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Kinetics and Mechanism of the Aminolysis of Methyl 4-Nitrophenyl, Methyl 2,4-Dinitrophenyl, and Phenyl 2,4-Dinitrophenyl Carbonates

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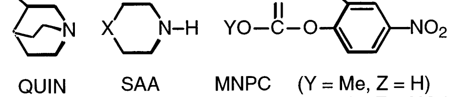
The reactions of methyl 4-nitrophenyl carbonate (MNPC) with a series of secondary alicyclic amines (SAA) and quinuclidines (QUIN), methyl 2,4-dinitrophenyl carbonate (MDNPC) with QUIN and 1-(2-hydroxyethyl)piperazinium ion (HPA), and phenyl 2,4-dinitrophenyl carbonate (PDNPC) with SAA are subjected to a kinetic investigation in aqueous solution, at 25.0 °C and an ionic strength of 0.2 M. By following spectrophotometrically the nucleofuge release (330−400 nm) under amine excess, pseudo-first-order rate coefficients (k_{obsd}) are obtained. Plots of k_{obsd} vs [amine] at constant pH are linear, with the slope (k_N) being pH independent. The Brönsted-type plot (log k_N vs amine pK_a) for the reactions of SAA with MNPC is biphasic with slopes $\beta_1 = 0.3$ (high pK_a region) and $\beta_2 = 1.0$ (low pK_a region) and a curvature center at p$K_a{}^0 = 9.3$. This plot is consistent with a stepwise mechanism through a zwitterionic tetrahedral intermediate ($T^{\pm}$) and a change in the rate-determining step with SAA basicity. The Brönsted plot for the quinuclidinolysis of MNPC is linear with slope $\beta_N = 0.86$, in line with a stepwise process where breakdown of $T^{\pm}$ to products is rate limiting. A previous work on the reactions of SAA with MDNPC was revised by including the reaction of HPA. The Brönsted plots for the reactions of QUIN and SAA with MDNPC and SAA with PDNPC are linear with slopes $\beta = 0.51$, 0.48, and 0.39, respectively, consistent with concerted mechanisms. Since quinuclidines are better leaving groups from $T^{\pm}$ than isobasic SAA, yielding a less stable $T^{\pm}$, it seems doubtful that the quinuclidinolysis of PDNPC is stepwise, as reported.

Introduction

Although much attention has been drawn to the kinetics and mechanism of the aminolysis of aryl esters,[1] the aminolyses of alkyl aryl carbonates[2−4] and diaryl carbonates[5,6] have been less studied. The latter investigations include reports on the reactions of alkyl aryl carbonates with pyridines,[2] secondary alicyclic amines (SAA),[3] and benzylamines[4] and the reactions of diaryl carbonates with quinuclidines (QUIN)[5] and SAA.[6] Most of these reactions were found to proceed through a zwitterionic tetrahedral addition intermediate (stepwise mechanism),[2−5] and others were found to occur in a single step with no intermediate (concerted mechanism).[6] In all these studies, the Brönsted-type plot has been employed as an important tool for the diagnosis of the reaction mechanism.

To shed more light on the mechanisms of the aminolysis of carbonates, we describe in this work a kinetic study of the reactions of SAA and QUIN with methyl 4-nitrophenyl carbonate (MNPC), QUIN with methyl 2,4-dinitrophenyl carbonate (MDNPC), and SAA with phenyl 2,4-dinitrophenyl carbonate (PDNPC). We compare our results with those obtained for the same aminolysis of similar carbonates[3,5,6] to assess the effect of the nonleaving and leaving groups and the amine nature on the kinetics and mechanism of these reactions.



QUIN SAA MNPC ($Y = Me$, $Z = H$)
MDNPC ($Y = Me$, $Z = NO_2$)
PDNPC ($Y = Ph$, $Z = NO_2$)

In view of our kinetic results, in this work we also revise the kinetic data obtained for the reactions of SAA

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TABLE 1. Experimental Conditions and k_{obsd} Values for the Aminolysis (SAA and QUIN) of Methyl 4-Nitrophenyl Carbonate (MNPC)[a]

amine	pH	F_N[b]	10^3 [N]$_{tot}$/M[c]	10^3 k_{obsd}/s^{-1}	no. of runs
piperidine	10.93	0.33	1.06−10.6	13.7−83.7	10
	11.24	0.50	1.06−10.6	28.0−118	9
	11.55	0.67	1.06−10.6	44.2−191	10
piperazine	9.63	0.33	2.51−25.1	4.80−54.5	9
	9.94	0.50	2.51−25.1	10.7−79.2	10
	10.25	0.67	2.51−25.1	13.7−112	10
1-(2-hydroxyethyl)-piperazine	9.07	0.33	0.49−4.94	3.90−26.4	10
	9.38	0.50	0.49−4.94	6.00−41.2	10
	9.69	0.67	0.49−4.94	12.3−58.2	10
morpholine	8.41	0.33	1.14−11.4	0.72−6.42	10
	8.78	0.50	1.14−11.4	1.64−9.33	9
	9.09	0.67	1.14−6.86	2.25−8.05	6
1-formylpiperazine	7.67	0.33	1.07−9.60	0.12−0.784	8
	7.98	0.50	1.07−10.7	0.20−1.38	9
	8.29	0.67	1.07−9.60	0.31−1.66	9
piperazinium ion	5.51	0.33	9.92−99.2	0.013−0.073	6
	5.81	0.50	11.9−83.0	0.019−0.126	5
	6.12	0.67	25.0−100.2	0.031−0.210	6
1-(2-hydroxyethyl)-piperazinium ion	4.60	0.0233	40.0−126	0.0055−0.0343	4
	4.90	0.0304	43.0−97.0	0.0154−0.0503	4
quinuclidine	8.5[d]	0.00126	0.80−8.0	0.67−2.78	7
	8.8[d]	0.00251	0.80−8.0	1.15−4.51	6
	9.0[d]	0.00397	0.80−8.0	2.20−7.26	7
3-hydroxy-quinuclidine	9.4	0.285	0.82−8.22	4.70−17.1	7
	9.7	0.443	0.82−8.22	4.30−20.9	6
	10.0	0.613	0.82−8.22	7.50−34.1	6
3-chloroquinuclidine	8.4	0.20	1.50−15.0	1.10−4.40	7
	8.7	0.33	1.50−15.0	1.70−7.70	7
	9.0	0.50	1.50−15.0	2.60−13.8	6
3-quinuclidinone	7.5	0.50	3.27−13.1	0.302−0.797	6
	7.8	0.67	1.31−13.1	0.361−1.04	7
	8.0	0.76	1.31−13.1	0.429−1.29	7

[a] In water, at 25.0 °C, ionic strength 0.2 M (KCl). [b] Free amine fraction. [c] Concentration of total amine (free base plus protonated forms). [d] In the presence of borate buffer 0.01M.

with MDNPC[3a] and discuss the mechanism proposed by Jencks for the reactions of quinuclidines with PDNPC.[5]

Experimental Section

Materials. The SAA were purified as described.[7] The substrates MNPC,[2a] MDNPC,[2b,8] and PDNPC[5] were synthesized as described previously. One of the products of the reactions of piperidine with MNPC and PDNPC, the methyl carbamate and phenyl carbamate of piperidine, respectively, were synthesized by the reactions of methyl and phenyl chloroformates with piperidine, as described.[9] Their NMR and IR spectra were in accordance with their structures.

Kinetic Measurements. These were carried out by means of a diode array spectrophotometer in aqueous solution, at 25.0 ± 0.1 °C, ionic strength 0.2 M (maintained with KCl). The reactions of MNPC, except those with piperazinium and 1-(2-(hydroxyethyl)piperazinium (HPA) ions, were followed at 400 nm (appearance of the 4-nitrophenoxide anion). The reactions of MNPC with the above ions, carried out at low pH, were followed at 330 nm (appearance of 4-nitrophenol). The quinuclidinolysis of MDNPC and the reactions of this substrate with HPA, as well as the reactions of PDNPC with all the SAA were studied at 360 nm (following the appearance of 2,4-dinitrophenoxide anion).

All reactions were investigated under an excess of the amine over the substrate (13-fold at least). The initial substrate concentration was 2.5×10^{-5} M.

TABLE 2. Experimental Conditions and k_{obsd} Values for the Aminolysis (QUIN and HPA) of Methyl 2,4-Dinitrophenyl Carbonate (MDNPC)[a]

amine	pH	F_N[b]	10^3 [N]$_{tot}$/M[c]	10^3 k_{obsd}/s^{-1}	no. of runs
quinuclidine	8.5[d]	0.00126	0.42−4.2	29.6−139	7
	8.8[d]	0.00251	0.42−4.2	61.0−326	6
	9.0[d]	0.00397	0.42−4.2	106−539	7
3-hydroxy-quinuclidine	9.4	0.285	0.49−4.89	14.3−138	6
	9.7	0.443	0.49−4.19	17.7−195	6
	10.0	0.613	0.49−4.89	26.7−245	7
3-chloro-quinuclidine	8.4	0.20	1.53−15.3	17.0−126	7
	8.7	0.33	1.53−15.3	23.0−221	6
	9.0	0.50	1.53−15.3	32.0−312	7
3-quinuclidinone	7.5	0.50	0.95−9.54	1.50−13.8	7
	7.8	0.67	0.95−9.54	3.20−22.2	6
	8.0	0.76	0.95−9.54	2.30−20.0	6
1-(2-hydroxyethyl)-piperazinium ion (HPA)	4.16	0.0128	10−40	0.07−0.35	3
	4.36	0.0174	10−45	0.11−0.71	3
	4.60	0.0233	10−100	0.21−2.2	6

[a] In water, at 25.0 °C, ionic strength 0.2 M (KCl). [b] Free amine fraction. [c] Concentration of total amine (free base plus protonated forms). [d] In the presence of borate buffer 0.01M.

Pseudo-first-order rate coefficients (k_{obsd}) were found for all the reactions; these were determined by means of the spectrophotometer kinetic software for first-order reactions.

Three pH values were employed in the reactions with each amine. These pH values were maintained by the amine as its own buffer (pH near the pK_a of its conjugate acid), except in the reactions of MNPC and MDNPC with quinuclidine and that of PDNPC with piperidine, where external buffer was used. For the reactions of the three substrates with HPA, the pH was maintained by partial ionization of 1-(2-hydroxyethyl)-piperazinium dication, whose pK_a is 4.56 under the kinetic conditions.[10] Under these conditions, the pK_a value of the conjugate acid of HPA is 5.9.[10]

The k_{obsd} values and the experimental conditions for the reactions of MNPC with SAA and QUIN are shown in Table 1. Those for the reactions of MDNPC with QUIN and HPA are exhibited in Table 2, and those for the reactions of PDNPC with SAA can be seen in Table 3.

Product Studies. 4-Nitrophenoxide anion and 2,4-dinitrophenoxide anion were identified as one of the products of the aminolysis of MNPC and PDNPC, respectively. This was achieved by comparison of the UV−vis spectra after completion of these reactions with those of authentic samples of sodium 4-nitrophenoxide or sodium 2,4-dinitrophenoxide, under the experimental kinetic conditions. The other product of the reactions of MNPC and PDNPC with piperidine was identified as the methyl carbamate of piperidine and the phenyl carbamate of piperidine, respectively. The identification was carried out by HPLC through a comparison of the retention times of authentic samples with those after completion of the reactions. HPLC conditions: column, Supelcosil LC-18-DB (25 cm, 5 μm); eluant, acetonitrile/water = 50/50; isocratic mode, 0.4 mL/min.

Results and Discussion

The kinetic law obtained under the reaction conditions is that described in eq 1,

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

where P is 4-nitrophenoxide anion (4-nitrophenol in the reaction of MNPC with piperazinium ion and HPA) or 2,4-dinitrophenoxide anion, S is the substrate, and k_{obsd}

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TABLE 3. Experimental Conditions and k_{obsd} Values for the Aminolysis (SAA) of Phenyl 2,4-Dinitrophenyl Carbonate (PDNPC)[a]

amine	pH	F_N[b]	10^3 $[N]_{tot}$/ M[c]	10^3 k_{obsd}/s^{-1}	no. of runs
piperidine	7.70[d]	0.00029	4.27−21.3	0.383−0.593	5
	8.00[d]	0.00058	4.27−21.3	0.563−1.22	12
	8.30[d]	0.00115	4.27−21.3	1.32−1.94	8
piperazine	9.64	0.333	4.21−25.3	55.8−27.5	6
	9.94	0.500	4.21−25.3	101−367	6
	10.24	0.667	4.07−24.4	111−260	6
1-(2-hydroxyethyl)-piperazine	9.08	0.333	6.85−41.1	26.4−139	11
	9.38	0.500	5.80−34.8	42.8−161	6
	9.68	0.667	5.30−26.5	33.8−154	6
morpholine	8.48	0.333	4.02−24.1	15.8−86.5	11
	8.78	0.500	4.02−24.1	17.6−113	11
	9.08	0.667	4.02−24.1	43.0−151	6
1-formylpiperazine	7.68	0.333	3.23−11.3	11.8−39.9	5
	7.98	0.500	4.68−29.1	14.4−44.0	5
	8.28	0.667	3.24−22.6	20.0−68.9	7
piperazinium ion	5.51	0.333	4.03−24.2	1.09−3.78	6
	5.81	0.500	4.18−25.1	1.29−5.70	6
	6.11	0.667	4.32−26.0	1.21−1.08	10
1-(2-hydroxyethyl)-piperazinium ion	4.60	0.0233	4.38−30.7	0.365−0.681	7
	4.80	0.0282	4.58−27.5	0.42−0.756	6

[a] In water, at 25.0 °C, ionic strength 0.2 M (KCl). [b] Free amine fraction. [c] Concentration of total amine (free base plus protonated forms). [d] In the presence of borate buffer 0.01M.

TABLE 4. Values of pK_a for the Conjugate Acids of Secondary Alicyclic Amines (SAA) and k_N Values for the Reactions of SAA with Methyl 4-Nitrophenyl Carbonate (MNPC), Methyl 2,4-Dinitrophenyl Carbonate (MDNPC) and Phenyl 2,4-Dinitrophenyl Carbonate (PDNPC)[a]

		k_N/s^{-1} M^{-1}		
amine	pK_a	MNPC	MDNPC[b]	PDNPC
piperidine	11.24	26 ± 1	280 ± 17	520 ± 24
piperazine	9.94	6.4 ± 0.1	166 ± 17	318 ± 12
1-(2-hydroxyethyl)-piperazine	9.38	1.7 ± 0.1	73 ± 10	85 ± 3
morpholine	8.78	1.6 ± 0.1	41 ± 4	83 ± 3
1-formylpiperazine	7.98	0.26 ± 0.01	9 ± 1	31 ± 2
piperazinium ion	5.81	0.031 ± 0.002	1.4 ± 0.1	5.4 ± 0.4
1-(2-hydroxyethyl)-piperazinium ion	5.9	0.067 ± 0.005	1.1 ± 0.1[c]	5.0 ± 0.2

[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). [b] Data from ref 3a, except otherwise stated. [c] Datum obtained in this work.

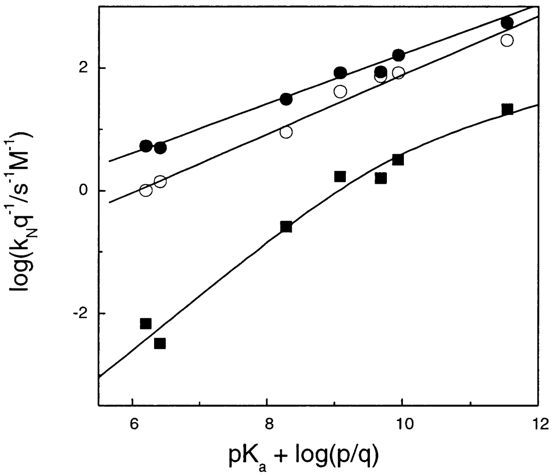

FIGURE 1. Bronsted-type plots for the reactions of SAA with MNPC (■), MDNPC (○), and PDNPC (●) in aqueous solution, at 25.0 °C and an ionic strength of 0.2 M (KCl).

TABLE 5. Values of pK_a for the Conjugate Acids of Quinuclidines (QUIN) and k_N Values for the Reactions of QUIN with Methyl 4-Nitrophenyl Carbonate (MNPC) and Methyl 2,4-Dinitrophenyl Carbonate (MDNPC)[a]

		k_N/s^{-1} M^{-1}	
amine	p*K*a	MNPC	MDNPC
quinuclidine	11.4	20 ± 1	305 ± 11
3-hydroxyquinuclidine	9.8	0.58 ± 0.03	81 ± 5
3-chloroquinuclidine	9.0	0.17 ± 0.01	41 ± 1
3-quinuclidinone	7.5	0.009 ± 0.0004	3.0 ± 0,2

[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).

is the pseudo-first-order rate coefficient (excess of amine was used throughout).

Plots of k_{obsd} against [amine] at constant pH were linear, in accordance with eq 2,

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

where k_0 and k_N are the rate coefficients for hydrolysis and aminolysis of the substrates, respectively. In general, k_0 and k_N were pH independent, except in the reaction of MNPC with piperidine, where k_0 was dependent on pH. The values of k_0 for the hydrolysis of MNPC are $10^2k_0/s^{-1} = 0.5$, 1.5, and 2.4 at pH = 10,93, 11.24, and 11.55, respectively.

The values of k_N (obtained as the slopes of plots of eq 2) for the reactions of SAA with MNPC, MDNPC, and PDNPC are shown in Table 4. The data for MDNPC, mostly taken from a previous study,[3a] include the datum for HPA (this work). These values, as well as those of the pK_a of the conjugate acids of the amines, were statistically corrected with $q = 2$ for piperazine and $p = 2$ for all the conjugate acids of the amines, except that for piperazinium ion with $p = 4$.[10,11] With these corrected values the Brönsted-type plots (shown in Figure 1) were obtained.

The k_N values found for the quinuclidinolysis of MNPC and MDNPC are shown in Table 5; the corresponding Brönsted plots are exhibited in Figure 2.

The nonlinear Brönsted plot for the reactions of SAA with MNPC (Figure 1) can be explained by the mechanism described in Scheme 1, where NH represents a SAA. The Brönsted break results from a change in the rate-determining step, from breakdown of the zwitterionic tetrahedral intermediate ($T^{\pm}$) to products (k_2 step) to $T^{\pm}$ formation (k_1 step) as the amine basicity increases.[2,3a,5−7,10]

The curved line for MNPC in Figure 1 was calculated by means of a semiempirical equation based on the existence of the intermediate $T^{\pm}$ in Scheme 1.[2,5−7,10] This equation contains four parameters: β_1 and β_2, which are the Brönsted slopes at high and low pK_a, respectively, and $k_N{}^0$ and p$K_a{}^0$, which are the corresponding values at the center of the curvature. The Brönsted curve for MNPC was calculated with the following parameters: log $k_N{}^0 = 0.232$, p$K_a{}^0 = 9.3$, $\beta_1 = 0.3$ and $\beta_2 = 1.0$ ($n = 7$, R = 0.994). The errors of the slopes are ±0.1, and those of p$K_a{}^0$ and log $k_N{}^0$ are ±0.2 and ±0.1, respectively.

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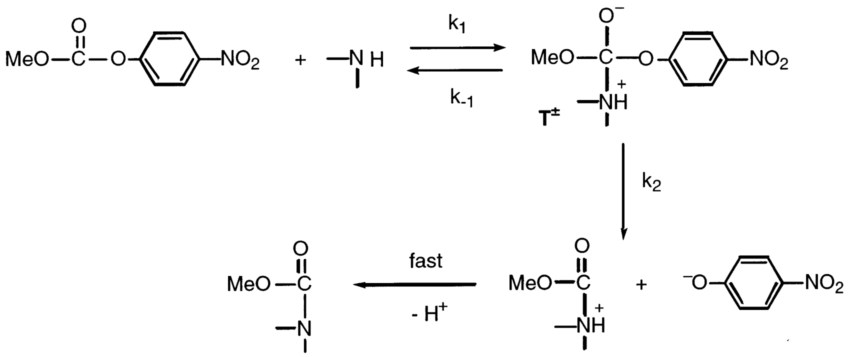
SCHEME 1



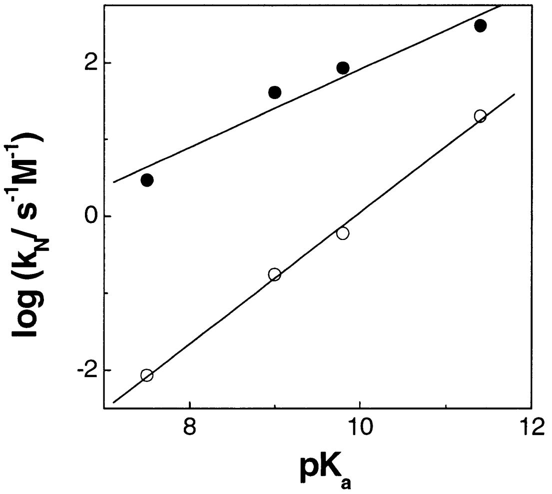
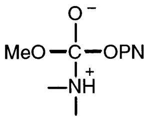


FIGURE 2. Bronsted-type plots for the quinuclidinolysis of MNPC (○) and MDNPC (●) in aqueous solution, at 25.0 °C and an ionic strength of 0.2 M (KCl).

The values of β_1 and β_2 for the aminolysis of MNPC are in accord with those reported for other reactions governed by stepwise mechanisms: $\beta_1 = 0.1-0.3$ and $\beta_2 = 0.8-1.1$.[2,5–7,10]

The simple mechanism shown by the reactions of SAA with MNPC (Scheme 1) is in contrast with the more complex one exhibited by the reactions of the same amines with methyl 4-nitrophenyl thionocarbonate (MNPTOC)[12] and ethyl 4-nitrophenyl thionocarbonate (ENPTOC).[13] In these cases there is an additional path for the intermediate T$^{\pm}$ in Scheme 1: its deprotonation by the corresponding amine to yield an anionic tetrahedral intermediate (k_3 step). On the basis of the nonlinear upward k_{obsd} vs [SAA] plots obtained in these reactions, it was concluded that the rate constant for proton transfer (k_3[SAA]) is similar to that for the nucleofuge expulsion from T$^{\pm}$ (k_2).[12,13] Since the value of k_3 and the concentration range of SAA are similar for the reactions of MNPC and the thiono derivatives (see below), it follows that the simpler reaction scheme for the carbonate arises from its larger k_2 value compared to that for the thionocarbonates MNPTOC and ENPTOC.

The k_3 values for MNPC and the thiono derivatives should be similar, since the proton transfers from the intermediates **1**, **2**, and **3** (PN = 4-nitrophenyl) to the corresponding free amine are thermodynamically favorable.[12,13] Therefore, these processes are diffusion-controlled and a value of 10^{10} s^{-1} M^{-1} has been estimated for k_3.[12–14]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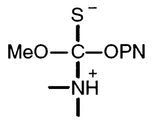
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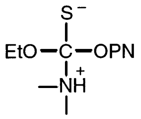
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The faster 4-nitrophenoxide expulsion (larger k_2 value) from intermediate **1** relative to that from **2** or **3** is reasonable in view of the greater ability of O$^-$ in **1** compared to S$^-$ in **2** or **3** to form a double bond with C and expel the nucleofuge. This has been ascribed to the stronger π-bonding energy of the carbonyl group than that of thiocarbonyl.[15]

The quinuclidinolysis of MNPC shows a linear Brönsted plot (Figure 2) of slope $\beta = 0.86 \pm 0.05$. This slope value is consistent with a pathway through a zwitterionic tetrahedral intermediate (T$^{\pm}$) whose breakdown to products is rate determining. 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).

The linear Brönsted plot for the reactions of MNPC with QUIN, in contrast to the biphasic plot for the reactions of this substrate with SAA, can be attributed to the fact that QUIN are better nucleofuges from a tetrahedral intermediate than isobasic SAA.[16] The pK_a value at the Brönsted curvature center (pK_a^0) is related to the k_{-1}/k_2 ratio, as described in eq 3,[17]

$$\log(k_{-1}/k_2) = (\beta_2 - \beta_1)\,(\mathrm{p}K_a^{\,0} - \mathrm{p}K_a) \qquad (3)$$

where β_1 and β_2 are the Brönsted slopes for formation and breakdown of the intermediate T$^{\pm}$, respectively.

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Since β_1 and β_2 are little dependent on the amine nature[1b,c,2,5,7,10] and pK_a^0 is larger for the QUIN reactions (its pK_a^0 value is larger than 11.4, according to Figure 2), it follows from eq 3 that the k_{-1}/k_2 ratio is larger for a given QUIN compared to an isobasic SAA. Since the k_2 value should be independent of the amine nature and basicity,[5] it follows that the value of k_{-1} is larger for a QUIN than for an isobasic SAA. Therefore, the lack of Brönsted curvature within the pK_a range 7.5−11.4 for the reactions of MNPC with QUIN can be explained by a larger nucleofugality from $T^{\pm}$ of QUIN compared to an isobasic SAA. A similar result was found in the reactions of QUIN and SAA with ethyl S-(4-nitrophenyl) thiolcarbonate.[16]

The Brönsted plots (statistically corrected) for the reactions of MDNPC and PDNPC with SAA are shown in Figure 1. The Brönsted plot for the quinuclidinolysis of the former substrate is exhibited in Figure 2. The three plots are linear with slope (β) values of 0.48 ± 0.05, 0.39 ± 0.05, and 0.51 ± 0.08, respectively.[18] The magnitude of these β values suggests that these reactions are concerted. Similar β values have been found in the concerted aminolysis of related substrates. Linear Brönsted plots with slopes $\beta = 0.56$ and 0.48 are exhibited in the reactions of SAA with *S*-(2,4-dinitrophenyl) and *S*-(2,4,6-trinitrophenyl) ethyl thiolcarbonates.[19] In the reactions of the same amines with methyl 2,4,6-trinitrophenyl carbonate, a β value of 0.36 was found.[3b] Also, the concerted methoxycarbonyl transfer from *N*-(methoxycarbonyl)isoquinolinium to pyridines shows a linear Brönsted plot of slope $\beta = 0.58$.[20]

The value of the Brönsted β alone is not sufficient for the diagnosis of a concerted mechanism.[21] It is also important to calculate the hypothetical pK_a^0 value (pK_a at the center of the Brönsted curvature) for a stepwise mechanism; the lack of Brönsted curvature within the pK_a range of the nucleophiles employed is a clear indication of a concerted mechanism.[21]

A biphasic Brönsted plot was found in the stepwise pyridinolysis of MDNPC in water, with $pK_a^0 = 7.8$.[2b] It is known that SAA are better nucleofuges from a tetrahedral intermediate than isobasic pyridines, as judged by the larger pK_a^0 values found for the former amines. For instance, the pK_a^0 values for the reactions of 2,4-dinitrophenyl acetate with pyridines and SAA are 7.3 and 9.1, respectively.[2c,22] Similarly, for the reactions of 2,4-dinitrophenyl thiolacetate with pyridines and SAA, the pK_a^0 values obtained are 6.6 and 8.9, respectively.[10] Namely, there is a pK_a^0 increase of ca. 2 units in going from pyridines to SAA. Assuming a similar increase for the reactions of carbonates, a pK_a^0 value of 9.8 (7.8 + 2) can be estimated for the hypothetical stepwise reactions of SAA with MDNPC. Nevertheless, this pK_a^0 value cannot be larger than that for the same aminolysis of MNPC (9.3, this work), since 2,4-dinitrophenoxide is a better leaving group than 4-nitrophenoxide.[1b,c,5] Therefore, it seems that the pK_a^0 increase (from pyridines to SAA) of ca. 2 pK_a units for acetates cannot be applied to carbonates. We can only assume that the pK_a^0 value for the hypothetical stepwise reactions of SAA with MDNPC should be larger than 7.8 but smaller than 9.3.

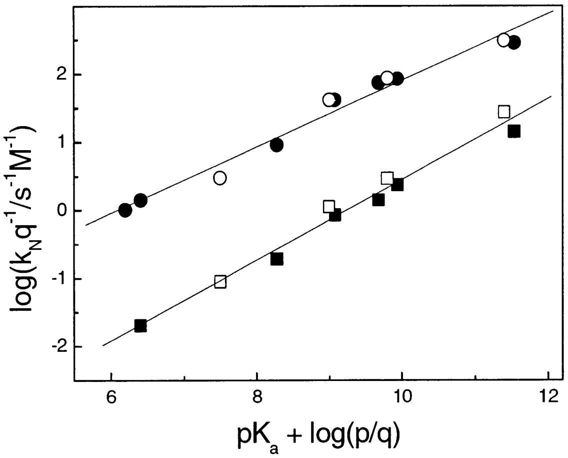

FIGURE 3. Bronsted-type plots for the reactions of MDNPC (this work) with QUIN (○) and SAA (●) and those of EDNPTC with QUIN (□, ref 16) and SAA (■, ref 19a) in aqueous solution, at 25.0 °C and an ionic strength of 0.2 M (KCl).

As seen in Figure 1, there is no break within this pK_a range in the corresponding Brönsted plot. Therefore, we conclude that the reactions of SAA with MDNPC are concerted. Since QUIN are better leaving groups from a tetrahedral intermediate than isobasic SAA (see above), it follows that the reactions of QUIN with MDNPC should also be concerted, in view of the greater instability of the hypothetical intermediate formed with QUIN than that with SAA.

Another proof for concertedness of the above reactions is the similar reactivity pattern of QUIN and SAA toward MDNPC and its thiol derivative ethyl S-(2,4-dinitrophenyl) thiolcarbonate (EDNPTC, see Figure 3).[23,24] It is known that the latter reactions are concerted.[16,19a] As seen in this figure, these two amine series are equally reactive toward a given substrate, and the Brönsted slope values for the aminolysis of these substrates are very similar.

The fact that the reactions of SAA with MNPC are stepwise, whereas those of these amines with MDNPC are concerted, means that the tetrahedral intermediate $T^{\pm}$ is greatly destabilized by the introduction of a second nitro group in the nucleofuge. This should be due to the much greater nucleofugality of 2,4-dinitrophenoxide from the hypothetical dinitro intermediate compared to that of 4-nitrophenoxide from **1**, which destabilizes it kinetically. A similar situation was found in the reactions of

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[18] The Brönsted-type plot for the reactions of SAA with MDNPC appeared as nonlinear in our original work (ref 3a) and the stepwise mechanism was preferred to the concerted one. The reason for the curved plot was that the point for the piperazinium ion was wrongly located in the plot, although the k_N value in the table was correct. In this work we checked this k_N value and obtained a similar one. With this point rightly located, the Brönsted plot becomes linear. To be sure of the linearity, we also measured (in this work) the k_N value for the reaction of this substrate with 1-(2-hydroxyethyl)piperazinium ion (see Table 2). As seen in Figure 1, with these two new points, the Brönsted plot for MDNPC looks linear.

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[23] The change of methoxy to ethoxy as the nonleaving group of carbonates has very little effect on the rate constants involved in these reactions.[24]

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SAA with the corresponding thiol derivatives: The reactions of ethyl *S*-4-nitrophenyl thiolcarbonate are stepwise,[25] in contrast to those of EDNPTC, which are concerted.[19a]

The reactions of SAA with 4-methylphenyl 4-nitrophenyl carbonate in aqueous ethanol have been found to be stepwise.[6] It is known that a zwitterionic tetrahedral intermediate ($T^{\pm}$) is more stabilized in the more polar solvents.[5] Therefore, these reactions should also be stepwise in water. On the other hand, the change of Me to H in the nonleaving group of the substrate should not change the mechanism, as indicated by the similar inductive effects[26,27] of 4-MePhO and PhO.[6] Therefore, it is very likely that the reactions of SAA with PNPC in water are stepwise.

Another indication that the above reactions are stepwise is the fact that the quinuclidinolysis of PNPC is stepwise, as evidenced by the linear Brönsted plot of slope 1.0 obtained.[5] If these reactions are stepwise, it is more likely that the reactions of this substrate with SAA are stepwise in view of the slower nucleofugality of SAA from the intermediate $T^{\pm}$ than isobasic QUIN (see above), which stabilizes this intermediate.[16]

The fact that the reactions of SAA with PDNPC in water are concerted, whereas those of the same amines with PNPC in the same solvent are stepwise, is another example of the great destabilization caused to the $T^{\pm}$ species by the addition of a second nitro group to the nucleofuge of the substrate.

The greater reactivity of PDNPC than MDNPC toward SAA (Table 4 and Figure 1) is in contrast to the larger rate constant for SAA attack, to form the zwitterionic tetrahedral intermediate (k_1), on methyl 4-nitrophenyl thionocarbonate compared to that on phenyl 4-nitrophenyl thionocarbonate.[12] The latter result was attributed to the greater steric hindrance of phenyl relative to methyl toward SAA attack, despite the greater electron-withdrawing effect of PhO compared to MeO in the corresponding thionocarbonates.[12] These contradicting results could be explained by assuming that steric hindrance is less important for a concerted mechanism than a stepwise process through the tetrahedral species.

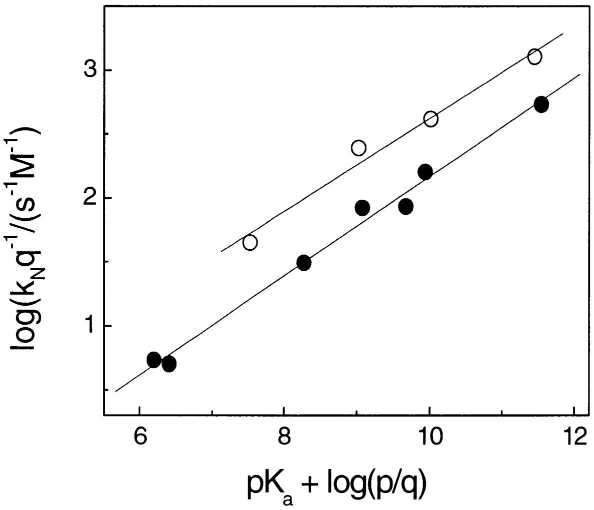

FIGURE 4. Bronsted-type plots for the reactions of PDNPC with QUIN (○) and SAA (●) in aqueous solution, at 25.0 °C and an ionic strength of 0.2 M (KCl). The data for QUIN was replotted from ref 5.

The quinuclidinolysis of PDNPC in water has been described as stepwise, through a zwitterionic tetrahedral intermediate.[5] On the other hand, quinuclidines are known to be better nucleofuges from a zwitterionic intermediate than isobasic SAA (see above).[16] This means that quinuclidines destabilize the tetrahedral intermediate relative to isobasic SAA.[16] Since we have found in this work that the reactions of SAA with PDNPC are concerted, it is doubtful that the reactions of quinuclidines with the same substrate be stepwise. Careful examination of the Brönsted-type plot obtained for the latter reactions shows that the points are better accommodated by a linear relation rather than a biphasic one (see Figure 4). The linear plot shows a slope $\beta = 0.36 \pm 0.05$ ($R^2 = 0.98$), which is very similar to that found by us in the reactions of SAA with the same substrate (Figure 4, $\beta = 0.39 \pm 0.05$).

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