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Chlorine Isotope Effects in the Reactions of Benzyl and Substituted Benzyl Chlorides with Various Nucleophiles[1,2]

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The kinetics and chlorine isotope effects in the nucleophilic substitution reactions of benzyl and substituted benzyl chlorides with water, cyanide ion and thiosulfate ion have been investigated. For those reactions exhibiting first-order kinetics, the kinetic isotope effect (k^{35}/k^{37}) observed was close to 1.0078, while for reactions displaying second-order kinetics the value was 1.0058. Those reactions proceeding by borderline kinetics gave isotope effects intermediate between these two extremes. Detailed analysis of the kinetic and isotope effect data for the reactions with cyanide and thiosulfate ions leads to the conclusion that there is a smooth transition in the reaction mechanism from near ideal S$_N$1 to near ideal S$_N$2 as the electron-donating power of the substituent decreases. It appears that the magnitude of the chlorine isotope effect may be used to differentiate between S$_N$1 and S$_N$2 reactions.

Introduction

Substitution of one isotope of an element for another in a bond undergoing rupture or formation in the rate-controlling step of a reaction influences the rate of the reaction. The magnitude of this effect is quite small in the case of substitution of chlorine-37 for chlorine-35. Bartholomew, Brown and Lounsbury[4] observed chlorine isotope effects (k^{35}/k^{37}) of 1.008 ± 0.001 for the reactions of *t*-butyl chloride with sodium hydroxide and with silver nitrate in aqueous alcohol. Nair and Fry[5] in an isotope effect study of the reaction between chloride and cyanide ions in aqueous ethanol observed a chlorine isotope effect of 1.0074 ± 0.0005.

Theoretical equations have been developed by Bigeleisen[6] for the prediction of the magnitude of kinetic isotope effects. These have been applied to two-center and three-center reactions by Bigeleisen and Wolfsberg.[7] These descriptions fit the type of covalency changes that are associated with the mechanistic categories, S$_N$1 and S$_N$2, of nucleophilic substitution reactions. Bender and Hoeg[8] and Bender and Buist[9] have investigated the carbon-14 kinetic isotope effects in S$_N$1 and S$_N$2 reactions. They have concluded from the results obtained and from calculations using Bigeleisen's equation that the magnitude of the kinetic isotope effect is of little value in differentiating between the two categories.

From calculations made in this Laboratory, however, it seems that a different approach to the problem, *viz.*, a study of the isotope effects in displacement reactions in which the terminal position, rather than the central carbon atom, is isotopically substituted might be fruitful. Simple calculations of temperature-independent factors[7,8] of isotope effects $[(k/k^*\text{-}1)100]$ for the systems (a) $O\cdots C^*\cdots Cl$ and (b) $O\cdots C\cdots Cl^*$ (where the asterisk indicates the isotopically labeled atom) reveal that there is only 5% variation for system (a) ($C^* = C^{14}$) as the mechanism changes from ideal S$_N$1 (unassisted bond rupture) to ideal S$_N$2 (concerted, equal bond formation and bond rupture), while for system (b) the corresponding change is 74% (from 1.0069 to 1.0018 in k^{35}/k^{37}). Although a complete theoretical treatment must also include the temperature-dependent factor, it seemed very likely that a study of (b) (chlorine isotope effect) would be more profitable in attempting to assess mechanistic changes.

The reactions of benzyl halides fall into the borderline region in nucleophilic displacements, and the mechanism can be shifted toward S$_N$1 or S$_N$2 by introducing appropriate substituents into the benzene ring. It was decided here to investigate the chlorine isotope effects (k^{35}/k^{37}) in the reactions of unsubstituted, *p*-methoxy-, *p*-methyl-, *p*-chloro- and *p*-nitrobenzyl chlorides with each of three nucleophiles: water, cyanide ion and thiosulfate ion.

Experimental

Materials.—*p*-Methoxybenzyl chloride was prepared from *p*-methoxybenzyl alcohol by a procedure of Quelet and Allard,[10] yielding material of b.p. 82° (0.9 mm.) [lit.[11] b.p. 95° (5 mm.)]. Fisher reagent grade benzyl chloride was dried over Drierite and fractionated under reduced pressure, b.p. 55° (1 mm.) [lit.[12] b.p. 63° (8 mm.)]. Eastman Kodak Co. reagent grade *p*-methylbenzyl chloride was dried over Drierite and fractionated under reduced pressure, b.p. 78° (1.5 mm.) [lit.[13] b.p. 80° (2 mm.)]. Eastman Kodak Co. reagent grade *p*-chlorobenzyl chloride was dried over Drierite and fractionated under reduced pressure, b.p. 79° (2 mm.) [lit.[14] b.p. 96° (15 mm.)]. Eastman Kodak Co. reagent grade *p*-nitrobenzyl chloride was twice recrystallized from hot *n*-heptane and air-dried in a hood, m.p. 71° (lit.[15] m.p. 71°). Distilled water was redistilled in a glass still from alkaline permanganate. It was protected from carbon dioxide during distillation and in storage. Commercial 1,4-dioxane was purified by the method of Fieser[16] and stored over sodium. It was freshly distilled as needed. Merck reagent grade potassium cyanide and Fisher reagent grade sodium thiosulfate were used without further purification. All other materials used were reagent grade.

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[2] From the Ph.D. thesis of J. W. H.; presented at the 16th Southwest Regional Meeting, American Chemical Society, Oklahoma City, Okla., December, 1960.

[3] N.S.F. Predoctoral Fellow.

[4] R. M. Bartholomew, F. Brown and M. Lounsbury, *Can. J. Chem.*, **32**, 979 (1955); *Nature*, **174**, 133 (1954).

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[7] J. Bigeleisen and M. Wolfsberg, *ibid.*, **21**, 1972 (1953); **22**, 1264 (1954).

[8] M. L. Bender and D. F. Hoeg, *J. Am. Chem. Soc.*, **79**, 5649 (1957).

[9] M. L. Bender and G. J. Buist, *ibid.*, **80**, 4304 (1958).

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[11] G. R. Robertson, in H. Gilman and A. H. Blatt, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1948, p. 396.

[12] I. Heilbron, "Dictionary of Organic Compounds," Vol. I, Oxford University Press, New York, N. Y., 1953, p. 272.

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[14] J. von Braun, M. Kuhn and J. Weismantel, *Ann.*, **449**, 267 (1926).

[15] F. Beilstein and P. Geitner, *ibid.*, **139**, 337 (1866).

[16] L. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., Boston, Mass., 1957, p. 368.

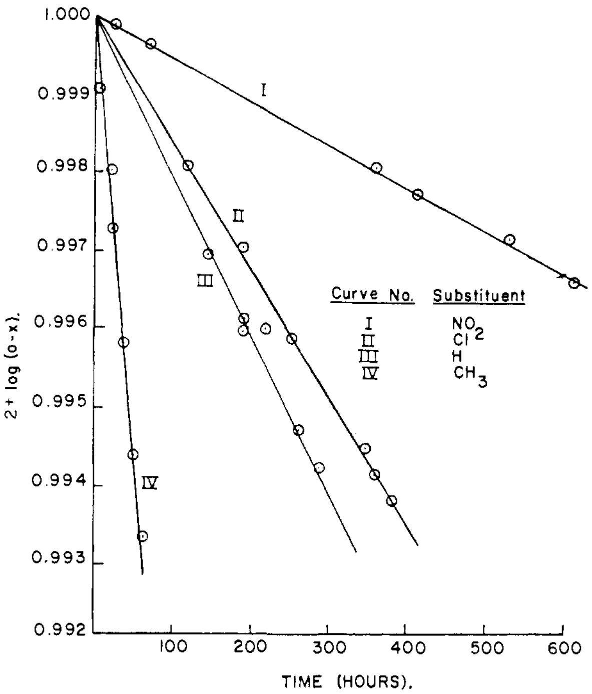

Fig. 1.—Kinetics of the hydrolyses of benzyl and p-substituted benzyl chlorides in 80% aqueous dioxane at 30°; [p-XC$_6$H$_4$CH$_2$Cl] = 0.1000 *m*.

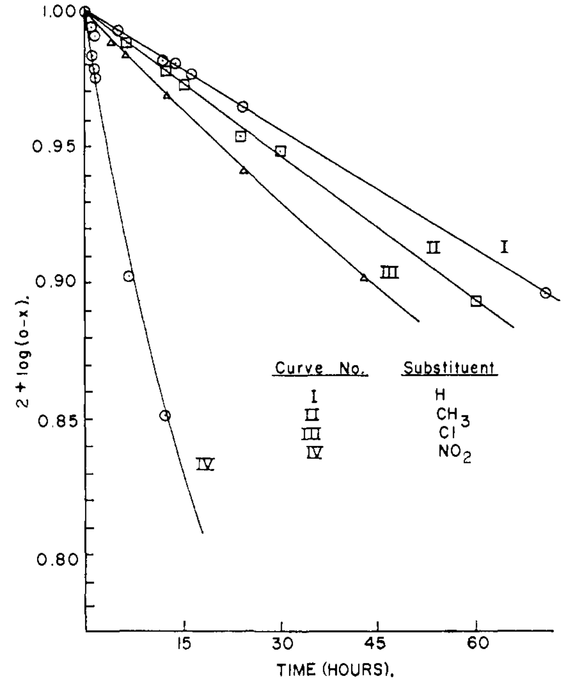

Fig. 2.—First-order plots of the reactions of benzyl and p-substituted benzyl chlorides with potassium cyanide in 80% aqueous dioxane at 30°; [p-XC$_6$H$_4$CH$_2$Cl] = 0.1000 *m*, [KCN] = 0.05002 *m*.

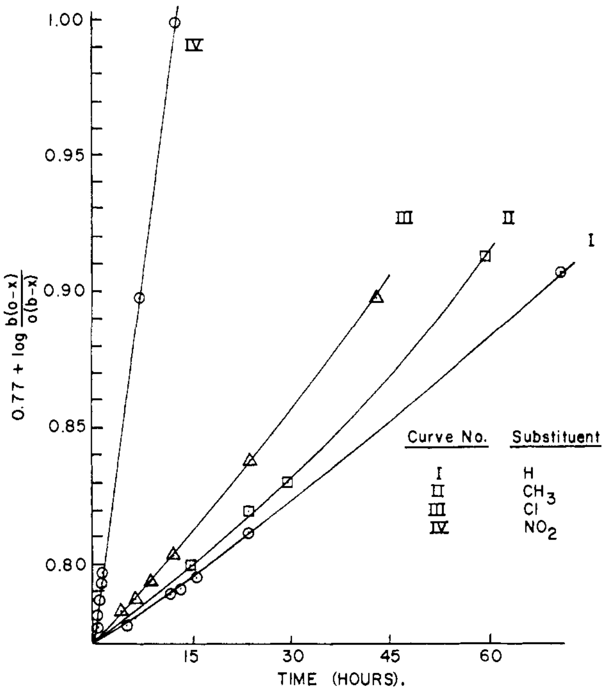

Fig. 3.—Second-order plots of the reactions of benzyl and p-substituted benzyl chlorides with potassium cyanide in 80% aqueous dioxane at 30°; [p-XC$_6$H$_4$CH$_2$Cl] = 0.1000 *m*, [KCN] = 0.05002 *m*.

Kinetics.—The kinetics of the reactions of benzyl and substituted benzyl chlorides with water, cyanide ions and thiosulfate ions were measured in aqueous dioxane solution (80% dioxane by weight) at 30.00 ± 0.02°. For the very slow reactions, the amount of aralkyl chloride required to make a 0.1000 *m* solution, the dioxane and the water or aqueous solution containing the amount of potassium cyanide or sodium thiosulfate needed to make a 0.05 *m* solution were weighed directly into the reaction flask, which was immediately shaken thoroughly and placed in the constant temperature bath. Zero time was taken as the time of addition of the water or aqueous solution. For faster reactions where the time required for the reaction flask contents to reach bath temperature might be an appreciable fraction of the shortest sampling time, the organic and aqueous phases were weighed separately into two flasks which were connected so as to enable mixing after the two solutions had reached bath temperature. After appropriate times, the reactions were stopped by immersing the reaction vessels in a Dry Ice–isopropyl alcohol mixture. The contents of the reaction flasks were washed into separatory funnels containing 100 ml. of water and 100 ml. of benzene, and the chloride ions separated by fractional extraction. If the combined aqueous fractions contained cyanide ions, these were rendered innocuous in a chloride ion determination by treatment with a few drops of 40% formalin.[17] If the aqueous mixture contained thiosulfate ions, these were made innocuous by treatment with hydrogen peroxide in basic solution.[18] The chloride ions were then determined gravimetrically as silver chloride. Blank runs, omitting the aralkyl chloride, gave no silver chloride. Control runs omitting the aralkyl chloride and containing known amounts of sodium chloride, gave essentially quantitative yields of silver chloride.

In order to investigate the temperature dependence of the kinetic isotope effects, the hydrolysis of benzyl chloride and the reaction of p-nitrobenzyl chloride with potassium cyanide were also carried out at 50.00 ± 0.05°, and the hydrolysis of p-nitrobenzyl chloride was performed at 90.0 ± 0.1°.

Representative data on the three reactions using p-methoxybenzyl chloride are given in Table I. In all cases first-order plots (log $(a - x)$ *vs.* t, where a is the initial concentration of aralkyl chloride, x is the extent of reaction taken place and t is the reaction time) of the data were made. For the reactions with cyanide ion and thiosulfate ion, second-order plots (log $[b(a-x)/a(b-x)]$ *vs.* t, where b is the initial concentration of cyanide or thiosulfate ion) were also made. The kinetic data for the compounds other

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(17) W. E. Williams, "Cyanogen Compounds," Arnold, New York, N. Y., 1948, p. 337.

(18) J. S. N. Cramer, *Chem. Weekblad*, **28**, 316 (1931).

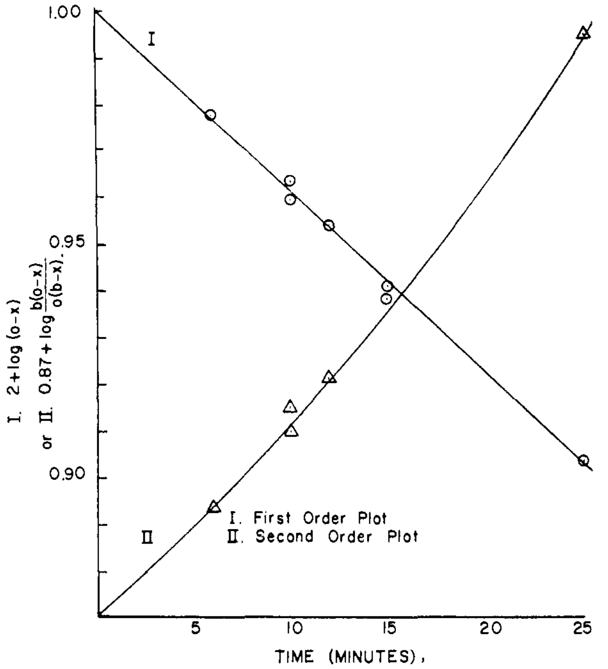

Fig. 4.—Kinetic order of the reaction of *p*-methoxybenzyl chloride with sodium thiosulfate in 80% aqueous dioxane at 30°; [p-$CH_3OC_6H_4CH_2Cl$] = 0.1000 *m*, [$Na_2S_2O_3$] = 0.05001 *m*.

than *p*-methoxybenzyl chloride (for which see Table I) are summarized in these plots as shown in Figs. 1 through 7.

TABLE I

KINETICS OF THE REACTIONS OF *p*-METHOXYBENZYL CHLORIDE WITH WATER, POTASSIUM CYANIDE AND SODIUM THIOSULFATE IN 80% AQUEOUS DIOXANE AT 30°

Water		0.05001 *m* KCN		0.05001 *m* $Na_2S_2O_3$	
Time, sec. × 10^{-2}	Reaction, %	Time, sec. × 10^{-2}	Reaction, %	Time, sec. × 10^{-2}	Reaction, %
		p-$CH_3OC_6H_4CH_2Cl$ = 0.1000 *m*			
1.8	2.458	6.0	6.526	3.6	4.937
6.0	4.900	6.0	6.720	6.0	8.056
7.2	5.535	6.0	7.117	6.0	8.915
7.2	5.611	6.6	7.668	7.2	10.102
9.6	6.977	7.8	8.834	9.0	12.779
14.4	9.677	9.0	10.090	15.0	20.006
69.6	39.727	19.5	20.511		
96.0	49.374				

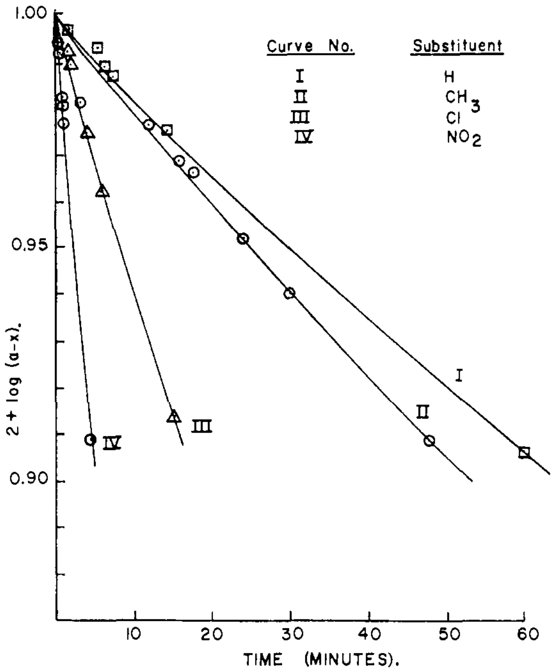

Fig. 5.—First-order plots of the reactions of benzyl and *p*-substituted benzyl chlorides with sodium thiosulfate in 80% aqueous dioxane at 30°; [p-$XC_6H_4CH_2Cl$] = 0.1000 *m*, [$Na_2S_2O_3$] = 0.05001 *m*.

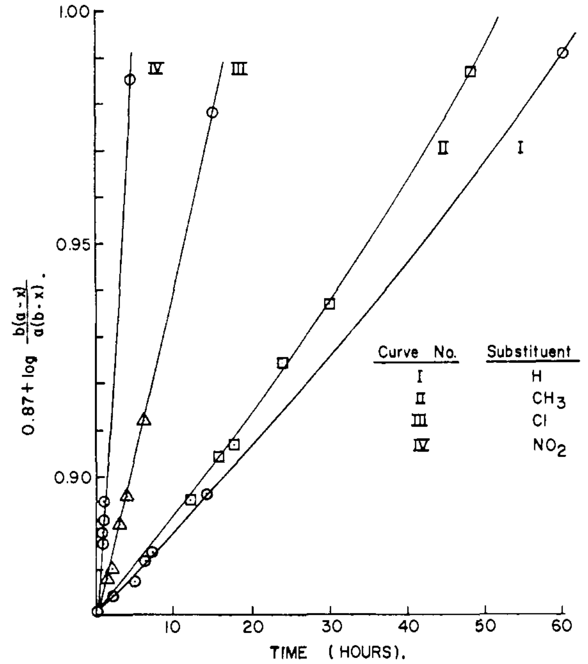

Fig. 6.—Second-order plots of the reactions of benzyl and *p*-substituted benzyl chlorides with sodium thiosulfate; [p-$XC_6H_4CH_2Cl$] = 0.1000 *m*, [$Na_2S_2O_3$] = 0.05001 *m*.

Preparation of the Mass Spectrometer Gas.—The silver chloride samples obtained in the kinetic runs were converted to methyl chloride by a modification of the method of Langvad.[19] The silver chloride was treated with a 50% excess of methyl iodide in a sealed tube for 12 hours at 110°. This procedure resulted in an 89% conversion. The methyl chloride formed and the excess methyl iodide were frozen by means of liquid air into a tube containing potassium hydroxide pellets (to remove any hydrogen chloride which might have been formed). The methyl chloride from the sample was then fractionally distilled by means of a Dry Ice–isopropyl alcohol mixture into a ampoule provided with a stopcock and a ground glass joint intended for connection to the mass spectrometer. That there is no chlorine isotope fractionation in this procedure was demonstrated in the following manner. Tank methyl chloride was decomposed by reaction with sodium in a sealed tube. The chloride formed was precipitated as silver chloride, which was converted to methyl chloride by the above procedure. This methyl chloride sample was shown to have the same isotopic composition as the original tank methyl chloride by comparison on the mass spectrometer. As a further check, another conversion of the above-mentioned silver chloride was started and then stopped after approximately 20% conversion. This methyl chloride was also found to have the same isotopic composition as the original tank methyl chloride within the precision of the mass spectrometer.

Isotope Ratio Measurements.—The variations in Cl^{37}/Cl^{35} ratios in the methyl chloride samples were determined with a

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[19] T. Langvad, *Acta Chem. Scand.*, **8**, 526 (1954).

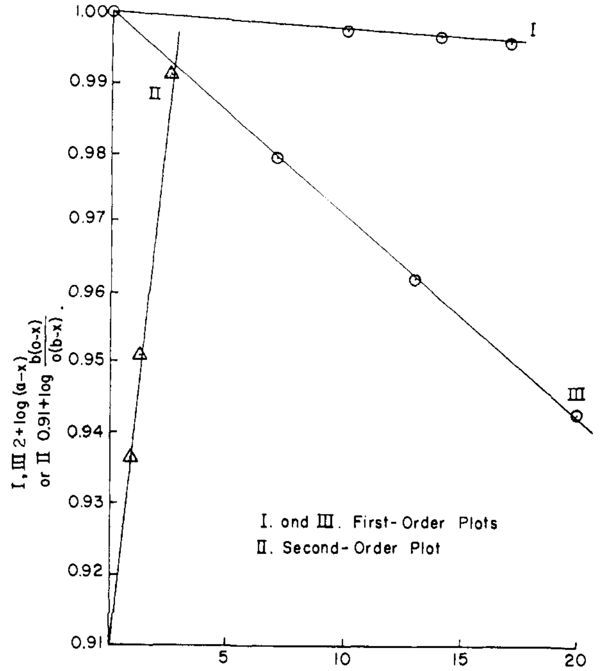

Fig. 7.—I. The hydrolysis of benzyl chloride at 50°; II. The reaction of *p*-nitrobenzyl chloride; with potassium cyanide at 50°; III. The hydrolysis of *p*-nitrobenzyl chloride at 90°; [*p*-$XC_6H_4CH_2Cl$] = 0.1000 *m*, [KCN] = 0.05002 *m*.

Nier type[20,21] 60° sector isotope ratio mass spectrometer with a dual inlet system and a dual collector. The sample was placed in one inlet system, and the standard in the other. The physical arrangement of the mass spectrometer is such that when the $C^{12}H_3Cl^{37}$ (*m/e* 52) positive ion beam is focused on one collector plate, the positive ion beams for *m/e* 51, 50 and 49 (which includes the $C^{12}H_3Cl^{35}$ positive ion) are focused on the other collector plate. In practice, the mass spectrometer is arranged so that the difference between the ion current ratio for the two collector plates for a sample and the ion current ratio for the two collector plates for the standard is recorded. By suitable corrections for other ion beams collected with the $C^{12}H_3Cl^{35}$ positive ion and by assuming an arbitrary isotopic ratio for the standard sample (approximately the natural abundance ratio), it is possible to calculate the ratio $C^{12}H_3Cl^{37}/C^{12}H_3Cl^{35} = Cl^{37}/Cl^{35}$ for the samples. Frequent switching from sample to standard served to minimize errors due to instrumental variations. In each reactant, the standard sample used for comparison purposes was prepared from the silver chloride obtained by reaction of the particular aralkyl chloride with excess alcoholic silver nitrate in a sealed tube. The sealed tube, which was well protected from light, was heated at 100° for 72 hours.

The mass spectrometer was calibrated using a series of samples of known chlorine-37 enrichment in the range encountered in the isotope effect work. These samples were prepared from an enriched (60.51 atom % Cl^{37}) sodium chloride sample by adding appropriate weighed quantities of unenriched sodium chloride. The sodium chloride samples were converted to methyl chloride and analyzed in the usual manner. A plot of the calculated difference from normal in the Cl^{37}/Cl^{35} ratio *versus* the measured difference was an excellent straight line. Furthermore, the slope was 1.00, indicating that our procedure results in accurate ratio difference measurements.

Results

Kinetics.—Examination of large scale graphs of the kinetic data (similar to Figs. 1 through 7) reveals that the first-order plots for many of the reactions are good straight lines; for others, the second-order plots are linear; and for the rest, both the first-order and second-order plots show considerable curvature. A complete kinetic study (variations of the reagent concentrations, effects of added salts, etc.) of these reactions would be of interest (and some future work along these lines is planned), but for correlation with the isotope effect data, the linearity or non-linearity of the first- and second-order plots was taken as a criterion of molecularity (for further consideration of this point, see the Discussion). Thus, all five hydrolysis reactions, the reactions of *p*-methoxy- and *p*-methylbenzyl chlorides with potassium cyanide, and the reaction of *p*-methoxybenzyl chloride with sodium thiosulfate, appear to be kinetically first order. The reactions of *p*-nitro- and *p*-chlorobenzyl chlorides with sodium thiosulfate and of the former with potassium cyanide exhibit second-order kinetics. The other reactions, *viz.*, those of unsubstituted and *p*-chlorobenzyl chlorides with potassium cyanide and of unsubstituted and *p*-methylbenzyl chlorides with sodium thiosulfate appear to display mixed order kinetics. The rate constants for those reactions showing linear kinetic plots were calculated from the slopes of the appropriate lines by the least squares method. These constants are given in Table II. Also given (in parentheses) in Table II are the pseudo-first-order rate constants for those reactions which do not show linear first-order plots, as calculated from the initial rates (least squares analysis of the first few points of the first-order plots).

TABLE II

RATE CONSTANTS FOR THE REACTIONS OF BENZYL AND SUBSTITUTED BENZYL CHLORIDES WITH VARIOUS NUCLEOPHILES IN 80% AQUEOUS DIOXANE

[*p*-$XC_6H_4CH_2Cl$] = 0.1000 *m*, [KCN] = 0.05002 *m*, [$Na_2S_2O_3$] = 0.05001 *m*

Substituent	Temp., °C.	Added nucleophile None[a]	 CN^-	 $S_2O_3^=$
CH_3O	30	709.0	1177[a]	1500[a]
CH_3	30	0.680	11.37[a]	(12.86)[b]
H	30	0.1279	(8.90)[b]	(11.36)[b]
	50	1.592		
Cl	30	0.1043	(16.33)[b]	0.923[c]
	30			(40.39)[b]
NO_2	30	0.0360	2.381[c]	3.384[c]
	30		(117.0)[b]	(154.0)[b]
	50		4.37[c]	
	50		(192.9)[b]	
	90	18.28		

[a] k_1, sec.$^{-1}$ × 10^7. [b] Pseudo-first-order rate constant (sec.$^{-1}$ × 10^7) (initial reaction). [c] k_2, l. mole^{-1} sec.$^{-1}$ × 10^4.

Isotope Effects.—The relationship[22] expressing the fractionation of two isotopes in a single stage reaction, where the isotopic species appears only once and in only one of the products, is

$$\ln\left(1 - f\frac{1 + R_0}{1 + R}\right) = \frac{k}{k^*}\ln\left(1 - f\frac{R}{R_0}\frac{1 + R_0}{1 + R}\right)$$

where *R* is the ratio of the heavier isotope to the lighter isotope in the product at any fraction, *f*,

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(20) A. O. Nier, *Rev. Sci. Inst.*, **18**, 398 (1940).

(21) C. R. McKinney, J. M. McCrea, S. Epstein, H. A. Allen and H. C. Urey, *ibid.*, **21**, 724 (1950).

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

TABLE III

FRACTIONATION OF CHLORINE ISOTOPES IN THE REACTIONS OF *p*-SUBSTITUTED BENZYL CHLORIDES, *p*-$XC_6H_4CH_2Cl$, WITH WATER, POTASSIUM CYANIDE AND SODIUM THIOSULFATE IN 80% AQUEOUS DIOXANE AT 30°

X = CH_3O			CH_3			H			Cl			NO_2		
Reacn., %	Cl^{37}/Cl^{35}	k/k^*	Reacn., %	Cl^{37}/Cl^{35}	k/k^*	Reacn., %	Cl^{37}/Cl^{35}	k/k^*	Reacn., %	Cl^{37}/Cl^{35}	k/k^*	Reacn., %	Cl^{37}/Cl^{35}	k/k^*
Part I. Reaction with water														
2.458	0.32083	1.0078	0.218	0.32077	1.0079	0.712	0.32080	1.0078	0.443	0.32080	1.0078	0.453	0.32090	1.0075
4.900	.32096	1.0075	.462	.32069	1.0082	.901	.32073	1.0080	.691	.32080	1.0078	.527	.32080	1.0078
5.535	.32093	1.0076	.634	.32090	1.0075	.934	.32073	1.0080	.960	.32086	1.0076	.666	.32090	1.0075
5.611	.32086	1.0078	.972	.32093	1.0074	.948	.32093	1.0074	1.280	.32077	1.0079	.790	.32083	1.0077
6.977	.32080	1.0081	1.302	.32104	1.0071	1.227	.32086	1.0076	1.348	.32073	1.0081	.808	.32104	1.0071
9.677	.32093	1.0078	1.542	.32107	1.0070	1.332	.32080	1.0078	1.428	.32090	1.0075	.817	.32077	1.0079
49.37	.32158	1.0077	100.0	.32330		100.0	.32330		100.0	.32330		.822	.32090	1.0075
100.0	.32330											100.0	.32330	
	Mean	1.0078 ± 0.0001		Mean	1.0075 ± 0.0004		Mean	1.0078 ± 0.0002		Mean	1.0078 ± 0.0002		Mean	1.0076 ± 0.0002
Part II. Reaction with potassium cyanide														
6.526	0.32096	1.0075	2.438	0.32073	1.0081	1.631	0.32096	1.0074	2.789	0.32145	1.0058	1.656	0.32155	1.0055
6.720	.32096	1.0076	4.845	.32080	1.0080	4.107	.32110	1.0070	3.649	.32138	1.0061	1.660	.32142	1.0059
7.117	.32077	1.0082	6.028	.32083	1.0079	4.253	.32114	1.0069	4.892	.32142	1.0060	3.717	.32145	1.0059
7.668	.32104	1.0073	9.722	.32090	1.0079	4.334	.32107	1.0071	6.863	.32131	1.0064	4.893	.32158	1.0055
8.834	.32083	1.0081	11.108	.32096	1.0077	5.100	.32103	1.0073	12.570	.32152	1.0059	5.463	.32155	1.0056
10.090	.32077	1.0083	21.858	.32114	1.0076	7.772	.32096	1.0076	20.220	.32169	1.0056	29.112	.32176	1.0057
100.0	.32330		100.0	.32330		100.0	.32330		100.0	.32330		100.0	.32330	
	Mean	1.0078 ± 0.0004		Mean	1.0079 ± 0.0003		Mean	1.0072 ± 0.0002		Mean	1.0060 ± 0.0002		Mean	1.0057 ± 0.0002
Part III. Reaction with sodium thiosulfate														
4.937	0.32069	1.0083	5.231	0.32097	1.0075	0.809	0.32131	1.0062	1.726	0.32131	1.0062	1.354	0.32138	1.0060
8.056	.32083	1.0080	7.032	.32100	1.0074	1.711	.32135	1.0061	2.018	.32152	1.0056	1.460	.32155	1.0055
8.915	.32086	1.0080	7.477	.32100	1.0075	2.520	.32121	1.0066	4.290	.32142	1.0060	3.813	.32142	1.0060
10.102	.32080	1.0082	10.515	.32110	1.0072	2.523	.32131	1.0063	5.646	.32142	1.0060	4.139	.32155	1.0056
12.799	.32090	1.0080	10.908	.32117	1.0070	2.961	.32118	1.0067	8.434	.32163	1.0054	5.218	.32142	1.0060
20.006	.32100	1.0080	19.060	.32113	1.0075	5.510	.32135	1.0062	18.033	.32169	1.0055	18.901	.32169	1.0056
100.0	.32330		100.0	.32330		100.0	.32330		100.0	.32330		100.0	.32300	
	Mean	1.0081 ± 0.0001		Mean	1.0074 ± 0.0002		Mean	1.0064 ± 0.0002		Mean	1.0058 ± 0.0003		Mean	1.0058 ± 0.0002

of reaction; R_0 is the same ratio at $f = 1$; and k and k^* are the velocity constants for the reactants containing the lighter and heavier atoms, respectively.

The kinetics previously described were utilized to determine the fraction of reaction. It should be noted that the k/k^* ratio is very insensitive to small variations in the fraction of reaction. R_0 was assumed to be 0.3233, the natural abundance ratio for the chlorine isotopes, and R was calculated from R_0 and the observed difference in ratios. The experimental data and isotope effects calculated by using the above equation are given in Tables III and IV.

TABLE IV

FRACTIONATION OF CHLORINE ISOTOPES IN THE REACTIONS OF BENZYL HALIDES IN 80% AQUEOUS DIOXANE AT TEMPERATURES OTHER THAN 30°

Reaction, %	Cl^{37}/Cl^{35}	k/k^*
Hydrolysis of benzyl chloride at 50°		
0.524	0.32077	1.0079
.809	.32086	1.0076
.963	.32086	1.0076
100.0	.32330	
	Mean	1.0077 ± 0.0001
Reaction of *p*-nitrobenzyl chloride with potassium cyanide at 50°		
5.608	0.32145	1.0059
8.318	.32152	1.0058
14.655	.32158	1.0058
100.0	.32330	
	Mean	1.0058 ± 0.00003
Hydrolysis of *p*-nitrobenzyl chloride at 90°		
4.599	0.32080	1.0080
8.447	.32086	1.0080
12.290	.32086	1.0081
100.0	.32330	
	Mean	1.0080 ± 0.00003

Discussion

It is seen from Tables II and III that in all cases where the first-order plots are linear, the chlorine isotope effect (k^{35}/k^{37}) is close to 1.0078, while for those reactions where the second-order plots are linear, the value is 1.0058. Reactions showing borderline kinetic behavior have isotope effect values intermediate between these two extremes. Thus, it is seen that there is a very clear relationship between chlorine isotope effect and kinetic behavior. For a given nucleophile (*i.e.*, cyanide ion or thiosulfate ion), the reaction is shifted from first-order kinetics and a maximum isotope effect to second-order kinetics and a minimum isotope effect by changing the *p*-substituent from powerful electron donor groups to those with increasing electron-withdrawing power. For a particular one of the three compounds, *p*-methyl, *p*-chloro and unsubstituted benzyl chloride, the kinetics may be shifted toward second order by increasing the nucleophilicity of the displacing group, the isotope effect being decreased accordingly. It is, therefore, concluded that the relative magnitudes of these effects may be used empirically as a mechanistic criterion.

The direction of the observed trend in isotope effects is in line with the theoretical calculations on the temperature independent factor mentioned in the Introduction. That is, the more the participation by the incoming nucleophile in the displacement reaction, the smaller the isotope effect. However, the variation from the kinetically first-order reactions to the kinetically second-order reactions is much smaller than that predicted on the basis of our calculations using the three-center equation of Bigeleisen and Wolfsberg.[7]

The experiments at higher temperatures summarized in Fig. 7 and Tables II and IV were done in an attempt to determine whether these chlorine isotope effects are strongly temperature dependent. It is evident by comparison of the values in Tables III and IV that there is no temperature dependence of these chlorine isotope effects within the error limits of the measurements. However, the temperature range was not very great, and unless the temperature dependent factor makes up a large fraction of the total isotope effect, it would be undetectable by these experiments.

Although there seems to be little hope of making exact isotope effect calculations for systems as complicated as this, some effort in this direction was made. Most models tried, using Bigeleisen's equations,[6,7] gave theoretical values of the isotope effect which were much higher than experiment. Some encouragement may be taken from the fact that our most complicated model, a bent XYZ molecule for the reactant (similar to ethyl chloride[23]) and a T-shaped molecule for the activated complex, gave results (1.0089 for ideal SN1 to 1.0033 for ideal SN2) which bracketed the experimental results (1.0078 for first order to 1.0058 for second order). However, in this case the temperature-independent factor was calculated using atomic fragment masses in calculating frequency shifts. In all cases, the calculated variation between ideal SN1 and ideal SN2 was much greater than the observed range of isotope effects, and we are not optimistic about getting better agreement by an improvement in models. However, this should not impair the usefulness of the chlorine isotope effect as a mechanistic criterion, since the empirical and qualitative theoretical correlations stand.

On the basis of the isotope effect data, it appears that the hydrolysis reactions are all proceeding by way of very similar transition states, and that the mechanism is very close to ideal SN1. The vastly different rates (see Table II) are attributed to the different abilities of the substituent group to disperse the developing positive charge on the methylene carbon. The possible involvement of water in the rate-determining transition state is insignificant in comparison to the electronic effect of the substituent group. Even for *p*-nitrobenzyl chloride, where participation by water might be expected to be greatest, no rate enhancement or isotope effect lowering is noted. However, a Hammett plot,[24] Fig. 8, of the data (using σ^{+}[25]

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[23] P. C. Cross and J. H. Van Vleck, *J. Chem. Phys.*, **1**, 350 (1933).

[24] L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, Chap. 7.

[25] H. C. Brown and Y. Okamoto, *J. Am. Chem. Soc.*, **79**, 1913 (1957).

since the developing positive charge can interact directly with the ring and substituent) has a pronounced concave upward curvature. This type of behavior has been noted before for benzyl derivative sand has been interpreted in terms of increasing nucleophilic participation in the displacement as the electron-donating power of the substituent decreases.[26] Any such change in mechanism would be expected to show up in a lowered isotope effect, but that this criterion is not extremely sensitive can be seen from the kinetic data for the reactions of *p*-methoxy- and *p*-methylbenzyl chlorides with cyanide ions and of *p*-methoxybenzyl chloride with thiosulfate ions. The first-order plots for these three reactions are all more nearly linear than the second-order plots. Nevertheless, borderline kinetic behavior might well be implied in all these cases by the enhanced rates compared to hydrolysis. Alternatively, the rate enhancement in the case of *p*-methoxybenzyl chloride in the presence of potassium cyanide (a factor of 1.66) or sodium thiosulfate (a factor of 2.12) might be due to a salt effect or to repression of the original ionization step due to the favorable competition for the organic cation of cyanide and thiosulfate ions compared to chloride ions. These factors would also be expected to contribute to a rate enhancement in the case of *p*-methylbenzyl chloride in the presence of potassium cyanide. However, it does not seem likely that these factors would cause a greater rate increase here than in the case of the *p*-methoxy compound. The greater rate enhancement, then (a factor of 16.7), is probably due to weak bonding at the transition state between the benzyl carbon and the cyanide ion. This would probably show up in a curvature of the first-order plot at higher fractions of reaction. The sensitivity of the isotope effect measurements at the present precision, at least, is not sufficient to detect this borderline behavior.

From examination of the pseudo-first-order rate constants (values in parentheses in Table II) for the reactions proceeding by mixed and second-order kinetics, it is clear that the incoming nucleophile is strongly affecting the rate. The increased rates in going from benzyl to *p*-nitrobenzyl chloride in the reactions with cyanide and thiosulfate ions must be due to the increasing amount of bond formation, and hence stabilization by the greater electron-withdrawing ability of the substituent. The Hammett plot of these data (Fig. 8) shows a very pronounced minimum near the unsubstituted compound. When coupled with the hydrolysis data, this kinetic behavior can be attributed to a change in mechanism from near ideal SN1 (no participation by nucleophiles other than solvating water) for *p*-methoxybenzyl chloride to near ideal SN2 (concerted, equal bond formation and bond rupture) for *p*-nitrobenzyl chloride.

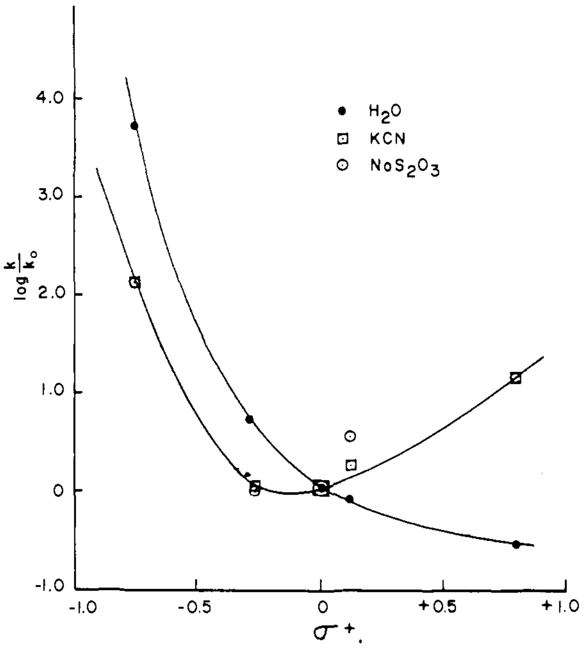

Fig. 8.—Hammett plot of initial first-order rate constants for reactions with water, potassium cyanide and sodium thiosulfate of benzyl and substituted benzyl chlorides in 80% aqueous dioxane at 30°.

This is the same conclusion arrived at by consideration of the isotope effect data, and it is thus clear that the kinetic isotope effect can be a valuable tool in mechanism studies. Further experiments are under way to see if this correlation of mechanism and chlorine isotope effect holds for purely aliphatic compounds.

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[26] For references to other examples and an excellent discussion of this matter, see C. G. Swain and W. P. Langsdorf, Jr., *J. Am. Chem. Soc.*, **73**, 2813 (1951).