Simultaneous Proton Removal from Open and Closed Forms of Hydrogen-bonded Phenylazoresorcinols by General Bases

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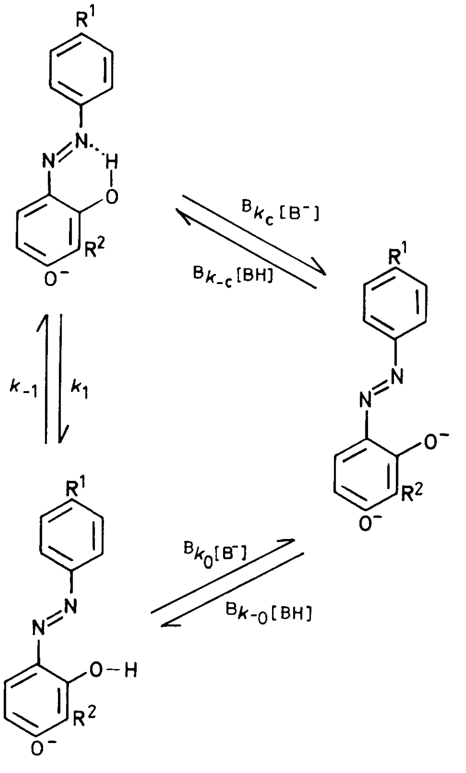
The kinetics of equilibration between the monoanions and dianions of substituted phenylazoresorcinols has been studied in buffered 70% (v/v) Me_2SO-H_2O. Kinetic terms arising from proton removal by buffer base and hydroxide ion from hydrogen-bonded and non-hydrogen-bonded forms of the monoanions have been observed. The rate coefficients ($^{B}k_c$) for proton removal from the hydrogen-bonded forms are several orders of magnitude below those for reaction of the open forms and depend on the strength of the catalysing base; $^{B}k_c$ for hydroxide ion is *ca.* 70-fold higher than $^{B}k_c$ for indazole ion. For reaction of 2-methyl-4-(4-nitrophenylazo)resorcinol with indazole ion, the kinetic solvent isotope effect is negligibly small, $^{B}k_c(H_2O)/^{B}k_c(D_2O)$ *ca.* 1.2.

The proton transfer behaviour of phenylazoresorcinol monoanions is extremely complex. In aqueous solution and 70% (v/v) Me_2SO-H_2O containing hydroxide ion the rate of equilibration between the monoanion and dianion of several phenyl azoresorcinols[1] and bis(phenylazo)resorcinols[2] goes through a minimum as the hydroxide ion concentration is increased. This behaviour has been explained in terms of the mechanism in the Scheme involving reaction of hydroxide ion ($B^- = OH^-$) with open and closed forms of the monoanions. It is assumed that the rate of proton removal from the open form is greater than the rate at which the open form reverts to the hydrogen-bonded form ($^{B}k_o[B^-] > k_{-1}$).

In aqueous solution in the presence of buffers, the similar reaction of 4-(4-sulphonatophenylazo)resorcinol ($R^1 = SO_3^-$, $R^2 = H$) (2',4'-dihydroxyazobenzene-4-sulphonate) is first-order in buffer and this was interpreted in terms of the reaction of buffer with the closed form of the monoanion.[3] However, for the reaction of the monoanion of 4,6-bis(phenylazo)resorcinol with buffers in 70% (v/v) Me_2SO-H_2O a curvilinear dependence of rate on buffer concentration was observed[4] and this was explained as corresponding to rate-limiting proton removal from the open form of the monoanion at low buffer concentrations ($^{B}k_o[B^-] < k_{-1}$) and rate-limiting opening of the intramolecular hydrogen bond at high concentrations ($^{B}k_o[B^-] > k_{-1}$). No evidence was found for reaction of the buffer with the hydrogen-bonded monoanion under these conditions. We have now studied the reactions of monophenylazoresorcinols with buffers in 70% (v/v) Me_2SO-H_2O in order to understand the difference in behaviour of the mono- and bis(phenylazo)resorcinols. The reaction of phenylazoresorcinols (**1**)—(**4**) with the anions (B^-) of benzimidazole and indazole under buffered conditions and with hydroxide ion in the presence and absence of buffer have been investigated, equation (1).

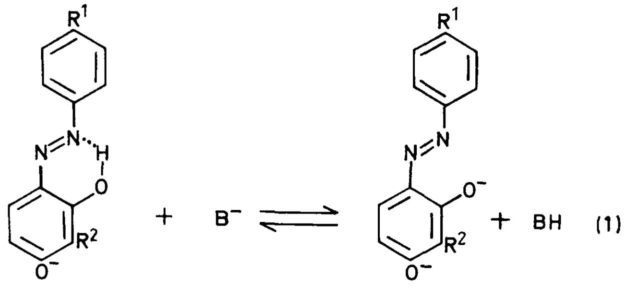


Scheme.

Experimental

Materials.—Commercial samples of 4-phenylazoresorcinol (**4**) and 4-(4-nitrophenylazo)resorcinol (**1**) were used. The preparations of 2-methyl-4-(4-nitrophenylazo)resorcinol (**2**) and 4-(4-chlorophenylazo)resorcinol (**3**) were achieved by reaction of the appropriate diazonium salt with 2-methylresorcinol and resorcinol, respectively. The products were recrystallised from $EtOH-H_2O$; (**2**) had m.p. 238—240 °C; δ(250 MHz; $CDCl_3$) 14.1 (s, 1 H, 3-OH), 8.36 (d, 2 H, 3'- and 5'-H), 7.92 (d, 2 H, 2'- and 6'-H), 7.64 (d, 1 H, 5-H), 6.59 (d, 1 H, 6-H), 5.60 (s, 1 H, 1-OH), and 2.18 (s, 3 H, Me); and (**3**) had m.p. 198—200 °C; δ([$^2H_6$]acetone) 13.0 (s, 3 H, 3-OH), 7.88 (d, 2 H, 2'- and 6'-H), 7.76 (d, 1 H, 5-H), 7.58 (d, 2 H, 3'- and 5'-H), 6.63 (dd, 1 H, 6-H), and 6.42 (d, 1 H, 2-H). A signal for 1-OH was not observed

Kinetic and Equilibrium Studies.—Kinetic and equilibrium measurements of reaction (1) were made spectrophotometrically in 70% (v/v) Me_2SO-H_2O at 288 K and ionic strength 0.1 mol dm^{-3}. Observations were usually made at a wavelength where the dianions absorb most strongly (*ca.* 600 nm) although some measurements were also made at *ca.* 450 nm where the absorbance is due mostly to the monoanion. Measurements were made with the phenylazoresorcinols in deficit (1×10^{-5}—10^{-4} mol dm^{-3}) in tetramethylammonium hydroxide solutions



	R^1	R^2
(1)	NO_2	H
(2)	NO_2	Me
(3)	Cl	H
(4)	H	H

and in buffer solutions prepared by partial neutralisation of the buffer acid (indazole or benzimidazole) with tetramethylammonium hydroxide. Tetramethylammonium chloride was added to keep constant ionic strength. In buffer solutions, values of the equilibrium constant for reaction (1), ${}^{B}K$ = [dianion][BH]/[monoanion][B^-], were determined from measurements at different buffer ratios, $r = [B^-]/[BH]$. In solutions of tetramethylammonium hydroxide, the equilibrium constant for reaction (1) with $B^- = OH^-$, ${}^{OH}K$ = [dianion]/[monoanion][OH^-], was determined from measurements over a range of hydroxide ion concentrations. The results for (**1**)—(**4**) are given in the Table. The dissociation of 2-methyl-4-(4-nitrophenylazo)resorcinol was also studied in 70% (v/v) $Me_2SO–D_2O$ containing indazole buffers.

The kinetics of the equilibration between the monoanions and dianions of (**1**)—(**4**) were studied by use of the temperature-jump technique.[5] The equilibrium was disturbed by a rapid perturbation of 2.6 K and the reactions were followed by observing the change in absorbance due to the decrease in concentration of the dianion. Reciprocal relaxation times were determined in solutions of tetramethylammonium hydroxide at different concentrations of hydroxide ion and in buffer solutions over a range of buffer concentrations at fixed buffer ratio. For each solution at least five determinations of the reciprocal relaxation time were made and the data points in Figures 1—3 show the average value with error limits equal to twice the standard deviation. The reaction of 2-methyl-4-(4-nitrophenylazo)resorcinol was studied in 70% (v/v) $Me_2SO–D_2O$ with indazole buffers in order to determine the kinetic solvent isotope effect for this reaction.

Results and Discussion

The phenylazoresorcinol monoanions studied in this work cover a 50-fold range of acid dissociation constant from the strongest acid (**1**) to the weakest (**4**). Although aqueous p*K* values cannot be calculated from the data in 70% (v/v) $Me_2SO–H_2O$, relative acidities can be deduced from the values of the equilibrium constants for dissociation in the presence of the various bases. The values relative to (**1**) (1.00) are (**2**) (0.077), (**3**) (0.068), and (**4**) (0.020). For (**1**), (**3**), and (**4**) the change in acidity is due to the decreasing electron-withdrawing ability of the group R^1 (NO_2 > Cl > H) in stabilising the phenylazoresorcinol dianions. The introduction of a methyl substituent as R^2 has a surprisingly large 20-fold acid-weakening effect on (**2**) in comparison with (**1**). A similar difference in the acidities of the monoanions of 4,6-bis(phenylazo)resorcinol and 2-methyl-4,6-bis(phenylazo)resorcinol has been found.[2] The methyl substituent may lead to steric inhibition of solvation of the dianion[6] or to a strengthening of the intramolecular hydrogen bond as a result of increased steric compression.[7]

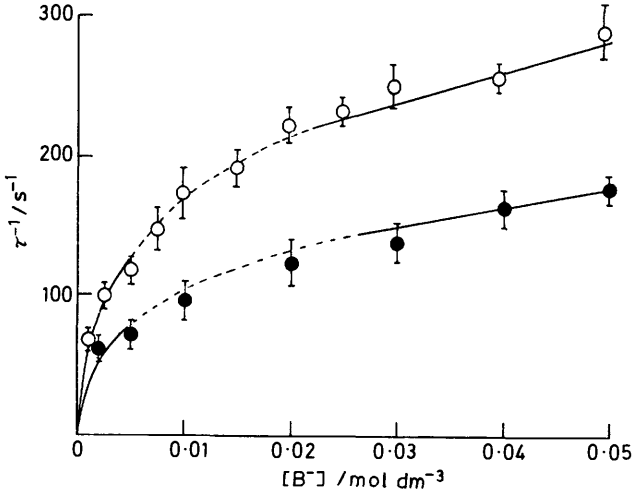


Figure 1. Reciprocal relaxation times for proton removal from 4-(4-nitrophenylazo)resorcinol monoanion in 70% (v/v) $Me_2SO–H_2O$ in the presence of benzimidazole buffers (B^-) at buffer ratios r = 1.0 (solid points) and 0.5 (open points)

The kinetics of proton transfer from (**1**) differs from that for the other phenylazoresorcinol monoanions and will be considered first. For the equilibration of (**1**) in 70% (v/v) $Me_2SO–H_2O$ containing benzimidazole buffers, equation (1), the dependence of reciprocal relaxation time on buffer concentration is curved as shown in Figure 1. A curved rate dependence on buffer concentration has previously been observed[4] for the reaction of 4,6-bis(phenylazo)resorcinol monoanion with phenol buffers and was explained by reaction through the steps in the Scheme to which the rate coefficients k_1, k_{-1}, and ${}^{B}k_o$, ${}^{BH}k_{-o}$ apply. For these steps, assuming the direct pathway from the closed form to the dianion occurs negligibly slowly, the dependence of reciprocal relaxation time on buffer concentration is given by equation (2). In equation (2),

$$\tau^{-1} = k_1(1 + 1/{}^{B}Kr)[B^-]/(k_{-1}/{}^{B}k_o + [B^-]) \qquad (2)$$

r is the buffer ratio ([B^-]/[BH]) and ${}^{B}K$ is the equilibrium constant for dissociation of the phenylazoresorcinol monoanion in the presence of buffer. A value of ${}^{B}K$ is known from equilibrium measurements. It is predicted from equation (2) that the reciprocal relaxation time becomes independent of buffer at high concentration. However, for (**1**) in benzimidazole buffers, the reciprocal relaxation time shows a small linear increase with buffer concentration at high buffer concentrations. Hence it appears for reaction of (**1**) in benzimidazole buffers that the results fit equation (2) at low buffer concentrations, but that at high buffer concentrations reaction of the hydrogen-bonded species with buffer becomes important and the dependence of reciprocal relaxation time on buffer concentration is given by equation (3).

$$\tau^{-1} = k_1(1 + 1/{}^{B}Kr) + {}^{B}k_c(1 + 1/{}^{B}Kr)[B^-] \qquad (3)$$

The first term corresponds to equation (2) with the condition ${}^{B}k_o[B^-] > k_{-1}$ and the second term refers to reaction of the hydrogen-bonded species with buffer. The data for (**1**) at low and high buffer concentrations can be fitted using equations (2) and (3), respectively. Good fits were obtained to the experimental data at three buffer ratios. The fits at buffer ratios

Table. Kinetic and equilibrium results[a]

Substrate	Solvent/ (v/v) Me_2SO–H_2O	Base	K	r	$10^{-2}\,k_1/s^{-1}$	$10^{-4}\,{}^{B}k_c/$ $dm^3\,mol^{-1}\,s^{-1}$
(1)	70%	Benz$^-$	0.66 ± 0.08	4.0	0.43 ± 0.1	0.055 ± 0.005
	70%	Benz$^-$		1.0		
	70%	Benz$^-$		0.5		
	50%	Benz$^-$	3.3 ± 0.3	0.5	2.8 ± 0.2	0.350 ± 0.05
(2)	70%	Ind$^-$	1.17 ± 0.1	1.0		0.0086 ± 0.001
	70%	Ind$^-$		0.33		
	70% Me_2SO–D_2O	Ind$^-$	1.38 ± 0.15	1.0		0.0072 ± 0.001
	70% Me_2SO–D_2O	Ind$^-$		0.33		
	70%	OH$^-$	1 580 ± 100			0.49 ± 0.05
(3)	70%	Ind$^-$	1.03 ± 0.1	1.0		1.48 ± 0.2
	70%	Ind$^-$		0.33		
	70%	OH$^-$	1 311 ± 60		4.5 ± 1	110 ± 10
(4)	70%	Ind$^-$	0.30 ± 0.03	1.0		0.74 ± 0.2
	70%	Ind$^-$		0.5		
	70%	Ind$^-$		0.18		
	70%	Benz$^-$	0.013 ± 0.002			<0.4
	70%	OH$^-$	393 ± 50		4.6 ± 0.5	53 ± 5

[a] Conditions are 288 K and ionic strength 0.1 mol dm^{-3}. Benz$^-$ = benzimidazole anion and Ind$^-$ = indazole anion.

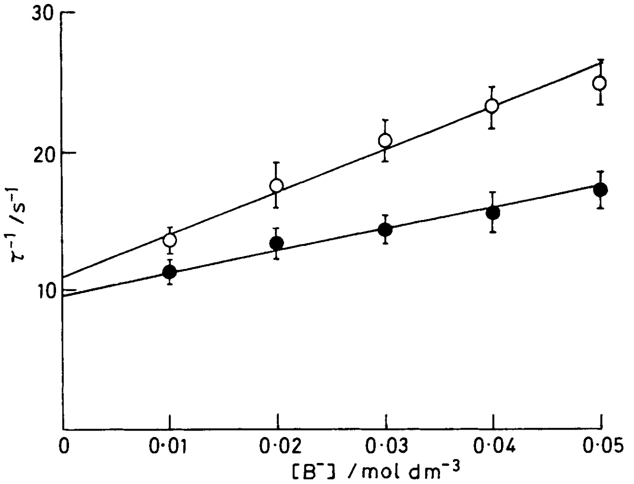


Figure 2. Reciprocal relaxation times for proton removal from 2-methyl-4-(4-nitrophenylazo)resorcinol in 70% (v/v) Me_2SO–H_2O in the presence of indazole buffers at buffer ratios r = 1.0 (solid points) and 0.33 (open points)

of r = 0.5 and 1.0 are shown in Figure 1 in which the solid lines at low and high buffer concentrations are plots of equations (2) and (3), respectively, using the values k_1 43 s^{-1}, $k_{-1}/{}^{B}k_o$ 1.2 × 10^{-3} mol dm^{-3}, and ${}^{B}k_c$ 550 dm^3 mol^{-1} s^{-1}. The result for $k_{-1}/{}^{B}k_o$ compares with the value $k_{-1}/{}^{B}k_o$ *ca.* 5 × 10^{-3} mol dm^{-3} previously obtained for 4,6-bis(phenylazo)resorcinol monoanion.[4] The behaviour of (**1**) in 50% (v/v) Me_2SO–H_2O was similar and the values k_1 280 s^{-1}, $k_{-1}/{}^{B}k_o$ 1.1 × 10^{-3} mol dm^{-3}, and ${}^{B}k_c$ 3.5 × 10^3 dm^3 mol^{-1} s^{-1} were obtained.

The data for the reactions of the less acidic phenylazoresorcinol monoanions (**2**)—(**4**) differ from the results for (**1**). In these cases it was necessary to study the reactions under more basic conditions in the presence of indazole buffers and the contribution of hydroxide ion to the rate cannot be neglected. However, to assist the analysis in buffer solutions the reaction with hydroxide ion was studied separately in dilute solutions of tetramethylammonium hydroxide. For (**2**)—(**4**) in indazole buffers, a linear dependence of rate against buffer concentration was found. Typical results are given in Figure 2 for the reaction of 2-methyl-4-(4-nitrophenylazo)resorcinol (**2**). For the hydrogen bonds in (**2**)—(**4**) under these more basic conditions, the inequality ${}^{B}k_o[B^-] > k_{-1}$ is satisfied at the lowest buffer concentrations and equation (3) is more appropriate than equation (2). However, it is also necessary to consider the possibility of proton removal by hydroxide ion from the hydrogen-bonded species and this gives rise to the second term in equation (4). The first term is identical with the first term in equation (3) but has been expressed in an alternative form with ${}^{B}Kr$ replaced by ${}^{OH}K[OH^-]$. In equation (4) the first two terms correspond to the intercept in the plots of reciprocal relaxation time against buffer concentration and the third term determines the gradient. The solid lines in Figure 2 are plots of equation (4) for (**2**), using the experimental value ${}^{OH}K$ 1 580 dm^3 mol^{-1} together with the value ${}^{B}k_c$ 86 dm^3 mol^{-1} s^{-1} and best-fit values for the intercepts at each buffer ratio. Values of ${}^{B}k_c$ for the phenylazoresorcinol monoanions (**3**) and (**4**) were calculated in a similar way and are given in the Table. The results are rather inaccurate because the dependence of reciprocal relaxation time on buffer concentration is shallow and the first two terms in equation (4) make a large contribution to the rate. For (**4**) in indazole buffers the result ${}^{B}k_c$ 7.4 × 10^3 dm^3 mol^{-1} s^{-1} was found but in benzimidazole buffers the rate was independent of buffer concentration within experimental error and for this weaker base an upper limit ${}^{B}k_c$ < 4 × 10^3 dm^3 mol^{-1} s^{-1} was estimated. To analyse the first two terms in equation (4) more fully it is necessary to consider the data for reaction of the phenylazoresorcinols in solutions of tetramethylammonium hydroxide.

$$\tau^{-1} = k_1(1 + 1/{}^{OH}K[OH^-]) + {}^{OH}k_c([OH^-] + 1/{}^{OH}K) + {}^{B}k_c(1 + 1/Kr)[B^-] \quad (4)$$

A linear dependence of reciprocal relaxation time on hydroxide ion concentration was observed for (**2**)—(**4**) in solutions of tetramethylammonium hydroxide over the range 0.001—0.025 mol dm^{-3} as shown for (**4**) in Figure 3. Under these conditions the third term in equation (4) vanishes. The data points at hydroxide ion concentrations below 0.001 mol dm^{-3} refer to the intercepts at zero buffer concentration of the plots of reciprocal relaxation time against buffer concentration in indazole and benzimidazole buffers. The concentrations of hydroxide ion present in indazole or benzimidazole buffers could not be measured directly. However, hydroxide ion con-

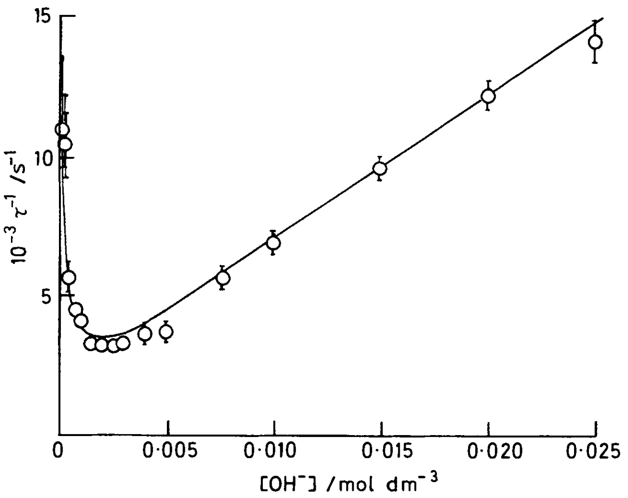


Figure 3. Reciprocal relaxation times for proton removal from 4-(phenylazo)resorcinol in 70% (v/v) Me_2SO–H_2O by hydroxide ion

centrations were calculated from the values of ^{B}K and ^{OH}K for each substrate determined from equilibrium measurements in the buffer (B) and in dilute solutions of tetramethylammonium hydroxide. The dependence of τ^{-1} on $[OH^-]$ in Figure 3 is similar to that which has been observed for mono- and bis-phenylazoresorcinols[1,2] in aqueous solution and is explained by the first two terms in equation (4). The line in Figure 3 is a plot of these terms for (4) using k_1 460 s^{-1} and $^{OH}k_c$ 5.3×10^5 dm^3 mol^{-1} s^{-1} and the value ^{OH}K 393 dm^3 mol^{-1} determined from separate equilibrium measurements. The results of a similar analysis for (**3**) are given in the Table but for (**2**) the first term in equation (4) made a small contribution and a value for $^{OH}k_c$ only was obtained.

The observation of a kinetic term identified as involving attack of buffer base on the hydrogen-bonded monoanions (**1**)—(**4**) ($^{B}k_c$) differs from the results for bis(phenylazo)-resorcinols.[4] This may be due to the fact that the bis(phenylazo)resorcinols are more strongly acidic and were therefore studied with weaker bases. The values of the rate coefficients $^{OH}k_c$ for reaction of hydroxide ion with (**2**)—(**4**) are each *ca.* 70-fold higher than the corresponding values of $^{B}k_c$ for reaction with indazole anion. It is calculated from the values of ^{OH}K and ^{B}K for (**2**)—(**4**) that hydroxide ion is *ca.* 1 310-fold more basic than indazole under the present conditions. The 70-fold difference in rate for the attack of hydroxide ion compared with indazole anion on the hydrogen-bonded proton shows that the value of $^{B}k_c$ depends on the strength of the attacking base. For reaction of (**4**) the value $^{B}k_c$ 7.4×10^3 dm^3 mol^{-1} s^{-1} was found with indazole as base but for the *ca.* 23-fold weaker base benzimidazole, attack on the hydrogen-bonded monoanion was not detectable and an upper limit of $^{B}k_c < 4.0 \times 10^3$ dm^3 mol^{-1} s^{-1} was estimated. The values of $^{OH}k_c$ and $^{B}k_c$ show a scattered change along the series (**1**)—(**4**). The slowest reaction was found for (**4**) and in the presence of 0.05 mol dm^{-3} indazole at a buffer ratio $r = 1.0$ the reaction has a half-life of 40 ms. The low rates may reflect an increased strength of the hydrogen bond in this case.

The present data permit an estimate of the relative rates of proton removal from the hydrogen-bonded and non-hydrogen-bonded forms of the phenylazoresorcinol monoanions. For (**1**) the curved dependence of τ^{-1} against $[B^-]$ at low buffer concentration in Figure 1 arises because the rate of proton transfer from the non-hydrogen-bonded monoanion and the rate at which the non-hydrogen-bonded species returns to the hydrogen-bonded monoanion are comparable. The results $k_{-1}/^{B}k_o$ *ca.* 1.2×10^{-3} mol dm^{-3}, k_1 43 s^{-1} and $^{B}k_c$ 550 dm^3 mol^{-1} s^{-1} were deduced. If it is assumed that proton transfer from the open form occurs at the diffusion-limited rate ($^{B}k_o$ *ca.* 1×10^{10} dm^3 mol^{-1} s^{-1}), the values k_{-1} *ca.* 1.2×10^7 s^{-1} and k_1/k_{-1} *ca.* 3.6×10^{-6} are obtained. The latter result for the equilibrium constant for opening of the intramolecular hydrogen bond is reasonable for this type of hydrogen bond. Further, the assumption $^{B}k_o$ *ca.* 1×10^{10} dm^3 mol^{-1} s^{-1}, leads to the conclusion that proton transfer from the open monoanion occurs *ca.* 2×10^7-fold more rapidly than from the hydrogen-bonded monoanion. The two processes can compete only because the open species is present in much lower concentration.

It was chosen to study the kinetic isotope effect for the reaction of 2-methyl-4-(4-nitrophenylazo)resorcinol with indazole anion because the equilibrium constant is close to unity and a maximum value in the kinetic isotope effect is expected when the p*K* values of the ionising proton and of the conjugate acid of the catalysing base are closely balanced.[8] Despite this, the observed value was negligibly small, $^{B}k_c(H_2O)/^{B}k_c(D_2O)$ *ca.* 1.2. Previously, reaction of hydrogen-bonded naphthylammonium ions[9] and bis(phenylazo)resorcinol monoanions[10] through low concentrations of the open forms has been found to occur with negligibly small isotope effects. Thus it is not possible to distinguish between direct removal of the hydrogen-bonded proton and two-step proton removal through the open form by measurements of the kinetic isotope effect.

Although the proton transfer behaviour of mono- and bis(phenylazo)resorcinols is explained by the mechanism in the Scheme, quite different kinetic behaviour is obtained depending on the relative values of the rate coefficients for the individual steps. For bis(phenylazo)resorcinols the resorcinol ring possesses an additional electron-withdrawing group and the monoanions are quite acidic. The direct step $^{B}k_c$, $^{BH}k_{-c}$ is unimportant and reaction from the monoanion to the dianion occurs by opening of the intramolecular hydrogen bond followed by proton removal from the non-hydrogen-bonded species.[4] The relative rate of the proton transfer step ($^{B}k_o[B^-]$) and the closing of the intramolecular hydrogen bond (k_{-1}) in phenol buffers depends on the buffer concentration and a curvilinear dependence of rate on buffer concentration is observed[4] with opening of the hydrogen bond becoming rate-limiting at high buffer concentration. The most acidic of the mono(phenylazo)resorcinols studied in the present work, compound (**1**), shows a similar curved rate dependence in benzimidazole buffers but in addition at high buffer concentrations attack of buffer on the hydrogen-bonded monoanion is observed. This latter reaction is also found for the phenylazoresorcinols (**2**)—(**4**), and at all buffer concentrations proton removal from the open species occurs more rapidly than closing of the hydrogen bond ($^{B}k_o[B^-] > k_{-1}$). These differences in mechanism are a result of a gradual change in the properties of the intramolecular hydrogen bonds in going from the bis(phenylazo)resorcinols with strongly electron-withdrawing substituents to the more weakly acidic mono-phenylazoresorcinols.

Acknowledgements

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