NUCLEAR MAGNETIC RESONANCE STUDIES OF HYDROGEN BONDING

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Hydrogen bonding is a very significant type of interaction, and is of widespread occurrence. According to Pimentel and McClellan[1], a hydrogen bond exists between a functional group A-H and an atom or a group of atoms D in the same or a different molecule when there is evidence of bond formation, and when the bond linking A-H and D involves the hydrogen atom already bonded to A. Infrared method, based mainly on intensity measurements of the band assigned to the monomeric species, has been used extensively in the determination of equilibrium constants of hydrogen-bonded systems. It offers the advantages that different hydrogen-bonded complexes can be distinguished, and that relatively low concentrations can be used. For very weak complexes however, the infrared method has not proved to be a sufficiently sensitive probe of the quantitative aspects of hydrogen bonding. High resolution nuclear magnetic resonance (nmr) scores easily in providing a sensitive measure of interaction, because it permits the measurements of frequencies which can be done very accurately, rather than intensities which are more subject to uncertainty. This paper describes several ways in which nmr is used to obtain equilibrium constants and thermodynamic functions of various hydrogen-bonded systems. In addition, an application of hydrogen-bonding data to the determination of the preferred form of a beta-diketone is given.

It is well known that the formation of hydrogen bonds usually shifts the nmr signals to lower field, except in certain cases involving aromatic molecules or electron donors in which unusual magnetic anisotropic effects are present[2,3]. Virtually all hydrogen bonds are broken and re-formed at a sufficiently fast rate, so that separate resonances for both hydrogen-bonded and nonhydrogen-bonded states in the same medium are not observed. Consequently, the observed frequency v will correspond to the average of the characteristic frequencies of the complexed and uncomplexed protons (v_c, v_f), weighted according to the equilibrium fraction in each form (X_c, X_f):

$$v = X_f v_f + X_c v_c \qquad (1)$$

For an equilibrium between a monomeric hydrogen donor, A-H, and an electron-donor, D, to form a 1:1 complex C, the following equation may be derived[4] when the concentration of the electron-donor is much greater than that of C:

$$\frac{1}{v - v_f} = \frac{1}{K(v_c - v_f)}\,\frac{1}{d} + \frac{1}{v_c - v_f} \qquad (2)$$

In eq. 2, v is the measured nmr frequency of the hydrogen-bonding proton at a concentration $\underline{d}$ of D, v_f is the frequency of monomeric A-H proton signal at $\underline{d} = 0$, and K is the association constant

$$K = \frac{(C)}{(A\text{-}H)d} \qquad (3)$$

It is interesting to note that this equation is of the same form as one used for treatment of ultraviolet spectral data on 1:1 complexes,

$$\frac{1}{E-E_f} = \frac{1}{K(E_c-E_f)}\frac{1}{d} + \frac{1}{E_c-E_f} \qquad (4)$$

where the E's are molar extinction coefficients[5]. For the treatment of infrared spectral data for 1:1 complexes, the following equation can be derived

$$\frac{1}{E_f-E} = \frac{1}{K\,E_f}\frac{1}{d} + \frac{1}{E_f} \qquad (5)$$

if intensity measurements are made on the band assigned to the monomeric and uncomplexed species and if complexed species do not absorb radiation at the same frequency, so that $E_c = 0$.

Benzenethiol complexes. Mathur, et al.[4], report nmr studies of hydrogen bonding of benzenethiol with N,N-dimethylformamide (DMF), tributyl phosphate (TBP), pyridine, N-methylpyrazole, and benzene to serve as models of bonding of -SH to the carbonyl oxygen, phosphoryl oxygen, organic nitrogen bases, and an aromatic π electron system, respectively. Table I lists the results obtained.

Table I
Thermodynamic data for benzenethiol bonding to electron-donors

Electron donor	v_c-v_f (ppm)	K_{26^o} l./mole	$-\Delta H$ kcal./mole
Pyridine	1.2	0.22	2.4
N-methylpyrazole	1.5	.14	2.1
TBP	1.8	.43	2.0
DMF	2.2	.24	1.8
Benzene	-2.5	.039	0.5

The extent of hydrogen-bonding in these systems, as measured by the equilibrium constants and enthalpy changes, is much smaller than that for the same electron donors interacting with phenol. For example, the values of K for phenol-pyridine and phenol-DMF are 77 and 64 l./mole, respectively [6,7]. These suffice to show the weakness of -SH hydrogen bonding relative to -OH. It is only because of the fairly large association shift, v_c-v_f, and the precision of nmr frequency measurements, that the thermodynamic functions of -SH bonding systems can be obtained. In benzene the ring current effect dominates the sign and magnitude of (v_c-v_f). As shown in Table I, benzene behaves as π-electron donor and hence capable of forming weak hydrogen bond with benzenethiol.

2-Propanol complexes. When 2-propanol is used as the hydrogen donor, eq. 2 has to be modified since self-association of the alcohol occurs, and this may affect the equilibrium involving its complex formation with D. Takahashi and Li[8] have derived the following modified equation

$$\frac{1}{v-v'} = \frac{1}{K(v_c-v')}\frac{1}{dx} + \frac{1}{v_c-v'} \qquad (6)$$

in which x is the fraction of 2-propanol in the form of monomer at a concentration of alcohol which is not hydrogen-bonded to D (assuming the alcohol to be a mixture of monomeric and polymeric species), and v' is the weighted average OH frequency of the 2-propanol which is not hydrogen-bonded to D. Table II lists the results obtained with N-methylacetamide and N,N-dimethylacetamide as electron donors.

Table II: Thermodynamic data for 2-propanol bonding to acetamides

Temp., °C	K, l./mole	v_c, ppm
	(A) N-methylacetamide	
36	3.61	5.00
24	5.02	5.17
14	6.01	5.23
0	8.94	5.35
	(B) N,N-dimethylacetamide	
40	2.23	4.20
29	2.56	4.30
21	2.88	4.33

Muller and Reiter[9] suggest that the nmr frequency of the complexed species depends quite strongly on the degree of excitation of the hydrogen-bond-stretching vibrational mode. They reason that because this is an unusually low-frequency motion, several excited states are significantly populated even at temperatures as low as 200°K, and their calculations show a temperature dependence of v_c. The data of Table II on the values of v_c at different temperatures do indicate that v_c increases slightly with decrease in temperature. This is not in agreement with the assumption of several authors[4,10-12] that the hydrogen bond shifts do not vary with temperature.

Amine complexes. Takahashi and Li[13] report nmr studies of hydrogen bonding between the amino protons of t-butylamine and aniline, and several electron donors, in chloroform medium. CCl_4 cannot be used because of its reaction with amine. When $CHCl_3$ is used as the solvent, eq. 2 has to be modified since the proton in $CHCl_3$ also acts as a hydrogen donor to the electron donor. The modified equation is

$$\frac{1}{v-v_f} = \frac{1}{K(v_c-v_f)} \cdot \frac{1+K_s(S)}{d} + \frac{1}{v_c-v_f} \qquad (7)$$

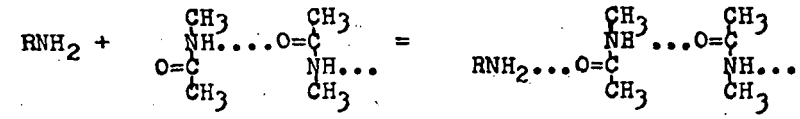
where K and K_s are equilibrium constants of the reactions

$$\text{Amine} + D = \text{amine}\ldots D \qquad K$$
$$Cl_3CH + D = Cl_3CH\ldots D \qquad K_s$$

and (S), d are the total concentrations of $CHCl_3$ and D, respectively. The experiments were carried out so that (S) is much greater than d and d much greater than the total concentration of the amine. From eq. 7, a plot of $1/(v-v_f)$ vs. $(1+K_s(S))/d$ therefore should yield a straight line, from which K can be determined. The value of K_s is determined in separate experiments by measuring

the nmr frequency of the chloroform proton signal in CCl_4 solutions containing 0.05M $CHCl_3$ and various amounts of the electron donor.

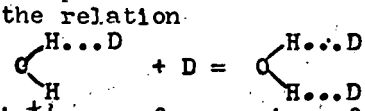
The hydrogen-bonding of N-methylacetamide (NMA) to the amines may be represented by the equation



(8)

The values of $v_c - v_f$ for NMA bonding to the amines are independent of temperature between -19 and 36°. This means that in this system, the hydrogen-bond shift is temperature independent and that the self-association of NMA does not interfere with its bonding with the amines. The relative hydrogen-donor strength of $-NH_2$, -OH, and -SH may be obtained by noting that the association constant for aniline bonding to NMA (K = 58 at 36°) is smaller than for phenol bonding to NMA (K = 105 at 30°) and larger than for benzenethiol bonding to NMA (K = 0.13 at 37°).

<u>Water complexes.</u> Takahashi and Li[14] and Ting, et al.[15], report nmr studies of water as hydrogen donor to tetrahydrofuran, acetone, N,N-dimethylacetamide, N,N-dimethylformamide and dimethyl sulfoxide. In their experiments water is the hydrogen donor at low concentrations (mole fraction in the range of X_w= 0.003 to 0.02), in the presence of an electron donor (mole fraction in the range X_d = 0.5 to 0.99), and cyclohexane as an inert solvent. Since water is not soluble in the inert solvent, the presence of an appreciable excess concentration of D is necessary. In the region of low water content, linear plots of the nmr frequency of the water protons vs. the mole fraction of water, at a given value of X_d, are obtained. The extrapolation of the water proton frequency to zero water concentration is easily made, and in the limit of X_w = 0, only two species are considered: the 1:1 complex, $OH_2 \cdots D$, and the 1:2 complex, $OH_2 . D_2$. The two species are considered to be in equilibrium according to the relation



(9)

The characteristic nmr frequencies of the 1:1 and 1:2 complexes are designated v_{11} and v_{12}, respectively, and the following equation is derived

$$\frac{1}{v_o - v_{11}} = \frac{1}{K(v_{12} - v_{11})} \cdot \frac{1}{X_d} + \frac{1}{v_{12} - v_{11}} \qquad (10)$$

In eq. 10, v_o is the extrapolated frequency of the water protons at zero water concentration and K is equilibrium constant of eq. 9. The authors assume that $(v_{12} - v_{11})$ is approximately independent of temperature and draw plots of $1/(v_o - v_{11})$ vs. $1/X_d$. The correct v_{11} is taken to be the value which makes the

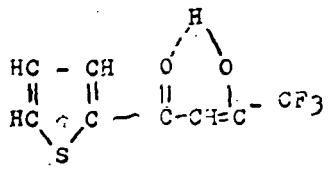
plots at different temperatures come to a common intercept. From the plots and eq. 10, the values of K and v_{12} are obtained.

Equilibrium constants and enthalpy changes for water bonding to N,N-dimethylformamide (DMF) are larger than the corresponding values for water-N,N-dimethylacetamide (DMA). This order is surprising, since DMF is a weaker electron-donor than DMA towards phenol. It may be that the CH proton in DMF functions as a weak hydrogen donor to the oxygen of water, the protons of which are bonded to other DMF molecules. This would result in a greater hydrogen-donor strength of water toward DMF than toward DMA.

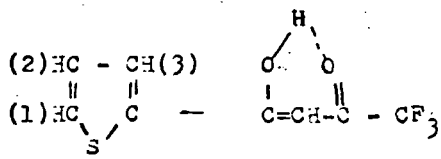
It is of interest to note that Muller and Simon[16] determine proton chemical shifts for dilute solutions of water in mixtures of dioxane and carbon tetrachloride. When the mole fraction of water is below 1.5×10^{-3}, self-association of water is negligible, and the authors treat the data assuming that there are three solute species, free water, a 1:1 water-dioxane complex, and a 1:2 complex. The characteristic frequencies of the complexes appear to be independent of temperature in the range 11-70°, in accordance with the assumption made by Takahashi and Li[14] and Ting, et al.[15]

<u>β-Diketone complexes.</u> Pukanic, et al.[17], report nmr studies of hydrogen bonding between β-diketones- thenoyltrifluoroacetone, hexafluoroacetylacetone, and trifluoroacetylacetone- and several neutral organophosphorus compounds- tributyl phosphate, diethyl ethyl phosphonate, and tri-n-octyl phosphine oxide. Of the three diketones studied, hexafluoroacetylacetone gives the most stable complex with a given phosphorus compound and this is as expected, since it has two electron-withdrawing CF_3 groups in the same molecule. Its greater hydrogen-donor strength is in line with its greater acid strength (pK_a of hexafluoroacetylacetone, thenoyltrifluoroacetone and trifluoroacetylacetone = 4.35, 5.70 and 6.40, respectively). With a given diketone, the equilibrium constant of hydrogen bond formation with the phosphorus compounds increases in the order tributyl phosphate, diethyl ethyl phosphonate, and tri-n-phosphine oxide and is in line with the relative basicity of the phosphorus compounds.

Pukanic, et al.[17], give an example of the application of hydrogen bonding data to the determination of the preferred enol form of thenoyltrifluoroacetone (HTTA). In CCl_4 as solvent, two possible enol structures (I and II) can be postulated



I



II

Intermolecular hydrogen bonding between HTTA molecules is negligible because HTTA remains monomeric and the nmr frequencies remain constant over wide range of HTTA concentrations in CCl_4 at constant temperature and in the absence of a second solute. In the presence of tributyl phosphate up to 1M, the fluorine-19 nmr resonance remains the same as in the absence of it. Under the same conditions, with hexafluoroacetylacetone in place of HTTA, the fluorine-19 signal moves upfield by 0.25 ppm. The data show that the preferred enol form of HTTA is II, rather than I, because tributyl phosphate would bond with HTTA through the enolic -COH. If the preferred enol form of HTTA were I, then the presence of tributyl phosphate should have affected the fluorine frequency, as it does with hexafluoroacetylacetone. Since no effect was observed with HTTA, the conclusion is that the preferred enol form is II, where the fluorine atoms are farther away from the hydrogen-bonding site.

Current studies. Dr. S. Nishimura and Mr. C.H.Ke in our Laboratory are carrying out nmr studies with water and chloroform bonding to organophosphorus compounds and several amines. At the Symposium in September I hope to include a discussion of their important results.

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