

## Structure–Reactivity Correlations in the Aminolysis and Pyridinolysis of Bis(phenyl) and Bis(4-nitrophenyl) Thionocarbonates

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The reactions of a series of secondary alicyclic amines with bis(phenyl) and bis(4-nitrophenyl) thionocarbonates (BPTOC and BNPTOC, respectively), and a series of pyridines with the latter substrate, are subjected to a kinetic investigation in water, 25.0 °C, ionic strength 0.2 M (KCl). All the reactions obey pseudo-first-order kinetics under amine excess over the substrate. The reactions of piperidine with BPTOC are first order in amine, but those of the same substrate with the other secondary alicyclic amines exhibit a complex order, consistent with the existence of both a zwitterionic ( $T^\pm$ ) and an anionic ( $T^-$ ) tetrahedral intermediates on the reaction pathway. Deprotonation of  $T^\pm$  by a secondary amine to give  $T^-$  (rate coefficient  $k_3$ ) competes with expulsion of the amine moiety from  $T^\pm$  ( $k_{-1}$ ), except in the reactions of 1-formylpiperazine whereby  $k_{-1} \gg k_3$  [1-formylpiperazine], and a kinetics second order in amine is observed. The reactions of secondary alicyclic amines with BNPTOC are all first order in amine and show a nonlinear Brønsted-type plot with limiting slopes  $\beta = 0.1$  (high amine  $pK_a$ ) and  $\beta = 0.5$  (low amine  $pK_a$ ). This slight curvature is consistent with a concerted mechanism (one step). The intermediate  $T^\pm$  is not formed because of its high kinetic instability due to a large  $k_{-1}$  value. The pyridinolysis of BNPTOC exhibits a first order in amine kinetics and a linear Brønsted-type plot of slope  $\beta = 1.0$ , which is consistent with the existence of  $T^\pm$  whereby the expulsion of the leaving group from  $T^\pm$  is the rate-determining step. This intermediate is less unstable than that with a secondary amine due to the fact that  $k_{-1}$  is smaller for a pyridine compared to an isobasic secondary alicyclic amine.

### Introduction

Lately, we have been interested on the mechanisms of the aminolysis of thiono derivatives and particularly thionocarbonates. We have kinetically studied the reactions of phenyl and 4-nitrophenyl ethyl thionocarbonates with secondary alicyclic amines, where a stepwise mechanism through two tetrahedral intermediates on the reaction pathway was found.<sup>1</sup>

Recently we have performed a kinetic study on the pyridinolysis of methyl and ethyl 4-nitrophenyl thionocarbonates and ethyl 2,4-dinitrophenyl thionocarbonate.<sup>2</sup> In this work a biphasic Brønsted-type plot was obtained for the latter reactions whereas linear plots were found for those of the alkyl 4-nitrophenyl derivatives. These Brønsted plots were interpreted through a zwitterionic tetrahedral intermediate ( $T^\pm$ ) on the reaction path, whereby there is a change in the rate-determining step depending on the pyridine basicity (for the dinitro derivative) and whereby the expulsion of 4-nitrophenoxide ion from  $T^\pm$  is rate determining (for the two mononitro thionocarbonates).<sup>2</sup>

In order to extend our mechanistic investigations we perform in the present work a kinetic study on the reactions of secondary alicyclic amines with bis(phenyl) and bis(4-nitrophenyl) thionocarbonates, and the reactions of pyridines with the latter substrate. The object is to assess the influence of the nonleaving and leaving groups of the substrate and the amine nature on these mechanisms by comparing these reactions among them and with those of alkyl aryl thionocarbonates.<sup>1,2</sup>

### Experimental Section

**Materials.** The secondary alicyclic amines and pyridines were purified as reported.<sup>3,4</sup> Bis(4-nitrophenyl) thionocarbonate (BNPTOC) was synthesized as follows: To a solution of 4-nitrophenol (3.62 g, 26 mmol) dissolved in THF (20 mL) in a Schlenk round-bottomed flask was added slowly a solution (16.3 mL) of 1.6 M butyllithium (Aldrich) under nitrogen atmosphere. The product, lithium 4-nitrophenoxide, was rapidly transferred to a compensation funnel, under nitrogen. In another Schlenk round-bottomed flask, thiophosgene (1 mL, Aldrich) was dissolved in anhydrous THF (20 mL) under nitrogen and the flask placed in an ethanol–liquid nitrogen bath. The compensation funnel was attached to the flask and the lithium 4-nitrophenoxide solution added dropwise with stirring during 2 h. The mixture was left overnight with stirring under nitrogen at ambient temperature. Chloroform (50 mL) was added to this mixture and the solution washed with water. The organic layer was dried with  $MgSO_4$  and filtered under vacuum and the solvent evaporated off. The crystallized BNPTOC melted at 195–196 °C (lit.<sup>5</sup> mp 196–197 °C) and was identified as follows:

BNPTOC: <sup>1</sup>H NMR (200 MHz,  $CDCl_3$ )  $\delta$  7.40 (sd, 2H,  $J = 7.0$  Hz), 8.36 (sd, 2H,  $J = 7.0$  Hz); <sup>13</sup>C NMR (50 MHz,  $CDCl_3$ )  $\delta$  123.09 (C-2/6), 125.60 (C-3/5), 146.35 (C-4), 157.19 (C-1), 192.02 (C=S); IR (KBr) 1532 and 1351 (C–NO<sub>2</sub>), 1209 (C=S), 1192 (C–O), 865 (CH, arom)  $cm^{-1}$ .

Bis(phenyl) thionocarbonate (BPTOC) was prepared in the same way but using phenol (2.47 g) and sodium (0.6 g) in order to obtain sodium phenoxide. The product BPTOC melted at 103–104 °C (lit.<sup>6</sup> mp 105–106 °C) and was identified as follows:

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(5) Al-Kazimi H. R.; Tarbell, D. S.; Plant, D. *J. Am. Chem. Soc.* **1955**, *77*, 2479.

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<sup>o</sup> Abstract published in *Advance ACS Abstracts*, August 15, 1997.

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**Table 1. Experimental Conditions and  $k_{\text{obsd}}$  Values for the Aminolysis of Bis(phenyl) Thionocarbonate (BPTOC)<sup>a</sup>**

amine	pH	$F_N^b$	$10^2[N]_{\text{tot}}, ^c \text{ M}$	$10^3 k_{\text{obsd}}, \text{ s}^{-1}$	no. of runs
piperidine	10.94	0.33	0.50–5.0	1.10–39.0	7
	11.24	0.50	0.50–5.0	4.80–72.1	7
	11.54	0.66	0.50–5.0	4.86–108	7
piperazine	9.64	0.33	0.90–9.0	2.81–99.7	7
	9.94	0.50	1.0–7.0	10.8–106	7
	10.24	0.66	0.40–4.0	1.92–87.5	7
1-(2-hydroxyethyl)piperazine	9.08	0.33	0.30–3.0	0.37–8.53	6
	9.38	0.50	0.20–1.8	0.26–6.60	6
	9.68	0.66	0.30–1.5	0.72–9.07	6
morpholine	8.48	0.33	1.5–30.0	0.99–148	9
	8.78	0.50	2.5–19.0	2.02–112	7
	9.08	0.66	0.75–15.0	0.86–126	10
1-formylpiperazine	7.68	0.33	7.5–30.0	0.014–0.23	4
	7.98	0.50	5.0–35.0	0.019–0.77	7
	8.28	0.66	3.75–30.0	0.017–1.12	8

<sup>a</sup> In aqueous solution at 25.0 °C, ionic strength 0.2 M (KCl). <sup>b</sup> Free amine fraction. <sup>c</sup> Concentration of total amine (free base plus protonated forms).

**Table 2. Experimental Conditions and  $k_{\text{obsd}}$  Values for the Aminolysis of Bis(4-nitrophenyl) Thionocarbonate (BNPTOC)<sup>a</sup>**

amine	pH	$F_N^b$	$10^2[N]_{\text{tot}}, ^c \text{ M}$	$10^3 k_{\text{obsd}}, \text{ s}^{-1}$	no. of runs
piperidine	10.94	0.33	0.30–2.4	6.25–46.7	7
	11.24	0.50	0.20–1.6	11.7–54.8	7
	11.54	0.66	0.30–1.2	18.8–66.6	6
piperazine	9.64	0.33	0.05–1.5	0.89–29.2	9
	9.94	0.50	0.05–1.0	1.22–26.0	9
	10.24	0.66	0.05–1.0	1.76–31.5	9
1-(2-hydroxyethyl)piperazine	9.08	0.33	0.15–3.0	2.07–32.9	9
	9.38	0.50	0.10–2.0	1.21–28.7	9
	9.68	0.66	0.075–1.5	1.52–40.6	9
morpholine	8.48	0.33	0.30–3.0	3.69–27.1	7
	8.78	0.50	0.20–2.0	3.64–25.8	7
	9.08	0.66	0.15–1.5	3.10–30.0	7
1-formylpiperazine	7.68	0.33	3.0–30.0	11.0–82.0	8
	7.98	0.50	2.0–19.0	9.22–77.4	7
	8.28	0.66	1.5–15.0	9.34–90.0	7
piperazinium ion	5.51	0.33	1.5–7.5	2.13–6.75	6
	5.81	0.50	1.0–10.0	1.80–11.0	5
	6.11	0.66	7.5–9.76	2.26–15.7	7

<sup>a</sup> In aqueous solution at 25.0 °C, ionic strength 0.2 M (KCl). <sup>b</sup> Free amine fraction. <sup>c</sup> Concentration of total amine (free base plus protonated forms).

BPTOC: <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>)  $\delta$  7.21–7.51 (m); <sup>13</sup>C NMR (50 MHz, CDCl<sub>3</sub>)  $\delta$  121.86 (C-2/6), 126.86 (C-4), 129.70 (C-3/5), 153.59 (C-1), 194.85 (C=S); IR (KBr) 1252 (C=S), 1158 (C–O), 775 and 693 (CH, arom) cm<sup>-1</sup>.

**Kinetic Measurements.** These were performed spectrophotometrically by following the production of phenoxide and 4-nitrophenoxide ions at 250 and 400 nm, respectively, for the aminolyses of BPTOC and BNPTOC, respectively. The reactions were measured using a Perkin-Elmer Lambda-3 spectrophotometer. The reactions were studied in aqueous solutions, 25.0  $\pm$  0.1 °C, ionic strength 0.2 M (maintained with KCl), and at least a 10-fold excess of total amine over the substrate.

Pseudo-first-order rate coefficients ( $k_{\text{obsd}}$ ) were found through-out, by means of the method described.<sup>3</sup> The experimental conditions of the reactions and the  $k_{\text{obsd}}$  values obtained are shown in Tables 1–3. The initial concentration of BPTOC and BNPTOC was  $3 \times 10^{-5}$  M in all the reactions.

**Product Studies.** The phenyl thionocarbamates of piperidine and morpholine, 1-(phenoxythiocarbonyl)piperidine, and 1-(phenoxythiocarbonyl)morpholine, were identified as the final products of the reactions of BPTOC with these two amines. This was carried out by comparison of the UV-vis spectra at the end of these reactions with those of authentic samples under the same experimental conditions. The UV-vis spectra after completion of the reactions of BPTOC with all the amines were also compared with those at the end of the reactions of phenyl chlorothionoformate with the same amines. It was deduced from these comparisons that the phenyl thionocarbamates derivatives of these amines are one of the products of these reactions. Phenoxide ion was identi-

fied as the other reaction product by comparison of the UV-vis spectra after completion of these reactions with those of authentic samples of phenol in the same reaction conditions.

The identification of 4-nitrophenol and the 4-nitrophenyl thionocarbamates of some secondary alicyclic amines and pyridines as the products of the reactions of BNPTOC with these amines was carried out by comparison of the UV-vis spectra after completion of these reactions with those of authentic samples of 4-nitrophenol under the same experimental conditions and also with those at the end of the reactions of 4-nitrophenyl chlorothionoformate with the secondary amines.

## Results and Discussion

The rate law obtained for all the reactions under study is given by eq 1, where Ar is either phenyl or 4-nitrophenyl, S represents the substrate (either BPTOC or

$$\frac{d[\text{ArO}^-]}{dt} = k_{\text{obsd}}[\text{S}] \quad (1)$$

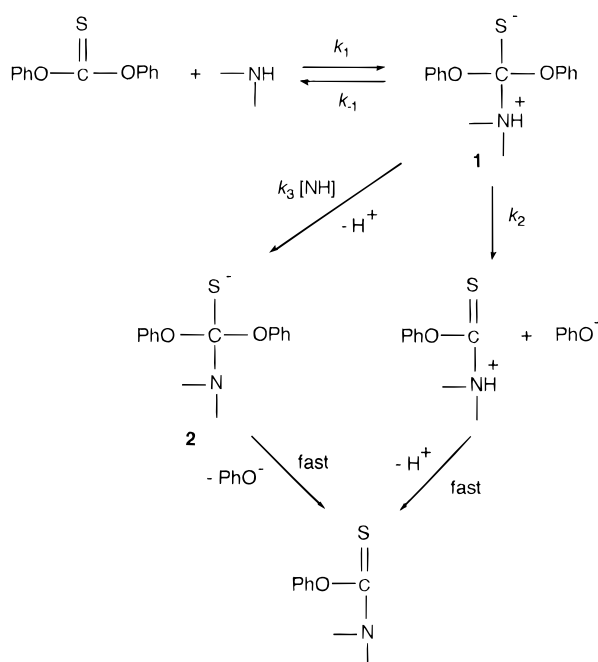
BNPTOC) and  $k_{\text{obsd}}$  is the pseudo-first-order rate coefficient (excess of amine over the substrate was used throughout).

The dependence of  $k_{\text{obsd}}$  on the concentration of the free amine varied according to the nature of both the substrate and the amine.

**Table 3. Experimental Conditions and  $k_{\text{obsd}}$  Values for the Pyridinolysis of Bis(4-nitrophenyl) Thionocarbonate (BNPTOC)<sup>a</sup>**

pyridine substituent	pH	$F_N^b$	$10^2[\text{N}]_{\text{tot}}, ^c \text{M}$	$10^3 k_{\text{obsd}}, \text{s}^{-1}$	no. of runs
4-dimethylamino <sup>d</sup>	8.2	0.021	0.15–0.60	6.8–10.1	6
	8.5	0.041	0.04–0.09	2.3–4.34	6
	9.0	0.119	0.03–0.08	3.98–8.24	6
4-amino <sup>d</sup>	8.2	0.057	0.10–0.425	3.33–11.2	7
	8.5	0.107	0.08–0.25	4.03–11.9	7
	9.0	0.275	0.03–0.08	4.49–9.77	6
3,4-dimethyl <sup>e</sup>	8.0	0.946	5.0–9.0	1.78–2.69	4
	8.2	0.964	4.0–18.0	1.57–7.49	5
	8.5	0.982	5.0–15.0	1.91–5.77	7
3-methyl <sup>e</sup>	8.2	0.995	5.0–15.0	0.60–1.66	5
	8.5	0.997	4.0–13.5	0.37–1.56	5
	8.8	0.999	3.0–13.0	0.19–1.49	6
none <sup>e</sup>	8.5	0.999	7.0–15	0.13–0.25	5
	8.8	0.999	6.0–21	0.12–0.32	6
	9.0	0.999	10.0–25	0.24–0.35	7

<sup>a</sup> In aqueous solution at 25.0 °C, ionic strength 0.2 M (KCl). <sup>b</sup> Fraction of amine free base. <sup>c</sup> Concentration of total amine (free base + protonated forms). <sup>d</sup> In the presence of carbonate buffer  $5 \times 10^{-2}$  M. <sup>e</sup> In the presence of borate buffer  $5 \times 10^{-3}$  M.

**Scheme 1**

Linear plots of  $k_{\text{obsd}}$  vs  $[\text{NH}]$ , where NH represents a free secondary alicyclic amine, at constant pH were found for the reactions of these amines with BNPTOC and in the reactions of piperidine with BPTOC. For the reactions of the secondary amines (except piperidine) with BPTOC, the plots of  $k_{\text{obsd}}$  vs  $[\text{NH}]$  were concave upward, indicating a kinetic order greater than unity in the amine. The reaction of 1-formylpiperazine with this substrate was the only one showing a clear second-order dependence on  $[\text{NH}]$ .

On the other hand the above plots for the pyridinolysis of BNPTOC were linear for the reactions of all the series of pyridines.

The reactions of secondary alicyclic amines with BPTOC can be described by the mechanism depicted in Scheme 1. This was arrived at by taking into account the kinetic results, the product studies, and the shape of the Brønsted-type plots obtained (see below). In this scheme the  $k_3$  step is deprotonation of the zwitterionic tetrahedral intermediate **1** by an amine to yield the anionic intermediate **2**.

Applying the steady state condition to both tetrahedral intermediates of Scheme 1, eq 2 can be obtained.

**Table 4. Values of the Rate Microcoefficients for the Reactions of Secondary Alicyclic Amines with BPTOC and Values of  $k_N$  for the Reactions of the Same Amines with BNPTOC<sup>a</sup>**

amine	$\text{p}K_a^a$	BPTOC		$k_N$ , $\text{s}^{-1} \text{M}^{-1}$
		$k_1$ , $\text{s}^{-1} \text{M}^{-1}$	$10^{-8} k_{-1}$ , $\text{s}^{-1}$	
piperidine	11.24	3.2	0.02 <sup>b</sup>	7.0
piperazine	9.94	4.2	1.0	6.4
1-(2-hydroxyethyl)piperazine	9.38	2.6	2.3	3.5
morpholine	8.78	2.0	3.0	2.6
1-formylpiperazine	7.98	1.8 <sup>c</sup>	65 <sup>d</sup>	0.85
piperazinium ion	5.81			0.22

<sup>a</sup> The reactions and  $\text{p}K_a$  determinations were carried out in aqueous solution, 25.0 °C, ionic strength 0.2 M (KCl). <sup>b</sup> Value obtained by extrapolation of the Brønsted-type plot for  $k_{-1}$ . <sup>c</sup> Value obtained by extrapolation of the Brønsted-type plot for  $k_1$ . <sup>d</sup> Value obtained from the values of  $K_1$  and  $k_1$  ( $k_{-1} = k_1/K_1$ ). The value of  $K_1$  was determined from the slope of a  $k_{\text{obsd}}$  vs  $[\text{NH}]^2$  plot (see text).

$$k_{\text{obsd}} = \frac{k_1(k_2 + k_3[\text{NH}])[\text{NH}]}{k_{-1} + k_2 + k_3[\text{NH}]} \quad (2)$$

For the reactions BPTOC with piperidine, it is reasonable that  $k_2 + k_3[\text{NH}] \gg k_{-1}$ , since this amine is by far the most basic of the series of secondary amines and therefore should show the smallest leaving ability ( $k_{-1}$ ) from **1** compared to the other amines of the series (see below the values of the rate microcoefficients involved). This fact leads to the kinetic law shown in eq 3 for these reactions, which explains the linear  $k_{\text{obsd}}$  vs  $[\text{NH}]$  plots

$$k_{\text{obsd}} = k_1[\text{NH}] \quad (3)$$

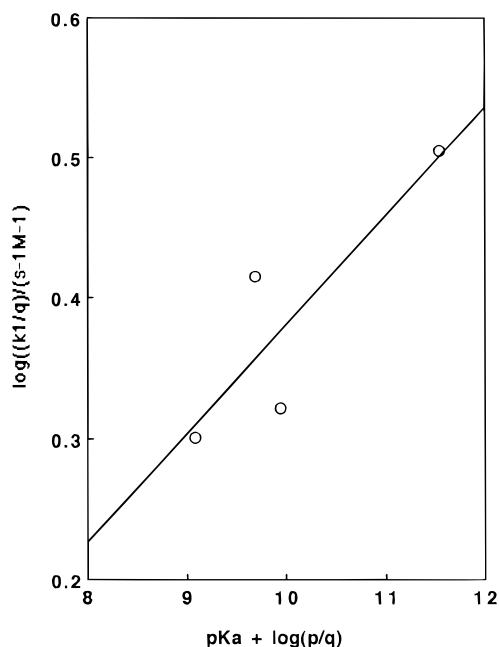
observed. The value of  $k_1$  was obtained as the slope of this plot and is shown in Table 4.

For the reactions of 1-formylpiperazine with BPTOC, a kinetics second-order in amine was found. The only way to achieve this in eq 2 is by assuming  $k_{-1} \gg k_3[\text{NH}] \gg k_2$ , which leads to eq 4. These inequalities are reasonable in view of the magnitude of the rate micro-

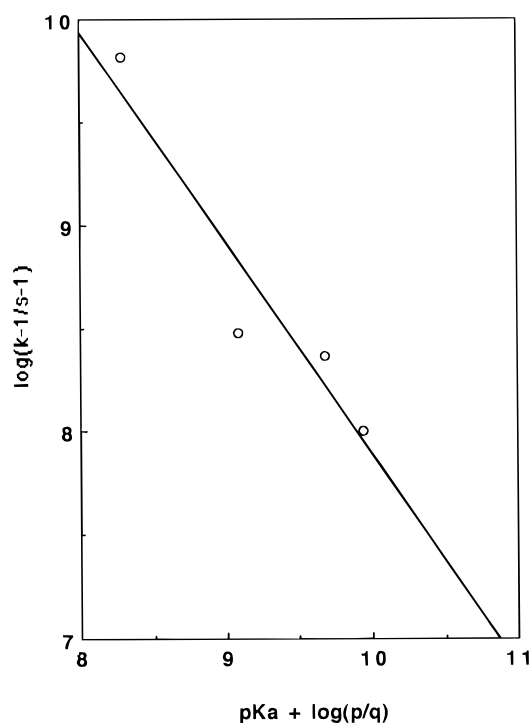
$$k_{\text{obsd}} = \frac{k_1 k_3}{k_{-1}} [\text{NH}]^2 = K_1 k_3 [\text{NH}]^2 \quad (4)$$

coefficients found (Table 4) and the concentration range of free amine employed (see Table 1). From the slope of



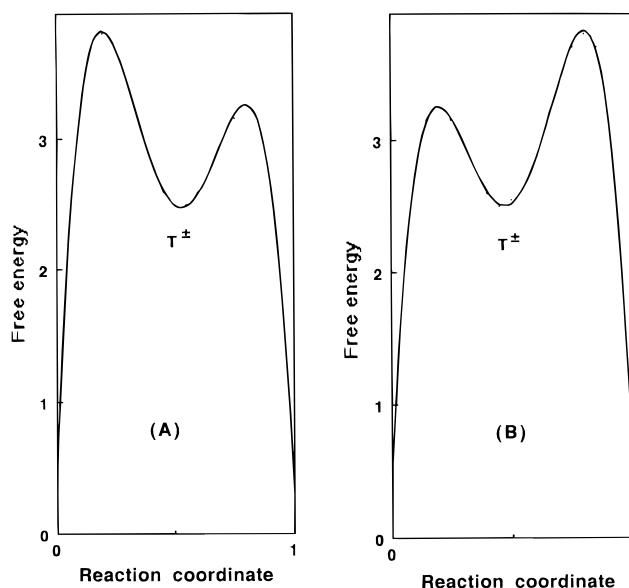


**Figure 2.** Brønsted-type plot for  $k_1$  (statistically corrected<sup>7</sup>) obtained in the reactions of BPTOC with secondary alicyclic amines. The value of the slope is  $\beta_1 = 0.1$ .



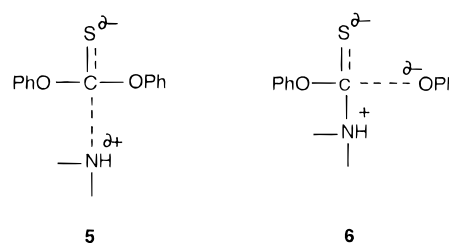
**Figure 3.** Brønsted-type plot for  $k_{-1}$  (statistically corrected<sup>7</sup>) obtained in the reactions of BPTOC with secondary alicyclic amines. The value of the slope is  $\beta_{-1} = -1.0$ .

We believe the reactions of BPTOC with secondary amines are stepwise not only because satisfactory fittings were found through eq 5, but also because of the magnitudes of the Brønsted slopes for  $k_1$  and  $k_{-1}$  (Figures 2 and 3). The former value ( $\beta_1 = 0.1$ ) is in agreement with the Brønsted slopes obtained in many aminolyses of carbonyl and thiocarbonyl derivatives when formation of the zwitterionic tetrahedral intermediate ( $T^\pm$ ) is the rate-determining step (see Figure 4A).<sup>1,3,12-16</sup> This low value is due to the little effective charge development on the amine nitrogen atom in going from the amine



**Figure 4.** Free energy (arbitrary units) reaction profiles for the aminolysis of BPTOC when the formation of  $T^\pm$  (A) or the breakdown of  $T^\pm$  to products (B) is the rate-determining step.

reactant to the transition state for the formation of the intermediate (structure **5** for the aminolysis of BPTOC).<sup>13</sup>



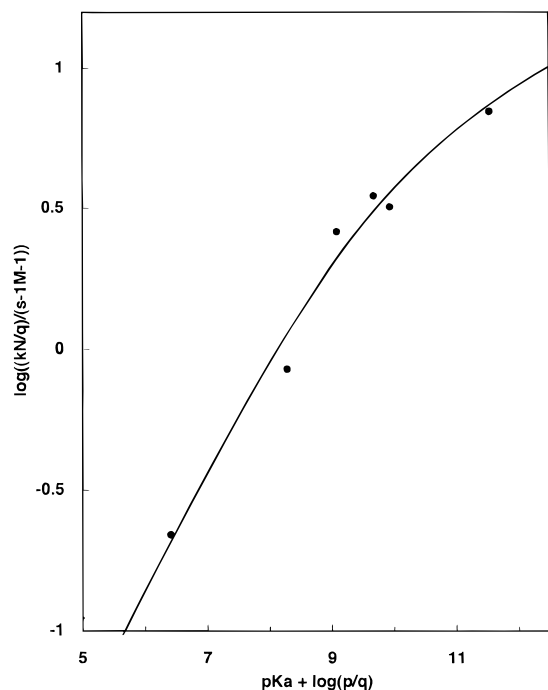
On the other hand, the Brønsted slope for  $k_{-1}$  in Figure 3 is  $\beta_{-1} = -1.0$ . Since the Brønsted slope when breakdown of the intermediate is rate determining ( $\beta_2$ ) is  $\beta_1 - \beta_{-1}$ ,<sup>1,13</sup> it follows that  $\beta_2 = 0.1 - (-1.0) = 1.1$ . This value is in accord with the Brønsted-type slopes at low amine  $pK_a$  for numerous aminolyses of carbonyl and thiocarbonyl compounds.<sup>1-4,12-16</sup> The larger value of  $\beta_2$  compared to  $\beta_1$  arises from the fact that there is a large effective charge development on the amine nitrogen from reactant to the transition state for breakdown to products of the intermediate (see Figure 4B and structure **6** for the aminolysis of BPTOC), since there is a full bond formation between amine and the carbonyl or thiocarbonyl carbon in this transition state.<sup>13</sup>

For the reactions of BNPTOC with secondary alicyclic amines, linear plots of  $k_{\text{obsd}}$  vs  $[\text{HN}]$  at constant pH were found. The nucleophilic rate constant ( $k_N$ ) were obtained as the slopes of these plots, and the values are shown in Table 4. After statistical correction of the  $k_N$  and  $pK_a$  values of the conjugate acids of the amines,<sup>7</sup> the Brønsted-type plot shown in Figure 5 was obtained. The line in this figure was calculated by an equation based on the existence of a tetrahedral intermediate on the reaction path and a change in the rate-determining step from

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**Figure 5.** Brønsted-type plot for  $k_N$  (statistically corrected<sup>7</sup>) found in the reactions of BNPTOC with secondary alicyclic amines. The line is calculated (see text) and the points are experimental. The values of the limiting slopes are  $\beta = 0.1$  (high  $pK_a$ ) and 0.45 (low  $pK_a$ ).

breakdown to formation of this intermediate as the amine gets more basic.<sup>4</sup> An analogous equation was derived by Jencks.<sup>13</sup> By nonlinear least-squares fitting,<sup>4</sup> the following parameters were found:  $\beta_1 = 0.1$  (slope at high  $pK_a$ ),  $\beta_2 = 0.45$  (slope at low  $pK_a$ ) and  $pK_a^\circ = 9.5$  ( $pK_a$  value at the curvature center).

Although the value of  $\beta_1 = 0.1$  is in agreement with previous ones when the  $k_1$  step is rate determining (see above), the value of  $\beta_2 = 0.45$  is not in line with the Brønsted slopes when the  $k_2$  step is rate limiting. The latter values are usually 0.8–1.0.<sup>1–4,12–16</sup>

On the other hand, in the concerted reactions of secondary alicyclic amines with *S*-(2,4-dinitrophenyl) and *S*-(2,4,6-trinitrophenyl) *O*-ethyl thiolcarbonates, linear Brønsted plots with slopes  $\beta \approx 0.5$ –0.6 were found.<sup>17</sup>

Also a linear Brønsted plot with  $\beta \approx 0.5$  was exhibited in the concerted reactions of the above amines with 2,4,6-trinitrophenyl *O*-ethyl dithiocarbonate in aqueous ethanol.<sup>18</sup> Methoxycarbonyl transfer between isoquinoline and pyridines is also believed to be concerted as indicated by the linear Brønsted plot of  $\beta \approx 0.58$  found.<sup>19</sup>

In some concerted aminolysis such as those of benzoyl fluorides, slightly curved Brønsted-type plots were obtained, with slopes  $\beta \approx 0.23$  and 0.67 at high and low  $pK_a$  values, respectively.<sup>20</sup> The difference between these extremes  $\beta$  values is small compared to that of typical stepwise aminolyses.<sup>1–4,12–16</sup> These type of Brønsted plots are not usually biphasic, as those for stepwise reactions, but rather show a continuous curvature.<sup>20</sup>

**Table 5.** Values of  $k_N$  for the Pyridinolysis of BNPTOC and  $pK_a$  Values for the Conjugate Acids of Pyridines<sup>a</sup>

pyridine substituent	$pK_a$	$k_N, s^{-1} M^{-1}$
4-dimethylamino	9.87	74
4-amino	9.42	44
3,4-dimethyl	6.77	$3.5 \times 10^{-2}$
3-methyl	5.80	$1.2 \times 10^{-2}$
H	5.37	$1.4 \times 10^{-3}$

<sup>a</sup> Both the  $k_N$  and  $pK_a$  values were obtained in aqueous solution, 25.0 °C, ionic strength 0.2 M (KCl).

The Brønsted-type plot in Figure 5 can be explained by a gradual decrease of  $\beta$  with increasing amine  $pK_a$  in a single step. This represents a normal Hammond effect for a concerted reaction, with an earlier transition state for more reactive nucleophiles.<sup>20,21</sup>

Although for the reactions of the alicyclic amines with BNPTOC the concerted mechanism seems preferable to the stepwise process, the latter cannot be rigorously excluded, although if this were the case, the tetrahedral intermediate formed would be extremely unstable.

The instability of the hypothetical zwitterionic tetrahedral intermediate formed in the reactions of secondary amines with BNPTOC should be extremely high in view of the two 4-nitrophenoxy groups attached to the central carbon of the intermediate. Therefore, this intermediate should have a lifetime comparable to a vibration period (ca.  $10^{-13}$  s), and therefore the intermediate would not be formed (would be too unstable to exist) and the concerted mechanism is enforced.<sup>20,22</sup>

For the pyridinolysis of BNPTOC, the nucleophilic rate constants ( $k_N$ ) were found as the slopes of the linear  $k_{obsd}$  vs  $[N]$  plots at constant pH, where N is the substituted pyridine free base. The values of  $k_N$  obtained and the  $pK_a$  values of the conjugate acids of the pyridines are shown in Table 5. The corresponding Brønsted type plot is shown in Figure 6.

The slope of the linear Brønsted-type plot in Figure 6 has a value of  $\beta = 1.0$ , which is in accord with the values shown by the Brønsted slopes in numerous aminolysis reactions of carbonyl and thiocarbonyl derivatives when breakdown of a tetrahedral intermediate is the rate-determining step.<sup>1–4,12–16</sup>

The fact that the reactions of BNPTOC with alicyclic amines seem to be concerted while those of the same substrate with pyridines are stepwise is in line with previous findings: The reactions of the above secondary alicyclic amines with *S*-(2,4-dinitrophenyl) and *S*-(2,4,6-trinitrophenyl) *O*-ethyl thiolcarbonates are concerted,<sup>17</sup> while the pyridinolysis of these substrates are stepwise.<sup>23</sup>

The above results have been explained by a high instability of the putative tetrahedral intermediate formed by the alicyclic amines due to a large nucleofugality rate of these amines from the intermediate. This kinetic instability prevents the intermediate to be formed, and the mechanism is enforced concerted.<sup>17</sup> Substitution of an alicyclic amine by an isobasic pyridine as the amine moiety of the tetrahedral intermediate decreases the kinetic instability of the latter species since pyridines are worse nucleofuges than isobasic secondary alicyclic amines from a tetrahedral intermediate.<sup>24</sup> This makes possible the existence of the intermediate formed by pyridines.

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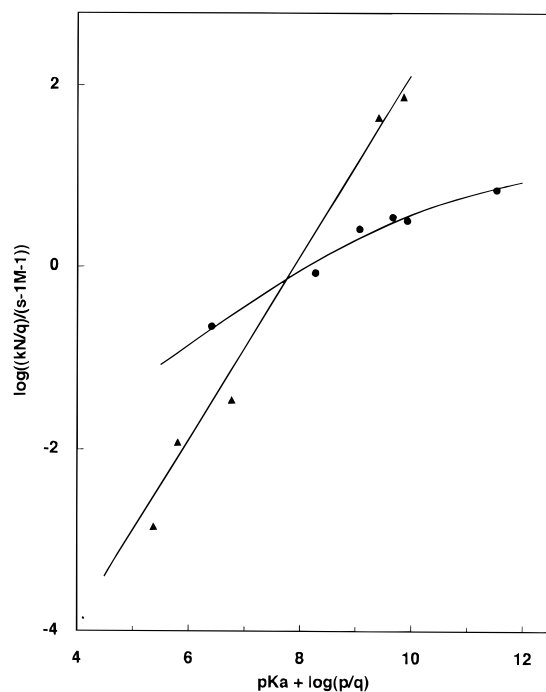
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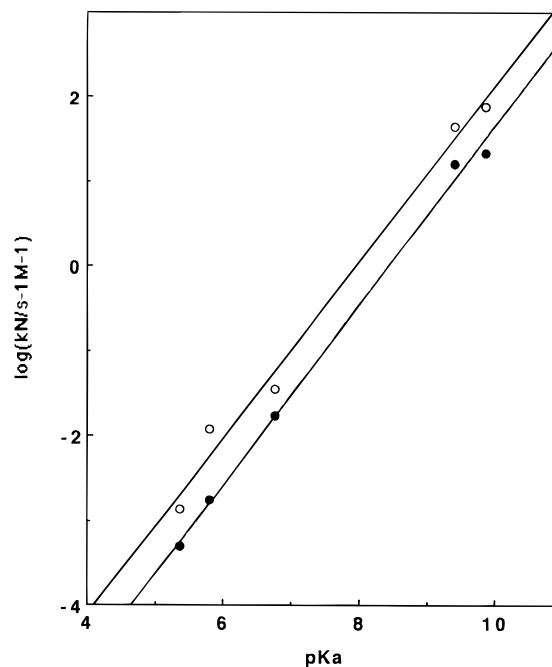
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**Figure 6.** Brønsted-type plot for  $k_N$  (statistically corrected<sup>7</sup>) found in the reactions of BNPTOC with secondary alicyclic amines (●) and pyridines (▲).

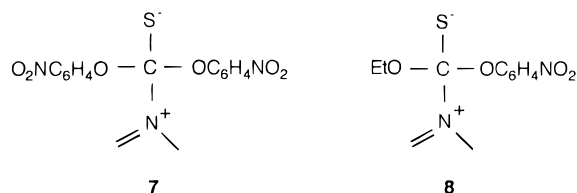
Our results are also in line with the work of Gresser and Jencks.<sup>13</sup> They found that in the aminolysis of phenyl 4-nitrophenyl carbonate, pyridines are expelled more slowly from the tetrahedral addition intermediate formed in these reactions than isobasic quinuclidines (the latter are tertiary alicyclic amines).<sup>13</sup>

From a comparison of the Brønsted-type plots obtained in the pyridinolyses of BNPTOC and ethyl 4-nitrophenyl thionocarbonate (ENPTOC),<sup>2</sup> shown in Figure 7, it can be observed that the former substrate is more reactive toward pyridines than the latter. Since breakdown to products of the corresponding tetrahedral intermediate is the rate-determining step for both reactions, it means that  $k_N = K_1k_2$  is greater for BNPTOC ( $K_1 = k_1/k_{-1}$  and  $k_2$  are defined in Scheme 1). The value of  $k_1$  should be larger for the reactions of BNPTOC in view of the larger electron-withdrawing effect of the nitro group in this substrate compared to the ethoxy group in ENPTOC. This effect should leave the thiocarbonyl carbon atom of BNPTOC more positively charged than that of ENPTOC, which should result in a faster attack of the amine on the former substrate.



**Figure 7.** Brønsted-type plot for  $k_N$  found in the reactions of pyridines with BNPTOC (○, this work) and ENPTOC (●, ref 1).

On the other hand, the value of  $k_{-1}$  (expulsion of the pyridine from **7** or **8**) should be greater for **8** than for **7** in view of the stronger push exerted by EtO in **8** than



that of 4-nitrophenoxy in **7** to expel the amine.<sup>13</sup> The value of  $k_2$  (expulsion of 4-nitrophenoxide ion) should be similar for **7** and **8** since the stronger push by EtO in **8** is compensated by the fact that there are two leaving groups in **7** (see above). Therefore, the larger value of  $K_1k_2$  for the pyridinolysis of BNPTOC relative to that of ENPTOC (Figure 7) can be explained by a larger  $K_1$  (larger  $k_1$  and smaller  $k_{-1}$ ) value for BNPTOC and similar  $k_2$  for the reactions of both substrates.

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