Monomeric and Cluster States of Water Molecules in Organic Solvent

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Measurements of the ^{1}H-NMR chemical shifts and their temperature dependence have disclosed that sparingly soluble water is monomeric at room temperature in hydrophobic solvents, such as carbon tetrachloride, benzene, chloroform, and that some water clusters are formed even in dilute solution in the apolar and slightly polar solvents at low temperatures, controlled by energy instead of entropy.

Water is one of the most important hydrogen-bonding substances for the living, and has been studied comprehensively.[1] Some nontrivial problems however remain unsolved: one may ask in which state water exists in hydrophobic environment, monomeric or cluster, how it depends on temperature, on what time scale the molecule rotates, how it is influenced by hydrogen bonds between water molecules or between water and solvent. Solving these problems is indispensable for a better understanding of a key role played by water molecules in controlling thermodynamic properties, reactivities, structures, and functions of chemically and biochemically interesting species in solution.[2]

Driven by entropy, though energetically unstable, water is dissolved to a small extent in such hydrophobic solvents as CCl_4 and C_6H_6 (C_6D_6) around room temperature. Early studies on the proton NMR spectra are confined to room temperature,[3-5] and there have been no comprehensive discussions about the water dissolution state and in particular, nothing about the dynamics.

Using a modern NMR machine, we could obtain the proton and deuteron spectra for "immiscible" water in the above-mentioned organic solvents over a wide temperature range. The proton spectra taken in elaborately purified solvents are given in Fig. 1. At room temperature, a single signal is observed at a high field compared with the chemical shift δ = 4.8 ppm for the bulk water protons involved in hydrogen bonding; the obtained chemical shifts (δ = 1.2 ppm in CCl_4, δ = 0.4 ppm in C_6D_6 at 30 °C) correspond to the early data[3] when the latter are properly converted into the present δ scale.

The high-field signals around 1 ppm are assigned to water monomers, because when hydrogen bonds in bulk water are broken in the gaseous phase (ca. 200 mM; M = mol dm^{-3}) instead of hydrophobic solvent environments, the proton signal shifts upfield by 4.6 ppm,[6] and because the dominant contribution of the monomer has been revealed by the detailed infrared spectroscopic analysis of water in carbon tetrachloride at room temperature.[7]

As can be seen in Fig. 2, the chemical shifts of water monomers (f, g, and h) depend little on temperature because hydrogen bonds between water molecules are already broken in hydrophobic solvents. The chemical shifts of water clusters in CCl_4 and C_6D_6 (a and c) are sensitive to temperature as in the case of bulk water (b). The chemical shifts due to hydrogen bonds between a water molecule and solvent molecules (d and e) are linearly dependent on temperature and the slope value is intermediate between the two extreme cases (a and h). It is to be noted that water contained in CCl_4 does not freeze even below 0 °C. This indicates that clusters found at low
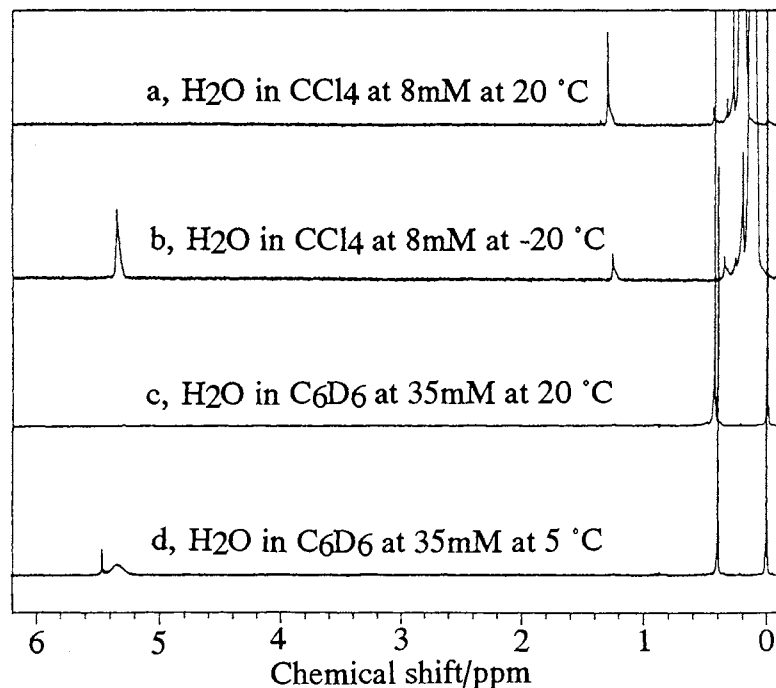
a, H2O in CCl4 at 8mM at 20 °C

b, H2O in CCl4 at 8mM at -20 °C

c, H2O in C6D6 at 35mM at 20 °C

d, H2O in C6D6 at 35mM at 5 °C

Chemical shift/ppm

Fig. 1. ^{1}H-NMR spectra for water (H2O) at low concentration in CCl4 and C6D6 at different temperatures. Chemical shifts are expressed in ppm relative to tetramethylsilane (TMS); the scale for the abscissa is given for water in benzene (c and d), and spectra a and b are slightly shifted to the left. In each spectrum, the strongest peak at the highest field is due to TMS. Solutions are saturated with water at room temperature and supersaturated at lower temperatures. Carbon tetrachloride of spectro-grade supplied by Nacalai were distilled and dried with a molecular sieve (4A, Nacalai). CCl4 purified thus was mixed with highly pure water several days before use. All proton spectra were taken using a JEOL JNM-EX270 wide-bore type spectrometer at 270 MHz and integrating 16 times.
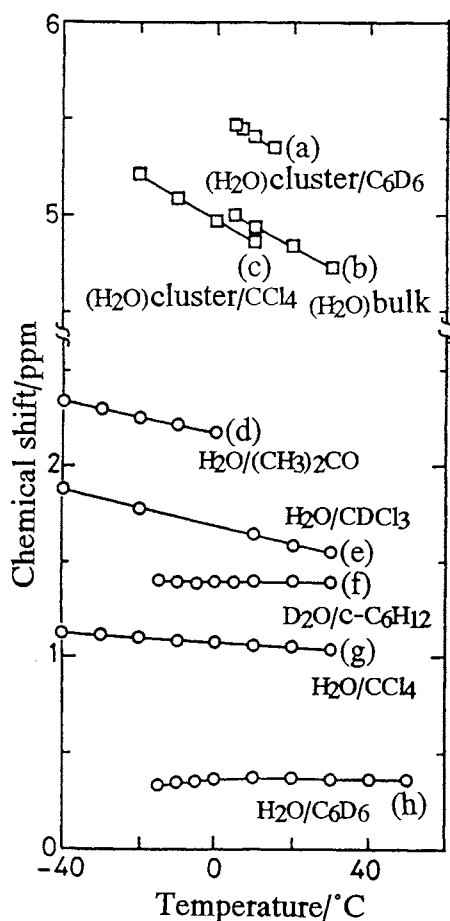

(a)
(H2O)cluster/C6D6

(c)   (b)
(H2O)cluster/CCl4   (H2O)bulk

(d)
H2O/(CH3)2CO

H2O/CDCl3
(e)

(f)
D2O/c-C6H12

(g)
H2O/CCl4

H2O/C6D6 (h)

Temperature/°C

Fig. 2. Temperature dependence of the proton chemical shifts for water (H2O) at low concentrations in apolar and polar solvents. a, cluster, ca. 35 mM H2O in C6D6; b, bulk water (H2O); c, cluster, ca. 8 mM H2O in CCl4; d, 50 mM H2O in (CH3)2CO; e, ca, 67 mM H2O in CDCl3; f, ca. 2 mM D2O in c-C6H12; g, ca. 8 mM H2O in CCl4; h, ca. 35 mM H2O in C6D6. All chemical shifts are given relative to TMS.

temperatures is not large enough in size to be transformed into a microcrystalline nucleus of ice as a prerequisite for the long-range order.

The unusually high-field signal in benzene, which is about 1 ppm higher than that in cyclohexane, suggests a weak hydrogen bond between a water molecule and π-electrons of the surrounding benzene molecules at the out-of-plane site where the local shielding is higher due to the ring current.[9] This type of location of a water molecule is found also in other phases at low temperatures,[9-11] and supported by the quantum mechanical calculations of the potential energy surface for a water-benzene pair[12] as well as the computer simulation studies for a benzene molecule in water.[13] In the solution studied here, the host benzene molecules are considered to form a solvent cage by a T-shaped packing with the molecular planes faced to the guest water molecule.

By lowering temperature closer to the solvent freezing point, in addition, we discovered a new signal near the position where the bulk water protons involved in hydrogen bonding are located; see low-temperature spectra b and d in Fig. 1. The low-field signals for water in CCl_4, C_6D_6, and $CDCl_3$, which result in phase separation on equimolar mixing, are assigned to water clusters whose structure is unknown at present and to be studied further. The sharp and broad signals for water clusters in benzene are at a position lower than that for bulk water, which suggests that the clusters are formed at the more hydrophobic in-plane sites of benzene. When we replaced the nonpolar solvents by such dipolar aprotic solvents as acetonitrile and acetone, we observed no low-field signals for water at 50 mM even at low temperatures. This implies that water molecules at such low concentrations tend to hydrogen bond to others rather than themselves driven by the mixing entropy. The site preference of hydrogen bonding is controlled thermodynamically and depends on water concentration as well as temperature, as observed for catalytic activities of enzymes in hydrophobic solvents.[2] The exchange of the different water states is not very fast because of the absence of coalescence of the high- and low-field signals.

To see how fast solitary water molecules can rotate in hydrophobic environments, we have measured the deuteron spin-lattice relaxation times T_1 for isolated heavy water molecules in the apolar and dipolar solvents by the inversion-recovery methods. The orientational correlation time τ_{2R} was obtained from the measured T_1; the quadrupole coupling constants (e^2Qq/h) necessary for the conversion were taken to be 250 and 308 kHz, respectively, for bulk and isolated water molecules according to the literature.[14] Solitary water (D_2O) molecules are found to reorient very fast on the time scale of 0.1 ps in CCl_4, which is composed of apolar spherical molecules, and the τ_{2R} values for a water molecule are in the sequence

D_2O (2.2) > $(CH_3)_2CO$ (0.83) > CH_3CN (0.63) > $CHCl_3$ (0.23) > C_6H_6 (0.22) > CCl_4 (0.10)
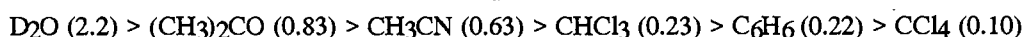
where the parenthesized numbers indicate the τ_{2R} values in ps at 30 $^\circ$C. Thus, non-hydrogen bonded water molecules in apolar solvents are rotating very fast almost like a gas molecule in a solvent cage. The solvent effect on the correlation time is almost linearly related to the proton chemical shifts which can be taken as a measure of the strength of solute-solvent interactions, indicating a dominant role of the attractive solute-solvent interactions in the short range in controlling the short time behavior. In fact, the τ_{2R} values for solitary water molecules in solution are not proportional but almost inversely proportional to the long-range property, bulk solvent viscosity, which is in the order

D_2O > CCl_4 > C_6H_6 > $CHCl_3$ > CH_3CN > $(CH_3)_2CO$

This tells us that the dynamics of solitary water molecules with an extremely small moment of inertia reflects on the time scale of our interest the molecular environment in the short range, say, the solvent cage composed of heavy and slowly moving molecules; bulk solvent properties, such as viscosity (or even a "microscopic viscosity") and dielectric constant, become useless in the proximity effects in question.

In this work we have found orientational motion of the small, nearly spherical, dipolar molecule is more

sensitive to solvent environment than that of the larger, planar, nonpolar benzene molecule previously studied[15] because of the hydrogen-bonding ability of the former. Since any nonpolar solvents and proteins contain a small amount of water, reactivities and functions of chemical and biochemical species at low concentrations in hydrophobic environments can be affected by the very active solitary water molecules characterized here.

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