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Inclusion of Water by a Crown Amide. First Crystal Structure of a Respective Host-Guest Combination

EDWIN WEBER*
Institut für Organische Chemie und Biochemie der Universität Bonn, Gerhard-Domagk-Strasse 1, D-5300 Bonn-1, F.R.G.

GEORGE R. NEWKOME, FRANK R. FRONCZEK
Department of Chemistry, Louisiana State University, Baton Rouge, LA 70803, U.S.A.

and

SYBILLE FRANKEN
Department of Chemical Physics, RUG, Nijenborgh 16, 9747 AG Groningen, The Netherlands

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Abstract. Crown amide (**1**) forms a stoicheiometric 1 : 1 inclusion complex with water, the X-ray crystal structure of which is reported. Crystals of $\mathbf{1}\cdot H_2O$ are triclinic, space group $P\bar{1}$, with $a = 7.503(1)$, $b = 11.394(3)$, $c = 13.443(2)$ Å, $\alpha = 107.066(18)$, $\beta = 96.627(10)$, $\gamma = 106.377(14)°$, and $Z = 2$. $R_F = 0.039$ for 1697 Mo$K\alpha$ reflections $[I > 3\sigma(I)]$ measured at 24 °C. The structure features a hydrogen bonded host-guest relationship with concrete $\mathbf{1}\cdot H_2O$ units. Hydrogen bonds are between the water oxygen and O(4), N(4), respectively. The crystal packing shows a cavity arrangement of four ligands around each water molecule.

Key words: Crown amide, host-guest complex, water inclusion, crystal structure, hydrogen bonding.

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1. Introduction

Unlike hydrogen bonded crystalline complexes between crown compounds and NH- or CH-acidic uncharged organic molecules, analogous complexes involving OH-acidic organic molecules or water are relatively rare in the literature [1–3]. As a further documented restriction, water is mostly found in the intermolecular crystal space [4] rather than accommodated in a preformed molecular void [5]. In other cases, water behaves merely as a go-between to bind a second guest individual to the crown (ternary complex) [6]. Cram [7] and Newkome [8] have shown some prerequisites which take advantage of a crown constitution and/or intramolecular proton donors to allow complete encircling of water, and very recently Reinhoudt [9] has given a systematic approach to the water binding of pyridino crowns. But he is restricted to the use of a protonated site of the crown ring (charged complex).

Surprisingly, no inclusion complex of water with a simple amide crown has been reported as yet, e.g., by crystallography, except for a cyclic urea spherand [10]. In

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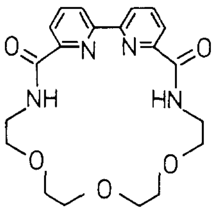
* Author for correspondence.



(1)

order to elucidate the nature and orientation of the binding of water in this context, we have determined the X-ray crystal structure of the readily available 1 : 1 complex formed between diamide crown **1** and water. The study of such molecular interactions may lead to a better understanding of secondary interactions that occur at biological receptor sites and enzyme pockets since water molecules and amide functions play a fundamental role in this area [11].

2. Experimental

A single crystal of $\mathbf{1}\cdot H_2O$ suitable for the crystallographic study was obtained by recrystallization of **1*** [12] from an aqueous benzene/petrol ether mixture. Data were collected from a colorless plate of dimensions $0.06 \times 0.36 \times 0.45$ mm sealed in a thin-walled glass capillary on an Enraf-Nonius CAD4 diffractometer equipped with Mo$K\alpha$ radiation ($\lambda = 0.71073$ Å) and a graphite monochromator. Cell dimensions and crystal orientation were determined from setting angles of 25 reflections having $13^\circ < \theta < 14^\circ$.

Crystal Data: $C_{20}H_{24}N_4O_5 \cdot H_2O$; $M = 418.5$, triclinic space group $P\bar{1}$, $a = 7.502(7)$, $b = 11.394(3)$, $c = 13.443(2)$ Å, $\alpha = 107.066(18)$, $\beta = 96.627(10)$, $\gamma = 106.377(14)^\circ$, $V = 1029.2(8)$ Å^3, $Z = 2$, $D_c = 1.350$ gcm^{-3}, $T = 24$ °C, $\mu(\mathrm{Mo}K\alpha) = 0.94$ cm^{-1}. Data having $0 \leqslant h \leqslant 7$, $-12 \leqslant k \leqslant 12$, $-14 \leqslant l \leqslant 14$, $2^\circ < 2\theta < 47^\circ$ were collected by $\omega - 2\theta$ scans with rates varying between 0.37–5.0 degmin^{-1}, designed to achieve $I = 25\sigma(I)$ subject to a maximum scan time of 180 sec. Three standard reflections, 200, 030, and 003, showed no significant decrease in intensity during data collection. Data reduction included corrections for background, Lorentz, and polarization effects; no absorption correction was made. Of 3027 unique data, 1697 had $I > 3\sigma(I)$ and were used in the refinement.

The structure was solved by direct methods using MULTAN78 [13], and refined by full-matrix least squares based on F with weights $w = 4F_o^2[\sigma^2(I) + (0.002F_o^2)^2]^{-1}$, using the Enraf-Nonius SDP programs. Nonhydrogen atoms were treated anisotropically; hydrogen atoms were located in difference maps (0.29–0.42 eÅ^{-3}). Amide H atoms were refined isotropically, while other macrocyclic H atoms were placed in calculated positions (C—H 1.05 Å) with isotropic $B = 5.0$ Å^2. Water hydrogen atoms could not be localized. Convergence was achieved with maximum shift 0.01σ, $R = 0.039$, $R_w = 0.052$, and goodness of fit 1.507 for 279 variables.

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* Systematic name (phane nomenclature) of **1**: 1,15-Dioxo-5,8,11-trioxa-2,14-diaza[15](6,6′)2,2′-bipyridinophane.

3. Results and Discussion

The final atomic coordinates of the nonhydrogen atoms of **1** · H_2O are given in Table I; atom labelling is in accordance with Figure 1. Table II shows bond distances and angles, and Table III gives a selection of torsion angles. Lists of anisotropic thermal parameters (Table IV), coordinates of the H atoms (Table V), and structure factors have been deposited. The molecular structure of the complex **1** · H_2O is shown in Figure 1 and the packing diagram is illustrated in Figure 2.

The host molecule reveals a nonsymmetric over-all geometry (Figure 1). This is mainly apparent from the conformations at C(13)—O(2)—C(14)—C(15) and at C(18)—C(19)—N(4)—C(20) which are *gauche* (–68.9 and –84.3°, respectively) instead of the usual *anti* for C—X—C—C (X = O, N) [14]. The endocyclic torsion

Table I. Final fractional coordinates ($\times 10^4$) and equivalent isotropic thermal parameters for **1** · H_2O[a]

Atom	*x*	*y*	*z*	B_{eq}
O(1)	5634(3)	9899(2)	7261(2)	5.31(5)
O(2)	8651(3)	6609(2)	7161(2)	5.13(6)
O(3)	7232(3)	3696(2)	6162(1)	4.95(6)
O(4)	3381(3)	2114(2)	5918(2)	4.60(5)
O(5)	1357(3)	2065(2)	8808(2)	4.97(5)
O(1W)	3755(4)	5032(2)	6612(2)	8.16(8)
N(1)	2499(3)	5401(2)	9102(2)	3.21(5)
N(2)	4089(3)	7827(2)	8736(2)	3.13(5)
N(3)	6667(3)	8335(2)	7546(2)	4.11(6)
N(4)	1437(4)	3068(2)	7594(2)	4.14(6)
C(1)	2307(4)	4386(2)	9434(2)	3.35(7)
C(2)	2568(4)	4500(3)	10505(2)	4.19(8)
C(3)	3004(5)	5720(3)	11261(2)	4.64(8)
C(4)	3150(4)	6772(3)	10927(2)	4.18(8)
C(5)	2898(4)	6575(2)	9840(2)	3.21(7)
C(6)	3001(4)	7688(3)	9448(2)	3.19(7)
C(7)	2008(4)	8526(3)	9821(2)	3.85(8)
C(8)	2137(4)	9540(3)	9440(2)	3.86(7)
C(9)	3234(4)	9699(2)	8717(2)	3.64(7)
C(10)	4201(4)	8831(2)	8392(2)	3.17(7)
C(11)	5553(4)	9066(2)	7670(2)	3.41(7)
C(12)	8200(4)	8512(3)	6982(2)	4.30(8)
C(13)	8425(5)	7240(3)	6418(2)	5.34(9)
C(14)	9731(4)	5758(3)	6890(3)	4.86(8)
C(15)	8758(4)	4559(3)	5925(2)	4.83(8)
C(16)	6224(5)	2574(3)	5257(2)	4.81(9)
C(17)	4848(5)	1621(3)	5593(3)	4.97(9)
C(18)	2131(5)	1285(3)	6334(2)	4.72(9)
C(19)	666(5)	1882(3)	6681(2)	4.61(9)
C(20)	1686(4)	3062(2)	8587(2)	3.56(7)
H(3N)	652(4)	781(2)	782(2)	5.0(7)[b]
H(4N)	185(4)	379(2)	752(2)	4.3(6)[b]

[a] Estimated standard deviation in the least significant digits are shown in parentheses.

[b] Isotropic thermal parameters.

Table II. Bond distances (Å) and bond angles (deg) for **1** · H_2O[a]

Atoms	Distance (Å)	Atoms	Distance (Å)
O(1)—C(11)	1.220(3)	C(3)—C(4)	1.379(4)
O(2)—C(13)	1.412(3)	C(4)—C(5)	1.393(3)
C(2)—C(14)	1.426(3)	C(5)—C(6)	1.496(3)
O(3)—C(15)	1.420(3)	C(6)—C(7)	1.387(3)
O(3)—C(16)	1.420(3)	C(7)—C(8)	1.378(4)
O(4)—C(17)	1.426(3)	C(8)—C(9)	1.364(4)
O(4)—C(18)	1.420(3)	C(9)—C(10)	1.385(3)
O(5)—C(20)	1.226(3)	C(10)—C(11)	1.507(3)
N(1)—C(1)	1.334(3)	C(12)—C(13)	1.492(4)
N(1)—C(5)	1.338(3)	C(14)—C(15)	1.503(4)
N(2)—C(6)	1.343(3)	C(16)—C(17)	1.487(4)
N(2)—C(10)	1.340(3)	C(18)—C(19)	1.497(4)
N(3)—C(11)	1.328(3)	O(1W)—O(2)	3.484(3)
N(3)—C(12)	1.448(3)	O(1W)—O(3)	3.399(3)
N(3)—H(3N)	0.78(3)	O(1W)—O(4)	3.098(3)
N(4)—C(19)	1.445(4)	O(1W)—N(1)	3.521(3)
N(4)—C(20)	1.328(3)	O(1W)—N(2)	3.522(3)
N(4)—H(4N)	0.84(3)	O(1W)—N(3)	3.530(4)
C(1)—C(2)	1.393(4)	O(1W)—N(4)	3.138(3)
C(1)—C(20)	1.503(4)	O(1W)—H(3N)	3.08(3)
C(2)—C(3)	1.383(4)	O(1W)—H(4N)	2.41(3)

Atoms	Angle (deg)	Atoms	Angle (deg)
C(13)—O(2)—C(14)	113.5(2)	C(5)—C(6)—C(7)	120.3(2)
C(15)—O(3)—C(16)	111.8(2)	C(6)—C(7)—C(8)	118.6(3)
C(17)—O(4)—C(18)	111.7(2)	C(7)—C(8)—C(9)	119.6(3)
C(1)—N(1)—C(5)	117.8(2)	C(8)—C(9)—C(10)	118.4(2)
C(6)—N(2)—C(10)	117.1(2)	N(2)—C(10)—C(9)	123.5(3)
C(11)—N(3)—C(12)	123.6(3)	N(2)—C(10)—C(11)	117.5(2)
C(11)—N(3)—H(3N)	118.0(2)	C(9)—C(10)—C(11)	118.9(2)
C(12)—N(3)—H(3N)	118.0(2)	O(1)—C(11)—N(3)	123.4(3)
C(19)—N(4)—C(20)	122.4(3)	O(1)—C(11)—C(10)	121.4(3)
C(19)—N(4)—H(4N)	121.0(2)	N(3)—C(11)—C(10)	115.2(2)
C(20)—N(4)—H(4N)	116.2(2)	N(3)—C(12)—C(13)	111.1(3)
N(1)—C(1)—C(2)	123.3(3)	O(2)—C(13)—C(12)	108.8(2)
N(1)—C(1)—C(20)	116.8(2)	O(2)—C(14)—C(15)	114.6(3)
C(2)—C(1)—C(20)	119.9(3)	O(3)—C(15)—C(14)	110.0(2)
C(1)—C(2)—C(3)	118.4(3)	O(3)—C(16)—C(17)	109.2(2)
C(2)—C(3)—C(4)	118.9(3)	O(4)—C(17)—C(16)	110.0(2)
C(3)—C(4)—C(5)	119.0(3)	O(4)—C(18)—C(19)	108.5(2)
N(1)—C(5)—C(4)	122.6(3)	N(4)—C(19)—C(18)	113.3(3)
N(1)—C(5)—C(6)	116.9(2)	O(5)—C(20)—N(4)	123.4(3)
C(4)—C(5)—C(6)	120.4(2)	O(5)—C(20)—C(1)	121.8(3)
N(2)—C(6)—C(5)	117.0(2)	N(4)—C(20)—C(1)	114.8(2)
N(2)—C(6)—C(7)	122.7(2)		

[a] Estimated standard deviations in the least significant digits are shown in parentheses.

Table III. Selected torsion angles (deg) for 1 · H_2O

Atoms	Angle	Atoms	Angle
N(1)—C(5)—C(6)—N(2)	-50.1	C(15)—O(3)—C(16)—C(17)	171.4
N(2)—C(10)—C(11)—N(3)	-7.5	O(3)—C(16)—C(17)—O(4)	68.0
C(10)—C(11)—N(3)—C(12)	-172.9	C(16)—C(17)—O(4)—C(18)	-174.8
C(11)—N(3)—C(12)—C(13)	-146.4	C(17)—O(4)—C(18)—C(19)	178.7
N(3)—C(12)—C(13)—O(2)	-54.2	O(4)—C(18)—C(19)—N(4)	-68.2
C(12)—C(13)—O(2)—C(14)	-151.9	C(18)—C(19)—N(4)—C(20)	-84.3
C(13)—O(2)—C(14)—C(15)	-68.9	C(19)—N(4)—C(20)—C(1)	-173.8
O(2)—C(14)—C(15)—O(3)	-71.1	N(4)—C(20)—C(1)—N(1)	1.3
C(14)—C(15)—O(3)—C(16)	177.5		

angles at N—C—C—N including the amide function are eclipsed (angles of -7.5 or 1.3°). The bipyridine moiety possesses the *syn* conformation with the N(1)—C(5)—C(6)—N(2) torsion angle being 50.1°. This is almost twice the value recently found for a comparable *n*-propanol complexed bipyridine macrocycle of the same ring size (25.6°) [15]. Other bipyridino-containing macrocycles have *anti* conformation at the very same unit [16]. Thus it is shown that the rotation around the central C—C

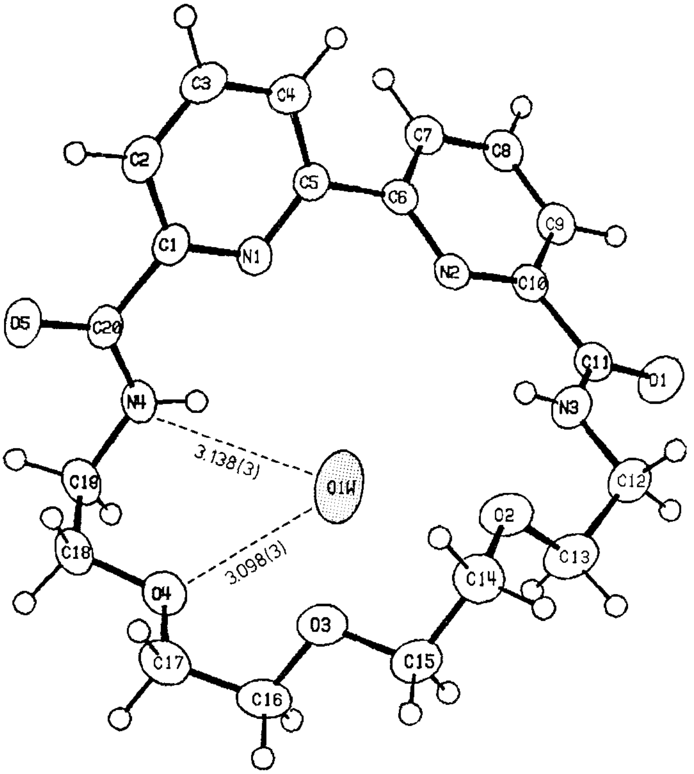

Fig. 1. Molecular structure of 1 · H_2O: top view giving indication of the numbering scheme for the atoms (water oxygen shaded; solid and dashed lines represent covalent and hydrogen bonds, respectively; non-bonding distances between O(1W) and endocyclic heteroatoms are specified in Table II).

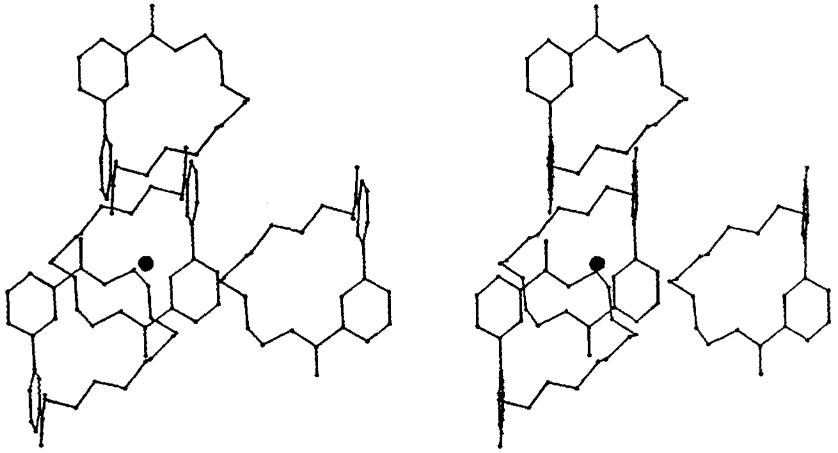

Fig. 2. Stereoview of the inclusion cavity encapsulating the water molecule. The host molecules are given as line drawings, the water molecule is represented by the O(1W) atom (cf. Figure 1, arbitrary radius).

bond of a bipyridine moiety, e.g., in crown compounds, is a relatively soft parameter and may be influenced by coordination or crystal packing forces.

Despite the nonsymmetric conformation of the host molecule all hetero-atoms, except for the carbonyl oxygens, point inside the ring and give rise to a hydrophilic core. Consequently, the amide hydrogens also point inside. Unlike other crowns with nonsymmetric conformation [15], the endocyclic heteroatoms are relatively distant (0.126–0.732 Å) from their mean plane. A more suitable plane related to heteroatoms is that including only N(3), O(2), O(3), O(4), N(4) (mean deviation 0.393 Å). Those sites are equivalent to the nearest neighbour heteroatoms of the water molecule.

The water molecule is 0.920 Å away from this plane in a perching position and adopts moderately weak H bonding interactions to O(4) and N(4) [3.098(3) Å and 3.138(3) Å, respectively, N(4)—H(4N)···O(1W) 146.2°]. All other heteroatoms around O(1W) are beyond bonding distance (Table II). Hence, the water molecule is located rather unsymmetrical with respect to the (intramolecular) opening and the surrounding set of heteroatoms of the ring (cf. refs. [5, 8, 17]).

This is possibly the result of a (short) intermolecular contact [3.360(5) Å] between the water oxygen and C(14) of a neighbouring host molecule (generated by translation). On the whole, the general packing in the crystal is relatively dense ($D_c = 1.350$ gcm^{-3}) which makes the water molecules encapsulated in nearly spherical cavities formed by four neighbouring host entities (Figure 2).

Compared with other complexes of crown compounds where water is in the role of a guest [1–3], the present crystal structure reveals several special features. (1) For the first time water is included by a crown amide. (2) The water molecule is close to the ring interior and is coordinated to the host. (3) A mixed set of ligand sites (NH, O) is used for hydrogen bonding with the included water. (4) Neither the pyridino nitrogens nor the carbonyl oxygens are involved in H bridges. (5) Although the host (considering its ring size and the number of donor/acceptor atoms) is likely to accommodate more than one guest, e.g., from both sides of the macroring (cf. refs. [1–3]), only a single water molecule per crown ligand is complexed. (6) A cavity relationship between four ligands and the water molecule in the crystal packing is shown to be a stabilizing factor of the molecular complex.

A challenge exists to develop new host-guest inclusions based on these results.

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