Acid–Base Equilibria of Nitropyridines in Protium Oxide and in Deuterium Oxide

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Equilibrium constants for the dissociation of 2-, 3-, and 4-$NO_2{\cdot}C_5H_4NH^+$ in H_2O have been measured as a function of temperature in the range 3—70 °C by spectrophotometric determination of acid–base concentration ratios in aqueous solution of constant ionic strength (0·02M) or in aqueous sulphuric acid. Thermodynamic functions (ΔG°, ΔH°, and ΔS°) have been calculated for these equilibria as well-behaved functions of temperature and compared with those relative to acid–base equilibrium of unsubstituted pyridine. Entropy values for the above reactions are nearly equal, so that the free-energy differences, due to the different acidities, are mainly found as differences between the corresponding enthalpies. Equilibrium constants for the dissociation of 2-, 3-, and 4-$NO_2{\cdot}C_5H_4ND^+$ in D_2O have also been measured at 298·2 K. Isotope effects seem to be mainly determined by solvation characteristics of the system.

SOME recent studies[1-3] on amino- and nitro-substituted pyridines have provided evidence supporting the interpretation of solvatochromism observed with the highly polar aminonitropyridines in terms of inter- and intramolecular hydrogen bonding, as well as of transition polarizability. The influence of amino- and nitro-groups in the pyridine ring on protonation equilibria was discussed[3] on the basis of electrical characteristics of substituents and electron availability of reaction site. Being interested in the acid–base equilibria of amino- and nitro-substituted pyridines as a means of examining protonation thermodynamically, we have investigated dissociation equilibria (1) and (2) of nitropyridinium ion in protium oxide and in deuterium oxide, with R = 2-, 3-, and 4-NO_2.

$$\mathrm{RC_5H_4NH^+} \underset{\mathrm{H_2O}}{\overset{K_a}{\rightleftharpoons}} \mathrm{RC_5H_4N + H^+} \qquad (1)$$

$$\mathrm{RC_5H_4ND^+} \underset{\mathrm{D_2O}}{\overset{K_a}{\rightleftharpoons}} \mathrm{RC_5H_4N + D^+} \qquad (2)$$

EXPERIMENTAL

Materials.—The preparation and purification of nitropyridines have been described.[3] Solvents and reagents used earlier were employed as indicated.[3,4] Concentrated D_2SO_4 was a Merck product (isotopic purity 99·4%).

Measurements of pK_a.—The technique has been described.[3,4] For equilibria (1) and (2) with R = 2-NO_2, equation (3) was used, the activity coefficients ratio being assumed equal

$$\mathrm{p}K_a = \log([\text{acid}]/[\text{base}]) + H_0\ (D_0) \qquad (3)$$

to the corresponding ratio of amine indicators employed for the measurement of the Hammett acidity function H_0 (D_0). Variation of H_0 values with temperature was evaluated from literature data.[5]

RESULTS AND DISCUSSION

Equilibrium (1) in protium oxide (R = 3- and 4-NO_2) or protium oxide–protiosulphuric acid solutions (R = 2-NO_2), depending on pK_a values, was measured as a function of temperature in the range 3—70 °C. Equilibrium (2) in deuterium oxide or deuterium oxide–deuteriosulphuric acid solutions was studied only at 25 °C.

The acid–base concentration ratio was determined spectrophotometrically in buffered solutions at constant ionic strength (0·02M) or in acid solutions with known values of the Hammett acidity function. Results in the form of pK_a values and their standard deviations are in Table 1. Plots of log K_a against $1/T$ showed a slight but significant curvature indicating that the assumption of temperature-independent enthalpy (ΔH°) and entropy (ΔS°) values is not valid for reaction (1). The very slight departure from linearity suggested, however, a low value of ΔC_p, the difference between molar heat capacities of products and reactants.

TABLE 1

pK_a (K_a in mol l^{-1}) for reactions (1) and (2)

pK_a Values for reaction (1) as a function of temperature

T/K	2-$NO_2{\cdot}C_5H_4NH^+$ in H_2O	3-$NO_2{\cdot}C_5H_4NH^+$ in H_2O	4-$NO_2{\cdot}C_5H_4NH^+$ in H_2O
276·2	−2·40 ± 0·02	0·68 ± 0·02	1·18 ± 0·04
298·2	−2·06 ± 0·04	0·79 ± 0·03	1·23 ± 0·03
313·7	−1·78 ± 0·05	0·87 ± 0·03	1·28 ± 0·03
329·3	−1·57 ± 0·05	0·91 ± 0·03	1·31 ± 0·02
343·6	−1·50 ± 0·03	0·98 ± 0·03	1·33 ± 0·03

pK_a Values for reaction (2) at 298·2 K

2-$NO_2{\cdot}C_5H_4ND^+$ in D_2O	3-$NO_2{\cdot}C_5H_4ND^+$ in D_2O	4-$NO_2{\cdot}C_5H_4ND^+$ in D_2O
−1·58 ± 0·03	1·26 ± 0·02	1·72 ± 0·02

The free-energy changes ΔG° of reaction (1) were fitted to the thermodynamic equation (4) that represents

$$\Delta G^\circ = \Delta H_0{}^\circ - AT\ln T + IT\ (\text{cal mol}^{-1}) \qquad (4)$$

ΔG° as a function of temperature in the particular case in which A ($= \Delta C_p = \mathrm{d}\Delta H^\circ/\mathrm{d}T$) can be considered constant in the temperature range investigated or, more properly, when precision of data does not allow a greater complexity to give the statistically best representation. The values of the constants $\Delta H_0{}^\circ$/cal mol^{-1}, A, and I/cal mol^{-1} K^{-1} for data of reaction (1) were obtained by

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[3] I. R. Bellobono and G. Favini, *J. Chem. Soc.* (*B*), 1971, 2034.

[4] I. R. Bellobono and P. Beltrame, *J. Chem. Soc.* (*B*), 1969, 620.

[5] C. D. Johnson, A. R. Katritzky, and S. A. Shapiro, *J. Amer. Chem. Soc.*, 1969, **91**, 6654.

an optimisation procedure. They are given in Table 2. Thermodynamic functions ΔG° [equation (4)], ΔH° [$= \Delta H_0^\circ + AT$], and ΔS° [$= A(1 + \ln T) - I$] for reaction (1) could thus be evaluated as continuous, well-behaved functions of temperature. Their values at 298·2 K are reported in Table 2, together with those relative to acid–base equilibrium of unsubstituted pyridine [4] for comparison.

It can be observed that entropy values for the above reactions are nearly equal. This is not surprising, since reaction (1) in aqueous solution is an isoelectronic reaction.[6] Hence solvation factors, associated with entropy changes, are not expected to be appreciably influenced by substituents. Further, differences in entropy for an acid and its conjugate base have been shown to remain approximately constant for a series of similar acids.[7] The free-energy differences, due to the different acidities, are therefore mainly found as differences between the corresponding enthalpies. This fact indicates that thermodynamics of acid–base equilibria of nitropyridines and parent compound is principally governed by the enthalpy of protonation, the entropy contribution being almost independent of the presence and position of the nitro-group. A similar situation, although not so pronounced as in the present case, was found for the proton dissociation of substituted anilinium ions.[8]

TABLE 2

Thermodynamic functions and constants for reaction (1)

	$C_5H_5NH^+$ [4]	$2\text{-}NO_2\cdot C_5H_4NH^+$	$3\text{-}NO_2\cdot C_5H_4NH^+$	$4\text{-}NO_2\cdot C_5H_4NH^+$
A/cal mol^{-1} K^{-1}	−2·73	−2·46	−1·97	−2·12
ΔH_0°/cal mol^{-1}	4830	−4986	−1257	−468
I/cal mol^{-1} K^{-1}	−7·85	−6·73	−3·40	−4·88
ΔG°/cal mol^{-1} at 298·2 K *	7102 ± 30	−2810 ± 30	1078 ± 8	1680 ± 20
ΔH°/cal mol^{-1} at 298·2 K †	4020	−5720	−1844	−1100
ΔS°/cal mol^{-1} K^{-1} at 298·2 K †	−10·4	−9·76	−9·80	−9·32

* Experimental values (and standard deviation). † Calculated values [equation (4)]

The similarity of ΔC_p and the low values of the dissociation equilibrium of pyridinium and nitropyridinium ions, which is of the charge type (acid)$^+$/(base), whereas greater values of ΔC_p are not unusual [8-10] for acid ionization processes of the same or of different charge type such as (acid)/(base)$^-$, suggest that differences in hydrogen bonding of the acid–base species concerned and the oxonium ion may be the main contributing factors to ΔC_p.

Conclusions along the same lines may be drawn from the examinations of isotope effects. ΔpK_a ($\equiv pK_a$ in $D_2O - pK_a$ in H_2O), which includes primary and solvent isotope effects, is 0·48, 0·47, and 0·49 at 25 °C for 2-, 3-, and 4-nitropyridinium ions respectively. The best linear correlation between ΔpK_a and pK_a for pyridine and nitropyridines, over a range of 7 pK_a units, satisfies equation (5). The low value of the slope, denoting that ΔpK_a is scarcely influenced by pK_a, seems to point out that isotope effects are principally determined by solvation characteristics of the system.

$$\Delta pK_a \text{ (at 25 °C)} = 0{\cdot}48 + 0{\cdot}005\, pK_a \qquad (5)$$

[2/355 *Received, 17th February,* 1972]

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