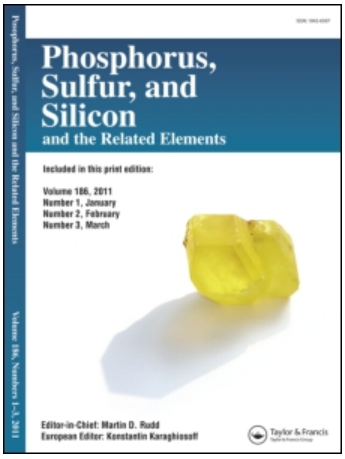

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CONFORMATIONAL AND STRUCTURAL STUDIES OF 2-FLUORO-2-OXO-1,3,2-DIOXAPHOSPHORINANES

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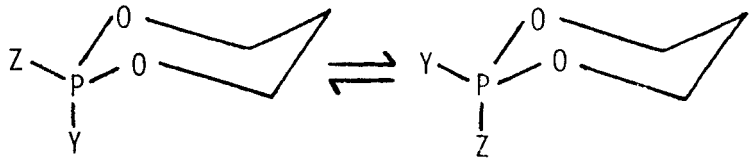
Reaction of 2-chloro-2-oxo-4,6-dimethyl-1,3,2-dioxaphosphorinane with KF and a catalytic amount of 18-crown-6-ether gives a mixture of two isomers (**5a** and **5b**) which are anancomeric at phosphorus. While the stable isomer could be obtained pure, attempts to isolate the unstable isomer resulted in mixtures. Nmr (^{31}P, ^{13}C and ^{19}F) and dipole moment measurements on the stable isomer and the isomer mixture are consistent with the presence of an axial fluorine in the stable isomer. This is strongly supported by the observation that the 5,5-dimethyl analogue of **5**, contains an axial fluorene as determined by x-ray diffraction techniques. The earlier conclusion (Ref. 3) that $^{1}JPF_{ax} > {}^{1}JPF_{eq}$ in the isomeric 4-methyl analogues of **5a** and **5b** is supported by our investigations and a rationale for this unusual coupling relationship is put forth.

INTRODUCTION

Considerable effort has been focused in the past decade on the conformational behavior and structural properties of phosphorus-containing cyclohexanes.[1] Of particular interest in the 1,3,2-dioxaphosphorinane class of compounds has been the determination of the differing tendencies of various *Y* groups to be axial or equatorial in the chair form. Rationales for these variations have been advanced

Y = e.g., R,OR,NR_2, halogen

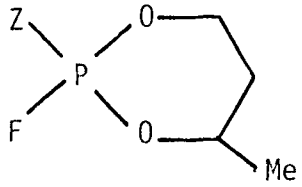


Z = lone pair, chalcogen

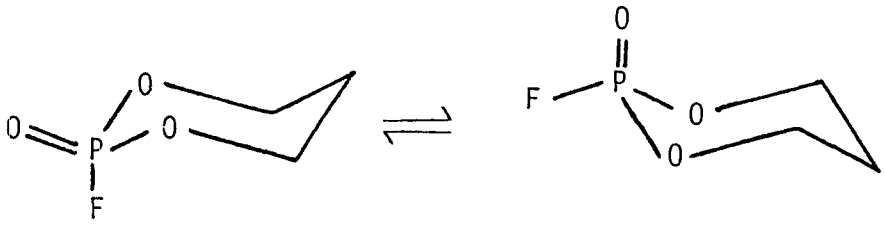
which involve the interplay of steric and electronic factors. One approach to evaluating the conformational bias of a compound in phosphorinane systems has been the examination of spectroscopic, dipole moment and structural parameters of analogues which are anancomeric at phosphorus because of rigidity of the chair conformation imposed by equatorial methyl groups on the 4 and 6 positions of the ring.[2] Comparison of the spectroscopic parameters derived from such studies frequently permit estimation of the equilibrium constants of the conformationally mobile parent systems.[2a] This approach as well as other studies of phosphorinane systems possessing differing degrees of conformational rigidity conferred on the ring by substituents have given rise to nmr and ir parameters and dipole moments, which with varying degrees of certainty characterize axial and equatorial groups on

phosphorus.[1] The evidence put forth for the axial preference of fluorine in 2-fluoro-2-oxo-1,3,2-dioxaphosphorinanes has been somewhat ambiguous. For the isomers of 2-*Z*-2*Y*-4-methyl-1,3,2-dioxaphosphorinanes the usual observation that $^1JPY_{ax} < {}^1JPY_{eq}$ (Y = C,H,SeR) and $^1JPZ_{ax} < {}^1JPZ_{eq}$ (Z = Se) also includes Y = F for **1–3**.[3] However, the opposite result is

1 Z = lone pair
2 Z = S
3 Z = Se
4 Z = O

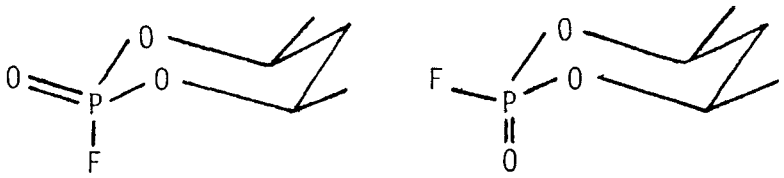


obtained in the case of **4**.[3] The latter observation along with the unusually small differences in $\delta^{31}P$ for **1–4** led to the postulation of an equilibrium which in the case of **4** lies toward conformer **B**.[3]



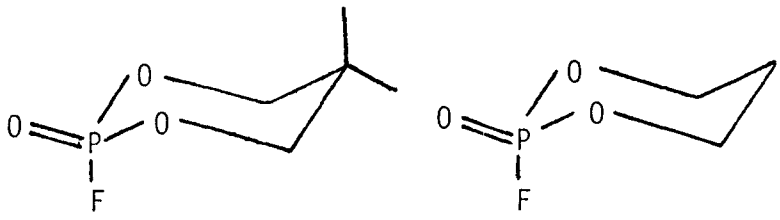
A B

Because 4,6-dimethyl-1,3,2-dioxaphosphorinane systems are considerably less conformationally mobile[2c] and also have been found to follow the empirical rule that $^1JPY_{ax} < {}^1JPY_{eq}$ (Y = H)[4] and $^1JPZ_{ax} < {}^1JPZ_{eq}$ (Y = Se)[5], it was of interest to examine the isomers of **5** for possible confirmation of the somewhat surprising conclusion by Stec *et al.* that $^1JPF_{ax} > {}^1JPF_{eq}$.[3] Here we show that the



5a **5b**

thermodynamically stable isomer of **5** has a larger dipole moment and that the stable conformer of **6** in the crystalline state possesses an axial fluorine. Comparison



6 **7**

of the ^{31}P and ^{13}C nmr data for these compounds and also for **7** is strongly confirmatory of the earlier conclusion[3] that $^{1}JPF_{ax} > {}^{1}JPF_{eq}$ when Z is oxygen.

EXPERIMENTAL

The stable isomer of **5** and compounds **6** and **7** were prepared as described earlier.[6] The unstable isomer of **5** was prepared as a mixture with the stable isomer as follows. A 50% excess of finely ground anhydrous KF was added to 5.0 g of the 2-chloro precursor in 5 mL of benzene along with a catalytic amount (2–5%) of 18-crown-6 ether. The mixture was stirred at room temperature for 24 h or refluxed for 2 h. After cooling to room temperature the reaction mixture was filtered, the benzene evaporated from the filtrate and the oily residue distilled (bp 100–101° at 0.2 Torr; yield, 40%; m/e 168 (p-1), calc MW 169).

A suitable crystal of **6** for x-ray diffraction (0.32 × 0.26 × 0.44 mm) was grown by slow sublimation to a water-cooled probe (30–35° at 0.5 mm) and mounted in a Lindemann capillary to protect it from reaction with atmospheric moisture.

Preliminary examination of **6** showed that the crystals belonged to the orthorhombic crystal class with $a = 13.078(1)$ $b = 10.854(1)$ and $c = 11.416(2)$ Å and four molecules of **6** per unit cell. The assignment of a space group was unambiguous since the systematic extinctions (*hoo* absent if $h = 2n + 1$, *oko* absent if $k = 2n + 1$, *ool* absent if $l = 2n + 1$) are only consistent with $P2_12_12_1$.

A total of 1278 unique reflections were measured using CuK_α radiation (1.5418 Å) in a variable ω-scan technique (minimum 1°/min) on a Syntex $P2_1$ computer-controlled four-circle diffractometer. During data collection the intensities of three standard reflections, (602), (512) and (341), were monitored periodically and observed not to change significantly. After correction for Lorentz, polarization and background effects, 672 reflections were judged observed [$F_o \geq 3\sigma(F_o)$].

Solution of the crystal structure was begun by routine application of direct methods using a multiple solution weighted tangent formula.[7] The positions of the phosphorus, three oxygen and fluorine atoms were located in the resulting electron density calculation. After four cycles of least squares refinement[8] of those positions, the conventional agreement factors R and ωR were 0.407 and 0.395, respectively. The phased E synthesis[8] revealed the positions of the rest of the non-hydrogen atoms which refined to $R = 0.270$ and $\omega R = 0.255$. The isotropic temperature factors were then varied giving $R = 0.15$ and $\omega R = 0.146$. Refinement of the anisotropic parameters yielded values of 0.085 and 0.070 for R and ωR, respectively. Subsequent difference calculations[8] located all of the hydrogen atoms and full matrix least squares refinement resulted in final crystallographic residuals of $R = 0.050$ and $\omega R = 0.042$. Fractional coordinates and thermal parameters, for this model are listed in Tables 1 and 2. The atomic scattering factors used in the refinement were those of Hanson, *et al.*[9] Corrections,[10] real and imaginary, for anomalous dispersion of phosphorus were also used in the calculations.

RESULTS AND DISCUSSION

Although the halogen exchange described in the Experimental gives two isomers of **5** as indicated by the nmr data in Table I, the predominant isomer in a fresh preparation quickly isomerizes to give a 19/81 ratio of unstable/stable which is stable on the order of several hours. In the presence of free halide ions, this mixture progresses to a 10/90 ratio. Attempts to achieve a pure sample of unstable isomer by crystallizing the stable form, column chromatography or reverse-phase hplc with high efficiency columns, always gave rise to mixtures. The stable isomer can, however, be obtained pure by recrystallization from CH_2Cl_2/*n*-hexane mixtures.

Differentiation between the isomers in the 19/81 mixture was not possible using ^{1}H nmr or ir spectroscopy. Thus a mixture of **5a** and **5b** exhibited the same ^{1}H spectrum as a sample of pure stable isomer (60 MHz, $CDCl_3$: 4.54m (2H, OCH) $^{3}JPH = 6$ Hz; 1.73m (2H, CCH_2); 1.29dd (6H, CH_3) $^{4}JPH = 3$ Hz). The ir spectra ($CHCl_3$) in the $\nu P=O$ region showed two peaks (1329 and 1319 cm^{-1}) which in the cases of **6** (1316 cm^{-1}) and **7** (1332 cm^{-1}) appeared as a single broadened peak. Whether these observations are consistent with the presence of conformer equilibria which are more rapid for **6** and **7** than for **5a** and **5b** is speculative.

TABLE I

Final atomic positional parameters

	x	*y*	*z*
P	0.1837(1)	0.8054(1)	0.0447(1)
F	0.1405(2)	0.9310(3)	0.0137(3)
O_1	0.1213(3)	0.7062(4)	0.0032(4)
O_2	0.1940(2)	0.8131(4)	0.1779(3)
O_3	0.2917(2)	0.8094(3)	−0.0072(2)
C_1	0.2720(4)	0.8933(6)	0.2305(5)
C_2	0.3695(4)	0.8890(5)	0.0469(5)
C_3	0.3753(3)	0.8684(4)	0.1767(4)
C_4	0.4113(5)	0.7396(6)	0.2063(7)
C_5	0.4512(6)	0.9649(7)	0.2248(7)
H_1	0.257(4)	0.980(6)	0.217(5)
H_{1A}	0.275(3)	0.873(4)	0.320(5)
H_2	0.349(3)	0.977(5)	0.034(4)
H_{2A}	0.429(4)	0.857(5)	0.007(5)
H_4	0.415(5)	0.728(7)	0.278(7)
H_{4A}	0.477(4)	0.727(5)	0.173(5)
H_{4B}	0.357(5)	0.677(6)	0.165(5)
H_5	0.519(6)	0.944(7)	0.199(6)
H_{5A}	0.451(5)	0.947(6)	0.295(6)
H_{5B}	0.420(5)	1.056(8)	0.201(6)

TABLE II

Final thermal parameters[a]

	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
P	7.9(1)	15.3(1)	12.7(1)	−1.3(1)	−1.2(1)	0.6(1)
F	13.9(3)	20.5(4)	21.2(4)	2.1(3)	−4.2(3)	2.7(3)
O_1	12.6(3)	22.3(5)	23.5(5)	−6.9(3)	−4.6(3)	−0.4(5)
O_2	7.9(2)	22.2(4)	13.0(3)	−1.7(3)	1.8(2)	1.5(3)
O_3	9.7(2)	18.7(4)	10.6(3)	−2.3(2)	0.5(2)	−3.0(3)
C_1	10.3(4)	15.7(6)	10.1(5)	1.2(4)	0.0(3)	−1.7(5)
C_2	8.9(3)	13.7(5)	11.5(5)	−1.5(4)	0.8(4)	1.2(4)
C_3	7.0(3)	11.4(4)	9.6(4)	0.0(3)	−0.1(3)	0.1(3)
C_4	11.0(4)	15.6(6)	17.5(7)	4.0(4)	0.8(5)	3.6(5)
C_5	12.5(4)	19.5(8)	16.7(7)	−1.8(5)	−4.6(5)	−0.9(6)

[a] The β_{ij} are defined by: $T = \exp\{-(h^2\beta_{11} + k^2\beta_{22} + l^2\beta_{23} + 2hk\beta_{12} + 2hl\beta_{13} + 2kl\beta_{23})\}$.

Except for the ^{31}P-^{19}F spin-spin coupling constants, the $\delta^{31}P$, $\delta^{19}F$ and $^3JPC(H_2)$ nmr data in Table III suggest the assignment of an axial and equatorial fluorine in **5a** and **5b**, respectively. The upfield $\delta^{31}P$ value of **5a** relative to **5b** is consistent with evidence adduced earlier for 2-*R* analogues of **5a** and **5b** (except where $R = H$).[2a] The ^{31}P chemical shifts for **6** and **7**, for which an axial fluorine in the dominant conformer would be expected since sterically unhindered *R* groups have a strong tendency to be axial,[1] are also upfield of **5b**. It can also be seen that the $\delta^{19}F$ values for **5a**, **6** and **7** are similar whereas that of **5b** is further upfield. The smaller $POCCH_2$ coupling observed for **5a** (4.9 Hz) compared to **5b** (11.8 Hz) has been correlated with the presence of an equatorial P=O group in similar systems.[11]

Arguments concerning the expected dipole moments of **5a**, **5b** and **6** are now presented which lend support to the stereochemical assignments at phosphorus in these molecules. The gas-phase dipole moments of PF_3 (1.03 D) and $O{=}PF_3$

TABLE III

NMR Data for Compounds **5-7**[a]

Cmpd	$\delta^{31}P$	$\delta^{19}F$	^{1}JPF	$\delta^{13}C(O_3)$	^{2}JPC	$\delta C(H_2)$	$^{3}JPC(H)_2$	$\delta^{13}C(H_3)$	$^{3}JPC(H_3)$
5a	−16.5	−85.5	1000	−78.0	6.9	−39.7	4.9	−21.4	14.4
5b	−15.2	−66.1	987	−77.9	6.9	−38.6	11.8	−21.5	10.8
6	−17.8	−87.1	1008	−79.3	7.4	−32.1	7.4	−21.1,19.4	—
7	−16.6	−85.1	1001	−71.0	7.9	−25.0	7.9	—	—

[a] Chemical shifts upfield of the standard (^{31}P, 85% H_3PO_4, external; ^{13}C, Me_4Si, internal ^{19}F, $FCCl_3$, internal) are negative. Coupling constants are in Herz. Measurements were carried out on a Bruker HX-90 instrument in the FT mode.

TABLE IV

Intramolecular bond distances (Å) and angles (°)

P—F	1.516(3)	C_3—C_5	1.544(7)	O_2—C_1—C_3	111.3(3)
P—O_1	1.431(3)	O_1—P—F	112.7(2)	O_3—C_2—C_3	110.4(3)
P—O_2	1.532(3)	O_1—P—O_2	114.8(2)	C_2—C_3—C_1	109.3(3)
P—O_3	1.529(3)	O_1—P—O_3	114.8(2)	C_2—C_3—C_4	110.7(4)
O_2—C_1	1.470(5)	F—P—O_2	103.2(2)	C_2—C_3—C_5	111.9(4)
O_3—C_2	1.468(5)	F—P—O_3	102.4(2)	C_1—C_3—C_4	106.4(4)
C_1—C_3	1.500(6)	O_2—P—O_3	107.6(2)	C_1—C_3—C_5	106.4(4)
C_2—C_3	1.508(6)	P—O_2—C_1	119.5(3)	C_4—C_3—C_5	110.3(4)
C_3—C_4	1.513(6)	P—O_3—C_2	120.0(3)		

(1.73 D) suggest that the P—F bond moment is toward F.[12] The O=P moment is about 3 D (in the indicated direction) as determined from the increment in the dipole moment of rigid phosphite esters such as $P(OCH_2)_3CR$ upon oxidation to $O{=}P(OCH_2)_3CR$.[13] Thus in order for the dipole moment of $O{=}PF_3$ to be only 0.7 D larger than that of PF_3, and if the O=P moment is *ca.* 3 D, then it is likely that the P—F and O=P bond moments are oppositely directed and that μ(O=P) is almost three times as large as μ(P—F). The expected dipole moment of **5a** should be larger than that of **5b**.[2c] From dielectric constant data taken in toluene at 25 ± 0.02°,[14] dipole moments of 5.98 D and 5.89 D for **5a** and a 19/81 mixture of **5b/5a**, respectively, were obtained. Using the equation $\gamma(\mu_A)^2 + (1 - Y)(\mu_B)^2 = \mu^2$ (where Y = the mole fraction of **5a**, μ_A = the dipole moment of **5a** and μ = the dipole moment of the mixture) the dipole moment of **5b** (μ_B) is calculated to be 5.49 D. The difference between the measured moments (0.09 D) is only about twice the probable error (±0.05 D), thus rendering this evidence for the stereochemical assignments of **5a** and **5b** supportive but weak.

The dipole moment of **6** in toluene is 5.96 D which suggests the same configuration at phosphorus as **5a**. An x-ray analysis of **6** was obtained assuming that the phosphorus stereochemistry in solution would be preserved in the solid state. This assumption has so far been borne out for 2*R*-2-oxo-1,3,2-dioxaphosphorinanes where *R* is an electronegative substituent such as Cl, Br and OR.[1] The structure of **6** shown in Figure 1 clearly shows the fluorine to be axial in the chair conformation of the ring. The bond distances and angles given in Table IV are comparable to the

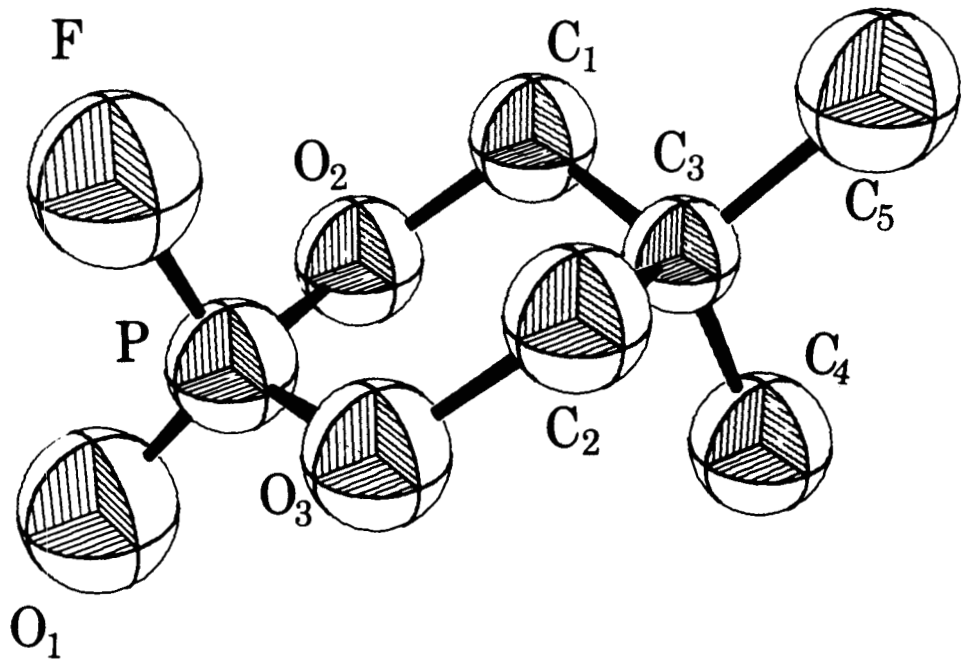
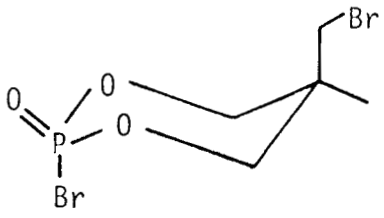


FIGURE 1 ORTEP drawing of **6**.

analogous structural parameters for **8**[15] and **9**.[16] This contrasts the observation that the XPX bond angle in $O{=}PX_3$



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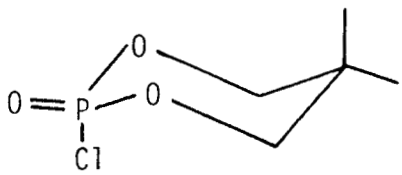

9

compounds decreases from X = Br to Cl to F.[17] The P—F distance in **6** compares well with that found for $O{=}PF_3$ (1.523(3) Å).[17]

Except for the ^1JPF couplings (which are opposite in magnitude to those expected for axial and equatorial stereochemistries) and the O=P stretching frequencies (which are uninformative) the rest of the data presented here favor the assignments given for **5a** and **5b** and hence also confirm those for the isomers of **4**.[3] The empirical observation that phosphorus couplings to equatorial substituents exceed those to axially positioned atoms has been rationalized in terms of the dominance of the Fermi contact term which includes a contribution from the positive charge on phosphorus.[2c] CNDO/2 calculations have shown that this charge is indeed larger as experienced by an equatorial proton than when it is axially disposed in **5a** and **5b**,

respectively.[18] Indeed, the contact contribution appears from calculations to be sufficient to account for one-bond phosphorus couplings such as $^{31}P—^{13}C$, $^{31}P—^{17}O$, $^{31}P—^{15}N$, $^{31}P—^{31}P$ and $^{31}P—^{35}Cl$.[19] Fluorine couplings, on the other hand appear to have significant contributions from the orbital and dipolar terms in Ramsey's formulation.[19] It is interesting to speculate that in compounds **1–4**, the latter terms are dominant in the 2-oxo derivative (**4**), while the Fermi contact term dominates in the compounds which possess less electronegative phosphorus substituents.

ACKNOWLEDGMENT

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