

Kinetic Study of the Aminolysis and Pyridinolysis of *O*-Phenyl and *O*-Ethyl *O*-(2,4-Dinitrophenyl) Thiocarbonates. A Remarkable Leaving Group Effect

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The reactions of a series of secondary alicyclic (SA) amines with *O*-phenyl and *O*-ethyl *O*-(2,4-dinitrophenyl) thiocarbonates (**1** and **2**, respectively) and of a series of pyridines with the former substrate are subjected to a kinetic investigation in water, at 25.0 °C, ionic strength 0.2 M (KCl). Under amine excess over the substrate, all the reactions obey pseudo-first-order kinetics and are first-order in amine. The Brønsted-type plots are biphasic, with slopes (at high pK_a) of $\beta_1 = 0.20$ for the reactions of SA amines with **1** and **2** and $\beta_1 = 0.10$ for the pyridinolysis of **1** and with slopes (at low pK_a) of $\beta_2 = 0.80$ for the reactions of SA amines with **1** and **2** and $\beta_2 = 1.0$ for the pyridinolysis of **1**. The pK_a values at the curvature center (pK_a^0) are 7.7, 7.0, and 7.0, respectively. These results are consistent with the existence of a zwitterionic tetrahedral intermediate (T^\ddagger) and a change in the rate-determining step with the variation of amine basicity. The larger pK_a^0 value for the pyridinolysis of **1** compared to that for **2** ($pK_a^0 = 6.8$) and the larger pK_a^0 value for the reactions of SA amines with **1** relative to **2** are explained by the greater inductive electron withdrawal of PhO compared to EtO. The larger pK_a^0 values for the reactions of SA amines with **1** and **2**, relative to their corresponding pyridinolysis, are attributed to the greater nucleofugalities of SA amines compared to isobasic pyridines. The smaller pK_a^0 value for the reactions of SA amines with **2** than with *O*-ethyl *S*-(2,4-dinitrophenyl) dithiocarbonate ($pK_a^0 = 9.2$) is explained by the greater nucleofugality from T^\ddagger of 2,4-dinitrophenoxide (DNPO⁻) relative to the thio derivative. The stepwise reactions of SA amines with **1** and **2**, in contrast to the concerted mechanisms for the reactions of the same amines with the corresponding carbonates, is attributed to stabilization of T^\ddagger by the change of O⁻ to S⁻. The simple mechanism for the SA aminolysis of **2** (only one tetrahedral intermediate, T^\ddagger) is in contrast to the more complex mechanism (two tetrahedral intermediates, T^\ddagger and T^- , the latter formed by deprotonation of T^\ddagger by the amine) for the same aminolysis of the analogous thionocarbonate with 4-nitrophenoxide (NPO⁻) as nucleofuge. To our knowledge, this is the first example of a remarkable change in the decomposition path of a tetrahedral intermediate T^\ddagger by replacement of NPO⁻ with DNPO⁻ as the leaving group of the substrate. This is explained by (i) the greater leaving ability from T^\ddagger of DNPO⁻ than NPO⁻ and (ii) the similar rates of deprotonation of both T^\ddagger (formed with DNPO and NPO).

Introduction

In recent years we have been interested in the mechanisms of the aminolysis of thionocarbonates. We have studied kinetically the reactions of *O*-phenyl and *O*-(4-nitrophenyl) *O*-ethyl thiocarbonates (EtO-CS-OC₆H₄X, X = H, NO₂) with secondary alicyclic (SA) amines, where we found a mechanism through two tetrahedral intermediates on the reaction pathway, one zwitterionic (T^\ddagger) and the other anionic.¹ A similar behavior was found for the aminolysis (SA amines) of *O*-methyl *O*-(4-nitrophenyl) thiocarbonate (MeO-CS-OC₆H₄NO₂).²

We have also carried out a kinetic study on the pyridinolysis of *O*-methyl and *O*-ethyl *O*-(4-nitrophenyl) thiocarbonates and *O*-ethyl *O*-(2,4-dinitrophenyl) thiocarbonate.³ For the reactions of the two former substrates, linear Brønsted-type plots of slopes $\beta = 1.0$ were found. These were interpreted by a stepwise mechanism through an intermediate T^\ddagger on the reaction path, whereby decomposition of T^\ddagger to products is rate-determining.³ In the pyridinolysis of *O*-ethyl *O*-(2,4-dinitrophenyl) thiocarbonate, a biphasic Brønsted-type plot was obtained, with limiting slopes $\beta = 0.1$ (high pyridine pK_a) and $\beta =$

* Corresponding author.

(1) Castro, E. A.; Cubillos, M.; Santos, J. G. *J. Org. Chem.* **1996**, *61*, 3501.

(2) Castro, E. A.; Saavedra, C.; Santos, J. G.; Umaña, M. I. *J. Org. Chem.* **1999**, *64*, 5401.

(3) Castro, E. A.; Cubillos, M.; Santos, J. G.; Téllez, J. *J. Org. Chem.* **1997**, *62*, 2512.

1.0 (low pyridine pK_a). This Brønsted plot was explained by a stepwise mechanism through an intermediate T^+ , with a change in the rate-determining step according to the pyridine basicity.³

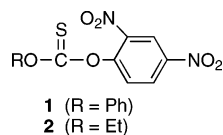
Also a kinetic study has been carried out on the reactions of SA amines with bis(phenyl) and bis(4-nitrophenyl) thionocarbonates and the reactions of pyridines with the latter substrate.⁴ The reactions of the SA amines (except piperidine) with the former substrate exhibit a complex order in amine, consistent with the existence of both a zwitterionic (T^+) and an anionic (T^-) tetrahedral intermediate on the reaction pathway, whereby T^+ is deprotonated by an amine to give T^- .⁴ On the other hand, the pyridinolysis of the nitro derivative shows first-order kinetics in pyridine and the Brønsted plot is linear, with slope $\beta = 1.0$, consistent with a stepwise mechanism where T^+ breakdown to products is the rate-determining step.⁴ The reactions of the SA amines with this substrate 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^+ is not formed because of its high kinetic instability due to the large nucleofugality of both leaving groups.⁴

The reactions of asymmetric diaryl thionocarbonates with SA amines in 44 wt % ethanol–water show curved upward plots of the pseudo-first-order rate constant vs amine concentration, in agreement with the formation of the tetrahedral intermediates T^+ , which transfers a proton to an amine to yield T^- .⁵

The reactions of SA amines with *O*-ethyl 2,4-dinitrophenyl dithiocarbonate exhibit a biphasic Brønsted plot with limiting slopes $\beta = 0.2$ and 0.8, in accordance with an intermediate T^+ on the reaction path and a change in the rate-limiting step, from T^+ breakdown to products to T^+ formation, as the amine basicity increases.⁶

On the other hand, the aminolysis (SA) of phenyl and methyl 2,4-dinitrophenyl carbonates were found to be concerted, on the basis of the linear Brønsted-type plots obtained with slopes ca. 0.4.⁷

To extend our mechanistic investigations on the aminolysis of thionocarbonates, in the present work we undertake a kinetic study of the reactions of SA amines with the thionocarbonates *O*-phenyl *O*-(2,4-dinitrophenyl) thiocarbonate (**1**) and *O*-ethyl *O*-(2,4-dinitrophenyl) thio-



carbonate (**2**) and of the reactions of pyridines with the former substrate. The object is to assess the influence of the different groups of the substrate and the amine

nature on these mechanisms by comparing these reactions between them and with those of alkyl aryl thionocarbonates,^{1–4} diaryl thionocarbonates,⁵ *O*-ethyl 2,4-dinitrophenyl dithiocarbonate,⁶ and phenyl and methyl 2,4-dinitrophenyl carbonates.⁷

According to our results, there is a remarkably different mechanism between the SA aminolysis of thionocarbonate **2** (only one tetrahedral intermediate, T^+ , on the reaction path) and the same aminolysis of the analogous thionocarbonate possessing 4-nitrophenoxide as leaving group (tetrahedral intermediates T^+ and T^-).^{1,2} Namely, this remarkable mechanistic change takes place by substitution of 2,4-dinitrophenoxy by 4-nitrophenoxy as the nucleofuge in T^+ . According to our records, this is the first report on this change in mechanism by the above change in the leaving group.

Experimental Section

Materials. The SA amines and pyridines were purified as reported.⁸ The thionocarbonates **1** and **2** were prepared as described elsewhere.^{3,9,10}

O-Ethyl thiocarbamates of piperidine and morpholine (one of the products of the reactions of these amines with thionocarbonate **2**) were prepared as described elsewhere;¹¹ *O*-phenyl thiocarbamates of piperidine and morpholine (products in the reactions of **1**) were synthesized by the reaction of *O*-phenyl chlorothioformate with the corresponding amines, as reported.¹²

Kinetic Measurements. These were carried out spectrophotometrically by following the production of 2,4-dinitrophenoxide ion at 400 nm. The reactions were studied in aqueous solutions, at 25.0 ± 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_{obsd}) were found throughout, by means of the spectrophotometer kinetic software for first-order reactions. The experimental conditions of the reactions and the k_{obsd} values obtained are shown in Tables S1–S3 (pages S2–S4 in the Supporting Information). The initial substrate concentration was 3×10^{-5} M in all the reactions.

Product Studies. In the reactions of thionocarbonates **1** and **2**, 2,4-dinitrophenoxide anion was identified as one of the reaction products, by comparison of the UV–vis spectra after completion of these reactions with that of an authentic sample of 2,4-dinitrophenol under the same reaction conditions.

In the reactions of thionocarbonate **2** with piperidine and morpholine, the presence of the corresponding *O*-ethyl thiocarbamates in the reaction media was determined by HPLC, as reported previously.¹³

The *O*-phenyl thiocarbamates of piperidine and morpholine were identified as the final products of the reactions of **1** 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.^{2,4}

Results and Discussion

The rate law obtained for all the reactions under study is given by eqs 1 and 2, where DNP is 2,4-dinitrophenyl

(4) Castro, E. A.; Santos, J. G.; Téllez, J.; Umaña, M. I. *J. Org. Chem.* **1997**, *62*, 6568.

(5) Castro, E. A.; García, P.; Leandro, L.; Quesieh, N.; Rebolledo, A.; Santos, J. G. *J. Org. Chem.* **2000**, *65*, 9047. Castro, E. A.; Leandro, L.; Quesieh, N.; Santos, J. G. *J. Org. Chem.* **2001**, *66*, 6130. Castro, E. A.; Gálvez, A.; Leandro, L.; Santos, J. G. *J. Org. Chem.* **2002**, *67*, 4309.

(6) Castro, E. A.; Ibáñez, F.; Salas, M.; Santos, J. G.; Sepúlveda, P. *J. Org. Chem.* **1993**, *58*, 459.

(7) Castro, E. A.; Aliaga, M.; Campodonico, P.; Santos, J. G. *J. Org. Chem.* **2002**, *67*, 8911.

(8) (a) Bond, P. M.; Castro, E. A.; Moodie, R. B. *J. Chem. Soc., Perkin Trans. 2* **1976**, 68. (b) Castro, E. A.; Ureta, C. *J. Org. Chem.* **1989**, *54*, 2153.

(9) Castro, E. A.; Pavez, P.; Santos, J. G. *J. Org. Chem.* **2003**, *68*, 6192.

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

(11) Herrera, M.; Ruiz, V. M.; Valderrama, J. A.; Vega, J. C. *An. Quim., Ser. C* **1980**, *76*, 183.

(12) Newman, M. S.; Karnes, H. A. *J. Org. Chem.* **1966**, *31*, 3980.

TABLE 1. Values of pK_a for the Conjugate Acids of Pyridines and k_N for the Pyridinolysis of Thionocarbonate **1**^a

pyridine substituent	pK_a	$k_N/s^{-1} M^{-1}$
4-(dimethylamino)	9.87	160 ± 16
4-amino	9.37	48 ± 7
3,4-dimethyl	6.77	19 ± 3
4-methyl	6.25	6.7 ± 1
3-methyl	5.86	2.9 ± 0.5
H-	5.37	1.1 ± 0.1
3-carbamoyl	3.43	0.013 ± 0.002

^a Both the k_N and pK_a values were obtained in aqueous solution, at 25.0 °C, ionic strength 0.2 M (KCl).

TABLE 2. Values of pK_a for the Conjugate Acids of SA Amines and k_N for the Reactions of SA Amines with Thionocarbonates **1** and **2**^a

SA amine	pK_a	$k_N/s^{-1} M^{-1}$	
		1	2
piperidine	11.24	6.2 ± 0.3	9.5 ± 0.4
piperazine	9.94	6.4 ± 0.2	8.3 ± 0.3
1-(2-hydroxyethyl)piperazine	9.38	2.9 ± 0.1	4.0 ± 0.1
morpholine	8.78	1.8 ± 0.1	3.4 ± 0.1
1-formylpiperazine	7.98	0.75 ± 0.08	1.8 ± 0.1
piperazinium ion	5.81	0.10 ± 0.01	0.27 ± 0.01

^a The rate constants and pK_a determinations were carried out in aqueous solution, at 25.0 °C, ionic strength 0.2 M (KCl).

and S and N represent the substrate and an amine, respectively.

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

$$k_{\text{obsd}} = k_N[\text{N}] \quad (2)$$

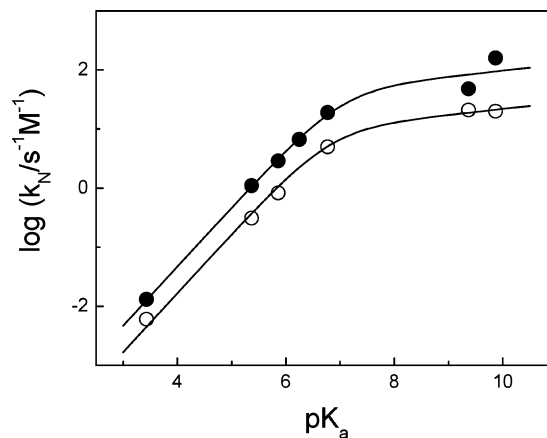
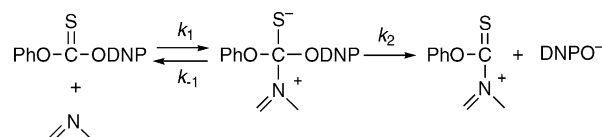
Linear plots of k_{obsd} vs $[\text{N}]$ at constant pH were found for the reactions of all amines with both substrates, with the slopes (k_N) independent of pH. The k_N values are shown in Table 1 for the reactions of pyridines and in Table 2 for the reactions of SA amines. The linear plots for the SA aminolysis of thionocarbonate **2** are in marked contrast to the nonlinear upward k_{obsd} vs $[\text{N}]$ plots found for the SA aminolysis of ethyl and methyl 4-nitrophenyl thionocarbonates.^{1,2}

With the pK_a values of the conjugate acids of pyridines and the k_N values for the pyridinolysis of **1** (Table 1), the Brønsted-type plot shown in Figure 1 was obtained. For comparison, this figure also includes the corresponding plot for the pyridinolysis of **2**.³ The Brønsted line for the reactions of **1** with pyridines was calculated by eq 3^a

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

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

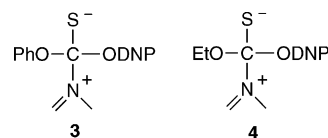
based on the existence of a zwitterionic tetrahedral intermediate (T^\ddagger) on the reaction path and a change in the rate-determining step, from breakdown to formation of T^\ddagger , as the amine becomes more basic.⁸ This mechanism is shown in Scheme 1, where DNP is 2,4-dinitrophenyl and N represents a pyridine. An analogous equation was derived by Gresser and Jencks.¹⁴ By nonlinear least-squares fitting, the following parameters were found: β_1

**FIGURE 1.** Brønsted-type plots for the reactions of pyridines with **1** (●, this work) and **2** (○, ref 3) in aqueous solution, at 25.0 °C and an ionic strength of 0.2 M (KCl).**SCHEME 1**

$= 0.1 \pm 0.1$ (slope at high pK_a), $\beta_2 = 1.0 \pm 0.1$ (slope at low pK_a) and $pK_a^0 = 7.0 \pm 0.2$ (pK_a value at the curvature center).

The value of $\beta_1 = 0.1$ is in agreement with previous ones obtained for similar aminolyses when the k_1 step of Scheme 1 is rate-determining (typical values are 0.1–0.3),^{1–8,14} and the value of $\beta_2 = 1.0$ is in line with the Brønsted slopes for analogous reactions when the k_2 step is rate-limiting (typical values are 0.8–1.1).^{2,6–8,13,14}

From a comparison of the Brønsted-type plots obtained in the pyridinolysis of **1** and **2**,³ shown in Figure 1, three observations can be made: (i) The values of k_1 (k_N values at high pK_a) are larger for the reactions of **1**; this can be attributed to a greater electron-withdrawing effect of phenoxy in **1**, compared to ethoxy in **2**, which would leave the former thiocarbonyl carbon more prone to a nucleophilic attack by the amine. (ii) The thionocarbonate **1** is also more reactive toward pyridines than **2** when the breakdown to products of the corresponding tetrahedral intermediate (T^\ddagger) is the rate-determining step. In this case $k_N = k_1 k_2 / k_{-1}$. It is known that inductive electron withdrawal by the nonleaving substituent in T^\ddagger decreases the k_2/k_{-1} ratio.^{14,15} This means that this ratio should be smaller for the reactions of **1**, since PhO in the tetrahedral intermediate **3** is more electron withdrawing induc-



tively than EtO in intermediate **4** ($\sigma_1 = 0.37$ and 0.26,

(13) Cabrera, M.; Castro, E. A.; Salas, M.; Santos, J. G.; Sepúlveda, P. *J. Org. Chem.* **1991**, *56*, 5324.

(14) Gresser, M. J.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 6963, 6970.

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

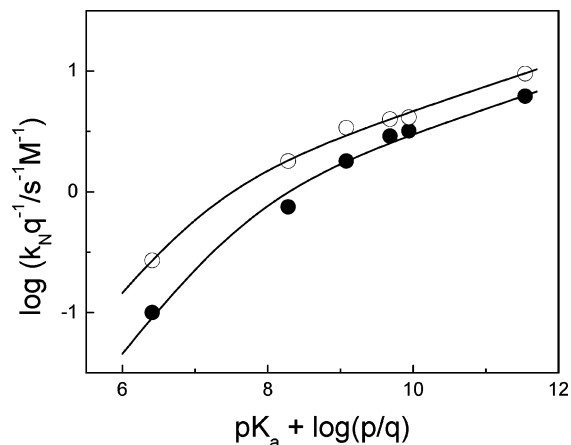


FIGURE 2. Brønsted-type plots (statistically corrected) for the reactions of SA amines with **1** (●) and **2** (○) in aqueous solution, at 25.0 °C and an ionic strength of 0.2 M (KCl).

respectively).¹⁶ Therefore, the greater k_N values for the pyridinolysis of **1** (compared to **2**) should be due to the much larger k_1 values for **1**, which are only partially counterbalanced by the smaller values of the k_2/k_{-1} ratio for the reactions of **1**. (iii) The center of the Brønsted curvature (pK_a^0) for the pyridinolysis of **1** ($pK_a^0 = 7.0$) is larger than that for the reactions of the same amines with **2** ($pK_a^0 = 6.8$).³ This result can be explained by the larger k_{-1}/k_2 ratio for intermediate **3** (relative to that for **4**), since it is known that $\log(k_{-1}/k_2)$ is linearly dependent on pK_a^0 .¹⁷

Figure 2 shows the Brønsted-type plots (statistically corrected) for the reactions of SA amines with thionocarbonates **1** and **2**. The statistical parameter q is the number of equivalent basic sites in the free amine and p is the number of equivalent protons in the conjugate acid of the amine.^{8b,18} The statistical corrections are $q = 2$ for piperazine, $p = 4$ for the conjugate acid of piperazinium cation, and $p = 2$ for the conjugate acids of the other SA amines.^{8b,18}

The curved lines in Figure 2 were obtained as for the reactions of pyridines (see above), with $\beta_1 = 0.2 \pm 0.1$ and $\beta_2 = 0.8 \pm 0.1$ for both reaction series and $pK_a^0 = 7.7 \pm 0.3$ and 7.0 ± 0.2 for the reactions of **1** and **2**, respectively. As discussed above, the β_1 and β_2 values are in accordance with the corresponding ones obtained for the stepwise aminolysis of similar compounds.^{1–8,13,14}

The larger pK_a^0 value for the reactions of SA amines with **1**, compared with that for the reactions of **2**, is in agreement with the larger σ_1 value for PhO than EtO, as discussed above. The larger pK_a^0 values for the reactions of SA amines with **1** and **2**, compared with those for the pyridinolysis of the corresponding substrates ($pK_a^0 = 7.0$ and 6.8 , respectively) can be attributed to the greater nucleofugality from the intermediate T^\ddagger of SA amines relative to isobasic pyridines.¹⁹ This means a larger k_{-1} value for an SA amine from intermediates **5**

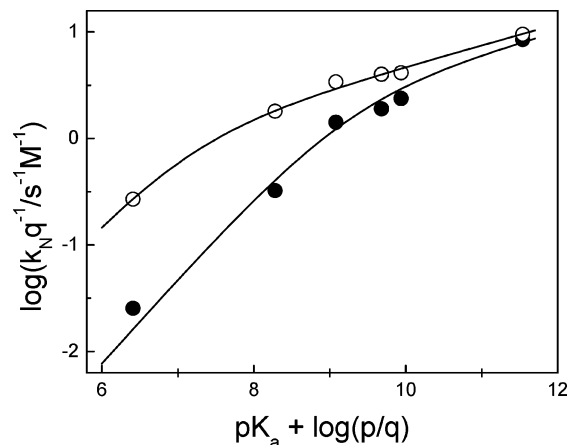
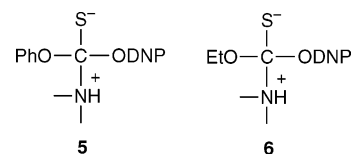


FIGURE 3. Brønsted-type plots for the reactions of SA amines with **2** (○, this work) and EDNPDTC (●, ref 6) in aqueous solution, at 25.0 °C and an ionic strength of 0.2 M (KCl).

and **6** than for an isobasic pyridine from intermediates



3 and **4**, respectively. Since the amine basicity and nature should not affect the rate of expulsion of the leaving group (k_2) from the zwitterionic tetrahedral intermediate,¹⁴ the k_{-1}/k_2 ratios for SA amines from **5** and **6** should be larger than those for isobasic pyridines from **3** and **4**, respectively. As discussed above, this means larger pK_a^0 values for the SA aminolysis of **1** and **2** compared with their corresponding pyridinolysis.

Contrary to what is observed for the pyridinolysis of thionocarbonates **1** and **2**, the latter substrate is more reactive than **1** toward SA amines. This could be explained by assuming that the phenyl group in **1** offers steric hindrance to SA attack, which may not be so important for pyridine attack. This could be due to the fact that pyridines are planar structures and SA amines are not. In other words, steric effects may be more important than electronic effects for SA aminolysis, whereas the opposite seems to be true for pyridinolysis.

The stepwise mechanisms found for the reactions of SA amines with thionocarbonates **1** and **2** are in agreement with the stepwise phenolysis of **1** and *O*-methyl *O*-(2,4-dinitrophenyl) thiocarbonate.^{9,20} This is because the change of an amino moiety in a tetrahedral intermediate by an aryloxy group destabilizes the intermediate.⁹ If the phenolysis of the above thionocarbonates is stepwise, it is more likely that the aminolysis of these substrates be driven by a stepwise mechanism.

For the reactions of SA amines with *O*-ethyl 2,4-dinitrophenyl dithiocarbonate (EDNPDTC),⁶ a nonlinear biphasic Brønsted-type plot has been found, with the following parameters: $\beta_1 = 0.2$, $\beta_2 = 0.8$, and $pK_a^0 = 9.2$. This has been attributed to a stepwise mechanism through a zwitterionic tetrahedral intermediate.⁶ Figure 3 shows the Brønsted-type plot obtained for the reactions of SA amines with EDNPDTC.⁶ For comparison reasons, the corresponding plot for the reactions of the same amines with **2** is also shown in Figure 3.

(16) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165.

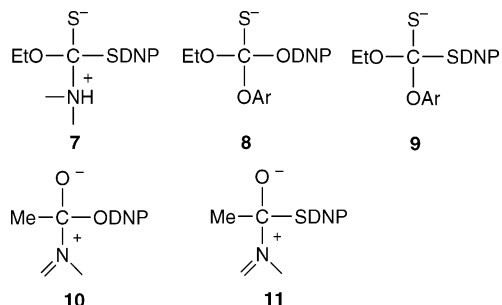
(17) Castro, E. A.; Araneda, C. A.; Santos, J. G. *J. Org. Chem.* **1997**, *62*, 126.

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

(19) Castro, E. A.; Ureta, C. *J. Chem. Soc., Perkin Trans. 2* **1991**, 63.

From Figure 3 three observations can be made:

(i) The pK_a value at the curvature center (pK_a^0) is larger for the SA aminolysis of the dithiocarbonate (EDNPDTC) than the thionocarbonate ($pK_a^0 = 9.2$ and 7.0 , respectively). This means that for a given SA amine the ratio k_{-1}/k_2 should be larger for tetrahedral intermediate **7** than for intermediate **6** (see above). This fact



suggests that 2,4-dinitrophenoxide ($DNPO^-$) leaves faster from intermediate **6** than 2,4-dinitrobenzenethiolate ($DNPS^-$) from **7** (k_2 larger for **6**). This result is surprising on the basis of the basicity of the leaving groups involved (pK_a values of $DNPOH$ and $DNPSH$ are 4.1 and 3.4 , respectively).¹⁹ Nonetheless, it is known that ArO^- is a better leaving group than an *isobasic* $Ar'S^-$;²¹ therefore, it is possible that $DNPO^-$ leaves faster from **6** than $DNPS^-$ from **7**. In contrast, $DNPO^-$ leaves at similar rates than $DNPS^-$ from intermediates **8** and **9**, respectively, formed in the phenolysis of **2** and EDNPDTC, respectively,⁹ and $DNPO^-$ leaves *slower* than $DNPS^-$ from intermediates **10** and **11**, respectively, formed in the pyridinolysis of the corresponding acetates.^{9,19} These contrasting results illustrate the influence on the k_{-1}/k_2 ratio of the other groups of an intermediate, as discussed by Gresser and Jencks.¹⁴

(ii) The k_N values are similar for the reactions of the two substrates with piperidine. Since the pK_a value for this amine is larger than that of pK_a^0 , the formation of the zwitterionic tetrahedral intermediate (T^\ddagger) is rate-limiting for these reactions, and $k_N = k_1$. The similar rate constants for formation of T^\ddagger is in line with the similar structures of the substrates involved.

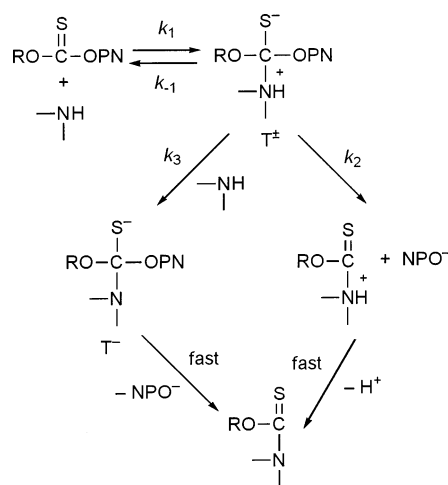
(iii) For SA amines whose pK_a are lower than pK_a^0 , the decomposition of T^\ddagger to products (k_2 step) is rate-determining and $k_N = K_1 k_2$. It can be seen in Figure 3 that the k_N values for the reactions of these amines with **2** are larger than those for EDNPDTC. Since the k_1 values are similar for both reactions, it follows that the k_2/k_{-1} ratio for intermediate **6** is larger than that for intermediate **7**, which agrees with the conclusions concerning point i.

It has been found that the reactions of SA amines with phenyl and methyl 2,4-dinitrophenyl carbonates are driven by a concerted mechanism,⁷ in contrast to the same aminolysis of **1** and **2**, which shows a stepwise path (this work). This indicates that substitution of S^- in the tetrahedral intermediate **5** or **6** by O^- destabilizes this intermediate to the point of a mechanistic change.²⁰

(20) It has been shown that the change of methoxy to ethoxy in a zwitterionic tetrahedral intermediate does not affect either the k_{-1} or the k_2 values or the stability of the intermediate in a significant manner.³

(21) Douglas, K. T.; Alborz, M. *J. Chem. Soc., Chem. Commun.* **1981**, 551. Douglas, K. T. *Acc. Chem. Res.* **1986**, *19*, 186.

SCHEME 2



The above result is in agreement with the fact that the reactions of SA amines with *S*-(2,4-dinitrophenyl) and *S*-(2,4,6-trinitrophenyl) *O*-ethyl thiolcarbonates are concerted,²² whereas the reactions of the same amines with *S*-(2,4-dinitrophenyl) and *S*-(2,4,6-trinitrophenyl) *O*-ethyl dithiocarbonates are stepwise.⁶ The destabilization of a tetrahedral intermediate by substitution of S^- by O^- has been explained by the greater ability of O^- in the intermediate to form a double bond and expel a nucleofuge, compared to S^- , due to the stronger π -bonding energy of the carbonyl group relative to thiocarbonyl.²³ The higher stability of a tetrahedral intermediate with S^- compared with O^- is in agreement with the greater stabilization of *S,S*-acetals relative to *O,S*- and *O,O*-acetals²⁴ and the fact that the stability of other similar tetrahedral intermediates increases as the number of sulfur atoms attached to the central carbon increases.²⁵

For the reactions of SA amines with *O*-alkyl *O*-aryl thiocarbonates^{1,2} and *O,O*-diaryl thiocarbonates,^{2,4,5} where the leaving groups are 3- or 4-nitrophenoxide (NPO^-), a complex kinetic order in amine (between 1 and 2) was found. This behavior was explained by a mechanistic scheme (Scheme 2) involving two tetrahedral intermediates, one zwitterionic (T^\ddagger), formed by the attack of the amine at thiocarbonyl group, and the other anionic (T^-), resulting from the deprotonation of T^\ddagger by the corresponding parent amine.

This complex mechanism for the reactions of SA amines with alkyl nitrophenyl thionocarbonates is in marked contrast to the simpler scheme (without the k_3 step in Scheme 2) for the same aminolysis of thionocarbonates **1** and **2**. The difference of these mechanisms should be due to the superior leaving ability from the intermediate T^\ddagger of $DNPO^-$ (larger k_2) relative to NPO^- . On the other hand, it is known that the proton transfer from the intermediate T^\ddagger to the amine is thermodynamically

(22) Castro, E. A.; Ibáñez, F.; Salas, M.; Santos, J. G. *J. Org. Chem.* **1991**, *56*, 4819. Castro, E. A.; Salas, M.; Santos, J. G. *J. Org. Chem.* **1994**, *59*, 30.

(23) Hill, S. V.; Thea, S.; Williams, A. *J. Chem. Soc., Perkin Trans. 2* **1983**, 437.

(24) Satchell, D. P. N.; Satchell, R. S. *Chem. Soc. Rev.* **1990**, *19*, 55, and references therein.

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

favorable, and therefore, the k_3 value for these reactions is diffusion-controlled ($k_3 = 10^{10} \text{ s}^{-1} \text{ M}^{-1}$).^{1,2,4,5,26} The change of NPO to DNPO should render the intermediate T^\ddagger more acidic still, and therefore, the k_3 value should remain the same. In conclusion, the reason for this remarkably different mechanisms should be due to the fact that for the aminolysis of thionocarbonates **1** and **2** the inequality $k_2 \gg k_3[\text{NH}]$ applies, whereas for the

(26) Eigen, M. *Angew. Chem., Int. Ed. Engl.* **1964**, 3, 1. Ahrens, M. L.; Maass, G. *Angew. Chem., Int. Ed. Engl.* **1968**, 7, 818.

reactions of the thionocarbonates with NPO as nucleofuge, k_2 is similar to $k_3[\text{NH}]$.

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Supporting Information Available: Pages S2–S4 containing Tables S1–S3. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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