Substituent Effects and Isotope Effects on the Rate Coefficients and Equilibrium Constant for Opening an Intramolecular Hydrogen Bond

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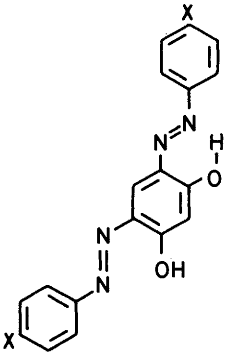
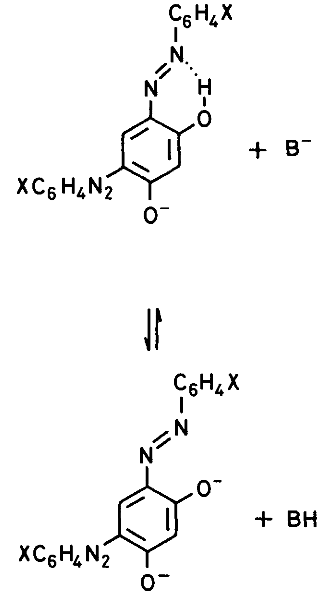
Proton removal from the intramolecularly hydrogen-bonded monoanions of substituted 4,6-bis(phenylazo)resorcinols in buffered 70% (v/v) $Me_2SO–H_2O$ involves opening of the hydrogen bond followed by proton transfer between open form and buffer. At low buffer concentration the proton transfer is rate-limiting but opening of the hydrogen bond becomes rate-limiting at higher buffer concentration. Typical values of the rate coefficients for opening (k_1) and closing (k_{-1}) of the hydrogen bond are k_1 $3.8 \pm 0.6 \times 10^4$ s^{-1} and k_{-1} *ca.* 8×10^7 s^{-1} found for 4,6-bis(phenylazo)-resorcinol monoanion. The rate coefficients and the corresponding equilibrium constant are almost unaffected by substituents and by changing the solvent to 70% (v/v) $Me_2SO–D_2O$.

The complex rate expression for deprotonation of the monoanions of 4,6-bis(phenylazo)resorcinol and 2,4-bis(phenylazo)-resorcinol by hydroxide ion in aqueous solution has been explained by postulating that proton removal can occur by direct single-step attack of hydroxide ion on the hydrogen-bonded monoanion and by slow formation of an open form of the monoanion from which the proton is removed rapidly.[1] Similar conclusions have been reached for the reactions of 4-phenylazoresorcinol.[2] To provide further information about these interesting reactions, we have studied the kinetics in the presence of buffer. In buffered aqueous solution the reaction is dominated by the hydroxide ion reaction. In 70% (v/v) $Me_2SO–H_2O$, because of a change in the value of the ionic product of water,[3,4] the concentration of hydroxide ion in phenol buffers is much lower than in aqueous phenol buffers, and this makes it possible to suppress the contribution of hydroxide ion. Accordingly the reaction of 4,6-bis(phenylazo)-resorcinol monoanion to give the dianion has been studied in 70% (v/v) $Me_2SO–H_2O$ containing phenol (B^-) buffers. Preliminary results referring to phenol and 2-methylphenol buffers each at a single buffer ratio have been published,[5] and we now present a full report. Kinetics studies of reaction (1) have been carried out in phenol, 2-methylphenol, and 2,6-di-isopropylphenol buffers at several buffer ratios for the phenylazoresorcinols (**1**)—(**4**). The isotope effect in changing the solvent to 70% (v/v) $Me_2SO–D_2O$ has been measured.



(**1**) X = H
(**2**) X = MeO
(**3**) X = Me
(**4**) X = Cl



(1)

Experimental

Materials.—A sample of 4,6-bis(phenylazo)resorcinol was available from a previous study.[1] Substituted bis(phenylazo)-resorcinols were prepared by reaction of resorcinol with a two-fold molar excess of the appropriate diazonium salt under alkaline conditions. After acidification the product mixture was separated by column chromatography. 4,6-Bis-(4-methoxyphenylazo)resorcinol was separated by flash chromatography[6] on silica with light petroleum (b.p. 40—60 °C)–ethyl acetate as eluant to give the pure solid (m.p. 219—221 °C) in 11% yield; $\delta(CDCl_3)$ 13.93 (s, 2 H, OH), 8.39—6.49 (m, 10 H, arom.), and 3.90 (s, 6 H, OCH_3). Samples of 4,6-bis-(4-chlorophenylazo)- and 4,6-bis-(4-methylphenylazo)-resorcinol were eluted from an alumina column with chloroform. The chloro derivative was obtained in 9% yield and had m.p. 257—259 °C with $\delta(CDCl_3)$ 13.76 (s, 2 H, OH) and 8.49—6.53 (m, 10 H, arom.); the methyl derivative was obtained in 34% yield, with m.p. 247—249 °C and $\delta(CDCl_3)$ 14.04 (s, 2 H, OH), 8.46—6.51 (m, 10 H, arom.), and 2.45 (s, 6 H, CH_3).

Phenols were purified by distillation and tetramethylammonium chloride was dried under vacuum. The solvent was made up by addition of 70 parts by volume of Me_2SO (B.D.H. AnalaR) to 30 parts by volume of double-distilled water. Buffers were prepared by partial neutralisation of the phenol with aqueous tetramethylammonium hydroxide solution and the ionic strength was adjusted to 0.1 mol dm^{-3} by addition of tetramethylammonium chloride.

Equilibrium and Kinetic Measurements.—Kinetic and equilibrium measurements of reaction (1) were made spectrophotometrically at 288 K in 70% (v/v) $Me_2SO–H_2O$ containing substituted phenol buffers at ionic strength 0.1 mol dm^{-3}. Equilibrium constants were calculated from absorbance

Table. Analysis of kinetic data for 4,6-bis(phenylazo)resorcinols (**1**)—(**4**)[a]

Compd.	Buffer	K	r	$10^{-4}k_1/s^{-1}$	$(10^3k_{-1}/k_2)/$ mol dm^{-3}
(**1**)	$4\text{-}ClC_6H_4OH$	0.025 ± 0.004			
	PhOH	0.28 ± 0.03	1.00	2.8 ± 0.3	4.4 ± 0.3
			3.38	3.8 ± 0.3	4.8 ± 0.3
			5.00	4.3 ± 0.2	4.9 ± 0.3
	$2\text{-}MeC_6H_4OH$	0.84 ± 0.02	0.48	2.7 ± 0.5	5.4 ± 0.8
			1.00	4.1 ± 0.3	7.9 ± 0.6
			2.01	4.2 ± 0.3	8.3 ± 0.6
			4.00	4.5 ± 0.4	8.4 ± 0.6
	$2,6\text{-}(Pr^i)_2C_6H_3OH$	3.4 ± 0.3	0.24	3.4 ± 0.2	9.5 ± 0.7
			0.47	3.5 ± 0.3	8.9 ± 0.7
			1.00	3.9 ± 0.4	9.1 ± 0.7
			1.90	4.6 ± 0.4	8.9 ± 0.7
		4.4 ± 0.2[b]	1.01	3.7 ± 0.3[b]	10.2 ± 0.8[b]
(**2**)	$2,6\text{-}(Pr^i)_2C_6H_3OH$	1.75 ± 0.06	1.00	4.1 ± 0.3	7.6 ± 0.8
(**3**)	$2,6\text{-}(Pr^i)_2C_6H_3OH$	2.49 ± 0.3	1.00	3.9 ± 0.3	8.2 ± 0.8
(**4**)	$2\text{-}MeC_6H_4OH$	2.81 ± 0.2	1.00	5.8 ± 0.3	6.3 ± 0.6

[a] 70% (v/v) $Me_2SO\text{–}H_2O$; ionic strength 0.1 mol dm^{-3}; 288 K. [b] 70% (v/v) $Me_2SO\text{–}D_2O$; ionic strength 0.1 mol dm^{-3}; 288 K.

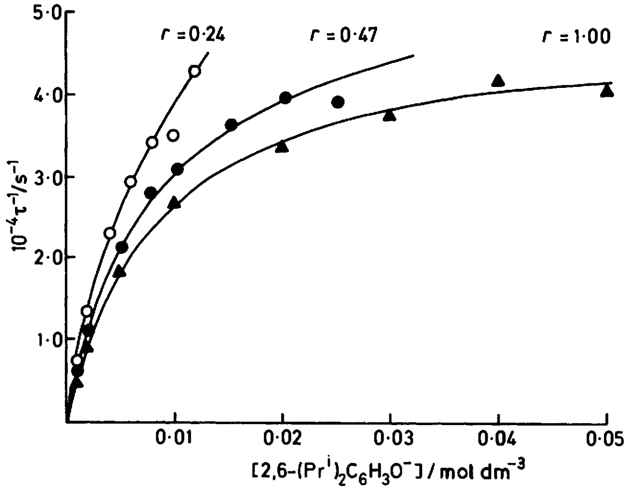


Figure. Dependence of reciprocal relaxation time on buffer concentration for the reaction of 4,6-bis(phenylazo)resorcinol in 2,6-di-isopropylphenol buffers at buffer ratios $r = [B^-]/[BH]$ of 0.24, 0.47, and 1.00

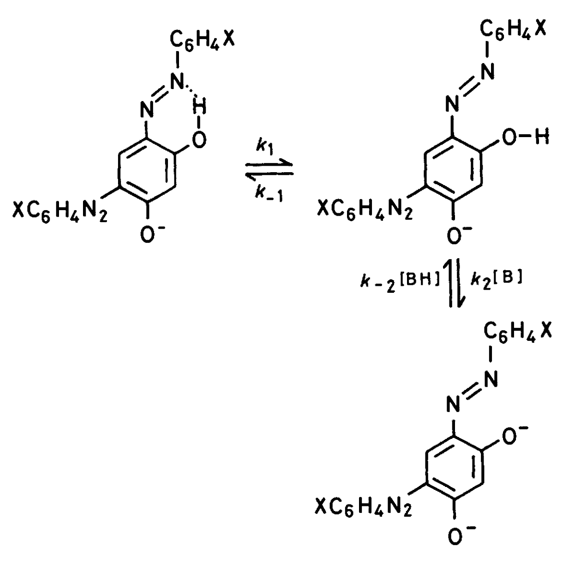
measurements at *ca.* 500 nm where the monoanion absorbs strongly [ε 3.1 ± 0.1 × 10^4 dm^3 mol^{-1} cm^{-1} for 4,6-bis(phenylazo)resorcinol] and at *ca.* 600 nm where the absorbance is mostly due to the dianion (ε 2.8 ± 0.1 × 10^4 dm^3 mol^{-1} cm^{-1}). The bis(phenylazo)resorcinols were present at a concentration of *ca.* 3 × 10^{-5} mol dm^{-3}; buffer concentrations were in the range 0.001—0.02 mol dm^{-3} and the buffer ratio was usually varied over a ten-fold range. Average values of the equilibrium constants (K) are given in the Table.

Kinetic studies were carried out using the temperature-jump technique. Readjustment of the equilibrium position following a temperature perturbation of 2.6 K was observed by measuring the change in absorbance at *ca.* 600 nm due to a decrease in concentration of the dianion. The total concentration of the bis(phenylazo)resorcinol was in the range (3—10) × 10^{-5} mol dm^{-3}. Relaxation times (τ) were determined at buffer concentrations over the range 0.001—0.05 mol dm^{-3} at a fixed buffer ratio, and in each buffer measurements were made at several buffer ratios. In all cases the dependence of reciprocal relaxation time on buffer concentration was rectilinear. Typical data for 4,6-bis(phenylazo)resorcinol in di-isopropylphenol buffers are given in the Figure.

Results and Discussion

A pK value of 11.3 has been found[1] for the second dissociation of 4,6-bis(phenylazo)resorcinol in aqueous solution at 5 °C and infinite dilution, to be compared with 10.6 observed for 2-methylphenol.[7] In 70% (v/v) $Me_2SO\text{–}H_2O$ the two phenols have very similar acidities (see Table). This may imply that the intramolecular hydrogen bond in the bis(phenylazo)resorcinol monoanion is weakened by the change of solvent, although other factors such as the stabilities of the phenolate ion and bis(phenylazo)resorcinol dianion will also contribute. The relative values of the equilibrium constants (K) for dissociation of 4,6-bis(phenylazo)resorcinol monoanion in 4-chlorophenol (K 0.025 ± 0.004) and phenol (K 0.28 ± 0.03) buffers are compatible with the pK values of 11.54 and 12.48 measured[3] for 4-chlorophenol and phenol, respectively, in 70% (v/v) $Me_2SO\text{–}H_2O$.

Kinetic data for the reaction of 4,6-bis(phenylazo)resorcinol in 2,6-di-isopropylphenol buffers are given in the Figure; very similar data were obtained in other buffers and for the other bis(phenylazo)resorcinols. The dependence of reciprocal relaxation time on buffer concentration shows that the order of reaction in buffer changes from first- to zero-order as the buffer concentration is increased. A mechanism and rate expression that are consistent with this observation are given in equations (2)—(4), in which r is the buffer ratio (= $[B^-]/[BH]$). The open



(2)

$$\tau^{-1} = k_1(1 + 1/Kr)[\mathrm{B}^-]/(k_{-1}/k_2 + [\mathrm{B}^-]) \quad (3)$$

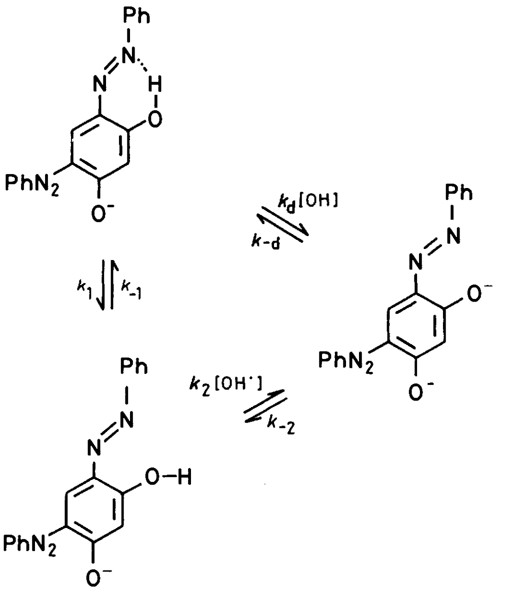
$$\tau = k_{-1}/k_1k_2(1 + 1/Kr)[\mathrm{B}^-] + 1/k_1(1 + 1/Kr) \quad (4)$$

non-hydrogen-bonded intermediate is assumed to be present in low concentration. At low buffer concentration where $k_{-1} > k_2[\mathrm{B}^-]$, proton transfer from the open intermediate is rate-limiting, but as the buffer concentration is increased opening of the intramolecular hydrogen bond becomes rate-limiting and $k_{-1} < k_2[\mathrm{B}^-]$. For each substituted bis(phenylazo)resorcinol in a particular buffer the values of the relaxation time were plotted against the reciprocal of buffer concentration according to equation (4). The plots were treated by linear regression analysis and gave correlation coefficients which were always greater than 0.985 and usually greater than 0.998. Values of k_1 and k_{-1}/k_2 calculated from the best-fit gradients and intercepts using the separately measured values of K for the particular bis(phenylazo)resorcinol and buffer are given in the Table. The solid lines in the Figure were constructed using the appropriate values of k_1, k_{-1}/k_2, and K given in the Table.

Analysis of the kinetic data for 4,6-bis(phenylazo)resorcinol at various buffer ratios in phenol, 2-methylphenol, and 2,6-di-isopropylphenol buffers leads to values of k_1, referring to opening of the intramolecular hydrogen bond, which vary somewhat. The average value is $(3.8 \pm 0.6) \times 10^4\ \mathrm{s}^{-1}$. The reasons for the variation are not known, but previous studies have shown that reactions in $\mathrm{Me_2SO–H_2O}$ are more susceptible to electrolyte effects than the same reactions in aqueous solution.[8] Significant buffer association occurs at concentrations above 0.1 mol dm^{-3} but is not an important factor under the present conditions.[3,9,10] We have shown recently that the rate coefficient for the base-catalysed hydrolysis of an ester depends on the electrolyte used to maintain constant ionic strength.[11] The variation in the k_1 values appears to be more severe at low buffer ratio in the more acidic buffers where the reverse reaction makes the larger contribution to the reciprocal relaxation time and the electrolyte effect may affect the reaction between the bis(phenylazo)resorcinol dianion and buffer acid. The derived values of k_{-1}/k_2 also show some variation with buffer ratio. The different values obtained in each phenol buffer could be the result of differences in the values of k_2. Proton removal from the open intermediate is strongly favoured thermodynamically and would be expected to occur with a diffusion-limited rate coefficient (k_2) independent of the particular buffer. However, the difference in the values of k_{-1}/k_2 between phenol, 2-methylphenol, and 2,6-di-isopropylphenol is in the direction that could be explained by a small steric effect resulting in a slightly lower value of k_2 for the more hindered buffers. The variation in k_{-1}/k_2 and k_1 can be regarded as small when it is considered that the results are obtained from work in different buffers in which the equilibrium constant for the overall reaction varies over a ten-fold range.

The assumption that proton transfer to buffer anion from the non-hydrogen-bonded species is diffusion-controlled can be used to deduce values for k_{-1} and for the equilibrium constant (K^*) for opening of the hydrogen bond. For bis(phenylazo)-resorcinol the estimated value of k_2 of $1 \times 10^{10}\ \mathrm{dm^3\ mol^{-1}\ s^{-1}}$ leads to k_{-1} *ca.* $8 \times 10^7\ \mathrm{s}^{-1}$ and K^* *ca.* 5×10^{-4}. The latter value is roughly the result which would be expected for an intramolecular hydrogen bond of this type.

The kinetic behaviour observed in the present work for the deprotonation of 4,6-bis(phenylazo)resorcinol monoanion by buffer species in 70% (v/v) $\mathrm{Me_2SO–H_2O}$ is different from the kinetics of the reaction with hydroxide ion in aqueous solution. The mechanism and rate expression deduced for the reaction with hydroxide ion are shown in equations (5) and (6). Direct reaction of hydroxide ion with the hydrogen-bonded species (k_d, k_{-d}) as well as reaction through the open form is involved. Reaction through the open form occurs with rate-limiting opening of the intramolecular hydrogen bond so that $k_2[\mathrm{OH}^-] > k_{-1}$ is satisfied at the lowest hydroxide ion concentration (0.001 mol dm^{-3}). For reaction with buffer in 70% (v/v) $\mathrm{Me_2SO–H_2O}$ the inequality $k_2[\mathrm{B}^-] > k_{-1}$ applies only for $[\mathrm{B}^-] > 0.05$. Even though the value of k_2 is expected to be *ca.* five-fold larger for diffusion-controlled reaction of the open intermediate with hydroxide ion as compared with B^-, the results mean that k_{-1} must be at least ten-fold lower in aqueous solution than in 70% (v/v) $\mathrm{Me_2SO–H_2O}$. A lower energy barrier for opening and closing of the hydrogen bond in 70% (v/v) $\mathrm{Me_2SO–H_2O}$ favours the route through the open intermediate and is therefore compatible with the failure to observe direct attack by buffer.



(5)

$$\tau^{-1} = (k_1 + k_d[\mathrm{OH}^-])(1 + 1/K[\mathrm{OH}^-]) \quad (6)$$

The kinetic and equilibrium data for substituted bis(phenylazo)resorcinols are given in the Table. The order of increasing values of K along the series X = MeO < Me < H < Cl is that expected on the basis of increasing stabilisation of the bis(phenylazo)resorcinol dianion by electron withdrawal. The values of k_1 and k_{-1}/k_2 show little variation although the value of k_1 for the chloro derivative is slightly higher than for the other bis(phenylazo)resorcinols. Making the assumption k_2 *ca.* $1 \times 10^{10}\ \mathrm{dm^3\ mol^{-1}\ s^{-1}}$ for each bis(phenylazo)resorcinol leads to the conclusion that K^* may also be somewhat higher for the chloro derivative. The higher values of k_1 and K^* can be accounted for by a weakening of the intramolecular hydrogen bond as a result of the lower basicity of the azo group in 4,6-bis-(4-chlorophenylazo)resorcinol monoanion. The effect of changing solvent to 70% (v/v) $\mathrm{Me_2SO–D_2O}$ on the data for 4,6-bis(phenylazo)resorcinol in di-isopropylphenol buffers is almost negligible. The largest effect is on the value of the overall equilibrium constant $K(\mathrm{H_2O})/K(\mathrm{D_2O})$ 0.77 ± 0.1. This can be explained by a reduced value of the fractionation factor for a hydrogen-bonded proton as compared with that for the proton in a typical phenol. The solvent isotope effect is close to that observed[12] for the dissociation of salicylate ion in the presence of triethylamine buffer, $K(\mathrm{H_2O})/K(\mathrm{D_2O})$ 0.73 ± 0.08. The similar kinetic results obtained for 4,6-bis(phenylazo)resorcinol in 70% (v/v) $\mathrm{Me_2SO–H_2O}$ and 70% $\mathrm{Me_2SO–D_2O}$ mean that the values of the kinetic isotope effects on opening and closing of the hydrogen bond and the value of the corresponding equilibrium isotope effect $K^*(\mathrm{H_2O})/K^*(\mathrm{D_2O})$ are unity within experimental error. Isotope effects on this type of process have not been measured previously.

The kinetic behaviour found for bis(phenylazo)resorcinols in buffered 70% (v/v) Me_2SO-H_2O identifies the mechanism of proton transfer and provides a procedure for the measurement of the rate coefficients and equilibrium constant for the opening of an intramolecular hydrogen bond. The procedure will be applied to the reaction of other hydrogen-bonded acids in future work.

Acknowledgements

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