Kinetic Investigation of the Reactions of *S*-4-Nitrophenyl 4-Substituted Thiobenzoates with Secondary Alicyclic Amines in Aqueous Ethanol

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The reactions of *S*-4-nitrophenyl 4-X-substituted thiobenzoates (X = H, Cl, and NO_2: **1**, **2**, and **3**, respectively) with a series of secondary alicyclic amines (SAA) were subjected to a kinetic investigation in 44 wt % ethanol−water, at 25.0 °C and an ionic strength of 0.2 M (KCl). The reactions were followed spectrophotometrically by monitoring the release of 4-nitrobenzenethiolate anion at 420−425 nm. Under excess amine, pseudo-first-order rate constants (k_{obsd}) are obtained for all reactions. The plots of k_{obsd} vs [SAA] at constant pH are linear with the slope (k_N) independent of pH. The statistically corrected Brønsted-type plots (log k_N/q vs pK_a + log p/q) for the reactions of **1** and **2** are nonlinear with slopes at high pK_a, $\beta_1 = 0.27$ and 0.10, respectively, and slopes at low pK_a, $\beta_2 = 0.86$ and 0.84, respectively. The Brønsted curvature is centered at pK_a (pK_a^0) 10.0 and 10.4, respectively. The reactions of SAA with **3** exhibit a linear Brønsted-type plot of slope 0.81. These results are consistent with a stepwise mechanism, through a zwitterionic tetrahedral intermediate ($\mathbf{T}^{\pm}$). For the reactions of **1** and **2**, there is a change in rate-determining step with amine basicity, from $\mathbf{T}^{\pm}$ breakdown to products at low pK_a, to $\mathbf{T}^{\pm}$ formation at high pK_a. For the reactions of **3**, breakdown to products of $\mathbf{T}^{\pm}$ is rate limiting for all the SAA series (pK_a^0 > 11). The increasing pK_a^0 value as the substituent in the acyl group becomes more electron withdrawing is attributed to an increasing nucleofugality of SAA from $\mathbf{T}^{\pm}$. The greater pK_a^0 value for the reactions of SAA with **1**, relative to that found in the pyridinolysis of 2,4-dinitrophenyl benzoate (pK_a^0 = 9.5), is explained by the greater nucleofugality from $\mathbf{T}^{\pm}$ of the former amines, compared to isobasic pyridines, and the greater leaving ability from $\mathbf{T}^{\pm}$ of 2,4-dinitrophenoxide relative to 4-nitrobenzenethiolate.

Introduction

Although there is abundant literature on the kinetics and mechanisms of the aminolysis of thiocarbonates[1,2] and thioalkanoates,[1,3] there is much less information on the kinetics of the same reactions of thiobenzoates.[1,4] The latter reports include the aminolysis (anilines) of *S*-aryl thiobenzoates (aryl thiolbenzoates, X-C_6H_4-CO-SAr) in methanol, where a concerted mechanism was found,[4a] in contrast to the reactions of the same substrates with benzylamines[4b] and pyridines[4c] in acetonitrile, where stepwise processes were observed, with the formation of a zwitterionic tetrahedral intermediate ($\mathbf{T}^{\pm}$). On the other hand, for the reactions of primary and secondary amines with 4-nitrophenyl thionobenzoate (C_6H_5-CS-$OC_6H_4NO_2$) in aqueous DMSO, stepwise mechanisms were found.[4d]

The pyridinolysis of 2,4-dinitrophenyl 4-substituted benzoates in aqueous ethanol proceeds through an intermediate $\mathbf{T}^{\pm}$; its breakdown to products is rate limiting for the reactions of all pyridines with substrates possessing electron-withdrawing substituents at the acyl group.[5a,b] On the other hand, formation of $\mathbf{T}^{\pm}$ is the rate-determining step for the reactions of the unsubstituted benzoate with the two more basic pyridines.[5c]

To shed some light on the kinetics and mechanisms of the aminolysis of *S*-aryl thiobenzoates (aryl thiolbenzoates), in this work we investigate the kinetics of the

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TABLE 1. Experimental Conditions and k_{obsd} Values for the Reactions of SAA with *S*-4-Nitrophenyl Thiobenzoate (1)[a]

SAA	pH	F_N[b]	10^3[NH]$_{tot}$/M[c]	$10^3 k_{obsd}$/s^{-1}	no. of runs
piperidine	10.52	0.33	1.0−10	1.21−12.7	10
	10.82	0.50	1.0−10	2.12−18.2	10
	11.12	0.67	1.0−9.0	3.68−24.0	9
piperazine	9.41	0.33	1.0−10	0.67−4.3	10
	9.71	0.50	1.0−10	0.77−5.95	10
	10.01	0.67	1.0−10	1.01−9.99	10
1-(2-hydroxyethyl)-piperazine	8.79	0.33	1.0−10	0.14−1.41	10
	9.09	0.50	1.0−10	0.25−2.52	10
	9.39	0.67	1.0−10	0.30−3.27	10
morpholine	8.18	0.33	1.0−10	0.12−0.76	8
	8.48	0.50	1.0−10	0.16−1.46	9
	8.78	0.67	4.0−10	0.58−1.77	7
1-formylpiperazine	7.33	0.33	28−140	0.27−1.23	9
	7.63	0.50	10−100	0.15−1.51	10
	7.93	0.67	10−100	0.23−1.93	10
piperazinium ion	5.07	0.33	10−80	0.0050−0.022	7
	5.37	0.50	10−90	0.0044−0.040	7

[a] In 44 wt % ethanol−water, at 25.0 °C, ionic strength 0.2 M (KCl). [b] Fraction of free amine. [c] Concentration of total amine (free amine plus its conjugate acid).

TABLE 2. Experimental Conditions and k_{obsd} Values for the Reactions of SAA with *S*-4-Nitrophenyl 4-Chlorothiobenzoate (2)[a]

SAA	pH	F_N[b]	10^3[NH]$_{tot}$/M[c]	$10^3 k_{obsd}$/s^{-1}	no. of runs
piperidine	10.52	0.33	1.0−9.0	3.92−20.5	8
	10.82	0.50	2.0−10	5.53−25.2	9
	11.12	0.67	1.0−9.0	7.30−38.0	8
piperazine	9.41	0.33	1.0−10	1.44−12.3	10
	9.71	0.50	1.0−10	2.40−16.7	9
	10.01	0.67	1.0−9.0	2.62−23.7	9
1-(2-hydroxyethyl)-piperazine	8.79	0.33	4.0−40	1.30−13.6	10
	9.09	0.50	4.0−40	1.55−14.6	10
	9.39	0.67	4.0−40	3.04−22.0	10
morpholine	8.18	0.33	20−200	3.31−33.2	10
	8.48	0.50	20−200	5.91−42.3	10
	8.78	0.67	20−200	5.40−55.4	10
1-formylpiperazine	7.63	0.50	40−400	1.11−9.55	10
	7.93	0.67	18−180	0.80−5.74	10
piperazinium ion	5.07	0.33	35−70	0.0080−0.020	6
	5.37	0.50	30−100	0.017−0.045	8
	5.67	0.67	15−150	0.013−0.11	10

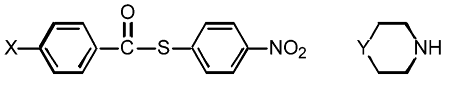
[a] In 44 wt % ethanol−water, at 25.0 °C, ionic strength 0.2 M (KCl). [b] Fraction of free amine. [c] Concentration of total amine (free amine plus its conjugate acid).

TABLE 3. Experimental Conditions and k_{obsd} Values for the Reactions of SAA with *S*-4-Nitrophenyl 4-Nitrothiobenzoate (3)[a]

SAA	pH	F_N[b]	10^3[NH]$_{tot}$/M[c]	$10^3 k_{obsd}$/s^{-1}	no. of runs
piperidine	10.52	0.33	1.0−10	27.7−215	9
	10.82	0.50	1.0−10	33.7−308	7
	11.12	0.67	1.0−9.0	58.6−376	7
piperazine	9.41	0.33	1.0−10	5.17−46.6	8
	9.71	0.50	1.0−9.0	6.26−56.7	9
	10.01	0.67	1.0−8.0	8.20−64.9	8
1-(2-hydroxyethyl)-piperazine	8.79	0.33	3.0−10	1.77−8.17	8
	9.09	0.50	2.0−10	2.11−11.7	8
	9.39	0.67	1.0−10	0.77−17.5	8
morpholine	8.18	0.33	1.0−10	0.69−4.44	8
	8.48	0.50	1.0−10	1.03−6.48	8
	8.78	0.67	1.0−9.0	1.12−9.54	8
1-formylpiperazine	7.33	0.33	3.0−10	0.030−0.48	7
	7.63	0.50	1.0−10	0.025−0.86	8
	7.93	0.67	2.0−9.0	0.26−1.11	7
piperazinium ion	5.07	0.33	20−100	0.0012−0.11	7
	5.37	0.50	30−100	0.020−0.16	7
	5.67	0.67	20−90	0.0063−0.23	7

[a] In 44 wt % ethanol−water, at 25.0 °C, ionic strength 0.2 M (KCl). [b] Fraction of free amine. [c] Concentration of total amine (free amine plus its conjugate acid).

reactions of *S*-4-nitrophenyl 4-X-substituted thiobenzoates (**1**, **2**, and **3**) with a series of secondary alicyclic



1 (X = H)
2 (X = Cl)
3 (X = NO$_2$)

SAA

amines (SAA) in aqueous ethanol. Specific goals are the assessment of the influence of the nature of the amine nucleophile, the solvent, and the substituents at both the acyl and leaving groups of the substrate on the kinetics and mechanisms of these reactions. These goals will be achieved by comparisons of the title reactions between them, and with the aminolyses of aryl thiolbenzoates in other solvents[4a−c] and aryl benzoates in aqueous ethanol.[5]

Experimental Section

Materials. The series of SAA employed were purified either by distillation or recrystallization.[6] The three thiolbenzoates **1**, **2**, and **3** were synthesized from the substituted benzoyl chloride and 4-nitrobenzenthiol, as described.[7] Their melting points were in accordance with literature values,[8] and their ^{1}H and ^{13}C NMR spectra and elemental analyses agreed with their structures.

The 4-X-substituted benzamides (X = H, Cl, NO$_2$) of piperidine and morpholine (one of the products of the reactions of these amines with **1**, **2**, and **3**, respectively) were prepared from the substituted benzoyl chloride and the corresponding amine, as reported.[9]

Kinetic Measurements. These measurements were carried out spectrophotometrically (420−425 nm) by following the release of 4-nitrobenzenethiolate anion (at pH values higher than 7), or a mixture of this anion and its conjugate acid (at pH ca. 5). The reactions were studied in 44 wt % ethanol−water solutions, at 25.0 ± 0.1 °C, and an ionic strength of 0.2 M (maintained with KCl). This particular solvent was chosen to compare the kinetics and mechanism of these reactions with those reported for the pyridinolysis of 2,4-dinitrophenyl 4-substituted benzoates in 44 wt % ethanol−water.[5] Three pH values were usually employed for the reactions of each amine; these were maintained by partial protonation of the amines. At least a 10-fold excess of total amine (free amine plus its conjugate acid) over the substrate was used in all reactions. The initial substrate concentration was 5 × 10^{-5} M in all runs.

Pseudo-first-order rate coefficients (k_{obsd}) were found in all cases. These were obtained by means of the kinetic software of the spectrophotometer, after at least 4 half-lives, except for the slowest reactions (piperazinium cation with **1** and **2**), where the initial rate method was used.[10]

The experimental conditions of the reactions and the k_{obsd} values are shown in Tables 1−3.

Product Studies. 4-Nitrobenzenethiolate anion was identified as one of the products in the aminolysis of **1**, **2**, and **3**. This was achieved by comparison of the UV−vis spectra after completion of these reactions with those of an authentic sample of 4-nitrobenzenethiol under the same reaction conditions.

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TABLE 4. Values of pK_a of the Conjugate Acids of SAA and k_N for the Reactions of SAA with *S*-4-Nitrophenyl Thiobenzoate (1), *S*-4-Nitrophenyl 4-Chlorothiobenzoate (2), and *S*-4-Nitrophenyl 4-Nitrothiobenzoate (3)[a]

		k_N/s^{-1} M^{-1}		
SAA	pK_a	**1**	**2**	**3**
piperidine	10.82	3.9 ± 0.2	5.2 ± 0.2	61 ± 2
piperazine	9.71	1.5 ± 0.1	3.7 ± 0.2	12.5 ± 0.5
1-(2-hydroxyethyl)piperazine	9.09	0.47 ± 0.02	0.79 ± 0.03	2.8 ± 0.1
morpholine	8.48	0.25 ± 0.01	0.42 ± 0.01	1.40 ± 0.1
1-formylpiperazine	7.63	0.028 ± 0.001	0.050 ± 0.002	0.19 ± 0.01
piperazinium ion	5.37	$(8.7 \pm 0.6) \times 10^{-4}$	0.0012 ± 0.0001	0.0043 ± 0.0002

[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).

In the reactions of piperidine and morpholine with **1**, **2**, and **3**, the corresponding 4-X-substituted benzamides (with X = H, Cl, and NO_2, respectively) were found as the other product (besides 4-nitrobenzenethiolate anion) of these reactions. All these products were identified by comparison of the UV−vis spectra at the end of the reactions with those of an equimolar mixture of the corresponding amide and 4-nitrobenzenethiol, under the same experimental conditions of the reactions.

Results and Discussion

The rate law obtained for all the reactions studied is given by eqs 1 and 2, where NPS$^-$, S, and NH represent 4-nitrobenzenethiolate anion, the substrate, and the free amine, respectively, and k_0 and k_N are the rate coefficients for solvolysis and aminolysis of the substrates, respectively.

$$\frac{\mathrm{d}[NPS^-]}{\mathrm{d}t} = k_{\mathrm{obsd}}[\mathrm{S}] \tag{1}$$

$$k_{\mathrm{obsd}} = k_0 + k_{\mathrm{N}}[\mathrm{NH}] \tag{2}$$

The value of k_0 was much lower than those of k_N[NH] in eq 2, except for the slow reactions of piperazinium cation with the three substrates, where the aminolysis term in eq 2 was also small. The values of k_N for all reactions were obtained as the slope of linear plots of k_{obsd} vs [NH]. The k_N values were found to be pH independent. These k_N values are shown in Table 4, together with the pK_a values of the conjugate acids of the series of amines (SAA) employed.

It can be seen in Table 4 that the values of k_N for the reactions of the substrates with a given amine increase with the increasing electron-withdrawing ability of the substituent on the acyl group of the thiolbenzoate. This could be interpreted by the greater electron attraction exerted by the 4-nitro substituent in **3**, which would leave its carbonyl carbon more positively charged, compared with the other less electron-attracting substituents, and therefore more prone to nucleophilic attack by the amine. Nevertheless, Neuvonen and co-workers have recently shown that electron-withdrawing substituents on both the acyl and leaving groups of esters *increase* the electron density at the carbonyl carbon.[11] The greater reactivity toward a nucleophile of esters with powerful electron-withdrawing substituents was explained by ground-state destabilization of the ester due to the decreased resonance stabilization.[11] This destabilization of the ground state should not be as great as that of the transition state, implying a smaller free energy of activation for the reaction of an ester with a stronger electron-withdrawing substituent.

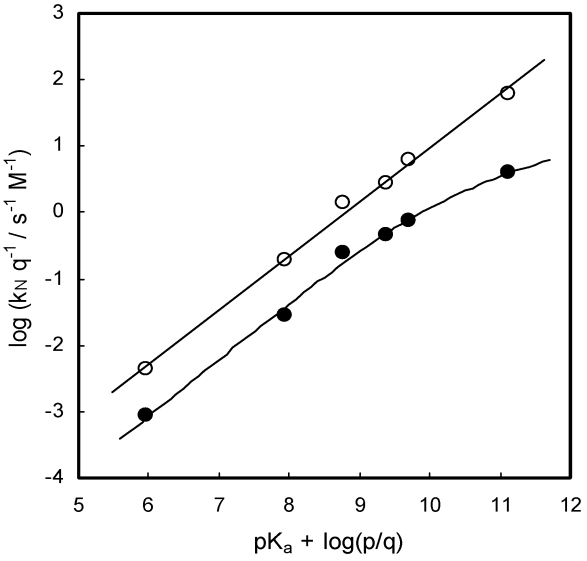

FIGURE 1. Brønsted-type plots (statistically corrected) for the reactions of SAA with **1** (●) and **3** (O) in 44 wt % ethanol−water, at 25.0 °C, ionic strength 0.2 M (KCl).

The values of k_N and pK_a of Table 4 were corrected statistically before plotting the Brønsted-type equation. The former values are corrected by dividing k_N by q, where q is the number of equivalent basic sites of the free SAA ($q = 2$ for piperazine and $q = 1$ for the other SAA).[6,12] The K_a values are corrected by multiplying K_a by q/p, where p is the number of equivalent protons of the conjugate acid of SAA ($p = 4$ for the conjugate acid of piperazinium cation and $p = 2$ for the conjugate acids of the other amines).[6,12]

Figure 1 shows the statistically corrected Brønsted-type plots for the aminolysis of thiolbenzoates **1** and **3**, and Figure 2 shows the corresponding plot for the reactions of the same amines with thiolbenzoate **2**. The plot for **3** is linear with slope $\beta = 0.81 \pm 0.03$, whereas the other plots are nonlinear.

The curved Brønsted-type plots for the aminolyis of **1** and **2** are consistent with a stepwise mechanism (shown in Scheme 1), through a zwitterionic tetrahedral intermediate ($\mathbf{T}^{\pm}$) and a change in the rate-determining step, from $\mathbf{T}^{\pm}$ decomposition to products (k_2 step in Scheme 1) to formation of $\mathbf{T}^{\pm}$ (k_1 step), as the amine becomes more

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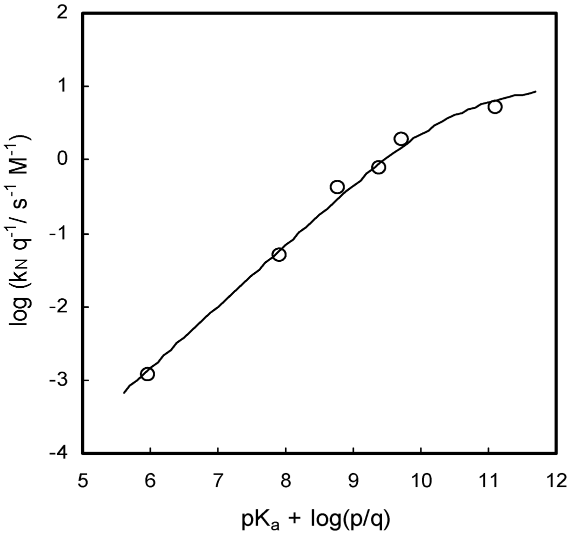
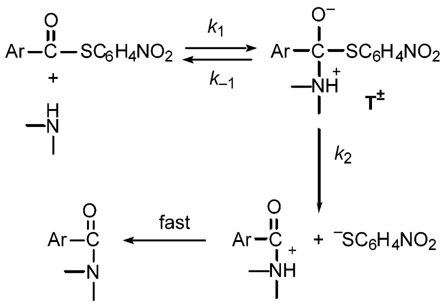


FIGURE 2. Brønsted-type plot (statistically corrected) for the reactions of SAA with **2** in 44 wt % ethanol−water, at 25.0 °C, ionic strength 0.2 M (KCl).

SCHEME 1



basic.[1,4c,d,5,6,13] The curved lines of the Brønsted plots for the reactions of **1** and **2** were calculated through a semiempirical equation (eq 3) based on the above hypothesis.[4d,5c,6,13] In this equation, $k_N{}^0$ and p$K_a{}^0$ are the corresponding parameters for the center of the Brønsted curvature, i.e., for an (hypothetical) amine that leaves $\mathbf{T}^{\pm}$ as fast as the leaving group of the substrate ($k_{-1} = k_2$ in Scheme 1). The parameters β_1 and β_2 are the slopes of the linear portions of the Brønsted plot, at high and low pK_a values, respectively. The parameters obtained in the fitting of eq 3 to the experimental points are the following: log $k_N{}^0 = 0.07$, p$K_a{}^0 = 10.0$, $\beta_1 = 0.27$, and $\beta_2 = 0.86$ for the reactions of thiolbenzoate **1** and log $k_N{}^0 = 0.56$, p$K_a{}^0 = 10.4$, $\beta_1 = 0.10$, and $\beta_2 = 0.84$ for the reactions of thiolbenzoate **2**. The errors of the values of p$K_a{}^0$ and the slopes are 0.2 and 0.03, respectively.

$$\log(k_N/k_N{}^0) = \beta_2(\mathrm{p}K_a - \mathrm{p}K_a{}^0) - \log[(1 + a)/2] \quad (3)$$

$$\log a = (\beta_2 - \beta_1)(\mathrm{p}K_a - \mathrm{p}K_a{}^0)$$

The linear Brønsted-type plot of slope $\beta_2 = 0.81$ found for the aminolysis of thiolbenzoate **3** (Figure 1) is in accordance with the mechanism depicted in Scheme 1, with decomposition of the intermediate $\mathbf{T}^{\pm}$ to products (step k_2) being rate limiting.

The values of β_1 and β_2 obtained in the reactions studied in the present work are in agreement with those obtained for the stepwise aminolysis of esters,[5,14,15] carbonates,[13,16,17] and their thio analogues[1,4c,d,6,18] ($\beta_2 = 0.1-0.3$ and $\beta_2 = 0.8-1.0$).

In light of the proposed mechanism for the present reactions (Scheme 1), deprotonation of the intermediate $\mathbf{T}^{\pm}$ by an amine to yield an anionic tetrahedral intermediate (k_3 step) is not fast enough to compete with the k_2 step. Competition between these two steps (k_3 and k_2) has been observed for relatively bad nucleofuges (compared with 4-nitrobenzenethiolate) and/or substrates with a thiocarbonyl group, instead of carbonyl.[1,2e,g−i] This has been explained by the lower ability of S^- in the zwitterionic tetrahedral intermediate formed in the aminolysis of thionocarbonates and dithiocarbonates to form a C=S double bond and expel the nucleofuge, compared with the ability of O^- in the corresponding intermediate to form a C=O bond. This means a lower k_2 value for breakdown of the intermediate with S^- relative to that for an intermediate with O^-.[1,2e,g−i]

According to our results, the p$K_a{}^0$ value increases as the substituent on the acyl group of the substrate becomes more electron withdrawing (p$K_a{}^0 = 10.0$, 10.4, and >10.8, for the reactions of **1**, **2**, and **3**, respectively). This is in accordance with the results of Gresser and Jencks in the reactions of quinuclidines with diaryl carbonates.[19] They found that electron attraction from the group that does not leave favors amine expulsion (compared to ArO^- expulsion) from the zwitterionic tetrahedral intermediate. This means that the value of p$K_a{}^0$ should increase with the increase of electron withdrawal from the nonleaving group of the substrate, according to eq 4.[20] The values of β_2 and β_1 do not change significantly with the amine or the substrate nature.[1,4c,d,5,6,13−19]

$$\log(k_{-1}/k_2) = (\beta_2 - \beta_1)(\mathrm{p}K_a{}^0 - \mathrm{p}K_a) \quad (4)$$

The shift of the p$K_a{}^0$ value with the change of the acyl substituent is another proof that the title reactions are stepwise. In the concerted aminolysis of benzoyl fluorides, where a *slight* Brønsted curve has been observed, the pK_a value at the center of the Brønsted curve does not change with the acyl substituents.[21] This was argued to be diagnostic of concerted mechanisms.[21]

The shift of p$K_a{}^0$ with acyl substituents observed in the present work is also in agreement with the results found for the stepwise reactions of 2,4-dinitrophenyl 4-X-substituted benzoates (X = H, Cl, and NO_2) with a series

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of pyridines in 44 wt % ethanol−water.[5] The reactions of the unsubstituted benzoate show a curved Brønsted-type plot centered at $pK_a^0 = 9.5$,[5c] whereas those exhibited in the pyridinolysis of the 4-chloro and 4-nitro derivatives are linear, with slope β_2 ca. 0.9, i.e., $pK_a^0 > 9.5$.[5a,b]

The greater value of pK_a^0 found for the aminolysis (SAA) of thiolbenzoate **1** in 44 wt % ethanol−water ($pK_a^0 = 10.0$, this work) compared with that obtained for the pyridinolysis of 2,4-dinitrophenyl benzoate in the same solvent ($pK_a^0 = 9.5$)[5c] can be explained through the following analysis. 2,4-Dinitrophenoxide anion should be a better nucleofuge from a zwitterionic tetrahedral intermediate ($\mathbf{T}^{\pm}$) than 4-nitrobenezenethiolate anion, as judged by the lower pK_a of the conjugate acid of the former (pK_a 4.1)[22] than that of the latter (pK_a 4.6).[6] Moreover, it is known that ArO^- is a better leaving group than an *isobasic* $Ar'S^-$.[23] This means a larger k_2 value for the dinitro derivative. On the other hand, pyridines are known to be worse nucleofuges from $\mathbf{T}^{\pm}$ than *isobasic* SAA,[18] which indicates a smaller k_{-1} value for pyridines. Therefore, for the reactions of 2,4-dinitrophenyl benzoate with pyridines the k_{-1}/k_2 ratios are lower than those for the reactions of thiolbenzoate **1** with *isobasic* SAA. According to eq 4, this means a lower pK_a^0 for the former reactions, as found.

The Hammett plot (not shown) for 4-X-acyl substituents ($\log k_N$ vs σ_X) for the title reactions exhibits an excellent linear correlation, with slope $\rho = 0.96 \pm 0.04$. This is in accordance with the ρ values obtained for the pyridinolysis of 2,4-dinitrophenyl 4-substituted benzoates ($\rho = 1.06$)[5] and the stepwise benzylaminolysis of *S*-4-bromophenyl 4-substituted thiobenzoates ($\rho = 0.94-1.2$).[4b]

The reactions of a series of SAA with *S*-4-nitrophenyl thioacetate in water are governed by a stepwise mechanism, as evidenced by the curved Brønsted-type plot obtained, with slopes $\beta_2 = 0.86$ (low pK_a region) and $\beta_1 = 0.10$ (high pK_a).[6] There is a striking greater reactivity toward SAA of the former thiolacetate in water compared to that of thiolbenzoates **1**−**3** in aqueous ethanol (this work), when either step is rate determining. This can be attributed to (i) the greater steric hindrance to SAA attack of the phenyl group in **1**−**3**, relative to methyl in *S*-4-nitrophenyl thioacetate, and (ii) the greater stabilization by water, relative to the less polar aqueous ethanol solvent, of the zwitterionic tetrahedral intermediate and the transition states for its formation and breakdown.[19] The same results were found by comparison of the pyridinolysis of aryl acetates in water[24,16c] with the same aminolysis of aryl benzoates in aqueous ethanol:[5] the values of k_N are much larger for the former reactions.

The reactions of anilines with *S*-4-nitrophenyl 4-X-thiobenzoates (X = H, Cl, NO_2) in methanol were subjected to a kinetic investigation and found to be concerted, i.e., these reactions proceed in a single step, with no formation of the zwitterionic tetrahedral intermediate ($\mathbf{T}^{\pm}$).[4a] These results are surprising taking into account those obtained in the present work, for the following reasons. We have shown that anilines are worse nucleofuges than isobasic SAA from the intermediate $\mathbf{T}^{\pm}$, i.e., the former amines stabilize kinetically $\mathbf{T}^{\pm}$ relative to isobasic SAA.[2d] On the other hand, methanol is a polar solvent and its polarity should not be so different than that of the solvent mixture used in the present investigation. Therefore, in the light of our results, it would be expected that the reactions of anilines with *S*-4-nitrophenyl thiobenzoates in methanol were stepwise, and not concerted, as found.

The reactions of benzylamines with *S*-aryl 4-X-thiobenzoates (X = H, Cl, NO_2) in acetonitrile are stepwise, with rate-determining breakdown of $\mathbf{T}^{\pm}$ to products.[4b] This is consistent with the results of the present work on the following grounds: it has been shown that aliphatic primary amines are worse leaving groups from $\mathbf{T}^{\pm}$ than isobasic SAA,[4d] which means that the former amines stabilize $\mathbf{T}^{\pm}$ relative to SAA. On the other hand, acetonitrile should destabilize the intermediate $\mathbf{T}^{\pm}$ compared with aqueous ethanol, in view of the lower polarity of the former solvent. The fact that both reactions are stepwise suggests that the amine effect is compensated by the solvent effect.

The pyridinolysis of *S*-aryl 4-nitrothiobenzoate in acetonitrile is stepwise, as shown by the curved (biphasic) Brønsted-type plot obtained.[4c] This is also in accordance with the stepwise reactions of SAA with thiolbenzoate **3**, since the stabilization of $\mathbf{T}^{\pm}$ provided by pyridines (compared to isobasic SAA)[6] should be compensated by its destabilization caused by acetonitrile (relative to aqueous ethanol).

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