

Kinetics and Mechanism of the Pyridinolysis of 4-Nitrophenyl and 2,4-Dinitrophenyl *S*-Methyl Thiocarbonates

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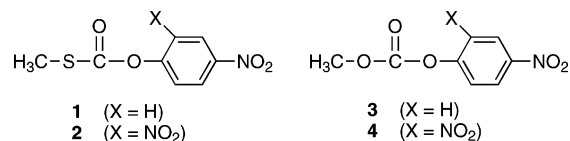
The reactions of 4-nitrophenyl and 2,4-dinitrophenyl *S*-methyl thiocarbonates (**1** and **2**, respectively) with a series of 3- and/or 4-substituted pyridines in aqueous solution, at 25.0 °C and an ionic strength of 0.2 M (KCl), are subjected to a kinetic investigation. The reactions are studied by following spectrophotometrically the release of 4-nitrophenoxide (400 nm) or 2,4-dinitrophenoxide (360 nm) anions. Under amine excess, pseudo-first-order rate coefficients (k_{obsd}) are found. Plots of k_{obsd} vs [pyridine] are linear and pH-independent, with slope k_{N} . The Brønsted-type plot ($\log k_{\text{N}}$ vs $\text{p}K_{\text{a}}$ of pyridinium ions) for the reactions of **1** is linear, with slope $\beta = 1.1$, in contrast to the plot for the reactions of **2**, which is biphasic, with slopes $\beta_1 = 0.25$ (high $\text{p}K_{\text{a}}$) and $\beta_2 = 0.90$ (low $\text{p}K_{\text{a}}$) and the curvature center at $\text{p}K_{\text{a}} = \text{p}K_{\text{a}}^0 = 7.3$. The latter Brønsted plot is consistent with a stepwise mechanism, through a zwitterionic tetrahedral intermediate (T^{\pm}) on the reaction path, and a change of the rate-determining step, from breakdown to formation of T^{\pm} , as pyridine basicity increases. For the reactions of **1** the β value indicates that the mechanism is also stepwise with expulsion of the nucleofuge from T^{\pm} as the rate-determining step. By comparison of the reactions under investigation among each other and with similar aminolyses, the following conclusions can be drawn. (i) Thiocarbonate **2** is more reactive than **1** toward pyridines. (ii) The $\text{p}K_{\text{a}}^0$ value for the pyridinolysis of 2,4-dinitrophenyl methyl carbonate (**4**) is larger than that for thiocarbonate **2**. (iii) The k_1 values (pyridine attack to form T^{\pm}) are smaller for thiocarbonates **1** and **2** than the corresponding oxy carbonates **3** and **4**, respectively. This is not in accordance with the electronic effects of MeS and MeO and could be attributed to steric hindrance of the MeS group toward pyridine attack. (iv) The k_{N} values for the pyridinolysis of carbonates **3** and **4** are larger than those for thiocarbonates **1** and **2**, respectively, when the k_2 step is rate-limiting.

Introduction

Although there have been many reports on the kinetics and mechanisms of the aminolyses (several types of amines) of alkyl aryl carbonates,^{1,2} *O*-ethyl *S*-aryl dithiocarbonates,³ *O*-alkyl *O*-aryl thiocarbonates^{3,4} and *O*-ethyl *S*-aryl thiocarbonates,^{3,5} there have been no reports, to our knowledge, on the kinetics of the aminolysis of *S*-alkyl *O*-aryl thiocarbonates.

To extend our investigations on the mechanism of the aminolysis of thiocarbonates and to study in particular the aminolysis of *S*-alkyl *O*-aryl thiocarbonates, in this

work we undertake a kinetic investigation on the reactions of pyridines with 4-nitrophenyl and 2,4-dinitrophenyl *S*-methyl thiocarbonates (**1** and **2**, respectively) in aqueous solution. A specific objective is to assess the influence of the leaving and nonleaving groups of the substrates on the kinetics and mechanisms of these reactions. This will be achieved by a kinetic comparison of the title reactions between them and with the pyridinolysis of 4-nitrophenyl and 2,4-dinitrophenyl methyl carbonates (**3** and **4**, respectively) in the same solvent.^{1a,b}



Experimental Section

Materials. The series of pyridines were purified either by distillation or recrystallization. *S*-Methyl 4-nitrophenyl thiocarbonate (**1**) and *S*-methyl 2,4-dinitrophenyl thiocarbonate (**2**) were prepared by a standard procedure.⁶ The ¹H and ¹³C

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TABLE 1. Values of pK_a for the Conjugate Acids of Pyridines and k_N Values for the Pyridinolysis of *S*-Methyl 4-Nitrophenyl Thiocarbonate (**1**), and *S*-Methyl 2,4-Dinitrophenyl Thiocarbonate (**2**)^a

pyridine substituent	pK_a	k_N ($s^{-1} M^{-1}$)	
		1	2
4-(dimethylamino)	9.87	4.3 ± 0.1	19 ± 1
4-amino	9.37	1.4 ± 0.04	9.1 ± 0.4
4-amino-3-bromo	7.40	$(7.1 \pm 0.1) \times 10^{-3}$	2.1 ± 0.1
3,4-dimethyl	6.77	$(8.4 \pm 0.3) \times 10^{-4}$	
4-methyl	6.25	$(6.6 \pm 0.3) \times 10^{-4}$	0.28 ± 0.02
3-methyl	5.86		0.13 ± 0.01
H	5.37		$(5.5 \pm 0.2) \times 10^{-2}$
3-carbamoyl	3.43		$(1.2 \pm 0.05) \times 10^{-3}$

^a Both the pK_a and k_N values were determined in aqueous solution, at 25.0 °C, and an ionic strength of 0.2 M (KCl).

NMR spectra of these compounds and their elemental analyses agreed with their structures.

Kinetic Measurements. The reactions were studied spectrophotometrically (300–500 nm) by means of a diode array instrument. The rate constants were determined at 400 nm (pyridinolysis of **1**) and 360 nm (pyridinolysis of **2**) by following 4-nitrophenoxide and 2,4-dinitrophenoxide anions, respectively. The reactions were studied in aqueous solutions, at 25.0 ± 0.1 °C and an ionic strength of 0.2 M (maintained with KCl). At least a 10-fold excess of total amine (free pyridine plus protonated pyridine) over the substrate was employed in all reactions.

Pseudo-first-order rate coefficients (k_{obsd}) were found in all cases. These were obtained by means of the kinetic software of the spectrophotometer, after at least four half-lives, except for the slowest reactions (thiocarbonate **1** with 4-methyl and 3,4-dimethylpyridines) where the initial rate method was used.⁷

The experimental conditions of the reactions and the values of k_{obsd} are shown in Tables S1 and S2 in Supporting Information.

Determination of pK_a Values. The pK_a value of 4-amino-3-bromopyridine was determined by a potentiometric method, in water, at 25.0 ± 0.1 °C and an ionic strength of 0.2 M (maintained with KCl). The value obtained was 7.4 ± 0.1.

Product Studies. 4-Nitrophenoxide and 2,4-dinitrophenoxide anions were identified as one of the products in the pyridinolysis of **1** and **2**, respectively. This was achieved by comparison of the UV-vis spectra after completion of these reactions with those of authentic samples of 4-nitrophenol and 2,4-dinitrophenol, under the same reaction conditions.

Results and Discussion

The rate law obtained for all of the reactions studied is given by eqs 1 and 2, where P, S, and N represent a product (4-nitrophenoxide or 2,4-dinitrophenoxide anion), the substrate, and the free pyridine, respectively, and k_0 and k_N are the rate coefficients for solvolysis and pyridinolysis of the substrates, respectively.

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

$$k_{obsd} = k_0 + k_N[N] \quad (2)$$

The value of k_0 was much lower than that of $k_N[N]$ in eq 2, except for the slow reactions of thiocarbonate **1** with 4-methyl and 3,4-dimethylpyridines, where the aminolysis term in eq 2 was also small. The values of k_N for all

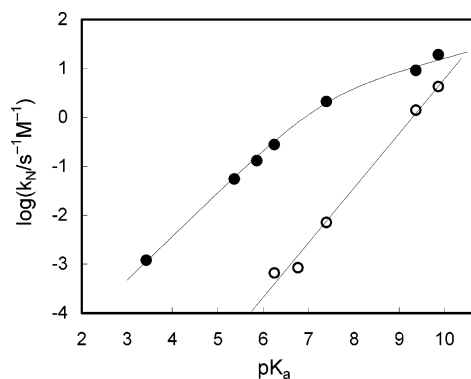
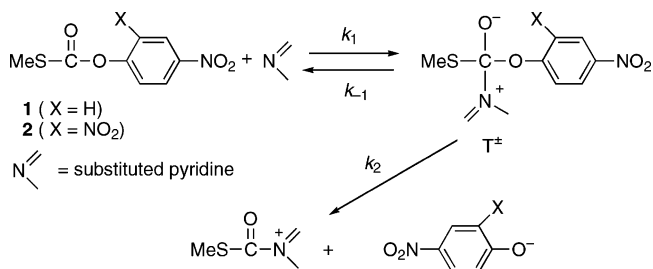


FIGURE 1. Brønsted-type plots for the pyridinolysis of thiocarbonates **1** (○) and **2** (●) in aqueous solution, at 25.0 °C and an ionic strength of 0.2 M (KCl).

SCHEME 1



reactions were obtained as the slopes of linear plots of k_{obsd} vs $[N]$. The k_N values were found to be pH-independent. The values of k_N for the reactions of pyridines with thiocarbonates **1** and **2** are shown in Table 1.

With the pK_a and k_N values in Table 1 the Brønsted-type plots of Figure 1 were obtained.

The curved Brønsted line in Figure 1 for the pyridinolysis of **2** was calculated by means of a semiempirical equation based on the existence of a zwitterionic tetrahedral intermediate (T^\pm) on the reaction pathway (see Scheme 1).^{1b-e,4b,8,9} This equation contains four parameters: β_1 and β_2 , which are the Brønsted slopes at high and low pK_a , respectively, and k_N^0 and pK_a^0 , which are the corresponding values at the center of the curvature. The Brønsted curve for thiocarbonate **2** was calculated by means of the following parameters: $\log k_N^0 = 0.24$,

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$pK_a^0 = 7.3$, $\beta_1 = 0.25$ and $\beta_2 = 0.90$ ($n = 7$, $R = 0.994$). The errors of the slopes are ± 0.1 , and those of pK_a^0 and $\log k_N^0$ are ± 0.2 and ± 0.1 , respectively.

The values of β_1 and β_2 for the pyridinolysis of thiocarbonate **2** are in accordance with those reported for other aminolyses governed by stepwise mechanisms: $\beta_1 = 0.1-0.3$ and $\beta_2 = 0.8-1.1$.^{1,3-5,7a,8,9}

The pyridinolysis of thiocarbonate **1** shows a linear Brønsted plot (Figure 1) of slope $\beta = 1.1 \pm 0.05$. This slope value is consistent with a pathway through a zwitterionic tetrahedral intermediate (T^\pm) whose breakdown to products is rate-determining;^{1,3-5,7a,8,9} namely, these reactions behave according to Scheme 1, with the formation of T^\pm as an equilibrium step and the k_2 step as rate-limiting ($k_{-1} \gg k_2$ in Scheme 1) along the whole pK_a range studied. Therefore, for this reaction the value of pK_a^0 must be greater than 9.87, which is the pK_a value for the most basic pyridine used in this plot.

The fact that the pK_a^0 value for the pyridinolysis of thiocarbonate **2** is smaller than that for **1** is in line with the results found in the aminolysis of aryl acetates,^{1c,d,7a} aryl phenyl carbonates,⁹ *S*-aryl thioacetates,¹⁰ aryl methyl carbonates,^{1a-d} and *S*-aryl *O*-ethyl dithiocarbonates;¹¹ the pK_a^0 value decreases as the leaving group becomes better. This can be explained on the basis of T^\pm in Scheme 1: the greater the nucleofugality of the leaving group from T^\pm (the larger k_2 in Scheme 1) the lower will be the basicity of a pyridine for which $k_{-1} = k_2$.^{3,9}

As seen in Figure 1, the values of k_N for the reactions of the two most basic pyridines with **2** are only little larger than those for **1**. In these cases formation of the intermediate T^\pm is rate-determining (k_1 step in Scheme 1). This means that addition of an *ortho* nitro group in the leaving group does not enhance much the pyridine attack. In contrast, the k_N values for the reactions of weakly basic pyridines (of $pK_a < pK_a^0$) with **2** are much larger than those for the reactions with **1**. In these cases, breakdown to products of the intermediate T^\pm (k_2 step in Scheme 1) is rate-limiting, and $k_N = K_1 k_2$, where K_1 is the equilibrium constant for the first step. This result can be explained by the much greater leaving ability from the intermediate (larger k_2 value) of 2,4-dinitrophenoxide than 4-nitrophenoxide.

Figure 2 shows a comparison of the Brønsted-type plots obtained for the pyridinolysis of thiocarbonate **1** (this work) and carbonate **3**.^{1a} Figure 3 shows the same plots for the pyridinolysis of **2** (this study) and carbonate **4**.^{1b}

Figure 2 shows that carbonate **3** is more reactive toward a given pyridine than thiocarbonate **1** when breakdown of T^\pm to products (k_2 step in Scheme 1) is the rate-determining step. In these cases, $k_N = k_1 k_2 / k_{-1}$. The value of the ratio k_2 / k_{-1} for a given pyridine is smaller for carbonate **3** than thiocarbonate **1** (see below). This means that the k_1 value should be much larger for the former compound. This is at first sight surprising because the electronic effects of MeS and MeO seem to favor amine attack toward thiocarbonate **1** rather than toward carbonate **3**. This is because the electron-releasing reso-

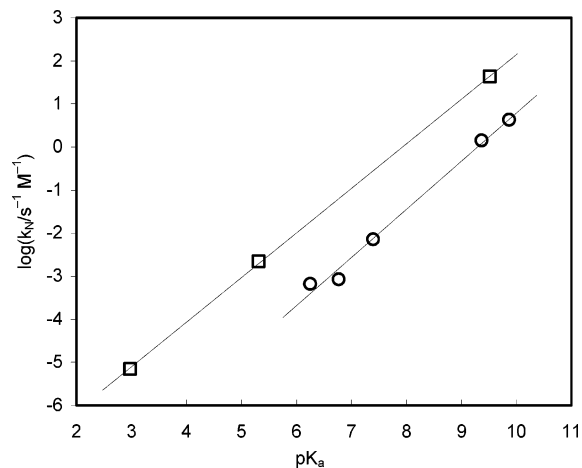


FIGURE 2. Brønsted-type plots obtained for the pyridinolysis of thiocarbonate **1** (○, this work) and carbonate **3** (□, ref 1a) in aqueous solution, at 25.0 °C and an ionic strength of 0.2 M.

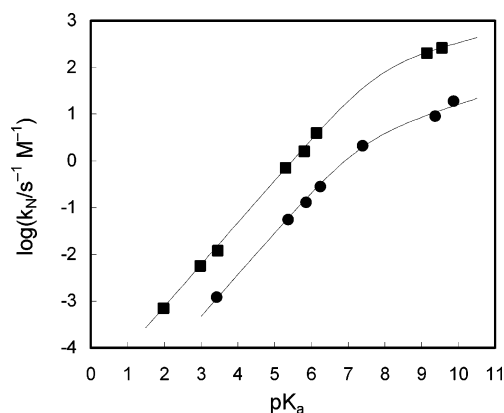


FIGURE 3. Brønsted-type plots obtained for the pyridinolysis of thiocarbonate **2** (●, this work) and carbonate **4** (■, ref 1b) in aqueous solution, at 25.0 °C and an ionic strength of 0.2 M.

nance effect of MeS is much smaller than that of MeO ($\sigma_R = -0.23$ and -0.56 , respectively),¹² and this effect is only partially compensated by the smaller electron-withdrawing inductive effect of MeS compared to that of MeO (σ_I of MeS and MeO are 0.23 and 0.29, respectively).¹² This is in line with the σ_P values (where both inductive and resonance effects are involved) of these groups ($\sigma_P = 0.00$ and -0.27 , respectively).¹² Therefore, the larger k_1 values shown by the pyridinolysis of **3** relative to those of **1** are not due to the electronic effects of the nonleaving groups. A reasonable explanation could be the much larger size of S compared to O, which due to steric hindrance should render the k_1 values for **1** smaller than those for **3**.

The larger k_1 values for carbonate **3** compared to those of thiocarbonate **1** are confirmed by inspection of Figure 3, which shows that at high pK_a (where the k_1 step is rate-determining) carbonate **4** is also more reactive toward pyridines than thiocarbonate **2**.

Figure 3 also shows that the value of the curvature center at the pK_a axis (pK_a^0) is larger for the pyridinolysis of carbonate **4** than for thiocarbonate **2** ($pK_a^0 = 7.8$ and 7.3, respectively). According to the hypothesis of the

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tetrahedral intermediate a larger pK_a^0 value means a larger k_{-1}/k_2 ratio for a given amine, as shown by an equation (eq 3) derived from the above hypothesis. The values of β_2 and β_1 are not much influenced by the substrate nature.^{1,3-5,7a,8-11}

$$\log\left(\frac{k_{-1}}{k_2}\right) = (\beta_2 - \beta_1)(pK_a^0 - pK_a) \quad (3)$$

According with the β_2 and β_1 values shown by the pyridinolysis of carbonate **4** and thiocarbonate **2** ($\beta_2 - \beta_1$ ca. 0.7), eq 3 predicts that, for a given substituted pyridine, the k_{-1}/k_2 ratio for carbonate **4** should be ca. two times larger than that for thiocarbonate **2**.

The larger k_{-1}/k_2 ratio for a given amine for the pyridinolysis of carbonate **4** compared to that of thiocarbonate **2** can be rationalized assuming that the inductive effects are more important than the resonance effects in a tetrahedral intermediate.¹³ The group MeO is inductively more electron-withdrawing than MeS ($\sigma_I = 0.29$ and 0.23, respectively),¹² leaving the central carbon of the tetrahedral intermediate (T^\pm) more positively charged, which facilitates the push provided by the oxygen atom in the leaving group to expel the pyridine. Nonetheless, the pyridino moiety in T^\pm cannot exert a push to expel the leaving group because its nitrogen atom lacks an electron pair.¹⁴ Our results are in accordance with those found in the quinuclidinolysis of diaryl carbonates:¹⁴ the pK_a^0 value increases as the substituent in the nonleaving group becomes more electron-withdrawing inductively.¹⁴

Figure 3 shows that the rate constant k_N for the pyridinolysis of carbonate **4** is larger than that for thiocarbonate **2** when the k_2 step in Scheme 1 is rate-limiting. As discussed above, in relation to the Brønsted plots for the corresponding mononitro derivatives, this can be attributed to a much greater k_1 value for carbonate

4, which is only partially offset by a lower value of the k_2/k_{-1} ratio.

The larger k_1 values found in this work for the pyridinolysis of a carbonate relative to those for the same aminolysis of the corresponding thiocarbonate with an S atom in the nonleaving group are in agreement with the kinetic results obtained for the pyridinolysis of carbonates and thiocarbonates that possess the S atom in the leaving group. For the reactions of 4-(dimethylamino)pyridine and 4-aminopyridine with carbonate **4** in water, at 25.0 °C, ionic strength 0.2 M, the values of k_1 are 260 and 200 $s^{-1} M^{-1}$, respectively,^{1b} whereas they are only 31 and 14 $s^{-1} M^{-1}$, respectively, for the reactions of the same amines with *S*-(2,4-dinitrophenyl) ethyl thiocarbonate under the same experimental conditions.¹⁵ Although the nonleaving groups of these two substrates are different, it is known that the change of methoxy to ethoxy as the nonleaving group does not affect the nucleophilic rate constants, within experimental error.¹⁶ Similarly, the values of k_1 for the reactions of the above pyridines with 2,4,6-trinitrophenyl methyl carbonate under the above conditions are 1390 and 807 $s^{-1} M^{-1}$, respectively,^{1d} in contrast to the values 38 and 21 $s^{-1} M^{-1}$, respectively, for the reactions of the same amines with *S*-(2,4,6-trinitrophenyl) ethyl thiocarbonate under the same conditions.¹⁵ Moreover, the values of k_1 for the reactions of these amines with *O*-(2,4-dinitrophenyl) *O*-ethyl thionocarbonate¹⁶ are larger than those for the reactions of the same amines with *S*-(2,4-dinitrophenyl) *O*-ethyl dithiocarbonate under the same experimental conditions.^{11b}

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Supporting Information Available: Experimental conditions of the reactions and the values of k_{obsd} . This material is available free of charge via the Internet at <http://pubs.acs.org>.

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