TABLE II

CALCULATED BOND ANGLES AND THEIR EXPERIMENTAL VALUES

Molecule	Angle[a]	Calcd.	Exptl.	Ref.
Pyridine	α	110°	117°	8
	β	121	124	
	γ	122	118.5	
	δ	123	118	
Pyrazine	α	112	115	9
	β	124	122.5	
Pyridazine	α	113		
	β	124		
	γ	123		
Pyrimidine	α	111	115	10
	β	124	128	
	γ	125	123	
	δ	124	116	
s-Triazine	α	114	113	4
	β	126	127	
s-Tetrazine	α	115	116	11
	β	130	127	

[a] The various angles are defined in Fig. 2.

in pyrimidine where we predict a value larger than 120° and the experimental result is smaller than 120°.

In judging the values in Table II we should bear in mind that we actually calculate the bond angle deviations from 120°. It follows then that the agreement between calculated and experimental values is good for s-triazine, reasonable for s-tetrazine and pyrazine and poor for pyridine and pyrimidine. It seems that the agreement becomes better as the molecules have higher symmetry.

In section I we already mentioned that our calculations contain so many approximations that it is difficult to judge the accuracy of the results from purely theoretical arguments. However, we can make some qualitative statements. The concept of sp²-hybridized lone pair orbitals on the nitrogen and the resulting theory tend to favor a decrease of the bond angles on the nitrogens and an increase of the bond angles on the carbons, as follows from the formulas in section II and from previous considerations.[3] It seems that the formulas that result from this concept give a reasonable quantitative prediction for these deviations for the more symmetric molecules; whether or not this is fortuitous is still undecided. This gives us some grounds for concluding that for the more asymmetric molecules like pyridine and pyrimidine there may be some additional effects, apart from the sp²-hybridization of the lone pair electrons, that play a role in determining the molecular dimensions; for example, the interaction between the π-electrons, the bending of bonds, etc. We are tempted to believe that the relative importance of these additional effects is less for s-triazine, s-tetrazine and pyrazine. Whatever the accuracy of our considerations is, they show clearly that serious errors may result if an attempt is made to calculate the molecular dimensions by considering the π-electron interactions only.

Finally, it may be interesting to speculate about the possibility of extending the above method to bond angle calculations in other molecules. In five-membered heterocycles, such as furan, thiophene, etc., it is fairly certain that the bonds are bent. This means that some additional parameters have to be introduced in the energy calculations, namely the angles between the directions of the hybridized orbitals and the corresponding actual bonds. For more complex aromatic molecules, containing more than one ring system, the interactions between the π-electrons probably play a significant role.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, NEW MEXICO INSTITUTE OF MINING AND TECHNOLOGY, SOCORRO, N. M.]

A Correlation of Volume of Activation, Solvent Polarity and Reactant Charge Type for Various Organic Reactions
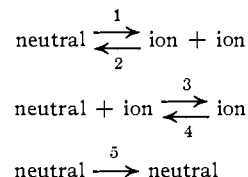
BY K. R. BROWER

The volumes of activation for organic reactions of various charge types, the partial molar volumes of several organic solutes, and the volume changes of several reactions have been measured for solvents of contrasting polarity. It is found that reactions which involve no change of polarization have essentially the same volume of activation in polar and non-polar solvents, whereas the variation of activation volume for reactions in which ions are created or destroyed amounts to a substantial fraction of the variation of partial molar volumes of electrolytes. A semiquantitative measurement of transition state polarization is thereby provided.

Introduction

It has long been recognized that the volume of activation for reactions in solution reflects not only the intrinsic difference in molecular dimensions of the transition state and reactants, but also the difference in their degrees of solvation.[1] For certain reactions of alkyl and aryl halides with amines the separation of these effects has been attempted by changing the polarity of the solvent and noting the effect on the volume of activation.[2] This method for diagnosing polarization changes in the activation process appeared sufficiently promising to warrant a test for its reliability for a variety of reactant charge types and solvents. The correlation of reaction rate with solvent polarity for

various charge types has been investigated by Ingold and others,[3] and the present study was planned along similar lines. The following set of charge types was selected

$$\text{neutral} \underset{2}{\overset{1}{\rightleftharpoons}} \text{ion} + \text{ion}$$

$$\text{neutral} + \text{ion} \underset{4}{\overset{3}{\rightleftharpoons}} \text{ion}$$

$$\text{neutral} \overset{5}{\longrightarrow} \text{neutral}$$

An effort was made to restrict the choices to reactions whose mechanism have already been thoroughly studied; thus, type 1 was exemplified by the Menschutkin reaction, 2 by nucleophilic substitution on quaternary ammonium ions and sulfonium ions by phenoxide ion, 3 by nucleophilic substitutions on an alkyl halide

(1) S. D. Hamann, "Physico-Chemical Effects of Pressure," Butterworths Scientific Publications, London, 1957.

(2) (a) K. R. Brower, J. Am. Chem. Soc., 83, 4370 (1961); (b) K. R. Brower, ibid., 81, 3504 (1959); (c) B. S. El'yanov and M. G. Gonikberg, Doklady Akad. Nauk SSSR, 130, 545 (1960); (d) A. P. Harris and K. E. Weale, J. Chem. Soc., 146 (1961).

(3) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, Chap. VII.

by anions, 4 by the decomposition of t-butyldimethylsulfonium ion, and 5 by the Claisen and Curtius rearrangements.

The entire basis of the effect of solvent polarity on the volume of activation is that the less polar solvents have higher compressibilities and are therefore more constricted by ionic or polar solutes. Adequate discussions of the phenomenon are available elsewhere.[4] In order to use the solvent dependence of the volume of activation for a semiquantitative estimation of the degree of polarization in the transition state, the rather scanty recorded data on partial molar volumes of polar and dipolar compounds in non-aqueous solvents were supplemented by appropriate new measurements.

Results and Discussion

Volumes of Activation.—The rates of the reactions chosen for this investigation were measured at various hydrostatic pressures up to 1400 atm., and the volumes of activation were obtained from the equation

$$RT(\delta \ln k/\delta P)_T = -\Delta V^*$$

in which k is the reaction rate constant and ΔV^* is the change in volume resulting from the transformation of one mole of reactant into activated complex. When the change of solvent entailed a change of temperature for the sake of accurate rate measurement the ΔV^* was adjusted to a standard temperature, usually one of the temperatures actually used. A justification for this type of comparison has been given previously.[14] In some cases involving solvents of low polarity the plot of ln k vs. P is curved, and the datum used is the estimated slope at zero pressure. This procedure has been recently criticized by Benson and Berson,[5] who advocate an extrapolation based on the use of the Tait equation to accommodate the difference in compressibility of the reactants and transition states. Application of their method to the present kinetic data gave essentially the same values of ΔV^* with about the same degree of uncertainty in the extrapolation to zero pressure. Their treatment involves plotting what might be termed the apparent ΔV^*, RT/P ln k/k_0, against $P^{0.523}$ and determining the intercept. It is easily seen, however, that the apparent ΔV^* will be widely scattered at low pressure unless the rate constants are very accurate. It is estimated that most of the present results have an uncertainty of about 1 ml./mole.

The volumes of activation are shown in Table I. Reactions 1, 2 and 3 yield ionic products from neutral reactants, and the volumes of activation show an increase of 15–17 ml. on changing from a non-polar to a predominantly aqueous solvent. This result is expected since the polar solvent should be less constricted by the partly ionic transition state.

Reactions 4, 5 and 6 involve ions but no net change of polarization. Electrical changes in the transition state should therefore be small, and the variation of ΔV^* with solvent polarity should also be small. When the solvent is water, and the ions act independently, the dispersal of charge between two centers in the transition state causes a slight release of solvent.[6] When the solvent is ethanol, however, ion-pair formation competes with solvation for reduction of the electrical potential, and it is not feasible to predict a priori whether the transition state would be more or less intensely solvated than the starting materials. Reactions 4, 5 and 6 give conflicting evidence. In

(4) R. W. Gurney, "Ionic Processes in Solution," McGraw–Hill Book Co., Inc., New York, N. Y., 1953, p. 193; W. C. Vosburgh, L. C. Connell and J. A. V. Butler, J. Chem. Soc., 933 (1933).
(5) S. W. Benson and J. A. Berson, J. Am. Chem. Soc., **84**, 152 (1962).
(6) C. T. Burris and K. J. Laidler, Trans. Faraday Soc., **51**, 1497 (1955).

TABLE I

	Reaction	Solvent	ΔV^*, ml.
1	2-Chloroquinoline + piperidine[a]	Pip.–C_6H_{12}	−46
		Piperidine	−43
		Pip.–HOH	−31
2	1-Bromonaphthalene + piperidine[a]	Piperidine	−53
		Pip.–HOH	−36
3	n-Butyl bromide + pyridine	Toluene	−42
		Ethanol	−33
		EtOH–HOH	−26
4	n-Butyl bromide + Na phenoxide	Ethanol	−12
		EtOH–HOH	− 9
5	n-Butyl bromide + K 2-pyridoxide[b]	Ethanol	−12
		EtOH–HOH	− 8
6	t-Butyldimethylsulfonium ion dec.	Ethanol	+10
		Water	+ 9
7	p-Cresyl allyl ether rearrangement[c]	Benzene	−18
		EtOH–HOH	−15
8	Benzazide rearrangement[c]	Ligroin	+ 5
		EtOH–HOH	+ 2
9	Trimethylphenylammonium phenoxide	Ethanol	+18
		Water	+ 7
10	Trimethylsulfonium phenoxide	Ethanol	+12
		Water	+ 7

[a] Ref. 2b. [b] Details of this reaction will be reported in a future paper. [c] Ref. 2a.

any case, the difference of ΔV^* for the two solvents ranges only up to 4 ml.

Reactions 7 and 8 produce neutral products from neutral reactants, and the volume of activation shows little variation with solvent polarity. Although the mechanisms of these reactions cannot be regarded as having been demonstrated with certainty, it seems probable that the transition states are also relatively nonpolar.

Reactions 9 and 10 involve the neutralization of a pair of ions, and the dominant contribution to ΔV^* should be the release of electrostricted solvent. Heretofore the only reliable published report of the volume of activation for a reaction of this type is due to Stewart and Weale,[7] who found +45 ml./mole for the reverse Menschutkin reaction of ethyldimethylanilinium iodide in nitrobenzene. For the present study the anilinium and sulfonium phenoxides were chosen because of favorable equilibrium positions, high solubility in water and alcohol, and freedom from competition of solvent with nucleophile. As in reactions 1, 2 and 3 the change of polarization in the activation process causes a substantial dependence of ΔV^* on solvent polarity. The change from water to ethanol causes an increase of 11 ml./mole in one case and 5 ml. in the other.

Partial Molar Volumes.—In order to assist the interpretation of the results in Table I the partial molar volumes of a variety of substances in solvents of different polarity were measured and are reported in Table II.[8,9]

The first group of solutes, all of which are electrolytes, illustrate the previously mentioned variation of solvent electrostriction. It is interesting to note that aqueous alcohol (60 mole % water) and dimethyl sulfoxide show approximately the same electrostriction as water. Another indication of the similarity of these solvents to water is that apparent molar volumes are nearly independent of solute concentration, whereas the pure alcohols give strongly sloping plots of $\phi(V_2)$ vs. $c^{1/2}$.

The second group of zwitterionic solutes demonstrates that the amino acids constrict more water than their uncharged structural isomers.[9] It is also found that

(7) J. M. Stewart and K. E. Weale, Proc. Chem. Soc., 389 (1961).
(8) S. D. Hamann and S. C. Lim, Australian J. Chem., **7**, 329 (1954).
(9) F. T. Gucker, Jr., I. M. Klotz and T. W. Allen, Chem. Rev., **30**, 181 (1942).

Table II
Partial Molar Volumes at Infinite Dilution (ML.)

Solute	Solvent				
	EtOH	CH₃OH	EtOH–HOH	DMS	HOH
NaBr	...	5[8]	25	..	24, 24[8]
KI	...	21[8]	..	..	45[8]
NaN₃	...	...	..	24	26
NaOPh	~50	...	..	..	68
Piperidine hydro-bromide	100[8]	...	..	..	114[8]
Glycine	...	...	..	..	43[9]
Glycolamide	...	...	..	..	56[9]
β-Alanine	...	...	..	..	59[9]
Lactamide	...	...	..	..	74[9]
Piperidinoacetic acid	112	...	..	..	117

Solute	Cyclohexane	EtOH	EtOH–HOH	DMS	HOH
2-Pyridone	...	74	...	79	77
Et₃N–O	...	109	...	..	109
Me₂S–O	69	...	...	71	69
Nitrobenzene	104	...	103	..	...
Toluene	109	...	109	..	...

piperidinoacetic acid causes less constriction in water than in alcohol, although the difference is far less than for piperidine hydrobromide. Piperidinoacetic acid is truly zwitterionic in alcohol solution since its carboxylate absorption frequency (1600 cm.⁻¹) agrees with that of sodium acetate (1580 cm.⁻¹) and differs from that of various carboxylic acids (1700–1720 cm.⁻¹). Evidently the amino acids constrict a much smaller volume of solvent than the strong electrolytes as a consequence of the exclusion of solvent molecules from the space directly between the charge centers. The magnitude of the difference between the uni-univalent electrolytes and the zwitterions may be appreciated by comparison of the value, 52 ml./mole, reported for the electrostriction of water for all examples of the former[10] with the 13–15 ml. difference between the amino acids and their neutral isomers. It is essential to the validity of this comparison that slight structural changes do not affect the intrinsic volume of molecules and that electrostriction by the amides is negligible.

The results for the third group of solutes in Table II indicate that the latter condition is probably satisfied. Although the dipole moment of nitrobenzene is 4 D. and that of toluene is 0.4 D., the partial molar volumes of both are independent of solvent polarity over the widest possible range. The molar volumes of the pure liquids (nitrobenzene, 103 ml.; toluene, 107 ml.) also agree closely with the partial molar volumes. Aside from these examples it is reported that volume changes of mixing for systems containing such polar substances as acetone, acetonitrile and nitromethane in alcohol and benzene are less than 1 ml. per mole.[11] The conclusion to be drawn is that polarized bonds even of the "coördinate covalent" type do not cause significant electrostriction of solvent. It is reassuring to note further that the volumes are not sensitive to variations in the external shape and geometrical fit of solute and solvent molecules.

The case of 2-pyridone is somewhat special. This highly polar, but not exactly zwitterionic, substance has its charge centers separated by an intermediate carbon atom unlike the N and S oxides. A small degree of electrostriction is indicated by its partial molar volumes.

Volume Changes of Reaction.—Another valuable aid in the interpretation of the volume of activation is the

(10) A. M. Couture and K. J. Laidler, *Can. J. Chem.*, **34**, 1209 (1956).
(11) I. Brown and F. Smith, *Australian J. Chem.*, **15**, 1 (1962).

measurement of the volume change of reaction. Several examples are shown in Table III. Unfortunately, the evaluation from density measurements is not feasible for every reaction owing to the requirement that the mixture remain homogeneous. All the examples offered involve the creation or destruction of ions, and solvent is accordingly constricted or released. The important point is that the volume of solvent constricted or released correlates well with the solvent polarity.

Table III
Volume Change of Reaction

Reaction	Solvent	ΔV, ml./mole
2-Chloroquinoline and piperidine[2b]	Piperidine	−40 ± 4
	Piperidine–water	−22 ± 4
Trimethylphenylammonium phenoxide	Ethanol	+39
	DMS	+32
Methyl iodide and MeEtaniline[2d]	Nitrobenzene	−56
Piperidinium methoxide neutralization[6]	Methanol	+50
Trialkylammonium hydroxide neutralization[12]	Water	+21-27

Conclusions.—In principle, the location of the transition state on the reaction coördinate as it is reflected by the fractional degree of polarization or depolarization could be found by taking the ratio of the difference in ΔV^* for two solvents of contrasting polarity to the difference in ΔV of reaction for the same two solvents.[13] It has only been possible to obtain all the necessary data for one reaction, 2-chloroquinoline and piperidine, and the error in ΔV due to poor miscibility is large. The indication is that the transition state is roughly 70% polarized. Fortunately, there is evidence in ref. 8 and Table II that a wide variety of uni-valent electrolytes show a difference of 18 to 20 ml. in partial molar volume between methyl or ethyl alcohol and water. Use of this datum together with the 7-ml. difference for ethanol and ethanol–water in reaction 3 indicates 40% polarization.

An alternate route to the characterization of the transition state for a group of related reactions might be provided by partition of the ΔV^* into two components of which one is associated with the reactant molecules and the other with the solvent. For example, the S_N2 reactions 3, 4, 5, 9 and 10 involve reactants of similar type and the activation free energies are not greatly different. The component of ΔV^* due to reactants should be approximately −10 ml. which is the average ΔV^* for the reactions not involving a change of polarization, 4 and 5. Application of this result to reactions 9 and 10 gives 22–28 ml. and 17 ml. for the solvent components of ΔV^* in ethanol and water, respectively. Since the total volume of ethanol released by reaction 9 is 39 ml. the depolarization is 28/39 or 70% complete in the transition state. A rough check on this result can be carried out by comparing the difference of ΔV^* for the two solvents, 11 ml., with the 18–20 ml. difference in partial molar volume of uni-univalent electrolytes referred to above. The ratio, 11/19 (60%), agrees reasonably well.

Experimental

Rate Measurements.—The high pressure equipment and sampling technique have been described elsewhere.[14] Stoichio-

(12) W. Kauzmann, A. Bodansky and I. Rasper, *J. Am. Chem. Soc.*, **84**, 1777 (1962).
(13) A linear relation between polarization and volume is assumed for the sake of simplicity. The classical continuum theory of electrostriction requires a z² dependence for ions, although the empirical equation of Couture and Laidler for volumes of ions in water is linear in z; *Can. J. Chem.*, **35**, 202 (1957).
(14) K. R. Brower, *J. Am. Chem. Soc.*, **80**, 2105 (1958).

TABLE IV

SUMMARY OF KINETIC MEASUREMENTS

n-Butyl bromide and pyridine in toluene, 98.7°

p, atm.	68	340	705	1020	1290
k, l./mole-hr.	0.0331	0.0495	0.0822	0.111	0.132

n-Butyl bromide and pyridine in ethanol, 69.2°

p, atm.	68	340	682	1330
k, l./mole-hr.	0.0682	0.0935	0.126	0.195

n-Butyl bromide and pyridine in 50 mole % ethanol–50 mole % water, 52.0°

p, atm.	68	340	682	1020	1360
k, l./mole-hr.	0.0537	0.0690	0.0917	0.109	0.135

n-Butyl bromide and sodium phenoxide in ethanol, 55.7°

p, atm.	3	340	680	1360
k, l./mole-hr.	0.748	0.874	1.01	1.22

n-Butyl bromide and sodium phenoxide in 49 mole % ethanol–60 mole % water, 54.0°

p, atm.	3	340	680	1020	1360
k, l./mole-hr.	0.95	1.13	1.23	1.44	1.58

t-Butyldimethylsulfonium iodide in water, 71.0°

p, atm.	1	340	680	1020	1360
k, hr.$^{-1}$	0.450	0.384	0.357	0.328	0.279

t-Butyldimethylsulfonium iodide in ethanol, 61.4°

p, atm.	1	340	680	1090	1230	1260
k, hr.$^{-1}$	0.374	0.344	0.293	0.246	0.232	0.206

Trimethylphenylammonium phenoxide in ethanol, 83.6°

p-atm.	1	340	680	1360
k, l./mole-hr.	0.126	0.099	0.084	0.063

Trimethylphenylammonium phenoxide in water, 128.3°

p, atm.	1	1360
k, l./mole-hr.	1.45	1.07

Trimethylsulfonium phenoxide in ethanol, 76.0°

p, atm.	1	680	1360
k, l./mole-hr.	0.404	0.320	0.249

Trimethylsulfonium phenoxide in water, 119.1°

p, atm.	1	680	1360
k, l./mole-hr.	0.334	0.315	0.261

metric reactant proportions were used in the bimolecular reactions so that the rate equation would take the simple form $dc/dt = -kc^2$. The reaction time was varied together with the pressure so that all reactions were 30–50% complete. In this way the effect of varying salt concentration was minimized. The temperature was adjusted for a reaction time of 2–4 hours so that the effect of the initially high heat flux from the thermostat bath and from adiabatic compression was slight. The reactant concentrations ranged from 0.25 to 1.00 M.

Analytical Methods.—The reactions involving butyl bromide were followed by potentiometric titration of bromide ion with silver nitrate solution. The decomposition of trimethylphenylammonium phenoxide was studied qualitatively by infrared spectrum analysis. A completely reacted mixture was separated into neutral and basic fractions by solvent extraction, and the spectra of these fractions were identical with those of anisole and dimethylaniline, respectively. Quantitative determination was accomplished by steam distillation of the sample followed by acid titration of the dimethylaniline in the distillate and unreacted phenoxide ion in the residue. An average of the two results was used in the calculations. The reaction of trimethylsulfonium phenoxide was investigated by direct titration of unreacted phenoxide ion since both products of the reaction are neutral.

Trimethylphenylammonium Phenoxide.—A 26-g. portion (0.1 mole) of N,N,N-trimethylanilinium iodide was dissolved in 60 ml. of water and causticized with 12 g. (0.1 mole) of silver oxide. When the clear liquid no longer gave a test for iodide ion it was filtered from the silver iodide and to it was added 9.4 g. (0.1 mole) of phenol. The mixture was evaporated under vacuum on a water-bath at 80° as rapidly as possible, and the residue solidified into waxy greenish crystals after cooling. The melting range was 66–72°, and attempts at purification by recrystallization were unsuccessful. The neut. equiv. was 261, calcd. 229.

Trimethylsulfonium Phenoxide.—The method described above was applied to trimethylsulfonium iodide. The melting range was 25–35°, and the material was used without further purification.

Piperidinoacetic Acid.—To a solution of 37 g. of chloroacetic acid and 20 g. of sodium hydroxide in 100 ml. of water was added 51 g. of piperidine. Heat was evolved in the first few minutes, and the mixture was allowed to react further and evaporate to dryness at room temperature in the course of several days. The residue was triturated with 100 ml. of absolute alcohol which dissolved the piperidinoacetic acid together with very little sodium chloride. After recrystallization from benzene–alcohol mixture the yield amounted to 52 g. (72%), m.p. 211–213°; rec. 215–217°.

Triethylamineoxide.—The method of Huisgen, *et al.*, was used.[15]

Measurements of Partial Molar Volumes and Volume Changes of Reaction.— Densities were measured with a pycnometer in the form of a 14-ml. glass bulb connected at both ends to graduated glass capillary arms of 0.5-mm. bore. The precision of density measurements is 2 parts in 10,000 and a temperature of 25.0 ± 0.1° was used. The partial molar volume at infinite dilution was obtained by plotting the apparent molar volume against $c^{1/2}$ and extrapolating to zero concentration. Only the strong electrolytes in non-aqueous solvents showed a variation of more than 1–2 ml. over the concentration range, 1.00–0.06 M.

The volume change of reaction was calculated from the change in density of the reaction mixture after heating for a time calculated to give <98% reaction. The solutions were 1 M in reactant, and the heating was done in sealed glass tubes.

(15) R. Huisgen, F. Bayerlein and W. Heydkamp, *Chem. Ber.*, **92**, 3223 (1959).