

## REACTION KINETICS AND SOLVATION IN NON-AQUEOUS SOLVENTS

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### INTRODUCTION

Rates of reactions in solution commonly depend not only on the making and breaking of bonds but on the accompanying motions of solvent molecules. The energy required to remove a solvent molecule from a reactive site so that another molecule can approach and react, or to reorganise solvent molecules as the charge distribution changes, is an important contribution to the activation energy in many reactions, especially those involving ions. This had long been suspected by kineticists even at a time when the direct evidence on solvation in solution was restricted to data on such properties of electrolyte solutions as solubilities, ionic mobilities, transport numbers in presence of an 'inert' reference substance, and ionic entropies (1-15, 16-19). Two articles by Bell show how the concept of ionic solvation could be used in kinetics even without the detailed knowledge that has been contributed by isotope-exchange studies and by n.m.r. spectroscopy since the 1950's (4). These new methods gave direct support for the view (proposed as early as 1930, on the basis of an electrostatic model; (20)) that around a metal ion in solution there is a first coordination shell composed of a definite small number of solvent molecules (21).

In the last twenty years n.m.r. methods have yielded much information on the coordination numbers and rates of exchange of these solvating molecules with bulk solvent (21-23). Infra-red and Raman spectroscopy have also begun to contribute to our knowledge of the structure of solvated ions, as many papers at this conference testify; X-ray diffraction and neutron diffraction have also been increasingly applied to solutions (24,25).

Molecular-relaxation measurements by dielectric and ultrasonic methods have been interpreted in terms of the motions of solvent and solute molecules, as have n.m.r. measurements (26,27); many of these experimental and theoretical approaches are exemplified in a recent Faraday Discussion (28). The thermodynamics of solution and solvation, studied in the 1930's (29) was given impetus by the work of H. S. Frank and others on solutions in water, which led to a model of aqueous ionic solutions in which three regions could be distinguished (30,31):

(a) next to the ion, a tightly-held first coordination shell, with a secondary shell more loosely attached; then (b) a relatively disordered region between the solvated ion and (c) the highly-ordered bulk water, which has a three-dimensional structure due to the ability of each water molecule to form four hydrogen bonds to neighbouring water molecules. This model requires modification for solvents which do not have such a three-dimensional structure, but retains its usefulness as a general picture.

Such investigations have confirmed that, as had long been suspected from the study of kinetic solvent effects, the energy associated with solvation is often large, especially for ions; that this solvation energy is a major factor influencing rates of reaction; that it varies considerably from one solvent to another; that interactions of solutes with solvents are often specific, not simply electrostatic; and that aqueous solutions show anomalous behaviour.

Kinetic investigations of non-aqueous systems can thus make use of a good deal of information on the structure and stability of ions and molecules in solution. Rates of reaction depend, however, not only on the properties of the initial reactants, but also on those of the transition state. This cannot be directly studied by spectroscopic methods, and nothing can replace experimental rate determinations if we wish to understand what actually happens in the course of a reaction. The rate law tells us the chemical composition of the transition state; the temperature-dependence and pressure-dependence of the rate constant give values for the changes in enthalpy, entropy and volume when the transition state is formed; variation of substituents and isotopes gives indications of the structure and energetics of the transition state; variation of the solvent throws light on solute-solvent interactions in the transition state, relative to the initial state. (The rate constant is a fairly sensitive indicator of energy differences; a change of 10% in the rate at 25°C corresponds to a change of only 60 calories per mole in the free energy of activation.) From studies of solvent effects, we can expect to learn more about solvation and solvent structure as well as about reaction mechanisms.

In what follows I shall attempt to summarise the position on some reactions that have been studied in a variety of non-aqueous solvents, classified according to charge-type. It will emerge that the solvent may appear in a whole range of roles, from passive spectator to dominant actor. Among the newer developments to be noticed are recent studies in gas-phase equilibria which give rather direct information on solvation; the attention given in recent years to the thermodynamics of transfer of ions and molecules from one solvent to another; the 'dissection' of changes in activation parameters into the separate contributions from initial and transition states; and the spread of new techniques, notable among which are techniques for fast reactions, for high-pressure studies (giving activation volumes), and for kinetic studies by n.m.r., which give information on solvent participation in reactions.

In a lecture on so broad a theme, there can be no attempt at a comprehensive review; the treatment is concerned to draw the outlines of a map rather than to fill in the details. The documentation in this account is correspondingly selective; some of the references are to primary papers and others to reviews, and some refer to the present state of the subject while others refer to its origins and development.

## 2. GAS-PHASE WORK ON SOLVATION

It has been known for many years that enthalpies of hydration of electrolytes in water are very large, being comparable with lattice energies (32). Recent mass-spectrograph work by Kebarle has given values of the enthalpy changes for successive addition of water molecules to simple anions and cations in the gas phase (33). The addition of the first water molecule is the most exothermic; for instance,  $\Delta H^\circ$  for  $K^+ + H_2O$  is  $-16.9 \text{ kcal mol}^{-1}$ , and for  $Cl^- + H_2O$  it is  $-13.1 \text{ kcal mol}^{-1}$ . The values of  $\Delta H^\circ$  decrease as the number of water molecules round the ion increases, and after addition of six water molecules  $\Delta H^\circ$  has a nearly constant value, which is close to the heat of condensation of water ( $-9.7 \text{ kcal mol}^{-1}$ ). This is in agreement with a model of a hydrated ion as having a tightly-held first coordination shell of six solvent molecules, as indicated by n.m.r. spectroscopy, the interaction with bulk solvent being considerably weaker. The results for anions are similar to those for cations, and the enthalpy changes on addition of water molecules are of the same order, though somewhat smaller. With acetonitrile, a typical dipolar aprotic solvent, the results for the first few molecules added are again similar, the value of  $\Delta H^\circ$  for  $K^+ + MeCN$  being  $-24.4 \text{ kcal mol}^{-1}$  and for  $Cl^- + MeCN$  about  $-13.4 \text{ kcal mol}^{-1}$ , but association becomes much less exothermic when the number of acetonitrile molecules reaches 4, presumably because they are more bulky than water molecules. The general result is that the enthalpy required to remove a "solvent" molecule S from an ion cluster in the gas phase is commonly in the region of  $10\text{-}20 \text{ kcal mol}^{-1}$  for a cation  $MS^+$ , and somewhat less for an isoelectronic anion.

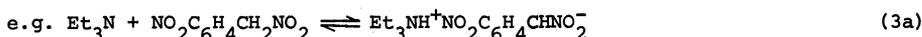
Gas-phase equilibrium constants have been determined in recent years for many proton-transfer reactions, by mass-spectrometry and pulsed ion-cyclotron resonance spectroscopy (34,35). The results give clear evidence that the energetics of reactions in solution are dominated by the effects of solvation. The range of pK's is much larger in the gas phase than in solution, whether in water or in DMSO; evidently pK's in solutions are strongly influenced by solvation differences between ions. There is a fair correlation between pK's in the gas and in DMSO solution, but in water the pK's often show enormous anomalies, attributable to hydrogen-bonding and to the effect of ions on the structure of water (35). For example, in the gas phase aniline is a much stronger base than ammonia, the relative pK changing by about 10 units from that in water and having its sign reversed; and the order of acidity of the monohaloacetic acids in the gas phase is the opposite of the order in water. We can therefore expect that solvation will be important in the kinetics of reactions in polar solvents, and that water will exhibit anomalies.

This brief survey must suffice to suggest the background needed for the interpretation of solvent effects on reaction kinetics. These will be classified according to the charge-type of the reaction. This mode of classification is chosen because, given that ions are more strongly solvated than uncharged molecules, we may expect that the kinetics of reaction will be largely influenced by the change of charge, or of charge distribution, which occurs on forming the transition state and of course is related to the charges on the initial reactants.

## 3. SOLVENT EFFECTS ON REACTIONS OF UNCHARGED MOLECULES PRODUCING IONS

We begin with reactions of uncharged molecules producing ions, since it is for these reactions that the widest range of solvents can be investigated. The most-studied reactions of this charge-type are (a) Menshutkin reactions, such as that of trimethylamine with p-nitrobenzyl chloride (equation 1), (b) solvolysis of alkyl halides such as that of t-butyl chloride (equation 2) and (c) some proton transfers from carbon acids (equation 3).





### Menschutkin Reactions

A wide range of solvents, from hydrocarbons to alcohols, has been investigated for the reaction of trimethylamine with p-nitrobenzyl chloride (36). The rate constant at 25°C varies over about four powers of ten, increasing with the 'polarity' (to use the common but imprecise term) of the solvent (Table 1). On the simplest view, the transition state (part-way to the products) may here be regarded as a dipole in which some fraction of an electronic charge has been transferred:  $\text{R}_3\text{N}^{\delta+}\text{R}'\cdot\text{X}^{\delta-}$ . Solvent molecules, being polar or at least polarisable, will tend to become orientated in the field set up by the dipolar transition-state. The work done can in principle be calculated by electrostatic theory in terms of the dipole moments and distances involved, and according to transition-state theory may be expressed as a contribution to the standard free energy of activation ( $\Delta G^\ddagger$ ), which is linearly related to the logarithm of the rate constant  $k$  (eq. 4):

$$\Delta G^\ddagger/RT = \ln(kT/h) - \ln k \quad (4)$$

so that the ratio of the rate constant in a particular solvent ( $k$ ) to that in a reference solvent ( $k_0$ ) is related to the difference of the corresponding free energies of activation ( $\delta\Delta G^\ddagger$ ) by equation 4a:

$$\delta\Delta G^\ddagger/RT = -\ln(k/k_0) \quad (4a)$$

TABLE 1. Kinetic solvent effects at 25°C on (a) the Menschutkin reaction between trimethylamine and p-nitrobenzyl chloride (b) the solvolysis of t-butyl chloride.

	$\epsilon$	Menschutkin reaction (1a)			Solvolysis of t-BuCl			$\Delta G_{\text{tr}}^{\text{O}}(\text{Et}_4\text{N}^+\text{Cl}^-)$
		$5 + \log_{10} k / \text{M}^{-1}\text{s}^{-1}$	$\delta\Delta G_{\text{tr}}^\ddagger$	$\Delta G_{\text{tr}}^{\text{X}}$	$16 + \log_{10} k / \text{s}^{-1}$	$\delta\Delta G_{\text{tr}}^\ddagger$	$\Delta G_{\text{tr}}^{\text{X}}$	
Water	78.4	-	-	-	14.46	-6.22	-1.65	-1.8
Methanol	32.6	3.26	0	0	9.90	0	0	0
Acetonitrile	36.0	4.41	-1.42	-1.61	7.27	+3.59	+3.20	+5.1
Benzene	2.3	2.18	+1.93	+0.98	3.84	+8.27	+7.21	+13.3
Hexane	1.9	0.94	+3.85	+5.02	-	-	-	+21.3
Pentane	1.8	-	-	-	0.0	+13.5	+12.5	-

$k$  = rate constant at 25°C.

$\epsilon$  = relative permittivity (dielectric constant) of solvent.

$\delta\Delta G_{\text{tr}}^\ddagger$  = free energy of activation in given solvent relative to that in methanol ( $\text{kcal mol}^{-1}$ ).

$\Delta G_{\text{tr}}^{\text{X}}$  = standard free energy of transfer of transition state from methanol to given solvent ( $\text{kcal mol}^{-1}$ ; calc. by eq. 6).

$\Delta G_{\text{tr}}^{\text{O}}(\text{Et}_4\text{N}^+\text{Cl}^-)$  = standard free energy of transfer of the ion-pair  $\text{Et}_4\text{N}^+\text{Cl}^-$  from methanol to given solvent ( $\text{kcal mol}^{-1}$ ).

Data from M. H. Abraham (36), Tables 31 and 37; *J. Chem. Soc., B*, 299 (1971); *J. Chem. Soc., Perkin II*, 1343 (1972).

This electrostatic calculation requires a model; the problem was solved by Kirkwood for the case of a point dipole in a spherical cavity (37). The result (simplified by omission of the smaller terms involving the dipole moments of the reactants) is equation 5, which expresses the rate constant  $k$  in a given solvent in terms of the relative permittivity (dielectric constant) of the solvent  $\epsilon$ , relative to the value  $k_0$  which it would have in a hypothetical medium of  $\epsilon=1$  in which the non-electrostatic forces are the same for the activated complex as for the reactants.

$$\ln(k/k_0) = -(kT)^{-1}(\mu_x^2/r^3)[(\epsilon-1)/(2\epsilon+1)] \quad (5)$$

This equation predicts a linear relation between  $\log k$  and the function  $(\epsilon-1)/(2\epsilon+1)$  (which for  $\epsilon > 7$  varies nearly linearly with  $1/\epsilon$ ), the slope depending on the dipole moment  $\mu_x$  of the transition state. Before testing this relation, the limitations of the approach should be noted. The dielectric constant is being used as a measure of solvent 'polarity', or better 'orientability'. This implies that only electrostatic interactions are being considered and all specific interactions such as hydrogen bonds are omitted. Further, the transition state is considered simply as a single dipole of negligible size compared to its cavity, regardless of the actual size, charge distribution, and polarisability. The appropriate value of  $\epsilon$  is assumed to be that determined under ordinary conditions at a field strength much less than that in the neighbourhood of an ion; effects of the local dipoles and quadrupoles are ignored. Equation 5 can thus only be an approximation. To refine the electrostatic account, however, would be a matter of great complexity.

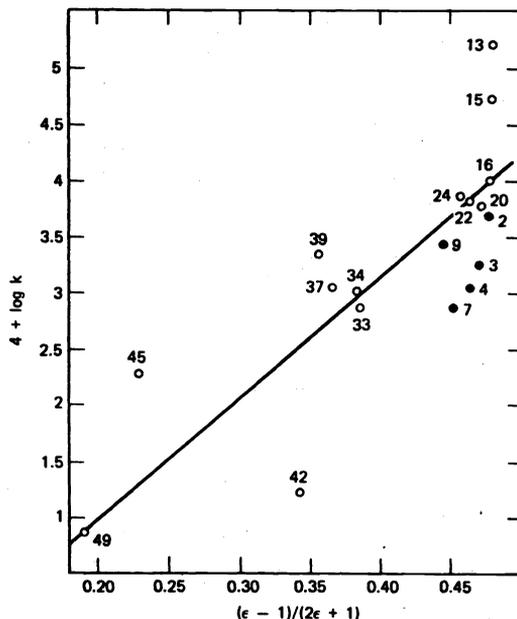


Fig. 1. Plot of  $\log k$  for the Menshutkin reaction of trimethylamine with *p*-nitrobenzyl chloride against the Kirkwood function  $(\epsilon-1)/(2\epsilon+1)$  at 25°C. Solvents: o, aprotic; •, hydroxylic. (From M. H. Abraham, (36), by permission of John Wiley and Sons, Inc.)

The plot of  $\log k$  against  $(\epsilon-1)/(2\epsilon+1)$  for the reaction of trimethylamine with *p*-nitrobenzyl chloride (eq. 1a) is shown in Fig. 1. The straight line is drawn through the points for some aliphatic solvents of low polarity (hexane, 49; ethyl benzoate, 34; acetone, 22); its slope corresponds (assuming a reasonable value for  $r$ ) to a dipole moment of about 8 Debye, which would imply a charge transfer of about 0.5 of the electronic charge. Hydroxylic solvents (2,3,4,7,9) give fairly high rate constants but their points lie below this line. Dipolar aprotic solvents such as acetonitrile (15) and nitromethane (13) give higher rate constants, although their dielectric constants are no higher; their points lie above the line. Benzene (45), with low dielectric constant but relatively high polarisability, gives a point above the line; diethyl ether (42), whose oxygen lone pair may give rise to specific interactions, gives a point well below.

We can already see the main lines of a classification of solvents. The electrostatic model is in general accord with the trend of the results from many solvents, and the slope of the line in Fig. 1 is reasonable in terms of a partial separation of charge in the transition state. Among polar solvents, hydroxylic liquids differ from aprotic solvents of similar dielectric constant. Among low-polarity solvents, aromatics may differ from aliphatics. These trends are compatible with the view that the role of the solvent is to stabilise the polar transition state.

A similar solvent classification emerges if we consider the thermodynamics of ion-pair formation in various solvents. The degree to which an ion-pair is stabilised in a given solvent, relative to a standard solvent (usually methanol), may be expressed in terms of the standard free energy of transfer,  $\Delta G_{tr}^{\circ}$ , a quantity which may be determined from experimental values

of solubilities and association constants. Values of the standard free energy of transfer of the ion-pair  $\text{Et}_4\text{N}^+\text{Cl}^-$  from methanol to various representative solvents are shown in Table 2. The stability is greatest ( $\Delta G_{\text{tr}}^{\circ}$  smallest) in hydroxylic solvents, which can solvate by hydrogen-bonding; less in dipolar aprotic solvents, which interact mainly by ion-dipole forces; less again in solvents of lower polarity, and least in non-polar aliphatic solvents.

TABLE 2. Stabilisation of the ion-pair  $\text{Et}_4\text{N}^+\text{Cl}^-$  in various solvents, at 25°C.

Solvent Type	Interactions	Solvent	$\epsilon$	$\mu$	$\alpha$	$\Delta G_{\text{tr}}^{\circ}$ ( $\text{Et}_4\text{N}^+\text{Cl}^-$ )
Hydroxylic	Hydrogen-bonding $\epsilon$ large, $\alpha$ small	Water	78.4	1.85	1.48	-1.8
		Methanol	32.6	1.68	3.24	0
		Ethanol	24.3	1.70		1.6
Dipolar aprotic	Ion-dipole $\epsilon$ and $\mu$ large	DMF	36.7	3.8	7.91	4.6
		Acetonitrile	36.0	4.1	4.45	5.1
Aromatic, low-polar	Polarisable; $\alpha$ large $\epsilon$ and $\mu$ small	Chlorobenzene	5.6	1.6	12.4	11.5
		Benzene	2.3	0	10.4	13.3
Aliphatic, low-polar	Short-range forces $\epsilon$ and $\mu$ small	$\text{CCl}_4$	2.2	0	10.5	18.5
		Hexane	1.9	0	11.4	21.3

$\Delta G_{\text{tr}}^{\circ}$  ( $\text{Et}_4\text{N}^+\text{Cl}^-$ ) = standard free energy of transfer of the ion-pair  $\text{Et}_4\text{N}^+\text{Cl}^-$  from methanol to a given solvent at 25°C (kcal mol<sup>-1</sup>).

Data from (36).

$\epsilon$  = relative permittivity (dielectric constant) at 25°C

$\mu$  = dipole moment (Debye).

$\alpha$  = molecular polarisability (10<sup>-24</sup>cm<sup>3</sup> mol<sup>-1</sup>) =  $[(\bar{n}^2-1)/(\bar{n}^2+2)](M/d)(3/4\pi N)$   
( $\bar{n}$  for sodium D-line).

**Solvent effects on initial and transition states.** Are these different rates in different solvents due to differing solvation of the reactants, or of the transition state, or of both? The enthalpy difference between solutions of a stable reactant A in two different solvents can be determined as the difference between its heats of solution in the two solvents; this is its enthalpy of transfer,  $\Delta H_{\text{tr}}^{\text{A}}$ . Similarly its free energy of transfer  $\Delta G_{\text{tr}}^{\text{A}}$  can be determined, by measurements of the solubility, or (for neutral species) the vapour pressure over the solutions, or (for electrolytes) the e.m.f. of appropriate cells. The corresponding quantities for the transition state,  $\Delta H_{\text{tr}}^{\ddagger}$  and  $\Delta G_{\text{tr}}^{\ddagger}$ , cannot be directly determined, but inspection of Fig. 2 shows that they can be determined from those for the initial state (i.e. the reactants A + B), together with the change of the enthalpy or free energy of activation from one solvent to the other ( $\delta\Delta H_{\text{tr}}^{\ddagger}$ ,  $\delta\Delta G_{\text{tr}}^{\ddagger}$ ):

$$\Delta H_{\text{tr}}^{\text{X}} = \delta\Delta H_{\text{tr}}^{\ddagger} + (\Delta H_{\text{tr}}^{\text{A}} + \Delta H_{\text{tr}}^{\text{B}})$$

$$\Delta G_{\text{tr}}^{\text{X}} = \delta\Delta G_{\text{tr}}^{\ddagger} + (\Delta G_{\text{tr}}^{\text{A}} + \Delta G_{\text{tr}}^{\text{B}}) \quad (6)$$

It is thus possible to achieve a 'dissection' of solvent effects on rates and activation parameters into contributions from solvent effects on the initial state and the transition state (38). These contributions are often very different.

The Menshutkin reaction that has been most thoroughly investigated in this way is that between trimethylamine and p-nitrobenzyl chloride (cf. Fig. 1). It turns out that the higher rates observed in the more polar solvents are due mainly to greater stabilisation of the transition state, rather than destabilisation of the reactants. For the transition state, the free energy of transfer  $\Delta G_{\text{tr}}^{\ddagger}$  (relative to methanol) varies from +5.0 kcal mol<sup>-1</sup> for the non-polar hexane to -2.2 kcal mol<sup>-1</sup> for nitromethane, while for the initial state the values lie mostly between +1 and -1 kcal mol<sup>-1</sup>. The solvent classification is confirmed. Some representative values are given in Table 1. The free-energy differences in hexane and in methanol are illustrated in Fig. 2.

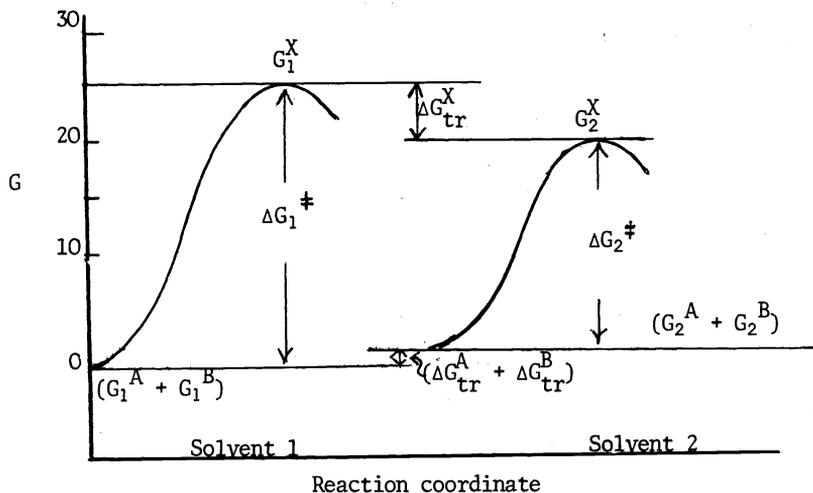
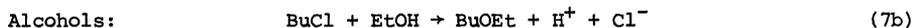


Fig. 2. Free-energy curves for reaction of trimethylamine with p-nitrobenzyl chloride in two solvents: 1 = hexane, 2 = methanol. Vertical distances to scale (zero arbitrary); otherwise schematic.

Some light may be thrown on the nature of the transition state for the reaction by comparing its behaviour towards solvents with that of an ion-pair such as  $\text{Et}_4\text{N}^+\text{Cl}^-$ . From the representative values of  $\Delta G_{\text{tr}}^{\circ}$  for this ion-pair given in Table 1, it is seen that the changes are much larger than those of  $\Delta G_{\text{tr}}^{\ddagger}$  for the transition state, and that for hydroxylic solvents the direction is different. The values for the transition state show indeed a better correlation with those for the reactant p-nitrobenzyl chloride. This comparison supports the view suggested by the apparent dipole moment: the transition state is intermediate between the reactants and the product ion-pair in its behaviour towards solvents; it may be regarded as a polarised and highly polarisable molecule. This is true also of the transition-states of other Menshutkin reactions (ref. 36, pp. 36-43) (Note a).

#### Solvolysis: the reactions of alkyl halides

Here the solvent is a reagent as well as a solvating agent; different solvents give different products, with t-butyl chloride for example:



The transition state for each of these reactions must involve a partial separation of charge ( $\text{Bu}^{\delta+}\text{Cl}^{\delta-}$ ), and we may reasonably expect an electrostatic model to have some success. In solvolysis, however, the solvent has an additional role; as a nucleophile, it attacks the alkyl group, besides acting (as in the Menshutkin reaction) as an electrophile in solvating the incipient chloride ion, and as an ionising medium in promoting further separation of charge. The effects of solvent nucleophilicity can in principle be distinguished (for instance) by comparison with a solvolysis where it is not involved, i.e. where the limiting  $\text{S}_{\text{N}}1$  mechanism holds. These effects have been shown to be significant in the solvolysis of many secondary substrates; scales of nucleophilic reactivity for solvents have been developed (39).

Note a. More limited data are available on a few other Menshutkin reactions (ref. 36, pp. 40 et seq.), for instance that of trimethylamine with methyl iodide, in which the solvent effects on the reactants appear to be more important than in the reaction of trimethylamine with p-nitrobenzyl chloride. The difference may be related to different effects of solvents on more and less polarisable molecules (ibid. p. 33).

The solvolysis of *t*-butyl chloride may be taken as an approximation to the limiting  $S_N1$  case. The solvent classification summarised in Table 2 is confirmed, though there are some interesting differences from Menschutkin reactions (36). The range of rates from pentane to methanol is 14 powers of ten, much greater than for Menschutkin reactions (Table 1). The plot of  $\log k$  against the Kirkwood function  $(\epsilon-1)/(2\epsilon+1)$ , shown in Fig. 3, is scattered, like the one for the Menschutkin reaction shown in Fig. 1, but the general trend gives a much higher slope, corresponding to a larger value of  $\mu_X$  (eqn.5); this indicates a markedly higher degree of charge separation in the transition state. Dissection shows that the solvent effect is again predominantly on the stability of the transition state, as represented by  $\Delta G_{tr}^\ddagger$ ; but this quantity is now almost linearly related to the free energy of transfer of the ion-pair  $Et_4N^+Cl^-$ , confirming that the transition state more nearly resembles the ion-pair product (Table 1). Water shows a special effect; the rate of solvolysis is  $10^4$  times higher than in methanol, and much larger than the ion-pair model would predict (Table 1). This, exceptionally, is due mainly to a large destabilisation of butyl chloride in water compared with methanol ( $\Delta G_{tr}^\circ = +4.57 \text{ kcal mol}^{-1}$ ); this destabilisation is attributable to the effect of *t*-butyl chloride on the structure of water (40).

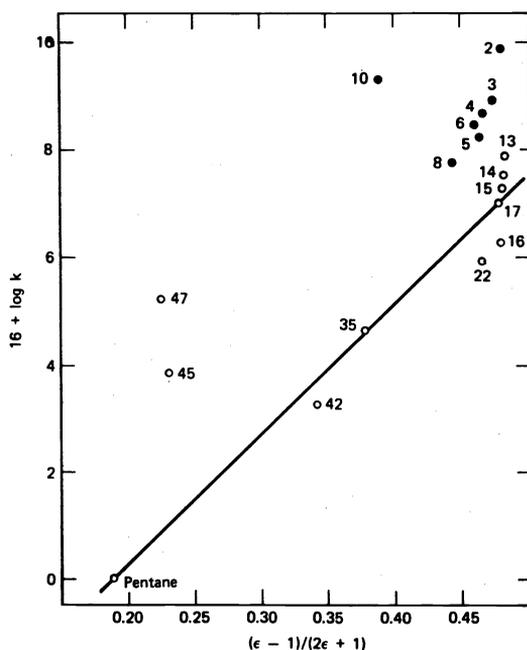


Fig. 3. Plot of  $\log k$  for the solvolysis of *t*-butyl chloride against the Kirkwood function  $(\epsilon-1)/(2\epsilon+1)$  at 25°C. Solvents: o, aprotic; •, hydroxylic.

(From M. H. Abraham, (36) by permission of John Wiley and Sons, Inc.)

For the alkyl halides as a class, there is a whole spectrum of transition-state structures, between the extremes of the  $S_N1$  mechanism where the solvent is simply a solvating medium and the  $S_N2$  mechanism where it is a reagent. There is a fine balance between the various factors at work - solvation, charge distribution, bond energies, and non-bonded interactions - on which the reader is referred to reviews concerned with mechanisms (41).

#### Proton-transfers between neutral molecules

Rates of proton transfer between neutral molecules producing charged species have of course been very extensively studied, but not often in a wide range of solvents (42). Reactions of oxygen acids, such as those of substituted phenols with amine bases, are often diffusion-controlled, with only minor effects due to solvation (43-46); an exception is bromophenol blue, whose reaction with pyridine in aprotic solvents behaves somewhat like the Menschutkin reaction considered above (47). Among reactions of carbon acids, that of 4-nitrophenylnitromethane with the strong base tetramethylguanidine (similar to eqn. 3a) has been studied in polar and non-polar aprotic solvents; the plot of  $\log k$  against  $(\epsilon-1)/(2\epsilon+1)$  is again reminiscent of the Menschutkin reaction (48).

#### 4. REACTIONS OF OPPOSITELY-CHARGED IONS TO FORM UNCHARGED SPECIES

The reverse of an ion-forming reaction is a reaction between oppositely-charged ions. The simplest reaction is the formation of an ion-pair. Ion-pairing between large ions in aprotic solvents, as exemplified by tetrabutylammonium and picrate ions in diphenyl ether, is

diffusion-controlled (49); solvation changes do not appear to be involved. Ion-pairing between small ions in water, by contrast, is a classic case where the rate is controlled by the dissociation of coordinated solvent molecules from anion and cation. In aqueous solutions of the sulphates of divalent metals, the rate is characteristic of the rate of dissociation of water from the cations (50). In the case of aqueous scandium sulphate solutions, it has been possible to determine by ultrasonic-relaxation methods the rates of all three processes affecting the overall rate, namely encounter, loss of water from anion, and loss of water from cation (51); the rate constants are respectively  $2 \times 10^{11} \text{ M}^{-1}\text{s}^{-1}$ ,  $1.4 \times 10^7 \text{ s}^{-1}$ , and  $1 \times 10^6 \text{ s}^{-1}$ . This is the limiting case of kinetic control by change of solvation (cf. section 6 below).

Reactions of carbonium ions with nucleophiles such as  $\text{F}^-$  or  $\text{N}_3^-$  have been extensively studied in hydroxylic and dipolar-aprotic solvents by Ritchie (52-54). The relative reactivities of the cations towards a given anion are strikingly independent of solvent, suggesting that the solvation of the cationic moiety is little changed on formation of the transition state. By contrast the relative reactivities of the anions in various solvents (water, methanol, DMSO) show variations of several powers of ten, corresponding to about half the free energy of transfer; this suggests that in the transition state desolvation of the anionic moiety is considerable. The effects of anion solvation are often large and are considered further below (section 5).

Proton-transfer reactions of this charge-type are those where the ions formed on dissociation of an uncharged acid recombine:  $\text{H}^+ + \text{A}^- \rightarrow \text{HA}$ . These have been extensively studied (42,53-58). For simple oxygen acids in water, the recombination rate approximates to the diffusion-controlled limit of ca  $10^{10} \text{ M}^{-1}\text{s}^{-1}$ ; the reactions are down-hill, there appears to be no activation barrier, and the role of the solvent is at most to provide a hydrogen-bridged path for the proton-transfer. The participation of water and other hydrogen-bonding solvents in proton-transfer reactions has been thoroughly studied by Grunwald and is considered below (59) (Section 6). Such participation is not essential, however; reactions of substituted phenols with nitrogen bases in chlorobenzene are also diffusion-controlled, although the solvent cannot take part in hydrogen bonding (43-46). For reactions of carbon acids, where hydrogen-bonding is much less important, the rate is usually much smaller than the diffusion-controlled limit, and much smaller in hydroxylic solvents than in dipolar aprotic solvents such as DMSO, probably because of the lower stability of anions in these latter solvents (53,57).

## 5. REACTIONS OF UNCHARGED MOLECULES WITH ANIONS

So far we have considered reactions involving simultaneously a cation and an anion, and have not enquired whether there is any difference between cations and anions in their behaviour towards solvents. The interactions of cations and anions separately are important, however, in the reactions considered in the two following sections.

### Reactions of Uncharged Molecules with Anions

Bimolecular reactions between anions and uncharged molecules, of the general type represented by equation 8, have been much studied (60-63).



For purposes of example, we consider  $\text{S}_{\text{N}}2$  substitution at a saturated carbon atom, such as the Finkelstein reaction:



Such reactions, in strong contrast with the ion-forming reactions considered above, are much slower in water than in dipolar aprotic solvents, often by a factor as large as  $10^6$ . The reason (to anticipate) is that in water, where anions are solvated by hydrogen-bonding ( $\text{A}^-\cdot\text{HOH}$ ), small anions are stabilised much more than large ones, because the hydrogen bond is stronger; whereas in dipolar aprotic solvents, where solvation is by non-specific ion-dipolar and dispersion forces, there is less difference between the stabilities of small and large anions. The result is that in water, relative to dipolar aprotic solvents, small anions are stabilised much more than the large transition-state anions, so the free energy of reaction is greater in water (see Fig. 4) and the reaction is therefore slower.

This situation is illustrated by the data in Table 3. The rate constant in the dipolar-aprotic solvents is  $10^4$  to  $10^6$  times larger than in water or methanol. The ratio of the rate constant for reaction between  $\text{Cl}^-$  and  $\text{CH}_3\text{I}$  in a given solvent ( $k$ ) to that in the standard solvent methanol ( $k_0$ ) is to be compared with the standard free energies of transfer from methanol to the given solvent of  $\text{Cl}^-$  and  $\text{CH}_3\text{I}$ , and hence (by use of equation 6) with that of the transition state. In accordance with equation 4a, we compare values of  $\log_{10} (k/k_0)$  with those of  $\Delta G_{\text{tr}}^\circ/2.3 \text{ RT}$  for the various species. It is evident that the large differences in  $k/k_0$  are to be attributed mostly to the differences in the free energy of transfer of  $\text{Cl}^-$ ;

the faster reactions in dipolar-aprotic solvents are due mostly to destabilisation of the chloride ion in these solvents, with only small contributions from a decrease in the free energy of the transition state. These relations are shown diagrammatically in Fig. 4.

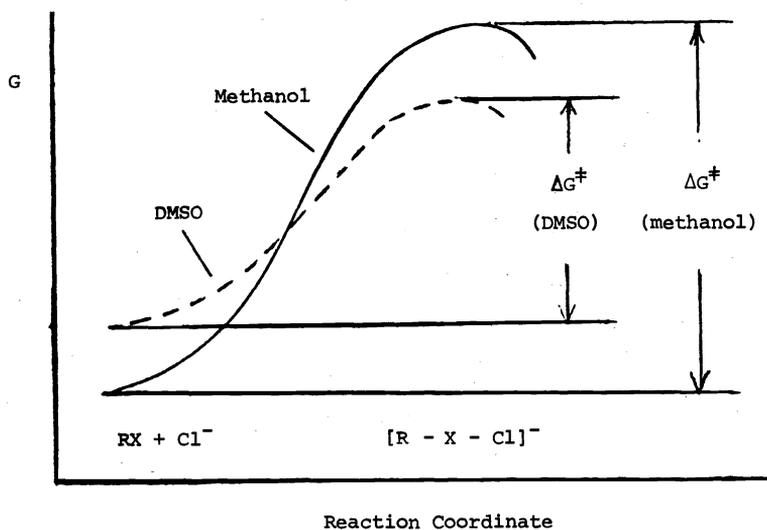


Fig. 4. Effect of change of solvent on free-energy changes for  $\text{Cl}^- + \text{RX} \rightarrow \text{ClR} + \text{X}^-$  (schematic).

TABLE 3. Rate constant ( $k$ ) for reaction  $\text{CH}_3\text{I} + \text{Cl}^- \rightarrow \text{CH}_3\text{Cl} + \text{I}^-$  in various solvents, compared with standard free energy of transfer ( $\Delta G_{\text{tr}}^\circ$ )

Solvent Type	Solvent	$\log (k/k_0)$	$-\Delta G_{\text{tr}}^\circ / 2.3RT$		
			$\text{Cl}^-$	$\text{CH}_3\text{I}$	T.S.
Hydroxylic	Water	0.05	-2.5	1.4	-1.1
	Methanol	0.0	0.0	0.0	0.0
Dipolar-aprotic	DMF	5.9	6.5	-0.5	0.1
	Acetonitrile	4.6	6.3	-0.4	1.3
	Nitromethane	4.2	4.9	-0.2	0.5

Reference solvent: methanol

Temperature: 25°C

T.S. = transition state  $[\text{Cl} \cdots \text{CH}_3 \cdots \text{I}]^-$

$$\log (k/k_0) = -\delta \Delta G^\ddagger / 2.3RT$$

Data from ref. 60, Table VIII. In deriving values of  $\Delta G_{\text{tr}}^\circ$  for individual ions such as  $\text{Cl}^-$ , the convention used is that the values for  $\text{BPh}_4^-$  and  $\text{AsPh}_4^-$  are equal.

This difference between the initial-state anion  $\text{Cl}^-$  and the transition-state anion  $(\text{Cl} - \text{CH}_3 - \text{I})^-$  may be attributed to weaker solvation of the latter in water due to its greater size, polarisability, and charge dispersion. The data in Table 4 show the effects of these factors (which of course are to some extent correlated) on the behaviour of simple anions.

These effects may be interpreted mainly in terms of the hydrogen-bonding properties of the anions and of the solvent molecules. In water, or methanol, anions are solvated by hydrogen bonding ( $\text{H}-\text{O}-\text{H}^{\delta+} \cdots \text{A}^-$ ). Anions with the charge localised on a small atom such as  $\text{Cl}^-$  will be stronger hydrogen-bond acceptors than those where the charge density is less, as on larger atoms ( $\text{I}^-$ ), or where the charge is dispersed ( $\text{ClO}_4^-$ ,  $\text{I}_3^-$ ).

TABLE 4. Stabilisation of ions by solvents, reactive to water.

Ion	Quantity	Hydroxylic		Dipolar-aprotic			
		Water	MeOH	DMSO	DMF	MeCN	PC
<b>(i) Anions</b>							
Cl <sup>-</sup>	$\Delta G_{tr}^{\circ}$	0	3.0	9.2	11.0	(12.0)	9.0
Br <sup>-</sup>		0	2.7	6.1	7.2	7.6	7.1
I <sup>-</sup>		0	1.6	2.2	4.5	4.5	4.2
ClO <sub>4</sub> <sup>-</sup>		0	1.4	-0.3	0.1	-	-
I <sub>3</sub> <sup>-</sup>		0	-3.0	-7.9	(-4.2)	-3.6	-
<b>(ii) Cations</b>							
Li <sup>+</sup>	$\Delta G_{tr}^{\circ}$	0	0.9	-3.5	-2.3	-	5.7
Na <sup>+</sup>		0	2.0	-3.3	-2.5	3.3	3.6
K <sup>+</sup>		0	2.4	-2.9	-2.3	1.9	1.4
Rb <sup>+</sup>		0	2.4	-2.6	-2.4	1.6	-0.7
Cs <sup>+</sup>		0	2.3	-3.0	-2.2	-	-2.9
NET <sub>4</sub> <sup>+</sup>		0	0.2	-3.0	-2.0	-2.1	-
<b>(iii) Anions</b>							
Cl <sup>-</sup>	$\Delta G_{tr}^{\circ}$	0	3.0	9.2	11.0	(12.0)	9.0
	$\Delta H_{tr}^{\circ}$	0	2.0	4.5	5.1	-	6.7
	-298 $\Delta S_{tr}^{\circ}$	0	1.0	4.7	5.9	-	2.3
Br <sup>-</sup>	$\Delta G_{tr}^{\circ}$	0	2.7	6.1	7.2	7.6	7.1
	$\Delta H_{tr}^{\circ}$	0	1.1	0.8	0.8	2.0	4.2
	-298 $\Delta S_{tr}^{\circ}$	0	1.6	5.3	6.4	5.6	2.9
ClO <sub>4</sub> <sup>-</sup>	$\Delta G_{tr}^{\circ}$	0	1.4	-0.3	0.1	-	-
	$\Delta H_{tr}^{\circ}$	0	-0.6	-4.6	-5.4	-	-
	-298 $\Delta S_{tr}^{\circ}$	0	2.0	4.3	5.5	-	-
<b>(iv) Cations</b>							
Na <sup>+</sup>	$\Delta G_{tr}^{\circ}$	0	2.0	-3.3	-2.5	3.3	3.6
	$\Delta H_{tr}^{\circ}$	0	-4.9	-6.6	-7.9	-3.1	-1.6
	-298 $\Delta S_{tr}^{\circ}$	0	6.9	3.3	5.4	6.4	5.2
Cs <sup>+</sup>	$\Delta G_{tr}^{\circ}$	0	2.3	-3.0	-2.2	-	-2.9
	$\Delta H_{tr}^{\circ}$	0	-3.3	-7.7	-8.8	-	-6.2
	-298 $\Delta S_{tr}^{\circ}$	0	5.1	4.7	6.6	-	3.3
NET <sub>4</sub> <sup>+</sup>	$\Delta G_{tr}^{\circ}$	0	0.2	-3.0	-2.0	-2.1	-
	$\Delta H_{tr}^{\circ}$	0	2.2	1.0	-0.2	-0.3	-
	-298 $\Delta S_{tr}^{\circ}$	0	-2.0	-4.0	-1.8	-1.8	-

$\Delta G_{tr}^{\circ}$  = standard free energy of transfer from water to a given solvent at 25°C in kcal mol<sup>-1</sup>. A positive value implies that stability is higher in water. Data from Table 6 of ref. 62, or in a few cases (shown by brackets) from Table V of ref. 60. The assumption is made that  $\Delta G_{tr}^{\circ}$  is the same for BPh<sub>4</sub><sup>-</sup> and AsPh<sub>4</sub><sup>-</sup>. DMSO = dimethyl sulphoxide, DMF = dimethylformamide, PC = propylene carbonate.

Besides these solute-solvent interactions, however, one must consider the solvent-solvent interactions. The molecules of hydroxylic solvents can act both as donors and as acceptors of hydrogen bonds, and so can form chains or rings, so the solvent has some degree of structure. Water, uniquely, can form a continuous three-dimensional structure, because each  $\text{H}_2\text{O}$  molecule can act as donor in two hydrogen bonds and acceptor in two more. The arrangement of solvent molecules around an ion is very different, however, from the arrangement in the pure solvent; in water especially, the ion with its six oriented water molecules cannot fit into the three-dimensional ice-like structure of the bulk water. There must be a region of relatively disordered solvent between the solvated ion and the bulk water (Fig. 5).

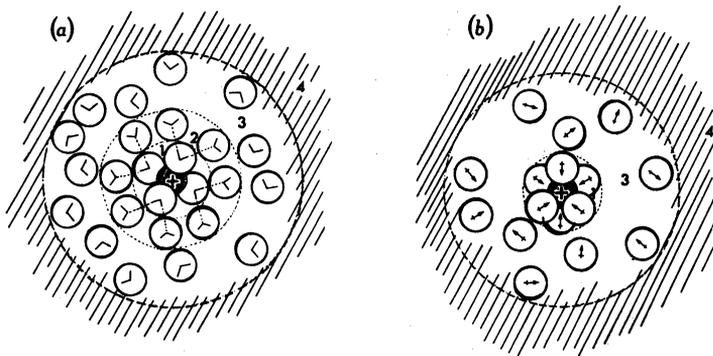


Fig. 5. Schematic diagram to indicate the molecular environment in the solvation of a particular cation (a) in water and (b) in an aprotic solvent. (reproduced from ref. 62 by permission).

The introduction of an ion into water has therefore two effects: it promotes order insofar as water molecules become oriented around the ion, but disorder insofar as the structure of the bulk water is partly destroyed (31). For this reason the entropy loss on dissolving an ion in water is less than would result from the formation of an oriented solvation shell alone (30). The same is true of the dipolar-protic solvents, but to a much smaller degree; there is less order in these solvents to begin with and therefore much less gain of entropy when ions are dissolved in them (see Note a). This incidentally gives us the reason why many salts dissolve more readily in water than in dipolar-protic solvents, even though the heat of solution is less favourable in water; it is that the entropy change is much more favourable in water, because the structure-breaking effect of the ions is greater because there is initially more order than in other solvents.

Referring now to Table 4, we can understand, firstly, why chloride ion, for example, is much less stabilised in DMSO or acetonitrile than in water, or even in methanol ( $\Delta G_{\text{tr}}^{\circ}$  positive); the free energy decrease on dissolution of  $\text{Cl}^-$  is greatest in the solvent whose structural order is greatest (water). Secondly, in the series of halide ions we can see the effect of increasing size and decreasing charge density; the advantage of the dipolar aprotic solvents is progressively reduced as the size increases and the interaction of the ion with hydrogen-bonded solvents decreases. The advantage is further reduced when the charge is dispersed (in the  $\text{ClO}_4^-$  ion) and when the ion is more polarisable ( $\text{I}_3^-$ ). This general picture must be expected to apply also to an anionic transition state. This will necessarily be larger and more polarisable than the reactant anion, and so may be expected to have a smaller value of  $\Delta G_{\text{tr}}^{\circ}$ . The energetics are therefore as shown in Fig. 4; thus  $\Delta G^{\ddagger}$  for reaction will be smaller in dipolar aprotic solvents, and the acceleration in these solvents, as compared with water, can be understood (see Note b).

**Note a.** For entropies and enthalpies of solution in water and other solvents, see Tables 2 and 4 of ref. 62. The independent evidence on solvent structure in DMSO and acetonitrile, for instance, has been reviewed by Coetzee (64). It appears that because of the strong dipolar forces DMSO may contain two-dimensional sheets while acetonitrile contains dimers or chains of solvent molecules.

**Note b.** It will be noted that we have assumed the behaviour of the transition state to be like that of stable species. More direct evidence on free energies of transfer of transition states, analogous to that available for Menshutkin reactions (section 3), is much to be desired.

This acceleration is sometimes attributed to 'poor solvation' of the reactant anion in the dipolar aprotic solvents, but this is not a fully satisfactory explanation. The rate constant of the reaction is controlled by the difference of free energy between two anions, the reactant and the transition state, not by the free energy of solvation of either anion alone. This difference is smaller in dipolar aprotic solvents, apparently because the non-specific ion-solvent interactions involved are less sensitive to the size and polarisability of the anion than is the hydrogen-bonding interaction which is responsible for solvation in water and other hydroxylic solvents. It is the specific hydrogen-bonding of anion to water which leads to a specific retardation of the reaction in water. As regards solvation, the gas-phase results mentioned above show that anions are solvated by dipolar-protic solvents and that the enthalpy of solvation is comparable with that in water. The relatively high stability of small anions in water (Table 4) is not apparently due to a stronger anion-solvent bond (the enthalpy of solution is indeed more favourable in dipolar aprotic solvents), but to a much more favourable entropy contribution (Table 4, Section iii), which may be attributed to partial disruption of the structure of the bulk water, as discussed above. This entropy contribution, incidentally, is relatively independent of anion size (see the table); the higher relative stability of smaller anions in water is an enthalpy effect due to the stronger hydrogen bonding of water to the anion. Hydrogen bonding is concerned both in the difference of reaction rate (attributed to the different anion-solvent interaction in water, depending on size of anion) and with the difference in solubility (attributable to the disruption of water structure by anions); but in the rate difference it is the anion-solvent interaction which is important, while in the solubility difference it is the solvent-solvent interactions.

#### 6. REACTIONS OF UNCHARGED MOLECULES WITH CATIONS

Ligand substitution and solvent exchange at labile metal cations such as  $\text{Ni}^{2+}$  and  $\text{Co}^{2+}$  in a variety of polar solvents have been much studied (64-83). The reactions of a bivalent cation  $\text{M}^{2+}$  and an uncharged ligand L in a solvent S are represented by equations 10 and 11 (charges are omitted). Solvent exchange is evidently a special case of ligand substitution.



The solvent in these reactions is a leaving group as well as a solvating and dissociating medium, and in solvent exchange it is also a nucleophilic reagent, so solvent effects may be expected to be complex. These reactions have been studied only relatively recently because the ligand substitution reactions require fast-reaction techniques such as stopped-flow, temperature-jump, pressure-jump, or ultrasonic absorption, and solvent exchange is best investigated by n.m.r. methods (74).

Thermodynamics of solvation. The interaction of cations with solvents may be compared with that of anions. Some data for univalent cations are shown in Table 4. There is not the same contrast between hydroxylic and dipolar aprotic solvents as for anions. For the alkali metal cations, the entropies of transfer from water to other solvents are all negative; the non-aqueous solvents have less structure than water, so there is less structure-breaking when a cation is introduced, just as with simple anions. But the free energies of transfer of the cations depend markedly also on the enthalpy term; for the alkali metal cations, unlike the halide anions, the transfer from water to non-aqueous solvent is exothermic, especially for the highly polar solvents DMSO and DMF, so the contributions of the entropy and enthalpy terms have opposite signs. The data are in accordance with the view that the solvation of these cations is largely influenced by ion-dipole forces. (That these are more prominent in cation-solvation than in anion-solvation is presumably because the dipolar solvent molecules have a localised negative charge but a dispersed positive charge.) An analysis in terms of the Frank and Wen model is given in ref. 62, where contributions to the entropy of transfer due to each of the regions are semi-quantitatively estimated.

For the doubly-charged metal cations which mostly concern us in this section, there is unfortunately not much thermodynamic information, but since the ions are small the charge density is high and we may expect ion-dipole forces to dominate the energetics.

Solvent exchange at transition-metal cations. The rate of solvent exchange at bivalent cations in the first transition-metal series has been measured for various solvents by n.m.r. methods (23,82,83). This type of reaction (eqn. 11), by reason of its symmetry, is simple as regards thermodynamics ( $\Delta G^\circ = \Delta H^\circ = \Delta S^\circ = 0$ ), but not as regards kinetics; the solvent has four different roles (as entering group, leaving group, solvating group, and medium), and is present at a constant high concentration. Not surprisingly, the results are not fully understood.

In the series of cations  $\text{Cr}^{2+}$ ,  $\text{Mn}^{2+}$ ,  $\text{Fe}^{2+}$ ,  $\text{Co}^{2+}$ ,  $\text{Ni}^{2+}$ ,  $\text{Cu}^{2+}$ ,  $\text{Zn}^{2+}$ , the rate constants run parallel with the crystal-field stabilisation energies, in accordance with the expectation that the ion-solvent interaction will be important. The widest range of solvents has been studied with  $\text{Ni}^{2+}$  and  $\text{Co}^{2+}$ . For these ions, the rate constants in various solvents lie in the same order (Table 5). The results differ strikingly from those for the reactions of uncharged molecules with anions considered in the preceding section. The range of rate constants for a given cation is relatively small (ca.  $10^2$  for  $\text{Ni}^{2+}$ ); and in water the reaction is faster than in dipolar aprotic solvents, and about 30 times faster than in methanol. Both these results contrast with those in Table 3. The physical properties of the bulk solvents do not yield satisfactory correlations, nor would they be expected to do so, since the solvent is here also a reagent. Factors that might be expected to be important are the ion-solvent interaction energies, the nucleophilicity of the solvent molecule and its steric requirements, the solvation differences between the initial and transition states, and (for some cations) the possibility of a change of coordination number. No single factor appears to dominate. A fuller interpretation must await more quantitative data on the various factors. Experiments in progress on the determination of activation volumes should provide useful additional clues (84).

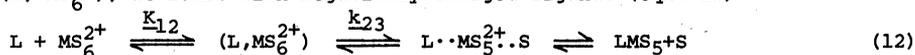
TABLE 5. Solvent exchange rates for Ni(II) and Co(II) ions in various solvents.

	$\text{NH}_3$	WATER	DMF	DMSO	MeCN	MeOH
$\text{Ni}^{2+}$	5.0	4.5	3.9	3.6	3.5	3.0
$\text{Co}^{2+}$	6.8	6.1	5.4	5.2	5.2	4.2

Values of  $\log_{10} k_s$  at 25°C ( $k_s$  in  $\text{s}^{-1}$ ).

Ligand substitution at transition-metal cations. In the study of ligand substitution (eqn. 10) it is possible to vary the nature and concentration of the incoming ligand, so that far more information is available than for solvent exchange. Moreover since both types of reaction involve the breaking of an ion-solvent bond, some of the factors are common to both types of reaction and others not, so a comparison of the two sets of results is helpful. The field has recently been admirably reviewed by Coetzee, Hague, and others, and will be considered only briefly here (64,77,78) (66,67).

The mechanism of the reaction was first studied in aqueous solution, with ligands of various charge-types. The rate law corresponds to the simple scheme  $A + B \rightleftharpoons C$ . The forward rate constants for various cations with a given ligand run roughly parallel with those for solvent exchange, and for ligands of various charges with a given cation they are related to the product of the charges. These results are compatible with an intermediate-dissociative ( $I_d$ ) mechanism, in which the formation of the transition state involves both the entering of a ligand molecule L and the departure of a solvent molecule S, the energetics being largely controlled by the latter; there must also be a preliminary formation of an outer-sphere complex ( $L, MS_6^{2+}$ ), at least with negatively-charged ligands (eqn. 12).



This mechanism was put forward by Eigen and Wilkins, who also assumed that  $k_{23}$  could be identified with the solvent-exchange rate constant  $k_s$  determined by n.m.r. methods (i.e., that the rate of solvent loss is unaffected by the presence of the ligand), and that  $K_{12}$  is controlled by electrostatic forces if the ligand is charged, or by random encounters if it is uncharged (75,76) (see Note a).

The result ( $k_f = K_{12}k_{23} = K_{ES}k_s$ ) gives values of the forward rate constant  $k_f$  for ligand substitution in aqueous solution which agree with the observed values within a power of ten.

In non-aqueous solvents, there are important deviations from this scheme. When the ligand is varied in a given solvent, the rate constant shows much more specificity than in water; and although the rate constants with monodentate ligands agree quite well with the Eigen-Wilkins equations, those with bidentate and tridentate ligands do not agree, and show much more specificity when the solvent is varied. These general features are illustrated by the data in Table 6. Water, as Coetzee notes, is in these respects anomalous, not a typical solvent, and the apparent simplicity of the results in aqueous solutions masks important factors in the part played by the solvent.

Note a. The Fuoss equation used to calculate the electrostatic value  $K_{ES}$  reduces, for neutral ligands, to a form identical with that for random encounters.

TABLE 6. Kinetics of ligand substitution and solvent exchange at nickel(II) ion in various solvents.

SOLVENT	LIGAND	log $k_f$	log $k_s$	log $R_1$	COMMENTS
Water	water	-	4.5	0	$R_1$ varies < 10-fold in aqueous solution for various ligands.
	pyridine	3.6	4.5	-0.3	
	bipy	3.2	4.5	-0.7	
	phen	3.5	4.5	-0.4	
	SCN <sup>-</sup>	4.5	4.5	-0.7	
	oxalate <sup>2-</sup>	4.9	4.5	-0.7	
MeCN	pyridine	2.9	3.4	-0.4	$R_1$ varies < 10-fold for monodentate ligands in various solvents.
water		3.6	4.5	-0.3	
DMSO		3.4	3.9	+0.1	
MeCN	SCN <sup>-</sup>	5.0	3.4	-0.1	
Water		4.5	4.5	-0.7	
DMSO		4.9	3.9	0.0	
MeCN	bipy	3.61	3.4	+0.3	$R_1$ varies 100-fold for bidentate ligands in various solvents.
Water		3.2	4.5	-0.7	
DMSO		1.84	3.9	-1.7	
MeCN	phen	4.70	3.4	+1.4	
Water		3.5	4.5	-0.4	
DMSO		2.6	3.9	-0.9	

$k_f$  = rate constant ( $M^{-1}s^{-1}$ ) at 25°C for forward reaction  $M + L \rightarrow ML$ .

$k_s$  = rate constant ( $s^{-1}$ ) at 25°C for solvent exchange.

$R_1$  =  $(4/3) k_f / K_{12} k_s$

$K_{12}$  =  $10^3 (4\pi N/3) a_1^3$  for neutral ligands, where  $a_1$  is the distance of closest approach of the centre of the solvated cation to the reaction site on the ligand. For charged ligands this expression is multiplied by a term representing the electrostatic interaction.

Data mainly from Coetzee, refs. 65, 77, 78.

These deviations from simple behaviour in the reactions of bidentate ligands in non-aqueous solvents might conceivably have their origin (a) in the first step of the reaction, i.e., formation of the outer-sphere complex, if this is influenced by specific interactions as well as electrostatic ones; or (b) in the second step, if  $k_{23}$  is influenced by the adjacent ligand and cannot be identified with the  $k_s$  which is measured in absence of L; or (c) possibly in a third step, namely the formation of the second metal-ligand bond (ring-closure), which so far we have assumed to be relatively fast. The third possibility has been considered by Coetzee but is regarded by him as unlikely (64,77,78). The second possibility was investigated by Bennetto, Caldin *et al.*, as an explanation of the correlations of rate and activation parameters with physical properties of solvents related to the strengths of their structures, such as their enthalpies of evaporation; a general picture based on the Frank-Wen model was developed, with stress on the influence of L on the local solvent structure (79,80,81). Of these possible explanations, the first is favoured by Coetzee, partly because (as we have noted) monodentate ligands show much smaller deviations (77,78). As a result of his survey, he concludes that the deviations originate mainly in the outer sphere. The stability of the outer-sphere complex and the orientation of the ligand in the outer sphere are both concerned; both are influenced by ion-dipolar and hydrogen-bonding interactions. In consequence, "the kinetics of a pyridine-type ligand are influenced by its polarity and steric requirements, as

well as by the electron-donor ability, hydrogen-bond donor ability and steric requirements of the solvent". Deviations from simple behaviour will depend on a combination of factors: the hydrogen-bonding donor strength of the solvent (much greater for hydroxylic solvents than for dipolar aprotic ones); the strength of the cation-solvent interaction, as revealed by the free energies of transfer; and the steric requirements in the inner sphere, which depend on the sizes of the solvent and ligand molecules, and (for the large bidentate ligands) on their flexibility. These factors may oppose or reinforce one another to produce the observed variety of behaviour in different solvents. It is not easy to distinguish these effects from those attributable to the structure of the solvent, which is directly influenced by several of these factors. The matter should become clearer when we know more about the effects of the solvent on the initial and transition states, through studies on the energies of transfer of ligands and metal ions from one solvent to another; so far there have been few studies permitting a 'dissection' of the kind that has proved so useful in other fields.

Proton transfer in hydroxylic solvents from cations to uncharged bases. For proton-transfer reactions in hydroxylic solvents ( $AH^+ + B \rightarrow A + HB^+$ ), we have a special source of information; by proton n.m.r. line-broadening measurements, it is possible to study the role of the solvent as well as the overall proton transfer (59). For instance, in the exchange of protons between ammonium ions and bases in water, the overall rate of exchange with  $NH_4^+$  is given by the broadening of the line due to the ammonium-ion protons, while the broadening of the line due to the solvent protons gives the rate of exchange of  $NH_4^+$  with solvent. The results show that there are two concurrent processes, one with participation of solvent and one without:



The rate constants for both reactions can be determined. The series of methylamines has been studied in this way. For their reactions such as 13b where proton transfer is via a solvent bridge, the rate constant in water ( $10^8 - 10^9 M^{-1}s^{-1}$ ) varies roughly with the base strength of the anion, as might be expected. For the direct bimolecular reactions such as 13a, however, the rate constant drops markedly as more methyl groups are introduced; this does not appear to be due to a steric effect, but to an increasing activation energy for the desolvation of the  $NH_4^+$  ion which must occur before the reactant molecules can come into contact. Similar studies in methanol, n-butanol and acetic acid likewise indicate that such desolvation requires an activation energy, though a small one, in these solvents, just as does desolvation of metal cations in ligand substitution. The multiplicity of the roles of the solvent is noteworthy; in reactions such as 13b, the solvent acts as reagent (hydrogen-ion donor and acceptor), as solvating agent (hydrogen-bond donor and acceptor), and as dissociating medium for the ions.

## 7. THE VARIOUS ROLES OF THE SOLVENT

From this brief survey of reaction types, it is clear that the solvent has a wide spectrum of roles in influencing the kinetics.

(1) The solvent may take no part in the reaction, apart from helping to maintain the Boltzmann distribution of energy. For such a reaction, the rate and activation parameters should be the same in the gas phase and in all solvents, as is approximately the case for the dimerisation of cyclopentadiene (85); if the reaction is unimolecular, the rate should also be the same in a solid matrix and in solution, as it is for the intramolecular H-atom transfer in the tri-t-butylphenyl radical in hydrocarbon media (86). The solvent is then simply a medium in which the reactant molecules meet in the course of their random motion; the encounter rate is diffusion-controlled, and the rate of reaction depends on the activation energy. If there is no activation barrier, reaction occurs at every encounter and the rate will depend on the viscosity of the solvent; an example is the recombination of iodine atoms in carbon tetrachloride (87).

(2) The solvent may act simply as a dissociating and ionising medium, reducing the forces between charges, as appears to be the case for the Menshutkin reaction mentioned above (section 3) in aliphatic solvents, where the polar transition state is stabilised in line with the dielectric constant of the solvent.

(3) Without taking part in the reaction, in the sense of undergoing covalent-bond changes, the solvent may influence the energetics of reaction, since the solvation of the initial and transition states will usually be different and solvent-dependent. We have seen examples of this in the reactions of anions or cations with uncharged molecules. Here the solvation of ions and their effects on solvent structure dominate the kinetic solvent effects.

(4) The solvent may be involved as a reagent, as well as a solvating medium; for instance in solvolysis, in solvent exchange at metal cations (where it is both reagent and product), in ligand substitution, and in proton transfer. Here the whole range of solvent properties may be involved, and we have to consider solvents as electron donors and acceptors (nucleophiles and electrophiles) as well as solvating agents.

Proton-transfer reactions, which are of all charge types, give examples of all these types of solvent involvement, as we have seen. Diffusion control (with slight modification) is

illustrated by the reactions of 2,4-dinitrophenol and some other substituted phenols with amine bases in aprotic solvents (43-46). The reactions of 4-nitrophenylnitromethane with neutral bases show the solvent as an ionising medium (48). Solvation change appears to dominate in the reaction of bromophenol blue with pyridine bases (45-47). In hydroxylic solvents, as we have noted, the solvent can act as a reactant, providing an independent pathway for the proton-transfer, besides its role in solvation which is also important for the kinetics (59).

Because of these diverse roles of the solvent, the relative rates of a given reaction in a series of solvents depend greatly upon the reaction, as we have seen.

## 8. SOLVENT 'POLARITY' PARAMETERS

At this point it is appropriate to say a word about various parameters that have been used as measures of the 'polarity' (using the word in a loose sense) of solvents.

(a) Physical properties of solvents and solvent molecules. The relative permittivity or dielectric constant of a solvent, as we have noted, is related to the ability of solvent molecules to orient in a field, a process which reduces the forces between charged particles, thus helping ions of opposite charge to separate. The magnitude depends on the dipole moment and polarisability of the solvent molecules, the number of molecules per unit volume, and any specific interactions, notably hydrogen-bonding of one solvent molecule to another. The dielectric constant may be expected to bear some relation to ion-solvent interactions, but there are limitations, as we have noted earlier; in the strong field of an ion, local dipoles and quadrupole moments may be important, and specific ion-solvent interactions such as hydrogen-bonding may dominate. The dielectric constant is probably better as an index of the ability of a solvent to separate the ions once formed.

Since solvent effects depend, as we have seen, on polarisability as well as dipole moment or dielectric constant, and also on specific solute-solvent interactions such as hydrogen-bonding in which the solvent may behave either as donor or acceptor, it appears unprofitable to seek for a single property that will characterise the behaviour of a solvent towards all solutes. We do, however, wish to understand solute-solvent interactions eventually in terms of the properties of individual solvent molecules such as size, shape, dipole moment, charge distribution and polarisability; as aids towards such understanding we can also use macroscopic properties such as dielectric constant, free volume, viscosity (79), heat capacity (88), enthalpy and entropy of evaporation (89), and cohesive energy density (90).

(b) Empirical solvent parameters based on rates of reaction, heats of reaction, or spectroscopic measurements. Various empirical parameters have been proposed, based on the behaviour of a particular system towards a change of solvent. The rate of solvolysis of t-butyl chloride (or other solvolysis reaction in which nucleophilic solvent assistance appears to be slight) has been used; the resulting 'Y-values' give a measure of the ability of the solvents to assist the formation of an ion-pair (39,98). The enthalpy of the interaction of the solvent with the acceptor molecule antimony pentachloride ( $S \rightarrow SbCl_5$ ) in an 'inert' solvent (sym-dichloroethane) gives a scale of 'donor numbers' (DN), which reflect the electron-donating or nucleophilic properties of solvents; and a scale of 'acceptor numbers' (AN) reflecting the electron-accepting or electrophilic properties is based on the extent of the interaction of the solvent with the donor molecule triethyl phosphine oxide ( $S \rightarrow OPET_3$ ) (91-95).

Spectroscopic parameters ( $Z$ ,  $E_T$ ) are based on the shift of the absorption maximum for a particular ion-pair (a substituted-pyridinium iodide) in a given solvent; they relate to the ability of the solvent to stabilise the ion-pair relative to its less polar electronically-excited state (96-98). These and other parameters show correlations of varying precision with each other, with the physical properties of the solvents, and with the behaviour (kinetic, thermodynamic, and spectroscopic) of other systems. They are useful in estimating the likely effect of a change in solvent, even in synthetic chemistry (99). Whether a given system conforms accurately to any of them depends, however, on how closely the system behaves analogously to the reference system. Fundamental understanding of solvent effects requires that these parameters should be related to molecular properties of the system concerned, not simply to its analogies with other systems.

## 9. RATES OF SOLVATION CHANGES

Changes of solvation during reaction are an integral part of the interpretation of solvent effects, and it is of interest to ask what evidence is available on molecular motions in liquids and on the rates of solvent reorganisation and of solvation changes. We first note that there are two types of solvation change which affect kinetics (13,57). (a) Where a solvating molecule blocks the reaction site, it must be removed before the reactants can approach closely enough to react; this process requires activation energy, and may indeed be the rate-limiting step. Ligand substitution at transition-metal cations provides many examples, as does proton-transfer in hydroxylic solvents. Another example is the reaction

$\text{HO}^- + \text{H}_2 \rightarrow \text{H}_2\text{O} + \text{H}^-$ , where the activation energy of about  $25 \text{ kcal mol}^{-1}$  has been attributed entirely to the need to desolvate  $\text{OH}^-$  before the reactants can react (57); for some early expressions of such views, see refs 1 and 6. (b) In reactions involving ions, the changes of covalent bonding are usually accompanied, as we have seen, by changes in the number of bound solvent molecules. These solvation and desolvation processes influence the rate of reaction, and the energy and entropy of activation, but are not rate-limiting steps.

Do these solvent-reorganisation processes precede the changes of bonding and internuclear distances, or do they follow them, or occur synchronously with them? The assumption of effectively synchronous changes allows transition-state theory to give a coherent interpretation of the effects of temperature, pressure and solvent on reaction kinetics; a vast mass of experimental data is rendered intelligible. But if we take the simplest view of the equations of transition-state theory, and base them on the assumption that throughout the lifetime of the reactive complex there is complete equilibration both of chemical species and of energy distribution, the difficulty arises that the lifetime is presumably about  $10^{-13}$ s (comparable with the time for one vibration), whereas a much longer time is required for rotation of the molecules of common solvents (according to dielectric-relaxation measurements, this time is around  $10^{-11}$ s). For water, it is true, the time required for molecular librations (wagging) is only about  $0.5 \times 10^{-13}$ s, and even for hindered translation it is about  $2 \times 10^{-13}$ s, while for other common solvents the infra-red spectra indicate that librations require something of the order of  $3 \times 10^{-13}$ s (27). Thus if librational motion is sufficient, the time required may not be excessive (the longer time required for dielectric relaxation corresponds to rotation through a large angle against the solvent-solvent interactions). It may be, however, that the assumption of complete equilibration requires revision.

Experimental work of various kinds is beginning to throw light on the rates of solvent motions. N.m.r. work gives rather detailed information, and confirms that small angular motions are much faster than the rotations controlling dielectric relaxation (27). Neutron-diffraction (100,101), infra-red, Raman, and light-scattering techniques (102) and picosecond laser methods (103-106) can all be expected to produce important results. The extension of the formalism of Marcus' theory of outer-sphere electron-transfer to proton-transfer reactions raises the question whether solvent reorganization precedes reaction (107). Solvent isotope effects and curved Brønsted plots are here relevant; but the data so far refer mainly to aqueous solutions. Some recent results on isotopic effects in the proton-transfer reaction of the carbon acid 4-nitrophenylnitromethane with the strong base tetramethylguanidine have been interpreted as suggesting that polar solvent molecules undergo rotation coupled with the motion of the proton while low-polar molecules do not, but this work awaits confirmation (48). Kinetic evidence in this field is far from plentiful.

Note on omissions. In this brief account there is too little space for numerous important aspects of the general theme. I have dealt only with molecular solvents, and even so have omitted consideration of strongly acidic and basic solvents (108), mixed solvents (109), and liquid crystals (110), as well as molten salts and molten metals. I have also excluded excited molecules. Various interesting investigations of reactions in a series of solvents are omitted, and I have not discussed the uses of solvent effects in mechanistic studies (41, 111,112), or in synthetic chemistry (99,113).

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