Kinetics and Mechanism of the Aminolysis of Thiophenyl Methylacetates in Acetonitrile

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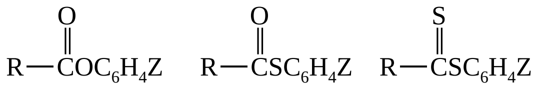
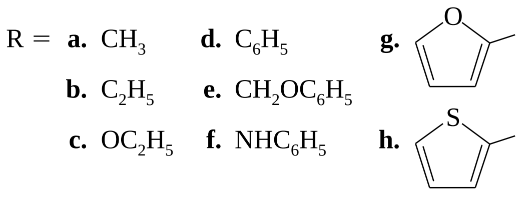
ABSTRACT: The aminolysis of Z-thiophenyl methylacetates ($C_2H_5C({=}O)SC_6H_4Z$) with X-benzylamines in acetonitrile has been investigated at 45°C. The reaction is found to proceed by a stepwise mechanism in which the rate-determining step is the breakdown of the zwitterionic tetrahedral intermediate, $T^{\pm}$, with possibly a hydrogen-bonded four-center-type transition state. These mechanistic conclusions are drawn based on (i) the large magnitude of β_X ($= 1.2 \sim 2.5$) and β_z ($= -0.9 \sim -1.5$), (ii) the normal kinetic isotope effects ($k_H/k_D \cong 1.2$) involving deuterated benzylamines ($XC_6H_4CH_2ND_2$), (iii) a large positive ρ_{xz} ($= 2.4$) and (iv) adherence to the reactivity-selectivity principle in all cases. The extremely large β_X (β_{nuc}) values can be accounted for by the loss of a strong localized cationic charge on the N atom of benzylamines in the expulsion from the $T^{\pm}$. The pK_a^{o} (≥ 10.0) is high due to a large ratio of the expulsion rates of the amine (k_{-a}) to thiophenolate (k_b) (k_{-a}/k_b) from the $T^{\pm}$. © 2000 John Wiley & Sons, Inc. Int J Chem Kinet 32: 485–490, 2000

INTRODUCTION



$R{-}C({=}O)OC_6H_4Z$ $R{-}C({=}O)SC_6H_4Z$ $R{-}C({=}S)SC_6H_4Z$

I **II** **III**



R = **a.** CH_3 **d.** C_6H_5 **g.**
b. C_2H_5 **e.** $CH_2OC_6H_5$
c. OC_2H_5 **f.** NHC_6H_5 **h.**

The mechanism of aminolysis of oxyesters **(I)** has been extensively studied. In contrast, relatively little is known about the mechanism for the aminolysis of thiol esters **(II)**. The Brønsted-type plots for the reactions of primary, secondary, and tertiary amines with oxyesters [e.g., substituted phenyl acetates **(Ia)** and benzoates **(Id)**], show a break at pK_a^{o} from a large ($\beta_{nuc} = 0.9 \pm 0.1$) to a small ($\beta_{nuc} = 0.2 \pm 0.2$) dependence of the rate on the basicity of the attacking amine, which has been interpreted to indicate a mechanistic changeover from a breakdown to formation of the tetrahedral intermediates, $T^{\pm}$ [1–3]. Our previous work on the aminolysis of thiol esters [e.g., thiophenyl benzoates **(IId)**] with benzylamines [4], however, showed an unusually large $\beta_{nuc}(\beta_X)$ value of 1.86 in acetonitrile, which was considered to proceed through a rate-limiting breakdown of $T^{\pm}$. Benzylamines are primary amines with relatively high basicities ($pK_a \geq 9.0$) due to localized cationic charge on the benzylam-

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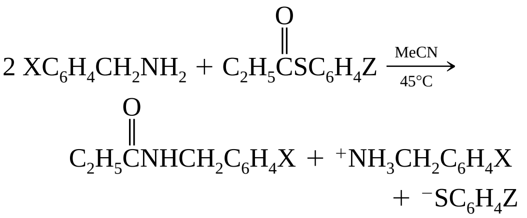
Correspondence to: I. Lee (ilee@dragon.inha.ac.kr) monium ion. Benzylamines' relative leaving ability from $T^{\pm}$ can be much different from that of anilines (also a primary amine, but the positive charge in the anilinium ion delocalizes into the ring leading to smaller pK_a values) and the secondary and tertiary amines, especially from a sulfur zwitterionic tetrahedral intermediate, since it is known that ArS^- is a poorer nucleofuge from a tetrahedral intermediate than an isobasic ArO^- group [5–8].

In this work, we carried out kinetic studies on the aminolysis of thiophenyl methylacetates **(IIb)** with benzylamines in acetonitrile at 45°C, Eq. (1). We aim to elucidate the mechanism of the aminolysis, Eq. (1), of thiol esters with an ethyl group, C_2H_5 **(IIb)** rather than phenyl, C_6H_5 **(IId).** Our interests in this work also lie in the unusually large $\beta_{nuc}(\beta_X)$ values obtained in the aminolysis of thiol esters with benzylamines in acetonitrile, and application of the cross-interaction constant [9–10], ρ_{xz} in Eq. (2), where X and Z denote substituents in the nucleophile and leaving group, respectively, as a mechanistic tool.



$$2\,XC_6H_4CH_2NH_2 + C_2H_5\overset{\overset{O}{\|}}{C}SC_6H_4Z \xrightarrow[45^\circ C]{MeCN} C_2H_5\overset{\overset{O}{\|}}{C}NHCH_2C_6H_4X + {}^+NH_3CH_2C_6H_4X + {}^-SC_6H_4Z \quad (1)$$

$$\log(k_{XZ}/k_{HH}) = \rho_X\sigma_X + \rho_Z\sigma_Z + \rho_{XZ}\sigma_X\sigma_Z \quad (2a)$$

$$\rho_{XZ} = \partial\rho_Z/\partial\sigma_X = \partial\rho_X/\partial\sigma_Z \quad (2b)$$

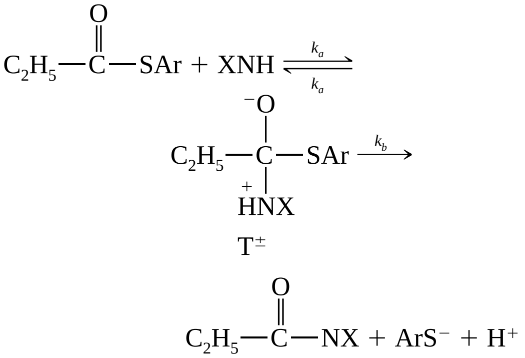
RESULTS AND DISCUSSION

The aminolysis of thiophenyl methylacetates **(IIb)** with a large excess of benzylamines in acetonitrile obeyed the simple kinetic law given by Eqs. (3) and (4), where P is thiophenolate anion and N is benzylamine. Plots of k_{obs} against [N] were linear, and the k_N values were determined from the slopes of these plots. The k_N values are summarized in Table I, where the ρ_x, $\beta_x(\beta_{nuc})$, ρ_Z, and $\beta_Z(\beta_{lg})$ values are also shown.

$$d[P]/dt = k_{obs}\,[\text{substrate}] \quad (3)$$

$$k_{obs} = k_N\,[N] \quad (4)$$

The clean second-order kinetics obtained, Eqs. (3) and (4), is an indication that there are no complications arising from competition of the fast proton transfer from an intermediate $T^{\pm}$, nor from general base catalysis by the amines. The mechanism of the reaction can, therefore, be described completely by Eq. (5), where $Ar = C_6H_4Z$, XNH represents benzylamines with substituent X. The proton transfer can occur during or after the rate-limiting step, k_b. The proton is of course rapidly consumed as XNH_2^+ under the excess amine concentration, as shown in Eq. (1).



$$C_2H_5-\overset{\overset{O}{\|}}{C}-SAr + XNH \underset{k_a}{\overset{k_a}{\rightleftharpoons}} \underset{T^{\pm}}{C_2H_5-\underset{\underset{HNX}{+|}}{\overset{\overset{^-O}{|}}{C}}-SAr} \xrightarrow{k_b} C_2H_5-\overset{\overset{O}{\|}}{C}-NX + ArS^- + H^+ \quad (5)$$

$$k_N = \frac{k_a}{k_{-a}}\,k_b = K\,k_b \quad (6)$$

Since the reactions were conducted in acetonitrile, the magnitude of $\beta_X(\beta_{nuc})$ and $\beta_Z(\beta_{lg})$ determined using the pK_a values in water may not be reliable. However, as we have pointed out previously [11–12], the β_X values can be considered to represent reliable values, although the absolute values of pK_a in MeCN differ from those in water, a constant ΔpK_a ($pK_{CH3CN} - pK_{H2O} \cong 7.7 \pm 0.3$) was experimentally found [13]. Our recent theoretical work of the solvent effects on the basicities of pyridines [14] has shown that the ΔpK_a ($\cong 7.7$) value arises solely from the ion solvation energy difference of H^+ ion in water and in acetonitrile, $\delta\Delta G_s^o(H^+) = 10.5$ kcal mol^{-1}, which corresponds to $\Delta pK_a = 7.7$, at the MP2/6-31G*//MP2/6-31G* level [15] of theory. Moreover, we are comparing the magnitude of β_X and β_Z values determined for the reactions carried out under the same reaction condition (i.e., in acetonitrile). Since we used pK_a values of thiophenolates in water, the comparison of β_Z values may not be entirely reliable.

We note that the magnitude of β_X in Table I ($\beta_X = 1.2 \sim 2.5$) is considerably larger than those for the corresponding reactions with anilines [16] and other secondary and tertiary amines ($\beta_X = 0.6 \sim 1.0$) proceeding by rate-limiting breakdown (k_b) of a zwitterionic tetrahedral intermediate, $T^{\pm}$, Eq. (5). On this account (i.e., large β_X values), the aminolysis of thiophenyl methylacetates with benzylamines in acetonitrile, Eq. (1), is most likely to occur by rate-limiting expulsion, k_b, in Eq. (5), of thiophenolate ion, ArS^-, from $T^{\pm}$.

Table I The Second-Order Rate Constants $k_N \times 10^3$ dm^3 mol^{-1} s^{-1} for the Reactions of Z-Thiophenyl Methylacetates with X-Benzylamines in Acetonitrile at 45°C

	Z					
X	*p*-Me	H	*p*-Cl	*m*-Cl	ρ_Z[a]	β_Z[b]
p-OMe	13.6 10.7[c] 8.29[d]	26.8	92.1	185 146 114	2.12 ± 0.09	−0.90 ± 0.01
p-Me	78.2	16.2	66.0	141	2.37 ± 0.11	−1.01 ± 0.01
H	3.08	7.37	34.4	90.6	2.74 ± 0.11	−1.18 ± 0.02
p-Cl	0.759	2.34	14.6	47.5	3.33 ± 0.10	−1.39 ± 0.05
ρ_X[a]	−2.48 ± 0.03	−2.09 ± 0.02	−1.62 ± 0.01	−1.18 ± 0.01		
β_X[e]	2.51 ± 0.01	2.11 ± 0.01	1.64 ± 0.02	1.20 ± 0.01		

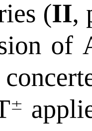
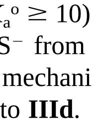
[a] The σ values were taken from Dean, J. A. Handbook of Organic Chemistry; McGraw-Hill: New York, 1987; Table 7–1. Correlation coefficients were better than 0.998 in all cases.

[b] The pK_a values were taken from Buckingham, J. Dictionary of Organic Chemistry; Chapman and Hall; New York, 1982; 5th, ed. The pK_a value for Z = m-Cl was estimated using p$K_a = -2.36\sigma + 6.45$ ($n = 3$, $r = 0.996$). Correlation coefficients were better than 0.998 in all cases.

[c] At 35°C.

[d] At 25°C.

[e] The pK_a values were taken from Fischer, A.; Galloway, W. J.; Vaughan, J. J Chem Soc 1964, 3588. Correlation coefficients were better than 0.999 in all cases. The pK_a value for X = p-CH$_3$O was estimated using the relation: p$K_a = -1.057\sigma \pm 9.355$ ($n = 13$, $r = 0.984$).

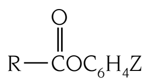
We have compared β_X and β_Z values for the aminolysis reactions of various thiol esters with benzylamines in acetonitrile in Table II. The magnitude of both β_X and β_Z is large compared to those for the corresponding reactions with anilines and other secondary and tertiary amines proceeding by rate-limiting breakdown of $T^\pm$. For example, the aminolysis of phenyl dithiobenzoates **(IIId)** with anilines [17] gave the β_X values ranging from 0.80 to 1.07 in acetonitrile at 55°C. This reaction is believed to proceed by rate-limiting breakdown of $T^\pm$. Similarly, for the aminolysis of dithioacetates [11] **(IIIa)** with anilines and *N,N*-dimethylanilines in acetonitrile, the β_X values of 0.80 ~ 0.87 were obtained. For these two series, **IIIa** and **IIId**, the push provided by ArS from $T^\pm$ to expel the amine, benzylamine, is much hindered (i.e., k_{-a}/k_b is reduced) due to change of  $-\overset{O^-}{\underset{|}{\overset{|}{C}}}-$ to  $-\overset{S^-}{\underset{|}{\overset{|}{C}}}-$ in $T^\pm$ [18]. It is known that the decrease in k_{-a}/k_b either by increasing k_b with a better nucleofuge or by decreasing k_{-a} with a weakly basic amine leads to a lowering of pK_a^o, where $k_{-a} = k_b$ [8].Thus the pK_a^o value should be lower in the dithio series (**III**, p$K_a^o \leq 9.0$) than that in the corresponding thiol series (**II**, p$K_a^o \geq 10$). This is the reason why the expulsion of ArS$^-$ from $T^\pm$ is rate-limiting for **IId**, while a concerted mechanism or a rate-limiting formation of $T^\pm$ applies to **IIId**.

The β_X (β_{nuc}) values for the aminolysis with benzylamines for which breakdown of $T^\pm$ is rate-limiting are large ($\beta_X = 1.2 \sim 2.5$). For such mechanism, the observed k_N is a complex quantity given by Eq. (6). Therefore, the dependence of log k_N on the basicity of amines becomes

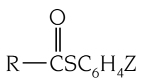
$$\begin{aligned}\beta_X\ (= \beta_{nuc}) &= d\log k_N/dpK_a(X)\\ &= d\log k_a/dpK_a(X)\\ &\quad - d\log k_{-a}/dpK_a(X)\\ &\quad + d\log k_b/dpK_a(X) \qquad (7)\end{aligned}$$

The rate constant for leaving group expulsion from $T^\pm(k_b)$ can be safely assumed to be independent of the nature of the attacking amine nucleophile [2,19], so that the last term in Eq. (7) vanishes. On the other hand, it is well known that the β_X values for the rate-limiting formation of $T^\pm(\beta_a)$ is lower with 0.2 ~ 0.3, β_a ($= d\log k_a/dpK_a(X)$) $\cong$ 0.2 ~ 0.3 [2]. This means that the observed $\beta_X(\beta_{nuc}) = 1.2 \sim 2.5$ for the aminolysis with benzylamines lead to the β_{-a} ($= d\log k_{-a}/dpK_a(X)$) value of $-0.9 \sim -2.2$ [$= (0.2 \sim 0.3) - (1.2 \sim 2.5)$]. For aniline nucleophiles, $\beta_X \cong 0.8 \sim 1.0$ so that $\beta_{-a} = -0.5 \sim -0.7$. Thus the loss of a strong localized cationic charge on the nitrogen atom of benzylammonium ion in the $T^\pm$ is so large that the benzylamine expulsion rates from $T^\pm$ are 2 ~ 3 times more sensitive to the substituent variation in the benzylamine than the sensitivity of aniline expulsion rates from the corresponding $T^\pm$ to the substituent charge in the aniline. For this reaction, the ratio k_{-a}/k_b is also high so that the pK_a^o lies above the pK_a's of the con-

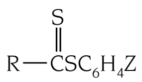
Table II The $\beta_X(\beta_{nuc})$ and $\beta_Z(\beta_{lg})$ Values for Acyl Transfer Reactions with Benzylamine Nucleophiles in Acetonitrile


$R{-}\overset{\overset{\displaystyle O}{\|}}{C}OC_6H_4Z$

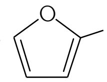
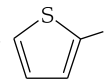
I


$R{-}\overset{\overset{\displaystyle O}{\|}}{C}SC_6H_4Z$

II


$R{-}\overset{\overset{\displaystyle S}{\|}}{C}SC_6H_4Z$

III

R = **a.** CH_3 **d.** C_6H_5 **g.** 
b. C_2H_5 **e.** $CH_2OC_6H_5$
c. OC_2H_5 **f.** NHC_6H_5 **h.** 

Substrate	β_X[a]	β_Z[a]	Remarks	Ref.
Ic	1.66	−1.71	Z = p-NO_2, 25°C	12
Ie	1.57	−1.77	Z = p-NO_2, 25°C	b
If	1.65		Z = p-NO_2, 25°C	c
Ig	1.06	−1.03	Z = p-NO_2, 25°C	d
IIb	2.11	−1.18	45°C	This work
IId	1.86	−1.63	55°C	e
IIg	1.40	−1.41	50°C	22
IIh	1.53	−1.42	50°C	22
IIIa	0.55	−0.50	20°C	11
IIId	0.60	−0.24	30°C	f
IIIg	1.40	−0.81	15°C	23
IIIh	1.02	−0.56	15°C	23

[a] Unless otherwise noted, β_X is for Z = H and β_Z is for X = H.
[b] Koh, H. J.; Kim, T. Y.; Lee, B. S.; Lee, I. J Chem Res (S) 1996, 482.
[c] Koh, H. J.; Kim, O. S.; Lee, H. W.; Lee, I. J Phys Org Chem 1997, 10, 725.
[d] Koh, H. J.; Lee, J. W.; Lee, H. W.; Lee, I. New J Chem 1997, 21, 447.
[e] Lee, I.; Koh, H. J. New J Chem 1996, 20, 131.
[f] Oh, H. K.; Shin, C. H.; Lee, I. Bull Korean Chem Soc 1995, 16, 657.

jugate acids of benzylamines used in this work. This high ratio of k_{-a}/k_b can be attributed to several factors. (i) The low stability of $T^{\pm}$ formed (larger k_{-a}) by benzylamines due to highly localized cationic charge on the $N^+{-}H$ moiety. The tetrahedral intermediates $T^{\pm}$ formed by anilines and secondary and tertiary amines are relatively stable (smaller k_{-a}) due to cationic charge delocalization to the ring and/or alkyl groups (inductive donors, +I groups) within $T^{\pm}$. (ii) The poorer nucleofugality of ArS^- than ArO^- (smaller k_b) and the stronger "push" provided by the ArS group in $T^{\pm}$ (larger k_{-a}) to expel the amine than that exerted by an isobasic ArO group in an analogous $T^{\pm}$ [8]. The pK_a^o was lower for pyridines than for alicyclic amines under the same reaction conditions due to the lower k_{-a}, whereas it was lower for a more delocalized phenolate ion (2,4,6-trinitrophenolate ion) expulsion due to the higher k_b value [8,20]. (iii) The aprotic solvent,

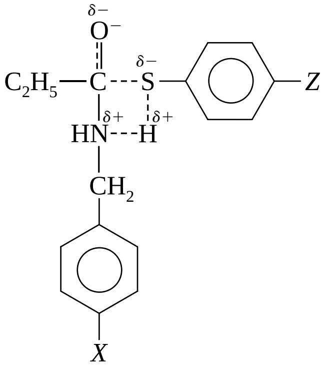
Table III The Secondary Kinetic Isotope Effects for the reactions of Z-Phenyl Thiolmethylacetates with Deuterated X-Benzylamines in Acetonitrile at 45°C

X	Z	$k_H \times 10^4 (M^{-1}\ s^{-1})$	$k_D \times 10^4 (M^{-1}\ s^{-1})$	k_H/k_D
p-OMe	p-Me	1.36 (± 0.02)	1.11 (± 0.02)	1.23 ± 0.03[a]
p-OMe	H	2.68 (± 0.05)	2.19 (± 0.04)	1.22 ± 0.04
p-OMe	pCl	9.21 (± 0.06)	7.62 (± 0.05)	1.21 ± 0.01
p-OMe	m-Cl	18.5 (± 0.3)	15.6 (± 0.2)	1.19 ± 0.02
p-Cl	p-Me	0.0759 (± 0.0004)	0.0612 (± 0.0005)	1.24 ± 0.01
p-Cl	H	0.234 (± 0.003)	0.192 (± 0.004)	1.22 ± 0.03
p-Cl	p-Cl	1.46 (± 0.02)	1.22 (± 0.03)	1.20 ± 0.04
p-Cl	m-Cl	4.75 (± 0.04)	4.03 (± 0.06)	1.18 ± 0.02

[a] Standard deviations.

MeCN, stabilizes the TS for the breakdown of $T^{\pm}$ to form uncharged products (k_{-a}) relative to that for the formation of thiophenolate anion and cationic amide (k_b).

The proposed mechanism is also supported by a large positive cross-interaction constant [9] (ρ_{XZ} = 2.36 ± 0.16, r = 0.999) and adherence to the reactivity–selectivity principle (RSP), which are believed to constitute necessary conditions for the rate-limiting breakdown of $T^{\pm}$ [20,21]. The secondary kinetic isotope effects (Table III) involving deuterated nucleophiles [10], $XC_6H_4CH_2ND_2$, are greater than unity, $k_H/k_D \cong 1.2$. This suggests a possibility of forming hydrogen-bonded, four-center-type TS as has often been proposed [22,23]. However, due to a lower charge on the thiophenolate leaving group, the k_H/k_D values are not high and variations depending on the substituents, X and Z, are small. The low activation parameters, $\Delta H^{\neq}$ and $\Delta S^{\neq}$ (Table IV) are also in line with the mechanism proposed. The expulsion of thiophenolate anion is aided by hydrogen bonding by the benzylamine present in $T^{\pm}$ requiring not much energy in the activation, but highly structured TS leads to large negative entropies of activation.



Proposed TS

SUMMARY

The aminolysis of thiophenyl methylacetates with benylamines in acetonitrile proceeds by rate-limiting expulsion of thiophenolate anion from a tetrahedral zwitterionic intermediate $T^{\pm}$. The extremely large $\beta_X(\beta_{nuc})$ values can be accounted for by a strong localized cationic charge on the nitrogen atom of benzylamines in $T^{\pm}$, which is lost in the benzylamine expulsion from $T^{\pm}$ (k_{-a}). The breakdown rate ratio of k_{-a} (expulsion of amine)/k_b (expulsion of ArS^-) is large due to large k_{-a} and relatively small k_b. The cross-interaction constant ρ_{XZ} is large positive and the RSP is adhered to in all cases. These are in line with the proposed mechanism.

Table IV Activation Parameters[a] for the Reactions of Z-Phenyl Thiolmethylacetates with X-Benzylamines in Acetonitrile

X	Z	$\Delta H^{\neq}$/kcal mol^{-1}	$-\Delta S^{\neq}$/cal mol^{-1} K^{-1}
p-OMe	*p*-Me	4.1 ± 0.1	55 ± 1
p-OMe	*m*-Cl	4.0 ± 0.1	53 ± 1
m-Cl	*p*-Me	4.6 ± 0.1	60 ± 1
m-Cl	*m*-Cl	3.9 ± 0.1	53 ± 1

[a] Calculated by the Eyring equation. Errors shown are standard deviations.

EXPERIMENTAL

Materials

Merk GR acetonitrile was used after three distillations. The benzylamine nucleophiles, Aldrich GR, were used without further purification. Thiophenols and propionyl chloride were Tokyo Kasei GR grade.

Preparations of Phenyl Thiolmethylacetates

Thiophenol derivatives and propionyl chloride were dissolved in anhydrous ether and KOH was added carefully, keeping the temperature at 0 ∼ 5°C. Ice was then added to the reaction mixture and the ether layer was separated, dried over $MgSO_4$, and distilled under reduced pressure to remove solvent. IR (Nicolet 5BX FT-IR) and ^1H and ^{13}C NMR (JEOL 400 MHz) data are as follows.

p-*Methylphenyl Thiolmethylacetate.* Liquid, IR (KBr), 2979 (C—H, CH_2), 2938 (C—H, CH_3), 1494, 1459 (C═C, aromatic), 1710 (C═O); ^1H NMR (400 MHz, $CDCl_3$), 1.61 (3 H, t, CH_3, J = 6.35 Hz), 2.31 (3 H, s, CH_3), 2.60 (2 H, q, CH_2, J = 6.35 Hz), 7.16–7.26 (4 H, m, aromatic ring); ^{13}C NMR (100.4 MHz, $CDCl_3$), 198.4 (C═O), 139.4, 134.4, 129.9, 124.3 (aromatic), 36.9 (CH_2), 21.2 (CH_3), 9.57 (methyl).

Phenyl Thiolmethylacetate. Liquid, IR (KBr), 2993 (C—H, CH_2), 2939 (C—H, CH_3), 1477, 1440 (C═C, aromatic), 1710 (C═O); ^1H NMR (400 MHz, $CDCl_3$), 1.19 (3 H, t, CH_3, J = 6.35 Hz), 2.63 (2 H, q, CH_2, J = 6.44 Hz), 7.41–7.36 (5 H, m, aromatic ring); ^{13}C NMR (100.4 MHz, $CDCl_3$), 198.1 (C═O), 134.5, 129.8, 129.3, 129.0, 127.4 (aromatic), 37.1 (CH_2), 9.58 (methyl).

p-*Chlorophenyl Thiolmethylacetates.* Liquid, IR (KBr), 2980 (C—H, CH_2), 2946 (C—H, CH_3), 1477, 1460 (C═C, aromatic), 1712 (C═O); ^{1}H NMR (400 MHz, $CDCl_3$), 1.18 (3 H, t, CH_3, J = 7.81 Hz), 2.64 (2 H, q, CH_2, J = 7.81 Hz), 7.28–7.35 (4 H, m, aromatic ring); ^{13}C NMR (100.4 MHz, $CDCl_3$), 197.5 (C═O), 135.7, 135.6, 126.3 (aromatic), 37.1 (CH_2), 9.51 (methyl).

m-*Chlorophenyl Thiolmethylacetate.* Liquid, IR (KBr), 2972 (C—H, CH_2), 2932 (C—H, CH_3), 1462, 1408 (C═C, aromatic), 1714 (C═O); ^{1}H NMR (400 MHz, $CDCl_3$), 1.20 (3 H, t, CH_3, J = 7.33 Hz), 2.67 (2 H, q, CH_2, J = 7.33 Hz), 7.27–7.41 (4 H, m, aromatic ring); ^{13}C NMR (100.4 MHz, $CDCl_3$), 197.2(C=O), 134.6, 134.2, 132.6, 130.1, 129.5, 129.4(aromatic), 37.2(CH_2), 9.52(methyl).

Kinetic Measurement

Rates were measured conductometrically at 45.0 ± 0.05°C. The conductivity bridge used in this work was a self-made computer automatic A/D converter conductivity bridge. Pseudo-first-order rate constants, k_{obs}, were determined by the Guggenheim method [24] with large excess of benzylamine, [substrate] ≅ 0.01 M and [benzylamine] = 0.05 ~ 0.1 M. Second-order rate constants, k_N, were obtained from the slope of a plot of k_{obs} vs. [benzylamine] with more than five concentrations of benzylamine in more than three runs and were reproducible to within ±3%.

Product Analysis

Substrate (0.05 M) and benzylamine (0.5 M) were added to acetonitrile and reacted 45°C under the same condition as the kinetic measurements. After more than 15 half lives, the solvent was removed under reduced pressure and the product was separated by column chromatography (silica gel, 20% ethylacetate-*n*-hexane). Analysis of the product gave the following results.

$CH_3CH_2C({=}O)NHCH_2C_6H_4{-}OCH_3$. : m.p, 55–57°C, IR (KBr), 3249 (N—H), 3080 (C—H, benzyl), 2993 (C—H, CH_2), 2946 (C—H, CH_3), 1711 (C═O), 1460 (C═C, aromatic); ^{1}H NMR (400 MHz, $CDCl_3$), 1.12 (3 H, t, CH_3, J = 7.81 Hz), 2.19 (2 H, q, CH_2, J = 7.81 Hz), 3.75 (3 H, s, OCH_3), 4.08 (1 H, br, N—H), 4.29 (2 H, d, J = 5.86 Hz, CH_2), 6.81–7.16 (4 H, m, aromatic ring); ^{13}C NMR (100.4 MHz, $CDCl_3$), 198.2 (C═O), 130.8, 129.3, 129.1 (aromatic), 55.4 (CH_2), 42.87 (CH_2), 21.0 (methyl), 14.18.

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