Kinetic and Mechanistic Investigation of the Aminolysis of 3-Methoxyphenyl 3-Nitrophenyl Thionocarbonate, 3-Chlorophenyl 3-Nitrophenyl Thionocarbonate, and Bis(3-nitrophenyl) Thionocarbonate

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The reactions of the title thionocarbonates (**6**, **7**, and **8**, respectively) with a series of secondary alicyclic amines are subjected to a kinetic investigation in 44 wt % ethanol−water, 25.0 °C, ionic strength 0.2 M (KCl). Under excess amine, pseudo-first-order rate coefficients (k_{obsd}) are obtained for all reactions. Reactions of substrates **6** and **7** with piperidine and of thionocarbonate **8** with the same amine and piperazine, 1-(2-hydroxyethyl)piperazine, and morpholine show linear k_{obsd} vs [amine] plots, with slopes (k_1) independent of pH. On the other hand, these plots are nonlinear upward for the reactions of substrates **6** and **7** with all the amines, except piperidine, and also for the reactions of compound **8** with 1-formylpiperazine and piperazinium ion. For all these reactions a mechanistic scheme is proposed with the formation of a zwitterionic tetrahedral intermediate ($T^{\pm}$), which can transfer a proton to an amine to give an anionic intermediate (T^{-}). Rate and equilibrium microcoefficients of this scheme, k_1, k_{-1}, K_1 (= k_1/k_{-1}), and k_2, are obtained by fitting the nonlinear plots through an equation derived from the scheme. The Brönsted-type plots for k_1 are linear with slopes $\beta_1 = 0.19$, 0.21, and 0.26 for the aminolysis of **6**, **7**, and **8**, respectively. This is consistent with the hypothesis that the formation of $T^{\pm}$ (k_1 step) is the rate-determining step. The k_1 values for these reactions follow the sequence **8** > **7** > **6**, consistent with the sequence of the electron-withdrawing effects from the substituents on the "nonleaving" group of the substrates. The k_1 values for the aminolysis of **6**, **7**, and **8** are smaller than those for the same aminolysis of 3-methoxyphenyl, 3-chlorophenyl, and 4-cyanophenyl 4-nitrophenyl thionocarbonates (**2**, **3**, and **4**, respectively). The k_2 values (expulsion of the nucleofuge from $T^{\pm}$) increase as the electron withdrawal from the nonleaving group increases. These values are smaller for the aminolysis of **6**, **7**, and **8** compared to those for the same aminolysis of **2**, **3**, and **4**, respectively.

Introduction

Although much work has been devoted to the study of the kinetics of reactions involving dithiocarbonates and thiolcarbonates,[1,2] especially their aminolysis,[2,3] less is known on the kinetics of the aminolysis of thionocarbonates.[4,5] Among the latter studies, there are only a few (as far as we are aware) on diaryl thionocarbonates.[4c,5]

To shed light on the mechanism of the aminolysis of diaryl thionocarbonates, we have reported a kinetic investigation on the reactions of sec alicyclic amines with 4-methylphenyl,[5a] 3-methoxyphenyl, 3-chlorophenyl, and 4-cyanophenyl 4-nitrophenyl thionocarbonates (**1**−**4**, respectively) in 44 wt % ethanol−water.[5b] We have chosen these thionocarbonates in view of the wide span of electron-withdrawing abilities of the substituents attached to the "nonleaving" group of the substrates. We have also studied kinetically the same aminolysis of 4-methylphenyl 3-nitrophenyl thionocarbonate (**5**) in the same solvent.[5a]

To extend our investigations on the mechanisms of the aminolysis of diaryl thionocarbonates, in this work, we study the reactions of sec alicyclic amines with 3-methoxyphenyl and 3-chlorophenyl 3-nitrophenyl thionocarbonates (**6** and **7**, respectively) and bis(3-nitrophenyl thionocarbonate) (**8**) in 44 wt % ethanol−water. These reactions will be compared with those of the thionocarbonates **1**−**5** with the aim of assessing the effect of both the leaving and "nonleaving" groups of the substrates on the kinetics and mechanisms of these reactions.

Experimental Section

Materials. The secondary alicyclic amines were purified as reported.[6] Thionocarbonates **6**−**8** have not been previously prepared, to our knowledge. They were synthesized according

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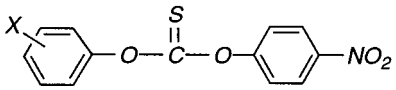
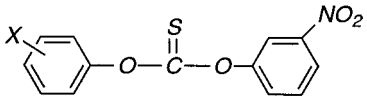


1 *(X = 4-Me)*
2 *(X =3-MeO)*
3 *(X = 3-Cl)*
4 *(X = 4-CN*



5 *(X = 4-Me)*
6 *(X =3-MeO)*
7 *(X = 3-Cl)*
8 *(X = 3-NO_2*

to a reported procedure[4c,5,7] by the reactions of 3-methoxyphenyl, 3-chlorophenyl, or 3-nitrophenyl thionochloroformates with 3-nitrophenol. The thionochloroformates were synthesized as described.[7]

Thionocarbonate **6** melted at 109.1−109.8 °C and was characterized by ^{1}H and ^{13}C NMR (page S2 in Supporting Information) and elemental analyses. Anal. Calcd for $C_{14}H_{11}O_5NS$: C, 55.08; H, 3.63; N, 4.59; S, 10.50. Found: C, 54.54; H, 3.46; N, 4.74; S, 10.12.

Thionocarbonate **7** melted at 129.4−130.2 °C and was characterized by ^{1}H and ^{13}C NMR (page S2 in Supporting Information) and elemental analyses. Anal. Calcd for $C_{13}H_8O_4ClNS$: C, 50.41; H, 2.60; N, 4.52; S, 10.35. Found: C, 50.88; H, 2.55; N, 4.49; S, 10.67.

Thionocarbonate **8** melted at 184−185 °C and was characterized by ^{1}H and ^{13}C NMR (page S2 in Supporting Information) and elemental analyses. Anal. Calcd for $C_{13}H_8O_6N_2S$: C, 48.75; H, 2.52; N, 8.75; S, 10.01. Found: C, 48.79; H, 2.60; N, 8.76; S, 9.91.

Kinetic Measurements. Reactions were studied spectrophotometrically by monitoring the appearance of 3-nitrophenoxide anion and/or its conjugate acid at 336 nm. All reactions were carried out in 44 wt % ethanol−water, 25.0 ± 0.1 °C, ionic strength 0.2 M (maintained with KCl). The initial concentration of the substrates was (4−6) × 10^{-5} M.

Three pH values were employed for the reactions of each amine. The preparation of the kinetic samples as well as the pH adjustments were carried out as reported.[8]

Pseudo-first-order rate coefficients (k_{obsd}) were found in all reactions (at least a 20-fold excess of the total amine over the substrates was employed). The experimental conditions of the reactions and the k_{obsd} values obtained are shown in Tables 1−3.

Product Studies. In the reactions of the thionocarbonates **6**−**8** with morpholine and piperidine, the final products obtained were the corresponding 3-methoxyphenyl, 3-chlorophenyl, and 3-nitrophenyl thionocarbamates, respectively, and 3-nitrophenol (and/or its conjugate base). The identification of the final products 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.

Results and Discussion

The pseudo-first-order rate coefficient (k_{obsd}) was found to vary with the concentration of free amine in different ways, depending on the substrates and on the amine basicity.

A complex kinetic order in amine (between 1 and 2) was exhibited by the reactions of thionocarbonates **6** and **7** with piperazine, 1-(2-hydroxyethyl)piperazine, and morpholine and in the reactions of compound **8** with 1-formylpiperazine. The reactions of thionocarbonates **6** and **7** with 1-formylpiperazine and piperazinium ion and that of substrate **8** with the latter amine showed a kinetic behavior in accordance with a second-order polynomial equation. On the other hand, first-order kinetics with respect to amine were obtained for the reactions of compounds **6** and **7** with piperidine and those of thionocarbonate **8** with the four more basic amines.

According to these kinetic results, the product analysis, and the Brönsted-type plots obtained (see below), a mechanistic scheme is proposed for these reactions (Scheme 1). This reaction scheme is the same as that found in the aminolysis of similar thionocarbonates (**1**−**4**) with a better leaving group (4-nitrophenoxide anion instead of 3-nitrophenoxide anion).[5] In this scheme, the k_3 step is the deprotonation of the aminium moiety of a

Table 1. Experimental Conditions and k_{obsd} Values for the Aminolysis of 3-Methoxyphenyl 3-Nitrophenyl Thionocarbonate (6)[a]

amine	pH	F_N[b]	$10^3[N]_{tot}$, M[c]	10^3k_{obsd}, s^{-1}	no. of runs
piperidine	10.51	0.33	4.0−20	7.9−29	9
	10.82	0.50	1.9−18	8.1−29	9
	11.13	0.67	1.8−18	7.1−41	10
piperazine	9.40	0.33	1.9−13	1.0−12	7
	9.71	0.50	1.8−14	0.84−19	7
	10.02	0.67	1.8−15	3.0−32	8
1-(2-hydroxyethyl)-piperazine	8.79	0.33	1.1−11	0.18−2.3	8
	9.09	0.50	1.1−11	0.34−4.5	9
	9.37	0.66	1.2−9.5	0.34−4.7	8
morpholine	8.18	0.33	4.2−42	0.64−11	10
	8.48	0.50	5.0−45	0.66−19	8
	8.78	0.67	2.1−19	0.88−8.1	9
1-formylpiperazine	7.33	0.33	4.3−43	0.19−1.8	10
	7.63	0.50	4.9−49	0.33−3.8	10
	7.93	0.67	5.3−53	0.34−8.5	10
piperazinium ion	5.06	0.33	8.1−81	0.051−0.24	10
	5.37	0.50	10−100	0.10−0.56	10
	5.68	0.67	10−100	0.11−0.97	10

[a] In 44 wt % ethanol−water at 25.0 °C and an ionic strength of 0.2 M (KCl). [b] Free-amine fraction. [c] Concentration of total amine (free-base and protonated forms).

Table 2. Experimental Conditions and k_{obsd} Values for the Aminolysis of 3-Chlorophenyl 3-Nitrophenyl Thionocarbonate (7)[a]

amine	pH	F_N[b]	$10^3[N]_{tot}$, M[c]	10^3k_{obsd}, s^{-1}	no. of runs
piperidine	10.52	0.33	4.0−18	13−39	8
	10.82	0.50	4.8−24	22−82	8
	11.12	0.67	1.9−15	10−71	8
piperazine	9.40	0.33	1.9−19	4.0−27	9
	9.71	0.50	1.9−19	4.4−39	10
	10.02	0.67	2.0−20	8.0−64	10
1-(2-hydroxyethyl)-piperazine	8.78	0.33	2.5−22	0.91−11	8
	9.09	0.50	3.7−18	3.9−18	9
	9.40	0.67	1.9−19	1.5−25	8
morpholine	8.17	0.33	4.9−50	1.1−23	9
	8.48	0.50	4.3−43	2.1−29	9
	8.79	0.67	8.5−43	7.9−41	7
1-formylpiperazine	7.32	0.33	4.9−49	0.21−4.3	10
	7.63	0.50	3.8−38	0.24−6.0	10
	7.94	0.67	4.2−42	0.32−9.8	10
piperazinium ion	5.07	0.33	10−100	0.020−0.88	8
	5.37	0.50	9.8−98	0.10−1.8	10
	5.67	0.67	9.4−94	0.13−2.6	10

[a] In 44 wt % ethanol−water at 25.0 °C and an ionic strength of 0.2 M (KCl). [b] Free-amine fraction. [c] Concentration of total amine (free-base and protonated forms).

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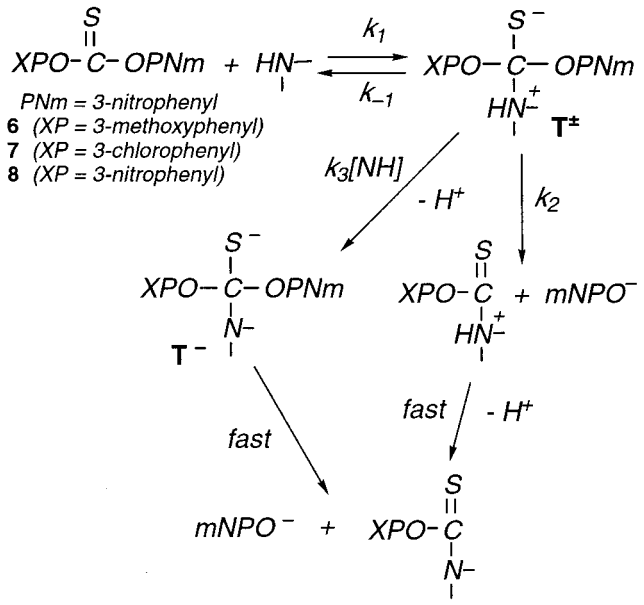
Table 3. Experimental Conditions and k_{obsd} Values for the Aminolysis of Bis(3-nitrophenyl) Thionocarbonate (8)[a]

amine	pH	F_N[b]	$10^3[N]_{tot}$, M[c]	10^3k_{obsd}, s^{-1}	no. of runs
piperidine	10.51	0.33	1.0−10	2.6−26	10
	10.82	0.50	1.0−10	6.5−54	10
	11.13	0.67	3.0−10	18−61	8
piperazine	9.40	0.33	1.6−16	3.4−49	10
	9.71	0.50	3.1−14	11−57	7
	10.02	0.67	1.5−15	3.8−65	10
1-(2-hydroxyethyl)-piperazine	8.78	0.33	4.9−49	4.0−51	9
	9.09	0.50	4.0−40	4.7−49	10
	9.40	0.67	3.2−32	5.6−59	10
morpholine	8.17	0.33	5.0−45	3.5−35	8
	8.48	0.50	5.0−50	5.5−61	8
	8.79	0.67	5.0−50	5.4−92	11
1-formylpiperazine	7.32	0.33	3.6−36	1.8−36	10
	7.63	0.50	4.8−48	3.4−53	10
	7.94	0.67	9.4−94	4.0−71	10
piperazinium ion	5.06	0.33	10−80	0.37−3.0	8
	5.37	0.50	10−90	0.55−5.9	9
	5.68	0.67	9.9−99	0.82−11	10

[a] In 44 wt % ethanol−water at 25.0 °C and an ionic strength of 0.2 M (KCl). [b] Free-amine fraction. [c] Concentration of total amine (free-base and protonated forms).

Scheme 1



zwitterionic tetrahedral intermediate $T^{\pm}$ by the corresponding amine to give an anionic tetrahedral intermediate T^{-}.

Since the tetrahedral intermediates in Scheme 1 are highly reactive, the steady-state condition can be applied to them, whereby eq 1 can be obtained. In this equation, k_0 is the solvolytic rate constant and NH represents a free secondary alicyclic amine.

$$k_{obsd} = k_0 + \frac{k_1(k_2 + k_3[NH])[NH]}{k_{-1} + k_2 + k_3[NH]} \qquad (1)$$

In the reactions of the two least basic amines, 1-formylpiperazine and piperazinium cation, with **6** and **7** and in those of the least basic amine, piperazinium cation, with compound **8**, the k_{obsd} vs [NH] plots are best fitted through a polynomial equation of second order in amine. This can be accounted for by assuming $k_{-1} \gg k_2 + k_3[NH]$, which is reasonable for weakly basic amines. This inequality reduces eq 1 to eq 2, where K_1 ($= k_1/k_{-1}$) is the equilibrium constant for the formation of the intermediate $\mathbf{T}^{\pm}$ in Scheme 1. An example of this type of plot is shown in Figure 1.

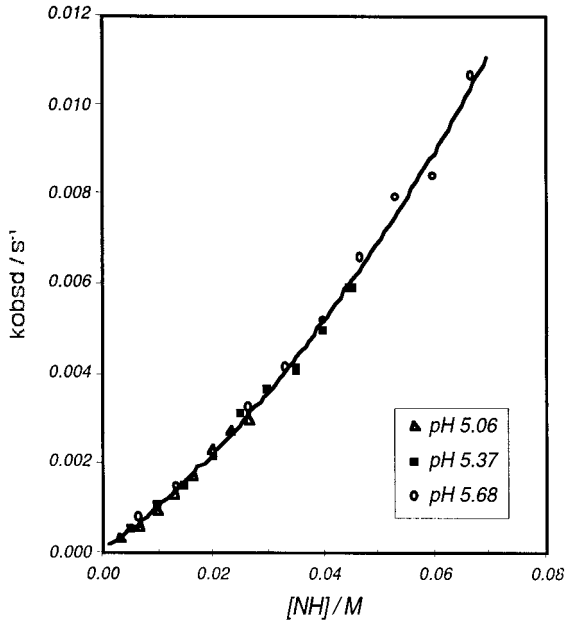


Figure 1. Plot of k_{obsd} against the free-amine concentration for the reaction of thionocarbonate **8** with piperazinium ion in 44 wt % ethanol−water, at 25.0 °C and an ionic strength of 0.2 M. The line was calculated using eq 2 with the microcoefficients shown in Table 4.

$$k_{obsd} = k_0 + K_1k_2[NH] + K_1k_3[NH]^2 \qquad (2)$$

The line in Figure 1 was calculated through eq 2 with the values of the equilibrium and rate coefficients shown in Table 4. These values were obtained by nonlinear least-squares fitting of eq 2 to the experimental points, introducing into this equation a known and constant value of k_3 (also shown in Table 4). The determination of the k_3 value is discussed below.

The reaction of 1-formylpiperazine with substrate **8** exhibits k_{obsd} vs [NH] plots that are best fitted with the general equation (eq 1) instead of the restricted one (eq 2). The values of the best fitting parameters, k_1, k_2, and k_{-1}, as well as the k_3 value, are shown in Table 4. The adherence of this reaction to eq 1, and not to eq 2, is presumably due to the fact that for this reaction k_{-1} is smaller and k_2 is larger than the corresponding values for the reactions of this amine with compounds **6** and **7** (see Table 4). This is why for the reaction of 1-formylpiperazine with **8**, $k_{-1} \approx k_2 + k_3[NH]$, and eq 1 applies.

The k_{obsd} vs [NH] plots found in the reactions of piperazine, 1-(2-hydroxyethyl)piperazine, and morpholine with thionocarbonates **6** and **7** were best adjusted to the general equation (eq 1). The best fitting parameters k_1, k_{-1}, and k_2 are shown in Table 4. The constant k_3 value used for the fittings was the same as that determined for the reactions of 1-formylpiperazine and that for the reaction of 1-formylpiperazine with thionocarbonate **8**. Figure 2 shows an example of the plots of k_{obsd} vs [NH] fitted through eq 1.

The reactions of the most basic amine of the series, piperidine, with the three substrates of this work show

Table 4. Values of the Rate and Equilibrium Microcoefficients Obtained in the Aminolysis of 4-Methylphenyl, 3-Methoxyphenyl, 3-Chlorophenyl, and 3-Nitrophenyl 3-Nitrophenyl Thionocarbonates (5−8, Respectively)[a]

		$k_1/s^{-1}\ M^{-1}$				$10^{-7}k_{-1}/s^{-1}$			
amine	pK_a	**5**[b]	**6**	**7**	**8**	**5**[b]	**6**	**7**	**8**
piperidine	10.82	3.0	3.2	5.8	9.4				
piperazine	9.71	2.2	3.8	5.2	8.0	2.9	1.9	1.5	
1-(2-hydroxyethyl)piperazine	9.09	1.0	1.3	2.3	2.8	4.0	2.9	2.2	
morpholine	8.48	0.9	1.2	2.0	2.5	8.1	5.6	5.3	
1-formylpiperazine	7.63	0.45			1.4	30			10
piperazinium cation	5.37								

other rate microcoefficients:

$10^{-7}k_2/s^{-1} = 0.5 \pm 0.1$ (**5**),[b] 2.0 ± 0.5 (**6**), 4 ± 1 (**7**), and 11 ± 1 (**8**)[c]
$k_3 = 2 \times 10^9\ s^{-1}\ M^{-1}$ (piperazinium ion)
$k_3 = 4 \times 10^9\ s^{-1}\ M^{-1}$ (other amines)

equilibrium microcoefficients:

$K_1 = 8.5 \times 10^{-10}\ M^{-1}$ (1-formylpiperazine + **6**)
$K_1 = 2.2 \times 10^{-9}\ M^{-1}$ (1-formylpiperazine + **7**)
$K_1 = 6.0 \times 10^{-11}\ M^{-1}$ (piperazinium + **6**)
$K_1 = 3.0 \times 10^{-10}\ M^{-1}$ (piperazinium + **7**)
$K_1 = 5.0 \times 10^{-10}\ M^{-1}$ (piperazinium + **8**)

[a] Values of both the pK_a and microcoefficients were determined in 44 wt % ethanol−water, 25.0 °C, ionic strength 0.2 M (KCl). [b] Values were taken from ref 5a, obtained under the same experimental conditions as those of this work. [c] For reactions of **8**, $k_2 = 5.5 \times 10^7\ s^{-1}$ after statistical correction.

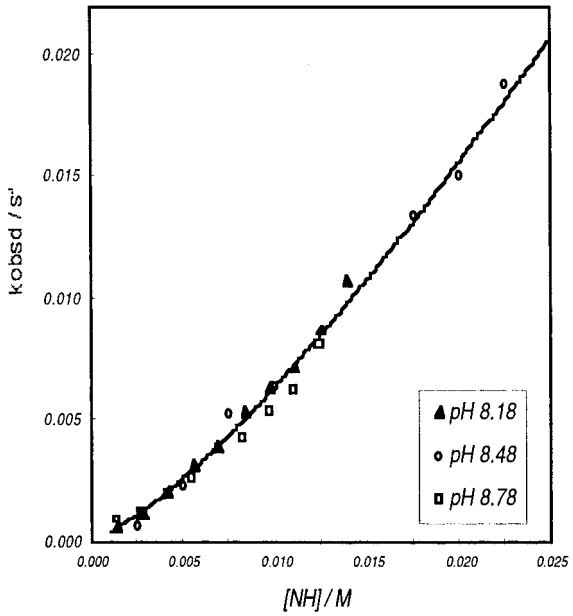


Figure 2. Plot of k_{obsd} against the free-amine concentration for the reaction of thionocarbonate **6** with morpholine in 44 wt % ethanol−water, at 25.0 °C and an ionic strength of 0.2 M. The line was calculated using eq 1 with the rate microcoefficients shown in Table 4.

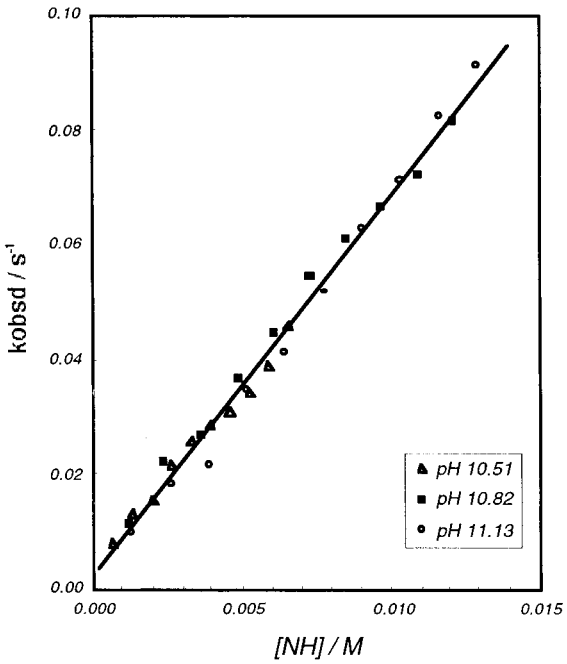


Figure 3. Plot of k_{obsd} against the free-amine concentration for the reaction of thionocarbonate **7** with piperidine in 44 wt % ethanol−water, at 25.0 °C and an ionic strength of 0.2 M.

linear k_{obsd} vs [NH] plots, with a pH-independent slope. This behavior can be explained by the poor leaving ability of this amine from the zwitterionic tetrahedral intermediate ($\mathbf{T}^{\pm}$ in Scheme 1), which means $k_{-1} \ll k_2 + k_3$[NH] in eq 1. This reduces this general equation to a linear dependence of k_{obsd} on [NH], with a slope k_1. The values of k_1 obtained are shown in Table 4. An example of these plots is exhibited in Figure 3.

The reactions of piperazine, 1-(2-hydroxyethyl)piperazine, and morpholine with thionocarbonate **8** also show linear k_{obsd} vs [NH] plots, with a pH-independent slope. These results can be accounted for by a larger value of k_2 and a smaller value of k_{-1} for the reactions of thionocarbonate **8** than the corresponding ones for the reactions of these amines with substrates **6** and **7** (see Table 4). The k_1 values obtained for these reactions are also included in Table 4.

Determination of k_3 Values. Since this rate coefficient measures the proton transfer from the aminium moiety of the zwitterionic tetrahedral intermediate ($\mathbf{T}^{\pm}$) to the corresponding free amine, knowledge of the pK_a values of both $\mathbf{T}^{\pm}$ and the conjugate acid of the free amine is requisite for the determination of the k_3 values.

The pK_a of the tetrahedral intermediates $\mathbf{T}^{\pm}$ in Scheme 1 can be estimated following the method of Jencks and co-workers,[9] which assumes that the inductive effect is the most important for assessing ionization constants of tetrahedral structures. By this method, the pK_a of intermediates similar to $\mathbf{T}^{\pm}$ can be estimated by the use of eq 3. In this equation, pK_a(ref) is the known pK_a of a

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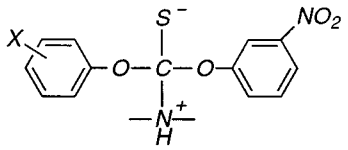
tetrahedral reference, ρ_I is the inductive reaction constant (− 9.2 for intermediates similar to $\mathbf{T}^{\pm}$ in Scheme 1),[10] and σ_I and σ_I(ref) are the inductive substituent constants for groups (variable and reference) attached to the central carbon atom of the intermediate.

$$pK_a - pK_a(\text{ref}) = \rho_I(\sigma_I - \sigma_I(\text{ref})) \qquad (3)$$

The pK_a of structure **9** has been found to be 7.1 pK_a units lower than that of the corresponding aminium cation.[5a] The pK_a of intermediate **10** can be estimated through eq 3 with the σ_I values of 4-methylphenoxy and 3-methoxyphenoxy, σ_I = 0.37 and 0.39, respectively.[5b] This gives pK_a(**10**) − pK_a(**9**) = − 9.2 (0.39−0.37) = ca. −0.2. Namely, the pK_a of **10** is 7.3 pK_a units lower than that of the corresponding aminium cation.



9 *(X = 4-Me)*
10 *(X = 3-MeO)*
11 *(X = 3-Cl)*
12 *(X = 3-NO$_2$)*

The pK_a of **11** and **12** can be determined with the σ_I values of 3-chlorophenoxy and 3-nitrophenoxy, respectively. These values have been estimated as ca. σ_I = 0.44.[5a,b] Obviously, these are rough estimations because the σ_I value of 3-nitrophenoxy should be larger than that of 3-chlorophenoxy, judging by the higher acidity of 3-nitrophenol than 3-chlorophenol (pK_a values in water at 25 °C are 8.4 and 9.0, respectively).[11] Taking compound **9** as a reference and assuming σ_I = 0.44 for 3-chlorophenoxy, eq 3 gives pK_a(**11**) − pK_a(**9**) = −9.2 (0.44−0.37) = ca. −0.6. This means that the pK_a of **11** is roughly 7.7 pK_a units lower than that of the corresponding conjugate acid of the amine. The pK_a of **12** should be lower than that of **11** for the reasons stated above.

Due to the fact that all the tetrahedral intermediates ($\mathbf{T}^{\pm}$) formed in the reactions under the present investigation exhibit pK_a values lower than those of the corresponding conjugate acid of the amine, the proton transfer from $\mathbf{T}^{\pm}$ to the corresponding amine is thermodynamically favorable. Therefore, these transfers are diffusion controlled, and according to Eigen, the value of k_3 should be ca. 10^{10} s^{-1} M^{-1} in water.[12,13] In 44 wt % ethanol−water, the value of k_3 has been reported as 4×10^9 s^{-1} M^{-1} in view of the 2.5 times larger viscosity coefficient of this medium compared to that of water.[14] This value should be independent of the amine since the amine moiety in $\mathbf{T}^{\pm}$ and the free amine are the same.[14] Nevertheless, for the proton transfer from the intermediate $\mathbf{T}^{\pm}$ formed in the reactions with piperazinium ion to this amine, the value of k_3 has been estimated as 2×10^9 s^{-1} M^{-1} in 44 wt % ethanol−water due to electrostatic repulsion of the positive charges involved.[14]

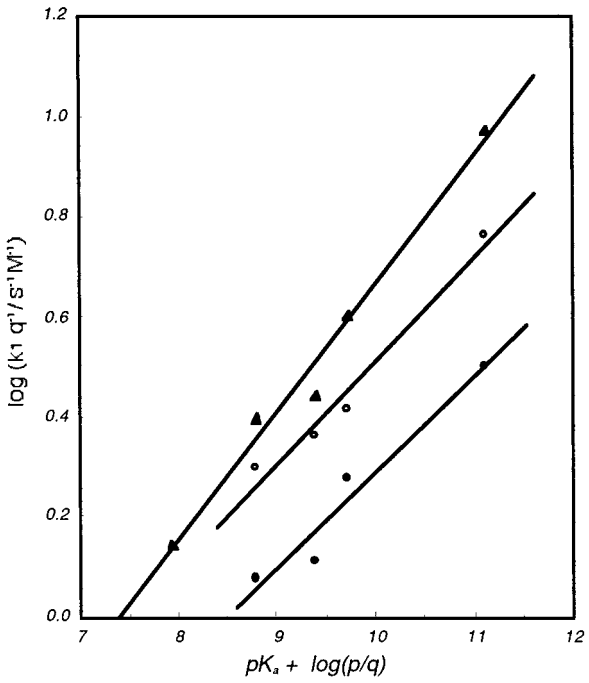


Figure 4. Brönsted-type plots (statistically corrected) for k_1 for the aminolysis of thionocarbonates **6** (●), **7** (○), and **8** (▲) in 44 wt % ethanol−water, at 25.0 °C and an ionic strength of 0.2 M. Slopes (β) are 0.19 ± 0.03, 0.21 ± 0.03, and 0.26 ± 0.02, respectively.

Brönsted-Type Plots. Figure 4 shows the Brönsted-type plots obtained (statistically corrected) with the k_1 values (shown in Table 4) found in the reactions of some secondary alicyclic amines with substrates **6**−**8**. The values of k_1 for the reactions of piperazine were corrected statistically by dividing them by q = 2, since this amine possesses two equivalent basic sites.[6,15] Similarly, the K_a values of the conjugate acid of the amines were corrected statistically by multiplying them by q/p, where p is the number of equivalent protons of the conjugate acid of the amine. The value of p is 2 for all amines, except piperazinium ion, whose p value is 4.[6,15]

The slopes (β) of the Brönsted plots in Figure 4 for the aminolysis of substrates **6**, **7**, and **8** are 0.19 ± 0.03, 0.21 ± 0.03, and 0.26 ± 0.02, respectively. The magnitudes of these slopes are consistent with a stepwise mechanism through a zwitterionic tetrahedral intermediate whereby its formation is the rate-determining step.[2−6,13,14,16] The order of reactivities toward these amines shown by the substrates is a consequence of the order of electron-withdrawing effects of the substituents in the nonleaving group of the substrates. As shown in Table 4, thionocarbonate **5** exhibits the lowest reactivity toward a given amine due to the slight electron-donating effect of the 4-methyl substituent. This leaves the thionocarbonyl carbon of **5** less positive relative to that of the other substrates and, therefore, less prone to nucleophilic attack by the amine.

The k_1 values found in the aminolysis of thionocarbonates **5**−**7** (Table 4) are smaller than those obtained in the same aminolysis of thionocarbonates **1**−**3**, respectively. This is understandable in terms of the lesser electron-withdrawing ability of 3-nitrophenoxy in the

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(15) Bell, R. P. *The Proton in Chemistry*; Methuen: London, 1959; p 159.

former substrates relative to that of 4-nitrophenoxy in the latter thionocarbonates. This leaves the thiocarbonyl carbon of compounds **5**−**7** less positive than that of **1**−**3**, decreasing, therefore, the rate of nucleophilic attack by the amine.

The aminolysis of **8** also exhibits values of k_1 (Table 4) lower than those obtained in the same aminolysis of thionocarbonate **4**.[5b] This should be due to the lower electron withdrawal of 3-nitro in **8** than that of both groups, 4-cyano and 4-nitro, in **4**, as reflected by the pK_a values of the corresponding phenols (pK_a = 8.4, 8.0, and 7.2, respectively, in water at 25 °C).[11]

Table 4 also shows the values of k_{-1} obtained by the fittings through eq 1. As expected, these values increase as the basicity of the amine decreases for the reactions of a given thionocarbonate. This is in accordance with the strength of the C−N bond between the central carbon atom and the amine in the zwitterionic tetrahedral intermediate. As the amine basicity decreases, this bond becomes weaker and the rate constant for amine expulsion (k_{-1}) becomes larger.

As seen in Table 4, the k_{-1} values increase slightly for the reactions of a given amine, as the substituent on the nonleaving group of the substrate becomes less electron withdrawing. Although this effect is small and just outside experimental error (ca. 30%), one could argue that this effect could be due to a greater "push" exerted by the oxygen atom of the nonleaving group (to expel the amine from the zwitterionic intermediate) as the substituent becomes less electron withdrawing. The same small effect was found in the reactions of 1-formylpiperazine with substrates **2**−**4**.[5b] The relatively long distance from these substituents in the zwitterionic intermediate to the central carbon and leaving amine has been claimed to be responsible for this small effect.[5b]

Table 4 shows the values of k_2 obtained in the aminolysis of thionocarbonates **5**−**8**. As seen in this table, these values are independent of the amine basicity but show dependence on the substituents in the nonleaving groups. The independence of these values on amine basicity can be explained by the lack of an electron pair on the aminium moiety of the zwitterionic tetrahedral intermediate, which prevents its push to expel the nucleofuge.[16]

For a comparison between the k_2 values in Table 4, k_2 for the reaction of substrate **8** must be divided by 2 due to the two identical nucleofuges in the corresponding tetrahedral intermediate (**12**). As seen in this table, the value of k_2 increases steadily in going from 4-methyl, the substituent in the nonleaving group of thionocarbonate **5**, to 3-methoxy, 3-chloro, and 3-nitro in thionocarbonates **6**, **7**, and **8**, respectively. This could be attributed to the greatest electron-withdrawal from the 3-nitro group (compared to the other groups), which leaves the central carbon atom of intermediate **12** the most positive. This facilitates the push provided by S^- in this intermediate to expel the nucleofuge.

As expected, the values of k_2 for the aminolysis of thionocarbonates **5**−**8**, with 3-nitrophenoxide as the leaving group (Table 4), are smaller than those for the same aminolysis of the similar thionocarbonates **1**−**4**, with 4-nitrophenoxide as the nucleofuge.[5a,b] This reflects the greater basicity of the 3-nitrophenoxide anion relative to that of 4-nitrophenoxide (pK_a values of the respective phenols are 8.4 and 7.2 in water at 25 °C),[11] which makes the former a worse nucleofuge from the zwitterionic intermediate compared to the latter.

For the aminolysis of thionocarbonates **6** and **7**, no significant amounts of 3-methoxyphenol and 3-chlorophenol were found, respectively. These results can be explained by the greater basicity of 3-methoxyphenoxide and 3-chlorophenoxide compared to that of 3-nitrophenoxide (pK_a values of the corresponding phenols in water at 25 °C are 9.7, 9.0, and 8.4, respectively).[11] This suggests a greater nucleofugality from the zwitterionic intermediate of the latter relative to that of the two other groups.[17]

The fact that neither 3-methoxyphenol nor 3-chlorophenol was found in the aminolysis of thionocarbonates **6** or **7**, respectively, indicates that the corresponding thionocarbamates are stable under the experimental conditions. This is in agreement with the fact that the 4-nitrophenyl thionocarbamate derived from morpholine (Mo−CS−OPNp, where Mo is morpholine and PNp is 4-nitrophenyl) at pH 8.5 did not show any signs of decomposition after 2 days at room temperature.[18]

The values of the equilibrium constant for formation of the zwitterionic tetrahedral intermediate (K_1), obtained by a fitting using eq 2, increase as the electron withdrawal from the substituent in the nonleaving group becomes greater (Table 4). This is a reflection of the larger k_1 and smaller k_{-1} values in going from 3-methoxy to 3-nitro as the above substituent. On the other hand, for the reactions of a given substrate, the value of K_1 increases with the increase of the amine basicity, as expected on the basis of a faster attack on the substrate (larger k_1) and a slower expulsion from the zwitterionic intermediate (smaller k_{-1}) for the more basic amines.

The reactions of piperazine and 1-(2-hydroxyethyl)-piperazine with thionocarbonates **2** and **3** show linear plots of k_{obsd} vs [NH].[5b] The Brönsted plots obtained with the slopes of these plots show β values in accord with the rate-determining formation (k_1 step) of a zwitterionic tetrahedral intermediate.[5b] These results are in great contrast to the nonlinear upward plots of k_{obsd} vs [NH], obeying eq 1, found in the reactions of the same amines with thionocarbonates **6** and **7** (this work). This apparent inconsistency can be explained by the larger k_2 values for the reactions of substrates **2** and **3**[5b] relative to those for **6** and **7** (6- and 4-fold, respectively) and the larger [NH] values employed in the reactions of the former substrates (from 4- to 9-fold). This makes $k_2 + k_3[NH] \gg k_{-1}$ for the reactions of thionocarbonates **2** and **3**, reducing eq 1 to $k_{obsd} = k_0 + k_1[NH]$.

Gresser and Jencks did not find any amine catalysis in the aminolysis of diaryl carbonates, including phenyl 3-nitrophenyl carbonate.[16b] Namely, the k_{obs} vs [amine] plots they obtained are linear for the reactions of all amines. The reaction mechanism proposed by these authors lacks the k_3 step found in the aminolysis of diaryl

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(17) A referee has commented that if the log of the relative nucleofugalities of 3-nitrophenoxide (NPO^-) and 3-chlorophenoxide ($ClPO^-$) is in direct proportion to their pK_a values, then $k_2^{NPO}/k_2^{ClPO} \approx 4$ and 20% of the 3-phenolic product should be $ClPO^-$. Unfortunately, the UV−vis technique does not allow us to detect this. Therefore, it could be possible that the k_2 value for the reaction of **7** (Table 4) could be slightly overestimated. In any case, the error in the determination in this value of k_2 is 25% (Table 4).

(18) Unpublished results from this laboratory.

thionocarbonates (Scheme 1). The difference in mechanism can be attributed to the faster nucleofugality of the leaving groups from the $\mathbf{T}^{\pm}$ intermediate formed with diaryl carbonates than that formed with diaryl thionocarbonates. The k_3 value is about the same for both systems since the proton transfer from $\mathbf{T}^{\pm}$ to the corresponding amine is diffusion controlled in both cases. This means that for diaryl thionocarbonates, $k_2 \approx k_3$[NH] in Scheme 1, whereas $k_2 \gg k_3$[NH] for diaryl carbonates.

The faster k_2 value for the $\mathbf{T}^{\pm}$ formed with carbonates relative to that formed with thionocarbonates has been explained by the greater ability of O^- in the former intermediate (compared to that of S^- in the latter intermediate) to form a double bond and expel the nucleofuge. This is consistent with the higher polarizability of the C═S bond compared to that of the C═O bond, which hinders the formation of the C═S bond from the thio $\mathbf{T}^{\pm}$ compared to the C═O bond from the oxy $\mathbf{T}^{\pm}$, thus decreasing the nucleofugality of the leaving group (and also the amine) from the former $\mathbf{T}^{\pm}$.[19,20]

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Supporting Information Available: Page S2 containing ^{1}H NMR and ^{13}C NMR data for compounds **6**−**8**. This material is available free of charge via the Internet at http://pubs.acs.org.

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