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S_N2 Reactions in Dipolar Aprotic Solvents. VII. Kinetic and Equilibrium Secondary α-Deuterium Isotope Effects in Chlorine Isotopic Exchange Reactions of Substituted Chloromethanes in Acetonitrile[1]

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Secondary α-deuterium isotope effects were studied in the symmetrical nucleophilic substitution of the substituted chloromethanes in acetonitrile. The apparent second order rate coefficients show a significant isotope effect for chloromethyl aryl ethers and sulfides (1.11—1.14 per D), and an intermediate value of 1.05 for cinnamyl chlorides. 2-Arylethyl chlorides were shown to give an appreciable isotope effect of 1.03—1.04, and arylchloromethanes to give varying amount of the isotope effect from 1.006 to 1.050 depending upon the ring substituent. The deuterium label also gave rise to a significant equilibrium isotope effect on the substrate-nucleophile association in the reaction mixture. The observation of an equilibrium isotope effect suggested a possibility that an apparent isotope effect was a composite of the thermodynamic and the kinetic isotope effects. Thus the dissection resulted in a uniform and a fairly large kinetic isotope effect for all the activated substrates studied and in a small kinetic isotope effect for 2-arylethyl chloride. The results are explained in a framework of loose–tight transition state.

In the studies of the Hammett type analysis of the Finkelstein reaction in a dipolar aprotic solvent acetonitrile, the present authors proposed the rate accelerating effect by the conjugative stabilization of the S_N2 transition state.[3]

When a hetero atom[3a] or an unsaturated linkage[3b,c] adjacent to the reaction center is available, the conjugative stabilization may be operative, superposing upon the nucleophilic approach of the attacking nucleophile, in the displacement reaction that proceeds through a loose transition state. The looseness or the tightness of the transition state has often been postulated. A successful example is found in the study of the solvent effect on the rate of the bimolecular reactions.[4]

Another approach to verify such a spectrum of the transition state may be tenable by the study of the secondary hydrogen isotope effect. The method, which was awarded with success, has mainly applied to the unimolecular solvolytic reactions.[5]

Formerly, the rate ratio k_2^H/k_2^D of unity has been believed to be a criterion of the S_N2 reaction and the secondary isotope effect has been considered not existent in this class of reactions.[6] Recent works show that the isotope effect is observable in some examples of the S_N2 reactions, and that the typical observed value is in the range of 0.95—1.06 per one α-deuterium atom.[7,8] However, the study with a systematic variation in the substrate reactivity was scarcely undertaken in the study of bimolecular substitutions.

In the present work, the substituted chloromethanes with the deuterium label at the reacting carbon were subjected to the chlorine-chlorine isotopic exchange reaction. The deuterium label also affected substrate-nucleophile interaction which accompanied with the symmetrical exchange reaction.[9] The kinetic deuterium isotope effect was discussed in relation to the reactivity of these model compounds and in relation to the potential role of the substrate-nucleophile association complex.

Results and Discussion

Substituted chloromethanes which have a variety of substituents adjacent to the reaction center were subjected to the chlorine isotopic exchange reaction in dry acetonitrile as shown in Scheme 1.

$$\text{X-C}_6\text{H}_4\text{-Y-CZ}_2\text{Cl} + \text{Et}_4\text{N*Cl} \rightleftharpoons \text{X-C}_6\text{H}_4\text{-Y-CZ}_2\text{*Cl} + \text{Et}_4\text{NCl}$$

X; H and other substituent
Y; O, S, CH^t=CH, none(benzyl), and CH_2
Z; H and D

Scheme 1.

The incorporation of the radioactive chlorine from the reagent tetraethylammonium chloride-^{36}Cl followed first-order kinetics and the plausible second-order rate coefficients were obtained as reported earlier.[3] This result definitely shows that the rate determining transition state should involve both the organic chloride and the nucleophile, chloride ion.

The results of the exchange reactions with the deuterated substrates as well as that with the unlabeled substrates are given in Table 1. As shown in Table 1, normal isotope effect was observed in every case. The magnitude of the effect was about 11—14% for chloromethyl aryl ethers and chloromethyl aryl sulfides. 2-Arylethyl chlorides gave about 3—4% of the effect while arylchloromethanes gave diverse normal effect of 0.6—5.0%. Cinnamyl chloride gave an intermediate value of 5%.

The constancy of the secondary deuterium isotope effect for chloromethyl aryl sulfides is excellent and possibly indicates an operation of a single mechanism for all these sulfides as are also indicated by the establishment of the good linear free energy relationship for exchange reactions.[3a,10]

The equilibrium constants for the formation of substrate-nucleophile complex were determined with deuterated substrates, as well as with unlabeled substrates. The formation of such a complex in the Finkelstein reaction mixture was already reported.[9] Equilibrium deuterium isotope effects were observed for the representative substrates and the results are shown in Table 2. Except for 2-(*p*-nitrophenyl)ethyl chloride, which shows essentially the absence of equilibrium

TABLE 1. RATE CONSTANTS AND ISOTOPE EFFECTS OF CHLORINE ISOTOPIC EXCHANGE REACTIONS OF SUBSTITUTED CHLOROMETHANES [$X-C_6H_4-Y-CZ_2Cl$]

Y	X	$\frac{t}{°C}$	$\frac{k_{obsd}{}^{a)}}{l/mol \cdot min} \times 10^2$ Z;H	Z;D	k_H/k_D b)
O	p-Cl	−20	20.0	16.2 c)	1.112
	m-Cl		11.6	9.46 c)	1.108
S	p-OCH_3	20	6.49	5.27	1.120
	H		3.10	2.44	1.128
	p-Cl		1.99	1.57	1.124
	m-Cl		1.60	1.23	1.141
	p-NO_2		0.652	0.519	1.121
CH=CH	H	20	2.54	2.30	1.050
None	p-OCH_3	20	4.52	4.13	1.046
	p-CH_3		1.83	1.66	1.050
	m-CH_3		1.25	1.23	1.006
	H		1.23	1.17	1.026
	p-Cl		1.81	1.72	1.025
	m-NO_2		2.46	2.38	1.017
	p-NO_2		3.47	3.28	1.028
CH_2	H	60	0.523	0.489	1.035
	p-Cl		0.889	0.836	1.031
	p-NO_2		1.92	1.78	1.039

a) [Substrate] = [*Cl^-] = 0.10 M. b) Per one D atom. c) 98% isotopic purity.

TABLE 2. EQUILIBRIUM CONSTANTS AND ISOTOPE EFFECTS OF THE FORMATION OF COMPLEX [$X-C_6H_4-Y-CZ_2Cl$]

Y	X	$\frac{t}{°C}$	$\frac{K_{Z;H}{}^{a)}}{M^{-1}}$	$\frac{K_{Z;D}{}^{a)}}{M^{-1}}$	K_H/K_D b)
S	p-NO_2	30.0	0.348	0.365	0.976
CH=CH d)	H	30.0	0.0964	0.104 c)	0.928
None	p-NO_2	19.7	0.365	0.400 c)	0.913
		27.2	0.303	0.322 c)	0.913
		31.0	0.277	0.308 c)	0.901
		32.7	0.266	0.322	0.909
CH_2 e)	p-NO_2	20.0	0.202	0.199	1.007

a) Errors estimated to be within 2% or better. b) Per one D atom. c) For $X-C_6H_4-Y-CHDCl$. d) At 30 °C, $\rho_K = 0.40 \pm 0.1$. For p-$NO_2-C_6H_4-CH=CH-CH_2Cl$, at 20 °C, $\Delta H° = (-1.52 \pm 0.5)$ kcal/mol, $\Delta S° = (-8.2 \pm 2)$ eu. e) At 30°C, $\rho_K = 0.65 \pm 0.1$. For p-$NO_2-C_6H_4-CH_2CH_2Cl$, at 20 °C, $\Delta H° = (-1.22 \pm 0.5)$ kcal/mol, $\Delta S° = (-7.3 \pm 2)$eu.

isotope effect, chloromethyl p-nitrophenyl sulfide, cinnamyl chloride, and (p-nitrophenyl)chloromethane all show an inverse equilibrium isotope effect. The observation of the inverse equilibrium isotope effect is not unexpected.[11]

The data of substrate-nucleophile association allow one to calculate the intrinsic second order rate coefficient corrected for the change of the concentration of both the substrate and the reagent upon complex formation (*vide infra*). In Table 3, the corrected isotope effects are summarized for the representative classes of the compounds. Table 3 also contains the results of the Hammett type analyses of the corresponding unlabeled substrates.

TABLE 3. SUMMARY OF THE α-SUBSTITUENT EFFECTS AND THE KINETIC ISOTOPE EFFECTS [$X-C_6H_4-Y-CZ_2Cl$]

Y	Rel rate a)	ρ (σ, r) b)	k_2^H/k_2^D c) (X)	$\frac{t}{°C}$
O	400000	−1.56(σ, 0.997)	1.112 d) (p-Cl)	−20
S	1020	−0.92(σ, 0.997)	1.119(p-NO_2)	20
CH=CH	680	−0.19 e) (σ, 0.962)	1.048(H)	20
None	330	— —	1.024(p-NO_2)	20
CH_2	1	0.57($\sigma°$, 0.991)	1.039(p-NO_2)	60

a) Ref. 3b. X; H, at 20 °C. b) Ref. 3. c) k_{obsd} was corrected for the formation of substrate-nucleophile complex. d) Uncorrected value. e) Obtained for m-substituted compounds.

The inspection of the results in Table 3 is quite intuitive. The spectrum of the secondary deuterium isotope effect obtained in the present study seems to have a parallelism to the degree of the electron-donating conjugative stabilization of the transition state. As suggested from the Hammett type analysis, and from the relative rate of the substituted chloromethanes studied, such a stabilization is most prevailing in the ethers ($\rho = -1.56$, $k_{rel} = 400000$) and in sulfides ($\rho = -0.92$, $k_{rel} = 1020$), less effective but still significant in cinnamyl chlorides ($\rho^m = -0.19$, $k_{rel} = 680$), and is apparently not operating in 2-arylethyl chlorides ($\rho = +0.57$, $k_{rel} = 1$).

The difficulty is encountered for arylchloromethanes. The observed isotope effects in the Table 1 seem too small for these activated Finkelstein substrates. This is also the case with cinnamyl chlorides (*cf.* Table 3).

The behavior of the arylchloromethanes is often a matter of controversy.[12] The significant change from tight transition state (p-NO_2) into loose transition state (p-OCH_3 or p-CH_3) was suggested by the studies of the substituent effect upon the rate of the Finkelstein reaction[3b] and upon the solvent activity coefficient of the reaction.[4]

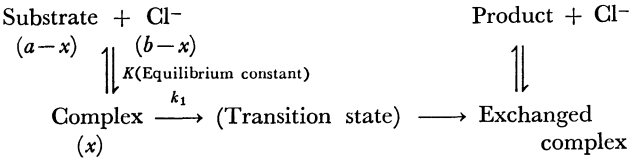
Table 1 shows the small and varying extent of the isotope effect. Thus (p-nitrophenyl)chloromethane, the transition state of which is considered to be tighter than that of (m-methyl- or unsubstituted phenyl)chloromethane, gives an appreciable isotope effect of about 3%. While (m-methylphenyl)chloromethane shows the isotope effect close to unity and phenylchloromethane shows a fair isotope effect of 2.6% contrary to the expectation from the looseness-tightness approach (*cf.* Table 1).

These findings seem to suggest that the (overall) isotope effect should tell something that is different from the implication of the rate studies.

A clue to answer this difficulty is found in an observation of an association complex in the Finkelstein reaction. The present authors have reported the presence of the substrate-reagent complex which possesses a structure quite similar to the traditional S_N2 transition state.[9] There are indications that the nucleophilic anion coordinates at the rear side of the potential leaving group resulting in the freezing of the intramolecular rotation, which is the necessary condition for the operation of an electron-donating p-π and(or) p-p

interaction by the neighboring functionality.

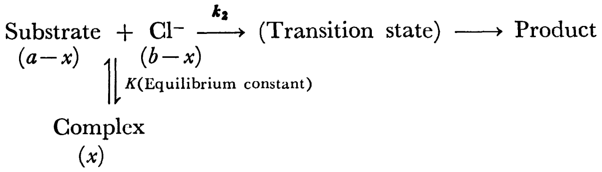
Such a complex can play one of the two quite distinct roles in the bimolecular reaction. One is the direct precursor that intervenes before the rate determining unimolecular scrambling (Scheme 2).



$$\text{Rate}=k_1K(a-x)(b-x)$$

Scheme 2.

The other is the indifferent entity in the subsidiary or parasitic equilibrium with the free substrate and the free nucleophile (Scheme 3).



$$\text{Rate}=k_2(a-x)(b-x)$$

Scheme 3.

The equilibrium isotope effect in Table 2 seems to support the operation of the association mechanism (Scheme 2), giving the more comprehensive picture of the observed kinetic isotope effect. When one postulates an operation of the mechanism in Scheme 2, the observed second order rate coefficient k_2 can be separated into the equilibrium constant K for the substrate-nucleophile association, and the rate constant k_1 for the unimolecular scrambling, as is shown in Eq. 1.

$$k_2 = k_1 \cdot K \tag{1}$$

Accordingly the kinetic isotope effect observed can be dissected into the equilibrium isotope effect of bimolecular association(K_H/K_D) and the kinetic isotope effect of unimolecular scrambling (k_1^H/k_1^D, Eq. 2).

$$k_2^H/k_2^D = k_1^H/k_1^D \cdot K_H/K_D \tag{2}$$

Combining the data from Table 1 and Table 2, the kinetic isotope effect k_1^H/k_1^D can be calculated postulating the intervention of the substrate-nucleophile complex. Results are shown in Table 4.

For the activated substrates, reflecting the inverse equilibrium isotope effects, the kinetic isotope effects calculated (that correspond to the rate determining unimolecular scrambling of the complex) are now close to that of the limiting solvolysis.[13] For 2-(*p*-nitrophenyl)ethyl chloride, the equilibrium isotope effect of about unity substantiates the figure of the isotope effect observed (k_2^H/k_2^D) is essentially intrinsic.

Thus the explanation in the framework of the looseness of the transition state seems to hold for the whole classes of the compounds studied. In a significantly loose transition state, the carbon under attack has essentially little difference from the carbonium ion having negligible nucleophilic attachment to both the leaving and the incoming group (chloride ion).[14] Thus 15.7% might be the limiting value for the secondary deuterium isotope effect in S_N2 reactions as it is the case with the unimolecular limiting solvolysis of organic chlorides.[15]

Table 4. Dissection of the isotope effect [$X-C_6H_4-Y-CZ_2Cl$]

Y	X	k_2^H/k_2^D a)	K_H/K_D a)	k_1^H/k_1^D a)
S	*p*-NO_2	1.119	0.976	1.147
CH=CH	H	1.048	0.928	1.129
None	*p*-NO_2	1.024	0.909	1.127
CH_2	*p*-NO_2	1.039	1.007	1.032

a) Per one D atom. There are some differences between the temperature for the kinetic measurement and that for the equilibrium measurement. However, the change of temperature in the range studied gave negligiblly small effect upon the equilibrium isotope effect, and an example is shown in Table 2 for (*p*-nitrophenyl)-chloromethane.

The S_N1 like behavior of the chloromethyl aryl ether was suggested in the nucleophilic displacement reaction of chloromethyl methyl ether.[16]

In the loose transition state, the change of the out-of-plane bending motion, caused by the bond breaking, may hardly be compensated by the bond formation with the incoming nucleophile.

The largest kinetic isotope effect observed in the present study, for chloromethyl aryl sulfides and ethers, is still smaller than the limiting value of S_N1 reactions. This is the indication of a nucleophilic interaction in the transition state.[7] The magnitude of the isotope effect seems to be smaller as the transition state becomes tighter. 2-(*p*-Nitrophenyl)ethyl chloride shows a small kinetic isotope effect which seems to be compatible with the implication from ρ_{k_1} (and with ρ_{k_2}).[17]

The nature of the unimolecular scrambling of the complex suggests that the nucleophile assists the expulsion of the leaving group. A quite similar suggestion was made by Schleyer as "nucleophilically assisted ion pair formation."[18]

Another explanation in a framework of traditional nucleophilic substitution may be pursued. The operation of an S_N2–C^+ or of the rate determining nucleophilic attack upon an ion pair may be one of the possibilities. The absence of a very high ρ value in the Hammett relationship[17] and the absence of k_Δ process[19] in the case of 2-arylethyl chlorides (and probably cinnamyl chloride) are the evidences against the classical S_N2–C^+ route.[3a]

As long as an S_N2–C^+ or an ion pair mechanism is operative, one should postulate a spontaneous ionization of the substrate.[20] Bearing in mind the existence of the substrate-nucleophile complex in the Finkelstein reaction mixture studied, and the feature of the complex which shows interesting similarities to the traditional S_N2 transition state, one can hardly imagine a spontaneous ionization without help of the nucleophile that locates at the rear side of the potential leaving group. The absence of the inert salt effect is also against the operation of S_N2–C^+ and(or) ion pair intervention.[3a] In addition, the classical explanation necessitates a significant attachment of the nucleophile for arylchloromethanes or cinnamyl chlorides, one of the classes of the activated substrates.

TABLE 5. PROTIC-APROTIC SOLVENT EFFECTS ON THE RATE OF THE CHLORINE EXCHANGE AND THE FORMATION OF COMPLEX IN ACETONITRILE [p-NO_2-C_6H_4-$CH_2Cl + Et_4N^*Cl$]

$\frac{[\text{MeOH}]}{\text{M}}$	$\frac{k_{\text{obsd}}\ ^{a)}}{\text{l/mol min}} \times 10^2$	$\frac{K\ ^{b)}}{\text{M}^{-1}}$
0	10.8	0.287
0.0493	8.16	0·242
0.0985	6.90	0.219
0.197	4.55	0.181
0.296	3.27	0.138
0.493	1.90	0.110

a) At 30 °C. Errors estimated to be within 1.5%.
b) At 30 °C. Errors estimated to be within 0.005.

TABLE 6. PHYSICAL CONSTANTS OF SUBSTITUTED CHLOROMETHANES [X-C_6H_4-Y-CZ_2Cl]

Y	X	$\frac{\text{Bp}}{\text{°C/mmHg}}\left(\frac{\text{Mp}}{\text{°C}}\right)$	
		Z; D	Z; H$^{a)}$
O	p-Cl	74.0—74.5/3.5	87.0—88.0/6
	m-Cl	71.0—71.5/3.5	82.0—83.0/6
S	p-OCH_3	109.0—109.5/1.0	105.0/0.7
	H	117.5—118.0/24	115.5—116.0/20
	p-Cl	98.0—99.0/1.0	109—111/4
	m-Cl	94.0/0.6	94.5/0.7
	p-NO_2	(62.5—63.0)	(63.5—64.0)
CH=CH	H	76.0/3 65.0/0.7$^{b)}$	116—118/16
None	p-OCH_3	82.0—82.5/3	70.5/0.5
	p-CH_3	99.5/30	88.5/17
	m-CH_3	97.0/26 45.5/0.8$^{b)}$	56.5—57.0/2.5
	H	77.5—78.0/26	76.8—77.0/24.5
	p-Cl	110.5—111.5/28	108.5/28
	m-NO_2	(45.0)	(45.0)
	p-NO_2	(72.0—72.5) (73.0)$^{b)}$	(72.5—73.0)
CH_2	H	93.0—94.0/26	86.0/18
	p-Cl	128.5—129.0/27	84.0/4
	p-NO_2	(48.8)	(49.0)

a) Ref. 3. b) X-C_6H_4-Y-CHDCl.

Thus the postulation of the substrate-nucleophile complex as the "intermediate" of the Finkelstein reaction opens up the new possibility to have a unified view of the behavior of the variety of the substrate. There is hardly available a good means to examine the possible equilibrium isotope effects of the substrate-nucleophile association in a protic medium. At present it is an open question if the present postulation can become a general proposal.

The preliminary result of the protic-aprotic solvent effect is also compatible with the association mechanism. Successive additions of the small amount of methanol to solvent acetonitrile give rise to the decrease in the equilibrium constant of the complex formation as well as the decrease in the rate of symmetrical exchange reactions (Table 5). However the decrease of the second order rate coefficient is much more profound than that of the equilibrium constant. According to the association mechanism (Scheme 2), the nucleophilic displacement reaction in the presence of methanol added should contain "deactivated anionic nucleophile"[4] both at the preliminary association and at the unimolecular scrambling, thus the overall rate should be doubly affected by the deactivation of the anionic nucleophile, as is envisaged by Eq. 1.

Experimental

Instruments. The radioactivity was measured with a Nuclear Chicago Model-6801 liquid scintillation counter. The PMR spectra were obtained on a JEOL JNM-PS-100 NMR spectrometer equipped with a Hetero Spin Decoupler JNM-SD-HC 1. The melting points were measured with a Yanagimoto Micro Melting Point Apparatus and were uncorrected.

Materials. Aryloxymethane-α,α-d_2-sulfonates were obtained as follows. Sodium p-chlorophenoxymethanesulfonate(8g) was dissolved in 10 ml of 1M-NaOD/D_2O (99.75% isotopic purity). The mixture was maintained at about 100 °C in a Teflon tube for four days. After cooling the solution was acidified with 1M-HCl and evaporated. The residue was subjected to the exchange once again according to the above procedure. Recrystallization from aqueous ethanol gave pure p-chlorophenoxymethane-α,α-d_2-sulfonate. The sulfonate was converted to p-chlorophenyl chloromethyl-d_2 ether with phosphorous pentachloride.[21]

Methyl-d_3 aryl sulfides were prepared from the corresponding thiophenols and CD_3I (99% isotopic purity) in ethanol in the presence of KOH. Chlorination of these sulfides with sulfuryl chloride gave chloromethyl-d_2 aryl sulfides.

(p-Nitro- and m-nitrophenyl)methan-α,α-d_2-ols were prepared from the corresponding methyl nitrobenzoates by mixed hydride reduction.[22] $LiAlD_4$(Merck, 99% isotopic purity, 0.75 g) was stirred in 40 ml of ether. To the solution anhydrous $AlCl_3$(2.5 g) in 40 ml of ether was added dropwise, and the solution was stirred for another few minutes. The methyl p-nitrobenzoate (3.2 g) in 20 ml of ether was added slowly. After stirring for an hour under reflux, the mixture was worked up as usual. The alcohols were purified by recrystallization or distillation after chromatographic purification on alumina.

(p-Nitrophenyl)methan-α-d-ol was prepared from p-nitrobenzaldehyde by mixed hydride reduction. (m-Methylphenyl)methan-α-d-ol was prepared from m-methylbenzaldehyde with $LiAlD_4$ as usual. Other arylmethan-α,α-d_2-ols were prepared from the corresponding methyl benzoates with $LiAlD_4$. Arylchloromethanes-α-d, and -α,α-d_2 were prepared from these alcohols by standard method.[23]

Cinnamyl-1,1-d_2 and cinnamyl-1-d derivatives were obtained by mixed hydride reduction from ethyl cinnamate and cinnamaldehyde, respectively.[24] Cinnamyl chlorides were proved to be trans isomers by PMR spectra and physical constants.

2-(p-Nitrophenyl)ethan-1,1-d_2-ol was prepared from ethyl (p-nitrophenyl)acetate by mixed hydride reduction. Other 2-arylethan-1,1-d_2-ols were obtained from the corresponding ethyl arylacetates by the reaction with $LiAlD_4$ as usual. The alcohols were subjected to the reaction with thionyl chloride which gave 2-arylethyl-1,1-d_2 chlorides.

After purification all these chlorides showed satisfactory NMR and IR spectra. Physical constants are listed in Table 6.

Kinetic Measurements. Batch method was undertaken as reported previously.[3a,b] In order to ensure the accuracy of the isotope effect measurement, the parallel reaction was always run with unlabeled compounds simultaniously in the same bath. The reproducibility of the isotope effect was within 0.01 for duplicate runs, though the difference in rate constants was within the range of 1.5% for independent series of measurements.

Equilibrium Measurements. Proton chemical shift measurements were undertaken as reported previously.[9] The shifts of α-proton of (*p*-nitrophenyl)chloromethane-α-*d*, (*m*-methylphenyl)chloromethane-α-*d*, and cinnamyl-α-*d* chloride were measured under the irradiation of D-frequences at 23000 G (15.349404, 15.349408, and 15.349589 MHz, respectively), noise-modulation was applied when necessary (white noise band width; 50 Hz).[25]

Some troubles are encountered in the preparation of chloromethyl-*d* *p*-nitrophenyl sulfide and of 2-(*p*-nitrophenyl)ethyl-1-*d* chloride. Accordingly α,α-d_2 labeled substrates were utilized to measure the equilibrium isotope effect observing the chemical shift of ortho hydrogens on the phenyl ring. The control experiment with (*p*-nitrophenyl)chloromethane-α-*d*, and -α,α-d_2 resulted essentially the identical equilibrium isotope effect. In the case of 2-(*p*-nitrophenyl)ethyl chloride two independent analyses from α- and *o*-proton(s) gave rise to the identical association constant.

Scott-Benesi-Hildebrand analyses for cinnamyl chlorides and 2-arylethyl chlorides were difficult because of their small low field shifts at the chloride concentrations studied.[26] However, the repeated measurements of the line position (up to 30 times and to the reproducibility of ±0.05 Hz or better) gave a reliable association constant.

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13) Beside *p*-nitrophenyl derivatives, the substrates give only a small low field shift upon complexing, thus one is not allowed to determine equilibrium isotope effect accurately. However, after repeated measurements, (*m*-methylphenyl)chloromethane gave K_H/K_D of about 0.91 (with fair error of ±5%). Dissection of k_2^H/k_2^D suggests a loose transition state for this arylchloromethane.

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17) As a corollary, the ρ_{k_2} obtained can be split into ρ_K and ρ_{k_1}, provided the linear free energy relationships hold for both K and k_2.

$$\log(k_2/k_2^\circ) = \log(Kk_1/K^\circ k_1^\circ) = \log(K/K^\circ) + \log(k_1/k_1^\circ)$$
$$= \rho_K\sigma + \rho_{k_1}\sigma = (\rho_K + \rho_{k_1})\sigma = \rho_{k_2}\sigma$$

For 2-arylethyl chlorides; $\rho_K=0.65$, $\rho_{k_2}=0.57$, $\therefore \rho_{k_1}=0.57-0.65=-0.08$. For chloromethyl aryl sulfides; $\rho_K=0.59$, $\rho_{k_2}=-0.92$, $\therefore \rho_{k_1}=-0.92-0.59=-1.51$. The value of ρ_K for the equilibrium of the complex formation between modified methyl chlorides and chloride ion was found essentially constant.[9] Using the average value of $\rho_K=0.57$, for chloromethyl aryl ethers; $\rho_{k_2}=-1.56$, $\therefore \rho_{k_1}=-1.56-0.57=-2.13$.

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20) Acetonitrile with the very low nucleophilicity and with a dielectric constant of about 30 seems not to be a good ionizing solvent. There is a report that the dissociation of 1,1-dimethyl-2-methylsulfonylhydrazine is quite facile in water but essentially absent in acetonitrile. *Cf.* D. M. Lemal, C. D. Underbrink, and T. W. Rave, *Tetrahedron Lett.*, **1964**, 1955.

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25) The line position of the proton in question did not change with or without the irradiation for heteronuclear decoupling. (*p*-Nitrophenyl)chloromethane-α-d_1 gave rise to a beautiful 1 : 1 : 1 triplet on ^1H spectra, which, on heteronuclear decoupling, coalesced to a sharp singlet centering at the center of the triplet mentioned above. The successful heteronuclear decoupling was experienced in every case.

26) The low field shift of α-proton at the concentration, [substrate]=0.1 M, [Et_4NCl]=1.0 M, at 30 °C, was 0.079 ppm for cinnamyl chloride, 0.085 ppm for 2-(*p*-nitrophenyl)ethyl chloride, whereas 0.398 ppm for chloromethyl *p*-nitrophenyl sulfide, 0.199 ppm for (*p*-nitrophenyl)chloromethane.