Temperature-jump Study of the Mechanism of Base Catalysed Removal of the Intramolecularly Hydrogen-bonded Proton from a Substituted Salicylate Ion in Aqueous Solution

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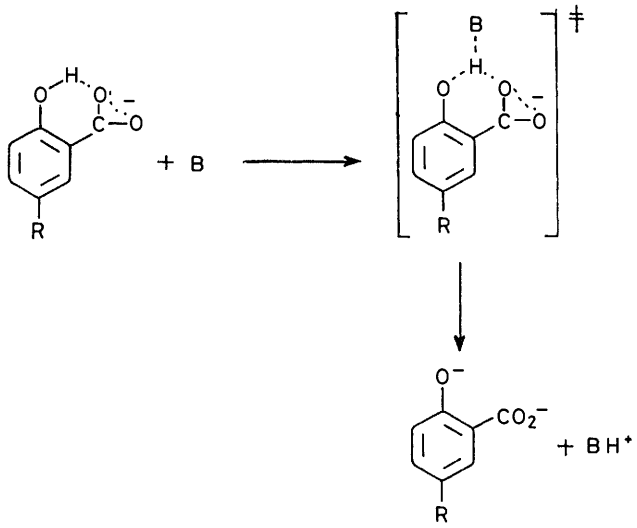
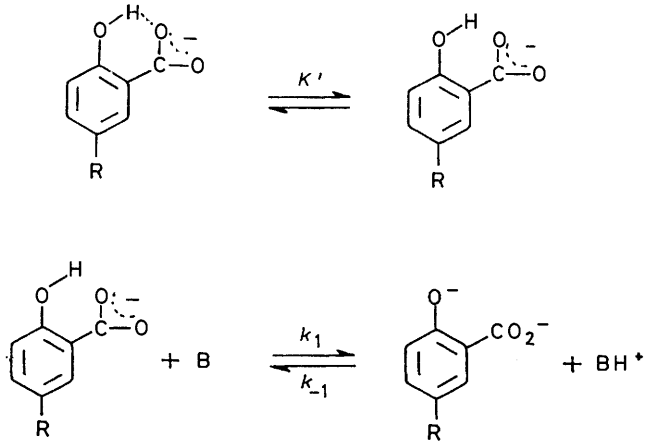
Rate coefficients and equilibrium constants for proton transfer from 4-(3-nitrophenylazo)salicylate ion to hydroxide ion and six amines have been measured in aqueous solution. The rate coefficients are approximately three orders of magnitude below the diffusion limited value and this is explained by the presence of a moderately strong intramolecular hydrogen bond in the salicylate ion. Although the amine bases vary in strength by over 1.5 pK units, the rate coefficients are the same within experimental error and this is accounted for by a two-step mechanism for proton transfer. The first step involves a rapid equilibrium between hydrogen-bonded and non-hydrogen-bonded forms of the salicylate ion and this is followed by base catalysed proton removal from the non-hydrogen-bonded form. A mechanism consisting of direct attack by base on the intramolecularly hydrogen-bonded species will not explain the results.

THERMODYNAMICALLY favourable proton transfer from most oxygen and nitrogen acids in aqueous solution occurs with a diffusion limited rate coefficient (*ca.* 1×10^{10} l mol^{-1} s^{-1}).[1] However when the proton is held in an intramolecular hydrogen bond ionisation occurs more slowly and the lowering in rate below the diffusion limit is often taken as an indication of the strength of the hydrogen bond.[2] The effect of an intramolecular hydrogen bond on the rate of proton transfer can be explained in two ways, as shown in Schemes 1 and 2 for a substituted salicylate ion. In Scheme 1 the proton is removed by direct attack by base on the intramolecularly hydrogen-bonded acid and in the transition state the proton is partially transferred to base (B) and the hydrogen bond is partially broken. In Scheme 2 the hydrogen-bonded acid is in rapid equilibrium with a low



SCHEME 1

concentration of a non-hydrogen-bonded form of the acid. The non-hydrogen-bonded acid presumably behaves as a normal oxygen acid and the proton is removed in a normal proton transfer step.[1] For Scheme 2 the rate



SCHEME 2

coefficient is low because the reaction occurs through a low concentration intermediate. Solvent effects,[3] isotope effects,[4] and variations in rate along a series of intramolecularly hydrogen-bonded acids [5] have been explained in terms of Scheme 1 although the results can be accounted for by Scheme 2.[6] There is no definite evidence to permit a choice between the two possible mechanisms.[6]

Schemes 1 and 2 can be distinguished by measuring rates of proton transfer from an intramolecularly hydrogen-bonded acid to a base B which is chosen so that the hydrogen-bonded acid and BH^+ have similar pK values. In this case the proton in the transition state in Scheme 1 will be roughly half-transferred. For proton transfer through Scheme 2, however, since the equilibrium constant for the first step will be much less than unity, the proton transfer step will be strongly thermodynamically favourable in the forward direction and

[1] M. Eigen, *Angew. Chem. Internat. Edn.*, 1964, **3**, 1; M. Eigen, W. Kruse, G. Maass, and L. de Maeyer, *Progr. Reaction Kinetics*, 1964, **2**, 285.

[2] (*a*) E. M. Eyring and D. L. Cole, 'Nobel Symposium 5,' Interscience, New York, 1967, p. 255; (*b*) M. C. Rose and J. Stuehr, *J. Amer. Chem. Soc.*, 1968, **90**, 7205; (*c*) A. Awwal and F. Hibbert, *J.C.S. Perkin II*, 1977, 1589.

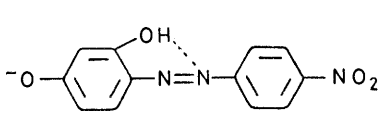
[3] R. P. Jensen, E. M. Eyring, and W. M. Walsh, *J. Phys. Chem.*, 1966, **70**, 2264.

[4] E. M. Eyring and J. L. Haslam, *J. Phys. Chem.*, 1966, **70**, 293.

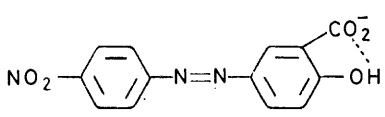
[5] M. H. Miles, E. M. Eyring, W. W. Epstein, and M. T. Anderson, *J. Phys. Chem.*, 1966, **70**, 3490.

[6] A. J. Kresge, *Chem. Soc. Rev.*, 1973, **2**, 475; *Accounts Chem. Res.*, 1975, **8**, 354.

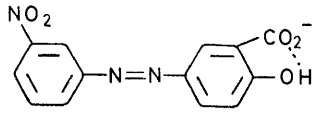
almost negligible proton transfer will have occurred when the transition state is reached. These two possibilities can be distinguished by the values of the Brönsted exponent for base catalysis and therefore it was decided to measure rates of proton transfer from an intramolecularly hydrogen-bonded acid to a series of bases of varying base strength. In choosing a suitable substrate, use was made of Stuehr's tabulations of the reactions of intramolecularly hydrogen-bonded acids



(I)



(II)

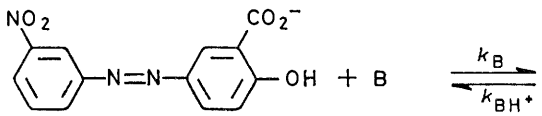


(III)

with hydroxide ion.[2b,7] Preliminary measurements were made with 4-(4-nitrophenylazo)resorcinol (I), 4-(4-nitrophenylazo)salicylate ion (II), and 4-(3-nitrophenylazo)salicylate ion (III). For (I) in aqueous buffer solutions, catalysis by hydroxide ion was predominant over catalysis by buffer species, but buffer catalysis was observed for (II) and (III). We now report the results of detailed measurements of base catalysed proton removal from 4-(3-nitrophenylazo)salicylate ion (III); a preliminary report of this work has been published.[8]

EXPERIMENTAL

Materials.—The substrates (I)—(III) were obtained commercially. Sodium 4-(3-nitrophenylazo)salicylate (III) was obtained from three sources (B.D.H., Eastman–Kodak, and Koch–Light) and the purity varied greatly. The free acid was obtained by acidifying an aqueous solution of the sodium salt, and after extraction with ether and recrystallisation from alcohol, orange crystals were obtained, m.p.



233—235 °C. The acetyl derivative was prepared, m.p. 180 °C (lit., 186 °C). Both the free acid and sodium salt were used in our experiments and gave identical results.

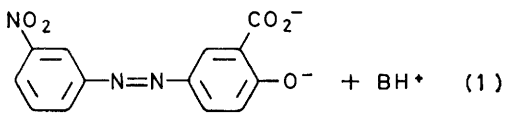
Aqueous amine buffers were used in this work. Triethylamine, *N*-methylpiperidine, and 2,6-dimethylpiperidine were distilled before use. Trimethylammonium chloride was recrystallised from chloroform. A sample of *cis*-1,2,6-trimethylpiperidine was obtained [9] from dimethylpiperidine by methylation with formic acid and formaldehyde and after distillation gave a satisfactory n.m.r. spectrum.[10] Methylation [11] of 2,2,6,6-tetramethylpiperidine with methyl iodide gave 1,2,2,6,6-pentamethylpiperidine [4] which was distilled to give the pure amine (n.m.r. spectrum [12]). Trimethylamine buffers were made up by partially neutralising a weighed amount of the hydrochloride with standard sodium hydroxide solution. The other buffers were made up by weighing out the amine and adding standard hydrochloric acid solution. The ionic strength of all the buffers was maintained at 0.5M by addition of potassium chloride.

Equilibrium Measurements.—Spectrophotometric equilibrium measurements were made with a Unicam SP 8000 spectrophotometer. The solutions were thermostatted at 6.5 °C by circulation of water from an external bath and nitrogen was passed through the cell compartment to prevent condensation. The temperature in the cell was measured using a thermocouple.

Kinetic Measurements.—Chemical relaxation times were measured using the temperature-jump instrument manufactured by Messanlagen Studiengesellschaft. The reaction solution initially thermostatted at 3.2 °C was subjected to a temperature rise of 3.3 °C using a 35 kV discharge from a 0.01 μF capacitor. The heating time under these conditions was measured for a solution of phenol red in a tris(hydroxymethyl)aminomethane buffer (ionic strength 0.5M). The acid–base equilibrium in this solution is established rapidly and measurements at 560 nm showed that heating was completed within 6 μs. A similar result was obtained from measurements with a solution of 4-(3-nitrophenylazo)-salicylate ion in a 0.2M-trimethylamine buffer containing 0.3M-potassium chloride.

RESULTS

Equilibrium Studies.—Measurement of p*K for* 4-(3-*Nitrophenylazo)salicylate Ion.*—The equilibrium between 4-(3-nitrophenylazo)salicylate monoanion and dianion (1) was observed spectrophotometrically in triethylamine



(1)

buffers at 6.5 °C and ionic strength 0.5M. Measurements were made at 348 nm where the monoanion (HA^-) absorbs most strongly and also at 442 nm where the absorbance is due mainly to the dianion (A^{2-}). Solutions were made up by injecting a solution of 4-(3-nitrophenylazo)salicylic acid in dioxan or methanol into aqueous triethylamine buffers of different buffer ratios. The concentration of the salicylic acid was 2.0—6.0 × 10^{-5}M and the final solution contained <0.2% by volume of methanol or dioxan. The hydronium ion concentrations were calculated using equation (2) in which $pK_{Et_3NH^+} = 11.433$ at 6.5 °C and ionic strength 0.5M. Actually the p*K* value of triethylamine is known [13] at 10.0 °C and ionic strength 0.5M and a precise value was calculated at 6.5 °C from the measured enthalpy of ionisation. Equation (3) was used to calculate a p*K* value for 4-(3-nitrophenylazo)salicylate ion from measurements at each buffer

[7] M. C. Rose and J. Stuehr, *J. Amer. Chem. Soc.*, (*a*) 1971, **93**, 4350; (*b*) 1972, **94**, 5532.
[8] F. Hibbert and A. Awwal, *J.C.S. Chem. Comm.*, 1976, 995.
[9] H. K. Hall, *J. Amer. Chem. Soc.*, 1957, **79**, 5444.
[10] J. C. N. Ma and E. W. Warnhoff, *Canad. J. Chem.*, 1965, **43**, 1849.
[11] H. Z. Sommer, H. I. Lipp, and L. L. Jackson, *J. Org. Chem.*, 1971, **36**, 824.
[12] J. J. Delpuech and M. N. Deschamps, *Tetrahedron*, 1970, **26**, 2723.
[13] M. C. Cox, D. H. Everett, D. A. Landsman, and R. J. Munn, *J. Chem. Soc.* (*B*), 19 68, 1373.

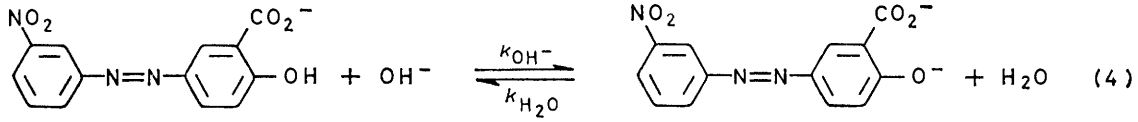
ratio and an average pK_{HA^-} 11.13 ± 0.06 was obtained from results at seven buffer ratios. An approximate result, $pK - \log_{10}[H_3O^+] =$

$$pK_{Et_3NH^+} - \log_{10}[Et_3NH^+]/[Et_3N] \quad (2)$$

$$pK_{HA^-} = -\log_{10}[H_3O^+] - \log_{10}[A^{2-}]/[HA^-] \quad (3)$$

ca. 10.9, under our conditions was calculated from a previous measurement referring to 15.0 °C and ionic strength 0.1M.

Differences in p*K* *between* 4-(3-*Nitrophenylazo*)*salicylate*



Ion and Buffer Species.—The acid dissociation constants of the buffers used in this work have not been measured under our experimental conditions (0.5M ionic strength; 6.5 °C). For trimethylamine [14] and triethylamine,[13] values at infinite dilution and 6.5 °C were calculated from accurate measurements of the heat of ionisation ($\Delta H°$) and p*K* at 10.0 °C. For *N*-methyl-, 2,6-dimethyl-, and 1,2,2,6,6-pentamethylpiperidine approximate values of $\Delta H°$ were calculated from p*K* measurements at two temperatures [9] and were used to calculate p*K* values at 6.5 °C and infinite dilution. A p*K* for *cis*-1,2,6-trimethylpiperidine is known [15] at 33 °C and in order to calculate a value at 6.5 °C it was necessary to use the average of $\Delta H°$ for the other amines. For all the amines it was assumed that the p*K* increased by 0.20 units in going from infinite dilution to ionic strength 0.5M which is the difference observed for triethylamine.[13] The results of these calculations, p*K*(calc.), are shown in Table 1. In

TABLE 1

p*K* Values for amines at 6.5 °C and ionic strength 0.5M

	p*K*(calc)	p*K*(expt)
Trimethylamine	10.42	10.46
N-Methylpiperidine	10.88	10.85
cis-1,2,6-Trimethylpiperidine	11.34	11.33
Triethylamine	11.43	11.43
2,6-Dimethylpiperidine	11.90	11.87
1,2,2,6,6-Pentamethylpiperidine	11.97	12.06

view of the assumptions involved it was thought necessary to make p*K* measurements under our experimental conditions.

The dissociation of 4-(3-nitrophenylazo)salicylate ion was observed spectrophotometrically in buffer solutions made up from the amines at ionic strength 0.5M and 6.5 °C. Measurements in triethylamine buffers have been described in the previous section. For the other amines two buffer ratios were chosen so that 4-(3-nitrophenylazo)salicylate ion was about half-dissociated and the buffer concentrations were 0.05—0.10M. The total concentration of the salicylate ion was also varied. For solutions in each buffer the optical densities were measured at 348 and 442 nm corresponding to the wavelength of maximum absorbance of the anion and dianion respectively. The degree of dissociation of 4-(3-nitrophenylazo)salicylate ion was calculated from the optical density readings at each wavelength and for each buffer an equilibrium constant for reaction (1) was obtained. From the p*K* value of the salicylate ion determined in triethylamine buffers, p*K* values for the amines were obtained, p*K*(expt), and these are compared in Table 1 with the calculated results.

Kinetic Measurements.—*Proton transfer to hydroxide ion.* Kinetic measurements for reaction (4) were made with solutions of 4-(3-nitrophenylazo)salicylate ion (8.4×10^{-5}M) in sodium hydroxide solutions (0.001—0.003M) at an ionic strength of 0.5M and at 6.5 °C. After a temperature jump chemical relaxations were observed at 442 nm. With hydroxide ion in excess the reciprocal relaxation time is given by equation (5) and a plot of the measured reciprocal relaxation time against hydroxide ion concentration was

$$1/\tau = k_{OH^-}[OH^-] + k_{H_2O}[H_2O] \quad (5)$$

accurately linear. The slope and intercept of this plot gave $k_{OH^-} = 2.4 \pm 0.2 \times 10^7$ l mol^{-1} s^{-1} and $k_{H_2O}[H_2O] = 1.1 \pm 0.2 \times 10^4$ s^{-1}. The ratio k_{OH^-}/k_{H_2O} $[H_2O] = 2.2 \pm 0.6 \times 10^3$ l mol^{-1} is in agreement with the value of the equilibrium constant (1.9×10^3 l mol^{-1}) calculated from the acid dissociation constant of 4-(3-nitrophenylazo)salicylate ion and the ionic product of water [16] under our conditions. The result $k_{OH^-} = 1.6 \times 10^7$ l mol^{-1} s^{-1} referring to 6.2 °C and an ionic strength 0.1M has been obtained previously.[7b]

Proton transfer to buffer species. Temperature-jump measurements were made to obtain values of the rate coefficients k_B and k_{BH^+} for reaction (1) with B as trimethylamine, *N*-methylpiperidine, *cis*-1,2,6-trimethylpiperidine, triethylamine, 2,6-dimethylpiperidine, and 1,2,2,6,6-pentamethylpiperidine. Chemical relaxation times were measured for 4-(3-nitrophenylazo)salicylate ion in buffer solutions made up from these amines and the experimental conditions were similar to those for the measurements in sodium hydroxide solutions. The temperature (6.5 °C) was chosen because at higher temperatures the reactions at high buffer concentrations are too fast to follow; even at 6.5 °C some of the reactions occur with half-lives of < 10 μs. The ionic strength (0.5M) was chosen so that the heating time of the solution was as short as possible. The buffers were always in excess over the substrate and over hydroxide ion. Under these conditions and providing the acid–base reaction of the buffer with hydroxide ion is rapid, the reciprocal relaxation time is given by equation (6), in which $r = [BH^+]/[B]$.

$$1/\tau = k_{OH^-}[OH^-] + k_{H_2O}[H_2O] + (k_B + k_{BH^+}r)[B] \quad (6)$$

For each amine, measurements of the reciprocal relaxation time were made at two buffer ratios and at different buffer concentrations. At a given buffer ratio and fixed pH, the observed relaxation times were linearly dependent on buffer concentration. The results are shown in Table 2. Typical results in *cis*-1,2,6-trimethylpiperidine buffers are shown in Figure 1. The gradients of these plots give values of $k_B + k_{BH^+}r$. For measurements in trimethylamine, *N*-methylpiperidine, *cis*-1,2,6-trimethylpiperidine, and triethylamine buffers, individual values for k_B and k_{BH^+} were calculated from the gradients of these plots at two buffer

[14] D. H. Everett and W. F. K. Wynne-Jones, *Proc. Roy. Soc.*, 1941, **A177**, 499.

[15] J. J. Delpuech, F. Sirieux, and M. N. Deschamps, *Org. Magnetic Resonance*, 1972, **4**, 651.

ratios. The ratios k_B/k_{BH^+} were compatible with the equilibrium constants obtained spectrophotometrically and this is shown in Table 3. The results in 2,6-dimethyl- and 1,2,2,6,6-pentamethyl-piperidine buffers were treated differently. In these cases, the gradients of the plots of reciprocal relaxation time against buffer concentration did not change very much with a change in the buffer ratio and individual values of k_B and k_{BH^+} could not be obtained accurately. For these buffers the values of k_B are much larger than the values of k_{BH^+}. In order to obtain individual rate coefficients, the gradients from the buffer concentration plots ($k_B + k_{BH^+}r$) were combined with the equilibrium constants (k_B/k_{BH^+}) determined spectrophotometrically. The results at two buffer ratios were averaged and these are shown in Table 3.

The intercepts of the plots of reciprocal relaxation time against buffer concentration at fixed buffer ratio are given by $k_{OH^-}[OH^-] + k_{H_2O}[H_2O]$. The values of k_{OH^-} and $k_{H_2O}[H_2O]$ are known from the measurements in sodium hydroxide solutions. For each buffer, the hydroxide ion concentration was calculated from the known pK of the buffer and the ionic product of water under our conditions [16] (3.92×10^{-15}). The calculated values of $k_{OH^-}[OH^-] + k_{H_2O}[H_2O]$ were in fair agreement with the measured intercepts.

[16] H. S. Harned and B. B. Owen, 'Physical Chemistry of Electrolyte Solutions,' Reinhold, New York, 1958, 3rd edn., pp. 635, 638, and 752.

TABLE 2

Proton transfer to buffer species at 6.5 °C and ionic strength 0.5M

Trimethylamine								
$[BH^+]/[B] = 0.33$								
$10^3[B]$/M	4.5	6.0	7.5	9.0	10.5	7.5		
$10^{-4}\tau^{-1}$/s^{-1}	4.0 ± 0.2	4.8 ± 0.3	5.9 ± 0.4	6.2 ± 0.4	7.6 ± 0.3	9.1 ± 0.6		
$[BH^+]/[B] = 1.0$								
$10^3[B]$/M	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0
$10^{-4}\tau^{-1}$/s^{-1}	2.2 ± 0.3	2.7 ± 0.4	3.1 ± 0.2	3.6 ± 0.3	4.1 ± 0.4	5.1 ± 0.3	6.2 ± 0.3	6.4 ± 0.6
N-Methylpiperidine								
$[BH^+]/[B] = 0.50$								
$10^2[B]$/M	1.0	1.5	2.0	2.5	3.0			
$10^{-4}\tau^{-1}$/s^{-1}	5.6 ± 0.2	6.0 ± 0.3	7.4 ± 0.5	9.4 ± 1.0	10.9 ± 1.0			
$[BH^+]/[B] = 2.0$								
$10^2[B]$/M	0.5	1.0	1.5	2.0				
$10^{-4}\tau^{-1}$/s^{-1}	5.1 ± 0.6	7.0 ± 0.4	9.7 ± 1.5	13.2 ± 1.0				
cis-1,2,6-Trimethylpiperidine								
$[BH^+]/[B] = 0.50$								
$10^2[B]$/M	1.0	1.5	2.0	2.5	3.0	3.5		
$10^{-4}\tau^{-1}$/s^{-1}	5.1 ± 0.2	5.8 ± 0.2	6.6 ± 0.3	7.4 ± 0.4	8.3 ± 0.8	9.4 ± 0.4		
$[BH^+]/[B] = 2.0$								
$10^2[B]$/M	0.5	1.0	1.5	2.0	2.5	3.0		
$10^{-4}\tau^{-1}$/s^{-1}	3.5 ± 0.2	4.8 ± 0.3	5.4 ± 0.2	6.2 ± 0.3	8.1 ± 0.3	9.5 ± 0.9		
Triethylamine								
$[BH^+]/[B] = 0.5$								
$10^2[B]$/M	1.0	1.5	2.0	2.5	3.0			
$10^{-4}\tau^{-1}$/s^{-1}	6.1 ± 0.4	6.7 ± 0.4	8.3 ± 0.5	9.2 ± 0.5	10.5 ± 0.4			
$[BH^+]/[B] = 2.0$								
$10^2[B]$/M	0.5	0.75	1.0	1.25	1.5	2.0	2.5	
$10^{-4}\tau^{-1}$/s^{-1}	3.5 ± 0.2	4.5 ± 0.2	5.2 ± 0.2	5.2 ± 0.2	6.0 ± 0.2	7.4 ± 0.3	8.7 ± 0.3	
2,6-Dimethylpiperidine								
$[BH^+]/[B] = 2.0$								
$10^2[B]$/M	1.0	1.5	2.0	2.5	3.0			
$10^{-4}\tau^{-1}$/s^{-1}	5.6 ± 0.2	7.0 ± 0.2	8.6 ± 0.3	10.0 ± 0.3	10.7 ± 0.3			
$[BH^+]/[B] = 5.0$								
$10^2[B]$/M	0.5	0.75	1.0	1.25	1.50	1.75	2.0	
$10^{-4}\tau^{-1}$/s^{-1}	3.6 ± 0.1	4.2 ± 0.4	4.9 ± 0.3	5.6 ± 0.2	6.3 ± 0.2	7.0 ± 0.3	7.4 ± 0.2	
1,2,2,6,6-Pentamethylpiperidine								
$[BH^+]/[B] = 5.0$								
$10^3[B]$/M	2.5	4.0	5.0	6.0	7.5	9.0	10.0	
$10^{-4}\tau^{-1}$/s^{-1}	3.3 ± 0.1	3.8 ± 0.1	4.2 ± 0.2	4.7 ± 0.2	4.6 ± 0.1	5.2 ± 0.2	5.4 ± 0.2	
$[BH^+]/[B] = 10.0$								
$10^3[B]$/M	2.5	5.0	7.5	10.0				
$10^{-4}\tau^{-1}$/s^{-1}	2.7 ± 0.1	3.1 ± 0.1	3.7 ± 0.1	4.4 ± 0.3				

DISCUSSION

The rate coefficients for proton transfer from 4-(3-nitrophenylazo)salicylate ion to hydroxide ion and to amines are approximately three orders of magnitude below the diffusion limited values expected for thermodynamically favourable proton transfer from an oxygen acid. This results from the presence of a moderately strong intramolecular hydrogen bond in 4-(3-nitrophenylazo)salicylate ion. The data in Table 3 provide two pieces of evidence to distinguish between the mechanisms

TABLE 3

	$10^{-6}k_B$	$10^{-6}k_{BH^+}$	K *
Trimethylamine	2.5 ± 1.0	9.5 ± 2.0	0.21
N-Methylpiperidine	1.7 ± 0.5	2.1 ± 0.3	0.52
cis-1,2,6-Trimethylpiperidine	1.3 ± 0.3	0.53 ± 0.1	1.6
Triethylamine	1.7 ± 0.3	0.47 ± 0.1	2.0
2,6-Dimethylpiperidine	1.85 ± 0.2	0.30 ± 0.06	5.5
1,2,2,6,6-Pentamethylpiperidine	1.4 ± 0.3	0.17 ± 0.03	8.5

* Measured spectrophotometrically.

shown in Schemes 1 and 2. For proton transfer through Scheme 2, the observed rate coefficients are given by equations (7) and (8) assuming the hydrogen-bond

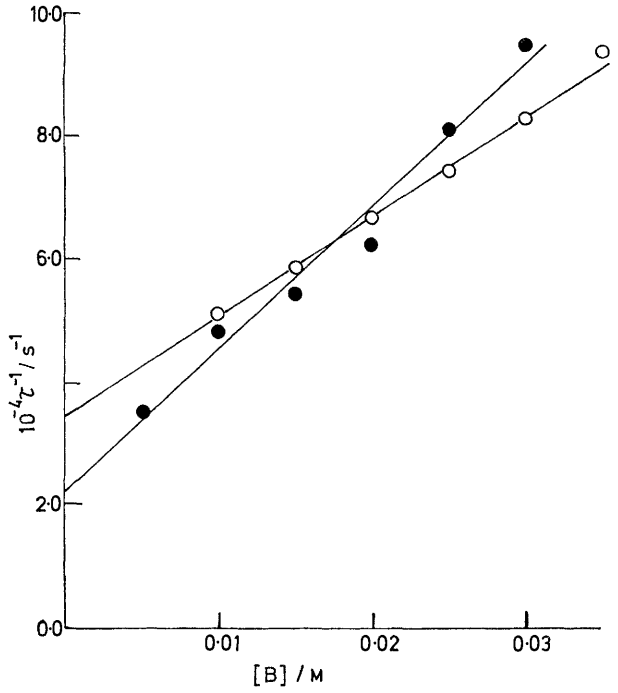


FIGURE 1 Variation of reciprocal relaxation time with buffer concentration for aqueous solutions of 4-(3-nitrophenylazo)-salicylate ion in *cis*-1,2,6-trimethylpiperidine(B) buffers at buffer ratio $[BH^+]/[B]$ 0.5 (○) and $[BH^+]/[B]$ 2.0 (●)

equilibrium is rapid compared with the proton transfer step. Since a moderately strong hydrogen bond is

$$k_B = K'k_1 \quad (7)$$

$$k_{BH^+} = k_{-1} \quad (8)$$

present in 4-(3-nitrophenylazo)salicylate ion the equilibrium constant for breakage of the intramolecular hydrogen bond in the first step of this Scheme is much less than unity ($K' < 1$). The equilibrium constants for the overall reaction between 4-(3-nitrophenylazo)-salicylate ion and the amines range from 0.21 to 8.5 (Table 3) and it therefore follows that the proton transfer step in Scheme 2 for all the amines is strongly thermodynamically favourable in the forward direction. This step involves the non-hydrogen-bonded form of the salicylate ion and if this species behaves as a normal oxygen acid, k_1 will be diffusion limited and independent of the basicity of B. From equation (7) it is therefore predicted that the base catalytic coefficient (k_B) should be the same for all the amine bases, and this is observed experimentally as shown in Table 3. The value of k_1 expected for diffusion controlled proton transfer from an oxygen acid to an amine [1] is *ca.* 2×10^9 l mol^{-1} s^{-1}. Hence from equation (7) the value of K' for the hydrogen-bonding equilibrium in 4-(3-nitrophenylazo)salicylate ion is *ca.* 1×10^{-3}. The measured rate coefficient for proton transfer from 4-(3-nitrophenylazo)salicylate ion to hydroxide ion (k_{OH^-} $2.4 \pm 0.2 \times 10^7$ l mol^{-1} s^{-1}) is higher than that observed for proton transfer to amines (k_B $1.8 \pm 0.3 \times 10^6$ l mol^{-1} s^{-1}). This arises because the diffusion controlled value for k_1 will be higher for hydroxide ion than for the amines.[1] If we assume $k_1 = 2 \times 10^{10}$ l mol^{-1} s^{-1} for proton transfer involving hydroxide ion then from equation (7) the same value $K' = 1 \times 10^{-3}$ is obtained from the results for proton transfer to hydroxide ion and to the amines. This value is compatible with the pK difference of *ca.* 3 units between phenol and salicylate ion assuming the pK difference results entirely from the presence of the intramolecular hydrogen bond in the latter.

The reverse rate coefficient (k_{BH^+}) in reaction (1) is identified in Scheme 2 with the rate coefficient k_{-1} which refers to thermodynamically unfavourable protonation of an oxygen anion. For a normal proton transfer this rate coefficient will vary inversely as the equilibrium constant of the proton transfer step. Since the value of the equilibrium constant for the first step in Scheme 2 is independent of the amine buffer, this variation is illustrated by the inverse dependence of k_{BH^+} on the equilibrium constant of the overall reaction (K) as given in Table 3.

The results are plotted in Figure 2 as an Eigen plot which expresses the dependence of $\log_{10}k_B$ and $\log_{10}k_{BH^+}$ on ΔpK = pK[4-(3-nitrophenylazo)salicylate ion] − pK(BH^+). The constancy of k_B with a variation in base strength is shown by the slope $\beta = 0.0 \pm 0.1$ of the plot

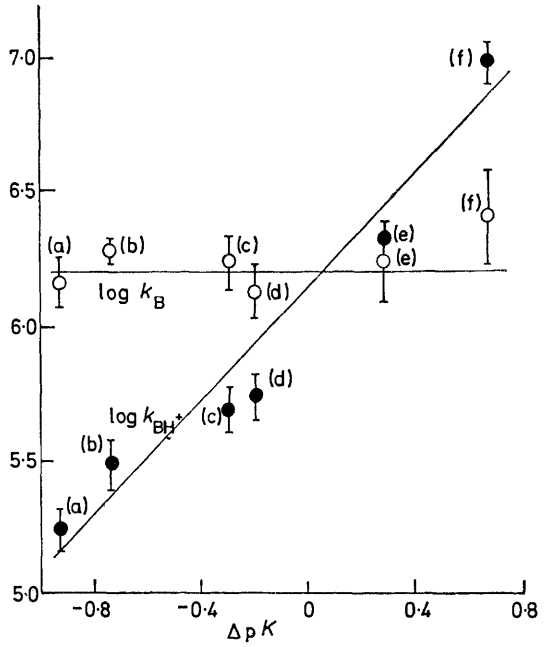


FIGURE 2 Eigen plot of $\log_{10}k_{BH^+}$ and $\log_{10}k_B$ against ΔpK = pK[4-(3-nitrophenylazo)salicylate ion] − pK(BH^+) where the points refer to B = (a) 1,2,2,6,6-pentamethylpiperidine; (b) 2,6-dimethylpiperidine; (c) triethylamine; (d) *cis*-1,2,6-trimethylpiperidine; (e) *N*-methylpiperidine; and (f) trimethylamine

of $\log_{10}k_B$ against ΔpK and the inverse relation between k_{BH^+} and equilibrium constant is shown by the slope $\alpha = 1.0 \pm 0.1$ of the plot of $\log_{10}k_{BH^+}$ against ΔpK. The

slopes α and β are Brönsted exponents for the proton transfer step in Scheme 2 and the values indicate that in the transition state the proton is firmly held by the salicylate ion and negligible transfer to the base has occurred, as expected for a diffusion controlled forward reaction.

The observed dependence of k_B and k_{BH^+} on base strength is incompatible with the mechanism shown in Scheme 1. For a single step proton transfer involving acid–base pairs with similar acidity, the transition state is expected to be roughly symmetrical with the proton half-transferred.[6] Evidence is available to support this hypothesis for proton transfers involving oxygen or nitrogen acids [1] and carbon acids.[17] In this case the values of k_B and k_{BH^+} should vary as the strength of the base is varied and if it is assumed that the value of the Brönsted exponent is related to the degree of proton transfer in the transition state, the slopes of the plots in Figure 2 would be $\alpha = \beta = ca.\ 0.5$. This is not observed.

The linear dependence of reciprocal relaxation time on base concentration is explained by Scheme 2 assuming the equilibrium between hydrogen-bonded and non-hydrogen-bonded forms of the salicylate ion is established more rapidly than the proton transfer step involving buffer. This means that formation of the intramolecular hydrogen bond occurs with a rate coefficient which is greater than $ca.\ 6 \times 10^7\ s^{-1}$. A rate coefficient of $3 \times 10^7\ s^{-1}$ has been obtained [18] for formation of the intramolecular hydrogen bond in methyl salicylate from ultrasonic absorption measurements in organic solvents.

Similar results to those in Table 3 have recently been found for proton transfer from an intramolecularly hydrogen-bonded ammonium ion to phenolate ions in 70% dimethyl sulphoxide–water (v/v).[19] The measured rate coefficients for phenolate ions differing in pK by 5 units were almost constant. However since all the reactions were strongly thermodynamically favourable with $\Delta pK < -1.8$ the results are also compatible with the single step mechanism through a transition state with a low degree of proton transfer. It is in the region around $\Delta pK = 0$ where the largest difference in Brönsted exponents for the two mechanisms will be observed.

Several studies have been carried out in which rates of proton transfer from a series of similar intramolecularly hydrogen-bonded acids to a single base (hydroxide ion) have been measured.[2b,5,7,20] However no definite mechanistic conclusions can be reached from the size of the Brönsted exponent. For the single step mechanism through a transition state in which the proton is partially transferred a Brönsted exponent of $\alpha\ ca.\ 0.5$ may be anticipated. However a Brönsted exponent of this size is equally compatible with the two-step mechanism in which a change in substituent on the hydrogen-bonded acid has two effects; the equilibrium between the hydrogen-bonded and non-hydrogen-bonded forms of the acids is affected as well as the proton transfer step.

Further evidence in support of the two-step mechanism can be deduced from the results for proton transfer to the bulky bases *cis*-1,2,6-trimethyl- and 1,2,2,6,6-pentamethyl-piperidine, although the evidence is much less compelling than that based upon the values of the Brönsted exponents. The values of k_B for the bulky bases are the same within experimental error as those for unhindered bases (Table 3). This is the expected result for Scheme 2 involving a normal proton transfer step. Normal proton transfers are thought to occur through bridging water molecules [1,21] and since the reactants do not therefore approach closely, the reactions are not sterically hindered. For the single-step mechanism it is unlikely that proton transfer would occur through a bridging water molecule since the intramolecularly hydrogen-bonded acid is unable to form an external hydrogen bond with solvent. For this mechanism a steric effect might have been expected. For example,[22] proton transfer between *cis*-1,2,6-trimethylpiperidine and its conjugate acid in water shows no steric effect (k 1.13×10^8 l mol^{-1} s^{-1}). However in dimethyl sulphoxide the reaction occurs slowly (k 2.6×10^4 l mol^{-1} s^{-1}) since direct proton transfer without a bridging water molecule now operates and steric hindrance is then observed.

Our conclusion in favour of the two-step mechanism for proton transfer from an intramolecularly hydrogen-bonded acid makes available a method for measuring the strengths of intramolecular hydrogen bonds. If it can be assumed that the two-step mechanism applies for proton transfer from all intramolecularly hydrogen-bonded acids, then the amount by which the rate coefficient for thermodynamically favourable proton transfer is lower than the diffusion limit can be identified with the equilibrium constant between hydrogen-bonded and non-hydrogen-bonded forms of the acid.

The distinction between the two mechanisms has further implications, in relation to the timing of solvation changes for proton transfers in general. Proton transfers in solution may involve several processes,[6] formation of an encounter complex, reorientation of the reactants and solvent within the encounter complex to give a reaction complex, proton transfer, and separation of products. It has been suggested [6] that a choice between the two possible mechanisms for proton transfer from an intramolecularly hydrogen-bonded acid will provide evidence as to whether solvation changes accompany proton transfer or whether solvent reorganisation and proton transfer occur as separate reaction steps. Our

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evidence in favour of a two-step mechanism indicates that for proton transfer from a hydrogen–bonded acid some solvation changes occur before the proton is transferred. The first step in the mechanism involves conversion of the internally hydrogen-bonded acid which is poorly solvated into a species which is able to form a hydrogen bond with solvent. The proton transfer then occurs as a separate reaction step.

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