Single Water Molecule Recognition: A 1:1 Complex of Crownophane with Water by Pseudo-tetrahedral Hydrogen Bond Formation

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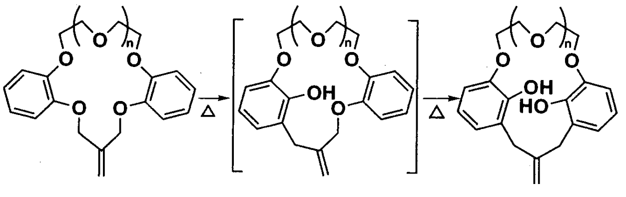
A 22-membered crownophane prepared via the "Tandem Claisen Rearrangement" was found to form stable 1:1 complex with water, which is incorporated into the cavity by pseudo-tetrahedral hydrogen bond formation and observed by DSC, TGA, and X-ray structural analysis.

The cooperation of both hydrogen-bond donating and accepting abilities in a receptor (host molecule) is of importance to exhibit molecular recognition in most cases of biological systems. Introduction of the both properties into a host molecule is significant to make sophisticated artificial receptors, especially to recognize neutral organic guests. In this context, topographical complementarity between the binding sites of the host and guest is required for the successful design of strongly binding host molecules.[1]

Above all, the complexation with water is of prime importance in biological systems, because the water molecules play a very important role to keep a highly organized structure and to achieve highly precise functions such as sensing and catalytic reactions. For these reasons, many molecular complexes of macrocycles such as crown ethers,[2,3] aza crown ethers in the protonated form,[4] cryptands both in the free form[5] and in the diprotonated form,[6] cyclodextrines,[7] and so on, with water molecules have also been reported and characterized by their crystal structure. To our knowledge, although a water molecule is enclosed in the formation of a 'water cryptate', in the cavity of the diprotonated macrobicycle, held by a tetrahedral array of hydrogen bonds,[6,8] there is no report on tetrahedral hydrogen bond formation like crystal of ice with water incorporated into the cavity of crown ether-like unprotonated macromonocyclic compounds. We report here the first example of a stable and neutral 1:1 complex of macromonocyclic crownophane[9] with water which is confirmed by X-ray crystallography and thermal analyses, where the complex has four hydrogen bonds forming a pseudotetrahedral conformation. These results show the importance of carefully designing the ring structure (size, shape, etc.).

Recently, we have developed a novel type of rearrangement reaction named the "Tandem Claisen Rearrangement",[10,11] by which novel crownophanes can be obtained from the corresponding macrocyclic polyethers by a one-step thermal reaction in moderate yields as shown in Scheme 1.[12] These crownophanes have two phenolic groups and oligoethylene glycol moieties. It has been found that crownophanes **1**, **2**, and **3** can form single crystals by recrystallization from cyclohexane or acetonitrile in the presence of a small amount of water.[13] As confirmed by elemental analysis and X-ray analysis, these crystals contain one water molecule for **1** and **3**, and two water molecules for **2**.[14]

Crystals of these compounds were measured using DSC and TGA. The DSC of crystals of **1**, **2**, and **3** gives a large endothermic peak at 124 °C (24.6 kcal/mole), 94 °C (38.6 kcal/mol), and 58 °C (10.7 kcal/mol), respectively.[15] Crownophane **1** shows a sharp peak at a higher temperature than crownophanes **2** and **3**, which show broad and irregular peaks. In TGA measurement, the weight loss of **2** and **3** begins at a lower temperature than that of **1**, which shows about 4% of weight loss corresponding to the loss of one water molecule from the 1:1 complex. These temperatures are very close to the peak temperatures observed in the DSC analysis, in all cases. Elemental analysis also confirmed that **1** can form a stable 1:1 complex with water after drying overnight under vacuum at room temperature, whereas the complexes of both **2** and **3** with water result in a higher host/guest ratio than expected, reflecting a less stable complexation and a higher lability of the included water.[14]



1 : n = 3, **2** : n = 4, **3** : n = 5

Scheme 1. Synthesis of crownophanes via thermal Claisen rearrangement.

X-ray structural analysis of single crystals of **1**, **2**, and **3** including water molecules was investigated by X-ray diffraction. These complexes with water were found to be a monohydrate for **1** and **3**, and a dihydrate for **2**. The ORTEP drawing of the complex of **1** with water is shown in Figure 1. In the case of the 1:1 complex of **1** with water,[16] a water molecule is enclosed in the macrocyclic cavity, interacting via hydrogen bonds with two phenolic hydroxy groups and two oxygen atoms of the polyethylene glycol ethers (Figure 1), where protons of water are directed towards the two ethereal oxygens O(4) and O(6). The five ethereal oxygen atoms are almost coplanar, the largest deviation from the mean plane being ± 0.5 Å. Two hydroxy groups are placed above and below the mean plane as described above. As shown by the value of the torsion angles, the overall conformation of the macrocyclic complex (**1**$\cdot 1H_2O$) is consistent with an approximate C_2 symmetry with the hypothetical rotation axis passing through O(5) and C(2). It is worth noting that two hydroxy protons of the phenolic moieties are located towards the molecular cavity, which enables their interaction with the oxygen atom of water located in the cavity. On the other hand, each hydrogen atom of the water molecule is hydrogen-bonded to two oxygen atoms (O(4) and O(6)) of the macrocyclic cavity.

As shown in Figure 1, the water oxygen atom O(8) almost lies in the center of the plane determined by the five ethereal oxygen atoms and on the center of a distorted tetrahedron with

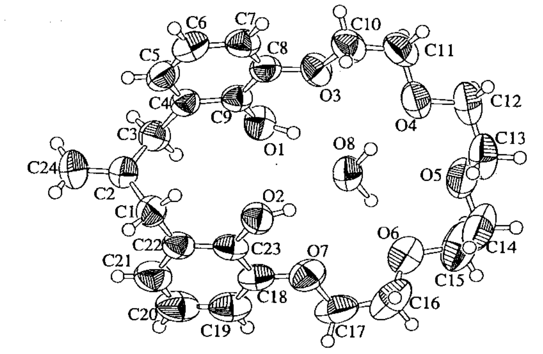


Figure 1. X-ray structural analysis of single crystals of the complex of **1** with water molecules. Thermal ellipsoids are scaled to the 50% probability level.

hydroxy oxygens O(1) and O(2), and ethereal oxygens O(4) and O(6) as four apices[distances between O(8) and O(n): O(8)–O(1) 2.82 Å, O(8)–O(2) 2.86 Å, O(8)–O(4) 2.97 Å, and O(8)–O(6) 3.15 Å]. In the crystals, crownophane **1** can act not only as a two *hydrogen-bonding donating* but also as a two *hydrogen-bonding accepting* host molecule towards the guest water molecule to give a stable 1:1 complex.

The ORTEP drawings (a and b) of the complexes of **2** and **3** with water are shown in Figure 2.[17] In the case of the complex of **2** with two water molecules, these are also incorporated into the cavity, but in a different manner for each other. Interestingly, only one water molecule is incorporated into the cavity of crownophane **3** and linked by three hydrogen bonds, although its cavity size of **3** is larger than that of **2** and the cavity shape of **3** is distorted. From these results, the water molecules included within the cavities of **2** and **3** seemed to be bound loosely with less stability than in the case of **1**. The crystal data might reflect the results of the thermal analysis.

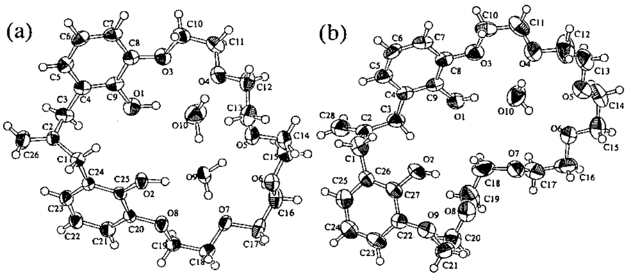


Figure 2. X-ray structural analyses of single crystals of the complex of **2** (a) and **3** (b) with water molecules. Thermal ellipsoids are scaled to the 50% probability level.

In conclusion, it has been found in this study that crownophane **1** can nicely work as hydrogen donor and acceptor in a complementary fashion (pseudo-tetrahedral hydrogen bond formation) toward single water molecule.

References and Notes

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13 Compound **3** had previously been reported to be liquid (see ref 12). When it is recrystallized from cyclohexane containing a small quantity of water, single crystals can be obtained.

14 Although satisfactory values are given as **1**·1H_2O, **2**·1.5H_2O, and **3**·0.5H_2O in the elemental analysis, it is confirmed in the X-ray structure analysis that the complexes of **1**, **2**, and **3** with water are the 1:1, 1:2, and 1:1 complexes, respectively; **1**·1H_2O: Found: C, 64.79, H, 7.14%. Calcd for $C_{24}H_{30}O_7 \cdot H_2O$: C, 64.27; H, 7.19%. **2**·1.5H_2O: Found: C, 62.17; H, 7.45%. Calcd for $C_{26}H_{34}O_8 \cdot 1.5H_2O$: C, 62.26; H, 7.44%. **3**·0.5H_2O: Found: C, 63.48; H, 7.69%. Calcd for $C_{28}H_{38}O_9 \cdot 0.5H_2O$: C, 63.74; H, 7.45%.

15 The DSC of the complexes was measured by using a small pan at the open system in which the sample was placed. Otherwise, when the DSC was measured in a closed system, the endothermic peak was observed to show a remarkably high temperature (>160 °C) in the case of **1**·1H_2O.

16 X-ray crystal data of **1**·1H_2O: $C_{24}H_{32}O_8$, MW 448, crystal size 0.25 × 0.30 × 0.20 mm^3. Orthorhombic, space group *P*bca(# 61), *a* = 15.305(1) Å, *b* = 23.086(1) Å, *c* = 13.123(1) Å, *V* = 4637(1) Å^3, *Z* = 8, *d* = 1.30 (obs) and 1.28 (calcd) g/cm^3; Mac Science MXC18 diffractometer, Mo Kα radiation (λ = 0.71073 Å), μ = 0.635/cm, 2θ (max) = 40°, 2573 measured and 2177 unique reflections (–14 ≤ h ≤ 0, 0 ≤ k ≤ 22, –12 ≤ l ≤ 0); direct methods, L.S. parameters 289, *R* = 0.042 (R_w = 0.067), *S* = 1.27. Hydrogen atoms of water of **1**·1H_2O were found from a difference electron density map.

17 a) X-ray crystal data of **2**·2H_2O: $C_{26}H_{38}O_{10}$, MW 511, crystal size 0.40 × 0.40 × 0.16 mm^3. Orthorhombic, space group $P2_12_12_1$(# 19), *a* = 13.180(1) Å, *b* = 11.783(1) Å, *c* = 17.176(1) Å, *V* = 2667.4(3) Å^3, *Z* = 4, *d* = 1.27 (calcd) g/cm^3; Enraf-Nonius diffractometer, Cu Kα radiation (λ = 1.5418 Å), μ = 8.12/cm, 2θ (max) = 120°, 2259 measured and 2259 unique reflections (0 ≤ h ≤ 14, 0 ≤ k ≤ 13, 0 ≤ l ≤ 19); direct methods, L.S. parameters 325, *R* = 0.049 (R_w = 0.067), *S* = 2.39. b) X-ray crystal data of **3**·1H_2O: $C_{28}H_{42}O_{10}$, MW 538, crystal size 0.20 × 0.20 × 0.30 mm^3. Orthorhombic, space group $P2_12_12_1$(# 19), *a* = 17.849(1) Å, *b* = 20.685(2) Å, *c* = 7.6703(8) Å, *V* = 2832.0(4) Å^3, *Z* = 4, *d* = 1.22 (calcd) g/cm^3; Mac Science MXC18 diffractometer, Mo Kα radiation (λ = 0.71073 Å), μ = 0.90/cm, 2θ (max) = 40°, 2577 measured and 1561 unique reflections (0 ≤ *h* ≤ 21, 0 ≤ *k* ≤ 24, 0 ≤ *I* ≤ 9); direct methods, L.S. parameters 343, *R* = 0.048 (R_w = 0.077), *S* = 0.82.