The Reactivity of 2-Bromo-1-phenylethanone (Phenacyl Bromide) toward Nucleophilic Species

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Summary A comparison of second-order rate constants for reactions of 2-bromo-1-phenylethanone (phenacyl bromide) and methyl iodide with various nucleophiles in acetonitrile at 25·0 °C reveals that the rate enhancement due to the carbonyl group in the position adjacent to the reacting carbon atom in alkyl halides is not a general effect but is very dependent upon the nucleophile.

Over 50 years ago Conant and his co-workers[1] published a series of studies on the reactivity of alkyl chlorides toward the iodide ion in acetone [equation (1)], drawing attention

$$\mathrm{RCl + KI \xrightarrow{Me_2CO} RI + KCl} \tag{1}$$

to the significant rate enhancement caused by a carbonyl group in the position adjacent to the reaction centre, an observation originally made by Slator and Twiss.[2] Conant's results have later received general acceptance and are repeatedly quoted, even in modern textbooks.[3] Several theories have been forwarded to account for the high reactivity of α-halogeno-ketones and related compounds.[4] However, reports in the literature where small rate enhancements have been observed[5] seem to have been neglected.

We have therefore performed a kinetic study at 25·0 °C in acetonitrile of reactions between a variety of nucleophiles and 2-bromo-1-phenylethanone (phenacyl bromide) and have compared the results with the corresponding rate constants for reactions of methyl iodide determined under similar experimental conditions. Methyl iodide was chosen as the reference alkyl halide since the MeI-nucleophilicity scale has been found to be a valuable measure of the discriminating power of the usual alkyl halides toward nucleophiles in bimolecular substitution reactions in both protic and aprotic solvents.

Our present results (Table) clearly illustrate that the often quoted rate enhancement due to the α-carbonyl group is not a general effect. Apparently, only for reactions with nucleophiles which are able to enter into a 'tight' transition state (a transition state containing a linear three-centre arrangement with an sp^2 hybridized central carbon atom), does the α-carbonyl group exert a significant influence upon reaction rates due to its $+E$ effect.[6] The effect appears to be especially pronounced for reactions of ionic nucleophiles, *e.g.* Finkelstein reactions, for which the transition states are rather symmetrical. For reactions of amines, on the other hand, a class of nucleophiles which are known to react with alkyl halides *via* 'early' transition states,[7] the central carbon atom is mainly sp^3 hybridized in the transition state and no conjugation with the α-carbonyl group is possible. For the remaining uncharged nucleophiles there is no detailed information with regard to the structure of the transition state in their reactions with alkyl halides, but it has recently been suggested that the ability of uncharged nucleophiles to enter into a 'tight' transition state should be related to the stability of the corresponding ylides.[8] (Compare rate ratios for triethylamine and pyridine and for dimethylsulphide and thiourea.) The calculated rate ratios listed in the Table may thus act as a valuable measure for the extent of bond making prior to bond breaking in alkylation reactions of the various nucleophiles.

From the data in the Table it is apparent that the MeI-nucleophilicity scale is a poor measure of the reactivity of nucleophiles toward 2-bromo-1-phenylethanone. Apparently charge and polarizability of the nucleophile are far more important for reactions with the latter substrate. Besides, low steric demands of the incoming nucleophile appear especially favourable for reactions with 2-bromo-1-phenylethanone which allow the nucleophile to adjust to a 'tight' transition state.

It should be emphasized that the reactions studied by Conant and his co-workers[1] are only forced to proceed owing to the insolubility of potassium chloride in acetone. Actually, under homogeneous conditions in acetone and other dipolar aprotic solvents, the reverse reactions take place since the carbon basicity of the chloride ion is

Table. Second-order rate constants (k_2 l mol^{-1} s^{-1}) in acetonitrile at 25·0 °C together with calculated rate ratios

Nucleophile	k_2(PhCOCH$_2$Br)	k_2 (MeI)	$\frac{k_2(\mathrm{PhCOCH_2Br})}{k_2\,(\mathrm{MeI})}$
Cl$^-$ [a]	*ca.* 8·0	$7{\cdot}0 \times 10^{-2}$	110
$(NH_2)_2CS$	$3{\cdot}3 \times 10^{-1}$ [b]	$6{\cdot}26 \times 10^{-3}$	53
NCS$^-$ [a]	$6{\cdot}2 \times 10^{-1}$	$2{\cdot}06 \times 10^{-2}$	30·5
NCSe$^-$ [a]	4·7	$1{\cdot}77 \times 10^{-1}$	26·6
Pyridine	$2{\cdot}95 \times 10^{-3}$	$4{\cdot}17 \times 10^{-4}$	7·07
Ph_3P	$2{\cdot}64 \times 10^{-2}$	$5{\cdot}94 \times 10^{-3}$	4·44
Me_2S	$7{\cdot}27 \times 10^{-4}$	$2{\cdot}26 \times 10^{-4}$	3·22
Ph_3As	$6{\cdot}76 \times 10^{-5}$	$3{\cdot}15 \times 10^{-5}$	2·15
Me_2NPh	*ca.* $7{\cdot}4 \times 10^{-5}$ [c]	$2{\cdot}00 \times 10^{-4}$	0·37
Et_3N	$5{\cdot}00 \times 10^{-3}$	$3{\cdot}61 \times 10^{-2}$	0·14

[a] The non-hygroscopic and very soluble bis(triphenylphosphine)-iminium salts, $[(Ph_3P)_2N]^+\ X^-$, were the source of the ionic nucleophiles (A. Martinsen and J. Songstad, *Acta Chem. Scand.*, 1977, **A31**, 645). [b] The product of the reaction is the substituted thiazolium bromide but the rate determining step is the formation of the isothiouronium salt. [c] Determined from the first 5—8% of the reaction by both second and pseudo-first-order kinetic runs.

superior to that of the iodide ion.[9] Furthermore, arguments based on results from kinetic studies of reactions of alkyl halides with iodide ions in dipolar aprotic solvents should be made with circumspection[4] when the weakly dissociated potassium iodide[10] is used as the source of the iodide ions.

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