Proton Magnetic Resonance Studies of Water as a Hydrogen Donor[1]

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Abstract: Proton magnetic resonance studies are reported of hydrogen bonding between water protons and the electron donors N,N-dimethylacetamide, acetone, and tetrahydrofuran in cyclohexane medium. Data on the variation of the water proton frequency as a function of the concentration of water, in the presence of a large excess concentration of an electron donor, D, are treated in a manner which permits the determination of the equilibrium constant of the reaction $OH_2 \cdot D + D = OH_2 \cdot D_2$. The enthalpy changes on the hydrogen bond formation were determined to be −2.5, −2.4, and −3.6 kcal/mole for tetrahydrofuran, acetone, and N,N-dimethylacetamide, respectively. The characteristic proton magnetic resonance frequency of the H–O–H···D species was found to be approximately half as large as the frequency of the D···H–O–H···D species.

Hydrogen bonding between peptide groups has been demonstrated in proteins, polypeptides, amino acids, and small peptides in the solid state,[2,3] and has often been assigned an important role in the stabilization of the configuration of protein molecules in solution. Klotz and Franzen,[4] however, have considered unlikely that interpeptide hydrogen bonds contribute significantly to the stabilization of macromolecular configuration in aqueous solution, "except in the regions with very low dielectric constants due to a specific high concentration of hydrocarbon-like residues." They further pointed out that a dielectric constant *per se* does not exert a dominant effect on the stability of interpeptide hydrogen bonds, and presume that solvents with H-donor groups may disrupt interpeptide hydrogen bonds by forming bonds between —C=O and the solvent.

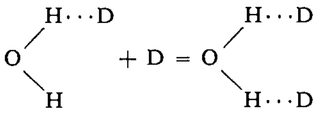
Using the same general line of thought, Tanford[5] states that water would be expected to interfere with —C=O···H—N— bonding in globular protein molecules by forming —C=O···H—O—H and H_2O···H—N— hydrogen bonds. Because of the predominance of water as a medium in living systems, we thought it to be of great importance to have available thermodynamic data on water as a hydrogen donor and as a hydrogen acceptor. A search of the literature reveals that only one paper[6] exists, which gives equilibrium constants of reactions involving water as a hydrogen donor. However, the constant was not determined as a function of temperature, so that the enthalpy of hydrogen bonding to an electron donor could not be obtained.

This paper presents the results of proton magnetic resonance (pmr) studies in the temperature range −14 to 53° on hydrogen bonding involving water. For the hydrogen acceptors, we have chosen acetone, N,N-dimethylacetamide, and tetrahydrofuran to serve as models for hydrogen bonding of OH_2 to the carbonyl oxygen and ethereal oxygen.

Calculation of Equilibrium Constants

In our 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 a large concentration 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 the electron donor, D, is necessary. The very small amount of water is probably present entirely as a mixture of the hydrogen-bonded complexes with the general formula $(OH_2)_x \cdot D_y$, where x and y take on different values when the concentrations are varied.

In the region of low water content, linear plots of the pmr frequency of the water protons *vs.* the mole fraction of water, at a given value of X_d, are obtained, as shown in Figure 1. As the concentration of water increases, water polymerizes to a greater extent, resulting in a downfield shift of the water proton signal. 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 will be assumed: the 1:1 complex, $OH_2 \cdot D$, and the 1:2 complex, $OH_2 \cdot D_2$. The two species are considered to be in equilibrium according to the relation



(1)

The characteristic pmr frequencies of the 1:1 and 1:2 complexes are designated ν_{11} and ν_{12}, respectively.

Since hydrogen-bonding equilibria usually involve very rapid reactions, the extrapolated frequency of the water protons at zero water concentration, ν_0, may be taken to be the weighted average of ν_{11} and ν_{12}, so that

$$\nu_0 = (X_{11}/X_w)_0\nu_{11} + (X_{12}/X_w)_0\nu_{12} \tag{2}$$

where $(X_{11}/X_w)_0$ and $(X_{12}/X_w)_0$ are the fractions of water present as the 1:1 and 1:2 complexes in the limit of zero water concentration, respectively, and $(X_{11}/X_w)_0 + (X_{12}/X_w)_0 = 1$.

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[1] This investigation was supported by PHS Research Grant No. GM-10539-03 from the National Institute of General Medical Sciences, Public Health Service.

[2] G. C. Pimentel and A. L. McClellan, "The Hydrogen Bond," W. H. Freeman and Co., San Francisco, Calif., 1960, p 296 ff.

[3] L. Pauling and R. B. Corey, *Proc. Natl. Acad. Sci. U. S.*, **37**, 251, 729 (1951).

[4] I. M. Klotz and J. S. Franzen, *J. Am. Chem. Soc.*, **84**, 3461 (1962).

[5] C. Tanford, "Physical Chemistry of Macromolecules," John Wiley and Sons, Inc., New York, N. Y., 1961, p 130.

[6] J. R. Holmes, D. Kivelson, and W. C. Drinkard, *J. Am. Chem. Soc.*, **84**, 4677 (1962).

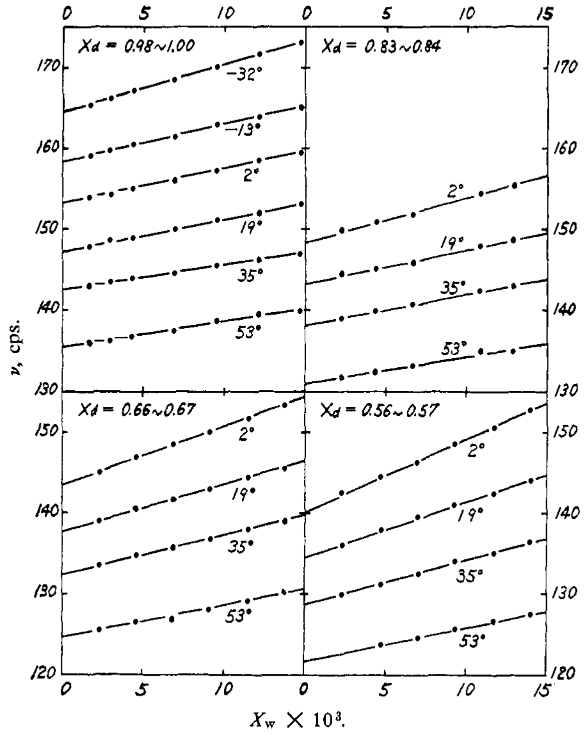

Figure 1. Plots of the water proton frequency *vs.* the mole fraction of water, $X_w \times 10^3$, in the presence of tetrahydrofuran of mole fraction X_d.

The equilibrium constant of eq 1 is given by the relation $K = X_{12}/(X_{11}X_d)$, so that

$$(X_{12}/X_w)_0 = KX_d(X_{11}/X_w)_0 \qquad (3)$$

Combination of eq 2 and 3 and rearrangement yield the equations

$$\nu_0 = \nu_{11} + \frac{KX_d}{1 + KX_d}(\nu_{12} - \nu_{11}) \qquad (4)$$

$$\frac{1}{\nu_0 - \nu_{11}} = \frac{1}{K(\nu_{12} - \nu_{11})}\frac{1}{X_d} + \frac{1}{\nu_{12} - \nu_{11}} \qquad (5)$$

According to eq 5, a plot of $1/(\nu_0 - \nu_{11})$ *vs.* $1/X_d$ yields a straight line, and the intercept is $1/(\nu_{12} - \nu_{11})$. Since it is safe to assume that $(\nu_{12} - \nu_{11})$ is approximately independent of temperature, we have taken trial values of ν_{11} and drawn plots of $1/(\nu_0 - \nu_{11})$ *vs.* $1/X_d$. The correct ν_{11} was taken to be the value which makes the plots at different temperatures come to a common intercept (see Figure 2). From the plots and eq 5, the values of K and ν_{12} are readily obtained.

Experimental Section

Materials. N,N-Dimethylacetamide was distilled twice; the fraction boiling at 165° was collected. Distilled cyclohexane was kept over molecular sieves. Acetone and tetrahydrofuran were Fisher Spectroanalyzed liquids.

Preparation of Samples. Samples were prepared by the same methods as described in previous papers.[7,8]

Pmr Measurements. All the pmr spectra were obtained with a Varian Associates Model A-60 nmr spectrometer. During the running of the spectra the temperature remained constant to within ±1°, as indicated by the separation in cps between two peaks in ethylene glycol or methanol.

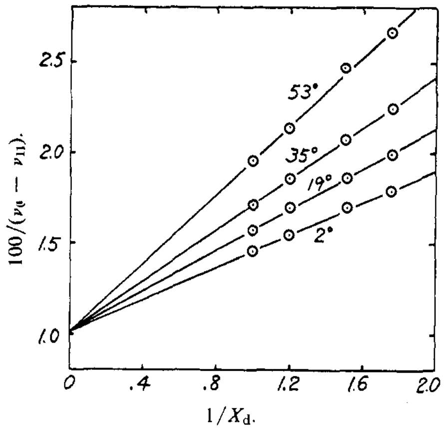

Figure 2. Plots of $10^2/(\nu_0 - \nu_{11})$ *vs.* $1/X_d$ for water hydrogen bonding to tetrahydrofuran.

Chemical shifts of the water proton signal were measured with respect to tetramethylsilane (TMS) used as an internal standard and are quoted as cps. All lines are downfield from TMS. The reported shifts are accurate to about 0.3 cps.

Results

The chemical shifts of the proton signal, ν, in ternary systems containing water (in the concentration range of $X_w = 0.003$ to 0.02), an electron donor of mole fraction X_d, and cyclohexane were determined at different temperatures. Plots of ν *vs.* X_w, at given values of X_d and temperature, are linear, and some examples are shown in Figure 1. The extrapolated values of ν_0 are summarized in Table I.

Table I. Values of ν_0 (cps) Obtained from Linear Plots of ν *vs.* X_w for the Ternary System Water–Electron Donor (D)–Cyclohexane

X_d	ν_0			
	(a) D = Tetrahydrofuran (THF)			
	53°	35°	19°	2°
0.99	135.5	142.5	147.1	153.2
0.84	131.0	138.3	143.3	148.5
0.67	124.6	132.3	137.6	143.5
0.57	121.8	128.8	134.6	139.9
	(b) D = Acetone			
	36°	19°	2°	−14°
0.99	163.0	169.7	178.0	184.3
0.85	157.0	164.4	173.0	179.7
0.68	150.2	157.8	165.3	174.5
0.59	147.5	155.0	163.5	174.7
	(c) D = N,N-Dimethylacetamide			
	70°	53°	35°	19°
0.99	189.1	196.6	205.3	211.8
0.83		190.2	199.4	207.0
0.64		182.0	191.9	199.9
0.54			187.0	195.2

Figure 2 gives plots of eq 5 for water hydrogen bonding to tetrahydrofuran. The values of K (dimensionless), ν_{11}, and ν_{12} (cps) for the three systems investigated are listed in Table II. From plots of log K *vs.* $1/T$, ΔH was obtained. The values of ΔS are calculated from the known relationship between equilibrium constant, enthalpy, and entropy changes, and are included in Table II.

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[7] R. Mathur, E. D. Becker, R. B. Bradley, and N. C. Li, *J. Phys. Chem.*, **67**, 2190 (1963).

[8] F. Takahashi and N. C. Li, *ibid.*, **68**, 2136 (1964).

Table II. Thermodynamic Data for $OH_2\cdot D + D = OH_2\cdot D_2$ in Cyclohexane

	D		
	THF	Acetone	DMA
K, 53°	1.1		1.9
35°	1.4	0.9 (36°)	2.6
19°	1.8	1.2	3.5
2°	2.3	1.5	
−14°		2.0	
ν_{11}	84	100	110
ν_{12}	183	230	240
ΔH, kcal/mole	−2.5	−2.4	−3.6
ΔS, eu	−7.6	−6.4	−11.9

Discussion

Treatment of Data. Equation 5 was also programmed[9] in Fortran II and the computations of ν_{12} and K, assuming different values of ν_{11}, were performed using an IBM 1620 computer. It was found that the intercept $1/(\nu_{12} - \nu_{11})$ became independent of temperature only with values of ν_{11} identical with those listed in Table II.

The results of our various computations indicate that the uncertainty in the K values listed in Table II is about 0.1 at 19° and above, and 0.2 at 2 and −14°. The uncertainty in the value of ΔH is about 0.1 kcal/mole.

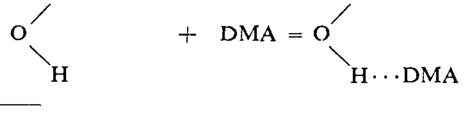
Comparison with Other Hydrogen-Bonded Systems. Searles and Tamres[10] determined the electron-donor ability of various hydrogen acceptors by measuring the heat of mixing with chloroform and the frequency shift of the OD band in the infrared spectrum of methanol-*d* solutions. They found that THF gives a greater heat of mixing with chloroform and greater frequency shift of the OD band than does acetone. Based on these criteria, THF is a stronger hydrogen acceptor than acetone. Becker[11] found that the equilibrium constants and enthalpies of the 1:1 dimethylformamide–alcohol complexes are always greater than the corresponding values for the acetone–alcohol (methyl, ethyl, and *t*-butyl alcohols) complexes.

The equilibrium constants and enthalpies listed in Table II show that the electron-donor ability to water increases in the order acetone, THF, DMA, in agreement with the order found in the literature for other hydrogen donors.

According to Table II, the K value at 35° for D = DMA is 2.6. Considering a very low water concentration in DMA, the molar equilibrium constant, K_m, is calculated to be 0.24 mole l.$^{-1}$. This value may be compared[8] to $K_m = 2.23$ for the formation of the DMA–2-propanol complex at 40°. It must be remembered, however, that the latter refers to the reaction

$$ROH + DMA = ROH\cdots DMA \qquad (6)$$

whereas the K in Table II refers to



$$O\genfrac{}{}{0pt}{}{\diagup H\cdots DMA}{\diagdown H} + DMA = O\genfrac{}{}{0pt}{}{\diagup H\cdots DMA}{\diagdown H\cdots DMA} \qquad (7)$$

If we assume the hydrogen-donor ability of ROH and OH_2 to be of the same order, then the equilibrium constants of eq 6 and 7 may be analogous to the first and second successive formation constants of metal complexes, respectively. Since the second successive formation constant is generally about an order smaller than the first,[12] the difference in K_m's for eq 6 and 7 becomes completely reasonable.

Holmes, *et al.*,[6] report equilibrium constants of the reaction

$$2OH_2\cdot S_2 = S_2\cdot H_2O\cdots HOH\cdot S + S \qquad (8)$$

where S is a solvent molecule and serves also as electron donor. Their equilibrium constants cannot be compared with the K values in Table II, since eq 8 involves dimerization of water and the formation of ordered O···H bonds in addition to the breaking of ordered S···H bonds. It is appropriate to mention here that Mohr, Wilk, and Barrow,[14] from the infrared spectra of water–base systems in carbon tetrachloride, found that at low base concentrations, a 1:1 complex (H–O–H···D) is formed, whereas at higher base concentrations, complexes involving one water molecule and two base molecules (D···H–O–H···D) are formed. These findings therefore support the relation expressed in our eq 1.

Mohr, *et al.*,[14] report that when the base concentration is around 0.2 *M* in carbon tetrachloride in the presence of about 0.01 *M* water, two absorption bands in the OH stretching region occurred; the higher frequency band, at around 3700 cm^{-1}, is ascribed to the antisymmetric ν_3 stretching mode of free water, while the lower frequency band is ascribed to the bonded OH stretching mode in the 1:1 complex, H–O–H···D. The difference in frequency, $\nu_{(\mathrm{free})} - \nu_{(\mathrm{bonded})}$, increases in the order acetone, dioxane, DMA, and is in line with the order of K and ΔH listed in Table II for acetone, THF, and DMA.

Characteristic Frequencies of Water Protons. It is not possible in our experiments to obtain the characteristic pmr frequencies of monomeric water, ν_M, since ν_0 and ν_{11} depend on the nature of the electron donor. However, ν_M may be taken to be the frequency of water vapor and has the value 50 cps.[15] As comparison, the characteristic pmr frequency of monomeric 2-propanol has been determined to be 46 cps.[8]

Infrared data have shown that as hydrogen-bonded polymers become larger, the hydrogen bonds become stronger,[18,19] and that for the OH stretching mode in

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[9] The authors thank Mr. G. Pukanic for aid in programming and operating the computer.

[10] S. Searles and M. Tamres, *J. Am. Chem. Soc.*, **73**, 3704 (1951); M. Tamres and S. Searles, Jr., *ibid.*, 81, 2100 (1959).

[11] E. D. Becker, *Spectrochim. Acta*, 17, 436 (1961).

[12] For example, the successive formation constants[13] of the following reactions, copper(II) + imidazole = copper(II) (imidazole) and copper(II) (imidazole) + imidazole = copper(II) (imidazole)$_2$, are 2.14 × 10^4 and 3.47 × 10^3, respectively.

[13] N. C. Li, J. M. White, and E. Doody, *J. Am. Chem. Soc.*, **76**, 6219 (1954).

[14] S. C. Mohr, W. D. Wilk, and G. M. Barrow, *ibid.*, **87**, 3048 (1965).

[15] Schneider, Bernstein, and Pople[16] report the frequency of water vapor as 0.60 ppm, or 36 cps, referred to methane. Since the chemical shift of methane referred to TMS is 14 cps,[17] the value of ν_M is calculated to be 50 cps.

[16] W. G. Schneider, H. J. Bernstein, and J. A. Pople, *J. Chem. Phys.*, **28**, 601 (1958).

[17] L. M. Jackson, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, New York, N. Y., 1959, p 60.

[18] L. P. Kuhn, *J. Am. Chem. Soc.*, **74**, 2494 (1952).

[19] R. F. Badger, *J. Chem. Phys.*, **8**, 288 (1940); E. R. Lippincott and R. Schroeder, *ibid.*, **23**, 1099 (1955).

phenol and 2-butanol, the change in frequency, $\Delta\nu$, for dimer formation is approximately half as big as $\Delta\nu$ for polymer formation. It is interesting that the characteristic pmr frequency of the 1:1 complex is approximately half as large as the frequency of the 1:2 complex. This is reasonable since the 1:1 species is associated through a hydrogen bond involving one of the OH bonds of the water molecule, the other bond remaining free, while the 1:2 species is associated through two hydrogen bonds.

It is unfortunate that in our experiments it is not possible to determine the equilibrium constant of the reaction

$$OH_2 + D = OH_2\cdots D \qquad (9)$$

The presence of a large excess concentration of D is necessary, not only from solubility consideration, but also because various water–water association species would be formed in the absence of a large concentration of D. Since water is in such large abundance, however, it is useful to have information on values of the equilibrium constant and enthalpy change of reactions represented by eq 1 for various electron donors.

The values of $(\nu_{12} - \nu_{11})$ and $(\nu_{11} - \nu_M)$ may be regarded as the hydrogen-bond shifts for eq 1 and 9, respectively. If the equilibrium constants for the reactions represented by these two equations had taken on identical values, it might be supposed that $(\nu_{12} - \nu_M)$ would be equal to $2(\nu_{11} - \nu_M)$, since $(\nu_{12} - \nu_M)$ may be considered to be the hydrogen-bond shift for the reaction

$$OH_2 + 2D = OH_2\cdot 2D \qquad (10)$$

However, our data show that $(\nu_{12} - \nu_M)$ is different from $2(\nu_{11} - \nu_M)$ and reflect the unequal equilibrium constants of eq 1 and 9.

The Stereochemistry of Complex Inorganic Compounds. XXX.[1] The Base Hydrolysis of Some Optically Active β-Dihalotriethylenetetraminecobalt(III) Cations

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Contribution from the William Albert Noyes Laboratory of Chemistry, University of Illinois, Urbana, Illinois. *Received August 5, 1965*

Abstract: The base hydrolysis of the optically active β-[CoX$_2$(trien)]$^+$ ion in aqueous solution proceeds, under all the conditions studied, with retention of configuration. A similar result is given by the reaction with both liquid and gaseous ammonia. The presence of silver(I) or mercury(II) ions in the aqueous solution has no effect on the configuration of the product of the base hydrolysis. Racemization of β-[Co(OH)$_2$(trien)]$^+$ in aqueous solution proceeds through the formation of the *trans* isomer as an intermediate.

In the previous paper,[1] it was pointed out that inversion takes place in the second step of base hydrolysis of the α-dihalotriethylenetetraminecobalt(III) ion.

$$\alpha\text{-}[CoX_2(trien)]^+ \xrightarrow{OH^-} \alpha\text{-}[CoXOH(trien)]^+ \quad \text{retention} \qquad (1)$$

$$\alpha\text{-}[CoXOH(trien)]^+ \xrightarrow{OH^-} \beta\text{-}[Co(OH)_2(trien)]^+ \quad \text{inversion} \qquad (2)$$

On the contrary, the first step of the base hydrolysis of *cis*-dichlorobis(ethylenediamine)cobalt(III) ion, at high OH$^-$ concentrations, proceeds largely with inversion of configuration.[2]

$$cis\text{-}[CoCl_2(en)_2]^+ \xrightarrow{OH^-} cis\text{-}[CoClOH(en)_2]^+ \quad \text{inversion} \qquad (3)$$

$$cis\text{-}[CoClOH(en)_2]^+ \xrightarrow{OH^-} cis\text{-}[Co(OH)_2(en)_2]^+ \quad \text{retention} \qquad (4)$$

Recently, the β isomer of the dichlorotriethylenetetraminecobalt(III) complex has been prepared in optically active form, and its behavior on acid hydrolysis has been studied.[3,4] The absolute configurations of both D-α- and D-β-[CoCl$_2$(trien)]$^+$ have been determined from optical rotatory dispersion (ORD), circular dichroism,[5] and kinetic studies[4,6] and are shown in Figure 1.

It has been found that under none of the conditions which we studied does the conversion of optically active *cis*-[CoF$_2$(en)$_2$]$^+$ to optically active [CoCO$_3$(en)$_2$]$^+$ result in a change of configuration,[7] but under some conditions, both optically active *cis*-[CoBrCl(en)$_2$]$^+$ and *cis*-[CoBr$_2$(en)$_2$]$^+$ give [CoCO$_3$(en)$_2$]$^+$ with optical inversion.[8] The differences in character between the Co–F, Co–Cl, and Co–Br bonds cause great differences in the mechanism of the base hydrolysis.

It has been shown that the D-*cis*-dichlorobis(L-propylenediamine)cobalt(III) ion, which is closely related to the ethylenediamine complex, can be converted to either D- or L-[CoCO$_3$(*l*-pn)$_2$]$^+$.[9] Finally, an optical inversion has been found in the reaction of *cis*-[CoCl$_2$(en)$_2$]$^+$ with ammonia at low temperatures, but not at room temperature or above.[10,11]

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(2) L. J. Boucher, E. Kyuno, and J. C. Bailar, Jr., *ibid.*, **86**, 3656 (1964).

(3) G. H. Searle, Thesis, Australian National University, 1963.

(4) A. M. Sargeson and G. H. Searle, *Nature*, **200**, 356 (1963).

(5) A. M. Sargeson and G. H. Searle, *Inorg. Chem.*, **4**, 45 (1965).

(6) A. M. Sargeson, *Australian J. Chem.*, **17**, 385 (1964).

(7) W. R. Matoush and F. Basolo, *J. Am. Chem. Soc.*, **78**, 3972 (1956).

(8) J. C. Bailar, Jr., and D. F. Peppard, *ibid.*, **62**, 820 (1940).

(9) J. C. Bailar, Jr., and J. P. McReynolds, *ibid.*, **61**, 3199 (1939).

(10) J. C. Bailar, Jr., J. H. Haslam, and E. M. Jones, *ibid.*, **58**, 2226 (1936).