

An alternative mechanism for formation of 1-phenylcyclobutene is shown in eq 7. In this instance, the



(7)

three-membered ring is generated in an irreversible step, an internal nucleophilic displacement of halide by the styrene-type radical anion. The entry to the possible equilibrium **12** ⇄ **13** now occurs through **13**. If ring opening of **13** is slow relative to its further reduction ($k_4 > k_{-2}$), then a competing normal Grignard formation would explain the observed result of limited scrambling of carbons in primary Grignard **6**. A similar mechanism could explain phenylcyclobutene formation in the methyllithium reaction. An argument against this mechanism is that both the internal displacement and Grignard formation should be affected by the change from bromine to chlorine in **1a**. It would be surprising that approximately the same balance of reaction paths should be found from both compounds.

Newman and Kaugars also found that 1,4-dichloro-1,2-diphenyl-1-butene yielded 90% of 1,2-diphenylcyclobutene on reaction with magnesium in ether. It is reasonable to presume that reaction follows a mechanism similar to the 1-phenylcyclobutene formation in the present study.

## Experimental Section

Nmr and ir spectra were run on a Varian Associates HA-100 spectrometer and a Beckman IR-8 spectrometer, respectively. Gas chromatography was carried out on an Aerograph A-90-P chromatograph, with columns of Dow Hi-vac silicone grease and QF-1 on Chromosorb P.

**1-Chloro-4-bromo-1-phenyl-1-butene.**—Aluminum chloride (40.7 g, 0.31 mol) was added in portions to 4-bromobutanoyl chloride (52.2 g, 0.30 mol) in 200 ml of benzene. The mixture was refluxed for 15 min more and poured over ice, and the organic product was worked up by distillation: bp 113–117° (0.4 mm); nmr ($CCl_4$) $\delta$ 2.20 (quintet, 2, $J$ = 6.5 Hz), 3.06 (t, 2, $J$ = 6.5 Hz), 3.45 (t, 2, $J$ = 6.5 Hz), 7.2 (m, 3), and 7.85 ppm (m, 2). The product (25 g, 0.11 mol) was allowed to react with phosphorus pentachloride (31.4 g, 0.15 mol) in 80 ml of carbon tetrachloride. The reaction mixture was poured over ice, and the product was taken up in benzene and distilled. After a forerun consisting largely of phosphorus oxychloride, a major product fraction, bp 105–110° (0.4 mm), was collected. Redistillation yielded a center cut: bp 111–112° (0.85 mm); nmr ($CCl_4$) $\delta$ 2.88 (q, 2, $J \sim 6.9$ Hz), 3.37 (t, 2, $J$ = 6.9 Hz, $CH_2Br$), 6.10 (t, 1, $J$ = 6.9 Hz, =CH), 7.15 (m, 3, aromatic), and 7.5 ppm (m, 2, aromatic). Chemical shifts were concentration dependent. A weak triplet at $\delta$ 5.9 may perhaps be attributed to a few per cent of the cis isomer.

*Anal.* Calcd for $C_{10}H_{10}ClBr$: C, 48.91; H, 4.11. Found: C, 49.17; H, 4.17.

**1-Chloro-4-bromo-1-phenyl-1-butene-*4,4-d*$_2$.**—4-Chloro-4-phenyl-3-buten-1-ol-*1,1-d*$_2$ was prepared in a manner similar to that described by Fry and Moore.[3] To the alcohol (3.2 g) and pyridine (0.6 g), phosphorus tribromide (1.4 g) was added dropwise with cooling on an ice bath. The mixture was heated 2 hr at 100°, hydrolized with water, extracted with ether, dried, and distilled. The nmr spectrum of the product was similar to that of the undeuterated compound, but the absorption at $\delta$ 2.9 was a broadened doublet ($J \cong 7$ Hz) and the absorption at $\delta$ 3.37 was completely absent (<2%). Triplets in the olefinic region at $\delta$ 6.12 and 5.92 ppm and an extra methylene absorption at $\delta$ 2.58 ppm indicated a mixture of isomers in a ratio of about 6:1. Undeuterated chloro bromide was prepared in this fashion with similar results.

**1-Phenyl-1-butene** was prepared as described by Newman and Kaugars. Cis and trans isomers were separated by gas chromatography, with the cis isomer eluted first: nmr ($CCl_4$) (cis) $\delta$ 1.09 (t, 3, $J$ = 7.5 Hz, $CH_3$), 2.33 (quintet, 2, $J \sim 7.5$ Hz, $CH_2$), 5.6 (triplet of doublets, 1, $J$ = 7.2 11.5 Hz, olefinic), 6.34 (d, 1, $J$ = 11.7 Hz, olefinic), and 7.19 ppm (s, 5, aromatic); (trans) $\delta$ 1.10 (t, 3, $J$ = 7.5 Hz, $CH_3$), 2.21 (m, 2, $J$ = 7.5, 5 Hz, $CH_2$), 6.2 (m, 2, olefinic), and 7.2 ppm (m, 5, aromatic).

**1-Chloro-1-phenyl-1-butene** was prepared as described by Newman and Kaugars. Cis and trans isomers were separated

(10) (a) H. R. Ward and R. G. Lawler, *J. Amer. Chem. Soc.*, **89**, 5518 (1967); (b) D. Bryce-Smith, *J. Chem. Soc.*, 1603 (1956).

by gas chromatography, with the cis isomer eluted first: nmr ($CCl_4$) (cis) $\delta$ 1.04 (t, 3, $J$ = 7.3 Hz, $CH_3$), 2.14 (quintet, 2, $J \sim 7.3$ Hz, $CH_2$), 5.88 (t, 1, $J$ = 7.5 Hz, olefinic), and 7.29 ppm (m, 5, aromatic); (trans) $\delta$ 1.12 (t, 3, $J$ = 7.5 Hz, $CH_3$), 2.40 (quintet, 2, $J \sim 7.2$ Hz, $CH_2$), 6.04 (t, 1, $J$ = 6.9 Hz, olefinic), and 7.2 and 7.5 ppm (m, 3 and 2, aromatic).

**1-Phenylcyclobutene.**—We are grateful for a sample received as a gift from Dr. M. McKinney of Marquette University: nmr ($CCl_4$) $\delta$ 2.47 (m, 2, $CH_2$), 2.73 (m, 2, $CH_2$), 6.17 (t, 1, olefinic, $J$ = 1.2 Hz), and 7.0–7.5 ppm (m, 5, aromatic). It was found that samples appeared to polymerize on standing for several days, and, on some occasions, isomerization or polymerization appeared to occur during gas chromatography. Since well-defined peaks were obtained, it appears that reaction may have occurred in the detector.

**Reaction of 1-Chloro-4-bromo-1-phenyl-1-butene with Magnesium.**—A Grignard reagent was prepared from 1.32 g (5.4 mmol) of the chloro bromide and 0.214 g (8.9 mg-atoms) of magnesium in 4 ml of ether. The magnesium was a sublimed grade obtained from the Dow Metal Products Co., and the ether was freshly distilled from lithium aluminum hydride under a flow of nitrogen. The nmr spectrum of this solution showed a somewhat broadened triplet at $\delta$ −0.37 ppm ($J$ = 8.5 Hz) attributable to the $CH_2Mg$ protons, and a triplet at $\delta$ 6.33 ppm ($J$ = 7 Hz), attributable to the olefinic hydrogens of the primary Grignard reagent **6**. A tight olefinic triplet at $\delta$ 6.17 ppm ($J$ = 1.2 Hz) and allylic methylene absorption at $\delta$ 2.47 and 2.76 ppm correspond to the spectrum of 1-phenylcyclobutene. Additional, poorly defined, olefinic absorption was present from $\delta$ 5.8 to 6.2 ppm. The spectrum remained unchanged on heating for up to 4 hr at 60°. Hydrolysis produced a mixture of products identified by gc retention times and nmr spectra as follows (relative yields in parentheses): *cis*-1-phenyl-1-butene (0.03), *trans*-1-phenyl-1-butene (0.10), 1-phenylcyclobutene (0.53), *cis*-1-chloro-1-phenyl-1-butene (0.11), and *trans*-1-chloro-1-phenyl-1-butene (1.00). Yields varied in different preparations. This was in part a consequence of a tendency of the 1-phenylcyclobutene to polymerize on standing. 1-Phenyl-1,3-butadiene[2] was not identified, though some minor fractions of short retention time were not investigated.

Solvent was distilled from the Grignard reagent under high vacuum, the semisolid residue was stirred with 3 ml of pentane, and the pentane was removed by syringe. After four such extractions, residual pentane was pumped off and replaced by fresh diethyl ether. The spectrum ascribed to phenylcyclobutene was no longer visible, while the absorptions at $\delta$ 6.33 and −0.37 ppm remined, as did some poorly defined olefinic resonances. The solution was heated for periods up to 4 hr at 115° in a sealed nmr tube. At the end of this time, the $\delta$ 6.33 and −0.37 ppm absorptions were decreased by about 50%, and the olefinic triplet of 1-phenylcyclobutene was the most prominent peak in the rather cluttered olefinic region. The nmr spectrum of the pentane extract clearly showed the presence of 1-phenylcyclobutene; additional absorption could be attributed to *trans*-1-chloro-1-phenyl-1-butene, and gas chromatography showed that the two components were present in a mole ratio of about 4:1. It is likely that much of the latter results from hydrolysis of some Grignard reagent entrained in the pentane extract, since the extract became cloudy on standing in air or addition of water. Hydrolysis of the remaining Grignard solution (not heated) gave mainly 1-chloro-1-phenyl-1-butene, along with smaller amounts of 1-phenyl-1-butene (1:0.2) and a trace of phenylcyclobutene.

A sample of Grignard solution was hydrolyzed with deuterium oxide, and the products were isolated by gas chromatography. The *trans*-1-chloro-1-phenyl-1-butene had aromatic and olefinic resonances similar to those of undeuterated material. The methyl absorption consisted of a 1:2:1 triplet of 1:1:1 triplets, corresponding to a vicinal $J_{H-H}$ = 7.7 Hz and a geminal $J_{H-D}$ = 1.9 Hz, respectively. The low-field component of each of the H–D triplets was slightly enhanced, and the splitting slightly reduced, suggesting the triplet corresponding to undeuterated material, and an up-field shift of about 0.017 ppm produced by geminal isotopic substitution. The methylene resonance was a broadened quartet. The ir spectrum showed C–D absorption at 2180 $cm^{-1}$. From nmr integrals and comparison of intensities within the methyl multiplet, it was concluded that the sample was 80–95% monodeuterated. The spectrum of the cis isomer was generally similar in appearance, but there was an insufficient amount for a quantitative analysis. The spectrum of the *trans*-1-phenyl-1-butene was similar in appearance in the methyl region but with probably 20% of undeuterated material. Integration of the olefinic and aromatic regions indicated 70–80% of one vinyl deuterium.

A sample of a reaction solution was stirred for 5 days under nitrogen, in the presence of excess magnesium, and hydrolyzed with deuterium oxide. None of the products were substantially deuterated, suggesting that little Grignard reagent remained. The product was significantly enhanced in 1-phenylcyclobutene. It is not certain whether this is a consequence of conversion of other products to phenylcyclobutene under the influence of magnesium or simply to destruction of the Grignard reagents present in a manner not leading to simple hydrolysis (as by reaction with oxygen).

In a reaction with undeuterated halide in tetrahydrofuran, the nmr of the reaction solution showed $CH_2Mg$ proton resonance at $\delta$ −0.42 ppm, somewhat weaker and less well resolved than in diethyl ether. There was a very broad absorption at $\delta$ 0.4 ppm, and the olefinic triplet of the primary Grignard reagent **6** was weak or absent. The presence of phenylcyclobutene was clear. The mixture was extracted with pentane as before. The extract contained phenylcyclobutene as the major identifiable product (from nmr), but there was a substantial amount of unidentified material, largely lacking in olefinic absorption and probably polymeric. The remaining Grignard reagent was hydrolyzed with deuterium oxide. The nmr spectrum of the product mixture indicated a $CH_2CH_2D$ group and an olefinic triplet, along with much other ill-defined absorption. Gas chromatography showed more 1-phenyl-1-butene than in the ether reaction. It is likely, judging from the spectra, that the Grignard solution contained largely the di-Grignard reagent.

**Reaction of 1-Chloro-4-bromo-1-phenyl-1-butene-4,4-$d_2$ with Magnesium.**—The reaction of 1 g of the halide with 0.16 g of magnesium in 4 ml of ether was carried out as with the undeuterated halide. The nmr spectrum of the original reaction solution was similar to that obtained previously with two exceptions: the methylene resonances of 1-phenylcyclobutene were collapsed into a pair of broadened singlets, and the $-CH_2Mg$ resonance was weak (about 20% of two protons, based on olefinic resonance) and was a broadened singlet. The mixture was extracted with pentane as before. The extract had broadened singlets at $\delta$ 2.47 and 2.73 ppm; the lack of splitting is consistent with assignment to the methylene resonances of 1-phenylcyclobutene-4,4-$d_2$ and -3,3-$d_2$, respectively. Since the higher field resonance was wider, it was assigned to the 4,4-$d_2$ isomer; the three-bond vinyl–allylic coupling of cyclobutene is known to be greater than the four-bond coupling.[11] The olefinic resonance appeared to be a superposition of the triplet ($J$ = 1.3 Hz) for the 4,4-$d_2$ isomer and a singlet, shifted $\delta$ 0.010 ppm to higher field, for the 3,3-$d_2$ isomer. The two isomers were present in nearly equal amounts (±10%). The residual Grignard solution had an olefinic triplet, most probably attributable to the primary Grignard reagent **6**-$d_2$, and a variety of weaker, ill-defined bands in the olefinic region.

**Reaction of 1-Chloro-4-bromo-1-phenyl-1-butene with Alkyllithium Reagents.**—To 1 g of the chloro bromide in 10 ml of tetrahydrofuran was added 12 ml of a 1.8 $M$ solution of methyllithium in ether. The reaction refluxed spontaneously. Toward the end of the addition, a long-lasting blue color was generated in the solution. The mixture was hydrolyzed with water and gas chromatographed. The major component was identified as 1-phenylcyclobutene. Similar reactions occurred with butyllithium.

The experiment was repeated with the deuterated chloro bromide. The crude product was distilled to a cold finger under aspirator vacuum. Its nmr spectrum was similar to that of the deuterated phenylcyclobutene isolated from the magnesium reaction, indicating a mixture of 3,3-$d_2$ and 4,4-$d_2$ isomers.

The reaction of **1b** with butyllithium was carried out in an nmr tube in an attempt to observe chemically induced dynamic nuclear polarization (CIDNP). In an nmr tube were placed 40 $\mu$l of chloro bromide **1b**, 0.25 ml of 1.6 $M$ butyllithium in hexane, and 0.035 g of diphenylacetylene. The nmr spectrum was scanned on a T-60 spectrometer and 100 $\mu$l of ether was added. Rapid scanning of the spectrum showed the appearance of positive and negative peaks similar to those observed in the analogous reaction with 1-bromobutane.[10a] These signals decayed and within about 4 min the spectrum remained constant. It appeared to have signals corresponding to olefinic protons of 1-butene and 1-

(11) E. A. Hill and J. D. Roberts, *J. Amer. Chem. Soc.*, **89**, 2047 (1967).

phenylcyclobutene, along with other olefinic resonances. No transient abnormalities were apparent in the position of the 1-phenylcyclobutene absorption.

**Reactions with Tri-*n*-butyltin Hydride.**—In an nmr tube, there were placed 0.55 ml of a 1.2 *M* stock solution of tri-*n*-butyltin hydride in benzene, 0.144 g (0.59 mmol) of 1-chloro-4-bromo-1-phenyl-1-butene, 0.0016 g of azobisisobutyronitrile, and 0.020 ml of tetrahydrofuran (as an internal reference). The sample was heated at 85° until the nmr spectrum showed complete disappearance of the Sn–H band (δ 2.24 ppm upfield from benzene). The nmr spectrum showed partial disappearance of the chlorobromide olefinic triplet δ 1.32 ppm upfield from benzene, and replacement by a new triplet at δ 1.28 ppm. By gas chromatography, components of the mixture were separated and identified as *cis*-1-phenyl-1-butene (by retention time), *trans*-1-phenyl-1-butene (by nmr), *cis*-1-chloro-1-phenyl-1-butene (by nmr), *trans*-1-phenyl-1-chloro-1-butene (by nmr), and cis and *trans* isomers of the starting halide (by retention time). The ratio of *trans*-1-phenyl-1-butene to *trans*-1-chloro-1-phenyl-1-butene was about 0.1. Reactions at lower concentrations gave less complete reduction and apparent side reactions.

A similar attempt at reduction of 1-phenyl-1-butene led to no disappearance of either hydride or alkene, based on nmr observation. With 1-chloro-1-phenyl-1-butene, disappearance of the hydride occurred, and a product was formed which was identified by nnr and by its retention time as *n*-butylbenzene. 1-Phenyl-1-butene was formed in less than 10% of the amount of *n*-butylbenzene.

A competitive reaction was carried out with 1-bromobutane and 1-phenyl-1-chloro-1-butene. No 1-phenyl-1-butene was found by gas chromatography.

**Registry No.**—**1b**, 28273-63-4; 4,4-dideuterio-**1b**, 28273-64-5; **2**, 3365-26-2; *cis*-**3**, 28273-67-8; *trans*-**3**, 3365-30-8; *cis*-**4**, 1560-0-94; *trans*-**4**, 1005-64-7.

# Conformational Analysis. LXXII. Solvolysis Studies with the 5-Phenylcyclooctanol System[1-3]

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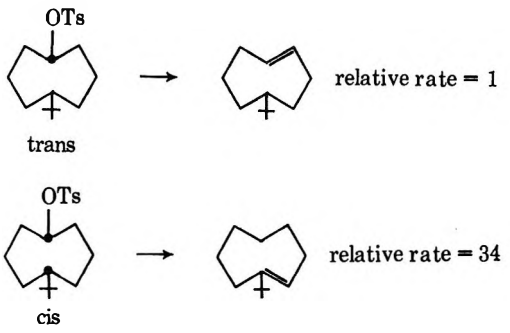
A rate and product study has been carried out on the solvolysis in aqueous ethanol of *cis*- and *trans*-5-phenylcyclooctanol tosylate and the corresponding *p*-anisyl derivatives. The results indicate that in these compounds, and by inference other cyclooctyl derivatives, neighboring group participation is not of importance in determining solvolysis rates. The rather fast rates observed, and rate differences between isomers, are attributed to steric effects.

Transannular hydride shifts across medium rings have been known for almost 20 years.[5] In an effort to understand the stereochemical features of these shifts, the solvolyses of a number of different stereoisomers of three- and five-substituted cyclooctane compounds were studied.[6-10] It was found that *cis*-5-*tert*-butylcyclooctyl tosylate solvolyzed much more rapidly than did the trans isomer, and the product obtained from the cis isomer was mostly rearranged olefin, while that from the trans isomer was mostly the olefin corresponding to simple elimination[6-8] (eq 1). From

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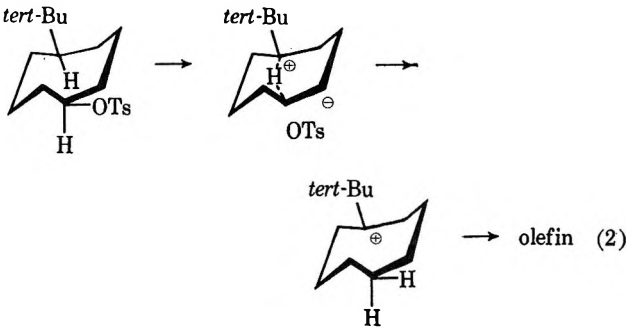
examination of the probable conformations of the molecules, participation by the transannular hydrogen of the cis isomer in the rate-determining step appeared to be indicated (eq 2). Only the cis isomer has a geometry




which will permit such participation. The trans isomer reacts without participation, and without much rearrangement. However, the difference in rate between the cis and trans isomers was only a factor of 34, and not large enough to be convincingly attributed to neighboring group participation. Since the *tert*-butyl group is obviously quite bulky, it may well deform appreciably the cyclooctane ring to which it is attached, and hence the earlier experiments did not conclusively rule out the possibility that the unusual rate for the cis isomer was a result of conformational distortion of the ring by the *tert*-butyl group, rather than of neighboring group participation in the usual sense. The rearranged product in that case would have to be formed by a trans-

(1) Paper LXXI: M. T. Tribble, M. A. Miller, and N. L. Allinger, *J. Amer. Chem. Soc.*, in press.

(2) Abstracted in part from the Ph.D. Dissertation of C. L. N., presented to Wayne State University, Sept 1966.

(3) Supported in part by Grant No. GP 15263 from the National Science Foundation.

(4) Correspondence regarding this paper should be directed to this author at the Department of Chemistry, University of Georgia.

(5) (a) A. C. Cope, S. W. Fenton, and C. F. Spencer, *J. Amer. Chem. Soc.*, **74**, 5884 (1952); (b) V. Prelog and K. Schenker, *Helv. Chim. Acta*, **35**, 2044 (1952). For reviews, see E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, New York, N. Y., 1962, p 252; A. C. Cope, M. M. Martin, and M. A. McKervey, *Quart. Rev., Chem. Soc.*, **20**, 119 (1966).

(6) N. L. Allinger and S. Greenberg, *J. Amer. Chem. Soc.*, **84**, 2394 (1962).

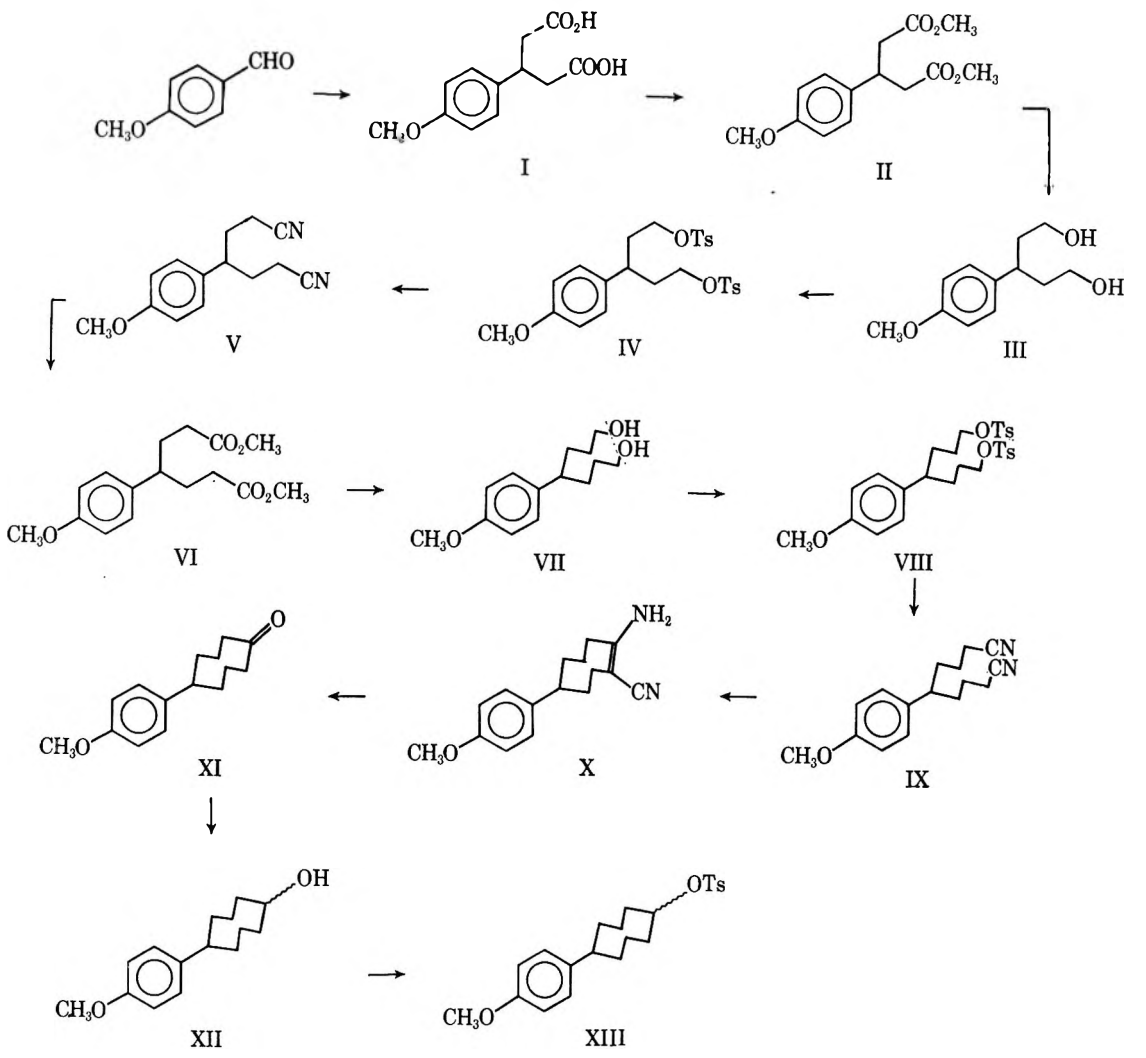
(7) N. L. Allinger and W. Szkrybalo, *Tetrahedron*, **24**, 4699 (1968).

(8) N. L. Allinger, I. Lillien, C. L. Neumann, H. Sugiyama, and N. A. Pamphilis, *J. Org. Chem.*, **35**, 1255 (1970).

(9) A. C. Cope and R. B. Kinnel, *J. Amer. Chem. Soc*, **88**, 752 (1966).

(10) A. C. Cope and D. M. Gale, *ibid.*, **85**, 3743 (1963).

CHART I




annular hydride ion transfer subsequent to the rate-determining step.

In order to differentiate steric and electronic effects in such a case, a convenient method involves carrying out parallel experiments on a phenyl compound, and on the *p*-anisyl derivative. The steric effects are essentially the same for these two, but the *p*-anisyl compound is able to supply electrons to a much higher degree if required to do so by an electronic demanding transition state. One might therefore predict that since a phenyl group has approximately the same, or somewhat smaller, bulk as a *tert*-butyl group[11] (depending on how it is measured), the 5-phenylcyclooctyl derivatives would solvolyze at rates similar to those of the corresponding *tert*-butyl compounds if neighboring group participation were unimportant in the transition state, but the cis isomer should be much faster if it were important. The *cis*-5-*p*-anisyl compound should either solvolyze at the same rate as the phenyl derivative, which would indicate no participation, or at a greatly accelerated rate, which would indicate a high degree of participation, or somewhere in between, while the trans isomer should have a rate similar to *trans*-phenylcyclooctyl tosylate in any case.

## Synthesis

During the early stages of this work, a paper by Cope[9] appeared, in which the syntheses of the isomeric 5-phenylcyclooctyl tosylates were described. We prepared a mixture of the two isomers by substantially the method described by Cope. There was no particular need to separate them; so we determined the rates of the two isomers directly from the mixture. Since the cis isomer solvolyzes over five times as fast as the trans isomer, this was easy to do experimentally. The analogous 5-anisylcyclooctyl tosylates were then prepared, by the scheme outlined on Chart I. Anisylaldehyde was converted to 3-anisylglutaric acid (I) *via* a Knovenagel reaction with ethyl acetoacetate, followed by basic cleavage (a reverse Claisen reaction) which yielded the acid. The acid I was esterified and reduced to 3-anisylpentane-1,5-diol (III) with lithium hydride. Chain extension of this diol *via* the tosylate IV and treatment with cyanide yielded 4-anisylpimelonitrile (V), which was converted to the ester VI, which was in turn reduced to 4-anisylheptane-1,7-diol (VII). Another chain extension *via* the tosylate VIII gave 5-anisylazelanitrile (IX). This compound was cyclized to yield 2-cyano-5-anisylcyclooctenylamine (X) by means of a Thorpe–Ziegler cyclization. Hydrolysis and decarboxylation furnished 5-anisylcyclooctanone (XI). The ketone was reduced with lithium aluminum hydride to give a mixture of the *cis*- and *trans*-5-*p*-anisylcyclooctanols (XII). The tosylates XIII were pre-

(11) J. A. Hirsch, *Top. Stereochem.*, 1, 207 (1967).

TABLE I

THE PRODUCT ANALYSIS FROM THE SOLVOLYSIS OF TOSYLATES IN 80% ETHANOL

| Compound solvolyzed | Rearranged products, % Olefin | Rearranged products, % Alcohol | Unrearranged products, % Olefin | Unrearranged products, % Alcohol | Other products, % |
|---|---|---|---|---|---|
| *cis*-5-*tert*-Butylcyclooctyl tosylate | 100 | 0 | 0 | 0 | 0 |
| *trans*-5-*tert*-Butylcyclooctyl tosylate[a] | 5–10 | 0 | 45–50 | 42 | 3 |
| 5-Phenylcyclooctyl tosylate (cis/trans ratio 1.32) | 34 | 8 | 46 | 9 | 3 |
| 5-Anisylcyclooctyl tosylate (cis/trans ratio 2.3) | 28 | 23 | 42 | 3 | 4 |
| *cis*-3-*tert*-Butylcyclooctyl tosylate | 10 | | | 40% *cis*-3-*tert*-butylcyclooctanol | 50% ether |
| Cyclooctyl tosylate | | | 53 | 47 | |

[a] Shown to contain 8% of the cis isomer during solvolysis.

pared and solvolyzed in the usual way; the solvolysis products are given in Table I. For comparison purposes, a number of other cyclooctyl tosylates were solvolyzed, or had previously been solvolyzed,[8] under identical conditions (in 80% ethanol, 25°, and pH 8.4). The relative rates of these compounds are summarized in Table II.

TABLE II

RATES OF SOLVOLYSIS OF CYCLOOCTYL TOSYLATES IN 80% ETHANOL–20% WATER AT 25° AND pH 8.4

| Compound | Absolute rate, $sec^{-1}$ | Rel rate |
|---|---|---|
| Cyclooctyl tosylate | $1.26 \times 10^{-4}$ | 39[b] |
| *cis*-5-*tert*-Butylcyclooctyl tosylate | $9.97 \times 10^{-4}$ | 312[b] |
| *trans*-5-*tert*-Butylcyclooctyl tosylate | $2.92 \times 10^{-5}$ | 9.1[b] |
| *cis*-5-Phenylcyclooctyl tosylate | $7.06 \times 10^{-5}$ | 22 |
| *trans*-5-Phenylcyclooctyl tosylate | $1.32 \times 10^{-5}$ | 4.1 |
| *cis*-5-*p*-Anisylcyclooctyl tosylate | $8.01 \times 10^{-5}$ | 25 |
| *trans*-5-*p*-Anisylcyclooctyl tosylate | $9.25 \times 10^{-6}$ | 2.9 |
| *cis*-3-*tert*-Butylcyclooctyl tosylate | $5.46 \times 10^{-4}$ | 171[b] |
| 2-Pentyl tosylate[a] | $3.2 \times 10^{-6}$ | 1[b] |

[a] A rate of $2.94 \times 10^{-6}$ $sec^{-1}$ has been found under similar conditions: S. H. Liggero, J. J. Harper, P. v. R. Schleyer, A. P. Krapcho, and D. E. Horn, *J. Amer. Chem. Soc.*, **92**, 3789 (1970). [b] Reference 8.

## Results and Discussion

The products of the solvolysis of *cis*- and *trans*-5-phenylcyclooctyl tosylate (in formic acid) were studied earlier by Cope and Kinnel.[9] They found that various alcohols were obtained as minor products; the cis isomer gave mostly the olefin obtained by hydride migration from C-5, while the trans isomer gave mostly unrearranged olefin, analogous to what was found earlier with the 5-alkylcyclooctyl tosylates.[6–8,10] In general our results seem to agree with Cope's, although our alcohol/olefin ratio was a little larger, as would be expected from the higher nucleophilicity of the solvent we employed. We did not separate our isomeric tosylates for separate study, but the products obtained are consistent with the cis isomer yielding mostly rearranged olefin and the trans isomer yielding mostly olefin without rearrangement (Table I).

The relative solvolysis rates of the tosylates are more informative than the reaction products. Looking now at Table II, we might first compare the relative rates of *trans*-5-*tert*-butylcyclooctyl tosylate (9.1) with the corresponding phenyl compound (4.1). The rates differ by only about a factor of 2, indicating that the steric effects are similar and the electronic effect is negligible, or there is some fortuitous cancellation of the two effects. Looking at the corresponding cis isomers, the 5-*tert*-butylcyclooctyl tosylate has a solvolysis rate of 312, compared to a *cis*-5-phenylcyclooctyl tosylate rate of 22. Any participation by the phenyl would be expected to accelerate the rate, and since the phenyl compound solvolyzes *more slowly* by a factor of 14, any acceleration must be pretty small, and more than counterbalanced by a steric or inductive effect. Looking only at the rates of the phenylcyclooctyl tosylates, then, one would conclude that there is no evidence for neighboring group participation by the phenyl.

If we now compare the *p*-anisylcyclooctyl tosylates with the corresponding *p*-phenyl compound, we notice that for the trans isomers the phenyl (rate 4.1) is just slightly faster than the *p*-anisyl (rate 2.9), a difference too small to be of much importance. Looking at the corresponding cis isomers, the *p*-anisyl (rate 25) is just slightly faster than the *p*-phenyl (rate 22). We thus conclude that there is no detectable neighboring group participation in the transition state in any of these phenyl- or anisyl-substituted cyclooctyl tosylates.

It might be argued that perhaps the phenyl group cannot achieve planarity with the carbonium ion being generated by hydride migration, and therefore it is unable to become involved in neighboring group participation in the transition state. While proof that this is not the case is lacking, it seems improbable that at least a small effect would not be observed if hydride migration is concerted with the solvolysis. For it not to occur, the phenyl would have to remain at almost exactly 90° to the plane of the carbonium ion being generated by hydride migration. This seems highly improbable. The large rate acceleration (34 times) brought about by the *cis*-5-*tert*-butyl group therefore seems best interpreted as a steric effect, that is, a relief of strain of some sort in the transition state. It might be noted that the *cis*-3-*tert*-butyl group also brings about a substantial rate acceleration (although not so large as in the 5-*tert*-butyl case), but here participation by hydride is unlikely, as the product obtained shows no hydride migration from the 3 position.

Since we conclude that neighboring group participation is negligible in the transition state, we must also conclude that the *cis*- and *trans*-cyclooctyl derivatives do not go through a common intermediate, since they give different products. The cis isomer is geometrically more favorably disposed toward transannular hydride transfer, and it undergoes such transfer in a fast

step subsequent to the rate-determining step. The corresponding trans isomer does not undergo much hydride transfer, and ordinary elimination–substitution is observed.

## Experimental Section

**3-*p*-Anisylglutaric Acid (I).**—To a mixture of 119.9 g of anisaldehyde and 225 g of ethyl acetoacetate was added dropwise 20 ml of piperidine, with stirring. After standing overnight the mixture had solidified. A solution of 200 g of sodium hydroxide in 1 l. of absolute ethanol was added to the solid product. After the solid had dissolved, the solution was heated under reflux with stirring for 24 hr. The majority of the ethanol was then evaporated, and 1 l. of ether was added to the cooled residue. The precipitate was filtered, washed with ether, and dissolved in 500 ml of water. Acidification with concentrated hydrochloric acid yielded the crude product, 165 g, mp 160–162°. Recrystallization from ethyl acetate gave crystals, mp 165–167° (lit.[12] mp 165°).

*Anal.* Calcd for $C_{12}H_{14}O_5$: C, 60.50; H, 5.92. Found: C, 60.71; H, 6.02.

**Dimethyl 3-*p*-Anisylglutarate (II).**—A mixture of 165 g of crude acid I, 500 ml of methanol, 1 l. of benzene, and 20 ml of concentrated sulfuric acid was heated under reflux for 72 hr. After the reaction mixture was cooled, 1 l. of water was added, the organic layer was separated, and the aqueous layer was extracted with benzene. The combined organic portions were washed again with water and dried over magnesium sulfate. The benzene was evaporated and the product was distilled, bp 164–165° (1 mm), yield 151 g, $n^{25}D$ 1.5073 [lit.[12] 205–210° (20 mm), mp 42°].

*Anal.* Calcd for $C_{14}H_{18}O_5$: C, 63.15; H, 6.81. Found: C, 63.41; H, 6.85.

**3-*p*-Anisylpentane-1,5-diol (III).**—To a stirred solution of 38 g of lithium aluminum hydride in 1 l. of dry ether was added dropwise 151 g of II in 450 ml of dry ether. The reaction mixture was refluxed for 2 hr, cooled, and treated with 500 ml of saturated aqueous ammonium chloride with stirring and cooling. The precipitate was filtered and washed with ether. The ether layer was separated and the aqueous layer was extracted with ether. The combined ether solutions were dried over magnesium sulfate and the solvent was evaporated. The residual solid was washed with a small amount of benzene to give crystals, mp 69–70°, yield 114 g. Recrystallization from benzene gave crystals, mp 70–71°.

*Anal.* Calcd for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63. Found: C, 68.57; H, 8.90.

**3-*p*-Anisylpentane-1,5-diol Bis(*p*-toluenesulfonate) (IV).**—To an ice-cooled solution of 2 g of III in 10 ml of dry pyridine was added 2 g of *p*-toluenesulfonyl chloride in 5 ml of pyridine. The reaction mixture was stirred in an ice bath for 2 hr. To the reaction mixture was then added 30 ml of ice water and 30 ml of ether. The ether layer was separated and washed with ice-cold 2 *N* hydrochloric acid, water, and saturated sodium bicarbonate solution. After drying over magnesium sulfate, the ether was removed, and the residue was recrystallized from methanol to yield 2.3 g of product, mp 64.5–65°.

*Anal.* Calcd for $C_{25}H_{30}O_7S_2$: C, 60.21; H, 5.83. Found: C, 60.46; H, 5.96.

**4-*p*-Anisylpimelonitrile (V).**—A mixture of 80 g of IV, 20 g of potassium cyanide, and 200 ml of 95% ethanol was heated under reflux with stirring for 16 hr. After most of the ethanol had been removed by distillation, 200 ml of water was added to the mixture, which was then extracted with ether. The ether layer was washed with water and dried over magnesium sulfate, and the ether was removed under reduced pressure. The oily residue was recrystallized from ethanol twice to yield 30 g of crystals, mp 60.5–61°.

*Anal.* Calcd for $C_{14}H_{16}ON_2$: C, 73.66; H, 7.06; N, 12.27. Found: C, 73.57; H, 7.21; N, 12.11.

**Dimethyl 4-*p*-Anisylpimelate (VI).**—A mixture of 30 g of V, 200 ml of methanol, and 10 ml of concentrated sulfuric acid was heated under reflux for 7 days. After most of the methanol was evaporated, the residual oil was poured into water and extracted with ether. The ether layer was washed with water and saturated sodium bicarbonate and dried over magnesium sulfate. After concentration, the residue was distilled, bp 163–164° (0.7 mm), $n^{25}D$ 1.5031, yield 34 g.

*Anal.* Calcd for $C_{16}H_{22}O_5$: C, 65.29; H, 7.53. Found: C, 65.31; H, 7.71.

**4-*p*-Anisylheptane-1,7-diol (VII).**—A solution of 34 g of VI in 170 ml of dry tetrahydrofuran was added dropwise to a stirred solution of 10 g of lithium aluminum hydride in 600 ml of dry ether. The reaction mixture was heated under reflux for 3 hr, cooled, and treated with 200 ml of saturated ammonium chloride with cooling and stirring. The precipitate was filtered and washed with ether. The organic layer was separated, and the aqueous layer was extracted with ether. The combined ether extracts were dried over magnesium sulfate and concentrated, yield 24.1 g, mp 41–42°. Recrystallization from ether in a Dry Ice–acetone bath gave mp 51–52°.

*Anal.* Calcd for $C_{14}H_{22}O_3$: C, 70.56; H, 9.30. Found: C, 70.81; H, 9.31.

**5-*p*-Anisylazelanitrile (IX).**—To a stirred solution of 1 g of VII in 10 ml of dry pyridine, in an ice–salt bath, 1.8 g of toxyl chloride was slowly added. The reaction mixture was stirred for 2 hr at 0° and treated with 20 ml of water. The aqueous solution was extracted with ether. The ether layer was washed with ice-cold 2 *N* hydrochloric acid, water, and saturated sodium bicarbonate and was dried over magnesium sulfate. After concentration, 2 g of the oily ditosylate VIII, which failed to crystallize, was obtained. A solution of 2 g of the tosylate and 4 g of potassium cyanide in 40 ml of 95% ethanol was refluxed with stirring for 17 hr. The reaction mixture was treated with 200 ml of water and extracted with ether. The ether layer was washed with water and dried over magnesium sulfate. After concentration, 0.9 g of crude crystal was obtained, mp 53–60°. Recrystallization several times from methanol gave crystals, mp 78–79°.

*Anal.* Calcd for $C_{16}H_{20}ON_2$: C, 74.97; H, 7.86; N, 10.93. Found: C, 74.73; H, 8.02; N, 11.14.

**2-Cyano-5-*p*-anisylcyclooctenylamine (X).**—To a well-stirred, boiling solution of sodium methylanilide, which was prepared from 12 g of sodium, 40.4 g of naphthalene, and 70 g of *N*-methylaniline in 800 ml of ether, a solution of 10.6 g of IX in 1.9 l. of dry ether was added dropwise through the high-dilution apparatus[13] over a period of 3 days. The reaction mixture was heated under reflux for 3 hr, cooled, and treated with 500 ml of water with stirring and cooling. The ether layer was separated and the aqueous layer was extracted with ether. After evaporation of solvent from the combined ether layers, the residue was steam distilled to remove methylaniline and dihydronaphthalene. The material remaining was extracted with chloroform, and the chloroform solution was dried over magnesium sulfate. Evaporation of the solvent gave a residue, mp 85–90°. Recrystallization from methanol gave 7.2 g of crystals, mp 136–137°.

*Anal.* Calcd for $C_{16}H_{20}ON_2$: C, 74.97; H, 7.86; N, 10.93. Found: C, 74.85; H, 8.01; N, 10.79.

**5-*p*-Anisylcyclooctanone (XI).**—The ketone was prepared by heating under reflux 4.8 g of X in 200 ml of 30% (volume) sulfuric acid for 17 hr with stirring. After cooling, the reaction mixture was extracted with chloroform, and the chloroform layer was washed with water. After drying over magnesium sulfate, the solution was evaporated to yield the crude ketone. Careful sublimation of this residue at 60° and 0.02 mm yielded white crystals, mp 35°, yield 2 g.

*Anal.* Calcd for $C_{15}H_{20}O$: C, 77.55; H, 8.68. Found: C, 77.44; H, 8.62.

**5-*p*-Anisylcyclooctanol (XII).**—To a slurry of 80 mg of lithium aluminum hydride in 25 ml of dry ether was added 275 mg of XI dissolved in a minimum amount of dry ether, at 0–10°. The reaction was allowed to warm and was stirred at 25° for 24 hr. The reaction was again cooled in an ice bath, and saturated aqueous ammonium chloride solution was carefully added until gas evolution ceased. The reaction was stirred for an additional half-hour, and 5 ml more of the ammonium chloride solution was added. The solid was filtered and washed with ether. The washings were combined and dried over magnesium sulfate, and the solvent was evaporated under reduced pressure. Sublimation at 70–90° and 0.02 mm yielded crystals, mp 50–59°.

*Anal.* Calcd for $C_{15}H_{22}O$: C, 76.88; H, 9.47. Found: C, 76.76; H, 9.21.

**5-*p*-Anisylcyclooctyl *p*-Toluenesulfonate (XIII).**—To a solution of 240 mg of XII in 5 ml of pyridine, cooled in Dry Ice–acetone so that the solution was slushy, was added with stirring 330 mg

(12) J. G. Jackson and J. Kenner, *J. Chem. Soc.*, 1657 (1928).

(13) D. J. Cram and M. F. Antar, *J. Amer. Chem. Soc.*, **80**, 3103 (1958).

of *p*-toluenesulfonyl chloride in 5 ml of pyridine. The reagent was added as fast as consistent with maintaining the reaction temperature. The resulting solution was then stored at −20° for 2 days. The flask was removed from the freezer, five drops of water were added to the reaction, and the solution was allowed to warm to 0°. The reaction was then poured into 30 ml of ice-cold 5% hydrochloric acid, and the solution was extracted with 30 ml of ether. The ether solution was washed with cold 5% acid and with sodium bicarbonate and was dried over magnesium sulfate. The solution was evaporated to dryness under reduced pressure, and the residue was recrystallized from ether–pentane at −20° to yield crystals, mp 77.5–82°. Kinetic runs were made on this product and showed different batches to be a mixture of epimers of variable composition.

**5-Phenylcyclooctyl *p*-Toluenesulfonate.**—This compound was prepared following the procedure used for XIII and gave crystals, from ether–pentane (−20°), mp 68–70° [lit.[9] 69.5–70.5 (cis isomer) and 70–71.5° (trans isomer)]. Kinetic runs were made on the mixture of epimers, and these runs showed the composition to be 1.3 parts cis epimer to one part trans.

**1-Phenylcyclooctene (XV).**—The preparation of this compound was accomplished by the dehydration of XIV in ether solution with iodine. This product was shown to be the olefin by thin layer chromatography, gas chromatography, and tetranitromethane tests.

**1-*p*-Anisylcyclooctanol.**—The method of preparation of this compound was identical with that described for the preparation of XIV, and the preparation of **1-*p*-anisylcyclooctene** was similarly analogous to the preparation of XV. Both compounds were used as ether solutions for the product analysis. Thin layer chromatography and gas chromatography were consistent with the above structures.

**Kinetic Experiments.**—The rates of solvolysis were measured on a Sargeant recording pH-Stat, as discussed earlier.[8]

**Preparation of Solvents and Reagents.**—The aqueous ethanol used in the kinetic runs was prepared all at once, and the same solvent was used for the base titrant and the solutions of tosylate. It was stored under dry nitrogen when not being used. Preparation consisted of dilution of commercial 95% ethanol with enough distilled water to make the solvent 80% ethanol by volume. Physical constants of the solution were as follows: $n^{25}D$ 1.3624, density 0.84985 g/ml at 25°. The basic titrant was prepared by dissolving reagent potassium hydroxide (0.65 g) in 500 ml of the above solvent. Titration against standard hydrochloric acid showed it to be 0.0182 *N*. An indicator consisting of 12 parts of cresol red to 36 parts of thymol blue was used in this titration, and also was used in the kinetic runs as a visual check of pH constancy.

**Treatment of Kinetic Data.**—The data obtained from the machine consisted of a graph of the milliliters of titrant used *vs.* time and was more or less smooth, depending on the rate of stirring, speed of reaction, etc. These graphs were smoothed out by means of a French curve, and then the points on the graph put in tabular form for each run. At least 10 points were taken, and in some cases as many as 75 were used. The factors that introduced the largest uncertainty in the treatment of these data were, first, that the infinity titer was uncertain in some cases, owing to errors inherent in the machine, and also because the weight of tosylate was known only to an accuracy of ±0.05 mg; second, when mixtures of two epimers were solvolyzed, the rate of solvolysis of the faster epimer may be determined accurately only if the rate of the slower one is known accurately.

For pure isomers then, when the infinity titer could be determined accurately, the rate was determined by plotting the logarithm of the concentration *vs.* time in seconds. When the infinity titer was not known, either the method developed by Guggenheim[14] was used, or the infinity titer was varied until the plot of log [ROTs] *vs.* time gave the straightest line, which corresponds to the correct infinity titer, within experimental error. The above methods, when they could be used on the same run, gave consistent results.

In the case of mixtures of epimers, one of the above-mentioned methods gave the absolute rate of the slower isomer. The absolute rate of the faster isomer was determined by extrapolating the concentration of the slower isomer back to zero time, and then subtracting the concentrations of the slower isomer away from the total concentrations of the isomers, thus obtaining the concentration of the faster, and, hence, the rate of disappearance of the faster isomer, uncontaminated with the slower. As a further check on this method of obtaining the rates of a mixture, synthetic mixtures of *cis*- and *trans*-5-*tert*-butylcyclooctyl *p*-toluenesulfonate of known composition were made and the individual rates determined from the mixture. These rates compared very favorably with those obtained on the pure epimers.

It should be noted that, since concentration does not enter into the rate equation for first-order kinetics, any convenient concentration units may be used. Here, 1 mm of chart paper is proportional to 1 mmol of alkyl toluenesulfonate remaining, and this is the most convenient measure of concentration. A sample run is reported in Table III.

TABLE III

SOLVOLYSIS OF *cis*- AND *trans*-5-PHENYLCYCLOOCTYL *p*-TOLUENESULFONATES IN 80% ETHANOL AT 25 ±0.05° [a]

| Time, hr | [ROTs], mm of chart | Log [ROTs] | Time, hr | [ROTs], mm of chart | Log [ROTs] |
|---|---|---|---|---|---|
| 0 | 207.8 | 1.3177 | 21 | 34.4 | 0.537 |
| 1 | 178.2 | 1.251 | 22 | 32.9 | 0.517 |
| 2 | 153.4 | 1.186 | 23 | 30.4 | 0.483 |
| 3 | 134.3 | 1.128 | 24 | 29.9 | 0.476 |
| 4 | 119.0 | 1.076 | 25 | 28.4 | 0.453 |
| 5 | 106.0 | 1.025 | 26 | 27.2 | 0.435 |
| 6 | 94.5 | 0.975 | 27 | 26.3 | 0.420 |
| 7 | 84.6 | 0.927 | 28 | 25.4 | 0.405 |
| 8 | 77.1 | 0.887 | 29 | 24.1 | 0.382 |
| 9 | 70.7 | 0.849 | 30 | 23.3 | 0.367 |
| 10 | 65.5 | 0.816 | 31 | 22.3 | 0.348 |
| 11 | 61.0 | 0.785 | 32 | 20.5 | 0.312 |
| 12 | 56.8 | 0.754 | 33 | 19.7 | 0.295 |
| 13 | 53.8 | 0.731 | 34 | 18.8 | 0.274 |
| 14 | 49.6 | 0.696 | 35 | 18.4 | 0.265 |
| 15 | 46.7 | 0.669 | 36 | 17.6 | 0.246 |
| 16 | 44.1 | 0.644 | 37 | 16.9 | 0.228 |
| 17 | 40.9 | 0.612 | 38 | 16.5 | 0.218 |
| 18 | 39.9 | 0.601 | 39 | 15.7 | 0.196 |
| 19 | 37.8 | 0.578 | 40 | 15.1 | 0.179 |
| 20 | 36.0 | 0.556 | 41 | 14.5 | 0.161 |

$k_{cis}$ = 7.07 × $10^{-5}$ $sec^{-1}$; $k_{trans}$ = 1.24 × $10^{-5}$ $sec^{-1}$
Ratio of cis/trans = 1.34

[a] Run no. 3: 13.50 mg of *p*-toluenesulfonate in 15 ml of 80% ethanol maintained at pH 8.4 ± 0.4.

**Product Analysis.**—Product analyses of the tosylate solvolyses were done by gas chromatography, and the results were checked by thin layer chromatography. The actual solvolysis runs were used for the analysis, rather than separate runs. This eliminated any uncertainty due to variable composition of epimers in the mixtures, which appears to occur with the *p*-anisyl derivative. A typical work-up of a solvolysis for analysis follows.

The reaction vessel was removed from the titrator, excess base was added to the solution, and the solution was transferred to a stoppered flask and stored at 25° until work-up was convenient. (In the case of the slower reactions, the reaction was left for several more half-lives to ensure complete reaction.) The reaction mixture was then diluted with 50 ml of pentane and extracted twice with 50 ml of distilled water. The water extracts were washed with pentane, and the organic fractions were combined and dried over magnesium sulfate. The pentane was then distilled carefully, using a 12-in. column packed with stainless steel gauze, and equipped with a head in which the reflux ratio could be varied. Distillation was continued until only 0.5–1 ml of liquid remained in the pot. This solution was stored in the freezer until needed.

The actual analyses were done on an aluminum column, 4 m × 0.25 in., packed with 10% SE-60 on 40–60 mesh Chromosorb B. One other column was used for the separation of the olefins obtained from the 5-*tert*-butylcyclooctyl tosylate solvolysis. It was a 20-ft dual column, the first half packed with XE-60 on 60–80 mesh firebrick, and the second half packed with tricresyl phos-

(14) E. A. Guggenheim, *Phil. Mag.*, **2**, 538 (1926).

phates on 60–80 mesh firebrick. This column separated the olefins but would not allow elution of the alcohols. The resuts are summarized in Table I.

**Registry No.**—III, 28252-86-0: IV, 28252-87-1; V, 28252-88-2; VI, 28252-89-3; VII, 28252-90-6; IX, 28252-91-7; X; 28252-92-8; XI, 28252-93-9; *cis*-XII, 28252-94-0; *trans*-XII, 28256-86-2; *cis*-XIII, 28252-95-1; *trans*-XIII, 28252-96-2; *cis*-5-phenylcyclooctyl *p*-toluenesulfonate, 7286-93-3; *trans*-5-phenylcyclooctyl *p*-toluenesulfonate, 7368-50-5.

# Base-Induced Rearrangement of Epoxides to Allylic Alcohols. III. Alkylidenecycloalkane Oxides[1]

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The lithium diethylamide induced rearrangement of a series of propylidenecycloalkane oxides to allylic alcohols exhibits marked regioselectivity, with endocyclic olefin product being formed preferentially. An exception is propylidenecyclohexane oxide which gives 95% of the alternate, tertiary allylic alcohol. A series of ethylidenecycloalkane oxides, where preference for endocyclic elimination competes with proton abstraction from primary carbon, was also examined. The results of both series support a syn elimination mechanism, with very specific cis-coplanar transition state geometrical requirements.

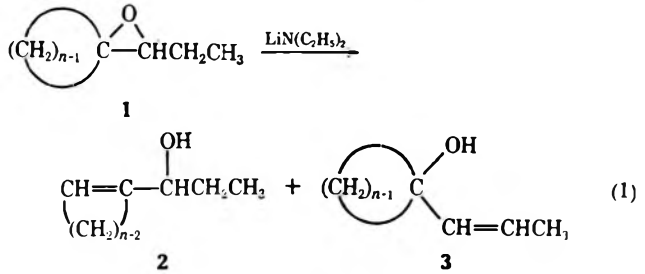
Cope and Tiffany[2] were apparently the first workers to observe an unusual base-catalyzed rearrangement of an epoxide when dealing with cyclooctatetraene oxide. Subsequent work with phenyl-substituted ethylene oxides,[3] medium-ring cycloalkene oxides,[4] and open-chain epoxides[5] established several novel reaction pathways on treatment with strong base. The extensive work of Crandall and his coworkers[6] amplified these and brought to light additional reactions.

This paper deals with our continuing[1,7] study of the lithium diethylamide induced rearrangement of epoxides to allylic alcohols. Formally an elimination, this reaction is remarkable for its very high selectivity, *e.g.*, stereoselectivity (exclusive formation of trans olefin in open-chain systems[5,7]) and regioselectivity[8] (exclusive, or nearly so, abstraction of proton from least substituted carbon[6,7]). Recently deuterium labeling studies[1] have established that syn elimination is the preferred pathway in cyclohexene oxide rearrangements.

The factors which influence the regioselectivity of the base-induced reaction are incompletely understood. We have undertaken a systematic study of substituted epoxides to examine this question; the results obtained with alkylidenecycloalkane oxides are presented here.

## Results and Discussion

A series of propylidenecycloalkane oxides (**1**) was prepared by standard procedures and treated with lithium diethylamide in refluxing ether–hexane (eq 1). The course of the reaction was followed by vpc, and the mixture quenched with water when the epoxide was consumed. The results are shown in Table I.



(1)

**1** **2** **3**

TABLE I

PRODUCT DISTRIBUTION FROM THE REACTION OF PROPYLIDENECYCLOALKANE OXIDES (1) WITH LITHIUM DIETHYLAMIDE

| 1 | *n* | Time, hr[a] | 2 | 3 |
|---|---|---|---|---|
| a | 4 | 6 | 77 | 15[b] |
| b | 5 | 1 | 100 | 0 |
| c | 6 | 49[c] | 5 | 95 |
| d | 7 | 5 | 98 | 2 |
| e | 8 | 2 | 100 | 0 |
| f | 12 | 22 | ≥84 | ...[d] |

[a] The reactions were followed by vpc; this is the time required for effective complete loss of starting epoxide. [b] The product mixture in this case contained 5% cyclobutyl ethyl ketone and 3% unidentified material. [c] At this time 9% unreacted epoxide remained. [d] Not directly determined; see Experimental Section.

In this series, proton abstraction from secondary cyclic carbon competes with that from a secondary acyclic center. The data in Table I show not only high selectivity depending on ring size, but a striking reversal in the direction of elimination in the series cyclopentyl (endocyclic), cyclohexyl (acyclic), and cycloheptyl (endocyclic olefin preferred).

It is apparent that subtle conformational effects can significantly diminish the activation energy for elimination into the carbocyclic ring. The propylidenecyclohexane oxide **1c** serves as a basis for comparison; reaction to form the acyclic double bond (as strongly favored in **1c**) requires in excess of 49 hr for complete conversion. All other systems shown in Table I react more rapidly, from a great deal faster in the completely

(1) Part II: R. P. Thummel and B. Rickborn, *J. Amer. Chem. Soc.*, **92**, 2064 (1970).

(2) A. C. Cope and B. D. Tiffany, *ibid.*, **73**, 4158 (1951).

(3) A. C. Cope, P. A. Trumbull, and E. R. Trumbull, *ibid.*, **80**, 2844 (1958).

(4) (a) A. C. Cope, H. Lee, and H. E. Petree, *ibid.*, **80**, 2849 (1958); (b) A. C. Cope, M. Brown, and H. Lee, *ibid.*, **80**, 2855 (1958); (c) A. C. Cope, G. A. Berchtold, P. E. Peterson, and S. H. Sharman, *ibid.*, **82**, 6370 (1960).

(5) A. C. Cope and J. K. Heeren, *ibid.*, **87**, 3125 (1965).

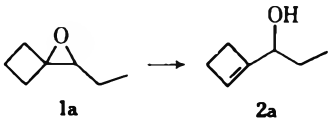
(6) (a) J. K. Crandall, *J. Org. Chem.*, **29**, 2830 (1964); (b) J. K. Crandall and L. Chang, *ibid.*, **32**, 435 (1967); (c) *ibid.*, **32**, 532 (1967); (d) J. K. Crandall and L. C. Lin, *J. Amer. Chem. Soc.*, **89**, 4526, 4527 (1967); (e) *J. Org. Chem.*, **33**, 2375 (1968).

(7) B. Rickborn and R. P. Thummel, *ibid.*, **34**, 3583 (1969).

(8) The terminology suggested by A. Hassner, *ibid.*, **33**, 2685 (1968).

endocyclic regiospecific reactions of **1b** and **1e** to the moderately faster, somewhat regioselective reaction of **1f**. In the limit a large ring should exhibit open-chain behavior, and the cyclododecyl system **1f** appears from both a rate and product (although incompletely analyzed) standpoint to be progressing in this direction.

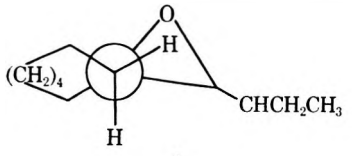
The cyclobutyl system **1a** is of interest in that it leads primarily to the strained cyclobutene product **2a** (eq 2)



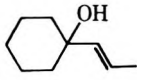
**1a** **2a** (2)

The data in Table I are best interpreted in terms of a syn elimination mechanism as earlier demonstrated in cyclohexene oxides.[1] DePuy and his coworkers[9] have presented convincing evidence of the importance of cis coplanarity of hydrogen and leaving group in the E2 syn elimination mechanism. Although other known syn eliminations do not necessarily serve as good models for the epoxide reaction, transition state cis coplanarity is apparently a dominant feature of the latter as well. Thus a cis coplanar arrangement of $\beta$ hydrogen and epoxygen in the cyclopentyl compound **1b** is easily attained, whereas trans coplanarity (needed for anti elimination) would involve excessive strain. The fact that **2b** is the exclusive product of this reaction strongly supports the syn elimination mechanism, although the degree of preference for endocyclic elimination is not so easily rationalized.

Compound **1c** offers a convincing demonstration of the importance of coplanarity in the base-induced rearrangement. In neither chair conformer (as seen from Newman projection **4**) of **1c** is cis (or trans) coplanarity of epoxygen with a $\beta$ hydrogen on the ring attained. Cis coplanarity is attainable with the acyclic $\beta$ proton;



**4**

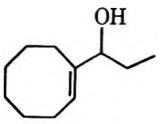


**5**

as a consequence, elimination is nearly exclusively in this direction (95%), in a slow reaction as expected for normal secondary proton abstraction. The product, in agreement with earlier work, is the trans olefin **5**. The small amount of endocyclic olefin which is formed in the reaction of **1c** may arise *via* a twist boat conformer, where cis coplanarity is feasible.

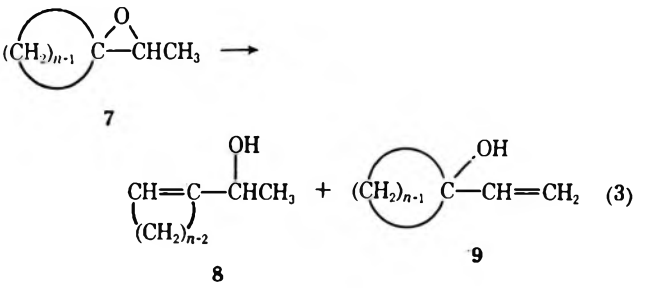
It is particularly interesting that the next higher ring system (cycloheptyl, **1d**) gives nearly exclusively endocyclic product. Apparently the cycloheptyl ring is sufficiently flexible that a conformationally favorable cis coplanar transition state is allowed. This behavior is even more pronounced with the cyclooctyloxirane **1e**, which in a quite rapid reaction yields the endocyclic olefin with complete regiospecificity. The product **2e** gives a single peak on vpc, and its nmr spectrum supports the *cis*-cyclooctene structure **6**; the formation of cis endocyclic olefin is of course mechanistically analogous to the generation of trans acyclic material.

(9) C. H. DePuy, G. F. Morris, J. S. Smith, and R. J. Smat, *J. Amer. Chem. Soc.*, **87**, 2421 (1965).



**6**

In view of the decided competitive advantage enjoyed by cyclic secondary proton abstraction over its acyclic equivalent, it was of interest to explore the competition between cyclic secondary and acyclic primary abstraction. It should be recalled that, in an open-chain model, 2-pentene oxide, no base attack at the secondary proton could be detected.[7] The systems studied are indicated in the generalized eq 3, and the results are given in Table II.



**7** **8** **9** (3)

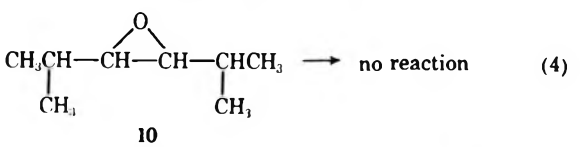
TABLE II

THE LITHIUM DIETHYLAMIDE INDUCED REARRANGEMENT OF ETHYLIDENECYCLOALKANE OXIDES (**7**)

| 7 | *n* | Time, hr | 8 | 9 |
|---|---|---|---|---|
| a | 5 | 1.5 | 70 | 30 |
| b | 6 | 2 | 0 | 100 |
| c | 7 | 2.5 | 38 | 62 |
| d | 8 | 2 | 66 | 34 |

Several points are worth noting. Although the cyclopentyl system **7a** no longer gives regiospecific results, endocyclic olefin formation is still preferred over primary proton abstraction, in contrast to the open-chain model. The ethylidenecyclooctane oxide **7d** gives results which are quite analogous to those obtained with **7a**. This behavior is anticipated from the results for **1b** and **1e** in Table I. Similarly, where the propylidenecycloheptane oxide **1d** gave incomplete specificity, the ethylidene analog **7c** reverts to slight preference for primary proton abstraction. As expected, ethylidenecyclohexane oxide yields only 1-vinylcyclohexanol (**9b**). Thus the results with the two sets of epoxides, ethylidene- and propylidenecycloalkane oxides, are mutually consistent.

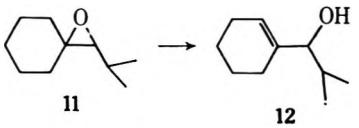
We had earlier observed that a system containing only tertiary $\beta$ protons, *i.e.*, 2,5-dimethyl-3-hexene oxide (**10**), gave no observable reaction when refluxed



**10** (4)

for 2 days with lithium diethylamide. Compound **11** was prepared in order to examine the competition between secondary cyclohexyl and tertiary proton ab-abstraction. The reaction was extremely slow; under the conditions normally employed, only 24% of the

epoxide had rearranged after 72 hr, giving **12** as the exclusive product. Again this behavior is anticipated




**11** **12** (5)

based on the inert nature of **10** and the formation of a small amount of **2c** in the reaction of **1c**.

The results presented here provide another example of the unusual and synthetically useful selectivity of the base-induced rearrangement of epoxides. We are continuing to explore other features of this interesting reaction.

## Experimental Section[10]

**Olefins.**—The method of Schlosser and Christmann,[11] involving the appropriate alkyltriphenylphosphonium bromide, was used to prepare olefins. The cyclic ketones used in this ylide reaction were all, with the exception of cyclobutanone, distilled commercial materials. Cyclobutanone was prepared using a literature method.[12] The product olefins had the following characteristics.

**Propylidenecyclobutane** (56%):[13] bp 96–104° (83% pure); nmr $\delta$ 5.15 (nonet, 1, $J$ = 2.5 Hz, C=CH), 2.7 (t, 4, $J$ = 7.5 Hz, $CH_2\mathbf{H}_2C$=CH), 2.3–1.5 (m, 4), and 0.95 ppm (t, 3); ir 1460, 1300, and 850 cm$^{-1}$.

**Propylidenecyclopentane**[14] (44%): bp 56–58° (43 mm); nmr $\delta$ 5.08 (nonet, 1, $J$ = 2.3 Hz, C=CH), 2.2–1.1 (m, 10), and 0.7 ppm (t, 3); ir 1460, 900, and 850 cm$^{-1}$.

**Propylidenecyclohexane**[15] (77%): bp 69–70.5° (70 mm); nmr $\delta$ 4.9 (t, 1, $J$ = 7 Hz, C=CH), 2.2–1.6 (m, 6), 1.6–1.0 (m, 6), and 0.7 ppm (t, 3); ir 1450, 983, 890, 841, 742, and 695 cm$^{-1}$.

**Propylidenecycloheptane** (78%): bp 90° (45 mm); nmr 5.0 (t, 1, $J$ = 7 Hz, C=CH), 2.5–1.1 (m, 14), and 0.9 ppm (t, 3); ir 2960 and 1460 cm$^{-1}$.

**Propylidenecyclooctane** (75%): bp 93–97° (30 mm); nmr $\delta$ 5.23 (t, 1, $J$ = 7 Hz, C=CH), 2.5–1.8 (m, 6), 1.55 (broad singlet, 10), and 0.95 ppm (t, 3); ir 2920 and 1460 cm$^{-1}$.

**Propylidenecyclododecane** (83%): bp 144–150° (20 mm); nmr $\delta$ 5.08 (t, 1, $J$ = 7 Hz, C=CH), 2.0 (m, 6), 1.3 (s, 18) and 0.92 ppm (t, 3); ir 1475, 1450, 880, and 725 cm$^{-1}$.

**Ethylidenecyclopentane**[16] (24%): bp 52–58° (80 mm); nmr $\delta$ 5.1 (m, 1), 2.1 (m, 4), and 1.6 ppm (m, 7); ir 3050, 945, and 805 cm$^{-1}$.

**Ethylidenecyclohexane** was a commercial sample purchased from the Aldrich Chemical Co.

**Ethylidenecycloheptane**[17] (62%): bp 71–74° (53 mm); nmr $\delta$ 5.3 (quartet, 1, $J$ = 7 Hz, C=CH), 2.25 (broad singlet, 4), and 1.8–1.4 ppm (m, 11); ir 2915, 1450, and 807 cm$^{-1}$.

**Ethylidenecyclooctane** (24%): bp 70–72° (50 mm) (81% pure by vpc); nmr $\delta$ 5.12 (quartet, 1, $J$ = 7 Hz, C=CH) and 2.4–1.1 ppm (broad multiplet, 17); ir 2920 and 1450 cm$^{-1}$.

**Isobutylidenecyclohexane** (9%): bp 88–92° (108 mm) (45% pure by vpc, contaminated with cyclohexanone); nmr $\delta$ 5.0 (d, 1, $J$ = 9 Hz, C=CH) and 0.9 ppm (d, 6).

**Epoxides.**—The epoxides were prepared from the olefins using peracetic acid[18] and had the following characteristics.

**Propylidenecyclobutane oxide** (82%): bp 75–77° (108 mm); nmr $\delta$ 2.8–0.8 ppm (multiplet); ir 1340, 1120, 920, and 830 cm$^{-1}$. *Anal.*[19] Calcd for $C_7H_{12}O$: C, 74.95; H, 10.78. Found: C, 74.73; H, 10.97.

**Propylidenecyclopentane oxide** (82%); bp 75–76° (39 mm); nmr $\delta$ 2.7 (t, 1, $J$ = 6 Hz, –O–CH[20]), 2.1–1.1 (m, 10), and 0.91 ppm (t, 3); ir 930 and 880 cm$^{-1}$. *Anal.* Calcd for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.32; H, 11.26.

**Propylidenecyclohexane oxide** (61%): bp 76° (20 mm); nmr $\delta$ 2.36 (t, 1, $J$ = 6 Hz, –O–CH[20]), 2.1–1.1 (m, 12), and 0.88 ppm (t, 3); ir 1040, 990, and 910 cm$^{-1}$. *Anal.* Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 77.09; H, 11.83.

**Propylidenecycloheptane oxide** (70%): bp 98° (30 mm); nmr $\delta$ 2.48 (t, 1, $J$ = 6 Hz, –O–CH[20]), 1.9–1.2 (m, 14), and 1.0 ppm (t, 3); ir 1460 and 910 cm$^{-1}$. *Anal.* Calcd for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 77.81; H, 11.89.

**Propylidenecyclooctane oxide** (70%): bp 110–112° (25 mm); nmr $\delta$ 2.57 (t, 1, $J$ = 6 Hz, –O–CH[20]), 1.6 (s) overlapping 1.5 (quartet, 16), and 1.03 ppm (t, 3); ir 955, 935, and 910 cm$^{-1}$. *Anal.* Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.24; H, 12.13.

**Propylidenecyclododecane oxide** (86%): bp 123–126° (3 mm); nmr $\delta$ 2.36 (t, 1, $J$ = 6 Hz, –O–CH[20]), 1.3 (broad singlet, 24), and 0.9 ppm (t, 3); ir 1255, 948, 885, and 723 cm$^{-1}$. *Anal.* Calcd for $C_{15}H_{28}O$: C, 80.29; H, 12.58. Found: C, 80.22; H, 12.79.

**Ethylidenecyclopentane oxide** (73%): bp 133–136°; nmr $\delta$ 3.25 (quartet, 1, $J$ = 6 Hz, –O–CH[20]), 2.3–1.5 (m, 8), and 1.4 ppm (d, 3, $J$ = 6 Hz, CH–$CH_3$); ir 1165, 1030, 1000, 980, 950, 930, and 865 cm$^{-1}$. *Anal.* Calcd for $C_7H_{12}O$: C, 74.95; H, 10.78. Found: C, 74.71; H, 10.94.

**Ethylidenecyclohexane oxide**[21] (64%): bp 158–160°; nmr $\delta$ 2.7 (quartet, 1), 2.55 (broad singlet, 10), and 1.25 ppm (d, 3); ir 1030, 897, and 849 cm$^{-1}$.

**Ethylidenecycloheptane oxide**[22] (83%): bp 80–82° (30 mm); nmr $\delta$ 2.7 (quartet, 1, $J$ = 6 Hz, –O–CH[20]), 1.65 (broad singlet, 12), and 1.23 ppm (d, 3, $J$ = 6 Hz, CH–$CH_3$); ir 1020 and 870 cm$^{-1}$.

**Ethylidenecyclooctane oxide** (75%): bp 87–91° (21 mm); nmr $\delta$ 268 (quartet, 1, $J$ = 5.5 Hz, –O–CH[20]), 1.54 (s, 14), and 1.2 ppm (d, 3, $J$ = 5.5 Hz, CH–$CH_3$); ir 1150 and 1100 cm$^{-1}$. *Anal.* Calcd for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 77.62; H, 11.35.

**Isobutylidenecyclohexane oxide** (63%): preparative vpc, collected on a Carbowax 6000 column at 125°; nmr $\delta$ 2.15 (d, 1, $J$ = 8.5 Hz, –O–CH[20]), 1.5 (broad singlet, 11), and 0.95 ppm (two overlapping doublets, 6, $J$ = 5.5 Hz, CH–$CH_3$); ir 1010 and 917 cm$^{-1}$. *Anal.* Calcd for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 78.33; H, 11.76.

**Epoxide Rearrangements.**—All reactions were run in refluxing ether solvent using 0.01 mol of epoxide; 0.025 mol of lithium diethylamide, prepared from the amine and commercial butyllithium in hexane, was used.

Aliquots were withdrawn, quenched with water, and examined by vpc to follow the course of the reaction. Carbowax 6M and 20M columns were employed for vpc analysis. Rearrangement product yields were obtained from vpc peak areas (uncorrected).

After quenching with water and evaporation of solvent, the products from the rearrangement reaction were isolated by preparative vpc and analyzed by nmr and ir. In cases where positive identification was not possible by spectral means, the product was catalytically reduced and then compared by gas chromatography to the saturated alcohols prepared by lithium aluminum hydride reduction of the epoxide or appropriate ketone.

The major products from **propylidenecyclobutane oxide** (66%) were catalytically reduced to give a mixture of 15% 1-propylcyclobutanol (ir 3350, 1270, 1175, 1038, and 963 cm$^{-1}$, identical with sole product from $LiAlH_4$ reduction of the epoxide), 72% 1-cyclobutylpropanol [nmr $\delta$ 3.1 (m, 2), 1.8 (m, 7), 1.25 (m, 2), and 0.9 ppm (t, 3); ir 3350, 1108, 1040, and 973 cm$^{-1}$], and 9%

(10) Nmr spectra were obtained in carbon tetrachloride solution using either a Varian A-60 or a Jeolco C-60H spectrometer. Infrared spectra were obtained on neat thin films using a Perkin-Elmer 337 grating spectrometer.

(11) M. Schlosser and K. F. Christmann, *Angew. Chem.*, **76**, 683 (1964).

(12) J. M. Conia and P. Leriverend, *C. R. Acad. Sci.*, **250**, 1078 (1960).

(13) The per cent yield is given in parentheses after the compound name throughout the Experimental Section.

(14) A. F. Plate and A. A. Melnikov, *Zh. Obshch. Khim.*, **29**, 1064 (1959).

(15) D. Seyferth, W. E. Hughes, and J. K. Heeren, *J. Amer. Chem. Soc.*, **87**, 2847 (1965).

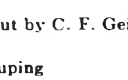
(16) R. B. Turner and R. H. Garner, *ibid.*, **80**, 1424 (1958).

(17) A. Maccioni and M. Secci, *Ann. Chim. (Rome)*, **54**, 226 (1964).

(18) M. Korach, D. R. Nielsen, and W. H. Rideout, *J. Amer. Chem. Soc.*, **82**, 4328 (1960).

(19) Analyses were carried out by C. F. Geiger, 312 E. Yale St., Ontario, Calif.

(20) –O–CH is from the grouping




(21) R. Jacquier, M. Mousseron, and R. Zagdourn, *Bull. Soc. Chim. Fr.*, 1042 (1959).

(22) A. Endo, M. Saito, M. Takahashi, K. Nagata, and Y. Fushizaki, *Nippon Kagaku Zasshi*, **86**, 1304 (1965).

cyclobutyl ethyl ketone (ir 1710, 1247, 1132, and 970 $cm^{-1}$, identical with product from Jones oxidation of 1-cyclobutylpropanol).

**Propylidenecyclopentane oxide** gave a single product in 84% yield: nmr $\delta$ 5.4 (s, 1), 4.0 (t, 1, $J$ = 6 Hz, CH–OH), 2.9 (d, 1, $J$ = 3 Hz, OH, shifts with formic acid), 2.5–1.2 (m, 8), and 0.85 ppm (t, 3, $J$ = 6.5 Hz, $CH_3$); ir 3320, 1090, and 900 $cm^{-1}$.

**Propylidenecyclohexane oxide** after 49 hr gave 9% unreacted epoxide and a 69% yield of two products. **3c** (95%): nmr $\delta$ 5.35 (m, 2), 2.3 (s, 1, shifts with formic acid, OH), 1.7 (d, 3, $J$ = 5 Hz, $CH_3$), and 1.55 ppm (broad singlet, 10); ir 3370 and 970 $cm^{-1}$. **2c** (5%): nmr $\delta$ 5.47 (t, 1, $J$ = 2.5 Hz, C=CH), 3.7 (t, 1, $J$ = 6.5 Hz, CH–OH), 2.5 (s, 1, OH), 2.2–1.2 (m, 10), and 0.8 ppm (t, 3, $J$ = 7 Hz, $CH_3$); ir 3330, 1003, 960, and 917 $cm^{-1}$.

**Propylidenecycloheptane oxide** was consumed within 5 hr, giving 76% of two volatile products. **2d** (98%): nmr $\delta$ 6.2 (t, 1, $J$ = 7 Hz, C=CH), 4.1 (t, 1, $J$ = 7 Hz, CH–OH), 2.7–1.3 (m, 13), and 0.9 ppm (t, 3, $J$ = 8 Hz, $CH_3$); ir 3320, 1020, and 850 $cm^{-1}$. The minor product, **3d** (2%), was identified by catalytic reduction to 1-propylcycloheptanol which was the major product from $LiAlH_4$ reduction of the epoxide.

**Propylidenecyclooctane oxide** after 2 hr gave 74% of a single product, **2e**: nmr $\delta$ 5.75 (t, 1, $J$ = 8 Hz, C=CH), 4.0 (t, 1, $J$ = 7 Hz, CH–OH), 2.2 (m, 4), 1.6 (broad singlet, 9), and 0.9 ppm (t, 3, $J$ = 8 Hz, $CH_3$); ir 3350, 1100, and 850 $cm^{-1}$.

**Propylidenecyclododecane oxide** was completely rearranged in 22 hr, yielding 66% of a product mixture. The major component (84%) was shown to be **2f**: nmr $\delta$ 6.0 (t, 1, $J$ = 8.5 Hz, C=CH), 4.9 (t, 1, $J$ = 7.5 Hz, CH–OH), 2.6–2.0 (m, 4), 2.0–1.2 (m, 19), and 1.0 ppm (t, 3, $J$ = 8 Hz, $CH_3$); ir 3370, 1090, 1010, and 970 $cm^{-1}$. Two lesser components, 12 and 4%, were not elucidated.

**Ethylidenecyclopentane oxide** after 1.5 hr gave 82% of two products. The major product (70%) was **8a**: nmr $\delta$ 6.2 (s, 1), 4.85 (quartet, 1, $J$ = 7.5 Hz, CH–OH), 3.5 (s, 1), 2.9–1.8 (m, 6), and 1.4 ppm (d, 3, $J$ = 7 Hz, $CH_3$); ir 3340, 1160, and 1075 $cm^{-1}$. The remainder (30%) was **9a**: nmr $\delta$ 6.1–4.8 (ABC pattern, 3) and 2.0–1.2 ppm (m, 8), OH peak variable; ir 3360, 3080, 990 (doublet), and 920 $cm^{-1}$.

**Ethylidenecyclohexane oxide** rearranged to a single product in 66% yield, **9b**: nmr $\delta$ 7.0–5.4 (ABC pattern, 3), 2.2 (s, 1, OH), and 1.7 ppm (broad singlet, 10); ir 3370, 3070, 1265, 995, 965, 925, and 910 $cm^{-1}$.

**Ethylidenecycloheptane oxide** gave a 74% yield of two allylic alcohols. The minor alcohol (38%) was **8c**: nmr $\delta$ 5.85 (t, 1, $J$ = 6.5 Hz, HC=C), 4.16 (quartet, 1, $J$ = 6.5 Hz, CH–OH), 2.8 (s, 1, OH), 2.4–1.9 (m, 4), 1.9–1.3 (m, 6), and 1.16 ppm (d, 3, $J$ = 7 Hz, $CH_3$); ir 3340, 1080, 1063, 986, and 848 $cm^{-1}$. The major product **9c** comprised 62% of the mixture: nmr $\delta$ 6.4–4.9 (ABC pattern, 3), 2.3 (s, 1, –OH), and 1.62 (broad singlet, 12); ir 3370, 1035, 1000, and 920 $cm^{-1}$.

**Ethylidenecyclooctane oxide** also led to a mixture of two alcohols in 73% overall yield. **8d** (66%): nmr $\delta$ 5.42 (t, 1, $J$ = 8 Hz, HC=C), 4.05 (quartet, 1, $J$ = 6 Hz, CH–OH), 3.2 (s, 1, OH), 2.1 (broad singlet, 4), 1.46 (s, 8), and 1.17 ppm (d, 3, $J$ = 6.5 Hz, $CH_3$); ir 3330, 1160, 1100, 1062, and 848 $cm^{-1}$. **9d** (34%): nmr $\delta$ 6.0–4.6 (ABC pattern, 3) and 1.55 ppm (broad singlet, 15, includes OH); ir 3375, 1160, 995, 972, and 919 $cm^{-1}$.

**Isobutylidenecyclohexane oxide**, after 72 hr reflux, was up to 76% unreacted. The sole product was **12**: nmr $\delta$ 5.4 (s, 1, HC=C), 4.6 (s, 1, OH), 3.36 (d, 1, $J$ = 7.5 Hz, CH–OH), 2.3–1.2 (m, 9), and 0.83 ppm (two overlapping doublets, 6); ir 3400, 1140, 1014, and 915 $cm^{-1}$.

**Registry No.**—Propylidenecyclobutane, 28253-07-8; propylidenecyclopentane, 4810-12-2; propylidenecyclohexane, 2129-93-3; propylidenecycloheptane, 17257-34-0; propylidenecyclooctane, 28256-52-2; propylidenecyclododecane, 28256-53-3; ethylidenecyclopentane, 2146-37-4; ethylidenecycloheptane, 10494-87-8; ethylidenecyclooctane, 19780-51-9; isobutylidenecyclohexane, 28256-56-6; **1a**, 28256-57-7; **1b**, 28256-58-8; **1c**, 28256-59-9; **1d**, 28256-60-2; **1e**, 28256-61-3; **1f**, 28256-62-4; **7a**, 28256-63-5; **7b**, 17328-74-4; **7c**, 28256-65-7; **7d**, 28256-66-8; **11**, 28256-67-9.

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# On the Rigidity to Carbanion Inversion of Four-, Five-, and Six-Membered Cyclic Organomagnesium Compounds

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Several 1,1-dimethylcycloalkylmagnesium halides were synthesized and their nmr spectra obtained as a function of temperature. Each reagent gave rise to an equal doublet for the methyl resonance. The nmr spectra were independent of the temperature, and it is concluded that carbanion inversion is slow on the nmr time scale up to 175°. The various effects responsible for this result are discussed in terms of what is known about the mechanism of inversion in primary Grignard reagents. It is concluded that carbon bridging in Grignard dimers is not favored when the bridging group is cycloalkyl.

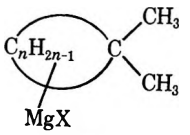
Inversion rates of carbon bonded to metal in primary organometallic compounds of lithium, magnesium, aluminum, and zinc have been reported.[1-5] However, so far there has been relatively little work on inversion in secondary systems. Letsinger found 2-octyllithium inverted slowly at low temperatures.[6] Jensen and Nakamaye determined the endo/exo ratio for 2-norbornylmagnesium bromide.[7] This reagent also inverted slowly.[7]

While our work on inversion in primary organometallic systems was proceeding, we initiated some experiments on secondary reagents. Meanwhile, Whitesides and Roberts[2] discussed the behavior of the nmr spectra of 3,3-dimethylcyclobutylmagnesium bromide and 2,4-dimethylpentylmagnesium bromide-3 and concluded carbanion inversion to be slow on the nmr time scale.[2] Also, Glaze and Selman have reported 4-*tert*-butylcyclohexyllithium to be configurationally stable.[8]

The approach we have chosen consists of synthesizing various 1,1-dimethylcycloalkylmagnesium halides, I, and obtaining their nmr spectra as a function of tem-

(1) G. M. Whitesides, M. Witanowski, and J. D. Roberts, *J. Amer. Chem. Soc.*, **87**, 2854 (1965).
(2) G. M. Whitesides and J. D. Roberts, *ibid.*, **87**, 4878 (1965).
(3) G. Fraenkel and D. T. Dix, *ibid.*, **88**, 979 (1966).
(4) M. Witanowski and J. D. Roberts, *ibid.*, **88**, 737 (1966).
(5) G. Fraenkel, D. T. Dix, and M. J. Carlson, *Tetrahedron Lett.*, 579 (1968).
(6) R. L. Letsinger, *J. Amer. Chem. Soc.*, **72**, 4842 (1950).
(7) F. R. Jensen and K. L. Nakamay, *ibid.*, **88**, 3437 (1966).
(8) W. H. Glaze and C. M. Selman, *J. Organometal. Chem.*, **11**, 3 (1968).

perature. From the results together with a consideration of what is known about ring inversion in these systems it should be possible to obtain at least qualitative information about carbanion inversion rates.

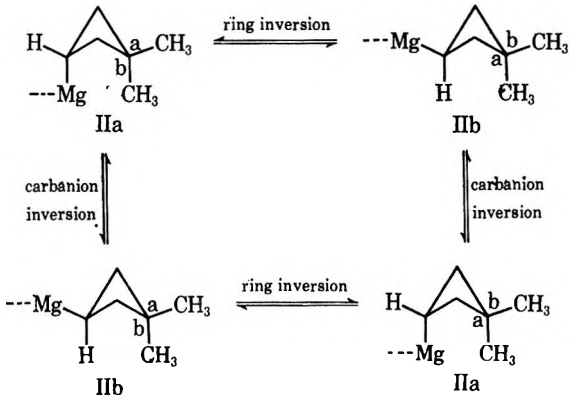



I

First, it is assumed that, although organomagnesium compounds exist in solution as mixtures of aggregates, carbon–magnesium bond exchange in ethers is still fast enough at −70° to average any shifts among species.[9,10] However, in the presence of organomagnesium alkoxides and certain diamines, carbon–magnesium bond exchange rates have been measured with the nmr line-shape method.[9]

By analogy to what is known about cyclobutanes, 3,3-dimethylcyclobutylmagnesium bromide should exist in two conformations.[11−14] The methyl groups in each should give rise to a doublet. Fast ring inversion and slow carbanion inversion should average the shifts between the conformers to a single doublet, while if both processes are fast all the methyl resonances will be averaged to a single line. It is already known that inversion in cyclobutanes is fast on the nmr time scale down to −100°.[15,16] Hence, it should be possible to estimate the rate of inversion from the methyl proton nmr line shape[17,18] (see Scheme I).

SCHEME I




The arguments for the other cyclic Grignard reagents follow those for the cyclobutyl reagent. In the case of cyclohexanes, shifts among conformers are usually averaged out by fast chair to chair inversion by 60°.[19] Finally, for 2,2-dimethylcyclopentylmagnesium bromide, we need not consider ring inversion and the pseudorotation discussed by Brutcher and Baur[20] is probably too fast to be detected by nmr spectroscopy.

We proceed below to describe the syntheses of the Grignard reagents and their precursors. It will be shown that inversion in cyclic organomagnesium compounds is slow compared to the primary reagents.

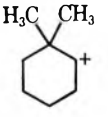
## Results and Discussion

3,3-Dimethylcyclobutanecarboxylic acid[21,22] was converted to 3,3-dimethylbromocyclobutane (III), by means of the Hunsdiecker reaction,[2] run in pentane.

Kishner's method,[22] the action of fuming HBr on cyclobutyldimethylcarbinol followed by work-up with base, afforded 2,2-dimethylcyclopentyl bromide (IV), together with two olefins which were identified to be 1,2-dimethylcyclopentene and isopropylidenecyclobutane.

The preparation of 2,2-dimethylcyclohexyl bromide (V) from cyclopentyldimethylcarbinol and fuming HBr[23] gave also two olefins identified to be isopropylidenecyclopentane and 1-isopropylcyclopentene.

When cyclopentyldimethylcarbinol was treated with 60% sulfuric acid at 80° for 4 hr, the products consisted of 1-isopropylcyclopentene (47%), isopropylidenecyclopentane (50%), and traces of isopropenylcyclopentane. The absence of ring-expanded products in this experiment is consistent with the finding of Johnson and Owyang that 2,2-dimethylcyclohexanol subjected to formolysis conditions slowly contracts to various five-membered ring compounds[24] and that the formation of cation VI is reversible.




VI

The synthesis of 4,4-dimethylcyclohexyl bromide (VII) was accomplished by halo decarboxylation of 4,4-dimethylcyclohexanecarboxylic acid (see Experimental Section for precursors).

Finally, 3,3-dimethylcyclohexyl bromide (VIII) was synthesized by a modification of Doering's procedure,[25] reacting the corresponding alcohol with hydrogen bromide.

The cyclic halides III, IV, V, VII, and VIII reacted with magnesium in ether, THF, and dimethoxymethane to give mainly coupling products and only low yields of the corresponding Grignard reagents IX–XIII. However, in diglyme at 60° these halides were smoothly

(9) H. O. House, R. A. Latham, and G. M. Whitesides, *J. Org. Chem.*, **32**, 2481 (1967).

(10) The possibility of degenerate shifts among species will not alter the interpretations.

(11) J. D. Dunitz and V. Schomaker, *J. Chem. Phys.*, **20**, 1703 (1952).

(12) G. W. Rathjens, Jr., and W. D. Gwinn, *J. Amer. Chem. Soc.*, **75**, 5629 (1953).

(13) G. W. Rathjens, N. K. Freeman, W. D. Gwinn, and K. S. Pitzer, *ibid.*, **75**, 711 (1961).

(14) A. Almennigen, O. Bastiansen, and P. N. Skancke, *Acta Chem. Scand.*, **15**, 711 (1961).

(15) R. P. Bauman and B. J. Balkin, *J. Chem. Phys.*, **45**, 496 (1966).

(16) S. Meiboom, Abstracts, 140th National Meeting of the American Chemical Society, Chicago, Ill., 1961, p 26T.

(17) H. S. Gutowsky, D. M. McCall, and C. P. Slichter, *J. Chem. Phys.*, **21**, 279 (1953).

(18) In the event of accidental degeneracy of all the methyl shifts, no conclusions can be drawn.

(19) (a) M. Friebolin, W. Faisst, M. G. Schmid, and S. Kabuss, *Tetrahedron Lett.*, 1317 (1966); W. Reusch and D. F. Anderson, *ibid.*, 253 (1966); R. J. Abraham and D. B. MacDonald, *Chem. Commun.*, 188 (1966); also reviewed in J. D. Roberts, *Chem. Brit.*, 529 (1966). (b) Exceptions to this generalization include 3,3-difluoromethylcyclohexane, 4,4-difluoromethylcyclohexane, and 4,4-difluorobutylcyclohexane: S. L. Spassov, P. L. Griffith, E. S. Glazer, N. Nagarajan, and J. D. Roberts, *J. Amer. Chem. Soc.*, **89**, 88 (1967).

(20) F. V. Brutcher and W. Baur, Jr., *Science*, **132**, 1489 (1960).

(21) A. Campbell and H. N. Ryden, *J. Chem. Soc.*, 3002 (1953).

(22) N. Kishner, *Chem. Zentralbl.*, I, 543 (1911); *ibid.*, II, 1859 (1908).

(23) S. S. Nametkin and M. A. Volodina, *Zh. Obshch. Khim.*, **21**, 331 (1951).

(24) W. S. Johnson and R. Owyang, *J. Amer. Chem. Soc.*, **86**, 5595 (1964).

(25) W. v. E. Doering and F. M. Beringer, *ibid.*, **71**, 2221 (1949).

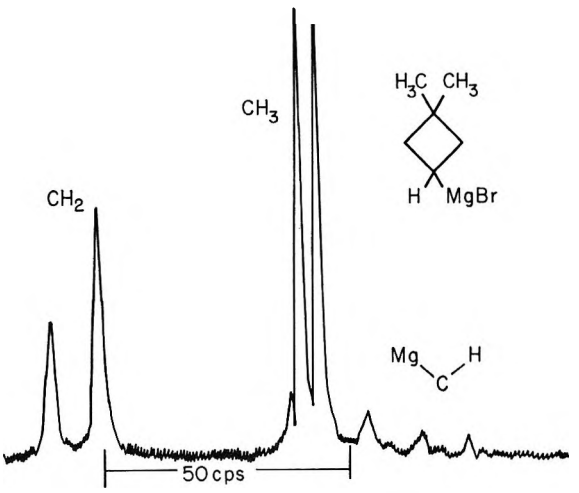



Figure 1.—Nmr spectrum (60 MHz) of 3,3-dimethylcyclobutylmagnesium bromide, 1.4 *M* in diglyme, 40°.

converted to Grignard reagents in nearly quantitative yields. Attempts were made to convert these halides to organolithium compounds. The only bromide which underwent this conversion in high yield was III. The nmr spectra of the hydrolysates of these organometallic reagents showed only absorption belonging to the corresponding hydrocarbon.

The nmr spectra of reagents IX–XIII are illustrated in Figures 1–4. Chemical shift assignments are labeled on the spectra. Methyl resonances of contained impurities are listed as RH or RBr.

Only in the case of 3,3-dimethylcyclobutylmagnesium bromide is it possible to resolve all the different hydrogens. Each reagent gives a single multiplet for the methine hydrogen, H–C–Mg. These shifts are listed in Table I. For all the reagents with the exception of 3,3-dimethylcyclobutylmagnesium bromide (Figure 1), the methylene hydrogens belong to strongly coupled systems and give rise to complex multiplets. Finally, each reagent in diglyme gives rise to two lines for the methyl hydrogens (Figure 3). The nmr spectrum of 3,3-dimethylcyclobutyllithium is shown in Figure 2b. This spectrum clearly shows magnetically nonequivalent methyls, also. Other details concerning these spectra will be discussed below.[26]

TABLE I

H–C–Mg SHIFT IN *x*,*x*-DIMETHYLCYCLOALKYLMAGNESIUM BROMIDES, 1 *M* IN DIGLYME

| Reagent | Ring size | *x* | τ |
|---|---|---|---|
| IX | 4 | 3 | 9.16 |
| X | 5 | 2 | 10.60 |
| XI | 6 | 2 | 10.30 |
| XIII | 6 | 3 | 10.05 |
| XII | 6 | 4 | 10.30 |

The nmr spectra of the Grignard reagents were obtained from 40 to 175°. Aside from changes in resolution which attend changes in viscosity, the line positions and intensities were independent of the temperature. However, at the higher temperatures, around 170°, each sample underwent slow irreversible changes as a result of which the spectrum of the Grignard reagent was eventually replaced by that of its hydrolysate. This behavior is illustrated for 3,3-dimethylcyclohexylmagnesium bromide in Figure 4. Evidently at the higher temperatures the reagents abstract protons from the solvent. Due to viscosity broadening it was not possible to obtain useful nmr data from these solutions below 10°. The sample of 3,3-dimethylcyclobutyllithium decomposed above 60° and was not further investigated.

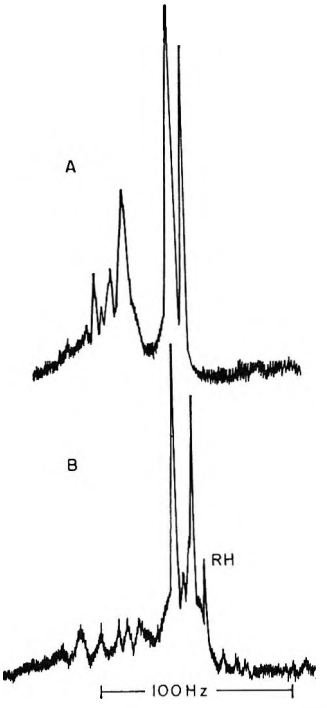



Figure 2.—Nmr spectra (60 MHz), 40°, of (a) 3,3-dimethylcyclohexylmagnesium bromide, 1.4 *M* in diglyme, and (b) 3,3-dimethylcyclobutyllithium, 1.3 *M* in benzene.

On the basis of the discussion in the introduction, the conclusions for the four- and five-membered ring reagents are quite clear. Down to −100° cyclobutanes invert at rates which are fast on the nmr time scale. The simplicity of the H–C–Br resonance in III, as well as the H–C–Mg resonances in its Grignard reagent IX, indicates ring flipping to be fast in the cyclobutyl compounds. The methyl resonance of 3,3-dimethylcyclobutylmagnesium bromide consists of two lines. Therefore, this reagent undergoes slow carbanion inversion up to 175°. Since pseudorotation in the five-membered reagent X is probably fast, the persistence of a methyl doublet up to 175° indicates slow carbanion inversion in this case, also. This same conclusion applies to the cyclohexylmagnesium bromides; carbanion inversion is slow up to 175° and ring inversion is fast above 40°. The latter is evident also from the simplicity of the H–C–Mg resonances of these Grignard reagents and is also found for their precursors.[27]

Jensen and Nakamaye have resolved shifts among the two chair conformers of cyclohexylmagnesium reagents[28] at low temperatures. The observation of two

(26) In one case, 3,3-dimethylcyclohexylmagnesium bromide in dimethoxymethane, there is fine structure in the methyl resonance indicative of slowly interconverting species. Above 50° the lines broaden slightly; however, the shifts remained constant.

(27) In contrast to this result we find that the carbinyl resonance of 3,3-dimethylcyclohexyl bromide is quite complicated and has the appearance of the resonance in a substituted cyclohexane undergoing slow ring inversion.

(28) F. R. Jensen and K. L. Nakamaye, *J. Amer. Chem. Soc.*, **90**, 3248 (1968).

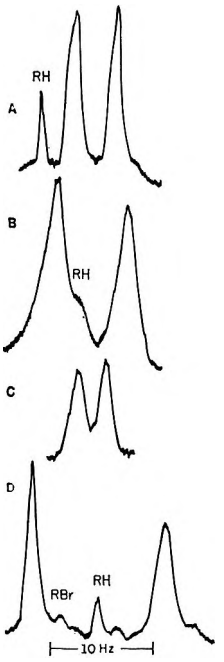



Figure 3.—Methyl group nmr from (a) 4,4-dimethylcyclohexylmagnesium bromide, (b) 3,3-dimethylcyclohexylmagnesium bromide, (c) 2,2-dimethylcyclohexylmagnesium bromide, and (d) 2,2-dimethylcyclopentymagnesium bromide. All reagents are 1.4 *M* in diglyme, 40°.

resonances for these materials at −85° implies both ring and carbanion inversion to be slow at this temperature. Either one or both of these processes could be responsible for averaging the two H–C–Mg resonances at higher temperatures. These authors assign the axial and equatorial H–C–Mg hydrogen shifts to be $\tau$ 10.25 and 9.76.[28] If these values apply to our solutions of substituted cyclohexylmagnesium reagents in diglyme, it would appear that the 2,2-dimethyl- and 4,4-dimethylcyclohexylmagnesium bromides exist mainly in the conformations with the C–Mg bond equatorial.

In view of the above discussion it would appear that the persistence of doublets for the methyl resonances of 2,2- and 4,4-dimethylcyclohexylmagnesium bromide indicates these reagents to be inverting slowly on the nmr scale up to 175°.

In summary, we find here that carbanion inversion in four-, five-, and six-membered cycloalkylorganomagnesium compounds is slow in the nmr time scale up to 175°. This situation applies also to cyclopropylmagnesium compounds. Walborsky has found these to be configurationally stable for long periods of time.[29]

The maximum reciprocal mean lifetime between inversions at 175° for the reagents studied here is 1 $sec^{-1}$, while the extrapolated value for 2-methylbutylmagnesium bromide is $1.2 \times 10^{-5}$ $sec^{-1}$. In spite of the qualitative nature of the results, it is worthwhile to consider why carbanion inversion in the cyclic organomagnesium compounds should be so much slower than in the primary reagents.

The most convincing rationale for the data presented here comes from a consideration of the results from kinetic studies on inversion in primary systems. The available data indicate that inversion takes place in

(29) H. M. Walborsky and F. J. Impasato, *J. Amer. Chem. Soc.*, **81**, 5835 (1959).

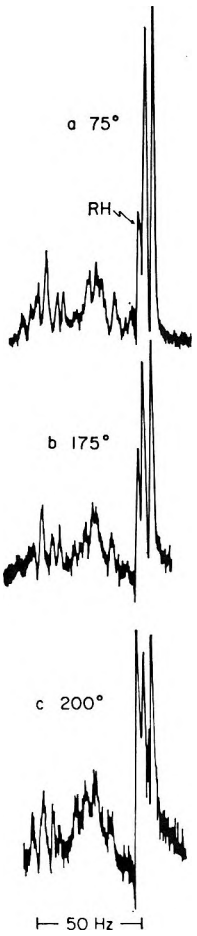



Figure 4.—Nmr spectra showing effect of heating 4,4-dimethylcyclohexylmagnesium bromide, 1.4 *M* in diglyme (a) after 10 min at 75°, (b) after 15 min at 175°, and (c) after 30 min at 200°.

dimers of 2-methylbutylmagnesium halides and that the transition state for inversion involves carbon bridging.[30] At the present time, it is not known whether carbon bridging is involved in Grignard dimers in the ground state. So far, there is no firm evidence for any of the structures which have been proposed for Grignard dimers.[31] If alkyl bridging takes place in the transition state for Grignard inversion, then bridging would be most likely for primary compared to secondary and tertiary groups, respectively. Such is the case among bridged organoaluminum compounds.[32]

The principle conclusion from this work is that carbanion inversion in cyclic organomagnesium bromides is slow on the nmr time scale up to 175°, and this effect is ascribed to the inability of secondary groups to bridge between magnesium centers.

## Experimental Section

**Physical Constants.**—All boiling points were those obtained during distillation and are uncorrected. All melting points were determined using a capillary apparatus or a Fisher-Johns apparatus and are uncorrected.

**Analyses.**—Elemental microanalyses of synthesized compounds were carried out by the microanalytical laboratories of Dr. A. Bernhardt, Mühlheim, Germany, or Galbraith Analytical Laboratories.

**Spectrometric Methods.**—Nuclear magnetic resonance spectra

(30) G. Fraenkel, C. Cottrell, and D. T. Dix, *ibid.*, submitted for publication.

(31) E. C. Ashby, *Quart. Rev., Chem. Soc.*, **21**, 259 (1967).

(32) E. G. Hoffmann, *Justus Liebigs Ann. Chem.*, **629**, 104 (1960).

were obtained on a Varian Model A-60 spectrometer. Infrared absorption spectra were obtained with a Perkin-Elmer Model 137 sodium chloride spectrometer. Vapor phase chromatographic work was undertaken with an Aerograph Hy-Fi Model 600 and an Aerograph "Autoprep" Model A-700. All analyses determined by vpc have been corrected for the weight:area factor utilizing an internal standard, except where otherwise designated. All vpc analyses were obtained with a 30% silicon gum rubber SE-30 on 45–60 Chromosorb W or 20% FFAP on 60–80 Chromosorb W.

**3,3-Dimethylcyclobutyl Bromide (III).**—A suspension of 3,3-dimethylcyclobutanecarboxylic acid (40 g, 0.312 mol) in 600 ml of distilled water was neutralized with 13 ml of 30% ammonium hydroxide. A solution of silver nitrate (53.2 g, 0.312 mol) in 200 ml of distilled water was added dropwise to the stirred solution of the acid. An additional 100 ml of water was added and the white precipitate was filtered, washed with water and then methanol, and dried in an oven at 50–60°. For the next step, the dried silver salt was powdered and sieved into a crystal dish. The silver salt was now dried in a vacuum oven at 80° for 60 hr. The yield consisted of 70 g (90.4%) of silver 3,3-dimethylcyclobutanecarboxylate.

The finely powdered silver salt (70 g, 0.298 mol) was placed in a 1-l. three-necked flask equipped with a dropping funnel, reflux condenser, and mechanical stirrer. All this equipment had been thoroughly dried in an oven at 100°. To the salt was added 360 ml of olefin-free dry pentane. While stirring, bromine (47.7 g, 0.298 mol), dried over phosphorus pentoxide, was slowly added through the dropping funnel over a period of 45 min. At first cooling was necessary, as the exothermic reaction was quite vigorous. When all the bromine had been added, the mixture was heated under reflux for 1 hr. It was then filtered and the silver bromide was washed on the filter with 100 ml of pentane. The filtrate was washed once with 200 ml of a 10% sodium bisulfite solution and then with distilled water and dried over magnesium sulfate. Evaporation of the solvent and distillation of the residue afforded 26.5 g (54.7%) of 3,3-dimethylcyclobutyl bromide as a colorless oil, bp 45.5–46.5° (32 mm) (lit.[2] bp 132°).

The purity of the compound was confirmed by vpc. The infrared spectrum (NaCl, neat) showed strong bands ($cm^{-1}$) at 2900, 1440, 1405, 1340, 1360, 1230, 990, and 788. The nmr spectrum (benzene, TMS internal standard) showed resonance at $\tau$ 5.80 (quintet, methine), 7.77 (multiplet), 8.99 (singlet, methyl), and 9.19 (singlet, methyl).

*Anal.* Calcd for $C_6H_{11}Br$: C, 44.18; H, 6.80; Br, 49.02. Found: C, 44.15; H, 6.76; Br, 49.09.

The Hunsdiecker reaction with 3,3-dimethylcyclobutane-*1-d*-carboxylic acid-*d* resulted in the formation of 3,3-dimethylcyclobutyl bromide-*1-d*.

**2,2-Dimethylcyclopentyl Bromide (IV).**—In a 250-ml two-necked flask equipped with a thermometer and a cooling tube was placed cyclobutyldimethylcarbinol (53.5 g, 0.468 mol). Approximately 50 ml of fuming hydrobromic acid was slowly added with cooling by means of an ice bath. The mixture was then heated in an oil bath with magnetic stirring at 100° for 2 hr. Much HBr was lost at this time. The resulting olive green solution was poured in a separatory funnel and washed a few times with distilled water. The lower layer of crude bromide was transferred to an erlenmeyer flask and heated with a solution of 20 g of potassium hydroxide in 50 ml of water at 100° for 2 hr. The bromide layer was separated, poured into a 100-ml flask, and, after addition of water, steam distilled. The bromide was dissolved in ether, washed with water, and finally dried over magnesium sulfate. The ether was then removed by distillation and the residual liquid distilled under reduced pressure to give 16 g of a fraction of isomeric olefins and 30.7 g (36.2%) of 2,2-dimethylcyclopentyl bromide, bp 55–56° (15 mm), as a colorless oil (lit.[22] bp 167°, partial dec). The purity of the bromide was confirmed by vpc. The infrared spectrum (NaCl, neat) showed strong bands at 2870, 1435, 1365, 1345, 1245, 1175, 838 and 804 $cm^{-1}$. The nmr spectrum ($CCl_4$, TMS internal standard) showed resonance at $\tau$ 6.13 (X portion of ABX, methine, $J_{AX} + J_{BX}$ − 15 cps), 7.55–8.60 (multiplet, methylene), and 8.96 (singlet, methyl).

*Anal.* Calcd for $C_7H_{13}Br$: C, 47.48; H, 7.39; Br, 45.13. Found: C, 47.31; H, 7.57; Br, 45.12.

Further evidence for the correct structure of the bromide came from the hydrocarbon obtained by hydrolysis of the corresponding Grignard reagent. The nmr spectrum of 1,1-dimethylcyclopentane (diglyme) showed at $\tau$ 8.15–8.85 (multiplet, methylene) and 8.98 (singlet, methyl). The peak areas were in ratio 4:3.

The isomeric olefins formed as side products from the preparation of the bromide were separated by vpc. Two components were obtained in the ratio of 4.5 to 95.5. The spectral properties of the lower boiling component established its structure to be isopropylidenecyclobutane: ir (NaCl, neat) max 2990, 2890, 2805, 1645, 1365, 1325, 1077, 1015, 915, and 797 $cm^{-1}$; nmr ($CCl_4$) $\tau$ 4.78 (center of complex multiplet, terminal vinyl protons), 7.38–8.15 (multiplet, methylene, methine), and 8.39 (singlet, methyl).

The second component was identified as 1,2-dimethylcyclopentene-1 by comparison of its nmr spectrum and retention time to those of an authentic sample: nmr ($CCl_4$) $\tau$ 7.51–8.35 (multiplet, methylene) and 8.44 (singlet, methyl).

**2,2-Dimethylcyclohexyl Bromide (V).**—In a 500-ml two-necked flask equipped with a thermometer and cooling tube were placed cyclopentyldimethylcarbinol (110 g, 0.858 mol) and 100 ml of fuming hydrobromic acid. The mixture was then heated in an oil bath with stirring at 100° for 3 hr. The heavier brown bromide layer was separated from the water. It was transferred to a 500-ml erlenmeyer flask and heated with stirring with a solution of 40 g of potassium hydroxide in 100 ml of water at 100° for 2 hr. The heavier crude bromide layer was separated, poured into a 1-l. flask, and steam distilled. The distilled product was dissolved in ether, washed with water, and dried over magnesium sulfate. The ether was removed and the residue distilled under reduced pressure to give a fraction of isomeric olefins, bp 40–60° (23 mm), and 99.4 g (60.6%) of colorless 2,2-dimethylcyclohexyl bromide, bp 85–85.5° (23 mm) [lit.[24] bp 85.5° (23 mm)]. The purity of the bromide was confirmed by vpc. The infrared spectrum (NaCl, neat) showed strong bands at 2870, 2885, 1448, 1430, 1367, 1348, 1200, 960, 854, 715, and 676 $cm^{-1}$. The nmr spectrum ($CCl_4$, TMS internal standard) showed resonance at $\tau$ 5.95 (ABX, methine, $J_{AX} + J_{BX}$ = 15.0 cps), 7.58–8.79 (multiplet, methylene), and 8.92 (singlet, methyl).

*Anal.* Calcd for $C_8H_{15}Br$: C, 50.28; H, 7 91; Br, 41.81. Found: C, 50.35; H, 7.87; Br, 41.78

The structure and identity of 2,2-dimethylcyclohexyl bromide was further proved by its chemistry.

A Grignard solution prepared in diglyme was hydrolyzed and the resulting hydrocarbon was compared in its spectral properties and retention time to a commercial sample of 1,1-dimethylcyclohexane. Their properties were the same: ir (NaCl, neat) max 2880, 2800, 1430, 1360, 1345, 1165, 957, and 846 $cm^{-1}$; nmr ($CCl_4$) $\tau$ 8.23–8.87 (multiplet, methylene) and 9.08 (singlet, methyl).

The Grignard reagent of the above bromide in ether was oxidized with molecular oxygen and the resulting alcohol compared to an authentic sample of 2,2-dimethylcyclohexanol. Both compounds showed the same spectral properties and vpc retention times. Treatment of the alcohol with phenyl isocyanate resulted in a phenylurethane which melted at 84.5–85° (lit.[33] mp 84–85°). The infrared spectrum (NaCl, neat) of the alcohol was characterized by a hydroxyl band at 330 $cm^{-1}$.

**Side Products from Cyclopentyldimethylcarbinol–HBr Reaction.**—The olefin fraction consisted of two components which were separated by vpc (XIV and XV). Samples (1 g) of these olefins were ozonized in methylene chloride at −78° for about 1 hr. The blue ozonide solution was poured into a flask containing 50 ml of water. The methylene chloride was removed on a steam bath. In both cases the water residue contained oils. The ozonized product of the lower boiling olefin XIV was soluble in a 5% solution of sodium bicarbonate, indicating an acid, whereas the product from olefin XV was insoluble. The alkaline solution from olefin XIV was acidified, extracted in ether, and gave a very high boiling oil. With semicarbazide hydrochloride it gave a semicarbazone, mp 183–185°. The melting point was close to that reported for the semicarbazone of 6-methyl-5-oxyheptanecarboxylic acid, mp 182.5–183.5°.[23]

Infrared and nuclear magnetic resonance spectra further proved the identity of olefin XIV as 1-isopropylcyclopentene-1: ir (NaCl, neat) max 3030, 2960, 1645, 1358, 1375, 1305, 1290, 1067, 1033, 948, and 807 $cm^{-1}$; nmr ($CCl_4$) $\tau$ 4.75 (singlet, vinyl), 7.50–8.52 (multiplet, methine, methylene), and 9.00 (doublet, methyl, $J$ = 6.0 cps).

The ozonized olefin XV was neutral and gave, after treatment with semicarbazide hydrochloride, a semicarbazone, mp 207–209°, very close to the reported melting point for the semicarbazone of

(33) H. Meerwein, *Justus Liebigs Ann. Chem.*, **405**, 142 (1914).

cyclopentanone,[34] mp 209–210°. The infrared and nuclear magnetic resonance spectra identified olefin XV as isopropylidinecyclopentane: ir (NaCl, neat) max 2910, 2820, 1645 (w), 1435, 1420, 1360, 1095, and 945 $cm^{-1}$; the nmr spectrum ($CCl_4$) showed no vinyl protons.

**Reaction of Dimethylcyclopentylcarbinol with Sulfuric Acid.**—When the dimethylcyclopentylcarbinol was heated with 60% sulfuric acid at 80° for 4 hr, it resulted in the formation of three compounds. All three decolorized bromine indicating alkenes. These were XIV (47%), isopropenylcyclopentane (2%) [XVI, 888 $cm^{-1}$ ($C{=}CH_2$)], and XV (51%) [bp 136° (lit.[23] bp 136–137°)].

**Preparation of 3,3-Dimethylcyclohexyl Bromide (VIII).**—The procedure used was a modification of that of Doering.[26] In a 100-ml three-necked flask equipped with a mechanical stirrer, reflux condenser, and insert tube was placed 3,3-dimethylcyclohexanol (32 g, 0.25 mol). A stream of hydrogen bromide was passed through the alcohol for 30 min at 5°, for 15 min at 100°, and for 2 hr at 130°. The reaction product was first washed with concentrated sulfuric acid with an equal amount of 50% methanol, with ammonium hydroxide until basic, and finally again with 50% methanol. Distillation of the dried product gave 31 g (64.8%) of colorless 3,3-dimethylcyclohexyl bromide, bp 63–63.5° (8 mm) [lit.[26] bp 80–82° (5 mm)].

The purity of the bromide was confirmed by vpc. The infrared spectrum (NaCl, neat) showed strong bands at 2880, 1445, 1373, 1350, 1330, 1312, 1285, 1250, 1235, 1205, 1170, 1130, 1042, 966, 945, 921, 840, 831, 715, and 695 $cm^{-1}$. The nmr spectrum ($CCl_4$, TMS internal standard) showed resonance at $\tau$ 5.64–6.30 (complex, multiplet, methine), 7.55–8.86 (complex, multiplet, methylene), 9.06 (singlet, methyl), and 9.09 (singlet, methyl).

*Anal.* Calcd for $C_8H_{15}Br$: C, 50.28; H, 7.91; Br, 41.81. Found: C, 50.22; H, 7.91; Br, 41.91.

Treatment of the Grignard reagent from VIII (0.02 mol) with 1-naphthyl isocyanate (1.69 g, 0.01 mol) gave, after recrystallization from methanol, a derivative with mp 201–202.5°, very close to the reported melting point of *N*-1-naphthyl-3,3-dimethylcyclohexanecarboxamide (lit.[25] bp 204–204.5°).

**1,5-Dibromo-3,3-dimethylpentane.**—Diethyl $\beta,\beta$-dimethylglutyrate was prepared by Perkin's procedure.[35] The ester was reduced to 3,3-dimethyl-1,5-pentanediol with lithium aluminum hydride.[36] To 3,3-dimethyl-1,5-pentanediol (71.5 g, 0.542 mol) was added, slowly, phosphorus tribromide (149 g, 0.55 mol) with stirring. The reaction mixture was heated at 90° for 12 hr. The ether layer was washed with sodium carbonate, dried over magnesium sulfate, and filtered. After evaporation of the ether, the residue was distilled under vacuum to give 116 g (83.2%) of colorless 1,5-dibromo-3,3-dimethylpentane: bp 86–86.5° (2 mm) [lit.[37] bp 80–81° (1.3 mm)]; ir (NaCl, neat) $\nu_{max}$ 2940, 1468, 1450, 1385, 1365, 1330, 1235, and 755 $cm^{-1}$.

**4,4-Dimethylcyclohexane-1,1-dicarboxylic Acid.**—The acid was prepared modifying the procedure of Otto.[37] In a 5-l. three-necked flask equipped with a mechanical stirrer, reflux condenser with a drying tube, and a dropping funnel was placed 2000 ml of absolute ethanol. The ethanol was slowly reacted with sodium (20.7 g, 0.96 g-atom) added over a period of 2 hr. Diethyl malonate (71 g, 0.45 mol) was added to the above solution followed by 1,5-dibromo-3,3-dimethylpentane (116 g, 0.448 mol). The reaction mixture was refluxed with stirring for 4 days. A solution of 100 g of sodium hydroxide in 500 ml of aqueous ethanol (50%) was then added and the refluxing continued for 10 hr. Ethanol was removed by steam distillation and the residual solution was acidified with hydrochloric acid, extracted with ether, and washed with distilled water. After the ethereal extract was dried over magnesium sulfate, the ether was evaporated and white crystals of 4,4-dimethylcyclohexane-1,1-dicarboxylic acid, mp 190–190.5° (reported[37] mp 190–192°), were obtained, yield 71 g (79.2%).

**4,4-Dimethylcyclohexanecarboxylic Acid.**—4,4-Dimethylcyclohexane-1,1-dicarboxylic acid (70.7 g, 0.353 mol) was heated with 0.3 g of powdered Pyrex glass in a 1-l. flask equipped with a reflux condenser carrying a thermometer. Evolution of carbon dioxide commenced soon after all the diacid had melted. The temperature was held for about 2 hr at 220°. Upon cooling, the residue solidified to shiny white needles. Recrystallization from ethanol–water gave 53.4 (95.8%) of 4,4-dimethylcyclohexanecarboxylic acid, mp 45–46° (reported[37] mp 45–47°).

**4,4-Dimethylcyclohexyl Bromide (VII).**—The acid just described was converted to the bromide by the Hunsdiecker reaction of the silver salt, in a procedure similar to that described above. Thus, 53.4 g of 4,4-dimethylcyclohexanecarboxylic acid gave with silver nitrate (58.3 g, 0.343 mol) and 82 g (91.2%) of dry silver salt.

The dry silver 4,4-dimethylcyclohexanecarboxylate (81.5 g, 0.31 mol) was allowed to react with bromine (49.5 g, 0.31 mol) in 500 ml of dry pentane. Work-up of the product in the usual manner resulted in 26.5 g (40.5%) of colorless VII, bp 57–58° (5 mm). The purity of the bromide was confirmed by vpc. The infrared spectrum (NaCl, neat) showed strong bands at 2850, 1455, 1440, 1325, 1305, 1285, 1250, 1205, 1172, 1135, 982, 973, 935, 842, 714, 699, and 686 $cm^{-1}$. The nmr spectrum ($CCl_4$, TMS internal standard) showed resonance at $\tau$ 5.87 (center of symmetrical multiplet, methine), 7.72–8.89 (multiplet, methylene), 9.04 (singlet, methyl), and 9.10 (singlet, methyl).

*Anal.* Calcd for $C_8H_{15}Br$: C, 50.28; H, 7.91; Br, 41.81. Found: C, 50.05; H, 7.84; Br, 42.05.

**Preparation of the Organometallic Compounds. Solvents.**—The solvents used for the preparation of organometallic compounds were distilled directly into the reaction vessel from a flask containing drying reagent. Diethyl ether was distilled from commercial methylmagnesium bromide. Dimethoxymethane, *n*-pentane, and benzene were distilled from lithium aluminum hydride. Diglyme was distilled twice from lithium aluminum hydride and then from methylmagnesium iodide under reduced pressure (50 mm).

**Metals.**—Lithium metal dispersed in wax and containing 1% of sodium was used for the preparation of the lithium compounds. The wax was removed just before reaction by washing the dispersion several times with dry solvent. Triply sublimed magnesium milled into fine shavings was used for the preparation of the Grignard compounds. The shavings were washed with dry ether, dried in a stream of helium, and stored in a desiccator.

**Apparatus.**—Hypodermic syringes were used for the addition of the bromides and the transfer of the organometallic compounds. The syringes were equipped with a stopcock and 6- or 8-in. 18-gauge needles.

Vacuum vials, fitted with a 1-mm straight bore stopcock and a 12/30 male joint, were used sometimes for storing or purification of organometallic reagents. All the above mentioned equipment was cleaned and dried in a current of argon prior to its use.

**Instrumentation.**—All nmr spectra of organometallic compounds were obtained with a Varian A-60 high resolution nmr spectrometer.

**Procedures for the Preparation of Organometallic Compounds. Grignard Reagents (General).**—The reaction vessel consisted of a 2.6-cm o.d. test tube equipped with a 24/40 outer joint at the open end and an 8-mm-o.d. side arm with straight bore Teflon stopcock. The apparatus was flamed out in a current of argon and loaded with a Teflon stirring bar together with the required amount of magnesium. It was then quickly attached to the receiving end of the still used to purify solvent. The solvent was then distilled over in two 20-ml portions. Each was removed by a hypodermic syringe. Finally, a 10-ml portion was distilled over, stirring was begun, and a few drops of the bromide were added to the reaction vessel through the Teflon stopcock. Sometimes reaction set in within a few minutes, but in some instances, heating or addition of 1–3 drops of 1,2-dibromoethane was necessary. The remaining bromide was then added at the rate of about 1 mmol/min, and the mixture heated afterward for 2 hr to complete reaction. Stirring was then discontinued, and the magnesium was allowed to settle. Aliquots were taken for nmr and base analysis. Most of the Grignard reagents were prepared in diglyme at 50°. Specific procedures follow.

**3,3-Dimethylcyclobutylmagnesium Bromide** —Into the helium-flushed reaction vial containing magnesium (0.965 g, 0.036 g-atom) was distilled 10 ml of dry diglyme. Stirring was started after the flask was immersed in an oil bath and heated to 50°. 3,3-Dimethylcyclobutyl bromide (29.3 g, 0.018 mol) was added slowly by means of a hypodermic syringe through the Teflon stopcock. The reaction mixture became cloudy after the first few drops, indicating initiation of the reaction. The rest of the bromide was added and stirring continued for 2 hr at 50°. A considerable amount of white solid precipitated after the solution had come to room temperature. One sample of the clear solution

(34) O. Aschau, *Ber.*, **45**, 1606 (1912).

(35) W. H. Perkin, *J. Chem. Soc.*, 1457 (1896).

(36) A. T. Blomquist and E. S. Wheeler, *J. Amer. Chem. Soc.*, **77**, 6307 (1955).

(37) B. Otto, Ph.D. Thesis, The Ohio State University, Columbus, Ohio, 1963.

was withdrawn from the reaction vessel and injected through a syringe cap into a dry nmr tube. The latter was cooled with liquid nitrogen and sealed with a hot flame. Another sample was titrated with 0.1 *N* hydrochloric acid (methyl orange as indicator), indicating a 1.5 *M* solution (95%). The nmr spectrum of the hydrolysate showed absorption only for 1,1-dimethylcyclobutane ($\tau$ 8.90).

**Registry No.**—3,3-Dimethylcyclobutyl bromide, 4237-75-6; 2,2-dimethylcyclopentyl bromide, 22228-38-2; isopropylidenecyclobutane, 1528-22-9; 2,2-dimethylcyclohexyl bromide, 28268-91-9; 1-isopropylcyclopentene, 1462-07-3; isopropylidinecyclopentane, 765-83-3; 3,3-dimethylcyclohexyl bromide, 25090-98-6; 4,4-dimethylcyclohexyl bromide, 25090-97-5; 3,3-dimethylcyclobutylmagnesium bromide, 4237-72-3; 3,3-dimethylcyclohexylmagnesium bromide, 28268-97-5; 4,4-dimethylcyclohexylmagnesium bromide, 28268-98-6; 2,2-dimethylcyclohexylmagnesium bromide, 28268-99-7; 2,2-dimethylcyclopentylmagnesium bromide, 28269-00-3.

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# Organophosphorus Compounds. XII.[1a] $^1$H and $^{31}$P Nuclear Magnetic Resonance Spectroscopic Studies of the Protonation and Cleavage of Trialkyl (Aryl) Phosphates and Phosphites, Dialkyl Phosphonates, and Phosphorus Oxy Acids in $FSO_3H$ and $FSO_3H$–$SbF_5$ Solution

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Protonation and cleavage of phosphoric acid, phosphonic acid, phosphinic acid, trialkyl (aryl) phosphates, trialkyl (aryl) phosphites, and dialkyl phosphonates were studied in fluorosulfuric acid and fluorosulfuric acid–antimony pentafluoride solution. $^1$H and $^{31}$P nmr spectra of the phosphonium ions [including the hydroxyphosphonium ions $H_nP(OH)_{4-n}^+$, $n$ = 0–2], as well as those of the precursors, were obtained generally at −60°. Tetravalent phosphoryl compounds were protonated on the phosphoryl oxygen atom; tervalent compounds were protonated at the phosphorus atom. The nmr data showed that in the protonated intermediates there was a substantial amount of back-donation of the oxygen nonbonded electron pairs to the empty phosphorus d orbital. By raising the temperature, several of the protonated compounds were subject to decomposition reactions, including carbon–oxygen bond cleavage and fluorination.

The chemical behavior of phosphates and phosphites under acidic conditions has long been a subject of interest to many investigators.[2] The acidic solvolyses[3] and the dealkylation by hydrogen halides[4] of phosphate triesters have been examined in detail. Arbuzov's classic paper[5] is the foundation of our understanding of the reactions of phosphite triesters with hydrogen halides.[4] Not only have interactions of phosphite triesters with other strong acids been studied,[6] but protonation by a variety of donors has also been invoked.[2] Dialkyl phosphonates are similarly dealkylated by hydrogen halides;[4] they also participate in other acid-catalyzed reactions.[7]

The chemistry of the parent monophosphorus oxy acids with regard to other acids is of interest as a model for the reactions of the organophosphorus compounds. The electrochemistry[8] and self-condensation[9] of orthophosphoric acid have been explained by autoprotolysis: $2H_3PO_4 \rightleftharpoons P(OH)_4^+ + H_2PO_4^-$. Oxygen isotope exchange between phosphoric acid and water is acid catalyzed.[10] The acid-catalyzed equilibration of the tautomeric forms of phosphonic acid[11] and phosphinic acid has been considered to be important in the many acid-catalyzed oxidation and isotope exchange experiments which have been conducted with these acids.[2]

However, fewer efforts have been made to obtain protonated phosphates and phosphites (the intermediates assumed to arise from the interactions with acids) sufficiently stable for direct observation. There are varying views on the stability of the complexes that phosphoric acid forms with hydrochloric acid and perchloric acid,[12] where phosphoric acid is thought to be a proton acceptor. Sulfuric acid is viewed as a proton donor to phosphoric acid,[12e,13] and $^{31}$P nuclear magnetic resonance chemical shifts of phosphates in sulfuric acid

(1) (a) Part XI: G. A. Olah and C. W. McFarland, *J. Org. Chem.*, **34**, 1832 (1969). (b) National Institutes of Health Predoctoral Research Fellow, 1968–1970. (c) Taken in part from the Ph.D. Dissertation of C. W. McFarland, Case Western Reserve University, 1971.

(2) The reactions with acids of the types of phosphorus compounds with which this paper is concerned, with emphasis on the involvement of protonated intermediates, have been thoroughly reviewed: C. W. McFarland, Ph.D. Thesis, Case Western Reserve University, Cleveland, Ohio, 1971.

(3) Recent reviews of acidic solvolyses can be found in (a) E. Cherbuliez, *Chimia*, **15**, 327 (1961); (b) C. A. Bunton, *Accounts Chem. Res.*, **3**, 257 (1970).

(4) W. Gerrard, *J. Chem. Soc.*, 218, 1464 (1940), and subsequent papers.

(5) A. E. Arbuzov, *Zh. Russ. Fiz.-Khim. Obshchest.*, **38**, 687 (1906); *J. Chem. Soc., London, Abstr.*, **92i**, 275 (1907).

(6) (a) A. E. Arbuzov, *Zh. Russ. Fiz.-Khim. Obshchest., Chast Khim.*, **46**, 291 (1914); *Chem. Abstr.*, **8**, 2551 (1914), and later papers; (b) A. N. Pudovik and V. K. Krupnov, *J. Gen. Chem. USSR*, **38**, 196, 306 (1968).

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(11) A. Finch, P. J. Gardner, and I. H. Wood, *ibid.*, 746 (1965).

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(13) (a) J. C. D. Brand, *J. Chem. Soc.*, 880 (1946); (b) R. A. Y. Jones and A. R. Katritzky, *J. Inorg. Nucl. Chem.*, **15**, 193 (1960); (c) R. J. Gillespie, R. Kapoor, and E. A. Robinson, *Can. J. Chem.*, **44**, 1203 (1966); (d) K. B. Dillon and T. C. Waddington, *J. Chem. Soc. A*, 1146 (1970).

TABLE I

$^{31}P$ AND $^{1}H$ NMR SPECTRAL PARAMETERS OF PROTONATED PHOSPHORUS OXYACIDS, TRIALKYL (ARYL) PHOSPHATES, TRIALKYL (ARYL) PHOSPHITES, AND DIALKYL PHOSPHONATES (−60°)

| | | | $\delta_{1H}$ | | | | | |
|---|---|---|---|---|---|---|---|---|
| | $\delta_{31P}$ (85% $H_3PO_4$ = 0) | | PH proton ($^{1}J_{PH}$, Hz) | | α-Alkyl protons ($^{3}J_{POCH}$, Hz) | | Other protons | |
| Phosphonium ion | Ion | Precursor | Ion | Precursor | Ion | Precursor | Ion | Precursor |
| $P(OH)_4^+$ | −2.3[a] | 0.0[b] | ... | ... | ... | ... | ... | ... |
| $HP(OH)_3^+$ | −19.0 | −5.4[b] | 7.62 (825) | 7.55 (683)[b] | ... | ... | ... | ... |
| $H_2P(OH)_2^+$ | −36.1 | −12.3[b] | 7.64 (687) | 7.47 (567)[b] | ... | ... | ... | ... |
| $HOP(OCH_3)_3^+$ | −2.0[a] | −2.3 | ... | ... | 4.42 (11.5)[a] | 4.15 (11.2) | ... | ... |
| $HOP(OC_2H_5)_3^+$ | +1.6[a] | +1.0 | ... | ... | 4.73 (8.5)[a] | 4.42 (8.6) | Methyl: 1.72[a] | 1.65 |
| $HOP(O\text{-}i\text{-}C_3H_7)_3^+$ | +4.5 | +3.4 | ... | ... | 5.19 (5.8) | 4.86 (7.1) | Methyl: 1.66 | 1.59 |
| $HOP(O\text{-}n\text{-}C_4H_9)_3^+$ | +1.2[a] | +0.6 | ... | ... | 4.76 (7.4)[a] | 4.32 (7.5) | Methyl: 1.30[a] | 1.28 |
| $HOP(OC_6H_5)_3^+$ | +16.0[a] | +17.9[c] | ... | ... | ... | ... | Aryl: 7.45[a] | 7.55[c] |
| $HP(OCH_3)_3^+$ | −24.7 | −139.7 | 7.47 (827) | ... | 4.34 (12.1) | 3.66 (10.8) | ... | ... |
| $HP(OC_2H_5)_3^+$ | −19.7 | −137.6 | 7.46 (811) | ... | 4.72 (7.4) | 4.00 (8.5) | Methyl: 1.67 | 1.40 |
| $HP(O\text{-}i\text{-}C_3H_7)_3^+$ | −15.7 | −137.5 | 7.44 (796) | ... | 5.23 (5.3) | 4.53 (8.8) | Methyl: 1.64 | 1.37 |
| $HP(O\text{-}n\text{-}C_4H_9)_3^+$ | −20.4 | −137.8 | 7.47 (812) | ... | 4.65 (5.5) | 4.07 (7.7) | Methyl: 1.15 | 1.20 |
| $HP(OC_6H_5)_3^+$ | −11.7 | −126.9 | 8.32 (875) | ... | ... | ... | Aryl: 7.24, 7.42 | 7.05 |
| $HP(O\text{-}n\text{-}C_3H_7)_2^+$ \| HO | −19.4 | −7.3 | 7.49 (820) | 7.03 (686) | 4.60 (7.1) | 4.25 (9.0) | β-Methylene: 2.01 | 1.94 |
| | | | | | | | Methyl: 1.18 | 1.20 |
| $HP(O\text{-}n\text{-}C_4H_9)_2^+$ \| HO | −19.3 | −7.2 | 7.47 (819) | 7.03 (686) | 4.62 (6.6) | 4.32 (8.8) | Methyl: 1.12 | 1.21 |

[a] At room temperature. [b] In $H_2O$. [c] In $CCl_4$.

solutions have been obtained.[13b,d] Such chemical shifts have also been very recently obtained for chlorosulfuric acid solutions and oleum solutions with varying sulfur trioxide content.[13d] Gillespie and his coworkers have cited conductometric and cryoscopic measurements as evidence for the generation of protonated phosphoric acid, $P(OH)_4^+$, from several precursors in sulfuric acid[13c] and disulfuric acid solution.[14] Their measurements indicated that triethyl phosphate is protonated in sulfuric acid solution but that phosphorus oxyfluoride is not.[13c] The conductivity of triphenyl phosphate in sulfuric acid has been explained by protonation.[9] Moedritzer observed changes in the $^{31}P$ chemical shifts of several phosphoric, phosphonic, and phosphinic acid derivatives upon addition of strong acids such as perchloric and hydrochloric acids.[15] Sheldrick[16] and Haas and Gillman[17] have studied the protonation of phosphonic acid and phosphinic acid in sulfuric and perchloric acid solutions by measuring the nmr coupling constant, $^{1}J_{PH}$, between phosphorus and the proton(s) bound directly to it. McFarlane and White have quite recently observed by nmr the protonation at phosphorus of several phosphites in 100% sulfuric acid.[18]

In continuation of our work on protonation of phosphines in strong acid solution,[1a] we extended our studies to the protonation and cleavage reactions of phosphates and phosphites in $FSO_3H$ and $FSO_3H$–$SbF_5$ solutions. We have found that phosphoric acid, trialkyl (aryl) phosphates, phosphonic acid, trialkyl (aryl) phosphites, dialkyl phosphonates, and phosphinic acid form in fluorosulfuric acid (at sufficiently low temperatures) stable protonated species which can be observed by nuclear magnetic resonance spectroscopy. $^{1}H$ and $^{31}P$ nmr spectra of the neutral starting compounds and of the corresponding protonated species in excess fluorosulfuric acid were obtained. We were particularly interested in the effect of protonation upon the phosphorus chemical shifts, as well as the nmr spectral parameters of protons bound directly to phosphorus. Another goal of our studies was to be able to identify the sites of protonation, and to follow subsequent cleavage reactions spectrally, as such information would be relevant to many important reactions in organophosphorus chemistry.

## Results and Discussion

The nmr data for protonated phosphorus oxy acids trialkyl (aryl) phosphates, trialkyl (aryl) phosphites, and dialkyl phosphonates in fluorosulfuric acid solution, at −60° unless otherwise indicated, are listed in Table I. The phosphorus precursors, except those which were dissolved in the indicated solvents, were examined as neat liquids. Room-temperature spectra of solutions of inorganic phosphates [$KH_2PO_4$, $(NH_4)_2HPO_4$] and the trialkyl (aryl) phosphates (except for triisopropyl phosphate) in excess fluorosulfuric acid were indicative of the protonated species. The 60-MHz proton spectra of the acid solutions were similar to those of the starting compounds, except for changes in peak positions and separations and the presence of a new, sharp singlet at δ 10.9 to 12.1 (ppm from external capillary tetramethylsilane). The 24.3-MHz phosphorus spectra likewise showed changes only in peak positions and separations.

Since sulfuric acid itself is sufficiently strong to protonate phosphoric acid and triethyl phosphate,[13c] the phosphates we have studied should be fully protonated in the stronger[19] fluorosulfuric acid. The $^{31}P$ chemical shift of phosphoric acid is practically the same when it is dissolved in aqueous sulfuric acid of $H_0$ −8.6 (−2.5 ppm relative to 85% $H_3PO_4$)[13b] as when it is dissolved in fluorosulfuric acid (−2.3 ppm) where $H_0$ is −13.9.[19] Dillon and Waddington have also recently expressed the opinion that the limiting value of the $^{31}P$ chemical

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(15) K. Moedritzer, *Inorg. Chem.*, **6**, 936 (1967).
(16) G. M. Sheldrick, *Trans. Faraday Soc.*, **63**, 1077 (1967).
(17) T. E. Haas and H. D. Gillman, *Inorg. Chem.*, **7**, 2051 (1968).
(18) W. McFarlane and R. F. M. White, *Chem. Commun.*, 744 (1969).
(19) R. J. Gillespie, *Accounts Chem. Res.*, **1**, 202 (1968).

shift of $P(OH)_4^+$ is −2.1 ppm.[13d] Protonation is assumed to take place on the phosphoryl oxygen atom, but no proton coupling with phosphorus is exhibited, nor is a new proton absorption observed directly. Exchange with excess solvent fluorosulfuric acid is evidently very rapid, so that only a single averaged acid peak is seen. This phenomenon is characteristic of hydroxyl groups bonded to phosphorus. Attempts to slow exchange through low-temperature experiments at 100 MHz were made. However, solutions of diammonium phosphate in fluorosulfuric acid at −50° or in fluorosulfuric acid–sulfuryl chlorofluoride at −90° exhibited only the usual singlet acid peak and an additional minor peak at δ 10.2 [attributed to hydronium ion ($H_3O^+$) impurity].[20] Phosphonic acid, phosphinic acid, and dialkyl phosphonates, which also are tetravalent phosphoryl compounds, similarly show no signal observable separately from the solvent acid peak when protonated on the phosphoryl oxygen atom.

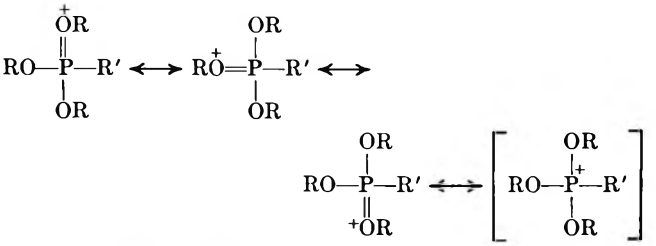
The $^{31}P$ chemical shifts of the protonated phosphates are comparable to values which have been reported for tetraalkoxy- and tetraphenoxyphosphonium ions. The first reported values for $P(OCH_3)_4^+$ and $CH_3OP(OC_2H_5)_3^+$ of −51.5 and −50 ppm[21] are in disagreement with subsequent shifts given for similar ions: −5,[22] −1.9,[23] −1.6,[24] and 0 ppm[25] for $P(OCH_3)_4^+$, and −3,[22] +2.4,[23] and +5 ppm[25] for $P(OC_2H_5)_4^+$. The more recent values are considered correct (in the early studies, the absorptions of the tetraalkoxyphosphonium ions may have been hidden by the reference peak[23b]). $^{31}P$ shifts of +18[26] and +24 ppm[25] have been found for $P(OC_6H_5)_4^+$. In certain cases the tetraalkoxyphosphonium ions were prepared by direct alkylation of the appropriate phosphates—the phosphoryl oxygen atom is clearly reactive toward sufficiently strong electrophiles.

Supplementing the nmr spectroscopic studies, it might be expected that protonated phosphoric acid, which should possess full tetrahedral symmetry, would produce a distinctive Raman spectrum. Laser Raman spectra of concentrated solutions of anhydrous phosphoric acid in fluorosulfuric acid led to no definite conclusions, for only lines due to the solvent fluorosulfuric acid and the major phosphoric acid lines observed by Simon and Weist[12d] in mixtures of phosphoric acid (which itself gives a spectrum characteristic of a tetrahedral environment) and perchloric acid were obtained.

In general, the protonated phosphorus compounds other than the phosphates are less stable, requiring their observation in solutions at −60°. The proton spectra of phosphonic acid, phosphinic acid, and dialkyl phosphonates showed sizable deshielding effects in fluorosulfuric acid solution. The coupling constants between a directly bound phosphorus and proton, $^1J_{PH}$, show large increases upon protonation. From a study of $^1J_{PH}$ obtained from solutions of phosphonic acid and phosphinic acid in aqueous sulfuric acid of variable acid strength, Sheldrick has calculated a value of 809–810 Hz for $^1J_{PH}$ in fully protonated phosphonic acid, $HP(OH)_3^+$, and a value of 675–681 Hz for $^1J_{PH}$ in fully protonated phosphinic acid, $H_2P(OH)_2^+$.[16] Haas and Gillman feel that their observed values of 804 and 671 Hz for $^1J_{PH}$ of phosphonic acid and phosphinic acid in 98% sulfuric acid are representative of the fully protonated species.[17] We obtained values of 819 to 825 Hz for phosphonic acid and the dialkyl phosphonates, and 687 Hz for phosphinic acid, when dissolved in fluorosulfuric acid (indicative of observation of the protonated compounds).

The tervalent trialkyl (aryl) phosphites are protonated at phosphorus in excess fluorosulfuric acid, yielding species similar to intermediates thought to occur in the Arbuzov reaction of organo phosphites.[27] The proton bound to phosphorus appeared in pmr spectra as a characteristic widely separated doublet, distinguishable from the strong low-field singlet due to excess fluorosulfuric acid. In all cases, this doublet was utilized to obtain the $^{31}P$ chemical shift by the internuclear double resonance (INDOR) method.

The $^{31}P$ chemical shifts of phosphoric acid and phosphates change very little upon protonation (and alkylation, as indicated before), whereas the α-alkyl protons in trialkyl phosphates become noticeably more deshielded. These protons exhibit chemical shifts which are comparable to values reported for $P(OCH_3)_4^+$ (δ 4.1,[25b] 4.32,[24] 4.37[23a]) and $P(OC_2H_5)_4^+$ (δ 4.5,[25b] 4.65[23a]). The $^{31}P$ shifts of the trialkyl (aryl) phosphites demonstrate startlingly large shielding effects upon protonation, moving upfield to values like that of protonated phosphonic acid and protonated dialkyl phosphonates. We conclude from these observations that in these hydroxy and alkoxy (aryloxy) phosphonium ions the positive charge is largely shifted from phosphorus to the oxygen atoms through the contribution of five-bond, phosphoryl-like structures in which the oxygen atoms donate nonbonded electron pairs to the formation of $d\pi$–$p\pi$ bonds.



R = H, alkyl, aryl; R′ = H, alkoxy, aryloxy, hydroxy

When R′ is an alkoxy, aryloxy, or hydroxy substituent, an additional contributing structure containing a phosphorus–oxygen double bond can be written. With hydroxy substitution going from the dihydroxyphosphonium ion $[H_2P(OH)_2^+]$ to the tetrahydroxyphosphonium ion $[P(OH)_4^+]$, the $^{31}P$ chemical shifts show

(20) A referee's inquiry prompted us to consider the concentration dependence of the chemical shift of the acid proton. In mixtures of trimethyl phosphate and fluorosulfuric acid, where the mole fraction of phosphate ranged from 0 to 0.9, the position of the acid peak varied correspondingly from δ 10.6 to 15.0.

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(22) H. Teichmann, M. Jatkowski, and G. Hilgetag, *Angew. Chem., Int. Ed. Engl.*, **6**, 372 (1967).

(23) (a) J. H. Finley, D. Z. Denney, and D. B. Denney, *J. Amer. Chem. Soc.*, **91**, 5826 (1969); (b) J. H. Finley and D. B. Denney, *ibid.*, **92**, 362 (1970).

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(25) (a) L. Kolditz and K. Lehmann, *Z. Chem.*, **7**, 356 (1967); (b) L. Kolditz, K. Lehmann, W. Wieker, and A. R. Grimmer, *Z. Anorg. Allg. Chem.*, **360**, 259 (1968).

(26) M. M. Crutchfield, C. H. Dungan, J. H. Letcher, V. Mark, and J. R. Van Wazer, "$P^{31}$ Nuclear Magnetic Resonance," Wiley, New York, N. Y., 1967, p 333.

(27) R. G. Harvey and E. R. DeSombre, *Top. Phosphorus Chem.*, **1**, 73 (1964).

the expected increasing shielding, indicating the degree of charge delocalization on oxygen. Protonation of phosphine oxide ($H_3PO$) would be expected to yield the monohydroxyphosphonium ion, but the instability and ease of oxidation of phosphine oxide[28] has so far prevented observation of the ion.

Protonated triisopropyl phosphate and phosphite, protonated tri-*tert*-butyl phosphate and phosphite, and protonated di-*tert*-butyl phosphonate cleave so rapidly at room temperature that nmr spectra of these species could not be obtained. For example, the $^{31}P$ spectrum of the fluorosulfuric acid solution of triisopropyl phosphate showed only a singlet at $-2.3$ ppm [$P(OH)_4^+$]. However, the isopropoxyphosphonium ions have limited stability at $-60°$, allowing their proton spectra to be obtained at that temperature.

Protonated tri-*n*-butyl phosphate and phosphite also cleave with time at room temperature. Two days after preparation of the fluorosulfuric acid solution of the phosphate, the $^{31}P$ spectrum showed only a singlet at $-2.5$ ppm [$P(OH)_4^+$]. When dissolved in the super acid, 1:1 $FSO_3H$–$SbF_5$, the proton spectra of the phosphate and phosphite showed primarily singlets at $\delta$ 10.9 to 11.4 (rapidly exchanging acid protons) and $\delta$ 4.37 to 4.43 (*tert*-butyl cation). It was found that formation of *tert*-butyl cation from the phosphate could be followed kinetically by nmr spectroscopy at $-60°$ in an excess of 5.5:1 $FSO_3H$–$SbF_5$, but that the data could not be interpreted according to a simple rate law, probably because the three *n*-butyl substituents are cleaved off (and rearrange to *tert*-butyl cations) sequentially.

$$HOP(OC_4H_9)_3^+ \xrightarrow[-C(CH_3)_3^+]{+H^+} (HO)_2P(OC_4H_9)_2^+ \xrightarrow[-C(CH_3)_3^+]{+H^+}$$

$$(HO)_3POC_4H_9^+ \xrightarrow[-C(CH_3)_3^+]{+H^+} (HO)_4P^+$$

By varying the $FSO_3H/SbF_5$ ratio (changing the acid strength) and temperature, a direct qualitative correlation of the rate of formation of *tert*-butyl cation with acid strength and temperature was observed.

It seems clear that carbon–oxygen bond cleavage in protonated trialkyl phosphates and phosphites is facilitated by the ability of the alkyl substituents to leave as carbonium ions. Thus the order tri-*n*-butyl < triisopropyl < tri-*tert*-butyl was observed for ease of cleavage, in accordance with the relative stabilities of the corresponding alkyl cations. The instability of the protonated tri-*tert*-butyl compounds is especially to be expected: *tert*-butyl phosphate is known to hydrolyze by an SN1 process, even at pH 4.[29]

Any warming of the protonated triisopropyl phosphate and phosphite solutions above Dry Ice temperature resulted in the pmr signal of the methine proton changing from a doublet of septets to a single septet: the coupling between phosphorus and the methine proton disappeared. The new methyl and methine resonances ($\delta$ 1.73–1.74 and 5.54–5.55, respectively; $^3J_{HCCH}$ = 6.2 Hz), as well as the appearance in the fluorine nmr spectrum of a new singlet at $-37.6$ to $-37.7$ ppm (relative to external $CCl_3F$), suggest that isopropyl fluorosulfonate is formed in solution. In the case of the triisopropyl phosphite–fluorosulfuric acid solution, the nmr parameters of the phosphorus species remaining after isopropyl group cleavage ($^1H$ shift $\delta$ 7.61, $^{31}P$ shift $-18.8$ ppm, $^1J_{PH}$ = 822 Hz) are indicative of protonated phosphonic acid. At certain times in a 60-MHz field (at $-60°$), it was possible to observe four different protons bound directly to phosphorus (there is some overlap of the absorptions at 100 MHz). We propose that the resonances arise from a mixture of all the possible ions of the type $HP(O\text{-}i\text{-}C_3H_7)_n(OH)_{3-n}^+$ ($n$ = 0, 1, 2, 3) which would result from sequential cleavage of the isopropyl substituents from protonated triisopropyl phosphite. This proposal is supported by the fact that from a combination of 60- and 100-MHz $^1H$ spectra, and $^{31}P$ INDOR spectra, we were able to obtain directly or calculate nmr parameters for each of the ions (see Table II). Unlike the corresponding phosphate, protonated trimethyl phosphite also demonstrates some instability. The pmr spectrum showed a new singlet in the O-methyl region ($\delta$ 4.47) which increased with time. In the fluorine spectrum a new singlet appeared at $-30.6$ ppm. In this case also it is suggested that the methyl groups are cleaved off to form methyl fluorosulfonate (literature values for $FSO_3CH_3$: $^1H$ shift $\delta$ 4.12, $^{19}F$ shift $-31.2$ ppm[30]). These observations are similar to the finding that methyl and ethyl fluorosulfonate can be prepared from fluorosulfuric acid and the corresponding dialkyl sulfates.[30]

TABLE II

$^{31}P$ AND $^1H$ NMR SPECTRAL PARAMETERS OF HYDROXYISOPROPOXYPHOSPHONIUM IONS, $HP[OCH(CH_3)_2]_n(OH)_{3-n}^+$ ($n$ = 0–3), AT $-60°$

| $n$ | $\delta_{^{31}P}$ (85% $H_3PO_4$ = 0) | $\delta_{^1H}$ PH proton | $^1J_{PH}$, Hz |
|---|---|---|---|
| 0 | −18.8 | 7.61 | 824 |
| 1 | −17.3 | 7.56 | 821 |
| 2 | −16.3 | 7.48 | 812 |
| 3 | −15.7 | 7.44 | 796 |

In studying the formation of protonated phosphonic acid by direct $^{31}P$ nmr spectroscopy (at 24.3 MHz), it was found that protonated phosphonic acid in fluorosulfuric acid undergoes further reaction at room temperature. After 45 min it was completely converted into phosphorus oxyfluoride ($^{31}P$ spectrum a quartet centered at +36.5 ppm, $^{19}F$ spectrum a doublet centered at +90.5 ppm, $^1J_{PF}$ = 1062 Hz). The nmr parameters are identical with those obtained when phosphorus oxyfluoride was dissolved in fluorosulfuric acid. The protonated phosphonic acid generated from protonated trimethyl phosphite by methyl group cleavage also reacts with fluorosulfuric acid to form phosphorus oxyfluoride (the only product observed after 8 days at room temperature). Protonated phosphinic acid reacts to give phosphorus oxyfluoride, which could be observed in the $^{19}F$ spectrum of the fluorosulfuric acid solution after 2 days. In these cases the fluorinating ability of fluorosulfuric acid is an important factor.[31]

(28) E. Wiberg and G. Müller-Schiedmayer, *Z. Anorg. Allg. Chem.*, **308**, 352 (1961).

(29) A. Lapidot, D. Samuel, and M. Weiss-Broday, *J. Chem. Soc.*, 637 (1964).

(30) M. G. Ahmed, R. W. Alder, G. H. James, M. L. Sinnott, and M. C. Whiting, *Chem. Commun.*, 1533 (1968).

(31) For example, phosphorus pentoxide in fluorosulfuric acid produces phosphorus oxyfluoride in good yield: E. Hayek, A. Aignesberger, and A. Engelbrecht, *Monatsh. Chem.*, **86**, 735 (1955).

## Experimental Section

**Materials.**—Potassium dihydrogen phosphate, diammonium hydrogen phosphate, 85% aqueous phosphoric acid, tri-*n*-butyl phosphate, phosphonic acid, trimethyl phosphite, triphenyl phosphite, di-*n*-propyl phosphonate, di-*n*-butyl phosphonate, 50% aqueous phosphinic acid, and phosphorus oxyfluoride were commercially obtained and purified by standard methods. Triethyl phosphite, triisopropyl phosphite, and tri-*n*-butyl phosphite were prepared by reaction of phosphorus trichloride and the appropriate alcohol in the presence of a tertiary nitrogen base[4,32] and distilled under reduced pressure. Trimethyl phosphate, triethyl phosphate, triisopropyl phosphate, and triphenyl phosphate were prepared by nitrogen dioxide oxidation of the corresponding phosphite.[33] The procedure for the preparation of tri-*tert*-butyl phosphite from phosphorus trichloride and *tert*-butyl alcohol[34] initially yielded, as had been reported, a mixture of tri-*tert*-butyl phosphite and di-*tert*-butyl phosphonate, along with a smaller amount of tri-*tert*-butyl phosphate. Commercially available fluorosulfuric acid and antimony pentafluoride were twice distilled before use in the preparation of solutions.

**Nmr Spectra.**—Pmr spectra were recorded with Varian Associates Models A-60, A-56/60A, and HA-100 nmr spectrometers. Proton chemical shifts are reported in parts per million ($\delta$) from external (capillary) tetramethylsilane. Fluorine nmr spectra were taken with the A-56/60A spectrometer operating at 56.4 MHz; fluorine chemical shifts are reported in parts per million relative to external fluorotrichloromethane. Direct phosphorus nmr spectra were obtained with a Varian Associates HA-60IL nmr spectrometer operating at 24.3 MHz and equipped with a Model V4331A probe. Samples were contained in 12- or 13-mm-o.d. thin-walled polished spinning tubes. A 5-mm-o.d. polished tube containing the reference material was inserted in the sample tube and maintained in a concentric position by two specially constructed Teflon inserts. Normally 85% phosphoric acid was used as the reference material; for samples (especially phosphates) whose resonance signals were masked by phosphoric acid, additional spectra using aqueous phosphonic acid (acid mole fraction $^1/_6$) and triphenyl phosphite as references were obtained. All phosphorus chemical shifts are reported in parts per million relative to 85% $H_3PO_4$. Whenever possible, direct $^{31}P$ spectra using 85% $H_3PO_4$ as the reference material were frequency swept under conditions of field-frequency stabilization. Otherwise, field sweep spectra calibrated by audiofrequency side-band modulation were obtained.

For obtaining phosphorus INDOR spectra (which include all of the low-temperature spectra), the HA-100 spectrometer was operated in the internal lock, frequency sweep mode, the first upper side-band of capillary TMS being used for the lock signal. The sweep 40.48-MHz frequency required for $^{31}P$ irradiation was obtained from the 20-MHz and 480-kHz outputs of a Monsanto Model 3100A Digital frequency synthesizer; the 20-MHz frequency was doubled and added to the 480-kHz output in an NMR Specialties Model SD-60B mixer and amplifier. The resultant frequency was fed to the probe *via* an attenuator and double-probe adapter and was monitored with a Hewlett-Packard Model 5245L electronic counter. The observing frequency (100 MHz) was determined using the same counter equipped with a Model 5253B frequency converter plug-in unit. $^{31}P$ resonance frequencies to $\pm 1$ Hz were obtained by monitoring a line in the proton spectrum known to arise from proton–phosphorus coupling, and varying the frequency synthesizer output and attenuation until minimum peak height was found. The $^{31}P$ chemical shifts were calculated with respect to 85% $H_3PO_4$ as reference using the equation

$$\delta_P = [(\nu_0/2.4703089) - f_i] \times 10^6/(\nu_0/2.4703089)$$

where $\nu_0$ is the sum of the observing frequency (derived from the V4311 unit) and the lock modulation frequency, and $f_i$ is the measured $^{31}P$ frequency. This equation holds only for upper side-band operation using TMS lock; it was derived from experimentally determined $\nu_0/f_i$ ratios for trimethyl phosphate (2.4703029) and 30% (w/w) aqueous phosphonic acid (2.4702969), and from the $^{31}P$ chemical shifts of these compounds (−2.3 and −5.0 ppm, respectively) determined from direct phosphorus nmr spectra.

**Preparation of the Ions.**—Phosphorus compounds were dissolved in a (usually) tenfold molar excess of fluorosulfuric acid or fluorosulfuric acid–antimony pentafluoride solution with stirring and cooling to generate the protonated species under conditions similar to those described previously.[1a]

The laser Raman spectrophotometer which was used has been described previously.[35]

**Registry No.**—$P(OH)_4^+$, 26902-99-8; $HP(OH)_3^+$, 21862-21-5; $H_2P(OH)_2^+$, 21862-20-4; $HOP(OCH_3)_3^+$, 28180-50-9; $HOP(OC_2H_5)_3^+$, 28206-36-2; $HOP(O\text{-}i\text{-}C_3H_7)_3^+$, 28180-51-0; $HOP(O\text{-}n\text{-}C_4H_9)_3^+$, 28180-52-1; $HOP(OC_6H_5)_3^+$, 28180-53-2; $HP(OCH_3)_3^+$, 28206-37-3; $HP(OC_2H_5)_3^+$, 28206-36-2; $HP(O\text{-}i\text{-}C_3H_7)_3^+$, 28206-39-5; $HP(O\text{-}n\text{-}C_4H_9)_3^+$, 28206-40-8; $HP(OC_6H_5)_3^+$, 28206-41-9; $HP(OH)(O\text{-}n\text{-}C_3H_7)_2^+$, 28206-42-0; $HP(OH)(O\text{-}n\text{-}C_4H_9)_2^+$, 28206-43-1; $HP[OCH(CH_3)_2](OH)_2^+$, 28206-44-2; $HP[OCH(CH_3)_2]_2(OH)^+$, 28206-45-3.

**Acknowledgments.**—Support of this work by a grant from the National Institutes of Health and by a Public Health Service Fellowship from the National Institute of General Medical Sciences (to C. W. M.) is gratefully acknowledged.

(32) A. H. Ford-Moore and B. J. Perry in "Organic Syntheses," Collect. Vol. IV, N. Rabjohn, Ed., Wiley, New York, N. Y., 1963, p 955.

(33) J. R. Cox and F. H. Westheimer, *J. Amer. Chem. Soc.*, **80**, 5441 (1958).

(34) V. Mark and J. R. Van Wazer, *J. Org. Chem.*, **29**, 1006 (1964).

(35) A. Commeyras and G. A. Olah, *J. Amer. Chem. Soc.*, **91**, 2929 (1969)

# Some Reactions of Dimethylphosphono-Substituted Diazoalkanes. $(MeO)_2P(O)CR$ Transfer to Olefins and 1,3-Dipolar Additions of $(MeO)_2P(O)C(N_2)R$[1]

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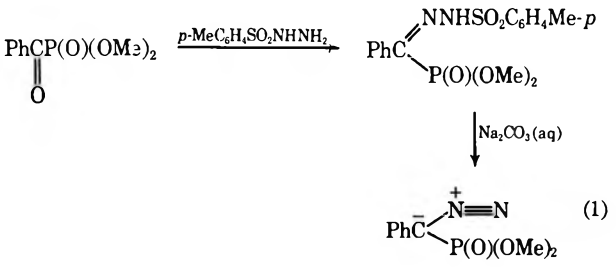
The dimethylphosphono-substituted diazoalkanes $PhC(N_2)P(O)(OMe)_2$ and $N_2CHP(O)(OMe)_2$ have been prepared, the first *via* the tosylhydrazone route, and the second by diazotization of the amine, and both could be isolated as the pure compounds. Their copper-catalyzed decomposition in the presence of olefins serves well in the preparation of dimethylphosphono-substituted cyclopropanes. Dimethyl α-diazobenzylphosphonate was found to react with triphenylphosphine to give the phosphazine and to methylenate mercuric chloride. 1,3-Dipolar addition to acrylonitrile, methyl vinyl ketone, and diethyl maleate gave stable $\Delta^2$-pyrazolines, and 1,3-dipolar additions to two vinylphosphonate esters were carried out in such a manner that the pyrazolines were decomposed to the cyclopropanes. Protolysis reactions of both diazo compounds are described and dimethyl diazomethylphosphonate could be metalated with mercury(II) and silver(I) acetylacetonates.

We have reported recently concerning the preparation and copper-catalyzed decomposition of a number of substituted α-dimethylphosphonodiazoalkanes.[2,3] In all these examples the intermediate carbene, $(MeO)_2P(O)CR$ [or its Cu(I) complex], underwent rapid intramolecular rearrangements, and attempted trapping of the divalent carbon species with olefinic substrates was not successful. We report here concerning two such reagents which are useful divalent carbon transfer reagents, dimethyl α-diazomethylphosphonate, $(MeO)_2P(O)CHN_2$, and dimethyl α-diazobenzylphosphonate, $(MeO)_2P(O)C(N_2)C_6H_5$. Also described are some other types of reactions of these diazoalkanes and of dimethyl α-diazoethylphosphonate, $(MeO)_2P(O)C(N_2)CH_3$.

## Results and Discussion

**Preparation of the Diazoalkanes.**—The preparation of dimethyl α-diazoethylphosphonate already has been described.[2] A very similar procedure, room-temperature decomposition of the *p*-toluenesulfonylhydrazone sodium salt, was used in the synthesis of the α-diazobenzylphosphonate ester (eq 1). This compound

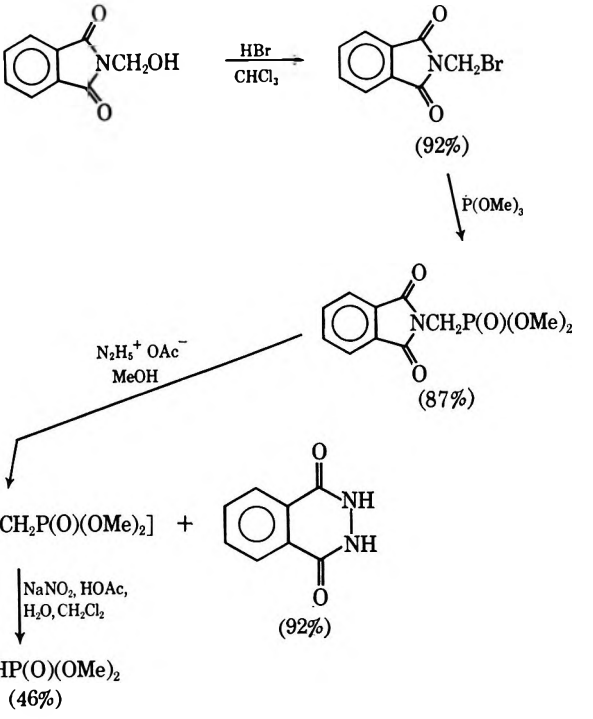



(1)

was isolated as an orange crystalline solid, mp 44.0–44.5°, which was unusually stable. It could be distilled at reduced pressure and was stable indefinitely at room temperature. It was recovered unchanged after its benzene solution had been heated at reflux for 48 hr but underwent complete decomposition when this treatment was carried out in the presence of copper powder. Pure $(MeO)_2P(O)C(N_2)Ph$ could be heated to 140° before evolution of a gas became apparent, and decomposition was not complete even at 190°.

A different synthetic sequence was employed in the preparation of dimethyl diazomethylphosphonate because of the nonexistence and presumed instability of the required carbonyl precursor [$HCOP(O)(OMe)_2 \rightarrow HP(O)(OMe)_2 + CO$] (Scheme I). The intermediate dimethyl aminomethylphosphonate was too unstable to be isolated in the free form but was stable as the unisolated acetate in solution. The presence of this amine in solution was demonstrated by the preparation of its *N*-tosyl derivative.

SCHEME I




Dimethyl diazomethylphosphonate was isolated as a distillable yellow liquid which was stable indefinitely when stored in a refrigerator.

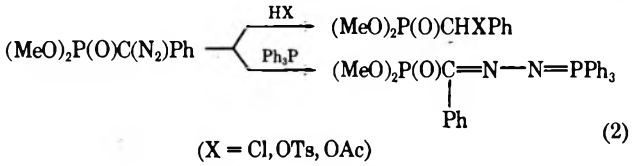
Both dimethylphosphono-substituted diazoalkanes reacted as expected with acids and with triphenylphos-

(1) Preliminary communications: (a) D. Seyferth, P. Hilbert, and R. S. Marmor, *J. Amer. Chem. Soc.*, **89**, 4811 (1967); (b) D. Seyferth and R. S. Marmor, *Tetrahedron Lett.*, 2493 (1970).

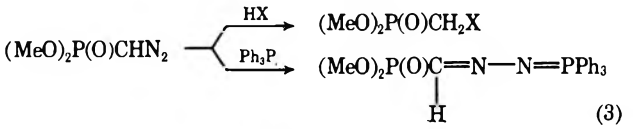
(2) D. Seyferth and R. S. Marmor, *J. Org. Chem.*, **36**, 128 (1971).

(3) A brief survey of the literature of phosphorus-substituted diazoalkanes is given in ref 2 and will not be repeated here.

phine (eq 2 and 3). Dimethyl diazomethylphosphonate could be metalated: with silver acetylacetonate to

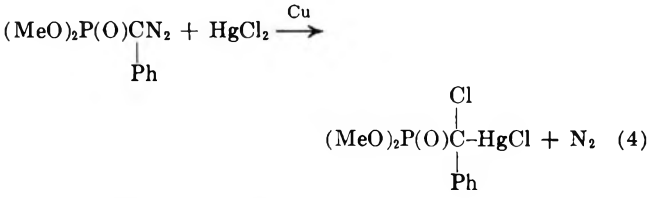


(X = Cl, OTs, OAc) (2)



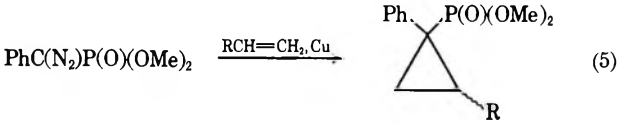
(X = OAc) (3)

give a surprisingly stable silver derivative as a yellow powder and with mercuric acetylacetonate to give the mercurial, $Hg[C(N_2)P(O)(OMe)_2]_2$. The well-known methylenation of mercuric halides by diazoalkanes[4,5] also could be effected using dimethyl α-diazobenzylphosphonate, but the yield of pure product was low (eq 4).

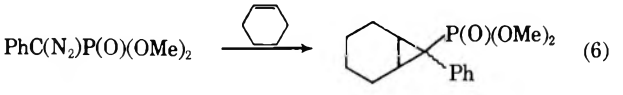


(4)

**Preparation of Dimethylphosphono-Substituted Cyclopropanes.**—Decomposition of $(MeO)_2P(O)C(N_2)Ph$ and $(MeO)_2P(O)CHN_2$ in the presence of copper powder and an excess of an olefin produced cyclopropanes.



(R = *n*-$C_5H_{11}$, $Me_3SiCH_2$) (5)



(6)

Dimethyl diazomethylphosphonate underwent divalent carbon transfer reactions with olefins when it was stirred at 0° with a large excess of the olefin, dichloromethane as a cosolvent, and copper powder. In the absence of dichloromethane the yields were markedly lower owing to the low solubility of the diazoalkane in the various olefins. In the reaction with cyclohexene, copper powder was found to be the most effective catalyst, giving higher yields and less tar than in reactions employing copper(I) chloride and copper(II) acetylacetonate. Scheme II summarizes these results.

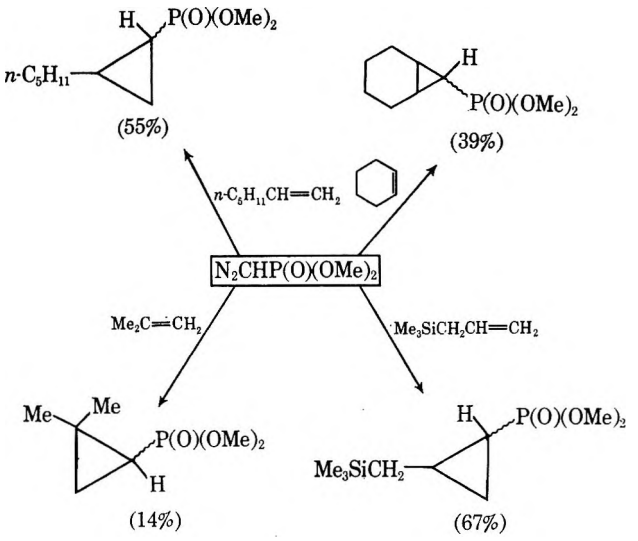
The available evidence[6] suggests that copper-catalyzed diazoalkane reactions involve intermediate carbene–Cu(I) complexes, and that it is these which react with the olefin to form the cyclopropane. In the present examples the possibility of forming the olefins *via* a 1,3-dipolar addition of the diazoalkane to the olefin

(4) L. Hellerman and M. D. Newman, *J. Amer. Chem. Soc.*, **54**, 2859 (1932).

(5) D. Seyferth, *Chem. Rev.*, **55**, 1155 (1955).

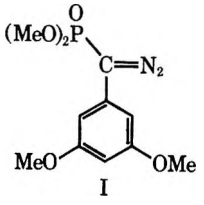
(6) W. Kirmse, "Carbene, Carbenoide und Carbenanaloge," Verlag Chemie, Weinheim/Bergstr., 1969, Chapter 5.

SCHEME II



followed by decomposition of the resulting Δ¹-pyrazoline to the cyclopropane also must be considered. The latter course is rather unlikely since we are dealing with unactivated (toward 1,3 dipoles) olefins. With activated olefins (see below), the latter course most certainly is operative. For the examples given above, however, a carbenoid process is the most likely.

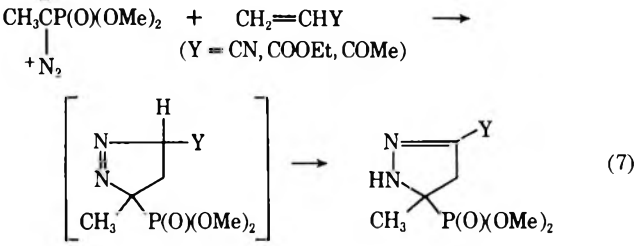
During the course of this study dimethyl α-diazo-3,5-dimethoxybenzylphosphonate (I) also was pre-



I

pared, but its chemistry was not investigated. Its copper-catalyzed decomposition gave a complex product mixture.

**1,3-Dipolar Additions.**—Dimethyl α-diazoethylphosphonate underwent 1,3-dipolar addition reactions with ethyl acrylate, acrylonitrile, and methyl vinyl ketone to give the corresponding dimethylphosphono-substituted Δ²-pyrazoline (eq 7). These adducts were not

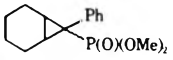
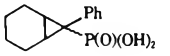
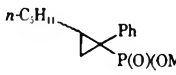
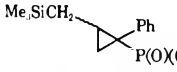
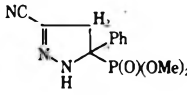
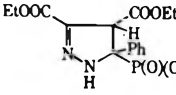
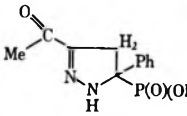
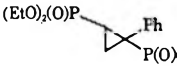
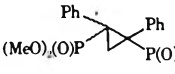
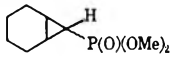
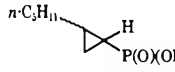
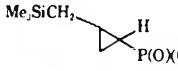
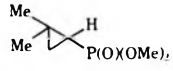
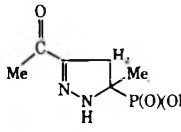
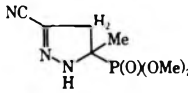
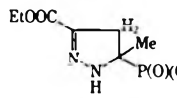


(7)

stable on storage at room temperature, presumably because of their ability to revert to the Δ¹-pyrazoline and lose nitrogen to form a cyclopropane contaminated with olefin and polymer. Dimethyl α-diazobenzylphosphonate showed similar reactivity toward activated olefins such as acrylonitrile, methyl vinyl ketone, diethyl maleate, diethyl vinylphosphonate, and dimethyl α-styrylphosphonate. The pyrazolines derived from the two dialkylphosphono-substituted olefins

TABLE I

PRODUCTS DERIVED FROM DIMETHYLPHOSPHONO-SUBSTITUTED DIAZOALKANES

| Compound | Registry no. | Obtained from reaction with (% yield) | Bp, °C (mm) | Mp, °C | $n^{25}D$ | —Carbon, %— Calcd | Found | —Hydrogen, %— Calcd | Found |
|---|---|---|---|---|---|---|---|---|---|
| **A. From $PhC(N_2)P(O)(OMe)_2$** | | | | | | | | | |
| $PhCHClP(O)(OMe)_2$ | 16965-75-6 | HCl (86) | 105 (0.07) | ... | 1.5276 | 46.07 | 46.28 | 5.16 | 5.36[a] |
| $PhCH(OAc)P(O)(OMe)_2$ | 16965-84-7 | HOAc (79) | 74 (0.03) | ... | 1.5010 | 51.16 | 50.91 | 5.86 | 5.96 |
| $PhCH(OTs)P(O)(OMe)_2$ | 28446-79-9 | $p$-$CH_3C_6H_4SO_3H$ (71) | ... | 86–87 | ... | 51.89 | 51.72 | 5.17 | 5.28 |
| $Ph_3P{=}NN{=}C(Ph)P(O)(OMe)_2$ | 16965-77-8 | $Ph_3P$ (20) | ... | 132–133 | ... | 66.39 | 66.50 | 5.37 | 5.69 |
| $PhC(Cl)P(O)(OMe)_2$ \| HgCl | 16965-74-5 | $HgCl_2$ (8) | ... | 151 | ... | 23.01 | 23.32 | 2.36 | 2.51[b] |
|  | 16965-86-9 |  (96) crude | ... | 187.5–188.0 | ... | 54.55 | 54.29 | 5.60 | 5.67 |
|  | 28446-82-4 | (95) | ... | 274–275 | ... | 61.89 | 62.16 | 6.79 | 6.92 |
|  | 16965-85-8 | $n$-$C_6H_{11}CH{=}CH_2$ (73) | 108 (0.04) | ... | 1.5025 | 64.84 | 65.01 | 8.50 | 8.63 |
|  | 28446-84-6 | $Me_3SiCH_2CH{=}CH_2$ (76) | 109–111 (0.02) | ... | 1.5050 | 57.66 | 57.43 | 8.07 | 8.01 |
|  | 28446-85-7 | $CH_2{=}CHCN$ (90) | ... | 137.5–138.5 | ... | 51.61 | 51.97 | 5.05 | 5.00 |
|  | 16965-78-9 | HC—COOEt (46) ‖ HC—COOEt | ... | 148.5–149.0 | ... | 51.25 | 51.48 | 5.82 | 5.88 |
|  | 16965-76-7 | O ‖ $CH_2{=}CHCMe$ (92) | ... | 70 | ... | 52.69 | 52.88 | 5.79 | 5.79 |
|  | 28446-88-0 | $CH_2{=}CHP(O)(OEt)_2$ (90) | >100 (0.10) | ... | 1.5078 | 49.73 | 49.64 | 6.68 | 6.62 |
|  | 28446-89-1 | $CH_2{=}C(Ph)PO(OMe)_2$ (30) | 190 (0.04) | 100–125 | ... | 55.61 | 55.39 | 5.90 | 6.31 |
| **B. From $HC(N_2)P(O)(OMe)_2$** | | | | | | | | | |
| $AcOCH_2P(O)(OMe)_2$ | 24630-57-7 | AcOH (78) | 63 (0.08) | ... | 1.4295 | 32.97 | 32.88 | 6.09 | 6.38 |
| $Ph_3P{=}NN{=}CHP(O)(OMe)_2$ | 27491-71-0 | $Ph_3P$ (12) | ... | 132–133 | ... | 61.16 | 61.12 | 5.38 | 5.30 |
| $Hg[C(N_2)P(O)(OMe)_2]_2$ | 27491-73-2 | Hg(acac)$_2$ (80) | ... | 106.5–107.0 | ... | 14.45 | 14.65 | 2.43 | 2.56 |
|  | 28446-93-7 |  (39) | 61–63 (0.02) | ... | 1.4721 | 52.93 | 52.50 | 8.39 | 8.33 |
|  | 28446-94-8 | $n$-$C_6H_{11}CH{=}CH_2$ (55) | 63–65 (0.03) | ... | 1.4439 | 54.33 | 54.14 | 9.61 | 9.59 |
|  | 28446-95-9 | $Me_3SiCH_2CH{=}CH_2$ (67) | 55–57 (0.02) | ... | 1.4489 | 45.74 | 45.63 | 8.96 | 8.92 |
|  | 26580-16-5 | $Me_2C{=}CH_2$ (14) | 52 (0.90) | ... | 1.4369 | 47.19 | 47.01 | 8.49 | 8.49 |
| **C. From $CH_3C(N_2)P(O)(OMe)_2$** | | | | | | | | | |
|  | 16965-81-4 | O ‖ $CH_2{=}CH{-}CMe$ (100) | ... | 111–112 | ... | 41.04 | 41.35 | 6.45 | 6.72 |
|  | 16965-83-6 | $CH_2{=}CHCN$ (100) | ... | 89–92 | ... | 38.71 | 38.80 | 5.57 | 5.76 |
|  | 16965-82-5 | $CH_2{=}CHCOOEt$ (98) | ... | 120–123 | ... | 40.91 | 40.52 | 6.49 | 6.57 |

[a] Cl: calcd, 15.11; found, 14.76. [b] Cl: calcd, 15.10; found, 14.93.

TABLE II

SPECTROSCOPIC PROPERTIES OF PRODUCTS DERIVED FROM DIMETHYLPHOSPHONO-SUBSTITUTED DIAZOALKANES

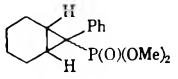
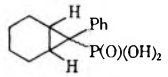
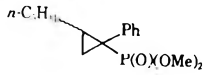
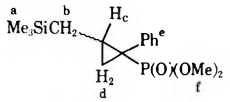
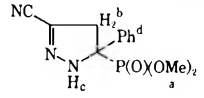
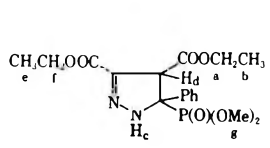
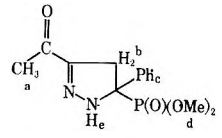
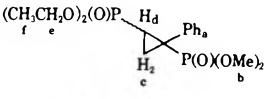
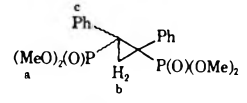
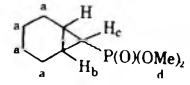
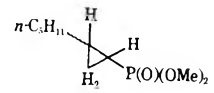
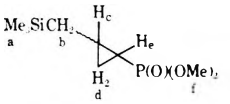
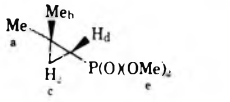
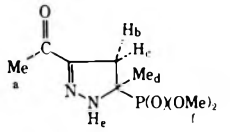
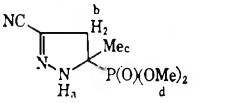
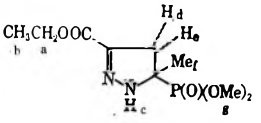
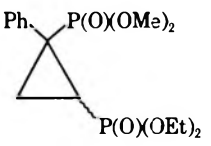
| Compound | Nmr (solvent), δ (ppm) | Ir (medium), cm$^{-1}$ (principal bands) |
|---|---|---|
| $PhCHClP(O)(OMe)_2$ | ($CCl_4$) 3.50, 3.74 (two d, 6, $J$ = 10.5 Hz), 4.97 (d, 1, $J$ = 14 Hz), 7.17–7.65 (m, 5) | (Neat liq) 1265 (s, P=O), 1185 (m), 1030 (s, POC) |
| $PhCH(OAc)P(O)(OMe)_2$ | ($CCl_4$) 2.02 (s, 3), 3.52, 3.58 (two d, 6, $J$ = 10.5 Hz), 6.13 (d, 1, $J$ = 13.5 Hz), 7.17–7.67 (m, 5). | (Neat liq) 1755 (s, C=O), 1265 (s, P=O), 1025 (s, POC). |
| $PhCH(OTs)P(O)(OMe)_2$ | ($CDCl_3$) 2.24 (s, 3), 3.47, 3.52 (two overlapping d, 6, $J$ = 10.5 Hz), 5.62 (d, 1, $J$ = 15.5 Hz), 6.9 7.6 (m, 9) | (Nujol) 1370 (s, $SO_2$), 1260 (s, P=O), 1175 (s, $SO_2$), 1030 (s, POC) |
| $Ph_3P{=}NN{=}C(Ph){-}P(O)(OMe)_2$ | ... | (Nujol) 1240 (s, P=O), 1110 (s, P=N), 1020 (s, POC) |
| $PhC(HgCl)P(O)(OMe)_2$ | ... | (Nujol) 1225 (s, P=O), 1035 (s, POC) |
|  | ($CDCl_3$), 0.2–1.3, 1.5–2.2 (m, 10), 3.58 (d, 6, $J$ = 10.5 Hz), 7.28 (s, 5) | (KBr) 1250 (s, P=O), 1030 (s, POC) |
|  | ... | (Nujol) 1210 (m), 1180 (m), 1135 (m), 1010 (s, POH), 705 (m) |
|  | ($CCl_4$) 0.2–2.0 (m, 14), 3.51, 3.57 (two d, 6, $J$ = 10.5 Hz), 7.25 (s, 5) | (Neat liq) 1260 (s, P=O), 1040 (s, POC) |
|  | ($CCl_4$) 0.00 [s, a (major isomer)], 0.02 [s, a (minor isomer)], 9], 0.5–1.9 (m, 5, b, c, and d), 3.52 [d, 6, $J$ = 11 Hz (major isomer; minor isomer seen as a doublet shoulder), f], 7.23 (s, 5, e) | Neat liq) 1250 (s, P=O and $Me_3Si$), 1030 (s, POC) |
|  | ($CDCl_3$) 2.8–3.9 [m with two d at 3.58 and 3.63 ($J$ = 10 Hz, a), 8, a and b], 7.26 (s, 5, d), 8.64 (s, 1, c) | (Nujol) 3205 (m, NH), 2210 (m, C≡N), 1225 (s, P=O), 1020 (s, POC) |
|  | ($CDCl_3$) 0.81 (t, 3, $J$ = 7 Hz, b or e), 1.29 (t, 3, $J$ = 7 Hz, b or e), 3.68 (t, 6, $J$ = 11 Hz, g, coincidental overlap of two d), 4.26 (quartet, 4, $J$ = 11 Hz, a and f), 3.0–4.6 (underlying peaks distorting major peaks, 1, d), 4.90 (impurity, 0.5), 7.32, 7.58 (two broad s, 5, Ph), 8.51 (s, 1, c) | (Nujol) 3205 (m, NH), 1735 (s, $COOCH_2CH_3$), 1725 (s, $COOCH_2CH_3$), 1050 (s), 1020 (s) |
|  | ($CDCl_3$) 2.40 (s, 3, a), 3.62, 3.68 (two d, $J$ = 10.2 Hz, d, 6), 2.9–4.2 (complex underlying pattern, 2, b), 7.2–7.6 (m, 5, c), 8.13 (broad s, 1, e) | (Nujol) 3220 (s, NH), 1660 (s, C=O), 1230 (s, P=O), 1030 (s, POC) |
|  | ($CCl_4$) 0.75–1.95 (m with max peak at 1.32, 9, c, d, and f), 3.3–4.3 (m, 10, b and e), 6.9–7.5 (m with max peak at 7.15, 5, a) | (Neat liq) 1250 (s, P=O), 1025 (s, POC) |
|  | ($CDCl_3$) 2.33 (t with underlying peaks, $J$ = 14.5 Hz, 2, b), 2.98, 3.20, 3.64 (three d with underlying peaks, $J$ = 11 Hz, 12, a), 7.2–7.8 (m with max peak at 7.36, 10, c) | (Neat liq) 1250 (s, P=O), 1030 (s, POC) |
| $AcOCH_2P(O)(OMe)_2$ | ($CCl_4$) 2.12 (s, 3), 3.78 (d, 6, $J$ = 10.5 Hz), 4.37 (d, 2, $J$ = 8.5 Hz) | (Neat liq) 1755 (s, C=O), 1220 (s, P=O), 1040 (s, POC) |
| $Ph_3P{=}NN{=}CHP(O)(OMe)_2$ | ($CDCl_3$) 3.54 (d, 6, $J$ = 10.5 Hz, c), 7.1–7.7 (m, 16, a + b) | (Nujol) 1290 (s), 1240 (s), 1110 (s, P=N), 825 (s), 720 (s) |
| $Hg[C(N_2)P(O)(OMe)_2]_2$ | ($CDCl_3$) 3.80 (d, $J$ = 11.5 Hz) | (Nujol) 2070 (s, C=N=N), 1245 (s, P=O), 1020 (s, POC) |
|  | ($CCl_4$) 0.43 (quartet, 1, $J_P$ = $J_{b,c}$ = 5 Hz, c), 1.1–2.2 (m with max peaks at 1.23 and 1.75, 10, a and b), 3.60 (d, 6, $J$ = 11 Hz, d) | (Neat liq) 1250 (s, P=O), 1030 (s, POC) |
|  | ($CCl_4$) 0.3–1.7 (m with max peaks at 0.90 and 1.36, 15), 3.65 (d, 6, $J$ = 10.7 Hz) | (Neat liq) 3060 (w), 1245 (s, P=O), 1030 (s, POC) |

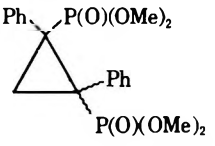
TABLE II (*Continued*)

| Compound | Nmr (solvent), δ (ppm) | Ir (medium), cm⁻¹ (principal bands) |
|---|---|---|
|  | ($CCl_4$) 0.06 (s, 9, a), 0.25–1.25 (m, 6, b, c, d, and e), 3.64 (d, $J$ = 10.7 Hz, minor isomer), 3.65 [d, $J$ = 10.7 Hz, major isomer), 6, f] | (Neat liq) 3060 (w), 1250 (s, P=O and $Me_3Si$), 1030 (s, POC) |
|  | ($CCl_4$) 0.3–1.3 (m with max peaks at 0.70, 3, c and d), 1.14 (d, 3, $J_P$ = 2.2 Hz, a or b), 1.29 (s, 3, a or b), 3.64 (d, 6, $J$ = 10.7 Hz, e) | (Neat liq) 3060 (w), 1250 (s, P=O), 1030 (s, POC) |
|  | ($CDCl_3$) 1.46 (d, 3, $J$ = 15 Hz, 3), 2.39 (s, 3, a), 2.88 (d, 1, $J$ = 11.5 Hz, b), 3.20 (d, 1, $J$ = 19 Hz, c), 3.83 and 3.86 (two d, 6, $J$ = 10 Hz, f), 7.85 (broad s, 1, e) | (Nujol) 3225 (s, NH), 1655 (s, C=O), 1240 (m, P=O), 1025 (s, POC) |
|  | ($CDCl_3$) 1.48 (d, 3, $J$ = 15 Hz, c), 2.77, 3.04, 3.41 (three s, 2, b), 3.82, 3.84 (two d, 6, $J$ = 10 Hz, d), 7.66 broad s, 1, a) | (Nujol) 3215 (s, NH), 2220 (s, C≡N), 1220 (s, P=O), 1045 (s, POC) |
|  | ($CDCl_3$) 1.33 (t, 3, $J$ = 7 Hz, b), 1.46 (d, 3, $J$ = 14.5 Hz, f), 2.95 (d, 1, $J$ = 13 Hz, d), 3.28 (d, 1, $J$ = 20 Hz, e), 3.81, 3.85 (two d, 6, $J$ = 10 Hz, g), 4.32 (quartet, 2, $J$ = 7 Hz, a), 6.54 (broad s, 1, c) | (Nujol) 3220 (s, NH), 1725 (s, C=O), 1240 (s, P=O), 1050 (s, POC) |

decomposed smoothly on distillation to give the cyclopropanes II and III, respectively, which contain two phosphorus substituents.



II



III

The results described here thus show $(MeO)_2P(O)C(N_2)R$ (R = H, Ph, and Me) to be useful reagents for organophosphorus syntheses, especially in the synthesis of phosphorus-substituted cyclopropanes. In view of the widely varied reactivity of their diazoalkane function, they should serve in the preparation of a wide variety of organophosphorus compounds.

## Experimental Section

**General Comments.**—All reactions involving preparation or use of the dimethylphosphono-substituted diazoalkanes were carried out under an atmosphere of prepurified nitrogen. Infrared spectra were recorded using Perkin-Elmer Infracord 237B and 337 grating spectrophotometers, nmr spectra using Varian A-60 or T-60 spectrometers. Chemical shifts are given in ppm downfield from internal TMS (δ units). Melting points are uncorrected. All gas–liquid partition chromatography (glc) was carried out using an F & M gas chromatograph.

All the products derived from the dimethylphosphono-substituted diazoalkanes, together with their physical properties and analytical data, are listed in Table I. Their spectroscopic properties are given in Table II.

**Preparation of Dimethyl α-Diazobenzylphosphonate.**—A solution of 186.2 g (1.0 mol) of *p*-toluenesulfonylhydrazine in 1 l. of THF in a 4-l. flask was chilled to 0°, and 37 ml of concentrated HCl (0.5 mol) was added. The resulting solution was stirred in an ice bath while 214.2 g (1.0 mol) of dimethyl benzoylphosphonate[7] ($n^{25}D$ 1.5248) was added over a 5-min period. The flask was stoppered and the mixture was allowed to warm to room temperature over a 6-hr period. The resulting heavy white precipitate was filtered and dried to give 304.9 g of solid, mp 168–169° (dec). The mother liquor was evaporated overnight at room temperature under an air stream to give a second crop, 47.6 g, mp 165–166° (dec); the total yield thus was 92%. Recrystallization from methanol gave an 84% recovery of pure product, mp 173–174°.

*Anal.* Calcd for $C_{16}H_{19}N_2O_5SP$: C, 50.25; H, 5.01. Found: C, 50.28; H, 5.04. Nmr ($CDCl_3$): δ 2.44 (s, 3, Ar $CH_3$), 3.73 (d, 6, $J$ = 11 Hz, $POCH_3$), 7.1–7.9 (m, 9, aryl), and 8.4 ppm (broad s, 1, NH).

A suspension of dimethyl benzoylphosphonate *p*-toluenesulfonylhydrazone (21.35 g, 55.9 mmol) in a solution of sodium carbonate (6.05 g, 57.0 mmol) in 100 ml of distilled water was stirred at room temperature for 15 hr, during which time the hydrazone slowly dissolved and the solution became orange and opaque. The mixture was extracted with two 100-ml portions of diethyl ether, each portion being washed with 50 ml of water. The combined ether extracts were dried ($Na_2SO_4$) and evaporated to a volume of 50 ml. The concentrated ether solution was chilled slowly in a −78° bath with scratching of the flask sides. This procedure gave 9.14 g of orange crystals, mp 38–42°. The mother liquor was concentrated to 20 ml and 20 ml of pentane was added; on chilling, a second crop of 2.70 g, mp 38–40°, was obtained, giving a total yield of 94%. Recrystallization from diethyl ether at −78° gave pure product (93% recovery), mp 44.0–44.5°.

*Anal.* Calcd for $C_9H_{11}N_2O_3P$: C, 47.78; H, 4.91. Found: C, 47.84; H, 5.03. Nmr ($CCl_4$): δ 3.67 (d, 6, $J$ = 11.7 Hz, $POCH_3$), 6.9–7.4 ppm (m, 5, aryl). Ir (liq film): 2950 (m), 2825 (m), 2975 (s, C=N=N), 1600 (m), 1500 (m), 1295 (s), 1265 (s, P=O), 1185 (s), 1025 (s, POC), 830 (s), 755 (s), and 685 (m) $cm^{-1}$.

**Preparation of Dimethyl Diazomethylphosphonate. A. Bromomethylphthalimide.**—An improved procedure is reported. A suspension of hydroxymethylphthalimide[8] in 3 l. of chloroform was stirred and refluxed gently in a 5-l. flask while gaseous hydrogen bromide (Matheson) was admitted through a submerged fritted glass gas inlet tube at a moderate rate for 2 hr. After 25 min the mixture became homogeneous, and after 70 min gas was no longer being absorbed rapidly. The solution was poured (while still warm) into a separatory funnel and the lower aqueous HBr layer was discarded. The organic layer was extracted with 500 ml of warm water (color change from orange to white). The organic layer then was dried ($Na_2SO_4$), filtered through Celite, and evaporated at reduced pressure. The crystalline residue was recrystallized from 2.1 l. of acetone to give 577 g of thick white needles, mp 150–152°. The mother liquor was concentrated to give a second crop of 82 g, mp 150–151°. The total yield was 659 g (92%), lit.[9] mp 148°. It must be emphasized that an adequate excess of HBr must be used in the above procedure; if this is not done, the yield is greatly reduced. Other routes to

(7) K. D. Berlin, D. M. Hellwege, and M. Nagabhushanam, *J. Org. Chem.*, **30**, 1265 (1965).

(8) S. R. Buc, *J. Amer. Chem. Soc.*, **69**, 254 (1947).

(9) G. W. Pucher and T. B. Johnson, *ibid.*, **44**, 817 (1922).

this product were tried (*via* HBr and $H_2SO_4$[9] and *via* $PBr_3$[10]), but the yields obtained were not so high.

**B. Dimethyl Phthalimidomethylphosphonate.**—A 2-l. flask equipped with a reflux condenser and a stirrer was charged with 240 g (1.0 mol) of bromomethylphthalimide, freshly distilled trimethyl phosphite (136.5 g, 1.1 mol), and 400 ml of xylene. The flask was swept with nitrogen and heated slowly to near reflux, at which time a vigorous but controllable reaction ensued. Heating was discontinued at this point and continued after the initial exothermic reaction had subsided. The reaction mixture was heated at reflux for 5 hr, then 300 ml of solvent was distilled away, and the remaining solution was allowed to cool overnight in a sealed flask. The crystalline product which had formed was collected, heated in 300 ml of dry ether for several hr, filtered again, and dried under vacuum to give 232.5 g of product (87%), mp 113–117° (prior softening). Several recrystallizations from ether and a final recrystallization from $CHCl_3$–$CCl_4$ afforded an analytical sample, mp 117.5–119°.

*Anal.* Calcd for $C_{11}H_{12}NO_5P$: C, 49.08; H, 4.49. Found: C, 48.98; H, 4.45. Nmr ($CDCl_3$): $\delta$ 3.85 (d, 6, $J$ = 10.7 Hz, $POCH_3$), 4.14 (d, 2, $J$ = 11.5 Hz, $NCH_2P$), 7.8 ppm (broad s, 4, aryl). Ir (Nujol mull, principal bands): 1720 (C=O), 1465, 1405, 1385, 1310, 1250 (P=O), 1190, 1070, 1050, 1020 (POC), 910, 840, and 715 $cm^{-1}$.

**C. Dimethyl Diazomethylphosphonate.**—A solution of 53.8 g (0.20 mol) of dimethyl phthalimidomethylphosphonate and 95% anhydrous hydrazine (0.21 mol) in 400 ml of methanol was stirred at room temperature under nitrogen for 45 hr. Then 20 ml of acetic acid was added and the mixture was stirred 5 min longer and filtered. The precipitated phthalhydrazide was dried, 29.7 g (92%). The filtrate was evaporated at reduced pressure and the residue was dissolved in 50 ml of acetic acid. A solution of sodium nitrite (21.7 g, 0.30 mol, in 50 ml of water) was added dropwise over 5 min while the flask was being swirled in an ice bath. The flask was kept in the ice bath, with occasional swirling, for another 5 min, and then 53 g of sodium carbonate was added slowly in portions, followed by 200 ml of ice water. The reaction mixture was extracted with three 100-ml portions of dichloromethane. The combined organic layers were extracted with 100 ml of saturated $NaHCO_3$ solution, dried ($Na_2SO_4$), and concentrated at reduced pressure. The orange liquid residue was short-path distilled to give 13.77 g (46%) of the diazo compound, bp 59° (0.42 mm), as a yellow liquid, $n^{25}D$ 1.4585.

*Anal.* Calcd for $C_3H_7N_2O_3P$: C, 24.01; H, 4.70. Found: C, 23.73; H, 4.85. Nmr (neat): $\delta$ 3.73 (d, 6, $J$ = 11.5 Hz, $POCH_3$), 4.49 ppm (d, 1, $J$ = 10.7 Hz, PCH). Ir (liq film): 3075 (w), 3020 (w), 2960 (m), 2860 (m), 2110 (s, C=N=N), 1760 (s), 1660 (w), 1465 (m), 1300 (s), 1250 (s, P=O), 1185 (m), 1160 (sh), 1030 (POC), 915 (w), 830 (s), 770 (w), 735 (w), and 710 (w) $cm^{-1}$.

The intermediacy of **dimethyl aminomethylphosphonate** was demonstrated in the following manner. A solution of dimethyl phthalimidomethyl phosphonate (8.7 mmol) and a slight excess of 95% anhydrous hydrazine in 15 ml of methanol was stirred at room temperature for 15 hr, as in the preparation above. The precipitated phthalhydrazide was filtered and the filtrate evaporated (near room temperature) to leave a yellow oil. Since acetic acid was not added as it had been in the diazo compound preparation, the free amine was present after evaporation of the solvent, and it was necessary to not allow the temperature to rise much above room temperature to prevent exothermic decomposition of the amine. Benzene (10 ml) was added and the mixture cooled to 0°. An ice-cold solution of 1.66 g of *p*-toluenesulfonyl chloride in 5 ml of pyridine was added and the mixture poured into 50 ml of water containing 10 ml of concentrated HCl after a 10-min reaction time. Extraction with chloroform, evaporation of the organic layer, and trituration of the residual oil with hexane followed. The resulting solid was recrystallized from benzene to give yellow needles, mp 117–118° (1.0 g, 38%). An analytical sample (from benzene), long thick white needles, had mp 118–119° and was shown to be **dimethyl *p*-toluenesulfonylaminomethylphosphonate**, $p$-$CH_3C_6H_4SO_2NHCH_2P(O)(OMe)_2$.

*Anal.* Calcd for $C_{10}H_{16}NO_5SP$: C, 40.95; H, 5.50; N, 4.78. Found: C, 41.23; H, 5.47; N, 4.69. Nmr ($CDCl_3$): $\delta$ 2.43 (s, 3, Ar-$CH_3$), 3.27 (d of d, 2, $J_{HCNH}$ = 6.5 Hz, $J_{HCP}$ = 13.5 Hz, $PCH_2N$), 3.78 (d, 6, $J$ = 10.5 Hz, $POCH_3$), 6.6 (broad s, 1, NH), 7.32 and 7.80 [two d, 4, $J$ (both) = 8 Hz, aryl].

(10) O. Mancera and O. Lemberger, *J. Org. Chem.*, **15**, 1253 (1950).

**Preparation of Dimethyl α-Diazo-3,5-dimethoxybenzylphosphonate.**—Dimethyl 3,5-dimethoxybenzoylphosphonate was prepared[7] on a 0.113-mol scale in 92% yield. The product was isolated as a viscous, yellow liquid, $n^{25}D$ 1.5337, bp *ca.* 153° (0.02 mm).

*Anal.* Calcd for $C_{11}H_{15}O_6P$: C, 48.18; H, 5.51. Found: C, 48.49; H, 5.45.

This compound (102.8 mmol) was converted to the *p*-toluenesulfonylhydrazone by the procedure described above for dimethyl benzoylphosphonate. The crude product was obtained as a yellow oil. This was washed with water and extracted with boiling ether to leave 30.16 g of presumed anti isomer, mp 158° (dec). The ether extracts were evaporated; the residual oil crystallized and was triturated with ether to give 10.40 g of presumed syn isomer, mp 107–108°. The total yield, 40.56 g, was 89%.

An analytical sample (from methanol) of the anti isomer had mp 164.5–165.5° (dec); the syn isomer (from methanol) had mp 113–114°.

*Anal.* Calcd for $C_{18}H_{23}N_2O_7SP$: C, 48.86; H, 5.24; N, 6.33. Found (anti isomer): C, 48.84; H, 5.23; N, 6.36. Found (syn isomer): C, 49.03; H, 5.30; N, 6.32.

To a solution of sodium carbonate (23.3 mmol) in 39 ml of water was added 8.57 g (19.4 mmol) of *syn*-dimethyl 3,5-dimethoxybenzoylphosphonate *p*-toluenesulfonylhydrazone. The reaction mixture was stirred under nitrogen for 24.5 hr, then was extracted with dichloromethane. Work-up of the organic layer gave 4.96 g of bright yellow powder (90%), mp 55–56° (from diethyl ether at −78°).

When the anti isomer was used, the reaction was noticeably slower in forming the yellow color, but work-up after 31 hr gave the diazo compound in 91% yield.

*Anal.* Calcd for $C_{11}H_{15}N_2O_5P$: C, 46.16; H, 5.28; N, 9.79. Found: C, 46.22; H, 5.43; N, 9.75. Nmr ($CCl_4$): $\delta$ 3.72 (s, 6, Ar $OCH_3$), 3.73 (d, 6, $J$ = 12 Hz, $POCH_3$), 6.1–6.3 (m, 3, aryl). The ir spectrum (Nujol mull) showed the bands due to C=N=N at 2090, to P=O at 1255, and to POC at 1020 $cm^{-1}$.

**Reactions of the Diazoalkanes with Acids.**—Physical properties and analytical data for the products are given in Table I.

**A. Dimethyl α-Diazobenzylphosphonate.**—Diethyl ether, 100 ml, in a three-necked flask equipped with a dropping funnel, a stirring unit, a gas inlet tube whose tip was submerged below the liquid level, and a drying tube, was saturated with anhydrous hydrogen chloride at −78°. While the HCl stream was continued, 1.40 g of the diazo compound in 50 ml of ether was added dropwise over 15 min, its orange color being discharged instantaneously. Evaporation of solvent, treatment of the residual oil with sodium bicarbonate solution, and ether extraction followed. Distillation of the ether extracts gave 1.25 g (86%) of **dimethyl α-chlorobenzylphosphonate.**

A solution of 10.0 mmol of the diazo compound and 20.0 mmol of glacial acetic acid in 20 ml of diethyl ether was heated at reflux for 15 hr, at which time nitrogen evolution was complete. Distillation of the reaction mixture gave 2.0 g (79%) of **dimethyl α-acetoxybenzylphosphonate.**

A warm solution of anhydrous *p*-toluenesulfonic acid in benzene (prepared by distilling 25 ml of benzene and water from a solution of 10 mmol of *p*-toluenesulfonic acid monohydrate in 50 ml of benzene) was added in portions to a solution of the diazo compound until the orange color was discharged. Evaporation of the reaction mixture was followed by extraction of the residual yellow oil with ether and washing of the ether solution with saturated sodium bicarbonate. Evaporation of the dried ether solution gave a solid which was recrystallized from methanol–water to give 1.32 g (71%) of **dimethyl α-(*p*-toluenesulfonyloxy)-benzylphosphonate**, mp 84–86°. An analytical sample (from $CCl_4$) had mp 86–87°.

**B. Dimethyl Diazomethylphosphonate.**—A solution of 4.36 mmol of the diazo compound in 15 ml of glacial acetic acid was heated on the steam bath with exclusion of moisture for 1.5 hr. Evaporation of the excess acid, treatment of the residue with saturated sodium bicarbonate solution, and extraction with chloroform followed. Distillation (short path) of the chloroform solutions gave 617 mg (78%) of the product, **dimethyl acetoxymethylphosphonate.**

**Miscellaneous Reactions of the Diazoalkanes. A. With Triphenylphosphine.**—A solution containing 5 mmol each of dimethyl α-diazobenzylphosphonate and triphenylphosphine in 10 ml of benzene was kept at room temperature under nitrogen for 56 hr. It then was warmed on the steam bath for 5 min and

diluted with heptane. The product separated out as an oil. The solution was decanted and the oil was triturated with pentane. The resulting powder was recrystallized twice from benzene–heptane to give the phosphazine $Ph_3P{=}NNC(Ph)P(O)(OMe)_2$.

When 2.41 mmol each of triphenylphosphine and dimethyl diazomethylphosphonate in 10 ml of benzene were stirred at room temperature under nitrogen for 12 hr, a white precipitate resulted. Recrystallization gave the phosphazine $Ph_3P{=}NN{=}CHP(O)(OMe)_2$ as long white silky needles in 12% yield.

**B. Reaction of Dimethyl α-Diazobenzylphosphonate with Mercuric Chloride.**—A THF solution (10 ml) of the diazo compound (9.08 mmol) and an equimolar quantity of mercuric chloride was heated at reflux for 30 min. No perceptible color change or gas evolution was apparent, but nitrogen evolution began after a trace of copper powder was added. The reaction mixture was heated at reflux for another hour. Removal of solvent at reduced pressure left a yellow oil. This was taken up in 150 ml of benzene, treated with activated charcoal, and filtered through Celite. Evaporation to 80 ml was followed by addition of 670 ml of hexane. The resulting solution was left to stand overnight; 0.35 g (8%) of light yellow crystals was deposited. An analytical sample was recrystallized once from benzene–cyclohexane and twice from benzene–heptane.

**C. Reaction of Dimethyl Diazomethylphosphonate with Mercury(II) and Silver(I) Acetylacetonates.**—To a solution of 10.0 mmol of the diazo compound in 10 ml of dichloromethane was added 2.19 g (5.5 mmol) of mercury(II) acetylacetonate. The reaction mixture was stirred in a sealed flask for 40 min and filtered through Celite: the filtrate was evaporated to *ca.* 5 ml. Diethyl ether (50 ml) was added slowly; 2.0 g (80%) of yellow needles formed. These were characterized as $Hg[C(N_2)P(O)(OMe)_2]_2$.

The silver derivative was prepared in an analogous manner, substituting a 50% molar excess of silver(I) acetylacetonate and carrying out the stirring and filtering operations in subdued light. The product was a yellow powder (95% yield), mp 125° (explodes), and was freely soluble in dichloromethane to give a deep orange solution. It was not shock sensitive. Ir (Nujol mull): 2310 (sh), 2270 (w), 2070 (s, C=N=N), 2030 (sh), 1525 (w), 1220 (s, P=O), 1185 (m), 1145 (m), 1055 (s), 1030 (s), 890 (s), 810 (s), and 745 (m) $cm^{-1}$.

**Copper-Catalyzed Reactions of the Diazoalkanes with Olefins. A. Dimethyl α-Diazobenzylphosphonate.**—A 200-ml three-necked flask equipped with a reflux condenser topped with a nitrogen inlet tube and a magnetic stirring assembly was charged with the olefin (100 ml, freshly distilled from lithium aluminum hydride), 6–10 mmol of the diazo compound, and 3.80 g (60 mg-atoms) of copper powder (J. T. Baker "purified grade"). The mixture was stirred at reflux under nitrogen until the orange diazoalkane color had been discharged (usually about a 12–24-hr reaction time was involved). The usually pale yellow mixture was filtered through Celite and the product cyclopropane was obtained by crystallization (in the case of cyclohexene) or distillation (in the case of 1-heptene and allyltrimethylsilane).

The product from cyclohexene, 7-(dimethylphosphono)-7-phenylnorcarane, was converted to the phosphonic acid by refluxing 331 mg of the dimethyl ester in 4 ml of concentrated HBr for 15 min. The mixture was cooled and the resulting white precipitate was filtered, washed with cold water, and dried to give 282 mg (95%) of 7-phenyl-7-phosphononorcarane, mp 271–273°. Recrystallization from aqueous methanol gave white needles, mp 274–275°.

**B. Dimethyl Diazomethylphosphonate.**—To a stirred mixture of the olefin (100 ml), 30 ml of dichloromethane, and 3.8 g of copper powder maintained in an ice bath under a nitrogen atmosphere was added 10 mmol of dimethyl diazomethylphosphonate. The reaction mixture was stirred at 0° for 8 hr and overnight at room temperature. Fractional distillation of the filtered (through Celite) reaction mixture gave the cyclopropane (yields in Table I) and the crude carbene "dimer," 1,2-bis(dimethylphosphono)ethylene (presumed identity; not obtained in pure state)[11] in variable (15–30%) yields.

The presence of dichloromethane was required in order to obtain good yields. Thus, in the case of cyclohexene, reaction with the diazo compound in the absence of dichloromethane gave the expected norcarane in 20% yield and "carbene dimer" in 68% yield. In the presence of dichloromethane these yields were 39 and 28%, respectively.

The reaction with isobutylene was carried out −7° for 16 hr.

**1,3-Dipolar Addition Reactions of Dimethyl α-Diazobenzylphosphonate. A. Reactions in Which the Initial Adduct Was Isolated.**—The diazo compound and the 1,3-dipolarophile (10- to 50-fold excess) in dry benzene were kept at room temperature for 1 or 2 days. The reaction mixture, if still orange at that time, was heated at reflux until a color change to yellow had occurred. Evaporation at reduced pressure and crystallization of the residue followed. Pure products were obtained by recrystallization from benzene–heptane (adducts from acrylonitrile, diethyl maleate) or chloroform–carbon tetrachloride (adduct from methyl vinyl ketone).

**B. Reactions in Which the Cyclopropane Was Isolated. (a) Reaction with Dimethyl α-Styrylphosphonate.**—α-Styrylphosphonic acid was prepared by the procedure of Conant and Coyne[12] and was esterified with an excess of diazomethane in diethyl ether. The reaction mixture was washed with saturated $NaHCO_3$, dried, and evaporated. The residual yellow oil was short-path distilled (141° at 4.3 mm) and redistilled at 101° (0.1 mm) to give dimethyl α-styrylphosphonate in 62% yield. A trace of hydroquinone prevented yellowing of the sample on storage in the freezer. A center cut had $n^{25}D$ 1.5267.

*Anal.* Calcd for $C_{10}H_{13}O_3P$: C, 56.60; H, 6.17. Found: C, 56.66; H, 6.37. Ir (liq film): 3050 (sh), 3000 (m), 2945 (s), 2840 (m), 1600 (w), 1575 (w), 1495 (s), 1445 (m), 1250 (s), 1180 (m), 1100 (m), 1050 (s), 960 (m), 935 (m), 850 (s), 830 (s), 785 (s), 765 (s), 720 (m), 700 (s), and 680 (m) $cm^{-1}$.

A solution of this vinylphosphonate ester (1.06 g, 5.0 mmol) and the diazo compound (1.13 g, 5.0 mmol) in 10 ml of benzene was heated at reflux under nitrogen for 7 days. Distillation of the reaction mixture gave 0.42 g of unconverted vinylphosphonate ester and then a viscous yellow syrup, boiling range 178–190° at 0.04 mm. Redistillation gave pure product, bp 190° (0.04 mm), presumably a mixture of isomers. The syrup changed to a white powder, melting range 100–125°, after it had stood for 2 weeks.

**(b) Reaction with Diethyl Vinylphosphonate.**—A solution containing 5.0 mmol of the diazo compound and 50 mmol of the vinylphosphonate ester was heated on the steam bath for 3 hr. The now colorless reaction mixture was distilled to remove the unconverted vinylphosphonate ester, and the yellow oil which remained, whose ir spectrum indicated the presence of some pyrazoline (N–H absorption), was distilled using a Hickman still (oil bath 90–160° at 0.10–0.05 mm) to give the cyclopropane as a colorless oil (no N–H absorption in the infrared).

**1,3-Dipolar Addition Reactions of Dimethyl α-Diazoethylphosphonate.**—The diazo compound and the respective 1,3-dipolarophile (1:1 molar ratio) were dissolved in toluene. An exothermic reaction ensued. Subsequently the reaction mixture was heated for *ca.* 30 min on the steam bath, until the diazo compound color had been discharged. The pyrazolines produced were isolated by removal of the solvent at reduced pressure. Pure samples were obtained by recrystallization from carbon tetrachloride (adduct from methyl vinyl ketone) or cyclohexane–carbon tetrachloride (adducts from ethyl acrylate and acrylonitrile).

**Registry No.**—Dimethyl α-diazobenzylphosphonate, 28447-22-5; dimethyl benzoylphosphonate *p*-toluenesulfonylhydrazone, 28447-23-6; dimethyl diazomethylphosphonate, 28447-24-7; bromomethylphthalimide, 5332-26-3; dimethyl phthalimidomethylphosphonate, 28447-26-9; dimethyl *p*-toluenesulfonylaminomethylphosphonate, 28447-27-0; dimethyl α-diazo-3,5-dimethoxybenzylphosphonate, 28447-28-1; *anti*-dimethyl 3,5-dimethoxybenzoylphosphonate *p*-toluenesulfonylhydrazone, 28434-43-7; *syn*-dimethyl 3,5-dimethoxybenzoylphosphonate *p*-toluenesulfonylhydrazone, 28434-44-8; dimethyl 3,5-dimethoxybenzoylphospho-

(11) Hydrogenation and saponification of this compound gave ethylenediphosphonic acid, mp 218–220°, which was not depressed on admixture with authentic acid: M. I. Kabachnik, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 631 (1947); *Chem. Abstr.*, **42**, 5845*h* (1948).

(12) J. B. Conant and B. B. Coyne, *J. Amer. Chem. Soc.*, **44**, 2530 (1922).

nate, 28446-76-6; dimethyl α-styrylphosphonate, 1707-07-9; dimethyl α-diazoethylphosphonate, 26584-15-6.

**Acknowledgments.**—The authors are grateful to the U. S. Public Health Service (Grant CA-08278) and to the U. S. Air Force Office of Scientific Research (SRC)-OAR (USAF Grant AFOSR-68-1350) for generous support of this work. This work was supported in part by Public Health Service Fellowship 1-F1-GM-32,679 (to R. S. M.).

# The Synthesis and Chemistry of 1′,1′,4′(*S*)-Trimethyl-3β-trityloxyandrost-5-eno[16β,17β-*b*]azetidinium Tosylate

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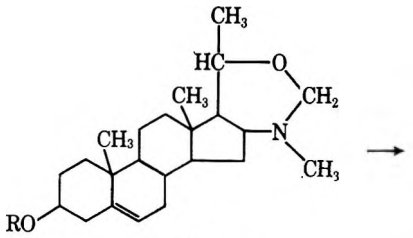
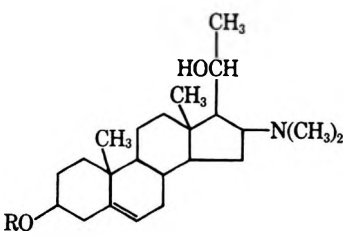
Treatment of 16β-dimethylamino-3β-trityloxypregn-5-en-20β-ol (**2b**) with *p*-toluenesulfonyl chloride in pyridine afforded 1′,1′,4′(*S*)-trimethyl-3β-trityloxyandrost-5-eno[16β,17β-*b*]azetidinium tosylate (**3a**). Reaction of the latter compound with refluxing ethanolamine (or potassium hydroxide in refluxing dioxane) yielded the Hofmann degradation product 16β-dimethylaminopregna-5,20-dien-3β-yl trityl ether (**4a**). The mother liquor of the ethanolamine reaction also contained the *N*-hydroxyethylamino compound **5a**. Reduction of **3a** with lithium aluminum hydride gave 16β-dimethylaminopregn-5-en-3β-yl trityl ether (**6**).

Published literature[1] in the steroid field has indicated that a tertiary amine grouping in a 1,4 relationship to a hydroxyl group may spontaneously cyclize under the influence of *p*-toluenesulfonyl chloride to form a pyrollidine ring. It was of interest, since 16β-dimethylaminopregn-5-ene-3β,20β-diol (**2a**)[2] was available, to know if the same conditions acting on this compound would produce an azetidine ring.[3] Such a transformation would establish a new heterocyclic-fused ring on the steroid system.

Since the 3β-hydroxyl group of the above-mentioned compound could conceivably interfere with a study of the reaction, it was thought best to protect this function preferentially. This was done by tritylation[4] of the *N*-methyloxazine **1a**[2] to form the 3-trityl ether **1b**,

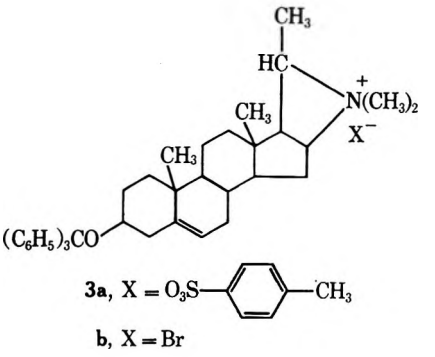


**1a**, R = H
**b**, R = $(C_6H_5)_3C$



**2a**, R = H
**b**, R = $(C_6H_5)_3C$

which was reduced with lithium aluminum hydride to afford 16β-dimethylamino-3β-trityloxypregn-5-en-20β-ol (**2b**). Reaction of **2b** with *p*-toluenesulfonyl chloride in pyridine at room temperature for 65 hr gave reasonable yields of the azetidine tosylate **3a**. This compound's structure was confirmed by its infrared spectrum, which



**3a**, X = $O_3S$—$C_6H_4$—$CH_3$
**b**, X = Br

had the tosylate ion bands previously reported,[1a] by the nmr spectrum confirming the quaternary alkylated nitrogen, and the mass spectrum which showed the expected molecular ion (minus *p*-toluenesulfonic acid) at *m/e* 586, and this ion minus the trityl grouping at *m/e* 343. Assuming a conventional rear-side attack of the nitrogen electrons to displace the $C_{20}$-β-toysl grouping, the resultant configuration of the steroidal $C_{20}$-methyl grouping on the azetidine ring would be *S*.

Since little is known of the chemistry of such azetidine systems, a modest chemical study of **3a** was undertaken. It has been shown that a condensed azetidinium ring structure, when it is nonplanar, will undergo reversal of the quaternization on reaction with nucleophiles.[5] In this case, however, treatment of **3a** with lithium bromide afforded only anion replacement to give the azetidinium bromide **3b**. The analogous iodide could be formed by treatment with sodium iodide, but the product was very labile to air and/or light and could not be characterized satisfactorily. This displacement reaction without ring opening may indicate that the azetidine ring is not distorted in

(1) (a) F. L. Weisenborn and D. Burn, *J. Amer. Chem. Soc.*, **75**, 259 (1953); (b) S. W. Pelletier and W. A. Jacobs, *ibid.*, **75**, 4442 (1953); (c) R. Ledger and J. McKenna, *Chem. Ind. (London)*, 1662 (1963); (d) L. Labler, J. Hora, and V. Cerny, *Collect. Czech. Chem. Commun.*, **28**, 2015 (1963).

(2) M. Heller and S. Bernstein, *J. Org. Chem.*, **32**, 3981 (1967).

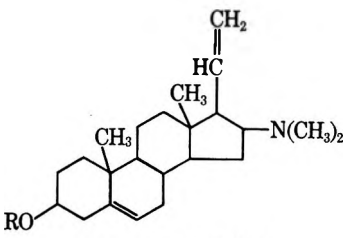
(3) This is similar to the general method of preparing azetidines by ring closure of γ-haloamines: see J. A. Moore in "Heterocyclic Compounds With Three- and Four-Membered Rings," Part Two, A. Weissberger, Ed., Interscience, New York, N. Y., 1964, p 891.

(4) R. T. Blickenstaff, *J. Amer. Chem. Soc.*, **82**, 3673 (1960).

(5) G. Fodor, *ibid.*, **88**, 1040 (1966).

this case, although the proof is by no means unequivocal (*vide infra*).

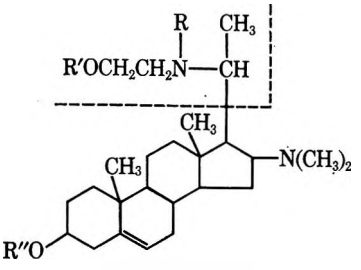
The observation of the variety of cleavages possible by heating a quaternary amine in ethanolamine[1d,6] suggested the application of this reaction to **3a**. The most easily isolated product was identified as the conventional Hoffmann degradation product **4a**[7] which was further heated in acetic acid to give the 3β-ol, **4b**. The nmr spectra of these compounds proved the



**4a**, R = $(C_6H_5)_3C$
**b**, R = H

proposed structures conclusively, since a normal basic dimethylamino band was seen at δ 2.18–2.19 ppm and the ABX splitting of the $C_{20,21}$-ethylene system was observed in the δ 4.74–5.15 ppm region. These two spectra also showed conclusively that the $C_6$-vinyl hydrogen is shielded by at least one of the phenyl rings of the trityl grouping since the trityl ether compounds herein prepared show this band at *ca.* δ 4.9 ppm, while the 3β-hydroxy compound **4b** has this band at the more normal location, δ 5.38 ppm.

Because a considerable amount of material was left in the mother liquor which resulted from the ethanolamine reaction, this mother liquor was subjected to partition chromatography on Celite to give one major component **5a**. Unfortunately, this component could not be crystallized; so it was acetylated in the hopes



**5a**, R = R′ = H; R″ = $(C_6H_5)_3C$
**b**, R = R′ = Ac; R″ = $(C_6H_5)_3C$
**c**, R = R′ = Ac; R″ = H
**d**, R = Ac; R′ = R″ = H

of attaining a crystalline compound. The new compound **5b** was amorphous, but it did show *O*-acetyl and *N*-acetyl absorption in its infrared spectrum. Its nmr spectrum also indicated such groupings, but further revealed a splitting of these signals in the acetyl region. Removal of the trityl group from **5b** with acetic acid finally gave a crystalline compound **5c** after preparative thin layer chromatography. The latter compound again showed ester and amide absorption in its infrared spectrum and revealed the same type of splitting of the acetyl signals in its nmr spectrum. The nmr spectrum also indicated a widening of the signal of the $C_{18}$-hydrogen atoms. The mass spectrum disclosed molecular weight of 488 for the largest mass ion, which supported an acetoxyethylamide structure for **5c**. This was further corroborated by a signal in the mass spectrum at *m/e* 316 (M − 172) which suggests the molecular ion minus a cleavage fragment consisting of the entire $C_{20}$ and $C_{21}$ moiety as indicated by the dotted line in the structure. Furthermore, a signal at *m/e* 172 for this moiety was noted. The balance of the nmr spectrum also supported this structure, so that the splitting of the acetyl signals and widening of the $C_{18}$-hydrogen signal in the nmr spectrum could be explained by the presence of rotamers of **5c** due to the interference of the $C_{18}$ hydrogens with the free rotation of the large substituent at $C_{20}$. This was further borne out by the coalescing of these signals when the nmr spectrum was taken at 90°. The indicated structure for **5c** then permitted the appropriate 3-trityl ether structures to be proposed for **5a** and **5b**.

It is apparent that **5a** was formed by the nucleophilic attack of the ethanolamine on the azetidine **3a** with the opening of the $C_{20}$-nitrogen bond. Since it appears most likely to be a concerted attack with bond cleavage, the stereochemistry of the hydroxyethylamine grouping about $C_{20}$ in **5a** has been assigned as β. No trace of the isomer of **5a** which would be formed by attack at the $C_{16}$ position with opening of the $C_{16}$-nitrogen bond was seen. This isomer would not have the *m/e* 316 signal or show rotamers in the nmr. Nucleophilic displacement of this type under very mild conditions has been discussed above.[5] It has also been achieved[8] under more vigorous conditions (heating with 10% sodium hydroxide or benzylamine). It is interesting that no Hoffmann degradation products are reported in this last reference.

A very small amount of more polar material recovered from the above-described preparative thin layer chromatography was assigned the structure of the alcohol–amide **5d** on the basis of its nmr and mass spectra. It is possible that this compound arose during the removal of the trityl group from **5b**.

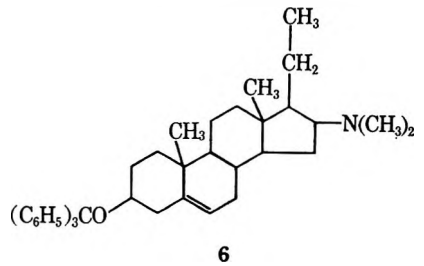
In the hope of achieving a chemical proof of the stereochemistry at $C_{20}$ of **5a**, the azetidinium tosylate **3a** was refluxed with potassium hydroxide in dioxane. For this purpose, the synthesis of **2a** was desired. Unfortunately, only the olefin **4a** was found as a product.

An attempt was made to functionalize **4a** at the $C_{21}$ position by reaction with 9-borabicyclo[3.3.1]nonane[9] as a selective hydroborating agent[10] relative to the $\Delta^5$ double bond. However, no reaction could be made to take place.

It has been observed that treatment of quaternary methylated amines with lithium aluminum hydride served to remove a methyl group from the salt, presumably by SN2 displacement by hydride ion on the *N*-methyl group.[1c,11] In this case, treatment of **3a** with lithium aluminum hydride in refluxing tetrahy-

(6) S. Hünig and W. Baron, *Chem. Ber.*, **90**, 395, 403 (1957).
(7) See ref 3, p 906.
(8) A. Ebnöther and E. Jucker, *Helv. Chim. Acta*, **47**, 745 (1964).
(9) E. F. Knights and H. C. Brown, *J. Amer. Chem. Soc.*, **90**, 5280 (1968).
(10) E. F. Knights and H. C. Brown, *ibid.*, **90**, 5281 (1968).
(11) G. W. Kenner and M. A. Murray, *J. Chem. Soc.*, 406 (1950); A. C. Cope, E. Ciganek, L. J. Fleckenstein, and M. A. P. Meisinger, *J. Amer. Chem. Soc.*, **82**, 4651 (1960).

drofuran opened the azetidine ring to form the pregnene **6**. The structure of the latter was confirmed



**6**

by reducing the diene **4a** catalytically to afford **6**. In this case, obviously, the hydride ion displacement was at $C_{20}$ followed by cleavage of the $C_{20}$-nitrogen bond. In general, reaction of the quaternary azetidine ring with nucleophiles may give Hoffmann degradation products and/or substitution products with ring opening besides simple displacement of the anion without ring opening.

## Experimental Section[12]

**3′6′(*R*)-Dimethyl-2′,3′,4′,5′-tetrahydro-3β-trityloxyandrost-5-eno[16β,17β-*d*]-1′,3′-oxazine (1b).**—A mixture of the oxazino compound **1a**[2] (0.77 g), trityl chloride (0.7 g), and pyridine (10 ml) was refluxed for 6 hr and poured into ice–water, and the resultant precipitate was collected. The solid was dissolved in methylene chloride and passed through a small pad of Magnesol. The solvent was removed *in vacuo* and the residue crystallized from methylene chloride–acetone to yield **1b** (0.54 g), mp 251–256°. The analytical sample had mp 257.5–258°; $[\alpha]^{25}D$ −31° ($CHCl_3$); ir 704 $cm^{-1}$; nmr ($CDCl_3$) δ 0.95 (s, 3, 19 H), 1.13 (s, 18 H), 1.35 (d, 3, $J$ = 7 Hz, 21 H), 1.99 (s, 3, $NCH_3$), 3.49 and 4.32 (pair of doublets, 2′,2′ H), 4.88 (m, 1, 6 H), and 7.18–7.62 ppm (m, 15, aromatic H).

*Anal.* Calcd for $C_{42}H_{51}NO_2$ (601.84): C, 83.81; H, 8.54; N, 2.33. Found: C, 83.65; H, 8.50; N, 2.30.

**16β-Dimethylamino-3β-trityloxypregn-5-en-20β-ol (2b).**—A mixture of the trityl ether **1b** (5.04 g), lithium aluminum hydride (5 g), and tetrahydrofuran (250 ml) was stirred and refluxed 22 hr. The mixture was cooled in an ice bath and a saturated solution of potassium sodium tartrate added dropwise until the excess lithium aluminum hydride was consumed. The mixture was filtered, and the residue was stirred with additional hot tetrahydrofuran and filtered. The combined filtrates were evaporated *in vacuo*. Crystallization of the residue in methylene chloride–acetone afforded **2b** (3.29 g), mp 226.5–228°. An additional 0.39 g, mp 221.5–223.5°, was collected from the mother liquor. The analytical sample had mp 227.5–229°; $[\alpha]^{25}D$ −28° ($CHCl_3$); ir 3450 and 708 $cm^{-1}$; nmr ($CDCl_3$) δ 0.97 (s, 3, 19 H), 1.00 (s, 3, 18 H), 1.28 (d, 3, $J$ = 6.5 Hz, 21 H), 2.30 (s, 6, $N(CH_3)_2$), 2.68–3.28 (m, 2, 16 H and 3 H), 4.40 (m, 1, 20 H), 4.91 (m, 1, 6 H), and 7.12–7.63 ppm (m, 15, aromatic H).

*Anal.* Calcd for $C_{42}H_{53}NO_2$ (603.85): C, 83.53; H, 8.85; N, 2.32. Found: C, 83.39; H, 8.99; N, 2.29.

**1′,1′,4′(*S*)-Trimethyl-3β-trityloxyandrost-5-eno[16β,17β-*b*]-azetidinium Tosylate (3a).**—A solution of the dimethylaminopregnene **2b** (0.177 g) and *p*-toluenesulfonyl chloride (0.2 g) in pyridine (5 ml) was allowed to stand at room temperature for 20 hr. The mixture was then poured into ice–water and extracted exhaustively with methylene chloride. The extract was dried ($Na_2SO_4$) and the solvent removed *in vacuo*. Crystallization from methanol–acetone afforded the tosylate **3a** (0.04 g): mp 245–246° dec; $[\alpha]^{25}D$ −6.5° ($CH_3OH$); ir 1200, 1125, 1040, 1016, 708, and 683 $cm^{-1}$; nmr (DMSO-$d_6$) δ 0.91 (s, 6, 18 H and 19 H), 1.38 (d, 3, $J$ = Hz, 21 H), 2.28 (s, 3, $CH_3$ ar), 2.89, 2.98 (two s, 6, $N(CH_3)_2^+$), 4.83 (m, 1, 6 H), and 7.11–7.57 ppm (m, 19, aromatic H); mass spectrum (70 eV) $m/e$ 586, 571, 343, 172.

*Anal.* Calcd for $C_{49}H_{59}NO_4S$ (757.97): C, 77.64; H, 7.85; N, 1.85; S, 4.23. Found: C, 77.72; H, 8.14; N, 1.95; S, 4.21.

In later runs it was found that increasing the reaction time to 65 hr increased the yield to 65–68%.

**1′,1′,4′(*S*)-Trimethyl-3β-trityloxyandrost-5-eno[16β,17β-*b*]-azetidinium Bromide (3b).**—To a solution of the tosylate **3a** (0.5 g) in methylene chloride (100 ml) was added a solution of lithium bromide (5 g) in acetone (50 ml). After standing 5 min at room temperature, the solution was concentrated *in vacuo* at room temperature to *ca.* 10 ml. Methylene chloride (150 ml) was added and the resultant precipitate collected. The filtrate was taken to dryness *in vacuo* and the residue crystallized from acetone to give **3b**: mp 175.5–176.5°; $[\alpha]^{25}D$ −7.6° ($CH_3OH$); ir 1050, 775, 765, 748, and 705 $cm^{-1}$; nmr (DMSO-$d_6$) δ 0.93 (s, 6, 18 H and 19 H), 1.42 (d, 3, $J$ = 7 Hz, 21 H), 2.93 and 3.02 (two s, 6, $N(CH_3)_2^+$), 4.87 (m, 1, 6 H), and 7.19–7.52 ppm (m, 15, aromatic H).

*Anal.* Calcd for $C_{42}H_{52}BrNO$ (666.76): C, 75.65; H, 7.86; Br, 11.99; N, 2.10. Found: C, 75.46; H, 7.84; Br, 11.63; N, 2.01.

**16β-Dimethylaminopregna-5,20-dien-3β-yl Trityl Ether (4a).**

**A.**—A mixture of the tosylate **3a** (0.31 g) and ethanolamine (12 ml) was refluxed 4 hr and then poured into ice–water. The resultant crude precipitate (0.24 g) was collected and crystallized from acetone–methanol to afford **4a** (0.088 g), mp 190–192°. The analytical sample had mp 196.5–197.5°; $[\alpha]^{25}D$ −43° ($CHCl_3$); ir 1048, 773, 760, and 704 $cm^{-1}$; nmr ($CDCl_3$) δ 0.72 (s, 3, 18 H), 0.96 (s, 3, 19 H), 2.18 (s, 6, $N(CH_3)_2$), 2.50 (m, 1, 16 H), 3.33 (m, 1, 3 H), 4.72–5.14 (m, 3. 6 H and 21 H), 6.0 (m, 1, 20 H), and 7.14–7.62 ppm (m, 15, aromatic H).

*Anal.* Calcd for $C_{42}H_{51}NO$ (585.84): C, 86.10; H, 8.78; N, 2.39. Found: C, 86.02; H, 8.93; N, 2.37.

**B.**—A mixture of the tosylate **3a** (0.95 g), potassium hydroxide (5 g), water (15 ml), and dioxane (50 ml) (two phase system) was stirred and refluxed for 19 hr. The mixture was poured into ice–water and the resultant precipitate (0.75 g) collected, mp 185–190°. A tlc showed essentially only **4a** as the product. This was crystallized to give 0.57 g of **4a**, mp 198–200°. A further 0.045 g, mp 195.5–197°, was isolated from the mother liquor. Each fraction had an identical ir spectrum with that of the sample characterized above.

**16β-Dimethylaminopregna-5,20-dien-3β-ol (4b).**—A solution of the trityl ether **4a** (0.64 g) in acetic acid (50 ml) was heated at 56° for 7.5 hr. Dilution of the solution with water precipitated triphenylcarbinol (0.28 g) which was removed. The solution was made basic with 30% potassium hydroxide and the resultant precipitate collected. Crystallization from acetone afforded **4b** (0.198 g), mp 209.5–211.5°. The analytical sample had mp 210–212°; $[\alpha]^{25}D$ −70° ($CHCl_3$); ir 3250 and 910 $cm^{-1}$; nmr ($CDCl_3$) δ 0.78 (s, 3, 18 H), 1.01 (s, 3, 19 H), 2.19 (s, 6, $N(CH_3)_2$), 3.47 (m, 1, 3 H), 4.75–5.15 (m, 2, 21 H), 5.38 (m, 1, 6 H), and 5.99 ppm (m, 1, 20 H).

*Anal.* Calcd for $C_{23}H_{37}NO$ (343.53): C, 80.41; H, 10.86; N, 4.08. Found: C, 80.22; H, 10.73; N, 4.01.

**16β-Dimethylamino-20β-(*N*-2′-acetoxyethylacetamido)pregn-5-en-3β-ol (5c).**—The mother liquors (*ca.* 3.25 g) from the reaction of the tosylate **3a** (4.6 g) and ethanolamine (150 ml) as in the preparation of **4a** by method A (1.45 g, of **4a** was recovered) was submitted to partition chromatography on Celite with the system heptane–Methyl Cellosolve. From the first half of a hold-back volume was isolated an additional 0.3 g of **4a**. An amorphous solid (1.45 g) was isolated from the fourth hold-back volume, but this could not be crystallized. Analysis by tlc suggested it was still a mixture. A repeated partition chromatography on Celite as above again gave a noncrystallizable amorphous solid **5a** (0.8 g). Its nmr spectrum ($CDCl_3$) had δ 0.82 (s, 3, 18 H), 0.96 (s, 3, 19 H), 1.23 (d, 3, $J$ = 7 Hz, 21 H), 2.25 (s, 6, $N(CH_3)_2$), 2.42–3.68 (m, 6, 3 H, 16 H, and $OCH_2CH_2N$), 4.92 (m, 1, 6 H), and 7.14–7.64 ppm (m, 15, aromatic H).

Compound **5a** (0.5 g) was acylated in the usual fashion with acetic anhydride (2 ml) in pyridine (4 ml) at room temperature. The mixture was poured into ice–water and the resultant amorphous solid **5b** (0.56 g) was collected. This solid also could not

(12) All melting points are uncorrected. The infrared spectra were determined in a potassium bromide disk. The nmr spectra were obtained in a Varian A-60 spectrometer with tetramethylsilane as internal reference. The mass spectra were determined on an AEI MS-9 spectrometer (Associated Electrical Industries, Ltd.). Celite (Johns-Manville Co.) is a diatomaceous silica product. Magnesol (Food Machinery Chemical Corp.) is a hydrous magnesium silicate. All the analytical samples were shown to be homogeneous by tlc (silica gel G) analysis. The elemental analyses were performed by L. M. Brancone and associates. The partition chromatography was done by C. Pidacks and associates. Spectral analyses and the optical rotational data were obtained from W. Fulmor and associates. We thank George O. Morton for discussions concerning some nmr spectra, Dr. George Van Lear for interpretation of the mass spectra, and Joseph Nocera for preparative assistance.

be crystallized but was essentially one component by tlc analysis: nmr ($CDCl_3$) $\delta$ 0.73 (s, 3, 18 H), 0.92 (s, 3, 19 H), 1.38 (d, 3, $J$ = 7 Hz, 21 H), 2.01, 2.03, 2.04, and 2.13 (4 s, 6, $OC(=O)CH_3$ and $NC(=O)CH_3$), 2.29 (s, 6, $N(CH_3)_2$), 2.58–3.88 (m, 5, 3 H, 16 H, 20 H, $NCH_2$), 4.18 (m, 2, $OCH_2$), 4.90 (m, 1, 6 H), and 7.14–7.68 ppm (m, 15, aromatic H).

Treatment of the acetate **5b** (0.295 g) in acetic acid (25 ml) for 7.5 hr at 56° and then pouring the mixture into ice–water afforded a precipitate which was collected. This was triphenylcarbinol (0.05 g). The filtrate was made basic with 30% potassium hydroxide. The resultant precipitate (0.156 g) was collected and put on two preparative thin layer chromatography plates (200 × 200 × 1 mm) (silica gel G) and developed in the system 85% of benzene–acetone–water (2:1:2) (upper phase) and 15% of methanol. The less polar band (0.127 g) (*ca.* 9–9.5 cm from the origin) was collected and crystallized from acetone–hexane to give **5c** (0.030 g): mp 203–203.5° dec; $[\alpha]^{25}D$ −9.6° ($CHCl_3$); ir 3410, 1750, 1642, 1630, and 1230 $cm^{-1}$; nmr ($CDCl_3$) $\delta$ 0.78, 0.79 (d, 3, 18 H), 0.99 (s, 3, 19 H), 1.41 (d, 3, $J$ = 6 Hz, 21 H), 2.03, 2.04 (d, 3, $NC(=O)CH_3$), 2.11, 2.17 (d, 3, $OC(=O)CH_3$), 2.31 (s, 6, $N(CH_3)_2$), 3.05–3.90 (m, 5, 3 H, 16 H, 20 H, $NCH_2$), 4.18 (m, 2, $OCH_2$), and 5.34 ppm (m, 1, 6 H); nmr at 90° ($CDCl_3$ + $CD_3OD$) $\delta$ 0.80 (s, 3, 18 H), 1.00 (s, 3, 19 H), 1.41 (d, 3, $J$ = 7 Hz, 21 H), 2.03 (s, 3, $NC(=O)CH_3$), 2.12 (s, 3, $OC(=O)CH_3$), and 2.32 ppm (s, 6, $N(CH_3)_2$); mass spectrum (70 eV) $m/e$ 488, 316, 172.

*Anal.* Calcd for $C_{29}H_{48}N_2O_4$ (488.69): C, 71.27; H, 9.90; N, 5.73. Found: C, 71.54; H, 9.86; N, 5.72.

The more polar band from the preparative plate (6.0 mm from the origin) gave a crude compound (0.03 g) which had physical measurement suggesting **5d** as its structure: nmr (DMSO-$d_6$) $\delta$ 0.68, 0.70 (d, 3, 18 H), 0.92 (s, 3, 19 H), 1.98 2.01 (d, 3, $NC(=O)CH_3$), 2.22 (s, 6, $N(CH_3)_2$), 4.50 (d, 1, CHOH), 4.75 (m, 1, $CH_2OH$), and 5.28 ppm (m, 1, 6 H); mass spectrum (70 eV) $m/e$ 446, 316, 130.

**16β-Dimethylaminopregn-5-en-3β-yl Trityl Ether (6). A.**—A mixture of the tosylate **3a** (0.5 g) and lithium aluminum hydride (1.0 g) in tetrahydrofuran (250 ml) (the steroid was not in solution) was stirred at room temperature for 15 min and then stirred and refluxed for 5 hr. The resultant mixture was worked up as in the preparation of **2b**. Removal of the solvent *in vacuo* afforded a glass which was crystallized from acetone–methanol to give **6** (0.26 g): mp 159–160° (recrystallization did not change the melting point); $[\alpha]^{25}D$ −27°; ir 765, 760, 747, 705, and 696 $cm^{-1}$; nmr ($CDCl_3$) $\delta$ 0.68 (s, 3, 18 H), 0.96 (s, 3, 19 H), 2.23 (s, 6, $N(CH_3)_2$), 4.91 (m, 1, 6 H), and 7.16–7.67 ppm (m, 15, aromatic H).

*Anal.* Calcd for $C_{42}H_{53}NO$ (587.85): C, 85.81; H, 9.09; N, 2.38. Found: C, 86.17; H, 9.25; N, 2.17.

**B.**—A mixture of the diene **4a** (0.29 g) and 10% palladium on charcoal (0.03 g) in tetrahydrofuran (20 ml) was stirred and treated with hydrogen at room temperature and atmospheric pressure for 1 hr when approximately 1 mol equiv of hydrogen was absorbed. After filtration of the catalyst, the tetrahydrofuran was removed from the filtrate *in vacuo* to give an amorphous solid. Crystallization from acetone–methanol afforded **6** (0.25 g), mp 160–161°. The infrared spectrum was identical with that of the sample prepared in A.

**Registry No.**—**1b**, 28463-69-6; **2b**, 28463-70-9; **3a**, 28463-71-0; **3b**, 28463-72-1; **4a**, 28463-73-2; **4b**, 28463-74-3; **5a**, 28463-75-4; **5b**, 28463-76-5; **5c**, 28463-77-6; **6**, 28463-78-7.

# The Reduction of Aromatic Nitro and Related Compounds by Dihydroflavins

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The reduction of nitrobenzene by dihydroflavins (or dihydroisoalloxazines) in organic solvents leads to *N*-phenylhydroxylamine and flavins (or isoalloxazines). Nitrosobenzene is very rapidly reduced to *N*-phenylhydroxylamine, and azobenzene leads to hydrazobenzene. Azoxybenzene is sluggishly reduced to hydrazobenzene and aniline. *N*-phenylhydroxylamine also slowly oxidizes reduced flavins, likely *via* disproportionation (to nitrosobenzene and aniline) followed by reaction of the product with dihydroflavin. The reactions of nitrobenzene and six para-substituted nitrobenzenes with dihydro-3-methyllumiflavin in DMF over a range of concentrations follow good second-order kinetics (first order in each reactant). The second-order rate constants fit a Hammett relationship using $\sigma^-$ substituent constants, $\rho^-$ = +3.6. On the basis of these data along with their relationship to electrochemical and other aromatic nitro reduction methods, a tentative initial step involving electron transfer is proposed. The azobenzene reaction also displays first-order behavior in each reactant (second order overall). No intermediates were observed spectrophotometrically in any of these systems. Aliphatic nitro compounds are unreactive to dihydroflavins.

As part of our studies of the redox chemistry of flavins with organic molecules related to substrates for flavoenzymes,[2] we have investigated reactions between oxidized and reduced flavins (see Scheme I) and the redox states between (and including) nitrobenzene and aniline. The flavoenzymes involved in nitrate reduction and in various metabolic pathways may perform reactions related to those described in this paper.[3] None of the compounds reported in this study reduced flavin, but as reported below several of the oxidation states of nitrobenzene oxidized reduced flavins. Aliphatic nitro compounds were unreactive.

## Results

**Nitrobenzene and Substituted Nitrobenzenes.**—Aromatic, but not aliphatic, nitro compounds oxidize reduced flavins to the normal oxidized flavins in organic solution (isolated chromatographically and identified by thin layer chromatography and spectrally). In the case of nitrobenzene itself the reaction is rather sluggish, requiring approximately 2 days for complete reoxidation of $10^{-4}$ *M* dihydroflavin with $10^{-2}$ *M* nitrobenzene in dimethylformamide (DMF), dimethyl sulfoxide (DMSO), or acetonitrile.

Thin layer chromatography of the reaction mixture showed major spots for *N*-phenylhydroxylamine and aniline plus unreacted starting material. Every work-up procedure that we have used in preparative experiments has, however, led to destruction of the phenylhydroxylamine with production of aniline. There is evidence as well that phenylhydroxylamine is reduced (by a circuitous route discussed below) to aniline by dihydroflavin. Ultimately in the nitrobenzene reaction

(1) NSF Undergraduate Research Participant, Summer 1969.

(2) M. J. Gibian and D. V. Winkelman, *Tetrahedron Lett.*, **44**, 3901 (1969).

(3) A leading reference is K. Yagi, Ed., "Flavins and Flavoproteins," University Park Press, Baltimore, Md., 1968.

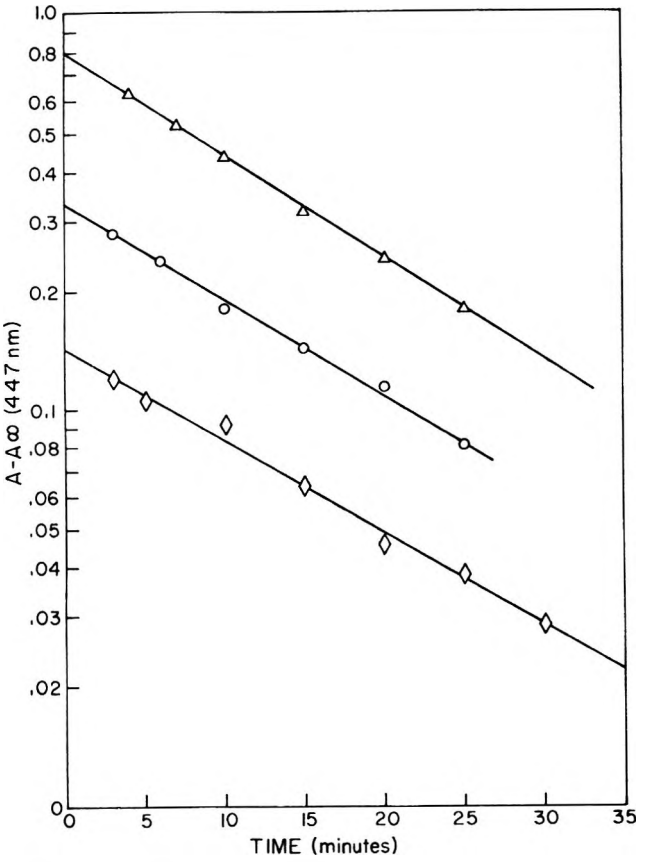
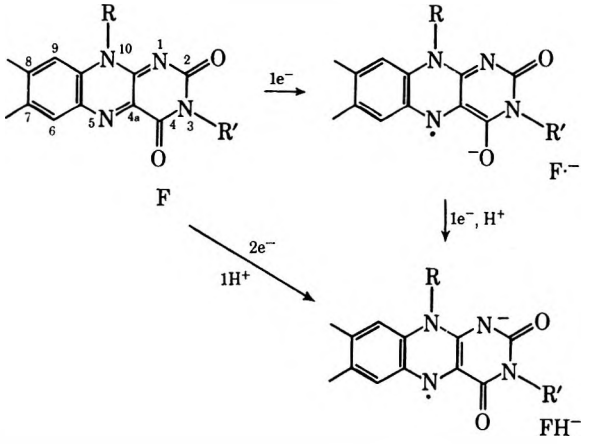



Figure 1.—Representative pseudo-first-order plots of the appearance of oxidized 3-methyllumiflavin (at 447 nm) with time in the presence of $4 \times 10^{-3}$ *M* *p*-chloronitrobenzene in DMF: △, $1.0 \times 10^{-4}$ *M* $FH_2$; ○, $5.0 \times 10^{-5}$ *M* $FH_2$; ◇, $2.5 \times 10^{-5}$ *M* $FH_2$.

SCHEME I[a]




[a] Only one tautomeric or resonance form for each state has been drawn. Flavins are 7,8-dimethylisoalloxazines.

mixture, a 59% yield of aniline is obtained as determined by gas chromatography (based on three successive 2-electron reductions; *i.e.*, a 3 to 1 stoichiometry of nitrobenzene to flavin).

The kinetics of the oxidation of dihydroflavin by nitrobenzene and by substituted nitrobenzenes were studied in DMF. Electron-withdrawing groups on the nitrobenzene ring significantly accelerate the rate of flavin oxidation. For reasons of experimental facility, the thorough kinetics of oxidation of dihydroflavins by *p*-chloronitrobenzene was studied. The concentration of 3-methyllumiflavin was varied from $2.5 \times 10^{-5}$ *M* to $1.0 \times 10^{-4}$ *M*, and that of *p*-chloronitrobenzene was varied from $2 \times 10^{-3}$ *M* to $8 \times 10^{-3}$ *M*. The reactions were run under argon in Schlenk tubes which were spectrophotometer cells at the bottom. A typical run was pseudo zero order in the nitro compound and first order in flavin (Figure 1). Variation of the concentration of each reactant showed the reaction to be second order overall (typical plot shown in Figure 2) over the range of our experiments. Table I gives the second-order rate constants for a series

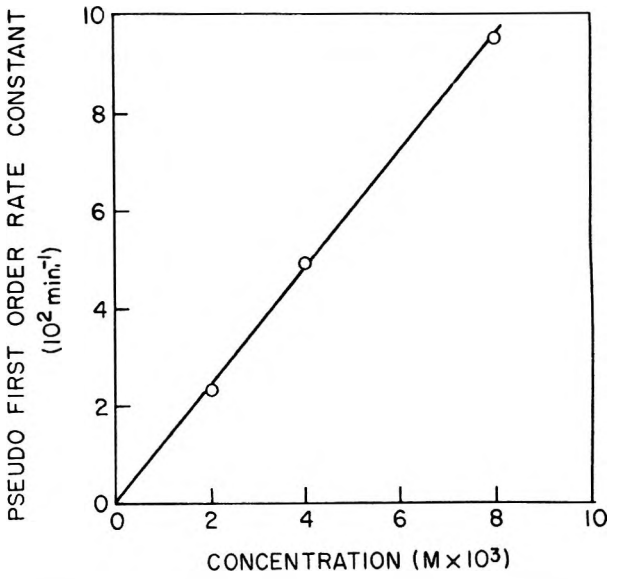



Figure 2.—Plot of the pseudo-first-order rate constants from the data in Figure 1 (from variation of initial dihydro-3-methyllumiflavin) *vs.* concentration of *p*-chloronitrobenzene. Each point represents at least duplicate runs of each of three different $FH_2$ concentrations. The slope is the second-order rate constant given in Table I.

TABLE I
SECOND-ORDER RATE CONSTANT FOR OXIDATION OF DIHYDRO-3-METHYLLUMIFLAVIN BY SUBSTITUTED NITROBENZENES

| X (X—C₆H₄—NO₂) | Registry no. | $k_2$ ($M^{-1}$ min$^{-1}$) |
|---|---|---|
| -OMe | 100-17-4 | ($\sim 3.3 \times 10^{-2}$) |
| $-CH_3$ | 99-99-0 | $1.3 \times 10^{-1}$ |
| -H | 98-95-3 | $3.3 \times 10^{-1}$ |
| -Cl | 100-00-5 | $1.3 \times 10^{+1}$ |
| $-\overset{O}{\overset{\|}{C}}CH_3$ | 100-19-6 | $6.3 \times 10^{+2}$ |
| -CN | 619-72-7 | $2.9 \times 10^{+3}$ |
| $-\overset{O}{\overset{\|}{C}}H$ | 555-16-8 | $4.4 \times 10^{+3}$ |

of substituted nitrobenzenes under the same conditions. Data were obtained by varying the concentration of each nitro compound over at least severalfold, good second-order kinetics being obtained in each case. Figure 3 is a Hammett plot for this reaction using $\sigma^-$ parameters. The fit using normal $\sigma$ substituent constants is quite poor for the *p*-cyano and *p*-formyl groups, predicting the wrong order of reactivity for these and the *p*-acetyl groups by large amounts.

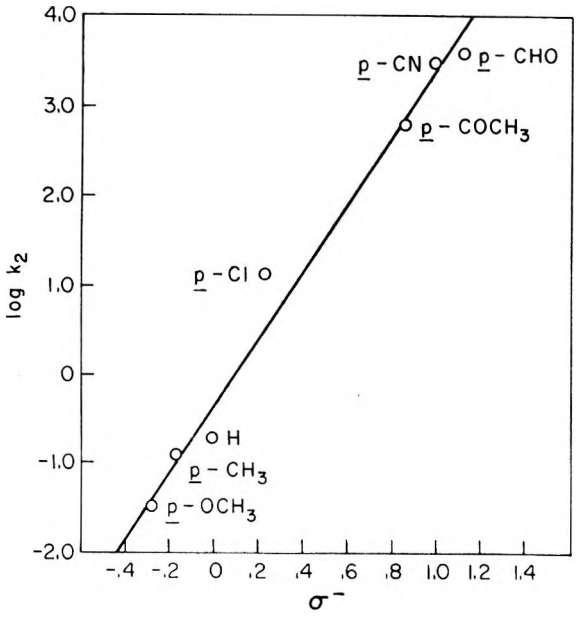



Figure 3.—Linear-free-energy correlation of the second-order rate constants in Table I ($M^{-1}$ min$^{-1}$) with Hammett $\sigma^-$ substituent constants.

Least-squares analysis gives $\rho^- = +3.62 \pm 0.23$ (intercept $= 0.28 \pm 0.15$), $r = 0.99$.

**Nitrosobenzene.**—Reduced flavins are oxidized by nitrosobenzene as fast as can be visually observed upon mixing. Normal oxidized flavin can be recovered quantitatively, and the substrate product is *N*-phenylhydroxylamine, as shown by recovery of azoxybenzene when a twofold excess of nitrosobenzene is added to flavin.[4,5] Reactions 1 and 2 describe the chemistry

$$C_6H_5NO + FH_2 \longrightarrow C_6H_5NHOH + F \quad (1)$$

$$C_6H_5NHOH + C_6H_5NO \longrightarrow C_6H_5N{=}NC_6H_5 + H_2O \quad (2)$$
$$\downarrow$$
$$O$$

involved here. We actually isolate a 39% yield of azoxybenzene from the reaction mixture. Thin layer chromatography shows that it is the only product, and we feel that the yield of isolated product is not higher because of the isolation procedure.

***N*-Phenylhydroxylamine.**—Dihydroflavins are very slowly oxidized to flavins by *N*-phenylhydroxylamine. After a significant number of days we find mostly aniline along with various condensation products (azoxy and azobenzenes) in the reaction mixture. It is known that disproportionation between two molecules of *N*-phenylhydroxylamine leads to aniline and nitrosobenzene (eq 3) and that subsequent condensation as

$$2C_6H_5NHOH \longrightarrow C_6H_5NO + C_6H_5NH_2 \quad (3)$$

in eq 2 leads to azoxybenzene. Both nitrosobenzene and azoxybenzene are capable of oxidizing reduced flavin. Furthermore, nitrosobenzene would lead to (a) phenylhydroxylamine on reduction (eq 1) which then recycles or (b) to azoxybenzene (eq 2) which is slowly reduced, so that ultimately the products should be aniline and those resulting from azoxybenzene reduction (*vide infra*).

(4) (a) S. Oae, T. Fukumoto, and M. Yamagami, *Bull. Chem. Soc. Jap.*, **36**, 728 (1963); (b) G. A. Russell, E. J. Geels, F. J. Smentowski, K.-Y. Chang, J. Reynolds, and G. Kaupp, *J. Amer. Chem. Soc.*, **89**, 3821 (1967).

(5) I. T. Millar and H. D. Springall, "Sidgwick's Organic Chemistry of Nitrogen," 3rd ed, Clarendon Press, Oxford, England, 1966, p 306.

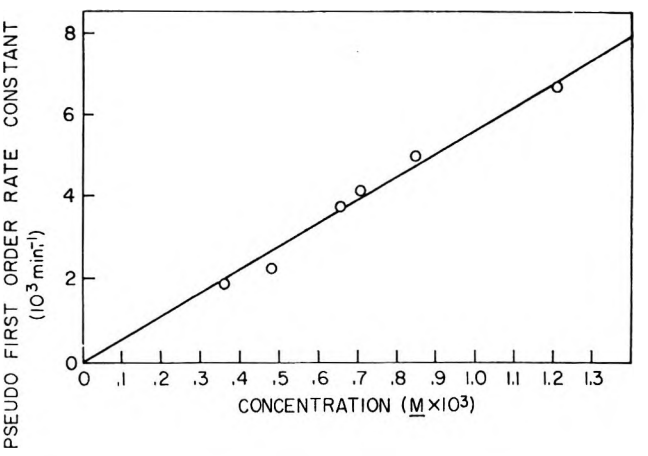



Figure 4.—Plot of the pseudo-first-order rate constants for the reduction of azobenzene obtained by varying dihydro-3-methyllumiflavin concentration (from $4 \times 10^{-5}$ *M* to $1.3 \times 10^{-4}$ *M*) *vs.* azobenzene concentration. The slope is the second-order rate constant (see text).

**Azobenzene.**—Azobenzene is an efficient oxidizing agent for dihydroflavin, producing a 62% isolated yield of hydrazobenzene along with a quantitative yield of oxidized flavin (eq 4). This reaction is second-

$$C_6H_5N{=}NC_6H_5 + FH_2 \longrightarrow C_6H_5NHNHC_6H_5 + F \quad (4)$$

order overall, first order in reduced flavin and first order in azobenzene. Figure 4 is a plot of the pseudo-first-order rate constant for dihydroflavin oxidation *vs.* initial azobenzene concentration. The slope, which is the second-order rate constant for the reaction, is $6.1 \pm 0.4$ $M^{-1}$ min$^{-1}$ (correlation coefficient 0.99). The rate is thus similar to that of the nitrobenzene reaction. Examination of spectra *vs.* time showed no buildup of intermediates, and hydrazobenzene was stable to both oxidized and reduced flavin.

**Azoxybenzene.**—Dihydroflavin and azoxybenzene slowly produce oxidized flavin (100%) along with aniline (~33%) and hydrazobenzene (~67%). This reaction is quite slow compared to the azobenzene and nitrobenzene reactions but of about the same rate as the reaction of *N*-phenylhydroxylamine.

## Discussion

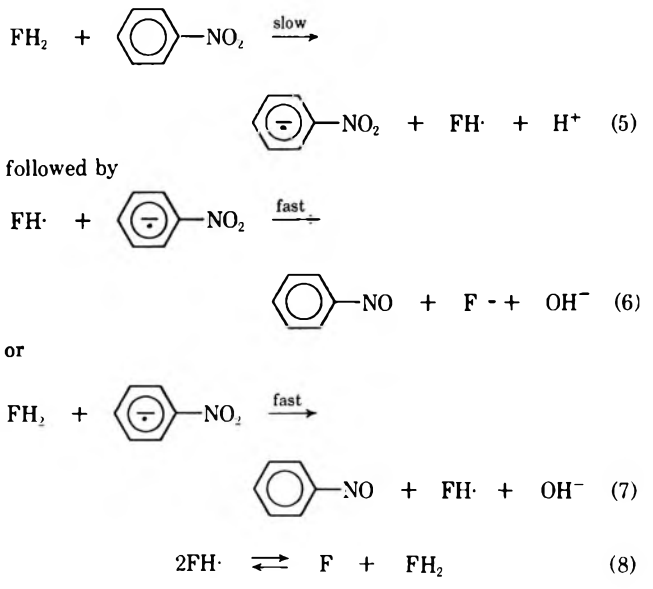
The patterns for reduction of nitrobenzene and its partially reduced derivatives by dihydroflavin follow a pattern not dissimilar from that of other organic reducing agents. The mechanisms of reduction of these functional groups have not been studied in detail for many of the normal reducing agents, but the general observations in this study would seem to place dihydroflavin at approximately the strength and specificity of metallic zinc in neutral aqueous solution. Lithium aluminum hydride sluggishly reduces most of these derivatives, but most of the other metal hydrides are inert (except that all reducing agents essentially are rapid and efficient with nitroso compounds).[6] Catalytic hydrogenation, on the other hand, is quite efficient in the reduction of all the oxidation states. Dihydroflavin is thus placed between $LiAlH_4$ and catalytic

(6) J. March, "Advanced Organic Chemistry," McGraw-Hill, New York, N. Y., 1968, p 890 ff.

hydrogenation in specificity and similar to the dehydropyridines.[7]

We tend to favor, from several lines of reasoning, a pathway involving successive one-electron transfers as the mode of reduction of the nitro compounds by dihydroflavins. Although *p*-nitrobenzaldehyde is very rapidly reduced by dihydroflavin, only the nitro group reacts. With metal hydrides (direct hydride donors), on the other hand, aldehyde functionalities are *more* readily reduced than are nitro compounds.[6] Radical anions of nitroaromatic compounds are highly stabilized, and evidence for their intermediacy in the reduction of nitrobenzenes by sodium arsenite, sodium ethoxide, or glucose is the observation of the transient epr spectrum of the nitrobenzene radical ion, the nitrosobenzene radical ion, and $^{18}O$ and $^{15}N$ scrambling.[4a] Scheme II depicts a pathway involving a slow one-

SCHEME II




electron transfer step (eq 5) followed by reaction 6 or by reactions 7 and 8 to arrive at nitrosobenzene for the nitrobenzene reaction. Rapid reduction by eq 1 would follow.

The necessity of using $\sigma^-$ substituent parameters in our Hammett plot indicates that negative charge is directly conjugated with substituents in the transition state. This could, of course, be either a two- or one-electron transfer, but the following consideration may shed some light on this question. The substituent effect on the half-wave reduction potential of substituted nitrobenzenes in DMF has been investigated,[8] it having been found that $\rho_\pi$ (volts) is equal to approximately +0.35 to +0.40 V. The $\sigma^-$ parameters gave a better fit of the data. Converting $\rho_\pi$(v) into the same units as that obtained in normal mechanistic organic chemistry[9] $[(\alpha n_a F/RT)\rho_\pi = \rho]$, $\rho^-$ for the electrochemical reduction is equal to +3.0 to +3.4. In the present study, $\rho^-$ was +3.6. It is highly probably that the electrochemical reduction is in fact a one-electron process as the rate-determining step.[9b] The implication is that, in the transition state for the flavin reduction and in the electrochemical process, roughly the same negative charge is transferred onto a nitrobenzene nucleus. Russell, *et al.*,[10] have studied the substituent effects on the one-electron transfer from fluorenide anion and from acetophenone enolate to substituted nitroaromatics. Solvents were different from those used in our study, but the two $\rho$ values were approximately 2.0 and 2.7, respectively.

The literature contains numerous references to a value of $\sigma$ for the *p*-formyl group of +0.21, which was found to be in error because of an unrecognized chemical reaction taking place in the original study. By ionization of terephthalaldehyde, Humffray, *et al.*,[11] report a more reasonable value of +0.45. In the course of our studies we had to choose a value for this group (ultimately, the $\sigma^-$ parameters were found to give the best fit) and calculated it from Taft's nmr data, using $\sigma^0 = \sigma_0^R + \sigma_I$.[12] The value was +0.55. Thus the value of approximately +0.5 is clearly preferred from two independent studies and is more in accord with that expected, based on the acetyl ($\sigma_p$ = +0.52) and the carbethoxyl groups ($\sigma_p$ = +0.52).[13]

## Experimental Section

**Reagents.**—Solvents used in product studies were reagent grade materials, distilled before use for kinetic studies. Riboflavin (Aldrich) was recrystallized from 2 *M* acetic acid. Lumiflavin,[14] 3-methyllumiflavin,[15] 3-benzyllumiflavin (*via* 3-benzylbarbituric acid),[16] 10-phenylisoalloxazine,[17] and 3-benzyl-10-phenylisoalloxazine (*via* benzyl bromide and 10-phenylisoalloxazine analogously to the flavin series[15]) were synthesized by published routes. Nitrobenzene (MCB) was distilled before use. Substituted nitrobenzenes (MCB reagents), azoxybenzene (Eastman), azobenzene (MCB), hydrazobenzene (Aldrich), and nitrosobenzene (Aldrich) were recrystallized from ether–pentane. All gave satisfactory melting points. *N*-Phenylhydroxylamine was synthesized by a standard procedure, mp 80–82° (lit. 81°).[18]

**Exploratory and Kinetic Experiments.**—All reactions were run in the rigorous absence of oxygen. This was accomplished by bubbling argon through all solvents and reagent solutions for at least 0.5 hr before initiating reactions. Care was taken to rigorously exclude light from all stock solutions and reactions except while spectra were being recorded.

Reactions were run in several types of vessels, but all of these were modified to effectively be Schlenk tubes. In many of these experiments, the tubes were constructed from 1.5 in. of 1-cm square Pyrex tubing rounded off and sealed at the bottom and fused at the top onto ordinary cylindrical Pyrex tubing terminating in an $\overline{\$}$ 14/20 or 19/22 inner joint. Just below the joint was a side arm with a stopcock at approximately 45° from the vertical. This sidearm was used for blowing argon over the top of the solution while adding reagents. To cover the tube an outer $\overline{\$}$ joint of the same bore terminating in a stopcock was used. In this manner, solutions could be deoxygenated, reagents added rapidly, and spectra recorded very shortly after mixing. Additional reagents could be injected at any time without admit-

(7) D. C. Dittmer and J. M. Kolyer, *J. Org. Chem.*, **27**, 56 (1962).

(8) (a) P. Zuman, "The Elucidation of Organic Electrode Processes," Academic Press, New York, N. Y., 1969, p 132; (b) A. H. Maki and D. H. Geske, *J. Amer. Chem. Soc.*, **83**, 1852 (1961).

(9) (a) C. L. Perrin, *Progr. Phys. Org. Chem.*, **3**, 292 (1965). (b) We have assumed, arbitrarily, that $\alpha n_a$ = 0.5. This would seem not unreasonable for this chemical situation, since $\alpha$ is generally between 0.3 and 0.7, and $n_a$ in a kinetic sense may realistically be assumed to be close to 1.0 electron.

(10) G. A. Russell, *et al.*, *Advan. Chem. Ser.*, **51**, 1112 (1965).

(11) A. A. Humffray, J. J. Ryan, J. P. Warren, and Y. H. Yung, *Chem. Commun.*, **23**, 610 (1965).

(12) R. W. Taft and I. C. Lewis, *J. Amer. Chem. Soc.*, **81**, 5343 (1959).

(13) C. D. Ritchie and W. F. Sager, *Progr. Phys. Org. Chem.*, **2**, 334, (1964).

(14) P. Hemmerich, S. Fallab, and H. Erlenmeyer, *Helv. Chim. Acta*, **39**, 1242 (1956).

(15) P. Hemmerich, *ibid.*, **47**, 464 (1964).

(16) J. B. Dickey and A. R. Gray, "Organic Syntheses," Collect. Vol. II, Wiley, New York, N. Y., 1943, p 60.

(17) R. Kuhn and F. Weygand, *Ber.*, **68**, 1282 (1935).

(18) O. Kamm, "Organic Syntheses," Collect. Vol. I, Wiley, New York, N. Y., 1941, p 445.

ting air by reattaching the vessel to the manifold, keeping a stream of argon blowing, and adding deoxygenated reagents *via* a gas-tight syringe. Flavins at the reduced level could be retained in the vessels for quite extended periods without any reoxidation, and many reopenings and closings of the tubes could be performed without the introduction of air.

Flavins were reduced by the addition of very small aliquots of freshly prepared sodium dithionite ($Na_2S_2O_4$) solution in $10^{-3}$ *M* NaOH or by catalytic hydrogenation over Pd on activated silica gel (followed by anaerobic filtration of reduced flavin). The dithionite solutions were standardized by titration of oxidized flavin in separate experiments and were stable in dilute base for several hours. Catalytic hydrogenation was used primarily for product isolation experiments, but it was shown that spectral observations were identical with those in dithionite-reduced flavin experiments.

Kinetic runs were followed in the visible region on a Cary 14 spectrophotometer by observing the increase in flavin absorbancy upon oxidation. For slow reactions the spectrum was scanned at appropriate time intervals while faster runs were continuously monitored at the $\lambda_{max}$ for oxidized material (447 nm for flavins, 437 nm for isoalloxazines).

**Product Isolations. Nitrobenzene.**—A DMF solution (100 ml) of 3-methyllumiflavin (0.138 g, 0.511 mmol) in a 250-cc round-bottom flask equipped with a Schlenk adapter at top was thoroughly deoxygenated by argon bubbling and reduced with 1.0 equiv of dithionite solution. Nitrobenzene (3.0 g, 24 mmol) was added anaerobically and the solution allowed to stand under a positive pressure of argon in the dark for 1 day. Upon opening, tlc showed major spots for nitrobenzene, *N*-phenylhydroxylamine, aniline, and a very slight amount of azoxybenzene. The bulk of the solution was passed through a silica gel column using ether–pentane (3:1) as eluent to remove the flavin (which is strongly retarded). Tlc of the chromatographed solution still contained *N*-phenylhydroxylamine and aniline. The solution was stripped down and then vacuum distilled. At this point, large amounts of aniline were observed on tlc (see *N*-phenylhydroxylamine below).

10-Phenylisoalloxazine (0.870 g, 3.00 mmol) in 1.5 l. of methanol was deoxygenated and reduced as above, 6.0 g (48 mmol) of nitrobenzene was added, and the reaction was allowed to proceed for 3 days. Methanol was removed at room temperature and the residue passed through silica gel to remove isoalloxazine. The total product mixture was then taken down to 45.0 ml and analyzed by glpc. Comparison to an external standard showed there to be a total of 0.055 g (0.59 mmol) of aniline. Based on net six-electron reduction, the theoretical yield of aniline (based on flavin) is 0.093 g (1.0 mmol); thus the yield represents 60% of the reducing equivalents from reduced flavin.

**Nitrosobenzene.**—Preliminary experiments with equimolar dihydroflavin and nitrosobenzene showed aniline and hydrazobenzene to be present. The reaction is complete almost immediately. In two careful experiments, 0.270 g (1.0 mmol) of 3-methyllumiflavin in 110 ml of DMF was deoxygenated and reduced as usual. Analysis on the Cary 14 showed that the flavin was 66% reduced (0.66 mmol). To this solution 0.21 g (2.02 mmol) of nitrosobenzene was added. Tlc showed only azoxybenzene as the product before and after removal of the DMF by vacuum distillation. Extraction with pentane and crystallization yielded 0.050 g (0.25 mmol) of azoxybenzene of high purity, a 38% overall yield.

***N*-Phenylhydroxylamine.**—*N*-Phenylhydroxylamine, allowed to stand in either methanol or DMF in the presence or absence of flavin or dihydroflavin, produced significant amounts of aniline in a few days. Upon removal of solvents from these solutions, significant quantities of tarry material were obtained. It was concluded that further attempts at product isolation would not be worthwhile.

**Azobenzene.**—3-Methyllumiflavin (0.0880 g, 0.32 mmol) in 100 ml of DMF was deoxygenated and reduced as usual with dithionite. Azobenzene (0.338 g, 1.86 mmol) was added and the solution allowed to stand for 3 days. Tlc showed that both hydrazobenzene and azobenzene were present in the reaction mixture. After passing the reaction mixture through a silica gel column to remove flavin and rechromatographing the eluate, the isolated yield of hydrazobenzene was 0.037 g (0.20 mmol), 62% overall based on dihydroflavin.

**Azoxybenzene.**—3-Methyllumiflavin (0.0071 g, 0.026 mmol) in 250 ml of methanol was deoxygenated and reduced as usual, 0.047 g (0.24 mmol) of azoxybenzene was added, and the solution was allowed to stand for 3 days. At the end of this time gas chromatography showed the presence of azoxybenzene, hydrazobenzene, and aniline. The ratio of hydrazobenzene to aniline was about 2 to 1. Flavin was removed from the solution by the usual method, and then the entire product mixture was taken down to 5.0 ml for glpc analysis. Based on an external standard added to this solution, the total yield of hydrazobenzene and aniline is close to 100% with a ratio of hydrazobenzene to aniline of 2 to 1.

**Registry No.**—Dihydro-3-methyllumiflavin, 23542-57-6; nitrosobenzene, 586-96-9; azobenzene, 103-33-3; azoxybenzene, 495-48-7.

**Acknowledgments.**—The authors thank the National Institutes of Health (GM-15100) and the Research Corporation for financial support of this work. We are also grateful to Mr. James Rynd, who made some of the initial observations upon which this paper is based.

# The Alkaline Decomposition of Organic Disulfides. V. Experimental Variants of α Elimination

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*Received October 9, 1970*

Several compounds, which might have been expected to undergo α elimination in aqueous alkaline solution, failed to give the anticipated mixtures of thiol, carbonyl compound, and hydrogen sulfide. Rather, fairly stable hemidithioketals were formed, apparently by the rapid conversion of the initially formed carbanions into stable thiolate anions. *meso*-1,2-Dithiane-3,6-dicarboxylic acid (1) in 0.1 *N* NaOH was transformed into *trans*-2-mercaptothiolane-2,5-dicarboxylic acid about 100 times as rapidly as the corresponding racemic disulfide was transformed into the cis isomer. The bicyclic anhydride of 1 decomposed at pH 8.6 in the same fashion, but even faster than did 1 in 0.1 *N* NaOH. The diethyl ester of 1 is about as sensitive to alkali as is the anhydride. Dithiodisuccinic acid decomposed predominantly by the alternative method and to a small extent by α elimination.

Organic disulfides appear to undergo alkaline decomposition by one of three alternative pathways, as determined by their molecular structures.[2] In the cases of disulfides in which a proton on a carbon atom α to a sulfur is sufficiently acidic, abstraction of this proton is the initiating step in alkaline decomposition, followed by the completion of an α elimination.[3] These reactions are characterized by the formation of carbonyl compounds and of thiol and hydrogen sulfide in a simple, integral ratio. Authenticated cases of β elimination are much less common,[4] although some version of this mechanism is invoked to explain transformation of cystinyl residues into lanthionyl residues, a process which is still not understood. Finally, direct nucleophilic displacement of sulfur from sulfur by hydroxide ion appears to cover the majority of all cases reported.[2,4]

Quantitative data in support of α elimination have been obtained for dithiodiacetate, which gives mercaptoacetic acid and hydrogen sulfide in the ratio of 3:1, and for 2,2′-dithiodipropionate, which gives 2-mercaptopropionic acid, hydrogen sulfide, and pyruvate in a ratio of 1:1:1.[3] It was expected that *meso*-1,2-dithiane-3,6-dicarboxylic acid (1), because of its structural analogy to 2,2′-dithiodipropionic acid, would decompose in a similar fashion to afford 2-keto-5-mercaptohexanedioic acid and an equivalent amount of hydrogen sulfide. Actually, they decompose at about the same speed (see Table I), but the cyclic compound gives not a trace of hydrogen sulfide, and the disappearance of each disulfide group corresponds quantitatively to the appearance of one thiol group. To account for these facts we suggest that the carbanion formed by the abstraction of the proton from the α carbon is rapidly converted into a stable thiolate anion, a five-membered cyclic hemidithioketal, *trans*-2-mercaptothiolane-2,5-dicarboxylic acid (2) (Scheme I). Actually, 2 was recovered as a crystalline product whose thiol content and neutralization equivalent corresponded to the assigned structure. 2 was readily alkylated in good yield by ethyl iodide to furnish 3, a crystalline product whose elemental analysis, neutralization equivalent, and nmr spectrum corresponded to the structure assigned.

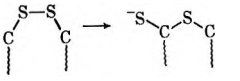
Fredga,[5] who first prepared the meso compound 1, showed that it could easily be converted into the more stable racemic one (4) by heating above its melting point for a few minutes. The racemic compound 4 decomposes (see Table II) in exactly the same fashion as does the meso one (1), but the decomposition of 1 is approximately 100 times as rapid as that of 4 under comparably alkaline conditions. In order to account for this substantial difference it should be noted that in 1 one of the α protons must be axial and the other equatorial, while in 4, since both carboxyl groups can scarcely be axial, both α protons probably are axial and therefore equally difficult to abstract.

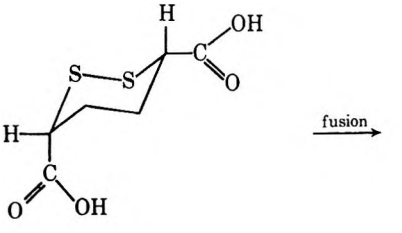
TABLE I

DECOMPOSITION OF *meso*-1,2-DITHIANE-3,6-DICARBOXYLIC ACID (1) IN AQUEOUS ALKALINE SOLUTIONS AT 35.2°

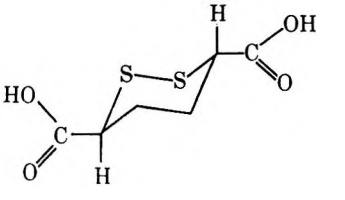
| Time, hr | RSSR | RSH | % dec | % S accounted for[c] |
|---|---|---|---|---|
| 0 | 15.9[a] | 0[a] | 0 | 100 |
| 1 | 13.0 | 3.50 | 18.2 | 103 |
| 2 | 10.2 | 5.91 | 35.3 | 102 |
| 4 | 6.10 | 9.10 | 61.0 | 96 |
| 6 | 4.67 | 11.40 | 71.0 | 101 |
| 0 | 14.1[b] | 0[b] | 0 | 100 |
| 0.5 | 11.7 | 3.15 | 17.3 | 105 |
| 1 | 9.21 | 5.45 | 34.7 | 104 |
| 2 | 6.16 | 8.40 | 56.4 | 103 |
| 3 | 4.36 | 10.13 | 69.1 | 103 |

[a] $M \times 10^4$ in 0.0580 *N* NaOH. [b] $M \times 10^4$ in 0.1188 *N* NaOH. [c] On assumption that





1



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(1) Postodoctoral Research Associate, 1969–1970.
(2) J. P. Danehy and K. N. Parameswaran, *J. Org. Chem.*, **33**, 568 (1968).
(3) J. P. Danehy and J. A. Kreuz, *J. Amer. Chem. Soc.*, **83**, 1109 (1961).
(4) J. P. Danehy and W. E. Hunter, *J. Org. Chem.*, **32**, 2047 (1967).
(5) A. Fredga, *Ber.*, **71B**, 289 (1938).

SCHEME I

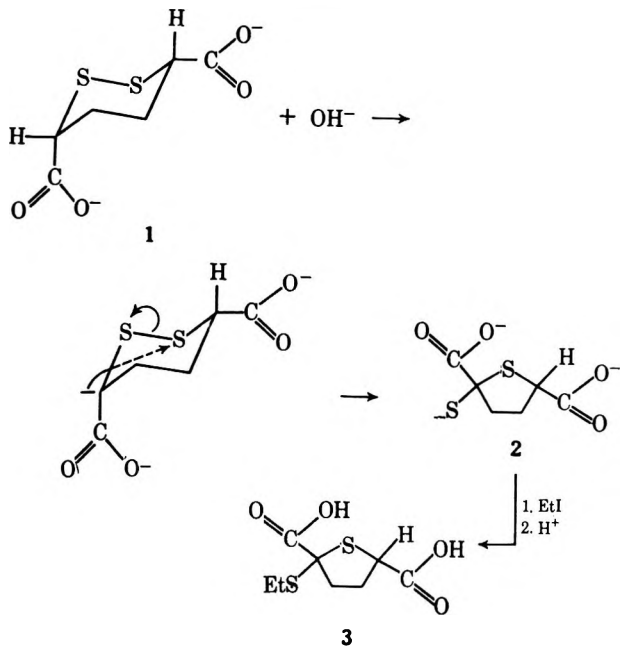


TABLE II

DECOMPOSITION OF RACEMIC 1,2-DITHIANE-3,6-DICARBOXYLIC ACID (4) IN AQUEOUS ALKALINE SOLUTIONS AT 35.2°

| Time, hr | RSSR | RSH | % dec | % S accounted for |
|---|---|---|---|---|
| 0 | 17.1[a] | 0[a] | 0 | 100 |
| 7 | 16.7 | 0.35 | 2.0 | 100 |
| 24 | 16.5 | 0.48 | 3.0 | 99.7 |
| 0 | 16.3[b] | 0[b] | 0 | 100 |
| 3 | 15.8 | 0.52 | 3.1 | 100.1 |
| 8 | 15.0 | 1.07 | 8.2 | 98.4 |
| 24 | 13.7 | 2.72 | 16.2 | 100.3 |
| 0 | 15.9[c] | 0[c] | 0 | 100 |
| 1 | 15.5 | 0.64 | 2.3 | 99.6 |
| 4 | 14.2 | 2.18 | 10.7 | 96.3 |
| 6 | 12.6 | 2.95 | 20.9 | 97.8 |
| 9 | 11.7 | 3.92 | 26.6 | 98.4 |

[a] $M \times 10^4$ in 0.0578 $N$ NaOH. [b] $M \times 10^4$ in 0.1984 $N$ NaOH. [c] $M \times 10^4$ in 0.500 $N$ NaOH.

Consideration of a difference between the reaction products from the alkaline decompositions of **1** and **4** supports the mechanism proposed. Decomposition of **1**, in which the carboxyl groups are cis, should give **2** (and **3**) in which the carboxyl groups are trans. Decomposition of **4**, in which the carboxyl groups are trans, should give the hemidithioketal **5** and its *S*-ethyl derivative **6** in which the carboxyl groups are cis. As a matter of fact, **3** and **6** are diastereomers;[6] the former melts at 115°, and the latter at 156–158°. That **3** and **6** have almost identical nmr spectra is not inconsistent with their structures. The known structures of **1** and **4**, and the considerations just given, are the bases for assigning trans configurations to **2** and **3** and cis configurations to **5** and **6**.

(6) As shown in detail in the Experimental Section, **1** gives both **2** and **3** in the ratio of 65:35, and **4** gives both **2** and **3** in the ratio of 30:70, respectively. While the reactions are not stereochemically clean, perhaps because of some scrambling at the carbanion stage, the observed predominances support our conclusion.

The bicyclic anhydride **7**[7] of **1** is exceedingly sensitive to alkaline decomposition, more sensitive than any other disulfide that has ever been reported (see Table III). At pH 8.6, **7** decomposed much more rapidly

TABLE III

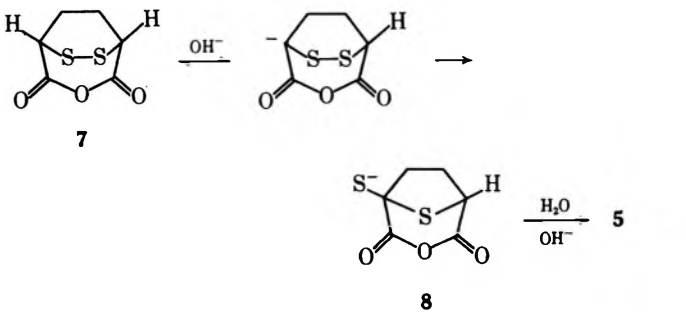
DECOMPOSITION OF THE ANHYDRIDE OF *meso*-1,2-DITHIANE-3,6-DICARBOXYLIC ACID (**7**) IN AQUEOUS ALKALINE SOLUTIONS AT 35.2° AT pH 8.68

| Time, min | RSSR | RSH | % dec | % S accounted for |
|---|---|---|---|---|
| 0 | 16.60[a] | | | |
| 20 | 11.39 | 5.21[a] | 31.3 | 100 |
| 40 | 9.18 | 6.75 | 44.7 | 96 |
| 60 | 8.42 | 7.58 | 49.3 | 96 |
| 90 | 7.50 | 8.62 | 54.9 | 97 |
| 120 | 6.86 | 9.14 | 58.7 | 96 |
| 180 | 5.53 | 10.42 | 66.7 | 96 |

[a] $M \times 10^4$ in 0.2 $M$ phosphate buffer at pH 8.68.

than did **1** in 0.1 $N$ NaOH. The analytical results certainly are in accord with the idea that decomposition proceeds in the same manner (see Scheme II), and

SCHEME II



the observed speed precludes the possibility that hydrolysis of **7** to **1** is followed by alkaline decomposition of **1**. However, the isolation and characterization of the 2-mercaptothiolane-2,5-dicarboxylic acid anhydride (**8**) is not claimed. Indeed, by reason of the rotation required for the attack of the carbanion on the remote sulfur, it may be that **8** is never formed; the breaking of the sulfur–sulfur bond may induce the simultaneous hydrolysis of the anhydride bond to give **5**. Two supplementary factors probably account for the large difference in sensitivity. In **7** the inductive effect of the oxygens, which increases the lability of the $\alpha$ protons, is not mitigated by the negative charge which is necessarily present in **1**. Construction of a model shows that both $\alpha$ protons are unequivocally equatorial. That the first of these factors is more important than the second is indicated by the fact that the alkaline decomposition of the diethyl ester of **1** is almost as facile as that of **7** (see Table IV). Nor should it be overlooked that ring strain makes some contribution to the ease with which the hypothetical carbanion attacks the remote sulfur. While the dihedral angle about the sulfur–sulfur bond is ~90° in a wide variety of acyclic disulfides,[8] it has been shown to be only 60° in **4**[9] and presumably is about the same in **1**.

(7) L. DeMytt, U. S. Patent 2,930,799 (March 29, 1960).

(8) O. Foss in "Organic Sulphur Compounds," Vol. I, N. Kharasch, Ed., Pergamon Press, Oxford, 1961.

(9) O. Foss and T. Reistad, *Acta Chem. Scand.*, **11**, 1427 (1957).

TABLE IV

DECOMPOSITION OF *meso*-1,2-DITHIANE-3,6-DICARBOXYLIC ACID DIETHYL ESTER IN AQUEOUS ALKALINE SOLUTIONS AT 35.2°

| Time, min | RSSR | RSH | % dec | % S accounted for |
|---|---|---|---|---|
| 0 | 11.35[a] | | 0 | 100 |
| 20 | 9.42 | 1.79[a] | 16.7 | 99 |
| 40 | 7.91 | 2.91 | 30.3 | 96 |
| 60 | 7.43 | 3.50 | 34.6 | 97 |
| 90 | 6.51 | 3.91 | 42.6 | 92 |
| 120 | 6.22 | 4.43 | 45.3 | 94 |
| 180 | 5.67 | 5.18 | 49.0 | 96 |
| 0 | 9.30[b] | | 0 | 100 |
| 4 hr | 8.12 | 1.10[b] | 12.7 | 99 |
| 22 hr | 7.97 | 1.19 | 14.3 | 99 |

[a] $M \times 10^4$ in 0.2 $M$ phosphate buffer at pH 8.68. [b] $M \times 10^4$ in 0.2 $M$ phosphate buffer at pH 7.00; no hydrogen sulfide detectable at any time.

In view of the extreme sensitivity of the anhydride **7** to decomposition in mildly alkaline solution, it is particularly interesting that in order to hydrolyze it to the corresponding dicarboxylic acid (**1**) it is necessary to reflux it in aqueous 2 $N$ HCl for several hours. The disulfide linkage survives this treatment quantitatively.

However, a cyclic disulfide is not a necessary condition for the kind of reaction described here. Howard[10] found that diethyl dithiodiacetate was cleaved at a low temperature by sodium methoxide in anhydrous methanol to give the rather unstable ester of 2-mercapto-3-thiaglutaric acid and proposed a mechanism essentially the same as the one invoked here. It was expected that dithiodisuccinic acid (**9**) would decompose readily by $\alpha$ elimination to give equivalent amounts of oxaloacetate (ketosuccinate), mercaptosuccinate, and hydrosulfide. The determination of relatively small amounts of hydrogen sulfide (a maximum of 5% of the total sulfur rather than the expected 50%) gave evidence that this may be a minor pathway. An approximate sulfur balance is obtained (see Table V) when the

TABLE V

DECOMPOSITION OF DITHIODISUCCINIC ACID (**9**) IN AQUEOUS ALKALINE SOLUTIONS AT 35.2°

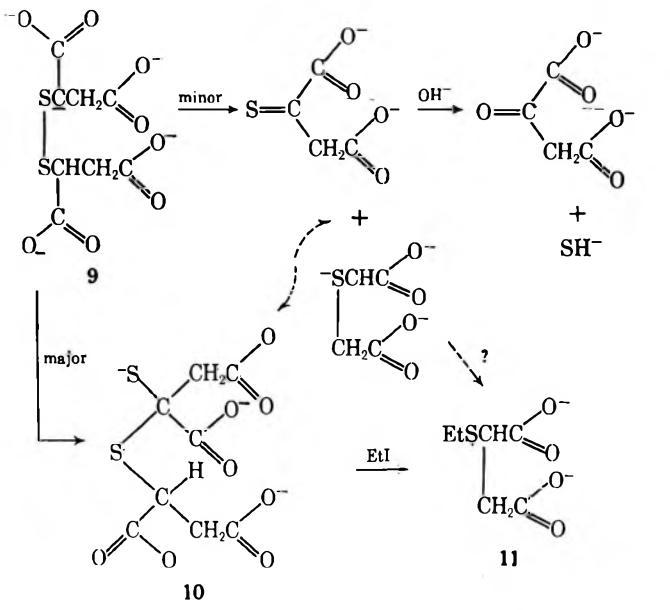
| Time, hr | RSSR | RSH | % dec | % S accounted for |
|---|---|---|---|---|
| 0 | 8.30[a] | 0 | 0 | 100 |
| 24 | 6.10 | 2.47[a] | 26.5 | 103 |
| 48 | 4.80 | 4.50 | 42.2 | 112 |
| 0 | 8.95[b] | 0[b] | 0 | 100 |
| 1 | 8.14 | 1.28 | 9.1 | 105 |
| 3 | 6.68 | 2.75 | 25.4 | 105 |
| 6 | 5.64 | 3.90 | 37.0 | 106 |

[a] $M \times 10^4$ in 0.1492 $N$ NaOH. [b] $M \times 10^4$ in 0.5112 $N$ NaOH.

data are treated on the assumption that a hemidithioketal **10** is the principal product (Scheme III). However, attempts to prepare the $S$-ethyl derivative of **10** resulted only in the formation of 2 mol of the $S$-ethyl derivative of mercaptosuccinic acid (**11**) for each mole of the original disulfide **9**. It would not be difficult to account for the formation of 1 mol of **11**; **10** might be

(10) E. G. Howard, *J. Org. Chem.*, **27**, 2212 (1962).

SCHEME III




in equilibrium with a very small amount of the same products which would result directly from an $\alpha$ elimination (dotted arrow in Scheme III), and under alkylating conditions the mercaptosuccinate might compete for the ethyl iodide to the exclusion of its precursor. The formation of a small but significant amount of hydrogen sulfide is in agreement with this view. However, we are at a loss to account for the repeated recovery of almost 2 mol of **11** for each mol of **10**.

At least two other experimental facts support the view that the hemidithioketal **10** is formed and persists in alkaline solution. During the alkaline decomposition of **9**, absorption with a well-defined maximum at 296 nm gradually increases to a maximal value which persists indefinitely. Treatment with ethyl iodide dissipates the absorption. Also, acidification of an alkaline solution to pH 1–2 destroys the absorption, and it does not reappear upon making the solution alkaline again. However, when an alkaline solution is neutralized only to pH 10, evaporated to dryness, and redissolved in water, the absorption at 296 nm is still present. Aliphatic thiolate ions absorb maximally in the range of 235–250 nm and aromatic ones in the range of 265–305 nm.[11] Fleury and Tohier[12] have observed the development of absorption at 315 nm, which gradually passes over to 335 nm, during the alkaline decomposition of dithiodiacetic acid. Earlier, Rosenthal and Oster[13] observed the absorption at 335 nm and attributed it to thioglyoxylic acid, $S{=}CHCO_2H$. It seems reasonable, then, that the persistent absorption at 296 nm is attributable to the alkali-stable **10** and that the absorption at 315 nm is attributable to the transient 2-mercapto-3-thiaglutarate ion which Fleury and Tohier have isolated.

All of these facts furnish a basis for resolving the apparent contradiction between our earlier results on the alkaline decomposition of dithiodiacetate and the report of Fleury and Tohier who, following the decomposition spectrophotometrically and polarographically, could find no evidence for hydrogen sulfide. In our

(11) J. P. Danehy and K. N. Parameswaran, *J. Chem. Eng. Data*, **13**, 386 (1968).

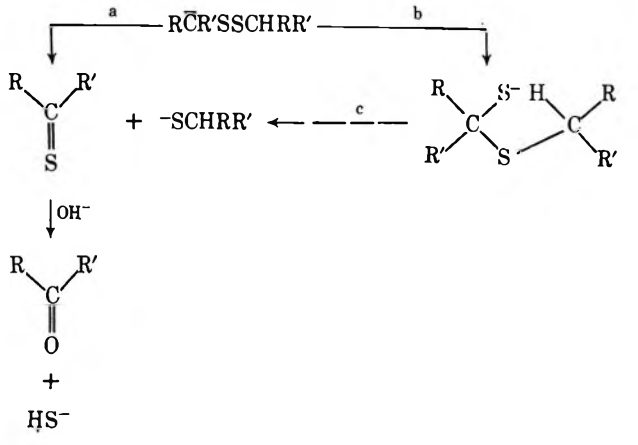
(12) M. Fleury and J. Tohier, *C. R. Acad. Sci., Ser. C*, **264**, 693 (1967).

(13) N. A. Rosenthal and G. Oster, *J. Amer. Chem. Soc.*, **83**, 4445 (1961).

work, aliquots of the reaction mixture were quenched in acid before analysis, and it might be that the hemidithiomercaptal undergoes hydrolysis and that hydrogen sulfide appears only at that stage. We have recently followed the decomposition of dithiodiacetate in aqueous alkali spectrophotometrically and have found that under the same conditions that led to ~50% decomposition[3] according to our analyses the absorption at 315 nm was still maximal. The conditions under which Fleury and Tohier oberved the transition from 315 to 335 nm were much more alkaline.

It appears likely then that in the cases of those disulfides in which a proton on a carbon $\alpha$ to sulfur is sufficiently acidic so that proton abstraction is the operative initial step in alkaline decomposition, three alternatives are possible (Scheme IV), and the one most difficult to

SCHEME IV




authenticate, direct $\alpha$ elimination (a), is the one we have until recently considered to be the most likely. It is now clear that pathway b can lead to stable cyclic products. After the fact, this is not too surprising since Owen[14] has shown that cyclic hemimonothioacetals are more stable than their oxygen analogs, and Field[15] has reported several quite stable hemimercaptals. With acyclic disulfides, pathway b can lead to relatively unstable intermediates and final products *via* pathway c, as in the case of dithiodiacetate, or to relatively stable products whose final disposition is not completely understood, as in the case of dithiodisuccinate.

Recently, Reeve and Nees[16] reported that 2,2′-diphenyldithiodiacetic acid (12) was resistant to attack by aqueous ammonia at 80° and by 15% KOH in methanol at 50°. These results are surprising for two quite different reasons. First, Schöberl[17] found that this disulfide decomposes readily in aqueous alkali. Second, it is to be expected that the phenyl groups would labilize the protons on the $\alpha$ carbons so that carbanion formation in this disulfide would be more facile than in the already sensitive dithiodiacetic acid.[3] We have investigated the behavior of 12 in aqueous alkali and find that it is indeed more sensitive than dithiodiacetic acid (see Table VI) and that the results correspond formally to an $\alpha$ elimination (Scheme IV, pathway a), irrespective of whether the reaction proceeds *via* a or b plus c. As expected, the order of decreasing sensitivity is $(\text{-SCHPhCO}_2\text{H})_2 > (\text{-SCH}_2\text{CO}_2\text{H})_2 > (\text{-SCHMeCO}_2\text{H})_2$.

TABLE VI

DECOMPOSITION OF 2,2′-DIPHENYLDITHIODIACETIC ACID (12) IN AQUEOUS ALKALINE SOLUTIONS AT 35.2°

| Time, hr | RSSR | RSH | $H_2S$ | % dec | % S accounted for |
|---|---|---|---|---|---|
| 0 | 9.65[a] | | | 0 | 100 |
| 1 | 5.08 | 4.86[a] | 3.88[a] | 47.3 | 98 |
| 2 | 4.44 | 6.03 | 5.06 | 54.0 | 102 |
| 0 | 9.70[b] | | | 0 | 100 |
| 1 | 8.22 | 1.66[b] | 0.82[b] | 15.2 | 98 |
| 2 | 7.18 | 2.90 | 1.44 | 26.0 | 97 |
| 3 | 6.96 | 3.24 | 1.82 | 28.2 | 98 |
| 5 | 6.68 | 3.68 | 2.56 | 31.1 | 101 |
| 10.5 | 5.49 | 4.64 | 3.73 | 43.4 | 100 |
| 24 | 4.00 | 6.04 | 5.13 | 68.8 | 99 |

[a] In 0.100 *N* NaOH. [b] In 0.0180 *N* NaOH.

## Experimental Section

**Materials.**—*meso*-2,5-Dimercaptoadipic acid, melting at 175–177° (lit.[5] mp 188°), 94.5% thiol by titration with aqueous potassium triiodide, *meso*-2,5-dimercaptoadipic acid diethyl ester, melting at 54–56°, 97.4% thiol by titration with aqueous potassium triiodide, *meso*-1,2-dithiane-3,6-dicarboxylic acid anhydride (7), melting at 74–76° (lit.[6] mp 77°), and 2,2′-diphenyldithiodiacetic acid (12), melting at 201–205° (lit.[16] mp 210–212°), were gifts from the Toni Division of the Gillette Co., Chicago, Ill. Mercaptosuccinic acid, melting at 154° (lit.[18] mp 149–150°), 99.3% pure by determination of neutralization equivalent, was a gift from Evans Chemetics, New York, N. Y. *meso*-1,2-Dithiane-3,6-dicarboxylic acid (1) was prepared by oxidation of the corresponding thiol in aqueous solution with either aqueous potassium iodide or aqueous hydrogen peroxide. After recrystallization from water, 1 melted at 197–199° (lit.[5] mp 199°). Racemic 1,2-dithiane-3,6-dicarboxylic acid (4) was prepared by heating ~5 g of 1 in a porcelain dish at ~230° for 7–8 min until the melt resolidified. After recrystallization from glacial acetic acid, 4 melted at 267–279° (lit.[5] mp 275° dec). *meso*-1,2-Dithiane-3,6-dicarboxylic acid diethyl ester was prepared by oxidation of the corresponding thiol in ethanol solution with a solution of iodine in ethanol; evaporation, extraction of the residue with ethyl ether, and evaporation of the ethereal extract gave an oil which distilled at 117° (0.5 mm). Dithiodisuccinic acid (9) was prepared by oxidation of the corresponding thiol in aqueous solution with aqueous hydrogen peroxide. After recrystallization from acetic acid–benzene, it melted at 171–173° (lit.[19] mp 168.5°).

**Transformation of *meso*-1,2-Dithiane-3,6-dicarboxylic Acid (1) into 2-Mercaptothiolane-2,5-dicarboxylic Acid and of the Latter into 2-Ethylmercaptothiolane-2,5-dicarboxylic Acid.**—1 (4.9 g) was dissolved in 200 ml of aqueous sodium hydroxide (10 g of NaOH) under nitrogen at 35.2°. After 4 hr analysis[3] showed that the decomposition was substantially complete. The solution was acidified to pH 1 with hydrochloric acid and extracted with ethyl ether, and the ethereal extract was dried with magnesium sulfate and evaporated to dryness to give 3.5 g of a solid thiol. Extraction of this solid with chloroform left 2.3 g (65%) of a thiol insoluble in chloroform which, after recrystallization from ethyl ether–Skellysolve B, melted at 139–142°: ir (KBr) 3000 (CH), 2600 (SH), and 1690 $cm^{-1}$ (COOH); nmr ($D_2O$) $\delta$ 2.58 ($J$ = 155 Hz, multiplet, 4 H, methylene), 4.38 ($J$ = 263 Hz, t, 1 H, methine). This compound is considered to be 2, the trans isomer. Evaporation of the chloroform solution gave 1.2 g (35%) of a thiol which, after recrystallization from chloroform–Skellysolve B, melted at 117–120°: ir (KBr) 3000 (CH), 2600 (S H), and 1690 $cm^{-1}$ (COOH); nmr ($CF_3COOH$) $\delta$ 2.71 ($J$ = 163 Hz, multiplet, 4

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H, methylene), 4.38 ($J$ = 264 Hz, t, 1 H, methine). This compound is considered to be **5**, the cis isomer. To 0.300 g of **2** dissolved in 50% aqueous ethanol was added sufficient aqueous sodium hydroxide to give a pH value of 10. Ethyl iodide (0.30 g) was added, the solution stirred until a negative value for sulfhydryl group was obtained (Folin's reagent), the solution acidified to pH 1, the ethanol removed by flash evaporation under reduced pressure, the residual aqueous solution extracted with ethyl ether, and the ethereal extract evaporated to leave 0.180 g of **3** which, after recrystallization from ethyl ether–Skellysolve B, melted at 115–117°: neutralization equivalent, 120.5 (calcd 118.2); nmr ($CF_3COOH$) $\delta$ 1.31 ($J$ = 79 Hz, t, 3 H, methyl), 2.75 ($J$ = 165 Hz, multiplet, 6 H, methylene), 4.47 ($J$ = 257 Hz, t, 1 H, methine). *Anal.* Calcd: C, 40.66; H, 5.12; S, 27.14. Found: C, 41.11; H, 5.38; S, 26.64.

Treatment of 0.300 g of **5** with 0.30 g of ethyl iodide as above gave 0.245 g of **6** which, after recrystallization from chloroform–ethyl ether, melted at 156–158°: nmr ($CF_3COOH$) $\delta$ 1.31 ($J$ = 79 Hz, t, 3 H, methyl), 2.75 ($J$ = 165 Hz, multiplet, 6 H, methylene), 4.47 ($J$ = 258 Hz t, 1 H, methine.) *Anal.* Calcd: C, 40.66; H, 5.12; S, 27.14. Found: C, 40.78; H, 5.14; S, 26.91.

**Transformation of Racemic 1,2-Dithiane-3,6-dicarboxylic Acid (4) into 2-Mercaptothiolane-2,5-dicarboxylic Acid and of the Latter into Its *S*-Ethyl Derivative.**—In a procedure that differed from the immediately preceding one only in that the concentration of sodium hydroxide was ~3 $N$, 3.30 g of **4** was transformed into 2.70 g of solid thiol which was fractionated into 0.80 g of **2** (30%) and 1.90 g of **5** (70%). From both **2** and **5** the *S*-ethyl derivatives, **3** and **6**, were prepared as before.

**Transformation of Dithiodisuccinic Acid (9) into 2-Mercapto-3-thiapentane-1,2,4,5-tetracarboxylic Acid (10) and of 10 into *S*-Ethylmercaptosuccinic Acid (11).**—**9** (1.12 g) was dissolved in a solution of 12.5 g of sodium hydroxide in 100 ml of water at room temperature under nitrogen. After ~2 hr the absorbance at 296 nm had reached a maximum. Ethyl iodide and sufficient ethanol to give a homogeneous solution were then added. When the test for the sulfhydryl group was negative, the solution was acidified to pH 2 and partially evaporated under reduced pressure, the residual aqueous solution extracted with ethyl ether, and the ethereal extract dried with magnesium sulfate and evaporated to dryness to give 1.17 g of a product which, after recrystallization from chloroform–Skellysolve B, melted at 95–97°. This product was identical in melting point and nmr spectrum with an authentic specimen of **11** prepared by alkylating mercaptosuccinate with ethyl iodide. Again, 3.14 g of **9** was dissolved in a solution of 6.0 g of sodium hydroxide in 100 ml of water under nitrogen. When the absorbance maximum at 296 nm was attained, the solution was neutralized to pH 10.0 and evaporated to dryness. After holding the residue over phosphorus pentoxide for some time, it was redissolved in water and the absorbance at 296 nm was found to be comparable to the previous value.

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**Registry No.**—**1**, 28463-60-7; **2**, 28463-61-8; **3**, 28463-62-9; **4**, 2611-41-8; **5**, 28463-64-1; **6**, 28463-65-2; **7**, 28463-66-3; **9**, 3384-95-0; **12**, 4695-07-2; *meso*-1,2-dithiane-3,6-dicarboxylic acid diethyl ester, 28463-67-4.

# The Synthesis of 6,6′-Diethynyldiphenic Anhydride[1]

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The synthesis of 6,6′-diethynyldiphenic anhydride (**10**) is described (Scheme I). Methyl 2,3-diiodobenzoate (**2**) was heated with copper bronze to yield dimethyl 6,6′-diiododiphenate (**3**). Heating **3** with carbethoxyethynylcopper in pyridine yielded dimethyl 6,6′-bis(carbethoxyethynyl)diphenate (**6**) which, by preferential alkaline hydrolysis, was converted into dimethyl 6,6′-bis(carboxyethynyl)diphenate (**8**). After decarboxylation of **8**, the resulting ester was hydrolyzed to 6,6′-diethynyldiphenic acid (**9**). Treatment of **9** with ethoxyacetylene afforded **10** which is stable thermally up to about 200° when decomposition to yield dark polymeric material occurs. A few attempts at photolysis of **10** yielded unchanged **10** in almost quantitative yield. Heating of **2** with copper in dimethylformamide at 55° yielded 1,5-dicarbomethoxybiphenylene (**4**). In pyridine **3** yielded a small amount of 1,8-dicarbomethoxybiphenylene (**5**) on heating with copper. Intramolecular Ullmann coupling of 2-iodo-3-ethylbenzoic anhydride (**15**) proceeded in 90% yield on refluxing in DMF for 15 min, whereas conventional Ullmann coupling of methyl 2-iodo-3-ethylbenzoate (**14**) was much slower.

In this paper, the synthesis of 6,6′-diethynyldiphenic anhydride (**10**) is reported. This compound was synthesized because we wished to know whether or not the substituted tetrahedrane (**11**) would be formed on pyrolysis or photolysis. The most highly strained and condensed ring system containing carbon–carbon single bonds is that of tricyclo[1.1.0.0.$^{2,4}$]butane (tetrahedrane). The strain energy for tetrahedrane has been calculated to be 90 and 151 kcal/mol, respectively.[3,4]

Since attempted syntheses of tetrahedranetricarboxylic acid were reported,[5,6] a number of papers[7–11] dealing with unsuccessful attempts to prepare tetrahedranes have appeared. The synthesis of 6,6′-diethynyldiphenic anhydride (**10**) was undertaken because **10** seemed to offer the greatest chance to yield a tetrahedrane compound. Molecular models indicated that the two ethyl groups cross each other at about an 80° angle and the anhydride function supposedly would force the two ethynyl groups as close to each other as nonbonded interaction would allow. Furthermore, nmr analysis would readily show the loss of the acetylenic hydrogens in any product.

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(2) Holder of the Sinclair Oil Fellowship, The Ohio State University, 1966–1967. Further details may be found in the Ph.D. Thesis of M. W. L., The Ohio State University, 1969.

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Theoretical considerations[12] predict that the transformation of two acetylenes to tetrahedrane would be a chemically allowed process. Two crossed acetylenes, 2,2′-bis(phenylethynyl)biphenyl (**12**)[8] and 2,2′-diethynylbiphenyl (**13**),[10] have been studied previously; however, the acetylenic groups in **12** and **13** are not forced together in a crossed position as they are in **10**. Whereas **12** gave 9-phenyldibenz[*a*,*c*]anthracene both photochemically and thermally, photolysis of **13** resulted in an almost quantitative recovery of starting material.

A modified isatin synthesis[13] was used for the preparation of 3-iodoanthranilic acid (**1**) from *o*-iodoaniline. Treatment of methyl 2,3-diiodobenzoate (**2**) with copper bronze at 110° afforded dimethyl 6,6′-diiododiphenate (**3**) in 61% yield. Ullmann reactions on 2,3-dihalogenated aromatic compounds which contain nitro and carbomethoxy activating groups yield only products derived from coupling at the ortho position.[14] The structure of **3** was established by conversion to **5** (see Experimental Section).

Interestingly, when **2** was heated with copper bronze in DMF at 55°, 1,5-dicarbomethoxybiphenylene (**4**) was produced in 75% yield.[15,16] On heating **3** with copper in pyridine, the isomeric 1,8-dicarbomethoxybiphenylene (**5**) was formed in 11% yield (Scheme I).

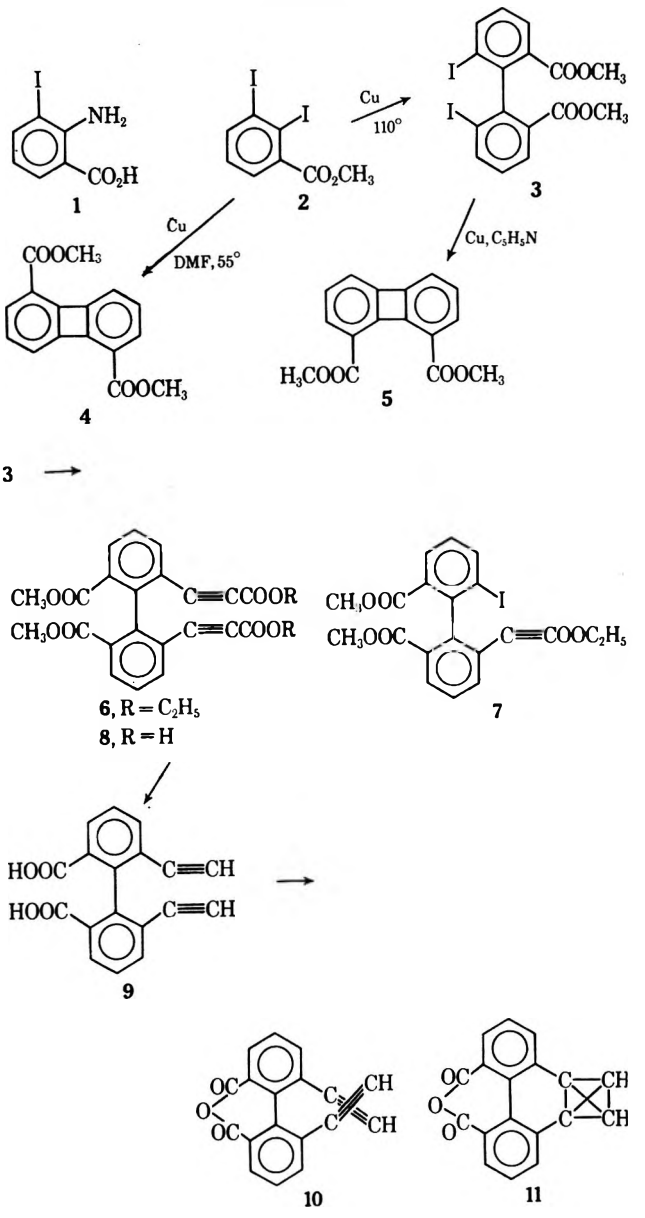
Dimethyl 6.6′-bis(carbethoxyethynyl)diphenate (**6**) was synthesized from **3** and carbethoxyethynylcopper (2 equiv) in pyridine at reflux.[17] Despite numerous attempts, yields of only 4–5% of **6** (about 50% recovery of **3**) were obtained. Some dimethyl 6-iodo-6′-carbethoxyethynyldiphenate (**7**) and biphenylene (**5**) were also produced. **7** was converted into **6** in 18% yield by treatment with additional carbethoxyethynylcopper.

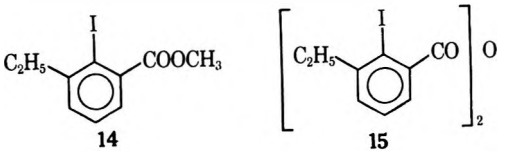
Selective saponification of **6** with sodium hydroxide (2 equiv) afforded dimethyl 6,6′-bis(carboxyethynyl)-diphenate (**8**) which was smoothly converted into 6,6′-diethynyldiphenic acid (**9**) by decarboxylation[18a] followed by alkaline hydrolysis. By treatment with ethoxyacetylene[18b] **9** was cyclized to the anhydride (**10**). Correct analysis for C and H of **10** was unsuccessful owing to its great tendency to react with water to form **9**. This tendency was also annoying in attempts to run photolyses on dilute solutions and to take nmr spectra. However, sharp melting points for **10** could be obtained in sealed tubes and the practically quantitative conversions of **10** to **9** indicated that **10** was pure. A precise mass spectral analysis on **10** gave the expected values.

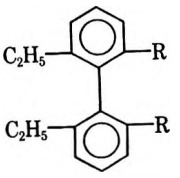
Photolyses of **10** in methylene chloride were performed in Pyrex and quartz nmr tubes, with and without benzophenone as a sensitizer. After each run the nmr and ir spectra were identical with those obtained before irradiation, and unchanged **10** was recovered. Pyrolyses of **10** in *sym*-tetrachloroethane in sealed tubes at temperatures of 180° and below showed that no reaction had occurred. At 200° dark solutions were obtained which gave no acetylenic hydrogen bands at 6.80, but only polymeric material was present.

During work on an alternate (but unsuccessful) synthesis of **10**, the Ullmann coupling of methyl 2-iodo-3-ethylbenzoate (**14** to **16b**) was effected in 41% yield by heating with copper bronze in refluxing DMF for 15

Scheme I




**16a**, R = $CO_2H$
**b**, R = $CO_2Me$

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min. However, when **14** was hydrolyzed to the corresponding acid and the latter converted into the anhydride (**15**), similar Ullmann treatment yielded (after hydrolysis) **16a** in 90% yield. Judging from this example, if Ullmann couplings are converted into intramolecular couplings as above, improved yields may result.[19]

## Experimental Section[20]

**2-Iodoaniline** (**17**).—The preparation of **17**, mp 58.0–58.5°, from *o*-nitroaniline was effected essentially as described[21] in 90% yield.

**2-Iodo-α-isonitrosoacetanilide** (**18**).—To a well-stirred solution of 371 g (2.25 mol) of chloral hydrate, 345 g (5.0 mol) of hydroxylamine hydrochloride, and 1.42 kg (10.0 mol) of anhydrous $Na_2SO_4$ in 7 l. of water was added a mixture of 160 g of concentrated HCl, 328 g (1.5 mol) of **17**, and 1 l. of water. The resulting mixture was slowly heated to 37° during 2.5 hr, at which time a yellow solid began to appear. The temperature of the reaction mixture was then slowly raised to 45° (2 hr). After cooling to room temperature, the product was filtered to yield 355 g (82%) of **18**, mp 158–160°. Recrystallization from ethanol gave colorless crystals, mp 167–168° (lit.[22] mp 162°).

**7-Iodoisatin** (**19**).—To 550 ml of 86% (by weight) $H_2SO_4$ at 55° was added 140 g (0.49 mol) of **18** during 25 min with efficient stirring. After the final portion of **18** had been added, the reaction mixture was allowed to warm to 70° and then stirred for an additional 20 min. The purplish-red mixture was then poured over crushed ice and the resulting precipitate collected. The filter cake was dissolved in 10% aqueous KOH and filtered through Celite. The filtrate was carefully acidified with 10% HCl until a precipitate just began to form, and then an additional 20 ml was added. After filtration through Celite, the filtrate was acidified with concentrated HCl to give 101 g (80%) of **19**. A sample was recrystallized from methanol to give bright red crystals, mp 221–222° (lit.[22] mp 209°).

**3-Iodoanthranilic Acid** (**1**).—To a well-stirred solution of 164 g (0.6 mol) of **19** and 40.4 g (0.7 mol) of KOH in 350 ml of $H_2O$ at 0° was added a chilled solution of 117 g (1.0 mol) of 30% $H_2O_2$ and 57.6 g (2.1 mol) of KOH in 800 ml of $H_2O$ during 1.25 hr with the temperature kept below 10° throughout the addition. After an additional 45 min of stirring, 220 ml of glacial acetic acid was added during 30 min with an occasional addition of a few drops of 2-octanol to reduce extreme foaming. Filtration afforded 154 g (95%) of **1**. A sample was recrystallized (aqueous-acetone) to give light yellow needles, mp 182–183° (lit.[22] mp 176–177°).

**Methyl 2,3-Diiodobenzoate** (**2**).—To a well-stirred mixture of 29 g (110 mmol) of **1**, 32 g (330 mmol) of concentrated HCl, and 100 ml of water at 0° was added a chilled solution of 9.4 g (110 mmol) of $KNO_2$ in 100 ml of water during 10 min. After a stirring period of 1 hr at 0°, a chilled solution of 39.8 g (240 mmol) of KI in 100 ml of water was added. The reaction mixture was allowed to warm to room temperature and decolorized with excess $NaHSO_3$. The light tan precipitate was filtered to afford 34.5 g (82%) of 2,3-diiodobenzoic acid. A sample was recrystallized from ethanol to give colorless crystals, mp 183–185° (lit.[23] mp 178–181°). Treatment with diazomethane yielded **2**, the nmr spectrum of which showed three aromatic hydrogens in the τ 2–3 region and a $CH_3$ peak at τ 5.5 (3 H).

*Anal.* Calcd for $C_8H_6I_2O_2$: C, 24.8; H, 1.6. Found: C, 25.2; H, 1.6.

**Dimethyl 6,6′-Diiododiphenate** (**3**).—To 50 g (129 mmol) of **2** at 110° was added 24.6 g of activated[24] copper bronze during 1 hr with stirring. After 1 hr at 110°, another 24.6 g of activated copper bronze was added in one portion. The mixture was held at 110–115° for 3 hr, cooled, and extracted with $CH_2Cl_2$. The solvent was removed under reduced pressure and the residue washed with cold ether to afford 20.3 g (61%) of **3**. The ether was removed from the washings to give 15.1 g (31%) of recovered **2**. Recrystallization of the ether residue from ethanol gave colorless crystals of **3**: mp 147–148°; ir (KBr) bands at 5.72 and 5.80 μ; nmr ($CDCl_3$) at τ 6.38 (s, 6, $OCH_3$), 2.92 (t, 2, $J$ = 8 Hz, 4- and 4′-Ar H), 2.05 (q, 2, $J$ = 1.8 Hz, 5- and 5′-Ar H), 1.95 (q, 2, $J$ = 1.8 Hz, 3- and 3′-Ar H).

*Anal.* Calcd for $C_{16}H_{12}I_2O_4$: C, 36.8; H, 2.3; I, 48.6. Found: C, 36.9; H, 2.4; I, 48.8.

**1,8-Dicarbomethoxybiphenylene** (**5**).—To a solution of 520 mg (1.0 mmol) of **3** in 20 ml of dry pyridine was added 130 mg of activated copper bronze.[24] After having been stirred at reflux for 20 hr, the reation mixture was cooled and worked up as usual with ether to give a brown oil. Column chromatography of the oil on silica (10% ether–benzene) afforded 440 mg (87%) of recovered **3** and 30 mg (11%) of **5**. Recrystallization from ethanol gave bright yellow needles: mp 147–148°; ir ($CHCl_3$) 5.85 μ; uv (ethanol) $\lambda_{max}$ 250 mμ (ε 30,700), 350 (sh, 3410), 365 (5270); nmr ($CDCl_3$) τ 6.17 (s, 6, $OCH_3$), 3.17 (m, 6, Ar H).

*Anal.* Calcd for $C_{16}H_{12}O_4$: C, 71.6; H, 4.5. Found: C, 71.8; H, 4.6.

**1,5-Dicarbomethoxybiphenylene** (**4**).—To a stirred solution of 1.9 g (5 mmol) of **2** in 15 ml of dry DMF at 55° was added 1.9 g of activated copper bronze. After stirring for 2 hr at 55°, the reaction mixture was diluted with $CH_2Cl_2$ and filtered. The filtrate was worked up as usual to afford a yellow semisolid. The semisolid was collected and washed with cold acetone to give 500 mg (75%) of **4**. From the filtrate 270 mg (14%) of **2** was recovered. Recrystallization (acetone) of **4** gave light yellow needles: mp 187–188°; ir ($CHCl_3$) 5.85 μ; uv (ethanol) $\lambda_{max}$ 254 mμ (ε 38,900), 263 (42,300), 372 (8850), 393 (11,400); nmr ($CDCl_3$), τ 6.17 (s, 6, $OCH_3$), 3.05 (m, 4, Ar H), 2.88 (dd, 2, $J$ = 7.5 and 3 Hz, Ar H).

*Anal.* Calcd for $C_{16}H_{12}O_4$: C, 71.6; H, 4.5. Found: C, 71.5; H, 4.5.

A sample of **3** was saponified to yield the diacid, mp >360° dec. This diacid was stirred for 15 hr with ethoxyacetylene in methylene chloride. The resulting anhydride, mp 240° dec, ir ($CH_2Cl_2$) 5.6 and 5.7 μ, was obtained in high yield.

*Anal.*. Calcd for $C_{14}H_8I_2O_4$: C, 34.0; H, 1.6. Found: C, 34.3; H, 1.7. Calcd for $C_{14}H_6I_2O_3$: C, 35.2; H, 1.3. Found: C, 35.5; H, 1.3.

Mass spectra of **4** and **5** gave parent peaks at $M^+$ 268. A strong peak at $M^+$ 237 in **5** (much weaker in **4**) provides additional evidence for the 1,8 location of the carbomethoxy groups as the acylium ion formed by loss of $CH_3O$ is stabilized by the adjacent carbomethoxy group.[25]

**Carbethoxyethynylcopper.**—To a well-stirred mixture of 19 g (50 mmol) of cuprous iodide,[26] 31.2 g (400 mmol) of $(NH_4)_2CO_3$, and 400 ml of distilled water under nitrogen was added a solution of 9.8 g (100 mmol) of ethyl propiolate in 150 ml of ethanol. After having been stirred for 30 min under nitrogen, the reaction mixture was filtered and the filter cake was washed successively with 200 ml each of water, ethanol, and ether. The filter cake was air-dried to give 16.1 g (100%) of canary yellow carbethoxyethynylcopper: ir (mineral oil) 5.2, 5.86, and 5.95 μ.

**Dimethyl 6,6′-Bis(carbethoxyethynyl)diphenate** (**6**).—In the best of many experiments 60 ml of pure degassed dry pyridine was added to a mixture of 10.0 mmol of **3** and 22.0 mmol of carbethoxyethynylcopper which had been stirred under dry $N_2$ for 15 min. After 24 hr at 110°, the mixture was cooled, diluted with $CH_2Cl_2$, filtered through Celite, and worked up as usual. By column chromatography on silica gel (2 and 4% ether–benzene for **7** and **6**, respectively) and crystallization from ethanol there was isolated about 16% of **7** [mp 105–107°; ir (KBr) bands at 4.48, 5.8, and 5.9 μ] and 5% of **6** (mp 87.5–89.5°; ir bands as for **7**): nmr ($CDCl_3$) for **6**, τ 8.83 (t, 6, $J$ = 7.5 Hz, $OCH_2CH_3$),

(19) We thank Dr. John S. Swenton for valuable advice concerning the photochemical experiments.

(20) All melting points and boiling points are uncorrected. All microanalyses were by Galbraith Laboratories, Inc., Knoxville, Tenn. Ir spectra were obtained with Perkin-Elmer 237 and/or 137 instruments. Uv spectra were obtained on a Bausch and Lomb Spectronic 505 or a Cary Model 15 spectrophotometer. Nmr spectra were obtained with a Varian A-60 spectrometer in reference to tetramethylsilane as an internal standard. All column chromatography was performed on Grace Davison 950 silica gel. The term "worked up as usual" means that a solution of the products in an organic solvent after washing with dilute alkali and/or acid, water, and saturated salt solution was filtered through 10–20 mesh Drierite (anhydrous calcium sulfate). The solvent was then removed on a rotary evaporator.

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6.38 (s, 6, $OCH_3$), 5.91 (q, 4, $J$ = 7.5 Hz, $OCH_2CH_3$), 2.55 (t, $J$ = 8 Hz, 4- and 4′-Ar H), 2.16 (dd, 2, $J$ = 8 and 1.5 Hz, 5- and 5′-Ar H), 1.84 (dd, 2, $J$ = 8 and 1.5 Hz, 3- and 3′-Ar H); for **7**, 8.82 (t, 3, $J$ = 7.5 Hz, $OCH_2CH_3$), 6.37 (s, 3, $OCH_3$), 6.33 (s, 3, $OCH_3$), 5.90 (q, 2, $J$ = 7.5 Hz, $OCH_2CH_3$), 2.20 (complex m, 6, Ar H).

*Anal.* Calcd for $C_{16}H_{22}O_8$ (**6**): C, 67.5; H, 4.8. Found: C, 67.7; H, 4.8. Calcd for $C_{21}H_{17}IO_6$ (**7**): C, 51.2; H, 3.5. Found C, 51.4; H, 3.4.

**Dimethyl 6,6′-Bis(carboxyethynyl)diphenate (8).**—Alkaline hydrolysis of **6** for 1 hr in boiling aqueous methanol containing 2 equiv of NaOH yielded **8** quantitatively. Recrystallization from chloroform gave colorless **8**: mp 158–162° dec; nmr (acetone-$d_6$) $\tau$ 6.39 (s, 6, $OCH_3$), 2.48 (t, 2, $J$ = 8 Hz, 4- and 4′-Ar H), 2.15 (dd, 2, $J$ = 8 and 1.5 Hz, 5- and 5′-Ar H), 1.81 (dd, 2, $J$ = 8 and 1.5 Hz, 3- and 3′-Ar H).

*Anal.* Calcd for $C_{22}H_{14}O_8$: C, 65.0; H, 3.5. Found: C, 64.9; 3.5.

**6,6′-Diethynyldiphenic Acid (9).**—To 834 mg (2.1 mmol) of **8** was added 10 ml of *N*,*N*-dimethylaniline. After having been stirred for 1.75 hr at 110–120°, the reaction mixture was cooled, poured into excess 10% HCl, and worked up as usual with ether to give a brown residue. Chromatography on silica (benzene) afforded 606 mg of colorless material. To 110 mg of the above material was added 10 ml of 5% methanolic NaOH. After the mixture was refluxed for 20 hr, it was cooled, poured into excess 10% HCl, and worked up as usual with ether to give 100 mg (92% based on **8**) of **9**. Recrystallization from ethyl acetate gave colorless crystals of **9**: mp 251–254°; ir bands at 3.03 and 5.9 $\mu$; nmr (DMSO-$d_6$) $\tau$ 6.17 (s, 2, ≡CH), 2.54 (t, 2, $J$ = 8 Hz, 4- and 4′-Ar H), 2.24 (dd, 2, $J$ = 8 and 1.5 Hz, 5- and 5′-Ar H), 1.96 (dd, 2, $J$ = 8 and 1.5 Hz, 3- and 3′-Ar H).

*Anal.* Calcd for $C_{18}H_{10}O_4$: C, 74.5; H, 3.5. Found: C, 74.7; H, 3.6.

**6,6′-Diethynyldiphenic Anhydride (10).**—To a stirred suspension of 20.2 mg (0.07 mmol) of **9** in dry $CH_2Cl_2$ was added 0.75 ml of 0.1 *M* ethoxyacetylene in $CH_2Cl_2$. After a stirring period of 24 hr, the solvent was removed under reduced pressure to afford 18.8 mg (100%) of **10**: mp 155° dec; ir ($CHCl_3$) bands at 3.03, 5.6, and 5.7 $\mu$; nmr ($CH_2Cl_2$) at $\tau$ 6.80 (s, 2, ≡CH), 2.25 (m, 6, aromatic); uv (ether) $\lambda$ 232 m$\mu$ ($\epsilon$ 29,500), 253 sh (10,000) 300 (2050); mass spectrum (70 eV) *m*/*e* (rel intensity) 274 (2.5), 273 (20), 272 (100), 229 (10), 228 (52), 201 (16), 200 (92), 199 (27), 174 (19), 150 (13), 100 (31); mol wt (calcd for $C_{18}H_8O_3$) 272.047339, found 272.047418 (by mass spectrographic analysis).

On hydrolysis **10** was converted into **9**.

**Photolyses of 6,6′-Diethynyldiphenic Anhydride (10).**—A number of attempts to effect photochemical reactions were carried out at 0° in Pyrex and quartz nmr tubes strapped to a quartz immersion-well of a 450-W Hanovia medium-pressure lamp. All photolyses were conducted in $CH_2Cl_2$ and were $1.4 \times 10^{-1}$ *M* in **10**. The sensitized photolyses were 1.1 *M* in benzophenone. The direct photolyses were conducted in Pyrex for periods of 0.5, 1.5, and 10.5 hr and in quartz for periods of 0.5 and 2.0 hr. The sensitized (Pyrex) photolyses were conducted for periods of 0.5 and 9.5 hr. In each case **10** was recovered essentially quantitatively.

**Pyrolyses of 6,6′-Diethynyldiphenic Anhydride (10).**—The pyrolyses of **10** were performed at 140, 160, 180, and 200° in sealed nmr tubes in 1,1,2,2-tetrachloroethane for 1 hr. Unchanged **10** was recovered in high yield in all but the 200° run. Pyrolyses at 200° were also performed for 15 and 30 min. Tarry material resulted.

**2-Ethyl-α-isonitrosoacetanilide (20).**—The procedure used for the preparation of **18** was used to prepare **20** in 86% yield from *o*-ethylaniline.[27] Recrystallization from water of **20** gave colorless needles, mp 105–106°.

*Anal.* Calcd for $C_{10}H_{12}N_2O_2$: C, 62.5; H, 6.3. Found: C, 62.4; H, 6.4.

**7-Ethylisatin (21)** was prepared in 81% yield as for **19**. Recrystallization (MeOH) of **21** gave rust colored crystals, mp 189–190° (lit.[28] mp 193°).

**3-Ethylanthranilic acid (22)** was prepared in 96% yield as for **1**. Recrystallization from acetic acid gave light tan needles, mp 147–148° (lit.[29] mp 146–147°).

**Methyl 2-Iodo-3-ethylbenzoate (14).**—To 832 g of concentrated HCl that was cooled in a Dry Ice–acetone bath was added a solution of 394 g (2.4 mol) of **22**, 118 g (2.9 mol) of NaOH, and 181 g (2.6 mol) of $NaNO_2$ in 2 l. of water at 10° during 1 hr with stirring. After 15 min, 20 g of urea was added followed by 830 g (5 mol) of KI during 15 min. After stirring for 1 hr, the dark mixture was decolorized with excess $NaHSO_3$ and the resulting light yellow precipitate collected to give crude 2-iodo-3-ethylbenzoic acid. To a solution of the crude acid in 2 l. of MeOH were added 250 g of 2,2-dimethoxypropane and 25 g of concentrated $H_2SO_4$. After 40 hr at reflux, 68 g of pyridine was added and the reaction mixture was concentrated under reduced pressure. After work-up with ether as usual, the residue was distilled to give 399 g (58%) of **14**, bp 114–116° (0.35 mm). A sample of **14** was saponified with 5% ethanolic KOH to give pure 2-iodo-3-ethylbenzoic acid, mp 110–112°, on crystallization from $CCl_4$.

*Anal.* Calcd for $C_9H_9IO_2$: C, 39.1; H, 3.3. Found: C, 38.9; H, 3.1.

**2-Iodo-3-ethylbenzoic Anhydride (15).**—To a solution of 6.8 g (23.5 mmol) of 2-iodo-3-ethylbenzoic acid in 25 ml of dry $CH_2Cl_2$ that was cooled in an ice bath was added 0.8 g (11.8 mmol) of ethoxyacetylene in 15 ml of $CH_2Cl_2$. After 24 hr, 6.3 g (100%) of **15** was obtained. Low-temperature recrystallization from ethyl acetate–hexane yielded colorless crystals of **15**: mp 50.0–50.5°; ir (neat) 5.55, 5.75 $\mu$.

*Anal.* Calcd for $C_{18}H_{16}I_2O_3$: C, 40.4; H, 3.0; I, 47.6. Found: C, 40.3; H, 3.1; I, 47.3.

**Ullmann Reaction on 2-Iodo-3-ethylbenzoic Anhydride (15).**—To a refluxing solution of 3.8 g (7.1 mmol) of **15** in 100 ml of dry DMF was added 2.7 g of activated copper bronze. After having been stirred for 15 min, the reaction mixture was cooled, diluted with ether, filtered, and worked up as usual. The product was hydrolyzed with alkali. On acidification 1.9 g (90%) of 6,6′-diethyldiphenic acid (**16a**) was obtained. Recrystallization from ethyl acetate gave colorless crystals, mp 226–229°.

*Anal.* Calcd for $C_{18}H_{18}O_4$: C, 72.5; H, 6.1. Found: C, 72.5; H, 6.1.

**Ullmann Coupling of Methyl 2-Iodo-3-ethylbenzoate (14).**—To a refluxing solution of 1.50 g (5.3 mmol) of **14** in 50 ml of dry DMF was added 1.50 g of activated copper bronze. The reaction mixture was stirred for 15 min, cooled, diluted with ether, and filtered. The filtrate was worked up in the usual manner to give a yellow oil. Column chromatography on silica afforded 700 mg (46%) of recovered **14** (benzene) and 360 mg (41%) of dimethyl 6,6′-diethyldiphenate (**16b**) (1% ether in benzene) which was saponified to **16a** for identification.

**Registry No.**—**2**, 14192-14-4; **3**, 28444-05-5; **3** diacid, 28444-06-6; **3** anhydride, 28444-07-7; **4**, 20275-25-6; **5**, 20275-26-7; **6**, 28444-10-2; **7**, 28455-59-6; **8**, 28455-60-9; **9**, 28455-61-0; **10**, 27287-05-4; **14**, 28455-63-2; **15**, 28455-64-3; **16a**, 7509-70-8; **20**, 7509-61-7.

(27) We thank the Ethyl Corp. for a generous gift of *o*-ethylaniline.

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# Unsaturated Heterocyclic Systems. LXXIX. The Alkali Metal Reduction of Oxepins[1]

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The alkali metal reduction of 2,7-dimethyloxepin and 3-benzoxepin was investigated for comparison with 2-methoxyazocines which undergo ready conversion to azocinyl dianions. In agreement with MO theory, these oxepins do not give rise to oxepinyl dianions. 2,7-Dimethyloxepin was found to give initially octa-4,6-dien-2-one which with excess potassium was further reduced to 4-octen-2-one. Under analogous conditions, 3-benzoxepin afforded equimolar mixtures of *o*-ethyl- and *o*-ethynylphenylacetaldehydes. Whereas the former substance is a reduction product, the latter arises from base-induced ring cleavage of the oxepin ring. The divergent behavior of $\pi$-excessive and $\pi$-equivalent heterocyclic analogs of cyclooctatetraene on reduction is briefly discussed.

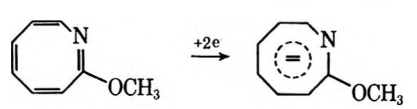
An understanding of the chemical reactivity of monoheterocyclic eight-$\pi$-electron systems isoelectronic with cyclooctatetraene has received considerable attention in the recent literature. Such $4n\pi$ molecules, which obviously do not satisfy the Hückel rule, are recognized to be divisible into two general classes. In the case of oxepin (**1a**), azepine (**1b**), thiepin (**1c**), and their derivatives, the eight $\pi$ electrons are potentially delocalizable over seven atoms, a condition which is clearly $\pi$ excessive.[3,4] In contrast, azocine (**2**) and

**1a**, X = O
**b**, X = NH
**c**, X = S

**2**

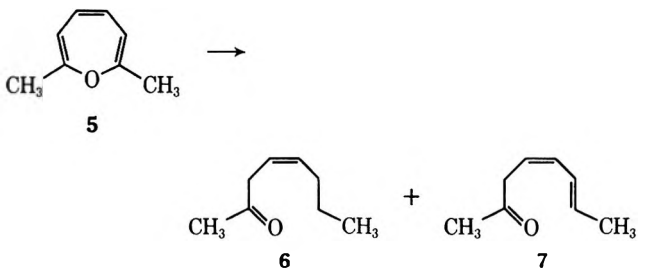
its congeners are endowed with the capability for $\pi$-electron delocalization over eight atoms and may therefore be termed $\pi$-equivalent analogs of the parent hydrocarbon.[5]

The classification is readily seen to be more than a formalistic distinction. In molecular orbital terms, the fourth MO of the heterotropylidines (**1**) can be shown to possess little bonding character.[6] Accordingly, localization of the $\pi$ electrons is prevalent, a condition which fosters comparatively facile oxidation.[7] An important consideration for the present study is the realization that the fifth MO in such systems is unequivocally antibonding. The situation with regard to azocine (**2**) is quite different,[8] as attested to experimentally, for example, by the ready two-electron reduction of 2-methoxyazocines (*e.g.*, **3**) to stable aromatic azocinyl dianions (*e.g.*, **4**).[8,9] Similar reduction of heterotropylidines to their dianions was not considered possible on the basis of the above theoretical considerations. However, the manner in which such heterocyclic polyenes would interact with alkali metals was not readily predictable. The present study has concerned itself with an examination of the reactivity of two representative oxepins toward potassium metal reduction. The selection of 2,7-dimethyloxepin (**5**) and 3-benzoxepin (**12**) was dictated by the knowledge that these derivatives exhibit little tendency for valence isomerization to their respective arene oxide forms.[3]



**3** **4**

Incremental addition of small pieces of potassium metal to cold (−70°) solutions of 2,7-dimethyloxepin (**5**) in anhydrous liquid ammonia–tetrahydrofuran (5:1) resulted in the formation of a reddish brown heterogeneous mixture. Although this complication caused difficulty in estimation of the "end point" (persistent blue coloration), approximately 3 g-atom equiv of the alkali metal were seen to be required. Addition of water and subsequent vpc analysis of the volatile product mixture revealed the formation of **6** (75%) and **7** (20%), together with a third minor substance of unknown composition.



**5** **6** **7**

The two ketones were identified by their elemental analyses and spectra. Thus, the infrared spectrum of **6** exhibits an intense carbonyl band at 1720 $cm^{-1}$ which is characteristic of nonconjugated acyclic ketones. The nmr spectrum ($CDCl_3$) shows a narrow two-proton multiplet in the vinyl region ($\delta$ 5.56) confirming the location of the double bond at a nonconjugated site. Additionally, there was revealed absorption indicative of the presence of a $-CH_2CO-$ grouping ($\delta$ 3.14, d, $J$ = 6 Hz), an acetyl methyl substituent (2.13, s), two allylic protons (2.00, m), and a terminal ethyl group (1.38, sextuplet, and 0.89, t, $J$ = 7 Hz).

(1) For the previous paper in this series, see L. A. Paquette and J. F. Kelly, *J. Org. Chem.*, **36**, 442 (1971).

(2) University Postdoctoral Fellow, 1969–1970.

(3) For recent reviews of heterotropylidine chemistry, see (a) L. A. Paquette in "Nonbenzenoid Aromatics," Vol. I, J. Snyder, Ed., Academic Press, New York, N. Y., 1969, pp 249–310; (b) E. Vogel and H. Günther, *Angew. Chem.*, **79**, 429 (1967); *Angew. Chem., Int. Ed. Engl.*, **6**, 385 (1967).

(4) This terminology was originally proposed by A. G. Anderson, Jr., W. F. Harrison, and R. G. Anderson, *J. Amer. Chem. Soc.*, **85**, 3448 (1963).

(5) (a) L. A. Paquette, T. Kakihana, J. F. Hansen, and J. C. Philips, *ibid.*, **93**, 152 (1971); (b) L. A. Paquette and T. Kakihana, *ibid.*, **90**, 3897 (1968); (c) L. A. Paquette and J. C. Philips, *ibid.*, **90**, 3898 (1968).

(6) A. Streitwieser, Jr., "Molecular Orbital Theory for Organic Chemists," Wiley, New York, N. Y., 1961, p 280.

(7) R. W. Schmid, *Helv. Chim. Acta*, **45**, 1982 (1962).

(8) L. A. Paquette, J. F. Hansen, and T. Kakihana, *J. Amer. Chem. Soc.*, **93**, 168 (1971).

(9) L. B. Anderson, J. F. Hansen, T. Kakihana, and L. A. Paquette, *ibid.*, **93**, 161 (1971).

By comparison, the carbonyl stretching frequency of ketone **7** was also seen at 1720 $cm^{-1}$. Its nmr spectrum shows four vinyl protons in the $\delta$ 5.4–6.5 region, $-CH_2CO-$ absorption at 3.34 (d, $J$ = 7.5 Hz), an acetyl methyl at 2.18, and an allylic methyl substituent at 1.82 (d, $J$ = 6 Hz). The presence of four vinyl protons, the terminal methyl group, and the nonconjugated acetyl function is consistent only with structure **7**. In both **6** and **7**, the geometry of the double bonds has been tentatively assigned by spectral correlation with model compounds.

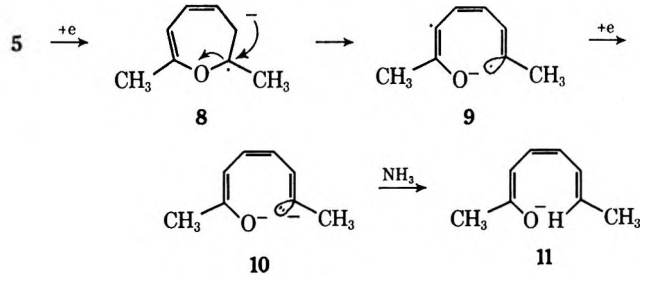
Final confirmation of these assignments was achieved by independent catalytic hydrogenation of **6** and **7** to 2-octanone.

Not unexpectedly, when the reduction was worked up by addition of deuterium oxide, the enone and dienone exhibited complicated patterns of deuterium incorporation as a result of base-catalyzed exchange of the $\alpha$-carbonyl protons. For example, enone **6** was isolated as a mixture of $d_1$–$d_7$ species with the $d_3$ (24%), $d_4$ (37%), and $d_5$ (27%) forms predominating.

Repetition of the reduction with one-half the previous amount of potassium led to a substantially different product composition. Under these conditions, **7** was the major component (70%), accompanied by lesser amounts of **6** (10%), unreacted oxepin (15%), and the same unknown minor constituent (5%). The obvious inference that **7** is the first-formed product and that this dienone undergoes reduction to give **6** under the reaction conditions was substantiated as follows. Resubmission of a product mixture rich in **7** to reduction with excess potassium in liquid ammonia–tetrahydrofuran led almost exclusively (~95%) to **6**.

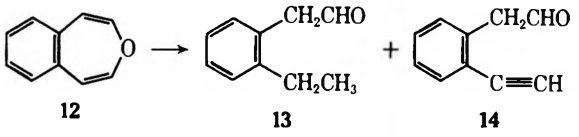
To account for these results, it is suggested that the reduction of **5** proceeds initially by one-electron addition to the oxepin nucleus leading to radical anion **8**. The instability of this species results in ring cleavage to give vinyl radical **9**, which can reasonably be expected to accept a second electron.[10] Protonation of the resulting dianion (**10**) at the vinylic center by the ammonia provides the enolate of **7** (Scheme I). The

SCHEME I



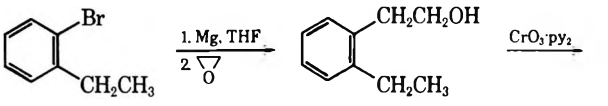

reduction of **7** to enone **6** would seem to be possible not only from the neutral molecule (established by independent experiment), but also by electron transfer to **11**.

Similar reduction of 3-benzoxepin (**12**) at −70° likewise resulted in the appearance of a brownish suspension. Approximately 2.5 g-atom equiv of potassium metal were required to produce a permanent blue coloration. Work-up led in 30% yield to a mixture of two aldehydes ($\nu_{max}^{CCl_4}$ 1727 $cm^{-1}$) that resisted separation by preparative vpc and tlc methods, as well as fractional crystallization of their semicarbazones. The mass spectrum of the mixture showed two substances to be present, one isomeric with **12** (parent ion at $m/e$ 144) and the other a tetrahydro product (parent ion at $m/e$ 148). The nmr spectrum suggested the mixture to consist of approximately equimolar amounts of **13** and **14**. These assignments were subsequently confirmed by independent synthesis.



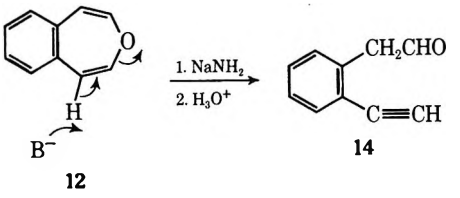

**12** **13** **14**

Starting with *o*-bromoethylbenzene (**15**), alcohol **16** was prepared by reaction of the derived Grignard reagent with ethylene oxide. Controlled oxidation of **16**




**15** **16**

with Collins reagent[11] conveniently afforded **13**. The unequivocal preparation of **14** was founded on the mechanistic rationalization of its formation, *viz.*, base-induced ring cleavage of **12**. In point of fact, exposure of **12** to sodium amide in liquid ammonia–tetrahydrofuran (5:1) at −33° led to **14** in a straightforward

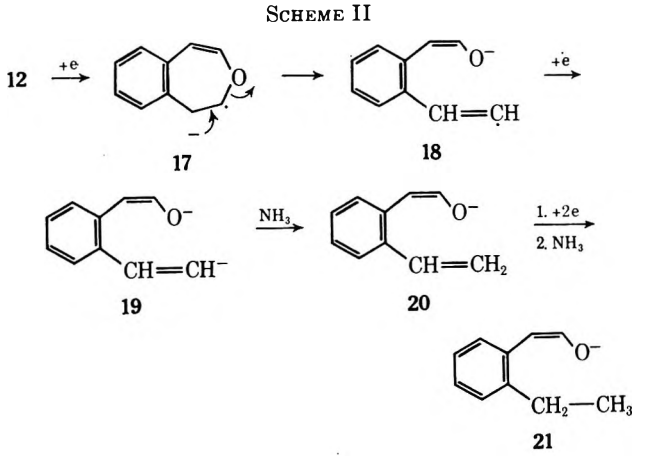



**12** **14**

way. When a composite of the nmr and ir spectra of these two aldehydes was made, it was found to be indistinguishable from the spectra of the mixture isolated in the reduction experiments.

A grossly reasonable mechanism for the formation of **13** (Scheme II) parallels exactly that advanced

SCHEME II




(10) For an excellent discussion of dissolving metal reductions, see H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, New York, N. Y., 1965, Chapter 3.

(11) J. C. Collins, W. W. Hess, and F. J. Frank, *Tetrahedron Lett.*, 3363 (1968).

earlier for **6**. Reductive cleavage of a C–O bond leads *via* **17** to **18**. This transient intermediate undergoes further reduction and protonation to afford the styrene alkoxide **20** which undergoes ultimate conversion to **21**, the enolate of **13**.

The formation of **14** by base-induced ring opening of 3-benzoxepin (**12**), although somewhat unusual, has some analogy in the cleavage reactions of 3-benzofuryllithiums.[12,13] Since no potassium amide was employed directly in the reduction, the source of base was necessarily the amide ion released upon protonation of **19** and its dihydro counterpart, or alkoxides **20**, **21**, and the like. The fact that no acetylenic material was isolated from the reduction of **5** is presumably a reflection of either the diminished acidity of its $\beta$ protons relative to those in **12**, or the susceptibility of the internal acetylene so generated to reduction. We favor the first alternative. The position that **13** may possibly result from further reduction of first-formed **14** is not tenable, since terminal acetylenes are known to be inert to the action of alkali metals.[14]

In conclusion, we note the inability of oxepins to undergo reduction to 10-$\pi$-electron oxepinyl dianions in agreement with MO theory and contrast such behavior with the ready passage of azocines to azocinyl dianions.[8,9] Thus, the divergent chemical properties of $\pi$-excessive and $\pi$-equivalent heterocyclic analogs of cyclooctatetraene are made particularly evident in such electron-transfer reactions.[15]

## Experimental Section

In all experiments involving liquid ammonia, predrying was achieved by stirring with sodium metal for 1 hr at −70°, followed by direct distillation into the predried reaction vessel under anhydrous conditions.

**Reduction of 2,7-Dimethyloxepin (5). A. Potassium (3 Equiv).**—To a stirred solution of 344 mg (2.82 mmol) of 5[16] in 30 ml of liquid ammonia and 6 ml of anhydrous tetrahydrofuran (freshly distilled from $LiAlH_4$), cooled in a Dry Ice–acetone bath, was slowly added small pieces of potassium metal. The solution developed a turbid brown-red color which darkened with progressive addition of the metal (3 g-atom equiv were added). The addition required approximately 2 hr, at which time the blue color persisted for more than 5 min. The cooling bath was removed and the ammonia was allowed to evaporate under a gentle dry nitrogen stream. With stirring, water (6 ml) was added and the resulting dark brown solution was extracted with ether. The combined ether layers were washed well with brine, dried, and evaporated to yield 196 mg of a brown oil. This material was seen to consist of three components (ratio of 5:75:20) on vpc analysis (10% SE-30 at 85°). Preparative vpc isolation was successful in separating the two major components.

The major component (80 mg) was identified as **6**:[17] $\nu_{max}^{CCl_4}$ 1720 cm$^{-1}$; $\delta_{max}^{CDCl_3}$ 5.56 (m, 2, vinyl), 3.14 (d, $J$ = 6 Hz, 2, $CH_2CO$), 2.13 (s, 3, $CH_3CO$), 2.0 (m, 2, allyl), 1.38 (sextuplet, 2, $CH_2CH_3$), and 0.89 (t, $J$ = 7 Hz, $CH_3CH_2$).

*Anal.* Calcd for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.10; H, 11.11.

The minor product was subsequently identified as **7**.

**B. Potassium (1.5 Equiv).**—Treatment of 183 mg (1.5 mmol) of **5** for 1 hr with 89 mg (2.2 mg-atoms) of potassium as above provided, after work-up, a brown oil which consisted (vpc analysis) of 15% unreacted **5**, 10% **6**, and 70% **7**.

Approximately 85% of this material was subjected to preparative vpc purification. In addition to 4 mg of **6**, there was obtained 25 mg of **7**:[18] $\nu_{max}^{CCl_4}$ 1720 cm$^{-1}$; $\delta_{TMS}^{CDCl_3}$ 5.4–6.5 (m, 4, vinyl), 3.34 (d, $J$ = 7.5 Hz, 2, $CH_2CO$), 2.18 (s, 3, $CH_3CO$), and 1.82 (d, $J$ = 6 Hz, 3, methyl).

*Anal.* Calcd for $C_8H_{12}O$: C, 77.37; H, 9.74. Found: C, 77.24; H, 9.47.

The remaining portion of the brown oil was further reduced with 70 mg of potassium in liquid ammonia–tetrahydrofuran (5:1) for 1 hr. The principal product (~95%) was enone **6**.

**Reduction of 3-Benzoxepin (12).**—To a pale yellow suspension of 12[19] (295 mg, 2.05 mmol) in 20 ml of liquid ammonia and 4 ml of anhydrous tetrahydrofuran was added slowly approximately 200 mg (2.5 mg-atom equiv) of potassium metal with stirring under nitrogen at −70°. The ammonia was evaporated under a gentle stream of nitrogen, water (10 ml) was added, and the mixture was thoroughly extracted with ether. The combined ether extracts were washed with brine, dried, and evaporated to give a brown oil which showed one peak on vpc analysis. Preparative vpc afforded 88 mg (30%) of an inseparable mixture of **13** and **14**, $\nu_{max}^{CCl_4}$ 1727 cm$^{-1}$. The physical properties of these aldehydes are presented in the ensuing paragraphs.

**1-Ethyl-2-(2-hydroxyethyl)benzene (16).**—A solution of 6.23 g (37.7 mmol) of *o*-bromoethylbenzene in 20 ml of dry tetrahydrofuran was added under nitrogen to a stirred suspension of magnesium turnings (1 g, 41.5 mg-atoms) in 20 ml of the same solvent, to which had previously been added a crystal of iodine and 0.1 g of ethylene dibromide. The resulting mixture was refluxed for 45 min and cooled to 0°, and ethylene oxide (25 g, tenfold excess) was distilled directly into the flask. After being stirred at 0° for 3 hr and at room temperature for 12 hr, the mixture was treated with 100 ml of 30% aqueous ammonium chloride solution and extracted with ether. Processing of the ether extract and distillation furnished 2.8 g (56%) of **16** as a colorless oil: bp 65–70° (2.3 mm); $\nu_{max}^{film}$ 3200–3300 cm$^{-1}$; $\delta_{max}^{CDCl_3}$ 7.12 (br s, 4, aryl), 3.75 (t, $J$ = 7 Hz, 2, $CH_2OH$), 2.96 (br s, 1, OH), 2.85 (t, $J$ = 7 Hz, 2, $CH_2CH_2OH$), 2.64 (q, $J$ = 7.5 Hz, 2, $CH_2CH_3$), and 1.20 (t, $J$ = 7.5 Hz, 3, methyl).

The 3,5-dinitrobenzoate of **16** was obtained as small white needles, mp 138.5–139°, from ethanol.

*Anal.* Calcd for $C_{17}H_{16}N_2O_6$: C, 59.30; H, 4.68; N, 8.14. Found: C, 59.23; H, 5.06; N, 8.11.

***o*-Ethylphenylacetaldehyde (13).**—Alcohol **16** (400 mg, 2.67 mmol) was stirred at 20° for 16 hr with a suspension of $CrO_3 \cdot py_2$[11] (7 g, approximate tenfold excess) in 50 ml of methylene chloride. The red suspension was filtered, the filtrate evaporated, and the residue taken up in ether. The ether extract was washed with 5% hydrochloric acid solution and brine, dried, and evaporated. The residual yellow oil was purified by preparative vpc to give 60 mg (15%) of **13** as a colorless oil: $\nu_{max}^{CCl_4}$ 1725 cm$^{-1}$; $\delta_{max}^{CDCl_3}$ 9.63 (t, $J$ = 2.5 Hz, 1, CHO), 7.0–7.3 (m, 4, aryl), 3.65 (d, $J$ = 2.5 Hz, 2, $CH_2CHO$), 2.60 (q, $J$ = 7.5 Hz, 2, $CH_2CH_3$), and 1.18 (t, $J$ = 7.5 Hz, 3, methyl).

The semicarbazone of **13** was obtained as lustrous white sheetlets, mp 164–165°, from ethanol–water (2:3).

*Anal.* Calcd for $C_{11}H_{15}N_3O$: C, 64.36; H, 7.37; N, 20.47. Found: C, 64.24; H, 7.52; N, 20.42.

***o*-Ethynylphenylacetaldehyde (14).**—To a suspension of sodium amide (prepared from 500 mg of sodium and a crystal of hydrated ferric nitrate) in 30 ml of liquid ammonia at −33° was added a solution of 330 mg (2.3 mmol) of 3-benzoxepin (**12**)[19] in 5 ml of anhydrous tetrahydrofuran. The mixture was stirred for 3.5 hr

(12) (a) H. Gilman and D. S. Melstrom, *J. Amer. Chem. Soc.*, **70**, 1655 (1948); (b) A. S. Angeloni and M. Tramontini, *Boll. Sci. Fac. Chim. Ind. Bologna*, **21**, 243 (1963); *Chem. Abstr.*, **60**, 15808 (1964).

(13) The formation of open anions from dihydrooxepin also bears some similarities: H. Kloosterziel and J. A. A. van Drunen, *Recl. Trav. Chim. Pays-Bas*, **89**, 667 (1970).

(14) (a) Reference 10, p 72; (b) N. A. Dobson and R. A. Raphael, *J. Chem. Soc.*, 3558 (1955).

(15) The alkali metal reduction of 1,2,7-trimethylazepine [L. A. Paquette, D. E. Kuhla, J. H. Barrett, and R. J. Haluska, *J. Org. Chem.*, **34**, 2866 (1969)] has been examined in a preliminary way. Dianion formation was again not evidenced. However, product characterization was seriously thwarted because of the extreme lability of the products to hydrolysis and air oxidation.

(16) L. A. Paquette and J. H. Barrett, *Org. Syn.*, **49**, 62 (1969).

(17) An isomer of 4-octen-2-one has been prepared earlier by A. P. Meshcheryakov, L. V. Petrova, and A. D. Petrov: *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 98 (1960). However, stereochemical and spectral details are lacking.

(18) Two stereoisomers of octa-4,6-dien-2-one have previously been synthesized, but no stereochemical details are available in either instance: (a) J. Wiemann and H. Danechpejouh, *C. R. Acad. Sci.*, **266**, 1165 (1968); (b) F. Hoffmann-La Roche and Co., A.-G., Belgian Patent 660,099 (Aug 23, 1965); *Chem. Abstr.*, **63**, 19706e (1965).

(19) G. R. Ziegler, *J. Amer. Chem. Soc.*, **91**, 446 (1969).

at this temperature and subsequently treated with solid ammonium chloride. Evaporation of the ammonia was followed by the addition of water and ether extraction. The customary work-up afforded a yellow oil, purification of which by preparative vpc (10% SE-30, 150°) afforded 56 mg (17%) of **14**: $\nu_{max}^{CCl_4}$ 1727 cm$^{-1}$; $\delta_{TMS}^{CDCl_3}$ 9.66 (t, $J$ = 2 Hz, 1, CHO), 7.0–7.7 (m, 4, aryl), 3.82 (d, $J$ = 2 Hz, 2, $CH_2CHO$), and 3.30 (s, 1, C≡CH).

The semicarbazone of **14** was obtained as a fawn-colored solid, mp 183–184° dec, from ethanol.

*Anal.* Calcd for $C_{11}H_{11}N_3O$: C, 65.67; H, 5.51; N, 20.88. Found: C, 65.40; H, 5.47; N, 20.58.

**Registry No.**—**5**, 1487-99-6; **6**, 28362-73-4; **7**, 28362-74-5; **12**, 264-13-1; **13**, 28362-76-7; **13** semicarbazone, 28362-77-8; **14**, 28362-78-9; **14** semicarbazone, 28362-79-0; **16**, 22545-12-6; **16** 3,5-dinitrobenzoate, 22532-40-7.

**Acknowledgment.**—The authors are indebted to the National Institutes of Health for partial financial support of this research.

# Thermally Disallowed Valence Tautomerization of an Indano[1,2-*b*]aziridine to an Isoquinolinium Imine[1a,b]

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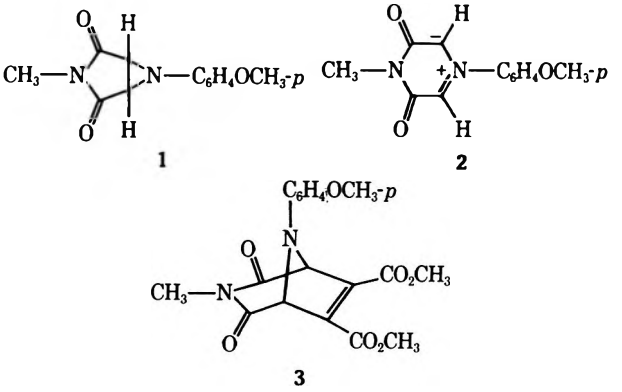
1-Cyclohexyl-6-(cyclohexylimino)-1a-phenylindano[1,2-*b*]aziridine (**4**) at 135° in toluene undergoes conversion to an aromatic valence tautomer, the red isoquinolinium imine **5**, despite the geometrical restrictions imposed by the molecule on the formally required conrotatory opening. Both the thermal and analogous photochemical isomerizations are reversible. The chemistry of **5** is discussed, in particular its trapping as an azomethine ylide in a series of 1,3-dipolar cycloadditions.

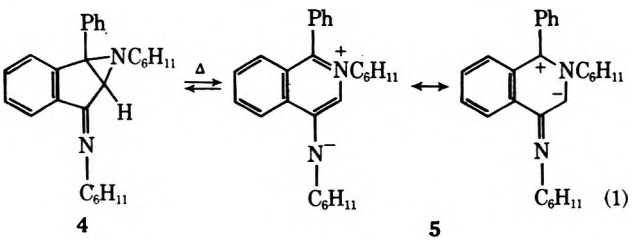
The thermal conrotatory opening of the cyclopropyl anion to the allyl ion predicted by the Woodward–Hoffman rules[2] has yet to receive experimental verification. However, Huisgen and his coworkers have convincingly demonstrated both the expected thermal conrotatory and photochemical disrotatory opening of examples of the isoelectronic analog aziridine to azomethine ylides.[3] Subsequent 1,3-dipolar cycloadditions of the azomethine ylide intermediates to homomultiple and heteromultiple bonds to give a variety of heterocycles are firmly established by several groups of workers.[4] When the aziridine ring is constrained in a bicyclic structure of medium size (five-or six-membered ring) at the 2,3 bond, disrotatory photochemical opening is allowed, but thermal conrotatory ring opening is not permitted by the geometry of the system. The latter reaction is therefore a disallowed process. In agreement with this prediction Huisgen reported[5] that the bicyclic aziridine **1**, while it undergoes facile photochemical disrotatory opening to species **2** which was subsequently trapped with dimethyl acetylenedi-



carboxylate to give **3** in 70% yield, was totally unreactive when heated to temperatures of even 180°.

Oida and Ohki similarly recognized that in a bicyclic aziridine closely related to **1**, while photochemical disrotatory opening is allowed, thermal conrotatory ring opening is disallowed.[4j]

We report the thermally disallowed valence tautomerization of 1-cyclohexyl-6-(cyclohexylimino)-1a-phenylindano[1,2-*b*]aziridine **4** to the isoquinolinium imine **5** (see eq 1) and subsequent trapping of the



(1)

latter as an azomethine ylide in a series of cycloadditions. The phenylindano[1,2-*b*]aziridine[6] is a white

(1) (a) A preliminary report of this work has appeared previously: J. W. Lown and K. Matsumoto, *Chem. Commun.*, 692 (1970). (b) We are indebted to the National Research Council of Canada (Grant A2305) for financial aid. (c) National Research Council of Canada Postdoctoral Fellow, 1969–present.

(2) R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry," Academic Press, New York, N. Y., 1970, p 57.

(3) R. Huisgen, W. Scheer, and H. Huber, *J. Amer. Chem. Soc.*, **89**, 1753 (1967).

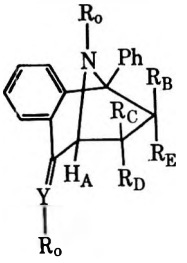
(4) (a) P. B. Woller and N. H. Cromwell, *J. Heterocycl. Chem.*, **5**, 579 (1968); (b) H. W. Heine and R. Peavy, *Tetrahedron Lett.*, 3123 (1965); (c) R. Huisgen, W. Scheer, G. Szeimies, and H. Huber, *ibid.*, 397 (1966); (d) A. Padwa and L. Hamilton, *ibid.*, 4363 (1965); (e) R. von Capeller, R. Griot, M. Haring, and T. Wagner-Jauregg, *Helv. Chim. Acta*, **40**, 1652 (1957); (f) H. W. Heine, A. B. Smith, and J. D. Bower, *J. Org. Chem.*, **33**, 1097 (1968); (g) H. W. Heine, R. E. Peavy, and A. J. Durbetaki, *ibid.*, **31**, 3924 (1966); (h) A. Padwa and L. Hamilton, *J. Heterocycl. Chem.*, **4**, 118 (1967); (i) A. Padwa and W. Eisenhardt, *Chem. Commun.*, 380 (1968); (j) S. Oida and E. Ohki, *Chem. Pharm. Bull.*, **16**, 764 (1968); (k) H. W. Heine and R. Henzel, *J. Org. Chem.*, **34**, 171 (1969); (l) J. W. Lown and J. P. Moser, *Chem. Commun.*, 247 (1970); (m) G. Dallas, J. W. Lown, and J. P. Moser, *ibid.*, 278 (1970); (n) J. W. Lown, J. P. Moser, and R. Westwood, *Can. J. Chem.*, **47**, 4335 (1969); (o) J. W. Lown, T. W. Maloney, and G. Dallas, *ibid.*, **48**, 584 (1970); (p) J. W. Lown, G. Dallas, and T. W. Maloney, *ibid.*, **47**, 3557 (1969); (q) J. W. Lown, R. K. Smalley, G. Dallas, and T. W. Maloney, *ibid.*, **48**, 89 (1970); (r) J. W. Lown, R. K. Smalley, G. Dallas, and T. W. Maloney, *ibid.*, **48**, 103 (1970); (s) J. W. Lown, R. Westwood, and J. P. Moser, *ibid.*, **48**, 1682 (1970).

(5) R. Huisgen and H. Mader, *Angew. Chem., Int. Ed. Engl.*, **8**, 604 (1969).

(6) N. H. Cromwell and M.C. McMaster, *J. Org. Chem.*, **32**, 2145 (1967).

TABLE I

ADDUCTS OF 1-ALKYL-6-(ALKYLIMINO)-1a-PHENYLINDANO[1,2-*b*]AZIRIDINES WITH OLEFINIC DIPOLAROPHILES[a]

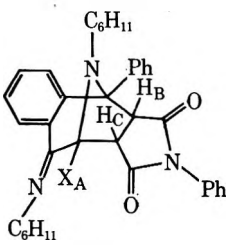


| Adduct[b] | $R_o$ | $R_B$ | $R_C$ | $R_D$ | $R_E$ | Mp, °C | Yield, % | Chemical shifts and coupling constants of methine protons[d] δ in ppm from $(CH_3)_4Si$[e] $H_A$[g] | $H_B$ | $H_C$ | Hz[f] $J_{AC}$ | $J_{BC}$ | $J_{AD}$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 6 | $C_6H_{11}$ | H | H | CONPhCO | | 235–237 | 82 | 5.14, d (0.1 H) | 4.32, d | 3.87, t | 9 | 9 | |
| 9a | $C_6H_{11}$ | H | $CO_2CH_3$ | H | $CO_2CH_3$ | 155–156 | 68 | 5.01, d (0.28 H) | 4.30, d | 3.37, q | 1.8 | 7.3 | |
| 13 | $C_6H_{11}$ | H | H | $(CH_2)_4$ | | 154–155 | 37 | 4.78, d (1 H) | 2.6–3.2, m | 2.1–2.6, m | 8 | | |
| 14 | $C_6H_{11}$ | H | H | CH—$(CH_2)_2$CH | | 174–175 | 39 | 4.66, d (0.57 H) | 2.74, d | 2.34, t | 8 | 10 | |
| 15 | $C_6H_{11}$ | H | H | CHCH=CHCH | | 143–144 | 32 | 4.49, d | 3.18, d | 2.69, t | 9 | 9 | |
| 19a | $CH_3$ | H | H | CONPhCO | | 216–217 | 85 | 4.94, d | 4.55, d | 4.17, q | 8.5 | 9.5 | |
| 19b | $CH_3$ | H | H | $(CH_2)_4$ | | 128–129 | 56 | 4.56, d | 2.9–3.2, m | 2.5–2.9, m | 8 | | |
| 20 | $C_6H_{11}$ | H | H | H | CN | 206–207 | 45 | 4.73, q (0.1 H) | 3.61, q | 2.5, m | 8 | 10 | 1.5 |
| 21a[c] | $CH_3$ | H | H | H | CN | 146–148 | 66 | 3.7–4.1, m | 3.7–4.1, m | 2.7–3.2, m | 8.5 | 11 | 1.5 |
| 21b | $C_6H_{11}$ | H | H | H | $CONH_2$ | 183 | 53 | 4.74, q | 3.85, q | 2.3–2.7, m | 8 | 11 | 1.5 |
| 22[h] | $C_6H_{11}$ | H | H | $CH_3$ | CN | 192–193 | 51 | 4.78, d (0.5 H) | 3.87, d | 2.5–3.0, m | 8 | 11 | |

[a] Satisfactory analytical data (±0.4% for C, H, and N) and mass spectral molecular masses (±0.001) were reported for all compounds in table: Ed. [b] Y = N except as noted. [c] Y–$R_o$ = O. [d] All adducts showed absorption due to aromatic and vinyl protons in the range δ 6.0–8.4 with the appropriate integration and absorption in the range δ 0.5–2.7 due to $C_6H_{11}$ with the cyclohexyl methine protons absorbing in the range δ 2.1–2.8 and 3.3–3.8. [e] $H_D$ octet line positions for **20**, **21a**, and **21b** were 1.80, 1.94, and 1.85, respectively. [f] $J_{BD}$ values for **20**, **21a**, and **21b** were 7 Hz. $J_{CE}$ values for **20** and **21a** were 13 and 14 Hz, respectively. [g] Reduced in intensity to the value shown in parentheses in the bridgehead deuterated analog. [h] Contains a small amount of an isomer (<5%).

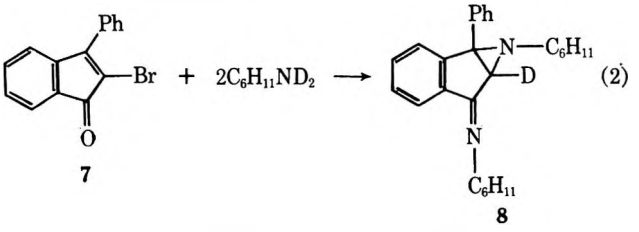
crystalline solid which is very sensitive to visible light, and, on exposure to daylight, adopts a red-purple color which fades in the dark. Solutions of **4** in toluene or xylene at about 135° assume an intense purple color which fades upon cooling or is bleached rapidly by sunlight. This purple species proved to be sensitive to oxygen, peroxides, halogens, acids, bases, and mercaptans, all of which added in trace quantities resulted in rapid bleaching of the color. The assignment of the purple species as the isoquinolinium imine **5** was supported by efficient trapping with a variety of dipolarophiles.

Heating of a degassed solution of **4** with an equimolar quantity of *N*-phenylmaleimide in toluene at 135° for 12 hr or refluxing in *p*-xylene under nitrogen afforded the crystalline adduct **6**, mp 235–237°, in 82% yield corresponding to 1,3-dipolar cycloaddition[7] across the azomethine ylide system (see Table I). Com-



**6a**, X = H
**b**, X = D

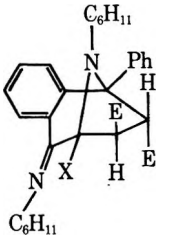
pound **6** was assigned a configuration in which the *N*-phenylmaleimide moiety is endo with respect to the cyclohexylimino group on the basis of the nmr spectrum which showed 9-Hz coupling to the bridgehead proton, in agreement with a dihedral angle of approximately 20° predicted from an examination of molecular models and by comparison with other adducts **14**, **15**, **19a**, **20**, **21a**, **21b**, and **22** (see Figure 1A and Table I). The nmr assignments of the methine protons in **6** could be made unambiguously by examination of the analogous adduct **6a** obtained with specifically 2a-deuterated **8** prepared from the monobromo precursor **7** and cyclohexylamine-*N*-$d_2$[8] with 91% deuterium incorporation.



(2)

**7** **8**

A characteristic property of 1,3-dipolar cycloadditions is the stereospecificity of addition with respect to the dipolarophile.[7] However, reaction of **4** with an equimolar quantity of dimethyl fumarate or dimethyl maleate in degassed toluene at 135° for 48 hr afforded the identical adduct **9a**, mp 156–157°.



**9a**, X = H
**b**, X = D
E = $COOCH_3$

(7) R. Huisgen, *Angew. Chem., Int. Ed. Engl.*, **2**, 565 (1963).

(8) D. B. Denney and M. A. Greenbaum, *J. Amer. Chem. Soc.*, **79**, 3701 (1957).

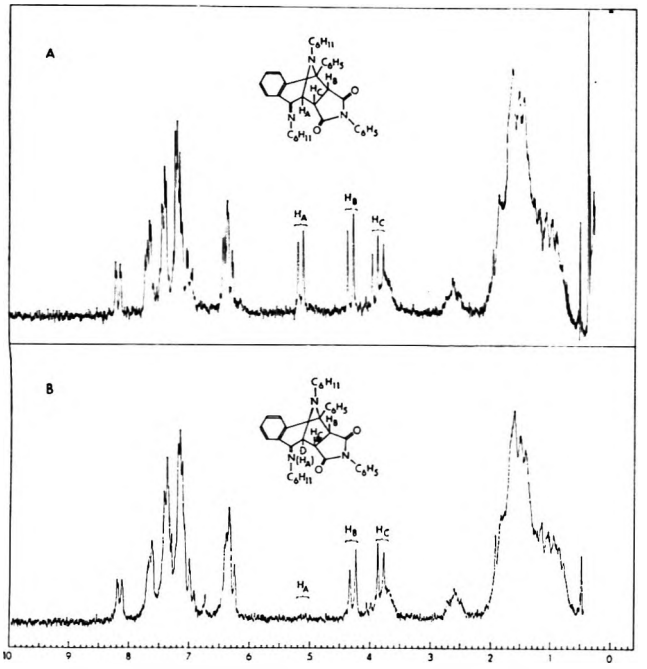


Figure 1.—Nuclear magnetic resonance spectrum at 100 MHz in $CDCl_3$ of (A) *N*-phenylamaleimide adduct of 1-cyclohexyl-6-(cyclohexylimino)-1a-phenylindano[1,2-*b*]aziridine, and (B) *N*-phenylamaleimide adduct of 1-cyclohexyl-6-(cyclohexylimino)-2a-deuterio-1a-phenylindano[1,2-*b*]aziridine (91% deuterium).

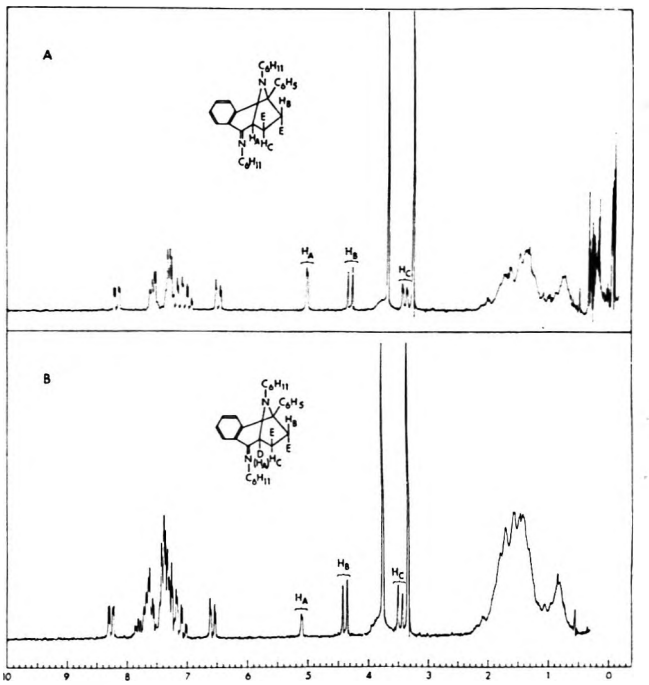
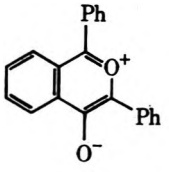


Figure 2.—Nuclear magnetic resonance spectrum at 100 MHz in $CDCl_3$ of (A) dimethyl maleate adduct of 1-cyclohexyl-6-(cyclohexylimino)-1a-phenylindano[1,2-*b*]aziridine, and (B) dimethyl maleate adduct of 1-cyclohexyl-6-(cyclohexylimino)-2a-deuterio-1a-phenylindano[1,2-*b*]aziridine (91% deuterium); E = carbomethoxy group.

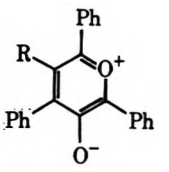
in 68 and 54% yields, respectively, corresponding in geometry to the addition of a fumarate moiety. Evidently the prolonged heating at 135° required to effect the disallowed ring opening of **4** results in isomerization of dimethyl maleate to dimethyl fumarate prior to cycloaddition.[9]

The orientation of the addition of the fumarate moiety in **9a** together with unambiguous assignment of the nmr methine line positions was possible by examination of the bridgehead deuterated analog **9b** (see Figures 2A and B). The diminution of the $\delta$ 5.01 doublet upon deuteration confirms the assignment of the bridgehead proton and its 1.8-Hz coupling to proton C confirms that the orientation of these protons is opposite to that which obtains in adduct **6**. The assignment of the 7.3-Hz splitting to a trans $H_B$–$H_C$ coupling receives support by examination of adduct **20** described below.

Although the thermal valence tautomerization of **4** to **5** is formally a forbidden process, substantial driving force for this process is provided by the relief of ring strain[10] in **4** and the gain in resonance energy in **5**. This process is analogous to the observed reversible tautomerization of 2,3-diphenylindenone oxide to the red pyrylium 4-oxide **10** and of cyclopentadienone oxides to the red pyrylium oxides **11**.[11] Huisgen pointed



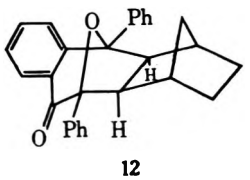
**10**



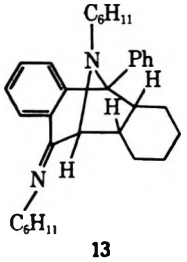
**11**

out[7] the carbonyl ylide nature of the pyrylium oxides **10** and **11** which readily react with dipolarophiles in 1,3-dipolar additions or dimerize readily. While an analogy may therefore be drawn between species **5** and **10** and **11**, significant differences in their properties may be noted.

The pyrylium oxide **10** forms an exo adduct **12** with norbornadiene, whereas **5** forms exclusively endo adducts. For example, **5** forms **6**, and **13**, which was obtained in 37% yield from cyclohexene. Compound



**12**



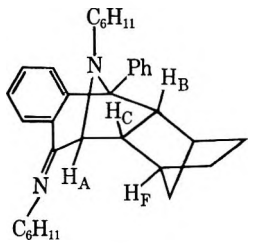
**13**

(9) Dimethyl maleate retains its configuration during the addition to 3-benzoyl-1-cyclohexyl-2-(2-thienyl)aziridine in refluxing benzene [J. W. Lown and K. Matsumoto, *Can. J. Chem.*, **48**, 2215 (1970)], whereas addition of dimethyl maleate to 1,2,3-triphenylaziridine in refluxing toluene gave a fumarate adduct.[4g] Partial isomerization of dimethyl maleate occurs during the addition to 4-oxazolines to give 3-aroyl-4,5-dihydrofurans[4r] and Huisgen reported complete thermal isomerization of maleate in an attempt to observe stereospecific cycloaddition of a ketocarbene to maleate and fumarate: R. Huisgen, H. Konig, G. Binsch, and H. J. Sturm, *Angew. Chem.*, **73**, 368 (1961).

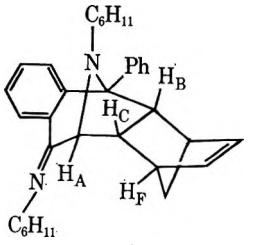
(10) For example, although the analogy is not exact, D. R. Arnold and L. A. Karnishky [*J. Amer. Chem. Soc.*, **92**, 1404 (1970)] point out that the thermal bond homolysis of the central bond of bicyclopentane requires *ca.* 20 kcal $mol^{-1}$ less energy than bond homolysis in dimethylcyclopropane: J. P. Chesick, *J. Amer. Chem. Soc.*, **84**, 3250 (1962); M. C. Flowers and H. M. Frey, *Proc. Roy. Soc., Ser. A*, **257**, 22 (1960).

(11) (a) E. F. Ullman and J. E. Milks, *J. Amer. Chem. Soc.*, **84**, 1315 (1962); (b) E. F. Ullman, *ibid.*, **85**, 3529 (1963); (c) E. F. Ullman and J. E. Milks, *ibid.*, **86**, 3814 (1964); (d) E. F. Ullman and W. A. Henderson, *ibid.*, **86**, 5050 (1964); (e) J. M. Dunston and P. Yates, *Tetrahedron Lett.*, 505 (1964).

**14** was obtained by reaction of **4** with norbornene in 40% yield, and **15** was similarly obtained from

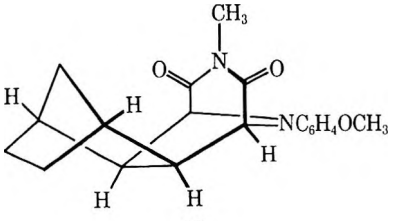


**14**

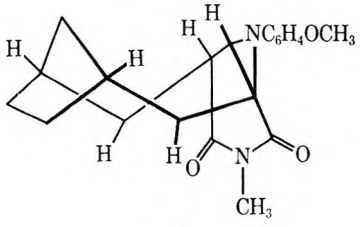


**15**

norbornadiene in 32% yield. The configuration of the adduct **13** was established by the 8-Hz coupling to the bridgehead proton by analogy with **6**. Similarly adducts **14** and **15** were assigned structures endo with respect to the isoquinolinium moiety because of the magnitude of the coupling $J_{AC}$ to be bridgehead proton (8 and 9 Hz, respectively) but exo structures with respect to the norbornene and norbornadiene moieties because $J_{CF} = 0$ Hz in agreement with assignments made on adducts **16** and **17** by Huisgen and his coworkers.[5] In accordance with this assignment, it may be noted that norbornene and norbornadiene normally form exo Diels–Alder and 1,3-dipolar adducts.[12]

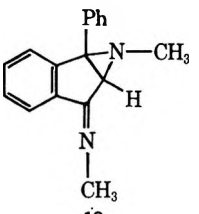


**16**

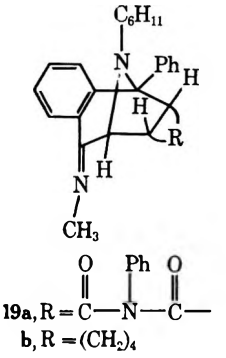


**17**

An additional difference in properties between **5** and **10** or **11** is that, whereas **4** could be recovered in good yield after pyrolysis in the absence of a dipolarophile (see later discussion), the unrecovered 2,3-diphenylindenone oxide in comparable experiments performed by Ullman and Milks[10c] proved to be a mixture of dimers. The *N*-cyclohexyl group in the isoquinolinium group of **5** probably exerts substantial steric hindrance during the 1,3-dipolar cycloaddition which directs a dipolarophile into the endo configuration and prevents dimerization of **5**. Tetrasubstituted dipolarophiles such as tetracyanoethylene failed to react with **4**. However, the fact that the smaller *N*-methyl substituent in **18** similarly results in the exclusive formation of endo adducts **19a** and **19b** suggests that other factors besides steric hindrance direct the mode

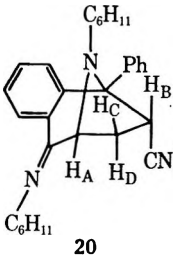


**18**



**19a**, R = $C_6H_{11}$; **b**, R = $(CH_2)_4$

of addition of the dipolarophile. We examined unsymmetrical dipolarophiles to establish any possible orientation preference in the addition. Reaction of **4** with an excess of acrylonitrile afforded only one isolable adduct in 52% yield to which structure **20** could be



**20**

assigned unambiguously by examination of the nmr spectrum together with critical double irradiation experiments (see Table II).

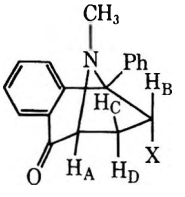
TABLE II

DOUBLE IRRADIATION EXPERIMENTS ON ADDUCTS OF INDANO[1,2-*b*]AZIRIDINE AT 100 MHz[a]

| Adduct | Proton irradiated | Decoupling frequency (Hz)[b] | Lines collapsed: Original form | Lines collapsed: Final form | Measured coupling constant, Hz |
|---|---|---|---|---|---|
| **14** | $H_A$ | 466 | t, 2.34, $H_C$ | d | $J_{AB} = 10$ |
| | $H_A$ | 466 | d, 2.74, $H_B$ | Unaffected | |
| **20** | $H_C$ | 266 | q, 4.73, $H_A$ | d | $J_{AD} = 1.5$ |
| | $H_C$ | 266 | q, 3.61, $H_B$ | d | $J_{BD} = 7$ |
| **21a** | $H_D$ | 206 | q, 3.88, $H_A$ | d | $J_{AC} = 8.5$ |
| | $H_D$ | 206 | q, 3.87, $H_B$ | d | $J_{CB} = 11$ |
| **21b** | $H_A$ | 470 | m, 2.5, $H_C$ | q | $J_{BC} = 11$ |
| | | | | | $J_{CD} = 14$ |
| | $H_C$ | 252 | q, 4.74, $H_A$ | d | $J_{AD} = 1$ |

[a] Double irradiation experiments performed with Varian HA-100 nmr spectrometer. [b] From $(CH_3)_4Si$.

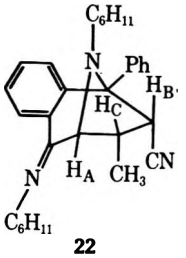
Similarly aziridine **18** reacted with acrylonitrile to give adduct **21a** in which, however, the 3-methylimino group from **18** was eliminated by hydrolysis during the work-up procedure. Acrylamide reacted with **4** to give adduct **21b** in 53% yield, the structure of which was proven by deuterium labeling and spin decoupling.



**21a**, X = CN
**b**, X = $CONH_2$

(12) J. K. Stille and D. A. Frey, *J. Amer. Chem. Soc.*, **81**, 4273 (1959).

The operation of strong directional effects in the approach of the dipolarophile to **5** is demonstrated by the reaction of **4** with a cis–trans mixture of crotonitrile. The adduct obtained proved to be that formed from *cis*-crotonitrile exclusively, *i.e.*, **22** in which both larger groups may be accomodated remote from the bridge-*N*-cyclohexyl group. The stereochemical assignment of **22** is confirmed by observation of $J_{AC} = 8$ Hz and $J_{BC} = 11$ Hz both typical of cis vicinal coupling in a pyrrolidine structure.[4g] The appearance of $H_B$ as a simple

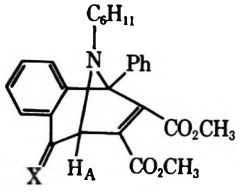


**22**

11-Hz doublet and its line position at $\delta$ 3.87 supports **22** and excludes the structure in which the dipolarophile is added in the alternative orientation.

The structure of the minor isomer produced in this reaction could not be assigned with confidence owing to the relatively low intensity of its nmr spectrum.

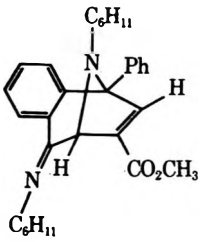
Reaction of **4** with dimethyl acetylenedicarboxylate in toluene gave **23a** in 70% yield. The nmr spectrum of **23a** consisted of a closely similar pair of isomers showing two distinct singlets for the bridgehead proton



**23a**, X = $NC_6H_{11}$
**b**, X = O

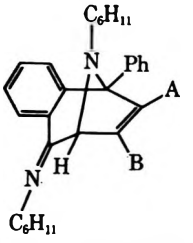
(*both* of which disappear in the adduct formed from **8** and dimethyl acetylenedicarboxylate) and two sets of signals for the ester methyl groups in the same proportion. This we attribute to the existence of syn and anti stereoisomerism about the 6-cyclohexylimino group, since mild acid hydrolysis of the mixture of isomers **23a** gave a single keto compound **23b**. The nmr spectrum of **23b** showed one sharp singlet for the bridgehead proton at $\delta$ 4.80. This phenomenon of syn–anti stereoisomerism, which occurred in the case of acetylenic adducts of **4**, was not encountered in adducts of olefinic dipolarophiles. Presumably the operation of directional effects which place larger groups endo to the cyclohexylimino group in **6**, **13**, **14**, **15**, **19a**, **19b**, and **22** preclude the existence of a syn configuration analogous to **23a**.

Similarly, reaction of methyl propiolate with **4** gave a mixture of stereoisomeric adducts in 63% yield, the major portion of which (>90%) consisted of structure **24** which like **23** exists as a syn–anti stereoisomeric mixture. Both of these stereoisomers showed doublets from AB quartets ($J_{AB} = 2.7$ Hz) for the bridgehead protons at $\delta$ 4.46 and 5.08, respectively, which were confirmed by deuteration to the extent of 90%. The intensity of these signals was 10% of one proton in a sample separately prepared from **8**. The magnitude of this vicinal coupling corresponds with that reported for the model compound norbornene in which $J_{AB} = 2.2$–$3.3$ Hz.[13]



**24**

Methyl phenyl propiolate reacted with **4** to give a mixture of isomers **25a** and **25b**. In this instance, as in the case of the diphenylacetylene adduct **26**, distinct nmr signals due to each syn and anti isomer were not observed.



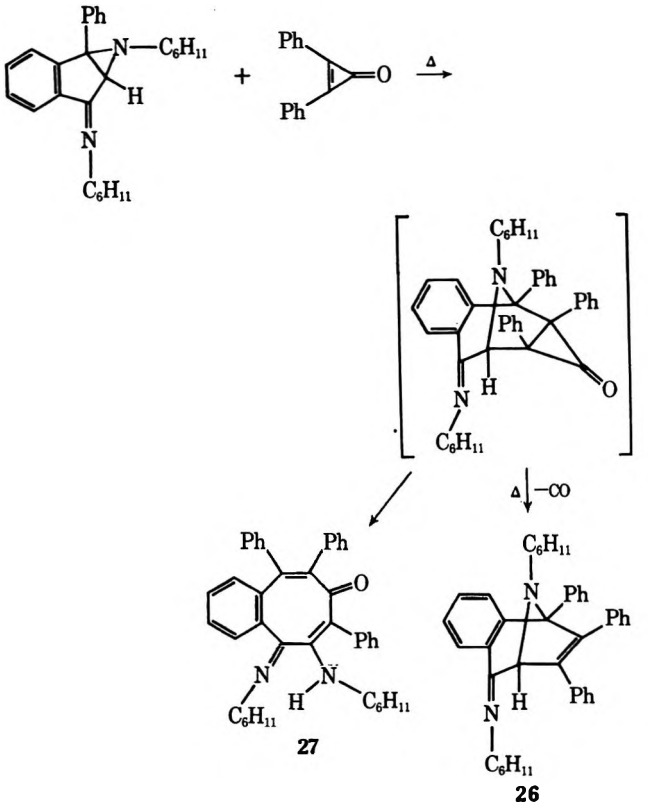
**25a**, A = $CO_2CH_3$; B = Ph
**b**, A = Ph; B = $CO_2CH_3$

The dipolarophilic capacity of the carbon–carbon double bond in diphenylcyclopropenone is considerable,[4o] and in many of its 1,3-dipolar cycloadditions to 3-aroylaziridines it forms pyrrolines by expulsion of carbon monoxide and thus behaves as a more reactive form of diphenylacetylene. Reaction of diphenylcyclopropenone[14] with **4** in toluene at 135° gave two products formulated as **26** and **27**. The former was identical with that obtained from diphenylacetylene and its formation is rationalized in Scheme I. The second product **27** proved to be a 1:1 adduct (*i.e.*, carbon monoxide was not eliminated), and the spectral data were consistent with structure **27**: ir 3400 (NH), 1624 (diconjugated C=O), 1600 $cm^{-1}$ (C=C and C=N); nmr 3.30 (broad singlet exchangeable by deuterium oxide NH). The latter product resembles those obtained by reaction of diphenylcyclopropenone and enamines by Ciabattoni and Berchtold.[15]

**Nature of the Ring-Opened Species.**—Rapid determination of the visible absorption spectrum of the colored species obtained by heating **4** to 135° in xylene showed an intense absorption maximum at 505 m$\mu$ with shoulders at 534 and 570 m$\mu$. The ring opening depicted by eq 1 is demonstrably reversible as shown by parallel experiments carried out in the presence and in the absence of *N*-phenylmaleimide, a powerful dipolarophile. The fraction of **5** consumed in the presence of a trapping agent (>80%) exceeded the fraction used up in its absence (39%), and hence the untrapped isoquinolinium imine **5** must be thermally reconverted back to the indanoaziridine **4**. A similar argument

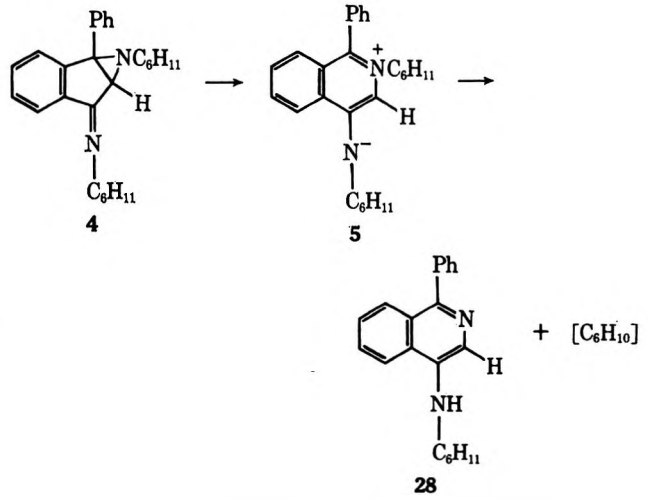
(13) P. Laszlo, *Science*, 58 (1963).
(14) R. Breslow, T. Eicher, A. Krebs, R. A. Peterson, and J. Posner, *J. Amer. Chem. Soc.*, **87**, 1320 (1965).
(15) J. Ciabattoni and G. A. Berchtold, *J. Org. Chem.*, **31**, 1336 (1966).

SCHEME I



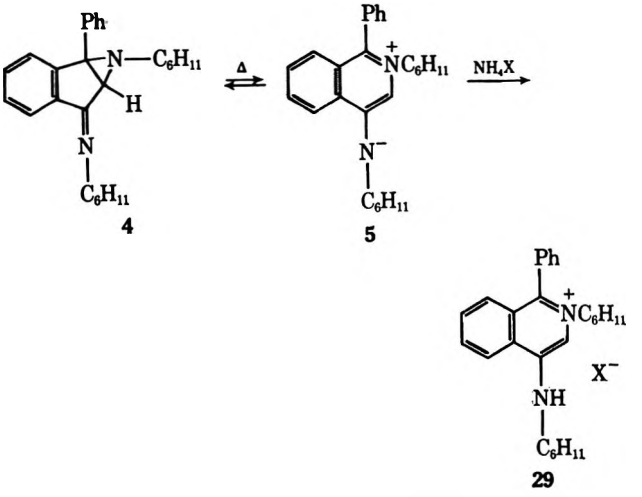
was employed by Ullman and Milks to demonstrate the reversibility of the valence tautomerism of 2,3-diphenylindenone oxide.[10c]

Prolonged pyrolysis of **4** in the absence of dipolarophiles or in the presence of very unreactive dipolarophiles such as cyclohexanone or benzonitrile resulted in the formation of **28**.

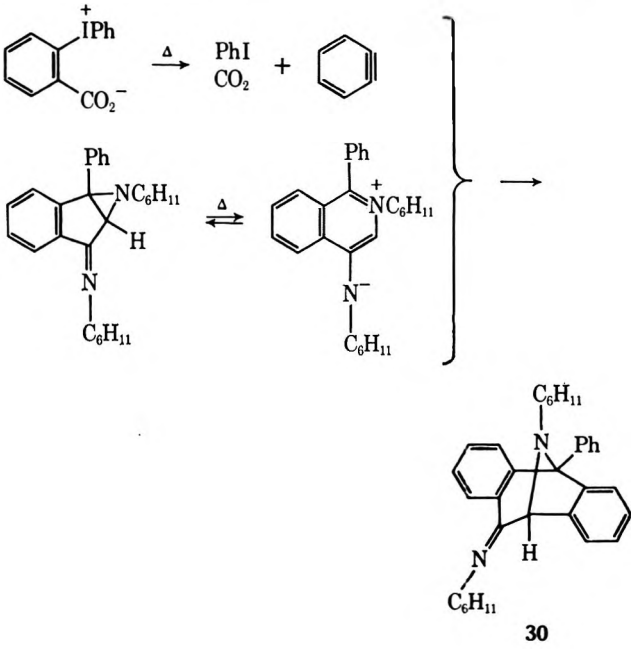


The elimination of cyclohexene from **5** to form the stable aromatic product **28** finds a parallel in the elimination of hydrocarbons from intermediate 4-oxazolines to form aromatic oxazoles reported by Padwa and Hamilton.[16]

The observed thermal opening of **4** to **5** complements the recently described[17] allowed solvolytic disrotatory opening of the *N*-chloroindano[1,2-*b*]aziridine to a nitrenium ion, which is an electrocyclic process with the same orbital symmetry control as a cyclopropyl to allyl cation rearrangement.[18] The intermediate nitrenium ion is converted to isoquinoline by loss of a proton. A parallel is provided in the present work; when the ylide **5** abstracts a proton from added ammonium halide, it is converted into the more stable salt **29**[19] which is the conjugate acid of the ylide.



Some measure of the resonance stabilization available to **5** and its consequent relatively long lifetime is provided by its successful trapping with benzyne. Heating a mixture of **4** with the benzyne precursor diphenyliodonium-2-carboxylate[20] in mesitylene gave the adduct **30**. This indicates qualitatively that **5** is relatively



stable and long-lived, since repeated attempts to trap the azomethine ylide from 1,2,3-triphenylaziridine with benzyne proved unsuccessful. Another factor contributing to the relative stability of species **5** is that

(16) A. Padwa and L. Hamilton, *Tetrahedron Lett.*, 1861 (1967).

(17) D. C. Horwell and C. W. Rees, *Chem. Commun.*, 1428 (1969).

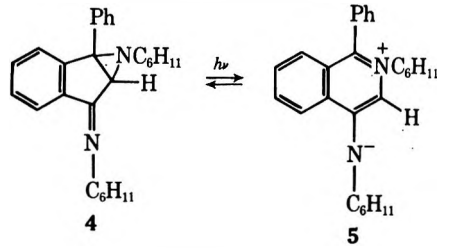
(18) B. Capon, M. J. Perkins, and C. W. Rees, "Organic Reaction Mechanism," Wiley, New York, N. Y., 1965, p 44; 1966, p 37; 1967, p 50; 1968, p 49.

(19) This reaction of **5** results in a sensitivity of the azomethine ylide to dipolarophiles possessing mobile protons; *e.g.*, while *N*-phenylmaleimide gave **6** in 82% yield, the apparently closely related dipolarophile maleimide gave in addition to only a small amount of adduct a complex mixture of unidentified products.

(20) F. M. Beringer and S. J. Huang, *J. Org. Chem.*, **29**, 445 (1964).

ring closure of the azomethine ylide by a symmetry-allowed conrotatory process[21] would result in a trans-fused ring which is clearly not permitted by the geometry of the system.

**Photochemical Valence Tautomerization of the Indano[1,2-*b*]aziridine.**—Whilst the geometry of **4** should not allow conrotatory opening to species **5** under thermal conditions, the corollary is that photochemical disrotatory cleavage should be facile. Photolysis of dilute solutions of **4** in dioxane or ether at 0° in a quartz reaction vessel produced an immediate deep red color, the absorption spectrum of which corresponded closely with that of the colored species produced thermally. The red color is discharged rapidly upon exposure to visible light and the infrared spectrum of the bleached solution was superimposable with that of **4**. Photolysis of solutions of **4** in dichloroethylene resulted in photolytic abstraction of hydrogen chloride from the sol-




**4** **5**

vent and production of the yellow salt **29** (X = Cl) in good yield.

This compound was identical in properties with that produced thermally and thus represents the photochemical stabilization of **5** by proton abstraction.

A control experiment involving irradiation of solutions of **4** in the epr cavity of a Varian instrument generated the deep red color but produced no evidence of a diradical species even at low temperatures. We conclude that **4** undergoes facile reversible photochemical disrotatory cleavage to an azomethine ylide identical with that produced thermally.

Repeated attempts to trap this species generated photolytically at low temperature with dipolarophiles such as *N*-phenylmaleimide proved unsuccessful. However, this result is not unexpected since, while 3-aroylaziridines readily give 1,3-dipolar cycloaddition adducts in good yield with a variety of dipolarophiles in refluxing benzene, Padwa and Hamilton were unable to trap the analogous azomethine ylides produced photolytically.[4h] Similarly, in Huisgen's classic demonstration of the thermal conrotatory and photolytic disrotatory opening of aziridine derivatives,[3] the yields of 1,3-dipolar adducts obtained thermally were superior to those obtained photochemically. In the recently announced photolytic disrotatory cleavage of oxiranes to carbonyl ylides[22] and thermal cleavage to similar species,[21d] 1,3-dipolar addition adducts were formed thermally but not under photolytic conditions.

## Experimental Section

**General.**—Melting points were determined on a Fisher-Johns apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 421 spectrophotometer, and only the principal, sharply defined peaks are reported. Nuclear magnetic resonance spectra were recorded on Varian A-60 and A-100 analytical spectrometers. The spectra were measured on approximately 10–15% (w/v) solutions in $CDCl_3$, with tetramethylsilane as a standard. Line positions are reported in parts per million from the reference. Absorption spectra were recorded in "spectro" grade solvents on a Beckman DB recording spectrophotometer. Mass spectra were determined on an Associated Electrical Industries MS-9 double-focusing high-resolution mass spectrometer. The ionization energy, in general, was 70 eV. Peak measurements were made by comparison with perfluorotributylamine at a resolving power of 15,000. Kieselgel DF-5 (Camag, Switzerland) and Eastman Kodak precoated sheets were used for thin layer chromatography. Microanalyses were carried out by Dr. C. Daesslé, Organic Microanalysis Ltd., Montreal, Quebec, and by Mrs. D. Mahlow of this department.

**1-Cyclohexyl-6-(cyclohexylimino)-1a-phenylindano[1,2-*b*]aziridine and 1-Methyl-6-(methylimino)-1a-phenylindano[1,2-*b*]aziridine.**—These compounds were prepared according to the method of Cromwell.[6] The cyclohexylindanoaziridine had mp 158–159° (lit.[6] 159–160°). The methylindanoaziridine had mp 98–99° (lit.[6] 98–99°).

**Reaction of 1-Cyclohexyl-6-(cyclohexylimino)-1a-phenylindano[1,2-*b*]aziridine with Olefinic Dipolarophiles.**—*N*-Phenylmaleimide, dimethyl maleate, dimethyl fumarate, acrylonitrile, acrylamide, norbornene, norbornadiene, and cyclohexene were successfully employed as dipolarophiles. The reaction procedure is exemplified by the following three reactions.

**Reaction of 1-Cyclohexylimino-6-(cyclohexylimino)-1a-phenylindano[1,2-*b*]aziridine with *N*-Phenylmaleimide.**—A solution of 0.770 g (2 mmol) of the indano[1,2-*b*]aziridine **4** and 0.346 g (2 mmol) of *N*-phenylmaleimide in 30 ml of *p*-xylene was heated under reflux under nitrogen for 12 hr. Removal of the solvent *in vacuo* gave a red oil, trituration of which with hexane afforded adduct **6a** as a slightly purple solid, 0.925 g (82%), purified by recrystallization from ethyl acetate–hexane: mp 235–237°; ir ($CHCl_3$) 1649 (C=N), 1713, 1775 $cm^{-1}$ (C=O); nmr $\delta_{TMS}$ ($CDCl_3$) 0.5–2.2 (m, 20, $C_6H_{11}$), 2.2–2.9 (m, 1, CHN), 3.5–4.1 (m, 1, C=NCH), 3.87 (t, 1, $J_{AC}$ = 9 Hz, $H_C$), 4.32 (d, 1, $J_{BC}$ = 9 Hz, $H_B$), 5.14 (d, 1, $J_{AC}$ = 9 Hz $H_A$), 6.0–8.3 (m, 14, aromatic protons) (see Figure 1A); $uv_{max}$ (95% EtOH) 247 mμ (log ε 4.12), 290 (sh, 3.06), 304 (sh, 2.62); mass spectrum (70 eV) 557.3042 (calcd for $C_{37}H_{39}N_2O_2$, 557.3042).

*Anal.* Calcd for $C_{37}H_{39}N_2O_2$: C, 79.68; H, 7.05; N, 7.54. Found: C, 79.86; H, 6.86; N, 7.53.

**Reaction of 1-Cyclohexylimino-6-(cyclohexylimino)-1a-phenylindano[1,2-*b*]aziridine with Dimethyl Fumarate.**—A deoxygenated solution of 1.15 g (3 mmol) of the indano[1,2-*b*]aziridine **4** and 0.432 g (3 mmol) of dimethyl fumarate in 30 ml of toluene was heated to 135–145° in a sealed vessel for 48 hr. Removal of the solvent *in vacuo* gave **9a** as a slightly purple solid, 1.074 g (68%): mp 156–157° (ether-pentane); ir ($CHCl_3$) 1642 (C=N), 1731 $cm^{-1}$ (C=O); nmr $\delta_{TMS}$ ($CDCl_3$) 0.5–2.2 (m, 21, $C_6H_{11}$), 3.23 (s, 3, $CO_2CH_3$), 3.37 (q, 1, $J_{BC}$ = 7.3 Hz, $J_{AC}$ = 1.8 Hz, $H_C$), 3.65 (s, 3, $CO_2CH_3$), 4.30 (d, 1, $J_{BC}$ = 7.3 Hz, $H_B$), 3.5–3.9 (m, 1, C=NCH), 5.01 (d, 1, $J_{AC}$ = 1.8 Hz, $H_A$), 6.4–8.3 (m, 9, aromatic protons) (see Figure 2A); $uv_{max}$ (95% EtOH) 242 mμ (log ε 4.16), 278 (sh, 3.14); mass spectrum (70 eV) 528.2995 (calcd for $C_{33}H_{40}N_2O_4$, 528.2988).

*Anal.* Calcd for $C_{33}H_{40}N_2O_4$: C, 74.97; H, 7.63; N, 5.30. Found: C, 74.77; H, 7.49; N, 5.55.

**Reaction of 1-Cyclohexylimino-6-(cyclohexylimino)-1a-phenylindano[1,2-*b*]aziridine with Dimethyl Maleate.**—A deoxygenated solution of 1.15 g (3 mmol) of the indano[1,2-*b*]aziridine **4** and 0.432 g (3 mmol) of dimethyl maleate in 30 ml of toluene was heated to 135–145° in a sealed vessel for 48 hr. Removal of the solvent *in vacuo* gave an adduct **9a** identical in all respects with that obtained above from dimethyl fumarate, 0.857 g (54%), mp 156–157° (ether-pentane).

**Reactions of 1-Cyclohexylimino-6-(cyclohexylimino)-1a-phenylindano[1,2-*b*]aziridine with Other Olefinic Dipolarophiles.**—Similar reactions were carried out with 3 mmol of either indano[1,2-*b*]aziridine and 10 ml each of acrylonitrile, crotonitrile, norbornadiene, or cyclohexene or 10 equiv of norbornene in 30 ml of toluene for reflux periods of up to 48 hr. Analytical and spectroscopic data on the adducts thus obtained are summarized in Tables I and II. Critical double irradiation experiments on selected adducts used to determine coupling constants and to assign structures are reported in Table II.

(21) (a) R. Hoffmann, *J. Amer. Chem. Soc.*, **90**, 1475 (1968); (b) R. J. Crawford and A. Mishra, *ibid.*, **88**, 3963 (1966); (c) B. G. Gill, *Quart. Rev., Chem. Soc.*, **22**, 338 (1968); (d) D. R. Arnold and L. A. Karnishky, *J. Amer. Chem. Soc.*, **92**, 1404 (1970).

(22) T. Do-Minh, A. M. Trozzolo, and G. W. Griffin, *ibid.*, **92**, 1402 (1970).

**6-Cyclohexylimino-2a-deuterio-1a-phenylindano[1,2-*b*]aziridine (9).** A. **2-Bromo-3-phenylindenone[6] (8).**—2-Bromo-3-phenylindenone was prepared by the following improved procedure. A mixture of 33.6 g (0.1 mol) of 2,3-dibromo-3-phenylindenone[23] and 10.8 g (0.11 mol) of potassium acetate in 700 ml of 95% ethanol was refluxed for 6 hr. Concentration of the solution *in vacuo* gave 2-bromo-3-phenylindenone (7) as orange crystals from ethanol, 24.8 g (97%), mp 112–113° (lit.[23] mp 112–113°).

B. **6-Cyclohexylimino-2a-deuterio-1a-phenylindano[1,2-*b*]aziridine.**—To a slurry of 25.5 g (0.1 mol) of 2-bromo-3-phenylindenone in 200 ml of dry benzene, a solution of 40 g (0.4 mol) of cyclohexylamine-*N*-$d_2$[8] was added dropwise with stirring, and stirring was continued 3 days in the dark. Removal of the solvent gave a brown solid, trituration of which with 95% ethanol gave pure aziridine **8** as a white solid, 30.8 g (80%): mp 159–160°; nmr $\delta_{TMS}$($CDCl_3$) 0.5–2.2 (m, 21, $C_6H_{11}$), 3.23 (s, 0.09, bridgehead proton), 3.4–4.0 (m, 1, C=NCH), 7.0–8.0 (m, 9, aromatic protons). An average of several integrations confirmed 91% deuterium incorporation at the bridgehead position.

**Reaction of 6-Cyclohexylimino-2a-deuterio-1a-phenylindano[1,2-*b*]aziridine with Olefinic Dipolarophiles.**—In order to elucidate the stereochemistry of some of the adducts obtained by reaction of indano[1,2-*b*]aziridines **4** with olefinic dipolarophiles, additions of the 2a-deuterated analog were carried out as exemplified by the reaction with *N*-phenylmaleimide. The results of other similar experiments are summarized in Table I.

**Reaction of 6-Cyclohexylimino-2a-deuterio-1a-phenylindano[1,2-*b*]aziridine with *N*-Phenylmaleimide.**—A deoxygenated solution of 1.16 (3 mmol) of 6-cyclohexylimino-2a-deuterio-1a-phenylindano[1,2-*b*]aziridine (**8**) and 0.519 g (3 mmol) of *N*-phenylmaleimide in 30 ml of toluene was heated at 135–145° for 24 hr. Evaporation of the solvent gave a purple oil, trituration of which with hexane gave a pale purple solid **6b**, 1.322 g (79%): mp 236–237° (ethyl acetate–hexane); nmr $\delta_{TMS}$($CDCl_3$) 0.5–2.2 (m, 20, $C_6H_{11}$), 2.2–2.9 (m, 1, CHN), 3.5–4.1 (m, 1, C=NCH), 3.87 (d, 1, $J_{AC}$ = 9 Hz, $H_C$), 4.32 (d, 1, $J_{BC}$ = 9 Hz, $H_B$), 5.14 (d, 0.1, $H_A$), 6.0–8.3 (m, 14 aromatic protons). An average of several integrations confirmed 90% deuterium incorporation at the bridgehead position.

**Reaction of 1-Cyclohexyl-6-(cyclohexylimino)-1a-phenylindano[1,2-*b*]aziridine with Acetylenic Dipolarophiles.**—Dimethyl acetylenedicarboxylate, methyl propiolate, diphenylacetylene, methyl phenylpropiolate, diphenylcyclopropenone, and benzyne were successfully employed as dipolarophiles. The reaction procedure and structure proof of the adducts for the first three dipolarophiles was similar to that described in detail for typical olefinic dipolarophile additions. The reactions involving the latter three acetylenic dipolarophiles are discussed in detail.

**Reaction of 1-Cyclohexyl-6-(cyclohexylimino)-1a-phenylindano[1,2-*b*]aziridine with Methyl Phenylpropiolate.**—A deoxygenated solution of 1.15 g (3 mmol) of the indano[1,2-*b*]aziridine **4** and 0.480 g (3 mmol) of methyl phenylpropiolate in 30 ml of toluene was heated to 135–145° for 40 hr. Evaporation of the solvent gave a purple oil which was subjected to chromatography on alumina. Elution with benzene gave one main fraction. Removal of the solvent *in vacuo* and trituration of the residual solid with hexane afforded adducts **25a** and **25b**, 0.914 g (56%): mp 172–173° (ether–hexane); ir ($CHCl_3$) 1638 (C=N), 1701 $cm^{-1}$ (C=O); nmr $\delta_{TMS}$ ($CDCl_3$) 0.3–2.5 (m, 21, $C_6H_{11}$), 3.52 and 3.58 (s, 3 each, $CO_2CH_3$), 3.7–4.4 (m, 1, =NCH), 5.53 and 5.57 (s, 1, bridgehead proton; line position confirmed by deuteration to the extent of 71%), 6.8–8.4 (m, 14, aromatic protons); $uv_{max}$ (95% EtOH) 248 mμ (log ε 4.34), 236 (sh, 4.30); mass spectrum (70 eV) 544.3084 (calcd for $C_{37}H_{40}N_2O_2$, 544.3090).

*Anal.* Calcd for $C_{37}H_{40}N_2O_2$: C, 81.55, H, 7.40, N, 5.14. Found: C, 81.12; H, 7.31; N, 5.19.

From the nmr spectrum it appears that two orientational isomers are present; however, repeated attempts at chromatographic separation were unsuccessful.

**Reaction of 1-cyclohexyl-6-cyclohexylimino-1a-phenylindano[1,2-*b*]aziridine with (A) dimethyl acetylenedicarboxylate** similarly gave adduct **23a** (71%): mp 68–70°; ir ($CHCl_3$) 1637 (C=N), 1724 $cm^{-1}$ (ester C=O); nmr $\delta_{TMS}$ ($CDCl_3$) 0.3–2.5 (m, 21, $C_6H_{11}$), 3.5–4.2 (m, 1, C=NCH), 3.57, 3.78 (s, 3 each, $CO_2CH_3$), 4.9 (s, 0.4), 5.55 (s, 0.6, bridgehead proton), 6.8–8.3 (m, 9, aromatic protons).

B. **Methyl propiolate** similarly gave adduct **24** (61%): mp 73°; ir 1635 (C=N), 1716 $cm^{-1}$ (ester C=O); nmr $\delta_{TMS}$ ($CDCl_3$) 0.3–2.4 (m, 21, $C_6H_{11}$), 3.3–3.7 (m, 1, C=NCH), 3.45, 3.50 (s, 3, $CO_2CH_3$), 4.46 (d, 0.5, $J$ = 2.8 Hz), 5.08 (d, 0.5, $J$ = 2.5 Hz, bridgehead proton), 6.8–8.3 (m, 10, aromatic protons).

**Acid Hydrolysis of Adduct of 1-Cyclohexyl-6-cyclohexylimino-1a-phenylindano[1,2-*b*]aziridine with Dimethyl Acetylenedicarboxylate.**—To a stirred solution of 0.526 g (1 mmol) of adduct **23a** in 20 ml of methanol was added 20 ml of 2 *N* hydrochloric acid. Stirring was continued for 5 hr at room temperature, the methanol was evaporated, and the residue was extracted with chloroform. Evaporation of the solvent from the dried ($MgSO_4$) extract gave a yellow solid **23b** which purified by recrystallization from chloroform–hexane, 0.307 g (69%): mp 134–135; ir $\nu_{max}$ ($CHCl_3$) 1640 (C=O), 1720 $cm^{-1}$ (ester C=O); nmr $\delta_{TMS}$ ($CDCl_3$) 0.5–2.2 (m, 11, $C_6H_{11}$), 3.72 (s, 6, $CO_2CH_3$), 4.80 (3, 1, bridgehead proton), 6.7–8.0 (m, 9, aromatic protons); mass spectrum (70 ev) 445.1892 (calcd for $C_{27}H_{27}NO_5$, 445.1889).

**Reaction of 1-Cyclohexyl-6-(cyclohexylimino)-1a-phenylindano[1,2-*b*]aziridine with Diphenylcyclopropenone.**—A deoxygenated solution of 2.30 g (6 mmol) of the indano[1,2-*b*]aziridine **4** and 1.236 g (6 mmol) of diphenylcyclopropenone in 60 ml of toluene was heated for 48 hr at 135–145°. Removal of the solvent gave a dark red oil, trituration of which with 95% ethanol gave initially crude **27** as a yellow solid, 1.469 g (42%), purified by recrystallization from 95% ethanol: mp 223–224°; ir ($CHCl_3$) 1624 (C=O), 1618, 1595 $cm^{-1}$ (C=N); nmr $\delta_{TMS}$ ($CDCl_3$) 0.3–2.5 (m, 21, $C_6H_{11}$), 3.28 (s, 1, exchangeable with $D_2O$, NH), 3.3–4.0 (m, 1, C=NCH), 6.7–7.7 (m, 19, aromatic protons); $uv_{max}$ (95% EtOH) 250 mμ (log ε 4.22), 295 (3.79), 414 (3.97); mass spectrum (70 eV) 590.3297 (calcd for $C_{42}H_{42}N_2O$, 590.3297).

*Anal.* Calcd for $C_{42}H_{42}N_2O$: C, 85.38, H, 7.17, N, 4.74. Found: C, 84.95; H, 6.71; N, 4.98.

The filtrate obtained from the isolation of **27** was subjected to chromatography on alumina using benzene as eluent which gave adduct **26** as a colorless solid, 0.762 g (23%): mp 169–170° (95% ethanol); ir ($CHCl_3$) 1634 $cm^{-1}$ (C=N); nmr $\delta_{TMS}$ ($CDCl_3$) 0.5–2.5 (m, 21, $C_6H_{11}$), 3.2–3.7 (m, 1, C=NCH), 5.62 (s, 1, bridgehead proton; line position confirmed by deuteration to the extent of 50%), 6.8–8.5 (m, 19, aromatic protons); $uv_{max}$ (95% EtOH) 224 mμ (log ε 3.81), 257 (ε 3.63); mass spectrum (70 eV) 562.3340 (calcd for $C_{41}H_{42}N_2$, 562.3348).

*Anal.* Calcd for $C_{41}H_{42}N$: C, 87.50; H, 7.53; N, 4.98. Found: C, 87.45; H, 7.42; N, 5.07.

This compound was identical in all respects with that obtained directly by reaction of **4** with diphenylacetylene.

**Reaction of 1-Cyclohexyl-6-cyclohexylimino-1a-phenylindano[1,2-*b*]aziridine with Diphenyliodonium-2-carboxylate.**—A solution of 1.15 g (3 mmol) of the indano[1,2-*b*]aziridine **4** and 1.94 g (6 mmol) of diphenyliodonium-2-carboxylate[20] in 50 ml of 1,2,3-trimethylbenzene was heated under reflux for 10 hr under nitrogen. Removal of the solvent *in vacuo* gave a dark red oil which was subjected to chromatography on alumina. Initial elution with pentane removed aromatic by-products, while the main fraction was obtained by elution with benzene. Evaporation of the solvent *in vacuo* and several recrystallizations of the residue from 95% ethanol afforded adduct **30** as a pale yellow solid, 0.258 g (19%): mp 83–86° (95% ethanol); ir ($CHCl_3$) 1635 $cm^{-1}$ (C=N); nmr $\delta_{TMS}$ ($CDCl_3$) 0.5–2.5 (m, 21, $C_6H_{11}$), 3.2–3.7 (m, 1, C=NCH), 5.65 (s, 1, bridgehead proton), 6.5–8.2 (m, 13, aromatic protons); $uv_{max}$ (95% EtOH) 258 mμ (log ε 3.51), 226 (3.94); mass spectrum (70 eV) 460.2883 (calcd for $C_{33}H_{36}N_2$, 460.2878).

**Reaction of 1-Cyclohexyl-6-(cyclohexylimino)-1a-phenylindano[1,2-*b*]aziridine with Dipolarophiles of Low Reactivity and in the Absence of Dipolarophiles.**—A deoxygenated solution of 1.15 g (3 mmol) of the indano[1,2-*b*]aziridine **4** and 15 ml of cyclohexanone in 15 ml of toluene was heated to 135–145° for 48 hr. Removal of the solvent *in vacuo* gave a dark purple oil which was subjected to chromatography on alumina. Elution with benzene gave an oil from the main fraction, trituration of which gave **28** as a yellow solid, 0.346 g (38%): mp 123–124°; ir ($CHCl_3$) 3432 (NH), 1577 $cm^{-1}$ (C=N); nmr $\delta_{TMS}$ ($CDCl_3$) 0.5–2.5 (m, 10, $C_6H_{11}$), 3.2–3.8 (m, 1, CHN), 4.10 (s, 1, exchangeable with $D_2O$ NH), 7.2–8.3 (m, 10, aromatic protons); $uv_{max}$ (95% EtOH) 262 mμ (log ε 4.06), 340 (sh, 3.91), 363 (4.03); mass spectrum (70 eV) 302.1787 (calcd for $C_{21}H_{22}N_2$, 302.1783).

*Anal.* Calcd for $C_{21}H_{22}N_2$: C, 83.40; H, 7.34; N, 9.27. Found: C, 83.19; H, 7.27; N, 9.14.

The identical compound was obtained by similar reaction of **4** with benzonitrile and vinylene carbonate in 19 and 23% yields,

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respectively. No unreacted aziridine could be detected after these prolonged reactions at high temperature.

**Reversibility of the Thermal Valence Isomerization of 1-Cyclohexyl-6-(cyclohexylimino)-1a-phenylindano[1,2-*b*]aziridine. A. Reaction in the Absence of Dipolarophile.**—A deoxygenated solution of 1.15 g (3 mmol) of **4** in 30 ml of toluene was heated to 135–145° for 24 hr giving a deep red color. Evaporation of the solvent and trituration of the residue with ethanol gave recovered indano[1,2-*b*]aziridine **4** as a slightly yellow solid, mp 158–159°, 0.702 g (61% recovery). Evaporation of the ethanol mother liquor afforded 0.068 g (19%) of **28**, 123–124°.

**B. Parallel Reaction in the Presence of a Dipolarophile.**—A similar experiment was performed with 1.5 g (3 mmol) of **4** and 0.519 g (3 mmol) of *N*-phenylmaleimide under exactly comparable conditions and resulted in the isolation of adduct **6** (see above), 1.34 g (80%), mp 235–236°, but no aziridine **4** could be recovered.

**Reversibility of Photochemical Valence Isomerization of 1-Cyclohexyl-6-(6-cyclohexylimino)-1a-phenylindano[1,2-*b*]aziridine**—A solution of 1.063 g (2.8 mmol) of the indano[1,2-*b*]aziridine **4** in 100 ml of tetrahydrofuran was irradiated under nitrogen at 0 to −10° in a quartz cell using a 450-W Hanovia high-pressure lamp for 8 hr. A deep red solution was obtained[24] and when exposed to visible light the color rapidly faded to a pale yellow resulting in a virtually complete restoration of the infrared absorption spectrum of the original compound **4**.

**Photochemical Reaction between 1-Cyclohexyl-6-(cyclohexylimino)-1a-phenylindano[1,2-*b*]aziridine and Cyclohexylamine Hydrobromide.**—A mixture of 1.15 g (3 mmol) of the indano[1,2-*b*]aziridine **4** and 1.08 g (6 mmol) of cyclohexylamine hydrobromide in 150 ml of ether and 20 ml of methanol was irradiated for 8 hr under nitrogen with a 450-W high-pressure Hanovia lamp in a quartz reaction vessel. The resulting yellow solid **29** was collected and recrystallized from ether–methanol, 0.527 g (38%): mp 298–299°; ir ($CHCl_3$) 1617 (C=N), 3230 $cm^{-1}$ (NH); nmr $\delta_{TMS}$ ($CDCl_3$) 0.6–2.4 (m, 20, $C_6H_{11}$), 3.0–3.6 (m, 1, CHNHC=), 3.9–4.5 (m, 1, $=N^+CH$), 6.8–8.1 (m, 9, aromatic protons), 8.51 (d, 1, $D_2O$ exchangeable NH), 9.65 (d, 1, $J$ = 7 Hz, aromatic protons); $uv_{max}$ (95% EtOH–HBr) 393 mμ (log ε 4.12), 335 (3.77), 324 (sh, 3.72), 288 (3.86), 279 (3.89); mass spectrum (70 eV) 384.

*Anal.* Calcd for $C_{27}H_{33}N_2Br$: N, 6.02. Found: N, 5.56.

The identical compound was obtained by heating the indano[1,2-*b*]aziridine with cyclohexylamine hydrobromide or ammonium bromide in toluene.

**Photochemical Reaction between 1-Cyclohexyl-6-(cyclohexylimino)-1a-phenylindano[1,2-*b*]aziridine and *cis*-1,2-Dichloromethylene.**—A mixture of 1.15 g (3 mmol) of the indano[1,2-*b*]aziridine **4** and 20 ml of *cis*-1,2-dichloroethylene in 100 ml of absolute ether was irradiated under nitrogen at 0 to 10° in a quartz reaction vessel for 8 hr. The resulting yellow solid was collected and purified by recrystallization from methanol–ether, 1.08 g (86%): mp 283–285°; ir ($CHCl_3$) 1618 (C=N), 3220 $cm^{-1}$ (NH); nmr $\delta_{TMS}$ ($CDCl_3$) 0.7–2.5 (m, 20, $C_6H_{11}$), 3.3–3.7 (m, 1, =CNHCH), 4.1–4.5 (m, 1, $=^+NCH$), 7.1–8.2 (m, 9, aromatic protons), 8.54 (d, 1, $D_2O$ exchangeable, NH), 8.68 (d, 1, $J$ = Hz, aromatic proton); $uv_{max}$ (95% EtOH) 222 mμ (log ε 4.59), 278 (3.66), 288 (3.64), 324 (sh, 3.47), 334 (3.55), 393 (3.99); mass spectrum (70 eV) 384.

*Anal.* Calcd for $C_{27}H_{33}N_2Cl$: N, 6.66. Found: N, 6.55.

The identical compound was obtained by heating the indano[1,2-*b*]aziridine with ammonium chloride in toluene.

**Registry No.**—**6a**, 27409-74-1; **6b**, 28443-72-3; **8**, 28443-73-4; **9a**, 27284-06-6; **13**, 28443-75-6; **14**, 28443-76-7; **15**, 28443-77-8; **19a**, 28443-78-9; **19b**, 28443-79-0; **20**, 28443-80-3; **21a**, 28443-81-4; **21b**, 28443-82-5; **22**, 28443-83-6; **23b**, 28443-84-7; **24**, 28443-85-8; **25a**, 28443-86-9; **25b**, 28443-87-0; **26**, 28443-88-1; **27**, 28443-89-2; **28**, 28443-90-5; **29** (X = Br), 28443-91-6; **29** (X = Cl), 28443-92-7; **30**, 28443-93-8.

(24) The very close similarity of the absorption spectrum of this species [$\lambda_{max}$ (dioxane) 500 mμ, 520 (sh), 565 (sh)] to that obtained by heating **4** [$\lambda_{max}$ (xylene) 505 mμ, 534 (sh), and 570 (sh)] may be noted.

# Aromatic Demethoxylation in the Cyclization of 3-(β-Dialkoxyarylethylamino)phthalides to 2,3-Dihydro-7*H*-dibenzo[*de,h*]quinolines

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Whereas polyphosphoric acid cyclization of β-phenylethylaminophthalide (**1a**) gives lactam **3**, similar cyclizations of methylenedioxyphenyl (**1c**) and dimethoxyphenyl (**1b**) analogs proceed in the direction of respective 5,6-dialkoxy-2,3-dihydro-7-dibenzo[*de,h*]quinolones (**4**). In **1b** closure, the 6-methoxy group in the tetracyclic base is partly demethylated and for the most part lost, giving **4a** as the major product, together with monophenolic congener. Structure **4a** was established by spectral data, aromatization to **5**, and reduction to basic carbinol **6**, in turn further characterized as acetates **7** and **8**.

Closures of cyclic carbinolamides or enamides leading to 1-substituted (or spiro) tetrahydroisoquinoline or β-carboline acid derivatives or lactams played a prominent role in the chemistry of erythroidines[1-3] and are now well known.[4-9] These and other Pictet–Spengler closures of *N*-(β-arylethyl)enamines being our point of departure, we examined cyclizations of condensation products **1** obtained from typical primary β-arylethylamines and phthalaldehydic acid under mild conditions (azeotropic reflux, benzene or toluene).

In the first place, such products of the reaction of phthalaldehydic acid with primary amines, like those formed with secondary amines and other nucleophiles,[10] are for the most part aminophthalides **1** rather than hydroxyphthalimidines. This is apparent from their infrared spectra, in which lactone bands (5.70 μ) predominate. Further evidence for structure **1** is the fact that mild hydrogenation of **1b** and **1c** gives amino acids **2b** and **2c**, respectively, products which would not arise from hydroxyphthalimidines. By contrast, as is well known, reactions of the ring tautomeric acid chlorides

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(10) D. D. Wheeler, D. C. Young, and D. S. Erley, *J. Org. Chem.*, **22**, 547 (1957).

corresponding to phthalaldehydic and *o*-benzoylbenzoic acids with amines lead to hydroxyphthalimidines.[8,9,11,12]

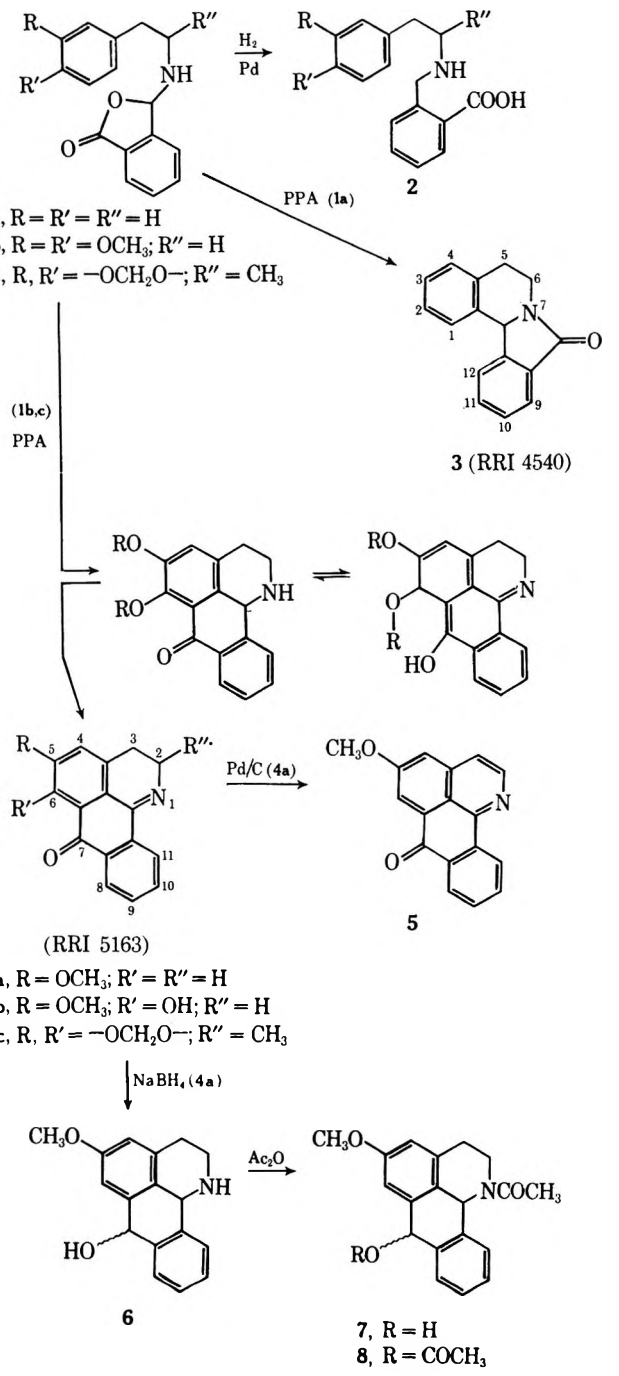
We found that polyphosphoric acid (PPA) cyclization at 100° of crude material consisting largely of **1a** gave a colorless lactam **3**, the same as that reported[8] as the product of $H_2SO_4$ cyclization of 3-hydroxy-*N*-(β-phenylethyl)phthalimidine. Similar cyclizations of **1b** and **c**, however, gave quite different results. The main product (yield *ca.* 30%) from **1b** was not a lactam but rather a basic, yellow (or orange) substance. Its analytically determined empirical formula was $C_{17}H_{13}NO_2$ (mol wt 263), although $FeCl_3$ tests, together with mass spectra, indicated the presence of a phenolic impurity, $C_{17}H_{13}NO_3$ (mol wt 279), as well as a trace of another substance, $C_{18}H_{15}NO_3$ (mol wt 293). As it was practically impossible to remove the (crypto)phenolic constituent completely by extraction with bases, the $C_{17}H_{13}NO_2$ compound was difficult to purify completely; nonetheless, good analyses were secured, and further work as follows established its structure as **4a**. Although basic (giving red solutions with acids), it did not react with dimethyl sulfate, iodomethane, or acetic anhydride except under drastic conditions. The uv spectrum closely resembled that of 2-methoxyanthraquinone. The nmr spectrum with six aromatic protons, one of them meta (but not ortho) coupled, and three methoxyl protons (δ 3.9), agreed with structure **4a**. The ir spectrum, lacking NH absorption, had a strong 6.05-μ peak, evidently conjugated C=O and/or C=N. The presence of both these unsaturated groups became apparent on $NaBH_4$ reduction, when the ir 6.05-μ peak disappeared, and a basic carbinol **6** was obtained. From this compound in turn by treatment with $Ac_2O$ at 100° there was obtained hydroxy *N*-acetyl derivative **7**, and further $Ac_2O$ reaction (reflux) gave the *O*,*N*-diacetyl derivative **8**. Finally, aromatization of **4a** to **5** with Pd/C under mild conditions (refluxing xylene) afforded evidence of a dihydroisoquinoline moiety in **4a**.

Thus it was evident that PPA cyclization of **1b** led, *via* two ring closures[7] and loss of the elements of methanol, mainly to **4a** and in part, by loss of the elements of methane, to a minor amount of phenolic congener, probably **4b**, and to very little **4** (R = R′ = $OCH_3$).

Similar cyclization of methylenedioxy compound **1c** gave **4c**, which however was rather unstable and formed in much lower yield than **4a**. Correct analysis and spectra (ir 6.03 μ; uv similar to that of **4a**; nmr consistent with **4c**; mass spectrum 291) having established structure **4c**, it was evident that a similar loss of 2 H without accompanying dealkoxylation had occurred. Phenolic substances were also present after this cyclization, but they were not amenable to isolation and characterization.

The course of these ring closures seems fairly clear, although certain questions remain unanswered. After cyclization of iminium acids corresponding to **1b**,**c** to tetrahydroisoquinolines, the reactivity of position 8 therein owing to the 7-alkoxy group is such that further carbonylium ion attack, very similar to that leading from 2-(*m*-methoxybenzoyl)benzoic acids to corresponding anthraquinones,[13] occurs, giving a 10-aminoanthrone relative. The driving force for dehydrogenation of such an intermediate to an anthraquinone imine very likely is in itself great and, as shown by the isolation of **4c**, is not necessarily related to loss of oxygen from the aromatic carbon ortho to the anthraquinone C=O. The loss of this oxygen, an unusual phenomenon, predominating in **1b** → **4a**, could proceed *via* first demethylation to chelated hydroxy ketone **4b** (a well-known type) and then loss of water, or it might involve direct loss of methanol. One tautomeric form of a possible intermediate, 5,6-dioxytetrahydro-7-dibenzo[*de*,*h*]quinolone which might lose ROH directly, is indicated in Scheme I, although we do not necessarily claim its validity. In any event there is at least one

SCHEME I




(11) W. Graf, E. Girod, E. Schmidt, and W. G. Stoll, *Helv. Chim. Acta*, **42**, 1085 (1959).

(12) J. M. Sprague, F. C. Novello, and A. A. Deana, U. S. Patent 3,322,631 (1967).

(13) D. S. Noyce and P. A. Kittle, *J. Org. Chem.*, **32**, 2459 (1967), and references therein.

excellent analogy to our findings to be found in work with liriodenine analogs,[14] wherein from a partially hydrogenated azabenzanthrone (aporphinone) of a similar type there was eliminated in the course of work-up an *o*-methoxyl group situated (vinylogously) in respect to C=O so as to resemble a methyl enol ether, as in the present case.

Aromatic methoxyl loss is an unusual synthetic reaction, but the possibility may exist that it occurs in critical intermediates at appropriate oxidation levels in some biogenetic cyclizations leading to series of related alkaloids in which the number of oxy groups varies. In view of current interest in aporphines and other isoquinoline alkaloids,[15-18] the findings presented here may be of interest.

## Experimental Section[19]

**5,6,8,12b-Tetrahydro-8-isoindolo[1,2-*a*]isoquinolone (3).**—The condensation product 1a from 13.9 g (0.115 mol) of β-phenylethylamine and 17 g (0.113 mol) of phthaldehydic acid (200 ml of toluene, Dean–Stark trap, refluxed 1 hr, solvent evaporated; mp 156–158°, acid-soluble; ir 5.70–5.88 μ) and 250 g of PPA were heated 1 hr on a steam cone with stirring. Treatment with ice and water, extraction with ether, isolation of neutral product by evaporation of washed (dilute NaOH, dilute HCl, water) and dried ($MgSO_4$) ether solution, and recrystallization from ether gave 17 g (64%) of colorless crystals: mp 116–118° (lit.[8] mp 114–116°); ir 5.96 μ; uv 278 nm (ε 1840).

*Anal.* Calcd for $C_{16}H_{13}NO$: C, 81.68; H, 5.57; N, 5.95. Found: C, 81.58; H, 5.82; N, 5.92.

Reaction of **3** (20 g) with $LiAlH_4$ (40 g) in THF (250 ml; refluxed and stirred 10 hr) and work-up (150 ml of water, filtration, evaporation, residue separated into neutral and basic components) gave 3.4 g of the corresponding tetracyclic, tertiary amine, characterized as the hydrochloride, mp 221–225° dec (from ethanol–ether).

*Anal.* Calcd for $C_{16}H_{15}N \cdot HCl$: C, 74.55; H, 6.26; N, 5.34. Found: C, 74.82; H, 6.51; N, 5.35.

A neutral product (5.1 g) was also obtained from this $LiAlH_4$ reaction and assigned the structure **12b-hydroxy-5,6,8,12b-tetrahydro-8-isoindolo[1,2-*a*]isoquinolone**, colorless crystals from ethyl acetate: mp 200–203° dec; ir 3.06 and 5.99 μ; uv 248–254 nm (ε 4420) and inflections 264 (3860) and 272 (2950).

*Anal.* Calcd for $C_{16}H_{13}NO_2$: C, 76.47; H, 5.22; N, 5.57. Found: C, 76.35; H, 5.20; N, 5.51.

**2,3-Dihydro-5-methoxy-7(7*H*)-dibenzo[*de*,*h*]quinolone (4a).**—Condensation of 27 g (0.149 mol) of homoveratrylamine and 22.5 g (0.150 mol) of phthaldehydic acid in 300 ml of toluene or benzene, with or without 0.5–1.0 g of $TSO_3H$ (1.5-hr reflux under water trap), gave a crude, acid-soluble, viscous oil, ir 5.68 μ (**1b**). This syrup and 425 g of PPA were heated 0.7 hr on a steam cone with stirring. The cooled material was treated with 1.5 l. of ice and water and stirred 1–2 hr. The deep red, aqueous solution was separated from dark, tarry residue by decantation and filtration and made basic by gradual addition (ice bath) of 20% NaOH solution. Crude, orange-brown crystals which separated were collected, washed with water, and dried, yield 13.5 g (34%). On trituration with methanol there was obtained 10.3 g (26%) of orange-yellow crystals: mp 163–166° dec; mass spectrum M 293 (very weak), 279 (*ca.* 6–10%), and 263 (90% or more). Recrystallization from ethanol or methanol gave **4a** as yellow crystals, mp *ca.* 170° dec, still somewhat contaminated with phenolic material although sufficiently pure for further reactions: mass spectrum $M^+$ 263 with *m/e* 236 (−HCN), 248 (−$CH_3$), and 219, as well as *m/e* 279 (relative intensity *ca.* 5%) and 262 (−OH). The 279 phenolic constituent was still present after treatment of the material with warm 21% NaOH solution.

The compound was relatively insoluble in EtOAc, acetone, and DMSO. It did not react with diazomethane, with iodomethane (DMF) or methyl sulfate, or with $Ac_2O$ at 100°.

The crude cyclization product, before recrystallization or trituration with solvents, was found to consist of 15% of the phenolic compound, which was isolated and characterized as follows. Preparative tlc ($CHCl_3$ solution, on silica) with 0.65 g of crude, orange crystals gave (fraction 1) 110 mg (17%) of orange crystals: mp 163–167° dec; $R_f \simeq 2.5$; $FeCl_3$ test deep blue-green; mass spectrum $M^+$ 293:$M^+$ 279 (1:8 intensity ratio). Trituration and recrystallization of the sample from EtOAc gave orange needles (**4b**): mp 173.5–174.5° dec; ir 6.10–6.18 (rel weak, chelated) and 6.29 μ; uv 240, 278, 324, and 428–430 nm (log ε 4.53, 4.13, 3.82, and 3.71, respectively); $M^+$ 279.

*Anal.* Calcd for $C_{17}H_{13}NO_3$: C, 73.11; H, 4.69; N, 5.02. Found: C, 73.31; H, 4.82; N, 4.94.

Fraction 2 from tlc [529 mg (81%), mp 166–170° dec, $R_f \simeq 3.5$, $FeCl_3$ negative, $M^+$ 263] was essentially pure **4a**. Recrystallization from methanol gave yellow crystals: mp 168–170° dec; ir 6.05 and 6.28 μ; uv 226, 248–252, 259, 275, 316, 364, and 380 nm (log ε 4.43, 4.34, 4.37, 4.26, 3.68, 3.57, and 3.62, respectively); nmr ($CDCl_3$) δ 8.5–7.5 (m, 5, aromatic protons at positions 6, 8, 9, 10, and 11), 6.95 (m, 1, $J \leq 3$ Hz, meta-coupled 4-proton), 4.13 (t, 2, $J$ = 7 Hz, 3-methylene), 3.9 (s, 3, $OCH_3$), and 2.85 (t, 2, $J$ = 7 Hz, 2-methylene).

*Anal.* Calcd for $C_{17}H_{13}NO_2$: C, 77.55; H, 4.98; N, 5.32. Found: C, 77.42; H, 4.97; N, 5.22.

Fraction 3 from tlc [16 mg (2.5%), mp *ca.* 165–170°, $R_f \simeq 5.5$, $FeCl_3$ negative], had mass spectral peaks at 261 and 231 (intensity ratio 2:1), presumably representing monomethoxy (**5**) and deoxy aromatized compounds, respectively.

**2,3-Dihydro-2-methyl-5,6-methylenedioxy-7(7*H*)-dibenzo[*de*,*h*]quinolone (4c).**—Similar cyclization of 15 g of the crude condensation product (benzene) of phthalaldehydic acid and β-(3,4-methylenedioxyphenyl)isopropylamine (ir 5.68–5.72 μ) with 150 g of PPA at 100° for 20 min was accompanied by decomposition (dark brown, foaming). After hydrolysis with 1 l. of ice and water, the clarified, red solution was neutralized with NaOH. From the deep green solution there was slowly deposited (3 days, 0°) *ca.* 0.5 g of crystalline material, which was collected, washed with water, dried, and recrystallized from ethyl acetate, light orange crystals, tending to become greenish in air especially in the presence of solvents: mp 214–217° dec; ir 6.03 μ; uv 233 nm (ε 35,030), 405 (5480), and a series of inflections at 251 (21,540), 272 (16,270), and 319 (5750); nmr ($CDCl_3$) δ 8.4–8.2 (m, 2, protons 8 and 11), 7.8–7.5 (m, 2, protons 9 and 10), 6.9 (s, 1, 4-proton), 6.25 (s, 2, $OCH_2O$), 4.0 (m, 1, 2-methine), 3.2–2.5 (m, 2, 3-methylene), and 1.63 (d, 3, $CH_3$); mass spectrum $M^+$ 291 with peaks 276 (−$CH_3$), 263 (−CO), 264 (−HCN), 248 (−CO, −$CH_3$).

*Anal.* Calcd for $C_{18}H_{13}NO_3$: C, 74.21; H, 4.50; N, 4.81. Found: C, 73.97; H, 4.75; N, 4.75.

***o*-[β-(3,4-Dimethoxyphenylethyl)aminomethyl]benzoic Acid (2b).**—Hydrogenation (40 psi) of 8.7 g of crude **1b** in EtOAc (150 ml) in the presence of 5 g of 10% Pd/C at 50° for 2 hr afforded crystals: mp 165.5–167° dec (from ethanol); water soluble; ir broad aminium and carboxylate (6.12 μ) bands; uv 226 nm (ε 13,580) and 277 (3640).

*Anal.* Calcd for $C_{18}H_{21}O_4N$: C, 68.55; H, 6.71; N, 4.44. Found: C, 68.26; H, 6.80; N, 4.67.

Compound **2c**, similarly prepared from **1c**, had comparable properties, crystals from ethanol, mp 172.5–173.5° dec.

*Anal.* Calcd for $C_{18}H_{19}NO_4$: C, 68.99; H, 6.11; N, 4.47. Found: C, 68.64; H, 6.31; N, 4.40.

**5-Methoxy-7(7*H*)-dibenzo[*de*,*h*]quinolone (5).**—Compound **4a** (1.5 g) in xylene (250 ml) with 10% Pd/C catalyst (1.3 g) was refluxed 1 hr, and the suspension was filtered while hot. Evaporation of the solvent gave (quantitatively) crystalline residue. Recrystallization from ethyl acetate afforded golden yellow crystals: mp 180–181°; ir 6.03 μ and doublet 6.18–6.25 μ; uv 247, 311, and 382 nm (log ε 4.70, 3.72, and 3.99, respectively) with inflections at 275 (3.81), 302 (3.69), and 394 (3.99); nmr ($CDCl_3$) δ 8.8–7.1 (m, 8, aromatic protons, with one meta-

(14) J. Cohen and W. I. Taylor, *J. Org. Chem.*, **28**, 3567 (1963).

(15) S. F. Dyke and M. Sainsbury, *Tetrahedron*, **21**, 1907 (1965).

(16) T. Kametani, *et al.*, *J. Chem. Soc. C*, 1295 (1969).

(17) J. L. Neumeyer, K. H. Oh, K. K. Weinhardt, and B. R. Neustadt, *J. Org. Chem.*, **34**, 3786 (1969).

(18) M. Shamma and C. D. Jones, *ibid.*, **35**, 3119 (1970).

(19) Melting points were obtained using Thomas-Hoover silicone oil bath; uv curves (MeOH solutions) were measured with a Cary 14 recording spectrophotometer; ir spectra (Nujol mulls) were taken on a Perkin-Elmer 21 double-beam instrument; mass spectra were recorded using a MS-902 double-focusing apparatus. We are indebted to Miss Ruth Behnke for nmr spectra (Varian A-60; TMS internal standard) and interpretation thereof, as well as to Mr. George Robertson, Mr. Rudolf Oeckinghaus, Dr. Reginald Puckett, Miss Barbara Biffar, Miss Natalie Cahoon, Mr. Charles Navarro, Mr. Anis Hamden, and Mr. Mike Hotolski of the staff of Mr. Louis Dorfman for microanalytical and spectral data, and to Mr. B. Korzun for chromatographic work.

coupled 6-proton discernible *ca.* δ 8.04; $J$ = 2.5 Hz), 3.92 (s, 3, $OCH_3$); mass spectrum $M^+$ 261 with 231 ($-OCH_3$), 203 ($-CO$), and $M^+$ 277 (low intensity).

*Anal.* Calcd for $C_{17}H_{11}NO_2$: C, 78.15; H, 4.24; N, 5.36. Found: C, 77.91; H, 4.36; N, 5.47.

**5-Methoxy-7-hydroxy-1,2,3,11b-tetrahydro-7*H*-dibenzo[*de*,*h*]quinoline (6).**—Treatment of a suspension of **4a** in methanol with an excess (4–5 parts by weight) of $NaBH_4$ resulted in effervescence and solution of the material. After heating on a steam cone 20 min while evaporating most of the methanol, the cooled residue was treated with water. The collected, washed (water), and dried product, on recrystallization from methanol, gave colorless crystals: mp 191–193°; ir 6.18 μ (weak) together with bonded OH and NH bands; uv 276 nm (ε 1960) and 284 (2010).

*Anal.* Calcd for $C_{17}N_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.65; H, 6.58; N, 5.28.

The compound gave temporary, intense blue (or red) colors with strong acids.

***N*-Acetyl derivative 7** was obtained by warming a sample of the basic carbinol **6** with excess acetic anhydride at 100° for 1.5 hr. The solution was evaporated and the residue recrystallized from ethyl acetate, giving colorless crystals: mp 225–227°; ir 2.92 and 6.14 μ; uv 276 nm (ε 1810) and 283 (1870); nmr (DMSO) δ 7.83–6.6 (m, 6, aromatic protons), 6.36 (d, 1, $D_2O$ exchange, OH), 5.9–5.4 (m, 2, benzhydryl protons), 3.74 (s, 3, $OCH_3$), 3.1–2.6 (m, 4, methylene protons), and 2.33–2.07 (complex s, 3, $NHCOCH_3$).

*Anal.* Calcd for $C_{19}H_{19}NO_3$: C, 73.76; H, 6.19; N, 4.53. Found: C, 73.84; H, 6.25; N, 4.38.

***O*,*N*-Diacetyl derivative 8** was obtained by refluxing **6** or **7** (1 g) with acetic anhydride (45 ml) for 4 hr. Evaporation, trituration of the brown-yellow residue with ether–ethyl acetate, and recrystallization from methanol gave slightly yellowish crystals: mp 188–190°; ir 5.71 and 6.07 μ; uv 278–279 nm (ε 1900); nmr ($CDCl_3$) δ 7.4–6.55 (m, 6, aromatic protons), 6.08 (broad s, 1, 7-proton), 5.43 (s, 1, 11b-proton), 3.8 (s, 3, $OCH_3$), 3.1–2.7 (m, 4, methylene protons), and 2.5–2.17 (m, 6, $COCH_3$; complexity of the latter signals indicating more than one isomer and/or slight contamination with a phenol acetate).

*Anal.* Calcd for $C_{21}H_{21}NO_4$: C, 71.78; H, 6.02; N, 3.99. Found: C, 71.76; H, 6.12; N, 3.93.

Hydrogenation of **7** or **8** in glacial HOAc in the presence of 10% Pd/C at 60–70° (3 hr) apparently led to hydrogenolysis of both benzhydryl (9,10-dihydroanthracene) groups and also to reduction of one of the aromatic rings, *i.e.*, to a crystalline **2-methoxy-4-(β-acetylaminoethyl)octahydroanthracene**, crystals from ether: mp 147–148°; ir 3.04, 6.12, and 6.45 μ; uv 274 nm (ε 1510) and 283 (1690).

*Anal.* Calcd for $C_{19}H_{27}NO_2$: C, 75.71; H, 9.03; N, 4.65. Found: C, 75.76; H, 9.06; N, 4.58.

**Registry No.**—**2b**, 28399-68-0; **2c**, 28455-52-9; **3**, 17416-64-7; **3** HCl, 28399-70-4; **4a**, 28399-71-5; **4b**, 28399-72-6; **4c**, 28399-73-7; **5**, 28399-74-8; **6**, 28399-75-9; **7**, 28399-76-0; **8**, 28399-77-1; 12b-hydroxy-5,6,8,-12b-tetrahydro-8-isoindolo[1,2-*a*]isoquinolone, 28455-53-0; 2-methoxy-4-(β-acetylaminoethyl)ctahydroanthracene, 28390-69-4.

# Polycyclic Orthoquinonoidal Heterocycles. Thieno[3,4-*b*]quinoline and Naphtho[2,3-*c*]thiophene

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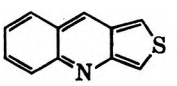
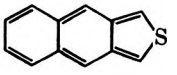
The formation of transient thieno[3,4-*b*]quinoline (**1**) and naphtho[2,3-*c*]thiophene (**2**) has been demonstrated in the synthesis of the exo NPMI adduct of **1** and a mixture of the exo and endo NPMI adducts of **2**. These adducts were isolated and characterized. Attempts to prepare **1** by the dehydration of 1,3-dihydrothieno[3,4-*b*]-quinoline 2-oxide (**8**) and dehydrogenation of 1,3-dihydrothieno[3,4-*b*]quinoline (**7**) were unsuccessful as were attempts to prepare **2** *via* the analogous dehydration of 1,3-dihydronaphtho[2,3-*c*]thiophene 2-oxide (**10**) The stabilities of **1** and **2** are discussed relative to one another and with regard to systems incorporating similar structural features.

This paper describes the attempted synthesis of thieno[3,4-*b*]quinoline (**1**) and naphtho[2,3-*c*]thiophene (**2**) from their precursor sulfoxides, 1,3-dihydrothieno-



**1**

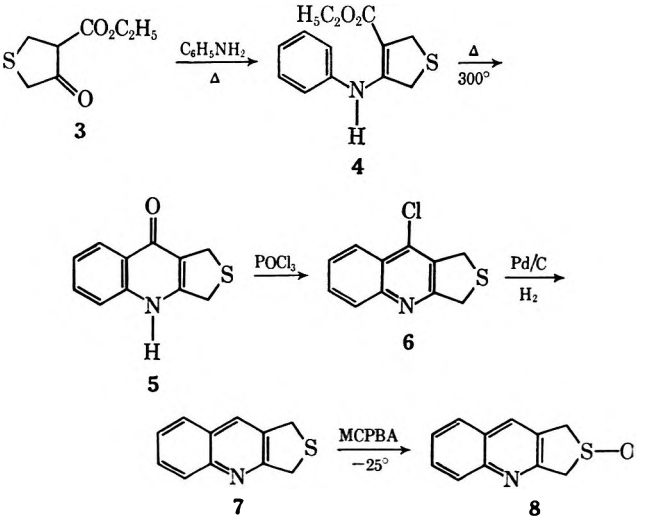


**2**

[3,4-*b*]quinoline 2-oxide (**8**) and 1,3-dihydronaphtho-[2,3-*c*]thiophene 2-oxide (**10**), or their precursor sulfides, 1,3-dihydrothieno[3,4-*b*]quinoline (**7**) and 1,3-dihydronaphtho[2,3-*c*]thiophene (**9**), in order to ascertain their relative stabilities compared to naphtho[1,2-*c*]thiophene.[2]

**Synthesis of 1,3-Dihydrothieno[3,4-*b*]quinoline 2-Oxide (8).**—The synthesis of **8** was accomplished as outlined in Scheme I. Reaction of aniline and ethyl 3-ketotetrahydrothiophene-4-carboxylate (**3**) following the procedure of Brown, *et al.*,[3] gave ethyl 3-anilino-2,5-dihydrothiophene-4-carboxylate (**4**) in 78% yield.

Scheme I




The occurrence of the imino tautomer of **4** was excluded by the presence of a sharp N–H stretching band at 3200 $cm^{-1}$ in its infrared spectrum. Thermal ring closure to 4*H*-1,3,4,9-tetrahydrothieno[3,4-*b*]-quino-

(1) NDEA Fellow, 1967–1970.

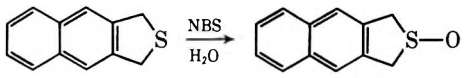
(2) M. P. Cava and N. M. Pollack, *J. Amer. Chem. Soc.*, **88**, 4112 (1966).

(3) R. J. Brown, F. W. S. Carver, and B. L. Hollingsworth, *J. Chem. Soc.*, 2624 (1962).

lin-9-one (**5**) was accomplished in 69–84% yield.[3] The ketone **5** was oxidized to 9-chloro-1,3-dihydrothieno[3,4-*b*]quinoline (**6**) by brief treatment with refluxing phosphoryl chloride in 80% yield. Reduction to **7** was accomplished in 63% yield using 5% Pd on charcoal in 2% ethanolic potassium hydroxide solution.[4] Selective oxidation of **7** to **8** was carried out in 63–66% yield using 1 equiv of *m*-chloroperbenzoic acid in methylene chloride at −25° to −30°.[5] The use of sodium metaperiodate to attain this product gave unsatisfactory results.

**Synthesis of 1,3-Dihydronaphtho[2,3-*c*]thiophene 2-Oxide (10).**—The synthesis of **10** is shown in Scheme II. Oxidation of 1,3-dihydronaphtho[2,3-*c*]thiophene[6]

SCHEME II




**9** **10**

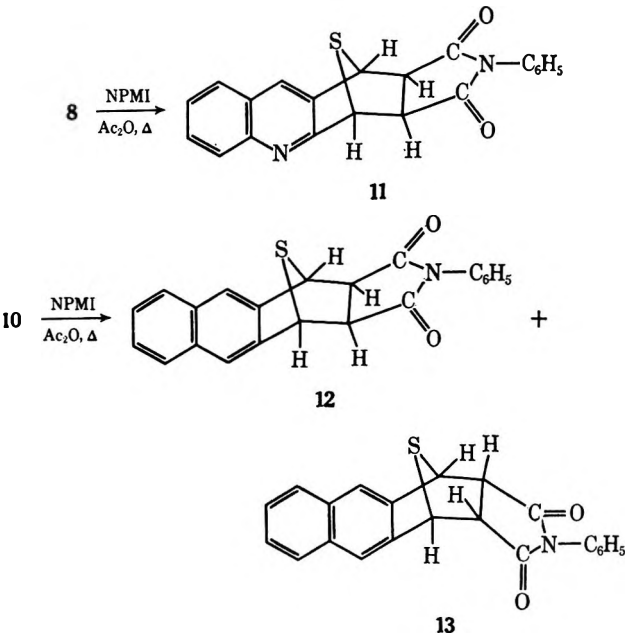
(**9**) was carried out in 69–73% yield using aqueous NBS as described by Oae and coworkers.[7]

**Pyrolysis Experiments.**—Attempts to isolate **1** and **2** by pyrolytic dehydration of mixtures of **8** and **10** with neutral alumina yielded only unreacted starting material and some colored amorphous material. Attempts to prepare **1** by the catalytic pyrolytic dehydrogenation technique of Meyer, *et al.*,[8] were also unsucessful.

**Trapping Experiments.**—The transient existence of **1** was demonstrated when its exo NPMI adduct was isolated in low yield from a mixture of **8** and NPMI in refluxing acetic anhydride. Monitoring the reaction by tlc indicated that all of **8** was consumed after 20 min. The basis for the structure of **11** lies in its elemental analysis and ir, nmr, and mass spectra.

In an identical manner **10** was dehydrated in the presence of NPMI in refluxing acetic anhydride. The isolation of a mixture of the exo and endo NPMI adducts **12** and **13** in 68% yield confirms the existence of **2**. Tlc separation of the mixture afforded the individual components **12** and **13** which were present in an approximately 1:1 ratio (Scheme III).

SCHEME III




## Discussion

Although **11** and **12** are similar systems, their nmr spectra show significant differences. The spectrum of **12** (DMSO-$d_6$) exhibits singlets at $\tau$ 4.90 and 6.50 for the bridgehead hydrogens and hydrogens $\alpha$ to the imido carbonyls, respectively. Compound **11** ($CDCl_3$), on the other hand, also shows a singlet at $\tau$ 4.90 for the bridgehead hydrogens when, in theory, one would expect two singlets due to their chemical nonequivalence. Attempts to record the spectrum of **11** in DMSO-$d_6$ and chlorobenzene were unsuccessful due to solubility problems. The hydrogens $\alpha$ to the imido carbonyls in **11** show an AB pattern at $\tau$ 6.50. It is interesting that the bridgehead hydrogens of **11** are a singlet even though they are closer to the point of nonequivalence than the hydrogens $\alpha$ to the imido carbonyls which show an AB pattern. In **13** the splitting patterns and chemical shifts of the aliphatic hydrogens and the 1 and 4 hydrogens on the naphthalene ring are different due to the stereochemistry of the endo adduct. A broad two-proton multiplet between $\tau$ 3.80 and 4.15 arises from the 1 and 4 hydrogens on the naphthalene ring. These hydrogens are shifted out of the normal aromatic region of the $\alpha$-imido carbonyl groups. A similar phenomenon has been observed by Cava[2] in the endo NPMI adduct of benzo[*c*]thiophene. The chemical shifts of the bridgehead hydrogens and the hydrogens $\alpha$ to the imido carbonyls of **13** are centered at $\tau$ 4.85 and 5.85 and are multiplets.

Both **11** and **12** exhibit identical infrared spectra from 800 to 600 $cm^{-1}$ which are easily distinguishable from that of **13**. These distinctive patterns provide a useful means of distinguishing between the two NPMI stereoisomers.

The failure to isolate **1** and **2** under the conditions of the pyrolytic dehydration reaction is due to the polycyclic orthoquinonoidal structures of **1** and **2** arising from *c* fusion of the thiophene nucleus at the 2,3 bond of the quinoline and naphthalene nuclei, respectively. Naphtho[1,2-*c*]thiophene[2] which precludes structures of the type drawn for **1** and **2** has been isolated in 50% yield by the pyrolytic dehydration method. In addition, it is well known that the reactivity in the acene series increases with increasing linear annelation within the series. This enhanced reactivity is caused by the increased amount of orthoquinonoidal character present in these molecules.[9] A similar explanation can be evoked for the failure of the dehydrogenation of **7** to give **1**.

It is interesting to note the increased stability incorporated into several otherwise very unstable orthoquinoid type systems by the symmetrical addition of

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(6) M. P. Cava and R. L. Shirley, *J. Amer. Chem. Soc.*, **82**, 654 (1960).

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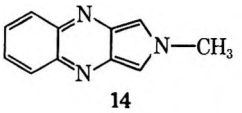
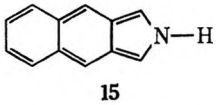
(8) R. Meyer, H. Kleinert, S. Richter, and K. Gewald, *J. Prakt. Chem.*, **20**, 244 (1963).

(9) (a) E. Clar, "Polycyclic Hydrocarbons," Vol. 1, Academic Press, New York, N. Y., 1964, Chapters 6 and 7; (b) G. M. Badger, "Aromatic Character and Aromaticity," Cambridge University Press, New York, N. Y., 1969, pp 18–24.

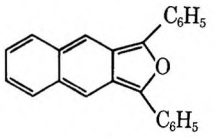
two nitrogen atoms. Thus, 2-methyl-2*H*-pyrrolo[3,4-*b*]quinoxaline[10] (**14**) is a stable solid, whereas 2*H*-naphtho[2,3-*c*]pyrrole (**15**) could only be trapped as its exo NPMI adduct.[11] Cava[12] has reported that 1,3-diphenylnaphtho[2,3-*c*]furan (**16**) decomposes in the solid state but 1,3-diphenylfuro[3,4-*b*]quinoxaline (**17**) is a stable crystalline solid.[13] Likewise, naphtho[2,3-*c*]-2,1,3-thiadiazole (**18**)[13] is a stable solid, but up until now only 2 has been trapped.



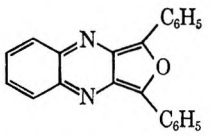

**14**



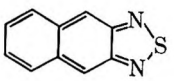

**15**



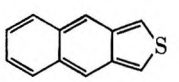

**16**




**17**




**18**




**2**

## Experimental Section[14]

**Ethyl 3-Anilino-2,5-dihydrothiophene-4-carboxylate (4).**—Aniline (43.6 g, 0.470 mol) was mixed with ethyl 3-ketotetrahydrothiophene-4-carboxylate[15] (**3**, 79.6 g, 0.457 mol) and refluxed for 7 min. After cooling, removal of 8.5 ml of water by azeotropic distillation with benzene, followed by work-up, gave 114 g of crystalline solid which was recrystallized from 2:1 acetone–hexane to give 63.3 g (55%) of solid: mp 73–76°; the analytical sample (acetone–hexane) melted at 72–73°; ir (KBr) 3200 (NH), 1655 $cm^{-1}$ (ester C=O); nmr ($CCl_4$) $\tau$ 0.10 (s, 1, NH), 2.8–3.2 (m, 5, aromatic), 5.8 (q, 2, $J$ = 7 Hz), 8.68 (t, 3, $J$ = 7 Hz).

*Anal.* Calcd for $C_{13}H_{15}NO_2S$: C, 62.65; H, 6.02; N, 5.62; S, 12.85. Found: C, 62.76; H, 6.02; N, 5.72; S, 13.10.

**4*H*-1,3,4,9-Tetrahydrothieno[3,4-*b*]quinoline (5).**—Ethyl 3-anilino-2,5-dihydrothiophene-4-carboxylate (**4**, 12 g, 0.0518 mol) was heated under reflux in a nitrogen atmosphere at 300°. After the initial temperature drop, the mixture was maintained at 290–300° until a vigorous evolution of ethanol accompanied by a cloud of smoke occurred. The solid residue was triturated with benzene to yield 69–84% of solid material which was used in the next step without further purification. An analytical sample (EtOH) had mp 345–347°; ir (KBr) 3000 (NH), 1600 $cm^{-1}$ (ketone C=O); nmr ($CF_3CO_2H$) $\tau$ 1.4–1.6 (mound, 1, NH), 2.0–2.6 (m, 4, aromatic), 5.3 (s, 2, $NCH_2$), 5.6 (s, 2, $CCH_2$).

*Anal.* Calcd for $C_{11}H_9NOS$: C, 65.02; H, 4.43; N, 6.89; S, 15.77. Found: C, 64.89; H, 4.49; N, 7.60; S, 15.48.

**9-Chloro-1,3-dihydrothieno[3,4-*b*]quinoline (6).**—4*H*-1,3,4,9-Tetrahydrothieno[3,4-*b*]quinolin-9-one (**5**, 10.0 g, 0.049 mol) and distilled phosphoryl chloride (85 ml) were refluxed together for 4 min. The mixture was cooled and poured onto ice and then neutralized with 2 l. of cold 2 *M* ammonium hydroxide. The resulting gray solid was filtered and air-dried to leave 8.73 g (81%) of solid, mp 140–141°. The solid was best purified by chromatography of a benzene solution over aluminum. An analytical sample was obtained by recrystallization from ethanol: mp 151–155°; nmr ($CDCl_3$) $\tau$ 1.7–2.5 (m, 4, aromatic), 5.4 (s, 2, $NCH_2$), 5.5 (s, 2, $CCH_2$).

*Anal.* Calcd for $C_{11}H_8ClNS$: C, 59.59; H, 3.61; N, 6.33; S, 14.47. Found: C, 59.79; H, 3.55; N, 6.17; S, 14.65.

**1,3-Dihydrothieno[3,4-*b*]quinoline (7).**—9-Chloro-1,3-dihydrothieno[3,4-*b*]quinoline (**6**, 1.0 g, 4.5 mmol) was dissolved in 300 ml of warm ethanol containing 2.8 g of potassium hydroxide. To this solution was added 0.50 g of 5% palladium on carbon, and the mixture was hydrogenated under a pressure of 40 lb/in.$^2$ for 1.5 hr, hydrogen uptake *ca.* 0.5 lb/in.$^2$ The filtrates from five such 1-g experiments were evaporated nearly to dryness and then dissolved in ethyl acetate. The solution was washed with water and brine and dried ($MgSO_4$). Evaporation left 3.11 g (73%) of yellow solid, mp 105.5–107.5°. In this manner 35 g of **6** was converted to **7** in yields ranging from 73 to 87% after recrystallization (63%, mp 106–108°). An analytical sample was prepared by recrystallization from hexane followed by sublimation: mp 110–111°; nmr ($CDCl_3$) $\tau$ 1.9–2.7 (m, 4, aromatic), 5.65 (s, 2, $NCH_2S$), 5.75 (s, 2, $CCH_2S$).

*Anal.* Calcd for $C_{11}H_9NS$: C, 70.55; H, 4.85; N, 7.48; S, 17.12. Found: C, 70.59; H, 4.88; N, 7.49; S, 17.11.

**1,3-Dihydrothieno[3,4-*b*]quinoline 2-Oxide (8).**—To a 1-l., three-necked flask fitted with an addition funnel, a low temperature thermometer, and a calcium chloride drying tube was added 1,3-dihydrothieno[3,4-*b*]quinoline (**7**, 4.0 g, 0.002 mol) in 250 ml of methylene chloride. This solution was cooled in a Dry Ice–acetone bath and was maintained between −25 and −30° during the addition of *m*-chloroperbenzoic acid (4.40 g, 83.4% purity, 0.002 mol) dissolved in 400 ml of methylene chloride. The addition required about 10 min. The temperature was maintained for an additional 5 min before *ca.* 20 ml of liquid ammonia was added to the solution. The cooling bath was removed and the turbid solution was allowed to warm to room temperature, filtered through Super-Cel, and dried ($MgSO_4$).

Removal of the solvent left 2.90 g (66%) of solid, mp 127–129°. Recrystallization from benzene afforded an analytical sample: mp 133–134°; ir (KBr) 1045 $cm^{-1}$ (SO); nmr ($CDCl_3$) $\tau$ 1.8–2.7 (m, 5, $C_9H_5N$), 5.61 (s, 2, $NCH_2S$), 5.68 (s, 2, $CCH_2S$).

*Anal.* Calcd for $C_{11}H_9NOS$: C, 65.00; H, 4.46; N, 6.89; S, 15.77. Found: C, 64.83; H, 4.55; N, 6.84; S, 15.64.

**1,3-Dihydronaphtho[2,3-*c*]thiophene 2-Oxide (10).**—1,3-Dihydronaphtho[2,3-*c*]thiophene[6] (**9**, 10.0 g, 5.38 × $10^{-3}$ mol) was dissolved in 900 ml of acetone. This solution was slowly diluted with 150 ml of water. To this yellow solution was added recrystallized *N*-bromosuccinimide (9.70 g, 5.45 × $10^{-2}$ mol) contained in 400 ml of 1:1 acetone and water over a 12-min period. The solution became colorless during addition but became yellow momentarily near the end of the addition period. The solution was allowed to stir 0.5 hr at room temperature and then the acetone was removed under reduced pressure. The white suspension was filtered and dried overnight under vacuum to leave 9.5 g (89%) of a gray solid. Recrystallization from methanol (Norite) left 7.6 g (69%) of a white solid, mp 199–201°. An analytical sample was obtained by recrystallization from methanol: mp 200.5–201°; nmr ($CDCl_3$) $\tau$ 2.0–2.65 (m, 6 H, aromatic), 5.75 (s, 4 H, $CH_2$).

*Anal.* Calcd for $C_{12}H_{10}OS$: C, 71.25; H, 4.98; S, 15.85. Found: C, 71.09; H, 5.11; S, 16.08.

***exo*-*N*-Phenylmaleimide Adduct of Thieno[3,4-*b*]quinoline.**—A mixture of 1.00 g (4.93 × $10^{-3}$ mol) of sulfoxide **8** and 0.855 g (4.94 × $10^{-3}$ mol) of *N*-phenylmaleimide were dissolved in 35 ml of freshly distilled acetic anhydride. The solution was protected under an atmosphere of dry nitrogen and refluxed for 20 min. The dark reaction mixture was poured into an ice–water mixture and extracted with chloroform. The chloroform solution was washed three times with water and twice with brine and dried ($Na_2SO_4$). Evaporation left 1.92 g of solid.

A portion of this solid (1.52 g) was partially dissolved in boiling benzene and placed on a column containing 140 g of neutral alumina. Elution with 1800 ml of benzene followed by elution with 5% ether:95% benzene caused the separation of a red band from the column. Evaporation of the appropriate benzene–ether fraction left 1.10 g of a brick red solid. Recrystallization from acetonitrile gave 0.30 g of a pink solid (17%), mp 268–269°. Further recrystallization produced an analytical sample: mp 278.5–279°; ir (KBr) 1775, 1700, 785 (m), 750 (s), 745 (sh), 685 $cm^{-1}$ (m); nmr ($CDCl_3$) $\tau$ 1.9–2.8 (m, 10), 4.90 (s, 2, bridgehead), 6.30–6.45 (q, 2, *endo* H, $J$ = 7 Hz); mass spectrum (70 eV; source 125°, probe, 225°) *m/e* (rel intensity) 330 (4), 359 (13),

(10) R. C. Anderson and R. H. Fleming, *Tetrahedron Lett.*, 1581 (1969).

(11) J. E. Shields and J. Bornstein, *Chem. Ind. (London)*, 1404 (1967).

(12) M. P. Cava and J. P. van Meter, *J. Org. Chem.*, **34**, 538 (1969).

(13) M. J. Haddadin, A. Yavroian, and C. Issidorides, *Tetrahedron Lett.*, 1409 (1970).

(14) All temperature readings are uncorrected. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn. Nuclear magnetic resonance spectra were recorded on a Varian HA-60 spectrometer using tetramethylsilane as an internal standard ($\tau$ 10) and solvents as specified. Infrared spectra were recorded on a Perkin-Elmer Model 127 and Beckman IR-8 spectrophotometer.

(15) G. B. Brown, B. R. Baker, S. Bernstein, and S. R. Safir, *J. Org. Chem.*, **12**, 155 (1947).

358 (82), 211 (3), 187 (7), 186 (16), 185 (100), 179 (11), 118 (4), 167 (4), 140 (3).

*Anal.* Calcd for $C_{21}H_{14}O_2N_2S$: C, 70.37; H, 3.94; N, 7.82; S, 8.95. Found: C, 70.62; H, 3.82; N, 7.89; S, 8.72.

*N*-Phenylmaleimide Adducts of Naphtho[2,3-*c*]thiophene.—Into a 250-ml flask was added 1,3-dihydronaphtho[2,3-*c*]thiophene 2-oxide (**10**, 1.0 g, 4.95 mmol), *N*-phenylmaleimide (0.86 g, 4.96 mmol), and 20 ml of acetic anhydride under dry nitrogen. The mixture was refluxed for 20 min. The yellow solution was cooled slightly and the excess acetic anhydride removed under reduced pressure to leave 1.80 g (101%) of a yellow crystalline solid. The separation of the isomeric adducts is detailed as follows.

Exo Adduct.—The yellow solid was recrystallized from acetonitrile to give 0.60 g (34%) of white solid. An analytical sample was obtained by recrystallization from chloroform–hexane: mp 281.5–282.5°; ir (KBr) 1765, 1700 (broad, imido C=O), 790 (m), 745 (s), 740 (sh), 690 $cm^{-1}$ (m); nmr (DMSO-$d_6$) $\tau$ 2.2–3.05 (m, 11, aromatic), 4.89 (s, 2, bridgehead), 6.50 (s, 2, endo H); mass spectrum (70 eV; source 250°, probe 150°) *m/e* (rel intensity) 357 (9.7), 325 (3.1), 186 (5.9), 185 (13.8), 184 (100), 178 (10).

*Anal.* Calcd for $C_{22}H_{15}NO_2S$: C, 73.92; H, 4.23; N, 3.92; S, 8.97. Found: C, 73.89; H, 4.06; N, 3.73; S, 9.10.

Endo Adduct.—This isomer was separated by preparative thin layer chromatography on a 20 × 20 cm 1000-$\mu$ silica gel $PF_{254}$ plates which had been activated 3 hr at 120°. Samples of 100 mg each, obtained in ether, were spread on the plates. Each plate was developed twice in 95% benzene–5% ethyl acetate in a presaturated chamber. Each plate was allowed to dry thoroughly between developments. The slower moving band from seven plates was scraped off and extracted with chloroform to yield 0.318 g of white solid. An analytical sample was obtained by recrystallization from ethanol: mp 214.5–215.5°; ir (KBr) 1775, 1700 (broad, imido C=O), 745 (s), 715 (s), 680 $cm^{-1}$ (m); nmr ($CDCl_3$) $\tau$ 2.2–2.85, 2.9–3.3 (m, 9, aromatic), 3.8–4.15 (m, 2, H-1 and -4 on the naphthalene ring), 4.9 (m, 2, bridgehead), 5.8–6.0 (m, 2, exo hydrogens); mass spectrum (70 eV; source 275°, probe 110°) *m/e* 357 (9.3), 325 (2), 186 (6.4), 185 (13.7), 184 (100), 178 (6.4).

*Anal.* Found: C, 73.96; H, 4.23; N, 3.99; S, 9.05.

**Registry No.**—**4**, 28237-98-1; **5**, 28237-99-2; **6**, 28238-00-8; **7**, 28238-01-9; **8**, 28312-62-1; **10**, 28238-02-0; **11**, 28238-03-1; **12**, 28238-04-2; **13**, 28238-04-2.

**Acknowledgment.**—The authors wish to thank Messrs. Bruce Heitke and James C. Wisowaty for recording the nmr spectra and Mr. Robert Smith for recording the mass spectra.

# The Aromatization of Some Cyclopropene Adducts. An Approach to the Naphtho[*b*]cyclopropene System

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*Received September 1, 1970*

1,3-Diphenylisobenzofuran (**4**) reacts with cyclopropene, 1-methylcyclopropene, and 1,2,3-triphenylcyclopropene to give the Diels–Alder adducts **5**, **16**, and **17**, all of which are the exo isomers. Attempted dehydration of **5** to 2,7-diphenylnaphtho[*b*]cyclopropene (**3**) could not be effected, although a variety of transformation products of **5** was isolated and identified. Several acid-catalyzed transformations of **16** and **17** were also studied. All evidence points to the nonintermediacy of **3** in the acid-catalyzed reactions of **5**.

Benzocyclopropene (**1**) is the most highly strained member of the benzocycloalkene series. Since 1964 the synthesis of the very reactive but isolable **1**[2a] and of a number of its substitution products[2b] has been reported. No example of any other condensed cyclopropane aromatic system exists in the literature.[3]

The work described in this paper had as its main goal the synthesis of a derivative of naphtho[*b*]cyclopropene (**2**), a system in which the central ring might be expected to show a high degree of bond fixation. 2,7-Diphenylnaphtho[*b*]cyclopropene (**3**) was chosen as a convenient synthetic objective, since it appeared to be readily accessible by the Diels–Alder addition of cyclopropene to 1,3-diphenylisobenzofuran (**4**), followed by acid-catalyzed dehydration of the resulting adduct **5**. The corresponding naphtho[*b*]cyclobutene derivative **6** has indeed been synthesized from cyclobutene by an exactly analogous route.[4]

## Results and Discussion

Cyclopropene was found to add to 1,3-diphenylisobenzofuran (**4**) to give a single crystalline adduct, mp 95–96°. This adduct was assigned the structure of the exo isomer **5** on the basis of its nmr spectrum, which indicated considerable deshielding of one of the two cyclopropane methylene protons ($\delta$ ~1.75 and ~1.15) by the oxido bridge.[5,6]

Reaction of adduct **5** with hydrogen chloride in benzene at room temperature led to a good yield of 1,4-diphenyl-2-chloromethylnaphthalene (**7**), no other product being detectable by tlc. The formation of chloride **7** could be explained as involving the formation of the desired cyclopropene **3** as a transient intermediate, followed by ring opening of **3** by hydrogen chloride. On the other hand, **3** might never be formed and formation of **7** could proceed by way of direct nucleophilic attack of chloride ion on the methylene of the cyclopropyl carbinyl cation **8**.

In an attempt to dehydrate **5** under milder conditions, it was heated in chloroform solution in the presence of a cation exchange resin (Dowex 50W X-2), which was later found to contain some chloride ion. The minor reaction product (16%) was again chloride **7**, but the

(1) Author to whom correspondence should be directed.

(2) (a) E. Vogel, W. Grimme, and S. Korte, *Tetrahedron Lett.*, 3625 (1965). (b) R. Anet and F. A. L. Anet, *J. Amer. Chem. Soc.*, **86**, 525 (1964); G. L. Closs, *Advan. Alicycl. Chem.*, **1**, 64 (1966); G. L. Closs, L. R. Kaplan, and V. I. Bendall, *J. Amer. Chem. Soc.*, **89**, 3376 (1967); E. Vogel, S. Korte, W. Grimme, and H. Günther, *Angew. Chem., Int. Ed. Engl.*, **7**, 289 (1968).

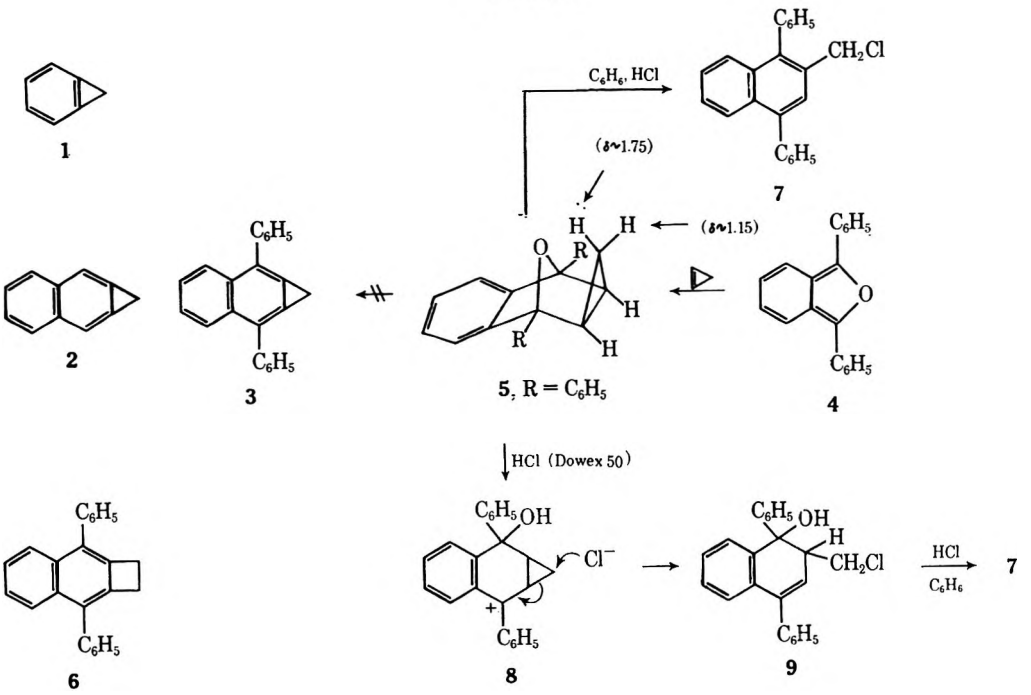
(3) A compound originally believed to be a keto tautomer of a naphtho[*b*]cyclopropenediol was subsequently shown not to contain a three-membered ring: L. F. Fieser and M. A. Peters, *J. Amer. Chem. Soc.*, **53**, 4080 (1931); A. R. Bader and M. G. Ettlinger, *ibid.*, **75**, 730 (1953).

(4) C. D. Nenitzescu, M. Avram, I. G. Dinulescu, and G. Mateescu, *Justus Liebigs Ann. Chem.*, **653**, 79 (1962).

(5) M. P. Cava and F. M. Scheel, *J. Org. Chem.*, **32**, 1304 (1967).

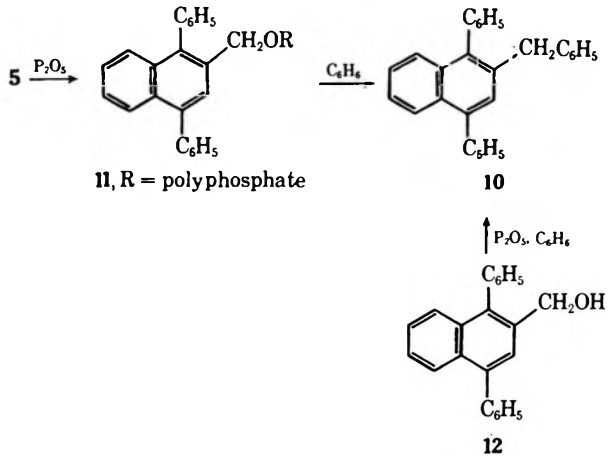
(6) Other investigators have mentioned in the footnote of a recent paper that they have synthesized adduct **5**: M. A. Battiste and C. T. Sprouse, Jr., *Tetrahedron Lett.*, 3165 (1969).

SCHEME I

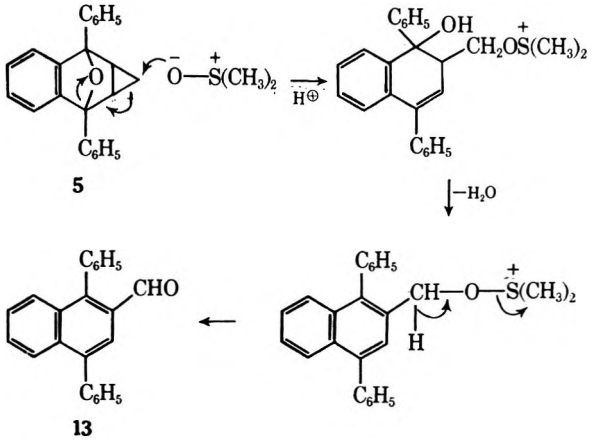


major reaction product (70%) was a compound which was assigned the chlorohydrin structure **9** on the basis of mass spectral, nmr, and analytical data. In accord with structure **9**, the mass spectrum of the compound showed significant peaks due to the loss of either water or hydrogen chloride. Its nmr spectrum showed an exchangeable hydroxyl proton at $\delta$ 2.35 and a single olefinic proton doublet ($J$ = 2.5 Hz) at $\delta$ 6.15, as well as aromatic protons and a three-proton multiplet in the region $\delta$ 3.45–3.65. As anticipated, **9** reacted immediately with hydrogen chloride in benzene to give the fully aromatic halide **7**. The isolation of chlorohydrin **9** in this experiment strongly suggests that the naphthocyclopropene **3** is in fact not an intermediate in the conversion of adduct **5** to the benzylic chloride **7** (Scheme I).

The reaction of adduct **5** with phosphorus pentoxide in benzene afforded a single product which was assigned the structure of 1,4-diphenyl-2-benzylnaphthalene (**10**) on the basis of mass spectral, nmr, and analytical data. The initial naphthalenic reaction product is probably a polyphosphate ester **11** of the benzyl alcohol **12**, which then attacks the solvent in a Friedel–Crafts alkylation process. In accord with this scheme, the known alcohol **12** was found to give hydrocarbon **10** on reaction with phosphorus pentoxide in benzene.



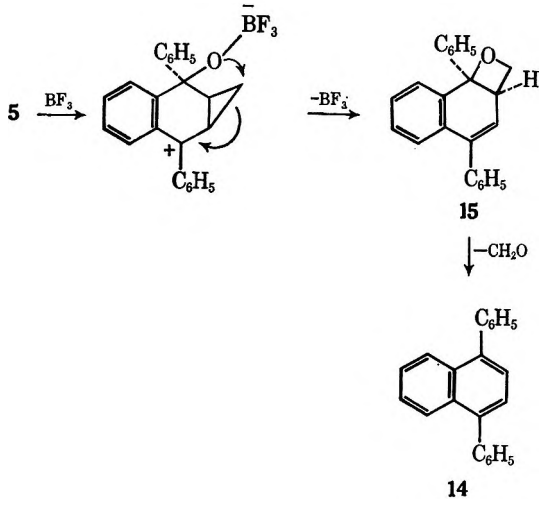
In an attempt to dehydrate **5** thermally under neutral conditions, the adduct was heated for a short time to 180° in dimethyl sulfoxide solution. The sole reaction product isolated (42% yield) was the known 1,4-diphenylnaphthalene-2-carboxaldehyde (**13**). The key step in the formation of **13** would appear to be a nucleophilic opening of the cyclopropane ring of **5** by the sulfoxide oxygen as shown below. Related ring-opening reactions of three-membered heterocycles by dimethyl sulfoxide have been recorded.[7]



Still different results were obtained when adduct **5** was treated with boron trifluoride etherate in ether solution. In addition to an unidentified product of molecular weight 392, 1,4-diphenylnaphthalene (**14**) was isolated. The unexpected formation of **14** may be rationalized by a reaction path involving formation of an oxetane intermediate **15** which aromatized to a naph-

(7) T. Durst, *Advan. Org. Chem.*, **6**, 354 (1965).

thalene by loss of formaldehyde. It will be noted that the assigned exo configuration of **5** is required for this mechanism.

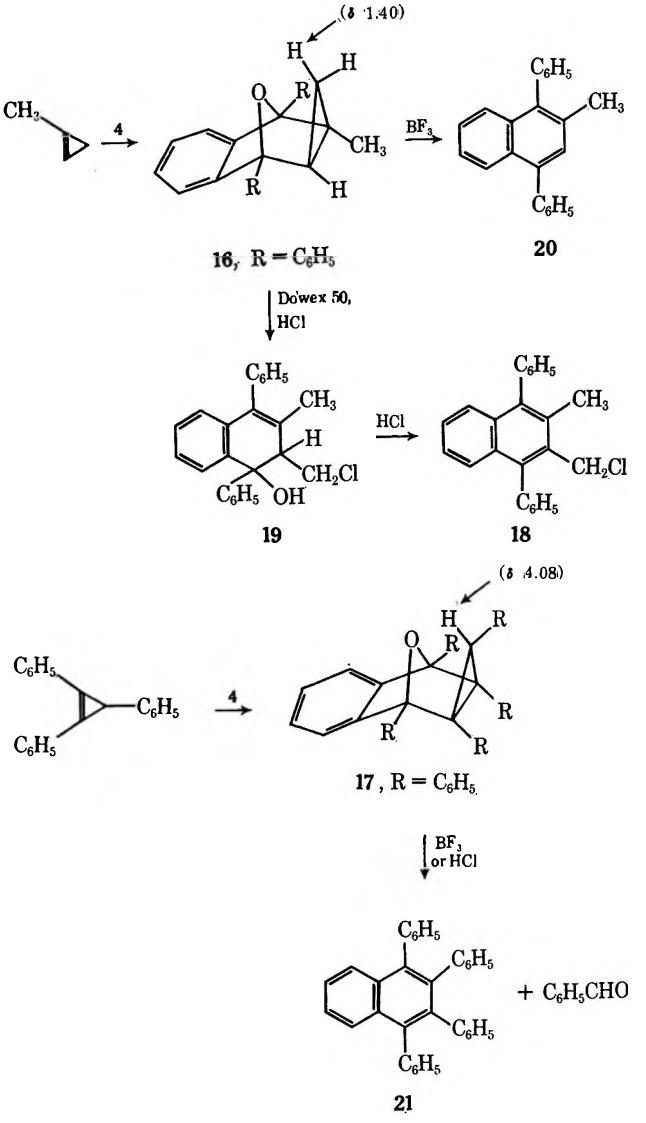



It seemed of interest to compare a few of the aromatization reactions of **5** with those of some related adducts which differ from **5** structurally in being incapable of giving a naphthocyclopropene by any direct dehydration process. In this connection, the adducts **16** and **17** were prepared from 1,3-diphenylisobenzofuran, 1-methylcyclopropene, and 1,2,3-triphenylcyclopropene, respectively. Although **16** was an oil, both **16** and **17** were homogeneous; they were assigned the exo configuration on the basis of their nmr spectra, both of which showed deshielding of one of the cyclopropane methylene protons by the oxido bridge.[5] The observed values for **16** ($\delta$ 1.40 and 1.00, $J$ = 7 Hz) were comparable to the corresponding values for **5**; coupling of the proton at 1.40 with the *trans*-cyclopropane proton at the ring junction ($\delta$ 2.10, $J$ = 2.5 Hz) was readily discernible. It should be pointed out, however, that these apparently obvious values were obtained by a first-order analysis, and they may not be entirely accurate. In the case of **17**, the deshielded proton appeared at $\delta$ 4.08, or 1.33 ppm further downfield than the aliphatic protons of the model compound *cis*-1,2,3-triphenylcyclopropane.[8-10]

Hydrogen chloride reacted with **16** in a manner strictly analogous to its reaction with the unmethylated adduct **5**. Thus, hydrogen chloride in benzene gave the naphthylmethyl chloride **18**; using Dowex 50 resin, the intermediate chlorohydrin **19** could be isolated. The reaction of boron trifluoride etherate with **16** was also similar to that of **5**; 1,4-diphenyl-2-methylnaphthalene (**20**) and an unidentified compound of mol wt 406 were isolated.

Adduct **17** underwent the expected fragmentation reaction in the presence of boron trifluoride etherate, affording 1,2,3,4-tetraphenylnaphthalene (**21**) in high yield. Hydrocarbon **21** was also formed from **17** by treatment with hydrochloric acid in acetic acid; in this experiment the second cleavage product, benzaldehyde, was also isolated in quantitative yield as its 2,4-dinitrophenylhydrazone (Scheme II).

SCHEME II




## Conclusion

We conclude from the experiments described that the naphtho[*b*]cyclopropene derivative **3** is not formed, even as an intermediate, in any of the aromatization reactions of adduct **5** which we have studied.[11] The reaction of **5** with acidic reagents follows a course quite different from that of the corresponding adduct of **4** with cyclobutene, which affords the normal dehydration product **6**.

(8) R. Breslow and P. Dowd, *J. Amer. Chem. Soc.*, **85**, 2729 (1963).

(9) The tendency of cyclopropenes to give exo adducts with **4** was pointed out during our study in a paper in which some adducts of **4** with various chlorinated cyclopropenes were reported: R. Breslow, G. Ryan, and J. T. Groves, *ibid.*, **92**, 988 (1970).

(10) For a very recent report of the formation of an exo adduct from **4** and 1,2-diphenylcyclopropene, see D. T. Longone and D. M. Stehouwer, *Tetrahedron Lett.*, 1017 (1970).

(11) After the completion of the manuscript of our paper, the following communication appeared [K. Geibel and J. Heindl, *ibid.*, 2133 (1970)] in which the reaction of cyclopropene with furan **4** was reported to give a 5.8:1 mixture of isomeric adducts, for which no physical data were given. The major adduct was converted by hydrochloric acid into compound **7** as in our study. The minor adduct was apparently obtained only in impure form and suffered ring cleavage (unlike the major adduct) simply on being passed through neutral alumina. Since our Diels–Alder products from cyclopropene and methylcyclopropene were purified by initial neutral alumina chromatography, it is apparent why we did not detect minor adducts from our reactions. Geibel and Heindl have assigned the endo configuration to their major stable adduct (our **5**) and the exo configuration to their minor unstable adduct. We believe that these assignments, for which no justification was given, must be reversed for reasons given in our discussion and in ref 9. (Note particularly in ref 9 the detection by nmr of a minor endo adduct, from **4** and chlorocyclopropene, which was too unstable to survive isolation by silica chromatography.)

## Experimental Section

Melting points were taken with a Thomas-Hoover apparatus and are uncorrected. Nmr spectra were obtained in deuteriochloroform with a Varian A-60 nmr spectrometer. Infrared spectra were taken with a Perkin-Elmer Model 137 infrared spectrophotometer. Elemental analyses were carried out by Midwest Microlab, Inc., Indianapolis, Ind. Molecular weights of all new compounds were confirmed by mass spectrometry using a Perkin-Elmer Model 270 instrument.

Isolation in the usual manner refers to extraction with ether or the organic solvent mentioned, washing the organic extract with water, followed by drying over magnesium sulfate, and evaporation of solvent under reduced pressure. Preparative tlc was carried out using silica gel (EM Reagent GF-254) coated on 20 × 20 cm glass plates (1-mm thickness) with hexane as the developer unless otherwise stated. The zones were detected by ultraviolet light, collected, and extracted with chloroform containing 3% MeOH.

The identity of known compounds was established by a comparison of ir spectra and by mixture melting point determinations with authentic samples obtained according to literature references given.

**Reaction of 1,3-Diphenylisobenzofuran (4) with Cyclopropene. Adduct 5.**—A stream of cyclopropene in nitrogen, generated from sodium amide (12 g, 0.3 mol) and allyl chloride (25 g, 0.3 mol),[12] was passed through a trap cooled in Dry Ice and then led into a solution of 1,3-diphenylisobenzofuran (4.05 g, 0.015 mol) in 250 ml of benzene at 20°. After the fluorescence had disappeared (2 hr), the benzene solution was worked up in the usual manner and the residue was chromatographed over neutral alumina using benzene as the eluent. The resulting oil (3.1 g), which was homogeneous by tlc, crystallized from hexane (50 ml) to give adduct **5** as colorless plates (1.95 g), mp 93–94°. In another run **5** was obtained from the same solvent as prisms, mp 66–67°. The two products are dimorphous as shown by comparison of nmr and ir spectra: nmr δ 1.1 (m, 1 H), 1.7–1.8 (m, 3 H), 7.0 (t, 4 H), 7.3–7.4 (m, 6 H), and 7.7 (m, 4 H).

*Anal.* Calcd for $C_{23}H_{18}O$: C, 89.00; H, 5.85. Found: C, 89.27; H, 5.99.

**Reaction of 5 with Hydrogen Chloride in Benzene.**—Adduct **5** (50 mg) was dissolved in 10 ml of dry benzene, and the solution was saturated with dry hydrogen chloride and then stirred at room temperature for 10 hr. The benzene solution was worked up in the usual manner to give a residue (45 mg) which crystallized from hexane to give chloride **7** (33 mg, 62%), mp 115–117° (lit.[13] 123°). Tlc examination of the mother liquor revealed the absence of any other product.

**Reaction of 5 with Phosphorus Pentoxide in Benzene. 1,4-Diphenyl-2-benzylnaphthalene (10).**—Adduct **5** (50 mg) was dissolved in 10 ml of dry benzene, 100 mg of $P_2O_5$ was added, and the reaction mixture was stirred at room temperature for 10 hr. The dark brown reaction mixture was then decomposed with ice and the product was isolated in the usual manner after preparative tlc as colorless crystals (31 mg, 52%) of **10**: mp 125–126°; nmr δ 3.95 (s, 2 H), 7.1 (t, 4 H), 7.2 (s, 1 H), 7.4 (m, 13 H), and 7.8 (m, 1 H).

*Anal.* Calcd for $C_{29}H_{22}$: C, 94.01; H, 5.99. Found: C, 93.71; H, 5.98.

Hydrocarbon **10** was prepared independently by stirring a solution of 1,4-diphenylnaphthalene-2-methanol[13] (**12**, 200 mg) in benzene (10 ml) with phosphorus pentoxide (500 mg) at room temperature for 2.5 hr. Isolation in the usual manner (ether) followed by preparative tlc (hexane–benzene, 5:1) afforded **10** (0.110 g) as feathery needles, mp 126–127°, after crystallization from hexane.

**Reaction of 5 with Cation Exchange Resin.**—Adduct **5** (500 mg) was dissolved in 20 ml of chloroform, Dowex 50W X-2 cation exchange resin (1 g) was added, and the mixture was stirred at room temperature for 4 hr. The solution was filtered and the filtrate was evaporated. The residue was resolved by preparative tlc into 70 mg of **7** (14.7%) and 406 mg (70%) of **9**. Compound **9** was purified by recrystallization from benzene–hexane (1:1) to give colorless plates: mp 125–127° (320 mg); nmr δ 2.35 (s, 1 H), 3.45 (m, 2 H), 3.65 (d, $J$ = 2.5 Hz, 1 H), 6.15 (d, $J$ = 2.5 Hz, 1 H), 6.92 (m, 1 H), 7.1 (q, 4 H), and 7.3 (m, 10 H).

Only erratic carbon analyses for this compound were obtained, although it analyzed well for chlorine and its molecular weight was confirmed by mass spectrometry.

*Anal.* Calcd for $C_{23}H_{19}ClO$: Cl, 10.22. Found: Cl, 10.48.

**Reaction of 9 with Hydrogen Chloride in Benzene.**—Compound **9** (30 mg) was dissolved in 10 ml of dry benzene, and the solution was saturated with dry hydrogen chloride and then stirred at room temperature for 10 min. Isolation in the usual manner gave chloride **7** (12 mg, 47%). Tlc examination of the mother liquor showed the absence of any other product.

**Reaction of 5 with Dimethyl Sulfoxide.**—Adduct **5** (50 mg) was dissolved in 3 ml of dimethyl sulfoxide and the solution was maintained at mild reflux for 15 min. After dilution with water, the product was isolated in the usual manner followed by silica gel chromatography (benzene eluent). Crystallization from hexane gave 23 mg (42%) of 1,4-diphenyl-2-naphthaldehyde (**13**) as colorless crystals, mp 146–148 (lit.[14] mp 145–147°).

**Reaction of 5 with Boron Trifluoride Etherate.**—Adduct **5** (50 mg) was dissolved in 10 ml of dry ether, a few drops of freshly distilled $BF_3$ etherate were added, and the colorless solution was stirred at room temperature for 12 hr. The usual isolation, followed by careful separation by preparative tlc, gave the following products: (a) 1,4-diphenylnaphthalene (**14**) (11 mg), colorless needles (hexane), mp 135–136° (lit.[14] mp 135–137°); (b) unidentified compound of mol wt 392, prisms (20 mg) from hexane.

**Reaction of Furan 4 with 1-Methylcyclopropene. Adduct 16.**—1-Methylcyclopropene, generated by the reaction of methallyl chloride (12 g) and sodium amide (5 g),[15] was led into a solution of furan **4** (1.0 g) in 30 ml of benzene. After the fluorescence had disappeared (5 hr), the solvent was removed and the residue was purified by chromatography over neutral alumina. A viscous oil (homogeneous by tlc) was obtained which could not be crystallized. However, the compound could be purified by distillation [bath temperature 160–180° (6 mm)]. A pale yellow liquid (602 mg) was obtained: nmr δ 1.0 (d, $J$ = 7 Hz, 1 H), 1.12 (s, 3 H), 1.4 (dd, $J$ = 7 Hz, $J$ = 2.5 Hz), 2.1 (t, $J$ = 2.5 Hz), 7.0–7.3 (m, 10 H), and 7.5–7.8 (m, 4 H).

*Anal.* Calcd for $C_{24}H_{20}O$: C, 88.85; H, 6.21. Found: C, 89.13; H, 6.27.

**Reaction of Adduct 16 with Hydrogen Chloride in Benzene.**—Adduct **16** (200 mg) was dissolved in 30 ml of dry benzene. The solution was saturated with hydrogen chloride and stirring was continued at room temperature for 0.5 hr. Isolation in the usual manner gave 162 mg (77%) of crystalline product which was recrystallized from hexane: mp 164–165°; 129 mg; nmr δ 2.35 (s, 3 H), 4.58 (s, 2 H), 7.2–7.6 (m, 14 H).

*Anal.* Calcd for $C_{24}H_{19}Cl$: C, 84.10; H, 5.58; Cl, 10.34. Found: C, 83.85; H, 5.58; Cl, 10.27.

**Reaction of Adduct 16 with Cation Exchange Resin.**—Adduct **16** (95 mg) was dissolved in 20 ml of dry chloroform, Dowex 50W X-2 cation exchange resin (1 g) was added, and the mixture was refluxed with stirring for 5 hr. The solution was filtered and the filtrate was evaporated. The residue was separated by preparative tlc into 11 mg of chloride **18** (4.7%) and 32 mg of chlorohydrin **19** (14.4%). Recrystallization of compound **19** from hexane gave colorless prisms, mp 150–152°. Its nmr spectrum showed, in addition to aromatic protons (14 H) centered around δ 2.8 and a methyl (3 H, s) at 1.62, the following pattern due to the nonequivalent protons ($H_A$ and $H_B$) of the chloromethyl group and a single proton ($H_C$) of the adjacent carbon: δ 4.12 ($H_A$, q), 3.66 ($H_B$, q), 3.10 ($H_C$, q), $J_{AB}$ = 10 Hz, $J_{AC}$ = 6 Hz and $J_{BC}$ = 7.5 Hz. Since attempted recrystallization of **19** resulted in decomposition, a satisfactory sample could not be prepared for analysis, although mass spectrometry confirmed its molecular weight.

**Reaction of Adduct 16 with Boron Trifluoride Etherate.**—Adduct **16** (100 mg) was dissolved in 10 ml of dry ether, a few drops of $BF_3$ etherate were added, and the solution was stirred at room temperature overnight. Tlc separation led to the isolation of the following products: (a) 1,4-diphenyl-2-methylnaphthalene (**20**, 25 mg), colorless needles (hexane), mp 128–129° (lit.[16] 129°); (b) unidentified compound of mol wt 406 (14 mg).

**Reaction of Furan 4 with 1,2,3-Triphenylcyclopropene. Adduct 17.**—A solution of 1,2,3-triphenylcyclopropene[8] (1.00 g)

(12) G. L. Closs and K. D. Krantz, *J. Org. Chem.*, **31**, 638 (1966).
(13) J. Robert, *C. R. Acad. Sci., Ser. C*, **223**, 906 (1946).
(14) A. Weiss, *Monatsh. Chem.*, **61**, 167 (1932).
(15) F. Fischer and D. E. Applequist, *J. Org. Chem.*, **30**, 2089 (1965).
(16) A. Etienne, A. Spire, and E. Toromanoff, *Bull Soc. Chim. Fr.*, 750 (1952).

and furan 4 (1.00 g) in benzene (10 ml) was refluxed for 5 hr. Crystallization from benzene–hexane yielded adduct 17 (1.50 g, 75%): mp 222–224° dec; nmr δ 4.1 (s, 1 H), 6.1–7.1 (m, 13 H), and 7.15–7.4 (m, 16 H).

*Anal.* Calcd for $C_{41}H_{30}O$: C, 91.41; H, 5.61. Found: C, 91.67; H, 5.90.

**Reaction of Adduct 17 with Acetic Acid and Hydrochloric Acid.**—Adduct 17 (100 mg) was dissolved in 2 ml of glacial acetic acid, two drops of concentrated hydrochloric acid were added, and the solution was heated under reflux for 3 hr. The solvent was removed *in vacuo* and the residue, which had a strong odor of benzaldehyde, was diluted with water. Isolation in the usual manner (ether) and separation by preparative tlc gave 1,2,3,4-tetraphenylnaphthalene (21), 64 mg (80%), mp 198–200°, identical with an authentic sample.

In another run, before extraction with ether, the reaction mixture was treated with 40 mg of 2,4-dinitrophenylhydrazine in ethanol solution. After stirring for 10 min, the precipitated hydrazone was filtered and washed with hexane to give 52 mg of 2,4-dinitrophenylhydrazone, mp 220–250°. Recrystallization from ethanol gave the pure derivative, mp 237–238°, identical with an authentic sample.

**Registry No.**—**5**, 28273-58-7; **9**, 28273-59-8; **10**, 28273-60-1; **16**, 28273-66-7; **17**, 28312-69-8; **18**, 28273-61-2; **19**, 28273-62-3.

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# The Tricyclo[5.2.0.0$^{2,5}$]nonane System[1,2]

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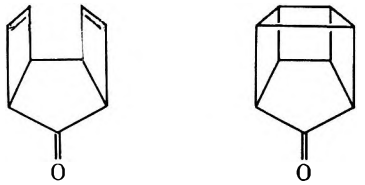
This paper describes the synthesis of *anti*-tricyclo[5.2.0.0$^{2,5}$]nonan-6-one (6), *syn*- and *anti*-tricyclo[5.2.0.0$^{2,5}$]-non-3-en-6-one (4 and 5), and *anti*-tricyclo[5.2.0.0$^{2,5}$]nona-3,8-dien-6-one (21), as well as some methylated derivatives of these tricyclic ketones. Irradiation of dienone 21 leads efficiently to homocubanone (2) *via* the syn dienone 1. Some transformations of the above tricyclic ketones, especially the β,γ-unsaturated ketones, are discussed.

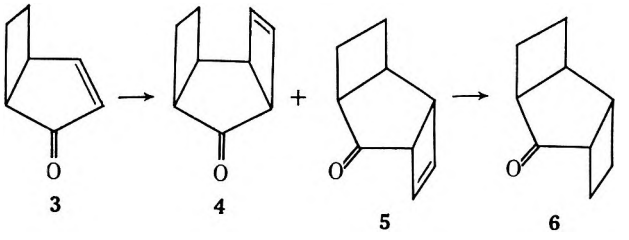
The obvious relationship of *syn*-tricyclo[5.2.0.0$^{2,5}$]-nona-3,8-dien-6-one (1) and homocubanone (2) led



1 2

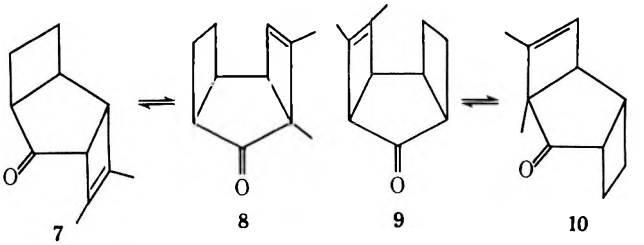
us to explore synthetic approaches to 1. In this paper we report syntheses of several members of the tricyclo-[5.2.0.0$^{2,5}$]nonane family as well as some of the transformations of these compounds.[3] In particular, the details of an efficient synthesis of homocubanone from cyclopentenone (14% overall yield) are presented.

Irradiation of bicyclo[3.2.0]hept-3-en-2-one (3)[4] with 1,2-chloroethylene followed by ketalization of the cycloadducts, dehalogenation, and hydrolysis provided a mixture of tricyclic ketones 4 and 5, ratio 2:98, in 75% overall yield.[5] The major isomer is assigned the anti configuration 5, since cycloaddition should occur predominantly from the less hindered face of 3. This assignment was confirmed by the identity of the hydrogenation product of the major enone and an authentic sample of *anti*-tricyclo[5.2.0.0$^{2,5}$]nonan-6-one (6) obtained as outlined later in this paper.



3 4 5 6

Photocycloaddition of ketone 3 and 2-butyne in methylene chloride produced a mixture of four isomeric tricyclic ketones 7–10 in 66% yield. The primary adducts 7 and 9 undergo subsequent photisomerization *via* the well-known allylic shift of carbonyl[6] to the isomeric ketones 8 and 10, respectively. Separate irradiation of pure 7 and of pure 8 gave the same photostationary-state mixture containing 73% of 7 and 27% of 8. Lack of material precluded similar experiments with 9 and 10.



7 8 9 10

In contrast to the photoisomerizations of the substituted enones 7–10, irradiation of the unsubstituted anti enone 5 in methylene chloride yielded the saturated

(1) Grateful acknowledgment is made to the Donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

(2) A preliminary report of a portion of this work has appeared: R. L. Cargill and T. Y. King, *Tetrahedron Lett.*, 409 (1970).

(3) The tricyclo[5.2.0.0$^{2,5}$]nonane system has previously been described by L. I. Smith, C. L. Agre, R. M. Leekley, and W. W. Prichard, *J. Amer. Chem. Soc.*, **61**, 7 (1939); R. Criegee, J. Dekker, and H. A. Brune, *Chem. Ber.*, **96**, 2368 (1963).

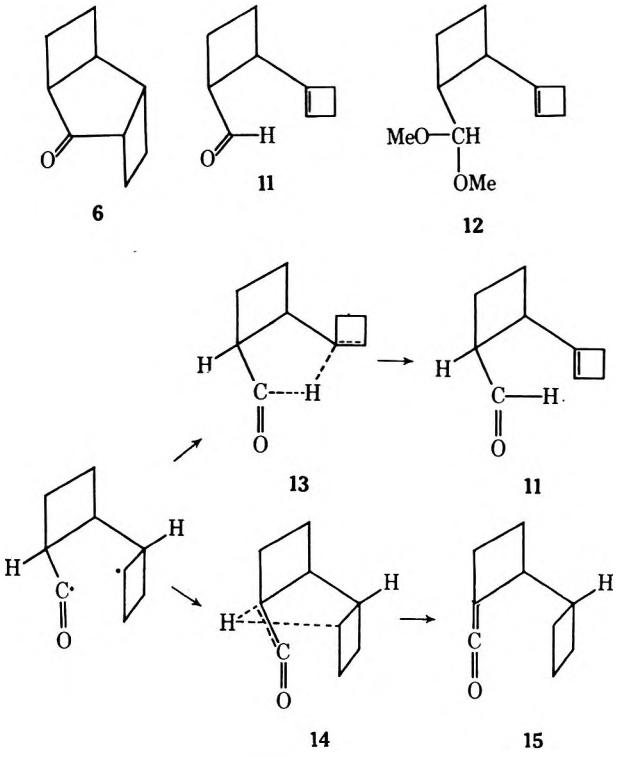
(4) R. L. Cargill, B. M. Gimarc, D. M. Pond, T. Y. King, A. B. Sears, and M. R. Willcott, *J. Amer. Chem. Soc.*, **92**, 3809 (1970).

(5) Spectroscopic data for all new compounds are presented in the Experimental Section.

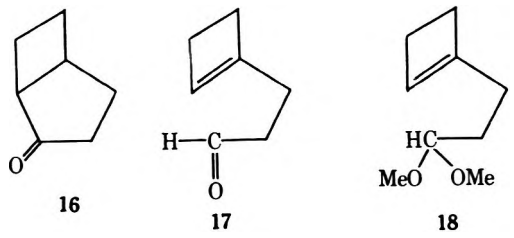
(6) G. Büchi and E. M. Burgess, *J. Amer. Chem. Soc.*, **82**, 4333 (1960).

ketone **6** and tetrachloroethane. No evidence for isomerization of **5** to the syn isomer **4** could be obtained. Photoreduction of the olefinic bond in $\beta,\gamma$-unsaturated ketones is not uncommon when mixing of carbonyl and olefinic orbitals is relatively inefficient, $\epsilon_{max}$ <150.[7,8] Here it appears that intramolecular triplet energy transfer from carbonyl to olefin yields the olefin triplet, the presumed reactive species in the photoreduction.[9] The Büchi rearrangement (**7** ⇄ **8**), on the other hand, appears to be a singlet reaction since sensitized irradiations of $\beta,\gamma$-unsaturated ketones result in oxadi-$\pi$-methane reactions,[10] and quenching of the rearrangement has been impossible.[11,12]

Irradiation of the saturated tricyclic ketone **6** in methanol yielded the acetal **12**. Presumably the acetal arises from the aldehyde **11** in a nonphotochemical step. Sufficient acidic material to catalyze acetal formation could be generated from photolysis of methanol.[13] The absence of any ester in the photolysate reflects the relative energy contents of transition states **13** and **14** which lead to aldehyde **11** and ketene **15**, respectively.

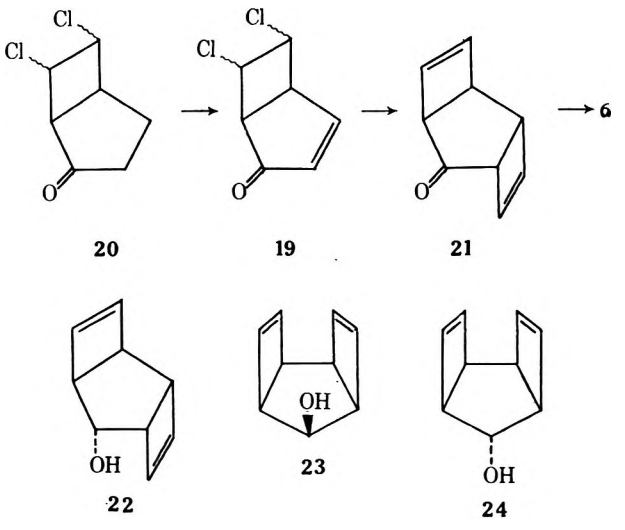



Similar irradiation of bicyclo[3.2.0]heptan-2-one (**16**) in methanol yielded only aldehyde **17** and the corresponding acetal **18**.[14] The absence of ester (from ketene) in this case is more difficult to rationalize.




We turn now to the tricyclo[5.2.0.0$^{2,5}$]nona-3,8-dien-6-ones. Attempts to induce cycloaddition of dichloroethylene and bicyclo[3.2.0]hepta-3,6-dien-2-one were unsuccessful. Therefore, a bicyclo[3.2.0]hept-3-en-2-one having a potential double bond in the cyclobutane ring was clearly necessary, dichloro ketone **19**, for example. Attempts to produce **19** by $\alpha$ bromination–dehydrobromination of **20** or its ethylene ketal gave only recovered starting material or products of double dehydrohalogenation. Dehydrogenation of **20** with selenium dioxide in *tert*-butyl alcohol,[15] on the other hand, gave **19** in 51% yield.

Photocycloaddition of ketone **19** and 1,2-dichloroethylene followed by ketalization of the adducts, dechlorination, and removal of the ketal function gave the anti dienone **21** in 46% yield from **19**. Confirmation of the anti stereochemistry in **21** was obtained by reduction to the corresponding alcohol **22**. In passing from ketone **21** to alcohol **22** the $C_2$ symmetry of **21** is destroyed, rendering the two sets of vinyl protons in **22** nonequivalent. Had the syn ketone **1** been obtained, reduction could have given either or both of two alcohols, **23** and **24**, both of which retain the plane of symmetry present in ketone **1**. The nmr spectrum of alcohol **22** exhibits two two-proton AB quartets[5] establishing the anti stereochemistry in ketone **21**. Catalytic hydrogenation of **21** provided the previously described saturated ketone **6**; therefore, the stereochemistry of **6** and enone **5** are firmly established




(7) (a) R. L. Cargill, J. R. Damewood, and M. M. Cooper, *J. Amer. Chem. Soc.*, **88**, 1330 (1966); (b) P. S. Engel and H. Ziffer, *Tetrahedron Lett.*, 5181 (1969).

(8) D. E. Bays, R. C. Cookson, and S. MacKenzie, *J. Chem. Soc. B*, 215 (1967), and references cited therein.

(9) Hydrogen abstraction by the triplets of cyclopentene and norbornene has been noted: P. J. Kropp, *J. Amer. Chem. Soc.*, **91**, 5783 (1969), and references cited therein.

(10) W. G. Dauben, M. S. Kellog, J. I. Seeman, and W. A. Spitzer, *ibid.*, **92**, 1786 (1970), and references cited therein.

(11) (a) E. Baggiolini, K. Schaffner, and O. Jeger, *Chem. Commun.*, 1103 (1969); (b) E. Baggiolini, H. P. Hamlow, and K. Schaffner, *J. Amer. Chem. Soc.*, **92**, 4906 (1970).

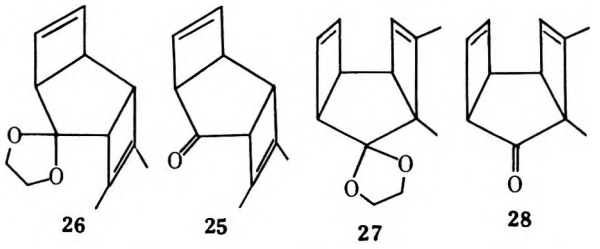
(12) Schuster has reported that the Büchi rearrangement has a quantum yield of 0.04 at 313 nm in benzene and that the reaction can be sensitized with compounds having $E_T$ > 65 kcal/mol, but compounds having $E_T$ < 62 kcal/mol quench the rearrangement. He concludes, however, that at least 75% of the reaction occurs in the singlet state with the remainder occurring in a quenchable triplet state: D. I. Schuster and D. H. Sussman, *Tetrahedron Lett.*, 1661 (1970); see also J. Ipaktschi, *ibid.*, 3179 (1970).

(13) P. Yates, *Pure Appl. Chem.*, **16**, 93 (1968). In other experiments addition of solid potassium carbonate to the irradiation mixture prevented acetal formation.

(14) T. S. Cantrell and J. S. Soloman, *J. Amer. Chem. Soc.*, **92**, 4656 (1970).

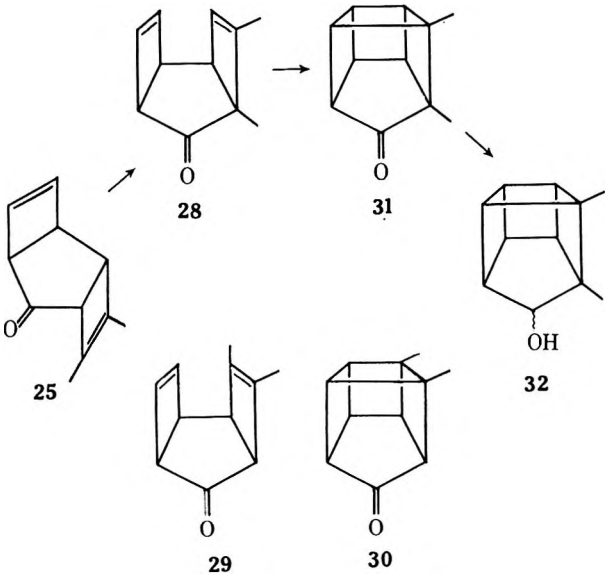
(15) M. Heller and S. Bernstein, *J. Org. Chem.*, **26**, 3876 (1961).

Photocycloaddition of ketone **19** with 2-butyne, followed by the sequence outlined above, provided ketone **25** in 45% yield. Although two ketals were obtained in this series, presumably **26** and **27**, hydrolysis of the ketal mixture gave a single ketone **25**. Whether the syn ketone **28** was formed and subsequently underwent acid-catalyzed isomerization to **25**[6] was not ascertained.



**26** **25** **27** **28**

Irradiation of anti dienone **21** in methylene chloride with "blacklights" gave homocubanone **2** in 68% yield.[16] Similar irradiation of **25** gave a single dimethylhomocubanone. The formation of homocubanones from the anti dienones most likely involves isomerization of the latter to the corresponding syn isomers *via* the Büchi rearrangement (see above), followed by photocycloaddition of the two olefinic bonds. An alternative route is isomerization of starting anti dienone to cyclononatetraenone which could conceivably undergo cyclization to homocubanone.[17] Isomerization of **25** *via* the latter route could produce only homocubanone **30**, whereas cyclization after isomerization of **25** to one of the syn isomers, **28** or **29**, could yield either **30** or **31**.



**28** **31** **25** **32** **29** **30**

We have already noted above that the Büchi rearrangement appears to be a singlet-state reaction. Further, we find that all those bicyclo[3.2.0]hept-6-en-2-ones which undergo the photoinduced allylic shift of carbonyl to the near exclusion of all competing processes exhibit efficient mixing of olefinic and carbonyl orbitals in the spectroscopically observed n,$\pi^*$ singlet state,[8] $\epsilon_{max} > 150$. Since orbital mixing increases with increased substitution of electron donors on the double bond,[8] we expect that Büchi rearrangement will occur most efficiently when the double bond involved is most highly alkyl substituted. Irradiation of **25** should therefore produce **28** rather than **29** as the major (or sole) syn isomer. If homocubanone formation proceeds *via* isomerization of anti to syn dienone followed by cyclization in the syn dienone, we expect homocubanone **31** rather than **30**.

In order to establish whether dienone **25** yields homocubanone **30** or **31**, the product was reduced with lithium aluminum hydride to an epimeric mixture of secondary alcohols **32** in a ratio of *ca.* 2:1. The 100-MHz nmr spectrum of the mixture exhibits two doublets (relative areas, *ca.* 2:1)[5] for the carbinol hydrogens. The presence of a single $\alpha$ proton in the homocubanone is thus established and structure **30** is eliminated. The data are consistent with, but do not prove, the formation of **31** in the irradiation of **25**. We conclude that homocubanone formation is a two-photon process involving first Büchi rearrangement of the anti dienone to the syn isomer followed by photocycloaddition of the double bonds in the latter. The final ring closure probably results from excitation of the carbonyl, intersystem crossing to the n,$\pi^*$ triplet, energy transfer to the $\pi$ system of the diene, and ring closure in the extended $\pi,\pi^*$ triplet.

## Experimental Section[18]

**Bicyclo[3.2.0]hept-3-en-2-one (3).**—This ketone was prepared in 47% yield from cyclopentenone by the previously described procedure:[19] bp 58–62° (4 Torr); uv max (95% $C_2H_5OH$) 226 nm ($\epsilon$ 12,600), 321 (70); ir ($CCl_4$) 1710 and 1575 cm$^{-1}$; nmr ($CCl_4$) $\delta$ 7.57 (q, 1, $J_{\alpha,\beta}$ = 5.5 Hz, $J_{\beta,\gamma}$ = 3.0 Hz, OCCH=CH-CH), 6.18 (d, 1, $J_{\alpha,\beta}$ = 5.5 Hz, OCCH=CH), 3.33 (m, 1, C-5 bridgehead), and 1.62–3.00 (m, 5).

***syn*- and *anti*-Tricyclo[5.2.0.0$^{2,5}$]non-3-en-6-one (4 and 5).**—A solution of 1.56 g (11.6 mmol) of bicyclo[3.2.0]hept-3-en-2-one (**3**) and 30 ml of a mixture of *cis*- and *trans*-1,2-dichloroethylene in 100 ml of purified methylene chloride was irradiated (Corex) for 2 hr. Progress of the reaction was followed by glpc [3% diethylene glycol succinate (DEGS), 8 ft × 0.125 in., 120°, 25 cc/min of He]. Removal of the methylene chloride and excess dichloroethylene by distillation resulted in a brown oil. To the crude mixture of cycloadducts were added 70 ml of ethylene glycol, 120 ml of benzene, and 5 drops of concentrated sulfuric acid. The solution was refluxed for 48 hr with removal of water. A 5% solution of sodium bicarbonate (200 ml) was added and the dichloro ketal isomers were extracted with three 200-ml portions of ether. The extracts were combined and dried ($CaCl_2$). Approximately 300 ml of the ether was removed by distillation and to the remaining solution was added 300 ml of ammonia in a 1-l. three-necked flask. Sodium metal was added until the solution remained dark blue for 30 min. Ammonium chloride was added to destroy the excess sodium. Water (300 ml) was added after the ammonia had evaporated and the aqueous layer was extracted with two 200-ml portions of ether. To the combined extracts was added 100 ml of 3 *M* hydrochloric acid, and this mixture was allowed to stir at room temperature for 12 hr.

(16) Homocubanone was identified by comparison of ir and nmr spectra of authentic material. We thank Professor W. G. Dauben for these spectra.

(17) We thank Professor J. A. Berson for calling this possibility to our attention.

(18) All boiling points and melting points are uncorrected. Microanalyses were performed by Bernhardt Miroanalytisches Laboratorium, Elbach uber Engelskirken, Germany, or by Gailbraith Laboratories, Inc., Knoxville, Tenn. Infrared spectra were determined in carbon tetrachloride unless otherwise stated, using a Perkin-Elmer Model 337 or 257 grating spectrophotometer. All nmr spectra were determined in carbon tetrachloride containing tetramethylsilane as an internal standard using a Varian A-60 nmr spectrometer. Analytical gas–liquid partition chromatograms were determined using a Varian Aerograph Model 1200 chromatograph, and preparative glpc separations were conducted using a Varian Aerograph 90-P-3 chromatograph. Irradiations were carried out using a Hanovia high-pressure mercury arc (450 W), internal probe, type L, and the filter specified.

(19) R. L. Cargill, A. C. Miller, D. M. Pond, P. deMayo, M. F. Tchir, K. R. Neuberger, and J. Saltiel, *Mol. Photochem.*, **1**, 301 (1969); see ref 4 also.

Sodium bicarbonate (200 ml of 15% solution) was added to destroy the acid, the resulting solution was washed with 200 ml of water, and the aqueous layer was extracted with two 100-ml portions of ether. The extracts were combined and dried ($CaCl_2$) and the ether was removed by distillation. The remaining brown residue was distilled, bp 39–41° (0.50 Torr), yielding 1.46 g (75.3% based on **3**) of **4** and **5** as a colorless oil. Analysis by preparative glpc (20% DEGS, 5 ft × 0.25 in., 115°, 30 cc/min of He) showed this oil to be a mixture of *syn*- and *anti*-tricyclo[5.2.0.$0^{2,5}$]non-3-en-one (**4** and **5**) in the ratio 2:98, respectively.

*syn*-Tricyclo[5.2.0.$0^{2,5}$]non-3-en-6-one (**4**): uv max (95% $C_2H_5OH$) 310 nm ($\epsilon$ 102); ir ($CCl_4$) 3110 and 3035 (CH=CH), and 1725 $cm^{-1}$ (C=O); nmr ($CCl_4$) $\delta$ 6.37 (AB q, 2, $J_{AB}$ = 2.5 Hz, $\Delta_{AB}$ = 10.0 Hz, CH=CH; each peak of the upfield doublet is split further into a doublet by $J_{BX}$ = 1.4 Hz) and 1.0–3.7 (m, 8).

*Anal.* Calcd for $C_9H_{10}O$ (134.11): C, 80.56; H, 7.51. Found: C, 80.40; H, 7.55.

*anti*-Tricyclo[5.2.0.$0^{2,5}$]non-3-en-6-one (**5**): uv max (95% $C_2H_5OH$) 310 nm ($\epsilon$ 146); ir ($CCl_4$) 3110 and 3035 (CH=CH) and 1725 $cm^{-1}$ (C=O); nmr ($CCl_4$) $\delta$ 6.13 (AB q, 2, $J_{AB}$ = 2.5 Hz, $\Delta_{AB}$ = 10.0 Hz, CH=CH; each peak of the upfield doublet is split further into a doublet by $J_{BX}$ = 1.4 Hz), 3.39 (d, br, 1, bridgehead, spacing 2.5 Hz), 3.02 (d, 1, bridgehead, spacing 2.5 Hz), and 1.40–2.95 (m, 6); mass spectrum (70 eV) *m/e* molecular ion 134.

*Anal.* Calcd for $C_9H_{10}O$ (134.11): C, 80.56; H, 7.51. Found: C, 80.52; H, 7.57.

**Irradiation of Bicyclo[3.2.0]hept-3-en-2-one (3) with 2-Butyne.**—A solution of 1.09 g (10.1 mmol) of **3** in 80 ml of methylene chloride and 15 ml of 2-butyne was irradiated (Corex) for 1.5 hr. Progress of the reaction was followed by glpc (3% Carbowax, 8 ft × 0.125 in., 128°, 25 cc/min of He). The solvent and excess 2-butyne were removed by distillation leaving a pale yellow residue. Distillation, bp 39–60° (0.24 Torr), gave 1.07 g (65.6%) of a colorless oil. Analysis by glpc (3% Carbowax, 8 ft × 0.125 in., 114°, 25 cc/min of He) showed the distillate to be a mixture of four components (**10**, **8**, **7**, and **9**) in a ratio of 1:10:7.5:1, respectively. Pure samples of **10**, **8**, **7**, and **9** were obtained by preparative glpc (20% Carbowax, 8 ft × 0.25 in., 152°, 100 cc/min of He).

*anti*-3,4-Dimethyltricyclo[5.2.0.$0^{2,5}$]non-3-en-6-one (**7**): uv max (95% $C_2H_5OH$) 311 nm ($\epsilon$ 349); ir ($CCl_4$) 1730 (CO) and 1700 $cm^{-1}$ (C=C); nmr ($CCl_4$) $\delta$ 1.5–3.2 (m, 8) and 1.57 (s, 6, $CH_3C{=}CCH_3$); mass spectrum (70 eV) *m/e* molecular ion 162.

*Anal.* Calcd for $C_{11}H_{14}O$ (162.22): C, 81.44; H, 8.70. Found: C, 81.36; H, 8.72.

*syn*-4,5-Dimethyltricyclo[5.2.0.$0^{2,5}$]non-3-en-6-one (**8**): uv max (95% $C_2H_5OH$) 319 nm ($\epsilon$ 140); ir ($CCl_4$) 3030 (>C=CH), 1725 (C=O), and 1650 $cm^{-1}$ (C=C); nmr ($CCl_4$) $\delta$ 6.02 (d, 1, $J$ = 2.0 Hz, >C=CH), 2.91 (m, 3, bridgehead), 2.12 (m, 4), 1.65 (s, br, 3, $CH_3C{=}CH$), and 1.17 (s, 3, $CH_3C$); mass spectrum (70 eV) *m/e* molecular ion 162.

*Anal.* Calcd for $C_{11}H_{14}O$ (162.22): C, 81.44; H, 8.70. Found: C, 81.33; H, 8.60.

*syn*-3,4-Dimethyltricyclo[5.2.0.$0^{2,5}$]non-3-en-6-one (**9**): uv max (95% $C_2H_5OH$) 310 nm ($\epsilon$ 229); ir ($CCl_4$) 1720 (C=O) and 1675 $cm^{-1}$ (C=C); nmr ($CCl_4$) $\delta$ 3.05 (m, 4, bridgehead protons), 2.08 (m, 4), and 1.70 (s, 6, $CH_3C{=}CCH_3$); mass spectrum (70 eV) *m/e* molecular ion 162.

*Anal.* Calcd for $C_{11}H_{14}O$ (162.22): C, 81.44; H, 8.70. Found: C, 81.56; H, 8.77.

*anti*-4,5-Dimethyltricyclo[5.2.0.$0^{2,5}$]non-3-en-6-one (**10**): uv max (95% $C_2H_5OH$) 309 nm ($\epsilon$ 301); ir ($CCl_4$) 3045 (CH=CH), 1725 (C=O), and 1640 $cm^{-1}$ (C=C); nmr ($CCl_4$) $\delta$ 5.71 (s, poorly resolved, >C=CH), 1.8–3.2 (m, 7, bridgehead and methylene protons), 1.53 (s, br, 3, $CH_3C{=}CH$), and 1.30 (s, 3, $CH_3C<$); mass spectrum (70 eV) *m/e* molecular ion 162.

*Anal.* Calcd for $C_{11}H_{14}O$ (162.22): C, 81.44; H, 8.70. Found: C, 81.39; H, 8.76.

**Photoequilibration of 7 and 8.**—A solution of 52 mg of **7** in 25 ml of methylene chloride was irradiated through Pyrex with ten "blacklights" for 8.5 hr, at which time a photostationary-state mixture containing 73% of **7** and 27% of **8** was obtained. Similar irradiation of 64 mg of **8** for 10 hr provided an identical photostationary-state mixture.

**Irradiation of *anti*-Tricyclo[5.2.0.$0^{2,5}$]non-3-en-6-one (5).**—A solution of 339 mg (2.53 mmol) of **5** in 90 ml of methylene chloride was irradiated (Pyrex) for 7 hr. Progress of the reaction was followed by glpc (3% Carbowax, 8 ft × 0.125 in., 128°, 25 cc/min of He). The solvent was removed by distillation to give 325 mg of a yellow oil. Analysis by glpc (3% Carbowax, 8 ft × 0.125 in. 128°, 25 cc/min of He) showed the presence of three products, **6**, **11**, and tetrachloroethane, in a ratio of 3.8:3.4:1.0, respectively. Pure samples were obtained by preparative glpc (20% DEGS, 5 ft × 0.25 in., 110°, 50 cc/min of He). Nmr and ir spectra of **6** and tetrachloroethane were compared with those of authentic samples. The third product, which decomposed upon attempted collection, was presumed to be **11**.

***anti*-Tricyclo[5.2.0.$0^{2,5}$]nonan-6-one (6).**—A solution of 1.464 g (10.92 mmol) of a mixture of **4** and **5** (ratio 2:98) in 50 ml of absolute methanol and 30 mg of platinum oxide was hydrogenated in a Parr shaker for 10 hr. The solution was filtered and the solvent was removed leaving 966 mg (65.0%) of a pale yellow oil. A pure sample of **6** was obtained by preparative glpc (20% DEGS, 5 ft × 0.25 in., 125°, 60 cc/min of He). *anti*-Tricyclo[5.2.0.$0^{2,5}$]-nonan-6-one (**6**): uv max (95% $C_2H_5OH$) 306 nm ($\epsilon$ 22); ir ($CCl_4$) 1730 $cm^{-1}$; nmr ($CCl_4$) $\delta$ 1.3–3.2 (m, 12); mass spectrum (70 eV) *m/e* molecular ion 136.

*Anal.* Calcd for $C_9H_{12}O$ (136.12): C, 79.37; H, 8.88. Found: C, 79.30; H, 8.93.

**Irradiation of *anti*-Tricyclo[5.2.0.$0^{2,5}$]nonan-6-one (6) in Methanol.**—A solution of 432 mg (3.18 mmol) of **6** in 80 ml of absolute methanol was irradiated (Corex) for 1.75 hr. Progress of the reaction was followed by glpc (3% Carbowax, 8 ft × 0.125 in., 123°, 25 cc/min of He). Two products, **12** and **11** (13:1), were formed. The solvent was removed at atmospheric pressure resulting in 547 mg of a pale yellow oil. Pure samples of **12** were obtained by preparative glpc (20% DEGS, 5 ft × 0.25 in., 113°, 30 cc/min of He). The minor component of the mixture was presumed to be **11**. 2-(1-Cyclobutenyl)cyclobutanecarboxaldehyde dimethyl acetal (**12**): ir ($CCl_4$) 3045 (>C=CH) and 1605 $cm^{-1}$ (C=C); nmr ($CCl_4$) $\delta$ 5.70 (s, br, 1, >C=CH), 4.30 (d, 1, $J$ = 8.0 Hz, $>CHCH(OCH_3)_2$), 3.10 (s, 3, $>CHOCH_3$), 3.15 (s, 3, $>CHOCH_3$), and 1.7–3.0 (m, 10); mass spectrum (70 eV) *m/e* molecular ion 182.

*Anal.* Calcd for $C_{11}H_{18}O_2$ (182.27): C, 72.49; H, 9.96. Found: C, 72.47; H, 9.92.

**Irradiation of Bicyclo[3.2.0]heptan-2-one (16) in Methanol.**—A solution of 1.47 g (13.4 mmol) of **16** in 90 ml of absolute methanol was irradiated (Corex) for 3 hr. Progress of the reaction was followed by glpc (3% Carbowax, 8 ft × 0.125 in., 109°, 25 cc/min of He). The solvent was removed and the pale yellow residue was distilled, bp 60–70° (8 Torr), yielding 1.21 g of a colorless oil. Analysis by glpc (3% Carbowax, 8 ft × 0.125 in., 109°, 25 cc/min of He) showed two products, **17** and **18**, and a small amount of starting material. Pure samples of **17** and **18** in the ratio 3:2 were obtained by preparative glpc (20% Carbowax, 8 ft × 0.25 in., 122°, 86 cc/min of He).

3-(1-Cyclobutenyl)propionaldehyde (**17**): ir ($CCl_4$) 3025 (>C=CH), 2705 (CHO), 1725 (C=O), and 1625 $cm^{-1}$ (C=C); nmr ($CCl_4$) $\delta$ 9.87 (t, 1, $J$ = 1.5 Hz, CHO), 5.58 (t, 1, $J$ = 1.5 Hz, >C=CH), and 2.33 (m, 8); mass spectrum (70 eV) *m/e* molecular ion 110.

*Anal.* Calcd for $C_7H_{10}O$ (110.15): C, 76.32; H, 9.15. Found: C, 76.05; H, 9.15.

3-(1-Cyclobutenyl)propionaldehyde dimethyl acetal (**18**): ir ($CCl_4$) 3025 (>C=CH) and 1630 $cm^{-1}$ (C=C); nmr ($CCl_4$) $\delta$ 5.38 (s, br, 1, >C=CH), 4.07 (t, 1, $J$ = 5.5 Hz, $CH_2CH(OCH_3)_2$), 3.03 (s, 6, $CH(OCH_3)_2$), 2.17 (s, 4, cyclobutane protons), and 1.3–2.1 (m, 4); mass spectrum (70 eV) *m/e* molecular ion 156.

*Anal.* Calcd for $C_9H_{16}O_2$ (156.23): C, 69.19; H, 10.32. Found: C, 69.23; H, 10.32.

**6,7-Dichlorobicyclo[3.2.0]hept-3-en-2-one (19).**—A solution of 6.492 g (79.19 mmol) of 2-cyclopentenone and 30 ml of a mixture of *cis* and *trans*-1,2-dichloroethylene in 70 ml of methylene chloride was irradiated (Corex) for 6 hr. The progress of the reaction was followed by glpc (3% Carbowax, 8 ft × 0.125 in., 105°, 25 cc/min of He). Removal of the solvent and excess dichloroethylene left a mixture of isomeric dichloro ketones. Vacuum distillation of this brown oil afforded 12.050 g of a pale yellow oil. To this was added 10 g of selenium dioxide and 500 ml of *tert*-butyl alcohol. The stirred solution was allowed to reflux for 13 hr under a nitrogen atmosphere. The solution was then cooled to room temperature and filtered twice using a Celite cake. The solvent was removed by distillation at aspirator pressure. The crude, reddish brown viscous residue was then distilled, bp up to 150° (0.07–0.10 Torr), yielding 6.048 g (43.6% from 2-cyclopentenone) of a yellow oil, **19**, which partially crystallized upon standing. Pure samples of **19** obtained

by vacuum distillation using a cold finger apparatus had uv max (95% $C_2H_5OH$) 229 nm ($\epsilon$ 3700); ir ($CCl_4$) 3060 (CH=CH), 1720 (C=O), and 1575 cm$^{-1}$ (C=C); nmr ($CCl_4$) $\delta$ 7.58 (q, 1, $J_{\alpha,\beta}$ = 6.5 Hz, $J_{\beta,\gamma}$ = 3.0 Hz, COCH=CH), 6.32 (q, 1, $J_{\alpha,\beta}$ = 6.5 Hz, $J_{\alpha,\gamma}$ = 2.0 Hz, COCH=CH), 4.58 (q, 1, $J$ = 9.0 Hz, $J$ = 6.0 Hz, CHCl), 4.00 (m, 2, bridgehead and CHCl), and 3.00 (t, 1, $J$ = 5.5 Hz, bridgehead); mass spectrum (70 eV) $m/e$ molecular ion 176 and 178.

*Anal.* Calcd for $C_7H_6OCl_2$ (177.03): C, 47.49; H, 3.32; Cl, 40.04. Found: C, 47.59; H, 3.40; Cl, 40.23.

***anti*-Tricyclo[5.2.0.0$^{2,5}$]nona-3,8-dien-6-one (21).**—A solution of 3.09 g (16.9 mmol) of 6,7-dichlorobicyclo[3.2.0]hept-3-en-2-one (19) in 50 ml of purified methylene chloride and 40 ml of a mixture of *cis*- and *trans*-1,2-dichloroethylene was irradiated (Corex) for 3.5 hr. Progress of the reaction was followed by glpc (3% Carbowax, 8 ft × 0.125 in., 170°, 25 cc/min of He). Solvent and excess dichloroethylene were removed by distillation leaving a brown oily residue. To this were added 125 ml of benzene, 70 ml of ethylene glycol, and 6 drops of concentrated sulfuric acid. This solution was allowed to reflux for 40 hr with water removal. The solution was cooled to room temperature and 200 ml of 5% sodium bicarbonate solution was added. The aqueous layer was extracted with four 200-ml portions of ether–methylene chloride (1:1), and the extracts were combined and dried ($CaCl_2$). The solvent was removed by distillation. The brown residue was dissolved in 50 ml of dry ether and added to 400 ml of ammonia contained in a 1-l. three-necked flask. Sodium metal was added to this stirred solution until the blue color persisted for 20 min. The reaction was then quenched with ammonium chloride. After complete evaporation of the ammonia 350 ml of water was added. The aqueous solution was extracted with three 200-ml portions of ether. The extracts were combined and 100 ml of 1.5 *M* hydrochloric acid was added to the ethereal solution. The solution was then allowed to stir at room temperature for 4 hr. The organic layer was washed with 100 ml of 5% sodium bicarbonate and then with 100 ml of water. The aqueous layer was extracted with two 100-ml portions of ether and the combined ethereal extract was washed with 50 ml of sodium bicarbonate and 50 ml of water and dried ($CaCl_2$). The ether was removed and the resulting oil was distilled, bp 34° (0.50 Torr), yielding 955 mg (41.8% overall) of a colorless oil, **21**. Pure samples of **21** were obtained by preparative glpc (20% DEGS, 5 ft × 0.25 in., 122°, 60 cc/min of He). *anti*-Tricyclo[5.2.0.0$^{2,5}$]nona-3,8-dien-6-one (21): uv max (95% $C_2H_5OH$) 306 nm ($\epsilon$ 267); ir ($CCl_4$) 3115 and 3040 (CH=CH) and 1725 cm$^{-1}$ (C=O); nmr ($CCl_4$) $\delta$ 6.07 (AB q, 4, $J_{AB}$ = 2.7 Hz, $\Delta_{AB}$ = 7.5 Hz, CH=CH; each peak of the upfield doublet is split further into a doublet by $J_{BX}$ = 1.3 Hz), 3.60 (s, br, 2, bridgehead protons), and 3.12 (m, 2, bridgehead protons); mass spectrum (70 eV) $m/e$ molecular ion 132.

*Anal.* Calcd for $C_9H_8O$ (132.15): C, 81.79; H, 6.10. Found: C, 81.73; H, 6.14.

***anti*-Tricyclo[5.2.0.0$^{2,5}$]nona-3,8-dien-6-ol (22).**—To 205 mg (5.12 mmol) of lithium aluminum hydride in 20 ml of dry ether was added 245 mg (1.85 mmol) of **21** in 10 ml of ether. The resulting mixture was stirred at room temperature for 17 hr and then 10 ml of 10% sodium hydroxide was slowly added to destroy the excess lithium aluminum hydride. The solid was filtered and washed three times with 20-ml portions of ether. The layers were separated and the ethereal solution was washed with 40 ml of saturated sodium chloride solution and dried ($Na_2SO_4$). The solvent was removed at atmospheric pressure leaving 177 mg of an oil. Analysis by glpc (3% Carbowax, 8 ft × 0.125 in., 125°, 25 cc/min of He) showed one product, **22**. Pure samples of **22** were obtained by preparative glpc (20% DEGS, 5 ft × 0.25 in. 133°, 65 cc/min of He). *anti*-Tricyclo[5.2.0.0$^{2,5}$]nona-3,8-dien-6-ol (22): mp 49.7–50.8°; ir ($CCl_4$) 3600, 3575, and 3350 (broad, >CHOH), 3115 and 3030 cm$^{-1}$ (CH=CH); nmr ($CCl_4$) $\delta$ 6.02 (AB q, 2, $J_{AB}$ = 3.0 Hz, $\Delta_{AB}$ = 3.3 Hz, CH=CH), 5.97 (A'B' q, 2, $J_{A'B'}$ = 2.8 Hz, $\Delta_{A'B'}$ = 17.5 Hz, CH=CH), 3.91 (s, 2, bridgehead), 3.44 (d, 1, $J$ = 3.0 Hz, <CHOH), 3.09 (d, 2, $J$ = 3.0 Hz, bridgehead), and 2.54 (s, 1, >CHOH); mass spectrum (70 eV) $m/e$ molecular ion 134.

*Anal.* Calcd for $C_9H_{10}O$ (134.17): C, 80.56; H, 7.51. Found: C, 80.65; H, 7.42.

**Hydrogenation of *anti*-Tricyclo[5.2.0.0$^{2,5}$]nona-3,8-dien-6-one (21).**—A solution of 148 mg (1.12 mmol) of *anti*-tricyclo[5.2.0.0$^{2,5}$]nona-3,8-dien-6-one (21) in 25 ml of absolute methanol and 20 mg of platinum oxide was hydrogenated in a Parr shaker for 6 hr. The methanolic solution was filtered and concentrated to give 91 mg of an oil. Analysis by glpc (3% Carbowax, 8 ft × 0.125 in., 125°, 25 cc/min of He) showed a single product. Pure samples of **6** were obtained by preparative glpc (20% DEGS, 5 ft × 0.25 in., 130°, 60 cc/min of He). Nmr and ir spectra of this product were identical with those of *anti*-tricyclo[5.2.0.0$^{2,5}$]-nonan-6-one (6) prepared from the hydrogenation of *anti*-tricyclo[5.2.0.0$^{2,5}$]non-3-en-6-one (5).

***anti*-3,4-Dimethyltricyclo[5.2.0.0$^{2,5}$]nona-3,8-dien-6-one (25).**—A solution of 3.28 g (18.5 mmol) of 6,7-dichlorobicyclo[3.2.0]-hept-3-en-2-one (19) in 90 ml of purified methylene chloride and 20 ml of 2-butyne was irradiated (Corex) for 2 hr. Progress of the reaction was followed by glpc (3% Carbowax, 8 ft × 0.125 in., 170°, 25 cc/min of He). The solvent and excess 2-butyne were removed by distillation leaving a brown residue. To this were added 125 ml of benzene, 70 ml of ethylene glycol, and 6 drops of concentrated sulfuric acid. This solution was allowed to reflux (110°) for 40 hr with water removal. The solution was cooled to room temperature and 200 ml of a 5% sodium bicarbonate solution was added. The aqueous layer was extracted with three 200-ml portions of ether–methylene chloride (1:1), and the extracts were combined and dried ($CaCl_2$). The solvent was removed by distillation. The brown residue was dissolved in 50 ml of dry ether and added to 400 ml of ammonia contained in a 1-l. three-necked flask. Sodium metal was added to this stirred solution until the blue color persisted for 25 min. The reaction was quenched with ammonium chloride. After evaporation of the ammonia, 350 ml of water was added. The aqueous solution was extracted with three 200-ml portions of ether. The ethereal extracts were combined and stirred overnight with 150 ml of 2.0 *M* hydrochloric acid. The ether layer was separated and the aqueous phase was neutralized with sodium bicarbonate solution and extracted with ether. All the ether extracts were combined and dried ($CaCl_2$). The solvent was removed and the residue was distilled, bp 55–56° (0.27 Torr), yielding 2.32 g of a colorless oil. Analysis by glpc (20% DEGS, 5 ft × 0.25 in., 115°, 70 cc/min of He) showed the presence of one major product, **25**, and an impurity, *ca.* 30%, presumed to be bicyclo[3.2.0]hept-6-en-2-one. Pure samples of **25** were obtained by preparative glpc (20% DEGS, 5 ft × 0.25 in., 115°, 70 cc/min of He). *anti*-3,4-Dimethyltricyclo[5.2.0.0$^{2,5}$]nona-3,8-dien-6-one (25): uv max (95% $C_2H_5OH$) 309 nm ($\epsilon$ 323); ir ($CCl_4$) 3085 and 3015 (CH=CH), 1720 (C=O), and 1680 cm$^{-1}$ (weak, $CH_3C$=$CCH_3$); nmr ($CCl_4$) $\delta$ 6.07 (AB q, 2, $J_{AB}$ = 2.5 Hz, $\Delta_{AB}$ = 8.5 Hz, CH=CH; each peak of the upfield doublet is split further into a doublet by $J_{BX}$ = 1.3 Hz), 3.47 (m, 1, bridgehead), 3.25 (m, 1, bridgehead), 3.10 (m, 1, bridgehead), 2.78 (m, 1, bridgehead), and 1.60 (s, 6, $CH_3C$=$CCH_3$); mass spectrum (70 eV) $m/e$ molecular ion 160.

*Anal.* Calcd for $C_{11}H_{12}O$ (160.21): C, 82.46; H, 7.55. Found: C, 82.30; H, 7.66.

**Irradiation of *anti*-Tricyclo[5.2.0.0$^{2,5}$]nona-3,8-dien-6-one (21).**—A solution of 570 mg (4.32 mmol) of **21** in 200 ml of purified methylene chloride was irradiated in a Pyrex tube with ten 15-W "blacklights" for 30 hr. Progress of the reaction was followed by glpc (3% Carbowax, 8 ft × 0.125 in., 128°, 25 cc/min of He) and analysis showed the formation of a single product, **2**. Solvent was removed (50–70°) and the resulting oil was distilled to give 390 mg (68.5%) of **2** as a colorless oil which crystallized upon standing. Pure samples of **2** were obtained by preparative glpc (20% SE-30, 5 ft × 0.25 in., 128°, 100 cc/min of He). Homocubanone (2) was identified by comparison of the nmr and ir spectra with those of an authentic sample.[16]

**Irradiation of *anti*-3,4-Dimethyltricyclo[5.2.0.0$^{2,5}$]nona-3,8-dien-6-one (25) in Methylene Chloride.**—A solution of 814 mg (5.04 mmol) of **25** in 190 ml of purified pentane was irradiated as above for 50 hr. Progress of the reaction was followed by glpc (3% Carbowax, 8 ft × 0.125 in., 122°, 25 cc/min of He). Two products were evident, one of which diminished upon further irradiation, leaving one final product. Solvent was removed and the product distilled in a short-path still to give 598 mg of **31**, bp 50–70° (bath temperature) (0.1 Torr). An analytical sample of **31** was obtained by preparative glpc (20% DEGS, 5 ft × 0.25 in., 105°, 70 cc/min of He). 1,2-Dimethylpentacyclo[4.3.0.0$^{2,5}$.0$^{3,8}$.0$^{4,7}$]nonan-9-one (31): ir ($CCl_4$) 1755 cm$^{-1}$ (C=O); nmr ($CCl_4$) $\delta$ 2.2–3.8 (m, 6, methine protons), 1.11 (s, 3, $CH_3C\lessdot$), and 1.07 (s, 3, $CH_3C\lessdot$).

*Anal.* Calcd for $C_{11}H_{12}O$ (160.21): C, 82.46; H, 7.55. Found: C, 82.52; H, 7.50.

**Reduction of Dimethylhomocubane (31).**—Reduction of **31** with lithium aluminum hydride as above gave a mixture of epi-

meric alcohols **32**. Analysis by glpc (3% Carbowax, 8 ft × 0.125 in., 120°, 25 cc/min of He) showed two peaks in a ratio of *ca.* 2:1. The mixture of carbinols was purified by preparative glpc (20% XF-1150, 10 ft × 0.125 in., 130°, 100 cc/min of He). Carbinols **32** have $\delta$ ($CCl_4$) 3.73 and 3.68 (doublets, $J$ = 2.2 and 2.0 Hz, respectively, relative areas *ca.* 2:1, respectively, carbinol), 1.15, 1.12 (pair of equally intense singlets), and 1.07, 1.03 (pair of equally intense singlets, the former pair having *ca.* twice the area of the latter pair, methyls). The high resolution mass spectrum of **32** exhibits $m/e$ 162.1040 (calcd for $C_{11}H_{14}O$: 162.1045).[20]

**Registry No.**—**3**, 28256-69-1; **4**, 28256-70-4; **5**, 28256-71-5; **6**, 28256-72-6; **7**, 28256-73-7; **8**, 28256-74-8; **9**, 28256-75-9; **10**, 28256-76-0; **12**, 28256-77-1; **17**, 28256-78-2; **18**, 28256-79-3; **19**, 25995-00-0; **21**, 25995-02-2; **22**, 26121-77-7; **25**, 28256-82-8; **31**, 28256-83-9; **32a**, 28256-84-0; **32b**, 28256-85-1.

(20) We thank Dr. D. M. Rosenthal and Mr. F. Williams, Research Triangle Institute, for the high-resolution mass spectrum.

# The Photochemistry of Bicyclo[6.1.0]nonanones[1a]

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The solution photochemistry of three bicyclic ketones containing formally nonconjugated chromophores in a medium ring has been examined. Bicyclo[6.1.0]nonan-3-one (**1**) affords *trans*-5,8-nonadienal (**4**), 2-allylcyclohexanone (**5**), and 3-vinylcycloheptanone (**6**). Photolysis in methanol also gives methyl 8-nonenoate (**7**). In addition to photoreduction to the corresponding alcohols, bicyclo[6.1.0]nonan-4-one (**2**) forms aldehydes **15** and **16** and ester **17**. A distinct solvent effect on the product distribution was observed in this system. 4,5-Epoxycyclooctanone (**3**) undergoes simple photoreduction of the ketone function. These results are discussed in relation to similar systems.

As part of a continuing study[2,3] on the photochemical interaction of formally nonconjugated chromophores contained within the same molecule, we have examined the photochemistry of the modified cyclooctanones **1–3**. Compound **1** is the cyclopropyl analog of the $\beta,\gamma$-unsaturated ketone, 3-cyclooctenone, upon which we have reported earlier.[2] The remaining ketones are functionalized in the $\gamma,\delta$ position with a cyclopropane and an epoxide unit. These compounds can be considered as derivatives of 4-cyclooctenone.[3] These specific systems have been chosen in a search for photochemical interplay of remote functional groups, since the medium-ring framework provides the geometrical proximity which has been effective in inducing transannular processes.[4]

**Bicyclo[6.1.0]nonan-3-one.**—The synthesis of **1** was accomplished from 3-cyclooctenol[5] by the sequence: acetylation, Simmons–Smith reaction, saponification, and chromic acid oxidation. Acetylation was critical to this synthetic scheme since the Simmons–Smith method failed on the alcohol itself. The ultraviolet spectrum of **1** suggests weak interaction of the cyclopropyl moiety with the carbonyl group as evidenced by an enhancement of the extinction coefficient [uv max (hexane) 289 nm ($\epsilon$ 44)]. This spectrum is similar to that of 3-cyclooctenone [292 nm ($\epsilon$ 47)][2] for which some overlap of the two $\pi$ bonds seems certain.[6] The ability of a cyclopropane to function in this fashion has only recently been documented.[7]

Irradiation of **1** leads to the rapid formation of three major products in approximately a 1:2:1 ratio in either benzene or cyclohexane. Photoisomer **4** displays spectroscopic properties (detailed in the Experimental Section) which suggest the presence of aldehyde, terminal vinyl, and a nonconjugated trans-disubstituted double bond. The relative position of the double bonds is evidenced by a doubly allylic methylene group at $\delta$ 2.7 in the nmr. The carbon skeleton of this compound was shown by the isolation of *n*-nonanal from a photolysis mixture which had subsequently been catalytically hydrogenated. 2-Allylcyclohexanone (**5**) was identified by comparison with a synthetic sample derived from allyl Grignard addition to cyclohexene oxide and subsequent chromic acid oxidation of the resulting alcohol. The structure of **6** rests on spectral data which show a cycloheptanone carbonyl (5.90 $\mu$) and a terminal vinyl group. The absence of a signal at *ca.* $\delta$ 3.0 ($CH_2$=CHCHCO) in the nmr indicates that the vinyl substituent is not adjacent to the carbonyl group,[2] and, therefore, the presence of an important fragment at $m/e$ 81 in the mass spectrum of **6** establishes the indicated locus of the vinyl substituent.[8]

Irradiation of **1** in methanol solvent gave methyl 8-nonenoate (**7**) in addition to the above three products. Methyl ester and terminal vinyl groups were manifest spectroscopically, and catalytic hydrogenation converted **7** to methyl *n*-nonanoate.

Examination of the photoisomers under the irradiation conditions demonstrated the absence of interconversion. In fact, except for aldehyde **4** which decomposed to an unidentified material of short retention time, the products were surprisingly stable to the photolysis conditions.

These results parallel closely those obtained by Heck-

(1) (a) Supported by a research grant from the National Science Foundation; (b) Alfred P. Sloan Research Fellow, 1968–1970; (c) NDEA Title IV Predoctoral Fellow, 1965–1968; NSF Trainee, 1968–1969.

(2) J. K. Crandall, J. P. Arrington, and J. Hen, *J. Amer. Chem. Soc.*, **89**, 6208 (1967).

(3) J. K. Crandall, J. P. Arrington, and R. J. Watkins, *Chem. Commun.*, 1052 (1967).

(4) A. C. Cope, M. M. Martin, and M. A. McKervey, *Quart. Rev., Chem. Soc.*, **20**, 119 (1966).

(5) J. K. Crandall, D. B. Banks, R. A. Colyer, R. J. Watkins, and J. P. Arrington, *J. Org. Chem.*, **33**, 423 (1968).

(6) R. C. Cookson and N. S. Wariyar, *J. Chem. Soc.*, 2302 (1956).

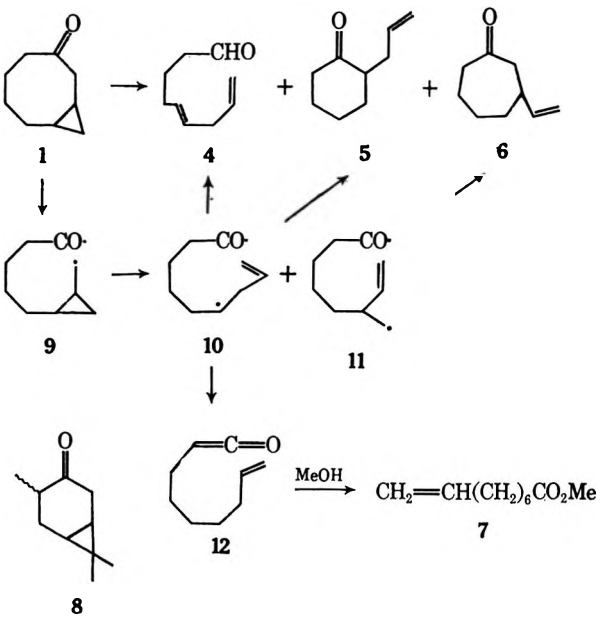
(7) A recent report describes the uv spectra of **1** and its trans isomer: K. B. Wiberg and A. deMeijere, *Tetrahedron Lett.*, 59 (1969).

(8) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, San Francisco, Calif., 1967, Chapter 3.

ert and Kropp[9] in their study of the isomeric 4-caranones (8), which are smaller ring analogs of 1. A related rationale can be applied to the transformations of 1 as illustrated below. Excitation of 1 is followed by virtually exclusive $\alpha$ cleavage in the direction to yield diradical 9. This selective ring fission is attributed to the delocalizing ability of the cyclopropyl substituent[10] which apparently exerts itself effectively in the transition state for bond rupture of electronically excited 1. In this regard, 1 parallels the behavior of its double bond analog.[2] Once generated the cyclopropylcarbinyl radical moiety is postulated to readily unravel in a well-established manner[11] to produce isomeric biradicals 10 and 11. Radical coupling processes from these intermediates give cyclic ketones 5 and 6, respectively. Alternatively, 10 can partake of favorable six-center hydrogen transfers to give aldehyde 4 and ketene 12, the precursor of ester 7. The absence of products from ketene 12 in benzene and cyclohexane is probably only a reflection of the propensity of this reactive intermediate to take part in further thermal and photochemical decomposition under conditions where it is not rendered inert by reaction with the solvent.

One aspect of this photochemical system which differs from that of 3-cyclooctenone is the lack of interconversion of the ketone products or their reversion to starting material. In principle, $\alpha$ cleavage of 5 and 6 in the correct manner would regenerate the postulated biradical intermediates 10 and 11, respectively. These transients should interconvert *via* the cyclopropylcarbinyl intermediate 9 in view of the known chemistry of homoallylic radical species.[11] The observed photostability of 5 and 6 relative to 1 can be attributed to an especially efficient decomposition of 1, an exceptionally inefficient $\alpha$ cleavage for 5 and 6, or both. Ordinarily, a certain degree of reversibility of the $\alpha$-cleavage step appears to obtain in the photolysis of saturated ketones.[12] thereby decreasing the efficiency of observed reaction. In the case of 1, the propensity of the cyclopropylcarbinyl radicals to spring open could promote more judicious utilization of the initial diradical derived from $\alpha$ cleavage. Inefficiency in the photolysis of 5 and 6 may result from a special route for relaxation of the excited states of these ketones, namely intramolecular energy transfer from the carbonyl group to the double bond. Such an explanation had been advanced previously to account for exceptional photostability of $\gamma,\delta$-unsaturated ketones (Scheme I).[13]

SCHEME I




**Bicyclo[6.1.0]nonan-4-one.**—This ketone was prepared by two different routes, each of which utilized 1,5-cyclooctadiene as the starting material. Simmons–Smith reaction followed by the oxymercuration–reduction procedure[14] for hydration gave a mixture of epimeric alcohols 13 and 14 which were smoothly converted to ketone 2 by chromic acid oxidation. Alternatively, the epimeric mixture of alcohols could be obtained from 4-cyclooctenol[5] by the sequence: acetylation, Simmons–Smith reaction, and saponification. As before, masking of the alcohol function was critical for the success of the cyclopropanation step. The ultraviolet spectrum of 2 [uv max (hexane) 287 nm ($\epsilon$ 15)] was normal for saturated cycloalkanones.[15]

The photochemistry of 2 was markedly dependent upon the solvent utilized. In benzene only slow decomposition without the formation of characterizable products was observed. Photolysis in cyclohexane or isopropyl alcohol resulted in reduction to the epimeric alcohols. In methanol, however, a more complex product mixture was obtained. The products were 3-(*cis*-2-allylcyclopropyl)propanal (15), 4-(*cis*-2-vinylcyclopropyl)butanal (16), methyl 3-(*cis*-2-propylcyclopropyl)propanoate (17), alcohols 13 and 14, starting ketone, and an unidentified material in the ratio of 20:3:25:15:36:1.

Structure 15 was assigned on the basis of spectral data which show an aldehyde, a terminal vinyl group, cyclopropyl protons, and methylene groups adjacent to both aldehyde ($\delta$ 2.45) and vinyl ($\delta$ 2.0) functions.[16] Double resonance experiments confirm these assignments which distinguish between the two probable structures 15 and 16 since only the former possesses an allylic methylene group. Retention of the cis stereochemistry at the cyclopropyl ring is confirmed by the observation of two multiplets ($\delta$ 0.75 and −0.2) for the cyclopropyl methylene group. The trans isomer should give a single absorption for the methylene protons.[17]

The structural assignment for 16 is considered tentative owing to the small amount of this material obtained. The nmr spectrum was quite similar to that

(9) D. C. Heckert and P. J. Kropp, *J. Amer. Chem. Soc.*, **90**, 4911 (1968). See also M. S. Carson, W. Cocker, S. M. Evans, and P. V. R. Shannon, *Tetrahedron Lett.*, 6153 (1968); R. G. Carlson and E. L. Biersmith, *Chem. Commun.*, 1049 (1969).

(10) J. K. Kochi, P. J. Krusic, and D. R. Eaton, *J. Amer. Chem. Soc.*, **91**, 1877, 1879 (1969).

(11) L. K. Montgomery and J. W. Matt, *ibid.*, **89**, 6556 (1967), and earlier papers in this series.

(12) P. J. Wagner and R. W. Spoerke, *ibid.*, **91**, 4437 (1969).

(13) L. D. Hess, J. L. Jacobson, K. Schaffner, and J. N. Pitts, Jr., *ibid.*, **89**, 3684 (1967).

(14) H. C. Brown and P. Geoghegan, Jr., *ibid.*, **89**, 1522 (1967).

(15) Cyclooctanone, for example, exhibits a uv max (EtOH) at 283 nm ($\epsilon$ 17): N. J. Leonard and F. H. Owens, *ibid.*, **80**, 6039 (1958).

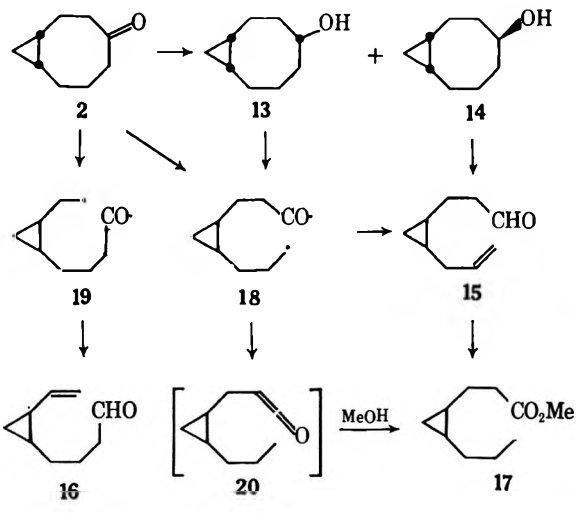
(16) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," 2nd ed, Pergamon Press, Oxford, 1969, pp 181–183.

(17) L. K. Montgomery, personal communication of unpublished results, 1969; D. T. Longone and A. H. Miller, *Chem. Commun.*, 447 (1967), and references therein.

of **15** except for a simplified pattern in the olefinic region.

The assignment of structure **17** follows from the presence of a methyl ester, cyclopropyl protons, and an aliphatic methyl group. The carbon skeleton was shown to be the same as **15** by transforming this latter compound to **17** by the sequence: catalytic hydrogenation, chromic acid oxidation, and diazomethane esterification (Scheme II).

SCHEME II




The alcohol product was homogeneous to all gc conditions utilized but was readily recognized as an epimeric mixture by the presence of two nonintegral signals for the carbinol hydrogen in the nmr at $\delta$ 4.0 and 3.5. Conversion of the mixture to the trimethylsilyl ethers allowed for the separation and characterization of the two products. Examination of molecular models suggests that the cis isomer has available reasonably good conformations which place the carbinol hydrogen in the plane of the cyclopropyl ring where it can experience deshielding from the magnetic anisotropy of the cyclopropyl ring.[18] The isomer whose signal appears at $\delta$ 4.0 is thus assigned as **13**. The trans epimer **14** appears to be more or less uninfluenced by the cyclopropyl ring, and its carbinol proton ($\delta$ 3.5) is similar to the analogous hydrogen in cyclooctanol ($\delta$ 3.65). The silyl ethers show a similar effect. The ratio of **13** to **14** from the photolysis is 3:1, whereas lithium aluminum hydride reduction of ketone **2** gives a 7:1 ratio.

The gross aspects of the photochemistry of **2** appear to be quite typical of simple cycloalkanones. Reduction of the carbonyl function to an alcohol by hydrogen abstraction from the solvent is a well-established process, as is transformation to acyclic aldehydes and esters (*via* the corresponding ketenes). Intermediate biradicals **18** and, to a much lesser extent, **19** serve as suitable reactive species which can undergo further transformations leading to the observed products. The large preference for reaction *via* **18** over **19** is striking. However, interpretation of this fact in terms of a special effect of the cyclopropyl group appears to be unwarranted in view of a similar discrimination in the case of 3-methylcyclohexanone.[12] In both instances the preferred product is derived from bond cleavage on the side of the carbonyl group farther from the substituent. The potential reversibility of the $\alpha$-cleavage step could be utilized to rationalize these results,[12] but clearly more information is required before an adequate explanation for the effects of substituents on these cleavage reactions can be tendered. Nonetheless, it should be noted that relatively subtle structural changes are apparently capable of markedly influencing the course of cycloalkanone photoisomerizations.

A second noteworthy point arises from the pronounced solvent effect which leads to competition between bimolecular reduction and $\alpha$ cleavage in methanol, but only the former in cyclohexane or isopropyl alcohol. A plausible explanation for this novel observation is that in methanol the carbonyl group is surrounded by oriented solvent molecules which retard bimolecular hydrogen atom abstraction from the methyl group of the solvent. This allows for competitive $\alpha$ cleavage. On the other hand, in cyclohexane the bare carbonyl function experiences little difficulty in abstracting hydrogen from the solvent, and reduction predominates. According to this view, isopropyl alcohol, which hydrogen bonds less effectively than methanol and offers a better hydrogen abstraction reaction, behaves more like cyclohexane than methanol. The factors which determine the relative efficiencies for $\alpha$ cleavage *vs.* reduction for a given ketone are poorly understood, but further studies on solvent effects are indicated. The potential control of these competitive pathways has important implications for synthetic uses.[19]

**4,5-Epoxycyclooctanone.**—Epoxide **3** was obtained from peracid oxidation of 4-cyclooctenone. The ultraviolet spectrum gave no evidence for transannular interaction between the epoxide and ketone functions: uv max (hexane) 288 nm ($\epsilon$ 13).

Assessment of the photochemical behavior of **3** was complicated by the propensity of the initially formed photoproduct mixture to undergo further nonphotochemical transformation. Thus, irradiation of **3** in cyclohexane gave a mixture of alcohols which was difficult to analyze and whose composition appeared to change on standing. Treatment of the crude product with hexamethyldisilazane allowed the isolation of two silylated materials in a 2:1 ratio. The same two products were obtained by lithium aluminum hydride reduction of **3** and subsequent silylation. The major component retained the epoxide ring as demonstrated by its spectroscopic properties and by comparison with a sample obtained by silylation and epoxidation of 4-cyclooctenol.[20] However, the second silyl ether lacked ir and nmr characteristics of the epoxide function. The results from hydride reduction of **3** suggest initial formation of the expected *cis*- and *trans*-epoxy alcohols (**20** and **21**), followed by intramolecular displacement of the suitably disposed *trans*-hydroxyl of **21** on the transannular epoxide moiety which transforms it into a bridged bicyclic ether. Two

(18) D. J. Patel, M. E. H. Howden, and J. D. Roberts, *J. Amer. Chem. Soc.*, **85**, 3218 (1963).

(19) During the preparation of this work for publication, we learned of a related study of the photochemistry of **1** and **2** by Professor S. Moon whom we thank for a helpful exchange of information.

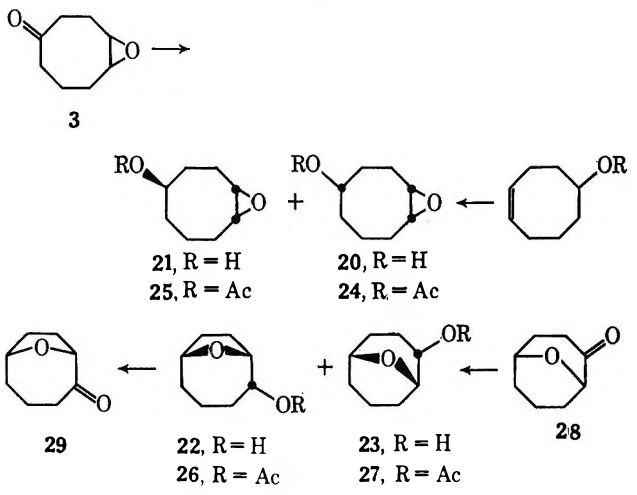
(20) This epoxidation apparently proceeds with high stereoselectivity presumably by attack of peracid cis to the silyl ether group.

different bicyclic ethers, **22** and **23**, are possible depending on the mode of transannular attack.[21]

Gas chromatographic studies utilizing acetate esters confirmed this hypothesis. Photolysis of **3** followed immediately by exposure to acetic anhydride–pyridine gave the same two peaks as obtained by epoxidation of 4-cyclooctenyl acetate. These are assigned as the *cis*- and *trans*-4,5-epoxycyclooctyl acetates (**24** and **25**). However, acetylation of the alcohol mixture obtained by epoxidation of 4-cyclooctenol gave only one of these peaks plus a second peak of the same retention time as an authentic unresolved mixture of bicyclic acetates **26** and **27**.[22] Treatment of the bicyclic acetate from either source with hydride followed by chromic acid oxidation gave a mixture of bicyclic ketones **28** and **29**.

The complicated set of interrelations described above establishes that the initial photoproducts are **20** and **21** and that under certain conditions **21** is further transformed to a mixture of the isomeric bicyclic ethers **22** and **23** (*e.g.*, under the conditions of silylation of the photoproduct, hydride reduction of **3**, and epoxidation of 4-cyclooctenol) (Scheme III).

SCHEME III




The recovery of volatile products from the photolysis of **3** in cyclohexane was poor, and only decomposition was observed from irradiation in benzene. The photolysis was not examined in methanol owing to an unexplored dark reaction of **3** with the solvent. Thus, the only characterized photoreaction of **3** is simple reduction.

## Experimental Section

General.—Nmr spectra were obtained with Varian A-60 or HR-100 instruments ($CCl_4$) and infrared spectra with Perkin-Elmer 137 and 137G spectrophotometers (neat samples unless noted otherwise). Gas chromatography (gc) was performed on Aerograph A1200 (analytical) and A90-P3 (preparative) instruments. Analytical columns were 10 ft × 1/8 in. 15% Carbowax 20M on 60–80 Chromosorb W and 10 ft × 1/8 in. 15% diethylene glycol succinate on 60–80 Chromosorb W. Mass spectra were obtained at 70 eV on an AEI-MS 9 instrument. Anhydrous magnesium sulfate was used for all drying operations.

Preparative photolyses were carried out on 1% solutions with a 450-W medium-pressure Hanovia Type L mercury vapor lamp in an immersion-well apparatus using a Vycor filter. The solution was degassed by bubbling nitrogen through it prior to photolysis, and a positive nitrogen pressure was maintained during photolysis. The course of the reaction was monitored by analytical gc.

**3-Cyclooctenyl Acetate.**—A solution of 6.3 g of 3-cyclooctenol and 12 ml of acetic anhydride in 50 ml of pyridine was stirred at room temperature for 18 hr. The solution was poured into 10% hydrochloric acid and extracted four times with pentane. The pentane solution was washed with saturated aqueous sodium bicarbonate and water and dried, and the solvent was removed by evaporation on a steam bath. Distillation gave 6.2 g of 3-cyclooctenyl acetate: bp 108–110° (30 mm); ir 3.3, 5.76, 7.3, 8.1, and 9.7 μ; nmr δ 5.65 (m, 2, CH=CH), 4.8 (broad m, 1, CHOAc), and 2.6–1.1 (broad m, 13). A sharp singlet at 1.9 ($CH_3CO$) was superimposed over the methylene absorption.

**Preparation of Bicyclo[6.1.0]nonan-3-yl Acetate.**—A solution of 95 g of methylene iodide, 26 g of zinc–copper couple, and 100 mg of iodine in 250 ml of ether was stirred at reflux for 0.5 hr. The oil bath was removed, and 4.5 g of 3-cyclooctenyl acetate in 25 ml of ether was added dropwise. Heating was then resumed and the mixture stirred at reflux for 48 hr. The mixture was filtered through HyFlo Super Cel and the filtrate was washed with five 50-ml portions of 5% hydrochloric acid, then with saturated sodium bicarbonate solution, and water, and dried. Concentration, followed by distillation, gave 4.7 g (96%) of bicyclo[6.1.0]nonan-3-yl acetate: bp 110–115° (30 mm); ir 3.25, 3.33, 5.75, 7.3, 8.0, and 9.8 μ; nmr δ 4.8 (m, 1, CHOAc), 2.2–0.5 (m, 16, $CH_2$, $CH_3$, cyclopropyl H), and −0.2 (m, 1, cyclopropyl H). The presence of sharp singlets of nearly equal intensity at 1.85 and 1.90 indicates that the product is a mixture of isomers, even though it was homogeneous to gc.

*Anal.* Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.23; H, 10.00.

**Bicyclo[6.1.0]nonan-3-ol.**—To a solution of 3 g of potassium hydroxide in 50 ml of methanol was added 4.5 g of bicyclo[6.1.0]nonan-3-yl acetate, and the resulting mixture was stirred at reflux for 3 hr. The reaction mixture was poured into water and pentane, and the layers were separated. The organic layer was washed twice with water and dried. The solvent was removed on a flash evaporator, and the residue was distilled through a short-path distillation head to give 2.7 g (90%) of bicyclo[6.1.0]nonan-3-ol: bp 115–120° (20 nm); ir 3.0, 3.2, 3.3, and 9.6 μ; nmr δ 3.7 (m, 2, CHOH), 2.4–0.5 (m, 13, $CH_2$, cyclopropyl H), and −0.3 (m, 1, cyclopropyl H).

**Bicyclo[6.1.0]nonan-3-one (1).**—Five milliliters of 8 *N* chromic acid was added dropwise to a cooled, stirred solution of 2.9 g of bicyclo[6.1.0]nonan-3-ol in 50 ml of acetone. The mixture was stirred for 0.75 hr, poured into water, and extracted with four 50-ml portions of pentane. The organic solution was washed with water and dried, and the solvent was removed on a flash evaporator. Distillation gave 2.6 g (91%) of **1**: bp 98–105° (20 mm); uv max (hexane) 289 nm (ε 44) [lit.[7] 298 nm (ε 34)]; ir 3.24, 3.32, 5.88, and 11.7 μ; nmr δ 2.8–1.0 (m, 10), 0.7 (m, 3, cyclopropyl H), and −0.1 (m, 1, cyclopropyl H).

*Anal.* Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.24; H, 9.95.

**Photolysis of 1.**—A solution of 0.9 g of **1** in 110 ml of methanol was photolyzed for 15 min. The solvent was removed by evaporation on a steam bath, and the residue was distilled (0.2 mm) to give 0.76 g of crude photoproduct. The products were isolated by preparative gc. The first product (27%) was identified as *trans*-5,8-nonadienal (**4**): ir 3.22, 3.33, 3.68, 5.80, 6.1, 10.1, 10.3, and 11.0 μ; nmr δ 9.5 (t, 1, $J$ = 1 Hz, CHO), 6.1–4.7 (m, 5, CH=CH), and 3.0–1.3 (m, 8).

*Anal.* Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.09; H, 10.27.

The second product (18%) was methyl 8-nonenoate (**7**): ir ($CCl_4$) 3.24, 5.74, 6.1, 7.3, 8.4, 8.6, 10.1, and 11.0 μ; nmr δ 5.7 (m, 1, CH=$CH_2$), 4.9 (m, 2, CH=$CH_2$), 3.6 (s, 3, $CH_3O$), and 2.5–1.0 (m, 10).

*Anal.* Calcd for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66. Found: C, 70.53; H, 10.71.

The third component (35%) was 2-allylcyclohexanone (**5**), identified by comparison with an authentic sample. The fourth product (10%) was identified as 3-vinylcycloheptanone (**6**) on spectroscopic grounds: ir ($CCl_4$) 3.24, 5.90, 6.1, 10.1, and 11.0 μ; nmr (100 MHz) δ 5.8 (m, 1, CH=$CH_2$), 5.0 (m, 2, $CH_2$=CH),

(21) Related reactions are well precedented. See, for example, A. C. Cope, R. S. Bly, M. M. Martin, and R. C. Petterson, *J. Amer. Chem. Soc.*, **87**, 3111 (1965).

(22) S. Moon and L. Haynes, *J. Org. Chem.*, **31**, 3067 (1966); A. C. Cope, M. A. McKervey, and N. M. Weinshenker, *J. Amer. Chem. Soc.*, **89**, 2932 (1967).

and 2.6–1.2 (m, 11); mass spectrum *m/e* (rel intensity) 138 (30), 82 (32), 81 (100), 68 (46), 67 (67), 56 (61), and 55 (33).

*Anal.* Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.00; H, 10.16.

The fifth component (12%) was **1**.

Photolysis of 1 in cyclohexane or benzene required 45 min and gave **4** (14%), **5** (32%), **6** (14%), **1** (33%), and an unknown of short retention time (7%). No equilibration of **4**, **5**, or **6** with each other or starting material was observed when each of these products was irradiated in separate experiments.

**Catalytic Hydrogenation of 7.**—A solution of 25 mg of **7** in 5 ml of methanol was hydrogenated at atmospheric pressure with 5% palladium on carbon for 24 hr. The catalyst was removed by filtration and the filtrate was poured into water and pentane. The layers were separated and the aqueous layer was washed twice with pentane. The pentane extracts were washed with water and dried, and the solvent was removed by distillation to give 20 mg of methyl pelargonate, identical in all respects with an authentic sample.

**Catalytic Hydrogenation of the Photoproducts of 1.**—A solution of 450 mg of the crude photoproduct mixture from photolysis of 1 in benzene was hydrogenated in 15 ml of methanol at atmospheric pressure using 10% palladium on carbon as catalyst. After 24 hr, the catalyst was removed by filtration, and the filtrate was poured into water and extracted three times with pentane. The pentane extract was washed with water and dried, and the solvent was removed by distillation. Separation by preparative gc yielded *n*-nonanal, 2-*n*-propylcyclohexanone (each of which was identified by comparison of its ir spectrum with that of a known sample), and a material tentatively identified as 3-ethylcycloheptanone, ir 5.88 μ.

**2-Allylcyclohexanone (5).**—To 75 ml of a 0.8 *M* solution of commercial allylmagnesium bromide in ether was added dropwise 5 g of cyclohexene oxide in 25 ml of ether. The mixture was stirred at reflux for 12 hr and then poured into 75 ml of cold 5% hydrochloric acid and 50 ml of pentane. The layers were separated and the aqueous portion was washed with three 50-ml portions of pentane. The combined extracts were washed with water and dried, and the solvent was removed by distillation. The residue was distilled through a short-path distillation head to give 5.9 g (83%) of 2-allylcyclohexanol: bp 46–48° (0.8 mm); ir 3.0, 3.26, 6.1, 9.5, 9.7, 10.1, and 11.0 μ; nmr δ 6.1–4.7 (m, 3, $CH{=}CH_2$), 3.85 (s, 1, OH), 3.2 (m, 1, CHOH), and 2.6–0.9 (m, 11).

To a cooled, stirred solution of 4.2 g of 2-allylcyclohexanol in 50 ml of acetone was added dropwise 8 ml of 8 *N* chromic acid. The resulting mixture was stirred at room temperature for an additional 30 min, poured into water, and extracted with three 50-ml portions of pentane. The pentane solution was washed with water, dried, and concentrated. The residue was distilled to give 3.2 g (76%) of **5**: bp 82–86° (15 mm); ir 3.24, 5.84, 6.1, 10.1, and 11.0 μ; nmr δ 6.1–4.7 (m, 3, $CH{=}CH_2$) and 2.6–1.0 (m, 11).

**4-Cyclooctenyl Acetate.**—A solution of 10.5 g of 4-cyclooctenol and 15 ml of acetic anhydride in 40 ml of pyridine was stirred at room temperature for 18 hr. The reaction mixture was poured into 250 ml of 10% hydrochloric acid and 500 ml of pentane, and the layers were separated. The pentane was washed with two 50-ml portions of 10% hydrochloric acid, saturated aqueous sodium bicarbonate, and water and dried. The solvent was removed by distillation and the residue was distilled to give 12 g (86%) of 4-cyclooctenyl acetate: bp 110–113° (20 mm); ir, 3.3, 5.78, 7.3, and 8.1 μ; nmr δ 5.6 (m, 2, CH=CH), 4.7 (broad m, 1, CHOAc), 2.4–1.4 (m, 13). A sharp singlet ($CH_3CO$) at 1.9 was superimposed over the methylene multiplet.

**Bicyclo[6.1.0]nonan-4-yl Acetate.**—A solution of 75 g of methylene iodide, 20 g of zinc–copper couple, and 100 mg of iodine in 250 ml of ether was stirred at reflux for 30 min. The heating bath was removed, and 4.5 g of 4-cyclooctenyl acetate in 25 ml of ether was added dropwise. The resulting mixture was stirred at reflux for 48 hr. The mixture was filtered through HyFlo Super Cel and the filtrate was washed with five 50-ml portions of 5% HCl, then with saturated aqueous sodium bicarbonate, and water and dried. The solvent was removed by flash evaporation and the residue was distilled to give 4.7 g (86%) of bicyclo[6.1.0]nonan-4-yl acetate: bp 120–125° (2 mm); ir 3.2, 3.3, 5.76, 7.3, and 8.1 μ; nmr δ 4.9 and 4.7 (m, 1, CHO), 2.4–0.3 (m, 16), and −0.3 (m, 1, cyclopropyl H). A sharp singlet ($CH_3CO$) at 1.9 was superimposed upon the broad methylene absorption.

**Bicyclo[6.1.0]nonan-4-ol. A.**—To a stirred, cooled slurry of 20 g of mercuric acetate in 120 ml of 50% aqueous tetrahydrofuran was added dropwise 7.0 g of bicyclo[6.1.0]non-4-ene. The yellow color disappeared before addition was complete (*ca.* 5 min), and the solution was stirred at room temperature for 45 min. The reaction mixture was again cooled in an ice bath, and 60 ml of 3 *N* sodium hydroxide and 60 ml of 0.5 *M* sodium borohydride in 3 *N* sodium hydroxide were added slowly. The solution was saturated with sodium chloride and the layers were separated. The aqueous solution was washed twice with tetrahydrofuran, the combined tetrahydrofuran extracts were washed with water and dried, and the solvent was removed by distillation. The residue was distilled through a short-path distillation head to give 6.5 g (81%) of bicyclo[6.1.0]nonan-4-ol: bp 60–63° (1 mm); ir 3.0, 3.26, 3.34, 9.6, 9.7, 10.0, 10.6, and 11.9 μ; nmr (100 MHz) δ 4.0 and 3.5 (two complex multiplets in a ratio of 6:4, together integrating for 1 hydrogen, CHOH), 2.5 (s, 1, OH), 2.3–0.5 (m, 13, $CH_2$, cyclopropyl H), and −0.7 (m, 1, cyclopropyl H). The sample was homogeneous on a variety of gc columns.

*Anal.* Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 76.89; H, 11.46.

**B.**—To a solution of 3.2 g of potassium hydroxide in 55 ml of methanol was added 4.2 g of bicyclo[6.1.0]nonan-4-yl acetate, and the resulting solution was stirred at reflux for 2.5 hr. The reaction mixture was poured into water and pentane, and the layers were separated. The pentane layer was washed three times with water and dried, and the solvent was removed by flash evaporation. Distillation gave 2.5 g (77%) of bicyclo[6.1.0]-nonan-4-ol.

**Trimethylsilylation of Bicyclo[6.1.0]nonan-4-ol.**—A mixture of 227 mg of the product obtained in the previous experiment and 550 mg of hexamethyldisilazane was stirred at 85–90° for 12 hr. Gc analysis showed two products of shorter retention time than the starting alcohol in a ratio of 56:44. Preparative gc gave two products which are assigned as the trimethylsilyl ethers of *cis*- and *trans*-bicyclo[6.1.0]nonan-4-ol (**13** and **14**). The 56% isomer shows absorptions in the nmr at δ 3.9 (m, 1, CHO), 2.2–0.3 (m, 13), 0.0 (s, 9, $CH_3Si$), and −0.3 (m, 1, cyclopropyl H). The 44% isomer exhibits an nmr identical with that of the first component, except that the downfield multiplet is shifted to 3.3.

**Bicyclo[6.1.0]nonan-4-one (2).**—To a cooled, stirred solution of 6.2 g of bicyclo[6.1.0]nonan-4-ol in 60 ml of acetone was added dropwise 12 ml of 8 *N* chromic acid, and the solution was stirred for an additional 15 min. The reaction mixture was poured into 40 ml of water and extracted with five 50-ml portions of pentane. The combined pentane extracts were washed with water and dried and the solvent was removed by flash evaporation. Distillation of the residue gave 4.0 g (66%) of **2**: bp 99–101° (15 mm); uv max (hexane) 287 nm (ε 15); ir 3.25, 3.33, and 5.85 μ; nmr δ 2.3 (m, 4, $CH_2CO$), 2.1–1.3 (m, 6, $CH_2$), 0.6 (m, 3, cyclopropyl H), and −0.2 (m, 1, cyclopropyl H).

*Anal.* Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.34; H, 10.24.

**Photolysis of 2. A. Methanol.**—A solution of 1.0 g of **2** in 110 ml of methanol was photolyzed for 1 hr. The solvent was removed by evaporation on a steam bath and the residue distilled (0.1 mm) to give 0.8 g of crude photoproduct. The products were isolated by preparative gc (20 ft × 0.25 in. 20% UCON 2000 Polar, 160–180°). The first component was ethylene glycol. The second product (20%) was identified as **15** on the basis of its spectral properties: ir 3.24, 3.33, 3.67, 5.80, 6.1, 10.1, and 11.0 μ; nmr (100 MHz) δ 9.57 (t, 1, $J$ = 1 Hz, CHO), 5.8 (m, 1, $CH{=}CH_2$), 5.0 (m, 2, $CH{=}CH_2$), 2.45 (triplet of t, 2, $J$ = 7, 1 Hz, $CH_2CHO$), 2.0 (m, 2, $CH_2{=}CHCH_2$), 1.6 (m, 2, $CH_2$), 0.75 (m, 3, cyclopropyl H), and −0.2 (m, 1, cyclopropyl H). Double irradiation experiments confirmed this structure, since irradiation of the methylene multiplet at 2.0 effected a simplification of the vinyl resonance, thereby demonstrating that the vinyl group was part of a side chain terminated by an allyl group. Irradiation of either the aldehyde resonance at 9.57 or the methylene absorption at 2.45 clearly demonstrated the mutual coupling of these two groups.

*Anal.* Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.10; H, 10.32.

The third component (3%) is tentatively identified as 4-(*cis*-2-vinylcyclopropyl)butanal (**16**): ir 3.25, 3.33, 5.80, 6.1, 10.1, and 11.0 μ; the nmr shows a spectrum nearly identical with that of **15** except that the vinyl resonance is somewhat simpler.

The fourth product (25%) was identified as methyl 3-(*cis*-2-*n*-propylcyclopropyl)propanoate (**17**): ir 3.25, 3.33, 5.74, 7.3, and 8.6 $\mu$; nmr $\delta$ 3.61 (s, 3, $CH_3O$), 2.3 (m, 2, $CH_2CO$), 2.0–0.5 (m, 14), and −0.2 (m, 1, cyclopropyl H). In addition, a multiplet typical of an aliphatic methyl was observed at 1.0. This product was homogeneous to a variety of gc columns and was identical with a sample prepared from aldehyde **15**.

*Anal.* Calcd for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66. Found: C, 70.46; H, 10.71.

The fifth component (1%) was not isolated in sufficient quantity to identify it. The sixth component (36%) was starting ketone. The seventh component (15%) was identified as a mixture of the bicyclo[6.1.0]nonan-4-ols (**13** and **14**) by comparison with authentic material.

**B. Cyclohexane.**—A solution of 1.0 g of **2** was photolyzed for 45 min; gc analysis showed two major products in addition to starting material. Concentration and distillation gave 0.8 g of crude product. The first product was identified as bicyclohexyl by comparison with authentic material. The other two components were identified as starting material (33%) and the isomeric bicyclo[6.1.0]nonan-4-ols (67%).

**C. Isopropyl Alcohol.**—Photolysis of a 50-mg sample of **2** in 5 ml of isopropyl alcohol led to a mixture of starting material (30%) and the isomeric bicyclo[6.1.0]nonan-4-ols (3:1) (70%).

**D. Benzene.**—Photolysis of a 10-mg sample of **2** in 1 ml of benzene in a Rayonet photochemical reactor with 3100-Å lamps led to a very slow decomposition of starting material with no discrete product formation.

**4,5-Epoxycyclooctanone (3).**—A solution of 17 ml of 40% peracetic acid was added dropwise to a cooled, stirred mixture of 5.4 g of 4-cyclooctenone, 29 g of anhydrous sodium carbonate, and 100 ml of methylene chloride. The reaction was stirred at room temperature for 48 hr, and the solid salts were removed by suction filtration and washed thoroughly with additional methylene chloride. The filtrate was washed with water, dried, and concentrated. The pasty residue was purified by sublimation to give 5.0 g (82%) of **3**. Low-temperature recrystallization from ether and sublimation gave a pure sample: mp 85–86°; uv max (hexane) 288 nm ($\epsilon$ 13); ir ($CCl_4$) 5.86, 9.9, 10.4, 11.0, and 11.6 $\mu$; nmr very sharp, complex absorption pattern from $\delta$ 2.9 to 1.5.

*Anal.* Calcd for $C_8H_{12}O_2$: C, 68.55; H, 8.63. Found: C, 68.54; H, 8.88.

**Photolysis of 3.**—A solution of 1.1 g of **3** in 110 ml of cyclohexane was irradiated for 1.25 hr. The solvent was removed to give 0.7 g of crude product: ir 3.0, 5.85, and 9.6 $\mu$. The crude product was stirred at 90° in excess hexamethyldisilazane for 18 hr. Three components in addition to **3** (32%) were isolated from the product thus obtained by preparative gc. The first product was bicyclohexyl. The second product (23%) displayed ir 3.5, 8.0, 9.4, 11.4, and 11.9 $\mu$; nmr (100 MHz), $\delta$ 4.4–3.5 (m, 3, CHO), 2.3–1.1 (m, 10, $CH_2$), and 0.1 (s, 9, $CH_3Si$).

*Anal.* Calcd for $C_{11}H_{22}O_2Si$: C, 61.66; H, 10.34. Found: C, 61.72; H, 10.44.

The third product (45%) was 4,5-epoxycyclooctyl trimethylsilyl ether: ir 3.5, 8.0, 9.1, 9.6, 10.9, 11.1, 11.4, 11.9, and 13.4 $\mu$; nmr (100 MHz) $\delta$ 3.9 (m, 1, CHOSi), 2.75 (m, 2, epoxide H), 2.2–1.0 (m, 10, $CH_2$), and 0.05 (s, 9, $CH_2Si$).

*Anal.* Calcd for $C_{11}H_{22}O_2Si$: C, 61.66; H, 10.34. Found: C, 61.58; H, 10.29.

A solution of 46 mg of **3** in 4.6 ml of cyclohexane in a Pyrex test tube was degassed and irradiated in a Rayonet photochemical reactor with 3000-Å bulbs for 6 hr. The solvent was removed under reduced pressure, the residue was dissolved in 1 ml of dry pyridine, and 0.4 ml of acetic anhydride was added. After standing for 17 hr at room temperature, the mixture was diluted with water and extracted with pentane. The pentane extract was washed with 1 *N* hydrochloric acid and saturated sodium carbonate solution and dried, and the solvent was removed. Gc assay of the residue displayed two peaks in a 4:1 ratio. These peaks were shown to have the same gc elution times as *cis*- and *trans*-4,5-epoxycyclooctyl acetates (**24** and **25**) prepared by peracid oxidation of 4-cyclooctenyl acetate.

When the photolysis was repeated with an internal standard, it was observed that more than half of the **3** was converted to nonvolatile products.

**Reaction of 3.**—To a cooled, stirred slurry of 200 mg of lithium aluminum hydride in 50 ml of anhydrous ether was added dropwise 1.0 g of **3** in 10 ml of ether. The resulting mixture was stirred at 0° for 3 hr, and hydrolysis was effected by addition of 2 ml of water. Magnesium sulfate was added, and the solid material was removed by suction filtration and washed with additional solvent. The filtrate was concentrated to give 0.9 g of a viscous liquid which was stirred at 85° with 6 ml of hexamethyldisilazane for 30 hr. Gc analysis showed two products in a ratio of 1:8 which were collected by preparative gc and were found to be identical with the silyl ethers obtained from the photolysis of **3**.

**4,5-Epoxycyclooctyl Trimethylsilyl Ether.**—A mixture of 0.75 g of 4-cyclooctenol in 3 ml of hexamethyldisilazane was stirred at 85° for 48 hr. The resulting trimethylsilyl ether (0.5 g) was collected by preparative gc and added to 25 ml of ice-cold methylene chloride containing 10 g of anhydrous sodium carbonate, and a methylene chloride solution of acetic acid–free peracetic acid[23] obtained from 1 ml of 40% peracetic acid was added. The resulting solution was stirred for 18 hr and then suction filtered. The solid filter cake was washed with methylene chloride, and the filtrate was concentrated to give a crude product from which the trimethylsilyl ether of **20** was collected by preparative gc. This material was identical with that obtained from the reactions described above except for minor differences in the nmr attributable to small amounts of the epimeric ether.

***cis*- and *trans*-4,5-Epoxycyclooctyl Acetate (24 and 25).**[24]—To a solution of 0.78 g of 4-cyclooctenyl acetate in 50 ml of methylene chloride at 0° was added 0.79 g of *m*-chloroperoxybenzoic acid in small portions with swirling. After standing for 18 hr, the solution was washed with saturated sodium carbonate solution and dried. Removal of the solvent gave a colorless oil: ir 5.77, 8.0, 9.7, and 9.8 $\mu$. Gc analysis showed a 3:1 ratio of **24** to **25**.

**Epoxidation of 4-Cyclooctenol.**—To an ice-cold solution of 1.0 g of 4-cyclooctenol in 50 ml of methylene chloride was added 1.46 g of *m*-chloroperoxybenzoic acid in small portions with swirling. After standing for 13 hr at room temperature, the solution was washed with two 20-ml portions of saturated sodium carbonate solution and dried, and the solvent was removed to give 1.28 g of colorless oil.

To a solution of 0.5 g of the above mixture in 5 ml of dry pyridine was added 1.88 ml of acetic anhydride. The solution was allowed to stand at room temperature for 20 hr. After being cooled to 0°, water was added slowly to hydrolyze the excess acetic anhydride before dilution to 50 ml. The resulting solution was extracted with pentane. The pentane solution was washed with 1 *N* hydrochloric acid and dried. Removal of the solvent gave a colorless oil: ir 5.77, 8.0, 9.4, 9.6, 9.7, and 9.8 $\mu$. Gc assay showed a 3:2 ratio of two peaks. The smaller of these corresponds in gc elution time to the peak assigned as **24**. The larger peak corresponds in retention time to a gc inseparable mixture of *endo*-9-oxabicyclo[4.2.1]non-2-yl acetate (**26**) and *endo*-9-oxabicyclo[3.1.1]non-2-yl acetate (**27**) obtained by treatment of 4-cyclooctenol with lead tetraacetate.[22]

To a stirred, ice-cold solution of 0.5 g of the original epoxidation mixture in 10 ml of acetone was added dropwise 8 *N* chromic acid solution until the reagent color persisted. Excess oxidizing agent was destroyed by the addition of isopropyl alcohol. The mixture was diluted to 50 ml with water and stirred until the chromium salts dissolved. The solution was extracted with pentane, and the pentane solution was dried. The solvent was removed to give a colorless oil. Gc analysis showed two peaks, one of which corresponded to **3**. The mixture was separated by gc, and the second peak was shown by nmr analysis to be a 1:2 mixture of **28** and **29** by comparison of the ir and nmr spectra to those of pure **29**[25] and to a 1:1 mixture of the two ketones obtained by lithium aluminum hydride reduction of the acetates from treatment of 4-cyclooctenol with lead tetraacetate followed by chromic acid oxidation.

**Registry No.**—**1**, 28399-86-2; **2**, 22562-46-5; **3**, 28399-88-4; **4**, 28399-92-0; **5**, 94-66-6; **6**, 28399-94-2; **7**, 20731-23-1; **15**, 28405-41-6; **17**, 28405-54-1; 3-cyclooctenyl acetate, 28339-89-5; bicyclo[6.1.0]nonan-3-yl acetate, 28399-90-8; bicyclo[6.1.0]nonan-3-ol, 28399-91-9; 2-allylcyclohexanol, 21895-83-0; 4-cyclooctenyl acetate, 22445-58-5; bicyclo[6.1.0]nonan-4-yl acetate, 28405-39-2; bicyclo[6.1.0]nonan-4-ol, 28405-40-5; 4,5-epoxycyclooctyl trimethyl silyl ether, 28405-53-0.

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# The Photochemistry of Bicyclo[6.1.0]nonan-3-one, Bicyclo[6.1.0]nonan-4-one, and Cyclooctanone

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Irradiation of bicyclo[6.1.0]nonan-3-one (1) in *tert*-butyl alcohol gave 2-allylcyclohexanone (2), 3-vinylcycloheptanone (3), and *tert*-butyl non-8-enoate (4). When irradiated in ether, the ketone 1 gave bicyclo[6.1.0]nonan-3-ol (5) and the isomeric 3-(1-ethoxyethyl)bicyclo[6.1.0]nonan-3-ol (6). In ether, bicyclo[6.1.0]nonan-4-one (7) gave bicyclo[6.1.0]nonan-4-ol (8) and the isomeric 4-(1-ethoxyethyl)bicyclo[6.1.0]nonan-4-ol (9). In *tert*-butyl alcohol, the ketone 7 gave mixtures of aldehydes 10 and 11 and *tert*-butyl esters 12 and 13. Irradiation of cyclooctanone (14) in *tert*-butyl alcohol gave the isomeric 2-(3-buten-1-yl)cyclobutanol (15) and *tert*-butyl octanoate (16). In ether, the ketone 14 gave cyclooctanol (17) and 1-(1-ethoxyethyl)cyclooctanol (18).

Cyclopropyl groups have been known to affect the course of a photoreaction. Most attention has centered on cyclopropyl rings $\alpha$ to or conjugated with a carbonyl group. Many of these studies have indicated that the cyclopropyl bond which best overlaps with the $\pi$ lobes of the carbonyl group undergoes a rapid photoreaction in a highly specific manner.[1,2]

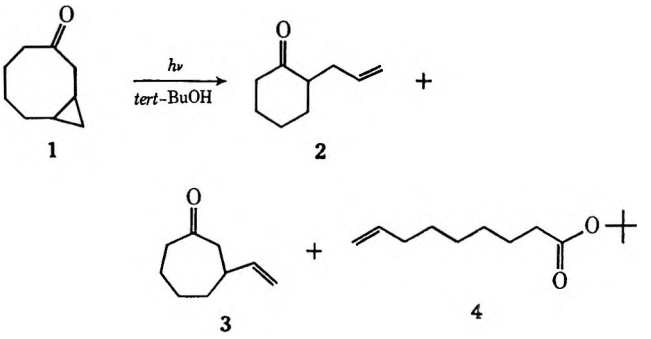
In ring compounds of $C_5$ and $C_6$ the conformation is rigid, permitting overlap of only one of the cyclopropyl bonds with the carbonyl group. In the case of the bicyclo[6.1.0]nonan-2-one, it has been shown by Paquette[3] that the ring has enough flexibility to permit the overlap of the two adjacent cyclopropyl bonds with the $\pi$ lobes of the carbonyl group.

While there has been considerable attention cast upon the photochemistry of conjugated cyclopropyl ketones, there is little information available on the effect of a cyclopropane ring that is not conjugated with a carbonyl group. Wiberg[4] has noted that there is an interaction between the cyclopropane ring and the carbonyl group in both bicyclo[6.1.0]nonane-2-one and bicyclo[6.1.0]nonan-3-one, but none was observed in bicyclo[6.1.0]nonan-4-one. In the photochemistry of 3- and 4-cyclooctenone, the double bond has been shown to have a very distinct effect on the course of the reaction[5,6] leading to ring-contracted products. It was therefore of interest to study the photochemistry of a ketone with a nonconjugated cyclopropane ring. We wish to report here such a study on bicyclo[6.1.0]nonan-3-one and bicyclo[6.1.0]nonan-4-one. As a comparison, we also studied the photochemistry of cyclooctanone. Past evidence indicates that the cyclopropane ring not conjugated with the carbonyl group can influence the course of the reaction.[7,8]

The photolyses were carried out in an immersion well apparatus using a 550-W Hanovia medium-pressure mercury vapor lamp using a Corex filter. The photolyses were conducted for 3 hr in dilute solutions (less than 1%).

Bicyclo[6.1.0]nonan-3-one (1) was prepared by the oxidation of bicyclo[6.1.0]nonan-3-ol (5) which was obtained from 3-cyclooctenol by the Simmons–Smith reaction.

After 3 hr of irradiation of 1 in *tert*-butyl alcohol, all of the starting ketone was consumed and the photoproduct[9] gave four major peaks on the gas chromatograph in a ratio of 46:15:23:14. They were 2-allylcyclohexanone (2), 3-vinylcycloheptanone (3), and *tert*-butyl non-8-enoate (4). The fourth component appeared to be a mixture in which an aldehyde appeared to be the major product.




2-Allylcyclohexanone (2) was identified by comparison with an authentic sample, prepared by alkylation of the pyrrolidine enamine of cyclohexanone with allyl bromide.

The nmr spectrum of 3 showed absorption for a terminal vinyl group. It also showed a sharp 4-proton peak at $\tau$ 7.6. The structure of this compound was determined by hydrogenating the photolysate of 1 and isolating 3-ethylcycloheptanone, which was identified by comparison with an authentic sample prepared by treating 2-cycloheptenone with ethylmagnesium iodide in the presence of a catalytic amount of cuprous chloride.

The nmr spectrum of 4 also showed absorption for a terminal vinyl group. The ir spectrum showed an ester absorption at 1730 $cm^{-1}$ and peaks at 1400 and 1375 $cm^{-1}$ accounting for a *tert*-butyl group. The structure of 4 was determined by isolating it by glpc and hydrogenating it to the *tert*-butyl nonanoate, which was also independently synthesized from nonanoic acid and isobutylene.

An attractive rationale for the mechanism of this reaction would be the formation of the cyclopropyl carbinyl radical by $\alpha$ cleavage, followed by rearrange-

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(6) (a) J. K. Crandall, J. P. Arrington, and J. Hen, *J. Amer. Chem. Soc.*, **89**, 6208 (1967); (b) L. A. Paquette and R. F. Eizember, *ibid.*, **89**, 6205 (1967).
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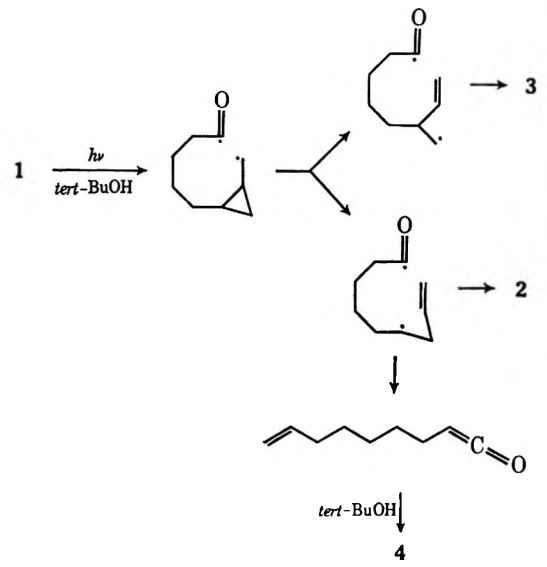
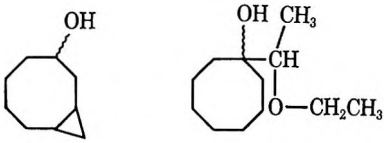
(9) We have learned that Professor Crandall has also studied the photochemistry of this compound. We thank Professor Crandall for informing us of his results prior to publication.

ments to the homoallylic radicals leading to the products, as shown below.




In ether, the photolysis of **1** took a somewhat different course. Photoreduction competed significantly with ring opening. The products were **2**, **3**, bicyclo[6.1.0]-nonan-3-ol (**5**), and the isomeric 3-(1-ethoxyethyl)-bicyclo[6.1.0]nonan-3-ol (**6**) in a ratio of 32:10:32:26.




**5** **6**

The ir spectrum as well as the retention time on glpc of **5** was identical with that of the reduction product of **1** with either sodium in alcohol or lithium aluminum hydride. Glpc analysis on several polar and nonpolar columns did not separate **5** into the isomeric alcohols, and the stereochemistry of **5** was not assigned.

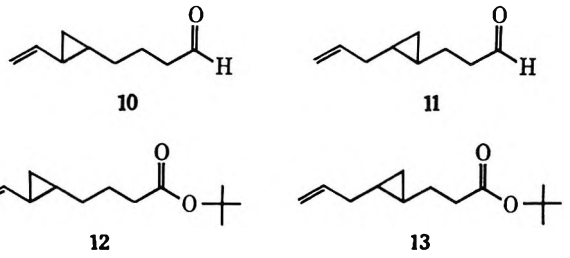
The mass spectrum of **6** showed a parent peak at *m/e* 212 and strong peaks at *m/e* 139 and 73 indicating the loss of the ether group. The ir spectrum showed a peak for a hydroxyl group, and the nmr spectrum confirmed the presence of a cyclopropyl proton.

Bicyclo[6.1.0]nonan-4-one (**7**) was synthesized by oxidation of 4-cyclooctenol to 4-cyclooctenone, followed by the Simmons–Smith reaction. This route was found to be superior to the alternative route of the Simmons–Smith reaction on 4-cyclooctenol, followed by oxidation to **7**.

The irradiation of **7** in ether yielded a mixture of three components in a ratio of 8:32:60. The first component was the ketone **7** and the second was identified as bicyclo[6.1.0]nonan-4-ol (**8**). The product had the same ir spectrum as the product obtained from the oxymercuration of bicyclo[6.1.0]non-4-ene. The stereochemistry of **8** was not determined.

The third component was assigned the structure of 4-(1-ethoxyethyl)bicyclo[6.1.0]nonan-4-ol (**9**). The mass spectrum of this compound showed apparent peak at *m/e* 212 and strong peaks at *m/e* 138 and 73 indicating the loss of the ether group. The infrared spectrum showed bands for a hydroxyl group and an ether group, and the nmr spectrum indicated the presence of a cyclopropane proton.

In *tert*-butyl alcohol, the ketone **7** gave a mixture of three components in a ratio of 22:15:63. The presence of an aldehyde group in the first component was indicated by the ir and nmr spectra. The nmr spectrum also indicated that a terminal vinyl group was present. A cyclopropyl group was also indicated in the nmr at $\tau$ 10.1. On the basis of this evidence, structures **10** and **11** were tentatively assigned to this component.

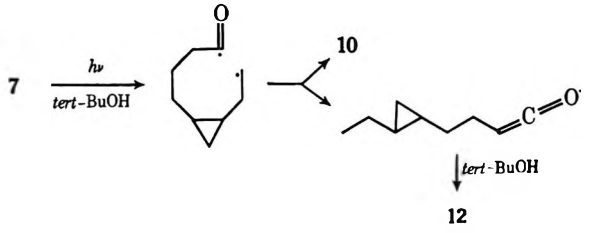


**10** **11**

**12** **13**

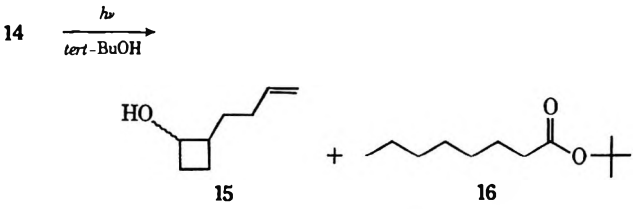
The second component was the ketone **7** while the third was a mixture of *tert*-butyl esters. The ir spectrum showed a carbonyl absorption at 1735 $cm^{-1}$, and bands at 1400 and 1365 $cm^{-1}$, indicating the presence of a *tert*-butyl group. The cyclopropyl absorption was also indicated in the nmr spectrum at $\tau$ 10.15. Based on this evidence, the isomeric structures of **12** and **13** were assigned to this component.

A plausible mechanism for this reaction is primary $\alpha$ cleavage followed by hydrogen abstraction to form either the aldehydes or the ketenes. The ketenes then can react with the *tert*-butyl alcohol to form the products.




**12**

For purposes of comparison, cyclooctanone (**14**) was photolyzed.[10] Irradiation of **14** in *tert*-butyl alcohol yielded a mixture which contained three components in a ratio of 15:79:6. The structure of the first component was assigned as 2-(3-buten-1-yl)cyclobutanol (**15**). The nmr spectrum of this component indicated a




**15** **16**

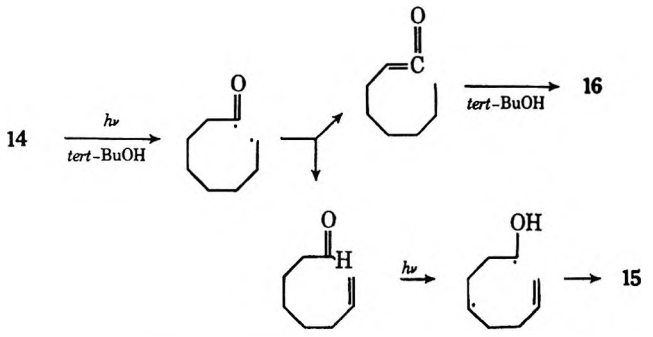
terminal vinyl group and two different protons $\alpha$ to the hydroxyl group each integrating to $^1/_2$ of a proton. Confirmation of this structure was made by oxidizing the crude photolysate and isolating the cyclobutanone formed, which had an infrared absorption for the carbonyl group at 1775 $cm^{-1}$.

The second component of the mixture was cyclooctanone and the third product, which showed an ester absorption in the ir spectrum, was shown to be *tert*-

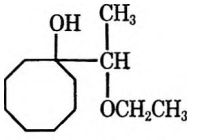
(10) N. C. Yang, Abstracts, 137th National Meeting of the American Chemical Society, Cleveland, Ohio, 1960, No. O-53.

butyl octanoate (16) by independent synthesis from octanoic acid and isobutylene.

The products 15 and 16 probably arise from $\alpha$ cleavage followed by hydrogen atom transfer to form either the aldehyde or the ketene. The aldehyde then rearranges to the alcohol by a type II rearrangement, while the ketene reacts with *tert*-butyl alcohol to give the ester.




The photolysis of cyclooctanone in ether also gave a mixture of three components, but in a ratio of 6:48:46. They were identified as 14 and cyclooctanol (17) by their retention times. The structure of the third component was assigned as 1-(1-ethoxyethyl)cyclooctanol (18) based on carbon–hydrogen analysis and spectral data. The nmr showed a 3-proton absorption at $\tau$ 6.2–7.0 (protons $\alpha$ to the ethereal oxygen) and a 6-proton absorption at $\tau$ 8.9 (two methyl groups). There was also a peak at $\tau$ 8.45 which integrated for 14 protons. The ir showed a band at 3570 $cm^{-1}$, suggesting a *tert*-hydroxyl group.




18

In cyclohexane, the photolysis of 14 gave cyclooctanol (38%) and several high-molecular-weight hydrocarbons (52%) in addition to 14 (9%). In our hands, in the solvents we used, we were unable to find bicyclo[3.3.0]octan-1-ol previously reported by Yang.[10] However, the exact experimental conditions under which this bicyclic alcohol was formed was not available in the literature.[10]

The photochemistry of ketones 1 and 7 and cyclooctanone are remarkably solvent dependent. In polar, nonhydrogen donating solvents, such as *tert*-butyl alcohol, $\alpha$ cleavage is the primary mode of photoreaction. In less polar solvents where hydrogen donation is possible, such as ether, photoreduction becomes the predominant pathway.

How the cyclopropyl group affects the reactivity of these compounds can be seen by comparing the photochemistry of 1 and 7 to that of cyclooctanone. The ketone 1 splits open quickly in *tert*-butyl alcohol to yield ring-contracted products and esters. The ketone 1 in this case is completely consumed within 15 min. In a similar manner, the ketone 7 splits open rapidly in *tert*-butyl alcohol, but 15% of it is left unchanged at the end of 3 hr. In contrast, cyclooctanone is consumed more slowly and 79% of the ketone is left at the end of 3 hr. Thus the cyclopropyl group must have a definite influence on the reactivity of the two bicyclic ketones.

It is significant that the components of the products from the photolysis of the ketone 7 maintain the cyclopropane ring, whereas those from the ketone 1 do not.

In ether, the results are quite different. The ketone 1 splits open rapidly again and also shows photoreduced products. Thus, the cyclopropane ring must still have considerable influence on the reactivity of this molecule. In the ketone 7 and cyclooctanone, only photoreduced products are observed. Here the cyclopropane ring in 7 does not seem to influence the reactivity of this ketone.

Two generalizations seem to come from the photochemistry of these bicyclic ketones. The first is that the solvent seems to have a distinct effect on the course of the reaction. The second is that the proximity of the cyclopropyl group with respect to the carbonyl group plays an important role in the formation of these products.

## Experimental Section[11]

**Bicyclo[6.1.0]nonan-3-ol (5).**[12]—To a rapidly stirring solution of 46.8 g of the zinc–copper couple[13] in 150 ml of anhydrous ether was added a small crystal of iodine. When the brown color was discharged, a mixture of 3-cyclooctenol[14] (25.6 g, 0.203 mol) and methylene iodide (69 g, 0.257 mol) was added dropwise. When all the alcohol was added, the mixture was refluxed for 72 hr.[15] The mixture was then cooled and the solids were removed by filtration. The solids were washed with ether and the combined ether extracts were washed with two 50-ml portions of saturated ammonium chloride solution and two 50-ml portions of saturated sodium carbonate solution, dried ($MgSO_4$), and concentrated. Glpc analysis indicated that the product consisted of an equal amount of 3-cyclooctenol and 5. Fractional distillation gave 7.6 g of 3-cyclooctenol, bp 108–112° (20 mm), and 11.4 g (40%) of 5, bp 128–132° (20 mm): ir ($CCl_4$) 3350, 3060, 1110, 1050 $cm^{-1}$; nmr ($CCl_4$) $\tau$ 6.2 (m, 1 H), 7.6–9.7 (m, 14 H), 10.2 (m, 1 H).

*Anal.* Calcd for $C_9H_{16}O_1$: C, 77.08; H, 11.50. Found: C, 77.16; H, 11.32.

**Bicyclo[6.1.0]nonan-3-one (1).**—To 4.0 g (0.0285 mol) of bicyclo[6.1.0]nonan-3-ol (5) in 100 ml of acetone was added dropwise a chromic acid solution prepared from 3.7 g of chromic anhydride, 3.3 ml of concentrated sulfuric acid, and 13 ml of water. The temperature of the reaction flask was not allowed to rise above 35° and the addition was continued until the orange color persisted for 1 min. The residual green salts were removed by filtration and washed with two 25-ml portions of acetone. The combined acetone extract was stirred with 5 g of solid $NaHCO_3$ for 0.5 hr. The solids were removed and the acetone layer was concentrated by distillation over a steam bath until 90 ml of acetone was collected. The residual water layer was extracted with three 50-ml portions of ether and the ether layer was dried ($MgSO_4$) and concentrated. Distillation of the crude product afforded 2.5 g (63%) of 1, bp 44–48° (0.3 mm): ir ($CCl_4$) 3060, 1700 $cm^{-1}$; nmr ($CCl_4$) $\tau$ 6.95–8.9 (broad, 13 H), 9.85 (m, 1 H).

**Irradiation of 1 in Ether.**—A solution of 0.73 g (0.0053 mol) of 1[16] in 250 ml of anhydrous ether was irradiated for 3 hr with a

(11) Nmr spectra were determined on a Varian A-60 spectrophotometer; chemical shifts are reported in $\tau$ values in parts per million using tetramethylsilane (TMS) as an internal standard. Infrared spectra were recorded on a Perkin-Elmer Model 257 grating infrared spectrophotometer. Gas chromatography was performed on an F & M Model 720 thermal conductivity gas chromatograph using 2- or 4-ft columns containing 20% neopentyl glycol succinate (NGS) on Chromosorb W, 20% silicone grease on Chromosorb W, and 30% silicone fluid F50 on Chromosorb P. Boiling points are uncorrected.

(12) A. C. Cope and G. L. Woo, *J. Amer. Chem. Soc.*, **85**, 3601 (1963).

(13) R. D. Smith and H. E. Simmons, *Org. Syn.*, **41**, 72 (1961).

(14) (a) A. C. Cope and P. E. Peterson, *J. Amer. Chem. Soc.*, **81**, 1643 (1959); (b) J. K. Crandall, D. B. Banks, R. A. Colyer, R. J. Watkins, and J. P. Arrington, *J. Org. Chem.*, **33**, 423 (1968).

(15) The reaction can be very exothermic in the first 2 hr.

(16) All compounds which were photolyzed were purified by distillation followed by isolation by glpc.

550-W Hanovia mercury vapor lamp in an immersion well apparatus fitted with a Corex filter.

Gas chromatographic analysis (silicon grease, 140°) of the photolysis product indicated the presence of four products: 2-allylcyclohexanone (**2**, 32%), 3-vinylcycloheptanone (**3**, 10%), bicyclo[6.1.0]nonan-3-ol (**5**, 26%), and the isomeric 3-(1-ethoxyethyl)bicyclo[6.1.0]nonan-3-ol (**6**, 26%).

A sample of **2** was isolated by glpc and identified by comparison of its glpc retention time and nmr and infrared spectra with those of an authentic sample prepared by the method of Stork.[17] A sample of **2** isolated by glpc exhibited the following spectral properties: ir ($CCl_4$) 3090, 2940, 2870, 1715, 1645, 1000, 922 $cm^{-1}$; nmr ($CCl_4$) $\tau$ 4.5 (m, 1 H), 4.9 (m, 1 H), 5.2 (m, 1 H), 7.5–8.9 (m, 11 H).

A sample of **3**, also isolated by glpc, exhibited the following spectral properties: ir ($CCl_4$), 3080, 1705, 1645, 1000, 922 $cm^{-1}$; nmr ($CCl_4$) $\tau$ 4.05–4.8 (m, 1 H), 5.0 (d, 1 H), 5.2 (m, 1 H), 7.5–9.1 (11 H).

*Anal.* Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.20; H, 9.92.

A sample of **6** had the following spectral properties: ir ($CCl_4$) 3580, 3080, 2990, 2930, 1100 $cm^{-1}$; nmr ($CCl_4$) $\tau$ 6.3–6.9 (3, m), 7.6–9.5 (20), 10.3 (1, m); mass spectrum (70 eV) *m/e* 212, 139, 73.

*Anal.* Calcd for $C_{13}H_{24}O_2$: C, 73.53; H, 11.39. Found: C, 73.61; H, 11.22.

**Irradiation of 1 in *tert*-Butyl Alcohol.**—A solution of 1.0 g of **1** in 250 ml of freshly distilled *tert*-butyl alcohol was irradiated through a Corex filter for 3 hr. Removal of the *tert*-butyl alcohol by distillation through a Vigreux column afforded 0.97 g of a colorless liquid. Gas chromatographic analysis (silicone grease, 140°) indicated the presence of **2** (46%), **3** (15%), and *tert*-butyl non-8-enoate (**4**, 23%). In addition, there was a component (14%) which was an unresolvable mixture of compounds. Its infrared and nmr spectra indicated the presence of an aldehyde. A sample of **4**, isolated by glpc, exhibited the following spectral properties: ir ($CCl_4$) 3080, 1735, 1400, 1375, 1160, 1000, 920 $cm^{-1}$; nmr ($CCl_4$) $\tau$ 4.1–4.6 (m, 1 H), 4.75–4.95 (m, 1 H), 5.25 (m, 1 H), 7.8 (m, 4 H), 8.65 (m, 17 H).

*Anal.* Calcd for $C_{13}H_{24}O_2$: C, 73.53; H, 11.39. Found: C, 73.50; H, 11.24.

**Hydrogenation of the Photoproduct of 1.**—A solution of 0.410 g of the photoproduct of **1** in *tert*-butyl alcohol in 100 ml of ether was hydrogenated at 40 lb of pressure over 5% palladium on charcoal for 24 hr. Isolation of the crude product yielded 0.305 g (74.5%).

Glpc analysis (silicone oil, 160°) indicated the presence of nine peaks. 2-Propylcyclohexanone (**19**, 43%), isolated by glpc, was identified by comparison of the ir and nmr spectra with those with an authentic sample obtained by hydrogenating 2-allylcyclohexanone. 3-Ethylcycloheptanone (**20**, 12%), isolated by glpc, was identified by comparison of the ir and nmr spectra with those of an authentic sample prepared as described below. Nonanoic acid (**21**, 8%) and *tert*-butyl nonanoate (**22**, 8%) were not separated on the silicone column, but they could be separated on the NGS column. Samples of **21** and **22** were first isolated on the silicone oil column as one peak and further isolated on the NGS column and identified by comparison of their infrared spectrum with those of authentic samples. There were five other components corresponding to 21% which were not identified.

**3-Ethylcycloheptanone (20).**[18]—To a solution of ethylmagnesium iodide prepared from 0.8 g of magnesium turnings and ethyl iodide (2.12 g, 0.9136 mol) in 50 ml of dry ether was added 0.1 g of cuprous chloride. The mixture was stirred for 5 min. The solution was cooled to 0° and a solution of 1.0 g (0.0091 mol) of 2-cycloheptenone[19] in 10 ml of ether was added slowly. The mixture was stirred overnight at room temperature and poured into ice, and 2 ml of 20% $H_2SO_4$ was added. The mixture was extracted with three 25-ml portions of ether and the combined ether layers were washed with 25 ml of 10% sodium thiosulfate solution, dried ($MgSO_4$), and concentrated. Glpc analysis (NGS, 140°) of the crude material indicated that it was homogeneous. The crude product was distilled yielding 0.4 g (40%) of **20**, bp 75–77° (20 mm) [lit.[18] 122–125° (100 mm)]: ir ($CCl_4$) 2940, 2870, 1705, 1415, 1405, 1390, 1365, 1330, 1260 $cm^{-1}$; nmr ($CCl_4$) $\tau$ 7.45 (m, 4 H), 7.65–8.55 (broad, 9 H), and 8.9 (t, 3 H).

***tert*-Butyl Nonanoate (22).**—A solution of 10 g (0.064 mol) of nonanoic acid, 7 ml (*ca.* 0.127 mol) of isobutylene, 1 ml of concentrated $H_2SO_4$, and 75 ml of ether was placed in a pressure bottle and shaken overnight. The contents were then poured into an ice-cold mixture of 7 g of NaOH in 50 ml of water. The mixture was kept cold and stirred for 10 min. The ether layer was then washed with two 25-ml portions of water, dried ($MgSO_4$), and concentrated. The crude product was distilled yielding 5.4 g (39%) of **22**, bp 70–71° (0.4 mm): ir ($CCl_4$) 2940, 2870, 1735, 1400, 1375, 1150 $cm^{-1}$; nmr ($CCl_4$) $\tau$ 8.0 (m, 2 H), 8.8 (m, 21 H), 9.2 (t, 3 H).

*Anal.* Calcd for $C_{13}H_{26}O_2$: C, 72.84; H, 12.22. Found: C, 72.84; H, 12.05.

**Reduction of 1 with Lithium Aluminum Hydride.**—A solution of 0.2 g (0.0145 mol) of **1** and 0.1 g (0.00264 mol) of lithium aluminum hydride in 50 ml of ether was heated to reflux for 2 hr. At the end of this period, 2 ml of water was added and the mixture was dried ($MgSO_4$). The solids were removed and the ether layer was concentrated. Glpc analysis of the crude product indicated that it consisted of one major peak which had the same retention time as **5**. The ir spectrum of this product was also identical with that of **5**.

**Reduction of 1 with Sodium in Ethanol.**—A solution of 0.2 g (0.0014 mol) of the ketone **1**, 0.2 g (0.0087 g-atom) of sodium, and 25 ml of ethanol in 50 ml of toluene was refluxed for 2.5 hr, cooled, and washed with two 25-ml portions of 3% HCl. The toluene layer was dried ($MgSO_4$) and concentrated. Glpc analysis of the crude mixture indicated that one major peak was present which had the same retention time as **5**. The ir spectrum of this fraction was identical with that of **5**.

**Irradiation of Cyclooctanone (14) in *tert*-Butyl Alcohol.**—A solution of 2.2 g of cyclooctanone in 250 ml of ether was irradiated for 3-hr through a Corex filter. The *tert*-butyl alcohol solution was then concentrated. Glpc analysis of the crude photolysate indicated the presence of three products in a ratio of 15:79:6. The first component was assigned the structure of 2-(3-buten-1-yl)cyclobutanol (**15**) based on the ir and nmr spectra: ir ($CCl_4$) 3620, 3340, 3080, 1645, 1120, 1000, 920 $cm^{-1}$; nmr ($CCl_4$) $\tau$ 4.0–4.7 (m, 1 H), 4.8–5.3 (t, 2 H), 5.7 (m, 1/2 H), 6.3 (m, 1/2 H), 6.4 (s, 1), 7.6–8.4 (m, 9 H).

*Anal.* Calcd for $C_8H_{14}O$: C, 76.13; H, 11.18. Found: C, 75.94; H, 10.87.

The second component was shown to be cyclooctanone (**14**) by comparison of the retention time on glpc and by comparison of the ir spectrum of the product isolated from chromatography with those of the authentic sample.

The third product was identified as *tert*-butyl octanoate (**16**) by comparison of its ir and nmr spectra with those of an authentic sample prepared as described below.

**Irradiation of Cyclooctanone (14) in Ether.**—A solution of 5 g of cyclooctanone in 250 ml of ether was irradiated for 3 hr through a Corex filter. The ether layer was concentrated. Glpc analysis of the crude product indicated the presence of three components in a ratio of 6:48:46. The first and second components were identified as cyclooctanone and cyclooctanol, respectively, by comparison of the retention times and ir spectra with those of authentic samples.

The structure of the third product was assigned as 1-(ethoxyethyl)cyclooctanol (**18**): ir ($CCl_4$) 3570, 2930, 1100 $cm^{-1}$; nmr ($CCl_4$) $\tau$ 6.2–6.9 (m, 3 H), 8.05 (s, 1 H), 8.15–8.65 (14 H), 8.7–9.1 (m, 6 H).

*Anal.* Calcd for $C_{12}H_{24}O_2$: C, 71.95; H, 12.08. Found: C, 72.16; H, 12.21.

***tert*-Butyl Octanoate (16).**—A solution of 10.0 g (0.069 mol) of octanoic acid, 2 ml of $H_2SO_4$, and 20 ml of isobutylene (*ca.* 0.364 mol) in 75 ml of ether was placed in a pressure bottle and shaken overnight. The mixture was then poured into an ice-cold solution of 7 g of NaOH in 50 ml of water and stirred for 10 min. The ether layer was separated and washed with two 25-ml portions of water, dried ($MgSO_4$), and concentrated. The product was distilled yielding 4.7 g (33.7%) of **16**, bp 55–57° (0.5 mm): ir ($CCl_4$) 2940, 1735, 1400, 1375, 1155 $cm^{-1}$; nmr ($CCl_4$) $\tau$ 7.8 (m, 2 H), 8.3–8.9 (m, 19 H), 9.0–9.3 (m, 3 H).

*Anal.* Calcd for $C_{12}H_{24}O_2$: C, 71.95; H, 12.08. Found: C, 71.90; H, 12.00.

**Bicyclo[6.1.0]nonan-4-one (7).**—To a mixture of 18 g of the zinc–copper couple in 100 ml of ether was added a crystal of iodine. When the brown color was discharged, a mixture of 31 g

(17) G. Stork, A. Brizzolarra, H. Landesman, J. Szmuskovicz, and R. Terrell, *J. Amer. Chem. Soc.*, **85**, 207 (1963).

(18) T. Nozoe, T. Mukai, and S. Matsumoto, *Proc. Jap. Acad.*, **27**, 110 (1951).

(19) N. Heap and G. Whitham, *J. Chem. Soc. B*, 164 (1966).

(0.248 mol) of 4-cyclooctenone[19] and 73 g (0.27 mol) of methylene iodide was added in one portion. The mixture was refluxed for 2 days, after which glpc analysis of the ether solution indicated that the reaction had only gone to a small extent (*ca.* 30%). Another 18 g of the zinc–copper couple was added to the mixture and this was followed by another 73 g (0.27 mol) of methylene iodide. The mixture was then refluxed for another 2 days. The mixture was then filtered and the filtrate was washed with two 100-ml portions of a 5% HCl solution, two 100-ml portions of saturated $Na_2CO_3$ solution, and two 100-ml portions of water, dried ($MgSO_4$), and concentrated. The product was distilled, yielding 16.2 g (47%) of **7**, bp 97–100° (15 mm). Glpc analysis of the distilled product indicated that two products were present in a ratio of 16:84. The first product was 4-cyclooctenone, while the second was bicyclo[6.1.0]nonan-4-one (**7**): ir ($CCl_4$) 3075, 3000, 2940, 2870, 1705, 1355, 1345, 1170 $cm^{-1}$; nmr ($CDCl_3$) $\tau$ 7.4–8.7 (10 H), 9.3 (m, 3 H), 10.15 (m, 1 H).[4]

**Irradiation of 7 in Ether.**—A solution of 0.66 g of **7** in 250 ml of ether was irradiated for 3 hr through a Corex filter. At the end of this period, the ether layer was concentrated. Glpc analysis of the crude product indicated the presence of three products ratio of 8:32:60. The first product had the same retention time and ir spectrum as **7**. The second product was bicyclo-[6.1.0]nonan-4-ol (**8**): ir ($CCl_4$) 3610, 3320, 3070, 3000, 2920, 2860, 1030 $cm^{-1}$; nmr ($CCl_4$) $\tau$ 5.9 (m, 1 H), 6.6 (s, 1 H), 7.5–9.1 (m, 13 H), 10.1 (m, 1 H).

*Anal.* Calcd for $C_9H_{16}O$: C, 77.08; H, 11.50. Found: C, 77.11; H, 11.65.

The third product was assigned the structure of 4-(1-ethoxyethyl)bicyclo[6.1.0]nonan-4-ol (**9**): ir ($CCl_4$) 3570, 3080, 1110 $cm^{-1}$; nmr ($CCl_4$) $\tau$ 6.1–7.0 (m, 3 H), 7.6–9.0 (broad, 17 H), 9.2 (m, 3 H), 10.15 (m, 1 H); mass spectrum (70 eV) *m/e* 212, 139, 73.

*Anal.* Calcd for $C_{13}H_{24}O_2$: C, 73.53; H, 11.39. Found: C, 73.70; H, 11.20.

**Oxymercuration of Bicyclo[6.1.0]non-4-ene.**—To a solution of 3.19 g (0.01 mol) of $Hg(OAc)_2$ in 10 ml of tetrahydrofuran and 10 ml of water was added 1.08 g (0.01 mol) of bicyclo[6.1.0]non-4-ene.[20] The mixture was stirred for 10 min. To the solution was added a 10-ml solution of 3 *M* NaOH and this was followed by a 10-ml solution of 3 *M* $NaBH_4$ in 3 *M* NaOH solution. The mercury was allowed to settle, and the mixture was saturated with NaCl. The upper layer was separated, dried ($MgSO_4$), and concentrated. Glpc analysis indicated that one major fraction is present which has the same retention time and ir spectrum as those of **8**.

**Irradiation of 7 in *tert*-Butyl Alcohol.**—A sample of 1.24 g of bicyclo[6.1.0]nonan-4-one (**7**) was irradiated through a Corex filter for 3 hr. The solution was then concentrated. Glpc analysis of the crude product on silicone grease (130°) indicated the presence of three products in a ratio of 22:15:62. The first product is believed to be a mixture of the aldehyde **10** and **11**: ir ($CS_2$) 3080, 3000, 2720, 1730 $cm^{-1}$; nmr ($CCl_4$) $\tau$ 0.34 (m, 1 H), 3.7–4.7 (m, 1 H) 4.75–5.25 (m, 2 H), 7.2–9.5 (m, 9), 10.05 (m, 1 H). The second product had the same retention time and ir spectrum as **7**.

The third product is believed to be a mixture of the *tert*-butyl esters **12** and **13**: ir ($CCl_4$) 3070, 2990, 1735, 1400, 1375, 1160 $cm^{-1}$; nmr ($CCl_4$) $\tau$ 7.6–8.0 (m, 2 H), 8.2–8.9 (15 H), 8.9–9.2 (m, 3 H), 9.35 (m, 3 H), 10.2 (m, 1 H).

*Anal.* Calcd for $C_{13}H_{24}O_2$: C, 73.53; H, 11.39. Found: C, 73.37; H, 11.05.

**Registry No.**—**1**, 28399-86-2; **2**, 94-66-6; **3**, 28399-94-2; **4**, 28405-45-0; **6**, 28405-46-1; **7**, 28405-47-2; **8**, 28405-40-5; **9**, 28405-48-3; **14**, 502-49-8; **15**, 28405-49-4; **16**, 5457-66-9; **18**, 28405-50-7; **22**, 28405-52-9.

(20) H. E. Simmons, E. P. Blanchard, and H. D. Hartsler, *J. Org. Chem.*, **31**, 295 (1966).

# Notes

## Ynamines from 1,1-Difluoro-2-aryl- and -2-alkylethylenes

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*Contribution No. 1721 from the Central Research Department, Experimental Station, E. I. du Pont de Nemours and Company, Wilmington, Delaware 19898*

*Received October 29, 1970*

The ynamines (**3** and **4**) are a well-known class of organic compounds and have been the subject of a review article.[1] We observed recently that the action of lithium diethylamide on a 1,1-difluoroalkene (**1**) or a $\beta,\beta$-difluorostyrene (**2**) is a convenient, general laboratory route to ynamines (**3** and **4**).[2] **1** and **2** are obtained readily from aliphatic or aromatic aldehydes and sodium chlorodifluoroacetate by the procedure of Fuqua, *et al.*,[3] and an overall yield of 30–40% of the ynamine was obtained from the commercially available aldehyde. The aromatic ynamines were pale yellow liquids, whereas the aliphatic compounds were colorless. All were stable at room temperature and, as expected, each had a characteristic strong band at 2220 $cm^{-1}$ in the infrared spectrum.[1]

$$\underset{\mathbf{1}}{RCH{=}CF_2} + 2LiN(C_2H_5)_2 \longrightarrow \underset{\mathbf{3}}{RC{\equiv}CN(C_2H_5)_2}$$

$$\underset{\mathbf{2}}{ArCH{=}CF_2} + 2LiN(C_2H_5)_2 \longrightarrow \underset{\mathbf{4}}{ArC{\equiv}CN(C_2H_5)_2}$$

The proton and fluorine nmr spectra of **1** and **2** were recorded (Table I). All the spectra were 12-line ABX patterns and were readily interpreted on this basis assuming that $J_{HF}(trans) > J_{HF}(cis)$. It is interesting to note that the chemical shifts of the fluorine atoms of $\beta,\beta$-difluorostyrene are at lower field than those of the 1,1-difluoroalkenes, and, significantly, F-1 (cis to the phenyl ring) is at lower field than F-2 (trans to the phenyl ring). A similar pattern is seen in the pmr spectra of the protonated series where the proton cis to the phenyl ring of styrene appears at lower field than the trans

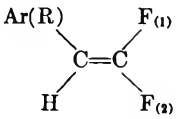
(1) H. G. Viehe, *Angew. Chem., Int. Ed. Engl.*, **6**, 767 (1967).

(2) When this work was initiated, the author was unaware of H. G. Viehe, U. S. Patent 3,369,047 (1968), which claims but does not give examples of the preparation of ynamines from lithium dialkylamides and 1,1-difluoroethylenes.

(3) S. A. Fuqua, W. G. Duncan, and R. M. Silverstein, *J. Org. Chem.*, **30**, 1027 (1965).

TABLE I

NMR PARAMETERS FOR 1,1-DIFLUORO-2-ARYL(ALKYL)ETHYLENES




| Ar or R group | Registry no. | Chemical shift H, δ | Chemical shift F-2, ppm | Chemical shift F-1, ppm | (F-2) − (F-1), ppm | J, Hz HF-1 | J, Hz HF-2 | J, Hz FF |
|---|---|---|---|---|---|---|---|---|
| $CH_3(CH_2)_4$ | 4980-67-0 | 4.07 | 90.1 | 92.8 | −2.7 | 25 | 3.5 | 49 |
| $CH_3(CH_2)_5$ | 592-93-8 | 4.06 | 90.5 | 93.0 | −2.5 | 25 | 3.5 | 50 |
| $C_6H_5$ | 405-42-5 | 5.13 | 85.4 | 83.6 | 1.8 | 26 | 4.5 | 33 |
| 4-$CH_3C_6H_4$ | 28321-07-5 | 5.13 | 86.4 | 84.3 | 2.1 | 26 | 4.5 | 34 |
| 4-$CH_3OC_6H_4$ | 1608-24-8 | 5.13 | 87.7 | 86.0 | 1.7 | 25 | 4.5 | 38 |
| 4-$ClC_6H_4$ | 28321-09-7 | 5.15 | 83.7 | 82.0 | 1.7 | 26 | 4.5 | 31 |
| 2-$CH_3C_6H_4$ | 28321-10-0 | 5.25 | 85.1 | 86.0 | −0.9 | 24 | 5.5 | 32 |
| 2-$ClC_6H_4$ | 28321-11-1 | 5.65 | 86.8 | 87.9 | −1.1 | 25 | 4.5 | 28 |
| $C_6H_5$ H>C=C H | 28321-12-2 | 4.90 | 88.4 | 86.7 | 1.7 | 24 | 2.0 | 28 |

proton,[4] which is at lower field than the *gem*-vinyl protons of 1-alkenes.[5] The anomalous low-field chemical shift of the vinyl protons of styrene has been explained in terms of the diamagnetic anisotropy of the phenyl ring.[4] A similar argument can be applied to explain qualitatively the low F-1 and F-2 chemical shift values of β,β-difluorostyrene relative to 1,1-difluoroalkenes. If the 4 position of β,β-difluorostyrene is substituted, both F-1 and F-2 are shifted by the same amount and in the same direction of field. The shifts observed are those anticipated based on the inductive and mesomeric effects of the particular substituent. The effect of a 2 substituent on the fluorine chemical shift is more complex and the paucity of data precludes the establishment of a discernible pattern. Drieding molecular models show that the aryl ring and vinyl system are not coplanar in the 2-substituted compounds and, as a result, one would expect F-1 to be shielded by the aromatic ring currents. Presumably the electronic effects of the substituent are also important; however, a better understanding of all the systems presented in Table I must await future studies.

### Experimental Section

Infrared spectra were obtained on neat samples. Proton nmr (pmr) spectra were recorded at 60 MHz and fluorine spectra at 56.4 MHz in carbon tetrachloride solution. Internal references, tetramethylsilane and trichlorofluoromethane, were used. Proton chemical shifts are δ values; fluorine chemical shifts are upfield from the reference. The abbreviations s, d, t, q, and m refer to singlet, doublet, triplet, quartet, and multiplet.

**β,β-Difluorostyrenes and 1,1-Difluoroalkenes.**—The procedure of Fuqua, *et al.*,[3] was used with only minor modification.

**2-Chloro-β,β-difluorostyrene** was obtained from *o*-chlorobenzaldehyde: bp 60–61° (13 mm); 66% yield; $n^{25}D$ 1.5118; infrared bands at 1730, 1470, 1430, 1340, 1275, 1235, 1175, 1125, 1030, 945, 815, and 748 $cm^{-1}$.

*Anal.* Calcd for $C_8H_5ClF_2$: C, 55.03; H, 2.89; F, 21.76. Found: C, 54.8; H, 2.98; F, 22.3.

**4-Chloro-β,β-difluorostyrene** was obtained from *p*-chlorobenzaldehyde: bp 67–71° (15 mm); 17% yield; $n^{25}D$ 1.5169; infrared bands at 1730, 1485, 1350, 1245, 1165, 1090, 1010, 938, and 840 $cm^{-1}$.

*Anal.* Calcd for $C_8H_5ClF_2$: C, 55.03; H, 2.89; Cl, 20.31. Found: C, 54.8; H, 2.91; Cl, 20.5.

**2-Methyl-β,β-difluorostyrene** was obtained from *o*-tolualdehyde: bp 59–61° (20 mm); 44% yield; $n^{25}D$ 1.4909; infrared bands at 1730, 1450, 1335, 1235, 1205, 1165, 935, 815, and 745 $cm^{-1}$.

*Anal.* Calcd for $C_9H_8F_2$: C, 70.10; H, 5.23; F, 24.65. Found: C, 69.7; H, 5.13; F, 24.7.

**4-Methyl-β,β-difluorostyrene** was obtained from *p*-tolualdehyde: bp 63–64° (22 mm); 35% yield; $n^{25}D$ 1.4909; infrared bands at 1725, 1340, 1240, 935, and 830 $cm^{-1}$.

*Anal.* Found: C, 69.8; H, 5.41; F, 24.6.

**1,1-Difluoro-4-phenyl-*trans*-1,3-butadiene** was obtained from *trans*-cinnamaldehyde: bp 66–67° (2.0 mm); 40% yield; $n^{25}D$ 1.5535; infrared bands at 1730, 1355, 1330, 1295, 1275, 1190, 965, 935, 830, 745, and 688 $cm^{-1}$.

*Anal.* Calcd for $C_{10}H_8F_2$: C, 72.26; H, 4.85; F, 22.86. Found: C, 72.0; H, 4.96; F, 23.2.

**1,1-Difluoro-1-heptene** was obtained from hexanal: bp 94–96°; 49% yield; $n^{25}D$ 1.3669; infrared bands at 2960, 2880, 1740, 1460, 1315, 1200, 1170, 1120, 1040, 930, and 800 $cm^{-1}$.

*Anal.* Calcd for $C_7H_{12}F_2$: C, 62.66; H, 9.02; F, 28.32. Found: C, 62.8; H, 9.10; F, 28.1.

**Preparation of Ynamines. General Procedure.**—The apparatus consisted of a 1-l. two-necked flask equipped with magnetic stirrer and fitted with a serum cap and Claisen adapter on which were placed a dropping funnel and a condenser with nitrogen bubbler. From a syringe, 90 ml (144 mmol) of 1.6 *M* *n*-butyllithium in hexane[6] was placed in the flask through the serum cap in a nitrogen atmosphere. A solution of 14.85 ml of diethylamine in 55 ml of ether was placed in the dropping funnel and the butyllithium solution was cooled in an ice bath. The amine solution was added, with stirring, over 30 min. After the addition, 64.3 mmol of neat difluoro compound was placed in the dropping funnel and the ice bath was replaced with a Dry Ice–acetone bath. The difluoro compound was added during 10–15 min and the funnel was rinsed with several milliliters of ether which was also added to the reaction vessel. The cooling bath was removed and the mixture warmed slowly. In the case of the *aryl difluoro compounds*, at some temperature below 0°, *a rapid reaction occurred with vigorous gas evolution.* This was not noted with the alkyl derivatives where the reaction was much more moderate. The reaction mixture was brought to room temperature and stirred overnight under nitrogen. Solids were removed by filtration and washed with hexane, all under a nitrogen blanket. The filtrates were concentrated on the water pump and the residue was distilled *in vacuo*.

***N,N*-Diethylphenylethynylamine** was obtained from β,β-difluorostyrene: bp 87–91° (45 mm); 73% yield; $n^{25}D$ 1.5618; infrared bands at 2980, 2880, 2220, 1600, 1375, 1355, 1330, 1185, 1070, 750, and 688 $cm^{-1}$ (the spectrum was essentially identical

(4) C. N. Banwell and N. Sheppard, *Mol. Phys.*, **3**, 351 (1960).

(5) A. A. Bothner-By and C. Naar-Colin, *J. Amer. Chem. Soc.*, **83**, 231 (1961).

(6) Foote Mineral Co., Exton, Pa.

with the published spectrum);[7] pmr resonances at δ 1.22 (t, 6 H), 2.95 (q, 4 H), 7.20 (m, 5 H).

*N,N*-**Diethyl-4-methoxyphenylethynylamine** was obtained from 4-methoxy-β,β-difluorostyrene: bp 98–100° (0.08 mm); 77% yield; $n^{25}D$ 1.5106; infrared bands at 2950, 2220, 1600, 1500, 1455, 1405, 1390, 1365, 1320, 1280, 1240, 1180, 1030, 830, and 760 $cm^{-1}$; pmr resonances at δ 1.22 (t, 6 H), 2.93 (q, 4 H), 3.68 (s, 3 H), 6.73 and 7.20 (AB quartet, 4 H).

*Anal.* Calcd for $C_{13}H_{17}NO$: C, 76.80; H, 8.43; N, 6.89. Found: C, 76.6; H, 8.64; N, 7.17.

*N,N*-**Diethyl-2-chlorophenylethynylamine** was obtained from 2-chloro-β,β-difluorostyrene: bp 84–86° (0.03 mm); 84% yield; $n^{25}D$ 1.5785; infrared bands at 2980, 2850, 2220, 1600, 1435, 1415, 1380, 1340, 1250, 1190, 1080, 1050, 1030, and 745 $cm^{-1}$; pmr resonances at δ 1.27 (t, 6 H), 3.00 (q, 4 H), 7.10 (m, 4 H).

*Anal.* Calcd for $C_{12}H_{14}ClN$: C, 69.39; H, 6.79; Cl, 17.07; N, 6.74. Found: C, 69.0; H, 6.96; Cl, 16.8; N, 7.36.

*N,N*-**Diethyl-4-chlorophenylethynylamine** was obtained from 4-chloro-β,β-difluorostyrene: bp 87–89° (0.03 mm); 67% yield; $n^{25}D$ 1.5772; infrared bands at 2950, 2220, 1490, 1185, 1170, 1090, 1060, 1010, and 823 $cm^{-1}$; pmr resonances at δ 1.22 (t, 6 H), 2.95 (q, 4 H), 7.28 (s, 4 H).

*Anal.* Found: C, 69.1; H, 6.96; Cl, 16.9; N, 7.23.

*N,N*-**Diethyl-*o*-tolylethynylamine** was obtained from 2-methyl-β,β-difluorostyrene: bp 74–76° (0.03 mm); 80% yield; $n^{25}D$ 1.5563; infrared bands at 2950, 2220, 1600, 1460, 1370, 1280, 1200, 1070, 1040, 750, and 710 $cm^{-1}$; pmr resonances at δ 1.22 (t, 6 H), 2.93 (q, 4 H), 2.33 (s, 3 H), 7.00 (m, 4 H).

*Anal.* Calcd for $C_{13}H_{17}N$: C, 83.36; H, 9.14; N, 7.48. Found: C, 82.8; H, 9.04; N, 8.34.

*N,N*-**Diethylamino-*p*-tolylethynylamine** was obtained from 4-methyl-β,β-difluorostyrene: bp 72–75° (0.03 mm); 73% yield; $n^{25}D$ 1.5578; infrared bands at 2950, 2900, 2850, 2220, 1600, 1500, 1440, 1365, 1185, 1100, 1065, and 813 $cm^{-1}$; pmr resonances at δ 1.22 (t, 6 H), 2.95 (q, 4 H), 2.26 (s, 3 H), 6.93 and 7.11 (AB quartet, 4 H).

*Anal.* Found: C, 82.3; H, 9.20; N, 7.87.

*N,N*-**Diethyl(4-phenyl-but-*trans*-3-ene-1-ynyl)amine** was obtained from 1,1-difluoro-4-phenyl-*trans*-1,3-butadiene: bp 99–104° (0.03 mm); 43% yield; $n^{25}D$ 1.6288; infrared bands at 3000, 2850, 2200, 1620, 1590, 1490, 1440, 1410, 1370, 1350, 1250, 950, 750, and 690 $cm^{-1}$; pmr resonances at δ 1.20 (t, 6 H), 2.92 (q, 4 H), 6.16 and 6.52, (AB quartet, 2 H, $J$ = 16 Hz (vinyl protons)), 7.18 (m, 5 H).

*Anal.* Calcd for $C_{14}H_{17}N$: C, 84.36; H, 8.60; N, 7.03. Found: C, 83.3; H, 9.00; N, 7.17.

*N,N*-**Diethylamino-1-heptyne** was obtained from 1,1-difluoro-1-heptene: bp 59–61° (0.70 mm); 74% yield; $n^{25}D$ 1.4454; infrared bands at 2950, 2850, 2220, 1460, 1375, 1320, 1250, 1180, 1090, and 1065 $cm^{-1}$; pmr resonances at δ 1.12 (t, 2.78 (q), 0.80–1.7 (m), 2.18 (t, $CH_2C{\equiv}C$).

*Anal.* Calcd for $C_{11}H_{21}N$: C, 78.97; H, 12.66; N, 8.38. Found: C, 78.8; H, 12.4; N, 8.64.

*N,N*-**Diethylamino-1-octyne** was obtained from 1,1-difluoro-1-octene: bp 56–58° (0.10 mm); 45% yield; $n^{25}D$ 1.4490; infrared bands at 2950, 2850, 2220, 1450, 1360, 1290, 1240, 1170, 1080, and 790 $cm^{-1}$; pmr resonances at δ 1.12 (t), 2.78 (q), 0.80–1.7 (m), 2.18 (t, $CH_2C{\equiv}C$).

*Anal.* Calcd for $C_{12}H_{23}N$: C, 79.49; H, 12.79; N, 7.73. Found: C, 78.6; H, 12.8; N, 6.90.

**Registry No.**—*N,N*-Diethylphenylethynylamine, 4231-26-9; *N,N*-diethyl-4-methoxyphenylethynylamine, 28321-14-4; *N,N*-diethyl-2-chlorophenylethynylamine, 28321-15-5; *N,N*-diethyl-4-chlorophenylethynylamine, 28321-16-6; *N,N*-diethyl-*o*-tolylethynylamine, 28321-17-7; *N,N*-diethylamino-*p*-tolylethynylamine, 28321-18-8; *N,N*-diethyl(4-phenylbut-*trans*-3-ene-1-ynyl)amine, 28321-19-9; *N,N*-diethylamino-1-heptyne, 28321-20-2; *N,N*-diethylamino-1-octyne, 4231-37-2.

**Acknowledgment.**—The author is indebted to Dr. F. J. Weigert for helpful discussions about nuclear magnetic resonance and Mrs. Sharon Wheeler for technical assistance.

(7) V. Wolf and F. Kowitz, *Justus Liebigs Ann. Chem.*, **638**, 33 (1960).

## 2,3-Dimethyl-1-phenylnaphthalene from Thermal Dimerization of Phenylallene[1]

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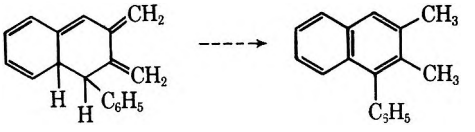
We report that phenylallene may be thermally converted to 2,3-dimethyl-1-phenylnaphthalene and suggest initial Diels–Alder cycloaddition producing a pentaene system, followed by tautomerization, as a mechanistically likely sequence.




A solution of phenylallene in inert solvents at 175° for 1 hr gave a low yield of colorless crystalline product, mp 84–85°, after recrystallization and sublimation. It proved to be a $C_{18}H_{16}$ isomer having ultraviolet absorption bands, $\lambda_{max}$ 230 nm (log ε ~5), 276 (4.1), 285 (4.15), and 294 (4.0) in $CCl_4$, unlike those expected for a 2-phenylnaphthalene[4] but in close correspondence with those reported for 1-phenylnaphthalene,[4] 2-methyl-1-(*o*-tolyl)naphthalene[4] [227 (4.91), 275 (3.84), 281 (3.87), 284 (3.87), and 292 (3.76) in petroleum ether], and 2,3-dibenzyl-1-phenylnaphthalene[5] [$\lambda_{max}$ 237.5 nm (4.87) and 286 (3.85) in $CH_2Cl_2$].

The nmr spectrum of the phenylallene dimer had methyl singlets at δ 2.10 and 2.43, and ten aromatic protons at δ 6.9–7.8 ppm.

The physical data and mechanistic possibilities prompted an assignment of 2,3-dimethyl-1-phenylnaphthalene as the probable structure for the $C_{18}H_{16}$ compound. The picrate derivative had mp 110–111°, in good agreement with the literature value, mp 112°, for authentic 2,3-dimethyl-1-phenylnaphthalene.[6] The melting point observed for the phenylallene dimer, 84–85°, was close to that for 2,3-dimethyl-1-phenylnaphthalene cited by Müller and K. Körmendy,[6] 85–86°.

Allene–allene thermal dimerizations giving dimethylenecyclobutanes and derived structures are common.[7–9] The present result, isolation of a 2,3-dimethyl-1-phenylnaphthalene as a thermal dimer from phenylallene, indicates a new mode of dimerization available to arylallenes. Formation of 2,3-dibenzyl-1-phenylnaphthalene through elimination of hydrogen chloride from 2-chloro-1,3-diphenylpropene[5] may well go by way of 1,3-diphenylallene and may then represent another example of this type of arylallene dimerization.

(1) Supported in part by National Science Foundation Grant GP-5226.

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(3) National Science Foundation Cooperative Graduate Fellow, 1963–1966.

(4) "UV Atlas of Organic Compounds," Vol. II, Plenum Press, New York, N. Y., 1966, plates E 1/2, E 1/3, and E 1/4.

(5) H. A. Staab and H. A. Kurmeier, *Chem. Ber.*, **101**, 2397 (1968).

(6) A. Müller and K. Körmendy, *J. Org. Chem.*, **18**, 1237 (1953).

(7) J. D. Roberts and C. M. Sharts, *Org. React.*, **12**, 1 (1962).

(8) D. R. Taylor, *Chem. Rev.*, **67**, 317 (1967).

(9) J. E. Baldwin and R. H. Fleming, *Fortschr. Chem. Forsch.*, **15** (3), 281 (1970).

### Experimental Section

**Phenylallene** was prepared through the reaction of 2,2-dibromo-1-phenylcyclopropane[10] with methyllithium in ether at −50°;[11] it had bp 64–65° (10 mm), $n^{20}$D 1.5819 [lit.[11] bp 64–65° (11 mm), $n^{24}$D 1.5809], and the expected spectral properties.

**2,3-Dimethyl-1-phenylnaphthalene from Phenylallene.**—A solution containing 5 g of phenylallene and 0.5 g of hydroquinone in 50 ml of 1:1 benzene–vinyl acetate in a glass liner was sealed in a steel reactor and heated to 175° for 1 hr. Concentration of the reaction mixture and short-path distillation give a yellow liquid, bp 100–130° (0.15 mm). A portion of this distillate soluble in carbon tetrachloride gave, upon concentration, 100 mg of colorless rosettes, mp 67–75°. Sublimation gave material of close to analytical purity: mp 78–80°; $\lambda_{max}^{CCl_4}$ 230 nm (log $\epsilon$ ~5), 276 (4.1), 285 (4.15), and 294 (4.0); nmr 2.10 (3 H, s), 2.43 (3 H, s), 6.9–7.8 ppm (10 H, m). Recrystallization from ethanol and vacuum sublimation gave crystals of mp 84–85° (lit.[6] mp 85–86° for 2,3-dimethyl-1-phenylnaphthalene). A solution of the hydrocarbon in 95% ethanol saturated with picric acid gave the picrate derivative, mp 110–111° (lit.[6] mp 112°).

**Registry No.**—2,3-Dimethyl-1-phenylnaphthalene, 27521-96-6; phenylallene, 2327-99-3.

(10) P. S. Skell and A. Y. Garner, *J. Amer. Chem. Soc.*, **78**, 5430 (1956).
(11) L. Skattebøl, *Acta Chem. Scand.*, **17**, 1683 (1963).

## Diarylmethylene–Tetracyanoethylene Cycloadditions[1]

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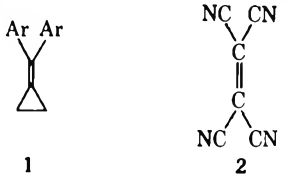
*Received September 3, 1970*

As one potential route to cyclopentane derivatives through (2 + 3) cycloadditions, the reaction between diarylmethylenecyclopropanes (**1**) and tetracyanoethylene (TCNE, **2**) has been examined.

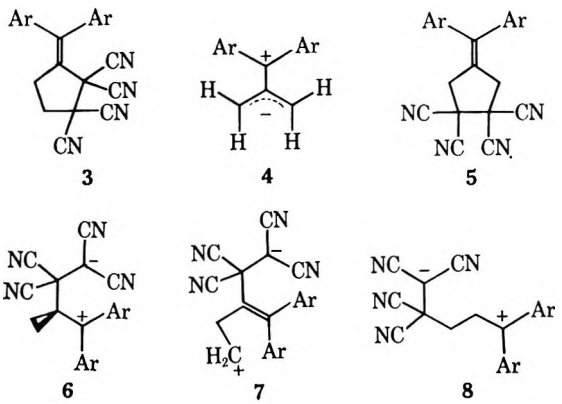


**1** **2**

**a**, Ar = $C_6H_5$; **b**, Ar = *p*-$CH_3OC_6H_4$

Both concerted and nonconcerted mechanistic possibilities leading to cyclopentane systems seem available. As a homoallene, the methylenecyclopropane unit would be potentially able to add TCNE across its $C_1$–$C_2$ bond to give **3** in what could be formally described as a thermally allowed [$\pi_s^2 + \pi_s^2 + \sigma_s^2$] cycloreaction.[4] By analogy with the behavior of appropriately substituted aziridines,[5–8] and with one perception of the cycloaddition behavior of cyclopropanones,[9,10] prior isomerization to dipolar intermediate **4**, followed by an allowed [$\pi_s^4 + \pi_s^2$] cycloaddition, might produce **5**.

Initial formation of one new bond linking methylenecyclopropane **1** at $C_1$ to TCNE, generating a dipolar species **6**, might also yield **3** through a cyclopropylcarbinyl to allylcarbinyl (**6** → **7**) rearrangement before the second bond-making step. A two-step process with a somewhat similar dipolar intermediate **8** has been proposed as one means to account for production of 1,1-diphenyl-2,2,3,3-tetracyanocyclopentane from 1,1-diphenylcyclopropane and TCNE.[11]



**3** **4** **5**

**6** **7** **8**

Cycloadducts from diphenylmethylenecyclopropane (**1a**) and bis(*p*-methoxyphenyl)methylenecyclopropane (**1b**) were obtained when these homoallenes were heated to 120° with TCNE in toluene. The adducts, mp 215 and 191°, respectively, had nmr spectra which immediately ruled out structure **5** as well as spiroheptane (2 + 2) adducts; the methylene protons appeared as two sets of 2 H triplets, centered at $\delta$ 3.22 and 2.63 (adduct **a**) and at $\delta$ 3.19 and 2.59 (adduct **b**), with $J$ = 8 Hz, implicating $CH_2CH_2$ as one moiety in these products. The methoxyl methyl signals in adduct **b** came at $\delta$ 4.00 and 3.93 ppm; both adducts had aromatic protons evident at $\delta$ 7–8 ppm.

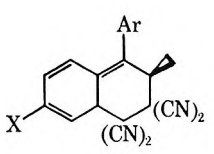
Structure **3** seemed consistent with the nmr data, but for two troubling points. In the adduct **a**, one aromatic proton appeared at an unusually low field (8.35 ppm) as a doublet of doublets ($J$ = 8, ~2 Hz), and the signals for the methylene protons were appropriate to an $A_2M_2$ system, rather than to the AA′MM′ pattern expected for **3**.

Elemental analyses and mass spectral determinations of molecular weight firmly excluded structure **3**, since both adducts corresponded to 1:1 adducts . . . less HCN! Their ultraviolet spectra revealed them to be 1-arylnaphthalene derivatives: for adduct **a**, $\lambda_{max}^{CH_2Cl_2}$ 253 (log $\epsilon$ 4.67), 305 (3.56), 318 (3.61), 341 (3.45), and 356 (3.56); for adduct **b**, $\lambda_{max}^{CH_2Cl_2}$ 265 (4.77), 298 (3.64), 313 (3.63), 372 sh (3.67), and 385 (3.72).[12] The substantial bathochromic shift for both the $^1B_a$ and $^1L_a$ bands (253 → 265 nm, 356 → 385 nm) on going from adduct **a** to the methoxy-substituted system **b** suggested a con-

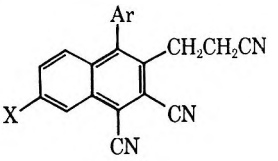
(1) Supported initially by Public Health Service Research Grant GM 16576 and subsequently by National Science Foundation Grant GP 9259 and the Research Corporation.
(2) Address correspondence to the University of Oregon.
(3) National Defense Education Act Fellow, 1967–1970.
(4) R. B. Woodward and R. Hoffmann, *Angew. Chem., Int. Ed. Engl.*, **8**, 781 (1969).
(5) H. W. Heine and R. E. Peavy, *Tetrahedron Lett.*, 3123 (1965).
(6) H. W. Heine, R. Peavy, and A. J. Durbetaki, *J. Org. Chem.*, **31**, 3924 (1966).
(7) R. Huisgen, W. Scheer, and H. Mäder, *Angew. Chem., Int. Ed. Engl.*, **8**, 602 (1969).
(8) R. Huisgen, W. Scheer, H. Mäder, and E. Brunn, *ibid.*, **8**, 604 (1969).
(9) N. J. Turro, *Accounts Chem. Res.*, **2**, 25 (1969).
(10) N. J. Turro, S. S. Edelson, J. R. Williams, T. R. Darling, and W. B. Hammond, *J. Amer. Chem. Soc.*, **91**, 2283 (1969).
(11) T. Martini and J. A. Kampmeier, *Angew. Chem., Int. Ed. Engl.*, **9**, 236 (1970).
(12) Compare ultraviolet spectral data reported for 1-phenylnaphthalene and 1-cyclonaphthalene: "UV Atlas of Organic Compounds," Vol. II, Plenum Press, New York, N. Y., 1966, plates E 1/2 and E 1/36.

jugative interaction between MeO– and NC– groups separated by four carbon atoms.

These data and mechanistic considerations led to formulation of the adducts as 1-phenyl-2-(2-cyanoethyl)-3,4-dicyanonaphthalenes, derived from an initial Diels–Alder addition between **1** and TCNE giving the relatively unstable triene system **9**, which through loss of HCN and a cyclopropylcarbinyl to allylcarbinyl rearrangement may give the isolated products **10**.



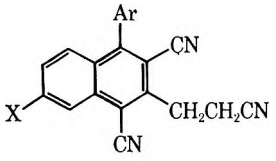

**9**




**10**

The $A_2M_2$ nmr pattern for methylene protons is in accord with the conformationally mobile cyanoethyl group, and the low field aromatic proton in **10a** may be ascribed to H–$C_5$, strongly deshielded by the peri-positioned NC–$C_4$ function, and in **10b**, counter shielded by the adjacent $CH_3O$ group.[13]

The experimental data seem compatible with both formulation **10** and with structure **11** for the adducts; only a substantial discrepancy in mechanistic plausibility favors the former alternative.




**11**

This cycloaddition behavior parallels one mode of reaction available to arylallenes: Diels–Alder dimerization followed by rearrangement, as in the conversion of phenylallene to 2,3-dimethyl-1-phenylnaphthalene[14] or of 1,3-diphenylallene to 2,3-dibenzyl-1-phenylnaphthalene.[15]

Further efforts to achieve additions across the $C_1$–$C_2$ or the $C_2$–$C_3$ bond of methylenecyclopropanes **1** will be made with other olefins and with other systems lacking vinyl or phenyl substitution at the exocyclic methylene carbon.

## Experimental Section

Melting points were obtained on a Kofler Micro Hot Stage apparatus and are uncorrected. Infrared spectra were run in chloroform solution on a Beckman Model IR-5 spectrophotometer, and ultraviolet spectra were recorded on a Cary 15 spectrophotometer. Proton magnetic resonance spectra (in $CDCl_3$) were determined on Varian Models A-60, A-60A, A-56/60A, HA-100 spectrometers. Mass spectra were run on a CEC 21-110B spectrometer by Mrs. Mary Mitchell. Elemental analyses were determined by Chemalytics Inc., Tempe, Ariz. Tetrahydrofuran (THF) was distilled from lithium aluminum hydride and stored over sodium wire.

**α-Triphenylphosphoniumbutyrolactone Bromide.**[16]—A solution of 9.86 g (0.03 mol) of triphenylphosphine and 4.96 g (0.03 mol) of α-bromo-γ-butyrolactone in 15 ml of THF was heated at reflux for 4 hr. The mixture was cooled, filtered, and washed with THF. The crude material was dissolved in 50 ml of hot methanol, 150 ml of ethyl acetate was added, and the cloudy solution was cooled. Filtration and drying gave 6.90 g (53.8%) of product, mp 188° (lit.[16] mp 196–197°).

Further purification was accomplished by grinding the crystalline material to a fine powder with a mortar and pestle and washing the solid several times with ether. Thorough drying in a vacuum oven at 60° (20 mm) gave salt sufficiently pure for synthetic utilization: ir 3500, 3250, 2900, 1710, 1600, 1485, 1110, 1025, and 956 $cm^{-1}$; nmr τ 2.10 (m, 15), 5.30 (m, 3), and 6.70 (m, 2).

**Cyclopropyltriphenylphosphonium bromide**[17,18] was prepared from α-triphenylphosphoniumbutyrolactone bromide in 98% yield, crushed to a fine powder with a mortar and pestle, washed thoroughly with ether, and dried in a vacuum oven at 60° (20 mm) to give material of melting point 190° (lit.[18] mp 189–190°): ir 3300, 2870, 1590, 1480, 1340, 1220, 1115, 1000, and 900 $cm^{-1}$; nmr τ 2.17 (m, 15), 6.60 (m, 1), 8.21 (m, 2), and 9.37 (m, 2).

*Anal.* Calcd for $C_{21}H_{20}BrP$: C, 65.79; H, 5.22; Br, 20.88. Found: C, 64.13; H, 5.35; Br, 20.66.

**Diphenylmethylenecyclopropane.**[19]—Under a dry nitrogen atmosphere and with stirring, a mixture of 3.54 g (7.8 mmol) of cyclopropyltriphenylphosphonium bromide in 45 ml of THF was treated with 4.5 ml of 1.6 *M* *n*-butyllithium in hexane (Foote Chemicals). The reaction mixture was stirred and heated gently for 2 hr, and then 1.42 g (7.8 mmol) of benzophenone in THF was slowly added. The mixture was gently heated at reflux for 21 hr. Tetrahydrofuran was distilled from the mixture, the residue was extracted with chloroform, and the extracts were washed with water and dried ($Na_2SO_4$). Evaporation of the chloroform and chromatography of the remaining material with hexane on 21 g of silica gel afforded 657 mg (41%) of product.

A pure sample was obtained by recrystallization from petroleum ether (bp 30–60°) to give material of mp 61–64° (lit.[19] mp 65°): ir 3080, 2950, 1960, 1890, 1820, 1595, 1490, 1075, and 895 $cm^{-1}$; nmr τ 2.81 (m, 10) and 8.65 (s, 4).

**Bis(*p*-methoxyphenyl)methylenecyclopropane.**—To a stirred slurry of 4.31 g (11.2 mmol) of cyclopropyltriphenylphosphonium bromide in 35 ml of THF was added 7.5 ml (12.9 mmol) of *n*-butyllithium. The solution was warmed gently and stirred for about 1 hr, and 2.7 g (11.2 mmol) of 4,4′-dimethoxybenzophenone in 10 ml of THF was slowly added. The reaction mixture was heated to reflux for 18 hr and then cooled; solvent was removed by distillation, and the residue was dissolved in chloroform. The chloroform solution was washed with water, dried ($Na_2SO_4$), filtered, and concentrated. The remaining oil was chromatographed with hexane on 30 g of silica gel. The desired product, 830 mg (28%), eluted with the first 100 ml of hexane. Recrystallization from hexane gave pure material: mp 106–107°; ir 2950, 2840, 1605, 1560, 1490, 1105, 1030, 895, and 828 $cm^{-1}$; nmr τ 2.76 (m, 8), 6.12 (s, 6), and 8.61 (s, 4).

*Anal.* Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 80.91; H, 6.74.

**Diphenylmethylenecyclopropane–TCNE Addition.**—A solution of 114 mg (0.55 mmol) of **1a** and 78 mg (0.61 mmol) of TCNE in 10 ml of toluene was heated gently to reflux under nitrogen for 17 hr. The toluene was removed by distillation, and the dark residue was chromatographed on 6 g of silica gel with chloroform. The first 20-ml fraction contained 62 mg of material shown by nmr to be a mixture of 75% adduct and 25% **1a**. From the second fraction eluted, 39 mg (total yield 85 mg, 46%) of adduct was obtained.

A pure sample of adduct, mp 215°, was obtained by recrystallization from methanol: mass spectrum (10 eV) *m/e* 307 ($M^+$); ir 2250, 1560, 1450, 1420, and 1380 $cm^{-1}$; for nmr and ultraviolet data, see text above.

*Anal.* Calcd for $C_{21}H_{13}N_3$: C, 82.07; H, 4.26. Found: C, 81.74; H, 4.23.

**Bis(2-methoxyphenyl)methylenecyclopropane–TCNE Addition.**—A solution of 122 mg (0.46 mmol) of **1b** and 60 mg (0.47 mmol) of TCNE was heated to reflux in 10 ml of toluene under nitrogen for 13 hr. Concentration and chromatography led to

(13) *Cf.* J. W. Emsley, J. Feeney, and L. H. Sutcliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy," Pergamon Press, Elmsford, N. Y., 1966, pp 405, 752.

(14) J. E. Baldwin and L. E. Walker, *J. Org. Chem.*, **36**, 1440 (1971).

(15) H. A. Staab and H. A. Kurmeier, *Chem. Ber.*, **101**, 2697 (1968).

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(17) (a) H. J. Bestmann and R. Kunstmann, *Tetrahedron Lett.*, 2895 (1968); (b) H. J. Bestmann, H. Hartung, and I. Pils, *Angew. Chem., Int. Ed. Engl.*, **4**, 957 (1965); (c) A. Maercker, *ibid.*, **6**, 557 (1967); (d) D. T. Longone and R. R. Doyle, *Chem. Commun.*, 300 (1967).

(18) E. E. Schweizer, C. J. Berninger, and J. G. Thompson, *J. Org. Chem.*, **33**, 336 (1968).

(19) K. Sisdo and K. Utimoto, *Tetrahedron Lett.*, 3267 (1966).

53 mg (29%) of yellow adduct: mp 190–191° from methanol; mass spectrum (9 eV) *m/e* 367 ($M^+$); ir 2245, 1625, 1465, 1430, 1225, 1033, and 837 $cm^{-1}$; the nmr and ultraviolet data are given above.

*Anal.* Calcd for $C_{23}H_{17}N_3O_2$: C, 75.19; H, 4.66. Found: C, 75.02; H, 4.53.

**Registry No.**—**1a**, 7632-57-7; **1b**, 28228-81-1; **2**, 670-54-2; α-triphenylphosphoniumbutyrolactone bromide, 28228-78-6; cyclopropyltriphenylphosphonium bromide, 14114-05-7.

## Catalytic Behavior of Some Ziegler–Natta Catalysts in the Norbornadiene–Butadiene Codimerization

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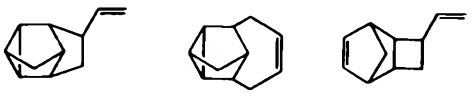
*Received October 1, 1970*

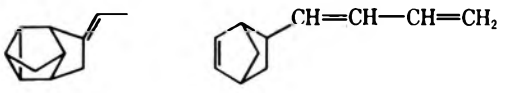
In a previous paper[1] we described the reaction between norbornadiene (NBD) and 1,3-butadiene (BD) catalyzed by organometallic iron compounds. The reaction products are 1:1 adducts, two of them (I and II) with the nortricyclenic and one (III) with the norbornenic structure.



I II III

In an attempt to set up selective syntheses of the above compounds and to discover new NBD–BD adducts, we investigated the behavior of catalysts containing transition metals different from iron. We employed two- as well as three-component systems, the third component always being a phosphorus-containing ligand. The most significant new results are summarized in Table I.

A new isomer was obtained employing the catalyst system $NiCl_2$–$Et_2AlCl$–$2PPh_3$. On the basis of chemical and physicochemical data, formula IV was attributed to it. The same product, but with lower con-




IV V

version, was obtained using a phosphine-free catalyst, prepared from a soluble nickel compound such as the diacetylacetonate.

Adduct IV is always accompanied by smaller amounts of adduct I. Since I and IV only differ in the position of the double bond of the side chain, we tried to isomerize I to IV by contact with the above nickel catalysts (under the same conditions in which IV is synthesized) but were unsuccessful. Also, other catalysts known for their activity in the isomerization of vinyl derivatives of cycloolefins to ethylidene compounds,

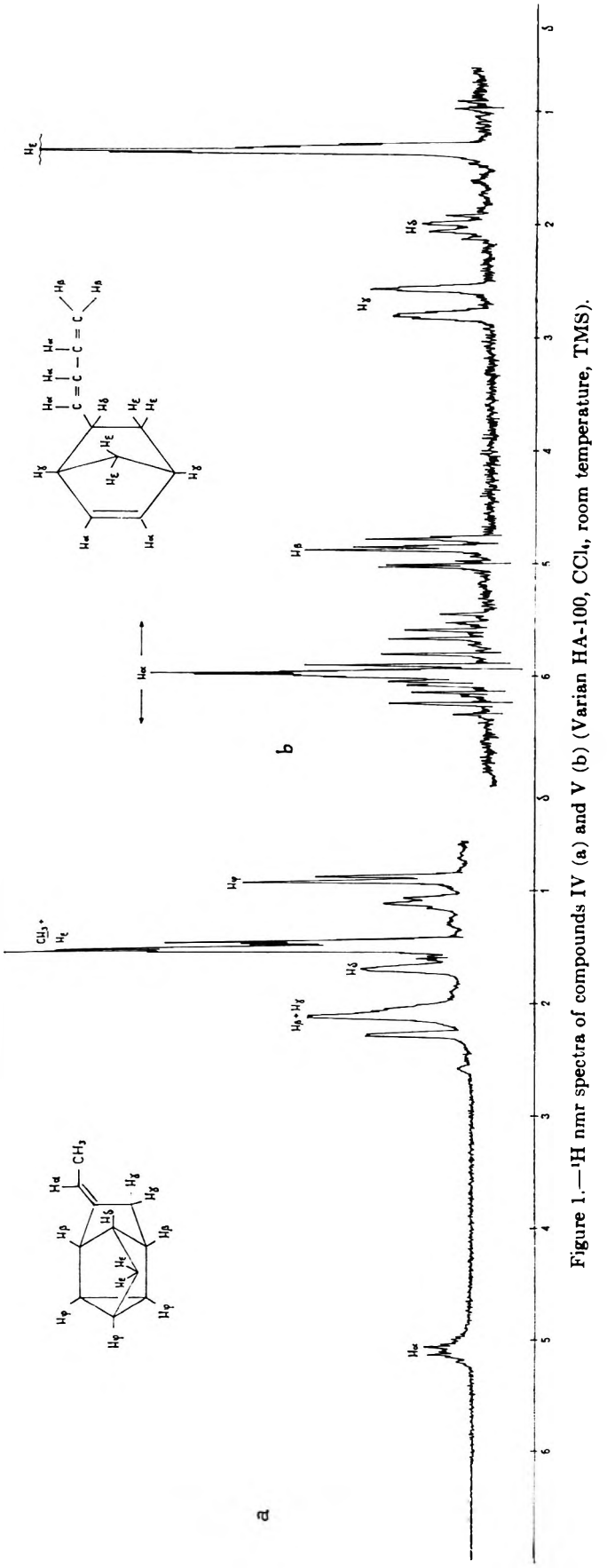



Figure 1.—$^1H$ nmr spectra of compounds IV (a) and V (b) (Varian HA-100, $CCl_4$, room temperature, TMS).

(1) A. Greco, A. Carbonaro, and G. Dall'Asta, *J. Org. Chem.*, **35**, 271 (1970).

TABLE I[a]

NORBORNADIENE–1,3-BUTADIENE CODIMERIZATION INDUCED BY DIFFERENT ORGANOMETALLIC CATALYST SYSTEMS

| Catalyst system | | | | Main products[b] | |
|---|---|---|---|---|---|
| Transition metal compd, mmol | Organometallic compd, mmol | Ligand, mmol | Solvent,[c] ml | Structure | % yield[d] |
| $NiCl_2$,[e] 0.04 | $(C_2H_5)_2AlCl$, 0.5 | $P(C_6H_5)_3$,[e] 0.08 | TOL, 30 | IV | 8 |
| | | | | I | 2.5 |
| $CoCl_2$, 0.36 | $(i\text{-}C_3H_7)MgCl$, 3.6 | | DEE, 30 | V | 12 |
| $CoA_3$,[f] 0.09 | $(C_2H_5)_3Al$, 0.9 | | TOL, 25 | V | 43 |
| $CoCl_2$,[e] 0.03 | $(C_2H_5)_3Al$, 0.4 | $[(C_6H_5)_2PCH_2]_2$,[e] 0.06 | TOL, 20 | II | 44 |
| $CoCl_2$,[e] 0.07 | $(C_2H_5)_2AlCl$, 0.7 | $[(C_6H_5)_2PCH_2]_2$,[e] 0.14 | TOL, 35 | II | 68 |
| $MnA_2$,[f] 0.12 | $(i\text{-}C_3H_7)MgCl$, 1.2 | | DEE, 15 | V | 4.5 |
| | | | | III | 3 |
| $MnA_2$,[f] 0.19 | $(C_2H_5)_3Al$, 1.9 | | HEX, 25 | V | 5 |
| | | | | III | 3 |
| $MnA_2$,[f] 0.13 | $(i\text{-}C_3H_7)MgCl$, 1.3 | $(C_6H_5)_2P(OC_4H_9)$, 0.6 | DEE, 15 | V | 13 |
| | | | | III | 8 |

[a] NBD = 19.7 mmol; BD = 24 mmol; temperature, 75°; time, 5 hr. [b] By-products mainly consist of NBD dimers. [c] TOL = toluene, DEE = diethyl ether, HEX = *n*-hexane. [d] Moles of the main product/moles of NBD introduced. [e] Transition metal compound/ligand complex preformed. [f] A = acetylacetonate.

such as $Fe(CO)_5$ or cobalt diacetylacetonate–$Et_3Al$,[2] were found to be almost uneffective at 150°.[3]

Isomerization of I to IV (to more than 90%: Experimental Section) could be achieved in the presence of the $Ti(OBu)_4$–$Et_3Al$ catalytic system at 150° for 1 hr. No other catalysts, among those investigated, yield appreciable amounts of oligomer IV. We should therefore deduce that IV is a primary product of the NBD–BD codimerization induced by organometallic nickel catalysts.

The behavior of the soluble cobalt catalysts is strongly influenced by the presence or absence of the bidentate 1,2-bis(diphenylphosphino)ethane ligand. The complex of $CoCl_2$ with the said phosphine, when combined with both $Et_3Al$ and $Et_2AlCl$ (Table I), yields adduct II in a very selective way. By contrast, the system obtained from an acetylacetonate of Co and $Et_3Al$ or from $CoCl_2$ and $(i\text{-}C_3H_7)MgCl$ in diethyl ether yields, in an equally specific way, a new adduct to which structure V was assigned.[3a]

Other catalysts examined are those prepared from a manganese compound and $Et_3Al$ or from a chloroisopropyl Grignard reagent. NBD and BD are induced to codimerize to a mixture of III and V, the latter being the main compound.[4] The presence of mono- and bidentate phosphorus ligands does not influence, in the case of manganese catalysts, the nature of the final products, but only the conversion.

Among the NBD–BD codimers, compound V is the only one formed through a hydrogen shift from one to the other reacting olefin. This type of addition of a butadiene to one cycloolefinic double bond was never observed before, as far as we know. It may be formally compared with one of the ethylene–butadiene codimers, *i.e.*, 1,3-hexadiene, formed by hydrogen shift from these two monomers by the action of analogous $CoCl_2$–$Et_3Al$ catalysts.[5]

**Assignment of Structures IV and V. Adduct IV.**—The mass spectrum parent peak is at *m/e* 146. The $^1H$ nmr spectrum (Figure 1a) shows multiplets centered at $\delta$ 5.1 (1 H), 2.27 (1 H), 2.1 (3 H), 1.59 (1 H), 1.48 (5 H), 1.1 (1 H), and 0.9 ppm (2 H). The signal at $\delta$ 5.1 may be attributed to the only hydrogen attached to an unsaturated carbon atom. The methyl protons, together with two others, originate the signal at $\delta$ 1.48; this position is justified by the presence of the double bond in $\alpha$. All other signals are derived from the nortricyclenic protons.

The ir spectrum shows absorptions at 790 (vs) and 821 $cm^{-1}$, attributed to the nortricyclenic system,[6] whereas a band at 3040 $cm^{-1}$ is due to the C—H stretching of the C=C double bond. The spectrum is rich in bands especially in the region between 500 and 1350 $cm^{-1}$.[7]

**Adduct V.**—The mass spectrum parent peak is at *m/e* 146. The $^1H$ nmr spectrum (Figure 1b) shows a peak system between $\delta$ 6.35 and 5.45 (5 H), as well as multiplets centered at about $\delta$ 4.9 (2 H), 2.8 (1 H), 2.56 (1 H), 2.02 (1 H), and 1.35 ppm (4 H). The two protons of the cycloolefin double bond and the three CH groups of the butadienyl residue should originate the system of bands at $\delta$ 6.35–5.45,[8] whereas the vinyl protons of the butadienyl residue should be attributed to the signal at about $\delta$ 4.9 (system of three bands). The two nonequivalent protons at $\delta$ 2.8 and 2.56 should be those $\alpha$ to the cycloolefinic unsaturation,[8] whereas at about $\delta$ 2 there should be the proton at the ring carbon atom bearing the side group. The remaining four saturated methylene hydrogens likely originate the signal at $\delta$ 1.35.[8]

The ir spectrum of V shows characteristic absorptions of the norbornenic system[5] at 3060, 1568, 1332, and 712 $cm^{-1}$; of the vinyl group at 1415, 1000, and 900 $cm^{-1}$; and of the internal trans double bonds at 951 $cm^{-1}$.[9] The uv maximum at 230 nm (log $\epsilon$ 4.59) is due to the trans double bond.

(2) M. W. Schneider (to B. F. Goodrich), French Patents 1,555,199 and 1,556,198 (priority 1967).

(3) According to our results, compound III isomerizes to the corresponding ethylidene derivative in the presence of said Fe or Co catalysts.

(3a) NOTE ADDED IN PROOF.—Compound V has recently been described also by A. Takahashi and T. Inukai, *Chem. Commun.*, 1473 (1970).

(4) Our unpublished results show that manganese-based catalysis selectively trimerizes butadiene to *trans,trans,trans*-1,5,9-cyclododecatriene.

(5) D. Wittenberg, *Angew. Chem.*, **75**, 1124 (1963); A. Carbonaro, G. Dall'Asta, and A. Greco, *Chim. Ind.* (*Milan*), **52**, 49 (1970).

(6) J. J. Mrowca and T. J. Katz, *J. Amer. Chem. Soc.*, **88**, 4012 (1966), and references quoted therein.

(7) The main ir bands of IV are at 2920 (vs), 2845, 1683, 1447 (s), 1428 (s), 1371, 1309 (s), 1290 (s), 1250 (s), 1167, 1122, 1049, 980 (s), 960, 950, 883, 841 (s), 700, 589, and 511 $cm^{-1}$ (s).

(8) P. Laszlo and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, **86**, 1171 (1964).

(9) Other significant ir bands of V are at 3087, 3038, 2965 (vs), 2870, 1648 (s), 1601, 1460, 1446 (s), 1415, 1282 (s), 1250 (s), 1135, 1098, 1082, 869 (s), 835, and 650 $cm^{-1}$.

### Experimental Section

**Reagents.**—Toluene, *n*-hexane, and diethyl ether were dried by distillation over $LiAlH_4$ and stored under nitrogen. Norbornadiene (Fluka, practical grade) and butadiene (Phillips, special purity) were used as supplied. Triphenylphosphine (BDH) and other phosphines (Strem) were commercial products. Cobalt and nickel chlorides were dried by treatment with $SOCl_2$. ($i$-$C_3H_7$)MgCl Grignard reagent was prepared from 2-chloropropane (Fluka, practical grade) and Mg turnings. $Et_3Al$ and $Et_2AlCl$ (Fluka, practical grade) were used as supplied.

**Oligomerizations.**—The reactions were run in glass vials under nitrogen. The reagents were introduced into the reactor in the following order: transition metal compound, ligand (when used), solvent, BD, NBD, and organometallic compound. A small amount of *n*-decane was added as internal standard for quantitative estimations in the glc analysis. The mixture was normally prepared at −78° and kept in a thermostatic bath. At the end of the reaction small amounts of methanol and phenyl-β-naphthylamine were added.

**Characterization of the Compounds.**—The quantitative composition of the reaction products was determined by glc (C. Erba, Fractovap C, methylsilicone SE 30, P 30–60 mesh, 2 m, 80°, He) on the crude mixture. Isolation of pure $C_{11}$ compounds was accomplished by preparative glc (C. Erba, Fractovap P 100, Apiezon L, Chromosorb W 50-60, 8 m, 220°, He) on fractions enriched by distillation. Spectroscopic characterizations were performed on a Perkin-Elmer 125 ir spectrophotometer (NaCl optics), Varian HA 100-MHz nmr spectrometer ($CCl_4$, room temperature, TMS reference), and Hitachi RMU 6 E (70 eV, 250°) mass spectrometer.

*Anal.* Calcd for $C_{11}H_{14}$: C, 90.42; H, 9.58. Found for IV: C, 90.19; H, 9.22. Found for V: C, 90.78; H, 9.61. Physical properties of IV and V: IV, bp 187–189°, $n^{24}D$ 1.4955; V, bp 190–192°, $n^{24}D$ 1.5188.

**Registry No.**—IV, 28229-18-7; V, 28229-10-9.

## Facile Olefin Hydrogenation with Soluble Lithium-Based Coordination Catalysts

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There has been considerable interest in soluble hydrogenation catalysts in recent years. Numerous Ziegler-type catalysts have been developed to effect facile hydrogenation of olefins using alkylaluminum compounds as reducing agents.[1-5] Although Sloan, *et al.*,[1] mention the use of alkyllithiums as reducing agents combined with transition metal salts of groups IV–VIII metals, they prefer alkylaluminums, claiming shorter reduction times. Several patents have also briefly mentioned alkyllithiums as cocatalysts in olefin reductions, but the use of alkylaluminums was preferred.[2-5] We have now found that previous investigators severely underestimated the reactivity of reduction catalysts prepared from alkyllithiums. In our studies Ziegler-type hydrogenation catalysts made from organolithium compounds and transition metal salts of 2-ethylhexanoic acid were fully as active as alkylaluminum-based catalyst systems at convenient concentration levels of catalyst. They are preferable because of the ease of handling of organolithiums compared with alkylaluminums. While these catalysts are generally referred to as soluble, they might exist in a finely divided suspended form. They do not deteriorate when aged for several months.

Active lithium-based hydrogenation catalysts may be prepared by slowly adding a solution of transition metal 2-ethylhexanoate in cyclohexane to a solution of an alkyl- or aryllithium dissolved in cyclohexane or benzene under a nitrogen atmosphere. This catalyst, in the presence of hydrogen, will reduce a variety of cyclic and acyclic olefins, as shown in Table I, utilizing mild conditions of temperature, 50°, and pressure, 50 psi of hydrogen. Cyclic, mono-, and disubstituted acyclic olefins are easily reduced quantitatively in 30 min or less. Trisubstituted olefins such as 1-methylcyclohexene and 2-methylpentene-2 are more resistant to hydrogenation, and the tetrasubstituted olefin 2,3-dimethylbutene-2 is the most resistant. Unsaturation adjacent to an aromatic nucleus is easily hydrogenated, as evidenced by the quantitative reduction of the vinyl group in styrene in 20 min.

TABLE I

HYDROGENATION OF OLEFINS WITH SOLUBLE HYDROGENATION CATALYSTS[a]

| Olefin | Catalyst level, mol % | Li/Co | Time, min | % conversion[b] |
|---|---|---|---|---|
| Cyclooctene | 0.6 | 4.0 | 30 | 100 |
| Cyclohexene | 0.5 | 4.0 | 20 | 100 |
| Cycloheptene | 0.5 | 3.0 | 30 | 100 |
| 1-Methylcyclohexene | 0.2 | 6.0 | 90 | 44 |
| *cis*-Pentene-2 | 0.4 | 4.0 | 20 | 100 |
| Hexene-1 | 0.5 | 4.0 | 20 | 100 |
| 2-Methylpentene-2 | 0.5 | 4.0 | 60 | 92 |
| *trans*-Pentene-2 | 0.4 | 4.0 | 30 | 100 |
| Styrene[c] | 0.6 | 4.0 | 20 | 100 |
| 2,3-Dimethylbutene-2 | 0.5 | 4.0 | 90 | 37 |

[a] Hydrogen pressure, 50 psi; 50°; *n*-butyllithium–cobalt 2-ethylhexanoate cocatalysts. [b] Determined by gas chromatography. [c] Reduction of the vinyl moiety.

The catalytic activity of lithium–cobalt hydrogenation catalysts compares favorably with an aluminum–cobalt catalyst having an aluminum to cobalt ratio (3.3:1) shown by Sloan, *et al.*,[1] to give facile hydrogenations.[6]

The activity of hydrogenation catalysts prepared from alkyl- or aryllithium and transition metal salts of 2-ethylhexanoic acid is a function of the molar ratio of lithium to cobalt (Table II, entries 1–5). At low lithium/transition metal ratios, Li/Co = 1.7, active hydrogenation catalysts are not formed, while at a higher lithium/cobalt ratio, 9.9, hydrogenation activity is greatly diminished. Intermediate ratios give quite active hydrogenation catalysts.

The rate of hydrogenation increases with an increase in catalyst concentration (Table II, entries 6–8). At 0.3 mol % catalyst cyclooctene is rapidly hydrogenated, while at 0.1 mol % catalyst the reaction is slightly slower. At 0.05 mol % catalyst, reduction ceases. The failure to observe hydrogenation of cyclooctene

(1) M. F. Sloan, A. S. Matlack, and D. S. Breslow, *J. Amer. Chem. Soc.*, **85**, 4014 (1963); U. S. Patent 3,113,986 (Dec 10, 1963).
(2) W. R. Kroll, U. S. Patent 3,412,174 (Nov 19, 1968).
(3) French Patent 1,575,046 (June 9, 1969).
(4) Belgian Patent 718,658 (Sept 30, 1968).
(5) S. J. Lapporte, U. S Patent 3,205,278 (Sept 7, 1965); *J. Org. Chem.*, **28**, 1947 (1963).
(6) A triethylaluminum–cobalt 2-ethylhexanoate catalyst having an Al/Co of 3.3 and at a concentration of 0.3 mol % quantitatively hydrogenated cyclooctene in cyclohexane in 20 min at 50° and 50 psi of hydrogen.

TABLE II
HYDROGENATION OF CYCLOOCTENE WITH SOLUBLE HYDROGENATION CATALYSTS AS A FUNCTION OF Li/Co RATIO AND CATALYST LEVEL[a]

| Entry | Li/Co[b] | Catalyst level, mol % | Time, min | % conversion |
|---|---|---|---|---|
| 1 | 1.7 | 0.3 | 90 | 8 |
| 2 | 4.0 | 0.3 | 30 | 100 |
| 3 | 5.6 | 0.3 | 20 | 99 |
| 4 | 6.0 | 0.3 | 20 | 100 |
| 5 | 9.9 | 0.3 | 90 | 16 |
| 6 | 5.6 | 0.05 | 90 | 0 |
| 7 | 5.6 | 0.1 | 30 | 93 |
| 8 | 5.6 | 0.3 | 20 | 99 |
| 9 | 4.7[c] | 0.3 | 90 | 98 |

[a] Hydrogen pressure 50 psi, 50°. [b] Molar ratio. [c] *n*-Butyllithium–nickel octoate cocatalysts.

with 0.05 mol % catalyst may be due to loss of catalyst by oxidation or other impurities.

Transition metal salts other than cobalt 2-ethylhexanoate may be used as cocatalysts in the hydrogenation of olefins. Nickel 2-ethylhexanoate–*n*-butyllithium hydrogenation catalyst is less active than its cobalt counterpart (Table II, entry 9).

A number of alkyl- or aryllithiums have been used in place of *n*-butyllithium as cocatalysts with cobalt 2-ethylhexanoate in the hydrogenation of olefins. Comparative data at 50°, 50 psi of hydrogen pressure, Li/Co = 4.0, are listed in Table III. Similar reactivity is observed with aromatic and primary and secondary alkyllithiums. Hydrogenation activity is diminished significantly if cyclopentyllithium is used as the cocatalyst, but this may reflect the unknown purity of cyclopentyllithium.

TABLE III
HYDROGENATION OF OLEFINS WITH SOLUBLE HYDROGENATION CATALYSTS AS A FUNCTION OF LITHIUM SOURCE[a]

| Lithium source | Olefin | Time, min | % conversion |
|---|---|---|---|
| *n*-Butyllithium | *cis*-Pentene-2 | 20 | 100 |
| Ethyllithium | Cyclooctene | 10 | 100 |
| *sec*-Butyllithium | Cyclooctene | 10 | 100 |
| Cyclopentyllithium | Cyclooctene | 90 | 63 |
| Phenyllithium | Hexene-1 | 10 | 100 |

[a] Hydrogen pressure 50 psi, Li/Co = 4.0, 50°, 0.3 mol % catalyst.

Cycloolefins may be selectively reduced in the presence of their 1-methyl counterparts. Cyclohexene in a 50% mixture of cyclohexene and 1-methylcyclohexene is quantitatively reduced in 10 min while 18% reduction of 1-methylcyclohexene occurs. A *n*-butyllithium–cobalt 2-ethylhexanoate catalyst was used having a Li/Co of 6.0 at a 0.2 mol % catalyst level at 50°, 50 psi of hydrogen pressure. In an analogous experiment with a 50% mixture of cycloheptene and 1-methylcycloheptene, cycloheptene is quantitatively reduced in 10 min while 25% reduction of the 1-methyl derivative occurs. The selectivity is not absolute and higher ratios of Li/Co may show improved selectivity.

An active soluble lithium-based hydrogenation catalyst system has been discussed in terms of several reaction parameters. This catalyst system is as active as aluminum-based systems at convenient catalyst concentrations and offers as an advantage the ease of handling of organolithiums compared with other hydrogenation catalysts such as alkylaluminums.

### Experimental Section

**Materials.**—Aryl- and alkyllithium reagents were purchased from the Foote Chemical Co. A solution of cobalt 2-ethylhexanoate in cyclohexane was purchased from the Harshaw Chemical Co. and nickel 2-ethylhexanoate was purchased from K & K Laboratories. The olefins were purchased from either the Eastman Kodak Co. or the Aldrich Chemical Co. and were distilled and stored over molecular sieves prior to use. Solvents were passed through molecular sieves. All reactions and reagent transfers were carried out under a dry nitrogen atmosphere.

**Catalyst Preparation.**—A 0.285 *M* solution of catalyst (molarity based upon the amount of lithium) was prepared by adding 14.1 g of cobalt 2-ethylhexanoate solution (12.0% cobalt, w/w) over a period of 90 min to a solution of 0.0854 mol of *n*-butyllithium in 287 ml of cyclohexane; Li/Co = 3.0. Other ratios were prepared in the same manner.

**Olefin Hydrogenation.**—In a typical example, cycloheptene (44.9 g) was dissolved in 1500 ml of cyclohexane and placed with 0.5 mol % of a *n*-butyllithium–cobalt 2-ethylhexanoate catalyst having a lithium/cobalt ratio of 3.0:1 in a 2-l. reactor thermostated at 50°. The reactor was kept at a constant hydrogen pressure of 50 psi throughout the hydrogenation. Aliquots of the reaction mixture were withdrawn periodically, and the per cent conversion was determined by measuring the amounts of cycloheptane and cycloheptene using a F & M Dual Flame Model 810 gas chromatograph with an activated alumina column at 200°.

**Registry No.**—Cyclooctene, 931-88-4; cyclohexene, 110-83-8; cycloheptene, 628-92-2; 1-methylcyclohexene, 591-49-1; *cis*-pentene-2, 627-20-3; hexene-1, 592-41-6; 2-methylpentene-2, 625-27-4; *trans*-pentene-2, 646-04-8; styrene, 100-42-5; 2,3-dimethylbutene-2, 563-79-1; *n*-butyllithium, 109-72-8; cobalt 2-ethylhexanoate, 136-52-7; nickel octanoate, 4995-91-9; ethyllithium, 811-49-4; *sec*-butyllithium, 598-30-1; cyclopentyllithium, 23473-12-3; phenyllithium, 591-51-5.

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## The Deconjugation of Isophorone[1]

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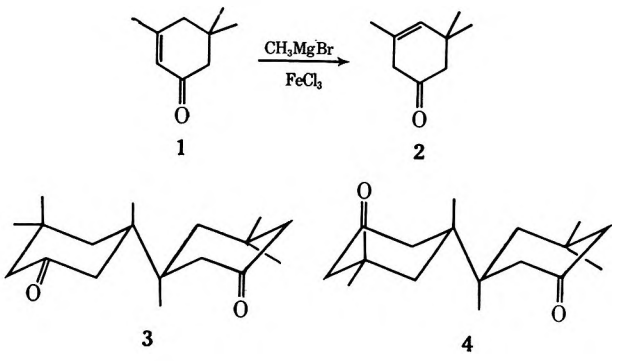
We were interested in an efficient procedure for the deconjugation of isophorone (1) to β-phorone (2) in connection with our recent synthesis of an allenic sesquiterpene.[2] While Kharasch and Tawney[3] have described a procedure for accomplishing this transformation, we found that the results were disappointingly erratic, giving sometimes large amounts of viscous, black material and sometimes a mixture of two crystalline products.

(1) Supported by NIH Training Grant 5RO1 GM00834-09.

(2) J. Meinwald and L. Hendry, *Tetrahedron Lett.*, 1657 (1969).

(3) M. S. Kharasch and P. O. Tawney, *J. Amer. Chem. Soc.*, **63**, 2308 (1941).

The crystalline by-products (mp 124 and 163°) were recognized from spectral evidence to result from reductive dimerization; their properties are well accounted for on the basis of formulas **3** and **4**, although we were unable to decide which isomer corresponds to the racemic mixture **3** and which to the meso form **4**. Earlier




workers[4,5] have described these reductive dimers from the sodium or lithium metal reductions of **1**. In our case, reductive dimerization seems to be brought about by the presence of excess magnesium metal in the methylmagnesium bromide reagent used to bring about the desired deconjugation.

On the basis of many experiments, we find that high yields of **2** are obtained when no excess of magnesium is present in the Grignard reagent, when the isophorone is added very rapidly to this reagent, and when other precautions noted in the Experimental Section are observed.

### Experimental Section

All melting points and boiling points are uncorrected. Infrared spectra were taken on a Perkin-Elmer 257 grating infrared spectrophotometer. The nuclear magnetic resonance spectra were obtained on Varian Associates A-60 and A-60A instruments. Mass spectra were taken on an Associated Electrical Industries MS-902 mass spectrometer.[6]

**β-Phorone (2).**—To a stirred solution of 51.5 g of Mallinckrodt Grignard magnesium in 300 ml of ether in a 3-l. flask, 200 g of cooled methyl bromide in 300 ml of ether was added. The dropwise addition was carried out over a 3-hr period, keeping the mixture under nitrogen and just below reflux temperature with an ice bath. When all of the magnesium was dissolved, 4 g of anhydrous ferric chloride in 100 ml of ether was added dropwise over 15 min. A solution of 207 g of distilled isophorone (**1**) [bp ~90° (10 mm)] in 300 ml of ether was added with rapid stirring over a 25-min interval. This step is dangerous and requires adequate venting of methane; moreover, the reaction mixture should not be allowed to cool, since large amounts of polymer are formed under those conditions. The reaction mixture was refluxed for 1 hr and poured into a 6-l. separatory funnel containing 50 g of ammonium chloride and 100 g of ice. After dropwise addition of 120 ml of glacial acetic acid, the mixture was shaken, and the aqueous phase was extracted twice with ether. The combined ether extract was washed with water, 5% aqueous sodium bicarbonate, and again with water. The ether was dried with anhydrous magnesium sulfate and filtered. Evaporation of the solvent and two distillations of the product using a Vigreux column gave 150 g of 96% pure β-phorone (**2**) [bp ~70° (10 mm)]; the purity was tested by gas chromatography on a 4% SE-30 column at 135°. The yield of β-phorone was 73%; however, reconjugation to isophorone (**1**) occurred at room temperature. This process was slowed by rapid distillation of the products and subsequent refrigeration.

**Isophorone Dimers 3 and 4.**—To a suspension of 25 g of magnesium in a 2-l. flask containing 200 ml of ether was added 100 g of cooled methyl bromide in 300 ml of ether. The system was flushed with nitrogen and 2 g of anhydrous ferric chloride in 50 ml of ether was added. (Specks of magnesium metal were visible in the mixture.) A solution of 125 g of isophorone (**1**) in 150 ml of ether was added carefully over a 1-hr period. A viscous material formed while refluxing for 1 hr which made stirring very difficult. Ice and 60 ml of acetic acid were used to hydrolyze the reaction mixture. After washing with water, 5% aqueous sodium bicarbonate, and water again, the ether layer was dried with anhydrous magnesium sulfate. Evaporation of the solvent yielded a semisolid viscous residue. The oil partially dissolved in pentane yielding 8.5 g of a crystalline dimeric species, mp 163°. Fractional crystallization in pentane yielded 15 g of a more soluble dimeric species, mp 123–124°. The total yield of dimer was about 20%; however, other experiments under varying conditions produced as much as 50% yield of dimers. Spectral data for both isomers were indistinguishable.

The dimer, mp 163°, had the following spectra: mass spectrum (70 eV) *m/e* 278.2239 ($C_{18}H_{30}O_2$ requires 278.2246), 263.2000 ($C_{17}H_{27}O_2$ requires 263.2010), 245.1875 ($C_{17}H_{25}O_2$ requires 245.1905), $263 \xrightarrow{m^* 228.1} 245$, 139 (M − $C_9H_{15}O$); nmr ($CDCl_3$) δ 1.05 (s, 6 H), 1.10 (s, 12 H), 1.27, 1.51, 1.70, 1.94 (AB quartet, $J_{AB} \sim 14$ cps, 4 H), 1.94, 2.18, 2.30, 2.54 (AB quartet, $J_{AB} \sim 14$ ops, 4 H), 2.18 (s, 4 H); nmr (pyridine) δ 0.99 (s, 18 H), 1.20, 1.43, 1.72, 1.95 (AB quartet, $J \sim 14$ cps, 4 H), 1.95, 2.18, 2.37, 2.60 (AB quartet, $J \sim 14$ cps, 4 H), 2.18 (s, 4 H); ir ($CH_2Cl_2$) 5.86 μ.

The dimer, mp 123–124°, had the following spectra: mass spectrum (70 eV) *m/e* 278, 263, 245, $263 \xrightarrow{m^* 228.1} 245$, 139; nmr ($CDCl_3$) δ 1.09 (s, 18 H), 1.28, 1.52, 1.71, 1.95 (AB quartet, $J \sim 14$ cps, 4 H), 1.92, 2.15, 2.31, 2.54 (AB quartet, $J \sim 14$ ops, 4 H), 2.18 (s, 4 H); nmr (pyridine) δ 0.99 (s, 18 H), 1.18, 1.42, 1.65, 1.89 (AB quartet, $J \sim 14$ cps, 4 H), 1.92, 2.16, 2.34, 2.58 (AB quartet, $J \sim 14$ cps, 4 H), 2.18 (s, 4 H); ir ($CH_2Cl_2$) 5.86 μ.

**Registry No.**—**1**, 78-59-1; **3**, 28192-72-5; **4**, 4994-12-1.

## A New Synthesis of Symmetrical Diaroylmethanes

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Sieglitz and Horn[2] prepared a series of symmetrical β-diketones by the reaction of vinyl acetate with the appropriate acid chloride in the presence of aluminum chloride. This method suffers from the disadvantage that appreciable amounts of unsymmetrical diketones, $RCOCH_2COCH_3$, are also formed. Rothman and Moore[3] have reported a route to β-diketones [$(RCO)_2CH_2$; R = alkyl] starting from isopropenyl esters. Recently, we described the preparation of symmetrical and unsymmetrical diaroylmethanes containing the pentafluorophenyl group.[4] We now report a simple general method for the preparation of symmetrical diaroylmethanes.

Vinyl esters of benzoic acids (Table I), prepared in

(4) W. Baker, *J. Amer. Chem. Soc.*, **47**, 663 (1925)

(5) J. Morizur, B. Furth, and J. Kossanyi, *Bull. Soc. Chim. Fr.*, 1422 (1967).

(6) Cornell High Resolution Mass Spectrometer Facility supported by NIH Grant No. RR00355.

(1) To whom inquiries should be addressed.

(2) A. Sieglitz and O. Horn, *Chem. Ber.*, **84**, 607 (1951).

(3) E. S. Rothman and G. G. Moore, *Tetrahedron Lett.*, 2553 (1969); E. S. Rothman, G. G. Moore, and A. N. Speca, *ibid.*, 5205 (1969).

(4) R. Filler, Y. S. Rao, A. Biezais, F. N. Miller, and V. D. Beaucaire, *J. Org. Chem.*, **35**, 930 (1970).

TABLE I

VINYL BENZOATES

| $CH_2$=CHOCOAr Ar = | Registry no. | Yield, % | Bp (mm) or mp, °C | Formula | Calcd, % C | Calcd, % H | Found, % C | Found, % H |
|---|---|---|---|---|---|---|---|---|
| 4-$ClC_6H_4$ | 7561-01-5 | 74 | 33 (5) | $C_9H_7O_2Cl$ | 59.18 | 3.89 | 59.32 | 3.83 |
| 4-$CH_3C_6H_4$ | 2653-44-3 | 70 | 33 (5) | $C_{10}H_{10}O_2$ | 74.07 | 6.17 | 73.9 | 6.1 |
| 4-$CH_3OC_6H_4$ | 13351-86-5 | 75 | 40 (5) | $C_{10}H_{10}O_3$ | 67.4 | 5.6 | 67.3 | 5.61 |
| 4-$NO_2C_6H_4$ | 831-69-6 | 80 | 73 | $C_9H_7O_4N$ | 60.3 | 3.9 | 60.2 | 3.87 |
| $C_6F_5$ | 28541-28-8 | 75 | 80 (5) | $C_9H_3F_5O_2$ | 45.3 | 1.26 | 45.15 | 1.24 |

75–80% yield by ester interchange (eq 1),[5] are treated with anhydrous aluminum chloride in tetrachloroethane at 70° to give the diketones in yields of 58–98% (Table II) (eq 2).[6]

$$CH_2{=}CHOCCH_3 \xrightarrow[HgSO_4]{ArCO_2H} CH_2{=}CHOCAr \qquad (1)$$

Ar = $C_6H_5$, *p*-$ClC_6H_4$, *p*-$CH_3OC_6H_4$, *p*-$CH_3C_6H_4$, *p*-$NO_2C_6H_4$, $C_6F_5$

$$CH_2{=}CHOCAr \xrightarrow{AlCl_3} ArCCH_2CAr \qquad (2)$$

The formation of the diaroylmethanes may proceed through the intermediacy of the diaroylacetaldehyde, $(ArCO)_2CHCHO$, which would then undergo decarbonylation to give the diketone.

### Experimental Section

**Vinyl Interchange Reaction.**—In a three-necked, round-bottomed flask, provided with a thermometer and water-cooled condenser, was placed 42.4 g (0.2 mol) of pentafluorobenzoic acid. Vinyl acetate (110 g, 1.28 mol) was added to the flask along with powdered mercuric sulfate (1.71 g). The contents of the flask were stirred with a magnetic bar and heated under reflux for 3 hr. At the end of this period, the contents of the flask were cooled and diluted with petroleum ether (bp 30–60°). Sodium acetate hydrate was added to remove acidic materials. The organic layer was filtered from the inorganic materials and concentrated on a rotary evaporator. Unreacted vinyl acetate and petroleum ether were thus removed. The residue in the flask was dissolved in ether and the ether solution washed with a solution of sodium bicarbonate to remove last traces of pentafluorobenzoic acid. The oily layer was distilled under reduced pressure to give 32 g (75%) of vinyl pentafluorobenzoate, bp 80° (5 mm). The following benzoates (see Table I) were prepared in the same fashion. Vinyl benzoate was obtained from Monomer-Polymer Labs, Philadelphia, Pa. If, when other other acids are used, the acid does not dissolve in vinyl acetate, it is beneficial to add 10–20 ml of absolute ethyl alcohol to dissolve the acid.

**Reaction of Vinyl Ester with Aluminum Chloride.**—In a three-necked flask provided with a thermometer, condenser, and a stirrer was placed 4.76 g (0.02 mol) of vinyl pentafluorobenzoate in 150 ml of tetrachloroethane. Anhydrous aluminum chloride (6 g, 0.046 mol) was added. The mixture was heated at 70° for 45 min. The reaction mixture was cooled and decomposed with 100 ml of 10% hydrochloric acid. Tetrachloroethane was removed by steam distillation and the residual organic material in the aqueous layer was recovered by extraction with ether. The ether layer was washed with water and dried over anhydrous sodium sulfate. Ether was removed on a rotary evaporator leaving behind a solid residue which was crystallized from a benzene–methanol mixture to give 3.85 g of bispentafluorobenzoylmethane, mp 119°.

A similar procedure was employed in preparing other diaroylmethanes (Table II).

TABLE II

DIAROYLMETHANES

| Vinyl ester, $CH_2$=CHOOCAr Ar = | Registry no. | Yield, % | Mp of β-diketone, °C |
|---|---|---|---|
| $C_6H_5$ | 120-46-7 | 95 | 78[a] |
| 4-$ClC_6H_4$ | 18362-49-7 | 85 | 159[b] |
| 4-$CH_3C_6H_4$ | 3596-36-3 | 90 | 127[c] |
| 4-$CH_3OC_6H_4$ | 18362-51-1 | 58 | 116[b] |
| 4-$NO_2C_6H_4$ | 13586-91-9 | 98 | 241[b] |
| $C_6F_5$ | 23074-29-5 | 95 | 119[d] |

[a] F. G. Young, F. C. Frostick, Jr., J. J. Sanderson, and C. R. Hauser, *J. Amer. Chem. Soc.*, 72, 3635 (1950). [b] See ref 2. [c] A. Behal and V. Auger, *Bull. Soc. Chim. Fr.*, 9, 699 (1893). [d] See ref 4.

(5) W. J. Toussaint and L. G. McDowell, Jr., U. S. Patent 2,299,862 (1942) [*Chem. Abstr.*, **37**, 1722 (1943)]; R. L. Adelman, *J. Org. Chem.*, **14**, 1057 (1949).

(6) After the present work was completed, Rothman and Moore, *ibid.*, **35**, 2351 (1970), have shown that under similar conditions, diacylmethanes, $(RCO)_2CH_2$, where R = $C_{11}H_{23}$, $C_{15}H_{31}$, and $C_{17}H_{35}$, are obtained from vinyl alkanoates. With shorter reaction times, only β-ketoaldehydes were isolated. We have not isolated any β-ketoaldehydes in our work.

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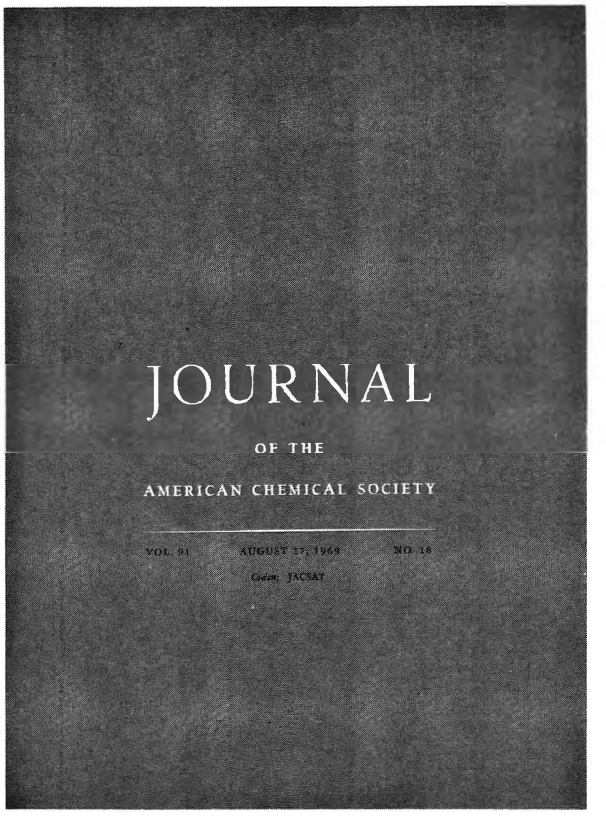


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