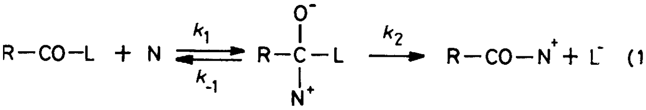
Kinetics and Mechanism of the Pyridinolysis of 2,4-Dinitrophenyl *p*-Nitrobenzoate

Enrique A. Castro * and Gloria B. Steinfort
Facultad de Quimica, Pontificia Universidad Catolica de Chile, Casilla 114-D, Santiago, Chile

The nucleophilic reactions of a series of 3- and 4-monosubstituted pyridines with 2,4-dinitrophenyl *p*-nitrobenzoate are studied in 44 wt% aqueous ethanol at 25 °C, and ionic strength 0.2 mol dm^{-3} (sodium perchlorate). The Brönsted-type plot obtained (log second-order rate constant against basicity of the pyridine) is straight, in contrast to the ones found in the pyridinolyses of 2,4-dinitrophenyl acetate and 2,4-dinitrophenyl methyl carbonate, and in the reactions of substituted quinuclidines with 2,4-dinitrophenyl phenyl carbonate, which all exhibit curved Brönsted plots centred at pK_a° 7.3—7.8. The higher pK_a° value obtained in the title reactions (>8.9) is explained mainly by the large influence of the electron-withdrawing power of the non-leaving group of the substrate.

A substantial number of Brönsted-type plots for nucleophilic reactions (log k_N against basicity of nucleophile, where k_N is the second-order rate constant for nucleophilic attack on the substrate) involving carboxylic acid derivatives have appeared in the literature. It is well known that when structurally homogeneous series of nucleophiles react with carboxylic substrates which are not very reactive, linear Brönsted-type plots are obtained.[1,2] For the more reactive substrates the Brönsted-type plots are curved.[2-8]

The curved Brönsted-type plots have been interpreted in terms of a tetrahedral intermediate in the reaction path and a change in the rate-determining step from breakdown to formation of the intermediate, as the basicity of the nucleophile increases [3-8] [equation (1), where N and L represent the nucleophile and the leaving group of the substrate, respectively]. The position of the centre of the curvature along the basicity axis of the Brönsted-type plot (pK_a°) corresponds to the basicity of the nucleophile which has the same leaving ability from the tetrahedral intermediate as the leaving group of the substrate.[3-8] In other words, it is the pK_a value of the conjugate acid of the nucleophile for which $k_{-1} = k_2$ in equation (1).



$$\mathrm{R{-}CO{-}L} + \mathrm{N} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{R{-}}\overset{\displaystyle \mathrm{O^-}}{\underset{\displaystyle \mathrm{N^+}}{\mathrm{C}}}\mathrm{{-}L} \xrightarrow{k_2} \mathrm{R{-}CO{-}N^+} + \mathrm{L^-} \qquad (1)$$

In the nucleophilic reactions of a given series of amines with reactive carboxylic acid derivatives (R–CO–L) it is of interest to know whether the value of pK_a° is dependent on the leaving group of the substrate (L), or the 'acyl' substituent group (R), or both. From a comparison of the Brönsted-type plots obtained in the pyridinolyses of methyl chloroformate (pK_a° 3.6)[4] and 2,4-dinitrophenyl methyl carbonate (pK_a° 7.8),[5] an important influence of the basicity of the leaving group on the pK_a° value can be inferred. On the other hand, the nature of the R group does not seem to play an important role in influencing the pK_a° value when comparison is made of the Brönsted-type plots obtained in the pyridinolyses of 2,4-dinitrophenyl methyl carbonate and 2,4-dinitrophenyl acetate (pK_a° 7.3).[6] This is confirmed by the reactions of substituted quinuclidines with 2,4-dinitrophenyl phenyl carbonate,[5] where pK_a° is 7.5. In other words, substitution of methyl by methoxy or phenoxy as the R group does not bring about significant changes of the pK_a° values found for these reactions. A small dependence of the basicity of the R group on the pK_a° value was also found in the reactions of substituted quinuclidines with substituted-aryl 3,4-dinitrophenyl carbonates.[8] The same authors report a large influence of the basicity of the L group on the pK_a° value in the reactions of quinuclidines with substituted-aryl phenyl carbonates.[7]

The present paper reports the Brönsted-type plot obtained in the pyridinolysis of 2,4-dinitrophenyl *p*-nitrobenzoate; comparison of its pK_a° value with the ones found in the aminolyses of the 2,4-dinitrophenyl carboxylates mentioned above is made, and hence the influence of another type of R group on the pK_a° value is assessed.

Experimental

Materials.—The 3- and 4-monosubstituted pyridines and other reagents were purified as previously described.[4] 2,4-Dinitrophenyl *p*-nitrobenzoate was prepared according to Burtle and Turek.[9]

Kinetic Measurements.—The reactions were followed at 360 nm, monitoring the appearance of 2,4-dinitrophenolate by means of a Pye–Unicam SP 1800 spectrophotometer. The reactions were started by adding a solution of the substrate in acetonitrile (10 µl) to a solution of the pyridine pre-heated to 25 ± 0.1 °C in a 1 cm cell (3 ml). The initial concentration of the substrate was 4×10^{-5} mol dm^{-3} in all reactions.

The reactions were studied under pseudo-first-order conditions, with the substituted pyridine in excess, in 44 wt% aqueous ethanol at ionic strength 0.2 mol dm^{-3} (maintained with sodium perchlorate). Good pseudo-first-order rate constants (k_{obs}) were obtained for each run by means of Guggenheim plots.

The experimental conditions for the reactions and the values of k_{obs} are shown in Table 1.

Products Studies.—2,4-Dinitrophenolate was quantitatively obtained as one of the products of the reactions as indicated by the comparison of the final u.v. spectra (340—400 nm) of some reaction samples at pH 5—7 with those of authentic samples at the same concentration as that of the substrate at zero time and under the same experimental conditions.

Determinations of pK_a.—These were carried out potentiometrically and spectrophotometrically under the same conditions as those of the kinetic measurements.

The potentiometric determinations involved the use of a Radiometer titration equipment composed of a PHM-62

Table 1. Experimental conditions and pseudo-first-order rate constants (k_{obs}) for the reactions of 2,4-dinitrophenyl *p*-nitrobenzoate with substituted pyridines in 44 wt% aqueous ethanol at 25 °C and ionic strength 0.2 mol dm^{-3} (maintained with sodium perchlorate)

Substituent	$[N]_t$/mol dm^{-3} [a]	pH [b]	$10^4 k_{obs}$/s^{-1}	Number of runs
3-Chloro	0.53—2.13	6.1	0.83—1.52	7
	0.53—2.66	6.4	0.95—1.83	8
	0.53—2.66	6.7	0.97—1.93	8
3-Carbamoyl	0.25—1.75	6.1	0.93—3.72	7
	0.25—1.62	6.4	1.19—3.73	7
	0.25—1.75	6.7	1.39—3.95	7
None	(2.5—19.8) × 10^{-2}	4.2	2.67—18.2	8
	(2.5—19.8) × 10^{-2}	4.5	3.26—25.9	8
	(2.5—19.8) × 10^{-2}	4.8	5.03—32.3	7
3-Methyl	(2.6—20.6) × 10^{-2}	4.4	5.57—33.2	8
	(1.0—8.3) × 10^{-2}	4.7	2.70—25.6	8
	(0.5—8.3) × 10^{-2}	5.0	2.13—31.2	8
4-Methyl	(0.5—4.1) × 10^{-2}	5.65	5.90—47.7	8
	(0.5—4.1) × 10^{-2}	5.95	6.42—53.1	9
	(0.5—4.1) × 10^{-2}	6.25	6.73—53.0	8
4-Amino	(1.3—10.0) × 10^{-3}	6.1	4.42—39.1	8
	(0.5—4.0) × 10^{-3}	6.4	3.75—28.1	8
	(0.5—3.5) × 10^{-3}	6.7	7.42—25.8	8
4-Dimethylamino	(0.5—4.0) × 10^{-3}	6.1	1.83—16.1	8
	(0.5—4.0) × 10^{-3}	6.4	4.00—31.2	8
	(0.5—3.5) × 10^{-3}	6.7	7.97—58.5	7

[a] Total concentration of substituted pyridine (free base plus acidic form). [b] Corrected pH by adding 0.1 to the value given by the pH-meter. The correction value was obtained by interpolation between 35 and 50 wt% aqueous ethanol.[10] During the runs, the pH was maintained by the presence of phosphate buffer (total concentration 0.02 mol dm^{-3}), except in the cases of 3- and 4-methyl and unsubstituted pyridines, where no external buffer was used.

Table 2. Values of pK_a for substituted pyridinium ions and second-order rate constants (k_N) for the reactions of 2,4-dinitrophenyl *p*-nitrobenzoate with substituted pyridines [a]

Substituent	pK_a [b]	k_N/dm^3 s^{-1} mol^{-1} [c]
3-Chloro	1.7 [d]	$(9.2 \pm 0.9) \times 10^{-5}$
3-Carbamoyl	2.4 [d]	$(3.6 \pm 0.2) \times 10^{-4}$
None	4.2 [d]	0.018 ± 0.001
3-Methyl	4.7 [e]	0.06 ± 0.004
4-Methyl	5.0 [e]	0.14 ± 0.02
4-Amino	8.7 [e]	160 ± 20
4-Dimethylamino	8.9 [e]	243 ± 20

[a] Both pK_a and k_N were determined in 44 wt% aqueous ethanol at 25 °C and ionic strength 0.2 mol dm^{-3} (maintained with sodium perchlorate). [b] ' Mixed pK_a ': $K_a = a_H[N]/[NH^+]$. This is the same type of pK_a reported in refs. 4—6. It was obtained by adding 0.1 to the experimental ' mixed pK_a ' value, in order to correct the pH meter readings (see footnote *b* of Table 1). [c] Errors shown are standard deviations. [d] Determined potentiometrically. [e] Determined spectrophotometrically.

pH-meter, ABU-11 autoburette, TTA-60 titration assembly, TTT-60 titrator, and REA-160 recorder. The electrodes were Radiometer G 2040G (glass) and K 4040 (calomel). Solutions (10 ml) containing 0.01 mol dm^{-3} of the protonated substituted pyridines in 44 wt% aqueous ethanol and ionic strength 0.2 mol dm^{-3} (maintained with sodium perchlorate) were thermostatted at 25 ± 0.1 °C and titrated with aqueous solutions (*ca.* 0.2 ml) of 0.5 mol dm^{-3} sodium hydroxide.

The spectrophotometric measurements were carried out by scannings (240—280 nm) of buffered solutions (3 ml in 1 cm cells) of the pyridines and their conjugate acids in the reaction conditions by means of a Pye–Unicam SP 1800 spectrophotometer. The measurements of pH were made through a Radiometer PHM-62 pH-meter, and the pH readings corrected for the ethanol present in the solutions[10] (see also footnotes *b* of Tables 1 and 2). Acetic and citric acids at various degrees of neutralisation were used as buffers.

The pK_a values obtained by the potentiometric as well as the spectrophotometric methods are shown in Table 2.

Results and Discussion

The pseudo-first-order rate constant observed (k_{obs}) for the title reactions is of the form given by equation (2), where k_0

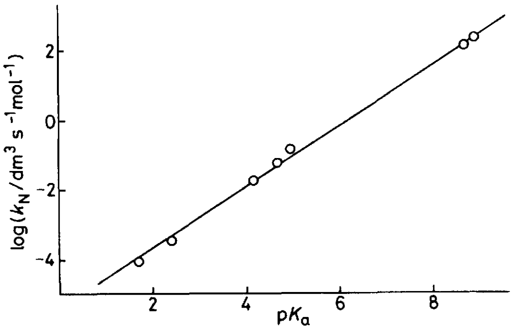
$$k_{obs} = k_0 + k_N[N] \qquad (2)$$

is the rate constant for the substrate solvolysis in the absence of substituted pyridine, k_N is the second-order rate constant for nucleophilic attack on the substrate by the substituted pyridine, and N represents the free-base form of the nucleophile. In most cases the values of k_N were obtained from plots of k_{obs} against total concentration of amine (free base plus acidic forms) at constant pH. Straight lines were exhibited in these cases, and the k_N values were obtained from k_N = slope/F_N where F_N is the molar fraction of the free base substituted pyridine at the pH concerned. As the k_N values did not show a pH dependence, the final value was taken as the average of the individual k_N values obtained at each pH.

In the cases where high concentrations of substituted pyridine had to be used (the two less basic pyridines) and in the case of 3-methylpyridine at pH 4.4 (where a relatively large concentration was employed), a non-linear dependence of k_{obs} on [N] was found. This was attributed to dimerisation of the substituted pyridines. The concentration of monomeric substituted pyridine ([N]) can be related to total concentration of monomeric plus dimeric forms ($[N]_{m,d}$) by means of equation (3), where K is the dimerisation constant.[11] Solving

$$[N]^2 + \frac{[N]}{2K} - \frac{[N]_{m,d}}{2K} = 0 \qquad (3)$$

this quadratic expression and substituting in equation (2), one gets equation (4). The values of k_0 were obtained by extra-



Brönsted-type plot for the pyridinolysis of 2,4-dinitrophenyl *p*-nitrobenzoate in 44 wt% aqueous ethanol at 25 °C and ionic strength 0.2 mol dm^{-3} (maintained with sodium perchlorate). The pK_a values were obtained experimentally under the same conditions

$$k_{obs} = k_0 + \frac{k_N}{4K}(\sqrt{1 + 8K[N]_{m,d}} + 1) \qquad (4)$$

polation, to zero $[N]_{m,d}$, of the k_{obs} *versus* $[N]_{m,d}$ experimental curves in the low concentration region (where the plots are linear). The k_N values were found by non-linear least-squares fitting of the experimental curves to equation (4). Since no clear dependence of k_N on the pH was found, the final k_N value for the reactions of each substituted pyridine was obtained as an average of the values found at each pH.

The average k_N values for the reactions of the substrate with all the substituted pyridines, determined by equations (2) and (4), are shown in Table 2.

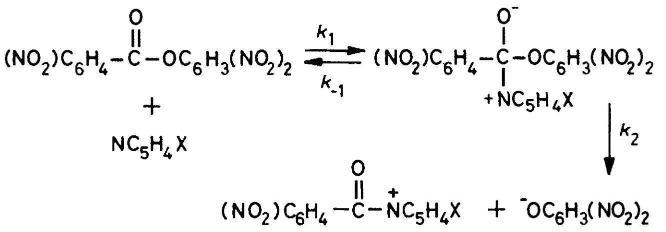
The Figure shows the Brönsted-type plot obtained for the present reactions, using the values of k_N and pK_a given in Table 2. The plot is linear, with a slope of 0.9. The linearity of the plot is in marked contrast with the breaks found in the Brönsted-type plots of the similar reactions of substituted pyridines with 2,4-dinitrophenyl methyl carbonate[5] and 2,4-dinitrophenyl acetate.[6]

Similar Brönsted slopes (β) to that of the plot in the Figure have been found in the nucleophilic reactions of substituted pyridines with methyl chloroformate and *p*-nitrophenyl acetate (β 0.93),[4] 2,4-dinitrophenyl methyl carbonate (β 0.9),[5] 2,4-dinitrophenyl acetate (β 0.85),[6] and acetic anhydride (β 1.0).[3b] Also, the aminolyses of phenyl acetates,[1] aryl phenyl carbonates,[7,8] acylpyridinium ions,[12] and phthalic and succinic anhydrides[13] have shown Brönsted-type plots with similar slopes.

Most of the above Brönsted plots are composed of two straight lines (one in the region of low basicities of the nucleophiles, with β 0.8—1.0, and the other at high basicities, with β 0.2—0.3) and a curvature in between (only *p*-nitrophenyl acetate shows a linear plot). In all these reactions the occurrence of a tetrahedral intermediate in the reaction path has been proposed, and the magnitude of the higher Brönsted slope has been connected with the decomposition to products of the intermediate as being the rate-determining step. In the reactions reported here, this is the k_2 step of Scheme 1.

The macroscopic rate constant from reactants to products of Scheme 1 is k_N, which can be related to the microscopic rate constants of the scheme through application of the steady-state treatment to the tetrahedral intermediate [equation (5)]. If the second step of Scheme 1 is rate determining for the present reactions, it follows that $k_{-1} \gg k_2$, and equation (5) leads to $k_N = k_1k_2/k_{-1} = K_1k_2$, where K_1 is the equilibrium constant for the first step. Therefore, Scheme 1 consists of a pre-equilibrium step followed by the rate-determining one.

$$k_N = k_1k_2/(k_{-1} + k_2) \qquad (5)$$



$$(NO_2)C_6H_4{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}OC_6H_3(NO_2)_2 + NC_5H_4X \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} (NO_2)C_6H_4{-}\overset{\overset{\displaystyle O^-}{|}}{\underset{\underset{\displaystyle {}^{+}NC_5H_4X}{|}}{C}}{-}OC_6H_3(NO_2)_2 \xrightarrow{k_2} (NO_2)C_6H_4{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}\overset{+}{N}C_5H_4X + {}^{-}OC_6H_3(NO_2)_2$$

Scheme 1

The breaks in the Brönsted-type plots, from large to small sensitivity of the nucleophilic rate constant upon basicity, have been attributed to a change in the rate-determining step from breakdown to formation of the tetrahedral intermediate (for the reactions reported here this would mean a change from the k_2 to the k_1 step of Scheme 1). For the first step to be rate determining requires $k_2 \gg k_{-1}$; equation (5) then leads to $k_N = k_1$. At the centre of the Brönsted curvature, $k_2 = k_{-1}$, and in the curved region equation (5) holds without approximations. It is clear from the Figure that for the present reactions the centre of the curvature has not been reached even by the most basic substituted pyridine used.*

The u.v. detection of the substituted *p*-nitrobenzoylpyridinium ion (one of the products of Scheme 1) could not be achieved due to high blank absorption, but also because its decomposition may be fast in aqueous solution. In fact, the rates of hydrolyses of substituted 1-methoxycarbonyl-[4,14] and 1-acetyl-pyridinium[3b,12] ions have been measured, the acetyl derivatives being 200—300 times more reactive than the methoxycarbonyl ones. Substitution of acetyl by *p*-nitrobenzoyl should increase the rates of hydrolyses of the *p*-nitrobenzoylpyridinium ions, as shown for example by the comparison between the rates for alkaline hydrolyses of substituted phenyl acetates and *p*-nitrobenzoates. The rate constant for hydroxide attack is about three times larger for *p*-nitrophenyl *p*-nitrobenzoate[15] than for the corresponding acetate.[2] Similarly, 2,4-dinitrophenyl *p*-nitrobenzoate is four times as reactive towards hydroxide ion[16] as the similar acetate.[1,] †

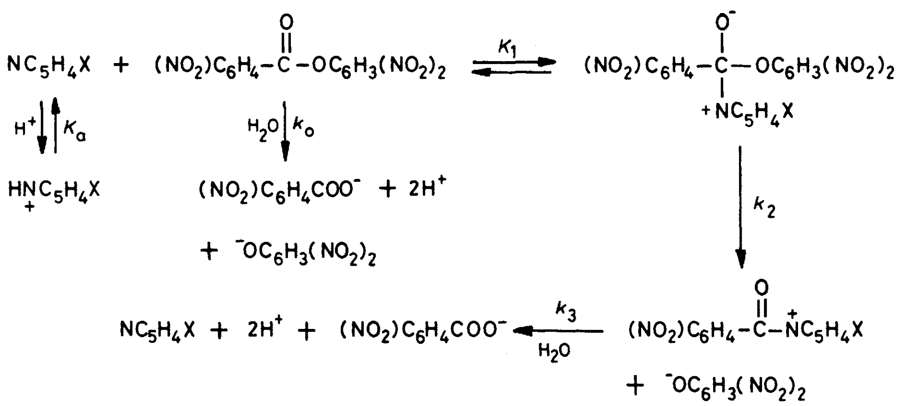
Considering all what has been discussed so far and the experimental results obtained, the most probable mechanism for the reactions reported here, in the experimental conditions used, appears to be the one shown in Scheme 2. For clarity reasons, ethanol has been omitted from Scheme 2; its molar concentration is 3.2 times smaller than that of water and, besides, it should react in a way similar to water.

From the comparison of the Brönsted-type plots obtained in the pyridinolyses of 2,4-dinitrophenyl *p*-nitrobenzoate (Figure), 2,4-dinitrophenyl methyl carbonate,[5] and 2,4-dinitrophenyl acetate,[6] and in the reactions of substituted quinuclidines with 2,4-dinitrophenyl phenyl carbonate,[7] the following observations and conclusions can be drawn.

---

* Unfortunately, the aqueous ethanol media of the reactions lower the basicities of the substituted pyridines, limiting the extent of the upper end of the Brönsted plot. For example, the pK_a values for 4-(dimethylamino)pyridinium ion at 25 °C and ionic strength 0.2 mol dm^{-3} are 9.55 (water) and 8.90 (44 wt% aqueous ethanol).

† Nevertheless, substituted pyridines are *less* reactive towards 2,4-dinitrophenyl *p*-nitrobenzoate than towards the corresponding acetate (*cf.* Table 2 of this work with Table 1 of ref. 1). This fact must be due to a higher steric hindrance of the substituted pyridine than the hydroxide ion towards the attack on the *p*-nitrobenzoate ester.



Scheme 2

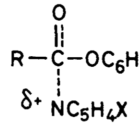
(1) The acetate and carbonate esters show curved Brönsted plots, with the centre of the break along the basicity coordinate (pK_a°) at very similar positions, which means that the nature of the non-leaving (R) group of the substrate does not alter significantly the value of pK_a°. This is in accord with previous findings[8] (see Introduction), where a plot of pK_a° against the basicity of R gives a straight line with slope *ca.* −0.4 for the reactions of quinuclidines with substituted-aryl 3,4-dinitrophenyl carbonates. This is in contrast to the large sensitivity of the pK_a° value upon the basicity of the L group (slope 1.7) found in the similar reactions[7] mentioned in the Introduction.

(2) The change to *p*-nitrophenyl as the R group of the 2,4-dinitrophenyl ester derivatives brings about a major shift of the position of the centre of the Brönsted break. Since the Brönsted-type plot shown in the Figure is linear up to pK_a 8.9, it follows that for the reactions reported here, $pK_a^\circ > 8.9$. This change in the pK_a° value is much larger than the one found in the aminolyses of substituted-aryl 3,4-dinitrophenyl carbonates[8] discussed above. In fact, Gresser and Jencks found a small increase of the pK_a° value upon the increase of the electron-withdrawing power of the R group,[8] which is qualitatively in accord with our results.

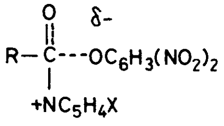
The fact that the Brönsted-type plot obtained in the title reactions has a pK_a° value >8.9 means that only for a (hypothetical) extremely basic pyridine (of $pK_a > 8.9$) will $k_{-1} = k_2$ (Scheme 1); *i.e.* this substituted pyridine will have the same leaving ability from the tetrahedral intermediate as 2,4-dinitrophenolate. For the pyridines of lower basicity ($pK_a \leqslant 8.9$) $k_{-1} \gg k_2$, *i.e.*, the pyridines leave the tetrahedral intermediate much faster than 2,4-dinitrophenolate. Thus, even 4-(dimethylamino)pyridine leaves the intermediate more readily than the phenolate in spite of being 10^5 times more basic in the water–ethanol media of the reactions (pK_a of 2,4-dinitrophenol 3.9 under the reaction conditions).

The much higher pK_a° value found in the present reactions, compared to the ones found in the aminolyses of the other 2,4-dinitrophenyl esters, implies that k_{-1}/k_2 (Scheme 1) is much larger for the reaction of the title substrate with a given substituted pyridine than for the reactions of the same pyridine with the other substrates. In other words, amine expulsion from the tetrahedral intermediate relative to 2,4-dinitrophenolate expulsion is favoured in the reactions reported here.

Although a change to a less polar solvent should increase k_{-1} and have little or no effect on k_2, we do not think this medium effect alone could account for the much higher value of k_{-1}/k_2 found for the title reactions. The main reason for the larger value of pK_a° must be due to the larger electron-withdrawing ability of the R group of the tetrahedral intermediate of Scheme 1 compared to the corresponding ones of similar intermediates in the reactions with the other 2,4-dinitrophenyl substrates. This electron-withdrawing effect will stabilise the ester product and the transition state for amine expulsion (1) more than the cationic amide product and the transition state for the phenolate expulsion[8] (2). The greater stabilisation of (1) relative to (2) with the increasing electron-withdrawing ability of R should result in an increase of the k_{-1}/k_2 value.



(1)



(2)

We are at present studying the pyridinolyses of several 2,4-dinitrophenyl substituted-benzoates in order to assess more precisely the magnitude of the dependence of the pK_a° value on the electron-withdrawing power of the non-leaving group of the substrate.

Acknowledgement

The financial assistance of Direccion de Investigacion de Universidad Catolica de Chile (DIUC) through project No. 85/80 is gratefully acknowledged.

References

1 S. L. Johnson, *Adv. Phys. Org. Chem.*, 1967, **5**, 237.
2 W. P. Jencks and M. Gilchrist, *J. Am. Chem. Soc.*, 1968, **90**, 2622.
3 (*a*) D. H. Hupe and W. P. Jencks, *J. Am. Chem. Soc.*, 1977, **99**, 451; (*b*) C. Castro and E. A. Castro, *J. Org. Chem.*, 1981, **46**, 2939.
4 P. M. Bond, E. A. Castro, and R. B. Moodie, *J. Chem. Soc., Perkin Trans. 2*, 1976, 68.
5 E. A. Castro and F. J. Gil, *J. Am. Chem. Soc.*, 1977, **99**, 7611.
6 E. A. Castro and M. Freudenberg, *J. Org. Chem.*, 1980, **45**, 906.
7 M. J. Gresser and W. P. Jencks, *J. Am. Chem. Soc.*, 1977, **99**, 6963.
8 M. J. Gresser and W. P. Jencks, *J. Am. Chem. Soc.*, 1977, **99**, 6970.
9 J. G. Burtle and W. N. Turek, *J. Org. Chem.*, 1954, **19**, 1567.
10 B. Gutbezahl and E. Grunwald, *J. Am. Chem. Soc.*, 1953, **75**, 565.

11 A. J. Kirby and W. P. Jencks, *J. Am. Chem. Soc.*, 1965, **87**, 3209; A. R. Fersht and W. P. Jencks, *ibid.*, 1970, **92**, 5432; L. Sacconi, P. Paoletti, and M. Ciampolini, *ibid.*, 1960, **82**, 3828; J. E. Del Bene, *ibid.*, 1980, **102**, 5191; P. L. Huyskens, R. S. Smets, and D. H. Mas, *Bull. Soc. Chim. Belg.*, 1977, **86**, 741.

12 A. R. Fersht and W. P. Jencks, *J. Am. Chem. Soc.*, 1970, **92**, 5442.

13 W. E. Hall, T. Higuchi, I. H. Pitman, and K. Uekama, *J. Am. Chem. Soc.*, 1972, **94**, 8153.

14 P. J. Battye, E. M. Ihsan, and R. B. Moodie, *J. Chem. Soc., Perkin Trans. 2*, 1980, 741.

15 J. F. Kirsch, W. Clewell, and A. Simon, *J. Org. Chem.*, 1968, **33**, 127.

16 C. D. Hubbard and J. F. Kirsch, *Biochemistry*, 1972, **11**, 2483.

Received 14th *June* 1982; *Paper* 2/993