Mechanisms of Nucleophilic Substitution. Kinetics of the Reactions of Benzyl and Diphenylmethyl Chlorides in Aqueous Acetone

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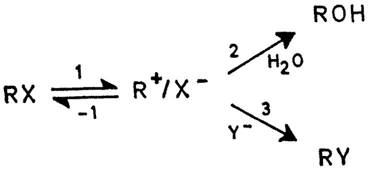
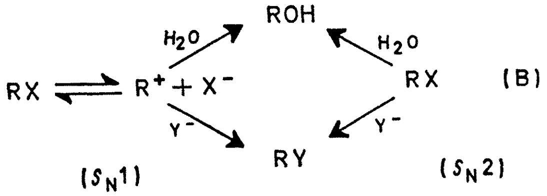
Summary The unified mechanism of nucleophilic substitution cannot account for the present observations on the rates of decomposition of benzyl and diphenylmethyl chlorides in aqueous acetone; this also applies to any extension of the unified mechanism which does not include carbonium ions as intermediates (mechanism S_N1) and a separate reaction path involving direct nucleophilic attack on the substrate (mechanism S_N2).

CONSIDERATIONS of the decomposition of toluene-*p*-sulphonates[1a] and halides[2] (RX) in aqueous organic solvents containing nucleophilic anions (Y^-) have led to the suggestion[1] of a unified mechanism for nucleophilic substitution (Scheme A) which differs from the long accepted S_N mechanisms (Scheme B) in requiring the same initial step (ion-pair formation) for all such reactions. The well-established classification into ***unimolecular*** and ***bimolecular*** processes was rationalised in terms of $k_{-1}/k_2 << 1$ and $k_{-1}/k_2 >> 1$, respectively, a logical extension of Ingold's original definition.[3] Doubts have already been expressed[4,5] about the validity of Scheme A which is now shown to be inapplicable to results for the decomposition of benzyl chlorides, 4-$ZC_6H_4CH_2Cl$(I), in aqueous acetone where some observations demand direct nucleophilic attack on RX (mechanism S_N2), a process explicity omitted[1] from Scheme A.



(A)



The argument rests on the almost entirely *unimolecular* solvolysis of (I; Z = MeO, PhO) and the *bimolecular* solvolysis of (I; Z = H, NO_2) in aqueous acetone, a conclusion demanded by the activation parameters,[6] and the sensitivity of k_{RX} with respect to solvent changes, the nature of Z, and additions of the weakly nucleophilic perchlorate ions. Table 1 compares the relevant results with those for the corresponding diphenylmethyl chlorides, 4-$Z^1C_6H_4$(4-Z^2-C_6H_4)CHCl (II), which are generally considered to react *unimolecularly*;[6] (I; Z = MeO,PhO) and (II) show striking similarities but (I; Z = H, NO_2) behaves quite differently (substituent effects in Table 1a, solvent and salt effects in 1b)

TABLE 1

Solvolysis of benzyl and diphenylmethyl chlorides in aqueous acetone

(I) 4-$ZC_6H_4CH_2Cl$ (II) 4-$Z^1C_6H_4$(4-$Z^2C_6H_4$)CHCl
$k^0_{RX} = k_{RX}$ at initially zero ionic strength

(a) $\log \frac{k^0_{RX}\ (Z = Z_A)}{k^0_{RX}\ (Z = Z_B)}$, 70% acetone, 20°

RX				
	Z_A	MeO	MeO	H
	Z_B	PhO	NO_2	NO_2
(I)		2·192	5·036	0·773
(II; $Z^2 = NO_2$)		1·922	9·217	3·805

(b) Solvent and salt effects

RX	$\log \frac{k^0_{RX}\ (50\%\ Me_2CO)^a}{k^0_{RX}\ (70\%\ Me_2CO)}$	$\frac{k_{RX}(0{\cdot}05\text{M-}NaClO_4)^b}{k^0_{RX}}$	
(I; Z = NO_2)	3·5	0·961[c]	—
(I; Z = H)	7·4	0·990[c]	—
(I; Z = PhO)	18·1	—	1·128[d]
(I; Z = MeO)	17·7	1·062[c]	1·159[d]
(II; Z^1 = H, $Z^2 = NO_2$)	16·4	1·039[c]	—
(II; Z^1 = H, Z^2 = H)	—	—	1·151[d]
(II; Z^1 = Ph, $Z^2 = NO_2$)	—	—	1·171[d]

[a] At 50°; [b] at 20°, standard error *ca.* 0·003; [c] 50% acetone; [d] 70% acetone.

TABLE 2

The effect of 0·05M-*salts* (k_{RX}/k^0_{RX}) *on rates of decomposition*

(All figures refer to reaction in 70% acetone at 20°)

4-$ZC_6H_4CH_2Cl$ (I)

	Z			
Salt	MeO[a]	PhO[a]	NO_2[b]	Ph_2CHCl (II)[a]
$NaClO_4$	1·159	1·128	—	1·151
$NaBF_4$	1·131	1·110	—	1·120
$NaNO_3$	1·144	1·109	1·61	1·070
NaBr	1·255	2·49	261	1·091
NaN_3	1·735[c]	20·0	5430	1·136
$k^0_{RX}(s^{-1})$	$2{\cdot}50 \times 10^{-4}$	$1{\cdot}61 \times 10^{-6}$	$2{\cdot}30 \times 10^{-9}$	—
$10^4k_1(s^{-1})$	2·5[d]	—	0·5[e]	—

[a] Standard error of k_{RX}/k^0_{RX} 0·002—0·003; [b] standard error of k_{RX}/k^0_{RX} *ca.* 0·006; [c] the rate coefficient for hydrolysis is reduced by 20% under these conditions; [d] assuming $k_1 = k^0_{RX}$; [e] assuming $k_1 = 2k_{RX}$ (0·1M-NaN_3)—see equation (1).

Assuming the stationary state approximation for the ion-pair, R^+/X^-, scheme A requires the rate law

$$k_{RX} = -\frac{1}{[RX]}\frac{d[RX]}{dt} = k_1\frac{k_2 + k_3[Y^-]}{k_{-1} + k_2 + k_3[Y^-]}$$

$$= \frac{k_1}{1+x}\left(1 + x\frac{\beta[Y^-]}{1 + \beta[Y^-]}\right)$$

where $x = k_{-1}/k_2$ and $\beta = k_3/(k_{-1} + k_2)$. Using the superscript 0 to indicate $[Y^-] = 0$, it then follows that

$$\left.\begin{array}{l} k^0_{RX} \sim k_{RX} \simeq k_1\ (x << 1,\ \textit{unimolecular}\ \text{solvolysis}) \\ k^0_{RX} < k_{RX} < k_1\ (x >> 1,\ \textit{bimolecular}\ \text{solvolysis}) \end{array}\right\} \quad (1)$$

Neither *unimolecular* nor *bimolecular* reaction with Y^- can be kinetically significant if RX undergoes *unimolecular* solvolysis ($x << 1$, $k_{RX} \simeq k_1$) so that the addition of Y^- should then only increase k_{RX} by the amount expected from the salt effect on k_1 ($\leqslant 15\%$ for 0·05 M-salt), as observed for (II) (see Table 2). However, k_{RX}/k^0_{RX} for (I; Z = MeO,PhO) is found to increase progressively with increasing nucleophilic power of Y^- (see Table 2) and attains values greatly in excess of the limit (1·15) predicted by Scheme A from the *unimolecular* solvolysis of these compounds.

Other results reveal further inconsistencies in Scheme A. First, the rate coefficient (k_1) for ion-pair formation by (I) decreases about 5-fold† when Z is changed from MeO to NO_2 (see Table 2) while the same structural alteration in (II) (where $k_1 \simeq k_{RX}$) leads to a 10^9-fold decrease (see Table 1); such a large difference between these two very similar systems would be most surprising. Secondly, the *bimolecular* solvolysis of (I; Z = NO_2) would require the free energy of the activated complex for the attack by water on R^+/X^- (step 2) to be much greater than that for its formation (step 1), with the converse for the *unimolecular* reactions of (II). Diametrically opposite behaviour would however be expected on steric grounds.

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† An even smaller decrease is suggested for reaction in methanol by the results[7] for the effect of added thiophenoxide ions.

Some objections to Scheme A disappears by extension to scheme C, where R^+/X^-, $R^+//X^-$ and R^+ can all react

$$RX \rightleftharpoons R^+/X^- \rightleftharpoons R^+//X^- \rightleftharpoons R^+ + X^- \qquad (C)$$

independently with the solvent and other nucleophiles, though others arise. A detailed discussion of this scheme is deferred but, for example, k_{RX} for (I; Z = NO_2) + N_3^- can then only be explained if azide ions attack one of the ion-pairs at the encounter rate (*k ca.* 10^{11} l mol^{-1} s^{-1}), requiring the relevant ion-pair to be a highly unselective reagent which should react at similar rates with other nucleophiles so that k_{RX} is virtually independent of the nature of Y^-. This is not observed (see Table 2).

Scheme B, however, accounts for all the present results, with concurrent S_N1 and S_N2 reactions of (I; Z = MeO, PhO) with nucleophiles stronger than water (as originally envisaged[2,8]) and S_N2 reactions for (I; Z = NO_2). Mechanism S_N1 is also demanded by the retardation of the hydrolysis of many of the present compounds (RX) by X^- ions,[9]‡ indicative of R^+ as an intermediate since any such retardation by attack of X^- on R^+/X^- or $R^+//X^-$ contradicts the principle of microscopic reversibility. Any general discussion of the mechanism of nucleophilic substitution must therefore include S_N1 and S_N2 processes, as originally suggested by Hughes and Ingold, but it must be stressed that Scheme C with an additional S_N2 reaction path is not excluded by the present observations.

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‡ Chloride ions retard the hydrolysis of (I; Z = MeO) about twice as much as that of (II; Z^1,Z^2 = H) under the same conditions.

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