

Structure-Reactivity Relationships in the Aminolysis of *O*-Ethyl *S*-Aryl Dithiocarbonates in Aqueous Solution

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The reactions of *O*-ethyl *S*-(*X*-phenyl) dithiocarbonates (*X* = *p*-Cl, *p*-Me, and *p*-MeO) with a series of secondary alicyclic amines and those of the same substrates and analogous derivatives (*X* = H, *p*-NO₂, and 2,4-(NO₂)₂) with pyrrolidine are subjected to a kinetic study in water, 25.0 °C, ionic strength 0.2 M (KCl). The reactions of piperidine and pyrrolidine show second-order kinetics (first order in amine) with the formation of a zwitterionic tetrahedral intermediate (T[±]) as the rate-determining step. The reactions of the other amines exhibit orders in amine different from one, compatible with the presence of an anionic intermediate (T⁻), resulting from a kinetically important proton transfer from T[±] to the amine. The rate of this proton transfer is faster than that of expulsion of arylthiolate from T[±] (*k*₂) as evidenced by the estimation of these rate coefficients. The rate constants for formation of T[±] (*k*₁) are obtained experimentally, and those for amine expulsion from T[±] (*k*₋₁) are estimated. Equations for *k*₁ and *k*₋₁ are derived as functions of the basicity of the amine and leaving (aryl thiolate) groups. Comparison of the *k*₋₁ and *k*₂ values found in the present reactions with those obtained in the aminolysis of aryl dithioacetates shows that substitution of Me by EtO as the "acyl" group of the zwitterionic tetrahedral intermediate destabilizes this species.

Introduction

The mechanisms of the aminolysis of aryl acetates,¹ diaryl carbonates,² and aryl thioacetates^{3,4} have been well established. These reactions are known to proceed through a zwitterionic tetrahedral intermediate, whose existence has been deduced from nonlinear structure-reactivity relationships, notably from curved Brønsted-type plots.¹⁻⁴ In the aminolysis of phenyl and *p*-nitrophenyl dithioacetates the existence of a tetrahedral intermediate was inferred from curved *k*_{obs} vs [N] plots, where *k*_{obs} is the pseudo-first-order rate constant and N represents the free amine.^{5,6} In these works the values of the microscopic rate coefficients for formation and decomposition of the zwitterionic intermediate were obtained.^{5,6} Linear structure-reactivity relationships have been found for the microscopic rate coefficients for the departure of the amine and aryl thiolate anion from the zwitterionic tetrahedral intermediate formed in the aminolysis of aryl thioacetates.⁴

We have recently studied the kinetics of the aminolysis of *O*-ethyl *S*-(*X*-phenyl) dithiocarbonates (*X* = H, *p*-nitro, 2,4-dinitro, and 2,4,6-trinitro),^{7,8} where curved Brønsted-type plots were found for the three more reactive dithiocarbonates. These were explained by the presence of a zwitterionic tetrahedral intermediate and a change in rate-determining step.^{7,8} We now report a kinetic study on the aminolysis (secondary alicyclic amines) of the above substrates with *X* = *p*-Cl, *p*-Me, and *p*-MeO and the

reactions of pyrrolidine with six of these substrates. Our aim is (i) to extend our mechanistic studies to other substituents less electron-withdrawing than the nitro groups, (ii) to obtain structure-reactivity relationships for the rate microcoefficients concerning the tetrahedral intermediate formed in the reactions of dithiocarbonates, and (iii) to compare the above rate microcoefficients with those found in the aminolysis of aryl dithioacetates^{5,6} in order to assess the influence of the ethoxy group on the nucleofugalities of amines and aryl thiolate anions from the zwitterionic tetrahedral intermediate and hence on its stability.

Experimental Section

The UV-vis spectra of the different kinetic samples were obtained in a Perkin-Elmer Lambda-3 spectrophotometer. Elemental analysis of *O*-ethyl *S*-(*p*-chlorophenyl) dithiocarbonate (CIPDTC) was carried out at the Instituto de Química Orgánica General (CSIC), Madrid, Spain. High-resolution mass spectroscopy (HRMS) spectra of *O*-ethyl *S*-(*p*-methylphenyl) dithiocarbonate (MPDTC) and *O*-ethyl *S*-(*p*-methoxyphenyl) dithiocarbonate (MOPDTC) were taken at the Mass Spectrometry Laboratory, University of Kansas. IR spectra were obtained on a Bruker IFS 25 spectrophotometer. ¹H NMR and ¹³C NMR spectra were recorded on a Bruker AC-200 spectrometer with TMS as internal standard.

Materials. The alicyclic amines were purified as described.⁹ Phenyl, *p*-methoxyphenyl, *p*-nitrophenyl, and 2,4-dinitrophenyl *O*-ethyl dithiocarbonates were prepared as reported.^{8,9} To our knowledge CIPDTC and MPDTC have not been previously synthesized. These compounds were prepared by the same procedure used for the synthesis of the unsubstituted dithiocarbonate and MOPDTC.⁹ The preparation of CIPDTC, MPDTC, and MOPDTC was carried out similarly and was as follows: *p*-chloro-, *p*-methyl-, and *p*-methoxyanilines (0.05 mol) were dissolved in a solution prepared by mixing concd sulfuric acid (10 mL) with water (120 mL). After rapid cooling in an ice-salt mixture a solution of 0.05 mol of sodium nitrite in water (40 mL) was added at once. The neutralized solution was added to an

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aqueous solution (10 mL) containing 0.05 mol of potassium *O*-ethyl dithiocarbonate. The crude oil formed was chromatographed on a Merck GF-254 silica gel column, using petroleum ether (40–60) as eluant. CIPDTC had mp 30–32 °C, and MPDTC and MOPDTC were liquids. The analyses of these compounds were as follows.

CIPDTC: ¹H NMR (200 MHz, CDCl₃) δ 1.34 (t, 3H, *J* = 7.1 Hz), 4.62 (q, 2H, *J* = 7.2 Hz), 7.42 (m, 4H); ¹³C NMR (50 MHz, CDCl₃) δ 13.57 (CH₃), 70.47 (CH₂), 128.59 (C-1), 129.25 (C-3/5), 136.37 (C-2/6), 136.42 (C-4), 212.31 (C=S); IR (KBr) 1230 (C=S), 1050 (C-S), 825 (CH-arom), 750 (C-Cl) cm⁻¹. Anal. Calcd for C₉H₉ClO₂S₂: C, 46.45; H, 3.87; Cl, 15.27; S, 27.53. Found for C, 46.22; H, 3.91; Cl, 14.98; S, 27.80.

MPDTC: ¹H NMR (200 MHz, CDCl₃) δ 1.34 (t, 3H, *J* = 7.1 Hz), 2.40 (s, 3H), 4.61 (q, 2H, *J* = 7.1 Hz), 7.24 (d, 2H, *J* = 8.2 Hz), 7.38 (d, 2H, *J* = 8.2 Hz); ¹³C NMR (50 MHz, CDCl₃) δ 13.71 (CH₃), 21.51 (CH₃), 70.27 (CH₂), 126.85 (C-1), 130.08 (C-3/5), 134.87 (C-2/6), 140.31 (C-4), 213.77 (C=S); IR (KBr) 1230 (C=S), 1030 (C-S), 800 (CH-arom.) cm⁻¹; HRMS calcd for C₁₀H₁₂O₂S₂ *m/z* 212.0330, found for *m/z* 212.0326.

MOPDTC: ¹H NMR (200 MHz, CDCl₃) δ 1.34 (t, 3H, *J* = 7.1 Hz), 3.84 (s, 3H), 4.61 (q, 2H, *J* = 7.1 Hz), 6.95 (d, 2H, *J* = 6.7 Hz), 7.41 (d, 2H, *J* = 6.7 Hz); ¹³C NMR (50 MHz, CDCl₃) δ 13.75 (CH₃), 55.41 (CH₃), 70.31 (CH₂), 114.72 (C-3/5), 121.13 (C-1), 136.80 (C-2/6), 161.06 (C-4), 214.45 (C=S); IR (KBr) 1257 (C=S), 1042 (C-S), 826 (CH-arom) cm⁻¹; HRMS calcd for C₁₀H₁₂O₂S₂ *m/z* 228.0279, found for *m/z* 228.0290.

Kinetic Measurements. These were carried out by following spectrophotometrically the corresponding benzenethiolate anion release at 257 nm (substrates with X = H, *p*-Cl, *p*-Me, and *p*-MeO) and 412 nm (X = *p*-NO₂ and 2,4-(NO₂)₂), using the equipment and method previously described.³ This was done in aqueous solution at 25.0 ± 0.1 °C, ionic strength 0.2 M (KCl). Under amine excess, pseudo-first-order rate coefficients (*k*_{obsd}) were found throughout, as reported.³ Experimental conditions for the reactions and *k*_{obsd} values are shown in Tables I and II.

Determination of *pK*_a. The values for *p*-chloro, *p*-methyl, and *p*-methoxybenzenethiols and pyrrolidinium ion were obtained spectrophotometrically at 270, 264, 265, and 205 nm, respectively, under the same conditions as the kinetic measurements by means of a Perkin-Elmer Lambda-3 spectrophotometer. The measurement of pH was made on a Radiometer PHM-62 pH-meter. The *pK*_a values of the benzenethiols are shown in Table III. The value for pyrrolidinium ion is 11.52.

Product Studies. The presence of benzenethiolate ions was determined spectrophotometrically by comparison of the UV-vis spectra at the end of the reactions with those of the corresponding benzenethiolate ion under the same conditions. The presence of thiocarbamates was determined chromatographically in two cases by comparison of the retention times at the end of the reactions with those of authentic samples of piperidinyl and morpholinyl thiocarbamates, by the instruments and methods previously described.⁷

Results and Discussion

The pseudo-first-order rate coefficients (*k*_{obsd}) obtained in the present reactions, except those of piperidine and pyrrolidine, are in accord with eq 1, where the *m*'s are

$$k_{\text{obsd}} = \frac{m_1[\text{N}]^2}{1 + m_2[\text{N}]} \quad (1)$$

constants and N represents the free amine. Linear plots of [N]/*k*_{obsd} vs 1/[N] were found in these reactions; the values of *m*₁ and *m*₂ were obtained from the slope and intercept, respectively, of these plots. In the reactions of piperidine and pyrrolidine the plots *k*_{obsd} vs [N] were linear (*m*₂[N] ≫ 1 in eq 1).

According to the rate law exhibited, the products obtained, and the mechanism found for similar reactions,^{7,8} the present reactions can be described by Scheme I.

Table I. Experimental Conditions and *k*_{obsd} Values for the Aminolysis of *O*-Ethyl *S*-(Para-substituted phenyl) Dithiocarbonates^a

amine	pH	10 ² [N] _{tot} , ^b M	10 ² <i>k</i> _{obsd} , s ⁻¹	<i>n</i> ^c
<i>O</i>-Ethyl <i>S</i>-(<i>p</i>-Chlorophenyl) Dithiocarbonate (CIPDTC)				
piperidine (PI)	10.94	2–12	0.76–6.8	5
	11.24	2–18	1.7–16.0	8
	11.54	2–8	1.7–8.6	4
piperazine (PA)	9.64	1–14	0.094–4.3	7
	9.94	1–16	0.21–8.8	8
	10.24	1–12	0.29–10.0	7
1-(2-hydroxyethyl)piperazine (BHPA)	9.08	4–20	0.18–2.2	9
	9.38	6–20	0.54–3.8	8
	9.68	8–24	1.3–6.7	8
morpholine (MO)	8.48	6–20	0.16–1.2	8
	8.78	4–20	0.18–1.9	9
	9.08	4–26	0.28–4.0	12
1-formylpiperazine (FPA)	7.98	22–32	0.43–0.78	5
	8.28	16–26	0.39–0.93	6
	8.78	10–30	0.27–1.8	10
<i>O</i>-Ethyl <i>S</i>-(<i>p</i>-Methylphenyl) Dithiocarbonate (MPDTC)				
piperidine (PI)	10.94	2–14	0.66–5.8	6
	11.24	2–18	1.8–11.9	9
	11.54	4–12	3.1–10.6	5
piperazine (PA)	9.64	1–14	0.088–3.9	6
	9.94	4–18	1.1–10.0	7
	10.24	1–12	3.1–7.8	7
1-(2-hydroxyethyl)piperazine (BHPA)	9.08	4–20	0.21–2.1	9
	9.38	2–20	0.11–3.5	10
	9.68	8–24	1.3–5.7	7
morpholine (MO)	8.48	6–20	0.16–1.0	8
	8.78	2–20	0.038–1.8	10
	9.08	4–26	0.26–5.0	12
1-formylpiperazine (FPA)	7.98	18–32	0.25–0.69	8
	8.28	16–28	0.37–0.95	4
	8.78	18–30	0.71–1.8	7
<i>O</i>-Ethyl <i>S</i>-(<i>p</i>-Methoxyphenyl) Dithiocarbonate (MOPDTC)				
piperidine (PI)	10.94	2–14	0.68–6.3	7
	11.24	2–18	1.5–12.4	8
	11.54	4–12	3.3–11.7	4
piperazine (PA)	9.64	1–14	0.11–3.6	8
	9.94	1–16	0.21–6.8	9
	10.24	2–10	0.78–6.1	5
1-(2-hydroxyethyl)piperazine (BHPA)	9.08	2–20	0.058–1.8	10
	9.38	2–20	0.11–3.4	10
	9.68	8–24	1.3–5.8	8
morpholine (MO)	8.48	6–20	0.18–0.99	8
	8.78	2–20	0.053–1.9	10
	9.08	4–26	0.31–3.8	12
1-formylpiperazine (FPA)	7.68	14–28	0.10–0.28	8
	7.98	18–32	0.27–0.80	8
	8.28	14–28	0.36–0.95	8
	8.78	6–30	0.12–1.8	13

^a In aqueous solution at 25 °C, ionic strength 0.2 M (KCl). ^b Total amine concentration (free amine plus protonated forms). ^c Number of runs.

Applying the steady-state condition to the tetrahedral intermediates T[±] and T⁻ of the scheme the rate law described by eq 2 can be deduced. Assuming *k*₃[N] ≫ *k*₂, eq 2 yields eq 3, which agrees with the experimental rate

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

$$k_{\text{obsd}} = \frac{k_1 k_3 [\text{N}]^2}{k_{-1} + k_3 [\text{N}]} = \frac{(k_1 k_3 / k_{-1}) [\text{N}]^2}{1 + (k_3 / k_{-1}) [\text{N}]} \quad (3)$$

equation (eq 1), with *m*₁ = *k*₁*k*₃/*k*₋₁ and *m*₂ = *k*₃/*k*₋₁. From the values of *m*₁ and *m*₂ the values of *k*₁ and *k*₃/*k*₋₁ were obtained. Since *k*₃ ≈ 10¹⁰ s⁻¹ M⁻¹ (see below), the values

Table II. Experimental Conditions and Rate Constants Found in the Reactions of Pyrrolidine with *O*-Ethyl *S*-(Substituted phenyl) Dithiocarbonates^a

substrate substituent	pH	10 ² [N] _{tot} , ^b M	10 ⁸ k _{obsd} , s ⁻¹	n ^c	k ₁ , ^d s ⁻¹ M ⁻¹
2,4-(NO ₂) ₂	10.62	0.01–4.0	0.52–13	7	28.3
	10.70	0.02–3.0	1.2–11	7	
	10.92	0.01–2.0	2.6–11	7	
	11.22	0.01–1.2	2.2–11	7	
<i>p</i> -NO ₂	10.80	0.5–1.6	4.7–22	7	9.6
	11.10	0.5–2.4	9.0–59	12	
	11.40	0.3–1.5	6.3–60	7	
<i>p</i> -Cl	10.66	1.5–19	8.6–120	6	5.5
none	10.66	1.5–19	8.2–110	7	4.9
<i>p</i> -CH ₃	10.66	1.5–15	7.0–76	6	5.0
<i>p</i> -OCH ₃	10.66	2.0–19	12–110	4	4.8

^a In aqueous solution at 25 °C, ionic strength 0.2 M (KCl). ^b Total amine concentration (free amine plus protonated forms). ^c Number of runs. ^d The *k*₁ values were obtained as slopes of linear *k*_{obsd} vs [N] plots, at constant pH.

Table III. Values of the Microconstants Obtained in the Aminolysis of *O*-Ethyl *S*-(Substituted phenyl) Dithiocarbonates^a

substrate substituent (p <i>K</i> _a) ^b	amine ^c	p <i>K</i> _a ^d	k ₁ , s ⁻¹ M ⁻¹	10 ⁻⁸ k ₋₁ , s ⁻¹
<i>p</i> -Cl (6.0)	PI	11.24	1.7 ± 0.1	
	PA	9.94	1.2 ± 0.1	1.4 ± 0.2
	BHPA	9.38	0.49 ± 0.03	3.5 ± 0.4
	MO	8.78	0.31 ± 0.03	6.0 ± 0.7
	FPA	7.98	0.13 ± 0.01	22 ± 3
<i>p</i> -CH ₃ (6.4)	PI		1.3 ± 0.1	
	PA		1.1 ± 0.1	1.2 ± 0.2
	BHPA		0.38 ± 0.02	2.4 ± 0.3
	MO		0.31 ± 0.03	6.3 ± 0.4
	FPA		0.12 ± 0.01	25 ± 4
<i>p</i> -OCH ₃ (6.5)	PI		1.4 ± 0.1	
	PA		1.0 ± 0.05	1.6 ± 0.2
	BHPA		0.38 ± 0.02	2.4 ± 0.4
	MO		0.29 ± 0.02	6.3 ± 0.8
	FPA		0.13 ± 0.01	26 ± 3
none ^e (6.4)	PI		1.1	0.13
	PA		0.82	1.2
	BHPA		0.40	2.7
	MO		0.37	5.5
<i>p</i> -NO ₂ ^e (4.6)	PI		3.0	
2,4-(NO ₂) ₂ ^f (3.4)	PI		8.5	
	PA		8.0	

^a In aqueous solution at 25 °C, ionic strength 0.2 M (KCl). ^b Of the conjugate acid of the substituted benzenethiolate ion under the experimental reaction conditions. ^c Symbols as in Table I. ^d Of the conjugate acid of the amine under the experimental reaction conditions. ^e Data from ref 7. ^f Data from ref 8.

of *k*₋₁ can also be found. The final *k*₋₁ values were obtained by nonlinear least-squares fitting of eq 3 to the experimental *k*_{obsd} vs [N] data. The final and initial *k*₋₁ values differed by 20% at most. In the reactions of piperidine and pyrrolidine only the values of *k*₁ could be obtained, as the slopes of the linear *k*_{obsd} vs [N] plots. This is so because for these two highly basic amines *k*₋₁ ≪ *k*₃[N], therefore, eq 3 yields *k*_{obsd} = *k*₁[N]. The values of *k*₁ and *k*₋₁ found in the present reactions, together with those obtained in similar reactions,^{7,8} are shown in Table III.

Figure 1 is an example of the fit of the calculated curve (through eq 3 with the values of the microconstants of Table III) to the experimental points (Table I).

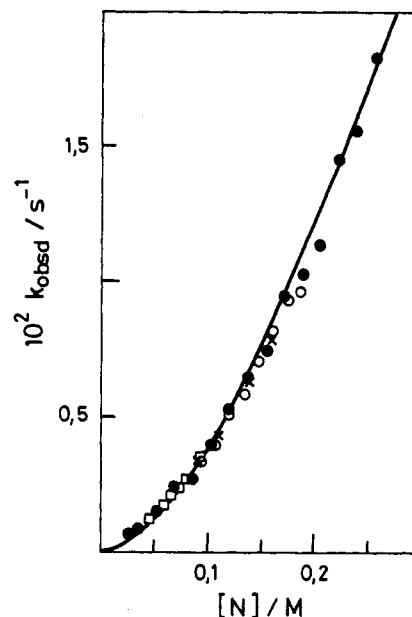
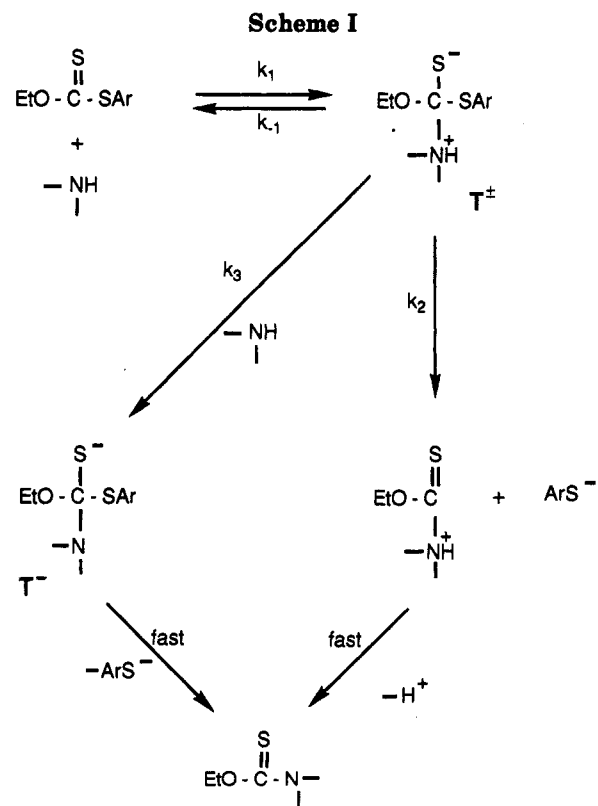
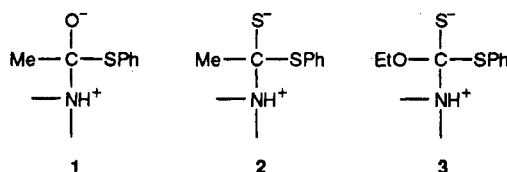


Figure 1. Plot of *k*_{obsd} vs [N] for the reaction of CIPDTC with 1-formylpiperazine at pH 7.68 (□), 7.98 (×), 8.28 (○), and 8.78 (●). The curve was calculated through eq 3 and the microscopic rate coefficients of Table III. The points are experimental.



In order to justify that *k*₃[N] ≫ *k*₂, it is necessary first to assess the p*K*_a of T[±] of Scheme I. The p*K*_a of 1 has been estimated as equal to that of the parent aminium ion.³



Jencks and co-workers have estimated the pK_a of intermediates similar to 1 assuming that the effects of α -substituents on the pK_a are mainly inductive.¹⁰ Hammett correlations using σ_I and ρ_I have satisfactorily been used to evaluate these pK_a .¹⁰ Starting with the pK_a of 1 and knowing that $\sigma_I(O^-) = -0.26$,¹¹ $\sigma_I(S^-) = 0.03$,¹¹ and $\rho_I = -7.3$ for the pK_a of XCH_2N -morpholinium ions,¹⁰ it follows by Jenck's procedure¹⁰ that the pK_a of 2 is changed relative to 1 by $\Delta pK_a = -7.3 (0.03 - (-0.26)) = ca. -2$. Therefore, the pK_a of 2 is ca. 2 pK_a units lower than that of the parent aminium ion. Substitution of Me by EtO in 2 should change the pK_a of 2 by $\Delta pK_a = -7.3 (0.26 - 0.01) = -1.8$ (σ_I for EtO and Me are 0.26 and 0.01,¹¹ respectively). Therefore, the pK_a of 3 should be ca. 3.8 pK_a units lower than that of the parent aminium ion. Since the basicity of PhS^- (pK_a 6.4) is not very different from that of the *p*-chloro, *p*-methyl, and *p*-methoxy derivatives ($pK_a = 6.0, 6.4, \text{ and } 6.5$, respectively), it is expected that the pK_a of the T^\ddagger formed in the reactions under study should be similar to that of 3 (except those for the nitro derivatives). This is confirmed by the following treatment.

The pK_a of $ArCH_2NH_3^+$ in water at 25 °C has been satisfactorily correlated with $\rho = -1.05$ and σ° values.¹² A fall-off factor of 1.63 can be estimated for transmission of substituent effects through a sulfur atom, by comparison of $\rho = 0.49$ for acid dissociation of $ArCH_2COOH$ with $\rho = 0.30$ for ionization of $ArSCH_2COOH$ in water at 25 °C.^{3,13} Since for *p*-Cl $\sigma^\circ = +0.27$,¹³ the pK_a change in going from 3 to the *p*-chloro derivative is $\Delta pK_a = -(1.05/1.63) \times 0.27 = -0.17$. Similar calculations for *p*-Me and *p*-MeO ($\sigma^\circ = -0.15$ and -0.16 ,¹³ respectively) yield $\Delta pK_a \approx +0.1$. The pK_a of the two nitro derivatives of 3 should be even lower than 3 in view of the strong electron-withdrawing effect of the nitro group.

Since the pK_a values of the intermediates T^\ddagger formed in the present reactions are much lower than that of the parent aminium ions, it follows that the proton transfers from T^\ddagger to the corresponding amines are thermodynamically favorable; therefore, k_3 of Scheme I can be estimated as ca. $10^{10} \text{ s}^{-1} \text{ M}^{-1}$, in analogy with similar proton transfers reported in the literature.^{1,4-8,10,14}

Let us now assess the value of k_2 of Scheme I. The rate of expulsion of PhS^- from 2 has been estimated as 10^6 – 10^7 s^{-1} .⁵ The rate of PhS^- leaving from 3 should be larger in view of the extra "push" exerted by EtO to expel the nucleofuge.¹⁵ In fact, a value of $k_2 = 7 \times 10^7 \text{ s}^{-1}$ for 3 has been estimated, although based on few data.^{8,16} The k_2 values for some of the zwitterionic tetrahedral intermediates found in this work (*p*-Cl, H, *p*-Me, and *p*-MeO derivatives of 3) should not be significantly different from that obtained for 3, in view of the similar basicities of the leaving groups involved. The k_2 values for the nitro derivatives should be larger since good leaving groups are involved.

According to the values of the free-amine concentrations used in the reactions of *O*-ethyl *S*-phenyl dithiocarbonate

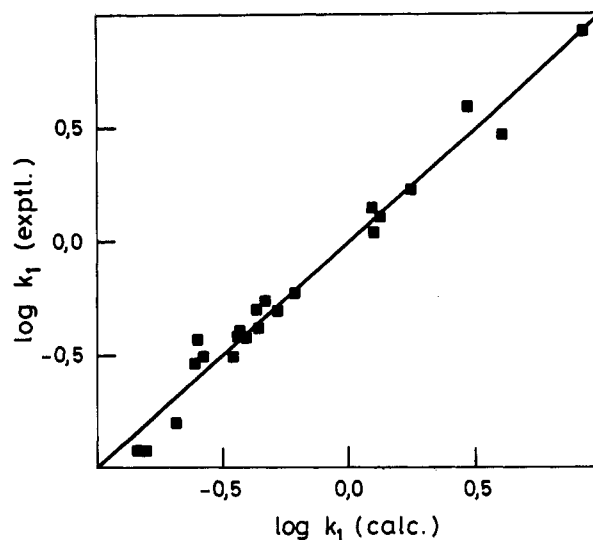


Figure 2. Logarithmic plot of the experimental vs the calculated values of k_1 (Scheme I) for the aminolysis of *O*-ethyl *S*-(substituted phenyl) dithiocarbonates. Data from Table III. The line was calculated by a linear least-squares procedure.

(PDTTC), CIPDTC, MPDTC and MOPDTC, and the estimated values of k_3 and k_2 , it is clear that in the great majority of the runs $k_3[N] > k_2$,¹⁷ justifying therefore the assumption made above, which accounts for the experimental rate law (eqs 1 and 3).

With the k_1 values found in the present reactions together with those obtained in similar reactions (Table III), eq 4 can be deduced by dual regression analysis (n

$$\log(k_1/q) = -1.46 + 0.29pK_a(N) - 0.27pK_a(lg) \quad (4)$$

$= 22$, $R^2 = 0.97$, st. error = 0.08). In this expression both k_1 and $pK_a(N)$ have been statistically corrected.^{3,7,18} The pK_a coefficients (β) are subject to an error of ± 0.1 and are similar to those reported in the aminolysis of phenyl dithioacetate,⁵ *p*-nitrophenyl thionbenzoate,¹⁹ aryl acetates,¹ phenyl aryl carbonates,² and aryl thioacetates.^{3,4}

A confirmation of the sensitivity of k_1 to the basicity of the leaving group (β_{lg}) was obtained by the kinetic study of the reactions of pyrrolidine with several *O*-ethyl *S*-(substituted phenyl) dithiocarbonates (Table II). Since this amine is still more basic than piperidine it is reasonable that k_1 is the rate-determining step in all these reactions. The Brønsted plot of $\log k_1$ vs $pK_a(lg)$ has a slope $\beta_{lg} = -0.23 \pm 0.1$, confirming the value found above (eq 4). A logarithmic plot of the experimental k_1 vs the calculated k_1 , through eq 4, is shown in Figure 2.

With the k_1 data of Table III, eq 5 can be deduced by regression analysis ($pK_a(N)$ statistically corrected, $n = 16$, $R^2 = 0.98$, st. error = 0.09). The amine sensitivity on

$$\log k_{-1} = 15.4 - 0.7pK_a(N) \quad (5)$$

k_{-1} ($\beta_N = -0.7 \pm 0.1$) is similar to that found in the aminolysis of aryl thioacetates,^{3,4} aryl acetates,¹ and phenyl aryl carbonates.² In contrast, the leaving group (arylsulfonate) sensitivity on k_{-1} ($\beta_{lg} \approx 0 \pm 0.1$, by the above

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

(12) Wells, P. R. *Linear Free Energy Relationships*; Academic: London, 1968; p 12.

(13) Shorter, J. *Correlation Analysis in Organic Chemistry: An Introduction to Linear Free-Energy Relationships*; Oxford: Oxford, 1973.

(14) Eigen, M. *Angew. Chem., Int. Ed. Engl.* 1964, 3, 1.

(15) Castro, E. A.; Ibáñez, F.; Salas, M.; Santos, J. G. *J. Org. Chem.* 1991, 56, 4819 and references cited therein.

(16) Since k_2 should not change with amine basicity,^{1,2} the values calculated for each amine were averaged.⁸

(17) $[N] = 0.005 \text{ M}$ in only a few runs, which gives $k_3[N]$ of $5 \times 10^7 \text{ s}^{-1}$, a value comparable to that of k_2 .

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

(19) Campbell, P.; Lapinskas, B. A. *J. Am. Chem. Soc.* 1977, 99, 5378.

regression analysis) is lower than that obtained in the aminolyses of aryl thiolacetates, aryl acetates, and diaryl carbonates ($\beta_{lg} = +0.4$).¹⁻⁴

The fact that β_{lg} for k_{-1} is approximately zero means that there is little or no charge development on the sulfur atom of the arylthio group when going from T^\ddagger of Scheme I to the transition state for the first step. The reason why this charge development is less here than in aryl thiolacetate derivatives ($\beta_{lg} = +0.4$) could be due to a greater charge delocalization of the CS_2 group in the transition state for the first step of the present reactions compared to the corresponding delocalization of the COS group in the aryl thiolacetate reactions. The similar k_{-1} values found in the aminolyses of phenyl⁵ and *p*-nitrophenyl dithioacetates⁶ is in accord with this explanation.

The k_{-1} values found in the aminolysis of PDTTC (Table III) are larger than those obtained for the corresponding reaction of phenyl dithioacetate.⁵ This result is in line with those found in the aminolysis of monothio and oxy derivatives, i.e., substitution of Me by EtO or MeO as the "acyl" group of the zwitterionic tetrahedral intermediate enhances the nucleofugality of the amine from the intermediate.^{4,7,8,15,20} In the pyridinolysis of 2,4,6-trinitrophenyl acetate (TNPA) and 2,4,6-trinitrophenyl methyl carbonate (TNPMC) curved Brønsted plots were found, with the center of curvature (pK_a°) at 5.0 and 6.5 pK_a units, respectively.²¹ This means that the change from Me to MeO as the "acyl" group of the zwitterionic tetrahedral intermediate favors amine leaving,^{1,2,22} also in agreement with the above result.

Since in the present reactions both k_{-1} and k_2 increase

(20) Fersht, A. R.; Jencks, W. P. *J. Am. Chem. Soc.* 1970, 92, 5442. Chrystiuk, E.; Williams, A. *J. Am. Chem. Soc.* 1987, 109, 3040.

(21) Castro, E. A.; Ibáñez, F.; Lagos, S.; Schick, M.; Santos, J. G. *J. Org. Chem.* 1992, 57, 2691.

(22) A higher pK_a° value indicates a larger k_{-1}/k_2 ratio.^{1,2} The k_2 value is also larger for **3** compared to **2** (see Discussion above) which means that substitution of Me by EtO increases k_2 . It is reasonable therefore that the change of Me by MeO in any zwitterionic tetrahedral intermediate similar to T^\ddagger also enlarges k_2 . A higher k_{-1}/k_2 for the TNPMC reactions relative to TNPA means, therefore, a larger k_{-1} for TNPMC.

by the change of Me by EtO or MeO in the zwitterionic tetrahedral intermediate, it is clear that this intermediate becomes less stable by this change. This is in accord with the fact that a stepwise reaction was found in the aminolysis of 2,4-dinitrophenyl thiolacetate⁴ whereas a concerted process was observed in the aminolysis of *O*-ethyl *S*-(2,4-dinitrophenyl) thiocarbonate.¹⁵ The faster expulsion of both the amine and 2,4-dinitrobenzenethiolate anion from the latter transition state was attributed to the superior "push" exerted by EtO from the transition state relative to Me.¹⁵ The above result is also in line with the findings of a stepwise mechanism (through a tetrahedral intermediate) in the aminolysis of acetylpyridinium ion and a concerted transfer of methoxycarbonyl between isoquinoline and pyridines.²⁰

Conclusions

(1) The reaction scheme found in the present reactions (Scheme I) is similar to that obtained for the aminolysis of aryl dithioacetates. (2) The Brønsted sensitivities of k_1 to the basicity of the amine (β_N) and the leaving group of the substrate (β_{lg}) are similar to those found in the aminolysis of aryl dithioacetates, thiolacetates, acetates, and carbonates. (3) The β_N value for k_{-1} is similar to those exhibited in the aminolysis of the above substrates; however, the β_{lg} value for k_{-1} is smaller than those found in the aminolysis of aryl thiolacetates, acetates, and carbonates. (4) The values of k_{-1} and k_2 are larger than the corresponding values found in the aminolysis of aryl dithioacetates. This means that the zwitterionic tetrahedral intermediate becomes kinetically more unstable by the change of methyl by ethoxy as its "permanent" group.

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