

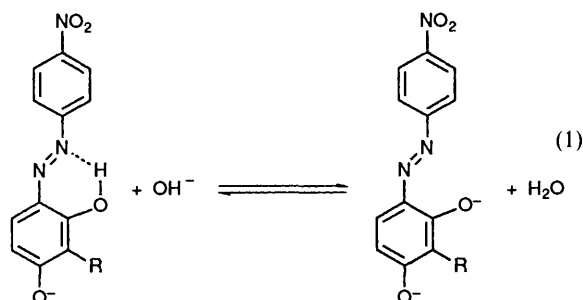
Kinetic and Equilibrium Solvent Isotope Effects on the Ionisation of a Hydrogen-bonded Proton and Studies of the Intramolecular Hydrogen Bond in Phenylazoresorcinols

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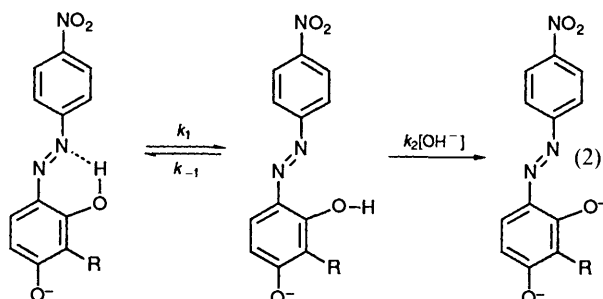
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The kinetic solvent isotope effect on the removal of the hydrogen-bonded proton from 2-methyl-4-(4-nitrophenylazo)resorcinol monoanion by hydroxide ion has been measured at different hydroxide-ion concentrations in 60% (v/v) Me₂SO–L₂O (L = H or D) and in 80% (v/v) Me₂SO–L₂O. The isotope effect in 80% (v/v) Me₂SO–L₂O has been analysed to give isotope effects on the rate coefficient (k_1) and equilibrium constant (K_1) for formation of an open non-hydrogen-bonded species from the intramolecularly hydrogen-bonded form and the results (k_1)^H/ (k_1) ^D 1.26 and (K_1)^H/ (K_1) ^D 0.65 were obtained. One contribution to the equilibrium isotope effect is made by the difference in the values of the isotopic fractionation factors (ϕ) for the protons in the hydrogen-bonded and open forms. To provide estimates of these values, fractionation factors have been measured in 80% (v/v) Me₂SO–L₂O for the hydrogen-bonded proton in 2-isopropyl-4-(4-nitrophenylazo)resorcinol monoanion (ϕ 0.97) and for the hydroxy proton in phenol (ϕ 1.08). The isotope effect on the chemical shift of the hydrogen-bonded proton in 2-isopropyl-4-(4-nitrophenylazo)resorcinol monoanion has been determined and the result $\Delta[\delta(^1\text{H}) - \delta(^2\text{H})]$ 0.61 shows that the hydrogen bond is of the double minimum type.

The kinetics of the ionisation of the hydrogen-bonded proton from 2-alkyl-4-(4-nitrophenylazo)resorcinol monoanions (R = H, Me, Et or Prⁱ) have been studied¹ in 80 and 90% (v/v) Me₂SO–H₂O in the presence of hydroxide ion, eqn. (1). Under



these conditions the equilibrium in eqn. (1) is strongly displaced towards products. The equilibrium constant for the reaction in 80% (v/v) Me₂SO–H₂O has a value in excess of 2000 and in 90% the value is larger still. The dependence of the observed first-order rate coefficient (k_{obs}) on hydroxide-ion concentration is curved and the mechanism in eqn. (2) was proposed to account



for this behaviour.¹ Values of k_1 and k_{-1}/k_2 were deduced from the fit of eqn. (3) to the kinetic results. By assuming that the proton transfer step in eqn. (2) is a diffusion controlled process

$$k_{\text{obs}} = k_1 k_2 [\text{OH}^-] / (k_{-1} + k_2 [\text{OH}^-]) \quad (3)$$

($k_2 \times 10^{10} \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$) it was then possible to estimate values for the rate coefficient k_{-1} and the equilibrium constant (K_1) for the hydrogen bond equilibrium.

In the present work we have extended these studies to include the measurement of solvent isotope effects in 60% and 80% (v/v) Me₂SO–L₂O (L = H or D). The isotopic fractionation factor and the isotope effect on the NMR chemical shift of the hydrogen-bonded proton in 2-isopropyl-4-(4-nitrophenylazo)resorcinol monoanion have also been measured to provide information about the nature of the intramolecular hydrogen bond and to permit detailed analysis of the kinetic isotope effects.

Experimental

Samples of 2-methyl- and 2-isopropyl-4-(4-nitrophenylazo)resorcinol were available from an earlier study.¹ The equilibrium ionisation of 2-methyl-4-(4-nitrophenylazo)resorcinol in 60 and 80% (v/v) Me₂SO–H₂O and in 60 and 80% (v/v) Me₂SO–D₂O containing Me₄NOH was observed spectrophotometrically and kinetic results were obtained using the stopped-flow method with spectrophotometric detection as described previously.¹ Reaction temperatures were 15 °C and ionic strength was maintained at 0.1 mol dm⁻³ by addition of tetramethylammonium chloride. For measurement of the isotopic fractionation factor and the isotope effect on the chemical shift of the hydrogen-bonded proton in 2-isopropyl-4-(4-nitrophenylazo)resorcinol monoanion, ¹H NMR spectra were recorded at 360 MHz and ²H spectra were obtained at 38.4 MHz (Bruker AM 360 and WM 250 respectively). The fractionation factor of the acidic proton in phenol was obtained from measurements of proton decoupled ¹³C spectra recorded at 90.6 MHz (Bruker AM 360).

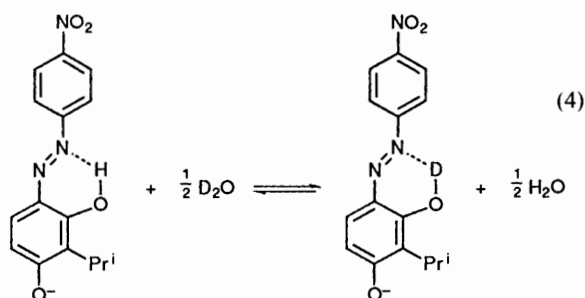
For studies in 80% (v/v) Me₂SO–D₂O the procedure for making up solutions from solid Me₄NOH·5H₂O and 99.7% D₂O resulted in the aqueous component containing ca. 2% H₂O and 98% D₂O at the highest concentrations of hydroxide

ion studied (0.05 mol dm^{-3}). If these solutions were kept for long periods, the fraction of H_2O increased due to the exchange of protons from Me_2SO with deuterons in the aqueous component. This exchange was monitored by observing the decrease in the peak due to the methyl protons in Me_2SO and the increase in the peak due to H_2O in the ^1H NMR spectrum. In the ^2H NMR spectrum the exchange resulted in the appearance of a peak at δ ca. 2.6 corresponding to the formation of deuterium-substituted Me_2SO . It was found that exchange occurred five- to ten-fold more rapidly in 80% than in 60% (v/v) $\text{Me}_2\text{SO}-\text{D}_2\text{O}$ and that the reaction was catalysed by tetramethylammonium hydroxide. Our results are compatible with previous observations² of tritium exchange into the methyl groups of Me_2SO from tritiated water in $\text{Me}_2\text{SO}-\text{H}_2\text{O}$ mixtures containing Me_4NOH . For this reaction a half-life of 1.5 h was found in 80% $\text{Me}_2\text{SO}-\text{H}_2\text{O}$ at 25 °C with $0.027 \text{ mol dm}^{-3}$ Me_4NOH . To minimise the problems of exchange in equilibrium and kinetic studies, solutions in 60% and 80% (v/v) $\text{Me}_2\text{SO}-\text{D}_2\text{O}$ were made up and used immediately.

Results and Discussion

Values of the isotopic fractionation factor (ϕ) and the isotope effect on the chemical shift, $\Delta[\delta(^1\text{H}) - \delta(^2\text{H})]$, for the hydrogen-bonded proton in 2-isopropyl-4-(4-nitrophenylazo)-resorcinol monoanion were measured in 80% (v/v) $\text{Me}_2\text{SO}-\text{L}_2\text{O}$. The monoanion at a concentration of 0.1 mol dm^{-3} was generated in the presence of a 4-chlorophenol/4-chlorophenolate ion buffer (0.15 mol dm^{-3}). Under these conditions exchange of the hydrogen-bonded proton of the monoanion with aqueous protons is slow on the NMR timescale and a fairly sharp peak at $\delta 17.50 \pm 0.01$ (referenced to TMS) was found in the ^1H spectrum. In similar experiments with 2-methyl-4-(4-nitrophenylazo)resorcinol monoanion a sharp peak for the hydrogen-bonded proton could not be observed because of a more rapid exchange with solvent. In the ^2H spectrum of a solution of 2-isopropyl-4-(4-nitrophenylazo)resorcinol monoanion in 80% (v/v) $\text{Me}_2\text{SO}-10\% \text{ H}_2\text{O}-10\% \text{ D}_2\text{O}$ the peak for the hydrogen-bonded proton appeared at $\delta 16.89 \pm 0.04$. This spectrum was referenced to CDCl_3 at $\delta 8.15$ since it was shown that a solution of CHCl_3 in 80% (v/v) $\text{Me}_2\text{SO}-\text{H}_2\text{O}$ gives a peak in the ^1H spectrum at $\delta 8.15$ relative to TMS at $\delta 0$ and it is reasonable to assume³ that for the proton of CHCl_3 , $\Delta[\delta(^1\text{H}) - \delta(^2\text{H})] = 0$. Thus for the hydrogen-bonded proton in 2-isopropyl-4-(4-nitrophenylazo)resorcinol monoanion, the result $\Delta[\delta(^1\text{H}) - \delta(^2\text{H})] 0.61 \pm 0.05$ is found. Positive values of $\Delta[\delta(^1\text{H}) - \delta(^2\text{H})]$ are characteristic of strong or moderately strong hydrogen bonds with double minimum potential functions.^{4,5}

The isotopic fractionation factor (ϕ) for the hydrogen-bonded proton in 2-isopropyl-4-(4-nitrophenylazo)resorcinol monoanion was measured to provide information about the nature of the hydrogen bond and to permit a detailed analysis of the kinetic solvent isotope effect on the proton transfer reaction, eqn. (1). The fractionation factor (ϕ) is the equilibrium constant



for the isotope exchange reaction in eqn. (4). The value of ϕ was measured by observing the reduced integral of the ^1H peak at $\delta 17.50$ in the NMR spectrum of the monoanion in 80% (v/v) $\text{Me}_2\text{SO}-10\% \text{ H}_2\text{O}-10\% \text{ D}_2\text{O}$ compared with 80% (v/v) $\text{Me}_2\text{SO}-20\% \text{ H}_2\text{O}$ as solvent. The conditions for generating the monoanion were the same as those used for the measurement of $\Delta[\delta(^1\text{H}) - \delta(^2\text{H})]$ and the average of two determinations gave $\phi = 0.97 \pm 0.08$.

To provide a value for the fractionation factor of a non-hydrogen-bonded proton, ϕ was measured for phenol in 80% (v/v) $\text{Me}_2\text{SO}-10\% \text{ H}_2\text{O}-10\% \text{ D}_2\text{O}$. In this case, exchange of the phenolic proton with solvent protons is fast on the NMR timescale and a separate peak for the phenolic proton was not observed. A technique for measuring the fractionation factor under these conditions has been devised and depends upon the effect of deuterium substitution on the ^{13}C chemical shift of a nearby carbon atom.⁶ A solution of 0.3 mol dm^{-3} phenol in 80% (v/v) $\text{Me}_2\text{SO}-\text{H}_2\text{O}$ was placed in the inner compartment of a concentric double-walled 5 mm NMR tube. The outer compartment contained 0.1 mol dm^{-3} phenol in solvents of different isotopic composition varying from 80% (v/v) $\text{Me}_2\text{SO}-\text{H}_2\text{O}$ to 80% (v/v) $\text{Me}_2\text{SO}-\text{D}_2\text{O}$. The difference in ^{13}C chemical shift of the quaternary carbon ($\delta = 14\,504.409 \text{ Hz}$) of phenol in the inner and outer compartments was then measured. The difference in chemical shift observed between 80% (v/v) $\text{Me}_2\text{SO}-\text{H}_2\text{O}$ and 80% (v/v) $\text{Me}_2\text{SO}-\text{D}_2\text{O}$ was 14.898 Hz corresponding to the effect of 100% deuterium substitution in the hydroxy group. For three solvents of intermediate isotopic composition the fraction of deuterium substitution was measured from the difference in the observed shift in that solvent compared with the chemical shift in 80% (v/v) $\text{Me}_2\text{SO}-\text{H}_2\text{O}$. From the known deuterium fraction in the solvent the fractionation factor for the phenolic proton was then calculated. The average value from several determinations was $\phi = 1.075 \pm 0.015$. For phenol in aqueous solution the result $\phi = 1.13 \pm 0.02$ has been measured.⁶ The difference in the values of ϕ for 2-isopropyl-4-(4-nitrophenylazo)resorcinol monoanion and phenol in 80% (v/v) $\text{Me}_2\text{SO}-\text{L}_2\text{O}$, although barely outside experimental uncertainty, is in the direction to be expected for the effect of an intramolecular hydrogen bond of moderate strength.⁵

In 80% (v/v) $\text{Me}_2\text{SO}-\text{H}_2\text{O}$, 2-methyl-4-(4-nitrophenylazo)resorcinol monoanion is practically fully dissociated into the dianion at the lowest hydroxide-ion concentrations that could be studied. The value $K > ca. 2000$ was estimated¹ for the equilibrium constant for the reaction in eqn. (1). In 60% (v/v) $\text{Me}_2\text{SO}-\text{H}_2\text{O}$ and 60% (v/v) $\text{Me}_2\text{SO}-\text{D}_2\text{O}$ the results $K 452 \pm 15 \text{ dm}^3 \text{ mol}^{-1}$ and $K 1013 \pm 40 \text{ dm}^3 \text{ mol}^{-1}$ respectively were obtained in the present work.

The first-order rate coefficient (k_{obs}) for ionisation of the hydrogen-bonded proton from 2-methyl-4-(4-nitrophenylazo)resorcinol monoanion was measured at different hydroxide ion concentrations (0.001 to 0.05 mol dm^{-3}) in 80% (v/v) $\text{Me}_2\text{SO}-\text{H}_2\text{O}$ and 80% (v/v) $\text{Me}_2\text{SO}-\text{D}_2\text{O}$. The curved dependence of k_{obs} on hydroxide-ion concentration is shown in Fig. 1. Measurements were also obtained in 60% (v/v) $\text{Me}_2\text{SO}-\text{H}_2\text{O}$ and 60% (v/v) $\text{Me}_2\text{SO}-\text{D}_2\text{O}$ with hydroxide-ion concentrations in the range 0.001 to $0.01 \text{ mol dm}^{-3} [\text{OH}^-]$. Under these conditions the dependence of k_{obs} on $[\text{OH}^-]$ was linear within experimental error as shown in Fig. 2.

In 80% (v/v) $\text{Me}_2\text{SO}-\text{L}_2\text{O}$ (L = H or D) the results were fitted by the expression in eqn. (3). A fit to the kinetic results was obtained from a linear regression analysis of the data plotted in the form of $1/k_{\text{obs}}$ against $1/[\text{OH}^-]$ which gives values for k_1 and k_{-1}/k_2 . Variation of the values of k_1 and k_{-1}/k_2 showed that a range of results gave satisfactory fits within the estimated experimental error of the data. For example, for the 13 data points in 80% (v/v) $\text{Me}_2\text{SO}-\text{H}_2\text{O}$ the following values of k_1/s^{-1} and $(k_{-1}/k_2)/\text{mol dm}^{-3}$ gave fits which deviated from the

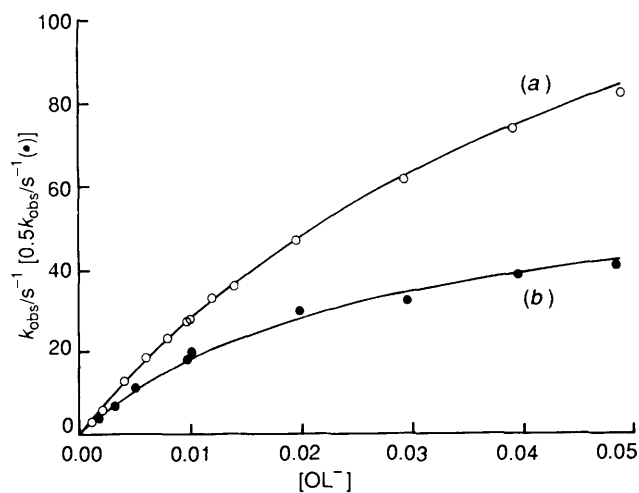


Fig. 1 Dependence of rate coefficient for the ionisation of 4-methyl-(4-nitrophenylazo)resorcinol monoanion in (a) 80% (v/v) Me₂SO-H₂O (k_{obs}) and (b) 80% (v/v) Me₂SO-D₂O ($k_{\text{obs}}/2$) against hydroxide-ion (OL^-) concentration

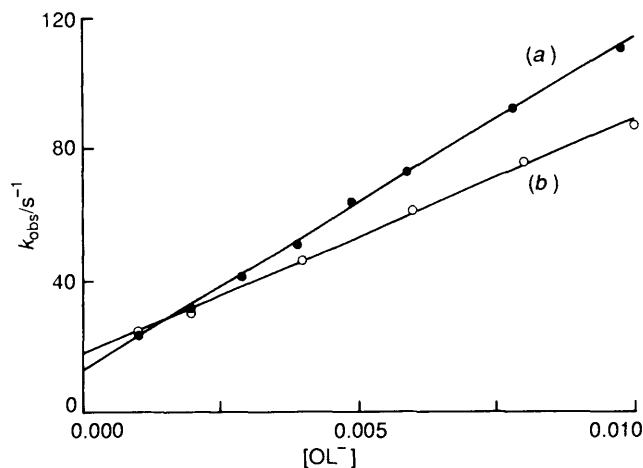


Fig. 2 Dependence of rate coefficient (k_{obs}) for the ionisation of 4-methyl-(4-nitrophenylazo)resorcinol monoanion in (a) 60% (v/v) Me₂SO-H₂O and (b) 60% (v/v) Me₂SO-D₂O against hydroxide-ion (OL^-) concentration

experimental values with an average deviation shown in brackets: k_1/s^{-1} 200 and $(k_{-1}/k_2)/\text{mol dm}^{-3}$ 0.063 (2.5%); 180 and 0.055 (1.5%); 170 and 0.050 (2.6%); 160 and 0.050 (2.4%); 155 and 0.045 (2.7%); 136 and 0.037 (5.5%). The solid line in Fig. 1 for the results in 80% (v/v) Me₂SO-H₂O was plotted using 170 and 0.050, chosen as being in the middle of the range of acceptable values. For the results in 80% (v/v) Me₂SO-D₂O, the average deviations of the experimental points from the fits were larger. The best fits were obtained with the following values: k_1/s^{-1} 145 and $(k_{-1}/k_2)/\text{mol dm}^{-3}$ 0.030 (6.2%); 140 and 0.030 (5.0%); 140 and 0.028 (3.7%); 135 and 0.028 (6.0%); 130 and 0.025 (3.0%); 125 and 0.025 (5.3%). The solid line through the experimental points in 80% (v/v) Me₂SO-D₂O was drawn using the values k_1 135 s⁻¹ and k_{-1}/k_2 0.028 mol dm⁻³.

The values of k_1 and k_{-1}/k_2 used to fit the data in Fig. 1 give isotope effects of $(k_1^{\text{H}}/k_1^{\text{D}})$ 1.26 and $(k_{-1}/k_2)^{\text{H}}/(k_{-1}/k_2)^{\text{D}}$ 1.79. These values are subject to considerable uncertainty as shown by the range of values of k_1 and k_{-1}/k_2 that provide a satisfactory fit to the data. However the uncertainties on the values of $(k_1 k_2/k_{-1})^{\text{H}}$ and $(k_1 k_2/k_{-1})^{\text{D}}$ obtained by taking the ratio of k_1 and k_{-1}/k_2 values in 80% (v/v) Me₂SO-H₂O and 80% (v/v) Me₂SO-D₂O are much lower and the results 3.17×10^3 , 3.27×10^3 , 3.40×10^3 , 3.20×10^3 , 3.44×10^3 , and 3.68×10^3

for $(k_1 k_2/k_{-1})^{\text{H}}$ and 4.70×10^3 , 5.00×10^3 , 4.82×10^3 , 5.20×10^3 , and 5.00×10^3 for $(k_1 k_2/k_{-1})^{\text{D}}$ are calculated. The solvent isotope effect $(k_1 k_2/k_{-1})^{\text{H}}/(k_1 k_2/k_{-1})^{\text{D}}$ 0.71 ± 0.15 is therefore known with greater precision.

If it is assumed that the proton transfer step in eqn. (2) is a diffusion limited process the kinetic solvent isotope effect on this step will be determined by the difference in viscosities of 80% (v/v) Me₂SO-H₂O and 80% (v/v) Me₂SO-D₂O. For the 70% solvent the ratio of viscosities⁷ is 1.09 and assuming the same value for the 80% solvent gives $(k_2^{\text{H}}/k_2^{\text{D}})$ 1.09. From the result $(k_1 k_2/k_{-1})^{\text{H}}/(k_1 k_2/k_{-1})^{\text{D}}$ 0.71 ± 0.15 it follows that the solvent isotope effect on the hydrogen bond equilibrium in eqn. (2) has a value $(K_1^{\text{H}}/K_1^{\text{D}})$ 0.65 ± 0.14 . According to fractionation factor theory,⁸ this isotope effect is given by eqn. (5) in which φ_c

$$(K_1^{\text{H}}/K_1^{\text{D}}) = \varphi_c/\varphi_o\varphi_{\Delta} \quad (5)$$

and φ_o are the fractionation factors of the proton in the closed and open forms of 2-methyl-4-(4-nitrophenylazo)resorcinol monoanion. The term φ_{Δ} is the differential medium effect and is equal to the ratio of fractionation factors of the solvating water molecules of the open and closed forms of 2-methyl-4-(4-nitrophenylazo)resorcinol monoanion. It is reasonable to assume that the values of φ_c and φ_o are the same as those for the fractionation factors of the hydrogen-bonded form of 2-isopropyl-4-(4-nitrophenylazo)resorcinol monoanion (φ 0.97) and of phenol (φ 1.08) respectively. The relative values of these results explain why the equilibrium isotope effect on the opening of the hydrogen bond is inverse. Substitution into eqn. (5) leads to a medium effect of φ_{Δ} 1.38.

In 60% (v/v) Me₂SO-L₂O the dependence of k_{obs} on $[\text{OL}^-]$ is linear within experimental error, Fig. 2. In 60% (v/v) Me₂SO-H₂O, k_{obs} was measured in the presence of hydroxide ion concentrations up to 0.100 mol dm⁻³ and no significant departure from linearity was detected. One explanation for the difference in kinetic behaviour in 60% and 80% (v/v) Me₂SO-L₂O is that the value of k_{-1}/k_2 is higher in 60% (v/v) Me₂SO-L₂O so that curvature in the plots of k_{obs} against $[\text{OL}^-]$ would only be detected at much higher hydroxide-ion concentrations. This explanation is supported by the observation from previous work¹ that the value of k_{-1}/k_2 is ca. ten-fold higher in 80% than in 90% (v/v) Me₂SO-H₂O. Since the equilibrium position in 60% (v/v) Me₂SO-L₂O is less displaced to the product side of eqn. (1) than in 80% (v/v) Me₂SO-H₂O the expression in eqn. (6) is needed to account for the dependence of k_{obs} on hydroxide-

$$k_{\text{obs}} = k_f[\text{OL}^-] + k_r \quad (6)$$

ion concentration. In eqn. (6), k_f and k_r are the forward and reverse rate coefficients for the reaction in eqn. (1). If the reaction is assumed to occur by the mechanism in eqn. (2) and the assumption $k_{-1} > k_2[\text{OL}^-]$ is made, eqn. (7) is obtained in

$$k_f = k_1 k_2/k_{-1}; \quad k_r = k_{-2} \quad (7)$$

which k_2 and k_{-2} are the rate coefficients in the forward and reverse directions for the proton transfer step.

The plots of k_{obs} against $[\text{OL}^-]$ in Fig. 2 yield the following values in 60% (v/v) Me₂SO-H₂O: k_f $7.1 \pm 0.5 \times 10^3$ dm³ mol⁻¹ s⁻¹ and k_r 17.7 ± 2 s⁻¹; in 60% (v/v) Me₂SO-D₂O k_f $1.10 \pm 0.05 \times 10^4$ dm³ mol⁻¹ s⁻¹ and k_r 12.8 ± 2 s⁻¹. The ratios of rate coefficients k_f/k_r 400 ± 80 dm³ mol⁻¹ in 60% (v/v) Me₂SO-H₂O and 860 ± 200 dm³ mol⁻¹ in 60% (v/v) Me₂SO-D₂O are compatible with the values of the equilibrium constants (K) for the reaction in eqn. (1) determined in separate experiments, K 452 ± 15 dm³ mol⁻¹ in 60% (v/v) Me₂SO-H₂O and K 1013 ± 40 dm³ mol⁻¹ in 60% (v/v) Me₂SO-D₂O. Use of eqn. (7) gives the value of the kinetic solvent isotope effect

$(k_1k_2/k_{-1})^H/(k_1k_2/k_{-1})^D$ 0.65 ± 0.09 for the reaction in 60% (v/v) $\text{Me}_2\text{SO}-\text{L}_2\text{O}$ and this is similar to the result $(k_1k_2/k_{-1})^H/(k_1k_2/k_{-1})^D$ 0.71 ± 0.15 obtained in 80% (v/v) $\text{Me}_2\text{SO}-\text{L}_2\text{O}$.

In previous work⁹ the kinetic solvent isotope effect on the deprotonation of 4,6-bis(phenylazo)resorcinol monoanion was investigated in 70% (v/v) $\text{Me}_2\text{SO}-\text{L}_2\text{O}$ containing phenol buffers. The reaction was shown to occur by a similar mechanism to that in eqn. (2) for the hydroxide-ion-catalysed deprotonation of 2-methyl-4-(4-nitrophenylazo)resorcinol monoanion except that in the second step the proton is removed by phenolate ion rather than hydroxide ion. Analysis of the data in 70% (v/v) $\text{Me}_2\text{SO}-\text{H}_2\text{O}$ and 70% (v/v) $\text{Me}_2\text{SO}-\text{D}_2\text{O}$ gave the following kinetic isotope effects: $(k_1)^H/(k_1)^D$ 1.04 ± 0.2 , $(k_{-1}/k_2)^H/(k_{-1}/k_2)^D$ 0.89 ± 0.15 , and $(k_1k_2/k_{-1})^H/(k_1k_2/k_{-1})^D$ 1.17 ± 0.2 . Although the uncertainties are large, the results differ significantly from the values deduced from the data for the hydroxide-ion-catalysed deprotonation of 2-methyl-4-(4-nitrophenylazo)resorcinol monoanion in 80% (v/v) $\text{Me}_2\text{SO}-\text{H}_2\text{O}$.

One possible reason for the difference in results is that the species from which the hydrogen-bonded proton is removed are different. For the monoanion of 2-methyl-4-(4-nitrophenylazo)resorcinol the hydrogen-bonded proton is less acidic by 2 pK units and the equilibrium constant (K_1) for opening the hydrogen bond is smaller by a factor of 10^2 to 10^3 than for 4,6-bis(phenylazo)resorcinol monoanion. However it seems more likely that the difference in behaviour of the two systems arises from differences in the second steps involving proton removal by hydroxide ion and phenolate ion. For the reaction of 4,6-bis(phenylazo)resorcinol monoanion with phenolate ion the equilibrium constant for the overall reaction has a value⁹ of 3.4. Assuming that the proton transfer step is diffusion limited (k_2 ca. $1 \times 10^{10} \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$) the value k_1k_2/k_{-1} 4.0×10^6 gives an equilibrium constant for the first step in eqn. (2) K_1 4.0×10^{-4} . It follows that the equilibrium constant for the proton transfer step has a value of 8.5×10^3 . In contrast the reaction of 2-methyl-4-(4-nitrophenylazo)resorcinol monoanion with hydroxide ion in 80% (v/v) $\text{Me}_2\text{SO}-\text{H}_2\text{O}$ occurs with an overall equilibrium constant of >2000 , K_1 is estimated to have a value of ca. 3×10^{-7} and it follows that the proton transfer step to hydroxide ion occurs with an equilibrium constant $>7 \times 10^9$. For proton transfer reactions between oxygen and nitrogen acids and bases it has been found¹⁰ that the kinetic solvent isotope effect has a maximum value when the species between which the proton is being transferred have similar pK values. The isotope effect falls to a value close to unity, as expected for a diffusion controlled process, when the pK values differ by greater than ca. 5 pK units. In the case of proton transfer from the open form of 4,6-bis(phenylazo)resorcinol monoanion to buffer, the value of the equilibrium constant for this step (8.5×10^3) means that the pK values of the two species are sufficiently close that the isotope effect $(k_2)^H/(k_2)^D$ could be expected to have a larger value than that predicted for a diffusion controlled process. For proton transfer from the open form of 2-methyl-4-(4-nitrophenylazo)resorcinol

monoanion to hydroxide ion for which the equilibrium constant has a value greater than 7×10^9 it would be expected that the isotope effect $(k_2)^H/(k_2)^D$ would be that for a diffusion controlled proton transfer $(k_2)^H/(k_2)^D$ 1.09. The isotope effects on proton transfer from 2-methyl-4-(4-nitrophenylazo)resorcinol monoanion to hydroxide ion and from 4,6-bis(phenylazo)resorcinol monoanion to buffer can be rationalised if, for the latter reaction, the isotope effect on the proton transfer step has a value of $(k_2)^H/(k_2)^D$ ca. 1.9.

The present results show that the kinetic solvent isotope effect on the opening of an intramolecular hydrogen bond is slightly above unity. The fractionation factors of intramolecularly hydrogen-bonded protons are lower than for non-hydrogen-bonded protons and this explains why the solvent isotope effect on the equilibrium constant for opening of an intramolecular hydrogen bond will normally be less than unity. For some intermolecularly hydrogen-bonded complexes, fractionation factors much lower than unity have been observed¹¹ and reactions involving these species should show kinetic and equilibrium solvent isotope effects which differ substantially from unity.¹²

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