[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, NEW MEXICO INSTITUTE OF MINING AND TECHNOLOGY]

Kinetic Study of Aromatic Nucleophilic Substitution under High Pressure. II. Variation of Solvent and Reactant Charge Type

BY K. R. BROWER

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The volume changes of activation for the reactions of several bromoquinolines and bromonaphthalenes with pure piperidine, piperidine in water, piperidine in cyclohexane and alkoxides in alkanol have been measured. The results indicate that the unactivated halides pass through transition states which closely resemble the sp^3 intermediates. Any change of nucleophile or solvent has the least effect on the most reactive halide. Sodium methoxide in methanol reduces 6- and 8-bromoquinoline to quinoline.

Introduction

In the first paper of this series[1] it was reported that the displacement reactions of bromoquinolines and bromonaphthalenes with piperidine are characterized by large negative volume changes of activation which can be ascribed partly to electrostriction of the solvent, piperidine, by the polarized transition states, and partly to motion along the reaction coördinate. This paper reports the results of an effort to separate these effects by measurement of the volume changes of activation for the reactions of the same halides with 40% piperidine–60% water (variation of solvent polarity), sodium methoxide in methyl alcohol and sodium isopropoxide in isopropyl alcohol (variation of reactant charge type) and of 2-chloroquinoline with the above reagents and conditions and with piperidine in cyclohexane.

The volume change caused by the introduction of an electric charge or dipole into a solvent is known to increase as the polarity of the solvent decreases.[2] This effect is thought to be a consequence of the inverse correlation between solvent polarity and compressibility. The influence of solvent polarity and pressure on the volume change of solution of electrolytes in water and methanol has been treated quantitatively in terms of the compressibility of the ions and the pressure dependence of the dielectric constant of the solvent.[3] Volume changes of activation for several ionic reactions in water have been measured[4] and were found to be relatively insensitive to charge type. The range was +8.5 ml./mole for the reaction of a divalent positive ion with a univalent negative ion to −6.1 ml./mole for the reaction of two univalent negative ions. The former involves a decrease and the latter an increase in the electrostriction of water as the transition state is formed. In consequence of the foregoing it seems reasonable that the chief effect of an increase in solvent polarity on a reaction producing a polar activated complex from neutral reactants should be a reduction of that component of the volume change of activation which is due to electrostriction of solvent. On the other hand, the component associated with motion along the reaction coördinate should increase since an increase in the dielectric constant of the environment permits a higher polarization (increased contraction) for any given total potential energy. It will be shown later that this effect must be small because the total volume of the space between reacting molecules is small in comparison with the observed volume changes of activation. For the reactions under discussion here the change of solvent from pure piperidine to piperidine–water should not only reduce all volume changes of activation but also reduce the range, since both components of volume change increase with increasing contraction along the reaction coordinate.

The change of nucleophilic reagent and solvent from piperidine to methoxide ion in methanol or isopropoxide ion in 2-propanol alters too many parameters to permit direct comparison of the reactions of a single halide, although one reaction series may be compared in certain respects with another. The reaction of a neutral molecule with an ion involves a dispersal of charge and a slight release of solvent.[4] The volume changes of activation for such reactions should therefore lie in a narrower range than those of the type discussed above. If the correlation between reactivity and the magnitude of the volume change previously noted for the reactions in piperidine[1] should persist, it would be indicated that there are important differences in the lengths of the bonds being formed. If on the other hand, the correlation should weaken appreciably or even be reversed it would appear that electrostriction of solvent is the dominant factor.

Results and Discussion

The rates of reaction were measured at various pressures up to 1360 atm., and the volume changes of activation were calculated from the equation

$$RT(\delta \ln k/\delta P)_T = -\Delta V^* \qquad (1)$$

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. As before, the value of the derivative at zero pressure was used in the calculation. Since the compounds vary widely in reactivity, each was studied at a temperature which gave convenient rates. Comparison of volume changes measured at different temperatures is justified by previous experiments on the same series of compounds which indicate that the derivative in equation 1 is practically independent of temperature. The results are shown in Table I which lists the volume changes of activation reduced to a standard temperature of 422°K.

A rough estimate of the component of volume change due to contraction along the reaction coör-

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[1] K. R. Brower, THIS JOURNAL, **80**, 2105 (1958).

[2] R. W. Gurney, "Ionic Processes in Solution," McGraw-Hill Book Co., Inc., New York, N. Y., 1953, p. 193.

[3] W. Strauss, *Australian J. Chem.*, **10**, 359 (1957).

[4] C. T. Burris and K. J. Laidler, *Trans. Faraday Soc.*, **51**, 1497 (1955).

dinate may be obtained from the equation[5]

$$-\Delta V^{\pm} = \frac{1\ \text{Å.} \times \Sigma V}{\Sigma l_i + \Sigma r_i + 2\text{Å.}} \qquad (2)$$

in which ΣV is the sum of the molar volumes of the reactants, l_i is the component of length of the ith bond along the reaction coördinate, and r_1 and r_2 are the covalent radii of the terminal atoms. It is assumed that the average separation of reactant molecules is reduced by 1 Å. as the activated complex is formed. Allowing for a reasonable uncertainty in Σl_i, which depends on configurational details, the volume change of activation for the reaction of any of the halides with piperidine should be -20 ± 5 ml. The measured values are all considerably greater, and in the case of 2-bromonaphthalene and 6-bromoquinoline the discrepancy amounts to some 40 ml. It can be concluded that the larger volume changes result chiefly from electrostriction of solvent and that the corresponding activated complexes are strongly polarized. By the argument given in the introduction the change of solvent to 40% piperidine–60% water (0.9 mole fraction of water) should reduce the volume changes and bring them into closer agreement with the value estimated from equation 2. The results in Table I show that the volume changes are reduced by 25% for activated halides and 33% for unactivated halides.

TABLE I

VALUES OF $-\Delta V^{*}$ 422° (Ml.) FOR VARIOUS REACTANT COMBINATIONS

Halide	Nucleophilic reagent Piperidine	Piperidine–water	2.8 *N* NaOMe
2-Bromoquinoline	36[a]	27	15 ± 2
8-Bromoquinoline	41[a]	27	..
2-Chloroquinoline	43	31	13
1-Bromonaphthalene	53[a]	36	22
2-Bromonaphthalene	63[a]	41	28
6-Bromoquinoline	64[a]	42	..
	Piperidine–cyclohexane	0.2 *N* NaOMe	0.2 *N* Na-i-OPr
2-Bromoquinoline	..	19	16 ± 2
2-Chloroquinoline	46	18	8

[a] Ref. 1.

In an effort to determine the difference in the partial molar volumes of a pair of ions in the solvents, piperidine and piperidine–water, the volume change of reaction of 2-chloroquinoline in each of these media was calculated from the change in density before and after reaction. For piperidine a contraction of 40 ± 4 ml./mole was observed and for piperidine–water, 22 ± 4 ml./mole. If the transition state involves a full electronic unit of charge separation, the volume change of activation should be approximately 20 ml. greater in piperidine than in piperidine–water, and for the unactivated halides this much difference is found. It can be concluded that their transition states are almost completely polarized and must closely resemble the sp^3 intermediates. The volume changes for 2-chloro- and 2-bromoquinoline show a decrease of about 10 ml./mole and their transition states should be approximately 50% polarized. Unfortunately, the volume change of reaction cannot be compared with the volume change of activation since the over-all reaction involves two molecules of piperidine

$$\text{Ar-Cl} + 2\text{C}_5\text{H}_{10}\text{NH} \longrightarrow \text{Ar-NC}_5\text{H}_{10} + \text{C}_5\text{H}_{10}\text{NH}_2{}^+\text{Cl}^-$$

The data obtained from the reactions of methoxide ion show that the separation of the reactants in the transition state is small. Although some solvent is released in these reactions, the volume changes have substantial negative values, and the ranges for methoxide ion and piperidine–water even overlap slightly. The value for 2-bromonaphthalene and methoxide ion lies near the upper limit for the transition state model on which equation 2 is based.

There has been some speculation about the relative extent of bond formation in the transition states of the reactions of *o*- and *p*-nitrochlorobenzene with amines and alkoxides with the object of explaining the curious inversion of relative reaction rates on changing from the *ortho* to the *para* isomer.[6] It has been supposed that the transition state in the reaction with alkoxide ion involves less contraction along the reaction coördinate since the formation of the new bond does not cause charge separation and should therefore be less endothermic than the corresponding process for the amine. In order to test this conclusion with the present data on activated halides (2-bromo- and 2-chloroquinoline), one must apply a downward revision to the volume changes in piperidine–water to compensate for residual solvent electrostriction and an upward revision to the volume changes for methoxide ion to compensate for the partial release of electrostricted solvent. It is difficult to decide whether the results for 2.8 or 0.2 *N* sodium methoxide should be used in the comparison but, if the latter is chosen, it seems likely that amines and alkoxides have similar locations on the reaction coördinate in their respective transition states.

The variation of the volume change of activation with concentration of methoxide ion is surprising in direction and magnitude. The apparent molar volume of sodium methoxide in methanol (Table II) increases with increasing concentration, and it might be expected that reactions in dilute solution should have smaller volume changes of activation since a greater volume of electrostricted solvent would be released. No simple explanation of the contrary experimental evidence can be offered at present.

TABLE II

APPARENT MOLAR VOLUME OF SODIUM METHOXIDE IN METHANOL

Concn., *M*	2.98	1.19	0.477	0.191
$\phi(V_2)$ (ml.)	17.5	9.9	4.7	2.0

The reactions with isopropoxide ion show smaller volume changes of activation than methoxide ion at the same concentration. Since isopropyl alcohol is less polar than methanol, this effect may be ascribed to increased solvent release in the former. The volume change for the reaction of 2-chloroquinoline with piperidine in cyclohexane is 3 ml. larger than the value for pure piperidine, and it is shown

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(5) A. E. Stearn and H. Eyring, *Chem. Revs.*, **29**, 509 (1941).

(6) M. F. Hawthorne, THIS JOURNAL, **76**, 6358 (1954); G. Hammond and M. F. Hawthorne in Newman, "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc. New York, N. Y., 1956, p. 191.

TABLE III

SUMMARY OF KINETIC DATA

6-Bromoquinoline and piperidine–water, 184.0°

p (atm.)	143	211	272	354	680	955	1360
k (hr.$^{-1}$)	0.0275	0.0285	0.0312	0.0342	0.0457	0.0542	0.0748

8-Bromoquinoline and piperidine–water, 163.3°

p (atm.)	65	273	354	560	966	1360
k (hr.$^{-1}$)	0.0093	0.0110	0.0120	0.0139	0.0178	0.0214

2-Bromoquinoline and piperidine–water, 22.4°

p (atm.)	1	545	834	1360
k (hr.$^{-1}$)	0.0190	0.0287	0.0385	0.0572

2-Bromoquinoline and piperidine–water, 43.2°

p (atm.)	1	300	408	680	950	1360
k (hr.$^{-1}$)	0.120	0.156	0.172	0.217	0.269	0.361

1-Bromonaphthalene and piperidine–water, 187.5°

p (atm.)	65	340	545	885	1360
k (hr.$^{-1}$)	0.00397	0.00551	0.00663	0.00868	0.0124

2-Bromonaphthalene and piperidine–water, 186.0°

p (atm.)	65	204	408	477	748	1360
k (hr.$^{-1}$)	0.00466	0.00581	0.00691	0.00770	0.00928	0.0143

2-Bromonaphthalene and 2.81 N sodium methoxide, 174.0°

p (atm.)	65	136	231	340	694	1360
k (hr.$^{-1}$)	0.0303	0.0326	0.0356	0.0372	0.0440	0.0570

1-Bromonaphthalene and 2.81 N sodium methoxide, 174.4°

p (atm.)	65	185	340	680	1360
k (hr.$^{-1}$)	0.0311	0.0335	0.0369	0.0438	0.0570

2-Bromoquinoline and 2.81 N sodium methoxide, 0.0°

p (atm.)	1	204	408	612	920	1360
k (hr.$^{-1}$)	0.0089	0.0098	0.0111	0.0120	0.0128	0.0158

2-Chloroquinoline and 2.81 N sodium methoxide, 18.2°

p (atm.)	1	197	408	612	952	1360
k (hr.$^{-1}$)	0.0448	0.0474	0.0484	0.0549	0.0644	0.0731

2-Chloroquinoline and piperidine, 50.6°

p (atm.)	1	197	408	612	1000	1360
k (hr.$^{-1}$)	0.133	0.162	0.217	0.286	0.435	0.670

2-Chloroquinoline and piperidine–water, 50.6°

p (atm.)	1	218	408	612	953	1360
k (hr.$^{-1}$)	0.0559	0.0678	0.0837	0.0946	0.130	0.176

2-Chloroquinoline and 0.2 N sodium methoxide, 59.8°

p (atm.)	1	204	408	612	952	1360
k (l./mole hr.)	0.0212	0.0227	0.0257	0.0291	0.0356	0.0400

2-Chloroquinoline and 0.2 N sodium isopropoxide, 77.6°

p (atm.)	1	204	408	612	952	1294
k (l./mole hr.)	0.101	0.102	0.108	0.112	0.124	0.130

2-Chloroquinoline and piperidine in cyclohexane, 105.2°

p (atm.)	65	204	408	612	970	1300
k (l./mole hr.)	0.0319	0.0403	0.0535	0.0639	0.0925	0.126

2-Bromoquinoline and 0.2 N sodium methoxide, 49.7°

p (atm.)	1	272	612	952	980	1290
k (l./mole hr.)	0.0132	0.0158	0.0178	0.0210	0.0214	0.0261

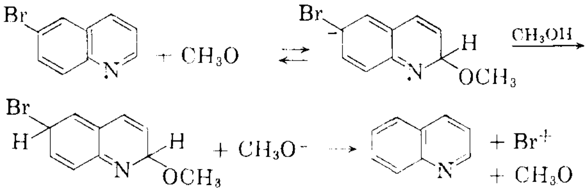
2-Bromoquinoline and 0.2 N sodium isopropoxide, 50.6°

p (atm.)	1	204	408	612	954	1415
k (l./mole hr.)	0.0887	0.0917	0.1052	0.1062	0.1350	0.1527

again that volume changes associated with the solvent (electrostriction in this case) increase as the polarity of the solvent decreases.

In summary, it can be shown that in every case the effect of a change in solvent or reactant on the volume change of activation increases as the reactivity decreases. This result is concordant with the postulate of Hammond[7] that the extent of molecular reorganization in a transition state increases with increasing free energy change of activation.

The reactions of 6- and 8-bromoquinoline with sodium methoxide gave erratic rate constants having very large pressure coefficients, and it was found that the major reaction product in both cases is quinoline. Since 7-bromoquinoline is reported to give 7-methoxyquinoline,[8] it seems likely that the reaction involves a quinonoid intermediate as



The reactions of 1- and 2-bromonaphthalene with excess sodium methoxide produce the corresponding naphthoxide ions, presumably by the S_N2 reaction of methyl naphthyl ether with methoxide ion.

Experimental

Rate Measurements.—The apparatus, procedures and preparations of reagents already have been described.[1] The reactions of 0.2 *M* halide with 2.81 *M* sodium methoxide or 40% by volume of piperidine in water were treated as pseudo-unimolecular since the fraction of base consumed at the time of measurement was always less than 3%. The reactions of 0.2 *M* halide with 0.2 *M* alkoxide or 0.2 *M* piperidine in cyclohexane were treated as bimolecular. Any errors in $-\Delta V^{*}_{422°}$ which are larger than the previously estimated 9% are indicated in Table I.

Measurement of Apparent Molar Volumes and Volume Changes of Reaction.—Densities were measured with a pycnometer consisting of a 14-ml. glass bulb connected to two graduated capillary tubes of 0.5 mm. bore. The precision of density measurements is 2 parts in 10,000, and a temperature of 25.00 ± 0.05° was used. The relatively large error in the measurement of the volume change of reaction of 2-chloroquinoline with pure piperidine and piperidine–water is due to the low solubility of piperidine hydrochloride in piperidine which made it necessary to use 0.02 *M* solutions.

Reaction of 6- and 8-Bromoquinoline with Sodium Methoxide.—A solution of 2.0 g. of 8-bromoquinoline and 1.5 g. of sodium methoxide in 10 ml. of methanol was heated at 125° for 48 hr. in a sealed glass tube. The reaction mixture was poured into water and diluted to 100 ml. A 2-ml. aliquot was analyzed for bromide ion and 96% of the theoretical amount was found. The remainder of the mixture was distilled until the distillate became clear, at which point 60 ml. had been removed and a polymeric residue remained. A solution of 2.0 g. of picric acid in 20 ml. of ethanol was added to the distillate and a picrate separated. The product after being washed with ethanol and dried weighed 2.35 g. and melted at 201–203°. A small sample recrystallized from ethanol had m.p. 203–204° and was identified as quinoline picrate (rec. m.p. 203°) by the undepressed m.p. of a mixture with an authentic sample. The yield of quinoline picrate based on bromide ion released was 71%.

The experiment was repeated using 6-bromoquinoline and a heating period of 96 hr. (100% reaction). A 48% yield of quinoline picrate was obtained.

Reaction of 1- and 2-Bromonaphthalene with Sodium Methoxide.—A solution of 7.0 g. of 2-bromonaphthalene and 29.0 g. of sodium methoxide in 80 ml. of methanol was heated in a sealed glass tube at 160–170° for 7 days. The reaction mixture was diluted with 40 ml. of water and distilled until most of the methanol had been removed. The residual mixture was washed with ether to remove unreacted 2-bromonaphthalene and an aliquot was analyzed for bromide ion to determine the extent of replacement (75%). The aqueous layer was acidified, and 3.05 g. of white solid was obtained. After recrystallization from alcohol–water, the substance melted at 121–122° and was identified as 2-naphthol (rec. m.p. 122–123°) by the undepressed m.p. of a mixture with an authentic sample. The yield based on bromide ion released was 84%.

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(7) G. S. Hammond, THIS JOURNAL, **77**, 334 (1955).

(8) L. Bradford, T. Elliot and F. Rowe, *J. Chem. Soc.*, 437 (1947).

The procedure above was applied to 1-bromonaphthalene which released 88% of the theoretical amount of bromide ion and gave 3.5 g. (84%) of crude 1-naphthol. The phenylurethan derivative melted at 173–175° (rec. m.p. 176°), and the melting point of a mixture with an authentic sample was not depressed.

CAMPUS STATION, SOCORRO, NEW MEXICO

[CONTRIBUTION FROM THE RADIATION LABORATORY, CONTINENTAL OIL COMPANY]

The Role of Free Radical Processes in the γ-Radiolysis of Methane, Ethane and Propane

BY KANG YANG AND PETER J. MANNO

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Nitric oxide inhibits the formation of hydrogen and saturated hydrocarbons in the γ-radiolysis of methane, ethane and propane. From these inhibition data, the $F_M(X)$-value (per cent. free radical contribution to the production of a species X in the γ-radiolysis of a compound M) has been determined. The $F_M(X)$-values for the chain degradation products are smaller than the $F_M(X)$-values for the products having carbon numbers larger than M. For example, $F_{C_3H_8}(X)$-values for various products are: H_2, 58; CH_4, 36; C_2H_6, 32; n-C_4H_{10}, 75; i-C_4H_{10}, 91; i-C_5H_{10}, 100. At present, nitric oxide appears to be most satisfactory for the estimation of radical energy yields, as well as contributions of free radical reactions to radiolysis of gaseous hydrocarbons.

Introduction

Interpretation of products yield in radiolysis of hydrocarbons is complicated by a number of potential processes which may contribute to the over-all mechanism. The problem may be partially simplified by the use of "so-called" radical scavengers[1-4] (as well as isotopic exchange method)[1,5-7] to determine the relative contribution of thermalized free radical processes, as compared to other possible processes. While the results of such observations are not unambiguous, as will be noted later, they may serve well as starting points for the complete elucidation of the radiolysis mechanism.

In the following sections, it is convenient to present our data in terms of a derived parameter $F_M(X)$, which we define as the % decrease in the yield of product X resulting from the addition of a radical scavenger during the radiolysis of compound M. The scavenger used in our work was nitric oxide. If it is assumed that the scavenged portion represents the free radical contribution and the remainder the contribution of non-free radical processes, then $F_M(X)$ is equivalent to the % free radical contribution to the formation of species X. It probably is safe to conclude that few, if any, free radical processes occur in the presence of a sufficient concentration of NO. However, it is possible that a charge transfer reaction of the type

$$RH^+ + NO \longrightarrow NO^+ + RH \qquad (1)$$

may occur, complicating interpretation of the inhibition data. In any case, this reaction probably could not compete with the ion–molecule reaction of the type[8,9]

$$RH^+ + M \longrightarrow \text{Products} \qquad (2)$$

under the condition of $[NO]/[M] \simeq 0.06$, where maximum inhibition has been reached already. In fact, comparison of the values obtained from our data with those obtained by other methods suggests that the error attributable to the reactions of type 1 is not great and the $F_M(X)$ is a reasonable approximation to the % free radical contribution.

Experimental

Phillips research grade methane was purified by bulb-to-bulb distillation in a high vacuum line. Phillips research grade ethane and propane and Matheson nitric oxide (min. 99%) were degassed by a freeze-pump technique and subjected to bulb-to-bulb distillation on a high vacuum line. The only detectable impurities in the resulting gases were 0.1% ethane in methane (GLPC) and 0.3% nitrous oxide in nitric oxide (mass spectrometric analysis). The irradiation vessel was made of Pyrex glass and equipped with breakoff seal and capillary constrictions at opposite ends. This vessel was charged with purified hydrocarbons (at 60 cm.) and varying amounts of nitric oxide (maximum 12%). Four spent fuel elements (150 days cool), from the Materials Testing Reactor, Arco, Idaho, shielded by 5.5 meters of water were used as an irradiation source. All experimental data were obtained at 22.5 ± 1° (the ambient temperature of the water). Gamma field intensity was determined by an air-gap ionization chamber calibrated with a cerous–ceric sulfate chemical dosimeter.[10] Ionization chamber readings before and after each run were averaged. To calculate the amounts of energy absorbed by each sample, it was assumed that the absorption coefficients were proportional to the electron density of the material. The energy input rate was approximately 2×10^{19} e.v. per g. per hour. After irradiation, the gaseous products were analyzed by gas chromatography. The products did not exceed 1% of the reactant. The analytical conditions were

Gas analyzed	Anal. conditions
Hydrogen and methane	Silica gel column, 2 m., 25°, nitrogen carrier, 25 cc./min.
Ethane and ethylene	High-activity charcoal column, 2 m., 149°, helium carrier, 84 cc./min.
Propane, propylene and acetylene	Silica gel column, 2 m., 87°, helium carrier, 30 cc./min.
Butanes, butenes and pentanes	Hexamethylphosphoramide, 4.6 m., 25°, helium carrier, 75 cc./min.

Results

Methane Radiolysis.—The effect of nitric oxide on the radiolysis of methane is summarized in Table I and depicted in Fig. 1. The various prod-

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[4] J. G. Burr, *ibid.*, **61**, 1483 (1957).

[5] L. M. Dorfman, *ibid.*, **60**, 826 (1956).

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[9] G. G. Meisels, W. H. Hamill and R. R. Williams, Jr., *ibid.*, **25**, 790 (1956).

[10] J. Weiss, *Nucleonics*, **10**, No. 7, 28 (1952).