

Studies of Hydrogen Bonding. Part XXXV.* Proton NMR Spectral Studies of Hydrogen Bonding between Phenol and Various Proton Acceptors. Concentration Effects

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The Higuchi plot has been used to evaluate the association of phenol with various proton acceptors. When the ratio of the concentration of phenol to that of proton acceptor was high, the NMR chemical shift data suggest the presence of $n:1$ proton donor–acceptor associates in addition to a 1:1 complex. At low concentration ratio, the 1:1 associate is solvated by acceptor molecules.

The chemical shift of the hydrogen bonded O–H proton has been found to be dependent on both the temperature and the concentration of the proton acceptor. A linear correlation exists between the logarithm of the association constant and the solvatochromic parameters β and π^* of Taft *et al.*

Higuchi *et al.*² have developed an iterative NMR method of calculating the association constant of a hydrogen-bonded complex. In previous publications^{3–7} it was shown that the Higuchi plot was an excellent method of studying weak hydrogen bonds such as for the systems chloroform/phosphoryl compounds and chloroform/amides. In this work it has been demonstrated that the method is less usable for the evaluation of the association constant of stronger hydrogen bonds like phenol/triethyl phosphate and phenol/amides. The main reason for this is that the association constant value for a strong hydrogen bond is very sensitive to small changes in the intercept value of the final regression line in the Higuchi plot. The observed sensitivity has now been utilized to study the effect of the proton acceptor concentration on complex formation.

Experimental

The chemicals were purified and dried as previously reported.^{8–10} All compounds were manipulated in a dry box under a dry nitrogen atmosphere. The concentrations used are given in Tables 1 and 2. The NMR data were obtained on a JMN-C-60H spectrometer with temperature accessories. The measurements were carried out in carbon tetrachloride at 20, 35, and 50 °C. The temperature accuracy was estimated to be ± 1 °C. The chemical shift of the O–H proton donor signal was measured with respect to Me₄Si by internal locking. By sweeping with a 100 Hz sweep width three times in each direction, the reported shifts are accurate to at least 0.003 ppm. The observed NMR chemical shift, δ_{obs} , of

a proton donor in equilibrium with a donor–acceptor complex is, in general, given by eqn. (1), where δ_f is the chemical shift of the non-bonded donor proton, δ_x is the chemical shift of the donor proton in the 1:1 hydrogen-bonded complex, C_d is the total proton donor concentration and C_x is the proton donor concentration in the 1:1 complex. By combining eqn. (1) with the equilibrium expression (2), the Higuchi eqn. (3) is obtained, where C_a is the total concentration of the proton acceptor.

$$\delta_{\text{obs}} = \frac{C_d - C_x}{C_d} \delta_f + \frac{C_x}{C_d} \delta_x \quad (1)$$

$$K_{\text{ass}} = \frac{C_x}{(C_d - C_x)(C_a - C_x)} \quad (2)$$

$$\frac{C_a}{\delta_{\text{obs}} - \delta_f} = \frac{1}{\delta_x - \delta_f} (C_a + C_d - C_x) + \frac{1}{K_{\text{ass}}(\delta_x - \delta_f)} \quad (3)$$

The Higuchi plot (3) contains two unknowns, K_{ass} and δ_x . The δ_f value is found by a dilution study of phenol in carbon tetrachloride.¹¹ The plot $C_a/(\delta_{\text{obs}} - \delta_f)$ vs. $(C_a + C_d)$ yields, according to eqn. (3), an approximate value of δ_x . This value can then be substituted into eqn. (1) to give the first approximate values of C_x . The C_x values thus obtained are then substituted into eqn. (3) to give an improved value of the slope and hence of the δ_x value. These steps are repeated, in this work four times, until two successive cycles yield essentially identical convergent values of the slope. The final association constant, K_{ass} , and the NMR chemical shift, δ_x , of the bonded O–H proton in the hydrogen bond are then calculated from the limiting slope and the intercept value. The slope value

* For Part XXXIV see Ref. 1.

Table 1. Thermodynamic and proton NMR spectral data for the interaction of phenol with various acceptors.^a

Proton acceptor	T/°C	[Phenol]/ 10 ⁻² M	[Acceptor] range/10 ⁻² M	δ_{obs} range	δ_x	$K_{\text{ass}}/\text{M}^{-1}$	$-\Delta H^\circ/\text{kJ mol}^{-1}$	$-\Delta S^\circ/\text{J K}^{-1} \text{mol}^{-1}$
Benzonitrile	20	5.25	2.83–210.39	4.700–6.413	6.621	4.5	17.7	47.9
	35	5.16	2.78–206.69	4.530–6.538	6.502	3.0		
	50	5.07	2.74–203.26	4.420–6.055	6.429	2.3		
Benzyl cyanide	20	5.22	15.76–250.90	5.343–6.360	6.510	5.3	20.8	57.4
	35	5.12	15.48–245.90	5.062–6.243	6.490	3.3		
	50	5.04	15.22–241.80	4.848–6.073	6.382	2.4		
Acetonitrile	20	4.83	1.81–179.81	4.563–6.387	6.605	5.3	19.7	55.2
	35	4.75	1.78–176.65	4.433–6.177	6.508	3.5		
	50	4.67	1.75–173.71	4.348–5.987	6.412	2.5		
Cyclohexanone	20	5.22	0.52–101.75	4.695–7.587	7.686	18.5	19.5	42.1
	35	5.13	0.51–99.96	4.542–7.418	7.583	13.0		
	50	5.04	0.50–98.30	4.413–7.193	7.452	8.8		
<i>N,N</i> -Dimethylformamide- <i>d</i> ₇	20	5.07	0.52–102.27	4.983–8.713	8.533	76.1	21.0	35.6
	35	4.98	0.51–100.48	4.790–8.578	8.433	52.1		
	50	4.90	0.50–98.30	4.618–8.408	8.296	34.1		
<i>N,N</i> -Dimethylacetamide	20	5.22	10.04–266.39	8.352–9.243	8.915	120.0	20.8	31.3
	35	5.12	9.87–261.96	8.055–9.130	8.824	78.2		
	50	5.04	9.70–257.36	7.690–9.005	8.707	54.4		
Tetramethylurea	20	5.22	10.51–205.80	8.157–8.875	8.632	128.0	22.0	34.5
	35	5.12	10.28–202.39	7.856–8.772	8.532	86.7		
	50	5.04	10.10–198.83	7.513–8.652	8.428	55.3		
Triethyl phosphate	20	4.94	0.11–206.40	4.572–8.655	8.494	264.0	21.6	27.1
	35	4.85	0.10–202.70	4.487–8.587	8.432	184.0		
	50	4.77	0.10–199.40	4.398–8.515	8.332	116.0		

^a Solvent: carbon tetrachloride. K_{ass} and δ_x are calculated by using the Higuchi plot.

was calculated by the least-squares method by using a HP-41C calculator. In the Higuchi plot the following assumptions have been made: (a) there is only an 1:1 proton donor–acceptor complex equilibrium throughout the concentration range, (b) the chemical shift is due exclusively to hydrogen bonding, (c) the monomer, δ_f , and the dimer, δ_x , chemical shifts are constant throughout the concentration range and (d) the observed chemical shift, δ_{obs} , is a weighted average of monomer and dimer chemical shifts. The final results are summarized in

Table 1. The thermodynamic quantities were calculated in the usual way. The enthalpy of association, ΔH° , was assumed to be constant in the temperature range 20–50 °C. The K_{ass} values were estimated to be accurate to within 10%, ΔH° values to within $\pm 2 \text{ kJ mol}^{-1}$ and δ_x values to within 0.02 ppm.

Results and Discussion

Fig. 1 shows the observed chemical shifts, δ_{obs} , of the phenol O–H proton as a function of the concentration

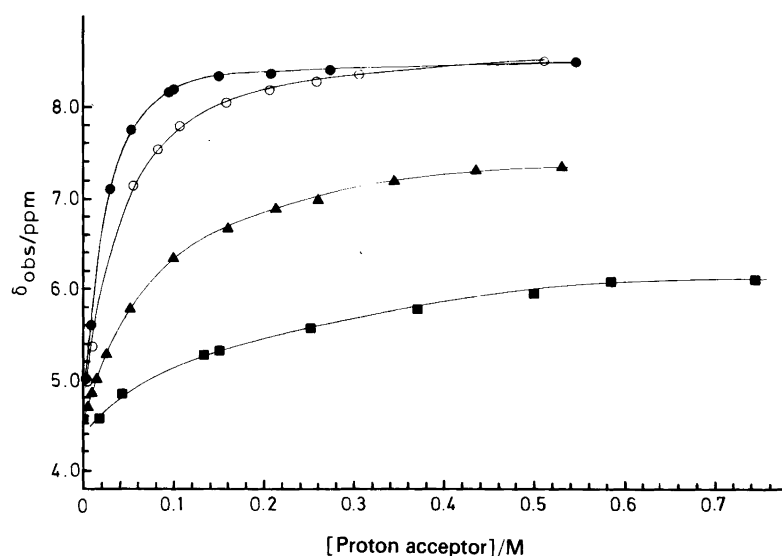


Fig. 1. The observed chemical shift, δ_{obs} , of phenol O–H proton vs. the concentration of, respectively, triethyl phosphate (●), *N,N*-dimethylformamide-*d*₇ (○), cyclohexanone (▲) and acetonitrile (■) in carbon tetrachloride at 20 °C.

of, respectively, triethyl phosphate, *N,N*-dimethylformamide-*d*₇, cyclohexanone and acetonitrile. The plots are characterized by a rapid change in δ_{obs} at low concentration with a much smaller variation above the acceptor concentration of about 0.2 M, the sequence of decreasing slope being, triethyl phosphate > *N,N*-dimethylformamide-*d*₇ > cyclohexanone > acetonitrile which is in accordance with the tendency of the acceptor to form a hydrogen bond.

Fig. 2 shows the final Higuchi plots of the systems phenol/triethyl phosphate and phenol/cyclohexanone. Theoretically, all data points for each system should, if the determination of K_{ass} is totally independent of the acceptor concentration, converge into one straight line after an appropriate number of the iteration cycles. As can be seen, however, the data points at low acceptor concentration do not converge into the final convergent line. The observed deviations were progressively greater as the acceptor concentration was decreased (the proton donor concentration was kept constant, about 0.05 M). We believe that the deviations are due to the formation of *n*:1 proton donor-acceptor associates. Furthermore, since the acceptor concentrations are relatively low, the mixture contains, in accordance with infrared spectroscopic results,¹¹ predominantly 1:1 and 2:1 associates. The effect of self-association of phenol has been minimized by working at low concentration.¹¹ At high acceptor concentration the data points are situated on or close to the regression line (not shown in Fig. 2).

The system phenol/triethyl phosphate was subjected to a careful NMR investigation by using seventeen solutions in the acceptor concentration range 0.001–2.064 M. The final convergent line in the Higuchi plot by using all seventeen data points at 20 °C gave $K_{\text{ass}} = 768.9 \text{ M}^{-1}$ and $\delta_x = 9.627 \text{ ppm}$. The K_{ass} value obtained is, however, far too large in comparison with the value of 268 M^{-1} found

by IR spectroscopy.¹² By cancellation of the four deviating points at low acceptor concentration (see Fig. 2), the final convergent line of the remaining thirteen data points yielded $K_{\text{ass}} = 91.6 \text{ M}^{-1}$ and $\delta_x = 8.657 \text{ ppm}$, i.e., there is a substantial difference in the K_{ass} values whereas the change in δ_x is moderate. We have previously¹¹ shown that the chemical shift, δ_x , of a proton in a hydrogen bond depends on the acceptor concentration. For the system phenol/triethyl phosphate¹¹ δ_x decreases linearly and gradually as C_a decreases and then increases rapidly at $C_a < 0.08 \text{ M}$. The linear correlation at high acceptor concentration was assumed to be due to solvent effects and the deviations at low concentration to the formation of *n*:1 proton donor-acceptor complexes. With respect to these findings, we found it reasonable to continue our successive cancellation of the data points by starting with the highest acceptor concentration. After cancellation of seven data points, the K_{ass} value increased gradually from 91.6 to 264.4 M^{-1} which corresponds well with the IR spectroscopic value. The δ_x value is simultaneously decreased from 8.657 to 8.494 ppm. This means that only six of the seventeen data points, within the concentration range 0.0529–0.2730 M, gave the correct K_{ass} value. The correlation by using six data points is given by eqn. (4),

$$\frac{C_a}{(\delta_{\text{obs}} - \delta_f)} = 0.2380(C_a + C_d - C_x) + 0.0009 \quad (4)$$

$n = 6 \qquad r = 1.000$

The systems phenol/tetramethylurea, phenol/*N,N*-dimethylacetamide, phenol/*N,N*-dimethylformamide-*d*₇, phenol/cyclohexanone and phenol/nitriles have been evaluated similarly by combined use of IR and NMR data. The approximate acceptor concentration range in which the 1:1 associate predominates is tabulated in Table 2. It should be noted that weak proton acceptors, like the nitriles, also form *n*:1 associates with phenol at

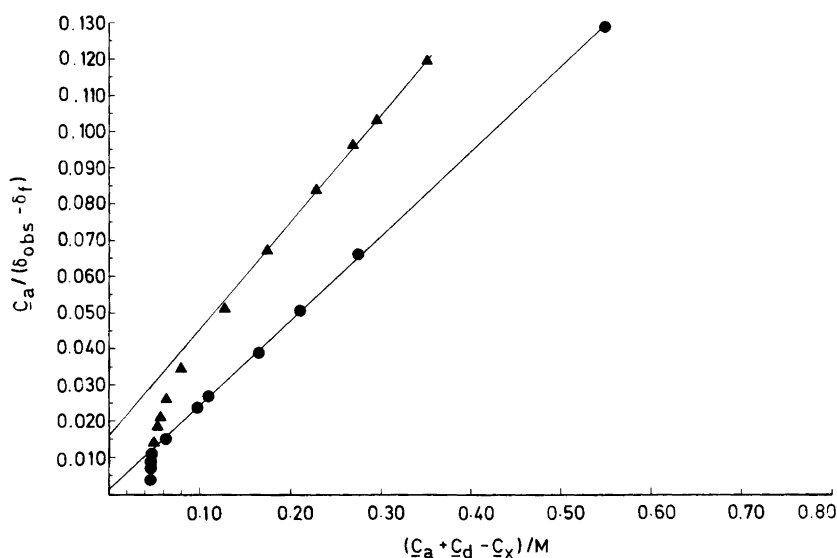


Fig. 2. Final plots of $C_a/(\delta_{\text{obs}} - \delta_f)$ vs. $(C_a + C_d - C_x)$ for the systems phenol/triethyl phosphate (●) and phenol/cyclohexanone (▲) in carbon tetrachloride at 20 °C.

Table 2. The approximate proton acceptor concentration range for the 1:1 associate between phenol and various proton acceptors in carbon tetrachloride at 20 °C.

Proton acceptor	[Phenol]/ 10 ⁻² M	[Acceptor] range/10 ⁻² M
Benzonitrile	5.25	23.83–210.39
Benzyl cyanide	5.22	22.90–250.90
Acetonitrile	4.83	25.26–179.81
Cyclohexanone	5.22	10.49–53.11
<i>N,N</i> -Dimethylformamide- <i>d</i> ₇	5.07	8.20–30.41
<i>N,N</i> -Dimethylacetamide	5.22	10.04–33.57
Tetramethylurea	5.22	13.53–26.26
Triethyl phosphate	4.94	5.29–27.30

low acceptor concentration. The decrease in the K_{ass} value on increasing acceptor concentration is probably due to the effect of variation of the medium surrounding the 1:1 associate from essentially pure carbon tetrachloride to a mixture of carbon tetrachloride and the acceptor. This solvation effect may also be looked upon as the associate is surrounded by loosely bound clusters of acceptor molecules on the formation of a more specific complex. In any case, the surrounding medium will give a small additional deshielding effect on the O–H proton bound in the 1:1 associate, i.e., we will observe an additional increase in the δ_{obs} value. As a consequence, the intercept value in the Higuchi plot will increase and hence the calculated K_{ass} value will be smaller. In general, to prevent the formation of 1:*n* proton donor–acceptor associates, the concentration of a strong acceptor should not exceed more than about 5–6 times the donor concentration. A weak acceptor seems, however, not to form 1:*n* associates. This may be only apparently correct because the association constant for a weak complex is different from a strong H-bond which is not sensitive to a small change in the intercept value of the final regression line in the Higuchi plot. On the other hand, to avoid the formation of *n*:1 associates, the acceptor concentration should not be less than the donor concentration. We have also observed that the weaker the proton acceptor, the greater the excess of the acceptor must be used to prevent the formation of *n*:1 associates (see Fig. 2 and Table 2). It should be emphasized, however, that the acceptor ranges for 1:1 association in Table 2 are certainly not valid for other proton donors or in other solvents.

Previously^{4,6,11} it has been shown that the magnetic anisotropy effect of a doubly bound oxygen causes increased deshielding in the order $\text{S}=\text{O} < \text{P}=\text{O} < \text{C}=\text{O}$, i.e., that the δ_x shift of the donor proton in a $\text{C}=\text{O} \cdots \text{H}$ hydrogen-bonded complex is shifted further downfield, in relation to the $\Delta\nu_{\text{OH}}$ value ($\Delta\nu_{\text{OH}} = \text{IR stretching frequency of free phenol O–H bond minus the frequency of the hydrogen-bonded O–H}$), than the corresponding proton in a $\text{P}=\text{O} \cdots \text{H}$ and an $\text{S}=\text{O} \cdots \text{H}$ complex. The present work also confirms that a $\text{C}=\text{O}$ group exercises a larger deshielding effect than a $\text{P}=\text{O}$ group on the donor proton in a hydrogen bond (see Table 1). We have

also shown that the chemical shift δ_x is lowered on increasing temperature. The variation with temperature probably arises from excitation of the effective length of the O–H \cdots O bond.¹¹ The temperature dependence of δ_x is found to lie between 0.005 and 0.008 ppm/°C. Our data show, however, no obvious correlation between the strength of the hydrogen bond and the temperature dependence of the chemical shift.

The correlations δ_x vs. $\log K_{\text{ass}}$, δ_x vs. ΔH , δ_x vs. $\Delta\nu_{\text{OH}}$ and $\log K_{\text{ass}}$ vs. $\Delta\nu_{\text{OH}}$ for the various systems in Table 1, are not linearly related. Such linear correlations have been shown to exist only within families of compounds.^{4,12–14} Taft *et al.*^{14–16} have shown, however, that the free energy change for an equilibrium reaction in ternary solutions of the types given in Table 1, can be correlated with the solvatochromic parameters β and π^* . The correlation is given by eqn. (5).

$$\log K_{\text{ass}} = \log K_{\text{ass}}^{\circ} + s\pi^* + b\beta \quad (5)$$

In this work the β term is a measure of the ability of the proton acceptor to accept a proton to form a hydrogen bond, the π^* term is the ability of the acceptor to interact by dipolarity/polarizability effects and $\log K_{\text{ass}}^{\circ}$ is the association constant measured in cyclohexane. The coefficients b and s give the relative importance of hydrogen bond strength and dipolar interactions to the free energy. The π^* and β values for the various proton acceptors are given in Table 3. Since the complex formation in this work is mainly solute–solute interaction in a non-hydrogen bonding solvent (CCl_4), it was expected that the hydrogen bond formation should show a major dependence on the β term with only a minor, if any, dependence on the π^* . Regression analyses of the data in Table 3 gives eqn. (6).

$$\log K_{\text{ass}} = 3.615\beta - 1.881\pi^* + 0.921 \quad (6)$$

$n = 7 \quad r = 0.988$

The dipolarity/polarizability term plays an unexpectedly important part in the free energy. The complexes are, however, destabilized by dipolar interaction. The reason for this might be a dipolar interaction of the

Table 3. The solvatochromic parameters π^* and β for the various proton acceptors.

Proton acceptor	$\log K_{\text{ass}}^a$	$\pi^*{}^b$	β^b
Benzonitrile	0.65	0.90	0.41
Benzyl cyanide	0.72	0.99	—
Acetonitrile	0.72	0.75	0.31
Cyclohexanone	1.27	0.76	0.53
<i>N,N</i> -Dimethylformamide- <i>d</i> ₇	1.88	0.88	0.69
<i>N,N</i> -Dimethylacetamide	2.08	0.88	0.76
Tetramethylurea	2.11	0.83	0.80
Triethyl phosphate	2.42	0.72	0.77

^a $\log K_{\text{ass}}$ = the logarithm of the 1:1 association constant between phenol and the various acceptors in carbon tetrachloride at 20 °C. ^b Data from Ref. 14.

solvent ($\pi^* = 0.29$, $\beta = 0$) with the proton donor and acceptor and hence carbon tetrachloride acts as a hydrogen bond breaker. It is well known that carbon tetrachloride interacts with proton acceptors containing a lone electron pair or pairs. Ott *et al.*¹⁷ have shown by phase diagram studies that carbon tetrachloride forms addition compounds with proton acceptors such as 1,4-dioxane and *N,N*-dimethylacetamide. Hence, it is reasonable to conclude that carbon tetrachloride will also interact with the acceptors listed in Table 1. The interaction of phenol with carbon tetrachloride should be of minor importance since O-H...CCl₄ interaction has been shown to be very small.¹⁸⁻²¹

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