JOC Note

Kinetics and Mechanism of the Reactions of *S*-2,4-Dinitrophenyl 4-Substituted Thiobenzoates with Secondary Alicyclic Amines

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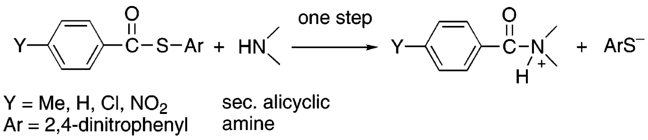

The title reactions, in 44 wt % ethanol−water at 25.0 °C, exhibit slightly curved Brønsted-type plots (log k_N versus pK_a of amines) with slopes $\beta_1 = 0.1-0.44$ (at high pK_a) and β_2 ca. 0.7 (at low pK_a). The magnitude of some of these slopes, together with the fact that the curvature center ($pK_a^0 = 9.5-10.8$) does not change with the electronic effects of the benzoyl substituent, suggests that these reactions are not stepwise, but concerted.

The kinetics and mechanisms of the reactions (especially aminolysis) of aryl benzoates are well-documented.[1−4] Nevertheless, the kinetics and mechanisms of the same reactions of aryl thiobenzoates are not well understood.[5−9] Concerning the kinetics of the aminolysis of *S*-aryl thiobenzoates (aryl thiolbenzoates, Ph−CO−SAr), there have been only a few reports in the literature.[7,9]

The reactions of aryl thiolbenzoates with anilines in methanol were claimed to be concerted,[7a] in contrast to the benzylaminolysis[7b] and pyridinolysis of the same substrates in acetonitrile,[7c] which were found to be stepwise, through a zwitterionic tetrahedral intermediate ($T^{\pm}$) on the reaction pathway. We have recently found that the reactions of secondary alicyclic (SA) amines[9a] and pyridines[9b] with 4-nitrophenyl 4-substituted thiolbenzoates and the latter amines with 2,4-dinitrophenyl 4-substituted thiolbenzoates[9c] in aqueous ethanol are stepwise.

On the other hand, we have reported that the pyridinolysis of 2,4-dinitrophenyl 4-Y-substituted benzoates (Y = H, Cl, CN, and NO_2) in aqueous ethanol is stepwise.[3a−d] In contrast, we have found that the reactions of SA amines with 2,4-dinitrophenyl 4-cyanobenzoate in the same solvent mixture are concerted.[3e]

Another question that needs clarification is the influence of the benzoyl Y-substituent on the kinetics and mechanism. Um and co-workers have reported that the reactions of 2,4-dinitrophenyl Y-substituted benzoates with SA amines in 20 mol % DMSO−water are stepwise, on the basis of the curved Brønsted-type plots (log *k* versus amine pK_a) obtained.[4a] These were explained by the existence of a $T^{\pm}$ intermediate and a change in the rate-determining step.[4a] It was found that the curvature center of these plots (pK_a^0) does not change with the nature of the Y substituent.[4a] The same conclusion was drawn for the reactions of the same amines with the corresponding 4-nitrophenyl derivatives in the same solvent.[4b]

In contrast to the above conclusion, Gresser and Jencks have found that, for the stepwise reactions of quinuclidines (tertiary alicyclic amines) with diaryl carbonates in water, the pK_a^0 value increases as the substituent in the nonleaving group of a diaryl carbonate becomes more electron-withdrawing.[10]

In accordance to the findings of the latter authors, we have found that, for the stepwise pyridinolysis of 2,4-dinitrophenyl Y-benzoates in aqueous ethanol, the pK_a^0 value increases with the increasing electron attraction from the Y-substituent in the benzoyl group.[3a−d] A similar conclusion was reached for the stepwise reactions of 4-nitrophenyl 4-Y-substituted thiolbenzoates with SA amines[9a] and pyridines[9b] and those of 2,4-dinitrophenyl

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(1) (a) Kirsh, J. F.; Clewell, W.; Simon, A. *J. Org. Chem.* **1968**, *33*, 127. (b) Nummert, V.; Piirsalu, M. *Org. React.* **1977**, *14*, 263. (c) Guanti, G.; Dell'Erba, C.; Pero, F.; Leandri, G. *J. Chem. Soc., Perkin Trans. 2* **1977**, 966. (d) Machacek, V.; Mareckova, S.; Sterba, V. *Collect. Czech. Chem. Commun.* **1979**, *44*, 1779. (e) Sawada, M.; Ichihara, M.; Ando, T.; Yukawa, Y.; Tsuno, Y. *Tetrahedron Lett.* **1981**, *22*, 4733. (f) Thea, S.; Guanti, G.; Petrillo, G.; Hopkins, A.; Williams, A. *J. Chem. Soc., Chem. Commun.* **1982**, 577. (g) Anvia, F.; Bowden, K. *J. Chem. Soc., Perkin Trans. 2* **1990**, 1805. (h) El Seoud, O. A.; Martins, M. *J. Phys. Org. Chem.* **1995**, *8*, 637. (i) Um, I. H.; Oh, S. J.; Kwon, D. S. *Bull. Korean Chem. Soc.* **1996**, *17*, 802. (j) Nummert, V.; Piirsalu, M. *J. Chem. Soc., Perkin Trans. 2* **2000**, 583. (k) Bauerova, I.; Ludwig, M. *Collect. Czech. Chem. Commun.* **2001**, *66*, 770. (l) Fife, T. H.; Singh, R.; Bembi, R. *J. Org. Chem.* **2002**, *67*, 3179. (m) El Seoud, O. A.; Ruasse, M. F.; Rodrigues, W. A. *J. Chem. Soc., Perkin Trans. 2* **2002**, 1053. (n) Neuvonen, H.; Neuvonen, K.; Pasanen, P. *J. Org. Chem.* **2004**, *69*, 3794.

(2) (a) Menger, F. M.; Smith, J. H. *J. Am. Chem. Soc.* **1972**, *94*, 3824. (b) Ciuffarin, E.; Loi, A.; Isola, M.; Lupetti, A.; Sagramora, L.; Senatore, L. *J. Org. Chem.* **1983**, *48*, 1047. (c) Bell, K. H. *Aust. J. Chem.* **1987**, *40*, 1723. (d) Koh, H. J.; Lee, H. C.; Lee, H. W.; Lee, I. *Bull. Korean Chem. Soc.* **1995**, *16*, 839.

(3) (a) Castro, E. A.; Santander, C. L. *J. Org. Chem.* **1985**, *50*, 3595. (b) Castro, E. A.; Steinfort, G. B. *J. Chem. Soc., Perkin Trans. 2* **1983**, 453. (c) Castro, E. A.; Valdivia, J. L. *J. Org. Chem.* **1986**, *51*, 1668. (d) Castro, E. A.; Becerra, M. C. *Bol. Soc. Chil. Quim.* **1988**, *33*, 67. (e) Castro, E. A.; Hormazabal, A.; Santos, J. G. *Int. J. Chem. Kinet.* **1998**, *30*, 267.

(4) (a) Um, I.-H.; Min, J.-S.; Lee, H.-W. *Can. J. Chem.* **1999**, *77*, 659. (b) Um, I.-H.; Min, J.-S.; Ahn, J.-A.; Hahn, H.-J. *J. Org. Chem.* **2000**, *65*, 5659. (c) Um, I.-H.; Baek, M.-H.; Hahn, H.-J. *Bull. Korean Chem. Soc.* **2003**, *24*, 1245. (d) Um, I.-H.; Park, H.-R.; Kim E.-Y *Bull. Korean Chem. Soc.* **2003**, *24*, 1251. (e) Um, I.-H.; Kim, K.-H.; Park, H.-R.; Fujio, M.; Tsuno, Y. *J. Org. Chem.* **2004**, *69*, 3937.

(5) Castro, E. A. *Chem. Rev.* **1999**, *99*, 3505 and references therein.

(6) (a) Um, I.-H.; Lee, J.-Y.; Kim, H.-T.; Bae, S.-K. *J. Org. Chem.* **2004**, *69*, 2436. (b) Cevasco, G.; Thea, S. *J. Org. Chem.* **2005**, *70*, 4203.

(7) (a) Lee, I.; Shim, C. S.; Lee, H. W. *J. Chem. Res., Synop.* **1992**, 90. (b) Lee, I.; Koh, H. J. *New J. Chem.* **1996**, *20*, 131. (c) Koh, H. J.; Han, K. L.; Lee, I. *J. Org. Chem.* **1999**, *64*, 4783.

(8) (a) Um, I.-H.; Lee, S.-E.; Kwon, H.-J. *J. Org. Chem.* **2002**, *67*, 8999. (b) Um, I.-H.; Seok, J.-A.; Kim, H.-T.; Bae, S.-K. *J. Org. Chem.* **2003**, *68*, 7742. (c) Um, I.-H.; Han, H.-J.; Baek, M.-H.; Bae, S.-Y. *J. Org. Chem.* **2004**, *69*, 6365. (d) Oh, H. K.; Lee, J. M.; Lee, H. W.; Lee, I. *Int. J. Chem. Kinet.* **2004**, *36*, 434.

(9) (a) Castro, E. A.; Bessolo, J.; Aguayo, R.; Santos, J. G. *J. Org. Chem.* **2003**, *68*, 8157. (b) Castro, E. A.; Vivanco, M.; Aguayo, R.; Santos, J. G. *J. Org. Chem.* **2004**, *69*, 5399. (c) Castro, E. A.; Aguayo, R.; Bessolo, J.; Santos, J. G. *J. Org. Chem.* **2005**, *70*, 3530.

(10) (a) Gresser, M. J.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 6970.

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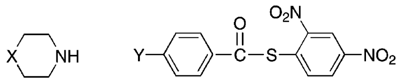
TABLE 1. Values of pK_a for the Conjugate Acids of SA Amines and Those of k_N for the SA Aminolysis of *S*-2,4-Dinitrophenyl 4-Methylthiobenzoate (1), *S*-2,4-Dinitrophenyl Thiobenzoate (2), *S*-2,4-Dinitrophenyl 4-Chlorothiobenzoate (3), and *S*-2,4-Dinitrophenyl 4-Nitrothiobenzoate (4)[a]

		k_N/s^{-1} M^{-1}			
SA amine	pK_a	**1**	**2**	**3**	**4**
piperidine	10.82	63 ± 4	88 ± 5	340 ± 20	1770 ± 120
piperazine	9.71	32 ± 2	46 ± 3	130 ± 7	460 ± 30
1-(2-hydroxyethyl)piperazine	9.09	9.7 ± 0.7	12 ± 1	35 ± 2	200 ± 15
morpholine	8.48	5.2 ± 0.3	7.7 ± 0.5	17 ± 1	85 ± 6
1-formylpiperazine	7.63	0.93 ± 0.05	1.4 ± 0.1	3.2 ± 0.2	16 ± 1
piperazinium ion	5.37	0.054 ± 0.003	0.071 ± 0.004	0.14 ± 0.01	0.61 ± 0.04

[a] Both the pK_a and k_N values were determined in 44 wt % ethanol−water, at 25.0 °C, ionic strength 0.2 M (KCl).

4-substituted thiolbenzoates[9c] with the latter amine series, all in aqueous ethanol.

To clarify the mechanisms of the aminolysis of aryl thiolbenzoates and the corresponding benzoates and to shed more light on the influence of the benzoyl substituent on the pK_a^0 value, in this work we investigate the reactions of 2,4-dinitrophenyl 4-substituted thiolbenzoates (**1**−**4**) with SA amines in aqueous ethanol. We have chosen these amines because of the constancy of the structures and for comparison with other reactions of these amines. Other goals are to determine the effects of the amine nature and the leaving group on these mechanisms.



SA amines

1 (Y = Me)
2 (Y = H)
3 (Y = Cl)
4 (Y = NO$_2$)

The rate law exhibited by the title reactions is given by eq 1, where k_{obsd}, k_0 and k_N are the pseudo-first-order, the solvolysis and the aminolysis rate constants, respectively, and N represents the SA amine.

$$k_{obsd} = k_0 + k_N\,[\mathrm{N}] \qquad (1)$$

The values of k_N (obtained as slopes of plots of eq 1) are shown in Table 1, together with the pK_a values of the conjugate acids of the SA amines.

For the reactions of a given SA amine with thiolbenzoates **1**−**4**, the k_N values (Table 1) are lower (ca. 5−10-fold) than those for the reactions of an isobasic pyridine with the same substrates in the same solvent.[9c] This is an indication that the carbonyl carbon of these substrates is relatively soft (due to the sulfur atom in the leaving group) and prefers to bind to the softer pyridine nucleophile relative to the relatively harder SA amine. This is in accordance with the principle of "Hard and Soft Acids and Bases (HSAB)" of Pearson.[11]

The pK_a and k_N values were statistically corrected before obtaining the Brønsted-type plots.[12] These plots are shown in Figures 1 and 2. The q parameter represents the number of equivalent basic sites in the free amine: $q = 1$ for all SA amines, except the symmetrical piperazine, for which $q = 2$. The p parameter is the number of equivalent protons in the conjugate acid of the amine: $p = 2$ for all the conjugate acids of the SA amines, except piperazinium cation, for which $p = 4$.[13]

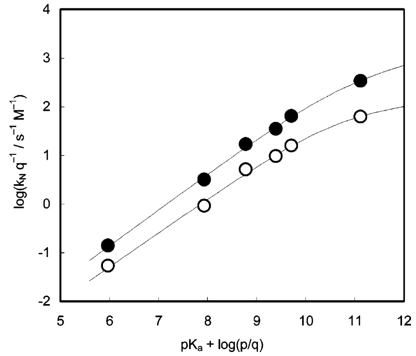


FIGURE 1. Brønsted-type plots (statistically corrected) for the SA aminolysis of **1** (○) and **3** (●) in 44 wt % ethanol−water, at 25.0 °C, and an ionic strength of 0.2 M (KCl).

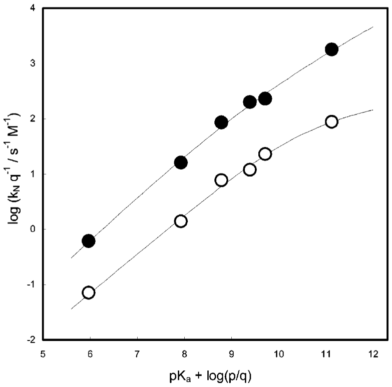


FIGURE 2. Brønsted-type plots (statistically corrected) for the SA aminolysis of **2** (○) and **4** (●) in 44 wt % ethanol−water, at 25.0 °C, and an ionic strength of 0.2 M (KCl).

The lines in the Brønsted-type plots of Figures 1 and 2 were calculated through an equation (eq 2) based on the existence of a zwitterionic tetrahedral intermediate (T$^{\pm}$) on the reaction pathway and a change in the rate-limiting step, from T$^{\pm}$ breakdown to its formation, as the amine basicity increases.[14] Equation 2 contains four parameters: log k_N^0 and pK_a^0 (which are the corresponding values at the center of the Brønsted curvature) and β_1 and β_2 (which are the slopes at high and low pK_a,

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[11] (a) Pearson, R. G. *J. Chem. Educ.* **1968**, *45*, 581, 643. (b) Pearson, R. G. *J. Org. Chem.* **1989**, *54*, 1423.

[12] Bell, R. P. *The Proton in Chemistry*; Methuen: London, U.K., 1959; p 159.

[13] Castro, E. A.; Ureta, C. *J. Org. Chem.* **1989**, *54*, 2153.

[14] Bond, P. M.; Castro, E. A.; Moodie, R. B. *J. Chem. Soc., Perkin Trans. 2* **1976**, 68.

TABLE 2. Values of the Fitting Parameters in Eq 2, Obtained for the SA Aminolysis of Thiolbenzoates 1−4

parameter	1	2	3	4
$\log k_N{}^0$	1.62 ± 0.26	1.69 ± 0.33	2.40 ± 0.26	2.31 ± 1.27
$pK_a{}^0$	10.59 ± 0.55	10.43 ± 0.69	10.81 ± 0.50	9.49 ± 2.0
β_1	0.10 ± 0.26	0.14 ± 0.24	0.20 ± 0.24	0.44 ± 0.16
β_2	0.70 ± 0.03	0.71 ± 0.04	0.74 ± 0.03	0.80 ± 0.08
$R^{2\,a}$	0.9970	0.9962	0.9986	0.9973

[a] *R* is the correlation coefficient. Errors are standard errors.

respectively). A similar equation was reported by Gresser and Jencks.[15]

$$\log(k_N/k_N{}^0) = \beta_2(pK_a - pK_a{}^0) - \log[(1 + a)/2]$$
$$\log a = (\beta_2 - \beta_1)(pK_a - pK_a{}^0) \qquad (2)$$

The best parameters obtained for the fit of this equation to the experimental points are shown in Table 2. The values of $\Delta\beta/\Delta pK_a$ for the Brønsted curvatures are ca. 0.1 for the reactions of **1**−**3** and 0.07 for **4**.

Although the fittings of eq 2 to the experimental points (Figures 1 and 2) seem reasonable and some β_1 values (those for the reactions of thiolbenzoates **1**−**3**) are in accordance with those usually obtained for stepwise reactions when formation of the $T^\pm$ intermediate is rate determining,[5,9,10,13−16] we have reasons to believe that these reactions are more likely to be concerted rather than stepwise.

The reasons are:

(1) The β_1 value 0.44 for the reaction of thiolbenzoate **4** is not in agreement with those usually found in stepwise reactions when formation of $T^\pm$ is rate-determining ($\beta_1 = 0.1−0.3$).[5,9,13−16]

(2) The β_2 values for the reactions of thiolbenzoates **1**−**3** are not in accordance with those obtained for stepwise mechanisms with rate-limiting breakdown to products of $T^\pm$ ($\beta_2 = 0.8−1$).[5,9,13−16] Moreover, the difference ($\beta_2 - \beta_1$) found for the reactions of all four thiolbenzoates, ($\beta_2 - \beta_1$) ≈ 0.36−0.60, is smaller than that obtained for stepwise reactions, ($\beta_2 - \beta_1$) ≈ 0.6−0.9.[5,9,13−16]

(3) The concerted reactions of primary amines with substituted benzoyl fluorides in water show slightly curved Brønsted-type plots ($\beta_1 = 0.23$, $\beta_2 = 0.67$).[17] The slight Brønsted curvature has been explained by a normal Hammond effect for a concerted reaction, with an earlier transition state for a more reactive nucleophile.[17,18] Brønsted-type plots with a small curvature ($\beta_1 = 0.10$, β_2 ca. 0.5) have also been found in the concerted reactions of SA amines with bis(4-nitrophenyl) thionocarbonate[19a] and 2,4-dinitrophenyl 4-methylphenyl carbonate.[19b]

(4) An important feature of the concerted reactions that show slight Brønsted curvatures is that $pK_a{}^0$ does not change with the change of acyl substituents.[17] This is the case of the title reactions (Table 2). For the aminolysis of substituted benzoyl fluorides the Brønsted plots show the same value of $pK_a{}^0$ (= 9.1). This is a clear indication that these reactions are concerted.[17] This is in contrast to the feature shown by stepwise reactions, where the $pK_a{}^0$ value increases as the substituent in the acyl or nonleaving group becomes more electron-withdrawing.[9,10]

(5) The reactions of SA amines with 2,4-dinitrophenyl 4-cyanobenzoate in aqueous ethanol are concerted, as shown by the obtained linear Brønsted-type plot of slope 0.6.[3e] The magnitude of this slope is within the usual range ($\beta = 0.4−0.7$) of those obtained for the concerted aminolysis of esters and carbonates and their thio analogues.[5,20] Taking into account that the above reaction is concerted, it is more likely that the title reactions are concerted, since the same nucleophiles and solvent mixture are involved in both reactions and the main difference is the better leaving group of the title substrates. This should further destabilize the hypothetical tetrahedral intermediate formed in the latter reactions.

Um and co-workers have reported that the reactions of SA amines with 2,4-dinitrophenyl and 4-nitrophenyl 4-substituted benzoates in water-20 mol % DMSO are stepwise.[4a,b] For the latter reactions, linear Brønsted-type plots of slopes ca. 0.8−0.9 were obtained,[4b] which are in agreement with stepwise mechanisms. Nevertheless, for the SA aminolysis of 2,4-dinitrophenyl 4-Y-substituted benzoates (Y = NO_2, H, and MeO) slightly curved Brønsted-type plots were found, with slopes 0.55, 0.40, and 0.42 (at high pK_a) and 0.76, 0.66, and 0.63 (at low pK_a), respectively.[4a] These slope values are not in accordance with those obtained in the aminolysis of esters and carbonates and their thio analogues, neither when formation of the tetrahedral intermediate ($T^\pm$) is rate-limiting ($\beta_1 = 0.1−0.3$) nor when $T^\pm$ breakdown to products is the rate-determining step ($\beta_2 = 0.8−1$).[5,9,13−16] Moreover, the differences of the slope values at low and high pK_a ($\Delta\beta = 0.21$, 0.26, and 0.21, respectively) are much lower than those found in stepwise aminolysis of the substrates mentioned above ($\Delta\beta = 0.6−0.9$).[5,9,13−16] Therefore, it is very likely that the SA aminolysis of 2,4-dinitrophenyl benzoates in aqueous DMSO are concerted, as is the same aminolysis of 2,4-dinitrophenyl 4-cyanobenzoate in aqueous ethanol.[3e]

According to the arguments above, it is not surprising that the SA aminolysis of 2,4-dinitrophenyl Y-substituted benzoates in aqueous DMSO exhibits curved Brønsted-type plots with the curvature center ($pK_a{}^0$) independent of the Y substituent.[4a]

In contrast to the concerted mechanisms found in the SA aminolysis of 2,4-dinitrophenyl Y-substituted thiolbenzoates in aqueous ethanol (this work), we have reported that the pyridinolyses of the same substrates in the same solvent mixture are stepwise.[9c] The change in mechanism can be ascribed to the greater leaving ability of SA amines from a hypothetical $T^\pm$ intermediate, relative to isobasic pyridines.[5,16,21,22] This means that the $T^\pm$ intermediate formed with a given pyridine is greatly

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[15] Gresser, M. J.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 6963.

[16] Castro, E. A.; Ureta, C. *J. Chem. Soc., Perkin Trans. 2* **1991**, 63.

[17] Song, B. D.; Jencks, W. P. *J. Am. Chem. Soc.* **1989**, *111*, 8479.

[18] Hammond, G. S. *J. Am. Chem. Soc.* **1955**, *77*, 334.

[19] (a) Castro, E. A.; Santos, J. G.; Tellez, J.; Umaña, M. I. *J. Org. Chem.* **1997**, *62*, 6568. (b) Castro, E. A.; Andujar, M.; Campodonico, P.; Santos, J. G. *Int. J. Chem. Kinet.* **2002**, *34*, 309.

[20] (a) Chrystiuk, E.; Williams, A. *J. Am. Chem. Soc.* **1987**, *109*, 3040. (b) Castro, E. A.; Cubillos, M.; Santos, J. G. *J. Org. Chem.* **2001**, *66*, 6000. (c) Castro, E. A.; Aliaga, M.; Campodonico, P.; Santos, J. G. *J. Org. Chem.* **2002**, *67*, 8911. (d) Castro, E. A.; Campodonico, P.; Toro, A.; Santos, J. G. *J. Org. Chem.* **2003**, *68*, 5930.

[21] Castro, E. A.; Araneda, C. A.; Santos, J. G. *J. Org. Chem.* **1997**, *62*, 126.

destabilized by the change of the pyridine to an isobasic SA amine. This great destabilization of T± by SA amines means that the intermediate either does not exist (enforced concerted mechanism) or it does exist, but it is so unstable that the concerted path is favored energetically. There are some precedents of pyridinolysis of substrates that are stepwise and SA aminolysis of the same substrates in the same solvent that are concerted.[5,19a,20b,c,23] In agreement with these results, Gresser and Jencks found that quinuclidines (tertiary alicyclic amines) are better nucleofuges from a T± intermediate than isobasic pyridines.[10] The relatively poor leaving ability of pyridines has been explained by a significant contribution of resonance stabilization by electron donation from the pyridine to the oxygen (or thio) leaving group in the transition state for the breakdown of T± with loss of ArO^- or ArS^-.[10] The greater nucleofugality of SA amines could also be explained by their greater steric hindrance compared with that of pyridines. There are also examples of stepwise pyridinolysis, in contrast to concerted phenolysis.[24]

The reactions of SA amines with 4-nitrophenyl 4-Y-substituted thiolbenzoates (Y = H and Cl) in aqueous ethanol are stepwise, as evidenced by the obtained nonlinear Brønsted-type plots of slopes $\beta_1 = 0.27$ and 0.10 and $\beta_2 = 0.86$ and 0.84.[9a] The same aminolysis of the thiolbenzoate with $Y = NO_2$ in the same solvent is also stepwise, as indicated by the linear Brønsted-type plot found of slope $\beta_2 = 0.81$.[9a] Another proof that these reactions are stepwise is the fact that pK_a^0 increases as electron withdrawal from Y improves.[9a] The change in mechanism, from stepwise for the 4-nitrophenyl derivatives[9a] to concerted for the title reactions, should be due to the greater nucleofugality of 2,4-dinitrobenzenethiolate than that of 4-nitrobenzenethiolate from the T± intermediate. In accordance with this result are the reactions of SA amines and quinuclidines with *O*-ethyl *S*-4-nitrophenyl thiocarbonate in water, which are stepwise,[25a,b] while the same aminolyses of the 2,4-dinitrophenyl derivative in the same solvent are concerted.[25b,c] Similarly, the SA aminolysis and quinuclidinolysis of methyl 4-nitrophenyl carbonate in water are stepwise,[20c] whereas those of the dinitro analogue in water are concerted.[20c]

The SA aminolysis of 2,4-dinitrophenyl thiolacetate in water exhibits a nonlinear Brønsted plot with slopes 0.2 (high pK_a) and 0.85 (low pK_a), which was explained by a stepwise mechanism.[16] The fact that the same aminolysis of the corresponding thiolbenzoate (Y = H) in aqueous ethanol is concerted (this work) can be explained as follows: (i) The change of the acyl group in the substrate, from methyl to phenyl, should destabilize the T± intermediate due to a greater steric compression caused by the latter group in T±. This should result in a greater nucleofugality of both the SA amine and 2,4-dinitrobenzenethiolate from the hypothetical intermediate formed with thiolbenzoate. (ii) The change of solvent, from water to aqueous ethanol, should also bring destabilization to T±, due to the zwitterionic nature of the intermediate. This is in accordance with the fact that the SA aminolysis of *O*-ethyl 2,4,6-trinitrophenyl dithiocarbonate in water is stepwise[26a] in contrast to the same reaction in aqueous ethanol, which is concerted.[26b]

Experimental Section

Materials. The series of SA amines were purified as described.[13] The aryl thiolbenzoates **1**−**4** were synthesized as reported.[9c]

Kinetic Measurements. These were carried out spectrophotometrically (diode array), by following the appearance of 2,4-dinitrobenzenethiolate at 420 nm. The reactions were studied in 44 wt % ethanol−water, at 25.0 ± 0.1 °C, and an ionic strength of 0.2 M (KCl). Two or three pH values were employed for the reactions of each SA amine. At least a 10-fold excess of total amine over the substrate was used in all cases. The initial substrate concentration was $(2-5) \times 10^{-5}$ M in all runs.

Pseudo-first-order rate coefficients (k_{obsd}) were obtained throughout by means of the kinetic software of the spectrophotometer. The experimental conditions of the reactions and k_{obsd} values are shown in Tables S1−S4 in the Supporting Information.

Determination of pK_a. The pK_a of 2,4-dinitrobenzenethiol was determined spectrophotometrically[27] in 44 wt % ethanol−water, at 25.0 ± 0.1 °C, and an ionic strength of 0.2 M (maintained with KCl). The value obtained was 3.5 ± 0.1. A similar value (pK_a 3.4) was found in aqueous solution, at 25.0 °C, and an ionic strength of 0.2 M (maintained with KCl).[16]

Product Studies. The products of the reactions, at the kinetic conditions, were identified as 2,4-dinitrobenzenethiolate anion and the corresponding benzamide. The identification of the products was achieved by comparison of the UV−vis spectra after completion of the reactions with those of an equimolar mixture of authentic samples of 2,4-dinitrobenzenethiolate and the corresponding benzamide, under the same experimental conditions.[9a]

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Supporting Information Available: Tables S1−S4 containing values of k_{obsd}, total amine concentration and pH, and experimental conditions. This material is available free of charge via the Internet at http://pubs.acs.org.

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[22] Oh, H. K.; Ku, M. H.; Lee, H. W.; Lee, I. *J. Org. Chem.* **2002**, *67*, 8995.

[23] Castro, E. A.; Pizarro, M. I.; Santos, J. G. *J. Org. Chem.* **1996**, *61*, 5982.

[24] Renfrew, A. H. M.; Taylor, J. A.; Whitmore, J. M. J.; Williams, A. *J. Chem. Soc., Perkin Trans. 2* **1993**, 1703; **1994**, 2383.

[25] (a) Castro, E. A.; Cubillos, M.; Santos, J. G. *J. Org. Chem.* **1994**, *59*, 3572. (b) Castro, E. A.; Muñoz, P.; Santos, J. G. *J. Org. Chem.* **1999**, *64*, 8298. (c) Castro, E. A.; Ibañez, F.; Salas, M.; Santos, J. G. *J. Org. Chem.* **1991**, *56*, 4819.

[26] (a) Castro, E. A.; Ibañez, F.; Salas, M.; Santos, J. G.; Sepulveda, P. *J. Org. Chem.* **1993**, *58*, 459. (b) Castro, E. A.; Cubillos, M.; Muñoz, G.; Santos, J. G. *Int. J. Chem. Kinet.* **1994**, *26*, 571.

[27] Albert, A.; Serjeant, E. P. *The Determination of Ionization Constants*; Chapman and Hall: London, 1971; p 44.