Kinetics and Mechanism of the Pyridinolysis of Alkyl Aryl Thionocarbonates

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The reactions of methyl 4-nitrophenyl, ethyl 4-nitrophenyl, and ethyl 2.4-dinitrophenyl thionocarbonates (MNPTOC, ENPTOC, and EDNPTOC, respectively) with a series of 3- and 4-substituted pyridines are subjected to a kinetic investigation in water, 25.0 °C, ionic strength 0.2 M (maintained with KCl). Under amine excess, pseudo-first-order rate coefficients (k_{obsd}) are obtained, which are linearly proportional to the free-pyridine concentration. The second-order rate coefficients $(k_{\rm N})$ are obtained as the slopes of these plots. The Brönsted-type plots found for the two mononitro derivatives coincide in one straight line (same slope and intercept) of slope $\beta = 1.0$. The EDNPTOC pyridinolysis shows a curved Brönsted-type plot with slopes $\beta_1 = 0.1$ (high pKa), $\beta_2 = 1.0$ (low pKa), and $pK_{a^0} = 6.8$ (pK_a value at the center of curvature). These plots are consistent with the existence of a zwitterionic tetrahedral intermediate (T^{\pm}) on the reaction pathway whereby expulsion of aryloxide anion from T[±] is rate determining (k_2 step) at low p K_a for EDNPTOC (and in the whole pK_a range for MNPTOC and ENPTOC), and there is a change to rate-limiting formation of T[±] (k_1 step) at high pK_a for EDNPTOC. Comparison of these Brönsted plots among them and with similar ones permits the following conclusions: (i) There is no variation of $k_{\rm N}$ by substitution of methoxy by ethoxy as the nonleaving group of the substrate. (ii) The $pK_{a^{0}}$ value is smaller for the less basic aryloxide nucleofuge due to a larger k_2 value. (iii) The change of C=S by C=O as the electrophilic center of the substrate results in larger values for both k_{-1} (amine expulsion rate) and k_2 , and also a larger k_{-1}/k_2 ratio for the carbonyl derivative. There is also an increase of k_1 by the same change. The K_1k_2 (= k_1k_2/k_{-1}) values are larger for the pyridinolysis of methyl 2,4-dinitrophenyl and methyl 4-nitrophenyl carbonates compared to the corresponding thionocarbonates (EDNPTOC and MNPTOC, respectively). (iv) Pyridines are more reactive than isobasic secondary alicyclic amines toward ENPTOC when either the k_1 step or the k_2 step is rate limiting. This is explained by the softer nature of pyridines than alicyclic amines (k_1 step) and the greater nucleofugality (k_{-1}) of the latter amines than isobasic pyridines, leading to a larger k_2/k_{-1} ratio for pyridines (k_2 is little affected by the amine nature), and therefore a larger K_1k_2 value when the k_2 step is rate determining.

Introduction

Although the aminolysis reactions of aryl acetates,^{1,2} benzoates,³ and carbonates⁴⁻⁷ have been extensively studied and their mechanisms have been clarified, less is known on the mechanism of the aminolysis of their thio derivatives.

We have recently studied the kinetics and mechanism of the reactions of secondary amines with aryl thiolacetates and dithioacetates.⁸ Also, the reactions of the above and other amines with aryl thiobenzoates have been subjected to kinetic investigations.⁹ We have also examined the reactions of secondary alicyclic amines with aryl thiolcarbonates¹⁰ and thionocarbonates.¹¹

In spite of the above works on the aminolysis (mainly secondary alicyclic amines) of aryl thioesters and thiocarbonates, little is known on the influence of the amine nature and the nonleaving, leaving, and electrophilic groups of the substrate on the kinetics and mechanism of these reactions.

We perform in the present work a kinetic study on the pyridinolysis of methyl 4-nitrophenyl thionocarbonate (MNPTOC), ethyl 4-nitrophenyl thionocarbonate (ENP-TOC), and ethyl 2,4-dinitrophenyl thionocarbonate (ED-NPTOC). The aim is to analyze the effect of the following groups on the kinetics and mechanism of these reactions: (i) Nonleaving (or acyl) group, by comparison of the pyridinolysis of MNPTOC and ENPTOC; (ii) leaving group, by comparison of the pyridinolysis of EDNPTOC

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with those of ENPTOC and *O*-ethyl 2,4-dinitrophenyl dithiocarbonate;¹² (iii) electrophilic group (C=O or C=S), by comparison of the pyridinolysis of MNPTOC and methyl 4-nitrophenyl carbonate;⁶ (iv) nucleophilic group, by comparison of the pyridinolysis of ENPTOC with the reactions of secondary alicyclic amines with the same substrate.¹¹

Experimental Section

Materials. The pyridines were purified as reported.¹³ Ethyl 4-nitrophenyl thionocarbonate (ENPTOC) was synthesized as described previously.^{11,14} Methyl 4-nitrophenyl thionocarbonate (MNPTOC) and ethyl 2,4-dinitrophenyl thionocarbonate (EDNPTOC) have not been synthesized before, to our knowledge. EDNPTOC was prepared by a general method, using *O*-ethyl chlorothioformate and 2,4-dinitrophenol in pyridine.¹⁴ MNPTOC could not be prepared in satisfactory yield by the general method¹⁴ employed for ENPTOC and EDNPTOC. MNPTOC was synthesized from potassium methoxide and bis(4-nitrophenyl) thionocarbonate. The latter was prepared by a modification of a reported procedure.¹⁴

The synthesis of MNPTOC was carried out as follows: To methanol (20 mL) in a Schlend round-bottomed flask was added potassium (0.024 g) slowly under N₂ atmosphere. After all potassium was reacted, the excess of methanol was evaporated off at room temperature. The product, potassium methoxide, was dissolved in anhydrous THF (20 mL) and rapidly transferred to a compensation funnel, under N₂. In another Schlend round-bottomed flask bis(4-nitrophenyl) thionocarbonate (0.2 g) was dissolved in anhydrous THF under N₂ and the flask placed in an ethanol-liquid N_2 bath. The $\ensuremath{\tilde{\text{n}}}$ compensation funnel was attached to the flask and the potassium methoxide solution added dropwise with stirring during 2 h. The mixture was left overnight with stirring under N₂ at ambient temperature. The final mixture was dissolved in chloroform and 4-nitrophenoxide anion extracted with water. The organic layer was dried with MgSO₄ and filtered under vacuum and the solvent evaporated off. The product was purified by column chromatography on GF-254 Merck silica gel, eluent ether-chloroform 3:1 (v/v); mp 109-110 °C. MNPTOC and EDNPTOC were characterized as follows:

MNPTOC: ¹H NMR (200 MHz, CDCl₃) δ 4.20 (s, 3H), 7.30 (sd, 2H, J = 9.1 Hz), 8.30 (sd, 2H, J = 9.1 Hz); ¹³C NMR (50 MHz, CDCl₃) δ 60.80 (CH₃), 123.28 (C-2/6), 125.37 (C-3/5), 145.96 (C-4), 157.56 (C-1), 194.69 (C=S); IR (KBr) 1593 (C=C), 1520 and 1346 (C-NO₂), 1295 (C=S), 1159 (C-0), 865 (CH, arom) cm⁻¹. Anal. Calcd for C₈H₇O₄NS: C, 45.08; H, 3.31; N, 6.57; S, 15.01. Found: C, 45.34; H, 3.24; N, 6.27; S, 15.54.

EDNPTOC: ¹H NMR (200 MHz, CDCl₃) δ 1.51 (t, 3H, J = 7.1 Hz), 4.66 (q, 2H, J = 7.1 Hz), 7.52 (d, 1 H, J = 8.9 Hz), 8.56 (dd, 1H, J = 2.7, 8.9 Hz), 9.02 (d, 1H, J = 2.7 Hz); ¹³C NMR (50 MHz, CDCl₃) δ 15.59 (CH₃), 72.13 (CH₂), 121.94 (C-3), 127.43 (C-5), 129.28 (C-1), 141.50 (C-6), 145.49 (C-4), 150.12 (C-2), 195.94 (C=S); IR (KBr) 1611 (C=C), 1542 and 1380 (C-NO₂), 1308 (C=S) cm⁻¹. Anal. Calcd for C₉H₈O₆N₂S: C, 39.72; H, 2.96; N, 10.29; S, 11.78. Found: C, 39.94; H, 2.92; N, 10.38; S, 11.49.

Kinetic Measurements. These were performed spectrophotometrically by following the release of 4-nitrophenol or 2,4-dinitrophenol (and/or their conjugate bases) at 400 nm, by the method and instrument previously described.¹⁵ The reactions were studied under the following conditions: aqueous solutions, 25.0 ± 0.1 °C, ionic strength 0.2 M (maintained with KCl), and a 10-fold excess (at least) of total amine over the substrate. **Product Studies.** 4-Nitrophenol and 2,4-dinitrophenol (and/or their conjugate bases) were identified as one of the final products of the corresponding reactions. This was carried out by comparison of the UV-vis spectra after completion of the reactions with those of authentic samples at the same experimental conditions.

The appearance and later disappearance of an intermediate was spectrophotometrically detected during the reactions. For example, the intermediate found in the reaction of MNPTOC with 4-aminopyridine has a $\lambda_{max} = 315$ nm. We identified this intermediate as 1-(methoxythiocarbonyl)-4-aminopyridinium ion.

Results and Discussion

The reactions subjected to the present investigation can be kinetically described by eqs 1 and 2, where Ar is 4-nitrophenyl or 2,4-dinitrophenyl, S represents the

$$\frac{\mathrm{d}[\mathrm{ArO}^{-}]}{\mathrm{d}t} = k_{\mathrm{obsd}}[\mathrm{S}] \tag{1}$$

$$k_{\rm obsd} = k_{\rm o} + k_{\rm N}[{\rm N}] \tag{2}$$

substrate, k_{obsd} is the pseudo-first-order rate coefficient, k_o and k_N are the rate coefficients for hydrolysis and pyridinolysis of the substrate, respectively, and N represents the substituted pyridine free base.

The values of k_{obsd} and the experimental conditions of the reactions are shown in Table 1.

The values of k_0 and k_N were obtained as the intercept and slope, respectively, of plots of k_{obsd} against [N] at constant pH, using at least three pH values. The values of k_N were found to be pH independent over the pH range employed.

The k_0 values were in general negligible compared to those of k_N [N] in eq 2, except in the slow aminolysis of the substrates with the two less basic pyridines (3-carbamoyl and unsubstituted pyridines).

The Brönsted-type plots of Figure 1 were obtained from the k_N values and the pK_a values of the pyridines shown in Table 2.

The linear and single Brönsted-type plot found for the pyridinolysis of ENPTOC and MNPTOC with slope $\beta =$ 1.0 is consistent with a stepwise mechanism where a zwitterionic tetrahedral intermediate (T^{\pm}) is formed on the reaction pathway and its breakdown to products is rate determining. Similar slope values have been found in the aminolysis of phenyl and 4-nitrophenyl acetates,¹ phenyl and 4-nitrophenyl methyl carbonates,^{6,16} 4-nitrophenyl benzoate,^{9b,17} 2,4-dinitrophenyl 4-chlorobenzoate,^{3d} and other reactive carbonyl compounds, 1,4,5,13,16,18 where a stepwise mechanism has been invoked with the breakdown of T^{\pm} to products being the rate-determining step. The value of $\beta = 1.0$ for the above Brönsted plot is also similar to those obtained in the aminolysis of thioesters and thiocarbonates when the breakdown of the tetrahedral intermediate is rate limiting.^{8,9a,b,10c,11,15,17}

The nonlinear Brönsted type plot found in the pyridinolysis of EDNPTOC (Figure 1), with slopes $\beta_1 = 0.1$ and $\beta_2 = 1.0$ at high and low p K_a values, respectively, is

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 Table 1. Experimental Conditions and kobsd Values for the Pyridinolysis of Alkyl Aryl Thionocarbonates^a

pyridine substituent	nH	10 ³ [N]/M	$10^{3}k_{\rm abod}/{\rm s}^{-1}$	no. of		
				Tuno		
Methyl 4-Nitrophenyl Thionocarbonate (MNPTOC)						
4-(dimethylamino) ^b	8.Z	1.0-6.0	4.0-5.8	8		
	8.5	0.4 - 1.0	0.71-1.9	6		
• • •	9.0	0.3 - 1.0	1.4-4.0	7		
4-amino ^b	8.2	1.0-4.3	1.4-6.0	7		
	8.5	1.0 - 2.5	2.4-6.2	6		
0 4 H - 1 I	9.0	0.2 - 1.0	1.4-6.3	8		
3,4-dimethyl	8.0	10-90	0.22-0.89	7		
	8.2	10-180	0.22-2.6	7		
0 1 10	8.5	50-150	1.0-2.3	7		
3-methyl ^c	8.2	60 - 150	0.11-0.25	5		
	8.5	50-135	0.10-0.23	6		
	8.8	40 - 130	0.091 - 0.23	6		
none ^c	8.5	70-170	0.032 - 0.083	6		
	8.8	60 - 190	0.033 - 0.10	5		
	9.0	100 - 180	0.085 - 0.13	5		
Ethyl 4-Nitrophenyl Thionocarbonate (ENPTOC)						
4-(dimethylamino)	9.6	0.4-4.0	2.4-28	7		
r (unneenglunnio)	99	0.2 - 2.0	2.1 - 19	7		
	10.2	0.2 - 2.0	31-28	7		
4-amino	91	0.2 2.0 07-85	35-44	7		
i unnio	94	0.7 - 7.0	5.3 - 57	7		
	97	0.7 7.0 0.5 - 5.0	4 5-49	7		
3 1-dimethyl	8.0	85-70	0.24 - 1.2	6		
5,4-unicenyi	8.2	10 - 110	0.24 1.2 0.24-1.8	7		
	85	10 - 100	0.24 1.0 0.18-1.7	7		
3 mothyl	82	10 100 11 - 120	0.10 1.7 0.045 - 0.23	6		
5-metriyi	85	80-130	$0.045 \ 0.23$	7		
	88	25 - 140	$0.043 \ 0.24$ 0.052 = 0.27	7		
nonol	0.0 9.5	20-150	0.032 0.27	5		
none	0.5	60-180	0.029 - 0.077 0.024 - 0.10	5		
	0.0	80 100	0.034 - 0.10	5 6		
	9.0	80-190	0.045-0.10	0		
Ethyl 2,4–Dinit	ropheny	l Thionocarb	onate (EDNPTO	C)		
4-(dimethylamino)	9.6	0.40 - 4.0	1.8 - 27	7		
	9.9	0.20 - 2.0	2.7 - 21	7		
	10.2	0.20 - 2.0	3.3 - 27	7		
4-amino	9.1	0.70 - 8.5	5.0 - 65	7		
	9.4	0.70 - 7.0	7.7 - 71	7		
	9.7	0.50 - 5.0	5.4 - 78	7		
3,4-dimethyl ^c	8.0	1.0 - 12	4.0 - 61	7		
5	8.2	3.0 - 25	10-123	6		
	8.5	4.0 - 25	16-120	6		
3-methyl ^c	8.2	15 - 300	1.6 - 25	7		
5	8.5	20 - 400	1.8 - 34	7		
	8.8	10 - 250	1.1 - 20	7		
none	5.1	40-200	3.4 - 20	7		
	5.4	25-250	3.6-39	7		
	5.7	15 - 160	3.6 - 31	7		
3-carbamovl ^c	8.5	10-100	0.16 - 0.68	7		
	8.8	20-105	0.20 - 0.69	7		
	9.0	15-110	0.18 - 0.74	6		
				v		

 a In aqueous solution at 25.0 °C, ionic strength 0.2 M (KCl). b In the presence of 0.05 M carbonate buffer. c In the presence of 0.005 M borate buffer.

similar to those obtained in the aminolysis of reactive aryl esters^{1,7c,16} and carbonates,^{4,5,7c,d} and in other carbonyl derivatives,^{13,18} thioesters,^{8a,17} and thiocarbonates.^{12,19} All these reactions have been explained by the mechanism described in eq 3, where R and L are the nonleaving

and leaving groups, and N represents an amine. The





Figure 1. Brönsted-type plots obtained in the pyridinolysis of MNPTOC (\triangle), ENPTOC (\bigcirc), and EDNPTOC (\blacksquare), in aqueous solution, at 25.0 °C, ionic strength 0.2 M (this work). Also shown for comparison is the Brönsted-type plot found in the pyridinolysis of methyl 2,4-dinitrophenyl carbonate (\bigcirc , ref 5) under the same conditions.

nonlinear plot results from a change in the ratedetermining step, from that for k_2 at low amine basicity to that for k_1 at high amine basicity.^{1,4,5,7c,d,8,9,13,15–19} Applying the steady state condition to T^{\pm} in eq 3, the equation $k_{\rm N} = k_1 k_2 / (k_{-1} + k_2)$ is obtained, and this accounts for the curvature of the Brönsted plot. At high p K_a values $k_{-1} \ll k_2$ and $k_N = k_1$ (first step of eq 3 is rate limiting). At low p K_a values $k_{-1} \gg k_2$ and $k_N = k_1 k_2 / k_{-1}$ $= K_1 k_2$ (second step limiting), where K_1 is the equilibrium constant for the first step of eq 3. Based on this, a semiempirical equation has been deduced,^{4,12,13} which satisfactorily accounts for the experimental points obtained in the pyridinolysis of EDNPTOC (see Figure 1). The parameters used in the semiempirical equation are: $\beta_1 = 0.1, \beta_2 = 1.0$, and p $K_{a^0} = 6.8$; the latter is the p K_{a} value at the center of curvature, i.e., it represents the pK_a of an amine for which $k_{-1} = k_2$ in eq 3. In other words, an amine of this basicity will leave T^{\pm} as readily as L⁻.^{4,5,8,13,19}

There are other explanations for curved Brönsted-type plots, based mainly on a structural variation of the transition state as the reactivity of the amine changes in a single step,²⁰ as predicted by the Hammond postulate.²¹ Nevertheless, as in other reactions, we have had no success in trying to fit equations based on the above hypothesis²⁰ to our experimental log k_N vs p K_a points.^{7d,19,22}

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Table 2. Values of pKa of Pyridinium Ions and kN for the Pyridinolysis of Alkyl Aryl Thionocarbonates^a

pyridine	$k_{ m N}/{ m s}^{-1}~{ m M}^{-1}$				
substitment	pK _a	MNPTOC	ENPTOC	EDNPTOC	
4-(dimethylamino)	9.87	32 ± 3	21 ± 1	20 ± 2	
4-amino	9.42	23 ± 1	16 ± 1	21 ± 2	
3,4-dimethyl	6.77	0.015 ± 0.001	0.017 ± 0.001	5.0 ± 0.2	
3-methyl	5.80	$(1.5\pm 0.1) imes 10^{-3}$	$(1.8\pm 0.2) imes 10^{-3}$	0.83 ± 0.03	
none	5.37	$(5.2 \pm 0.2) imes 10^{-4}$	$(5.0 \pm 0.1) imes 10^{-4}$	0.31 ± 0.02	
3-carbamoyl	3.43			(6.0 \pm 0.4) $ imes$ 10 $^{-3}$	

^{*a*} Both p K_a and k_N values were obtained in aqueous solution at 25.0 °C, ionic strength 0.2 M (KCl). For abbreviations of the substrates see Table 1.

A referee has pointed out that the nonlinear Brönstedtype plot for the pyridinolysis of EDNPTOC can be explained by a requirement for structural reorganization of the two aminopyridines upon bond order reorganization in the transition state, which significantly decreases the rate. Nevertheless, it can be seen in Figure 1 that the two aminopyridines correlate well with the other less basic amines in the pyridinolyses of both ENPTOC and MNPTOC.

Moreover, good Brönsted-type correlations (including the two mentioned aminopyridines) are also shown in the pyridinolyses of substrates with good leaving groups, such as 2,4-dinitrophenyl 4-X-substituted benzoates (X = NO₂, CN, and Cl). These linear Brönsted-type plots exhibit a slope β ca.1, which indicates that a tetrahedral intermediate is formed and its breakdown to products is the rate-determining step.^{3d,23} Furthermore, in the pyridinolysis of methyl chloroformate there is a good linear Brönsted correlation between the above two aminopyridines and other X-substituted pyridines (X = H, 3-methyl and 4- methyl).¹³ Also, in the pyridinolysis of acetyl chloride there is a good Brönsted linearity between 4-(dimethylamino)pyridine and other pyridines (X = H, 4-methyl and 3,4-dimethyl).^{18b}

Moreover, Williams has recently found that 4-(dimethylamino)- and 4-amino pyridines correlate well with N-pyrid-4-ylmorpholine and 4-methoxy and 3,5-dimethyl pyridines on the Brönsted-type plot obtained in the pyridinolysis of 1'-(4,6-diphenoxy-1,3,5-triazin-2-yl)pyridinium chloride.²⁴ Also the above two aminopyridines correlate linearly with five other pyridines ranging from pK_a 6.7 down to 3.5 on the Brönsted-type plot found in the pyridinolysis of 4,6-diphenoxy-1,3,5-triazin-2-yl chloride.²⁴

Another referee has suggested that the pyridinolysis of EDNPTOC (Figure 1) could be concerted, as found by Jencks^{25,26} and Williams^{27,28} in related reactions. Nevertheless, the Brönsted curvature exhibited by the ED-NPTOC reaction is far too *sharp* for a concerted process. Jencks found a *slight* Brönsted curvature in the aminolysis of benzoyl fluorides, which together with the fact that the curvature center does not shift with the change of acyl substituents led him to the conclusion that the mechanism is concerted.²⁵ Jencks also found that the reactions of *phenolate* anions with acetate and formate esters are concerted, but this conclusion was arrived at from the *linear* Brönsted-type plots obtained for structurally homogeneous series of phenolate anions.²⁶

Williams has found that acetyl and other groups transfers between phenolate ions are concerted.²⁷ He has also found that methoxycarbonyl transfer between isoquinoline and pyridines is a concerted process.²⁸ In all these reactions a *linear* Brönsted-type plot was obtained.^{27,28} Williams has argued that acyl group transfers between a given phenolate and pyridines (and other amines) are *stepwise*, through a tetrahedral intermediate which is stable enough to exist.^{27a} Williams has agreed with our claim that the pyridinolysis of acetic anhydride,^{27b} 2,4,6-trinitrophenyl acetate,^{27c} 2,4-dinitrophenyl methyl carbonate (Brönsted-type plot shown in Figure 1), and other reactive carbonyl derivatives are all stepwise reactions where a tetrahedral intermediate is formed.^{27a}

On the other hand, Palling and Jencks have claimed that the pyridinolysis of acetyl chloride is stepwise.^{18b} It is noteworthy that this substrate possesses a better leaving group than EDNPTOC, and therefore if a tetrahedral intermediate is formed in the former reaction, it should be more likely to exist in the latter reaction (this work) where it should be less unstable.

Therefore, according to what has been discussed above, and in agreement with the kinetic law and the products and intermediate studies, we believe that the reactions under the present investigation can be depicted by the mechanism shown in eq 4, where **1** is a tetrahedral intermediate. In this equation, R is either methyl or ethyl, Ar is either 4-nitrophenyl or 2,4-dinitrophenyl, and -N= represents a given pyridine.

Intermediate **2**, 1-(alkoxythiocarbonyl)-substituted pyridinium ion, was detected as explained in the Experimental Section, although its decomposition rate was not measured. Compound **2** does not absorb at 400 nm where the production of ArO^- was followed and the kinetics of the reactions were measured. Therefore, the k_N values obtained are the macroscopic rate coefficients for the formation of **2** and ArO^- from reactants.

Similar intermediates to **2** have been found in the reactions of pyridine and 3-carbamoylpyridine (nicotinamide) with *O*-ethyl 2,4-dinitrophenyl dithiocarbonate,¹² and in the pyridinolysis of methyl chloroformate^{6,13,29} and methyl 2,4-dinitrophenyl carbonate.⁵ Also 1-acetylsubstituted pyridinium ions have been detected in the pyridinolysis of acetic anhydride.³⁰

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The fact that the experimental points for the pyridinolysis of both ENPTOC and MNPTOC fall on the same straight line of the Brönsted-type plot (Figure 1) means that the value of k_1k_2/k_{-1} (eq 4) is the same for both reactions (see above). It is known that electron withdrawal from R in the tetrahedral intermediate T^{\pm} (eq 3) increases the p K_a^{0} value, and therefore the k_{-1}/k_2 ratio, favoring amine expulsion from T^\pm relative to $L^{-,4}~$ Since the electronic effects from R in T^\pm and RO in 1 (eq 4) are mainly inductive, due to the fact that the central carbon atom is tetrahedral,³¹ similar values for the k_{-1}/k_2 ratios are expected for R = Me and Et in eq 4, in view of the similar $\sigma_{\rm I}$ values involved (0.29 and 0.26, respectively).³² Moreover, since the other groups attached to the central carbon in **1** are the same, the similar σ_{I} values for R = Me and Et in **1** should imply similar k_{-1} and k_2 values for both intermediates. The k_1 values for the two reactions concerned (eq 4) should be governed by both resonance and inductive effects since there is a trigonal central carbon involved in the substrates. The σ_{R} value for MeO is -0.56, the absolute value of which is slightly greater than that for EtO ($\sigma_{\rm R} = -0.50$);³² nevertheless, the slightly stronger electron donation by resonance of MeO relative to EtO is counterbalanced by a slightly stronger electron-withdrawing inductive effect (see above) of MeO. This suggests that the k_1 values could also be similar for the pyridinolysis of MNPTOC and ENPTOC. Therefore, if the $k_1k_2/k_{-1} = K_1k_2$ values are the same (within experimental error) for both reactions, the conclusion from the above discussion is that both K_1 and k_2 should be similar for both reactions.

The p K_a value for the center of the Brönsted curvature for the pyridinolysis of EDNPTOC is $pK_a^{0} = 6.8$, which is lower than that for the pyridinolysis of ENPTOC (pK_a^{0} > 10, see Figure 1). This is in accordance with the results found in the aminolysis of aryl acetates,³³ diaryl carbonates,⁴ aryl methyl carbonates,^{5,6,7c} aryl thiolacetates,^{8a} and aryl O-ethyl dithiocarbonates,¹⁹ i.e. the pK_{a^0} value decreases as the basicity of the nucleofuge diminishes. This fact is in agreement with the stepwise mechanism, since the lower the leaving group basicity the larger the value of k_2 in eqs 3 and 4, and therefore the lower the amine pK_{a} for which $k_{-1} = k_2 \cdot \frac{4-6,8,13}{2}$

The above value of $pK_a^{0} = 6.8 \ (\pm 0.1)$ is the same within experimental error as that found in the pyridinolysis of O-ethyl 2,4-dinitrophenyl dithiocarbonate (EDNPDTC, $pK_{a^{0}} = 6.9 \pm 0.1$).¹² This is somewhat surprising in view of the lower basicity of 2,4-dinitrobenzenethiolate anion (DNPS⁻) compared to 2,4-dinitrophenoxide anion (DNPO⁻) $(pK_a 3.4 \text{ and } 4.0 \text{ at } 25 \degree \text{C}, \text{ respectively}).^{8a,34}$ Nevertheless,

the nature of the leaving groups involved is different. In fact, it has been reported that any oxide anions are better nucleofuges from a tetrahedral intermediate than isobasic arylthiolate anions.³⁵ The higher basicity of DNPOrelative to DNPS⁻ should be partly counterbalanced by the higher *intrinsic* nucleofugality of aryloxide anions. On the other hand the push exerted by DNPO in 1 to expel the amine should be slightly stronger than that by DNPS.^{8a,35a} Taking into account the pull and push effects of these two groups in the corresponding tetrahedral intermediates, one concludes that the k_{-1}/k_2 value for a given amine should be slightly larger for DNPO compared to DNPS, producing a little larger pK_{a^0} value for the pyridinolysis of EDNPTOC relative to EDNPDTC, according to the tetrahedral intermediate hypothesis.^{4,8} The fact that the $pK_{a^{0}}$ values for the two reactions concerned are equal within experimental error indicates that the nonleaving RO group in 1 must also play a significant role by affecting the k_{-1}/k_2 ratio. This is evident by comparison of the p K_a^{0} values in the pyridinolysis of 2,4dinitrophenyl acetate (DNPA) and 2,4-dinitrophenyl thiolacetate (DNPTA). There is a *decrease* in pK_{a^0} of 0.6 unit by the change of DNPO by DNPS as the L group of T^{\pm} in eq 3 (R = Me).^{8a,16} There is also a smaller decrease of $pK_{a^{0}}$ (0.2 units) by the same change in the reactions of secondary alicyclic amines with the same substrates.^{8a,36}

A linear Brönsted-type plot of slope $\beta = 1.0$ can be obtained in the pyridinolysis of methyl 4-nitrophenyl carbonate,^{6,37} with the same slope as that found in the same reactions of MNPTOC (this work), although, the $k_{\rm N}$ values are larger for the former reactions. Similarly the $k_{\rm N}$ values are larger in the reactions of secondary alicyclic amines with 4-nitrophenyl benzoate compared to the same aminolysis of 4-nitrophenyl thionobenzoate.9b

As seen in Figure 1, the change of R = Me by Et in the tetrahedral intermediate 1 of eq 4 does not alter the $k_{\rm N}$ values, nor is K_1 or k_2 changed significantly (see above). Taking this into account a comparison between the pyridinolysis of EDNPTOC and methyl 2,4-dinitrophenyl carbonate (MDNPC) should be valid; the Brönsted-type plot for the latter reactions is included in Figure 1 for this purpose.⁵ It can be seen in this figure that the substitution of the thiocarbonyl group in EDNPTOC by a carbonyl in MDNPC shifts the center of the Brönsted curvature to higher pK_a values, that is from $pK_a^{0} = 6.8$ to 7.8.5 A similar effect has been found in the aminolysis of 4-nitrophenyl thionobenzoate and benzoate: A nonlinear Brönsted-type plot with $pK_{a^0} = 9.2$ was exhibited by the former reactions, whereas a linear plot ($pK_{a^{0}}$ > 11) was obtained for the latter reactions.¹⁷ The larger $pK_{a^{0}}$ value means a larger k_{-1}/k_{2} ratio (for a given amine and leaving group) for the carbonyl compound compared to the thiocarbonyl derivative.^{4,8} It has been reported that the change of S⁻ by O⁻ in **3** increases both k_{-1} and k_2 , with k_{-1} bearing the larger increase.¹⁵ It seems that the same situation holds for the reactions discussed above.

The $k_{\rm N}$ values for the pyridinolysis of EDNPTOC are smaller than those for MDNPC (Figure 1) in the entire pK_a region. Namely, this is independent of the ratedetermining step. When expulsion of DNPO⁻ is rate limiting (linear portion of the Bronsted plot at low pK_a)

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(37) This plot can be obtained with the data in Table 1 of ref 6.

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 $k_{\rm N} = k_1 k_2 / k_{-1}$. Since k_2 / k_{-1} is *smaller* for MDNPC, its larger $k_{\rm N}$ value must rise for a much larger k_1 relative to that for EDNPTOC. This is evident in Figure 1 at high p K_a values, where the formation of the tetrahedral intermediate (k_1 step) is the rate-determining step. The k_1 values are ca. 10-fold larger for the carbonate. Larger k_1 values for the aminolysis of phenyl acetate relative to those for the same reactions of phenyl thionoacetate have been reported.¹⁵ This has been ascribed to the hard nature of a carbonyl center (compared to the softer thiocarbonyl) which prefers to bind a relatively hard alicyclic amine.^{15,38} Pyridines should be softer than alicyclic amines,³⁸ but still show higher nucleophilicity toward the C=O electrophilic center of MDNPC compared to the C=S in EDNPTOC.

The reactions of ENPTOC with secondary alicyclic amines have been subjected to a kinetic investigation whereby the rate microcoefficients k_1 , k_{-1} , and k_2 have been measured.¹¹ From these data it is possible to draw a Brönsted-type plot for $k_N = k_1k_2/(k_{-1} + k_2)$ with the purpose of comparing it with that for the pyridinolysis of the same substrate (this work). Figure 2 shows such plots, together with a Brönsted-type plot for k_1 for the former reactions. The plots for the reactions of secondary amines are statistically corrected.³⁹ Some conclusions can be drawn from these plots:

(i) The $k_{\rm N} = K_1 k_2$ values for the two most basic pyridines are larger than the k_1 values for isobasic secondary alicyclic amines. This means that for pyridines of higher pK_a values (hypothetical) for which the formation of the tetrahedral intermediate would be rate determining (k_1 step), the k_1 values for these pyridines would be larger than those of isobasic secondary alicyclic amines. This is in agreement with what was discussed above regarding hard and soft acids and bases. If pyridines show larger k_1 values than isobasic secondary alicyclic amines toward carbonyl compounds, the k_1 values should be even larger for pyridines toward a softer thiocarbonyl center.³⁸ The higher reactivity of pyridines than isobasic secondary alicyclic amines is also reasonable in terms of the lower steric hindrance of the former amines.40

(ii) The k_N values for both reaction series at low pK_a (where $k_N = K_1k_2$ for both series of reactions) are also

(40) We thank a referee for this comment.



Figure 2. Brönsted-type plots found in the pyridinolysis of ENPTOC (\bullet , this work), and in the reactions of secondary alicyclic amines with the same substrate (\triangle , k_N values; \blacksquare , k_1 values, ref 11). The Brönsted plots for the reactions of secondary amines are statistically corrected (see text). Experimental reaction conditions as in Figure 1.

larger for pyridines relative to the other isobasic amines. This can be explained as follows: It has been estimated that the value of k_2 should be independent of the amine nature or basicity since the cationic amine cannot exert a push to expel an aryloxide leaving group from the zwitterionic tetrahedral intermediate due to the lack of an electron pair on its nitrogen atom.⁴ On the other hand it has been found that the value of k_{-1} is larger for secondary alicyclic amines than isobasic pyridines.^{8,10,36} Therefore, it is reasonable that the K_1k_2 (= k_1k_2/k_{-1}) values be larger for pyridines since both k_1 and the ratio k_2/k_{-1} are larger for the reactions of these amines compared to isobasic alicyclic amines. In line with our finding is the larger reactivity of pyridines toward 2,4dinitrophenyl and 2,4,6-trinitrophenyl O-ethyl dithiocarbonates relative to isobasic secondary alicyclic amines when expulsion of the corresponding benzenthiolate anion is rate limiting.^{12,19}

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