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Ions and Ion-pairs in Nucleophilic Aliphatic Substitution

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A survey is made of the involvement of ions and ion-pairs formed both by the nucleophilic reagent and by the substrate. Evidence is given for the existence of ion-pairs of different types (contact and solvent-separated) in S_N1 reactions, and the possible participation of the former type in S_N2 processes is examined. A list of 338 references is included.

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I. INTRODUCTION

A most important current problem of theoretical organic chemistry is the involvement not only of covalent molecules but also of various ionic intermediates, free ions, and different types of ion-pairs in the reactions of organic compounds. These species change significantly the reactivity of the substrate and the mechanism of the reaction. The participation of carbonium ions in nucleophilic substitutions is based on evidence of the mechanism of unimolecular substitution (S_N1), first put forward by Ingold and his coworkers [1], and whose classic formulation presupposes the formation of a steady concentration of a free ion in the rate-determining stage of the reaction. Later, nucleophilic substitutions involving stable carbonium ions were studied. A vast amount of information has now accumulated on the role and the reactivity of free ions (carbonium ions [2] and carbanions [3,4]), but special attention has been paid during the past decade to the fact that these species are frequently present in solution and take part in a reaction not in the free state but associated with their gegenion. The "ion-pair" concept, well known in the chemistry of electrolytes [5], was introduced into organic chemistry by Winstein (on Grunwald's suggestion).

As early as 1960 Winstein wrote: "It is important to distinguish between ionisation and dissociation, and to consider explicitly the role of different ionic intermediates, representing various stages of ionisation and dissociation" [6]. The idea that ionic intermediates other than the carbonium ion might be present during nucleophilic substitutions occurred to him after he had established that solvolysis in allylic systems is accompanied by intramolecular rearrangement of the initial compound [7]. Proof of the existence of such ionic intermediates, which it was proposed to term "ion-pairs" (internal and external, but in present-day literature contact or intimate and solvent-separated or loose), was obtained from many studies not only of allylic isomerisations but also of rearrangements in systems containing a 2-arylethyl group, from a comparison of rates of solvolysis, racemisation, isotopic exchange in ArC*HXR systems, and randomisation in esters $ROC^{18}OAr$, and also from a study of salt effects. These results led to the idea [8] that a covalent compound dissociates into free ions in stages involving the formation of at least two types of ion-pairs, return from which may result in isomerisation of either the cationic or the anionic moiety of the molecule:

$$RX \rightleftharpoons R^+X^- \rightleftharpoons R^+ \,\|\, X^- \rightleftharpoons R^+ + X^-$$
$$\quad\;\; \downarrow\uparrow \qquad\quad \downarrow\uparrow$$
$$\quad\;\; R^+X'^- \qquad R'^+ \,\|\, X'^-$$

It was suggested that reactions of type S_N1 may involve not only free ions but also solvent-separated ion-pairs.

An attempt has been made during recent years to demonstrate that ion-pairs of contact type may take part in S_N2 reactions of non-activated secondary (and even primary) substrates, although efforts to suggest a "unified" mechanism of nucleophilic substitution encounter serious difficulties. However, the idea that a substrate reacts in various forms depending on structure and conditions, with all differences in mechanism determined by the relative rates of individual stages, is an extremely tempting approach. Thus evidence of the existence in solution not only of carbonium ions but also of different types of ion-pairs is based on an analysis of kinetic and stereochemical results.

A completely different situation became evident when the existence of ion-pairs was examined in the chemistry of carbanions. Physical investigations in this field, which has developed vigorously during recent years, have provided direct evidence of the existence of various types of ion-pairs in solutions of salts of carbanions and radical-anions [9]. Especially valuable studies were made by Weissman [10], who in 1958 was the first to obtain physical proof of the existence of ion-pairs from the electron spin resonance spectra of salts of radical-anions, after which further work showed the existence of two types of ion-pairs [11-13]; Smid and his collaborators [14-16] have demonstrated the existence of contact and solvent-separated ion-pairs in a study of the spectra of salts of carbanions. It was Smid's papers which attracted the special attention of organic chemists to this problem. By now it has become possible not only to identify the different types of ion-pairs but also to establish their physical properties, energetics, solvation, and dynamics [17].

The present situation is somewhat paradoxical in that ion-pairs of carbanions have been thoroughly studied by various physicochemical methods, but very little is known of their reactivity in electrophilic substitution [18-20], whereas ion-pairs of carbonium ions are widely enlisted to explain the rules of nucleophilic substitution, although

objective data on their structure are lacking. However, the immense successes achieved in connection with this problem in the chemistry of carbanions have overshadowed the achievements in the field of carbonium ions, although the actual concept of ion-pairs was formulated by Winstein precisely in application to carbonium ions and nucleophilic substitution. The present Review examines the evidence for the existence of ions and ion-pairs in S_N reactions and the role of ion-pairs in uni- and bi-molecular nucleophilic substitution.

II. IONS AND ION-PAIRS MX IN S_N2 REACTIONS

Among nucleophilic substitutions those involving ionic nucleophilic reagents are some of the most important, both practically and theoretically. Here a special position is occupied by the exchange of halogens $RX-X^-$, termed the Finkelstein exchange [1]. The reactivity of the anions—their nucleophilicity in these reactions—is determined by the electronegativity, polarisability, and solvation, which in turn depend on the nature of the reaction centre under attack, the leaving group, and the solvent.

An important factor determining the reactivity of an ion, which for a long time was not taken into account, is the ability to associate with a gegenion [5], which is especially marked in media of low dielectric constant. With incomplete dissociation of the ionophore [21] the reaction rate constant will fall as its concentration increases. This phenomenon has been observed for quite a long time with halogen salts. Thus in 1948–1949 Evans et al. [22,23] discovered that the second-order rate constant for the reaction of n-butyl bromide with lithium bromide in acetone at 25°C decreases by a factor of 3.6 with increase in the lithium bromide concentration by a factor of 400, and explained this on the hypothesis that the reactant species was the bromide ion. A similar observation was made at that time by Moelwyn-Hughes in a study of the reaction of methyl bromide with potassium iodide in acetone [24].

Table 1. Relative RX + Hal^- reaction rate constants.

RX*	Solvent**	Cl⁻	Br⁻	I⁻	Ref.
n-PrBr	acetone	11	5	1	27
n-BuOBs	acetone	16	4	1	27
MeOTs	DMF	9.1	3.4	1	28
MeOTs***	83.3Py-DMF	2.8	1.5	1	29
EtOTs	HMPA	14 4	2.0	k_2 M^{-1} min^{-1}	30

*Bs = p-$SO_2C_6H_4Br$; Ts = p-$SO_2C_6H_4CH_3$.
**DMF = dimethylformamide; Py = pyridine; HMPA = hexamethylphosphoramide.
***K_{eq} was obtained from the kinetic data.

In many later papers, however, the degree of dissociation of the salts was disregarded, with a consequent distortion of the true reactivity of the halide ions [25]. In work on the Finkelstein exchange in $RHal-Hal^-$ systems in acetone Ingold et al. [26] observed in 1955 that the reaction rate constant increases with decrease in the lithium halide concentration, which they attributed to a negative salt effect. They regarded this as confirmed by the diminution in rate on the addition of lithium perchlorate, actually due to suppression of dissociation of the lithium halide. The reaction sequence of halide ions obtained by these workers—$I^- > Br^- > Cl^-$—was analogous to that observed in water and protonic media [25], which for a long time was considered an effect of polarisability varying in the same sequence. However, Winstein et al. [27] recalculated these results taking into account the degree of dissociation of the lithium halide, and found that the reaction sequence of halide ions in aprotic solvents was exactly the opposite, and the observed nucleophilicity diminished in the sequence $Cl^- > Br^- > I^-$ (Table 1). The ion-pair $\rightleftharpoons$ ions equilibrium constant increases in this sequence in acetone, but depends in general on the nature of the solvent [31]. The results obtained by Winstein et al. [27] show that the difference in reactivity between lithium and tetrabutylammonium halides towards n-butyl p-bromobenzenesulphonate in acetone is determined solely by the difference in their dissociation (Table 2). If the degree of dissociation is ignored, the true reactivity sequence for the reaction of methyl toluene-p-sulphonate in a mixture of pyridine and dimethylformamide is reversed when the salt concentration is increased to 0.35 M. [29]

Table 2. Observed and true rate constants for reaction of n-butyl p-bromobenzenesulphonate with lithium and tetra-n-butylammonium halides.

Salt	10^4K_{diss}	10^3k_{obs}, M^{-1} s^{-1}	$k_2 = 10^3k_{obs}/\alpha$, M^{-1} s^{-1}
n-Bu_4NCl	22.8	33.5	58
LiCl	0.027	0.493	51
n-Bu_4NBr	32.9	9.09	13
LiBr	5.22	2.81	12
n-Bu_4NI	64.8	1.68	2.0
LiI	69	2.97	3.6

Inspection of available results shows that salts of alkali metals with various anions are strongly associated into ion-pairs in ambipolar aprotic solvents [31,32], and neglect of this effect distorts the results significantly. With lithium bromide in acetone, for example, the order of the reaction with respect to the nucleophile is distorted [33]. For the reaction of 1-iodo-2,4-dinitrobenzene with potassium iodide in acetone [34] disregard of association to ion-pairs leads to an apparent change in the mechanism from S_N2 to S_N1.

It is no less important for the assessment of true reactivity to take into account the dissociation of alkoxides [35], wnich, in aprotic solvents such as dimethyl sulphoxide, are frequently used as nucleophiles in aromatic substitution and as bases in the elimination and generation of carbanions. Alkoxides are present in dimethyl sulphoxide predominantly as ion-pairs [35].

Crown polyethers have recently been used to increase the degree of dissociation of metal halides and alkoxides [36]. Addition to 18-crown-6 to a solution of potassium fluoride in acetonitrile increases sharply the observed nucleophilicity (and basicity), leading e.g. to ready substitution of fluorine for bromine in benzyl bromide [37]. Potassium ethoxide in the presence of dicyclohexyl-18-crown-6 is able to intervene in nucleophilic aromatic substitution, converting o-dichlorobenzene into o-chloroanisole in 40–50% yield [38]. In the presence of a crown polyether the nucleophilicity of the acetate ion is sharply increased, and

alkyl derivatives AlkX (where X = Cl, $OSO_2C_6H_4CH_3$, and especially Br) are readily converted into acetates [39]. Addition of a crown polyether has a similar influence on the reaction of alkyl halides with the cyanide ion [40].

It was accepted in most of the studies, however, that a free ion was the active species in nucleophilic substitution, and that the contribution by ion-pairs to the reactivity could be neglected, i.e. that $k_i \gg k_{ip}$ and that $k_{obs} = \alpha k_i$. Nevertheless, this contribution $(1 - \alpha)k_{ip}$ may be comparable with the contribution by the free ion αk_i if dissociation of the salt is slight ($\alpha \ll 1$) even when $k_i \simeq 10k_{ip}$. During recent years several workers [41-50], notably Beronius, have used Acree's equation [51] to estimate the reactivity both of free ions and also of ion-pairs in nucleophilic substitutions involving halides:

$$k_2 = \alpha k_i + (1-\alpha)k_{ip}; \qquad K_{eq} = \frac{c_\alpha^2 f_\pm^2}{1-\alpha},$$

where k_i is the reaction rate constant of the free ion, k_{ip} that of an ion-pair, α the degree of dissociation, $f_\pm$ the activity coefficient of the ion, and K_{eq} the equilibrium constant.

It was natural to expect that k_i would be independent of the nature of the cation, unlike k_{ip}. It has in fact been shown [27,50] that k_i has the same value for various cations. However, Lichtin et al. [41] did observe some dependence of k_i on the nature of the cation, with a regular increase in the ratio k_i/k_{ip} as K_{eq}^{-1} increased (Table 3). Although we usually find that $k_i \gg k_{ip}$, [50] the accompanying data show that the two rate constants may be comparable. Thus in the case of tetraethylammonium chloride $k_{ip} = \frac{1}{2}k_i$. In such cases, of course, it is not permissible to neglect the part played by ion-pairs and calculate $k_2 = k_{obs}/\alpha$, as is usually done [27,52-55].

Table 3. Rate constants for reactions of ions and ion-pairs of *p*-nitrobenzyl bromide with various bromides and chlorides.

MX	$10^5 k_i$, $M^{-1} s^{-1}$	$10^5 k_{ip}$, $M^{-1} s^{-1}$	$\frac{k_i}{k_{ip}}$	MX	$10^5 k_i$, $M^{-1} s^{-1}$	$10^5 k_{ip}$, $M^{-1} s^{-1}$	$\frac{k_i}{k_{ip}}$
p-$NO_2C_6H_4CH_2Br$+$M^{36}Cl$ in liq. SO_2, at 0°C				*p*-$NO_2C_6H_4CH_2Br$+ $M^{82}Br$ in liq. SO_2			
RbCl	2.69	0.076	35	KBr	7.89	0.38	21
Me_4NCl	2.92	0.47	5.2	Me_4NBr	7.24	1.07	6.8
Et_4NCl	3.17	1.61	1.97	Et_4NBr	7.07	2.86	2.5

Ion-pairs are the sole reactant species [42] in the reaction between 1-alkylpyridinium iodides and methyl toluene-*p*-sulphonate in chloroform, dichloroethane, and methyl formate. In solvents of high dielectric constant such as acetone and acetonitrile, however, ions and ion-pairs make comparable contributions to the observed rate-constants (e.g. for 4-cyano-1-ethylpyridinium iodide in acetonitrile k_i and k_{ip} have the respective values 0.175 and 0.12 $M^{-1} s^{-1}$).

For the reaction of *p*-nitrobenzyl chloride with lithium chloride in acetone the contribution by k_{ip} is <1% of that by k_i according to Beronius [43]; similarly, k_{ip} can be neglected in the reaction of n-butyl bromide with lithium bromide in acetone [45] or in a mixture of acetone with a large quantity of water [48]. When the lithium salts are replaced in these reactions by the corresponding tetrabutylammonium halides, however, the contribution by ion-pairs cannot be neglected in calculating the true rate constants, since k_{ip} amounts to 10% and 20% of k_i respectively. It was shown, in agreement with Lichtin's results [41?], that k_i is somewhat higher for lithium chloride than for tetrabutylammonium chloride (2.4 and 2.0 M^{-1} min^{-1} respectively).

The complexity of determining the true value of k_i lies in the uncertainty attached to the salt effect. An attempted estimate by Beronius for the reaction of iodoalkanes with the iodide ion in aqueous ethanol [47] revealed that the assumption of minimum and maximum salt effects (on $f_{RX}f_{X^-}/f_{\neq}$) produced a marked change in k_{ip} from negative to large positive values of 30–50% of k_i.

It must be noted also that the values of K_{eq} calculated from electrical conductivity data, and hence the estimated contribution by ion-pairs, depend not only on the accuracy of the measurements (the conductivity of electrolytes in non-aqueous media has only recently been measured accurately) but also on the method of calculating them [56].

Considerable attention has been paid to the reactivity of ions and ion-pairs of ambident anions. Thus Smith et al. [57,58] determined the rate constants for the methylation of the ion and the sodium ion-pair of fluorenone oxime in a mixture of acetonitrile and t-butyl alcohol by methyl iodide, and found the ion to be more reactive than the ion-pair by a factor of 500.

It is especially interesting to estimate the true rate constant k_i and the contribution by ion-pairs in the reactions of ambident organic ions such as enoxide ions containing two nucleophilic centres joined by a single mesomeric system. Brändstrom showed [59] that both the ion and the ion-pair are kinetically active in the methylation of alkali-metal enoxides in alcohol†. A similar observation was made by Forsblad [60] in a study of the alkylation of alkali-metal methyl $o\beta$-dihydroxycinnamates. With the dipiperidinium bisenoxide in methanol the ion-pair was more active than the free ion in both *C*- and *O*-alkylation, probably because of selective solvation of the anion by hydrogen bonding. Thus the diminution in reactivity due to formation of a hydrogen bond may be greater than that resulting from electrostatic interaction with a gegenion of large radius and low charge density.

The most thorough study of the dual reactivity of ions and ion-pairs of ambident enoxide ions in alkylation has been reported in a series of papers [61-66]. At concentrations <0.1 M in hexametapol [hexamethylphosphortriamide, HMPT] the only reactive species is the "free" enoxide ion of acetoacetic ester [61] and other acyclic β-keto-esters [62], and its rate of alkylation by ethyl toluene-*p*-sulphonate parallels the basicity of the ambident anion. In a less basic medium such as dimethylformamide not only the ion but also ion-pairs of alkali-metal enoxides of acetoacetic ester take part in the reaction [63]. The rate constant of the reaction involving the anion was determined from experiments in the presence of macrocyclic polyethers. The greater reactivity of the ion-pair of sodium ethyl acetoacetate than of the potassium enoxide definitely indicates that the solvent-separated form of the ion-pairs of alkali-metal enoxides undergoes alkylation in dimethylformamide. In the presence of a crown polyether in such a weakly polar and feebly basic medium as dioxan [64], and even in the more strongly basic tetraglyme [65], contact ion-pairs of alkali-metal enoxides of acetoacetic ester take part in the reaction. This conclusion is based on the excellent linear

† Alkylation of an enoxide ion at a carbon atom can be regarded not only as an S_N2 reaction but also as an S_E reaction, and this field overlaps the study of carbanionic reactions.

correlation between $\lg k_{ip}$ and the reciprocal of the crystallographic radius of the cation—a relation that is typical of contact ion-pairs.

It is interesting that the stereochemical results of the *O*-alkylation of alkali-metal enoxides of acetoacetic ester depends on the nature of the ionic species involved [66], since the ion and the solvent-separated and contact ion-pairs may have different conformations.

III. PROOFS OF THE EXISTENCE OF CARBONIUM IONS IN S_N1 REACTIONS

Proofs of the existence of carbonium ions in nucleophilic substitutions are usually based on study of the kinetics and the stereochemistry of an S_N1 type of reaction. The classic theory of such reactions requires that the observed constant should be independent of the concentration and the nature of the nucleophile [1]:

$$RX \underset{k_1,\ \text{slow}}{\overset{}{\rightleftharpoons}} R^+ + X^- \xrightarrow[k_2,\ \text{rapid}]{N^-} RN;$$

$$w = \frac{k_1 k_2 [RX][N^-]}{k_{-1}[X^-] + k_2[N^-]};$$

when $k_2[N] \gg k^{-1}[X^-]$, we have $w = k_1[RX]$. Such regularities have been observed in the reactions of t-butyl bromide with various nucleophiles in nitromethane [67-69].

Another criterion of the involvement of carbonium ions in reactions is the "common-ion effect" [70-76] (the mass-action effect" or, as defined by Winstein [7], "external return"), depression of the observed constant on introduction of a common ion or on its accumulation during the reaction. The mechanism of the effect involves return of the ion as a result of reaction with the gegenion to form the initial compound, and operates when the contribution $k_2[N^-]$ is comparable with $k_{-1}[X^-]$. The common-ion effect is the more strongly developed the more stable is the resulting carbonium ion [71,77-81]. The common ion is thus acting as a nucleophilic "trap" for the carbonium ion. A foreign nucleophile such as the azide ion may be used as ionic trap, and would not affect the rate of the process but would influence the composition of the products, since the rate-determining stage in S_N1 processes does not coincide with the stage governing the products formed:

$$RX \underset{\text{slow}}{\rightleftharpoons} X^- + R^+ \begin{cases} \xrightarrow{HOS^-} ROS \\ \xrightarrow{N^-} RN \end{cases}.$$

Precisely this result was obtained for the reactions of di- and tri-phenylmethyl derivatives with sodium azide and tetrahydroborate used as traps [72-74,82-86].

Use of a nucleophilic trap combined with change in the nature of the leaving group provides another indication of formation of a carbonium ion in S_N1 reactions:

$$\left.\begin{matrix} RCl \\ RBr \end{matrix}\right\} \rightleftharpoons R^+ \begin{cases} \xrightarrow{HOS^-} ROS \\ \xrightarrow{N^-} RN \end{cases}.$$

Thus the reaction of diphenylmethyl chloride and bromide with the azide ion in 90% aqueous acetone yielded mixtures of the same products, although the reaction velocities of these halides differed thirty-fold [74,82].

An important criterion of formation of a carbonium ion is the stereochemical result of the reaction: a racemic product formed from an optically active compound undoubtedly indicates an S_N1 mechanism [1]. Because of the participation not only of free ions but also of ion-pairs in reactions of S_N1 type, however, the stereochemistry of these processes may in general be extremely diverse, as will be seen later, varying from substantial inversion to complete retention of the stereochemical configuration.

Finally, mention may be made of a further criterion, which is especially significant for diagnosing the mechanism of solvolytic reactions and consists in the influence of structural effects on the reaction velocity.

Schleyer et al. [87] recently proposed the addition of sodium azide as a test for the mechanism of solvolytic reactions. It is quite clear that, if the reaction velocity is unaffected by such addition, the solvent, being the weaker nucleophile, is incapable of nucleophilic participation in the rate-determining stage, i.e. that the reaction takes place by an S_N1 mechanism.

With sufficiently stable carbonium ions an S_N2C^+ mechanism [68] is possible, when the carbonium ion is formed in the pre-equilibrium stage and reacts slowly with the nucleophile: $k_2[N] \ll k_1[X^-]$. This probably occurs most often in the reactions of triphenylmethyl derivatives. However, such reactions may involve not only free ions but also ion-pairs, whose concentration in the solution may not be stationary, since these compounds may already be present in an ionised and partly dissociated state.

IV. IONS AND ION-PAIRS IN SOLUTIONS OF TRIPHENYLMETHYL DERIVATIVES

In strongly acid solutions even carbonium ions such as isopropylium, which are classified as unstable, can exist for a long time [88]. The more stable triarylmethyl cations are formed in theoretical yield by the action of sulphuric acid on the corresponding carbinols, and are entirely stable in these solutions [89]. Carbonium ions can be obtained from triarylmethyl derivatives also in other media or in the presence of Lewis acids [90].

In less strongly ionising media a covalent compound is in equilibrium with ion-pairs, as is shown by spectral investigations. Thus according to Evans [91] triphenylmethyl chloride dissolved in nitromethane and other nitroalkanes does not dissociate but merely undergoes ionisation (in nitromethane $K_{ion} \simeq 4 \times 10^{-4}$); tri-*p*-tolylmethyl chloride behaves similarly in nitrobenzene [92]. In dichloroethane solution triphenylmethyl chloride is capable only of ionisation ($K_{ion} \simeq 7.9 \times 10^{-3}$), whereas tri-*p*-tolylmethyl chloride undergoes partial dissociation [93]. The establishment of two equilibria in this case follows from the linearity of the plots of $([R^+] + [R^+Cl^-])/[RCl]$ against $([RCl])^{-1/2}$. In fact

$$RCl \overset{K_1}{\rightleftharpoons} R^+Cl^-;$$

$$R^+Cl^- \overset{K_2}{\rightleftharpoons} R^+ + Cl^-;$$

$$RCl \overset{K_3}{\rightleftharpoons} R^+ + Cl^-;$$

$$K_3 = \frac{[R^+]^2}{[RCl]} = K_1 K_2;$$

$$\frac{[R^+] + [R^+Cl^-]}{[RCl]} = K_1 + \frac{[R^+]}{[RCl]} = K_1 + K_3 \frac{1}{\sqrt{[RCl]}}.$$

Triphenylmethyl bromide is assumed to be completely dissociated in *m*-cresol solution [94]; the degree of dissociation is diminished by the addition of benzene or hexane to the *m*-cresol [95]. Dissociation is increased in chlorinated ethanes compared with nitroalkanes, but no direct relation is observed between the dissociating or ionising power of a solvent and its dielectric constant [93]. Liquid sulphur dioxide is a good ionising solvent, in spite of its low

dielectric constant (ϵ = 15.4 at 0°C).[96,97] Solutions of triphenylmethyl chloride in liquid sulphur dioxide conduct electricity, and comparison of spectral and conductivity data[98] permitted calculation of the ionisation constant and of the constant of dissociation of the ion-pair into free ions (K_1 = 0.013 and K_2 = 0.003 M at 0°C)[99,100]. Liquid sulphur dioxide is a stronger ionising solvent that nitrobenzene by a factor[97] of 5×10^{10} ($K_1 = 2 \times 10^8$ and 0.004 respectively).

It has recently been shown[101] that the ionisation of triphenylmethyl chloride in ether, assessed from the rate of isotopic exchange with $*Cl^-$, is promoted by lithium perchlorate, which in this solution forms aggregates of diverse structure. The dissociation and ionisation of triarylmethyl halides is increased by complex formation with Lewis acids[90,102]. The influence of salts on these processes diminishes in the sequence[103]

$$SbCl_5 \gg FeCl_3 \gg SnCl_4 \gg BiCl_3 > HgCl_2 > SbCl_3 .$$

The complexes $(XC_6H_4)_3CCl.HgCl_2$ (where X = H, *p*-Cl, *p*-CH_3) in nitromethane undergo not only ionisation but also dissociation[104,105], and the bromides dissociate still more readily under these conditions[106]. Similar results were obtained in other solvents[105]. Spectroscopic results indicate that solvents form the sequence—nitromethane > chlorobenzene > benzene—according to their ability to ionise the complex; the ability of a solvent to solvate both the anion and the carbonium ion must, of course, be taken into account, as well as the possibility of variation in the extinction coefficient of the carbonium ion under the influence of solvation[107]. Furthermore, the ratio of dissociated to covalent form may change during the reaction as a consequence of the common-ion effect[108].

Increase in ionicity on passing from triarylmethyl halides to the perchlorates is indicated by conductivity data[109-111] and by the absorption spectra[112,113]. Triethyl perchlorate is completely ionised and partly dissociated in chlorinated solvents—chloroform, dichloromethane, and the dichloroethanes[114].

The presence of ions and ion-pairs in a solution of tropylium isothiocyanate

$$RNCS \rightleftharpoons R^+NCS^- \rightleftharpoons R^+ + NCS^-$$

has been demonstrated by nuclear magnetic resonance[115]. The ratio between the covalent form and the ionic species depends on the composition of the solvent and the temperature. Thus in trideuteroacetonitrile only free ions are formed, whereas in its mixture with deuterochloroform (1 : 3) at 40°C ion-pairs are also present.

In order to describe the reactivity of dissociating and ionising organic compounds it is necessary to estimate separately the contributions made by each of the reactant species, as in the case of metal halides.

In media of low dielectric constant nucleophilic substitutions can take place in the triarylmethyl series by an S_N1 mechanism, when dissociation (or ionisation) occurs in the limiting stage, and ions and ion-pairs are present in steady concentrations. Nucleophiles capable of forming a hydrogen bond with the leaving group may assist the ionisation; since they may be associated in these media, their observed kinetic order is complicated[99,116-118]. At one time this and other complications connected with the return mechanism gave rise to bitter controversy between Ingold et al.[119-123] and Swain et al.[124-128]. Kinetic complications may arise also from aggregation of the ion-pairs[129,130].

It may be assumed that in these media the S_N1 mechanism involves only the formation of solvent-separated ion-pairs. This hypothesis is supported by the absence of depression of the rate constant by the common ion in the methanolysis of diphenyl-*p*-tolylmethyl toluene-*p*-sulphonate in a mixture of oxolan and methanol (10%), and by the considerable acceleration of this reaction on the addition of lithium perchlorate[131].

A considerable number of studies have now been made on the reactivity of free triarylmethyl cations. They originally covered the most stable amino-substituted triarylmethane dyes, whose rates of reaction were not very high[132-135]. However, application of the stopped-flow method extended considerably the range of carbonium ions investigated[136-140]. Study of the effect of additions of salts on the reaction of triarylmethyl cations with water[141,142] showed that variation in the rate was due to association of the carbonium ion with the anion of the added salt, in particular to formation of ion-pairs with the perchlorate anion.

A special position among this work is occupied by Ritchie's superb investigations[143-150], which included a study of reaction rates and equilibria for triarylmethyl and also substituted tropylium and benzenediazonium ions with various nucleophiles in several solvents. Unusual results were obtained, which have not yet been fully explained. This work showed firstly that the "stability–reactivity" principle breaks down. Although the required opposition between the stability of an ion pK_{R^+}[151] and its rate of reaction with nucleophiles was observed in a series of ions, Brønsted's equation was on the whole inapplicable, and in several cases no correlation was evident between the logarithms of rate and equilibrium constants. Absence of correlation was also mentioned earlier between $\lg k$ for the reaction of triarylmethyl cations with water and pK_{R^+} with variation in the number of *para*-substituents from 1 to 3.[136] However, a "reactivity–stability" correlation was observed in the hydride reduction of triarylmethyl cations[137,138].

Secondly, Ritchie discovered the surprising fact that carbonium ions differing considerably in stability had the same selectivity. The distribution of products of competing S_N1 reactions had shown that the selectivity of a carbonium ion towards nucleophiles depended on its stability. In 1966 a linear relation‡ was found[152] for a series of S_N1 reactions between $\lg k_1$ and $\lg(k_N/k_S)$ (where k_N and k_S are the reaction rate constants with the azide ion and with water respectively; the ratio $k_N[N_3^-]/k_S$ can be found from the distribution of the reaction products $[RN_3]/[ROH]$. This relation was extended by Schleyer et al.[153] and by Harris et al.[154].

Ritchie's results show that the rate of reaction of a carbonium ion increases with the nucleophilicity of the other reactant, but the ratio k_N/k_S remains almost constant for all the carbonium ions investigated. The reactions of substituted tropylium ions with hydroxide ions and with water may be cited as examples (Table 4). Although reactivities varied by 10^2, and stabilities by $10^{2.5}$, the k_{OH^-}/k_{H_2O} ratios were very closely similar[143]. A possible explanation[155] is that the reaction velocity is governed by desolvation of the nucleophile, which is independent of the cation.

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‡ It must be borne in mind that a linear dependence may be distorted by the return mechanism, although it is supposed[154] that the fractional return is small in aqueous ethanol, in which the correlation was obtained.

The quantity $N_+ = \lg(k_N/k_{H_2O})$, where k_N is the reaction rate constant in a given solvent and k_{H_2O} the rate constant for reaction of the same cation with water in pure water, was proposed[147] as a measure of the nucleophilicity of the nucleophile N in the solvent. The nucleophilicity sequence thus obtained, quite apart from the absolute values, differed very markedly from published results determined in relation to other substrates[156-159].

Table 4. Comparison of stability of substituted tropylium ions with their reactivity towards OH^- and H_2O.

Cation	pK_{R+}	k_{H_2O}, s^{-1}	k_{OH^-}, $M^{-1}s^{-1}$
$C_7H_7^+$	4.76	2.6	$3.1\cdot10^5$
$C_6H_5C_7H_6^+$	4.86	1.0	$7.9\cdot10^4$
p-$ClC_6H_4C_7H_6^+$	4.55	1.2	$1.4\cdot10^5$
p-$CH_3C_6H_4C_7H_6^+$	5.75	0.27	$4.0\cdot10^4$
p-$Me_2NC_6H_4C_7H_6^+$	6.90	0.02	$1.7\cdot10^3$

Dorfman et al.[160] have recently obtained unique data on the reactivity of the benzyl cation. They used pulsed radiolysis to generate benzylium from various benzyl derivatives, and to determine rate constants for its reactions with methanol, ethanol, and the bromide and iodide ions as ($k_2^{24°}$, $M^{-1}\,s^{-1}$) respectively 7.4×10^7, 1.3×10^8, 5.2×10^{10}, and 4.9×10^{10}.

V. PROOFS OF THE EXISTENCE OF ION-PAIRS IN S_N1 REACTIONS

1. Special Salt Effect

An attempt to test the possible involvement of various types of ionic intermediates in solvolytic reactions led Winstein et al. to undertake a series of studies of salt effects in the solvolysis of sulphonates and halides[8,161-170]. In the normal salt effect additions of such a salt as lithium perchlorate, not containing a common ion, produce an increase in the titrimetrically determined solvolysis rate constant: $k_t = k_t^0(1 + b[\text{Salt}])$, where b is a measure of the normal salt effect. Such a relation has been observed in the solvolysis of several primary and even secondary systems in aqueous acetone and in acetic acid[161,164]. In some cases, however, the introduction of small quantities of lithium perchlorate produced a sharp increase in reaction velocity (Fig. 1). This phenomenon was termed a "special salt effect" and was observed e.g. with *o*- and *p*-methoxyphenethyl toluene-*p*-sulphonates in alcoholic acetic acid[162] and with *trans*-2-*p*-methoxyphenyl-cyclopentyl and -cyclohexyl *p*-bromobenzenesulphonates, *p*-methoxy-α-methylphenethyl toluene-*p*-sulphonate, *erythro*-*p*-methoxy-$\alpha\beta$-dimethylphenethyl *p*-bromobenzenesulphonate[163], and 2,4-dimethoxyphenethyl toluene-*p*-sulphonate in acetic acid[165]. With further increase in the lithium perchlorate concentration only the normal salt effect was observed in conformity with the equation $k_t = k^0_{ext}(1 + b[LiClO_4])$, so that the special salt effect is defined by the ratio k^0_{ext}/k^0_t (Fig. 1).

Winstein and his coworkers suggested that the solvolytic product ROS could be formed from the carbonium ion or from the solvent-separated ion-pair, and return to the covalent form could take place at all stages—external ion return k_{-3} involving the anion X^- and hence depending on its concentration, external ion-pair return k_{-2}, and internal ion-pair return k_{-1}:

$$\underset{(I)}{RX} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \underset{(II)}{R^+X^-} \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \underset{(III)}{R^+\|X^-} \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} \underset{(IV)}{R^+ + X^-}$$
$$\overset{k_S^{III}}{\downarrow}\text{HOS} \qquad \overset{k_S^{IV}}{\downarrow}\text{HOS}$$
$$\text{ROS} \qquad \text{ROS}$$

It was assumed also that exchange of anions could occur only by means of a solvent-separated ion-pair, which would be converted into a different, more reactive ion-pair, with suppression of the return stage k_{-2}:

$$R^+\|X^- + M^+\|Y^- \rightleftharpoons R^+\|Y^- + M^+\|X^-$$

(exchange involving the ion-pair $M^+\|Y^-$), and

$$R^+\|X^- + Y^- \rightleftharpoons R^+\|Y^- + X^-$$

(exchange involving the ion Y^-). However, the effect of lithium perchlorate on the ratio k_1/k_{-1} corresponds to the normal salt effect.

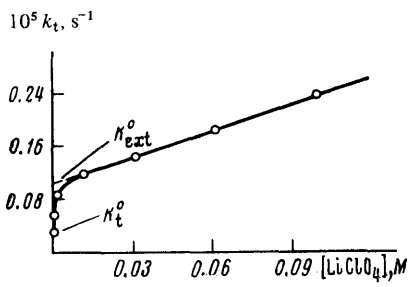


Figure 1. Typical dependence of solvolysis rate constant on $LiClO_4$ concentration in presence of a special salt effect. The points represent values of k^0_t, and the broken line indicates k^0_{ext}.

Thus the action of lithium perchlorate consists in the usual "chemical capture", which, unlike capture by other nucleophiles (N^-), does not yield a stable compound RN but a well ionised compound formed in solution by a reactive ionic intermediate. This mechanism of the action of lithium perchlorate is confirmed by the suppression of the special salt effect on addition of a salt having a common ion, e.g. lithium toluene-*p*-sulphonate in the reaction of an alkyl toluene-*p*-sulphonate[166] because of competition for the ion-pair (III). It is noteworthy that lithium toluene-*p*-sulphonate exhibits a positive salt effect in the acetolysis of *p*-methoxy-α-methylphenethyl toluene-*p*-sulphonate. The absence of depression of k_t by the toluene-*p*-sulphonate anion suggests absence of a return stage involving the free ion, i.e. an intramolecular return stage.

Depression of the constant by a common ion may in principle be absent in two cases—(i) with very reactive ions, for which $k_S^{IV} \gg k_{-3}$ and (ii) when a solvolytic reaction involves only a loose ion-pair ($k_S^{III} \gg k_3$). In several

other reactions, e.g. in the acetolysis of *p*-methoxy-α-methylphenethyl or norbornyl toluene-*p*-sulphonate, the addition of lithium toluene-*p*-sulphonate led to a decrease in the solvolytic constant[168]. An exhaustive kinetic analysis by Winstein et al. yielded a formula for the titrimetric solvolysis constant in the absence of a common-ion effect ($k_{-3}[X^-] = 0$) and with complete depression ($k_{-3}[X^-] \gg k_S^{IV}$). Under certain conditions this method permits not only detection of ion-pairs but also quantitative calculation of the fractional return at different stages.

Winstein repeatedly emphasised that the presence of a special salt effect proves the existence of return stages, but a return mechanism is possible even in the absence of a special salt effect.

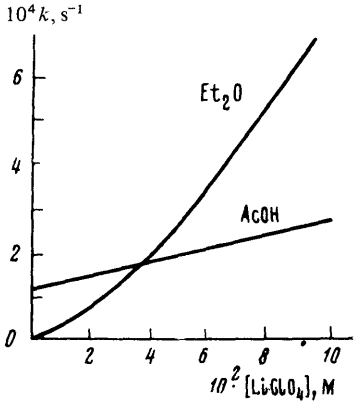


Figure 2. Dependence of ionisation rate constant for *p*-methoxy-$\beta\beta$-dimethylphenethyl toluene-*p*-sulphonate on the concentration of lithium perchlorate in diethyl ether and in acetic acid.

The bromide ion can also function as a trap for a solvate-separated ion-pair[167]. Formation of a bromo-derivative from *p*-methoxy-$\alpha\beta$-dimethylphenethyl *p*-bromobenzenesulphonate and *p*-methoxy-α-methylphenethyl toluene-*p*-sulphonate in acetic acid is a first-order reaction, and the exchange is subject to a normal salt effect.

Especially large salt effects are observed in slightly polar and weakly ionising media. Acetic acid, in which most of the studies of salt effects have been made, is a weakly polar but quite strongly ionising solvent[169,170]. The rate of ionisation of *p*-methoxyneophyl [*p*-methoxy-$\beta\beta$-dimethylphenethyl] toluene-*p*-sulphonate in ether increases on addition of 0.1 M lithium perchlorate by the immense factor of 10^5 (in acetic acid and in diethyl ether *b* has the respective values 12.2 and 298 000).[169] At a certain concentration of the lithium salt (>0.036 M) ether becomes a more strongly ionising medium than is acetic acid (Fig. 2). In solvents of this type it is supposed[170] that the added salt, present as an ion-pair, coordinates with the substrate to form a quadrupole:

$$RX + M^+Y^- \rightleftharpoons [R^+X^-M^+Y^-]$$

and such electrophilic assistance promotes the ionisation of RX.

The use of lithium perchlorate in poorly dissociating solvents may lead to distortions of the dependence $\lg k = f([LiClO_4])$. This may be responsible for the criticism of Winstein's work resulting from a study of the effect of additions of salts on the rate of reaction of triphenylmethyl chloride with methanol in benzene[171] which disregarded the dissociation of the added tetrabutylammonium chloride and perchlorate.

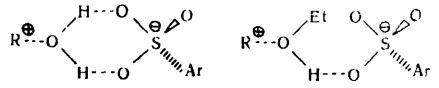
2. Distribution of Products in Competing Reactions. Nucleophilic "Traps" for Ion-pairs

Effect of leaving group

One method already noted for demonstrating the existence of a carbonium ion is the use of nucleophilic "traps", which affect the composition of the products without changing, in the case of a classic S_N1 process, the reaction velocity[2,74,83]. Competition between a strong nucleophile and the solvent for an ionic intermediate is expressed by a competition factor[172], which is easily determined from experimental data on the yield of products: $F_N = k_N/k_S = [RN]/[ROS][N]$, where F_N increases with the stability of the cationic intermediate[152,153,173]. For an unstable carbonium ion, exhibiting poor selectivity, the factor F_N should approach unity.

As already mentioned, one test for an S_N1 mechanism is that F_N should be unaffected by the nature of the leaving group. Thus the ratio $[RN_3]/[ROH] = 1.94$, the same for the reactions of diphenylmethyl chloride and bromide in aqueous acetone[74]. However, F_N depends§ not only on the nature of R in RX but also on that of the leaving group[175], which suggested that certain S_N1 reactions involve not the free carbonium ions but ion-pairs.

Thus the alkene/alcohol ratio in the reaction of t-butyl derivatives depends on the nature of the leaving group[176]. This result, may, of course, be due to partial involvement of an S_N2 mechanism. Variation in selectivity depending on the leaving group has been observed also in the reaction of 2-adamantyl arenesulphonates in aqueous alcohol[177]. The ROC_2H_5/ROH ratio diminished with increase in stability (with rise in $\lg k$), although the opposite relation might have been expected with attack on a free carbonium ion, in view of the great nucleophilicity of ethanol. Ion-pairs



are assumed to be involved in the reactions, and of these the pair separated by a water molecule is the more stable. The nature of the leaving group has a considerable effect on $F_N = k_{N_3^-}/k_{H_2O}$ in the reactions of triphenylmethyl chloride and bromide in 80% acetone[175]. The yield of hydrocarbon relative to that of the alcohol increases on passing from the chloride to the bromide in the reactions of diphenylmethyl and especially 1-phenylethyl halides with sodium tetrahydroborate in aqueous diglyme[178]. The

§ Detailed analysis[174] of various effects on the competition factor (not only by the structure of the substrate, the nature of the leaving group, and the nucleophile but also by the medium, the temperature, and even the rate of stirring) shows that a cautious approach must be made to comparing values obtained in different investigations.

leaving group has been found to affect the composition of the solvolysis products in the reactions of cyclobutyl arenesulphonates [179].

The selectivity factor in the solvolysis of triphenylmethyl chloride (0.013 M) in the presence of sodium azide (0.039 M) in 95% aqueous dioxan changed sharply on the addition of lithium nitrate and especially perchlorate [180] (0.089 M $LiClO_4$ increased [ROH]/[RN_3] from 20.2/79.8 to 41/59), which can be regarded as an argument in support of the formation from $R^+\|Cl^-$ of the more stable and less selective ion-pair $R^+\|ClO_4^-$. However, another possible explanation [180] is the influence of the ionic strength on the rates of the two "product-determining" reactions and the greater retardation by the salt effect of the ion–ion reaction (of the triphenylmethyl cation with the azide anion) than of the ion–dipole reaction (of this cation with water).

Comparison of stability of ion-pairs based on competitive substitution

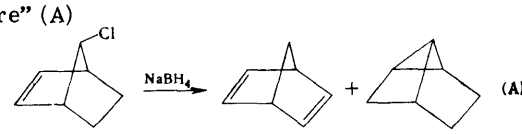
The solvolysis of 1,1- and 3,3-dimethylallyl [3-methylbut-2-enyl] chlorides yields mixtures of primary and tertiary alcohols, which suggests a common ionic intermediate. However, the action of sodium tetrahydroborate in aqueous ethanol results in different ratios (12.0 and 6.25) of the hydrocarbons $(CH_3)_2C:CH.CH_3$ to $CH_2:CH.CH(CH_3)_2$. [181] This difference is not due to simultaneous reaction by mechanisms S_N1 and S_N2 or S_N2', since doubling the concentration of sodium tetrahydroborate produces no significant change in these ratios. Hence it may be concluded that ion-pairs of similar but not identical structure are formed: i.e. they are distinguished by charge delocalisation in the cationic component, which is significant for attack by the hydride ion.

An interesting comparison was made [182] of reactivities and product compositions in the hydrolysis in aqueous diglyme of cyclopropylmethyl (V) and cyclobutyl (VI) methanesulphonates and of their 1-methylated derivatives in the presence of sodium tetrahydroborate or sodium azide. The reactivity of (V) was almost tenfold that of (VI), but the alcohols formed were almost identical in composition—almost equal quantities of (V)–OH and (VI)–OH with a little allyl alcohol. The suggested that a common intermediate was formed in the limiting stage, which might be a "non-classical" bicyclobutonium ion. However, the competition factors $F_N = k_N/k_{H_2O}$ (N = BH_4^-, N_3^-) were different, larger for (V)¶. Furthermore, different ratios of hydrocarbons are formed also with sodium tetrahydroborate: the ratios of methylcyclopropane to cyclobutane obtained on reaction with (V) and (VI) are respectively 3 and 2. Hence the reaction involves not a free carbonium ion but an ion-pair, having similar but not identical structures with (V) and (VI). Reactivity and selectivity data indicate that the ion-pair of (V) is more stable than that of (VI): i.e. a primary pair is more stable than a secondary pair. The same conclusion is reached from a study of competition factors for 1-methylated (V) and (VI): introduction of the methyl group diminishes selectivity, so that, in contrast to the free carbonium ions, the selectivity (and probably the stability) of the ion-pairs diminishes in the sequence—primary > secondary > tertiary.

An analogous relation has been found [174] for the sulphonates and halides of several "classical" systems for the study of S_N1 processes. However, it was noted that ambiguity was associated with use of the F_N criterion for assessing the mechanism in the intermediate region, where results could be interpreted in terms either of competition between S_N1 and S_N2 mechanisms or of the ion-pair S_N2 mechanism suggested by Sneen [183], since in this case the relation between competition factor and structure might be quite complicated.

Nucleophilic "traps" for ion-pairs

The use of lithium tetrahydroaluminate in ether as a nucleophilic trap for the "non-classical" carbonium ion in the reaction of 7-chloronorbornadiene led to the formation not only of norbornadiene but also of a "non-classical structure" (A)



which was regarded [184] as formed from a contact ion-pair, since it is difficult to assume an S_N1 mechanism in this solvent or S_N2 attack by a hydride ion on the double bond.

An interesting "trap" for ion-pairs in the reactions of diphenylmethyl and *p*-chlorodiphenylmethyl chlorides in 80% acetone is cobalt(II) nitrate [185]. Since this salt greatly affects the rate of solvolysis but has no effect on the polarimetric constant, it was deduced that racemisation involves ion-pairs of the same type (probably contact), while "capture" involves solvent-separated ion-pairs.

3. Stereochemistry

Comparison of rates of racemisation, solvolysis, and isotope exchange

The idea of the participation of ion-pairs and the occurrence of a return stage in solvolytic processes of S_N1 type were used by Winstein et al. [186] to explain the difference between the rate constants for loss of optical activity and for the solvolytic reaction of *exo*-norbornyl *p*-bromobenzenesulphonate ($k_\alpha > k_t$). These workers discovered a rule, which has since been confirmed: the fractional return increases as the nucleophilicity of the solvent decreases (Table 5). With $\alpha\beta$-dimethylphenethyl toluene-*p*-sulphonate as example it was shown [187] that the "excess" of racemisation was due to return of an ion-pair, not of the free ions, since the addition of sodium toluene-*p*-sulphonate hardly affected the ratio k_α/k_t, which had the respective values 2, 4.5–5, and 1.18 in ethanol, acetic acid, and formic acid. In the solvolysis of *threo*-*p*-methoxy-$\alpha\beta$-dimethylphenethyl *p*-bromobenzenesulphonate the ratio varies from 4.1 in acetic acid to 16 in a mixture of 10% of formic acid with dioxan [188]. Both constants increase on the addition of lithium perchlorate in conformity with the equation for the salt effect, in which $b_\alpha = 16.2$ and $b_t = 21.6$.

An analogous proof of the existence of ion-pairs in the reactions of dimethylphenyl systems is based on comparing k_α (determined polarimetrically) with k_t or the rate

¶ It is significant that the rate of reaction in the presence of sodium azide varies little, only a slight positive salt effect being observed, which does not support an S_N2 mechanism.

constant k_e for exchange between the halides and a radioactive halide ion. Thus the rate of loss of optical activity by the compounds $C_6H_5CHClC_6D_5$ and $C_6H_5CDClC_6D_5$ exceeds the aggregate rate of solvolysis and exchange with the radioactive chloride ion[189]: k_α/k_t has the values ~3, 20, and 100 in 50% acetone, nitromethane, and liquid sulphur dioxide respectively.

Table 5.

Solvent	AcOH	EtOH	75% Acetone
k_α/k_t	3.45	2.94	1.40

Winstein and his coworkers[6,190-195] made a series of determinations of the constants k_α, k_t, and k_e using *p*-chlorodiphenylmethyl chloride in various aprotic and other solvents. Values of the constants obtained by extrapolating to zero salt concentration were compared. Table 6, which lists the dielectric constants of the solvents together with the values obtained for the rate constants and the ratio k^0_α/k^0_e or k^0_α/k^0_t, shows that $k_\alpha > k_t$ or k_e in all the solvents, i.e. that the rate of return exceeds the rate of chemical capture. The value of k_α is strongly dependent on the ionising power of the solvent. It is interesting that a linear dependence of $\lg k^0_\alpha$ on $\lg k_1$ for the solvolysis of *p*-methoxy-$\beta\beta$-dimethylphenethyl toluene-*p*-sulphonate was obtained[196] for all six solvents at 75°C: $\lg k^0_\alpha = 4.22 + 2.02 \lg k_1$.

Table 6. Effect of solvent on the constants k^0_α, k^0_t, and k^0_e and their ratios for the reaction of *p*-chlorodiphenylethyl chloride with the chloride ion.

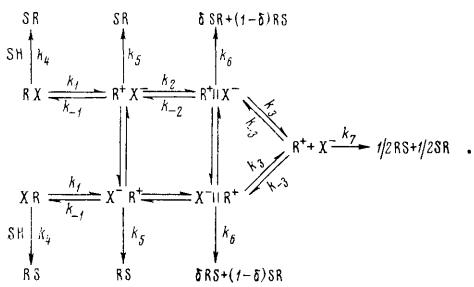
t, °C	Solvent	ε	$10^6 k^0_\alpha$, s^{-1}	$10^6 k^0_t$, s^{-1}	$10^6 k^0_e$, s^{-1}	k_{2e}**, $M^{-1} s^{-1}$	k^0_α/k^0_t	k^0_α/k^0_e
25	AcOH	6	68	1.8	—	—	38	—
25	80% CH_3COCH_3	30	60	23.1	—	—	2.6	—
75	CH_3NO_2	37	145	—	3.25	1.03	—	44
11	CH_3CN	37	60.7	—	0.2	1.23	—	304
11	$HCONMe_2$	37	18.9	—	5.0	2.00	—	4
11	CH_3COCH_3*	21	1.38	—	0.03	1.90	—	50

*Both processes, characterised by k_α and k_e, are slightly accelerated by lithium salts (chloride and perchlorate) and very strongly accelerated by the corresponding tetrabutylammonium salts, but their ratio varies little.
**The rate constant k_{2e} for bimolecular exchange with covalent RCl is found as the slope of the dependence of k_e on [MCl] at a low concentration of the isotopically labelled salt: $k_e = k^0_e + k_{2e}[(C_4H_9)_4NCl]$. The value of k_{2e} is almost the same in all solvents.

The ratio of the constants (k^0_α/k^0_t or k^0_α/k^0_e), of course, represents the ratio of the lower limit of the rate of ionisation to the rate of chemical capture, since part of the return may occur with retention of stereochemical configuration. As already noted, this ratio is strongly dependent on the nature of the solvent and decreases with increase in its nucleophilicity. For solvolytic reaction this occurs as a consequence of increase in the rate constant k_N for reactions of the ion-pair with the solvent. Initial attack on the pair $R^+||X^-$ by a solvent molecule is assumed also for exchange, with formation of an intermediate that is more reactive in exchange, e.g. $RO.CH:N^+(CH_3)_2$ [or the less stable $CH_3C:N^+R$ and $(CH_3)_2C:O^+R$]. The results indicate that most of the ion-pairs in the majority of the ambipolar aprotic solvents used are converted back into the initial compound, and only a proportion of them undergo exchange.

Rates of exchange of chlorine and loss of optical activity have similarly been compared for the compounds $C_6H_5CHClCH_3$ and $C_6H_5CHClCH(CH_3)_2$ in various solvents[197]. In all cases k_α exceeds k_e, although their ratio is, of course, influenced by the variation in structure and solvent. Detailed investigation of the solvolysis of 1-phenylethyl chloride in 60% aqueous dioxan showed[198] that addition of lithium perchlorate produces a considerable increase in rate†, whereas lithium chloride has hardly any effect on the rate (k_α and k_t), which indicates an ionisation process, not dissociation. The ratio k_α/k_t remains almost unchanged: 1.18, 1.40, and 1.42 in the absence of additive and in the presence of 0.23 M LiCl and 0.23 M $LiClO_4$ respectively. An explanation was based[198] on Winstein's concept of equilibrium among various ionic intermediates, including solvated ion-pairs.

A similar relationship ($k_\alpha > k_t$) has been observed[199] in the solvolysis of 1-phenylethyl chloride in trifluoroethanol and in aqueous ethanol. Both solvent-separated contact ion-pairs, whose interaction with the solvent was accompanied by inversion, were regarded[199] as taking part. Thus the general scheme involves several equilibria and processes:



The results show that, of 100 contact ion-pairs in trifluoroethanol (97–100%), 80 undergo return, 18 are solvolysed (through solvent-separated ion-pairs), and 7 invert the configuration; the corresponding proportions in 60% ethanol are 70, 28, and 1.4.

Exchange in the systems comprising 1-phenylethyl chloride or bromide with the corresponding halide ions, as well as reactions with other nucleophiles, were studied by Pocker[200,201] in liquid sulphur dioxide and in nitromethane. Here, too, it was found that the rate of racemisation k_α exceeded the rate of exchange k_e together with the rate of the accompanying dehydrochlorination k_D.

† With *p*-chlorodiphenylmethyl chloride in 80% acetone k_t is larger in the absence of lithium perchlorate than in its presence in small concentrations: i.e. the dependence of the rate constant on the concentration passes through a minimum.

The ratio of return with racemisation to chemical capture was respectively 9 and 4 in the two solvents. However, as also with diphenylethyl bromide, a significant proportion of the exchange under these conditions took place by an S_N2 mechanism [202], when it was found that $k_{2\alpha} = 2k_{2e}$: i.e. every act of bimolecular exchange was accompanied by inversion of configuration, in conformity with theory.

The unimolecular racemisation rate constant for phenyl-*p*-tolylmethyl chloride in nitromethane exceeds the rate constant for reaction with various nucleophiles by a factor of 20 (in conformity with an S_N1 mechanism the same constant $k_1 \simeq 2 \times 10^{-7}$ was obtained at 0°C for various nucleophiles—the azide and chloride ions, pyridine, triethylamine [200]).

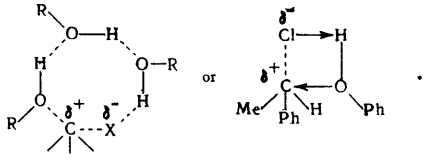
The involvement of ion-pairs in the "solvolysis" of s-butyl chloride in dimethylformamide in the presence of $Li^{36}Cl$ (the products are but-1- and but-2-ene and s-butyl formate) is also confirmed by comparing the rates of solvolysis, racemisation, and exchange [203].

Stereochemical "anomalies"

Various "anomalies" in the stereochemical results of unimolecular reactions are readily explained by the involvement of ion-pairs. Thus in several S_N1 solvolytic reactions inversion of configuration predominates over racemisation. For example, the methanolysis of 1-ethyl-1,3-dimethylbutyl phthalate, i.e. substitution at a tertiary carbon atom, is accompanied 54% by inversion and 46% by racemisation [204]. Such a result is usually attributed to shielding by the leaving group from nucleophilic attack, which in effect acknowledges the participation of ion-pairs in the reaction.

An analogous stereochemical effect of the leaving group, leading to predominant though not exclusive inversion, has been observed in the acetolysis of isomeric 4-t-butylcyclohexyl trifluoromethanesulphonates (triflates) (I). [204] The main product was an alkene, with only a certain quantity of acetates, inversion amounting to 94% for the equatorial compound and 75% for the axial compound. This suggested [205] that contact ion-pairs, not free carbonium ions, were involved in the reaction. The same conclusions had been reached earlier to explain incomplete inversion in the reactions of vinyl trifluoromethanesulphonates [206-208].

From the point of view of the mechanism and the possibility of the involvement of ion-pairs the greatest interest attaches to nucleophilic substitutions with retention of stereochemical configuration when this is not due to neighbouring-group participation but is a consequence of direct attack by the nucleophile [209,210]. A series of studies by Okamoto et al. [211-219] on the stereochemistry of the solvolysis of optically active 1-phenylethyl chloride showed extremely diverse results depending on the composition of the solvent. Thus solvolysis in the methanol–phenol–triethylamine system gave both products (of phenolysis and of methanolysis) with inversion of configuration when the initial phenol content has been 50% (by weight); from a phenol content of 85–95% both ethers exhibited complete retention of configuration; but in 75% phenol the methyl ether was formed with inversion, and the phenyl ether with retention [217]. A possible explanation suggested by Okamoto [217,218] was oriented coordination of attack by a solvent molecule on an ion-pair on the side of the leaving group. This explanation much resembles Cram's scheme [3] put forward to explain the retention of configuration at a carbanionic centre in reactions involving ion-pairs:



Retention of configuration can be explained also by differences between the uniform solvation of a carbonium ion and the possibly unsymmetrical solvation of an ion-pair on the side of the carbonium centre. If such solvation partly acquires the status of a bond, i.e. achieves directionality and some overlap of orbitals, though weaker than in nucleophilic attack‡, a situation may arise in which it is easier for the nucleophile to attack the carbonium centre from the direction of the leaving group than on the opposite side, which is shielded by a solvent molecule. Such a hypothesis was used to explain the partial retention of configuration in the reaction of optically active 2-bromooctane with the thiocyanate ion in dimethyl sulphoxide [220]. The considerable retention of configuration in the S_N1 reaction of *laevo*-biphenylyl-1-naphthylphenylmethyl benzoate in aqueous acetone, aqueous dioxan, and absolute alcohol was explained [221] on the same basis.

Retention of configuration by participation of the solvent was used by Okamoto [222] to explain the stereochemical result of the reaction of 1-phenylethyl chloride with a carboxylic acid in acetonitrile, when the fractional retention increased with the content of this solvent. Reaction was assumed to involve the "tail-solvated" ion-pair $CH_3CN...R^+...X^-$, in which the reaction centre interacts more strongly with the solvent than with the leaving group. However, the solvated ion-pairs considered here are not solvent-separated, and their involvement in the reaction presupposes that the S_N1 (or S_N2?) reaction may occur through another ionic intermediate, a solvated contact ion-pair. Solvation of an ion-pair from the "tail", as a result of which the reaction of 1-phenylethyl chloride with silver nitrate in diethyl ether takes place with retention of configuration, was considered also by Kornblum [223], but in acetonitrile the same reaction was accompanied by inversion; competition probably takes place between the solvent and the nitrate ion.

Complete retention of configuration was observed in the nucleophilic substitution of axial bromine in *trans,trans*-2-bromodecahydronaphthalene by the action of acetonitrile in the presence of silver perchlorate or tetrafluoroborate to give *N*-*trans,trans*-decahydro-2-naphthylacetamide [224]. Retention was observed in the solvolysis of menthyl toluene-*p*-sulphonate in aqueous alcohol (58%) and in trifluoroethanol (83%). [225]

There was a tendency [226,227] to explain the considerable retention of configuration in the acetolysis and the formolysis of *anti*-2,3-dideutero-7-norbornyl *p*-bromobenzenesulphonate (90% and 95% respectively) by frontal collapse of the ion-pair formed. An S_N1 mechanism is clearly indicated by the lack of effect of added sodium acetate on the stereochemical result of acetolysis. On the other hand, the lower percentage retention accompanying formolysis may be some argument that retention of configuration is not a consequence of the development of

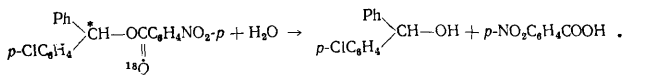
‡ This shows how blurred is the boundary between electrostatic solvation and formation of a covalent bond, leading to S_N1 and S_N2 mechanisms in solvolytic reactions.

synartesis and the formation of a non-classical carbonium ion. Thus reaction of a solvate-separated ion-pair and exchange in it of an anion without change in configuration provide yet another possibility. In other words, it must be supposed that attack on a contact ion-pair that is not solvated at a carbon atom takes place from the "tail", for exchange of an anion in a solvent-separated pair occurs at the front. However, the possibility of explaining retention of configuration by "non-classical" participation cannot be completely excluded[228].

Thus steric orientation is considerably more ambiguous in S_N1 than in S_N2 reactions, and can be explained only in terms of ion-pairs.

4. Isomerisation of Anionic Component

A powerful method for proving the occurrence of various types of ion-pairs in solvolytic reactions, proposed by Goering[229], consisted in simultaneous study of rates of randomisation (equilibration), racemisation, and solvolysis of labelled (at carbonyl or ethereal oxygen atoms) optically active alkyl *p*-nitrobenzoates, e.g.[209]



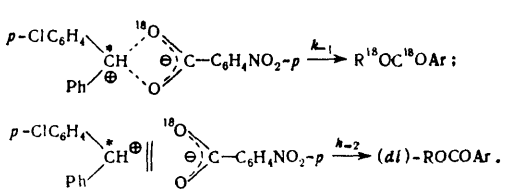
Analysis of the initial compound at various degrees of conversion revealed "scrambling" (equilibration) of the tracer in the returned product and loss of stereochemical configuration; however, these processes take place at different rates:

$$ROCOAr \xrightarrow{k_t} ROH + ArCOOH; \quad (1)$$

$$ROC^{18}OAr \xrightarrow{k_{eq}} R^{18}OC^{18}OAr; \quad (2)$$

$$(d \text{ or } l)\text{-}ROCOAr \xrightarrow{k_{rac}} d, l\text{-}ROCOAr. \quad (3)$$

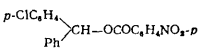
Thus for *p*-chlorodiphenylethyl *p*-nitrobenzoate in 80% and 90% aqueous acetone the rate of randomisation exceeds the rate of the solvolytic reaction ($k_{eq} > k_t$). The fact that k_t does not coincide with k_{eq} and k_{rac} implies that processes (2) and (3) result not only from the return of ions to the original covalent compound but also from the return of other ionic intermediates, as the difference between k_{eq} and k_{rac} indicates the existence of at least two such ionic intermediates. Usually $k_{eq} > k_{rac}$: e.g. for the system under discussion their ratio is 1.5 and 2.5 in 80% and 90% acetone respectively. This suggests that equilibration of the label has already occurred at the stage of return of the contact ion-pair, but racemisation on return of a solvate-separated ion-pair (the anionic component "slides" over the surface of the cation), while the solvolytic reaction involves solvate-separated ion-pairs and free ions:



The results show that in 90% acetone 72% of the ion-pairs formed are converted back into the original covalent compound, and 81% of the return occurs with retention of configuration. The rate constant k_{eq} may not represent the total return of ion-pairs (on the assumption that part takes place without randomisation) but be its lower limit.

Proof that return of an internal ion-pair may occur with complete retention of stereochemical configuration and proof of the existence of various types of ion-pairs were obtained in a study of the effects of additions of sodium azide on k_t, k_{eq}, and k_{rac}.[210] The presence of this additive was found to increase the rate of solvolysis, somewhat to diminish the rate of randomisation, and completely to suppress racemisation of the initial compound.

Table 7. Values of k_t, k_{eq}, and k_{rac} in the hydrolysis of *p*-chlorodiphenylethyl *p*-nitrobenzoate in 80% acetone at 99.0°C, in the presence and in the absence of sodium azide



(80% acetone with $c_0 \simeq 0.028$ M at 99.6°C).

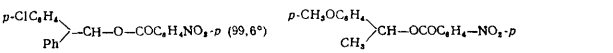
10^3k, h^{-1}	NaN_3 absent	0.14 M NaN_3
k_t	4.41	30.0
k_{eq}	6.5	5.9
k_{rac}	2.76	0.0

These results are consistent with the view that sodium azide is a nucleophilic "trap" for external ion-pairs. Exchange of anions between the ion-pairs

$$R^+\|X^- + Na^+\|N_3^- \rightleftharpoons R^+\|N_3^- + Na^+\|X^-$$

produces a more reactive ion-pair, which almost completely suppresses return from the solvent-separated ion-pair. Hence loss of stereochemical configuration is a consequence of return of this particular ion-pair (Table 7). Some change in k_{eq} under the influence of sodium azide implies that part of the randomisation is due to the return of loose ion-pairs. The fractional return increases with increase in the stability of the ion-pair. Thus k_t = 0.0064 h^{-1} and k_{eq} = 0.0187 h^{-1} even for diphenylethyl *p*-nitrobenzoate in 90% acetone (at 118.6°C).

Table 8. Effect of water content of acetone on proportion and stereochemistry of return for



Acetone	90%	80%	90%	70%
k_t (rel.)	1	9	1	45
k_{eq}/k_t	2.1	1.46	2.59	0.57
k_{rac}/k_{eq}	0.38	0.43	0.45	0.71

Increasing the water content in aqueous acetone affects both the fractional return (k_{eq}/k_t) and the stereochemistry of return (k_{rac}/k_{eq}).[230] The rates of solvolysis of

p-chlorodiphenylethyl and 1-*p*-methoxyphenylethyl *p*-nitrobenzoates increase, while the ratio k_{eq}/k_t decreases (for the latter compound in 70% acetone it even becomes <1) and k_{rac}/k_{eq} increases (Table 8). This observation is fully consistent with the above hypothetical shift in equilibrium, in a more strongly ionising medium, from contact to loose ion-pairs.

The fractional return from a solvate-separated ion-pair depends on its stability. A more stable ionic intermediate is in general less susceptible to nucleophilic attack, and is therefore more strongly racemised. Another possible explanation is that the forces of interaction between the ionic components become weaker in such an ion-pair, which increases the fractional return with racemisation. This may be illustrated by comparing results obtained for the solvolysis of 1-phenylethyl *p*-nitrobenzoate in 70% acetone, when no appreciable racemisation was observed, and for that of the 1-*p*-methoxyphenylethyl ester, which was more reactive by a factor of ~30 000, and 71% return occurred with racemisation [230]. Thus increase in the stability of $R^+\|X^-$ leads to increases both in the ionisation constant and in the fractional return k_N/k_S (the ratio of the rate constants for reaction with its own gegenion and for reaction of the ion-pair with the solvent).

Winstein et al. [162] noted an increased contribution by return of the solvent-separated pair accompanied by increase in the rate of solvolysis in acetic acid on passing from 1-phenylethyl to 1-*p*-methoxyphenylethyl toluene-*p*-sulphonate, as shown by the increase in the salt effect from normal to special ($k^0_{ext}/k^0_t = 1$ and 3.2 respectively). A similar relationship was observed for *para*-substituted diphenylethyl *p*-nitrobenzoates [231]: k_t increased rapidly in the sequence Cl < H < CH_3 < CH_3O ($\rho = -3.9$ in agreement with an S_N1 mechanism), while k_{eq}/k_t showed little change, and k_{rac}/k_{eq} increased with k_t, i.e. with increase in stability of the ionic intermediate.

The species through which return takes place to the original compound is recognised from the common-ion effect, the salt effect, and the rate constants k_{eq} and k_{rac}. Thus it was deduced from the absence of depression by a common ion that with 1-*p*-methoxyphenylethyl toluene-*p*-sulphonate return occurs only from solvent-separated ion-pairs, whereas free ions are also involved in the case of the 1-(2,4-dimethoxyphenyl)ethyl ester [188]. The special salt effect and the greater selectivity observed in the solvolysis of *threo*-*p*-methoxy-$\alpha\beta$-dimethylphenethyl toluene-*p*-sulphonate in comparison with the $\alpha\beta$-dimethylphenethyl ester correspond also to the nature of the ion-pairs involved in return: in the former case solvolysis is accompanied by the return of 83% of loose and 38% of contact ion-pairs; whereas in the latter case return takes place only from contact ion-pairs, although the total amount of return (78%) is the same in the two cases [188]. Passing from 2-phenylpropyl to 2-*p*-methoxyphenylpropyl toluene-*p*-sulphonate is also accompanied by an increase in the fractional return from loose ion-pairs [232].

A more complex question is the effect of additions of sodium azide on the ratios k_{eq}/k_t and k_{rac}/k_{eq}. Thus, in contrast to the above reaction of *p*-chlorodiphenylethyl *p*-dinitrobenzoate, the addition of sodium or tetrabutylammonium azide in the reactions of 1-*p*-methoxyphenylethyl [230] and phenyl-*p*-tolylmethyl [231] *p*-nitrobenzoates leads not only to an increase in k_t but also to a considerable decrease in the fractional return (k_{eq}/k_t), though the stereochemistry of return (k_{rac}/k_{eq}) remains almost unchanged, for which no simple explanation is available. It may be linked [230,231] with a diminution in the forces of interaction in the contact ion-pair (resulting from increased delocalisation of charge in the cationic component), so that racemisations may already occur on return of the contact ion-pair.

Redistribution of the label in the anionic component was used by Winstein et al. [233] to prove the presence of ion-pairs in the reactions of non-activated secondary alkyl sulphonates, such as 1-methylheptyl and *trans*-4-t-butylcyclohexyl toluene-*p*-sulphonates, for which bimolecular attack on the contact ion-pair is assumed in conformity with Sneen's mechanism [183]. Randomisation was demonstrated, and k_{eq} was unaffected by addition of the same anion. The proportion of this process

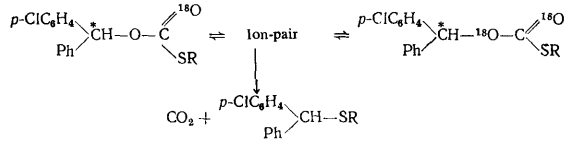
$$ROS^{18}O_2Ar \underset{}{\overset{k_{eq}}{\rightleftharpoons}} R^{18}OS^{18}O_2Ar$$

increases as the solvent becomes less strongly nucleophilic (Table 9).

Table 9.

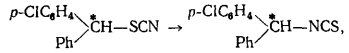
Solvent	MeOH	AcOH	HCOOH	CF_3COOH
$\frac{k_{eq}}{k_{eq}+k_t}$	1.1 (75°)	6.5 (75°)	8.1(25°)	19.9 (25°)

Equilibration of the label and loss of optical activity in the initial compound have been observed in the decomposition of *p*-chlorodiphenylmethyl *S*-alkyl(or aryl) thiocarbonates in various solvents [234] (S_Ni mechanism), with the ratio of the constants depending on the nature of the solvent. The results indicate that return of the ion-pairs took place predominantly with retention of configuration ($k_{eq} > k_\alpha$): [235]



In the corresponding reaction of $RCH(CH_3)OCOCl$ in dioxan, however, no exchange of the tracer between ethereal and carbonyl oxygen atoms was observed [236]. The above results on equilibration of the oxygen label in the carboxylate and other anions show that this process occurs mainly at the stage of return of internal ion-pairs.

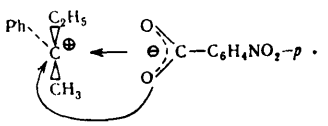
Similar results were obtained for isomerisation in a system containing thiocyanate, another ambident anion. Optically active *p*-chlorodiphenylmethyl thiocyanate underwent isomerisation in various solvents with complete retention of configuration [236–240]:



i.e. most probably as a result of return of a contact ion-pair.

Thus considerable return was usually observed with secondary alkyl *p*-nitrobenzoates (k_{eq}/k_t = 2.2–3.2 for 90% acetone), and a substantial proportion of the return (38–53% depending on structure) involved racemisation, but different rules were obtained for tertiary alkyl systems. In the reaction of α-ethyl-α-methylbenzyl-*p*-nitrobenzoate

$k_{eq} < k_t$ ($k_{eq}/k_t = 0.6$),[241] although both constants increased on passing to the tertiary alkyl, and only 8% of the return involved racemisation. The reason for the diminished return is not clear, although it may be linked with greater instability of a tertiary than of a secondary ion-pair due to an enhanced tendency to dissociation. The greater stereospecificity of return was attributed[242] to a heightened barrier to rotation of the anion around the sterically hindered cation



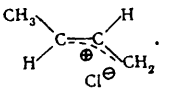
Fundamentally, however, the situation was unchanged: solvolytic reactions of tertiary systems involve ion-pairs capable of conversion into the original compound.

Return, as indicated by randomisation, was observed with triphenylmethyl *p*-nitrobenzoate dissolved in anhydrous acetone[242], i.e. in the absence of reaction. However, contradictory results were obtained for the effect of the azide ion[242-244]. According to Swain et al.[242] lithium azide converts the whole of the ester into triphenylmethyl azide and completely inhibits return (k_{eq} falls to zero), from which it was concluded that rearrangement took place in the intermediate that was captured by the azide ion. According to Winstein et al.[243], however, tetrabutylammonium azide does not suppress return, although in 99.2% acetone its addition, without changing the overall rate of the process, completely suppressed solvolysis: i.e. then $k_t = k_{N_3^-}$. In contrast to the quaternary ammonium azide, the lithium salt greatly diminishes return and sharply increases $k_t = k_{N_3^-}$. Since lithium perchlorate exerts an unusually marked influence on the rate of ionisation, it is supposed that in aprotic media lithium salts are able to form quadrupoles with ion-pairs, thereby promoting ionisation.

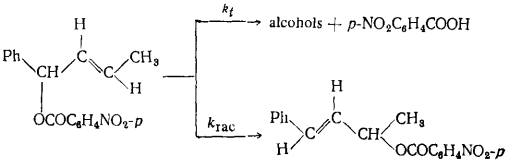
5. Isomerisation in Allyl Systems

Evidence of the occurrence of ion-pairs in solvolytic reactions and of a return mechanism is provided by isomerisation of the allyl fragment during the reaction of unsymmetrically substituted allyl systems, which have been studied in very great detail[245-253]. The intramolecular character of the isomerisation must first be demonstrated before the presence of ion-pairs can be assumed in these reactions. The actual idea of the existence of ionic intermediates other than free carbonium ions, through which both solvolysis and intramolecular rearrangements can be effected, was first put forward[7] in a study precisely of the allyl rearrangement: acetolysis of 1,1-dimethylallyl chloride was shown to be accompanied by its rearrangement into 3,3-dimethylallyl chloride, the rate of rearrangement being unchanged (allowing for the salt effect) when the reaction was conducted in the presence of the chloride ion. On the addition of $*Cl^-$ only a small proportion of the label entered the initial compound[25].

Thus the observed isomerisation is due to return of an ion-pair. The action of aqueous silver nitrate on *cis*- and *trans*-but-2-enyl and 1-methylallyl chlorides gives mixtures of isomers (nitrates and alcohols) with retention of geometrical configuration, which was attributed to a fairly high barrier opposing rotation in the ionic intermediate[245]

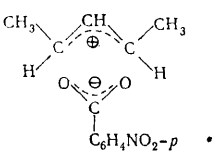


Solvolysis of 1-phenylbut-2-enyl *p*-nitrobenzoate in aqueous acetone[246,247], dioxan, and methanol[248,249] is accompanied by its intramolecular isomerisation into the less reactive α-methylcinnamyl ester:

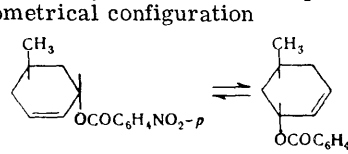


Use of the labelled optically active ester showed[247] that, in 90% aqueous acetone at 99.4°C, the relative rate constants (in 10^2 h^{-1}) were $k_t : k_{rac} : k_{eq} = 5.16 : 7.04 : 10.88$: i.e. under these conditions 65% of the return was accompanied by loss of stereochemical configuration. As noted earlier, the fractional return, i.e. the ratio k_{eq}/k_t, diminished with increase in the water content of the acetone, but, in contrast to other alkyl benzoates, the fractional return with racemisation k_{rac}/k_{eq} also decreased (to 16% in 70% acetone at 49.04°C).

The solvolysis of optically active *trans*-1-methylbut-2-enyl *p*-nitrobenzoate in aqueous acetone also was accompanied by randomisation and racemisation of the starting material, since the rate of loss of optical activity $k_\alpha = k_t + k_{rac}$ exceeded considerably the rate of solvolysis ($k_\alpha/k_t = 5.4$ and 2.17 in 90% acetone at 99.6°C and in 60% acetone at 59.9°C respectively)[250,251], so that by the time of 50% reaction the initial ester has been 95% racemised. The intramolecular character of the isomerisation (racemisation) was proved by the absence of exchange between the anions and *p*-nitrobenzoic acid and by the lack of effect of salt additions on k_t and k_α. It it interesting that $k_{eq} = k_{rac}$ (in 80% and 60% acetone): i.e. the two processes take place via the same symmetrical ion-pair (probably a contact pair, since exchange is absent), in which the two oxygen atoms and the two allyl carbon atoms are equivalent (cationic and anionic components are assumed to be located in perpendicular planes)



A similar relation was observed in the solvolysis of *cis*-5-methylcyclohex-2-enyl *p*-nitrobenzoate[252]. In the allyl isomerisation of the optically active *trans*-ester in 80% acetone, however, which also takes place with retention of the geometrical configuration



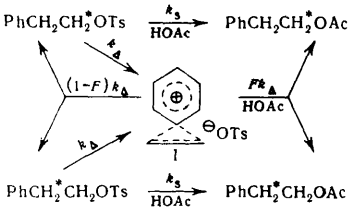
the rate of randomisation is double the rate of racemisation[253]. This system thus presents a more general situation, with two intermediates present in equilibrium: one is common to the two enantiomers, and its return leads both to racemisation and to randomisation; the other is not common, and only equilibration without loss of stereochemical configuration takes place in it (i.e. return occurs

without change in the carbon reaction centre). However, the reason for the differing behaviour of the two geometrical isomers is obscure.

6. Rearrangements with Aryl Participation

The concept of ion-pairs proved necessary to explain results connected with aryl migration and the stereochemistry of solvolysis in systems containing a 2-arylethyl fragment. From the very first steps in investigating the problem of "non-classical" (bridging) carbonium ions and anchimeric assistance it was demonstrated that this problem is closely connected with that of the formation of ion-pairs in these reactions [186,254].

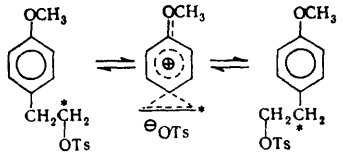
If migration of an aryl group during solvolysis in such systems is intramolecular, i.e. if it is independent of addition of a common ion, investigation of the rate of migration can be used to determine the fractional return from ion-pairs ("non-classical") formed with anchimeric assistance (k_Δ). Occurrence of a migration process can be assessed by using an unsymmetrically substituted system or, most simply, by examining the distribution of an isotropic tracer in a (carbon or hydrogen) labelled symmetrical system:



$$k_t = k_s + Fk_\Delta$$

The acetolysis rate constants for phenethyl toluene-*p*-sulphonate at 90°C are [255] $k_S = 8.92 \times 10^{-7}$ s^{-1} and $k_\Delta = 1.18 \times 10^{-6}$ s^{-1}, while the ion-pair return rate constant is 8.00×10^{-7} s^{-1}, which is comparable with k_S.

Many papers have appeared [255-270,273] on the effect of the aryl group and the medium on the distribution of a radioactive label in the initial compound, with calculations of the proportions of the process occurring with and without anchimeric assistance (k_Δ and k_S). Unfortunately, the nature of the ionic intermediate from which return occurred was not always studied. Return may involve not only ion-pairs but also free ions depending on structure and solvent, and these processes may occur together [271]. In some cases, however, the intramolecular character of return has been proved [255]. Thus solvolysis of carbon-labelled *p*-methoxyphenethyl toluene-*p*-sulphonate results in dissemination of the tracer both in the solvolysis product and in the initial ester [258], the latter process being a consequence of intramolecular rearrangement:



The intramolecular character of the rearrangement has been shown also in the acetolysis of β-methylphenethyl *p*-bromobenzenesulphonate [272] and *p*-methoxy-2-methylphenethyl toluene-*p*-sulphonate [232]. Hence participation of ion-pairs is possible even in the reactions of primary alkyl systems, providing that the substrate contains groups capable of assisting ionisation.

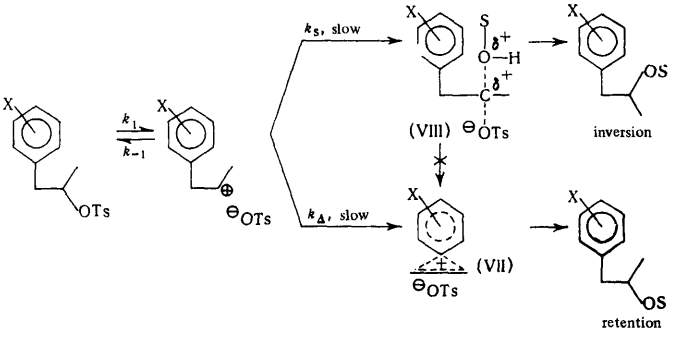
Results for the trifluoroacetolysis of phenethyl toluene-*p*-sulphonate [271], in which the path with anchimeric assistance is greatly enhanced, ($k_\Delta/k_S = 23\,000$), can be explained only if all three types of ion-pairs are involved in the process. Their contributions to the total return are indicated by the scheme

$$\mathrm{ROTs} \underset{15\%}{\rightleftharpoons} \mathrm{R^{\oplus}OTs^{\ominus}} \underset{87\%}{\overset{85\%}{\rightleftharpoons}} \underset{\text{Product}}{\mathrm{R^{\ominus}\,\|\,{}^{\ominus}OTs}} \overset{11.8\%}{\rightleftharpoons} \underset{\text{Product}}{\mathrm{R^{\oplus}}} + {}^{\ominus}\mathrm{OTs}\ .$$

Similarly for the *p*-methoxyphenethyl ester [258,271]

$$\mathrm{ROTs} \underset{8\%}{\rightleftharpoons} \mathrm{R^{\oplus}OTs^{\ominus}} \overset{92\%}{\underset{95\%}{\rightleftharpoons}} \underset{\text{Product}}{\mathrm{R^{\ominus}\,\|\,{}^{\ominus}OTs}} \overset{2.5\%}{\rightleftharpoons} \underset{\text{Product}}{\mathrm{R^{\oplus}}} + {}^{\ominus}\mathrm{OTs}\ .$$

Thus systems with a bridging capability undergo solvolysis in two ways—attack by the solvent on the substrate and attack by the aryl group on the carbonium centre—corresponding to the rate constants k_S and k_Δ. In the case of secondary substrates the first process gives a product with inversion of configuration [272]. The present Review will not discuss the mechanism of stabilisation of the carbonium centre by neighbouring groups, nor methods of resolving the observed constant k_t into k_S and k_Δ (we mention merely that this is effected both from the percentage rearrangement and the stereochemistry and from a correlation analysis [274,275]). Nor shall we consider the controversial question [276,277] of the existence of two rapidly rearranging classical ion-pairs instead of a "non-classical" ion-pair. The fundamental question here will be the presence of a stage of intramolecular return, indicating that structure (VII) is an intermediate, not the transition state of the dissociation stage.



An important aspect of the reaction mechanism, especially in secondary systems, is possible participation by ion-pairs even at a stage not involving anchimeric assistance. In these systems both processes (attack by the solvent and by the aryl group) may be supposed to involve not the covalent compound but an intimate ion-pair formed in a pre-equilibrium stage [277]. It is possible also that an ion-pair differing from (VII) (e.g. a nucleophilically solvated ion-pair) may be formed along the k_S path, from which return may occur also (this is important, since return from (VII) diminishes the anchimerically assisted proportion of the process). It is important only to remember that the k_S and k_Δ paths do not intersect [255]: i.e. the ion-pairs formed (VIII) are unable (e.g. because solvation prevents aryl attack) to pass into (VII) (otherwise it would have been impossible to explain the good agreement between kinetic results and analyses of the products).

However, a test for the reaction mechanism shows the possibility of direct S_N2 attack by the azide ion on the covalent compound in primary and secondary systems [270,278].

Table 10.

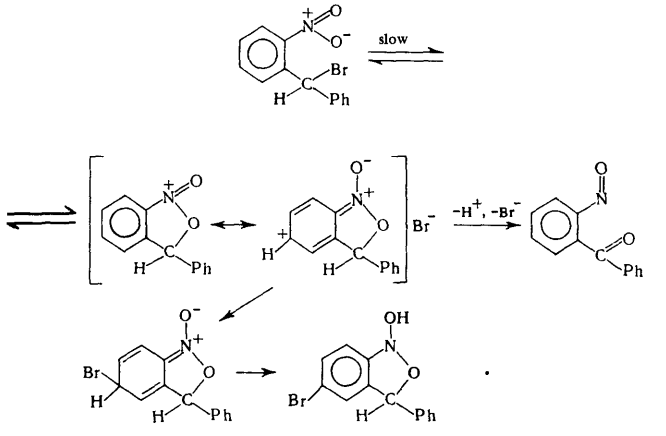
	CF_3COOH	HCOOH	AcOH
erythro-	92	61	29
threo-	89	49	22

Although proofs of the existence of ion-pairs have been obtained mainly in connection with aryl-group participation, k_Δ processes involving other β-donor groups may reasonably be expected to occur similarly. An example is the rearrangement of *erythro*- and *threo*-isomers of 4-chloro-1-methylpentyl toluene-*p*-sulphonate [279], in which considerable retention of configuration was observed. Table 10 shows that the fractional retention increases with increase in the ionising power of the solvent and decrease in its nucleophilicity. The concept of ion-pairs is especially reasonable for explaining rearrangements in primary systems, where the formation of free carbonium ions is unlikely.

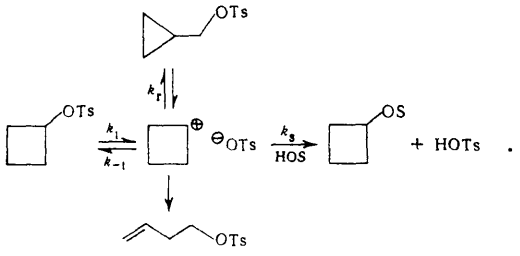
7. Other Cases of Isomerisation of the Cationic Component

Besides the above cases of allyl rearrangement and migration of an aryl group, other examples are known of rearrangements in the cationic component, which also are easily explained by the formation of ionic intermediates.

The nature of the product is changed by a curious isomerisation discovered recently [280]. In the solvolysis of *o*-nitrodiphenylmethyl bromide in 90% aqueous acetone, acidification with aqueous hydrobromic acid yields 5-bromo-3-phenyl-1-2,1-benzisoxazole instead of *o*-nitrosobenzophenone, which is the reaction product in neutral solution. The two reactions are assumed to occur via the same ion-pair formed by intramolecular attack by the nitro-group. Abstraction of a proton from this ion-pair (by the action of water or of added sodium acetate) yields the ketone, and reversible return of the pair in acid medium is accompanied by entry of bromine into the ring to give a product converted into the isoxazole derivative:



The formation of ion-pairs (probably of contact type) explains the isomerisation observed in the solvolysis of cyclopropylmethyl [281] and cyclobutyl [179,282] arenesulphonates:



It has been shown above, on the basis of the effect of the leaving group and data on competing reactions, that free ions are not formed, and the ratio k_r/k_S depends on the nature of the leaving group [179], as should be the case in reactions involving an ion-pair.

VI. CONTACT ION-PAIRS IN S_N2 REACTIONS

The concept of ion-pairs has thus provided explanations of the relations among rates of solvolysis, racemisation, randomisation, and rearrangement, as well as the special salt effect, in solvolytic reactions of type S_N1. Formation of ionic intermediate has recently been considered also in S_N2 reactions of secondary alkyl systems. Since 1965 the possibility has been discussed that bimolecular nucleophilic substitution may result from nucleophilic attack not on the covalent compound but on a contact ion-pair formed in the pre-equilibrium stage:

$$RX \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} R^+X^- \xrightarrow[\text{slow}]{N^-,k_2} RN + X^- \ .$$

Since secondary compounds should be less reactive than primary compounds by an S_N2 mechanism, and less reactive than tertiary compounds by an S_N1 mechanism, Sneen supposed [183,283-294] that the nucleophile may be attacking a contact ion-pair. He based this suggestion on two facts—(i) formation of the completely inverted alcohol on the hydrolysis of optically active 1-methylheptyl methanesulphonate [283] and (ii) the non-coincidence of the rate-determining stage and the stage governing the ratio of the products (alcohol and azide) of the solvolysis of this compound in the presence of sodium azide in 25% and 30% aqueous dioxan [284].

In the classic S_N1 mechanism the reaction velocity is indeed unaffected by addition of sodium azide, since attack occurs after the rate-determining stage. Addition of the azide ion may than serve as a test for the S_N1 character of a solvolytic process [87], since, if reaction does not occur by an S_N2 mechanism even with a strong nucleophile, this should apply even more to a weaker nucleophile (water, alcohols). In the classic S_N2 mechanism the rate should increase in proportion to the increase in concentration of sodium azide:

$$RX \begin{cases} \xrightarrow{k_S} ROS \\ \xrightarrow{k_N\cdot[N_3^-]} RN_3 \end{cases} ; \quad k_{obs} = k_S + k_N[N_3^-] \ .$$

An intermediate case was observed with s-octyl sulphonates: the rate of reaction measured by the consumption of the initial compound increases with the sodium azide concentration, but considerably less rapidly than in

an S_N2 process (the order with respect to the azide ion lies between zero and unity). However, the selectivity with respect to the azide ion is about a thousandfold that for an S_N1 reaction. Thus addition of the azide ion provided Sneen and his coworkers with a convincing argument that an S_N2 reaction results from attack by the nucleophile on a contact ion-pair, which explained both the stereochemical inversion, the kinetic data, and the distribution of the products. Application of the steady-state principle to the scheme

$$RX \underset{\text{rapid}}{\rightleftharpoons} R^+X^- \begin{cases} \xrightarrow[\text{slow}]{k_S} ROS \\ \xrightarrow{k_N} RN_3 \end{cases}$$

yields the equation

$$k_{obs} = \frac{k_1 (k_S + k_N \cdot [N_3^-])}{k_{-1} + k_S + k_N \cdot [N_3^-]},$$

showing that k_{obs} is a complicated function of k_1, k_{-1}, k_S, and k_N. The ratio k_N/k_S is determined from the proportions of products formed in the presence of various concentrations of sodium azide:

$$\frac{k_N [N_3^-]}{k_S} = \frac{[RN_3]}{[ROH]}.$$

This approach removes objections based on the variation of the reactivity of sodium azide with concentration. Of course, F_N can be determined from the plot of $[RN_3]/[ROH]$ against $[N_3^-]$ if the latter is a straight line. However, the dependence would not be linear over a wide concentration range, since sodium azide may be incompletely dissociated in these solutions. Indeed, according to Ritchie [145] the graph for the reaction of di-*p*-methoxyphenylmethyl 2,4,6-trimethylbenzoate in methanol is not linear. The observed fractional order with respect to the azide ion may then be a consequence of its incomplete dissociation. However, this aspect has not been discussed in the publications of Sneen and his collaborators. It is noteworthy that departures from the first order with respect to the bromide ion, observed in a study of the rate of racemisation of 1-phenylethyl bromide in acetone, were due to the existence of lithium bromide in this solvent not only as ions but also as ion-pairs [33], although they could easily have been attributed to an ion-pair S_N2 mechanism.

The ratio of the observed rate constant to the solvolytic rate constant k_{NA} in the absence of sodium azide, allowing for a possible slight positive salt effect (assumed to correspond to that produced by salts such as lithium perchlorate, sodium nitrate, and sodium bromide), is given by

$$\frac{k_{obs}}{k_{NA}} = \frac{(x+1)(1+m[N_3^-])}{(x+1+m[N_3^-])}$$

$$m = \frac{k_N}{k_S}, \quad x = \frac{k_{-1}}{k_S}$$

$$k_{NA} = k^0_{NA}(1 + b \cdot [NaN_3]).$$

The S_N2 and S_N1 mechanisms are extreme cases of this equation (as $x \to \infty$ and 0 respectively). The variation of k_{obs}/k_{NA} at intermediate values of x is represented by curve *1* in Fig. 3. The experimental constant for 1-methylheptyl methanesulphonate coincides with the value calculated for 25% and 30% dioxan with $x = 2.4$ and and 2.59 on the assumption that $b = 1.08$ and 1.04 respectively [287]. However, Schleyer et al. [295] have shown that observed rate constants obtained at different concentrations can be described by the equation for an S_N2 reaction (i.e. they can be correlated with the distribution of products) on the assumption that sodium azide exerts a negative salt effect ($b = -0.3$ and -1.0 for 25% and 30% dioxan respectively). The dependence of the ratio k_{obs}/k_{NA} on the sodium azide concentration will then be linear, in conformity with an S_N2 mechanism. However, values of b for closely similar media may then differ very greatly. Furthermore, Schleyer et al. [295] showed that the reaction of 1-methylheptyl *p*-bromobenzenesulphonate and of isopropyl toluene-*p*-sulphonate with the azide ion in 80% aqueous ethanol is the usual S_N2 type of process, in which the rate-determining stage coincides with the stage determining the composition of the products.

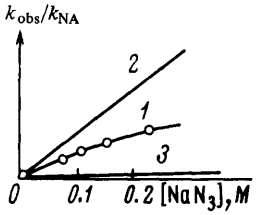
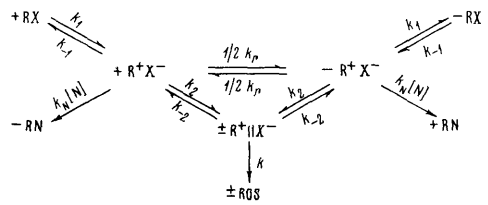


Figure 3. Dependence of k_{obs}/k_{NA} on $[NaN_3]$ for the reaction of 1-methylheptyl methanesulphonate with the azide ion and with water in 25% aqueous dioxan based on experimental value of $k_N/k_S = 8.22$ and different values of x: 1) 2.40; 2) ∞ (S_N2 mechanism); 3) 0 (S_N1).

The above procedure was applied by Sneen et al. to various systems, e.g. the reaction of *p*-methoxybenzyl chloride with water and the azide ion in 70% aqueous dioxan and that of benzoyl chloride with *o*-nitroaniline and water in 50% aqueous acetone [288]. On the assumption of a positive salt effect calculated and observed ratios k_{obs}/k_{NA} can be reconciled with $x = 1.98$ and 1.1 respectively ($m = 21.6$ and 4.42 from experiment).

An S_N2 mechanism with nucleophilic attack on a contact ion-pair has been suggested by Sneen et al. for the reactions of 1-arylethyl halides in ethanol [289] and of sulphonium salts [290]. The proposed scheme explains also results obtained in allyl systems [292-294]. In the solvolysis of 1-methylbut-2-enyl chloride in the presence of azide or thiocyanate ions in absolute ethanol $x = k_{-1}/k_S = 4.0$ for both ions [291]. This was regarded as supporting the scheme, which can in general be written



where k_r is the allyl isomerisation rate constant.

A similar view was expressed by Streitwieser et al. [296], who showed [297] that acetolysis of 1-methylheptyl toluene-*p*-sulphonate entails inversion but is accompanied by racemisation of the initial compound, the rate of which is

increased by the presence of lithium toluene-*p*-sulphonate[296]. According to Streitwieser solvolysis and substitution are not independent processes, but occur via the same ionic intermediate, together with slight rearrangement

$$ROTs \rightleftharpoons R^+OTs^- \rightleftharpoons R'^+OTs^- \rightleftharpoons R'OTs$$
$$\searrow \quad \swarrow$$
$$\text{Solvolysis products}$$

The observed effect of additions of lithium perchlorate on the rates of solvolysis, racemisation, and rearrangement were attributed to "capture" of the ion-pair, similar to that effected by the azide ion. Thus in the reactions of non-activated secondary systems, in contrast to Winstein's description of S_N1 processes, all events (anion exchange, return, solvolysis) involve contact ion-pairs, which in Winstein's scheme played no part in chemical "capture". It is significant also that the limiting stage is not the formation of these ion-pairs but their further transformation. The reason for these differences is that nucleophilic attack on a secondary ion-pair is more favoured than is its further ionisation and dissociation.

When the various secondary systems for which Winstein's scheme was used are recalled, many questions arise, to which it is difficult to give an unequivocal answer. It must be admitted, for example, that all processes involving solvent-separated ion-pairs formed in the limiting stage should be more rapid than any process described by an ion-pair S_N2 mechanism, otherwise it would be impossible to explain why they did not result from attack on a contact ion-pair. Unfortunately, no comparison was made of the rates of various processes under identical conditions.

It was shown in the same year (1965) that the reaction of 1-methylheptyl bromide with silver nitrate in acetonitrile, with formation of an alkene and an alkyl nitrate, entails inversion of the stereochemical configuration (the optical purity of the alkyl nitrate was 87%)[298]. A similar rule was observed in the reaction of the bromide with silver perchlorate in benzene: formation of the alkyl perchlorate was 80% accompanied by inversion of configuration[299]. The slow stage was considered to be attack by the nucleophile on the complex $RX\ldots Ag^+$, and a quadrupole $[N^-\ldots R^+\ldots X^-\ldots Ag^+]$ was assumed, in the traditions of the English school, to be involved in the reaction. Such a structure had been suggested earlier as a transition state[300]. The reactions of alkyl halides with silver nitrate or silver perchlorate in acetonitrile had the same mechanism (not S_N1Ag^+ [1])[301]. However, it is easily seen that the differences from Sneen's treatment are mainly terminological[302,303].

In view of the possibility that ion-pairs of contact type may take part in nucleophilic substitution Winstein's scheme should be expanded, and should include in modified form the various mechanisms that can in principle operate with variation in the relative rates of the different stages:

$$\begin{array}{ccccccc}
 & S_N^I1 & & S_N^{II}1 & & S_N^{III}1 & \\
 & k_1 & & k_2 & & k_3 & \\
RX & \rightleftharpoons & R^+X^- & \rightleftharpoons & R^+\,\|\,X^- & \rightleftharpoons & R^+ + X^- \\
\text{(I)} & k_{-1} & \text{(II)} & k_{-2} & \text{(III)} & k_{-3} & \text{(IV)} \\
S_N^I2 \downarrow & k_S & S_N^{II}2 \downarrow & k_S^{II} & S_N^{III}2 \downarrow & k_S^{III} & S_N^{IV}2 \downarrow\ k_S^{IV} \\
\text{ROS} & & \text{ROS} & & \text{ROS} & & \text{ROS}
\end{array}$$

Participation of ion-pairs in reactions of secondary systems, including Sneen's ion-pair mechanism ($S_N^{II}2$), follows from the efforts by Shiner et al.[304-310] to determine the mechanism of solvolytic reactions from α- and β-deuterium isotope effects. For example, the α-effect in the reactions of isopropyl *p*-bromobenzenesulphonate[305], 1-methylbut-2-enyl derivatives[306], cyclopentyl *p*-bromobenzenesulphonate[310], etc. is close to unity in aqueous ethanol, but increases to 1.22–1.23 as the ionising power of the solvent increases and its nucleophilicity diminishes (ethanol with a high water content, aqueous trifluoroethanol, carboxylic acids). This was regarded as evidence of a change in mechanism from "purely" S_N2 to S_N^I1 or $S_N^{II}2$, in the limit $S_N^{II}1$; the classification is based on a scheme which differentiates between the mechanisms of the formation of a contact ion-pair in the limiting stage (S_N^I1) and of its conversion into a solvent-separated ion-pair ($S_N^{II}1$). α-Deuterium effects of 1.00–1.05, ~1.15, and 1.22 are regarded as representing S_N^I2, S_N^I1 or $S_N^{II}2$, and $S_N^{II}1$ mechanisms respectively (the last indicates conversion of a contact into a solvent-separated ion-pair). A large isotope effect is associated with formation of a carbonium ion[311]. However, the presence of a certain effect of the azide ion on the rate of reaction of secondary systems would probably indicate $S_N^{II}2$, not an S_N^I1 mechanism.

Nevertheless, it seems to the Reviewer premature to regard the criterion proposed by Shiner and his coworkers as absolutely reliable, and to try to identify reaction mechanisms on the basis of relatively small (1.08–1.22) α-deuterium isotope effects. Other grounds also exist for a cautious attitude to this criterion. Thus the observed isotope effect develops differently at different stages[312], and would depend on the relative rates of conversion of the ion-pair and of the return stage, since

$$\frac{k_2^D}{k_{-1}^D} \Big/ \frac{k_2^H}{k_{-1}^H} \neq 1.$$

Furthermore, this approach does not apply to reactions in which elimination and rearrangement occur as well as substitution[313], and such competing processes usually accompany reactions in secondary systems[314]. Finally, the maximum isotope effect was assigned to an $S_N^{II}1$ reaction on the basis of results[305] that have since proved incorrect[315].

Bordwell et al.[316-319] give arguments supporting the involvement of ion-pairs in S_N2 nucleophilic substitution at a tertiary carbon atom in the allylic systems

$$p\text{-}MeC_6H_4SO_2\diagdown \quad H \qquad \xrightarrow[\text{MeOH or DMF}]{N^-} RN$$
$$\quad\quad C{=}C \qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad$$
$$H\diagup \quad C(Me_2)X$$

in which X = Cl, Br, OSO_2CH_3; N = OCH_3, OH, N_3, SCN, $S:C(NH_2)_2$. With the first order with respect to the nucleophile (which corresponds to an S_N1 mechanism) the dependence of reaction velocity on salt effect, polarity of medium, nature of nucleophile, leaving group, and the β-deuterium effect is different from that found for a system having a primary carbon atom. Introduction of an arenesulphonyl group is assumed to inhibit the dissociation but not the formation of ion-pairs.

Sneen's mechanism has recently been supported[320] by examination of the kinetic chlorine isotope effect $^{35}k/^{37}k$ in the reaction of *p*-methoxybenzyl chloride with sodium azide in 70% aqueous acetone. The isotope effect varied with the nucleophile concentration, which should not occur[320] in S_N1 and S_N2 processes, but is consistent with an ion-pair S_N2 mechanism.

An attempt was made to transfer Sneen's mechanism to reactions of non-activated primary systems [321,322]. It had earlier been suggested, in the reactions of AlkX with silver salts AgY (where Y = NO_3^-, $OSO_2C_6H_4CH_3$, etc.), that an ion pair Y^-R^+ is formed in the slow stage [323,324], and recombines or forms an alkene in the rapid stage. Scott [321] concluded that reactivity and selectivity data for methyl halides with various nucleophiles in water were best explained by the involvement of contact ion-pairs in the slow stage (i.e. that $k_{obs} = K_{eq} k_2$). However, such a hypothesis gives rise to grave objections [325]. Abraham's calculation [326] of the free energy required to form a primary ion-pair in water makes the hypothesis improbable, although ion-pairs may be formed with isopropyl and t-butyl bromides. Furthermore, the α-deuterium isotope effect in primary systems is close to unity [313].

Kohnstam and his coworkers [327,328] disputed the involvement of contact ion-pairs in the S_N2 mechanism and opposed attempts to establish a "unified" mechanism of nucleophilic substitution. In their view the influence of sodium azide on the hydrolysis of s-octyl methanesulphonates could be described, within the framework of the classic mechanisms, as occurring in a boundary region in which reaction took place simultaneously by S_N1 and S_N2 mechanisms§. These workers showed [328] that the hydrolysis of *para*-substituted (methoxylated and phenoxylated) benzyl chlorides and diphenylmethyl chloride takes place by an S_N1 mechanism, and that addition of sodium azide produces only a slight change caused by the salt effect; when the *para*-position is occupied by hydrogen or a nitro-group, however, the mechanism changes to S_N2, and the rate of disappearance of the initial compound is increased considerably by the addition of sodium azide. Table 11 shows the effect of such addition (0.05 M) on the hydrolysis of p-$XC_6H_4CH_2Cl$.

Table 11.

X	MeO	PhO	NO_2	Ph_2CHCl
$\frac{k_{RX}}{k^0_{RX}}$	1.74	20	5430	1.14

The same view arose [329] from a study of the reaction of 1-phenylethyl bromide with potassium and sodium ethoxides in alcohol: the results were described better by competition between $E1$, $E2$, S_N1, and S_N2 mechanisms involving the covalent compound than by Sneen's ion-pair S_N2 mechanism. Analysis of carbon and α-hydrogen isotope effects ($^{12}k/^{14}k$ and k_H/k_D)¶ led to the conclusion [330] that the hydrolysis of benzyl and p-methylbenzyl chlorides in the presence of sodium azide is a classic S_N2 process, while the corresponding reaction of 1-methylheptyl p-bromobenzenesulphonate is described by competition between S_N2 and S_N1 processes with the former predominating.

§ In the cases which they studied, however, the possibility of the formation of a free carbonium ion (by the S_N1 path) is doubtful.

¶ Theory predicts a considerable carbon isotope effect in an S_N2 process, a small effect in an S_N1 process, and the opposite behaviour of the α-hydrogen isotope effect [304].

Thus Sneen's ion-pair S_N2 mechanism has both protagonists and antagonists, and at the present time can be regarded only as debatable [331]. In the Reviewer's opinion recent very significant results have cast doubt on the existence of such a mechanism. Although the chief argument for an ion-pair S_N2 mechanism has been the fractional order with respect to sodium azide, as well as inversion of configuration in the final product, the result may be due to the existence of sodium azide not only as free ions but also as ion-pairs. One author considers [332] that use of concentrations of this salt instead of activities of the azide ion in the kinetic equations is responsible. He showed that such a change will linearise the non-linear relations between k_{obs}/k_{NA} and $[N_3^-]$ in the reaction of 1-methylheptyl methanesulphonate in 25% and 30% aqueous dioxan. However, the slopes of the dependence on $a_{N_3^-}$ of $[RN_3]/[ROH]$ and k_{obs}/k_{NA} differ in both media (addition of sodium azide has a smaller effect on the rate than on the yield—Fig. 4): i.e. there is indeed a difference between the stages determining the rate and the formation of products. However, this difference has been attributed [320] to the occurrence of solvolysis by an intermediate (borderline) mechanism [333]†.

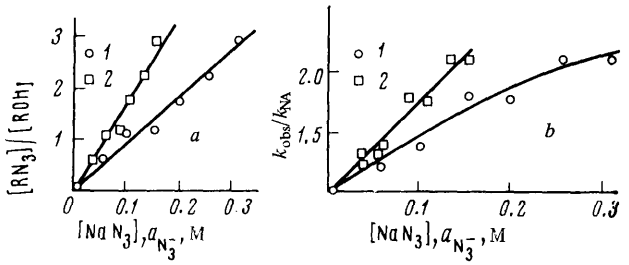


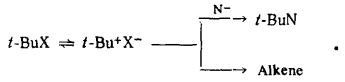
Figure 4. Effect of: 1) concentration of sodium azide; 2) activity of azide ion on reaction of 1-methylheptyl methanesulphonate with sodium azide and water in 30% aqueous dioxan: *a*) ratio of products; *b*) k_{obs}/k_{NA}.

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In the present Review we have discussed the involvement of ion-pairs only in S_N reactions, although it has been noted that in secondary systems they are often accompanied by elimination processes. In tertiary systems elimination may become predominant, so that we have almost ignored such systems. Yet in these cases also there are clear indications that ion-pairs, as well as carbonium ions, may take part in the reaction. Thus Winstein et al. [335] showed that, in the solvolysis of t-C_4H_9X compounds in water, a small quantity of an alkene is formed, which is approximately the same for all X, but in a less strongly dissociating solvent (ethanol) the proportion of elimination is sharply increased, and varies significantly with X in the sequence $S(CH_3)_2 < I < Br < Cl$.

† The nature of this mechanism was at one time widely discussed. Cases are known in which the total effect of competing S_N1 and S_N2 mechanisms is unable to describe behaviour characteristic of the "intermediate" region [334].

The yield of alkene in the solvolysis of t-butylethylmethylsulphonium salts in ethanol and in acetic acid increased on passing from the perchlorate to the bromide [336]. All these results were interpreted in terms of ion-pairs:



Finally, we have only mentioned the participation of ion-pairs in reactions at an sp^2-hybridised carbon atom, although study of the solvolytic reactions of the "vinyl cation" is providing increasing evidence of the involvement of ion-pairs even in these reactions [337].

The theoretical foundations of organic chemistry first formulated by Ingold and his school were based mainly on a study of nucleophilic substitution in aliphatic systems, and were then transferred with additions to other types of substitution. There was a period when it seemed that this field, having become classical, was almost exhausted. This was apparent in a change in the number of publications on the theory of nucleophilic substitution and in the increasing attention paid to other types of reactions, which exhibited interesting and novel features. However, as had already happened repeatedly, new ideas and a new standard of research revealed that established views, in this case concerning S_N2 and S_N1 mechanisms, were inadequate. Whatever the fate of the ion-pair S_N2 mechanism, around which heated arguments are currently raging, it is evident that the whole field of nucleophilic substitution will survive the new stage of development, primarily because of the great attention paid by investigators to the role of various types of ionic intermediates. New ideas have led to a new terminology, and writers on mechanisms of solvolytic reactions prefer to speak of the nucleophilic participation of the solvent in the reaction—which is more or less strongly developed depending on the nature of substrate and solvent, and may be completely absent—not about S_N2 and S_N1 mechanisms [313]. The nucleophilic intervention of the solvent in the solvolysis of several secondary systems has been estimated relative to trifluoroacetic acid, whose intervention was equated to zero [338]. The same approach can in principle be extended to other nucleophilic substitutions. However, the new terminology should not conceal the fundamental problem of elucidating the nature of the species involved in the primary stages.

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