# The Alkaline Hydrolysis of Some Tri-(2-thienyl)phosphonium Salts. Inductive Effects on the Rate of Nucleophilic Attack at Phosphorus

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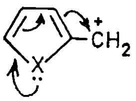
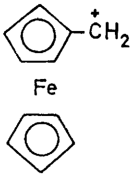
The kinetics of alkaline hydrolysis of the heteroarylphosphonium salts, methyltri-(2-thienyl)phosphonium iodide (IV) and benzyltri-(2-thienyl)phosphonium bromide (V), which proceed with cleavage of a phosphorus–thiophen bond, have been studied at different temperatures in 50% (v/v) aqueous ethanol, and the rates of hydrolysis have been compared with those for the hydrolysis of analogous triphenylphosphonium salts. The hydrolysis of both the above thienylphosphonium salts follows a third-order rate law; under the same conditions at 40·2°, methyltri-(2-thienyl)phosphonum iodide (IV) hydrolyses $1{\cdot}45 \times 10^8$ times more rapidly than methyltriphenylphosphonium iodide. Similarly, benzyltri-(2-thienyl)phosphonium bromide hydrolyses $2{\cdot}5 \times 10^5$ times faster than benzyltriphenylphosphonium bromide.

It is suggested that in the alkaline hydrolysis of the above salts, the inductive effect of the 2-thienyl group and the stability of the 2-thienyl carbanion are of the greatest importance in controlling the rate of the reaction; $d_\pi$–$p_\pi$ bonding between the ' π-excessive ' heterocycle and the phosphorus 3*d* orbitals does not appear to play a significant role in controlling the rate of nucleophilic attack at phosphorus.

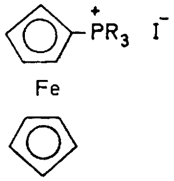
FURAN, thiophen, and pyrrole are classed as π-excessive heterocycles, and this view is supported by the readiness with which they undergo electrophilic substitution reactions. Further, the very ready hydrolysis of halogenomethyl derivatives of these systems (analogues of benzyl halides) can be understood in terms of resonance stabilisation of the intermediate carbonium ion (I; X = O, S, or NH) by $p_\pi$–$p_\pi$ overlap between the ring system and the carbonium ion centre.[1] The stability of the ferrocenyl carbonium ion (II) has been similarly explained by the overlap of either filled iron 3*d* orbitals or cyclopentadienyl *p* orbitals with the vacant *p* orbital on the carbonium ion carbon.[2] Recently, McEwen and co-workers[3] have suggested a similar $p_\pi$–$d_\pi$ (or $d_\pi$–$d_\pi$) stabilisation for the ferrocenylphosphonium ion, involving the phosphorus 3*d* orbitals, to account for the markedly lower rate of alkaline hydrolysis of phosphonium salts with ferrocenyl substituents when compared with the rates of hydrolysis of typical phenylphosphonium compounds.



(I)



(II)



(III)

As part of a study of the interactions between the phosphorus atom and the ring system, in phosphorus compounds bearing a heterocyclic ring directly attached to phosphorus, the possibility of a similar stabilisation of heteroarylphosphonium salts by $p_\pi$–$d_\pi$ overlap between the ring π-system and the empty phosphorus 3*d* orbitals has been investigated. Recently, the $^1$H n.m.r. spectra of some heteroaryl-phosphine oxides and -phosphonates have been discussed,[4] and it has been suggested that the spectra are in accord with some degree of $p_\pi$–$d_\pi$ bonding between the ring system and the phosphorus. Similarly, an earlier paper[5] describing the u.v. spectra of the above compounds also suggests the occurrence of $p_\pi$–$d_\pi$ overlap, indicating such effects to be more important in the pyrryl and furyl than in the thienyl derivatives, in contrast with the above $^1$H n.m.r. data which indicate that such interactions are more important in the furyl and thienyl than in the pyrryl derivatives.

The mechanism of the alkaline hydrolysis of phosphonium salts has been extensively studied,[6,7] and involves steps (i)—(iv).

$$[\mathrm{R_4\overset{+}{P}}] + \mathrm{OH^-} \xrightleftharpoons{\text{fast}} \mathrm{R_4POH} \qquad \text{(i)}$$

$$\mathrm{R_4POH} + \mathrm{OH^-} \xrightleftharpoons{\text{fast}} [\mathrm{R_4PO}]^- + \mathrm{H_2O} \qquad \text{(ii)}$$

$$[\mathrm{R_4PO}]^- \xrightarrow{\text{slow}} \mathrm{R_3P{=}O} + \mathrm{R^-} \qquad \text{(iii)}$$

$$\mathrm{R^-} + \mathrm{H_2O} \xrightarrow{\text{fast}} \mathrm{RH} + \mathrm{OH^-} \qquad \text{(iv)}$$

As indicated, the reaction gives a phosphine oxide and a hydrocarbon, the relative ease of departure of the group R in the rate-determining step (iii) being in parallel with its stability as a carbanion. Thus a benzyl group departs more rapidly than a methyl,[7] ethyl,[7] phenyl,[7] ferrocenyl,[3] *p*-methoxybenzyl,[6] or *p*-methylbenzyl[6] group, and less rapidly than a *m*-bromobenzyl[6] or a *p*-chlorobenzyl[6] group. As required by the above mechanism, investigations of the kinetics of such reactions have established that a third-order rate law (rate ∝[phosphonium salt] $[\mathrm{OH^-}]^2$) is followed.

In addition to the stability of the leaving group, other factors influence the overall rate of the reaction; it has been shown that the relative ease of departure of a given group is influenced by the nature of the

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[1] M. H. Palmer, ' The Structure and Reactions of Heterocyclic Compounds,' E. Arnold Ltd., London, 1967.

[2] M. L. H. Green, ' Organometallic Compounds,' Methuen and Co., London, 1968, vol. 2, p. 142, and references therein.

[3] A. W. Smalley, C. E. Sullivan, and W. E. McEwen, *Chem. Comm.*, 1967, **5**.

[4] R. H. Kemp, W. A. Thomas, M. Gordon, and C. E. Griffin, *J. Chem. Soc.* (*B*), 1969, 527.

[5] C. E. Griffin, R. P. Peller, K. R. Martin, and J. A. Peters, *J. Org. Chem.*, 1965, **30**, 97.

[6] W. E. McEwen, G. Axelrad, M. Zanger, and C. A. VanderWerf, *J. Amer. Chem. Soc.*, 1965, **87**, 3948.

[7] W. E. McEwen, K. F. Kumli, A. Blade-Font, M. Zanger, and C. A. VanderWerf, *J. Amer. Chem. Soc.*, 1964, **86**, 2378.

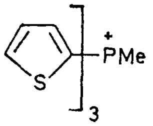
non-departing groups.[6,8] Thus the presence of electron-withdrawing substituents accelerates the reaction, whereas electron-donating systems tend to retard the reaction. Such inductive effects are best understood in terms of their ability to promote (or inhibit) the utilisation of the phosphorus 3*d* orbitals in the formation of the hydroxyphosphorane in the initial step of the reaction; electron-withdrawing substituents cause a contraction of the normally diffuse 3*d* orbitals, and the latter are therefore more readily available for overlap, whereas for electron-donating substituents, the converse is true.[9,10]

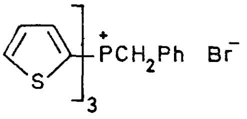
Third-order rate constants and activation parameters for the alkaline hydrolysis of heteroaryl- and aryl-phosphonium salts in 50% aqueous ethanol

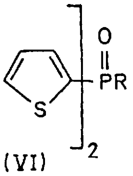
| Compound | Concentration (M) | *k* (l.² mole⁻² min.⁻¹) 5° | 14·8° | 40·2° | $E_A$ (kcal. mole⁻¹) | log *A* |
|---|---|---|---|---|---|---|
| (IV) | 0·001 | 1·13 × 10⁶ | 2·66 × 10⁶<br>2·56 × 10⁶<br>2·68 × 10⁶ | 2·06 × 10⁷ * | 14·55<br>(60·82 kJ mole⁻¹) | 17·46 |
| | 0·0015 | 1·015 × 10⁶ | — | — | | |
| | 0·002 | 1·072 × 10⁶ | — | — | | |
| (V) | 0·001 | 0·161 × 10⁶ | 0·430 × 10⁶<br>0·491 × 10⁶<br>0·461 × 10⁶ | 3·14 × 10⁶ * | 13·57<br>(56·72 kJ mole⁻¹) | 15·96 |
| | 0·0015 | 0·237 × 10⁶ | — | — | | |
| | 0·002 | 0·199 × 10⁶ | — | — | | |
| $[Ph_3P^+Me]I^-$ | 0·05 | — | — | 0·014 | 31·4 †<br>(131·25 kJ mole⁻¹) | 21·6 † |
| $[Ph_3P^+CH_2Ph]Br^-$ | 0·01 | — | — | 12·57 | 18·0 ‡<br>(75·24 kJ mole⁻¹) | — |

* Calculated value. † Ref. 9. ‡ Ref. 11.

Reduction of the positive charge on phosphorus by means of $p_\pi$–$d_\pi$ overlap with the π-system of a π-excessive heteroaryl ring system might also be expected to lead to a reduction in the overall rate of the alkaline decomposition of phosphonium salts. The course and rate of hydrolysis of the salts, methyltri-(2-thienyl)-phosphonium iodide (IV) and benzyltri-(2-thienyl)-phosphonium bromide (V), have therefore been studied and the kinetic data have been compared with those for the hydrolysis of the corresponding phenylphosphonium salts. The methylphosphonium salt (IV) hydrolyses with the loss of thiophen to give methyldi-(2-thienyl)-phosphine oxide (VI; R = Me); loss of thiophen also occurs on hydrolysis of the benzyl salt (V) to give benzyldi-(2-thienyl)phosphine oxide (VI; R = $PhCH_2$). The course of the latter reaction contrasts with the hydrolysis of benzyltriphenylphosphonium bromide which proceeds with loss of the benzyl group to give triphenylphosphine oxide. The above reactions indicate that the 2-thienyl anion is distinctly more stable than the benzyl anion, and that the order of carbanion stabilities among the above groups is: 2-thienyl > benzyl > phenyl > alkyl.


(IV)


(V)


(VI)

The kinetics of the above reactions in 50% (v/v) aqueous ethanol have been studied. The hydrolyses proceed very rapidly at room temperature, even when the starting concentration of phosphonium salt and of sodium hydroxide is 0·001M. At 5°, however, the reactions may be followed conveniently if the decrease in conductance of the solution is monitored as the reaction proceeds. The hydrolyses of both salts at 5° follow a third-order rate law, in accordance with the generally accepted mechanism. Studies of the temperature dependence of the rate constants (Table) give for the hydrolysis of the salt (IV) an energy of activation of 14·5 kcal./mole (60·8 kJ mole⁻¹) and for the hydrolysis of (V) an energy of activation of 13·6 kcal./mole (56·7 kJ mole⁻¹). Both energies of activation for the cleavage of a 2-thienyl–phosphorus bond are markedly lower than for hydrolyses in which a phenyl carbanion is the leaving group, for which [9] the energy of activation is in the region of 32 kcal./mole (133·7 kJ mole⁻¹). Studies of the hydrolysis of $[Ph_3\overset{+}{P}Me]I^-$ in solvents containing a much higher proportion of ethanol (which accelerates the reaction) than that used in the above study have been reported,[9] but no data appear to be available for 50% v/v aqueous ethanol solutions. In order that a comparison of the rates of hydrolysis of $[Ph_3\overset{+}{P}Me]I^-$ and the salt (IV) could be made, the hydrolysis of the former has been studied in this solvent at 40·2°, at initial concentrations of phosphonium salt and sodium hydroxide of 0·05M, although reaction was then very slow. Extrapolation of rate data at 5° for the salt (IV) shows that at 40·2°, the hydrolysis of the thienyl

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[8] M. Zanger, C. A. VanderWerf, and W. E. McEwen, *J. Amer. Chem. Soc.*, 1959, **81**, 3806.

[9] G. Aksnes and L. J. Brudvick, *Acta Chem. Scand.*, 1963, **17**, 1616.

[10] D. P. Craig, A. Maccoll, R. S. Nyholm, L. E. Orgel, and L. E. Sutton, *J. Chem. Soc.*, 1954, 332.

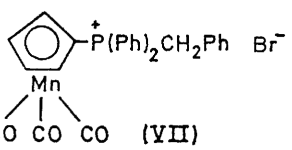
salt (IV) occurs 1·45 × 10$^8$ times faster than that of $[Ph_3\overset{+}{P}Me]I^-$. Similarly, the benzyl salt (V) hydrolyses some 2·5 × 10$^5$ times more rapidly than $[Ph_3\overset{+}{P}CH_2Ph]$-$Br^-$, under the same conditions; although in this case the validity of comparison between the rates is limited by the different course of the reactions. The hydrolyses of both $[Ph_3\overset{+}{P}Me]I^-$ and $[Ph_3\overset{+}{P}CH_2Ph]Br^-$ in 50% (v/v) aqueous ethanol at 40·2° follow a third-order rate law, as established for these reactions under other conditions.[9,11]

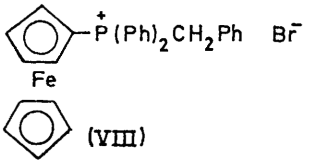
The very rapid rate of hydrolysis of the 2-thienylphosphonium salts [(IV) and (V)] would suggest that stabilisation of the phosphonium ion by $p_\pi$–$d_\pi$ overlap is of little importance; if it occurs at all, its effect must be masked by the facile cleavage of the ring-phosphorus bond in the rate-determining step due to the apparent over-riding stability of the 2-thienyl carbanion.

That the 2-thienyl group has a powerful electron-withdrawing (—*I*) character, due to the electronegative sulphur atom, is revealed by a comparison of the p$K_a$ data for thiophen-2-carboxylic acid (p$K_a$ 3·5), thiophen-3-carboxylic acid (p$K_a$ 4·1), and benzoic acid (p$K_a$ 4·20).[12] Thus in addition to being π-excessive, a 2-thienyl group is more electronegative than a phenyl group. As discussed above, the presence of electron-withdrawing substituents attached to the phosphorus in a phosphonium salt would be expected to accelerate the hydrolysis reaction; this factor, together with the relative stability of the 2-thienyl anion, doubtless accounts for the very rapid hydrolysis of the salts [(IV) and (V)].*

It is of interest to consider the factors promoting stabilisation of the 2-thienyl anion. Either inductive stabilisation due to the electronegative sulphur atom or overlap of the carbanion *sp*$^2$ orbital with a sulphur 3*d* orbital, or both, may be suggested. The importance of the influence of inductive effects on carbanion stability has recently been demonstrated.[13]

The importance of the inductive effect of substituents on the rates of hydrolysis of phosphonium salts has recently been discussed further by Reilly and McEwen,[14] who showed that the cyclopentadienyl-phosphonium salt of tricarbonylmanganese (VII) hydrolysed faster than $[Ph_3\overset{+}{P}CH_2Ph]Br^-$, which in turn hydrolysed faster than the ferrocenylphosphonium salt (VIII). It was suggested that the electron-withdrawing effect of the carbonyl groups in the cymantryl group promoted attack at the phosphorus, in contrast to the 'electron-rich' ferrocenyl group. The question of stabilisation of the ferrocenylphosphonium salt by π-overlap suggested earlier [3] to explain the lower rate of hydrolysis, was not discussed further. The relative electron-withdrawing nature of the above organometallic substituents was further supported by a comparison of the p$K_a$ values of the carboxylic acid derivatives.


(VII)


(VIII)

It would seem likely, therefore, that in the alkaline hydrolysis of phosphonium salts, the inductive effects of the substituents and the stability of the leaving group as a carbanion are of greatest importance in determination of the rate of the reaction. Any π-bonding effects between substituents and the empty 3*d* orbitals of phosphorus do not appear to play a significant role. Further studies of the chemistry of heteroarylphosphorus compounds are in progress.

## EXPERIMENTAL

$^1$H. n.m.r. spectra were recorded at 60 MHz on a Perkin-Elmer R10 Spectrophotometer. G.l.c. analyses were carried out with a Pye series 104 chromatograph equipped with a 25 ft. column of 10% silicone oil on Celite, and a flame ionisation detector.

*Preparation of Phosphonium Salts.*—Tri-(2-thienyl)-phosphine was prepared by the Grignard procedure from 2-iodothiophen as described by Issleib and Brack.[15] The phosphine in benzene solution with methyl iodide gave *methyltri-(2-thienyl)phosphonium iodide* (IV), m.p. 189° (Found: C, 37·73; H, 3·05. $C_{13}H_{12}IPS_3$ requires C, 37·0; H, 2·85%); τ ($CF_3COOH$): 1·71 (3H, sextuplet), 2·05 (3H, octet), 2·42 (3H, octet), and 7·10 (3H, d, $^2J_{PCH}$ = 14·1 Hz). The n.m.r. spectrum of this compound in the aromatic region closely resembles the published spectrum of tri-(2-thienyl)phosphine oxide.[4]

The phosphine in benzene solution with benzyl bromide gave *benzyltri-(2-thienyl)phosphonium bromide* (V), m.p. 273—275° (Found: C, 50·2; H, 3·55. $C_{19}H_{16}BrPS_3$ requires C, 50·55; H, 3·55%); τ ($CF_3COOH$): 1·72 (3H, sextuplet), 2·1—3·1 (11H, m), and 5·5 (2H, d, $^2J_{PCH}$ = 14·0 Hz). The salts $[Ph_3\overset{+}{P}Me]I^-$ and $[Ph_3\overset{+}{P}CH_2Ph]Br^-$ were prepared by alkylation of triphenylphosphine, and had m.p. values in accord with literature.

*Alkaline Hydrolysis of Thienylphosphonium Salts.*—(a) *Methyltri-(2-thienyl)phosphonium iodide* (IV). To the salt (0·2 g., 1 mol.) dissolved in aqueous ethanol (50% v/v, 25 ml.), was added sodium hydroxide solution (0·02M in aqueous ethanol, 50% v/v, 25 ml., 1 mol.) After 2 hr., the

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* A referee has commented that rate increases of the order of 1 × 10$^8$ are rather large to be accounted for by 'inductive effects'. However, it should be borne in mind that the overall rate constant for the hydrolysis of a phosphonium salt, although largely governed by the slow step (iii), is composite, and can be expressed as the product of the equilibrium constants of steps (i) and (ii) and the rate constant of step (iii). Consequently, moderate increases in these constants of the order of 10$^2$—10$^3$ would result in an overall rate increase of *ca.* 10$^8$ for the above reactions.

[11] G. Aksnes and J. Songstad, *Acta Chem. Scand.*, 1962, **16**, 1426.

[12] A. Albert, 'Heterocyclic Chemistry,' Athlone Press, London, 1968.

[13] A. Streitwieser and D. Holtz, *J. Amer. Chem. Soc.*, 1967, **89**, 692.

[14] G. J. Reilly and W. E. McEwen, *Tetrahedron Letters*, 1968, 1231.

[15] K. Issleib and A. Brack, *Z. anorg. Chem.*, 1957, **292**, 245.

solution was evaporated on a steam-bath. The residue was extracted with water (10 ml.) and chloroform (2 × 10 ml.). The chloroform layer was dried ($Na_2SO_4$) and evaporated to give *methyldi-*(2-*thienyl*)*phosphine* oxide (VI; R = Me), m.p. 57—60° (after drying over $P_2O_5$) (Found: C, 47·3; H, 3·95. $C_9H_9OPS_2$ requires C, 47·35; H, 3·95%); $\tau$ ($CDCl_3$): 2·0—2·4 (4H, m), 2·65 (2H, m), and 7·74 (3H, d, $^2J_{PCH}$ = 14·2 Hz). The presence of thiophen in the reaction mixture was confirmed by g.l.c.

(b) *Benzyltri-*(2-*thienyl*)*phosphonium bromide* (V). To the salt (0·22 g., 1 mol.), in aqueous ethanol (50% v/v, 25 ml.) was added sodium hydroxide solution (0·02M in aqueous ethanol, 50% v/v, 25 ml., 1 mol.). After 2 hr. the solution was diluted with an equal volume of water and allowed to stand for a further period. A mass of fine needle-like crystals of *benzyldi-*(2-*thienyl*)*phosphine oxide* (VI; R = $CH_2Ph$), m.p. 131—132°, was deposited (Found: C, 59·7; H, 4·3. $C_{15}H_{13}OPS_3$ requires C, 59·2; H, 4·25%); $\tau$ ($CDCl_3$): 2·1—3·0 (11H, m) and 6·31 (2H, d, $^2J_{PCH}$ = 15·25 Hz). The presence of thiophen in the reaction mixture was confirmed by g.l.c.

*Kinetic Studies*.—(a) *Tri-*(2-*thienyl*)*phosphonium salts*. The hydrolyses were carried out at 5 and 14·8° in 50% (v/v) aqueous ethanol, at equal initial concentrations of phosphonium salt and sodium hydroxide in the range 0·001—0·002M, and were followed by measurement of the decrease in conductance of the solution as the reaction proceeded, using a Lock conductance bridge. The solutions were thermostatted in a bath controlled to ±0·1°. The reactions were followed to 70% completion, and the data were evaluated as follows.

At $t = 0$ (sec.), the conductance of the solution $\Lambda_{(t=0)}$, is proportional to the concentrations of phosphonium salt and sodium hydroxide,

$$i.e. \qquad \Lambda_{(t=0)} \propto \{[R_4P^+X^-] + [Na^+OH^-]\}$$

At $t = \infty$, the concentration of $[R_4P^+OH^-]$ is zero, and the conductance of the solution is given by:

$$\Lambda_\infty \propto [Na^+X^-]$$

$$\text{Hence} \qquad [R_4P^+OH^-]_{t=0} \propto (\Lambda_{(t=0)} - \Lambda_\infty)$$

$$\text{and} \qquad [R_4P^+OH^-]_{t=0} = P(\Lambda_{(t=0)} - \Lambda_\infty)$$

where $P$ is a proportionality constant which may be evaluated, the initial concentration ($a$) of phosphonium hydroxide being known.

The zero-time reading, $\Lambda_{(t=0)}$, was evaluated from the sum of the individual conductivities of solutions of the phosphonium salt and sodium hydroxide, under the same conditions. Plots of the conductance of individual solutions of the phosphonium salt and sodium hydroxide against concentration in the range 0·001—0·002M were linear.

At time $t$ after the start of the reaction, the conductance of the solution has fallen to $\Lambda_t$, and the concentration of the unchanged phosphonium hydroxide ($a - x$) is given by

$$[R_4P^+OH^-] = P(\Lambda_t - \Lambda_\infty)$$

Thus the concentration of the unchanged phosphonium hydroxide at time $t$ may be evaluated from the conductance data.

The order of the reaction was then evaluated by the method of integration. In every case, a plot of $1/(a - x)^2$ *vs.* $t$ was linear up to 70% completion, whereas a second-order plot of $1/(a - x)$ *vs.* $t$ had a pronounced curvature over the range studied. Third-order kinetics were also confirmed by the 'half-life method', a plot of $\log t_{\frac{1}{2}}$ *vs.* $-\log a$ being linear, the slope giving the order of the reaction as three. Rate constants were independent of the initial concentration of phosphonium salt and sodium hydroxide over the range 0·001—0·002M, and were reproducible. Rate and activation data are tabulated in the text.

(b) *Triphenylphosphonium salts*. The hydrolysis reactions were carried out at 40·2° in 50% (v/v) aqueous ethanol, at equal initial concentrations of phosphonium salt and sodium hydroxide, and were followed by a conventional back-titration procedure, in which the concentration of $OH^-$ was determined. The reactions were followed to 50% completion, and the data were evaluated by the method of integration, which confirmed third-order kinetics as reported by other workers.[9,11] The rate data are given in the text.

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