Kinetics and mechanism of the reactions of S-4-nitrophenyl 4-methylthiobenzoate with secondary alicyclic amines and pyridines[†]

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ABSTRACT: The reactions of the title substrate with a series of six secondary alicyclic amines and a series of eight pyridines are subjected to a kinetic investigation in 44 wt% ethanol-water, at 25.0°C, and an ionic strength of $0.2 \, mol \cdot dm^{-3}$. Under amine excess pseudo first-order rate coefficients (k_{obs}) are obtained. Plots of k_{obs} against free amine concentration at constant pH are linear, with the slope (k_N) independent of pH. The Brønsted-type plots (log k_N against pK_a of the conjugate acids of the amines) are non-linear, with the curvature center located at pK_a (pK_a^0) 9.7 and 9.4, for the reactions of secondary alicyclic amines and pyridines, respectively. The plots are consistent with a zwitterionic tetrahedral intermediate ($T^{\pm}$) on the reaction path and a change in rate-determining step. The greater pK_a^0 value for secondary alicyclic amines than pyridines is explained by the greater nucleofugality from $T^{\pm}$ of secondary alicyclic amines compared to isobasic pyridines. These pK_a^0 values are lower than those found for the reactions of S-4-nitrophenyl 4-Y-substituted thiolbenzoates (Y = H, Cl, NO_2) with the corresponding amine series. These results indicate that electron donation from the non-leaving group in $T^{\pm}$ favors leaving group expulsion from $T^{\pm}$ relative to amine expulsion. Copyright © 2006 John Wiley & Sons, Ltd.

KEYWORDS: kinetics and mechanism; thiobenzoate; aminolysis; pyridinolysis; Brønsted plot; tetrahedral intermediate

INTRODUCTION

The kinetics and mechanisms of the aminolyses (several types of amines) of aryl benzoates has been the subject of many reports.[1–5] In contrast, the aminolyses of aryl thionobenzoates (ArCSOAr),[6,7] dithiobenzoates (ArCSSAr),[6,8] and thiolbenzoates (ArCOSAr)[9,10] have received little attention.

The pyridinolysis of 2,4-dinitrophenyl 4-Y-substituted benzoates in aqueous ethanol shows a curved Brønsted-type plot for Y = H,[5a] and linear plots for Y = Cl and NO_2.[5b,c] The curvature of the former plot is centered at a pK_a value (pK_a^0) of 9.5. This curve was explained by the presence of a zwitterionic tetrahedral intermediate ($T^{\pm}$, Scheme 1) on the reaction pathway and a change in the rate-determining step, from breaking to products of $T^{\pm}$ to its formation, as basicity of the pyridine increases.[5a] The linear Brønsted-type plots for Y = Cl and NO_2 show slope values of *ca.* 0.9, which indicates that breaking to products of $T^{\pm}$ is rate limiting.[5b,c] This means that the pK_a^0 values for these reactions are greater than 9.5. These

results suggest that the pK_a^0 value increases as Y becomes more electron withdrawing.[5]

The above findings are in accordance with the results obtained by Gresser and Jencks for the quinuclidinolysis of diaryl carbonates in water:[11] the pK_a^0 value increases as the substituent in the non-leaving aryloxy group of the intermediate increases its electron withdrawing ability.[11] Also in agreement are the results obtained for the benzylaminolysis of 4-nitrophenyl Y-benzoates in acetonitrile:[2] the ratio of rate coefficients for amine (k_{-1}) and 4-nitrophenoxide (k_2) expulsion from the intermediate $T^{\pm}$ increases with the increasing electron attraction of Y.[2] Since it is known that log (k_{-1}/k_2) depends linearly on pK_a^0,[10,12] the above means that the pK_a^0 value increases as Y becomes more electron withdrawing.

A similar trend was found for the reactions of S-4-nitrophenyl 4-Y-substituted thiobenzoates (thiolbenzoates) with secondary alicyclic amines in aqueous ethanol: the pK_a^0 values obtained are 10.0, 10.4, and >10.8 for Y = H, Cl, and NO_2, respectively.[10a] Also in accordance is the fact that for the pyridinolysis of the same thiolbenzoates in the same solvent, the pK_a^0 values are 9.7 for Y = H and >9.9 for Y = Cl and NO_2.[10b] Moreover, for the pyridinolysis of S-2,4-dinitrophenyl 4-Y-substituted thiobenzoates (Y = Me, H, Cl, and NO_2) in aqueous ethanol the pK_a^0 values obtained are 8.5, 8.9, 9.5, and 9.9, respectively.[10c]
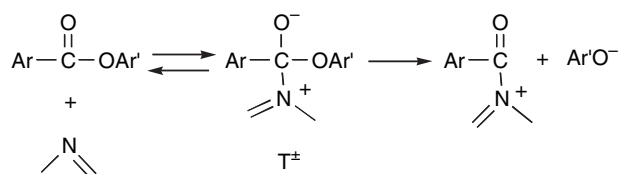
Scheme 1

In contrast to the above findings Um *et al.* have found that for the reactions of secondary alicyclic amines with 2,4-dinitrophenyl and 4-nitrophenyl Y-substituted benzoates in aqueous dimethyl sulfoxide the pK_a^0 value is independent of the Y substituent.[3]

To try to solve the above controversy and to extend our investigations on the mechanisms of the aminolysis of aryl thiolbenzoates, in this work we study kinetically the reactions of secondary alicyclic amines and pyridines with S-4-nitrophenyl 4-methylthiobenzoate (**1**) in aqueous ethanol. To quantify more precisely the pK_a^0 values for these reactions we have added a new pyridine (4-oxypyridine) with $pK_a = 11.5$ in order to extend the amine pK_a range previously employed.[10b] In this work we also determine the rate coefficients (k_N) for the reactions of this pyridine with the other S-4-nitrophenyl 4-Y-substituted thiolbenzoates (Y = H, Cl, and NO$_2$, **2**, **3**, and **4**) previously studied. This is to obtain more accurate pK_a^0 values for these reactions than those previously reported.[10b] The main goal of this work is to compare the pK_a^0 values for the title reactions with those obtained for the same aminolyses of

thiolbenzoates **2**, **3**, and **4**,[10a,b] in order to confirm or reject the hypothesis of the increase of pK_a^0 with the electron attraction from the Y substituent.[2,5,10,11]

EXPERIMENTAL

Materials

The series of secondary alicyclic amines and pyridines were purified as reported.[5,13] 4-Hydroxypyridine was purified by recrystallization in acetone. Thiolbenzoate **1** was synthesized as described.[14] Its melting point agreed with that reported,[15] and its ^{1}H and ^{13}C NMR spectra and elemental analysis were in accordance to its structure. Thiolbenzoates **2–4** were synthesized as reported.[10a]

Kinetics

The reactions were followed spectrophotometrically by monitoring the appearance of 4-nitrobenzenethiolate anion at 425 nm by means of a Hewlett-Packard 8453 instrument. The reactions were studied in 44 wt% ethanol-water solution, at $25.0 \pm 0.1°C$ and an ionic strength of $0.2\ mol \cdot dm^{-3}$ (maintained with KCl). All reactions were carried out under excess amine over thiolbenzoate **1**; the initial concentration of the latter was *ca.* $5 \times 10^{-5}\ mol \cdot dm^{-3}$.

Most of the reactions were followed for at least three half-lives, where pseudo first-order rate coefficients (k_{obs}) were found. The k_{obs} values for the slow reactions of piperazinium ion and the four less basic pyridines with substrate **1** were obtained by the initial rate method.[16] This procedure was used due to the slow reactions and also to avoid kinetic interference with the very slow oxidation of 4-nitrobenzenethiolate to yield bis(4-nitrophenyl) disulfide.[10b]
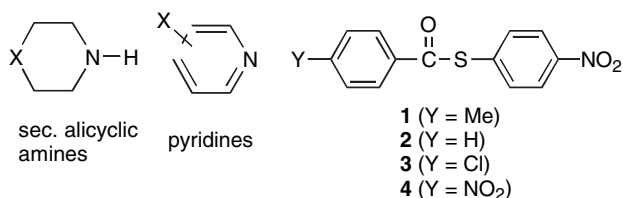
Table 1. Values of k_{obs} and experimental conditions for the reactions of thiolbenzoate **1** with secondary alicyclic amines[a]

Amine	pH	F_N[b]	$10^2\ [N]_{tot}$[c]/mol $\cdot$ dm^{-3}	$10^3 k_{obs}$/s^{-1}	Number of runs
Piperidine	10.52	0.33	0.50–5.0	2.1–22	8
	10.82	0.50	0.50–5.0	3.8–38	10
	11.12	0.67	1.0–5.0	13–61	8
Piperazine	9.41	0.33	0.50–1.7	0.99–4.0	6
	9.71	0.50	0.25–2.2	0.92–7.4	9
	10.01	0.67	0.25–2.2	1.9–11	7
1-(2-Hydroxyethyl)piperazine	8.79	0.33	1.0–10	0.70–7.4	9
	9.09	0.50	1.0–10	1.1–11	8
	9.39	0.67	1.0–10	1.4–14	8
Morpholine	8.48	0.50	2.5–20	1.6–13	8
	8.78	0.67	2.5–17	3.7–14	7
1-Formylpiperazine	7.63	0.50	4.0–32	0.31–2.3	7
	7.93	0.67	7.9–32	0.81–2.9	6
Piperaziniun cation	5.37	0.50	1.0–9.9	0.0001–0.011	7
	5.67	0.67	1.0–9.9	0.0008–0.020	8

[a] In 44 wt% ethanol-water, at 25.0°C, and an ionic strength of $0.2\ mol \cdot dm^{-3}$.
[b] Free amine fraction.
[c] Concentration of total amine (free amine plus its conjugate acid).

Table 2. Values of k_{obs} and experimental conditions for the reactions of thiolbenzoate **1** with pyridines[a]

Pyridine substituent	pH	F_N[b]	10^2 [N]$_{tot}$[c]/mol·dm^{-3}	$10^3 k_{obs}$/s^{-1}	Number of runs
4-Oxypyridine	11.20	0.33	0.10–1.0	5.2–41	7
	11.50	0.50	0.10–0.90	22–57	8
	11.80	0.67	0.10–1.0	18–90	7
3,4-Diamino	9.15	0.33	0.50–4.5	3.6–28	8
	9.45	0.50	0.50–4.0	4.8–32	7
	9.75	0.67	0.50–4.5	9.1–40	7
4-Dimethylamino	8.84	0.33	1.0–8.9	4.0–35	6
	9.14	0.50	1.0–8.9	6.3–46	7
	9.44	0.67	1.0–10	8.7–76	8
4-Amino	8.68	0.33	3.0–13	6.4–36	7
	8.98	0.50	3.0–13	9.8–52	7
	9.28	0.67	1.5–15	8.9–83	8
4-Amino-3-bromo[d]	7.55	0.817	0.25–2.5	0.027–0.13	7
	7.85	0.899	0.17–1.2	0.020–0.076	5
3,4-Dimethyl[d]	7.55	0.987	15–50	0.095–0.24	8
	7.85	0.993	9.9–50	0.030–0.19	9
4-Methyl[d]	7.55	0.994	8.9–27	0.0070–0.036	7
	7.85	0.997	1.5–13	0.00082–0.020	6
3-Methyl[d]	7.55	0.998	9.9–45	0.00081–0.026	7
	7.85	0.999	9.9–45	0.0045–0.031	7

[a] In 44 wt% ethanol-water, at 25.0°C, and an ionic strength of 0.2 mol·dm^{-3}.
[b] Free amine fraction.
[c] Concentration of total amine (free amine plus its conjugate acid).
[d] In the presence of phosphate buffer 0.01 mol·dm^{-3}.

Table 3. Values of k_{obs} and experimental conditions for the reactions of thiolbenzoates **2–4** with 4-oxypyridine[a]

Thiolbenzoate	pH	F_N[b]	10^2 [N]$_{tot}$[c]/mol·dm^{-3}	$10^3 k_{obs}$/s^{-1}	Number of runs
2	11.50	0.50	0.10–0.80	4.4–50	8
	11.80	0.67	0.10–0.80	12–106	8
3	11.20	0.33	0.10–0.90	17–159	8
	11.50	0.50	0.10–1.0	23–253	8
4	11.50	0.50	0.01–0.10	45–340	10
	11.80	0.67	0.01–0.10	6.6-452	10

[a] In 44 wt% ethanol-water, at 25.0°C, and an ionic strength of 0.2 mol·dm^{-3}.
[b] Free amine fraction.
[c] Concentration of total amine (free amine plus its conjugate acid).

The values of k_{obs} and the experimental conditions for the reactions of thiolbenzoate **1** are shown in Tables 1 and 2; those for the reactions of thiolbenzoates **2–4** with 4-oxypyridine are shown in Table 3.

Product studies

The products of the reactions of secondary alicyclic amines with the title thiolbenzoate (**1**) are 4-nitrobenzenethiolate anion and the corresponding 4-methylbenzamide. The same benzenethiolate and 4-methylbenzoate anions were found as products of the reactions with pyridines. The latter product is due to rapid hydrolysis of the cationic benzamides formed with pyridines, as found in the pyridinolysis of thiolbenzoates **2–4**.[10b]

The identification of the above products was carried out by comparison of the UV-Vis spectra of the kinetic samples at the end of the reactions (but before the slow oxidation of 4-nitrobenzenethiolate)[10b] with those of the authentic products under identical experimental conditions.

RESULTS AND DISCUSSION

Under amine excess the rate law obtained for the reactions of thiolbenzoate **1** is given by Eqns (1) and (2), where NPS$^-$ and N represent 4-nitrobenzenethiolate anion and the free amine, respectively, and k_0 and k_N are the rate coefficients for solvolysis and aminolysis, respectively, of thiolbenzoate **1**. Similar rate equations were found for the reactions of thiolbenzoates **2–4** with 4-oxypyridine.

$$\frac{d[NPS^-]}{dt} = k_{obs}[\mathbf{1}] \tag{1}$$

$$k_{obs} = k_0 + k_N[N] \tag{2}$$

Plots of k_{obs} against [N] at constant pH are linear, with the slopes (k_N) independent of pH. The k_N values are shown in Table 4. With the k_N values and the pK_a of the conjugate acids of the amines, the Brønsted-type plots for

Table 4. Values of pK_a for the conjugate acids of secondary alicyclic amines and pyridines, and k_N values for the reactions of thiolbenzoate **1** with secondary alicyclic amines and pyridines[a]

Amine	pK_a	$k_N/s^{-1} \cdot mol^{-1} \cdot dm^3$
Piperidine	10.82	1.6 ± 0.1
Piperazine	9.71	0.70 ± 0.04
1-(2-Hydroxyethyl)piperazine	9.09	0.22 ± 0.01
Morpholine	8.48	0.11 ± 0.01
1-Formylpiperazine	7.63	0.014 ± 0.001
Piperaziniun cation	5.37	$(2.7 \pm 0.2) \times 10^{-4}$
4-Oxypyridine[b]	11.50	11 ± 1
3,4-Diaminopyridine	9.45	1.5 ± 0.1
4-(Dimethylamino)pyridine	9.14	1.1 ± 0.1
4-Aminopyridine	8.98	0.84 ± 0.05
4-Amino-3-bromopyridine	6.90	$(5.8 \pm 0.3) \times 10^{-3}$
3,4-Dimethylpyridine	5.68	$(4.2 \pm 0.3) \times 10^{-4}$
4-Methylpyridine	5.35	$(1.6 \pm 0.2) \times 10^{-4}$
3-Methylpyridine	4.92	$(7.5 \pm 0.5) \times 10^{-5}$

[a] Both the pK_a and k_N values were obtained in 44 wt% ethanol-water, at 25.0°C, and an ionic strength of $0.2 \, mol \cdot dm^{-3}$.
[b] The k_N values obtained for the reactions of 4-oxypyridine with thiolbenzoates **2**, **3**, and **4** are 16, 53, and 650 $s^{-1} \cdot mol^{-1} \cdot dm^3$, respectively.

the reactions of thiolbenzoate **1** with secondary alicyclic amines and pyridines were obtained. These are shown in Figure 1. The plot for secondary alicyclic amines was statistically corrected,[13b,17] using the values of $q = 2$ for piperazine, $p = 4$ for piperazinium dication and $p = 2$ for the conjugate acids of the other secondary alicyclic amines. The parameter q is the number of equivalent basic sites in the free amine and p is the number of equivalent protons in the conjugate acid.[13b,17]

The curved lines in Figure 1 were calculated through a semi-empirical equation, Eqn (3), derived on the basis of the existence of a zwitterionic tetrahedral intermediate ($T^{\pm}$) on the reaction pathway and a change in the rate-determining step, from breakdown to products of $T^{\pm}$ to its formation, as the basicity of the amine increases.[13] In this equation, k_N^0 and pK_a^0 are the corresponding parameters at the curvature center and β_2 and β_1 are the Brønsted slopes at low and high pK_a values, respectively. The best parameters for the non-
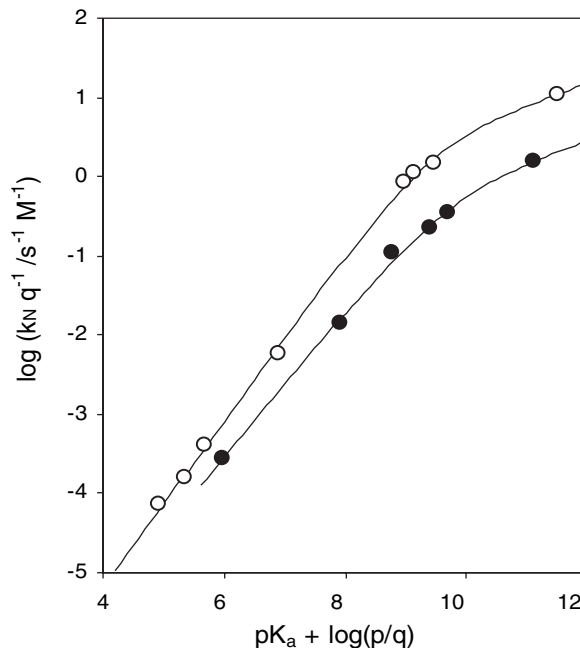

Figure 1. Brønsted-type plots (statistically corrected) for the reactions of thiolbenzoate **1** with secondary alicyclic amines (●) and pyridines (○) in 44 wt% ethanol-water, at 25.0°C, ionic strength $0.2 \, mol \cdot dm^{-3}$

linear least-squares fitting of Eqn (3) to the experimental points are: $\log k_N^0 = -0.43 \pm 0.05$, $pK_a^0 = 9.7 \pm 0.1$, $\beta_2 = 0.92 \pm 0.05$, and $\beta_1 = 0.26 \pm 0.05$ for the reactions of secondary alicyclic amines, and $\log k_N^0 = 0.18 \pm 0.05$, $pK_a^0 = 9.4 \pm 0.1$, $\beta_2 = 1.05 \pm 0.05$ and $\beta_1 = 0.27 \pm 0.08$ for the reactions of pyridines.

$$\log(k_N/k_N^0) = \beta_2(pK_a - pK_a^0) - \log[(1 + a)/2] \quad (3)$$
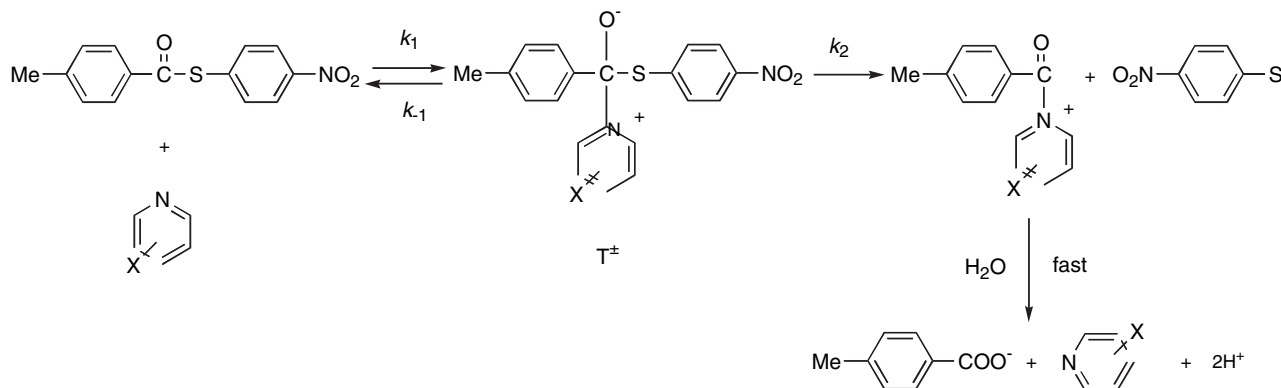
where

$$\log a = (\beta_2 - \beta_1)(pK_a - pK_a^0)$$

According to the rate law, the product studies and the Brønsted-type plots obtained for the reactions under scrutiny, the most likely mechanism for these reactions is that described in Scheme 2 for secondary alicyclic amines and Scheme 3 for pyridines. As found for the
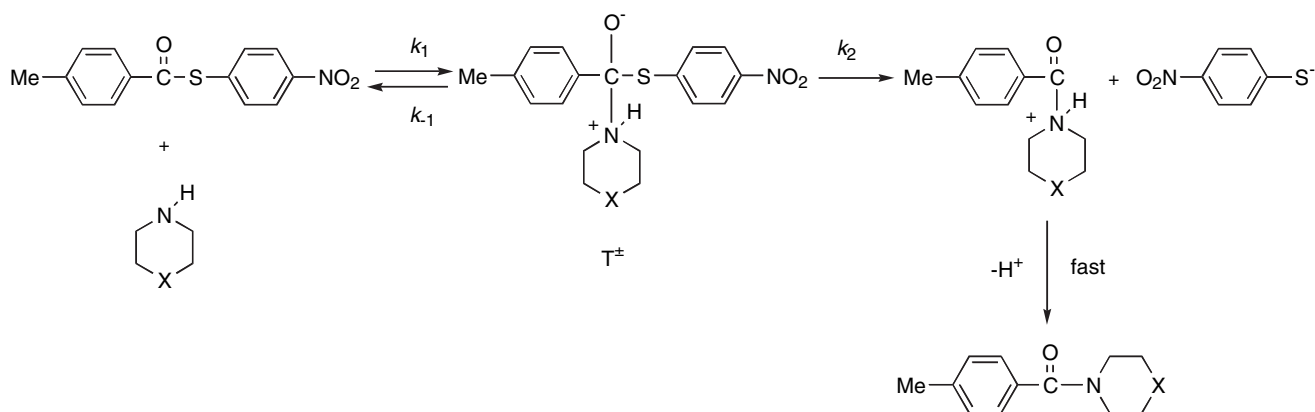
Scheme 2

Scheme 3

pyridinolysis of thiolbenzoates **2–4**,[10b] a good isosbestic point was obtained for the same aminolysis of thiol-benzoate **1** (except for the reactions of the three more basic pyridines), indicating, therefore, that the hydrolysis of the cationic amidinium intermediate is fast. For the reactions with the three more basic pyridines, a small increase and fast decrease of absorbance was observed at 300 nm, which indicates that these intermediates are also rapidly hydrolyzed, but not as fast as the cationic intermediates formed from the less basic pyridines.

The larger pK_a^0 value obtained for the reactions of thiolbenzoate **1** with secondary alicyclic amines in aqueous ethanol ($pK_a^0 = 9.7$) relative to that with pyridines ($pK_a^0 = 9.4$) is in accordance with the results found for the reactions of these series of amines with thiolbenzoate **2** in the same solvent.[10a,b] For the pyridinolysis of thiolbenzo-ates **3** and **4**, linear Brønsted-type plots up to a pK_a value of 9.45 were obtained.[10b] Quantification of the pK_a^0 value for these reactions was not possible due to the fact that the most basic pyridine employed was 3,4-diaminopyridine, of pK_a 9.45.[10b]

In order to quantify the pK_a^0 value for the pyridinolysis of thiolbenzoates **3** and **4** and to obtain a more precise value for the same aminolysis of thiolbenzoate **2**, we have determined in this work the k_N values for the reactions of 4-oxypyridine (pK_a 11.5) with these three thiolbenzoates. These k_N values are shown in Table 4.

With the values of k_N reported for the reactions of thiolbenzoates **2–4** with seven pyridines,[10b] and those found in this work for the reactions of these substrates with 4-oxypyridine, the Brønsted-type plots shown in Figures 2 and 3 were obtained. The best fitting parameters of Eqn (3) to the experimental points are: $\log k_N^0 = 0.54 \pm 0.04$, $pK_a^0 = 9.7 \pm 0.1$, $\beta_2 = 0.94 \pm 0.04$, and $\beta_1 = 0.22 \pm 0.03$ for the reactions thiolbenzoate **2**; $\log k_N^0 = 1.11 \pm 0.06$, $pK_a^0 = 10.1 \pm 0.1$, $\beta_2 = 0.96 \pm 0.04$, and $\beta_1 = 0.25 \pm 0.04$ for the reactions of thiolbenzoate **3**; and $\log k_N^0 = 2.43 \pm 0.07$, $pK_a^0 = 10.7 \pm 0.2$, $\beta_2 = 1.01 \pm 0.06$, and $\beta_1 = 0.22 \pm 0.03$ for the reactions of thiolbenzoate **4**. The pK_a^0 values obtained for these reactions, together with those found in the secondary alicyclic aminolysis of thiolbenzoates **1–4** are summar-

ized in Table 5. The pK_a^0 value found for the pyridinolysis of **2** including the new pyridine (4-oxypyridine) is the same ($pK_a^0 = 9.7$) as that obtained previously without this amine.[10b] Due to this new pyridine, quantification of the pK_a^0 value for the pyridinolysis of **3** and **4** is now possible.

As seen in Table 5, the pK_a^0 value for the reactions of a given thiolbenzoate with secondary alicyclic amines is larger than that with pyridines. This can be attributed to the greater nucleofugality from the intermediate $T^\pm$ (larger k_{-1} in Schemes 2 and 3) of secondary alicyclic amines relative to isobasic pyridines.[18] This means a larger k_{-1}/k_2 ratio for former amines since k_2 should be independent of the amine basicity and nature.[19] A larger k_{-1}/k_2 ratio means a larger pK_a^0, according to Eqn (4),
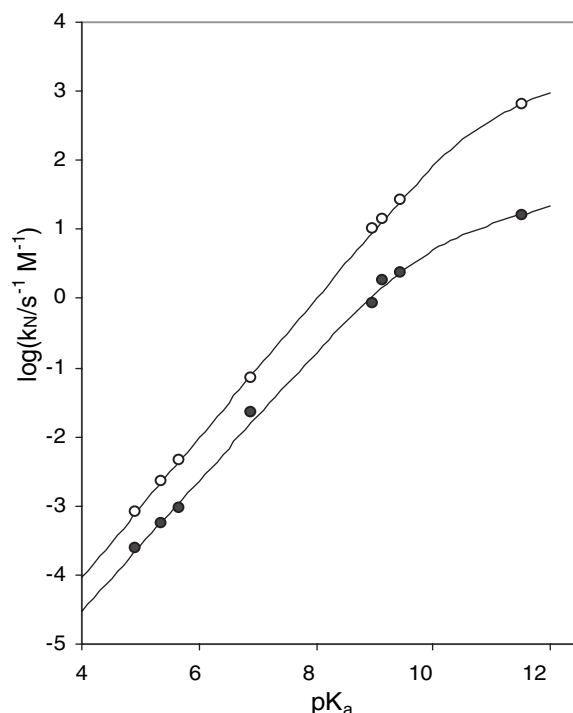

Figure 2. Brønsted-type plots for the pyridinolysis of thiol-benzoates **2** (●) and **4** (○) in 44 wt% ethanol-water, at 25.0°C, ionic strength 0.2 mol·dm^{-3}
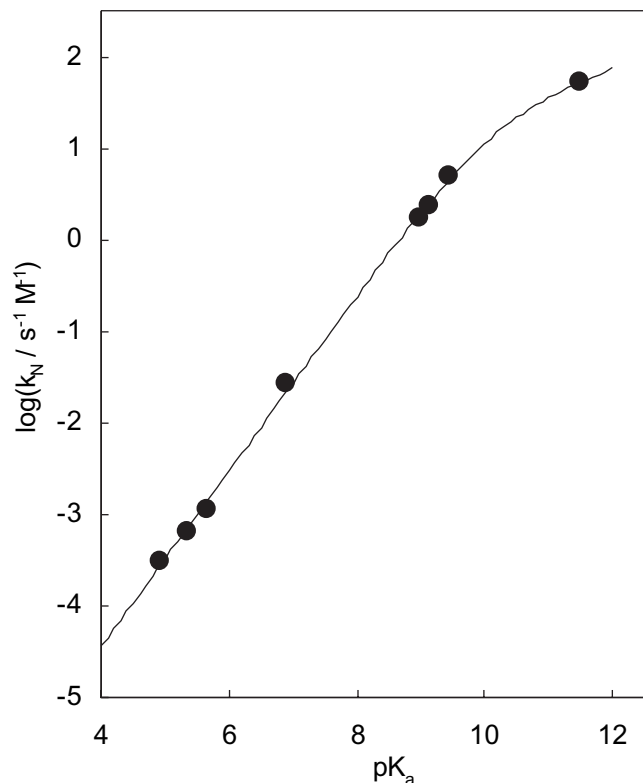
Figure 3. Brønsted-type plot for the pyridinolysis of thiolbenzoate **3** in 44 wt% ethanol-water, at 25.0°C, ionic strength 0.2 mol · dm^{-3}

which was derived from the hypothesis of the tetrahedral intermediate.[10,12]

$$\log(k_{-1}/k_2) = (\beta_2 - \beta_1)(pK_a^0 - pK_a) \qquad (4)$$

As seen in Table 5 for the reactions of a given series of amines, the pK_a^0 value increases as the substituent Y in the benzoyl group becomes more electron withdrawing.

The same effect was found by Gresser and Jencks for the aminolysis of diaryl carbonates in water.[11] Electron attraction from the substituent in the non-leaving group of

Table 5. Values of pK_a for the center of the Brønsted curvature (pK_a^0) for the reactions of 4-nitrophenyl 4-Y-thiolbenzoates (**1**–**4**) with secondary alicyclic (SA) amines and pyridines[a]

Thiolbenzoate	SA amines	Pyridines
1 (Y = Me)	9.7 ± 0.1[b]	9.4 ± 0.1[b]
2 (Y = H)	10.0 ± 0.2[c]	9.7 ± 0.1[d]
3 (Y = Cl)	10.4 ± 0.2[c]	10.1 ± 0.1[d]
4 (Y = NO$_2$)	>10.8[c]	10.7 ± 0.2[d]

[a] Reactions carried out in 44 wt% ethanol-water, at 25.0°C, and an ionic strength of 0.2 mol · dm^{-3}.
[b] Data from this work.
[c] Data from Ref. 10a.
[d] Values of pK_a^0 obtained from the Brønsted data for seven pyridines (Ref. 10b) and the data for 4-oxypyridine (this work).

the carbonate favors amine (relative to leaving group) expulsion from the zwitterionic tetrahedral intermediate, increasing, therefore, the pK_a^0 value.[11] The same trend was obtained for the reactions of benzylamines with 4-nitrophenyl Y-benzoates in acetonitrile:[2] the ratio of rate coefficients arising from the intermediate T$^\pm$ (k_{-1}/k_2) increases with the increasing electron attraction of Y.[2] This means that the pK_a^0 value increases as Y becomes more electron withdrawing.

The above effect has been explained as follows:[10,11] as electron attraction from Y in the intermediate T$^\pm$ increases, the central carbon of this intermediate becomes more positively charged and this enhances the push provided by the oxygen (or sulfur) atom in the leaving group to expel the amine (larger k_{-1}). The amine nitrogen atom in T$^\pm$ lacks an electron pair to exert its push to expel the leaving group. Therefore, electron withdrawal from Y favors amine leaving from T$^\pm$, compared to leaving group expulsion, enlarging the k_{-1}/k_2 ratio and, according to Eqn (4), increasing the pK_a^0 value.

In contrast to the above results, Um *et al.* have found that in some aminolysis reactions, the substituents in the acyl group of aryl benzoates do not affect the pK_a^0 value.[3] For instance, for the reactions of 2,4-dinitrophenyl 4-Y-substituted benzoates with secondary alicyclic amines in aqueous DMSO, these workers found curved Brønsted-type plots centered at $pK_a = pK_a^0 = 9.1$ for Y = MeO, H, and NO$_2$.[3a] Nonetheless, these plots exhibit slope values of $\beta_1 = 0.40$–0.55 (at high pK_a) and $\beta_2 = 0.63$–0.76 (at low pK_a).[3a] These slopes are not typical of stepwise mechanisms through a tetrahedral intermediate. For a two-step mechanism in aqueous solution the usual slopes are $\beta_1 = 0.10$–0.3 and $\beta_2 = 0.80$–1.1.[5a–c,6,10,13,16,18,19] The magnitude of the Brønsted slopes obtained in the secondary alicyclic aminolysis of 2,4-dinitrophenyl benzoates in aqueous DMSO, together with the small Brønsted curvatures suggests that a concerted mechanism, rather than a stepwise, governs these reactions. This is based on the following grounds.

(1) We have found that the reactions of secondary alicyclic amines with 2,4-dinitrophenyl 4-cyanobenzoate in aqueous ethanol are ruled by a concerted mechanism, on the basis of the linear Brønsted-type plot of slope 0.6 obtained.[5d]

(2) Song and Jencks obtained slightly curved Brønsted plots in the aminolysis of substituted benzoyl fluorides.[20] The values of the slopes at low and high pK_a are *ca.* 0.67 and 0.23, respectively.[20] The magnitude of these slopes and the small difference between their values at low and high pK_a (i.e., small curvatures) were interpreted as concerted mechanisms.[20] Furthermore, the fact that the center of the Brønsted curvature (pK_a^0) is the same for all the benzoyl fluorides investigated indicates that these mechanisms are concerted.[20]

The gradual decrease of the Brønsted slope with increasing amine pK_a in a single step has been explained by a manifestation of a normal Hammond effect, with an earlier transition state for the more reactive nucleophiles.[20,21]

Acknowledgements

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