J. Am. Chem. Soc. **1983**, *105*, 6053-6061

The Reactions of Ethoxy Radicals with Optically Active Tertiary Phosphines. Stereochemistry of the Substitution Process and the Question of Permutation Modes for the Possible Phosphoranyl Radical Intermediates

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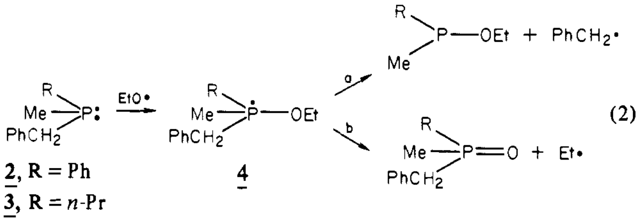
Abstract: The reactions of (−)-(*S*)-2, MePhPCH$_2$Ph, and (+)-(*S*)-3, *n*-PrMePCH$_2$Ph, with EtO· were shown to yield substitution products MePhPOEt and *n*-PrMePOEt, respectively. Both reactions occur with net *inversion* of configuration at phosphorus. The maximum optical yields, determined at very low phosphine conversions, were 96 ± 5% for (−)-(*S*)-2 and 78 ± 4% for (+)-(*S*)-3. Optical yields are very sensitive to reaction times and conversions, because the product phosphonites are readily racemized by EtOH formed during reaction. *If indeed these substitutions take place via phosphoranyl radicals*, then the stereochemistry for reaction of (−)-(*S*)-2 is consistent with the π^* electronic configuration and presumed tetrahedral geometry normally assigned to phenyl-substituted phosphoranyl radicals such as [MePhP(OEt)CH$_2$Ph]·. Potential trigonal-bipyramidal intermediates are considered for [*n*-PrMeP(OEt)CH$_2$Ph]· with the assumption that the EtO· in initial adducts is apical and that the PhCH$_2$ departs exclusively from the apical position. From consideration of possible intramolecular rearrangements of various modes available to these intermediates, it is concluded that mode 1 permutations with the vacant equatorial position (odd electron) remaining equatorial are not operative. Thus TBP phosphoranyl radicals do not mimic truly pentacovalent phosphorus intermediates in their permutational properties. The stereochemistry is readily accounted for by single mode 4 rearrangements which leave the odd electron equatorial and bring the PhCH$_2$ apical. A single mode 5 permutation before α-scission would accomplish the inversion of phosphorus configuration but is discounted on the basis of perceived stereochemical difficulties associated with the mode 5 process. *Overall* mode 4 rearrangements via two successive mode 2 or mode 1 rearrangements via an odd-electron-apical intermediate cannot be excluded, but are again not reflective of the properties of truly pentacovalent phosphorus intermediates. A new three-dimensional mode 4 topological graph is presented. The graph is used to discuss the overall stereochemistries of the reactions in terms of the formation, possible mode 4 permutational isomerizations, and α-scissions of phosphoranyl radical intermediates from reaction of both (*S*)- and (*R*)-3 with EtO· *These conclusions must remain provisional being based on the presumed intermediacy of phosphoranyl radicals and assumptions concerning their initial geometries.*

Free-radical substitutions occur on carbon atoms only in specially constructed molecules.[1,2] Trivalent phosphorus, and certain other heteroatoms, however, undergo substitution with ease, when X· and Y· of eq 1 are appropriately chosen.[2] Such systems also

$$Y\cdot + PX_3 \xrightarrow{a} \underset{\mathbf{1}}{Y\dot{P}X_3} \xrightarrow{b} YPX_2 + X\cdot \qquad (1)$$

offer the opportunity to study the stereochemistry of substitution because of the stability of trivalent phosphorus toward pyramidal inversion. These reactions are of additional interest because of the possibility that they proceed via phosphoranyl radical intermediates, 1.[3] The overall stereochemistry of substitution via 1 could be strongly dependent on the configuration of such an intermediate and on the nature of potential ligand exchange processes which could permute the positions of the substitutents on phosphorus prior to α-scission, step 1b. The opportunity to study the stereochemistry of a free-radical substitution reaction taking place at a hetero atom is rare even though such reactions occur with a variety of elements. The substitution reactions of free radicals with optically active tertiary phosphines have not been previously investigated.

The reactions of ethoxy radicals with the optically active phosphines 2 and 3 were chosen for study. The replacement of a P–Et bond with an EtO–P bond should be favorable by about 20 kcal/mol, on the basis of average bond strengths.[3a,d] The substitution sequence shown in eq 2 would be driven by another approximately 15 kcal/mol, the resonance energy of the benzyl radical.[4] The alternative β-scission reaction (reaction 2b), also



2, R = Ph
3, R = *n*-Pr

4

(2)

available to intermediate 4, is disfavored kinetically by the relatively unstable Et· formed, although it is nonetheless strongly exothermic. The substitution reactions of both 2 and 3 with ethoxy radical were found to proceed with predominant inversion of configuration at phosphorus in the phosphinites formed. This finding provides experimental evidence supportive of the earlier postulation that phosphoranyl radicals like 4 when R is Ph are ligand-π species, 5.[5] Further, if the trigonal-bipyramidal sort of phosphoranyl radical 6 or 14 which should result from reaction of ethoxy radical with phosphine 3 is actually the intermediate through which the great majority of the reaction proceeds, then conclusions relative to permissible permutation modes[6] consistent

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(1) As an example, see: Incremona, J. H.; Upton, C. J. *J. Am. Chem. Soc.* **1972**, *94*, 301.

(2) Ingold, K. U.; Roberts, B. P. "Free-Radical Substitution Reactions"; Wiley-Interscience: New York, 1971.

(3) For reasonably comprehensive recent reviews, see: (a) Bentrude, W. G. In "Reactive Intermediates"; Abramovitch, R. A., Ed.; Plenum: London, 1983; Vol. 3, pp 199–298. (b) Bentrude, W. G. *Acc. Chem. Res.* **1982**, *15*, 117. (c) Roberts, B. P. In "Advances in Free Radical Chemistry"; Williams, G. H., Ed.; Heyden and Sons: London, 1979; Vol. 6, pp 225–289. (d) Bentrude, W. G. In "Free Radicals"; Kochi, J. K., Ed.; Wiley-Interscience: New York, 1973; Chapter 22. (e) Schipper, P.; Janzen, E. H. J. M.; Buck, H. M. *Top. Phosphorus Chem.* **1977**, *9*, 407. More brief reviews emphasize our work: (f) Bentrude, W. G. In "Organic Free Radicals"; Pryor, W. A., Ed.; American Chemical Society: Washington, DC, 1978; ACS Symp. Ser. No. 69, Chapter 20 (g) Bentrude, W. G. *Phosphorus Sulfur* **1977**, *3*, 109.

(4) From data of: Benson, S. W. *J. Chem. Educ.* **1965**, *42*, 502. Kerr, J. A. *Chem. Rev.* **1966**, *66*, 465.

(5) Boekstein, G.; Jansen, E. H. J. M.; Buck, H. M. *J. Chem. Soc., Chem. Commun.* **1974**, 118. Davies, A. G.; Parrott, M. J.; Roberts, B. P. *Ibid.* **1974**, 973.

(6) Permutation modes discussed are among those codified (M$_1$–M$_5$) by Musher (Musher, J. I. *J. Am. Chem. Soc.* **1972**, *94*, 5662. Musher, J. I. *J. Chem. Educ.* **1974**, *51*, 94). Each mode designation specifies, within the context of TBP geometry, a particular and unique rearrangement with respect to the number and types of ligands (apical or equatorial) involved and the stereochemistry of the process without any regard to pathway (mechanism).

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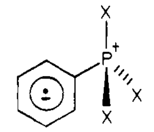
Table I. Reaction of (+)-(*S*)-3 with EtO· in C_6H_5 at 70 °C

	reaction conditions			product yields (%)[b] and optical purities (OP)[d]					
expt	4[a]	$(EtO)_2N_2$[a]	*T*, min	4-oxide[i] (OP)	10-oxide (OP)	MeP(O)-$(OEt)_2$	$(EtO)_3$-PO	$(PhCH_2)_2$[f]	% OY[l]
1	1.5	0.10[g]	70	91 (*j*)	5.3 (9 ± 1)	0[c]	0[c]	6.4	9 ± 1
2	1.7	0.10[g]	30	95 (46 ± 1)	3.1 (29 ± 1)	0[c]	0[c]	3.8	63 ± 4
3	1.2	0.07[h]	30	*e* (52 ± 2)[j]	*e* (42 ± 2)	*e*	*e*	2	78 ± 4[k]

[a] mmol dissolved in 40 mL of argon-purged C_6H_6. [b] Measured by GLC after oxidation with 1 to 3 molar equiv of *t*-BuOOH. [c] Less than 1%, limit of GLC detection. [d] On material isolated after stereospecific *t*-BuOOH oxidation, (−)-*t*-BuPhP(S)OH method. [e] Not determined in this case. [f] Corrected for the fact that 2 mol of $PhCH_2$ gives 1 mol of bibenzyl. [g] Old sample containing EtOH. [h] Freshly prepared. [i] Corrected for 85 ± 5% yield of *t*-BuOOH oxidation. [j] OP of 4-oxide from *t*-BuOOH oxidation of 4 before reaction with EtON=NOEt, 54 ± 1%. [k] Based on 54 ± 1% OP of starting 4, footnote *j*. [l] OY = optical yield.

with the observed stereochemistry can be made. The permissible rearrangements (modes 4 and 5) will be discussed along with the conclusion that mode 1 permutations, those operative with trigonal-bipyramidal pentacovalent phosphorus intermediates, are not rapid for the potential phosphoranyl radical, 4, formed from 3 unless intermediates with the vacant position (or odd electron) of the trigonal-bipyramid apical (6) are of relatively low energy.



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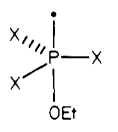

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Results

The optically active phosphines, (−)-(*S*)-2 and (+)-(*S*)-3, were prepared via a recently devised route using chiral *S*-alkyl *O*-isopropyl methylphosphonothioates as the highly optical pure precursors.[7] As a convenient source of ethoxy radicals, ethyl hyponitrite was chosen. Alkyl hyponitrites undergo thermal decomposition at convenient temperatures to yield nitrogen and alkoxy radicals.[8] The half-life for the first-order decomposition of $EtON_2OEt$ is about 25 min at 65 °C.[8c] Before the stereochemistry of free-radical displacement could be determined, it was necessary to identify the main products of reaction and examine in cursory fashion the effects of certain reaction variables on product distribution.

Products of Reaction of Phosphine 2. Products from the reaction of phosphine 2 (ca. 0.17 M) with EtO· in deoxygenated benzene solution at 70 °C are shown in Figure 1. All products which accounted for more than 1% of total product area as determined by GLC were identified. Each product in Figure 1 is plotted in terms of its accountability for reacted 2 using GLC areas determined with a thermal conductivity detector. The formation of EtOPMePh is consistent with the displacement of benzyl radical by ethoxy radical according to process a of eq 2. (Of course no evidence regarding the presence of 4 can be inferred.) 1,2-Diphenylethane formation (eq 3) is the normal course of reaction

$$2PhCH_2\cdot \rightarrow PhCH_2CH_2Ph \qquad (3)$$

for benzyl radicals formed in solution. Over a range of consumption of 2 of 9 to 80%, $PhCH_2CH_2Ph$ accounted for a nearly constant 82 ± 8% of consumed 3. (Accountability percentage assumes stoichiometry of reaction 3.) As the consumption of 2 increases, accountability in terms of EtOPMePh falls sharply. This is in part because this product itself begins to be consumed by oxidation reaction 4. In addition reaction 4 produces ethyl radicals

$$EtO\cdot + EtOPMePh \rightarrow Et\cdot + EtOP(O)MePh \qquad (4)$$

which in turn are able to displace benzy radicals 2 (equation 5) providing a second route for its consumption. The occurrence of reaction 4, once the levels of EtOPPhMe become increased, is not surprising as *n*-PrPMePh gives largely oxidation on reaction with *tert*-butoxy radicals.[9] Evidently, after the stable benzyl radical

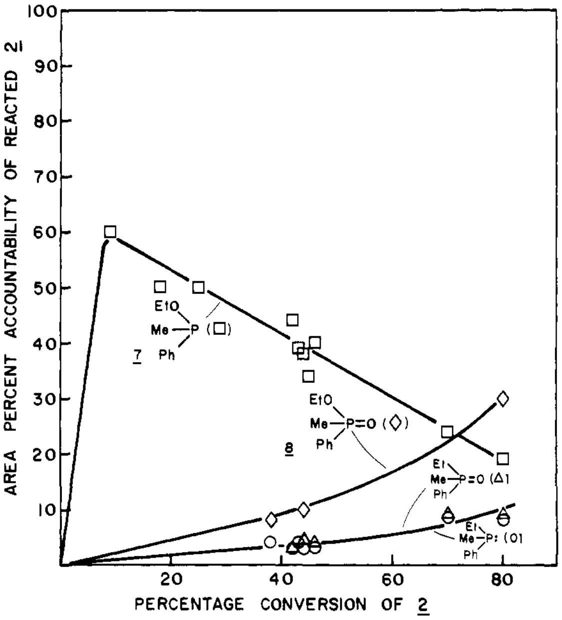

Figure 1. Products of reaction of 0.17 M benzene solutions of 2 with EtO·. Plots show GLC area percentage accountability of reacted 2 in terms of each product as a function of percentage consumption of 2.

$$Et\cdot + 2 \rightarrow MePhPEt + PhCH_2\cdot \qquad (5)$$

is displaced, the remaining methyl substituent is not replaced by EtO· even though process 4 yields only the relatively unstable ethyl radical. Reaction 5 is fully consistent with substitution reactions we have observed on reaction of ethyl radicals with various RP-$(OEt)_2$.[10] The product MePhPEt is further oxidized by EtO·. The constancy of accountability of 2 in terms of $PhCH_2CH_2Ph$ throughout the reaction is consistent with the generation of $PhCH_2\cdot$ in *both* of the reactions, (2a) and (5), which consume 2. Ethoxy radicals may also generate some EtOPMePh via reaction 6. A radical Arbuzov-like process involving Et· and EtOPMePh also may lead to some MePhP(O)Et.

$$EtO\cdot + MePhPEt \rightarrow MePhPOEt + Et\cdot \qquad (6)$$

In the stereochemical studies described below, the optically active EtOPMePh is oxidized by *t*-BuOOH to EtOP(O)MePh before isolation. To avoid the inclusion in the isolated EtOP(O)MePh of material of uncertain stereochemistry formed by reaction 4 and from oxidation of MePhPOEt formed via process 6, reactions were run to low conversions in which EtOPMePh arises only from reaction 2a.

Products of Reactions of Phosphine 3. Products from reaction of 3 with EtO· from $(EtO)_2N_2$ decomposition in argon-flused benzene solution are given in Figure 2 and Table I. Products

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[7] Bentrude, W. G.; Moriyama, M. *J. Am. Chem. Soc.* **1983**, *105*, 4727. Moriyama, M.; Bentrude, W. G. *Tetrahedron Lett.* **1982**, 4547.

[8] (a) Kiefer, H.; Traylor, T. G. *Tetrahedron Lett.* **1966**, 6163. (b) Partington, J. R.; Shaw, C. S. *J. Chem. Soc.* **1932**, 2589. (c) Bentrude, W. G.; Min, T. B. *J. Am. Chem. Soc.* **1976**, *98*, 2918.

[9] Bentrude, W. G.; Hargis, J. H.; Johnson, N. A.; Min, T. B.; Rusek, P. E., Jr.; Tan, H. W.; Wielesek, R. A. *J. Am. Chem. Soc.* **1976**, *98*, 5348.

[10] Hansen, E. R., unpublished results from this laboratory.

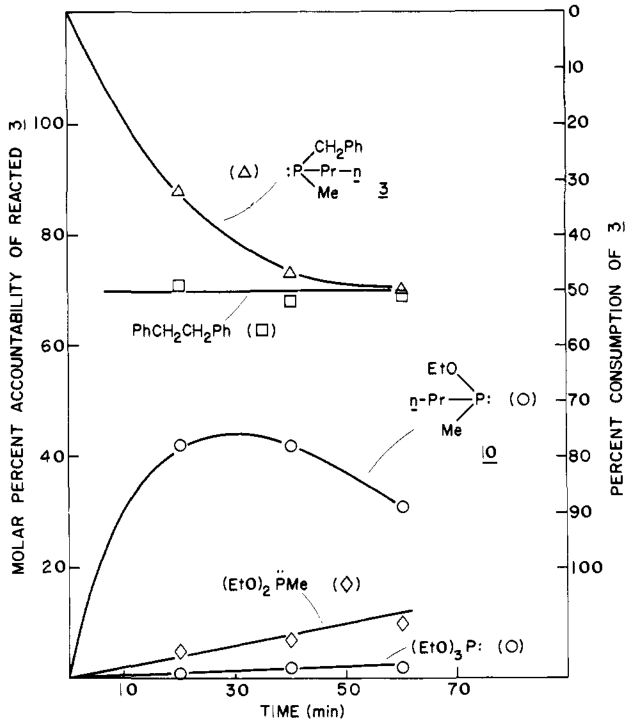


Figure 2. Products of reactions of 0.06 M benzene solutions of 3 with EtO·. Plots show molar accountability of reacted 3 in terms of each product as a function of reaction time. The percentage of 3 reacted (right-hand *Y* axis) is also shown.

shown in Table I are those determined by GLC analysis *following* addition of *t*-BuOOH. This oxidation usually proceeds quantitatively[11] but with 3 gave only 85 ± 5% yields of 3-oxide. (Yields given are so-corrected.) For the other products, the oxidation with *t*-BuOOH was presumed to be quantitative. GLC analyses were carried out in all cases before *t*-BuOOH oxidation to show the presence of EtOPMePr-*n* and unreacted 3 and to be certain that oxide formation had not occurred accidentally. The products found are consistent with the operation of the following reactions:

$$n\text{-PrMePCH}_2\text{Ph} + \text{EtO}\cdot \rightarrow \underset{\mathbf{10}}{n\text{-PrMePOEt}} + \text{PhCH}_2\cdot \quad (7)$$

$$2\text{PhCH}_2\cdot \rightarrow \text{PhCH}_2\text{CH}_2\text{Ph} \quad (8)$$

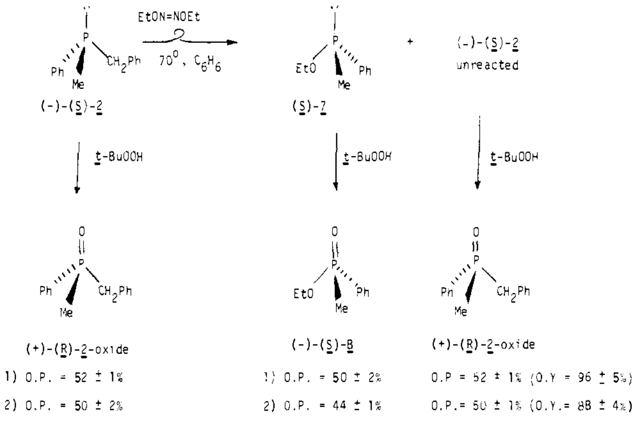
$$n\text{-PrMePOEt} + \text{EtO}\cdot \rightarrow \text{MeP(OEt)}_2 + n\text{-Pr}\cdot \quad (9)$$

$$\text{MeP(OEt)}_2 + \text{EtO}\cdot \rightarrow (\text{EtO})_3\text{P} + \text{Me}\cdot \quad (10)$$

In Figure 2 molar percent accountabilities of consumed 3 in terms of each product are plotted as a function of time during a single reaction of 3 run to only moderate conversions. Percent consumption of 3 is also shown. (Although each product and remaining 3 were determined as the oxide, all are shown in Figure 2 in trivalent form in accordance with eq 7, 9, and 10.) The importance of reaction 7 peaks early as does that of reaction 2a (Figure 1). Processes 9 and 10 do not occur at the low conversions of Table I, but they become increasingly important, as would be expected, at high conversions. Thus in Figure 2, as the amount of remaining phosphine decreases from 70 to 50% (20–60 min), there is a steady increase in MeP(OEt)_2 and $(\text{EtO})_3\text{P}$. Again the accountability of 3 in terms of $\text{PhCH}_2\text{CH}_2\text{Ph}$ formed is nearly constant, ca. 70% (yield corrected for the formation of only 0.5 mol of $\text{PhCH}_2\text{CH}_2\text{Ph}$ for each 1 mol of $\text{PhCH}_2\cdot$ formed). In the very low conversions of experiments 1 and 2 of Table I, the accountabilities of reacted 3 in terms of 10-oxide appear to be over 60%.

Total molar accountabilities (sum of remaining 3-oxide, EtOP(O)MePr-*n*, $(\text{Et}_2\text{O})_2\text{P(O)Me}$, and $(\text{EtO})_3\text{PO}$) after *t*-BuOOH oxidation, which are not easily determined directly from Figure 2, go down progressively from 84% (20 min) to 69% (60 min). In the very low conversions of Table I, total accountability as high as 98% is seen. Evidently, unidentified processes consume phosphine and 10 to an increasing extent at higher conversions. A minor product was tentatively identified as $n\text{-Pr}_2\text{PMe}$ from substitution analogous to process 5.

Scheme I



Further oxidations of the substitution products, EtOPMePr-*n*, MeP(OEt)_2, and $(\text{EtO})_3\text{P}$, by EtO·, e.g., eq 11, are not major

$$\text{EtO}\cdot + \text{EtOPMePr-}n \rightarrow \text{Et}\cdot + \text{EtOP(O)MePr-}n \quad (11)$$

components of this reaction system as shown by GLC analysis prior to *t*-BuOOH oxidation. In the absence of phenyl substituents on phosphorus, alkyl radical displacement rather than oxidation is the rule when the transfer of oxygen would yield a relatively unstable radical such as Et·.[10]

GLC analysis of the reaction mixtures before heating, but after $(\text{EtO})_2\text{N}_2$ addition, showed less than 1% of the phosphine oxide to be present and that EtOPMePr-*n* was not formed. After heating but before oxidation with *t*-BuOOH, 2–3% of the phosphine oxide from 3 was sometimes present. We showed the air oxidation of both 2 and 3 to be stereospecific and retentive in stereochemistry. Therefore air oxidation does not affect the analyses of optical yield.

Stereochemistry of Reactions of EtO· with (−)-(*S*)-2. Following reaction of 1.0–1.4 mmol of (−)-(*S*)-2 with ethoxy radicals from decomposition of hyponitrite in deoxygenated benzene, the reaction mixtures were oxidized at 5 °C with an excess of *t*-BuOOH. The volatile materials were removed under vacuum, and the phosphinate 8 and phosphine oxide, formed from the remaining 2, were separated by preparative TLC. The optical purity of the isolated (+)-2 oxide was determined either by comparison to that of optically pure material (+51.4°)[12] or by ^{1}H NMR through use of the optically active shift reagent, (−)-*t*-BuPhP(S)OH, as described in the Experimental Section. The latter is preferred, because it avoids the errors which come from contaminants. Similarly, the specific rotation for isolated EtOP(O)MePh was measured in early work (lit.[13] −49°, *S* enantiomer); but later on, the (−)-*t*-BuPhP(S)OH method was used for it as well. The results of these studies, done under a variety of conditions, appear in Table II. The formation of (−)-(*S*)-8 from (−)-(*S*)-2 establishes that *the predominant route of the substitution process in which 2 is converted to EtOPPhMe (7) involves inversion of configuration at phosphorus.* The stereochemistry of the conversion of (−)-(*S*)-2 to (*S*)-7 and subsequently to (−)-(*S*)-8 is depicted in Scheme I. The optical purities (OP) and optical yields (OY) given are for the two best cases of Table II. (See Discussion below.) Errors are simple averages of the deviations of individual measurements of optical purity and optical yield (See Experimental Section) from the average value.

In many cases a portion of the starting optically active phosphine was oxidized with *t*-BuOOH and its optical purity compared to

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(11) Denney, D. B.; Hanifin, J. W., Jr. *Tetrahedron Lett.* **1963**, 2177. Marsi, K. L. *J. Org. Chem.* **1974**, *39*, 265.

(12) Nauman, G.; Zon, G.; Mislow, K. *J. Am. Chem. Soc.* **1969**, *91*, 7012.

(13) DeBruin, K. E.; Perin, D. E. *J. Org. Chem.* **1975**, *40*, 1523.

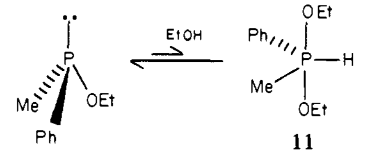
Table II. Reactions of (−)-(*S*)-2 with EtO· in C_6H_6 at 70 °C[a]

expt	mmol of phosphine	mmol of $(EtO)_2N_2$	reaction time, min	mmol of added EtOH	area percentage[j] MePhP(O)-CH_2Ph[f]	MePhP(O)-OEt[f] (8)	$(PhCH_2)_2$	optical purity, % MePhP(O)-CH_2Ph[f]	MePhP(O)-OEt[f]	method	% OY[k]
1	1.0	0.10[b]	60	0	92	5	3	43	22	A[d]	51
2	1.0	0.10[b]	60	0.26	89	8	3	41	7	A	17
3	1.0	0.10[c]	60	0	84	11	5	26	20	A	77
4	1.0	0.10[c]	60	1.7	89	8	3	25	1	A	4
5	1.3	0.10	80	0	89	7	4	69	48	B[g]	70
6	1.4	0.10	30	0	93	5	2	64	51	B	80
7	1.2	0.09	30	0	94	5	1	50 (51[h])	44	B	88
8	1.0	0.1	60	0	91	6	3	58	43	A	74
9[i]	1.0	0.4	60	0	64	23	13	54	5	A	9
10	1.0	0.4	60	0	54	28	18	56	8	A	15
11	1.1	0.09[c]	15	0	97 (96[e])	2 (3[e])	0.5 (1[e])	52 (52[h])	50	B	96

[a] In 40 mL of argon-flushed benzene. [b] Sample refrigerated several months. [c] Freshly prepared sample. [d] From $[\alpha]^{25}{}_D$ in MeOH(MePhP(O)OEt)[13] or C_6D_6 (MePhP(O)CH_2Ph). [e] Trivalent products before *t*-BuOOH oxidation. [f] From *t*-BuOOH oxidation. [g] ^{1}H NMR with added *t*-BuPhP(S)OH. [h] OP of oxide from *t*-BuOOH oxidation before reaction. [i] Volume of benzene 3 mL. Three percent MePhP(O)Et also formed. [j] Minor amounts of other products are ignored. [k] OY = optical yield.

that of 2-oxide isolated after the reaction. In no case was there a difference of more than 3% in optical purities. Thus, 2 is not racemized under the reaction conditions. We believe that the optical purity of the phosphine oxide resulting from *t*-BuOOH oxidation is a better indication of the optical purity of phosphine 2 than is its own specific rotation.[14] (Use of the latter gave higher optical purities.) The *t*-BuOOH oxidation is generally stereospecific[11] and proved to be so with phosphine 3 which was reoxidized with *t*-BuOOH to oxide of the same optical purity (rotation or ^{1}H NMR) as that from which the phosphine was formed by reduction with $PhSiH_3$.[11]

The results in Table II clearly show that the optical yield of the conversion of (−)-(*S*)-2 to (*S*)-7 is strongly dependent on the extent of conversion of 2, the concentration of reactants, and the amount of EtOH present. The area percentages of unreacted 2 (oxide) and product MePhPOEt (oxide) give a rough indication of the degree of conversion of 2. Thus in experiments 1–4 in which conversions of 2 are similar, the presence of EtOH greatly reduces the optical yield of the reaction. $(EtO)_2N_2$ which has been stored in the refrigerator for several months shows ^{1}H NMR spectral evidence for the formation of traces of EtOH. The use of freshly prepared hyponitrite in experiment 3 raises the optical yield to 77% from the 51% obtained with hyponitrite which was several months old (experiment 1). Deliberate addition of EtOH greatly reduced optical yields in experiments 2 and 4. When not otherwise indicated, the hyponitrite used was reasonably fresh. Of course at higher conversions and with larger amounts of hyponitrite (experiments 9 and 10), more EtOH from abstraction of hydrogen by EtO· would be expected to result. The effect of EtOH, which we surmise is probably the result of the formation of symmetrical intermediate **11**, would also be greater kinetically at higher concentrations of reactants, experiment 9. Extensive racemization of the product results. With reactions 3, 6, 7, 8, and 11, optical yields ranging 74–96% were encountered, each case being one in which conversion of 2 was low. Indeed, the highest optical yield, 96 ± 5%, was obtained with freshly prepared hyponitrite and a very short reaction time, experiment 11.



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Stereochemistry of Reactions of EtO· with (+)-(*S*)-3. In view of the above reaction variable studies, it was not necessary to do the same with the reactions of ethoxy radicals with (+)-(*S*)-3. Thus, reactions were run to low conversions as shown in Table I. The optical purity of the starting phosphine was determined by its reoxidation to 3-oxide following reaction with EtO·. This we showed to be a stereospecific process in connection with the preparation of optically active 3.[7] (See also earlier comment.) In other experiments, the optical purities of 3-oxide formed from starting 3 and that isolated following oxidation were the same; i.e., no racemization occurred during the radical reaction. Immediately following reaction, *t*-BuOOH oxidation was carried out on the products (see Scheme II), which had been examined by GLC to determine that prior oxidation had not occurred. Phosphinate 10 and (+)-(*S*)-3-oxide were isolated by preparative TLC and their optical purities determined by use of (−)-*t*-BuPhP(S)OH and ^{1}H NMR. The results of these studies appear in Table I. Reduced reaction times clearly increase optical yield (experiments 1 and 2). The use of freshly prepared hyponitrite, experiment 3, is also essential to obtaining an optimum optical yield (78 ± 4%). Scheme II summarizes experiment 3.

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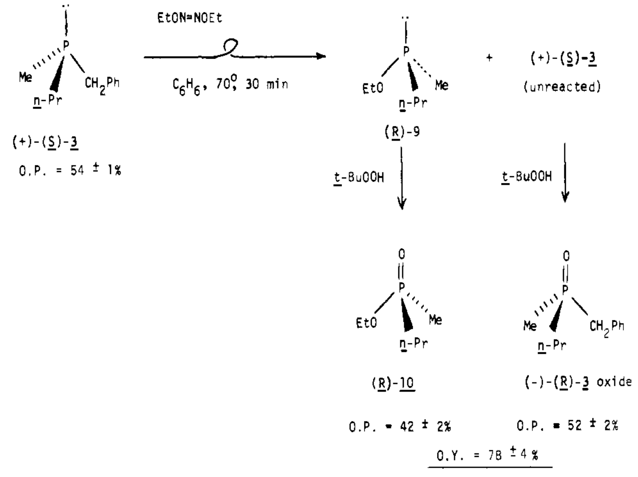
[14] It seems to us quite possible that the value of the specific rotation reported for phosphine 2, believed to be at least 95% optically pure (Kyba, E. P. *J. Am. Chem. Soc.* **1975**, *97*, 2554), is still too low because of the extreme ease of oxidation under conditions for determination of optical rotation.

Scheme II

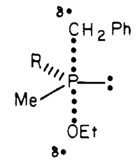


The absolute configuration of the predominant enantiomer of product 10 was determined by comparing the relative chemical shift of its MeP doublet in the presence of added (−)-*t*-BuPhP(S)OH to that of a sample of (*R*)-10 supplied to us by C. R. Hall.[15] Addition of the latter enhanced the intensity of the *upfield* pair of MeP doublets, $\delta\Delta = 2.6$ Hz at 300 MHz.

Discussion

The reactions of both (−)-(*S*)-2 and (+)-(*S*)-3 with ethoxy radicals yield substitution products, the corresponding ethyl phosphinites, (*S*)-7 and (*R*)-9, with high optical efficiencies and inversion of configuration at phosphorus. Indeed, were one able to study the reactions at extremely low phosphine conversions, 100% optical yields might be obtainable.

The simplest and mechanistically most economical way to view these reactions is in terms of a one-step, inline displacement process of the type represented by 12 which nicely accounts for the



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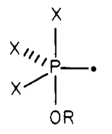
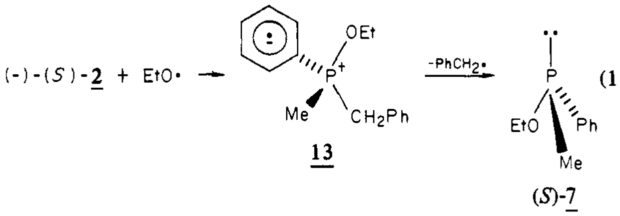


14

predominant observed stereochemistry. However, in a very large number of systems (more than 350) in which free radicals are generated in the presence of trivalent phosphorus compounds, transient phosphoranyl radical species have been detected,[3a] the breakdown of which gives the overall chemistry observed. Equation 2 depicts the observed substitutions of this study in terms of such an intermediate, 4. Though such intermediates have not been observed in substitution reactions in which a benzyl radical is displaced, their presence has been observed in ESR investigations of the reactions of *t*-BuO· with (PhO)$_3$P in which the very stable PhO· is generated.[16] Of course the formation of phosphoranyl radicals does not prove that they are necessarily intermediates along the major reaction pathway in any case. Chemical labeling studies, nonetheless, have indicated that this is so in reactions of alkoxy radicals with trialkyl phosphites.[8c,17] Therefore, it seems reasonable to consider the above stereochemical results in terms of possible phosphoranyl radical intermediates which could lie along the reaction pathway in the substitution processes investigated.

Potential Intermediate from (*S*)-2. Phenyl-substituted phosphoranyl radicals are generally ligand-π species, 5, unless the other substituents on phosphorus destabilize the positive charge on phosphorus.[5] Ligand-π radicals include (PhP(OR)$_2$OBu-*t*)·, (Ph$_2$P(OR)$_2$)·, (Ph$_3$POBu-*t*)·, and numerous radicals containing only aryl substituents on phosphorus.[3,5] If indeed the reaction of (−)-(*S*)-2 does proceed via a phosphoranyl radical intermediate, it most surely is a ligand-π species. Assuming that the low isotropic phosphorus hyperfine splittings (<50 G) typical of these radicals mean not only that the odd electron is primarily located in the π system but also that the configuration about phosphorus is tetrahedral, then the inversion of stereochemistry observed in the displacement of PhCH$_2$· by EtO· is just what would be predicted for a ligand-π intermediate, 13. This is shown in reaction 12. Loss of benzyl radical from intermediate 13 yields (*S*)-7.



(12)

Potential Intermediates from (*S*)-3 and Possible Rearrangement Modes. Consideration of the stereochemical outcome of the reaction of ethoxy radicals with (+)-(*S*)-3 is not so straightforward since, if an intermediate is involved, one is most likely dealing with a trigonal-bipyramidal (TBP) species, as illustrated by 14. Thus, Me$_3\dot{P}$OBu-*t* has a structure which corresponds to 14 with X = Me.[18,19b] It is very clear from variable temperature ESR results that radical 14 with X = Me, H, or F undergoes a very rapid isomerization, probably of an intermolecular nature, in which the positions of the X groups are permuted over the TBP framework.[19] The stereochemical outcome of a substitution reaction of the type under consideration, were it to proceed via an intermediate like 14, would depend on the position of RO in the initially formed adduct and on the stereochemical mode[6] of the process which permutes the substituents, X. We have argued elsewhere[17a-d,3b,20] for the reasonableness of the initial irreversible, site-specific, apical introduction of the alkoxy group in a species such as 14. Kinetic ESR evidence for the microscopic reverse process, stereospecific apical α-scission, has been presented.[19b,21] Therefore, if the substituent to be displaced is not initially in the apical position, the overall stereochemistry of substitution will depend on the particular permutation mode which must of necessity move the leaving substituent to the apical position. This is illustrated by eq 13. (The numbers in parentheses are from Figure 3 and will be used later.) The intermediate 15 of eq 13 is one of two TBP species (15 and 16) with odd electron equatorial and benzyl non-apical formed from apical introduction of the ethoxy radical on reaction of (+)-(*S*)-3 with EtO·.

A reasonable argument can be made for the idea that in fact a majority of the initial attack by ethoxy radical should give 15 and 16. Statistically, 15 and the other benzyl-equatorial isomer, 16, would result 66% of the time. In fact for trialkylphosphines with various combinations of alkyl groups such as *t*-Bu, *n*-Bu, *n*-Pr, and *i*-Pr on phosphorus, ESR results[19b] suggest that on reaction

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[15] A sample of (*R*)-10 received from C. R. Hall was shown by use of (−)-*t*-BuPhP(S)OH at 300 MHz to be identical with the predominant enantiomer formed in our system. The material provided us had been prepared according to the procedure of Hall and Williams (Hall, C. R.; Williams, N. E. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2746), applied in their paper (Scheme 7) to the preparation of (*R*)-methyl methylphenylphosphinate.

[16] Davies, A. G.; Parrott, M. J.; Roberts, B. P. *J. Chem. Soc., Perkin Trans. 2*, **1976**, 1066.

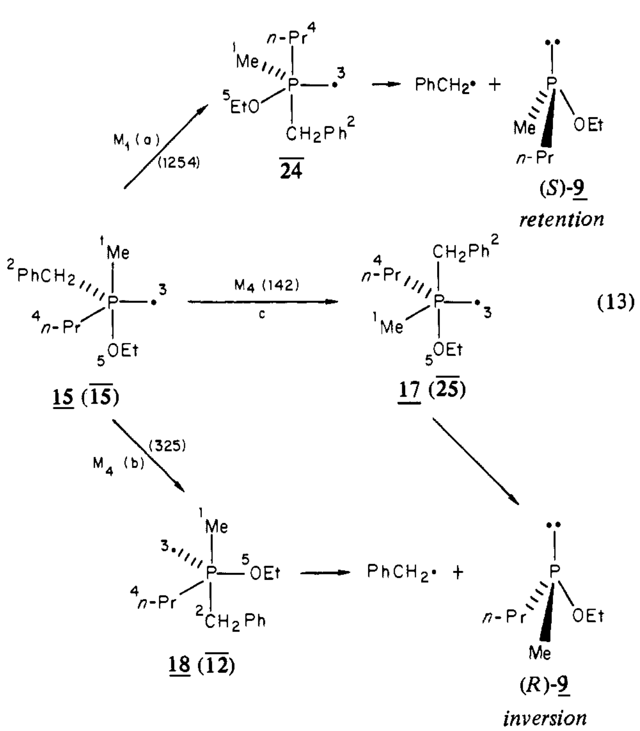
[17] (a) Bentrude, W. G.; Wielesek, R. A. *J. Am. Chem. Soc.* **1969**, *91*, 2406. (b) Bentrude, W. G.; Min, T. B. *Ibid.* **1972**, *94*, 1025. (c) Nakanishi, A.; Nishikida, K.; Bentrude, W. G. *Ibid.* **1978**, *100*, 6403. (d) Nakanishi, A.; Nishikida, K.; Bentrude, W. G. *Ibid*, **1978**, *100*, 6398. (e) Hay, R. S.; Roberts, B. P. *J. Chem. Soc., Perkin Trans 2* **1978**, 770.

[18] Krusic, P. J.; Mahler, W.; Kochi, J. K. *J. Am. Chem. Soc.* **1972**, *94*, 6033.

[19] (a) Krusic, P. J.; Meakin, P. *Chem. Phys. Lett.* **1973**, *18*, 347. (b) Copper, J. W.; Roberts, B. P. *J. Chem. Soc., Perkin Trans. 2* **1976**, 808. (c) Elson, I. H.; Parrott, M. J.; Roberts, B. P. *J. Chem. Soc., Chem. Commun.* **1975**, 586.

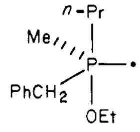
[20] Nakanishi, A.; Bentrude, W. G. *J. Am. Chem. Soc.* **1978**, *100*, 6271.

[21] Davies, A. G.; Dennis, R. W.; Roberts, B. P. *J. Chem. Soc., Perkin Trans. 2* **1974**, 1101.

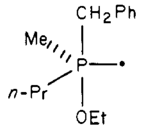


(13)

with RO· the three alkyl groups distribute themselves rather unselectively into the apical site from which they are rapidly lost by α-scission with little regard for the stability of the alkyl radical. Unless the benzyl group by virtue of its slightly greater electronegativity biases the process of formation of the intermediates, a fairly unselective distribution of **15**, **16**, and **17** should prevail. Since Me_2N and EtO which have quite different electronegativities have only small apicophilicity differences,[22] it is unlikely that the benzyl group should be strongly biased toward the apical position.



16



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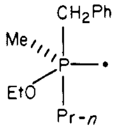

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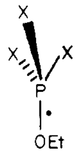


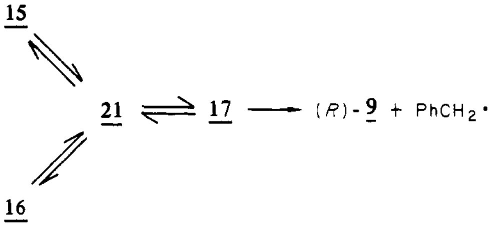
21

Route a, eq 13, is a mode 1 (M_1) permutation[6] to give an intermediate which on loss of apical benzyl radical yields a product of retained configuration at phosphorus, (*S*)-**9**. Mode 1 is that permutation characteristic of pentacovalent phosphorus intermediates.[23] Step 13a keeps the odd electron equatorial as would be expected if it were a sort of electropositive fifth ligand in a pentacovalent-phosphorus-like intermediate for which movement of an electropositive substituent apical occurs only with the sacrifice of considerable energy.[23] Clearly, such an M_1 process involving initial intermediates **15** (path a) does not apply in this case since the observed stereochemistry is very largely inversion. In this regard it *appears that if intermediate* **15** *is the predominant initial intermediate along the pathway by which* (+)-(*S*)-**3** *is converted to* **9**, *then its permutational properties are not those predicted by simple extrapolation of what is known concerning truly pentacovalent phosphorus species*. The same is true of **16**. (The more complex consideration involving successive M_1 isomerization via odd electron apical intermediates will be examined below.) In routes 13b and 13c, a single mode 4 (M_4) permutation preceeds α-scission. The overall stereochemistry following α-scission of intermediates **17** and **18** is inversion, the predominant outcome observed experimentally. Route 13c should be the more rapid process since the ethoxy group remains apical in **17**. Overall M_4 isomerization is observed in variable temperature ESR work with phosphoranyl radicals which involve phosphorus as part of a 5-membered ring[22,24] and is consistent with the stereochemistry of free-radical reactions (oxidation, substitution, radical-Arbuzov) occurring at phosphorus in cyclic systems.[9,20,25] Unfortunately, the mode of permutation for the radicals *t*-$BuOPX_3$ cannot be determined from their variable temperature ESR spectra. The observed stereochemistry for reaction of (+)-(*S*)-**3**, of course, does not require that intermediates such as **15**, (**16**) lie along the major reaction pathway nor does it require that an M_4 permutation occur. It is, however, consistent with both possibilities.

There are two other permutation modes[6] which would involve apical-equatorial ligand exchange in **15** (or **16**) and could thus serve to bring the benzyl group into the apical position prior to α-scission. *Mode 2* (M_2) is a pairwise apical-equatorial exchange of two substituents (here benzyl and Me of **15**) resulting in **19** from which, however, (*S*)-**9** is generated. Simultaneous pairwise exchange of two sets of ligands in **15** via a *mode 5* (M_5) (anti-Berry) permutation gives **20** which on loss of the benzyl radical yields the required (*R*)-**9**. ESR ruled out the M_5 option for the cyclic phosphoranyl radical,[24] but cannot do so here. The *mode 3* (M_3) exchange of two equatorial substituents is not a consideration, because it cannot move the benzyl group into the apical position.

Since the optical yield for the substitution reaction undergone by (+)-(*S*)-**3** is only about 80%, approximately 10% of the reaction could go by a route giving retention of configuration at phosphorus. One possibility is that 90% of the reaction involves initial formation of **17**, from which the benzyl radical departs directly to yield (*R*)-**9**. The other 10% of radical attack might then give **15** or **16** and by way of an M_1 isomerization (reaction 13a) account for a 10% formation of (*S*)-**9**. For the reasons given earlier, it is probable that much greater than 10% of the initially formed intermediate is **15** or **16**. In view of the demonstrated effects of EtOH, it is more likely that the apparent 80% optical yield is actually a result of partial (10%) racemization of (*R*)-**9** prior to its oxidation by *t*-BuOOH.

A plausible unifying explanation for the observed stereochemistry of reaction of EtO· with (+)-(*S*)-**3** in terms of M_4 processes involves initial addition of EtO· to form an intermediate (or transition state) of C_{3v} geometry, a σ^* species, like **21**. Radical **12** could randomly (or selectively) give **15**, **16**, and **17** and also would provide the common intermediate for their interconversion via an M_4 permutation mode:



(14)

Initial formation of σ^* phosphoranyl radicals and their possible intermediacy in M_4 processes has been proposed earlier by Roberts.[17e,24] That σ^* phosphoranyl radicals should not be very much higher in energy than their TBP counterparts is suggested by the fact that certain phosphoranyl radicals, e.g., $(Ph_3PCl)\cdot$[26] and $(Z_3P)_2{}^{+}\cdot$,[27] have lowest energy σ^* configurations. CNDO

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[22] Cooper, J. W.; Parrott, M. J.; Roberts, B. P. *J. Chem. Soc., Perkin Trans. 2* **1977**, 730. Dennis, R. W. Robert, B. P. *Ibid.* **1975**, 140.

[23] Holmes, R. R. "Pentacoordinated Phosphorus"; American Chemical Society: Washington, DC; 1980; Vol. 2, ACS Monograph 176, Chapter 2. For earlier reviews, see: (a) Ramirez, F. *Acc. Chem. Res.* **1968**, *1*, 168. (b) Westheimer, F. H. *Ibid.* **1968**, *1*, 70. (c) Mislow, K. *Ibid.* **1970**, *3*, 321. (d) Muetterties, E. L. *Ibid.* **1970**, *3*, 266. (e) Holmes, R. R. *Ibid.* **1972**, *5*, 296. (f) Ramirez, F.; Ugi, I. *Bull. Soc. Chim. Fr.* **1974**, 453.

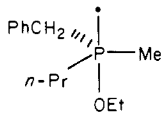
[24] Roberts, B. P.; Singh, K. *J. Chem. Soc., Chem. Commun.* **1979**, 980 and references therein.

[25] Bentrude, W. G.; Alley, W. D. Johnson, N. A.; Murakami, M.; Nishikida, K.; Tan, H. W. *J. Am. Chem. Soc.* **1977**, *99*, 4383.

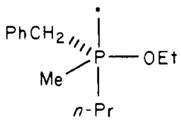
[26] Berclaz, T.; Geoffroy, M.; Lucken, E. A. C. *Chem. Phys. Lett.* **1975**, *36*, 677.

calculations also predict that ($MeO\dot{P}Me_3$) should have a σ^* configuration only 3.4 kcal/mol above that of the TBP one.[28]

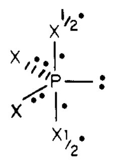
When dealing with possible permutation modes, it is always necessary to remember that observed stereochemistries of reactions are being reconciled with potential *overall* modes. Thus the overall M_4 rearrangement of $\underline{15}$ to $\underline{17}$ can result from two successive M_2 processes by way of intermediate $\underline{22}$ or two successive M_1 permutations via intermediate $\underline{23}$. (The latter is permutationally equivalent to a $(TR)^2$ process.[23f]) In both of these intermediates, however, the odd electron is in the apical position. Once again the permutational property of the phosphoranyl radical would differ from that of a truly pentacovalent phosphorus intermediate, since in such a context, the odd electron should serve as an electropositive ligand which would not enter the apical position without considerable sacrifice of energy. Sulfranes (X_4S:) do indeed behave permutationally as though the lone pair were an electropositive substituent.[29] However, representation of the phosphoranyl radical as in structures $\underline{6}$, $\underline{15}$–$\underline{20}$, $\underline{22}$–$\underline{24}$, etc., is only a convenient approximation. Electronically, a second resonance contributor which must be considered for $\underline{24}$ is $\underline{25}$, a Rundle structure which places the odd electron in a nonbonding orbital with the odd electron entirely on the apical ligands. Molecular orbital representations of the SOMO similar to $\underline{26}$ have been suggested in which the odd electron occupies an orbital with antibonding character and which distributes electron densities between the vacant equatorial position and the apical ligands.[30] Both ab initio and CNDO calculations show that distortion of phosphoranyl radical structures like $\underline{24}$ with C_{2v} symmetry toward the C_{4v} structure, $\underline{27}$, requires a large amount of energy compared to that required to convert $\underline{24}$ into $\underline{28}$ or other odd-electron-apical-like intermediates or transition states.[28,31] Thus an overall M_4 process via successive M_1 steps is worth consideration.



$\underline{22}$



$\underline{23}$



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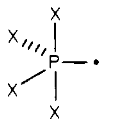

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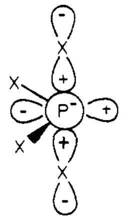

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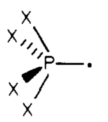
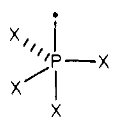


$\underline{27}$



$\underline{28}$

Three-Dimensional Topological Representation of M_4 Permutations. Because of the unusual nature of the M_4 permutation processes to which TBP phosphoranyl radicals may be subject, it is instructive to provide and discuss a topological diagram which shows the possible initial intermediates and accounts systematically for their permutational interconversions. Figure 3 is one of two disjoined, enantiomeric, three-dimensional graphs required to fully describe the reaction of (*S*)- and (*R*)-$\underline{3}$ with the ethoxy radical.[32] The vertices of the polygon represent the four individual TBP radicals formed from (*S*)-$\underline{3}$ (right of the *R*–*S* vertical plane) and the six from (*R*)-$\underline{3}$ (left side of the same plane). The remaining ten structures would be found on the enantiomeric graph which is not shown. The numbering system for the isomers is according to the usual convention.[23c] Thus, e.g., species $\overline{45}$ is the permutamer in which groups 4 and 5 are apical and the substituents 1, 2, and 3 are arranged in counterclockwise fashion when viewed from the lower number apical substituent, 4. The enantiomeric species would be **45**. (See structures for (*R*)-$\underline{3}$ and (*S*)-$\underline{3}$, Figure 3, for numbering of substituents.) The edges of the polygon connect interconvertable permutamers. For each permutamer, the connectivity is six. There is no connectivity between the two disjoined graphs. Thus, enantiomeric structures, e.g., **12** and $\overline{12}$, **24** and $\overline{24}$, etc, cannot be interconverted since they are on different graphs. Similarly, the six permutamers formed on equatorial introduction of EtO on attack on (*S*)-$\underline{3}$ cannot be formed by isomerization of **15**, $\overline{25}$, **35**, or $\overline{45}$. (A similar M_4 graph for substitution in cyclic systems omitted certain permutations perceived to be sterically difficult.[3b])

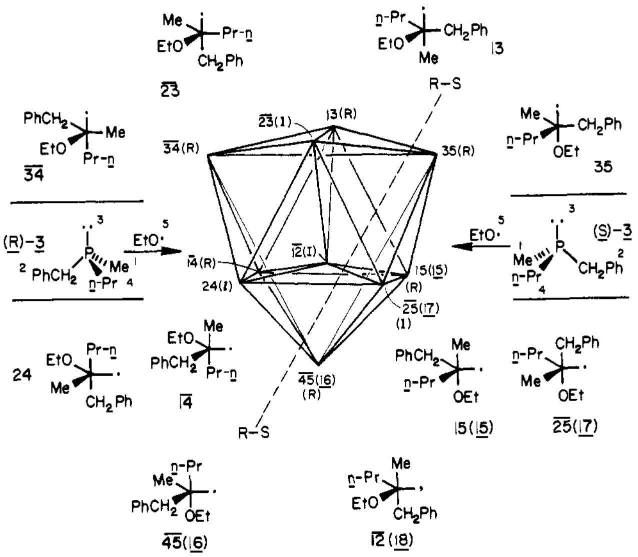


Figure 3. Three-dimensional topological representation for the formation and M_4 isomerization of phosphoranyl radicals from the reaction of (*S*)-$\underline{3}$ and (*R*)-$\underline{3}$ with ethoxy radicals. Underlined numbers, e.g., $\underline{15}$, refer to structures given in the text. Other numbers either barred (e.g., $\overline{15}$) or unbarred (e.g., 15) designate permutational isomers of the above graph.

Species **15**, $\overline{25}$, and $\overline{45}$ are those formed directly from (*S*)-$\underline{3}$ by *apical* introduction of the ethoxy radical and correspond to $\underline{15}$, $\underline{17}$, and $\underline{16}$, respectively, of reactions 13 and 14 discussed above. (Initial formation of **35** can be excluded since RO· oxidations of trivalent phosphorus compounds always occur with retention of configuration at phosphorus. β-Scission of **35** (oxidation) would give inversion.) The designations I and R indicate whether the *overall stereochemistry of the reaction of* (*S*)-$\underline{3}$ *with EtO· would be inversion* (*I*) *or retention* (*R*) if loss of $PhCH_2$· by α-scission were to occur from that particular intermediate, i.e., **15**, $\overline{25}$, **35**, $\overline{45}$, or the others formed thereform by isomerization. The stereochemistry of loss of $PhCH_2$· is *assumed* to be the same as for Z_5P intermediates,[23c] i.e., the reverse of edge or facial attack on pyramidal product phosphinite $\underline{10}$.

As noted in the sequence of reaction 13, from initial $\underline{15}$

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(27) Gara, W. B.; Roberts, B. P. *J. Chem. Soc., Perkin Trans. 2* **1978**, 150. Claxton, T. A.; Fullam, B. W.; Platt, E.; Symons, M. C. R. *J. Chem. Soc., Dalton Trans.* **1975**, 1395.

(28) Gorlov, Y. I.; Penkovsky, V. V. *Chem. Phys. Lett.* **1975**, *35*, 25. Penkovsky, V. V. *Dokl. Akad. Nauk SSSR* **1978**, *243*, 375.

(29) Martin, J. C.; Astrologes, G. W. *J. Am. Chem. Soc.* **1977**, *99*, 4390. Klemperer, W. G.; Krieger, J. K.; McCreary, M. D.; Muetterties, E. L.; Traficante, D. D.; Whitesides, G. M. *Ibid.* **1975**, *97*, 7023.

(30) Representations similar to 26 have been given by Gillbro, T.; Williams, F. *J. Am. Chem. Soc.* **1974**, *96*, 5032. Nishikida, K.; Williams F. *Ibid.* **1975**, *97*, 5462. Hasegawa, A.; Ohnishi, K.; Sogabe K.; Miura, M. *Mol. Phys.* **1975**, *30*, 1367.

(31) Howell, J. M.; Olsen, J. F. *J. Am. Chem. Soc.* **1976**, *98*, 7119.

(32) Other topological graphs of M_4 processes are available. (See: Gielen, M. In "Chemical Applications of Graph Theory"; Balaban, A. T., Ed.; Academic Press: New York, 1976; Chapter 9). However, no *three*-dimensional graph showing all possible isomers seems to be available. The graph of Figure 3 was formed from the ones found in ref 23c by connecting alternate isomers. The relationship of permutational restraints for M_4 isomerizations to stereochemistry in substitution reactions of tetrahedrally substituted phosphorus has been described. Gielen, M.; Willem, R. *Phosphorus Sulfur* **1977**, *3*, 339.

($\overline{\mathbf{15}}$), one M_4 permutation gives $\overline{\mathbf{12}}$ or $\overline{\mathbf{25}}$ ($\underline{\mathbf{15}}$ → $\underline{\mathbf{18}}$, $\underline{\mathbf{15}}$ → $\underline{\mathbf{17}}$, reaction 13) with $PhCH_2$ apical. Not shown in reaction 13 is $\overline{\mathbf{45}}$ ($\underline{\mathbf{16}}$) formation and its potential isomerization to $\overline{\mathbf{25}}$ ($\underline{\mathbf{16}}$ → $\underline{\mathbf{17}}$) or **24**, both with $PhCH_2$ apical as required[19,21] prior to α-scission. Loss of $PhCH_2\cdot$ from **24** or $\overline{\mathbf{25}}$ gives the overall *inversion* at phosphorus required by experiment. Since EtO is in the thermodynamically favored apical position in $\overline{\mathbf{25}}$, its formation from $\overline{\mathbf{45}}$ ($\underline{\mathbf{16}}$) should be especially favored. *Retention* would demand that one of the isomerizations—(1) $\overline{\mathbf{12}}$ → **13** or $\overline{\mathbf{14}}$, (2) $\overline{\mathbf{25}}$ → $\overline{\mathbf{12}}$ or **35**, or (3) $\overline{\mathbf{25}}$ → **24** → $\overline{\mathbf{14}}$ or $\overline{\mathbf{34}}$—occur more rapidly than loss of $PhCH_2\cdot$ from $\overline{\mathbf{12}}$ or $\overline{\mathbf{25}}$. Moreover, all of the retention routes require at the very least the increase in energy associated with the EtO becoming equatorial ($\overline{\mathbf{12}}$, **24**, $\overline{\mathbf{14}}$). Permutamers **35**, $\overline{\mathbf{34}}$, and **13** have the odd electron apical as well. All of these factors make retention highly improbable.

Consideration of the stereochemical consequences of initial formation of the remaining intermediates of Figure 3, which are formed directly from (*R*)-$\underline{3}$ by *equatorial* introduction of EtO, is also instructive. (Comparable intermediates from (*S*)-$\underline{3}$ are on the enantiomeric graph.) Only **24**, $\overline{\mathbf{14}}$, and $\overline{\mathbf{12}}$ are likely as possible initial intermediates as $\overline{\mathbf{34}}$, $\overline{\mathbf{23}}$, and **13** all have the odd electron apical and should be kinetically disfavored. Both $\overline{\mathbf{12}}$ and **24** have the $PhCH_2$ apical from which it should quickly depart with overall *retention* at phosphorus. (The R and I designations on this graph refer to overall stereochemistries of reactions via initial $\overline{\mathbf{45}}$, $\overline{\mathbf{25}}$, **15**, or **35** from (*S*)-$\underline{3}$. See above. They should be reversed when considering initial **24**, $\overline{\mathbf{14}}$, etc., from (*R*)-$\underline{3}$.) They also would be readily convertible to the more stable $\overline{\mathbf{25}}$ which also would yield substitution product of *retained* phosphorus configuration. *Therefore, there is thus no reason to believe that* ***24*** *and* $\overline{\mathbf{12}}$ *are formed initially from* (*R*)-$\underline{3}$, *or* $\overline{\mathbf{24}}$ *and* ***12*** from (*S*)-$\underline{3}$. This is consistent with the idea that the ethoxy group enters the TBP axially.[3b,17a–d,20] Were $\overline{\mathbf{14}}$ generated initially from (*R*)-$\underline{3}$, it would have to be isomerized to $\overline{\mathbf{12}}$ or **24** in order for the $PhCH_2$ to depart from the apical position, but again with overall retention. Clearly, *if phosphoranyl radicals are indeed involved*, the most probable route for the reaction of (*S*)-$\underline{3}$ with EtO· to expell $PhCH_2\cdot$ with inversion of phosphorus configuration is via $\overline{\mathbf{25}}$, **15**, and $\overline{\mathbf{45}}$ with loss of $PhCH_2\cdot$ from $\overline{\mathbf{25}}$, i.e, eq 14.

Conclusions

The most straightforward explanation of the net inversion observed with $\underline{2}$ and $\underline{3}$ is by way of a concerted, inline process, transition state $\underline{\mathbf{12}}$. However, the stereochemical result (*inversion*) from the reaction of EtO· with phosphine $\underline{2}$ is completely consistent with the intervention of a phosphoranyl radical intermediate of π^* electronic configuration and tetrahedral geometry ($\underline{\mathbf{13}}$). If indeed the experimentally observed substitution reaction of phosphine $\underline{3}$ (*also inversion*) proceeds in large fraction via initial phosphoranyl radicals $\underline{\mathbf{15}}$ and $\underline{\mathbf{16}}$ (which has not been proved), then it is quite certain that these TPB species do not isomerize prior to α-scission via M_1 processes which involve the odd electron as a stationary equatorial substituent. Instead, one-step, M_4 processes, e.g., eq 14 (perhaps via intermediates like $\underline{\mathbf{21}}$), or two successive M_1 or other permutations (overall M_4) in which the odd electron is allowed to be apical should be considered. One-step M_5 processes to give $\underline{\mathbf{20}}$ also are not excluded by the observed stereochemistry. However, such a rearrangement appears to be stereochemically improbable and for cyclic phosphoranyl radicals was ruled out by ESR measurements.[22,24] Its transition state would have to be planar or square planar to minimize steric repulsions. Ab initio calculations place such a geometry 40–50 kcal/mol above that of $\underline{\mathbf{24}}$ (X = H, F).[31] Additionally, EtO is equatorial, increasing the energy of $\underline{\mathbf{20}}$. For cyclic phosphoranyl radicals ESR observations are only consistent with the operation of *overall* M_4 permutations,[22,24] a finding supported by stereochemical studies.[9,20,25] Until evidence to the contrary is presented, the simplest approach is to assume that this also is true of noncyclic ones. One should not rule out M_1 processes for all phosphoranyl radicals, since the route a of eq 13 moves the EtO equatorial at a considerable cost of energy. (Indeed, it should be noted that M_2 formation of $\underline{\mathbf{23}}$ leaves the EtO apical.)

The choice between one-step M_4 and two-step, overall M_4 processes cannot be made experimentally. Calculations at the CNDO level[28] a favor a σ^* intermediate or barrier state ($\underline{\mathbf{21}}$) for $F_4P\cdot$ and $(HO)_4P\cdot$ over one like **28**. Unfortunately, ab initio methods have not been applied to σ^* configurations. They assign similar energy increases to $\underline{\mathbf{24}}$ → $\underline{\mathbf{27}}$ (X = H, F) and to one-step M_4 processes.[31] In any event, TBP phosphoranyl radicals do not appear to possess permutational properties parallel to those of truly pentacovalent phosphorus containing species. However, with respect to the trialkylphosphines of the present study, this conclusion must remain provisional being based on the presumed intermediacy of phosphoranyl radicals and assumptions concerning their initial geometries, neither of which has been experimentally verified.

Experimental Section

Materials and Methods. Thiophene-free benzene was extracted with concentrated H_2SO_4 and washed with distilled H_2O (4×), with 7% aqueous NaOH, and finally distilled H_2O. After being dried overnight over $CaCl_2$, it was refluxed for 8 h over $LiAlH_4$, distilled, and stored over 4A molecular sieves. GLC analyses were carried out on silanized 0.25-in. × 10-ft glass columns packed with 2–3% QF-1 on 80/100 Gas Chromosorb Q. After being packed and baked, the columns were treated with Silyl-8 and then baked again before use. Quantitative elemental analyses were done by Galbraith Laboratories, Knoxville, Tenn. Continuous wave ^1H NMR spectra were obtained on a Varian EM390 instrument. FT ^{31}P and ^1H NMR spectra wre taken on a Varian SC 300 or FT 80 spectrometer. Neat *t*-BuOOH from Pfaltz and Bauer was used without further purification. Optical rotations were measured with a Perkin-Elmer Model 141 polarimeter at 25 ± 1 °C in a 1-mm cell.

Preparative TLC. Plates were prepared by vigorously shaking for 5 min a mixture of 20 g of SiO_2 (GF-254, type 60, E.M. Laboratories) and 45 mL of distilled H_2O. The resulting slurry was poured onto a 20 cm × 20 cm glass plate and spread in homogeneous fashion by moving the plate from side to side and up and down. The plate was allowed to stand at room temperature for 20 min and was then heated in an oven for 2 h at 110 °C.

Preparation of EtON=NOEt. Silver hyponitrite was prepared in 6.7-g amounts by the procedure of Mendenhall.[33] It could be stored in the dark for weeks before its use to make EtON=NOEt, for which a typical procedure adopted from the literature[8b] follows. $Ag_2N_2O_2$ (5.5 g, 0.020 mol) was slowly added in a dark room over a 2-h period to an ice-cooled solution of ethyl iodide (6.2 g, 0.040 mol) in 20 mL of ether. The reaction mixture was placed in a refrigerator for 36 h and then filtered. The filter cake (AgI) was washed with 20 mL of ether, and the ether from the combined solutions was removed on a rotary evaporator. Residual ether was removed with a stream of dry nitrogen passed over the agitated hyponitrite, an oil. The product hyponitrite (0.7 g (29%) yield), completely pure as judged by ^1H NMR, was stored in a refrigerator, preferably in a bottle with a Teflon-lined serum top.

Preparations of $\underline{2}$, $\underline{3}$, $\underline{2}$-Oxide, $\underline{3}$-Oxide, $\underline{8}$, and $\underline{10}$. Phosphines $\underline{2}$ and $\underline{3}$ and their corresponding oxides were prepared according to a method developed recently in this laboratory.[7] Successive Grignard reactions of nearly optically pure *i*-PrO(RS)P(O)Me gave the phosphine oxides which were reduced by Ph_3SiH to the phosphines. Phosphinate $\underline{\mathbf{10}}$ was prepared by reaction of Me(EtO)P(O)SMe (2.2 g, 14 mmol) with *n*-PrMgI (ca. 34 mmol) in a refluxing mixed solvent of benzene (200 mL) and ether (34 mL) for 3 h. The desired product was easily isolated by preparative GLC (8 ft × 0.25 in. 10% QF-1 Gas-Chromosorb Q, 140 °C). Its structure was confirmed by ^1H NMR analysis at 300 MHz. The absolute configurations of its enantiomers were assigned by comparison of the relative intensities of the two well-separated PMe doublets in the ^{31}P NMR spectrum at 121 MHz seen on addition of (−)-*t*-BuPhP(S)OH to a CCl_4 solution of $\underline{\mathbf{10}}$ before and after addition of an authentic sample of (*R*)-$\underline{\mathbf{10}}$ supplied by C. R. Hall.[15] Phosphinate $\underline{\mathbf{8}}$ was isolated from reaction mixtures, subjected to GLC analysis, and identified by its 300-MHz ^1H NMR spectrum. In early studies its optical purity was determined from its specific rotation in MeOH and compared to the literature value, $[\alpha]^{25}_D$ −49°, optically pure.[13]

Determination of Optical Purities of $\underline{2}$-Oxide, $\underline{3}$-Oxide, $\underline{8}$, and $\underline{10}$ by

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(33) Mendenhall, G. D. *J. Am. Chem. Soc.* **1974**, *96*, 5000.

use of (−)-*t*-BuPhP(S)OH. The thio acid (−)-*t*-BuPhP(S)OH, readily prepared in complete optical purity,[34] was used. Phosphine oxides and phosphinates were dissolved at the 1–5% level in $CDCl_3$ or C_6D_6. Addition of 0.6 to 2.7 molar equiv of thio acid was sufficient to effect separations of peaks for the individual enantiomers. Peaks examined and typical separations ($\Delta\delta$, Hz) were as follows: *n*-PrMeP(O)OEt, CH_3CH_2O, 2.1 Hz (90 MHz), 7.2 Hz (300 MHz); CH_3P, 2.6 Hz (300 MHz). *n*-PrMeP(O)CH_2Ph, MeP, 2.7 Hz (90 MHz), 12.4 Hz (300 MHz). MePhP(O)OEt, MeP, 6.3 Hz (90 MHz); CH_3CH_2OP, 3.9 Hz (90 MHz). MePhP(O)CH_2Ph, MeP, 6.6–7.8 Hz (90 MHz), 22.4 Hz (300 MHz). Optical purities were determined from peak heights and from areas measured by electronic integration, triangulation, and cut and weight methods. The numbers given in Tables I and II are average values with errors in Table I demarking average deviations from the average. In most instances the measurements made at 300 MHz using 100-Hz expansions were considered to be the most accurate and were used in the calculations.

Product Analyses. Reaction mixtures were cooled in ice water and then oxidized with 1 to 5 molar equiv of *t*-BuOOH, added slowly at 5 °C. After 30 min to 1 h, GLC analyses were conducted. Hexadecane, added before the reaction, served as internal standard. Yields of products from the reaction of *n*-PrMePCH$_2$Ph are based on sensitivity factors relative to hexadecane calculated in the usual manner from excellent linear plots of molar ratio vs. area ratio and are corrected for the fact that the pure phosphine gave only 85 ± 5% yields of the oxide. The oxidation is assumed to be quantitative for the other compounds. In Figure 1 and Table I, percentages of products and accountabilities given are based on TC GLC areas and are not corrected for sensitivity differences. The points for phosphine in Figure 1 are from GLC areas normalized relative to internal hexadecane. Values in Table I are percentages of total areas. All products were identified by co-injection with authentic samples and for the phosphine oxides and phosphinates by isolation and ^{1}H NMR spectra.

Oxidation Stereochemistries. Glass reaction tubes were carefully cleaned in sequence with dichromate, distilled water (10×), 30% NH_4OH, distilled water (10×), purified acetone (3×), Et_3N (3×), and purified acetone (3×) and then oven dried (110 °C) before being tightly capped with a rubber septum. Benzene (40 mL) was added and thoroughly flushed with argon. The phosphine (ca. 1.7 mmol) and hexadecane internal standard were then added and a GLC analysis done to determine the amount of phosphine relative to the amount of standard present before the addition of EtON=NOEt (ca. 0.07 mmol). The reaction solution was heated in a bath at 70 °C for the prescribed amount of time and then analyzed by GLC. The reaction mixture was cooled in an ice bath, and an amount of *t*-BuOOH equal to or greater than that of the starting phosphine was added. After about 1 h at room temperature, the reaction was analyzed by GLC. If an excess of *t*-BuOOH had been added, the reaction mixtures were sometimes first passed through a short Al_2O_3 column to destroy excess *t*-BuOOH after which the phosphine oxide and phosphinate, whose optical purities were to be determined, were isolated by preparative TLC as described below.

Product Isolation. For the studies of **2**, solvent and excess *t*-BuOOH were removed under vacuum with gentle warming. The residue was spotted in $CHCl_3$ solvent on a TLC plate which was developed with 25:1 $CHCl_3$:MeOH. The products were detected by exposure of the edge of the plate to I_2. PhMeP(O)OEt and PhMeP(O)CH_2Ph (smaller R_f) developed as bands close to each other. The products were isolated by stirring the SiO_2 with 50:50 $CHCl_3$:MeOH for 1 h. Following filtration and solvent evaporation, the residue was dissolved in benzene and dried over $MgSO_4$. Removal of benzene gave material suitable for determination of optical purity. In the same manner following reaction of **3**, *n*-PrMeP(O)CH_2Ph and *n*-PrMeP(O)OEt were separated except that these products were first removed from most of the phosphine oxide under vacuum. Products of purities 92–98% resulted (GLC). If a single TLC separation did not give adequate purity material, it was repeated. Because of concern that **8** or **10** might undergo resolution during workup, a portion of **8**-oxide was mixed with optically enriched **2**-oxide. The mixture was separated by TLC in the normal way to give **8** which was unchanged in optical purity.

The amounts of unreacted **2** and **3** recovered by TLC as their oxides were generally 70–90% of that indicated by GLC. While the amounts of the EtOPPhMe and EtOMePr-*n* recovered as their oxides were 30–80% depending on the conversion of **2** or **3**. Lower isolation yields (30–50%) of the latter sometimes were obtained at low conversions and amounted to about 1–3 mg of oxide.

Acknowledgment. We gratefully acknowledge the support of this research by grants from the National Science Foundation and N.C.I. of the Public Health Service (CA 11045). We especially thank Dr. C. R. Hall for the sample of authentic (*R*)-**10**.

Registry No. (−)-(*S*)-**2**, 34868-25-2; (+)-(*S*)-**3**, 85248-81-3; EtO·, 2154-50-9; EtON=NOEt, 4549-46-6; $Ag_2N_2O_2$, 7784-04-5; ethyl iodide, 75-03-6.

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(34) Harger, M. J. P. *J. Chem. Soc., Perkin Trans. 2* **1980**, 1505. Harger, M. J. P. *Ibid.* **1978**, 326.

(35) **Note Added in Proof**: After this paper was submitted, results of a single crystal ESR study of the phosphoranyl radical generated from the cyclene tetraamino hydridophosphorane were published which were interpreted in terms of a Mode 1 Berry pseudorotation with the odd electron as pivot (Hamerlinck, J. H. H.; Schipper, P.; Buck, H. M. *J. Am. Chem. Soc.* **1983**, *105*, 385). This suggests the possibility that the preferred mode of permutation could be influenced by medium or the detailed structure of the radical. The equilibrating structures are isoenergetic in the radical in question.