formations, which we find convenient for working models, the half-chair, C_s-type conformations with C-4 or C-5 and one heteroatom lying above and below the plane defined by the remaining three atoms are essentially equivalent (±0.2 kcal) energetically to the corresponding envelopes.

It is interesting that the minimized bond angles and dihedral angles for 2-methyl-1,3-oxathiolane agree within ±1.2 and ±4°, respectively (Table II), with those for the steroidal oxathiolane determined by Cooper and Norton.[7] Also, the existence of only two discrete minima 1 kcal apart for the 2-methyl compound agrees with the finding of two preferred pseudorotamers and with the conformational free energy of the methyl group in oxathiolanes as previously determined by Pasto and coworkers.[3]

We may clearly identify three factors which control the conformational population of the oxathiolanes. Most important of these is the minimization of transannular van der Waals interactions of the substituents at C-2 with the methylene units at the 4 and 5 positions. Second in importance is minimization of torsional energies achieved by maintaining a heteroatom not bearing a proton or other group β to the flap atom in the nearly planar portion of the ring. Finally, of approximately equal importance is maximization of group staggering by having one carbon atom of an ethylene unit at the flap position. These minima are simultaneously achieved in the oxathiolanes by allowing a substituent at the 2 position to adopt a position β to the flap atom and anti to it with respect to the ring plane.

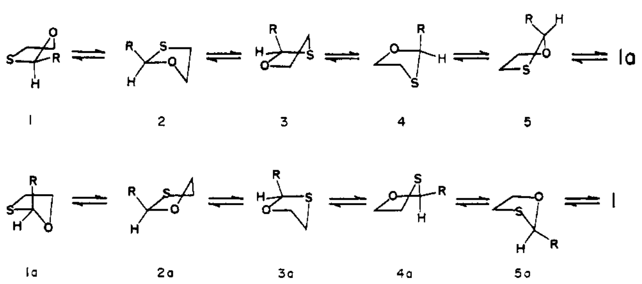

Figure 6. Envelope conformations of the pseudorotamers of 1,3-oxathiolanes.

In a number of other studies on heterocycles containing sulfur, the thiophane ring,[8] 1,3-thiazolidines,[4] and 1,3-dithiolanes[5] these principles may be seen to apply. We suggest that they may, indeed, be quite general, and we are pursuing efforts to extend our capability of predicting preferred geometry to other systems and other substitution patterns.

Acknowledgment. Numerous discussions with Professor G. Allegra of the University of Trieste and Drs. E. Benedetti and C. Pedone are gratefully acknowledged, as is the assistance of the staff of the Polytechnic Institute of New York computer center.

Oxyphosphorane Models for Displacement Reactions of Pyrophosphates

Fausto Ramirez,*[1a,b] Yu Fen Chaw,[1b] James F. Marecek,[1b] and Ivar Ugi[1c]

Contribution from the Department of Chemistry, State University of New York, Stony Brook, New York 11790, and the Organisch-Chemisches Laboratorium, Technische Universität, München, West Germany. *Received August 10, 1973*

Abstract: The reactions of hexafluorobiacetyl, $CF_3COCOCF_3$, with mixed anhydrides of phosphorous and phosphoric acids, $(RO)_2POP(O)(OC_2H_5)_2$ ($R = CH_3$, C_2H_5), give relatively stable 4,5-bis(trifluoromethyl)-2,2-dialkoxy-2-diethylphosphato-2,2-dihydro-1,3,2-dioxaphospholenes. These compounds are oxyphosphorane models of the hypothetical intermediates derived from the addition of nucleophiles to the phosphorus of pyrophosphates, such as ADP and ATP.

Numerous publications have described the synthesis and the molecular structure of oxyphosphoranes, *i.e.*, of P(5) compounds[2] having at least one phosphorus–oxygen bond.[3,4] The existence of the relatively stable trigonal bipyramidal oxyphosphoranes has provided increasing support for the hypothesis that metastable oxyphosphoranes are intermediates in displacement reactions of P(4) compounds.[2,5-10] When applied to the biochemically important pyrophosphates, *e.g.*, ADP[2] and ATP,[2] these concepts lead to oxyphosphoranes of the type shown in Scheme I.

Due to the occurrence of relatively rapid PI[2,11] in

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(1) (a) This research was supported by the Cancer Institute of the U. S. Public Health Service (Grant CA-04769) and by the National Science Foundation (Grant GP-23018); (b) State University of New York; (c) Technische Universität.

(2) The following abbreviations will be used in this paper: P(3), P(4), P(5) = three-, four-, and five-coordinate phosphorus; ADP = adenosine 5′-diphosphate; ATP = adenosine 5′-triphosphate; PI = permutational isomerization of trigonal bipyramidal P(5) compounds.

(3) (a) F. Ramirez, *Accounts Chem. Res.*, 1, 168 (1968); (b) F. Ramirez, *Bull.Soc. Chim. Fr.*, 3491 (1970); (c) F. Ramirez and I. Ugi, *Advan. Phys. Org. Chem.*, 9, 25 (1971).

(4) P. Gillespie, F. Ramirez, I. Ugi, and D. Marquarding, *Angew. Chem., Int. Ed. Engl.*, 12, 91 (1973).

(5) The literature pertaining to the participation of oxyphosphorane intermediates in displacement reactions of P(4) compounds has been reviewed in ref 4 and 6–10.

(6) W. E. McEwen, *Top. Phosphorus Chem.*, 2, 1 (1965).

(7) G. Kamai and G. M. Usacheva, *Russ. Chem. Rev.*, 35, 601 (1966).

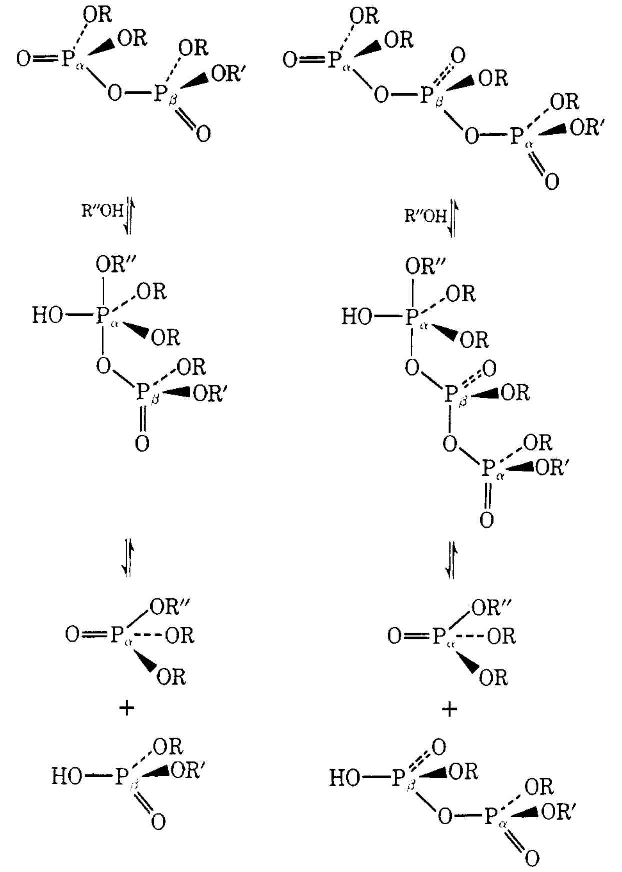
(8) F. H. Westheimer, *Accounts Chem. Res.*, 1, 70 (1968).

(9) K. Mislow, *Accounts Chem. Res.*, 3, 321 (1970).

(10) R. F. Hudson and C. Brown, *Accounts Chem. Res.*, **5**, 204 (1972).

(11) (a) P. Gillespie, P. Hoffmann, H. Klusacek, D. Marquarding, S. Pfohl, F. Ramirez, E. A. Tsolis, and I. Ugi, *Angew. Chem., Int. Ed. Engl.*, **10**, 687 (1971); (b) I. Ugi and F. Ramirez, *Chem. Brit.*, **8**, 198 (1972).

Scheme I

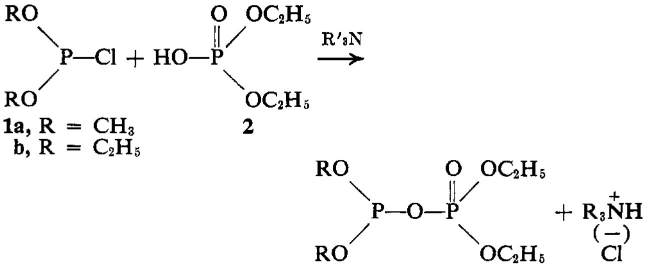


the oxyphosphoranes, it is necessary to consider also isomers of these oxyphosphoranes in which the phosphato, OP(O)(OR)(OR′), and pyrophosphato, OP(O)(OR)OP(O)(OR)(OR′), groups occupy equatorial positions in the trigonal bipyramid. Moreover, since the two phosphorus atoms in ADP, and the three phosphorus atoms in ATP, are structurally nonequivalent, one must also consider other structural isomers of the oxyphosphoranes derived from these compounds. Oxyphosphoranes of this type should decompose with elimination of phosphate and pyrophosphate, respectively, since these are relatively good leaving groups.

The present investigation was undertaken in order to provide isolable oxyphosphoranes which would serve as models for the hypothetical oxyphosphoranes shown in Scheme I. The data pertaining to the molecular structure, and the chemical reactions of these model compounds, should aid our understanding of the behavior of pyrophosphates.

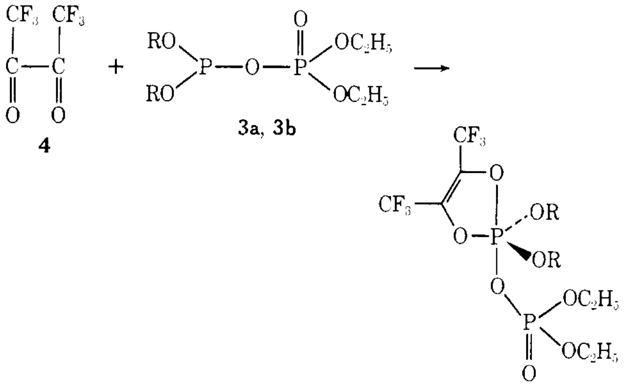
Results

Dimethyl phosphorochloridite[12,13] (**1a**) reacts with diethyl phosphate[14] (**2**) to give the unsymmetrically substituted mixed anhydride, **3a**, containing P(3) and P(4).[2] The symmetrically substituted analog, **3b**, is also obtained in this manner, as has already been reported by Michalski and his coworkers.[15–17] The spectral data of these compounds is given in Table I.



1a, R = CH_3
b, R = C_2H_5
2
3a, R = CH_3
b, R = C_2H_5

The mixed P(3)·O·P(4)[2] anhydrides, **3a** and **3b**, react rapidly with hexafluorobiacetyl[18] (**4**) to yield the corresponding oxyphosphorane anhydrides, **5a** and **5b**. These P(5)·O·P(4)[2] compounds are assumed to have the trigonal-bipyramidal geometry about P(5) by analogy with other related oxyphosphoranes.[3,4] Probably, the favored configuration of the molecule is as shown, with the more apicophilic[4,11] phosphato ligand in the apical position and the five-membered ring in the apicoequatorial position. The possible PI[11] in these oxyphosphoranes will be considered in the Discussion section.



4
3a, 3b
5a, R = CH_3
b, R = C_2H_5

The nmr data for the oxyphosphoranes **5a** and **5b** are given in Table I. Note the significant increase in the shielding of the phosphorus nucleus by electrons when P(3) is converted into P(5), as reflected in a displacement of the ^{31}P chemical shifts by approximately 186 ppm toward higher magnetic field: **3a** → **5a** and **3b** → **5b**. The chemical shift of P(4), which is not directly involved in the reaction, is displaced by only 3 ppm toward higher magnetic field.

The two trifluoromethyl groups in the oxyphosphoranes, **5a** and **5b**, give rise to one ^{19}F nmr signal, respectively. The two methoxy ligands on the P(5) of **5a** give one ^1H nmr signal, which is a doublet with a relatively large coupling constant, J_{HCOP} = 16.0 Hz. The oxyphosphorane **7a**, made from the reaction of hexafluorobiacetyl (**4**) with trimethyl phosphite (**6a**), has a slightly smaller methoxy coupling constant.[19] The hexafluorobiacetyl–triethyl phosphite oxyphosphorane, **7b**, is also reported in order to provide a closer com-

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[12] A. E. Lippman, *J. Org. Chem.*, **30**, 3217 (1965).

[13] H. G. Cook, J. D. Ilett, B. C. Saunders, G. J. Stacey, H. G. Watson, I. G. E. Wilding, and S. J. Woodcock, *J. Chem. Soc.*, 2921 (1969).

[14] A. D. F. Toy, *J. Amer. Chem. Soc.*, **70**, 3882 (1948).

[15] J. Michalski, T. Modro, and A. Zwierzak, *J. Chem. Soc.*, 4904 (1961).

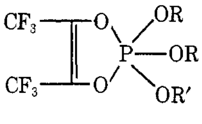
[16] R. K. Harris, A. R. Katritzky, S. Musierowicz, and B. Ternai, *J. Chem. Soc. A*, 37 (1967).

[17] J. M. Cheymol, P. E. Chabrier de Lassauniere, and M. Selim, French Patent 1,513,206 (1968); *Chem. Abstr.*, **70**, 77307h (1969).

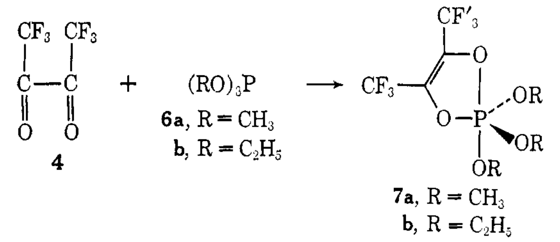
[18] (a) L. O. Moore and J. W. Clark, *J. Org. Chem.*, **30**, 2472 (1965); (b) *ibid.*, **35**, 3999 (1970).

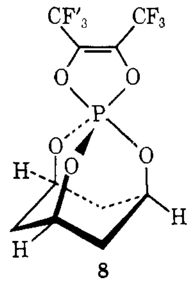
[19] F. Ramirez, J. Marecek, I. Ugi, and D. Marquarding, *Phosphorus*, **3**, 91 (1973).

Table I. Spectral Data[a] of Oxyphosphoranes and Related Compounds Derived from the Reactions of Hexafluorobiacetyl, $CF_3\cdot CO\cdot CO\cdot CF_3$, with Three-Coordinate Phosphorus Compounds, $P(OR)_2(OR')$

Formula no.	Substituents on P compound R	R′	$\delta^{31}P$	$\delta^{19}F$	^1H nmr τ	J_{HP}	Mp or bp, deg (mm)	Main ir bands, cm^{-1}
			Three-Coordinate P Compounds, $P_\alpha(OR)_2(OR')$					
6a	CH_3	CH_3	−140.0	None	6.70 (CH_3)	10.5		
3a	CH_3	$P_\beta(O)(OC_2H_5)_2$	−129.5 +9.4	None	6.34 (CH_3) 5.87, 8.67 (C_2H_5)	10.8 8.0[b] 2.5	73–79[c] (0.05)	1220, 1042, 980
6b	C_2H_5	C_2H_5	−138.5	None				
3b	C_2H_5	$P_\beta(O)(OC_2H_5)_2$	−128.4[d] +9.7	None	*ca.* 5.83 *ca.* 8.85 (C_2H_5)	*e*	78–80[c] (0.05)	1160, 1035, 975
			Oxyphosphoranes, 					
7a	CH_3	CH_3	+46.7	−12.9[f]	6.30 (CH_3)	14.0	*g*	
5a	CH_3	$P_\beta(O)(OC_2H_5)_2$	+55.6 +12.4	−13.1[f]	6.08 (CH_3) 5.86, 8.66 (C_2H_5)	16.0 *e*	*h*	1715, 1355, 1282, 1163, 1042, 980
7b	C_2H_5	C_2H_5	+49.3	−13.1[f]	5.95, 8.75 (C_2H_5)	*e*	39–40[c] (0.2)	1701, 1346, 1147, 1057
5b	C_2H_5	$P_\beta(O)(OC_2H_5)_2$	+58.6 +12.4	−12.9[f]	*ca.* 5.8, *ca.* 8.8 (C_2H_5)	*e*	*h*	1710, 1350, 1240, 1150, 1035, 990
8	1-Phospha-2,8,9-trioxaadamantane		+41.7	−14.3[f]	5.00 (CH)	26.0	*i*	
			Phosphates, $CF_3\cdot CO\cdot CH(CF_3)[OP_\alpha(O)(OR)(OR')]$					
7a	CH_3	CH_3	+0.8	−2.1[j] −4.5[k]	6.10 (CH_3)[l] 6.14 (CH_3)	11.5 11.5	36–37 (0.2)	1786, 1282, 1205, 1053
9a[m]	CH_3	$P_\beta(O)(OC_2H_5)_2$	+13.0	−2.3[j]	6.16 (CH_3)	11.8	*h*	1785, 1260, 1200, 1030
			+11.8	−4.4[k]	5.76, 8.65 (C_2H_5)[n]	*e*		
7b	C_2H_5	C_2H_5	+2.9	−2.4[j] −4.9[k]	5.76, 8.64 (C_2H_5)[o]	*e*	44–45° (0.2)	1786, 1282, 1205, 1176, 1036
9b[m]	C_2H_5	$P_\beta(O)(OC_2H_5)_2$	+13.8 +12.7	−2.3[j] −4.6[k]	5.88, 8.64 (C_2H_5)[p]	*e*	*h*	1785, 1270, 1200, 1040

[a] All nmr spectra at 25°. ^1H spectra in $CDCl_3$ at 60 or 100 MHz; signals in ppm from TMS = 10 (τ values); coupling constants, J, in Hz; all integrated intensities were as expected from the structures given. ^{31}P spectra in $CDCl_3$ at 40.5 MHz; $\delta^{31}P$ in ppm *vs.* H_3PO_4 = 0. ^{19}F spectra in $CDCl_3$ at 94.1 MHz; $\delta^{19}F$ in ppm *vs.* CF_3COOH = 0. Ir spectra in CH_2Cl_2. [b] Couplings in CH_3CH_2OP group; J_{HCCH} = 7.2 Hz. [c] Short-path distillation. [d] Reference 16 gives $\delta^{31}P = -127.7$ and +9.5 ppm *vs.* H_3PO_4; ref 15 gives bp 74° (0.01 mm). [e] Complex multiplets. [f] One signal from six fluorines in two CF_3 groups. [g] Reference 19. [h] Not distillable, noncrystalline material. [i] Reference 19. [j] Quartet, J = *ca.* 4 Hz assumed to result from $CF_3CO\cdot$ coupled with CF_3. [k] Broad multiplet, probably a doublet, J_{FCCH} = 6.0 (from the ^1H spectrum), of quartets, J = *ca.* 4 Hz, due to CF_3 coupled with CH and CF_3CO. [l] The two CH_3O groups are magnetically nonequivalent. The methine ^1H gives a signal at τ = 4.15 ppm, J_{HCOP} = 10.5 Hz, J_{HCCF} = 6.0 Hz. [m] One of two possible diastereomers of the phosphate. The two ethoxy groups on P_β are magnetically nonequivalent; the ^1H nmr signals are complex multiplets. [n] The methine ^1H gives a signal at τ = 3.94 ppm, J_{HCOP} = 10.0 Hz, J_{HCCF} = 6.0 Hz. [o] The methine ^1H gives a signal at τ = 4.18 ppm, J_{HCO} = 10.0 Hz, J_{HCCF} = 6.0 Hz. [p] The methine ^1H gives a signal at τ = 4.10 ppm, J_{HCOP} = 10.0 Hz, J_{HCCF} = 6.0 Hz.





8

parison with the P(5)·O·P(4) analog, **5b**. The first phosphorane derived from hexafluorobiacetyl contained three phenoxy ligands.[20]

Another type of oxyphosphorane derived from hexafluorobiacetyl (**4**) is the caged polycyclic system[19] **8**, and its nmr data are also included in Table I. In all these cases, the equivalency of the six fluorine nuclei in the nmr has been taken as an indication of the existence of a relatively rapid positional exchange of ligands on the trigonal-bipyramidal skeleton, *i.e.*, a manifestation of the general phenomenon of PI[2] in the oxyphosphoranes.

The oxyphosphorane anhydrides, **5a** and **5b**, react with hydrogen chloride to yield the corresponding tetraalkyl pyrophosphates, **9a** and **9b**. It is assumed that the pyrophosphates are formed *via* the intermediate tetraalkoxyphosphonium chlorides shown.

The oxyphosphoranes **7a** and **7b**, made from the

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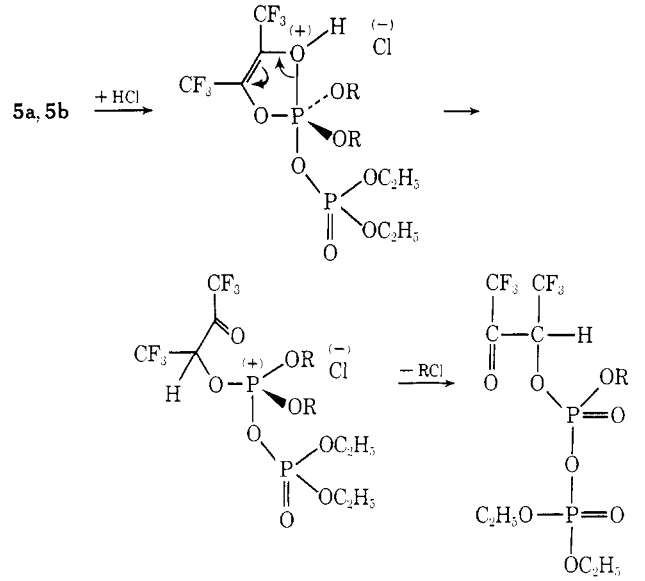
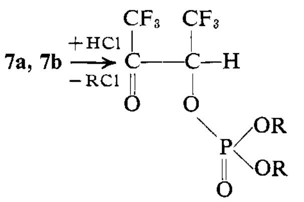
(20) F. Ramirez and H. J. Kugler, *Phosphorus*, 2, 203 (1973).



9a, R = CH$_3$
b, R = C$_2$H$_5$

trialkyl phosphites and hexafluorobiacetyl, react also with hydrogen chloride and give the corresponding phosphate esters, namely, the hexafluorophosphoacetoins, **10a** and **10b**. These reactions are significantly faster than the corresponding reactions of the oxyphosphorane anhydrides, **5a** and **5b**, with hydrogen chloride.

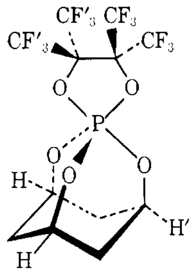


10a, R = CH$_3$
b, R = C$_2$H$_5$

Discussion

This investigation shows that oxyphosphorane anhydrides **5a** and **5b** can be synthesized and are, in fact, relatively stable substances. Therefore, it is entirely reasonable to assume that the hypothetical oxyphosphoranes depicted in Scheme I, which are formed by the addition of nucleophiles R''OH to the P(4) of ADP and ATP, have also a significant degree of stability and can be formed by processes of reasonably low activation energy. As discussed elsewhere,[3c,4,11] acyclic oxyphosphoranes are, in general, somewhat less stable than cyclic oxyphosphoranes of comparable type.

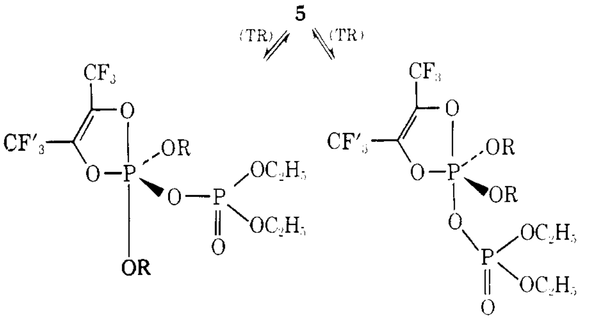
Extensive research[3,4,11] has shown that derivatives of the 1,3,2-dioxaphospholene and 1,3,2-dioxaphospholane ring systems, with three additional alkoxy ligands attached to the P(5), undergo relatively rapid PI[2] in solutions at ambient temperatures. The variable temperature nmr spectra of the trimethyl phosphite–hexafluorobiacetyl, **7a**, and the adamantanoid–hexafluorobiacetyl, **8**, oxyphosphoranes[19] have been examined to −50° without any evidence of inhibition of the PI.[2] The ^{19}F nmr spectrum of the adamantanoid–hexafluoroacetone, **11**, oxyphosphorane has been followed to −165° in the solvent mixture 70% vinyl chloride + 30% CHFCl$_2$ without any evidence for the occurrence of an inhibition of PI.[21-23] The ^{13}CFT nmr of this caged oxyphosphorane **11**, studied in CH$_2$Cl$_2$ solution at ambient temperature,[21] leaves no doubt concerning the existence of the PI. That the PI isomerization of **11** occurs by a bond deformation or regular process,[3,4,11] and not by an ionization process, is supported by the insensitivity of the ^{31}P nmr shift to the nature of the solvent, including the acidic hexafluoroisopropanol, and by the existence of the couplings of the ^{31}P nuclei with the nuclei in the ligands, J_{FCCOP} = 0.3 Hz and J_{HCOP} = 28.0 Hz.[21] Although we have had no opportunity to detect the expectedly small J_{FCCOP} coupling in the hexafluorobiacetyl derivatives, **7a** and **8**, the insensitivity of the ^{31}P nmr shifts of these compounds to the nature of the solvent, and the observation of the J_{HCOP} couplings, support the regular PI process in them.



11

By analogy, we suggest that the PI[2] indicated in the oxyphosphorane anhydrides, **5a** and **5b**, by the magnetic equivalency of the six fluorine nuclei, is also due to a regular process. This can occur in two ways. (a) A single turnstile rotation mechanism[3c,11,23] which must utilize the five-membered ring as the "pair," leads to the new isomer **12** (Scheme II), with the strongly apicophilic[4] phosphato ligand in an equatorial position.[24] (b) A triple turnstile rotation,[3c,11,23] which must also utilize the ring as the "pair," leads to the original isomer **5'** with exchange of the two trifluoromethyl groups among the skeletal positions and retention of the apical placement of the apicophilic phosphato ligand. In general, the triple turnstile

Scheme II



12 **5'**

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(21) F. Ramirez, I. Ugi, F. Lin, S. Pfohl, P. Hoffmann, and D. Marquarding, *Tetrahedron*, in press.

(22) A preliminary investigation (ref 3c, 11a, and 23) of the variable temperature ^{19}F nmr spectrum of the adamantanoid–hexafluoroacetone oxyphosphorane, **11**, which was carried out in pure vinyl chloride as solvent, led to the erroneous conclusion that the PI of **11** was inhibited at temperatures close to −120°. The same erroneous conclusion was reached from the results of the variable temperature ^{1}H nmr of **11**.

(23) F. Ramirez, S. Pfohl, E. A. Tsolis, J. F. Pilot, C. P. Smith, I. Ugi, D. Marquarding, P. Gillespie, and P. Hoffmann, *Phosphorus*, **1**, 1 (1971).

(24) Isomer **12** can also be generated from **5** by one Berry pseudorotation mechanism: R. S. Berry, *J. Chem. Phys.*, **32**, 933 (1960).

rotation has a higher energy barrier than the single turnstile rotation. However, this situation could change when one permutational isomer, *e.g.*, **5** ≡ **5′**, is of significantly lower energy than another, *e.g.*, **12**. The available data do not permit a choice between the single and the triple turnstile in the present case.

Experimental Section

Analyses were performed by Galbraith Laboratories, Knoxville, Tenn. All reactions of oxyphosphoranes were carried out in anhydrous solvents. The physical constants and the nmr data at ambient temperature are given in Table I.

Hexafluorobiacetyl (4). The following procedure, adapted from that given in ref 18, gave the α-diketone, reproducibly, in 50% yield based on reacted 2,3-dichlorohexafluoro-2-butene. The olefin (70.0 g, 0.3 mol) was added dropwise (2 hr) to a stirred mixture of CrO_3 (70.0 g, 0.7 mol) and 20% fuming H_2SO_4 (250 ml), contained in a three-necked flask fitted with an *air* condenser leading to two traps cooled by Dry Ice. The flask was kept in a bath at 65–70° during the addition of the olefin and was kept 2 additional hr at 70°. A slow N_2 stream was passed through the reaction mixture for 2 hr at 70°. The contents of the first trap were distilled through a 5-in. Vigreux column. Fraction no. 1 boiled below 25° (760 mm) and was collected in an ice-cooled receiver. The higher boiling fraction no. 2 was 17 g of recovered olefin. Fraction no. 1 consisted of hexafluorobiacetyl contaminated with traces of trifluoroacetyl chloride. This mixture was immersed in a Dry Ice bath and was kept 90 sec (*not longer*) at 0.5 mm using an oil pump; the residue was pure hexafluorobiacetyl (**4**) (15.8 g). The acid mixture was cooled to room temperature and poured cautiously over 2 kg of ice. The dark green solution was extracted with methylene chloride (3 × 150 ml); the organic layers were combined and dried over sodium sulfate and the methylene chloride removed under reduced pressure. An oily cyclic sulfate remained (13 g) which was mixed with dimethylformamide (6 ml) and slowly heated to 120°. Decomposition of the sulfate afforded additional hexafluorobiacetyl (6.7 g).

Reaction of Hexafluorobiacetyl with Triethyl Phosphite. The α-diketone **4** (2.20 g, 12 mmol) dissolved in 20 ml of cold CH_2Cl_2 was added dropwise with stirring over 15 min to the phosphite (1.74 g, 11 mmol) dissolved in 25 ml of CH_2Cl_2 and cooled to −78°. The reaction was run under an argon atmosphere. The colorless solution was stirred a further 10 min at −78° and then allowed to warm to 20°. The solvent was evaporated at 20° (40 mm) and the residue distilled to give 2.7 g (75%) of **4,5-bis(trifluoromethyl)-2,2,2-triethoxy-2,2-dihydro-1,3,2-dioxaphospholene (7b)**.

Anal. Calcd for $C_{10}H_{15}O_5PF_6$: C, 33.3; H, 4.2; F, 31.6. Found: C, 33.5; H, 4.2; F, 31.4.

Reaction of Dimethyl Phosphorochloridite (1a) with Diethyl Phosphate (2). (a) The $(CH_3O)_2PCl$ (**1a**; $\delta^{31}P$ = −168.9 ppm; τCH_3 = 6.07, J_{HP} = 11.0 Hz; bp 28–29° (20 mm)) was made by a significant modification of Lippman's procedure.[12] Trimethyl phosphite and phosphorus trichloride in a 2.5:1 molar proportion were stirred 2 hr at 0° and 30 hr at 25°. One short-path distillation (bp *ca.* 25–30° (25 mm)), followed by one fractional distillation through a 4-in. Vigreux column (bp *ca.* 96–108° (760 mm) and a bath at 128°), gave pure $(CH_3O)_2PCl$ (**1a**).

(b) The $(C_2H_5O)_2P(O)OH$ (**2**; $\delta^{31}P$ = +2.5 ppm; multiplets at τ = 5.85 (CH_2) and 8.62 (CH_3); τOH = −1.7; bp 118–128° (0.01 mm)) was made by Toy's procedure.[14] A mixture of water (6.07 g, 0.34 mol) and pyridine (53.34 g, 0.67 mol) was added to a cooled solution of diethyl phosphorochloridate (116.0 g, 0.67 mol) dissolved in benzene (100 ml), over a period of 1.5 hr. The mixture was stirred at 0° then left overnight. The pyridinium hydrochloride was filtered with suction and washed with benzene. The benzene solution was dried over sodium sulfate and then removed under reduced pressure (30 mm) at 40°. The residue was distilled *in vacuo* yielding 85 g of tetraethyl pyrophosphate.

Tetraethyl pyrophosphate (30.0 g, 0.10 mol) and water (4.5 g, 2.5 mol equiv) were heated with stirring at 65° for 2 days. The excess water was removed under reduced pressure (2 mm) at 50° and the residue vacuum distilled. There was isolated 25 g (83% yield), bp 124° (0.05 mm). of **2**.

(c) Dimethyl phosphorochloridite (**1a**) (1 mol equiv) was added over a 1.5-hr period to a stirred 0.7 *M* benzene solution containing equimolar amounts of diethyl phosphate (**2**) and pyridine at 0° The mixture was stirred an additional 3.5 hr at 0° and then filtered. The filtrate was evaporated at 30° (30 mm), and the residue was submitted to a fractional short-path distillation to give **dimethylphosphorous diethylphosphoric anhydride (3a)** in *ca.* 67% of the theoretical yield (Table I).

Anal. Calcd for $C_6H_{16}O_6P_2$: C, 29.3; H, 6.5; P, 25.2. Found: C, 29.2; H, 6.6; P, 25.0.

(d) Large quantities of the anhydride, **3a**, were conveniently prepared by addition of the mixture of $(CH_3O)_3P$, $(CH_3O)_2PCl$, and CH_3OPCl_2 ($\delta^{31}P$ = −180.8 ppm), which was obtained from a above *without distillation*, to the diethyl phosphate–pyridine mixture. In this case, 1.1 g of $(C_2H_5O)_2P(O)OH$ was used per gram of the mixture. The anhydride was obtained in 65% of the theory based on $(CH_3O)_2PCl$ used.

Reaction of Hexafluorobiacetyl (4) with Dimethylphosphorous Diethylphosphoric Anhydride (3a). A cold solution of hexafluorobiacetyl, **4** (0.200 g, 1 mmol), dissolved in CH_2Cl_2 (10 ml) was added over a 1-hr period to a stirred solution of the anhydride, **3a** (0.223 g, 0.9 mmol), in CH_2Cl_2 (10 ml), at −78°. The mixture was kept 15 min at −78° and then allowed to reach 20°, and the solvent was evaporated at 30° (30 mm). The residue was kept 1 hr at 25° and *ca.* 0.1 mm to remove any volatile contaminants and was submitted to elemental and nmr spectroscopic analysis.

4,5-Bis(trifluoromethyl)-2,2-dimethoxy-2-diethylphosphato-2,2-dihydro-1,3,2-dioxaphospholene (5a) was obtained in *ca.* 100% of the theoretical yield (Table I).

Anal. Calcd for $C_{10}H_{16}O_8P_2F_6$: C, 27.3; H, 3.6; P, 14.0; F, 25.9. Found: C, 27.3; H, 3.7; P, 14.0; F, 25.7.

Reaction of Diethyl Phosphorochloridite (1b) with Diethyl Phosphate (2). The $(C_2H_5O)_2PCl$ (**1b**: $\delta^{31}P$ = −162.5 ppm; multiplets at τ = 6.20 (CH_2) and 9.05 (CH_3) in benzene solution) was purchased from Aldrich Chemical Co. and was freshly distilled. The reaction of **1b** with diethyl phosphate (**2**) was carried out as in the case of the dimethyl phosphorochloridate; see procedure c. **Diethylphosphorous diethylphosphoric anhydride (3b)** was obtained in 75% of the theoretical yield.

Reaction of Hexafluorobiacetyl (4) with Diethylphosphorous Diethylphosphoric Anhydride (3b). The same procedure as for the dimethyl analog was followed; **4,5-bis(trifluoromethyl)-2,2-diethoxy-2-diethylphosphato-2,2-dihydro-1,3,2-dioxaphospholene (5b)** was obtained in 100% of the theoretical yield (Table I).

Reaction of 4,5-Bis(trifluoromethyl)-2,2,2-trimethoxy-2,2-dihydro-1,3,2-dioxaphospholene (7a) with Hydrogen Halides. (a) Hydrogen chloride was passed slowly through a cooled solution (0°) of the dioxaphospholene, **7a** (2.08 g), in benzene (20 ml), containing a few crystals of methyl orange, until a pink color was noted in the solution. The solvent was evaporated at 30° (30 mm), and the residue was distilled through a 5-in. Vigreux column to give **dimethyl-(1-trifluoromethyl-2-oxo-3,3,3-trifluoro)propyl phosphate (10a)** in 73% of the theoretical yield. The compound was found to slowly decompose when left at room temperature but could be stored for several weeks at −10° with little decomposition.

Anal. Calcd for $C_6H_7O_5PF_6$: C, 23.7; H, 2.3. Found: C, 23.8; H, 2.5.

(b) The reaction was also carried out with hydrogen bromide to give the phosphate ester, **10a**, in approximately the same yield.

Reaction of 4,5-Bis(trifluoromethyl)-2,2,2-triethoxy-2,2-dihydro-1,3,2-dioxaphospholene (7b) with Hydrogen Chloride. The reaction was carried out as described above. **Diethyl-(1-trifluoromethyl-2-oxo-3,3,3-trifluoro)propyl phosphate (10b)** was obtained in 70% yield.

Anal. Calcd for $C_8H_{11}O_5PF_6$: C, 28.9; H, 3.3; F, 34.3. Found: C, 29.1; H, 3.5; F, 34.2.

Reaction of 4,5-Bis(trifluoromethyl)-2,2-dimethoxy-2-diethylphosphato-2,2-dihydro-1,3,2-dioxaphospholene (5a) with Hydrogen Chloride. About 100 cc of hydrogen chloride was slowly (1 hr) passed through a cooled solution (10°) of the dioxaphospholene, **5a**, (1.65 g) in benzene (15 ml). The solution was stirred a further 30 min at 10° and the solvent evaporated at 30° (30 mm). The crude reaction mixture was found to contain the desired product, **9a**, together with some unreacted **5a** and small amounts of phosphates. Attempts to drive the reaction to completion using more hydrogen chloride resulted in extensive decomposition of the product. The pyrophosphate could not be isolated in the pure state from the crude mixture due to its rapid decomposition. The spectral data are reported in Table I.

Reaction of 4,5-Bis(trifluoromethyl)-2,2-diethoxy-2-diethyl-2-phosphato-2,2-dihydro-1,3,2-dioxaphospholene (5b) with Hydrogen Chloride. The procedure and results are the same as described above for **5a**. The spectral data are reported in Table I.