Reactivity–Selectivity Relationships. Part 6.[1] Application of the Reactivity–Selectivity Principle to Solvolytic Reactions. Possible Evidence for Ion Pair Intermediates in S_N2 Solvolyses

By **Addy Pross,*** **Haim Aronovitch,** and **Rodi Koren,** Department of Chemistry, Ben Gurion University of the Negev, Beer Sheva, Israel

The reactivity–selectivity principle has been applied to the study of the solvolytic behaviour of octyl, 1-methylheptyl, and benzyl derivatives toward the competing nucleophiles, ethanol and water. Low selectivity values, k_E/k_W, are observed for these substrates. The results are interpreted as possible evidence for ion pair intermediates in S_N2 solvolyses. The effect of changes in substrate, solvent polarity, leaving group, and temperature are consistent with this interpretation. In the presence of a strong nucleophile, such as azide ion, a traditional S_N2 pathway is indicated.

THE first major step in the understanding of solvolytic substitution reactions was made by Hughes and Ingold over 30 years ago.[2] Their classification of nucleophilic substitution reactions as either unimolecular, S_N1, or bimolecular, S_N2, has formed the basis of much of the research since conducted on this subject.[2-4] Nonetheless, it has become increasingly apparent with the passage of time that the nature of such reactions is considerably more complex than was first appreciated.[3-6]

The problem of 'borderline' behaviour has been particularly troublesome. Secondary substrates, for example, exhibit characteristics intermediate between those expected for limiting S_N1 and S_N2 mechanisms.[3a,4] As a consequence, the study of 'borderline' cases has been the subject of considerable interest in recent years.[3,4]

In an attempt to resolve the problem of 'borderline' behaviour Sneen and his co-workers proposed a universal ion pair mechanism as the basis of all substitution reactions at carbon.[3d] This proposal was particularly controversial with regard to the traditional S_N2 mechanism since the possibility of attack of nucleophiles on neutral substrate was discounted. The Sneen ion pair

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[1] (*a*) Part 5, Y. Karton and A. Pross, *J.C.S. Perkin II*, 1977, 1860. For preliminary communications see (*b*) A. Pross and H. Aronovitch, *J.C.S. Chem. Comm.*, 1976, 817; (*c*) A. Pross and R. Koren, *Tetrahedron Letters*, 1975, 3613.

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

[3] For recent reviews see (*a*) D. J. Raber, J. M. Harris, and P. v. R. Schleyer in 'Ions and Ion Pairs in Organic Reactions.' ed. M. Szwarc, Wiley, New York, 1974, vol. 2; (*b*) J. M. Harris, *Progr. Phys. Org. Chem.*, 1974, **11**, 89; (*c*) D. J. McLennan, *Accounts Chem. Res.*, 1976, **9**, 281; (*d*) R. A. Sneen, *Accounts Chem. Res.*, 1973, **6**, 46 and references therein; (*e*) T. W. Bentley and P. v. R. Schleyer, *Adv. Phys. Org. Chem.*, 1977, **14**, 1.

[4] T. W. Bentley and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, 1976, **98**, 7658.

[5] S. Winstein, B. Appel, R. Baker, and A. Diaz, Chem. Soc. Special Publication, 1965, No. 19, p. 109.

[6] H. L. Goering and H. Hopf, *J. Amer. Chem. Soc.*, 1971, **93**, 1224.

mechanism has since been challenged on a number of counts and now appears to lack general support.[3a–c,4,7] However, the proposal that ion pair intermediates are formed in S_N2 and 'borderline' reactions cannot be entirely ignored since there are other possible mechanisms invoking ion pair intermediates which are nonetheless compatible with the characteristics of traditional S_N2 behaviour. One such mechanism has recently been proposed by Bentley and Schleyer who termed it S_N2 (intermediate).[4] It is the aim of this paper to explore the possibility of ion pair intermediates in S_N2 reactions by the study of the selectivity of octyl and 1-methylheptyl as well as benzyl derivatives during solvolysis in aqueous ethanol.

The method is based on application of the reactivity–selectivity principle (r.s.p.).[8] This principle asserts, what is to many chemists an intuitive belief, that reactivity and selectivity are related for a family of closely related species. Highly reactive species exhibit low selectivity, that is, they show little discriminating ability when reacted with two or more competing reagents. In the limit, diffusion controlled reactions exhibit no selectivity at all; the reaction rate is encounter determined. Species of low reactivity, on the other hand, exhibit a clear ability to discriminate between different reagents. Such species show a definite preference for the more reactive of a number of competing reagents.

On this basis it is apparent that the r.s.p. might be able to answer the question whether ion pair intermediates are formed in S_N2 substitution reactions. For the traditional one-step mechanism the entire reaction pathway represents the product-determining step. If an ion pair intermediate is formed, however, only that part of the pathway *following* the intermediate comprises the product-determining step. Thus for the one-step mechanism the selectivity observed would be that of the neutral substrate, while for the two-step pathway, the observed selectivity would be that of a highly active and short lived ion pair intermediate. Since neutral substrate and ion pair intermediate are expected to show markedly different reactivities, an examination of reaction selectivity may provide a means of distinguishing between the two mechanistic possibilities.

This discussion of course presupposes that the r.s.p. may be applied to solvolytic reactions.[9] A general survey of the r.s.p. over a varied range of reaction types, indeed suggests it to be of wide applicability.[8] For solvolytic reactions in particular, a significant number of reactivity–selectivity relationships have been observed,[1a,7a,10–12] though the systems studied are now recognized as being more complex than originally thought.[11]

The closely related nucleophile–electrophile combination reactions represent a rather striking breakdown of the r.s.p.[13] This is because electrophiles over a wide reactivity range exhibit constant selectivity. It has recently been proposed that compensating solvation effects bring about this breakdown in the principle.[14] This suggests that even though experimental verification of the r.s.p. has been obtained by a number of workers, some caution in its application is required.[8] Solvation effects play a dominant, yet often subtle, role in such reactions, so that any conclusions might be considered somewhat speculative till greater understanding of the scope and limitations of the r.s.p., in general, and for solvolysis reactions, in particular, is obtained.

RESULTS

The aqueous ethanolysis of alkyl derivatives yields a mixture of ether and alcohol products. The selectivity, k_E/k_W, may be obtained from product analysis and equation (1).[11a] k_E and k_W are the rate constants for ethanol and

$$k_E/k_W = [ROEt][H_2O]/[ROH][EtOH] \qquad (1)$$

water attack, respectively, in the product-determining step, [ROEt]/[ROH] is the ether : alcohol product ratio, and $[H_2O]$ and [EtOH] are the molar concentrations of water and ethanol, respectively, in the solvolytic mixture. The value k_E/k_W is a selectivity measure since, as a ratio of two

TABLE 1

Selectivity [a] of octyl, 1-methylheptyl, and benzyl derivatives in aqueous ethanol

	% (v/v) Ethanol					
Substrate	50	60	70	80	90	95
Octyl X [b]						
X = Cl	1.97	1.74	1.53	1.32	1.06	0.97
X = Br	1.78	1.59	1.46	1.27	1.03	0.89
X = OTs	1.82	1.57	1.51	1.27	1.04	0.93
1-Methylheptyl X [c]						
X = Cl	0.88	0.83	0.86	0.79	0.73	0.67
X = Br	0.84	0.76	0.73	0.75	0.68	0.71
X = OBs	0.90	0.73	0.70	0.70	0.63	0.65
Benzyl X [d]						
X = Cl	3.33	3.09	2.87	2.45	2.17	1.86
X = Br	3.61	3.30	2.95	2.56	2.12	1.80

[a] Selectivity defined as k_E/k_W and determined from $[ROCH_2CH_3]/[ROH]$: $[EtOH]/[H_2O]$. Product ratios determined by g.l.c. in the presence of excess of lutidine or pyridine. Data based on at least five determinations. Error is estimated to be ±5% though the standard error generally did not exceed 3%. [b] 120°, lutidine as base. [c] 120°, pyridine as base. Selectivity values replace earlier data obtained with lower precision.[1c] [d] 75°, pyridine as base.

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[7] (*a*) D. J. Raber, J. M. Harris, R. E. Hall, and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, 1971, **93**, 4821; (*b*) D. J. McLennan, *J.C.S. Perkin II*, 1974, 481; (*c*) D. J. McLennan, *Tetrahedron Letters*, 1975, 4689; (*d*) B. J. Gregory, G. Kohnstam, A. Queen, and D. J. Reid, *Chem. Comm.*, 1971, 797; (*e*) M. H. Abraham, *J.C.S. Chem. Comm.*, 1973, 51; (*f*) G. A. Gregoriou, *Tetrahedron Letters*, 1974, 233; (*g*), V. F. Raaen, T. Juhlke, F. J. Brown, and C. J. Collins, *J. Amer. Chem. Soc.*, 1974, **96**, 5928.

[8] For a review of the r.s.p. see A. Pross, *Adv. Phys. Org. Chem.*, 1977, **14**, 69.

[9] For a critical view of the r.s.p. see C. D. Johnson, *Chem. Rev.*, 1975, **75**, 755.

[10] R. A. Sneen, J. V. Carter, and P. S. Kay, *J. Amer. Chem. Soc.*, 1966, **88**, 2594.

[11] (*a*) J. M. Harris, D. C. Clark, A. Becker, and J. F. Fagan, *J. Amer. Chem. Soc.*, 1974, **96**, 4478; (*b*) J. M. Harris, A. Becker, J. F. Fagan and F. A. Walden, *ibid.*, p. 4484.

[12] K. Okamoto and T. Kinoshita, *Chem. Letters*, 1974, 1037.

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

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

rate constants, it signifies the ability of a particular species to discriminate between ethanol and water molecules in the product determining step.

The selectivity data for octyl, 1-methylheptyl, and benzyl derivatives are listed in Table 1. Data are provided for various leaving groups as well as for different solvent compositions.

The effect of the solvent on selectivity was examined by an additional method as well. Variable amounts of acetone were added to fixed ethanol–water mixtures. The data for octyl bromide in 50 and 90% aqueous ethanol as well as benzyl chloride in 50 and 95% aqueous ethanol are presented in Table 2.

TABLE 2

Effect of acetone on selectivity [a] of octyl and benzyl derivatives

Substrate	Solvent % ethanol [b]	% Acetone [b,c]				
		0	20	40	60	80
Octyl Br [d]	50	1.78	1.48	1.30	1.12	0.91
	90	1.03	0.87	0.85	0.79	0.78
Benzyl Cl [e]	50	3.33	2.88	2.59	2.18	1.78
	95	1.86	1.73	1.56	1.35	[f]

[a] From equation (1). Error estimated as ±5%. [b] Volume %. [c] Solution composed of x% of the indicated aqueous ethanol solution and $(100 - x)$% acetone. [d] 120°, lutidine as base. [e] 75°, pyridine as base. [f] This value could not be estimated with sufficient accuracy due to the low yield of solvolysis products formed.

For the benzyl chloride solutions the absolute yield of ether and alcohol products dropped drastically with a corresponding increase in acetone concentration. This appears to be due to polymerization side reaction which becomes significant as the concentration of available nucleophiles decreases. Nonetheless, we consider the data significant since the presence of a competing side reaction is not expected to affect the selectivity data. This is because the side reaction does not stem from further reaction of substitution products. This is known since all products were found to be stable under the reaction conditions. Only for the case in which substitution products are formed *via* two separate pathways is the side reaction liable to influence the selectivity data. We consider this possibility unlikely, particularly in view of the similar effect of acetone on the selectivity of octyl bromide.

TABLE 3

Effect of temperature on selectivity [a]

Substrate	Solvent % ethanol [b]	Temperature (°C)			
		75	100	120	140
Octyl Br [c]	50	1.80		1.78	1.66
	95	0.80		0.89	0.93
1-Methylheptyl OBs [d]	50	0.87		0.90	
	90	0.66		0.63	
Benzyl Cl [d]	50	3.33	3.03	2.73	2.61
	95	1.86	1.98	1.98	1.86

[a] From equation (1). Error is estimated to be ±5%. [b] Volume % in water. [c] Lutidine as base. [d] Pyridine as base.

The effect of temperature on selectivity for all three substrates for two aqueous ethanol solutions is illustrated in Table 3. With the exception of benzyl chloride in 50% aqueous ethanol there is no marked influence of changes in temperature. For this system a plot of log k_E/k_W against $1/T$ gave a linear correlation as shown in Figure 1.

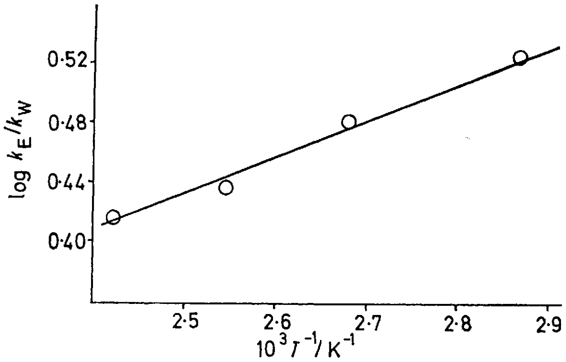

FIGURE 1 Plot of the logarithm of selectivity (log k_E/k_W) for benzyl chloride in 50% ethanol against $1/T$

From the slope $\Delta\Delta H^‡$ may be calculated since $\log k_E/k_W = -\Delta\Delta H^‡/2.303RT +$ constant. A least squares estimate of $\Delta\Delta H^‡$ was calculated to be -1.10 ± 0.09 kcal mol^{-1}.

DISCUSSION

The most significant feature of the data listed in Table 1 is the low selectivity values observed, particularly for octyl and 1-methylheptyl derivatives and the total absence of a leaving group effect. Product data for the aqueous ethanolysis of cyclopentyl brosylate recently reported by Shiner,[15] may be utilized to calculate selectivity data for this substrate as well. The selectivities observed in four different aqueous ethanol solutions (70—96% v/v) fall in the range 0.99—1.08.

These low selectivity values are unexpected and one possible interpretation is that they indicate product-determining attack on highly reactive ion pair intermediates. This is because for a highly reactive species exhibiting no discriminating ability at all (*i.e.* one whose rate is diffusion controlled) a selectivity value k_E/k_W of 1 is anticipated. The closeness of the selectivity values we obtained to this limiting figure suggests that reactive species, which show little tendency to discriminate between ethanol and water molecules, may be responsible for this result.

An alternative, and equally feasible explanation, should not be overlooked. The absence of selectivity could simply be due to the fact that ethanol and water possess similar nucleophilicities. Clearly, if this is the case, low selectivity values would result.

Evidence that the absence of selectivity is not simply due to identical ethanol and water nucleophilicities stems from the fact that diphenylmethyl derivatives exhibit significant selectivity during solvolysis in aqueous ethanol. We have noted selectivity values in the range 1.9—4.7 [1a] while Harris has observed a value of 11 for bis-(*p*-methylphenyl)methyl chloride.[11,16] Now diphenylmethyl derivatives undergo product formation

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[15] K. Humski, V. Sendijarevic, and V. J. Shiner, jun., *J. Amer. Chem. Soc.*, 1973, **95**, 7722.

[16] J. M. Harris, A. Becker, D. C. Clark, J. F. Fagan, and S. L. Kennan, *Tetrahedron Letters*, 1973, 3813.

on reactive ion pair intermediates, yet, despite this, they display significant discriminating ability between ethanol and water. Of particular interest is the fact that diphenylmethyl selectivity correlates with the Hammett σ^+ substituent constants.[1a] In other words, diphenylmethyl derivatives substituted with electron-withdrawing substituents (which yield less stable ion pairs) exhibit lower selectivity than those substituted with electron-releasing substituents (which yield more stable ion pairs). The low selectivity values obtained for octyl and 1-methylheptyl derivatives suggest, therefore, that product formation takes place on a species even *more* reactive than diphenylmethyl ion pairs. This expectation is not consistent with nucleophilic attack on neutral substrate (classical S_N2).

The above argument suggests that were nucleophilic attack in the product-determining step to take place on neutral substrate (*i.e.*, in a concerted S_N2 process) large selectivity values would result. This is not readily demonstrated since a model substrate which undergoes a concerted S_N2 reaction in aqueous ethanol may not exist in view of our results on octyl derivatives.

A possible S_N2 model, however, is the reaction of a primary alkyl system with a powerful nucleophile such as azide ion. For such a nucleophile the concerted process is far more favoured than for the corresponding reaction with the relatively poor nucleophiles, ethanol and water. We have measured the selectivity of octyl bromide toward the competing nucleophiles, azide ion, a most powerful nucleophile, and water, and compared the result with the corresponding values for other substrates. The data are listed in Table 4.

TABLE 4

Selectivity values [a] of alkyl derivatives towards azide ion and water in 80% aqueous acetone

Substrate	k_N/k_W
Octyl	11 800 [b]
1-Methylheptyl	770 [c]
Bis-(*p*-methylphenyl)methyl	180 [d]
Diphenylmethyl	34 [d]
exo-Norbornyl	11 [d]
2-Adamantyl	1.7 [d]

[a] Selectivity defined as k_N/k_W. [b] Data obtained on octyl bromide at 100°. [c] Data from R. A. Sneen and J. W. Larson, *J. Amer. Chem. Soc.*, 1969, **91**, 362. [d] Data from ref. 7*a*.

It is apparent that the octyl substrate exhibits exceptionally high selectivity (k_N/k_W 11 800), substantially *higher* than the value for diphenylmethyl ion pair derivatives (k_N/k_W 34). Attack on even more reactive ion pair intermediates results in a further decrease in selectivity which approaches the limiting value of 1 for the highly unstable 2-adamantyl ion pair. The conclusion we reach, therefore, is that nucleophilic attack on neutral substrate of low reactivity *is* a relatively selective process compared to such attack on reactive ion pair intermediates. This lends support to our earlier conclusion that the low selectivity values observed for octyl and 1-methylheptyl derivatives in aqueous ethanol may signify that attack of ethanol and water molecules in the product-determining step takes place on highly active ion pair intermediates. In the presence of a strong nucleophile, such as azide ion, a concerted S_N2 process appears to take place, resulting in the observation of high selectivity.

A plot of two measures of selectivity, k_E/k_W and k_N/k_W, against each other is of interest (Figure 2). Solvolytic species which show high selectivity by one measure generally do so by another measure,[1c] by analogy with electrophilic substitution reactions.[17] Octyl and 1-methylheptyl derivatives are notable exceptions. Both octyl and 1-methylheptyl derivatives show almost no selectivity toward the binary ethanol–water system. However, both show exceptionally high selectivity toward the azide ion–water system (Table 4). These data as well as literature selectivity data[11] for various alkyl derivatives are presented in Figure 2. It is readily seen that for most of the substrates there appears to be an approximate correlation between the azide ion–water and the ethanol–water selectivity measures. We interpret this correlation to mean that for those points falling on the selectivity–selectivity plot, the same species, *i.e.* ion pair intermediates, are formed in both solvolytic systems. Species exhibiting high selectivity in ethanol–water due to the stable nature of the ion pair intermediates exhibit high selectivity toward the azide ion–water system. Those highly active species showing inverse selectivity as a result of front side attack in the solvent separated ion pair show low selectivity in the azide ion–water system. We interpret the failure of the octyl and 1-methylheptyl derivatives to fall on this plot as evidence that each of these two substrates react *via* different product-determining steps in the two solvolytic systems. In the binary ethanol–water system both react *via* nucleophilically solvated ion pairs, hence the low selectivity.

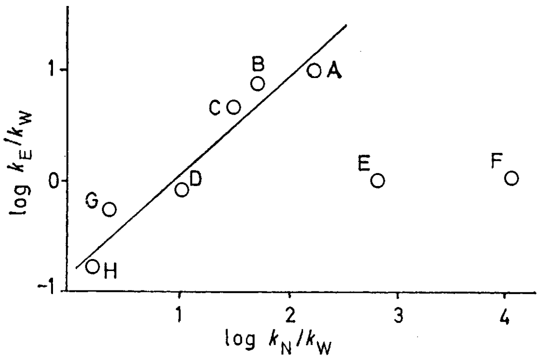

FIGURE 2 Plot of the logarithm of azide ion–water selectivity (log k_N/k_W) against the logarithm of ethanol–water selectivity (log k_E/k_W) for various alkyl substrates: A, bis-(*p*-methylphenyl)methyl; B, *p*-chlorophenyl(phenyl)methyl; C, diphenylmethyl; D, *exo*-2-norbornyl; E, 1-methylheptyl; F, octyl; G, 1-adamantyl; H, 2-adamantyl

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[17] L. M. Stock and H. C. Brown, *Adv. Phys. Org. Chem.*, 1963, **1**, 35.

In the azide ion–water system the particularly high selectivity values indicate that product formation occurs *via* attack on neutral substrate. This means that the highly nucleophilic azide ion, once over the transition state barrier for nucleophilic attack collapses directly to product *without* the transient formation of an intermediate of low discriminating ability. This suggests that with powerful nucleophiles the classic S_N2 pathway is possible but with relatively weak nucleophiles, such as the aqueous ethanol system the S_N2 (intermediate) mechanism operates.

The observation of selectivity values <1 for 1-methylheptyl derivatives requires comment since this would appear to be less than the limiting value. Selectivity values <1 imply that for these cases water is more nucleophilic than ethanol. This is contrary to the accepted nucleophilic order.[18] Only for cases where the product-determining step occurs *via* front side attack in the solvent separated ion pair has such inversion been observed.[11,19] This is because in such a process leaving group stabilization is important as well. For 1-methylheptyl derivatives this explanation is unacceptable since it is well established that nucleophilic attack on these derivatives occurs *via* back side attack with inversion of configuration.[20] We attribute the inverse selectivity, *i.e.* k_E/k_W less than the limiting value, 1, to slight solvent sorting. This suggests that in the solvent shell surrounding the reaction intermediate there exists a somewhat different distribution of solvent molecules than in the bulk. Harris [11a] has considered the possibility of solvent sorting governing the magnitude of selectivity in the binary ethanol–water mixture and rejected it as insignificant. In essence, we agree with his conclusion on the basis of the following points.

(1) There is a definite correlation between ion pair reactivity and selectivity for a number of competing systems. In addition to ethanol–water, this is true for both the azide ion–water system [7a,10] and the ambident nucleophile, phenol.[12] What this means is that three separate methods of measuring selectivity correlate with each other since all three correlate with reactivity. This is similar to the selectivity relationship [17] for aromatic substitution reactions, where intermolecular and intramolecular selectivity were found to correlate. Species which show high selectivity by one measure also show high selectivity by another quite independent measure. The three measures of selectivity utilized to date in solvolysis reactions are so different it is difficult to see how they could measure some spurious effect such as variable solvent sorting. The ethanol–water system involves a binary solvent mixture, the azide ion–water system involves the competition between a dissolved anion and solvent, and the phenol system is an ambident nucleophile capable of attack through either C or O. This argument, of course, cannot exclude some slight contribution from solvent sorting; however we suggest that the overall measure of selectivity is primarily determined by the discriminating ability of the intermediate and that solvent sorting introduces no more than a small systematic error. We believe this is responsible for the inverse selectivity observed in 1-methylheptyl derivatives.

(2) We exclude the possibility of ground state solvent which carries over into the product-determining step on the basis of the absence of any leaving group effect on selectivity. If ground state solvation were structure dependent and also influenced selectivity then it is reasonable to assume that the change in leaving group introduced into the substrates studied (Cl, Br, OTs) is sufficiently drastic and close to the reaction site to bring about a significant selectivity change. The absence of any such effect essentially rules out such a possibility.

Solvent Effects.—We have examined the selectivity of the substrates studied as a function of solvent polarity. This was achieved by two separate means: (*a*) a change in the relative amounts of ethanol and water in the binary system and (*b*) the addition of varying amounts of acetone to a fixed ethanol–water mixture. The data appear in Tables 1 and 2 and Figures 3 and 4. From Figure 3 it can be seen that all three compounds, octyl, 1-methylheptyl, and benzyl chlorides exhibit higher selectivity in the more aqueous and hence more polar mixtures. The effect of acetone operates in the same direction: higher selectivity is observed in media of low acetone concentration. This is seen in Figure 4.

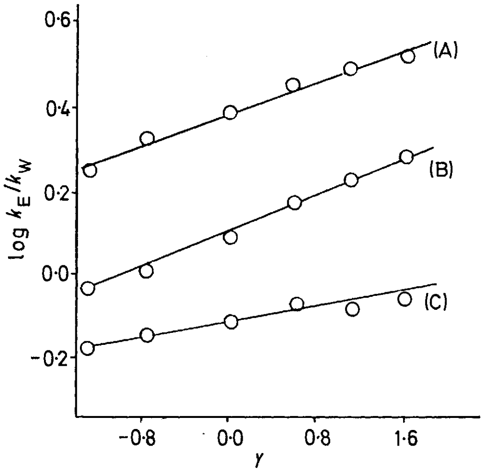

FIGURE 3 Plot of the logarithm of selectivity (log k_E/k_W) against Y values for (A) benzyl, (B) octyl, and (C) 1-methylheptyl chlorides in aqueous ethanol

These data may be interpreted in a number of ways.[1a] (*a*) One way of influencing the stability of an active intermediate is by varying the nature of the solvent. Such an effect has been previously reported. The selectivity of chlorine radicals was found to be solvent

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[18] (*a*) T. W. Bentley, F. L. Schadt, and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, 1972, **94**, 993; (*b*) F. L. Schadt, T. W. Bentley, and P. v. R. Schleyer, *ibid.*, 1976, **98**, 766.

[19] A. Pross, *Tetrahedron Letters*, 1975, 637.

[20] (*a*) A. Streitwieser, jun., T. D. Walsh, and J. R. Wolfe, jun., *J. Amer. Chem. Soc.*, 1965, **87**, 3682; (*b*) H. Weiner and R. A. Sneen, *ibid.*, 1965, **87**, p. 287.

dependent.[21] In aromatic solvents it appears that the radical is stabilized through complexation. The result is that in such solvents the chlorine atom exhibits higher selectivity. An increase in basicity of the aromatic solvent increases both the stability and the selectivity of the radical.[21] For a polarized intermediate in which there is substantial charge separation an increase in solvent polarity might be expected to operate in a similar way; the solvent stabilized species is likely to exhibit enhanced selectivity. The data are consistent with such an interpretation and lend support to the ion pair scheme.

(*b*) Harris [11a] has also considered the question of variable selectivity as a function of solvent ionizing power and proposed an alternative explanation. The variation in selectivity was attributed to a shift in the equilibrium of the species undergoing attack in the product-determining step. This means that at least two species must be present for such an effect to occur. Applying this analysis to octyl derivatives implicates attack on an ion pair intermediate in addition to attack on neutral substrate, and is therefore at least partially consistent with the ion pair scheme.*

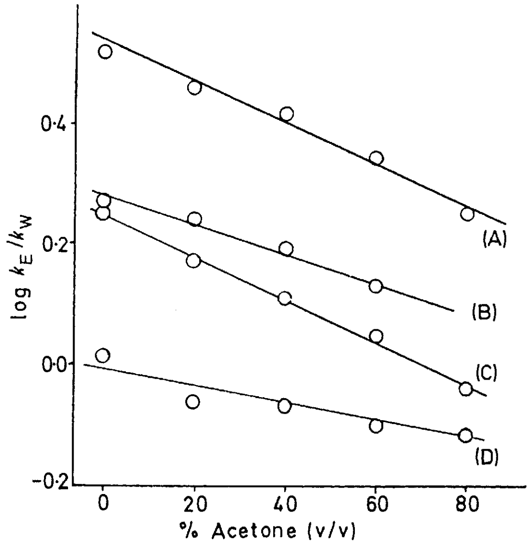

FIGURE 4 Plot of the logarithm of selectivity (log k_E/k_W) against % acetone for benzyl chloride in (A) 50% and (B) 95% aqueous ethanol, and octyl bromide in (C) 50% and (D) 90% aqueous ethanol for aqueous ethanol–acetone solutions

(*c*) It is also possible to interpret the data in a way that does not require the postulation of ion pair intermediates. The observed increase in the relative nucleophilicity of ethanol compared to water may be due to a variation in nucleophilicity brought about by the change in solvent composition. Since the effect of solvent polarity on nucleophilicity is not understood at present, the increase in the nucleophilic character of ethanol relative to water may stem from the change in solvent properties alone. This point requires further clarification and will be the subject of additional study. At this stage, therefore, the effect of solvent changes on selectivity should not be considered as definitive evidence for ion pair intermediates in these systems.

Effect of Structure.—There appears to be a general trend toward an increase in selectivity as the ability of the alkyl group to stabilize charge increases. Thus octyl and 1-methylheptyl derivatives show low selectivity. Benzyl derivatives exhibit intermediate selectivity while most diphenylmethyl derivatives [1a,11a] show relatively high selectivity. This trend conforms to expectation since more stabilized ion pairs are expected to exhibit greater selectivity. The relative selectivities for octyl and 1-methylheptyl derivatives, however, appear to be anomalous. On the basis of ion pair stabilities one would anticipate 1-methylheptyl derivatives to show greater selectivity than octyl derivatives when in fact the opposite order is observed. The reason for this reversal is not clear. One possible explanation lies in the degree of solvation of the ion pairs. The less hindered octyl ion pair being more strongly solvated may exhibit somewhat higher selectivity than the 1-methylheptyl ion pair.

Effect of Temperature.—The effect of temperature on selectivity for all three substrates for two aqueous ethanol solutions is illustrated in Table 3. With the exception of benzyl chloride in 50% aqueous ethanol there is no marked influence of changes in temperature. The absence of a temperature dependence on selectivity means that $\Delta\Delta H^{\ddagger}$, the difference in the enthalpy of activation for ethanol attack and water attack in the product determining step, must be close to zero. This could, of course, merely mean that the enthalpy of activation for both ethanol and water attack are very similar. However, the fact that $\Delta\Delta H^{\ddagger}$ for benzyl chloride in 50% ethanol is measurable (a least squares estimate of $\Delta\Delta H^{\ddagger}$ was calculated to be -1.10 ± 0.09 kcal mol^{-1}) argues against this possibility (see Figure 1).

If, for octyl derivatives, the product is formed *via* nucleophilic attack on a highly active ion pair species then $\Delta\Delta H^{\ddagger}$ is expected to be close to zero since $\Delta H^{\ddagger}$ for both ethanol and water attack are small. For the concerted S_N2 pathway the magnitude of $\Delta\Delta H^{\ddagger}$ would be expected to be significant since $\Delta H^{\ddagger}$ for the entire reaction is of the order of 20—25 kcal mol^{-1}. The lack of temperature dependence lends further support to the view that product formation takes place on a high energy intermediate.

Nature of Ion Pair Intermediates.—While we feel the data may support the existence of ion pair intermediates in certain S_N2 reactions, we have not addressed ourselves to the question of the nature of the ion pair proposed.

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* One difficulty with this interpretation for these systems is that an increase in solvent polarity would be expected to decrease the measured selectivity. This is because at higher solvent polarity a shift in equilibrium toward greater dissociation will favour attack on ion pair species. Since the ion pair is expected to be less selective than the neutral substrate, a decrease in selectivity would be anticipated.

[21] G. A. Russell (*a*) *J. Amer. Chem. Soc.*, 1958, **80**, 4987; (*b*) *Tetrahedron*, 1960, **8**, 101.

The proposal that ion pair intermediates are formed in S_N2 solvolyses was first made by Sneen and his coworkers[3d] who considered their data to support the scheme shown in equation (2) where k_2 is the rate-determining step. For an S_N2 process they proposed

$$\mathrm{RX} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{R^+X^-} \xrightarrow{k_2} \mathrm{ROS} \qquad (2)$$

an initial rapid equilibrium between neutral substrate and ion pair intermediate followed by rate-determining nucleophilic attack on the ion pair in the product-determining step ($k_{-1} \gg k_2$).

Extensive study on Sneen's proposal has been conducted.[7,22,23] At present, a general consensus appears to have rejected this possibility. Though our data are consistent with Sneen's ion pair mechanism there is an alternative ion pair mechanism proposed by Schleyer[4] which resembles the classical S_N2 mechanism more closely. This scheme which has been termed S_N2 (intermediate) is shown in equation (3). In contrast to Sneen's proposal, the first step may be rate determining resulting in the formation of a nucleophilically solvated ion pair. The ion pair intermediate then reacts with solvent in a rapid product-determining step.

$$\mathrm{RX} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \left[\begin{array}{l}\mathrm{HO} \cdots \mathrm{R} \cdots \mathrm{X} \\ \ \ | \\ \ \ \mathrm{S}\end{array}\right] \xrightarrow{k_2} \mathrm{ROS} \qquad (3)$$

In order to account for the low selectivity we must presume that the nucleophilically solvated ion pair intermediate is not bound to react with the solvating solvent molecule. That is, an ethanol solvated ion pair is capable of reaction with water to give alcohol product and a water solvated ion pair is capable of reaction with ethanol to give the ether product. Two possible mechanisms may be postulated to account for such behaviour.

(*a*) Crossover occurs so that the solvating molecule is rapidly replaced by an alternative molecule [reaction (4)]. This process is necessarily more rapid than collapse of the ion pair to form product.

$$\begin{array}{l}\mathrm{H{-}O} \cdots \mathrm{R} \cdots \mathrm{X} + \mathrm{EtOH} \longrightarrow \\ \ \ \ \ | \\ \ \ \ \mathrm{H}\end{array} \qquad \begin{array}{l}\mathrm{Et{-}O} \cdots \mathrm{R} \cdots \mathrm{X} + \mathrm{H_2O} \\ \ \ \ \ \ \ | \\ \ \ \ \ \ \mathrm{H}\end{array} \qquad (4)$$

(*b*) Alternatively, the solvated ion pair may undergo product formation *via* direct substitution from a solvent molecule other than a solvating one. This would suggest that while one molecule of solvent may be primarily responsible for the solvation process, a second molecule may be responsible for product formation. We know of no way of distinguishing between these two possibilities. However, it is possible that one of these processes does occur. If neither process were to occur, *i.e.* for the case in which the solvating molecule is ultimately responsible for product formation, ion pair selectivity would be identical to that of neutral substrate. As a consequence, the study of substrate selectivity would not provide a means of distinguishing between the S_N2(intermediate) mechanism and the traditional, concerted S_N2 pathway. However, in view of the low selectivity values observed for octyl derivatives we suggest that ion pair intermediates may be indicated for these substrates as well as 1-methylheptyl and benzyl derivatives.

As Bentley and Schleyer[4] have suggested, 'borderline' behaviour fits readily into this scheme. At the S_N2 end of the spectrum the reaction proceeds through either a classical one-step pathway with strong nucleophiles or through the nucleophilically solvated ion pair for weak nucleophiles. At the S_N1 end of the spectrum ion pair formation is nucleophilically unassisted. 'Borderline' behaviour is consistent with partial nucleophilic assistance in the formation of the ion pair. The importance of nucleophilic assistance to the kinetic behaviour of secondary substrates has recently been demonstrated and is consistent with this view.[4,24] Thus the major difference between S_N1 and S_N2 solvolytic pathways may be attributed to the degree of nucleophilic assistance leading to the transition state.

Conclusions.—This paper presents unexpected selectivity data which may be interpreted as evidence for ion pair intermediates in S_N2 processes. The conclusion, which is based on application of the r.s.p., cannot be considered as definitive since no standard measure of k_E/k_W based on a concerted S_N2 reaction was obtained. In other words, the argument assumes that the r.s.p. is applicable over a wide range of different substrates. While no proof for this supposition exists at present, the general validity of the r.s.p. in solvolytic reactions is well documented, and, we believe, may therefore be utilized as a mechanistic tool. However, it should be emphasized that due to the controversial nature of our conclusions and the degree of uncertainty surrounding the limitations of the r.s.p., the results and conclusions presented here must be considered speculative.

The question that needs to be answered is the following: are the results, which fall into a rather well defined pattern, in fact due to nucleophilic attack on a highly active ion pair species, or is the pattern observed, entirely coincidental, and that for some obscure reason, neutral substrates show lower selectivity than ion pair derivatives toward ethanol and water?

Further work to resolve this dilemma is in progress.

EXPERIMENTAL

Materials.—Alkyl halides were commercially available and were distilled prior to use. The absence of hydrolysis products in the starting material was established by g.l.c. Alkyl arenesulphonates[25] were prepared as previously

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[22] J. Koskikallio, *Acta Chem. Scand.*, 1972, **26**, 2101.

[23] (*a*) R. E. Robertson, A. Annesa, and J. M. W. Scott, *Canad. J. Chem.*, 1975, **53**, 3106; (*b*) J. M. W. Scott, *ibid.*, 1970, **48**, 3807.

[24] A. Pross and R. Koren, *Tetrahedron Letters*, 1974, 1949.

[25] L. F. Fieser and M. Fieser, 'Reagents in Organic Synthesis', Wiley, New York, 1967, p. 1180.

reported and recrystallised from light petroleum at −50°. All gave satisfactory n.m.r. spectra.

Reagents.—Pyridine and lutidine were distilled and stored over potassium hydroxide pellets or molecular sieves. Analytical grade absolute ethanol and acetone (Merck) were stored over molecular sieves and used directly.

Product Determination.—Reactions were performed in pressure tubes containing substrate (0.01M), lutidine or pyridine as base (0.013M), and solvent (5 ml). For octyl and 1-methylheptyl derivatives results with and without base were found to be identical. Reactions were conducted in thermostatted oil-baths (±0.05 °C) for 10—20 half-lives. For all materials, product ratios were established as stable under the reaction conditions. Product ratios were determined by response calibrated g.l.c. on a 1.5 m × 1/4 in column packed with 3% Carbowax 20M on 60—70 mesh Chromasorb WAW DMCS for octyl and benzyl derivatives and a 2 m 4% column for 1-methylheptyl derivatives. Results are the average of between two and four determinations on at least duplicate runs. An error of 5% is estimated for product ratios. Alcohols and ethers accounted for over 90% of the solvolysis product. For octyl and 1-methylheptyl substrates up to 10% yield of alkenes were formed. Addition of acetone to the solvolysis mixtures of benzyl chloride resulted in a polymeric side reaction which at high acetone concentration accounted for *ca.* 90% of the products.

The selectivity of octyl bromide in 80% acetone in the presence of 0.1M-NaN_3 at 100° was obtained by titration of the acid produced from hydrolysis. The ratio $[RN_3] : [ROH]$ was obtained by comparison of the experimental titre with the theoretical titre expected in the absence of azide ion.

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