ALLEGED S_N2 FINKELSTEIN SUBSTITUTIONS OF T-BUTYL BROMIDE[1]

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The relative reactivity of t-butyl halides in bimolecular nucleophilic substitution represents an important anchor point for our quantitative understanding of the subject,[2,3] and thus there is considerable interest in the recently reported rate constants for S_N2 reactions of t-butyl bromide with lithium bromide[4,5] and lithium chloride[6] in anhydrous acetone. These results are being widely quoted.[7] However, careful examination of the papers in question reveals that the S_N2 designation for these reactions was merely an assumption. In this Communication we show that the published experimental evidence and the results of further work by us make it clear that the reported rate constants do not correspond to the S_N2 mechanism.

The rates of the exchange reaction between t-butyl bromide and lithium

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[1] Research supported by the National Science Foundation.

[2] C. K. Ingold et al., J. Chem. Soc. 3200 (1955).

[3] C. K. Ingold, Quarterly Reviews 11, 1 (1957).

[4] L. J. LeRoux and E. R. Swart, J. Chem. Soc. 1475 (1955).

[5] P. B. de la Mare, ibid. 3180 (1955).

[6] E. D. Hughes, C. K. Ingold and J. D. H. Mackie, ibid. 3173 (1955).

[7] e.g., (a) A. Streitwieser, Jr., Chem. Reviews 56, 571 (1956); (b) E. Eliel, "Steric Effects in Organic Chemistry", John Wiley and Sons, New York, N. Y., 1956, p. 73; (c) E. S. Gould, "Mechanism and Structure in Organic Chemistry", Henry Holt and Co., New York, N. Y., 1959, pp. 234-235, 274-276.

radio-bromide in acetone were treated by LeRoux and Swart with the aid of equation (1), the first and second terms on the right hand side of the

$$(R/a) = k_1 + k_2 [\alpha (LiBr)] \qquad (1)$$
$$(dx/dt)/(a-x) = k_1 + k_2 (b-x) \qquad (2)$$

equation representing unimolecular and bimolecular substitution, respectively. In the second term, the concentration of lithium bromide was multiplied by α, the degree of dissociation of the salt, in order to correct for the negligible reactivity of lithium bromide ion pairs compared to dissociated bromide ions.[8] The fit of the data by equation (1) was good, and at $40°$ unimolecular and bimolecular paths were judged to be of nearly equal importance at a lithium bromide concentration of 0.01 N. The bimolecular rate constant, k_2, was about one seventh that for isopropyl bromide.

In the work of the group at University College, London, on the reaction of t-butyl bromide with both lithium radio-bromide[5] and lithium chloride[6] in acetone, some disturbance from a unimolecular contribution was reported, but the main reactions were regarded as bimolecular substitutions. In the reaction with lithium radio-bromide a small amount of acid was observed and ascribed to the elimination component of the unimolecular reaction of t-butyl bromide. However, roughly second order kinetics were followed and second order rate constants were evaluated.

Although the treatment of t-butyl bromide with lithium chloride gave rise to more acid than does lithium bromide, Hughes, Ingold and Mackie[6] claim to have shown that the reaction is predominantly a substitution. There are disturbances from reversibility and other causes, which these workers hoped to avoid by confining the quantitative treatment of the

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[8] C. C. Evans and S. Sugden, *J. Chem. Soc.* 270 (1949).

measurements to the first 30-40% of the reaction. The specific rate of development of bromide ion, $[dx/dt)/(a-x)]$, was plotted against the concentration of chloride ion, $(b-x)$, according to equation (2), the intercept and slope supposedly giving k_1, the rate constant of the El reaction, and k_2, the S_N2 rate constant, respectively. At $55.20°$, k_2 was reported to be 0.76×10^{-5} sec $^{-1}$ l. mole^{-1}, about one fifth the value for isopropyl bromide.

The main evidence for the S_N2 mechanism of reaction of t-butyl bromide offered by LeRoux and Swart[4] and Ingold and coworkers[5,6] was the observed kinetic form, and this is far from an unambiguous guide to mechanism. The use of equations such as (1) and (2) to separate unimolecular and bimolecular contributions involves the assumption that k_1 is insensitive to the salt concentration. This is known to be incorrect in acetone.[9,10c] The value of k_1 can be expected to increase with increased salt concentration in the approximately linear fashion reported by Salomaa[11] for alcoholysis of α-haloethers and by Winstein and coworkers[10] for ionization of various alkyl arenesulfonates and halides in acetic acid and other solvents including acetone.

An approximately linear pattern of salt effects in ionization reactions serves to make salt-promoted ionization take the same kinetic form

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[9] J. C. Charlton and E. D. Hughes, J. Chem. Soc. 2939 (1954).

[10] e.g., (a) S. Winstein, E. Clippinger, A. H. Fainberg and G. C. Robinson, J. Am. Chem. Soc. 76, 2597 (1954); Chemistry and Industry, 664 (1954); (b) A. H. Fainberg and S. Winstein, J. Am. Chem. Soc. 78, 2763 (1956); (c) S. Winstein, S. Smith and D. Darwish, ibid. in press.

[11] P. Salomaa, Ann. Univ. Turkuensis A14 (1953).

as bimolecular substitution. The ambiguity may be seen most clearly with equation (3), which shows how a linear pattern of acceleration of an ionization rate by a salt, MY, can be mistaken for contributing unimolecular and bimolecular contributions with rate constants k_1^o and $k_1^o b$, respectively. Ingold and coworkers, who have actually reported salt effects which follow the linear pattern quite well in the case of chloromethyl ether in ether-alcohol[12] and t-butyl bromide in nitromethane[13] (Table I), failed to recognize this ambiguity.

As summarized in Table I, the data on t-butyl bromide-lithium radio-bromide exchange are fit by equation (4) for an ionization reaction with a linear pattern of salt effects. In actual fact, equation (4) reproduces the first order rate constants of LeRoux and Swart[4] with just as low a

$$k_1 = k_1^o [1 + b (MY)] = k_1^o + k_1^o b (MY) \qquad (3)$$

$$R/a = k_1^o [1 + b (LiBr)] \qquad (4)$$

mean deviation as does equation (1). Since the rate constants reported by de la Mare[5] are in essential agreement with those of LeRoux and Swart, they also fit well to equation (4) (Table I). Obviously, kinetic form provides no argument for the S$_N$2 mechanism for the t-butyl bromide radio-bromide exchange.

With regards to the kinetics of the reaction of t-butyl bromide with lithium chloride, Hughes, Ingold and Mackie[6] report the actual data for one sample run at 55.20°, the concentration of t-butyl bromide being 0.1191 M and that of lithium chloride being 0.0634 M. Our own plot of the reported

[12] P. Ballinger, P. B. D. de la Mare, G. Kohnstam and B. M. Prestt, J. Chem. Soc. 3641 (1955).

[13] P. B. D. de la Mare, E. D. Hughes, C. K. Ingold and Y. Pocker, ibid. 2930 (1954).

Table I

Reactions of t-Butyl Bromide in Various Solvents

Solvent	°C	Salt	$10^6 k_1^0$ sec^{-1}	b	Salt Range 10^2M	Ave. Fit % of k_1	Ref.
90% Me_2CO	50.0	$LiClO_4$	187	3.4	0-10	2.0	14
		LiBr	187	4.2	0-10		14
		LiCl	187	5.6	0-10		14
$AcOH^a$	50.0	$LiClO_4$	79	13	0-3.4		14
$MeNO_2$	25.0	Et_4NCl	3.62	20.7	0.5-14	1.0	13
$HCONMe_2$	50.7	Et_4NBr	52	6.3	0-10		15
		NaBr	52	6.5	0-10		15
		Et_4NNO_3	52	3.2	0-17	2.4	15
Me_2CO	20.0^b	LiBr	0.040	27.8	0.5-5	0.9	4
	40.0^b	LiBr	0.38	27.4	0.5-10	4.7	4
	44.4^b	LiBr	0.734	32.5	2.4-9	2.6	5
	60.0^b	LiBr	2.46	29.0	0.5-5	4.8	4
	50.0	LiBr	1.23	33.8	0-8	7.8	
	50.0	$LiClO_4$	1.23	11.5	0-8	3.8	
	50.0	Bu_4NClO_4	1.23	12.2	0-8	5.5	
	50.0	LiCl	1.23	24	0-3		

[a] 0.068 M in LiOAc

[b] Radio-bromide exchange

$[(dx/dt)/(a-x)]$ values vs. $(b-x)$ according to equation (2) leads to a k_1 value of 1.8×10^{-6} sec^{-1} and a k_2 value of 7.6×10^{-5} sec^{-1} l. mole^{-1}, ten times the value reported by Hughes, Ingold and Mackie.[6] This new figure is twice the rate constant for isopropyl bromide.[6]

Ingold and coworkers[6] offered no evidence for S_N2 substitution based

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[14] A. H. Fainberg and S. Smith, unpublished work.

[15] S. D. Ross and M. M. Labes, *J. Am. Chem. Soc.* **79**, 4155 (1957).

on the nature of the products from the action of lithium chloride on t-butyl bromide. The reported acid titers for the one sample run corresponded to ca. 60% elimination, so that elimination was clearly more important than substitution. No direct evidence for formation of t-butyl chloride was obtained.

In our own experiments on the behavior of t-butyl bromide in acetone, acid was observed to develop at a substantial rate initially, but the amount of acid tended to level off at a low value and then to rise again eventually as side reactions of the solvent occur and water develops. This behavior has been noted previously.[16] The addition of excess tetrabutylammonium chloride caused acid formation to be nearly quantitative, hydrogen chloride presumably being diverted as the bichloride salt. The addition of 2,6-lutidine tends to prevent loss of acid, nearly quantitative acid formation being observed in the absence or presence of lithium or tetrabutylammonium perchlorate, chloride or bromide. Vapor phase chromatographic analysis of aliquots of the reaction mixture showed (3 ± 1)% of t-butyl chloride was formed during runs with excess lithium or tetrabutylammonium chloride whether lutidine was present or not. Isobutylene was the major organic product, comparing favorably in amount with that of acid.

The rate of acid formation from t-butyl bromide in acetone was independent of lutidine concentration in the 0.02-0.09 M range. The first order rate constants were increased somewhat by addition of salt, the values at .03 M salt being compared in Table II. While the pattern of the variation of rate constant with salt concentration is not exactly the linear one, equation (3) fits the data fairly well, as is summarized in Table I for

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[16] L. C. Bateman, K. A. Cooper and E. D. Hughes, _J. Chem. Soc._ 913 (1940).

Table II

First Order Rate Constants at 50.0° for Acid Formation from

t-Butyl Bromide in Acetone Containing 0.02 M 2,6-Lutidine

and 0.03 M Salt

Salt	$10^6 k_1$ sec.$^{-1}$	Salt	$10^6 k_1$ sec.$^{-1}$
None	1.23	LiCl	2.11
LiClO$_4$	1.65	Bu$_4$NClO$_4$	1.78
LiCl	2.0[a]	LiBr	2.66

[a] Without lutidine

several of the salts.

Summing up the behavior of t-butyl bromide towards lithium chloride in acetone, it is clear that the reaction is nearly quantitatively elimination, only ca. 3% of the substitution product, t-butyl chloride, being formed. It would appear that Hughes, Ingold and Mackie[6] assumed not only the mechanism, but the reaction product as well. As regards the exchange reaction between t-butyl bromide, and lithium radio-bromide, it is significant that the initial rate of acid formation from t-butyl bromide in the presence of lithium bromide is approximately equal to the first order exchange rate. Further, the k_1^o and b values from the exchange rates are nearly identical with those from the elimination rates (Table I), suggesting that exchange and elimination have the same rate-determining step. Very probably, exchange involves elimination and re-addition of hydrogen bromide, just as in nitromethane solvent.[13] The S_N2 designation is certainly unwarranted.

Except for a lower rate level, the behavior of t-butyl bromide towards bromide and chloride salts in acetone is exactly parallel to that in nitro-

methane, but Ingold and coworkers have somehow given quite different inter-
pretations for the two solvents. The dependence of rates on salt concen-
tration is not too different in the two solvents, judging by the b values
in Table I, and yet the reaction of t-butyl bromide with tetraethylammonium
chloride in nitromethane[13] has been labelled a unimolecular one, zero order
in salt, and the reaction with lithium chloride in acetone[6] has been termed
predominantly bimolecular substitution.

While more needs to be known about ion pair return and salt effect
patterns in acetone, and the mechanistic details of the proton removal, the
most likely mechanism of elimination in acetone appears to be one involving
initial ionization of the t-butyl bromide. As far as we now know, the
sequence of relative rates and b values in the different solvents summarized
in Table I are consistent with an ionization mechanism in acetone. The
mechanism of formation of the very small amount of t-butyl chloride from
t-butyl bromide is less clear.

The present change in the account of what is occurring when t-butyl
bromide is treated with halide salts in acetone has a bearing on Ingold's
quantitative treatment[2] of steric effects in S_N2 displacements. For the
bimolecular Finkelstein reactions of methyl, ethyl and isopropyl bromides
and the alleged bimolecular substitutions of t-butyl bromide, the energies
of activation rise continuously with α-methyl substitution, while the entropy
of activation decreases from methyl to isopropyl bromide and then rises
again. This behavior of the entropy of activation was not associated with
a change of mechanism. Instead, it was accounted for by a treatment[2] in-
volving ponderal, steric and polar structural entropic effects, rates being
fitted to within a small factor. This fit of the t-butyl bromide rates may
no longer be regarded as support for the quantitative treatment.