

412. The Kinetics of Alkaline Hydrolysis of the Ethyl β -Pyridylacrylates and their 1-Oxides.

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Rates of alkaline hydrolysis, in 70% (w/w) ethanol-water, of the ethyl β -pyridylacrylates have been measured in the temperature range 15–35°. Further evidence of the operation of a "direct" effect in the 1-oxides is given.

BRYNMOR JONES and WATKINSON¹ found that a simple relationship existed between the rates of alkaline hydrolysis of a series of *meta*- and *para*-substituted ethyl cinnamates and those of the corresponding ethyl benzoates. If the non-exponential factor (A) is constant, this implies that the effect of a given substituent on the activation energy (E) is only about half as great in the former series as in the latter. The present investigation was designed to determine whether a similar relation exists between the rates of hydrolysis of ethyl β -pyridylacrylates and of ethyl pyridinecarboxylates.²

EXPERIMENTAL

β -Pyridylacrylic acids, prepared by the method of Marvel, Coleman, and Scott,³ were esterified by use of ethanol-sulphuric acid and the products purified by fractional distillation (2- and 3-esters) or by recrystallisation; the purified 2- and 3-esters solidified: 2-, m. p. 25° (lit.,⁴ 26–27°); 3-, b. p. 159°/14 mm. (lit.,⁵ 156–158°/14 mm.), m. p. 18° (not previously reported as a solid); 4-, m. p. 65–66° (lit.,⁶ 64.5–66°).

β -Pyridylacrylic acid 1-oxides and their ethyl esters were prepared as described by Katritzky and Monro⁷ and by Katritzky, Monro, and Beard.⁸ Although melting (decomposition) points are quoted for the acids,^{7,8} we find that decomposition occurs over a considerable range of temperature and the values obtained give no indication of purity. Hence melting points of the esters only are recorded here: 2-, m. p. 70–71° (lit.,⁸ 68–68.5°); 3-, m. p. 100–101° (lit.,⁷ 99–101°); 4-, m. p. 144–146° (lit.,⁷ 145°).

Rates of hydrolysis were measured by the conductometric method described previously,² the solvent being aqueous ethanol d_{25}^{25} 0.8646 (70.55% w/w). Mean values of the second-order rate constants are given in Table 1.

pK values of the β -pyridylacrylic acid 1-oxides were determined potentiometrically by using 50% aqueous ethanol as the solvent. The values obtained were: 2-acid, 4.78; 3-acid, 4.81; 4-acid, 4.82.

TABLE 1.Rates of hydrolysis of $\text{RCH}:\text{CH}\cdot\text{CO}_2\text{Et}$, expressed as $\log_{10} k$ (k in l. mole⁻¹ sec.⁻¹).

R	15°	20°	25°	30°	35°	$\log A$	E (kcal. mole ⁻¹)
2-Pyridyl	-2.239	-2.067	-1.855	-1.692	-1.529	8.7	14.5
3-Pyridyl	-2.307	-2.109	-1.903	-1.721	-1.545	9.4	15.5
4-Pyridyl	-1.851	-1.670	-1.478	-1.299	-1.148	9.3	14.6
2-Pyridyl 1-oxide	-1.550	-1.396	-1.228	-1.096	-0.950	7.7	12.2
3-Pyridyl 1-oxide	-1.640	-1.484	-1.314	-1.177	-1.015	7.9	12.7
4-Pyridyl 1-oxide	-1.673	-1.504	-1.340	-1.186	-1.024	8.2	13.0

DISCUSSION

For the ethyl β -pyridylacrylates, $\log A$ values are constant (even for the 2-isomer) within the limits of experimental error, and are of the same order as for ethyl benzoate

¹ Brynmor Jones and Watkinson, *J.*, 1958, 4064.² Falkner and Harrison, *J.*, 1960, 1171.³ Marvel, Coleman, and Scott, *J. Org. Chem.*, 1955, **20**, 1785.⁴ McElvain and Johnson, *J. Amer. Chem. Soc.*, 1941, **63**, 2213.⁵ Pannizzon, *Helv. Chim. Acta*, 1941, **24**, 24E.⁶ Katritzky, *J.*, 1955, 2581.⁷ Katritzky and Monro, *J.*, 1958, 150.⁸ Katritzky, Monro, and Beard, *J.*, 1958, 3721.

in the same solvent.² A similar observation was made by Brynmor Jones and Watkinson¹ in discussing the rates of alkaline hydrolysis of substituted ethyl cinnamates. In view of the sensitivity to experimental error of the E values obtained from the Arrhenius plot, we have calculated a quantity $\Delta E = 2.303RT (\log_{10} k - \log_{10} k_0)$ (k_0 is the rate constant for ethyl benzoate). $\log A$ being assumed constant, ΔE is the difference in activation energies for the two esters. ΔE was calculated for each of the five temperatures and mean values are recorded in Table 2; the quantities in parentheses were calculated similarly for the ethyl pyridinecarboxylates. Rate constants for the hydrolysis of ethyl benzoate at 15°, 20°, and 30° were interpolated from an Arrhenius plot of the values given previously.²

TABLE 2.
RCH:CH:CO₂Et.

R	2-Pyridyl	3-Pyridyl	4-Pyridyl
ΔE (kcal. mole ⁻¹)	1.58	1.52 (2.19)	2.11 (3.18)

In both series the ring nitrogen atom exerts a powerful electron-attracting effect leading to a decrease in activation energy at all positions. As expected, the effect is greater at the 4- than at the 3-position, and is considerably reduced by transmission through the -C:C- system. The value of ΔE for the 2-position is lower than expected; although steric hindrance to attack on the ethoxycarbonyl group is unlikely, conjugative transmission of electronic effects at a ring carbon atom through the -CH:CH·CO₂Et system may be adversely affected by steric hindrance in the 2-isomer.

We have previously shown² that an equation $\log k = \chi + \rho\sigma$ is consistent with the rates of alkaline hydrolysis of the ethyl pyridine-3- and -4-carboxylates and their 1-oxides, and of several other reactions. In all these reactions the reaction site is a carbon atom directly attached to the heterocyclic ring. The quantity $1/\rho \log_{10} (k_4/k_3)$, *i.e.*, $\sigma_4 - \sigma_3$, has the value 0.31 for the pyridines and 0.12 for the 1-oxides. To test the applicability of this equation in the present case, a value of ρ for the alkaline hydrolysis of ethyl cinnamates in 70% aqueous ethanol is needed. The results obtained by Brynmor Jones and Watkinson¹ for the hydrolysis of ethyl cinnamates in 85% aqueous ethanol give a satisfactory linear plot of $\log k$ against σ , from which an approximate value of $\rho = 1.35$ can be deduced. Since results on a series of substituted ethyl benzoates⁹ suggest that the accuracy with which the individual rates fit the Hammett equation is probably less than the variations in ρ associated with small changes in solvent composition, and in the absence of the required data for 70% aqueous ethanol, we assume that the value $\rho = 1.35$ is of the correct order for this solvent also. For the ethyl β -pyridylacrylates the present results then give $1/\rho \log_{10} (k_4/k_3) = 0.32$. This suggests that the modified Hammett equation is applicable here also, and that conjugative transmission of electron withdrawal from the ring carbon atoms to the ethoxycarbonyl group differs little in the pyridylacrylates and cinnamates.

For the 1-oxides the $\log A$ values are again closely similar, although unexpectedly low; the average value is 7.9 as compared with 9.1 for the pyridines. In consequence, despite their relatively low activation energies, the ethyl β -pyridylacrylate 1-oxides hydrolyse at only about one twentieth of the rate of the ethyl pyridinecarboxylate 1-oxides. The order of rates for the ethyl β -pyridylacrylate 1-oxides is $2 > 3 \simeq 4$. The expression $1/\rho \log_{10} (k_4/k_3)$ (taking $\rho = 1.35$) in this case gives the value 0.02; the expected value is 0.12. The pK values of the β -pyridylacrylic acid 1-oxides also fail to satisfy the modified Hammett equation, the values for the 3- and 4-acids being almost identical (4.81 and 4.82).

We have previously suggested,² that the pronounced electron withdrawal brought about by the 1-oxide group is primarily a "direct" effect. The present observations provide further evidence for this. Since the effect should diminish rapidly with increase in distance from the 1-oxide group, the ethyl β -pyridylacrylate 1-oxides would be expected

⁹ Falkner, unpublished observations.

to hydrolyse much more slowly than the ethyl pyridinecarboxylate 1-oxides. Further, although insufficient information is at present available to permit a quantitative estimate of the relative distances of the ethoxycarbonyl group from the 1-oxide function in the three esters to be made, it seems likely that the distance will not differ greatly in the 3- and 4-isomers, as required if our explanation is correct.

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