The Chemistry of Heteroarylphosphorus Compounds. Part 7.[1] Heteroaryl-, Heteroarylmethyl-, and Substituted Aryl-phosphonate Esters. Electronic Effects of Substituents at Phosphorus on the Rates of Alkaline Hydrolysis, and Phosphorus-31 Nuclear Magnetic Resonance and Phosphoryl Infrared Stretching Frequency Studies

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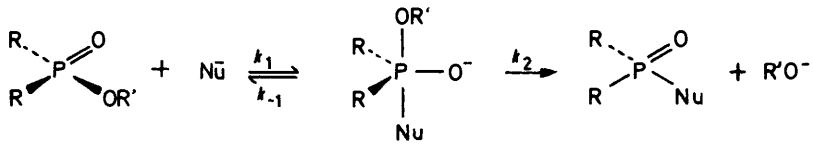
The rates of alkaline hydrolysis of a series of ethyl and phenyl esters of heteroarylphosphonic acids derived from furan, thiophen, and 1-methylpyrrole have been determined, and the variation of the rate of hydrolysis with the nature of the heterocycle is discussed. It is concluded that the heteroaryl substituent interacts with the phosphorus atom mainly by a σ-electron-withdrawing effect. Mesomeric $p_\pi \longrightarrow d_\pi$ electron donation from the ring systems to phosphorus seems to be of little importance. ^{31}P N.m.r. and phosphoryl i.r. stretching frequencies are also presented and discussed in relation to the electronic effects of the heteroaryl substituents.

In addition a study has been made of the rates of alkaline hydrolysis of a related series of heteroarylmethylphosphonate esters, and also of a series of substituted phenylphosphonates. In the latter case, a good correlation between the rate data and the Hammett σ constants of the aromatic substituents has been obtained. For both series of esters ^{31}P n.m.r. data are presented and discussed.

THE mechanism of nucleophilic displacement at phosphorus in phosphyl compounds has received considerable attention. Such displacement reactions at a tetrahedral phosphorus atom (as in the alkaline hydrolysis of phosphate, phosphonate, and phosphinate esters) are predominantly bimolecular, being first-order in nucleophile and first-order in phosphyl compound, and in general are believed to proceed by a two-step mechanism involving a trigonal bipyramidal pentacovalent intermediate phosphorane [2] (see Scheme). The observed second-order rate constant can be expressed as in equation (i). Such phosphorane intermediates are short-

$$k_{obs} = k_1/(1 + k_{-1}/k_2) \qquad \text{(i)}$$

lived, having a route for ready decomposition by ejection of either the leaving group OR' or nucleophile Nu^-. Many examples of nucleophilic displacement in phosphyl compounds have been interpreted on the basis of an S_N2P direct displacement process proceeding *via* a high-energy transition state which resembles a phosphorane rather than *via* an actual intermediate.[3] However, some evidence of the involvement of recognisable phosphorane intermediates in such reactions has recently become available,[4,5] and in view of the large number of stable pentacovalent oxyphosphoranes which are known,[6] a discussion of the course of nucleophilic displacement at phosphyl phosphorus in terms of the involvement of unstable pentacovalent intermediates seems reasonable.



SCHEME

Our earlier papers in this series have discussed the effect of heteroaryl *P*-substituents on the rate and course of nucleophilic displacement reactions at phosphorus in the alkaline hydrolysis of phosphonium salts and in the decomposition of phosphonium betaines. We hav ow extended our studies to include nucleophilic dis ce-ments at phosphorus in phosphyl compounds wit one or more heteroaryl *P*-substituents. In this paper, we report the rates of hydrolysis of a series of ethyl and phenyl esters of heteroarylphosphonic acids derived from furan, thiophen, and 1-methylpyrrole. In addition, we report the rates of alkaline hydrolysis of a related series of diethyl heteroarylmethylphosphonates and also of a series of diethyl arylphosphonates. ^{31}P N.m.r. and phosphonyl i.r. stretching frequency data for the esters are also presented and discussed in relation to the rate data.

RESULTS

The kinetics of alkaline hydrolysis of the diethyl and diphenyl esters of 2-furyl-, 2-thienyl-, and 1-methylpyrrol-2-yl-phosphonic acids (1; X = O, S, or NMe, R = Et or Ph) and phenylphosphonic acid (2; X = H) in 50% aqueous dioxan (0.1M in potassium chloride) have been

[1] Part 6, D. W. Allen, B. G. Hutley, and M. T. J. Mellor, *J.C.S. Perkin II*, 1974, 1690.

[2] P. Gillespie, F. Ramirez, I. Ugi, and D. Marquading, *Angew. Chem. Internat. Edn.*, 1973, **12**, 91, and references therein.

[3] See *e.g.* R. F. Hudson, 'Structure and Mechanism in Organophosphorus Chemistry,' Academic Press, New York, 1965; B. J. Walker, 'Organophosphorus Chemistry,' Penguin, 1972; J. Emsley and D. Hall, 'The Chemistry of Phosphorus,' Harper and Row, London, 1976; and references therein.

[4] R. D. Cook, C. E. Diebert, W. Schwarz, P. C. Turley, and P. Haake, *J. Amer. Chem. Soc.*, 1973, **95**, 8088.

[5] M. Gallagher, A. Munoz, G. Gence, and M. Koenig, *J.C.S. Chem. Comm.*, 1976, 321.

[6] S. Trippett, 'Organophosphorus Chemistry,' Chem. Soc. Specialist Periodical Reports, Vols. 1—7, 1969—1976; and references therein.

studied by a titrimetric procedure. The esters undergo hydrolysis on treatment with 1 mol. equiv. of sodium hydroxide to give the half esters, and a second-order rate law is observed. The rate data are presented in Table 1.

(3; X = O or S) and diethyl benzylphosphonate (4), together with their ^{31}P n.m.r. chemical shifts and phosphoryl i.r. stretching frequencies, are presented in Table 2.

The second-order rate data for the hydrolysis of a series

TABLE 1

Second-order rate constants and activation parameters for the alkaline hydrolysis of heteroarylphosphonate esters [$R^1P(O)(OR^2)_2$] in aqueous dioxan (50% v/v; 0.1M inKCl); phosphoryl infrared stretching frequencies and ^{31}P n.m.r. chemical shifts (in chloroform) of the esters

R^1	R^2	Temp. (°C)	k_{obs} / l mol^{-1} s^{-1}	E_A / kJ mol^{-1}	$\Delta S^{\ddagger}$ / J K^{-1} mol^{-1}	ν_{PO}/cm^{-1}	$\delta(^{31}P)$(p.p.m. relative to 85% H_3PO_4) *
2-Furyl	Et	59.7	$(4.53 \pm 0.08) \times 10^{-3}$	56.4	−121.0	1 261	−3.9
	Et	49.9	$(2.44 \pm 0.02) \times 10^{-3}$				
Phenyl	Et	59.7	$(9.74 \pm 0.39) \times 10^{-4}$	63.6	−112.2	1 252	−16.7
	Et	50.0	$(4.89 \pm 0.07) \times 10^{-4}$				
2-Thienyl	Et	59.7	$(8.88 \pm 0.18) \times 10^{-4}$	54.8	−139.5	1 255	−10.9
	Et	50.0	$(4.90 \pm 0.08) \times 10^{-4}$				
1-Methylpyrrol-2-yl	Et	69.8	$(8.45 \pm 0.02) \times 10^{-5}$	75.5	−103.6	1 250	−9.4
	Et	59.8	$(3.81 \pm 0.01) \times 10^{-5}$				
2-Furyl	Ph	39.8	$(10.50 \pm 0.06) \times 10^{-2}$	28.6	−172.4	1 265	+3.0
	Ph	29.7	$(7.28 \pm 0.05) \times 10^{-2}$				
Phenyl	Ph	39.8	$(11.06 \pm 0.04) \times 10^{-2}$	39.9	−135.6	1 265	−10.3
	Ph	29.7	$(6.61 \pm 0.19) \times 10^{-2}$				
2-Thienyl	Ph	39.8	$(6.42 \pm 0.12) \times 10^{-2}$	34.8	−156.3	1 268	−4.1
	Ph	29.7	$(4.11 \pm 0.08) \times 10^{-2}$				
1-Methylpyrrol-2-yl	Ph	39.8	$(4.71 \pm 0.19) \times 10^{-3}$	55.6	−112.1	1 265	−2.5
	Ph	29.7	$(2.27 \pm 0.01) \times 10^{-3}$				

* Shifts upfield of 85% H_3PO_4 (δ = 0 p.p.m.) are denoted as positive.

TABLE 2

Second-order rate constants and activation parameters for the alkaline hydrolysis of heteroarylmethylphosphonate esters [$R^1P(O)(OR^2)_2$] in aqueous dioxan (50% v/v; 0.1M in KCl); phosphoryl infrared stretching frequencies, and ^{31}P n.m.r. chemical shifts (in chloroform) of the esters

R^1	R^2	Temp. (°C)	k_{obs} / l mol^{-1} s^{-1}	E_A / kJ mol^{-1}	$\Delta S^{\ddagger}$ / J K^{-1} mol^{-1}	ν_{PO} / cm^{-1}	$\delta(^{31}P)$ (p.p.m. relative to 85% H_3PO)
Benzyl	Et	60	$(10.83 \pm 0.27) \times 10^{-5}$	63.3	−131.3	1 250	−22.8
	Et	50	$(5.34 \pm 0.02) \times 10^{-5}$				
2-Thenyl	Et	60	$(3.71 \pm 0.04) \times 10^{-4}$	64.7	−117.0	1 250	−21.0
	Et	50	$(1.80 \pm 0.01) \times 10^{-4}$				
Furfuryl	Et	60	$(6.78 \pm 0.03) \times 10^{-4}$	65.7	−109.2	1 250	−19.8
	Et	50	$(3.27 \pm 0.01) \times 10^{-4}$				

^{31}P N.m.r. chemical shifts and phosphoryl i.r. stretching frequency data for the above phosphonate esters are also presented in Table 1.

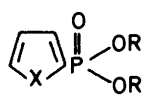
TABLE 3

Second-order rate constants for the alkaline hydrolysis of substituted phenylphosphonate esters in aqueous dioxan (50% v/v 0.1M in KCl) at 59.7 °C; ^{31}P n.m.r. chemical shifts of the esters in chloroform

	$k_{obs.}$ / l mol^{-1} s^{-1}	$\delta(^{31}P)$(p.p.m. relative to 85% H_3PO_4)
Diethyl (*m*-chlorophenyl)-phosphonate	$(37.17 \pm 0.48) \times 10^{-4}$	−14.1
Diethyl (*p*-bromophenyl)-phosphonate	$(25.33 \pm 0.33) \times 10^{-4}$	−15.5
Diethyl phenylphosphonate	$(9.74 \pm 0.39) \times 10^{-4}$	−16.7
Diethyl (*m*-tolyl)-phosphonate	$(5.50 \pm 0.16) \times 10^{-4}$	−17.0
Diethyl (*p*-methoxy-phenyl)phosphonate	$(2.56 \pm 0.08) \times 10^{-4}$	−17.3
Diethyl (*m*-formyl-phenyl)phosphonate	Not studied	−14.2

The second-order rate data for the alkaline hydrolysis of the corresponding diethyl heteroarylmethylphosphonates

of diethyl arylphosphonates (2; X = H, *m*-Cl, *p*-Br, *m*-Me, or *p*-MeO, R = Et), together with their ^{31}P chemical shifts, are presented in Table 3.



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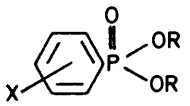

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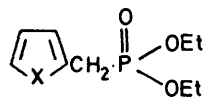

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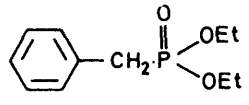

(4)

DISCUSSION

In order to facilitate discussion of the kinetic data, we have attempted to gain some indication of the electronic effects of the heteroaryl substituents in the series of phosphonate esters by studying (i) the variation in the phosphoryl i.r. stretching frequency (ν_{PO}) and (ii) the ^{31}P n.m.r. chemical shifts of the esters.

For both series of heteroarylphosphonate esters (1; X = O, S, or NMe, R = Et or Ph) and the corresponding phenylphosphonate esters, the data in Table 1 shows that ν_{PO} increases in the order 1-methylpyrrol-2-yl ≤ phenyl < 2-thienyl < 2-furyl. On the basis of the work of Bell *et al.*[7] and of Davis,[8] this order is therefore the order of apparent increasing electron-withdrawing ability of the substituent ring systems, in keeping with the order previously indicated.[1] The higher values of ν_{PO} for the phenyl esters is in keeping with the greater electron-withdrawing ability of phenoxy- than of ethoxy-groups. The observed shifts in ν_{PO} in each series are small; for comparison, the phosphonyl stretching frequencies of the diethyl esters of methyl-, chloromethyl-, and dichloromethyl-phosphonic acid have been given[9] as 1 243, 1 271, and 1 281 cm^{-1}, respectively. On the basis of the above i.r. data, there appears little evidence of significant $p_\pi \longrightarrow d_\pi$ conjugation between the ring systems and phosphorus; such interactions would be expected to lead to a decrease in ν_{PO} for the heteroaryl substituents relative to phenyl. It is well known that for $p_\pi \longrightarrow p_\pi$ interactions the above heteroaryl systems are much better electron donors than phenyl.[10]

It was hoped that ^{31}P n.m.r. studies might also give some indication of the relative electron-withdrawing effects of the heteroaryl *P*-substituents. Freedman *et al.*[11,12] have investigated the effect of various substituents on the phenyl ring on the ^{31}P n.m.r. chemical shifts of a series of *meta*- and *para*-substituted phenylphosphonic acids and related esters, and obtained a correlation of the chemical shift with the corresponding Hammett σ substituent constants,[13] and also with the Taft[14] σ_I or σ_R components of the Hammett σ constants. In the case of *ortho*-substituted phenylphosphonic acids, a similar correlation was observed between the ^{31}P chemical shifts and substituent constants derived by Taft[14] from the esterification and hydrolysis of *ortho*-substituted benzoic acids and their esters. In each case, the correlation was opposite to that expected on the basis of the electron-withdrawing ability of the substituents. Thus the more electron-donating substituents *decrease* the shielding of the phosphorus nucleus, and *vice versa*. This effect was predicted on the basis of theoretical considerations by Van Wazer and Letcher.[15]

The ^{31}P chemical shifts (solvent chloroform) of the arylphosphonate esters prepared in the present study (2; X = *p*-MeO, *m*-CHO, *p*-Br, *m*-Cl, or *m*-Me, R = Et) are presented in Table 3. In agreement with the results obtained by Freedman *et al.*[11,12] the data indicate the shift of the ^{31}P resonance to be in a direction opposite to that expected from the electronegativity of the substituent. In addition a linear relationship between the ^{31}P chemical shifts and the corresponding Hammett σ substituent constants[13] is indicated (correlation coefficient 0.96). The largest deviation from the correlation is obtained for the *p*-methoxyphenylphosphonate (2; X = *p*-OMe). The ^{31}P chemical shift is more positive than is predicted by the σ_p constant and therefore the result possibly indicates that the σ-inductive electron-withdrawing effect of the *p*-methoxy-group is more important in comparison with the mesomeric electron donation in the determination of ^{31}P chemical shift. Evidence in favour of this proposal is provided by the improved correlation coefficient of 0.98 which is obtained when the σ^0 constants for the substituents are plotted against the ^{31}P chemical shifts.

Consideration of the ^{31}P chemical shifts of the above heteroarylphosphonate esters (1; R = Et or Ph) indicates that the phosphorus in the 2-furyl esters is more shielded than that in the 2-thienyl and phenyl esters, in keeping with the earlier indication from i.r. spectroscopy that the 2-furyl group is more electron-withdrawing than the 2-thienyl and phenyl groups. It is apparent, however, that the ^{31}P shift for the 1-methylpyrrol-2-yl ester is anomalously high to be consistent with an interpretation in terms of the apparent electron-withdrawing character of the pyrrolyl ring system as indicated by the i.r. study. Clearly, factors other than simple inductive effects are also important in influencing ^{31}P shifts in this series of related compounds. In addition to inductive and resonance ($p_\pi \longrightarrow d_\pi$) effects, shielding is doubtless influenced by diamagnetic anisotropy effects, which would be expected to be different for each heterocyclic system. The difficulties in interpreting chemical shift data for spin nuclei other than hydrogen have been highlighted in a recent paper.[16]

There is a general increase in the shielding of the phosphorus nuclei of the diphenyl phosphonate esters as compared with the corresponding diethyl phosphonate analogues, in keeping with the greater electron-withdrawing ability of phenoxy- relative to ethoxy-groups.

Kinetic Data.—In the heteroarylmethylphosphonate esters (3) and the related benzylphosphonate (4), there can be no possibility of $p_\pi \longrightarrow d_\pi$ overlap between the (hetero)aromatic ring system and phosphorus. The relative rates of hydrolysis are in the order furfuryl (6) > 2-thienyl (3) > benzyl (1), and reflect the relative electron-withdrawing abilities of the substituent ring systems. Electron-withdrawing groups attached to phosphorus increase the magnitude of the observed rate constant for the reaction. Such groups favour phosphorane formation [*i.e.* an increase in k_1 in equation (i)] but this effect will be partly compensated by the decrease in k_2. However k_{-1} also decreases; thus k_{-1}/k_2 [equation (i)] will not change significantly in comparison to k_1, and therefore the latter will be dominant. Large

[7] J. V. Bell, J. Heisler, H. Tannenbaum, and J. Goldenson, *J. Amer. Chem. Soc.*, 1954, **76**, 5185.
[8] N. A. Davis, *J. Org. Chem.*, 1967, **32**, 1161.
[9] G. Aksnes and J. Songstad, *Acta Chem. Scand.*, 1965, **19**, 893.
[10] M. H. Palmer, 'The Structure and Reactions of Heterocyclic Compounds,' Arnold, London, 1967.
[11] C. C. Mitsch, L. D. Freedman, and C. G. Moreland, *J. Magnetic Resonance*, 1970, **3**, 446.
[12] C. C. Mitsch, L. D. Freedman, and C. G. Moreland, *J. Magnetic Resonance*, 1971, **5**, 140.
[13] H. H. Jaffe, *Chem. Rev.*, 1953, **53**, 191.
[14] R. W. Taft, jun., *J. Amer. Chem. Soc.*, 1952, **74**, 2729.
[15] J. R. Van Wazer and J. H. Letcher, *Topics Phosphorus Chem.*, 1967, **5**, 179.
[16] H. J. Kroth, H. Schumann, H. G. Kuivila, C. D. Schaeffer, jun., and J. J. Zuckerman, *J. Amer. Chem. Soc.*, 1975, **97**, 1754.

rate differences between individual members of a given series would not be expected or found in the alkaline hydrolysis of phosphorus(v) esters in general. For example the relative rate constants for the alkaline hydrolysis [9] of various phosphonate esters $RP(O)(OEt)_2$ are in the order R = Et (0.13) < Me (1.0) < $ClCH_2$ (15.6) < Cl_2CH (108), whereas the relative rate constants for hydrolysis of the corresponding carboxylic acid esters RCO_2Et (in which bond formation is of paramount importance) are estimated as R = Et (0.9) < Me (1.0) < $ClCH_2$ (258) < Cl_2CH (5 000). In addition, steric effects are more important in the alkaline hydrolysis of phosphorus(v) esters (which have a basically tetrahedral structure about phosphorus) than for carboxylic acid esters (in which nucleophilic attack at a trigonal planar carbon occurs). In general therefore activation entropies for the hydrolysis of phosphonate esters are more negative than for the corresponding carboxylic acid esters.[9]

The relative rates of hydrolysis of the heteroarylphosphonate esters (1; R = Et) and diethyl phenylphosphonate (2; X = H, R = Et) are in the order 2-furyl (120) > phenyl ≈ 2-thienyl (25) > 1-methylpyrrol-2-yl (1). The 2-furylphosphonate ester undergoes hydrolysis *ca.* 7 times faster than the furfurylphosphonate (3; X = O), whereas the 2-thienylphosphonate undergoes hydrolysis only twice as fast as the 2-thenyl analogue (3; X = S). In the case of the corresponding phenyl esters (1; R = Ph) and (2; X = H, R = Ph), the relative rates are in the order 2-furyl ≈ phenyl (25) > 2-thienyl (16) > 1-methylpyrrol-2-yl (1). The reduction in relative rates and the change in ranking order are significant. Whereas in the case of the ethyl esters (1; R = Et) the 2-furylphosphonate is hydrolysed *ca.* 5 times faster than the 2-thienyl analogue, in the phenyl ester series (1; R = Ph) there is only a 1.5 : 1 difference in rate between the 2-furyl- and 2-thienyl-phosphonates. A marked levelling effect appears to be operating.

The increased rate of hydrolysis of the diphenyl esters as compared with the diethyl esters can be explained readily in terms of equation (i). The greater electron-withdrawing ability of phenoxy relative to ethoxy should result in an increase in k_1 for the diphenyl esters, but more particularly, since PhO^- is a much better leaving group than EtO^-, there should be a more considerable increase in k_2 for the former than for the latter.

In the diethyl ester series, electron-withdrawing groups should increase the rate constant k_1 of equation (i) by relatively stabilising the electron-rich transition state for phosphorane formation. The rate constants k_{-1} and k_2 should be decreased by electron-withdrawing substituents because their effect on the stability of the phosphorane with its full negative charge should be greater than their effect on the stability of the transition states (having a partial negative charge) leading back to reactants and forward to products. Because of the similarity of the two potential leaving groups (OH^- and OEt^-) in the decomposition of the phosphorane, the effects of substituents on k_{-1} and k_2 will be partly compensatory, and therefore k_1 will be the dominant factor in the rate equation. Thus one would expect the rate of hydrolysis of the ethyl esters to be in the order 2-furyl > 2-thienyl > phenyl > 1-methylpyrrol-2-yl. Obviously, the relative values of k_{-1} and k_2 for the thienyl- and phenyl-phosphonic acid esters are such that the observed rate constants are of the same order.

In the case of the diphenyl esters, electron-withdrawing *P*-substituents will also tend to stabilise the intermediate anionic phosphorane and to a lesser extent the transition states flanking it on the reaction co-ordinate. The stabilisation of the transition state for loss of OH^- from the intermediate will be more marked than that for loss of PhO^- because in the latter case the negative charge is already extensively delocalised over the phenyl ring. Consequently, there will be a levelling effect on the energies of the transition states for loss of PhO^- which will have the effect of increasing k_{-1}/k_2 relative to that for a less electron-withdrawing substituent and hence decreasing the observed rate constant. Thus the relative effects of *P*-substituents will be more difficult to predict; *e.g.* for the 2-furyl substituent relative to phenyl, both k_1 and k_{-1}/k_2 should be increased, and it will be the relative magnitudes of these changes which will control the observed order.

In both the diethyl and diphenyl series of esters, the 1-methylpyrrol-2-ylphosphonates undergo hydrolysis significantly more slowly than the 2-furyl, 2-thienyl, or phenyl analogues. This is attributable to the reduced electron-withdrawing effect of the 1-methylpyrrol-2-yl substituent which will directly affect k_1 and hence the overall rate of hydrolysis. In addition, a possible steric effect by the *N*-methyl group should also be borne in mind. We have previously noted a small steric effect in the quaternisation of phosphines bearing 1-methylpyrrol-2-yl substituents as compared with the parent pyrrol-2-yl system.[17] In the above phosphonate ester study, we were unable to investigate the rates of alkaline hydrolysis of the pyrrol-2-yl esters (1; X = NH) since these compounds undergo cleavage of the ring C–P bond on treatment with alkali.[18]

The difference in electronic character between the 2-furyl and 2-thienyl substituents and the 1-methylpyrrol-2-yl substituent is of considerable interest. The differences cannot simply be attributable to the different electronegativities of the heteroatoms since both oxygen and nitrogen have similar electronegativities, and both are more electronegative than sulphur. It is of interest that the direction of the dipole moment in pyrrole (and 1-methylpyrrole) is from the heteroatom to the ring system whereas the opposite is true for furan and thiophen.[19,20] In discussing the relative inductive effects of

[17] D. W. Allen, J. R. Charlton, and B. G. Hutley, *Phosphorus*, 1976, **6**, 191.
[18] C. E. Griffin, R. P. Peller, and J. A. Peters, *J. Org. Chem.*, 1965, **30**, 91.
[19] G. Marino, *J. Heterocyclic Chem.*, 1972, **9**, 817.
[20] T. J. Barton, R. W. Roth, and J. G. Verkade, *J. Amer. Chem. Soc.*, 1972, **94**, 8854.

the above heteroaryl substituents, one should bear in mind that what is being considered is the overall inductive effect of the ring system, which is related to the direction of the dipole moment in the parent heterocycle and includes a contribution from both σ and π electron systems. The 1-methylpyrrol-2-yl substituent appears to be a weaker electron-withdrawing system than 2-furyl or 2-thienyl because of a significant contribution to the overall inductive effect by electron donation from the nitrogen atom to the π-system of the ring.

A Hammett plot of the rate data for the alkaline hydrolysis of the substituted phenylphosphonate esters (2; X = *p*-MeO, *p*-Br, *m*-Cl, *m*-Me, or H, R = Et) reveals that the rate of hydrolysis is increased by electron-withdrawing substituents, and this is reflected in a reaction constant of 1.8 when $\log_{10}(k/k_0)$ values are plotted against the appropriate σ constant; a correlation coefficient of 0.99 is obtained. Of particular note is the excellent fit of data for the *p*-methoxy-compound, indicating the possible importance of resonance interactions on the hydrolysis reaction. Inherent in the Hammett σ_p constant for the methoxy-substituent is a small contribution due to direct resonance between the methoxy-group and the reaction site in the defining reaction for σ (*i.e.* the ionisation of benzoic acids). The fit of the data for the *p*-methoxyphenyl ester to the Hammett correlation *might* indicate that a similarly small resonance contribution operates in the hydrolysis of the above phosphonates, but such a resonance contribution would have to be of the $p_\pi \longrightarrow d_\pi$ type. However, many electronic factors govern the magnitude of σ and it is possible and probably more likely that the fit of the *p*-methoxyphenyl compound results from electron delocalisation from the oxygen of the methoxy-group to the π-electron system of the benzene ring, *i.e.* a π-inductive effect. This would have the effect of placing electron density adjacent to the phosphorus atom bearing a partial positive charge and thus stabilising it without the necessity of invoking $p_\pi \longrightarrow d_\pi$ resonance interactions.

EXPERIMENTAL

^{1}H N.m.r. spectra were recorded at 60 MHz with a JEOL spectrometer. ^{31}P N.m.r. data were recorded at 24 MHz with the same instrument, with phosphoric acid (85%) as external standard. I.r. spectra were recorded for liquid films or for potassium bromide discs with a Grubb Parsons Spectromaster double-beam spectrometer (calibration accurate to ±1 cm^{-1}). G.l.c. analyses were carried out with a Pye 104 chromatograph equipped with a 25 ft column of 10% silicone oil on Celite, and a flame ionisation detector. Spinning-band distillations were carried out with a Nester-Faust spinning-band column equipped with an 18 in stainless steel band and a partial take-off head. M.p.s were determined with a Kofler hot-stage apparatus.

Preparation of Phosphonate Esters.—Diethyl (2-furyl)-phosphonate (1; X = O, R = Et), (2-thienyl)phosphonate (1; X = S, R = Et), and phenylphosphonate (2; X = H, R = Et) were prepared as described previously.[21]

Diphenyl (2-furyl)phosphonate (1; X = O, R = Ph). 2-Furylmagnesium iodide (0.09 mol) [from 2-iodofuran (18 g, 0.09 mol) and magnesium (2.43 g, 0.1 mol) in ether (80 cm^3)] was added dropwise, with stirring under nitrogen, to a gently refluxing solution of diphenyl phosphorochloridate (18.8 g, 0.07 mol) in ether (100 cm^3). The resulting solution was heated under reflux for 1 h, cooled in ice, and hydrolysed with dilute hydrochloric acid. The organic layer was separated, and the aqueous phase extracted with ether. The combined organic layers were dried (Na_2SO_4) and evaporated. The residue, which solidified, was re-recrystallised from n-hexane to yield white *needles* (5.8 g, 27.6%), m.p. 50° (Found: C, 64.05; H, 4.45. $C_{16}H_{13}O_4P$ requires C, 64.0; H, 4.35%); τ($CDCl_3$) 2.25—2.4 (1 H, m), 2.5—3.0 (11 H, m), and 3.45—3.65 (1 H, m); δ(^{31}P)-($CHCl_3$) + 3.0 p.p.m.

Diphenyl (2-thienyl)phosphonate (1; X = S, R = Ph). 2-Thienylmagnesium bromide (0.1 mol) [from 2-bromothiophen (16.3 g, 0.1 mol) and magnesium (2.43 g, 0.1 mol) in ether (80 cm^3)] was added dropwise, with stirring under nitrogen, to a refluxing solution of diphenyl phosphorochloridate (17.9 g, 0.067 mol) in ether (50 cm^3). The resulting solution was heated under reflux for 3 h, cooled in ice, and hydrolysed with dilute hydrochloric acid. The organic layer was separated, and the aqueous phase extracted with ether. The combined organic layers were dried (Na_2SO_4) and evaporated. The residue, which solidified, was recrystallised from n-hexane to give a white *solid* (15.83 g, 75.4%), m.p. 75° (Found: C, 60.8; H, 4.3. $C_{16}H_{13}O_3PS$ requires C, 60.75; H, 4.1%); τ($CDCl_3$) 2.15—2.45 (2 H, m) and 2.55—3.0 (11 H); δ(^{31}P)($CHCl_3$) — 4.1 p.p.m.

The ester was also prepared by reverse addition of 2-thienyl-lithium to diphenyl phosphorochloridate in ether; however, the yield in this case was only 8% after recrystallisation. Hence the foregoing procedure is to be preferred.

Diethyl (1-methylpyrrol-2-yl)phosphonate (1; X = NMe, R = Et), prepared according to the procedure described by Griffin *et al.*,[18] had b.p. 109—120° at 0.3 mmHg (lit.,[18] 122.5—126° at 3.0 mmHg). Further purification was effected by distillation through a spinning-band column until the product had 99% purity by g.l.c. analysis (Found: C, 49.4; H, 7.35; N, 6.45. Calc. for $C_9H_{16}NO_3P$: C, 49.75; H, 7.35; N, 6.45%); τ($CDCl_3$) 3.2 (2 H, m), 3.9 (1 H, m), 5.7—6.2 (4 H, m), 6.22 (3 H, s), and 8.7 (6 H, t); δ(^{31}P)($CHCl_3$) — 9.45 p.p.m.

Diphenyl (1-methylpyrrol-2-yl)phosphonate (1; X = NMe, R = Ph). A slurry of 1-methylpyrrol-2-yl-lithium (0.1 mol) [from 1-methylpyrrole (10 g, >0.1 mol) and n-butyl-lithium (0.1 mol)] in ether (100 cm^3) was added dropwise, with stirring under nitrogen to a solution of diphenyl phosphorochloridate (26.8 g, 0.1 mol) in ether (100 cm^3). The mixture was maintained at ice-bath temperature during the addition, then heated under reflux for 2 h, cooled in ice, and hydrolysed with ammonium chloride solution (10% w/v; 100 cm^3). The organic layer was separated and the aqueous phase extracted with ether. The combined organic layers were dried ($MgSO_4$) and evaporated. The residue, which solidified, was recrystallised from n-hexane to give a white *solid* (3.4 g, 11%), m.p. 73° (Found: C, 66.1; H, 5.35. $C_{17}H_{16}NO_3P$ requires C, 65.2; H, 5.1%); τ($CDCl_3$) 2.6—3.2 (12 H, m), 3.7—3.9 (1 H, m), and 6.12 (3 H, s); δ(^{31}P)($CHCl_3$) — 2.5 p.p.m.

Diphenyl phenylphosphonate (2; X = H, R = Ph). This was prepared by the reaction of phenylphosphonic

[21] D. W. Allen, B. G. Hutley, and M. T. J. Mellor, *J.C.S. Perkin II*, 1972, 63.

dichloride with phenol (>2 mol. equiv.) in dry benzene, in the presence of pyridine (2 mol. equiv.), according to the general procedure described by Kosolapoff,[22] m.p. 73.5° (from n-hexane) (lit.,[22] 73—74°); τ($CDCl_3$) 2.05—3.38 (15 H, m); δ(^{31}P)($CHCl_3$) − 10.4 p.p.m.

Diethyl furfurylphosphonate (3; X = O). Furfuryl bromide (*ca.* 0.14 mol) in ether (60 cm^3) was added dropwise with constant stirring under nitrogen to a suspension of diethyl sodiophosphonate (0.14 mol) [from diethyl phosphonate (19.3 g, 0.14 mol) and sodium (3.2 g, 0.14 mol)] in ether (100 cm^3). The mixture was stirred for 12 h, heated under reflux for a further 4 h, cooled, filtered, and evaporated. The residue was distilled to give the ester (15.5 g, 51%), b.p. 104—108° at 0.7 mmHg (lit.,[23] 117—120° at 2 mmHg), further purified by distillation through a spinning-band column (Found: C, 49.45; H, 6.65. Calc. for $C_9H_{15}O_4P$: C, 49.55; H, 6.9%); τ($CDCl_3$) 2.64 (1 H, m), 3.70 (2 H, m), 5.7—6.2 (4 H, m), 6.78 (2 H, d, $^2J_{PCH}$ 21 Hz), and 8.73 (6 H, t); δ(^{31}P)($CHCl_3$) — 19.75 p.p.m.

Diethyl (2-thenyl)phosphonate (3; X = S). This was similarly prepared by the addition of 2-thenyl chloride (11.5 g, 0.09 mol) to diethyl sodiophosphonate (0.09 mol) in ether, according to the foregoing procedure. Concentration of the filtrate followed by distillation of the residue gave the ester (9.8 g, 48%), b.p. 138—140° at 2.2 mmHg (lit.,[24] 112° at 0.1 mmHg) (Found: C, 46.3; H, 6.6. Calc. for $C_9H_{15}O_3PS$: C, 46.15; H, 6.4%); τ($CDCl_3$) 2.7—3.18 (3 H, m), 5.68—6.18 (4 H, m), 6.65 (2 H, d, $^2J_{PCH}$ 21 Hz), and 8.7 (6 H, t); δ(^{31}P)($CHCl_3$) − 21 p.p.m.

Diethyl benzylphosphonate (4). This was similarly prepared by addition of benzyl chloride (12.65 g, 0.1 mol) to diethyl sodiophosphonate (0.1 mol) in ether. Concentration of the filtrate followed by distillation of the residue gave the ester (15.1 g, 66.2%), b.p. 124—126° at 0.2 mmHg (lit.,[25] 155° at 14 mmHg) (Found: C, 58.1; H, 7.4. Calc. for $C_{11}H_{17}O_3P$: C, 57.9; H, 7.45%); τ($CDCl_3$) 2.71 (5 H, s), 5.77—6.25 (4 H, m), 6.88 (2 H, d, $^2J_{PCH}$ 21 Hz), and 8.77 (6 H, t); δ(^{31}P)($CHCl_3$) −22.75 p.p.m.

Diethyl (p-bromophenyl)phosphonate (2; X = *p*-Br, R = Et). *p*-Bromophenylmagnesium bromide (0.1 mol) [from *p*-dibromobenzene (23.6 g, 0.1 mol) and magnesium (2.43 g, 0.1 mol) in ether (75 cm^3)] was added dropwise, with constant stirring under nitrogen, to a solution of diethyl phosphorochloridate (17.3 g, 0.1 mol) in ether (100 cm^3) maintained at ice-bath temperature. The resulting solution was heated under reflux for 2 h, cooled, and hydrolysed with dilute hydrochloric acid. The organic layer was separated, dried (Na_2SO_4), and evaporated. The residue was distilled to give the ester (8.3 g, 24%), b.p. 117—120° at 0.4 mmHg (lit.,[22] 126—128° at 0.5 mmHg), further purified by spinning-band fractionation until it had >99% purity by g.l.c.; τ($CDCl_3$) 2.0—2.5 (4 H, m), 5.65—6.15 (4 H, m), and 8.7 (6 H, t); δ(^{31}P)($CHCl_3$) −15.5 p.p.m.

Diethyl (m-chlorophenyl)phosphonate (2; X = m-Cl, R = Et). This was similarly prepared by reverse addition of *m*-chlorophenylmagnesium bromide (0.15 mol) to diethyl phosphorochloridate (25.9 g, 0.15 mol) in ether. The residue was distilled to give the ester (16.8 g, 45%), b.p. 108—110° at 0.3 mmHg (lit.,[26] 100—101° at 0.3 mmHg), further purified by spinning-band fractionation; τ($CDCl_3$) 1.9—2.7 (4 H, m), 5.55—6.05 (4 H, m), and 8.65 (6 H, t); δ(^{31}P)($CHCl_3$) — 14.1 p.p.m.

Diethyl (p-methoxyphenyl)phosphonate (2; X = *p*-OMe, R = Et). This was prepared by the reaction of triethyl phosphite (66.4 g, 0.4 mol) with *p*-bromoanisole (62.3 g, 0.33 mol) in the presence of anhydrous nickel chloride (2.2 g), according to the general procedure described by Tavs;[27] yield 47 g (58.4%), b.p. 129—130° at 0.35 mmHg (lit.,[27] 113—114° at 0.1 mmHg). Further purification was effected by distillation through a spinning-band column, until the product had >99% purity by g.l.c. analysis; τ($CDCl_3$) 2.0—2.45 (2 H, m), 2.85—3.15 (2 H, m), 5.67—6.2 (4 H, m), 6.17 (3 H, s), and 8.7 (6 H, t); δ(^{31}P)($CHCl_3$) — 17.3 p.p.m.

Diethyl (m-tolyl)phosphonate (2; X = *m*-Me, R = Et). A solution of *m*-iodotoluene (17.5 g, 0.08 mol) in triethyl phosphite (66.4 g, 0.4 mol) in a silica glass vessel was degassed by flushing with nitrogen and irradiated at room temperature with a medium-pressure quartz mercury discharge lamp for 24 h. The excess of triethyl phosphite was then removed under vacuum and the residue distilled to give the ester (8 g, 44%) further purified by distillation through a spinning-band column; b.p. 108° at 0.44 mmHg (lit.,[28] 104—105° at 0.4 mmHg); τ($CDCl_3$) 2.1—2.67 (4 H, m), 5.6—6.1 (4 H, m), 7.57 (3 H, s), and 8.66 (6 H, t); δ(^{31}P) ($CHCl_3$) − 17.0 p.p.m.

Diethyl (m-formylphenyl)phosphonate (2; X = *m*-CHO, R = Et). This was prepared similarly by irradiation of a solution of *m*-iodobenzaldehyde (18.6 g, 0.08 mol) in triethyl phosphite (66.4 g, 0.4 mol) for 45 h. Distillation of the residue gave the ester (9.9 g, 51%), b.p. 128—136° at 0.25 mmHg, further purified by distillation through a spinning-band column. G.l.c. analysis and examination of the peak intensities in the n.m.r. spectrum, however, indicated the product to be *ca.* 90% pure. Further distillation did not improve the purity, and the compound was not used in the kinetic studies; τ($CDCl_3$) — 4.2 (s, CHO), 1.4—2.75 (m, ArH), 5.55—6.05 (m, OCH_2), and 8.65 (t, $OCH_2{\cdot}CH_3$); δ(^{31}P)($CHCl_3$) — 14.2 p.p.m.

Hydrolysis of Diethyl Phosphonate Esters.—General procedure. The phosphonate was heated under reflux in aqueous sodium hydroxide (10% w/v) until a homogeneous mixture was formed. The solution was then cooled and acidified with concentrated hydrochloric acid, whereupon an oil separated. The oil was extracted with chloroform, and the combined extracts were dried (Na_2SO_4) and evaporated to leave the monoester, which was recrystallised. In cases where the monoester could not be induced to crystallise, the product was isolated as the dicyclohexylamine salt.

Hydrolysis of Diphenyl Phosphonate Esters.—The phosphonate was heated under reflux in aqueous sodium hydroxide (10% w/v) until a homogeneous mixture was formed. The solution was then cooled and acidified. The monoester and phenol formed during the hydrolysis were then extracted with chloroform. The chloroform solution was then extracted with aqueous sodium hydrogen carbonate (10% w/v). Acidification of the aqueous solution yielded the monoester, which was filtered off and recrystallised.

Preparation of Dicyclohexylamine Salts.—To the mono-

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ester dissolved in 4—5 volumes of benzene was added dicyclohexylamine (0—20% excess) in 4—5 volumes of benzene. The salt slowly crystallised from the solution and was collected. If the salt did not crystallise, the benzene was evaporated off and the solid residue recrystallised. The yields in most cases were quantitative.

Data for Monophosphonate Esters.—*Ethyl hydrogen (2-furyl)phosphonate dicyclohexylamine salt*, m.p. 132° (from n-hexane) (Found: C, 60.65; H, 8.9; N, 3.8. $C_{18}H_{32}NO_4P$ requires C, 60.5; H, 8.95; N, 3.9%). *Ethyl hydrogen (2-thienyl)phosphonate dicyclohexylamine salt*, m.p. 159° (from n-hexane) (Found: C, 58.2; H, 8.7; N, 3.85. $C_{18}H_{32}NO_3PS$ requires C, 57.9; H, 8.6; N, 3.75%). *Phenyl hydrogen (2-thienyl)phosphonate dicyclohexylamine salt*, m.p. 151—152° (from n-hexane) (Found: C, 63.0; H, 7.5; N, 3.3. $C_{22}H_{32}NO_3PS$ requires C, 62.7; H, 7.6; N, 3.3%). *Ethyl hydrogen (1-methylpyrrol-2-yl)phosphonate dicyclohexylamine salt*, m.p. 150° (from n-hexane) (Found: C, 61.8; H, 9.5; N, 7.4. $C_{19}H_{35}N_2O_3P$ requires C, 61.6; H, 9.45; N, 7.55%). *Phenyl hydrogen (1-methylpyrrol-2-yl)phosphonate*, m.p. 93° (from n-hexane) (Found: C, 55.95; H, 5.1; N. 5.9. $C_{11}H_{12}NO_3P$ requires C, 55.7; H, 5.1; N, 5.9%). Ethyl hydrogen phenylphosphonate dicyclohexylamine salt, m.p. 141° (from n-hexane) (lit.,[29] 140.7—141.8°). *Phenyl hydrogen phenylphosphonate*, m.p. 78—79° (from n-hexane) (Found: C, 61.75; H, 4.75. $C_{12}H_{11}O_3P$ requires C, 61.55; H, 4.7%). *Ethyl hydrogen furfurylphosphonate dicyclohexylamine salt*, m.p. 133° (from n-hexane) (Found: C, 61.7; H, 4.94; N, 3.9. $C_9H_{34}NO_4P$ requires C, 61.45; H, 9.15; N, 3.8%). *Ethyl hydrogen (2-thenyl)phosphonate dicyclohexylamine salt*, m.p. 132° (from n-hexane) (Found: C, 59.2; H, 8.85; N, 3.55. $C_{19}H_{34}NO_3PS$ requires C, 58.9; H, 8.8; N, 3.6%). Ethyl hydrogen benzylphosphonate, m.p. 64° (from n-hexane) (lit.,[29] 63—64°). *Ethyl hydrogen (p-bromophenyl)phosphonate dicyclohexylamine salt*, m.p. 164° (from n-hexane) (Found: C, 54.15; H, 7.65; N, 3.15. $C_{20}H_{33}BrNO_3P$ requires C, 53.8; H, 7.4; N, 3.15%). *Ethyl hydrogen (m-chlorophenyl)phosphonate dicyclohexylamine salt*, m.p. 145° (from n-hexane) (Found: C, 59.6; H, 8.3; N, 3.4. $C_{20}H_{33}ClNO_3P$ requires C, 59.8; H, 8.2; N, 3.5%). *Ethyl hydrogen (p-methoxyphenyl)-phosphonate dicyclohexylamine salt*, m.p. 126—128° (from n-hexane) (Found: C, 63.35; H, 9.05; N, 3.4. $C_{21}H_{36}NO_4P$ requires C, 63.5; H, 9.05; N, 3.55%). *Ethyl hydrogen (m-tolyl)phosphonate dicyclohexylamine salt*, m.p. 130° (from n-hexane) (Found: C, 66.25; H, 9.3; N, 3.65. $C_{21}H_{36}NO_3P$ requires C, 66.15; H, 9.45; N, 3.7%).

Kinetics of Alkaline Hydrolysis.—The hydrolyses were carried out in aqueous 50% (v/v) dioxan, 0.1M in KCl, at equal initial concentrations of phosphonate ester and sodium hydroxide, and were followed by a conventional back-titration procedure, in which the decrease in sodium hydroxide was determined. The solutions were in a thermostatted bath controlled to within ± 0.1 °C. The data were evaluated by the method of integration, using the least squares program on an I.M.E. 120 electronic desk calculator, and in all cases a plot of $1/[OH^-]$ *versus* time was linear, confirming a second-order rate law.

The Hammett reaction constants and linear correlation coefficients were similarly calculated by using the least-squares program on the desk calculator.

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