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EFFECT OF NEIGHBORING PYRIDINIUM GROUPS ON THE BASIC HYDROLYSIS OF ARYLBENZOATE ESTERS

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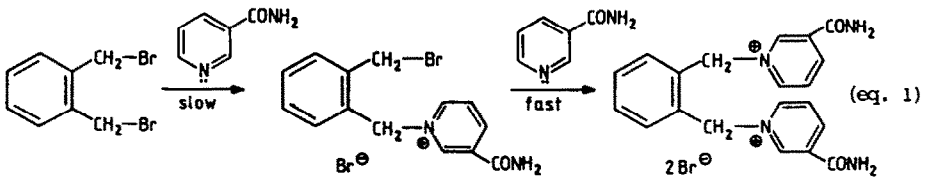
Abstract. - Arylbenzoate esters with a quaternary pyridinium group ortho to the ester function exhibit enhanced reactivity towards basic hydrolysis relative to their para analogs in the order pyridinium < 4-aminocarbonylpyridinium < 3-aminocarbonylpyridinium < 3-aminocarbonylquinolium. In contrast, a trimethylammonium group in the ortho position shows a decelerating effect relative to the para analog. It is concluded that the catalytic effect of a neighboring pyridinium group is based upon interaction of the negatively charged transition state of ester hydrolysis with the electron deficient π-system of the pyridinium ring. For the p-methoxyphenolate ester containing the 3-aminocarbonylpyridinium group in the ortho position this interaction leads to a change in mechanism from rate limiting hydroxide ion attack to hydroxide ion catalyzed expulsion of the leaving group as became apparent from deviation of the Hammett plot and second-order dependence on OH^- concentration. For the p-nitrophenolate ester it was observed that decrease of the solvent polarity by addition of dioxane results in an increase of the rate of hydrolysis and a marked increase of the neighboring group effect.

Study of interactions between the positively charged 3-aminocarbonylpyridinium group and negatively charged intermediates or transition states are of particular interest in view of the relevance to biological NAD^+ reactions. For example, one of the steps in the oxidation of alcohols by NAD^+ and alcoholdehydrogenase is the formation of a ternary enzyme-NAD^+-alcoholate complex. It is proposed that formation of alcoholate ion is catalyzed by hydroxyl ion bound to zinc at the active site of the enzyme and it might be anticipated that the proximity of the positively charged nicotinamide moiety promotes the formation of alcoholate complex by favorable charge interactions.[1] However, it is difficult to obtain a quantitative idea about the importance of such charge interactions since under non-enzymical conditions the ethanolate anion readily forms an adduct with the quaternary nicotinamide group.[1,2] Nevertheless, the work of Kosower and others has clearly demonstrated that there can be a significant charge transfer interaction between relative electron-poor pyridinium groups and electron-rich anions.[3,4] Some experimental evidence for the importance of charge interactions in chemical reactivity we obtained from our efforts to prepare the monosubstituted derivative 2 from α,α'-dibromo-o-xylene (1) and nicotinamide. Even in the presence of a 100-fold excess of nicotinamide in chloroform only the bis-product 3 could be obtained (eq. 1). In contrast, α,α'-dibromo-p-xylene reacts readily with nicotinamide to give the monoproduct in high yield. It seems probable that in 2 the leaving ability of the bromide ion is largely enhanced by the proximity of the positively charged nicotinamide group, giving rise to the fast formation of 3.



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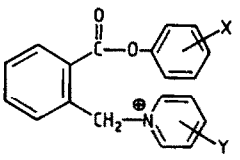
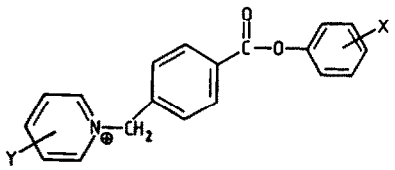
In order to get a more quantitative insight how far the proximity of a quaternary pyridinium group can affect the rate of formation of transient negatively charged species (intermediates, transition states), we have investigated the alkaline hydrolysis of a series of ortho- and para-substituted arylbenzoates (**4-12**)**a,b**. The base-catalyzed hydrolysis of arylbenzoates has been studied by several groups in the past and it has been established that, in water, the rate determining step involves nucleophile attack of hydroxide ion to the carbonyl moiety.[5]



(4-10) a



(4-10) b

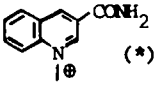
Esters a and b differ by the position of the quaternary group relative to the ester function (ortho vs. para). In comparing the rates of hydrolysis of the two compounds, inductive effects are largely eliminated and the neighboring group effect of the quaternary group becomes apparent. Besides esters containing the pyridinium group (**4-10**)**a,b** also esters containing the 3-aminocarbonylquinolinium group (**11a,b**) and the trimethylammonium group (**12a,b**) have been studied in order to establish the effect of enlargement and of complete deletion of the π-system of the neighboring group, respectively.

RESULTS AND DISCUSSION

The hydrolysis of the esters (**4-12**)**a,b** was studied in series of dilute buffer solutions (carbonate, phosphate) and in series of dilute NaOH solutions with ionic strength 0.1 M (NaCl). It was found that the rate of hydrolysis was slightly dependent on the buffer concentration, indicating a low contribution of buffer anions to the catalysis. Therefore, second-order rate constants for OH^- contribution, k_{OH^-}, have been determined by extrapolation to zero buffer concentration. Alternatively, k_{OH^-} has been determined by linear regression from the rates in a series of dilute NaOH solutions. The rate constants obtained by the two methods were in close agreement.

The hydrolysis of the esters was carried out at pH conditions sufficiently low to prevent interference of adduct formation by attack of OH^- or other nucleophiles to the pyridinium ring.[6] Consequently, esters **11a** and **11b**, containing the quinolium ring, were hydrolyzed in aqueous solutions below pH 9.70; the other esters below pH 12.0. Uncomplicated pseudo-first-order hydrolysis was observed under these conditions. In water-organic solvent mixtures the pyridinium ring is more susceptible to OH^- attack and solutions of lower pH have been employed (vide infra).

Table I Second-order rate constants (M^{-1},s^{-1}) for hydroxide ion promoted hydrolysis of esters (4-12)a,b)

Ester	X	Y	k_{OH}^{ortho}(a)	k_{OH}^{para}(b)	k ortho / k para
4a,b	4-NO_2	H	22.6	19.6	1.15
5a,b	4-NO_2	4-$CONH_2$	27.5	20.8	1.32
6a,b	4-NO_2	3-$CONH_2$	38.6	19.5	1.98
7a,b	3-NO_2	3-$CONH_2$	36.6	18.5	1.98
8a,b	H	3-$CONH_2$	8.88	4.00	2.22
9a,b	4-OCH_3	3-$CONH_2$	8.20	2.71	3.03
10a,b	4-OCH_3	4-$CONH_2$	3.70	2.70	1.37
11a,b	4-NO_2	 (*)	311	20.4	15.2
12a,b	4-NO_2	$-\overset{\oplus}{N}(CH_3)_3$ (*)	9.70	21.7	0.45

*) pyridinium group completely replaced by this group.

In Table I second-order rate constants for hydrolysis by hydroxide ion, k_{OH^-}, are presented. From the data in this Table it is apparent that the proximity of a positively charged pyridinium group to the ester function has a rate enhancing effect since the ortho-substituted esters (4-10)a, react 15 to 300% faster than the para-substituted analogs (4-10)b. For the quinolinium substituted ester the neighboring group effect is even much larger; i.e. ortho-substituted ester 11a hydrolyses 15 times faster than the para-substituted analog 11b. The rate enhancements for the ortho-substituted esters are striking because substituents ortho to an ester group generally exhibit a rate retarding effect on hydrolysis.[7] In evaluating the neighboring group effect on these esters it is important to point out that, in addition to steric hindrance, the effective hydration of the cationic group by the solvent and the conformational flexibility of the compounds is such that the influence of the neighboring group on the ester function is considerably less than optimal.

The rate enhancements induced by the proximity of the positively charged pyridinium group, in principle, may originate from (i) increased localization of OH^- ion in the neighborhood of the ester group due to electrostatic interactions, (ii) favorable charge interaction of the incipient negative charge on carbonyl oxygen upon attack of OH^-, (iii) stabilization of negative charge on the leaving group. Since the proximity of a trimethylammonium group induces a decelerating effect on the rate of ester hydrolysis, as is shown for 11a,b, it is not very likely that increased localization of OH^- in the neighborhood of the ester group is responsible for the observed effects because in that case similar effects should be expected for the trimethylammonium group and the pyridinium groups.

Notably, the neighboring group effect for esters (4-11)a is different from the effect exerted by cationic head groups of micelles. The presence of cetyltrimethylammonium bromide[8] and cetyldimethylammonium chloride[9] accelerates the alkaline hydrolysis of p-nitrophenylbenzoate, whereas little or no effect is observed by micelles of n-dodecylpyridinium chloride on the basic hydrolysis of p-nitrophenyl alkylate esters.[10]

Inspection of the data in Table I shows that variation of the Y substituent in the pyridinium group does not affect the rate of hydrolysis for the para-substituted esters. Almost the same rates are found within the series (**4-7**)**b** (X = NO_2) and (**9-10**)**b** (X = OCH_3). For the ortho-substituted esters, however, the hydrolysis rate increases in the order Y = H < 4-$CONH_2$ < 3-$CONH_2$, which is in correlation with the relative stabilities of the pyridinium cations, based upon their pK_a values.[11] The increased reactivity of the ortho-substituted esters is indicative for a transition state interaction of the ester group with the π-system of the pyridinium moiety. Hydrogen bonding interactions from the carbonamide group to the ester function do not contribute to the enhanced reactivity since replacement of the carbonamide group of **6a,b** by the N,N-dimethylaminocarbonyl group has no significant effect. Of larger importance seems to be a coplanar orientation of pyridinium ring and ester function in order to allow maximum interaction between incipient negative charge in the ester moiety and the π-system of the pyridinium ring in the transition state. Strong support for this conclusion is found the much larger ortho/para ratio of 15 for hydrolysis of **11a,b**. Since in **11a** the 3-aminocarbonylquinolinium group is more restricted in its rotation and possesses a larger π-system than the pyridinium group, stronger π-interaction with the ester group is possible.

It is remarkable that a change of leaving group from p-nitrophenolate to p-methoxyphenolate reduces the rate of hydrolysis considerably more for the para-than for the ortho-substituted esters. Obviously, for the latter compounds the lower leaving ability of p-methoxyphenolate group is partly compensated by interaction with the neighboring pyridinium group.

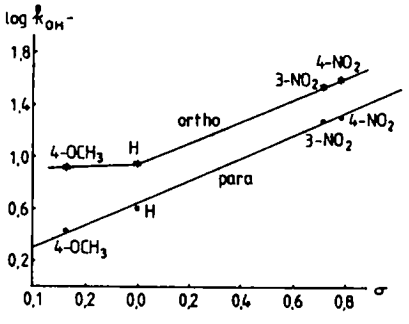


Fig. 1 Hammett plots for ortho- and para-substituted esters (**6-9**)**a,b**.

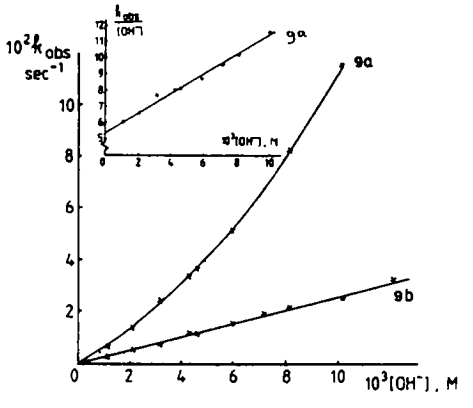
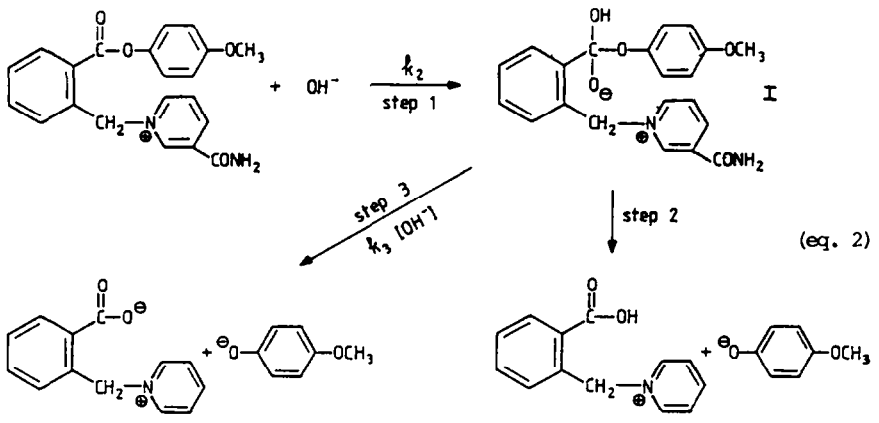


Fig. 2 Rate of hydrolysis of **9a,b** as a function of the hydroxide ion concentration. Inset: Second-order [OH^-] dependence of hydrolysis of **9a**.

Fig. 1 gives the Hammett plots for the nicotinamide substituted esters (**6-9**)**a** and **b**, respectively. For the ortho-substituted benzoates, the methoxyphenyl ester **9a** shows a positive deviation from the plot, indicating an extra effect of the neighboring nicotinamide group. This deviation from the Hammett plot may point to a mechanistic change from rate limiting hydroxide attack to rate limiting breakdown of the tetrahedral intermediate. This is confirmed by the non-linear increment of the reaction rate at hydroxide concentrations above ca. 3×10^{-3} M, which points out that a second-order hydroxide term ($k_3[OH^-]$) becomes important in hydrolysis (Fig. 2). A plot of $k_{obs}/[OH^-]$ vs. $[OH^-]$ gives a straight line with slope k_3 = 607 $M^{-2}s^{-1}$ and intercept k_2 = 5.38 $M^{-1}s^{-1}$. The appearance of second-order hydroxide ion catalysis indicates that the tetrahedral intermediate I becomes sufficiently stabilized by the neighboring 3-aminocarbonylpyridinium group to make the hydroxide-ion catalyzed breakdown of I (step 3) kinetically significant (eq. 2).



Furthermore, we have investigated the effect of addition of dioxane on the rates of hydrolysis. It was expected that decrease of the solvent polarity would result in a more distinct neighboring group effect, since charged species involved in the reaction will become less stabilized by the solvent. Generally, addition of organic cosolvents results in an increase of the nucleophilicity and basicity of anions in water. However, the base catalyzed hydrolysis of phenylbenzoate is slowed down upon addition of ethanol[12] and the same effect was observed for p-nitrophenylbenzoate upon addition of t-butyl alcohol, t-amyl alcohol and acetonitrile.[8] This is a clear indication that increase of the OH^- activity is not the dominating effect governing the reaction rate. Moreover, for the neutral hydrolysis of aryl dichloroacetates, it has been established that the rate decrease upon addition of dioxane and acetonitrile is primarily caused by initial state stabilization of the ester.[13] The data in Table II show that in the presence of a cationic substituent to the ester addition of dioxane enhances the hydrolysis of **6a,b** and **11a,b**. An explanation for this dramatic change in solvent effect for both the ortho- and para-substituted esters is most probably that the inductive effect of the cationic group increases as the result of

Table II Observed rate constants for hydrolysis of **6a,b** and **12a,b** in dioxane-carbonate buffer 0.01 M, pH 10.00 at 25°C.

dioxane % (vv)	$10^4 k_{obs}$ (sec^{-1})		$\frac{k\ ortho}{k\ para}$	$10^4 k_{obs}$ (sec^{-1})		$\frac{k\ ortho}{k\ para}$
	6a	**6b**		**12a**	**12b**	
-	38.6	19.5	1.98	9.70	21.7	0.45
10	88.7	45.5	1.95	29.2	60.6	0.48
20	177	74.9	2.36	54.5	94.2	0.58
30	368	99.7	3.69	108	135	0.80
40	1130	131	8.64	198	182	1.08
50	3310	190*)	17.4	366	224	1.63

*) Adduct formation to nicotinamide ring becomes concurrent side reaction.

diminished hydration at lower water content. Furthermore, Fig. 3 clearly shows that the effect of the neighboring 3-aminocarbonylpyridinium group becomes much more mani-

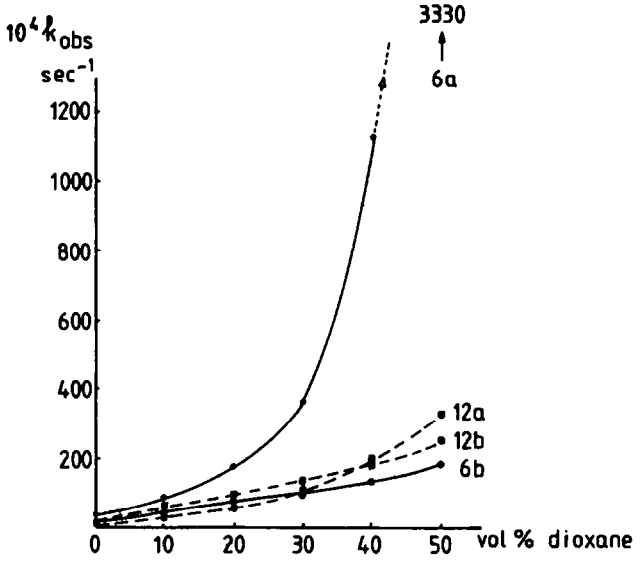


Fig. 3 Effect of dioxane addition on the basic hydrolysis of **6a,b** and **12,b** (carbonate buffer 0.01 M, pH = 10.00, 25°C).

fest in solutions of lower water content, whereas only a moderate effect is observed for the trimethylammonium group.[14] Solvent effects for the p-methoxyphenyl ester could not be obtained since under the more basic conditions needed for hydrolysis of this compound, addition of cosolvent results in concurrent addition of hydroxide ion to the nicotinamide moiety. This became apparent from the appearance of an absorption peak in the spectrum at 357 nm.

In conclusion, the positively charged quaternary nicotinamide group and the related pyridinium and quinolinium groups are able to stabilize transient negative charges developed in the ester function by interaction with their electron deficient π-electron system. This effect is exhibited more pronounced when the polarity of the solvent is reduced. Considering the conformational flexibility of the compounds examined and the polarity of the solvents used, the observed neighboring group effects most probably represent only a fraction of what might occur in more constraint systems in less polar environment.

EXPERIMENTAL SECTION

Materials

The aryltoluate esters were prepared by adding dropwise 15.5 g of ortho- or para-toluyl chloride to a solution of 0.1 mole of the appropriate phenol and 7.9 g of pyridine in 100 ml of dry ether. The reaction mixture was stirred for 2 h and after filtration, the filtrate was evaporated in vacuo.
The products were recrystallized from ethanol-water, except phenyl-o-toluate which was a liquid.

Phenyl-o-toluate. Column chromatography on silica with chloroform-cyclohexane 1:1 yielded 60% of a colorless liquid (lit.[15] bp 306°C/754 mm). ^{1}H NMR ($CDCl_3$), δ (TMS): 2.65 (s, CH_3), 6.55-8.17 (m, arom).
Phenyl-p-toluate, yield 92%, mp 76-77°C (lit.[5c] 75-76.5°C). ^{1}H NMR (CCl_4), δ (TMS): 2.34 (s, CH_3), 6.85-8.15 (m, arom).
3-Nitrophenyl-o-toluate, yield 71%, mp 82-83°C. ^{1}H NMR ($CHCl_3$), δ (TMS): 2.62 (s, CH_3), 7.25-8.25 (m, arom). Anal. Calcd for $C_{14}H_{11}NO_4$: C, 65.36; H, 4.31. Found: C, 65.64; H, 4.24.
3-Nitrophenyl-p-toluate, yield 78%, mp 105-107°C (lit.[5c] 106-107°C). ^{1}H NMR ($CHCl_3$), δ (TMS): 2.40 (s, CH_3), 7.10-8.20 (m, arom).
4-Nitrophenyl-o-toluate, yield 89%, mp 107-108°C (lit.[11] 108-109°C). ^{1}H NMR ($CDCl_3$), δ (TMS): 2.66 (s, CH_3), 7.15-8.35 (m, arom).
4-Nitrophenyl-p-toluate, yield 91%, mp 119-120°C (lit.[5c] 120.3-121.3°C). ^{1}H NMR ($CDCl_3$), δ (TMS): 2.42 (s, CH_3), 7.15-8.30 (m, arom).
4-Methoxyphenyl-o-toluate, yield 82%, mp 59-60°C. ^{1}H NMR ($CDCl_3$), δ (TMS): 2.39 (s, CH_3), 3.66 (s, OCH_3), 6.60-8.20 (m, arom). Anal. Calcd for $C_{15}H_{14}O_3$: C, 74.36; H, 5.83. Found: C, 74.14; H, 5.91.
4-Methoxyphenyl-p-toluate, yield 93%, mp 93-95°C. ^{1}H NMR ($CDCl_3$), δ (TMS): 2.58 (s, CH_3), 3.64 (s, OCH_3), 6.57-8.07 (m, arom).

Conversion of the methyl group of the toluate esters into the α-bromomethyl group was accomplished by refluxing the ester (30 mmole), N-bromosuccinimide (30 mmole) and benzoylperoxide (0.2 mmole) in tetra (90 ml). The progress of the reaction was followed by NMR by monitoring the appearance of the $-CH_2-Br$ signal in the range δ 4.40-4.95 ppm. Usually it took 12 or more hours to bring the reaction to completion. After cooling and filtration, the filtrate was evaporated in vacuo. The crude product was chromatographed on silica with cyclohexane-acetone 9:1 and was used without further purification for reaction to the quarternary compounds (**4-12**)**a,b**.
The general procedure for the esters (**4-12**)**a,b** was as follows: a mixture of 5 mmole of the α-bromotoluate ester and 5 mmole of the appropriate pyridine (or 3-aminocarbonylquinoline for **11a,b** or trimethylamine for **12a,b**) was refluxed for 12 h in 40 ml of dry THF. After cooling, the precipitate was washed with THF and acetone and recrystallized from ethanol-ether.
1-[2-[(4-Nitrophenoxy)carbonyl]benzyl]pyridinium bromide (**4a**), yield 82%, mp 178-180°C. ^{1}H NMR (DMSO-d6), δ (DSS): 6.31 (s, CH_2): 7.1-8.8 (m, arom), 9.06 (dd, pyr H2,6). Anal. Calcd for $C_{19}H_{15}BrN_2O_4$: C, 54.95; H, 3.64. Found: C, 54.71; H, 3.63.
1-[4-[(4-Nitrophenoxy)carbonyl]benzyl]pyridinium bromide (**4b**), yield 92%, mp 225-230d°C. ^{1}H NMR (DMSO-d6), δ (DSS): 6.25 (s, CH_2), 7.5-9.0 (m, arom), 9.45 (dd, pyr H2,6). Anal. Calcd for $C_{19}H_{15}BrN_2O_4$: C, 54.95; H, 3.64. Found: C, 54.95; H, 3.64.
1-[2-[(4-Nitrophenoxy)carbonyl]benzyl]-4-(aminocarbonyl)pyridinium bromide (**5a**), yield 73%, mp 245-255d°C. ^{1}H NMR (DMSO-d6), δ (DSS): 6.42 (s, CH_2), 7.5-8.9 (m, arom), 9.30 (d, pyr H2,6). Anal. Calcd for $C_{20}H_{16}BrN_3O_5$: C, 52.41; H, 3.52. Found: C, 52.69; H, 3.45.
1-[4-[(4-Nitrophenoxy)carbonyl]benzyl]-4-(aminocarbonyl)pyridinium bromide (**5b**), yield 87%, mp 230-235d°C. ^{1}H NMR (DMSO-d6), δ (DSS): 6.25 (s, CH_2), 7.5-9.5 (m, arom), 9.60 (d, pyr H2,6). Anal. Calcd for $C_{20}H_{16}BrN_3O_5$: C, 52.41; H, 3.52. Found: C, 52.41; H, 3.34.
1-[2-[(4-Nitrophenoxy)carbonyl]benzyl]-3-(aminocarbonyl)pyridinium bromide (**6a**), yield 90%, mp 239-241°C. ^{1}H NMR (DMSO-d6), δ (DSS): 6.42 (s, CH_2), 7.4-9.4 (m, arom), 9.55 (s, pyr H2). Anal. Calcd for $C_{20}H_{16}BrN_3O_5$: C, 52.41; H, 3.52. Found: C, 52.24; H, 3.70.
1-[4-[(4-Nitrophenoxy)carbonyl]benzyl]-3-(aminocarbonyl)pyridinium bromide (**6b**), yield 92%, mp 235-237°C. ^{1}H NMR (DMSO-d6), δ (DSS): 6.20 (s, CH_2), 7.5-9.6 (m, arom), 9.78 (s, pyr H2). Anal. Calcd for $C_{20}H_{16}BrN_3O_5$: C, 52.41; H, 3.52. Found: C, 52.25; H, 3.62.
1-[2-[(3-Nitrophenoxy)carbonyl]benzyl]-3-(aminocarbonyl)pyridinium bromide (**7a**), yield 87%, mp 243-246°C. ^{1}H NMR (DMSO-d6), δ (DSS): 6.30 (s, CH_2), 7.4-9.3 (m, arom), 9.40 (s, pyr H2). Anal. Calcd for $C_{20}H_{16}BrN_3O_5$: C, 52.41; H, 3.52. Found: C, 52.64; H, 3.43.
1-[4-[(3-Nitrophenoxy)carbonyl]benzyl]-3-(aminocarbonyl)pyridinium bromide (**7b**), yield 85%, mp 233-235°C. ^{1}H NMR (DMSO-d6), δ (DSS): 6.10 (s, CH_2), 7.4-9.5 (m, arom), 9.70 (s, pyr H2). Anal. Calcd for $C_{20}H_{16}BrN_3O_5$: C, 52.41; H, 3.52. Found: C, 52.66; H, 3.45.
1-[2-(Phenoxycarbonyl)benzyl]-3-(aminocarbonyl)pyridinium bromide (**8a**), yield 71%, mp 209-212°C. ^{1}H NMR (DMSO-d6), δ (DSS): 6.34 (s, CH_2), 7.4-9.5 (m, arom), 9.45 (s, pyr H2). Anal. Calcd for $C_{20}H_{17}BrN_2O_3$: C, 58.12; H, 4.15. Found: C, 58.22; H, 4.03.
1-[4-(Phenoxycarbonyl)benzyl]-3-(aminocarbonyl)pyridinium bromide (**8b**), yield 88%, mp 245-247°C. ^{1}H NMR (DMSO-d6), δ (DSS): 6.12 (s, CH_2), 7.4-9.5 (m, arom), 9.75 (s, pyr H2). Anal. Calcd for $C_{20}H_{17}BrN_2O_3$: C, 58.12; H, 4.15. Found: C, 58.03; H, 4.11.
1-[2-[(4-Methoxyphenoxy)carbonyl]benzyl]-3-(aminocarbonyl)pyridinium bromide (**9a**), yield 90%, mp 198-199°C. ^{1}H NMR (DMSO-d6), δ (DSS): 3.80 (s, OCH_3), 6.36 (s, CH_2), 6.9-9.3 (m, arom), 9.49 (s, pyr H2). Anal. Calcd for $C_{21}H_{19}BrN_2O_4$: C, 56.89; H, 4.32. Found: C, 56.81; H, 4.26.
1-[4-[(4-Methoxyphenoxy)carbonyl]benzyl]-3-(aminocarbonyl)pyridinium bromide (**9b**), yield 91%, mp 253-256°C. ^{1}H NMR (DMSO-d6), δ (DSS): 3.75 (s, OCH_3), 6.22 (s, CH_2), 6.8-9.5 (m, arom), 9.79 (s, pyr H2). Anal. Calcd for $C_{21}H_{19}BrN_2O_4$: C, 56.89; H, 4.32. Found: C, 56.98; H, 4.31.

1-[2-[(4-Methoxyphenoxy)carbonyl]benzyl]-4-(aminocarbonyl)pyridinium bromide (**10a**), yield 79%, mp 206-208°C. ^{1}H NMR (DMSO-d6), δ (DSS): 3.70 (s, OCH_3), 6.30 (s, CH_2), 7.1-9.2 (m, arom), 9.40 (d, pyr H2,6). Anal. Calcd for $C_{21}H_{19}BrN_2O_4$: C, 56.89; H, 4.32. Found: C, 57.01; H, 4.38.

1-[4-[(4-Methoxyphenoxy)carbonyl]benzyl]-4-(aminocarbonyl)pyridinium bromide (**10b**), yield 85%, mp 229-231°C. ^{1}H NMR (DMSO-d6), δ (DSS): 3.66 (s, OCH_3), 6.10 (s, CH_2), 7.1-9.2 (m, arom), 9.40 (d, pyr H2,6). Anal. Calcd for $C_{21}H_{19}BrN_2O_4$: C, 56.89; H, 4.32. Found: C, 56.80; H, 4.21.

1-[2-[(4-Nitrophenoxy)carbonyl]benzyl]-3-(aminocarbonyl)quinolinium bromide (**11a**), yield 76%, mp 245-247°C. ^{1}H NMR (DMSO-d6), δ (DSS): 6.85 (s, CH_2), 7.5-8.9 (m, arom), 10.07 (s, quin H4), 10.12 (s, quin H2). Anal. Calcd for $C_{24}H_{18}BrN_3O_5$: C, 56.71; H, 3.57. Found: C, 56.53; H, 3.54.

1-[4-[(4-Nitrophenoxy)carbonyl]benzyl]-3-(aminocarbonyl)quinolinium bromide (**11b**), yield 73%, mp 215-217°C. ^{1}H NMR (DMSO-d6), δ (DSS): 6.45 (s, CH_2), 7.2-9.0 (m, arom), 10.05 (s, quin H4), 10.45 (s, quin H2). Anal. Calcd for $C_{24}H_{18}BrN_3O_5$: C, 56.71; H, 3.57. Found: C, 56.62; H, 3.61.

2-[(4-Nitrophenoxy)carbonyl]benzyltrimethylammonium bromide (**12a**), yield 90%, mp 201-204°C (lit.[11] 190-192°C). ^{1}H NMR (DMSO-d6), δ (DSS): 3.18 (s, $N(CH_3)_3$), 5.12 (s, CH_2), 7.5-8.5 (m, arom). Anal. Calcd for $C_{17}H_{19}BrN_2O_4$: C, 51.66; H, 4.85. Found: C, 51.40; H, 4.68.

4-[(4-Nitrophenoxy)carbonyl]benzyltrimethylammonium bromide (**12b**), yield 92%, mp 269-272°C. ^{1}H NMR (DMSO-d6), δ (DSS): 3.09 (s, $N(CH_3)_3$), 4.71 (s, CH_2), 7.4-8.5 (m, arom). Anal. Calcd for $C_{17}H_{19}BrN_2O_4$: C, 51.66; H, 4.85. Found: C, 51.81; H, 4.67.

Kinetic measurements

The water used in the kinetic measurements was distilled twice in an all quartz distillation unit. The ester hydrolysis was carried out in 1 cm quartz cells in a thermostated cell compartment maintained at 25.0 ± 0.1°C of a Varian DMS 90 spectrophotometer. About 5 μl of a concentrated solution of the ester in water was added to 2 ml of buffer or NaOH solution. The buffers used were borax buffer pH = 9.20 (**11a,b**), carbonate buffer, pH = 10.50 (**4-7a,b**; **12a,b** and phosphate buffer pH = 11.50 (**8-10a,b**). Alternatively, dilute NaOH solutions (μ = 0.1 with NaCl) were employed. The rate of hydrolysis was measured by following the appearance of the formed phenolate (400 nm, X = 4-NO_2; 390 nm, X = 3-NO_2; 287 nm, X = H; 303 nm, X = OCH_3). All ester hydrolysis reactions were followed to greater than 75% completion and infinity points A_∞ were taken after 10 half lives. In all cases straight lines were obtained by plotting ln (A_∞-A_t) against t, showing first-order kinetics. The pseudo first-order rate constant was calculated from the tangent of the slope of the line. Rate constants were determined at least in duplo and were reproducible to within 3%. The second-order rate constant for hydroxide ion k_{OH^-} has been determined by measurement of the rate in a series of diluted buffer solutions (dilution with 0.1 M NaCl to keep the ionic strength constant) and extrapolation to zero buffer concentration or by linear regression of the data obtained from series of dilute NaOH solutions.

REFERENCES AND NOTES

1. C.-I. Brandén, H. Jornvall, H. Eklund and B. Furugren in "The Enzymes" 3rd ed., Vol. XI, P.D. Boyer, Ed. Academic Press, New York, p. 103 (1975).
2. W.H. Gündel, Z. Naturforsch B, Anorg. Chem., Org. Chem., **38B**, 873 (1983).
3a. E.M. Kosower in "The Enzymes" 2nd ed., Vol. 3, Academic Press, New York, p. 171-193 (1960);
b. E.M. Kosower, Progr. Phys. Org. Chem., **3**, 82 (1965).
4. W.P. Jencks, "Catalysis in Chemistry and Enzymology", McGraw-Hill, New York, chapter 9, 1969.
5a. C.A. Bunton and D.N. Spatcher, J. Chem. Soc., 1099 (1956);
b. M. Caplow and W.P. Jencks, Biochemistry, **1**, 883 (1962);
c. J.F. Kirsch, W. Clewell and A. Simon, J. Org. Chem., **33**, 127 (1968);
d. A.A. Humffray and J.J. Ryan, J. Chem. Soc. B, 468 (1967).
6. S.L. Johnson and D.L. Morrison, Biochemistry, **9**, 1460 (1970).
7. J.G. Watkinson, W. Watson and B.L. Yates, J. Chem. Soc., 5437 (1963).
8. V. Athanassakis, C.A. Bunton and D.C. McKenzie, J. Phys. Chem., **90**, 5158 (1986).
9. P.S. Raghavan, V.S. Srinivasan, S. Vangalur, N. Venkat-Subramanian, Indian J. Chem., Sect. B, **218**, 423 (1982).
10. F.M. Menger and C.E. Portnoy, J. Amer. Chem. Soc., **89**, 4698 (1967).
11. A. Albert in "Physical Methods in Heterocyclic Chemistry", Vol. I, A.R. Katritzky, Ed., Academic Press, New York, p. 1 (1963).
12. J. Mollin and A.A. Baisa, Coll. Czech. Chem. Comm., **43**, 304 (1978).
13. J.F.J. Engbersen, PhD Thesis, Groningen, 1976.
14. In aprotic solvents the presence of a quaternary ammonium group ortho to the ester function enhances the rate of acyl transfer from α-substituted p-nitrophenyl-o-toluates to carboxylate ion ca. 3000-fold. J. Hajdu and G.M. Smith, J. Amer. Chem. Soc., **103**, 6192 (1981).
15. A.W. Titherley and L. Stubbs, J. Chem. Soc., **105**, 302 (1914).