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# Kinetics and Mechanism of the Aminolysis of *O*-Aryl *S*-Methyl Thiocarbonates

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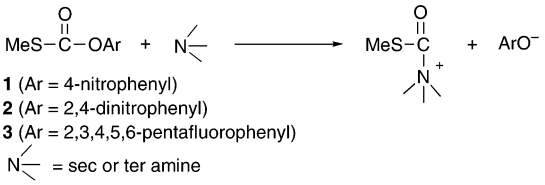


Stepwise mechanisms for aminolysis of **1**
Concerted mechanisms for aminolysis of **2** and **3**

The reactions of secondary alicyclic (SA) amines and quinuclidines (QUI) with 4-nitrophenyl and 2,4-dinitrophenyl *S*-methyl thiocarbonates (**1** and **2**, respectively) and those of SA amines with 2,3,4,5,6-pentafluorophenyl *S*-methyl thiocarbonate (**3**) are subjected to a kinetic study in aqueous solution, at 25.0 °C, and an ionic strength of 0.2 M (KCl). The reactions of thiocarbonates **1**, **2**, and **3** were followed spectrophotometrically at 400, 360, and 220 nm, respectively. Under amine excess, pseudo-first-order rate coefficients ($k_{obsd}$) are found. Plots of $k_{obsd}$ vs amine concentration at constant pH are linear, with the slope ($k_N$) independent of pH. The Brønsted-type plots (log $k_N$ vs p$K_a$ of aminium ions) are linear for all the reactions, with slopes $\beta = 0.9$ for those of **1** with SA amines and QUI, $\beta = 0.36$ and 0.57 for the reactions of **2** with SA amines and QUI, respectively, and $\beta = 0.39$ for the reactions of SA amines with **3**. The magnitude of the slopes indicates that both aminolyses of **1** are governed by stepwise mechanisms, through a zwitterionic tetrahedral intermediate ($T^{\pm}$), where expulsion of the nucleofuge from $T^{\pm}$ is the rate-determining step. The values of the Brønsted slopes found for the aminolyses of thiocarbonates **2** and **3** suggest that these reactions are concerted. By comparison of the reactions under investigation between them and with similar aminolyses, the following conclusions arise: (i) Thiocarbonate **2** is more reactive than **1** toward the two amine series. (ii) The change of the nonleaving group from MeO in 4-nitrophenyl methyl carbonate to MeS in thiocarbonate **1** results in lower $k_N$ values. (iii) The greater reactivity of this carbonate than thiocarbonate **1** is attributed to steric hindrance of the MeS group, compared to MeO toward amine attack. (iv) The change of a pyridine to an isobasic SA amine or QUI destabilizes the $T^{\pm}$ intermediate formed in the aminolyses of **2**. (v) The change of 4-nitrophenoxy to 2,3,4,5,6-pentafluorphenoxy or 2,4-dinitrophenoxy as the leaving group destabilizes the tetrahedral intermediate formed in the reactions with SA amines, changing the mechanism from a stepwise process to a concerted reaction.

## Introduction

The kinetics and mechanisms of the aminolysis of aryl alkyl carbonates have been well documented.[1–3] Nevertheless, less is known on the kinetics and mechanism of the aminolysis of *S*-aryl *O*-alkyl thiocarbonates,[4,5] and, as far as we know, there has been only one work on the kinetics of the aminolyses of *O*-aryl *S*-alkyl thiocarbonates.[6]

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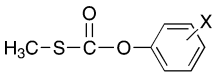
**TABLE 1. Experimental Conditions and $k_{obsd}$ Values for the Aminolysis (SA and QUI) of 4-Nitrophenyl *S*-Methyl Thiocarbonate (1)[a]**

| amine | pH | $F_N$[b] | $10^2[N]_{tot}$/M[c] | $10^5 k_{obsd}/s^{-1}$ | no. of runs |
|---|---|---|---|---|---|
| piperidine | 10.94 | 0.33 | 0.101−1.01 | 54.6−589 | 7 |
| | 11.24 | 0.50 | 0.101−1.01 | 91.2−916 | 7 |
| | 11.54 | 0.67 | 0.101−1.01 | 163−1270 | 7 |
| piperazine | 9.64 | 0.33 | 0.189−1.89 | 16.5−140 | 7 |
| | 9.94 | 0.50 | 0.202−2.02 | 23.1−238 | 7 |
| | 10.24 | 0.67 | 0.189−1.89 | 32.0−278 | 7 |
| 1-(2-hydroxyethyl)piperazine | 9.07 | 0.33 | 0.574−5.74 | 11.1−101 | 7 |
| | 9.38 | 0.50 | 0.497−4.97 | 17.3−131 | 7 |
| | 9.69 | 0.67 | 0.465−4.65 | 21.2−185 | 7 |
| morpholine | 8.48 | 0.33 | 1.02−10.2 | 7.42−71.2 | 7 |
| | 8.78 | 0.50 | 0.856−8.56 | 8.48−78.0 | 7 |
| | 9.08 | 0.67 | 0.714−7.14 | 10.8−96.8 | 7 |
| 1-formylpiperazine | 7.68 | 0.33 | 0.608−6.08 | 0.381−5.32 | 7 |
| | 7.98 | 0.50 | 0.591−5.91 | 1.28−8.21 | 7 |
| | 8.28 | 0.67 | 0.609−6.09 | 2.00−9.43 | 7 |
| piperazinium ion | 5.51 | 0.33 | 1.70−14.2 | 0.050−0.282 | 6 |
| | 5.81 | 0.50 | 1.70−14.3 | 0.231−0.525 | 6 |
| | 6.11 | 0.67 | 1.47−14.7 | 0.207−1.01 | 7 |
| quinuclidine | 11.10 | 0.33 | 0.261−2.61 | 40.6−198 | 6 |
| | 11.40 | 0.50 | 0.272−2.72 | 71.0−304 | 7 |
| 3-hydroxyquinuclidine | 9.50 | 0.33 | 0.322−3.22 | 2.91−8.89 | 6 |
| | 9.80 | 0.50 | 0.386−3.86 | 2.23−19.7 | 7 |
| | 10.10 | 0.67 | 0.450−4.50 | 4.33−25.8 | 7 |
| 3-chloroquinuclidine | 8.70 | 0.33 | 0.189−1.89 | 0.129−1.09 | 7 |
| | 9.00 | 0.50 | 0.242−2.42 | 0.587−3.20 | 7 |
| | 9.30 | 0.67 | 0.191−1.91 | 1.05−4.30 | 7 |
| 3-quinuclidinone | 7.50 | 0.50 | 1.97−19.7 | 0.128−0.597 | 7 |
| | 7.80 | 0.67 | 1.91−19.1 | 0.155−0.692 | 6 |

[a] In water, at 25.0 °C, ionic strength 0.2 M (KCl). [b] Free amine fraction. [c] Concentration of total amine (free base plus protonated forms).

In the latter work we found that the pyridinolysis of *O*-4-nitrophenyl *S*-methyl thiocarbonate (**1**) shows a linear Brønsted-type plot with slope $\beta = 1.1$, which is consistent with a stepwise mechanism, through a zwitterionic tetrahedral intermediate ($T^{\pm}$), where $T^{\pm}$ breakdown to products is the rate-limiting step.[6] On the other hand, the pyridinolysis of *O*-(2,4-dinitrophenyl) *S*-methyl thiocarbonate (**2**) exhibits a curved (biphasic) Brønsted-type plot with slopes $\beta = 0.9$ (at low amine $pK_a$) and $\beta = 0.25$ (at high amine $pK_a$).[6] The Brønsted curvature can be explained by a stepwise mechanism where there is a change in the rate-determining step, from breakdown of the intermediate $T^{\pm}$ to products, to its formation as the substituted pyridine increases its basicity.[6]

To extend our studies on the kinetics and mechanisms of the aminolysis of *O*-aryl *S*-alkyl thiocarbonates, in this work we study the reactions of secondary alicyclic (SA) amines with thiocarbonates **1** and **2** and *O*-(2,3,4,5,6-pentafluorophenyl) *S*-methyl thiocarbonate (**3**). We also examine the reactions of quinuclidines (QUI) with thiocarbonates **1** and **2**. By comparing the kinetics and mechanisms of the title reactions with the pyridinolysis of the same substrates[6] and with the reactions of SA amines and QUI with similar carbonates and thiocarbonates,[3−5] we evaluate the effects of the amine nature and the leaving and nonleaving groups of the substrates on the kinetics and mechanisms of these reactions. One specific objective is to assess the influence of the sulfur atom in the nonleaving group, by comparing the title reactions with the aminolysis of the corresponding *O*-aryl *O*-methyl carbonates.



**1** : X = 4-$NO_2$
**2** : X = 2,4-$(NO_2)_2$
**3** : X = 2,3,4,5,6-$F_5$

## Experimental Section

**Materials.** The SA amines and QUI were purified as reported.[7,8] Thiocarbonates **1** and **2** were synthesized as described.[6,9] Thiocarbonate **3** was also prepared by the same standard procedure,[9] and its spectral signals are in accordance with its structure: $^1$H NMR (200 MHz, $CDCl_3$) $\delta$ 2.49 (s); $^{13}$C NMR (200 MHz, $CDCl_3$) $\delta$ 12.9, 124.9, 135.6, 138.9, 141.1, 169.2; $^{19}$F NMR (200 MHz, $CDCl_3$) $\delta$ −145.60, −150.67, −155.42.

**Kinetic Measurements.** The reactions were followed spectrophotometrically (210−500 nm) by means of a diode array instrument. The rate constants were measured following the absorbance change due to the appearance of the corresponding phenoxide ions at 400 nm (reactions of **1**), at 360 nm (reactions of **2**), and at 220 nm (reactions of **3** with all amines except with formylpiperazine, which was measured at 260 nm). The reactions were investigated in aqueous solutions, at 25.0 ± 0.1 °C, and an ionic strength of 0.2 M (maintained with KCl). In all reactions the concentration of total amine (free amine plus its protonated form) was much greater (at least 10-fold) than that of the substrate.

In all cases, pseudo-first-order rate coefficients ($k_{obsd}$) were obtained by means of the kinetic software of the spectrophotometer, after at least four half-lives, except for the slowest

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**TABLE 2. Experimental Conditions and $k_{obsd}$ Values for the Aminolysis (SA and QUI) of 2,4-Dinitrophenyl *S*-Methyl Thiocarbonate (2)[a]**

| amine | pH | $F_N$[b] | $10^3[N]_{tot}$ /M[c] | $10^3k_{obsd}/s^{-1}$ | no. of runs |
|---|---|---|---|---|---|
| piperidine | 10.94 | 0.33 | 1.01−10.1 | 2.90−30.6 | 7 |
| | 11.24 | 0.50 | 1.01−10.1 | 6.00−45.9 | 7 |
| | 11.54 | 0.67 | 1.01−10.1 | 10.2−67.0 | 7 |
| piperazine | 9.64 | 0.33 | 0.325−3.25 | 0.335−3.61 | 7 |
| | 9.94 | 0.50 | 0.269−2.69 | 1.04−5.20 | 7 |
| | 10.24 | 0.67 | 1.57−15.7 | 5.61−36.7 | 7 |
| 1-(2-hydroxyethyl)piperazine | 9.08 | 0.33 | 0.372−3.72 | 0.375−2.58 | 7 |
| | 9.38 | 0.50 | 0.518−5.18 | 1.00−6.05 | 7 |
| | 9.68 | 0.67 | 0.240−2.40 | 0.454−3.35 | 7 |
| morpholine | 8.48 | 0.33 | 0.826−8.26 | 0.460−4.45 | 7 |
| | 8.78 | 0.50 | 0.849−8.49 | 1.16−7.32 | 7 |
| | 9.08 | 0.67 | 0.597−5.97 | 1.19−7.22 | 7 |
| 1-formylpiperazine | 7.68 | 0.33 | 6.08−60.8 | 2.52−22.6 | 7 |
| | 7.98 | 0.50 | 5.91−59.1 | 3.55−33.6 | 7 |
| | 8.28 | 0.67 | 6.09−60.9 | 4.76−45.8 | 7 |
| piperazinium ion | 5.81 | 0.50 | 16.9−169 | 1.12−9.21 | 7 |
| | 6.11 | 0.67 | 16.5−165 | 1.19−12.9 | 7 |
| 1-(2-hydroxyethyl)piperazinium ion | 4.20 | 0.0137 | 3.05−25.9 | 0.0125−0.0450 | 6 |
| | 4.50 | 0.0208 | 2.55−25.5 | 0.0191−0.0733 | 7 |
| quinuclidine | 11.10 | 0.33 | 2.33−19.8 | 56.2−309 | 6 |
| | 11.40 | 0.50 | 4.78−19.1 | 132−435 | 6 |
| 3-hydroxyquinuclidine | 9.50 | 0.33 | 2.92−24.8 | 9.15−68.9 | 6 |
| | 9.80 | 0.50 | 3.86−38.6 | 21.7−172 | 7 |
| | 10.10 | 0.67 | 1.95−19.5 | 14.1−116 | 7 |
| 3-chloroquinuclidine | 8.70 | 0.33 | 1.89−16.0 | 3.02−23.8 | 6 |
| | 9.00 | 0.50 | 2.42−24.2 | 4.10−50.6 | 7 |
| | 9.30 | 0.67 | 1.91−19.1 | 5.57−51.7 | 7 |
| 3-quinuclidinone | 7.20 | 0.33 | 2.99−29.9 | 0.283−2.67 | 7 |
| | 7.50 | 0.50 | 2.76−29.9 | 0.389−4.27 | 14 |
| | 7.80 | 0.67 | 2.63−26.3 | 0.445−4.50 | 7 |

[a] In water, at 25.0 °C, ionic strength 0.2 M (KCl). [b] Free amine fraction. [c] Concentration of total amine (free base plus protonated forms).

**TABLE 3. Experimental Conditions and $k_{obsd}$ Values for the Aminolysis (SA) of 2,3,4,5,6-Pentafluorophenyl *S*-Methyl Thiocarbonate (3)[a]**

| amine | pH | $F_N$[b] | $10^3[N]_{tot}$/ M[c] | $10^3k_{obsd}/s^{-1}$ | no. of runs |
|---|---|---|---|---|---|
| piperidine | 10.94 | 0.33 | 3.40−34.0 | 9.27−76.4 | 7 |
| | 11.24 | 0.50 | 3.60−36.0 | 11.2−119 | 7 |
| | 11.54 | 0.67 | 3.69−36.9 | 20.2−191 | 7 |
| piperazine | 9.64 | 0.33 | 2.46−26.4 | 4.77−37.5 | 6 |
| | 9.94 | 0.50 | 2.46−26.4 | 6.24−54.9 | 7 |
| | 10.24 | 0.67 | 2.62−26.2 | 8.44−85.3 | 6 |
| Piperazine + piperazinium ion | 8.20[d] | *e* | 10.6−106 | 1.93−22.6 | 7 |
| | 8.50[d] | *f* | 11.5−115 | 3.69−38.5 | 7 |
| | 8.80[d] | *g* | 10.5−105 | 6.31−58.4 | 7 |
| 1-(2-hydroxyethyl)piperazine | 9.08 | 0.33 | 3.74−37.4 | 3.90−28.5 | 7 |
| | 9.38 | 0.50 | 3.57−30.3 | 4.36−36.2 | 6 |
| | 9.68 | 0.67 | 3.45−34.5 | 6.03−49.5 | 6 |
| morpholine | 8.48 | 0.33 | 9.20−92.0 | 5.37−40.4 | 7 |
| | 8.78 | 0.50 | 10.2−102 | 4.36−58.1 | 7 |
| | 9.08 | 0.67 | 7.12−71.2 | 6.90−55.2 | 7 |
| 1-formylpiperazine | 8.29 | 0.67 | 6.98−69.8 | 0.870−11.5 | 7 |
| | 9.00[d] | 0.91 | 7.11−60.5 | 1.51−16.0 | 6 |

[a] In water, at 25.0 °C, ionic strength 0.2 M (KCl). [b] Free amine fraction. [c] Concentration of total amine (free base plus protonated forms). [d] In 0.01 M borate buffer. [e] Free piperazine and piperazinium ion fractions are 0.0178 and 0.978, respectively. [f] Free piperazine and piperazinium ion fractions are 0.0349 and 0.963, respectively. [g] Free piperazine and piperazinium ion fractions are 0.0675 and 0.932, respectively.

reactions (thiocarbonate **1** with 3-quinuclidinone and piperazinium ion), where the initial rate method was used.[10] The experimental conditions of the reactions and the $k_{obsd}$ values are shown in Tables 1−3.

**Product Studies.** One of the products in the aminolysis of thiocarbonates **1**, **2**, and **3** was identified as 4-nitrophenoxide, 2,4-dinitrophenoxide, and 2,3,4,5,6-pentafluorophenoxide anions, respectively. The identification was carried out by comparison of the UV−vis spectra at the end of these reactions with those of authentic samples of 4-nitrophenol, 2,4-dinitrophenol, and 2,3,4,5,6-pentafluorophenol, respectively, under the same reaction conditions.

In the reactions of thiocarbonates **1**-**3** with piperidine the other product was identified as 1-(*S*-methylthiocarbonyl)-piperidine, by comparison of the UV−vis spectra at the end of the reactions with that obtained after completion of the reaction of piperidine with *S*-methyl chlorothioformate.

## Results and Discussion

The reactions investigated in this work are governed by the rate law given by eqs 1 and 2, where P, S, and NH represent a product (see the Experimental Section),

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**TABLE 4. Values of p$K_a$ for the Conjugate Acids of Secondary Alicyclic (SA) Amines and $k_N$ Values for the Reactions of SA Amines with 4-Nitrophenyl *S*-Methyl Thiocarbonate (1), 2,4-Dinitrophenyl *S*-Methyl Thiocarbonate (2), and 2,3,4,5,6-Pentafluorophenyl *S*-Methyl Thiocarbonate (3)[a]**

| | | $10^2k_N/s^{-1}M^{-1}$ | | |
|---|---|---|---|---|
| amine | p$K_a$ | **1** | **2** | **3** |
| piperidine | 11.24 | 185 ± 6 | 881 ± 17 | 736 ± 28 |
| piperazine | 9.94 | 21.7 ± 0.5 | 336 ± 7 | 481 ± 17 |
| 1-(2-hydroxyethyl)piperazine | 9.38 | 5.6 ± 0.1 | 226 ± 10 | 206 ± 6 |
| morpholine | 8.78 | 1.93 ± 0.06 | 176 ± 6 | 111 ± 5 |
| 1-formylpiperazine | 7.98 | 0.217 ± 0.009 | 111 ± 2 | 31 ± 2 |
| piperazinium ion | 5.81 | 0.0088 ± 0.0007 | 10.7 ± 0.6 | 10 ± 1 |
| 1-(2-hydroxyethyl)piperazinium ion | 5.9 | | 11.4 ± 0.6 | |

[a] Both the p$K_a$ and $k_N$ values were determined in aqueous solution, at 25.0 °C, and an ionic strength of 0.2 M (KCl).

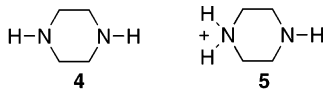
the substrate, and the free amine (SA amine or QUI), respectively, and $k_0$ and $k_N$ are the rate coefficients for hydrolysis and aminolysis of the substrates, respectively.

$$\frac{d[P]}{dt} = k_{obsd}[S] \quad (1)$$

$$k_{obsd} = k_0 + k_N[NH] \quad (2)$$

The value of $k_0$ was much smaller than that of $k_N$[NH] in eq 2, except for the slow reactions of piperazinium cation with **1**, where the aminolysis term ($k_N$[NH]) was also small. The values of $k_N$ for all the reactions were determined as the slope of linear plots of $k_{obsd}$ vs [NH] and were found to be pH independent.

The reactions of **3** with mixtures of piperazine (**4**) and piperazinium ion (**5**) were studied at pH 8.2−8.8, where a mixture of both amines are present, instead of at pH 5.81, which is the p$K_a$ of piperazinium dication. This is due to the fact that the absorbance change by the appearance of pentafluorophenoxide is greater than that of the corresponding phenol. In these cases the $k_N$ values were obtained through eqs 3 and 4. In these equations $k_{Nobsd}$ is a global nucleophilic rate constant (corresponding to the mixture of nucleophiles), $[N]_{tot}$ is the total piperazine (species **4** and **5**) concentration, $F_4$ and $F_5$ are the molar fractions of **4** and **5**, respectively, and $k_4$ and $k_5$ are their corresponding nucleophilic rate constants. The values of $k_{Nobsd}$ were obtained as the slopes of linear $k_{obsd}$ vs $[N]_{tot}$ plots at constant pH. The $k_N$ values for the reactions of thiocarbonate **3** with species **4** and **5** were determined through eq 4, as described.[11]



**4** **5**

$$k_{obsd} = k_0 + k_{Nobs}[N]_{tot} \quad (3)$$

$$k_{Nobsd} = F_4 k_4 + F_5 k_5 \quad (4)$$

The values of $k_N$ for the reactions of SA amines with thiocarbonates **1**, **2**, and **3** are shown in Table 4. These values, as well as those of the p$K_a$ of the conjugate acids of the amines, were statistically corrected with $q = 2$ for piperazine and $p = 2$ for all the conjugate acids of the amines, except that for piperazinium ion with $p = 4$.[11,12]

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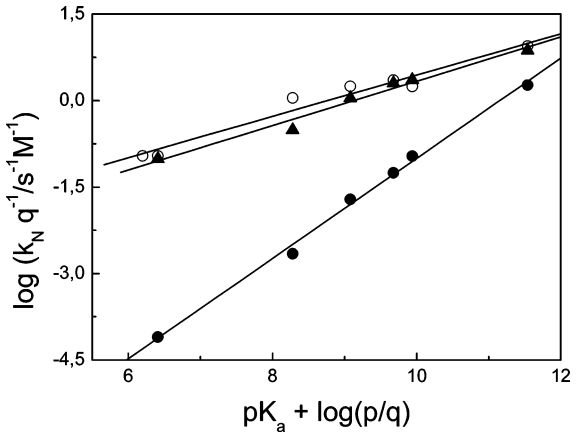



**FIGURE 1.** Brønsted-type plots (statistically corrected) for the reactions of SA amines with thiocarbonates **1** (●), **2** (○), and **3** (▲), in aqueous solution, at 25.0 °C and an ionic strength of 0.2 M (KCl).

**TABLE 5. Values of p$K_a$ for the Conjugate Acids of Quinuclidines (QUI) and $k_N$ Values for the Reactions of QUI with 4-Nitrophenyl *S*-Methyl Thiocarbonate (1) and 2,4-Dinitrophenyl *S*-Methyl Thiocarbonate (2)[a]**

| | | $10^2k_N/s^{-1}M^{-1}$ | |
|---|---|---|---|
| amine | p$K_a$ | **1** | **2** |
| quinuclidine | 11.4 | 21 ± 1 | 4100 ± 100 |
| 3-hydroxy quinuclidine | 9.8 | 0.83 ± 0.03 | 860 ± 30 |
| 3-chloroquinuclidine | 9.0 | 0.25 ± 0.02 | 407 ± 6 |
| 3-quinuclidinone | 7.5 | 0.0054 ± 0.0002 | 25.5 ± 1 |

[a] Both the p$K_a$ and $k_N$ values were determined in aqueous solution, at 25.0 °C and an ionic strength of 0.2 M (KCl).

With these corrected values the Brønsted-type plots (shown in Figure 1) were obtained.

The $k_N$ values found for the quinuclidinolysis of thiocarbonates **1** and **2** are shown in Table 5; the corresponding Brønsted plots are exhibited in Figure 2.

The aminolysis (SA) and quinuclidinolysis of thiocarbonate **1** show linear Brønsted plots (Figures 1 and 2) of slopes $\beta = 0.9 \pm 0.1$ for both reaction series. These slope values are consistent with a pathway through a zwitterionic tetrahedral intermediate ($T^{\pm}$) whose breakdown to products is rate determining.[2−4,6−8,10,11] Namely, these reactions behave according to Scheme 1, with the formation of $T^{\pm}$ as an equilibrium step and the $k_2$ step as rate limiting ($k_{-1} \gg k_2$ in Scheme 1) along the whole p$K_a$ range studied.

The Brønsted plots (statistically corrected), for the reactions of thiocarbonates **2** and **3** with SA amines

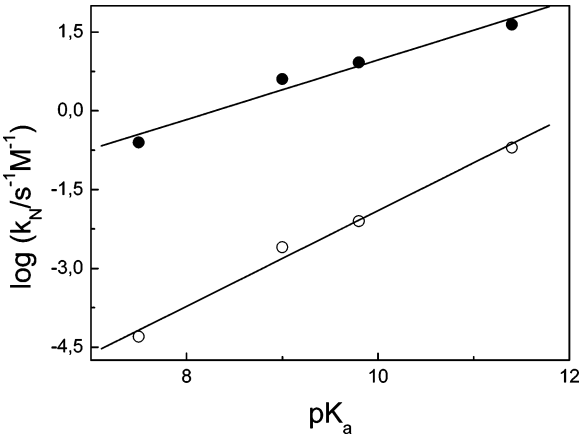
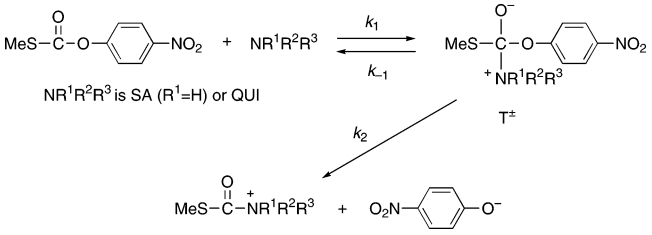



**FIGURE 2.** Brønsted-type plots for the quinuclidinolysis of thiocarbonates **1** (○) and **2** (●) in aqueous solution, at 25.0 °C and an ionic strength of 0.2 M (KCl).

**SCHEME 1**




(shown in Figure 1) are linear with slope ($\beta$) values of $0.36 \pm 0.05$ and $0.39 \pm 0.05$, respectively. The magnitude of this $\beta$ value is at the upper limit of those found for stepwise mechanisms in aminolysis of similar substrates, when formation of a zwitterionic tetrahedral intermediate is the rate-determining step ($\beta_1 = 0.1-0.3$).[2−4,6−8,13,14] On the other hand, these $\beta$ values are also in the lower limit of the Brønsted slopes exhibited by the concerted aminolysis of similar reactive carbonates and thiocarbonates governed by concerted mechanisms.[4,5] Although the $\beta$ values shown by the SA aminolysis of thiocarbonates **2** and **3** seem consistent with both mechanisms, we think the concerted pathway is more likely to drive these reactions for the following reasons.

(a) It was found that the pyridinolysis of thiocarbonate **2** is stepwise, as judged by the biphasic Brønsted-type plot obtained, with slope values $\beta_1 = 0.25$ (high p$K_a$), $\beta_2 = 0.90$ (low p$K_a$) and the center of the Brønsted curvature at p$K_a^0 = 7.3$.[6] The change of the series of nucleophiles from pyridines to SA amines is known to enlarge the p$K_a^0$ value. For instance, the aminolyses (pyridines and SA amines) of *O*-phenyl *O*-2,4-dinitrophenyl thiocarbonate show biphasic Brønsted-type plots with p$K_a^0$ values of 7.0 and 7.7, respectively.[15] Similarly, the same aminolyses of *O*-ethyl *S*-2,4-dinitrophenyl dithiocarbonate exhibit p$K_a^0$ values of 6.9 and 9.2, respectively.[16] Namely, there is a p$K_a^0$ increase of 0.7−2.3 units by the change of nucleophiles from pyridines to SA amines in these 2,4-dinitrophenyl thiocarbonates derivatives. Therefore, it is expected that the p$K_a^0$ value for the SA aminolysis of **2** be 7.3 + (0.7−2.3) units (p$K_a^0$ ranging from 8.0 to 9.6) if this reaction were stepwise. As seen in Figure 2 there is no break in the Brønsted-type plot, within the p$K_a$ 8.0−9.6, for the SA aminolysis of **2**. This fact rules out the stepwise mechanism for this reaction.

(b) Even if for some reason the predicted p$K_a^0$ value for the stepwise SA aminolysis of **2** were beyond 11.54 (the p$K_a$ of piperidine, the most basic amine employed), then the breakdown to products of the tetrahedral intermediate would be rate limiting. In this case the Brønsted slope would be 0.8−1.1,[2−4,6−8,10] which is inconsistent with the $\beta$ value of 0.36 found. The same applies to the SA aminolysis of **3** since this thiocarbonate possesses a worse leaving group than **2** and, therefore, a larger p$K_a^0$ value for the aminolysis of **3** (relative to that of **2**) would be expected if these mechanisms were stepwise.[8] This means that the p$K_a^0$ value for the reactions of **3** would be within the p$K_a$ range of the SA amines used or greater than 11.5. Since no break is observed in the corresponding Brønsted-type plot and its slope value ($\beta$ 0.39) is inconsistent with a stepwise mechanism with rate-limiting breakdown of the intermediate T$^\pm$, we can safely exclude this mechanism for the SA aminolysis of **3**.

(c) The reactions of SA amines with 2,4-dinitrophenyl acetate and 2,4-dinitrophenyl thiolacetate are stepwise,[11,17] in contrast to the reactions of the same amines with methyl 2,4-dinitrophenyl carbonate and *O*-ethyl *S*-2,4-dinitrophenyl thiocarbonate, which are concerted.[3c,5a] Namely, substitution of Me by MeO or EtO as the nonleaving group of a 2,4-dinitrophenyl ester derivative changes the mechanism of its SA aminolysis from stepwise to concerted. This has been ascribed to destabilization of the zwitterionic tetrahedral intermediate (T$^\pm$) by the above change, due to the greater inductive electron withdrawal of MeO or EtO than Me ($\sigma_I = 0.29$, 0.26, and 0.01, respectively)[18] in the intermediate T$^\pm$.[3c,5a,19] Jencks has argued that electron-withdrawing substituents in the nonleaving group favor amine expulsion from T$^\pm$ compared to aryloxide leaving.[19] This destabilization can be attributed to a faster nucleofugality of the amine from T$^\pm$ for substituents in the nonleaving group with greater inductive electron withdrawing ability.[5a] Since $\sigma_I$ for MeS is 0.23,[18] it is reasonable to assume that the inductive electron withdrawal of MeS in T$^\pm$ destabilizes this intermediate as much as MeO or EtO, changing the mechanism from stepwise for the SA aminolysis of 2,4-dinitrophenyl acetate to concerted for the same aminolysis of thiocarbonate **2**.

(13) A reviewer has indicated that the $\beta$ values for the $k_1$ step in Scheme 1 should be large since the corresponding transition state (TS) should be late. It is true that the TS for the formation of the tetrahedral intermediate T$^\pm$ should resemble this intermediate, according to the Hammond postulate. Nevertheless, the Brønsted $\beta$ values for rate limiting formation of T$^\pm$ ($\beta_1$) reported in the literature are 0.1-0.3.[2−4,6−8] An explanation for the discrepancy is that charge development and bond formation in the TS usually do not occur synchronically. Jencks has called this "imbalanced transition state" and Bernasconi "The Principle of Nonperfect Synchronization".[14] For the title reactions, it means that in the TS for the first step, bond formation is well advanced relative to charge development

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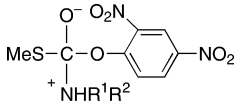
On the other hand, the Brønsted plot for the quinuclidinolysis of **2** (Figure 2) is linear with slope $\beta$ 0.57, similar to those found in the concerted aminolysis of similar substrates ($\beta$ values ranging from 0.4 to 0.7).[4,5a,b,6] It is known that QUI are better leaving groups than isobasic SA amines from a $T^{\pm}$ intermediate, destabilizing, therefore, this intermediate.[3c,4,5d,19] If the SA aminolysis of thiocarbonate **2** is concerted it is reasonable that the quinuclidinolysis of this substrate be concerted, due to the more unstable $T^{\pm}$ intermediate that would be formed had this reaction been stepwise.

**Effect of Amine Nature.** The pyridinolysis of **2** has been found to be stepwise,[6] whereas the SA aminolysis and quinuclidinolysis of this substrate are concerted (this work). The same change in mechanism has been found for the reactions of these amine series with *O*-ethyl *S*-2,4-dinitrophenyl and *O*-ethyl *S*-2,4,6-trinitrophenyl thiocarbonates: The pyridinolysis of these substrates are stepwise,[20] in contrast to their SA and QUI aminolyses, which are concerted.[5a,b,d] Other examples are the stepwise pyridinolysis of methyl 2,4-dinitrophenyl carbonate,[2b] compared to the concerted reactions of this compound with SA amines and QUI.[3c] The mechanistic change has been attributed to the superior nucleofugality of SA amines and QUI from the intermediate $T^{\pm}$ relative to isobasic pyridines.[3c,4,5a,b,d,19]

As seen in Tables 4 and 5, the $k_N$ values for the SA aminolysis of thiocarbonate **1** are larger than those for the quinuclidinolysis of the same substrate. The same is true for the reactions of these amines with *O*-ethyl *S*-4-nitrophenyl thiocarbonate.[5d] Since for the reactions of these amines with thiocarbonate **1** the $k_2$ step of Scheme 1 is rate determining, the nucleophilic macroscopic rate constant ($k_N$) is $k_N = K_1 k_2$, where $K_1$ is the equilibrium constant for the first step. Since the $k_2$ value should not change significantly with the amine basicity or nature,[8] it follows that the $K_1$ values should be larger for the reactions of **1** with SA amines relative to those with isobasic QUI. In view that the $k_1$ values should be slightly larger for the reactions of QUI compared to isobasic SA amines,[5d] it means that the $k_{-1}$ values should be larger for QUI relative to isobasic SA amines. This is in line with what was discussed above: QUI are better nucleofuges from the intermediate $T^{\pm}$ than isobasic SA amines.[3c,4,5d,19]

The $k_N$ values for the concerted reactions of **2** with QUI are larger than those of the same substrate with isobasic SA amines (see Tables 4 and 5). This is in opposition to the kinetic results obtained for the stepwise reactions of **1**. Nonetheless, since the $k_1$ values toward **1** are larger for QUI relative to isobasic SA amines,[5d] it is reasonable to assume that for the concerted reactions of **2** the nucleophilic attack of a given QUI would be faster than that of an isobasic SA amine.

**Effect of the Leaving Group.** The fact that the reactions of SA amines with thiocarbonate **1** are stepwise whereas those of the same amines with **3** are concerted indicates that the tetrahedral intermediate $T^{\pm}$ in Scheme 1 is greatly destabilized by the change of 4-nitrophenoxy to 2,3,4,5,6-pentafluorophenoxy as leaving group. This should be due to the lower basicity of 2,3,4,5,6-pentafluorophenoxide ($pK_a$ of conjugate phenol 5.2),[21] compared to that of 4-nitrophenoxide ($pK_a$ 7.1),[22] which should result in a greater nucleofugality of the former group from the hypothetical intermediate, destabilizing, therefore, this intermediate. Similarly, the fact that the reactions of SA amines and QUI with **1** are stepwise whereas those of these amines with **2** are concerted means that the intermediate $T^{\pm}$ in Scheme 1 is also greatly destabilized by the introduction of a second nitro group in the nucleofuge. This lowers its basicity from 7.1 to 4.1,[22] which means a much greater nucleofugality of 2,4-dinitrophenoxide from the hypothetical intermediate (**6**), compared to that of 4-nitrophenoxide, which destabilizes it kinetically. This means that intermediate **6** either exists but it is so unstable that the concerted path becomes more favorable energetically than the stepwise, or it is so unstable that does not exist (lifetime less than a vibration period) and the mechanism is enforced concerted.[23] A similar situation was found for the reactions of SA amines with the corresponding carbonates and *S*-aryl thio derivatives: The reactions of methyl 4-nitrophenyl carbonate[3c] and ethyl *S*-4-nitrophenyl thiocarbonate[5c] are stepwise, in contrast to those of methyl 2,4-dinitrophenyl carbonate[3c] and ethyl *S*-2,4-dinitrophenyl thiocarbonate[5a] which are concerted.




**6**

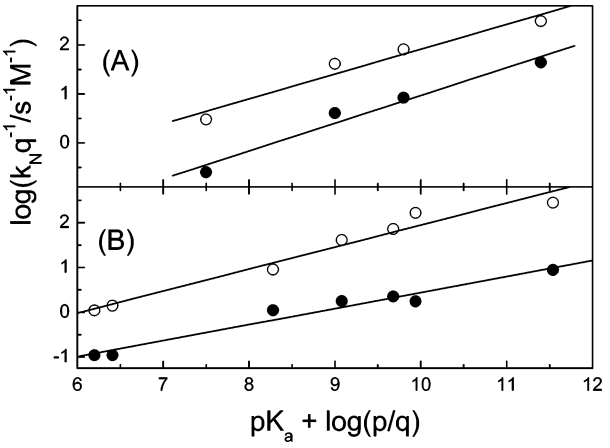



**FIGURE 3.** Brønsted-type plots obtained for the reactions of QUI (A) and SA amines (B) with 2,4-dinitrophenyl methyl carbonate (○, ref 3c) and thiocarbonate **2** (●, this work), in aqueous solution, at 25.0 °C and an ionic strength of 0.2 M (KCl).

**Comparison with Carbonates.** Figure 3 shows the Brønsted-type plots for the concerted reactions of SA amines and QUI with methyl 2,4-dinitrophenyl carbonate[3c] (**7**) and thiocarbonate **2** (this work). The higher reactivity of these amines toward carbonate **7** seem at first sight

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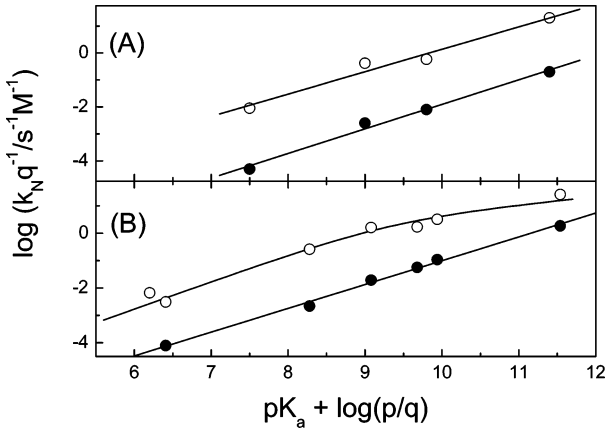


**FIGURE 4.** Brønsted-type plots obtained for the reactions of QUI (A) and SA amines (B) with 4-nitrophenyl methyl carbonate (○, ref 3c) and thiocarbonate **1** (●, this work), in aqueous solution, at 25.0 °C and an ionic strength of 0.2 M (KCl).

surprising in view of the favorable electronic effects of MeS in thiocarbonate **2** compared to MeO in carbonate **7**, which should result in the carbonyl carbon of **2** being more positively charged and therefore more prone to nucleophilic attack by the amine, relative to attack at carbonate **7**.[6] The lower $k_N$ values for the aminolysis of **2** can be attributed to steric hindrance toward amine attack by the bulkier sulfur atom in **2** compared to the oxygen atom in **7**. The same trend was observed for the stepwise pyridinolysis of these substrates: the $k_N$ values are larger for carbonate **7** relative to thiocarbonate **2**.[6] This is also true when the *S* and *O* atoms are in the leaving group: the $k_N$ values for the pyridinolysis of 2,4-dinitrophenyl and 2,4,6-trinitrophenyl methyl carbonates[2b,d] are larger than those for the same aminolysis of *S*-2,4-dinitrophenyl and *S*-2,4,6-trinitrophenyl *O*-ethyl thiocarbonates, respectively.[20] Likewise, the $k_N$ values for the pyridinolysis of *O*-2,4-dinitrophenyl *O*-ethyl thionocarbonate[24] are larger than those for *S*-2,4-dinitrophenyl *O*-ethyl dithiocarbonate.[14b]

Figure 4 shows the Brønsted-type plots for the reactions of SA amines and QUI with 4-nitrophenyl methyl carbonate[3c] (**8**) and thiocarbonate **1** (this work). All these reactions were shown to be governed by stepwise mechanisms, where breakdown to products of the zwitterionic intermediate ($T^{\pm}$) is the rate-determining step, except the reactions of the strongly basic SA amines ($pK_a > 9.3$) with carbonate **8**, for which formation of $T^{\pm}$ is rate limiting.[3c] Therefore, for most of the reactions depicted in Figure 4, $k_N = k_1k_2/k_{-1}$ holds. As seen in Figure 4, carbonate **8** is more reactive toward these amines than thiocarbonate **1**. The $k_1$ value should be larger for the reaction of the former substrate with a given amine in view of the lower steric hindrance offered by the *O* atom compared to *S* toward amine attack (see above). On the other hand, the value of the $k_2/k_{-1}$ ratio, for a given amine and leaving group, should be larger for carbonate **8** since it is known that the smaller the $pK_a^0$ value, the larger is the $k_2/k_{-1}$ ratio.[16b] These two effects can explain the larger $k_N$ values exhibited by the reactions of carbonate **8** compared to thiocarbonate **1**.

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