The Hydrogen Bonding of Alcohols, Cholesterol and Phenols with Cyanate and Azide Ions

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The hydrogen bonding between ROH hydrogen bond donors (alcohols, cholesterol and phenols) and the cyanate and azide anions has been investigated in CCl_4 solution by FTIR spectroscopy. Equilibrium constants K_a and enthalpies of complex formation have been determined by using the intensity of the antisymmetric vibration $\nu_a(X)$ of the uncomplexed anions X^-. The $\nu_a(X)$ frequency shifts in the $NBu_4X \cdots HOR$ complexes have also been measured. The cyanate and azide anions are found to be the strongest hydrogen bond acceptors ever reported. The correlations between the frequency shifts and log K_a values reveal a strong influence of steric effects on association constants. The very strong basicity of the cyanate ion allows a significant discrimination of the hydrogen bond acidity of the three classes of alcohol.

The hydrogen bond acidity of a given compound is more or less dependent on its state of aggregation: gas, liquid or diluted in an inert solvent. Acidities can be measured in the liquid state by solvatochromic effects[1–3] and in the gas state by ion cyclotron resonance[4,5] or high resolution mass spectrometry.[6,7] In the dissolved state the acidity of a hydrogen bond donor is usually measured by its free enthalpy of hydrogen bonding with a common base used as a reference *i.e.* by the logarithm of the equilibrium constant K_a of the association.[8]

Abraham[8c] derived the scales of hydrogen bond acidity α_2^H and basicity β_2^H from an exhaustive analysis of the literature on log K data. However the foundation of the α_2^H scale appears to be less general because: (*i*) the number of hydrogen bond donors involved is comparatively much smaller; (*ii*) some important classes of carbon and nitrogen acids are excluded from the general statistical calculations; and (*iii*) none of the selected sets can emerge as a reference series.

In our view the development of a hydrogen bond acidity scale requires the definition of a reference set giving accurate primary data for a large number of diverse donors. This procedure has proved useful in the current extension of the β_2^H scale with *p*-fluorophenol as a reference acid.[9] The aim of this work is to test whether some anionic bases may be considered as suitable for this purpose.

Several papers were published in the past on hydrogen bonding with halide anions[10–12] and the ν(OH) frequency shifts of alcohols were measured in order to estimate the basicities of these anions.[13–15]

The two similar pseudo halide X^- anions (X = OCN and N_3) are most favourable for this kind of measurement because: (*i*) they exhibit an intense IR absorption in the 2000–2200 cm^{-1} range where most organic molecules have no absorption—this band is characteristic of the antisymmetric $\nu_a(N_3)$ or pseudo antisymmetric ν_{CN}(OCN) stretching vibration of the anion; (*ii*) the frequency shifts $\Delta\nu$ (bonded minus free) may serve as secondary probes of the hydrogen bonding interactions and (*iii*) they are stronger hydrogen bonding acceptors† than SCN^-

Experimental

Tetrabutylammonium azide NBu_4N_3 was prepared[16] by the reaction of NBu_4OH with gaseous hydrazoic acid. The salt was recrystallized three times in methanol. Tetrabutylammonium cyanate NBu_4OCN was obtained from Fluka. Both salts were dried under vacuum until they reached a constant weight. The solutions in CCl_4 were stored for several days over molecular sieves (Merck, 3 Å) in order to remove last traces of water. The solutions were titrated with monitoring by IR spectroscopy after calibration by Volhard's method.

The alcohols of the best available commercial grade were dried over molecular sieves without further purification. Cholesterol (Sigma, standard for chromatography) was dried under vacuum for several days at 80 °C. Phenols were either distilled when liquids or sublimed when solids.

The IR spectra were obtained with a FTIR spectrometer, Bruker IFS 85, with 2 cm^{-1} resolution. The calcium fluoride cells were thermostatted with a ±0.1 °C accuracy. Relative permittivity measurements were made at 2 MHz on a WTW DM01 dipolemeter with a DFL1 cell.

Method and Results

In this work a series of ROH proton donors was investigated: alcohols, cholesterol and substituted phenols. The equilibrium constants K_a and the enthalpies ΔH_a of formation of the 1:1 complexes were determined from the intensity changes of the free ν_{CN} and $\nu(N_3)$ absorptions after decomposition of the IR spectra by a band fitting procedure.

In CCl_4 solutions of NBu_4X, only one $\nu_a(X)$ IR band is observed and its position is nearly the same as in ionizing solvents: ν_{CN} = 2134 and $\nu_a(N_3)$ = 1995 cm^{-1}. Moreover the shape of the absorption band is independent of the concentration. The behaviour of such tetraalkylammonium salt solutions is well known[17] and the X^- anions are said to be 'spectroscopically free'. In this case the perturbation brought by the large NR_4^+ cation to the anion is so small that no spectral difference can be detected between free and bonded anions.

The extremely low conductivity of the solution makes dielectric measurements possible at low frequency. In the CCl_4 solutions the NBu_4OCN ion pairs are found in equilibrium with non-polar aggregates. As the solubility of NBu_4OCN is quite low we could measure the variations of dielectric permittivity only in a narrow range of concentration [*ca.* (4–6) × 10^{-5} mol dm^{-3}]. The apparent dipole moment of NBu_4OCN was calculated by using Exner's procedure.[18] The aggregation state was represented by an ion pair–quadrupole (dimer) equilibrium

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† The values of $\Delta\nu$(OH) of methanol in CCl_4 solutions are: SCN^- 301, N_3^- 360 and OCN^- 436 cm^{-1}.

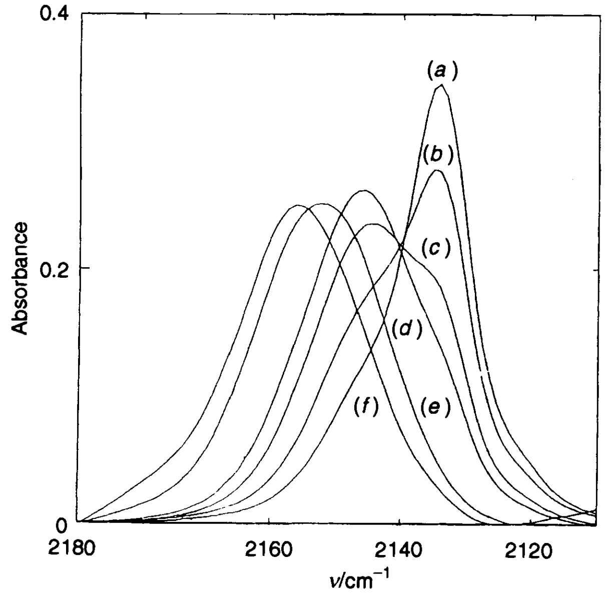

Fig. 1 IR spectra of cholesterol–NBu_4OCN solutions in CCl_4. Concentrations: NBu_4OCN 4×10^{-4}; cholesterol (*a*) 8×10^{-4}, (*b*) 3.5×10^{-3}, (*c*) 0.016, (*d*) 0.032, (*e*) 0.064, (*f*) 0.2 mol dm^{-3}; cell thickness 0.5 cm.

as usual for electrolytes in non-polar or slightly polar solvents.[19] By using an electrostatic model the dipole moment μ of the ion pair was estimated to be 12–13 D[21–23] while the dimer was supposed to be a pure quadrupole ($\mu = 0$).[20] Within this model the dimerization constant K_q of the ion pair was found to be $K_q \simeq 10^4$ dm^3 mol^{-1} at 25 °C. These results are close to those obtained by other authors for NBu_4X in benzene: 1.6×10^3 (X = I) and 3×10^3 dm^3 mol^{-1} (X = Br).[22]

Additions of small amounts of ROH compounds (cholesterol, 2,2,2-trichoroethanol and 4-fluoroethanol) to a NBu_4OCN solution cause an increase of the dielectric permittivity in significant excess to the additivity rule. A similar effect on the dielectric permittivity through addition of methanol to NBu_4Br solutions in benzene was observed by Richardson and Stern.[23] Consequently, the addition of alcohol causes a separation of quadrupoles into ion pairs which form 1 : 1 complexes with the added ROH. Therefore the association equilibrium will be writen as

$$NBu_4X + HOR \rightleftharpoons NBu_4X \cdots HOR$$

and assuming the activity coefficient ratio to be unity the equilibrium constant K_a/dm^3 mol^{-1} is calculated as shown in eqn. (1).

$$K_a = [NBu_4X \cdots HOR]/[NBu_4X][HOR] \qquad (1)$$

Owing to the high values of the extinction coefficients it was possible to investigate NBu_4X at very low concentrations ($5 \times 10^{-5} < c_o < 5 \times 10^{-3}$ mol dm^{-3}). The ROH concentrations were kept in the same range and it was checked in the ν_{OH} region that the self-association of ROH was negligible.

Larger concentrations of alcohols give 1:2 or higher complexes which causes an important increase of $\Delta\nu_{CN}$ shifts. This can be seen on Fig. 1 in the case of cholesterol.

The enthalpies of association were deduced from the dependence of equilibrium constants on temperatures between 5 and 55 °C. The variations of the extinction coefficients were taken into account. A typical example of spectral changes with temperature has been reported in Fig. 2.

The experimental results are summarized in Table 1. The values of log K_a and of frequency shifts are reported for both anions. The ΔH_a values are also reported for the hydrogen bonding with cyanate.

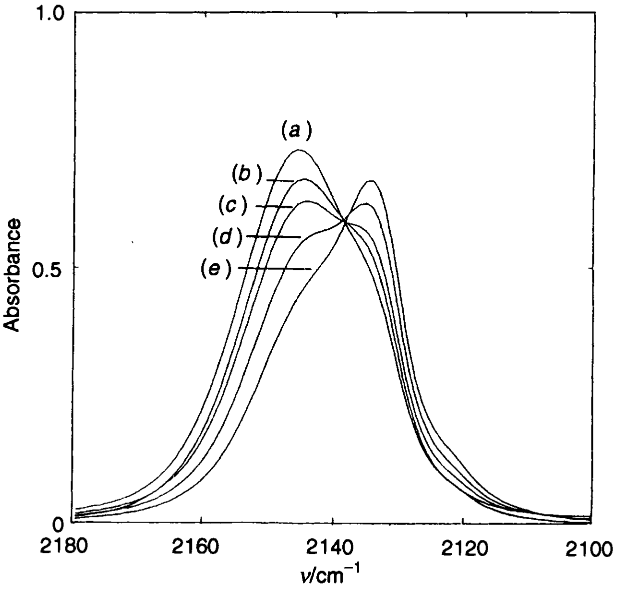

Fig. 2 IR spectra of cholesterol (9.8×10^{-3} mol dm^{-3})–NBu_4OCN (1.2×10^{-3} mol dm^{-3}) solutions in CCl_4 at various temperatures. (*a*) 5, (*b*) 15, (*c*) 25, (*d*) 40 and (*e*) 55 °C; cell thickness 0.5 cm.

Discussion

The association constants with *p*-fluorophenol allow a direct calculation of the β_2^H values for the two anionic species from eqn. (2).

$$\beta_2^H = [\log K_a(p\text{-fluorophenol}) + 1.1]/4.636 \qquad (2)$$

The calculated values $\beta_2^H(OCN^-) = 1.333$ and $\beta_2^H(N_3^-) = 1.210$ give these anions the strongest hydrogen bond basicities known. The basicities of the strongest molecular bases are around the 1.0 value of hexamethylphosphoramide. When a statistical correction of log 2 due to the bidentate character of N_3^- is applied, the ratio $\beta_2^H(OCN^-):\beta_2^H(N_3^-) = 1.17$ is equal to the ratio of the donor numbers of the two anions $DN(OCN^-)/DN(N_3^-) = 1.18$, measured recently by Linert.[24] On the other hand the pK_a of HN_3 (4.7) in water is higher than that of HNCO (3.5).[25] Consequently the order of the basicities of OCN^- and N_3^- is reversed when protonation in water is compared with hydrogen bonding.

The larger hydrogen bonding basicity of the cyanate ion is reflected in the positive intercept and the greater than unity slope of the linear free energy relationship [eqn. (3)] between the two sets of data.

$$\log K_a(OCN^-) = 0.42\,(\pm 0.10) + 1.04\,(\pm 0.03) \log K_a(N_3^-) \qquad (3)$$

n (number of points) = 18; R (correlation coefficient) = 0.992; sd (standard deviation) = 0.15

The subsequent correlations are relative to OCN^- which gives more accurate data than N_3^-. The values of equilibrium constants of the $NBu_4X \cdots HOR$ association (as log K_a) are well correlated to the enthalpy of the complex formation ΔH_a [eqn. (4)].

$$\log K_a(OCN^-) = -0.40\,(\pm 0.09) + 0.122\,(\pm 0.003)\,\Delta H_a$$

$$n = 17 \quad R = 0.996 \quad sd = 0.11 \qquad (4)$$

Table 1 Thermodynamic properties at 25 °C and wavenumber shifts of hydrogen bonded complexes in CCl_4[a]

Compound	$\log K_a(OCN^-)$	$\Delta H_a(OCN^-)$/kJ mol^{-1}	$\Delta\nu_{CN}$/cm^{-1}	$\log k_a(N_3^-)$	$\Delta\nu(N_3^-)$/cm^{-1}
1 2-Methylpropan-2-ol	1.65	−18.0	10.4	1.48	11.2
2 Cyclohexanol	1.90	−19.0	11.1	1.53	12.1
3 Cholesterol	2.04	−20.0	11.5	1.54	12.4
4 Propan-2-ol	2.15	−21.0	11.3	1.60	12.3
5 Butan-1-ol	2.20	−22.0	12.0	1.65	12.9
6 Ethanol	2.27	−22.5	12.2	1.69	13.1
7 Methanol	2.41	−23.0	12.9	1.76	13.9
8 2,6-Diisopropylphenol	2.48	−24.0	16.8	1.87	17.3
9 2-Chloroethanol	2.70	−24.5	15.0	2.23	14.8
10 2,4,6-Trimethylphenol	2.95	−27.0	15.3	2.34	17.4
11 2,2,2-Trichloroethanol	3.65	−33.5	17.8	3.38	16.8
12 2-*tert*-Butylphenol	4.08		18.8	3.56	18.0
13 2-Methylphenol	4.23	−36.0	17.8	3.51	17.0
14 3-Methylphenol	4.30	−38.0	17.8	3.87	17.3
15 3,5-Dimethylphenol	4.32	−39.5	17.5	3.75	16.6
16 4-Methylphenol	4.49	−41.5	18.9	3.85	16.7
17 Phenol	4.78	−43.0	18.9	3.98	17.2
18 4-Fluorophenol	5.08	−45.5	20.6	4.51	19.1
[a] Estimated accuracy	±0.08	±2	±0.3	±0.1	±0.3

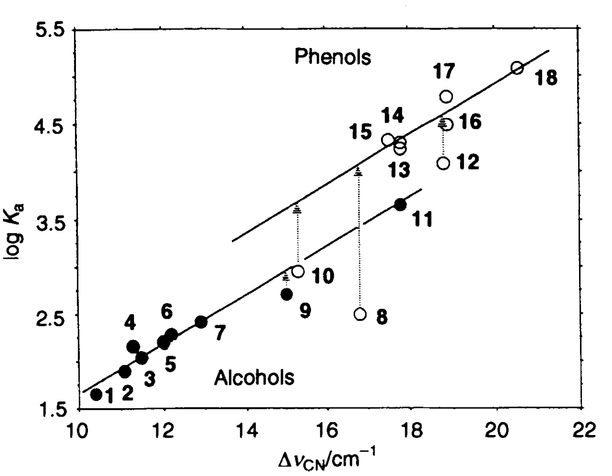

Fig. 3 The correlation $\log K_a$ *vs.* $\Delta\nu_{CN}$ in the hydrogen bonding between OCN^- and ROH. The numbers are the same as in Table 1 and the arrows indicate deviations due either to steric hindrance (*ortho* substituted phenols) or to chelation (2-chloroethanol).

Table 2 A comparison between both sets of α_2^H values

	α_2^H Values	
Compound	Abraham[a]	This work[b]
1 2-Methylpropan-2-ol	0.319 ± 0.042	0.27
2 Cyclohexanol	0.32[c]	0.30
3 Cholesterol	0.32[c]	0.31
4 Propan-2-ol	0.324 ± 0.037	0.33
5 Butan-1-ol	0.328 ± 0.032	0.33
6 Ethanol	0.328 ± 0.017	0.34
7 Methanol	0.367 ± 0.014	0.35
8 2,6-Diisopropylphenol		0.36
9 2-Chloroethanol	0.35[d]	0.38
10 2,4,6-Trimethylphenol	0.374 ± 0.037	0.41
11 2,2,2,-Trichloroethanol	0.500 ± 0.006	0.48
12 2-*tert*-Butylphenol	0.500 ± 0.028	0.53
13 2-Methylphenol	0.519 ± 0.034	0.54
14 3-Methylphenol	0.572 ± 0.014	0.55
15 3,5-Dimethylphenol	0.57[c]	0.55
16 4-Methylphenol	0.569 ± 0.010	0.57
17 Phenol	0.596 ± 0.016	0.60
18 4-Fluorophenol	0.629 ± 0.014	0.63

[a] Ref. 8(*a*). [b] Estimated accuracy ±0.02. [c] Value for simple secondary alcohols. [d] Secondary value based upon one determination only.

Any one of the two parameters can measure the hydrogen bond acidity of a proton donor. However $\log K_a$ must be preferred because most physicochemical phenomena are free energy related processes.

The frequency shifts of $\Delta\nu_a(X)$ in the complexes are of the same order of magnitude for both anions, as in MX ion pairs.[26] As for $\log K_a$, the $\Delta\nu_{CN}$ is preferred to $\Delta\nu_a(N_3)$ for its greater sensitivity to the OH acidity. The plot $\log K_a$ *vs.* $\Delta\nu$(CN) (Fig. 3) reveals: (*i*) the greater sensitivity of the thermodynamic scale to the steric effect of the substituents in the *ortho* position to the hydroxy group—the deviation exceeds 1.5 log unit for the strongly hindered 2,6-diisopropylphenol; (*ii*) the separation of the alcohol donors from the unhindered phenols family—the two sets of donors belong to two approximately parallel lines separated by 0.6 log units; (*iii*) the negative vertical deviation of 2-chloroethanol corresponding to the chelation.

The separation in two different families as well as the greater sensitivity of $\log K$ data to steric effects has already been reported by Kamlet *et al.*[27] and Abraham *et al.*[9] and it is interpreted as a consequence of entropic losses arising from steric strain and/or different geometric arrangements of the hydrogen bond.

The potential of these anions to serve as reference bases can be tested by means of the relationship between $\log K_a(OCN^-)$ and the Abraham α_2^H parameter [eqn. (5)].

$$\log K_a(OCN^-) = -0.99\,(\pm 0.23) + 9.63\,(\pm 0.46)\alpha_2^H \qquad (5)$$

$$n = 17 \quad R = 0.984 \quad sd = 0.216$$

The high standard deviation and the low correlation coefficient of regression of eqn. (5) are attributed mainly to the lack of precision of some α_2^H values (see Table 2) since successive removal of the compounds having the most imprecise α_2^H systematically leads to a significant improvement of both statistical tests. However the overall goodness of fit as measured by an F-test is not increased by this elimination procedure. Hence eqn. (5) has been retained for the calculation of our α_2^H values presented in the last column of Table 2. The estimated error on our calculated α_2^H values is taken as sd/slope = 0.02.

As shown in this table, both scales are in agreement to within experimental error. However some important features can be extracted from our experimental results. (*a*) The very strong basicity of the cyanate ion allows a better discrimination between the three classes of alcohols: tertiary (0.27) < secondary (0.30–0.33) < primary (0.33–0.35). (*b*) Methanol is confirmed to be the most acidic aliphatic alcohol (0.35). (*c*) 2-Chloroethanol (0.38) is now found to be more acidic than ethanol and methanol in line with the inductive effects of the CH_2Cl substituent. (*d*) A value $\alpha_2^H = 0.36$ is assigned to the strongly hindered 2,6-diisopropylphenol. (*e*) The behaviour of cholesterol is the same as expected for a secondary alcohol. This fact has already been noticed in the complexes with covalent proton donors.[28]

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