Chlorine Kinetic Isotope Effects in Nucleophilic Substitution Reactions. Support for the Ion Pairs Mechanism in the Reactions of *p*-Methoxybenzyl Chloride in 70% Aqueous Acetone

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Abstract: The possibility that the variation of the chlorine leaving group kinetic isotope effects with nucleophile concentration might serve to detect the intervention of ion pairs has been examined for the competitive reactions of *p*-methoxybenzyl chloride with solvent water and added sodium azide in 70% aqueous acetone at 20°. The observed isotope effect value increases more than 30% (1.00786 ± 0.00010 to 1.01049 ± 0.00025) as the azide concentration is varied from zero to approximately 0.25 *M*. It is demonstrated that this observation is consistent with the ion pairs mechanism but not with simultaneous SN1 and SN2 processes. The solvolysis reaction carried out in the presence of 0.200 *M* potassium nitrate is shown to be complicated by nucleophilic participation by the nitrate anion. The increased isotope effect observed with the nitrate nucleophile also supports the ion pairs hypothesis for the *p*-methoxybenzyl chloride substrate.

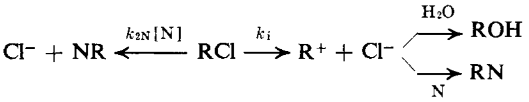
Heavy-atom kinetic isotope effects (KIE) have shown promise as a powerful tool for the study of organic reaction mechanisms.[1-3] In particular, leaving group KIE measurements on nucleophilic displacement reactions offer a probe of the transition state structure and, hence, of the fundamental chemical processes involved in these reactions.[4-7] The development of precise and reliable methods for the determination of chlorine leaving group KIE was an early goal in these laboratories[8] and has been followed by experiments designed to test the validity of this probe and its application to real chemical systems.[5,9,10]

During this testing, Sneen and coworkers[11] advanced a mechanistic alternative to the classical SN theories[12] of nucleophilic attack which invokes the participation of a configurationally stable ion pair intermediate to explain the relationship between rate and product data. Because of the success of Sneen's treatment in explaining the experimental data from a few well-characterized systems, it became of interest to inquire what implications this treatment might have to the interpretation of kinetic isotope effects and, conversely, what new information might the KIE give which would be useful in distinguishing between the classical and ion pairs hypotheses.

Kinetic Considerations

Although a number of possible mechanistic interpretations can be postulated as descriptive of the classical hypothesis, the simultaneous operation of SN1 and SN2 processes, shown as Scheme I, is a reasonable representation of this category. This scheme can explain "borderline" behavior[13,14] and reduces in a simple manner (under appropriate conditions) to the kinetic situations for which the SN processes were defined.

Scheme I



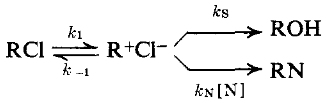
$$Cl^- + NR \xleftarrow{k_{2N}[N]} RCl \xrightarrow{k_i} R^+ + Cl^- \begin{cases} \xrightarrow{H_2O} ROH \\ \xrightarrow[N]{} RN \end{cases}$$

For Scheme I, the rate constant for the production of chloride (or disappearance of reactant) is given by eq 1 where k is the (experimentally observable) overall rate constant for the reaction, k_i is the rate constant for the production of the carbonium ion R^+, and k_{2N} is the second-order rate constant for reaction with the nucleophile N at the concentration [N].

$$k = k_i + k_{2N}[N] \tag{1}$$

The ion pairs mechanism in its simplest form[11] is presented as Scheme II. For Scheme II, application of the Bodenstein approximation, assuming no accumulation of intermediate products, provides an expression for the rate constant[15] as given by eq 2.

Scheme II



$$RCl \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} R^+Cl^- \begin{cases} \xrightarrow{k_S} ROH \\ \xrightarrow[k_N[N]]{} RN \end{cases}$$

$$k = \frac{k_1(k_S + k_N[N])}{(k_{-1} + k_S + k_N[N])} \tag{2}$$

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(1) A. Fry in "Isotope Effects on Chemical Reactions," C. J. Collins and N. S. Bowman, Ed., Van Nostrand-Reinhold, New York, N. Y., 1970.

(2) L. Melander, "Isotope Effects on Reaction Rates," Roland Press, New York, N. Y., 1960.

(3) A. Fry, *Pure Appl. Chem.*, **8**, 409 (1964).

(4) J. W. Hill and A. Fry, *J. Amer. Chem. Soc.*, **84**, 2763 (1962).

(5) E. P. Grimsrud and J. W. Taylor, *J. Amer. Chem. Soc.*, **92**, 739 (1970).

(6) C. G. Swain and E. R. Thornton, *J. Org. Chem.*, **26**, 4808 (1961).

(7) T. M. Bare, N. B. D. Hershey, H. O. House, and C. G. Swain, *J. Org. Chem.*, **37**, 997 (1972).

(8) J. W. Taylor and E. P. Grimsrud, *Anal. Chem.*, **41**, 805 (1969).

(9) R. C. Williams and J. W. Taylor, *J. Amer. Chem. Soc.*, **95**, 1710 (1973).

(10) C. R. Turnquist, J. W. Taylor, E. P. Grimsrud, and R. C. Williams, *J. Amer. Chem. Soc.*, **95**, 4133 (1973).

(11) R. A. Sneen, *Accounts Chem. Res.*, **6**, 46 (1973), and references cited therein.

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

(13) V. Gold, *J. Chem. Soc.*, 4633 (1956).

(14) G. Kohnstam, A. Queen, and B. Shillaker, *Proc. Chem. Soc., London*, 157 (1959).

(15) R. A. Sneen and J. W. Larsen, *J. Amer. Chem. Soc.*, **91**, 362 (1969).

For convenience in applying eq 2 to experimental data, a quantity k_{NA} has been defined by Sneen[15] which is the rate constant for the reaction in the absence of added nucleophile corrected for normal salt effects. Using this quantity and the definitions $x = k_{-1}/k_S$ and $m = k_N/k_S$, the expression for the rate constant according to Scheme II is derived.[15] This expression is presented as eq 3. The kinetic implications of eq 1 through 3 have been discussed at length[15-17] and will not be considered here.

$$\frac{k}{k_{NA}} = \frac{(x + 1)(1 + m[N])}{(x + 1 + m[N])} \quad (3)$$

Kinetic Isotope Effects

From eq 1 and the definition of the KIE, one obtains for Scheme I

$$\mathrm{KIE_I} = \frac{^{35}k}{^{37}k} = \frac{^{35}k_i + {}^{35}k_{2N}[N]}{^{37}k_i + {}^{37}k_{2N}[N]} \quad (4)$$

where the superscript indicates the respective rate constant for the ^{35}Cl and ^{37}Cl isotopes in the process indicated by the subscript. Similarly, on the basis of eq 2, assuming an isotope effect only in the ion pair formation equilibrium, one obtains for Scheme II

$$\mathrm{KIE_{II}} = \frac{^{35}k_1(^{37}k_{-1} + k_S + k_N[N])}{^{37}k_1(^{35}k_{-1} + k_S + k_N[N])} \quad (5)$$

In order to apply the relationships given by eq 4 and 5 to the interpretation of experimental KIE values, some assumptions must be made concerning the relative values for the various parameters. The first assumption is that the isotope effect for each process is normal and not inverse. This assumption arises from a consideration of the relative importance of the various terms which comprise the isotope effect. From Bigeleisen's theory as applied to heavy atoms,[18] eq 6

$$\mathrm{KIE} = \frac{k_1}{k_2} = \left(\frac{\nu_{1L}^{\ddagger}}{\nu_{2L}^{\ddagger}}\right)\left[1 + \sum_i^{3n-6} G(u_i)\Delta u_i - \sum_i^{3n-7} G(u_i^{\ddagger})\Delta u_i^{\ddagger}\right] \quad (6)$$

may be derived. In this expression, the $\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$ term, representing the ratio of the imaginary frequencies of the vibration along the reaction coordinate in the transition state, is always greater than unity.[19] The terms in the square brackets evaluate the partition function ratios for the reactants and transition state, respectively. For all but the internal return case, there will be less bonding to the labeled center (fewer vibrations or lower frequency vibrations) in the transition state than in the reactants, and the term in square brackets will be greater than one. For the case of internal return, an inverse effect can arise if the sum in the brackets is sufficiently less than one that the product of that sum with the $\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$ term is also less than one. The probability of this occurring can be evaluated by seeking the factors which drive the sum to small values. In the limiting case where the ion pair contains no covalent bonding to chlorine, the first summation collapses to zero and the term arising from one minus the second summation must be compared to the $\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$ term. If the decomposition mode is identified with the C–Cl stretching mode in the transition state, the $G(u^{\ddagger})\Delta u_L^{\ddagger}$ term will be composed, primarily, of contributions from bending modes which involve chlorine, along with any other bonding changes which directly involve the chlorine atom, such as specific solvent effects. The bending modes could become important in cases where the transition state is of such high symmetry that coupling becomes significant, but, in the specific case to be considered, this argument does not apply. Also, preliminary experiments in these laboratories[20] aimed at probing the effect of solvents on the chlorine KIE show effects too small to alter the stated assumption.

The second assumption is that the KIE for a three-center transition state involving both bond formation and bond breaking (an SN2 type transition state) is lower than that for a two-center transition state involving primarily bond breaking (an SN1 type situation) as predicted by theory.[21] This assumption is based primarily on the relative magnitudes of the $\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$ terms in eq 6 for the two cases. For a three-center case (SN2 reactions) the term is smaller. For the assumption to fail, the term in brackets must contribute an opposing effect sufficiently large to offset the difference in the primary term. Since the first term in the brackets is the same in the two cases, any reversal must occur from the $G(u_i^{\ddagger})\Delta u_i^{\ddagger}$ term. The choice of chlorine as the KIE probe excludes the possibility of contributions from bonding and hybridization changes in the transition state to produce such effects. Solvent bonding to the chlorine, if significant, would be expected to occur more for the SN1 case than for the SN2 case but, as discussed previously, this effect appears to be quite small and certainly insufficient to invert the theoretical order of SN1 > SN2. Specifically, then, this assumption leads to the prediction that the KIE for ionization is greater than the KIE for substitution in Scheme I or that $^{35}k_i/^{37}k_i$ is greater than $^{35}k_{2N}/^{37}k_{2N}$.

For Scheme I, then, if the solvolysis is strictly SN1, KIE$_I$ in the absence of added nucleophile will be given only by $^{35}k_i/^{37}k_i$, the KIE for the ionization process. As the concentration of nucleophile is increased, this value should approach the value $^{35}k_{2N}/^{37}k_{2N}$. Using the second assumption, the predicted variation in KIE$_I$ with increasing nucleophile concentration is a decrease from the solvolysis value toward some limiting value characteristic of the SN2 substitution process.

In contrast, the assumption of normal isotope effects for the various processes in Scheme II predicts an increase in the value of the observed KIE$_{II}$, as the nucleophile concentration is raised, from the solvolysis value to the limit $^{35}k_1/^{37}k_1$ for infinite nucleophile concentration. Thus, a significant dependence of the chlorine leaving group kinetic isotope effects on nucleophile concentration should provide a simple and possibly conclusive test of the mechanism involved in the reaction. If the KIE increases as the nucleophile concentration is increased, ion pairs are indicated. If the KIE decreases

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(16) B. J. Gregory, G. Kohnstam, M. Paddon-Row, and A. Queen, *Chem. Commun.*, 1032 (1970).

(17) D. J. Raber, J. M. Harris, R. E. Hall, and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, 93, 4821 (1971).

(18) M. J. Stern and M. Wolfsberg, *J. Pharm. Sci.*, 54, 849 (1964).

(19) J. Bigeleisen, *Can. J. Chem.*, 30, 443 (1952).

(20) C. R. Turnquist, Ph.D. Dissertation, University of Wisconsin, Madison, Wis., 1972.

(21) J. Bigeleisen and M. Wolfsberg, *J. Chem. Phys.*, 21, 1972 (1953); 22, 1264 (1954).

with increasing nucleophile concentration, then the classical description is the more probable one.

In cases where the reaction kinetics are strictly first or second order, there may not be an observable dependence of KIE on nucleophile concentration. These cases would correspond to the situation where, for example, either k_i or k_{2N} in Scheme I is zero, for which no concentration dependence is predicted according to eq 4. In terms of Scheme II and eq 3, these would be the cases in which the parameter x is either very small (first order) or very large (second order). In these cases, eq 5 suggests that the KIE dependence on nucleophile concentration would be determined by the relative values of k_{-1}, k_S, and k_N.

In order to test the concepts derived above, a model system was chosen whose kinetic behavior has been interpreted in terms of both schemes under consideration. This system was the competitive reaction of solvent water and added azide ions with *p*-methoxybenzyl chloride in 70% aqueous acetone at 20°. This reaction was carefully studied by Kohnstam, Queen, and Shillaker[14] who interpreted the observed "borderline" kinetics in terms of an SN1 ionization process concurrent with a second-order reaction between azide ion and the substrate. Sneen and Larsen[22] later interpreted Kohnstam's data in terms of the ion pairs hypothesis. Chloride ions are generated as one of the products of the reaction; it is therefore amenable to our method for determining the chlorine leaving group KIE.

Experimental Section

Materials. *p*-Methoxybenzyl chloride was prepared from *p*-methoxybenzyl alcohol (Aldrich) by the procedure of Quelet and Allard.[23] The product was stored as the ether solution and distilled no more than 24 hr before being used. A small amount of potassium carbonate added to the distillation pot was found to minimize decomposition of the chloride during the distillation: bp 75° (∼0.5 mm) (lit.[23] bp 113–114° (15 mm)).

Commercial sodium azide (Matheson Coleman and Bell) was purified by fractional precipitation according to the procedure described by Weiner and Sneen.[24] The precipitated salt was dried under vacuum and stored in a desiccator.

Reagent grade acetone (Mallinckrodt Chemical) was distilled through an 18-in. column packed with glass beads; the fraction used boiled over a range of not more than 0.1°.

Laboratory distilled water was further purified by distilling it from an alkaline permanganate solution and then again from a sulfuric acid solution in an all glass still.

70% Aqueous acetone solvent was prepared by weighing 553.56 g of distilled acetone (700 ml assuming a density of 0.7908 g/ml at 20°) into a glass-stoppered 1-l. container and pipetting 300 ml of triply distilled water into it. It was found that better reproducibility between solvent batches could be obtained through this procedure than through volumetric methods since the volatility and large temperature dependence of the volume of acetone prohibit accurate volumetric transfers.

Kinetic Procedure. The reactions were run in a calibrated temperature bath controlled at 20 ± 0.02°. The reaction vessel was a 500-ml round-bottom flask fitted with an air-driven magnetic stirrer and immersed in the bath. For the runs involving added salts, the quantity of salt necessary to prepare a solution of the desired concentration was weighed into a 250-ml volumetric flask and the flask filled to just below the mark with solvent at room temperature. The flask was then placed in the temperature bath and allowed to equilibrate for several hours. Additional solvent was then added and additional time allowed for temperature equilibration.

In a typical run, 200 ml of solvent salt solution was added to the reaction vessel and was allowed to come to temperature by standing (with stirring) overnight. The reaction was started by adding, *via* syringe, sufficient *p*-methoxybenzyl chloride to give a solution of *ca.* 0.05 *M* reactant. A timer was started coincidentally with this addition. Periodically, 10–25-ml aliquots of the reaction mixture were transferred from the reaction vessel to a 125-ml separatory funnel containing very cold toluene (cooled in a Trichlor/Dry Ice bath) and 5 ml of triply distilled water. The times at the beginning and end of the pipet drain were recorded and the midpoint taken as the sample time. The organic layer was then subjected to a second water wash and the combined aqueous layers extracted with a second portion of toluene. This procedure served both to quench the reaction and to isolate the chloride ion produced.

When all the samples had been collected, the ionic strength of each was adjusted to approximately 1 *M* with potassium nitrate (Baker), and each was titrated potentiometrically with standard (*ca.* 0.01 *M*) silver nitrate. A silver wire electrode, in combination with a saturated calomel reference electrode through a chloride free potassium nitrate–agar salt bridge, was used to follow the titration progress. For the runs involving added azide, the samples were also made 1 *M* in nitric acid to inhibit silver azide formation during the titration. For the run with 0.200 *M* sodium nitrate added, the acid liberated during reaction was titrated to the phenolphthalein end point with standard sodium hydroxide before addition of the potassium nitrate. The samples were then acidified with 0.01 *M* nitric acid and the chloride determined as usual. The silver chloride obtained was washed and dried at 105°.

Isotopic Analysis. The conversion of the microcrystalline, dry silver chloride *via* reaction with excess methyl iodide to methyl chloride, purification of the methyl chloride, and chlorine isotopic analysis by isotope ratio mass spectrometry have been described previously.[8] For this work, however, a twofold excess of methyl iodide, positive ion ratios, and the collector configuration leading to a correction factor of 1.036 as described by Turnquist, *et al.*,[10] were used.

Kinetics Data Analysis. First-order kinetics plots for the production of chloride as a function of time according to the relation $\ln C_\infty/(C_\infty - C) = kt$ were made for each reaction studied. Even the solvolysis reaction showed significant, though very slight, curvature in this plot. With added azide, the decrease in slope with increasing time was more pronounced due to the decrease in azide concentration as the reaction proceeded. The initial rate constants were therefore determined by application of the method employed by Hammett and McCleary[25] in their study of the reactions of ethyl-*p*-toluenesulfonate ester.

Briefly, the method consists of fitting the experimental data to a polynomial function of enough terms to describe the data to a desired precision. The derivative of this function then gives the value of the rate constant as a function of time, and evaluation of the derivative at $t = 0$ provides the initial rate coefficient. The solvolysis data were found to be described adequately by the expression (derived from a least-squares fit of the data to the function $y = a_1 + b_1t + c_1t^2$)

$$y = -\ln\left(\frac{C_\infty - C_t}{C_\infty}\right) = 0.01594 + 2.3820 \times 10^{-4}t - 7.18 \times 10^{-10}t^2 \quad (7)$$

which yields the value for $k\ (t = 0)$ of 2.38×10^{-4}.

For the runs with added azide, the first-order plots could not be described well even by the quadratic expression. Second-order plots, however, were amenable to this procedure and least-squares fits of the data to the expression

$$y = \frac{1}{(b_0 - a_0)}\ln\left(\frac{a_0(b_0 - x)}{b_0(a_0 - x)}\right) = a_2 + b_2t + c_2t^2 \quad (8)$$

followed by evaluation of the derivative at $t = 0$ provided initial second-order rate constants which when multiplied by the initial azide concentration gave the pseudo-first-order rate constants at $t = 0$.

Calculation of Isotope Effects. The chlorine leaving group kinetic isotope effects were calculated from isotopic abundance ratios measured for the reaction product chloride and for the

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[22] R. A. Sneen and J. W. Larsen, *J. Amer. Chem. Soc.*, **91**, 6031 (1969).

[23] R. Quelet and J. Allard, *Bull. Soc. Chim. Fr.*, **4**, 1468 (1937).

[24] H. Weiner and R. A. Sneen, *J. Amer. Chem. Soc.*, **87**, 287 (1965).

[25] H. R. McCleary and L. P. Hammett, *J. Amer. Chem. Soc.*, **63**, 2254 (1941).

Table I. Summary of Kinetics and Chlorine Leaving Group Kinetic Isotope Effects Data for the Reaction of *p*-Methoxybenzyl Chloride with Solvent Water and Added Salts in 70% Aqueous Acetone at 20°

Solvolysis			0.100 M NaN$_3$			0.1491 M NaN$_3$			0.2506 M NaN$_3$			0.200 M KNO$_3$		
Time[a]	f	$^{35}k/^{37}k$	Time[a]	f	$^{35}k/^{37}k$	Time[a]	f	$^{35}k/^{37}k$	Time[a]	f	$^{35}k/^{37}k$	Time[a]	f	$^{35}k/^{37}k$
148	0.0484	1.00677[b]	85	0.0666	1.00864[b]	162	0.1280	1.00914[b]	135	0.1496	1.00989[b]	127	0.0588	1.00783[b]
320	0.0881	1.00747[b]	233	0.1353	1.00922[b]	291	0.2081	1.00957[b]	262	0.2391	1.01036	278	0.1017	1.00838
451	0.1157	1.00755[b]	382	0.2022	1.00930	448	0.2838	1.00985	431	0.3462	1.01046	398	0.1385	1.00851
684	0.1653	1.00781	772	0.3471	1.00972	619	0.3592	1.00983	582	0.4381	1.01041	615	0.1982	1.00853
1019	0.2281	1.00788	1127	0.4525	1.00944	866	0.4524	1.00984	836	0.5533	1.01060	794	0.2442	1.00856
1504	0.3094	1.00784	1538	0.5465	1.00936	1031	0.5025	1.01004	1204	0.6799	1.01083	1009	0.3024	1.00846
1864	0.3676	1.00782	1841	0.6020	1.00944	1363	0.5950	1.00990	1455	0.7383		1304	0.3579	1.00858
2348	0.4360	1.00828	2281	0.6753	1.00932	1751	0.6790	1.00987	1983	0.8347	1.01047	1565	0.4121	1.00841
2905	0.5026	1.00796	2830	0.7420	1.00931	2038	0.7190	1.00974	2256	0.8662		1847	0.4566	1.00835
3437	0.5632	1.00783	3389	0.7962		2543	0.7923	1.00975	2621	0.8999	1.01029	2358	0.5428	1.00827
			3931	0.8341		3519	0.8774		3037	0.9315		2931	0.6165	1.00812
						3962	0.9034		3496	0.9552		3464	0.6719	1.00831
												3816	0.7068	
	Mean	1.00786		Mean	1.00936		Mean	1.00985		Mean	1.01049		Mean	1.00845
		±0.00010			±0.00015			±0.00015			±0.00025			±0.00015

[a] Time is measured in seconds. [b] Initial value contaminated by blank (see text); not included in calculation of the mean.

starting material by means of the relation derived by Tong and Yankwich.[26]

$$\text{KIE} = {}^{35}k/{}^{37}k = \frac{\ln\left(1 - f\dfrac{(1 + R_0)}{(1 + R)}\right)}{\ln\left(1 - f(R/R_0)\dfrac{(1 + R_0)}{(1 + R)}\right)} \qquad (9)$$

R is the ratio of ^{37}Cl to ^{35}Cl in the product chloride at fraction of reaction f; R_0 is the same ratio for the starting material (or chloride product at infinite time) and is assumed to be equal to 0.31977, the natural abundance of the chlorine isotopes.[27] The calculated values of the KIE were found to be significantly lower at small values of f than at higher f values. Above about 20% reaction, however, the KIE values were constant within experimental error and are considered reliable. The source of this variation was traced to a small chloride blank (*ca.* 1%) present in the reactant at the outset of the reaction, which altered the isotopic composition of the samples at low f so that the measured ratios were not representative of the isotopic composition of the chloride product from the reaction. It was not possible chemically to remove the blank, but the data could be treated to eliminate its influence by using the change in isotopic composition with changes in f for consecutive data points. This procedure yielded an average value for the KIE that was essentially the same as that determined from the average of the points calculated from eq 9 at high f. The agreement of results from the two methods indicates that the isotopic composition of the blank was not very much different from that of the samples in the range studied, and at its low concentration level its influence upon the sample ratio was negligible when the product chloride concentration was relatively high. The kinetics and isotope effects data are summarized in Table I.

Results and Discussion

The reaction of *p*-methoxybenzyl chloride with solvent water and added azide ion in 70% aqueous acetone was studied for four different azide concentrations in the range 0 to 0.25 M. The concentrations of azide used were chosen for two reasons. First of all, the concentration of reactant was necessarily high (*ca.* 0.05 M) in order to provide a tractable amount of chloride product for isotopic analysis. If the nucleophile were to be in excess, its concentration had to be greater than 0.05 M. Secondly, because the dependence of the chlorine leaving group KIE on nucleophile was to be determined, a wide concentration range of nucleophile was chosen to minimize the uncertainty in evaluating any trends observed. The rate and isotope effects data from these runs are summarized in Table II.

Table II. Rate Constants and Chlorine Leaving Group Kinetic Isotope Effects for the Reaction of *p*-Methoxybenzyl Chloride with Solvent Water and Added Salts in 70% Aqueous Acetone at 20°

Salt	[Salt], M	10^4k, sec^{-1} [a]	$^{35}k/^{37}k$ [b]
None		2.38 ± 0.02	1.00786 ± 0.00010
NaN$_3$	0.1001	5.87 ± 0.15	1.00936 ± 0.00015
	0.1491	7.27 ± 0.09	1.00985 ± 0.00015
	0.2506	9.76 ± 0.14	1.01049 ± 0.00025
KNO$_3$	0.200	3.36 ± 0.05	1.00845 ± 0.00015
NaNO$_3$	0.200	3.48 ± 0.06	

[a] Initial pseudo-first-order rate constants. Error limits estimated on the basis of the standard deviation from a least-squares fit of the kinetics data. [b] Error limits estimated from propagation of probable experimental error or scatter in observed values, whichever was greater.

In order to compare the observed kinetics with those predicted for Schemes I and II, it is necessary to ob-

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(26) J. Y. Tong and P. E. Yankwich, *J. Phys. Chem.*, **61**, 540 (1957).

(27) W. R. Shields, T. J. Murphy, E. L. Garner, and V. H. Dibeler, *J. Amer. Chem. Soc.*, **84**, 1519 (1962).

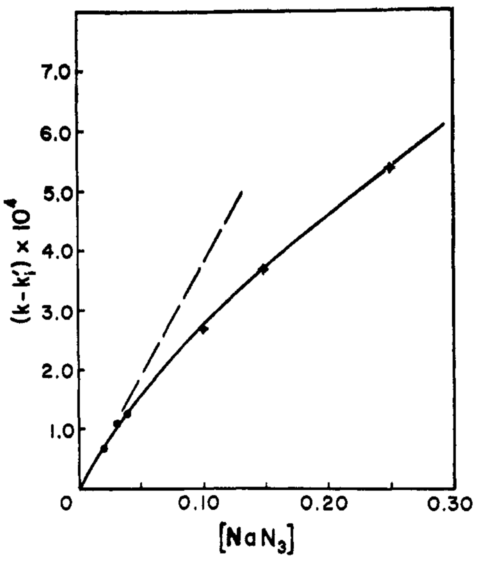

Figure 1. Plot for the reaction of *p*-methoxybenzyl chloride with solvent water and added sodium azide in 70% aqueous acetone at 20°: data from ref 14 (●); data from present study (✦).

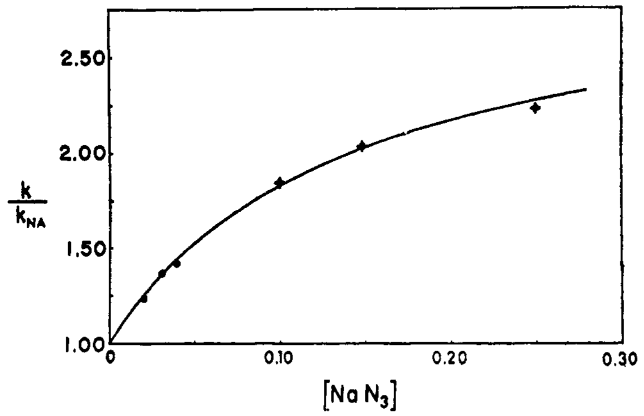

Figure 2. Plot for the reaction of *p*-methoxybenzyl chloride with solvent water and added sodium azide in 70% aqueous acetone at 20°. The solid line is given by eq 3 with $x = 1.98$, $m = 21.6$: data from ref 14 (●); data from present study (✦).

tain an estimate of the salt effects of sodium azide on the solvolysis reaction. Kohnstam's data[14] suggest a nonlinear relationship between the rate and salt concentration for this reaction. Thus, the apparent value of b in the Winstein equation[28] ranges from approximately 3.24 at 0.02 M NaN_3 to approximately 3.31 at 0.04 M NaN_3. At the higher concentrations employed in this study, a value of $b = 3.35$ and a linear dependence of rate on salt concentration was assumed as a reasonable extrapolation of these data.

For Scheme I, eq 1 prescribes that the rate of the reaction in the presence of azide be given by eq 10. In

$$k = k_i' + k_{2N}[N_3^-] \qquad (10)$$

this expression, k_i' is the rate constant for the ionization reaction corrected for salt effects and is given by

$$k_i' = k_i^0(1 + b[N_3^-]) \qquad (11)$$

where k_i^0 is the rate constant for ionization in the absence of added salts. It is assumed that the observed salt effect acts only upon the ionization process. Under these conditions, the operation of Scheme I requires that a plot of $(k - k_i')$ *vs.* $[N_3^-]$ be linear with a slope of k_{2N}, the second-order rate constant for SN2 substitution by azide ion on the substrate.[29] Such a plot is shown in Figure 1, where both the quantities calculated from the data in ref 14 and the data from this study are included. The observed slope does not fit the linear prediction and would suggest that Scheme I does not describe the mechanism. Scheme I can remain a viable alternative, however, if a negative salt effect for the second-order component of the reaction is postulated. An argument of this type was advanced[16,17] and effectively refuted[30] where negative salt effects were proposed for a solvolytic reaction. Negative salt effects upon the reaction between an anion and a neutral molecule are, however, not unexpected.[31] These effects are usually smaller than that necessary to rationalize the data in Figure 1, but the possibility of their operation does exist.

For Scheme II, the variation of reaction rate as a function of nucleophile concentration is expected to vary in accordance with eq 3. The parameter k_{NA} in this case is identical with k_i' as calculated by means of eq 11. The values of x and m have been determined by Sneen and Larsen[22] to be 1.98 and 21.6, respectively, for this reaction. Figure 2 shows a plot of k/k_{NA} values calculated from both the data in ref 14 and that of the present study as a function of azide concentration. The solid line is given by eq 3 using the values given above for the various constants. The ability of this expression to describe the experimental data is readily apparent; there is little doubt that the data are consistent with the operation of Scheme II. A definitive choice between the alternative mechanisms on the basis of the kinetics data alone is not possible, however, because of the uncertainty in the possible negative salt effect contribution.

Since the test reaction falls into the "borderline" classification, it was expected that the observed chlorine leaving group kinetic isotope effects would exhibit a dependence on nucleophile concentration according to eq 4 or 5 depending upon whether the classical or the ion pairs mechanism were operative. Under the assumptions made, an increase in KIE with increasing nucleophile concentration is indicative of the operation of the ion pairs mechanism; a decrease in KIE with increasing nucleophile concentration indicates that the classical description is the more probable one. The chlorine leaving group KIE values in Table I do, indeed, show a substantial dependence upon azide concentration. The KIE increases more than 30% (1.00786 to 1.01049, see Table II) as the azide concentration is raised from zero to approximately 0.25 M. This increasing trend is consistent only with the ion pairs

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[28] S. Winstein, B. Appel, R. Baker, and A. Diaz, *Chem. Soc., Spec. Publ.*, **No. 19,** 109 (1965).

[29] This criterion is not the same as that used by Sneen and coworkers[11] to test the operation of simultaneous SN1 and SN2 processes. Their treatment is based on the prediction that linear combinations of SN1 and SN2 processes will lead to a linear plot of k/k_{NA} *vs.* [N].[22] If k_{NA} is identified with k_i' in eq 11, the expression

$$k/k_{NA} = 1 + [k_{2N}[N]/k_i^0(1 + b[N])]$$

results. It is apparent that this expression is not a linear function of [N].

[30] R. A. Sneen and H. M. Robbins, *J. Amer. Chem. Soc.*, **94,** 7868 (1972).

[31] L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill, New York, N. Y., 1970, p 211.

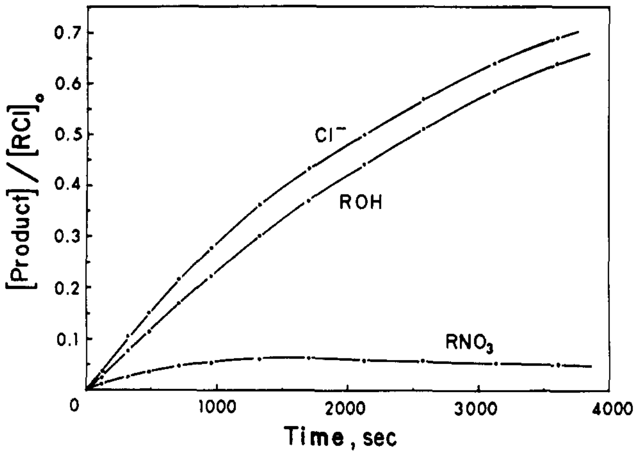

Figure 3. Product distribution as a function of time for the reaction of *p*-methoxybenzyl chloride with solvent water and 0.200 *M* sodium nitrate in 70% aqueous acetone at 20°.

hypothesis and provides strong evidence for the operation of this mechanism.

In addition, the functional form of the dependence of KIE on azide concentration is in accord with eq 5. This expression may be rewritten in the form

$$\mathrm{KIE_{II}} = \frac{^{35}k_1}{^{37}k_1}\,\frac{^{37}x + 1 + m[\mathrm{N}]}{^{35}x + 1 + m[\mathrm{N}]} \qquad (12)$$

where $x = k_{-1}/k_{\mathrm{S}}$ and $m = k_{\mathrm{N}}/k_{\mathrm{S}}$. By substituting the experimental values for $\mathrm{KIE_{II}}$, m, and [N] and making the approximation that $^{37}x = 1.98$ (the experimental value of x for the over-all reaction), an estimate of the values of $^{35}k_1/^{37}k_1$ and $^{35}k_{-1}/^{37}k_{-1}$, the isotope effects for the forward and reverse reactions involved in the ion pair formation equilibrium can be obtained. These values are approximately 1.0117 for the forward reaction and 1.0057 for the reverse process. The magnitudes of these effects may be interpreted as arising from a transition state involving substantial carbon–chlorine bond rupture consistent with the ion pairs postulate.

Because the treatment of salt effects upon the kinetics of the reaction represented the primary source of uncertainty in the application of kinetics data to the differentiation between Schemes I and II, it was felt that this aspect should receive more attention. It is sometimes assumed[30] that all salts affect the reaction similarly and that the effect is linear in salt concentration. The fallacy of this assumption for *p*-methoxybenzyl chloride was powerfully demonstrated by the results of an emperiment performed in the course of this study. Solvolysis of *p*-methoxybenzyl chloride in 70% aqueous acetone in the presence of 0.200 *M* potassium nitrate was found to give an isotope effect value (1.00845 ± 0.00015) substantially higher than that obtained for the solvolysis in the absence of added salts. It had been assumed that the nitrate would be a typical "inert" salt and that little, if any, difference in KIE would be observed because the inert salts are believed to affect the reaction rate by altering only the physical environment of the reacting molecules and should not influence the KIE. In addition, the observed rate for the reaction was considerably lower than that predicted on the basis of the salt effect constant used for the sodium azide cases.

An extensive study[32] of the effects of a variety of salts upon the type of reaction under consideration here has shown that significant differences exist between the salts in their effectiveness in increasing the reaction rate. Sodium azide was found to produce a rate enhancement more than twice that of sodium nitrate at the same concentration for the hydrolysis of diphenylmethyl chloride in 70% aqueous acetone.[32] It has also been demonstrated[33] that the nitrate anion is capable of acting as a nucleophile, albeit weakly, in the reactions of *p*-methoxybenzyl chloride in 70% aqueous acetone.

In order to test whether or not these were reasonable causes for our surprising results, a detailed study of the kinetics of the reaction of *p*-methoxybenzyl chloride with 0.200 *M* sodium nitrate in 70% aqueous acetone was carried out in which the concentrations of the various products as a function of time were determined. The results of this study are shown in Figure 3. The data suggest that, indeed, nitrate does act as a nucleophile but that the organic nitrate produced is not stable and undergoes hydrolysis to the alcohol. Thus, no evidence of a nitrate product was found in samples taken after more than 20 reaction half-lives even though reaction to the nitrate was found to account for approximately 36% of the initial over-all reaction rate. On the basis of the initial rates, a value for the parameter m in eq 3 for nitrate as nucleophile was estimated as 2.81. Comparison of the observed KIE of 1.00845 ± 0.00015 with the value 1.00846 calculated on the basis of eq 12 using $m = 2.81$, $^{37}x = 1.98$, $^{35}k_1/^{37}k_1 = 1.0117$, and $^{35}k_{-1}/^{37}k_{-1} = 1.0057$ (*vide supra*) suggests that the nucleophilicity of the nitrate anion is sufficient to explain the difference between the KIE measured with and without added salt. The agreement between the prediction based on eq 12 and experiment is remarkably good, indicating that the main cause of the change in isotope effect with salt concentration is a nucleophilic interaction and not a salt effect upon the isotope effect. Here, again, the increased KIE for reaction in the presence of potassium nitrate over that for the solvolysis is inconsistent with predictions based upon the classical scheme and adds further support to Scheme II in describing the mechanism.

Summary and Conclusions

The observation of a substantial increase in the value of the chlorine leaving group kinetic isotope effects with increasing nucleophile concentration for the borderline kinetics test reaction of *p*-methoxybenzyl chloride with solvent water and added azide ion in 70% aqueous acetone cannot be reconciled with Scheme I but is consistent with the Scheme II explanation of the mechanism. The higher KIE value observed for the reaction in the presence of 0.200 *M* potassium nitrate was shown to result from nucleophilic participation by the nitrate anion. The organic nitrate product is not stable but undergoes subsequent hydrolysis by the solvent. The increased KIE for the nitrate nucleophile also supports the ion pairs hypothesis for the *p*-methoxybenzyl chloride substrate.

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(32) B. J. Gregory, G. Kohnstam, A. Queen, and D. J. Reid, *Chem. Commun.*, 797 (1971).

(33) G. Kohnstam, A. Queen, and T. Ribar, *Chem. Ind.* (*London*), 1287 (1962).

These results demonstrate that the chlorine leaving group KIE can indeed serve to differentiate between the operation of the classical SN mechanisms of nucleophilic attack and that of the ion pairs mechanism under appropriate conditions and within the limits of the assumptions made. In this case, the data support the ion pairs mechanism to the exclusion of simultaneous SN1 and SN2 processes and indicate that further investigation and theoretical development of the KIE probe based upon this hypothesis are warranted. The question of the generality of the ion pairs mechanism[22] remains open. Perhaps the results of future work based upon these preliminary findings and directed toward the goals mentioned above will help to resolve the controversy evoked by its suggestion.

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Solvent Effects on the Proton Magnetic Resonance Spectra of Tetraalkylammonium Tetraalkylborides

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Abstract: Solvent effects on proton chemical shifts of molten tetraalkylammonium tetraalkylborides have been measured in binary molten salt–solvent mixtures containing 0–90 mol % solvent at 50 and 90°. Hydrocarbon analogs of the molten salt ions are shown to be the best reference compounds for solvent-induced shifts. Aromatic solvents cause upfield shifts of the cation resonances as large as 1.5 ppm and downfield shifts of the anion resonances as large as 1.0 ppm. The sizes of the solvent shifts are linearly related to the volume magnetic susceptibility anisotropy of the solvent. Although the aromatic solvent-induced shifts are large, the ion–dipole and ion–induced dipole interactions which cause them are weak. Simple equilibrium models for formation of collision complexes between solvents and tetraalkylammonium tetraalkylborides do not fit the chemical shift data.

The preparation of large quantities of tetraalkylammonium tetraalkylborides which are liquid at or near room temperature makes available a class of solvents different from any previously studied.[1] These viscous liquid salts are miscible with many organic compounds but not with water or paraffins. Since they cannot participate in Lewis acid–base interactions with solutes or with each other, their intermolecular and interionic interactions are limited to coulombic, ion–dipole, ion–induced dipole, and dispersion forces. To determine qualitatively the nature of interactions between these molten salts and organic compounds, we have measured pmr chemical shifts of 0–90 mol % solutions of a wide variety of organic solvents in the homologous series of molten salts $N_{1116}B_{1116}$, $N_{2226}B_{2226}$, $N_{3333}B_{3336}$, and $N_{4446}B_{4446}$.[2]

The screening constant σ_{solvent} for the difference in chemical shifts of a molecule in the gas phase and in solution has been expressed as a sum of four terms (eq 1), which are contributions from the bulk sus-

$$\sigma_{\text{solvent}} = \sigma_b + \sigma_a + \sigma_w + \sigma_E \qquad (1)$$

ceptibility of the medium σ_b, magnetic susceptibility anisotropy of solvent molecules σ_a, van der Waals forces between solute and solvent σ_w, and a polar (electric field) effect of solvent molecules on the solute σ_E.[3] To these four terms is added sometimes a fifth term, σ_c, for specific complexation between solute and solvent. Bulk susceptibility corrections σ_b are readily made from volume magnetic susceptibilities. Numerous attempts to evaluate the other terms for uncharged solutes both experimentally and theoretically have led to the conclusions that σ_a is usually the major contributor in aromatic solvents, that σ_w is important in most solvents, particularly ones containing heavy atoms, and that σ_E is negligible in nonpolar solvents and difficult to distinguish from σ_w in polar solvents.[4–18] In principle, σ_c can be evaluated from concentration-dependent chemical shifts of the two complexing species

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(1) W. T. Ford, R. J. Hauri, and D. J. Hart, *J. Org. Chem.*, **38**, 3916 (1973).

(2) In the structural abbreviations subscripts refer to the numbers of carbon atoms in *n*-alkyl groups bound to nitrogen or boron. For example, $N_{2226}B_{2226}$ is triethyl-*n*-hexylammonium triethyl-*n*-hexylboride.

(3) A. D. Buckingham, T. Schaefer, and W. G. Schneider, *J. Chem. Phys.*, **32**, 1227 (1960).

(4) P. Laszlo, *Progr. Nucl. Magn. Resonance Spectrosc.*, **3**, 231 (1967).

(5) J. Ronayne and D. H. Williams, *Annu. Rev. NMR (Nucl. Magn. Resonance) Spectrosc.*, **2**, 83 (1969).

(6) R. Foster and C. A. Fyfe, *Progr. Nucl. Magn. Resonance Spectrosc.*, **4**, 1 (1969).

(7) J. C. Schug, *J. Phys. Chem.*, **70**, 1816 (1966).

(8) P. Laszlo, A. Speert, R. Ottinger, and J. Reisse, *J. Chem. Phys.*, **48**, 1732 (1968).

(9) F. H. A. Rummens, W. T. Raynes, and H. J. Bernstein, *J. Phys. Chem.*, **72**, 2111 (1968).

(10) J. K. Becconsall, *Mol. Phys.*, **15**, 129 (1968); **18**, 337 (1970).

(11) F. H. A. Rummens, *Mol. Phys.*, **19**, 423 (1970).

(12) E. R. Malinowski and P. H. Weiner, *J. Amer. Chem. Soc.*, **92**, 4193 (1970).

(13) P. H. Weiner and E. R. Malinowski, *J. Phys. Chem.*, **75**, 1207, 3160, 3971 (1971).

(14) E. M. Engler and P. Laszlo, *J. Amer. Chem. Soc.*, **93**, 1317 (1971).

(15) F. H. A. Rummens and R. J. Krystynak, *J. Amer. Chem. Soc.*, **94**, 6914 (1972).

(16) F. H. A. Rummens and F. J. A. Louman, *J. Magn. Resonance*, **8**, 332 (1972).

(17) H. J. Bernstein, *Pure Appl. Chem.*, **32**, 79 (1972).

(18) M. R. Bacon and G. E. Maciel, *J. Amer. Chem. Soc.*, **95**, 2413 (1973).