

## The Chemistry of Heteroarylphosphorus Compounds. Part III.<sup>1</sup> The Alkaline Hydrolysis of Heteroarylmethyl Analogues of Benzyltriphenylphosphonium Bromide; Relative Stabilities of Heteroarylmethyl Carbanions

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The kinetics of alkaline hydrolysis of a series of (heteroarylmethyl)triphenylphosphonium bromides (V)—(VIII) [ $\text{R}^+\text{PPh}_3\text{Br}^-$  (R = 2- or 3-furylmethyl or 2- or 3-thenyl)] which produce triphenylphosphine oxide and the respective methyl-substituted heterocyclic compound, have been studied at different temperatures in aqueous 50% ethanol in the presence of potassium chloride, and the rate data have been compared with those for the hydrolysis of benzyltriphenylphosphonium bromide.

The hydrolysis of all the salts follows a third-order rate law; under the same conditions at 30°, the rates of hydrolysis decrease in the order R = 2-furylmethyl > 2-thenyl > benzyl > 3-thenyl > 3-furylmethyl. The rate data are discussed in terms of the electron-withdrawing nature of the heteroaryl substituent, and the relative stability of the heteroarylmethyl carbanions.

In earlier papers<sup>1,2</sup> we have shown that the heteroarylphosphonium salts (I and II; R = PhCH<sub>2</sub> or Me, X = Br or I) undergo alkaline hydrolysis very rapidly in comparison to the phenyl analogues (III; R = PhCH<sub>2</sub> or Me, X = Br or I) to produce the alkyldi-(heteroaryl)phosphine oxides (IV; Z = O or S, R = PhCH<sub>2</sub> or Me) and the respective heterocyclic compounds.

The increased rate of hydrolysis of the heteroarylphosphonium salts has been attributed to the electron-

withdrawing effect of the heteroaryl substituent and the greater stability of the heteroaryl carbanions produced in the rate-determining step of the reaction, the mechanism of which is generally considered to involve stages (i)—(iv).<sup>3-5</sup> As required by this mechanism, the reactions proceed with third-order kinetics (rate =  $k_{\text{obs}}[\text{R}_4\text{P}^+][\text{OH}^-]^2$ ). The observed rate constant,  $k_{\text{obs}}$ , is composite, and can be expressed as the product of  $k_s$ ,  $K_1$ , and  $K_2$ , where  $K_1$  and  $K_2$  are the equilibrium constants of steps (i) and (ii), and  $k_s$  is the rate constant

<sup>1</sup> Part II, D. W. Allen, B. G. Hutley, and M. T. J. Mellor, preceding paper.

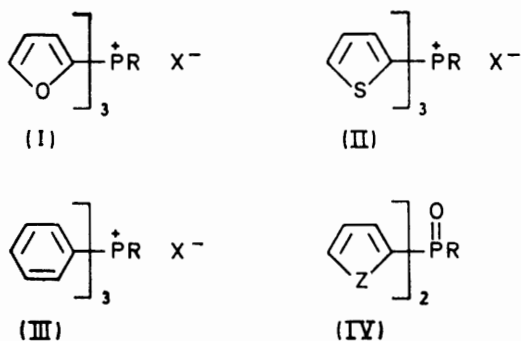
<sup>2</sup> D. W. Allen, *J. Chem. Soc. (B)*, 1970, 1490.

<sup>3</sup> W. E. McEwen, K. F. Kumli, A. Blade-Font, M. Zanger, and C. A. VanderWerf, *J. Amer. Chem. Soc.*, 1964, **86**, 2378.

<sup>4</sup> W. E. McEwen, G. Axelrad, M. Zanger, and C. A. VanderWerf, *J. Amer. Chem. Soc.*, 1965, **87**, 3948.

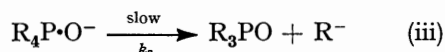
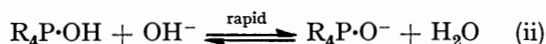
<sup>5</sup> M. Zanger, C. A. VanderWerf, and W. E. McEwen, *J. Amer. Chem. Soc.*, 1959, **81**, 3806.

for the rate-determining step (iii). The presence of electron-withdrawing groups attached to phosphorus

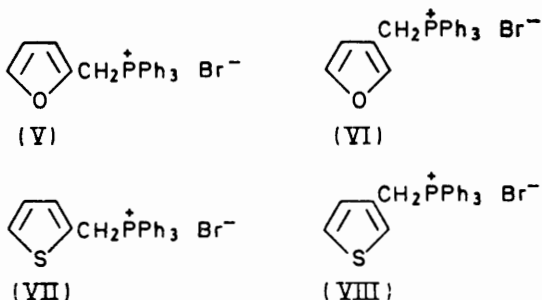


leads to increases in each of these constants, and is thus reflected in an increase in  $k_{\text{obs}}$ .

In order to investigate the influence of the heterocycle on the stability of an adjacent carbanionic carbon,



we have studied the kinetics of alkaline hydrolysis of a series of (heteroarylmethyl)triphenylphosphonium bromides [(V)—(VIII)]. Alkaline hydrolysis of these



phosphonium salts occurs readily to form triphenylphosphine oxide and the respective methyl-substituted heterocyclic compound; the course of the reactions is

maintain a constant ionic strength) have been studied at various temperatures; the third-order rate data and activation parameters, together with both  $^1\text{H}$  and  $^{31}\text{P}$  n.m.r. data for the phosphonium salts, are given in the Table.

The kinetic data reveal several features of interest. Over the temperature range studied, the rates of hydrolysis decrease in the order 2-furylmethyl- > 2-thenyl- > benzyl- > 3-thenyl- > 3-furylmethyl-triphenylphosphonium bromide, the decrease in rate being accompanied by a steady increase in energy of activation for the reactions.

At  $30^\circ$ , the 2-furylmethyl salt (V) undergoes hydrolysis almost two hundred times as fast as the 3-isomer (VI), the energy of activation for the hydrolysis of the former being significantly smaller than for the latter. The rate data undoubtedly reflect increases in the values of  $K_1$ ,  $K_2$ , and  $k_s$  for the hydrolysis of the salt (V), compared to those for that of the salt (VI). The electron-withdrawing effect of the 2-furylmethyl group on the phosphorus atom is greater than that of the 3-isomer (n.m.r. evidence in support of this assumption is discussed later), and hence the pre-equilibria involved in the hydrolysis of the salt (V) will lie further to the right. In addition, owing to the greater possibility of resonance stabilisation and the proximity of the electronegative oxygen atom to the negative charge, the 2-furylmethyl carbanion should be more stable than the 3-isomer.

A similar situation is apparent for the thenylphosphonium salts (VII) and (VIII), the 2-thenyl salt (VII), at  $30^\circ$ , undergoing hydrolysis *ca.* sixty times as fast as the 3-isomer (VIII). The differences in rates and activation energies between the 2- and 3-thenyl salts are significantly smaller than for the corresponding 2- and 3-furylmethyl salts (V) and (VI), respectively. This may indicate some additional stabilisation of the 3-thenyl carbanion due to participation of the  $3d$  orbital of sulphur (see later), which is not possible in the oxygen analogue. However, in this instance, other explanations may be advanced.

The greater electron-withdrawing nature of the 2-furylmethyl substituent relative to the 3-isomer, and of 2-thenyl relative to 3-thenyl is indicated by both  $^{31}\text{P}$  and  $^1\text{H}$  n.m.r. studies. In the preceding paper,<sup>1</sup>

Third-order rate constants and activation parameters, for the alkaline hydrolysis of the phosphonium salts  $\text{Ph}_3\text{P}^+\text{RBr}^-$  in aqueous 50% (v/v) ethanol, 0.1M in KCl;  $^1\text{H}$  and  $^{31}\text{P}$  n.m.r. data for the salts in  $\text{CF}_3\cdot\text{CO}_2\text{H}$

$\text{Ph}_3\text{P}^+\text{RBr}^-$	$k_{\text{obs}}/l^2 \text{ mol}^{-2} \text{ min}^{-1}$		$E_A/\text{kJ mol}^{-1}$	$\delta^{31}\text{P}/\text{p.p.m. (rel. to } 85\% \text{ H}_3\text{PO}_4)$	$\tau_{\text{CH}_2} (\text{CF}_3\cdot\text{CO}_2\text{H})$	$^2J_{\text{PCH}}/\text{Hz}$
	$30^\circ$	$40^\circ$				
R = Benzyl	2.76	7.25	76.2	-19.9	5.44	13.65
R = 2-Thenyl	75.1	183.3	70.3	-18.25	5.19	12.96
R = 3-Thenyl	1.21	3.64	86.9	-19.75	5.34	13.02
R = 2-Furylmethyl	157.7	356.5	64.3	-17.45	5.34	12.90
R = 3-Furylmethyl	0.81	2.95	101.8	-18.1	5.52	13.65

thus analogous to that of the hydrolysis of benzyltriphenylphosphonium bromide, which gives triphenylphosphine oxide and toluene. The kinetics of the reactions in aqueous 50% (v/v) ethanol (0.1M in KCl to

it was shown that  $^{31}\text{P}$  chemical shifts of a series of phosphonium salts of comparable structure reflect the electron-withdrawing nature of the substituents attached to phosphorus, the phosphorus becoming in-

creasingly shielded as the electron-withdrawing power of the attached groups increase. A comparison of the  $^{31}\text{P}$  chemical shifts (Table) of the salts (V) and (VI) reveals that the phosphorus is shielded in the 2-isomer relative to the 3-isomer, indicating the 2-furylmethyl group to be more electron-withdrawing than the 3-isomer. Similarly, the phosphorus in the 2-thenyl salt (VII) is shielded relative to the 3-isomer (VIII). These conclusions are supported by  $^1\text{H}$  n.m.r. studies. In phosphonium salts of the type  $\text{Ph}_3\text{P}^+\text{CH}_2\text{X Y}^-$ , where X is an electronegative substituent, the geminal coupling constants,  $^2J_{\text{POCH}}$ , of the methylene protons are significantly smaller than those of  $\alpha$ -protons of unsubstituted alkylphosphonium salts, and a relationship has been established between the magnitude of  $^2J_{\text{POCH}}$  and the electronegativity of the substituent X. The data have been interpreted on the basis of an increase in the s character of the C-H and C-P bonds caused by the electronegative substituent X, resulting in a positive contribution to a negative coupling constant, thus reducing the numerical value of  $^2J_{\text{POCH}}$ .<sup>6</sup> While such effects in the above phosphonium salts are far less marked than for salts in which X = OH, Cl, Br, or I, they are nevertheless in the expected direction.

A comparison of the relative rates of hydrolysis of the 2-furylmethyl- (V), 2-thenyl- (VII), and benzylphosphonium salts, is also of interest. At 30°, the 2-furylmethyl salt (V) undergoes hydrolysis twice as fast as the 2-thenyl analogue (VII), and fifty-seven times as fast as the benzyl salt. One might conclude from the rate data that the transition state for the formation of the 2-furylmethyl carbanion is more stable than that for the formation of the 2-thenyl analogue, which in turn is more stable than that for the formation of the benzyl carbanion. In the preceding paper, we showed that the 2-furyl group is more electron-withdrawing than 2-thienyl, and that this factor is of considerable importance in influencing the position of the pre-equilibria involved in the hydrolysis of the salts (I) and (II). It is therefore reasonable to assume that the 2-furylmethyl group is more electron-withdrawing than 2-thenyl, and evidence in support of this assumption is adduced from  $^1\text{H}$  and  $^{31}\text{P}$  n.m.r. data on the salts. The phosphorus nucleus becomes increasingly shielded from benzyl-, to 2-thenyl-, to 2-furylmethyl-triphenylphosphonium bromide, and the geminal coupling constant  $^2J_{\text{POCH}}$  decreases accordingly. Thus in the hydrolysis reactions, the pre-equilibria [steps (i) and (ii)] should lie further to the right in the case of the 2-furylmethyl salt (V) than for the 2-thenyl analogue (VII); likewise the pre-equilibria for the latter will lie further to the right than for the benzyl salt. However, since it has been shown<sup>1</sup> that it is only for the tri-2-furylphosphonium salts (I) that the pre-equilibria might lie substantially in favour of the products, it is likely that for all of the above salts the position of the

step (i) pre-equilibrium will lie predominantly to the left. In addition, the difference in activation energy for the hydrolyses of the 2-furylmethyl and the 2-thenyl salts is small (6 kJ mol<sup>-1</sup>), and therefore the position of the pre-equilibria for the 2-furylmethyl salt could so much outweigh the corresponding equilibria for the 2-thenyl salt, that the former would undergo hydrolysis faster, but the latter might give rise to the more stable carbanion. The experiments do not throw any appreciable light on the possibility of stabilisation by *d* orbitals of the transition state leading to the 2-thenyl carbanion. In the case of the heteroarylmethyl carbanions, the forming negative charge is extensively delocalised in both the 2-furylmethyl and 2-thenyl systems, and hence further stabilisation of the 2-thenyl carbanion by participation of the *d* orbitals of sulphur is probably minimal. The 2-thenyl carbanion may well involve participation of the 3*d* orbitals of sulphur, but if so, this does not have an over-riding effect.

In the case of the benzylphosphonium salt, the step (i) pre-equilibrium should lie further over to the reactant side, and although the forming carbanion is extensively delocalised mesomerically, it would appear that the electronegativity of the heteroatom in the 2-furylmethyl and 2-thenyl groups completely outweighs the greater mesomeric delocalisation in the benzyl case. Thus, the observed rate differences between the hydrolyses of the (heteroarylmethyl)phosphonium salts (V) and (VII), and that of the benzyl salt, could still be largely due to the relative position of the pre-equilibria.

Finally, a comparison of the rates of hydrolysis of 3-furylmethyl- (VI), 3-thenyl- (VIII), and benzyl-triphenylphosphonium bromide is of particular interest, in that the relative rates and activation energies for the oxygen and sulphur heterocycles are reversed relative to the data for the 2-isomers. Thus at 30°, the 3-thenyl salt (VIII) undergoes hydrolysis 1.5 times as fast as the 3-furylmethyl analogue (VI), and both salts undergo hydrolysis more slowly than the benzyl analogue, in marked contrast to the situation for the 2-isomers. The benzyl salt undergoes hydrolysis twice as fast as the 3-thenyl salt (VIII) and over three times as fast as the 3-furylmethyl salt (VI). As for the 2-isomers, the  $^{31}\text{P}$  chemical shifts indicate that the phosphorus is increasingly shielded in passing from the benzyl-, to the 3-thenyl-, to the 3-furylmethyl-phosphonium salt, indicating that the electron-withdrawing nature of the substituents increases in this order as expected. [In the case of the (3-heteroarylmethyl)phosphonium salts, the geminal coupling constants,  $^2J_{\text{POCH}}$ , are not in the expected order;  $^2J_{\text{POCH}}$  for the 3-furylmethyl salt (VI) is unexpectedly high.] On the basis of the  $^{31}\text{P}$  n.m.r. data, and by analogy with the 2-isomers, it is reasonable to assume that for the hydrolysis of the (3-heteroarylmethyl)phosphonium salts, the pre-equilibria will lie further to the right on passing from benzyl-, to 3-thenyl-, to 3-furylmethyl-triphenylphosphonium bromide, yet the observed relative rates are not in the expected order. On the basis of the observed rate and activation energy

<sup>6</sup> D. W. Allen, I. T. Millar, and J. C. Tebby, *Tetrahedron Letters*, 1968, 745.

data, one must conclude that the transition state leading to the 3-thenyl carbanion is more stable than that for the formation of the 3-furylmethyl carbanion. A reasonable explanation of this would seem to be in terms of participation by the  $3d$  orbitals of sulphur. In the 3-heteroarylmethyl carbanions, the delocalisation of the negative charge is more limited than for the 2-isomers, and the additional delocalisation due to involvement of the  $3d$  orbitals of sulphur could be significant, such an effect not being possible for the 3-furylmethyl carbanion. From the rate data, it must be concluded that the benzyl carbanion is more stable than the two 3-heteroarylmethyl carbanions, the energy of activation for the hydrolysis of the benzylphosphonium salt being significantly lower. The extensive delocalisation of the negative charge possible in the benzyl carbanion overshadows 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  $3d$  orbitals of sulphur.

#### EXPERIMENTAL

$^1\text{H}$  N.m.r. spectra were recorded at 60 MHz on a JEOL spectrometer.  $^{31}\text{P}$  N.m.r. spectra were recorded at 24 MHz on the same instrument, with phosphoric acid (85%) as external standard. Coupling constants were measured on scale-expanded spectra. G.l.c. analyses were carried out with a Pye series 104 chromatograph (25 ft column of 10% silicone oil on Celite; flame ionisation detector). M.p.s were determined with a Kofler hot-stage apparatus.

**Phosphonium Salts.**—2-Furylmethyltriphenylphosphonium bromide (V) was prepared according to the procedure of Schweizer *et al.*<sup>7</sup> and had m.p. 268–270° (lit.,<sup>7</sup> 269–271°) (Found: C, 65.5; H, 4.65. Calc. for  $\text{C}_{23}\text{H}_{20}\text{BrOP}$ : C, 65.25; H, 4.75%);  $\tau$  ( $\text{CF}_3\text{CO}_2\text{H}$ ) 2.2 (15H, m), 2.6 (1H, m), 3.7 (2H, m), and 5.34 (2H, d,  $^2J_{\text{POCH}}$  12.90 Hz);  $\delta$   $^{31}\text{P}$  –17.45 p.p.m.

**3-Furylmethyltriphenylphosphonium bromide (VI).** Furan-2,3,4,5-tetracarboxylic acid<sup>8</sup> was converted into 3-furoic acid and 3-furylmethanol as described by Sherman *et al.*<sup>9</sup> To a stirred ice-cold solution of 3-furylmethanol (2.8 g) in anhydrous ether (30 ml), redistilled phosphorus tribromide (2.8 g) in anhydrous ether (5 ml) was added dropwise. The solution was then allowed to attain ambient temperature, and was left for 90 min. The ether layer was decanted, cooled to 0°, and then treated cautiously, with stirring, with sodium hydroxide solution (40% w/v; 15 ml). After 10 min, the ether layer was separated, dried (NaOH) and filtered into a solution of triphenylphosphine (8.0 g) in anhydrous ether (40 ml). The resulting

solution was stirred at room temperature for 13 days, and the precipitated salt was then removed (6.7 g, 50%), m.p. (from EtOAc–EtOH) >290° (decomp.) (Found: C, 65.6; H, 5.15.  $\text{C}_{23}\text{H}_{20}\text{BrOP}$  requires C, 65.25; H, 4.75%);  $\tau$  ( $\text{CF}_3\text{CO}_2\text{H}$ ) 1.8–2.9 (17H, m), 4.0 (1H, m), and 5.52 (2H, d,  $^2J_{\text{POCH}}$  13.65 Hz);  $\delta$   $^{31}\text{P}$  ( $\text{CF}_3\text{CO}_2\text{H}$ ) –18.1 p.p.m.

**2-Thenyltriphenylphosphonium bromide (VII).** To a solution of 2-thenyl bromide<sup>10</sup> (5 g) in anhydrous ether (30 ml), triphenylphosphine (9 g) in anhydrous ether (70 ml) was added with stirring. The resulting solution was then stirred at room temperature for 10 days, and the salt was removed (9.7 g, 79%), m.p. >300° (decomp.) (lit.,<sup>11</sup> m.p. 320°) (Found: C, 63.2; H, 4.6. Calc. for  $\text{C}_{23}\text{H}_{20}\text{BrPS}$ : C, 62.9; H, 4.55%);  $\tau$  ( $\text{CF}_3\text{CO}_2\text{H}$ ) 2.4 (16H, m) and 5.19 (2H, d,  $^2J_{\text{POCH}}$  12.96 Hz);  $\delta$   $^{31}\text{P}$  ( $\text{CF}_3\text{CO}_2\text{H}$ ) –18.25 p.p.m.

**3-Thenyltriphenylphosphonium bromide (VIII).** 3-Thenyl bromide<sup>10</sup> (5 g) and triphenylphosphine (9 g) in anhydrous ether (120 ml) gave the salt (VIII) (8.7 g, 71%), m.p. 313–315° (from EtOAc–EtOH) (Found: C, 62.8; H, 4.6.  $\text{C}_{23}\text{H}_{20}\text{BrPS}$  requires C, 62.9; H, 4.6%);  $\tau$  ( $\text{CF}_3\text{CO}_2\text{H}$ ) 2.4 (16H, m), 3.0 (1H, m), 3.35 (1H, m), and 5.34 (2H, d,  $^2J_{\text{POCH}}$  13.02 Hz);  $\delta$   $^{31}\text{P}$  ( $\text{CF}_3\text{CO}_2\text{H}$ ) –19.75 p.p.m.

**Benzyltriphenylphosphonium bromide.**—The salt was prepared from benzyl bromide and triphenylphosphine in toluene and had m.p. 275–276° (lit.,<sup>12</sup> 274–275°);  $\tau$  ( $\text{CF}_3\text{CO}_2\text{H}$ ) 1.9–3.2 (19H, m) and 5.44 (2H, d,  $^2J_{\text{POCH}}$  13.65 Hz);  $\delta$   $^{31}\text{P}$  ( $\text{CF}_3\text{CO}_2\text{H}$ ) –19.9 p.p.m.

**Alkaline Hydrolysis of Phosphonium Salts.**—The following general procedure was used: the phosphonium salt (1 g) dissolved in aqueous ethanol (50% v/v; 5 ml) was treated with sodium hydroxide solution (10% w/v; 5 ml) and the resulting solution was heated under reflux for 2 h. The cooled mixture was neutralised, poured into water, and extracted with chloroform. The extract was dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated to give triphenylphosphine oxide. The volatile hydrocarbon product was identified by g.l.c., by comparison with the authentic material. Compound (V) gave 2-methylfuran, (VI) gave 3-methylfuran, (VII) gave 2-methylthiophen, (VIII) gave 3-methylthiophen, and benzyltriphenylphosphonium bromide gave toluene.

**Kinetics.**—The hydrolysis reactions were carried out in aqueous 50% (v/v) ethanol, 0.1M in KCl, at initial concentrations of phosphonium salt and sodium hydroxide of 0.01M, and were followed by a conventional back-titration procedure, in which the decrease in sodium hydroxide concentration was determined. The solutions were in a thermostatted bath controlled to  $\pm 0.1^\circ$ . The reactions were followed to 70% completion, and the data were evaluated by the method of integration. In all cases, a plot of  $1/[\text{OH}]^2$  vs. time was linear, confirming a third-order rate law.

[1/1537 Received, August 24th, 1971]

<sup>7</sup> E. E. Schweizer, W. S. Creasy, K. K. Light, and E. T. Shaffer, *J. Org. Chem.*, 1969, **34**, 212.

<sup>8</sup> T. Reichstein, A. Grussner, K. Schindler, and E. Hardmeier, *Helv. Chim. Acta*, 1933, **16**, 276.

<sup>9</sup> E. Sherman and E. D. Amstutz, *J. Amer. Chem. Soc.*, 1950, **72**, 2195.

<sup>10</sup> K. Dittmer, R. P. Martin, W. Herz, and S. J. Cristol, *J. Amer. Chem. Soc.*, 1949, **71**, 1201.

<sup>11</sup> T. R. Pampalona, *Org. Preparative Proc.*, 1969, **1**, 209.

<sup>12</sup> G. M. Kosolapoff, 'Organophosphorus Compounds,' Wiley, New York, 1950.