Kinetics and Mechanism of the Pyridinolysis of *S*-2,4-Dinitrophenyl 4-Substituted Thiobenzoates

Enrique A. Castro,* Raul Aguayo, Jorge Bessolo, and José G. Santos

Facultad de Química, Pontificia Universidad Católica de Chile, Casilla 306, Santiago 22, Chile

ecastro@puc.cl

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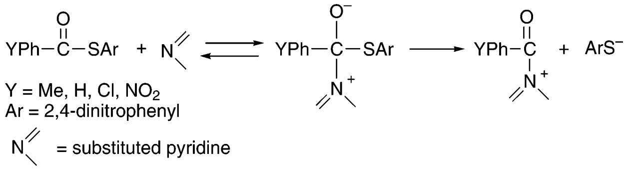

The pK_a value at the center of the Bronsted plot (pK_a^0) increases with the electron withdrawing ability of substituent Y.

The reactions of *S*-2,4-dinitrophenyl 4-methyl (**1**), *S*-2,4-dinitrophenyl 4-H (**2**), *S*-2,4-dinitrophenyl 4-chloro (**3**), and *S*-2,4-dinitrophenyl 4-nitro (**4**) thiobenzoates with a structurally homogeneous series of pyridines are 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 are studied spectrophotometrically (420 nm) by monitoring the appearance of 2,4-dinitrobenzenethiolate anion. Pseudo-first-order rate coefficients (k_{obsd}) are obtained for all the reactions, employing excess of amine. The plots of k_{obsd} vs [free pyridine] at constant pH are linear with the slopes (k_N) independent of pH. The Brønsted-type plots (log k_N vs pK_a of the conjugate acid of the pyridines) are curved for all the reactions. The Brønsted curves are in accordance with stepwise mechanisms, through a zwitterionic tetrahedral intermediate ($T^{\pm}$), and a change in the rate-limiting step. An equation based on this hypothesis accounts well for the experimental points. The Brønsted lines were calculated with the following parameters: Reactions of thiolbenzoate **1**: β_1 0.33 (slope at high pK_a), β_2 0.95 (slope at low pK_a), and p$K_a^0 = 8.5$ (pK_a at the curvature center); thiolbenzoate **2**: β_1 0.30, β_2 0.88, and p$K_a^0 = 8.9$; thiolbenzoate **3**: β_1 0.33, β_2 0.89, and p$K_a^0 = 9.5$; thiolbenzoate **4**: β_1 0.21, β_2 0.97, and p$K_a^0 = 9.9$. The increase of the pK_a^0 value with the increase of the electron-withdrawing effect of the acyl substituent is explained by the argument that the rate of pyridine expulsion from $T^{\pm}$ (k_{-1}) is favored over that of 2,4-dinitrobenzenethiolate leaving (k_2), i.e., k_{-1}/k_2 increases, as the acyl group becomes more electron withdrawing. The pK_a^0 values for the title reactions are smaller than those for the reactions of the corresponding 4-nitrophenyl 4-substituted thiolbenzoates with the same pyridine series. This is explained by the larger k_2 value for 2,4-dinitrobenzenethiolate leaving from $T^{\pm}$ compared with 4-nitrobenzenethiolate, which results in lower k_{-1}/k_2 ratios for the dinitro derivatives. The pK_a^0 value obtained for the pyridinolysis of thiolbenzoate **2** (p$K_a^0 = 8.9$) is smaller than that found for the same aminolysis of 2,4-dinitrophenyl benzoate (p$K_a^0 = 9.5$). This is attributed to the greater nucleofugality from $T^{\pm}$ of 2,4-dinitrobenzenethiolate (pK_a of conjugate acid 3.4) relative to 2,4-dinitrophenoxide (pK_a of conjugate acid 4.1). The title reactions are also compared with the aminolysis of similar esters to assess the effect of the amine nature and leaving and acyl groups on the kinetics and mechanism.

Introduction

Although the kinetics and mechanisms of the aminolysis of alkyl aryl and diaryl thiocarbonates have been extensively investigated,[1,2] the kinetics of the aminolyses (various types of amines) of thiobenzoates have attracted less attention.[3,4]

The reactions of secondary alicyclic amines with *S*-4-nitrophenyl 4-Y-substituted thiobenzoates (Y = H, Cl, NO$_2$) in aqueous ethanol are governed by a stepwise mechanism, through a zwitterionic tetrahedral intermediate ($T^{\pm}$), as shown by the nonlinear Brønsted-type plots obtained for the unsubstituted and 4-chloro-substituted derivatives.[4a] The Brønsted curves are consistent with a change in the rate-determining step, from $T^{\pm}$ breakdown to its formation, as the amine becomes more basic.[4a] The

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

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pK_a values at the center of the Brønsted curvature (pK_a^0) obtained for Y = H and Cl are pK_a^0 = 10.0 and 10.4, respectively. For the reactions of the 4-nitro derivative the Brønsted-type plot is linear, indicating that pK_a^0 > 11. Namely, these results suggest that pK_a^0 increases as the electron-withdrawing effect of substituent Y increases.[4a]

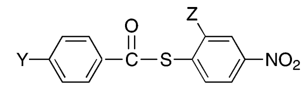
The pyridinolysis of the above thiolbenzoates in the same solvent shows a nonlinear Brønsted-type plot for Y = H, with pK_a^0 = 9.7, and linear Brønsted-type plots for Y = Cl and NO$_2$ (pK_a^0 > 9.7).[4b] These results are not conclusive in view that quantification of the pK_a^0 values was not possible for the reactions of thiolbenzoates with chloro and nitro substituents, due to the lack of pyridines with pK_a > 9.5.[4b]

The pyridinolysis of 2,4-dinitrophenyl benzoate in aqueous ethanol exhibits a nonlinear Brønsted-type plot with pK_a^0 = 9.5.[5a] The corresponding plots for the pyridinolyses of 2,4-dinitrophenyl 4-Y-substituted benzoates (Y = Cl, CN, NO$_2$) in the same solvent are linear, indicating that for these reactions pK_a^0 > 9.5.[5b–d] Again, no firm conclusions regarding the effect of the acyl substituent on the pK_a^0 value can be derived due to lack of very basic pyridines for pK_a^0 quantification.

For the quinuclidinolysis of diaryl carbonates in water Gresser and Jencks found that the pK_a^0 value increases as the electron-withdrawing ability of the substituent (Y) in the nonleaving group increases.[6] This was explained through the argument that amine leaving from the zwitterionic tetrahedral intermediate is favored, over that of the nucleofuge of the substrate, as Y becomes more electron withdrawing.[6]

In contrast, for the aminolysis of 2,4-dinitrophenyl 4-Y-substituted benzoates (Y = MeO, Me, H, Cl, NO$_2$) in aqueous solution (20 mol % DMSO) it was concluded that the pK_a^0 value does not change by the change of substituent Y in the benzoyl group.[7,8] This conclusion was achieved by pK_a^0 quantification of the nonlinear Brønsted-type plots obtained for these reactions.[7,8] The same conclusion was drawn by these authors for the aminolyses of 4-nitrophenyl Y-benzoates[9] and 2,4-dinitrophenyl Y-benzenesulfonates in the same solvent.[10]

To shed more light on the kinetics and mechanisms of the aminolysis of aryl thiolbenzoates and to clarify the effect of the substituent in the nonleaving group on the pK_a^0 value, in the present work we undertake a kinetic investigation of the pyridinolysis of 2,4-dinitrphenyl Y-substituted thiolbenzoates **1**–**4**. We have increased the range of electronic abilities of the substituents, relative to that in our previous studies,[4] by adding a thiolbenzoate with Y = Me. We have also extended the pK_a range of the series of pyridines by including a very basic one with pK_a = 11.5. By introducing a very good leaving group in the thiolbenzoates, quantification of the pK_a^0 value will be easier in view that smaller pK_a^0 values are expected for these reactions compared with those for the corresponding 4-nitrophenyl derivatives.[6]



1 (Y = Me; Z = NO$_2$)
2 (Y = H; Z = NO$_2$)
3 (Y = Cl; Z = NO$_2$)
4 (Y = NO$_2$; Z = NO$_2$)
5 (Y = H; Z = H)
6 (Y = Cl; Z = H)
7 (Y = NO$_2$; Z =H)

By comparison of the title reactions with the pyridinolysis of *S*-4-nitrophenyl 4-substituted thiolbenzoates **5**–**7** in the same solvent (aqueous ethanol),[4b] the effect of the nucleofuge basicity will be examined. Another objective of the present work is to assess the influence of the sulfur atom in the nucleofuge on the kinetics and mechanism. This will be achieved by comparison of the title reactions in aqueous ethanol with the pyridinolysis of the corresponding 2,4-dinitrophenyl 4-Y-substituted benzoates in the same solvent.[5]

Experimental Section

Materials. The series of pyridines were purified as reported.[5a,11] Thiolbenzoates **1**–**4** were synthesized by the same method used for the synthesis of *S*-4-nitrophenyl 4-substituted thiolbenzoates.[12] The procedure described for the synthesis of thiolbenzoates **1**–**4** gave low yields.[13] Previously, 2,4-dinitrobenzenethiol was prepared as reported.[14] The IR spectra of thiolbenzoates **1**–**4** agreed with those in the literature,[15] and their ^{1}H and ^{13}C NMR spectra and elemental analyses were in accordance with their structures.

Kinetic Measurements. The reactions were followed spectrophotometrically through diode array equipment, monitoring the release of 2,4-dinitrobenzenethiolate anion at 420 nm. The reactions were carried out in 44 wt % ethanol–water solutions, at 25.0 ± 0.1 °C, and an ionic strength of 0.2 M (maintained

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TABLE 1. Experimental Conditions and k_{obsd} Values for the Pyridinolysis of *S*-2,4-Dinitrophenyl 4-Methylthiobenzoate (1)[a]

pyridine substituent	pH	F_N[b]	$10^3[N]_{tot}$[c]/ M	10^3k_{obsd}/ s^{-1}	no. of runs
4-oxy	11.2	0.333	0.55−5.5	39.4−584	9
	11.5	0.500	0.55−5.5	105−898	9
3.4-diamino	9.15	0.333	0.50−5.0	10.3−105	9
	9.45	0.500	0.50−5.0	13.1−140	9
4-dimethylamino	8.84	0.333	0.50−5.0	7.22−77.3	10
	9.14	0.500	0.50−5.0	8.54−94.4	9
4-amino	8.98	0.500	0.99−9.9	12.3−125	10
	9.28	0.667	0.50−5.0	8.80−93.3	10
4-amino-3-bromo	6.90	0.500	2.0−20	0.720−9.21	10
	7.20	0.667	2.0−20	0.853−12.8	10
3,4-dimethyl	5.68	0.500	16.5−165	0.585−5.50	9
	5.98	0.667	16.5−165	0.815−7.43	7
4-methyl	5.35	0.500	39.6−396	0.681−6.26	10
	5.65	0.667	49.5−495	1.18−9.92	10
3-methyl	4.92	0.500	39.6−356	0.402−2.73	9
	5.22	0.667	49.5−446	0.503−4.12	9

[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 Pyridinolysis of *S*-2,4-Dinitrophenyl Thiobenzoate (2)[a]

pyridine substituent	pH	F_N[b]	$10^3[N]_{tot}$[c]/ M	10^3k_{obsd}/ s^{-1}	no. of runs
4-oxy	11.2	0.333	0.55−5.5	51.1−890	9
	11.5	0.500	0.55−5.5	167−1450	9
3.4-diamino	9.15	0.333	0.10−1.0	2.83−25.8	10
	9.45	0.500	0.20−0.90	3.72−30.0	8
	9.75	0.667	0.10−1.0	3.49−47.2	10
4-dimethylamino	8.84	0.333	0.10−1.0	2.33−20.3	7
	9.14	0.500	0.10−0.90	3.36−27.6	8
	9.44	0.667	0.10−1.0	4.25−38.7	9
4-amino	8.68	0.333	0.10−1.0	0.516−16.0	9
	8.98	0.500	0.10−1.0	1.61−22.8	9
	9.28	0.667	0.10−0.9	1.03−27.4	8
4-amino-3-bromo	6.60	0.333	1.0−10	0.934−5.69	8
	6.90	0.500	1.0−9.0	0.828−7.41	9
	7.20	0.667	1.0−10	1.18−8.89	8
3,4-dimethyl	5.38	0.333	1.0−10	0.110−0.435	8
	5.68	0.500	1.0−10	0.135−0.635	8
	5.98	0.667	1.0−10	0.123−0.753	7
4-methyl	5.05	0.333	1.0−10	0.0635−0.241	8
	5.35	0.500	1.0−10	0.0706−0.368	10
	5.65	0.667	1.0−10	0.0918−0.416	8
3-methyl	4.62	0.333	1.0−9.0	0.0506−0.139	7
	4.92	0.500	1.0−10	0.0502−0.207	8
	5.22	0.667	1.0−10	0.0365−0.238	8
unsubstituted	4.33	0.333	10−90	0.101−0.533	8
	4.63	0.500	10−100	0.120−0.820	7
	4.93	0.667	10−100	0.130−0.928	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 3. Experimental Conditions and k_{obsd} Values for the Pyridinolysis of *S*-4-Nitrophenyl 4-Chlorothiobenzoate (3)[a]

pyridine substituent	pH	F_N[b]	$10^3[N]_{tot}$[c]/ M	10^3k_{obsd}/ s^{-1}	no. of runs
4-oxy	7.25[d]	0.000056	1.5−15	0.237−1.86	10
	7.85[d]	0.00024	1.5−15	0.805−6.67	10
3,4-diamino	9.15	0.333	0.25−2.5	14.2−172	10
	9.45	0.500	0.25−2.5	22.5−213	10
	9.75	0.667	0.25−2.5	22.1−278	9
4-dimethylamino	8.84	0.333	0.25−2.5	7.36−133	10
	9.14	0.500	0.25−2.5	7.09−174	10
4-amino	8.68	0.333	0.54−3.4	14.4−109	10
	8.98	0.500	0.99−5.0	51.8−246	9
4-amino-3-bromo	6.90	0.500	0.50−5.0	0.746−5.36	8
	7.20	0.667	0.99−5.0	1.31−6.39	8
3,4-dimethyl	5.68	0.500	66−330	5.99−32.5	7
	5.98	0.667	33−165	4.04−21.6	8
4-methyl	5.35	0.500	39.6−396	1.56−16.9	9
	5.65	0.667	49.5−495	2.71−28.5	10
3-methyl	4.92	0.500	39.6−396	0.959−8.84	10
	5.22	0.667	99−495	2.00−13.6	9

[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). [d] Under the presence of phosphate buffer 0.01 M.

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

pyridine substituent	pH	F_N[b]	$10^3[N]_{tot}$[c] / M	10^3k_{obsd}/ s^{-1}	no. of runs
4-oxy	7.25[d]	0.000056	5.0−50	3.37−43.8	10
	7.85[d]	0.00024	0.50−5.0	0.745−7.24	9
3.4-diamino	7.25[d]	0.00627	0.50−5.0	6.52−681	10
	7.55[d]	0.0124	0.50−4.5	12.1−123	9
4-dimethylamino	7.25[d]	0.0127	0.50−5.0	5.78−68.7	9
	7.55[d]	0.0251	0.50−5.0	10.0−124	9
4-amino	7.25[d]	0.0182	0.50−4.5	5.90−54.8	9
	7.55[d]	0.0358	0.50−4.0	10.3−95.8	8
4-amino-3-bromo	6.90	0.500	0.50−5.0	2.38−25.6	10
	7.20	0.667	0.50−5.0	3.61−32.3	10
3,4-dimethyl	5.68	0.500	4.13−41.3	1.58−14.0	10
	5.98	0.667	4.13−41.3	2.45−18.2	10
4-methyl	5.35	0.500	4.13−41.3	0.743−4.72	9
	5.65	0.667	4.13−41.3	0.810−7.31	10
3-methyl	4.92	0.500	2.5−25	0.472−1.73	6
	5.22	0.667	2.5−25	0.362−2.14	9

[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). [d] Under the presence of phosphate buffer 0.01 M.

with KCl). Two or three pH values were employed for the reactions of each pyridine. For most reactions the pH was kept constant by partial protonation of the pyridines. For the very fast reactions of thiolbenzoate **3** with the most basic pyridine and thiolbenzoate **4** with the four more basic pyridines, phosphate was employed as buffer. At least a 10-fold excess of total amine over the substrate was used throughout. The initial substrate concentration was (2−5) × 10^{-5} M in all runs.

Pseudo-first-order rate coefficients (k_{obsd}) were obtained in all cases by means of the kinetic software of the spectrophotometer. The experimental conditions of the reactions and k_{obsd} values are shown in Tables 1−4.

Determination of pK_a. The pK_a value of the conjugate acid of 4-oxypyridine anion was determined by a spectrophotometric method,[16] in 44 wt % ethanol−water, at 25.0 ± 0.1 °C, and an ionic strength of 0.2 M (maintained with KCl). The value found is 11.5 ± 0.1. A similar value (pK_a = 11.3) was obtained by Um and co-workers in 80 mol % water/20 mol % DMSO at the same temperature.[3g]

Product Studies. One of the products of the title reactions was identified as 2,4-dinitrobenzenethiolate anion. The other final product is the corresponding benzoate anion. This was concluded by comparison of the UV−vis spectra after completion of the reactions with those of an equimolar mixture of

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TABLE 5. Values of pK_a for the Conjugate Acids of Pyridines and Those of k_N for the Pyridinolysis of *S*-2,4-Dinitrophenyl 4-Methylhiobenzoate (1), *S*-2,4-Dinitrophenyl Thiobenzoate (2), *S*-2,4-Dinitrophenyl 4-Chlorothiobenzoate (3), and *S*-2,4-Dinitrophenyl 4-Nitrothiobenzoate (4)[a]

pyridine substituent	pK_a	k_N/s^{-1} M^{-1}			
		1	**2**	**3**	**4**
4-oxy	11.5	320 ± 20	500 ± 30	2100 ± 150	15000 ± 1000
3,4-diamino	9.45	59 ± 4	79 ± 6	190 ± 14	2200 ± 140
4-dimethylamino	9.14	43 ± 2	60 ± 4	160 ± 12	1050 ± 70
4-amino	8.98	27 ± 2	49 ± 3	100 ± 7	680 ± 40
4-amino-3-bromo	6.90	1.0 ± 0.1	1.5 ± 0.1	2.0 ± 0.1	14 ± 1
3,4-dimethyl	5.68	0.068 ± 0.004	0.11 ± 0.01	0.20 ± 0.01	0.65 ± 0.04
4-methyl	5.35	0.031 ± 0.002	0.060 ± 0.004	0.089 ± 0.006	0.26 ± 0.02
3-methyl	4.92	0.014 ± 0.001	0.033 ± 0.002	0.044 ± 0.003	0.12 ± 0.01
none	4.63		0.015 ± 0.001		

[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).

authentic samples of 2,4-dinitrobenzenethiolate and the corresponding benzoate anion, under the same experimental conditions of the kinetic measurements.

An intermediate was detected spectrophotometrically (300−302 nm) in some reactions. This is presumably the amidic cation, 1-(4-substituted-benzoyl)pyridinium, as described for the pyridinolysis of thiolbenzoates **5**−**7**.[4b]

For some of the slowest reactions studied a slow decrease of absorbance at 420 nm was observed This is presumably due to dimerization of 2,4-dinitrobenzenethiolate anion to form bis-(2,4-dinitrophenyl) disulfide, as found for 4-nitrobenzenethiolate anion.[4b] This reaction was not a problem for the determination of the k_{obsd} values for the title reactions (as was for the pyridinolysis of thiolbenzoates **5**−**7**),[4b] since the title reactions are much faster than those involving the mononitrophenyl derivatives (**5**−**7**).

Results and Discussion

The kinetic behavior shown by the reactions under the present investigation is given by eqs 1 and 2, where DNPS$^-$, S, and N represent 2,4-dinitrobenzenethiolate anion, the corresponding thiolbenzoate, and the free pyridine, respectively. The rate coefficients k_0 and k_N are those for solvolysis and pyridinolysis of the substrates, respectively.

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

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

For all reactions the value of k_0 was much lower than that of k_N[N] in eq 2. The values of k_N were obtained as the slopes of linear plots of k_{obsd} against [N], and found to be pH independent. The values of k_N are shown in Table 5, together with the pK_a values of the conjugate acids of the pyridines.

As seen in Table 5 the k_N values increase as both amine basicity and electron withdrawal from the benzoyl substituent increases, as was found for the aminolysis of similar esters and carbonates.[1,3−9,17] The k_N values in Table 5 are larger than the corresponding ones obtained for the pyridinolysis of thiolbenzoates **5**−**7**.[4b] This is reasonable taking into account the two nitro groups in the nucleofuge of substrates **1**−**4** (compared to only one in thiolbenzoates **5**−**7**), which increases both amine attack toward the former compounds and the nucleofugality of 2,4-dinitrobenzenethiolate, compared to that of 4-nitrobenzenethiolate.

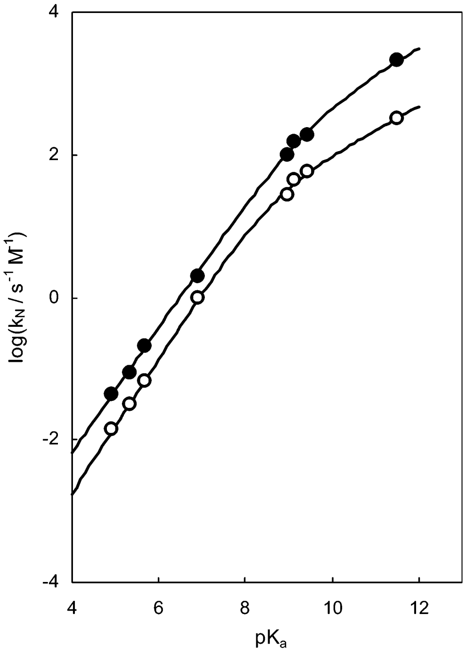

FIGURE 1. Brønsted-type plots obtained for the pyridinolysis of **1** (○) and **3** (●) in 44 wt % ethanol−water, at 25.0 °C, and an ionic strength of 0.2 M (KCl).

Figures 1 and 2 show the Brønsted-type plots obtained with the data in Table 5. According to the shape and slope values of these plots the most likely mechanism for these reactions is the stepwise process (Scheme 1), through a zwitterionic tetrahedral intermediate (T$^\pm$) and a change in the rate-determining step, from breakdown of T$^\pm$ to products (k_2 step) to formation of T$^\pm$ (k_1 step), as the amine becomes more basic.[1−8,11,17]

On the basis of the hypothesis of the intermediate T$^\pm$ on the reaction pathway a semiempirical equation (eq 3) can be derived that involves four parameters:[1,4−6,11,17] $k_N{}^0$ and p$K_a{}^0$, which are the values of k_N and pK_a at the curvature center (where $k_{-1} = k_2$), and β_1 and β_2, which are the slopes at high and low pK_a values, respectively. The best fitting parameters of this equation to the experimental points are shown in Table 6. The curved lines exhibited in Figures 1 and 2 were calculated by this equation with the parameters shown in Table 6.

$$\log(k_N/k_N{}^0) = \beta_2(\mathrm{p}K_a - \mathrm{p}K_a{}^0) - \log((1 + a)/2)$$
$$\log a = (\beta_2 - \beta_1)(\mathrm{p}K_a - \mathrm{p}K_a{}^0) \tag{3}$$

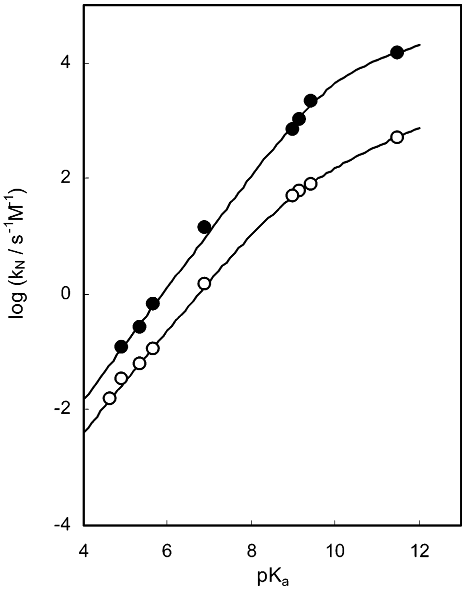

FIGURE 2. Brønsted-type plots obtained for the pyridinolysis of **2** (○) and **4** (●) in 44 wt % ethanol−water, at 25.0 °C, and an ionic strength of 0.2 M (KCl).

SCHEME 1

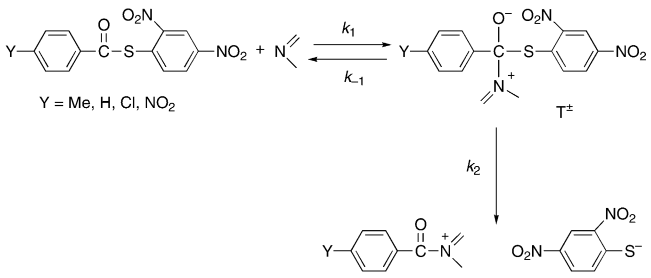

TABLE 6. Values of the Fitting Parameters of the Equation Based on the Stepwise Mechanism for the Pyridinolysis of Thiolbenzoates 1−4

parameter	1	2	3	4
log $k_N{}^0$	1.23 ± 0.20	1.63 ± 0.25	2.36 ± 0.44	3.56 ± 0.47
p$K_a{}^0$	8.5 ± 0.3	8.9 ± 0.4	9.5 ± 0.6	9.9 ± 0.7
β_1	0.33 ± 0.04	0.30 ± 0.05	0.33 ± 0.07	0.21 ± 0.09
β_2	0.95 ± 0.04	0.88 ± 0.04	0.89 ± 0.04	0.97 ± 0.07
$R^{2\,a}$	0.9995	0.9994	0.9995	0.9985

[a] *R* is the correlation coefficient.

The values of β_1 and β_2 in Table 6 are in accordance with those obtained in the aminolysis of similar esters and carbonates, and their thio analogues, when formation and breakdown of the tetrahedral intermediate (T$^\pm$), respectively, is the rate-determining step.[1−6,11,17] The usual β values are 0.1−0.3 for rate-limiting formation of T$^\pm$, and β = 0.8−1 for decomposition to products of this intermediate.[1−6,11,17]

Table 6 shows that the pK_a values at the curvature center of the Brønsted-type plots (p$K_a{}^0$) increase as the Y substituent in the benzoyl moiety becomes more electron withdrawing. This effect is in accordance with the results found in the quinuclidinolysis of diaryl carbonates[6] and in the aminolysis of dithioesters.[18] The same influence of substituent Y on p$K_a{}^0$ was suggested for the aminolyses of thiolbenzoates **5**−**7** and 2,4-dinitrophenyl benzoate.[4,5]

For the reactions of quinuclidines (tertiary alicyclic amines) with Y-substituted-phenyl 3,4-dinitrophenyl carbonates (Y = H, 4-acetyl, and pentafluoro) in water it was found that the p$K_a{}^0$ value increases with the increasing electron withdrawal of the Y substituent in the nonleaving group of the carbonate.[6]

In accordance with the results above, Lee and coworkers have reported a larger p$K_a{}^0$ value for the aminolysis of a dithioester possessing 2-furyl as the substituent in the acyl group relative to the corresponding values for the same aminolysis of the corresponding dithioesters with Me and Ph as acyl substituents.[18] The larger p$K_a{}^0$ for the former reactions was attributed to the stronger electron-withdrawing effect exerted by 2-furyl compared to those by the other substituents.[18]

The effect of the substituent in the nonleaving group of a diaryl carbonate or in the acyl group of a thiolester upon the p$K_a{}^0$ value has been explained as follows:[4b,6,19] as the substituent increases its electron attraction the central carbon of the zwitterionic tetrahedral intermediate (T$^\pm$) becomes more positive and favors the push provided by the oxygen or sulfur atom in the leaving group of T$^\pm$ to expel the amine. The cationic amino moiety in T$^\pm$ cannot exert its push to expel the nucleofuge due to the lack of an electron pair. Therefore, electron-withdrawing substituents in the nonleaving or acyl group favor amine expulsion from T$^\pm$ relative to that of the nucleofuge, increasing therefore the ratio k_{-1}/k_2 (see Scheme 1).[4b,6,19] By applying the steady-state treatment to the tetrahedral intermediate in a stepwise reaction, eq 4 can be deduced.[20] Since the values of β_1 and β_2 do not change significantly with the nature of the substrate,[1,3−5,11,17] eq 4 shows that p$K_a{}^0$ increases with the increase of the k_{-1}/k_2 ratio.

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

The same effect of Y on p$K_a{}^0$ was suggested for the reactions of secondary alicyclic amines with thiolbenzoates **5**−**7**, where the p$K_a{}^0$ values are 10.0 and 10.4 for the reactions of the substrates with Y = H (**5**) and Cl (**6**), respectively.[4a] The reactions of the thiolbenzoate with Y = NO$_2$ (**7**) exhibit a linear Brønsted-type plot of slope 0.81, indicating that p$K_a{}^0$ > 11.[4a]

The pyridinolysis of thiolbenzoate **5** in 44 wt % ethanol−water shows a nonlinear Brønsted-type plot with p$K_a{}^0$ = 9.7, whereas thiolbenzoates **6** and **7** exhibit linear plots of slopes 0.94 and 1.0, respectively, indicating p$K_a{}^0$ > 9.7 for Y = Cl and NO$_2$.[4b] These results also suggest the above effect of the Y substituent on the p$K_a{}^0$ value, although these results are not conclusive due to the lack of quantification of the p$K_a{}^0$ values for the two latter thiolbenzoates. This quantification was not possible since pyridines more basic than 9.7 were not employed in the kinetic study.[4b] It is noteworthy that, for the title reactions, quantification of the p$K_a{}^0$ values for thiolbenzoates with Y = Cl and NO$_2$ was possible due to the inclusion

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of a much more basic pyridine (4-oxypyridine) and a better leaving group, compared to those used in the pyridinolysis of thiolbenzoates **5**−**7**.

The smaller pK_a^0 value obtained in the pyridinolysis of thiolbenzoate **2** ($pK_a^0 = 8.9$, Table 6), relative to that found in the same aminolysis of thiolbenzoate **5** ($pK_a^0 = 9.7$),[4b] can be explained by the superior leaving ability from $T^{\pm}$ of 2,4-dinitrobenzenethiolate, relative to that of 4-nitrobenzenethiolate, as reflected by the lower basicity of the former: the pK_a values of conjugate acids are 3.4 and 4.6, respectively.[21] This means a larger k_2 value for the reactions of thiolbenzoate **2**, and therefore, a smaller pK_a^0 value, according to eq 4.

A curved Brønsted-type plot has been found for the pyridinolysis of 2,4-dinitrophenyl benzoate in 44 wt % ethanol−water, with $pK_a^0 = 9.5$.[5a] The corresponding plots for the pyridinolysis of analogous 4-substituted benzoates with 4-Cl-, 4-CN-, and 4-NO_2-substituents are linear with slopes ca. 0.9, indicating $pK_a^0 > 9.5$.[5b−d] Again, it was not possible to quantify the pK_a^0 values for the latter reactions, preventing, therefore, a clear conclusion regarding the influence of the acyl substituents on the pK_a position at the center of the Brønsted curvature. The smaller pK_a^0 value found in the pyridinolysis of thiolbenzoate **2** in the same solvent ($pK_a^0 = 8.9$, this work) can be explained by the greater nucleofugality of 2,4-dinitrobenzenethiolate ($pK_a = 3.4$)[21] from $T^{\pm}$ than 2,4-dinitrophenoxide (pK_a 4.1).[22] According to eq 4, a larger k_2 implies a lower pK_a^0 value, as found.

In contrast to the results obtained in the title reactions, and others,[6,18] concerning the influence of the substituent in the acyl or nonleaving groups upon the pK_a^0 values, Um and co-workers have claimed that for the aminolysis of 2,4-dinitrophenyl and 4-nitrophenyl 4-substituted benzoates[7−9] and 2,4-dinitrophenyl substituted benzenesulfonates,[10] all in water−20 mol % DMSO, there is no effect of the acyl substituents on the pK_a^0 values.

For the reactions of a series of secondary alicyclic amines with 2,4-dinitrophenyl 4-Y-substituted benzoates, Um and co-workers found curved Brønsted-type plots for Y = MeO, Me, H, Cl, and NO_2, with the center of the plots located at $pK_a = 9.1$ for all substituents.[7] The Brønsted curves were attributed to a stepwise mechanism and a change in the rate-determining step, and it was claimed that no change in the pK_a^0 value was observed with the change of substituents.[7] Nevertheless, for the reactions of the benzoates with Y = MeO, H, and NO_2 the values of the Brønsted slopes obtained at high pK_a (β_1) are 0.48, 0.38, and 0.55, respectively, which are too large compared to those normally found ($\beta_1 = 0.1−0.3$) for rate-determining formation of the zwitterionic tetrahedral intermediate ($T^{\pm}$).[1,4−6,11,17−20] On the other hand, for the reactions of the benzoates with Y = MeO and H, the slope values found at low pK_a (β_2) are 0.64 and 0.66, respectively, which are too small relative to those usually obtained ($\beta_2 = 0.8−1.1$) for rate-limiting breakdown of $T^{\pm}$ to products.[1,4−6,11,17−20] Therefore, for all these reactions the Brønsted curvatures are too slight (the difference of $\beta_2 - \beta_1$ values are too small) compared to those observed in stepwise aminolysis; these Brønsted plots are more in agreement with those found in some concerted reactions.[23]

Song and Jencks have studied kinetically the reactions of primary amines with substituted benzoyl fluorides in water and found slightly curved ($\beta_1 = 0.23$, $\beta_2 = 0.67$) Brønsted-type plots, with the pK_a value at the curvature center ($pK_a^0 = 9.1$) independent of the benzoyl substituent.[23a] This independence is typical of concerted reactions.[23a] The slight Brønsted curvature represents a normal Hammond effect for a concerted reaction, with an earlier transition state for a more reactive nucleophile.[23a,24] Brønsted-type plots slightly curved ($\beta_1 = 0.10$, $\beta_2 =$ ca. 0.5) were also obtained in the concerted reactions of secondary alicyclic amines with bis(4-nitrophenyl) thionocarbonate[23b] and 2,4-dinitrophenyl 4-methylphenyl carbonate.[23c]

Another kinetic result that suggests that the reactions of secondary alicyclic amines with 2,4-dinitrophenyl 4-Y-substituted benzoates in water−20 mol % DMSO are concerted is the linear Brønsted-type plot of slope 0.6 obtained for the reactions of the same amines with 2,4-dinitrophenyl 4-cyanobenzoate in aqueous ethanol.[25] The value of the Brønsted slope for the latter reactions is within the typical range ($\beta = 0.4−0.7$) of those found in the concerted aminolysis of esters and carbonates and their thio derivatives.[1,26]

If the reactions of secondary alicyclic amines with 2,4-dinitrophenyl 4-Y-substituted benzoates are concerted it is more likely that those of the same amines with thiolbenzoates **1**−**4** be concerted in view of the better leaving group involved in the latter reactions.

The reason for the stepwise pyridinolysis of the title thiolbenzoates in contrast to the probable concerted reactions of secondary alicyclic amines with these substrates can be found in the superior nucleofugality from the tetrahedral intermediate ($T^{\pm}$) of the latter amines compared to isobasic pyridines.[1,4,18,20,25] Therefore, the change of a pyridino moiety in $T^{\pm}$ by an isobasic secondary alicyclic amino destabilizes $T^{\pm}$, in some cases to the point of nonexistence, and the mechanism becomes enforced concerted.[27] There are many examples in the literature of reactions of reactive esters and carbonates and their thio analogues with pyridines that are stepwise, in contrast to those of the same substrates with secondary alicyclic amines which are concerted.[1,25,26b,c,28]

For the reactions of secondary alicyclic amines with 4-nitrophenyl Y-substituted benzoates in water−20 mol % DMSO, linear Brønsted-type plots of slope 0.8−0.9 were obtained, which are in accordance with stepwise mechanisms where breakdown to products of the intermediate $T^{\pm}$ is rate determining.[9] The pK_a value of the

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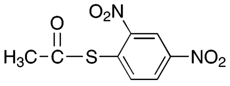
conjugate acid of the most basic amine employed (piperidine) is ca. 11; therefore, for all these reactions the Brønsted break is centered at pK_a^0 > 11. It was claimed in this work that since no change in the rate-determining step with the change of Y substituents was observed, there is no influence of Y on the pK_a^0 value.[9] We think this is not the right conclusion from the kinetic results. It must be taken into account that it is very likely that the pK_a^0 value for these reactions be much larger than 11. This is because of the following: (i) 4-Nitrophenoxide is a relatively poor nucleofuge (for instance compared to 2,4-dinitrophenoxide), which means a relatively small k_2 and, according to eq 4, high pK_a^0. This is why almost always the Brønsted-type plots involving 4-nitrophenoxide as leaving group are linear with high slopes and quantification of pK_a^0 is not possible. (ii) Secondary alicyclic amines are relatively good leaving groups (for instance compared to isobasic pyridines, see above), which means large k_{-1} values (relative to those for isobasic pyridines). According to eq 4 this means larger pK_a^0 values. Therefore, it is very unlikely that the change of a Y substituent, even from 4-NO_2 to 4-MeO, could be so drastic as to change the rate-limiting step, from the k_2 step for NO_2 to the k_1 step for MeO. According to Um and co-workers to produce such a change in rate-determining step a Y substituent of $\sigma = -6.4$ would be needed, which does not exist.[9]

For the pyridinolysis of 2,4-dinitrophenyl thiolacetate (**8**) a curved Brønsted-type plot centered at pK_a = 6.6 was found.[21] The values of the slopes at high and low pK_a (β_1 = 0.2 and β_2 = 0.85, respectively) and the value of the Brønsted break are all consistent with a stepwise mechanism.[21] The k_N values obtained in these reactions are larger than those found in the reactions of the same amines with thiolbenzoate **2** (this work, Table 5),[21] both when formation and breakdown of the tetrahedral intermediate is rate limiting. For the reactions of 4-(dimethylamino)pyridine, for which the first step of Scheme 1 is rate determining, the k_N (k_1 in Scheme 1) value is 10-fold larger for thiolacetate **8**, whereas for the reactions of 4-methylpyridine, 3-methylpyridine, and pyridine (second step rate limiting) the k_N values are 480-, 520-, and 400-fold larger for the thiolacetate. The former result can be explained by steric hindrance toward amine attack by phenyl in the acyl group of thiolbenzoate **2**, compared to the methyl group in thiolacetate **8**. The larger k_N values for the reactions of the thiolacetate when the second step of Scheme 1 is rate determining ($k_N = k_1k_2/k_{-1}$) can be attributed to a greater k_1 and a much greater k_2/k_{-1} ratio for thiolacetate **8**. The latter is due to a greater electron-donating effect by Me compared to Ph.[29] The larger pK_a^0 value found for the pyridinolysis of thiolbenzoate **2** (8.9, this work), relative to that obtained in the same aminolysis of thiolacetate **8** (6.6),[21] can also be explained by the greater electron-withdrawing ability of phenyl in the former compound compared to that of methyl in thiolacetate **8**. This results in a larger k_{-1}/k_2 ratio for thiolbenzoate **2** and, according to eq 4, a larger value of pK_a^0 for the latter reactions, as found.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