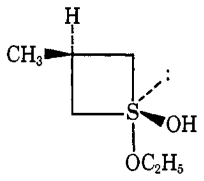
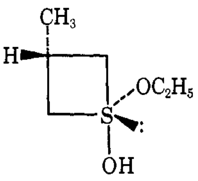
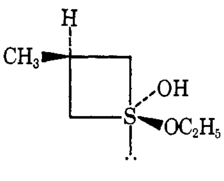


4A



4B



4C

leads to a structure which is not ruled out on energetic grounds.[16] Similarly, if **4B** is first formed, only **4A** is accessible[16] by pseudorotation. It follows that if the rate of departure of the leaving group is faster than pseudorotation to an unfavorable intermediate,[16] loss of ethoxide from **4A** or **4B** results in net retention of configuration.[17,18] Since this is not what is observed, we conclude that the displacement at sulfur occurs by way of a high-energy transition state or intermediate: either the thietane ring spans the ee positions (I strain) and the entering (hydroxide) and leaving (ethoxide) groups occupy a positions, or the ring spans the ae positions but the entering and leaving groups now occupy e positions, with the lone pair in the *a* position (stereoelectronic strain). Hence, either pseudorotation in the family of "pentacoordinate" sulfur compounds, if it occurs at all,[13,19] is less facile than in the phosphoranes, or the reaction does not proceed through an intermediate of significant lifetime and is better described as a direct nucleophilic substitution.[20]

[16] Intermediates ruled out are those in which the thietane ring spans other than ae positions, and those in which the unfavorable energetics detailed for 4C obtain.

[17] The principle of microscopic reversibility,[15] as applied to the present case, obtains for equatorial attack (3A → 2A → 4A → 4B → 3A) *or* apical attack (3A → 2A → 4B → 4A → 3A).

[18] Arguments entirely analogous to the above apply to the *trans* series of 2 and 3.

[19] E. L. Muetterties and W. D. Phillips, *J. Chem. Phys.*, **46**, 2861 (1967).

[20] Note Added in Proof. The present analysis is applicable *in toto* to nucleophilic substitution at phosphorus in 1-chloro-2,2,3,4,4-pentamethylphosphetane, which is also reported to proceed with inversion of configuration (D. J. H. Smith and S. Trippett, *Chem. Commun.*, 855 (1969)).

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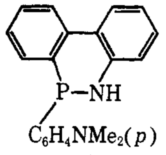
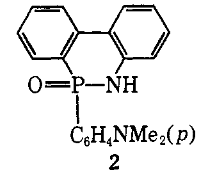
Stereomutation of Phosphine Oxides by Lithium Aluminum Hydride[1]

Sir:

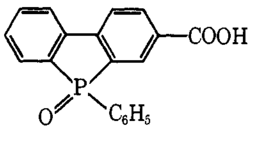
Phosphine **1**, prepared by lithium aluminum hydride (LAH) reduction of optically active **2**, provided the first example of a compound whose optical activity could be attributed to stably pyramidal tervalent phosphorus.[2] Surprisingly, however, reduction of optically active **3** with LAH gave racemic **4**,[3] even though phosphines are configurationally stable at temperatures employed in the reduction.[2,4] We now report our finding that phosphine oxides undergo rapid stereomutation in the presence of LAH *prior* to reduction.



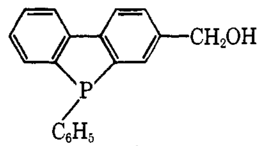
1



2



3



4

Solutions of (+)-methylphenyl-*n*-propylphosphine oxide (**5**, 1 mmol) and LAH (0.5 mmol) in tetrahydrofuran (THF) were allowed to stand at room temperature, and their compositions were examined at hourly intervals. The results for two runs are collected in Table I and clearly demonstrate that *racemization of the phosphine oxide is virtually complete before more than 10% has been reduced to phosphine.* A control experiment showed that quenching of the reduction mixture with $H_2{}^{18}O$ does not lead to incorporation of ^{18}O into the recovered phosphine oxide. Exposure of optically active **5** to LAH in refluxing THF or di-*n*-butyl ether at 80–90° for 30 min leads to racemic **5**. Sodium borohydride in ethanol at room temperature is ineffective as either a racemizing or reducing agent.

Table I. Racemization and Reduction of (+)-Methylphenyl-*n*-propylphosphine Oxide (**5**) by Lithium Aluminum Hydride in Tetrahydrofuran

	Recovered phosphine oxide[a]				
	Run no. 1		Run no. 2		
Reaction time, hr	$[\alpha]D$, deg	Racemization, %	$[\alpha]D$, deg	Racemization, %	Yield of phosphine, %[b]
0	9.8	0	18.0	0	0
1	8.1	17	15.3	15	1
2	7.5	23			2
3	4.9	50	9.8	46	5
4	4.5	54	6.8	62	7
5	3.2	67	6.4	64	
6	1.7	83	3.6	80	9

[a] Rotations of **5** refer to methanol. Starting materials are 49% (run 1) and 90% (run 2) optically pure, based on the absolute rotation of $[\alpha]D$ 20°: J. P. Casey, R. A. Lewis, and K. Mislow, *J. Amer. Chem. Soc.*, **91**, 2789 (1969). Recovery of **5** was generally about 70%. [b] These figures, assessed by glpc (2 ft, 10% SE-30 on 60–80 Chromosorb W), are approximate, and refer to both runs. In addition to phosphines, some other unidentified decomposition products were also observed.

Exposure of either *cis*- or *trans*-1-phenyl-2,2,3,4,4-pentamethylphosphetane 1-oxide[5] to LAH in THF at room temperature produces the *same* mixture of isomers (70% recovery) consisting of 95% of the higher melting (presumably *cis*[6]) and 5% of the lower melting (presumably *trans*[6]) isomer. Significantly, the epimerization of the two diastereomers is complete within 10 min or less under the stated reaction conditions.

[1] We are grateful to the Air Force Office of Scientific Research for support of this research under Grant No. AF-AFOSR-1188-B, and to the Public Health Service for a Special Research Fellowship (P. D. H.).

[2] I. G. M. Campbell and J. K. Way, *J. Chem. Soc.*, 5034 (1960).

[3] I. G. M. Campbell and J. K. Way, *ibid.*, 2133 (1961).

[4] L. Horner and H. Winkler, *Tetrahedron Lett.*, 461 (1964); L. D. Quin, J. P. Gratz, and R. E. Montgomery, *ibid.*, 2187 (1965); H. E. Shook, Jr., and L. D. Quin, *J. Amer. Chem. Soc.*, **89**, 1841 (1967); S. E. Cremer, R. J. Chorvat, C. H. Chang, and D. W. Davis, *Tetrahedron Lett.*, 5799 (1968); K. L. Marsi, *Chem. Commun.*, 846 (1968); *J. Amer. Chem. Soc.*, **91**, 4724 (1969).

[5] S. E. Cremer and R. J. Chorvat, *J. Org. Chem.*, **32**, 4066 (1967).

[6] These assignments are tentative (ref 5; S. E. Cremer, private communication).

All of the above observations are readily accommodated by invoking *reversible* addition of LAH to the phosphine oxide. Similar addition products have been described and have been assigned a structure, Li[Al(OPHR$_3$)$_4$], in which a pentacoordinate phosphorus atom is linked to hydrogen.[7] We suggest that pseudorotation of the phosphorane, followed by dissociation into phosphine oxide and LAH, leads to the observed stereomutation.[8–11]

Reduction of optically active benzylphosphonium salts with LAH also gives racemic phosphines under conditions where such phosphines are optically stable.[12] However, we have found that while reduction of (+)-benzylmethylphenyl-*n*-propylphosphonium bromide with LAH in THF at room temperature gives racemic methylphenyl-*n*-propylphosphine, the recovered salt has suffered no change in optical purity. It is therefore likely, as has been suggested,[13] that racemization here occurs by pseudorotation of the *irreversibly* formed phosphorane (R$_4$PH) intermediate prior to loss of the benzyl anion.

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(7) K. Issleib and G. Grams, *Z. Anorg. Allg. Chem.*, **299**, 58 (1959).

(8) Pseudorotation in phosphoranes containing a P–H bond is not without precedent: R. R. Holmes and R. N. Storey, *Inorg. Chem.*, **5**, 2146 (1966); D. Houalla, R. Wolf, D. Gagnaire, and J. B. Robert, *Chem. Commun.*, 443 (1969).

(9) The small amount of phosphine produced in the reduction of (+)-**5** is 80–90% racemized after 4–5 hr, even though the phosphine is optically stable under conditions which cause complete racemization of **5** by LAH (control experiment). An additional racemization mechanism must therefore play a minor role. The residual activity indicates net retention of configuration in the reduction, similar to the retention observed[2] in the reduction of **2**.

$$(+)\text{-}\mathbf{2} \xrightarrow{\text{LAH}} (-)\text{-}\mathbf{1} \xrightarrow{\text{H}_2\text{O}_2} (+)\text{-}\mathbf{2}$$

(10) The rapidity of the stereomutation of phosphetane 1-oxides by LAH is a useful diagnostic, since an enhancement in reaction rate, relative to the acyclic analogs, characterizes intermediate phosphorane formation in reactions of closely related phosphetane P(IV) derivatives: K. Bergesen, *Acta Chem. Scand.*, **21**, 1587 (1967); W. Hawes and S. Trippett, *Chem. Commun.*, 577 (1968); P. Haake, R. D. Cook, W. Schwarz, and D. R. McCoy, *Tetrahedron Lett.*, 5251 (1968); S. E. Cremer, R. J. Chorvat, and B. C. Trivedi, *Chem. Commun.*, 769 (1969); K. E. DeBruin, G. Zon, K. Naumann, and K. Mislow, *J. Amer. Chem. Soc.*, in press.

(11) (a) In the light of these results, the *absence* of racemization in the LAH reduction of **1** represents an anomaly, the source of which is likely to be the presence of the neighboring NH group. (b) Retention of configuration in the reduction of phosphine oxides with trichlorosilane (L. Horner and W. D. Balzer, *Tetrahedron Lett.*, 1157 (1965)) implies that the rate of loss of trichlorosiloxide ion from the intermediate Cl$_3$SiOPHR$_3$ is faster than the rate of pseudorotation (K. Naumann, G. Zon, and K. Mislow, *J. Amer. Chem. Soc.*, in press).

(12) W. E. McEwen, K. F. Kumli, A. Bladé-Font, M. Zanger, and C. A. VanderWerf, *J. Amer. Chem. Soc.*, **86**, 2378 (1964).

(13) T. J. Katz, C. R. Nicholson, and C. A. Reilly, *ibid.*, **88**, 3832 (1966); M. J. Gallagher and I. D. Jenkins in "Topics in Stereochemistry," Vol. 3, N. L. Allinger and E. L. Eliel, Ed., John Wiley & Sons, Inc., New York, N. Y., 1968, pp 29 and 74.

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The Solvomercuration–Demercuration of Representative Olefins in the Presence of Alcohols. Convenient Procedures for the Synthesis of Ethers

Sir:

Recently a remarkably simple procedure was described for the synthesis of alcohols from representative olefins *via* a Markovnikov hydration.[1] The synthesis involves oxymercuration of the unsaturated compound with mercuric acetate in the presence of a 50:50 tetrahydrofuran–water medium, followed by *in situ* reduction of the oxymercurial with sodium borohydride in the presence of sodium hydroxide.

This combined solvomercuration–demercuration procedure is capable of considerable variation and may be widely utilized for the addition of various nucleophilic reagents to olefinic double bonds under very mild conditions. For optimum results it is necessary to vary the mercuric salt so as to avoid competition of the anion of the salt with the desired nucleophile for the mercuric intermediate.

Thus, mercuric acetate achieves a satisfactory synthesis of methyl, ethyl, and isopropyl ethers from the corresponding alcohols and representative olefins, utilizing essentially the original procedure.[1,2] However, the synthesis of more hindered derivatives, such as the *t*-butyl ethers, required a shift to a mercuric salt containing a less nucleophilic anion, such as mercuric trifluoroacetate. Finally, to achieve the synthesis of amines by adding acetonitrile as the nucleophilic reagent, it proved desirable to utilize a salt containing an even less nucleophilic anion, mercuric nitrate.[3]

Since the olefins are quite soluble in the pure alcohols, we utilized the latter for the reaction mixture in place of the 50:50 tetrahydrofuran–water mixture utilized in the hydration procedure. In the great majority of cases involving mercuric acetate, the alkoxymercuration stage proceeded quite rapidly, with a reaction time of 10 min being quite satisfactory. In a few cases involving relatively hindered reactants, longer reaction times were necessary.

For the most part the yields are quite satisfactory. Only in the case where *t*-butyl alcohol was utilized as the nucleophilic reagent were the yields relatively low.

The following procedure is representative. In the flask were placed 100 ml of anhydrous isopropyl alcohol and 100 mmol of mercuric acetate. Then, 100 mmol of 2-methyl-1-butene was introduced into the vigorously stirred suspension. Ten minutes after the addition of the olefin, the reduction of the mercurial intermediate was achieved by adding 100 ml of 3 *M* sodium hydroxide and 100 ml of 0.5 *M* sodium borohydride in 3 *M* sodium hydroxide, both in water. The mixture was allowed to stir for 2 hr, until the mercury had coagulated and settled. The product, *t*-amyl isopropyl ether, was extracted with pentane and isolated in 81% yield, bp 112–114°, $n^{20}\text{D}$ 1.3946.

In all cases involving mercuric acetate and methyl or ethyl alcohol the reaction mixture became homogeneous in 1 to 5 min following addition of the olefin, and high yields of the corresponding ethers were obtained. It was gratifying that even tertiary olefins, such as 2-methyl-1-butene and α-methylstyrene, reacted smoothly to produce the corresponding *t*-alkyl ethers. In the case of mercuric acetate and isopropyl alcohol, the rates were appreciably slower and these reactions

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(1) H. C. Brown and P. J. Geoghegan, Jr., *J. Amer. Chem. Soc.*, **89**, 1522 (1967).

(2) It should be pointed out that the synthesis of cyclohexyl methyl ether was achieved previously by treating cyclohexene in methanol with mercuric acetate, precipitation of the mercurial as the chloride, and reduction of the chloride with sodium borohydride (F. G. Bordwell and M. L. Douglass, *ibid.*, **88**, 993 (1966)). The present procedure is not only more convenient in allowing the reaction to be carried out in a single vessel, but it possesses the enormous advantage of making unnecessary the isolation and handling of the toxic intermediate.

(3) H. C. Brown and J. T. Kurek, *ibid.*, **91**, 5647 (1969).