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Kinetics and mechanism of the reactions of aryl chlorodithioformates with pyridines and secondary alicyclic amines

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The reactions of pyridines and secondary alicyclic (SA) amines with phenyl and 4-nitrophenyl chlorodithioformates (PClDTF and NPClDTF, respectively) are subjected to a kinetic study in aqueous ethanol (44 wt% ethanol) solution, at 25.0 °C, and an ionic strength of 0.2 M (KCl). The reactions are studied spectrophotometrically. Under amine excess, pseudo-first-order rate coefficients (k_{obs}) are found. Plots of k_{obs} *versus* [amine] are linear and pH independent, with slope k_N. The Brønsted-type plots (log k_N *vs.* pK_a of aminium ions) are linear for the reactions of PClDTF with SA amines (slope β of 0.3) and pyridines ($\beta = 0.26$) and those of NPClDTF with pyridines ($\beta = 0.30$). For the reaction of NPClDTF with SA amines the Brønsted-type plot is biphasic, with slopes $\beta_1 = 0.2$ (at high p*K*a) and $\beta_2 = 1.1$ (at low p*K*a). The pK_a value at the center of curvature (pK_a^0) is 7.7. The magnitude of the slopes indicates that the mechanisms of these reactions are stepwise, with the formation of a zwitterionic tetrahedral intermediate as the rate-determining step, except for the reaction of NPClDTF with SA amines where there is a change in the rate-determining step, from formation to breakdown of the tetrahedral intermediate, as the amine basicity decreases. Copyright © 2009 John Wiley & Sons, Ltd.

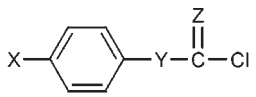
Keywords: kinetics; mechanism; aminolysis; aryl chlorodithioformates; Brønsted plot; tetrahedral intermediates

INTRODUCTION

The solvolysis reactions of aryl chloroformates (ArO—CO—Cl),[1–3] phenyl chlorothiolformate (PhS—CO—Cl),[4,5] phenyl chlorothionoformate (PhO—CS—Cl),[6–8] and phenyl chlorodithioformate (PhS—CS—Cl)[8–10] have been studied kinetically and their mechanisms clearly established. By comparison of the solvolysis of phenyl chloroformate with those of the corresponding thiol and dithio analogues, it was concluded that the substitution of the oxygen atoms in phenyl chloroformate by sulfur atoms (to give the corresponding thiol and dithio chloroformates, respectively) gradually changes the mechanism from addition–elimination, for the chloroformate, to an S_N1 ionization process for phenyl chlorodithioformate.[8]

On the other hand, the reactions of aryl chloroformates with secondary alicyclic (SA) amines[11,12] and quinuclidines,[13] and those of aryl chlorothionoformates with pyridines,[14] SA amines[15] and quinuclidines[16] show stepwise mechanisms with the formation of a zwitterionic tetrahedral intermediate as the rate-limiting step. The rate-determining step has been suggested to change at pK_a^0 (pK_a at the center of the Brønsted curvature), thereby indicating that the pK_a^0 value is governed by the basicity of the amine, solvent effects, the nucleophile–nucleofuge interaction, and the nucleofugality of the leaving group.[17–21] However, the effect of the nonleaving-group on the reaction mechanism is not yet completely understood. It has been found that the pK_a^0 value increases as the substituent in the nonleaving group increases its electron-withdrawing ability,[22] this argument being in agreement with the results reported by Gresser and Jencks.[23]

To extend our kinetic studies on the aminolysis of chlorothioformates and with the aim to shed some light on these mechanisms, in the present work we investigate the reactions of pyridines and SA amines with phenyl and 4-nitrophenyl chlorodithioformates (PClDTF and NPClDTF, respectively, Scheme 1). Specific objectives are (i) to assess the effect of the nonleaving group on the kinetics and mechanism, by comparing the reactions of PClDTF and NPClDTF with a given amine series; (ii) to analyze the influence of the sulfur atoms in aryl chlorodithioformates, by comparison of the present reactions with the same aminolyses of the corresponding thiono derivatives (PClTF and NPClTF, respectively, Scheme 1) and aryl chloroformates (PClF and NPClF, respectively, Scheme 1). It is of special interest to see whether there is a change of mechanism by the substitution of an



PClDTF (X = H ; Y = Z = S)
NPClDTF (X = NO_2 ; Y = Z = S)
PClTF (X = H ; Y = O ; Z = S)
NPClTF (X = NO_2 ; Y = O ; Z = S)
PClF (X = H ; Y = Z = O)
NPClF (X = NO_2 ; Y = Z = O)

Scheme 1.

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O-aryl group by *S*-aryl in the reactant structure; (iii) to assess the influence of the amine nature on the kinetics and mechanisms of these reactions. This will be achieved by a kinetic comparison of the reactions of the title substrates with both amine series.

RESULTS AND DISCUSSION

The kinetic law obtained under the reaction conditions is that described by Eqn (1), where P is the corresponding dithiocarbamate product, S the substrate, and k_{obs} is the pseudo-first-order rate coefficient (excess of amine was used throughout). The experimental conditions of the reactions and the k_{obs} values obtained are shown in Tables 1–4.

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

Plots of k_{obs} against [amine] at constant pH were linear in accordance with Eqn (2), where k_0 and k_N are the rate coefficients for solvolysis and aminolyses (SA amines and pyridines) of the substrates, respectively. The values of k_0 and k_N were pH independent.

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

The reactions of PClDTF with piperazine and piperazinium ion were studied at pH values ranged over 6.5–7.5, where mixtures of both amines are present. In these cases, the k_N values were obtained through Eqns (3) and (4).[24] In these equations $k_{N,obs}$ is a global nucleophilic rate constant (corresponding to the mixture of nucleophiles), $[N]_{tot}$ is the total piperazine (piperazine + piperazinium ion) concentration, F_N and F_{NH} are the molar fractions of piperazine and piperazinium ion, respectively, and k_N and k_{NH} are their corresponding nucleophilic rate constants. The values of $k_{N\,obs}$ were obtained as the slopes of linear plots of k_{obs} *versus* $[N]_{tot}$ at constant pH. The nucleophilic rate constants for the reactions of PClDTF with piperazine (k_N) and piperazinium ion (k_{NH}) were determined through Eqn (4), as described in Reference [24].

$$k_{obs} = k_0 + k_{Nobs}[N]_{tot} \quad (3)$$

$$k_{Nobs} = F_N\,k_N + F_{NH}\,k_{NH} \quad (4)$$

The k_0 values obtained for the reactions of PClDTF in this study (with both SAA and pyridines) ranged from 0.01 to 0.02 s^{-1}. These values are in the expected order of magnitude based on the work of Kevill and D'Souza[8] on the solvolysis reactions of PDTClF in ethanol and in 60–90% ethanol aqueous solutions. For instance, the k_0 values at 70 and 60% ethanol are 0.0018 and 0.007 s^{-1}, respectively. This shows that k_0 increases with the increase of water content in the solvent mixture.

Table 1. Experimental conditions and k_{obs} values for the reactions of secondary alicyclic (SA) amines with phenyl chlorodithioformate (PClDTF)[a]

SA amine	pH	F_N[b]	10^3 $[N]_{tot}$ (M)[c]	10^3 k_{obs} (s^{-1})	No. of runs
Piperidine	10.52	0.33	0.510–5.10	55.7–131	6
	10.82	0.50	0.500–5.00	30.5–207	6
	11.12	0.67	0.510–5.10	72.0–335	7
Piperazine	6.5[d]	[e]	2.00–5.00	21.4–27.9	5
	6.8[d]	[f]	0.500–5.00	16.1–25.0	6
	7.0[d]	[g]	0.500–5.00	21.2–33.8	6
	7.2[d]	[h]	2.75–5.00	30.8–34.9	4
	7.5[d]	[i]	2.00–5.00	31.9–45.8	5
	9.41	0.33	1.25–5.00	40.0–121	6
	9.71	0.50	0.250–2.50	15.8–109	6
	10.01	0.67	0.500–5.00	53.4–245	7
1-(2-Hydroxyethyl)piperazine	9.09	0.50	0.500–5.00	25.3–73.5	6
	9.39	0.67	1.28–5.10	35.0–76.6	6
Morpholine	8.08	0.294	1.38–2.50	38.8–45.1	4
	8.48	0.50	0.613–5.21	32.3–97.9	8
	9.78	0.67	0.500–4.92	37.1–111	6
Formylpiperazine	7.33	0.33	0.500–5.00	18.5–33.0	6
	7.63	0.50	0.500–4.25	17.8–37.4	6
	7.93	0.67	2.89–5.26	38.1–56.5	4
Piperazinium ion	5.37	0.50	1.25–5.00	112–170	5

[a] In 44 wt% ethanol–water, at 25 °C, ionic strength 0.2 M (KCl).
[b] Free amine fraction.
[c] Concentration of total amine (free base plus protonated forms).
[d] 0.005 M phosphate buffer.
[e] Free piperazine and piperazinium ion fractions were 0.0005737 and 0.93045, respectively.
[f] Free piperazine and piperazinium ion fractions were 0.001185 and 0.96303, respectively.
[g] Free piperazine and piperazinium ion fractions were 0.0019015 and 0.97524, respectively.
[h] Free piperazine and piperazinium ion fractions were 0.003036 and 0.98243, respectively.
[i] Free piperazine and piperazinium ion fractions were 0.005083 and 0.98660, respectively.

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Table 2. Experimental conditions and k_{obs} values for the reactions of secondary alicyclic (SA) amines with 4-nitrophenyl chlorodithioformate (NPClDTF)[a]

SA amine	pH	F_N[b]	10^3 $[N]_{tot}$(M)[c]	10^3 k_{obs} (s^{-1})	No. of runs
Piperidine	8.5[d]	0.00476	0.500–3.50	3.64–8.28	5
	9.0[d]	0.0149	0.500–4.25	4.51–17.8	6
	9.5[d]	0.0457	0.500–2.75	8.75–38.0	4
Piperazine	9.4	0.33	0.500–5.00	38.3–328	6
	9.7	0.50	0.500–0.425	75.9–522	6
1-(2-Hydroxyethyl)piperazine	8.5	0.205	0.500–5.00	20.7–101	7
	9.0	0.448	0.500–5.00	27.6–101	7
	9.5	0.720	0.500–5.00	31.2–289	7
Morpholine	6.5[e]	0.0104	0.500–5.00	3.75–10.9	7
	7.0[e]	0.0321	0.500–5.00	4.00–22.5	7
	7.5[e]	0.0948	0.500–5.00	9.32–56.4	7
Formylpiperazine	7.33	0.33	0.500–5.00	5.24–43.2	7
	7.63	0.50	0.500–5.00	11.8–75.6	7
	7.93	0.67	0.500–5.00	12.7–105	7
Piperazinium ion	5.07	0.33	10.4–104	3.50–17.5	7
	5.37	0.50	10.4–104	4.88–29.9	7
	5.67	0.67	10.4–104	5.13–38.7	7

[a] In 44 wt% ethanol–water, at 25 °C, ionic strength 0.2 M (KCl).
[b] Free amine fraction.
[c] Concentration of total amine (free base plus protonated forms).
[d] 0.005 M borate buffer.
[e] 0.005 M phosphate buffer.

Table 3. Experimental conditions and k_{obs} values for the reactions of pyridines with phenyl chlorodithioformate (PClDTF)[a]

Pyridine substituent	pH	F_N[b]	10^3 $[N]_{tot}$ (M)[c]	10^3 k_{obs} (s^{-1})	No. of runs
3,4-Diamino	9.15	0.33	3.25–32.5	24.6–138	7
	9.45	0.50	3.35–33.5	25.7–177	7
	9.75	0.67	3.13–31.3	31.8–236	7
4-Dimethylamino	8.84	0.33	5.01–50.1	28.7–181	7
	9.14	0.50	4.91–68.7	31.6–352	6
	9.44	0.67	3.70–37.0	53.6–237	7
4-Amino	8.5	0.25	4.60–18.4	22.1–60.0	6
	9.0	0.51	1.84–18.4	14.9–82.6	7
	9.5	0.77	1.06–10.6	21.4–77.7	7
4-Amino-3-bromo	6.6	0.33	10.0–25.0	21.6–40.0	4
	6.9	0.50	2.48–24.8	12.7–48.5	7
	7.2	0.67	2.32–23.2	16.3–55.4	7
3,4-Dimethyl	5.38	0.33	5.03–50.3	19.2–61.1	7
	5.68	0.50	5.14–51.4	18.8–66.3	7
	5.98	0.67	4.78–47.8	25.7–90.3	7
None	4.33	0.33	7.32–73.2	27.3–48.3	6
	4.93	0.67	12.2–48.9	27.8–54.1	6
3-Carbamoyl	2.37	0.33	42.3–89.8	13.3–16.2	4
	2.67	0.50	10.1–101	9.33–16.7	7
	2.97	0.67	25.8–103	8.50–16.7	6
3-Chloro	2.17	0.50	25.5–102	12.2–15.6	6
	2.47	0.67	10.3–103	14.3–21.1	6

[a] In 44 wt% ethanol–water, at 25 °C, ionic strength 0.2 M (KCl).
[b] Free amine fraction.
[c] Concentration of total amine (free base plus protonated forms).

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Table 4. Experimental conditions and k_{obs} values for the reactions of pyridines with 4-nitrophenyl chlorodithioformate (NPClDTF)[a]

Pyridine substituent	pH	F_N[b]	10^3 $[N]_{tot}$ (M)[c]	10^3 k_{obs} (s^{-1})	No. of runs
4-Oxy	8.5[d]	0.000315	12.7–50.8	2.84–10.3	6
	9.0[d]	0.001	5.02–50.2	4.37–20.9	7
	9.5[d]	0.0099	4.84–48.4	5.50–43.6	7
3,4-Diamino	9.05	0.285	0.541–5.41	9.40–62.0	7
	9.45	0.50	0.491–4.91	11.2–93.3	7
	9.75	0.67	0.541–5.41	15.5–125	7
4-Dimethylamino	9.14	0.50	0.501–5.01	13.4–62.7	7
	9.44	0.67	0.524–5.24	15.9–94.8	6
4-Amino	8.60	0.294	0.671–6.71	16.8–75.6	6
	8.90	0.454	0.693–6.93	30.1–123	7
	9.10	0.60	0.516–5.16	16.6–158	7
4-Amino-3-bromo	6.60	0.33	0.679–6.79	4.55–27.8	4
	6.90	0.50	0.674–4.72	5.73–26.4	5
	7.20	0.67	0.670–3.69	6.14–24.6	4
3,4-Dimethyl	5.38	0.33	0.526–2.89	4.78–9.30	4
	5.68	0.50	0.526–4.47	5.86–10.9	6
	5.98	0.67	0.543–54.3	4.18–17.5	7
None	4.33	0.33	6.07–60.7	6.20–24.6	7
	4.63	0.50	4.88–48.8	7.89–28.0	7
	4.93	0.67	4.89–41.6	9.14–25.3	5
3-Carbamoyl	3.13	0.74	5.34–53.4	2.39–10.7	7
	3.43	0.85	5.05–50.5	3.14–11.1	7
	3.73	0.92	5.41–54.1	3.18–12.4	7
	4.00	0.955	13.3–53.4	3.80–13.6	6
3-Chloro	1.89	0.33	10.4–104	1.90–7.13	5
	2.17	0.50	10.2–102	1.28–9.40	7
	2.47	0.67	10.3–103	2.06–11.2	7

[a] In 44 wt% ethanol–water, at 25 °C, ionic strength 0.2 M (KCl).
[b] Free amine fraction.
[c] Concentration of total amine (free base plus protonated forms).
[d] 0.005 M borate buffer.

For the reactions of PClDTF and NPClDTF with SA amines the values of k_N, obtained as the slopes of plots of Eqns (2) or (4), and the pK_a of the conjugate acids of the amines are summarized in Table 5. Similar values for the reactions of these substrates with pyridines are shown in Table 6.

Figures 1 and 2 show the Brønsted-type plots for the reactions studied. The k_N values for the reactions of SA amines, as well as those of the pK_a of their conjugate acids, were statistically corrected with $q = 2$ for piperazine ($q = 1$ for all the other SA amines) and $p = 2$ for the conjugate acids of the amines, except that for the piperazinium dication with $p = 4$.[24] The parameter q is the number of equivalent basic sites on the free amine and p is the number of equivalent dissociable protons on the conjugate acid of the amine.[25] The Brønsted-type plots are linear for the reactions of both substrates with pyridines and for the reaction of PClDTF with SA amines. The corresponding plot for the reaction of the latter amines with NPClDTF is biphasic.

The slopes (β) of the linear Brønsted plots for the reactions of PClDTF with SA amines and pyridines and those of NPClDTF with pyridines are 0.30, 0.26, and 0.30, respectively. These values are in accordance with a stepwise process (as in Scheme 2, where Nu represents a pyridine or SA amine), whereby the formation (k_1 step) of the zwitterionic tetrahedral intermediate ($T^{\pm}$) is the rate-determining step for all the pK_a range studied. These β values are in agreement with those found in the stepwise reactions of PClTF and NPClTF with pyridines,[14] SA amines,[15] and quinuclidines in water.[16] They are also in accordance with those obtained for the stepwise reactions of a series of aryl chloroformates with SA amines[11,12] and quinuclidines[13] in water and the pyridinolysis of phenyl and 4-nitrophenyl chloroformates in acetonitrile,[26] where the formation of the intermediate $T^{\pm}$ is the rate-determining step.

The biphasic curve for the reaction of NPClDTF with SA amines in Fig. 2 was calculated by means of Eqn (5),[27] with $pK_a^0 = 7.7$ and $\log k_N^0 = 1.5$ (parameters for the center of curvature), $\beta_1 = 0.2$ and $\beta_2 = 1.1$ (the slopes at high and low amine basicity, respectively). The shape of this plot is in accordance with a stepwise mechanism through a zwitterionic tetrahedral intermediate ($T^{\pm}$) and a change in the rate-limiting step, from formation of $T^{\pm}$ (k_1 step in Scheme 2) to its breakdown to products (k_2 step in Scheme 2), as the amine basicity decreases.[27]

$$\log (k_N/k_N^0) = \beta_2 (pK_a - pK_a^0) - \log [(1 + a)/2]$$
$$\log a = (\beta_2 - \beta_1)(pK_a - pK_a^0) \quad (5)$$

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Table 5. Values of pK_a for the conjugate acids of secondary alicyclic (SA) amines and k_N values for the reactions of SA amines with phenyl chlorodithioformate (PClDTF) and 4-nitrophenyl chlorodithioformate (NPClDTF)[a]

				k_N ($s^{-1} M^{-1}$)	
SA amine	p[b]	q[c]	pK_a	PClDTF	NPClDTF
Piperidine	2	1	10.82	82 ± 3	260 ± 10
Piperazine[d]	2	2	9.71	71 ± 3	210 ± 10
1-(2-Hydroxyethyl)piperazine	2	1	9.09	17 ± 1	77 ± 2
Morpholine	2	1	8.48	26 ± 1	111 ± 2
1-Formylpiperazine	2	1	7.63	11.8 ± 0.5	32 ± 1
Piperazinium ion	4	1	5.37	3.3 ± 0.5	0.52 ± 0.01
Piperazinium ion[e]	4	1	5.37	2.2 ± 0.1	

[a] Both the pK_a and k_N values were determined in 44 wt% ethanol–water, at 25.0 °C, ionic strength 0.2 M (KCl).
[b] Number of equivalent protons on the conjugate acid of the amine.
[c] Number of equivalent basic sites on the free amine.
[d] Value obtained at the 9.41–10.01 pH range.
[e] Value obtained at the 6.5–7.5 pH range with Eqns (3) and (4).

From these results, it can be concluded that the substitution of an oxygen atom in chlorothionoformates by a sulfur atom (to yield chlorodithioformates) does not change the mechanism of their SA aminolysis or pyridinolysis (it remains stepwise and only the rate limiting step for SA amines changes).

The fact that the pK_a^0 value for the reaction of NPClDTF with SA amines (p$K_a^0 = 7.7$) is larger than that for the reaction of the same amines with PClDTF (p$K_a^0 \leq$ca. 5) is in line with the results obtained for the pyridinolysis of aryl 4-X-substituted thiolbenzoates (ArS—CO—C_6H_4—X) in aqueous ethanol:[28] the greater the electron-withdrawing ability of the nonleaving group, the larger the pK_a^0 value. This has been explained in the following way:[28,29] as the X substituent in the nonleaving phenyl group becomes more electron-withdrawing, the push provided by the leaving group from the tetrahedral intermediate ($T^{\pm}$) becomes greater and the amine leaves faster from $T^{\pm}$ (larger k_{-1}). Since the amine cannot exert its push to expel the leaving group (it lacks an electron pair), this means a larger k_{-1}/k_2 ratio and, according to Eqn (6),[30] a larger pK_a^0 value.[28,29] It is not clear why the reactions

Table 6. Values of pK_a for the conjugate acids of pyridines and k_N values for the reactions of pyridines with phenyl chlorodithioformate (PClDTF) and 4-nitrorophenyl chlorodithioformate (NPClDTF)[a]

		k_N ($s^{-1} M^{-1}$)	
Pyridine substituent	pK_a	PClDTF	NPClDTF
4-Oxy	11.50		88.0 ± 1.0
3,4-Diamino	9.45	10.4 ± 0.4	34.0 ± 1.0
4-Dimethylamino	9.14	8.8 ± 0.4	24.0 ± 1.0
4-Amino	8.98	8.2 ± 0.5	22.4 ± 0.6
4-Amino-3-bromo	6.90	2.9 ± 0.1	10.1 ± 0.5
3,4-Dimethyl	5.68	2.2 ± 0.1	3.5 ± 0.3
None	4.63	1.0 ± 0.1	0.82 ± 0.06
3-Carbamoyl	2.67	0.17 ± 0.01	0.22 ± 0.01
3-Chloro	2.17	0.10 ± 0.03	0.16 ± 0.01

[a] Both the pK_a and k_N values were determined in 44 wt% ethanol–water, at 25.0 °C, ionic strength 0.2 M (KCl).

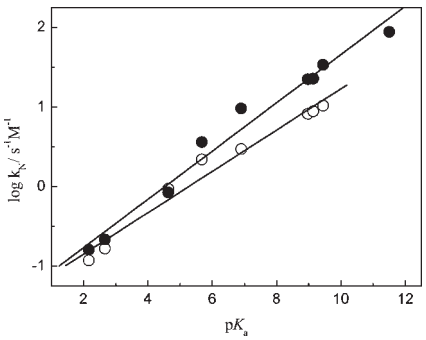

Figure 1. Brønsted-type plots obtained for the reactions of pyridines with phenyl chlorodithioformate (PClDTF) (○) and 4-nitrophenyl chlorodithioformate (NPClDTF) (●) in 44 wt% aqueous ethanol, at 25.0 °C and an ionic strength of 0.2 M (KCl)

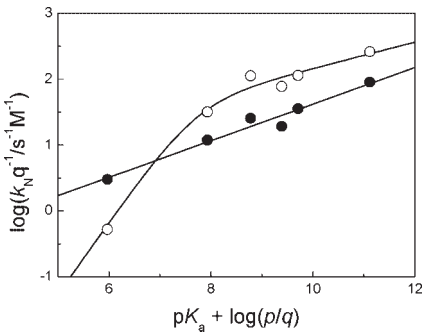

Figure 2. Brønsted-type plots (statistically corrected) obtained for the reactions of SA amines with phenyl chlorodithioformate (PClDTF) (●) and 4-nitrophenyl chlorodithioformate (NPClDTF) (○), in 44 wt% aqueous ethanol, at 25.0 °C and an ionic strength of 0.2 M (KCl)

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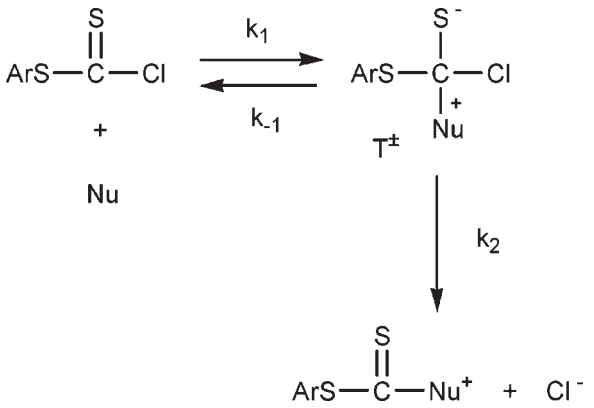

Scheme 2.

of NPClDTF with pyridines did not exhibit a biphasic Brønsted plot, apparently not showing the same tendency as found for SA amines. An explanation would be that for pyridines the pK_a^0 value for their reactions with PClDTF is $<<3$ and the expected increase of this value did not show up in the plot for NPClDTF, i.e., the pK_a^0 value for the latter was 3 or less. It is reasonable that the pK_a^0 value for pyridines is lower than that for SA amines, since it is known that k_{-1} for a given pyridine is lower than that for an isobasic SA amine.[24] A lower k_{-1} (and the same k_2 for both amines)[29] means a smaller pK_a^0 value, according to the following equation:[30]

$$\log (k_{-1}/k_2) = (\beta_2 - \beta_1)(pK_a{}^0 - pK_a) \quad (6)$$

Figure 3 shows a comparison of the Brønsted-type plots obtained for the pyridinolysis of PClDTF and NPClDTF in aqueous ethanol (this work) with the corresponding plots found for the same aminolysis of PClTF and NPClTF in water.[14]

Considering (a) the greater electron withdrawal of PhS ($\sigma_P = 0.07$) than PhO ($\sigma_P = -0.03$)[31] and (b) that pyridines are considered relatively soft bases and that the thiocarbonyl group of PClDTF and NPClDTF should be softer than that of PClTF and NPClTF,[32,33] respectively, greater values of k_1 for PClDTF relative to PClTF should be expected. The larger k_1 values observed for the pyridinolysis of PClTF[14] relative to PClDTF (this study) can be attributed to a steric hindrance caused by the second sulfur atom in PClDTF. The greater k_1 values found for the reactions of NPClTF[14] relative to NPClDTF (this work) can be explained the same way. On the other hand, the change of solvent, from aqueous ethanol (reactions of dithioformates) to water (reactions of thionoformates), should also increase the k_1 values. Nevertheless, in view of the fact that both media are very similar, it is doubtful that the reactivity difference can be entirely accounted for by the change of solvent.

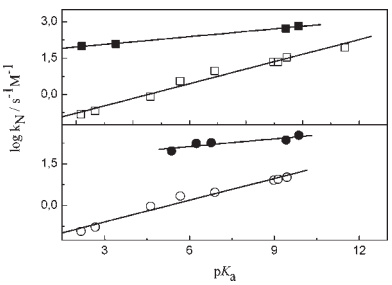

Figure 3. Brønsted plots for the pyridinolysis of PClDTF (○, this work), PClTF (●, Reference 14), NPClDTF (□, this work), and NPClTF (■, Reference 14)

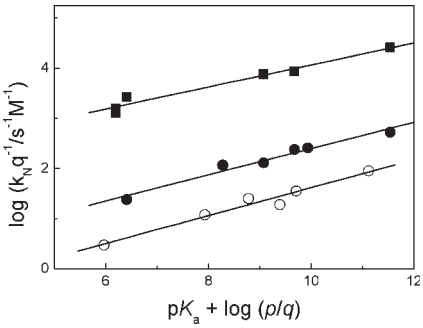

Figure 4. Brønsted plots (statistically corrected) for the reactions of SA amines with PClDTF (○, this work), phenyl chlorothionoformate (●, Reference 15), and phenyl chloroformate (■, Reference 11)

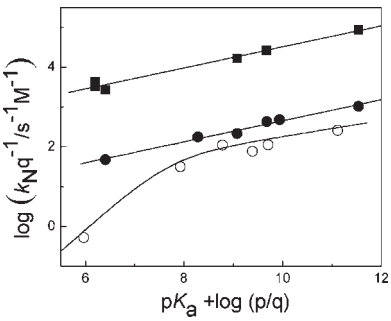

Figure 5. Brønsted plots (statistically corrected) for the reactions of SA amines with NPClDTF (○, this work), 4-nitrophenyl chlorothionoformate (●, Reference 15), and 4-nitrophenyl chloroformate (■, Reference 11)

Figure 4 shows a comparison of the Brønsted-type plot obtained for the SA aminolysis of PClDTF in aqueous ethanol (this work) and those of PClTF[15] and PClF[11] in water. Figure 5 shows the same plots for the 4-nitrophenyl derivatives. It can be observed in these figures that k_1 increases according to the sequence PClDTF < PClTF < PClF and NPClDTF < NPClTF < NPClF.

The highest reactivity shown by the formates, compared with thionoformates and dithioformates, can be explained by the same argument mentioned above: as sulfur atoms are changed by oxygen atoms in the substrates, there is less steric hindrance toward amine attack, and therefore, higher reactivity.

CONCLUSION

The reactions of pyridines and SA amines with phenyl and 4-nitrophenyl chlorodithioformates (PClDTF and NPClDTF, respectively) show Brønsted-type plots in agreement with a stepwise mechanism, through a zwitterionic tetrahedral intermediate ($T^{\pm}$).

The slope values of the Brønsted-type plots are in accordance with the formation of a the $T^{\pm}$ intermediate as the rate-determining step, except for the reaction of NPClDTF with SA amines where there is a change in the rate-determining step, from formation to breakdown of $T^{\pm}$, as the amine basicity decreases.

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The substitution of the oxygen atoms in phenyl chloroformate by sulfur atoms (to give the corresponding thiono and dithio chloroformates, respectively) does not produce changes in the reaction mechanism, but progressively reduces the reactivity toward the amine.

EXPERIMENTAL

Materials

The pyridines and SA amines were purified as reported.[24] Phenyl chlorodithioformate (PClDTF) is a commercial product and was used as purchased. 4-Nitrophenyl chlorodithioformate (NPClDTF) was synthesized as reported,[34,35] and identified as follows: ^{1}H-NMR (400 MHz, $CDCl_3$) 7.72 (d, 2H, $J = 8.9$Hz) and 8.35 (d, 2H, $J = 8.9$Hz). ^{13}C-NMR (100 MHz,) δ ppm 124.85, 135.69, 138.70, 149.22, and 194.36.

The phenyl dithiocarbamate formed with morpholine was prepared by the reaction of phenyl chlorodithioformate with morpholine in acetonitrile, following the general method used for the synthesis of aryl carbamates.[11] The product obtained was identified by its melting point and ^{1}H-NMR and ^{13}C-NMR analyses: mp 139–140.5 °C (lit.[36] mp 141 °C; lit.[37,38] mp 138–141 °C). ^{1}H-NMR (400 MHz, $CDCl_3$) 7.45–7.52 (5H), 4.21 (4H), and 3.82 (4H). ^{13}C-NMR (100 MHz,) δ ppm 51.30, 66.30, 129.18, 130.22, 130.97, 137.08, and 198.02.

Kinetics

These were carried out by means of a diode array spectrophotometer in 44 wt% ethanol aqueous solution, at 25.0 ± 0.1 °C, and ionic strength 0.2 M (KCl). Phosphate and borate buffers were used in some reactions. The reactions, studied under excess of the amine over the substrate, were started by the injection of a substrate stock solution in acetonitrile (10 μl) into the amine aqueous solution (2.5 ml in the spectrophotometric cell). The initial substrate concentration was 5×10^{-5} M.

Pseudo-first-order rate coefficients (k_{obs}) were found for all reactions; these were determined by means of the spectrophotometer kinetic software for first order reactions. The experimental conditions of the reactions and the k_{obs} values are shown in Tables 1–4.

As in the reactions of aryl chloroformates and chlorothionoformates with tertiary amines (pyridinolysis and quinuclidinolysis),[13,14,16] in this work, a consecutive reactions behavior was observed for the pyridinolysis of the title substrates: the formation and later hydrolysis of the cationic pyridinium dithiocarbamate (CP) formed.[13,14,16] For the reactions with basic pyridines, the hydrolysis of CP is more than 10 times slower than its formation, so that both reactions can be considered kinetically independent. In these cases, the reactions were followed by the increase of a band at 315–340 nm, attributed to the appearance of CP. For the reactions of PClDTF with weakly basic pyridines, the disappearance of the substrate was followed at 308 nm. For the reactions of NPClDTF with weakly basic pyridines, the disappearance of CP is fast. In these cases, the appearance of 4-nitrobenzenethiolate was followed at 340–350 nm.

Product studies

In the reactions of PClDTF and NPClDTF with SA amines, the increase of a band centered at 275–280 nm was observed; this band is attributed to the corresponding dithiocarbamate. Phenyl dithiocarbamate formed with morpholine was identified as the final product of the reaction of PClDTF with morpholine. This was achieved by comparison of the UV–Vis spectra after completion of this reaction with that of an authentic sample under the same conditions.

For the reactions with some pyridines, an increase followed by a slow decrease of a band centered at 315–340 nm is attributed to the corresponding dithiocarbamate cation (CP).

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