Properties of Hydrogen Bonds in 5,8-Dihydroxy-1,4-naphthoquinone and 1,4-Dihydroxy-9,10-anthraquinone; Reaction with Bases in Aqueous Solution

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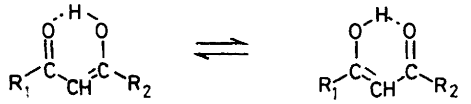
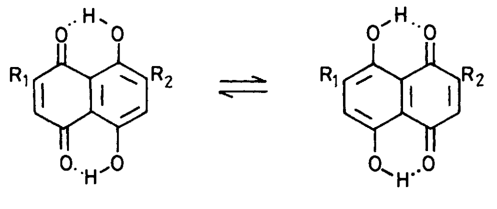
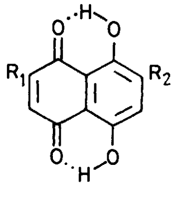
Rate coefficients and equilibrium constants for the dissociation of 5,8-dihydroxy-1,4-naphthoquinone (**1**), pK_1^0 8.51 and pK_2^0 11.49, and 1,4-dihydroxy-9,10-anthraquinone (**3**), pK_1^0 9.85 and pK_2^0 12.28, have been measured in aqueous solution. The effects of a methyl substituent in (**1**) and a sulphonate substituent in (**3**) have been studied. The rate coefficients for the first and second dissociation are 25- and 1 000-fold respectively lower than those for normal proton transfers because of a weak intramolecular hydrogen bond in the undissociated acids and a moderately strong hydrogen bond in the monoanions.

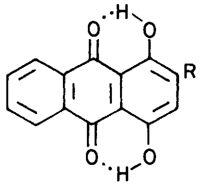
The intramolecular hydrogen bond in the enol form of β-diketones[1] has an important effect on their acid–base behaviour[2] and tautomerism. The hydrogen bond is non-centred and best described by a potential function with two minima[1,3] between which the proton oscillates sufficiently rapidly that the ^{13}C n.m.r. spectra of the enol forms of unsymmetrically substituted β-diketones correspond to the spectra for a time average of the two isomers in equation (1).[4]


(1)

There is evidence from the i.r. spectrum that equilibration takes place on the picosecond time-scale.[5] This is the usual observation for intramolecular hydrogen bonds.[6] As for other intramolecularly hydrogen-bonded species,[7] the rate coefficient for proton transfer from the enol of pentane-2,4-dione to an external base is reduced compared with that for normal proton transfer from a hydroxy group.[8] In some of these respects, the closely related intramolecular hydrogen bond in substituted 5,8-dihydroxy-1,4-naphthoquinones shows different properties. For 5,8-dihydroxy-2-methyl-1,4-naphthoquinone [R_1 = Me, R_2 = H in equation (2)], the ^1H n.m.r. spectrum of a solution in CD_2Cl_2 has been interpreted[9,10] in terms of a predominance of the isomer on the reactant side of equation (2). Although it was considered that the tautomers would not differ greatly in energy, the minor tautomer was not detected. Furthermore, from the n.m.r. spectrum it was concluded that the equilibrium in equation (2) was established slowly.[9] With 5,8-dihydroxy-2,7-dimethyl-1,4-naphthoquinone [R_1 = R_2 = Me in equation (2)], one singlet was observed for the methyl resonance in the ^1H n.m.r. spectrum, indicating that the tautomerisation is now established rapidly, as is the case for 5,8-dihydroxy-1,4-naphthoquinone,[11] [R_1 = R_2 = H in equation (2)]. These differences were attributed to the occurrence of proton tunnelling for 5,8-dihydroxy-1,4-naphthoquinone and the 2,7-dimethyl derivative.[10,12] Since 5,8-dihydroxy-2-methyl-1,4-naphthoquinone (**2**) appears to be unusual in comparison with 5,8-dihydroxy-1,4-naphthoquinone (**1**) and with other intramolecularly hydrogen-bonded species, we have undertaken a comparative study of the proton-transfer behaviour of (**1**) and (**2**) and their monoanions towards an external base. The similar reactions of (**3**) and (**4**) have also been investigated. Some studies with (**4**) have previously been carried out.[13]


(2)


(**1**) R_1 = R_2 = H
(**2**) R_1 = CH_3, R_2 = H


(**3**) R = H
(**4**) R = SO_3^-

Experimental

Materials.—A sample of 5,8-dihydroxy-2-methyl-1,4-naphthoquinone (**2**) was prepared according to published procedures.[14]

Equilibrium Measurements.—The first and second dissociations of the substrates (**1**)—(**4**) occur at sufficiently different pH values that they can be studied separately, although there is some overlap at intermediate pH. Measurements were made spectrophotometrically in aqueous solution at 15 °C and ionic strength 0.1 mol dm^{-3}. The first dissociations, equations (3) and (4), were studied in solutions containing *ca.* 5×10^{-5} mol dm^{-3}

$$H_2A + B \underset{k_{-1}^{BH^+}}{\overset{k_1^{B}}{\rightleftharpoons}} HA^- + BH^+ \qquad (3)$$

$$H_2A + OH^- \underset{k_{-1}^{H_2O}}{\overset{k_1^{OH^-}}{\rightleftharpoons}} HA^- + H_2O \qquad (4)$$

of the substrate [H_2A = (**1**), (**2**), or (**4**)] in the presence of an excess of either carbonate, 2-amino-2-(hydroxymethyl)propane-1,3-diol, or 2-amino-2-methylpropane-1,3-diol as buffer (B), with sodium chloride to maintain constant ionic strength. Because of the lower solubility of (**3**), measurements were made at a concentration of *ca.* 4×10^{-6} mol dm^{-3} in carbonate buffers. For each substrate, absorbance readings (A) were taken at several buffer ratios (r = $[BH^+]/[B]$) at a wavelength where the dissociated species HA^- absorbed strongly [610 nm for (**1**) and (**2**) and 540 nm for (**3**) and (**4**)]. The absorbance (A_{H_2A}) of a solution in which the substrate was entirely in the form of the undissociated acid was obtained from measurements in 0.1 mol dm^{-3} HCl. The absorbance (A_{HA^-}) for a solution in which

Table. Kinetic and equilibrium results for first and second dissociation of dihydroxy-diones (**1**)—(**4**) in aqueous solution[a]

First dissociation

	(**1**)	(**2**)	(**3**)	(**4**)
pK_1^0	8.51 ± 0.05	8.86 ± 0.06	9.85 ± 0.03	9.35 ± 0.05
$10^{-5}K_1^{OH^-}$/dm^3 mol^{-1}	7.5 ± 0.9	3.4 ± 0.4	0.35 ± 0.03	1.9 ± 0.3
$10^{-9}k_1^{OH^-}$/dm^3 mol^{-1} s^{-1}	*ca.* 10	*ca.* 2		*ca.* 7
$10^{-4}k_{-1}^{H_2O}$/s^{-1}	*ca.* 1	*ca.* 0.6		*ca.* 4
K_1^B [B = CO_3^{2-}]	55.7 ± 7		2.6 ± 0.2	14.1 ± 2
K_1^B [B = $(HOCH_2)_3CNH_2$]	1.30 ± 0.2	0.51 ± 0.07		0.32 ± 0.03
K_1^B [B = $(HOCH_2)_2C(Me)NH_2$]		3.64 ± 0.2		
$10^{-7}k_1^B$/dm^3 mol^{-1} s^{-1} [B = $(HOCH_2)_3CNH_2$]	2.1 ± 0.5			1.02 ± 0.2
$10^{-7}k_{-1}^{BH^+}$/dm^3 mol^{-1} s^{-1} [B = $(HOCH_2)_3CNH_2$]	1.6 ± 0.4			3.1 ± 0.6
$10^{-7}k_1^B$/dm^3 mol^{-1} s^{-1} [B = $(HOCH_2)_2C(Me)NH_2$]		2.85 ± 0.1		
$10^{-7}k_{-1}^{BH^+}$/dm^3 mol^{-1} s^{-1} [B = $(HOCH_2)_2C(Me)NH_2$]		0.78 ± 0.03		

Second dissociation

	(**1**)	(**2**)	(**3**)	(**4**)
pK_2^0	11.49 ± 0.1	11.88 ± 0.02	12.28 ± 0.02	12.94 ± 0.03
$10^{-2}K_2^{OH^-}$/dm^3 mol^{-1}	13.6 ± 0.2	5.62 ± 0.3	2.22 ± 0.1	0.84 ± 0.07
$10^{-7}k_2^{OH^-}$/dm^3 mol^{-1} s^{-1}	1.42 ± 0.1	1.45 ± 0.2	1.35 ± 0.3	0.41 ± 0.08
$10^{-4}k_{-2}^{H_2O}$/s^{-1}	1.16 ± 0.3	2.45 ± 0.2	8.0 ± 1	7.0 ± 1

[a] Ionic strength 0.1 mol dm^{-3} and temperature 288 K.

dissociation into HA^- was complete could not be obtained because under conditions where H_2A was almost fully dissociated into HA^-, some dissociaton into A^{2-} was also occurring. Hence the value of the equilibrium constant (K_1^B) for equilibrium (3) was determined from a plot of A against $(A - A_{H_2A})r$, equation (5). The values of K_1^B determined in this way

$$A = -(A - A_{H_2A})r/K_1^B + A_{HA^-} \qquad (5)$$

for each of the substrates with various buffers are given in the Table. These results were used to calculate values of the equilibrium constant $K_1^{OH^-}$ for reaction (4) and values for the first acid dissociation constants (K_1). The latter were converted into pK_1^0 at infinite dilution using the Debye–Huckel approximation.

The second dissociations of (**1**)—(**4**), equation (6), were studied

$$HA^- + OH^- \underset{k_{-2}^{H_2O}}{\overset{k_2^{OH^-}}{\rightleftharpoons}} A^{2-} + H_2O \qquad (6)$$

in aqueous sodium hydroxide and in carbonate buffers with sodium chloride to maintain constant ionic strength (0.1 mol dm^{-3}). Absorbance readings (A) of solutions containing 5×10^{-5} mol dm^{-3} substrate were taken over a range of hydroxide ion concentrations at the same wavelengths as those used to study the first dissociation. The absorbance ($A_{A^{2-}}$) corresponding to complete dissociation into A^{2-} was obtained from measurements in 0.1 and 1.0 mol dm^{-3} sodium hydroxide. Since the absorbance A_{HA^-} could not be measured, the equilibrium constant ($K_2^{OH^-}$) of reaction (6) was determined from plots of A against $(A_{A^{2-}} - A)[OH^-]$, equation (7). These

$$A = K_2^{OH^-}(A_{A^{2-}} - A)[OH^-] + A_{HA^-} \qquad (7)$$

results were converted into values for the second acid dissociation constants (K_2) and corrected to give pK_2^0.

Kinetic Measurements.—The kinetics of the first and second dissociations were studied by use of the temperature-jump technique. The reactions were followed spectrophotometrically at the same wavelengths and under the same conditions as those used for equilibrium measurements. For the first dissociation in the presence of buffer, equations (3) and (4), the time constant (τ^{-1}) for the re-equilibration between H_2A and HA^- following a rapid temperature perturbation is given by equation (8). For (**1**),

$$\tau^{-1} = k_1^{OH^-}[OH^-] + k_{-1}^{H_2O} + (k_1^B + k_{-1}^{BB}\overset{+}{r})[B] \qquad (8)$$

(**2**), and (**4**), values of the reciprocal relaxation time (τ^{-1}) were determined over a range of buffer concentration at several buffer ratios. For (**3**), the solubility was too low to permit kinetic studies of the first dissociation. Plots of τ^{-1} against buffer concentration were accurately linear and values of k_1^B and $k_{-1}^{BH^+}$ were obtained by combining the value of the gradient at a particular buffer ratio with the value of the equilibrium constant (K_1^B) for the reaction determined from equilibrium measurements. Average values of k_1^B and $k_{-1}^{BH^+}$ for (**1**), (**2**), and (**4**) are given in the Table. The intercepts of the plots of τ^{-1} against buffer concentration correspond to the first two terms in equation (8). The hydroxide ion concentration was calculated at each buffer ratio and from the magnitude of the intercept at that buffer ratio and the value of $K_1^{OH^-}$ determined from equilibrium measurements the values of $k_1^{OH^-}$ and $k_{-1}^{H_2O}$ given in the Table were obtained. These results are approximate since under the conditions of the experiment the intercepts were small and equation (8) was dominated by the buffer term.

The kinetics of the second dissociation, equation (6), were studied in aqueous sodium hydroxide. The variation of reciprocal relaxation time for the equilibration between HA^- and A^{2-} was accurately linear in hydroxide ion concentration, equation (9). The values obtained for $k_2^{OH^-}$ and $k_{-2}^{H_2O}$ were

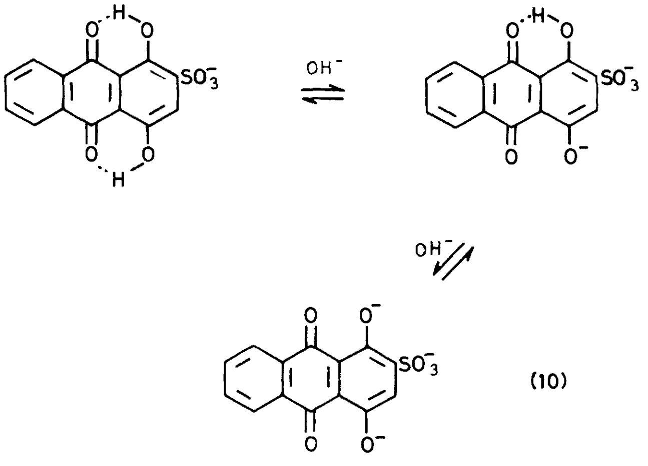
$$\tau^{-1} = k_2^{OH^-}[OH^-] + k_{-2}^{H_2O} \qquad (9)$$

compatible with the independently measured values of the equilibrium constant for the reactions ($K_2^{OH^-}$), and are given in the Table.

Discussion

On the basis of n.m.r. studies[10] and theoretical calculations[12] there appear to be differences in the properties of the intramolecular hydrogen bonds in 5,8-dihydroxy-1,4-naphthoquinone (**1**) and 5,8-dihydroxy-2-methyl-1,4-naphthoquinone (**2**). One of the purposes of the present work was to find out whether these differences affect the kinetic and equilibrium results for dissociation of the hydrogen-bonded protons from (**1**) and (**2**) and from the related species (**3**) and (**4**).

The first dissociation of (**2**) and (**4**) may lead to a mixture of anions depending on whether the proton is lost from the 5- or 8-, or the 1- or 4-hydroxy group, respectively. The equilibrium results for (**1**) and (**2**) show that a methyl substituent increases $pK_1{}^0$ and $pK_2{}^0$ by 0.35 and 0.39 units respectively. These are the effects expected from the differences in the pK of phenol (pK^0 9.99) and 2-methylphenol (pK^0 10.28).[15] The sulphonate group in (**4**) has the effect of decreasing $pK_1{}^0$ by 0.5 units and increasing $pK_2{}^0$ by 0.74 units compared with the values found for (**3**). A sulphonate group would have been expected to have an acid-strengthening effect on $pK_1{}^0$ and $pK_2{}^0$ by comparison with the 0.5—1.0 unit decrease in pK brought about by the introduction of a 2-, 3-, or 4-sulphonate group into phenol. The most reasonable explanation of the higher $pK_2{}^0$ of (**4**) compared with (**3**) is that the sulphonate substituent inhibits solvation[16] of the adjacent ionised hydroxy group and dissociation then occurs as shown in equation (10). Alternatively the higher $pK_2{}^0$ value could be accounted for if the intramolecular hydrogen bond in the product of the first dissociation is strengthened by the sulphonate group. If the sulphonate acts as hydrogen-bond acceptor instead of the keto group, as has been proposed by Stuehr,[13] and if this is the stronger of the two hydrogen bonds, ionisation will occur first at the 4-hydroxy group and $pK_2{}^0$ will be increased. However it is unlikely that this effect will be sufficiently large to account for the higher $pK_2{}^0$ of (**4**) compared with (**3**). The pK value of hydroxybenzene-2-sulphonate (pK^0 9.35) which is able to form a similar intramolecular hydrogen bond, is only slightly higher than that of hydroxybenzene-3-sulphonate (pK^0 9.07) and hydroxybenzene-4-sulphonate (pK^0 8.95) and lower than the pK value of phenol (pK^0 9.99).[15] It will be argued later that the similar kinetic results for (**4**) compared with (**1**)—(**3**) are not compatible with a stronger hydrogen bond in (**4**).



(10)

For proton transfer from phenol to amines (B), equation (11) holds; the values of $k_1{}^B$ and $k_{-1}{}^{BH^+}$ vary as the equilibrium constant ($K_1{}^B$) for the reaction changes.[8]

$$PhOH + B \underset{k_{-1}{}^{BH^+}}{\overset{k_1{}^B}{\rightleftharpoons}} PhO^- + BH^+ \qquad (11)$$

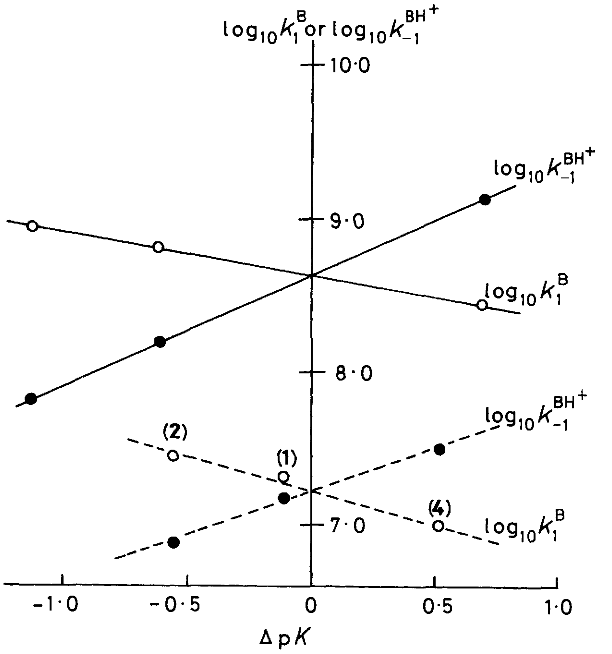


Figure. Variation of $\log_{10} k_1{}^B$ and $\log_{10} k_{-1}{}^{BH^+}$ with ΔpK for reaction of phenol (solid lines) and dihydroxy-diones (dashed lines) with amines

This variation is shown in the Figure in which values of $\log_{10}k_1{}^B$ and $\log_{10}k_{-1}{}^{BH^+}$ for three amines are plotted against $\Delta pK = -\log_{10}K_1{}^B$. The rate coefficients obtained for reaction of (**1**), (**2**), and (**4**) with buffer, equation (3), vary with ΔpK in the same way (see Figure) but the reactions occur 25-fold more slowly than for phenol. The reduction in rate is due to a weak intramolecular hydrogen bond in the undissociated acids which hinders proton transfer[6,7] and since the reduction in rate is the same for (**1**), (**2**), and (**4**), it can be concluded that the hydrogen bonds have very similar properties. Values of the rate coefficients ($k_1{}^{OH^-}$) for reaction of (**1**), (**2**), and (**4**) with hydroxide ion, equation (4), are also given in the Table. These results are very approximate (see Experimental section). The result $k_1{}^{OH^-}$ 1.0 × 10^8 dm^3 mol^{-1} s^{-1} has been measured previously[13] for (**4**) but the data were extremely scattered and this value is also approximate.

The second dissociations of (**1**)—(**4**) occur with $pK_2{}^0$ values which are 2.5—3.5 units higher than $pK_1{}^0$. The rate coefficients ($k_2{}^{OH^-}$) for removal of the second proton from (**1**), (**2**), and (**3**) by hydroxide ion have values which are quite similar to the result 1.9 × 10^7 dm^3 mol^{-1} s^{-1} observed for proton removal from the enol form of pentane-2,4-dione.[8] The results are about 1 000-fold below the diffusion-limited value observed for the reaction of phenol with hydroxide ion.[8] For (**4**), the rate coefficient is about 3-fold lower than for (**1**), (**2**), and (**3**), but this could be explained by the different charge type of this reaction. The kinetic results for the first and second dissociation of (**1**), (**2**), and (**4**) are sufficiently similar for the conclusion to be reached that both hydrogen bonds in (**4**) involve the keto groups as proton acceptors, equation (10). The value $k_2{}^{OH^-}$ 4.1 ± 0.8 × 10^6 dm^3 mol^{-1} s^{-1} determined for (**4**) is somewhat different from the result 2.7 × 10^6 dm^3 mol^{-1} s^{-1} found previously.[13] However, this latter result was obtained from scattered data over a limited range of hydroxide ion concentrations (0.004—0.015 mol dm^{-3}) compared with the present result obtained from an accurately linear dependence (correlation coefficient 0.996, 7 data points) of τ^{-1} on hydroxide ion concentration in the range 0.0025—0.04 mol dm^{-3}.

The kinetic and equilibrium results show that the intramolecularly hydrogen-bonded protons in (**1**)—(**4**) have very similar acid–base properties. The observation that the rates of the first and second dissociations are 25-fold and 1 000-fold respectively below the normal rates of proton transfer of phenol means that the intramolecular hydrogen bonds in the HA^- species are moderately strong and in the H_2A species are weak.

Acknowledgements

The S.E.R.C. and Royal Society are thanked for financial support.

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Received 20*th October* 1986; *Paper* 6/2044