

<Original> **Kinetic Studies on Halogen Exchange
Reactions of Phenethyl Chloride in Acetone**

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(Received November 23, 1974)

Abstract

Kinetics of halogen exchange reaction of 1-phenethyl chloride and 2-phenethyl chloride using radioisotopic tracer halide ions in acetone have been studied.

The reactions were believed to be S_N2 processes and the orders of relative nucleophilicity of halide ions were $Cl^- > Br^- > I^-$.

The reaction rate is slower than that of benzyl chloride.

These were interpreted in terms of solvation effect of halide ions and HSAB principle.

요 약

1-Phenethyl Chloride 와 2-Phenethyl Chloride 의 할로젠 교환반응 속도를 아세톤 용매속에서 방사성 할라이드 이온을 사용하여 측정하였으며, 활성화 엔탈피와 활성화 엔트로피를 결정하였다.

이 반응은 S_N2 반응이며 할라이드 이온의 상대적 친핵성의 순서는 $Cl^- > Br^- > I^-$ 이고 반응 속도는 Benzyl Chloride 와 비교해 볼때 대체적으로 느리다. 이 결과를 할라이드 이온의 용매화 효과와 HSAB 원리로 설명하였다.

1. Introduction

Extensive studies on halogen exchange reactions have been reported for benzyl chloride¹⁾.

It has been shown that substituents at active sites (starred ortho- or para-position) of benzyl system increase rates considerably while substituent at inactive site decrease rate.



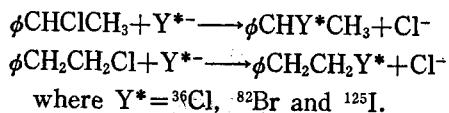
For phenethyl system, which is not con-

jugated, the effect of benzene ring is expected to decrease or to have no effect on rate, and thus slower reaction rate than benzyl chloride is predicted.

Only report appeared so far concerning the halogen exchange reaction on phenethyl chloride is a chloride-chloride exchange in acetonitrile solvent with tetraethyl ammonium chloride²⁾.

In this work, the kinetics of halogen exchange of 1-phenethyl chloride and 2-phenethyl chloride in acetone, a dipolar aprotic solvent, carried out by using radioisotopic tracer halide

ions is reported.



The rate constants k which were corrected for effect of ion-pair association, and activation parameter, $\Delta H^\ddagger, \Delta S^\ddagger$ calculated are reported and the reaction mechanism is discussed.

2. Experimental

1) Materials

1-Phenethyl chloride (Tokyo Kashei industrial Co. Ltd) and 2-phenethyl chloride (Aldrich chemical Co. Inc.) were purified by distillation under reduced pressure.

$\text{LiCl}, (\text{C}_2\text{H}_5)_4\text{NBr}, \text{KI}$ were Merck G.R. reagents, which were used without further purification.

Acetone was purified by drying over calcium chloride before fractional distillation using a Todd Column (reflux ratio 10:1) and was dehydrated by flowing through the alumina column. This treatment reduces the water content to 0.08% or less³⁾

Radioactive ${}^{36}\text{Cl}$ (HCl form) and ${}^{125}\text{I}$ (NaI form) were purchased from the Radiochemical Center, Amersham, Buckinghamshire, England, and ${}^{82}\text{Br}[(\text{C}_2\text{H}_5)_4\text{NBr form}]$ was supplied by the radioisotope Production Group, Korea Atomic Energy Research Institute.

2) KINETIC RUNS were conducted as described before⁴⁾. ${}^{36}\text{Cl}$ activity was counted by using Aloka-1600 Liquid Scintillation Counter, and ${}^{82}\text{Br}$ and ${}^{125}\text{I}$ Activities were measured by using Well-type Scintillation Counter.

Exchange rate were calculated by the equation.

$$k = -\frac{1}{a+b} \cdot \frac{1}{at} (1-F)$$

for chloride exchange, and

$$k = -\frac{c-b}{a-b} \cdot \frac{1}{Dt} (1-F)$$

for bromide and iodide exchange reactions where a and b are initial concentration of substrate and salt, respectively, and

$$C = \frac{1}{2} (D + K + 4b)$$

$$D = (K^2 + 4Kb)^{\frac{1}{2}}$$

where K is the ion pair dissociation constants in acetone, F is the fraction reacted at time t , α is the degree of dissociation of salt.

Activation parameters were calculated by general method based on absolute rate theory.

The plot of $-\log(1-F)$ versus t was linear. A typical plot is given in Fig 1.

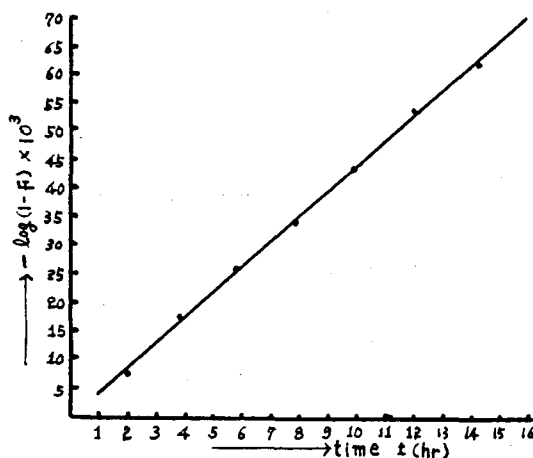
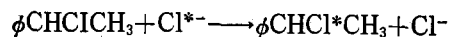


Fig 1. A typical plot of $-\log(1-F)$ vs. t of chloride-chloride exchange at 65°C for the reaction.



The rate constant determined in this way proved reproducible to $\pm 5\%$. Thus the accuracy of ΔH^\ddagger and ΔS^\ddagger was estimated ± 1.0 Kcal/mole and ± 2.0 e.u., respectively.

The accuracy of ΔH^\ddagger and ΔS^\ddagger will not improve greatly even though they were calculated with rate constant at more than two temperatures.

Thus we have calculated the activation

parameters from rate constant k at two temperatures since we are only concerned with general trends of the activation parameters in this work.

3. Results and Discussion

Halogen exchanges of 1-phenethyl chloride and 2-phenethyl chloride in acetone are second order and typical direct displacement reactions. The rate constant at 55°C and 65°C are summarized in Table 1.

Table 1. Summary of rate constants $k \times 10^4 (M^{-1} \text{sec}^{-1})$ for halogen exchange of 1-phenethyl chloride and 2-phenethyl chloride in acetone.

		Cl ⁻	Br ⁻	I ⁻
$\phi\text{CH}\cdot\text{Cl}\cdot\text{CH}_3$	$k_1(55^\circ\text{C})$	5.91	1.34	0.87
	$k_2(65^\circ\text{C})$	17.6	3.41	1.84
$\phi\text{CH}_2\cdot\text{CH}_2\text{Cl}$	$k_1(55^\circ\text{C})$	14.3	1.46	0.50
	$k_2(65^\circ\text{C})$	40.4	3.78	1.17

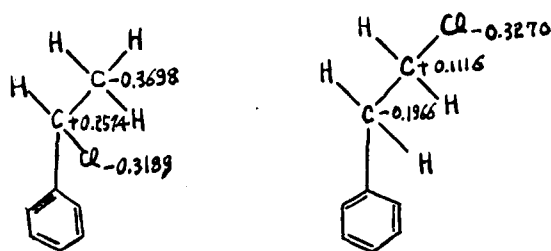
The exchange reaction rate constant in Table 1 shows that the order of reaction rate coincide with the nucleophilicity of halide ion, $\text{Cl}^- > \text{Br}^- > \text{I}^-$, in dipolar aprotic solvent such as acetone⁹. It is the reverse order of that found in water, a protic solvent, and in good accord with solvation effect of the halide ions.

According to HSAB principle^{7,8,9,10} the hard base Cl^- is better solvated than soft I^- in water, hard solvent, and soft I^- is better solvated than hard Cl^- in soft solvent such as acetone¹⁰. The better solvated ion is more difficult to disolvate in forming transition state¹⁰ and the reaction rate decreases. Consequently, we can understand that the order of nucleophilicity of halide ions reversed when solvent changed from water to acetone.

The rate of 2-phenethyl chloride is faster,

more than two times, in Cl^- exchange, and slower, about two third times in I^- exchange, as compared with that of 1-phenethyl chloride.

According to the EHT analysis (Fig 2)¹¹, the carbon atom at the reaction center of 1-phenethyl chloride is more positive than that of 2-phenethyl chloride.



1-Phenethyl chloride.

2-Phenethyl chloride.

Fig 2. Results of EHT analysis (from ref-11)

In spite of the larger positive charge, the chloride ion exchange rate of the 1-phenethyl chloride is believed to be smaller owing to the steric hindrance by CH_3 -group.

In the case of I^- exchange however the rate of 1-phenethyl chloride becomes faster than that of 2-phenethyl chloride as expected from the calculated positive charges on the reaction center. This can be explained when the transition state structures including the attacking halides are considered. Thus in the case of I^- exchange, loose transition state seems to develop as well solvated I^- ion is still in the early attacking stage and hence no steric hindrance with the CH_3 -group is expected.

Table 2 shows that the orders of nucleo-

Table 2. Relative nucleophilicity ($k_{\text{Y}^-}/k_{\text{Cl}^-}$) at 55°C

	Y ⁻		
	Cl ⁻	Br ⁻	I ⁻
$\phi\text{CH}_2\text{CH}_2\text{Cl}$	1.0	0.1	0.04
ϕCHClCH_3	1.0	0.22	0.15
* $\phi\text{CH}_2\text{Cl}$	1.0	0.64	0.57

* from ref (1)

Table 3. Summary of activation parameters for halogen exchange of 1-phenethyl chloride and 2-phenethyl chloride in acetone.

		Cl ⁻	Br ⁻	I ⁻
ϕCHClCH_3	ΔH^\ddagger (Kcal/mole)	23.4	20.0	15.8
	ΔS^\ddagger (e. u)	-2.10	-15.7	-27.8
$\phi\text{CH}_2\text{CH}_2\text{Cl}$	ΔH^\ddagger (Kcal/mole)	22.2	20.3	18.1
	ΔS^\ddagger (e. u)	-3.8	-14.5	-23.2

philicity of free halide ions in acetone are $\text{Cl}^- > \text{Br}^- > \text{I}^-$ for 1-phenethyl chloride, 2-phenethyl chloride, and benzyl chloride.

But relative nucleophilicity of Br^- and I^- decreases in sequence $\phi\text{CH}_2\text{Cl} > \phi\text{CHClCH}_3 > \phi\text{CH}_2\text{CH}_2\text{Cl}$. This is not unexpected since Br^- and I^- are softer than Cl^- and the hardness of the reaction center carbon atom increases in that order $\phi\text{CH}_2\text{Cl} < \phi\text{CHClCH}_3 < \phi\text{CH}_2\text{CH}_2\text{Cl}$, successively.

The rate constant k decreases in the same order for iodide exchange and this is also in accord with the above argument.

Table 3 shows the activation enthalpy ΔH^\ddagger and entropy ΔS^\ddagger which were calculated from rate constants, k at two temperatures. It shows that the order of the activation enthalpy ΔH^\ddagger is similar to the order of nucleophilicity, $\text{Cl}^- > \text{Br}^- > \text{I}^-$.

This implies that the greater nucleophilicity is, the tighter the transition state (I) becomes.

Therefore I^- ion forms loose transition state (II) as compared with Cl^- ion and bond

formation is more important in controlling the reaction rate.

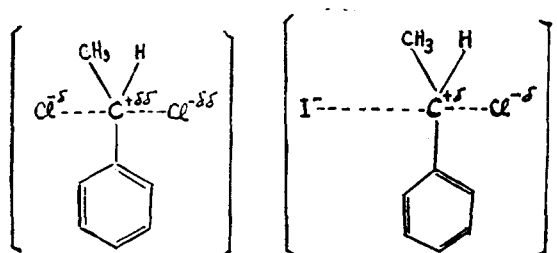
In case of Cl^- , bond-formation proceeds to the same degree as bond breaking, thus forms a symmetrical transition state, while in the case of I^- bond-formation proceeds in much less degree as compared with that of Cl^- , requiring relatively less energy.

These tendencies are also shown in activation entropy ΔS^\ddagger value, *i.e.*, the charge of Cl^- is dispersed in the transition state and therefore do not show so large entropy decrease, but in case of I^- , the loose transition state accompanies charge separation, and will bring about great entropy decrease.

In conclusion, the reaction rate of 1-, 2-phenethyl chloride is slower than benzyl chloride, expectedly, but the relative reactivity of halide ion shows the same tendencies.

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