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S_N2 Reactions in Dipolar Aprotic Solvents. VIII.[1] Chlorine Isotopic Exchange Reaction of (Arylsulfonyl)chloromethanes, (Arylsulfinyl)chloromethanes, and 2-Chloro-1-arylethanones in Acetonitrile. A Role of the Nucleophile-substrate Interaction in the Finkelstein Reaction

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Chlorine isotopic exchange reactions of substituted chloromethanes [(arylsulfonyl)chloromethanes (**1**), (arylsulfinyl)chloromethanes (**2**), and 2-chloro-1-arylethanones (**4**)] with tetraethylammonium chloride-^{36}Cl were studied in acetonitrile. This study enabled, for the first time, the accurate rate study of the former two classes of compounds (**1** and **2**) of extremely low reactivity. Both the large enthalpies of activation and the positive entropies of activation were the characteristics for these two substrates (**1**-p-NO_2 and **2**-p-NO_2). High reactivity of 2-chloro-1-phenylethanone was substantiated, and was not associated with the significant secondary kinetic deuterium isotope effect. A nucleophile-substrate association that proceeds the reaction was suggested and the possible role of such an interaction was examined in the light of the intermediary of the nucleophile-substrate complex in the Finkelstein reaction.

The present authors have been investigating the symmetrical Finkelstein reaction between the substituted chloromethanes and radioactive chloride ion in dipolar aprotic solvent.[3] Through the Hammett type analysis of the reaction rates, two factors were pointed out to govern the reactivity of this reaction system: One is the approach of the nucleophile to the substrate, and the other is the electron-donating stabilization of the incipient electro-positive reaction center at the transition state. These findings were accomodated in the framework of the traditional S_N2 reactions.[4]

However, in a recent work, the authors confirmed the presence of an 1 : 1 complex between the substrate and the anionic nucleophile in the Finkelstein reaction mixture. This complex shows many characteristics of the approach of a nucleophile in the S_N2 reactions.[5]

In a separate study, secondary kinetic deuterium isotope effect at the α-hydrogen of the S_N2 reaction center was substantiated for S_N2 substrates of high reactivity.[6] Inverse equilibrium deuterium isotope effects were also found for the substrate-nucleophile association, suggesting that the secondarty isotope effects are explained in terms of the intervention of the complex as the direct precursor of the Finkelstein reaction and in terms of the operation of the electron-donating conjugation at the loose transition state of the unimolecualr scrambling of the complex.[7]

In the present work, chlorine isotopic exchange reactions of (arylsulfonyl)chloromethanes (**1**), (arylsulfinyl)chloromethanes (**2**), and 2-chloro-1-arylethanones (**4**) with tetraethylammonium chloride-^{36}Cl were studied in acetonitrile to get an insight of the rate-controlling factors of the S_N2 reactions.

Results and Discussion

In dry acetonitrile as the solvent, substituted chloromethanes were treated with tetraethylammonium chloride-^{36}Cl as are shown in Scheme 1.

Good second-order kinetics was followed for this isotopic exchange reaction in the every instance. Good linear free energy relationships held for Hammett σ in each classes of substrates, giving positive ρ values. The accurate rate study for the substrates of diminished reactivity, (arylsulfonyl) and (arylsulfinyl)chloromethanes (**1** and **2**) was achieved for the first time.[8] Results are shown in Table 1.

$$\text{X-C}_6\text{H}_4\text{-Y-CH}_2\text{Cl} + (\text{C}_2\text{H}_5)_4\text{N}\ {}^*\text{Cl} \rightleftharpoons \text{X-C}_6\text{H}_4\text{-Y-CH}_2{}^*\text{Cl} + (\text{C}_2\text{H}_5)_4\text{NCl}$$

X: a) p-NO_2, b) p-Cl, c) H, d) p-CH_3, e) p-CH_3O.
Y: a) SO_2 (**1**), b) SO (**2**), c) CO (**4**).

Scheme 1.

In Table 2, the second-order rate constants for the substituted chloromethanes with unsubstituted phenyl ring are collected to show the effect of the functional group adjacent to the S_N2 reaction center. Substituent effects on the phenyl moiety are also shown by the Hammett ρσ relationship.

As is shown in Table 2, reactivity spreads in wide range (10^{10}) between the most reactive compound [(phenoxy)chloromethane] and the least reactive one [(phenylsulfonyl)chloromethane]. In 2-chloro-1-arylethanones (**4**), which are about 10^9 times as reactive

Table 1. Observed second-order rate coefficients of symmetrical Finkelstein reactions
$\text{X-C}_6\text{H}_4\text{-Y-CH}_2\text{Cl} + (\text{C}_2\text{H}_5)_4\text{N}^{36}\text{Cl}$

X	$\frac{k_{\text{obsd}}}{\text{M}^{-1}\,\text{min}^{-1}}$ Y; SO_2[a)]	Y; SO[b)]	Y; CO[c)]
p-NO_2	4.30	5.15	10.4
p-Cl	1.78	1.86	2.71
H	1.24	0.918	1.46
p-CH_3	0.942	0.758	0.962
p-CH_3O	0.801	0.647	0.859
ρ	0.70 (r=0.999)	0.88 (r=0.997)	1.02 (r=0.998)

Throughout this paper, 1 M=1 mol dm^{-3}, 1 cal$_{\text{th}}$=4.184 J, °C=K−273.15. a) At 66.5 °C, ×10^6. b) At 66.5 °C, ×10^4. c) At 0 °C, ×10.

TABLE 2. EFFECT OF THE FUNCTIONAL GROUP ADJACENT TO THE REACTION CENTER. RELATIVE RATES AND ρ VALUES FOR SYMMETRICAL FINKELSTEIN REACTION OF SUBSTITUTED CHLOROMETHANES
(20 °C)
$Ph\text{-}Y\text{-}CH_2Cl + (C_2H_5)_4N^{36}Cl$

Y	k_{obsd} / $M^{-1}\,min^{-1}$	Relative rate	ρ	$\left(\frac{t}{°C}\right)$
O	$15.0^{a,b)}$	3.98×10^{10}	-1.56	(-15.9)
CO	1.22	3.24×10^{9}	1.02	(0.0)
S	$3.81\times10^{-2\ b)}$	1.01×10^{8}	-0.92	(20.0)
CH=CH	$2.54\times10^{-2\ b)}$	6.74×10^{7}	U-shape	(20.0)
NONE	$1.23\times10^{-2\ b)}$	3.26×10^{7}	U-shape	(20.0)
C≡C	$9.14\times10^{-3\ b)}$	2.42×10^{7}	-0.19	(20.0)
CH_2	$3.72\times10^{-5\ a,b)}$	9.87×10^{4}	0.57	(60.0)
SO	$1.14\times10^{-7\ a)}$	3.02×10^{2}	0.88	(66.5)
SO_2	$3.77\times10^{-10\ a)}$	1.00	0.70	(66.5)

a) Calculated from the data at other temperatures.
b) Ref. 3.

as (arylsulfonyl)chloromethanes (**1**), electron-withdrawing groups on the phenyl ring facilitate the isotope exchange raection. While in all the other reactive substrates studied [especially in (arylthio)chloromethanes (**3**) and (aryloxy)chloromethanes] the effect of the substituent on the phenyl ring is reversed. Therefore, a quite different accelerating factor seems to be operative in the reaction of the halo ketone **4**.

Reaction of 2-Chloro-1-Arylethanone (4). A marked reactivity was shown by 2-chloro-1-arylethanones, which were about 10^7—10^9 times more reactive than (arylsulfinyl)chloromethanes, and (arylsulfonyl)-chloromethanes.

The enhanced reactivity of an α-halo carbonyl compound is often cited[9] and is a matter of controversy considering the presence of the carbonyl group which is an electron-withdrawing group as effective as the sulfinyl and sulfonyl groups.[10]

To get the insight of the reactivity of the 2-chloro-1-arylethanones **4**, substrate–nucleophile interaction was examined first, as the importance of the approach of the nucleophile was implicated by the positive ρ_{obsd}.

On the addition of nucleophile, chloride ion, to the solution of 2-chloro-1-arylethanone in acetonitrile, a significant PMR shift was observed.[5b] As are shown in the left side column of Table 3 for 2-chloro-1-phenylethanone (**4**-H), the representative compound of the class, the enthalpy of formation of the complex ($\Delta H°$) was the most negative among the substrates studied, implicating some interaction other than hydrogen bonding.[11] However, this stabilization (deactivation) is counterbalanced by the extensive decrease in the entropy of formation of the complex ($\Delta S°$) giving rise a fairly small formation constant for the nucleophile-substrate association (Tables 4 and 5).[5b]

A study on the proton spin-lattice relaxation time (T_1) suggested that such a large decrease of the entropy

TABLE 3. ACTIVATION PARAMETERS AND THERMODYNAMIC PARAMETERS IN THE SYMMETRICAL FINKELSTEIN REACTION

Y	$\Delta H°$ / kcal·mol^{-1} $^{a)}$ ($\rho°$)	$\Delta S°$ / eu $^{a,b)}$	$\Delta H_1^{\ddagger}$ / kcal·mol^{-1} (ρ_1)	$\Delta S_1^{\ddagger}$ / eu $^{b)}$	$\Delta H_{obsd}^{\ddagger}$ / kcal·mol^{-1} (ρ_{obsd})	$\Delta S_{obsd}^{\ddagger}$ / eu $^{b)}$
(a) $Ph\text{-}Y\text{-}CH_2Cl + (C_2H_5)_4N^{36}Cl$						
CO	-4.3_0	$-18._1$	21.0	$6._8$	$16.7^{c)}$	$-11._3{}^{c)}$
[**4**-H]	(0.52)		(0.50)		(1.02)	
(b) Substrates with sulfur-containing functional groups $p\text{-}NO_2\text{-}C_6H_4\text{-}Y\text{-}CH_2Cl + (C_2H_5)_4N^{36}Cl$						
SO_2	-1.2_2	$-3._5$	35.1	$12._0$	33.9	$8._5$
[**1**-*p*-NO_2]	(0.54)		(0.16)		(0.70)	
SO	-1.4_0	$-4._2$	30.0	$6._6$	28.6	$2._4$
[**2**-*p*-NO_2]	(0.66)		(0.22)		(0.88)	
S	-1.7_5	$-7._2$	21.3	$-2._8$	19.5	$-10._0$
[**3**-*p*-NO_2]	(0.59)		(-1.51)		(-0.92)	

$\Delta H°$, $\Delta S°$, $\rho°$ are for the association equilibria, $\Delta H_1^{\ddagger}$, $\Delta S_1^{\ddagger}$, ρ_1 are for the rate-determining scrambling in the postulated scheme 2, and $\Delta H_{obsd}^{\ddagger}$, $\Delta S_{obsd}^{\ddagger}$, ρ_{obsd} are for the overall isotope exchange reaction.
a) Throughout this paper, errors for $\Delta H°$ and $\Delta S°$ are estimated to be within 0.5 kcal/mol, and with in 2 eu.
b) At 20 °C. c) $K_{obsd}/M^{-1}\,min^{-1}$: 1.46×10^{-1} (0.0 °C); 4.20×10^{-1} (10.0 °C); 1.22 (20.0 °C). $k_2/M^{-1}\,min^{-1}$: 1.50×10^{-1} (0.0 °C); 4.25×10^{-1} (10.0 °C); 1.23 (20.0 °C). Errors for $\Delta H_{obsd}^{\ddagger}$ and $\Delta S_{obsd}^{\ddagger}$ are estimated to be within 0.5 kcal/mol, and within 2 eu.
* $k_2 = k_{obsd}\times ab/(a-x)(b-x)$, $x/(a-x)(b-x) = K$
where a = chemical concentration of the substrate [0.1 M for $X\text{-}C_6H_4\text{-}Y\text{-}CH_2Cl$; Y = SO_2, SO, and S. 0.05 M for $X\text{-}C_6H_4\text{-}CO\text{-}CH_2Cl$], b = chemical concentration of the nucleophile ($^{36}Cl^-$) [0.1 M for $X\text{-}C_6H_4\text{-}Y\text{-}CH_2Cl$; Y = SO_2, SO, and S. 0.05 M for $X\text{-}C_6H_4\text{-}CO\text{-}CH_2Cl$], x = chemical concentration of the association complex, K = formation constant of the association complex.
** k_2 is the second-order rate constant corrected for the decrease in the concentration of both the free nucleophile and the free substrate on the formation of complex. Such correction gave essentially no effect on the Arrhenius parameters.

on complexing was accompanied by the extensive freezing of the intramolecular rotation in the substrate.11) The examination of the limiting PMR shift and of the thermodynamic parameters of the association equilibria pointed out the possibility that the nucleophilic anion interacts with the carbonyl group, as well as with the α-methylene protons.11)

Another indication of such an interaction was obtained by the ^{13}C-NMR study. Carbon-13 NMR (CMR) spectra were obtained for 2-chloro-1-phenylethanone-1-^{13}C (C_6H_5–^{13}CO–CH_2Cl), with phenylchloromethane-1-^{13}C (C_6H_5–$^{13}CH_2Cl$) as the reference compound. As are shown in Table 4, α-methylene carbon of phenylchloromethane, carbon at the potential reaction center, showed no significant CMR shift (about 0.1 ppm or less) by the addition of chloride ion.

Table 4. ^{13}C-NMR shift induced by the formation of complex
Ph-Y-CH_2Cl + $(C_2H_5)_4NCl$ a)

Y	δ b) ppm	δ c) ppm	δ_c d) ppm
NONE (Ph-$^{13}CH_2Cl$)	47.2	47.3	(<0.5)
CO (Ph-^{13}CO-CH_2Cl)	192.2	193.3	8.3

a) At 25 °C, in acetonitrile-d_3. b) δ from TMS. 0.1 M standard solution. c) δ from TMS. TEA-Cl (1.0 M) is added to the standard solution. d) $\delta_c = \delta/f$; "f" is the fraction of the complexed substrate. K/M^{-1} (25 °C); 0.132 (Ph-$^{13}CH_2Cl$), 0.157 (Ph-^{13}CO-CH_2Cl).

On the other hand, carbonyl carbon of 2-chloro-1-phenylethanone, located at α-position to the reaction center, gave the low field shift, amounting to 1.1 ppm, on the addition of tetraethylammonium chloride (1.0 M). The amount of the shift is evidently larger than the errors inherent in the present CMR measurements (±0.1 ppm).12)

When correction is made of the fraction of the complex in the equilibrium, with the due assumption that the equilibration is rapid for the time scale of the NMR spectroscopy, the limiting shift of the complex of 8.3 ppm is obtained for 2-chloro-1-phenylethanone. In PMR spectra, α-methylene proton of this substrate showed limiting complexing shift of −1.52 ppm, indicating the attacking nucleophile resides in the proximity of the methylene protons, at the site of the potential S_N2 displacement.5b)

These results suggest that, preceding the isotopic exchange reaction, a nucleophilic anion coordinates to both α-methylene protons and the carbonyl group. Hindrance of the internal rotation thus sets in, as reflected on the sharp decrease in $\Delta S°$ and the increase in the rotational correlation time (τ_c) of the substrate in the complex.5b)

Thus, a quite similar structure to that of the transition state of the nucleophilic displacement reaction accompanying "orbital overlap" is suggested for the nucleophile-substrate complex of **4**. In this complex, a coordination of the nucleophile is already accomplished and the "entropy activation", necessary for the S_N2 reaction to take place, is essentially attained.9a,13)

There seems to be no reason to suppose that such a complex should dissociate to the free components to enter the classical "S_N2" displacement. Possible intermediary of such an association complex was already discussed.8,9)

As a second approach, the measurement of the secondary α-deuterium isotope effect (α-d effect) using 2-chloro-1-phenylethanone-2-d_2 (**4**-H-d_2) was undertaken to present a clue to the nature of the transition state of the displacement reaction of this chloro ketone. The results are shown in Table 5 along with the results of another reactive substrate, **3**-p-NO_2.

Table 5. α-Deuterium isotope effect of the Finkelstein reaction system in acetonitrile

Substrate	k_2^H/k_2^D	K^H/K^D	k_1^H/k_1^D
Ph-CO-CH_2Cl (0 °C)	0.96_2 a)	0.94_2 b)	1.02_1
p-NO_2-C_6H_4-S-CH_2Cl (20 °C)	1.11_9 c)	0.97_6 c)	1.14_7 c)

a) k_2/M^{-1} min^{-1}: 1.50×10^{-1} (for Ph-CO-CH_2Cl), 1.62×10^{-1} (for Ph-CO-CD_2Cl). b) K/M^{-1}: 0.307 (for Ph-CO-CH_2Cl), 0.326 (Ph-CO-CHDCl). c) Ref. 7.

In the symmetrical Finkelstein reaction, the chloro ketone **4**-H gave an inverse α-d effect ($k_2^H/k_2^D = 0.96_2$) for the second order rate coefficient.

Such an inverse kinetic isotope effect seems to be too large for a reaction that proceeds through a symmetrical transition state. In a symmetrical S_N2 reaction, Seltzer suggested an operation of a normal isotope effect or an isotope effect of close to unity when the nucleophilicities of the incoming and leaving nucleophile are equal.14) Interestingly, PMR experiments showed that the α-d effect on the complex formation equilibrium for **4**-H is appreciable and inverse ($K^H/K^D = 0.94_2$).

Now an explanation in terms of the operation of an association-scramble mechanism, which was applied to accomodate the kinetic isotope effect of the reactive substrates,7) is worth trying.

This mechanism postulates an intervention of the nucleophile-substrate association complex as a direct precursor of the rate-determining (unimolecular) scrambling and is depicted in Scheme 2.5)

As expressed in Scheme 2, α-d effect (k_2^H/k_2^D), kinetic parameters ($\Delta H^{\ddagger}_{obsd}$, $\Delta S^{\ddagger}_{obsd}$), and ρ_{obsd} values can be separated into those parameters, both for the complex-forming step and for the unimolecular-scrambling step.

When one postulates the operation of the association-scramble mechanism, α-d effect ascribable to the rate-determining scrambling step of this halo ketone is calculated to be normal and is very close to unity, suggesting a very tight transition state16) (Table 5).

For the chloro ketone **4**, there is no intramolecular functionality among the substrate itself to stabilize the incipient electropositive center developing in the course of the S_N2 reaction. This is in contrast to the

$$\begin{tikzcd}
\text{X-C}_6\text{H}_4\text{-Y-CH}_2\text{Cl} + {}^*\text{Cl}^- \arrow[d, shift right, "K"'] & \text{X-C}_6\text{H}_4\text{-Y-CH}_2{}^*\text{Cl} + \text{Cl}^- \arrow[d, shift right, "(rapid)"'] \\
{[\text{X-C}_6\text{H}_4\text{-Y-CH}_2\text{Cl}\cdot{}^*\text{Cl}^-]} \arrow[u, shift right, "(rapid)"'] \arrow[r, "k_1", "(slow)"'] & {[\text{X-C}_6\text{H}_4\text{-Y-CH}_2{}^*\text{Cl}\cdot\text{Cl}^-]} \arrow[u, shift right, "K"']
\end{tikzcd}$$

K: Equilibrium constant of the complex formation.

k_1: Rate coefficient of the (unimolecular) scrambling in the complex.

$$K = \frac{[\text{Complex}]}{[\text{Substrate}]\ [\text{Nucleophile}]}$$

$$\text{Rate} = k_1\cdot[\text{Complex}]$$
$$= K\cdot k_1\ [\text{Substrate}]\ [\text{Nucleophile}]^{15)}$$
$$k_2 = K\cdot k_1$$
$$k_2^{\mathrm{H}}/k_2^{\mathrm{D}} = (K^{\mathrm{H}}/K^{\mathrm{D}})(k_1^{\mathrm{H}}/k_1^{\mathrm{D}})$$
$$\Delta H^{\ddagger}_{\mathrm{obsd}} = \Delta H^{\circ} + \Delta H^{\ddagger}_1$$
$$\Delta S^{\ddagger}_{\mathrm{obsd}} = \Delta S^{\circ} + \Delta S^{\ddagger}_1$$
$$\rho_{\mathrm{obsd}} = \rho^{\circ} + \rho_1$$

(*Cf.* Table 3, footnote)

Scheme 2. Association-scramble mechanism.

TABLE 6. ACTIVATION PARAMETERS FOR THE SUBSTRATES WITH SULFUR-CONTAINING FUNCTIONAL GROUPS
$\text{X-C}_6\text{H}_4\text{-Y-CH}_2\text{Cl} + (\text{C}_2\text{H}_5)_4\text{N}^{36}\text{Cl}$

Y	X	$\Delta H^{\ddagger}_{\mathrm{obsd}}$ / kcal·mol^{-1}	$\Delta S^{\ddagger}_{\mathrm{obsd}}$ / eu (20 °C)
SO$_2$[a)]	p-NO$_2$	33.9±0.6	$8._5$±2.0
SO[b)]	p-NO$_2$	28.6±0.5	$2._4$±2.0
S[c)]	p-NO$_2$	19.5±0.5	$-10._0$±2.0

a) k_{obsd}/M^{-1} min^{-1}: 4.30×10^{-6} (66.5 °C); 1.23×10^{-4} (89.6 °C); 1.42×10^{-3} (110.0 °C). k_2/M^{-1} min^{-1}: 5.15×10^{-6} (66.5 °C); 1.45×10^{-4} (89.6 °C); 1.65×10^{-3} (110.0 °C). b) k_{obsd}/M^{-1} min^{-1}: 5.15×10^{-4} (66.5°C); 8.69×10^{-3} (89.6 °C); 6.95×10^{-2} (110.0 °C). k_2/M^{-1} min^{-1}: 6.09×10^{-4} (66.5 °C); 1.01×10^{-2} (89.6 °C); 7.96×10^{-2} (110.0 °C). c) k_{obsd}/M^{-1} min^{-1}: 7.15×10^{-3} (20.0 °C); 2.27×10^{-2} (30.0 °C); 6.46×10^{-2} (40.0 °C). k_2/M^{-1} min^{-1}: 7.92×10^{-3} (20.0 °C); 2.50×10^{-2} (30.0 °C); 7.03×10^{-2} (40.0 °C). [*Cf.* Ref. 3a.]

cases of the chloromethyl sulfide **3** and other reactive compounds.

However, it is conceivable that the incoming chloride ion which resides at a position close enough to perturb the carbonyl group keeps interacting in the course of the rate-determining scrambling. This sort of an interaction could energetically be favored by the "orbital overlap" among the π-orbital of the carbonyl group, the incipient p-orbital of the reaction center, and the p-orbital of the nucleophile.[9a)]

Thus a kind of the attraction-dissociation process is feasible. In fact, very small α-d effect can be reasonably interpreted assuming a tight transition state where no significant charge separation around the reaction center is expected.[17)] Positive ρ_1 value in Table 3(a) also are in accord with the above explanation, since the electron-withdrawing group on the phenyl ring facilitates the attraction of the nucleophile.

Effect of the Sulfur-containing Functional Group on the Finkelstein Reactions. As shown in Table 2, marked retardation in reaction was observed for (arylsulfonyl)- and (arylsulfinyl)chloromethanes (**1** and **2**), in contrast to the appreciable rate acceleration in (arylthio)-chloromethanes (**3**). In the present study, the reactivity gap between **2** and **3** was significantly larger than that reported earlier by Bordwell and coworkers.[8)]

For (p-nitrophenylsulfonyl)chloromethane (**1**-p-NO$_2$) and for (p-nitrophenylsulfinyl)chloromethane (**2**-p-NO$_2$), as the representatives for these classes of the substrates, activation parameters were evaluated. In Table 6, these parameters are given with those for (p-nitrophenylthio)chloromethane (**3**-p-NO$_2$) as the reference substrate.

The observed enthalpies of activation ($\Delta H^{\ddagger}_{\mathrm{obsd}}$) increase in the order of **3**-p-NO$_2$<**2**-p-NO$_2$<**1**-p-NO$_2$, reflecting the relative reactivities of these substrates. As to the observed entropies of activation ($\Delta S^{\ddagger}_{\mathrm{obsd}}$) incontestable positive values were obtained for **1**-p-NO$_2$ and **2**-p-NO$_2$.

This is quite a contrast with the Bordwell's experiment. They found large negative entropies of activation in the reaction of **2** and potassium iodide in acetone. They also claimed only a small difference in the enthalpies of activation between **2** and **3**.[8)]

These findings led Bordwell to accomodate the rate retardation in terms of the steric hindrance (and of the electrostatic repulsion) by sulfinyl (and possibly by sulfonyl) group.[8)] A similar explanation was made of the ring opening of the episulfonium ion, under the nucleophilic attack by chloride ion, substituted with alkylsulfonyl group.[13)]

However, positive entropy of activation obtained in the present study cannot be accomodated in terms of increased steric restriction in the transition state. Thus the cause of the rate retardation other than the steric hindrance must be sought for the least reactive substrates **1** and **2**.

There is a possibility that an isokinetic relationship holds for the symmetrical exchange reaction of **1**, **2**, and **3**, although the apparent linear relationship found can probably be fallacious. If the present observation is not fortuitous in nature, an operation of a common mechanism should be postulated among the three classes of compounds.[19)] This implies a possible intervention of the nucleophile-substrate complex playing a role of the direct precursor of the rate-determining step, as behaviors of the chloromethyl sulfide **3** were better accomodated in the frame work of this mechanism.[7)]

In Table 3(b), there are also shown kinetic and thermodynamic parameters which are obtained by taking into account the intervention of the complex.

Interestingly, an isokinetic relationship about $\Delta H_1^{\ddagger}$-$\Delta S_1^{\ddagger}$ suggests a different interaction between chloro ketone **4** and the three classes of the sulfur-containing substrates, while $\Delta H^{\ddagger}_{\mathrm{obsd}}$-$\Delta S^{\ddagger}_{\mathrm{obsd}}$ relationship suggests a single interaction among those four classes of the substrates.

The postulation of the association-scramble mechanism suggests a more comprehensive picture. The effect of a facilitated approach of a nucleophile is separated from k_{obsd} into K, thus the rate retardation observed in **1** and **2** could be an outcome of the lack of the electron-donating capacity of both the sulfinyl and the sulfonyl groups to the reaction center in the (unimolecular) scrambling step of the nucleophilic displacement reaction. There are examples of the difference in the electron-donating capacity of these three sulfur-containing groups.[20]

A conceivable presence of the isokinetic relationship(s) among the nucleophilic displacement reactions studied, suggests a prevailing positive entropy of activation for substrates with extremely high activation enthalpy. However, no indication is obtained from this reasoning about the physical meaning of the positive entropy of activation where a tight transition state can plausibly be ascribed.[21]

At present, the postulation of the intermediary of the nucleophile-substrate complex remains as a proposal. Further studies to support (or disprove) the role of such a complex are necessary to help clarify the situation on the possibility of the intermediary in the Finkelstein reaction system.

Experimental

Preparative gas chromatography was performed on a Varian Model-920 gas chromatograph. The CMR spectra were obtained on a JEOL JNM-FX60 spectrometer. The mass spectra were recorded on a Hitachi M-52 spectrometer. The radioactivity was measured with a Nuclear Chicago Model-6801 liquid scintillation counter.

Materials. Substituted chloromethanes were synthesized according to the standard procedures.[3,8]

2-Chloro-1-phenylethanone-1-^{13}C: (a) Benzoic-*carboxy*-^{13}C Acid:[22] A Grignard solution was prepared from 480 mg (20 mmol) of magnesium turning and 3.1 g (20 mmol) of bromobenzene in absolute ether (20 ml). Phenylmagnesium bromide was carbonated with carbon-^{13}C dioxide liberated from 1 g (5 mmol) of barium carbonate-^{13}C (isotopic enrichment 90%, Prochem). Following hydrolysis with aqueous ammonium chloride, the ethereal solution was extracted repeatedly (5 ml × 5) with saturated aqueous sodium hydrogencarbonate solution. Then the alkaline solution was washed with ether, acidified and extracted with a small amount of saturated aqueous sodium hydrogencarbonate solution. The hot aqueous solution was acidified with hydrochloric acid, and cooled to precipitate the product, yield 556 mg (91%). (b) Benzoyl-*carbonyl*-^{13}C Chloride. A mixture of 556 mg (4.6 mmol) of benzoic acid and 4 ml (30 mmol) of purified thionyl chloride was refluxed for 1 h and the excess thionyl chloride was removed under reduced pressure. The residual liquid was used without further purification. (c) 2-Diazo-1-phenylethanone-^{13}C: To a stirred and ice-cooled ethereal solution of diazomethane (65 ml) [from 10.8 g (50 mmol) of *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide] was added dropwise a solution of crude benzoyl chloride in 20 ml of absolute ether. The mixture was stirred for 15 min at 0 °C and for additional 2 h at room temperature. The product was used for the following process without further purification. (d) 2-Chloro-1-phenylethanone-1-^{13}C; Into a stirred dry ethereal solution (20 ml) containing 2-diazo-1-phenylethanone was introduced anhydrous hydrogen chloride for 1 h at 0 °C. Then the solution was concentrated, and the resulting crude material was recrystallized from ethanol, to give a pure product, 506 mg, 72% based on the benzoic acid. Mass; 156 (M$^+$) (isotopic enrichment 90%).

2-Chloro-1-phenylethanone-2-d_2: To a stirred and ice-cooled solution of 2-diazo-1-phenylethanone (400 mg, 2.7 mmol) in dry ether (20 ml) was bubbled anhydrous deuterium chloride, generated by the reaction between phosphorus pentachloride (24 g, 0.1 mol) and deuterium oxide (2 g, 0.1 mol). The mixture was stirred for 1 h at 0 °C, then concentrated to give the crude material. Recrystallization from ethanol gave a pure product, 407 mg, 82% based on the 2-diazo-1-phenylethanone. Mass; 157 (M$^+$) (isotopic enrichment 99.7%).

Benzyl-α-^{13}C Chloride: (a) Methyl Benzoate-*carbonyl*-^{13}C; An ethereal solution (10 ml) of 500 mg (4.0 mmol) of benzoic-^{13}CO acid was treated with a cold ethereal solution (65 ml) of diazomethane prepared from 10.8 g (50 mmol) of *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide. The solution was concentrated under reduced pressure, and used for the following step without further purification. (b) Phenylmethanol-1-^{13}C; An ethereal solution (3 ml) of the ester was added dropwise to a stirred ethereal solution (15 ml) of 455 mg (1.2 mmol) of lithium aluminum hydride. The mixture was then refluxed for 2 h, cooled with ice bath, and acidified with dilute hydrochloric acid. The aqueous layer was separated, and extracted with several portions of ether. The ether layer and the extracts were combined and the combined solution was dried over anhydrous magnesium sulfate. Concentration of the solution gave the cited compound as an almost colorless liquid. This product was used without further purification. The yield was essentially quantitative. (c) Benzyl-α-^{13}C chloride; To the crude benzyl alcohol, was added slowly 5 ml (25 mmol) of purified thionyl chloride, and the mixture was refluxed for 1 h. The excess thionyl chloride was distilled off, and the product was purified by preparative gas chromatography. The yield was 370 mg, 71% based on the benzoic acid. Mass; 127 (M$^+$) (isotopic enrichment, 90%).

Kinetic Measurements. Batch method was employed for kinetic measurements. Procedures were almost similar as previously reported.[3] At the appropriate intervals, the reaction mixture was quenched by cooling and dilution with cold (−78 °C) toluene, while tetraethylammonium chloride was extracted in water. Chlorine-36 radioactivity was measured by liquid scintillation counter. In the measurement of the less reactive substrate, tetraethylammonium chloride-^{36}Cl with high specific activity (10 μCi/mmol) was utilized. In such cases, to avoid the experimental error caused by the contamination of unreacted tetraethylammonium chloride-^{36}Cl to the organic layer, the organic layer was washed repeatedly with water (at least six times) until the radioactivity of the aqueous layer was reduced to that of the natural backgound.

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For the sake of simplicity and to show the experimental results, rate data in Tables 1 through 2 are not corrected. As is exemplified in the footnote of Table 3, the due correction is often close to 20% for the substrates with a high K. However, as are given in the footnote of Table 3, $\Delta H^{\ddagger}_{\mathrm{i}}$ and $\Delta S^{\ddagger}_{\mathrm{i}}$ (also $\Delta H^{\ddagger}_{\mathrm{obsd}}$ and $\Delta S^{\ddagger}_{\mathrm{obsd}}$) are affected little by the due correction of the decrease in the concentrations of the reactants and, accordingly, of the rate constants on the complex formation.

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