

Phenolysis and Aminolysis of 4-Nitrophenyl and 2,4-Dinitrophenyl S-Methyl Thiocarbonates in Aqueous Ethanol

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ABSTRACT: The reactions of S-methyl O-(4-nitrophenyl) thiocarbonate (**1**) and S-methyl O-(2,4-dinitrophenyl) thiocarbonate (**2**) with a series of secondary alicyclic (SA) amines and phenols are subjected to a kinetic investigation. Under nucleophile excess, pseudo-first-order rate coefficients (k_{obs}) are obtained. Plots of k_{obs} against the free nucleophile concentration at constant pH are linear with slopes k_{N} . The Brønsted plots ($\log k_{\text{N}}$ vs. nucleophile $\text{p}K_{\text{a}}$) for the reactions are linear with slope (β) values in the 0.5–0.7 range, in accordance with concerted mechanisms. Comparison of the SA aminolysis of **1** with the same one carried out in water shows that the change of solvent from water to aqueous ethanol destabilizes the zwitterionic tetrahedral intermediate, changing the mechanism from stepwise to concerted. This destabilization is greater than that due to the change from SA amines to quinuclidines. For the phenolysis reactions, the k_{N} values in aqueous ethanol are smaller than those for the same reactions in water. Considering that the nucleophile is an anion, this result is unexpected because the anion should be more stabilized in the more polar solvent. This result is explained by the facts that the phenoxide reactant has a negative charge that is delocalized in the aromatic ring and the transition state is highly polar. © 2011 Wiley Periodicals, Inc. *Int J Chem Kinet* 43: 353–358, 2011

INTRODUCTION

The nucleophilic substitution reactions of carbonyl and thiocarbonyl derivatives in a solution with reagents of varying nucleophilicity have been studied by several groups. To date there is a suitable database since the kinetics and mechanisms of these processes have been fully described [1–18]. Taking into account these studies, several factors have been reported to affect the

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kinetics and mechanisms of these reactions: (i) nucleophile nature and basicity, (ii) nonleaving group, (iii) leaving group (nucleofuge), and (iv) electrophilic group.

In addition, other studies involving different nucleophilic substitution reactions on carbonyl derivatives show that the solvent plays an important role in controlling the dynamics of a chemical reaction [19,20]. Nevertheless, there have been relatively few reports on the effect of the solvent on the mechanisms of these reactions. One of these is the reaction of *O*-ethyl *S*-2,4,6-trinitrophenyl dithiocarbonate with secondary alicyclic (SA) amines, which changes from stepwise in water [21] to concerted in aqueous 44 wt% ethanol [22].

With the purpose to enhance the knowledge about the solvent effect on these reactions, in this work we study the aminolysis (SA amines) and phenolysis of *S*-methyl *O*-(4-nitrophenyl) thiocarbonate (**1**) and *S*-methyl *O*-(2,4-dinitrophenyl) thiocarbonate (**2**) in aqueous 44 wt% ethanol. By comparison of these reactions with the same ones carried out in water, the effect of the solvent on the kinetics and mechanism will be assessed.

EXPERIMENTAL

Materials

Phenols and secondary alicyclic (SA) amines were purified by recrystallization or distillation. Thiocarbonates **1** and **2** were samples from previous studies [23,24].

Kinetic Measurements

The kinetics of the reactions were analyzed through a diode array spectrophotometer in 44 wt% ethanol-water at $25.0 \pm 0.1^\circ\text{C}$ and an ionic strength of 0.2 M (maintained with KCl). The reactions were followed at the 300–500 nm wavelength range.

The reactions were studied under at least a 10-fold excess of nucleophile over the substrate, the initial concentration of the latter being 2.5×10^{-5} M. Under these conditions, pseudo-first-order rate coefficients (k_{obs}) were found throughout, the kinetics being measured for at least five half-lives at 400 and 360 nm following 4-nitrophenoxide and 2,4-dinitrophenoxide ions formation, respectively. In most of the reactions, the pH was maintained constant by the nucleophile, except in some reactions where the pH was maintained by 0.01 M borate buffer.

Pseudo-first-order rate coefficients (k_{obs}) were found throughout and determined by means of the kinetics software for first-order reactions of the spectrophotometer. Errors in the k_{obs} values were less than 3%. The experimental conditions of the reactions and the values of k_{obs} are shown in Tables S1–S21 in the Supporting Information.

Product Studies

For the aminolysis and phenolysis reactions of thiocarbonates **1** and **2**, 4-nitrophenoxide and 2,4-dinitrophenoxide anions, respectively, were identified as one of the products. 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 kinetics of all the studied reactions is in accordance with Eqs. (1) and (2), where [P] and [S] are the product and substrate concentrations, respectively, and k_0 and k_N are the rate coefficients for solvolysis and phenolysis or aminolysis of the substrates, respectively. The values of k_0 and k_N showed no dependence on pH within the pH range employed. These values were obtained as the intercept and slope, respectively, of linear plots of k_{obs} against the nucleophile concentration, at constant pH. The pseudo-first-order rate constants (k_{obs}), obtained under an excess of phenol or secondary alicyclic (SA) amine, and the experimental conditions for the studied reactions are detailed in Tables S1–S21 in the Supporting Information.

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

$$k_{\text{obs}} = k_0 + k_N[\text{nucleophile}] \quad (2)$$

The k_0 values were much smaller than the k_N [nucleophile] term in Eq. (2) for the studied reactions. The values of k_N for the reactions of thiocarbonates **1** and **2** with SA amines are shown in Table I, and those with phenols are shown in Table II.

The k_N values, as well as those of the $\text{p}K_a$ of the conjugate acids of these amines, in Table I, were statistically corrected [21] with $q = 2$ for piperazine ($q = 1$ for all the other SA amines) and $p = 2$ for all the conjugate acids of the amines [21]. The parameter q is the number of equivalent basic sites in the free amine, and p is the number of equivalent dissociable protons in

Table I Values of pK_a for the Series of Secondary Alicyclic (SA) Amines and Nucleophilic Rate Constants (k_N) for the SA Aminolysis of S-methyl O-(4-nitrophenyl) Thiocarbonate (**1**) and S-methyl O-(2,4-dinitrophenyl) Thiocarbonate (**2**)^{a,b}

Amine	pK_a	$10^3 k_N (M^{-1} s^{-1})$	
		1	2
Piperidine	10.82	197 ± 9	1030 ± 50
Piperazine	9.71	202 ± 6	590 ± 20
1-(2-Hydroxyethyl) piperazine	9.09	41 ± 2	152 ± 6
Morpholine	8.48	11.8 ± 0.4	124 ± 6
1-Formylpiperazine	7.63	14.0 ± 0.4	75 ± 5
Piperazinium ion	5.57	0.25 ± 0.01	–

^a pK_a and k_N values were determined in aqueous 44 wt% ethanol.

^bErrors shown are standard deviations.

Table II Values of pK_a for the Series of Phenols and Nucleophilic Rate Constants (k_N) for the Phenolysis of S-methyl O-(4-nitrophenyl) Thiocarbonate (**1**) and S-methyl O-(2,4-dinitrophenyl) Thiocarbonate (**2**)^{a,b}

Phenol	pK_a	$10^3 k_N (M^{-1} s^{-1})$	
		1	2
4-Methoxyphenol	11.55	149 ± 9	970 ± 50
Phenol	11.16	42 ± 2	288 ± 1
3-Chlorophenol	10.23	19.0 ± 0.5	170 ± 1
4-Cyanophenol	8.60	1.18 ± 0.06	28.6 ± 0.1
2,6-Difluorophenol	7.21	0.83 ± 0.04	6.9 ± 0.1

^a pK_a and k_N values were determined in aqueous 44 wt% ethanol.

^bErrors shown are standard deviations.

the conjugate acid of the amine [25]. Figure 1 shows the statistically corrected Brønsted-type plots for the SA aminolysis of thiocarbonates **1** and **2** in aqueous ethanol. This figure also includes the statistically corrected Brønsted plot for the reactions of thiocarbonate **2** with SA amines in water [23].

The Brønsted-type plots for the reactions of SA amines with thiocarbonates **1** and **2** in aqueous ethanol are linear with slope values (β) 0.57 and 0.40, respectively. These β values are in accordance with those reported for other concerted reactions that show Brønsted slopes within the range 0.5–0.7 [13,14,22,23].

Nonetheless, it is known that the β value alone is not enough to conclude that a mechanism is concerted. It is also necessary to make sure that the expected pK_a value at the center of the Brønsted curvature (pK_a^0) for a hypothetical stepwise mechanism is within the pK_a range used [26,27]. Unfortunately, there are no relevant

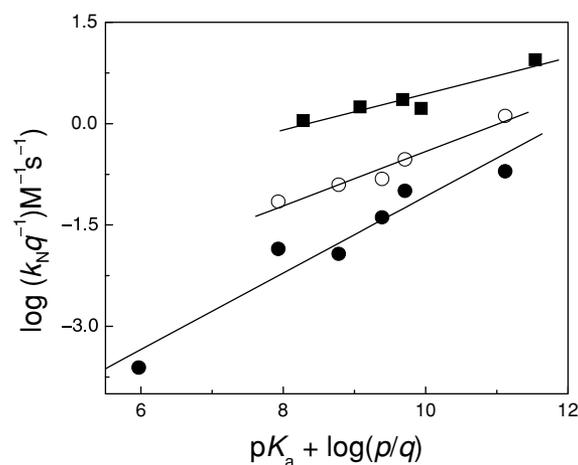
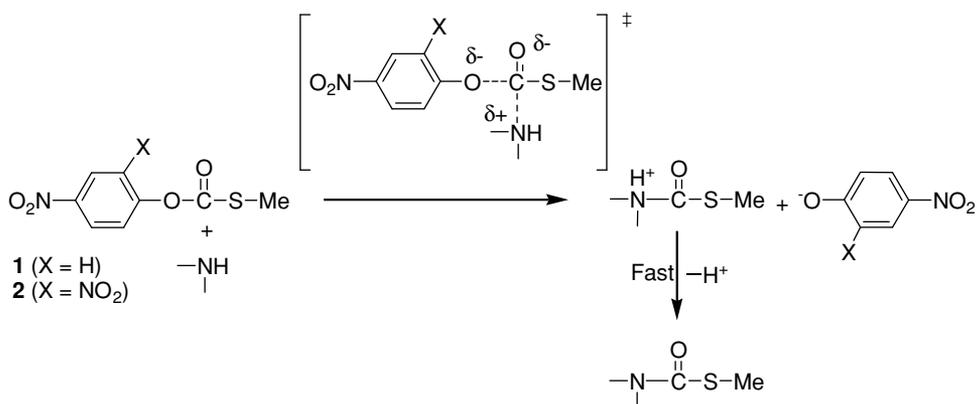


Figure 1 Brønsted-type plots (statistically corrected, see the text) obtained for the reactions of SA amines with thiocarbonate **1** (●) and thiocarbonate **2** (○) in 44 wt% ethanol–water at 25.0°C; ionic strength 0.2 M (KCl). Also shown is the plot for the SA aminolysis of **2** (■, [23]) in water at 25.0°C; ionic strength 0.2 M (KCl).

data in the literature to predict a good estimation of the pK_a^0 for these reactions.

Nevertheless, the following argument can be useful to decide about the mechanism: For the SA aminolysis of thiocarbonate **1** in water, a linear Brønsted plot with slope 0.9 was found [23]. This indicates the presence of a zwitterionic tetrahedral intermediate (T^\pm) on the reaction pathway, its breakdown to products being the rate-determining step [3,4,8,9]. This means that the pK_a^0 value for the SA aminolysis of **1** in water is larger than 10.8 (the pK_a for the most basic SA amine studied) [3,4,8,9]. It is known that the change of solvent from water to a less polar solvent fastens amine expulsion from T^\pm (larger k_{-1}), but does not affect significantly the expulsion of aryloxy (similar k_2) [9]. This is because the transition state (TS) for T^\pm formation is less polar than T^\pm , but the TS for T^\pm breakdown is of similar polarity as T^\pm [9]. A larger k_{-1}/k_2 ratio signifies a larger pK_a^0 value [3,4,8,9]. Therefore, the pK_a^0 value for the SA aminolysis of **1** in aqueous ethanol should be much higher than 10.8 if this reaction were stepwise, and the Brønsted plot for this reaction should be linear with slope ca. 0.8–1 (the same rate-determining step as that in water). In view that the actual Brønsted slope is 0.57, one can safely conclude that the reaction of **1** with SA amines in aqueous ethanol is concerted; see Scheme 1 ($X = H$).

For the reactions of **2** with the same amine series in water, a concerted mechanism was proposed [23]. These reactions are between neutral reactants that produce ionic products; therefore, if the mechanism were



Scheme 1

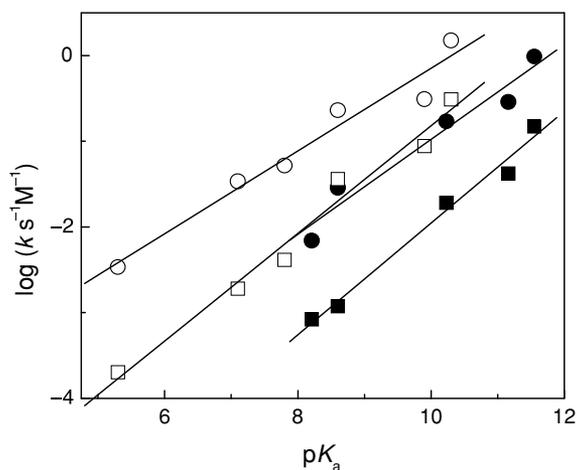


Figure 2 Brønsted-type plots for the reactions of phenoxide ions with thiocarbonates **1** (■) and **2** (●), in 44 wt% ethanol–water, at 25.0°C, ionic strength 0.2 M (KCl). Also included are the same reactions of **1** (□) and **2** (○) in water, at 25.0°C, ionic strength 0.2 M (KCl), from [24].

stepwise, the putative tetrahedral intermediate would have a charge separation. As this zwitterionic intermediate is unstable for the SA aminolysis of **2** in water, then it would be even more unstable in aqueous ethanol. According to this argument, it is highly probable that the mechanism for the reactions of **2** with SA amines in the less polar solvent is concerted, in accordance with Scheme 1 (X = NO₂).

With the k_N values for the phenolysis of thiocarbonates **1** and **2**, as well as those of the pK_a of the phenols in Table II, the Brønsted-type plots of Fig. 2 were obtained. The plots are linear with slope (β) values of 0.65 and 0.55, respectively. This figure also includes the plots for the same reactions in water, which are concerted, with $\beta = 0.51$ and 0.66 for the phenolysis of **1** and **2**, respectively [24]. The β values

obtained for the reactions in aqueous ethanol are in accordance with those found in the concerted reactions of the same reactants in water [24]. They also agree with the β values found in other concerted processes, which show Brønsted slopes within the range 0.5–0.7 [3,4,13,14,23].

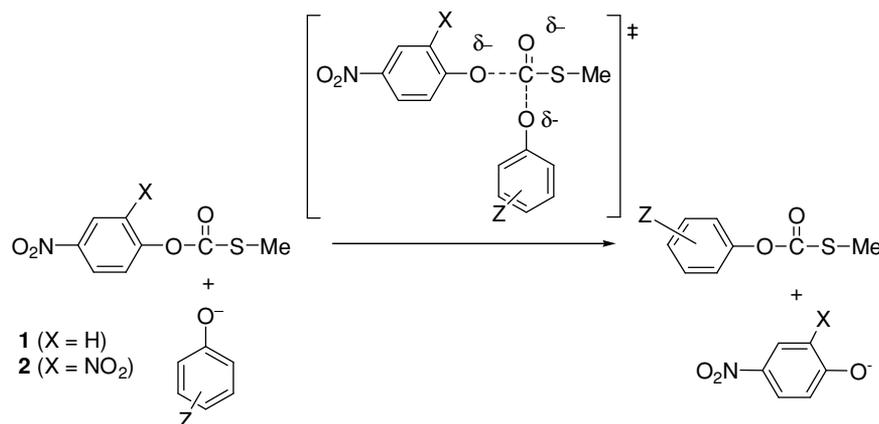
As was mentioned above, the β value alone is not enough to conclude that a mechanism is concerted. For the phenolysis of **1**, where 4-nitrophenoxide anion is the leaving group, the absence of a break (pK_a^0 at 7.5 (the pK_a of 4-nitrophenol in aqueous 44 wt% ethanol) allows to rule out a stepwise process and confirms the concerted mechanism. This is shown in Scheme 2 (X = H).

On the other hand, the hypothetical pK_a^0 for the phenolysis of **2** is out of the pK_a range studied (pK_a of 2,4-dinitrophenol is 4.0). Nevertheless, since 2,4-dinitrophenoxide anion is a better nucleofuge than 4-nitrophenoxide anion, the putative anionic tetrahedral intermediate in the reaction of **2** would be even more unstable than that in the phenolysis of **1**, and therefore, the mechanism for the phenolysis of **2** in aqueous ethanol should also be concerted as shown in Scheme 2 (X = NO₂).

From the k_N values shown in Tables I and II and from Figs. 1 and 2, it can be observed that thiocarbonate **2** is more reactive than **1** toward amines and phenoxides. This result is in accordance with the greater electron-withdrawing effect of the 2,4-dinitro group in **2**, compared with 4-nitro in **1**, which leads to a more electrophilic carbonyl carbon in **2** and, therefore, more prone to the nucleophilic attack.

Solvent Effect on Mechanism

The aminolysis (SA amines) of **1** in aqueous ethanol (this study) is in accordance with a concerted



Scheme 2

mechanism, as shown in Scheme 1 ($X = \text{H}$). It is noteworthy that the same reaction in water proceeds by a stepwise mechanism [23] (see above). Therefore, the change of solvent from water to a less polar one, such as aqueous ethanol, greatly destabilizes the zwitterionic tetrahedral intermediate. Two situations could then be possible: (i) The intermediate could be destabilized to the point of nonexistence (enforced concerted mechanism) or (ii) the intermediate could still exist but the free energy of activation of the stepwise process could be larger than that of the concerted mechanism [2,28,29]. The same behavior was described for the reactions of SA amines with *O*-ethyl *S*-(2,4,6-trinitrophenyl) dithiocarbonate, which shows a stepwise mechanism in water [21] and a concerted process in aqueous 44 wt% ethanol [22].

On the other hand, the reactions of **1** with quinuclidines in water are stepwise [23]; therefore, the corresponding tetrahedral intermediate exists. It is known that quinuclidines destabilize the zwitterionic tetrahedral intermediate relative to isobasic SA amines [30]. In consequence, the solvent change from water to aqueous 44 wt% ethanol destabilizes this tetrahedral intermediate more than the change from SA amines to quinuclidines.

For the phenolysis reactions of thiocarbonates **1** and **2**, and the SA aminolysis of **2**, no changes in mechanism were found by the solvent change from water [23,24] to aqueous 44 wt% ethanol.

Kinetic Solvent Effect

From Fig. 1, it can be observed that the k_N values for the reactions of **2** with SA amines are greater in water [23] relative to aqueous ethanol (this study), both being concerted mechanisms. Taking into account that the

reactants are neutral and the transition state presents charge dispersion, it is possible to expect a greater stabilization of the transition state (relative to reactants) in the more polar medium (water).

For the phenolysis reactions, the k_N values in aqueous ethanol (this study) are smaller (about 15 times) than those for the same reactions in water [24]. Considering that the nucleophile is an anion (phenoxide), this result is unexpected because the anion should be more stabilized in the more polar solvent.

A possible explanation is that the negative charge on the TS is localized mainly in the leaving group (a late TS) and, therefore, the TS would be more solvated by water relative to aqueous ethanol. On the other hand, it is necessary to consider that the phenoxide reactant has a negative charge that is delocalized in the aromatic ring; therefore, it is less stabilized in a polar solvent than could be expected for an anion with localized charge, such as an alkoxide anion [24]. Because of this, the delocalization of charge makes the nucleophile a less anionic species, producing a decrease in the total solvation energy, which is particularly strong for a solvent such as water [24]. In accordance with this, it is possible that the activation free energy for the phenolysis of **1** and **2** in water be smaller than those in 44 wt% aqueous ethanol, therefore, being greater the nucleophilic rate constants in the former solvent.

CONCLUSIONS

(i) The aminolysis (SA amines) and phenolysis reactions of thiocarbonates **1** and **2** in aqueous 44 wt% ethanol are concerted. (ii) For the aminolysis of **1**, the solvent change from water to aqueous 44 wt% ethanol changes the mechanism from stepwise to concerted.

(iii) For the aminolysis of **1**, the solvent change from water to aqueous 44 wt% ethanol destabilizes the tetrahedral intermediate more than the change from SA amines to quinuclidines in water. (iv) The concerted phenolysis reactions of **1** and **2** are faster in water than in aqueous 44 wt% ethanol; this is mainly attributed to charge delocalization in the phenoxide reactant.

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