

We thank Dr J. L. Briansó (Universidad Autónoma de Barcelona) for the use of computer facilities at this University and Dr E. Giralt for providing the samples and for discussions. This work was sponsored by the University of Barcelona.

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Acta Cryst. (1981). **B37**, 2114–2117

18⟨O₅(2,6-Pyridino)1·2₄·1-coronand-6⟩₂,16-dione Dihydrate*

BY GEORGE R. NEWKOME,[†] FRANK R. FRONCZEK AND DALIP K. KOHLI

Department of Chemistry, Louisiana State University, Baton Rouge, Louisiana 70803, USA

(Received 23 January 1981; accepted 18 May 1981)

Abstract. C₁₅H₁₉NO₇·2H₂O, monoclinic, *P*2₁/*n*, *a* = 9.622 (3), *b* = 8.791 (6), *c* = 21.353 (3) Å, β = 96.40 (2)°, *Z* = 4, *d*_c = 1.339 Mg m⁻³, *R* = 0.055 for 994 observations measured by diffractometer. The macrocyclic polyetheral bis-lactone exists in a nearly flat conformation, in which six potential hydrogen-bond acceptor atoms (N and O) approximate a circle of radius 2.8 Å. A water molecule lies beneath this circle, 1.49 (1) Å from its center, and forms its best hydrogen bond *not* with the N atom, but with the polyetheral O atom most distant from the N atom. A second water molecule is hydrogen bonded to the first with an O···O distance of 3.01 (1) Å.

Introduction. Crown ethers and substituted analogs have been shown to play an active role in the catalysis of organic reactions and the dissolution of inorganic cations (Lehn, 1979; Izatt & Christensen, 1979; Bradshaw, Maas, Izatt & Christensen, 1979; Newkome, Sauer, Roper & Hager, 1977). Application of these macrocycles, *e.g.* (I), to catalyze the decom-

position of aryldiazonium salts (Bartsch & Juri, 1980, and references cited therein; Kuokkanen & Virtanen, 1979) prompted us to ascertain the molecular geometry of (I) prior to inclusion of the diazonium moiety. Force-field calculations (Gandour, 1980) on a simple model, dimethyl 2,6-pyridinedicarboxylate (II), support the favored orientation to be (IIa) by *ca* 13 kJ mol⁻¹. Thus, the question of whether (I) should possess a similar geometry (III) in the crystalline state was addressed. We herein report the crystal structure of the unexpected dihydrate of (I), which exhibits the conformation given in (IIb), and from the results suggest the possible necessity of inclusion of water (or solvent) in the cavity to ensure the anticipated circular orientation (Lehn, 1978) as a prerequisite to inclusion of a larger guest.

The bis-lactone (I), prepared by known procedures (Frensch & Vögtle, 1977), was shown by satisfactory elemental analysis to exist as a hydrate (m.p. 338–339 K), which can be liberated of the water molecule(s) by warming (333 K) *in vacuo* to give the free molecule (m.p. 356–357 K) as an anhydrous, ill-defined microcrystalline solid. In order to obtain a suitable single crystal, (I) was recrystallized from hexane to regenerate the unexpected dihydrate.

* IUPAC nomenclature: 3,6,9,12,15-pentaoxa-21-azabicyclo-[15.3.1]henicosa-1(21),17,19-triene-2,16-dione dihydrate.

[†] To whom correspondence should be addressed.

Intensity data were obtained from a colorless crystal of dimensions 0.20 × 0.36 × 0.36 mm mounted in random orientation on an Enraf–Nonius CAD-4 automatic diffractometer. One quadrant of data having $1^\circ \leq \theta \leq 21^\circ$ was measured using graphite-mono-chromatized Mo $K\alpha$ radiation ($\lambda = 0.71073 \text{ \AA}$). The ω - 2θ scans were made at rates varying from 0.31 to 5.0° min⁻¹ in order to measure all significant data with approximately equal precision. Reflections having $I_{\text{obs}} < \sigma(I_{\text{obs}})$ in a 5.0° min⁻¹ prescan were flagged as unobserved and not scanned slowly. No significant decrease in the intensities of standard reflections was noted, although the data crystal clouded and ceased to diffract X-rays several months after data collection. A total of 1973 independent data were measured in this manner, of which 994 had $F_{\text{obs}} > 3\sigma(F_{\text{obs}})$ and were used in further calculations. Data were corrected for background, Lorentz and polarization effects, but not for absorption [$\mu(\text{Mo } K\alpha) = 0.120 \text{ mm}^{-1}$].

The space group was determined from systematic absences $0k0$ with k odd and $h0l$ with $h + l$ odd. The structure was solved by routine application of multiple-solution direct methods employing *MULTAN* 78 (Main, Hall, Lessinger, Germain, Declercq & Woolfson, 1978), and refined by full-matrix least squares using *SHELX* 76 (Sheldrick, 1976). Refinement was based upon F with weights $w = \sigma^{-2}(F_{\text{obs}})$, treating non-H atoms anisotropically. H atoms were located from difference maps as peaks of density 0.21–0.51 e \AA^{-3} . H atoms of the macrocycle were allowed to ride on the C atoms to which they are bonded (C–H 1.08 \AA), with a common temperature factor. Water H atoms were in fixed positions and refined with a second common temperature factor. A final difference Fourier map yielded no residuals greater than 0.19 e \AA^{-3} .*

Discussion. Refined coordinates and equivalent isotropic temperature factors for non-H atoms are given in Table 1. Macrocycle (I) exists in an approximately planar conformation (Fig. 1) with its six potential donor atoms lying in a plane to within 0.26 \AA . The ethereal-coordinated water molecule lies below this plane, 1.49 (1) \AA from its center, to optimize the hydrogen bond with O(4) [O–O 2.92 (1) \AA] and to minimize heteroatom repulsion. Due to the electron-withdrawing properties of the carbonyl group(s), possible hydrogen bonding with O(2) and O(6) is less favored. Also, the pyridyl N atom in (I), generally considered a good donor atom (Bradshaw, Asay, Baxter, Fore, Jolley, Lamb, Maas, Thompson, Izatt &

Table 1. Positional and equivalent isotropic thermal parameters for ligand (I)·2H₂O

U_{eq} is defined according to Hamilton (1959).

	x	y	z	$U_{\text{eq}} (\text{\AA}^2)$
N(1)	0.0645 (10)	0.4083 (8)	0.6093 (3)	0.047 (6)
O(1)	0.3569 (7)	0.5803 (7)	0.5516 (3)	0.125 (7)
O(2)	0.3204 (6)	0.3464 (7)	0.5819 (3)	0.049 (5)
O(3)	0.4633 (6)	0.0722 (8)	0.6261 (3)	0.070 (5)
O(4)	0.2875 (7)	-0.1441 (7)	0.6816 (3)	0.077 (6)
O(5)	0.0342 (8)	-0.0545 (7)	0.7287 (3)	0.076 (6)
O(6)	-0.0876 (6)	0.2064 (7)	0.6654 (2)	0.058 (5)
O(7)	-0.2535 (6)	0.3810 (8)	0.6762 (3)	0.097 (6)
C(1)	-0.0667 (13)	0.4444 (12)	0.6163 (4)	0.051 (8)
C(2)	-0.1371 (10)	0.5750 (13)	0.5916 (5)	0.070 (8)
C(3)	-0.0607 (15)	0.6720 (12)	0.5582 (5)	0.086 (10)
C(4)	0.0740 (14)	0.6459 (13)	0.5513 (5)	0.075 (9)
C(5)	0.1317 (12)	0.5115 (13)	0.5791 (5)	0.050 (8)
C(6)	0.2774 (14)	0.4872 (11)	0.5691 (4)	0.070 (9)
C(7)	0.4667 (10)	0.3082 (11)	0.5746 (5)	0.087 (9)
C(8)	0.4831 (10)	0.1426 (11)	0.5686 (4)	0.087 (9)
C(9)	0.4710 (10)	-0.0897 (12)	0.6210 (5)	0.091 (10)
C(10)	0.4354 (12)	-0.1575 (11)	0.6794 (5)	0.098 (11)
C(11)	0.2431 (13)	-0.1951 (12)	0.7404 (5)	0.097 (10)
C(12)	0.0911 (12)	-0.2046 (12)	0.7343 (5)	0.099 (10)
C(13)	-0.1004 (11)	-0.0514 (11)	0.6982 (4)	0.072 (8)
C(14)	-0.1649 (9)	0.1030 (10)	0.7030 (4)	0.069 (8)
C(15)	-0.1477 (10)	0.3434 (12)	0.6550 (4)	0.061 (8)
O(W1)	0.1268 (5)	0.0541 (5)	0.5907 (2)	0.060 (4)
O(W2)	0.3268 (5)	0.4556 (6)	0.0330 (2)	0.073 (5)

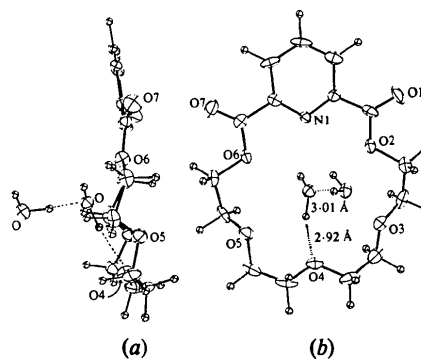


Fig. 1. (a) Side and (b) top perspective drawings of macrocycle (I)·2H₂O and associated water molecules. Hydrogen bonds are indicated by dotted lines. Thermal ellipsoids are drawn to enclose the 30% probability level.

Christensen, 1980; Bradshaw, Maas, Lamb, Izatt & Christensen, 1980; Bradshaw, Baxter, Scott, Lamb, Izatt & Christensen, 1979), is a minor contributor to the electron density within the cavity. It has been suggested (Bradshaw, Baxter, Scott, Lamb, Izatt & Christensen, 1979) that in ligand (I), the 'pyridine N atom is the best hydrogen-bond acceptor'. As herein demonstrated for (I)·2H₂O, the most favored hydrogen bond is with O(4). A second potential hydrogen bond with O(6) [O(W1)–O(6) 3.05 \AA ; O(4)–O(W1)–O(6) 104°] is considered less likely since no electron density indicative of an H atom was located at a reasonable position. All other

* Lists of structure factors, anisotropic thermal parameters and assigned H-atom coordinates have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 36185 (15 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

interactions between water and ring heteroatoms, including the pyridine N atom (distances > 3·20 Å), are deemed improbable as hydrogen-bond acceptors. The second water molecule is hydrogen bonded to the first [O...O 3·01 (1) Å]. The crystal structure of the analogous macrocycle, lacking the carbonyl groups, has been determined as a host-guest complex with the *tert*-butylammonium ion (Maverick, Grossenbacher & Trueblood, 1979). In that structure, lack of electron withdrawal by carbonyl groups allows hydrogen-bond acceptance by the pyridyl N atom, as well as by O atoms corresponding to our O(3) and O(5).

Bond distances and angles are given in Figs. 2 and 3. Averages for important bond types are 1·383 (16) Å for aromatic C—C, 1·324 (2) Å for C—N, 1·207 (1) Å for C=O, 1·471 (10) Å for aliphatic C—C, and 1·421 (9) Å for polyetheral C—O. Selected torsion angles are listed in Table 2. Of particular interest are the torsion angles involving linkage of the carboxylate functions to the aromatic ring. The first and last entries

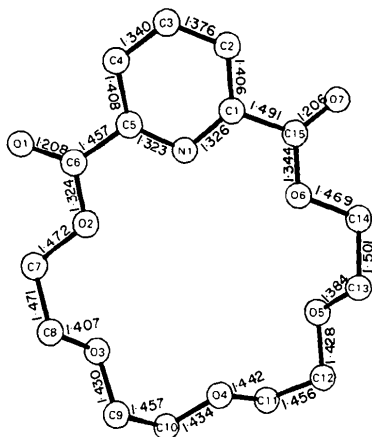


Fig. 2. Bond distances (Å) and numbering scheme. E.s.d.'s are 0·008–0·010 Å for C—O, 0·010 Å for C—N, and 0·009–0·012 Å for C—C.

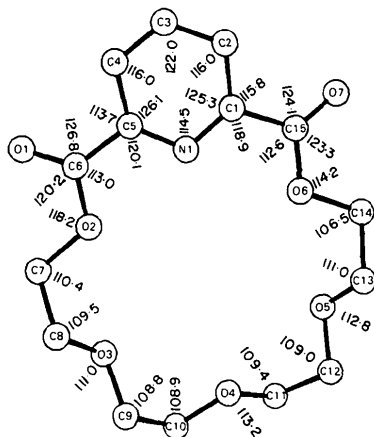


Fig. 3. Bond angles (°). Standard deviations are 0·7–1·3°.

Table 2. Selected torsion angles (°)

E.s.d.'s are 1·0–1·4°.

N(1)—C(5)—C(6)—O(2)	12·0	O(4)—C(11)—C(12)—O(5)	−68·9
C(5)—C(6)—O(2)—C(7)	−179·0	C(11)—C(12)—O(5)—C(13)	155·5
C(6)—O(2)—C(7)—C(8)	−160·0	C(12)—O(5)—C(13)—C(14)	170·3
O(2)—C(7)—C(8)—O(3)	−67·9	O(5)—C(13)—C(14)—O(6)	67·9
C(7)—C(8)—O(3)—C(9)	176·9	C(13)—C(14)—O(6)—C(15)	168·4
C(8)—O(3)—C(9)—C(10)	−174·1	C(14)—O(6)—C(15)—C(1)	−179·6
O(3)—C(9)—C(10)—O(4)	73·9	C(15)—C(1)—N(1)—C(5)	−174·2
C(9)—C(10)—O(4)—C(11)	−174·5	C(1)—N(1)—C(5)—C(6)	176·0
C(10)—O(4)—C(11)—C(12)	−169·4	O(6)—C(15)—C(1)—N(1)	−15·7

in Table 2 indicate that the carboxylates are twisted out of the plane of the pyridine ring by an average of 13·8° towards the same side of the ring. Analogous torsion angles in dipicolinic acid monohydrate (Takusagawa, Hirotsu & Shimada, 1973) are −4·9° and −177·0°, reflecting its conformation to be that given in (IIb).

Of particular interest for the purposes of comparison is the recently reported structure of (I).KSCN (Larson & Dalley, 1980). The macrocycle in that determination has exact *m* symmetry, and exists in a conformation almost identical to that of the dihydrate. The r.m.s. difference between the 18 endocyclic torsion angles of the KSCN and H₂O complexes is 10·7°, with the largest individual difference only 32°. Dimensions of the molecule in the two determinations agree within experimental uncertainties with a few exceptions. The chemically equivalent bonds C(9)—C(10) and C(11)—C(12) in the present structure average 1·457 (12) Å in length, *vs* 1·504 (4) Å in the KSCN complex. This difference is 3·7 times its standard deviation. This apparent anomaly is probably the effect of thermal motion, as this portion of the molecule exhibits the largest thermal parameters of the structure. Atoms C(9) to C(12) have *U*_{eq} values approximately double those of corresponding atoms in the KSCN complex. Although water of hydration is quite common in structures of macrocyclic complexes, only a few structures involving free cyclic ligands containing water(s) of inclusion have been determined (Zahn & Spoor, 1959; Borgen & Dale, 1970; de Jong, Reinhoudt & Smit, 1976; Cradwick & Poonia, 1977; Gokel & Garcia, 1977; Goldberg, 1978). Although 'anhydrous' solvents were used in the recrystallization, (I) crystallizes as a dihydrate in the presence of only trace amounts of moisture. The recent works of Vögtle (Vögtle, Muller & Weber, 1980; Vögtle & Muller, 1980) and Knochel (von Deuten, Knochel, Kopf, Oehler & Rudolph, 1979) indicate that solvent and reagent inclusion by similar macrocycles may play an important role in the stabilization and manipulation of toxic and noxious reagents.

Thus we herein suggest that extreme care must be exercised in the preparation and purification of these macrocyclic, hydrophilic reagents, if the subsequent data are sensitive to the presence of water.

We thank the National Institutes of Health for partial support of this research and Professor F. Vögtle (Bonn) and R. D. Gandour (Louisiana State Univ.) for helpful suggestions.

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Acta Cryst. (1981). **B37**, 2117–2120

Structure of the Complex 3-Indoleacetic Acid: Tyramine (1:1)*

BY TOSHIMASA ISHIDA AND MASATOSHI INOUE

Osaka College of Pharmacy, 2-10-65 Kawai, Matsubara-City, Osaka 580, Japan

(Received 9 March 1981; accepted 18 May 1981)

Abstract. C₁₀H₈NO₂⁻·C₈H₁₂NO⁺, monoclinic, *P*2₁/*c*, *a* = 9.069 (1), *b* = 11.745 (2), *c* = 16.136 (2) Å, β = 100.33 (1)°, *U* = 1690.8 (4) Å³, *Z* = 4, *D_m* = 1.225 (1), *D_x* = 1.227 Mg m⁻³, μ(Cu Kα) = 0.7988 mm⁻¹. The structure was solved by a direct method and refined to *R* = 0.054 for 2889 independent reflections. No prominent interaction between the indole and phenol rings is observed in the crystal. Both molecules are held together by the hydrogen bonds between the

carboxyl group of 3-indoleacetic acid and the amino group of tyramine, forming a tetrameric complex unit.

Introduction. Electron transfer within proteins is of general importance in biological oxidation–reduction systems. It has been thought possible that aromatic amino acids such as tryptophan and tyrosine could be implicated in such a process (Prütz, Butler, Land & Swallow, 1980; Winfield, 1965). On the other hand, it has been shown that a tyrosine residue is involved in the specific indole binding site of human serum albumin (Fehske, Müller & Wollert, 1979). In order to elucidate

* Structural Studies of the Interaction between Indole Derivatives and Biologically Important Aromatic Compounds. VIII.