Reactions of 2,4-Dinitrophenyl 5-substituted-2-thiophenecarboxylates with $R_2NH/R_2NH_2^+$ in 20 Mol % DMSO(aq). Effects of 5-Thienyl Substituent and Leaving Group on the Reaction Mechanism

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Reactions of 2,4-dinitrophenyl 2-thiophenecarboxylate (**2a–d**) with $R_2NH/R_2NH_2^+$ in 20 mol % DMSO(aq) have been studied. The reactions are overall second order, first order to the substrates, and first order to the nucleophiles. The Brönsted plots showed downward curves with pK_a^0 = 9.5, β_1 = 0.22–0.34, and β_2 = 0.85–0.92. The k_1 values increased with a stronger electron-withdrawing 5-thienyl substituent and a stronger nucleophile, whereas the k_2/k_{-1} values remained nearly the same for all 5-thienyl substituents. The influence of 5-thienyl substituent on the reaction rates showed excellent correlations on the Yukawa-Tsuno plots with ρ = 1.28–2.16 and r = 0.20–0.60. The ρ value increased and r value decreased with a stronger nucleophile, indicating an increase in the electron density at the carbonyl carbon and a decrease in the resonance demand. From these results, a stepwise mechanism with a change in the rate-determining step has been proposed.

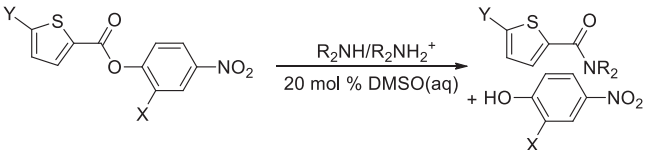
Keywords: Aminolysis, Bronsted-plot, Hammett plot, Yukawa-Tsuno plot

Introduction

Acyl transfer reactions from $XC_6H_4C(O)OC_6H_4Y$ have been the subject of intensive investigation because of their mechanistic diversity.[1–7] The most important question is whether the reaction proceeds through a stepwise or a concerted mechanism.[1–8] For example, the acyl transfer reactions of aryl phenyl carbonates and 4-nitrophenyl acetate with aryloxides proceed through a concerted mechanism.[9–11] When amine was used as the nucleophile, the reaction proceeded through a stepwise mechanism via a Zwitterionic tetrahedral intermediate.[12–15] A change in the rate-determining step (rds) from the second to the first step was noted by the change in the nucleophile from weakly basic amines to strongly basic ones. Compared with large diversity of mechanism studies on the acyl transfer reactions of aryl acetates, little is known about the reactions of heterocyclic aromatic compounds.

Earlier, we reported the mechanism of the reactions of 4-nitrophenyl 5-substituted 2-thiophenecarboxylates (**1a–d**) with $R_2NH/R_2NH_2^+$ in 20 mol % DMSO(aq).[16] The Brönsted plots were linear with reasonable correlations. The results have been interpreted with an addition-elimination mechanism in which the break-down of the intermediate (second step) is the rds. On the other hand, Um *et al.* reported curved Brönsted plots with downward curvature in the aminolysis for 2,4-dinitrophenyl 2-thiophenecarboxylate under the same condition.[17] This result has been attributed to a change in the rds.[9–11] It was noted that the rds changed from the second to the first step when the pK_a of the amine nucleophile was higher than that of the leaving group by 4–5 units.[12–15] However, the electronic effect on the transition state on this reaction was not studied.

In this work, we have studied the reactions of 2,4-dinitrophenyl 5-substituted-2-thiophenecarboxylates (**2a–d**) with $R_2NH/R_2NH_2^+$ in 20 mol % DMSO(aq) (Equation 1). We have introduced different 5-thienyl substituents (**2a–d**) to study the electronic effect and employed $R_2NH/R_2NH_2^+$ buffer as the nucleophile to keep the pH constant. All reactions proceeded through a stepwise mechanism with a change in the rds. Comparison with existing data for **1a–d** revealed the origin of the change in the rds wrought by the change in the basicity of the nucleophile.



X = H (**1**), NO_2 (**2**); Y = H (**a**), MeO (**b**), Me (**c**), Cl (**d**)
R_2NH = 1-formylpiperazine, morpholine, *N*-(2-hydroxyethyl)piperazine, piperazine, 3-methylpiperazine, piperidine

Table 1. Rate constants for the aminolysis of 5-$XC_4H_2(S)C(O)OC_6H_3$–2,4-$(NO_2)_2$[a] promoted by $R_2NH/R_2NH_2^{+}$[b] in 20 mol % DMSO(aq) at 25.0 °C

Amine[c]	pK_a[d]	K_N, M^{-1} s^{-1}[e,f] When X is			
		H (**2a**)	OCH_3 (**2b**)	CH_3 (**2c**)	Cl (**2d**)
1-Formylpiperazine	7.98	3.14	0.710	1.90	7.0
Morpholine	8.65	14.4	2.43	7.39	31.2
N-(2-hydroxylethyl)-piperazine	9.38	15.9	3.69	10.9	40.8
Piperazine	9.85	74.2	13.3	38.9	180
3-Methylpiperidine	10.8	143	23.1	53.0	389
Piperidine	11.02	151	24.5	62.2	448

[a] [Substrate] = 5.0×10^{-5} M. [b] $[R_2NH]/[R_2NH_2^{+}] = 1.0$. [c] $[R_2NH] = (5.0 \times 10^{-4})$ M. [d] pK_a data in 20 mol % DMSO(aq) taken from Ref. 8d. [e] Average of three or more rate constants. [f] Estimated uncertainty, ±3%.

Results

2,4-Dinitrophenyl 2-thiophenecarboxylates (**2a–d**) were prepared by the reaction 5-substituted-2-thiophenecarboxylic acid chloride with 2,4-dinitrophenol in the presence of Et_3N in CH_2Cl_2 as described.[18] The yields of 2,4-dinitrophenoxide determined by comparing the absorbance of the infinity samples from the kinetic studies with those of the authentic aryloxides were in the range of 96–98%.

Rates of aminolysis were determined by monitoring the increase in the absorption at the λ_{max} = 426 nm of 2,4-dinitrophenoxide. Excellent pseudo-first order kinetics plots, which covered at least three half-lives were obtained. Pseudo-first order rate constants (k_{obs}) are summarized in Tables S1–S6 (File S1, Supporting Information). The plots of k_{obs} vs. amine concentration are straight lines passing through the origin, indicating that the reactions are second order, first order to the ester and 1st order to the amine (Figures S1–S7).

The rate equation can be expressed as Equation 2. The second-order rate constants k_N were obtained either from the slopes of straight lines or by dividing the k_{obs} by nucleophile concentration. The k_N values for the reactions of **2a–d** are summarized in Table 1.

$$\text{Rate} = k_{obs}[\mathbf{2}], \text{where} k_{obs} = k_N[\text{nucleophile}] \quad (2)$$

The rate increased with increasing in the electron-withdrawing ability of the 5-thienyl substituent and the pK_a value of the amine (Table 1). The Brönsted plots for the aminolysis from **2a–d** showed downward curvature (Figure 1). The values of pK_a^0, β_1, and β_2 that best fit with Equation 3 have been calculated using a nonlinear regression analysis program.8b,19,25

$$\log(k_N/k_N^0) = \beta_2(pK_a - pK_a^0) - \log(1+\alpha)/2$$
$$\text{where } \log\alpha = (\beta_2 - \beta_1)(pK_a - pK_a^0) \quad (3)$$

For the aminolysis of **2a–d**, the calculated pK_a^0 value is 9.5, while the values of β_1 and β_2 are in the range of 0.22–0.34 and 0.85–0.92, respectively (Figure 1 and Figure S8). The k_2/k_{-1} values increased with a stronger nucleophile and remained nearly the same for all 5-thienyl substituent (Table 2).

The k_1 values increased with a stronger nucleophile and a stronger the electron-withdrawing 5-thienyl substituent (Table 3). The Brönsted plots of log k_2/k_{-1} and log k_1 vs. pK_a + log(p/q) values of R_2NH are straight lines with excellent correlations (Figures 2 and 3). Their slopes (β_{-1} and β_1) are in the ranges of 0.58–0.63 and 0.21–0.34, respectively. Similar β_1 values calculated from the data in Tables 1 and 3 demonstrates the reliability of these analysis (Figures 1 and 3).

The Hammett plots for the aminolysis from **2a–d** are shown in Figure 4. The influence of the 5-thienyl substituents on the aminolysis rates could be correlated with the

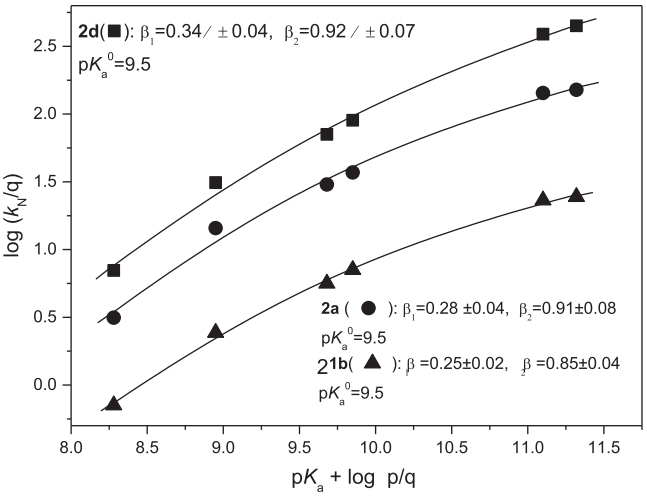


Figure 1. Brönsted plots for the reactions of 5-$XC_4H_2(S)C(O)OC_6H_3$–2,4-$(NO_2)_2$ with $R_2NH/R_2NH_2^{+}$ in 20 mol % DMSO(aq) at 25.0 °C [X = H (**2a**, ●), OCH_3 (**2b**, ▲), Cl (**2d**, ■)].

Table 2. k_2/k_{-1} values for the reactions of 5-$XC_4H_2(S)C(O)OC_6H_3$–2,4-$(NO_2)_2$[a] with $R_2NH/R_2NH_2^{+}$[b] in 20 mol % DMSO(aq) at 25.0 °C.

		k_2/k_{-1}[e,f]			
Amine[c]	pK_a[d]	H (**2a**)	OCH_3 (**2b**)	CH_3 (**2c**)	Cl (**2d**)
1-Formylpiperazine	7.98	0.170	0.185	0.17	0.196
Morpholine	8.65	0.450	0.467	0.450	0.479
N-(2-hydroxylethyl)-piperazine	9.38	1.30	1.28	1.30	1.27
Piperazine	9.85	1.66	1.62	1.66	1.60
3-Methylpiperidine	10.8	10.2	9.12	10.2	8.47
Piperidine	11.02	14.0	12.4	14.0	11.4

[a] [Substrate] = 5.0×10^{-5} M.
[b] $[R_2NH]/[R_2NH_2^{+}] = 1.0$.
[c] $[R_2N] = 7.0 \times 10^{-4}$ to 2.0×10^{-2} M.
[d] pK_a data in 20 mol % DMSO(aq) taken from Ref. 8d.
[e] Average of three or more rate constants.
[f] Estimated uncertainty, ±3%.

Table 3. k_1 values for the reactions of 5-$XC_4H_2(S)C(O)OC_6H_3$–2,4-$(NO_2)_2$[a] with $R_2NH/R_2NH_2^{+}$ [b] in 20 mol % DMSO(aq) at 25.0 °C.

		k_1/ M^{-1} s^{-1}[e,f]			
Amine[c]	pK_a[d]	H (**2a**)	OCH_3 (**2b**)	CH_3 (**2c**)	Cl (**2d**)
1-formylpiperazine	7.98	21.6	4.55	13.1	42.7
morpholine	8.65	46.4	7.63	23.8	96.3
N-(2-hydroxylethyl)- piperazine	9.38	53.5	10.0	25.0	127
piperazine	9.85	119	23.0	62.5	293
3-methylpiperidine	10.8	157	25.6	58.2	435
piperidine	11.02	162	26.5	66.6	487

[a] [Substrate] = 5.0×10^{-5} M.
[b] $[R_2NH]/[R_2NH_2^{+}] = 1.0$.
[c] $[R_2N] = 7.0 \times 10^{-4}$ to 2.0×10^{-2} M.
[d] pK_a data in 20 mol % DMSO(aq) taken from Ref. 8d.
[e] Average of three or more rate constants.
[f] Estimated uncertainty, ± 3%.

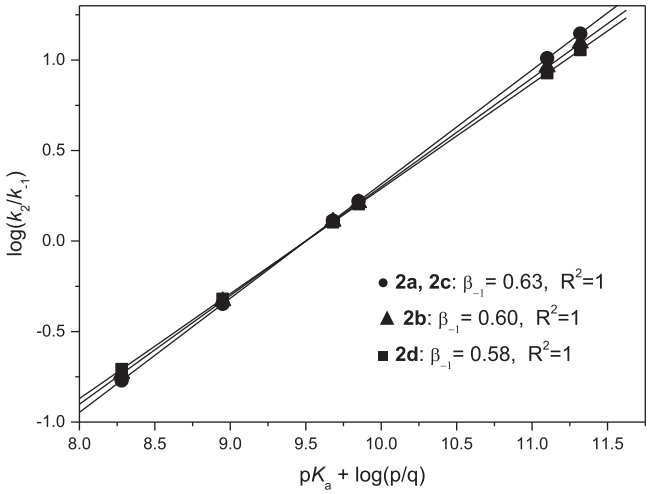


Figure 2. Plots of $\log(k_2/k_{-1})$ vs. $pK_a + \log(p/q)$ values for the reactions of 5-$XC_4H_2(S)C(O)OC_6H_3$–2,4-$(NO_2)_2$ with $R_2NH/R_2NH_2^{+}$ in 20 mol % DMSO(aq) at 25.0 °C [X = H (**2a**, ●), OCH_3 (**2b**, ▲), CH_3 (**2c**, ●), Cl (**2d**, ■).

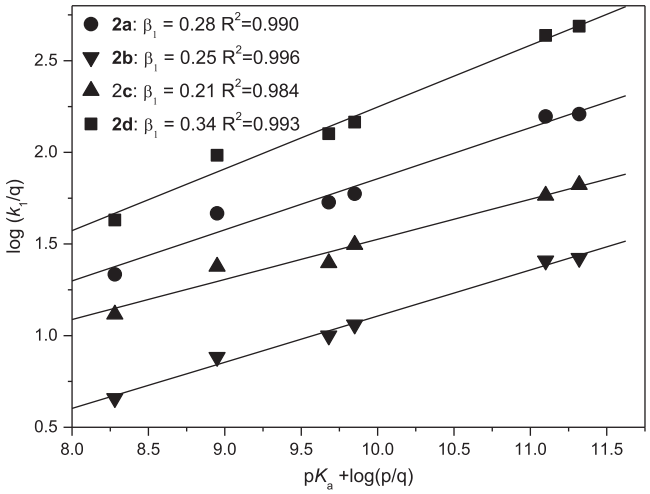


Figure 3. Plots of $\log(k_1)$ vs. $pK_a + \log(p/q)$ values for the reactions of 5-$XC_4H_2(S)C(O)OC_6H_3$–2,4-$(NO_2)_2$ with $R_2NH/R_2NH_2^{+}$ in 20 mol % DMSO(aq) at 25.0 °C [X = H (**2a**, ●), OCH_3 (**2b**, ▲), CH_3 (**2c**, ●), Cl (**2d**, ■).

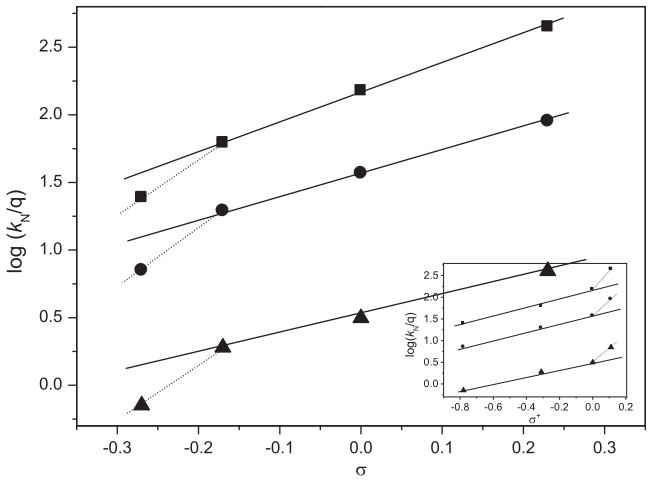


Figure 4. Hammett plots of log(k_N/q) vs. σ values for the reactions of 5-$XC_4H_2(S)C(O)OC_6H_3$–2,4-$(NO_2)_2$ with $R_2NH/R_2NH_2^+$ in 20 mol % DMSO(aq) at 25.0 °C. [R_2N = piperidine (■), piperazine (●), 1-formylpiperazine (▲)]. Inset: Plots of log(k_N/q) vs. σ^+ values for the same reaction.

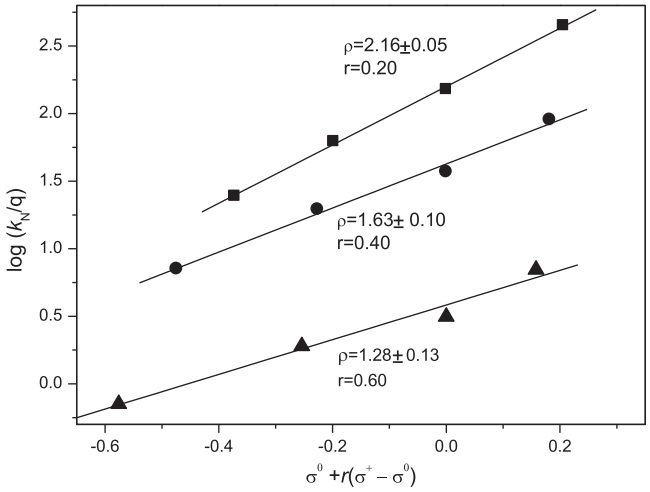


Figure 5. Yukawa-Tsuno plots for the reactions of 5-$XC_4H_2(S)C(O)OC_6H_3$–2,4-$(NO_2)_2$ with $R_2NH/R_2NH_2^+$ in 20 mol % DMSO(aq) at 25.0 °C [R_2N = piperidine (■), piperazine (●), 1-formylpiperazine (▲)].

Hammett σ values, if the data for **2b** is excluded. It showed negative deviation when plotted against σ (Figure 4). However, all of the data showed excellent correlations on the Yukawa-Tsuno plots (Figure 5). The ρ and r values calculated from these plots are in the range of 1.28–2.16 and 0.20–0.60, respectively (Table 4). The ρ value decreased and *r* value increased as the nucleophile was less basic.

Discussion

Mechanism of Aminolysis. The reactions of **2a–d** with $R_2NH/R_2NH_2^+$ in 20 mol % DMSO(aq) produced 2,4-dinitrophenoxide almost quantitatively. The reactions

Table 4. The ρ and *r* values for the reactions of 5-$XC_4H_2(S)C(O)OC_6H_3$–2,4-$(NO_2)_2$ with $R_2NH/R_2NH_2^+$ in 20 mol % DMSO(aq) at 25.0 °C.

Entry	Amine	pK_a[a]	ρ	*r*
1	Piperidine	11.02	2.16 ± 0.05	0.20
2	3-Methyl piperidine	10.80	2.06 ± 0.04	0.25
3	Piperazine	9.85	1.63 ± 0.10	0.40
4	1-(2-Hydroxyethyl) piperazine	9.38	1.59 ± 0.09	0.45
5	Morpholine	8.65	1.50 ± 0.09	0.55
6	1-Formylpiperazine	7.98	1.28 ± 0.13	0.60

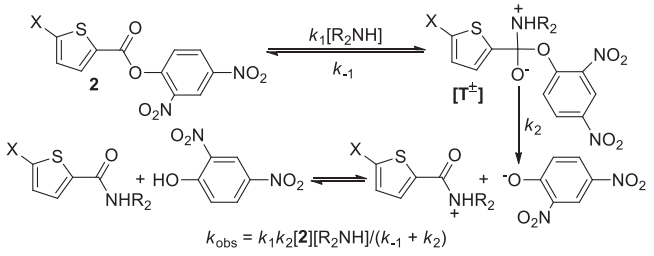
[a] pK_a data in 20 mol % DMSO(aq) taken from Ref. 8d.

are overall second order, first order to **2a–d** and first order to the amine nucleophiles. This result is consistent with both concerted and stepwise mechanisms. However, Brönsted plots exhibit downward curvature. Since the Brönsted plots for the concerted reactions are linear with β_{nuc} = 0.5–0.6, the curved Brönsted plots observed in this study can be most reasonably attributed to the stepwise mechanism with change in the rds (Scheme 1).[9–11]

To provide additional evidence for the stepwise mechanism, the pK_a^0, β_1, and β_2 values have been calculated. The pK_a^o was defined as the pK_a at the midpoint of the curved Brönsted plot, while the β_1 and β_2 values represent the slopes of the curved Brönsted plots for the reactions with strongly and weakly basic nucleophiles, respectively, that is, the β values when the second and first step is the rds, respectively (Figure 1). For reactions of **2a–d**, pK_a^o = 9.5, β_1 = 0.22–0.34, and β_2 = 0.85–0.92 have been calculated. The β_1 and β_2 values are in the same range as those reported for acyl transfer reactions of 3,4-dinitrophenyl aryl carbonate with quinuclidines[20] and of 2,4-dinitrophenyl benzonates with pyridine in aqueous ethanol,4a-4c both of which have been interpreted with a change in the rds.[9–11]

We also calculated the k_1 and k_2/k_{-1} values using Eqs. (4)–(10).[19] If the reaction proceeds as shown in Scheme 1, one can apply steady-state approximation with respect to $T^{\pm}$. The rate equation can be expressed as Eq. (4).

$$k_N = k_1k_2/(k_{-1}+k_2) = k_1(k_{-1}/k_2+1) \quad (4)$$



Scheme 1. Stepwise mechanism for the acyl transfer reaction.

If $k_2 << k_{-1}$, Eq. (4) reduces to Eq. (5).

$$k_N = k_1k_2/k_{-1}, \text{ when } k_2 << k_{-1} \quad (5)$$

(second step is rds)

If $k_2 >> k_{-1}$, the rate expression becomes Eq. (6).

$$k_N = k_1, \text{ when } k_2 >> k_{-1} \quad (6)$$

(first step is rds)

On the other hand, the β_1 and β_2 can be expressed by the Eqs. (7) and (8), respectively.4e

$$\beta_1 = d(\log k_1)/d(pK_a) \quad (7)$$

$$\begin{aligned}\beta_2 &= d[\log(k_1k_2/k_{-1})]/d(pK_a) \\ &= \beta_1 + d(\log k_2/k_{-1})/d(pK_a)\end{aligned} \quad (8)$$

Rearrangement of Eq. (8) provides an expression for β_2–β_1.

$$\beta_2 - \beta_1 = d(\log k_2/k_{-1})/d(pK_a) \quad (9)$$

Integration of Eq. (9) yields Eq. (10),

$$\log(k_2/k_{-1}) = (\beta_2 - \beta_1)(pK_a - pK_a^0) \quad (10)$$

where $pK_a = pK_a^0$ when $k_2 = k_{-1}$.

The k_2/k_{-1} values can be calculated from Eq. (10) using the β_1, β_2, and pK_a values. The k_1 values can then be calculated from Eq. (5) using the values of k_N and k_2/k_{-1} calculated as above.

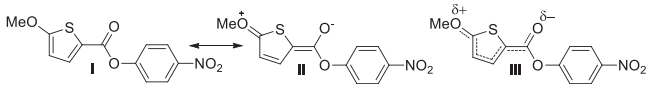
The values of pK_a^0, k_1, and k_2/k_{-1} provide strong support for a stepwise mechanism; (1) the k_2/k_{-1} value increased with a stronger nucleophile (Table 2). This outcome is as expected because k_{-1} should decrease with a stronger base and k_2 should remain constant. More importantly, values of $k_2/k_{-1} << 1$, $k_2/k_{-1} \approx 1$, and $k_2/k_{-1} >> 1$ have been calculated for nucleophiles with $pK_a < 9.0$, $pK_a = 9.38$–9.85, and $pK_a > 10.8$, respectively (Table 2). As stated above, an increase in the pK_a value of the nucleophile should increase the k_2/k_{-1} value, thereby resulting in a gradual shift of the rds from the second ($k_2/k_{-1} << 1$) to the first step ($k_2/k_{-1} >> 1$). This outcome is consistent with that of Um except that the change in the rds occurs when the pK_a of the amine nucleophile is larger than that of the leaving group by 6–7 units rather than 4–5 units.[12–15] (2) The k_2/k_{-1} values are nearly the same for all 5-thienyl substituents (Table 2). Also, the β_{-1} values, the slopes of the plots of log k_2/k_{-1} vs. pK_a of the amines, are very similar (Figure 2). A stepwise mechanism predicts that the electron density at the carbonyl carbon should decrease as the intermediate ($T^{\pm}$) is converted to either reactant (k_{-1}) or product (k_2) (Scheme 1). Hence, an electron withdrawing 5-thienyl substituent should decrease both of k_{-1} and k_2 values, thereby keeping the k_2/k_{-1} value more or less a constant. Similar results have been reported for the aminolysis from 2,4-dinitrophenyl X-substituted benzonates7j and 2,4-dinitrophenyl X-substituted benzene sulfonates.[20] (3) The pK_a^0 values, pK_a of the nucleophile when $k_2 = k_{-1}$, are the same for all 5-thienyl substituents (Figure 1). Since the k_2 values for the departure of the common leaving group should be identical, the basicity of the nucleophiles (pK_a^0) required to keep k_{-1} a constant should also be the same. (4) The k_1 increased as the nucleophile becomes a stronger base, while the 5-thienyl substituent changes from an electron donating group to an electron withdrawing group. This is because the reactivity of the nucleophile and the carbonyl carbon are increased by these changes. (5) The β_1 values are in the range of 0.25–0.34, indicating modest sensitivity of the k_1 to the amine basicity. The values are smaller by about 2-fold than the β_{-1} values of 0.58–0.63 (Figures 1 and 2). Since k_1 and k_{-1} are reversible steps involving common transition states, the moderate values of the β_1 predict that k_{-1} should be more sensitive than k_1 to the amine basicity. On the other hand, the k_2 value should be relatively insensitive to the amine basicity (see above). This would predict that the k_2/k_{-1} values should be more sensitive than k_1 to the amine basicity and a larger β_{-1} than β_1 values.

Effect of 5-Thienyl Substituent. The rate of the reaction increased as the 5-thienyl substituent changes from an electron donating group to an electron withdrawing group (Table 1). The rate data could be correlated with the Hammett plots, if the data for **2b** is excluded. It showed negative deviation when plotted against σ (Figure 4). In sharp contrast, all of the rate data showed excellent correlations on the Yukawa-Tsuno plots when plotted against [$\sigma + r(\sigma^+ - \sigma)$] values (Figure 5). The extra resonance stabilization by the **π** donor substituents can be evaluated with Eq. (10) using the Yukawa-Tsuno equation.[21]

$$\log(k/k_0) = \rho\{\sigma + r(\sigma^+ - \sigma)\} \quad (10)$$

The ρ value indicates the extent of negative charge development at the reaction site, ($\sigma^+ - \sigma$) is the resonance substituent constant measuring the π-delocalization capability of the donor group, and r is a parameter characteristic of the given reaction, measuring the extent of resonance demand, *i.e.*, the degree of resonance interaction between the aryl group and the reaction site in the rds.[21] This equation is identical to the Hammett equation when $r = 0$ and Brown equation when $r = 1$. The much better correlation of the rate data with Eq. (10) than with Hammett and Brown equations indicates that the extra resonance stabilization by the π-donor substituent in **2b** can be represented by the resonance hybrid (**III**) of **I** and **II**, not by **I** (Hammett σ) or **II** (Brown σ^+) alone (Scheme 2).[22]

For the aminolysis of **2a**–**d**, the ρ value increased from 1.28 to 2.16 and r value decreased from 0.60 to 0.20 as the amine was changed to a stronger base (Table 4). This



Scheme 2. Extra resonance stabilization by the π-donor substituent.

Table 5. Transition state parameters for reactions of $C_4H_3(S)C(O)OY$ with $R_2NH/R_2NH_2^+$ in 20 mol % DMSO(aq) at 25.0 °C.

	$Y = 4\text{-}NO_2C_6H_4$[16]	$Y = 2,4\text{-}(NO_2)_2C_6H_3$
pK_a[23]	7.14	4.11
Relative rate[a]	1	260
β_{nuc}	0.89 ± 0.05	—
β_1	—	0.28 ± 0.04
β_2	—	0.91 ± 0.08
β_{-1}	—	0.63
ρ[a]	0.89 ± 0.05[a]	1.50 ± 0.09
r	0.90	0.55
Brönsted plot	Linear	Downward curve

[a] R_2NH = morpholine.

indicates an increase in the electron density at the carbonyl carbon and a decrease in the resonance demand. Since the electron density at the carbonyl carbon increases in the first step and decreases in the second step, the ρ value for the acyl transfer reaction should be larger when the first step is rds than when the second step is rds due to the opposite substituent effect. Therefore, the increase in the ρ value with a stronger nucleophile provides additional support for the change in the rds from the second to the first step. The decrease in the r value is also consistent because the resonance demand should decrease as the electron density is increased.

Effect of Leaving Group. Comparison of the kinetic data for the aminolysis of **1a–d** and **2a–d** provides additional evidence for the proposed mechanism; (1) the rate of morpholine-promoted aminolysis from **2a** is faster than that from **1a** by 270-fold (Table 5). Since the second step is the rds for both reactions, the rate equation should be $k_N = k_1k_2/k_{-1}$. For a given nucleophile, k_1 and k_{-1} values should remain almost the same regardless of the leaving group. Therefore, the 270-fold faster rate of **2a** is undoubtedly due to the enhanced leaving group ability. (2) For the aminolysis of **1a–d**, the second step is rds ($k_2/k_{-1} << 1$) for all nucleophiles, whereas those of **2a–d** proceed by the stepwise mechanism with the change in the rds (Table 2). Since the k_2 step of **2a** is much faster than that of **1a**, and k_{-1} decreases as the nucleophile becomes more basic, the k_2/k_{-1} value of **2a** could become greater than **1** with a strong nucleophile, thereby changing the rds to the first step. On the other hand, the k_2 step of **1a** should be slower than that of **2a** by more than 270-fold in order for the first step to become rds. However, this is not possible because the k_{-1} values for the two compounds should be same for a given nucleophile. Therefore, the stepwise mechanism with a change in the rds observed for **2a–d** can be attributed to the enhanced leaving group ability. (3) The $\beta_{nuc} = 0.89$ for **1a** is very similar to $\beta_2 = 0.91$ for **2a** measured using weak nucleophiles (Figure 1). Since the reactions of **1a** and **2a** with weakly basic nucleophiles proceed through the same mechanism in which the k_2 step is the rds, the extent of N─C bond formation in the transition state should be similar. This would predict similar Brönsted β values, as observed. (4) The ρ value increased from 0.89 to 1.50 while the r values decreased from 0.90 to 0.55 by the change in the leaving group from 4-nitrophenoxide (**1a**) to 2,4-dinitrophenoxide (**2a**). This result can be attributed to the different extent of participation of the first step to the rds. As stated above, the electron density at the carbonyl carbon increases in the first step and decreases in the second step, thereby resulting in a larger ρ value when the first step is rds than when the second step is rds. For the aminolysis from **1a**, the second step is always rds for all nucleophiles. On the other hand, the rds in the aminolysis from **2a** changes from the second step to the first step as the basicity of the nucleophile is increased (see above). Therefore, the larger ρ value determined for **2a** can be attributed to the partial involvement of the first step in the rds. The smaller r value reflects the reduced resonance demand caused by the enhanced electron density at the carbonyl carbon. All of these results are in excellent agreement with the stepwise mechanism with the change in the rds.

Conclusions

In this work, we have studied the aminolysis reactions of 2,4-dinitrophenyl 5-substituted-2-thiophene carboxylate (**2a–d**) with $R_2NH/R_2NH_2^+$ in 20 mol % DMSO(aq). The curved Brönsted plots with identical $pK_a^0 = 9.5$, $\beta_1 = 0.22–0.34$, $\beta_2 = 0.85–0.92$, gradual increase in the k_1 values with electron-withdrawing 5-thienyl substituents and stronger nucleophiles, and values of $k_2/k_{-1} << 1$, $k_2/k_{-1} \approx 1$, and $k_2/k_{-1} >> 1$ for nucleophiles with $pK_a < 9.0$, $pK_a = 9.38–9.85$, and $pK_a > 10.8$, respectively, provide strong evidence for the stepwise mechanism with the change in rds. Moreover, the excellent correlation of the rate data on the Yukawa-Tsuno plots, the gradual increase in the ρ values with concomitant decrease in the r value with a stronger nucleophile indicated the gradual increase in the N─C bond formation in the transition state. Comparison with the previously reported data for **1a–d** revealed that the change in the rds in the reactions of **2a–d** from the second to the first step with a stronger nucleophile originated from the increased leaving group ability of 2,4-dinitrophenoxide.

Experimental Section

Materials. All of the 2,4-dinitrophenyl 5-substituted-2-thiophenecarboxylates **2a-d** were prepared by the reactions of 2,4-dinitrophenol with 5-substituted-2-thiophenecarboxyl chloride in the presence of Et_3N in methylene chloride.[18]

The spectral and analytical data of the compounds were consistent with the proposed structures. The yield (%), IR (KBr, C⊠O, cm^{-1}), ^1H NMR (400 MHz, $CDCl_3$, *J* values are in Hz), and ^{13}C NMR (100 MHz), and mass spectral data for the new compounds are as follows.

$C_4H_3(S)C(O)OC_6H_3$–2,4-$(NO_2)_2$ (2a): Yield 83%; IR 1710 cm^{-1}; ^1H NMR δ 7.24 (dd,1H, *J* = 3.68, 8.8), 7.67 (d, 1H, *J* = 9.14), 7.79 (d, 1H, *J* = 1.44), 8.06 (dd, 1H, *J* = 1.44, 3.68), 8.56 (dd, 1H, *J* = 2.74, 9.14), 9.01 (d, 1H, *J* = 2.74); ^{13}C NMR δ 121.8, 126.7, 128.6, 128.9, 130,3, 135.6, 136.7, 141.9, 145.1, 148.3, 158.2.; LRMS(EI); *m/z* 294[M^+] (3), 112(100), 111(92), 83(32), 63(16), 39(77), 30(14).

5-$MeOC_4H_2(S)C(O)OC_6H_3$–2,4-(NO_2) (2b): Yield 79%; IR 1716 cm^{-1}; ^1H NMR δ 4.03 (s, 3H), 6.37 (d, 1H, *J* = 4.11), 7.65 (d, 1H, *J* = 8.96), 7.82 (d, 1H, *J* = 4.11), 8.53–8.56 (dd, *J* = 3.26, 8.96, 1H), 8.97 (d, 1H, *J* = 3.26); ^{13}C NMR δ 60.9, 101.1, 115.1, 121.9, 126.9, 129.0, 137.5, 142.2, 145.1148.8, 158.7, 175.7. LRMS(EI); *m/z* 324[M^+] (6), 141(100), 126(15), 98(48), 85(8), 70(26), 69(14), 30(12).

5-$MeC_4H_2(S)C(O)OC_6H_3$–2,4-$(NO_2)_2$ (2c): Yield 81%; IR 1715 cm^{-1}; ^1H NMR δ 2.61 (s, 3H), 6.90 (d, 1H, *J* = 3.48), 7.65 (d, 1H, *J* = 8.98), 7.87 (d, 1H, *J* = 3.48), 8.55 (dd, 1H,*J* = 2.76, 8.8), 8.98 (d, 1H, *J* = 2.76); ^{13}C NMR δ 160.0, 121.7, 127.3, 121.4, 128.8, 137.2, 141.9, 144.9, 148.5, 152.0, 158.3.; LRMS(EI); *m/z* 308[M^+] (9), 126(100), 97(49), 70(16), 63(37), 53(99), 39(14), 30(37).

5-$ClC_4H_2(S)C(O)OC_6H_3$–2,4-$(NO_2)_2$ (2d): Yield 82%; IR 1715 cm^{-1}; ^1H NMR δ 7.08 (d, 1H, *J* = 4.05), 7.65 (d, 1H, *J* = 8.96), 7.85 (dd, 1H, *J* = 4.05), 8.56–8.59 (dd, 1H, *J* = 2.76, 8.96), 9.00 (d, 1H, *J* = 2.76); ^{13}C NMR δ 121.8, 126.7, 128.1, 128.3, 129.0, 136.3, 141.0, 141.7, 145.2, 148.0, 157.5.; LRMS(EI); *m/z* 328[M^+] (4), 147(73), 145 (100), 117(18),73(46), 63(15),30(14).

Reagent grade methylene chloride and secondary amine were fractionally distilled from CaH_2.

The solutions of R_2N/R_2NH^+ in 20 mol % DMSO(aq) were prepared by dissolving equivalent amount of R_2NH and R_2NH^+ in 20 mol % DMSO(aq), as reported.[24]

Kinetic Studies. The solution of R_2N/R_2NH^+ in 20 mol % DMSO(aq) (3.0 mL) was placed in a 10 mm quartz cuvette and allowed to equilibrate in the cuvette compartment for 15 min. The cuvette was removed and 5 μL of the freshly prepared solution (0.03 M) of **2a-d** in MeCN was injected with microsyringe. Rates of the eliminations from **2a–d** promoted by R_2N/R_2NH^+ in 20 mol % DMSO(aq) were followed by monitoring the change in the UV absorption with the reaction time using a UV–vis or stopped-flow spectrophotometer as described.[16] Reactions were followed by monitoring the increase in the absorbance of the aryloxides at 426 nm under pseudo-first-order conditions employing at least a 14-fold excess of nucleophiles. In almost every case, plots of $\ln(A_\infty - A_t)$ vs. time were linear over at least two half-lives. The plots of k_{obs} vs. base concentration for **2a–d** were straight lines passing through the origin, indicating that the reactions are second-order, first-order to the substrate and first-order to the base. The second-order rate constants k_2 were obtained either from the slopes of straight lines or by dividing the k_{obs} by the base concentration.

Product Studies. The products were identified by periodically monitoring the UV absorption of the reactions mixtures under the reaction condition. The yields of aryloxides determined by comparing the UV absorptions of the infinity samples with those for the authentic aryloxides were in the range of 96–98%.

Control Experiments. The stabilities of **2a–d** were determined as reported earlier.[16] The solutions of **2a–d** in MeCN were stable for at least 2 days when stored in the refrigerator.

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Supporting Information. Observed rate constants for elimination from **2a–d** promoted by R_2N/R_2NH^+ in 20 mol % DMSO(aq), plots of k_{obs} vs. base concentration, and NMR spectra for all compounds are available on request from the correspondence author (14 pages).

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