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Water Molecules as a Gluing Factor in Organic Crystals and Biological Systems

Tadeusz M. Krygowski*, Sławomir J. Grabowski+ and Jerzy Konarski#

* Department of Chemistry, University of Warsaw, ul. L. Pasteura 1, 02-093 Warsaw, Poland

+ Institute of Chemistry, University in Białystok, 15-443 Białystok, Al.Piłsudskiego 11, Poland

\# Department of Chemistry, University of A.Mickiewicz, Poznań, ul. Grunwaldzka 6, Poland

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Abstract. Variability of two independent geometrical parameters (interatomic distances R(O-H) and bond angles φ(HOH)) of water molecules in crystal structures of hydrated organic systems, is studied on the basis of precise neutron diffraction measurements of molecular geometry retrieved from the Cambridge Structural Database. The large values of variance for both these parameters suggest that the molecule of water is very elastic, and hence may readily be employed as a particular kind of glue between other molecules building up the condensed phase. We postulate that elasticity of water molecule and its amphoteric acid/base properties in the Brönsted and Lewis sense are the main reasons of its unique properties as a gluing factor in chemical and biological systems. The energetic gain due to the water molecules acting in this way, observed for simple inorganic hydrates in crystalline state, is as large as 20 Kcal/mole per water molecule. © 1998 Published by Elsevier Science Ltd. All rights reserved.

Introduction

Crystal structure determination of organic systems is now a routine way of inspection of the molecular structure of organic compounds,[1,2] and provides excellent information about the intra- and inter- molecular interactions in crystalline state of organic solids.[3-8] Fundamental ideas of structural organic chemistry are much facilitated due to an easy access to a large number of structural data collected in the Cambridge Structural Database (CSD).[9] Despite many approaches taking into account the geometric structure of large organic molecules (or their fragments) in crystals, much less is known about the role of water molecules in many molecular and ionic crystals of organic compounds.

The aim of this paper is to show how water molecules behave in organic crystals, and their role in building them. Water as a solvent is a very important factor for many chemical reactions and most life processes - organic chemists and biochemists should be aware of a great flexibility of the shape of water molecules and the energy gain during the hydration - both factors playing a fundamental role in determining chemical processes. The paper demonstrate clearly these points. To study these problems, an analysis of the shape of water molecules based on neutron diffraction structure determination of water molecules embedded in ionic and molecular crystals of organic compounds, is presented in this report.

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Variation of the geometry of water molecules

The molecular geometry of water molecules is of course well-recognised. Table 1 presents the relevant data for the gas phase determination[10] and in the condensed phase in a liquid [11,12] and in the crystalline state in ice.[13]

Table 1. Molecular geometry of water in gaseous, liquid and solid states. Interatomic distances in Å, angles in degrees. E.s.d.'s for the molecular geometry of water in liquid are given in parentheses.

State	O-H bond length	H-O-H bond angle	O...O distance	Reference
gas	0.9572	104.52	-	10
liquid	0.966(6)	102.8(2)	2.9-3.0	11,12
solid - ice I	1.010	~104	2.75	13

A substantial diversity of the geometrical parameters R(OH) and HOH bond angle φ are observed when comparing the three phases of water. If the water molecules are embedded in crystals of hydrated chemical compounds, they exhibit a much greater variation in magnitude of these parameters. This report shows how widely these geometrical parameters vary depending on the molecular environment in the crystal lattice, indicating a specific feature of the water molecules (i.e. their elasticity). 52 water molecules were taken from the most precise neutron diffraction measurements (with e.s.d's < 0.005 Å for bond lengths, and R < 8.0% retrieved from the Cambridge Structural Database,[9] May 1997 release) removing all structures which were biased by disorder connected with water molecules. Figs 1 and 2 show how dramatically they differ from the values determined for the isolated molecule (gas phase and liquid phase data marked in both figures).

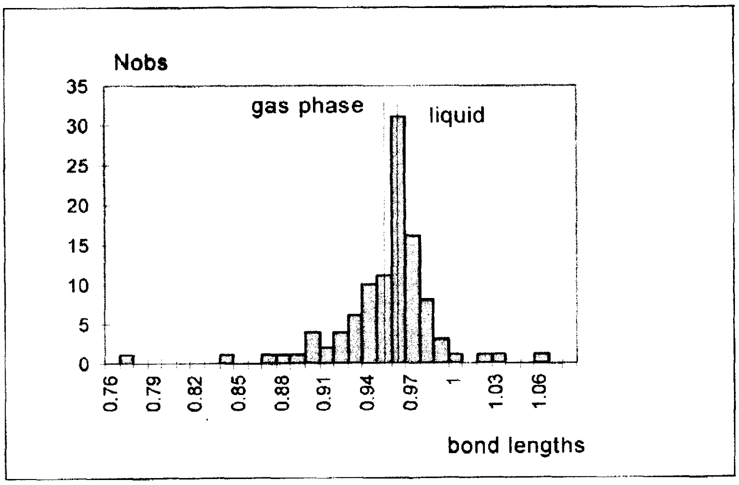

Fig 1. Distribution of R(O-H) bond lengths (in Å) of water molecules in hydrates of organic crystalline solids from neutron structure determinations. The mean value is 0.956 Å (e.s.d. = 0.033 Å). The values for gas phase and liquid water are indicated.

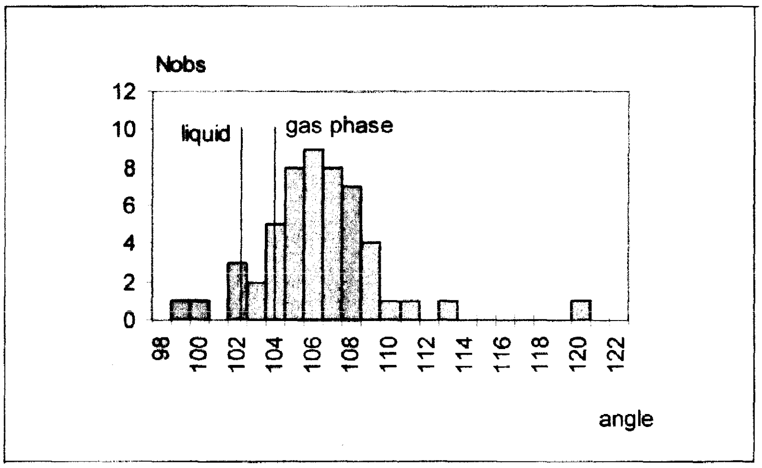

Fig 2. Distribution of φ(HOH) bond angles (in degrees) of water molecules in hydrates of organic crystalline solids from neutron structure determinations. The mean values is 106.8° (e.s.d. = 3.6°). The values for gas phase and liquid water are indicated.

Moreover, the distribution of OH interatomic distances exhibits substantial asymmetry, ranging over as much as 0.14 Å. Fig 3. shows the distribution of differences. Only 6 of the total number of water molecules in question (i.e. 11.5%) exhibited C_{2v} symmetry.

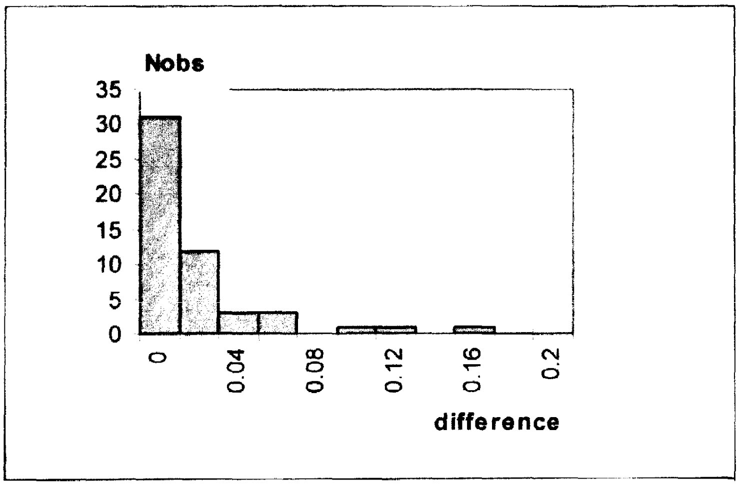

Fig 3. Distributions of R(O-H) bond length differences (in Å)

Having used in these graphs only the most precise neutron diffraction determinations, we may reject the hypothesis that these differences are simply due to the error of measurements. The mean value of R(OH) is in the range of values for an isolated molecule and that in a liquid phase. A substantial lengthening is observed for water molecules in ice: the difference is statistically significant at $\alpha = 0.01$. The lengthening of R(OH) may easily be attributed to the H-bond formation,[14] but its significant shortening has no simple interpretation. However 37.5% of the data exhibit shorter bonds than in the gas phase, and 22.2% bonds are shorter by more than the 3σ of the least precise measurements for these class of data retrieved from CSD, i.e. 0.015 Å. Even more dramatic is the variability of bond angles, as shown in Fig 2.

Very important is the observation that the bond angle φ is considerably greater than those measured for isolated molecule, as well as for molecules in the condensed phases. In all three cases the difference is statistically significant at $\alpha = 0.01$. These are significant findings. It simply means that the water molecule is a very elastic and readily deformable moiety.

From a simple model of deformation based on the harmonic approximation, it is understable that bond angles are more easily deformed than the bond lengths, as the force constants for bond angle deformations are approximately one order of magnitude smaller than those for the bond stretching.[15] As a tentative explanation[16,17] one may consider a model in which a water molecule due to the interaction with its environment, undergoes a semidissociation leading to a form H^+OH^- and in consequence to variation in R(OH) value. As another explanation of these effects one may consider water molecules in their dynamics. It means that we should take into account rotational-vibrational motion of water molecules which leads to considerable changes in molecular geometry.[18] Based on experimental results,[10,19] we suggest the consideration of changes in molecular geometry of water as due to the intermolecular interactions in the frame of deformations brought about by rotational-vibrational excitations.

On the other hand, the water molecule represents a rather strange features. In the ground state, the three modes of a vibrating molecule are not correlated. However even a small vibrational excitation leads to a considerable coupling between these motions, leading to localization.[20] It means that each OH bond vibrates indepedently. Taking this into account, we propose that the external force fields (e.g. intermolecular interactions) imposed on the water molecule by its environment may cause these changes in molecular geometry and molecular electric properties in a way similar to the deformations due to vibrations. A fundamental consequence of the proposed point of view is that changes in molecular geometry of a water molecule caused by intermolecular interactions associated with partial ionic structures, leads to their new electric properties, giving rise to potentially new kinds of intermolecular interactions. Looking at the examples presented above, it is possible to suppose that the water molecule is very flexible and easily deformed.

A very good illustration of the important role of water molecules in stabilising the crystal structures is provided by investigations in the thermochemistry of simple inorganic hydrates.[21] The heat of formation of water in the gas phase is 57.78 Kcal/mole and in the liquid phase 68.29 Kcal/mole. Table 2 contains values of the heat of formation for hydrates of $MgCl_2$ and $CuSO_4$ in the first column, and the additive sum of heats of formation of the components in the second column. The difference in the third column presents the stabilising effect due to the interactions of these salts with water molecules in crystalline hydrates, whereas the last column presents the stabilising effect per molecule of water.

Table 2. Heats of formation of $MgCl_2$ and $CuSO_4$ and their hydrates in Kcal/mole. n stands for number of water molecules in the hydrate unit.

Salt	ΔH_f	additive sum of ΔH_f of components	Differenc	difference / n
$MgCl_2$	153.4	-	-	-
$MgCl_2.H_2O$	231.2	211.2	20.0	20.0
$MgCl_2.2H_2O$	306.0	269.0	37.0	18.5
$MgCl_2.4H_2O$	454.0	384.5	69.5	17.4
$MgCl_2.6H_2O$	597.4	500.1	97.3	16.2
$CuSO_4$	184.0	-	-	-
$CuSO_4.H_2O$	259.0	241.8	17.2	17.2
$CuSO_4.3H_2O$	402.3	357.4	44.9	15.0
$CuSO_4.5H_2O$	544.4	472.9	71.5	14.3

The above results may be compared with the stabilizing effect in going from the gas phase (isolated molecules) to the liquid phases. It yields 10.5 Kcal/mole. The data in the last column show that the effect of stabilization due to the interaction of water molecules with $CuSO_4$ is significantly larger - by 4-10 Kcal/mole. This may be interpreted as a "gluing" activity of the water molecule in crystalline structures.

We postulate that this particular and unique property of water molecule(s) is due to the following factors:

(i) water exhibits amphoteric behaviour in both the Brönsted and Lewis acid/base sense,[22] since each molecule contains two donating H-bonds and two accepting H-bond centres,

(ii) as shown in this report, water molecules exhibit a substantial elasticity and may easily adopt to the spatial requirements of the closest environment.

The most important consequence resulting from these properties is a great propensity of the water molecule to accommodate in the crystal lattice. These effects may be studied in a precise way in the solid state by use of diffraction and spectroscopic techniques. An important consequence may be deduced for biopolymers and even larger biological systems since it is well-known that proteins, even in the crystalline state, contain 30 to 70% per volume[23] of water, not to mention native forms and systems in live cells. The above presented data and their interpretation show that the water molecules exhibit unique features which determine the significant role of these molecules in chemistry and biology.

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REFERENCES

1. Dunitz, J.D. *X-Ray Analysis and the Structure of Organic Molecules,* Cornell University Press, Ithaca, **1979**.
2. Mak,T.C.W.; Zhou, Gong-Du *Crystallography in Modern Chemistry*, John Wiley & Sons, New York, **1992**.
3. Domenicano, A.; Vaciago,A.; Coulson,C.A. *Acta Cryst.*, **1975**, B31, 221 and 1630.
4. e.g. Bürgi,H.B.; Shefter,E.; Dunitz,J.D. *Tetrahedron*, **1975**, 31, 3089. Bürgi,H.B.; Dunitz,J.D.; Lehn.J.M.; Wipff,G. *Tetrahedron*, **1974**, 30, 1563.
5. Bürgi,H.B.; Dunitz,J.D. *Structure Correlation*, vol. 1 and 2, VCH Weinheim, **1994**.
6. Krygowski,T.M. *Progr.Phys.Org. Chem.*, **1991**, 17, 239.
7. Krygowski,T.M.; Cyrański,M.K. *Advances in Molecular Structure Research*, M.Hargittai and I.Hargittai Edts, JAI Press Inc., **1997**, vol.3, p.227.
8. Krygowski,T.M.; Cyrański,M.K. *Theoretical Organic Chemistry - Theoretical and Computational Chemistry*, C.Parkanyi Ed., Elsevier **1998**, vol.5 p. 153.
9. Allen,F.H.; Davies,J.E.; Galloy,J.E.; Johnson,J.J.; Kennard,O.; Macrave,C.F.; Mitchel,E.M.; Smith,J.M.; Watson,D.G. *J.Chem.Inf.Comput.Sci.*, **1991**, 31, 187.
10. Shostak,S.L.; Ebenstein,W.L.; Muenter,J.S. *J.Chem.Phys.*, **1991**, 94, 5875.
11. Thiessen,W.E.; Narten,A.H. *J.Chem.Phys.*, **1982**, 77, 2656.
12. Postorino,P.; Tromp,R.H.; Ricci,M-A.; Soper,A.K.; Neilson,G.W. *Nature*, **1993**, 366, 668.
13. Franks,F. *The Properties of Ice*, in *Water, A Comprehensive Treatise*, Vol.1, ed. by F.Franks, Plenum Press, New York, London **1972**.
14. Jeffrey,G.A.; Saenger,W., *Hydrogen Bonding in Biological Structures,* Springer, Berlin, **1991**.
15. Berstein,J. *Effect of crystal environment on molecular structure,* in *Accurate Molecular Structures,* ed. by A.Domenicano and I.Hargittai, Oxford Science Publications, Oxford University Press, **1992**, pp 469 - 497.
16. Ceccarelli,C.; Jeffrey,G.A.; Taylor,R. *J.Mol.Struct.*, **1981**, 70, 255.
17. Huet,T.R.; Pursell,C.J.; Ho,W.C.; Dinelli,B.M.; Oka,T. *J.Chem.Phys.*, **1992**, 97, 5977.
18. Makarewicz,J.; Pyka,J. *Mol.Struct.*, **1989**, 68, 107.
19. Shostak,S.L.; Muenter,J.S. *J.Chem.Phys.*, **1991**, 94, 5883.
20. Camy-Peyret,C.; Flaud,J.M.; Lechuga-Fossat,L. *J.Mol.Spectr.*, **1985**, 109, 300.
21. Landolt-Bernstein; *Zahlenwerte und Funktionen aus Physik-Chemie-Astronomie-Geophysik und Technik,* Zweiter Band, 4 Teil - Kalorimetrische Zustandgrossungen, Springer-Verlag, Berlin, **1961**, pp 209 ff.
22. Reichardt,C. *Solvents and Solvent Effects in Organic Chemistry,* VCH, Weinheim, **1988**. Krygowski,T.M.; Fawcett,W.R. *J.Am.Chem.Soc.*, **1975**, 97, 2143.
23. Matthews,B.W. *Annu.Rev.Phys.Chem.*, **1976**, 27, 493. Gunsteren,W.F. and Berendsen,H.J.C. *J.Mol.Biol.*, **1984**, 176,559.