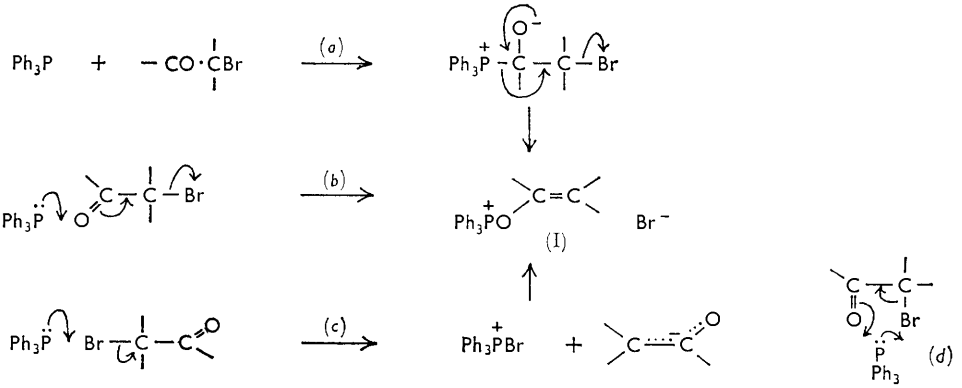
947. *The Reaction of Triphenylphosphine with α-Bromo-ketones*

By F. Hampson and S. Trippett

Triphenylphosphine reacts with α-bromo-ketones to give in general enolphosphonium salts (I).[1] The reaction has been envisaged as proceeding *via* nucleophilic attack of the phosphine (*a*) on the carbon of the carbonyl group, (*b*) on the carbonyl oxygen, and (*c*) on the halogen. A cyclic mechanism (*d*) is also possible.[2] Borowitz and Virkhaus [3] showed that the enolate anion (II) is the probable intermediate in the reaction of triphenylphosphine with phenacyl bromide to give the quaternary salt, for in the presence of proton donors acetophenone is a major product.



We have studied the kinetics of the reaction of triphenylphosphine with the ketones $R^1CO{\cdot}CHBr{\cdot}R^2$ (III; R^1 = 2,4,6-trimethylphenyl, R^2 = H, Me) in methanol and ethanol by following the change in absorption at 262 mμ. The reactions were strongly acid-catalysed which precluded their study in aprotic solvents because of the production of acid by reaction with traces of water and which also led to slightly curved second-order plots for reactions in weakly acid solution. In the presence of alkali or in more strongly acid solution the reactions gave good second-order plots to >70% completion. The Table gives the activation parameters for the non-acid-catalysed and the acid-catalysed reactions:

	Non-catalysed			Acid-catalysed
R^2	Solvent	ΔH^*	ΔS^* (e.u.)	ΔH^* (kcal. mole^{-1})
H	MeOH	7·8 ± 0·3	−41	10·5 ± 1·0
H	EtOH	9·8 ± 0·9	−36	—
Me	MeOH	10·5 ± 0·6	−37	9·8 ± 1·0

Mesityl ketones are highly hindered to addition and mechanism (*a*) cannot here be operating. For the non-catalysed reactions the high negative entropies of activation and the increase in ΔH^* on going from methanol to ethanol indicate a dipolar transition state and preclude a fully synchronous cyclic mechanism. The increase in ΔH^* on placing a methyl on the halogen-bearing carbon suggests that this carbon acquires a negative charge in the transition state. This conclusion is supported by the fact that the reactions of di- and tri-bromomethyl 2,4,6-trimethylphenyl ketones with triphenylphosphine were too fast to measure under the conditions employed. The results are consistent either with mechanism (*c*) or with a non-synchronous cyclic mechanism in which charge accumulates on the α-carbon.

The acid-catalysed reactions, which must involve protonation of the bromo-ketones, are much faster than the competing non-catalysed reactions despite the similar enthalpies of activation. This must be a consequence of the more positive entropies of activation

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[1] S. Trippett, *J.*, 1962, 2337; I. J. Borowitz and L. I. Grossman, *Tetrahedron Letters*, 1962, 471; H. Hoffmann and H. J. Diehr, *ibid.*, p. 583.

[2] H. Hoffmann and H. J. Diehr, *Angew. Chem. Internat. Edn.*, 1964, **3**, 737.

[3] I. J. Borowitz and R. Virkhaus, *J. Amer. Chem. Soc.*, 1963, **85**, 2783.

expected for reactions between ions and neutral molecules, in which charge is dispersed in the transition state. Protonation of the bromo-ketones could be on oxygen or on halogen; a decision is not possible on the available evidence.

The mechanism of the Perkow reaction between α-halogenocarbonyl compounds and trialkyl phosphites has been the subject of much speculation.[4] Tribromomethyl 2,4,6-trimethylphenyl ketone reacts vigorously with triethyl phosphite to give a vinyl phosphate; the Perkow reaction can not here be proceeding by a mechanism analogous to (*a*) above.

Experimental.—Bromomethyl 2,4,6-trimethylphenyl ketone,[5] b. p. 120—126°/1 mm., was recrystallised from ethanol and then repeatedly from light petroleum (b. p. 40—60°), m. p. 55—56°; α-bromoethyl 2,4,6-trimethylphenyl ketone,[6] b. p. 125—128°/1·5 mm., crystallised repeatedly from light petroleum (b. p. 40—60°) at −20° had m. p. 18°; triphenylphosphine was recrystallised repeatedly from ethanol, m. p. 80·5°.

The reactions were conducted at initial concentrations of both phosphine and ketone of $7{\cdot}40 \times 10^{-3}$M, in thermostats accurate to $\pm 0{\cdot}02°$. Aliquot portions of 1 ml. were diluted to 100 ml., with the alcohol employed, for measurement of optical density. In the fast acid-catalysed reactions the diluent was alcoholic 10^{-3}N-NaOH. The initial absorbances were calculated from those of the reactants; the final absorbances agreed with those calculated for the products. In methanolic 0·0128N-NaOH at 40°, the reactions with di- and tri-bromomethyl 2,4,6-trimethylphenyl ketones were complete in less than 1 min.

To obtain the rate of an acid-catalysed reaction the rate of the reaction at the same temperature in the presence of base was subtracted from the observed rate.

Bromomethyl ketone in methanol

Temp.	10^3N	10^2k (l. moles^{-1} sec.$^{-1}$)	Temp.	10^3N	10^2k
40°	5·48-NaOH	6·24	50	13·3-HBr	40·6
25	10·8-NaOH	3·32	40	17·8-HBr	28·4
40	10·8-NaOH	6·50	40	9·7-HCl	18·3
50	10·8-NaOH	9·06	25·3	8·1-NaOEt*	0·166
40	0·91-HBr	10·68	40	8·1-NaOEt*	0·38
40	4·52-HBr	13·84	50	8·1-NaOEt*	0·586
40	8·82-HBr	19·78			
25	13·3-HBr	11·38			
40	13·3-HBr	24·6			

* In EtOH.

α-Bromoethyl ketone in methanol

Temp.	10^3N	10^3k	Temp.	10^3N	10^3k
25°	5·48-NaOH	2·68	40°	8·0-HBr	75·2
40	5·48-NaOH	5·84	25·3	12·8-HBr	54·4
50	5·48-NaOH	10·34	40	12·8-HBr	129·2
40	140·9-NaOH	5·86	50	12·8-HBr	202
40	4·04-HBr	56·2	40	1·68-HBr	150·8

Reaction of triphenylphosphine with bromomethyl 2,4,6-*trimethylphenyl ketone*. A solution of the ketone (4·43 g.) and triphenylphosphine (4·83 g.) in methanol (150 ml.) containing constant-boiling hydrobromic acid (1 ml.) was kept at 50° for 15 hr. Solvent was then removed under reduced pressure and the residue triturated with light petroleum (b. p. 40°). Filtration gave triphenylphosphine oxide (4·82 g.) m. p. and mixed m. p. 153—154° [from light petroleum (b. p. 100—120°)]. Evaporation of the filtrate and distillation gave acetomesitylene (1·75 g.), b. p. 120—125°/14 mm., having an infrared spectrum identical with that of an authentic sample,

Reaction of tribromomethyl 2,4,6-*trimethylphenyl ketone with triethyl phosphite*. A solution of the ketone (21·5 g.) in benzene (20 ml.) was added slowly to a stirred solution of triethyl phosphite (8 g.) in benzene (50 ml.) at 0°. Fractional distillation then gave ethyl bromide (3·04 g.), b. p. 36—38°. Removal of solvent from the residue and trituration with light petroleum (b. p. 40—60°) at −15° gave *diethyl* 1-(2′,4′,6′-*trimethylphenyl*)-2,2-*dibromovinyl phosphate* (14·8 g.), m. p. 66—66·5° [from light petroleum (b. p. 40°)] (Found: C, 39·8; H, 4·75. $C_{15}H_{21}Br_2O_4P$ requires C, 39·5; H, 4·7%), having no absorption in the infrared between 5·8 and 6·2 μ.

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[4] F. W. Lichtenthaler, *Chem. Revs.*, 1961, **61**, 607.

[5] W. A. Jacobs and M. Heidelberger, *J. Biol. Chem.*, 1915, **21**, 459.

[6] C. H. Fisher, H. R. Snyder, and R. C. Fuson, *J. Amer. Chem. Soc.*, 1932, **54**, 3665.