JOURNAL
OF THE AMERICAN CHEMICAL SOCIETY

VOLUME 90, NUMBER 19 SEPTEMBER 11, 1968

Physical and Inorganic Chemistry

Solvation of Ions. XIV.[1] Protic–Dipolar Aprotic Solvent Effects on Rates of Bimolecular Reactions. Solvent Activity Coefficients of Reactants and Transition States at 25°

R. Alexander, E. C. F. Ko, A. J. Parker,[2] and T. J. Broxton

Contribution from the Department of Organic Chemistry, University of Western Australia, Nedlands, Western Australia. *Received January 9, 1968*

Abstract: Rates of 78 bimolecular nucleophilic substitution (SN2) and elimination (E2) reactions in solvents water, methanol, formamide, dimethylformamide (DMF), dimethylacetamide (DMAC), sulfolane (TMS), acetonitrile, dimethyl sulfoxide (DMSO), N-methyl-2-pyrrolidone (NMePy), acetone, hexamethylphosphoramide (HMPT), nitromethane, and 80% v:v DMSO–methanol are considered. Solvent effects on rate are interpreted in terms of solvent activity coefficients, with methanol as reference solvent, for reactants and for transition states. If our extrathermodynamic assumptions are valid, then solvation of small, "hard" reactant anions (*e.g.*, Cl^-) decreases strongly in the order of solvents: $H_2O > MeOH > HCONH_2 \gg$ DMSO, $CH_3NO_2 > CH_3CN$, DMF > TMS > DMAC > HMPT, NMePy. Solvation of polar reactants (*e.g.*, CH_3I) and uncharged transition states decreases slightly and roughly in the order of solvents: HMPT, NMePy > DMSO; DMAC, DMF > $CH_3CN > CH_3NO_2 > MeOH > HCONH_2 \gg H_2O$; solvation of large polarizable SNAr transition state anions decreases in the order HMPT, DMSO > DMF > CH_3OH, NMePy > CH_3NO_2, CH_3CN, just as does a "model" transition state anion. Evidence is presented for the following observations, which are independent of extrathermodynamic assumptions. Solvation of SN2 transition-state anions depends on the nature of the entering and displaced groups. The susceptibility of SN2 and E2 transition states to transfer from protic to dipolar aprotic solvent depends very much on the type of carbon atom being attacked. Transition states for reaction of benzyl Hal > secondary RHal > primary RHal > CH_3Hal > 4-nitrobenzyl Hal tend to be more solvated by methanol than by DMF in the order shown. Transition states for E2C and for SN2 reactions of similar substrates respond in much the same way to solvent transfer. Solvation of SN2 transition states varies by > 4 kcal mole^{-1} according to the nature of the atom being attacked. "Solvation of substituents," both in reactant and the transition state, influences rates of SNAr reactions. Protic–dipolar aprotic effects on rate usually are reflected in changes in enthalpy rather than in the entropy of activation. HMPT is the "fastest" solvent studied.

Bimolecular reactions of anions, Y^-, with molecules, RX, such as substitution (*e.g.*, eq 1), elimina-

$$Y^- + RX \longrightarrow [YRX^-]^{\ddagger} \longrightarrow YR + X^- \quad (1)$$

tion, proton abstraction, and addition, are often much faster in dipolar aprotic than in protic solvents of comparable dielectric constant.[3-5] This simple observation is of great practical significance.[4,6] Also, because the majority of measurements have been hitherto made in water, a very special protic medium, it is leading us to a reassessment of the chemistry of rate[5] and

---

[1] Part XIII: A. J. Parker and R. Alexander, *J. Amer. Chem. Soc.*, **90**, 3313 (1968).

[2] Author to whom enquiries should be addressed at the Department of Organic Chemistry, University of Western Australia, Nedlands, Western Australia 6009.

[3] Solvent effects on rate cannot be treated successfully in terms of any function of solvent dielectric constant, except in most exceptional and limited circumstances.

[4] A. J. Parker, *Quart. Rev.* (London), 163 (1962).

[5] A. J. Parker, *Advan. Phys. Org. Chem.*, **5**, 173 (1967). This article is most relevant to this paper. The data discussed were only preliminary and are now modified.

[6] A. J. Parker, *Advan. Org. Chem.*, **5**, 1 (1965).

equilibrium[1,7,8] processes, involving anions. As we hope to show here, the principles underlying this observation provide a powerful method of studying the nature of transition states, and this leads to useful thoughts about reaction mechanisms and rate processes.

For our purposes, eq 2 is the most profitable way of considering solvent effects on the rate constants k^S and k^0 for any bimolecular reaction, such as (1), between Y^- and RX in a solvent S and a reference solvent 0 at 25°.[5] The solvent activity coefficients, ${}^0\gamma_i{}^S$, are for

$$\log \frac{k^S}{k^0} = \log {}^0\gamma^S{}_{Y^-} + \log {}^0\gamma^S{}_{RX} - \log {}^0\gamma^S{}_{YRX\neq^-} \quad (2)$$

transfer of hypothetically ideal unimolar i from the reference solvent to the solvent S at 25°.

Equation 2 follows from the absolute rate theory[9] in which reactions like (1) are considered to involve an equilibrium between the reactants and transition state.[10,11] In this way, solvent effects on rate can be treated in much the same way as we have treated protic–dipolar aprotic solvent effects on acid–base equilibria,[7] on solubilities,[1,8] and on instability constants.[1,8] It should be remembered though that transition states are not true solutes; they are models whose structure is based on our knowledge of the reaction mechanism. The behavior of these models, upon solvent transfer, can be predicted sometimes from the behavior of real molecules or of ions of comparable structure.[10,11] Quite often, if the mechanism is well understood, solvent effects on rate can be predicted through appropriate linear free-energy relationships,[11] based on (2).[5] An alternative way in which (2) is useful arises if our knowledge of the mechanism is scanty. A value of $\log {}^0\gamma^S{}_{YRX\neq}$ is calculated from (2), and this is compared with known solvent activity coefficients for a variety of relevant solutes and established transition states. In this way, the best model for the "unknown" transition state can be set up, thus defining the new mechanism. These approaches, which of course are not new[5,11] but have not been used as much as they might have been, will be illustrated in this and succeeding papers.

It is a fundamental assumption of our comparison between transition-state solvation and solvation of real molecular species or ions *that the transition states of our reactions, as well as being in equilibrium with reactants, are in equilibrium with their surroundings.* The assumption is an important one[12] in terms of our understanding of solvent effects on rate, but at this time we merely wish to show that the consequences are reasonable, if it is accepted.

The terms in eq 2 were obtained as follows. Rate constants have been measured by a variety of routine procedures, with reactants at *ca.* 4×10^{-2} *M*. Solvent activity coefficients of nonelectrolytes were determined from solubility, distribution, or vapor-pressure measurements (*vide infra*). Up until now, a serious difficulty has been the estimation of solvent activity coefficients of individual anions or cations.[5] Values of $({}^0\gamma^S{}_{M^+})({}^0\gamma^S{}_{Y^-})$ are known from solubilities of the salt MY, but it will always be impossible to determine ${}^0\gamma^S{}_{M^+}$ or ${}^0\gamma^S{}_{Y^-}$ separately.[1] This leaves two alternatives, either to split $({}^0\gamma^S{}_{M^+})({}^0\gamma^S{}_{Y^-})$ by extrathermodynamic assumptions[1,13] or to choose an ion as a reference standard.[8] We have used both procedures in the past, but, now that we have greater confidence in the extrathermodynamic assumptions, we will use them in this paper. If the assumptions prove to be invalid, appropriate adjustments are very easily made.[14]

Extrathermodynamic Assumptions.[5] A survey of several extrathermodynamic assumptions used to split solvent activity coefficients of electrolytes has been given in part XIII.[1] Assumptions such as (3) and (4) seem reasonable and lead to values of $\log {}^0\gamma^S{}_{Ag^+}$. The principle behind these assumptions is that a pair of large solutes, with low or no charge density and of similar structure, behave in much the same way on transfer through a series of solvents of comparable dielectric con-

$$\log {}^0\gamma^S{}_{Ph_4B^-} = \log {}^0\gamma^S{}_{Ph_4As^+} \quad (3)$$

$$\log {}^0\gamma^S{}_{I_2} = \log {}^0\gamma^S{}_{I_3^-} \quad (4)$$

stant (30–45). Other assumptions,[1] not related to (3) or (4), give comparable values of ${}^0\gamma^S{}_{Ag^+}$. Our estimates of $\log {}^0\gamma^S{}_{Ag^+}$ give values of $\log {}^0\gamma^S{}_{Y^-}$ and thus of $\log {}^0\gamma^S{}_{M^+}$, when applied to solubilities of the salts AgY and MY at 25° as in (5) and (6). In (5) and (6), *K* is the solubility product (mole² liter⁻²) of the salt shown in parentheses.

$$\log K^0/K^S(\text{AgY}) - \log {}^0\gamma^S{}_{Ag^+} = \log {}^0\gamma^S{}_{Y^-} \quad (5)$$

$$\log K^0/K^S(\text{MY}) - \log {}^0\gamma^S{}_{Y^-} = \log {}^0\gamma^S{}_{M^+} \quad (6)$$

Some solubilities of electrolytes, which we have not reported previously, are in Table I, and mean values, on the molar scale, of $\log {}^M\gamma^S{}_{Y^-}$ and $\log {}^M\gamma^S{}_{M^+}$ are in Table II. These are for transfer from methanol, as reference solvent, to other solvents, *e.g.*, water, formamide, dimethylformamide (DMF), dimethylacetamide (DMAC), sulfolane (TMS, at 30°), acetonitrile, dimethyl sulfoxide

Table I. Solubilities[a] and Solvent Activity Coefficients of Ionic Substrates (Reference Solvent: Methanol at 25°)

Electrolyte	p*K* (MeOH)	Log ${}^M\gamma^S{}_{A^+}$ (CH$_3$CN)	${}^M\gamma^S{}_{B^-}$[b] (DMF)
2-Cl-3,5-$(NO_2)_2C_6H_2CO_2Ag$	5.6	...	−3.9
4-Cl-3-$NO_2C_6H_3NMe_3I$	3.2	...	−2.0
Me_3SI[c]	1.5	+0.9	−0.5

[a] By analysis of saturated solutions, no allowance for ion association. [b] *I.e.*, pK^S − pK^M, where *K* is the solubility product in moles² liter⁻². [c] Measured by Mr. I. P. Evans.

---

(7) B. W. Clare, D. Cook, E. C. F. Ko, Y. C. Mac, and A. J. Parker, *J. Amer. Chem. Soc.*, **88**, 1911 (1966).

(8) R. Alexander, E. C. F. Ko, Y. C. Mac, and A. J. Parker, *ibid.*, **89**, 3703 (1967).

(9) The collision theory of reaction rates and interpretations of mechanism in terms of electrostatic interactions in the reactant state, despite their simplicity, are of little value to our understanding of mechanisms. Their influence on the understanding of solvent effects on rate has been equally unfortunate.

(10) W. F. K. Wynne-Jones and H. Eyring, *J. Chem. Phys.*, **3**, 492 (1935).

(11) J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1963.

(12) C. D. Ritchie, G. A. Skinner, and V. G. Badding, *J. Amer. Chem. Soc.*, **89**, 2063 (1967).

(13) R. Alexander and A. J. Parker, *ibid.*, **89**, 5549 (1967).

(14) The values of $\log {}^0\gamma^S{}_{M^+}$ and $\log {}^0\gamma^S{}_{Y^-}$ used in this paper can be put on a strict thermodynamic basis, if it is realized[1] that $\log {}^0\gamma^S{}_{Y^-} \approx \log {}^0\bar{\gamma}^S{}_{Y^-} + \log {}^0\gamma^S{}_{I_2} - \log {}^0\gamma^S{}_{I_3^-} \approx \log {}^0\bar{\gamma}^S{}_{Y^-} + {}^1/_2 \log {}^0\bar{\gamma}^S{}_{Ph_4As^+} - {}^1/_2 \log {}^0\bar{\gamma}^S{}_{Ph_4B^-}$, where ${}^0\bar{\gamma}^S$ is the actual (but forever unknown for ions) solvent activity coefficient of the solute.

Table II. Solvent Activity Coefficients of Anions and Cations (Reference Solvent: Methanol at 25°[a])

Ion	Log $^{M}\gamma^{S}_{ion}$ ± 0.3[a,b]										
	H_2O	$HCONH_2$	DMF	DMAC	DMSO	CH_3CN	HMPT	CH_3NO_2	NMePy	80DMSO-M	TMS[c,i]
CH_3O^-	...	...	...	...	(5.3)[c,f]	...	...	...	...	(4.0)[c]	...
$CH_3CO_2^-$	−2.9	(0.6)[c]	+9.2	+10.2	+6.5	+7.8	...	...	...	...	...
$4\text{-}NO_2C_6H_4O^-$	...	...	(4.1)[c]	...	...	+4.2[g]	...	...	...	...	...
$2,4\text{-}(NO_2)_2C_6H_3O^-$	...	...	(3.9)[c]	...	...	...	...	...	...	...	...
$2,4,6\text{-}(NO_2)_3C_6H_2O^-$	+0.6	...	(−0.4)[c]	...	...	+0.1	...	...	...	...	...
$4\text{-}CH_3C_6H_4SO_3^-$	−1.1	...	+3.5	...	...	...	...	...	...	...	...
ClO_4^-	−0.8	...	−0.4	...	−0.3	...	...	...	...	...	...
$2\text{-}Cl\text{-}3,5\text{-}(NO_2)_2C_6H_2CO_2^-$	...	...	+1.2[e]	...	...	...	...	...	...	...	...
$C_6H_5S^-$	...	...	(4.9)[c]	...	...	...	...	...	...	...	...
$C_6H_5O^-$	...	...	(7.7)[c]	...	...	...	...	...	...	...	...
$4\text{-}NO_2C_6H_4S^-$	...	...	(2.9)[c]	...	...	...	...	...	...	...	...
Cl^-	−2.5	0.0	+6.5	+7.8	+5.5	+6.3	+8.8	+4.9	8.1	+4.2	+5.8
N_3^-	−1.8	+0.2	+4.9	+6.2	+3.5	+4.7	+7.2	+4.6	6.3	...	+5.4
CN^-	(−1.5)[c]	(0.4)[c]	(6.2)[c]	...	...	...	...	...	...	...	...
Br^-	−2.1	−0.1	+4.9	+5.9	+3.6	+4.2	+7.1	...	(6.1)[c]	...	...
SCN^-	−1.2	−0.3	+2.7	+3.2	+1.4	+2.6	+3.4	+2.4	2.9	+1.6	+2.6
I^-	−1.5	−0.1	+2.6	+3.0	+1.3	+2.4	...	+2.6	3.0	+1.5	+2.4
$SeCN^-$	...	...	(2.7)[c]	...	...	...	...	...	...	...	...
NO_2^-	...	...	...	...	(3.7)[c]	...	...	...	...	...	...
BPh_4^-	+4.1	−0.1	−2.7	−2.7	−2.6	−1.6	−2.7	...	...	−2.2	−2
$AgCl_2^-$	−2.9	...	−0.2	+0.2	−0.6	+0.9	−2.5	+0.1	0.0	...	0
$AgBr_2^-$	−1.8	...	−1.2	−1.0	−1.6	−1.0	−3.8	...	...	...	...
AgI_2^-	+0.0	...	−2.7	−3.1	−3.1	...	...	...	...	...	...
I_3^-	+2.2	+1.0	−2.0	−3.0	−4.1	−0.4	...	...	...	...	...
Ag^+	−0.8[d]	−3.7[d]	−5.1[d]	−6.6[d]	−8.2[d]	−6.3[d]	−10[d]	+1.7[d]	−6.8[d]	−7.4[d]	−2
Na^+	...	...	−3.9	...	−3.6	+1.4	−6.3	...	...	...	...
K^+	−1.5	...	−3.7	...	−4.5	−1.6	−4.8	...	...	...	...
Cs^+	−1.1	−2.1	−3.3	...	...	−1.3	...	...	...	...	...
Me_3S^+	...	...	−3.1[e]	...	...	−1.6[h]	...	...	...	...	...
NEt_4^+	...	...	−1.3	...	...	...	...	...	...	...	...
NBu_4^+	+3.7	...	...	...	...	−1.5	...	...	...	...	...
Ph_4As^+	+4.1	−0.1	−2.7	−2.7	−2.6	−1.6	−2.7	...	...	−2.2	−2
$4\text{-}Cl\text{-}3\text{-}NO_2C_6H_3NMe_3^+$	...	...	−4.6[e]	...	...	...	...	...	...	...	...

[a] Because the values here are effectively calculated by applying the iodine–triiodide assumption and/or the tetraphenylarsonium tetraphenyl boride assumption to solubility products of appropriate salts,[1] the log $^{M}\gamma^{S}_{ion}$ values recorded for anions are in fact log $^{M}\bar{\gamma}^{S}_{ion}$ + log $^{M}\bar{\gamma}^{S}_{I_2}$ − log $^{M}\bar{\gamma}_{I_3^-}$ ≈ log $^{M}\bar{\gamma}^{S}_{ion}$ + $^1/_2$ log $^{M}\bar{\gamma}^{S}_{Ph_4As^+}$ − $^1/_2$ log $^{M}\bar{\gamma}^{S}_{Ph_4B^-}$, where $^{M}\bar{\gamma}^{S}$ denotes the true, but forever indeterminable, solvent activity coefficient of a single ion (*cf.* ref 14). [b] Unless stated otherwise, data are from ref 1, 8, or 13 with the values derived from solubilities of silver and other salts adjusted to a mean value, after the survey in ref 1 of *all* extrathermodynamic assumptions used to split log ($^{M}\gamma^{S}_{A^+}$)($^{M}\gamma^{S}_{B^-}$). The values previously given in Table III of ref 13 are from the TATB assumption only, and some small adjustments have been made according to the new values of log $^{M}\gamma^{S}_{Ag^+}$ in ref 1. [c] Calculated from a linear free-energy relationship (7), using mean values of C = log $^{M}\gamma^{S}_{RX}/^{M}\gamma^{S}_{\pm}$ from Table IV for the same R and X groups and related Y groups and values of log k^S/k^M for this Y group. These values are in parentheses because they are subject to greater uncertainty (±0.3 log unit) than other values in the table and of course cannot be used in later papers to test whether such free-energy relationships are valid. [d] Reference 1. [e] From Table I, using log $^{M}\gamma^{D}_{Ag^+}$ = −5.1. [f] This value almost certainly is low for free methoxide ion, because of ion pairing of sodium methoxide in DMSO. It is actually the value for *ca.* 10^{-3} *M* OMe^- in the presence of 10^{-3} *M* Na^+ in DMSO. [g] From solubilities in ref 8 (Table VIII), using values of log $^{M}\gamma^{S}_{K^+}$ or log $^{M}\gamma^{S}_{Na^+}$ from this table. [h] From Table I using log $^{M}\gamma^{CH_3CN}_{Ag^+}$ = −6.3. [i] At 30.0°.

(DMSO), N-methyl-2-pyrrolidone (NMePy), acetone, hexamethylphosphoramide (HMPT), nitromethane, and 80% v:v DMSO–methanol (80DMSO-M) at 25°. They have been calculated through eq 5 and 6 or related expressions, as shown in earlier papers.[1,13] The values in Table II which are in parentheses have been estimated from a rough linear free-energy relationship, eq 7. The values of the constant are estimated from log $^{M}\gamma^{S}_{RX}/^{M}\gamma^{S}_{\pm}$ for closely related reactions recorded in Table IV. This assumption leads to values with an uncertainty

$$\log \frac{k^{S}}{k^{M}} (RX + Y^-) = \log {}^{M}\gamma^{S}_{Y^-} + C \qquad (7)$$

estimated at ±0.3 log unit.

Solvation of Anions Y^-.[5] The values of log $^{M}\gamma^{S}_{Y^-}$ in Table II give quantitative significance to our qualitative discussion of the effects of solvation on the properties of anions in dipolar aprotic solvents.[4,6] Briefly, small anions which are strong hydrogen bond acceptors (*e.g.*, Cl^-, N_3^-, $CH_3CO_2^-$) are *ca.* 10^4–10^{10} times more solvated[15] by protic than by dipolar aprotic solvents. Large anions, which are polarizable but are poor hydrogen bond acceptors and fit poorly into hydrogen-bonded solvent structures (*e.g.*, ClO_4^-, picrate, $Ag(Hal)_2^-$), are *ca.* 10^0–10^3 times more solvated by dipolar aprotic solvents than by protic solvents. Protic solvents, such as water and formamide and to a lesser extent methanol, have highly developed structures. Their relatively small molecules are held together by very strong hydrogen bonds. Dipolar aprotic solvents have weaker structures. Their larger polarizable molecules are held together by strong dipole–dipole interactions and London dispersion forces, but there is no H bonding. The weaker structure of dipolar aprotic solvents is one reason why very large polar solutes, be they anions, cations, or polar molecules, are more solvated by dipolar aprotic

---

(15) To say that a solute is "10^x times more solvated" is perhaps a loose and confusing way of saying that the standard chemical potential of the solute is reduced by 2.303 × 298*Rx* kcal/mole upon solvent transfer at 25°. Nevertheless, we feel that it is an effective way of communicating our ideas about solvent effects on rate and equilibrium constants.

Table III. Solvent Activity Coefficients of Molecules at 25° (Reference Solvent: Methanol)

Solute, RX	Log h/c[b] (MeOH) ± 0.1	Solvent	Log ${}^{M}\gamma^{S}{}_{RX}$[c] ± 0.2	Solute, RX	Log S[a] (MeOH) ± 0.1	Solvent	Log ${}^{M}\gamma^{S}{}_{RX}$[c] ± 0.2
CH_3Cl	2.93	H_2O	+0.9	*trans*-TsCH=CHCl	−0.5	DMF	−1.1
		$HCONH_2$	+0.1	$CH_2{=}CH_2$	−1[f]	H_2O[f]	+1.3
		DMF	−0.45		−1[f]	DMF[g]	0.0
CH_3Br	2.44	H_2O	+1.2		−1[f]	DMSO[h]	−0.1
		$HCONH_2$	+0.2	CH_3CO_2Ar[e]	−0.5	DMF	−0.9
		DMF	−0.3	$(C_6H_5)_4C$	−3.7[i]	DMF	−1.6
		80DMSO-M	0.0		−3.7[i]	DMAC	−1.4
CH_3I	2.21	H_2O	+1.4		−3.7[i]	CH_3CN	−0.5
		$HCONH_2$	+0.5	$(C_6H_5)_4Sn$	−3.6[i]	DMF	−1.6
		DMF	−0.5	Ferrocene	−1.2[i]	H_2O	+3.6
		DMAC	−0.6		−1.2[i]	CH_3CN	−0.3
		DMSO	−0.5	Iodine	−0.6[j]	H_2O[j]	+2.3
		CH_3CN	−0.4		−0.6[j]	$HCONH_2$[j]	+0.5
		HMPT	−0.7		−0.6[j]	DMF[j]	−1.8
		NMePy	−0.7		−0.6[j]	DMAC[j]	−2.9
		Me_2CO	−0.45		−0.6[j]	DMSO[j]	−4.1
		80DMSO-M	−0.3		−0.6[j]	CH_3CN[j]	−0.2
		CH_3NO_2	−0.2	2,4-$(NO_2)_2C_6H_3Cl$	−0.3[f,k]	H_2O[f,k]	+4.2
n-BuCl	2.3	DMF	−0.6		−0.3[f,k]	DMF[k]	<−1
n-BuBr	1.8	$HCONH_2$	+0.5	4-$NO_2C_6H_4I$	−1.58	$HCONH_2$	+0.4
		DMF	−0.1		−1.58	DMF	−1.2
		DMAC	−0.1		−1.58	CH_3CN	−0.4
		DMSO	+0.1		−1.58	HMPT	−1.5
		CH_3CN	−0.2		−1.58	NMePy	−1.4
		HMPT	−0.4		−1.58	DMSO	−1.1
		Me_2CO	−0.1	CH_3OTs	−0.2[d]	DMF	−0.6[d]
$(CH_3O)_3PO$	1.8	DMF	−0.4	4-$NO_2C_6H_4CH_2Br$	−0.9	DMF	−1.2
4-Cl-3-$NO_2C_6H_3CF_3$	1.1	80DMSO-M	0.0	4-$NO_2C_6H_4I$	−1.58	80DMSO-M	−0.8
t-BuCl	2.2	DMF	−0.2		−1.58	CH_3NO_2	−0.6
t-BuBr	2.0	DMF	−0.3	2,4-$(NO_2)_2C_6H_3OAr$[e]	−1.8	DMF	−2.0
n-BuI	2.1	DMF	−0.3	[2,4-$(NO_2)_2C_6H_3S]_2$	−4.70	DMF	−2.3
		DMSO	0.0		−4.70	DMSO	−2.1
		CH_3CN	−0.3		−4.70	CH_3CN	−0.9
i-PrBr	2.1	DMF	−0.1		−4.70	CH_3NO_2	−1.5
		80DMSO-M	+0.1	4-Cl-3-$NO_2C_6H_3SO_2Me$	−1.34	80DMSO-M	−1.4
$C_6H_{11}Br$[e]	1.8	DMF	+0.1	2-$NO_2C_6H_4Cl$	+0.8[l]	80DMSO-M	−0.2
$C_6H_{11}I$[e]	1.7	DMF	0				
$C_6H_5CH_2Cl$	1.5	DMF	+0.15				
		80DMSO-M	+0.1				
$(i\text{-}Pr)_2POCl$	1.6	DMF	−0.3				

[a] S is the solubility in moles liter^{-1} of crystalline solutes. Saturated solutions are sometimes concentrated (*ca.* 1 *M*) and thus not ideal. [b] h/c is the Henry's law constant (mm mole^{-1} l.) for liquid and gaseous solutes, measured as described in ref 19 and in the text. [c] Values of ${}^{M}\gamma^{S}{}_{RX}$ were calculated from (8) or (9); see text. [d] OTs is *p*-toluenesulfonate; solubility was measured at 0°. [e] Ar is 4-nitrophenyl; C_6H_{11} is cyclohexyl. [f] A. Seidell, "Solubilities of Organic Compounds," Vol. 2, D. Van Nostrand Co., Inc., New York, N. Y., 1941. [g] "DMF Product Information," E. I. du Pont de Nemours and Co., Inc., Wilmington, Del., 1959. [h] "Dimethyl Sulfoxide Reaction Medium and Reactant," Chemical Products Division, Crown Zellerbach Corp., Camas, Wash., 1962. [i] Reference 13. [j] Reference 8, measured potentiometrically. [k] At 16°. [l] Saturated solution in methanol is 6 *M*, so γ is a very rough value.

Table IV. Bimolecular Reactions at 25° in Protic and Dipolar Aprotic Solvents (Reference Solvent: Methanol)

No.	Reactants	Log k^{M}[a]	Solvent	Log k^{S}/k^{M}[a]	Log ${}^{M}\gamma^{S}{}_{RX}$[b]	Log ${}^{M}\gamma^{S}{}_{Y^-}$[c]	Transn state[d]	Log ${}^{M}\gamma^{S}{}_{\ddagger}$[e]	Log ${}^{M}\gamma^{S}{}_{RX}/{}^{M}\gamma^{S}{}_{\ddagger}$[f]
1	$CH_3Cl + N_3^-$	−6.1[g]	$HCONH_2$	1.3[h]	0.1	0.2	I	−1.0	+1.1
		−6.1	DMF	3.3[g]	−0.4	4.9	I	1.2	−1.6
2	$CH_3Cl + SCN^-$	−5.8[g]	DMF	1.4[g]	−0.4	2.7	I	0.9	−1.3
3	$CH_3Br + Cl^-$	−5.2[h]	H_2O	0.1[i]	1.2	−2.5	I	−1.4	+2.6
		−5.2	DMF	4.8[j]	−0.3	6.5	I	1.4	−1.7
		−5.2	Me_2CO	5.7[j]	...	...	I	...	...
4	$CH_3Br + N_3^-$	−4.3[g]	$HCONH_2$	1.1[h]	0.2	0.2	I	−0.7	+0.9
		−4.3	DMF	3.9[g]	−0.3	4.9	I	0.7	−1.0
5	$CH_3Br + SCN^-$	−3.6[g]	DMF	1.7[g]	−0.3	2.7	I	0.7	−1.0
6	$CH_3Br + I^-$	−3.0[k]	H_2O	−0.2[i]	1.2	−1.5	I	−0.1	+1.3
		−3.0	Me_2CO	2.6[l]	...	...			
7	$CH_3I + Cl^-$	−5.5[l]	H_2O	0.05[m]	1.4	−2.5	I	−1.1	+2.5
		−5.5	$HCONH_2$	1.2[h]	0.5	0.0	I	−0.7	+1.2
		−5.5	DMF	5.9[n,o]	−0.5	6.5	I	0.1	−0.6
		−5.5	DMAC	6.4[l,o]	−0.6	7.8	I	0.8	−1.4
		−5.5	CH_3CN	4.6[h]	−0.4	6.3	I	1.3	−1.7
		−5.5	NMePy[r]	6.9[p]	−0.7	8.1	I	0.5	−1.2
		−5.5	Me_2CO	6.2[l]	−0.4	...	I	...	...
		−5.5	80DMSO-M[r]	3.7[h]	−0.3	4.2	I	0.2	−0.5
		−5.5	CH_3NO_2	4.2[q]	−0.2	4.9	I	0.5	−0.7

Table IV (*Continued*)

No.	Reactants	Log k^{Ma}	Solvent	Log k^{S}/k^{Ma}	Log $^{M}\gamma^{S}_{RX}{}^{b}$	Log $^{M}\gamma^{S}_{Y^-}{}^{c}$	Transn state^{d}	Log $^{M}\gamma^{S}_{\ddagger}{}^{e}$	Log $^{M}\gamma^{S}_{RX}/^{M}\gamma^{S}_{\ddagger}{}^{f}$
8	$CH_3I + N_3^-$	-4.1^{l}	$HCONH_2$	1.0^{h}	0.5	0.2	I	−0.3	+0.8
		−4.1	DMF	$4.6^{l,o}$	−0.5	4.9	I	−0.2	−0.3
9	$CH_3I + SCN^-$	-3.3^{l}	H_2O	-0.2^{m}	1.4	−1.2	I	0.4	+1.0
		−3.3	$HCONH_2$	0.5^{h}	0.5	−0.3	I	−0.3	+0.8
		−3.3	DMF	2.2^{l}	−0.5	2.7	I	0.0	−0.5
		−3.3	DMAC	2.5^{h}	−0.6	3.2	I	0.1	−0.7
		−3.3	CH_3CN	1.4^{h}	−0.4	2.6	I	0.8	−1.2
		−3.3	NMePy^{r}	3.5^{p}	−0.7	2.9	I	−1.3	+0.6
		−3.3	Me_2CO	$2.5^{h,s}$	−0.4	. . .	I	. . .	. . .
		−3.3	80DMSO-M^{r}	1.6^{h}	−0.3	1.6	I	−0.3	0.0
		−3.3	CH_3NO_2	1.3^{h}	−0.2	2.4	I	+0.9	−1.1
		−3.3	HCONHMe	0.9^{h}	. . .	. . .	I	. . .	. . .
10	$CH_3I + Br^-$	-4.1^{k}	H_2O	-0.3^{m}	1.4	−2.1	I	−0.4	+1.8
		−4.1	$HCONH_2$	0.7^{h}	0.5	−0.1	I	−0.3	+0.8
		−4.1	DMF	$4.2^{n,o}$	−0.5	4.9	I	0.2	−0.7
		−4.1	NMePy^{r}	5.4^{p}	−0.7	$(6.1)^{t}$	I	$(0.0)^{t}$	$(-0.7)^{t}$
		−4.1	Me_2CO	5.1^{l}	−0.4	. . .	I	. . .	. . .
11	$CH_3I + OAc^-$	-5.6^{u}	$HCONH_2$	1.4^{h}	0.5	$(0.6)^{t}$	I	$(-0.3)^{t}$	$(0.8)^{t}$
		−5.6	DMF	$6.9^{h,o,s}$	−0.5	9.2	I	1.8	−2.3
12	$CH_3I + ArO^{-\,r}$	-5.5^{u}	DMF	3.6^{u}	−0.5	$(4.1)^{t}$	I	$(0.0)^{t}$	$(-0.5)^{t}$
13	$CH_3I + 2,4\text{-}(NO_2)_2C_6H_3O^-$	-7.0^{u}	DMF	3.4^{u}	−0.5	$(3.9)^{t}$	I	$(0.0)^{t}$	$(-0.5)^{t}$
14	$CH_3I + ArS^{-\,r}$	$-1.2^{o,u}$	DMF	$2.4^{o,u}$	−0.5	$(2.9)^{t}$	I	$(0.0)^{t}$	$(-0.5)^{t}$
15	$CH_3I + SeCN^-$	$-2.4^{n,o}$	DMF	$2.2^{n,o}$	−0.5	$(2.7)^{t}$	I	$(0.0)^{t}$	$(-0.5)^{t}$
16	$CH_3I + CN^-$	-3.2^{h}	H_2O	0.0^{m}	1.4	$(-1.5)^{t}$	I	$(-0.1)^{t}$	$(1.5)^{t}$
		−3.2	$HCONH_2$	1.2^{h}	0.5	$(0.4)^{t}$	I	$(-0.4)^{t}$	$(0.9)^{t}$
		−3.2	DMF	$5.7^{h,o}$	−0.5	$(6.2)^{t}$	I	$(0.0)^{t}$	$(-0.5)^{t}$
17	$CH_3I + I^-$	-2.5^{v}	H_2O	-0.8^{m}	1.4	−1.5	I	0.7	+0.7
		−2.5	Me_2CO	3.4^{l}	−0.4	. . .	I	. . .	. . .
18	$CH_3I + OMe^-$	-3.6^{w}	DMSO	5.4^{w}	−0.5	$(5.3)^{t}$	I	$(-0.6)^{t}$	$(+0.1)^{t}$
		−3.6	80DMSO-M^{r}	3.5^{w}	−0.3	$(4.0)^{t}$	I	$(+0.2)^{t}$	$(-0.5)^{t}$
19	$CH_3OTs + N_3^-$	-3.3^{h}	H_2O	-0.4^{x}	. . .	−1.8	XVIII	. . .	+1.4
		−3.3	DMF	2.0^{h}	−0.6	4.9	XVIII	2.3	−2.9
20	$CH_3OTs + SCN^-$	-3.9^{h}	H_2O	-0.2^{x}	. . .	−1.2	XVIII	. . .	+1.0
		−3.9	DMF	0.8^{h}	−0.6	2.7	XVIII	1.3	−1.9
21	$CH_3OTs + Br^-$	-4.6^{h}	DMF	3.1^{h}	−0.6	4.9	XVIII	1.2	−1.8
22	$CH_3OTs + I^-$	-3.4^{h}	DMF	1.4^{h}	−0.6	2.6	XVIII	0.6	−1.2
23	$CH_3OTs + ArS^-$	-1.8^{h}	DMF	1.6^{h}	−0.6	$(2.9)^{t}$	XVIII	$(+0.7)^{t}$	$(-1.3)^{t}$
		−1.8	Me_2CO	$1.7^{h,s}$	. . .	. . .	XVIII	. . .	. . .
24	$n\text{-}BuBr + ArS^{-\,r}$	−3.1	Me_2CO	$2.2^{h,s}$	. . .	. . .	I	. . .	. . .
25	$CH_3S^+Me_2 + N_3^-$	-7.4^{y}	DMF	3.1^{y}	-3.1^{c}	4.9	II	−1.3	−1.8
		−7.4	CH_3CN	3.7^{y}	-1.6^{c}	4.7	II	−0.6	−1.0
		−7.4	Me_2CO	4.9^{y}	. . .	. . .	II	. . .	. . .
26	$CH_3S^+Me_2 + SCN^-$	-7.2^{y}	DMF	1.2^{y}	-3.1^{c}	2.7	II	−1.6	−1.5
27	$CH_3OPO(OMe)_2 + N_3^-$	-6.6^{h}	DMF	1.8^{h}	−0.4	4.9	I	2.7	−3.1
28	$n\text{-}BuBr + N_3^-$	-5.1^{z}	H_2O	0.8^{z}	. . .	−1.8	I	. . .	. . .
		−5.1	$HCONH_2$	1.1^{z}	0.3	0.2	I	−0.6	+0.9
		−5.1	DMF	3.4^{z}	0.0	4.9	I	1.5	−1.5
		−5.1	DMAC	3.9^{h}	−0.1	6.2	I	2.2	−2.3
		−5.1	DMSO	3.1^{z}	+0.1	3.5	I	0.5	−0.4
		−5.1	CH_3CN	3.7^{z}	−0.2	4.7	I	0.8	−1.0
		−5.1	HMPT^{r}	4.3^{z}	−0.4	7.2	I	2.5	−2.9
		−5.1	Me_2CO	$3.6^{h,s}$	−0.1	. . .	I	. . .	. . .
29	$n\text{-}BuI + Cl^-$	-6.4^{h}	DMF	5.2^{h}	−0.3	6.5	I	1.0	−1.3
		−6.4	DMSO	4.6^{h}	0.0	5.5	I	0.9	−0.9
30	$n\text{-}BuI + Br^-$	-5.5^{h}	DMSO	3.6^{h}	0.0	3.6	I	0.0	0.0
31	$n\text{-}BuI + I^-$	-4.2^{aa}	CH_3CN	1.8^{aa}	−0.3	2.4	I	0.3	−0.6
		−4.2	Me_2CO	3.1^{bb}	. . .	. . .	I	. . .	. . .
32	$n\text{-}BuI + SCN^-$	-4.5^{h}	DMF	1.9^{h}	−0.3	2.7	I	0.5	−0.8
		−4.5	DMSO	1.7^{h}	0.0	1.4	I	−0.3	+0.3
		−4.5	HMPT^{r}	3.3^{h}	. . .	3.4	I	. . .	−0.1
33	$n\text{-}BuI + N_3^-$	-4.6^{h}	DMF	4.0^{h}	−0.3	4.9	I	0.6	−0.9
		−4.6	DMSO	3.5^{h}	0.0	3.5	I	0.0	0.0
		−4.6	CH_3CN	3.1^{h}	−0.3	4.7	I	1.3	−1.6
34	$n\text{-}BuI + NO_2^-$	-5.2^{h}	DMSO	3.8^{h}	0.0	$(3.7)^{t}$	I	$(-0.1)^{t}$	$(+0.1)^{t}$
35	$i\text{-}BuBr + N_3^-$	-6.3^{h}	DMF	3.3^{j}	. . .	4.9	I	. . .	−1.6
36	$n\text{-}BuBr + C_6H_5S^-$	-2.3^{h}	DMF	4.0^{h}	0.0	$(4.9)^{t}$	I	$(0.9)^{t}$	$(-0.9)^{t}$
37	$i\text{-}PrBr + C_6H_5S^-$	-3.8^{h}	DMF	3.1^{h}	−0.1	$(4.9)^{t}$	III	$(1.7)^{t}$	$(-1.8)^{t}$
38	$t\text{-}BuBr + C_6H_5S^-$	-3.5^{h}	DMF	$<0.5^{h}$	−0.3	$(4.9)^{t}$	IV	$(>4.1)^{t}$	$(<-4.4)^{t}$
39	$t\text{-}BuBr + C_6H_5S^-$	-3.3^{h}	DMF	1.6^{h}	−0.3	$(4.9)^{t}$	V	$(3.0)^{t}$	$(-3.3)^{t}$
40	$i\text{-}PrBr + N_3^-$	-5.1^{h}	DMF	2.7^{h}	−0.1	4.9	III	2.1	−2.2
41	$CH_3Br + OMe^-$	-3.8^{h}	80DMSO-M^{r}	3.5^{h}	0.0	$(4.0)^{t}$	I	(0.5)	$(-0.5)^{t}$
42	$i\text{-}PrBr + OMe^-$	-5.7^{h}	80DMSO-M^{r}	3.3^{h}	0.1	$(4.0)^{t}$	XVI	$(0.6)^{t}$	$(-0.5)^{t}$
43	$c\text{-}C_6H_{11}Br^{r} + N_3^-$	-6.8^{h}	DMF	2.8^{h}	0.1	4.9	III	2.2	−2.3
44	$c\text{-}C_6H_{11}Br^{r} + N_3^-$	-7.7^{h}	DMF	2.9^{h}	0.1	4.9	V	2.1	−2.2
45	$c\text{-}C_6H_{11}I^{r} + N_3^-$	-6.5^{h}	DMF	3.9^{h}	0.0	4.9	III	1.0	−1.0
46	$c\text{-}C_6H_{11}I^{r} + N_3^-$	-6.7^{h}	DMF	3.4^{h}	0.0	4.9	V	1.5	−1.5
47	$c\text{-}C_6H_{11}OTs^{r} + ArS^-$	-2.7^{h}	Me_2CO	$-0.3^{h,s}$	. . .	. . .	III	. . .	. . .

Table IV (*Continued*)

No.	Reactants	Log k^{M}[a]	Solvent	Log k^S/k^M[a]	Log ${}^M\gamma^S_{RX}$[b]	Log ${}^M\gamma^S_{Y^-}$[c]	Transn state[d]	Log ${}^M\gamma^S_{\ddagger}$[e]	Log ${}^M\gamma^S_{RX}/{}^M\gamma^S_{\ddagger}$[f]
48	c-$C_6H_{11}OTs$[r] + ArS^-	−2.5[h]	Me_2CO	−0.4[h,s]	...	...	V	...	...
49	4-$NO_2C_6H_4CH_2Cl$ + N_3^-	−4.2[cc]	Me_2CO	3.5[r,cc]	...	...	I	...	...
50	4-$NO_2C_6H_4CH_2Br$ + N_3^-	−2.4[h]	DMF	3.9[h]	−1.2	4.9	I	−0.2	−1.0
		−2.4	Me_2CO	4.2[s,cc]	...	...	I	...	...
51	$C_6H_5CH_2Cl$ + N_3^-	−4.3[h]	DMF	2.4[h]	0.2	4.9	VI	2.7	−2.5
52	$C_6H_5CH_2Cl$ + OMe^-	−4.6[dd]	80DMSO-M[r]	2.5[dd]	0.1	(4.0)[t]	VI	(1.4)[t]	(−1.3)[t]
53	*trans*-TsCH═CHCl[ee] + N_3^-	−2.8[h]	DMF	3.2[h]	−1.1	4.9	VII	0.6	−1.7
54	$CH_3CO_2C_6H_4NO_2$-4 + N_3^-	−1.6[h]	H_2O	0.2[ff]	...	−1.6	VIII	...	+1.8
		−1.6	DMF	1.4[h]	−0.9	4.9	VIII	2.6	−3.5
55	(i-Pr)$_2$POCl + OAr^-	−1.6[h]	DMF	2.3[h]	−0.3	(4.1)[t]	IX	(1.5)[t]	(−1.8)[t]
56	4-$NO_2C_6H_4F$ + N_3^-	−7.2[gg]	$HCONH_2$	0.8[h]	...	0.2	X	...	+0.6
		−7.2	DMF	4.5[gg]	...	4.9	X	...	−0.4
		−7.2	DMAC	5.0[gg]	...	6.2	X	...	−1.2
		−7.2	DMSO	3.9[gg]	...	3.5	X	...	+0.4
		−7.2	CH_3CN	3.9[gg]	...	4.7	X	...	−0.8
		−7.2	CH_3NO_2	3.5[gg]	...	4.6	X	...	−1.1
		−7.2	TMS[r]	4.5[h]	...	5.4	X	...	−0.9
		−7.2	NMePy[r]	5.3[h]	...	6.3	X	...	−1.0
		−7.2	HMPT[r]	7.3[h]	...	7.2	X	...	+0.1
		−7.2	Me_2CO	4.9[s,gg]	...	...	X	...	...
57	4-$NO_2C_6H_4F$ + $C_6H_5S^-$	−3.8[hh]	DMF	4.4[g,o]	...	(4.9)[t]	X	...	(−0.5)[t]
58	4-$NO_2C_6H_4I$ + N_3^-	−9.5[gg]	DMF	4.2[gg]	−1.2	4.9	X	−0.5	−0.7
		−9.5	CH_3CN	3.8[h]	−0.4	4.7	X	+0.5	−0.9
		−9.5	NMePy[r]	4.7[h]	−1.4	6.3	X	+0.2	−1.6
		−9.5	HMPT[r]	6.3[h]	−1.5	7.2	X	−0.6	−0.9
59	4-$NO_2C_6H_4I$ + $C_6H_5S^-$	−4.2[ii]	DMF	3.6[ii]	−1.2	(4.9)[t]	X	(+0.1)[t]	(−1.3)[t]
60	4-$NO_2C_6H_4I$ + $C_6H_5O^-$	−8.7[ii]	DMF	7.0[h,jj]	−1.2	(7.7)[t]	X	(−0.5)[t]	(−0.7)[t]
61	2,4-$(NO_2)_2C_6H_3Cl$ + N_3^-	−3.3[g]	DMF	4.1[h,q]	<−1	4.9	X	<−0.2	−0.8
62	2,4-$(NO_2)_2C_6H_3Cl$ + SCN^-	−6.5[g]	DMF	2.5[g]	<−1	2.7	X	<−0.8	−0.2
63	2,4-$(NO_2)_2C_6H_3Br$ + SCN^-	−5.5[g]	DMF	2.0[g]	...	2.7	X	...	−0.7
64	2,4-$(NO_2)_2C_6H_3Br$ + I^-	−8.5[n]	DMF	2.6[n]	...	2.6	X	...	−0.0
65	2,4-$(NO_2)_2C_6H_3I$ + SCN^-	−5.4[g]	NMePy[r]	2.0[h]	...	2.9	X	...	−0.9
		−5.4	DMF	1.7[g]	...	2.7	X	...	−1.0
		−5.4	Me_2CO	2.8[gg]	...	...	X	...	...
		−5.4	$HCONH_2$	−0.3[h]	...	−0.3	X	...	0.0
		−5.4	DMAC	2.1[h]	...	3.2	X	...	−1.1
		−5.4	CH_3CN	1.6[h]	...	2.6	X	...	−1.0
		−5.4	DMSO	1.2[h]	...	1.4	X	...	−0.2
		−5.4	CH_3NO_2	1.3[h]	...	2.4	X	...	−1.1
		−5.4	TMS[r]	1.7[h]	...	2.6	X	...	−0.9
66	2,4-$(NO_2)_2C_6H_3I$ + Cl^-	−10.2[h]	DMF	6.5[h]	...	6.5	X	...	0.0
		−10.2[h]	HMPT[r]	8.8[h]	...	8.8	X	...	0.0
67	2,4-$(NO_2)_2C_6H_3I$ + Br^-	−9.0[h]	DMF	4.9[h]	...	4.9	X	...	0.0
68	2,4-$(NO_2)_2C_6H_3OAr$ + N_3^-	−2.7[h]	DMF	3.4[h]	−2.0	4.9	X	−0.5	−1.5
69	2-Cl-3,5-$(NO_2)_2C_6H_2CO_2^-$ + N_3^-	−4.6[h, kk]	DMF	3.3[h, kk]	1.2[c]	4.9	XI	2.8	−1.6
70	4-Cl-3-$NO_2C_6H_3CO_2^-$ + OMe^-	−5.4[kk−mm]	80DMSO-M[r]	2.4[h,kk,ll]	...	(4.0)[t]	XII	...	(−1.6)[t]
71	2-Cl-5-$NO_2C_6H_3CO_2^-$ + OMe^-	−6.2[h,kk,ll]	80DMSO-M[r]	2.7[h, kk,ll]	...	(4.0)[t]	XI	...	(−1.3)[t]
72	4-Cl-3-$NO_2C_6H_3N^+Me_3$ + N_3^-	−4.7[kk,mm]	DMF	3.3[h,kk]	−4.6[c]	4.9	XIII	−3.0	−1.6
73	4-NO_2-malachite green + N_3^-	+4.8[nn]	DMF	>2.2[nn]	...	4.9	XV	...	>−2.7
		4.8[nn]	DMSO	>2.9[nn]	...	3.5	XV	...	>−0.6
74	4-Cl-3-$NO_2C_6H_3NMe_3^+$ + OMe^-	−2.5[h,kk]	80DMSO-M[r]	2.4[h,kk]	...	(4.0)[t]	XIII	...	(−1.6)[t]
75	4-Cl-3-$NO_2C_6H_3CF_3$ + OMe^-	−3.8[mm]	80DMSO-M[r]	3.4[h]	0.0	(4.0)[t]	X	(0.6)[t]	(−0.6)[t]
76	2-$NO_2C_6H_4Cl$ + OMe^-	−6.9[oo]	80DMSO-M[r]	3.3[h]	−0.2	(4.0)[t]	X	(0.5)[t]	(−0.7)[t]
77	4-$NO_2C_6H_4Cl$ + OMe^-	−6.4[oo]	80DMSO-M[r]	3.6[h]	...	(4.0)[t]	X	...	(−0.4)
78	4-Cl-3-$NO_2C_6H_3SO_2Me$ + OMe^-	−2.5[mm]	80DMSO-M[r]	2.8[h]	−1.4	(4.0)[t]	XIV	(−0.2)[t]	(−1.2)[t]

[a] k^M is the second-order rate constant (l. mole^{-1} sec^{-1}) for reaction in methanol; k^S is for reaction in solvent S. Log k^S = log (k^S/k^M) + log k^M. [b] From Table III. [c] From Table II unless stated otherwise. [d] Numbers refer to figures in text. [e] Calculated from log ${}^M\gamma^S_{\ddagger}$ = log ${}^M\gamma^S_{Y^-}$ + log ${}^M\gamma^S_{RX}$ − log k^S/k^M; $\ddagger$ denotes transition state. [f] Calculated from log (${}^M\gamma^S_{RX}$)(${}^M\gamma^S_{\ddagger}$) = log k^S/k^M − log ${}^M\gamma^S_{Y^-}$. [g] Reference 20. [h] This work. [i] R. H. Bathgate and E. A. Moelwyn-Hughes, *J. Chem. Soc.*, 2642 (1959). [j] D. Cook and A. J. Parker, *ibid.*, *B*, 142 (1968). [k] E. A. Moelwyn-Hughes and J. S. McKinley-McKee, *ibid.*, 838 (1952). [l] Reference 43. [m] G. C. Lalor and E. A. Molewyn-Hughes, *J. Chem. Soc.*, 2201 (1965). [n] A. J. Parker, *J. Chem. Soc.*, *A*, 220 (1966). [o] Rate constants extrapolated from data at 0° using an estimated activation energy of 16 ± 2 kcal mole^{-1} in aprotic solvents and 18 ± 2 kcal mole^{-1} in protic solvents, in line with related reactions (*cf.* Table XIII). [p] O. Virtanen, *Suomen Kemistilehti*, 257 (1966). [q] A. J. Parker, *Aust. J. Chem.*, **16**, 585, (1963). [r] Abbreviations are: NMePy = N-methyl-2-pyrrolidone, TMS = sulfolane (at 30°), 80DMSO-M = 80% v:v DMSO–methanol, HMPT = hexamethylphosphoramide, Ar = 4-nitrophenyl. [s] Using 0.03 *M* tetrabutylammonium salt, rate constants were not corrected for ion association. [t] These values are in parentheses because log ${}^M\gamma^S_{Y^-}$ is derived from a linear free-energy relationship (7) based on solvation of transition states and rate data (see text). [u] D. Cook, I. P. Evans, E. C. F. Ko, and A. J. Parker, *J. Chem. Soc.*, *B*, 404 (1966). [v] P. Beronius, *Acta Chem. Scand.*, **15**, 1151 (1961). [w] J. Murto, *Suomen Kemistilehti*, **B34**, 92 (1961). [x] R. E. Davis, *J. Amer. Chem. Soc.*, **87**, 3010 (1965). [y] I. P. Evans and A. J. Parker, unpublished data at ionic strength 3 × 10^{-3} *M*. [z] J. J. Delpuech, *Tetrahedron Lett.*, 2111 (1965). [aa] E. A. S. Cavell and J. A. Speed, *J. Chem. Soc.*, 226 (1961). [bb] E. A. S. Cavell and J. A. Speed, *ibid.*, 1453 (1960). [cc] U. Miotti, *Gazz. Chim. Ital.*, 254 (1967). [dd] E. Tommila and O. Savolainan, *Acta Chem. Scand.*, **20**, 946 (1966). [ee] *trans*-1-Chloro-2-(*p*-toluenesulfonyl)ethene. [ff] W. P. Jencks and J. Carrulio, *J. Amer. Chem. Soc.*, **82**, 1778 (1960). [gg] Reference 32. [hh] C. W. Bevan and J. Hirst, *J. Chem. Soc.*, 254 (1956). [ii] A. J. Parker, *ibid.*, 4398 (1961). [jj] Initial rate, using 0.01 *M* KOC_6H_5. Our result in footnote ii (above) is in error because we did not allow for ion association; *cf.* A. Berge and J. Ugelstadt, *Acta Chem. Scand.*, 19, 742 (1965). [kk] At zero ionic strength. [ll] At 45.6°. [mm] Reference 42c. [nn] Reference 12. [oo] Reference 42a.

solvents than by water or formamide. It is usually only strong hydrogen-bond acceptors (like small anions) which are more solvated by protic solvents.[16]

Solvation of RX.[18,19] Some values of log ${}^{M}\gamma^{S}{}_{RX}$ for transfer of nonelectrolytes RX from reference solvent methanol at 25° are in Table III. They were calculated as in (8) from solubilities, S (mole l.$^{-1}$), of solids or as in (9) from Henry's law constants, h/c (mm l. mole^{-1}), of gases or liquids. Distribution experiments and vpc analysis of the vapor phase above solutions of known concentration at atmospheric pressure gave results comparable (± 0.15 log unit) to the values from eq 8 and 9. Some of the solubilities are calculated

$$\log S^{M} - \log S^{S} = \log {}^{M}\gamma^{S}{}_{RX} \qquad (8)$$

$$\log\left(\frac{h}{c}\right)^{S} - \log\left(\frac{h}{c}\right)^{M} = \log {}^{M}\gamma^{S}{}_{RX} \qquad (9)$$

from rather concentrated (*ca.* 1 *M*) nonideal solutions, and the technique[19] used to determine Henry's law constants, although fast and efficient, is not the most precise available. The activity coefficients are not intended for manipulations requiring considerable precision. We would emphasize that our purpose is to survey large (10^{2}–10^{6}) solvent effects on the rates of a variety of reactions, to develop an over-all explanation for these effects, and to derive linear free-energy relationships, which predict behavior in new circumstances. An error of ± 0.15 log unit in the solvent activity coefficients of Table III does not interfere with our treatment of the rate data. Most values in Table III are more precise than this.

It is sometimes forgotten that solvation of RX may be an important factor in determining the rate of (1) in different solvents. Although it is true that ions have much greater solvation energies than nonelectrolytes, one should not concentrate only on ions, because *differences* in solvation are the important criteria.[5] As the reactants Y^{-} and RX of (1) are transferred through a series of strongly solvating media, of comparable dielectric constant, the standard chemical potential of RX may change much more than does that of the anion Y^{-}. One has only to recall the low solubility of many organic compounds in water and their extreme solubility in DMF or acetone to appreciate this. As shown in Table III, values of ${}^{M}\gamma^{S}{}_{RX}$ range from at least $10^{4.2}$ to $10^{-2.3}$. Organic compounds, especially the large ones such as ferrocene and 2,4-dinitrochlorobenzene, are much less soluble in water and formamide than in methanol. Polar nonelectrolytes are 10^{0} to at least 10^{2} times more soluble in dipolar aprotic solvents than in methanol. The greater solubility in dipolar aprotic solvents is most pronounced for large polar solutes (*e.g.*, nitro aromatics) and least for alkyl halides with large alkyl chains. Hexamethylphosphoramide and N-methylpyrrolidone are excellent solvents for polar molecules, exceeding DMF or DMSO in this respect.

The most likely qualitative explanation for the data in Table III lies in the fact, already mentioned, that water and formamide, and to a lesser extent methanol, have strong structures involving hydrogen bonds between rather small molecules, whereas dipolar aprotic solvents have weaker structures and high dipole moments and are very polarizable. Thus polar, polarizable, large solutes are much more solvated by dipolar aprotic than by protic solvents.

Remembering that methanol is a good H-bond donor and DMF is an excellent H-bond acceptor, we expect that polar nonelectrolytes, RX, which are strong hydrogen bond acceptors (*e.g.*, ketones, sulfones), would have log ${}^{M}\gamma^{D}{}_{RX}$ less negative than would those which are strong hydrogen bond donors (*e.g.*, phenols).[4] There is not sufficient data in Table III to substantiate this prediction, however.

Solvation of Cations.[4] Some of the substrates, RX, of eq 1 are cations. Values of log ${}^{M}\gamma^{S}{}_{M^{+}}$ for cations M^{+} are in Table II. They will not be discussed at length here; it is suffice to say that small cations are very well solvated by HMPT, DMF, and DMSO and are well solvated by acetonitrile, formamide, and water, relative to solvation by methanol. Some qualitative reasons for this have been given previously.[4] Silver cation has very strong and apparently specific interactions with N-methylpyrrolidone, formamide, DMF, DMSO, CH_3CN, DMAC, and HMPT, but the interactions with methanol, water, sulfolane, or nitromethane are much weaker. Large "organic" cations (*e.g.*, NBu_4^{+}) are very poorly solvated by water but are well solvated by dipolar aprotic solvents, relative to solvation by methanol.

Solvation of Transition States $YRX^{\neq}$.[5,20] Table IV contains rate data (log k^{M} and log k^{S}/k^{M}) and solvent activity coefficients for the reactants (log ${}^{M}\gamma^{S}{}_{RX}$ and log ${}^{M}\gamma^{S}{}_{Y^{-}}$) in 78 bimolecular reactions in protic and in dipolar aprotic solvents. Solvent activity coefficients for most of the 15 types of transition state have been calculated from eq 2 and are also in Table IV. We believe that these transition states can be represented by the conventional structures I–XVI. In these structures, the lengths of the partial bonds (one to six dots) indicate qualitatively the extent of covalent character in the bond and, where partial charge is shown, the extent to which that charge is developed. The species have the over-all charge recorded below their structure. Thus $A\cdots\cdots B^{\delta-}$ (charge -1) indicates an *anion* with a very poorly developed bond between A and B with considerable negative charge localized on B. $A\cdot\cdot B^{\delta-}$ (charge 0) indicates an uncharged species with a well-developed partial bond between A and B and little charge localized on B. We think that transition states VII–XIV are for the rate-determining step in effectively irreversible multistep reactions, proceeding through rather high-energy intermediates, but have not

---

[16] The transition from small to large anions is, of course, continuous, and there are anions (*e.g.*, F^{-} and OH^{-}) which we have found difficult to study because of solubility problems and ion association. These must be $\gg 10^{8}$ times more solvated by protic solvents than by some dipolar aprotic solvents.[4] There are also large anions (*e.g.*, I_3^{-}) which are $>10^{3}$ times more solvated by some dipolar aprotic than by protic solvents. The line of demarcation between protic (*e.g.*, N-methylformamide) and dipolar aprotic (*e.g.*, nitromethane) is of course not a sharp one. We have arbitrarily distinguished between dipolar aprotic (*e.g.*, acetone) and aprotic (*e.g.*, benzene) simply in terms of dielectric constant >15. Nevertheless the classification of anions as large or small and as strong or weak hydrogen bond acceptors, and of solvents as protic or dipolar aprotic, is a useful concept. Followers of the hard and soft acids and bases principle[17] may find it easy to think in terms of "hard" and "soft" anions in "hard" and "soft" solvents.

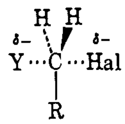
[17] R. G. Pearson and J. Songstad, *J. Amer. Chem. Soc.*, **89**, 1827 (1967).

[18] O. Dimroth, *Ann.*, **377**, 127 (1910).

[19] E. Grunwald and S. Winstein, *J. Amer. Chem. Soc.*, **70**, 846 (1948).

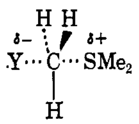
[20] B. O. Coniglio, D. E. Giles, W. R. McDonald, and A. J. Parker, *J. Chem. Soc., B*, 152 (1966).

had sufficient experience with transition states VIII and IX to know whether bond forming (as shown) or bond breaking takes place in the rate-determining transition state. Whatever the true situation, the transition states VIII and IX are thought to be close to the highly endoenergetic intermediate, so our interpretation is much the same, no matter which step is rate determining. Some of the representations, I–XVI, were drawn after considering the discussion which follows, but all are reasonable in terms of current mechanistic thinking.[21,22]



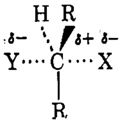
I

synchronous SN2 (charge −1)



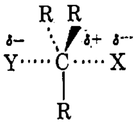
II

synchronous SN2 (charge 0)



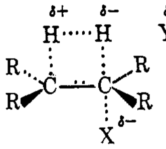
III

secondary carbonium SN2 (charge −1)



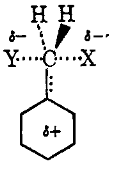
IV

tertiary carbonium SN2 (charge −1)



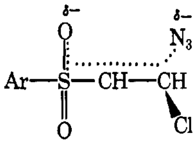
V

secondary or tertiary E2C (charge −1)



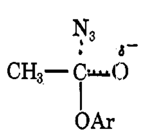
VI

benzyl carbonium SN2 (charge −1)



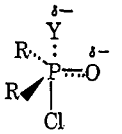
VII

vinyl SN2 (charge −1)



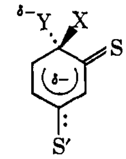
VIII

carbonyl SN2 (charge −1)



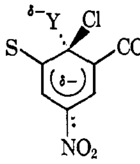
IX

phosphorus SN2 (charge −1)



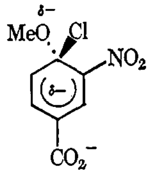
X

SNAr (charge −1)



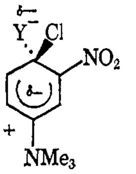
XI

SNAr (charge −2)



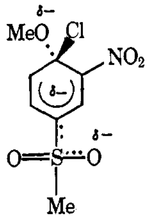
XII

SNAr (charge −2)



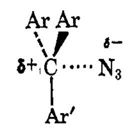
XIII

SNAr (charge 0)



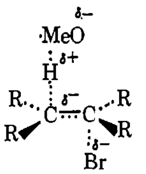
XIV

SNAr (charge −1)



XV

XV addition (charge 0)



XVI E2H (charge −1) (limiting)

It must be realized at the outset that these transition-state "structures" may change more drastically with solvent transfer than do the shape and the partition functions of real species.[11,20] A transition state can, in principle, exist at any point along the reaction coordinate. Its position along this coordinate will surely change with solvent transfer. We believe that it is legitimate, however, to take model structures (I–XVI) for bimolecular transition states and discuss expected solvent effects on the basis of these structures, *provided that the reaction has the same basic mechanism (e.g., SN2) in each solvent considered.* After all, "real species" also change their "structure" and partition functions with solvent transfer or from the crystal to the gas phase, as evidenced for example by changes in their spectra, but chemists still use the same representation for these species in all environments.

The major purpose of this paper is to see to what extent the change in the standard chemical potential of bimolecular transition states, $YRX^{\neq}$, with transfer from methanol to other solvents, depends on the nature of the entering group, Y, the attacked group, R, the leaving group, X, the charge developed on these groups in the transition state, C, the solvent receiving the transition state from methanol, S, and the geometry, G, of $YRX^{\neq}$ (SN2, E2H, E2C, etc.). The effect of any one of these variables can only be demonstrated if the others are held constant, but R, C, and G are rather closely interrelated so that a rigorous treatment is difficult.

In the Tables V–X, which we use to illustrate our arguments, we use a mathematical symbolism which attempts in part to follow the principles outlined by Leffler and Grunwald.[11] The comparisons are for systems at 25° in solution, so that T and P are understood to be constant. Thus a column as in Table V, headed δ_X-(log ${}^{M}\gamma^{DMF}_{N_3,MeX}$)$_{SN2,C}$ shows the changes in the standard chemical potential of a series of SN2 transition states, $N_3CH_3X^{\neq}$, with solvent transfer from methanol to DMF. The Y group (N_3), the R group (CH_3), the geometry (SN2), the solvent (DMF), and the charge distribution (−1) over Y, R, and X remain constant throughout the series of X groups.

The following points from Table IV will be discussed at this time.

1. *Changes in the standard chemical potential of SN2 and E2C transition states, with transfer from methanol to dipolar aprotic solvents, depend on the nature of the entering nucleophile and the displaced group.* The observation has been discussed for a few SN2 reactions, but at that time we only assumed that ${}^{0}\gamma^{S}_{RX}$ was constant for different X groups in the molecule RX.[20] Since this assumption now proves to be roughly correct (Table III), the previous discussion[20] is still valid, when applied to the new results in Table V. It should be noted that the conclusions reached previously and those which follow in this section are *quite independent of the validity of our extrathermodynamic assumptions.* The differences in Table V remain unchanged, although the actual numbers may be modified by a constant amount, if a better assumption becomes accepted.

In Table V, the presentation is in terms of leaving-group (δ_X) and entering-group (δ_Y) effects, but this is artificial because, in the reverse reactions, the leaving and entering groups switch roles, although the transition states remain the same for the forward as for the backward reaction.

It is expected that anionic and uncharged transition states, $YRX^{\neq}$, will behave in exactly the same way as

---

[21] J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1962; A. Streitwieser, Jr., *Chem. Rev.*, **56**, 573 (1956).

[22] C. K. Ingold, "Structure and Mechanism in Organic Chemistry," G. Bell and Sons, London, 1953.

Table V. Effect of Entering Group, Y, and Leaving Group, X, on Solvation of S_N2 Transition States, $YRX^{\ddagger}$ (Reference Solvent: Methanol at 25°)

Leaving group (X) effects			Entering group (Y) effects			Model[b]	
No.[a]	$YRX^{\ddagger}$	$\delta_X(\log {}^M\gamma^{DMF}{}_{N_3MeX})_{S_N2}{}^d$	No.[a]	$YRX^{\ddagger}$	$\delta_Y(\log {}^M\gamma^{DMSO}{}_{YBuI})_{S_N2,C}{}^e$	YRX	$\delta_X(\log {}^M\gamma^{DMSO}{}_{XAgX})_C{}^e$
27	$N_3CH_3OPO(OMe)_2^-$	2.7	29	$ClBuI^-$	0.9	$ClAgCl^-$	−0.6
19	$N_3CH_3OTs^-$	2.3	30	$BrBuI^-$	0.0	$BrAgBr^-$	−1.6
1	$N_3CH_3Cl^-$	1.2	33	N_3BuI^-	−0.0	$IAgI^-$	−3.1
4	$N_3CH_3Br^-$	0.7	32	$NCSBuI^-$	−0.3		
8	$N_3CH_3I^-$	−0.2					
25	$N_3CH_3SMe_2$	−1.3			$\delta_Y(\log {}^M\gamma^{CH_3CN}{}_{YBuI})_{S_N2,C}{}^e$		
			33	N_3BuI^-	+1.3		
		$\delta_X(\log {}^M\gamma^{DMF}{}_{NCSMeX})_{S_N2}{}^d$	31	$IBuI^-$	+0.3		
20	$NCSCH_3OTs^-$	1.3					
2	$NCSCH_3Cl^-$	0.9			$\delta_Y(\log {}^M\gamma^{DMF}{}_{YMeBr})_{S_N2,C}{}^e$		$\delta_X(\log {}^M\gamma^{DMF}{}_{XAgX})_C{}^e$
			3	$ClCH_3Br^-$	1.4	$ClAgCl^-$	−0.2
5	$NCSCH_3Br^-$	0.7	4	$N_3C_3HBr^-$	0.7	$BrAgBr^-$	−1.2
9	$NCSCH_3I^-$	0.0	5	$NCSCH_3Br^-$	0.7	$IAgI^-$	−2.7
26	$NCSCH_3SMe_2$	−1.6					
			10	ICH_3Br^-	0.2		$\log {}^M\gamma^{DMF}{}_{I_3}$
		$\delta_X(\log {}^M\gamma^{DMF}{}_{N_3C_6H_{11}X})_{E2,C}{}^e$				III^-	−2.0
44[c]	$N_3C_6H_{11}Br^-$	2.1[c]					
46[c]	$N_3C_6H_{11}I^-$	1.5[c]					

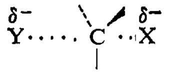
[a] Numbers refer to the appropriate reaction in Table IV. [b] These are solvent activity coefficients from Table II for real anions, which are regarded as models for the transition states (see text). [c] These are elimination reactions and the data are for E2C-like transition states; C_6H_{11} is cyclohexyl. [d] The charge distribution (*C*) is not constant in this set (see text). [e] The charge distribution on Y, R, and X is assumed to be constant within this set (see text and ref 20).

"real" anions and nonelectrolytes of comparable structure upon solvent transfer. In one sense, the real anions, $HalAgHal^-$ and Hal_3^-, can be thought of as models of transition states for S_N2 displacements of halide ion, by halide ion, from silver and halogen, respectively. Their behavior is compared in Table V with that of real transition states. As already noted,[20] one cannot concentrate on only one "end" of a transition state; solvation of the whole species $YRX^{-\ddagger}$ must be taken into account.

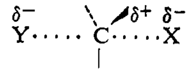
If the charge distribution over X, R, and Y remains effectively uniform, then we would expect[4-8, 20] that, for the situation where S is a particular dipolar aprotic solvent, $\delta_X(\log {}^M\gamma^S{}_{YRX^{\ddagger}})_{Y,R,S_N2,C}$, $\delta_Y(\log {}^M\gamma^S{}_{YRX})_{X,R,S_N2C}$, and $\delta_X(\log {}^M\gamma^S{}_{YRX^{\ddagger}})_{Y,R,E2,C}$ for transition states and $\delta_X(\log {}^M\gamma^S{}_{XAgX})_C$ for real anions, AgX_2^-, would be most positive (*i.e.*, well solvated by methanol) for the species in which X or Y was the most powerful hydrogen bond acceptor and least polarizable. This is observed in Table V for those cases where δ_X or δ_Y is a change through a series of halogens or halogenoids whose anions show increasing size and polarizability, but decreasing charge density and thus ability to accept hydrogen bonds (*i.e.*, Cl, N_3, Br, SCN, I). Where X or Y is chlorine, more positive values are observed within a set than when X or Y is iodine. This is true no matter whether we consider real anions or transition-state anions. The complex anion as a whole is smaller and a better hydrogen bond acceptor if it contains chlorine than is the case for an equivalent anion containing iodine.

We would emphasize that the expected behavior[20] outlined above is only observed (Table V) when δ_X or δ_Y involves halogen or halogenoids. When the leaving groups are dimethyl phosphate or tosylate anions or dimethyl sulfide, the behavior of transition states on solvent transfer is more difficult to account for. The OTs and $OP(OMe)_2$ groups are large, and the tosylate anion (and presumably $OP(OMe)_2^-$) is much less susceptible to solvent transfer than are chloride or bromide ions (Table II). Thus for a uniform negative charge distribution, the anion $N_3MeX^{-\ddagger}$ should be[20] less solvated by DMF relative to methanol when X = Cl or Br than when X = OTs or $OP(OMe)_2$. However, $\delta_X(\log {}^M\gamma^{DMF}{}_{N_3MeX})_{S_N2}$ is less positive (*i.e.*, more solvated by DMF) for X = Cl or Br than for X = OTs or $OP(OMe)_2$ (Table V). The only conclusion is that the charge distribution and/or the geometry of the transition state is not constant for a change in X from halogen to tosylate or $OP(OMe)_2$.

Hoffmann[23] has noticed that S_N2 and E2 reactions of tosylates have transition states whose position along the reaction coordinate seems to be very sensitive to reaction conditions. Phosphate esters may behave similarly. Two reasons for values of $\delta_X(\log {}^M\gamma^{DMF}{}_{YMeX})_{Y,S_N2}$ for X = OTs or $OP(OMe)_2$ in Table V being more positive than expected[20] are based on structures XVII and XVIII. Both assume that the negative charge localized on Y and/or X is greater when X is OTs or $OP(OMe)_2$ than when Y and/or X is halogen or halogenoid.



XVII (charge −1)



XVIII (charge −1)

In XVII, the transition states for these highly exoenergetic reaction occur early[24] along the reaction coordinate[11] in a synchronous process, in which no positive charge is developed at the carbon atom.[21,22] In the "loose" transition state XVIII, bond breaking is ahead of bond forming and there is some carbonium ion character at the methyl carbon atom. This could be described as a carbonium ion S_N2 mechanism. Both transition states allow considerable negative charge to be localized on the entering group, Y^-, but transition state XVIII also allows considerable negative charge to be localized on the tosylate or phosphate group (X). Thus these transition-state anions are good H-bond acceptors and are relatively well solvated by protic solvents, for reasons already given. In the limit of XVII (*i.e.*, very early on the reaction coordinate) where Y and RX have the same charge distribution in the transition

---

(23) H. M. R. Hoffmann, *J. Chem. Soc.*, 6753, 6762 (1965).
(24) G. S. Hammond, *J. Amer. Chem. Soc.*, 77, 334 (1955).

Table VI. Solvation of Selected SN2 and SNAr Transition-State Anions. Effect of Solvent Variation at 25° [a] (Reference Solvent: Methanol)

Reaction no.[a]	Transition-state YRX	Solvent										
		H_2O	$HCONH_2$	HMPT	DMSO	DMF	CH_3OH	80DMSO-M	NMePy	CH_3NO_2	DMAC	CH_3CN
$\delta_S(\log {}^M\gamma^S_{YRX})_{Y,R,X,S_NAr,C}$[f]												
56	N_3ArF^- [c]	...	...	−1.6[d]	−1.5[d]	−0.8[d]	0.0	...	−0.4[d]	+0.5[d]	...	+0.4[d]
58	N_3ArI^-	...	...	−0.6	...	−0.5	0.0	...	+0.2	...	...	+0.5
$\delta_S(\log {}^M\gamma^S_{YRX})_{Y,R,X,S\ 2,C}$[f]												
28	N_3BuBr^-	...	−0.6	+2.5	+0.5	+1.5	0.0	...	...	...	+2.2	+0.8
32	$NCSBuI^-$	...	...	−0.3[e]	−0.3	+0.5	0.0	...	...	...	...	...
33	N_3BuI^-	...	...	...	0.0	+0.6	0.0	...	...	...	...	+1.3
9	$NCSCH_3I^-$	+0.4	−0.3	...	...	+0.0	0.0	−0.3	−1.3	+0.9	+0.1	+0.8
7	$ClCH_3I^-$	−1.1	−0.7	...	...	+0.1	0.0	+0.2	+0.5	+0.5	+0.8	+1.3
$\delta_S(\log {}^M\gamma^S_{ClAgCl})_C$[f]												
Model	$ClAgCl^-$ [b]	−2.9	...	−2.5	−0.6	−0.2	0.0	...	0.0	+0.1	+0.2	+0.9

[a] Data from Table IV unless stated otherwise. [b] From Table II. [c] Ar is 4-nitrophenyl. [d] Values estimated on the assumption that 4-nitrofluorobenzene and 4-iodonitrobenzene have comparable solvent activity coefficients (*cf.* Table III). [e] Rough value, on the assumption that butyl iodide and butyl bromide have comparable solvent activity coefficients. [f] The variables Y, R, and X, mechanism, and charge distribution are held constant across each horizontal row, but vary down each column.

state as in the reactant state, the solvent effect on rate will be very small.

We cannot distinguish between transition states XVII and XVIII on the observations recorded in Table V, but intuitively we favor XVIII. We recall the notorious instability of tertiary alkyl tosylates,[25] which apparently ionize (SN1) much more readily than do tertiary alkyl halides and note that the nucleophilicity of azide ion, relative to halide ions, in methanol, is much greater toward tosylates than toward alkyl halides (Table IV). We have noted in other reactions[26] that azide ion is most nucleophilic when it is attacking carbon which has considerable positive charge in the transition state. Transition state XVIII is in line with a later discussion about primary, secondary, and tertiary alkyl transition states (*vide infra*). It may be that alkyl tosylates and phosphates have a greater tendency to react by carbonium ion SN2 mechanisms than do alkyl halides; *i.e.*, bond breaking gets further ahead of bond forming with the esters than with the halides.

The transition state for displacement of dimethyl sulfide from the trimethylsulfonium cation by an anion is best modeled by an ion pair or a polar molecule.[27,28] The value of log $^M\gamma^{DMF}_{N_3CH_3SMe_2^{\ddagger}}$ is −1.3, which is only slightly more negative than we would expect for log $^M\gamma^{DMF}_{CH_3N_3}$ + log $^M\gamma^{DMF}_{(CH_3)_2S}$, *i.e.*, the polar products of reaction. The change in charge type from −1 to 0 is the main reason for the more negative value of $\delta_X(\log {}^M\gamma^{DMF}_{N_3MeX})_{S_N2}$ when X is S^+Me_2 compared with X = I. Most anions have log $^M\gamma^{DMF}_{ion}$ positive (Table II) whereas most polar nonelectrolytes have log $^M\gamma^{DMF}_i$ negative (Table III).

2. *The solvent activity coefficients of transition-state anions for SN2 reactions of primary alkyl halides and for SNAr reactions of aryl halides change by up to 10^3 with solvent transfer. A model transition state, ClAgCl⁻, shows related behavior.* The evidence is in Table VI where sets of data are presented as $\delta_S(\log {}^M\gamma^S_{YRX^{\ddagger}})_{Y,R,X,S_N2,C}$ and $\delta_S(\log {}^M\gamma^S_{YRX})_{Y,R,X,S_NAr,C}$ for a number of transition states in various solvents. It is not possible to set up a universal order of "transition-state solvating power" on the limited evidence available. It would seem that acetonitrile and nitromethane solvate transition-state anions less strongly than many other solvents. DMSO and HMPT solvate SNAr transition-state anions (and nitro aromatic compounds, Table III) considerably more strongly than does methanol, but this is not the case for the smaller, less polarizable SN2 transition-state anions. The behavior of $ClCH_3I^{-\ddagger}$ (*i.e.*, $\delta_S(\log {}^M\gamma^S_{ClMeI})_{S_N2,C}$ through a number of solvents is not unlike that of the real anion $ClAgCl^-$ (*i.e.*, $\delta_S(\log {}^M\gamma^S_{ClAgCl})_C$). The conclusions reached here depend on the validity of our extrathermodynamic assumptions,[1] two of which involve assumptions about solvation of SN2 and SNAr transition-state anions.

3. *Rates of SN2 reactions of secondary alkyl and benzyl halides are less susceptible to protic–dipolar aprotic solvent transfer than are rates of SN2 reactions of primary alkyl, p-nitrobenzyl, and methyl halides, because of transition-state solvation effects.* Two possible explanations for the data presented in Tables IV and VII are represented by transition-state structures XVII and XVIII. In XVII, as already discussed, the SN2 reactions of alkyl halides are synchronous, but, as steric resistance to its formation increases, the transition state comes increasingly early along a reaction coordinate, which is recording loss of charge on Y with corresponding development of charge on the leaving group X. The transition state comes earlier in the order of transition states: Y-*i*-PrX‡ > Y-*n*-BuX > YCH$_3$X‡. The more hindered the situation the greater the tendency of Y and X in the transition state to have charge distribution tending toward that in the reactants; *i.e.*, Y⁻ carries localized negative charge but X carries little charge. In this way transition state and reactants tend toward being similarly solvated, and the solvent effect on rate is smaller than in a less hindered situation.

There are two objections to such an "explanation" in terms of steric hindrance. The *p*-nitrobenzyl, *p*-methylbenzyl, *p*-chlorobenzyl, and benzyl systems should have much the same steric resistance to formation of the SN2 transition state, and yet the corresponding transition states behave very differently with solvent transfer. An electronic explanation, in accord with the observed substituent effects, seems more likely. A

---

(25) H. M. R. Hoffmann, *J. Chem. Soc.*, 6748 (1965).

(26) A. J. Parker, unpublished work.

(27) I. P. Evans and A. J. Parker, *Tetrahedron Lett.*, 163 (1966).

(28) Y. C. Mac, W. A. Millen, A. J. Parker, and D. W. Watts, *J. Chem. Soc., B*, 525 (1967).

Table VII. Solvation of Transition-State Anions for SN2 Reactions at Saturated Carbon. Effect of Substituents on Carbon (Reference Solvent: Methanol at 25°)[a,d]

Reaction no.[a]	R in YRX‡ [b]	Structure[c]	$\delta_{R,G}(\log {}^{M}\gamma^{DMF}{}_{N_3RBr})_{SN2}$[f]
50	4-$NO_2C_6H_4CH_2$	I	−0.2
4	HCH_2	I	0.7
28	*n*-$PrCH_2$	I	1.5
40	Me_2CH	III	2.1
43	Cyclohexyl	III	2.2
			$\delta_{R,G}(\log {}^{M}\gamma^{DMF}{}_{N_3RI})_{SN2}$[f]
8	HCH_2	I	−0.2
33	*n*-$PrCH_2$	I	0.6
45	Cyclohexyl	III	1.0
			$\delta_{R,G}(\log {}^{M}\gamma^{DMF}{}_{N_3RCl})_{SN2}$[f]
1	HCH_2	I	1.2
51	$C_6H_5CH_2$	VI	2.7
			$\delta_{R,G}(\log {}^{M}\gamma^{60DMSO \cdot M}{}_{MeORCl})_{SN2}$[f] $- C$[d]
..	4-$NO_2C_6H_4CH_2$	I	−2.9[d,e]
..	4-$ClC_6H_4CH_2$	VI	−1.7[d,e]
..	$C_6H_5CH_2$	VI	−1.6[d,e]
..	4-$CH_3C_6H_4CH_2$	VI	−1.4[d,e]

[a] Data from Table IV unless stated otherwise. [b] Y is the entering group and X is the leaving group. [c] Numbers refer to structures in text. [d] Assuming that solvent activity coefficients of these benzyl chlorides are the same so that $\log {}^{M}\gamma^{60DMSO \cdot M}{}_{RX} + \log {}^{M}\gamma^{60DMSO \cdot M}{}_{OMe^-}$ is a constant, *i.e.*, *C*. This gives differences $\delta_{R,G}$, which are suitable for discussion. [e] Rate data from E. Tommila and A. Savolainan, *Acta Chem. Scand.*, **20**, 946 (1966), for the solvent 60% v:v DMSO–methanol. [f] Both the nature of R and the mechanism (charge distribution on X and Y) change (see text).

further objection to XVII is that such behavior could not occur for symmetrical, one-step exchange reactions, where entering and leaving group are equally bound to carbon. There is little reason to suspect that a symmetrical transition-state series, *e.g.*, $ClCH_3Cl^{\ddagger}$, Cl-*n*-$BuCl^{\ddagger}$, Cl-*i*-$PrCl^{\ddagger}$, $ClBzCl^{\ddagger}$, would behave in any significantly different way from the corresponding $N_3RBr^{\ddagger}$ series in Table VII.

In the second type of transition state, XVIII, C–X bond breaking moves increasingly ahead of C–Y bond formation as the alkyl group becomes more able to accommodate a lower energy carbonium ion.[11,21,29] The charge distribution is such that Y and X carry increasing negative charge and C_α carries increasing positive charge through a spectrum of transition states from "tight" synchronous SN2 toward "loose" carbonium ion SN2, *i.e.*, through $YCH_3X^{\ddagger}$, Y-*n*-$BuX^{\ddagger}$, Y-*i*-$PrX^{\ddagger}$, $YBzX^{\ddagger}$. A "carbonium ion SN2 transition state," XVIII, will be well solvated by protic solvents, because in the extreme case there is a single negative charge localized on each of the hydrogen bond acceptors X and Y. There is positive charge on carbon, but it is shielded by two anions, so that, although positive centers are generally more solvated by dipolar aprotic solvents than by methanol (Table II), the over-all effect is for this transition state to be more solvated by methanol; *i.e.*, $\log {}^{M}\gamma^{DMF}{}_{YRX^{\ddagger}}$ is positive. We would regard the extreme case of XVIII as an SN2 transition state for as long as both entering and leaving group are influencing the geometry and energy of the transition state and the kinetics suggest a bimolecular reaction. After this the reaction becomes SN1.

The data in Table VII for the transition states of reaction of azide ion with methyl and benzyl chloride and with methyl and 4-nitrobenzyl bromide, in methanol and in DMF, are strong evidence for a spectrum of transition states from synchronous to carbonium ion SN2. The 4-nitrobenzyl bromide transition state anion (I) is thought to be limiting SN2 with no carbonium ion character.[21] There is a complication though in the separation of effects due to R and those to transition-state geometry, G. The negative charge is distributed over a large polarizable nitrobenzyl system, so that, even if this transition state were of comparable tightness, it would be more solvated by DMF relative to methanol than would the smaller, less polarizable methyl bromide transition state anion (I). The behavior of the benzyl chloride transition state anion (VI), relative to the methyl chloride transition state (I), on the other hand, is even more convincing. The former is thought to be a carbonium SN2 type; *i.e.*, it has negative charge localized on chloride and azide ion and positive charge well dispersed over the benzyl system. Despite the presence of a positive benzyl system (well solvated by DMF), the negative Cl and N_3 ensure that this transition state (VI) is quite poorly solvated by DMF, relative to methanol. The tighter methyl chloride transition state (I), although smaller and lacking a polarizable aromatic system, has its negative charge spread over three atoms. It is thus a poorer hydrogen bond acceptor and solvation by DMF relative to methanol is more favored with I than with the benzyl transition state (VI).

The SN2 reactions of the substituted benzyl chlorides with methoxide ion in methanol and in 60% v:v DMSO–MeOH (Table VII) are explained in much the same way,[30] if it is remembered that the electron-donating *p*-methyl group encourages carbonium ion development, whereas the electron-withdrawing *p*-chloro (weak) and *p*-nitro (strong) substituents discourage carbonium ion development,[21] relative to the benzyl chloride transition state. It would seem useful, when considering a set of SN2 transition states having the same entering and leaving groups at saturated carbon, *i.e.*, when considering $\delta_R(\log {}^{M}\gamma^{S}{}_{YRX})_{Y,X,S,SN2}$ (R = saturated carbon, S = dipolar aprotic), to say that, the more positive this value, the greater the carbonium ion SN2 character (XVIII) of the transition state.

The conclusions in this section are independent of our extrathermodynamic assumptions about single-ion solvent activity coefficients.

4. *The standard chemical potentials of E2C (V) transition states change in much the same way with solvent transfer as do those of the corresponding SN2 transition states III and IV.* Winstein, Parker, and their coworkers[31] feel that many bimolecular elimination reac-

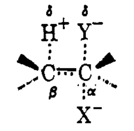
---

(29) Even in symmetrical exchange reactions, Y and X can be strongly or weakly bound, but equally bound in both cases.

(30) The $\log {}^{M}\gamma^{DMSO \cdot M}{}_{\ddagger}$ values in Table VII, for reactions in DMSO–methanol, are subject to the reservations that $\log {}^{M}\gamma^{DMSO \cdot M}{}_{RX}$ for the various benzyl chlorides was not measured. It was assumed that this value would be constant (*ca.* −0.5; *cf.* Table III) for the substituted benzyl chlorides, but, until these values are measured, the data should be interpreted with caution. The other data in Table VII give adequate support alone to our interpretation. The rate data are presented because they do not seriously conflict with our explanation.

(31) A. J. Parker, M. Ruane, G. Biale, and S. Winstein, *Tetrahedron Lett.*, 2113 (1968); S. Winstein, A. J. Parker, G. Biale, P. Beltrame, M. Ruane, D. Lloyd, D. Darwish, S. G. Smith, I. D. R. Stevens, and J. Takashi, unpublished work; A. J. Parker, 39th ANZAAS Congress, Melbourne, Australia, Jan 1967; S. Winstein, 144th National Meeting of the American Chemical Society, Los Angeles, Calif., April 1963, Abstracts, p 8M.

tions, which they define as E2C, proceed through transition states V, which are like the limiting E2C transition states XIX. E2C reactions are observed with very weakly acidic tertiary alkyl and secondary cycloalkyl compounds and with some secondary alkyl compounds, in the presence of strong carbon but weak hydrogen bases (*e.g.*, RS^-, Cl^-). The E2C transition state has Y^- bound to the α-carbon atom, but the C_α–Y bond is poorly developed. There must be weak (perhaps hydrogen) bonding between Y and the β-hydrogen. The double bond is very well developed. The C_α–X bond is poorly developed, and there is considerable negative charge localized on X and Y. The eliminations are strongly *trans* and Saytzeff. These reactions are accompanied by SN2 reactions, which have been shown *not* to proceed through the E2C transition state V, but which presumably pass through the carbonium ion SN2 transition states III and IV. We emphasize that SN2 and E2C reactions do *not* have a common or merged mechanism; *i.e.*, they do not have the same transition state.



XIX

The elimination reactions of more strongly acidic secondary alkyl and some reactions of tertiary alkyl and cycloalkyl compounds with strong hydrogen bases, but weak carbon nucleophiles (*e.g.*, RO^-), pass through transition states (V), which are very like XVI, the "classical" E2 transition state.[22] These are defined as E2H reactions.

Several E2C and one E2H transition states with corresponding SN2 transition states are represented in Table IV. As shown in Table VIII, E2C transition states respond in much the same way as does the corresponding (*i.e.*, same reactants) SN2 transition state, with transfer from protic to dipolar aprotic solvent, *i.e.*, $\delta_G(\log {}^{M}\gamma^{DMF}{}_{YRX})_{Y,R,X,C}$ is constant for the two geometries (G) corresponding to SN2 and E2C transition states. The transition states for E2C reactions of cycloalkyl compounds, like those already discussed for SN2 reactions of the same substrates (Table VII), tend to be rather more solvated in methanol, relative to DMF, than are the corresponding (same X, Y) methyl or primary alkyl synchronous SN2 transition states (I). In the E2C transition states, V like XIX, just as in the carbonium ion SN2 transition states, XVIII, and III and IV, it would seem that both Y and X had considerably more localized negative charge than in I. In the SN2 transition states XVIII, III and IV, C_α has some carbonium ion (sp^2) character, as already discussed; in the E2C transition state (V like XIX), C_α has considerable sp^2 hybridization, *i.e.*, a well-developed double bond but positive charge on β hydrogen. The transition state (V like XVI) for the E2H reaction of isopropyl bromide with methoxide behaves differently from that for the SN2 reaction; indeed it behaves in much the same way as the SN2 transition state for reaction of methyl bromide with methoxide ion (Table IV). This could mean that E2H transition states of secondary alkyl halides unlike E2C transition states, but like SN2 transition states of methyl halides, have well dispersed negative charge. More data are needed however.

Table VIII. Solvation of Transition States. Effect of Changing the Mechanism from Substitution to Elimination (Reference Solvent: Methanol at 25°)[a]

Reaction no.[a]	Reactants RX + Y	Mechanism G SN2[b]	E2C[c]	E2H[d]
		$\delta_G(\log {}^{M}\gamma^{DMF}{}_{N_3C_6H_{11}Br})_C$		
43, 44	$C_6H_{11}Br + N_3^-$	+2.2	+2.1	...
		$\delta_G(\log {}^{M}\gamma^{80DMSO\cdot M}{}_{MeO\cdot i\text{-}PrBr})_C$		
42	*i*-PrBr + OMe^-	>1.5[e]	...	0.6
		$\delta_G(\log {}^{M}\gamma^{DMF}{}_{N_3C_6H_{11}I})_C$		
45, 46	$C_6H_{11}I + N_3^-$	1.0	1.5	...
		$\delta_G(\log {}^{M}\gamma^{Me_2CO}{}_{ArSC_6H_{11}OTs})_C$		
47, 48	$C_6H_{11}OTs + ArS^-$ [g]	3.2[f]	3.2[f]	...

[a] Data from Table IV. [b] Structures are III or IV in text. [b] Structures are V like XIX. [d] Structures are V like XVI. [e] Value estimated from a reaction in which solvolysis interferes. Agrees with behavior of isopropyl bromide in reactions with other bases (*cf.* Table IV). [f] Assuming that the solvent activity coefficient of cyclohexyl tosylate for transfer from methanol to acetone is 1 (*cf.* Table III). This assumption does not influence the equality of the numbers, only their magnitude. [g] Abbreviations are Ar = 4-nitrophenyl, Ts = *p*-toluenesulfonyl, C_6H_{11} = cyclohexyl.

The conclusions in this section are independent of our extrathermodynamic assumptions.

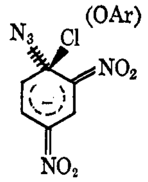
5. *The solvation of transition states for bimolecular nucleophilic substitutions varies by >4 kcal mole*$^{-1}$ *(10^3 log k units) according to the nature of the atom being attacked and the geometry of the transition state.* This is illustrated by the behavior of the two sets of SN2 transition states in Table IX on transfer from methanol to DMF, *i.e.*, by $\delta_{GR}(\log {}^{M}\gamma^{DMF}{}_{N_3RCl^{\ddagger}})_{SN2}$ and by $\delta_{GR}\cdot(\log {}^{M}\gamma^{DMF}{}_{N_3ROAr})_{SN2}$. The solvent activity coefficients are understandable in terms of the variation in the geometry and charge distribution, G, of transition states I, VI, VII, VIII, IX, and X, whose structures are based on well-accepted mechanisms.[21,22]

Table IX. Solvation of SN2 Transition States. Effect of Changing Geometry of Transition State and Nature of R through Aryl, Vinyl, Benzyl, Carbonyl, and Saturated Carbon Atoms and Phosphorus (Reference Solvent: Methanol at 25°)[a,b]

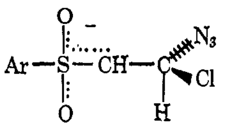
Reaction no.[a]	R in RCl + N_3^-	Transn state[c]	$\delta_{GR}(\log {}^{M}\gamma^{DMF}{}_{N_3RCl})_{SN2}{}^{d,e}$
61	2,4-$(NO_2)_2C_6H_3$	X	<−0.2
53	*trans*-TsCH=CH	VII	0.6
1	CH_3	I	1.2
51	$C_6H_5CH_2$	VI	2.7
	R in ROAr + N_3^-		$\delta_{GR}(\log {}^{M}\gamma^{DMF}{}_{N_3ROAr})_{SN2}{}^{d,e}$
68	2,4-$(NO_2)_2C_6H_3$	X	−0.5
55[f]	(*i*-Pr)$_2$P(O)[f]	IX	1.5[f]
54	$CH_3C(O)$	VIII	2.6

[a] Data from Table IV. [b] Ar = 4-nitrophenyl, Ts *p*-toluenesulfonyl. [c] Numbers refer to structures in text. [d] The geometry and the nature of R in the transition state are both variables. [e] The mechanism is SN2 in the broadest sense of this label. [f] This member of the set has been built up from an assumption (see text).

Transition state X, reaction 61, is like the SNAr intermediate complex XX, with the C–Cl and C–N_3 bonds completely, or almost completely, developed and negative charge well dispersed over the large polarizable aryl system. Such an anion is a poor hydrogen bond ac-



XX

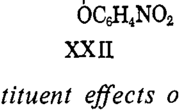


XXI

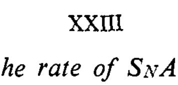
ceptor and is well solvated by DMF relative to methanol. It is interesting that the picrate anion, which could be a model for some SNAr transition states,[32] has log $^{M}\gamma^{DMF} = -0.4$, while related SNAr transition-state anions have log $^{M}\gamma^{DMF} =$ *ca.* -0.2. Structure VII is like the intermediate XXI, which is large and polarizable, favoring solvation by DMF, but the negative charge is somewhat localized on the sulfone oxygen, which thus becomes a good hydrogen bond acceptor, and this favors solvation by methanol. The over-all effect is that solvation by methanol is more favored (*i.e.*, $\delta_{GR}(\log {}^{M}\gamma^{DMF}{}_{N_3RCl})_{S_N2}$ is more positive) for the vinyl sulfone transition state VII than it is with the weaker hydrogen bond acceptor X. Reaction of an aryl sulfone is considered later (*vide infra*). Structure I is a considerably smaller and less polarizable anion than VII or X, so that solvation by methanol is more favored (*i.e.*, $\delta_{GR}(\log {}^{M}\gamma^{DMF}{}_{N_3RCl})_{S_N2}$ is more positive) when N_3RCl is I than when it is VII or X.

The situation shown in Table IX for the benzyl transition state VI, in which C_α has considerable carbonium ion character and azide and chloride carry localized negative charge has been discussed above. This transition state is considerably more solvated by methanol than by DMF. Transition state IX, reaction 55, because of the principle of microscopic reversibility, can be thought of as the transition state for displacement of OAr^- by Cl^- from phosphorus. Thus transition states X (reaction 68), VIII (reaction 54), and IX (reaction 55) have the same leaving group. A satisfactory assumption for our purposes is that azide would behave in much the same way as does chloride (Tables IV and V) in IX, so that these transition states can be compared as a set, $\delta_{GR}(\log {}^{M}\gamma^{DMF}{}_{N_3ROAr})_{S_N2}$.

Transition state X (like XX), reaction 68, is very large and polarizable but a poor hydrogen bond donor. It is thus better solvated by DMF than by methanol. Transition states VIII and IX resemble the high-energy intermediates XXII and XXIII, respectively. They are both large and polarizable, but negative charge is localized on oxygen,[21] so that they are excellent hydrogen bond acceptors at oxygen. Thus both are more solvated by methanol than by DMF, despite the size and polarizability, and $\delta_{GR}(\log {}^{M}\gamma^{DMF}{}_{N_3ROAr})_{S_N2}$ is considerably more positive for VIII and IX than for X.



XXII



XXIII

6. *Substituent effects on the rate of SNAr reactions are not solvent independent. Solvation of reactant molecules and of transition states depends on the nature of substituents. Substituents may interact differently with solvent when in the reactant vs. the transition state.* In a set of substituents, some of which may be hydrogen bond donors, others acceptors, and others fulfilling neither or both roles, there may be one type of interaction in the reactant state with a protic solvent and another type with a dipolar aprotic solvent. These interactions will often be stronger or weaker in the transition state, according to the charge distribution produced by the type of reaction, especially at the substituent.[33] As an example, the molecule $XArCOCH_3$ may become a better hydrogen bond acceptor at negative oxygen in the SNAr transition state anion, $XYArCOCH_3^{-\ddagger}$ than at carbonyl oxygen in the reactant state. In such a molecule, the substituent will be more effective, relative to hydrogen, at increasing the rate of an SNAr reaction in methanol than it is in aprotic DMF. A substituent such as CF_3, on the other hand, is not a good hydrogen bond acceptor in reactant or SNAr transition state and will behave similarly, relative to hydrogen, in both types of solvent.

These principles, which are not new,[11,34] but hitherto lacked quantitative numbers as to the extent of reactant and transition-state effects, are shown in a limited way as δ_R values (R is a substituent), for reactions of the same charge type in Table X. In some cases only the solvent effect on rate is available, but this establishes that substituent effects on SNAr reactions are not solvent independent. Therefore Hammett σ constants,[21] obtained in protic solvents, may not be applicable to dipolar aprotic solvents.[34] The solvent effect on substituents is seen to operate in both the reactant and transition state (Table X).

The effect of charge on transition-state solvation, $\delta_C(\log {}^{M}\gamma^{S}{}_{YArX})_{S_N\text{Ar},Y,X}$, and on rate, $\delta_C(\log k^S/k^M)_{Y,R,X,S_N\text{Ar}}$, is also shown in Table X. The comparison is not completely valid because Ar varies, but it serves to illustrate an important point. Polar *uncharged* SNAr transition states XIII, reaction 72, are much more solvated by DMF than by methanol.[27] SNAr transition-state *anions* (X) are similarly solvated by DMF and methanol, whereas a SNAr transition-state *dianion* (XI) is much more solvated by methanol than by DMF. A transition-state carboxylate dianion (charge −2) is a much better hydrogen bond acceptor than a reactant carboxylate anion (charge −1) (reaction 69, Table X).

7. *Protic–dipolar aprotic solvent effects on rate are usually reflected much more strongly in the enthalpy rather than in the entropy of activation.* This statement is supported by the data for all but one of the reactions in Table XI, in which enthalpies and entropies of activation are expressed so as to be directly comparable in the same terms as log *k*. Too little is known about enthalpies and entropies of transfer of electrolytes and nonelectrolytes, from protic to dipolar aprotic solvents, for the full significance of this observation to be understood. It may not be generally applicable and a wider spectrum of reactants and solvents must be studied. We merely note that the SN2 reactions studied are faster in dipolar aprotic than in protic solvents

---

[32] J. Miller and A. J. Parker, *J. Amer. Chem. Soc.*, **83**, 117 (1961).

[33] No matter how different or large the interaction of a substituted molecule with protic *vs.* dipolar aprotic solvents, substituent effects on rate will be solvent independent if these interactions are the same in the transition state.

[34] C. D. Ritchie and E. S. Lewis, *J. Amer. Chem. Soc.*, **84**, 591 (1962); R. W. Taft, E. Price, I. R. Fox, I. C. Lewis, K. K. Andersen, and G. T. Davis, *ibid.*, **85**, 3146 (1963).

Table X. Effect of Charge Type and Solvation of Substituents in Reactant and Transition State of SNAr Reactions[a] (Reference Solvent: Methanol at 25°)

Reaction no.[a]	Substituent R^f	Solvent	Log k^S/k^M	Log ${}^M\gamma^S{}_{ArX}$	Log ${}^M\gamma^S{}_{\ddagger}$	Transn state[b]
58	H	DMF	4.2	−1.2	−0.5	X (−1)
	R^g		$\delta_R(\log k^S/k^M)$	$\delta_R(\log {}^{M}\gamma^{80DMSO\text{-}M}_{RArCl})_{Ar}$[d]	$\delta_R(\log {}^{M}\gamma^{80DMSO\text{-}M}_{MeORArCl})_{Ar.SNAr}$[d,e]	
78	SO_2Me	80DMSO-M	2.8	−1.4	−0.2	XIV (−1)
75	CF_3	80DMSO-M	3.4	0	+0.6	X (−1)
76	H	80DMSO-M	3.3	−0.2	+0.5	X (−1)
			$\delta_C(\log (k^S/k^M))_{MeO.Ar.Cl.SNAr}$			
74	NMe_3^+	80DMSO-M	2.4	...	...	XIII (0)
76	H	80DMSO-M	3.3	−0.2	+0.5	X (−1)
70	CO_2^-	80DMSO-M	2.4	...	...	XII (−2)
	R^h		$\delta_C(\log (k^S/k^M))_{MeO.Ar.Cl.SNAr}$			
71	CO_2^-	80DMSO-M	2.7	...	...	XI (−2)
77	H	80DMSO-M	3.6	−0.8[c]	−0.4	X (−1)
	R^i		$\delta_C(\log k^S/k^M)$	$\delta_C(\log {}^{M}\gamma^{DMF}_{RArCl})_{Ar}$[d]	$\delta_C(\log {}^{M}\gamma^{DMF}_{N_3RArCl})_{Ar.SNAr}$[d]	
61	NO_2	DMF	4.1[e]	<-1[e]	<-0.2[e]	X (−1)
72	NMe_3^+	DMF	3.3	−4.6	−3.0	XIII (0)
	R^j					
69	CO_2^-	DMF	3.3	+1.2	+2.8	XI (−2)
61	H	DMF	4.1[e]	<-1[e]	<-0.2[e]	X (−1)

[a] Data from Table IV. [b] Charge on transition state is in parentheses: numbers refer to structures in text. [c] Estimated on the assumption that 4-chloronitrobenzene and 4-iodonitrobenzene respond in much the same way to solvent transfer (*cf.* Table III). [d] R is a substituent at the same position on a particular aromatic system (Ar). The nature of Ar varies through each set of results. [e] Compare reaction 58 for more precise numbers in a closely related reaction. [f] Reaction is azide ion with 4-iodonitrobenzene. [g] Reaction is methoxide ion with 4-Cl-3-$NO_2C_6H_3R$. [h] Reaction is methoxide with 2-Cl-5-$NO_2C_6H_3R$. [i] Reaction is azide with 4-Cl-3-$NO_2C_6H_3R$. [j] Reaction is azide with 2-Cl-3,5-$(NO_2)_2C_6H_5R$.

mainly because the enthalpy of activation is considerably less in the dipolar aprotic solvent. In SN2 reactions at saturated carbon, this is slightly compensated for by a larger entropy of activation in the protic solvent, but in some SNAr reactions the large enthalpy change is reinforced by a smaller entropy change.

The enthalpies of transfer of the tetraethylammonium halides, relative to tetraethylammonium iodide,[35] are compared in Table XII with the free energies of transfer of silver halides,[8] relative to silver iodide, from water to DMSO at 25°. The cation is constant in each set, so that, if iodide is set as reference anion, cation effects cancel and no extrathermodynamic assumptions are necessary. The data support our feeling that the changes in the chemistry of anions, on transfer from protic to dipolar aprotic solvents, are due mainly to significant differences in the solvation enthalpy of anions of different hydrogen bond acceptor tendency, in protic solvents, rather than to entropy differences. Solvation enthalpies of a series of salts of the same cation are "leveled" in dipolar aprotic solvents.[35]

The important point which emerges is that protic–dipolar aprotic solvent effects on the chemistry of anions are quite strongly temperature dependent, as expected for an effect, attributed mainly to hydrogen-bonding interactions. Up till now, most of our observations have been reported at 25°; differences between protic and dipolar aprotic solvents are greater at lower temperatures, less at higher temperatures.

8. *Reactions in HMPT are faster than in any other solvent studied and acetone is a typical dipolar aprotic solvent, with similar effects on rate to dimethylacetamide.* We have not attempted to estimate solvent activity coefficients for ions in acetone, because ion pairing is significant in this solvent. Table IV shows, however, that SN2 reactions of tetraalkylammonium salts <0.02 *M* in acetone proceed at much the same rate as do the corresponding reactions in dimethylacetamide. Nonelectrolytes are solvated to much the same extent in acetone, DMF, and DMAC. Bimolecular substitutions (eq 1), especially SNAr reactions, are very much faster in HMPT than in other dipolar aprotic solvents.

Experimental Section

Materials. Dipolar aprotic solvents and formamide were commercial products. DMSO was kindly donated by the Crown Zellerbach Corp. Solvents were dried over molecular seives and twice distilled under a reduced pressure of nitrogen. They were stored in dark bottles, over molecular seives, and were used within 1 week of distillation. Acetonitrile was shaken over KOH pellets, dried with P_2O_5, and then distilled as above. Tetraalkylammonium and trimethylsulfonium salts were prepared in methanol from the recrystallized iodide, using fresh silver oxide to convert to the methoxide, which was then neutralized to the desired salt with the appropriate acid, in methanol. The methanol was removed under reduced pressure at room temperature. Tetraethylammonium salts were recrystallized from acetone, acetone–ether, or DMAC; tetrabutylammonium salts were recrystallized from acetone or benzene–petrol. All analyzed satisfactorily for the appropriate anion and were free of acid. Many were hygroscopic and were handled in glove bags under dry nitrogen. Solutions were standardized before use. Sodium and potassium salts were AR materials and were used without further purification.

The alkyl and benzyl halides, the 4-nitrohalobenzenes, and 2,4-dinitrohalobenzenes were commercial products and were purified by recrystallization or by fractional distillation. They analyzed satisfactorily for halide ion after hydrolysis at 100° in 80% DMSO–water containing excess potassium hydroxide.

The following compounds were made by methods described in the literature (melting points corresponded to within 1° of literature values, and where applicable analysis of the group displaced by

---

(35) E. M. Arnett and D. R. McKelvey, *ibid.*, **88**, 2598 (1966).

Table XI. Effect of Transfer from Methanol to DMF or to 80% v:v DMSO–MeOH. Enthalpies and Entropies of Activation of SN2 Reactions at 25°

Reactants	$\frac{\Delta H_M^{\ddagger} - \Delta H_{DMF}^{\ddagger}}{(2.303R)298}$ [a]	$\frac{\Delta S_M^{\ddagger} - \Delta S_{DMF}^{\ddagger}}{2.303R}$ [a]
MeOH to DMF		
$(MeO)_3PO + N_3^-$ [f]	2.3	+0.4
$CH_3Cl + N_3^-$ [b]	4.3	+1.0
$CH_3Cl + SCN^-$ [b]	2.8	+1.4
$CH_3I + SCN^-$ [b]	3.2	+1.0
i-BuBr + N_3^- [c]	3.3	+0.1
$(CH_3)_3S^+ + N_3^-$ [d,e]	4.3	+1.1
$CH_3OTs + N_3^-$ [f]	1.9	+0.3
$C_6H_{11}Br + N_3^-$ (SN2)[f]	3.7	+0.8
$C_6H_{11}Br + N_3^-$ (E2C)[f]	2.8	−0.1
trans-TsCH═CHCl + N_3^-	2.9[f,g]	0.0[f,g]
$4\text{-}NO_2C_6H_4I + N_3^-$ [b]	4.1	−0.2
$4\text{-}NO_2C_6H_4F + N_3^-$ [b]	3.5	−0.9
$2,4\text{-}(NO_2)_2C_6H_3I + Cl^-$ [f]	6.2	−0.3
$2,4\text{-}(NO_2)_2C_6H_3I + SCN^-$ [b]	0.2	−1.6
$2,4\text{-}(NO_2)_2C_6H_3Cl + SCN^-$ [b]	2.2	+0.2
$2,4\text{-}(NO_2)_2C_6H_3Cl + N_3^-$ [b]	4.8	+0.7
$2\text{-}Cl\text{-}3,5(NO_2)_2C_6H_2CO_2^- + N_3^-$ [f,h]	3.1	−0.2
MeOH to 80% DMSO–MeOH		
$2\text{-}NO_2C_6H_4Cl + OMe^-$ [f]	2.9	−0.3
$4\text{-}NO_2C_6H_4Cl + OMe^-$ [f]	4.3	+0.6
$4\text{-}Cl\text{-}3\text{-}NO_2C_6H_3CO_2^- + OMe^-$ [d,f]	3.3	+0.5
$4\text{-}Cl\text{-}3\text{-}NO_2C_6H_3N^+Me_3 + OMe^-$ [d,f]	3.7	+1.7
$4\text{-}Cl\text{-}3\text{-}NO_2C_6H_3SO_2Me + OMe^-$ [f]	3.2	+0.4
$C_6H_5CH_2Cl + OMe^-$ [f]	3.7	+1.3

[a] Values are expressed in this way so as to be directly comparable with each other and with log k; *i.e.*, $\log k = (\Delta G^{\ddagger}/2.303RT) = (\Delta H^{\ddagger}/2.303RT) - (\Delta S^{\ddagger}/2.303R)$. [b] Reference 20. [c] A. J. Parker and D. Cook, *J. Chem. Soc., B*, 142 (1968). [d] At ionic strength (1–5) × 10^{-3} *M*. [e] I. Evans and A. J. Parker, unpublished work. [f] This work (Table XIV). [g] G. Modena and P. E. Todesco, *Gazz. Chim. Ital.*, **89**, 866 (1959), studied the reaction of *trans*-4-$ClC_6H_4SO_2CH$═CHCl with azide ion in methanol. We assume that $\Delta H^{\ddagger}$ for *trans*-4-$CH_3C_6H_4SO_2CH$═CHCl with azide ion in methanol is similar, *i.e.*, 15.3 kcal $mole^{-1}$, and that $\Delta S^{\ddagger}$ is the same. The $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ in DMF are from Table XIV. [h] After extrapolation to zero ionic strength.

Table XII. Enthalpies and Free Energies of Transfer from Water to DMSO of Halide Ions, Relative to Iodide Ion at 25°

X^-	Free energy,[a] kcal/g-ion	Enthalpy,[b] kcal/g-ion
Cl^-	7.0	7.4
Br^-	3.9	3.9
I^-	0.0	0.0

[a] Calculated from solubilities of silver salts in ref 8. [b] Reference 35, from heats of solution of NEt_4X.

excess base was quantitative): 4-Nitrophenyl acetate,[36] diisopropyl phosphorochloridate,[37] methyl tosylate,[38] cyclohexyl tosylate,[39] ferrocene,[39] bis-2,4-dinitrophenyl disulfide,[40] *trans*-1-chloro-2-(*p*-toluenesulfonyl)ethene.[41] The chloronitrobenzene derivatives were samples used by Miller and coworkers or were prepared by methods indicated in their papers.[42]

Rate Measurements. Details of runs are in Table XIII. The runs were performed in duplicate, but only mean values (±4%) are shown in the table. Rate constants are not corrected for solvent expansion. The low-temperature runs (<0°) were performed using an ice–salt bath (−10, −20°) and acetone–Dry Ice baths (−25, −30, −35, −40°) as "thermostats." The baths were in a plastic dish surrounded by ice–salt. Runs were performed in a cold room at *ca.* −2°. These runs had half-lives of <5 min, and temperature control was ±0.4° during this period. The rate constants obtained are satisfactory for our purpose. Arrhenius parameters are in Table XIV. Our main intention was to obtain suitable rate constants at 25°. Some of the parameters calculated from low-temperature or very high-temperature runs (Table XIII) could be in error by ±2 kcal $mole^{-1}$ in *E* and ±1 unit in log *B*.

In Table XIII the analytical procedures are abbreviated as follows. Appropriate blanks were carried out and substrates did not react during analysis.

Ag^+/H^+. The sample was poured into water, acidified with 1 *N* H_2SO_4, and titrated potentiometrically with silver nitrate. Silver azide does not precipitate from acid solution. Reactions of alkyl or aryl halides with azide ion were occasionally sampled by titration of a neutral solution with silver nitrate. If the total of $N_3^- + Hal^-$ was constant during reaction, this confirmed an SN2 process.

OH^-/H^+. The sample was poured into excess acid and back-titrated with barium hydroxide, using an indicator appropriate to the sample. On occasions sodium methoxide in methanol was the titrant.

$Ag^+/Ba(NO_3)_2$. The sample was poured into water containing solid barium nitrate. Mixtures of halide ions could be selectively titrated potentiometrically with silver nitrate in this way.

Ag^+. A neutral solution in 70% acetone–water was titrated potentiometrically with silver nitrate. This was used to estimate azide ion. Similar results were obtained by titrating azide ion as a base in 80% acetone with HCl in 80% acetone–water, using bromphenol blue as indicator.

H^+/ArS^-. The 4-nitrothiophenoxide ion was deep red in 80% acetone-water. Addition of HCl in 80% acetone-water gave a change to pale yellow at the end point. These titrations were performed as quickly as possible, under a nitrogen "blanket," to minimize oxidation of the mercaptide.

Extract/Ag^+/H^+. Where substrates were likely to solvolyze during analysis, the sample was poured into chloroform and extracted with water. The aqueous extract was analyzed potentiometrically with silver nitrate, after acidification.

H^+/Extract/Ag^+. Thiophenol was removed by extraction of acidified solutions with chloroform because it interfered with potentiometric halide estimations.

Spectro. The 4-nitrophenoxide ion was estimated spectrophotometrically in saturated aqueous sodium carbonate solutions.

H^+/Bromophenol Blue. The thiophenoxide ion was estimated by titration in cold ethanol with *p*-toluenesulfonic acid in ethanol, using bromphenol blue as indicator.

A few reactions in methanol are accompanied by a solvolysis reaction (Table XV). Methanolysis rates were determined in solutions containing 2,6-lutidine to prevent subsequent reactions of hydrogen halides with methanol. The initial rates were adjusted where necessary to allow for solvolysis.[43] Reactions of alkyl or aryl bromides with iodide ion and, of course, the reverse reactions, came to equilibrium. Rate constants were calculated so as to allow for this.[32] All our reactions followed second-order kinetics and are well established as straightforward bimolecular processes in related solvents. The E2 and SN2 reactions of azide ion both effectively remove azide ion, so that second-order kinetics are followed. The reaction of azide ion with trimethyl phosphate gave methyl azide by vpc analysis, confirming carbon–oxygen scission, rather than attack at phosphorus,[21] in both methanol and DMF.

Solvent Activity Coefficients of Molecules. The solubility of crystalline solids was estimated by saturating solutions at 35°, then thermostating at 25° for 12 hr. The saturated solutions were hydrolyzed with excess KOH at 100° in 80% DMSO–H_2O, acidified, and then analyzed for their labile halogen. Alternative analytical methods used were spectrophotometry or gravimetric analysis, after pouring into water.

The Henry's law constants of volatile liquids were determined exactly as described by Winstein and Grunwald,[19] using degassed

---

(36) F. D. Chattaway, *J. Chem. Soc.*, 2495 (1931).

(37) I. Dostrovsky and M. Halmann, *ibid.*, 508 (1953).

(38) H. T. Roos, H. Gilman, and N. J. Beaver, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, p 141.

(39) G. Wilkinson, *Org. Syn.*, **36**, 31 (1956).

(40) Houben-Weyl, "Methoden der Organischen Chemie," Vol. 9, Georg. Thieme, Stuttgart, 1955.

(41) F. Montanari, *Gazz. Chim. Ital.*, **86**, 406 (1956).

(42) (a) J. Miller, *J. Amer. Chem. Soc.*, **76**, 448 (1954); (b) N. J. Daly, G. Krueger, and J. Miller, *Aust. J. Chem.*, **11**, 290 (1958); (c) R. L. Heppolette, J. Miller, and V. A. Williams, *J. Chem. Soc.*, 2929 (1955); (d) R. L. Heppolette, I. R. Lantzke, and J. Miller, *Aust. J. Chem.*, **9**, 299 (1956).

(43) A. J. Parker, *J. Chem. Soc.*, 1328 (1961).

Table XIII. Experimental Rate Constants

Reactants RX + MY	[RX], 10^2 *M*	[MY], 10^2 *M*	Solvent	Temp, °C	10^4k,[l] M^{-1} sec^{-1} ± 5%	Analytical procedure[m]
$CH_3Cl + NaN_3$	1.01	4.10	$HCONH_2$	25.0	0.16	Ag^+/H^+
$CH_3Br + NaOMe$	2.22	3.98	80DMSO-M	25.0	5000	OH^-/H^+
$CH_3Br + NEt_4Cl$	2.01	4.83	MeOH	25.0	0.067	$Ag^+/Ba(NO_3)_2$
$CH_3Br + NaN_3$	2.02	5.13	$HCONH_2$	25.0	7.35	Ag^+/H^+
$CH_3I + NEt_4Cl$	4.25	2.08	CH_3CN	25.3	1260	$Ag^+/Ba(NO_3)_2$
	4.47	2.09	CH_3CN	0.1	50.0	$Ag^+/Ba(NO_3)_2$
$CH_3I + KCl$	1.50	2.96	80DMSO-M	25.0	153	$Ag^+/Ba(NO_3)_2$
	2.10	10.3	$HCONH_2$	25.0	0.55[a]	$Ag^+/Ba(NO_3)_2$
$CH_3I + NaN_3$	1.98	8.06	$HCONH_2$	25.0	8.0	Ag^+/H^+
$CH_3I + KSCN$	1.90	6.10	$HCONH_2$	25.0	18.2	$Ag^+/Ba(NO_3)_2$
	2.19	3.90	DMAC	25.0	1820	$Ag^+/Ba(NO_3)_2$
	4.33	2.10	CH_3CN	25.3	149	$Ag^+/Ba(NO_3)_2$
	4.00	2.23	HCONHMe	25.0	36.0	$Ag^+/Ba(NO_3)_2$
	2.80	6.30	80DMSO-M	25.0	205	$Ag^+/Ba(NO_3)_2$
$CH_3I + NBu_4SCN$	2.80	4.10	CH_3NO_2	25.0	100	$Ag^+/Ba(NO_3)_2$
	1.04	1.42	Me_2CO	25.0	1500	$Ag^+/Ba(NO_3)_2$
	1.98	4.26	Me_2CO	25.0	1200	$Ag^+/Ba(NO_3)_2$
$CH_3I + KBr$	2.41	4.83	$HCONH_2$	25.0	3.93[b]	$Ag^+/Ba(NO_3)_2$
$CH_3I + NaOAc$	1.90	4.80	$HCONH_2$	25.0	0.64[a]	Ag^+/H^+
$CH_3I + NBu_4OAc$	2.06	4.82	DMF	0.3	19,700	Ag^+/H^+
$CH_3I + KCN$	1.82	3.10	MeOH	25.0	6.4	Ag^+/H^+
	1.73	4.68	$HCONH_2$	25.0	92.2	Ag^+/H^+
	1.20	0.46	DMF	−21.3	20,600	Ag^+/H^+
$CH_3OTs + NaN_3$	2.05	3.99	MeOH	25.0	5.00	Ag^+ [d]
	1.70	4.84	MeOH	50.0	34.0	Ag^+ [d]
	1.88	4.84	MeOH	75.6	240	Ag^+ [d]
	1.97	4.12	DMF	25.0	458	Ag^+ [d]
	2.10	3.88	DMF	19.6	312	Ag^+ [d]
	1.85	3.88	DMF	17.1	260	Ag^+ [d]
	1.78	3.67	DMF	10.3	128	Ag^+ [d]
	1.30	2.91	DMF	0.0	58.2	Ag^+ [d]
$CH_3OTs + KSCN$	2.01	3.97	MeOH	25.0	1.43	Ag^+ [d]
	2.06	3.98	MeOH	50.0	17.2	Ag^+ [d]
	2.10	3.98	MeOH	60.1	35.8	Ag^+ [d]
	1.90	3.98	MeOH	75.6	111	Ag^+ [d]
	2.01	4.02	DMF	49.7	96.2	Ag^+ [d]
	2.01	4.02	DMF	34.9	22.6	Ag^+ [d]
	2.04	4.55	DMF	25.0	7.80	Ag^+ [d]
	1.22	2.72	DMF	60.0	280	Ag^+ [d]
$CH_3OTs + NEt_4Br$	1.96	9.60	MeOH	25.0	0.27[a]	Ag^+ [d]
	1.96	3.88	DMF	25.0	331	Ag^+ [d]
$CH_3OTs + KI$	2.05	4.04	MeOH	25.2	4.04	Ag^+ [d]
$CH_3OTs + NEt_4I$	1.92	4.02	DMF	25.0	100	Ag^+ [d]
$CH_3OTs + NaSAr$[c]	1.06	2.93	MeOH	25.0	148	H^+/ArS^- [d]
CH_3OTs NBu_4SAr[c]	1.50	3.62	DMF	25.0	6000	H^+/ArS^- [d]
	1.98	4.16	Me_2CO[c]	25.0	7800	H^+/ArS^- [d]
n-BuBr + NBu_4SAr[c]	2.01	4.54	MeOH	25.0	7.53	H^+/ArS^-
	0.82	4.64	Me_2CO	25.0	1080	H^+/ArS^-
n-BuBr + NEt_4N_3	1.61	2.63	DMAC	25.0	735	Ag^+/H^+
	4.08	1.93	CH_3CN	25.0	22.0	Ag^+/H^+
n-BuBr + NEt_4N_3	1.91	4.55	MeOH	75.0	1.51	Ag^+/H^+
	1.07	8.78	MeOH	100.0	12.5	Ag^+/H^+
	2.09	2.86	Me_2CO	25.0	267	Ag^+/H^+
n-BuI + NEt_4Cl	2.18	9.80	MeOH	40.4	0.043	$Ag^+/Ba(NO_3)_2$
	2.10	9.80	MeOH	50.0	0.14	$Ag^+/Ba(NO_3)_2$
	1.07	4.74	MeOH	90.0	6.4	$Ag^+/Ba(NO_3)_2$
	1.07	5.60	MeOH	114.0	47.2	$Ag^+/Ba(NO_3)_2$
	1.84	4.69	DMF	25.0	590	$Ag^+/Ba(NO_3)_2$
	1.85	4.14	DMSO	25.0	150	$Ag^+/Ba(NO_3)_2$
n-BuI + NEt_4Br[e]	1.96	3.71	MeOH	105.0	89	$Ag^+/Ba(NO_3)_2$
	2.35	4.75	MeOH	100.0	72	$Ag^+/Ba(NO_3)_2$
	1.94	3.93	MeOH	83.0	12	$Ag^+/Ba(NO_3)_2$
	1.97	3.58	MeOH	75.0	7.4	$Ag^+/Ba(NO_3)_2$
	1.96	3.80	DMSO	25.0	132	$Ag^+/Ba(NO_3)_2$
n-BuI + KSCN	2.02	4.02	MeOH	100.0	200	$Ag^+/Ba(NO_3)_2$
	2.02	4.12	MeOH	75.0	25.3	$Ag^+/Ba(NO_3)_2$
	2.02	4.12	MeOH	60.4	8.65	$Ag^+/Ba(NO_3)_2$
	2.00	4.14	DMF	25.0	22.0	$Ag^+/Ba(NO_3)_2$
	1.94	4.52	DMSO	25.0	13.2	$Ag^+/Ba(NO_3)_2$
	1.94	4.00	HMPT	25.0	522	$Ag^+/Ba(NO_3)_2$
n-BuI + NaN_3	1.85	4.50	MeOH	100.0	270	Ag^+/H^+
	1.85	4.50	MeOH	75.0	31.8	Ag^+/H^+
	1.85	4.50	MeOH	60.4	8.50	Ag^+/H^+
	1.87	4.08	DMSO	25.0	735	Ag^+/H^+
n-BuI + NEt_4N_3	1.94	3.86	DMF	25.0	2400	Ag^+/H^+
	1.83	3.41	CH_3CN	25.0	300	Ag^+/H^+

Table XIII (*Continued*)

Reactants RX + MY	[RX], 10^2 M	[MY], 10^2 M	Solvent	Temp, °C	10^4k,[l] M^{-1} sec^{-1}, ± 5%	Analytical procedure[m]
n-BuI + NaNO$_2$	1.99	4.52	MeOH	100.0	80.0	Ag$^+$
	1.85	3.90	MeOH	85.0	24.6	Ag$^+$
	2.08	3.97	MeOH	75.0	9.8	Ag$^+$
	2.10	3.90	DMSO	25.0	368	Ag$^+$
i-BuBr + NaN$_3$	1.67	9.87	MeOH	77.7	1.51	Ag$^+$/H$^+$
	2.08	9.87	MeOH	100.2	10.3	Ag$^+$/H$^+$
	2.28	9.77	MeOH	107.0	20.0	Ag$^+$/H$^+$
	2.16	9.77	MeOH	109.0	23.0	Ag$^+$/H$^+$
n-BuBr + NaSPh[c]	2.11	4.57	MeOH[f]	25.0	54.4	H$^+$/extract/Ag$^+$
	1.94	4.07	DMF	−21.0	5300	H$^+$/extract/Ag$^+$
	2.05	4.02	DMF	−25.0	4000	H$^+$/extract/Ag$^+$
	1.84	3.32	DMF	−30.0	1900	H$^+$/extract/Ag$^+$
n-BuBr + NaSPh[c]	1.74	3.60	DMF	−35.0	1370	H$^+$/extract/Ag$^+$
	1.88	4.14	DMF	−40.0	700	H$^+$/extract/Ag$^+$
i-PrBr + NaSPh[c]	2.37	6.54	MeOH[f]	50.0	21.8	H$^+$/bromphenol blue
	2.08	4.57	MeOH[f]	75.8	237	H$^+$/bromphenol blue
	2.30	4.57	MeOH[f]	86.0	470	H$^+$/bromphenol blue
	1.98	3.70	DMF	25.0	2250	H$^+$/bromphenol blue
t-BuBr + NaSPh[c]	2.16	4.57	MeOH[f]	25.0	13.6[l] (7.5)[a,l]	H$^+$/bromphenol blue
	1.94	9.15	MeOH[f]	25.0	11.0[l]	H$^+$/bromphenol blue
	3.06	7.37	DMF	25.0	169[l]	H$^+$/bromphenol blue
	3.06	7.37	DMF	25.0	170[l]	H$^+$/extract/Ag$^+$
i-PrBr + NEt$_4$N$_3$	1.76	3.40	MeOH	100.0	120	Ag$^+$/H$^+$
	2.14	7.28	MeOH	100.0	110	Ag$^+$/H$^+$
	1.80	3.64	MeOH	85.3	29.7	Ag$^+$/H$^+$
	1.84	3.64	MeOH	75.0	11.8	Ag$^+$/H$^+$
	1.82	3.90	DMF	25.0	40.5	Ag$^+$/H$^+$
i-PrBr + NaOMe	2.14	3.97	MeOH	100.0	110[a,l]	Ag$^+$/H$^+$
	2.40	3.97	MeOH	88.4	34.2[a,l]	Ag$^+$/H$^+$
	2.25	3.97	MeOH	75.0	9.15[a,l]	Ag$^+$/H$^+$
	2.22	3.97	80DMSO-M	25.0	23.8[l]	Ag$^+$/H$^+$
C$_6$H$_{11}$Br + NaN$_3$	2.04	7.44	MeOH	100.0	8.30[l]	Ag$^+$/H$^+$
	1.90	5.57	MeOH	87.0	2.85[l]	Ag$^+$/H$^+$
	1.90	7.44	MeOH	74.6	0.66[l]	Ag$^+$/H$^+$
C$_6$H$_{11}$Br + NEt$_4$N$_3$	2.08	3.58	DMF	100.0	930[l]	Ag$^+$/H$^+$
	2.11	3.86	DMF	74.6	330[l]	Ag$^+$/H$^+$
	2.02	3.86	DMF	87.0	134[l]	Ag$^+$/H$^+$
C$_6$H$_{11}$I + NaN$_3$	3.56	5.04	MeOH	100.0	30.0[l]	Ag$^+$/H$^+$
	2.13	4.05	MeOH	75.0	2.35[l]	Ag$^+$/H$^+$
	2.29	3.90	DMF	25.0	32.0[l]	Ag$^+$/H$^+$
C$_6$H$_{11}$OTs + NBu$_4$SAr[c,i]	2.09	4.46	MeOH	75.0	48.2[l]	H$^+$/ArS$^-$
	1.64	5.75	Me$_2$CO	75.0	22.3[l]	H$^+$/ArS$^-$
4-NO$_2$C$_6$H$_4$CH$_2$Br + NEt$_4$N$_3$	1.84	3.64	MeOH	25.0	39.2	Ag$^+$/H$^+$
	1.63	3.24	DMF	−21.1	3700	Ag$^+$/H$^+$
	1.89	3.72	DMF	−25.0	2950	Ag$^+$/H$^+$
	1.71	3.72	DMF	−30.0	1420	Ag$^+$/H$^+$
	2.05	3.72	DMF	−35.0	740	Ag$^+$/H$^+$
	1.89	3.72	DMF	−40.0	455	Ag$^+$/H$^+$
C$_6$H$_5$CH$_2$Cl + NaN$_3$	1.83	3.40	MeOH	64.0	27.3	Extract/Ag$^+$/H$^+$
	1.76	3.40	MeOH	75.0	63.0	Extract/Ag$^+$/H$^+$
	1.82	3.40	MeOH	100.0	490	Extract/Ag$^+$/H$^+$
C$_6$H$_5$CH$_2$Cl + NEt$_4$N$_3$	2.12	3.90	DMF	25.0	132	Extract/Ag$^+$/H$^+$
trans-TsCH=CHCl + NaN$_3$	2.05	3.72	MeOH	25.0	15.5	Ag$^+$/H$^+$
trans-TsCH=CHCl + NEt$_4$N$_3$	1.91	3.69	DMF	0.0	4100	Ag$^+$/H$^+$
	1.86	3.69	DMF	−8.0	2150	Ag$^+$/H$^+$
	1.19	3.69	DMF	−13.0	1040	Ag$^+$/H$^+$
	1.95	3.69	DMF	−20.0	618	Ag$^+$/H$^+$
CH$_3$CO$_2$Ar[i] + NaN$_3$	1.85	3.90	MeOH[g]	25.0	254	Spectro
	1.74	3.90	DMF	0.5	940	Spectro
	1.72	4.05	DMF	−10.0	460	Spectro
	1.59	3.04	DMF	−15.0	300	Spectro
	1.68	4.05	DMF	−20.5	220	Spectro
(MeO)$_3$PO + NEt$_4$N$_3$	2.0	4.0	MeOH	100.0	10.4	H$^+$/bromphenol blue
	2.0	4.0	MeOH	86.0	2.60	H$^+$/bromphenol blue
	2.0	4.0	MeOH	75.3	1.03	H$^+$/bromphenol blue
	2.0	4.0	DMF	75.3	33	H$^+$/bromphenol blue
	2.0	4.0	DMF	52.5	3.8	H$^+$/bromphenol blue
(i-Pr)$_2$POCl + NBu$_4$OAr[i]	2.05	3.87	MeOH	25.0	248[a]	Ag$^+$/H$^+$[d]
	2.01	3.93	DMF	−20.0	2650	Ag$^+$/H$^+$ [d]
	2.10	3.98	DMF	−25.0	1730	Ag$^+$/H$^+$ [d]
	1.96	4.04	DMF	−30.0	1380	Ag$^+$/H$^+$ [d]
	1.90	4.02	DMF	−36.0	650	Ag$^+$/H$^+$
	1.96	4.12	DMF	−40.0	515	Ag$^+$/H$^+$
4-NO$_2$C$_6$H$_4$F + NEt$_4$N$_3$	1.18	0.40	HMPT	25.0	11,600	Ag$^+$
	0.97	2.20	TMS	30.0	31.8	Ag$^+$

Table XIII (*Continued*)

Reactants RX + MY	[RX], 10^2 M	[MY], 10^2 M	Solvent	Temp, °C	10^4k,^{l} M^{-1} sec^{-1} ± 5%	Analytical procedure^m
4-NO$_2$C$_6$H$_4$I + NEt$_4$N$_3$	0.80	1.69	CH$_3$CN	101.0	45.6	Ag$^+$/H$^+$
	0.80	1.69	CH$_3$CN	76.5	4.51	Ag$^+$/H$^+$
4-NO$_2$C$_6$H$_4$I + NEt$_4$N$_3$	1.91	1.00	HMPT	25.0	5.50	Ag$^+$/H$^+$
	0.93	2.00	HMPT	25.0	6.10	Ag$^+$/H$^+$
4-NO$_2$C$_6$H$_4$I + NaN$_3$	0.56	1.34	NMePy	100.5	534	Ag$^+$/H$^+$
	0.56	1.34	NMePy	88.4	180	Ag$^+$/H$^+$
	1.00	2.16	NMePy	76.0	64	Ag$^+$/H$^+$
4-NO$_2$C$_6$H$_4$I + C$_6$H$_5$OK	2.01	1.02	DMF	25.0	202	Ag$^+$/H$^+$
2,4-(NO$_2$)$_2$C$_6$H$_3$I + NEt$_4$Cl	9.63	9.63	MeOH	133.0	1.14	Ag$^+$/Ba(NO$_3$)$_2$
	11.64	11.64	MeOH	100.0	0.0033	Ag$^+$/Ba(NO$_3$)$_2$
	4.12	1.99	DMF	45.5	20.4	Ag$^+$/Ba(NO$_3$)$_2$
	2.10	2.10	DMF	60.0	105	Ag$^+$/Ba(NO$_3$)$_2$
	2.10	2.10	DMF	75.3	504	Ag$^+$/Ba(NO$_3$)$_2$
	1.39	0.38	HMPT	25.4	460	Ag$^+$/Ba(NO$_3$)$_2$
2,4-(NO$_2$)$_2$C$_6$H$_3$I + NaCl	2.26	0.78	HMPT	25.0	281	Ag$^+$/Ba(NO$_3$)$_2$
2,4-(NO$_2$)$_2$C$_6$H$_3$I + NEt$_4$Br^h	4.20	2.08	DMF	45.5	1.02	Ag$^+$/Ba(NO$_3$)$_2$
	1.50	3.00	DMF	73.5	12.3	Ag$^+$/Ba(NO$_3$)$_2$
	2.10	2.10	DMF	84.2	84	Ag$^+$/Ba(NO$_2$)$_2$
	1.50	3.00	DMF	100.5	179	Ag$^+$/Ba(NO$_3$)$_2$
2,4-(NO$_2$)$_2$C$_6$H$_3$Br + KI	5.16	5.16	MeOH	138.8	3.6	Ag$^+$/Ba(NO$_3$)$_2$
	10.8	10.8	MeOH	120.6	0.85	Ag$^+$/Ba(NO$_3$)$_2$
	10.8	10.8	MeOH	100.5	0.16	Ag$^+$/Ba(NO$_3$)$_2$
2,4-(NO$_2$)$_2$C$_6$H$_3$Br + NEt$_4$Cl	2.10	2.10	DMF	75.3	1140	Ag$^+$/Ba(NO$_3$)$_2$
	4.20	2.08	DMF	60.0	455	Ag$^+$/Ba(NO$_3$)$_2$
	1.50	3.00	DMF	52.6	173	Ag$^+$/Ba(NO$_3$)$_2$
	1.50	3.00	DMF	45.5	87.5	Ag$^+$/Ba(NO$_3$)$_2$
2,4-(NO$_2$)$_2$C$_6$H$_3$Cl + NEt$_4$N$_3$	1.99	3.85	DMF	−15.5	2680	Ag$^+$/H$^+$
	2.09	3.85	DMF	−20.0	1530	Ag$^+$/H$^+$
	1.88	3.85	DMF	−33.0	490	Ag$^+$/H$^+$
	2.09	3.85	DMF	−40.0	260	Ag$^+$/H$^+$
2,4-(NO$_2$)$_2$C$_6$H$_3$OAr^i + NaN$_3$	1.64	3.90	MeOH	25.0	22.0	Spectro
2,4-(NO$_2$)$_2$C$_6$H$_3$OAr^i + NEt$_4$N$_3$	1.57	4.06	DMF	−20.0	2170	Spectro
	1.57	4.06	DMF	−25.0	1450	Spectro
	1.62	4.06	DMF	−30.0	760	Spectro
	1.66	4.06	DMF	−35.0	520	Spectro
	1.60	4.06	DMF	−40.0	350	Spectro
2-NO$_2$C$_6$H$_4$Cl + NaOMe	3.0	4.0	80DMSO-M	45.6	19.5	Ag$^+$/H$^+$
	3.0	4.5	80DMSO-M	55.2	46.8	Ag$^+$/H$^+$
	3.0	4.0	80DMSO-M	70.4	183	Ag$^+$/H$^+$
4-NO$_2$C$_6$H$_4$Cl + NaOMe	1.0	2.0	80DMSO-M	45.6	119	Ag$^+$/H$^+$
	1.0	2.0	80DMSO-M	56.0	290	OH$^-$/H$^+$
	2.0	4.0	80DMSO-M	38.8	72.0	OH$^-$/H$^+$
	2.0	4.0	80DMSO-M	25.3	17.4	OH$^-$/H$^+$
4-Cl-3-NO$_2$C$_6$H$_3$SO$_2$Me + NaOMe	1.0	2.0	80DMSO-M	0.3	2400	Ag$^+$/H$^+$
	1.0	1.0	80DMSO-M	4.0	3560	Ag$^+$/H$^+$
	1.0	2.0	80DMSO-M	6.0	4130	Ag$^+$/H$^+$
	1.0	1.0	80DMSO-M	8.2	4960	Ag$^+$/H$^+$
	3.0	1.0	80DMSO-M	11.2	6500	Ag$^+$/H$^+$
	1.0	1.0	80DMSO-M	15.5	9360	Ag$^+$/H$^+$
4-Cl-3-NO$_2$C$_6$H$_3$CF$_3$ + NaOMe	2.0	2.0	80DMSO-M	0.3	330	Ag$^+$/H$^+$
	2.0	2.0	80DMSO-M	7.5	778	Ag$^+$/H$^+$
	2.0	1.0	80DMSO-M	10.5	1070	Ag$^+$/H$^+$
	2.0	2.0	80DMSO-M	13.1	1380	Ag$^+$/H$^+$
	2.0	2.0	80DMSO-M	20.6	2930	Ag$^+$/H$^+$
4-Cl-3-NO$_2$C$_6$H$_3$NMe$_3$I + NaOMe	0.50	1.0	80DMSO-M	9.9	875^k	Ag$^+$/H$^+$
	1.0	1.0	80DMSO-M	9.9	717^k	Ag$^+$/H$^+$
	1.0	2.0	80DMSO-M	9.9	629^k	Ag$^+$/H$^+$
	2.0	2.0	80DMSO-M	9.9	582^k	Ag$^+$/H$^+$
	1.0	2.0	80DMSO-M	0.7	300^k	OH$^-$/H$^+$
	1.0	2.0	80DMSO-M	10.8	946^k	OH$^-$/H$^+$
	1.0	2.0	80DMSO-M	8.1	872^k	OH$^-$/H$^+$
	1.0	2.0	80DMSO-M	14.2	1470^k	OH$^-$/H$^+$
	1.0	2.0	80DMSO-M	7.2	589^k	OH$^-$/H$^+$
4-Cl-3-NO$_2$C$_6$H$_3$NMe$_3$I + NaN$_3$	1.0	2.0	MeOH	100.0	107^j	Ag$^+$/H$^+$
	1.0	2.0	MeOH	75.1	13.2^j	Ag$^+$/H$^+$
4-Cl-3-NO$_2$C$_6$H$_3$NMe$_3$NO$_3$ + NaN$_3$	0.40	0.60	MeOH	100.0	239^j	Ag$^+$/H$^+$
	4.0	6.0	MeOH	100.0	74^j	Ag$^+$/H$^+$
4-Cl-3-NO$_2$C$_6$H$_3$NMe$_3$I + NaN$_3$	1.0	1.0	DMF	25.0	163^k	Ag$^+$/H$^+$
4-Cl-3-NO-C$_6$H$_3$NMe$_3$I + NEt$_4$N$_3$	1.60	1.50	DMF	25.0	165^k	Ag$^+$/H$^+$
	8.5	0.77	DMF	25.0	209^k	Ag$^+$/H$^+$
2-Cl-3,5-(NO$_2$)$_2$C$_6$H$_2$CO$_2$Na + NaN$_3$	1.4	2.6	MeOH	75.1	40.1	Ag$^+$/H$^+$
	2.6	5.5	MeOH	75.1	50.1	Ag$^+$/m$^+$
	0.40	1.1	MeOH	75.1	32.8	Ag$^+$/H$^+$
	1.4	2.6	MeOH	50.2	4.7	Ag$^+$/H$^+$
	1.4	2.6	MeOH	87.0	100	Ag$^+$/H$^+$
	1.4	2.6	MeOH	100.7	287	Ag$^+$/H$^+$

Table XIII (*Continued*)

Reactants RX + MY	[RX], 10^2 *M*	[MY], 10^2 *M*	Solvent	Temp, °C	10^4k,[l] M^{-1} $sec^{-1} \pm 5\%$	Analytical procedure[m]
	0.4	0.4	DMF	0.4	134	Ag^+/H^+
	0.8	0.8	DMF	0.4	187	Ag^+/H^+
	3.2	0.8	DMF	1.0	351	Ah^+/H^+
	3.2	0.8	DMF	8.5	827	Ag^+/H^+
	3.2	0.8	DMF	−15.5	65.6	Ag^+/H^+
	3.2	0.8	DMF	−10.0	120	Ag^+/H^+
2-Cl-5-$NO_2C_6H_3CO_2Na$ + NaOMe	1.0	1.0	80DMSO-M	45.6	9.92	Ag^+/H^+
	2.0	4.0	80DMSO-M	45.6	25.2	Ag^+/H^+
	2.0	2.0	80DMSO-M	45.6	17.8	Ag^+/H^+
	1.0	2.0	80DMSO-M	45.6	14.2	Ag^+/H^+
	1.0	2.0	80DMSO-M	70.4	139	Ag^+/H^+
	1.0	2.0	80DMSO-M	55.2	35.0	Ag^+/H^+
4-Cl-3-$NO_2C_6H_3CO_2Na$ + NaOMe	0.5	1.0	80DMSO-M	45.6	14.2	Ag^+/H^+
	2.0	4.0	80DMSO-M	45.6	23.4	Ag^+/H^+
	2.0	2.0	80DMSO-M	45.6	21.0	Ag^+/H^+
	1.0	1.0	80DMSO-M	45.6	17.2	Ag^+/H^+
	1.0	2.0	80DMSO-M	65.7	93.0	Ag^+/H^+
	1.0	2.0	80DMSO-M	55.2	42.0	Ag^+/H^+
	1.0	2.0	80DMSO-M	45.6	19.6	Ag^+/H^+
2,4-$(NO_2)_2C_6H_3I$ + KSCN	1.04	2.00	DMAC	25.0	5.64	$Ag^+/Ba(NO_3)_2$
	1.00	1.72	CH_3CN	25.0	1.05	$Ag^+/Ba(NO_3)_2$
	1.00	2.03	DMSO	25.0	0.605	$Ag^+/Ba(NO_3)_2$
	1.03	2.02	$HCONH_2$	101.0	25.5	$Ag^+/Ba(NO_3)_2$
	1.03	2.03	$HCONH_2$	75.0	3.45	$Ag^+/Ba(NO_3)_2$
	1.02	2.05	TMS	30.0	3.03	$Ag^+/Ba(NO_3)_2$
	2.0	1.0	CH_3NO_2	25.0	0.82	$Ag^+/Ba(NO_3)_2$
	1.0	2.03	NMePy	25.0	4.1	$Ag^+/Ba(NO_3)_2$
4-$NO_2C_6H_4F$ + NaN_3	1.26	2.00	NMePy	25.0	130	Ag^+

[a] Corrected for solvolysis as in ref 43, using solvolysis rates in Table XV. [b] Equilibrium constant is 0.48, rate constant calculated over first 10% reaction. [c] Reaction under nitrogen in solutions flushed with nitrogen. [d] Solutions poured into cold ethanol and titrated immediately. [e] The equilibrium constant is 0.285 at 100° and 0.27 at 60° in methanol and 7.0 in DMSO at 25°. [f] Solution contained 50% excess thiophenol to minimize methanolysis and oxidation. [g] Reaction in the presence of 0.040 *M* lutidine. [h] Equilibrium constant is 3.0 at 100.5° and 3.3 at 73.5°. [i] Ar is 4-nitrophenyl. [j] Reaction is only 65% SNAr substitution; the remainder is 35% SN2 substitution at methyl. The rate of constant is for the SNAr reaction. [k] Reaction is 100% SNAr substitution. [l] Reactions sometimes have an elimination and a substitution path; the rate constants are for loss of RX, *i.e.*, the sum of the SN2 and E2 reactions, both of which effectively consume the basic nucleophile. This over-all rate constant is split into its SN2 and E2 components in Table IV, following vpc and volumetric analysis of products. [m] See Experimental Section.

Table XIV. Arrhenius Parameters for SN2 Reactions

Reactants[a]	Solvent	$E_a \pm 0.5$ kcal $mole^{-1}$	Log *B* ± 0.5
n-BuI + NEt_4Cl	MeOH	22.4	10.3
n-BuI + NEt_4Br	MeOH	21.9	10.5
n-BuI + KSCN	MeOH	18.8	9.3
n-BuI + NaN_3	MeOH	20.1	10.2
n-BuI + $NaNO_2$	MeOH	20.8	10.1
n-BuBr + C_6H_5SNa	DMF	13.3[c]	11.6[c]
i-PrBr + $NaSC_6H_5$	MeOH	19.7	10.7
$C_6H_5CH_2Cl$ + NaN_3	MeOH	20.1	10.5
$CH_3S^+Me_2$ + N_3^-	MeOH[b]	32.8	16.7
$CH_3S^+Me_2$ + N_3^-	DMF[b]	27.0	15.6
$C_6H_{11}Br$ + NEt_4N_3 SN2	MeOH	23.8	10.7
	DMF	18.8	9.9
CH_3OTs + KSCN	MeOH	18.0	9.4
CH_3OTs + KSCN	DMF	19.3	11.1
i-BuBr + NaN_3	MeOH	22.7	10.3
CH_3OTs + NaN_3	DMF	13.3	8.6
CH_3OTs + NaN_3	MeOH	15.8	8.3
4-$NO_2C_6H_4CH_2Br$ + NEt_4N_3	DMF	14.1[c]	11.6[c]
$(MeO)_3PO$ + NEt_4N_3	MeOH	24.1	11.1
	DMF	21.0	10.7
CH_3CO_2Ar + NEt_4N_3	DMF	9.3[c]	6.9[c]
(*i*-Pr)$_2$POCl + NaOAr	DMF	9.7[c]	7.8[c]
trans-TsCH=CHCl + NEt_4N_3	DMF	12.3	9.5
i-PrBr + NaOMe	MeOH	25.4	13.0
i-PrBr + NEt_4N_3	MeOH	23.5	12.2
$C_6H_5CH_2Cl$ + NaOMe	MeOH	22.5	11.9
	80DMSO-M	17.4	10.6
2,4-$(NO_2)_2C_6H_3Br$ + NEt_4Cl	DMF	18.8	10.8
2,4-$(NO_2)_2C_6H_3I$ + NEt_4Cl	MeOH	32.1[c]	13.4[c]
	DMF	23.7	13.6
2,4-$(NO_2)_2C_6H_3Cl$ + NEt_4N_3	DMF	11.4[c]	9.2[c]
2-Cl-3,5-$(NO_2)_2C_6H_2CO_2^-$ + NEt_4N_3	MeOH[b]	18.5	9.0
	DMF[b]	14.3	9.2
2,4-$(NO_2)_2C_6H_3OAr$ + NEt_4N_3	DMF	10.6[c]	8.5[c]

Table XIV (*Continued*)

Reactants[a]	Solvent	$E_a \pm 0.5$ kcal mole^{-1}	Log $B \pm 0.5$
$C_6H_{11}Br + NEt_4N_3$ E2C	MeOH	24.7	10.4
	DMF	20.9	10.5
2-$NO_2C_6H_4Cl$ + NaOMe	MeOH	23.6	10.4
	80DMSO-M	19.6	10.7
4-Cl-3-$NO_2C_6H_3CF_3$ + NaOMe	MeOH	19.7	10.6
	80DMSO-M	16.6	11.8
2,4-$(NO_2)_2C_6H_3Br$ + KI	MeOH	25[c]	10[c]
2,4-$(NO_2)_2C_6H_3I + NEt_4Br$	DMF	22.8	11.6
4-Cl-3-$NO_2C_6H_3CO_2^-$ + NaOMe	MeOH[b]	21.1	9.2
	80DMSO-M[b]	16.6	8.7
4-Cl-3-$NO_2C_6H_3NMe_3^+$ + NaOMe	MeOH[b]	22.2	13.7
	80DMSO-M[b]	17.1	12.0
4-Cl-3-$NO_2C_6H_3SO_2Me$ + NaOMe	MeOH	18.6	11.1
	80DMSO-M	14.2	10.7
4-Cl-$C_6H_4NO_2$ + NaOMe	MeOH	24.1	11.2
	80DMSO-M	18.3	10.6
2-Cl-5-$NO_2C_6H_3CO_2^-$ + NaOMe	MeOH[b]	26.9	12.2
	80DMSO-M[b]	20.9	11.5
4-$NO_2C_6H_4I + NEt_4N_3$	NMePy	23.8	12.6
	CH_3CN	24.0	11.6
2,4-$(NO_2)_2C_6H_3I$ + KSCN	$HCONH_2$	20.0	9.0

[a] Abbreviations are Ar = 4-nitrophenyl, Ts = *p*-toluenesulfonyl, 80DMSO-M = 80% v:v DMSO–methanol. [b] At ionic strength 10^{-3} *M*. [c] Uncertainty is ±2 kcal in E_a and ±1 in log *B*.

Table XV. Comparison of S_N2 and Solvolysis Rates in Methanol[a]

Reaction[f]	Reactants[b]	Temp, °C	Log k[c] (solv)	Log "k_1"[d] (S_N2)	Reaction[b]	Reactants[b]	Temp, °C	Log k[c] (solv)	Log "k_1" (S_N2)
1	$CH_3Cl + N_3^-$	75.0	Slow	...	44	$C_6H_{11}Br + N_3^-$ (E2)	100.0	−5.3	−4.7
7	$CH_3I + Cl^-$	25.0	−6.2	−5.5	45	$C_6H_{11}I + N_3^-$ (S_N2)	100.0	<−4.8	−4.0
21	$CH_3OTs + Br^-$	25.0	−6.2	−5.8	46	$C_6H_{11}I + N_3^-$ (E2)	100.0	<−4.8	−4.1
27	$(MeO)_3PO + N_3^-$	100.0	Slow	...	47	$C_6H_{11}OTs + SAr^{1-}$	25.0	Slow	...
28	*n*-BuBr + N_3^-	50.0	Slow	...	51	$C_6H_5CH_2Cl + N_3^-$	100.0	−4.1	−2.8
29	*n*-BuI + Cl^-	101.0	−4.7	−4.0	53	*trans*-TsCH=CHCl + N_3^-	25.0	Slow	...
35	*i*-BuBr + NaN_3	107	−5.2	−4.1	54	$CH_3CO_2Ar^1 + N_3^-$	25.0	Slow	...
38	*t*-BuBr + $C_6H_5S^-$ (S_N2)	25.0	−4.7[e]	−4.4	55	$(i\text{-}Pr)_2POCl + OAr^{1-}$	25.0	−3.6	−3.0
39	*t*-BuBr + $C_6H_5S^-$ (E2)	25.0	−5.0[e]	−4.2	68	$ArOAr^1 + N_3^-$	25.0	Slow	...
42	*i*-PrBr + OMe^- (E2)	100.0	−4.2	−3.4					
43	$C_6H_{11}Br + N_3^-$ (S_N2)	100.0	−5.3	−4.8					

[a] Containing 0.04 *M* 2,6-lutidine for solvolysis reactions. [b] Ar is 2,4-dinitrophenyl, Ar^1 is 4-nitrophenyl, C_6H_{11} is cyclohexyl, Ts is *p*-toluenesulfonyl. [c] Rates of solvolysis are in sec^{-1}, "slow" denotes that no solvolysis was observed during 50% of the S_N2 reaction. [d] Initial rate of the S_N2 reaction expressed as a first-order rate "constant" (in sec^{-1}), for comparison with the solvolysis rate. The S_N2 reactions shown here are the slowest, for the particular substrate, of those recorded in Table IV. All other reactions in Table IV of each substrate are less affected by methanolysis. [e] The solvolysis rate has been divided into that portion which gives isobutylene (30%) and that portion (70%) which gives *t*-butyl methyl ether. [f] See Table IV.

Table XVI. S_N2 and E2 Reactions

RX + MY	Solvent	Temp, °C	F_S[a] (vpc)	F_S[a] (Ag^+)	F_E[a] (vpc)	F_E[a] (H^+)
i-PrBr + NaSPh	MeOH	50.0	...	...	<0.01[b]	...
	DMF	25.0	...	...	<0.01[b]	...
i-PrBr + NaN_3	MeOH	100.0	...	...	<0.01[b]	...
	DMF	25.0	...	1.0	<0.01[b]	...
i-PrBr + NaOMe	MeOH	75.0	(0.05)[c]	...	0.96[d]	...
	80DMSO-M	25.0	0.03	...	0.97	...
t-BuBr + NaSPh	MeOH[e]	25.0	...	...	0.60[f]	0.7[g]
	DMF[e]	25.0	...	...	>0.98	1[g]
$C_6H_{11}Br + NEt_4N_3$	MeOH	100.0	...	...	0.32	0.33
	MeOH	87.0	...	...	...	0.29
	MeOH	74.6	...	...	...	0.25
	DMF	100.0	...	0.8	0.20	0.19
	DMF	87.0	...	...	...	0.17
	DMF	74.6	...	...	...	0.16
$C_6H_{11}I + NEt_4N_3$	MeOH	100.0	...	...	0.41	0.40
	MeOH	75.0	...	...	...	0.40
	DMF	25.0	...	...	0.17	0.20
$C_6H_{11}OTs + NBu_4SAr$[e]	MeOH	75.0	...	...	0.60	0.58[g]
	Me_2CO	75.0	...	...	0.56	0.50[g]

[a] F_S is the fraction of substitution; F_E is the fraction of elimination. They were measured by vpc as well as by titration of azide consumed (denoted Ag^+) after neutralization and by titration of the acid produced (denoted H^+) and comparison with total reaction. Analysis at 50% reaction and at 5 half-lives gave virtually the same result. [b] No propene detected by vpc. [c] Is most likely produced by methanolysis, not by the S_N2 reaction. [d] Mainly formed by the E2 reaction. [e] Under nitrogen, solution contains 0.10 *M* lutidine to prevent addition of mercaptan to olefin. [f] About 10% of the isobutylene may be formed in an E1 reaction. [g] Value at 50% reaction; the acid decreases with time, perhaps because oxidation of RS^- produces strong base.

solvents and solutions. The constants were reproducible to within ±20%. For solvents which were of low volatility, distribution between the two solvents in sealed dessicators (or for solutes of low volatility, distribution between each solvent and decalin) gave solvent activity coefficients agreeing to ±50%. Analysis by vpc of the vapor phase, above solutions of alkyl halides using a gas-circulating pump and a gas-sampling valve, attached to a Perkin-Elmer 880 gas chromatograph, followed by analysis of the liquid phase, was only suitable for very volatile solutes. Agreement between the solvent activity coefficients of the methyl halides by the three methods (Henry's law, distribution, and vpc) was to within ±30%. We used the Henry's law method to measure data in Table III, which are satisfactory for our purposes.

Elimination Reactions. Elimination or substitution products were determined by vpc analysis at 1 half-life and 5 half-lives of reaction. Details are in Table XVI. Reactions of thiophenoxide, for vpc analysis, were performed in the presence of a threefold excess of 2,6-lutidine, because thiophenol adds to alkenes in dipolar aprotic solvents. For reactions of azide ion, the fractions of elimination, as estimated by vpc and by titration of acid produced, were in good agreement. The reactions of thiophenoxide and *p*-nitrothiophenoxide were complicated by oxidation; the vpc analysis of products was considered more reliable than the titration procedures. The reaction of isopropyl bromide with sodium methoxide in methanol is accompanied by methanolysis. The small amount (5.4%) of isopropyl methyl ether, observed by vpc for reaction in methanol at 75°, could be accounted for by methanolysis, but 2.7% of this ether is produced by an SN2 reaction in 80% DMSO–methanol at 25°.

To estimate fractions of elimination in reactions of azide ion with alkyl bromides, the sample was poured into 80% acetone–water and the hydrazoic acid was estimated by titration with NaOMe–MeOH using thymol blue as indicator. Bromphenol blue was then added and the sample was titrated with HCl in 80% acetone–water to estimate the total azide ion present, *i.e.*, unconsumed by the SN2 reaction. The procedure was also used for reactions of thiophenoxide but was less satisfactory. The total (SN2 + E2) reaction was given by bromide ion produced.

Acknowledgment. We thank Mrs. Y. C. Smart and Miss S. H. Tay for technical assistance. This research was supported by a grant from the Australian Research Grants Commission.

Proton Magnetic Resonance Studies of Self-Association and Metal Complexation of Nucleosides in Dimethyl Sulfoxide[1]

Sung M. Wang and Norman C. Li

Contribution from the Chemistry Department, Duquesne University,
Pittsburgh, Pennsylvania 15219. *Received February 16, 1968*

Abstract: For the purpose of deciding whether a ternary complex is formed on mixing a metal salt and two nucleosides, we have carried out proton magnetic resonance studies in which the metal salt is $ZnCl_2$ and the nucleosides are adenosine (A), guanosine (G), cytidine (C), and uridine (U), in dimethyl sulfoxide medium. Although dimethyl sulfoxide is a hydrogen-bond acceptor, we take as reference state the one in which the nucleoside is bonded to solvent and look for further shifts of NH, NH_2, and CH proton signals at different temperatures as the nucleoside concentration is increased and as an increasing amount of $ZnCl_2$ is added. Formation constants of 1:1 Zn–nucleoside complexes are obtained. Of the four nucleosides studied, the ternary complexes formed are Zn–A–G and Zn–A–C.

The nucleosides are of prime biological importance, and proton magnetic resonance studies of these have been reported by a number of investigators.[2–8] In order to decide whether a ternary complex is formed on mixing a metal salt and two nucleosides, it is desirable to obtain data on self-association of the individual nucleosides and on formation of binary metal–nucleoside complexes. This paper presents the results of proton magnetic resonance (pmr) studies on these systems, using $ZnCl_2$ as metal salt and adenosine (A), guanosine (G), cytidine (C), and uridine (U) as nucleosides.

Dimethyl sulfoxide (DMSO) is a polar liquid and a powerful solvent for many aromatic compounds and inorganic salts. Since the use of water as solvent causes complications in that the bond-forming hydrogens exchange rapidly with the water protons, we have selected DMSO as solvent because it provides adequate solubility without proton transfer. Although DMSO is known to be a hydrogen-bond acceptor,[9,10] we can take as reference state the one in which nucleoside is hydrogen-bonded to the solvent *via* the protons attached to nucleoside nitrogens, and look for further shifts of the NH, NH_2, and CH proton signals at different temperatures as the nucleoside concentration is increased and as an increasing amount of $ZnCl_2$ is added.

Calculation of Formation Constants of Binary Metal Complexes. The downfield shifts of heterocyclic aromatic ring proton resonances upon protonation or metal complexation have been ascribed to extensive π-electron redistribution.[11,12] The ring proton res-

---

[1] This investigation was supported by Public Health Service Grant No. GM 10539-05 and by National Science Foundation Grant No. GB-4065.

(2) L. Katz and S. Penman, *J. Mol. Biol.*, **15**, 220 (1966).

(3) S. I. Chan, M. P. Schweizer, P. O. P. Ts'o, and G. K. Helmkamp, *J. Am. Chem. Soc.*, **86**, 4182 (1964).

(4) O. Jardetzky, *Biopolymers, Symp.*, [1] 501 (1964).

(5) J. P. Kokko, J. H. Goldstein, and L. Mandell, *J. Am. Chem. Soc.*, **83**, 2909 (1961).

(6) G. L. Eichhorn, P. Clark, and E. D. Becker, *Biochemistry*, **5**, 245 (1966).

(7) L. Gatlin and J. C. Davies, Jr., *J. Am. Chem. Soc.*, **84**, 4464 (1962).

(8) H. T. Miles, *ibid.*, **85**, 1007 (1963).

(9) T. Gramstad, *Spectrochim. Acta*, **19**, 829 (1963).

(10) S. F. Ting, S. M. Wang, and N. C. Li, *Can. J. Chem.*, **45**, 425 (1967).

(11) R. H. Carlson and T. C. Brown, *Inorg. Chem.*, **5**, 268 (1966).

(12) S. M. Wang and N. C. Li, *J. Am. Chem. Soc.*, **88**, 4592 (1966).