# The Hexafluoroacetone Adducts of Diphenyl Phosphoramidites; a Distinction between P–N Bond Rotation and Pseudorotation

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The low-temperature [19]F n.m.r. spectra of the 1,3,2-dioxaphospholans obtained from hexafluoroacetone and diphenyl phosphoramidites give barriers of 10—12 kcal mol^{-1} for the pseudorotations which involve switching equatorial amino- and apical phenoxy-groups consistent with a large difference in apicophilicity between these groups. The changes in the spectra at lower temperatures are explained in terms of topomer formation from the most stable conformer either by P–N bond rotation or by pseudorotation, the former having the larger free energy of activation.

WE previously [1] reported data on the free energies of activation of the pseudorotations (1) ⇌ (2) and in-

(1)   (2)
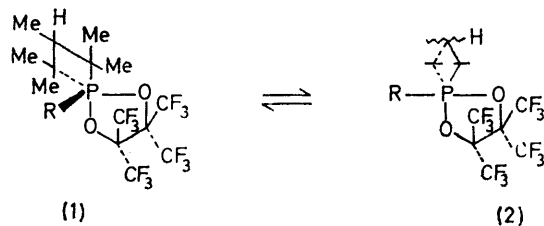
terpreted the variation with the nature of the group R in terms of the apicophilicity of groups in trigonal bipyramids being a function both of electronegativity, increase in which favours occupation of the apical position, and of greater back-bonding of available filled p-orbitals from equatorial than from apical positions.[2] The low observed apicophilicity of dimethylamino-relative to alkyl and the large difference in apicophilicity (>7 kcal mol^{-1}) between dimethylamino- and phenoxy-groups therefore became a consequence largely of efficient back-bonding from the filled p-orbital of an equatorial dimethylamino-group. Hoffmann, Howell, and Muetterties,[3] on the basis of calculations which emphasise the importance of lone-pair σ-framework repulsive interactions as well as of p_π–d_π back-bonding,

have also suggested that apicophilicity for groups having a lone pair on the atom bonded to phosphorus is a balance between electronegativity and lone-pair interactions. We now report experiments in which we sought additional evidence for a substantial difference in apicophilicity between oxygen and nitrogen.

The diphenyl phosphoramidites [(PhO)$_2$P·NR$_2$] with hexafluoroacetone gave the stable crystalline 1,3,2-dioxaphospholans (4; A—D = CF$_3$). The pseudorotations available to these without placing the five-membered ring diequatorial are shown in the cycle (3)—(8). Pseudorotations which place a 1,3,2-dioxaphospholan ring diequatorial without compensating gain in the apicophilicity of the groups occupying the apical positions are high energy processes and slow on the n.m.r. time-scale at room temperature. Thus the pseudorotation (9) ⇌ (10) [4] has ΔG* ca. 22 kcal mol^{-1}. The classical work of Westheimer [5] on the hydrolysis of methyl ethylene phosphate, in which rate accelerations of about 10^6 are ascribed to relief of strain in decreasing the ring angle at phosphorus from a theoretical 109 to 90°, would also lead one to expect that an increase in ring angle from 90 to 120° would require a great deal of energy. Of the pseudorotations in the cycle (3)—(8), those which involve (4) ⇌ (5) and (6) ⇌ (7) are

[1] R. K. Oram and S. Trippett, *J.C.S. Chem. Comm.*, 1972, 554; *J.C.S. Perkin I*, 1973, 1300.
[2] P. Gillespie, P. Hoffmann, H. Klysacek, D. Marquarding, S. Pfohl, F. Ramirez, E. A. Tsolis, and I. Ugi, *Angew. Chem. Internat. Edn.*, 1971, **10**, 687.
[3] R. Hoffmann, J. M. Howell, and E. L. Muetterties, *J. Amer. Chem. Soc.*, 1972, **94**, 3047.
[4] B. C. Chang, W. E. Conrad, D. B. Denney, D. Z. Denney, R. Edelman, R. L. Powell, and D. W. White, *J. Amer. Chem. Soc.*, 1971, **93**, 4004.
[5] F. H. Westheimer, *Accounts Chem. Res.*, 1968, **1**, 70.

between topomeric [6] trigonal bipyramids of identical energies. Such pseudorotations have never been slowed on the n.m.r. time-scale [5] and all available calculations [7]

(3) (4) (5)

(6) (7) (8)
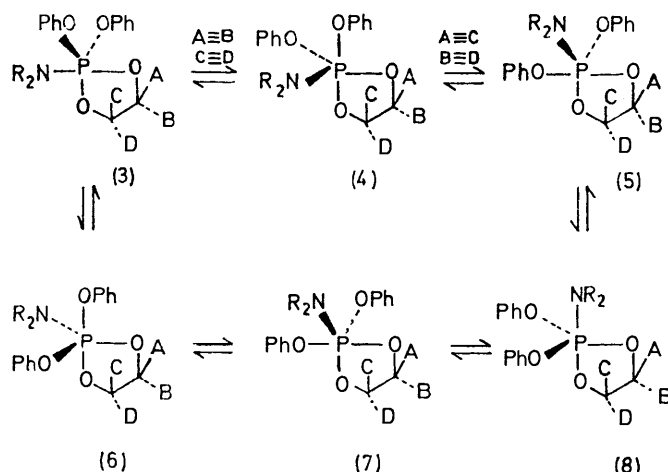
agree that the barriers to such pseudorotations will be small. The presence of a five-membered ring is not expected to increase the barriers between (4) and (5), and

(9) (10)
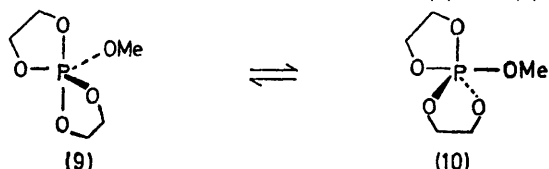
(6) and (7), as whatever the details of the pseudorotation process involved angle strain is not increased at any point.

The [19]F n.m.r. spectra of the adducts (4) show a singlet at room temperature implying that all the pseudo-rotations in the cycle (3)—(8) are rapid on the n.m.r. time-scale. The pseudorotation (4) ⇌ (5) leads to equivalence of A with C and of B and D, and the pseudo-rotation (3) ⇌ (4) leads to equivalence of A and B and of C and D (it is necessary to consider only one half of the symmetrical cycle). On cooling, the singlets broaden and then split, each into two equal signals. The free energies of activation for the processes leading to these changes, obtained by application of the Gutowsky-Holm equation, vary from 10 to 12 kcal mol^{-1}, and on the basis of the foregoing discussion of the cycle (3)—(8) must be ascribed to those pseudorotations which exchange phenoxy- and amino-groups at apical sites. Two situations could lead to the observed n.m.r. changes; (a) low energy (3) with (3) ⇌ (4) slow and (4) ⇌ (5) rapid, and (b) high energy (3) with (3) ⇌ (4) slow and (4) ⇌ (5) rapid. We prefer the latter alternative, in keeping with the assumed,[8] expected,[2,3] and found [1] greater apicophilicity of oxygen than of nitrogen. The observed barriers of 10—12 kcal mol^{-1} are greater than the energy differences between (3) and (4), but in view of the small

barriers (<5 kcal mol^{-1}) between topomeric trigonal bipyramids are probably consistent with the previously observed [1] difference in apicophilicity between amino- and phenoxy-groups of 7—8 kcal mol^{-1}.

The surprising feature of the data (Table) is the insensitivity of the barrier to the pseudorotations (3) ⇌

N.m.r. data for the adducts (4)

R$_2$N	Me$_2$N	[CH$_2$]$_4$N	Pr$_2^i$N	PhMeN
δ(^{31}P) [a]	+54·5	+56	+51	+57
^{19}F T_c/°C [b]	−58	−8	−31	−42
		−100	−62	−51
				−113
$\Delta\nu$/Hz [c]	156	186	188	156
		127	94	56
				ca. 50
ΔG^*/kcal mol^{-1}	10·0	12·3	11·2	10·8
		8·1	10·0	10·8
				7·9

[a] P.p.m. relative to 85% H$_3$PO$_4$; in CDCl$_3$. [b] In ether. [c] Limiting separation below coalescence temperature.

(4) to the nature of the groups attached to nitrogen. The extent of back-bonding from the equatorial nitrogen atoms was expected to vary with the basicity of the corresponding secondary amines R$_2$NH which spans a range greater than 10^6. Although one is comparing the extent of p_π–d_π overlap from the filled p-orbital of an sp^2-hybridised nitrogen with the availability for donation to a proton of the lone pair of an sp^3-hybridised nitrogen, the lack of correlation was unexpected. We have observed a similar lack of effect on the apicophilicity of the phenyl group as the para-substituent varies.[1]

The barrier to the pseudorotation (3) ⇌ (4) when R$_2$ = [CH$_2$]$_4$ is unchanged in hexafluoropropan-2-ol (pK$_a$ 9·3). This suggests that the observed changes in the ^{19}F spectrum are not due to dissociation to a betaine [2] and that the nitrogen atom is only feebly basic, as expected on the basis of the back-bonding hypothesis. Protonation would give the highly electronegative C$_4$H$_8$$\overset{+}{N}$H group and the barrier to pseudorotation would be lowered.

Further lowering of the temperature resulted in one component in the doublet in the ^{19}F n.m.r. spectra of the adducts (4; R^2 = Pr$^i_2$, [CH$_2$]$_4$, or PhMe) broadening and splitting into two equal signals, the other component remaining unchanged. At this point the para-fluorine atoms of the bis-(p-fluorophenyl) analogue of the adduct (4; R$_2$ = [CH$_2$]$_4$) also became non-equivalent. These changes, with ΔG^* values from 8·5 to 11 kcal mol^{-1}, we associate with slowing of rotation round the equatorial P–N bonds. A barrier of 5—12 kcal mol^{-1} to rotation round the equatorial P–N bond is well established experimentally [9,10] and theoretically.[3,10] Calculations [3] show that the lowest energy conformation has the nitrogen p-orbital in the equatorial plane but it has not been explicitly stated whether the barrier to rotation would be

[6] G. Binsch, E. L. Eliel, and H. Kessler, Angew Chem. Internat. Edn., 1971, 10, 570.

[7] E.g. A. Rauk, L. C. Allen, and K. Mislow, J. Amer. Chem. Soc., 1972, 94, 3035, and ref. 3.

[8] E.g. A. Klaebe, J.-F. Brazier, F. Mathis, and R. Wolf, Tetrahedron Letters, 1972, 4367.

[9] M. J. C. Hewson, S. C. Peake, and R. Schmutzler, Chem. Comm., 1971, 1454.

[10] E. L. Muetterties, P. Meakin, and R. Hoffmann, J. Amer. Chem. Soc., 1972, 94, 5674.

expected to be two-fold or four-fold. We assume that it is four-fold with the conformer in which the nitrogen p-orbital is in the apical plane having a higher energy than that in which the p-orbital is in the equatorial plane, but both being energy minima. In our cases, the topomers (11) and (13) are formed from (12), the lowest energy conformer of (4), by P–N bond rotation [(11) ⇌ (12)], and by pseudorotation [(12) ⇌ (13)]. These are distinct processes and may have different energies of activation,
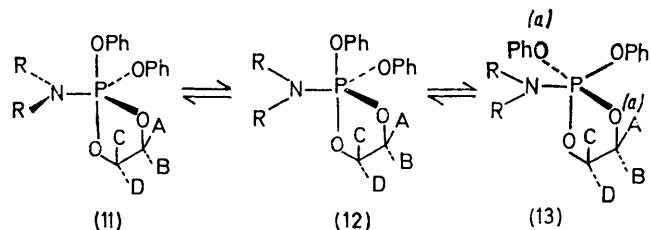
(11)   (12)   (13)

although the topomers have identical energies. If P–N bond rotation, i.e. (11) ⇌ (12), becomes slow on the n.m.r. time-scale while the pseudorotation (12) ⇌ (13) is still rapid, then the CF_3 groups A and C will be magnetically non-equivalent as will the two aryloxy-groups. The CF_3 groups B and D would also be expected to be non-equivalent, in that B is next to an equatorial oxygen atom when the nitrogen p-orbital is in the equatorial plane (12) while A is next to an equatorial oxygen atom when this orbital is in the apical plane (13), but they are on the opposite side of the molecule from the amino-group and are insulated from the effects of lone-pair orientation.

Further cooling would be expected to slow the pseudorotation (12) ⇌ (13) and lead to non-equivalence of B and D, the conformation now being effectively frozen at (12) on the n.m.r. time-scale. This is observed in the case of the adduct (12; $R_2 = PhMe$); below -113 °C the second component of the initial doublet splits and the spectrum consists of four equal signals due to four distinct CF_3 groups.*

The possibility of topomer formation by either bond rotation or Berry pseudorotation has been considered by Muetterties, Meakin, and Hoffmann.[10] They concluded that the two processes are inextricably coupled and that 'factoring would involve at best a circular argument of which process comes first.' Our tentative interpretation of the variable temperature [19]F n.m.r. spectrum of the 1,3,2-dioxaphospholan (4; $R_2 = PhMe$) requires that the barrier to conversion of (12; $R_2 = PhMe$) into (11) by bond rotation is 10·8 kcal mol^{-1} while the barrier to conversion into the topomer (13) by pseudorotation is 7·9 kcal mol^{-1}.

* With $R_2 = PhMe$ there are two possible isomers for the lowest energy trigonal bipyramid (12). From the observed phenomena and from steric considerations, the phenyl group is probably on the side of the 1,3,2-dioxaphospholan ring.

As expected, the [1]H n.m.r. spectrum of the isopropyl groups of the adduct (4; $R_2 = Pr^i_2$) showed complex changes around -60 °C, but we have not been able to quantify these.

EXPERIMENTAL

Reaction of Diphenyl Phosphoramidites with Hexafluoroacetone.—Hexafluoroacetone (22 mmol) was passed into a solution of the phosphoramidite (10 mmol) in ether–hexane (1 : 1; 30 ml) at $-78°$. In some cases, a white solid precipitated and quickly redissolved. Solvent was then removed under reduced pressure below room temperature and the crystalline residue was recrystallised from ethanol. In this way the following 4,4,5,5-tetrakis(trifluoromethyl)-1,3,2-dioxaphosph(v)olans were obtained in almost quantitative yields: 2-dimethylamino-2,2-diphenoxy-, m.p. 110—110·5°, m/e 574 $(M - F)$, 549, 524, and 500, τ 2·8 (10H, m) and 7·0 (6H, d, J 12 Hz), [19]F δ +5·2 (s) p.p.m. (Found: C, 40·7; H, 2·7; N, 2·5. $C_{20}H_{16}F_{12}NO_4P$ requires C, 40·5; H, 2·7; N, 2·4%); 2-dimethylamino-2,2-bis-(p-fluorophenoxy)-, m.p. 101—102°, m/e 629, 610, 585, 560, and 518, τ 3·13 (8H, m) and 7·0 (6H, d, J 11 Hz), [19]F δ +4·5 (s) and +55·5 (m) p.p.m., [31]P δ +53·5 p.p.m. (Found: C, 38·2; H, 2·2; F, 42·0; N, 2·4. $C_{20}H_{14}F_{14}NO_4P$ requires C, 38·2; H, 2·2; F, 42·3; N, 2·2%); 2-di-isopropylamino-2,2-diphenoxy-, m.p. 83·5—84°, m/e 630 $(M - F)$, 580, 556, and 549, τ 2·9 (10H, m), 6·0 (1H, m), and 8·6 (6H, d, J 7 Hz), [19]F δ +4·2 (s) p.p.m. (Found: C, 44·5; H, 3·8; F, 34·9. $C_{24}H_{16}F_{12}NO_4P$ requires C, 44·4; H, 3·7; F, 35·1%); 2-(pyrrolidin-1-yl)-2,2-diphenoxy-, m.p. 108—108·5°, m/e 619, 600, 549, and 526, [19]F δ +5·13 (s) p.p.m. (Found: C, 42·7; H, 2·8; N, 2·5. $C_{24}H_{18}F_{12}NO_4P$ requires C, 42·7; H, 2·9; N, 2·3%); 2-(pyrrolidin-1-yl)-2,2-bis-(p-fluorophenyl)-, m.p. 98·5—100·5°, m/e 655, 636, 582, 581, and 540, [19]F δ +4·55 (s) and +56·6 (m) p.p.m., [31]P δ +60 p.p.m. (Found: C, 40·4; H, 2·5; F, 40·5. $C_{22}H_{16}F_{14}NO_4P$ requires C, 40·3; H, 2·5; F, 40·6%); 2-N-methylanilino-2,2-diphenoxy-, m.p. 95—95·5°, m/e 636 $(M - F)$, 586, 562, and 549, [19]F δ +4·9 (s) p.p.m., τ 2·6—3·3 (15H, m) and 6·6 (3H, d, J 10 Hz) (Found: C, 46·0; H, 2·7; N, 2·8. $C_{25}H_{18}F_{12}NO_4P$ requires C, 45·8; H, 2·7; N, 2·15%); 2-N-methylanilino-2,2-bis-(p-fluorophenoxy)-, m.p. 68·5—69·5°, m/e 691, 672, 622, 585, and 580, τ 2·73 (5H, m), 3·22 (8H, m), and 6·65 (3H, d, J 11 Hz), [19]F δ +4·65 (s) and +53·5 (m) p.p.m., [31]P δ +58·5 p.p.m. (Found: C, 43·2; H, 2·35; F, 38·7; P, 4·5. $C_{25}H_{16}F_{14}NO_4P$ requires C, 43·4; H, 2·35; F, 38·5; P, 4·5%).