Nucleophilic Substitution Reactions of Thiophenyl Dimethylacetates and Trimethylacetates with Benzylamines in Acetonitrile

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The kinetics and mechanism of the reactions of thiophenyl dimethylacetates (TDA) and trimethylacetates (TTA) with benzylamines in acetonitrile are studied. The reactions are first order in both the amine and the substrate. Relatively large values of β_X (β_{nuc} = 1.1-1.5; TDA and 1.1-1.5; TTA) and β_Z (β_{lg} = -1.8~-2.0; DTA and -1.3~-1.6; TTA) for benzylamines, significantly large k_H/k_D values (=1.2-1.5; DTA and 1.2-1.5; TTA) involving deuterated benzylamines, and large ρ_{XZ} (=0.82; TDA and 1.05; TTA) values are interpreted to indicate stepwise acyl transfer mechanism, but with the hydrogen bonded four center type transition state for benzylamine. The relatively greater magnitudes of ρ_{XZ} and the secondary kinetic isotope effects involving deuterated nucleophiles are in line with the proposed mechanism.

Keywords : Aminolysis, Kinetics and mechanism, Acyl transfer reaction.

Introduction

The aminolyses of acyl compounds have been studied extensively. Brönsted plots were used in these reactions as mechanistic criteria.[1,2] In many of these nucleophilic reactions curved Brönsted type plots have been found, which have been attributed to a change in the rate-determing step from breakdown ($\beta_{nuc} \cong 0.8$-1.0) to formation ($\beta_{nuc} \cong 0.1$-0.3) of a tetrahedral intermediate, $T^{\pm}$, in the reaction path as a basicity of the amine nucleophile increases.[1-6] The aminolysis of thiophenyl benzoates with benzylamines, however, exhibited an unusually large β_X (β_{nuc} = 1.86) in acetonitrile, which was considered to proceed through a rate-limiting breakdown of a tetrahedral zwitterionic intermediate, $T^{\pm}$. Benzylamines are primary amines with relatively high basicities ($pK_a \geq 9.0$) due to localized cationic charge on the benzylammonium ion and their nucleofugality from $T^{\pm}$ may be much different from that of the secondary and tertiary amines, especially from a sulfur zwitterionic tetrahedral intermediate since it is known that ArS^- is a poorer leaving group from $T^{\pm}$ than an isobasic AeO^- group.[7]

In this work, we investigated the kinetics and mechanism of the aminolysis of thiophenyl dimethylacetates (1) and trimethylacetates (2) with benzylamines in acetonitrile at 55.0 and 60.0 °C, eq. 1 and 2. The objective of the present work is to elucidate the mechanism by determining β_X (β_{nuc}), β_Z (β_{lg}) and cross-interaction constant ρ_{XZ}, eq. 2[8] where X and Z denote substituents in the nucleophile and nucleofuge.

$$2\,XC_6H_4CH_2NH_2 + CH_3(CH_3)CHC(=O)SC_6H_4Z \xrightarrow[55.0\,^{\circ}C]{MeCN} CH_3(CH_3)CHC(=O)NHCH_2C_6H_4X + {}^{+}NH_3CH_2C_6H_4X + {}^{-}SC_6H_4Z \quad (1)$$

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$$2\,XC_6H_4CH_2NH_2 + (CH_3)_3CC(=O)SC_6H_4Z \xrightarrow[60.0\,^{\circ}C]{MeCN} (CH_3)_3CC(=O)NHCH_2C_6H_4X + {}^{+}NH_3CH_2C_6H_4X + {}^{-}SC_6H_4Z \quad (2)$$

respectively.

$$\log(k_{XZ}/k_{HH}) = \rho_X\sigma_X + \rho_Z\sigma_Z + \rho_{XZ}\sigma_X\sigma_Z \quad (3a)$$

$$\rho_{XZ} = \partial\rho_Z/\partial\sigma_X = \partial\rho_X/\partial\sigma_Z \quad (3b)$$

It has been shown that the ρ_{XZ} is large positive and a higher reactivity is invariably accompanied by a smaller magnitude of selectivity parameters, such as ρ and β, *i.e.*, the reactivity-selectivity principle (RSP)[9] holds, for the acyl transfer reactions with rate-limiting breakdown of an intermediate, $T^{\pm}$.[10]

Results and Discussion

The pseudo-first order rate constants observed (k_{obs}) for all reactions obeyed eq. 4 with negligible k_o ($\cong 0$) in acetonitrile. The second-order rate constants, k_2 ($M^{-1}\,s^{-1}$), were obtained as the slopes of the k_{obs} *vs.* benzylamine concentration [N]

$$k_{obs} = k_o + k_2\,[BA] \quad (4)$$

and are summarized in Table 1 and 2, respectively. No third-order or higher order terms in amine were detected and no complications were found neither in the determination of k_{obs} nor in the linear plots of eq. 4. This suggests that there is no base catalysis or noticeable side reactions. The rate is faster with a stronger nucleophile and a better nucleofuge as normally expected from a nucleophilic substitution reaction. The rates for the thiophenyl trimethylacetates are much lower, due most probably to steric effects, than those for the thiophenyl dimethylacetates.

The ρ_X (ρ_{nuc}) and β_X (β_{nuc}) values are presented in Table 1

Table 1. The Second Order Rate Constants, $k_N \times 10^4$ dm^3 mol^{-1} s^{-1} for the Reactions of Thiophenyl Dimethylacetates with X-Benzylamines in Acetonitrile at 55.0 °C

X	Z				ρ_Z[a]	β_Z[b]
	p-Me	H	*p*-Cl	*p*-Br		
p-OMe	5.59	24.8	251	259	4.19 ± 0.10	-1.78 ± 0.09
	3.20[c]			136		
	1.81[d]			72.3		
p-Me	4.03	20.4	195	205	4.26 ± 0.03	-1.81 ± 0.14
H	2.38	11.1	117	135	4.35 ± 0.12	-1.82 ± 0.09
p-Cl	1.13	5.70	61.9	71.7	4.47 ± 0.11	-1.87 ± 0.12
	0.497			39.7		
	0.276			21.9		
m-Cl	0.590	3.59	43.1	51.6	4.76 ± 0.09	-1.99 ± 0.16
ρ_X[e]	-1.49 ± 0.05	-1.33 ± 0.04	-1.21 ± 0.02	-1.11 ± 0.02	ρ_{XZ}[f] =	0.82 ± 0.16
β_X[g]	1.46 ± 0.08	1.30 ± 0. 07	1.18 ± 0.03	1.08 ± 0.03		

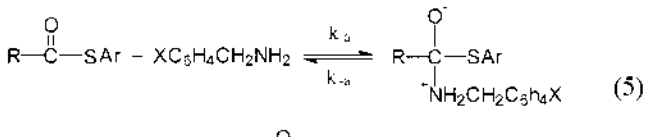
[a]The σ values were taken from J. A. Dean. *Handbook of organic Chemistry*. McGraw-Hill. New York. 1987. Table 7-1. Correlation coefficients were better than 0.999 in all cases. [b]The p*K*a values were taken from ed., J. Bukingham. *Dictionary of Organic Chemistry*. Chapman and Hall. New York. 1982. 5th. ed. Z=p-Br was excluded from the Brönsted plot for β_Z due to an unreliable p*K*a values. Correlation coefficients were better than 0.997 in all cases. [c]At 45 °C. [d]At 35 °C. [e]The σ values were taken from D. H. McDaniel and H.C. Brown. *J. Org. Chem*., 1958. **23**. 420. Correlation coefficients were better than 0.998 in all cases. [f]Correlation coefficients was 0.999. [g]The p*K*a values were taken from A. Fischer, W. J. Galloway and J. Vaughan. *J. Chem. Soc*., 1964. 3588. Correlation coefficients were better than 0.995 in all cases. pK_a= 9.67 was used for X= *p*-CH_3O. (reference H. K. Oh, J. Y. Lee, and I. Lee. *Bull Korean Chem. Soc*., **1998**. 19. 1198.)

Table 2. The Second Order Rate Constants, $k_N \times 10^4$ dm^3 mol^{-1} s^{-1} for the Reactions of Thiophenyl Trimethylacetates with X-Benzylamines in Acetonitrile at 60.0 °C

X	Z				ρ_Z[a]	β_Z[b]
	p-Me	H	*p*-Cl	*m*-Cl		
p-OMe	4.60	14.8	80.3	101	3.26 ± 0.14	-1.34 ± 0.09
	2.77[c]			61.9		
	1.65[d]			37.3		
p-Me	3.15	10.3	61.7	73.0	3.36 ± 0.12	-1.39 ± 0.08
H	1.51	5.52	37.2	47.6	3.65 ± 0.16	-1.49 ± 0.09
p-Cl	0.821	2.93	22.7	28.4	3.78 ± 0.18	-1.56 ± 0.06
m-Cl	0.441	2.03	13.8	19.4	3.94 ± 0.19	-1.59 ± 0.17
	0.260			11.6		
	0.149			6.87		
ρ_X[e]	-1.55 ± 0.07	-1.35 ± 0.06	-1.16 ± 0.05	-1.09 ± 0.03	ρ_{XZ}[f] =	1.05 ± 0.26
β_X[g]	1.53 ± 0.13	1.30 ± 0.08	1.17 ± 0.09	1.06 ± 0.04		

[a]The σ values were taken from J. A. Dean, *Handbook of organic Chemistry*. McGraw-Hill. New York. 1987. Table 7-1. Correlation coefficients were better than 0.998 in all cases. [b]The p*K*a values were taken from ed., J. Bukingham. *Dictionary of Organic Chemistry*. Chapman and Hall. New York. 1982. 5th. ed. Z=*m*-Cl was excluded from the Brönsted plot for β_Z due to an unreliable p*K*a values. Correlation coefficients were better than 0.995 in all cases. [c]At 50 °C. [d]At 40 °C. [e]The σ values were taken from D. H. McDaniel and H.C. Brown. *J. Org. Chem*., 1958. **23**. 420. Correlation coefficients were better than 0.997 in all cases. [f]Correlation coefficients was 0.998. [g]The p*K*a values were taken from A. Fischer, W. J. Galloway and J. Vaughan. *J. Chem. Soc*., 1964. 3588. Correlation coefficients were better than 0.995 in all cases. pK_a= 9.67 was used for X=*p*-CH_3O. (reference H. K. Oh. J. Y. Lee. and I. Lee. *Bull Korean Chem. Soc*., **1998**. 19. 1198.)

and 2. We note that the magnitude of the two selectivity parameters is large. As we have pointed out previously. these β_X values can be considered to represent reliable values since although the absolute values of pK_a in MeCN differ from those in water. a constant $\Delta pK_a(pK_{CH_3CN}-pK_{H_2O} \cong 7.7 \pm 0.3)$ was experimentally found for 22 alkyl and alicyclic amines.[11] Our recent theoretical work of the solvent effects on the basicities of pyridines has shown that the pK_a ($\cong$ 7.7) value arises solely from the ion solvation energy difference of H^+ ion in water and in acetonitrile, $\delta\Delta G_s^\circ$ (H^-)=10.5 kcal mol^{-1} which corresponds to ΔpK_a = 7.7. at the MP2/6-31G*// MP2/6-31G* level.[12] The β_X values (1.1-1.6) obtained in this work are considerably larger than those for the corresponding reactions with anilines[13] and other secondary and tertiary amines (β_X = 0.6-1.0) proceeding by rate-limiting breakdown of a zwitterionic tetrahedral intermediate. $T^\pm$, eq. 4. On this account, *i.e*.. large β_X values obtained. the aminolysis of thiophenyl dimethylacetates and trimethylacetates with benzylamines in acetonitrile is most likely to occur by rate-limiting expulsion of thiophenolate ion, ArS^-, from $T^\pm$ (k_b step). The large β_X values observed with benzylamine nucleophile in the present work are considered to represent a very sensitive change in the benzylamine expulsion rate (k_{-a}) with substrate (X) variation due to the loss of a strong localized charge on the nitrogen atom of the benzylammonium ion in the $T^\pm$.



$$k_2 = \frac{k_a}{k_{-a}}k_b = Kk_b \quad (6)$$

We note that the size of β_Z (=-1.1~-1.5) is large, which is again an indication of the rate-limiting leaving group expulsion mechanism. For example, the reactions of thiophenyl benzoates with benzylamines in acetonitrile at 55.0 and 60.0 °C have been proposed to proceed by the rate limiting expulsion of thiophenylate ion from $T^{\pm}$: the β_Z values for these reactions ranged from -1.4 to -1.7, which are quite similar to the values obtained in this work.

The cross-interaction constant ρ_{XZ} (=0.82: DTA and 1.05: TTA) is relatively large (the corresponding value for the reaction of thiophenyl benzoate is 0.3)[2]. The large positive ρ_{XZ} and adherence to the RSP (Table 1 and 2) also support our proposed mechanism.[10]

Secondary kinetic isotope effects involving deuteriated benzylamine nucleophiles are summarized in Table 3 and 4. Benzylamines have two mobile protons so that in a general base-catalysed nucleophilic attack in S_N2 type concerted processes one of the mobile hydrogens on the N atom will cause an inverse isotope effect due to steric hindrance to N-H bending vibration. Thus, in such causes, the k_H/k_D values are either less than unity (inverse effect) or marginally greater than unity (normal effect) due to cancellation of the primary kinetic effect of deprotonation process. The k_H/k_D values observed in Table 3 and 4 are all greater than 1.0.

Similarly, if the reactions proceed by a stepwise mechanism with rate-determining breakdown of $T^{\pm}$ the H-N-H moiety will be sterically relieved in the TS as the LG departs from $T^{\pm}$. This will cause a decrease in the N-H vibration frequencies and the k_H/k_D values will be greater than 1.0. Thus, the normal k_H/k_D values ($k_H/k_D > 1.0$) alone do not allow us to predict the correct mechanism. Previously we have noted that the k_H/k_D values are close to 1.0 in the rate-limiting breakdown of $T^{\pm}$.[14] The values in Table 3 and 4 are somewhat larger than those for such a mechanism. This can be rationalized by a cycle TS of the types shown as I and II, respectively, for the stepwise and concerted mechanism.

Table 3. The Secondary Kinetic Isotope Effects for the Reactions of Thiophenyl Dimethylacetates with Deuterated X-Benzylamines in Acetonitrile at 55.0 °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	5.59(±0.05)	4.47(±0.04)	1.22±0.02[a]
p-OMe	H	24.8(±0.2)	18.9(±0.09)	1.31±0.01
p-OMe	*p*-Cl	251(±4.5)	169(±3.0)	1.48±0.03
P-OMe	*p*-Br	259(±4.5)	171(±2.5)	1.51±0.03
p-Cl	*p*-Me	1.13(±0.01)	0.883(±0.008)	1.28±0.02
p-Cl	H	5.70(±0.06)	4.22(±0.05)	1.35±0.02
p-Cl	*p*-Cl	61.9(±0.8)	42.4(±0.4)	1.46±0.02
p-Cl	*p*-Br	71.7(±0.9)	46.9(±0.5)	1.53±0.03

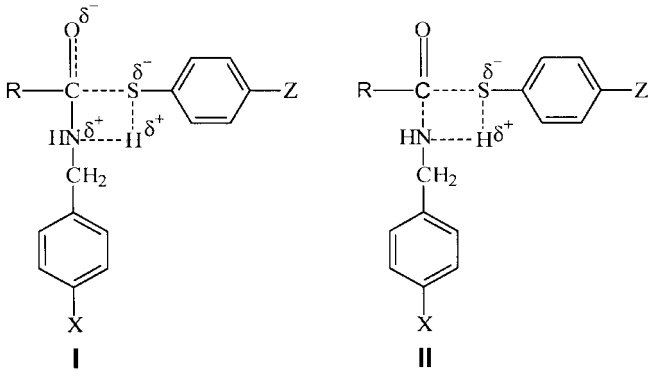
[a]Standard deviations.

Table 4. The Secondary Kinetic Isotope Effects for the Reactions of Thiophenyl Trimethylacetates with Deuterated X-Benzylamines in Acetonitrile at 60.0 °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	4.60(±0.05)	3.74(±0.04)	1.23±0.02[a]
p-OMe	H	14.8(±0.08)	11.5(±0.06)	1.29±0.01
p-OMe	*p*-Cl	80.3(±1.2)	59.5(±0.4)	1.35±0.02
P-OMe	*m*-Cl	101(±1.5)	68.2(±0.6)	1.48±0.03
p-Cl	*p*-Me	0.821(±0.008)	0.696(±0.006)	1.18±0.02
p-Cl	H	2.93(±0.03)	2.24(±0.03)	1.31±0.02
p-Cl	*p*-Cl	22.7(±0.2)	15.9(±0.08)	1.43±0.01
p-Cl	*m*-Cl	28.4(±0.3)	18.8(±0.09)	1.51±0.02

[a]Standard deviations.

The cyclic TSs are often suggested for reactions in solutions of low relative permittivity since the cyclic TSs minimize charge creation, or separation, and have an energetic advantage.[15] In such cyclic proton transfer, leaving group departure is facilitated in addition to charge dispersion. The assistance to bond cleavage of the LG is especially important in aprotic solvents since the solvent cannot stabilize the TS by hydrogen bonding. It is difficult to choose one from the two cyclic TSs, but as noted above the relatively large ρ_{XZ} values observed favour **I** rather than **II**: in the two structures. **I** and **II**, interaction between substituents X and Z will be strong since X and Z can interct *via* two routes (an additional one is provided by the hydrogen-bonding bridge):[16] however, a shorter route, therefore a stronger interaction with a larger ρ_{XZ} value, is provided in **I**.



The low activation parameters, $\Delta H^{\neq}$ ans $\Delta S^{\neq}$, (Table 5 and 6) are also in line with the mechanism proposed. The expulsion of thiophenolate anion is aided by hydrogen-bonding by the incoming benzylamine requiring not much energy in the activation but highly structured TS leads to large negative entropies activation.

In summary the aminolysis of thiophenyl dimethylacetates and trimethylacetates with benzylamines in acetonitrile proceeds by rate-limiting breakdown of a tetrahedral intermediate, $T^{\pm}$. The unusually large β_X (β_{nuc}) values can be accounted

Table 5. Activation Parameters[a] for the Reactions of Thiophenyl Dimethylacetates 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	10.6	41
p-OMe	*p*-Br	11.9	30
p-Cl	*p*-Me	13.2	37
p-Cl	*p*-Br	11.0	35

[a]Calculated by the Eyring equation. The maximum errors calculated (by the method of K. B. Wiberg, *Physical Organic Chemistry*, Wiley, New York. **1964**. p378) are = 0.6 kcal mol^{-1} and = 2 e.u. for $\Delta H^{\neq}$ and $\Delta S^{\neq}$, respectively.

Table 6. Activation Parameters[a] for the Reactions of Thiophenyl Trimethylacetates 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	10.0	44
p-OMe	*m*-Cl	9.9	39
m-Cl	*p*-Me	11.5	46
m-Cl	*m*-Cl	10.1	41

[a]Calculated by the Eyring equation. The maximum errors calculated (by the method of K. B. Wiberg, *Physical Organic Chemistry*, Wiley, New York. **1964**. p378) are ± 0.6 kcal mol^{-1} and ± 2 e.u. for $\Delta H^{\neq}$ and $\Delta S^{\neq}$, respectively.

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}/k_b is large due to large k_{-a} and relatively small k_b. The proposed mechanism is also supported by a large positive cross-interaction constant, ρ_{XZ} (=0.82 and 1.05), adherence to the RSP, and low activation parameters. The greater than unity k_H/k_D values involving deuterated benzylamines suggests a four-center type hydrogen-bonded TS.

Experimental Section

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

Preparartions of thiophenyl dimethylacetates and trimethylacetates. Thiophenol derivatives and isobutyryl or trimethylacetyl chloride were dissolved in anhydrous ether and added pyridine carefully keeping temperature to 0-5 °C. Ice was then added to the reaction mixture and ether layer was separated, dried on $MgSO_4$ and distilled under reduced pressure to remove solvent. The melting point, IR (Nicolet 5BX FT-IR) and ^{1}H and ^{13}C NMR (JEOL 400 MHz) data are cited next.

***p*-Thiotolyl dimethylacetate**: Liquid, IR (KBr), 3032 (C-H, C-H), 2972, 2932 (C-H, CH_3), 1709 (C=O), 1461 (C=C, aromatic); ^{1}H NMR (400 MHz, $CDCl_3$), 1.30 (6H, d, J = 7.32 MHz, CH_3), 2.40 (3H, s, CH_3), 2.88 (1H, sep, J = 6.84 MHz, CH), 7.24 (2H, d, J = 7.80 MHz, meta H), 7.33 (2H, d, J = 8.30 MHz, ortho H); ^{13}C NMR (100.4 MHz, $CDCl_3$), 201.6 (C=O), 139.0, 134.2, 129.6, 124.2, 42.7, 21.2, 19.3; Mass, *m/z* 194 (M^-). Anal. Calcd. for $C_{11}H_{14}OS$: C, 68.0; H, 7.31. Found: C, 68.2; H, 7.33.

Thiophenyl dimethylacetate: Liquid. IR (KBr). 3073 (C-H, C-H), 2972, 2925 (C-H, CH_3), 1702 (C=O), 1467 (C=C, aromatic); ^{1}H NMR (400 MHz, $CDCl_3$), 1.20 (6H, d, J = 7.30 MHz, CH_3), 2.79 (1H, sep, J = 6.84 MHz, CH), 7.38-7.28 (5H, m, aromatic); ^{13}C NMR (100.4 MHz, $CDCl_3$), 200.8 (C=O), 134.2, 128.7, 127.6, 42.7, 19.1; Mass, *m/z* 180 (M^-). Anal. Calcd. for $C_{10}H_{12}OS$: C, 66.6; H, 6.71. Found: C, 66.4; H, 6.69.

***p*-Chlorothiophenyl dimethylacetate**: Liquid. IR (KBr), 3059 (C-H, C-H), 2979, 2932 (C-H, CH_3), 1709 (C=O), 1575, 1474 (C=C, aromatic); ^{1}H NMR (400 MHz, $CDCl_3$), 1.23 (6H, d, J = 7.31 MHz, CH_3), 2.81 (1H, sep, J = 6.84 MHz, CH), 7.29 (2H, d, J = 8.30 MHz, meta H), 7.33 (2H, d, J = 8.30 MHz, ortho H); ^{13}C NMR (100.4 MHz, $CDCl_3$), 200.1 (C=O), 135.4, 135.2, 129.0, 126.2, 42.9, 19.1, 17.0; Mass, *m/z* 214 (M^+). Anal. Calcd. for $C_{10}H_{11}ClOS$: C, 55.9; H, 5.22. Found: C, 55.7; H, 5.24.

***p*-Bromothiophenyl dimethylacetate**: Liquid, IR (KBr), 3060 (C-H, C-H), 2979, 2932 (C-H, CH_3), 1702 (C=O), 1568 (C=C, aromatic); ^{1}H NMR (400 MHz, $CDCl_3$), 1.25 (6H, d, J = 6.80 MHz, CH_3), 2.88 (1H, sep, J = 6.84 MHz, CH), 7.25 (2H, d, J = 8.80 MHz, meta H), 7.51 (2H, d, J = 8.30 MHz, ortho H); ^{13}C NMR (100.4 MHz, $CDCl_3$), 200.8 (C=O), 135.8, 132.1, 126.8, 123.7, 43.1, 19.3; Mass, *m/z* 259 (M^-). Anal. Calcd. for $C_{10}H_{11}BrOS$: C, 46.3; H, 4.30. Found: C, 46.5; H, 4.28.

***p*-Thiotolyl trimethylacetate**: m.p 45-47 °C. IR (KBr), 2966, 2925 (C-H, CH_3), 1715 (C=O), 1463 (C=C, aromatic); ^{1}H NMR (400 MHz, $CDCl_3$), 1.29 (9H, s, J = 7.30 MHz, $3CH_3$), 2.35 (3H, s, CH_3), 7.18 (2H, d, J = 7.81 MHz, meta H), 7.26 (2H, d, J = 8.30 MHz, ortho H); ^{13}C NMR (100.4 MHz, $CDCl_3$), 197.4 (C=O), 142.3, 134.7, 130.6, 61.4, 32.7, 30.8, 20.3; Mass, *m/z* 208 (M^-). Anal. Calcd. for $C_{12}H_{16}OS$: C, 69.2; H, 7.71. Found: C, 69.4; H, 7.69.

Thiophenyl trimethylacetate: Liquid, IR (KBr), 2962, 2927 (C-H, CH_3), 1702 (C=O), 1467 (C=C, aromatic); ^{1}H NMR (400 MHz, $CDCl_3$), 1.34 (9H, s, J = 7.32 MHz, $3CH_3$), 7.21-7.41 (5H, m, aromatic); ^{13}C NMR (100.4 MHz, $CDCl_3$), 197.3 (C=O), 142.3, 133.5, 130.4, 127.1, 61.4, 32.7; Mass, *m/z* 194 (M^+). Anal. Calcd. for $C_{11}H_{14}OS$: C, 68.0; H, 7.31. Found: C, 68.3; H, 7.29.

***p*-Chlorothiophenyl trimethylacetate**: Liquid. IR (KBr), 2971, 2931 (C-H, CH_3), 1705 (C=O), 1573, 1474 (C=C, aromatic); ^{1}H NMR (400 MHz, $CDCl_3$), 1.26 (9H, s, J = 7.32 MHz, $3CH_3$), 7.24 (2H, d, J = 8.78 MHz, meta H), 7.33 (2H, d, J = 8.378 MHz, ortho H); ^{13}C NMR (100.4 MHz, $CDCl_3$), 197.4 (C=O), 142.3, 133.5, 130.4, 61.4, 32.7; Mass, *m/z* 228 (M^-). Anal. Calcd. for $C_{11}H_{13}ClOS$: C, 57.8; H, 5.71. Found: C, 57.6; H, 5.73.

***m*-Chlorothiophenyl trimethylacetate**: m.p. 60-62 °C. IR (KBr), 2973, 2933 (C-H, CH_3), 1708 (C=O), 1560 (C=C, aromatic); ^{1}H NMR (400 MHz, $CDCl_3$), 1.28 (9H, d, J = 6.90 MHz, CH_3), 7.22-7.36 (4H, m, aromatic); ^{13}C NMR (100.4 MHz, $CDCl_3$), 197.4 (C=O), 142.5, 133.3, 130.2, 61.4, 32.7; Mass, *m/z* 228 (M^-). Anal. Calcd. for $C_{11}H_{13}ClOS$:

C, 57.8; H, 5.71. Found: C, 58.0; H, 5.69.

Kinetic measurement. Rates were measured conductometrically at 55.0 and 60.0 ± 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[16] with large excess of benzylamine. 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 more than three runs and were reproducible to within ± 3%.

Product analysis. Substrate (0.05 mole) and benzylamine (0.5 mole) were added to acetonitrile and reacted 55.0 and 60.0 °C under the same condition as the kinetic measurements. After more than 15 half lives, solvent was removed under reduced pressure and product was separated by column chromatography (silica gel, 10% ethylacetate-n-hexane). Analysis of the product gave the following results.

$CH_3(CH_3)CHC(=O)NHCH_2C_6H_4$-$OCH_3$: m.p. 75-77 °C, IR (KBr), 3325 (N-H), 3032 (C-H, benzyl), 2973 (C-H, CH_2), 2942 (C-H, CH_3), 1695 (C=O), 1545 (C=C, aromatic), 1274, 1045 (C-O); ^{1}H NMR (400 MHz, $CDCl_3$), 1.01 (6H, d, J = 6.83 MHz, CH_3), 2.33-2.26 (1H, m, CH), 3.36 (2H, s, NH-CH_2), 3.64 (3H, s, OCH_3), 6.69-7.10 (4H, m, aromatic ring); ^{13}C NMR (100.4 MHz, $CDCl_3$), 176.8 (C=O), 158.2, 130.4, 129.4, 128.4, 113.5, 57.2, 45.1, 19.3, 18.0; Mass, *m/z* 207 (M^-). Anal. Calcd. for $C_{12}H_{17}NO_2$: C, 69.5; H, 8.31 Found: C, 69.7; H, 8.33.

$(CH_3)_3CC(=O)NHCH_2C_6H_4$-$OCH_3$: m.p. 115-117 °C, IR (KBr), 3328 (N-H), 3034 (C-H, benzyl), 2975 (C-H, CH_2), 2941 (C-H, CH_3), 1690 (C=O), 1546 (C=C, aromatic), 1274, 1043 (C-O); ^{1}H NMR (400 MHz, $CDCl_3$), 1.33 (9H, d, J = 6.83 MHz, $3CH_3$), 3.75 (2H, d, NH-CH_2), 3.62 (3H, s, OCH_3), 6.92-7.14 (4H, m, aromatic ring); ^{13}C NMR (100.4 MHz, $CDCl_3$), 197.4 (C=O), 155.2, 133.5, 130.4, 128.3, 75.2, 61.4, 32.7, 18.5; Mass, *m/z* 221 (M^-). Anal. Calcd. for $C_{13}H_{19}OS$: C, 70.6; H, 8.71. Found: C, 70.8; H, 8.69.

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