Barriers to Rotation in Intramolecularly Hydrogen-bonded 2-Phenylazoresorcinols

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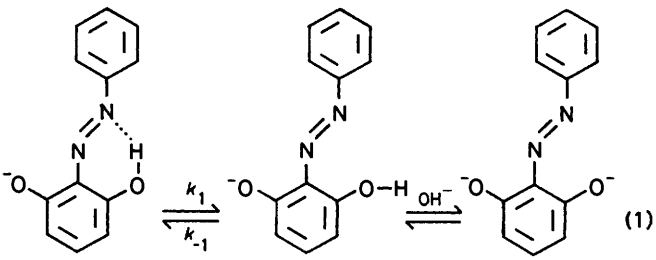
Separate peaks at δ 13.0 and 7.5 are observed for the intramolecularly hydrogen-bonded and non-hydrogen-bonded hydroxy groups in the ^{1}H n.m.r. spectrum of 2-phenylazoresorcinol in [$^2H_8$]toluene at temperatures below *ca.* 300 K. At 357 K, equilibration of the two conformers in which the phenylazo group is hydrogen-bonded to each hydroxy group is rapid (k 5.4 × 10^4 s^{-1}) and an averaged hydroxy peak at δ *ca.* 10 is observed. Energy barriers for substituted 2-phenylazoresorcinols in [$^2H_8$]toluene and CD_2Cl_2 have been obtained from linewidth measurements of the hydroxy peaks and from observation of coalescence temperatures of aromatic ^{1}H and ^{13}C signals.

Proton transfer from the monoanion of 2-phenylazoresorcinol to hydroxide ion in 95% (v/v) Me_2SO–H_2O is considered to occur by the mechanism in equation (1).[1] A non-hydrogen-bonded open form of the monoanion is present in low concentration, in equilibrium with the closed form and values of the rate coefficients k_1 4.2 ± 0.1 × 10^3 s^{-1} and k_{-1} < *ca.* 10^8 s^{-1} were deduced from the kinetic results. In similar studies[2] with 4,6-bis(phenylazo)resorcinol monoanion in 70% (v/v) Me_2SO–H_2O, values of 3.7 ± 0.8 × 10^4 s^{-1} for k_1 and 7 ± 2 × 10^7 s^{-1} for k_{-1} were found. Since these results appeared to us to be surprisingly low, we have carried out further studies of the opening and closing of the hydrogen bond between phenylazo and hydroxy groups. Studies by n.m.r. of the rate of equilibration in equation (2) occurring in [$^2H_8$]toluene for the phenylazoresorcinols (**1**)—(**4**) are now reported. Some data were also obtained in CD_2Cl_2 and $(CD_3)_2SO$.



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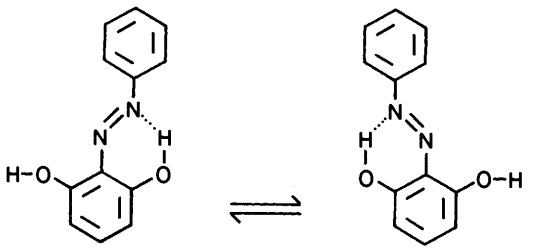
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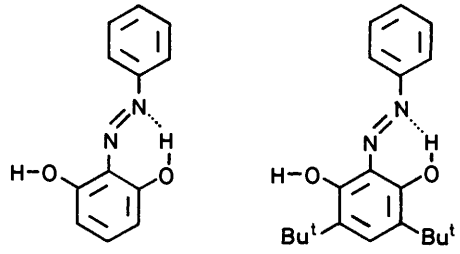
Experimental

Materials.—The preparation of 2-phenylazoresorcinol (**1**) has been described previously.[1,3] Samples of 4,6-di-t-butyl-2-phenylazoresorcinol (**2**) and 4,6-di-t-butyl-2-(4-nitrophenylazo)resorcinol (**4**) were prepared by reaction of the appropriate diazonium salt with 4,6-di-t-butylresorcinol. Recrystallisation of (**2**) from methanol gave red-brown plates, m.p. 130—132 °C; δ[$(CD_3)_2SO$] 11.97 (s, 2 H, OH), 8.2—7.5 (m, 5 H, $C_6H_5N_2$), 7.30 (s, 1 H, 5-H), and 1.40 (s, 18 H, Bu^t). A pure sample of (**4**) was obtained as a red solid by flash chromatography[4] on MN silica gel 60 with toluene as eluant; m.p. 195—197 °C; δ[$(CD_3)_2CO$] 11.60 (s, 2 H, OH), 8.40 (s, 4 H, $N_2C_6H_4NO_2$), 7.57 (s, 1 H, 5-H), and 1.43 (s, 18 H, Bu^t). Reaction of benzenediazonium chloride with 1,3,5-trihydroxybenzene gave a mixture of products from which 2-phenylazo-1,3,5-trihydroxybenzene (**3**) was separated by flash chromatography as the first fraction with toluene as eluant. The product was red, m.p. 192—194 °C; δ[$(CD_3)_2SO$] 12.24 (s, 2 H, 1- and 3-OH), 10.63 (s, 1 H, 5-OH), 7.9—7.3 (m, 5 H, $C_6H_5N_2$), and 5.88 (s, 2 H, 4- and 6-H).

Samples of (**1**), (**3**), and (**4**) were dried at room temperature under vacuum, and (**2**) was dried at 77 °C under vacuum. Gold label $(CD_3)_2SO$, CD_2Cl_2, and [$^2H_8$]toluene were dried over molecular sieves[5] and handled in a dry box.

N.m.r. Measurements.—Activation parameters for the reaction in equation (2) were determined for (**1**)—(**4**) by observation of the changes in n.m.r. spectra with temperature. Most results were obtained from the hydroxy proton resonances but observations of the aromatic ^{1}H and ^{13}C signals were also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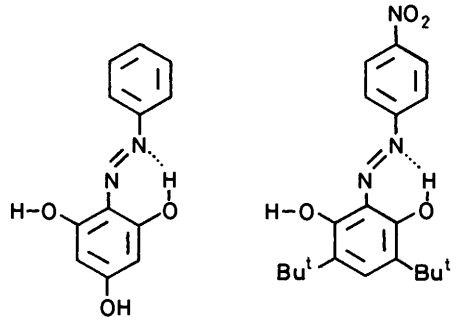

(3) (4)

made. Spectra were run with a Bruker WM 250 instrument and proton shifts were measured relative to Me_4Si. Proton-decoupled ^{13}C spectra were obtained at 62.896 MHz. Variable-temperature n.m.r. spectra were taken for (**1**)—(**4**) in [$^2H_8$]toluene over the range 207—377 K and for (**1**) and (**2**) in CD_2Cl_2 at 213—297 K. For 2-phenylazoresorcinol (**1**) in toluene, the ^1H and ^{13}C spectra were obtained at concentrations of 0.06 and 0.25 mol dm^{-3}, respectively, and similar concentrations were used for (**2**)—(**4**). Depending on the temperature, the solvent, and the particular substituted 2-phenylazoresorcinol, the hydroxy resonances were observed as a collapsed two-proton singlet at δ 10—11, or as two distinct singlets at δ 7—8 and 13—14, each integrating for one proton. Linewidth measurements were made at 10 K intervals of the expanded hydroxy peaks, either by hand or by a curve-fitting procedure. For (**1**) and (**2**) in toluene, linewidths were measured in the temperature range where broadening of the collapsed hydroxy peak occurred (fast exchange) and in the range where broadening of the two separate hydroxy peaks was observed (slow exchange). In most cases, the upfield hydroxy resonance overlapped with the aromatic ^1H signals and accurate widths could only be obtained for the downfield signal. However for (**2**) in toluene, linewidths were measured for both hydroxy resonances. With (**1**) and (**2**) in CD_2Cl_2, the temperature could not be raised sufficiently to observe sharpening of the collapsed resonance, and for (**3**) and (**4**) in toluene exchange was sufficiently slow even at 377 K that the collapsed peak was extremely broad. In these cases, linewidth measurements were limited to the slow exchange region.

For broadening of the averaged hydroxy resonance in the fast-exchange region, equation (3) was used to calculate the rate coefficient for exchange (k), and in the range where the hydroxy resonances were distinct equation (4) was used. In these

$$k = \pi(\delta\nu)^2(W^* - W_0) \quad (3)$$

$$k = \pi(W^* - W_0) \quad (4)$$

approximate equations,[6] W^* is the measured linewidth at half-height at a particular temperature, W_0 is the natural linewidth, and δν is the difference in shift of the hydroxy protons in the absence of exchange. Satisfactory results were obtained by taking the natural linewidth as that for Me_4Si. Within the limits of uncertainty of our experiments, the Me_4Si linewidth remained roughly constant in different solvents and over a range of temperatures. The values of δν for each compound were measured at the lowest temperature at which a spectrum was recorded. For each system plots of $\ln(k/T)$ against $1/T$ were used to calculate the activation parameters given in the Table. The plots were accurately linear. For example for 2-phenylazoresorcinol in toluene values of k at ten temperatures over the range 237 to 377 K gave a straight line with correlation coefficient 0.9998.

In some cases, approximate values of rate coefficients were calculated from observation of coalescence temperatures. The rate coefficient at the coalescence temperature is given[6] by $k = \pi(\delta\nu)/2$. For example in the ^{13}C spectrum of 2-phenylazoresorcinol in toluene, collapse of the aromatic ^{13}C signals of carbon at the 4- and 6-positions and at the 1- and 3-positions was observed at *ca.* 280 K. Rate coefficients calculated in this way were found to be compatible with the values calculated from the more detailed treatment of the broadening of the hydroxy resonances.

Results and Discussion

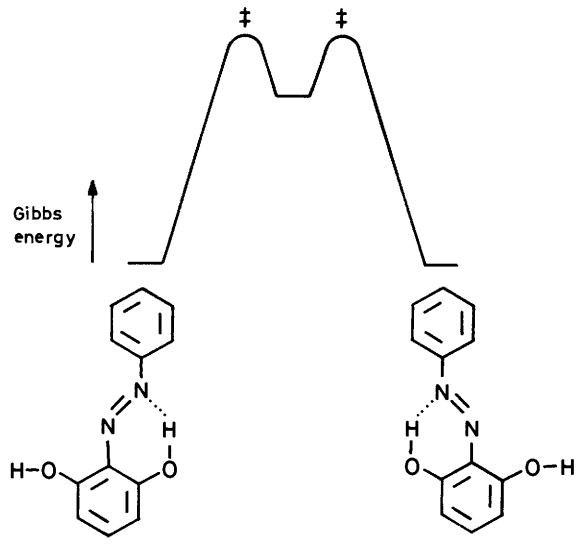
The ^1H spectra of solutions of 2-phenylazoresorcinol in $(CD_3)_2SO$ and CD_2Cl_2 at 298 K contain peaks at δ 11.80 and *ca.* 10, respectively, for the hydroxy protons. In CD_2Cl_2 at lower temperatures, the peak was observed to broaden and split into peaks at δ 13.03 and 7.85 which shifted slightly and sharpened as the temperature was lowered. At 298 K the aromatic region of the spectrum in CD_2Cl_2 contained a doublet for the equivalent protons at the 4- and 6-positions (δ 6.57), and the proton at the 5-position gave a triplet centred at δ 7.30. At lower temperatures the protons at the 4- and 6-positions were observed to become non-equivalent: the doublet and triplet first broadened and then each gave rise to two doublets as the temperature was lowered further. In [$^2H_8$]toluene, reaction (2) occurs more slowly, and even at 298 K the hydroxy protons gave separate broad peaks at δ *ca.* 13 and 7.5, although the latter was partially obscured by solvent protons. At lower temperatures the peaks sharpened and shifted slightly and at higher temperatures collapse to a broad singlet at δ 9.98 was observed. For 2-phenylazoresorcinol in [$^2H_8$]toluene, the ^{13}C spectrum at low temperatures contained one pair of peaks at δ 157.47 and 154.26 (carbon at positions 1 and 3) and another pair at δ 109.05 and 105.82 (carbon at 4- and 6-positions). As the temperature was raised, each pair coalesced to give peaks at δ 156.15 and 107.63, and the coalescence temperatures were 278 ± 2 and 280 ± 2 K, respectively. Activation parameters calculated for reaction (2) in toluene and CD_2Cl_2 are given in the Table.

Reaction (2) occurs more slowly for 4,6-di-t-butyl-2-phenylazoresorcinol (**2**). At 298 K in $(CD_3)_2SO$ a single peak (δ 11.97) was observed for the two hydroxy groups, but in CD_2Cl_2 and [$^2H_8$]toluene separate peaks were observed for each hydroxy group, δ 13.70 and 8.21 in CD_2Cl_2 and δ 13.86 and 7.94 in [$^2H_8$]toluene. Activation parameters for (**2**) in these solvents and for 4,6-di-t-butyl-2-(4-nitrophenylazo)resorcinol (**4**) and 2-phenylazo-1,3,5-trihydroxybenzene (**3**) in [$^2H_8$]toluene determined from observations of the hydroxy resonances are given in the Table. For (**3**), separate signals at δ 5.85 and 5.97 due to the protons at the 4- and 6-positions were observed at 287 K. As the temperature was raised the peaks coalesced to a single peak at δ 5.90 which sharpened as the temperature was raised further. Coalescence occurred at 307 ± 2 K.

Table. Rotational energy barriers in substituted 2-phenylazoresorcinols

	Solvent	δ_1[a]	δ_2[a]	δ_3[b]	$10^{-2}k$[c] / s^{-1}	$\Delta G^{\ddagger}$[c] / kJ mol^{-1}	$\Delta H^{\ddagger}$ / kJ mol^{-1}	$\Delta S^{\ddagger}$ / J K^{-1} mol^{-1}
(**1**)	*d*	13.01	7.49	9.98	19 ± 4	54.5 ± 1	47.3 ± 1	−24 ± 4
	e	12.92	7.85	*ca.* 10	30 ± 10	53.0 ± 2	40.0 ± 2	−45 ± 10
(**2**)	*d*	13.86	7.94	10.75	2.2 ± 0.4	59.8 ± 1	55.3 ± 1	−15 ± 4
	e	13.70	8.21	*f*	7 ± 3	57.0 ± 2	47.0 ± 2	−33 ± 10
(**3**)	*d*	13.84	7.53	*f*	0.44 ± 0.2	63.8 ± 2	56.9 ± 2	−23 ± 4
(**4**)	*d*	13.58	7.76	10.63	0.49 ± 0.2	63.4 ± 2	57.7 ± 2	−19 ± 4

[a] Hydroxy resonance (slow exchange) at 250 K. [b] Hydroxy resonance (fast exchange) at 377 K in toluene and 298 K in CD_2Cl_2. [c] 298 K. [d] [$^2H_8$]Toluene. [e] CD_2Cl_2. [f] No coalescence.

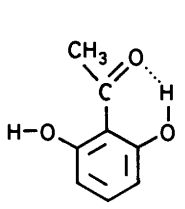


Scheme.

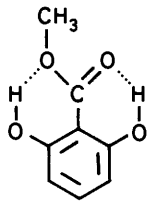
The signal at δ 13—14 in the spectra of (**1**)—(**4**) is due to the intramolecularly hydrogen-bonded hydroxy group, and the peak for the free hydroxy group occurs at δ 7.5—8.5. There is no evidence[7] in the ^{13}C n.m.r. spectrum of simple azobenzenes for restricted rotation, and it is likely that the slow equilibration of the hydroxy groups in (**1**)—(**4**) is due to the presence of the hydrogen bond. The equilibration probably occurs by the Gibbs energy path in the Scheme, in which the intermediate is an open non-hydrogen-bonded conformer. The lowest energy barrier and the furthest upfield shift of the hydrogen-bonded hydroxy group are found for 2-phenylazoresorcinol and this species may contain the weakest hydrogen bond. The stronger hydrogen bond in (**2**) as compared with (**1**) may be the result of steric compression of the hydrogen-bonded conformer or steric destabilisation of the non-hydrogen-bonded conformer. The additional hydroxy group in the resorcinol ring of (**3**) increases the energy barrier as compared with that for (**1**), but the 4-nitro substituent in the phenylazo ring in (**4**) does not change the energy barrier significantly as compared with (**2**). Theoretical calculations[8] have estimated that in substituted 2-hydroxyazobenzenes the strength of the intramolecular hydrogen bond, defined as the difference in energy of hydrogen-bonded and non-hydrogen-bonded conformers, has a value of 34—38 kJ mol^{-1}. The value is predicted[8] to be relatively insensitive to substituents in the phenylazo ring.

The results for (**1**) and (**2**) in the Table show that changing the solvent from [$^2H_8$]toluene to CD_2Cl_2 has little effect on the energy barrier. However the barrier to equilibration of the hydroxy groups appears to be lower in $(CD_3)_2SO$, because for 4,6-di-t-butyl-2-phenylazoresorcinol at 298 K separate peaks for the hydroxy groups were observed in CD_2Cl_2 and [$^2H_8$]toluene, but a single peak integrating for two protons was found with $(CD_3)_2SO$ as solvent. This is compatible with stabilisation of the open form of the phenylazoresorcinol by intermolecular hydrogen-bonding of the hydroxy group with $(CD_3)_2SO$ and a lowering of the energy barrier.

The energy barriers in (**1**)—(**4**) are higher than those found[9] for 2-acetylresorcinol (**5**), for which the results at 298 K in



(**5**)



(**6**)

diethyl ether are $\Delta G^{\ddagger}$ 41 ± 2 kJ mol^{-1}, $\Delta H^{\ddagger}$ 19.2 ± 2 kJ mol^{-1}, and $\Delta S^{\ddagger}$ −75 ± 17 J K^{-1} mol^{-1}. With 2-methoxycarbonylresorcinol (**6**), for which two intramolecular hydrogen bonds may be present, the results in dichlorofluoromethane were $\Delta G^{\ddagger}$ 46.0 ± 0.5 kJ mol^{-1}, $\Delta H^{\ddagger}$ 28.4 ± 0.4 kJ mol^{-1}, and $\Delta S^{\ddagger}$ −59 ± 6 J K^{-1} mol^{-1}.

In proton transfer from the monoanion of 2-phenylazoresorcinol in Me_2SO–H_2O mixtures,[1] the kinetic barrier to opening and closing of the intramolecular hydrogen bond in the monoanion is sufficiently high to make this step rate-limiting in the overall reaction under certain conditions. The intramolecular hydrogen bond will be weaker in 2-phenylazoresorcinol than in the monoanion, but the present results show that there is a modest energy barrier to breakage of the hydrogen bond in substituted phenylazoresorcinols in toluene and methylene dichloride. It is of interest that the barrier to rotation is increased by t-butyl substituents. The conclusion has been reached from measurements of the acid dissociation constants of the monoanions of 2-phenylazoresorcinol and the 4,6-di-t-butyl derivative that the hydrogen bond is strengthened by t-butyl groups.[10] For example the second dissociation of 2-phenylazoresorcinol is half-complete in 95% (v/v) Me_2SO–H_2O in the presence of 0.016 mol dm^{-3} hydroxide ion, but dissociation of the monoanion of the t-butyl derivative is negligible in the presence of 0.1 mol dm^{-3} hydroxide ion.[10]

Acknowledgements

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