PERKIN 2

Structure–reactivity correlations in the aminolysis of aryl dithiomethyl- and dithiophenylacetates with anilines in acetonitrile

Hyuck Keun Oh,[a] **Sun Kyung Kim,**[a] **Hai Whang Lee**[b] **and Ikchoon Lee***[b]

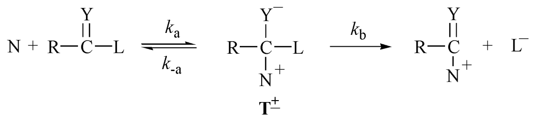
[a] *Department of Chemistry, Chonbuk National University, Chonju, 560-756, Korea*
[b] *Department of Chemistry, Inha University, Inchon, 402-751, Korea. E-mail: ilee@inha.ac.kr; Fax: +82-32-865-4855*

Received (in Cambridge, UK) 16th May 2001, Accepted 28th June 2001
First published as an Advance Article on the web 14th August 2001

The kinetics and mechanism of the anilinolysis ($XC_6H_4NH_2$) of dithio esters, $RC(=S)SC_6H_4Z$ with R = C_2H_5 and $C_6H_5CH_2$ are investigated in acetonitrile at 45.0 °C. By application of various structure–reactivity correlations, selectivity parameters ρ_X, β_X, ρ_Z, β_Z and ρ_{XZ} are determined. The reactions are predicted to proceed stepwise with rate-limiting expulsion of the ArS^- group. The dithio ester with R = C_2H_5 exhibits the fastest rate and the largest positive ρ_{XZ} value; this is interpreted to result from the strongest electron donating ability of the ethyl group in the intermediate and a crowded tetrahedral intermediate and transition state in which the nucleophile (X) and leaving group (Z) are in close proximity due to the bulky C_2H_5 group. Much faster rates are observed for the thiocarbonyl (C=S) rather than carbonyl (C=O) esters in the stepwise nucleophilic substitution reactions, which may be ascribed to the lower $\pi^*_{C=S}$ and σ^*_{C-LG} levels than those of the corresponding antibonding levels in the carbonyl esters. The normal kinetic isotope effects, $k_H/k_D > 1.0$, involving deuterated anilines suggest concurrent proton transfer with the expulsion of the ArS^- leaving group in a four-center hydrogen bonded transition state.

Introduction

The two common mechanisms for the aminolysis of carbonyl, **I**, and thiocarbonyl, **II**, esters and carbonates are (i) concerted through a tetrahedral transition state (TS) and (ii) stepwise through a tetrahedral intermediate.[1] The latter reaction pathway can be described by eqn. (1), where R and L are nonleaving and leaving groups, N represents an amine and Y is either O (**I**) or S (**II**). A nonlinear Brønsted plot results from a change in the rate-determining step, from that of k_b at low amine basicity (with $\beta_{nuc} \geq 0.8$) to that of k_a at high amine basicity (with $\beta_{nuc} \leq 0.3$). Applying the steady-state condition to $T^{\pm}$ in eqn. (1), the equation $k_N = k_a\ k_b/(k_{-a} + k_b) \cong (k_a/k_{-a}) \times k_b = Kk_b$ is obtained when the second step is rate-limiting, and this accounts for the change in the rate-determining step at $pK_a°$ where $k_{-a} = k_b$ applies. The aminolysis mechanisms naturally depend on Y, R, L, N in eqn. (1) and solvent. Fixing L (= SC_6H_4Z) and solvent (acetonitrile), we recently found an interesting mechanistic changeover due to changes in Y (O or S),[2] N (benzylamines or anilines)[2,3] and R (CH_3, C_2H_5, $C_6H_5CH_2$, C_6H_5 or C_2H_5O).[2–5] For example, change of Y from O to S resulted in lowering of $pK_a°$ for R = CH_3 and C_6H_5 so that the rate-limiting step of the aminolysis for carbonyl esters, **I**, with benzylamines[2a,b] changed from expulsion of thiolate anion, ArS^-, from $T^{\pm}$ (with $\beta_{nuc} = \beta_X = 1.36$ and 1.86, and $\rho_{XZ} > 0$) to formation of $T^{\pm}$ (with $\beta_X = 0.55$ and 0.63 and $\rho_{XZ} > 0$) for thiocarbonyl esters,[2c,d] **II**, Table 1. The aminolysis of all the carbonyl (**I**) series, except for R = C_2H_5O (concerted, with $\rho_{XZ} < 0$), in Table 1 proceeds through the stepwise path with rate-limiting expulsion of the leaving group (with $\beta_X = 1.36–2.11$ and $\rho_{XZ} > 0$).



$$N + R-\overset{\overset{\displaystyle Y}{||}}{C}-L \underset{k_{-a}}{\overset{k_a}{\rightleftharpoons}} \underset{T^{\pm}}{R-\overset{\overset{\displaystyle Y^-}{|}}{\underset{\underset{\displaystyle N^+}{|}}{C}}-L} \xrightarrow{k_b} R-\overset{\overset{\displaystyle Y}{||}}{\underset{\underset{\displaystyle N^+}{|}}{C}} + L^- \qquad (1)$$

Another important aspect of the change of R is that the cross-interaction constants, ρ_{XZ} in eqns. (2)[6] where X and Z are substituents in the nucleophile and leaving group, are exceptionally large with R = C_2H_5 for the carbonyl[5a] as well as the thiocarbonyl[5c] series, which suggests that the interaction between nucleophile (X) and leaving group (Z) is very strong in a very tight TS structure[6] for both carbonyl and thiocarbonyl thio esters with R = C_2H_5 only.

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

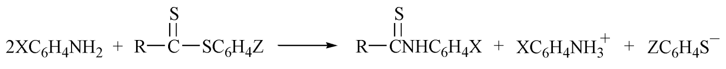
$$\rho_{XZ} = \partial\rho_X/\partial\sigma_Z = \partial\rho_Z/\partial\sigma_X \qquad (2b)$$

This surprising result prompts us to test whether the similar large ρ_{XZ} value persists with weakly basic amines (anilines) or not, and to explore the possible cause for this large ρ_{XZ} value.

In this work, we performed kinetic studies on the anilinolysis of the two dithio esters with R = C_2H_5 and $C_6H_5CH_2$, in acetonitrile at 45.0 °C, eqn. (3), and examined the aminolysis mechanism applying various structure–reactivity correlations.

Results and discussion

The reactions studied in this work followed the rate law described by eqns. (4) and (5), where S and N represent the substrate and nucleophile, aniline, and k_N is the rate constant for anilinolysis of the substrate. The reactions were run under pseudo-first-order conditions with a large excess of aniline



$$2XC_6H_4NH_2 + R-\overset{\overset{\displaystyle S}{||}}{C}-SC_6H_4Z \longrightarrow R-\overset{\overset{\displaystyle S}{||}}{C}NHC_6H_4X + XC_6H_4NH_3^+ + ZC_6H_4S^- \qquad (3)$$

with R = C_2H_5 or $C_6H_5CH_2$, X = *p*-OMe, *p*-Me, H, *p*-Cl or *p*-Br
and Z = *p*-Me, H, *p*-Cl or *p*-Br

DOI: 10.1039/b104295p

Table 1 Rates (k_N/dm^3 mol^{-1} s^{-1}) and selectivity parameters (ρ_X, β_X, ρ_Z, β_Z and ρ_{XZ}) for the aminolysis of thiol esters, **I** [RC(=O)SC$_6$H$_4$Z], and dithio esters, **II** [RC(=S)SC$_6$H$_4$Z], with benzylamines (XC$_6$H$_4$CH$_2$NH$_2$) in acetonitrile

		$R-\overset{O}{\overset{\|}{C}}-SC_6H_4Z$							$R-\overset{S}{\overset{\|}{C}}-SC_6H_4Z$						
Entry	R	k_N[a]	ρ_X[b]	β_X[b]	ρ_Z[c]	β_Z[c]	ρ_{XZ}[d]	Ref.	k_N[a]	ρ_X[b]	β_X[b]	ρ_Z[c]	β_Z[c]	ρ_{XZ}[d]	Ref.
1	CH_3	3.93 × 10^{-3} (45.0 °C)	−1.40	1.36	5.32	−2.21	0.90	2*b*	0.699 (20.0 °C)	−0.56	0.55	1.19	−0.50	0.40	2*d*
2	C_2H_5	7.32 × 10^{-3} (45.0 °C)	−2.09	2.11	2.74	−1.18	2.36	5*a*	9.84 (35.0 °C)	−2.24	2.19	2.77	−1.15	3.51	5*c*
3	$C_6H_5CH_2$	4.94 × 10^{-3} (55.0 °C)	−1.50	1.55	1.61	−1.66	0.92	5*b*	11.6 (25.0 °C)	−2.21	2.03	3.51	−1.38	2.05	5*d*
4	C_6H_5	2.51 × 10^{-3} (55.0 °C)	−1.88	1.86	3.84	−1.63	0.27	2*a*	3.82 × 10^{-1} (30.0 °C)	−0.65	0.24	0.56	−0.24	0.50	2*c*
5	C_2H_5O	2.18 × 10^{-2} (45.0 °C)	−0.63	0.63	1.51	−0.63	−0.47	4*a*							

[a] For X = Y = Z = H. [b] For Z = H. [c] For X = H. [d] For Y = H when Y is varied.

Table 2 The second order rate constants, $k_N \times 10^4$/dm^3 mol^{-1} s^{-1}, for the reactions of Z-aryl dithiophenylacetates with X-anilines in acetonitrile at 45.0 °C

	Z					
X	*p*-Me	H	*p*-Cl	*p*-Br	ρ_Z[a]	β_Z[b]
p-OMe	6.92 5.34[c] 4.07[d]	16.4	56.9	71.0 54.6[c] 41.2[d]	2.43 ± 0.14	−0.98 ± 0.07
p-Me	3.16	7.80	28.7	36.1	2.55 ± 0.14	−1.03 ± 0.07
H	1.06	2.76	11.2	14.1	2.72 ± 0.15	−1.10 ± 0.07
p-Cl	0.251	0.781	3.67	5.05	3.11 ± 0.19	−1.25 ± 0.12
m-Cl	0.0810 0.0610[c] 0.0459[d]	0.271	1.43	2.00 1.68[c] 1.28[d]	3.31 ± 0.20	−1.33 ± 0.11
ρ_X[e]	−2.95 ± 0.06	−2.64 ± 0.07	−2.42 ± 0.07	−2.34 ± 0.08		
					ρ_{XZ}[f] = 1.41 ± 0.31	
β_X[g]	1.04 ± 0.02	0.93 ± 0.03	0.85 ± 0.03	0.82 ± 0.03		

[a] The σ values were taken from ref. 17. Correlation coefficients were better than 0.996 in all cases. [b] The pK_a values were taken from ref. 18. Z = *p*-Br was excluded from the Brønsted plot for β_Z due to an unreliable pK_a value. Correlation coefficients were better than 0.996 in all cases. [c] At 35.0 °C. [d] At 25.0 °C. [e] The source of σ is the same as for footnote *a*. Correlation coefficients were better than 0.998 in all cases. [f] Correlation coefficient was 0.998. [g] The pK_a values were taken from ref. 19. Correlation coefficients were better than 0.998 in all cases.

Table 3 The second order rate constants, $k_N \times 10^3$/dm^3 mol^{-1} s^{-1}, for the reactions of Z-aryl dithiomethylacetates with X-anilines in acetonitrile at 45.0 °C

	Z					
X	*p*-Me	H	*p*-Cl	*p*-Br	ρ_Z[a]	β_Z[b]
p-OMe	9.72 19.1[c] 5.05[d]	19.8	81.2	89.5 175[c] 46.5[d]	2.42 ± 0.17	−1.00 ± 0.01
p-Me	4.05	8.50	38.3	39.8	2.53 ± 0.17	−1.06 ± 0.02
H	1.25	3.19	13.2	14.6	2.64 ± 0.08	−1.10 ± 0.06
p-Cl	0.223	0.669	3.50	3.89	3.08 ± 0.08	−1.29 ± 0.07
m-Cl	0.0551 0.128[c] 0.0242[d]	0.180	1.38	1.83 3.97[c] 0.842[d]	3.73 ± 0.24	−1.51 ± 0.03
ρ_X[e]	−3.42 ± 0.10	−3.08 ± 0.12	−2.72 ± 0.06	−2.60 ± 0.09		
					ρ_{XZ}[f] = 1.90 ± 0.26	
β_X[g]	1.20 ± 0.03	1.09 ± 0.04	0.96 ± 0.03	0.91 ± 0.04		

[a] The source of σ is the same as that for *a*, Table 2. Correlation coefficients were better than 0.995 in all cases. [b] The source of pK_a is the same as that for footnote *b*, Table 2. Correlation coefficients were better than 0.998 in all cases. [c] At 55.0 °C. [d] At 35.0 °C. [e] The source of σ is the same as for footnote *a*. Correlation coefficients were better than 0.998 in all cases. [f] Correlation coefficient was 0.998. [g] The source of pK_a is the same as that for footnote *g*, Table 2.

$$\text{Rate} = k_{obs}[S] \qquad (4)$$

$$k_{obs} = k_N[N] \qquad (5)$$

nucleophiles. The values of k_N were obtained as the slopes of plots of k_{obs} against [N], and are summarized in Tables 2 and 3 for aryl dithiophenyl- (R = $C_6H_5CH_2$) and dithiomethylacetates (R = C_2H_5), respectively. In these Tables, the selectivity parameters obtained as σ and pK_a dependence of the composite rate constant $k_N = Kk_b$, ρ_X, β_X, ρ_Z, β_Z and ρ_{XZ}, are also shown. In the determination of Brønsted coefficients, β_X and β_Z, the pK_a values in water are used; the pK_a (CH_3CN) values for structurally similar amines are known to change in parallel with the pK_a (H_2O) values.[5a,7] Although the absolute β_Z values may not be reliable, the comparison of β_Z values for different series of substrates is justified since we have determined the β_Z values in the same reaction medium, acetonitrile. In order to facilitate comparisons of rates and selectivity parameters between different substrates, (for different R groups), we have summarized them in Table 4. First of all, the anilinolysis of *O*-ethyl *S*-aryl

Table 4 Rates (k_N/dm^3 mol^{-1} s^{-1}) and selectivity parameters (ρ_X, β_X, ρ_Z, β_Z, and ρ_{XZ}) for the aminolysis of dithioesters, **II** [RC(=S)SC$_6$H$_4$Z], with anilines ($XC_6H_4NH_2$) in acetonitrile

Entry	R	k_N[a]	ρ_X[b]	β_X[b]	ρ_Z[c]	β_Z[c]	ρ_{XZ}[d]	Ref.
1	CH_3	9.46×10^{-4} (50.0 °C)	−3.05	0.84	1.90	−0.81	0.58	2*d*
2	C_2H_5	3.19×10^{-3} (45.0 °C)	−3.08	1.09	2.64	−1.10	1.90	This work
3	$C_6H_5CH_2$	2.76×10^{-4} (45.0 °C)	−2.64	0.93	2.72	−1.10	1.41	This work
4	C_6H_5	2.85×10^{-3} (55.0 °C)	−2.86	1.03	2.26	−0.76	0.60	3
5	C_2H_5O	1.71×10^{-2} (30.0 °C)	−1.46	0.54	0.45	−0.19	−0.56	4*b*

[a] For X = Y = Z = H. [b] For Z = H. [c] For X = H. [d] For Y = H when Y is varied.

dithiocarbonates[4b] (R = C_2H_5O) has been reported to proceed concertedly based on (i) the small magnitude of β_X (= 0.54) and β_Z (= −0.19) values relative to those reacting stepwise with large β_X (≥ 0.8) and $-\beta_Z$ (≤ −0.8)[1,8] and (ii) negative ρ_{XZ} (< 0).[6c] For the remaining Rs (entries 1–4), the same mechanism applies with positive ρ_{XZ}, large magnitude of $\beta_X$and β_Z, and adherence to the reactivity–selectivity principle (RSP),[6,9] *i.e.*, rate-limiting expulsion of thiolate anion (ArS^-) leaving group from the tetrahedral intermediate, $T^\pm$. Reference to Table 1 reveals that the rate is the fastest (k_N is the greatest) with R = C_2H_5 among the four stepwise reaction series (entries 1–4). This is also true for the aminolysis rates of carbonyl, **I**, and thiocarbonyl, **II**, series with benzylamines shown in Table 1. Albeit exact comparison is difficult due to the k_N values determined at different temperatures, the approximate rate order is R = C_2H_5 (σ^* = −0.10) > CH_3 (0.0) > $C_6H_4CH_2$ (+0.22) > C_6H_5 (+0.60), which is the order of decreasing electron donating ability of the R group represented by the Taft σ^* scale[10] as shown in parentheses. This is quite reasonable in view of the rate-limiting expulsion of the ArS^- group from $T^\pm$, since in the tetrahedral structure only the inductive effect is expected to apply and the greater the electron donation by R, the greater will be the leaving ability of the ArS^- group (k_b). If the electronic effect of R were predominant in the bond formation step (k_a), then the rate sequence should have been in the reverse order since a stronger electron acceptor R will lead to a stronger positive charge on the carbonyl carbon in the substrate.

Thus, the fastest rates for aminolyses of carbonyl as well as thiocarbonyl esters with R = C_2H_5 are in line with the stepwise mechanism with rate-limiting expulsion of ArS^-. The concerted reaction pathway predicted for R = C_2H_5O (σ^* = −0.18) both with anilines[4b] (Table 4) and benzylamines[4a] (Table 1, entry 5) can also be explained in a similar vein: substitution of ethoxy group destabilizes the tetrahedral intermediate so much as to prevent the existence of the putative intermediate, and therefore, the mechanism changes from stepwise to enforced concerted. This destabilization is mainly due to a strong electron donating effect of the ethoxy group in the TS leading to a greater nucleofugality and faster leaving from the tetrahedral intermediate of the ArS^- group.

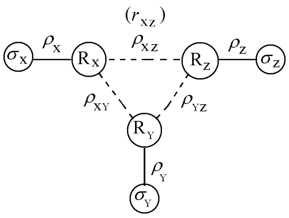
For R = CH_3 and C_6H_5 (entries 1 and 4) groups, a biphasic rate dependence on the amine basicity is observed; the aminolysis proceeds stepwise with rate-limiting expulsion of ArS^- with weakly basic anilines[2d,3] (entries 1 and 4 in Table 4) but with rate-limiting formation of $T^\pm$ with strongly basic benzylamines[2c,d] (entries 1 and 4 for the dithio series in Table 1). The change of the rate-determining step is apparent from (i) the change in β_X (and β_Z) from large to smaller magnitude and (ii) positive ρ_{XZ} throughout.[6c] Although $\beta_X \approx 0.6$ (entries 1 and 4 in Table 1) may be considered rather high for the rate-limiting formation of $T^\pm$, for which β_X values of less than 0.3 ($\beta_X \geq 0.3$)[8] are common and a concerted pathway may seem more appropriate, we nevertheless found that β_X values come out rather high in general for the aminolysis with benzylamines as the comparison of β_X values in Table 1 with those in Table 4 shows. This prediction of rate-limiting formation is also based on the positive ρ_{XZ} value,[6c] since in the concerted nucleophilic substitution reactions a negative ρ_{XZ} is expected as we found for R = C_2H_5O in Tables 1 and 4 (entry 5).

We find a mechanistic difference between the carbonyl (**I**) (Table 1) and thiocarbonyl (**II**) series (Tables 1 and 4): for the former series (**I**) the rate-limiting expulsion (k_b) applies even up to relatively strong basic amines (benzylamines),[2a,b] whereas for the latter dithio series, (**II**), the rate-limiting step changes from rate-limiting expulsion of ArS^- from $T^\pm$ with weakly basic amines, anilines[2d,3] (Table 4), to rate-limiting formation with strongly basic amines, benzylamines[2c,d] (Table 1). This means that the center of the Brønsted curvature for the thiocarbonyl series, **II**, shifted to a lower pK_a value, *i.e.*, from $pK_a° \geq pK_a = 9.51$ (for *p*-MeO-benzylamine in H_2O) for the carbonyl to $pK_a° \leq pK_a = 9.14$ (for *p*-Cl-benzylamine in H_2O) for the thiocarbonyl series. The smaller $pK_a°$ value results from a smaller k_{-a}/k_b ratio (for a given amine and leaving group)[11] for the thiocarbonyl compared to the carbonyl compound. It has been shown that the change of carbonyl to thiocarbonyl decreases both k_{-a} and k_b but the decrease in k_{-a} is greater.[11] A similar effect has been found in the aminolysis of *p*-nitrophenyl benzoate and thionobenzoate in aqueous solution. The $pK_a°$ value of greater than 11 was obtained for the former reactions, whereas $pK_a° = 9.2$ was found with the latter reactions.[12] Again $pK_a° = 7.8$ for the pyridinolysis of methyl 2,4-dinitrophenyl carbonate shifted to $pK_a° = 6.8$ for the same reactions with ethyl 2,4-dinitrophenyl thionocarbonate in aqueous solution.[11]

It has been shown by MO calculation that the possibility of an acyl transfer reaction through a tetrahedral intermediate is the greater, the lower the $\pi^*_{C=O}$ (or $\pi^*_{C=S}$) level and the higher the $\sigma^*_{C\text{–}LG}$ level, *i.e.*, the greater the level gap, $\Delta\varepsilon = \varepsilon(\sigma^*) - \varepsilon(\pi^*)$.[13] For $CH_3C(=O)Cl$ and $CH_3C(=S)Cl$ at the RHF/6-31+G*//B3LYP/6-31+G* level,[14] the $\pi^*_{C=S}$ level is much lower (by *ca.* 1.9 eV) but the $\sigma^*_{C\text{–}Cl}$ level is slightly lower (by *ca.* 0.3 eV) than the corresponding levels of the carbonyl compound so that the level gap, $\Delta\varepsilon$, is much greater for the thiocarbonyl transfers. This means that the thiocarbonyl transfer is more prone to proceed through a tetrahedral intermediate than the carbonyl transfers. Since both the $\pi^*_{C=S}$ and $\sigma^*_{C\text{–}LG}$ levels of thiocarbonyl compounds are lower than the corresponding levels of carbonyl compounds, both the initial attack on the thiocarbonyl π bond, C=S, by a nucleophile, *e.g.*, amines, (*i.e.*, k_a is greater) and the leaving group expulsion due to electron flow into the $\sigma^*_{C\text{–}LG}$ orbital in a stepwise mechanism are more facile (*i.e.*, k_b is greater) for the thiocarbonyl than the carbonyl derivatives. However, since the π^*–σ^* level gap is much narrower for the carbonyl compound, the concerted carbonyl transfer will be more facile for the carbonyl than the thiocarbonyl due to greater π^*–σ^* mixing. Theoretically, the carbonyl transfer through a tetrahedral TS is found to have a lower energy barrier.[14]

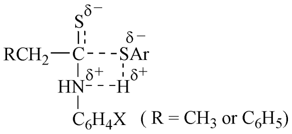
Although predictions from MO theory are applicable strictly in the gas phase, our experimental results in acetonitrile shown in Table 1 are in excellent agreement. Indeed, the rates for the thiocarbonyl series are seen to be much faster than those for the corresponding carbonyl series (comparisons are valid only for entries 2 and 3 which have a common mechanism of the rate-limiting breakdown of $T^\pm$; for entries 1 and 4, the thiocarbonyl and carbonyl compounds have different reaction mechanisms).

An important aspect we note in Tables 1 and 4 is that the magnitude of ρ_{XZ} is unusually large for R = C_2H_5 (entry 2 in both Tables). The size of ρ_{XZ} is considered to represent the intensity of interaction in the TS[6] between the two substituents in the nucleophile (X) and leaving group (Z), and hence the larger the ρ_{XZ}, the stronger is the interaction, *i.e.*, the closer are the two fragments, the nucleophile and leaving group, in the TS. In order to see whether this interpretation is correct or not and whether the size of ρ_{XZ} is indeed inversely related to the distance (r_{XZ} in Scheme 1) between the two, we attempted to optimize the MO theoretical structures of the intermediate, $T^{\pm}$, and the substrate. This was a rather difficult endeavour since the systems are so large that *ab initio* calculations, even at a relatively low level, require extremely long computational times and hence are very expensive. The intermediate structure at the RHF/6-31G* level revealed that the amine, aniline, and the leaving group, thiolate anion, are located nearer due to the bulky ethyl group in $T^{\pm}$, especially when the ethyl group rotates freely around the C–C bond, so that the TS structure corresponding to the k_b step should also be crowded and the closer distance between the two fragments, nucleophile (X) and leaving group (Z), can be explained. For other R groups, *e.g.*, with R = CH_3 or $C_6H_5CH_2$, the structures of the intermediates are less crowded, and hence the distance, r_{XZ}, is greater than that for R = C_2H_5.



Scheme 1

The kinetic isotope effects, k_H/k_D, involving deuterated amine nucleophiles ($XC_6H_4ND_2$) have been determined[6b] in acetonitrile as shown in Table 5. The k_H/k_D values are significantly greater than unity, *i.e.*, primary kinetic isotope effects are operative and the amine proton shift in the TS is implicated.[6b] This means that deprotonation of the amine hydrogen takes place concurrently with the expulsion (k_b) of the leaving group, ArS^-. In this proposed TS structure (Scheme 2), the leaving group departure is facilitated by a partial protonation of ArS^- and therefore the activation energy required for the C–S bond scission and reformation of the C=S bond may be partially lowered. Even though the proton is transferred to thiolate anion partially in the TS, the aniline, which is in large excess, will become protonated eventually and the reaction proceeds as represented by eqn. (3). The proposed TS structure (Scheme 2) should lead to relatively low activation enthalpies ($\Delta H^{\neq}$) and large negative activation entropies ($\Delta S^{\neq}$), as we have found for all the reactions listed in Tables 1 and 4 (except for entry 5, R = C_2H_5O). The activation parameters determined in the present work by the Eyring equation[15] are shown in Table 6. We note that the $\Delta H^{\neq}$ values for the reactions of dithio compounds with R = C_2H_5 are somewhat higher than the other corresponding values. In addition the k_H/k_D values for this series tend to be somewhat smaller than the other corresponding values. This could be related to the relatively tight TS in which the nucleophile (X) and the thiophenolate leaving group (Z) are in rather close proximity, as the large magnitude of ρ_{XZ} suggested, so that the protonation (on deprotonation) has progressed very little and hydrogen bonding assistance for bond cleavage is low.



Scheme 2

The magnitudes of the selectivity parameters in Tables 2 and 3 decrease as the rates become faster so that the reactivity–selectivity principle (RSP) holds.[9] This adherence to the RSP is considered another necessary condition for a stepwise acyl transfer reaction with rate-limiting breakdown of the tetrahedral intermediate.[6a–c]

Table 5 Kinetic isotope effects for the reactions of dithioesters, **II** [RC(=S)SC_6H_4Z] with deuterated X-anilines in acetonitrile at 45.0 °C

X	Z	R = C_2H_5 k_H/k_D	R = $C_6H_5CH_2$ k_H/k_D
p-OMe	*p*-Me	1.64 ± 0.02[a]	1.53 ± 0.02[a]
p-OMe	H	1.47 ± 0.02	1.39 ± 0.02
p-OMe	*p*-Cl	1.30 ± 0.03	1.32 ± 0.03
p-OMe	*p*-Br	1.13 ± 0.03	1.19 ± 0.03
p-Cl	*p*-Me	1.24 ± 0.02	1.74 ± 0.02
p-Cl	H	1.13 ± 0.02	1.66 ± 0.03
p-Cl	*p*-Cl	1.08 ± 0.03	1.51 ± 0.02
p-Cl	*p*-Br	1.04 ± 0.02	1.42 ± 0.02

[a] Standard deviations.

Conclusions

We conclude that: (i) the stepwise aminolysis reaction of carbonyl or thiocarbonyl esters or carbonates exhibits a positive ρ_{XZ}, irrespective of whether the rate-determining step is formation or breakdown of the tetrahedral intermediate, $T^{\pm}$. (ii) The concerted aminolysis mechanism, on the other hand, is characterized by a negative ρ_{XZ}. (iii) The stepwise mechanism is more likely to be obtained, the lower the $\pi^*_{C=O}$ or $\pi^*_{C=S}$ level and the higher the σ^*_{C-LG} level, *i.e.*, the wider the level gap $\Delta\varepsilon = \varepsilon(\sigma^*) - \varepsilon(\pi^*)$. (iv) Since both the π^* and σ^* levels of the thiocarbonyl (C=S) compound are lower than the corresponding levels of the carbonyl (C=O) compound, the reactivity of

Table 6 Activation parameters[a] for the reactions of dithioesters, **II** [RC(=S)SC_6H_4Z], with X-anilines in acetonitrile

R	X	Z	$\Delta H^{\neq}$/kcal mol^{-1}	$-\Delta S^{\neq}$/cal mol^{-1} K^{-1}
C_2H_5	*p*-OMe	*p*-Me	12.7	28
	p-OMe	*p*-Br	12.7	24
	m-Cl	*p*-Me	16.0	28
	m-Cl	*p*-Br	14.9	24
$C_6H_5CH_2$	*p*-OMe	*p*-Me	4.4	59
	p-OMe	*p*-Br	4.5	54
	m-Cl	*p*-Me	4.7	67
	m-Cl	*p*-Br	4.0	64

[a] Calculated by the Eyring equation. The maximum errors calculated (by the method in ref. 20) are ±0.6 kcal mol^{-1} and ±2 e.u. for $\Delta H^{\neq}$ and $\Delta S^{\neq}$, respectively.

the stepwise reaction is faster for the thiocarbonyl than for the carbonyl esters. (v) The reactivity order for the stepwise aminolysis follows roughly the order of the electron donating ability of the R group as represented by the Taft σ^* scale with the fastest rate for $R = C_2H_5$. (vi) The largest ρ_{XZ} value of $R = C_2H_5$ for the stepwise aminolysis among four R groups ($R = CH_3$, C_2H_5, $C_6H_5CH_2$ and C_6H_5) appears to result from the close proximity of nucleophile (X) and leaving group (Z) in the TS due to the steric crowding of the bulky C_2H_5 group in the tetrahedral intermediate $T^{\pm}$.

Experimental

Materials

Merck GR acetonitrile was used after three distillations. The Aldrich anilines were used without further purification.

Substrates

Preparations and analytical data are reported elsewhere.[5c,d]

Kinetic measurements

Rates were measured conductometrically in acetonitrile. Since the anilines were in large excess, $[S] \approx 10^{-3}$ M and $[N] = 0.02$–0.45 M in eqns. (4) and (5), the proton transfer can be considered to occur to aniline, instead of thiolate anion, and the conductivity of the medium increases with the progress of the reaction as expressed by eqn. (3). The conductivity bridge used in this work was a laboratory-made computer-automatic A/D converter conductivity bridge. Pseudo-first-order rate constants, k_{obs}, were determined by the Guggenheim method.[16] More than 4 concentrations of aniline were used in the determination of k_N [eqn. (5)] and the k_N values reported are averages of at least two determinations with reproducibility of ±3%.

Product analysis

Substrate, phenyl dithiophenylacetate (0.05 mol) (and phenyl dithiomethylacetate (0.05 mol)), was reacted with excess aniline (0.5 mol) with stirring for more than 15 half-lives at 45.0 °C in acetonitrile, and the products were isolated by evaporating the solvent under reduced pressure. The product mixture was treated with column chromatography (silica gel, 20% ethyl acetate–*n*-hexane). Analysis of the products gave the following results. IR absorptions are given in cm^{-1} and NMR shifts in ppm.

$C_6H_5CH_2C(=S)NHC_6H_5$. Liquid, IR (KBr) 1606 (N–H), 1512 (C–C, aromatic), 1492 (C=C, aromatic), 1461 (C–H, CH_2), 1209 (C=S), 705 (C–H, aromatic); ^1H NMR (400 MHz, $CDCl_3$) δ 3.14 (1H, s, NH), 4.14 (2H, s, CH_2), 7.36–7.51 (10H, m, aromatic ring); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 214.2 (C=S), 134.6, 132.7, 131.4, 129.0, 127.4, 126.5, 124.3, 122.7, 58.1.

$CH_3CH_2C(=S)NHC_6H_5$. Liquid, IR (KBr) 2989 (C–H, CH_2), 2938 (C–H, CH_3), 1607 (N–H), 1504 (C–C, aromatic), 1463 (C=C, aromatic), 1279 (C=S), 701 (C–H, aromatic); ^1H NMR (400 MHz, $CDCl_3$) δ 2.42 (3H, s, CH_3), 3.12 (1H, s, NH), 3.17 (2H, q, CH_2), 7.51–7.68 (4H, m, aromatic ring); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 224.4 (C=S), 134.6, 133.1, 131.8, 130.2, 58.0, 44.6.

Acknowledgements

This work was supported by a Korea Research Foundation Grant (KRF-2000-015-DP0209).

References

1 (*a*) M. I. Page and A. Williams, *Organic and Bio-organic Mechanisms*, Longman, Harlow, 1997; (*b*) A. Williams, *Concerted Organic and Bio-organic Mechanisms*, CRC Press, Boca Raton, 2000.

2 (*a*) I. Lee and H. J. Koh, *New J. Chem.*, 1996, **20**, 131; (*b*) H. K. Oh, J. H. Yang, H. W. Lee and I. Lee, *Bull. Korean Chem. Soc.*, 1999, **20**, 1418; (*c*) H. K. Oh, C. H. Shin and I. Lee, *Bull. Korean Chem. Soc.*, 1995, **16**, 657; (*d*) H. K. Oh, S. Y. Woo, C. H. Shin, Y. S. Park and I. Lee, *J. Org. Chem.*, 1997, **62**, 5780.

3 H. K. Oh, C. H. Shin and I. Lee, *J. Chem. Soc., Perkin Trans. 2*, 1995, 1169.

4 (*a*) H. K. Oh, Y. H. Lee and I. Lee, *Int. J. Chem. Kinet.*, 2000, **32**, 131; (*b*) H. K. Oh, J. Y. Lee, J. H. Yun, Y. S. Park and I. Lee, *Int. J. Chem. Kinet.*, 1998, **30**, 419.

5 (*a*) H. K. Oh, J. H. Yang, I. H. Cho, H. W. Lee and I. Lee, *Int. J. Chem. Kinet.*, 2000, **32**, 485; (*b*) H. K. Oh, S. K. Kim and I. Lee, *Bull. Korean Chem. Soc.*, 1999, **20**, 1017; (*c*) H. K. Oh, S. K. Kim, H. W. Lee and I. Lee, *New J. Chem.*, 2001, **25**, 313; (*d*) H. K. Oh, S. K. Kim, I. H. Cho, H. W. Lee and I. Lee, *J. Chem. Soc., Perkin Trans. 2*, 2000, 2306.

6 (*a*) I. Lee, *Adv. Phys. Org. Chem.*, 1992, **27**, 57; (*b*) I. Lee, *Chem. Soc. Rev.*, 1994, **24**, 223; (*c*) I. Lee and H. W. Lee, *Collect. Czech. Chem. Commun.*, 1999, **64**, 1529; (*d*) N. S. Isaacs, *Physical Organic Chemistry*, 2nd edn., Longman, Harlow, 1995, Ch. 4.

7 (*a*) I. Lee, C. K. Kim, I. S. Han, H. W. Lee, W. K. Kim and Y. B. Kim, *J. Phys. Chem. B*, 1999, **103**, 7302; (*b*) W. J. Spillane, G. Hogan, P. McGroth, J. King and C. Brack, *J. Chem. Soc., Perkin Trans. 2*, 1996, 2099.

8 M. J. Gresser and W. P. Jencks, *J. Am. Chem. Soc.*, 1977, **99**, 6963, 6970.

9 (*a*) A. Pross, *Adv. Phys. Org. Chem.*, 1997, **14**, 69; (*b*) E. Buncel and H. Wilson, *J. Chem. Educ.*, 1987, **64**, 475.

10 (*a*) R. W. Taft, in *Steric Effects in Organic Chemistry*, M. S. Newman, Ed., Wiley, New York, 1956; (*b*) F. Ruff and I. G. Csizmadia, *Organic Reactions, Equilibria, Kinetics and Mechanism*, Elsevier, Amsterdam, 1994, p. 191.

11 E. A. Castro, M. Cufillos, J. G. Santos and J. Tellez, *J. Org. Chem.*, 1997, **62**, 2512.

12 P. Campbell and B. A. Lapinskas, *J. Am. Chem. Soc.*, 1977, **99**, 5378.

13 (*a*) S. Yamabe and T. Minato, *J. Org. Chem.*, 1983, **48**, 2972; (*b*) C. K. Kim, H. G. Li, H. W. Lee, C. K. Sohn, Y. I. Chun and I. Lee, *J. Phys. Chem. A*, 2000, **104**, 4069.

14 I. Lee, C. K. Kim, H. G. Li, C. K. Sohn, C. K. Kim, H. W. Lee and B. S. Lee, *J. Am. Chem. Soc.*, 2000, **112**, 11162.

15 F. Ruff and I. G. Csizmadia, *Organic Reactions, Equilibria, Kinetics and Mechanism*, Elsevier, Amsterdam, 1994, p. 141.

16 E. A. Guggenheim, *Philos. Mag.*, 1926, **2**, 538.

17 C. Hansch, A. Leo and R. W. Taft, *Chem. Rev.*, 1991, **91**, 165.

18 *Dictionary of Organic Chemistry*, 5th edn., J. Buckingham, Ed., Chapman and Hall, New York, 1982.

19 A. Streitweiser, Jr. and C. H. Heathcock, *Introduction to Organic Chemistry*, 3rd edn., Macmillan, New York, 1989, p. 693.

20 K. B. Wiberg, *Physical Organic Chemistry*, Wiley, New York, 1964, p. 378.