Kinetics and Mechanism of the Aminolysis of Phenyl and 4-Nitrophenyl Ethyl Thionocarbonates

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The reactions of the title substrates (PTOC and NPTOC, respectively) with secondary alicyclic amines are subjected to a kinetic study in aqueous solution at 25.0 °C, ionic strength 0.2 M (KCl). Under amine excess, pseudo-first-order rate coefficients (k_{obsd}) are found throughout. The order in amine is one for the reactions of piperidine but is of intermediate order between 1 and 2 for the reactions of the other amines. The kinetic results can be accommodated by a reaction scheme with two hypothetical tetrahedral intermediates: a zwitterionic ($T^{\pm}$) and an anionic (T^{-}) one, whereby amine catalysis (deprotonation of $T^{\pm}$ to give T^{-}) is kinetically important. Both the pK_a of $T^{\pm}$ and the rate coefficient for proton transfer (k_3 ca. 10^{10} s^{-1} M^{-1}) are estimated. The values of the other rate microcoefficients of the scheme are found by a nonlinear least-squares fitting, and these values are compared with those exhibited in the aminolysis of phenyl thionoacetate (PTOA), and *S*-phenyl and *S*-(4-nitrophenyl) *O*-ethyl dithiocarbonates (PDTC and NPDTC, respectively). The Brönsted type plots for amine basicity have slopes β_N ca. 0.2 for rate-determining amine attack (k_1) and β_N ca. 0.8 for amine expulsion from $T^{\pm}$ (k_{-1}), in accord with the β_N values found in similar aminolyses. The general base catalysis by amine found in the aminolysis of NPTOC, in contrast with the lack of such catalysis in the aminolysis of 4-nitrophenyl methyl carbonate, is explained by a smaller rate coefficient for expulsion of 4-nitrophenoxide (k_2) from $T^{\pm}$ (which competes with amine deprotonation of $T^{\pm}$) relative to the same expulsion from the analogous oxy intermediate.

Introduction

Although the mechanisms of the aminolysis of aryl esters[1] and carbonates,[2] and their *S*-aryl derivatives[3] are well documented, little is known about the mechanism of thionoesters and thionocarbonates. Among the latter we are aware of kinetic studies on the aminolysis of 4-nitrophenyl thionobenzoate[4] and phenyl thionoacetate[5] and on the alcoholysis of the former compound.[6]

To our knowledge there have been no reports on the kinetics of the aminolysis of thionocarbonates. In the present work we carry out a kinetic and mechanistic study of the reactions of the title thionocarbonates with a series of secondary alicyclic amines in water. The aim is to compare these reactions with those of the same amines with phenyl thionoacetate[5] and *S*-phenyl and *S*-(4-nitrophenyl) *O*-ethyl dithiocarbonates in water,[7] in order to assess the influence of the nonleaving and leaving groups of the substrate on the kinetics and mechanism of these reactions. It is also of interest to examine the influence of the thiocarbonyl group by comparing the present reactions with those of similar oxycarbonates.[8]

Experimental Section

Materials. The amines were purified as described.[9] Phenyl ethyl thionocarbonate (PTOC) was synthesized as reported[10] and characterized by ^{1}H NMR and IR analyses. 4-Nitrophenyl ethyl thionocarbonate (NPTOC) has not been previously prepared to our knowledge. It was synthesized using a general literature method employing *O*-ethyl chlorothioformate and 4-nitrophenol in pyridine.[11] NPTOC was identified by the following analyses: ^{1}H NMR (200 MHz, CDCl$_3$) δ 1.48 (t, 3H, J = 7.1 Hz), 4.61 (q, 2H, J = 7.1 Hz), 7.28 (sd, 2H, J = 9.1 Hz), 8.30 (sd, 2H, J = 9.1 Hz); ^{13}C NMR (50 MHz, CDCl$_3$) δ 13.69 (CH$_3$), 71.05 (CH$_2$), 123.36 (C-2/6), 125.34 (C-3/5), 145.90 (C-4), 157.49 (C-1), 193.63 (C=S); IR (KBr) 1597 (C=C), 1532 and 1351 (C–NO$_2$), 1304 (C=S), 1196 (C–O), 865 (CH, arom) cm^{-1}. Anal. Calcd for C$_9$H$_9$O$_4$NS: C, 47.57; H, 3.99; N, 6.16; S, 14.11. Found: C, 47.55; H, 4.05; N, 6.00; S, 13.83.

Kinetic Measurements. These were carried out spectrophotometrically, in water at 25.0 ± 0.1 °C, ionic strength 0.2 M (KCl), by following the release of phenol and/or phenoxide ion (269 nm), or 4-nitrophenol and/or 4-nitrophenoxide ion (400 nm). The instrument employed and the kinetic procedure were previously described.[5] The initial substrate concentration was 2×10^{-5} M, and the amine was in excess over the substrate (at least 10-fold). Pseudo-first-order rate coefficients (k_{obsd}) were found throughout by the method reported.[5] The experimental reaction conditions and the values of k_{obsd} are shown in Tables 1 and 2.

Product Studies. The presence of phenol and 4-nitrophenol and their conjugate bases was determined by comparison of the UV–vis spectra at the end of the reactions with those of authentic samples in the same conditions. The presence of thiocarbamates was determined by HPLC, as reported.[7]

⊗ Abstract published in *Advance ACS Abstracts,* April 15, 1996.

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Table 1. Experimental Conditions and k_{obsd} Values for the Aminolysis of Phenyl Ethyl Thionocarbonate (PTOC)[a]

amine	pH	F_N[b]	$10^2[N]_{tot}$,[c] M	$10^3 k_{obsd}$, s^{-1}	no. of runs
piperidine	10.94	0.33	0.70−9.0	4.4−86	7
	11.24	0.50	0.50−5.0	5.8−74	8
	11.54	0.67	0.50−5.0	5.9−108	7
piperazine	9.64	0.33	0.10−1.4	0.17−4.2	9
	9.94	0.50	0.10−1.0	0.13−4.1	8
	10.24	0.67	0.10−1.0	0.14−8.4	7
1-(2-hydroxyethyl)- piperazine	9.08	0.33	5.0−15	3.4−35	7
	9.38	0.50	5.0−20	9.1−82	7
	9.68	0.67	5.0−20	16−117	7
morpholine	8.78	0.50	5.0−20	4.9−47	7
	9.08	0.67	5.0−20	7.3−71	7
	9.38	0.80	5.0−20	9.2−93	7
1-formylpiperazine	7.68	0.33	7.0−30	2.8−47	6
	7.98	0.50	7.0−40	4.8−123	7
	8.28	0.67	7.0−30	9.1−135	6

[a] In aqueous solution at 25.0 °C, ionic strength 0.2 M (KCl). [b] Free-amine fraction. [c] Concentration of total amine.

Table 2. Experimental Conditions and k_{obsd} Values for the Aminolysis of 4-Nitrophenyl Ethyl Thionocarbonate (NPTOC)[a]

amine	pH	F_N	$10^3[N]_{tot}$, M	$10^3 k_{obsd}$, s^{-1}	no. of runs
piperidine	10.94	0.33	0.5−15	1.7−43	7
	11.24	0.50	0.5−15	3.1−63	7
	11.54	0.66	0.3−10	3.1−55	7
piperazine	9.64	0.33	1.0−16	1.0−38	8
	9.94	0.50	0.5−10	1.1−31	9
	10.24	0.67	1.0 −10	3.4−46	7
1-(2-hydroxyethyl)- piperazine	9.08	0.33	8.5−60	4.4−61	7
	9.38	0.50	8.5−60	6.5−86	7
	9.68	0.67	5.5−40	7.0−82	7
morpholine	8.78	0.50	8.5−60	4.1−63	7
	9.08	0.67	8.5−60	4.6−101	7
	9.38	0.80	8.5−60	7.6−143	7
1-formylpiperazine	7.68	0.33	70−300	5.7−51	6
	7.98	0.50	10−400	0.60−142	11
	8.28	0.67	70−300	13−123	6
piperazinium ion	5.50	0.33	25−85	0.14−0.50	5
	5.80	0.49	10−100	0.08−0.83	7
	6.20	0.71	10−100	0.13−1.4	7

[a] Conditions and symbols as in Table 1.

Results and Discussion

The reactions of piperidine with phenyl ethyl thiono-carbonate (PTOC) and 4-nitrophenyl ethyl thionocarbon-ate (NPTOC), under the reaction conditions (see Table 1), obey the rate law given by eqs 1 and 2, where P is

$$\frac{d[P]}{dt} = k_{obsd}[S] \tag{1}$$

$$k_{obsd} = k_0 + k_N[\text{piperidine}] \tag{2}$$

either phenol or 4-nitrophenol (and/or their conjugate bases) and S represents the substrate; k_0 and k_N are the rate coefficients for hydrolysis and aminolysis of the substrate, respectively.

Plots of k_{obsd} against piperidine free base concentration at three pH values were linear, according to eq 2, with the intercept (k_0) and the slope (k_N) independent of pH. The value of k_0 was almost negligible compared to that of the aminolysis term in eq 2.

For the reactions of the other amines with PTOC and NPTOC the plots of k_{obsd} vs amine free base concentration at three pH values were nonlinear and pH independent (see Figure 1 as an example).
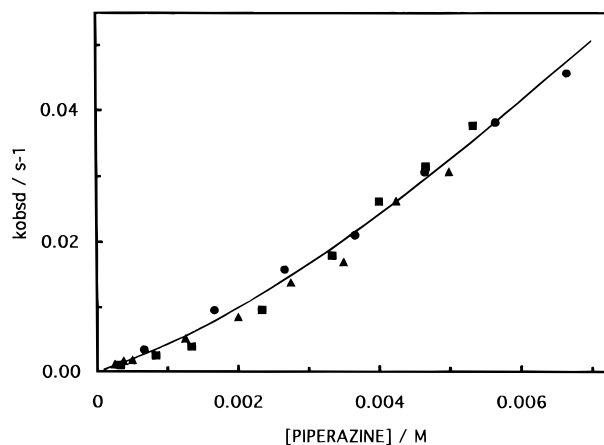

Figure 1. Plot of k_{obsd} vs free-amine concentration for the reaction of NPTOC with piperazine, at pH 9.64 (■), 9.94 (▲), and 10.24 (●), in aqueous solution at 25.0 °C, ionic strength 0.2 M. The solid line was calculated by eq 3 and the rate microcoefficients in Table 3.
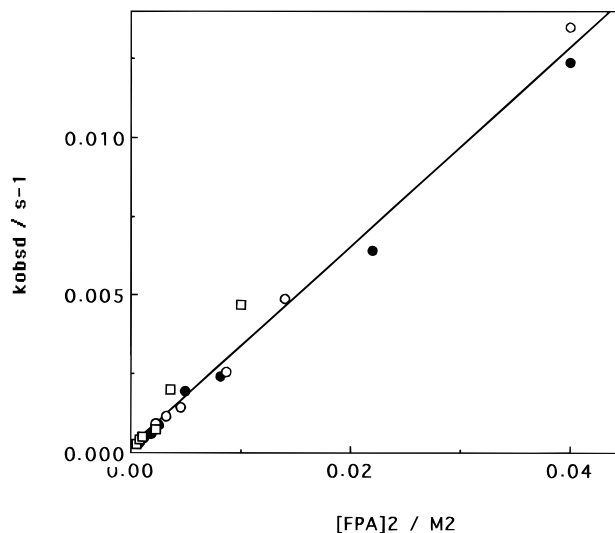

Figure 2. Plot of k_{obsd} vs the square of free-amine concentra-tion for the reaction of PTOC with 1-formylpiperazine (FPA) at pH 7.68 (□), 7.98 (●), and 8.28 (○), in aqueous solution at 25.0 °C, ionic strength 0.2 M.

For the reactions of PTOC with 1-formylpiperazine (FPA), the plots of k_{obsd} vs [FPA]^2 were linear, with both intercept and slope independent of pH. In order to be sure of the second order in amine, we extended the original amine concentration range up to a value of 0.2 M (see Figure 2).

According to the kinetic results, shown by the k_{obs} vs free-amine concentration plots, and the product studies, a likely mechanism for the present reactions is depicted in Scheme 1. In this scheme, HN< represents a second-ary alicyclic amine and Ar = phenyl or 4-nitrophenyl. The k_3 step is deprotonation by an amine of the zwitterionic tetrahedral itermediate T$^{\pm}$ to yield the anionic interme-diate T$^-$. Decomposition of T$^-$ to products should be fast;[12] therefore the k_3 step should be rate determining for the left hand side path of Scheme 1.

Assuming the steady-state condition for both hypo-thetical tetrahedral intermediates, eq 3 results, where HN represents the amine.

$$k_{obsd} = \frac{k_1(k_2 + k_3[\text{HN}])[\text{HN}]}{k_{-1} + k_2 + k_3[\text{HN}]} \tag{3}$$

Table 3. Values of the pK_a of the Conjugate Acids of Secondary Alicyclic Amines and Rate Microcoefficients of Scheme 1

amine	pK_a	k_1/s^{-1} M^{-1}		10^{-8} k_{-1}/s^{-1}	
		PTOC	NPTOC	PTOC	NPTOC
piperidine	11.24	3.2 ± 0.3	8.3 ± 0.5	0.1 [a]	0.03[a]
piperazine	9.94	3.0 ± 0.3	13.4 ± 1	1.6 ± 0.2	0.85 ± 0.09
1-(2-hydroxyethyl)piperazine	9.38	1.2 ± 0.1	3.9 ± 0.4	5.0 ± 0.4	1.0 ± 0.1
morpholine	8.78	0.9 ± 0.1	2.8 ± 0.3	9.0 ± 0.9	1.3 ± 0.2
1-formylpiperazine	7.98	0.6[a]	1.3 ± 0.2	44[a]	20 ± 2

$$k_2(\text{PTOC}) = (1.0 \pm 0.5) \times 10^7 \text{ s}^{-1}$$
$$k_2(\text{NPTOC}) = (3.0 \pm 0.4) \times 10^7 \text{ s}^{-1}$$
$$k_3 = (1.0 \pm 0.3) \times 10^{10} \text{ s}^{-1} \text{ M}^{-1}$$

[a] Values obtained by extrapolation of the Brönsted-type plots for the other amines.

Scheme 1
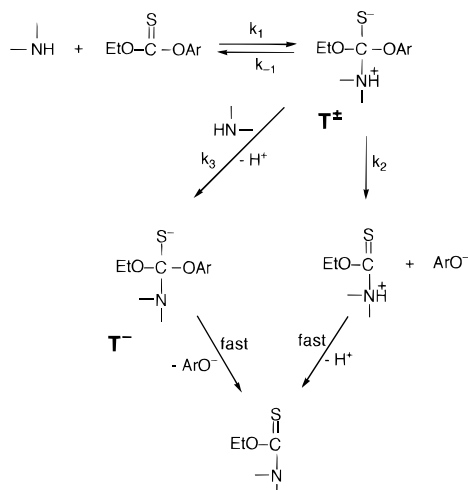
The linear k_{obsd} vs [HN] plots found for the reactions of piperidine can be explained by assuming k_{-1} is less than $k_2 + k_3$[HN]; hence $k_{obsd} = k_1$[HN]. This inequality is reasonable in view of the strong C–N$^+$H bond in T$^\pm$ for this very basic amine (see below).[13]

For the reactions of PTOC with 1-formylpiperazine, k_2 is less than k_3[HN] and k_{-1} is greater than $k_2 + k_3$[HN] (see below), and hence, according to eq 3, $k_{obsd} = (k_1/k_{-1})$-k_3[HN]^2, which has the same form as the rate law found experimentally.

For the other reactions, eq 3 applies as such. The value of k_3 of Scheme 1 for all reactions was estimated as 10^{10} s^{-1} M^{-1} (see below), and the rate microcoefficients k_1, k_{-1}, and k_2 were found by a nonlinear least-squares fitting of eq 3 to the experimental results. Figure 1 is an example of such fitting. The values of the rate microcoefficients are shown in Table 3.

The value of k_3 for the intermediates T$^\pm$ (Ar = phenyl and 4-nitrophenyl) of Scheme 1 can be estimated by knowledge of their pK_a values. The pK_a of one of these intermediates (Ar = Ph) can be estimated in the following way.

The pK_a of **1** has been found to be 2.8 pK_a units lower than that of the parent aminium ion (that is, the protonated amine itself),[5] by following Jencks' procedure.[14] The procedure involves the use of Hammett inductive parameters for substituents attached to a central tetrahedral carbon atom.[14] Considering that the
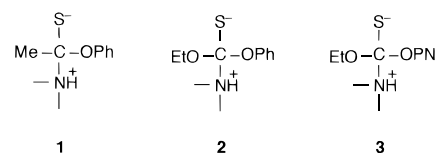
inductive effects are the most important in tetrahedral intermediates,[14] and using a value of $\rho_I = -9.2$ for the pK_a of X-substituted >(X)CN$^+$(H)< intermediates,[15] and $\sigma_I = -0.01$ for Me and $\sigma_I = 0.28$ for EtO,[15] one obtains pK_a(**2**) − pK_a(**1**) = −9.2 (0.28 − (−0.01)) = −2.7 pK_a units. Therefore, the pK_a of **2** should be 2.8 + 2.7 = 5.5 pK_a units lower than that of the parent aminium ion.

The pK_a of the other intermediate T$^\pm$ of Scheme 1 (species **3**, where NP = 4-nitrophenyl) can be estimated with $\sigma_I = 0.37$ for PhO,[16] and $\sigma_I = 0.47$ for 4-nitrophenoxy,[17] giving pK_a(**3**) − pK_a(**2**) = −9.2(0.47−0.37) = −0.9 pK_a unit. Hence pK_a(**3**) should be 5.5 + 0.9 = 6.4 pK_a units lower than that of the parent aminium ion.

Since the pK_a values of both intermediates **2** and **3** are lower than those of their parent aminium ions, it follows that the proton transfer from **2** or **3** to the corresponding amine is thermodynamically favorable. Therefore, a value for k_3 of ca. 10^{10} s^{-1} M^{-1} can be estimated for the proton transfers from both zwitterionic tetrahedral intermediates of Scheme 1.[3,5,7,18]

The inequalities stated above involving rate microcoefficients are justified when taking into account the values of the rate microcoefficients found in the fittings of the k_{obsd} vs [HN] plots (see Table 3).

The larger k_2 value for leaving group departure obtained in the reactions of NPTOC relative to that of PTOC (Table 3) is reasonable in view of the lower basicity

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(12) Since T$^-$ is a very reactive intermediate, complying with the steady state condition, the term "fast" for T$^-$ decomposition means that this step is faster than k_{-3}[NH$_2^+$] (not shown in Scheme 1). The k_3 protonation step is thermodynamically favorable since the pK_a of T$^\pm$ (Ar = Ph), for example, is 5.5 pK_a units lower than that of the parent aminium ion (see text). This means that the k_{-3} step is unfavorable with $k_{-3} = k_3$. K_a(NH$_2^+$)/K_a(T$^\pm$) = $10^{10} \times 10^{-5.5} \approx 3 \times 10^4$ s^{-1} M^{-1}.[1] Since [NH$_2^+$] was never greater than 0.2 M (see Tables 1 and 2), the value of the rate k_{-3} [NH$_2^+$] should not be greater than ca. 10^4 s^{-1}. It is known that the rate of expulsion of PhO$^-$ from intermediates similar to T$^\pm$ (e.g. those formed in the aminolysis of phenyl acetate) is k_2 ca. 10^6 s^{-1}.[9] Expulsion of ArO$^-$ from T$^-$ should be faster than from T$^\pm$ in view of the extra "push" provided by the amine moiety in T$^-$, which is not possible in T$^\pm$.[1,2] Therefore, it is reasonable that the rate of expulsion of PhO$^-$ from T$^-$ be larger than 10^4 s^{-1}, i.e. faster than k_{-3}[NH$_2^+$]. It is obvious that 4-nitrophenoxide expulsion from T$^-$ should be even faster than PhO$^-$.

(13) According to the microcoefficient values of Table 3 for PTOC, $k_{-1} = 1 \times 10^7$ s^{-1} (piperidine), $k_2 = 1 \times 10^7$ s^{-1}, and $k_3 = 10^{10}$ s^{-1} M^{-1}. With the [HN] values for piperidine of Table 1, the values of k_3[HN] were ca. (0.3–3) $\times 10^8$ s^{-1}, with only three values of 3×10^7 s^{-1}. Therefore, one can safely assume that $k_{-1} < k_2 + k_3$[HN], due to the fact that k_3[HN] > k_{-1} for this reaction.

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of 4-nitrophenoxide ion ($pK_a \approx 7$) compared to that of phenoxide ion ($pK_a \approx 10$). The rather small increase (ca. 3-fold) in k_2 for NPTOC with respect to PTOC is in line with the low sensitivity of k_2 to leaving group basicity (β_{lg}) found in the aminolysis of S-aryl O-ethyl dithiocarbonates.[19] This is in contrast to the large negative β_{lg} values for k_2 found in the aminolysis of aryl acetates ($\beta_{lg} = -0.5$) and diaryl carbonates ($\beta_{lg} = -0.7$).[2] This difference in β_{lg} can be ascribed to the higher polarizability of the C=S bond compared to C=O,[20] which has been found responsible for the low sensitivity of the rate of expulsion of an amine from a tetrahedral intermediate (k_{-1} in Scheme 1) on the leaving group basicity in the aminolysis of S-aryl dithioacetates.[5,21] In contrast, β_{lg} for k_{-1} is large in the aminolysis of aryl oxyesters,[1] diaryl carbonates[2] and S-aryl thioacetates.[3b]

The larger k_1 values for the reactions of NPTOC relative to PTOC (Table 3) are reasonable in view of the more positively charged thiocarbonyl carbon of the former substrate due to a larger electron withdrawal from the 4-nitrophenoxy group in NPTOC compared to phenoxy in PTOC.

On the other hand the larger k_{-1} values for the reactions of PTOC compared to NPTOC (Table 3) are in agreement with the larger "push" of the phenoxy group in T$^{\pm}$ (Scheme 1), relative to that of 4-nitrophenoxy, to expel the amine.[1,2]

The larger k_2 and k_{-1} values for expulsion of phenoxide ion and an amine from **2**, respectively, relative to the same expulsions from **1**,[5] are reasonable in view of the superior "push" provided by EtO in **2** to expel the nucleofuge and the amine, compared to that exerted by Me in **1**. This is in agreement with the results found in the aminolyses of S-aryl O-ethyl dithiocarbonates and S-aryl dithioacetates. Both k_{-1} and k_2 are larger for the former susbtrates.[7,19,21] Also in line with our results is the stepwise mechanism, through a tetrahedral intermediate, found in the aminolysis of S-(2,4-dinitrophenyl) thioacetate[3b] and a concerted process exhibited by the same aminolysis of S-(2,4-dinitrophenyl) O-ethyl thiocarbonate.[22] It was argued that a tetrahedral intermediate cannot be formed in the latter reaction due to its kinetic instability brought about by the larger values of both k_{-1} and k_2 concerning the "intermediate" with EtO, compared to that with Me.[22] Another example is the stepwise acetyl transfer between pyridines[23] and the concerted methoxycarbonyl transfer between isoquinoline and pyridines.[24] Electron donation from substituted phenyl as the "acyl" group of a potential zwitterionic tetrahedral intermediate has been found responsible for the kinetic destabilization of the "intermediate" in the concerted aminolysis of benzoyl fluorides.[25]

The k_1 values for the aminolysis of PTOC (Table 3) are lower than those for the same aminolysis of O-phenyl thionoacetate.[5] This result is in line with the general higher reactivity of acetates than carbonates, due to a larger electron donating resonance of EtO relative to Me
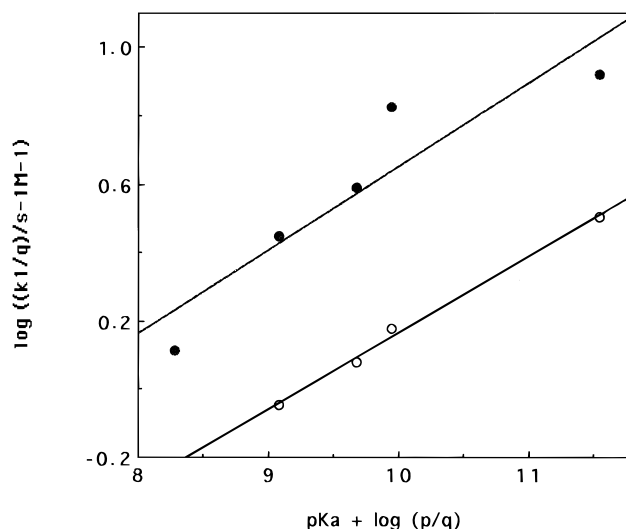
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Figure 3. Brönsted-type plots for k_1 (statistically corrected), obtained in the reactions of secondary alicyclic amines with PTOC (○) and NPTOC (●).

in the corresponding substrates.[2] Also, S-aryl dithioacetates[21,26] are more readily attacked by alicyclic amines to form a tetrahedral intermediate than S-aryl O-ethyl dithiocarbonates.[7]

The values of k_2 for the reactions of the present work are smaller than those estimated in the aminolysis of S-phenyl and S-(4-nitrophenyl) O-ethyl dithiocarbonates (PDTC and NPDTC): $k_2 = 7 \times 10^7$ and 3×10^8 s^{-1}, respectively.[19,21] This is in agreement with the results in the acetate series, where k_2 is larger for PhS$^-$ expulsion compared to PhO$^-$, and k_2 is also greater for 4-nitrobenzenethiolate ion expulsion compared to 4-nitrophenoxide.[2,4]

The k_1 values for the aminolysis of PTOC and NPTOC (Table 3) are slightly larger than those found in the same aminolysis of PDTC and NPDTC,[7] respectively. This seems surprising in view of the larger electron-donating resonance effect of PhO ($\sigma_R = -0.40$)[16] relative to PhS ($\sigma_R = -0.23$)[17] and, presumably, the same larger effect of 4-nitrophenoxy compared to the corresponding thio group. This should be in part counterbalanced by a greater electron-withdrawing inductive effect of PhO than of PhS ($\sigma_I = 0.37$ and 0.30, respectively)[16,17] and a larger effect of 4-nitrophenoxy than 4-nitrobenzenethio ($\sigma_I = 0.47$ and 0.36, respectively).[16c,17] The slightly higher rate of amine attack on the thionocarbonates compared to the dithio analogues could be due to the relatively hard nature of the series of secondary alicyclic amines used in this study which would prefer the moderately harder thiocarbonyl carbon of the thionocarbonates compared to the softer thiocarbonyl carbon of the dithiocarbonates.[27]

The larger k_{-1} value for a given amine found in the aminolysis of PTOC compared to that of PDTC[7] should be due to the greater "push" exerted by PhO compared to PhS from the corresponding tetrahedral intermediate.[28]

With the values of k_1, k_{-1}, and the pK_a of amines of Table 3, the Brönsted-type plots for both rate microcoefficients can be drawn (Figures 3 and 4). The plots are

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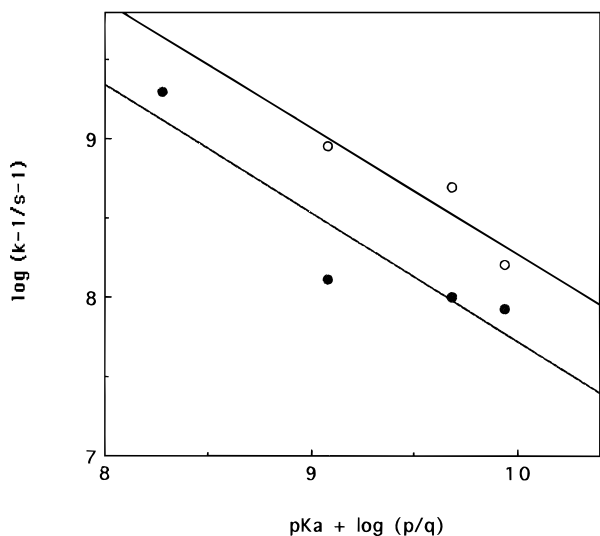
Figure 4. Brönsted-type plots for k_{-1} (pK_a statistically corrected), obtained in the reactions of secondary alicyclic amines with PTOC ($\bigcirc$) and NPTOC ($\bullet$).

statistically corrected[29] for k_1 and pK_a, with the values $p = 2$ and $q = 1$, except piperazine with $q = 2$.[3,5,7,9,19] The Brönsted slopes are $\beta_N(k_1)$ ca. 0.23 and $\beta_N(k_{-1})$ ca. 0.8, for the reactions of both PTOC and NPTOC.

By dual regression analysis, eqs 4 and 5 can be obtained for k_1 and k_{-1}, respectively. In these equations, $pK_a(N)$ and $pK_a(lg)$ are the statistically corrected pK_a of the conjugate acids of the amine and the leaving group of the substrate, respectively.

$$\log(k_1/q) = -0.53 + 0.24pK_a(N) - 0.17pK_a(lg) \quad (4)$$

$$\log k_{-1} = 14.5 - 0.81pK_a(N) + 0.18pK_a(lg) \quad (5)$$

The standard errors are 0.3, 0.03, and 0.02 for the coefficients of the constant, the $pK_a(N)$, and $pK_a(lg)$ terms, respectively, of eq 4, and 0.7, 0.1, and 0.05, respectively, for the three coefficients of eq 5. The correlation coefficients are 0.97 and 0.98 for eqs 4 and 5, respectively.

The β_N value for k_1 is similar to those found in other aminolysis[5,7,21,26] and also in accord to the slopes at high pK_a in biphasic Brönsted-type plots found in stepwise reactions.[1–4,8,9,19] In these plots at high pK_a the formation of the zwitterionic tetrahedral intermediate is rate determining, and little positive charge develops on the amine nitrogen atom in going from reactants to the transition state of the k_1 step.[1–5,7–9,19,21]

The β_N value found for k_{-1} in the present reactions is also in agreement with the values obtained in other aminolysis such as those of aryl acetates,[1,2] diaryl carbonates,[2] S-aryl O-ethyl dithiocarbonates,[3a] phenyl thionoacetate,[5] aryl thiolacetates,[9] and aryl dithioacetates.[21]

The Brönsted slope for equilibrium formation of $T^{\pm}$ in Scheme 1 is $\beta_{eq} = \beta_1 - \beta_{-1} = 0.23 - (-0.80) = $ ca. 1. According to the hypothesis of the tetrahedral intermediate, this should be the Brönsted slope at low pK_a for a biphasic Brönsted-type plot, since at this pK_a region $k_N = K_1 k_2$ and k_2 should be of little or no dependence on amine pK_a.[2] In fact, our value of β_{eq} is in agreement with the Brönsted slope at low pK_a of biphasic plots found the aminolysis of oxy- and thioesters and -carbonates.[1–4,7,9,19]

The general base catalysis by a second amine molecule found in the present reactions (except for piperidine) is in contrast to the lack of such catalysis in the reactions of primary amines (pK_a 4.7–10.7) and imidazole with 4-nitrophenyl methyl carbonate.[8a] The latter result was explained by a reaction scheme involving only the steps k_1, k_{-1}, and k_2 of Scheme 1.[8a] In the reactions of the present work the amine-catalysis step (k_3) successfully competes with the k_2 step; therefore the difference in the results of both reactions must lie in the values of k_3 and/or k_2.

The pK_a value of the zwitteronic tetrahedral intermediate formed in the aminolysis of 4-nitrophenyl methyl carbonate (**4**, PN = 4-nitrophenyl) can be estimated on the basis of the pK_a of **3** and $\sigma_I(O^-) = -0.26$ and $\sigma_I(S^-) = 0.03$.[16c] The change of EtO by MeO is irrelevant since σ_I

$$\begin{array}{c} O^- \\ | \\ MeO-C-OPN \\ | \\ -\overset{+}{NH} \\ | \end{array}$$

4
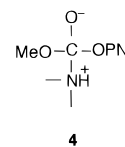
for these groups is almost the same.[15] This gives $pK_a(\mathbf{4}) - pK_a(\mathbf{3}) = -9.2(-0.26-0.03) = +2.7$ pK_a units. Since $pK_a(\mathbf{3})$ is 6.4 pK_a units lower than that of the parent aminium ion (see above), $pK_a(\mathbf{4})$ should be 3.7 pK_a units lower than the parent aminium ion, and the proton transfer from **4** to the parent amine should be thermodynamically favorable, with k_3 ca. 10^{10} s^{-1} M^{-1}.[18] Since the range of amine concentration is similar in the aminolysis of 4-nitrophenyl methyl carbonate[8a] and 4-nitrophenyl O-ethyl thionocarbonate (Table 2), the proton transfer rate, $k_3[HN]$, should be similar in both reactions. Therefore, k_2 should be larger in the oxycarbonate aminolysis compared to that of the thionocarbonate.

The above conclusion is reasonable in view of the difficulty of formation of the double C=S bond in **3** to expel the nucleofuge compared to the formation of the double C=O bond in **4**. The difficulty in forming the C=S bond in **3** seems to be due to a weaker π-bonding energy of the thiocarbonyl compared to the carbonyl group.[30] The change of S$^-$ by O$^-$ in T$^{\pm}$ of Scheme 1 should therefore increase the nucleofugality of ArO$^-$ (increase k_2).

This result is in line with the larger value of k_2 found in the aminolysis of phenyl acetate relative to that of phenyl thionoacetate[5] and the larger k_2 for the aminolysis of S-(4-nitrophenyl) thioacetate[9] than that for 4-nitrophenyl dithioacetate.[21] Also in agreement are the concerted mechanisms found in the aminolyses of S-(2,4-dinitrophenyl)[22] and S-(2,4,6-trinitrophenyl) O-ethyl thiocarbonates[31] in contrast to the stepwise aminolyses of the corresponding dithiocarbonates.[19] Kinetic instability of the "tetrahedral intremediate" with O$^-$ due to a larger k_2, relative to that with S$^-$, together with a larger k_{-1}, was attributed to the change in mechanism.[19,31]

Therefore, the larger nucleofugality of 4-nitrophenoxide ion from **4** than from **3** should be responsible for the lack of base catalysis in the aminolysis of 4-nitrophenyl methyl carbonate, since for this reaction k_2 is larger than $k_3[HN]$.

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