Free Radical Studies of Organophosphorus Compounds. 7.[1,2] The Stereochemistries of Alkoxy and Thiyl Radical Oxidations of Phosphines and Cyclic Phosphites. Possible Permutational Isomerization Modes for Phosphoranyl Radicals

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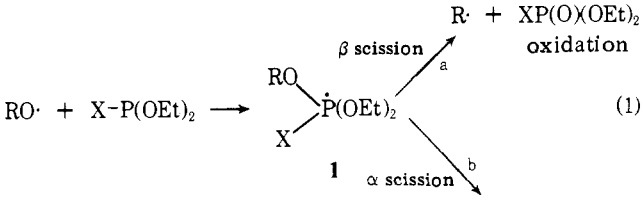
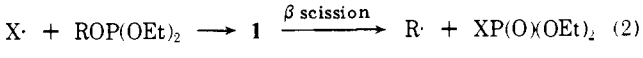
Abstract: Reactions of alkoxy radicals with cis/trans isomeric mixtures of certain 2-alkoxy-4-methyl-1,3,2-dioxaphospholanes and 2-alkoxy-5-*tert*-butyl-1,3,2-dioxaphosphorinanes (5- and 6-ring cyclic phosphites) were found to give the corresponding phosphorus oxides (cyclic phosphates) nearly stereospecifically with *retention* of configuration about phosphorus. The same stereochemical outcome was observed with a chiral phosphine and in the reaction of *n*-BuS· with 2-methoxy-5-*tert*-butyl-1,3,2-dioxaphosphorinane. It is concluded that free radical attack at trivalent phosphorus in these systems occurs in the sterically most favorable manner, i.e., toward the phosphorus lone pair electrons. An interpretation of the results is given in terms of the intermediacy of phosphoranyl radicals of trigonal-bipyramidal geometry. β scission appears to occur at both apical and equatorial positions. Extensive amounts of permutational isomerization of these intermediates via mode 1 (M_1) processes (as defined by Musher) prior to product formation by β scission are excluded. It is estimated that the most rapid potential M_1 permutation available to such intermediates must have $\Delta G^{\ddagger}$ greater than 11 kcal/mol. A complementary study of the reaction of *cis*-2-*tert*-butoxy-5-*tert*-butyl-1,3,2-dioxaphosphorinane with ^{14}C-labeled *tert*-butoxy radical showed that both cis and trans phosphates are products. Only the trans isomer contained carbon label, a result also consistent with the absence of rapid M_1 permutations in competition with β scission. When compared with their truly pentacovalent phosphorus counterparts, the tetraalkoxy phosphoranyl radical systems appear to have relatively high activation free energies for M_1 alkoxy exchange. However, it is pointed out that neither the stereochemical nor the radiochemical labeling results exclude the intervention of certain other permutational isomerizations (M_4 and M_5) prior to or competitive with β scission.

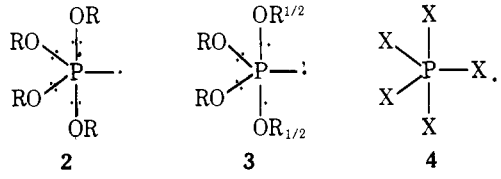
When free radicals are generated in the presence of trivalent phosphorus compounds, three important overall processes are observed:[3] oxidation (1a); substitution (1b); and a free-radical equivalent of the familiar Arbuzov reaction (2). The often-presumed intermediates in these reactions, phosphoranyl radicals (**1**),[4] give products primarily by either α or β scission processes as shown in eq 1 and 2. A number of ESR studies[5]





have shown that phosphoranyl radicals in fact are formed in systems depicted by eq 1 and in analogous reactions of RS·.[6] In at least one instance the presence of a phosphoranyl radical was confirmed in a free-radical Arbuzov reaction system as well[5d] (reaction 2, X· = Me·, R = $PhCH_2$·). Several reports of the kinetics of decay of phosphoranyl radicals via α or β scission also have appeared.[5b,c,d,g] In general, therefore, it is not unreasonable to assume the intermediacy of phosphoranyl radicals in reactions 1 and 2, although this has not been proved in all cases.

Configurationally, phosphoranyl radicals are usually characterized as being trigonal-bipyramidal species and have been described electronically in terms of two extreme structures. Most commonly a structure with the odd electron in an orbital with electron density primarily in the equatorial plane is written **2**.[3] More recently a hypervalent representation (**3**)



2 **3** **4**

has been proposed which places the odd electron in a primarily nonbonding molecular orbital distributed over the apical ligands.[2b,7] The superficial similarity of **2** and **3** to truly pentacovalent phosphorus systems, **4**, is obvious if the odd electron (or pair) is viewed as a phantom ligand. The stereochemical and configurational aspects of these radicals are unchanged by choice of **2** or **3**. Hence for the sake of simplicity we will use structures analogous to **2** in this paper.

The potential effects of configurations of phosphoranyl radicals on processes 1 and 2 have received little attention. In particular, little is known with regard to the following questions:

(1) In the formation of **1**, does the attacking radical enter the trigonal bipyramid (TBP) in a configurationally nonrandom fashion, i.e., preferentially apical or equatorial?

(2) Are there configurational preferences for α and β scission for either the apical or equatorial positions?

(3) Are there permutation processes which exchange substituents on phosphorus in phosphoranyl radical intermediates at rates competitive with or faster than α or β scission?

In this paper we report results of investigations of the stereochemistries of alkoxy and thiyl radical oxidations of certain trivalent organophosphorus compounds. Implications of our findings as far as the above questions are concerned will be stressed. (The utility of stereochemical studies in the investigation of permutation processes in systems involving pentacovalent phosphorus intermediates is well known.[8]) We also report some combined stereochemical and radioactive

Table I. Stereochemistry of Oxidation of Phosphine **7**

Phosphine[e] sample	$[\alpha]^{20}D$[f] phosphine	Solvent	Oxidant	T, °C	$[\alpha]^{20}D$[f] phosphine oxide	%[d] yield
1	−14.1°	CH_3CN	*t*-BuO· (DTBH[f])	69	−17.2° [a]	68
2	−16.6°	CH_3CN	*t*-BuO· (DTBH)	69	−16.6° [a]	74
3	−13.0°	CH_3CN	*t*-BuO· (DTBH)	69	−16.4° [a] (−16.2°)[b]	53
	−13.0°	*n*-Pentane	*t*-BuOOH	0	−16.8° [a] (−16.4°)[b]	49
4	−12.6°	CH_3CN	*t*-BuO· (DTBH)	69	−17.0° [a] (−15.6°)[b]	52
	−12.6°	*n*-Pentane	*t*-BuOOH	0	−16.5° [a] (−15.0°)[b]	61
5	−12.1°	CH_3CN	*t*-BuO· (DTBH)	69	−16.2° [c]	56

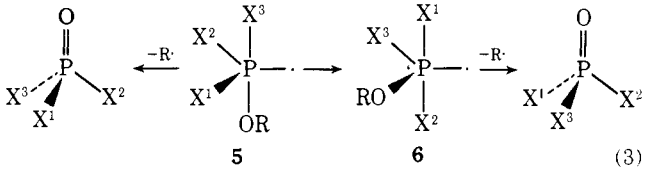
[a] Purified by recrystallization from hexane to constant rotation. [b] Oil isolated by solvent removal prior to crystallization. [c] Sublimed under vacuum from oil isolated by solvent removal. [d] Isolated and purified crystalline **7**-oxide. [e] Phosphine and DTBH both about 3 M in CH_3CN; *t*-BuOOH ~0.40 M and phosphine ~0.21 M in *n*-pentane. Different sample numbers refer to separate preparations. [f] Determined at concentrations 0.011 to 0.019 g per 2 ml of methanol.

Table II. Stereochemistries of Alkoxy- and Thiyl-Radical Oxidations of Phosphites **8–11**

Case	Phosphite	Radical (source[a])	Solvent	T, °C	Product	% yield	Cis/trans ratio: Reactants	Cis/trans ratio: Products
1	**8**	*t*-BuO· (DTBP)[b]	CH_3CN	*hν*,[d] 3	**8**-Oxide	52[f]	92/8[g]	94/6[f]
2	**8**	*t*-BuO· (DTBP)[b]	CH_3CN	*hν*, 3	**8**-Oxide	43[f]	92/8[g]	95/5[f]
3	**8**	*t*-BuO· (DTBH)[b]	CH_3CN	Δ,[e] 72	**8**-Oxide	43[f]	91/9[g]	96/4[f]
4	**8**	*t*-BuO· (DTBH)[b]	C_6H_6	Δ, 65	**8**-Oxide	56[f]	90/10[g]	95/5[f]
5	**8**	*t*-BuO· (DTBH)[b]	CH_3CN	Δ, 72	**8**-Oxide	52[f]	15/85[g]	21/79[f]
6	**8**	*t*-BuO· (DTBH)[b]	C_6H_6	Δ, 65	**8**-Oxide	43[f]	6/94[g]	9/91[f]
7	**8**	*n*-BuS· (DBD)[c]	CH_3CN	*hν*, 3	**8**-Sulfide	92[f]	92/8[g]	94/6[f]
8	**8**	*n*-BuS· (DBD)[c]	CH_3CN	*hν*, 3	**8**-Sulfide	94[f]	94/6[g]	95/5[f]
9	**8**	*n*-BuS· (DBD)[c]	CH_3CN	*hν*, 3	**8**-Sulfide	83[f]	79/21[g]	79/21[f]
10	**8**	*n*-BuS· (DBD)[c]	CH_3CN	*hν*, 3	**8**-Sulfide	83[f]	88/12[g]	85/15[g]
11	**9**	EtO· (DEP)[i]	C_6H_6	*hν*, 17	**12**	48[h]	**14**/86[g]	85/15[g]
12	**9**	EtO· (DEP)[i]	C_6H_6	*hν*, 17	**12**	52[h]	14/86[g]	87/13[f]
13	**9**	EtO· (DEP)[i]	C_6D_6	*hν*, 17	**12**	*n*	14/86[n,g]	86/14[n,g,f]
14	**10**	*t*-BuO· (DTBP[j]	C_6D_6	*hν*, 17	**10**-Oxide	72[f]	46/54[k]	45/55[k] (46/54)[f]
15	**10**	*t*-BuO· (DTBP)[j]	C_6D_6	*hν*, 17	**10**-Oxide	*t*	45/55[k,t]	47/53[k,t]
16	**10**	*t*-BuO· (DTBP)[j]	C_6D_6	*hν*, 17	**10**-Oxide	71[f]	33/67[k]	33/67[k] (33/67)[f]
17	**10**	*t*-BuO· (DTBH)[j]	C_6D_6	Δ, 65	**10**-Oxide	86[f]	34/66[k]	33/67[k] (31/69)[f]
18	**10**	*t*-BuO· (DTBH)[j]	C_6D_6	Δ, 65	**10**-Oxide	86[f]	34/66[k]	33/67[k] (32/68)[f]
19	**10**	*t*-BuO· (DTBH)[j]	C_6D_6	Δ, 25[s]	**10**-Oxide	*s*	33/67[k,s]	33/67[k,s]
20	**11**	EtO· (DEP)[l]	C_6D_6	*hν*, **17**	**13**	68[f]	42/58[o]	57/43[f]
21	**11**	EtO· (DEP)[l]	C_6D_6	*hν*, 17	**13**	74[f]	42/58[o]	56/44[f]
22	**11**	EtO· (DEP)[l]	C_6D_6	*hν*, 17	**13**	*p*	40/60[o,p]	57/43[o,p]
23	**9**	*t*-BuO· (DTBH)[q]	C_6H_6	Δ, 65	**9**-Oxide	*r*	98/2[g,m]	67/33[g]
24	**11**	*t*-BuO· (DTBP)[u]	C_6D_6	*hν*, 17	**11**-Oxide	82[o]	44/56[o]	40/60[o]

[a] Sources are di-*tert*-butyl peroxide (DTBP), di-*tert*-butyl hyponitrite (DTBH), di-*n*-butyl disulfide (DBD), diethyl peroxide (DEP). [b] Radical source is excess. Solutions 0.3–0.6 M in **8**, 0.2–0.4 M in DTBP or DTBH. [c] Solutions 0.4–0.6 M in phosphite, 0.3–0.4 M in disulfide. [d] Photochemical decomposition. [e] Thermal decomposition. [f] By GLC. Internal standard for yield determinations added following reaction. [g] By integration of 5-*tert*-butyl ^1H NMR resonances at 60 or 100 MHz, as required by peak separations. [h] By ^1H NMR. Internal standard added after reaction. [i] **9**, 0.7 M; DEP, 1.5 M. [j] **10**, 0.5 M; DTBP or DTBH, 0.34 M. [k] By integration of 4-methyl and/or 2-methoxy ^1H NMR resonances at 100 MHz. [l] **11**, 0.7 M; DEP, 1.5 M. [m] Minimum ratio. ^1H NMR showed no *cis*-**9** to be present. [n] Experiment interrupted at 45% conversion of **9**. Cis/trans ratios for **9** and **12** are those at 45% conversion. Initial ratio 14/86. [o] By ^1H NMR at 100 MHz using both 4-Me and 2-*t*-BuO resonances. [p] Interrupted at ~60% conversion of **11**. Cis/trans ratios for **11** and **13** are for 60% conversion. Initial ratio 42/58. [q] **9**, 0.2 M; DTBH, 0.3 M. [r] Not determined. For other cis/trans ratios, ~65%. [s] At room temperature for 5 h, 20% conversion of phosphite. Cis/trans ratios are at 20% conversion. Initial ratio 34/66. [t] Phosphite **10** 50% consumed. Cis/trans ratios are at 50% conversion. Initial ratio 46/54. [u] **11**, 0.3 M; DTBP, 0.3 M.

labeling experiments designed to help to answer the above questions. An example of the potential effect of a ligand permutation on the stereochemistry of oxidation is illustrated in (3) for a pairwise mode of which the Berry pseudorotation process[9] is a specific mechanism. Whereas β scission of **5** gives an oxide of one chirality, a single prior permutation (**5** to **6**) leads then to the enantiomeric oxide.

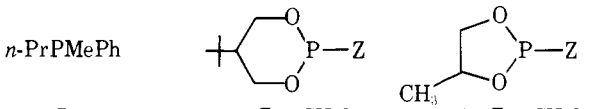


5 **6** (3)

It should be emphasized at the outset that although **2** and **4** bear a superficial resemblance to each other, there is no reason to predict that they necessarily should have similar permutation modes or barriers to such isomerizations. As our results will show, the permutational properties of phosphoranyl radicals may well be quite different from those of truly pentacovalent phosphorus species.

Results

Oxidations. The stereochemistries about phosphorus of the oxidations of phosphine **7** and phosphites **8–11** by reaction with RO· and of **8** or RS· were investigated. Results of these studies are presented in Tables I and II which also list the attacking



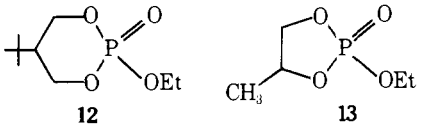
n-PrPMePh

7

8, Z = CH_3O
9, Z = *t*-BuO

10, Z = CH_3O
11, Z = *t*-BuO

free radical and oxidation product for each case. The corresponding oxidation product formed from transfer of oxygen or sulfur from RO· or RS· to a given trivalent phosphorus reactant is designated merely as **7**-oxide, **8**-oxide, etc. With phosphites **9** and **11,** addition of an ethoxy radical (cases 11–13 and 20–22 Table II) was followed by β scission of the alkoxy group (*t*-BuO) already attached to phosphorus. The product in these cases is phosphate **12** (from **9**) or phosphate **13** (from **11**).



12 **13**

Syntheses and Stereochemistries. Phosphine **7**, (−)-(*R*)-methylphenyl-*n*-propylphosphine, was prepared by Cl_3SiH/Et_3N reduction[10] of **7**-oxide made according to Mislow et al.,[11] and the stereochemistry of *tert*-butoxy radical reaction was compared with that of the known *t*-BuOOH oxidation process which retains configuration at phosphorus.[12] Table I records specific rotations for isolated **7**-oxide from both types of reactions. Considering the fact that the rotations were determined on 11–19-mg samples with consequent accompanying small weighing errors, the agreement between rotations on oxide from the two types of reactions with different preparations of phosphine is excellent (compare samples 3 and 4). Rotations obtained on the isolated, oily **7**-oxide prior to purification are quite high compared with the purified material. Note also that similar results are found when **7**-oxide was purified *either* by recrystallization or by sublimation. We conclude that the *tert*-butoxy radical oxidations of **7** give **7**-oxide almost quantitatively with *very nearly complete retention of configuration about phosphorus.*

Phosphites **8–11** had either been prepared previously[13,14] or were synthesized by well-known methods. Assignments of the cis/trans geometries of isomers of **8**,[13] **10**,[14] and **11**[14] were reported earlier. Identical ^1H and ^{31}P NMR methods were applied to **9** (see Experimental Section). The geometries of the phosphite precursor to **12,** the 2-ethoxy-5-*tert*-butyl-1,3,2-dioxaphosphorinane, were determined on the basis of ^{31}P and 5-*tert*-butyl ^1H chemical shift data and the relative thermodynamic stabilities of the two isomers (methods we reported earlier[13,15]). Cis/trans geometries were assigned to isomers of the phosphite precursor to **13,** the 2-ethoxy-4-methyl-1,3,2-dioxaphospholane, by use of their ^{31}P chemical shifts, a well-documented criterion.[14] N_2O_4 oxidation of the phosphites then gave **12** and **13** with known isomer geometries, based on the well-studied retentive stereochemistry of this reaction.[16] The thiyl radical oxidations of **8** were referred to those using S_8, also known[17] to retain configuration at phosphorus.

Inspection of the results of Table II shows the *tert*-butoxy radical oxidations of **7** and **10** (cases 1–6) to be nearly stereospecific with *retention* of configuration at phosphorus. The same is true of the thiyl radical cases (7–10). Ethoxy radicals react with **9** and **11** nearly stereospecifically as well (cases 11–13 and 20–22) but lead by contrast to *inverted* phosphorus configuration in the product ethyl phosphates, **12** and **13.** In case 23, however, *both* cis and trans isomers of the phosphate, **9**-oxide, are formed. The radiochemical labeling studies outlined below show that this results from β scission of both *tert*-butoxy groups in the phosphoranyl radical intermediate.

At this point it would be well to acknowledge the fact that the oxidations of Table II proceed in less than quantitative fashion. Were the correspondence between starting isomer ratios and those of products not strong (cases 23 and 24 are excluded at this point obviously), it would be difficult to make stereochemical conclusions. However, in these systems several lines of evidence are consistent with the conclusion that the reactions are in fact stereospecific and that the phosphoranyl radical intermediates give other products (unidentified) by competitive processes (ring scission,[5d] dimerization[5k]) at rates which are the same for cis and trans isomers. First, yields are high enough that for say a 90/10 cis/trans ratio of phosphite a 90/10 cis/trans ratio of phosphate could not arise by an *inversion* process in which the cis phosphite gives only a low yield of trans phosphate and the trans phosphite near-quantitative amounts of cis phosphate. Second, such an accidental appearance of near stereospecificity of reaction at phosphorus is ruled out by experiments using different starting cis/trans ratios of phosphite. At a single ratio, proportioning of reaction pathways between retention, inversion, and side product in different manners for the two isomeric phosphoranyl radicals might give *coincidentally* apparent complete retention of configuration from both. But this would not occur with two different ratios. Third, ratios of products are unaffected by the extent of conversion or lengthened reaction times, ruling out a role of selective consumption of one product or of product interconversion in determining final ratios. Fourth, in cases examined there is no major effect on overall yield of changing the starting isomer ratio as would be expected if one phosphoranyl radical were more rapidly consumed than the other by side reactions.

Reaction Conditions, Radical Sources, and Controls. All reaction solutions were carefully deoxygenated, most often by freeze-thaw methods at 10^{-5}–10^{-6} Torr. Careful control reactions showed all reactants to be inert to reaction conditions in the absence of a free radical source. In addition, in the reactions using peroxide or disulfide as radical source, no reaction occurred in controls held in the dark, and the phosphite–peroxide reaction mixtures were stable to GLC conditions where that method of analysis was applied. In certain cases (1 and 2 vs. 3–6; 16 vs. 17–19) both di-*tert*-butyl peroxide (DTBP) and di-*tert*-butyl hyponitrite (DTBH) were used as *t*-BuO· sources with no effect on results. We previously reported[1] the lack of effect of added *sec*-$BuOP(OEt)_2$ (0.5–2.0 M) on the rate of thermal decomposition of EtON=NOEt (1.0 M) at 65 °C indicating the independence from phosphite attack of ethoxy radical formation. The peroxides, DTBP and diethyl peroxide (DEP), have been shown to be ready photolytic sources of alkoxy radicals in ESR studies of $(RO)_4P\cdot$.[5] The *n*-butylthiyl radicals were generated by photolysis of the disulfide at 3 °C. No reaction occured at all in the dark. (The photolysis of MeSSMe in the presence of $(EtO)_3P$ gives rise to a radical detected by ESR[6] with structure assignable to $MeS(EtO)_3P\cdot$.

Cis/trans isomer ratios of phosphite reactants **8** and **10** can be measured by ^1H NMR integrals of the 5-*tert*-butyl or 4-methyl peaks or by conversion by N_2O_4 or S_8 to the corresponding phosphate or thiophosphate with results nearly identical, i.e., percentages within a range ±2. This has been demonstrated earlier[13-15] for these and other 1,3,2-dioxaphospholanes and 1,3,2-dioxaphosphorinanes. Only ^1H NMR methods were applicable to **9** and **11** because of thermal instability of the oxides and sulfides. For the sake of convenience the ^1H NMR technique was used to determine cis/trans ratios for all of **8–11.**

Both quantitative GLC and ^1H NMR methods were used for product analyses. Except for **9**-oxide, which was totally unstable to GLC conditions, all products were confirmed not only by ^1H NMR of the reaction mixtures but also by GLC

Table III. ^{14}C Labeling of Product Oxide from Decomposition of Labeled Di-*tert*-butyl Hypernitrite in the Presence of **9** in Degassed Benzene at 65 °C

Case	[9][a]	[DTBH][a]	Mole fraction[b,d] *trans*-**9**-Oxide	Fraction[c,d] activity
1	0.206	0.279	0.44	0.44
2	0.206	0.279	0.16	0.17
3	0.206	0.279	0.077	0.088
4	0.344	0.100		0.028[e]
5	0.147[f]	0.257		0.01[g]

[a] Concentration in mol/l. [b] (Moles trans)/(moles trans plus moles cis) by integration of 5-*tert*-butyl resonances, ^1H NMR. [c] Based on total label available in *t*-BuO· from DTBH. [d] From repeated crystallizations of a single product phosphate mixture. [e] In unreacted **9** recovered as thiophosphate. [f] Unlabeled **9**-oxide as reactant. [g] Activity in recovered reactant **9**-oxide.

analysis in which reaction product mixtures were doped with authentic materials. As noted later **9**-oxide was confirmed by quantitative elemental microanalysis.

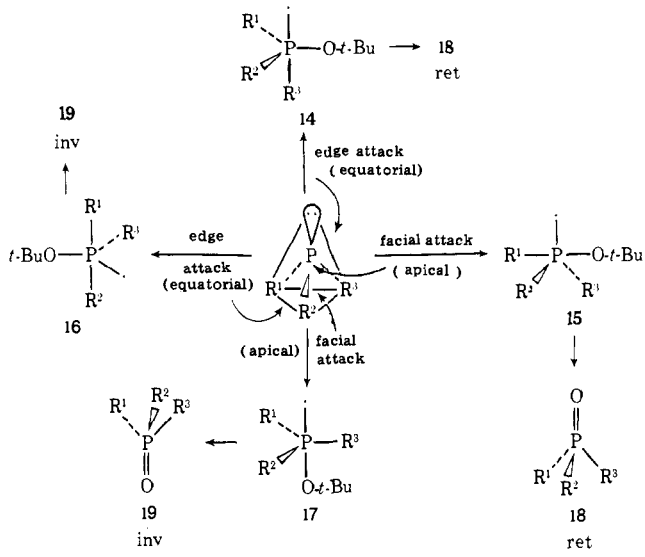
An important concern in stereochemical investigations of this type is that product ratios may not reflect kinetic control because of equilibration of reactants or products during the reaction. Prolonged reaction times failed to give any indication of selective decay or consumption of one isomer of a given product. Reactions in Table II were most usually run to complete consumption of reactants with more than one starting cis/trans ratio. Since these cases (1-10 and 14-19) gave near-stereospecific outcomes, there was no concern that cis ⇌ trans starting material equilibration might occur during reaction. Where only one cis/trans ratio of reactant was examined (cases 11-13 and 20-22 of Table II), it was a thermodynamically nonequilibrated one; and the reaction was interrupted before completion to show that no change in reactant or product isomer ratio occurred during reaction. Apparently the exceedingly rapid nature of the reaction of alkoxy radicals with phosphites[5c] (k = 10^8-10^9 M^{-1} s^{-1} at 60 °C) confers equal reactivities on cis and trans isomers. Case 15 also was interrupted at 50% completion. Again, product and reactant ratios were unchanged during the course of reaction. The same was true of the thiyl radical reactions of **8** at two different starting phosphite ratios. However, only product thiophosphates were examined.

^{14}C Label Studies. We earlier reported[18] the use of ^{14}C label techniques in the study of $(t\text{-BuO})_4P\cdot$. In the present work the stereochemical and radioactive labeling approaches have been combined. ^{14}C-labeled *tert*-butoxy radicals were generated thermally from di-*tert*-butyl hyponitrite in the presence of *cis*-**9**. Results of these experiments appear in Table III in which is recorded the degree of incorporation of label into both **9** and product phosphate. The fraction activity is the activity in a given molecule compared with the total possible activity based on the level of label in the *tert*-butoxy radicals generated. Label in unreacted **9** (isolated as the sulfide) was negligible (case 4 of Table III). In Table III are compared also the fractions of available label found in various mixtures of **9**-oxide isomers with the fractions of trans isomer of the oxides. The **9**-oxide mixtures resulted from successive fractional recrystallizations of the initial product mixture. Note the parallel between phosphate activity and the fraction of the minor phosphate (*trans*-**9**-oxide) in the isomer mixtures. This probably means that only a single phosphate isomer is labeled, and such an interpretation is employed in the Discussion section. The **9**-oxides were thermally stable to the reaction conditions. No change in isomer ratio or appreciable incorporation of label occurred when labeled hyponitrite was decomposed in the presence of unlabeled phosphate (case 5).

Discussion

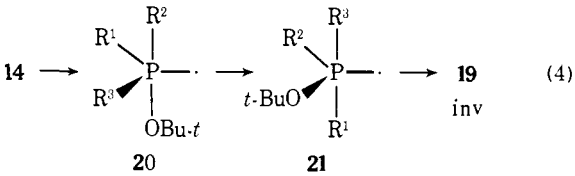
In the discussion which follows, it will be assumed that the formation of the intermediate phosphoranyl radical can be viewed as the result of either a facial (apical introduction) or edge (equatorial introduction) attack of RO· on the trivalent phosphorus compound taken as a pyramidal species with the lone pair at the apex. This is shown in Scheme I which depicts

Scheme I



only four of six possible edge and four possible facial attacks. Clearly demonstrated is the dependence of the overall stereochemistry of such a reaction on the direction of RO· attack. Attack on any of the top three faces or edges which involve the lone pair results in retention of configuration about phosphorus whereas inversion is the result of attack away from the lone pair (bottom face and three edges).

In addition to the effect of direction of RO· attack, the stereochemical outcome of reactions of the type shown in Scheme I may be altered by permutational isomerizations which precede β scission. This was shown above for intermediate **5** of eq 3 (**5** is equivalent to **15** of Scheme I). In eq 4 below, the product **14** (from Scheme I) of attack on a top edge of the phosphine undergoes *two* such rearrangements prior to β scission. In both



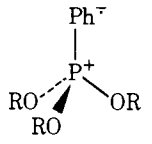
(4)

eq 3 and 4, the product oxide is *inverted* in configuration about phosphorus.

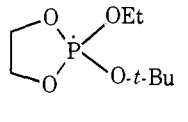
The sort of permutation shown in (3) and (4) is that classified as mode 1 (M_1) by Musher[19] and implies no specific physical mechanism such as the Berry pseudorotation or Turnstile[20] processes which are of this mode. We do not wish to imply that only M_1 isomerizations need be considered for phosphoranyl radicals. However, this is the mode most generally recognized for truly pentacovalent phosphorus, Z_5P, and gives us an initial point of comparison. The stereochemical consequences of other isomerization modes will be considered later.

Phosphine 7 Oxidation. Clearly, the retentive stereochemistry of the oxidations of phosphine **7** (Table I) is indicative of *t*-BuO· attack in the direction of the phosphorus lone pair and the absence of extensive amounts of M_1 isomerizations of the phosphoranyl radical intermediate prior to β scission. There

is a considerable amount of ESR evidence,[5i,j,21] which appeared after our studies were completed, that has been interpreted to show that many phenyl-substituted phosphoranyl radicals have the odd electron distributed largely over the π orbital system and may well be tetrahedral in geometry as represented by **22.** This postulation has recently found support



22



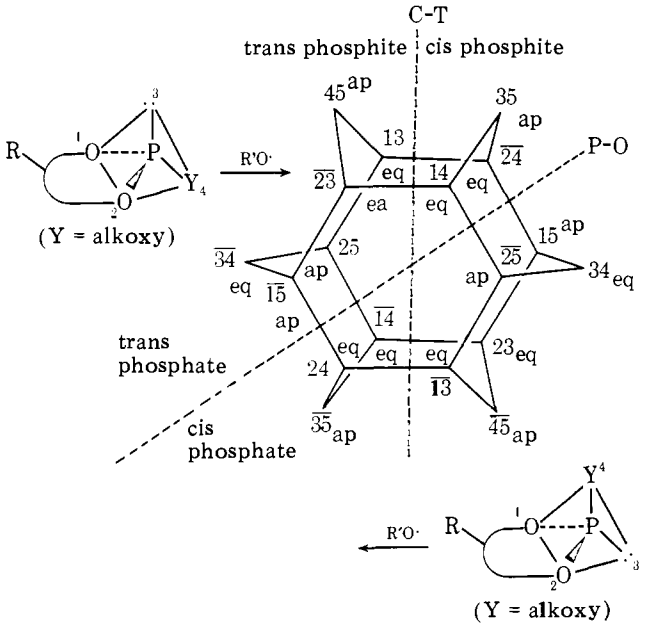
23

in CNDO/2 calculations.[22] For these reasons the phosphine system may not represent the best case for testing the ease of M_I permutation processes. However, the results with **7** do show that *t-BuO· attacks in the direction of the phosphorus lone pair.*

Oxidations of Phosphites 8 and 10. An abundant amount of ESR evidence has been amassed to demonstrate the formation of tetraalkoxy phosphoranyl radicals, $(RO)_4P\cdot$, when alkoxy radicals are generated thermally or photochemically from initiator molecules in the presence of trialkyl phosphites.[5] The tetraalkoxy phosphoranyl radicals present a very attractive system in that they are clearly trigonal bipyramidal in geometry, a configuration most likely to undergo permutational isomerization. In addition, based on pentacovalent phosphorus[8] and what is known about substituent affinities for apical vs. equatorial positions in phosphoranyl radicals,[5] it seems probable that the barrier to substituent exchange in tetraalkoxy phosphoranyls would be much lower than in those derived from phosphines. With the alkoxy systems, interconversions between various species would exchange substituents with nearly identical electronic and steric properties; i.e., all intermediates will be of similar energies.

Scheme II is a Desargues-Levi graph of the type often

Scheme II

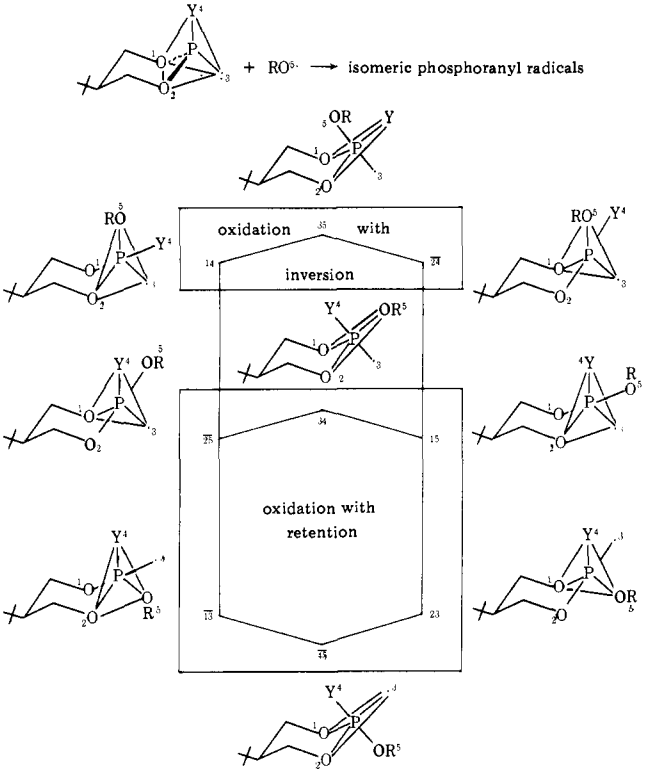


used[23] to aid in following systematically the M_I permutational isomerizations available to pentacovalent phosphorus systems but here adapted to the reactions of cis and trans phosphites with R'O·. The numbers at the vertices of the graph, by referring to the two ligands which are apical, designate the configuration of a given phosphoranyl radical formed by R'O· attack. Unbarred numbers, e.g., 23, designate a clockwise arrangement of the equatorial substituents in increasing numerical order (1, 4, and 5) when viewed from the apical substituent with the lowest number, in this case 2. The barred number permutamer, $\overline{23}$, is the geometrical (cis-trans) isomer of 23. In this scheme note that both the electron pair in reactant phosphite and the odd electron in the resulting phosphoranyl radical bear the number 3, while the attacking R'O· is substituent 5. Adjacent to each vertex the abbreviation ap or eq indicates whether the R'O· has been introduced apical or equatorial and thus in which position it is potentially able to undergo β scission. Lines in the graph connect interconvertible isomers. The C-T plane divides cis and trans phosphite reactants. On one side of the P-O plane are permutamers which on β scission give trans oxide (phosphate), while those on the other side give the cis phosphate. By following the lines connecting various vertices in Scheme II, one can easily see how permutamers are interconverted by M_I isomerizations and the effect of such isomerizations on the stereochemical outcome of the oxidation.

What Scheme II shows very clearly is that in certain cases only a single isomerization prior to β scission is required to lead to inversion of configuration about phosphorus in the overall oxidation process; e.g., attack by R'O· on cis phosphite to give phosphoranyl radical intermediate 15 followed by rapid β scission of the C-O bond of R'O in the apical position into which it was introduced prior to isomerization gives cis phosphate, i.e., retention of configuration. However, *a single permutation* of substituents ($15 \rightarrow \overline{24}$) gives a permutamer which on equatorial β scission would yield trans phosphate (inversion). Even if 23 or $\overline{13}$ (mirror images) were initial intermediates or β scission were only apical requiring $15 \rightarrow \overline{24} \rightarrow 35$, configuration inversion at phosphorus would require only two or three permutations prior to phosphate formation.

This is seen more clearly in Scheme III which shows struc-

Scheme III



tural detail for the permutamers on the right of the C-T plane in Scheme II. These are the phosphoranyl radicals which result from RO· attack on the specific phosphite, *cis*-2-alkoxy-5-

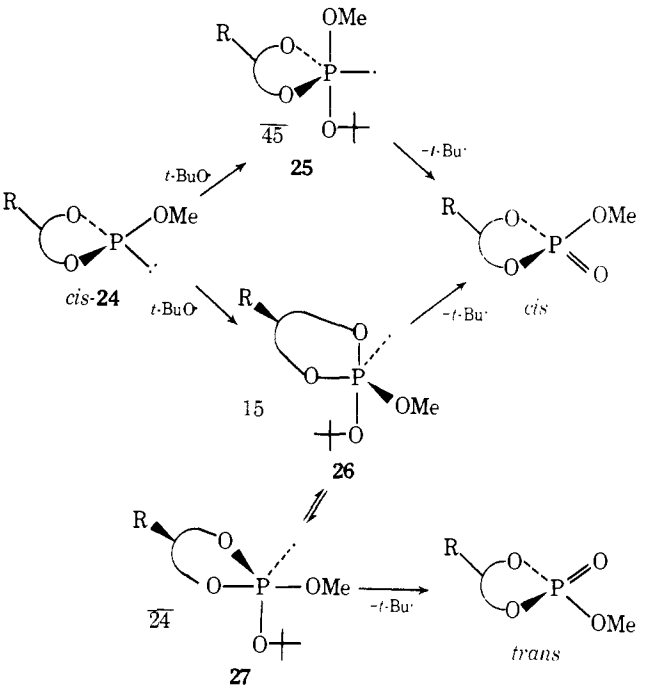
tert-butyl-1,3,2-dioxaphosphorinane. In Scheme III substituent Y is an alkoxy. From consideration of Schemes II and III along with the evidence from Table II for the highly retentive oxidation of phosphites **8** and **10**, *it is clear that an extensive amount of M_1 isomerization of initially formed phosphoranyl radical does not precede β scission.* Though our attention is focused primarily on the alkoxy radical oxidations, the conclusions throughout are valid for the RS· reactions as well, which is not surprising since β scission is even more rapid for such systems.[4]

Two very reasonable assumptions with experimental basis will allow us to further simplify Scheme III and make estimates of lower limit values of $\Delta G^{\ddagger}$ for particular M_1 isomerizations: (a) Permutamers 14, $\overline{24}$, and 35 may be disregarded as initial adducts or at least undergo very rapid isomerizations before β scission. (b) Formation of 13, 34, and 23 as initial adducts, in which the odd electron is apical and the attacking RO equatorial, need not be considered.

Justification for assumption a comes from the experimental observations of the phosphine **7** oxidations which showed that attack occurs in a direction toward the phosphorus lone pair and by the radioactive labeling results discussed below. (With the six-membered ring phosphites, normal steric arguments against approach to a bottom face or edge are reinforced by the presence of axial hydrogens when methoxy is axial in the phosphite substrate.) No inverted phosphate which could have arisen from 14($\overline{24}$) was found as well. With regard to assumption b, all ESR evidence to date favors a strong equatorial preference for the odd electron (lone pair), as no species possessing an apical odd electron has been observed.[3,5] Theoretical calculations[5f,24] are also consistent with this view. (Extrapolation of principles from pentacovalent phosphorus chemistry[8] to these systems of course requires the apical introduction of the attacking radical.) Any initial 34, 13, or 23 should be quickly converted to 15($\overline{25}$) or $\overline{45}$. Recent ESR work[25] may be interpreted to indicate an apical kinetic preference for attacking H· in $H(OR)_3P$·.

This leaves only $\overline{25}$ and its mirror image 15 along with $\overline{45}$ as initial adducts to be considered. ($\overline{25}$ and 15 are not strictly speaking mirror images where the phosphoranyl radicals formed from **10** are concerned, since the methyl in **10** is not in a symmetry plane. The conclusions drawn, however, are not changed by this simplification.) Note that a *single isomerization* of one of the enantiomeric adducts, $\overline{25}$ → 14 or 15 → 24, prior to β scission would lead to *inversion* of configuration at phosphorus. A minimal set of permutamers derived from the above considerations comprises Scheme IV in which the phosphite has been generalized in structures **24–27** so that both five- and six-membered rings can be discussed. Clearly, if **25** is the phosphoranyl radical preferred kinetically in these systems, it is to be expected that oxidation would be stereospecifically retentive. M_1 permutations of **25** (corresponds to $\overline{45}$ in Scheme III) by way of intermediates 13 and 23 of Scheme III should be relatively slow since both have apical odd electrons (see above). On the other hand, strong arguments can be made that at least a portion, and in the five-membered rings a major portion, of these reactions should involve initial formation of **26** or its enantiomer ($\overline{25}$) or at least a high subsequent population of that form. ESR studies[5d,e,m] of alkoxy radical attack on five-membered ring compounds containing two oxygens, two nitrogens, or an oxygen and a nitrogen at the 1 and 3 positions all show hyperfine splittings interpretable only in terms of a ring attached apical-equatorial to phosphorus. Even the alkoxy radical adducts from reaction with a six-membered ring diamino compound, a 1,3,2-diazaphosphorinane, had the ring attached apical-equatorial.[5m] Statistical factors alone would predict the formation of **26** and its enantiomer two-thirds of the time. Effects of the ring should enhance this preference, especially where five-membered rings are concerned.

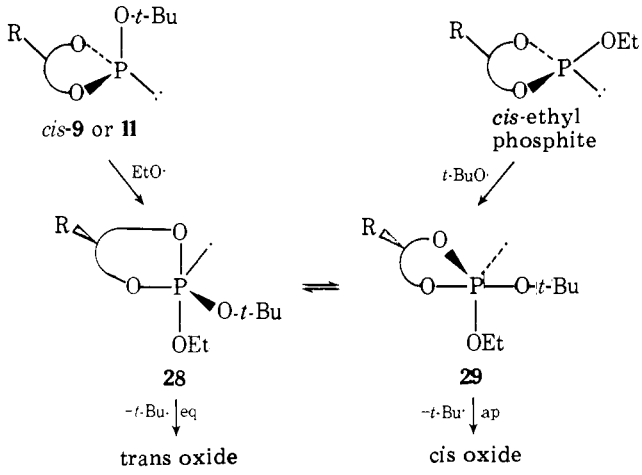
Scheme IV



If, in fact, **26** and its enantiomer are formed in significant amounts in reactions of **8** and **10**, then failure to observe at least some inversion of phosphorus configuration suggests that the isomerization **26** → **27** is slow compared with the rate of β scission. The rate of β scission for **23**[5d] at −60 °C is about five times slower than that of *t*-$Bu(EtO)_3P$·. Using the experimentally determined values of E_a and A for β scission of *t*-$BuO(EtO)_3P$·,[5b,c] one can calculate a rate constant and thus $\Delta G^{\ddagger}$ for that process at 17 °C, the temperature at which the present studies were run. The $\Delta G^{\ddagger}_{17}$ of 10.5 kcal/mol is presumably a lower limit value for the slower β scission of **26**. Since permutation **26** → **27** ($\overline{25}$ → 14 or 15 → $\overline{24}$ of Scheme III) of Scheme IV is unable to compete with β scission, *it must have $\Delta G^{\ddagger}$ greater than about 11 kcal/mol.* There remains the possibility that the bulk of such reactions proceed via $\overline{45}$, which reacts too rapidly to be detected by ESR. At the very least, however, these results require $\Delta G^{\ddagger}$ for $\overline{45}$ → 14($\overline{24}$) to be >11 kcal/mol.

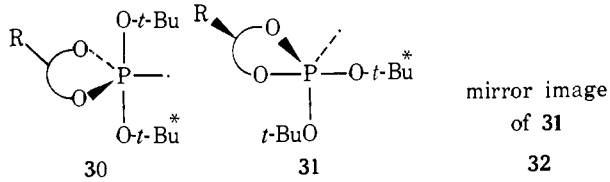
Ethoxy Radical Reactions of 9 and 11. As an alternate to the above conclusion about isomerization rates, it could be argued that **26** → **27** may well be very fast but undetectable if in fact β scission cannot take place at the equatorial position as required for **27** to give product with inverted phosphorus configuration. However, this idea can be discounted in view of the results of cases 11–13 and 20–22 of Table II. Scheme V shows a treatment of the reactions of the *tert*-butyl phosphites **9** and **11** with EtO· which is completely analogous to that given in Scheme IV. The *cis*-ethyl phosphite included in Scheme V would react in exactly the same manner as its methyl counterpart (**8** or **10** in Scheme IV). Thus reaction of **9** or **11** with EtO· allows us to generate directly the radical **28** (**27** of Scheme IV) which would result from isomerization of **29** (**26** of Scheme IV). Were only apical β scission of the *tert*-butoxy group allowed, then *cis*-**9** and **11** would yield cis oxide from reaction with EtO·. That instead trans oxide results (cases 11–13 and 20–22 go with inversion) indicates that presumed **28** gives β scission *directly* without isomerization to **29**. Isomerization in competition with β scission in reactions of any of **8–11** should have lead to loss of stereospecificity. The EtO· reactions of **9** and **11** provide evidence that *β scission occurs in both apical and equatorial positions in such intermediates.* These and the reations of **7**, **8**, and **10** with *t*-BuO· *rule out the*

Scheme V



suggestion[5b] *that an* M_1 *permutation must precede* β *scission.*

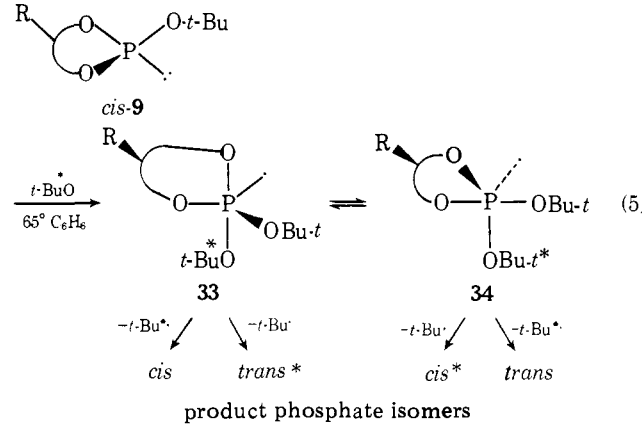
***tert*-Butoxy Radical Reactions of 9 and 11.** The most striking aspect of cases 23 and 24 is the nonstereospecificity observed. (Cis-trans equilibration of phosphites was not observed under reaction conditions.) The most obvious interpretation requires that both *tert*-butoxy groups in the phosphoranyl radical intermediate undergo β cleavage as confirmed by radiochemical label work (see below). Possible intermediates following reaction of cis phosphite are given below (**30–32**) with the incoming *tert*-butoxy marked with an asterisk.



It is likely that the predominance of *cis*-**9**-oxide is a reflection of the effect on its rate of formation of the fact that the cis isomer should be more stable thermodynamically than its trans counterpart. The *cis*-**9**-oxide exists[26] in solution in a single chair conformation with both 5-*tert*-butyl and phosphoryl oxygen in equatorial positions as preferred by these substituents. The *trans*-**9**-oxide, however, should be destabilized by the fact that the 5-*tert*-butyl and phosphoryl oxygen must compete for the equatorial position. It is difficult to estimate the relative thermodynamic stabilities of the oxides of **11.**

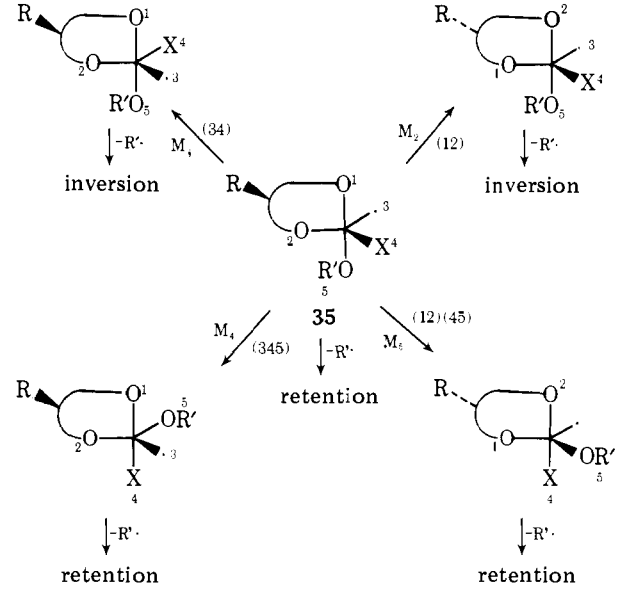
Reactions of 9 with ^{14}C-Labeled *t*-BuO·. In the reactions of *tert*-butoxy radical with **9** and **11** discussed above, an interpretation which involved β scission of both *tert*-butoxy groups of the phosphoranyl radical intermediate was given. The radioactive labeling results of Table III point clearly to the loss of *both* labeled and unlabeled *tert*-butyl radical in reactions of ^{14}C-labeled *tert*-butoxy radicals with *cis*-**9.** This provides further evidence for the actual intermediacy of such a species in the oxidation processes. The irreversibility of the *tert*-butoxy radical addition is a reconfirmation of an important finding we reported[18] earlier in the reaction of *t*-BuO· with $(t\text{-BuO})_3$P.

The results in Table III are readily interpreted as showing that only the trans isomer is labeled. Intermediate **30** could account for this. However, if it is assumed that some portion of intermediate **33** (reoriented mirror image of **31**) is formed by labeled *tert*-butoxy radical attack on *cis*-**9,** then it can be concluded again that the M_1 sort of permutation of substituents shown in eq 5 is not competitive with loss of *tert*-butyl radical. Both intermediates **33** and **34** give cis and trans phosphate product. However, the isomerization **33** ⇌ **34** would lead to a scrambling of label which is not observed.



Finally, the initial formation of 14($\overline{24}$) (Scheme III) can be ruled out now with surety. In the other cases a rapid isomerization following generation of 14($\overline{24}$) might have removed all evidence of its formation. When both RO and Y are *t*-BuO, there is no driving force for conversion to $\overline{25}$(15) since 14($\overline{24}$) and $\overline{25}$(15) are enantiomers. Labeled cis phosphate would necessarily result, but was not found.

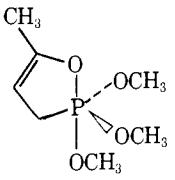
Alternative Permutation Modes. Shown below are various permutational modes (as designated by Musher[19]) applied to intermediates like **26–29,** along with the *stereochemical* effect on subsequent formation of phosphate by loss of R′·. (The effect of an M_1 permutation has been discussed above.) A single example of each type is shown. No physically meaningful reaction mechanism is implied by the numbers in parentheses which are only given to aid in keeping track of changes in locations of ligands. Other orderings of ligands within a mode can be given to designate a given permutation of ligands. It is assumed that the ring attachment must remain ap–eq and that the odd electron stays equatorial. What is seen is that while M_1 rearrangements do not fit with the stereochemical outcome of our experiments (nor do M_2 or M_3), the occurrence of very rapid M_4 or M_5 processes would not alter the stereochemistry but would give retention just as would β scission directly from **35.** It is easy to show that the labeling results of Table III allow



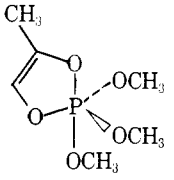
for rapid M_4 or M_5 steps as well. The stereochemical outcome of free-radical substitutions at phosphorus also is consistent with this conclusion.[27] *While we can exclude rapid* M_1*–*M_3 *processes in competition with* α *scission,* M_4 *and* M_5 *processes are not ruled out.* It should be mentioned also that modes M_2–M_5 can arise from a succession of other rearrangement

processes[19] (e.g., $M_1 \times M_1 = M_4$; $M_2 \times M_2 = M_4$, etc.) The restrictions placed on the locations of the ring (ap-eq) and add electron (eq) minimize this possibility.

Comparisons with Phosphoranes and Other Phosphoranyl Radical Systems. The barrier to presumed M_1 methoxy exchange in **36,** which likely requires that the ring CH_2 be placed in the electronically unfavorable apical position, is 10 kcal/mol.[28] That for the oxy analogue, **37,** must be considerably



36



37

lower. The implication of our work is that M_1 isomerization **26** → **27** and analogous processes in cyclic tetraalkoxy phosphoranyl radicals has a barrier of at least 11 kcal/mol. *This suggests strongly that the idea the phosphoranyl radicals are simply analogues of their well-studied phosphorane counterparts is an oversimplification.*

Several theoretical calculations comparing energies of trigonal-bipyramidal (equatorial odd electron) and square-pyramidal (apical odd electron) structures show that the energy difference between the two forms is much greater for the phosphoranyl radicals ($\cdot PH_4$,[24f,29] $\cdot PF_4$,[24f] $\cdot PO_4^{-4}$ [30]) than for the analogous pentacovalent system (PH_5,[24f,29] PF_5[8e,24f]). Berry pseudorotation, a mechanistic example of an M_1 rearrangement, requires a square-pyramidal transition state with calculated $\Delta G^{\ddagger}$ of 34 kcal/mol compared with 1.8 kcal/mol for PH_5.[29] A turnstile process for $\cdot PH_4$ also is calculated[29] to have a very high barrier (15 kcal/mol).[29]

Experimentally, ESR studies have indicated the presence of rapid ligand permutations in $RO\dot{P}H_3$[5f] and $RO\dot{P}F_3$[5n] (modes not defined). For five-membered ring species like **23,** an M_1 rearrangement was excluded, and an M_4 process has been proposed.[5m] This is consistent (as noted above) with our oxidation results and with the stereochemistry of free radical substitutions on phosphorus. The stereochemistry of certain free-radical Arbuzov processes[31] also allows for rapid M_4 or M_5 permutations. However, in acyclic $(RO)_4P\cdot$ systems, results of our studies[1] are not consistent with the occurrence of any permutation mode for an exchange alkoxy groups between apical and equatorial sites with $\Delta G^{\ddagger}$ less than 10–12 kcal/mol. On the other hand, ESR results failed to reveal the presence of a memory effect on the β scission of five-membered ring intermediates similar to **30–32** (R = H), and a rapid ap/eq interchange was proposed.[5p] Clearly, the question of mode and rate of alkoxy radical exchange in phosphoranyl radical intermediates is worthy of further study.

Experimental Section

Gas chromatography was performed on an F & M Model 810 instrument equipped with TC detector. Both ¼ in. aluminum columns packed with about 20% SE-30 on 60–80 mesh Chromosorb W and ¼ in. glass columns packed with 3–4% QF-1 on 100 mesh Gas Chrom Q were employed in temperature-programmed analyses. The glass columns proved especially applicable with sensitive five-membered ring products. No correction was made for small differences possible in sensitivities of isomers. **^{1}H NMR spectra** were obtained on Varian A-60, EM-360, and XL-100-15 instruments. **^{31}P spectra** were recorded on the XL-100 operating in the CW mode with proton-phosphorus splitting noise decoupled. A Beckman 1R-5A infrared spectrophotometer was used to obtain infrared spectra. Microanalyses were performed by Schwartzkopf Microanalytical Laboratory, Woodside, N.Y., and Galbraith Laboratories, Knoxville, Tenn. Melting points are uncorrected.

Benzene was typically purified by washing with concentrated sulfuric acid, 5% NaOH, and then H_2O before drying over $CaCl_2$ and distillation from $LiAlH_4$. It was stored over 3A molecular sieves. **Acetonitrile** was purified according to Weissberger.[32] **Diethyl peroxide**[33] and **di-*tert*-butyl hyponitrite**[34] were prepared by literature procedures.

Oxidations of Phosphine 7. The phosphine, (−)-(*R*)-**7,** was prepared by Cl_3SiH/Et_3N reduction[10] of (+)-(*R*)-methylphenyl-*n*-propylphosphine oxide synthesized in near 100% optical purity according to the method of Mislow et al.[11] Rotations were measured in methanol using a recording polarimeter at the concentrations indicated in Table I. Oxidation of **7** by *tert*-butyl hydroperoxide to establish optical purity and for comparison with *tert*-butoxy radical oxidation was carried out as in the following example. Phosphine **7**, $[\alpha]^{20}D$ −13.0°, (0.60 g, 3.6 mmol) was dissolved in 24 ml of dry pentane previously flushed with pure nitrogen, and the solution was cooled to 0 °C. *tert*-Butyl hydroperoxide (1.1 g, 12 mmol) in 5 ml of pentane was then added dropwise with stirring. After the reaction mixture had been stirred an additional 30 min, the solvent was removed under vacuum to leave an oil $[\alpha]^{20}D$ −16.4°. Two recrystallizations (constant rotation) from *n*-hexane gave the white, solid **7**-oxide (0.32 g, 1.8 mmol, 49% yield), $[\alpha]^{20}D$ −16.8°.

For the reactions of **7** with DBH, the following is typical. Phosphine **7** (1.0 g, 6.0 mmol, $[\alpha]^{20}D$ −13.0°) and DTBH (1.0 g, 5.8 mmol) were dissolved in 2 ml of acetonitrile in a tube sealed with a rubber septum. The solution was thoroughly flushed with pure nitrogen and then heated at 65 °C for 2 h. GLC showed no remaining **7.** Removal of solvent under vacuum left an oil which showed only **7**-oxide on GLC analysis, $[\alpha]^{20}D$ −16.2°. Two crystallizations (constant rotation) from *n*-hexane yielded pure **7**-oxide, a white solid (0.59 g, 32 mmol, 53% yield), $[\alpha]^{20}D$ −16.4°.

Phosphites 8, 10, and 11. These materials were synthesized by standard methods and have been previously described stereochemically by us.[13,14]

Phosphite 9. This material was obtained in excellent purity without distillation (estimated 95% pure by ^{1}H NMR) from 2-chloro-5-*tert*-butyl-1,3,2-dioxaphosphorinane;[13] e.g., potassium (0.20 g, 5.1 mmol) was placed in 20 ml of dry benzene to which was then added *tert*-butyl alcohol (0.50 g, 7.2 mmol). The mixture was stirred under nitrogen atmosphere until the potassium was consumed. A solution of the phosphorochloridite (1.0 g, 5.1 mmol) in 20 ml of benzene was added dropwise to the alkoxide–benzene mixture which was stirred at 0 °C. Upon warming to room temperature, the mixture became clear. The solution was stirred for an additional 48 h. Following removal of solvent and addition of pentane, a white suspended solid, presumably KCl, was removed by centrifugation. Removal of the pentane left a light-yellow oil which decomposed on attempted GLC analysis. ^{1}H NMR indicated this to be highly pure single isomer of **9** (cis). This material was used without further purification in the radiochemical labeling work. ^{1}H NMR (C_6H_6) δ 0.65 (9 H, s, 5-*t*-Bu), 1.46 (9 H, s, *t*-BuO), 1.74–2.32 (1 H, m, methine H), 3.62–5.70 (4 H, m, CH_2); ir (thin film) 3.38 (s), 6.80 (s), 7.16 (w), 7.30 (m), 7.80 (s), 8.05 (s), 8.45 (w), 8.75 (s), 8.90 (m), 9.52 (s), 9.80–10.05 (broad, s), 10.45 (broad, s), 10.70 (m), 11.25 (m), 11.90 (s), 12.45 (s), 13.88 (m) μ.

9-Oxide. To a solution of the above sample of **9** (0.234 g, 1.00 mmol) in 10 ml of benzene at 0–5 °C was added dropwise *tert*-butyl hydroperoxide (0.100 g, 1.11 mmol) in benzene (5 ml). Following 1 h of stirring and removal of solvent, a white solid was obtained (in quantitative amounts based on **9**) which ^{1}H NMR (C_6H_6) showed to have a structure possessing only a single 5-*tert*-butyl group. Recrystallization from benzene gave pure *cis*-**9**-oxide, mp 111–113 °C. ^{1}H NMR ($CDCl_3$) δ 0.934 (9 H, s, 5-*t*-Bu), 1.53 (9 H, s, *t*-BuO), 1.81–2.34 (1 H, m, methine H), 4.10–4.54 (4 H, m, CH_2); ir (CCl_4) 3.50 (s), 7.15 (m), 7.29 (s), 7.65 (s), 8.04 (m), 8.45 (m), 8.75 (s), 9.42 (s), 9.63 (s), 10.0 (broad, s) μ.

Anal. Calcd for $C_{11}H_{23}PO_4$: C, 52.77; H, 9.27; P, 12.38. Found: C, 52.52; H, 9.15; P, 12.24.

9-Sulfide. To a cold solution of **9** (0.200 g, 0.856 mmol) in benzene (15 ml) was quickly added a cold slurry of sulfur (0.050 g, 1.6 mmol) in benzene (5 ml) while maintaining a nitrogen atmosphere. After stirring for 30 min, filtration, and solvent removal in vacuo, an oil was isolated which crystallized on cooling. Recrystallization from hexane gave a white solid: mp 80–81 °C; ^{1}H NMR (C_6H_6) δ 0.59 (9 H, s, 5-*t*-Bu), 1.47 (9 H, s, *t*-BuO), 1.64–1.82 (1 H, m, methine H), 3.74–4.18 (4 H, m, CH_2); ir (CCl_4) 3.44 (s), 3.51 (m), 6.80 (m), 7.15 (w), 7.32 (m), 7.82 (s), 8.05 (m), 8.60 (m), 8.92 (m), 9.24 (m), 9.50 (broad, s), 10.05 (s), 10.28 (s) μ.

Anal. Calcd for $C_{11}H_{23}PO_3S$: C, 48.58; H, 8.71; P, 12.04. Found:

C, 49.76; H, 8.58; P, 11.70.

In another preparation in benzene, **9** was obtained very pure in a 66/44 cis/trans ratio as shown by the presence of two distinct 5-*tert*-butyl peaks in the ^{1}H NMR spectrum (δ 5-*t*-Bu = 0.908 (trans), 0.625 (cis)). Oxidation of this mixture was effected by addition of a saturated solution of N_2O_4 in CH_2Cl_2 to the mixture of **9** isomers. Removal of solvent gave a solid. The ratio of phosphate isomers as determined by integration of the 5-*tert*-butyl peaks corresponded closely to that of the starting phosphite, **9.** ^{1}H NMR of mixture (C_6H_6) δ 0.469 (cis isomer) and 0.574 (trans) (9 H total, s pair, 5-*t*-Bu), 1.36 (9 H, s, *t*-BuO), 1.65–1.84 (1 H, m, methine H), 3.80–4.38 (4 H, m, CH_2).

Preparation of **9** by a procedure otherwise identical with that above but using ether instead of benzene as solvent gave extremely pure **9** in 5/95 cis/trans ratio. This sample of **9** was purified by short-path vacuum distillation. This ratio changed to 14/86 when the sample stood for several months in a refrigerator (cases 11–13). All attempts to analyze **9** or its oxide by GLC failed even on glass columns.

Assignment of Cis/Trans Geometries to Isomers of 9. Both cis-rich and trans-rich mixtures of **9** were subjected to computer-assisted ^{1}H NMR analysis using the LAOCN3 program as we have described earlier for **8**[13] and similar 1,3,2-dioxaphosphorinanes.[15] These ring systems represent AA′BB′XY spin systems. Key parameters in the assignment for the trans isomer were the vicinal couplings, J_{HH} and J_{HP} (Hz), for the $CH_XCH_AH_BOP$ grouping where H_X is the methine H, H_A, and H_B are the methylene hydrogens, and P is the Y spin: J_{AX} = 4.31; J_{BX} = 4.72; J_{AP} = 9.25; J_{BP} = 4.62. These parameters show, by analogy to *trans*-**8**,[13] the population of more than one conformer in solution. The corresponding coupling constants for *cis*-**9** are: J_{AX} = 12.0; J_{BX} = 4.15; J_{AP} = 3.07; J_{BP} = 11.39. *Cis*-**9** is assigned a single chair conformation with 5-*tert*-butyl equatorial. In addition the relative chemical shifts of the 5-*tert*-butyls are in the order noted for cis and trans isomers in similar compounds.

Phosphate 12. The phosphite precursor to **12** was synthesized as a mixture of cis and trans isomers in routine fashion from reaction of 2-chloro-5-*tert*-butyl-1,3,2-dioxaphosphorinane[13] with ethanol in the presence of Et_3N, and purified by vacuum distillation, bp 67–68° (0.5 mm). Assignment of geometries to the isomers was made on the basis of their relative ^{31}P chemical shifts[15b] (in ppm downfield from external 85% H_3PO_4): cis, 123.5; trans, 130.8. This was further confirmed by comparison of the 5-*tert*-butyl chemical shifts by reference to **8, 9** and other analogues.[13,15]

Anal. Calcd for $C_9H_{19}O_3P$: C, 52.43; H, 9.22; P, 15.05. Found: C, 52.25; H, 9.27; P, 15.22.

Oxidation of the above phosphite with N_2O_4 afforded the corresponding phosphate, **12**, as a mixture of isomers used to confirm by GLC and ^{1}H NMR the formation of **12** in cases 11–13 of Table II.

Phosphate 13. The phosphite precursor to **13,** the known 2-ethoxy-4-methyl-1,3,2-dioxaphospholane, was synthesized from the 2-chloro-4-methyl-1,3,2-dioxaphospholane on reaction with ethanol in the presence of Et_3N by a procedure exactly parallel to that reported earlier for **10** and **11.** This cis and trans geometries of the isomers formed were inferred from the relative ^{31}P chemical shifts[15] (downfield from external 85% H_3PO_4): cis, 140.5; trans, 136.7. The phosphite was better than 98% pure by GLC without distillation and was converted directly by stereospecific, retentive N_2O_4 oxidation to the mixture of cis/trans isomers of **13** which was used to dope the product samples for GLC identification of products of cases 20–22, Table II.

8-Sulfide. A mixture of the sulfides, cis/trans = 92/8, generated on reaction of S_8 with **8** at 0 °C in C_6H_6 for 2 h gave an oily solid on removal of solvent which recrystallized from hexane to give pure *cis*-**8**-sulfide (2-methoxy-2-thio-5-*tert*-butyl-1,3,2-dioxaphosphorinane): mp 134–135 °C; ^{1}H NMR ($CDCl_3$) δ 0.95 (9 H, s, 5-*t*-Bu), 2.15 (1 H, m, methine H), 3.77 (3 H, d, J_{HP} = CH_3O), 4.30 (4 H, m, CH_2); ir (Nujol) 8.97, 9.52, 9.63, 9.98, 10.3, 11.2, 11.9, 11.2, 15.2 μ.

Anal. Calcd for $C_8H_{17}O_3PS$: C, 42.84; H, 7.72; P, 13.81. Found: C, 42.98; H, 7.82; P, 13.72.

Pure ***trans*-8-sulfide** was isolated by preparative GLC (Varian Aerograph A90-P3) from a 23/77 cis/trans sulfide mixture generated by reaction of sulfur with **8** having cis/trans ratio 27/73: mp 44–45 °C; ^{1}H NMR ($CDCl_3$) δ 1.00 (9 H, s, 5-*t*-Bu), 1.97 (1 H, m, methine H), 3.77 (3 H, d, J_{HP} = 13 Hz, CH_3O), 4.60 (4 H, m, CH_2); ir (Nujol) 7.69, 8.97, 9.55, 10.0, 11.9 μ.

Anal. Calcd for $C_8H_{17}O_3P$: C, 42.84; H, 7.72; P, 13.81. Found: C, 43.13; H, 7.76; P, 13.72.

8-Oxide. The preparation and properties of the oxide isomers of **8** have been described previously.[13]

10-Oxide. A sample of **8** (3.65 g, 26.8 mmol) having cis/trans ratio 34/66 as determined by integration of the 4-methyl ^{1}H NMR resonances (δ cis, 1.18; δ trans, 1.03 in benzene) was dissolved in 20 ml of benzene. The resulting solution was cooled to about 10 °C and to it was added slowly and dropwise a benzene solution saturated with N_2O_4 until ^{1}H NMR analysis showed complete consumption of **10** and the formation of the phosphate of **10,** 2-methoxy-2-oxo-4-methyl-1,3,2-dioxaphospholane. The area ratio of the 4-methyl peaks assigned to the cis (δ = 0.883) and trans (δ = 0.933) isomers of **10**-oxide was 34/66. Removal of solvent and vacuum distillation yielded pure **10**-oxide (3.50 g, 23.0 mmol) in 86% yield: bp 70 °C (0.1 mm); ^{1}H NMR (C_6H_6) trans isomer δ 1.09 (3 H, d J_{HH} = 6.0 Hz, 4-CH_3), 3.57 (3 H, d, J_{HP} = 11.7 Hz, 2-CH_3O); cis isomer δ 1.05 (3 H, d, J_{HH} = 6.0 Hz, 4-CH_3), 3.55 (3 H, d, J_{HP} = 11.8 Hz, 2-CH_3O); cis and trans isomers δ 3.28–4.72 (3 H, m, $CHCH_2$). An independent experiment with purified **10**-oxide and internal standardized GLC methods gave a yield of **10**-oxide of 92%.

11-Oxide. Oxidation of **11** with N_2O_4 in benzene, as with **10,** afforded a product which appeared by ^{1}H NMR to be highly pure. Because of thermal instability, the resulting phosphate was not distilled nor could cis/trans isomer ratios be reliably obtained by GLC as the sensitivity and isomer ratios changed gradually on repeated injections. This sample was used to verify the formation of **11-oxide** by GLC as well as ^{1}H NMR in the *tert*-butoxy radical oxidations of **11,** but all quantitative analyses were done by ^{1}H NMR. The correspondence between cis/trans ratios in phosphite and N_2O_4 generated phosphate as determined by ^{1}H NMR was closely similar to that noted above for **10.**

Oxidations of 8–11 by Free Radicals. The oxidations with **8** in CH_3CN were run in tubes capped with a rubber septum. The solutions were flushed carefully with purified nitrogen after addition of all reactants and prior to reaction. In all other cases the reaction tubes were degassed at 10^{-5} to 10^{-6} mm by three or more freeze–thaw cycles and sealed under vacuum. Careful cleaning of all tubes followed by a Et_3N or NH_3 rinse and drying at 110 °C was required to prevent cis/trans isomer equilibration of trivalent reactants. Careful controls demonstrated the absence of oxidation without the presence of added free radical sources and, at temperature or under irradiation conditions (450-W Hanovia medium pressure lamp), the stability toward decomposition of **8–11** and lack of equilibrium of mixtures of cis and trans isomers not already at thermal equilibrium. Although mixtures of reactants containing DTBH could not be subjected to GLC analysis, in all other cases where yields or product ratios were determined by GLC, it was shown that the reactant mixtures were highly stable to GLC conditions. Product yields were determined by GLC or ^{1}H NMR analysis using an appropriate internal standard added after completion of the reaction. ^{1}H NMR spectra of products were run at 60 or 100 MHz depending on how well separated were the peaks. All phosphites were purified by distillation before use except **9.** In this instance material used in cases 11–13 had been distilled, but in case 23 was material initially made in highly pure form (^{1}H NMR). Phosphates and thiophosphates were identified in each case by ^{1}H NMR comparisons and, except for reaction to give **9-oxide**, by GLC retention time comparison using product samples doped with authentic phosphate. This was done even in reactions of **11** with *tert*-butoxy radicals although, as explained above, quantitative product data could not be obtained in this manner. As detailed in the paragraphs below describing labeling experiments, in one experiment, the **9-oxide** product mixture was subjected to quantitative analysis for C, H, and P.

Reactions of 9 with ^{14}C-Labeled *tert*-Butoxy Radicals. *tert*-Butyl chloride labeled at the 2 position, prepared from the corresponding labeled alcohol (New England Nuclear), was readily converted to the di-*tert*-butyl hyponitrite by the method of Kiefer and Traylor.[34] Liquid scintillation counting was carried out using a Packard Tri-Carb Model 3003 instrument. Samples to be counted were first dissolved in 1 ml of toluene to which was then added 10 ml of a solution of BBOT scintillator in toluene (15 g/3.8 l.). Activities were experimentally in the range 2000–5000 counts/min. Very small background corrections (20–30 cpm) were employed. The absence of self-quenching was evidenced by measurements at different substrate concentrations. The activity of the hyponitrite was precisely twice that of the alcohol counted as the urethane derivative. The fraction activity (f) of Table III is equal to (disintegrations min^{-1} $mmol^{-1}$ of phos-

phorus product)/(disintegrations min^{-1} $mmol^{-1}$ of *tert*-butyl alcohol).

Following deoxygenation of the reaction solutions by a pure nitrogen purge, the serum-cap-sealed tubes were heated for 8–10 di-*tert*-butyl hyponitrite decomposition half-lives[34] at 65 °C. Phosphite **9** used in these studies was the cis isomer, undistilled following preparation, but shown to be highly pure by ^{1}H NMR and by conversion by *tert*-butyl hydroperoxide to **9**-oxide in essentially quantitative yield. ^{1}H NMR analysis of the product mixture revealed the formation of the cis and trans phosphates in 66/34 ratio. Attempts to isolate the two phosphates by column chromatography (Florisil) or TLC (silica gel G) were unsuccessful. Separation was attained by TLC, but the phosphates could not be eluted from the solid phase. The R_f of one of the spots, however, was shown to be the same as that for the pure **9**-oxide prepared by *tert*-butyl hydroperoxide oxidation of **9**.

The above phosphate mixture could be changed in composition by repeated crystallizations from ether–hexane solvent. Following each crystallization, the phosphate mixture was counted and the proportions of isomers determined from integration of the 5-*tert*-butyl resonances in the ^{1}H NMR spectrum (see Table III). The recrystallized mixture was also subjected to microanalysis.

Anal. Calcd for $C_{11}H_{23}PO_4$: C, 52.77; H, 9.27; H, 12.38. Found: C, 52.55; H, 9.44; P, 12.56.

When an excess of phosphite **9** was used, the product mixture was treated with sulfur to convert unreacted **9** to its sulfide which was then isolated by column chromatography on Florisil and assayed for radioactivity. This sulfide was identical with the **9**-sulfide described above.

Solutions of unlabeled phosphate containing labeled hyponitrite were deoxygenated and heated at 65 °C. The phosphate isolated by crystallization from hexane had a negligible amount of incorporated radioactivity.

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