in vacuo. The residual solids were extracted with ether several times and the combined ether extracts were dried ($MgSO_4$) and concentrated, yielding dialkyl phosphates (**8**) which were identified as their dicyclohexyl amine salts (Table VI).

Table VI

Registry no.	$(RO)_2$-P(O)OH R =	Dicyclohexyl Amine Salt Mp, °C (solvent)	Mmp,[a] °C
34608-90-7	Et	132–134 (ligroin)	133.5–134.5
14530-43-9	*n*-Pr	131–133 (acetone)	133–134
13941-64-5	*i*-Pr	171–173 (acetone)	172–173
34638-10-3	*n*-Bu	104–105 (acetone)	106–107

[a] Preparation of the authentic samples was reported in A. F. Gasiecki, M. S. Thesis, University of Wisconsin—Milwaukee, 1970.

Registry No.—Benzene, 71-43-2; $AlCl_3$, 7446-70-0; phenylmagnesium bromide, 100-58-3.

Acknowledgment.—We gratefully acknowledge Mr. W. Mertz for his technical assistance. One of us (M. K.) would like to thank the National Science Foundation for a research fellowship during the summer of 1970 (144-A703). We wish to thank the Mobil Chemical Co., Richmond, Va., and the Hooker Chemical Corp., Niagara Falls, N. Y., for their generous samples of trialkyl phosphites, and the Signal Oil and Gas Co., Houston, Texas, and the Ethyl Corp., New York, N. Y., for samples of various alkylbenzenes used in this investigation.

Steric and Electronic Effects on the Stereochemistry of the Alkaline Hydrolysis of Acyclic Dialkoxyphosphonium Salts. Pseudorotation of Intermediates in Phosphorus Ester Reactions

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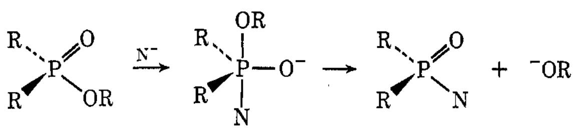
The stereochemistry of the alkaline hydrolysis of three acyclic dialkoxyphosphonium salts, (*R*)- and (*S*)-menthoxymethoxymethylphenylphosphonium hexachloroantimonate (**2**) and ethoxymethoxymethylphenylphosphonium hexachloroantimonate (**3**), was investigated and compared to the previous results obtained for the alkaline hydrolysis of (*R*)- and (*S*)-ethoxymenthoxymethylphenylphosphonium hexachloroantimonate (**1**). The extent to which the intermediate phosphorane containing one apical alkoxy group and one equatorial alkoxy group can undergo pseudorotation prior to direct loss of the apical alkoxide increases by a factor of 10 and 70 as the apical alkoxy group is varied from methoxy to ethoxy or menthoxy, respectively, but decreases by a factor of 0.6 and 0.3, respectively, as the same variation is made in the equatorial alkoxy group. Thus, depending only on the nature of the alkoxy ligands, a reaction can proceed either with predominant (>90%) direct loss of an alkoxide or predominantly by a pathway involving pseudorotation. In contrast to previous explanations, the "bulky" menthoxy group exerts no observable steric driving force to occupy the less hindered equatorial position of a phosphorane. The extension of these results to the relative stability of intermediates in nucleophilic displacement reactions of phosphorus esters is discussed.

In light of the demonstrated stability[1-3] of pentacoordinated phosphorus compounds containing alkoxy or aryloxy and carbon ligands (oxyphosphoranes[1]), analogous species containing a hydroxy ligand[4] must be considered as probable intermediates in displacement reactions at phosphorus in phosphorus esters. However, these hydroxyphosphoranes differ from the isolated aryl- or alkyloxyphosphoranes in that they have a facile route for decomposition (eq 1). Thus, at best, they would be unstable intermediates.



(1)

Several workers have obtained indirect evidence that such intermediates are formed in reactions of cyclic phosphorus esters and that they have sufficient stability to undergo pseudorotation[5] prior to or competitive with product formation. In the hydrolysis of five-membered ring phosphorus esters,[2,7] the product ratios obtained have been explained by formation of a phosphorane intermediate which may undergo pseudorotation or directly decompose to products, depending on the system. The retention of configuration[8,9] observed in the transesterification of four-membered ring esters (phosphetanes) has been credited to the formation of the cyclic phosphorane, pseudorotation, and decomposition to products. Pseudorotation has also been invoked in the hydrolysis[10] of these phosphetane esters.

In contrast to cyclic esters, there seems to be little information that reactions of acyclic esters involve intermediates of any detectable degree of stability. It has been argued[1a,2b] that acyclic oxyphosphoranes are less stable than cyclic oxyphosphoranes containing a five-membered ring; while the reverse order of stability is observed in the tetracoordinated phosphorus esters. These stability differences may imply that the

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[1] (a) F. Ramirez, *Accounts Chem. Res.*, **1**, 168 (1968); (b) F. Ramirez, *Bull. Soc. Chim. Fr.*, 3491 (1970).

[2] (a) F. H. Westheimer, *Accounts Chem. Res.*, **1**, 70 (1968), and references therein; (b) E. A. Dennis and F. H. Westheimer, *J. Amer. Chem. Soc.*, **88**, 3432 (1966).

[3] (a) D. B. Denney, D. Z. Denney, B. C. Chang, and K. L. Marsi, *ibid.*, **91**, 5243 (1969); (b) D. B. Denney and D. H. Jones, *ibid.*, **91**, 5821 (1969); (c) B. C. Chang, W. E. Conrad, D. B. Denney, D. Z. Denney, R. Edelman, R. L. Powell, and D. W. White, *ibid.*, **93**, 4004 (1971).

[4] Oxyphosphoranes containing one or more hydroxy ligands (OH or O^-) will be referred to as hydroxyphosphoranes.

[5] For the purpose of this paper, the term "pseudorotation" will refer to an intramolecular ligand exchange in phosphoranes where the two apical ligands are exchanged with two equatorial ligands; the stereochemistry being that predicted by the Berry mechanism.[6]

[6] R. S. Berry, *J. Chem. Phys.*, **32**, 933 (1960).

[7] (a) R. Kluger, F. Covitz, E. Dennis, L. D. Williams, and F. H. Westheimer, *J. Amer. Chem. Soc.*, **91**, 6066 (1969); (b) R. Kluger and F. H. Westheimer, *ibid.*, **91**, 4143 (1969).

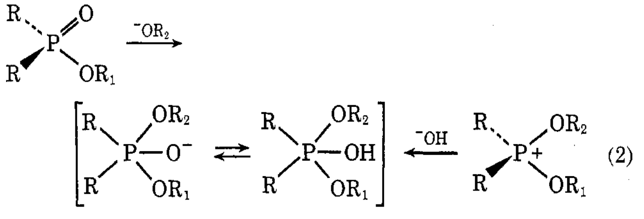
[8] S. E. Cremer and B. C. Trivedi, *ibid.*, **91**, 7200 (1969).

[9] K. E. DeBruin and J. J. Jacobs, *Chem. Commun.*, 59 (1971).

[10] B. W. Hawes and S. Trippett, *ibid.*, 578 (1968).

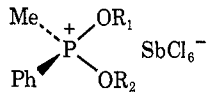
more exothermic decomposition of an acylic hydroxyphosphorane to an acyclic ester would have a relatively lower barrier for reaction, allowing pseudorotation to compete less favorably. As recently as 1968, authors[11] have argued against the existence of intermediates in nucleophilic displacements at acyclic phosphoryl[12] and thiophosphoryl[13] centers on the basis of labeling experiments. More recently, however, it has been reported that the hydrolysis of phosphonothioates[14,15] proceeds with lack of stereospecificity and may be attributed to the formation of a phosphorane intermediate with sufficient lifetime to undergo pseudorotation.

Indirect evidence that certain acyclic hydroxyphosphoranes do exist and have sufficient stability to be detected by virtue of their stereochemical nonrigidity[16] has been obtained from a study of the alkaline hydrolysis of dialkoxyphosphonium salts.[17] From a product analysis in the hydrolysis of (*R*)- and (*S*)-ethoxymenthoxymethylphenylphosphonium hexachloroantimonate, (*R*)- and (*S*)-**1**,[18] it was concluded that pseudorotation of the initially formed hydroxyphosphorane was competitive with direct loss of an alkoxy group to form the product phosphinate esters. The intermediate hydroxyphosphorane in this reaction contains the same ligands as the intermediate formed in the transesterification of a phosphinate ester (eq 2).

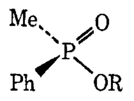


(2)

We decided to investigate the hydrolysis of two other dialkoxyphosphonium salts in order to probe the importance of factors such as steric and electronic effects on pseudorotation or decomposition barriers and to subsequently define the dividing line where pseudorotation becomes noncompetitive with product formation. The hydrolysis of dialkoxyphosphonium salts is a particularly good system for evaluating these factors, since the competition allows an evaluation of the relative energy barriers for pseudorotation *vs.* loss of alkoxide. Also, the product esters are configurationally stable to the reaction conditions. The dialkoxyphosphonium salts investigated in this paper are (*R*)- and (*S*)-menthoxymethoxymethylphenylphosphonium hexachloroantimonate, (*R*)- and (*S*)-**2**,[18] and ethoxymethoxymethylphenylphosphonium hexachloroantimonate (**3**). Phosphonium salts (*R*)- and (*S*)-**2** were chosen to determine the effect of the leaving ability of the nonbulky alkoxide and **3** was chosen to define the importance of steric effects postulated for the hydrolysis of (*R*)- and (*S*)-**1**.



(*S*)-**1**, R_1 = Et; R_2 = Men
(*R*)-**1**, R_1 = Men; R_2 = Et
(*S*)-**2**, R_1 = Me; R_2 = Men
(*R*)-**2**, R_1 = Men; R_2 = Me
(*S*)-**3**, R_1 = Me; R_2 = Et
(*R*)-**3**, R_1 = Et; R_2 = Me



(*S*)-**4**, R = Men
(*S*)-**5**, R = Me
(*S*)-**6**, R = Et

Results

Diastereomerically pure (*S*)-**2** was prepared by O-methylation of menthyl (*S*)-methylphenylphosphinate,[19] (*S*)-**4**. Reaction of (*S*)-**2** with 0.05 *M* NaOH in 50% v/v H_2O–dioxane for 1 min at room temperature afforded phosphinate ester products in greater than 80% yield. These products were identified as (*S*)- and (*R*)-**4** and (*S*)- and (*R*)-mentyl methylphenylphosphinate (**5**). Similarly, diastereomerically pure (*R*)-**2**, prepared by O-methylation of (*R*)-**4**,[19] was hydrolyzed under the same conditions to yield (*S*)- and (*R*)-**4** and (*S*)- and (*R*)-**5**. The ratio of the products from (*S*)-**2** differed from that obtained from (*R*)-**2**, indicating that stereochemical equilibration had not occurred prior to product formation.

The synthesis of (*S*)-**3** was accomplished by O-methylation of (*S*)-ethyl methylphenylphosphinate,[17] (*S*)-**6** (80% optically pure). When this sample of (*S*)-**3** was submitted to the same conditions used in the alkaline hydrolysis of (*S*)- and (*R*)-**2**, the phosphinate ester products consisted of **6** [48% optically pure with the predominance of the *R* isomer] and **5** [78% optically pure (*S*)-**5**]. It follows that optically pure (*S*)-**3** would yield (*R*)-**6** of 60% optical purity and (*S*)-**5** of 98% optical purity. Table I summarizes the results of the hydrolyses.

TABLE I

PRODUCTS OBTAINED FROM THE ALKALINE HYDROLYSIS OF DIALKOXYPHOSPHONIUM SALTS

	Yield of product, %,[a] from hydrolysis of		
Product	(*S*)-**2**	(*R*)-**2**	(*S*)-**3**[b]
(*S*)-**4**	55	32	
(*R*)-**4**	24	42	
(*S*)-**5**	21	8	37
(*R*)-**5**	0	18	1
(*S*)-**6**			12
(*R*)-**6**			50

[a] Per cent of total phosphinate ester products. Standard deviation of five determinations *ca.* 2%. Corrected for differential hydrolysis. [b] Corrected to optically pure phosphonium salt.

Under the reaction conditions for alkaline hydrolysis of the phosphonium salts, **2** and **3**, the product esters are partially hydrolyzed further to methylphenylphosphinic acid. A differential rate of hydrolysis changes the mole ratios of these products. The observed product ratios were corrected for this effect by submitting a known mixture of two phosphinate esters (A and B) to the same conditions used in the alkaline hydrolysis of the phosphonium salts and observing the ratio of

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[11] M. J. Gallagher and I. D. Jenkins in "Topics in Stereochemistry," Vol. III, E. L. Eliel and N. L. Allinger, Ed., Interscience, New York, N. Y., 1968, p 31.

[12] M. Green and R. F. Hudson, *Proc. Chem. Soc.*, 307 (1962).

[13] J. Michalski, M. Mikolajczyk, A. Halpern, and K. Proszynska, *Tetrahedron Lett.*, 1919 (1966).

[14] J. Michalski, M. Mikolajczyk, and J. Omelanczuk, *ibid.*, 3565 (1968).

[15] L. P. Reiff, L. J. Szafraniec, and H. S. Aaron, *Chem. Commun.*, 366 (1971).

[16] K. Mislow, *Accounts Chem. Res.*, **3**, 321 (1970).

[17] K. E. DeBruin and K. Mislow, *J. Amer. Chem. Soc.*, **91**, 7393 (1969).

[18] Configurational notation (*R*) and (*S*) refer to chirality at phosphorus. The menthoxy group is derived from (−)-menthol (MenOH).

[19] O. Korpiun, R. A. Lewis, J. Chickos, and K. Mislow, *J. Amer. Chem. Soc.*, **90**, 4842 (1968).

the two esters as a function of time. The difference in the pseudo-first-order rate constants ($k_A - k_B$) was obtained by eq 3, where A_t and B_t represent the

$$\ln\left(\frac{A_t B_0}{A_0 B_t}\right) = -(k_A - k_B)t \qquad (3)$$

concentration of esters A and B at time t, respectively. Thus, under the reaction time of 1 min for the hydrolysis of the phosphonium salts, (*S*)- and (*R*)-**2** and **3**, the product ratio of the two esters, **4** and **5** from **2** or **5** and **6** from **3**, deviates from the true product ratio by the exponential term in eq 4. Table II summarizes

$$\frac{A_0}{B_0} = \frac{A_t}{B_t}e^{+(k_A - k_B)t} \qquad (4)$$

Table II

Differential Hydrolysis Rates of Phosphinate Esters[a] at 25°

Ester A	Ester B	[NaOH], M	$k_A - k_B$, sec^{-1}	$e^{+(k_A-k_B)60}$
6	**4**	0.5[b]	1.6×10^{-3}	1.10 (0.010)[c]
6	**4**	0.05	1.6×10^{-4}	1.01 (0.001)
5	**4**	0.05	1.4×10^{-3}	1.09 (0.009)
5	**6**	0.05	1.2×10^{-3}	1.07 (0.007)
5	**6**	0.5	1.3×10^{-2}	2.18 (0.140)

[a] 50% v/v aqueous dioxane. Pseudo-first-order rate constants. Standard deviation of three determinations is ±5%. [b] Reference 17. [c] Error in parentheses.

the results of this study. As previously pointed out,[17] (*S*)-**4** and (*R*)-**4** are either hydrolyxed at the same state or not hydrolyzed under the reaction time. The results in Table I are corrected for any differential hydrolysis which may have occurred.

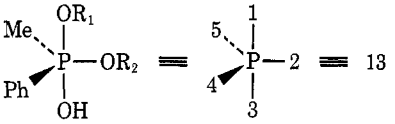
Haake and coworkers[20] have observed, under slightly different conditions, that the methyl ester of diphenylphosphinic acid or diethylphosphinic acid is hydrolyzed about ten times faster than the ethyl ester and from 100 to 300 times faster than the isopropyl ester. Thus, to a first approximation, the difference in rate constants (Table II, $k_A - k_B$) is equal to the rate constant for the hydrolysis of A. Our results are consistent with those of Haake.[20]

The hydrolyses of (*R*)- and (*S*)-**1** were previously carried out[17] using 0.5 M NaOH in 50% v/v H_2O–dioxane. As Table II shows, only a 10% correction is needed to account for any differential hydrolysis of the product esters, **6** and **4**. However, this base concentration results in a substantial hydrolysis of the methyl phosphinate, **5**. The lower base concentration of 0.05 M NaOH was used in the above hydrolyses to minimize the error resulting from correcting for a differential hydrolysis rate. Since a direct comparison of the product ratios from the respective hydrolyses is desired, the hydrolysis of (*S*)- and (*R*)-**1** was repeated using 0.05 M NaOH. Within error, the same product ratios were obtained, after correction, as were previously reported[17] for the hydrolysis in 0.5 M NaOH.

Discussion

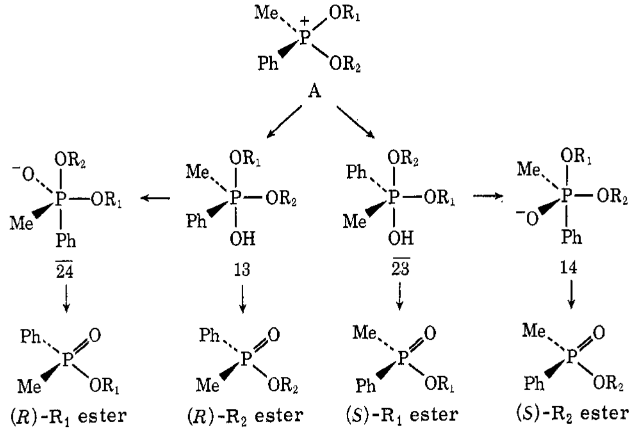
The alkaline hydrolysis of acyclic alkoxyphosphonium salts has been shown[17] to proceed, in general, by attack of hydroxide on phosphorus with resultant cleavage of a P–O bond and loss of alkoxide. In the case of unsymmetrical dialkoxyphosphonium salts, two phosphinate esters can be formed from cleavage of either alkoxy group. For the three chiral acyclic dialkoxyphosphonium salts studied in this paper, (*R*)-**2**, (*S*)-**2**, and **3**, as well as the two previously studied,[17] (*R*)-**1** and (*S*)-**1**, this hydrolysis proceeds with varying lack of stereospecificity. Presumably, attack of hydroxide ion on the dialkoxyphosphonium salt forms a hydroxyphosphorane which has sufficient lifetime to undergo pseudorotation prior to or competitive with loss of alkoxide to form products. Since each phosphonium salt yields products of different degrees of loss of stereospecificity, pseudorotation can be only competitive with product formation. From a product analysis, steric and electronic effects on this competition are obtainable as discussed below.

Phosphoranes and Pseudorotations.—In an earlier paper,[17] the general scheme for the alkaline hydrolysis of a dialkoxyphosphonium salt was developed. For the present discussion, the ligands of the phosphorane intermediates will be numbered as indicated by the equality below. The respective isomers will be noted by a two-digit number referring to the apical ligands of the phosphorane.[21]



Since the preferred mode of reaction of hydroxide on a phosphonium salt is assumed to involve apical attack,[2,16,21] the initially formed phosphoranes from attack on a dialkoxyphosphonium salt of the general structure A would be 13 and $\overline{23}$ (Scheme I). These

Scheme I



phosphoranes can either directly lose the apical alkoxy group (OR_1 from 13 and OR_2 from $\overline{23}$) or undergo pseudorotation by the lowest energy pathway to $\overline{24}$ and 14, respectively.[22] Thus, the general scheme for

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[20] (a) P. Haake, C. E. Diebert, and R. S. Marmor, *Tetrahedron Lett.*, 5247 (1968); (b) P. Haake, R. D. Cook, W. Schwarz, and R. R. McCoy, *ibid.*, 5251 (1968).

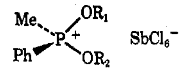
[21] K. E. DeBruin, K. Naumann, G. Zon, and K. Mislow, *J. Amer. Chem. Soc.*, **91**, 7031 (1969).

[22] Pseudorotations of 13 and $\overline{23}$ to $\overline{24}$ and 14, respectively, is assumed to be of lower energy than pseudorotations to 25 and $\overline{15}$, since the former have the more electronegative phenyl group in an apical position.[2,16,23] Even if these energetics were reversed, the conclusions in this paper would hold. Further pseudorotations are assumed to be insignificant, since the first pseudorotation is only competitive with direct loss of alkoxide and additional pseudorotations would require the formation of less stable phosphoranes.[17]

[23] E. L. Muetterties and R. A. Schunn, *Quart. Rev., Chem. Soc.*, **20**, 245 (1966).

TABLE III

PRODUCTS FROM THE ALKALINE HYDROLYSIS OF DIALKOXYPHOSPHONIUM SALTS



			Products						
			R₁ Ester		R₂ Ester				
R₁	R₂	Confn	(*R*)	(*S*)	(*R*)	(*S*)	$\frac{(R)\text{-R}_1}{(R)\text{-R}_2}$	$\frac{(S)\text{-R}_2}{(S)\text{-R}_1}$	(*R*)/(*S*)
Me	Et	(*S*)-**3**	1	37	50	12	0.02 (0.04)[a]	0.33 (0.05)	1.0 (0.2)
Et	Me	(*R*)-**3**[b]	12	50	37	1	0.33 (0.05)	0.02 (0.04)	1.0 (0.2)
Me	Men	(*S*)-**2**	0	21	24	55	(0)	2.6 (0.4)	0.3 (0.1)
Men	Me	(*R*)-**2**	42	32	18	8	2.3 (0.4)	0.25 (0.05)	1.5 (0.3)
Et	Men	(*S*)-**1**[c]	2	38	20	40	0.1 (0.1)	1.0 (0.2)	0.3 (0.05)
Men	Et	(*R*)-**1**[c]	39	27	26	8	1.5 (0.2)	0.3 (0.1)	1.8 (0.4)

[a] Error estimates in parentheses based on a standard deviation of 2% in the product percentages. [b] Calculated assuming enantiomers have identical energies in an achiral medium. [c] Reference 18.

the hydrolysis of dialkoxyphosphonium salts is shown in Scheme I.

The observation of (*R*)-R$_1$ ester and (*S*)-R$_2$ ester in the hydrolysis of phosphonium salts **2** and **3** (Table I) requires pseudorotation of the initially formed phosphoranes if loss of alkoxide proceeds from an apical position. Thus, the amount of either of these esters will reflect the fraction of the initially formed phosphorane which does not directly lose an alkoxy group, *i.e.*, the degree to which pseudorotation followed by loss of alkoxide competes with direct decomposition. It would be useful, for predictive reasons, to know the nature of the hydroxy ligand (*e.g.*, OH or O$^-$) in the initially formed phosphoranes, 13 and $\overline{23}$, as well as phosphoranes 14 and $\overline{24}$ and the energy surface connecting them. Westheimer and coworkers[7] have estimated the pK_a of a hydroxyphosphorane containing only oxygens attached to phosphorus to be *ca.* 9 by the empirical method of Branch and Calvin.[24] This value was consistent with a pH profile plot in their product analysis of the hydrolysis of a cyclic phosphate ester. A similar estimate of the pK_a of a phosphorane containing a phenyl and a methyl ligand such as in 13 or $\overline{23}$ would be *ca.* 12, which is in the region of the base concentration used in the above hydrolysis of the phosphonium salts (0.05 *M* NaOH in 50% aqueous dioxane). This empirical equation does not account for any differences in the pK_a of a phosphorane containing the hydroxy group in an apical *vs.* an equatorial position. Although some difference is expected, the magnitude is unknown. For the present discussion, we will assume that the OH group is in the form which satisfies the electronic requirement[2,23] of its position in the trigonal bipyramidal phosphorane, OH in the apical position and O$^-$ in the equatorial position. The formal mechanism for conversion of a phosphorane containing an apical OH ligand (*e.g.*, 13) to a phosphorane containing an equatorial O$^-$ ligand (*e.g.*, $\overline{24}$) may either involve a two-step process with ionization prior to or following pseudorotation or a general base catalyzed reaction involving simultaneous proton abstraction and pseudorotation. No information exists on this question; however, if proton transfers are much faster than pseudorotation, the latter mechanism would be more likely since these transfers will be occurring as the energy pathway for pseudorotation is being traversed.

Steric Constraints on Phosphorane Formation.—The products from the hydrolysis of the dialkoxyphosphonium salts investigated in this paper, (*R*)- and (*S*)-**2** and **3**, are listed in generalized form in Table III, along with the previous results for (*R*)- and (*S*)-**1**. That there exists a steric effect on the transition state for formation of the initially formed hydroxyphosphoranes 13 and $\overline{23}$ can be substantiated by contrasting the *R* to *S* product ratio obtained from **1** and **2** to that obtained from **3** (see the last column in Table III). As shown in Scheme I, *R* products can only arise from 13, the hydroxyphosphorane resulting from attack of hydroxide in the face of the tetrahedral phosphonium salt opposite the OR$_1$ ligand, while the *S* products can only originate from attack opposite ligand OR$_2$ with formation of $\overline{23}$. The ratio *R*/*S* is greater than 1 when R$_1$ is a menthyl group, whereas this ratio is less than 1 when R$_2$ is the menthyl group.[25] In contrast, when the alkoxy groups are methoxy and ethoxy (**3**), the amount of products arising from the two pathways is similar. Clearly, the bulky menthoxy group influences the partitioning between the two pathways. The magnitude of this steric effect, however, is small, ranging from a 1.5- to a 3-fold preference for attack opposite a menthoxy group, compared to attack opposite a primary alkyl group.

The similar ratios of *R*/*S* from **2** and **1** require the rate-limiting steps for formation of *R* products and *S* products, respectively, to be relatively insensitve to a change in OR$_1$ (or OR$_2$) from methoxy to ethoxy. Of the various possibilities, phosphorane formation from the phosphonium salt is the most consistent with this observation. Although loss of an alkoxy group from the hydroxyphosphorane (13 or $\overline{23}$) to form a hydroxyphosphonium salt should not differ greatly in energetics from loss of hydroxide to return to staring phosphonium salt, an alternate pathway involving the simultaneous abstraction of the proton with loss of the alkoxy group and formation of the P=O bond may be of lower energy. If this were the case, attack of hydroxide would be the rate-limiting step and the observed effect of the menthoxy group is a steric hindrance to approach of the attacking hydroxide.[26]

Steric and Electronic Effects on Pseudorotations and Product Formation.—From Table III, direct information on the degree of pseudorotation *vs.* loss of alkoxide of the initially formed phosphoranes 13 and $\overline{23}$ can be obtained by examining the product distribution. Since

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[24] G. E. Branch and M. Calvin, "The Theory of Organic Chemistry," Prentice-Hall, New York, N. Y., 1941, p 204.

[25] That these ratios from (*S*)-**2** *vs.* (*R*)-**2** or from (*S*)-**1** *vs.* (*R*)-**1** are not the exact inverse of each other has its origin in the chiral menthoxy group. In both cases, the phosphonium salt with the (*S*) configuration at phosphorus has the greater hindrance for approach of hydroxide.

[26] At present, we have been unable to develop conditions for kinetic measurements to test this postulate.

(*R*)-R_1 ester can only result after one pseudorotation of 13, a comparison of the product ratio, (*R*)-R_1 to (*R*)-R_2 ester, reflects the relative rates of pseudorotation compared to alkoxide loss to form products. Similarily, the ratio of (*S*)-R_2 to (*S*)-R_1 ester represents the competition from $\overline{23}$. These ratios are given in Table III. In Table IV,[27] the results are tabulated in a form which facilitates the discussion of factors influencing the competition between the two possible pathways for product formation from 13. The relative ratios in the last column and in the bottom row represent the relative competition between formation of (*R*)-R_1 *vs.* (*R*)-R_2 from 13 as a function of a change in R_1 or R_2, respectively.

Table IV

Effect of the Alkoxy Ligands on the Products Derived from 13

13, R_1	(*R*)-R_1/(*R*)-R_2[a]			Rel ratio[b]
	R_2 = Me	R_2 = Et	R_2 = Men	
Me		0.02	(0)	1.0
Et	0.33		0.1	10
Men	2.3	1.5		70
Rel ratio[b]	1.0	0.6	0.3	

[a] See Table III. [b] See text for definition.

Three factors can be postulated to have an influence on the product ratios obtained: (1) the leaving ability of the alkoxide group; (2) electronic effects on the alkoxy ligand which remains attached to phosphorus in the product on the decomposition rates; and (3) steric and electronic effects on pseudorotation rates.

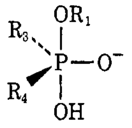
For any given R_2 group, the relative amount of product ((*R*)-R_2) resulting from direct loss of alkoxide (OR_1) decreases as R_1 is changed from methyl to ethyl to menthyl (the ratio of (*R*)-R_1 ester to (*R*)-R_2 ester increases from 1 to 10 to 70). In contrast, when R_1 is constant and R_2 is varied, the reverse order is observed (from 1 to 0.6 to 0.3). The relative order and magnitude in each of these two series is consistent with an inductive effect on the decomposition of 13 to (*R*)-R_2 ester. In the transition state for this reaction, the positive charge on phosphorus is increasing with a corresponding negative charge developing on the alkoxy leaving group. As might be expected, the effect of substituents in the leaving group is greater than that in the remaining alkoxy group. For this system, when the leaving group is methoxide, pseudorotation is virtually noncompetitive with direct decomposition.

Although steric factors were originally proposed to influence the barriers for pseudorotations in these systems,[17] the above order of reactivity does not require this hypothesis. If the "bulky" menthoxy group preferred to occupy an equatorial position, an abnormally low value (*R*)-R_1 ester/(*R*)-R_2 ester would be expected when R_2 is menthyl, while this ratio should be abnormally high when R_1 is menthyl. This behavior is not observed and suggests that the bulk of the menthyl group is sufficiently removed from the crowded phosphorus to exhibit little positional preference around the hydroxyphosphorane. Steric effects on pseudorotational barriers have nicely explained the chemistry of several systems[17,28,29] where a *tert*-butyl group is directly attached to phosphorus; however, in those cases, the crowding around phosphorus would be much more severe.

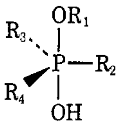
An alternate explanation for the above suggested lack of steric constraints on pseudorotational barriers is that both pseudorotation and decomposition barriers are affected to the same amount and therefore, not detectable by this study. Loss of alkoxide from 13 should be accelerated due to relief of strain when a menthoxy group is the leaving group (R_1) as well as when the menthoxy group is equatorial (R_2). Pseudorotations should be accelerated when the menthoxy group is apical and slowed down when it is equatorial. Thus, the steric effect may be nonobservable when R_1 is menthyl but should be magnified when R_2 is menthyl. Since this behavior is not observed, steric effects on positional preferences by a menthoxy group on a phosphorane must be small.

In summary, the fate of a phosphorane such as 13 in terms of its ability to undergo psuedorotation competitively with direct loss of an alkoxide group is determined primarily by the leaving ability of the alkoxide and, to a lesser extent, by electronic effects of the ligands which remain attached to the phosphorus. In the above system, when methoxide is the leaving group, pseudorotation is virtually noncompetitive. Also, in order for a bulky ligand to originate conformational preferences in a phosphorane, as measured by relative rates of pseudorotation, the bulk of the ligand must, apparently, be similar to that of a *tert*-butyl group.

Pseudorotation in Reactions of Phosphorus Esters.— If one assumes that nucleophilic displacement reactions at phosphorus in acyclic phosphorus esters proceed through the intermediacy of a phosphorane, and that axial attack is preferred over equatorial attack, the initially formed phosphorane would have the nucleophile and the most electronegative group in the apical positions. In alkaline hydrolyses, the hydroxyphosphoranes would have the general structure B. An analogous intermediate (C) would be formed in the alkaline hydrolysis of alkoxyphosphonium salts, the difference being only in the replacement of the electropositive oxy ligand (O^-) by an electropositive alkyl or aryl group (R_2). Granted that the transition state for loss of alkoxide may be stabilized by resonance when the phosphorane contains the oxy ligand compared to an alkyl or aryl ligand, the degree to which an initially formed phosphorane may undergo pseudorotation is at a maximum in the hydrolysis of alkoxyphosphonium salts, other things being equal.



B



C

It has been shown[30] that the alkaline hydrolysis of an acylic monoalkoxyphosphonium salt, ethoxymethyl-

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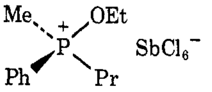
[27] Table IV and future discussion will be concerned only with the products derived from 13. The transition state for loss of alkoxide (OR_1) from 13 (R_2 = menthyl) has the same relative configuration of phosphorus and the menthyl group as the transition state for attack of hydroxide on (*R*)-**1** or (*R*)-**2**, the diastereomers which gave the least steric hindrance for formation of the phosphorane. Thus, steric constraints on decomposition are minimized.

[28] A. P. Stewart and S. Trippett, *Chem. Commun.*, 1279 (1970).

[29] D. Z. Denney, D. W. White, and D. B. Denney, *J. Amer. Chem. Soc.*, **93**, 2066 (1971).

[30] G. Zon, K. E. DeBruin, K. Naumann, and K. Mislow, *ibid.*, **91**, 7023 (1969).

phenylpropylphosphonium hexachloroantimonate (**7**), proceeds stereospecifically with inversion of configuration. Any pseudorotation of the initially formed phosphorane (C, R_2 = Pr; R_3 = Me; R_4 = Ph) requires exchanging the apical hydroxy and alkoxy groups for two electropositive groups, a process noncompetitive with direct loss of an alkoxide. Extension of this argument to the hydrolysis of an acyclic phosphinate ester (*e.g.*, ethyl methylphenylphosphinate, **8**), would predict that no pseudorotation of the intermediate phosphorane (B, R_3 = Me; R_4 = Ph) would occur prior to product formation. The absence of any ^{18}O exchange into the phosphoryl oxygen of recovered starting material[20] when the hydrolysis is carried out in $H_2{}^{18}O$ is consistent with this prediction in that the phosphoryl oxygen and the hydroxide oxygen cannot assume identical environments if pseudorotation is blocked.



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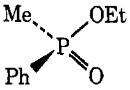

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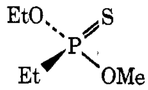

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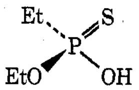

10

A similar extension of the results in this paper to the hydrolysis of acyclic phosphonate esters would suggest that pseudorotation of the initially formed phosphorane would only be competitive with loss of alkoxide when the leaving group is poorer than methoxide. The stereochemistry of the alkaline hydrolysis of a phosphonothioate, *O*-ethyl *O*-methylethylphosphonothioate (**9**) to *O*-ethylethylphosphonothioic acid (**10**) has been shown[14] to proceed with 85% inversion of configuration. Although labeling experiments were not carried out, the observed stereochemistry was postulated to result from partial C–O bond cleavage.

An alternative explanation would involve competitive formation of two hydroxyphosphoranes with either the methoxy ligand or the ethoxy ligand in the apical position. Direct loss of methoxide from the former and pseudorotation followed by loss of methoxide from the latter would result in the formation of **10** with inversion and retention, respectively. The stereospecificity of the hydrolysis would then be determined by the relative energies of the two pathways. Our results above would indicate that this alternative explanation is indeed possible.

In general, the results of this paper would indicate that nucleophilic displacements of alkoxide in acyclic phosphinate and phosphonate esters by a nucleophile of similar or greater electronegativity, when bonded to phosphorus, than hydroxide (*e.g.*, alkoxide in transesterification reactions) should proceed with little if any pseudorotation of the initially formed phosphorane. Further studies are underway to test the limits of this generalization.

Experimental Section[31]

Synthesis of Dialkoxyphosphonium Hexachloroantimonates. A. (*S*)-Menthoxymethoxymethylphenylphosphonium Hexachloroantimonate [(*S*)-**2**].—A solution of diastereomerically pure menthyl (*S*)-methylphenylphosphinate, (*S*)-**4** (500 mg, 1.7 mmol), $[\alpha]_D$ −95°, in dichloromethane (10 ml) was added to a heterogenous mixture of trimethyloxonium hexachloroantimonate[32] (600 mg, 1.6 mmol) in dichloromethane (20 ml). The mixture was stirred at room temperature until the solution became homogeneous (15 min) and then stirred for an additional 1 hr. Concentration of the solution under vacuum to 5 ml, followed by addition of this residue to anhydrous ether (100 ml), produced a white, crystalline material (970 mg, 95%), mp 102–103° dec, $[\alpha]_D$ −32° (*c* 3.77, CH_2Cl_2). The pmr spectrum of this material was consistent with that expected for diastereomerically pure (*S*)-**2**, and featured PCH_3 (d, 2.49 δ, J_{PCH} = 14 Hz), $POCH_3$ (d, 4.22 δ, J_{POCH} = 12 Hz).

Anal. Calcd for $C_{18}H_{30}PO_2SbCl_6$: C, 33.58; H, 4.70. Found: C, 33.69; H, 4.67.

B. (*R*)-Menthoxymethoxymethylphenylphosphonium Hexachloroantimonate [(*R*)-**2**].—The synthesis of (*R*)-**2** from diastereomerically pure (*R*)-**4**, $[\alpha]_D$ −17°, was similar to that of (*S*)-**2**, mp 90–92° (800 mg, 78%). The pmr spectrum of this material featured PCH_3 (d, 2.47 δ, J_{PCH} = 14 Hz), $POCH_3$ (d, 4.07 δ, J_{POCH} = 12 Hz). By analysis of the $POCH_3$ region of the pmr spectrum, (*R*)-**2** was found to be diastereomerically pure.

C. (*S*)-Ethoxymethoxymethylphenylphosphonium Hexachloroantimonate [(*S*)-**3**].—A solution of (*S*)-ethyl methylphenylphosphinate [(*S*)-**6**] (1.0 g, 5.4 mmol), $[\alpha]_D$ −36° (80% optically pure) in dichloromethane (10 ml) was added to a heterogeneous mixture of trimethyloxonium hexachloroantimonate (2.1 g, 5.4 mmol) in dichloromethane (20 ml) and stirred at room temperature for 4 hr. After 1 hr, the solution was homogeneous. Addition of this solution to anhydrous ether (100 ml) produced a white, crystalline material which was identified as (*S*)-ethoxymethoxymethylphenylphosphonium hexachloroantimonate [(*S*)-**3**] (2.5 g, 86%), mp 104–106° dec. The pmr spectrum (CH_2Cl_2) of this material featured PCH_3 (d, 2.30 δ, J_{PCH} = 14 Hz), $POCH_3$ (d, 4.07 δ, J_{POCH} = 12 Hz), $POCH_2CH_3$ (apparent quintet, 4.42 δ, J_{POCH} = 7 Hz), $POCH_2\mathbf{CH_3}$ (t, 1.47 δ, J_{HCCH} = 7 Hz).

Anal. Calcd for $C_{10}H_{16}PO_2SbCl_6$: C, 22.51; H, 3.02; P, 5.80. Found: C, 22.89; H, 3.25; P, 5.72.

Hydrolysis of Dialkoxyphosphonium Hexachloroantimonates. A. (*S*)- and (*R*)-Menthoxymethoxymethylphenylphosphonium Hexachloroantimonates [(*S*)- **and** (*R*)-**2**].—The hydrolyses of (*S*)-**2** and (*R*)-**2** were carried out by the identical procedure used in the hydrolysis of (*S*)-**1** and (*R*)-**1**[17] except that 0.05 *M* NaOH was used instead of 0.5 *M* NaOH. A solution (100 ml) of 0.05 *M* NaOH in 50% v/v aqueous dioxane was added to a solution of either (*S*)-**2** or (*R*)-**2** (300 mg, 5 mmol) in dioxane (0.5 ml), and the heterogeneous mixture was stirred for 1 min. The reaction mixture was extracted with dichloromethane and the combined organic layers were dried (magnesium sulfate). Removal of solvent under reduced pressure gave a mixture of (*S*)- and (*R*)-**4**, methyl methylphenylphosphinate (**5**), and *l*-menthol. The total products (*ca.* 100 mg) from the hydrolysis of (*S*)-**2** or (*R*)-**2** were analyzed as follows.

The PCH_3 group in each of the three products from hydrolysis of **2** [(*S*)-**4**, (*R*)-**4**, and **5**] has a characteristic signal in the pmr spectrum: (*S*)-**4**, 1.66 δ, J_{PCH} = 14.5 Hz; (*R*)-**4**, 1.62 δ, J_{PCH} = 14.5 Hz; and **5**, 1.63 δ, J_{PCH} = 14.5 Hz. The proportions of the three compounds were estimated by comparing peak heights of the upfield half of each doublet. The relative amounts of **4** and **5** were estimated by glpc analysis (6 ft, SE-30, 200°) of the crude mixture of products from the hydrolysis of (*S*)-**2** and (*R*)-**2**, and compared to the pmr results.

Pure samples of **4** and **5** were obtained by collection from a gas chromatograph. The entire peak corresponding to each compound was collected. The ratio thus obtained agreed well (within 2%) with that determined on the crude mixture.

The optical purity and absolute configuration of **5** was established by its conversion to methyl-β-naphthylphenylphosphine oxide (**7**) with β-naphthylmagnesium bromide.[17] A sample of **5**, $[\alpha]_D$ −21° yielded (*S*)-**7**, $[\alpha]_D$ +11° (chloroform). Thus, this sample of **5** was 40% optically pure based on the highest reported rotation of **7**, with a predominance of the *S* isomer, granted that the Grignard reaction proceeded with complete retention of configuration.[19] It follows that optically pure **5** would have an absolute rotation of 52°. The hydrolysis of diastereomerically

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[31] Elemental analyses were performed by Schwarzkopf Microanalytical Laboratories, Woodside, N. Y. Pmr spectra were recorded on a Varian A-60A spectrometer and refer to *ca.* 10% solution in deuteriochloroform, with tetramethylsilane as internal standard. Chemical shifts are reported in parts per million from TMS. Optical rotations were measured on a PE-141 polarimeter and refer to solvent benzene (*c* 1–3 g/100 ml), except as noted.

[32] H. Meerwein, E. Battenberg, H. Gold, E. Pfeil, and G. Willfang, *J. Prakt. Chem.*, **154**, 83 (1939).

pure (*S*)-**2** gave **5**, $[\alpha]_D$ −52° which would correspond to optically pure **5** of the *S* configuration.

The sample of **5**, $[\alpha]_D$ +19.7°, obtained from hydrolysis of (*R*)-**2** is therefore 38% optically pure with the predominance of the *R* isomer.

B. (*S*)-Ethoxymethoxymethylphenylphosphonium Hexachloroantimonate [(*S*)-3].—The hydrolysis of (*S*)-**3** (80% optically pure) was carried out by the identical procedure used for the hydrolysis of (*S*)- and (*R*)-**2**. A mixture of methyl methylphenylphosphinate (**5**) and ethyl methylphenylphosphinate (**6**) was obtained and analyzed by pmr and glpc for relative amounts. The two phosphinate esters, **5** and **6**, were separated by glpc (6 ft, SE-30, 150°) to give **5**, $[\alpha]_D$ −40° (77% optically pure), and **6**, $[\alpha]_D$ +22° (48% optically pure[17]). Thus, optically pure (*S*)-**3** would give, upon hydrolysis, a ratio of (*S*)-**5** to (*R*)-**5** of 98:2 and a ratio of (*S*)-**6** to (*R*)-**6** of 20:80.

Control Experiments.—That the phosphinate ester products are configurationally stable under the reaction conditions for hydrolysis was shown by submitting a sample of each to these exact conditions. Recovery of unreacted ester after 5 min yielded a product of unchanged stereochemistry.

The product ratios obtained from the hydrolyses of the dialkoxyphosphonium salts were corrected for the differential rate of hydrolysis of the various esters by the following procedure. A mixture of two phosphinate esters (A and B) of known mole per cent ratio was submitted to the conditions of the hydrolyses of the phosphonium salt. Aliquots were taken and quenched by extracting with dichloromethane and the recovered mixture of the two esters was analyzed by pmr. A plot of ln [A/B] against time yielded a slope ($k_A - k_B$, assuming pseudo-first-order kinetics). Table II contains the results of this study.

Registry No.—**2**, 34630-90-5; (*S*)-**3**, 34630-91-6; (*R*)-**3**, 34630-92-7; **4**, 34638-63-6; (*S*)-**5**, 34647-06-8; (*R*)-**5**, 34647-07-9; (*S*)-**6**, 33642-98-7; (*R*)-**7**, 34638-79-4; (*S*)-**7**, 34630-93-8.

Acknowledgment.—We are indebted to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

Three-Membered Rings. III.[1a] Ultraviolet Spectral Evidence of a Stereochemical Bias in Rigid *p*-Nitrophenylcyclopropanes[1b]

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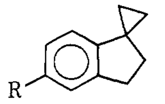
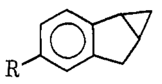
A study of the uv spectra of a series of conformatially rigid *p*-nitrophenylcyclopropanes and the parent hydrocarbons demonstrates the existence of a slight stereochemical bias for electronic interaction between the cyclopropyl group and the nitrobenzene or benzene chromophore. In the series studied, the orientation of the cyclopropane ring deviates from the bisected geometry from 0 to 90°.

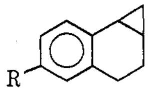
The ability of the para-enriched carbon–carbon orbitals of cyclopropane to conjugate with neighboring unsaturated systems has been demonstrated.[2-4] Several recent studies have dealt with the effects of the cyclopropyl substituent on the electronic spectra of π systems.[5-8] Goodman and Eastman[7] studied the uv spectra of a series of rigid phenylcyclopropanes (**1–3**) in order to ascertain the preferred geometry for expression of olefinic character. On the basis of small spectral variations, they concluded that there is no preferred geometry for conjugation of a cyclopropane ring with a phenyl nucleus. Strait, *et al.*,[9] have demonstrated the usefulness of the nitrobenzene chromophore in evaluating the electronic properties of three-membered rings. Hahn and coworkers[8] extended the study of Goodman and Eastman[7] by including **4** and **5** and in addition studied the para-nitro derivatives (**1′–5′**), and concluded that conjugation in cyclopropyl aromatic systems is a detectable function of cyclopropane geometry if the interacting chromophore is sufficiently electron attracting.



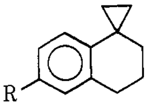
1,1′
$\theta = 0°$



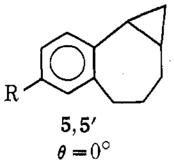
2,2′
$\theta = 25°$



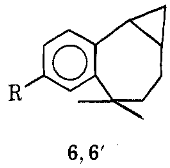
3,3′
$\theta = 10°$



4,4′
$\theta = 10°$



5,5′
$\theta = 0°$
$\theta = 90°$



6,6′
$\theta = 90°$

1–6, R = H
1′–6′, R = NO_2
θ = Deviation in degrees from bisected geometry

According to Bernett,[10] total overlap between the sp^5 bent bonds of the cyclopropane ring and an adjacent p orbital decrease only slightly for deviations up to 39° (Figure 1B) from the optimum geometry (Figure 1A) and thereafter decreases more rapidly to a minimum at 90° (Figure 1C).

Compound **5** and its nitration products are the most crucial in their study[8] because they represent the only compounds having a large deviation ($\theta = 90°$) from optimum geometry. There are two conformations of **5**; the sterically preferred conformation has the least preferred geometry for orbital overlap ($\theta = 90°$), whereas the sterically less preferred conformation has the optimum geometry for overlap ($\theta = 0°$). It

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(1) (a) Paper II: L. A. Strait, D. Jambotkar, R. Ketcham, and M. Hrenoff, *J. Org. Chem.*, **31**, 3976 (1966). (b) Taken in part from the Ph.D. Thesis of L. C. M. Presented, in part, at the 156th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept. 12, 1968. (c) U. S. Public Health Service Predoctoral Trainee.

(2) N. N. Kizhner, *Zh. Russ. Fiz.-Khim. Obshchest.*, **47**, 1102 (1915).

(3) M. T. Rogers, *J. Amer. Chem. Soc.*, **69**, 2544 (1947).

(4) H. C. Brown and J. D. Cleveland, *ibid.*, **88**, 2051 (1966).

(5) E. M. Kosower and M. Ito, *Proc. Chem. Soc.*, 25 (1962).

(6) W. G. Dauben and G. H. Berezin, *J. Amer. Chem. Soc.*, **89**, 3449 (1967).

(7) A. L. Goodman and R. H. Eastman, *ibid.*, **86**, 908 (1964).

(8) R. C. Hahn, P. H. Howard, S. Kong, G. A. Lorenzo, and N. L. Miller, *ibid.*, **91**, 3558 (1969).

(9) L. A. Strait, R. Ketcham, D. Jambotkar, and V. P. Shah, *ibid.*, **86**, 4628 (1964).

(10) W. A. Bernett, *J. Chem. Educ.*, **44**, 17 (1967). (Figure 1 is taken from this reference.)