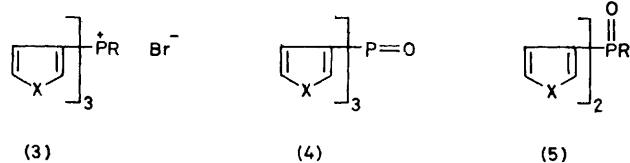
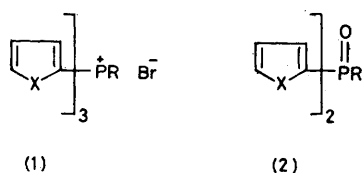


The Chemistry of Heteroarylphosphorus Compounds. Part 11.¹ The Effects of 3-Furyl and 3-Thienyl Substituents at Phosphorus on the Rate and Course of Alkaline Hydrolysis of Phosphonium Salts and on the Decomposition of Phosphonium Betaines

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Both benzyltri-(3-furyl)- and benzyltri-(3-thienyl)-phosphonium bromides (3: X = O or S, R = PhCH₂) undergo alkaline hydrolysis with preferential loss of the benzyl group, indicating that the latter is better able to support the forming carbanionic centre than are the 3-heteroaryl groups, in contrast to the situation for the corresponding 2-heteroaryl isomers. A comparison of the rates of hydrolysis of a series of methyltri(heteroaryl)phosphonium salts shows that the relative reactivities are in the order 2-furyl(10⁹) > 2-thienyl(3 × 10⁶) > 3-furyl(46) > 3-thienyl(33) > phenyl(1 × 10⁻²), indicating that the 3-heteroaryl substituents are much less strongly electron-withdrawing than the 2-isomers. The phosphonium betaine derived from the reaction of tri-(3-furyl)phosphine with styrene oxide decomposes to form styrene and the phosphine oxide, whereas the corresponding 3-thienyl derivative follows an alternative reaction pathway with the formation of the vinylphosphine oxide (9: Ar = 3-thienyl) and the re-arrangement product (8: Ar = 3-thienyl).

In earlier papers, we have shown that the presence at phosphorus of a 2-furyl or 2-thienyl substituent has a marked effect on the rate and course of reactions involving nucleophilic attack at a phosphonium centre, as in the alkaline hydrolysis of phosphonium salts^{2,3} and



in the decomposition of phosphonium betaines.^{4,5} In this paper we report for comparison a study of the effects of the 3-furyl and 3-thienyl groups in such reactions.

In the alkaline hydrolysis of non-crowded phosphonium salts, the group cleaved from phosphorus is generally that which is most stable as a carbanion,⁶⁻⁸ although the extent of carbanion formation in the transition state of the reaction is thought to be small.⁹ We have shown that on alkaline hydrolysis the salts (1; X = O or S, R = CH₂Ph) undergo exclusive loss of a heteroaryl substituent to form the oxides (2; X = O or S, R = CH₂Ph), indicating that the forming 2-heteroaryl carbanions are more stable than the forming benzyl

carbanion in spite of the resonance stabilisation possible for the latter.^{2,3} The presence of the electronegative heteroatom adjacent to the carbon bound to phosphorus is the key feature of these heteroaryl substituents in controlling the stability of the forming carbanions, and the results of hydrolysis of the corresponding 3-heteroarylphosphonium salts (3; X = O or S, R = CH₂Ph or Me) together with the mode of decomposition of related phosphonium betaines support this suggestion.

RESULTS AND DISCUSSION

In contrast to the hydrolysis of the salts (1; X = O or S, R = PhCH₂), hydrolysis of each of the salts (3; X = O or S, R = PhCH₂) gives a mixture of phosphine oxides, together with both the heteroarene and toluene. In each case, the phosphine oxides (4) and (5; R = PhCH₂) (X = O or S) are formed in ca. 3:1 molar proportions. From the product ratios, and taking statistical effects into consideration, there is apparently a preference for loss of the benzyl rather than the 3-heteroaryl substituent from phosphorus, presumably indicating that carbanion stability factors are favouring the former. Clearly the 3-heteroaryl substituents are less electron-withdrawing than the corresponding 2-heteroaryl systems owing to the greater distance of the carbon linked to phosphorus from the heteroatom. Furthermore, whereas in the case of the 2-isomers the forming 2-thienyl carbanion is more stable than the 2-furyl analogue,¹⁰ in the case of the 3-isomers, the stabilities of the forming carbanions are similar.

Comparison of the rates of alkaline hydrolysis of the corresponding methylphosphonium salts (1; X = O or S, R = Me) and (3; X = O or S, R = Me) provides

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further evidence of the reduced electron-withdrawing nature of the 3-heteroaryl substituents and the consequent reduction in ease of cleavage from phosphorus. As for the 2-heteroaryl systems (1), both the 3-heteroarylphosphonium salts (3; X = O or S, R = Me) undergo hydrolysis with exclusive loss of the hetero-arene to form the oxide (5; X = O or S, R = Me). The hydrolyses proceed according to a third-order rate law (as is generally found for the aqueous alkaline hydrolysis of phosphonium salts); the rate data are presented in the Table, together with the corresponding data for the

Third-order rate constants for the alkaline hydrolysis of heteroarylphosphonium salts $R_3P^+MeI^-$ in 50% aqueous ethanol at 30 °C

R	$k/l^2 \text{ mol}^{-2} \text{ min}^{-1}$
R = 2-furyl	ca. 10^9 *
R = 2-thienyl	2.7×10^6 *
R = 3-furyl	46.5
R = 3-thienyl	33.3
R = phenyl	1.4×10^{-2} *

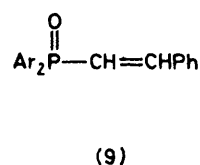
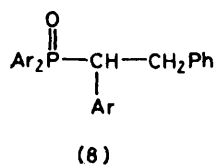
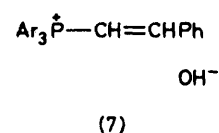
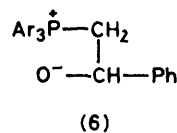
* Calculated from data given in refs. 2 and 3.

hydrolysis of the 2-heteroaryl isomers. In comparison with the 2-heteroarylphosphonium salts, the hydrolysis of the 3-isomers proceeds much more slowly. Nevertheless, the latter undergo hydrolysis significantly faster than the corresponding phenylphosphonium salt, indicating that the electron-withdrawing effect of the heteroatom is still significant in influencing the positions of the pre-equilibria involved and presumably also the stability of the forming carbanions.

We have shown recently that the course of decomposition (in protic solvents such as ethanol) of phosphonium betaines (6) (derived from the reactions of tertiary phosphines with styrene oxide) depends markedly on the nature of the groups bound to phosphorus.^{4,5} If the *P*-substituents are strongly electron-withdrawing, then betaine collapse occurs with formation of the normal products of a Wittig reaction, *viz.* styrene and the phosphine oxide. If, however, the *P*-substituents are less strongly electron-withdrawing, protonation of the betaine occurs to form a β -hydroxylalkylphosphonium salt which then loses water to form a vinylphosphonium salt (7). The mode of decomposition of the latter depends on the carbanionic stability of the other *P*-substituents. Groups of moderate carbanionic stability are generally involved in migration from phosphorus to carbon with formation of a rearranged phosphine oxide (8), whereas for carbanions of greater stability simple cleavage occurs with the formation of a substituted vinylphosphine oxide (9).

We have previously shown that when Ar = 2-furyl or 2-thienyl, betaine collapse is rapid and styrene and the phosphine oxide are formed in good yield, whereas when Ar = phenyl, the main product is the rearrangement product (8; Ar = Ph). We now find that when

Ar = 3-furyl, betaine collapse is still sufficiently rapid for the predominant formation of styrene and the phosphine oxide. However, when Ar = 3-thienyl, the main products are the vinylphosphine oxide (9; Ar = 3-thienyl), and the rearrangement product (8; Ar = 3-thienyl). Clearly, owing to the greater electronegativity of oxygen, the electron-withdrawing effect



of the 3-furyl substituent is still sufficient to cause betaine collapse to occur significantly faster than the competitive routes involving protonation of the betaine. In the case of the less strongly electron-withdrawing 3-thienyl substituent, betaine collapse must be slower, and the route involving formation of the vinylphosphonium intermediate (7) is followed predominantly. The formation of both the rearranged phosphine oxide (8; Ar = 3-thienyl) and the vinylphosphine oxide (9; Ar = 3-thienyl) suggests that the forming 3-thienyl carbanion is at the borderline of stability between those which are sufficiently stable to be cleaved completely from phosphorus and those which require the additional delocalisation of negative charge afforded in the transition state of the rearrangement. Of the range of heteroaryl substituents at phosphorus studied in the decomposition of vinylphosphonium salts, the 3-thienyl group is the only one which is involved in migration from phosphorus to adjacent carbon.

EXPERIMENTAL

¹H N.m.r. spectra were recorded at 60 MHz with a JEOL spectrometer (Me₄Si as internal standard). Mass spectra were recorded at 70 eV with an A.E.I. MS30 spectrometer.

Synthesis of Phosphines and Phosphonium Salts.—Tri-(3-furyl)phosphine and tri-(3-thienyl)phosphine were prepared and converted into their oxides and methiodides as described in the literature.¹¹⁻¹³ Treatment of the respective phosphines with an excess of benzyl bromide in benzene solution gave *benzyltri-(3-furyl)phosphonium bromide* (3; X = O, R = PhCH₂), m.p. 219–220° (from EtOAc–EtOH) (Found: C, 56.2; H, 4.25. C₁₉H₁₆BrO₃P requires C, 56.6; H, 4.0%); and *benzyltri-(3-thienyl)phosphonium bromide* (3; X = S, R = PhCH₂), m.p. 294° (Found: C, 50.65; H, 3.65. C₁₉H₁₆BrPS₃ requires C, 50.55; H, 3.55%).

Alkaline Hydrolysis of Phosphonium Salts.—(A) *Benzyltri-(3-furyl)phosphonium bromide.* To a solution of the

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phosphonium salt (81 mg) in ethanol (1 cm³) was added aqueous sodium hydroxide (2M; 1 cm³) and the resulting solution was heated under reflux for 3 h. G.l.c. confirmed the presence of both furan and toluene. The solution was poured into sulphuric acid (1M; 10 cm³) and extracted with chloroform (3 × 10 cm³). The extract was dried (Na₂SO₄) and evaporated to give a 3 : 1 mixture (according to ¹H n.m.r.) of tri-(3-furyl)phosphine oxide and benzyldi-(3-furyl)phosphine oxide which we were unable to separate by fractional crystallisation or by t.l.c.; τ(CDCl₃) 2.45 (m, ArH), 2.6 (m, ArH), 2.95 (ArH), 3.6 (m, ArH), and 6.6 (d, P-CH₂Ph, ²J_{POCH} 15 Hz), M⁺ 248 and 272.

(B) *Benzyldi-(3-thienyl)phosphonium bromide*. To a solution of the phosphonium salt (200 mg) in ethanol (2 cm³) was added aqueous sodium hydroxide (2M; 2 cm³) and the resulting solution was heated under reflux for 4 h. G.l.c. confirmed the presence of both thiophen and toluene. On cooling, the solution deposited white crystals which were filtered off and recrystallised to give *benzyldi-(3-thienyl)phosphine oxide*, m.p. 183–184° (from benzene–hexane) (Found: C, 58.8; H, 4.45. C₁₅H₁₃OPS₂ requires C, 59.2; H, 4.3%), τ(CDCl₃) 2.1–3.0 (m, 11 ArH), 6.4 (2 H, d, P-CH₂Ph, ²J_{POCH} 15 Hz). The filtrate from the above was poured into water (25 cm³) and extracted with chloroform (3 × 10 cm³). Evaporation of the dried extract gave tri-(3-thienyl)phosphine oxide, identical with an authentic specimen. In a subsequent experiment the mixture of both phosphine oxides was extracted into chloroform and, following evaporation, analysed by ¹H n.m.r. Integration data showed a 3 : 1 molar ratio of tri-(3-thienyl)phosphine oxide to benzyldi-(3-thienyl)phosphine oxide.

(C) *Tri-(3-furyl)methylphosphonium iodide*. To a solution of the salt (100 mg) in ethanol (1 cm³) was added aqueous sodium hydroxide (2M; 1 cm³) and the solution was set aside for 24 h. G.l.c. confirmed the presence of furan. The mixture was then poured into dilute sulphuric acid (1M; 10 cm³) and the products were extracted into chloroform. Evaporation of the dried extract gave *di-(3-furyl)methylphosphine oxide*, m.p. 87° (from MeOAc–hexane) (Found: C, 55.1; H, 4.75. C₉H₉O₃P requires C, 55.1; H, 4.65%); τ(CDCl₃) 1.8 (4 H, m), 2.2 (4 H, m), 3.2 (4 H, m), and 8.0 (3 H, d, ²J_{POCH} 13.5 Hz).

(D) *Methyldi-(3-thienyl)phosphonium iodide*. The salt was hydrolysed and the products were extracted as described in (C). G.l.c. confirmed the presence of thiophen. Evaporation of the extract gave *methyldi-(3-thienyl)-*

phosphine oxide, m.p. 110° (from MeOAc–hexane) (Found: C, 47.2; H, 4.0. C₉H₉OPS₂ requires C, 47.35; H, 4.0%), τ(CDCl₃) 1.9 (2 H, m), 2.4 (4 H, m), and 7.95 (3 H, d, ²J_{POCH} 13.5 Hz).

Kinetic Studies.—The hydrolyses of the methylphosphonium salts (3; R = Me, X = O or S) were carried out at 30 °C in 50% (v/v) aqueous ethanol, with equal initial concentrations of phosphonium salt and sodium hydroxide (0.005M). The course of each reaction was followed by the conductance procedure described previously.² The reactions followed a third-order rate law; the rate data are presented in the Table.

Reactions of Tri-(3-heteroaryl)phosphines with Styrene Oxide.—(a) *Tri-(3-furyl)phosphine*. The phosphine (0.232 g) and styrene oxide (0.24 g; excess) were dissolved in absolute ethanol (2 cm³) and the resulting solution was heated under reflux for 24 h. G.l.c. indicated the formation of styrene in 45% yield. Evaporation gave tri-(3-furyl)phosphine oxide, identical with an authentic sample.

(b) *Tri-(3-thienyl)phosphine*. The phosphine (0.28 g) and styrene oxide (0.24 g; excess) were dissolved in absolute ethanol and the solution was heated under reflux for 24 h. G.l.c. showed only a trace of styrene, the major volatile product being thiophen. Evaporation followed by preparative t.l.c. of the residue [on a 20 × 20 cm plate coated with a 1.0 mm thickness of Kieselgel, with EtOAc–hexane (1 : 1 v/v) as solvent] gave *methyldi-(3-thienyl)phosphine oxide*, m.p. 110°, *m/e* 228 (M⁺) (30 mg), identical with the hydrolysis product in (D) above; and *2-phenyl-1-(3-thienyl)ethyl-di-(3-thienyl)phosphine oxide* (8; Ar = 3-thienyl) (28 mg), m.p. 199° [from EtOH–petroleum (b.p. 60–80°)] (Found: C, 59.8; H, 4.45. C₂₀H₁₇OPS₃ requires C, 60.0; H, 4.3%); *m/e* 400 (M⁺), 214 [(C₄H₃S)₂POH], and 186 (C₄H₃SCH=CHPh), in accord with the very specific fragmentation pattern established for such compounds;¹⁴ also isolated was a mixture (105 mg) of β-styryl-di-(3-thienyl)phosphine oxide (9; Ar = 3-thienyl), *m/e* 316 (M⁺), and tri-(3-thienyl)phosphine oxide, *m/e* 296 (M⁺), which we were unable to separate. The u.v. spectrum of the mixture in ethanol showed an absorption at 270 nm consistent with the presence of PhCH=CH–P(O).

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