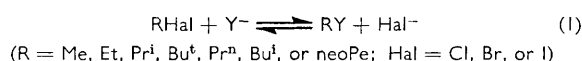


Halide Exchange at a Saturated Carbon Atom in Dimethylformamide Solvent. Comparison of Experimental Rates and Arrhenius Parameters with Values Calculated by Ingold

By D. Cook and A. J. Parker,* Department of Organic Chemistry, University of Western Australia, Nedlands, Western Australia

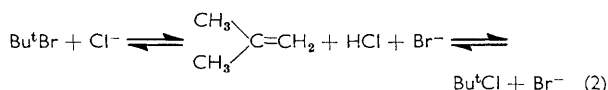
The rates of exchange of a strong electrolyte, tetraethylammonium chloride, with simple alkyl bromides in solvent dimethylformamide have been studied. The rate constants, activation energies, and Arrhenius $\log B$ terms are compared with those obtained by Hughes, Ingold, and Mackie, who studied reactions of the weak electrolyte lithium chloride in acetone. The results for dimethylformamide are also compared with the data calculated for Finkelstein substitutions in any solvent by de la Mare, Fowden, Hughes, Ingold, and Mackie. Special attention is given to the S_N2 and $E2$ reactions of *t*-butyl bromide with chloride ion. With one exception, Ingold's calculated values show remarkably good agreement with our experimental data.

An analysis of steric and polar effects of alkyl groups on rates of S_N2 reactions (1), with special reference to halogen exchanges ($Y = \text{Cl, Br, or I}$), was described by

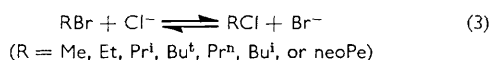


de la Mare, Fowden, Hughes, Ingold, and Mackie¹ in 1955, in a major contribution to our understanding of one of the most common reactions in organic chemistry. Unfortunately, the experimental data² used by Ingold^{1,3} for comparison with his calculated values have been criticised, and his calculations are regarded with scepticism by some chemists. Some of the criticism is well founded,^{4,5} but not all of it⁶ is justified.⁷

The main sources of complaint are, first, that the lithium halides, which were used as sources of halide ion in reaction (1) ($Y = \text{Hal}$), together with the product lithium halides, are weak electrolytes in acetone,^{5,6,8} and secondly, that reactions (1) of *t*-butyl halides in acetone are not S_N2 but $E2$, followed by addition as in (2).⁴ The paper describing the exchange reactions (3)



of chloride ions with simple alkyl bromides in acetone⁹ has received the most cogent criticism.⁴



We here examine reaction (3) in dimethylformamide as solvent. We have used tetraethylammonium chloride

† Rate constants, activation energies, and $\log B$ terms were not calculated by Ingold for reaction (3); attention was concentrated on the symmetrical exchange (1) ($Y = \text{Hal} = \text{Br}$) for rates and $\log B$ terms, and on the three symmetrical exchanges (1) ($Y = \text{Hal} = \text{Hal}$) for E_a .¹ Ingold makes it clear in his calculations, and it is confirmed experimentally, that the expressions $[\log k(\text{MeBr}) - \log k(\text{RBr})]$, $[E_a(\text{RBr}) - E_a(\text{MeBr})]$, and $[\log B(\text{MeBr}) - \log B(\text{RBr})]$ for exchange reaction of alkyl bromides with bromide ion are almost identical with the corresponding expressions for reaction with chloride ion.¹ We therefore feel that we are making a legitimate test of his theory by comparing these expressions for reaction (3) in dimethylformamide with the calculated values of $\log k$ and $\log B$ for reaction (1) ($Y = \text{Hal} = \text{Br}$). We use the mean of the calculated values of E_a for the three symmetrical exchange reactions (1) ($Y = \text{Hal} = \text{Hal}$), for comparison with our experimental activation energies of reaction (3).

($K_{\text{assoc}} 6.7 \text{ l. mole}^{-1}$; cf. Table 6) as the source of chloride ion, because, like the product tetraethylammonium bromide ($K_{\text{assoc}} 16 \text{ l. mole}^{-1}$),¹⁰ it is a moderately strong electrolyte in dimethylformamide at the concentrations ($< 0.04M$) that we used. We have given careful attention to the S_N2 reactions (3) and the $E2$ reactions (2) of *t*-butyl bromide.

Because our experimental results (Table 1) are not subject to the same criticisms as those of Hughes, Ingold, and Mackie,⁹ they provide a better set of experimental data with which to test Ingold's calculations.¹ †

Calculated and Experimental Rate Constants.—Our experimental rate constants for reaction (3) in dimethylformamide at 25° are in Table 1. When expressed as $\log k(\text{MeBr}) - \log k(\text{RBr})$ they can be compared (Figure 1) with Ingold's calculated values for reaction (1) ($Y = \text{Hal} = \text{Br}$).¹ The experimental rate constants for reaction (3) of 0.07M-lithium chloride in acetone⁹ at 25°, expressed in the same way, are included in Figure 1. The value for reaction (3) (R = Bu^t) of 0.07M-lithium chloride in acetone must be disregarded (see below), so our results agree better with the calculated rate constants than do the rate constants reported by Hughes, Ingold, and Mackie.⁹ The situation for reaction (3) (R = Bu^t) is discussed below.

Calculated and Experimental Arrhenius Activation Energies.—Our experimental activation energies for reaction (3) in dimethylformamide (Table 1) have been expressed as $E_a(\text{RBr}) - E_a(\text{MeBr})$ and then compared as in Figure 2 with the mean of Ingold's calculated values for reaction (1) ($Y = \text{Hal} = \text{Hal}$). The scale is chosen

¹ P. B. D. de la Mare, L. Fowden, E. D. Hughes, C. K. Ingold, and J. D. H. Mackie, *J. Chem. Soc.*, 1955, 3200.

² P. B. D. de la Mare, E. D. Hughes, C. K. Ingold, and their co-workers, *J. Chem. Soc.*, 1955, 3169.

³ C. K. Ingold, *Quart. Rev.*, 1957, 11, 1.

⁴ S. Winstein, S. G. Smith, and D. Darwish, *Tetrahedron Letters*, 1959, No. 16, 24.

⁵ S. Winstein, L. G. Savedoff, S. G. Smith, I. D. R. Stevens, and J. S. Gall, *Tetrahedron Letters*, 1960, No. 9, 24.

⁶ Farhat-Aziz and E. A. Moelwyn-Hughes, *J. Chem. Soc.*, 1959, 2635.

⁷ E. D. Hughes, C. K. Ingold, and A. J. Parker, *J. Chem. Soc.*, 1960, 4400.

⁸ L. G. Savedoff, *J. Amer. Chem. Soc.*, 1966, 88, 664.

⁹ E. D. Hughes, C. K. Ingold, and J. D. H. Mackie, *J. Chem. Soc.*, 1955, 3173.

¹⁰ P. G. Sears, E. D. Wilhoit, and L. R. Dawson, *J. Phys. Chem.*, 1955, 59, 373.

TABLE 1

Rate data for the exchange reactions $\text{RBr} + \text{Cl}^- \longrightarrow \text{RCl} + \text{Br}^-$

	R = Me	Et	Pr ⁱ	Bu ^t	Pr ⁿ	Bu ⁱ	neoPe
$-\log k^a$ (DMF) ^b	0.30	1.87	3.61	4.96 ^c	2.03	3.35	7.07
$-\log k^a$ (Me ₂ CO) ^d	2.22 ^h	4.01	5.89	6.54 ^e	4.19	4.82	8.59
$-\log k/\alpha^{a,g}$ (Me ₂ CO)	-0.52 ^h	1.18	3.06	3.71	1.37	1.99	5.76
E_a^a (DMF) ^b	17.9	19.2	20.9	21.2	19.8	19.7	26.3
E_a^a (Me ₂ CO) ^d	15.7 ^h	17.6	18.8	21.0 ^e	17.5	18.1	21.7
$\log B$ (DMF) ^b	12.8	12.2	11.7	10.6 ^e	12.5	11.1	12.2
$\log B$ (Me ₂ CO) ^d	9.3 ^h	8.9	7.9	8.9 ^e	8.6	8.4	7.4
$\log B^d - \log \alpha^g$ (Me ₂ CO)	12.0	11.7	10.7	11.7 ^e	11.4	11.2	10.2

^a Rate constants in l. mole⁻¹ sec.⁻¹ at 25.0° (note that they are recorded as $-\log k$), and E_a in kcal. mole⁻¹. ^b NEt_4Cl at 0.04 ± 0.005M for which $\alpha = 0.82$. Rates corrected for incomplete dissociation of NEt_4Cl by the Acree method (see text). ^c This work. NEt_4Cl is at 0.12M and is corrected for incomplete dissociation of NEt_4Cl ($\alpha = 0.70$). ^d Ref. 9, $[\text{LiCl}] = 0.070 \pm 0.007\text{M}$. ^e Reaction is chiefly elimination-addition (see text). ^f This work. $[\text{NBu}_4\text{Cl}] = 0.0481\text{M}$ in acetone; uncorrected for ion association. Rate constant and parameters are for the $\text{S}_{\text{N}}2$ reaction. ^g The degree of dissociation, α , of LiCl is calculated at 30% reaction from $k_{\text{diss}} = 3.3 \times 10^{-6}$ and 2.19×10^{-4} mole l.⁻¹ for LiCl and LiBr , respectively, at 25.0° in acetone. ^h $[\text{LiCl}] = 0.05\text{M}$.

so that ΔE_a in Figure 2 and $\Delta \log k$ in Figure 1 are directly comparable (*i.e.*, $1.36 \Delta \log k = \Delta E_a$). The experimental activation energies, expressed relative to methyl, for

formation of bromide ion. Roughly 2–10% of the formation of bromide ion (depending on the concentration of chloride ion) is solvolysis, and the remaining 83–91% is an $\text{E}2$ reaction. Small errors in the measurement of the fraction of substitution at different temperatures could make a substantial error in the activation energy. Nevertheless, the fraction of substitution over a 60° range is constant (Table 2), and the 'activation energy' for the combined $\text{E}2$ and $\text{S}_{\text{N}}2$ reaction of 21.2 ± 0.4 kcal. mole⁻¹ is precise. We estimate E_a as 21.2 kcal. mole⁻¹ for the $\text{S}_{\text{N}}2$ reaction. Clearly, Ingold's calculation¹ of E_a for reaction (3) ($\text{R} = \text{Bu}^t$) does not agree

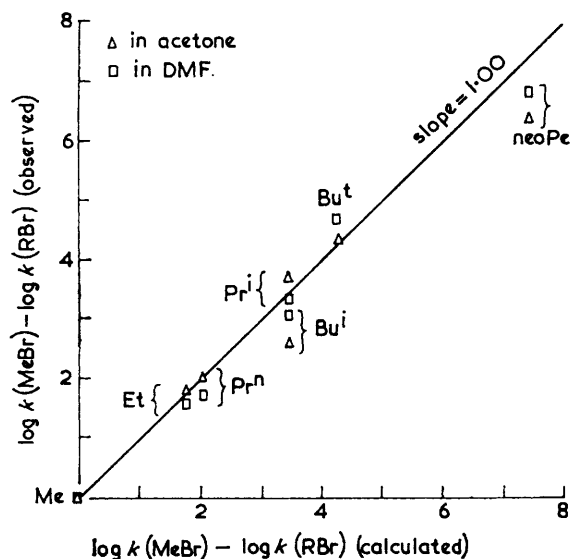


FIGURE 1 Comparison of experimental rate constants for reaction (3) of 0.07M-LiCl in acetone and of NEt_4Cl in dimethylformamide with rate constants calculated for bromide exchange with alkyl bromides. Effects of alkyl groups R are relative to methyl

reaction (3) of 0.07M-lithium chloride in acetone⁹ are included in Figure 2. The agreement with theory of our activation energy for $\text{R} = \text{neopentyl}$ is particularly striking, in view of the large deviation observed by Hughes, Ingold, and Mackie.⁹ Our experimental values for $\text{R} = \text{n-propyl}$ and isopropyl are almost identical with values obtained for acetone, and they agree well with theory. Both our value and that of Hughes, Ingold, and Mackie⁹ for isobutyl bromide show deviations from theory, our value showing the greater deviation.

The activation energy for reaction (3) ($\text{R} = \text{Bu}^t$) in dimethylformamide (Table 2) is only approximate, because $\text{S}_{\text{N}}2$ substitution is only $7 \pm 1\%$ of the total

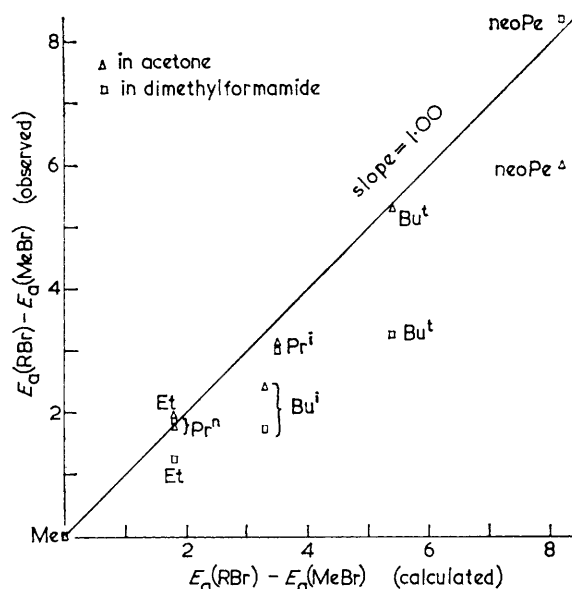


FIGURE 2 Comparison of experimental activation energies for reaction (3) of 0.07M-LiCl in acetone and of NEt_4Cl in dimethylformamide with mean activation energies calculated for symmetrical halide-ion-alkyl halide exchange reactions

at all well with our experimental value. Although the experimental activation energy obtained by Hughes, Ingold, and Mackie⁹ agrees with theory (Figure 2), this may not be significant, because they were following an

elimination-addition reaction.⁴ Also, they may have made an arithmetical error in the calculation of their rate constant ⁴ at 55.2° (see below). We repeated their reaction (3) (R = Bu^t) using 0.05M-tetra-n-butylammonium chloride, which is a stronger electrolyte than lithium chloride, in acetone containing 2,6-lutidine

TABLE 2

Reactions of t-butyl bromide with chloride ion; estimated maximum uncertainty in rate constants is $\pm 4\%$

Solvent: dimethylformamide						
Temp. (°C)	[Bu ^t Br] (M)	[Salt] * (M)	[NEt ₄ Cl] (M)	10 ⁵ k ₁ ^b (sec. ⁻¹)	10 ⁴ k ₂ ^a (l. mole ⁻¹ sec. ⁻¹)	100F ₈ ^e
25.0	0.0385	0.1205(A)	—	0.337 ^c	—	—
50.0	0.0385	0.1205(A)	—	5.21 ^c	—	—
74.9	0.0385	0.1205(A)	—	59.0 ^c	—	—
25.0	0.0522	0.1035(B)	0.0704	1.55	1.72	7.0
25.0	0.0407	0.1188(B)	0.0779	1.65	1.68	6.6
50.0	0.0511	0.0994(B)	0.0682	20.6	22.6	8.3
50.0	0.0518 ^a	0.0994(B)	0.0682	20.3 ^a	22.1 ^a	6.0
50.0	0.0520	0.2112(B)	0.1178	36.2	26.3	7.5
49.9	0.0407	0.1188(B)	0.0779	26.8	27.7	6.6
60.0	0.0407	0.1188(B)	0.0779	73.1	74.8	6.6
0.0	0.0407	0.1188(B)	0.0779	0.0656	0.0691	7.0

* A = NEt₄ClO₄; B = NEt₄Cl.

Solvent: acetone					
Temp.	[Bu ^t Br]	[NBu ₄ Cl]	[Lutidine]	10 ⁵ k ₂ ^f	100F ₈
25.0°	0.0485	0.0914	0.0573	5.31	3.8
25.0	0.0462	0.0474	0.0573	6.21	4.4
25.0	0.0461	0.0206	0.0573	6.51	4.3
25.0	0.0500	0.1741	0.0634	5.39	7.6
25.0	0.0510	0.0860	0.0630	5.92	5.1
25.0	0.0493	0.0487	0.1901	4.99	8.0
25.0	0.0482	0.0481	0.0883	5.77	4.2
49.9	0.0482	0.0481	0.0883	93.4	5.3
75.6	0.0482	0.0481	0.0883	1140	6.4
100.0	0.0482	0.0481	0.0883	—	8.5

^a Carried out in the presence of 0.0533M-lutidine. ^b Rate of bromide ion production by all reactions, with no corrections for solvolysis. ^c This is assumed to be the rate of solvolysis at formal ionic strength 0.12M. ^d Rate constant corrected for ion association and solvolysis. ^e Fraction of total bromide ion produced by the S_N2 reaction; corrected for solvolysis. ^f No correction for ion association.

(Table 2). Under these conditions the reaction is 91—96% bimolecular elimination and 4—9% bimolecular substitution.¹¹ Solvolysis is negligible in acetone.¹¹ The activation energy for the combined E2 + S_N2 production of bromide ion is 21.6 kcal. mole⁻¹ (*i.e.*, close to the value of 21.0 reported by Hughes, Ingold, and Mackie). The fraction of substitution increases from 4.2 to 8.5% over the range 25—100°, so the activation energy for the S_N2 reaction is 23.3 \pm 0.5 kcal. mole⁻¹.

Comparison of Calculated and Experimental log B Terms.—The log B terms for reaction (3) in dimethylformamide are compared with theory as log B(MeBr) — log B(RBr) in Figure 3. The scale is such that Δlog B and Δlog k (Figure 1) are directly comparable. Clearly, most of the polar and steric effects of alkyl substituents are accounted for by the activation energy, not by the log B term. There is only fair agreement between Ingold's calculated values¹ and the experimental values

for reaction (3) in either acetone or dimethylformamide, but the deviations should be evaluated by comparison on the scale of Figures 1 and 2. The deviation is significantly large only for reaction (3) of t-butyl bromide in dimethylformamide. As with the activation energy for this reaction, the calculated value of log B for reaction (1) (Y = Hal = Br) is not satisfactory.

Ingold's calculated rate for reaction (3) (R = Bu^t) agrees well with our experimental rate (Figure 1), but because his rate constant is calculated from compensating E_a and log B values, which deviate considerably from observed values, this agreement may not be significant. However, it should be noted that our experimental E_a and log B for t-butyl bromide are subject to much greater uncertainty than is our log k.

Although Ingold's calculations for reaction (1) of t-butyl bromide are far from satisfactory, we find it

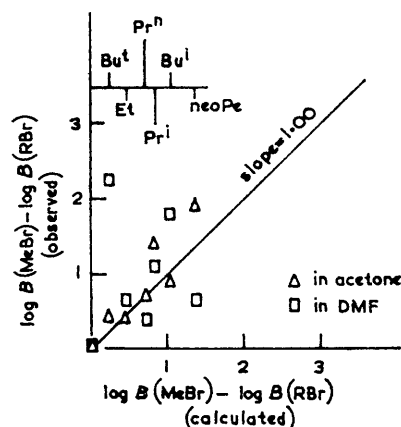


FIGURE 3 Comparison of experimental log B terms for reaction (3) of 0.07M-LiCl in acetone and of NEt₄Cl in dimethylformamide with log B terms calculated for bromide exchange with alkyl bromides

remarkable that, for six out of the seven reactions studied by us, calculations from first principles predict, to within a factor of five, effects ranging over 10⁷ in rate (Figure 1). Our experimental activation energies are spread over 8 kcal. mole⁻¹, but are predicted by theory to within 1 kcal. mole⁻¹ (Figure 2).

General Observations on S_N2 Halide Exchange in Acetone and in Dimethylformamide.—Our rate data for reaction (3) in dimethylformamide are compared in Table 1 with those of Hughes, Ingold, and Mackie⁹ for reaction (3) in acetone. Notice how the reaction (3) of 0.04M-tetraethylammonium chloride in dimethylformamide is *ca.* 10² times faster than the reaction of 0.07M-lithium chloride in acetone at 25°. This is because lithium chloride is a weak electrolyte in acetone⁸ but tetraethylammonium chloride is strong in dimethylformamide. When approximate rate constants for attack by dissociated chloride ion, rather than by a formal concentration of 0.07M-lithium chloride, are calculated by the Acree method,^{12,13} acetone and dimethylformamide are

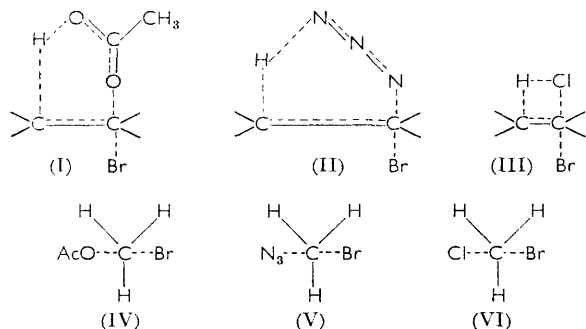
¹¹ D. Darwish, A. J. Parker, S. G. Smith, and S. Winstein, to be published.

¹² C. C. Evans and S. Sugden, *J. Chem. Soc.*, 1949, 270.

¹³ A. J. Parker, *J. Chem. Soc.*, 1961, 1328.

seen to exert comparable solvent effects on the rate of reaction (3), with reactions in acetone being faster. This is expected,¹⁴ because both are dipolar aprotic solvents and solvate alkyl bromides and chloride ion, relative to the transition state anion of (3), in much the same way. In our Acree type calculation, we have used the ion pair dissociation constants 8.3×10^{-6} mole l.⁻¹ for LiCl and 2.19×10^{-4} mole l.⁻¹ for LiBr in acetone at 25°. The degree of dissociation, α , of lithium chloride at 30% forward reaction (3), *i.e.*, in the presence of LiBr, was calculated, and then the rate constants reported by Hughes, Ingold, and Mackie were divided by α , to give the rate constants in Table I, for attack by dissociated chloride ion.

The reaction (1) ($Y = \text{OAc}$ or N_3) was studied because of our interest¹⁵ in a mechanism of merged substitution and elimination.¹⁶ The possibility existed that transition states (I)—(III) were utilised by the $\text{S}_{\text{N}}2$ reaction (1), when R contained a β -hydrogen. Of course, such transition states would not be available to reaction (1) ($\text{RBr} = \text{MeBr}$), which can use only $\text{S}_{\text{N}}2$ transition states



such as (IV)—(VI). We would expect that (I), and possibly (II), would be considerably more stable, relative to (IV) and (V), respectively, than would (III) be relative to (VI), because of the structurally more favourable six-membered ring and the greater hydrogen-bond acceptor tendencies of acetate in (I). Thus, if transition states such as (I)—(III) were used, we might expect a substantial decrease in the rate difference $\log k(\text{Pr}^i\text{Br}) - \log k(\text{MeBr})$ for reaction (1) of acetate or azide ion, when compared with experimental and especially with calculated values for reaction (1) of chloride ion. A small decrease is observed, but it is not substantial (Table 3), and we feel that transition states such as (I)—(III) do not lead to $\text{S}_{\text{N}}2$ products, although they may lead to $\text{E}2$ products.¹⁵

$\text{S}_{\text{N}}2$ and $\text{E}2$ Reactions of *t*-Butyl Bromide.—Hughes, Ingold, and Mackie⁹ did not appreciate that the overall reaction (2) in acetone was largely elimination followed by

¹⁴ A. J. Parker, *Quart. Revs.*, 1962, 163.

¹⁵ A. J. Parker, M. Ruane, G. Biale, and S. Winstein, *Tetrahedron Letters*, in the press; A. J. Parker and S. Winstein, Abstracts, 39th Congress of the Australian and New Zealand Association for the Advancement of Science, Melbourne, Jan. 1967, p. B15; S. Winstein, *et al.*, Abstracts of the 144th National Meeting of the American Chemical Society, Los Angeles, April, 1963, 8M; S. Winstein, *Accademia Nazionale dei Lincei (Roma)*, VIII Corso Estivo di Chimica, *Chimica Teorica*, 1965, 327.

addition.⁴ They concluded that (2) was *ca.* 40% an $\text{S}_{\text{N}}2$ reaction. An arithmetical error appears in their Paper, where they record a rate constant which is less by a factor of 10 than the rate constant which can be calculated⁴ from their published run.

The formation of bromide ion from *t*-butyl bromide in the presence of the moderately strong electrolyte

TABLE 3

Effect of alkyl groups and β -hydrogen atoms on rates of $\text{S}_{\text{N}}2$ reactions of alkyl bromides with chloride, azide, and acetate ion in dimethylformamide at 25°

	$\log k_2(\text{MeBr}) - \log k_2(\text{RBr})$				
	R = Me	Et	Pr ⁱ	Bu ^t	Bu ^t
LiOAc (0.009M) ^a ...	0.00	1.35	2.78	—	—
NET ₄ N ₃ (0.04M) ...	0.00 ^b	—	2.10 ^f	2.56 ^c	4.40 ^d
NET ₄ Cl (0.04M)	0.00	1.57	3.31	3.05	4.66
Calculated (Br ⁻) ^e ...	0.00	1.77	3.46	3.46	4.28

^a This salt is incompletely dissociated in dimethylformamide at this concentration, but since the same concentration was used for all three alkyl bromides, the comparison is not affected. ^b B. O. Coniglio, D. E. Giles, W. R. McDonald, and A. J. Parker, *J. Chem. Soc. (B)*, 1966, 152. ^c This work, using NaN₃ at 0.04M. This value has been corrected to compensate for the differing ion-pairing of NaN₃ relative to NET₄N₃ in dimethylformamide, from comparison of rate data for MeBr with NaN₃ and NET₄N₃ in dimethylformamide (see b). ^d This reaction is 80% $\text{E}2$ and 20% $\text{S}_{\text{N}}2$. The relative rate constant for the $\text{S}_{\text{N}}2$ reaction is recorded here. ^e Calculated rate data for Br⁻ + RBr reaction; ref. 1. ^f E. C. Ko, unpublished work.

TABLE 4

Reaction (3) of *t*-butyl bromide with NBu₄Cl in acetone at 75.6°. Concentrations expressed as ml. of 0.0239M standard titrant per 4.59 ml. of sample; estimated maximum uncertainty in rate constants is $\pm 4\%$

$[\text{Bu}^t\text{Br}]_0 = 0.0482\text{M} = 9.26$ ml. titrant; $[\text{NBu}_4\text{Cl}]_0 = 0.0481\text{M} = 9.24$ ml. titrant; $[\text{lutidine}] = 0.0883\text{M}$.

Time (min.)	$[\text{Br}^-]_t$ ^a (ml.)	$[\text{H}^+]_t$ ^b (ml.)	$[\text{Br}^- + \text{Cl}^-]_t$ ^a (ml.)	100 F_8 ^c (%)	10 ⁴ k_1 ^d (sec. ⁻¹)	10 ² k_2 ^e (l. mole ⁻¹ sec. ⁻¹)
0	0.01	0.03	9.24	—	—	—
10	2.16	1.78	11.25	6.7	4.43	1.05
20	3.63	3.08	12.62	6.6	4.15	1.12
30	4.54	4.06	13.47	6.6	3.75	1.11
40	5.23	4.80	14.06	7.7	3.47	1.13
50	5.62	5.40	14.61	4.3	3.12	1.07
630	9.35	—	17.97	6.5	—	—

Av. 6.4

^a Estimated by pouring reaction mixture into carbon tetrachloride (25 ml.), extracting with water (3×20 ml.), and titrating the aqueous extract with standard AgNO₃. ^b Estimated by pouring into cold acetone and titrating with standard NaOMe in MeOH, using Thymol Blue indicator. ^c 100 F_8 gives the fraction of substitution (as a percentage). F_8 was calculated here from the expression $F_8 = ([\text{Cl}^-]_0 - [\text{Cl}^-]_t) / ([\text{Br}^-]_t - [\text{Br}^-]_0)$. ^d First-order rate constant for the development of bromide ion by all reactions. ^e Second-order rate constant for overall bimolecular reaction [$\text{S}_{\text{N}}2 + \text{E}2$], not corrected for incomplete dissociation of NBu₄Cl in acetone.

tetra-*n*-butylammonium chloride in solvent acetone has been studied in detail by Winstein and his co-workers¹¹ and will be discussed in later papers. The reactions are bimolecular. Roughly 5% of reaction proceeds through an $\text{S}_{\text{N}}2$ transition state to give *t*-butyl

¹⁶ S. Winstein, D. Darwish, and N. J. Holness, *J. Amer. Chem. Soc.*, 1956, 78, 2915.

chloride and bromide ion, and the remaining 95% proceeds through an interesting non-classical *E2* transition state to give bromide ion, isobutene, and hydrogen chloride. A typical reaction is in Table 4. In the absence of base, the elimination reaction is succeeded by Markovnikov addition of HCl to isobutene.⁴ For this reason, Hughes, Ingold, and Mackie believed that the substitution reaction was of greater importance than is actually the case. In the presence of 2,6-lutidine, a base which does not promote the *E2* or *S_N2* reaction,¹¹ addition does not occur and only 4–9% t-butyl chloride is produced (Table 4). The t-butyl chloride has been estimated by gas chromatography, by chloride analysis, and by $[\text{Br}^-]-[\text{H}^+]$ analysis.¹¹ The fraction of substitution is constant (Table 4) throughout reaction. The fraction of substitution at 25° is not significantly changed by increasing the concentration of tetra-n-butylammonium chloride from 0.02 to 0.09M (Table 2). It seems most likely that, as in many reactions of chloride ion with secondary and tertiary alkyl halides and toluene-sulphonates, the alkyl chloride is produced by an *S_N2* reaction, which is competing with a chloride induced *E2* reaction.¹⁵ The t-butyl chloride is *not* produced by addition of HCl to isobutene or of chloride ion to the t-butyl carbonium ion.

In dimethylformamide as solvent, almost the same fraction (6–8%) of the total reaction is due to an *S_N2* reaction (3) ($\text{R} = \text{Bu}^t$) when t-butyl bromide reacts with >0.1M-tetraethylammonium chloride. This is expected in view of the similarity of acetone and dimethylformamide as dipolar aprotic solvents. Blank experiments showed that hydrogen chloride was stable in dimethylformamide at 50° over two half-lives of reaction (2), and that HCl did not add to isobutene at 50° in dimethylformamide, a solvent which is much more basic than acetone. Although the first-order rate constant for total bromide ion production was almost doubled, the fraction of substitution to elimination was not appreciably changed by a two-fold increase in the concentration of tetraethylammonium chloride (Table 2). Neither the rate of bromide ion formation, nor the fraction of substitution was changed by the addition of lutidine. A typical run is in Table 5. Note that reaction (3) ($\text{R} = \text{Bu}^t$) follows second-order kinetics in acetone containing 2,6-lutidine¹¹ (Table 4) and first-order kinetics in dimethylformamide containing lutidine (Table 5). This is because the heteroconjugate LutH^+Cl^- is stable in acetone but dissociates to chloride ion and lutidinium cation in dimethylformamide. Thus, the concentration of free chloride ion decreases with each act of elimination in acetone, but remains almost constant in dimethylformamide.

The bimolecular reaction (2) is accompanied by solvolysis, which is very much faster in dimethylformamide than in acetone. Rate constants for the bimolecular reactions in dimethylformamide (Table 2) were calculated from (4). Higher concentrations (*ca.* 0.1M) of tetraethylammonium chloride in dimethylformamide were used for reaction of t-butyl bromide than for reactions of

TABLE 5

Reaction (3) of t-butyl bromide with chloride ion in dimethylformamide at 50.0°. Concentrations expressed as ml. of 0.03035M standard titrant per 4.59 ml. of sample; estimated maximum uncertainty in rate constants is $\pm 4\%$

$[\text{Bu}^t\text{Br}]_0 = 0.0518\text{M} = 7.83$ ml. titrant; $[\text{NEt}_4\text{Cl}]_0 = 0.0994\text{M} = 15.03$ ml. titrant; $[\text{lutidine}] = 0.0533\text{M}$.

Time (min.)	$[\text{Br}]_t$ (ml.)	$[\text{Br}^- + \text{Cl}^-]_t$ (ml.)	$[\text{H}^+]_t$ (ml.)	100 F_s ^a	10 ⁴ k_1 ^b (sec. ⁻¹)
0	2.32	17.12	1.63	—	—
15	3.31	18.00	3.34	1.11	2.12
30	4.07	18.76	3.79	6.3	2.06
45	4.66	19.33	4.48	5.6	1.98
125	6.67	21.14	6.27	7.6	1.96
155	7.13	21.62	6.67	6.4	2.06
180	7.31	21.77	6.87	6.8	2.00
1485	7.91	22.45	7.48	4.7	—
1515	7.91	22.45	7.65	4.7	—

Av. 6.0

$$k_2^c = 2.21 \times 10^{-3} \text{ l. mole}^{-1} \text{ sec.}^{-1}$$

^a See footnote *c* to Table 4. ^b First-order rate constant for the development of bromide by all reactions. ^c Second-order rate constant, after correction for solvolysis (Table 2) and for incomplete dissociation of NEt_4Cl ($\alpha = 0.69$) as in equation (4).

the other alkyl bromides, in an effort to minimise the influence of the solvolysis reaction. In (4), k_1 is the solvolysis rate with tetraethylammonium perchlorate in place of tetraethylammonium chloride, *i.e.*, 3.37×10^{-6}

$$\left(\frac{d[\text{Br}^-]}{dt}\right)/[\text{Bu}^t\text{Br}]_t = k_1 + (k_2^B + k_2^S) \alpha [\text{NEt}_4\text{Cl}]_0 \quad (4)$$

sec.⁻¹ at 25°, and α is the degree of dissociation of tetraethylammonium chloride in dimethylformamide at 25° at the appropriate concentration. Values of α were calculated from the rates for the *S_N2* reaction of 0.01–0.19M-tetraethylammonium chloride with n-butyl iodide in dimethylformamide at 25°, by using the Acree method,¹² as re-published by Weaver and Hutchison¹⁷ (see Table 6).

TABLE 6

Reaction of NEt_4Cl with Bu^nI in dimethylformamide. Estimation of the degree of dissociation of NEt_4Cl in dimethylformamide at 25.0° by the method of Weaver and Hutchison¹⁷

$[\text{Bu}^n\text{I}] = 0.035\text{M}$.

$[\text{NEt}_4\text{Cl}]$ (M)	10 ² k ^a (l. mole ⁻¹ sec. ⁻¹)	α ^b	10 ² k^c (l. mole ⁻¹ sec. ⁻¹)
0.0102	6.80	0.936	7.26
0.0230	6.48	0.880	7.36
0.0784	5.32	0.724	7.35
0.0789	5.35	0.723	7.40
0.1952	4.20	0.572	7.34
0.1952	4.17	0.572	7.29

^a Observed second-order rate constant; estimated uncertainty $\pm 1\%$. ^b Calculated from $K_{\text{dissoc}} = 1.49 \times 10^{-1}$ mole l.⁻¹. This is the value of K_D which gives α , so the most constant value of k^c is obtained. ^c k^c is the rate constant for reaction of dissociated chloride ion.

The ratio of bimolecular elimination to total bimolecular production of bromide ion was calculated from the

¹⁷ W. M. Weaver and J. D. Hutchison, *J. Amer. Chem. Soc.*, 1964, **86**, 261.

ratio of acid to total bromide ion produced. The fraction of S_N2 reaction was calculated from the ratio of chloride ion consumed to total bromide ion produced by the bimolecular reaction. Allowance was made for the solvolysis reaction. Results are in Table 2. The fraction of substitution varies with temperature, so the 'activation energy' for the combined S_N2 and $E2$ reactions is modified to give the value in Table 1 for S_N2 substitution.

None of the reactions (3) of other alkyl bromides in dimethylformamide had an $E2$ component which was detectable, and the solvolysis reaction was not significant. No acid was produced and the total halide ion concentration remained constant. Reactions of neopentyl bromide were S_N2 and gave the expected neopentyl chloride, as confirmed by analysis and the n.m.r. spectrum.

EXPERIMENTAL

Alkyl Bromides.—Methyl, ethyl, isopropyl, n-propyl, isobutyl, and t-butyl bromide (all B.D.H.) were dried (P_2O_5) and fractionated through an efficient column before use. Isobutyl bromide, freed from traces of t-butyl bromide by repeatedly washing an ether solution with water until the washings were no longer acidic and contained no bromide ion, was dried (P_2O_5) and fractionated. The compounds all had boiling points within 0.5° of published values.⁹ All gave $100 \pm 1\%$ of the expected bromide ion when hydrolysed with an excess of alkali in 80% DMF- H_2O . Infinity samples in kinetic runs were always within 2% of the expected value for the complete forward reaction (3). All alkyl bromides, except t-butyl bromide, remained unchanged when allowed to stand in dimethylformamide for a period corresponding to two half-lives, at the highest temperature used for reactions of a particular alkyl bromide. Neopentyl bromide was prepared from neopentyl alcohol, using phosphorus tribromide in bromobenzene containing quinoline.¹⁸ An ether solution of the product was washed repeatedly with water to remove traces of an isomeric tertiary alkyl bromide, and the bromide was dried and fractionated, b. p. $105-106^\circ/760$ mm. The n.m.r. spectrum * showed only two absorptions: CH_3 protons, τ 8.95, and CH_2 protons, τ 6.77, integrating 9 : 2, as expected. The calculated quantity of bromide ion was liberated from the neopentyl bromide when it was heated with an excess of azide ion at 100° in dimethylformamide.

Other Materials.—Dimethylformamide and acetone were purified in the usual way.¹⁹ Tetra-alkylammonium salts were prepared by standard methods. The analyses of all salts were within 1% of the expected values. 2,6-Lutidine was fractionated before use.

Technique for Kinetic Runs.—Kinetic runs were performed in sealed tubes.^{13,19} Experimental rate constants are in Tables 2, 7, and 8. Typical runs are shown in Tables 4, 5, and 9. Reactions of primary and secondary alkyl bromides were quenched by pouring into cold 60% acetone-water, and the solutions were titrated potentiometrically without delay with silver nitrate, in the presence of barium nitrate which was added to reduce coprecipitation of the silver halides. The end-points for bromide ion and for

* N.m.r. spectra were run in analytical grade CCl_4 solution on a Varian A60 spectrophotometer using tetramethylsilane as an internal standard.

TABLE 7

Rate constants for reaction (3) in dimethylformamide at the temperature shown. Initially, $[RBr] = 0.02M$, $[NET_4Cl] = 0.04 \pm 0.004M$ unless otherwise indicated; estimated maximum uncertainty in rate constants is $\pm 4\%$. Rate data for $RBr = Bu^tBr$ are in Table 2

	10^4k_2 (l. mole ⁻¹ sec. ⁻¹)
MeBr ...	19.2 (-20.3°); 30.3 (-16.8°); 81.7 (-8.3°); 250 (0.5°); 233 (0.7°); 735, 745 (8.2°)
EtBr ...	7.79 (3.0°); 19.9 (10.0°); 40.3 (15.8°); 46.8 (16.2°); 108 (24.7°); 115, 121 (25.7°); 187 (30.8°)
Pr ⁱ Br ...	3.48, 3.53 (30.0°); 9.60 (38.9°); 16.5 (44.0°); 17.6 (44.1°); 109, 111, 121 (63.2°)
Pr ⁿ Br ...	5.43 (3.2°); 9.71 (7.1°); 15.6 (11.6°); 16.1 (11.7°); 59.8 (22.9°); 76.0 (26.6°); 77.4 (28.2°)
Bu ^t Br ...	3.90 (25.9°); 10.4, 10.8, 11.5 (35.0°); 32.0 (45.5°); 29.7 (45.4°); 103, 111 (59.5°); 119 ^a (60.0°), 29.5 (45.4°); 27.4 ^b (45.4°)
neoPeBr	0.715 (80.0°); 1.30 (85.7°); 5.45 (100.2°); 5.48 (100.4°); 13.9 (110.2°); 13.1 (110.5°); 18.4 (114.1°); 22.7 (115.9°); 25.8 (116.8°)

^a $[NET_4Cl] = 0.0112M$. ^b Reaction mixture contained 0.042M-lutidine, no acid was formed, and total halide was constant; therefore no elimination

TABLE 8

Rate constants for reaction (1) of NET_4N_3 and of LiOAc in dimethylformamide at the temperature shown. Initially, $[RBr] = 0.03M$, $[NET_4N_3] = 0.04M$, and $[LiOAc] = 0.0098M$; estimated maximum uncertainty in rate constants is $\pm 4\%$

Reactants	10^4k_2 (l. mole ⁻¹ sec. ⁻¹)
$CH_3Br + LiOAc$...	657 (25.0°)
$EtBr + LiOAc$...	29.2 (25.0°)
$Pr^iBr + LiOAc$...	1.08 (25.0°)
$Bu^tBr + NET_4N_3$...	11.5, 9.67 (23.9°); 21.4, 20.7 (31.1°); 73.3, 73.8 (44.8°)
neoPeBr + NET_4N_3	60.7 (100.0°)
$Bu^tBr + NET_4N_3$ ^a	1.14 (25.0°)

^a $[NET_4N_3] = 0.0940M$; $[Bu^tBr] = 0.0510M$; the second-order rate constant is for total bromide ion production; this reaction is 80% elimination and 20% substitution, but both processes effectively consume free azide ion, because HN_3 is a weak acid in dimethylformamide

TABLE 9

Typical S_N2 reaction of an alkyl bromide with NET_4Cl in dimethylformamide at 35.0° . Concentrations expressed as ml. of 0.0125M- $AgNO_3$ per 4.91 ml. of sample

$[Bu^tBr]_0 = 0.02209M = 8.67$ ml. $AgNO_3$; $[NET_4Cl]_0 = 0.04619M = 18.14$ ml. $AgNO_3$.

Time (min.)	$[Br^-]_t$ (ml.)	$[Br^- + Cl^-]_t$ (ml.)	$\log [Bu^tBr]_t$	10^3k_2 (l. mole ⁻¹ sec. ⁻¹)
0	0.60	18.17	0.3372	—
36	1.25	18.23	0.3572	1.06
60	1.82	17.90	0.3770	1.06
105	2.48	18.12 ^a	0.4031	1.00
135	2.98	18.15	0.4256	1.07
165	3.32	18.27	0.4425	1.02
195	3.72	18.22	0.4643	1.04
2000	8.62	18.10 ^a	—	—
2500	8.67	18.10 ^a	—	—

Mean $k_2 = 1.04 \pm 0.02 \times 10^{-3}$ l. mole⁻¹ sec.⁻¹.

^a Sample tested for acid; none found.

¹⁸ L. H. Sommer, H. D. Blankman, and P. C. Miller, *J. Amer. Chem. Soc.*, 1954, **76**, 803.

¹⁹ A. J. Parker, *J. Chem. Soc. (A)*, 1966, 220.

total halide were easily detected. Occasional checks revealed no formation of acid in any reaction. Total halide remained constant throughout reaction, confirming that a substitution reaction was occurring. Good second-order kinetics were followed in all cases. The run in Table 9 is typical.

The reaction samples of t-butyl bromide were poured into 20 ml. of carbon tetrachloride and shaken three times with 10-ml. portions of water. The combined aqueous extracts were then analysed for bromide ion and total halide ion, as described above. The acid formed by elimination was estimated by pouring aliquots of the reaction mixture into 20 ml. of cold acetone and titrating with sodium methoxide in methanol, using Thymol Blue as indicator. Appropriate blank experiments established the validity of our analytical procedures.

Reaction Products.—The products for the reaction of t-butyl bromide with chloride ion in acetone have been thoroughly investigated by Winstein and his co-workers, using gas chromatography and titration procedures.¹¹ The organic products are $5 \pm 1\%$ t-butyl chloride and 95% isobutene. The other alkyl bromide-chloride ion-exchanges are confirmed as pure S_N2 processes, because of the constancy of total halide ion. Solvolysis was not observed, except for t-butyl bromide (Table 2). Neopentyl chloride

and neopentyl azide were extracted with carbon tetrachloride from their respective reactions after ten half-lives (100% production of bromide ion). The n.m.r. spectrum of each extract showed only two peaks, and each spectrum closely resembled that of the starting material, neopentyl bromide: neoPeCl, τ 8.99 (CH_3), 7.73 (CH_2), rel. pk. area 9:2; neoPeN₃, τ 9.05 (CH_3), 6.94 (CH_2), 9:2.

The chemical shifts of starting material, neopentyl bromide, and of reaction products, neopentyl chloride and neopentyl azide, were close but spectra of each mixture of starting material and reaction product showed four peaks, two peaks corresponding to the starting material neopentyl bromide and two peaks corresponding to the reaction product, either neopentyl chloride or neopentyl azide. These spectra showed, in agreement with 100% formation of bromide ion, that the reaction products were not the starting reagent. Thus, the S_N2 reactions of neopentyl bromide with chloride or azide ion proceed without rearrangement.

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