Kinetics and Mechanism of the Aminolysis of 2,4-Dinitrophenyl and 2,4,6-Trinitrophenyl O-Ethyl Dithiocarbonates

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The reactions of a series of secondary alicyclic amines with the title substrates (DNPDTC and TNPDTC) are subject to a kinetic study in water at 25.0 °C, ionic strength 0.2 M (KCl). The reactions are first order in both the amine and the substrate. The Brönsted-type plots obtained are nonlinear and are explained by a stepwise mechanism through a zwitterionic tetrahedral intermediate ($T^{\pm}$), although a concerted process is not rigorously excluded for the reactions of the less basic amines with TNPDTC. An equation is reported which describes the dependence of the basicities of the amine and leaving group on the nucleofugality ratio of these groups from $T^{\pm}$ (k_{-1}/k_2). This equation satisfactorily predicts the pK_a values at the Brönsted breaks ($pK_a°$). The experimental $pK_a°$ values found in the present reactions correlate well with those in the aminolysis of *p*-nitro- and unsubstituted phenyl *O*-ethyl dithiocarbonates. The values of both k_{-1} and k_2 are larger in the reactions of phenyl *O*-ethyl dithiocarbonate than in the aminolysis of phenyl dithioacetate due to the additional push exerted by EtO in $T^{\pm}$. The $T^{\pm}$ formed in the aminolysis of DNPDTC is less unstable than that in the aminolysis of *S*-(2,4-dinitrophenyl) *O*-ethyl thiocarbonate (whose mechanism is concerted), and this is attributed to a smaller ability of S^- in $T^{\pm}$ to form a double bond and expel a nucleofuge.

Introduction

Although the mechanisms of hydrolysis and aminolysis of oxyesters and oxycarbonates have been well established,[1,2] those for the reactions of the thio analogues have received less attention.

We have recently studied the kinetics of the aminolysis (secondary alicyclic amines) of aryl thioacetates,[3] *S*-(2,4-dinitrophenyl) *O*-ethyl thiocarbonate (DNPTC),[4] and phenyl and *p*-nitrophenyl *O*-ethyl dithiocarbonates (PDTC and NPDTC, respectively).[5] We have found that the reactions of thioacetates and the dithiocarbonates PDTC and NPDTC proceed through tetrahedral addition intermediates,[3,5] whereas that of DNPTC apparently occurs by an enforced coupled concerted mechanism, without such intermediate.[4]

In order to extend our kinetic studies on the aminolysis of thiocarbonates we examine in this work the reactions of secondary alicyclic amines with 2,4-dinitrophenyl and 2,4,6-trinitrophenyl *O*-ethyl dithiocarbonates (DNPDTC and TNPDTC, respectively). The object is to analyze (i) the leaving group effect on the kinetics by comparison with the aminolysis of PDTC and NPDTC and (ii) the thiocarbonyl group effect by comparison with the reactions of the same amines with DNPTC.

Experimental Section

Materials. The secondary alicyclic amines were purified as reported.[6] DNPDTC and TNPDTC were prepared according to modifications of a reported procedure,[7] which were as follows: In the case of DNPDTC a solution of potassium *O*-ethyl xanthate in acetone was added dropwise to a cooled solution (−70 °C) of 1-chloro-2,4-dinitrobenzene in acetone. For TNPDTC, a solution of potassium *O*-ethyl xanthate in methanol was added dropwise to a cooled solution (−5 °C) of 1-chloro-2,4,6-trinitrobenzene in methanol–4% acetone.

Since we found large discrepancies between our mp's for the above compounds and those of literature,[7] we fully characterized these compounds as follows.

DNPTC: mp 43–45 °C (lit.[7] mp 185 °C); IR (KBr) 1528 and 1343 (CNO_2), 1274 (C=S), 1029 (CS) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$), δ 1.34 (t, 3 H, J = 7.2 Hz), 4.62 (q, 2 H, J = 7.2 Hz), 7.96 (d, 1 H, J = 8.6 Hz), 8.46 (dd, 1 H, J = 2.4, 8.6 Hz), 8.85 (d, 1 H, J = 2.4 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.31 (CH_3), 71.49 (CH_2), 120.38 (C-3), 125.9 (C-5), 132.1 (C-1), 138.03 (C-6), 147.99 (C-4), 150.38 (C-2), 205.44 (C=S). Anal. Calcd for $C_9H_8N_2O_5S_2$: C, 37.5; H, 2.77; N, 9.72; S, 22.2. Found: C, 37.8; H, 2.84; N, 9.86; S, 23.0.

TNPDTC: mp 76–78 °C (lit.[7] mp 100 °C); IR (KBr) 1541 and 1343 (CNO_2), 1270 (C=S), 1029 (CS) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.32 (t, 3 H, J = 7.2 Hz), 4.57 (q, 2 H, J = 7.2 Hz), 8.95 (s, 2 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.21 (CH_3), 72.16 (CH_2), 122.65 (C-3/5), 127.21 (C-1), 147.62 (C-4), 152.38 (C-2/6), 201.03 (C=S). Anal. Calcd for $C_9H_7N_3O_7S_2$: C, 32.4; H, 2.12; N, 12.6; S, 19.2. Found: C, 32.6; H, 2.29; N, 13.0; S, 18.6.

Kinetic Measurements. The reactions were studied in aqueous solution, 25.0 ± 0.1 °C, ionic strength 0.1 M (KCl), and followed spectrophotometrically by the method and instrument described.[3] In all cases the pH values were within the buffering capacity of the amines and the total amine was in excess over the substrate. Pseudo-first-order rate coefficients (k_{obsd}) were found from ln ($A_\infty - A$) vs time plots, where A_∞ and A are the absorbances at "infinity" and "t" times, respectively. The plots remained linear for at least 4 half-lives, showing correlation coefficients better than 0.9990. The experimental conditions and k_{obsd} values are shown in Tables I and II.

Product Studies. The presence of aryl thiolate anions[8] and thiocarbamates as products of the reactions was determined as reported.[5]

Results

The rate law obtained in the present reactions is given in eqs 1 and 2, where L^-, S, and N represent the leaving

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(8) At the pH values employed in the kinetic studies the aryl thiolate anions are well in excess over the corresponding aryl thiols (the pK_a values of 2,4-dinitrobenzenethiol and 2,4,6-trinitrobenzenethiol are 3.4 and 1.4, respectively, under the kinetic conditions).[3]

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Table I. Experimental Conditions and k_{obsd} for the Aminolysis of DNPDTC[a]

amine (pK_a)[b]	pH	F_N[c]	$10^2[N]_{tot}$,[d] M	10^2k_{obsd}, s^{-1}	no. of runs
piperidine (11.24)	10.5	0.15	0.50–7.00	0.555–8.63	10
	11.0	0.37	0.70–6.00	2.26–18.4	8
	11.3	0.53	0.50–4.00	2.26–17.7	6
piperazine (9.94)	9.5	0.27	0.50–5.00	0.834–7.13	7
	10.0	0.53	0.50–5.00	1.73–13.5	6
	10.5	0.78	0.50–4.00	2.91–14.8	6
1-(β-hydroxyethyl)-piperazine (9.38)	8.7	0.17	3.00–9.00	1.22–3.66	7
	9.0	0.29	2.00–8.00	1.37–5.50	6
	9.5	0.57	2.00–6.00	2.32–6.80	5
morpholine (8.78)	9.1	0.67	1.00–7.00	1.17–7.28	7
	9.3	0.77	1.00–7.00	1.16–8.18	7
	9.5	0.84	1.00–7.00	1.35–8.28	7
1-formylpiperazine (7.98)	7.5	0.25	1.00–6.00	0.124–0.511	6
	8.0	0.51	1.00–7.00	0.190–1.21	7
	8.5	0.77	5.00–20.0	1.21–5.39	7
piperazinium ion (5.81)	5.5	0.33	7.00–16.0	0.0569–0.122	5
	6.1	0.67	7.00–22.0	0.119–0.379	6
	6.6[e]	0.86	2.00–6.00	0.0469–0.144	4
	6.9[e]	0.92	2.00–9.00	0.0644–0.254	6

[a] In water at 25.0 °C, ionic strength 0.1 M (KCl). [b] Values from ref 6. [c] Molar fraction of free amine. [d] Concentration of total amine (free base plus protonated forms). [e] In the presence of 0.01 M phosphate buffer.

Table II. Experimental Conditions and k_{obsd} for the Aminolysis of TNPDTC[a]

amine (pK_a)	pH	F_N	$10^2[N]_{tot}$, M	10^2k_{obsd}, s^{-1}	no. of runs
piperidine (11.24)	10.0	0.058	3.00–13.0	0.699–3.63	6
	10.3	0.102	2.00–8.00	0.964–4.04	7
	10.5	0.15	1.00–7.00	0.770–5.62	6
	11.0	0.37	0.50–6.00	1.63–12.0	9
	11.2	0.48	0.50–4.00	2.30–11.6	6
	11.5	0.65	0.50–4.00	4.07–16.4	6
piperazine (9.94)	9.5	0.27	1.00–7.00	1.11–6.30	7
	10.0	0.53	1.00–6.00	1.92–10.6	6
	10.3	0.70	1.00–7.00	2.96–17.9	7
	10.6	0.82	1.00–7.00	3.38–21.1	7
1-(β-hydroxyethyl)-piperazine (9.38)	8.7	0.17	7.00–16.0	1.33–2.91	7
	9.0	0.29	3.00–8.00	0.995–2.52	6
	9.4	0.51	2.00–8.00	1.11–3.89	6
morpholine (8.78)	9.1	0.67	1.00–7.00	0.764–4.77	7
	9.3	0.77	1.00–7.00	0.961–5.20	7
	9.5	0.84	1.00–5.00	1.01–3.80	5
	9.7	0.89	1.00–7.00	0.963–6.12	7
1-formylpiperazine (7.98)	7.5	0.25	1.00–7.00	0.155–0.789	7
	8.0	0.51	1.00–7.00	0.259–1.20	7
	8.5	0.77	1.00–7.00	0.374–1.81	7
piperazinium ion (5.81)	5.5	0.33	8.00–20.0	0.164–0.297	6
	5.8	0.50	4.50–15.0	0.158–0.338	6
	6.1	0.67	3.00–20.0	0.142–0.493	8

[a] As in Table I.

aryl thiolate ion, the substrate, and the free amine, respectively, and k_o and k_N are the rate coefficients for hydrolysis and aminolysis of the substrate, respectively.

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

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

Plots of k_{obsd} vs [N] at constant pH were linear; the k_N values, obtained as the slope of the plots, were pH-independent. In the reactions of DNPDTC the value of k_o was negligible compared with that of k_N[N]. For the TNPDTC aminolysis k_o was significant and pH dependent at high pH, obeying eq 3, where k_w and k_{OH} are the rate coefficients for neutral and alkaline hydrolysis. A plot of

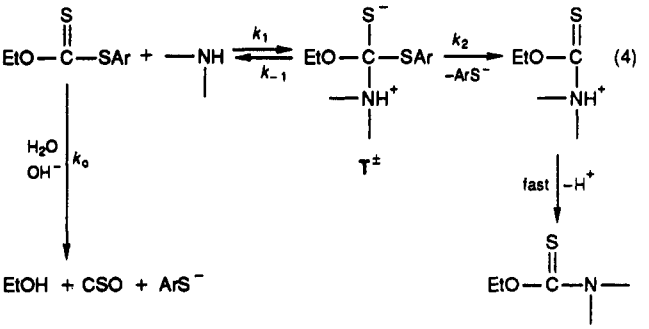
$$k_o = k_w + k_{OH}[OH^-] \quad (3)$$

k_o vs [OH^-] was linear with $k_w = (1.0 \pm 0.3) \times 10^{-3}$ s^{-1} and $k_{OH} = (7.3 \pm 0.4)$ s^{-1} M^{-1}. A more reliable k_w value was found in the reactions of TNPDTC with piperazinium ion at low pH, where the second term of eq 3 is negligible; this value is $k_w = (7.4 \pm 0.5) \times 10^{-4}$ s^{-1}.

With the statistically,[6,9] corrected values of k_N and pK_a, shown in Table III, the Brönsted-type plots of Figure 1 were drawn.

Discussion

According to the rate law, the Brönsted plots obtained and the product studies the present reactions can be described by the mechanism shown in eq 4, where –NH represents a secondary alicyclic amine.



Applying the steady-state condition to the zwitterionic tetrahedral intermediate ($T^{\pm}$) of eq 4, one obtains eq 5, where k_N is the macroscopic rate coefficient for the aminolysis of the substrates.

$$k_N = \frac{k_1k_2}{k_{-1} + k_2} \quad (5)$$

The curved Brönsted plots in Figure 1 can be explained by a change in the rate-limiting step from k_2 at low amine basicity (where $k_{-1} \gg k_2$, i.e., $k_N = K_1k_2$, where K_1 is the equilibrium constant for the first step) to k_1 at high amine basicity (where $k_{-1} \ll k_2$, i.e., $k_N = k_1$).[2,3,5,6,10] The Brönsted lines in Figure 1 were calculated by a semiempirical equation based on the existence of $T^{\pm}$ (eq 6)[2,6,10] with the

$$\log\frac{k_N}{k_N^\circ} = \beta_2(pK_a - pK_a^\circ) - \log\frac{1+a}{2} \quad (6)$$

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

following parameters: $\beta_1 = 0.2$, $\beta_2 = 0.8$ for the reactions of both substrates, $\log k_N^\circ = 0.15$ and $pK_a^\circ = 9.2$ for the reactions of DNPDTC, and $\log k_N^\circ = -0.30$ and $pK_a^\circ = 8.4$ for the reactions of TNPDTC. β_1 and β_2 are the Brönsted slopes at high and low pK_a values, respectively, and k_N° and pK_a° are the k_N and pK_a values at the center of curvature (for which $k_{-1} = k_2$ in eq 4).[2,3,5,6,10] The β_1 and β_2 values found in this work are similar (within an experimental error of ±0.05) to those found in the

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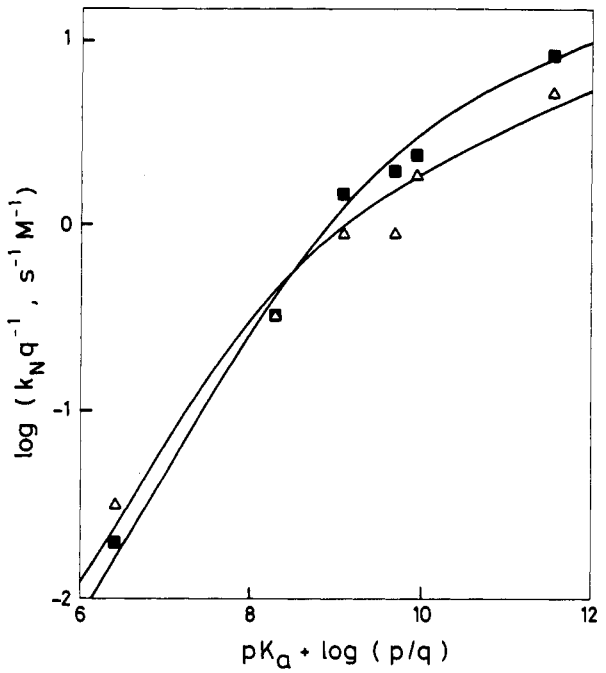

Figure 1. Statistically corrected Brönsted-type plots for the aminolysis of DNPDTC (■) and TNPDTC (△). The lines are calculated by an equation based on the hypothesis of a tetrahedral intermediate (eq 6) and the points are experimental.

Table III. Statistically Corrected Values of pK_a and k_N and Values of Rate Microcoefficients Obtained in the Aminolysis of DNPDTC and TNPDTC

amine	pK_a + log p/q	k_N/q, $s^{-1} M^{-1}$	k_1/q, $s^{-1} M^{-1}$	k_{-1}/k_2
	DNPDTC			
piperidine	11.54	8.47	8.47	
piperazine	9.94	2.37	4.0	0.70
1-(β-hydroxyethyl)-piperazine	9.68	1.90	3.5	0.75
morpholine	9.08	1.42	2.65	0.77
1-formylpiperazine	8.28	0.324	1.78	4.5
piperazinium ion	6.41	0.0254	0.8	32
	TNPDTC			
piperidine	11.54	5.1	5.1	
piperazine	9.94	1.85	2.81	0.3
1-(β-hydroxyethyl)-piperazine	9.68	0.94	2.45	1.3
morpholine	9.08	0.92	1.82	0.8
1-formylpiperazine	8.28	0.322	1.23	2.3
piperazinium ion	6.41	0.033	0.55	13

aminolysis of NPDTC,[5] aryl acetates,[1] aryl thioacetates,[3] acetyl chloride, and methyl chloroformate.[10]

The fact that the $pK_a°$ values for the aminolysis of *O*-ethyl *S*-aryl dithiocarbonates follows the sequence: TNPDTC < DNPDTC < NPDTC (the latter $pK_a° = 9.6$)[5] is in line with the results found in the aminolysis of aryl acetates,[1] aryl phenyl carbonates,[2] aryl thioacetates,[3] and aryl methyl carbonates;[11] namely, the $pK_a°$ value decreases as the leaving group becomes better. This can be explained on the basis of $T^{\pm}$ (eq 4); the greater the nucleofugality of the leaving group (the larger k_2 of eq 4) the lower will be the basicity of an amine for which $k_{-1} = k_2$.

The Brönsted data for TNPDTC can also be accommodated by a straight line, although a curve seems more likely. Therefore, a concerted process cannot be excluded for the TNPDTC reactions; nevertheless, we are more inclined toward the stepwise mechanism (see below).

The curved Brönsted-type plots of Figure 1 can also be explained in terms of structural variation of the transition state in a one-step process: The experimental points can also be accommodated by an equation based on Hammond,[12] Marcus, and Murdoch ideas,[13] which predict a continuous variation of the Brönsted slope (β) from a large value at low amine basicities to a smaller β at high basicities, in a concerted process.[13]

On the other hand, single electron transfer (SET) mechanisms have been found lately in reactions of OH^- with dinitrochlorobenzenes[14] and ethyl dinitrobenzoates in DMSO–water[15] and in those of anionic nucleophiles with reactive aryl acetates in water.[16] In the latter case the operation of the SET mechanism was demonstrated by the linear plot of $\Delta G^{\ddagger}$ vs IP*, where IP* is the vertical ionization potential of the anionic nucleophile.[16]

The IP* data for alicyclic amines is scarce in the literature; we have only found experimental IP* values for piperidine, piperazine, and morpholine: 8.66, 8.98, and 8.91 eV, respectively.[17] The plot log k_N vs IP* for these three points is not linear (not shown), and the IP* sequence is not the same as that of the reactivity. Nevertheless, in view of the scarcity of data and the fact that the IP* datum for pyrrolidine is available (8.77 eV),[17b] we used the k_N value for the reaction of this amine with DNPDTC (k_N = 28.3 $s^{-1} M^{-1}$, in the same conditions as the other reactions).[18] The new plot of log k_N vs IP* (with four points) looks more scattered still. Therefore, we can reasonably assume that SET is not involved in the rate-determining step of the mechanism. Nevertheless, a firm conclusion regarding this matter must await due to the scarcity of data.

We think that the two-step hypothesis is more likely to account for our experimental results than the concerted or SET mechanisms for the following reasons.

(1) There is a rather large variation of the $pK_a°$ value with the change of the leaving group of the substrate (from 9.2 for the DNPDTC reactions to 8.4 for those of TNPDTC). This is consistent with the stepwise mechanism, as explained above. Little or no variation of $pK_a°$, with either the leaving group or the nonleaving group of the substrate, is expected for a concerted reaction.[19]

(2) There is a steric effect caused by the third nitro group of TNPDTC in its aminolysis, compared to DNPDTC. This is manifested at high pK_a values (see Figure 1) where the k_1 step of eq 4 is rate determining and is due to steric inhibition caused by the second *o*-nitro group of the substrate. Table III shows that for piperine the k_1 ratio TNPDTC/DNPDTC is ca. 0.6. On the basis

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of a normal arylthiolate leaving group effect, k_1 for TNPDTC is 6-fold smaller than expected (see later). When the k_2 step is rate limiting, $k_N = K_1k_2$, one expects inhibition on K_1 but enhancement of k_2; therefore, the steric effect should not be so pronounced in this case (see the plots of Figure 1 at low pK_a).

Similar inhibition caused by the second *o*-nitro group, although less pronounced, is observed in the reactions of alicyclic amines with 2,4,6-trinitrophenyl thioacetate (TNPTA) compared to that of 2,4-dinitrophenyl thioacetate (DNPTA).[3] In this case the k_N ratio TNPTA/DNPTA for the three more basic amines is ca. 6 (where the k_1 step is rate-determining), whereas the same ratio is ca. 20 for the two less basic amines (where the k_2 step is rate-limiting).[3] For the pyridinolysis of the substrates, the above ratio is ca. 4 for the two more basic amines, whereas it is ca. 80 for the two less basic amines.[3]

A one-step reaction should show less steric hindrance by the leaving group than the k_1 step of a stepwise mechanism, since in the former process the leaving group has partially broken its bond with the central carbon in the transition state.

(3) In the reactions of piperidine with DNPDTC and TNPDTC the k_1 step is rate determining, assuming a stepwise mechanism. The Brönsted plot for k_1 obtained in the reactions of piperidine with PDTC,[5] NPDTC,[5] and DNPDTC (k_N value of Table III) is linear (plot not shown $\beta_{lg} = -0.3$). The value of β_{lg} agrees with those found in the aminolysis of aryl acetates and carbonates when the k_1 step is rate-determining.[1,2] Since the two former reactions are stepwise,[5] the linearity of the plot indicates that the latter is also a two-step process. Obviously, the k_1 value for the reaction of piperidine with TNPDTC does not correlate with the reactions of the same amine with PDTC, NPDTC, and DNPDTC, for steric reasons. Extrapolation of the Brönsted line to the pK_a of 2,4,6-trinitrobenzenethiol (TNPSH, $pK_a = 1.4$)[3] gives a value of k_1 for the reaction of piperidine with TNPDTC which is ca. 6 times larger than that of the experimental k_1. This quantifies the steric effect for the k_1 step assuming this reaction to be a two-step process.

It is also possible that most of the reactions studied here are stepwise but those of TNPDTC with the less basic amines are concerted due to the presence of two good nucleofuges in the putative tetrahedral intermediate ($T^{\pm}$). In any case if the reactions proceed through $T^{\pm}$ this should be highly unstable, with its lifetime near that of a bond vibration.[20]

The k_1 values for the reactions of the alicyclic amines with DNPDTC and TNPDTC can be determined by extrapolation of the Brönsted lines at high pK_a (Figure 1); therefore, the k_{-1}/k_2 ratios can also be found.[21] Table III shows the values of k_1 and the k_{-1}/k_2 ratios. With the latter values for the aminolysis of NPDTC,[5] DNPDTC and TNPDTC, eq 7 results by dual regression analysis,

$$\log (k_{-1}/k_2) = 4.0 - 0.5pK_a(N) + 0.2\ pK_a(lg) \qquad (7)$$

where N and lg refer to the amine and leaving group of the substrate, respectively. The errors of the coefficients of eq 7 are ±0.3, ±0.1, and ±0.1, respectively. Since it is known that log k_2 is not dependent on amine basicity,[2-6] the sensitivity of log k_{-1} to amine basicity is $\beta_{-1}(N) = -0.5$, according to eq 7. The $\beta_{-1}(N)$ value can also be calculated from $\beta_{-1}(N) = \beta_1(N) - \beta_{eq}(N) = 0.2 - 0.8 = -0.6$, where $\beta_{eq}(N)$ is the Brönsted sensitivity to the amine basicity of the equilibrium constant for the formation of $T^{\pm}$. $\beta_1(N)$ and $\beta_{eq}(N)$ are the Brönsted slopes at high and low pK_a. It can be seen that the experimental (eq 7) and calculated $\beta_{-1}(N)$ values are in agreement (within experimental error).

The dependence of $\log(k_{-1}/k_2)$ on the basicity of the leaving group is remarkable small (eq 7). This value is $\beta_{-1}(lg) - \beta_2(lg)$, and since the latter is negative, it follows that both β are very small. This is in contrast to the corresponding values found in the aminolysis of aryl acetates,[22] diaryl carbonates,[2] and aryl thioacetates,[3] where $\beta_{-1}(lg) = +0.4$ and $\beta_2(lg) = -0.5$, -0.7, and -0.3, respectively.

Equation 7 predicts that the pK_a value of an (hypothetical) amine which is expelled from $T^{\pm}$ as fast as the leaving group of the substrate is $pK_a^\circ = 8.6$, 9.4, 9.8, and 10.6, for the aminolysis of TNPDTC, DNPDTC, NPDTC, and PDTC, respectively.[23] The experimental pK_a° values are 8.4, 9.2, and 9.6 for the three first reactions. An experimental pK_a° value for the latter reaction could not be obtained since the k_2 step was much slower than the deprotonation of $T^{\pm}$ to yield an anionic intermediate.[5] An estimation of $pK_a^\circ = 10.3$ for this reaction can be deduced by extrapolation of the linear plot of the experimental pK_a° vs $pK_a(lg)$ for the other three reactions.

The values of the isobasic amine/ArS^- ratio from $T^{\pm}$, calculated through eq 7, are larger than unity in all cases. This is in accord with the results found in the aminolyses of diaryl carbonates,[2] aryl acetates,[11c,22] methyl aryl carbonates,[11] aryl benzoates,[24] aryl thioacetates,[3] and other compounds,[25] where the amine is expelled from a tetrahedral intermediate much faster than an isobasic aryl oxide (or aryl thioxide) ion.

By replacing in eq 7 the k_{-1} values found in the aminolysis of PDTC[5] values of k_2 can be found.[26] These values range from 4×10^7 to 1×10^8 s^{-1}. Since they should be independent of amine basicity we will take the average value as $k_2 = 7 \times 10^7$ s^{-1}. This is larger than the k_2 value for the same expulsion from the $T^{\pm}$ formed in the aminolysis of phenyl dithioacetate (PDTA): 10^6–10^7 s^{-1}.[27] The value of k_{-1} for a given amine in the PDTC aminolysis is also larger than that in the PDTA aminolysis.[27] The larger k_2 and k_{-1} values found in the PDTC reactions compared to PDTA are in agreement with the findings in other aminolyses: Replacement of Me by EtO in $T^{\pm}$ results in faster expulsion of both the amine and the leaving group of the substrate. In the aminolysis of DNPTA the existence of $T^{\pm}$ was deduced from a curved Brönsted-type plot,[3] whereas a concerted aminolysis of *S*-(2,4-dinitrophenyl) *O*-ethyl thiocarbonate (DNPTC) was inferred from a linear Brönsted plot of slope $\beta = 0.56$.[4] The instability

(20) Capon, B.; Matos-Sanchez, M. N. *Tetrahedron* **1983**, *39*, 4143. McClelland, R. A.; Santry, L. J. *Acc. Chem. Res.* **1983**, *16*, 394. Guthrie, J. P. *Acc. Chem. Res.* **1983**, *16*, 122 and references cited therein.

(21) Since the general expression for k_N is $k_N = k_1k_2/(k_{-1} + k_2) = k_1/(k_{-1}/k_2 + 1)$, knowing k_1 and k_N the values of the k_{-1}/k_2 ratio can be determined. Nevertheless, the errors involved in the latter values are large.

(22) Castro, E. A.; Ureta, C. *J. Org. Chem.* **1990**, *55*, 1676.

(23) This is the $pK_a(N)$ value of eq 7 when $k_{-1} = k_2$. The $pK_a(lg)$ values (at 25 °C, ionic strength 0.2 M) of TNPSH, DNPSH, NPSH, and PSH are 1.4, 3.4, 4.6, and 6.5, respectively.[3]

(24) Castro, E. A.; Santander, C. L. *J. Org. Chem.* **1985**, *50*, 3595.

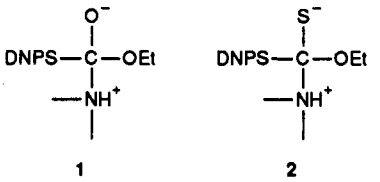
(25) Gravitz, N.; Jencks, W. P. *J. Am. Chem. Soc.* **1974**, *96*, 499.

(26) In eq 7, $pK_a(lg) = 6.5$ for PDTC. Substituting the experimental k_{-1} of ref 5 and the $pK_a(N)$ values of the different amines, the values of k_2 can be determined.

(27) Castro, E. A.; Ibáñez, F.; Santos, J. G.; Ureta, C. *J. Chem. Soc., Perkin Trans. 2* **1991**, 1919.

of the latter "intermediate" was attributed to the "push" given by EtO which enhances the nucleofugality of both the amine and aryl thiolate ion from the "intermediate", relative to Me.[4] In line with this is the change in mechanism from the stepwise acetyl transfer between pyridines[28] to the concerted methoxycarbonyl transfer between isoquinoline and pyridines.[29]

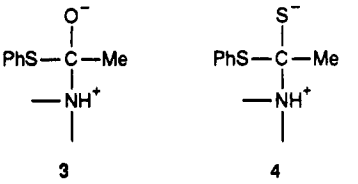
Comparison of the mechanisms of the reactions of alicyclic secondary amines with DNPDTC and DNPTC (probably stepwise and concerted, respectively) indicates that expulsion of an amine and/or 2,4-dinitrobenzenethiolate ion ($DNPS^-$) from 1 must be faster than from 2



1 2

rendering therefore the former "intermediate" more unstable than the latter. The same effect was found in the acetate system. Expulsions of a given amine and PhS^- from 3 are much faster than the same leavings from 4, which was attributed to the smaller ability of S^- in 4 than O^- in 3 to form a double bond and expel a nucleofuge,[27] due to a weaker π-bonding energy of the thiocarbonyl group compared to carbonyl.[30]

It should be mentioned that the driving force for thiolate displacement from $T^{\pm}$ (eq 4) depends not only on its pK_a



3 4

but on the fact that the acyl product initially formed is an unstable N-protonated thiocarbonate.[31]

The reactions of secondary alicyclic amines with PDTC are base-catalyzed by a second amine molecule.[5] The reasons we did not find this catalysis in the present reactions are as follows: (i) The value of k_2 must be smaller in the reactions of PDTC compared to DNPDTC and TNPDTC, and therefore, in the former aminolysis there is enough time for deprotonation of $T^{\pm}$ by a base to give an anionic intermediate. (ii) Deprotonation of the $T^{\pm}$ formed in all the above reactions by the corresponding amine is thermodynamically favorable;[5] therefore, we can assume a rate coefficient $k_3 = 10^{10}\ s^{-1}\ M^{-1}$ for all the above proton transfers, independent of both the amine and substrate.[5] Since the free-amine concentrations used are of the same order of magnitude in all these reactions, the deprotonation rate, $k_3[N]$, should also be similar. Therefore, the fact that amine catalysis was found in the PDTC aminolysis can be explained because in these reactions k_2 is smaller than the $k_3(N)$ is similar to the corresponding coefficients found in the present reactions.

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(28) Fersht, A. R.; Jencks, W. P. *J. Am. Chem. Soc.* **1970**, *92*, 5442.
(29) Chrystiuk, E.; Williams, A. *J. Am. Chem. Soc.* **1987**, *109*, 3040.
(30) Hill, S. V.; Thea, S.; Williams, A. *J. Chem. Soc., Perkin Trans. 2* **1983**, 437.
(31) We thank a reviewer for this comment.