Comments on the Putative Ion Pair Mechanism for Hydrolysis of Methyl Halides and Methyl Perchlorate

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Calculations based on a linear free energy approach to the mechanism of hydrolysis of methyl halides and methyl perchlorate by Scott and Robertson suggest that rate-limiting attack of water (and other nucleophiles) on a preformed ion pair is involved. This result contrasts strongly with that of Abraham, who calculates, *via* a thermodynamic cycle, that the relevant ion pairs have free energies too high to allow their participation in the reactions, which are thus most likely concerted S_N2 processes, and with experimental failure to detect ion pair intermediates in systems potentially more favourable for ion pair formation. The linear free energy approach of Scott is critically examined in the light of recent work by Ritchie, and is seen to rest on false premises. The quasi-thermodynamic treatment of Robertson, Annesa, and Scott is shown to be likewise unsound. The interpretation of the secondary k_H/k_D for methyl perchlorate hydrolysis in terms of an ion-pair intermediate is shown to be unnecessary in that a looser than usual S_N2 transition state is also compatible with the results. The molecular basis of this looseness is discussed.

WITHIN the traditional S_N1–S_N2 framework of nucleophilic aliphatic substitution, methyl halides are commonly considered as model S_N2 substrates [equation (1)].

$$\mathrm{N}\!: + \mathrm{MeX} \longrightarrow [\mathrm{N}\cdots\mathrm{Me}\cdots\mathrm{X}]^{\ddagger} \longrightarrow \mathrm{NMe} + \mathrm{X}\!:^{-} \qquad (1)$$

Sneen [1] has, however, questioned the very existence of the concerted S_N2 mechanism, and has instead proposed a universal ion-pair process, which, for observed second-order kinetic behaviour takes the form shown in equations (2) and (3). The experimental second-order rate

$$\mathrm{MeX} \overset{K_e}{\rightleftharpoons} \mathrm{Me^+X^-} \qquad (2)$$

$$\mathrm{N}\!: + \mathrm{Me^+X^-} \xrightarrow{k_n} \mathrm{NMe} + \mathrm{X^-} \qquad (3)$$

constant is then given by $k_{obs} = K_e k_n$ and the free energy of activation is given by $\Delta G_{obs}^{\ddagger} = \Delta G_e^{\circ} + \Delta G_n^{\ddagger}$. Since the methyl halides are generally regarded as model S_N2 substrates, any demonstration that they actually undergo substitution by the ion-pair mechanism, $S_N$ip, would strongly imply the universal nature of this latter mechanism.

Scott [2] has indeed applied equations (2) and (3) to the nucleophilic substitution of the four methyl halides in aqueous solution. Using a semi-empirical linear free energy approach, he has calculated values of K_e for these four halides and then deduced values of k_n for a variety of nucleophiles. It was shown that the k_n values could be related to a variety of thermodynamic and kinetic phenomena. The same method was later used by Robertson, Annesa, and Scott [3] in assigning the ion-pair mechanism to the neutral hydrolysis of methyl perchlorate. The K_e and ΔG_e° values calculated by Scott [3] for the methyl halides are, however, in serious disagreement with those calculated by Abraham [4] through a thermodynamic cycle. For example Scott [2] finds ΔG_e° for methyl bromide to be 9.8 kcal $\mathrm{mol^{-1}}$ (or 11.2 kcal $\mathrm{mol^{-1}}$ in the later paper [3]), whereas Abraham [4] calculated a value of no less than 66.2 kcal $\mathrm{mol^{-1}}$ for the standard free energy change in reaction (2; $\mathrm{X = Br}$); both calculations refer to aqueous solution at 298 K. Robertson, Annesa, and Scott [3] dismiss the thermodynamic calculation as crude, although they offer no explanation for the enormous discrepancies (above), and no explanation as to why the thermodynamic calculation yields values for the ionisation of the t-butyl halides that are in complete accord with observation.[4] Furthermore, the results of Scott's calculations conflict with a considerable body of recent work [5-12] that suggests that the classical S_N2 mechanism is operative in a number of cases.† McLennan and Martin [5] have put forward the view that the solvolysis of diphenylmethyl *p*-nitrobenzoate is solvent-assisted in ethanol–water mixtures to the extent that an S_N2 component may exist: note that the Sneen mechanism allows no specific assistance to

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† Bordwell [13] has interpreted nucleophilic reactions of allylic halides as involving ion-pair intermediates; this is not at the moment a matter of dispute. Graczyk and Taylor [14] have suggested, from a study of chlorine isotope effects, that the hydrolysis of *p*-methoxybenzyl chloride takes place by the ion-pair mechanism, but Collins [12] has argued that substitutions of benzyl chloride, *p*-methylbenzyl chloride, and 2-octyl brosylate proceed by the classical S_N2 reaction (in the latter case together with a competing classical S_N1 reaction). The Graczyk and Taylor interpretation has also been questioned by Friedberger and Thornton.[15]

[1] R. A. Sneen, *Accounts Chem. Res.*, 1973, **6**, 46; for a contrary viewpoint, see D. J. McLennan, *ibid.*, 1976, **9**, 281.

[2] J. M. W. Scott, *Canad. J. Chem.*, 1970, **48**, 3807.

[3] R. E. Robertson, A. Annesa, and J. M. W. Scott, *Canad. J. Chem.*, 1975, **53**, 3106.

[4] M. H. Abraham, *J.C.S. Perkin II*, 1973, 1893.

[5] D. J. McLennan and P. L. Martin, *Tetrahedron Letters*, 1973, 4215.

[6] D. J. McLennan, *J.C.S. Perkin II*, 1974, 481.

[7] D. J. McLennan, *Tetrahedron Letters*, 1975, 4689.

[8] K. C. Westaway and R. A. Poirier, *Canad. J. Chem.*, 1975, **53**, 3216.

[9] M. H. Abraham and R. J. Abraham, *J.C.S. Perkin II*, 1975, 1677.

[10] M. H. Abraham and P. L. Grellier, *J.C.S. Perkin II*, 1976, 1735.

[11] G. A. Gregoriou, *Tetrahedron Letters*, 1974, 233.

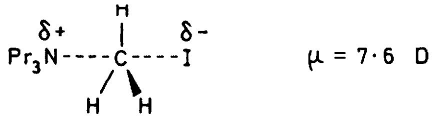
[12] V. F. Raaen, T. Juhlke, F. J. Brown, and C. J. Collins, *J. Amer. Chem. Soc.*, 1974, **96**, 5928.

[13] F. G. Bordwell and T. G. Mecca, *J. Amer. Chem. Soc.*, 1975, **97**, 123, 127; F. G. Hordwell, P. F. Wiley, and T. G. Mecca, *ibid.*, 132.

[14] D. G. Graczyk and J. W. Taylor, *J. Amer. Chem. Soc.*, 1974, **96**, 3255.

[15] M. P. Friedberger and E. R. Thornton, *J. Amer. Chem. Soc.*, 1976, **98**, 2861.

substrate ionisation. McLennan[7] has shown that in the nucleophilic substitution of 2-octyl mesylate by thiourea a concerted S_N2 reaction cannot be excluded, and Westaway and Poirier[8] have unequivocally concluded that substitution of *N*-benzyl-*NN*-dimethylanilinium nitrate by benzenethiolate ion cannot take place by an ion-pair mechanism but must occur *via* an S_N2 process. Other work has dealt with substitution at primary centres. Abraham and Abraham[9] have been able to calculate quantitatively the effect of solvent on values of $\Delta G^{\ddagger}$ for the substitution of methyl iodide by tripropylamine; their calculations were carried out with a transition state model (A) in which the nucleophile and halogen atom



(A)

are partially bonded to the primary centre in a classical S_N2 mode. The transition state in a related reaction, the substitution of ethyl iodide by triethylamine, has also been shown[10] not to resemble a highly polar species such as an ion pair, but rather to behave as a species of only moderate polarity.

It is the purpose of the present paper critically to examine the method of Scott, especially in the light of the work of Ritchie[16-20] which has appeared between 1972 and 1975. This work has neither been cited nor have its implications been discussed by Robertson, Annesa, and Scott.[3] We shall also examine the quasi-thermodynamic method of Robertson, Annesa, and Scott which in these workers hands leads also to conclusions favouring the ion-pair mechanism.

The Scott Linear Free Energy Relationship.—This has been fully and formally discussed by Scott.[2] We repeat the essence of the argument leading to the calculation of K_e and k_n values for clarity. If two nucleophiles N_1 and N_2 react with the ion pair produced by a given methyl halide, equations (4) and (5) apply. Clearly, one further

$$\log(k_n)_{N_1} = \log(k_{obs})_{N_1} - \log K_e \qquad (4)$$

$$\log(k_n)_{N_2} = \log(k_{obs})_{N_2} - \log K_e \qquad (5)$$

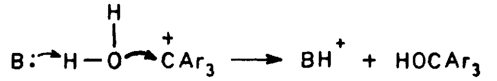
expression is needed before the two k_n values and the one K_e value may be obtained from the two experimental k_{obs} values. As a standard process for attack of nucleophiles on cationic carbon [*i.e.* equation (3)], Scott[2] selected the reaction of water (N_1) and OH^- (N_2) with four stable triarylmethyl cations, rate constants for which are known, $(k_n^\circ)_{N_1}$ and $(k_n^\circ)_{N_2}$. A linear free energy relationship is found, whence equation (6)

$$\log(k_n^\circ)_{N_1} = 1.51\,\log(k_n^\circ)_{N_2} - 5.97 \qquad (6)$$

applies.* It is then assumed that the relationship also holds for $\log(k_n)_{N_1}$ *versus* $\log(k_n)_{N_2}$, and the three simultaneous equations are then solved for K_e, $(k_n)_{N_1}$, and $(k_n)_{N_2}$. Values of $(k_n)_N$ for any other nucleophile N can then be calculated *via* equation (4) as long as $(k_{obs})_N$ is known.†

There are three crucial assumptions invoked in this method. The first is that water and HO^- act in the same way towards the methyl halides as they do towards the triarylmethyl cations. The second is that water and HO^- are typical nucleophiles, so that the constants in equation (6) can be transferred to equations (4) and (5) for any other nucleophiles. The third is that the triarylmethyl cation–nucleophile processes proceed by single elementary reactions [this assumption is demanded by the requirement that the triarylmethyl cation–nucleophile process is a model for the proposed elementary reaction (3)].‡

Recent work negates all these assumptions. Water is *not* a typical nucleophile towards triarylmethyl cations, since its reactions are subject to general base catalysis [equation (7)].[17,19,21] Furthermore, Ritchie[20] has argued



$$\mathrm{B{:}\;H{-}\overset{H}{O}{-}\overset{+}{C}Ar_3 \longrightarrow BH^+ + HOCAr_3} \qquad (7)$$

that HO^- is also an unusual nucleophile towards the triarylmethyl cations in that reaction can take place by an indirect process resembling the proton-jump mode of diffusion through aqueous solutions. These modes of substitution are not available to other foreign nucleophiles, and since general base catalysis has to date not been observed in solvolytic substitution[22] of the methyl halides it follows that (i) water and possibly also HO^- do not act in the same way towards methyl halides as they do towards the triarylmethyl cations, (ii) water and possibly HO^- are not typical nucleophiles towards the triarylmethyl cations, and (iii) at least one of the model reactions is not a unitary process. Thus none of the three required assumptions are fulfilled. To make this point further we invoke Ritchie's observation on the nucleophilic reactivity of a wide range of nucleophiles towards triarylmethyl cations and diazonium ions of diverse reactivity.[16,18,19] This can be summarised in equation (8) where N_+ is a parameter characteristic of

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* In ref. 3 a revised relationship is given, *viz.* $\log(k_n^\circ)_{N_1} = 1.285\,\log(k_n^\circ)_{N_2} - 5.545$.

† Scott's paper[2] is misleading regarding his procedure, since a misprint in column 1, line 35, page 3814 mentions equation (14) instead of equation (13).

‡ Scott is here placed in a logically untenable position. The Ar_3C^+, N reactions are either elementary reactions or they are not. If they are not elementary reactions, then this third assumption is not valid and the method is unreliable. If they are elementary reactions, then the reverse process, the dissociation of $Ar_3C–N$, must be an elementary reaction. But this is contrary to the universal ion-pair mechanism of Sneen, so that in order to deduce the ion-pair mechanism for the MeX substrates, Scott is forced to assume a non-ion-pair mechanism for $Ar_3C–N$.

[16] C. D. Ritchie, *Accounts Chem. Res.*, 1972, **5**, 348.

[17] C. D. Ritchie, *J. Amer. Chem. Soc.*, 1972, **94**, 3275.

[18] C. D. Ritchie and P. O. I. Virtanen, *J. Amer. Chem. Soc.*, 1972, **94**, 4966.

[19] C. D. Ritchie, D. J. Wright, D.-S. Huang, and A. A. Kamego, *J. Amer. Chem. Soc.*, 1975, **97**, 1163.

[20] C. D. Ritchie, *J. Amer. Chem. Soc.*, 1975, **97**, 1170.

[21] J. H. Ride, P. A. H. Wyatt, and Z. M. Zochowski, *J.C.S. Perkin II*, 1974, 1188.

[22] J. M. Harris, D. C. Clark, A. Becker, and J. F. Fagan, *J. Amer. Chem. Soc.*, 1974, **96**, 4478.

the nucleophile alone, having no dependence on the identity or class of substrate. Ritchie identifies (with reservations[20]) his N_+ scale with desolvation of the nucleophile and describes the rate-limiting step of the anion–cation recombination reactions as the removal of

$$\log(k_n)_{N_1} = \log(k_n)_{N_2} + N_+ \qquad (8)$$

the last but one molecule of water (specifically solvating the anion) separating anion and cation. The lack of cation selectivity implied by equation (8) is explained by Pross[23] in terms of cation solvation factors. His proposed mechanism for the anion–cation combination reactions of Ritchie involves the desolvation of a solvent-separated ion pair, to form an intimate ion pair, as the rate-limiting step. It then seems clear that the model processes are not simple elementary reactions and that the $\log(k_n)_N$ values do not pertain directly to formation of covalent product.

Re-analysis with HO^- *and* CN^- *as Standard Nucleophiles.*—Whatever the other failings of Scott's procedure, it is clear that water is eminently unsuitable as a standard nucleophile. We therefore re-analyse the situation by using the nucleophiles HO^- and CN^-, for which abundant data are available. Both these nucleophiles are singly-charged anions, both have first-row nucleophilic atoms and, since both are linear, their steric requirements should be similar. Equation (6) must be re-cast appropriately, and we draw on data for 13 substrates of the Ar_3C^+ and ArN_2^+ type[16,18,19,24,25] to generate the linear free energy relationship shown in Figure 1. Such a range of data was not available to Scott. Linearity is impressive (r 0.996 0), and the least-squares correlation is given by equation (9). This may favourably

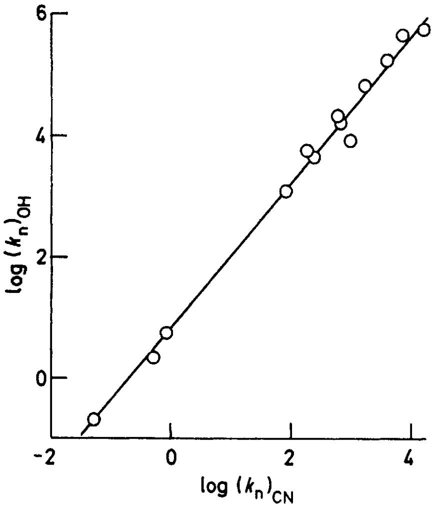

FIGURE 1 Plot of observed values of $\log(k_n)_{OH}$ *vs.* $\log(k_n)_{CN}$ pertaining to attack of the nucleophiles OH^- and CN^- on diazonium ions and stabilised carbocations

$$\log(k_n^\circ)_{OH} = (1.20 \pm 0.03) \log(k_n^\circ)_{CN} + (0.79 \pm 0.09) \qquad (9)$$

be compared with the prediction based on the N_+ scale, equation (8), which is equation (10).[16] Following

$$\log(k_n^\circ)_{OH} = \log(k_n^\circ)_{CN} + 0.7 \qquad (10)$$

Scott, we make the appropriate substitutions into equations (4) and (5), with $N_1 = HO^-$ and $N_2 = CN^-$, using the observed rate constants tabulated.[2] The resulting values of K_e are shown in Table 1. They are quite unreasonable. According to this treatment (more soundly based than the original version of Scott), methyl fluoride is 79% ionised in aqueous solution, and the three other methyl halides are virtually 100% ionised. But let us continue by calculating k_n values for various nucleophiles, using the new K_e values in Table 1. A sample set for the case of methyl iodide is shown in Table 2, similar data being calculated for the other halides. The outstanding feature is the calculated resistance of the putative ion pair Me^+I^- to nucleophilic attack, since the k_n values are many orders of magnitude lower than those observed for nucleophilic attack on stable carbocations.[16-21] It seems clear that the present calculations are falsely based.

TABLE 1

Ion-pair equilibrium constants as calculated by the modified Scott method[a]

Substrate:	MeF	MeCl	MeBr	MeI
K_e[b]	3.7	1.0×10^5	1.2×10^7	2.7×10^5

[a] Tabulations of observed rates in ref. 2 were employed. [b] In water.

We can demonstrate that this is indeed the case in a direct way, by combining equation (4) for a given nucleophile–methyl halide combination with the Ritchie expression for that nucleophile, equation (8). The result is that $\log(k_{obs})$ for a series of nucleophiles reacting with a given methyl halide in water should be linearly correlated with N_+, with a slope equal to unity. One such plot is shown in Figure 2, where the nucleophiles are H_2O, HO^-, CN^-, and N_3^-. Plots for the other halides have a similar appearance (azide points were here calculated *via* the Swain–Scott equation). If the points for water are rejected for the reasons given above, such plots have slopes of the wrong sign (if, indeed, one can assign slopes to plots with such poor correlations).

TABLE 2

Values of k_n for attack of nucleophiles on the Me^+I^- ion pair in water, as calculated by the modified Scott method[a]

Nucleophile	k_n/l mol^{-1} s^{-1}
H_2O	4.9×10^{-15}
OH^-	2.4×10^{-10}
$S_2O_3^{2-}$	1.3×10^{-7}
I^-	1.3×10^{-9}
F^-	2.5×10^{-13}
Br^-	1.5×10^{-10}
Cl^-	1.1×10^{-11}
CN^-	2.2×10^{-9}
SCN^-	1.3×10^{-9}

[a] Tabulations of observed rates in ref. 2 were employed.

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[23] A. Pross, *J. Amer. Chem. Soc.*, 1976, **98**, 776.

[24] C. A. Bunton and S. K. Huang, *J. Amer. Chem. Soc.*, 1974, **96**, 515.

[25] C. D. Ritchie, G. A. Skinner, and V. G. Badding, *J. Amer. Chem. Soc.*, 1967, **89**, 2063; C. D. Ritchie and D. J. Wright, *ibid.*, 1971, **93**, 6574.

It is obvious that Scott has chosen a most inappropriate pair of standard reactions. Our choice of a somewhat better pair of model reactions leads to ridiculous values for the equilibrium constants, K_e, and rate constants, k_n. This could perhaps have been foreseen, for Ritchie has emphasised the point that the reactivity order $HO^- > CN^-$ in anion–cation recombination reactions is opposite to that commonly encountered in second-order nucleophilic substitutions. We must stress that this is not the reason for our choice of the two anions HO^- and CN^- as standards in the present treatment. It turns out that they are the only two anions for which a satisfactory range of aqueous solution data is available.

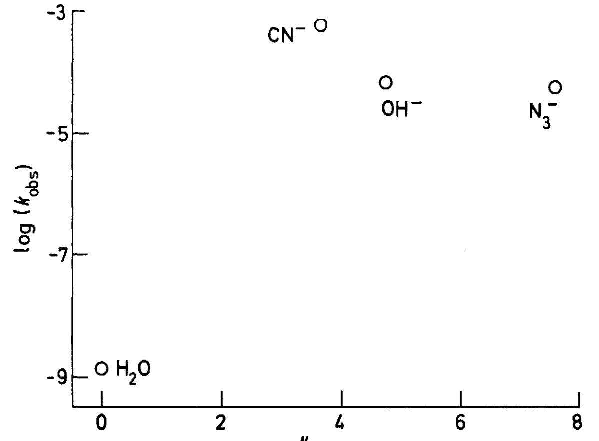

FIGURE 2 Plot of log(k_{obs}) for reactions of various nucleophiles with MeI in water against the nucleophiles' N_+ values

The Quasi-thermodynamic Analysis of Scott, Annesa, and Robertson.—These workers [3] have used a method due originally to Robertson, Heppolette, and Scott [26] to assign values to the charge development ($Z^‡$) in the transition states for hydrolysis of methyl halides, nitrate, and perchlorate. A quantity $S^‡$ is defined by the expression (11) in which $S°$(MeX) is the standard entropy of the substrate in the gas phase, $\Delta S_s°$(MeX) is the entropy of solution of the substrate and $\Delta S^‡$ is the entropy of activation. In effect, $S^‡$ is the standard entropy of the substrate in aqueous solution plus $\Delta S^‡$.

$$S^‡ = S°(\mathrm{MeX}) + \Delta S_s°(\mathrm{MeX}) + \Delta S^‡ \qquad (11)$$

$$S^‡ = S°(\mathrm{MeX, aq}) + \Delta S^‡ \qquad (12)$$

It is then assumed [26] that $S^‡$ is given by equation (13), where μ and α are constants. Since for a given alkyl

$$S^‡ = \mu S°\ (\mathrm{R^+, aq}) + \alpha S°(\mathrm{X^-, aq}) + \text{constant} \qquad (13)$$

group $S°$ (R^+, aq) is constant, equation (13) reduces to equation (14). Thus a plot of $S^‡$ for a series of com-

$$S^‡ = \alpha S°(\mathrm{X^-, aq}) + \text{constant} \qquad (14)$$

pounds of a given alkyl group against $S°$ (X^-, aq) should be a straight line the slope of which (α) is identified as the charge separation ($Z^‡$) in the transition state or alternatively [3] as $\sqrt{\alpha} = Z^‡$. Robertson and Scott [27] also discussed this treatment and inferred (but did not state explicitly) that similar equations would hold in terms of enthalpy, and hence of free energy. Indeed, if the method has any theoretical significance, values of α (and hence of $Z^‡$) should be obtainable from plots of $G^‡$ against $\Delta G_f°$ (X^+, aq) and of $H^‡$ against $\Delta H_f°$ (X^-, aq). Thermodynamic quantities for the methyl halides in aqueous solution can be derived from the known gas-phase values,[28,29] together with the accurate data of Alexander [30] for the solution process. In the case of the other alkyl halides, $\Delta G_f°$ (RX, aq) values can be obtained from gas-phase data [28] and solubility measurements [31] but the corresponding enthalpy and entropy data required for the most part an estimate for the solution process. The collected data are in Table 3, and in Table 4 are given activation parameters for the aqueous

TABLE 3

Thermodynamic parameters [a] for the formation of molecules and ions in aqueous solution (molar scale) at 298 K

	$\Delta G_f°$	$\Delta H_f°$	$S°$
MeF	−48.5	−60.2	33.1
MeCl	−13.7	−26.2	32.8
MeBr	−5.7	−15.2	34.3
MeI	4.7	−2.8	36.6
MeCN	23.0 [b]	11.1 [c]	33.0 [c]
$MeNO_3$	−9.7 [d]	−38.9 [c]	47.0 [c]
MeOH	−41.9 [e]	−58.8 [f]	31.8
EtF	−48.2 [c]	−67.8 [c]	39.2 [c]
EtCl	−12.8	−33.4 [c]	38.4 [c]
EtBr	−5.1	−22.3 [c]	41.2 [c]
EtI	6.3	−9.0 [c]	43.3 [c]
EtOH	−43.3 [d]	−68.6 [f]	35.8
Pr^iF	−46.8 [c]	−75.0 [c]	43.0 [c]
Pr^iCl	−13.2	−42.4 [c]	42.2 [c]
Pr^iBr	−5.0	−31.0 [c]	44.5 [c]
Pr^iI	6.2 [c]	−17.8 [c]	46.6 [c]
Pr^iOH	−44.4 [g]	−79.1 [f]	37.1
Bu^tF	−50.3	−85.5	52.0 [c]
Bu^tCl	−12.3	−48.7	50.5
Bu^tBr	−4.0	−37.4 [c]	52.0 [c]
Bu^tI	8.0 [c]	−23.2 [c]	54.8 [c]
Bu^tOH	−45.1 [h]	−90.0 [f]	35.2
H^+	0	0	0
F^-	−66.6	−79.5	−3.3
Cl^-	−31.4	−40.0	13.5
Br^-	−24.9	−29.1	19.7
I^-	−12.3	−13.2	26.6
CN^-	41.2	36.0	22.5
NO_3^-	−26.6	−49.6	35.0

[a] $\Delta G_f°$ and $\Delta H_f°$ in kcal mol^{-1}, $S°$ in cal K^{-1} mol^{-1}; data from refs. 28—31 unless otherwise noted. [b] Using $\gamma^\infty = 17.2$ from data by J. Hine and P. K. Mookerjee (*J. Org. Chem.*, 1975, **40**, 292). [c] Estimated values. [d] Using $\gamma^\infty = 25$ (the same as that for nitromethane) (M. H. Abraham and P. L. Grellier, *J.C.S. Perkin II*, 1975, 1856). [e] From data by J. A. V. Butler, D. W. Thomson, and W. H. Maclennan (*J. Chem. Soc.*, 1933, 674). [f] Using heats of solution by H. L. Friedman and C. V. Krishnan (*J. Phys. Chem.*, 1969, **73**, 1572). [g] From data by A. Wilson and E. L. Simons (*Ind. and Eng. Chem.*, 1952, **44**, 2214). [h] From data by W. F. Eberz and H. J. Lucas (*J. Amer. Chem. Soc.*, 1934, **56**, 1230).

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[26] R. E. Robertson, R. L. Heppolette, and J. M. W. Scott, *Canad. J. Chem.*, 1959, **37**, 803.

[27] R. E. Robertson and J. M. W. Scott, *J. Chem. Soc.*, 1961, 1597.

[28] National Bureau of Standards Technical Note 270–3, U.S. Department of Commerce, Washington, 1968.

[29] D. R. Stull, E. F. Westrum, jun., and G. C. Sinke, 'Chemical Thermodynamics of Organic Compounds,' Wiley, New York, 1969.

[30] D. M. Alexander, D. J. T. Hill, and L. R. White, *Austral. J. Chem.*, 1971, **24**, 1143.

[31] N. C. Deno and H. E. Berkheimer, *J. Chem. and Eng. Data*, 1960, **5**, 1.

hydrolysis and the derived values of $G^{\ddagger}$, $H^{\ddagger}$, and $S^{\ddagger}$. A plot of $G^{\ddagger}$ against $\Delta G_f^{\circ}(X^-, aq)$ is a good straight line for the methyl compounds of slope 0.93, but it is clear that there is little connection between this value for α and $Z^{\ddagger}$, since a similar plot of ΔG_f°(MeX, aq) against $\Delta G_f^{\circ}(X^-, aq)$ also yields a straight line of slope no less than 0.97! A similar result is obtained from the corresponding enthalpy plots; thus it is clear that the enthalpy and free energy plots cannot be used to find Z. In order to determine if the entropy plots are useful purely as an empirical method, we give in Table 5 the values of α obtained from various plots. Those involving the alkyl halides themselves are instructive; the four values of α average 0.33 so that for the simple reactants we have $Z = 0.33$ (from α) or $Z = 0.57$ (from $\sqrt{\alpha}$), whereas from known dipole moments [33] and bond lengths [33] it may be calculated that Z is only 0.21 units on average for these compounds. For these simple compounds, the method thus considerably overestimates the value of Z. Data on the $S^{\ddagger}$ plots (Table 5) shows that the calculated α values form a reasonable qualitative sequence, Me < $\text{Pr}^{\text{i}} \simeq \text{Bu}^{\text{t}}$. Unfortunately the $\Delta S^{\ddagger}$ values for the hydrolysis of the t-butyl halides are not known to any great accuracy and the value of $\alpha \simeq 1.0$ for the $\text{Bu}^{\text{t}}\text{X}$ transition states is very approximate. However, $\Delta S^{\ddagger}$ values are known for methanol as solvent,[34] and the ancillary data needed to calculate [4] $G^{\ddagger}$, $H^{\ddagger}$, and $S^{\ddagger}$ and also to calculate the thermodynamic quantities for the halide ions [35] are available. Details are in Tables 6 and 7, and in Table 8 are the values of α calculated from the various plots. It is clear that there is absolutely no relation between α and Z, the charge separation, when methanol is the solvent. Taking into account the results in aqueous solution as well as those in methanol, we conclude that there is no theoretical foundation for the quasithermodynamic method and that the value of α obtained from plots of $S^{\ddagger}$ against $S^{\circ}(X^-)$ cannot be equated with the charge separation in the transition states.

TABLE 4

Activation parameters for the aqueous hydrolysis of alkyl compounds, and derived values of $S^{\ddagger}$ through equation (12), at 298 K [a]

Compound [b]	$\Delta G^{\ddagger}$	$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$	$G^{\ddagger}$	$H^{\ddagger}$	$S^{\ddagger}$
MeF	29.9	27.3	−8.7	−18.6	−32.9	24.4
MeCl	27.9	26.6	−4.3	14.2	0.4	28.5
MeBr	26.2	25.3	−2.9	20.5	12.2	34.9
MeI	27.2	27.4	+0.6	31.9	24.6	37.2
MeNO_3	29.2	28.6	−1.9	19.5	−10.3	45.1
MeClO_4	21.2	21.5	+0.9			
EtCl	26.6	26.2	−1.2	13.8	−7.2	37.2
EtBr	26.4	25.5	−3.1	21.3	3.2	38.1
EtI	26.7	26.9	+0.4	33.0	17.9	43.7
$\text{Pr}^{\text{i}}\text{Cl}$	26.6	25.9	−2.1	13.4	−16.5	40.1
$\text{Pr}^{\text{i}}\text{Br}$	24.8	25.8	+3.1	19.8	−5.2	47.6
$\text{Pr}^{\text{i}}\text{I}$	25.0	27.0	+6.6	31.2	9.2	53.2
$\text{Bu}^{\text{t}}\text{F}$	26.3	23.9	−8	−24.0	−61.6	44
$\text{Bu}^{\text{t}}\text{Cl}$ [c]	19.5	22.6	10.2	7.2	−26.1	60.7
$\text{Bu}^{\text{t}}\text{Br}$ [d]	17.6	22.0	14.6	13.6	−15.4	66.6
$\text{Bu}^{\text{t}}\text{I}$ [d]	17.2			25.2		

[a] G and H in kcal mol^{-1}, S in cal K^{-1} mol^{-1}. [b] Activation parameters from refs. 3, 26, and R. L. Heppolette and R. E. Robertson, *Canad. J. Chem.*, 1966, **44**, 677; *Proc. Roy. Soc.*, 1959, *A*, **252**, 273. [c] Values from E. A. Moelwyn-Hughes, R. E. Robertson, and S. Sugamori, *J. Chem. Soc.*, 1965, 1965; S. Winstein and A. H. Fainberg (*J. Amer. Chem. Soc.*, 1957, **79**, 5937) record ΔH‡ 23.2 and ΔS‡ 12.2 [d] E. A. Moelwyn-Hughes, *J. Chem. Soc.*, 1962, 4301.

TABLE 5

Values of α obtained by the quasi-thermodynamic method

Plot			X	α
S°(MeX, aq)	*vs.*	$S^{\circ}(X^-, aq)$	Cl, Br, I	0.29 [a]
S°(EtX, aq)	*vs.*	$S^{\circ}(X^-, aq)$	Cl, Br, I	0.37 [a]
S°(Pr^{i}X, aq)	*vs.*	$S^{\circ}(X^-, aq)$	Cl, Br, I	0.34 [a]
S°(Bu^{t}X, aq)	*vs.*	$S^{\circ}(X^-, aq)$	Cl, Br, I	0.33 [a]
$S^{\ddagger}$(MeX, aq)	*vs.*	$S^{\circ}(X^-, aq)$	Cl, Br, 1	0.66 [a]
$S^{\ddagger}$(EtX, aq)	*vs.*	$S^{\circ}(X^-, aq)$	Cl, Br, I	*b*
$S^{\ddagger}$(Pr^{i}X, aq)	*vs.*	$S^{\circ}(X^-, aq)$	Cl, Br, I	1.00
$S^{\ddagger}$(Bu^{t}X, aq)	*vs.*	$S^{\circ}(X^-, aq)$	F, Cl, Br	*ca.* 1.0 [c]
ΔG_f°(MeX, aq)	*vs.*	$\Delta G_f^{\circ}(X^-, aq)$	F, Cl, Br, I	0.97
$G^{\ddagger}$(MeX, aq)	*vs.*	$\Delta G_f^{\circ}(X^-, aq)$	F, Cl, Br, I	0.93
ΔH_f°(MeX, aq)	*vs.*	$\Delta H_f^{\circ}(X^-, aq)$	Cl, Br, I	0.87 [a]
$H^{\ddagger}$(MeX, aq)	*vs.*	$\Delta H_f^{\circ}(X^-, aq)$	Cl, Br, I	0.93 [a]

[a] Values for X = F do not fall on the line for the other halides. [b] No straight line obtained. [c] Approximate value only.

TABLE 6

Thermodynamic parameters,[a,b] for the formation of molecules and ions in methanol (molar scale at 298 K)

	ΔG_f°	ΔH_f°	S°
$\text{Bu}^{\text{t}}\text{Cl}$	−16.4	−50.4	58.5
$\text{Bu}^{\text{t}}\text{Br}$	−8.1	−39.1	60.2
$\text{Bu}^{\text{t}}\text{I}$	3.7	−25.4	62.3
Cl^-	−26.5	−37.7	4.9
Br^-	−20.5	−27.7	9.8
I^-	−9.0	−13.4	14.9

[a] ΔG_f° and ΔH_f° in kcal mol^{-1}, S° in cal K^{-1} mol^{-1}. [b] Values of $\text{Bu}^{\text{t}}\text{X}$ from data in refs. 4 and 29, and values for X^- calculated from aqueous solution data in Table 3 together with transfer parameters from water to methanol (see ref. 35). Note that any arbitrary division into single-ion parameters will not alter the differences amongst Cl^-, Br^-, and I^-.

The Neutral Hydrolysis of Methyl Perchlorate.—Although the previous discussion has shown that neither Scott's linear free energy method nor the quasi-thermodynamic method leads to valid evidence for the S_N2 ion-pair mechanism, this does not necessarily mean that the

TABLE 7

Calculations of $G^{\ddagger}$, $H^{\ddagger}$, and $S^{\ddagger}$ for the methanolysis of the t-butyl halides at 298 K [a]

	$\Delta G^{\ddagger}$	$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$	$G^{\ddagger}$	$H^{\ddagger}$	$S^{\ddagger}$
$\text{Bu}^{\text{t}}\text{Cl}$ [b]	25.8	25.1	−2.2	9.4	−25.3	56.3
$\text{Bu}^{\text{t}}\text{Br}$ [c]	23.5	23.0	−1.8	15.4	−16.1	58.4
$\text{Bu}^{\text{t}}\text{I}$ [d]	22.8	22.1	−2.4	26.5	−3.3	59.9

[a] G and H in kcal mol^{-1}, S in cal K^{-1} mol^{-1}. [b] Average values of recorded activation parameters given in ref. 33*a*. [c] Ref. 34*b*; but note that a value of +1.8 for $\Delta S^{\ddagger}$ may be calculated from data in ref. 34*c*. [d] Calculated from data in ref. 34*c*.

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[32] C. K. Ingold, 'Structure and Mechanism in Organic Chemistry,' 2nd edn., Cornell University Press, Ithaca, 1969.

[33] 'Tables of Interatomic Distances and Configurations in Molecules and Ions,' Chem. Soc. Special Publ. No. 11, London, 1958.

[34] (*a*) M. H. Abraham, *J.C.S. Perkin II*, in the press; (*b*), P. O. I. Virtanen, *Suomen. Kem.*, 1967, **40B**, 179; (*c*) J. Biordi, and E. A. Moelwyn-Hughes, *J. Chem. Soc.*, 1962, 4291.

[35] M. H. Abraham, *J.C.S. Faraday I*, 1973, 1375.

[36] D. N. Kevill and B. Shen, *Chem. and Ind.*, 1971, 1466.

ion-pair mechanism for the substitution of methyl substrates can be rejected completely. Robertson, Annesa, and Scott [3] have indeed contended that their experimental results on the neutral hydrolysis of methyl perchlorate, the most reactive methyl substrate so far studied in hydrolysis,[3] cannot be understood on the basis of a unitary S_N2 process.* We believe, on the other hand, that these results can be explained in terms of a simple S_N2 substitution, and that thus there is no necessity to invoke an ion-pair mechanism for substitution of methyl substrates.

Robertson, Annesa, and Scott base much of their argument on the hydrolysis of methyl substrates around the Hammond postulate. The postulate refers to two states occurring consecutively along a reaction co-ordinate and having nearly the same energy content. It is thus totally inapplicable to a unitary S_N2 process, since the energy of the transition is far higher than the energy of either the reactants or the products. Furthermore, it is not even applicable to the ion-pair scheme of Robertson, Annesa, and Scott [3] because the transition state is still *ca.* 11—20 kcal mol^{-1} higher in energy than the Me^+X^- ion pair (that is, if their K_e values are used). Hence their arguments are based on a false premise; see for example ref. 37. Thornton's rules [38] are more appropriate for the assignment of comparative transition state structures in a situation where the leaving group is changed. In such a case, it is usually felt that the substituent effect of the leaving group is manifested parallel to the reaction co-ordinate (in the reaction co-ordinate decomposition mode).[39] However, Thornton himself has recently allowed that in $E2$ reactions change in leaving group may change the transition state geometry by altering the equilibrium nuclear geometry in stable (perpendicular) vibrational modes.[39] This agrees with experimental observations of Zollinger [40] pertaining to S_NAr reactions. The perturbing influence seems to be steric in nature, and it may be noted that exceptions to Thornton's rules in proton transfers have been rationalised in terms of steric effects.[41] A proviso to the rules for change of leaving group may be given: if a leaving group is changed so that on electronic grounds it becomes a better leaving group, but if the steric consequences of the change are such that the magnitudes of non-bonded steric repulsions between the substrate and leaving group in the transition state are increased, the substrate-to-leaving group separation in the transition state may increase.† An overall perpendicular effect may now operate and the nucleophile-to-substrate separation may also increase. In other words, the transition state will not change structure in the reactant-like–product-like dimension parallel to the reaction co-ordinate, but will change in the tight–loose dimension perpendicular to the reaction co-ordinate. This is seen in the transition states for S_N2 reactions of MeX and Bu^tX. Theoretical calculations [42,43] suggest that the incoming and outgoing groups are further from the central carbon atom in the Bu^tX case, and that this is due to steric effects and not electronic ones. In the case of methyl perchlorate, similar calculations indicate that in the S_N2 transition state there is steric interaction between the α-hydrogen atoms and one or more of the oxygen atoms in the ClO_3 moiety. Relief of this strain is most easily obtained by extension of the $C{-}{-}{-}{-}OClO_3$ bond in the transition state. No such relief is necessary in the case of the methyl halides (or methyl nitrate), so that instead of the comparative structures (i)—(iii) we have now the comparative structures (iv)—(vi), with the substituent effect being felt in the bond closer to the substituent, as required by Thornton. If we accept an almost constant nucleophile-to-substrate separation in a series of substrates MeX reacting with a common nucleophile (water), as suggested by Thornton's rules, the $CH_3{-}{-}{-}{-}X$ distance will normally decrease with increasing reactivity (the parallel effect), exceptions as in (iv)—(vi) arising through steric effects.

$$H_2O{-}{-}{-}{-}CH_3{-}{-}{-}{-}OClO_3 \qquad \text{(i)}$$

$$H_2O{-}{-}{-}{-}CH_3{-}{-}{-}{-}{-}I \qquad \text{(ii)}$$

$$H_2O{-}{-}{-}{-}CH_3{-}{-}{-}{-}{-}{-}{-}Cl \qquad \text{(iii)}$$

$$H_2O{-}{-}{-}{-}CH{-}{-}{-}{-}{-}{-}{-}OClO_3 \qquad \text{(iv)}$$

$$H_2O{-}{-}{-}{-}CH_3{-}{-}{-}{-}{-}I \qquad \text{(v)}$$

$$H_2O{-}{-}{-}{-}CH_3{-}{-}{-}{-}{-}{-}{-}Cl \qquad \text{(vi)}$$

TABLE 8

Values of α obtained by the quasi-thermodynamic method in solvent methanol

Plot			X	α
$S°(Bu^tX)$	*vs.*	$S°(X^-)$	Cl, Br, I	0.38
$S^‡(Bu^tX)$	*vs.*	$S°(X^-)$	Cl, Br, I	0.36
$\Delta G_f°(Bu^tX)$	*vs.*	$\Delta G_f°(X^-)$	Cl, Br, I	1.15
$G^‡(Bu^tX)$	*vs.*	$\Delta G_f°(X^-)$	Cl, Br, I	0.98
$\Delta H_f°(Bu^tX)$	*vs.*	$\Delta H_f°(X^-)$	Cl, Br, I	1.03
$H^‡(Bu^tX)$	*vs.*	$\Delta H_f\ (X^-)$	Cl, Br, I	0.98

We can now rationalise the α-deuterium kinetic isotope effect (k.i.e.) shown in Table 9, which in the case of $MeClO_4$ is inverse to about the same extent as with MeCl. If the $CH_3{-}{-}{-}{-}X$ distance decreases with increasing reactivity, the variable $H{-}C{-}{-}{-}{-}X$ out-of-plane bending frequencies will also decrease with increas-

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* Several workers are agreed that the S_N1 process is not reasonable for the hydrolysis of methyl perchlorate. Kevill and Shen [36] rejected an S_N1 mechanism after consideration of the $k(MeX)/k(EtX)$ values, and Abraham [4] showed that the activation parameters were not consistent with an S_N1 process. Robertson, Annesa, and Scott [3] have also put forward evidence against an S_N1 mechanism.

† Thornton's rules suggest that, in the absence of such steric effects, the substrate-to-leaving group separation would decrease if the leaving group is electronically a better leaving group.

[37] D. Fărcasiu, *J. Chem. Educ.*, 1975, **52**, 76.

[38] E. R. Thornton, *J. Amer. Chem. Soc.*, 1967, **89**, 2915; J. C. Harris and J. L. Kurz, *ibid.*, 1970, **92**, 349.

[39] D. A. Winey and E. R. Thornton, *J. Amer. Chem. Soc.*, 1975, **97**, 3102.

[40] W. Eggiman, P. Schmid, and H. Zollinger, *Helv. Chim. Acta*, 1975, 1365.

[41] D. J. McLennan, *J.C.S. Faraday I*, 1975, 1516.

[42] P. B. D. de la Mare, L. Fowden, E. D. Hughes, C. K. Ingold, and J. D. H. Mackie, *J. Chem. Soc.*, 1955, 3200.

[43] M. H. Abraham, P. L. Grellier, and M. J. Hogarth, *J.C.S. Perkin II*, 1975, 1365.

ing reactivity and should approach the reactant frequencies. The k.i.e. will then be dominated by the O - - - - C–H bending frequencies, which will necessarily result in an inverse k.i.e. since such frequencies are absent from the initial state.[44] As the leaving group becomes kinetically better, the dominant effect of the O - - - - C–H bending frequencies should result in the k.i.e. becoming more and more inverse. This indeed is found for the methyl halides, and a continuation of this trend would result in a very large inverse k.i.e. for methyl perchlorate. But as we have shown, the CH_3 - - - - $OClO_3$ distance is longer than expected, and by the above argument would result in a k.i.e. more positive (or less inverse) than expected from the overall reactivity of the substrate. A similar argument can be applied to the neutral hydrolysis of CH_3–OSO_2OMe and CH_3–SO_3Me since in these cases the k.i.e. is less inverse than expected. Theoretical k.i.e. calculations by Bron[45] substantiate the view that k_H/k_D should increase as the total bonding to the central carbon in the transition state decreases.* Experimental results for $ArCH_2NO_3$ and $ArCH_2Cl$ hydrolysis,[46] when viewed in the light of Thornton's rules for substitution on the central carbon atom,[38] are also in agreement.

TABLE 9

α-Deuterium isotope effects for hydrolysis of CH_3X at 298 K[a]

X:	Cl	Br	I	OSO_2OMe	SO_3Me	ClO_4	NO_3
k_H/k_D:	0.904	0.886	0.849	0.976	0.938	0.920	0.896

[a] From data and equation (11) of ref. 3, using $n = 3$ (CH_3X *vs.* CD_3X) and $T = 298$ K.

Thus the k.i.e. for the neutral hydrolysis of methyl perchlorate can be rationalised by using a unitary S_N2 scheme. Schowen[47] has already discussed the kinetic solvent isotope effect in hydrolyses, and has concluded that a simple S_N2 process operates in which the transition states are only 20% towards the products.† Since both the k.i.e. and the kinetic solvent isotope effect can be interpreted on the basis of a unitary S_N2 scheme, it is therefore not necessary to postulate an ion-pair mechansim for these S_N2 substitutions.

Conclusions.—In summary, we reject the Scott linear free energy approach to the mechanism of substitution of the methyl halides. We show that the kinetic isotope effect and (following Schowen[47]) the kinetic solvent isotope effect can be explained in terms of a traditional S_N2 mechanism that involves a rather looser than usual transition state for the hydrolysis of methyl perchlorate. We have also revealed the source of the very large discrepancy between the results of Scott[2] and the results of Abraham[4] on the energetics of ionisation of the methyl halides, since in our opinion Scott's values are based on an invalid method of treatment.

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* *Note added in proof:* Calculations on the benzyl chloride-oxyanion system which use a more acceptable force field also give this trend in k_H/k_D (G. W. Burton, personal communication).

† This is essentially the same conclusion as was reached by Abraham and Johnston,[48] who showed that charge separation in the transition states for solvolysis of the methyl halides was only *ca.* 0.30 units.

[44] V. J. Shiner, in 'Isotope Effects in Chemical Reactions,' eds. N. S. Bowman and C. J. Collins, Van Nostrand–Reinhold, New York, 1970. ch. 2; M. Wolfsberg, *Accounts Chem. Res.*, 1972, **5**, 225; A. V. Willi, *Canad. J. Chem.*, 1966, **44**, 1889; A. V. Willi and C. M. Won, *J. Amer. Chem. Soc.*, 1968, **90**, 5999; C. M. Won and A. V. Willi, *J. Phys. Chem.*, 1972, **76**, 427.

[45] J. Bron, *Canad. J. Chem.*, 1974, **52**, 903; note that the force field employed has been criticised by W. E. Buddenbaum and V. J. Shiner (*ibid.*, 1976, **54**, 1146) but it is not clear how k_H/k_D would be affected.

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[47] R. Schowen, *Progr. Phys. Org. Chem.*, 1972, **9**, 275.

[48] M. H. Abraham and G. F. Johnston, *J. Chem. Soc.* (*A*), 1971, 1610.