

<Original> Kinetic Studies on Halogen Exchange of Phenacyl Halides

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Abstract

Kinetics of halogen exchange reactions of phenacyl halides using radioisotope tracer halide ions in anhydrous acetone have been studied. The reactions were believed to be SN_2 processes and the orders of relative nucleophilicity of halide ions were $Cl^- > I^- > Br^-$ for the phenacyl chloride and $I^- > Cl^- > Br^-$ for the phenacyl bromide. These were interpreted in terms of solvation effect of halide ions and HSAB principle.

요 약

Phenacyl halides의 할로젠 교환반응을 무수 아세톤중에서 방사성 할라이드 이온을 사용하여 속도론적으로 연구하였다. 반응은 SN_2 반응이며 할라이드 이온의 상대적 친핵성의 순서는 Phenacyl chloride에 있어서는 $Cl^- > I^- > Br^-$ 이고 Phenacyl bromide에 있어서는 $I^- > Cl^- > Br^-$ 였다. 이것을 할라이드 이온의 용매화 효과와 그리고 HSAB 원리로 설명하였다.

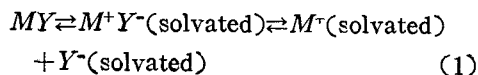
1. Introduction

Many halogen exchange reactions in various solvents have been studied extensively¹⁻⁹⁾. The most important factors which influence nucleophilic reactivity are: (1) Brnsted basicity of the nucleophile, (2) the polarizability of the nucleophile, (3) the nature of the solvent, (4) the bond strength in product, (5) the charges on the nucleophile and the substrate, (6) alpha-effect of nucleophile and (7) steric effect¹⁰⁾.

The characteristics of bimolecular nucleophilic displacement reaction generally accepted

are: (1) the order of reaction rate is unity for both nucleophile and substrate, which may be written as $Rate = k[R-X][Y]$, (2) the rate constant k depends on the natures of the nucleophile Y and the leaving group X , (3) they do not exhibit any of the properties typical of radical reactions, and (4) the values of entropy of activation, ΔS^\ddagger , are usually quite negative.

In acetone not having sufficient power to free the ions from each other, the equilibrium between ion pair and the separated ions

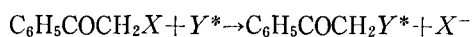


is not displaced completely to the right. The ion pair, however, is relatively unreactive to the bimolecular nucleophilic displacement⁴⁾

Relative nucleophilic reactivity of halide ions in dipolar aprotic solvent such as acetone is reported to decrease in the order of $\text{Cl}^- > \text{Br}^- > \text{I}^-$ on the other hand, it is reversed as the order of $\text{I}^- > \text{Br}^- > \text{Cl}^-$ in protic solvent. This is explained as the large sized I^- solvated less than the small Cl^- in protic solvent and the more polarizable I^- is the most reactive of the three anions.

On the other hand, Pearson *et al.*,¹¹⁻¹⁴⁾ argued that the anionic nucleophilicity depends on the softness of the substrate. As the softness of the substrate increases, the softer nucleophile is more reactive, so that the nucleophilicity order of halides ions even in dipolar aprotic solvent is maintained as $\text{I}^- > \text{Br}^- > \text{Cl}^-$.

In this work, the kinetics of halogen exchange of phenacyl halides in anhydrous acetone, dipolar aprotic solvent, was carried out using radioisotope tracer halide ions.



(2)

where $\text{X} = \text{Cl}$ and Br , $\text{Y}^* = {}^{36}\text{Cl}$, ${}^{82}\text{Br}$ and ${}^{131}\text{I}$.

This system is of particular interest since the phenacyl halides have the carbonyl group between C_6H_5- and $-\text{CH}_2\text{X}$, and then, relatively great reactivity will be expected for the existence of it by the suggestion¹⁵⁾, that is, when the carbon atom attached directly to the reaction center is unsaturated, the reactivity increases.

2. Experimental

(1) Materials

GR-grade phenacyl chloride(PC) and phenacyl bromide(PB) made by Tokyo Kashei Industrial Co. Ltd., were used without further purification.

Acetone was purified by drying over calcium

chloride before fractional distillation and was dehydrated by flowing through the alumina column. This treatment reduces the water content to 0.08% or less⁴⁾.

Radioactive chlorine-36 was purchased from The Radiochemical Center, Amersham, Buckinghamshire, England, as aqueous HCl solution, and radioactive bromine-82 in the form of NH_4Br and iodine-131 in the form of NaI were supplied by The Radioisotope Production Group of Atomic Energy Research Institute, Korea. 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.

(2) Kinetic Runs

A weighed amount of phenacyl halide was dissolved in 500ml flask with anhydrous acetone(PC: 5.491×10^{-3} M, PB: 3.771×10^{-3} M). Twenty ml of this substrate solution was transferred into the 50ml flask and maintained in the thermostat at desired temperature. The temperature of the bath was kept to the better than $\pm 0.05^\circ\text{C}$. About 10 minutes later, 15 ml of active salt solution was added to the substrate one. At timed interval, 5 ml of reaction mixture was withdrawn by pipette and immediately quenched by transferring it into the separatory funnel in which 10 ml of benzene and 5 ml of distilled water were already provided and extracting out the unreactive salt by shaking for more 30 seconds. After standing for 3-4 hours or more, 1 ml portion was pipetted out of each of the organic and the aqueous layers and counted. Chloride activity was measured by liquid scintillation counter, while bromide and iodide activities were measured by well-type scintillation counter. In the measurement of chloride activity, suitable amount of scintillator solution that was prepared by dissolving 2,5-

diphenyloxazole(PPO, 3.1 g/l) and 2,2'-p-phenylene-bis-(5-phenyloxazole) (POPOP, 0.15 g/l) in benzene or toluene was used. The error of concentration arisen from the expansion of the solvent with temperature was within the experimental error, and then it was neglected.

(3) Determination of Rate Constants

For the evaluations of second order rate constants, the method of Lee *et al.*⁴⁾ was adopted. The rate constants, k , for $X=Y$ exchange reactions were calculated by equation (3), and for $X \neq Y$ by equation (4).

$$\frac{1}{a+b} \log(1-F) = \frac{-akt}{2.303} \quad (3)$$

$$\frac{c-b}{a-b} \log(1-F) = \frac{-Dkt}{2.303} \quad (4)$$

where a and b are the initial concentrations of substrate and salt respectively, $D = (K^2 + 4Kb)^{\frac{1}{2}}$, $c = \frac{1}{2}(D + D^2/K)$, K is the ion pair dissociation constant of salt in anhydrous acetone, α is the degree of dissociation of salt, F is the fraction exchange and t is the reaction time.

Ion pair dissociation constants in acetone were taken from the literature¹⁶⁾.

3. Results and Discussion

The typical plots of $-\log(1-F)$ vs. t of

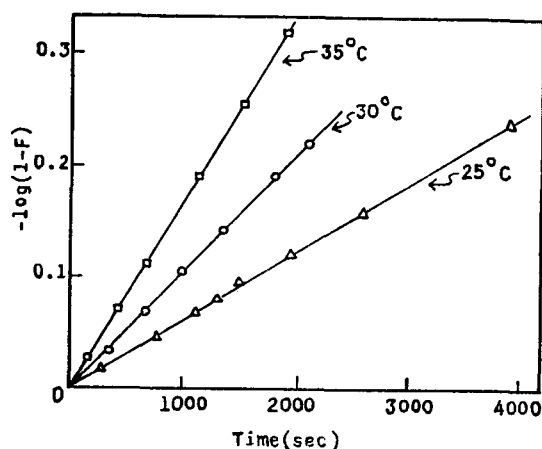


Fig. 1. Typical plots of $-\log(1-F)$ vs. time of phenacyl chloride-chloride system.

($PC+Cl^*$) system at various temperatures shown in Fig. 1 were satisfactorily linear in accordance with the equations (3). The values of the rate constants k given in Table 1 were calculated from the plots employing the least-squares technique. Consequently, the halogen exchange reaction of phenacyl halide in anhydrous acetone was first order for both nucleophile and substrate. This supports the view that the rate-controlling step of the reaction involves the collision of phenacyl halide and halide ion. The fact that the attacking group, Y^- , always has unshared pairs of electrons is evidence for the nucleophilic character of the attack. Since the displaced group, X^- , also has unshared pairs of electrons, it seems reasonable that the reaction consists of a nucleophilic attack of Y^- on carbon, in which the unshared pair on Y^- forms the new $C-Y$ bond and displaces X^- with its electron pair. This attack may occur on the side of the carbon atom opposite to that to which the displaced group is attached. Therefore, the halogen exchange of phenacyl halide in anhydrous acetone is believed to be a bimolecular

Table 1. Summary of rate constants for the reaction: $C_6H_5COCH_2X + Y^* \rightarrow C_6H_5COCH_2Y^* + X^-$ in acetone

		$k(1 \text{ mole}^{-1} \text{ sec}^{-1})^*$		
X	Temp	Cl	Br	I
	Y			
Cl	35°C	1.54		
	30	1.03	1.56×10^{-1}	2.33×10^{-1}
	25	5.93×10^{-1}	8.40×10^{-2}	1.56×10^{-1}
	0.1		6.31×10^{-3}	1.32×10^{-2}
Br	25**	41.09	30.38	80.96
	0.1	8.27	3.03	8.86
	-11	3.67	9.43×10^{-1}	2.87

*: Reproducibilities were better than $\pm 6\%$

**: This row contains calculated values.

displacement reaction, $\text{SN}_2^{15)}$.

Table 2 shows the ratio of the rate constants for halogen exchange of phenacyl halides to those of benzyl halides in anhydrous acetone.

Table 2.		k_p/k_b			
X	Temp.	Y	Cl	Br	I
Cl	25° C		210	47	96
Br	0*		—	48	269

*: k_p values were at 0.1°C

k_p : Rate constant for phenacyl halide.

k_b : Rate constant for benzyl halide.

Accordingly, phenacyl halide carbonyl carbon center is more reactive than benzyl carbon center,⁴⁾ and this trend is enhanced when the leaving group is bromine. This may be explained that when the β carbon atom attached directly to the reaction center is unsaturated to be sp^2 , the reactivity increases. The increased reactivity may be due in part to a steric effect. However, the steric effect is not the only factor of importance. Stabilization by overlap of the orbital by which X and Y are bound with the p orbitals on the adjacent sp^2 carbon atom and the oxygen as in Fig. 2 may also be important.¹⁷⁾ This overlap will be larger for the more bulky and polarizable group.

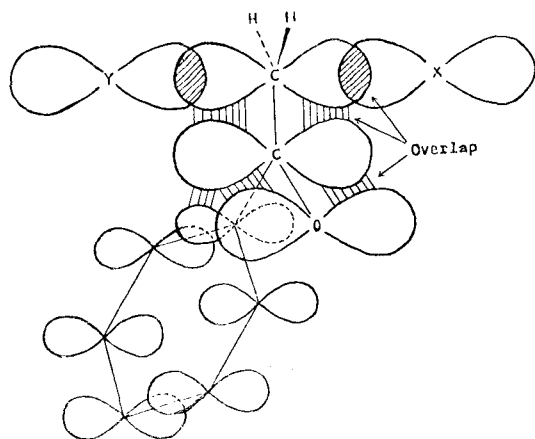


Fig. 2. Transition state model.

Table 3 shows that the orders of nucleophilicity of free halide ions in anhydrous acetone are $\text{Cl}^- > \text{I}^- > \text{Br}^-$ for PC and $\text{I}^- > \text{Cl}^- > \text{Br}^-$ for PB. The normal order expected in dipolar aprotic solvent is $\text{Cl}^- > \text{Br}^- > \text{I}^-$ as stated before. Therefore, it may be said that ground state solvation effect of halide ions is more important than the symbiotic stabilization effect at the transition state for PC, and that the softness of the substrate and solvation effect of the halide ions influence the reaction competitively for PB.

Table 3. Relative nucleophilicity

X	Temp	Y	Cl	Br	I
Cl	30° C		1.0	0.15	0.23
	25		1.0	0.14	0.26
	0.1			1.0	2.11
Br	25		1.0	0.37	1.07
	0.1		1.0	0.26	0.78
	-11		1.0	0.74	1.97

In other word, both solvation effect and polarizability are in general important in determining the nucleophilic reactivities of anionic nucleophile and they are competitive. By HSAB principle, the increased coordination number in transition state puts an increased negative charge on carbon center and makes it softer. So, if the softness of the substrate increases remarkably, the nucleophilic order of halide ions will be $\text{I}^- > \text{Br}^- > \text{Cl}^-$ even in dipolar aprotic solvents.

Relative leaving ability is shown in Table 4. The leaving ability between PC and PB differs very much and the order of leaving ability is $\text{Cl} < \text{Br}$ regardless of the variety of the nucleophile, which is in accord with the accepted general trends for these types of reactions.

Table 4. Relative leaving ability.

X \ Y			
	Cl	Br	I
Cl	1	1	1
Br	69.3	4813.8	6114.8

It will be concluded that the rate constant depends on the nature of the leaving group X. As the strength of the R-X bond increases, the rate with constant nucleophile Y decreases. And when the softnesses of both X and Y increase, leaving ability increases. Moreover, since acetone is a soft solvent, reactivity is accelerated. And also, the basicity difference will be important in determining the reactivity difference¹⁸⁾.

Activation parameters summarized in Table 5 and Table 6 were calculated by the following relationship.

$$K = \frac{kT}{h} e^{-\Delta H^* / RT} e^{\Delta S^* / R} \quad (5)$$

Activation enthalpies of PC are similar to those of PB except PB-Cl. While, the values of ΔH^* and ΔS^* of PC are smaller by about 10 to 22 Kcal and about 17 to 28 *e.u.* respectively than those of benzyl chloride⁴⁾. The unsaturation of β carbon atom and the overlapping of the orbital cause the increase of the reactivity as stated before, which means the decrease of ΔH^* by the equation (5). The decrease of ΔS^* of PC than that of benzyl chloride may be due to the interference with electron-withdrawing carbonyl group in rotation around the $C\alpha-C\beta$ bond in the transition state¹⁵⁾. Appearance of the negative activation entropy may be rationalized that the orderliness of the solvent in the whole reaction system is decreased by the formation of new polarity of transition state. While, the values, of ΔF^* and ΔS^* of PB show small differences than those of benzyl bromide.

Equation (5) gives the correlations of the

Table 5. Activation enthalpies, ΔH^* (Kcal)

X \ Y			
	Cl	Br	I
Cl	16.8	16.7	14.8
Br	9.9	14.4	13.9

Table 6. Activation entropies, ΔS^* (*e.u.*)

X \ Y			
	Cl	Br	I
Cl	-3.2	-7.0	-12.5
Br	-18.1	-3.4	-3.0

rate constant with ΔH^* and ΔS^* , that is, the smaller both ΔH^* and $-\Delta S^*$ are, the greater the rate constant is. In phenacyl halide, however, the compensation rule, which states that ΔH^* and ΔS^* compensate each other and the linearity exists between them, does not hold good. Among the various causes of that, overlap stabilization effect of the transition state may be an important factor¹⁾

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