The Chemistry of Heteroarylphosphorus Compounds. Part V.[1] The Alkaline Hydrolysis of 2-Furyldiphenyl-(2-thienyl)phosphonium Bromide, and Some Mixed Heteroarylmethylphosphonium Salts. Relative Stabilities of the Forming Carbanions

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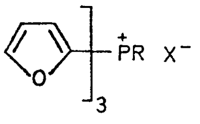
Alkaline hydrolysis of 2-furyl(diphenyl)-2-thienyl-phosphonium bromide (V) gives both furan and thiophen in a 1 : 3 molar ratio, indicating that the forming 2-thienyl carbanion is more stable than the 2-furyl analogue, and implying stabilisation of the forming negative charge in the former by sulphur 3*d* orbital participation. A kinetic isotope effect, $k_H/k_D \approx 1{\cdot}2$ is observed for the formation of both furan and thiophen in this reaction. The previously reported greater rate of alkaline hydrolysis of alkyltri-(2-furyl)phosphonium salts compared to the 2-thienyl analogues is now attributable to the greater electron-withdrawing effect of the 2-furyl substituent on the magnitude of the equilibrium constants of the pre-equilibria involved in the reactions. The products of alkaline hydrolysis of the mixed arylmethyldiphenylphosphonium salts (X)—(XII) indicate the relative stabilities of the forming carbanions to be in the order 2-furylmethyl > 2-thenyl > benzyl. The implications of this order are discussed in relation to earlier kinetic studies.

RECENTLY, we have shown that tri-(2-furyl)methylphosphonium iodide (I; R = Me, X = I) undergoes alkaline hydrolysis with loss of furan to form di-(2-furyl)methylphosphine oxide (II; R = Me) some 10^{10} times faster than the analogous hydrolysis of methyltriphenylphosphonium iodide. Furthermore the 2-furylphosphonium salt undergoes hydrolysis some 10^{2-3} times faster than the corresponding 2-thienylphosphonium salt (III; R = Me, X = I), which similarly yields thiophen and the oxide (IV; R = Me). A similar order of relative reactivity was noted in the hydrolysis of the corresponding benzylphosphonium salts (I and III; R = $PhCH_2$, X = Br), which again proceed with exclusive loss of furan or thiophen to give the oxides (II and IV; R = $PhCH_2$) respectively.[2,3]

The greater rate of hydrolysis of the heteroarylphosphonium salts compared to the phenyl analogues has been attributed to the greater electron-withdrawing character of the heteroaryl substituents, which cause increases in the equilibrium constants, K_1 and K_2, of the pre-equilibria involved in the hydrolysis reactions; in addition, the heteroaryl carbanions eliminated in the rate-determining step are more stable than the phenyl carbanion.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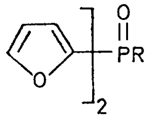
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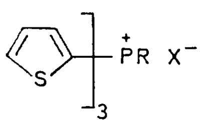
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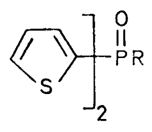
(IV)

The greater rate of hydrolysis of the 2-furylphosphonium salts compared to the 2-thienyl analogues is of interest. We have shown that the 2-furyl substituent is more electron-withdrawing than 2-thienyl and thus the pre-equilibria involved in the reaction will lie further to the right for the 2-furylphosphonium salts than for the (2-thienyl) analogues. The relative rate studies, however, do not necessarily indicate the relative stabilities of the two forming 2-heteroaryl carbanions. Simple inductive arguments would suggest that the 2-furyl carbanion would be the more stable due to the greater electronegativity of oxygen relative to sulphur. This approach, however, neglects the possibility of involvement of the sulphur 3*d* orbitals in stabilising the forming 2-thienyl carbanion. The possible utilisation of the sulphur 3*d* orbitals in the chemistry of thiophen and its derivatives has long attracted attention, and various experimental approaches have been devised in order to investigate this point. However, the results have often been in conflict.[4,5]

In order to investigate the relative stabilities of the transition states leading to the 2-furyl and 2-thienyl carbanions, we have studied the hydrolysis of the 'mixed' salt (V). It was considered that the relative proportions of furan and thiophen liberated on hydrolysis of this salt should reflect the relative stabilities of the forming carbanions, since the course of the reaction in the rate-determining step is determined by carbanion formation, and electronic effects of the substituents in the pre-equilibria would not be expected to influence the overall course. However, in competitive reactions of this type, the usual assumption is made that the electronic effects of the non-leaving groups are less important than those of the leaving group in stabilising the transition state.

The salt (V) was prepared by an extension of Horner's 'complex salt' synthesis of tetra-arylphosphonium

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[1] Part IV, D. W. Allen, B. G. Hutley, and T. C. Rich, *J.C.S. Perkin II*, 1973, 820.

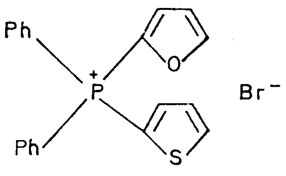
[2] D. W. Allen, *J. Chem. Soc.* (*B*), 1970, 1491.

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

[4] W. G. Salmond, *Quart. Rev.*, 1968, **22**, 253.

[5] K. A. R. Mitchell, *Chem. Rev.*, 1969, **69**, 157.

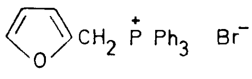
salts[6] to heterocyclic systems by heating together to 160° a mixture of 2-furyldiphenylphosphine, 2-bromothiophen, and anhydrous nickel(II) bromide. After extraction with water, the phosphonium salt was obtained in 40% yield. Alkaline hydrolysis of (V) gave furan and thiophen in a 1 : 3 molar ratio, indicating the preferential cleavage of the phosphorus–2-thienyl bond. Thus the forming 2-thienyl carbanion would appear to be more stable than the 2-furyl analogue, and the greater rate of hydrolysis of the 2-furylphosphonium salts (I) must therefore be due to the pre-equilibrium inductive effects of the 2-furyl substituents, which increase the pre-equilibrium constants K_1 and K_2 as compared to the corresponding 2-thienylphosphonium salts. Our observation of the preferential cleavage of the 2-thienyl group in the hydrolysis of the salt (V) is noteworthy, and suggests the stabilisation of the forming 2-thienyl carbanion in the transition state by sulphur 3*d* orbitals. It is of interest that in the competitive metallation of a mixture of furan and thiophen by n-butyl-lithium in non-polar solvents, the thiophen is almost exclusively metallated, indicating stabilisation of the fully formed carbanion by sulphur 3*d* orbitals.[7]



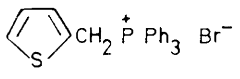
(V)

The extent of carbanionic character in the transition state of the rate-determining step of phosphonium salt hydrolysis has recently been investigated by Corfield and Trippett[8] who observed a kinetic isotope effect, $k_H/k_D \approx 1{\cdot}2$, in the alkaline hydrolysis of phenyl- and cumyl-phosphonium salts. This result has been interpreted as indicating that in the transition state, little cleavage of the phosphorus–carbon bond has occurred, and that there is correspondingly little transfer of a proton to the forming carbanion. We have also observed a kinetic isotope effect of 1·2 for the formation of both furan and thiophen in the alkaline hydrolysis of the salt (V) in 1 : 1 H_2O–D_2O. Although the 2-heteroaryl carbanions would seem to be more stable than both the phenyl and benzyl (and presumably cumyl) carbanions, the extent of carbanion formation in the transition state for the hydrolysis of the heteroarylphosphonium salts would appear to be the same as for the formation of the less stable carbanions.

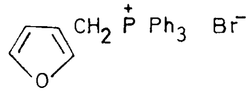
We have also recently reported a study of the kinetics of alkaline hydrolysis of a series of (heteroarylmethyl)-phosphonium salts (VI)—(IX) which produce triphenylphosphine oxide and the respective methyl-substituted heterocyclic compound.[9] Under the same conditions at 30°, the rates of hydrolysis decrease in the order 2-furylmethyl- > 2-thenyl- > benzyl- > 3-thenyl- > 3 furylmethyl-triphenylphosphonium bromide. The rate data were discussed in terms of the electron-withdrawing nature of the heteroaryl substituent, and the relative stability of the heteroarylmethyl carbanions. It was concluded that the transition state leading to the 3-thenyl carbanion is more stable than that for the formation of the 3-furylmethyl analogue, again indicating participation by the 3*d* orbitals of sulphur. In addition, it was concluded that the above 3-heteroarylmethyl carbanions are less stable than the benzyl carbanion, the more extensive delocalisation of the negative charge possible in the latter overshadowing the more restricted delocalisation possible for the 3-heteroarylmethyl carbanions, in spite of the possibility of inductive stabilisation by the electronegative heteroatoms and participation by the 3*d* orbitals of sulphur. However, the above rate data did not allow an unambiguous assignment of the relative order of stability of the 2-furylmethyl, 2-thenyl, and benzyl carbanions, since the contribution of the inductive effects of the substituents on the magnitude of the pre-equilibrium constants K_1 and K_2 is uncertain. In order to resolve this problem, we have investigated the products of alkaline hydrolysis of the salts (X)—(XII).



(VI)



(VII)



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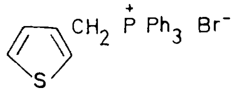

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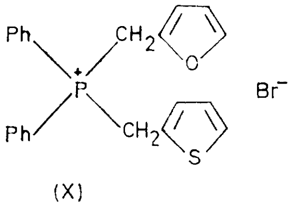
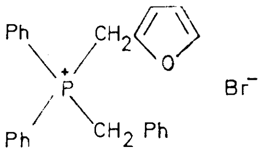
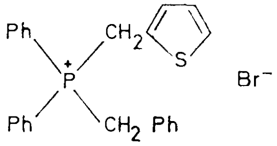


(X)



(XI)



(XII)

Alkaline hydrolysis of the salt (X) gave 2-methylfuran and 2-methylthiophen in a 1·3 : 1 mole ratio, indicating

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[6] L. Horner, G. Mummenthy, H. Moser, and P. Beck, *Chem. Ber.*, 1966, **99**, 2782.

[7] A. I. Shatenshtein, A. G. Kamrad, I. O. Shapiro, Yu. I. Ranneva, and E. N. Svyagintseva, *Proc. Acad. Sci. U.S.S.R.*, 1966, **168**, 502; Ya. L. Gol'dfarb and Y. L. Danyushevskii, *J. Gen. Chem. U.S.S.R.*, 1961, **31**, 3410; J. M. Mallan and R. L. Bebb, *Chem. Rev.*, 1969, **69**, 693.

[8] J. R. Corfield and S. Trippett, *Chem. Comm.*, 1970, 1267.

[9] D. W. Allen and B. G. Hutley, *J.C.S. Perkin II*, 1972, 67.

the 2-furylmethyl carbanion to be marginally more stable than the 2-thenyl analogue. Clearly, in this case, the inductive stabilisation by the more electronegative oxygen atom outweighs any contribution by the sulphur 3*d* orbitals in stabilising the forming 2-heteroarylmethyl carbanion. A comparison of this result with that for the hydrolysis of the salt (V) is of interest. Stabilisation of the forming 2-thienyl carbanion by the sulphur 3*d* orbitals is indicated, whereas in the case of the forming 2-thenyl carbanion, the *d* orbitals do not appear to play a significant role.

Alkaline hydrolysis of the salts (XI) and (XII) indicates that both the 2-furylmethyl and 2-thenyl carbanions are more stable than the benzyl analogue. Thus the salt (XI) gave on hydrolysis both 2-methylfuran and toluene in a 7 : 1 mole ratio; similarly, the salt (XII) gave both 2-methylthiophen and toluene in a 5 : 1 mole ratio. Clearly, the effect of the electronegative heteroatoms in the 2-heteroarylmethyl carbanions (together with possible 3*d* orbital participation in the 2-thenyl case) completely outweighs the greater possibilities of mesomeric delocalisation in the benzyl case. Thus the observed rate differences between the hydrolyses of the 2-heteroarylmethylphosphonium salts (VI) and (VII), and that of the benzyl analogue are due to *both* pre-equilibrium inductive effects and the greater stability of the forming carbanions.

EXPERIMENTAL

^{1}H N.m.r. spectra were recorded at 60 MHz on a JEOL spectrometer. G.l.c. analyses were carried out with a Pye series 104 chromatograph equipped with a 5 ft column of 10% silicone oil (SE 30) on Celite, and a flame ionisation detector. Operations involving phosphines or organolithium reagents were conducted under nitrogen.

2-Furyldiphenyl-(2-thienyl)phosphonium Bromide (V).—2-Furyldiphenylphosphine[1] (1·00 g, 1 equiv.), 2-bromothiophen (1·30 g, 1 equiv.), and anhydrous nickel bromide (0·44 g, 0·5 equiv.) were heated together at 160—170° for 5 h. On cooling, the deep green semi-crystalline mass was treated with water (10 ml) and the resulting emulsion extracted with ether (2 × 10 ml); the ether layer was discarded. The aqueous solution was then extracted with chloroform (3 × 10 ml) and the extracts evaporated to give the *salt* (V) (0·6 g, 40%), which after crystallisation from MeOAc–EtOH had m.p. 243—246° (decomp.) (Found: C, 57·9; H, 4·05. $C_{20}H_{16}BrPS$ requires C, 57·85; H, 3·85%), τ ($CDCl_3$) 1·46 (1H, m), 1·67 (1H, m), 2·05—2·8 (13H, m), and 3·05 (1H, m).

Hydrolysis of (V).—The salt (V) (29 mg) was added to a solution of sodium hydroxide (1·0 g) in aqueous diglyme (1 : 1; 3 ml) at 25°, and after mixing, the resulting solution was allowed to stand in a stoppered flask at 25° for 1 h. G.l.c. analysis of the solution indicated the presence of both furan and thiophen in a 1 : 3 mole ratio; benzene was not detected.

Kinetic Isotope Effect in the Hydrolysis of (V).—The salt (38 mg) was dissolved in H_2O–D_2O (1 : 1; 1 ml). To this solution was added a solution of 1N-NaOH (in H_2O–D_2O 1:1; 0·5 ml), resulting in the immediate formation of an emulsion. Redistilled dioxan was added dropwise to render the solution homogeneous. The resulting solution was then analysed by a combined g.l.c.–mass spectral system (using an AEI MS 30 mass spectrometer, with an ionising voltage of 13 eV, so as to minimise the formation of $M - 1$ fragments). Analysis of the molecular ions recorded for the partially deuteriated furan and thiophen indicated that for the formation of both components, $k_H/k_D \approx 1{\cdot}2$.

2-Furylmethyldiphenyl-(2-thenyl)phosphonium Bromide (X).—Diphenylphosphinous chloride (9·25 g) in dry tetrahydrofuran (50 ml) was added dropwise to a stirred suspension of lithium (1·0 g) in tetrahydrofuran (30 ml) during 40 min. The resulting red solution was stirred for a further hour and then separated from the excess of lithium by decantation under nitrogen. To this solution was added a solution of 2-chloromethylthiophen (5·0 g) in tetrahydrofuran (50 ml) during 45 min, and the mixture stirred for a further 12 h. The resulting solution was hydrolysed by the addition of dilute hydrochloric acid (100 ml). The organic layer was then separated, combined with ether (100 ml), and washed with sodium hydrogen sulphate solution and water, before drying over Na_2SO_4. Evaporation of the solvent gave the crude diphenyl-(2-thenyl)phosphine (9·2 g, 71%). The phosphine (2 g), in benzene (10 ml) was stirred with 2-furylmethyl bromide[10] (2·4 g; 10% solution in ether) for 12 h. The precipitated *salt* (X) (1·04 g, 38%) was filtered, washed with benzene, and after crystallisation from EtOAc–EtOH had m.p. 222—224° (Found: C, 59·45; H, 4·4. $C_{22}H_{20}BrOPS$ requires C, 59·6; H, 4·55%), τ (CF_3CO_2H) 2·4 (12H, m), 3·0 (2H, m), 3·6 (1H, m), 3·8 (1H, m), 5·45 (2H, d, $^2J_{PCH}$ 12·7 Hz), and 5·65 (2H, d, $^2J_{PCH}$ 12·9 Hz).

Benzyl-(2-furyl)diphenylphosphonium Bromide (XI).—Benzyldiphenylphosphine (2 g) was treated with 2-furylmethyl bromide (5 g; 10% solution in ether); the resulting solution was stirred overnight. The precipitated *salt* (XI; 2·15 g, 68%) was filtered, washed with ether, and recrystallised from EtOAc–EtOH to give crystals, m.p. 227—228° (Found: C, 65·55; H, 5·15. $C_{24}H_{22}BrOP$ requires C, 65·9; H, 5·05%), τ (CF_3CO_2H) 1·92—3·12 (16H, m), 3·67 (1H, m), 3·8 (1H, m), 5·7 (2H, d, $^2J_{PCH}$ 14·6 Hz), and 5·72 (2H, d, $^2J_{PCH}$ 12·75 Hz).

Benzyl-(2-thenyl)diphenylphosphonium Bromide (XII).—Diphenyl-(2-thenyl)phosphine (2·0 g), in benzene (10 ml), was heated under reflux with benzyl bromide (2·0 g) for 2 h. After allowing to stand overnight, the precipitated salt (1·2 g, 43%) was filtered, washed with benzene, and dried, m.p. 258—260° (from EtOAc–EtOH) (Found: C, 63·35; H, 5·05. $C_{24}H_{22}BrPS$ requires C, 63·55; H, 4·9%), τ (CF_3CO_2H) 2·0—3·4 (18H, m), 5·63 (2H, d, $^2J_{PCH}$ 12·7 Hz), and 5·78 (2H, d, $^2J_{PCH}$ 13·5 Hz).

Hydrolysis of the Salts (X)—(XII).—The following general procedure was used. The salt (0·2 g) was dissolved in diglyme (2 ml) and the solution added to aqueous sodium hydroxide solution (1N; 3 ml) at 30°. After 12 h, the resulting solution was analysed by g.l.c. Thus hydrolysis of (X) gave 2-methylfuran and 2-methylthiophen in a 1·3 : 1 mole ratio; hydrolysis of (XI) gave 2-methylfuran and toluene in a 7 : 1 mole ratio; hydrolysis of (XII) gave 2-methylthiophen and toluene in a 5 : 1 mole ratio. In each case, the aqueous alkaline diglyme solution was acidified, extracted with chloroform, and the extracts

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[10] J. E. Zanetti, *J. Amer. Chem. Soc.*, 1927, **49**, 1065.

(after drying over anhydrous $MgSO_4$) evaporated. The ^1H n.m.r. spectra of the residue was in accordance with that expected for a mixture of phosphine oxides. Integration of the signals due to the respective methylene protons in the mixture of phosphine oxides indicated the relative proportions of the components, and supported the g.l.c. data.

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