Formation of Extended Tapes of Cyclic Water Hexamers in an Organic Molecular Crystal Host**

Radu Custelcean,* Cerasela Afloroaei, Mircea Vlassa, and Mihai Polverejan

Water clusters have been extensively studied both theoretically and experimentally, as they can provide insight into the structure and characteristics of liquid water or ice.[1] Among the clusters, the water hexamer is particularly interesting. Recent studies indicated that this cluster is the smallest possible unit that can exhibit some of the properties found in bulk water.[2] Theoretical calculations found several different isomers for the water hexamer, of which the five lowest energy ones, that is, cage, prism, book, boat, and cyclic, are almost isoenergetic.[3] The cage structure, however, was predicted to be the most stable isomer at very low temperatures, and its existence was confirmed experimentally.[4] Recently, the less-stable cyclic hexamer was isolated, and its structure characterized by IR spectroscopy.[5] Fast cooling in liquid helium allowed its growth under kinetic control and prevented its transformation into more-stable three-dimensional structures. This isomer is particularly significant, as it is the building block of ice I_h,[6] and it appears to be relevant to liquid water as well.[7] It was also described as the simplest supramolecular analogue of cyclohexane.[1]

The lattice of a crystal host may offer an alternative environment for stabilizing various topologies of water clusters.[8] Herein we describe the formation of cyclic water hexamers with an icelike chair conformation and their self-assembly into unprecedented one-dimensional tapes with spectroscopic features similar to those of liquid water, along the channels of an organic molecular crystal host.

2,4-Dimethyl-5-aminobenzo[*b*]-1,8-naphthyridine[9] (**1**) crystallizes from MeOH or EtOH with 2.5 mol of H_2O, as revealed by X-ray crystallography.[10] Two of the five unique water molecules interconnect crystallographically different benzonaphthyridine units in hydrogen-bonded dimers (Figure 1a). The dimers further associate by N(3)–H$\cdots$O(2) and N(6)–H$\cdots$O(1) hydrogen bonds into one-dimensional chains (Figure 1b), which π stack along the *a* axis to generate two-dimensional extended layers. A closer examination of the packing reveals the presence of extended channels, approximately 9 Å × 6 Å wide, through the crystal (Figure 2). Their existence seems to originate in the highly asymmetric shape of the hydrogen-bonded building block dimers, which precludes efficient packing of the layers.

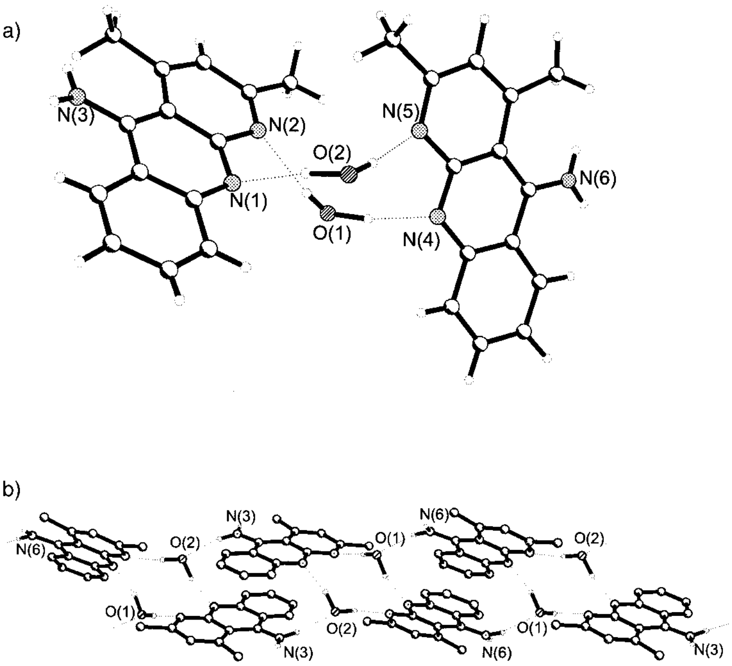

Figure 1. X-ray crystal structure of **1**. a) Hydrogen-bonded dimers. b) Self-assembly of the dimers into chains.

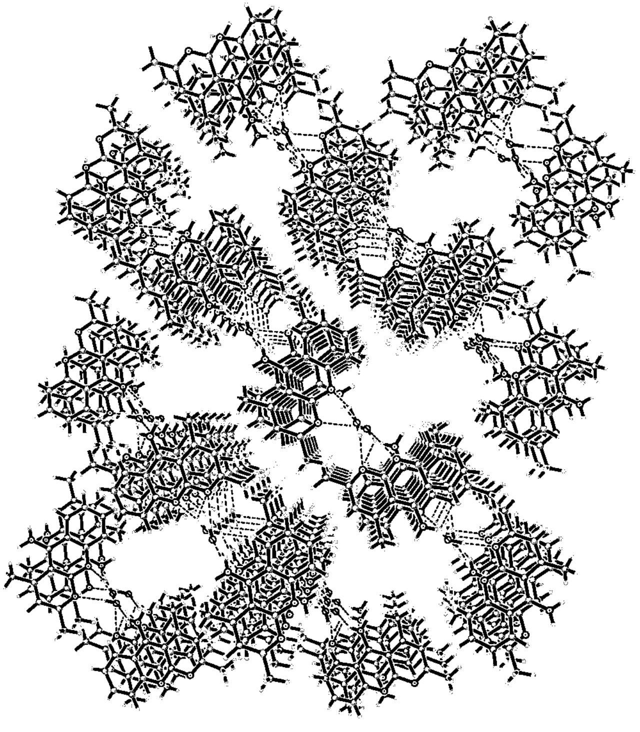

Figure 2. Crystal packing of **1**, viewed along the *a* axis. Water molecules from the channels are omitted for clarity.

The channels are occupied by the remaining water molecules, which are associated by strong O–H$\cdots$O hydrogen bonds into cyclic centrosymmetric hexamers that adopt an icelike chair conformation (Figure 3). The geometric parameters of the hexamers are summarized in Table 1. The average O–O distance is 2.776 Å. For comparison, the corresponding

---

[*] Dr. R. Custelcean, M. Polverejan
Department of Chemistry
Michigan State University
East Lansing, MI 48824 (USA)
Fax: (+1) 517-353-1793
E-mail: custelce@cem.msu.edu

C. Afloroaei, Prof. Dr. M. Vlassa
Department of Organic Chemistry
Babes-Bolyai University
11 Arany Janos
3400 Cluj-Napoca (Romania)

[**] We thank Prof. J. E. Jackson (MSU) for his generous support of this study.

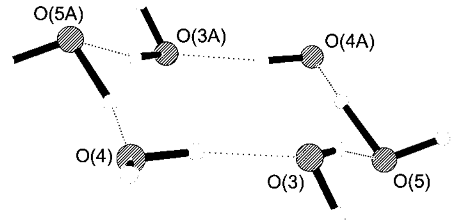

Figure 3. Representation of the chair conformation of the cyclic water hexamers found in the channels of **1**.

Table 1. Geometrical parameters [Å, °] for the cyclic water hexamers in **1**·2.5 H_2O.

O–H···O	O–H	O···O	H···O	O-H···O
O(4)-H···O(3)	0.960[a]	2.711	1.758	171.3
O(3)-H···O(5)	0.956	2.785	1.844	167.6
O(5)-H···O(4A)	1.264	2.833	1.703	145.0
O···O···O				
O(3)···O(5)···O(4A)	113.2			
O(5A)···O(4)···O(3)	96.0			
O(4)···O(3)···O(5)	140.2			
O···O···O···O				
O(5)···O(3)···O(4)···O(3A)	106.2			
O(5)···O(4A)···O(3A)···O(4)	105.9			

[a] Restrained.

value in ice I_h is 2.759 Å at – 90 °C.[6a] However, there is a wide variation in the O-O-O angles, with an average of 116.5°. This value deviates considerably from the corresponding value of 109.3° in hexagonal ice. The hexamers are self-assembled along the channels by O(5)–H···O(4) hydrogen bonds into extended tapes consisting of fused four- and six-membered water rings (Figure 4). The interhexamer O(5)–O(4) distance of 2.854 Å is very similar to the O–O distance of 2.85 Å in liquid water.[11] This supramolecular association of water molecules in tapes is presumably enforced by the shape of the host's channels, whose relatively narrow openings preclude the formation of more-stable three-dimensional clusters. Additional O(4)–H···O(2) hydrogen bonds anchor the water tapes to the organic framework. Although the O(3)···O(1) distance of 2.696 Å suggests strong hydrogen bonding between these oxygen atoms, the positions of the O(3)–H dangling protons, as found by X-ray diffraction, do not indicate any attractive interaction. Notably, there are no O–H···N hydrogen bonds between the water tapes and the organic host. This structure appears therefore to be unique, in the sense that the water molecules in the cluster experience a molecular surrounding that resembles more closely the environment found in liquid water or ice, as opposed to the previously described inclusion complexes of water clusters,[8] in which strong interactions with the host were present.[12]

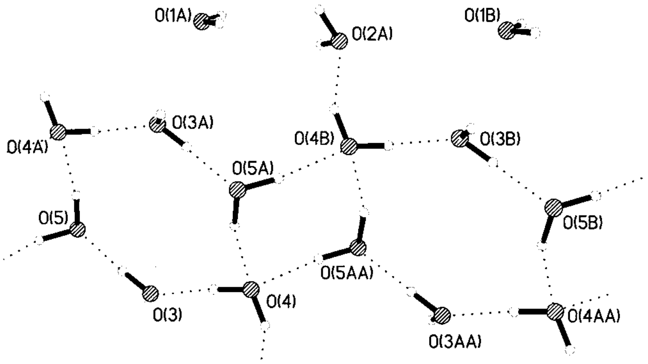

Figure 4. Self-assembly of the water hexamers into extended tapes. Hydrogen-bond lengths [Å] and angles [°]: O(5A)-H···O(4B): O···O 2.854, H···O 1.848; O-H···O 169.1; O(4)-H···O(2): O···O 2.743, H···O 1.879; O-H···O 148.3.

The relatively weak interactions with the host framework suggested that the water tapes are fairly loose inside the channels. Therefore, facile removal of this water was anticipated. Indeed, thermogravimetric analysis (TGA) showed an 11.65 % weight loss between room temperature and 70 °C, which corresponds to 1.73 of the 2.5 water molecules. Moreover, when a crystal of **1**·2.5 H_2O was examined with a hot-stage microscope, loss of liquid water and concomitant loss of crystal transparency were observed on heating. The remaining water is retained up to 166 °C and eventually lost before the melting point of **1** (227 °C) is reached. The water from the channels is also slowly released at room temperature, as indicated by a TGA taken on a five-month-old sample. It appears that the structure of the organic host is maintained after water release, as demonstrated by powder X-ray diffraction, which shows almost identical patterns for the initial and dehydrated compounds. However, N_2 absorption isotherms obtained under different conditions indicated no porosity for the latter, and this suggests that the channels become inaccessible after removal of the water.

We attempted to assign the O–H stretching vibrations of the water molecules of the tapes on the basis of the difference between the FT-IR spectrum of the initial complex and that of the solid obtained after removing the water from the channels by heating at 120 °C for 10 min. As illustrated in Figure 5, the bands centered around 3495 and 3359 cm^{-1} and the analogous bands at 2614 and 2469 cm^{-1} in the deuterated complex (obtained by recrystallization from deuterated methanol) disappear upon heating. We therefore assign these bands to the O–H and O–D bonds of the water tapes. These peaks do not reappear when the dehydrated complex is exposed to water vapor or stirred in liquid water for 24 h, and this suggests that the loss of water is irreversible, as is also supported by TGA. However, the IR spectrum of ice is significantly different, with the O–H (O–D) stretching vibration at 3220 (2420) cm^{-1}.[6a] In this respect, the water tapes described here appear to have more similarities with liquid H_2O (D_2O), which exhibits analogous bands at 3490 (2540) and 3280 (2450) cm^{-1}.[6a] Our measured band at 3359 cm^{-1} is also close to the value of about 3335 cm^{-1} reported for the cyclic water hexamer formed in liquid helium.[5]

In summary, we reported the supramolecular association of icelike cyclic water hexamers into one-dimensional tapes in an organic host. Further investigation of this unprecedented manifestation of H_2O, with characteristics reminiscent of both

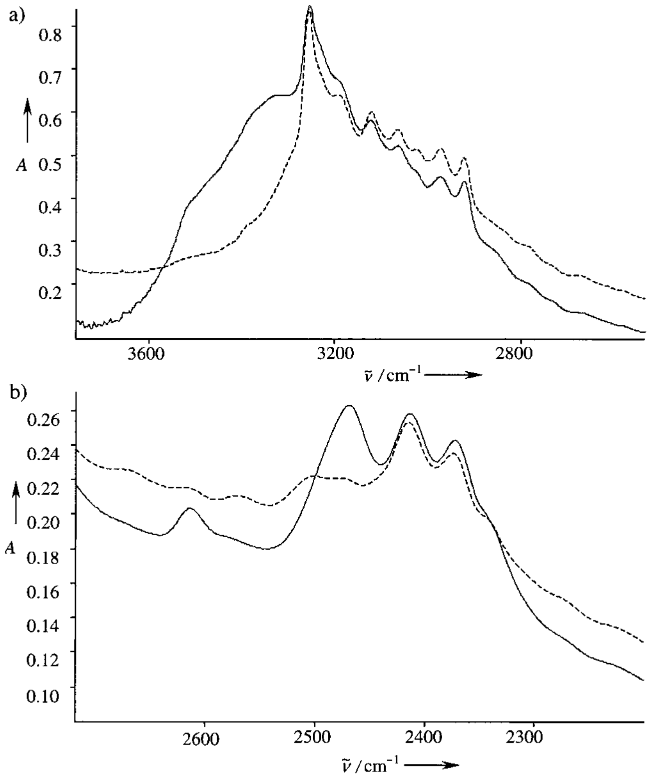

Figure 5. a) FT-IR spectra of the initial $\mathbf{1}\cdot 2.5\,H_2O$ (solid line) and after evacuation of water from the channels (dotted line); b) analogous spectra of $\mathbf{1}(ND_2)\cdot 2.5\,D_2O$. A = absorbance.

liquid water and ice, offers the prospect of improving our understanding of this fundamental, yet complex substance.

Received: April 6, 2000 [Z14948]

---

[1] J. M. Ugalde, I. Alkorta, J. Elguero, *Angew. Chem.* **2000**, *112*, 733–737; *Angew. Chem. Int. Ed.* **2000**, *39*, 717–721.

[2] J. K. Gregory, D. C. Clary, K. Liu, M. G. Brown, R. J. Saykally, *Science* **1997**, *275*, 814–817.

[3] The relative stability of these isomers is strongly dependent on temperature and zero-point energy (ZPE) corrections: J. Kim, K. S. Kim, *J. Chem. Phys.* **1998**, *109*, 5886–5895.

[4] K. Liu, M. G. Brown, C. Carter, R. J. Saykally, J. K. Gregory, D. C. Clary, *Nature* **1996**, *381*, 501–503.

[5] K. Nauta, R. E. Miller, *Science* **2000**, *287*, 293–295.

[6] a) D. Eisenberg, W. Kauzmann, *The Structure and Properties of Water*, Oxford University Press, Oxford, **1969**; b) N. H. Fletcher, *The Chemical Physics of Ice*, Cambridge University Press, Cambridge, **1970**.

[7] a) R. J. Speedy, J. D. Madura, W. L. Jorgensen, *J. Phys. Chem.* **1987**, *91*, 909–913; b) A. C. Belch, S. A. Rice, *J. Chem. Phys.* **1987**, *86*, 5676–5682.

[8] a) W. B. Blanton, S. W. Gordon-Wylie, G. R. Clark, K. D. Jordan, J. T. Wood, U. Geiser, T. J. Collins, *J. Am. Chem. Soc.* **1999**, *121*, 3551–3552; b) L. J. Barbour, G. W. Orr, J. L. Atwood, *Nature* **1998**, *393*, 671–673; c) C. Foces-Foces, F. H. Cano, M. Martinez-Ripoll, R. Faure, C. Roussel, R. M. Claramunt, C. Lopez, D. Sanz, J. Elguero, *Tetrahedron: Asymmetry* **1990**, *1*, 65–86.

[9] N. I. Shramm, M. E. Konshin, *Khim. Geterotsikl. Soedin.* **1982**, 674–678; N. I. Shramm, M. E. Konshin, *Chem. Heterocycl. Compd. (Engl. Transl.)* **1982**, *18*, 511–515.

[10] Crystal data for $\mathbf{1}\cdot 2.5\,H_2O$: A Siemens SMART CCD diffractometer with $Mo_{K\alpha}$ radiation ($\lambda = 0.71073$) was used for data collection. The structure was solved by direct methods and refined by full-matrix least-squares methods on F^2 by using the SHELXTL package (Structure Analysis Program 5.1, Brucker AXS, Inc., Madison, WI, **1997**). Absorption corrections were applied by using SADABS. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were located from difference Fourier maps and refined isotropically. However, the two hydrogen atoms on O(4) and the dangling hydrogen atom of O(3) became unstable during refinement, and therefore the corresponding O–H distances were constrained at 0.96 Å. Crystal dimensions: $0.41\times0.10\times0.05$ mm; $T = 173$ K; triclinic, space group $P\bar{1}$; $a = 7.4737(9)$, $b = 12.5474(15)$, $c = 14.5261(18)$ Å, $\alpha = 82.315(3)$, $\beta = 84.305(2)$, $\gamma = 80.020(2)^\circ$, $V = 1325.5(3)$ Å^3, $Z = 4$; $\rho_{\mathrm{calcd}} = 1.345\ \mathrm{g\,cm^{-3}}$; $2\theta_{\max} = 50^\circ$; 9901 reflections collected, of which 4624 were unique; 497 parameters, three restraints; $R_1 = 0.0656$, $wR_2 = 0.1387$ for $I > 2\sigma(I)$; residual electron density: 0.256 e Å^3. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-142220. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

[11] A. H. Narten, W. E. Thiessen, L. Blum, *Science* **1982**, *217*, 1033–1034.

[12] An N(3)–H···O(3) intermolecular contact was detected in the present complex. However, the relatively long H···O distance (2.58 Å) and tight N–H···O angle (135.8°) suggest a very weak interaction.

The First Solid-Phase Synthesis of a Peptide-Tethered Platinum(II) Complex**

Marc S. Robillard, A. Rob P. M. Valentijn,
Nico J. Meeuwenoord, Gijs A. van der Marel,
Jacques H. van Boom,* and Jan Reedijk*

It is well established that removal of cisplatin- and carboplatin-induced DNA adducts contributes to tumor resistance to these drugs.[1] To overcome this problem, a plethora of platinum(II) complexes which interact with DNA in a manner distinct from that of the parent drugs have been designed and evaluated with respect to the distortion of DNA, as well as the interaction with proteins and antitumor activity.[2] In addition, amino acid residues, peptides, and polyamides have been successfully employed as site-specific DNA-interacting elements conjugated to metal complexes.[3a–h] For example, Kelland et al.[4] reported minor-groove-directed platinum complexes derived from the polyamides netropsin and distamycin. Despite these efforts, only a few

---

[*] Prof. J. H. van Boom, Prof. J. Reedijk, M. S. Robillard,
Dr. A. R. P. M. Valentijn, N. J. Meeuwenoord,
Dr. G. A. van der Marel
Leiden Institute of Chemistry
Gorlaeus Laboratories, Leiden University
P.O. Box 9502, 2300 RA Leiden (The Netherlands)
Fax: (+31)71-527-4671 (J. Reedijk)
Fax: (+31)71-527-4307 (J.H. van Boom)
E-mail: j.boom@chem.leidenuniv.nl, reedijk@chem.leidenuniv.nl

[**] This research was supported by the Council for Chemical Sciences of The Netherlands Organization for Scientific Research (CW-NWO) and by The Netherlands Foundation for Technical Sciences (STW). Support and sponsorship by COST Action D8/00097 (biocoordination chemistry) is kindly acknowledged. The authors thank Johnson & Matthey (Reading, UK) for their generous loan of K_2PtCl_4.