90°). The ether concentration was increased gradually during elution. The major oxide, *trans*-2-dimethylamino-5-*tert*-butyl-2-oxo-1,3,2-dioxaphosphorinane (**3a**), was recrystallized from ether–ligroin (60–90°): mp 114.5–115.0°; ir (KBr) 2959, 2907, 2825, 1473, 1330, 1239, 1143, 1058, 1011, 898, 814, and 702 cm^{-1}; pmr ($CDCl_3$) δ 0.960 (9 H, singlet, *t*-Bu), 1.97 (1 H, multiplet, methine H), 2.71 (6 H doublet, J_{HP} = 10.0 Hz, Me_2N), and 4.09–4.57 (4 H, multiplet, CH_2O).

Anal. Calcd for $C_9H_{20}O_3PN$: C, 48.86; H, 9.11; P, 14.00. Found: C, 48.73; H, 9.38; P, 14.50.

The minor oxide, *cis*-2-dimethylamino-5-*tert*-butyl-2-oxo-1,3,2-dioxaphosphorinane (**3b**), was recrystallized from ether–ligroin (60–90°): mp 117.5–118.0°; ir (KBr) 2967, 2915, 2825, 1486, 1460, 1374, 1309, 1261, 1181, 1140, 1081, 1054, 1012, 991, 893, 848, 814, 784, and 680 cm^{-1}; pmr ($CDCl_3$) δ 0.955 (9 H, singlet, *t*-Bu), 2.23 (1 H, multiplet, methine H), 2.68 (6 H, doublet, J_{PH} = 10.6 Hz, Me_2N), and 3.98–4.58 ppm (4 H, multiplet, CH_2O).

Anal. Calcd for $C_9H_{20}O_3PN$: C, 48.86; H, 9.11; P, 14.00. Found: C, 49.06; H, 8.91; P, 14.00.

Synthesis of 2-Methylamino-5-*tert*-butyl-1,3,2-dioxaphosphorinane (4). Anhydrous ether (25 ml) was added to a 100-ml, round-bottom, three-necked flask equipped with a Dry Ice condenser, a 50-ml addition funnel topped with nitrogen bubbler, and an adapter with a disposable pipet connected to the valve of a methylamine gas cylinder (Matheson), and the flask was then chilled to −20°. A solution of 4.78 g (24.3 mmol) of 2-chloro-5-*tert*-butyl-1,3,2-dioxaphosphorinane[1b] in 40 ml of anhydrous ether was added dropwise over a period of 30 min. Simultaneously, methylamine was bubbled through the disposable pipet into the ether solution. A white precipitate of amine hydrochloride was formed. The mixture was stirred with continued methylamine addition at −20° for another 30 min. The addition of $MeNH_2$ was discontinued, and the reaction mixture was stirred under nitrogen at methylamine reflux for a final 3.5 hr. The solution was then quickly filtered under nitrogen pressure through a glass wool filter plug to remove the amine salt into a flask protected from moisture by a $CaCl_2$ drying tube. Most of the ether was short path distilled under nitrogen. The remaining liquid was then distilled under reduced pressure to give a mixture of two isomers of 2-methylamino-5-*tert*-butyl-1,3,2-dioxaphosphorinane (**4**) in 60% yield (2.80 g, 14.64 mmol), bp 82° (1.0 mm). Vpc analysis showed only one peak. However, pmr (benzene-d_6) showed the presence of two isomers in ratio about 90:10 as determined from the integrated intensities of the *tert*-butyl protons. The pmr (benzene-d_6) spectrum of the major isomer (**4a**) showed resonances at δ 0.650 (9 H, singlet, *t*-Bu), 1.70 (1 H, multiplet, methine H), 2.55 (4 H, broad multiplet, MeNH), and 3.65–4.41 (4 H, multiplet, CH_2O). The only resonance that could be assigned accurately to the minor isomer (**4b**) was at δ 0.667 (9 H, singlet) which is due to the *tert*-butyl protons. The resonances of the rest of the protons for the minor isomer overlap with those of the major isomer.

Synthesis of 2-Methylamino-5-*tert*-butyl-2-thio-1,3,2-dioxaphosphorinane (5). To a stirred solution of 0.24 g (1.26 mmol) of a 90:10 trans:cis mixture of 2-methylamino-5-*tert*-butyl-1,3,2-dioxaphosphorinane in 1 ml of benzene at 5–10° was added under nitrogen 0.04 g (1.26 mmol) of sulfur in small portions. The reaction was followed by vpc analysis. After the reaction was complete, vpc analysis (temperature programmed at 10°/min) showed two products at retention temperatures 201 and 204° in area ratio 91:9. Removal of solvent gave 0.28 g (~100%) of product. After purification by preparative vpc, a 91:9 (trans:cis) ratio mixture was used for analysis: pmr (**5a**, major isomer, $CDCl_3$) δ 0.967 (9 H, singlet, *t*-Bu), 1.98 (1 H, multiplet, methine H), 2.69 (3 H, quartet, J_{HP} = 13.0 Hz, J_{HH} = 5.2 Hz, MeNH), 3.17 (1 H, broad multiplet, MeNH), and 3.93–4.79 ppm (4 H, multiplet, CH_2O).

Following the above procedure, a 55:45 (trans:cis) ratio mixture of 2-methylamino-5-*tert*-butyl-1,3,2-dioxaphosphorinane was converted to the corresponding sulfides in a 58:42 (trans:cis) ratio.

Anal. Calcd for $C_8H_{18}PO_2NS$: C, 43.04; H, 8.13; P, 13.87. Found: C, 43.04; H, 8.27; P, 14.16.

Acknowledgment. This work was supported by Grant CA-11045 from the National Cancer Institute of the Public Health Service and by Grant 22885 from the National Science Foundation.

Relative Energetics of Modes for Phosphorane Formation and Decomposition in Nucleophilic Displacement Reactions at Acyclic Phosphorus. Alkaline Hydrolysis of Alkoxy(alkylthio)phosphonium Salts

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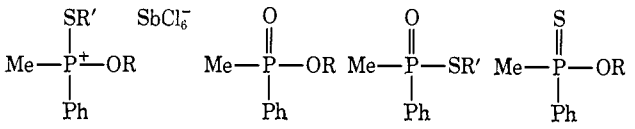
Abstract: A stereochemical and product study was carried out on the alkaline hydrolysis of various alkoxy(alkylthio)methylphenylphosphonium hexachloroantimonates (**1**). Two products, an alkyl phosphinothiolate (**3**) and an alkyl phosphinate (**2**), from cleavage of the alkoxy group or the alkylthio group, respectively, were obtained from all compounds studied except when the alkoxy group is menthoxy. The ratio of the two products was affected by the nature of the substitution in the alkoxy group but insensitive to substitution in the alkylthio group. In addition, when (*S*)-**1** (R = R′ = Me) was hydrolyzed, the two products, **2** (R = Me) and **3** (R′ = Me), were of the *R* configuration indicating cleavage of the alkoxy group with inversion and cleavage of the alkylthio group with retention of configuration at phosphorus. A mechanism involving axial attack of hydroxide ion in the face of the tetrahedral phosphonium salt opposite the alkoxy ligand, followed by a competition between direct loss of the axial alkoxy ligand and an isomerization with subsequent loss of the alkylthio ligand from an axial position, is implicated from the results.

There now appears to be ample evidence that pentacoordinate intermediates are involved in many nucleophilic displacement reactions at tetracoordinate phosphorus in both cyclic[1-4] and acyclic[5-10] phosphorus

(1) (a) F. H. Westheimer, *Accounts Chem. Res.*, 1, 70 (1968), and references therein; (b) R. Kluger, F. Covitz, E. Dennis, L. D. Williams,

compounds. However, particularly in the acyclic systems void of ring constraints, very little is known about the energetics controlling the modes of formation or decomposition of these intermediates or whether these intermediates have sufficient lifetimes to undergo the intramolecular isomerizations[11] available to pentacoordinate phosphorus. The empirical rules of Muetterties[15] concerning the relative stabilities of the various isomeric phosphoranes as a function of the ligand electronegatives provide a guess to the thermodynamically most stable intermediate expected in a displacement reaction. However, kinetic control may be at variance with thermodynamic control in determining the structure of the initially formed phosphorane.

To provide some information on the factors controlling the relative energetics of the various modes for phosphorane formation and decomposition, we decided to investigate the alkaline hydrolysis of alkoxy(alkylthio)methylphenylphosphonium hexachloroantimonates (**1**). The advantage of this system is that phosphorane formation is reasonably implicated involving a simple combination of oppositely charged ions, hydroxide and phosphonium ions. In addition, the two potential leaving groups, alkoxide and alkylthio, are widely different in electronegativity and leaving ability such that the importance of these two factors on the product composition and stereochemistry can be evaluated. The better leaving group (alkylthio) is the less electronegative ligand when attached to phosphorus. Trippett and coworkers[16] have previously investigated the hydrolysis of **1** (R = Men, R′ = Me) and made the important observation that displacement of the methyl-



1 **2** **3** **4**

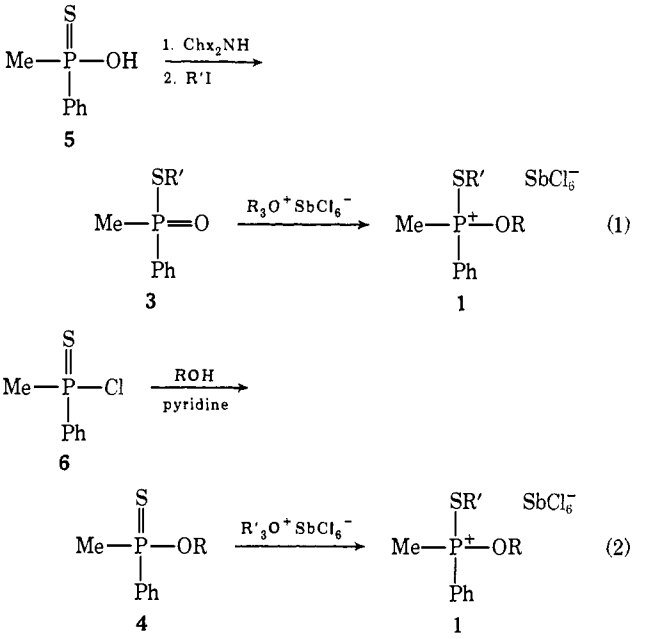
R = Me, Et, *i*-Pr, or Men

R′ = Me, Et, or *i*-Pr

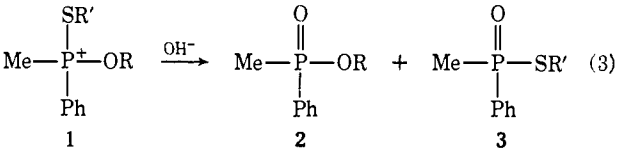
thio group occurs with retention of configuration at phosphorus; however, a number of mechanistic alternatives remain possible from this observation. Our study, which combines a stereochemical investigation with a probe of the effect the leaving abilities of the two groups, alkoxy and alkylthio, have on the product ratio, distinguishes among the alternatives and thus provides details of the mode for formation and decomposition of the intermediate phosphorane.

Results

The alkoxy(alkylthio)methylphenylphosphonium hexachloroantimonates (**1**), prepared by one of the two general synthetic routes in eq 1 or 2, were hydro-



lyzed with 0.01 *M* NaOH in 50% aqueous dioxane at room temperature. In all cases, except for **1** (R = Men, R′ = Me), hydrolysis yielded two ester products, a phosphinate ester (**2**) and a phosphinothiolate ester (**3**), from displacement of the alkylthio group and the alkoxy group, respectively (eq 3). No trace



of a phosphinothionate ester (**4**) from cleavage of the S–R′ bond could be detected. The relative amounts of the two products, **2** and **3**, as a function of the alkyl groups, R and R′, in the phosphonium salts (**1**), are given in Table I. It is apparent that *the ratio of the two products is insensitive to the nature of the alkylthio group but affected by a change in the alkoxy group.*

The conditions chosen for the hydrolysis study were necessitated by the possibility of further hydrolysis of the products, **2** and **3**, at differential rates. From control studies, **3** (R′ = Me) has a pseudo-first-order rate constant in 0.05 *M* NaOH of *ca.* 10^{-2}. Thus, at the base concentration of 0.01 *M* NaOH and with the extremely short reaction time (15 sec), the maximum correction in any of the percentages in Table I is within

and F. H. Westheimer, *J. Amer. Chem. Soc.*, **91**, 6066 (1969); (c) R. Kluger and F. H. Westheimer, *ibid.*, **91**, 4143 (1969).

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

(3) (a) K. E. DeBruin and M. J. Jacobs, *Chem. Commun.*, 59 (1971); (b) K. E. DeBruin, G. Zon, K. Naumann, and K. Mislow, *J. Amer. Chem. Soc.*, **91**, 7027 (1969); (c) K. E. DeBruin, K. Naumann, G. Zon, and K. Mislow, *ibid.*, **91**, 7031 (1969).

(4) B. W. Hawes and S. Trippett, *Chem. Commun.*, 578 (1968).

(5) (a) K. E. DeBruin and J. R. Petersen, *J. Org. Chem.*, **37**, 2272 (1972); (b) K. E. DeBruin and K. Mislow, *J. Amer. Chem. Soc.*, **91**, 7393 (1969).

(6) W. E. McEwen in *Top. Phosphorus Chem.*, **2**, 1 (1965), and references therein.

(7) R. Luckenbach, *Phosphorus*, **1**, 293 (1972).

(8) J. Michalski, M. Mikolajczyk, and J. Omelanczuk, *Tetrahedron Lett.*, 3565 (1968).

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

(10) R. D. Cook, P. C. Turley, C. E. Diebert, A. H. Fierman, and P. Haake, *J. Amer. Chem. Soc.*, **94**, 9260 (1972).

(11) Two popular mechanisms, of the same mode for intramolecular isomerizations, are Berry pseudorotation (BPR)[12] and turnstile rotation (TR).[13] An alternate mechanism which remains reasonable but is of a different mode is disrotatory pseudorotation (DPR).[14]

(12) R. S. Berry, *J. Chem. Phys.*, **32**, 933 (1960).

(13) I. Ugi, D. Marquarding, H. Klusacek, G. Gokel, and P. Gillespie, *Angew. Chem., Int. Ed. Engl.*, **9**, 702 (1970).

(14) J. I. Musher, *J. Amer. Chem. Soc.*, **94**, 5662 (1972).

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

(16) N. J. De'ath, K. Ellis, D. J. H. Smith, and S. Trippett, *Chem. Commun.*, 714 (1971).

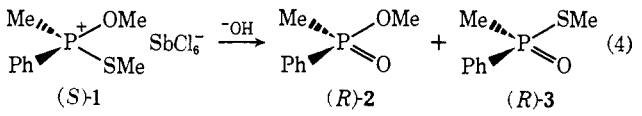
Table I. Products from the Hydrolysis of Alkoxy(alkylthio)methylphenylphosphonium Hexachloroantimonates (1)

Phosphonium salt R	R′	Products (%)[a] 2	3	3/2
Me	Me	65	35	0.54
Me	Et	67	33	0.50
Me	*i*-Pr	67	33	0.50
Et	Me	79	21	0.27
Et	Et	81	19	0.23
Et	*i*-Pr	80	20	0.25
i-Pr	Me	91	9	0.10
i-Pr	Et	90	10	0.11
Men	Me	>95	<5	<0.05

[a] Per cent of total ester products. Standard deviation of five separate hydrolyses was ±2%.

error of the measurement (±2%). The phosphinate esters (2) have previously been shown to be inert to these conditions.[5]

When optically active (*S*)-1 (R = R′ = Me), prepared by O-methylation of (*S*)-3 (R′ = Me),[17,18] was submitted to the hydrolysis conditions, (*R*)-2 (R = Me)[5] and (*R*)-3 (R′ = Me) were formed with complete or nearly complete stereospecificity. Equation 4 in-



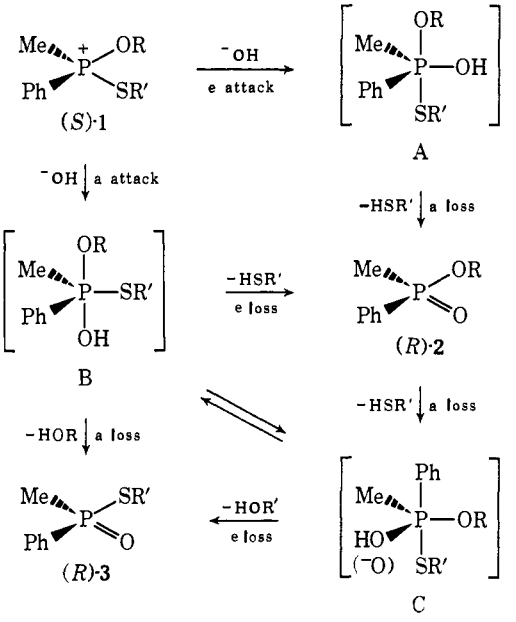
dicates the stereochemistry of this reaction. Apparently, displacement of the methoxy group proceeds with inversion of configuration at phosphorus while displacement of the methylthio group occurs with retention. The latter result is similar to that obtained by Trippett and coworkers[16] in the hydrolysis of 1 (R = Men, R′ = Me). Clearly, the hydrolysis must be proceeding entirely by attack at phosphorus with cleavage of the P–O and P–S bonds to give 3 and 2, respectively. Attack on carbon of the methoxy group would have resulted in C–O cleavage to give (*S*)-3 (R′ = Me), while attack on carbon of the alkylthio group would have yielded (*S*)-4 (R = Me). Neither of these products was observed.

Trippett and coworkers[16] also investigated the hydrolysis of *tert*-butylmethoxy(methylthio)phenylphosphonium hexachloroantimonate (7) and found displacement of the methylthio group with retention, a similar result to that observed for 1 (R = Men, R′ = Me). However, they reported no product resulting from displacement of the methoxy group. Since we observed 35% cleavage of the methoxy group in the hydrolysis of 1 (R = R′ = Me), we reinvestigated the hydrolysis of racemic 7 under the conditions used above and found 22% cleavage of the methoxy group to form methyl *tert*-butylphenylphosphinothiolate (8). The stereochemistry of this product was not investigated.

Discussion

Stereochemistry of the Hydrolysis. Our observation that (*S*)-1 (R = R′ = Me) undergoes hydrolysis either by cleavage of the methylthio group to give (*R*)-2 or by cleavage of the methoxy group to give (*R*)-3 places certain limitations on the intermediates which may be involved. Displacement of the methoxy group with inversion of configuration at phosphorus may, in theory, have resulted from the direct formation and decomposition of a phosphorane containing the hydroxide nucleophile and alkoxide leaving group in a diaxial or a diequatorial arrangement.[19] The latter arrangement would be energetically unlikely on the basis of Muetterties' rule,[1,15] since the two most electronegative ligands (OH and OR) would be occupying the unfavorable equatorial positions. In contrast, the displacement of the methylthio group with retention of configuration requires either an axial–equatorial or equatorial–axial arrangement of the nucleophile and the methylthio group, respectively, in the initially formed phosphorane. The possible intermediates and their pathways for formation and decomposition which would give the observed stereochemical results are shown in Scheme I.

Scheme I



Reaction of the phosphonium salt (1) with hydroxide ion to form phosphorane B (a attack) followed by direct loss of alkoxide ion from the axial position to give 3, or direct loss of the alkylthio group from the equatorial position to give 2, would result in the products of the observed stereochemistry. An alternative route to the formation of 2 from B would involve prior isomerization to a different phosphorane containing the alkylthio group in an axial position (*e.g.*, C) followed by axial loss.

Although either of the above pathways is intuitively pleasing, since the two products arise from a common intermediate, the stereochemical results cannot eliminate an additional pathway involving e attack of hydroxide ion on 1 to give the intermediate A. This intermediate contains both potential leaving groups in the axial positions. Since loss of the alkoxide group is expected to be less facile than loss of the alkylthio group from

(17) H. P. Benschop, G. R. van den Berg, and H. L. Boter, *Recl. Trav. Chim. Pays-Bas*, 89, 289 (1970).
(18) M. Mikolajczyk, M. Para, J. Omelanczuk, M. Kajtar, and G. Snatzke, *Tetrahedron*, 28, 4357 (1972).
(19) See K. Mislow, *Accounts Chem. Res.*, 3, 321 (1970), for a topological description of the stereochemical relationships between pentacoordinate and tetracoordinate phosphorus species.

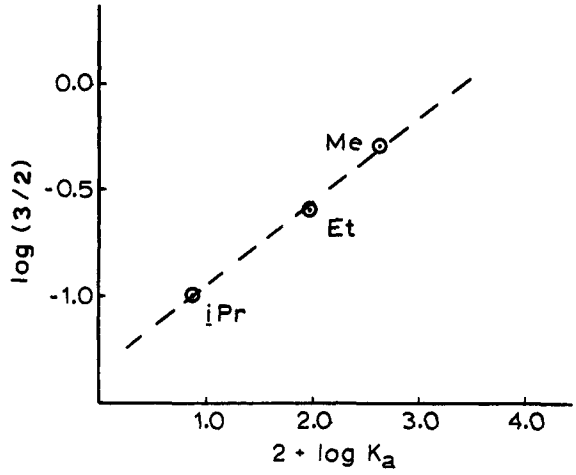
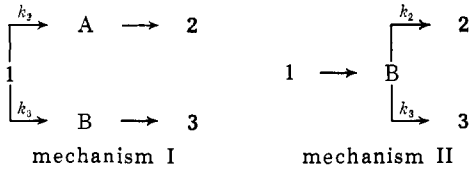


Figure 1. Plot of product ratios obtained from the hydrolysis of **1** against the relative acidities of the alcohol (ROH) form of the alkoxide leaving group as a function of the substituent R.

equivalent positions, A would result in the formation of only **2** with overall retention of configuration as observed. If any loss of the alkoxide group had occurred from A, (*S*)-**3** would have resulted which is contrary to observation. The fact that both **2** and **3** were obtained in the hydrolysis requires a separate pathway to form (*R*)-**3** perhaps *via* competitive a attack to form B, followed by alkoxide loss.

Leaving Group Effect on the Product Ratio. To provide some information on the various mechanistic pathways suggested from the stereochemical results (Scheme I), a study of the effect the nature of the alkoxy and alkylthio groups have on the product ratio, **3/2**, was carried out (Table I). As the alkoxy group was varied from methoxy to ethoxy to isopropoxy, the product ratio decreased from 0.5 to 0.25 to 0.1, respectively, corresponding to a decrease in the relative amount of cleavage of the alkoxy group. In contrast, a similar variation in the alkyl portion of the alkylthio group produced no substituent effect on the product ratio.[20]

Five possible detailed mechanisms for the hydrolysis of **1** present themselves from Scheme I and differ primarily in the point of divergence to form the two observed products, **2** and **3**. These mechanisms are indicated below where k_2 and k_3 represent the steps whose transition states determine the competition for formation of products **2** and **3**, respectively.



We have previously shown[5] that steric factors on isomerization rates (*e.g.*, B → C) in a similar system, dialkoxyphosphonium salts, are negligible when the bulk is located on the alkoxy ligand. Therefore, due to the remoteness of the substitution on the alkoxy or alkylthio group from the phosphorus center, the only transition states affected by substitution would be those which involve bond breaking between phosphorus and the alkoxy or alkylthio group being substituted.[22] Presumably, increased substitution by alkyl groups would destabilize these transition states involving buildup of negative charge on the alkoxy or alkylthio ligand.[23] With this in mind, Table II indicates the

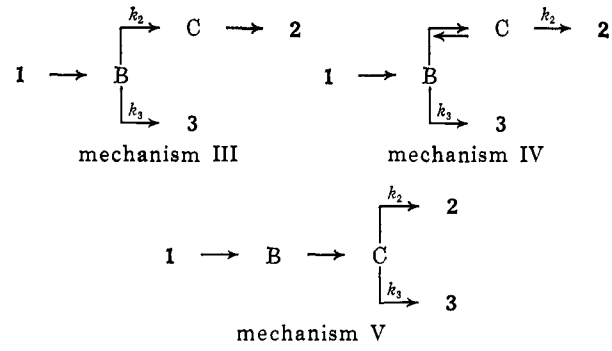


Table II. Predicted Effect of Substitution on Product Ratios from the Hydrolysis of **1**

Mechanism	Effect of substitution at OR	Effect of substitution at SR′
I	0	0
II	+	+
III	+	0
IV	+	+
V	+	+

predicted absence (0) or existence (+) of an effect on the product ratio by substituent changes in the alkoxy or alkylthio ligand as a function of the mechanism under consideration. Only mechanism III has the predicted effect consistent with the observed results. Thus, a attack of hydroxide ion on **1** produces an intermediate (**B**) containing the alkoxy group in the other axial position and the alkylthio group in an equatorial position of the trigonal bipyramidal intermediate. The degree to which this intermediate directly looses an alkoxy group in competition with isomerization and loss of the alkylthio group is determined primarily by the leaving ability of the alkoxy ligand.

In support of the above mechanistic conclusions, the product ratio, **3/2**, as a function of the nature of the alkoxy group follows a simple Brønsted relationship with the relative acidities of the corresponding alcohols (ROH). Table III lists the pertinent data which are plotted in Figure 1. The linear relationship between log (**3/2**) and log (K_a) requires that each of the transi-

(20) The ρ^* for the plot of mercaptan acidities *vs.* σ^* is similar to that for alcohol acidities ($\rho^*_{ROH} = 3.9$, $\rho^*_{RSH} = 3.4$)[21] indicating that the effect of a change in substituent in the alkylthio group would be as observable as the effect of a change in substituent in an alkoxy group if similar processes were operating.

(21) M. M. Kreevoy, E. T. Harper, R. E. Duvall, H. S. Wilgus, III, and L. T. Ditsch, *J. Amer. Chem. Soc.*, **82**, 4899 (1960).

(22) In the pH region corresponding to the pK_a of either B or C this isomerization rate may be pH dependent and, therefore, also dependent on the pK_a's of the variously substituted phosphoranes. We have assumed that variations in the alkyl portion of the alkoxy or alkylthio groups, four atoms removed from the oxygen containing the acidic proton, will have a negligible effect on the pK_a's of the phosphoranes. Thus, even if the pH of the NaOH solution employed in this study is near the pK_a of B or C, the isomerization rate should be independent of substitution.

(23) It is assumed that leaving abilities of alkoxy groups are proportional to the acidity of the corresponding alcohol in the aqueous medium.[24]

(24) J. Hine and M. Hine, *J. Amer. Chem. Soc.*, **74**, 5266 (1952).

Table III. Relationship between Product Ratios Obtained and Acidities[a] of the Protonated Alkoxy Leaving Groups

Alkoxy group	3/2	K_a's (rel)
OMe	0.5	4.0
OEt	0.25	0.95
O-*i*-Pr	0.1	0.076

[a] Reference 24.

tion states represented by k_2 and k_3, which control the product ratio, also follow the Brønsted relationship (*i.e.*, $\log k_3 = \alpha_3 \log K_a + C_3$ and $\log k_2 = \alpha_2 \log K_a + C_2$). This requirement is followed by mechanism III in that k_3 involves P–O bond cleavage with a development of negative charge on oxygen and k_2 is expected to be independent of the nature of the alkoxy group ($\alpha_2 = 0$). Thus, since log (**3**/**2**) is proportional to log (k_3/k_2) and k_2 is constant, the slope of the plot in Figure 1 represents the proportionality constant between log k_3 and log K_a of $\alpha_3 = 0.4$. A similar plot of the product ratio, **3**/**2**, as a function of the nature of the alkylthio group would give, within the error of our analysis, an α of ≤ 0.05. Since substituent effects are not attenuated by a sulfur atom compared to an oxygen atom,[20] this small value is inconsistent with P–S bond cleavage in a transition state which determines the product ratio.

The origin of the exclusive formation of phosphorane B containing the alkylthio ligand in an equatorial position and the hydroxy and alkoxy ligands in axial positions of the trigonal bipyramid is not obvious. Although a attack of a nucleophile on tetracoordinate phosphorus is generally postulated[1] as the mode of phosphorane formation, the above study provides the first test of the generality in an acyclic system containing two relatively electronegative ligands. Apparently, there is an inherent stabilization of the transition state for attack in a face of the tetrahedral phosphorus (a attack) as opposed to attack of the nucleophile leading directly to a phosphorane containing the nucleophile in an equatorial position.

In addition to providing evidence for a attack, the formation of B suggests a preference for attack of the nucleophile in the face opposite the alkoxy ligand rather than in the face opposite the alkylthio group. The relative thermodynamic stabilities of the two intermediates resulting from these two modes of a attack cannot be estimated. The application of Muetterties' rule,[15] which implies that the most electronegative ligands[25] will prefer the axial positions, has not been tested in comparisons between ligands involving first-row elements to ligands involving second-row elements attached to phosphorus. The possibility of multiple bonding[14,27] raises extreme doubt in extending Muetterties' rule to subtle comparisons of intermediates containing an alkoxy and an alkylthio ligand. However, even if B is the most stable intermediate having the alkoxy group in the axial position, thermodynamic stability may not necessarily be reflected in the kinetic control of the attack. Our results are consistent with a kinetic preference for attack of a hydroxide ion in the face of a tetrahedral phosphonium salt (**1**) opposite the alkoxy ligand.[16]

For the decomposition of B, our results indicate a competition exists between direct loss of the axial alkoxy group and isomerization of B to a different phosphorane. The extent of this competition is determined by the leaving ability[23] of the alkoxy group. The implication of these conclusions is that *equatorial loss of an alkylthio group from B is a relatively high energy process compared to loss of an alkoxy group from an axial position or isomerization of B to a new intermediate such as C.* If one makes the reasonable, but untested, assumption that an alkylthio group is a better leaving group than an alkoxy group, there exists a strong preference for axial loss of a group over equatorial loss.

Implications for General Nucleophilic Displacement Reactions at Phosphorus. An important consequence of our mechanistic study is that the course of a displacement reaction at phosphorus which involves the formation of a phosphorane intermediate is determined entirely by the energetics of the intermediate. For example, in a displacement reaction at phosphorus containing an alkoxy and an alkylthio ligand, if an intermediate such as B is formed with the alkylthio ligand in an equatorial position, loss of the alkylthio group will be competitive with loss of the alkoxy group *only if isomerization is possible* (*e.g.*, B to C). Thus, if isomerization in certain systems is a high energy process, loss of the alkylthio group would be blocked and products would arise from loss of the alkoxy group occupying the axial position.

Experimental Section[28]

Synthesis of Alkyl Methylphenylphosphinates (2). The procedure given below for the synthesis of **2** (R = Me) typifies the general procedure for the synthesis of alkyl methylphenylphosphinates. The pmr spectra of the various compounds are listed in Table IV.

A solution of methylphenylphosphinochloridate (5.0 g, 29 mmol) in ether (10 ml) was added dropwise to a solution of methanol (5 ml) and pyridine (5 ml) in ether (20 ml). After the mixture was stirred at room temperature for 1 hr, the solid precipitate was filtered from solution. Concentration of the filtrate followed by Kugelrohr distillation (75° (0.1 mm)) yielded methyl methylphenylphosphinate (**2**, R = Me) (4.5 g, 93% yield).

Synthesis of Alkyl Methylphenylphosphinothiolates (3). The synthesis of **3** (R = Me) from dicyclohexylammonium methylphenylphosphinothioate (**9**) is given later in the Experimental Section. This procedure was used in the synthesis of **3** (R = Et) from iodoethane and **9** in benzene except the solution was heated to reflux for 4 hr. Preparation of **3** (R = *i*-Pr) was similarly accomplished from **7** and isopropyl bromide requiring heating to reflux for 48 hr. Yields are quantitative. Table IV contains the pmr data on the phosphinothiolate esters (**3**).

Synthesis of Alkyl Methylphenylphosphinothionates (4). The general procedure for the synthesis of alkyl methylphenylphosphinothionates from methylphenylphosphinothionochloridate is similar to that employed above for the synthesis of **2** except longer reaction times are necessary to ensure complete reaction. For **4** (R = *i*-Pr), stirring for 6 hr was necessary to obain an 80% yield. The pmr spectra of the phosphinothionates are given in Table IV.

Synthesis of Alkoxy(alkylthio)methylphenylphosphonium Hexachloroantimonates (1). The general routes to the phosphonium salts (**1**) used in this study involved either O-alkylation of a phosphinothiolate ester (**3**) or S-alkylation of a phosphinothionate ester (**4**) with a trialkyloxonium hexachloroantimonate. The general procedure applicable to either route is exampled below in the syn-

(25) In any of the multiple methods for determining the electronegativity of an atom or group, an S atom or SMe group is less electronegative than an O atom or OMe group.[26]

(26) P. R. Wells, *Progr. Phys. Org. Chem.*, **6**, 111 (1968).

(27) R. Hoffmann, J. M. Howell, and E. L. Muetterties, *J. Amer. Chem. Soc.*, **94**, 3047 (1972).

(28) Pmr spectra were recorded on a Varian A-60A spectrometer and refer to *ca.* 10% solution with tetramethylsilane as internal standard. Chemical shifts are reported in ppm from TMS. Optical rotations were measured on a PE-141 polarimeter.

Table IV. Pmr Spectral Data of Organophosphorus Compounds[a]

Group containing proton	MePhP(O)OR[b]	MePhP(S)OR[b]	MePhP(O)SR[b]	MePhP(OR)SR$^+$SbCl$_6^-$[c]
PCH_3	1.65 (15)	1.95 (14)	1.93 (14)	2.49 (13)
$POCH_3$	3.58 (11)	3.52 (14)		4.09 (14)
$PSCH_3$			2.18 (12)	2.41 (15)
$POCH_2CH_3$	3.95 (14)	3.9		4.42 (9)
$PSCH_2CH_3$			2.68 (10)	2.90 (13)
$POCH_2CH_3$	1.27 (0)	1.23 (0)		1.49 (0)
$PSCH_2CH_3$			1.23 (7)	1.33 (0)
$POCH(CH_3)_2$	4.55 (8)	4.68 (7)		*d*
$PSCH(CH_3)_2$			3.35 (7, 9)	3.49
$POCH(CH_3)_2$	1.15, 1.38[e] (0)	1.05, 1.33[e] (0)		1.44, 1.52[e] (0)
$PSCH(CH_3)_2$			1.17, 1.40[e] (0)	1.34, 1.46[e] (0)

[a] Chemical shifts in ppm from TMS. Coupling constants J_{PH} in hertz are noted in parentheses. J_{HCCH} = 7 Hz for all compounds. [b] Solvent $CDCl_3$. [c] Solvent CH_2Cl_2. [d] Peaks under solvent. [e] Diastereotopic CH_3 groups.

thesis of (*S*)-**1** (R = R′ = Me). All reactions are complete within 1 hr. Table IV contains the spectral data of the various functionality in the phosphonium salts (**1**). The chemical shifts of the alkyl groups are insensitive (±0.02 ppm) to the nature of the other alkyl groups in the phosphonium salt.

Hydrolysis of Alkoxy(alkylthio)methylphenylphosphonium Hexachloroantimonates (1). Identical conditions and procedures were utilized in the hydrolysis of each of the phosphonium salts. A solution of 0.01 *M* NaOH in 50% aqueous dioxane (500 ml, 5 mmol) was added at once to a rapidly stirred solution of the phosphonium salt (0.5 mmol) in dioxane (2 ml). The resulting mixture was immediately added to dichloromethane (400 ml) in a separatory funnel and extracted. The total reaction time was less than 15 sec. Drying and concentration of the dichloromethane layer afforded a clear oil which was analyzed by pmr without purification. The only products detectable by pmr were the corresponding phosphinate and phosphinotholate esters, **2** and **3**. The relative amounts of these two products were determined by integration of the P–CH_3 region in the pmr. A duplicate check on the product ratios was carried out by glc analysis (SE-30, 6 ft) and corresponded within ±3% of the pmr analysis. The values obtained are listed in Table I.

Synthesis of (*S*)-Methylphenylphosphinothioic Acid [(*S*)-5].[16,29] A solution of (R_p)-menthyl methylphenylphosphinothionate (**10**) (1.0 g, 3.2 mmol), which was greater than 90% diastereomerically pure by pmr,[16,30] dissolved in dioxane (10 ml) was added to a solution of 1.0 *M* KOH in 30% aqueous dioxane (400 ml, 400 mmol) and the mixture was heated to reflux for 20 hr. The homogeneous solution was extracted with methylene chloride, strongly acidified with HCl, and extracted again with methylene chloride. The acid extracts were dried and concentrated to yield the desired product **5** (0.51 g, 90% yield). This sample was directly converted to the dicyclohexylammonium salt (**9**).

Synthesis of (*S*)-Dicyclohexylammonium Methylphenylphosphinothioate [(*S*)-9].[16] A solution of dicyclohexylamine (0.6 g, 3.3 mmol) in ether (5 ml) was added dropwise to a solution of methylphenylphosphinothioic acid (0.5 g, 2.9 mmol) in ether (10 ml) at room temperature. After the mixture was stirred for 5 hr, the white precipitate was filtered from solution and consisted of pure **9** (0.87 g, 85% yield, mp 157–159°), [α]D −9.25° (*c* 2.5, MeOH). Based on the highest reported rotation[16] for **9** of 11.3°, this sample is 83% optically pure, with the predominance of the *S*-(−) configuration.

Synthesis of (*S*)-Methyl Methylphenylphosphinothiolate [(*S*)-3] (R′ = Me). Iodomethane (2 g, 14 mmol) was added directly to a solution of (*S*)-**9** (0.8 g, 2.3 mmol, 83% optically pure) in benzene (30 ml) and the resulting mixture was stirred at room temperature for 15 hr. The solid precipitate which formed was filtered from solution and the filtrate was concentrated on a rotary evaporator. Kugelrohr distillation (80° (0.1 mm)) afforded pure **3** (0.40 g, 95% yield) by pmr and glc, [α]D −158° (*c* 4.1, benzene). Assuming a stereospecific reaction, this sample is 83% optically pure and of the *S*-(−) configuration.[18,29]

Synthesis of (*S*)-Methoxy(methylthio)methylphenylphosphonium Hexachloroantimonate [(*S*)-1] (R = R′ = Me). A solid sample of trimethyloxonium hexachloroantimonate (0.74 g, 1.9 mmol) was added to a solution of (*S*)-methyl methylphenylphosphonothiolate (**3**) (R′ = Me) (0.35 g, 1.9 mmol), [α]D −158°, in dichloromethane (15 ml) at room temperature. The mixture became homogeneous after *ca.* 15 min and was then stirred an additional hour. After concentrating to 5 ml, the solution was added rapidly to anhydrous ether (50 ml) causing a white precipitate to form. Filtering and drying afforded (*S*)-**1** (0.90 g, 90% yield), mp 133–135°, [α]D −11.1° (*c* 2.15, dichloromethane). Assuming a stereospecific reaction, this sample is 83% optically pure.

Hydrolysis of (*S*)-Methoxy(methylthio)methylphenylphosphonium Hexachloroantimonate [(*S*)-1] (R = R′ = Me). A solution of 0.05 *M* NaOH in 50% aqueous dioxane (200 ml, 10 mmol) was added rapidly to a solution of (*S*)-**1** (R = R′ = Me), [α]D = −11.1° (0.3 g, 0.65 mmol), in dioxane (2 ml). The resulting solntion was immediately added to dichloromethane (400 ml) in a separatory funnel and extracted. The total time necessary for these two processes was *ca.* 15 sec. The dichloromethane layer was separated, dried, and concentrated. The residue was submitted to a Kugelrohr distillation (80° (0.1 mm)), yielding a clear oil (0.08 g) consisting of a mixture of methyl methylphenylphosphinate (**2**, R = Me) and methyl methylphenylphosphinothiolate (**3**, R′ = Me), [α]D +66.0° (*c* 4.04, benzene).

The above procedure was repeated twice with reaction times of 50 sec and 3 min which gave rotations of [α]D +60.0° (*c* 3.2, benzene) and +45.5° [*c* 4.13, benzene), respectively. Table V compares the product ratio of **2** (R = Me) with **3** (R′ = Me) as determined by pmr with the absolute rotations obtained. Thus, both products have a dextrarotatory optical rotation and are of the *R* configuration.[5,18,29]

Table V. Optical Rotations of Product Mixtures from Hydrolysis of (*S*)-**1** (R = R′ = Me)

Reaction time, sec	Products (%)[a] **2** (R = Me)	**3** (R′ = Me)	[α]D(obsd), deg	[α]D(calcd),[b] deg
15	78	22	+66.0	+68
50	86	14	+60.0	+59
180	100	0	+45.5	+43

[a] Per cent of total ester products. Error *ca.* 2%. [b] See eq 5.

Based on the highest reported rotations of **2** (R = Me, [α]D 52°, optically pure, benzene)[5a] and **3** (R′ = Me, [α]D 158°, 83% optically pure, benzene), a stereospecific hydrolysis of (*S*)-**1** (R = R′ = Me, 83% optically pure) would have yielded (*R*)-**2** (R = Me) with a rotation of +43° and (*R*)-**3** (R′ = Me) with a rotation of +158°. Thus, the calculated optical rotation, [α]D (calcd), of a mixture of (*R*)-**2** and (*R*)-**3**, each 83% optically pure, would be given by eq 5. The calculated values are given in Table V as a

$$[\alpha]_D(\text{calcd}) = 115\left(\frac{[3]}{[2]+[3]}\right) + 43 \qquad (5)$$

function of the observed product percentages. If the reasonable assumption is made that the error in the percentages indicated in Table V is 2% or greater, [α]D (calcd) is within error of the observed absolute rotation [α]D (obsd). Thus, the hydrolysis of

(29) H. P. Benschop, G. R. van der Berg, and H. L. Boter, *Recl. Trav. Chim. Pays-Bas*, **87**, 387 (1968).
(30) A. Herriott, *J. Amer. Chem. Soc.*, **93**, 3304 (1971).

(*S*)-**1** (R = R′ = Me) is stereospecific within error of the measurements.

Control Experiments. The phosphinate and phosphinothiolate ester products, **2** (R = Me) and **3** (R′ = Me), from the hydrolysis of (*S*)-**1** (R = R′ = Me) were shown to be configurationally stable under the reaction conditions for hydrolysis by submitting a sample of each to the exact conditions. Recovery of unreacted **2** (R′ = Me) after 30 sec and unreacted **3** (R = Me) after 2 min yielded a product of unchanged stereochemistry.

Differential Hydrolysis Rates of the Two Products from Hydrolysis of 1. The phosphinate ester products, **2**, have previously been shown to be chemically stable to the hydrolysis reaction conditions of 0.01 *M* NaOH in 50% aqueous dioxane for a reaction time of less than 1 min. To test the possibility of hydrolysis of the phosphinothiolate esters (**3**), mixtures of each of esters **3** and **2** (R = *i*-Pr) were submitted to the reaction conditions for 2 min. The ratio of **3** to **2** (R = *i*-Pr) was unchanged for **2** (R′ = Et) and **2** (R′ = *i*-Pr), indicating the absence of any hydrolysis. For **2** (R′ = Me) a starting ratio of **2**/**3** of 0.8 was decreased to 0.6 indicating *ca.* 25% reaction of **2**. This corresponds to a pseudo-first-order rate constant of *ca.* 2×10^{-3} sec^{-1}. Thus, under the reaction time of 15 sec, less than 5% of **2** (R′ = Me) could have reacted.

Hydrolysis of *tert*-Butylmethoxy(methylthio)phenylphosphonium Hexachloroantimonate (7). By a procedure identical with that above for the hydrolysis of **1** except that a longer reaction time (*ca.* 40 sec) was necessary, the hydrolysis of **7**[16] (pmr ($CDCl_3$): $PCCH_3$, d, δ 1.41, J_{PCCH} = 20 Hz; $POCH_3$, d, δ 4.35, J_{POCH} = 12.5 Hz; $PSCH_3$, d, δ 2.56, J_{PSCH} = 13.0 Hz) afforded two products. These products were identified by pmr ($CDCl_3$) to be methyl *tert*-butylphenylphosphinate ($PCCH_3$, d, δ 1.13, J_{PCCH} = 15.9; $POCH_3$, d, δ 3.70, J_{POCH} = 10.9 Hz) and methyl *tert*-butylphenylphosphinothiolate ($PCCH_3$, d, δ 1.20, J_{PCCH} = 17.0 Hz; $PSCH_3$, d, δ 2.13, J_{PSCH} = 10.8 Hz) in the ratio of 78:22, respectively.

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Alkaline Hydrolysis of 1-X-1-Alkoxy-2,2,3,4,4-pentamethylphosphetanium Salts. An Unusual Order of Ligand Kinetic Axiophilicities

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Abstract: The stereochemistry of the products from the alkaline hydrolysis of *cis*- and *trans*-1-X-1-alkoxy-2,2,3,4,4-pentamethylphosphetanium hexachloroantimonates where X is methoxy, ethoxy, isopropoxy, dimethylamino, methylthio, or chloro has been investigated. Assuming a mechanism involving axial attack of the hydroxide ion and axial loss of the leaving group, an unusual order of ligand axiophilicities is implicated from the product analysis. Thus, the ability of a phosphorane to undergo an intramolecular isomerization involving the positional exchange of a ligand from an equatorial position to an axial position in a trigonal bipyramid depends on the nature of the ligand with increasing ability in the order: NMe_2 < OMe, OEt, O-*i*-Pr < SMe $\simeq$ Cl. An interpretation of the origin of this order is advanced involving the electronegativity of the ligand and the ability of the lone pairs of electrons in the heteroatom of the ligand to overlap with phosphorus.

The importance of pentacoordinate phosphorus species (phosphoranes) as intermediates in displacement reactions at tetrahedral phosphorus has become recognized in the last decade. Westheimer and coworkers,[1] in their elegant studies of the mechanism of the hydrolysis of cyclic phosphorus esters, have invoked phosphorane intermediates and emphasized the importance of isomerization pathways available to these intermediates in determining the product composition. We have observed a similar product control by intermediates and their isomerization pathways in displacements at acyclic phosphonium salts[2a-c] and phosphorus esters.[2d] Although gross empiricisms have resulted from these studies, it is of importance to further establish the factors controlling the geometry of the intermediates initially formed in a reaction and the relative energetics of possible isomerization and decomposition pathways available to these intermediates.

We have undertaken the present study to elucidate one aspect of the problem; namely, the effect various ligands have on the energies for intramolecular isomerizations. Specifically, our study has probed the relative kinetic ability of ligands such as alkoxy, dimethylamino, methylthio, and halo, which are common to many reactions of phosphorus, to undergo positional exchange from an equatorial position in a trigonal bipyramid to an axial position (axiophilicity). Other workers have been able to obtain similar information on saturated and unsaturated carbon ligands as well as phenoxy and dimethylamino,[3] which with our study, provide a wide range of ligands whose relative kinetic axiophilicities have now been established.

The system utilized in this study was the alkaline hydrolysis of 1-X-1-alkoxy-2,2,3,4,4-pentamethylphosphetanium hexachloroantimonates (**1** and **2**). Because of the small ring, the number of isomerization pathways of the pentacoordinate intermediates is limited. In addition, if one assumes axial approach of the nucleo-

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(3) R. K. Oram and S. Trippett, *J. Chem. Soc., Chem. Commun.*, 554 (1972).