KINETIC STUDIES ON HALOGEN EXCHANGE OF 1-NAPHTHYL METHYL HALIDES

by

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(Received May 26. 1969)

1-나프틸메틸 할라이드의 할로겐 교환반응

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(1969. 5. 26. 접수)

ABSTRACT

Kinetics of reactions of halide ions with 1-naphthyl methyl halide have been investigated in anhydrous acetone. Semi-quantitative analysis of the results shows that if the softness of the substrate increases remarkably, the nucleophilicity order of halide ions is $I^- > Br^- > Cl^-$ even in dipolar aprotic solvent.

But for 1-naphthyl methyl bromide, though the reaction center which was made soft by symbiosis of bromine atom raises the reactivity of soft nucleophile, nucleophilicity order indicates that soft-soft interaction is interfered by perihydrogen.

要　約

1-naphthyl methyl halide 와 halide ion 간의 反應을 無水 acetone 에서 反應 速度論的으로 연구하였다. Substrate 의 softness 가 현저하게 增加하면 halide ion 의 nucleophilicity 가 dipolar aprotic solvent 에서도 一般的으로 $I^- > Br^- > Cl^-$ 의 순서를 갖는다는 것을 보여 주고 있다.

Leaving group 이 bromide 일 때는 symbiotic effect 에 의해서 reaction center 의 softness 가 증가하여 soft halide ion 과의 反應이 커질 것이나 perihydrogen atom 의 steric effect 때문에 chloride 일 때에 비해서 약간 감소하고 있다.

INTRODUCTION

Halogen exchange reaction is a typical displacement reaction on carbon and has been studied extensively.[1][2][3][4][5] Hughes & Ingold suggested the SN2 mechanism for reactions of this type in the course of investigation on halide exchanges of alkyl halides. The first order dependence of reaction rate on both nucleophile and substrate concentration supports this view. It is generally accepted that during the SN2 displacement, the molecule passes through a state[1] in which carbon is pentavalent and has the configuration of a triangular

hipyramid[2]

(1)
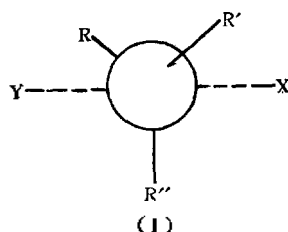
For the substrate which R and R′ are hydrogen and R″ is aromatic ring, i. e., the aryl methyl system, the rate of reaction is relatively large. Lee et al. [6] studied the reaction of benzyl halide in 90% aqueous ethanol solvent, concluding that in the transition state the p-orbital of the attacked carbon atom overlaps with the pd-hybrid orbitals of halide ion so that the transition state may be stablized and the reaction rate may be comparatively high. Thus it is certainly reasonable to expect the nucleophilic order of halide ions to be I⁻>Br⁻>Cl⁻, which is easiness of pd hybrid formation.

But in dipolar aprotic solvent as acetone, the nucleophilic reactivity of free halide ions was reversed, i. e., Cl⁻>Br_>I⁻. [5][7][8][9] This result was interpreted with solvation theory which was suggested by Parker et al., [9] such as, in anhydrous acetone, the more desolvated chloride ion may be the most reactive and the more solvated iodide ion may be the least reactive.

On the other hand, Pearson et al., [8] argued that the anionic nucleophilicity depend on the substrates softness. As the softness of the substrate increases, the softer nucleophile is more reactive, so that the nucleophilicity order of halide ion even in dipolar aprotic solvent, acetone, must be I⁻>Br⁻>Cl⁻.

If we make the reaction center softer, we can test the HSAB principle and solvation theory.

Thus, in this work, the kinetics of halogen exchange of 1-naphthyl methyl halide, the reaction center of which was made softer than the benzyl carbon center, was studied in anhydrous acetone.
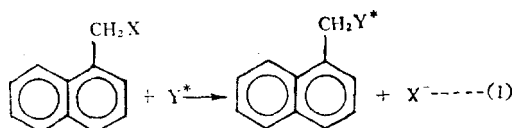
According to Lee et al., [7] the steric strain of peri-

hydrogen of 1-naphthyl system is also expected for the SN2 reaction of 1-naphthyl methyl halide with halide ion, which was suggested by Dewar & Sampson. [10]

EXPERIMENTAL

1) Materials:

1-naphthyl methyl chloride was prepared by chloromethylation[11] of naphthalene in the presence of catalyst, phosphoric acid. The final product obtained from vacum distillation had the physical constants, m. p. 31-32°, b. p. 135-9°. [12]

1-naphthyl methyl bromide was prepared by bromomethylation using the same procedure as for 1-naphthyl methyl chloride, m. p. 53.5-54.5, b. p. 183[8][12]

Acetone was dried over magnesium sulfate before fractional distillation and was dehydrated by flowing through the activated alumina coloumn, resulting in 0.08% or less water content. [13]

Radioactive bromine-82 and iodine-131 were supplied by the Isotope Production Group of AERI, Korea. Cl-36 isotope was purchased as aqueous HCl solution from the Isotope Center, Belgium. The radioactive chloride and bromide were converted to lithium halides by adding the equivalent amount of lithium hydroxide and then evaporated to dryness and diluted with anhydrous acetone to suitable activity (original form of Br-82, NH₄ Br and that of I-131, NaI).

2) Kinetic runs:

Weighed amount of 1-naphthyl methyl halide was dissolved in a volumetric flask with anhydrous acetone and desired amount of active stock solution was added. The flask was filled to the mark with anhydrous acetone, quenched by means of dry ice-acetone mixture.

This solution was divided into several portions and transfered to ampoules. After sealing, they were maintained in the thermostat at the desired temperature. The temperature of the bath containing the sealed ampoules was kept to the better than ±0.05°C.

At timed intervals, ampoules were withdrawn from the bath and immediately the reaction mixture was quenched before 5 ml sample solution was pipetted out of each ampoule, and extracted by means of 10

ml of benzene and 5 ml of distilled water.

One ml portion was pipetted out of each of the organic and the aqueous layer was counted. The bromine and iodine activities were measured in a well-type scintillation counter, while a liquid scintillation counter (Beckman L. S. -100) was used for chlorine-36.)[14]

The decay correction was made only for bromine at each counting because of its short half-life.

In the measurement of chlorine activity, suitable amount of scintillator solution that was prepared freshly by dissolving 2. 5-diphenyl xazole (P. P. O. 8g/1) and 2, 2'-p-phenylene-bis-(5-phenylo-xazole) (P. O. P. O. P. O. 1g/1) in benzene was used.

Becasuse the scintillator solution was immiscible with aqueous solution, desired amount of propyl alcohol was added to make the mixture of aqueous and scintillator solution homogeneous.

Quenching was generally compensated for using the equation, [14]

$$-\frac{N}{C}=Se^{-qc} \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots(2)$$

where N is the counting number, C, the concentration of quenching agent, S_q the specific activity, and q the quenching constant. If there exist more than one quenching agent, the equation (2) is modified as following;

$$-\frac{N}{\Pi c_i}=Se^{-\Sigma q_i c_i} \dots\dots\dots\dots\dots\dots\dots\dots(3)$$

The quenching constant of water was 0. 11, whose dimension is denoted by 20 ml scintillator solution per 1 ml aqueous layer sample, whereas that of isopropyl
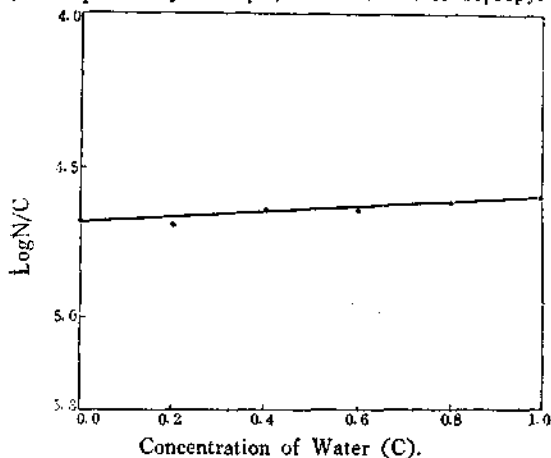

Fig 1. Typical Quenching Curve for water

alcohol was 0. 51, whose value is valid when using

alcohol concentration units as 10 ml sample per 20 ml solution. Typical quenching curve is demonstrted in Fig. 1.

The counting rate was high enough to require only a few minutes counting in reducing the counting error to less than 2%.

3. Determination of rate constants:

Since it is generally accepted that ion-pair of metal halide has no reactivity to the bimolecular nucleophilic substitution, neglecting the reverse reaction, the rate of exchange may be represented by the equation: [15][16]

$$R=k_i a ab \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots(4)$$

where k_i is the second-order rate constant for free halide ion and α is the degree of dissociation.

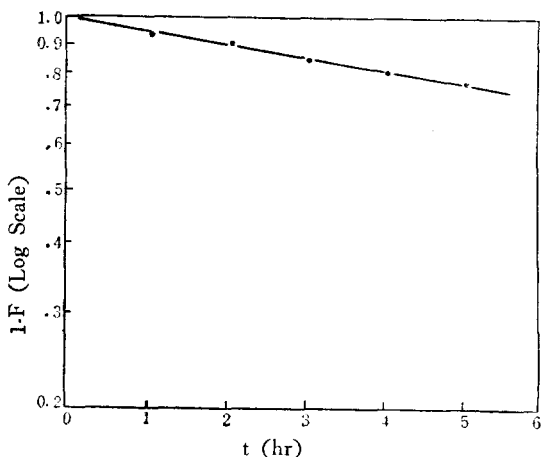For the evaluation of second-order rate constant the method of Lee et al. [7] was adopted.

Fig. 2. Typical Plot of Log (1-F) vs t for Iodine Exchange in 1-Naphthyl Methyl Chloride at 25°C

From the mass-action law,

$$K=\frac{a^2(b-x)}{1-\alpha}, \quad \text{or} \quad \alpha=\frac{-K\pm\sqrt{K^2+4K(b-x)}}{2(b-x)}$$
$$\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots(5)$$

Substituting equation (5) to eq. (4),

$$R=\frac{dx}{dt}=ki\ (a-x)\frac{1}{2}(-K+\sqrt{K^2+4K(b-x)}$$
$$\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots(6)$$

Rearranging the eq. [6], and integrating that,

$$-\frac{(a-c)}{(a-b)}\ \ln\left(\frac{a-x}{a}\right)+\frac{(c-b)}{(a-b)}\ \ln\left(\frac{b-x}{b}\right)$$
$$=-Dkit$$

where, $D=(K^2+4Kb)^{\frac{1}{2}}, \quad C=\frac{1}{2}\left(D+\frac{D}{K}\right) \dots\dots(7)$

In case, a$\gg$b, therefore, a$\gg$x, eq. (7) is simplified into

$$\frac{(c-b)}{(a-b)} \log (1-F) = \frac{-Dkit}{2.303} \quad \text{......................(8)}$$

where F is equivalent to $\frac{x}{b}$ in eq. (7).

In the case of isotope exchange reaction, where nucleophile and leaving group is the same species, the eq. (8) is modified to, [17][18]

$$\frac{(c-b)}{(a+b)} \log (1-F) = \frac{-Dkit}{2.303} \quad \text{..................(9)}$$

In this work the plot of log (1−F) vs. t showed good linearity, and from the slope of the plot, ki was evaluated.

Ion pair dissociation constant, K in acetone were taken from the literature. [19]

RESULTS AND DISCUSSION

Rate constants for halogen exchange reactions of 1-naphthyl methyl halides in an hydrous acetone are summarized in table 1.

TABLE 1. SUMMARY OF RATE CONSTANT

Y \ X	Cl		Br	
	25°	35°	−10°	0°
Cl	2.22×10^{-3}	6.63×10^{-3}	2.44×10^{-2}	1.11×10^{-1}
Br	3.01×10^{-3}	6.98×10^{-3}	2.56×10^{-2}	9.32×10^{-2}
I	3.58×10^{-3}	8.84×10^{-3}	5.63×10^{-2}	1.43×10^{-1}

※ Standard deviation was 3%

TABLE 2. kn/kb

Y \ X	Cl 25°	Br 0°
Cl	0.85	—
Br	1.67	2.33
I	2.21	4.62

※ kn: rate constant for 1-naphthyl methyl halide.
　 kb: rate constant for benzyl halide.

The ratio of rate constants for halogen exchange reactions of 1-naphthyl methyl halides to that of benzyl halides in anhydrous acetone shows that 1-naphthyl methyl carbon center is more reactive than benzyl carbon center, except for the case of 1-naphthyl methyl chloride-chloride exchange. (Table 2) According to HSAB principle, [8][20][21][22] the softer the substrate becomes, the faster the reaction proceeds.

From the above table, we can easily understand that 1-naphthyl methyl carbon center has the higher softness than benzyl carbon.

Table 2 also shows that the iodide exchange reaction rate of 1-naphthyl methyl chloride and bromide are 2.2 and 4.6 times of the rate for benzyl chloride and bromide, respectively. This indicates that the bromine atom in 1-naphthylmethyl bromide has the more rate enhancing effect than chlorine atom in 1-naphthylmethyl chloride, owing to the symbiotic effect of bromide atom. In the case of bromide ion nucleophile, the effect becomes also apparent.

But for attacking chloride ion, 1-naphthyl methyl chloride is less reactive compared to benzyl chloride at 25°C. Since 1-naphthyl methyl carbon center is fairly soft, the hard nucleophile, Cl⁻ has low soft-soft interaction, resulting in the rate decrease.

Activation parameters summarized in Table 3 and 4 also show comparable tendency.

Although activation entropies are lower by about 15-25 e. u. in the halogen exchange reaction of 1-naphthyl methyl chloride compared with that of benzyl

TABLE 3. ACTIVATION ENTHALPY ($\triangle H^{\neq}$ K cal)

Y \ X	Cl	Br
Cl	19.4	21.1
Br	14.7	15.4
I	15.9	11.4

TABLE 4. ACTIVATION ENTROPY ($\triangle S^{\neq}$ e. u.)

Y \ X	Cl	Br
Cl	−1.1	+14.6
Br	−20.7	−6.7
I	−16.4	−14.8

chloride, activation enthalpies, cause rate increase, compensating the unfavorable entropy change. On the other hand, the entropy and enthalpy of activation for the halogen exchange of 1-naphthyl methyl bromide show small variations, compared with that for benzyl bromide.

If we dissect $\triangle H^{\neq}$ into three contributing terms, i. e., electronic, steric, and solvational terms, $\triangle H^{\neq}$ is the sum of the three:

$$\triangle H^{\neq} = \triangle H^{\neq} \text{elect} + \triangle H^{\neq} \text{ster.} + \triangle H^{\neq} \text{sol...(10)}$$

where $\triangle H^*$ elect. is the part of enthalpy contributed from the electronic effect of the system, $\triangle H^*$ ster., that from steric effect, and $\triangle H^*$ sol. that from solvation effect.

When substrate is changed from benzyl to 1-naphthyl methyl, the change of activaton enthalpy is

$$\delta(\triangle H^*)=(\triangle H^*_n-\triangle H^*_b)$$
$$=\delta(\triangle H^* \text{ elect})+\delta(\triangle H^* \text{ ster})+\delta(\triangle H^* \text{ sol})$$
$$\cdots\cdots\cdots\cdots\cdots\cdots(11)$$

where, $\triangle H_n^*$ is activation enthalpy for the substrate of 1-naphthyl methyl, and $\triangle H_b^*$ is that of benzyl system.

Applying eq. (11) to halide exchanges of the two chloride substituted substrates, $\delta(\triangle H^*)$ is nearly —10- —20 kcal. If we assume that the main contributing effect to $\delta(\triangle H^* \text{ ster})$ is the steric strain of perihydrogen of 1-naphthyl system, $\delta(\triangle H^* \text{ ster})$ will be 2 or 3 kilocalories positive. According to Parker et al.,[6] $\delta(\triangle H^* \text{ sol})$ for the azide exchange of benzyl chloride and methyl chloride in DMF was about —1.3 kcal. The value of $\delta(\triangle H^* \text{ sol})$ for the halide exchange of 1-naphthyl methyl halides and benzyl halides in acetone can safely be assumed to be no greater than this. Hence the sum of $\delta(\triangle H^* \text{sol})$ and $\delta(\angle H^* \text{ ster})$ is at best 2 or 3 kcal. and the main contributing term in $\delta(\triangle H^*)$ is $\delta(H^* \text{ elect.})$.

This is mainly due to the change of interaction energy between substrate and nucleophile.

For bromide and iodide exchange reactions of both aryl methyl bromides, $\delta(\triangle H^*)$ values are ca. 1 or 0 kcal., respectively. Since it can easily be understood that $\delta(\triangle H^* \text{ elect})$ and $\delta(\triangle H^* \text{ sol.})$ have the same sign, and each of the terms, $\delta(\triangle H^* \text{ elect.})$ and $\delta(\triangle H^* \text{ sol.})$ has to be the smaller magnitude than the sum of both terms, from eq. (11), the sum of $\delta(\triangle H^* \text{ elect.})$ and $\delta(\triangle H^* \text{ sol})$ has to be as much magnitude as $\delta(\triangle H^* \text{ ster.})$, which have opposite signs. Judging from the preceding discussions, we can say that the effective factor contributing to $\delta(\triangle H^* \text{ elect.})$ is the symbiosis of leaving group in halogen exchange reaction of aryl methyl halides.

Table 5 shows that the sequence of nucleophilicity of free halide ions in anhydrous acetone for the 1-naphthyl methyl halides is I⁻>Br⁻>Cl⁻ except for the case of I⁻> Cl⁻> Br⁻ for 1-naphthyl methyl bromides at 0°C. This result is in accordance with

Pearson's suggestion[8] that if the softness of the substrate increases remarkably, the nucleophilicity order of halide ions will be I⁻>Br⁻>Cl⁻ even in dipolar aprotic solvents.

But for 1-naphthyl methyl bromide, halide ion nucleophilicity order, I⁻>Cl⁻>Br⁻, indicates that

TABLE 5. RELATIVE NUCLEOPHILICITY

Y \ X	Cl		Br	
	25°	35°	—10°	0°
Cl	1	1	1	1
Br	1.36	1.05	1.05	0.84
I	1.61	1.33	2.31	1.28

TABLE 6. RELATIVE LEAVING ABILITY

Y \ X	Cl, 25°	Br, 0°
Cl	1	50.2
Br	1	31.0
I	1	39.8

soft-soft interaction is interfered by a certain factor. In other words, even if the reaction center which was made soft by symbiosis of bromine atom raises the reactivity of soft nucleophile, bulky leaving group, Br, lowers the relative nucleophilicity of soft nucleophile Br⁻, I⁻ of large size, considerably. Such size effect was assumed to be steric strain of perihydrogen of 1-naphthyl system.

If we adopt the transition state model which was suggested by Lee et al.[6], this perihydrogen effect can be explained as follows.

As in Fig 3. seudo-allyl type delocalized MO, which was made by overlap of 1-orbital of reaction center carbon atom with the pd hybrid orbital of leaving and nucleophilic halogens can be distorted by perihydrogen, and the coplanarity between X, C and Y may partially be broken, and therefore the transition state can be destabilized. Thus the nucleophilicity of large halide ion can be lowered.

Table 5 also show the temperature dependence of nucleophilic reactivity. The nucleophilicity of soft and large nuclophile decreases as temperature rises. This could be due the increase of steric strain with temperature rise. Such steric strain can be considered as transition

state destabilization caused by C-H bond stretching of peri-hydrogen.

Table 6 indicates that the size effect of nucleophile minimizes the leaving ability of large sized leaving group. Through distorted MO of the transition state, the transfer of lone-pair election from nucleophile to leaving group should be difficult and this will destabilize the transition state.
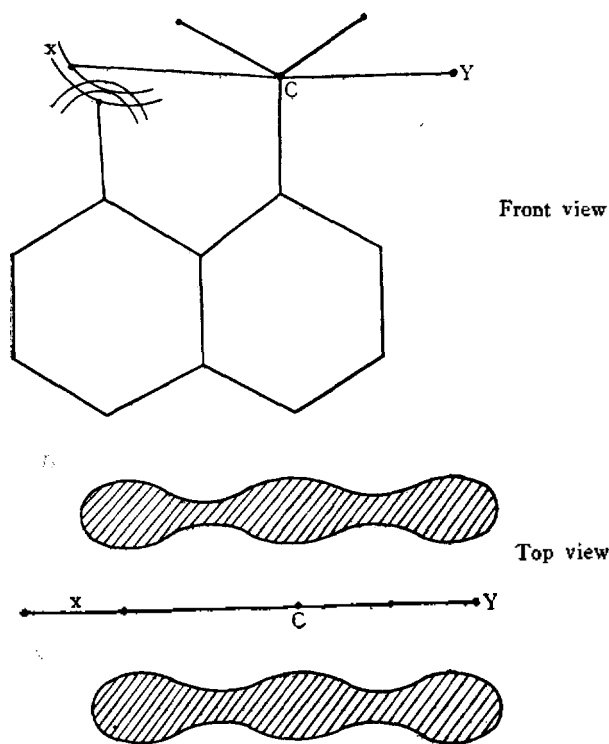
Front view

Top view

Fig 3. Schematic diagram of SN2 transition state model with steric strain of perihydrogen of 1-naphthyl methyl halide

Acknowledgement

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