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Reactions of *O*-aryl *S*-aryl dithiocarbonates with secondary alicyclic amines in aqueous ethanol. Kinetics and mechanism

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The reactions of *O*-(4-methylphenyl) *S*-(4-nitrophenyl), *O*-(4-chlorophenyl) (4-nitrophenyl), *O*-(4-chlorophenyl) *S*-phenyl, and *O*-(4-methylphenyl) *S*-phenyl dithiocarbonates (1, 2, 3, and 4, respectively) with a series of secondary alicyclic (SA) amines are subjected to a kinetic investigation in 44 wt% ethanol-water, at 25.0 °C and an ionic strength of 0.2 M. The reactions are followed spectrophotometrically. Under amine excess, pseudo-first-order rate coefficients (k_{obs}) are found. For some of the reactions, plots of k_{obs} *vs.* free amine concentration at constant pH are linear but others are nonlinear upwards. This kinetic behavior is in accordance with a stepwise mechanism with two tetrahedral intermediates, one zwitterionic ($T^{\pm}$) and the other anionic (T^{-}). In some cases, there is a kinetically significant proton transfer from $T^{\pm}$ to an amine to yield T^{-}. Values of the rate micro constants k_1 (amine attack to form $T^{\pm}$), k_{-1} (its back step), k_2 (nucleofuge expulsion from $T^{\pm}$), and k_3 (proton transfer from $T^{\pm}$ to the amine) are determined for some reactions. The Brønsted plots for k_1 are linear with slopes $\beta_1 = 0.2$–0.4 in accordance with the slope values found when $T^{\pm}$ formation is the rate-determining step. The sensitivity of log k_1 and log k_{-1} to the pK_a of the amine, leaving and non-leaving groups are determined by a multiparametric equation. For the reactions of 1–4 with 1-formylpiperazine and those of 3 and 4 with morpholine the k_2 and k_3 steps are rate determining. Copyright © 2010 John Wiley & Sons, Ltd.

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Keywords: Brønsted plots; dithiocarbonates; kinetics; mechanisms; secondary alicyclic amines

INTRODUCTION

The kinetics and mechanisms of the aminolysis of *O*-alkyl *S*-aryl dithiocarbonates are well documented.[1–4] Among these reports are those of the reactions of *S*-(2,4-dinitrophenyl) and *S*-(2,4,6-trinitrophenyl) *O*-ethyl dithiocarbonates with pyridines and secondary alicyclic (SA) amines in water, which proceed by a stepwise mechanism, through a zwitterionic tetrahedral intermediate ($T^{\pm}$).[1] On the other hand, the reactions of *S*-(4-X-phenyl) *O*-ethyl dithiocarbonates (X = H, MeO, Me, and Cl) with SA amines have been found to take place through two tetrahedral intermediates, one zwitterionic ($T^{\pm}$), and the other anionic (T^{-}).[1] In contrast, the reactions of *S*-(2,4-dinitrophenyl) and *S*-(2,4,6-trinitrophenyl) *O*-ethyl dithiocarbonates with quinuclidines are driven by a concerted mechanism (single step, with no intermediate).[2]

On the other hand, the aminolysis of diaryl dithiocarbonates has received less attention.[5–8] The reactions of SA amines with *O*-phenyl *S*-(4-nitrophenyl) dithiocarbonate in aqueous ethanol have been shown to proceed through $T^{\pm}$ and T^{-} intermediates.[8] We have recently described the pyridinolysis of *O*-(4-methylphenyl) *S*-(4-nitrophenyl) dithiocarbonate (**1**), *O*-(4-chlorophenyl) *S*-(4-nitrophenyl) dithiocarbonate (**2**), and *O*-(4-chlorophenyl) *S*-phenyl dithiocarbonate (**3**) in aqueous ethanol, showing that these reactions are stepwise and occur through a $T^{\pm}$ intermediate.[6] Also, a kinetic and mechanistic study of the reactions of dithiocarbonates **1** and **2** with anilines has demonstrated the presence of the above two ($T^{\pm}$ and T^{-}) intermediates.[7]

In order to shed more light on the mechanisms of the aminolysis of diaryl dithiocarbonates, in this work we report a kinetic study of the reactions of dithiocarbonates **1**, **2**, **3** and *O*-(4-methylphenyl) *S*-phenyl dithiocarbonate (**4**) with a series of SA amines. By a comparison between the kinetic results obtained in this work and those in the pyridinolysis and anilinolysis of the same substrates and the aminolysis (SA amines) of related compounds, we evaluate the effect of the amine nature, the

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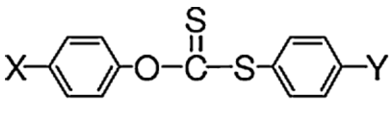
electrophile moiety, and the non-leaving and leaving groups of the substrates on the kinetics and mechanism.



1 X = Me ; Y = NO_2
2 X = Cl ; Y = NO_2
3 X = Cl ; Y = H
4 X = Me ; Y = H

RESULTS AND DISCUSSION

For all the reactions studied, under amine excess, pseudo-first-order rate constants (k_{obs}) were found. These were obtained by means of the kinetic software for first-order reactions of the spectrophotometer. The experimental conditions of the reactions and the values of k_{obs} are detailed in Supplementary Materials. The ranges of amine concentration and k_{obs} values are summarized in Tables 1–4.

Plots of k_{obs} against free amine concentration ([N]) show different behaviors depending on the amine basicity and the dithiocarbonate:

The reactions of **1**, **2**, and **3** with piperidine, those of **1** and **2** with piperazine and that of **2** with 1-(2-hydroxyethylpiperazine) show linear plots of k_{obs} against free amine concentration.

The reaction of **4** with 1-formylpiperazine shows a linear plot of k_{obs} against $[N]^2$.

For the reactions of **1**, **2**, and **3** with 1-formylpiperazine and those of **3** and **4** with morpholine, the plots of k_{obs} *vs.* [N] are in accordance with a second order polynomial equation.

The reactions of **3** and **4** with piperazine and 1-(2-hydroxyethyl)-piperazine, and those of **1** and **2** with morpholine, show nonlinear upwards plots of k_{obs} against [N]. The plots $[N]/k_{obs}$ *vs.* 1/[N] exhibit linear portions at high amine concentrations.

The different behavior exhibited by all these reactions can be explained by the mechanism shown in Scheme 1. A similar reaction mechanism has been obtained for the aminolysis (SA amines) of some *O*-alkyl *S*-aryl dithiocarbonates,[1] *O*-phenyl *S*-4-nitrophenyl dithiocarbonate,[8] alkyl aryl[1] and diaryl thionocarbonates,[5] and for the reactions of **1** and **2** with anilines.[7]

By application of the steady state condition to the tetrahedral intermediates $T^{\pm}$ and T^{-} in Scheme 1, Eqn (1) can be derived.

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

If $k_{-1} >> k_2 + k_3[N]$, Eqn (1) can be reduced to Eqn (2), where $K_1 = k_1/k_{-1}$. In this case, the plots correspond to a second order polynomial behavior, as was found in the reactions of **1**, **2**, and **3** with 1-formylpiperazine and those of **3** and **4** with morpholine. This is because these two amines are the least basic of the series and their nucleofugality from the intermediate $T^{\pm}$ (k_{-1}) is very large. In the particular case of the reaction of **4** with 1-formylpiperazine, the second order in amine term is much larger than that first order in amine, i.e., $k_3[N] >> k_2$ and $k_{obs} = K_1k_3[N]^2$.

$$k_{obs} = K_1k_2[N] + K_1k_3[N]^2 \tag{2}$$

On the other hand, if in Eqn (1) $k_2 + k_3[N] >> k_{-1}$, then Eqn (3) is obtained.

$$k_{obs} = k_1[N] \tag{3}$$

This is the case of the reactions of **2** with piperidine, piperazine, and 1-(2-hydroxyethyl)piperazine and those of **1** and **3** with piperidine. These amines are highly basic and it is reasonable that their nucleofugality from the intermediate $T^{\pm}$ (k_{-1}) is very low. This is why linear plots of k_{obs} *vs.* [N] were found for these reactions.

Table 1. Experimental conditions and k_{obs} values for the reactions of SA amines with *O*-(4-methylphenyl) 4-nitrophenyl dithiocarbonate (**1**)[a]

	pH	F_N[b]	$10^3[N]_{tot}$ (M)[c]	10^3k_{obs} (s^{-1})	No. of runs
Piperidine	10.52	0.33	3.43–34.3	1.22–9.56	6
	10.82	0.50	2.90–29.0	1.50–15.9	7
	11.12	0.67	2.47–24.7	2.20–18.5	7
Piperazine	9.41	0.33	4.58–38.9	0.926–9.72	6
	9.71	0.50	3.67–25.7	1.15–9.84	5
1-(2-Hydroxyethyl) piperazine	8.79	0.33	4.72–47.2	0.276–4.20	7
	9.09	0.50	4.34–80.6	0.277–9.66	10
	9.39	0.67	3.82–146	0.373–24.3	12
Morpholine	8.48	0.50	3.63–26.3	0.142–2.60	7
	8.78	0.67	3.50–121	0.230–15.2	11
	9.08	0.81	3.80–38.0	0.26–15.2	7
1-Formylpiperazine	7.33	0.33	5.71–57.1	0.0240–0.411	7
	7.63	0.50	6.39–160	0.0376–2.34	12
	7.93	0.67	5.79–160	0.0507–4.23	12

[a] In 44 wt% ethanol–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 2. Experimental conditions and k_{obs} values for the reactions of SA amines with *O*-(4-chlorophenyl) 4-nitrophenyl dithiocarbonate (**2**)[a]

	pH	F_N[b]	103[N]$_{tot}$ (M)[c]	$10^3 k_{obs}$ (s^{-1})	No. of runs
Piperidine	10.52	0.33	3.43–34.3	2.16–18.2	7
	10.82	0.50	2.92–29.2	2.62–27.6	7
	11.12	0.67	2.47–24.7	3.34–31.3	7
Piperazine	9.41	0.33	4.58–45.8	1.53–21.0	7
	9.71	0.50	3.67–36.7	1.93–27.2	7
	10.01	0.67	6.00–24.0	5.31–24.8	3
1-(2-Hydroxyethyl) piperazine	8.79	0.33	4.72–47.2	0.623–8.63	7
	9.09	0.50	4.34–80.6	0.661–20.7	10
	9.39	0.67	3.82–146	0.862–45.9	12
Morpholine	8.48	0.50	3.63–36.3	0.357–5.86	7
	8.78	0.67	3.50–143	0.546–46.6	11
	9.08	0.81	3.80–38.0	0.654–11.9	7
1-Formylpiperazine	7.33	0.33	5.71–57.1	0.0970–1.17	7
	7.63	0.50	6.40–53.9	0.122–1.56	7
	7.93	0.67	5.45–170	0.144–11.2	12

[a] In 44 wt% ethanol–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_{obs} values for the reactions of SA amines with *O*-(4-chlorophenyl) phenyl dithiocarbonate (**3**)[a]

	pH	F_N[b]	10^3[N]$_{tot}$ (M)[c]	$10^3 k_{obs}$ (s^{-1})	No. of runs
Piperidine	10.52	0.33	3.92–39.2	0.675–8.29	7
	10.82	0.50	4.18–41.8	1.56–15.8	7
	11.12	0.67	3.63–36.3	1.48–16.1	7
Piperazine	9.41	0.33	3.63–36.3	0.221–4.96	7
	9.71	0.50	4.71–47.1	1.72–12.6	6
	10.01	0.67	3.52–35.2	0.660–13.8	7
1-(2-Hydroxyethyl) piperazine	9.09	0.50	6.05–60.5	0.189–3.84	7
	9.39	0.67	5.79–57.9	0.373–5.43	7
Morpholine	8.48	0.50	5.95–50.6	0.138–3.21	6
	8.78	0.67	5.19–36.3	0.186–2.79	5
	9.08	0.81	5.50–46.8	0.283–5.67	6
1-Formylpiperazine	7.33	0.33	20.3–44.6	0.0680–0.215	3
	7.63	0.50	7.28–72.8	0.0364–0.680	7
	7.93	0.67	19.9–67.8	0.168–0.899	5

[a] In 44 wt% ethanol–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).

If experimentally the amine concentration is high enough, then $k_3[N] >> k_2$ and Eqn (1) can be simplified to Eqn (4), which by rearrangement leads to Eqn (5). If also $k_3[N] >> k_{-1}$ Eqn (4) transforms into Eqn (3).

$$k_{obs} = \frac{k_1 k_3 [N]^2}{(k_{-1} + k_3[N])} \tag{4}$$

$$\frac{[N]}{k_{obs}} = \frac{k_{-1}}{k_1 k_3 [N]} + \frac{1}{k_1} \tag{5}$$

For the reactions of **1**, **3**, and **4** with piperazine and 1-(2-hydroxyethyl)piperazine, and those of **1** and **2** with morpholine, Eqn (1) holds at low amine concentrations but at higher amine concentrations, the reaction conditions are described by Eqns (4) and (5). In accordance with Eqn (5), plots of $[N]/k_{obs}$ *vs.* $1/[N]$ are linear in the region where the amine concentration is high enough, but the plots exhibit a downward curvature as amine concentration decreases. Therefore, from the linear parts of the curved plots, the values of $1/k_1$ and k_{-1}/k_1k_3 were obtained from the intercept and slope, respectively.

In Scheme 1, the k_3 step corresponds to the proton transfer from the zwitterionic tetrahedral intermediate $T^{\pm}$ to the corresponding amine to give the anionic tetrahedral intermediate T^{-}. In order to determine the value of k_3, it is

Table 4. Experimental conditions and k_{obs} values for the reactions of SA amines with *O*-(4-methylphenyl) phenyl dithiocarbonate (**4**)[a]

	pH	F_N[b]	$10^3[N]_{tot}$ (M)[c]	10^3k_{obs} (s^{-1})	No. of runs
Piperidine	10.52	0.33	9.70–97.0	0.652–11.2	7
	10.82	0.50	9.83–98.3	1.25–19.4	7
	11.12	0.67	9.68–96.8	1.93–27.9	7
Piperazine	9.41	0.33	8.50–85.0	0.233–6.81	7
	9.71	0.50	8.60–86.0	0.314–12.2	7
	10.01	0.67	8.47–84.7	0.607–16.5	7
1-(2-Hydroxyethyl) piperazine	8.79	0.33	6.43–64.3	0.0285–1.03	7
	9.09	0.50	6.75–67.5	0.0486–2.08	7
	9.39	0.67	6.43–64.3	0.0584–2.66	7
Morpholine	8.18	0.33	11.9–119	0.0564–2.41	7
	8.48	0.50	11.1–94.3	0.0899–2.73	6
	8.78	0.67	10.9–109	0.112–5.05	7
1-Formylpiperazine	7.33	0.33	49.1–196	0.0306–0.392	6
	7.63	0.50	18.1–181	0.0263–0.521	7
	7.93	0.67	18.1–181	0.0301–1.15	7

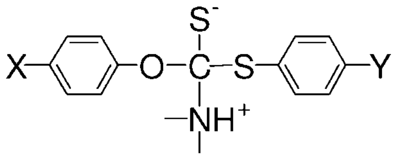
[a] In 44 wt% ethanol–water, at 25.0 °C, ionic strength 0.2 M (KCl).

[b] Free amine fraction.

[c] Concentration of total amine (free base plus protonated forms).

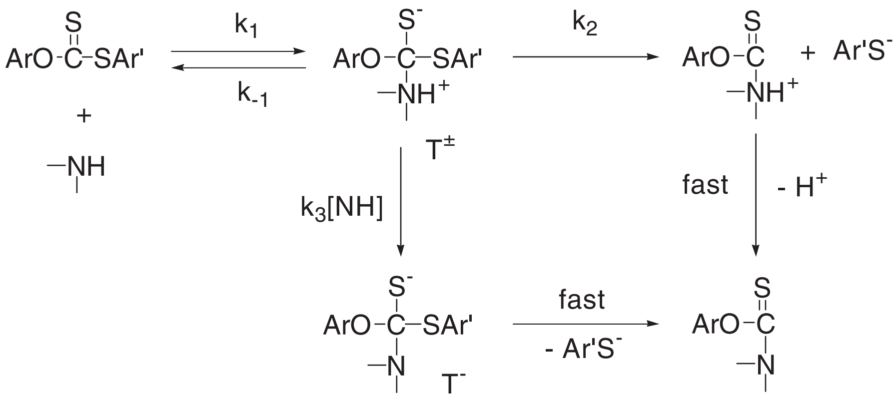
necessary to estimate the pK_a values of the corresponding $T^{\pm}$ intermediates.

For the tetrahedral intermediates $T^{\pm}$ derived from the reactions of **1** and **2** with anilines a pK_a value 5.4 and 6.0 units, respectively, lower than that of the respective amine has been estimated.[7] Since these values should be independent of the amine basicity and nature,[1] it means that the pK_a of the tetrahedral intermediates formed with SA amines (intermediates **5** and **6**) should also be 5.4 and 6.0 units, respectively, lower than that of the respective amine. Substitution of *S*-(4-nitrophenyl) in the intermediates **5** and **6** by the *S*-phenyl group yield the intermediates **8** and **7**, respectively. The pK_a of these species can be estimated by Jencks' method, which considers the Hammett inductive σ_I values for the substituents attached to the central carbon of a tetrahedral intermediate.[9,10] The σ_I values for *S*-phenyl and *S*-(4-nitrophenyl) are 0.30 and 0.36, respectively.[11] Using $\rho_I = -9.2$ for the Hammett inductive constant for the pK_a of the tetrahedral intermediates,[12] a pK_a for **8** and **7** of *ca.* 0.6 units larger than those of **5** and **6**, respectively, can be estimated. Therefore, the pK_a of intermediates **8** and **7** are 4.8 and 5.4 units lower, respectively, than those of the corresponding amine.



5 X = Me ; Y = NO_2
6 X = Cl ; Y = NO_2
7 X = Cl ; Y = H
8 X = Me ; Y = H

According to this estimation, the proton transfer from $T^{\pm}$ to the amine (k_3) must be thermodynamically favorable and, therefore,



Scheme 1.

Table 5. Values of k_1 obtained for the reactions of *O*-(4-methylphenyl) *S*-(4-nitrophenyl) dithiocarbonate (**1**), *O*-(4-chlorophenyl) *S*-(4-nitrophenyl) dithiocarbonate (**2**), *O*-(4-chlorophenyl) *S*-phenyl dithiocarbonate (**3**), and *O*-(4-methylphenyl) *S*-phenyl dithiocarbonate (**4**) with SA amines[a]

		k_1 (s^{-1} M^{-1})			
Amine	pK_a[b]	**1**	**2**	**3**	**4**
Piperidine	10.82	1.11[c]	1.86[c]	0.716[c]	0.528[d]
Piperazine	9.71	0.794[c]	1.51[c]	0.660[d]	0.375[d]
1-(2-Hydroxyethyl) piperazine	9.09	0.260[d]	0.481[c]	0.180[d]	0.0785[d]
Morpholine	8.48	0.210[d]	0.50[d]	—	—

[a] Values determined in 44 wt% ethanol–water, at 25.0 °C, ionic strength 0.2 M (KCl).
[b] Values of pK_a of the conjugate acid of the amine under the reaction conditions.
[c] Values of the slope of linear k_{obs} *vs.* [N] plots (Eqn (3)).
[d] Values of the reciprocal of the intercept of the linear portion of the [N]/k_{obs} *vs.* 1/[N] plots (Eqn (5)).

diffusion controlled.[8] A value of *ca.* 4×10^9 s^{-1} M^{-1} has been estimated for k_3 in 44 wt% ethanol–water.[7,8,13] It is noteworthy that this value is independent of the amine basicity and nature because the same amine that acts as a base is in the corresponding intermediate.[1]

Tables 5 and 6 summarize the k_1 and k_{-1} values obtained from Eqns (3) and (5) for some of the reactions studied.

Figure 1 shows the Brønsted plots for the k_1 values obtained for the reactions of the series of SA amines with dithiocarbonates **1**–**4** (Table 5). These plots are linear with slopes $\beta = 0.2$–0.4. The k_1 values, as well as those of the pK_a of the conjugate acids of these amines, were statistically corrected[1,14] with $q = 2$ for piperazine ($q = 1$ for all the other SA amines) and $p = 2$ for all the conjugate acids of the amines.[1] The parameter q is the number of equivalent basic sites in the free amine and p is the number of equivalent dissociable protons in the conjugate acid of the amine.[14]

The β values obtained for k_1 (Fig. 1) are in accordance with those found for similar stepwise reactions where the formation of $T^{\pm}$ is the rate determining step.[1,5]

With the k_1 corrected values obtained for the SA aminolysis of dithiocarbonates **1**–**4** (Table 5) and those for the same aminolysis of phenyl *S*-4-nitrophenyl dithiocarbonate,[8] and the corrected pK_a of the conjugate acid of the amines (pK_{Ncorr}), those of the

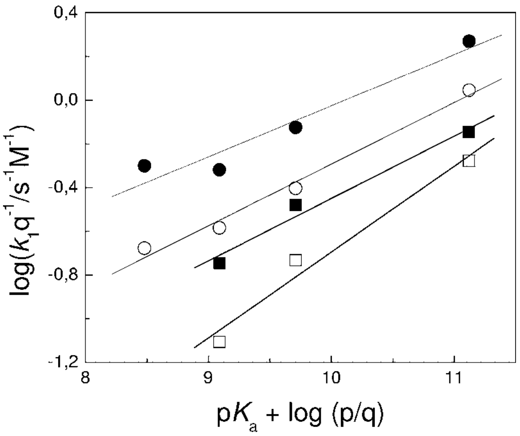


Figure 1. Brønsted-type plots (statistically corrected, see text) for the k_1 values obtained in the reactions of secondary alicyclic aminess with (○) *O*-(4-methylphenyl) *S*-(4-nitrophenyl) dithiocarbonate (**1**), (●) *O*-(4-chlorophenyl) *S*-(4-nitrophenyl) dithiocarbonate (**2**), (■) *O*-(4-chlorophenyl) *S*-phenyl dithiocarbonate (**3**), and (□) *O*-(4-methylphenyl) *S*-phenyl dithiocarbonate (**4**) in 44 wt% ethanol–water, at 25.0 °C, ionic strength 0.2 M (KCl)

Table 6. Values of k_{-1} obtained for the reactions of *O*-(4-methylphenyl) *S*-(4-nitrophenyl) dithiocarbonate (**1**), *O*-(4-chlorophenyl) *S*-(4-nitrophenyl) dithiocarbonate (**2**), *O*-(4-chlorophenyl) *S*-phenyl dithiocarbonate (**3**), and *O*-(4-methylphenyl) *S*-phenyl dithiocarbonate (**4**) with SA amines[a]

		$10^{-8}k_{-1}$ (s^{-1})			
Amine	pK_a[b]	**1**	**2**	**3**	**4**
Piperidine	10.82	—	—	—	1.05
Piperazine	9.71	—	—	0.314	1.9
1-(2-Hydroxyethylpiperazine	9.09	0.72	—	2.62	7.22
Morpholine	8.48	1.5	0.70	—	—

[a] Values of k_{-1}determined in 44 wt% ethanol–water, at 25.0 °C, ionic strength 0.2 M (KCl). These were determined from the slopes of the linear portion of [N]/k_{obs} *vs.* 1/[N] plots (Eqn (5)), with $k_3 = 4 \times 10^9$ s^{-1} M^{-1}(see text) and k_{-1} values in Table 5.
[b] Values of pK_a of the conjugate acid of the amine under the reactions conditions.

leaving (pK_{lg}) and the non-leaving (pK_{nlg}) groups, the multiparametric relationship shown in Eqn (6) ($n = 19$, $R^2 = 0.917$) was obtained. The β_N value (0.27) is in accordance with those found for stepwise mechanisms where the formation of the $T^{\pm}$ intermediate is the rate-determining step.

$$\log k_{1corr} = (0.6 \pm 0.6) + (0.27 \pm 0.03)pK_{Ncorr} - (0.22 \pm 0.05)\, pK_{nlg} - (0.23 \pm 0.03)\, pK_{lg} \qquad (6)$$

With the k_{-1} values of Table 6 and those for the SA aminolysis of phenyl *S*-4-nitrophenyl dithiocarbonate,[8] and the corrected pK_a of the conjugate acid of the SA amines and those of the leaving and non-leaving groups, Eqn (7) ($n = 13$, $R^2 = 0.815$) can be obtained.

$$\log k_{-1} = (6.3 \pm 1.8) - (0.66 \pm 0.11)pK_{Ncorr} + (0.47 \pm 0.16)pK_{nlg} + (0.49 \pm 0.1)pK_{lg} \qquad (7)$$

The negative value of β_N (-0.66) is in agreement with the fact that the more basic is the amine (higher pK_a) the lower is its nucleofugality from the $T^{\pm}$ intermediate. The positive β values for the non-leaving and leaving groups (0.47 and 0.49, respectively) are in accordance with the results of Gresser and Jencks: the leaving ability of the amine from $T^{\pm}$ increases with electron donation (higher basicity) from these two groups.[15,16]

By nonlinear least-squares fitting to Eqn (2) of the kinetic results for the reactions of **1**–**3** with 1-formylpiperazine and **3** and **4** with morpholine, the values for the coefficients for first and second order in amine, K_1k_2 and K_1k_3, respectively, were obtained. These are summarized in Table 7.

The k_2 values obtained from the reactions of **1** and **2** with 1-formylpiperazine are similar to those obtained for their anilinolysis under the same experimental conditions: $(3 \pm 2) \times 10^8\ s^{-1}$ and $(4 \pm 2) \times 10^8\ s^{-1}$ for **1** and **2**, respectively.[7] This is in accordance with the finding that the nucleofugality of the leaving group from the $T^{\pm}$ intermediate is independent of the amine basicity and nature.[15] This is because the cationic amino moiety in $T^{\pm}$ cannot exert a push to expel the leaving group since it lacks an electron pair.[15] On the other hand, the k_2 values obtained for 4-nitrobenzenethiolate expulsion should be larger than those for benzenethiolate. As seen in Table 7, the k_2 values for **2** are larger than those for **3**. Nonetheless, the k_2 value for **1** is smaller than that for **4** (morpholine), which is not reasonable and could be due to the large errors involved in the determination of K_1k_2 and K_1k_3 for the reaction of **4** with morpholine. Another possibility, as one of the referees suggested, is that it could be due to 'perhaps some small changes in local solvation of some centers'.

Effect of the amine nature

The reactions of dithiocarbonates **1** and **2** with pyridines,[6] anilines,[7] and SA amines (this work) under the same experimental conditions were found to be stepwise, albeit with an important difference: the reactions with pyridines proceed through only one tetrahedral intermediate ($T^{\pm}$), while in the reactions with SA amines and anilines two tetrahedral intermediates, the zwitterionic ($T^{\pm}$) and the anionic (T^{-}), are formed. The absence of the intermediate T^{-} in the reactions with pyridines is obvious since these tertiary amines lack a proton and, therefore, the proton transfer from $T^{\pm}$ to the amine is impossible.

In the studied reactions of **1**–**3** with 1-formylpiperazine and of **3** and **4** with morpholine, the formation of $T^{\pm}$ is an equilibrium step, as is in the anilinolysis of **1** and **2**.[7] This should be due to the weak basicity of these amines (pK_a for 1-formylpiperazine and morpholine are 7.63 and 8.48, respectively, and for anilines the pK_a range covered was 4.3–6.5), which means high nucleofugality from the $T^{\pm}$ intermediate (large k_{-1} value). Therefore, the condition $k_{-1} >> k_2 + k_3[N]$ is satisfied and Eqn (1) reduces to Eqn (2), which implies an equilibrium between reactants and $T^{\pm}$. Exceptions to this are the reactions carried out at very high amine concentrations, where both terms are comparable.

Effect of the leaving and non-leaving groups

The k_1 values are larger for the reactions of **1** and **2** than those of **4** and **3**, respectively. These results are reasonable in the light of the larger electron withdrawing effect of the 4-nitrobenzenethio group in the two former dithiocarbonates compared with the benzenethio group in the latter compounds. This leaves more positive the thiocarbonyl carbon atom of **1** and **2**, and, therefore, more prone to the amine attack.

On the other hand, the negative values for the sensitivity of the non-leaving and leaving groups on k_1 obtained ($\beta_{nlg} = -0.22$ and $\beta_{lg} = -0.23$) are reasonable since as the pK_a of the leaving and non-leaving groups increases, there is less electron-withdrawal

Table 7. Values of K_1k_2, K_1k_3, K_1, and k_2 obtained for some of the reactions of *O*-4-methylphenyl *S*-4-nitrophenyl dithiocarbonate (**1**), *O*-4-chlorophenyl *S*-4-nitrophenyl dithiocarbonate (**2**), *O*-(4-chlorophenyl) *S*-phenyl dithiocarbonate (**3**), and *O*-(4-methylphenyl) *S*-phenyl dithiocarbonate (**4**) with some SA amines[a,b,c]

Amine	Substrate	$10^3K_1k_2$ ($s^{-1}\,M^{-1}$)	$10^2K_1k_3$ ($s^{-1}\,M^{-2}$)	$10^{11}K_1$ (M^{-1})	$10^{-8}k_2$ (s^{-1})
Morpholine	**4**	38 ± 6	45 ± 8	11.3	3.4
Morpholine	**3**	80 ± 10	200 ± 30	50	1.6
1-Formylpiperazine	**1**	10 ± 2	26 ± 2	6.5	1.5
1-Formylpiperazine	**2**	40 ± 2	50 ± 2	13	3.2
1-Formylpiperazine	**3**	12 ± 2	18 ± 5	4.5	2.7
1-Formylpiperazine	**4**	—	7.5 ± 0.2	1.9	—

[a] The values of K_1k_2 and K_1k_3 were determined in 44 wt% ethanol–water, at 25 °C and ionic strength 0.2 M (KCl), by fitting of the experimental data to Eqn (2).

[b] The values of K_1 were calculated by dividing K_1k_3 by $k_3 = 4 \times 10^9\ s^{-1}\,M^{-1}$ (see text).

[c] The values of k_2 were calculated by dividing K_1k_2 by K_1.

from them and the thiocarbonyl carbon of the substrate becomes less positive and less susceptible to the amine attack. It is noteworthy that the values of β_{nlg} and β_{lg} are very similar. This means that the electronic abilities from these two groups in the substrate have a similar effect on the charge of the thiocarbonyl carbon.

The reactions of SA amines with **1** show the same mechanism as that exhibited by the same aminolysis of 4-methylphenyl 4-nitrophenyl thionocarbonate, under the same experimental conditions.[17] In fact, in both reactions the corresponding zwitterionic tetrahedral intermediate ($T^{\pm}$) transfers a proton to the amine to form the anionic intermediate (T^{-}). For both reactions, the k_3[N] values are comparable with those of k_2 despite the larger value of the rate constant k_2 for expulsion of 4-nitrobenzenethiolate, relative to 4-nitrophenoxide, from the corresponding intermediate $T^{\pm}$ (the k_2 values are $1.5 \times 10^8\ s^{-1}$ (this work) and *ca.* $1 \times 10^7\ s^{-1}$, respectively).[17]

The k_1 values for the reactions of 4-methylphenyl 4-nitrophenyl thionocarbonate with a given SA amine are 2 to 6 times larger than those of **1** with the same amine, probably due to the larger electron withdrawing effect of 4-nitrophenoxy relative to 4-nitrobenzenethio.[11]

From Table 5 and Fig. 1 it can be observed that the k_1 values obtained for the reactions of SA amines with **2** and **3** are larger than those for **1** and **4**, respectively. These results can be explained by the larger electron-withdrawing effect of Cl than CH_3 from the non-leaving group, which leads to a more positive thiocarbonyl carbon in **2** and **3**, which in turn facilitates the nucleophilic attack by the amine.

The positive values for the sensitivity of $\log k_{-1}$ on the pK_a of both the non-leaving and leaving groups ($\beta_{nlg} = 0.47$ and $\beta_{lg} = 0.49$ in Eqn (7)) can be attributed to the fact that as the basicity (i.e., pK_a) of both groups in the intermediate $T^{\pm}$ increase, they can exert a better push to expel the amine from this intermediate.[15,16]

The reactions of SA amines with *O*-ethyl *S*-(4-nitrophenyl) dithiocarbonate in aqueous ethanol are driven by a stepwise mechanism, with the formation of only one tetrahedral intermediate ($T^{\pm}$).[18] Namely, there is no competition between leaving group expulsion from $T^{\pm}$ (k_2 step) and proton transfer from $T^{\pm}$ to the amine to give T^{-} (k_3 step). The former step is faster than the latter. The difference with the SA aminolysis of **1** and **2** (this work, where both $T^{\pm}$ and T^{-} are kinetically significant) can be explained by the superior push provided by EtO in the corresponding $T^{\pm}$,[16] compared with that by 4-MePhO or 4-ClPhO in the respective intermediates $T^{\pm}$, to expel the leaving group. Therefore, it is reasonable that for the reactions of the *O*-ethyl derivative, $k_2 >> k_3$[N].

Effect of the electrophilic group

The reactions of **2** with SA amines in aqueous ethanol are stepwise (this work). In contrast, the reactions of the same amines with *O*-(4-chlorophenyl) *S*-(4-nitrophenyl) thiolcarbonate, in the same experimental conditions, are concerted.[19] These results indicate that the change of thiocarbonyl as the electrophilic group by carbonyl destabilizes the tetrahedral intermediate $T^{\pm}$, changing the mechanism from stepwise to concerted. This destabilization can be attributed to the larger ability of O^{-} than S^{-} in $T^{\pm}$ to form the double bond with carbon due to the stronger π-bonding energy of the C=O group relative to C=S.[20] This should increase the expulsion rates of both the amine (k_{-1}) and the nucleofuge (k_2) from the putative tetrahedral intermediate.[1] The same effect of the electrophilic group was found for the SA aminolysis of *O*-ethyl *S*-(2,4-dinitrophenyl) dithiocarbonate[21] and *O*-ethyl *S*-(2,4-dinitrophenyl) thiolcarbonate,[22] both in water: the former reactions are stepwise whereas the latter are concerted.

CONCLUDING REMARKS

From the results obtained in this work, several conclusions can be drawn: (i) The mechanism of the aminolysis (SA amines) of dithiocarbonates **1**–**4** is stepwise, with two tetrahedral intermediates, one zwitterionic ($T^{\pm}$) and other anionic (T^{-}). (ii) Multiparametric equations are determined for the dependence of k_1 and k_{-1} on the pK_a of the conjugate acids of the nucleophile (pK_N) and the non-leaving (pK_{nlg}) and leaving (pK_{lg}) groups. (iii) Dithiocarbonates **2** and **3** are more reactive toward SA amines than **1** and **4**, respectively, due to the larger electron withdrawal of 4-chloro than 4-methyl in the non-leaving group. (iv) The reactions of SA amines with **1** show the same mechanism as that exhibited by the same aminolysis of 4-methylphenyl 4-nitrophenyl thionocarbonate, under the same experimental conditions. The larger value of the rate constant k_2 for expulsion of 4-nitrobenzenethiolate, relative to 4-nitrophenoxide, from the corresponding intermediate $T^{\pm}$ should be due to the lower basicity of the former. (v) The k_1 values for the SA aminolysis of **1** are 2–6 times smaller than those of the corresponding thionocarbonate due to the smaller electron withdrawal of 4-nitrobenzenethio than 4-nitrophenoxy. (vi) The reactions of **2** with SA amines in aqueous ethanol are stepwise (this work). In contrast, the reactions of the same amines with *O*-(4-chlorophenyl) *S*-(4-nitrophenyl) thiolcarbonate, under the same experimental conditions, are concerted. These results indicate that the change of thiocarbonyl as the electrophilic group by carbonyl destabilizes the tetrahedral intermediate $T^{\pm}$, changing the mechanism from stepwise to concerted. (vii) The reactions of ethyl *S*-(4-nitrophenyl) dithiocarbonate with SA amines proceed by a stepwise mechanism with formation of the intermediate $T^{\pm}$ only. The change of *O*-ethyl by *O*-aryl as the non-leaving group diminishes the push exerted by this group to expel the nucleofuge. Therefore, the rate constant k_2 becomes smaller and comparable with the rate constant for deprotonation of the $T^{\pm}$ intermediate (k_3). (viii) The k_2 values obtained for the reactions of **1** and **2** with 1-formylpiperazine are similar to those obtained for their anilinolysis under the same experimental conditions, in accordance with the finding that the nucleofugality of the leaving group from the $T^{\pm}$ intermediate is independent of the amine basicity and nature.

EXPERIMENTAL

Materials

Dithiocarbonates **1**, **2**, and **3** were synthesized as described.[6] *O*-(4-methylphenyl) *S*-phenyl dithiocarbonate (**4**) was synthesized by the reaction of phenyl chlorodithioformate with 4-methylphenoxide, as previously described for the preparation of dithiocarbonate **3**.[6] The solid product **4** showed the following characteristics: m.p. 62–63 °C (lit[23] 59.5–60.5 °C); ^{1}H NMR (400 MHz, CDCl$_3$) δ_H 7.60 (m, 2H), 7.50 (m, 3H), 7.30 (d, $J = 8.2$ Hz, Hz, 2H), 6.96 (d, $J = 8.5$ Hz, 2H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 21.0, 117.9, 121.6, 129.5, 130.1, 130.3, 135.2, 136.5, 152.4, 214.5.

Kinetic measurements

The kinetics of the reactions were analyzed through a diode array spectrophotometer in 44 wt% ethanol–water, at 25.0 ± 0.1 °C and an ionic strength of 0.2 M (maintained with KCl). The reactions of dithiocarbonates **1** and **2** were followed at 420 nm (appearance of 4-nitrobenzenethiolate anion), and those of **3** and **4** at 260 nm (appearance of the corresponding aryl thionocarbamate).

The reactions were studied under at least 10-fold amine excess over the substrate, the initial concentration of the latter being 2.5×10^{-5} M. Under these conditions pseudo-first-order rate coefficients (k_{obs}) were found throughout, the reactions being followed for at least five half-lives.

For all the reactions, the pH was maintained constant (two or three pH values for each amine) by the buffer formed by partial protonation of the amine. The experimental conditions of the reactions and the values of k_{obs} are detailed in Supplementary Materials. The ranges of amine concentration and k_{obs} values are summarized in Tables 1–4.

Product studies

In the reactions of dithiocarbonates **1** and **4** with morpholine and piperazine, the corresponding 4-methylphenyl thionocarbamates were found as final products. Also, 4-nitrobenzenethiolate ion was identified as one of the products of the reactions of **1** and **2**. These identifications were carried out by comparison of the UV-vis spectra after completion of these reactions with those of authentic samples, under the same reaction conditions.

For the reactions of dithiocarbonates **2** and **3** with piperidine and morpholine, the corresponding 4-chlorophenyl thionocarbamates were identified as one of the products by comparing the final UV-vis spectra of the reactions with those of the product of the reactions of 4-chlorophenyl chlorothionoformate with the same amines under the same experimental conditions ($\lambda_{max} = 260$ nm).

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REFERENCES

[1] E. A. Castro, *Chem. Rev.* **1999**, *99*, 3505–3524.
[2] E. A. Castro, M. Gazitua, P. Rios, P. Tobar, J. G. Santos, *J. Phys. Org. Chem.* **2009**, *22*, 443–448.
[3] H. K. Oh, J. Y. Lee, J. W. Yun, Y. S. Park, I. Lee, *Int. J. Chem. Kinet.* **1998**, *30*, 419–423.
[4] H. K. Oh, J. Y. Oh, D. D. Sung, I. Lee, *Collect. Czech. Chem. Commun.* **2004**, *69*, 2174–2182.
[5] E. A. Castro, *J. Sulfur Chem.* **2007**, *28*, 401–429.
[6] E. A. Castro, M. Gazitua, J. G. Santos, *J. Phys. Org. Chem.* **2009**, *22*, 1003–1008.
[7] E. A. Castro, M. Gazitua, J. G. Santos, *J. Phys. Org. Chem.* **2010**, *23*, 176–180.
[8] E. A. Castro, L. Leandro, J. G. Santos, *Int. J. Chem. Kinet.* **1999**, *31*, 839–845.
[9] J. M. Sayer, W. P. Jencks, *J. Am. Chem. Soc.* **1973**, *95*, 5637–5649.
[10] J. P. Fox, W. P. Jencks, *J. Am. Chem. Soc.* **1974**, *96*, 1436–1449.
[11] C. Hansh, A. Leo, R. W. Taft, *Chem. Rev.* **1991**, *91*, 165–195.
[12] P. J. Taylor, *J. Chem. Soc. Perkin Trans. 2* **1993**, 1423–1427.
[13] E. A. Castro, M. Cabrera, J. G. Santos, *Int. J. Chem. Kinet.* **1995**, *27*, 49–57.
[14] R. P. Bell, *The Proton in Chemistry*, Methuen, London, **1959**. p 159.
[15] M. J. Gresser, W. P. Jencks, *J. Am. Chem. Soc.* **1977**, *99*, 6963–6970.
[16] M. J. Gresser, W. P. Jencks, *J. Am. Chem. Soc.* **1977**, *99*, 6970–6980.
[17] E. A. Castro, P. Garcia, L. Leandro, N. Quesieh, A. Rebolledo, J. G. Santos, *J. Org. Chem.* **2000**, *65*, 9047–9053.
[18] E. A. Castro, G. Muñoz, M. Salas, J. G. Santos, *Int. J. Chem. Kinet.* **1995**, *27*, 987–995.
[19] E. A. Castro, M. Aliaga, J. G. Santos, *J. Phys. Org. Chem.* **2008**, *21*, 271–278.
[20] S. V. Hill, S. Thea, A. Williams, *J. Chem. Soc. Perkin Trans. 2* **1983**, 437–446.
[21] E. A. Castro, F. Ibañez, M. Salas, J. G. Santos, P. Sepulveda, *J. Org. Chem.* **1993**, *58*, 459–463.
[22] E. A. Castro, F. Ibañez, M. Salas, J. G. Santos, *J. Org. Chem.* **1991**, *56*, 4819–4821.
[23] Y. Araki, *Bull. Chem. Soc. Jpn.* **1970**, *43*, 252–257.