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Kinetics and Mechanism of Ketophosphonate Formation from Triethyl Phosphite and Aryl Substituted α-Bromoacetophenones

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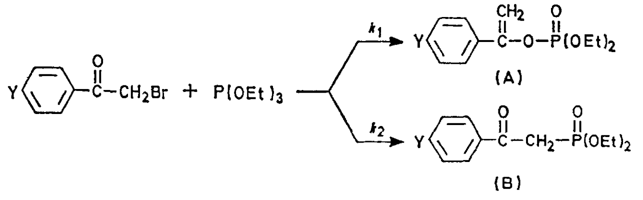
Summary A negative Hammett ρ value ($-0{\cdot}22$) suggests a mechanism involving initial attack on the brominated carbon atom by phosphorus, in the formation of ketophosphonate from triethyl phosphite and aryl substituted α-bromoacetophenones.

The reactions of α-bromoketones with triethyl phosphite lead to enol-phosphates (A) (Perkow reaction) and ketophosphonates (B) (Arbuzov reaction). Numerous studies have appeared on the scope and mechanism of the Perkow reaction.[1-6] The large negative entropies of activation[2-4] and positive ρ values, obtained in the case of aryl substituted-α-chloroacetophenones,[1] α-chloro- and α-bromoisobutyrophenones,[3] are best explained by a pathway involving a rate-determining addition of phosphite to carbonyl carbon.



The reaction of α-bromoketones with triphenylphosphine in aprotic media to give ketophosphonium bromides proceeds *via* S_N2 displacement of bromide ion.[7] The evidence for this conclusion included kinetic studies of reactions of α-bromoacetophenones or α-bromopropiophenones with triphenylphosphine (ρ 0·44, 0·67).[7]

Table

Kinetic data[a] on the reactions of triethyl phosphite with aryl-*p*-substituted α-bromoacetophenones

Y	k_1 (Y)/k_2 (Y)[b]	k_1 (Y)/k_1 (H)[c]	k_2 (Y)/k_2 (H)[c]
NO_2	29·0	18·1	0·641
Br	2·53	2·12	0·862
Cl	2·54	2·17	0·881
F	1·24	1·156	0·956
H	1·03	1·00	1·00
Me	0·43	0·437	1·05
MeO	0·173	0·183	1·09

[a] Reactions were carried out at 40 °C under nitrogen at 0·1 M concentration in benzene. [b] Kinetics of reaction were followed by n.m.r. or by v.p.c. on 5% SE-30 in 6 ft × $\frac{1}{8}$ in columns. [c] These values were determined from competition experiments by v.p.c. using calibration curves.

No kinetic studies have been reported on ketophosphonate formation and we now report the reactions of a series of aryl substituted α-bromoacetophenones with triethyl phosphite. The reaction mixture of (A) and (B) was studied in benzene using n.m.r.[8,9] and v.p.c. analysis.[10] The reactions are first order in halogenoketone and first order in triethyl phosphite. We have determined the rates for the Perkow and the Arbuzov reactions (see Table).

The use of σ values[11] gives a linear Hammett plot (ρ 1·64, confidence level 99·9%) with the data of the Perkow reaction. This positive ρ value is in good agreement with those obtained in other cases.[1,3]

Our most important finding is of a small Hammett ρ value (ρ − 0·22, confidence level 99·9%) calculated using σ values[1] with the data for ketophosphonate products. This observed ρ value is not consistent with attack on bromine. Thus, it is expected that initial attack on bromine to give an enolate bromotriethylphosphonium ion pair would be rate determining, and should give a positive ρ value comparable with that of the formation of benzoate from benzoic acid (ρ 1·00 in water, 1·96 in ethanol[11]). The negative value could be explained by a mechanism involving bimolecular nucleophile attack of the brominated carbon atom by triethyl phosphite.

This mode of attack explains the steric effects found with normally hindered bromoketones. Only 20% of ketophosphonate is obtained in the reaction of α-bromopropiophenone with triethyl phosphite,[9] and ketophosphonate formation is excluded in the cases of α-bromoisobutyrophenones or 2′,4′,6′-trimethyl-α-bromo-isobutyrophenone.[3] Trialkyl phosphites do not debrominate most α-bromoketones in the presence of alcohols or even acetic acid,[12] although triphenylphosphine debrominates α-bromoketones in protic media.[13]

The reactions of α-halogenoketones with tricovalent organophosphorus reagents can be correlated with hard and soft acid base theory.[14] The relatively 'soft' triphenylphosphine reacts with α-halogenoketones at the 'soft' halogen atom to give ketophosphonium or enol phosphonium halides.[15] The 'harder' trialkyl phosphites react with α-halogenoketones at the 'harder' sites; carbonyl carbon to give enol phosphate (major process) and the brominated carbon atom to give ketophosphonate (minor process).

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