Can Primary Alkyl Halides Hydrolyse by the Ion-pair Mechanism?

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Summary The standard free energy change for formation of $R^+X^-(aq)$ from $RX(aq)$ is so high in the case of R = Me and Et that primary alkyl halides are unlikely to undergo nucleophilic substitution by the ion-pair mechanism; this mechanism is slightly unfavourable for the case of $R = Pr^i$, but is energetically feasible for the t-butyl halides.

ALTHOUGH Sneen and Larsen's[1] unified ion-pair mechanism of nucleophilic substitution has not been well received,[2,3] even for the original cases of solvolyses of some s-alkyl substrates,[3] Scott[4] has interpreted S_N reactions of the methyl halides in terms of such a mechanism. In its simplest form the ion-pair mechanism reduces to reactions (1) and (2); Scott[4] suggests that for substitutions of methyl halides in water, $k_{obs} = K_1 \cdot k_2$ so that $\Delta G^{\ddagger}_{obs} = \Delta G^{\circ}_1 + \Delta G^{\ddagger}_2$.

$$RX \rightleftharpoons R^+X^- \qquad (1)$$

$$R^+X^- + N \rightarrow \text{Products} \qquad (2)$$

The mechanism thus requires that $\Delta G^{\ddagger}_{obs} > \Delta G^{\circ}_1$ and Scott deduces values of ΔG°_1 that are compatible with this inequality. Now if the ion-pair mechanism was indeed valid for S_N reactions of the methyl halides (the least likely substrates to undergo substitution by such a mechanism), then the general Hughes–Ingold scheme of nucleophilic substitution[5] would consequently be obsolete. An independent assessment of the feasibility of reaction (1) thus seems obligatory.

TABLE 1. *Calculation of* ΔG°_1 *for the reaction* $MeBr(aq) \rightarrow Me^+Br^-(aq)$, *in kcal mol*$^{-1}$ *at* 298 K.

Process[a]	ΔG°
$MeBr(aq) \rightarrow MeBr(g)$	-1[b]
$MeBr(g) \rightarrow Me\cdot(g) + Br\cdot(g)$	$+61$[c]
$Me\cdot(g) \rightarrow Me^+(g)$	$+227$[d]
$Br\cdot(g) \rightarrow Br^-(g)$	-81[e]
$Me^+(g) \rightarrow Me^+(aq)$	-73[f]
$Br^-(g) \rightarrow Br^-(aq)$	-68[f]
$Me^+(aq) + Br^-(aq) \rightarrow Me^+Br^-(aq)$	$+1$[g]
$MeBr(aq) \rightarrow Me^+Br^-(aq)$	$+66$

[a] Standard states are 1 atm(g) and 1 mol l^{-1}(aq). [b] D. M. Alexander, D. J. T. Hill, and L. R. White, *Austral. J. Chem.*, 1971, **24**, 1143. [c] From $\Delta H^{\circ} = 70$ kcal mol^{-1}, J. A. Kerr, *Chem. Rev.*, 1966, **66**, 465, and $\Delta S^{\circ} = 29$ cal K^{-1} mol^{-1} calculated from standard entropies of formation. [d] From $\Delta H^{\circ} = 226{\cdot}9$ kcal mol^{-1}, F. P. Lossing and G. P. Semeluk, *Canad. J. Chem.*, 1970, **48,** 955, together with $\Delta S^{\circ} = -1{\cdot}4$ cal K^{-1} mol^{-1}. [e] From $\Delta H^{\circ} = -82{\cdot}0$ kcal mol^{-1}, J. C. McCoubrey, *Trans. Faraday Soc.*, 1955, **51**, 743 together with $\Delta S^{\circ} = -1{\cdot}4$ cal K^{-1} mol^{-1}. [f] Footnote *e* and R. M. Noyes, *J. Amer. Chem. Soc.*, 1962, **84**, 513; the value for Me^+ has been calculated from a plot of ΔG°_{hyd} against the molar volume of the cations. [g] Compare a K_A value of 0·14- (CsBr), E. M. Hanna, A. D. Pethybridge, and J. E. Prue, *Electrochim. Acta*, 1971, **16**, 677.

In Table 1 is a calculation of the standard free-energy change for reaction (1) (RX = MeBr) in aqueous solution, and in Table 2 are presented results of calculations for a series of alkyl bromides (values of ΔG°_1 for the corresponding chlorides and iodides are quite similar). Although the calculated ΔG_1° values are subject to an error that could be as much as ± 5 kcal mol^{-1}, these calculated values for the primary alkyl halides are so much larger than values of $\Delta G^{\ddagger}_{\text{obs}}$ for the aqueous hydrolyses that it seems energetically quite improbable that simple primary halides hydrolyse (or undergo any S_N reaction) by the ion-pair mechanism. Judging from the data in Table 2, the ion-pair mechanism is slightly unfavourable for S_N reactions of simple secondary halides, though for other secondary substrates the reverse might hold. For the t-butyl halides $\Delta G^{\ddagger}_{\text{obs}} > \Delta G_1^\circ$ so that the ion-pair mechanism is energetically feasible. In these cases it has been suggested[6] that $\Delta G^{\ddagger}_{\text{obs}} = \Delta G_1^{\ddagger}$; the mechanism still demands, however, that $\Delta G^{\ddagger}_{\text{obs}} > \Delta G_1^\circ$, as observed (Table 2).

Table 2. *Comparison of* ΔG° *for reaction* (1) *with* $\Delta G^{\ddagger}_{\text{obs}}$ *for the aqueous hydrolysis of alkyl halides, in kcal mol*$^{-1}$ *at* 298 K.

	RX			
	MeBr	EtBr	Pr^{i}Br	Bu^{t}Br
ΔG_1°	66	43	28	12
$\Delta G^{\ddagger}_{\text{obs}}$	26[a]	26[a]	25[a]	18[b]

[a] R. E. Robertson, *Progr. Phys. Org. Chem.*, 1967, **4**, 213.
[b] E. A. Moelwyn-Hughes, *J. Chem. Soc.*, 1962, 4301.

It should be noted that the final step in the calculation (Table 1) refers to association of a pair of ions to closed ion-pairs plus solvent-separated ion-pairs. If the closed ion-pair[4] is only a fraction of the total, then the ΔG^0 value for association to a closed ion-pair will be more positive than the value tabulated (+1 kcal mol^{-1}). Hence the calculated value of ΔG_1° will be more positive and the discrepancies between ΔG_1° and $\Delta G^{\ddagger}_{\text{obs}}$ for primary alkyl halides (Table 2) will be even larger.

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[1] R. A. Sneen and J. W. Larsen, *J. Amer. Chem. Soc.*, 1969, **91**, 362, 6031.

[2] J. L. Kurz and J. C. Harris, *J. Amer. Chem. Soc.*, 1970, **92**, 4117; B. J. Gregory, G. Kohnstam, A. Queen, and D. J. Reid, *Chem. Comm.*, 1971, 797; M. H. Abraham, *J. Chem. Soc.* (*B*), 1971, 299.

[3] B. J. Gregory, G. Kohnstam, M. Paddon-Row, and A. Queen, *Chem. Comm.*, 1970, 1032; D. J. Raber, J. M. Harris, R. E. Hall, and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, 1971, **93**, 4821.

[4] J. M. W. Scott, *Canad. J. Chem.*, 1970, **48**, 3807; see also J. M. W. Scott and R. E. Robertson, *ibid.*, 1972, **50**, 167.

[5] C. K. Ingold, 'Structure and Mechanism in Organic Chemistry,' Bell, London, 1953.

[6] M. H. Abraham, *J.C.S. Perkin II*, 1972, 1343.