Kinetics and Mechanism of the Aminolysis of Phenyl Dithioacetate in Aqueous Solution

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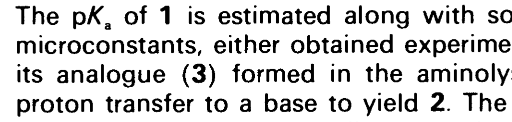
The reactions of the title substrate with a series of secondary alicyclic amines have been subjected to a kinetic study in water at 25 °C, ionic strength 0.2 mol dm^{-3}. Under amine excess pseudo-first-order rate coefficients (k_{obs}) are found throughout. The order in amine varies from 1–2 according to the amine basicity and the experimental conditions. A general reaction scheme with a zwitterionic and an anionic tetrahedral intermediate (**1** and **2**, respectively) accounts for the rate equations found. The pK_a of **1** is estimated along with some microconstants in the scheme. From the values of the microconstants, either obtained experimentally or estimated, it is deduced that **1** is more stable than its analogue (**3**) formed in the aminolysis of *S*-phenyl thioacetate, and therefore, **1** has time for proton transfer to a base to yield **2**. The rate coefficients for expulsion of an amine (k_{-1}) and PhS$^-$ (k_2) from **1** are both smaller than those for expulsion from **3**. The Brønsted plots for k_1 (rate coefficient for formation of **1**), K_1 ($=k_1/k_{-1}$) and k_{-1} have slopes $\beta = 0.2$, 1.2 and -1.0, respectively. The pK_a value of an (hypothetical)amine for which $k_{-1} = k_2$ is deduced: p$K_a^\circ = 10.3 \pm 0.5$, which is smaller than that derived from the aminolysis of *S*-phenyl thioacetate (p$K_a^\circ = 12.2$).

Although the mechanism of the hydrolysis and aminolysis of oxyesters and oxycarbonates is well established,[1,2] that of the corresponding reactions of thiolesters and thiocarbonates is not well understood, despite some studies carried out in water as well as in aprotic solvents.[3,4]

We have recently studied the aminolysis of *S*-aryl thioacetates in aqueous solution and deduced, through non linear structure–reactivity relationships, the existence of a zwitterionic tetrahedral intermediate (T$^\pm$) in the reaction path.[5,6] The mechanism of these reactions is described by eqn. (1), where –NH represents a secondary alicyclic amine. It was found that the k_2 step was faster than the rate of proton transfer from T$^\pm$ to a base to yield an anionic intermediate T$^-$.[5,6]



$$\mathrm{Me{-}C({=}O){-}SAr} + \mathrm{{-}NH{-}} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{Me{-}C(O^-)(SAr){-}NH^+{-}} \xrightarrow{k_2} \mathrm{Me{-}C({=}O){-}NH^+{-}} + \mathrm{ArS^-} \qquad (1)$$

In one of the works above we also analysed the influence of the nature of the amine on the reaction mechanism.[6] The effect of the non-leaving group of the substrate on the mechanism has also been studied in the aminolysis of oxyesters and oxycarbonates.[2,7]

In this work we examine the influence of the thiocarbonyl group of the substrate on the mechanism of the above reactions, by comparing the results of the present work with those found in the aminolysis of *S*-phenyl thioacetate.[5] We find in the present work that there is a remarkable difference in the mechanism of these two reactions caused by the much higher stability of T$^\pm$ formed in the present reactions. As a result of this the lifetime of the latter is long enough to allow proton transfer to a base to yield T$^-$. This rate of proton transfer is comparable or faster than the rate of PhS$^-$ expulsion from this T$^\pm$ species.

Experimental

Materials.—The secondary alicyclic amines were purified prior to use as described.[5] Boric acid from Riedel-de Häen and sodium phosphate dibasic from Fluka, both analytical reagent grade, were used without further purification to prepare some of the buffered solutions. Potassium chloride from Merck, analytical grade, was used to maintain the ionic strength of the solutions.

Phenyl dithioacetate (PDTA) was prepared from 2,4-bis-(phenylthio)-1,3-dithia-2,4-diphosphetane 2,4-disulfide (PDD) and acetic acid, according to a reported procedure.[8] PDTA was identified by its ^{1}H NMR and IR spectra. PDD was synthesized as described previously.[8]

Kinetic Measurements.—The reactions were studied spectrophotometrically, following the appearance of benzenethiol and/or its conjugate base at 264 nm, by means of a Perkin-Elmer Lambda 3 spectrophotometer. After thermal equilibration of the kinetic samples in 1 cm cells placed in the thermostatted compartment of the instrument (25.0 ± 0.1 °C), the reactions were started by addition (5–15 mm^3) of a stock solution of PDTA in acetonitrile. The initial PDTA concentration was (1–3) × 10^{-5} mol dm^{-3} and acetonitrile never exceeded 0.5% in the kinetic solutions.

Borate and phosphate buffers were used in some cases to maintain the pH. In other cases the amine and its conjugate acid acted as such. At least three pH values were employed in the reactions of each amine. The reaction conditions are described in Table 1.

Pseudo-first-order rate coefficients (k_{obs}) were obtained under amine excess (at least twenty-fold, although usually the excess was well over this). The values of k_{obs} found are shown in Table 1.

Product Studies.—The UV spectrum obtained at the end of the reaction of the substrate with piperidine, $[\mathrm{PDTA}]_0 = 2 \times 10^{-5}$ mol dm^{-3}, $[\mathrm{N}]_{tot} = 0.01$ mol dm^{-3}, borate buffer 0.01 mol dm^{-3} and pH = 8.7, was identical to the one found for benzenethiolate anion under the same conditions ($\lambda_{max} = 264$ nm).

Results and Discussion

The rate law obtained in all the present reactions is given by eqn. (2), the amine being in excess over the substrate (PDTA) in all

Table 1 Experimental conditions and k_{obs} values for the aminolysis of PDTA[a]

Amine	$[N]_{tot}$/ 10^{-3} mol dm^{-3} [b]	pH	k_{obs}/ 10^{-3} s^{-1}	Number of runs
Piperidine (PI)	10–100[c]	8.7	4.5–45.7	4
	7.5–75.0[c]	9.0	6.8–65.2	5
	5.0–50.0[c]	9.3	9.9–86.7	5
Piperazine (PA)	0.8–8.0[c]	8.1	0.8–11.1	5
	0.6–6.0[c]	8.4	1.5–20.6	5
	0.4–4.0[c]	8.7	2.6–31.6	5
	5.0[d]	8.7	32–63	5
1-(β-Hydroxyethyl)-piperazine (BHPA)	0.4–9.0	8.8	1.2–104	6
	0.4–6.0	9.1	6.4–122	11
	0.4–5.0	9.4	10.6–166	7
	0.2–2.5	9.7	11.1–117	7
	2.7[d]	9.4	92–115	6
	0.4–4.0[e]	8.8	6.9–69	3
	0.4–4.0[e]	9.1	11.7–116	3
	0.4–4.0[e]	9.4	19.2–174	3
Morpholine (MO)	6.6–49.7	7.6	3.5–123	4
	0.3–52.0	7.9	0.3–319	20
	0.4–1.0	8.2	0.4–1.3	6
	13.2[f]	7.6	10.1–47.9	4
	5.1–50.5[g]	7.0	5.1–57.5	5
	3.0–30.3[g]	7.3	7.2–60.1	5
	1.5–15.2[g]	7.6	7.4–59.7	4
1-Formylpiperazine (FPA)	3.5–35.0	7.7	1.7–108	4
	3.5–42.0	8.0	3.4–244	11
	1.8–17.5	8.3	1.8–102	5
	0.3–3.0[h]	8.4	2.4–24.2	3
	0.3–3.0[h]	8.7	2.3–36.4	3
	0.3–3.0[h]	9.0	5.2–51.4	8
Piperazinium ion (PAH)	2.0–76.5	5.5	0.1–9.5	9
	9.0–90.0	5.8	0.8–22.0	4
	9.0–90.0	6.2	1.2–45.3	7

[a] In aqueous solution at 25 °C, I 0.2 mol dm^{-3} (KCl). [b] Concentration of total amine (free amine plus its conjugate acid). [c] In the presence of 0.02 mol dm^{-3} borate buffer. [d] In the presence of 0.01–0.15 mol dm^{-3} borate buffer. [e] In the presence of 0.2 mol dm^{-3} borate buffer. [f] In the presence of 0.01–0.40 mol dm^{-3} phosphate buffer. [g] In the presence of 0.1 mol dm^{-3} phosphate buffer. [h] In the presence of 0.4 mol dm^{-3} borate buffer.

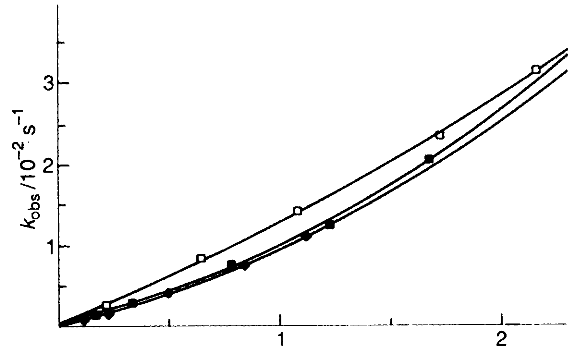


Fig. 1 Plots of k_{obs} *vs.* [N] for the reaction of PDTA with PA in 0.02 mol dm^{-3} borate buffer at pH 8.1 (◆), 8.4 (■) and 8.7 (□)

$$\frac{d[PhS^-]}{dt} = k_{obs}[PDTA] \qquad (2)$$

cases. The dependence of k_{obs} on the amine and/or buffer concentration varied according to the amine, as can be seen in Figs. 1–4, which describe some examples of the plots obtained in this work.

Linear plots of k_{obs} *vs.* [N] (where N represents the free amine) with the slope independent of pH were obtained in the reactions of PDTA with piperidine (PI), 1-(β-hydroxyethyl)-piperazine (BHPA) and morpholine (MO) under external buffer conditions (plots not shown).

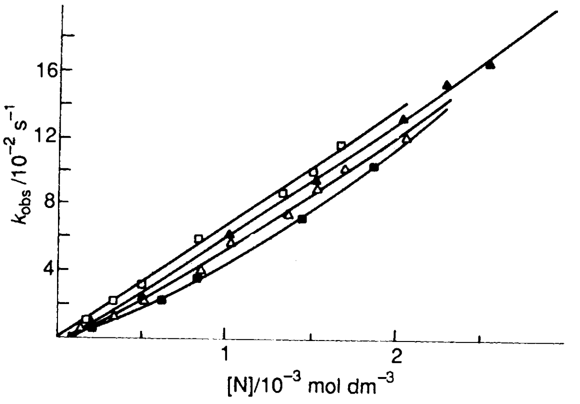


Fig. 2 Plots of k_{obs} *vs.* [N] for the reaction of PDTA with BHPA at pH 8.8 (■), 9.1 (△), 9.4 (▲) and 9.7 (□)

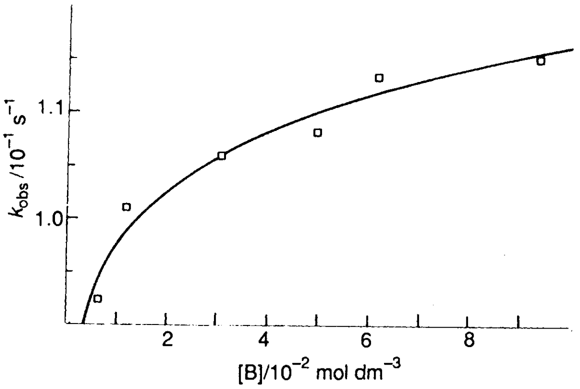


Fig. 3 Plot of k_{obs} *vs.* [B] for the reaction of PDTA with BHPA in borate buffer at pH 9.4, $[N]_{tot}$ 2.7 × 10^{-3} mol dm^{-3}

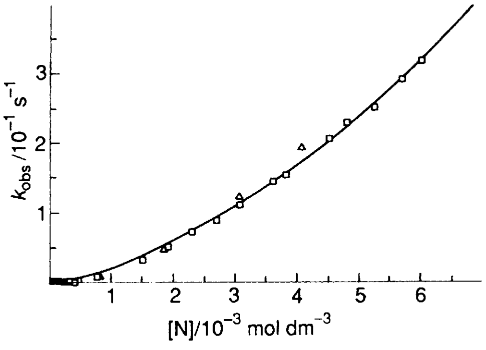


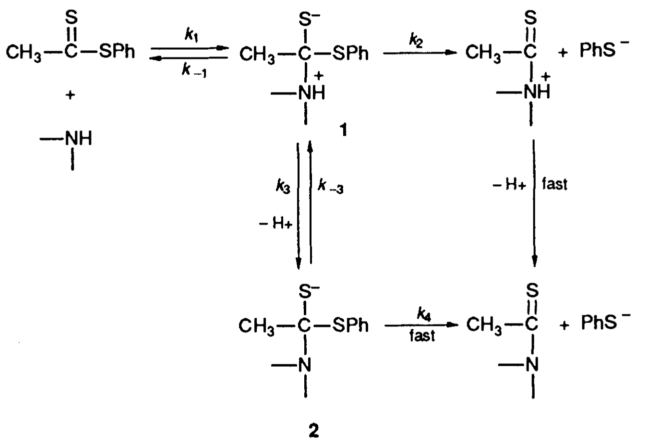
Fig. 4 Plot of k_{obs} *vs.* [N] for the reaction of PDTA with MO at pH 7.6 (△), 7.9 (□) and 8.2 (■)

The non-linear k_{obs} *vs.* [B] plot (B represents the free base of the external buffer) shown in the reaction of PDTA with BHPA (Fig. 3) is similar to the ones found in the reactions with piperazine (PA), MO and 1-formylpiperazine (FPA) (plots not shown). Linear plots of $[B]/k_{obs}$ *vs.* [B] were obtained in the reactions with BHPA, PA, MO and FPA (not shown).

The non-linear plot of k_{obs} *vs.* [N] found in the reaction of the substrate with MO in the absence of external buffer is pH independent (Fig. 4). Re-plotting this as $[N]/k_{obs}$ *vs.* 1/[N] results in a straight line (not shown). Similar plots were obtained in the reaction with FPA.

Linear k_{obs} *vs.* [N] plots, with the slopes increasing with pH, were found in the reaction of the substrate with FPA in the presence of 0.4 mol dm^{-3} borate buffer (plots not shown).

In the reaction of PDTA with piperazinium ion (PAH) in the



$$k_3 = k_3^{N}[N] + k_3^{B}[B] + k_3^{OH}[OH^-]$$

$$k_{-3} = k_{-3}^{NH}[NH^+] + k_{-3}^{BH}[BH] + k_{-3}^{W}[H_2O]$$

Scheme 1

Table 2 Values of the pK_a of the conjugate acids of the amines and of the microconstants obtained in this work[a]

Amine	pK_a[b]	k_1/dm^3 mol^{-1} s^{-1}	$k_{-1}/10^8$ s^{-1}	$K_1/10^{-6}$ mol^{-1} dm^3	$k_3^B/10^9$[c] dm^3 mol^{-1} s^{-1}
PI	11.24	150	0.002[d]	750[e]	0.2
PA	9.94	250	0.08	30	3
BHPA	9.38	85[f]	0.1	7	5
MO	8.78	67[g]	0.3	2	0.1
FPA	7.98	30	4	0.08	10
PAH	5.81	17[h]	160	0.001	—

[a] $k_2 = 10^6$–10^7 s^{-1}; $k_3^N = 10^{10}$ dm^3 mol^{-1} s^{-1}; $k_3^{OH} = 5 \times 10^{10}$ dm^3 mol^{-1} s^{-1}. In aqueous solution at 25 °C, I 0.2 mol dm^{-3} (KCl). The error involved in k_1 is 20%, except for FPA and PAH where it is 40%. The errors of k_{-1}, K_1, k_3^B, k_3^N and k_3^{OH} are *ca.* 100%. The value of k_2 is independent of the amine basicity,[2,5,6] and is estimated to be within the limiting values shown. [b] Values taken from ref. 5. [c] The k_3^B values refer to B = $H_2BO_3^-$, except in the MO reactions where B = HPO_4^{2-}. [d] Value obtained by extrapolation of the Brønsted plot for k_{-1}. [e] Value obtained as k_1/k_{-1}. [f] Average value of the ones obtained from the intercept of a plot of $[B]/k_{obs}$ *vs.* [B] and as the slope of a plot of k_{obs} *vs.* [N] in 0.2 mol dm^{-3} borate buffer; the individual k_1 values are 84.8 and 85.2 dm^3 mol^{-1} s^{-1}, respectively. [g] Average value of the ones obtained from the intercept of a plot of $[N]/k_{obs}$ *vs.* 1/[N], as the slope of a plot of k_{obs} *vs.* [N] in 0.1 mol dm^{-3} phosphate buffer and from the limiting value of k_{obs} at high [B]; the individual k_1 values are 76, 64 and 61 dm^3 mol^{-1} s^{-1}, respectively.

absence of external buffer a pH-independent linear plot of k_{obs} *vs.* $[N]^2$ was obtained (not shown).

According to the kinetic behaviour exhibited by the present reactions (Figs. 1–4 and the linear plots), a general expression for k_{obs} can be deduced, eqn. (3), which is consistent with the

$$k_{obs} = \frac{k_1(k_2 + k_3^N[N] + k_3^B[B] + k_3^{OH}[OH^-])[N]}{k_{-1} + k_2 + k_3^N[N] + k_3^B[B] + k_3^{OH}[OH^-]} \qquad (3)$$

general mechanism shown in Scheme 1. Applying the steady state condition to intermediates **1** and **2** of the scheme and assuming $k_4 \gg k_{-3} = k_{-3}^{NH}[NH^+] + k_{-3}^{BH}[BH] + k_{-3}^{W}[H_2O]$, one obtains eqn. (3) ($NH^+$ and BH are the conjugate acids of N and B; the latter represent the free bases of the amine and the external buffer, respectively).

Eqn. (3) can be simplified according to the conditions of the reactions (Table 1) and the nature of the amine.

In the reactions with PI, in the presence of borate buffer, $k_2 + k_3 \gg k_{-1}$, where $k_3 = k_3^N[N] + k_3^B[B] + k_3^{OH}[OH^-]$, and eqn. (3) reduces to eqn. (4). This inequality will be justified later,

$$k_{obs} = k_1[N] \qquad (4)$$

together with the ones below for the reactions of the other amines. The value of k_1 was obtained as the slope of a plot of k_{obs} *vs.* [N]. The value is shown in Table 2.

In the reactions of the substrate with PA, in the presence of borate buffer, $k_3^{OH}[OH^-]$ is negligible at the pH values used (Table 1), compared to the other terms in eqn. (3). Therefore, in this case eqn. (3) simplifies to eqn. (5), which accounts for the

$$k_{obs} = \frac{k_1(k_2 + k_3^N[N] + k_3^B[B])[N]}{k_{-1} + k_2 + k_3^N[N] + k_3^B[B]} \qquad (5)$$

plots shown in Fig. 1. The pH dependence of the curves can be attributed to the variation of [B] with the pH values.

In the reactions with PA at variable [B] (borate) and constant [N] and pH, according to the reaction conditions $k_3^B[B] \gg k_2 + k_3^N[N] + k_3^{OH}[OH^-]$; therefore eqn. (3) yields eqn. (6), which accounts for the plot found (similar to that in Fig. 3). Rearrangement of eqn. (6) gives eqn. (7), where K_1 =

$$k_{obs} = \frac{k_1K_3^B[B][N]}{k_{-1} + k_3^B[B]} \qquad (6)$$

k_1/k_{-1} is the equilibrium constant for the first step of Scheme 1. Eqn. (7) describes the linear plot obtained (not shown); the

$$\frac{[B]}{k_{obs}} = (K_1k_3^B[N])^{-1} + (k_1[N])^{-1}[B] \qquad (7)$$

values of $K_1k_3^B$ and k_1 were obtained from the intercept and slope, respectively, of this plot. From an estimation of the value of $k_3^B \approx 3 \times 10^9$ dm^3 mol^{-1} s^{-1} (see below), the value of K_1 can be found; the value of k_{-1} can also be determined knowing K_1 and k_1. These values are shown in Table 2.

In the reactions with BHPA in the absence of buffer the term $k_3^B[B] = 0$, so eqn. (3) reduces to eqn. (8), under the reaction

$$k_{obs} = \frac{k_1(k_2 + k_3^N[N] + k_3^{OH}[OH^-])[N]}{k_{-1} + k_2 + k_3^N[N] + k_3^{OH}[OH^-]} \qquad (8)$$

conditions (Table 1), which accounts for the plots in Fig. 2.

In the presence of 0.2 mol dm^{-3} borate buffer, however, the above reaction exhibits a linear plot of k_{obs} *vs.* [N] which obeys eqn. (4), *i.e.*, in this case k_{-1} is negligible compared to the sum of the other terms in the denominator of eqn. (3), and this equation reduces to eqn. (4). The value of k_1, obtained as the slope of the above plot, is shown in Table 2.

For the reaction of PDTA with BHPA at constant [N] and pH in the presence of varying [B], $k_3^B[B] \approx k_{-1} \gg k_2 + k_3^N[N] + k_3^{OH}[OH^-]$; hence eqn. (3) simplifies to eqn. (6), which accounts for the plot in Fig. 3. From the linear plot of $[B]/k_{obs}$ *vs.* [B] (not shown), $K_1k_3^B$ and k_1 were obtained from the intercept and slope, respectively [see eqn. (7)]. The value of k_1 agrees with that previously determined from eqn. (4) (Table 2). From an estimation of $k_B \approx 5 \times 10^9$ dm^3 mol^{-1} s^{-1} (see below), the values of K_1 and k_{-1} were obtained; these are shown in Table 2.

The reaction of PDTA with MO without external buffer obeys eqn. (9), under the reaction conditions (Table 1), *i.e.*, $k_3^{OH}[OH^-]$

$$k_{obs} = \frac{k_1(k_2 + k_3^N[N])[N]}{k_{-1} + k_2 + k_3^N[N]} \qquad (9)$$

is negligible compared with the other terms in eqn. (3). Eqn. (9) accounts for the plot of Fig. 4. If the [N] range is restricted to (2.3–60) × 10^{-4} mol dm^{-3}, instead of (1.0–60) × 10^{-4} mol dm^{-3}

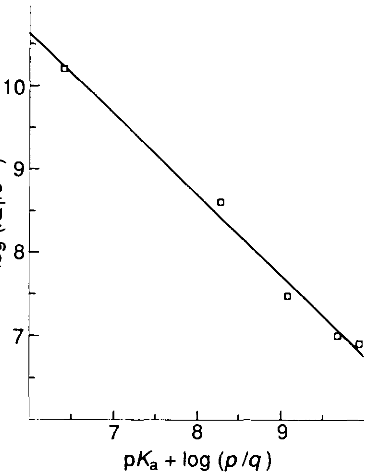


Fig. 5 Brønsted plot for k_{-1} (pK_a statistically corrected) obtained in the reactions of PDTA with PA, BHPA, MO, FPA and PAH

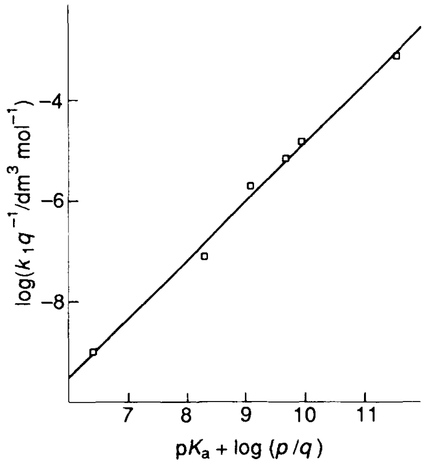


Fig. 6 Brønsted plot for K_1 (statistically corrected) obtained in the reactions of PDTA with PI, PA, BHPA, MO, FPA and PAH

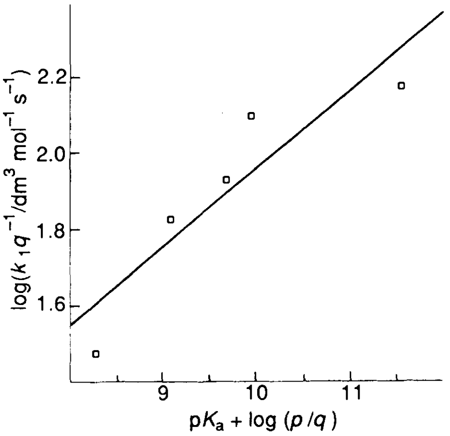


Fig. 7 Brønsted plot for k_1 (statistically corrected obtained in the reactions of PDTA with PI, PA, BHPA, MO and FPA

in Fig. 4, $k_3^N[N] > k_2$ and eqn. (9) reduces to eqn. (10), which

$$k_{obs} = \frac{k_1 k_3^N [N]^2}{k_{-1} + k_3^N[N]} \qquad (10)$$

rearranges to eqn. (11). This expression accounts for the linear

$$\frac{[N]}{k_{obs}} = k_1^{-1} + (K_1 k_3^N)^{-1}[N]^{-1} \qquad (11)$$

plot of $[N]/k_{obs}$ *vs.* $1/[N]$ found (not shown); the values of k_1 and $K_1 k_3^N$ were obtained from the intercept and slope, respectively, of this plot. From the estimation of $k_3^N = 10^{10}$ dm^3 mol^{-1} s^{-1} (see below) the values of K_1 and k_{-1} can be determined (Table 2).

For the above reaction in 0.1 mol dm^{-3} phosphate buffer, k_{-1} is negligible compared to the sum of the other terms in the denominator of eqn. (3), so this expression simplifies to eqn. (4), which accounts for the linear and pH independent plot of k_{obs} *vs.* [N] (not shown). The value of k_1 obtained as slope of this plot (Table 2) agrees with the value determined from the plot of eqn. (11).

Another determination of k_1 is possible from a plot of k_{obs} *vs.* [B] (phosphate) at constant [N] and pH (not shown; conditions in Table 1). The plot levels off (similarly to that in Fig. 3) and k_1 is the limiting value of $k_{obs}/[N]$, *i.e.*, in eqn. (6) $k_3^B[B] \gg k_{-1}$ at high [B]. This value of k_1 (shown in Table 2) agrees with the values determined above.

In the reaction of PDTA with FPA without external buffer, under the reaction conditions, $k_3^{OH}[OH^-]$ is negligible and eqn. (9) holds. This equation accounts for the k_{obs} *vs.* [N] plot obtained (not shown, but similar to that of Fig. 4). Using a more restricted [N] range, (3–20) × 10^{-3} mol dm^{-3} instead of (1–20) × 10^{-3} mol dm^{-3}, the plot $[N]/k_{obs}$ *vs.* $1/[N]$ is linear (not shown), *i.e.*, under the new conditions $k_3^N[N] > k_2$ and eqn. (9) reduces to eqns. (10) and (11). From a plot of the latter equation the values of k_1 and $K_1 k_3^N$ were obtained; since $k_3^N = 10^{10}$ s^{-1} mol^{-1} dm^3 (see below) the values of K_1 and k_{-1} can also be determined; all these values are shown in Table 2.

The above reaction in the presence of borate buffer shows linear plots of k_{obs} *vs.* [N], where the slopes increase with pH (plots not shown). In this case $k_3^B[B] \gg k_3^N[N] + k_2$, $k_3^{OH}[OH^-]$ is negligible and, therefore, eqn. (3) simplifies to eqn. (6). The latter accounts for the above linear plots; moreover, since [B] increases with pH ($[B]_{tot}$ is constant at the 3 pH values) the slopes should also do so.

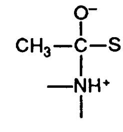
In the reaction of the substrate with PAH, $k_{-1} \gg k_3^N[N] \gg k_2$, $k_3^{OH}[OH^-]$ is negligible and $k_3^B[B] = 0$ (no external buffer was used), therefore eqn. (3) simplifies to eqn. (12). The linear and

$$k_{obs} = \frac{k_1 k_3^N [N]^2}{k_{-1}} \qquad (12)$$

pH-independent plot of k_{obs} *vs.* $[N]^2$ found (not shown) obeys eqn. (12); the value of $K_1 k_3^N$ was obtained as the slope of the plot. With the value of $k_3^N = 10^{10}$ dm^3 mol^{-1} s^{-1}, K_1 can be determined. The value of k_1 for this reaction was obtained by extrapolation of the Brønsted plot for k_1 in the reactions with the other amines, and the k_{-1} value was determined from K_1 and k_1. The values are shown in Table 2.

In order to justify the above inequalities we will estimate some of the microconstants involved in Scheme 1. To do so we will first estimate the pK_a of intermediate **1** in the scheme.

The pK_a of the tetrahedral intermediate **3** has been estimated, based on Jencks's method,[9] to be equal to that of the parent aminium ion.[5] On the other hand, an increasing acidity of NH in the series RNHCO$_2$Ar < RNHCOSAr < RNHCS$_2$Ar has been found.[10] There is also a pK_a lowering of 3.5 units when



$$\mathrm{CH_3{-}\overset{\overset{\Large O^-}{|}}{\underset{\underset{\Large —NH^+}{|}}{C}}{-}SPh}$$

3

going from *N*-protonated *N*-alkylcarbamates (RNH_2^+–COO^-) to the corresponding thiocarbamates and there is a further decrease in pK_a from the latter compounds to dithiocarbamates.[11] The pK_a lowering in going from **3** to **1** cannot be as large as 3.5 units,[4b] and according to our results we estimate this pK_a decrease to be *ca.* 0.3 units (see below). Therefore, the pK_a of **1** is *ca.* 0.3 pK_a units lower than that of the parent aminium ion.

Since proton transfer from **1** to the corresponding amine is thermodynamically favourable, it follows that k_3^N is *ca.* 10^{10} dm^3 mol^{-1} s^{-1}.[12] This proton transfer to OH^- is also favourable (pK_a of H_2O 15.7), therefore, k_3^{OH} is *ca.* 5 × 10^{10} dm^3 mol^{-1} s^{-1} (larger than k_3^N in view of the large diffusion coefficient of OH^- compared with that of the amine).[12]

The pK_a of the intermediate **1** formed with PI is $11.2 - 0.3 = 10.9$. The proton transfer to B (borate base, pK_a of BH = 9.2) is not thermodynamically favourable, therefore $k_{-3}^{BH} \approx 10^{10}$ dm^3 mol^{-1} s^{-1} and $k_3^B \approx 10^{10} \times 10^{-10.9}/10^{-9.2} \approx 2 \times 10^8$ dm^3 mol^{-1} s^{-1}.[12] In the reactions with PA a similar calculation yields k_3^B *ca.* 3 × 10^9 dm^3 mol^{-1} s^{-1}. The intermediate **1** formed with BHPA has a pK_a similar to that of BH, therefore k_3^B is *ca.* 5 × 10^9 dm^3 mol^{-1} s^{-1}.[12] For FPA, k_3^B is *ca.* 10^{10} dm^3 mol^{-1} s^{-1}, since the proton transfer from **1** to B (borate) is thermodynamically favourable. In the reactions with MO phosphate buffer was employed (pK_a = 6.7) and the pK_a of **1** (MO) is *ca.* 8.5; therefore k_3^B is *ca.* 1 × 10^8 dm^3 mol^{-1} s^{-1} in this case.

The results obtained in this work (Figs. 1–4 and other plots) are compatible with a value of k_2 within the range 10^6–10^7 s^{-1}. This value should be practically independent of the amine basicity,[2,5,6] so it is the same for all the zwitterionic intermediates formed in the present reactions. The uncertainty in k_2 is a consequence of its relatively small value compared to the sum of the other terms in the rate equations concerned [*e.g.* eqns. (5), (8) and (9)].

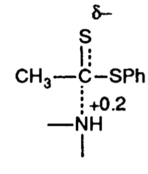
The values of the microconstants involved in Scheme 1 (either estimated or obtained experimentally, Table 2), although subject to rather large errors (see Table 2), justify the inequalities stated above regarding eqns. (4)–(12) and can describe satisfactorily the experimental plots found.

Another indication that the values of the microconstants of Table 2 are correct is given by the good correlations exhibited by the Brønsted plots for k_{-1} and K_1 (Figs. 5 and 6). The corresponding plot for k_1 shows a satisfactory correlation (Fig. 7).

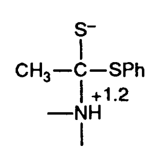
The absolute value of the Brønsted slope for k_{-1} (β_{-1} *ca.* -1, Fig. 5) is larger than those exhibited in the aminolyses of aryl acetates ($\beta_{-1} = -0.7$),[13] phenyl aryl carbonates ($\beta_{-1} = -0.7$)[2] and aryl thioacetates ($\beta_{-1} = -0.65$).[6] The Brønsted slope for K_1 ($\beta_{eq} = +1.2$, Fig. 6) is comparable to that found in the aminolysis of phenyl aryl carbonates ($\beta_{eq} = +1.0$),[2] and larger than those obtained in the aminolysis of aryl acetates and thiolacetates ($\beta_{eq} = +0.85$–0.9)[1,6,13] and 2,4-dinitrophenyl methyl carbonate and *p*-nitrophenyl benzoate ($\beta_{eq} = +0.85$–0.9).[4a,7a,c] The Brønsted slope for k_1 (β_1 *ca.* $+0.2$, Fig. 7) is the same as that found in the aminolysis of aryl acetates and thiolacetates and methyl aryl carbonates,[1,6,7] and a little smaller than that exhibited in the aminolysis of phenyl aryl carbonates ($\beta_1 = 0.3$).[2]

With the β values for k_{-1} and K_1 found in the present reactions the β value for k_1 can be deduced: $\beta_1 = \beta_{eq} + \beta_{-1} = 1.2 - 1.0 = 0.2$,[1,2] which coincides with the one obtained experimentally (Fig. 7).

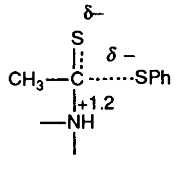
With the values of β_1 and β_{eq} the effective charges can be assigned on the nitrogen atoms of the transition state for the first step (**4**) and of intermediate **1**, respectively.[1,2] Since the sensitivity of the rate coefficient k_2 of Scheme 1 to the amine basicity is approximately zero in the aminolysis of aryl acetates and thiolacetates,[1,2,6,13] we will assume that it is also zero in the present reactions. This is reasonable in view of the impossibility of the amine moiety in intermediate **1** exerting the push to expel PhS^-.[1,2,6,13] Therefore, we can assume that the effective charge on the nitrogen atom of the transition state for the second step in Scheme 1 (**5**) is also +1.2.



4



1



5

The greater effective charge on the nitrogen atom of intermediate **1** (+1.2) compared to that of **3** (+0.7) means that the group MeC(S^-)SPh is more electron-withdrawing than MeC(O^-)SPh, and explains why the species **1** is more acidic than **3**.

The reason for observing base catalysis in the present reactions, as opposed to the aminolysis of aryl thiolacetates which shows no base catalysis,[5,6] is two fold: (i) In the present reactions proton transfer from **1** to a base to yield **2** is faster than in the aryl thiolacetates reactions due to the higher acidity of **1**. (ii) The rate of expulsion of both PhS^- and a given amine is slower from intermediate **1** than from **3**,[5,6] therefore **1** is more stable than **3** and proton transfer from **1** can successfully compete with k_2.

The higher stability of intermediate **1** relative to **3** is in agreement with the fact that *S,S*-acetals decompose in water more slowly than *O,S*-acetals and *O,O*-analogues.[14] There are also many examples of tetrahedral intermediates whose stability increases as the number of sulfur atoms attached to the central carbon increases.[15]

According to our results the ability of S^- in intermediate **1** to form a double bond with the tetrahedral carbon and expel a leaving group is less than that of O^- in **3**. This is in accord with the known C^+–S^- character of the thione 'double' bond resulting from a weaker π-bonding energy compared with that of the carbonyl group.[10b] There is a 170 kJ mol^{-1} difference between the π-bond energy of C=S and C=O.[16] As a result of this, k_1 is larger in the present reactions compared to the same reactions with *S*-phenyl thioacetate (PTA).[5,6,*] Once the intermediate **1** is formed the difficulty in reforming the CS double bond and expelling either the amine or PhS^- is greater compared with the formation of the CO double bond in **3**.[17] It is difficult to find analogies in the literature, but the slower expulsion of PhO^- from ArN^-CSOPh in comparison with the same expulsion from ArN^-COOPh and the slower leaving rate of PhS^- from ArN^-CSSPh relative to ArN^-COSPh,[10a] are somehow in agreement with our results in view of the contribution of the canonical structure ArN=C(X^-)(XPh), (X = O or S), to the ground state of the X-phenyl *N*-aryl(thio)carbamate.[10b]

The pK_a value for the centre of the hypothetical Brønsted plot for k_N (pK_a^0), *i.e.*, the value of the basicity of an amine for which $k_{-1} = k_2$,[6] can be obtained for the present reactions by equalising the Brønsted equation for k_{-1} † with the value of k_2 (Table 2).[6] For the lower and upper limits of k_2, the resulting values of pK_a^0 are 10.8 and 9.8, respectively. The pK_a^0 value deduced for the reactions of PTA with secondary alicyclic amines is 12.2.[6] The higher value of pK_a^0 for the PTA reactions

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* With the $k_N = K_1k_2$ values for the reactions of secondary alicyclic amines with PTA (ref. 5) and the values of k_2 and k_{-1}, deduced from the corresponding equations (ref. 6), the values of k_1 can be determined for these reactions.

† The k_{-1} values of Table 2 are correlated through the Brønsted equation: $\log k_{-1} = 16.47 - 0.97$ pK_a (Fig. 5).

is consistent with the fact that a linear Brønsted plot was found in the aminolysis of *p*-nitrophenyl benzoate ($pK_a^0 > 11$), whereas a curved one with $pK_a^0 = 9.2$ is exhibited in the same reactions with *O*-*p*-nitrophenyl thiobenzoate.[4a]

Campbell and Lapinskas[4a] have interpreted their results in terms of a lower stability of the tetrahedral intermediate formed in the reactions of the thioester compared to that formed in the aminolysis of the oxyesters; they claim that S^- in the former intermediate is able to expel *p*-nitrophenoxide ion with greater driving force than can O^- from the oxy intermediate.

Our results disagree with the above interpretation and indicate that the change of O^- in the intermediate to S^- increases the stability of the intermediate by decreasing the nucleofugalities of both the amine and PhS^- from this compound.

The ratio k_{-1}/k_2 for an amine isobasic with PhS^- (pK_a PhSH = 6.5)[5] from intermediate **3** is *ca.* 5×10^3,[5,6] whereas the same ratio from **1** is *ca.* 10^3–10^4, depending on the limiting k_2 values used (Table 2). In both cases, the conclusion is that amines are much better leaving groups than isobasic arylthiolate ions. It has also been found that amines are much better nucleofuges from a zwitterionic intermediate ($T^\pm$) than aryloxide ions of equal basicity.[1,2,4,7,13]

We disagree with the claim that the change of O^- to S^- in $T^\pm$ favours aryloxide ion (or arylthiolate ion) expulsion,[4a] since the k_{-1}/k_2 ratio will vary differently with amine basicity due to the different sensitivities of k_{-1} to this basicity ($\beta_{-1} = 0.65$ and 0.97 for the aminolysis of PTA and in this work, respectively). For instance, for an amine of pK_a 12 the k_{-1}/k_2 ratio is 1.4 and 0.01 * for the aminolysis of PTA and PDTA, respectively; nevertheless, for an amine of pK_a 4 the k_{-1}/k_2 ratio is 2×10^5 and 8×10^5,* respectively. In other words, the change from **3** to **1** favours PhS^- expulsion for the basic amine, but it favours the amine leaving for a weakly basic amine.

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* Assuming $k_2 = 5 \times 10^6\ s^{-1}$ in the present reactions.

References

1 A. C. Satterthwait and W. P. Jencks, *J. Am. Chem. Soc.*, 1974, **96**, 7018.

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

3 R. Barnett and W. P. Jencks, *J. Am. Chem. Soc.*, 1968, **90**, 4199; 1969, **91**, 2358; N. S. Tao, S. Scheithauer and P. Mayer, *Z. Chem.*, 1972, **12**, 133; T. Komives, A. F. Marton and F. Dutka, *Z. Naturforsch., Teil B*, 1975, **30**, 138; N. M. Oleinik, L. M. Litvinenko, L. P. Kurchenko, S. E. Terekhova and Z. P. Gelbina, *Zh. Org. Khim.*, 1976, **12**, 2374; V. A. Dadali, B. V. Pachenko and L. M. Litvinenko, *Zh. Org. Chem.*, 1980, **16**, 1725; I-H. Um, K-E. Choi and D-S. Kwon, *Bull. Korean Chem. Soc.*, 1990, **11**, 362.

4 (*a*) P. Campbell and B. A. Lapinskas, *J. Am. Chem. Soc.*, 1977, **99**, 5378; (*b*) E. A. Castro, N. Alvarado, S. A. Peña and J. G. Santos, *J. Chem. Soc., Perkin Trans. 2*, 1989, 635.

5 E. A. Castro and C. Ureta, *J. Org. Chem.*, 1989, **54**, 2153.

6 E. A. Castro and C. Ureta, *J. Chem. Soc., Perkin Trans. 2*, 1991, 63.

7 (*a*) E. A. Castro and F. J. Gil, *J. Am. Chem. Soc.*, 1977, **99**, 7611; (*b*) E. A. Castro and M. Freudenberg, *J. Org. Chem.*, 1980, **45**, 906; (*c*) E. A. Castro, M. T. Bórquez and P. M. Parada, *J. Org. Chem.*, 1986, **51**, 5072.

8 M. Yokoyama, Y. Hasegawa, H. Hatanaka, Y. Kawasoe and T. Imamoto, *Synthesis*, 1984, **10**, 827.

9 J. M. Sayer and W. P. Jencks, *J. Am. Chem. Soc.*, 1973, **95**, 5637; J. P. Fox and W. P. Jencks, *J. Am. Chem. Soc.*, 1974, **96**, 1436.

10 (*a*) J. Mindl, J. Sulzer and M. Vecera, *Collect. Czech. Chem. Comm.*, 1981, **46**, 1970; (*b*) S. V. Hill, S. Thea and A. Williams, *J. Chem. Soc., Perkin Trans 2*, 1983, 437.

11 S. P. Ewing, D. Lockshon and W. P. Jencks, *J. Am. Chem. Soc.*, 1980, **102**, 3072.

12 M. Eigen, *Angew. Chem., Int. Ed. Engl.*, 1964, **3**, 1.

13 E. A. Castro and C. Ureta, *J. Org. Chem.*, 1990, **55**, 1676.

14 D. P. N. Satchell and R. S. Satchell, *Chem. Soc. Rev.*, 1990, **19**, 55 and references therein.

15 B. Capon, A. K. Ghosh and D. M. A. Grieve, *Acc. Chem. Res.*, 1981, **14**, 306; B. Capon, M. I. Dosunumu and M. N. de Matus-Sánchez, *Adv. Phys. Org. Chem.*, 1985, **21**, 37 and references therein.

16 T. L. Cottrell, *The Strengths of Chemical Bonds*, Butterworth, London, 1959, 2nd edn., pp. 275–276.

17 D. S. Kwon, H. S. Park and I. H. Um, *Bull. Korean Chem. Soc.*, 1991, **12**, 93.

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