

Phenacy Bromide 와 置換아닐린類와의 反應에 關한 反應速度論的 研究

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Kinetics of the Reaction of Phenacyl Bromide with Anilines in Methanol and Dimethylformamide

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요 약. 페나실브로미드와 치환아닐린류와의 반응속도를 메탄올과 DMF 중에서 전기전도도 법으로 측정된 결과 반응속도는 치환기의 전자를 주는 능력이 강할 수록 빨랐으며, 메탄올 속에서 보다 DMF 속에서 더 빨랐다. ΔH^\ddagger 와 ΔS^\ddagger 사이에서는 등속 관계가 성립하였으며, 이때 등속 온도는 메탄올에서는 539 °K, DMF에서는 400 °K였다. 그러나 *p*-니트로 아닐린은 용매효과 때문에 직선에서 벗어났다. Brønsted plot의 경우 메탄올과 DMF에서 $\log k = 0.57pK_a - 1.28$ ($r = 0.996$) in MeOH at 45 °C; $\log k = 0.65pK_a - 0.88$ ($r = 0.970$) in DMF at 45 °C,로서 좋은 직선관계가 성립하였다.

Hammett σ 도식 결과 이 반응은 아닐린의 친핵치환 반응이었으며, 다음의 식이 얻어졌다.

$\log k/k_0 = -2.00\sigma + 0.06$ ($r = 0.985$) in MeOH; $\log k/k_0 = -2.22\sigma + 0.08$ ($r = 0.995$) in DMF.

그리고 DMF에서 4-NO₂기가 직선에서 벗어났다. 이는 치환기에 의한 용매효과에 기인하는 것이라고 생각된다. 이상의 결과로부터 본 반응의 친환기 효과는 전이상태에서 결합의 형성이 보다 우세한 S_N2 메카니즘으로 진행되고 있으며, 결합의 형성은 DMF 용매에서 더욱 진행되고 있다.

Abstract. The rates and the activation parameters for the reaction of phenacyl bromide with substituted anilines in methanol and dimethylformamide were measured. The effects of substituted anilines were discussed.

The rate of the reaction was increased with the electron donating power of substituent and showed larger value in DMF than in MeOH.

The isokinetic relationship was shown between ΔH^\ddagger and ΔS^\ddagger , isokinetic temperature was 539 and 400 °C in MeOH and DMF respectively, but *p*-nitro aniline was deviated from linearity in both solvents caused by solvent effects.

The excellent linear relationship between $\log k$ and pK_a of substituted anilines was observed by following equation. $\log k = 0.57pK_a - 1.28$ ($r = 0.996$) in MeOH at 45 °C, $\log k = 0.65pK_a - 0.88$ ($r = 0.970$) in DMF at 45 °C. From the Hammett plot, this reaction was a nucleophilic displacement of aniline to phenacyl bromide and the following equation was obtained at 45 °C

$\log k/k_0 = -2.00\sigma + 0.06$ ($r = 0.985$) in MeOH; $\log k/k_0 = -2.22\sigma + 0.08$ ($r = 0.995$) in DMF

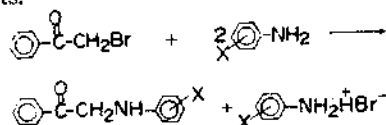
Large deviation of *p*-nitro aniline in DMF is resulted from solvent effects too.

From above results, the substituent effect of this reaction can be described as S_N2 mechanism and bond formation more proceeds in DMF relative to MeOH.

INTRODUCTION

The effects of the solvents and substituents upon the reaction of the substituted phenacyl bromides with substituted pyridines, Menshutkin reaction, had been shown to be important by many workers¹⁻⁴. The reaction, in which ions are formed from electrically neutral reagents, proceeds more rapidly in solvents of high dielectric constants. However a similar study of the phenacylation of aniline system does not seem to have been made so far, except for few substituted phenacyl bromide with aniline of S_N2 mechanism in methanol only by Cox⁵.

We therefore thought it of interest to investigate the solvent and substituent effect for the reaction of phenacyl bromide with many substituted anilines in dipolar aprotic and protic solvents.



For this purpose we chose methanol and dimethylformamide (DMF), two solvents having very similar dielectric constants, in order to focus, as much as possible, solely upon the differences between a protic and a dipolar aprotic solvents.

EXPERIMENTAL

Materials and Instruments: All materials used throughout were commercial products (Wako, Japan). Liquid anilines were a commercial product purified by several distillations over potassium hydroxide before use, but solide ones were recrystallized before use. All purified anilines were stored in brown ampoule or bottle filled with nitrogen gas. Dimethylformamide was purified by distillation after standing with anhydrous magnesium sulfate for 3 days at room

temperature. Conductance measurements were used with Chemtrix Type 70 Conductivity meter (U. S. A.)

Phenacyl Aniline. While stirring, the temperature was kept at 30 °C in water bath, 10 g (0.05 mol) of phenacyl bromide was dissolved in 40 cc of methanol and subsequently 10 g (0.11 mol) of aniline was added.

After stirring for 1 hour at same temperature, the products obtained were separated from solvent and washed with petroleum ether and cold water several times.

Recrystallization from methanol gave yellowish crystals m. p 92 °C (*lit*⁶, 93 °C), yields 82 %.

Kinetics. The rate of reaction was measured by means of electric conductivity because the reaction is a kind of formation of salt, anilinium bromide, which was made by hydrobromide produced in the reaction with anilines of excess. A typical kinetic run is briefly described as follows: The final concentration of phenacyl bromide prepared was made just 0.005 mole/l in 15 ml volume flask which was filled with nitrogen gas and solvent. That of aniline was made just 0.2 mole/l with above same method. A kinetic run was initiated by placing 15 ml of aniline solution in the conductivity cell and adding same amount of the phenacyl bromide solution to give a reaction mixture that was 0.10 mole/l in aniline and 0.0025 mole/l in phenacyl bromide. All measurements were done with anilines in large excess over phenacyl bromide. Pseudo first-order rate constant of the reaction of the phenacyl bromide with aniline was obtained. Generally, pseudo first-order rate constant was obtained by

$$\ln \frac{a}{a-x} = \frac{\lambda_\infty - \lambda_0}{\lambda_\infty - \lambda_t} = kt \quad (1)$$

where, λ_0 : Initial electric conductivity, λ_∞ : Electric conductivity at the terminal period as

the 100 % reaction, λ_t : Electric conductivity at time t .

The reproducibility of the data (λ_{∞} and λ_0) was difficult to be determined, so the pseudo first-order rate constant was calculated from the Guggenheim equation⁷

$$kt + \ln(\lambda' - \lambda) = \text{constant} \quad (2)$$

where, λ : Electric conductivity at time t , λ' : Electric conductivity at time $t + \Delta$, Δ is constant increment (ca. 2~3 times of half-time).

An example of the results obtained by the above procedure is in Table 1. The plot of $\ln(\lambda' - \lambda)$ against time shows good linearity (Fig. 1). Second order rate constants were calculated from the slopes of plots of the observed first order rate constant against pyridine concentration. Activation energies were calculated from Arrhenius plot and activation entropies were obtained using the theory of absolute reaction rate

$$k = \frac{KT}{h} e^{AS^\ddagger / R} e^{-\Delta H^\ddagger / RT}$$

RESULTS AND DISCUSSION

The present paper reports the results of an investigation to determine the substituent effects of anilines and solvent effects for the reaction of phenacyl bromide with substituted anilines.

nes.

The kinetic data and activation parameters for that reactions in methanol and DMF are given in Table 2 and 3.

Table 1. The rate of phenacyl bromide with aniline in MeOH at 35 °C.

Time (min)	λ_t (μmho)	$t + \Delta$ ($\Delta = 380 \text{ min}$)	$\lambda'_{t+\Delta}$	$\log(\lambda'_{t+\Delta} - \lambda_t)$
5	15.5	385	313	2.4735
10	29.0	390	314	2.4548
15	40.8	395	315	2.4381
20	52.0	400	316	2.4216
25	62.5	405	316.9	2.4057
30	72.7	410	317.9	2.3897
35	82.7	415	319	2.3735
40	92.0	420	320	2.3579
45	101.0	425	321	2.3424

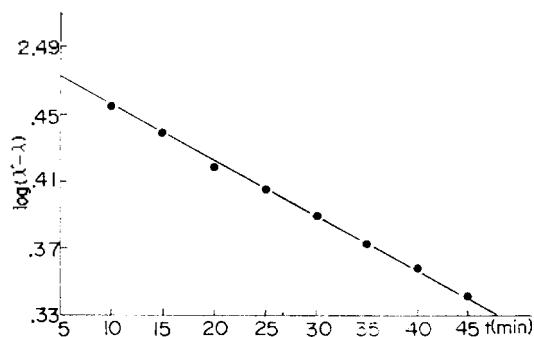


Fig. 1. The kinetic plot for the reaction of aniline with phenacyl bromide in MeOH at 35 °C.

Table 2. Kinetic data for the reaction of phenacyl bromide with anilines in MeOH.

No.	Substituent	$k_2 \times 10^4$ (l/mol·min)			ΔH^\ddagger (kcal/mol)	$-\Delta S^\ddagger$ (e. u)	ΔG^\ddagger (kcal/mol)
		35°C	45°C	55°C			
1	4-OCH ₃	46.0	87.5		11.9	30.7	21.7
2	4-CH ₃	20.1	45.0	93.4	15.1	22.0	22.1
3	3-CH ₃	15.1	32.8	58.3	14.4	24.6	22.2
4	H	12.3	21.8	43.0	13.4	28.7	22.5
5	3-OCH ₃	10.4	20.2		12.2	32.6	22.6
6	4-Cl	5.4	10.3		11.9	34.9	23.0
7	4-Br	4.5	7.9		10.3	40.6	23.2
8	3-Cl	1.3	3.2		17.0	21.3	23.8
9	3-NO ₂		0.9	2.2	18.1	20.4	24.6
10	4-NO ₂		0.8	1.7	16.2	26.6	24.7

Table 3. Kinetic Data for the Reaction of Phenacyl bromide with Anilines in DMF

No.	Substituent	$k \times 10^4$ (l/mol·min)			ΔH^\ddagger (kcal/mol)	$-\Delta S^\ddagger$ (e. u)	ΔF^\ddagger (kcal/mol)
		35°C	45°C	55°C			
1	4-OCH ₃	328.6	484.4		6.9	42.9	20.5
2	4-CH ₃	116.5	228.0	333.6	12.4	27.1	21.0
3	3-CH ₃	83.7	158.4	255.6	11.8	29.8	21.3
4	H	51.1	95.5	188.6	13.0	25.5	21.6
5	3-OCH ₃	45.0	93.5		13.6	25.3	21.6
6	4-Cl	22.2	44.3		12.8	29.1	22.0
7	4-Br	15.2	32.8		14.4	24.9	22.3
8	3-Cl	13.1	29.5		15.2	22.5	22.4
9	3-NO ₂		6.5	10.3	8.7	45.8	23.3
10	4-NO ₂		36.9	77.5	14.7	23.5	22.2

Rate constants and Activation parameters.

The rate constants for the reaction of phenacyl bromide with substituted anilines were shown that electron-donating substituents in the anilines increase the rate, while electron-attracting ones decrease in both solvents. Although the effect on the rate of a change from a polar protic to a dipolar aprotic solvent is not great and both rate increases and rate decreases have been reported, there does seem to be a consistent decrease in the enthalpy of activation in the dipolar aprotic solvent.

This decrease in ΔH^\ddagger can be attributed to two possible causes. The first, and most common, explanation is that desolvation of nucleophile or base in the aprotic solvent relative to the protic solvent raises the energy of the reactants, thus diminishing the energy gap between the reactants and the transition state. The second explanation is that the lowering of the activation energy is caused by increased solvation of the transition state in the dipolar aprotic solvent.

The decrease in the ΔH^\ddagger for the Menshutkin reaction on going from a polar protic to a dipolar aprotic solvent is quite large and is of the same order of magnitude as that observed for S_N2 reaction having a negatively charged

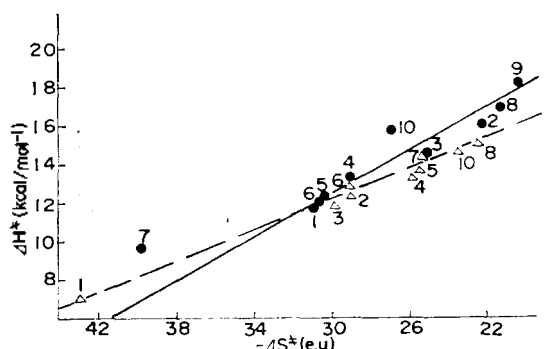


Fig. 2. The isokinetic relationship for the reaction of phenacylbromide with substituted anilines in MeOH (●) and DMF(Δ).

nucleophile³⁻⁹.

A plot of ΔH^\ddagger vs. ΔS^\ddagger for these reactions in a pair of solvents yielded good correlation line with an isokinetic temperature of 539, 400°K in MeOH and DMF respectively (Fig. 2).

The relationship,

$$\Delta\Delta H^\ddagger = \beta\Delta\Delta S^\ddagger \quad (4)$$

was first recognized by Leffler, who collated examples of experimental results illustrated this idea, where β is the constant of proportionality, the slope of the line obtained when $\Delta\Delta H^\ddagger$ is plotted against $\Delta\Delta S^\ddagger$: which is rearranged to give

$$\Delta\Delta G^\ddagger = (1 - T/\beta)\Delta\Delta S^\ddagger \quad (5)$$

When $\beta = T$, $\Delta\Delta G^\ddagger = 0$, and no variation of rate

will be expected when substituents or media are changed.

At temperature below β , the reaction rate is controlled mainly by $\Delta\Delta H^\ddagger$. In this region the reaction with the lowest activation energy will react fastest.

We have also found such a result from this present and other study,¹³⁻¹⁵ in which charge of N atom at the transition state has electronic interaction with substituents of anilines, consequently, this reaction was controlled by activation enthalpy.

Activation entropy caused by its interaction between charge and solvent was accompanied by activation enthalpy according to substituents.

Brønsted Linear Relationship. The efficiency of general base catalysts increases with increasing base strength of the catalyst, and the slope of a plot of $\log k_B$ against pK_a of a series of catalysts is a measure of the sensitivity of the reaction to the strength of the base catalyst. These relationships are defined by the Brønsted equations.

$$\log k_B = \beta pK_a + \log G_B \quad (6)$$

where k_B is the rate constant, β and G_B are constants characteristic of the reaction, solvent and temperature.

It was generally accepted that Brønsted linear relationship was shown between reaction rates and basicities of nucleophiles in which attacking atom is the same in S_N2 reaction.

Good linearity of this Brønsted relationship has been reported on quaternization of substituted N,N -dimethylanilines and pyridines. In the present paper reports the results of a good linear relationship between $\log k$ against pK_a of anilines (Fig. 3).

$$\log k = 0.57pK_a - 1.28 \quad (r=0.996)$$

in MeOH at 45°C

$$\log k = 0.65pK_a - 0.88 \quad (r=0.970)$$

in DMF at 45°C

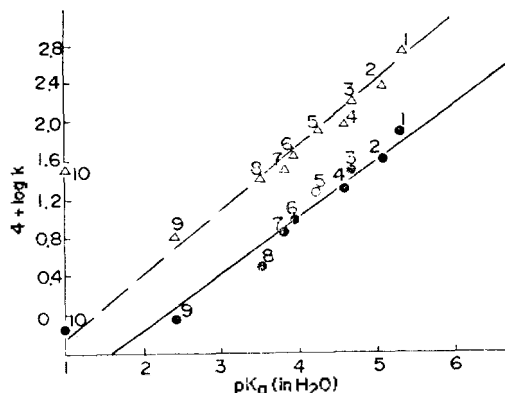


Fig. 3. Correlation between $\log k$ and pK_a for the reaction of phenacyl bromide with anilines in MeOH (●) and DMF (△) at 45°C.

These difference β values agreed with that of isokinetic temperature of the reaction of phenacyl bromide with anilines in MeOH and DMF. From the above β value, it can be inferred that C-N bond formation decreases from DMF to MeOH.

In Fig. 3, p -NO₂ aniline was deviated from the linearity in both solvents and so much faster than any other substituents. This may be resulted from solvent effect: pK_a values of anilines were determined in water, but these reaction were carried out in DMF and MeOH.

NO₂ group has hydrogen bond in water, but this bond become weaker in methanol and disappear entirely in DMF, so NO₂ group, especially p -NO₂ aniline causes in resonance, indicated stronger electron donating power than water.

This p -NO₂ aniline, therefore, accelerated the rates of reactions in both solvents.

$\log k - \log k_0$ plot for the reaction of phenacyl bromide with anilines in MeOH and DMF are good correlated with 0.90 of slope ($r=0.988$) (Fig. 4.). From good correlation, it was considered that the reaction mechanism has not

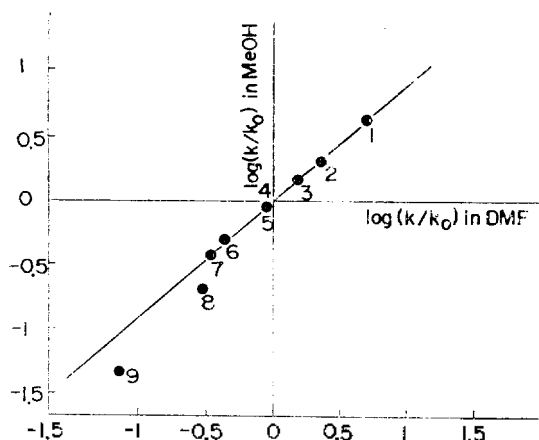


Fig. 4. Plot of the rate constant for the reaction of phenacyl bromide with anilines in DMF and MeOH at 45 °C.

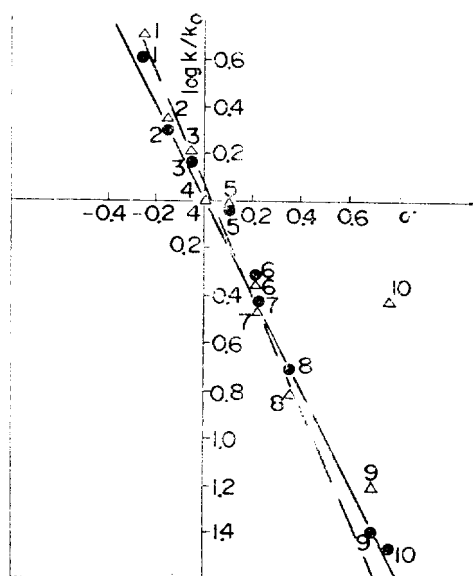


Fig. 5. Hammett plot for the reaction of phenacyl bromide with anilines in MeOH (●) and DMF (Δ) at 45 °C.

different from both solvent, but the slope for the reaction in DMF is larger than that in MeOH. The reason is, in DMF, greater susceptibility to the substituent effect than that in MeOH.

Hammett Relationship. The Hammett ρ

value for the reaction of phenacyl bromide with substituted anilines was large and negative: the reaction rate is very sensitive to substituents and increased with electron donating power of substituents of anilines.

This reaction, therefore, is a nucleophilic displacement of aniline to phenacyl bromide and the following equation was obtained from the Fig. 5

$$\log k/k_0 = -2.00\sigma + 0.06 \quad (r=0.985)$$

in MeOH at 45 °C

$$\log k/k_0 = -2.22\sigma + 0.08 \quad (r=0.995)$$

in DMF at 45 °C

The size of ρ is an indication of the extent of charge development at the atom of the reacting side chain adjacent to the ring in passing from ground to transitionstate. For the two reaction solvents shown, DMF and MeOH, there is some difference in ρ (-2.22 and -2.00 respectively), as well as in the rate constants of the unsubstituted aniline (0.0051 and 0.0012 mol⁻¹s⁻¹ respectively).

This reflects the difference in solvation properties of the solvents, the polar protic solvent stabilising the polar transition state more efficiently than the DMF and bond formation is less progressive than DMF. This result agreed with that of isokinetic temperature in two solvents, so S_N2 reaction is more proceeded in DMF relative to MeOH. Large deviation of 4-NO₂ aniline in DMF is resulted from solvent effect already discussed, *i.e.* no hydrogen bond with DMF so that 4-NO₂ group made not so stronger electron attracting power, these results caused an acceleration of the reaction rate.

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