Hydrogen-Bonding Effects on Oxygen-17 Chemical Shifts

Jacques Reuben[1]

Contribution from the Isotope Department, The Weizmann Institute of Science, Rehovoth, Israel. *Received March 14, 1969*

Abstract: The effects of solvents on the oxygen-17 chemical shifts of water and acetic acid have been investigated. The effects of added water on the ^{17}O shifts of methanol and acetone and the shift changes upon titration of acetic acid have also been studied. The results are interpreted in terms of fast equilibrium between various plausible hydrogen-bonded complexes. It is found that breaking of hydrogen bonds involving the oxygen atom of a hydroxyl group leads to an upfield shift of the ^{17}O resonance. Proton donation has an effect of -12 ppm and proton accepting an effect of -6 ppm on the ^{17}O shift. These values are tentatively rationalized in terms of the relative contribution of valence bond resonance structures describing the hydrogen bond. The major effect seems to be due to the charge-transfer structure $-O^{-}\ H-^{+}O<$. Its contribution is estimated to be between 6.3 and 10.5% depending on the value taken for the ^{17}O shift of H_3O^+ and ^{-}OH. The solvent effects on the ^{17}O chemical shift of acetic acid clearly reveal the features of the equilibrium between the complex species present in these solutions. The calculated equilibrium constants are in agreement with values obtained from nmr studies of other nuclei (^1H and ^{13}C). Upon titration a negative shift is observed and, if plotted against pH, a well-defined titration curve is obtained. Previous study of the dilution shift of acetone in water has been extended. The observed behavior cannot be described by one equilibrium constant and the existence of two equilibria in this system is suggested. Oxygen-17 magnetic resonance appears to be a suitable method for studying hydrogen-bonded systems.

Solvent effects are among the most important variables used for studying molecular structure and specific interactions by nmr spectroscopy.[2] Since the discovery in 1951 that protons involved in hydrogen bonding experience large shift in their resonance frequency,[3] proton magnetic resonance (pmr) became a convenient, although rather empirical, method for investigating systems with hydrogen bonding. The question whether additional understanding might be gained by observing the effects of hydrogen bonding on the nuclear resonance of other initmately involved atoms was raised more than 10 years ago,[4] but the pertinent information accumulated during the last decade is still very limited.[2]

Oxygen is undoubtedly one of the most important atoms in hydrogen-bonded systems since it acts both as a proton acceptor and as a proton donor. Its participation in hydrogen bonds may lead to changes in the electron charge distribution. In fact, considerable shift (about 11 ppm) toward higher field has been noted in the ^{17}O resonance of water dissolved in acetone relative to that in pure water.[5] More recently Florin and Alei[6] succeeded in measuring the shift between vapor and liquid phase (36 ppm) using water enriched to 30% in oxygen-17. With the high enrichments of oxygen-17 now available it seems that systematic studies of hydrogen bonding by oxygen-17 magnetic resonance (omr) are feasible. Although the experimental accuracy in measuring ^{17}O shifts rarely exceeds 1 ppm, it may appear that omr is methodically more suitable for such studies since, owing to the slow (on the nmr time scale) oxygen-exchange rates, it is less sensitive to impurities than, *e.g.*, pmr.[7]

This paper reports the results of a preliminary investigation of the solvent effects on the ^{17}O chemical shift of water and acetic acid. The effects of added water on the ^{17}O shifts of methanol and acetone are also studied. The possibilities of utilizing omr for studying chemical equilibria in hydrogen-bonded systems are considered. In this regard a titration of acetic acid has been carried out.

Experimental Section

Oxygen-17 nmr spectra were obtained with a Varian DP-60 spectrometer operating at 8.13 MHz and at ambient temperature (24 ± 1°). Magnetic field sweep was obtained from the Model V-K3507 slow-sweep unit in conjunction with the superstabilizer. The derivative of the absorption mode was recorded. The modulation frequency used was 20 Hz, and its amplitude was adjusted to give maximum intensity of the observed signal. This procedure makes unfeasible accurate line-width determinations due to large modulation broadening. Qualitatively it was noted that the line widths approximately followed the viscosity of the medium. This is consistent with the fact that ^{17}O relaxation in diamagnetic liquids is governed by the interaction of the quadrupole moment with intramolecular electric field gradients.[8]

The measurements were done with solutions contained in 15-mm o.d. tubes in which a small capillary tube containing water (or, for some of the experiments, methanol) enriched to *ca.* 8% in oxygen-17 was placed for reference purposes. Several measurements were repeated using spherical cells. No systematic difference between the two sets of data was noted. Susceptibility effects do not exceed 1 ppm which is also the usual limit of experimental error. At least four (usually six) spectra of each solution were recorded, and the average chemical shift was taken as the experimental value.

The enriched materials were obtained from the isotope separation plant of this Institute.[9] Before use they were subjected to bulb-

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[1] Address correspondence to the author at Johnson Research Foundation, The School of Medicine, University of Pennsylvania, Philadelphia, Pa. 19104.

[2] Recently this subject has comprehensively been reviewed by P. Laszlo in "Progress in NMR Spectroscopy," Vol. 3, J. W. Emsley, J. Feeney, and L. H. Sutcliffe Ed., Pergamon Press, Oxford, 1967, pp 231–402, 415 references.

[3] (a) J. T. Arnold and M. G. Packard, *J. Chem. Phys.*, 19, 1608 (1951); (b) V. Liddel and N. F. Ramsey, *ibid.*, 19, 1608 (1951).

[4] W. G. Schneider in "Hydrogen Bonding," D. Hadzi Ed., Pergamon Press, London, 1959, p 55.

[5] J. Reuben, A. Tzalmona, and D. Samuel, *Proc. Chem. Soc.*, 353 (1962).

[6] A. E. Florin and M. Alei, Jr., *J. Chem. Phys.*, 47, 4268 (1967).

[7] N. Muller and P. I. Rose, *J. Am. Chem. Soc.*, **85**, 2173 (1963). These authors have found that the carboxyl proton shift of acetic acid in acetone is extremely sensitive to small amounts of water.

[8] H. A. Christ and P. Diehl, "Magnetic Resonance and Relaxation," 12th Colloque Ampere, North-Holland Publishing Co., Amsterdam, 1963, p 296.

[9] The author is indebted to Mrs. Dora Sadeh, Miles-Yeda Ltd., Rehovoth, who was responsible for the synthesis and purification of the labeled methanol, acetone, and acetic acid.

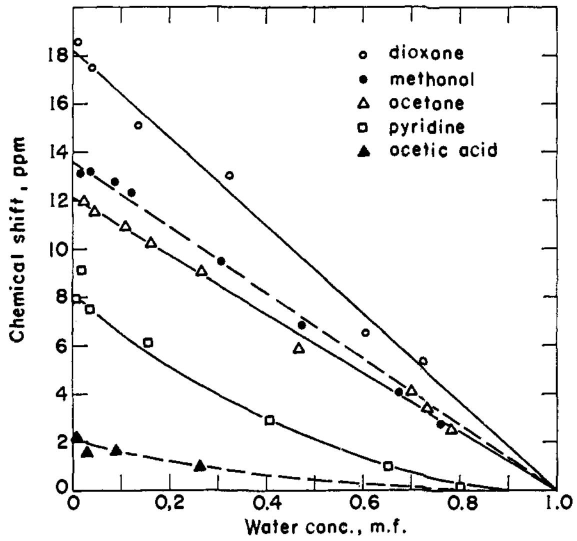

Figure 1. The oxygen-17 shift of water (relative to pure water) as a function of concentration (mole fraction) in various solvents.

to-bulb distillation *in vacuo*. The extent of enrichment was between 4 (acetic acid) and 8 (water) atom % oxygen-17.

The organic solvents were analytical products of BDH and Fluka AG. Before use they were distilled and the middle fractions collected. The concentrations were determined gravimetrically by weighing the components while preparing the solutions.

For the titration of acetic acid about 4 ml of a 0.437 *m* solution was prepared. It was titrated with standardized 1.01 *N* NaOH and 1.05 *N* HCl solutions.

Results and Discussion

Dilution of Water. The omr signal of water is shifted toward higher field upon dilution. The results are presented in Figure 1. The dilution curves in dioxane, methanol, and acetone appear to be linear (within the experimental error) throughout the whole range of concentrations. The extrapolated values are collected in Table I.

Table I. Oxygen-17 Shifts of Water in Various Media

Medium	Lowest concn, mole fraction × 10^2	Shift, ppm
Vapor (175–215°)	...	36[a]
Dioxane	0.9	18.3
Methanol	1.5	13.6
Acetone	2.4	12.1
Pyridine	0.8	8.3
Acetic acid	0.9	2.1
Water (24°)	(10^2)	(0)

[a] From ref 6.

Assuming that each water molecule in the liquid at room temperature is hydrogen bonded by four hydrogen bonds [two *via* the hydrogen atoms (hereafter referred to as *H-bonds*) and two by donating the oxygen hybrid orbitals (hereafter referred to as *O-bonds*)], the shift of the vapor indicates that breaking of all the hydrogen bonds leads to a positive shift of 36 ppm. In the proton-accepting solvents dioxane, acetone, and pyridine there is still considerable downfield shifts with respect to water vapor, although it is usually assumed that no significant water–water association takes place in these media. Thus, it may be concluded that breaking of both the H-bonds and the O-bonds leads to an upfield shift. An estimate of the shift due to each "type" of hydrogen bond may be obtained using the dioxane datum. Muller and Simon have shown in a pmr study,[10] that the two important equilibria in the dioxane–water system are

$$\mathrm{HOH} + \mathrm{D} \rightleftharpoons \mathrm{HOH}\cdots\mathrm{D} \qquad K_1 \cong 15\ (\text{mole fraction})^{-1} \quad (1)$$

$$\mathrm{D}\cdots\mathrm{HOH} + \mathrm{D} \rightleftharpoons \mathrm{D}\cdots\mathrm{HOH}\cdots\mathrm{D} \qquad K_2 \cong 1\ (\text{mole fraction})^{-1} \quad (2)$$

Calculations show that the concentration of free water molecules at a total water concentration of 0.01 mole fraction is negligibly low, whereas the concentrations of the two hydrogen-bonded complexes are almost equal. On the average each water molecule is hydrogen bonded to dioxane by $^3/_2$ H-bonds and no O-bonds. Breaking up two O-bonds and $^1/_2$ H-bond leads, therefore, to an upfield shift of 18 ppm, or formation of $^3/_2$ H-bonds causes a downfield shift of 18 ppm. Thus, roughly, breaking of an H-bond induces an upfield shift of 12 ppm and that of an O-bond is responsible for 6 ppm. It appears that in acetone (at concentrations less than 0.02 mole fraction) all the H-bonds are saturated and only the doubly complexed species are present. Apparently acetone is more basic than dioxane. A similar conclusion has been reached from an interpretation of pmr dilution shifts.[11]

The model emerging from the above interpretation of water ^{17}O shifts in various media cannot accommodate values less than 12 ppm for basic solvents. The shift in pyridine, however, is only 8.3 ppm. This low value may be rationalized considering the equilibrium.

$$\mathrm{P}\cdots\mathrm{HOH}\cdots\mathrm{P} \rightleftharpoons \mathrm{PH}^+ + \mathrm{OH}^- + \mathrm{P} \quad (3)$$

The chemical shift of OH^- is about −70 ppm.[12] Assuming the limit of rapid exchange and considering species with chemical shifts of 12 and −70 ppm the equilibrium constant is found to be about 2×10^{-5} (mole fraction)^2. If the same conditions hold also at a water mole fraction of $^1/_3$, the fraction of pyridine in the protonated form PH^+ is calculated to be 6.4%. This figure is in good agreement with that obtained from theoretical considerations (9.2%) and analysis of ^{14}N chemical shifts in the system pyridine–methanol (7 ± 3%).[13]

As inferred from the ^{17}O shifts, water in acetic acid is only slightly less hydrogen bonded than in the pure liquid. However, considering that some protonation may occur, the relative amount of broken hydrogen bonds may be greater than indicated by the dilution shift, since the shift of $\mathrm{H_3O^+}$ is about −40 ppm.[12]

Water–Methanol Mixtures. The structure of water–alcohol mixtures is undoubtedly more complex. Franks and Ives have recently reviewed the subject but reached a not too optimistic conclusion concerning the model for these mixtures.[14] One may regard liquid methanol as composed of hydrogen-bonded chains or, alternatively, as a mixture of cyclic trimers containing some

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(10) N. Muller and P. Simon, *J. Phys. Chem.*, 71, 568 (1967).

(11) I. Satake, M. Arita, H. Kamizuka, and R. Matuura, *Bull. Chem. Soc. Japan*, 39, 597 (1966).

(12) Z. Luz and G. Yagil, *J. Phys. Chem.*, 70, 554 (1966).

(13) H. Saito and K. Nukada, *Tetrahedron Lett.*, 111 (1965).

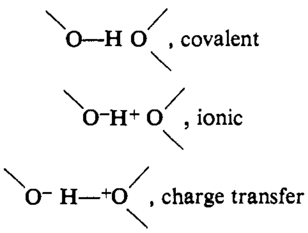
(14) F. Franks and D. J. G. Ives, *Quart. Rev.* (London), 20, 1 (1966).

fraction of monomers. (A more realistic, but difficult to handle, model is that of a composition of all three species mentioned.) Water accommodated in the chains, or in the trimers, is hydrogen bonded by one H-bond and one O-bond, and according to our model an upfield shift of 18 ppm relative to pure water is anticipated. The observed quantity at infinite dilution is only 13.6 ppm suggesting that considerable branching of the chains occurs when a water molecule is substituted for methanol. The relative amount of water molecules at which branching takes place is calculated to be 73%.

When methanol ($CH_3{}^{17}OH$) is dissolved in water, the number of hydrogen bonds involving the methanol molecule is expected to increase by at least one O-bond. The anticipated downfield ^{17}O shift is indeed observed (see Figure 2). The value extrapolated to infinite dilution is −9.4 ppm relative to pure methanol. Assuming that in the aqueous solution the methanol molecule is hydrogen bonded by one H-bond and two O-bonds, this value may be used to estimate the average chain length or the relative amounts of cyclic trimers and monomers in pure methanol. Thus, we find that the average number of methanol molecules in a hydrogen-bonded chain is 5.3 or, alternatively, if the cyclc trimer model is adopted, we find that 19% of the molecules are monomeric. Both figures are consistent with other data.[14]

On the Origin of the Oxygen-17 Hydrogen-Bond Shift. We propose the following tentative rationalization of oxygen-17 shifts of hydroxylic oxygen atoms induced by hydrogen bonding.

Theoretical discussions of hydrogen bonding consider usually four major effects:[15] (a) electrostatic interaction; (b) delocalization effects; (c) repulsive forces; (d) dispersion forces. The variation of oxygen-17 chemical shifts is determined mainly by the paramagnetic term of the nuclear shielding constant[16] and it seems, therefore, that the shifts induced by hydrogen bonding are due to delocalization effects. These have been represented[17] in terms of the valence bond resonance structure



A major perturbation of the oxygen atoms takes place in the charge-transfer structure in which, considering water molecules, the proton donor is converted to OH^- and the proton acceptor to H_3O^+. Now, the ^{17}O resonance of OH^- is expected to occur at a much lower field than that of H_3O^+, and thus the hydrogen-bond shift is greater when the oxygen atom acts as proton donor than when it is a proton acceptor. The true ^{17}O shifts of OH^- and H_3O^+ are difficult to obtain. Using the data of Luz and Yagil[12] three different estimates are obtained. These can be used in turn to estimate the relative contribution of the charge-transfer structure assuming that formation of an O-bond induces a downfield shift of 6 ppm and that of an H-bond 12 ppm (*vide supra*). The results are summarized in Table II. These estimates are only in qualitative agreement with the theoretical calculations of Coulson and Danielson.[17] They demonstrate, however, that the charge-transfer valence bond structure is of significant importance in the description of the hydrogen bond and may satisfactorily account for the observed solvent-induced ^{17}O shifts of the hydroxyl group.

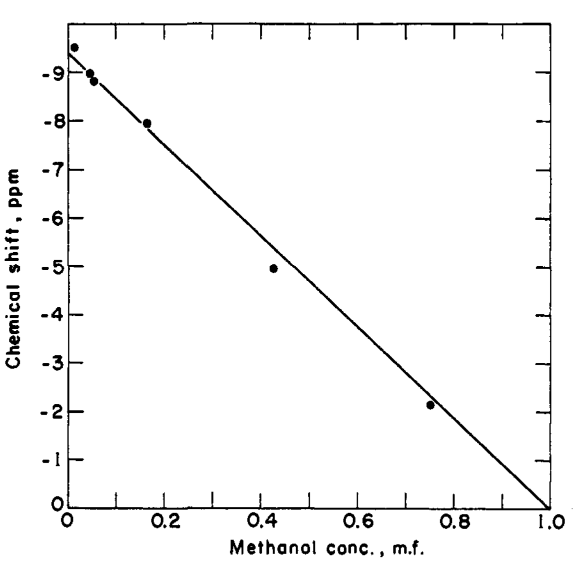


Figure 2. The oxygen-17 shift of methanol (relative to pure methanol) as a function of its concentration (mole fraction) in water.

Table II. Estimates of the Relative Contribution of the Charge-Transfer Structure

Method	Shifts[a] H_3O^+	Shifts[a] OH^-	Relative contribution, % From H_3O^+	Relative contribution, % From OH^-
Experimental shifts[b]	−76	−106	7.9	10.3
Molal shifts[c]	−94	−142	6.4	8.4
Ionic molal shifts[d]	−87	−191	6.9	6.3

[a] In ppm from water vapor. [b] From Figure 5 of ref 12. [c] From Table I of ref 12. [d] From Table II of ref 12.

Dilution of Acetic Acid. In solutions of acetic acid as well as in the pure liquid a single omr absorption is observed, the chemical shift of which is approximately the average of the chemical shifts of the carbonyl and hydroxyl oxygens.[18] Upon dilution a shift toward lower field is observed. The behavior is presented in Figure 3.[19] The extrapolated values of the ^{17}O shift (relative to pure acetic acid) are −13 ppm in acetone and acetonitrile and −1 ppm in cyclopentane. The latter value, which is within experimental error, suggests that in the pure liquid acetic acid is fully hydrogen bonded and this

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(15) See, *e.g.*, C. A. Coulson in ref 4, p 339.

(16) (a) B. N. Figgis, R. G. Kidd, and R. S. Nyholm, *Proc. Roy. Soc.* (London), **A269**, 469 (1962); (b) R. G. Kidd, *Can. J. Chem.*, **45**, 605 (1967).

(17) C. A. Coulson and U. Danielson, *Arkiv Fysik*, **8**, 239 (1954).

(18) H. A. Christ, P. Diehl, H. R. Schneider, and H. Dahn, *Helv. Chim. Acta*, **44**, 856 (1961).

(19) The effect of adding small amounts of water to dilute solutions of acetic acid in acetonitrile was checked. No change in the chemical shift was observed, suggesting that at low concentrations no water complex of acetic acid is formed.

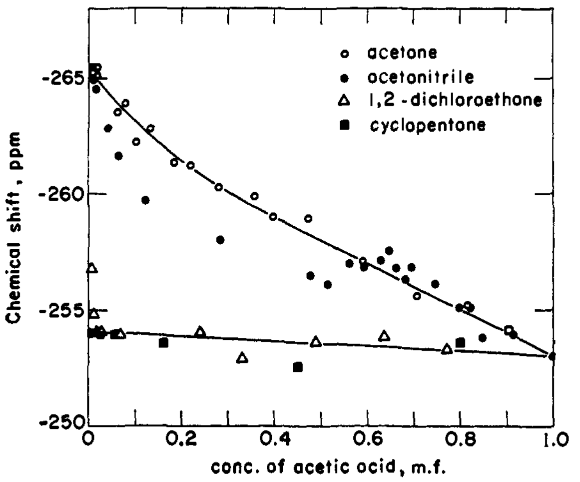


Figure 3. The oxygen-17 shift of acetic acid (relative to water) as a function of its concentration (mole fraction) in various solvents.

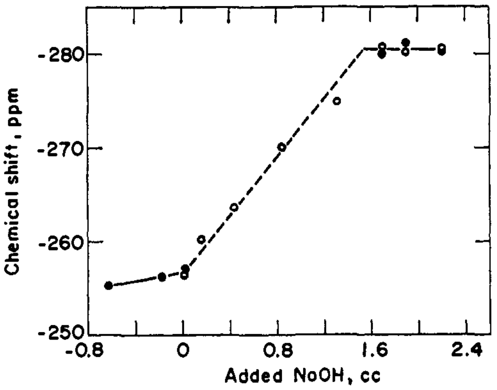


Figure 4. The oxygen-17 shift of the carboxyl group (relative to water) in a 0.437 *m* aqueous solution of acetic acid as a function of added volume of a 1.05 *N* NaOH solution: ○, added NaOH solution; ●, added HCl solution (back titration).

form, plausibly the dimer, persists upon dilution in the hydrocarbon, as may be expected from other data.[20]

The results in the basic solvents acetone and acetonitrile may be interpreted in terms of the equilibrium

$$\frac{1}{2}(CH_3COOH)_2 + A \rightleftarrows CH_3COOH\cdots A$$

The equilibrium constant was calculated from the experimental data at concentrations lower than 0.5 mole fraction and taking -266 and -254 ppm (relative to water) as the shifts of the complex and the dimer, respectively. For A = acetone, $K = (0.94 \pm 0.18)$ (mole fraction)$^{-1/2}$ is obtained. The value 1.2 ± 20% (mole fraction)$^{-1/2}$ obtained from recent estimates of equilibrium constants using proton dilution shifts is in good agreement.[21] For A = acetonitrile the equilibrium constant is (0.44 ± 0.04) (mole fraction)$^{-1/2}$. Carbon-13 chemical shifts of these systems have been studied by Maciel and Traficante.[22] From their results, which have been expressed in (mole/l.)$^{-1/2}$, one obtains $K_{\text{acetone}}/K_{\text{acetonitrile}} = 2.09$. This ratio is in excellent agreement with our value of 2.1 ± 0.4.

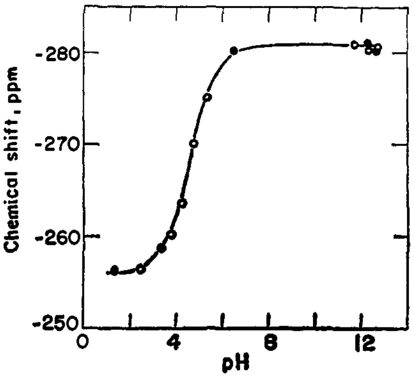
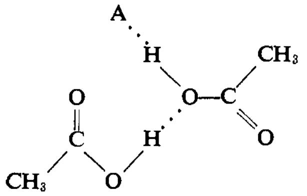


Figure 5. The titration curve of the oxygen-17 shift of acetic acid (see Figure 4).

Assuming that the action of the carboxyl group as a proton donor in hydrogen bonding has the same effect on the ^{17}O chemical shift in the acetic acid dimer and in the complexes with the basic solvents acetone and acetonitrile, the extrapolated dilution shift of -12 ppm may be ascribed to breaking the hydrogen bond involving the carbonyl oxygen of the acid. An oxygen-17 shift in this direction is expected in view of the upfield shifts observed upon hydrogen bonding of acetone[23] (*vide infra*). The shift of the free monomeric acetic acid has, therefore, a contribution of -12 ppm (relative to the dimer) from breaking the $C{=}O\cdots H$ bond and a contribution of $+6$ ppm/mole from breaking the $OH\cdots O$ bond (*vide supra*), *i.e.*, a total of -6 ppm. From the results in solutions of 1,2-dichloroethane and using a dimerization constant of 24.8 (mole fraction)$^{-1}$, which has been obtained by Perotti and Cola from pmr studies,[24] the shift of the monomer is found to be -5 ± 1 ppm, in very good agreement with the proposed model.

A "hump" of about 1 ppm at 0.66 mole fraction is observed in the dilution curve of acetic acid in acetonitrile (see Figure 3). This finding may be rationalized invoking the existence in equilibrium of considerable amounts of hydrogen-bonded ternary complexes of the type



Owing to the presence of the additional O-bond, the average ^{17}O shift of this complex is expected to be -1.5 ppm relative to that of the simple binary complex $CH_3COOH\cdots A$.

Titration of Acetic Acid. The change of the ^{17}O shift of the carboxyl group upon titration of a 0.437 *m* aqueous solution of acetic acid is depicted in Figures 4 and 5. The chemical shift of the acetate ion relative to aqueous acetic acid is -23.6 ppm.[25] The value per oxygen atom per negative charge, -47.2 ppm, is of the

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[20] G. Allen and E. F. Caldin, *Quart. Rev.* (London), 7, 255 (1953).

[21] N. Muller and P. I. Rose, *J. Phys. Chem.*, 69, 2564 (1965).

[22] G. E. Maciel and D. D. Traficante, *J. Am. Chem. Soc.*, 88, 220 (1966).

[23] H. A. Christ and P. Diehl, *Helv. Phys. Acta*, 36, 170 (1963).

[24] A. Perotti and M. Cola, *Gazz. Chim. Ital.*, 91, 1153 (1961).

[25] A similar shift (-21.3 ppm) has been observed between formic acid and sodium formate in one of the earliest observations of ^{17}O chemical shifts: H. E. Weaver, B. M. Tolbert, and R. C. LaForce, *J. Chem. Phys.*, 23, 1956 (1955).

same sign and order of magnitude as that of the hydroxyl ion with respect to water.[12] The pK calculated from the plot of the shift against pH is 4.7 in agreement with the well-established value of 4.756.[20] While omr can hardly be recommended as a method for measuring pK values of carboxylic acids, it may serve as a good indicator, using specific labeling, for determining the site of ionization in poly acids.

A Comment on the ^{17}O Dilution Shift of Acetone in Water. The solvent effects upon the oxygen-17 chemical shift of acetone have been investigated by Christ and Diehl using natural isotopic abundance.[23] We have extended the study using labeled acetone. The results, together with data from Figure 2 of ref 23, are shown in Figure 6. The oxygen-17 resonance of acetone is shifted toward higher field upon hydrogen bonding. The shift extrapolated to infinite dilution is 52 ppm relative to pure acetone. No deuterium isotope effect is observed. The upfield shift has been attributed to the increased contribution of the polar valence bond resonance structure $>C^+–O^-$.[23] This explanation has been found to be consistent with the ^{13}C solvent shifts of the carboxyl group.[26]

Attempting to calculate the constant of the plausible equilibrium

$$\mathrm{HOH} + \mathrm{A} \rightleftarrows \mathrm{HOH}\cdots\mathrm{A} \qquad K_1$$

using the experiment shifts, it is found that the equilibrium constant decreases with increasing acetone concentration. This observation suggests that the system cannot be described by one equilibrium constant. In fact, the water ^{17}O dilution shift (*vide supra*) indicates that at high acetone concentration the predominating species are A···HOH···A. The observed behavior can be explained assuming that a second equilibrium

$$\mathrm{HOH}\cdots\mathrm{A} + \mathrm{A} \rightleftarrows \mathrm{A}\cdots\mathrm{HOH}\cdots\mathrm{A} \qquad K_2$$

is important at high acetone concentrations. The equilibrium constants are estimated from the experimental data and found to be $K_1 = 9 \pm 3$ (mole fraction)$^{-1}$ and $K_2 = 0.15 \pm 0.05$ (mole fraction)$^{-1}$.

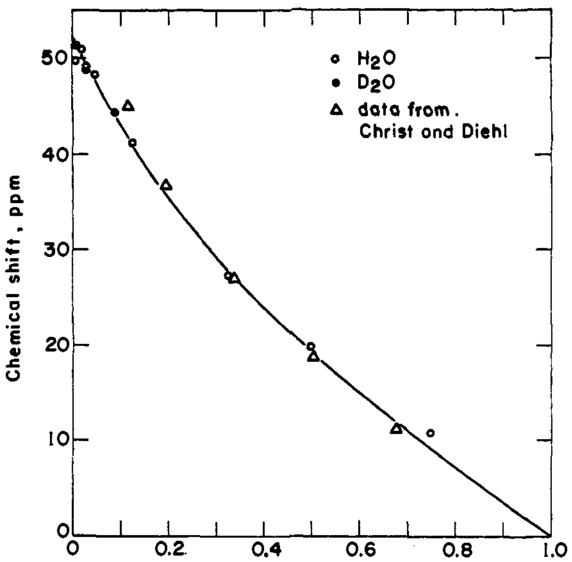

Figure 6. The oxygen-17 shift of acetone (relative to pure acetone) as a function of its concentration (mole fraction) in H_2O and D_2O. Included are data from ref 23.

Conclusions

Hydrogen bonding affects very much the oxygen-17 chemical shifts. It appears that the hydroxylic oxygen experiences greater downfield shifts when it acts as proton donor than when it serves as proton acceptor. Upfield shifts are observed upon hydrogen bonding of the carbonyl oxygen. The interpretation of the oxygen-17 shifts, although tentative, gives further insight into the chemical equilibria in hydrogen-bonded systems and the nature of the hydrogen bond. It seems that omr offers a very suitable method for further investigation in this direction.

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(26) G. E. Maciel and J. J. Natterstad, *J. Chem. Phys.*, **42**, 2752 (1965); see also G. E. Maciel, P. D. Ellis, and D. C. Hofer, *J. Phys. Chem.*, 71, 2160 (1967).