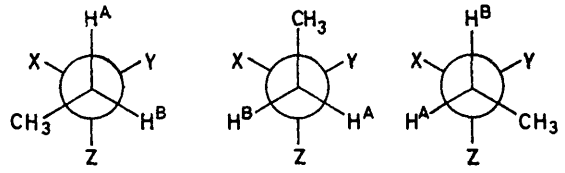
Magnetic Non-equivalence in Organophosphorus Esters

By **C. Dennis Hall,* Robert Ardrey, Robert Dyer,** and **Paul G. Le Gras,** Department of Chemistry, King's College, University of London, Strand, London WC2R 2LS

The ^{1}H n.m.r. spectra of a number of esters of phosphoric, phosphonic, phosphorothioic, phosphonothioic, phosphorodithioic, and phosphonodithioic acids are reported. In certain cases the methylene protons of the ethoxy-groups show non-equivalence and such spectra are analysed by full iterative calculations using the LAOCN 3 program. The effects of temperature and solvent changes on the non-equivalence are reported and the results are interpreted in terms of intrinsic non-equivalence (due to an asymmetric phosphorus atom) or unequal conformer populations or a combination of both factors.

THE literature is now replete with examples of magnetically non-equivalent methylene protons.[1-3] The non-equivalence occurs when the methylene protons lie in the vicinity of a centre which is asymmetric with respect to the sensor protons (*e.g.* a chiral or prochiral carbon atom) and the necessary condition for geminal groups to show non-equivalence (*i.e.* be anisochronous) is simply that they be ' diastereotopic [1] on the time scale of the measurement '.[4] Thus with a tetracoordinate organophosphorus ester, CH_3CH_2OPXYZ, the methylene group (of CH_3CH_2O) will, in principle, show non-equivalence provided X, Y, and Z are different. This is depicted in the Newman projections (I)—(III) † from which it may be seen that, assuming rapid rotation on the n.m.r. time-scale, even if (I)—(III) are equally populated, H^A never enjoys the same environment as



(I) (II) (III)

H^B,[2] and a chemical shift difference between H^A and H^B may therefore be expected. This is known as ' intrinsic

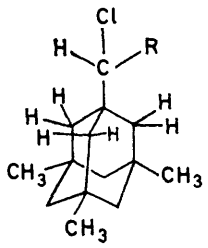
† The projection is simplified in that the oxygen atom between the phosphorus and carbon atoms has been omitted. In fact the C–O–P bond introduces two degrees of freedom about the C–O and the P–O bonds resulting in nine possible staggered conformations (see ref. 2).

[1] K. Mislow and M. Raban, *Topics Stereochem.*, 1967, vol. 1, ch. 1.
[2] M. van Gorkam and G. E. Hall, *Quart. Rev.*, 1968, **22**, 14.
[3] T. H. Siddall and W. E. Stewart, *Progr. NMR Spectroscopy*, 1964, **5**, 33.
[4] G. R. Franzen and G. Binsch, *J. Amer. Chem. Soc.*, 1973, **95**, 175.

non-equivalence '. The possibility of unequal residence time in any conformer may augment the non-equivalence of H^A and H^B. Hence Gutowsky represents the total chemical shift difference (Δ) as a sum of two terms involving a contribution from intrinsic non-equivalence, (Δ_i), and a contribution from a difference in conformer populations, (Δ_c) [equation (1)].[5] Obviously a knowledge of the magnitudes and relative signs of the two terms is

$$\Delta = \Delta_i + \Delta_c \qquad (1)$$

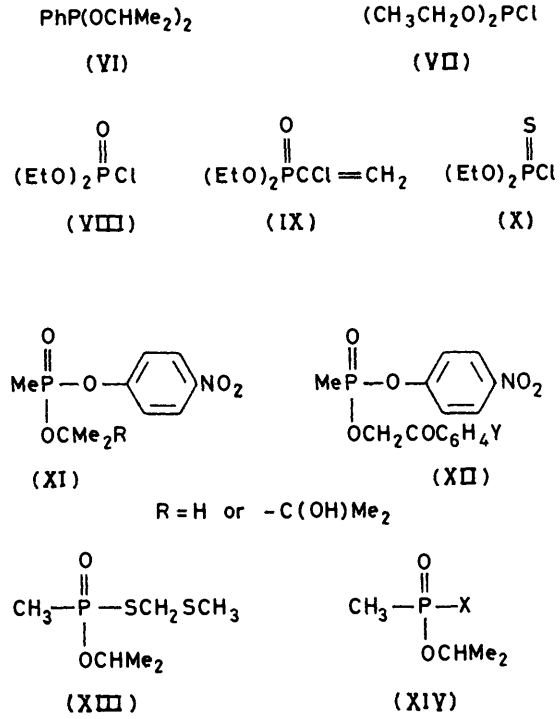
essential to the use of non-equivalence as a tool for conformational analysis. By devising a system of the type $(RCH^AH^B)_3C\text{-}CXYZ$ in which all three staggered conformations were of necessity equally populated, *i.e.* a system with trigonal symmetry, Binsch was able to assess the potential magnitude of the Δ_i term.[4] This was accomplished in a most elegant manner using compounds of type (IV) for which Δ_i varied between 0.162 and 0.293 p.p.m. (in $CDCl_3$) according to the nature of R. With R = CO_2H in benzene as solvent, Δ_i varied only marginally from 0.200 (at 39.5 °C) to 0.180 p.p.m.



(IV)

(at 100 °C). Furthermore, solvents varying in dielectric constant from dioxan (ε 2.21) to dimethyl sulphoxide (ε 48.9) had only a slight effect (0.197—0.162 p.p.m.) on Δ_i.[4] As Binsch pointed out, the intrinsic anisochronism in compounds of type (IV) may be magnified in comparison with open chain analogues by the geometric constraint of the bicyclic structure. Nevertheless, the observations that Δ_i was insensitive to changes in solvent, and more importantly, temperature, appear to provide useful criteria for the assignment of chemical shift differences to intrinsic anisochronism as distinct from differences in conformer population.

The origin of non-equivalence of protons in acyclic phosphorus esters has been the subject of debate for some time. In one of the earliest studies,[6] the non-equivalence of the methyl groups of (VI) was ascribed to intrinsic anisochronism on the basis of non-equivalence persisting to 190 °C. Similar evidence prompted the same explanation for the non-equivalence of methylene groups in (VII) [7] and in the same paper Williamson and Griffin ascribed the non-equivalence of methylene groups in (VIII)—(X) to the intrinsic term but did not offer conclusive evidence for their proposals. Conversely, Jardine *et al.*[8] noted that the non-equivalence of methyl groups in phosphonate esters of type (XI) was not maintained at 150 °C and hence the phenomenon



was ascribed to rotational conformers which could be frozen in one conformer by complex formation with uranyl nitrate. In a similar system, (XII), Frankel *et al.* suggested that the non-equivalence of the methylene protons (with a variety of groups Y) was due to intrinsic non-equivalence augmented by conformational effects.[9] A variable temperature study (in $CDCl_3$) revealed a slight fall in Δ from 0.164 at 0 °C to 0.159 p.p.m. at 58 °C (for Y = H) which suggests a substantial contribution from Δ_i but a change from $CDCl_3$ to DMSO caused a fall in Δ from 0.166 to <0.015 p.p.m. which at first sight is consistent with non-equivalence derived from conformational effects. An even more interesting example was provided by compounds of type (XIII) in which the methylene protons of the SCH_2SCH_3 group and the methyl groups of the $-OCHMe_2$ group both showed magnetic non-equivalence.[10] This is entirely consistent with both sets of protons lying in the proximity of a phosphorus atom bearing three different groups. However, a change in temperature from −62 to +57 °C changed Δ for the *S*-methylene protons from 0.165 to 0.098 p.p.m. whereas Δ for the methyl groups showed only a slight change from 0.077 to 0.060 p.p.m. over the same temperature range. Furthermore, the

[5] H. S. Gutowsky, *J. Chem. Phys.*, 1962, **37**, 2196.
[6] T. H. Siddall and C. A. Prohaska, *J. Amer. Chem. Soc.*, 1962, **84**, 3467.
[7] M. P. Williamson and C. E. Griffin, *J. Phys. Chem.*, 1968, **72**, 4043.
[8] R. V. Jardine, A. H. Gray, and J. B. Reesor, *Canad. J. Chem.*, 1969, **47**, 35.
[9] L. S. Frankel, H. Klapper, and J. Cargioli, *J. Phys. Chem.*, 1969, **73**, 91.
[10] L. Frankel, J. Cargioli, H. Klapper, and R. Danielson, *Canad. J. Chem.*, 1969, **47**, 3167.

solvent effects on Δ for the SCH_2 protons was substantial (0.216 to <0.01 p.p.m. from benzene to DMSO) but was less marked for the methyl groups (0.147 to 0.029 p.p.m. for the same solvent range). It would appear that a combination of Δ_i and Δ_c again determines the overall chemical shift difference but that the contribution of Δ_i may be larger for the methyl non-equivalence than for the *S*-methylene protons. A cursory examination of the structure of (XIII) suggests that the methyl groups lie in a less symmetric environment (P attached to C, O, and S) than the SCH_2 protons which are influenced by phosphorus bearing a carbon and two oxygen atoms. Hence one would anticipate a larger Δ_i term for the methyl groups. This hypothesis is borne out to some extent by examination of the Δ values for (XIV) [10] which range from 0.166 for X = SCH_2CH_3 through 0.08 for X = SH to <0.01 p.p.m. for X = OR, OH, and F.

The implication is clear. In order to observe a substantial Δ_i in organophosphorus esters, the potentially anisotropic sensor protons must be influenced by a highly unsymmetrically substituted phosphorus atom. The availability of a large number of phosphorus esters from earlier studies in an unrelated field [11-13] created the opportunity to examine this hypothesis in detail and the consequent results are the subject of this paper.

EXPERIMENTAL

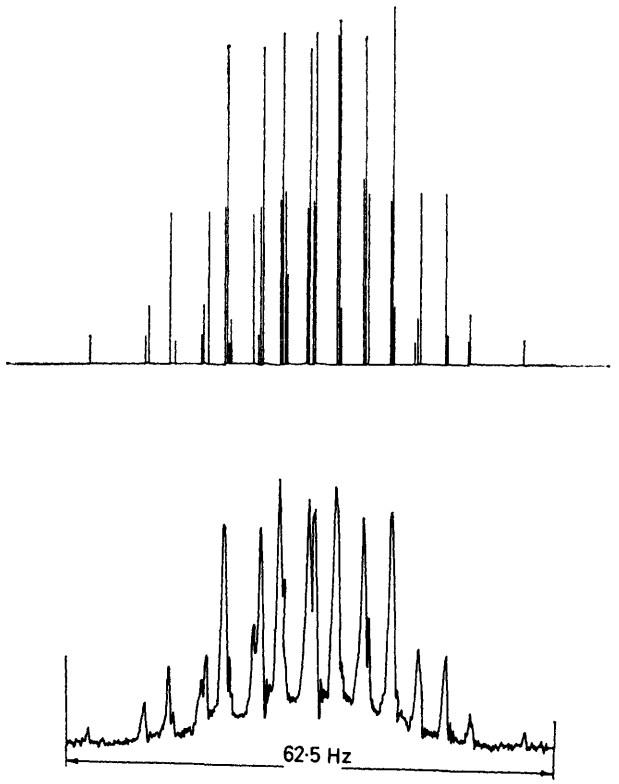
The phosphorus esters were prepared as described previously.[11-13] The n.m.r. spectra were obtained as solutions (*ca.* 10% v/v) in the appropriate solvent (usually $CDCl_3$) using either a Varian HA 100 instrument (PCMU, Harwell or Rutgers University, New Jersey) or more usually a Bruker HFX 90 spectrometer equipped with a Nicolet 1080 computer system and referenced to internal tetramethylsilane. Whenever non-equivalence was detected, the chemical shift region of the non-equivalent methylene protons was expanded (normally to 1 Hz cm^{-1}) and the spectra were analysed in the following manner.

Trial spectra were calculated using the NMRCAL program * and full iterative calculations were carried out using the LAOCN3 program [14] and assuming an ABC_3X, six-spin system. The line positions were taken as the average of at least two measurements each obtained from a 2 048 point, 150 Hz sweepwidth, 90 MHz Fourier transform spectrum.

It should also be noted that the errors in the chemical shifts are always less than the errors in the coupling constants. Our discussion is centred around chemical shift differences and it is reasonable to estimate the errors in individual chemical shifts to be < ±0.003 p.p.m. in each case.

RESULTS AND DISCUSSION

From a total of 22 phosphorus esters, ten showed non-equivalent methylene protons in ethoxy-groups within the molecules. Of the ten examples of non-equivalence, seven were fully analysed as described above and the results of the iterative calculations are shown in Table 1. The Figure provides a typical example of the close similarity between observed and calculated spectra. In a number of cases (compounds 1, 2, 4, and 7) spectra



90 MHz ^1H N.m.r. spectrum of the OCH_2 protons of $(EtO)_2$-P(S)Me in benzene at 28 °C: (a) calculated spectrum; (b) experimental spectrum

were recorded at temperatures up to 140 °C and the results of these variable temperature studies are presented in Table 2. The effects of solvent changes on the spectra of *OO*-diethyl methylphosphonothionate and *OS*-diethyl methylphosphonothionothiolate (compounds 1 and 7 in Table 1) are recorded in Table 3.

The data of Table 1 reveal that the chemical shift differences (Δ) between the methylene protons vary from 0.067 (6 Hz at 90 MHz) to 0.192 p.p.m. (17.3 Hz at 90 MHz) in $CDCl_3$ but there is no obvious correlation between Δ and the degree of asymmetry at phosphorus. It should be noted however, that in the two cases containing SEt groups in which the *S*-methylene protons were potentially anisochronous (compounds 3 and 7) no such non-equivalence was observed. In broad terms the data of Tables 2 and 3 show that variation in temperature and solvent have no significant effect on coupling constants (J_{AB}, J_{AX}, J_{BX}, J_{AC}, and J_{BC}) but do have significant effects on Δ.

It is then instructive to compare the types of phosphorus ester which reveal non-equivalent methylene

* Program available from the Nicolet Instrument Corporation, 5225, Verona Road, Madison, Wisconsin.

[11] C. D. Hall, *J. Chem. Soc.* (*B*), 1968, 708.
[12] R. L. Dyer, P. G. Le Gras, P. J. Clifford, and C. D. Hall, *J.C.S. Perkin II*, 1973, 2084.
[13] R. L. Dyer, and C. D. Hall, *Chem. and Ind.*, 1973, 1109.
[14] A. A. Bothner-By and S. M. Castellano in 'Computer Programmes for Chemistry,' ed. D. F. Detar, Benjamin, New York and Amsterdam 1968, vol. 1, p. 10.

TABLE 1

^{1}H N.m.r. parameters at 90 MHz for the *O*-methylene protons of the ethyl esters of phosphorus acids [a-c]

$$\geq P\text{-}O\text{-}CH_2\text{-}CH_3$$
(X) (A,B) (C)

Compound	δ_A (±0.003)	δ_B (±0.003)	$\Delta(\delta_B - \delta_A)$/ Hz	J_{AB} (±0.3)/ Hz	J_{AX} (±0.4)/ Hz	J_{BX} (±0.4) Hz	J_{AC} (±0.3)/ Hz	J_{BC} (±0.3)/ Hz
1 $(EtO)_2P(S)Me$	5.851	5.944	8.4 ± 0.4	−10.4	10.5	9.7	7.2	6.9
2 (EtO)(MeS)P(O)Me	5.844	5.924	7.2 ± 0.4	−10.4	8.7	10.1	7.0	7.0
3 (EtO)(EtS)P(O)Me *	5.910	6.102	17.3 ± 0.5	−9.9	10.2	9.9	6.9	6.9
4 $(EtO)_2P(S)SEt$	5.807	5.874	6.1 ± 0.3	−10.3	10.0	9.7	7.2	7.0
5 $(EtO)_2P(S)$S-1-methylheptyl	5.807	5.887	7.2 ± 0.3	−10.2	9.7	9.4	7.1	7.3
6 (EtO)(MeS)P(S)Me	5.829	6.024	17.3 ± 0.4	−9.7	9.8	9.0	7.0	7.0
7 (EtO)(EtS)P(S)Me *	5.833	6.026	17.3 ± 0.4	−10.1	10.2	9.9	7.0	7.1

[a] All data in Hz, except for δ_A and δ_B which are chemical shifts (in p.p.m.) relative to Me_4Si as internal standard. [b] Solvent, $CDCl_3$. [c] In view of the underestimate of errors alleged to be associated with LAOCN 3 the quoted errors are the (computed errors) × 5.

* SCH_2 protons show no non-equivalence.

TABLE 2

Effect of temperature on the 90 MHz n.m.r. spectra of the *O*-methylene protons of ethyl esters of phosphorus acids [a]

Compound	Solvent	T/K	Δ/Hz	J_{AB} [b]/Hz	J_{AX} [c]/Hz	J_{BX} [c]/Hz	J_{AC} [b]/Hz	J_{BC} [b]/Hz
$(EtO)_2P(S)Me$	TCE †	300	9.0 ± 0.4	−10.5	11.3	10.1	7.2	7.3
	TCE †	413	7.0 ± 0.4	−10.6	11.7	10.2	7.2	7.2
$(EtO)_2P(S)Me$	DMSO	297	6.3 ± 0.4	−10.2	11.2	9.4	7.1	7.0
	DMSO	318	5.6 ± 0.4	−9.9	11.2	9.3	7.0	7.0
	DMSO	337	5.2 ± 0.4	−10.0	11.3 ± 0.4	9.4	7.1	7.0
	DMSO	357	4.9 ± 0.4	−10.1	11.6 ± 0.5	9.4 ± 0.5	7.1 ± 0.3	6.9 ± 0.3
	DMSO	377	4.7 ± 0.4	−10.1	11.9 ± 0.5	9.3 ± 0.5	7.1 ± 0.3	6.9 ± 0.3
	DMSO	397	4.5 ± 0.6	−10.2	11.9 ± 0.6	9.4 ± 0.6	7.1 ± 0.3	6.9 ± 0.3
	DMSO	417	4.3 ± 0.6	−10.1	12.1 ± 0.6	9.3 ± 0.6	7.2 ± 0.3	6.8 ± 0.3
(EtO)(MeS)P(O)Me	$CDCl_3$	310	7.2 ± 0.4	−10.4	8.7 ± 0.4	10.1 ± 0.4	7.0	7.0 ± 0.3
	$CDCl_3$	328	7.5 ± 0.4	−10.3	9.0	9.9	7.1	7.0
	TCE †	310	7.5 ± 0.4	−10.7 ± 0.3	9.2 ± 0.5	10.1 ± 0.5	7.0 ± 0.3	7.3 ± 0.3
	TCE †	413	7.6 ± 0.2	−10.6	9.2	10.2	7.2	7.2
(EtO)(EtS)P(S)Me	DMSO	297	13.5 ± 0.4	−10.2	10.3	10.0	7.0	7.0
	DMSO	318	11.5 ± 0.4	−10.4	11.1	10.1	7.1	7.0
	DMSO	338	11.0 ± 0.4	−10.5	11.1	10.3	7.0	7.1
	DMSO	357	10.0 ± 0.4	−10.2	11.4	10.5	7.0	7.2
	DMSO	377	10.1 ± 0.4	−10.5	11.4	10.5	7.0	7.1
	DMSO	397	9.7 ± 0.4	−10.4	11.2	10.4	7.1	7.3
	DMSO	417	9.7 ± 0.4	−10.0	11.2	10.5	7.2	7.2
$(EtO)_2P(S)SEt$	$CDCl_3$	310	6.1 ± 0.4	−10.3	10.0	9.7 ± 0.4	7.2	7.0
	$CDCl_3$	328	4.3 ± 1.0	−10.7 ± 0.4	10.3 ± 0.9	10.1 ± 0.9	7.3 ± 0.7	6.8 ± 0.7
	TCE †	310	5.9 ± 0.4	−10.7	10.5 ± 0.5	10.6 ± 0.4	7.3 ± 0.3	7.5 ± 0.3
	TCE †	413	*d*					

[a] As in Table 1 errors are 5 × (computed errors). [b] Errors (±0.2 Hz) unless otherwise indicated. Errors (±0.3 Hz) unless otherwise indicated. [d] Δ is very small; spectrum approximates a doublet of quartets.

† TCE = 1,1,2,2-Tetrachloroethane.

TABLE 3

90 MHz N.m.r. spectra of the *O*-methylene protons of ethyl esters of phosphorus acids at ambient temperature [a]

Solvent	Δ/Hz (±0.3)	J_{AB} (±0.3)/Hz	J_{AX} (±0.4)/Hz	J_{BX} (±0.4)/Hz	J_{AC} (±0.2)/Hz	J_{BC} (±0.2)/Hz
(i) $(EtO)_2P(S)Me$						
C_6D_6	10.0	−10.2	11.0	9.7	7.2	7.0
CCl_4	9.1	−10.2	11.2	9.8	7.1	7.0
$CDCl_3$	8.4	−10.4	10.5	9.7	7.2	6.9
$(CD_3)_2CO$	7.2	−10.2	11.2	9.5	7.0	7.0
CD_3CN	6.6	−10.2	10.9	9.2	6.9	7.0
DMSO	6.3	−10.2	11.2	9.4	7.1	7.0
(ii) (EtO)(EtS)P((S)Me						
C_6D_6	23.4	−9.7	10.9	9.8	7.2	7.0
$CDCl_3$	18.4	−10.1	10.2	9.9	7.0	7.1
$(CD_3)_2CO$	13.9	−10.3	10.8	10.1	6.8	7.2
CD_3CN	13.3	−10.0	10.7	9.8	7.1	7.0
DMSO	13.5	−10.2	10.3	10.0	7.0	7.0

[a] Errors 5 × (computed errors) and values of Δ and J rounded to first decimal place.

protons with those which, although containing a chiral or prochiral phosphorus atom, do not display the phenomenon. To this end a large number of results on phosphorus and thiophosphorus esters derived from this and earlier work are collected in Table 4.

TABLE 4

Summary of the n.m.r. spectra of the *O*-ethyl or *O*-isopropyl (methyl groups) regions of organophosphorus esters with the potential to display non-equivalence

Compound	Non-equivalence in OCH_2, or $OCH(CH_3)_2$ protons, Δ (p.p.m.)	Reference
1 Phosphates, phosphoramidates, phosphorochloridates, and phosphonates		
$(EtO)_2P(O)O$-1-methylheptyl		This work
$(EtO)_2P(O)OPh$		7
$(EtO)_2P(O)NHEt$		7
$(EtO)_2P(O)Cl$	0.032 [a]	7
$(EtO)_2P(O)H$		7
$(EtO)_2P(O)R^1$ *		This work
$(EtO)(MeO)P(O)Et$		This work
$(EtO)_2P(O)CH=CH_2$		7
$(EtO)_2P(O)CCl=CH_2$	0.033 [a]	7
$(Pr^iO)(p\text{-}NO_2C_6H_4O)P(O)Me$	0.070 [a]	8
$(ArCOCH_2O)(p\text{-}NO_2C_6H_4O)P(O)Me$	0.160—0.186	9
$(EtO)(PhO)P(O)Et$		
2 Monothio-esters		
(a) Thiolo-esters		
$(EtO)_2P(O)SEt$		This work
$(Pr^nO)_2P(O)SEt$		This work
$(EtO)_2P(O)S$-1-methylheptyl		This work
$(EtO)(MeS)P(O)Me$	0.080 [b]	This work
$(EtO)(EtS)P(O)Me$	0.192 [b]	This work
$(EtO)(EtS)P(O)Pr^n$	†	This work
$(Pr^iO)(CH_3SCH_2S)P(O)Me$	0.108 (SCH_2); 0.063 (CH_3) [b]	10
(b) Thiono-esters		
$(EtO)_2P(S)O$-1-methylheptyl		This work
$(EtO)_2P(S)Cl$	0.042 [a]	7
$(EtO)_2P(S)Me$	0.093 [b]	This work
$(EtO)(MeO)P(S)Me$	†	This work
3 Dithio-esters		
$(EtO)_2P(S)(SEt)$ ‡	0.068 [b]	This work
$(EtO)_2P(S)S$-1-methylheptyl	0.080 [b]	This work
$(EtO)(MeS)P(S)Me$	0.191 [b]	This work
$(EtO)(EtS)P(S)Me$	0.192 [b]	This work

[a] In CCl_4. [b] In $CDCl_3$.

* R^1 = Me, Et, Pr^n, and Bu^n. † Observable, but not analysed. ‡ Non-equivalence almost disappears on heating to 140 °C.

For the phosphate, phosphoramidate, phosphorochloridate, and phosphonate esters, six distinct types of prochiral phosphorus atoms (XV)—(XX) are represented in Table 4. Of these, the phosphates (XV) and (XVI) and phosphoramidates (XVII) show no non-equivalence and the phosphorus centres are obviously not sufficiently asymmetric to allow the phenomenon to be observed. With the phosphorochloridates (XVIII) the non-equivalence is slight (Δ 2.9 Hz at 90 MHz) but there is no evidence from variable temperature or solvent variation studies to indicate the relative importance of intrinsic non-equivalence *versus* conformational effects. With *O*-alkyl alkylphosphonates (XIX) again the non-equivalence was not detectable but a small value for Δ (0.033 p.p.m.) was recorded with $R^2 = CCl=CH_2$. Since Δ = 0 for $R^2 = CH=CH_2$ it seems likely that the non-equivalence is derived from unequal conformer populations brought about by size of the chlorine atom

(XV) Y, Z = OR^1, OR^2 (R = alkyl)
(XVI) Y = OR, Z = OAr
(XVII) Y = OR, Z = NHR or NR_2
(XVIII) Y = OR, Z = Cl
(XIX) Y = R^1, Z = OR^2 (R^2 = H, alkyl, or alkenyl)
(XX) Y = R, Z = OAr
(XXI) Y = SR, Z = OR
(XXII) Y = SR, Z = R

(XXIII) Y, Z = OR^1, OR^2
(XXIV) Y = OR, Z = Cl
(XXV) Y = OR, Z = R
(XXVI) Y = OR, Z = SR
(XXVII) Y = R, Z = SR

on the carbon α to phosphorus. With *O*-aryl alkylphosphonates (XX) a different story emerges. Frankel *et al.*[9] were able to demonstrate that at least up to 58 °C (in $CDCl_3$) the non-equivalence of methylene protons was maintained and this suggests that intrinsic non-equivalence plays a substantial role for these molecules. In all the cases studied by Frankel however, increase in the dielectric constant of the medium reduced the value of Δ until in DMSO, non-equivalence was unobservable. This is reminiscent of the case for (EtO)(MeS)P(O)Me which shows only a slight variation of Δ with temperature (up to 140 °C, Table 2) but no non-equivalence in DMSO. It seems most unlikely that a change to DMSO would somehow equate conformer populations when a rise in temperature to 140 °C has virtually no effect whatsoever and one is drawn to the conclusion that solvation can substantially reduce the overall asymmetry at phosphorus. Presumably, the polarity of the phosphoryl oxygen bond (P=O ⟷ $\overset{+}{P}$–$\overset{-}{O}$) contributes substantially to the anisotropy of the sensor protons and solvation by dipole–dipole attraction between the phosphoryl group and a solvent like DMSO may be sufficient virtually to eliminate the asymmetric environment. It should be noted however, that if this explanation is correct, it must also apply to non-equivalence arising from different conformer populations since even if the conformers remained unequally populated, there would be no observable non-equivalence when each conformer was influenced by a virtually symmetric environment. Such an explanation therefore appears to negate the solvent criterion for intrinsic non-equivalence. As pointed out earlier however, if Δ is not removed by a substantial increase in temperature, it is hardly likely that a change in solvent would be capable of equating conformer populations to the extent of removing Δ. It seems therefore, that solvent effects by themselves, are not sufficient to determine the origin of non-equivalence and hence the major criterion is the effect of a substantial increase in temperature.

Of the available monothio esters, the thiolo-esters have two types of asymmetric phosphorus [(XXI) and

(XXII)] and the thiono-esters three types [(XXIII)—(XXV)].

The phosphorothiolo- (XXI) and phosphorothiono- (XXIII) esters show no non-equivalence and even diethyl phosphorothionochloridate (XXIV; R = Et) shows only a small value for Δ for which variable temperature and solvent studies are not available. The phosphonothiolate esters (XXII) discussed above do show non-equivalence which is virtually unaffected by a rise in temperature to 140 °C but is eliminated in DMSO. The phosphonothiono-esters (XXV) however, show a 30% decrease in Δ (from ambient to 140 °C) and a similar % decrease in Δ from benzene to DMSO (Tables 2 and 3). Thus neither solvation or temperature changes are able to remove the non-equivalence and it seems reasonable to conclude that a substantial proportion of Δ is due to the intrinsic effect. Since the thiophosphoryl group (P=S) would be less efficiently solvated than the phosphoryl group (P=O) the solvent effect would be expected to be less pronounced for the thiono- than for the thiolo-esters.

Two types of asymmetric phosphorus centre are available for the dithio-esters and these are depicted by (XXVI) (phosphoro-esters) and (XXVII) (phosphono-esters). As expected, both sets of esters show non-equivalence but with the phosphoro-series (XXVI) the effect virtually disappears on raising the temperature to 140 °C, a clear indication of a large contribution from unequal conformer populations. With the phosphono-esters (XXVII) however, non-equivalence is maintained, though somewhat reduced, at 140 °C and in DMSO. Once again, solvation is unable to destroy the asymmetric environment provided by a combination of the alkyl, thioalkyl, and thiophosphoryl groups and the Δ_i term remains substantial under all conditions.

On the basis of the empirical data it is possible to make the following predictions about non-equivalence in organophosphorus esters. (1) Phosphate and phosphoramidate esters will *not* show the effect but phosphorochloridates may show slight non-equivalence. (2) Dialkyl phosphites and *OO*-dialkyl alkylphosphonates will *not* show non-equivalence but certain *OO*-dialkyl alkenyl phosphonates (and by inference, alkynylphosphonates) may show small values of Δ which are probably due to conformational rather than intrinsic effects. (3) *O*-alkyl *O*-aryl alkylphosphonates will show substantial values of Δ which are due to a combination of intrinsic anisochronism and conformational effects. (4) *OO*-dialkyl alkylphosphorothiolates and trialkylphosphorothionates are not sufficiently asymmetric at phosphorus to afford measurable non-equivalence. (5) Phosphonothiolate and phosphonothionate esters will show non-equivalence which is due largely to intrinsic anisochronism; the non-equivalence will therefore be maintained at high temperatures but whereas the thionate esters will retain non-equivalence through a wide range of solvent polarity, the non-equivalence of thiolate esters may be negligible in dipolar, aprotic solvents. (6) Both *OO*-dialkyl alkylphosphorothiolothionates and *OS*-dialkyl alkylphosphonothiolothionates will show non-equivalence but conformational effects may be largely responsible for non-equivalence in the phosphoro-series whereas intrinsic non-equivalence provides the major contribution in the phosphono-series; hence, the dithiophosphoric esters will show a much lower degree of non-equivalence at high temperature.

These predictions are tentative and may well need to be modified in the light of subsequent data. Nevertheless, they should be useful as a guide to anticipating the occurrence of non-equivalence and hence may help to solve problems of structure determination in novel organophosphorus esters.

We thank PCMU (Harwell), Dr. D. Z. Denney (Rutgers University, New Jersey), and Dr. J. M. Briggs (King's College) for the provision of 100 and 90 MHz n.m.r. spectra and for helpful discussion.

[5/2358 *Received*, 4*th December*, 1975]