Bromo-*tert*-butyl Hydroperoxide. The preparation was similar to that reported previously[12b] for other β-bromohydroperoxides. The crude hydroperoxide (86% pure by iodometric titration) was obtained in 62% yield. Distillation with a molecular still connected to a vacuum line at 10^{-3} mm (bath temperature, 40°) gave a clear colorless liquid (95% pure) (lit.[12a] bp 33° (0.05 mm)): nmr $(CH_3)_2$ (1.33, s, 6.3), CH_2 (3.50, s, 2.0), OOH (8.28, s, 0.91), and OOH in DMSO (11.04, s).

3,3-Dimethyl-1,2-dioxetane (5). To a distillation apparatus under 10 mm pressure, 0.1 g of bromo-*tert*-butyl hydroperoxide was added dropwise to 1 ml of saturated aqueous potassium hydroxide solution contained in the pot at room temperature. The receiver was cooled in a Dry Ice–isopropyl alcohol bath (−78°). The distillate was redistilled at 0° under reduced pressure with the receiver at −78°. Chloro-*tert*-butyl hydroperoxide was also used to prepare **5** by this method.

Product Studies. The reactions were carried out in sealed tubes with the internal standard (*tert*-amyl alcohol) and were allowed to proceed through at least ten half-lives before analysis. Analyses were obtained by glc using a 5 ft × 1/8 in. PAR-2 column at 120°. Calculation of yields was made by comparison with the glc record of a standard mixture which contained the products and the internal standard. Gas analyses were made by standard vacuum line techniques combined with mass spectral analysis.

Kinetic Methods. The base and the hydroperoxide solutions, in separate volumetric flasks, were thermally equilibrated and then mixed in a thermally equilibrated vessel under a nitrogen atmosphere. Aliquots were periodically withdrawn and analyzed iodometrically.[16] A similar procedure was used for the acidometric measurements, except that the aliquots were quenched by addition to standard acid and then titrated with standard base to the phenolphthalein end point. In the glc procedure, the aliquots were quenched with acid to a pH of 8. The relative amounts of **1** in the aliquots were determined by reference to an internal standard (*tert*-amyl alcohol). Various concentrations of a standard mixture of **1** with the internal standard gave reproducible amounts of **2**, by comparison to a standard mixture of **2** and the internal standard. The analyses were carried out on a 10 ft × 1/8 in. Apiezon column at 90°. The light emission studies were obtained with a Beckman DU, equipped with an RCA 1P28 phototube, thermospacers, and output to a recorder. For rapid reactions, the base solution was thermally equilibrated in the spectrometer and then a small amount of hydroperoxide solution was injected into the base solution and rapidly mixed. The kinetic data were normally processed with the aid of a least-squares computer program.

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The Exchange Route to Oxyphosphoranes[1]

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Abstract: It has been found that acyclic phosphoranes which contain at least two alkoxy groups often undergo exchange with 1,2- and 1,3-glycols to give oxyphosphoranes containing one or two rings. These materials undergo pseudorotation at room temperature. Pseudorotation is restricted to equatorial–apical switching in the five-membered ring compounds. The six-membered ring compounds are not so restricted. In some cases variable-temperature nmr measurements have given information on inhibition of pseudorotation. 1,4-Butanediol and 1,5-pentanediol react with pentaethoxyphosphorane and triphenyldiethoxyphosphorane, respectively, to give tetrahydrofuran and tetrahydropyran in very good yield. Attempts to exchange benzyl alcohol with pentaethoxyphosphorane led to decomposition. Similarly the reaction of tribenzyl phosphite with diethyl peroxide produced a very unstable phosphorane which decomposed almost as fast as it formed.

In earlier work it was shown that pentaethoxyphosphorane (**1**), undergoes an exchange reaction with *n*-propyl alcohol to give new phosphoranes containing *n*-propyloxy groups.[5] More recently Ramirez and coworkers have shown that the cyclic unsaturated oxyphosphoranes derived from 1,2-dicarbonyl compounds and trialkyl phosphites also undergo exchange of the alkoxy groups when they are allowed to react with alcohols. The unsaturated ring is preserved during these transformations.[6a] They have also shown that pentaphenoxyphosphorane exchanges with catechol to give five-membered ring containing phosphoranes.[6b,c] This report concerns itself with the exchange of a variety of alkoxy containing phosphoranes with glycols and alcohols. In general the phosphoranes were prepared by allowing the appropriate trisubstituted phosphorus compound to react with diethyl peroxide.[7] This method is perhaps the most general one for producing oxyphosphoranes; however, during their formation tetrasubstituted phosphorus compounds are usually formed. In this work such materials were generally present and they were only partially removed in a few cases by distillation. There is no reason for suspecting that these substances had any effect on the reactions under investigation. The presence of these substances and the general hydrolytic instability of the oxyphosphoranes

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(5) D. B. Denney and L. Saferstein, *J. Amer. Chem. Soc.*, **88**, 1839 (1966).
(6) (a) F. Ramirez, K. Tasaka, N. B. Desai, and C. P. Smith, *ibid.*, **90**, 751 (1968); (b) F. Ramirez, A. J. Bigler, and C. P. Smith, *ibid.*, **90**, 3507 (1968); (c) F. Ramirez, A. J. Bigler, and C. P. Smith, *Tetrahedron*, **24**, 5041 (1968).
(7) (a) D. B. Denney and D. H. Jones, *J. Amer. Chem. Soc.*, **91**, 5821 (1969); (b) D. B. Denney, D. Z. Denney, B. C. Chang, and K. L. Marsi, *ibid.*, **91**, 5243 (1969).

Table I. Nmr Spectral Data for Five-Membered Ring Containing Phosphoranes[a]

Compd	$\delta^{31}P^b$	CH_2CH_2 δ	CH_2CH_2 J_{PH}	OCH_2 δ	OCH_2 J_{PH}	OCH_2 J_{HH}	CH_3 δ	CH_3 J_{PH}	CH_3 J_{HH}	P-CH_3 δ	P-CH_3 J_{PH}
9	50	3.64	14	3.86[c]			1.1	2	7		
10	36	3.71	13	3.64	7	7	*d*				
11	28	3.70	12	3.35	7	7	0.97		7		
12	32	3.68	13							1.85	11
13	33	3.58	14							1.45	9
14	35	3.61	13								
15	25	3.70	13	3.79	7	7	1.15		7	1.48	17
16	23	(3.54	15)[e]								
17	27	3.28–3.55[f]		3.78	10	7	1.13	2	7		
18	19	3.20–4.14[f]									
19	8	3.50–4.00[f]								1.54	17

[a] The spectra were recorded at 60 MHz in methylene chloride except for **9** which was taken on a neat sample and **17** which was taken at 100 MHz in toluene-d^8. [b] All shifts are positive relative to 85% phosphoric acid. [c] Probably two overlapping quartets. [d] Could not determine. [e] Tentative assignment because of decomposition and ethanol. [f] Multiplet.

Table II. Nmr Spectral Data for Six-Membered Ring Containing Phosphoranes[a]

Compd	$\delta^{31}P^b$	Ring CH_2 δ	Ring CH_2 J_{PH}	OCH_2 δ	OCH_2 J_{PH}	OCH_2 J_{HH}	CH_3 δ	CH_3 J_{PH}	CH_3 J_{HH}	Ring CH_3 δ	P-CH_3 δ	P-CH_3 J_{PH}
20	70	3.59	18	3.83	7	7	1.13	2	7	0.96		
21	52	3.60	17	3.82	7	7	1.16	2	7	0.96		
22	40	3.49	16	3.14	7	7	0.90		7	0.92		
23	42	3.60	16	3.78	8	7	1.13	1	7	0.95	1.48	17
24	66	3.59	18	*c*			1.16	2	7	0.90		
25	49	3.65	16							0.95		
26	39	3.66	16							0.98	1.52	18

[a] The spectra of **20**, **22**, **23**, and **26** were recorded at 60 MHz in methylene chloride. The rest were recorded at 100 MHz in methylene chloride. [b] All chemical shifts are positive relative to 85% phosphoric acid. [c] Could not assign.

has precluded the obtention of standard analytical data. Furthermore, attempts to obtain mass spectral data have never led to the observation of a parent ion. In general, peaks were observed for the phosphoryl containing compound(s) derived from the phosphorane. The structural assignments reported for these compounds rest therefore on ^1H and ^{31}P nmr spectroscopy, methods of preparation, and chemical reactions.

Results

The pentasubstituted phosphorus compounds **1–8**

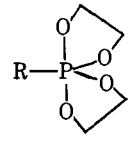
$$R_1R_2R_3P(OC_2H_5)_2 + HOCH_2CH_2OH \longrightarrow R_1R_2R_3P\langle O\rangle$$

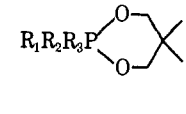
1, $R_1 = R_2 = R_3 = OC_2H_5$
2, $R_1 = C_6H_5$; $R_2 = R_3 = OC_2H_5$
3, $R_1 = R_2 = C_6H_5$; $R_3 = OC_2H_5$
4, $R_1 = R_2 = C_6H_5$; $R_3 = CH_3$
5, $R_1 = C_6H_5$; $R_2 = R_3 = CH_3$
6, $R_1 = R_2 = R_3 = C_6H_5$
7, $R_1 = CH_3$; $R_2 = R_3 = OC_2H_5$
8, $R_1 = R_2 = R_3 = C_4H_9$
9, $R_1 = R_2 = R_3 = OC_2H_5$
10, $R_1 = C_6H_5$; $R_2 = R_3 = OC_2H_5$
11, $R_1 = R_2 = C_6H_5$; $R_3 = OC_2H_5$
12, $R_1 = R_2 = C_6H_5$; $R_3 = CH_3$
13, $R_1 = C_6H_5$; $R_2 = R_3 = CH_3$
14, $R_1 = R_2 = R_3 = C_6H_5$
15, $R_1 = CH_3$; $R_2 = R_3 = OC_2H_5$
16, $R_1 = R_2 = R_3 = C_4H_9$

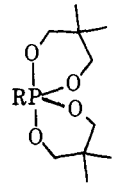
were allowed to react with equimolar amounts of ethylene glycol. The course of the reactions was monitored by ^{31}P nmr spectroscopy. In all cases absorptions appeared which are assigned to the phosphoranes **9–16**. These substances all show ^{31}P nmr chemical shifts which are considerably downfield from their precursors. Such a change in chemical shift is characteristic of the introduction of a five-membered ring into the phosphorane.[8,9] In general the major product was the monoring compound. Compounds **12**, **13**, and **16** were not very stable and decomposed to the phosphine oxides fairly rapidly. In particular, **16** was by far the least stable material of the series. Substance **9** could be distilled under reduced pressure. Treatment of **9**, **10**, and **11** with ethanol did not lead to their reversion to the acyclic phosphoranes.

The ^1H nmr spectral data for **9–16** are collected in Table I. It is instructive to note that the protons of the five-membered rings are all equivalent as are those of the methylene and methyl groups of the ethoxy groups. Similarly the methyl hydrogens of **13** are equivalent.

Treatment of **1**, **2**, and **7** with 2 mol or more of ethylene glycol led to changes in the ^{31}P nmr spectra which indicated that the bisring compounds **17–19** were







17, R = OC_2H_5
18, R = C_6H_5
19, R = CH_3
20, $R_1 = R_2 = R_3 = OC_2H_5$
21, $R_1 = C_6H_5$; $R_2 = R_3 = OC_2H_5$
22, $R_1 = R_2 = C_6H_5$; $R_3 = OC_2H_5$
23, $R_1 = CH_3$; $R_2 = R_3 = OC_2H_5$
24, R = OC_2H_5
25, R = C_6H_5
26, R = CH_3

formed. In these materials the ^{31}P nmr absorptions were found at lower fields than those of the monoring compounds.[9] Treatment of these substances with ethanol did not lead to reversion to monoring or acyclic phosphoranes. The ^1H nmr spectra of the ring methylene protons of **18** and **19** very clearly show that there is a nonequivalency present. On the other hand the spectrum of **17** at 60 MHz appeared deceptively simple

(8) F. Ramirez and N. Desai, *J. Amer. Chem. Soc.*, **85**, 3252 (1963).
(9) F. Ramirez, M. Nagabhushanam, and C. P. Smith, *Tetrahedron*, **24**, 1785 (1968).

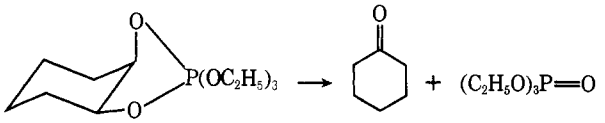
with the ring methylene hydrogens appearing as a distorted doublet. The spectrum was obtained in several solvents at various concentrations and at both 60 and 100 MHz. It has been shown quite conclusively that there is nonequivalency of the ring protons of **17**.

Exchange of **1**, **2**, and **3** with neopentyl glycol (1 mol) yielded compounds **20–22**. Once again exchange was essentially complete and the monoring compounds were the predominant products. Reaction of diethyl peroxide with the appropriate six-membered ring phosphonite afforded **23**. Compounds **20–22** did not revert to the acyclic phosphoranes on treatment with ethanol. They did decompose though to give tetrasubstituted materials at a more rapid rate than the five-membered ring compounds. The ^1H nmr spectral data for these substances, Table II, show that the hydrogens of the methyl groups on the ring are equivalent as are the methylene hydrogen atoms.

Treatment of **1**, **2**, and **23** with neopentyl glycol yielded the bisring compounds **24–26**. Once again the ^1H nmr spectra show that the ring methyl group hydrogens are equivalent as are the ring methylene group hydrogens.

Reaction of **1** with *trans*-1,2-cyclohexanediol led to the production of a new phosphorane, **27**, which absorbed in the ^{31}P nmr at $+56$. This material decomposed slowly at room temperature to give cyclohexene oxide. The mechanism of this decomposition has been discussed and the decomposition of **27** is in accord with it.[7a]

Reaction of **1** with *cis*-1,2-cyclohexanediol yielded one major product, **28**, which absorbed at $+53$. This material was stable at 100° but decomposed at higher temperatures to give cyclohexanone and triethyl phosphate.



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Other 1,2-glycols which gave monocyclic oxyphosphoranes by exchange with **1** are propylene glycol, *dl*-2,3-butanediol, and styrene glycol. The spectral data for the oxyphosphoranes agreed with the data obtained on the same materials prepared by allowing the corresponding cyclic phosphites to react with diethyl peroxide.[7a]

The reaction of **1** with pinacol took an interesting course; the major products after 3 days were triethyl phosphate, pinacol, and ethanol. Minor phosphorus containing compounds were observed by ^{31}P nmr.

Reaction of **1** with 1,4-butanediol was extremely exothermic and led under controlled conditions, 0°, to the formation of tetrahydrofuran in 87% yield. 1,5-Pentanediol reacted with **1** in the absence of solvent to give tetrahydropyran in 26% yield. The compound, **6**, in methylene chloride reacted with 1,5-pentanediol to give tetrahydropyran in 81% yield.

When **1** was allowed to react with benzyl alcohol, decomposition occurred. The major products were dibenzyl ether, ethanol, and triethyl phosphate. Tribenzyl phosphite reacted with diethyl peroxide to give a phosphorane which decomposed almost as rapidly as it was formed.

Discussion

The reactions of the acyclic phosphoranes with 1,2- and 1,3-glycols are generally good methods for the preparation of monoring and bisring compounds. Notable exceptions are found in the reactions of **1** with pinacol and that of **6** with neopentyl glycol. In the latter case exchange occurred but no cyclic phosphorane was obtained. The exchange route complements the peroxide–cyclic phosphite reaction and thus *two general methods* are now available for the preparation of a wide variety of cyclic oxyphosphoranes. The exchange of acyclic phosphoranes with alcohols occurs readily; however, the reactions have not been studied in sufficient detail to make their utility known.

The unsubstituted five-membered ring containing oxyphosphoranes appear to be thermodynamically more stable than their acyclic analogs. Similar observations have been made with a variety of cyclic unsaturated five-membered ring containing oxyphosphoranes.[6b,c,9] It is not necessarily true that all five-membered ring containing oxyphosphoranes are more stable than acyclic oxyphosphoranes. For example, reaction of tetramethylethylene ethyl phosphite with diethyl peroxide gave a very unstable oxyphosphorane which decomposed at room temperature to give triethyl phosphate and tetramethylethylene oxide.[7a] Formation of the first ring is generally fast and thus monoring compounds can be prepared in good yield even though the evidence strongly suggests that the bisring compounds are thermodynamically more stable. The same trend of thermodynamic and kinetic parameters seem to operate with the six-membered ring systems; however, they cannot be regarded as established. In fact one exception to the thermodynamic trend has already been noted, *i.e.*, the reaction of **6** with neopentyl glycol.

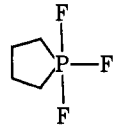
The reactions of 1,4-butanediol and 1,5-pentanediol with **1** and **6** undoubtedly involve monoexchange followed by a displacement reaction which yields the heterocycle and tetrasubstituted phosphorus compound. In fact **1** and **6** can be used as synthetic reagents for the preparation of a wide variety of heterocycles (unpublished research).

One of the more fascinating aspects of the chemistry of pentasubstituted phosphorus compounds is the intramolecular transposition of groups which has been dubbed pseudorotation.[10] During the years since its recognition some generalities concerning pseudorotation have been advanced. In general it is assumed that the pentasubstituted phosphorus compounds exist in solution as trigonal bipyramids. It has often been assumed that the positional exchange occurs by a motion of the two apical groups to equatorial positions with a similar shift of two equatorial groups to apical position. This change is the Berry mechanism for pseudorotation. One generality which has arisen is the electronegativity effect,[11] which states that within a pentasubstituted phosphorus compound the more electronegative groups will favor apical positions of the trigonal bipyramidal structure; thus compounds R_3PF_2 do not pseudorotate at room temperature and the fluorines are in apical positions; on the other hand RPF_4 compounds

(10) R. S. Berry, *J. Chem. Phys.*, **32**, 933 (1960).
(11) E. L. Muetterties, W. Mahler, and R. Schmutzler, *Inorg. Chem.*, **2**, 613 (1963).

do pseudorotate. Pseudorotation with these substances occurs in such a manner that the R group remains in an equatorial position and the fluorines exchange from apical to equatorial and *vice versa*.

Another generalization is that in ring-containing phosphoranes internal strain may restrict the ring to spanning from an equatorial to an apical position.[12] In particular it has been noted that five-membered rings containing at least one oxygen bonded to phosphorus highly prefer the apical–equatorial disposition.[12,13] On the other hand, compound **29** pseudorotates at



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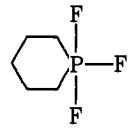


30

room temperature, but on cooling it adopts a structure in which the ring has two equatorial bonds. Compound **30** does not pseudorotate at room temperature and the ring has two equatorial bonds.[11]

It should also be noted that alternative mechanisms for pseudorotation have recently been discussed,[14] and diagrams have been proposed which permit a logical following of the consequences of pseudorotation.[15]

The ^{1}H nmr spectra of compounds **9–15** show an equivalency of hydrogens which can be accounted for by pseudorotation. It is important to note that the equivalency can arise *without* the rings adopting an equatorial–equatorial disposition; thus it is not necessary to invoke a violation of the strain rule nor is it necessary to describe a new mechanism for pseudorotation. In fact, the observation that the ring protons of **17–19** are nonequivalent is exactly that which would have been predicted if the two rings pseudorotate but only with a transposition from equatorial to apical and apical to equatorial positions. In this regard Ramirez and coworkers have made similar observations[9] as have Houalla, *et al.*[13e]

The variable-temperature ^{1}H nmr spectra at 100 MHz of **9–11** and **14** have been recorded down to *ca.* −60°. No dramatic changes were observed in any of these spectra and thus it appears that pseudorotation is still rapid on the nmr time scale. These substances will be studied at lower temperatures.

The variable-temperature spectrum of **17** shows that at 172° the multiplet for the ring protons collapses into a simple doublet. Each absorption is of the same intensity. Such behavior could well be due to the five-membered rings now adopting equatorial–equatorial positions either *via* a transition state or an intermediate. The ^{1}H nmr spectra of **18** and **19** also changed on heating; however, the ring protons never became a simple doublet.[16]

(12) (a) D. Gorenstein and F. H. Westheimer, *J. Amer. Chem. Soc.*, **92**, 634 (1970); (b) E. A. Dennis and F. H. Westheimer, *ibid.*, **88**, 3432 (1966); (c) P. C. Haake and F. H. Westheimer, *ibid.*, **83**, 1102 (1961).

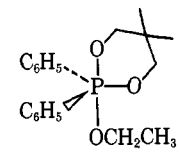
(13) (a) D. Gorenstein, *ibid.*, **92**, 644 (1970); (b) G. O. Doak and R. Schmutzler, *Chem. Commun.*, 476 (1970); (c) F. H. Westheimer, *Accounts Chem. Res.*, **1**, 70 (1968); (d) F. Ramirez, *ibid.*, **1**, 168 (1968); (e) D. Houalla, R. Wolf, D. Gagnaire, and J. B. Robert, *Chem. Commun.*, 443 (1969).

(14) E. L. Muetterties, *J. Amer. Chem. Soc.*, **91**, 4115 (1969).

(15) (a) P. C. Lauterbur and F. Ramirez, *ibid.*, **90**, 6722 (1968); (b) K. E. DeBruin, K. Naumann, G. Zon, and K. Mislow, *ibid.*, **91**, 7031 (1969); (c) Gorenstein and Westheimer, ref 12a, use a diagram which was originated by Professor D. J. Cram.

The ^{1}H nmr spectra of compounds **20–26** are best explained by an intramolecular exchange process. The ^{1}H nmr spectra of **24–26** require that the rings adopt equatorial–equatorial positions and obviously that the single group goes into an apical position, since the other ring cannot span two apical positions. These results clearly show that a six-membered ring containing two oxygens bonded to phosphorus can enter a diequatorial position in an oxyphosphorane. Ramirez, *et al.*,[9] have prepared mixed five-membered unsaturated ring and six-membered saturated ring pentaoxyphosphoranes. The ^{1}H nmr spectra of these compounds do not permit a decision as to whether the six-membered rings become diequatorial.

The variable-temperature spectra of **20–23** were observed down to *ca.* −60°. Only that of **22** underwent any material change. At −65° the methylene hydrogens of the ring were found as two distinct doublets, 3.88 (J = 19 Hz) and 2.96 (J = 16 Hz). The methyl group hydrogens remained as a single absorption. Such a spectrum can arise from the structure in which the two phenyls are in equatorial positions and the ring prefers an apical–equatorial orientation. The doublet at 2.96 is assigned to the apical methylene hydrogens both on the basis of coupling constant and the shielding effect of the benzene rings.[7b] The other doublet is



22 (−65°)

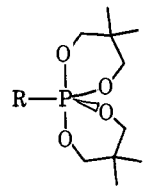
assigned to the equatorial methylene hydrogens. The structure is that predicted in that the two phenyl groups are in equatorial positions and the maximum number of oxygens are in apical positions. It should be noted that diphenyltriethoxyphosphorane showed the same kind of behavior.[7b]

The spectrum of **24** did not change on cooling to −65°. The spectra of **25** and **26** both underwent changes on cooling. In the case of **25** the single absorption for the hydrogens of the ring methyl groups split into two absorptions of equal intensity and the methylene doublet became two poorly resolved multiplets. The spectrum of **26** showed a similar behavior in the methyl group region. The methylene doublet broadened and began to show signs of asymmetry. The activation energy for the process which leads to equivalency of the methyl hydrogens of **26** was calculated from the coalescence temperature and the maximum chemical shift difference which could be observed. The value was 12 kcal/mol.[17] It probably represents a maximum value since the maximum chemical shift difference may not have been achieved.

The variable-temperature proton spectra are compatible with structures in which the R groups take up an equatorial position and the two rings are apical–equatorial. Pseudorotation is still occurring with the rings

(16) It should be remembered that the coalescence temperature for simple exchanges such as these is directly related to the chemical-shift differences between the two sites. As a consequence it is not safe to compare coalescence to lack of coalescence as a direct measure of the energies involved in the two processes.

(17) J. A. Pople, W. G. Schneider, and H. J. Berstein, "High Resolution NMR," McGraw-Hill, New York, N. Y., 1959, p 218 ff.



switching from apical to equatorial, etc. Under these circumstances two methyl groups remain cis to R and two remain trans; thus the nonequivalency. Similarly a set of four cis hydrogens and a set of four trans hydrogens arise from the previously equivalent methylene hydrogens. The methylene hydrogens should ultimately appear as part of an ABX pattern. If pseudorotation was completely inhibited then AB parts of two ABX patterns would be expected. Further support for the above conclusions is the finding that the ethoxy groups of phenyltetraethoxyphosphorane are equivalent at $-65°$.[7b]

The results from these systems are in accord with those obtained in other studies. More quantitative measurements over greater temperature ranges will allow an assessment of the magnitudes of the various effects. These studies are now in progress.

Experimental Section

General. Nmr spectra were obtained on a Varian A-60 and Varian HA-100. In particular low-temperature ^1H spectra were recorded with the HA-100. ^{31}P nmr spectra were recorded at 40.5 MHz with 85% phosphoric acid as external standard. Infrared spectra were recorded with an Infracord. Glpc analyses were conducted with an F & M 700 gas chromatograph.

Preparation of Diethyl Peroxide.[18] Diethyl sulfate, 308 g (2 mol), and hydrogen peroxide, 240 ml (30%), were mixed at room temperature in a 1-*l.* creased flask equipped with an efficient stirrer, dropping funnel, and condenser. The mixture was cooled to 20° in an ice-water bath and potassium hydroxide solution, 112 g (2 mol), in 100 ml of water was added dropwise at such a rate that the temperature was maintained between 20 and 25°. The ice bath was also used to maintain the temperature in this range. The addition required about 2 hr. The solution was then stirred for 2 hr with the temperature maintained in the 20–25° range; it was stirred for an additional 4 hr without cooling, 26–28°.

The organic layer was separated and washed with 100 ml of water. The ^1H nmr spectrum indicated that it consisted of diethyl peroxide, ether, and diethyl sulfate. The yield of diethyl peroxide was estimated to be 60 g (66%). The organic layer was dried overnight over magnesium sulfate. After decantation, the magnesium sulfate was washed with two 40-ml portions of anisole. The diethyl peroxide was distilled at room temperature (10 mm) and condensed in a liquid nitrogen trap. At the end of the distillation the temperature was raised to 60°. The distillate was allowed to melt and then it was dried over magnesium sulfate. Distillation through a short Vigreux column afforded 55 g (60%) of diethyl peroxide, bp 60–64°. This material is best stored in a refrigerator over molecular sieve.

Exchange of 1 with Ethylene Glycol. Ethylene glycol, 0.307 g (0.005 mol), and 2.52 g (0.005 mol) of 49% pure **1** were mixed and allowed to stand overnight. Distillation afforded a fraction, bp 55–58° (0.1 mm), which gave the spectral properties reported in Table I. In another experiment 10.3 g (0.0403 mol) of **1** in 10 ml of methylene chloride was added to 5.41 g (0.0872 mol) of ethylene glycol. The mixture was stirred and the ethylene glycol dissolved exothermically within 30 sec. The solvent and ethanol were removed under reduced pressure and the residue was distilled to give four fractions. The last fraction, bp 81–82° (0.01 mm), 3.53 g (45%), had the spectral properties reported in Table I. The material crystallized to give a low melting solid.

(18) All of the work with these phosphoranes ultimately requires a good source of diethyl peroxide. As a consequence the standard procedure [P. S. Wangia and S. W. Benson, *J. Org. Chem.*, 37, 1882 (1962)] has been checked in detail and certain modifications have been introduced which give good yields of peroxide in a relatively routine manner.

Several experiments were conducted in which varying amounts of ethylene glycol were added to **1** and the formation of **9** and **17** was observed by ^{31}P nmr. Addition of ethanol never caused formation of **1**.

Exchange of 1 with 1,2-Glycols. Essentially equimolar quantities of **1** and *dl*-2,3-butanediol were mixed. After 2 hr the ^{31}P nmr spectrum showed two absorptions at +1.1 (phosphates) and +53 (monocyclic oxyphosphorane). Propylene glycol gave a mixture of phosphates (+1) and monocyclic oxyphosphorane (+53). The reaction mixture from **1** and styrene glycol was distilled, bp 120° (0.17 mm). The oxyphosphorane had ^{31}P absorption at +52. Reaction of **1** with pinacol was monitored by ^{31}P nmr spectroscopy. Initially 2.09 g (0.0177 mol) of pinacol and 4.715 g (0.0175 mol) of **1**, 95% pure, were mixed and allowed to stand at room temperature. After 1 day the following absorptions were noted, +1.0, +47.7 (three overlapping peaks), +57, and +71. The approximate percentage of each was 45, 12, 7, and 36. After 3 days, the approximate percentages were 59, 18, 8, and 15. The reaction mixture was concentrated *in vacuo*. Glpc analysis of the volatiles showed it was mainly ethanol. The residue was analyzed by glpc which showed pinacol and triethyl phosphate were the major components.

Reaction of *cis*- and *trans*-1,2-Cyclohexanediols with 1. Reaction of various molar ratios of *trans*-1,2-cyclohexanediol with **1** led to a new absorption at +56; at no time was an absorption found in the ^{31}P nmr spectrum which could be due to a doubly exchanged phosphorane. The phosphorane was relatively unstable and decomposed over a period of *ca.* 24 days to give a reaction mixture which showed an absorption for phosphate. The volatiles were removed and analyzed by glpc. Ethanol and cyclohexene oxide were the major components both by retention time and peak augmentation.

Exchange of *cis*-1,2-cyclohexanediol gave a solution when quite pure **1** was used which showed one major absorption at +53. Injection of the solution into a gas chromatograph led to peaks which were due to cyclohexanone, triethyl phosphate, and ethanol.

Exchange of 1 with Neopentyl Glycol. A 1:1 molar ratio of **1** and neopentyl glycol was allowed to stand overnight. Distillation afforded a fraction, bp 58–63° (0.20 mm), which showed two absorptions at +1 and +73 whose relative areas were 21 and 79.

Reaction of **1** and neopentyl glycol in a 1:2 ratio gave, after distillation, bp 86–90° (0.1 mm), a material with one absorption in the ^{31}P nmr spectrum at +68.

Preparation of Tetraethoxymethylphosphorane (7). Diethylmethyl phosphonite, 0.150 g, in 0.2 ml of methylene chloride cooled in an ice bath and in an nmr tube was treated with 0.145 ml of diethyl peroxide. The mixture was shaken with cooling and allowed to stand overnight and then for 2 days in a refrigerator. The ^{31}P nmr showed one major absorption at +44 which is ascribed to **7**; *ca.* 22% diethyl methylphosphonate was also present. The volatiles were evaporated. The ^1H nmr spectrum of **7** showed a quintet at 3.72 ($J_{PH} = J_{HH} = 7$ Hz) CH_2; sextet at 1.12 ($J_{HH} = 7$ Hz; $J_{PH} = 1$ Hz) CH_2CH_3, and a doublet at 1.41 ($J_{PH} = 17$ Hz) PCH_3.

Exchange of 2–8 with Various Glycols. The acyclic phosphorane in an nmr tube was allowed to react with the appropriate amount of glycol. The monoring phosphoranes formed rapidly. Formation of the bisring compounds usually occurred on standing overnight in a refrigerator. The ^1H nmr spectra and ^{31}P spectra were recorded. The solvents and other volatiles were removed by pumping at a few millimeters for 2–3 hr. The residue was diluted with carbon disulfide or methylene chloride and the variable-temperature ^1H nmr spectra were recorded at 100 MHz.

Preparation of 23 and 26. The phosphonite, 2.06 g (0.0139 mol), in 12 ml of methylene chloride was cooled in an ice bath and treated with 1.56 g of diethyl peroxide. The reaction mixture was allowed to stand at room temperature in the dark for 4 days. The volatiles were removed and the ^{31}P and ^1H nmr spectra were recorded. The exchange with neopentyl glycol was carried out in the usual fashion.

Reaction of 1 with 1,4-Butanediol. 1,4-Butanediol and **1** were mixed at 0° in a 1:1 mole ratio. The reaction mixture was stirred at 0° for 15 min and stored overnight in a refrigerator. Glpc analysis with cyclohexane as an internal standard showed the yield of tetrahydrofuran was 87%.

Reaction of 6 with 1,5-Pentanediol. A solution of **6** in methylene chloride was treated with an equivalent amount of 1,5-pentanediol. After 4 days at room temperature analysis by ^{31}P nmr spectroscopy showed that most of the starting phosphorane had reacted to give triphenylphosphine oxide. The mixture was heated under reflux for 2 hr; at this time all of **6** had reacted. The yield (81%) of

tetrahydropyran was determined by glpc using cyclohexane as an internal standard.

Reaction of 1 with Benzyl Alcohol. Samples of **1** were mixed with benzyl alcohol, mole ratio 1:10 at room temperature, 1:5 at −20°, and 1:20 at 0°. In all cases decomposition of **1** occurred with the formation of trialkyl phosphate. Glpc analysis showed that dibenzyl ether was formed. Formation of benzyl ethyl ether could not be detected because of its similar retention time to that of benzyl alcohol.

Reaction of Tribenzyl Phosphite with Diethyl Peroxide. Tribenzyl phosphite, 7.04 g (0.02 mol), and diethyl peroxide, 2.7 g (0.0274 mol), were mixed with cooling. The flask and its contents were cooled to −60°, evacuated, and flushed with argon three times. The course of the reaction was monitored by ^{31}P nmr spectroscopy. After 4 days there was found 32% phosphate, 59% phosphite, and 9% phosphorane, +68. After 15 days only phosphate, 88%, and phosphite, 12%, were present. Glpc analysis showed dibenzyl ether and benzyl ethyl ether had been formed.

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Structure–Reactivity Correlation for the Hydrolysis of Phosphoramidate Monoanions

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Abstract: The structure–reactivity relationship which correlates the rate constants for the hydrolysis of phosphoramidate monoanions with the pK_a of the leaving amine is nonlinear. The inflection point in the data which occurs at $pK_a \approx 8$ is attributed to changes in the nonsteady-state zwitterion concentration which are directly proportional to the pK_a of the parent amine. The equilibrium favors the zwitterionic species in aqueous solution for those phosphoramidates whose second dissociation constant is greater than 7.2. On the basis of these data, a semiquantitative description of the transition state for nucleophilic attack on phosphoramidates is developed which features bond cleavage to the departing group as greatly exceeding bond formation to the incoming nucleophile. This finding in conjunction with data for *O*- and *S*-phosphate mono- and diesters suggests that pentacovalent intermediates probably do not occur on the reaction pathways for acyclic mono- and diester hydrolysis.

The involvement of various phosphoramidates either as substrates or intermediates in the enzyme-catalyzed phosphorylation of hexose and adenosine triphosphate is well established.[3–6] Two examples follow. Phosphoramidate–adenosine diphosphate phosphotransferase facilitates the interconversion of adenosine di- and triphosphate utilizing *N*-phosphorylglycine, *N*-phosphorylhistidine, or phosphoramidate as the $[PO_3^{2-}]$ source.[3] Glucose 6-phosphatase catalyzes the transfer of $[PO_3^{2-}]$ from glucose 6-phosphate to water or inorganic phosphate through an enzymic *N*-phosphorylhistidine intermediate.[4] Several quantitative studies have dealt with the nonenzymic hydrolysis of phosphoramidate and various *N*-acyl and *N*-aryl derivatives.[7–9] In addition it has been demonstrated that the hydrolysis of phosphoramidate monoanion[7,10] and a series of phosphorylpyridinium ions[11] is subject to nucleophilic catalysis by various amines, especially pyridines and in the case of phosphoramidate, the hydrolysis is accelerated by electrophilic catalysts including formaldehyde and nitrous and hypochlorous acid. Collectively these studies posed a problem concerning the description of the transition state for the catalyzed and spontaneous hydrolysis of the ester monoanion. The proposal of a "borderline" unimolecular elimination reaction, not involving a "free" metaphosphate species, for the phosphoramidates, in contrast to the metaphosphate mechanism suggested for *O*-phosphate monoesters, stemmed from investigations of product distribution in various mixed alcohol–water solvents.[7,10,12] The results indicated that the solvolysis proceeded *via* a species that was selective toward nucleophilic reagents, *e.g.*, methanol is tenfold more reactive than water. Moreover, interpretation of the low Brønsted β value (0.2) for nucleophilic catalysis by pyridines implied a transition state with minor but not negligible bond formation between the nucleophile and phosphorus atom. Left unspecified, however, is the degree of bond cleavage between phosphorus and the departing group.

The present study of the hydrolysis of a series of phosphoramidate monoesters was initiated in order to establish a structure–reactivity correlation for this

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