친핵치환반응에 미치는 용매효과 (제 1 보)
메탄올-아세토니트릴 혼합용매에서 *t*-Butylbromide
및 Benzoylchloride 의 가메탄올 분해반응

李海晃 · 羅相武* · 李金春

仁荷大學校 理科大學 化學科

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Effects of Medium on Nucleophilic Substitution Reactions (I).
Methanolysis of *t*-Butylbromide and Benzoylchloride
in Methanol-Acetonitrile Mixtures

Hai Whang Lee, Sangmoo La* and Ikchoon Lee

Department of Chemistry, College of Science, Inha University,
Incheon 160, Korea

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요 약. *t*-Butylbromide 와 benzoylchloride 의 가메탄올 분해반응을 메탄올-아세토니트릴 혼합용매 하에서 연구하였다. *t*-Butylbromide 의 가메탄올 분해반응 일차속도상수는 온도 변화가 25~50°C 일 때 메탄올의 몰분율 0.75~0.9 부근에서 최대치를 보였다. Benzoylchloride 의 경우에는 겉보기 2 차 반응속도 상수가 온도 변화 12~26°C 일때 메탄올의 몰분율 0.6~0.75 에서 역시 최대치를 보였다. 최대속도는 용매구조 변화에 기인함을 알았는데 메탄올에 아세토니트릴이 첨가됨에 따라 자유 메탄 올 분자가 증가하여 *t*-butylbromide 및 benzoylchloride 의 가메탄올 분해반응에서 천이상태의 안정 화에 기여함을 알았다. 메탄올은 *t*-butylbromide 의 가메탄올 분해반응의 경우 친전자 및 친핵 촉매 작용을, benzoylchloride 의 가메탄올 분해반응의 경우에는 친전자 촉매작용을 함을 알았다.

ABSTRACT. A kinetic study of the methanolysis of *t*-butylbromide and benzoylchloride in me-thanol-acetonitrile mixtures is reported. First order rate constants for the methanolysis of *t*-butyl bromide show maximum at $X_{MeOH} = 0.75 \sim 0.9$ and 25~50°C. Apparent second order rate constants for the methanolysis of benzoylchloride also show maximum at $X_{MeOH} = 0.6 \sim 0.95$ and 12~26°C. The maximum rate is ascribed to the solvent structure change; the addition of acetonitrile to me-thanol perturbs the methanol structure increasing the free methanol molecules available to stabilize the transition state for the methanolysis of *t*-butylbromide and benzoylchloride. It has been shown that methanol acts as nucleophilic and electrophilic catalyst upon methanolysis of *t*-butylbromide and as electrophilic catalyst upon methanolysis of benzoylchloride.

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*Deptartment of Chemical Engineering, Ajou Institute of Technology, Suweon 170, Korea

李海晃・羅相武・李益春

1. INTRODUCTION

It is well known that methanol–acetonitrile solvent mixtures can be treated as quasi-isodielectric solvents. But methanol ($D=32.63$: protic solvent) and acetonitrile ($D=36.02$: dipolar aprotic solvent) have different solvating properties and these can be used to obtain more information on specific solvent effects.

Some of the physical properties of methanol–acetonitrile mixtures show anomalies:

(1) The value of viscosity shows minimum at $X_{MeOH} \simeq 0.2$ and furthermore shows deviation from the curve at $X_{MeOH} \simeq 0.7$ in the plot of viscosity $vs.$ X_{MeOH} at 25°C. [1]

(2) Walden products for tetramethyl, tetraethyl, tetrabutyl and tetrahexylammonium perchlorate show a systematic deviation from the smooth curve at $X_{MeOH}=0.7 \sim 0.9$ in the plot of Walden product $vs.$ X_{MeOH} at 25°C. [2]

(3) The value of density shows maximum at the composition of $X_{MeOH} \simeq 0.8$, 25°C. [1]

(4) The value of excess molar volume shows minimum at the composition of $X_{MeOH} \simeq 0.75$, 25°C. [2]

Such behaviours seem to be related to the change in the structure of the solvent mixtures and solvent heterogeneity may be maximum at $X_{MeOH}=0.7 \sim 0.8$.

But the plot of dielectric constant $vs.$ X_{MeOH} shows smooth curve without notable deviations. [1] It means that the bulk solvent effect (electrostatic interaction) of methanol–acetonitrile mixtures upon any solutes does not change significantly in all the spectrum of solvent mixtures.

The aim of this work is to study the solvent effects on two reactions; methanolysis of t-butylbromide which proceeds via S_N1 [3] and methanolysis of benzoylchloride which proceeds via $S_A N$ [4] mechanism in methanol–acetonitrile mixtures.

2. EXPERIMENTAL

Materials. Benzoylchloride was purified by distillation under reduced pressure and t-butylbromide was purified by distillation. Methanol and acetonitrile were purified by conventional procedures.

Kinetic Measurements. First order rate constants were measured by conductivity method. Solvent mixtures were made up by weight.

3. RESULTS AND DISCUSSION

3.1 Methanolysis of t-Butylbromide. First order rate constants k_1 are summarized together with activation parameters in $Table$ 1.

$Table$ 1. First order rate constants* and activation parameters** for the methanolysis of t-butylbromide at various mole fraction of methanol in methanol–acetonitrile mixtures.

X_{MeOH}	k_1 (sec^{-1}) $\times 10^4$				ΔH^{*} (kcal)	$-\Delta S^{*}$ (e.u.)
	25 °C	35 °C	40 °C	50 °C		
1	0.397	1.56	2.65	8.41	22.8	2.2
0.901	0.531	1.79	3.05	10.1	22.0	4.4
0.799	0.540	1.94	3.31	10.3	22.0	4.3
0.749	0.555	1.89	3.22	9.90	21.5	6.0
0.698	0.525	1.74	3.08	9.32	21.4	6.2
0.601	0.484	1.55	2.74	8.12	21.0	8.2
0.502	0.430	1.31	2.32	7.25	21.0	8.1

*The values of k_1 were reproducible to $\pm 2\%$. **The values of activation parameters are at 25 °C.
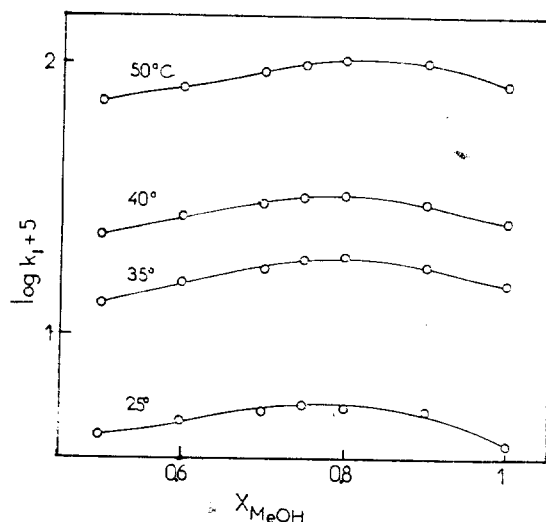
Fig. 1. Plot of log k_1 vs. X_{MeOH} for methanolysis of t-BuBr in MeOH-MeCN mixtures.

Fig. 1 shows a plot of log k_1 vs. X_{MeOH}.

From the tendency of changes in rate constants, it can be approximately seen that the rate constant at 25 °C shows maximum at X_{MeOH}=0. 75~0. 8, at 35 °C at X_{MeOH}≃0. 8, at 40 °C at X_{MeOH}≃0. 8, and at 50 °C at X_{MeOH}=0. 8~0. 9.

Arcoria et al.[5] reported that the second order rate constant for the reaction of 2-thiophenesulphonylchloride with p-anisidine in methanol-acetonitrile mixtures at 25 °C shows maximum at X_{MeOH}≃0. 9. A maximum rate in mixed solvents was also observed by Foon and Hambly[6] and by Ciuffarin et al.[7] for the neutral hydrolysis of aliphatic sulphonylchloride in water-acetone mixtures and for the reaction of benzenesulphonylchloride with pyridine and primary amines in water-dioxane, water-acetonitrile and water-ethanol mixtures. They have ascribed the maximum rate to the break up of the solvent structure for the cosolvent addition. Arcoria et al.[5] explained that the addition of the cosolvent to methanol depolymerises it by increasing the amount of protic solvent available to make hydrogen bonds with the negative end of intermediate and hence increases the reaction rate.

A further addition of the aprotic solvent, decreasing the electrophilic solvation power of the medium, makes the reaction rate lower.

If specific solvations do not play an important role for methanolysis of t-butylbromide which proceeds via S_N1 mechanism, the rate constants would be independent of solvent composition and have nearly constant values since bulk solvent effect is expected to remain approximately the same over all the solvent composition range in methanol-acetonitrile mixtures.

Neutral polar molecules, particularly those which are not strong H-bond acceptors, are known to be more solvated by aprotic solvent than by protic solvent because of highly ordered, hydrogen bonded structures, of protic solvent.[8] But the difference of degree of solvation would be small for t-butylbromide toward solvent changes from pure methanol to pure acetonitrile. Furthermore the addition of acetonitrile to methanol breaks up the highly ordered methanol structure and thus the solvation power of the solvent mixture for t-butylbromide which are not strong hydrogen bond acceptor would be nearly the same in mixed solvents. Therefore the problem of ground state solvation can be neglected for methanolysis of t-butylbromide and hence the rate maximum can be attributed to transition state solvation.

Protic solvents are known to be far more effective in solvation of small (hard) anions, e. g., for F⁻, OH⁻, Cl⁻, than dipolar aprotic ones, owing to their ability to act as hydrogen bond donors. On the other hand, dipolar aprotic solvents, although generally regarded as anion-desolvator[9,10], often interact strongly and specifically (mutual polarizability interaction) with large, polarizable (soft) anions[9,11], e. g., for SCN⁻, I_3^-, I⁻. Bromide anion is known as boderline ion, but still similar to hard anions. This can be supported by Parker's result.[12]

Parker indicated qualitatively that the crossover point, at which anions change from being more solvated in methanol to more solvated in dimethylformamide, may be thiocyanate ion, SCN^-.

D'Aprano *et al.*[13] reported that cation solvation by methanol is greatest for small cations, *e. g.*, Li^+, Na^+, K^+, and is least for large cations, *e. g.*, tetrahexyl, tetraisoamyl, tetrabutyl ammonium ions. On the other hand cation solvation by acetonitrile is greatest for large cations and least for small cations. They also showed[2] that cation solvation by methanol still plays an important role for tetramethylammonium ion. Therefore *t*-butylium ion may be more solvated by methanol than by acetonitrile.

The addition of acetonitrile to a methanolic solution perturbs the methanol structure and the amount of free methanol molecules which are not bound to polymer chain increases. The transition state for methanolysis of *t*-butylbromide may be a highly charge seperated ion pair $(CH_3)_3C^+\cdots Br^-$, and both sites, positive and negative sites, would be more solvated as increasing the amounts of free methanol molecules and hence the reaction rate increases. But further addition of acetonitrile decreasing the

electrophilic and nucleophilic solvation power of the solvent makes the reaction rate slower.

The fact that the maximum rate is attributed to the change of solvent structure can be proved by temperature effect. Methanol structure perturbation may increase when the temperature raises. The amount of acetonitrile to break up the methanol structure would be smaller at higher temperature than at lower temperature. So the solvent composition of the maximum rate changes from $X_{MeOH} \simeq 0.75$ at 25 °C to $X_{MeOH} \simeq 0.85$ at 50 °C.

It is notable that the maximum rate in methanol-acetonitrile solvent system can be observed even at relatively high temperature of 50 °C in comparison with the results of other workers[6,7] showing the maximum rate at the lowest temperature (0~15 °C) where the protic solvent has the most organised structure.

The activation parameters in *Table* 1 shows relatively large activation enthalpy values (21 ~23kcal) and relatively small negative activation entropy values (2~8 e. u.). This is consistent with general S_N1 reaction types.[14]

3. 2 Methanolysis of Benzoylchloride. First order rate constants are summarized in

Table 2. First order rate constants* and activation parameters** for the methanolysis of benzoylchloride at various mole fraction of methanol in methanol-acetonitrile mixtures.

X_{MeOH}	$k_1 (sec^{-1}) \times 10^3$				$\Delta H^{\ddagger}$ (kcal)	$-\Delta S^{\ddagger}$ (e. u.)
	0 °C	12 °C	20 °C	26 °C		
1	0.495	1.53	2.93	5.14	13.9	22.7
0.919	0.549	1.57	2.82	4.90	12.9	26.2
0.859	0.542	1.57	2.78	4.64	12.7	26.9
0.787	0.511	1.53	2.77	4.40	12.8	26.5
0.765	0.491	1.45	2.74	4.36	13.0	25.7
0.742	0.491	1.39	2.77	4.19	12.9	26.1
0.684	0.471	1.31	2.46	3.76	12.4	28.0
0.656	0.458	1.24	2.34	3.55	12.3	28.7
0.575	0.440	1.12	1.99	3.02	11.4	31.8
0.393	0.287	0.646	1.11	1.75	10.6	35.8

*The values of k_1 were reproducible to $\pm 2\%$. **The values of activation parameters are at 20 °C.
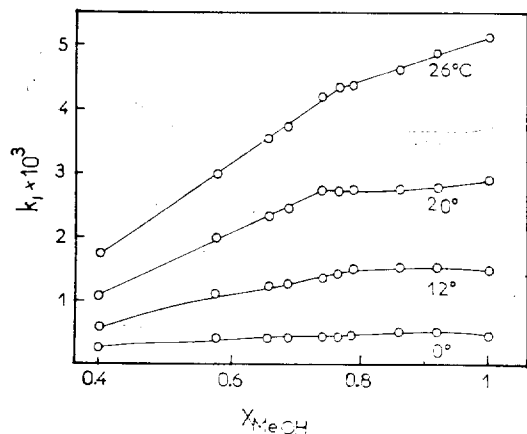
Fig. 2. Plot of k_1 vs. X_{MeOH} for methanolysis of benzoylchloride in MeOH–MeCN mixtures.

Table 2 and are plotted as a function of solvent composition in *Fig.* 2.

First order rate constants show maximum at the composition of $X_{MeOH} \simeq 0.9$ at lower temperature 0 and 12 °C. Raising the temperature to 20°C, rate constants roughly show isokinetics at $X_{MeOH} = 0.75 \sim 1$ and slows down rapidly at $X_{MeOH} < 0.75$. At higher temperature 26 °C, rate constant decreases as decreasing the mole fracti on of methanol but the decreasing curve shows deviation at $X_{MeOH} \simeq 0.75$ as shown in *Fig.* 2. These phenomena also indicate that the reaction system is strongly influenced by solvent structure changes as it was for methanolysis of t-butylbromide.

In order to investigate the actual solvent effect, we calculated apparent (although not real) second order rate constants by dividing first order rate constants by concentration of methanol since the methanolysis of benzoyl-chloride proceeds *via* bimolecular mechanism. The apparent second order rate constants, k_2, are summarized in *Table* 3 and are plotted as a function of solvent composition X_{MeOH}, in *Fig.* 3. *Table* 3 and *Fig.* 3 show that the rate at 26°C shows maximum at $X_{MeOH} \simeq 0.75$, at 20 °C at

Table 3. Apparent second order rate constants* for the methanolysis of benzoyl chloride at various mole fraction of methanol in methanol–acetonitrile mixtures.

X_{MeOH}	$k_2(l \cdot mole^{-1} \cdot sec^{-1}) \times 10^5$			
	0 °C	12 °C	20 °C	26 °C
1	2.02	6.23	11.9	20.9
0.919	2.49	7.12	12.8	22.2
0.859	2.62	7.58	13.4	22.4
0.787	2.80	8.40	15.2	24.1
0.765	2.79	8 23	15.5	24.7
0.742	2.89	8.18	16.3	24.7
0.684	3.06	8.50	16.0	24.4
0.656	3.13	8.46	16.0	24.2
0.575	3.47	8.83	15.7	23.8
0.393	3.49	7.85	13.5	21.2

*k_2 was obtained by $k_1/(CH_3OH)$ and the values of (CH_3OH) were taken from ref. (1)

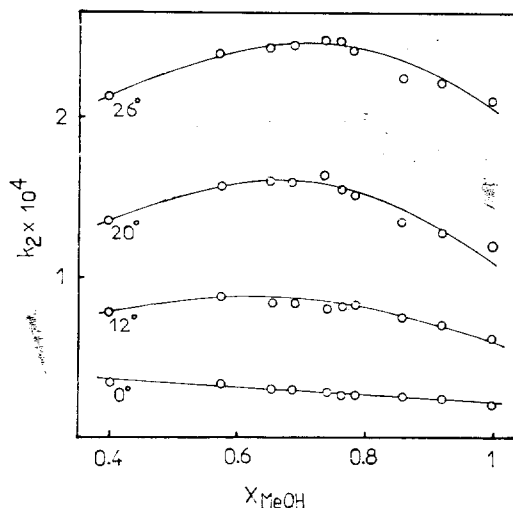*Fig.* 3 Plot of k_2 (apparent second order rate constant; $l \cdot mole^{-1} \cdot sec^{-1}$) vs. X_{MeOH} for methanolysis of benzoylchloride in MeOH–MeCN mixtures.

$X_{MeOH} = 0.7 \sim 0.75$, at 12 °C at $X_{MeOH} \simeq 0.6$ and the rate at 0 °C shows gradual increase as decreasing X_{MeOH} in the solvent composition studied. This is in accord with the results of methanolysis of t-butylbromide for which the solvent composition of maximum rate shifted to larger value of X_{MeOH} by raising temperature.

The reaction mechanism for methanolysis of benzoylchloride may be addition–elimination. It is reasonable to assume that the first transition state is bond formation and the second transition state is bond breaking. If the bond formation step is rate determining one, specific solvation of free methanol molecules will have no significant role to play in giving a rate maximum because the change seperation is much larger in the second transition state than in the first transition state. It means that the bond breaking step is rate determining and hence the electrophilic solvation of leaving group, Cl^-, by methanol is important. Once again without considering the problem of the ground state solvation (possibly increase in solvation by methanol) the second transition state stabilization increases due to the increment of free methanol molecules which results in the rate maximum.

The activation parameters in *Table* 2 shows relatively small activation enthalpy values (11 ~14 kcal) and relatively large negative activation entropy values (22~36 e. u.) which are different from what we found methanolysis of t-butylbromide. These activation parameters are consistent with the values for general S_N2 or S_AN reaction types.[14]

ACKNOWLEDGEMENT

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