Solvation of Ions. XV.[1] Solvation of "Tight" and "Loose" Transition States for SN2, E2C, and E2Hal Reactions of Thiophenoxide Ion in Ethanol, Methanol, and Dimethylformamide

E. C. F. Ko and A. J. Parker[2]

Contribution from the School of Chemistry, University of Western Australia, Nedlands, Western Australia 6009. *Received May 17, 1968*

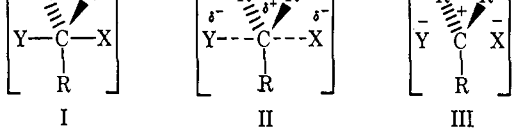
Abstract: The rates of some SN2 reactions, E2 dehydrobrominations (E2C reactions), and E2 debrominations (E2Hal reactions) have been measured in solvents ethanol, methanol, and dimethylformamide. The solvent activity coefficients of the appropriate transition states suggest that SN2 reactions of *p*-methoxybenzyl bromide have "looser" transition states than do the corresponding reactions of *p*-nitrobenzyl bromides and that as the carbon atom (C_α) being attacked changes from primary through secondary to tertiary, in a series of alkyl bromides, the SN2 and E2C transition states "loosen." A "loose" transition state has bond forming lagging behind bond breaking, so that negative charge is localized on the entering and leaving group and positive charge is localized on C_α. The E2C transition state is much looser than a corresponding E2Hal transition state. Nucleophilic tendencies of thiophenoxide, azide, chloride, and ethoxide ions toward a series of alkyl and benzyl bromides, as well as substituent effects on rates of SN2 reactions of benzyl bromides, are also in accord with a looser transition state, as C_α becomes more substituted and/or more able to accommodate positive charge.

The observation[3-5] that bimolecular reactions (1) are very much faster and cleaner in dipolar aprotic solvents than in protic solvents has been useful. However, we have noticed[1] that reactions (1) of primary alkyl bromides become much faster with transfer from protic to dipolar aprotic solvent than do the corresponding reactions of secondary alkyl bromides. Moreover bimolecular reactions (1) of tertiary alkyl bromides appear to be only slightly susceptible to such solvent transfer,[1] and some bimolecular reactions (1) of secondary tosylates are actually faster in methanol than in acetone. In this paper, we examine in detail an explanation[1] for this important observation on a set of reactions which are fundamental to organic chemistry. The explanation throws new light on one of the classical areas[6] of the SN1 and SN2 mechanistic pathways, the borderline region.

$$Y^- + RX \longrightarrow [YRX^-]^{\ddagger} \longrightarrow \begin{array}{l}\text{products of substitution,}\\ \text{elimination, addition, or}\\ \text{abstraction}\end{array} \qquad (1)$$

In part XIV,[1] we showed how comparison of solvent activity coefficients for model solutes with solvent activity coefficients ${}^{\circ}\gamma_{YRX\ddagger}{}^{s}$, for transfer of transition states of bimolecular reactions (1) from a protic reference solvent, o, to a dipolar aprotic solvent, s, could indicate something about the charge distribution in these transition states. The procedure is to examine a series of transition states, $YRX^{-\ddagger}$, in which Y and X are held constant and R changes in such a way that ${}^{\circ}\gamma_{RX}{}^{s}$ is roughly constant.[7] We then apply the principle[1] that the more positive[8] the value of log ${}^{\circ}\gamma_{YRX^{-}\ddagger}{}^{s}$ the greater the localization of negative charge on Y and X in the transition state and thus the greater the carbonium ion character of R.

Solvent activity coefficients already reported[1] for a limited number of transition states suggest that there is a spectrum of SN2 transition states, II, between the extremes of synchronous SN2 (I) and carbonium ion SN2 (III). From I to III, bond breaking moves increasingly ahead of bond formation, so that negative charge becomes increasingly localized on Y and X. It is convenient to describe I as a "tight" transition state and III as a "loose" transition state. We lay no claims as to the originality of this proposal,[6] but feel that solvation of transition states provides new evidence which strongly supports such a concept. The SN1 transition state can be a logical extension of II very like III, with bond breaking completely ahead of bond forming. The SN1 transition state is not necessarily III; this is an extreme in the SN2 spectrum, but III could resemble a transition state for a rate-determining attack on a preformed ion pair.



I II III

In this paper we study reactions (1) of thiophenoxide and azide ions ($Y = C_6H_5S^-, N_3^-$) with alkyl, benzyl,

---

[1] Part XIV: R. Alexander, E. C. F. Ko, A. J. Parker, and T. Broxton, *J. Am. Chem. Soc.*, **90**, 5049 (1968).

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

[3] A. J. Parker, *J. Chem. Soc.*, 1328 (1961).

[4] A. J. Parker, *Quart. Rev.* (London), **16**, 163 (1962).

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

[6] C. K. Ingold, "Structure and Mechanism in Organic Chemistry," G. Bell and Sons Ltd., London, 1953, Chapter 7; C. A. Bunton, "Nucleophilic Substitution at a Saturated Carbon Atom," Elsevier Publishing Co., New York, N. Y., 1963; E. S. Gould, "Mechanism and Structure in Organic Chemistry," Holt, Rinehart and Winston, New York, N. Y., 1959, Chapter 8; J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, Chapter 7; G. J. Frisone and E. R. Thornton, *J. Am. Chem. Soc.*, **90**, 1211 (1968).

[7] Thus solvation effects due solely to the nature of R, which are large, for example, when R changes from methyl to *p*-nitrobenzyl, can be ignored, relative to effects due to the changes at the reaction center.

[8] More positive when the reference solvent is protic and the solvent S is dipolar aprotic as in part XIV.[1] When the reference solvent is dipolar aprotic and the other solvent is protic, as had to be the case in Table III, then of course the more negative the value of log ${}^{\circ}\gamma_{YRX\ddagger}{}^{s}$, the greater the localization of negative charge on Y and X.

Table I. Rates of Bromide Ion Production from Reaction of Alkyl, Benzyl, and Cycloalkyl Bromides with Thiophenoxide and Azide Ions

RBr	T°, C	Solvent	[RBr], 10^2 M	[NaSC$_6$H$_5$], 10^2 M	[C$_6$H$_5$SH], 10^2 M	[Lut], 10^2 M	10^4k_2, M^{-1} sec^{-1}	10^2F_E[e]
n-BuBr	−21.0	DMF	1.94	4.07			5300	0.0
	−25	DMF	2.05	4.02			4000	
	−35	DMF	1.74	3.60			1370	
	−40	DMF	1.88	4.14			700	
	25.0	EtOH	1.91	4.19	1.8		120	0.0
C$_6$H$_{11}$Br	25.0	DMF	1.86	3.82			100	
	25.0	DMF	1.96	4.80		5.53		60[a]
	100.0	EtOH	2.03	4.36	0.40		365	
	86.5	EtOH	1.80	4.36	0.40		110	
	76.4	EtOH	1.90	4.36	0.40		49	
	100.0	EtOH	1.85	4.85		4.86		60[a]
	87.0	EtOH	1.85	4.85		4.86		60[a]
trans-1,2-C$_6$H$_{10}$Br$_2$	25.0	DMF	1.09	3.93			9200[b]	100[a]
	25.0	DMF	1.00	4.80		5.60		100[a]
	86.6	EtOH	0.97	4.02	0.53		310[b]	
	75.0	EtOH	0.80	4.02	0.31		100[b]	
	87.0	EtOH	1.02	4.93		5.72		100[a]
	100.0	MeOH	1.00	4.00	0.6		370[b]	
	87.2	MeOH	1.04	4.16			118[b]	
	75.0	MeOH	1.18	3.98	0.2		42[b]	
	100.0	MeOH	0.95	4.54		5.60		100[a]
4-MeOC$_6$H$_4$CH$_2$Br	0.0	EtOH	1.55	4.00			8200	
				[NEt$_4$N$_3$], 10^2 M				
4-MeOC$_6$H$_4$CH$_2$Br	−19	DMF	1.94	4.56			2600	
	−20	DMF	1.85	4.04			2800	
	−30	DMF	1.85	4.04			1050	
	−41	DMF	1.80	4.30			360	
	25.0	EtOH	1.88			3.70	44[c]	
	25.0	EtOH	1.67	4.08			660	
	0.0	EtOH	1.76	3.02			40	
	25.0	EtOH	2.22	4.15	4.64[d]		640[d]	
4-NO$_2$C$_6$H$_4$CH$_2$Br	25.0	EtOH	2.10	4.14			89	
C$_6$H$_5$CH$_2$Br	76.5	EtOH	2.07			4.60	25[c]	
	−21	DMF	2.00	4.56			660	
	0.0	DMF	1.92	4.56			4200	
	25.0	EtOH	2.19	4.14			53	

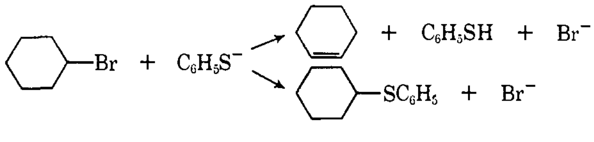
[a] By vpc analysis for cyclohexene; values agree with titrimetric estimates of elimination. [b] Rate expression allows for loss of 2 mol of thiophenoxide/mol of cyclohexene formed. [c] The first-order rate constant observed for solvolysis, k_1, is expressed here as an initial second-order rate constant, $k_2 = k_1/0.04$, so that competition between the solvolysis and S$_N$2 reactions can be evaluated. [d] This concentration of NEt$_4$Br added to see if there was a common ion retardation of an S$_N$1 process. The lower value is not significant. [e] Fraction of reaction proceeding with elimination.

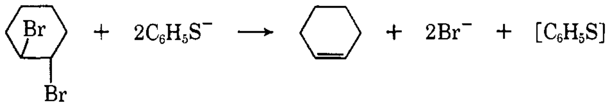
and cycloalkyl bromides (X = Br) in the protic solvents methanol and ethanol and the dipolar aprotic solvent dimethylformamide (DMF). The use of thiophenoxide ion, a very powerful nucleophile, in ethanol, a protic solvent of relatively low ionizing power, enables us to study reactions (1), which were previously studied[1] with weaker nucleophiles in more ionizing solvents (*e.g.*, methanol), a situation where E1 and S$_N$1 processes sometimes intrude. A disadvantage of ethanol as solvent is its low dielectric constant, so that rates are influenced by ion association, but provided the same initial concentration of electrolyte is used for all reactions (1) in ethanol, valid comparisons can be made. Reactions of thiophenoxide with benzyl bromide in DMF were too fast for us to measure, so we studied S$_N$2 reactions of azide ion.

Results

New rate and product data for reactions 2-5 are given in Table I. Appropriate second-order kinetics for loss of thiophenoxide ion as thiophenol and thioether or for loss of azide ion as benzyl azide, and for production of bromide ion, were obeyed. Solvolysis rates, measured in the presence of 2,6-lutidine to prevent reaction of HBr with the alcohols, were always less than 5% (usually much less) of the initial rates of reactions in the presence of 0.04 M sodium thiophenoxide or tetraethylammonium azide. Where data are available (ref 1 and Tables I and IV) reactions are faster with thiophenoxide than are the corresponding reactions with azide than with weaker nucleophiles in the same solvent. The reactions are thus bimolecular, depending on the nature and concentration of Y. Elimination (3a) and

$$n\text{-BuBr} + C_6H_5S^- \longrightarrow n\text{-BuSC}_6H_5 + Br^- \qquad (2)$$


(3a)
(3b)


(4)

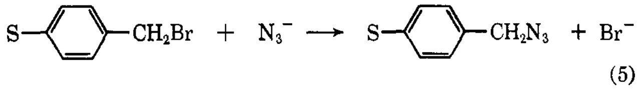

(5)

Table II. Reactions of *t*-Butyl Bromide

Solvent	T, °C	[t-BuBr], $10^2\ M$	Additive	[Add], $10^2\ M$	10^4k_2,[a] M^{-1} sec^{-1}	10^6k_2[Add]$_0$, sec^{-1}	10^2F_E[b]
EtOH	25.0	10.3				4.5[f,g]	19[f]
EtOH	75.0	2.12					14
EtOH	75.0	2.00	Lut[c]	10.5			48
EtOH	25.0	2.00	Lut[c]	34		3.2[g]	44
EtOH	25.0	1.71	NaOEt	2.4		5.2[f,g]	26[f]
EtOH	25.0	1.71	NaOEt	8.3		6.4[f,g]	46[f]
EtOH	25.0	3.84	NaOEt	201		42.0[f,g]	>91[f]
EtOH	25.0	1.46	$NaOC_6H_5$	3.24	1.6	5.2	
EtOH	25.0	1.40	$NaOC_6H_5$	8.50	1.1	9.4	
EtOH	25.0	1.59	$NaSC_6H_5$	3.07	4.0	12.3	
EtOH	25.0	1.42	$NaSC_6H_5$	6.16	4.1	25.3	
EtOH	25.0	1.55	$NaSC_6H_5$	9.22	3.5	32.3	
EtOH	25.0	2.02	$NaSC_6H_5$ +Lut	4.06[d]			61
EtOH	75.0	1.94	$NaSC_6H_5$ +Lut	27.6[e]			96
EtOH	100	1.89	$NaSC_6H_5$ +Lut	19.6			97
MeOH	25.0	2.10	Lut	20.0		25[g]	
MeOH	25.0	2.16	$NaSC_6H_5$	4.57	13.6	62	
MeOH	25.0	1.94	$NaSC_6H_5$	9.15	11.0	100	60
DMF	25.0	2.10				2.84[g]	98
DMF	25.0	2.02	$NaSC_6H_5$	4.06	170	680	
DMF	25.0	3.06	$NaSC_6H_5$	7.37	169	1200	
DMF	25.0	1.97	$NaSC_6H_5$	7.0			>98

[a] These reactions obeyed good second-order kinetics for over 50% of reaction. [b] Isobutylene estimated by vpc except for work described in ref 11. [c] 2,6-Lutidine. [d] Solution contained 0.34 M lutidine; this is the concentration of NaSPh. [e] Solution contained 0.53 M lutidine; this is the concentration of NaSPh. [f] Reference 11. [g] Observed first-order rate constant for bromide ion production. Reaction followed first-order kinetics.

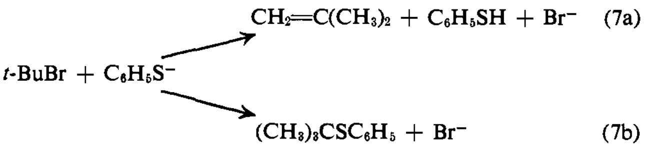
substitution (3b) compete in reaction 3, but both effectively remove thiophenoxide ion, so that second-order kinetics for loss of thiophenoxide are obeyed. The debromination reaction (4) is a bimolecular process, but 2 mol of thiophenoxide is consumed for each act of elimination, because of a subsequent reaction (6). An

$$C_6H_5SBr + C_6H_5S^- \longrightarrow (C_6H_5S)_2 + Br^- \qquad (6)$$

appropriate second-order expression was therefore used for reaction 4.

Reactions were carried out under dry nitrogen, to minimize oxidation of thiophenoxide; those in ethanol or methanol had a slight excess of thiophenol, to minimize alcoholysis of the thiophenoxide ion. Thiophenoxide and thiophenol were followed by acid–base titration with appropriate indicators. Production of bromide ion was followed potentiometrically with silver nitrate and proceeded as required by reactions 2–5. The cyclohexene formed in reactions 3a and 4 was monitored by vpc analysis of reaction mixtures containing a fivefold excess of 2,6-lutidine, to prevent addition of thiophenol to cyclohexene. The thiophenol produced in the first 20% of reaction 3 suggested the same fraction of elimination as obtained by vpc. Appropriate blanks confirmed the validity and necessity for these procedures.

Rate and product data for reactions (7) of *t*-butyl bromide are in Table II. We have devoted particular attention to these reactions,[9] because it is important to establish that the rates of production of bromide ion, thiophenol, *t*-butyl phenyl sulfide, and isobutylene are for bimolecular processes. We must consider the possibility of a rate-determining unimolecular ionization, which is independent of thiophenoxide, except insofar as sodium thiophenoxide exerts a general salt effect, which assists ionization.[6]



$$t\text{-BuBr} + C_6H_5S^- \longrightarrow CH_2{=}C(CH_3)_2 + C_6H_5SH + Br^- \qquad (7a)$$

$$t\text{-BuBr} + C_6H_5S^- \longrightarrow (CH_3)_3CSC_6H_5 + Br^- \qquad (7b)$$

The reactions of sodium thiophenoxide with *t*-butyl bromide in DMF, like reactions of chloride ion in acetone,[9] are clearly E2 reactions (7a) because they are so much faster than the solvolysis reaction. If there is an SN2 component, as there is with chloride and azide ion in acetone,[9] it is too small for us to detect. Solvolysis accounts for <0.5% reaction.

The reactions of $NaSC_6H_5$ with *t*-butyl bromide in ethanol are significantly faster and give higher yields of isobutylene than does the ethanolysis of *t*-butyl bromide either in the presence or absence of 2,6-lutidine (Table II). de la Mare and Vernon[10] concluded that the closely related reaction of *t*-butyl chloride with sodium thiophenoxide in ethanol was mainly E2, with perhaps a minor (<8%) SN2 component and a SN1 + E1 component, whose magnitude depended on the concentration of sodium thiophenoxide. Dhar, Hughes, and Ingold[11] decided that the loss of base and production of isobutylene from reaction of *t*-butyl bromide with sodium ethoxide in ethanol, which is slower than the reaction with sodium thiophenoxide in ethanol, was an E2 reaction with a significant SN1 + E1 component. Their results are also presented in Table II. If the sodium ethoxide reaction is E2, then the sodium thiophenoxide reaction is even more so. It is important to note the effect of 2,6-lutidine on the products of ethanol-

---

(9) D. Cook and A. J. Parker, *J. Chem. Soc., B*, 142 (1968).

(10) P. B. D. de la Mare and C. A. Vernon, *J. Chem. Soc.*, 41 (1956).

(11) M. L. Dhar, E. D. Hughes, and C. K. Ingold, *ibid.*, 2065 (1948).

Table III. Analysis of Rate Data for Reactions of Alkyl, Benzyl, and Cycloalkyl Bromides with Thiophenoxide and Azide Ion in Methanol, Ethanol, and Dimethylformamide at 25°; Reference Solvent, Dimethylformamide (D)

$RBr + Y^-$	Log k^D	Solvent	Log k^s	Log k^s/k^D	Log $^D\gamma_{RBr}{}^s$	Log $^D\gamma_{Y^-}{}^s$	Log $^D\gamma^s{}_\ddagger$
SN2 reactions							
n-BuBr + $C_6H_5S^-$	$+1.7^a$	MeOH	-2.26^a	-4.0	$+0.1^a$	-4.9^a	-0.8
		EtOH	-1.96^b	-3.7	$+0.2^b$	$-5.0 + C^c$	$-1.1 + C^c$
i-PrBr + $C_6H_5S^-$	-0.66^a	MeOH	-3.78^a	-3.1	$+0.1^a$	-4.9	-1.7
$C_6H_{11}Br + C_6H_5S^-$	-2.40^b	EtOH	-5.10^b	-2.7	$+0.2^b$	$-5.0 + C^c$	$-2.1 + C^c$
$4\text{-}NO_2C_6H_4CH_2Br + N_3^-$	$+1.5^a$	MeOH	-2.4^a	-3.9	1.2^a	-4.9^a	$+0.2$
		EtOH	-2.1^b	-3.6	1.2^b	$-5.0 + C'^c$	$-0.2 + C'$
$C_6H_5CH_2Br + N_3^-$	$+0.4^b$	EtOH	-2.17^b	-2.6	$+0.2^b$	$-5.0 + C'^c$	$-2.2 + C'$
$4\text{-}MeOC_6H_4CH_2Br + N_3^-$	$+0.8^b$	EtOH	-1.18^b	-2.0	0.0^b	$-5.0 + C'^c$	$-3.0 + C'$
E2C reactions							
$C_6H_{11}Br + C_6H_5S^-$	-2.22^b	EtOH	-4.92^b	-2.7	$+0.2^b$	$-5.0 + C$	$-2.1 + C$
t-BuBr + $C_6H_5S^-$	$-1.8^{a,b}$	MeOH	-3.4^a	-1.6	$+0.2^a$	-4.9	-3.1
		EtOH	-3.6^b	-1.8	$+0.4^b$	$-5.0 + C$	$-2.8 + C$
E2Hal reactions							
trans-$C_6H_{10}Br_2 + C_6H_5S^-$	-0.04^b	MeOH	-4.64^b	-4.6	$+0.3^b$	-4.9	0.0
		EtOH	-4.45^b	-4.4	$+0.4^b$	$-5.0 + C$	$-0.2 + C$

[a] Reference 1. [b] This work. [c] The constants C and C' are an unknown quantity, but because we expect[1] methanol and ethanol to solvate anions similarly they may be small. We have chosen a number (-5.0) close to log $^D\gamma_{Y^-}{}^M$ for log $^D\gamma_{Y^-}{}^E = -5.0 + C$ (or C') so that C and C' may be small. Since we are dealing with differences in behavior of transition states, the actual value of C or C' is irrelevant to our discussion. The constants C and C' allow also for ion association of 0.04 M $NaSC_6H_5$ and 0.04 M NEt_4N_3, respectively, in ethanol relative to other solvents.

ysis. The per cent of isobutylene is considerably increased in the presence of 2,6-lutidine, although the rate of ethanolysis is hardly affected. Decomposition of the t-butyl cation is influenced by the basic lutidine.

We cannot be sure that the enhanced rate of bromide ion production from t-butyl bromide in the presence of 0.083 M sodium ethoxide is not due to a salt effect assisting ionization,[6,12] because in the presence of the weaker base and usually weaker C-nucleophile 0.085 M sodium phenoxide, the production of bromide ion is slightly faster. The same behavior was observed by de la Mare and Vernon[10] in reactions of t-butyl chloride. The higher yield of isobutylene when the concentration of sodium ethoxide is increased is not as convincing as it might be, because of the related behavior of lutidine, which apparently encourages E1 elimination from the carbonium ion intermediate. Another note of caution is sounded by the fact that reaction 7 is about three times faster in methanol than in ethanol. Bimolecular reactions (1) of primary and secondary alkyl bromides, *e.g.*, reactions 2, 4, and 5, are usually faster in ethanol than in methanol[6] (Table I). Ionization is faster in methanol than in ethanol (Table II) so that the solvent effect on rate of reaction 7 suggests a process resembling ionization, at least in methanol. However, a "loose" E2 transition state, of the type we propose for reaction 7a, unlike tighter transition states for reactions 2 and 4 may well be more solvated by methanol, favoring reaction in this solvent. Thus the behavior in reactions 2 and 4 and reactions of primary alkyl bromides may not be good models for predicting the solvent effect on E2 reactions of t-butyl bromide.

With only very slight reservations, we feel that reaction 7a induced by 0.09 M sodium thiophenoxide is very largely an E2 reaction in ethanol. We are less certain about the situation in methanol, but favor an E2 process. Reaction[1] 7 follows good second-order kinetics and is considerably faster than elimination in the presence of other salts, like sodium ethoxide and sodium phenoxide, in ethanol. The comparisons which we will make (Table III) are most valid if we allocate a minimum rate for the E2 reaction (7a). For this reason, we have regarded the rate of bromide ion production in the presence of 0.09 M sodium phenoxide as being equal to the rate of the salt-assisted E1 portion of reaction 7a in the presence of the rather similar salt, 0.09 M sodium thiophenoxide. The difference between the total rate of reaction 7 and this maximum salt-assisted E1 rate gives the minimum E2 rate, which can be converted to the E2 rate constant which is recorded in Table III. The maximum E2 rate of reaction 7a could only be *ca.* 50% greater than this, so our discussion would not be changed.

We suspect, from the behavior in related reactions,[9,11] that reaction 7 has a small (<2%) SN2 component (reaction 7b). However, this is too small for us to identify with any certainty. We do observe *ca.* 2% t-butyl phenyl thioether as product, but this could arise from addition, or an SN1 process.

Solvent activity coefficients for the alkyl, benzyl, and cycloalkyl bromides were estimated by vapor pressure measurements.[13] An exception was 4-nitrobenzyl bromide which was determined by solubility. Data are in Table III. All the bromides, except the very polarizable 4-nitrobenzyl bromide,[1,4] are roughly twice as solvated by DMF as by ethanol or methanol, so that our requirement[1] that $^o\gamma_{RBr}{}^s$ be roughly constant, *i.e.*, solvation differences be due to charge distribution at the reaction center rather than to the structure of R in the transition state, is fulfilled with only one exception. t-Butyl chloride had a similar solvent activity coefficient to t-butyl bromide and since it is much less susceptible to interference by solvolysis, we regard this as support for our values of $^o\gamma_{t\text{-BuBr}}{}^s$.

Discussion

SN2 Reactions. The logarithms of the solvent activity coefficients in Table III, for transfer from DMF to methanol or ethanol, of transition states for SN2 reactions of thiophenoxide ion with alkyl bromides, or of

---

(12) S. Winstein, S. Smith, and D. Darwish, *J. Am. Chem. Soc.*, **81**, 5511 (1959).

(13) E. Grunwald and S. Winstein, *ibid.*, **70**, 846 (1948).

azide ion with benzyl bromides, RBr, become more negative, *i.e.*, the transition states become relatively more solvated by the protic solvent,[1,4] as RBr changes from primary to a secondary alkyl bromide or from 4-nitrobenzyl bromide to 4-methoxybenzyl bromide. This suggests[1] that the transition state, II, for reaction of the secondary alkyl bromide (secondary $\ddagger$) is a better hydrogen bond acceptor than the transition state, II, for the reaction of the primary alkyl bromide (primary $\ddagger$), and that the transition state, II, for the reaction of *p*-methoxybenzyl bromide is a better hydrogen bond acceptor than that for reaction of *p*-nitrobenzyl bromide. In terms of the spectrum of transition states between I and III, secondary $\ddagger$ has negative charge more localized on C_6H_5S and Br than has primary $\ddagger$, *i.e.*, secondary $\ddagger$ is the looser transition state and has a structure (II) more like III than has primary $\ddagger$. Similarly, the 4-methoxybenzyl transition state (II like III) has more negative charge localized on N_3 and Br than has the 4-nitrobenzyl transition state (II like I). The interpretation is clouded by the large difference in solvation of the 4-nitrobenzyl group, relative to the 4-methoxybenzyl group, in ethanol relative to DMF, but the effect is so much greater than is observed in the reactant species that part must be due to differences in charge distribution in the transition state. This situation could arise as outlined in the following argument, which is more or less along classical lines.[6]

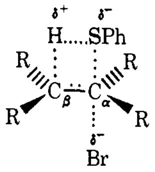
The position of the SN2 transition state, II, in the spectrum between I and III is determined by a delicate balance between at least four variables, *i.e.*, solvation, charge development, nonbonding interactions, and bond energy. The free energy of the transition state is lower the greater the contribution from partial C_α–Y and C_α–X bonds, but is raised by nonbonding interactions between X, Y, and the three R groups. Charge development on X, C_α, and Y will raise the energy of II, but a positive charge on C_α can be stabilized electronically by electron-donating R groups and a negative charge on X can be stabilized by being distributed over a number of atoms, as in X = tosylate. Solvation stabilizes charge, so that protic solvents favor structures II like III.

In changing C_α from a primary to a secondary carbon atom, in reactions in the same pair of solvents, where the entering and leaving group are constant, nonbonding interactions in II would be increased,[6] unless there were a loosening of the C_α–Y and C_α–X bonds. This produces more positive charge on C_α, but because of the electron-donating methyl groups, this is more readily accommodated than at a primary carbon atom.[6] Although there is less stabilization from C_α–Y and C_α–X bonding energy in a looser transition state, the over-all balance of effects is for a reaction path through a transition state, II, which is looser (more like III) for the secondary alkyl compound than for the primary alkyl compound.

Through the benzyl system, nonbonding interactions are constant, because changes are only at the *para* position of the benzyl group. The "loosening," from *p*-nitrobenzyl through benzyl to *p*-methoxybenzyl must be solely due to greater electronic stabilization of positive charge on C_α by the *p*-methoxybenzyl group and to a lesser extent by the benzyl group, relative to *p*-nitrobenzyl. Such behavior has long been suspected,[6] because of the unusual substituent effects on rates of SN2 reactions of benzyl systems. The solvent effect now provides strong support for such an explanation.

Nonbonding interactions between the R groups themselves are less in the trigonal bipyramid, II, than in the tetrahedral reactant, R_3CBr. A stage may be reached in II, very like III, where, as in SN1 reactions,[6] there is a net decrease in *non*bonding interactions from reactants to transition state, leading to steric acceleration of SN2 or E2C reactions.

E2C Reactions. The solvation of the transition state anion, IV, for the E2C reaction[1,9,14] (3a) changes in exactly the same way, on transfer from DMF to ethanol, as does the transition state anion, II, for the SN2 reaction (3b). It is logical to assume that the negative charge distribution is similar in II and IV. This is in line with our proposal that energies of SN2 and E2C transition states depend in much the same way on factors such as C-nucleophilicity,[14] leaving group tendencies,[15] and solvation.[1]



IV

The transition state, IV, for the E2C reaction (7a) of *t*-butyl bromide has a more negative value of log ${}^{\mathrm{D}}\gamma^{\mathrm{E}}{}_{\ddagger}$ than has that for the E2C reaction (3a) of cyclohexyl bromide (Table III). The tertiary E2C transition state is thus[1] a looser transition state than is the secondary E2C transition state; *i.e.*, it has negative charge more localized on SC_6H_5 and Br. This interpretation is along the same lines as given above for SN2 reactions. In IV, C_α is effectively a planar sp^2 hybridized atom with SPh and Br loosely incorporated in the p lobes, which are also overlapping with p lobes on C_β. The arrangement at C_α is effectively a trigonal bipyramid, as in II. The bulkier the R groups at C_α, and the greater their freedom to be bound to sp^2-hybridized C_α, and the stronger their tendency to stabilize the well-developed double bond, so the further the entering and leaving group will be from C_α in the transition state IV. This means greater localization of negative charge on SPh and Br in IV, when C_α is tertiary.

E2Hal Reactions. In line with our nomenclature[14] of E2C for bimolecular elimination reactions in which attack is mainly at C_α, and E2H when attack is mainly at H_β, we designate reactions 4 as E2Hal, because we agree that attack is mainly at halogen[16] when thiophenoxide is the base. The transition state, V, for E2Hal reactions (4) has a very much more positive solvent activity coefficient (Table III) than that for the corresponding E2C reaction (3a). Transition state V is thus a much weaker hydrogen bond acceptor than IV and we interpret this as meaning that it carries less negative charge localized on the entering and leaving group. In practical terms rates of E2Hal reactions of $NaSC_6H_5$

---

(14) M. Ruane, A. J. Parker, S. Winstein, and G. Biale, *Tetrahedron Letters*, 2113 (1968).

(15) D. Lloyd and A. J. Parker, submitted for publication.

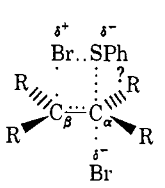
(16) D. V. Banthorpe, "Elimination Reactions," Elsevier Publishing Co., New York, N. Y., 1963.

Table IV. Nucleophilic Tendencies toward Alkyl Bromides

Y	Solvent	MeBr	n-BuBr	i-PrBr	$C_6H_{11}Br$	t-BuBr
			Log k(Y) − log k(Cl) at 25°			
$C_6H_5S^-$	DMF		3.8[a]	2.9[a]	2.8[c]	<1.5[c]
N_3^-	DMF	0.0[a]	0.4[a]	1.2[b]	1.2[a]	0.4[b]
Cl^-	DMF	0.0[b]	0.0[b]	0.0[b]	0.0[d]	0.0[b]
			Log k(Y) − log k(OEt) at 55°			
$C_6H_5S^-$	EtOH		2.8[e]	1.9[g]		1.1[c,h]
OEt^-	EtOH		0.0[f]	0.0[f]		0.0[f,h]
		n-BuBr	4-$NO_2C_6H_4CH_2Br$	$C_6H_5CH_2Br$	4-$MeOC_6H_4CH_2Br$	
			Log k(Y) − log $k(N_3^-)$ at 25°			
$C_6H_5S^-$	MeOH	2.8[a]	3.2[i]	2.4[i]	2.0[i]	
N_3^-	EtOH		0.0[c]	0.0[c]	0.0[c]	
N_3^-	MeOH	0.0[a]	−0.3[a]			

[a] Reference 1. [b] Reference 9. [c] This work. [d] Reference 15. [e] O. R. Quayles and E. E. Royals, *J. Am. Chem. Soc.*, **64**, 226 (1942). [f] Reference 11. [g] Estimated by assuming rate in methanol[1] is twice as slow as in ethanol (Table III). The actual value could be a little less than 1.9 but is not greater. [h] Rate constant is for an E2C reaction of t-butyl bromide at 25°; all other reactions are SN2. [i] Data from ref 20 have been arbitrarily multiplied by 1.6 to give our estimate of rate constants at 25°.

are over 100 times more susceptible to protic–dipolar aprotic solvent transfer than are rates of the corresponding E2C reactions.



V

We do not yet have evidence to show whether the entering group is bound to C_α in the E2Hal transition state V, but it would seem that the E2Hal reaction (4) is a much more synchronous process, with less negative charge on SPh and Br, a less broken C_α–Br bond, and a less developed $C_\alpha{=}C_\beta$ double bond in the transition state V, compared to IV. The PhS–Br bond in V is thought to be considerably more developed than is the corresponding PhS–H bond in IV. For structures IV and V, we use the system[1] of dotted bonds between the limits ...... (effectively not developed) and — (fully developed) to indicate bond development.

C-Nucleophilicity. Solvation effects suggest increasing looseness in SN2 and E2C transition states as the carbon atom being attacked (C_α) changes from methyl through primary and secondary to tertiary or from p-nitrobenzyl through benzyl to p-methoxybenzyl. This conclusion receives support from an interpretation, which is not original,[6] of the nucleophilic tendencies shown in Table IV. As the transition state II or IV becomes looser, we would expect less influence on its free energy from a covalent C_α–Y interaction because the interaction would become increasingly electrostatic, *i.e.*, tending toward that in an ion pair if Y is an anion, and as in the solvated carbonium ion if Y is the solvent. This interaction would continue to decrease with increasing separation from C_α. For this reason, the greater C-nucleophilicity of thiophenoxide ion, relative to chloride, ethoxide, or azide ion, will be leveled, as the transition state II or IV becomes looser. This is observed for three sets of reactions in Table IV. As already noted,[9] the linear azide ion may be able to approach closer to C_α in II than can the bulky thiophenoxide or chloride in an otherwise identical situation. This may be part of the reason why the C-nucleophilicity of azide ion relative to chloride ion increases from reaction with methyl bromide to reaction with isopropyl bromide:[9] the chloride-containing transition state is looser than the azide-containing transition state. For reaction with t-butyl bromide, all nucleophilic tendencies in Table IV appear to be leveled, but it is significant that azide ion gives a much higher yield (15–20%) of SN2 product than does thiophenoxide or chloride ion (<5%).[9] Followers of the hard acids–soft bases principle[17] would be encouraged by the data in Table IV for the "hard" azide *vs.* "soft" thiophenoxide to say that C_α becomes a "harder" center as the transition state II becomes more like the carbonium ion SN2 transition state III.

The data in Table IV for reactions of t-butyl bromide in ethanol are for an E2C reaction,[18] whereas the other reactions are SN2. However, we expect[14] E2C reactions to respond in much the same way to C-nucleophilicity as do the corresponding SN2 reactions, so that the values recorded probably give a good estimate of C-nucleophilicity in the undetected SN2 reactions of t-butyl bromide. The decrease in C-nucleophilicity of SPh^- relative to ethoxide in ethanol is in accord with a loosening of the SN2 transition state, from reactions of primary to tertiary alkyl bromides.

Substituent Effects. The effect of p-methoxyl and p-nitro substituents on rates of SN2 reactions of benzyl bromides[6,19,20] first led to the idea of tight and loose SN2 transition states. The usual substituent effects on rate are observed in Table V, *i.e.*, both p-methoxyl and

Table V. Effect of Substituents (S) on Rates of SN2 Reactions of Benzyl Bromides with Azide Ion at 25° [a]

		Substituent		
	Solvent	p-OMe	H	p-NO_2
Log k_S/k_H[b]	EtOH	1.0	0	0.1
Log k_S/k_H[b]	DMF	0.4	0	1.1

[a] Data from Table III. [b] That is, rate constant for reaction of S-substituted benzyl bromide relative to rate constant for same reaction of benzyl bromide.

---

(17) J. O. Edwards, *J. Am. Chem. Soc.*, 76, 1540 (1954); R. G. Pearson, *Science*, **151**, 172 (1966).

(18) For this discussion, we accept the claim[11] that the reaction of NaOEt with t-butyl bromide is in part an E2 process.

(19) C. G. Swain and W. P. Langsdorf, *J. Am. Chem. Soc.*, **73**, 2813 (1951).

(20) R. F. Hudson and G. Klopman, *J. Chem. Soc.*, 1062 (1962).

p-nitro groups are activating relative to hydrogen. In ethanol, which solvates anions strongly[4] and thus favors looser carbonium ion transition states like III, a *p*-methoxy substituent is more effective than a *p*-nitro substituent. In DMF, which solvates anions poorly,[4] but solvates polarizable solutes strongly, thus favoring a tight synchronous transition state like I, the *p*-nitro substituent is more effective than the *p*-methoxy substituent. Part of this effect may be due to solvation effects on the *p*-nitrobenzyl portion of the transition state, relative to the *p*-methoxybenzyl portion, in ethanol relative to DMF, but we feel that some of the solvent effect on the activating power of these substituents is due to differences of charge distribution at the actual reaction center.

Experimental Section

Materials. *trans*-1,2-Cyclohexyl dibromide[21] and cyclohexyl bromide,[22] 4-nitrobenzyl bromide,[22] and 4-methoxybenzyl bromide[19] were made by routine procedures. Other materials were commercial products and were dried, then purified by fractional distillation. All organic bromides analyzed for 100 ± 2% bromide in infinity samples of runs with excess base.

Kinetic Measurements. Reactions of azide ion were studied as in part XIV.[1] Reactions of sodium thiophenoxide were carried out under nitrogen in nitrogen-flushed solvents, using freshly prepared solutions. Thiophenoxide concentrations were estimated by titration with *p*-toluenesulfonic acid in ethanol, using brom phenol blue as indicator. Thiophenol was estimated by titration in ethanol with sodium methoxide in methanol, using thymol blue as indicator. Bromide ion was estimated by titration with silver nitrate in 10% sulfuric acid solution. Reactions of *t*-butyl bromide, benzyl bromide, and 4-methoxybenzyl bromide were poured into carbon tetrachloride and the electrolytes were extracted with water before estimation of thiophenoxide, azide, or bromide ion.[9] Solvolysis reactions were followed by estimation of hydrogen bromide as acid and as a source of bromide ion. Henry's law constants were measured to within ±25% as previously described.[1] Measurements with *t*-butyl bromide were performed without delay on fresh solutions to avoid solvolysis. Values for *t*-butyl chloride were similar, but our values are *ca.* 50% higher than those recorded by Winstein and Fainberg.[23] Uncertainties of this magnitude do not influence our discussion.

Reaction Products. Vpc analyses were made on a Perkin-Elmer 880 instrument with a flame ionization detector. Cyclohexene was estimated on a Porapak column at 180° and isobutylene was estimated on a 5% Ucon Polar 50-HB nonacid-washed Chromosorb W column at 30°. Propylene was not detected from reactions of isopropyl bromide with sodium thiophenoxide. The yields of olefin by vpc agreed with thiophenol produced as estimated by titration. A 2% yield of *t*-butyl phenyl thioether (n^{25}D 1.5325) was isolated[1] from the complete reaction of 0.07 *M* *t*-butyl bromide with 0.1 *M* sodium thiophenoxide in ethanol following de La Mare and Vernon.[10] The nmr spectrum of the thioether showed nine *t*-butyl protons at τ 8.72 (singlet) and five aromatic protons at τ 2.43–2.84. Acid was not produced and azide lost equalled bromide produced, confirming a substitution process for reactions of benzyl bromides with azide ion.

Acknowledgment. This work was supported by a grant from the Australian Research Grants Committee.

---

(21) H. R. Snyder and L. A. Brooks, "Organic Syntheses," Coll. Vol. II, John Wiley & Sons, Inc., New York, N. Y., 1957, p 171.

(22) A. I. Vogel, "Practical Organic Chemistry," Longmans, Green and Co., London, 1961.

(23) S. Winstein and A. H. Fainberg, *J. Am. Chem. Soc.*, 79, 5937 (1957).

The Protonation of Aromatic Carbonyl Compounds

C. C. Greig[1] and C. D. Johnson

Contribution from the School of Chemical Sciences, University of East Anglia, Norwich, England. *Received April 29, 1968*

Abstract: The protonation behavior in aqueous sulfuric acid solution of various aromatic carbonyl compounds, together with mesityl oxide, has been investigated by uv spectrophotometry. The separation of protonation and medium effects on the spectra is discussed. Earlier conclusions on the protonation of these compounds are shown to be apparently in error, the increases in extent of proton take-up with increasing acidity being significantly greater than for a base following the H_A scale.

The pK_a values of aromatic carbonyl compounds have been the subject of extensive studies by Canadian workers,[2–5] and correlations of such pK_a's with MO calculations,[6] carbonyl stretching frequencies,[7] excited pK_a's by the Forster cycle,[8] Hammett σ^+ constants,[2,3,5,9] and hydrogen bonding[10,11] have been reported. Such determinations have often involved the assumption that these compounds are Hammett bases.[12] Since it has now been shown that protonation of amides[13,14] (which take up a proton at the oxygen site[15]), and of pyridine 1-oxides,[16] does not follow the H_0 acidity scale,[17–19] but generates a new acidity function, H_A, it might reasonably be postulated that oxygen protonations in general follow H_A. This contention receives support from the fact that both the

---

(1) Science Research Council Advanced Course Studentship holder.

(2) R. Stewart and K. Yates, *J. Amer. Chem. Soc.*, 80, 6355 (1958).

(3) K. Yates and R. Stewart, *ibid.*, 82, 4059 (1960).

(4) R. Stewart, M. R. Granger, R. B. Moodie, and J. J. Muenster, *Can. J. Chem.*, 41, 1065 (1963).

(5) R. Stewart and K. Yates, *ibid.*, 37, 664 (1959).

(6) G. Culbertson and R. Pettit, *J. Amer. Chem. Soc.*, 85, 741 (1963).

(7) M. Liler, *Tetrahedron*, 23A, 139 (1967).

(8) A. C. Hopkinson and P. A. H. Wyatt, *J. Chem. Soc., B*, 1333 (1967).

(9) T. G. Bonner and J. Phillips, *ibid.*, 650 (1966).

(10) D. Cook, *J. Amer. Chem. Soc.*, 80, 49 (1958).

(11) W. Gordy and S. C. Stanford, *J. Chem. Phys.*, 9, 204, (1941).

(12) E. M. Arnett, *Progr. Phys. Org. Chem.*, 1, 223 (1963).

(13) K. Yates, J. B. Stevens, and A. R. Katritzky, *Can. J. Chem.*, 43, 1957 (1964).

(14) K. Yates and J. B. Stevens, *ibid.*, 43, 529 (1965).

(15) T. Birchall and R. J. Gillespie, *ibid.*, 41, 2642 (1963).

(16) C. D. Johnson, A. R. Katritzky, and N. Shakir, *J. Chem. Soc., B*, 1235 (1967).

(17) M. A. Paul and F. A. Long, *Chem. Rev.*, 57, 1 (1957).

(18) M. J. Jorgenson and D. R. Hartter, *J. Amer. Chem. Soc.*, 85, 878 (1963).

(19) R. S. Ryabova, *Russ. J. Phys. Chem.*, 46, 184 (1966).