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SYNTHESIS, CONFORMATIONAL NOVELTY, AND X-RAY CRYSTAL STRUCTURE OF THE SPHERICAL <N[O(2,6-PYRIDINO)O-2·1_2·2]$_3$CRYPTAND-11>.

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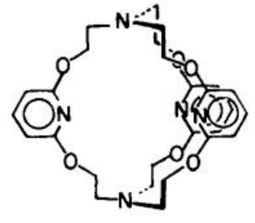
Summary. The synthesis and x-ray crystal structure of a spherical cryptand 2, in which the bridgehead N-electrons are in the in-in configuration and one of the pyridine rings is located inside the cavity of the cryptand, are described.

Previously, we reported[1] the synthesis of the smallest known cryptand possessing three subheterocyclic rings 1. The X-ray analysis showed that in cryptand 1 the bridgehead nitrogen atom possesses a planar configuration with crystallographically equivalent 120° bond angles. Because of our interest in studying the effects of structural constraints on the complexing ability of macrocyclic ligands[2], it was deemed of interest to attempt the synthesis of 2, a structural analog to 1, in which a methylene group was inserted between each pyridine ring and oxygen atom. It was expected that with the increased flexibility and the removal of the imposed steric constraints caused by the imidate[3] moieties (in 1), the bridgehead N-lone pairs of electrons could assume a nonplanar (sp^3) configuration and thus be available for internal complexation.

We herein report the synthesis and x-ray crystal structure of 2, in which the N-lone pairs are in the in-in configuration and one of the pyridine rings is located inside the cavity of the cryptand.



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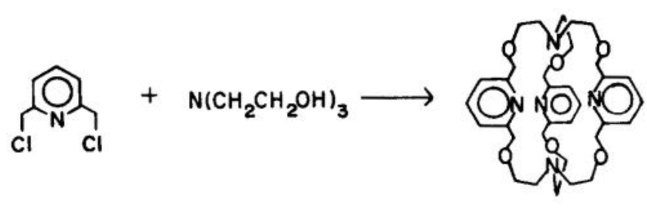

2

To a mixture of triethanolamine (6.6 mmol) and oil-free sodium hydride (20 mmol) in *N*,*N*-dimethylformamide, 2,6-bis(chloromethyl)pyridine[4] (10 mmol) in *N*,*N*-dimethylformamide was added. The mixture was stirred at 25°C for 72 hours, concentrated *in vacuo*, and the resulting oil was chromatographed (ThLC) on alumina with cyclohexane/ethyl acetate (1:1) to afford **2** (2%), as colorless crystals[5]: mp 118-119°C; ^{1}H NMR (200 MHz, CDCl_3) δ 2.82 (t, N-CH_3, J=5Hz, 12H), 3.56(t, O-CH_2, J=5Hz, 12H), 4.52 (s, Pyr-CH_2, 12H), 6.90 (t, 4-Pyr-H, J=8Hz, 3H), 7.30 (d, 3,5-Pyr-H, J=8Hz, 6H); IR(KBr) 1600, 1460, 1355, 1120, 1050, 970 cm^{-1}.

Crystal Data[6]: $\text{C}_{33}\text{H}_{45}\text{N}_5\text{O}_6$, triclinic space group $P\bar{1}$, *a*=8.762(1), *b*=9.198(1), *c*=23.122(3)Å, α=75.70(1), β=76.17(1), γ=67.27(1), Z=2, d=1.228 gcm^{-3}, R=0.045 for 2154 observed data having $2° \leqslant \theta \leqslant 25°$, λ=0.71073Å for MoK_α radiation. Intensity data were collected by the θ-2θ scan method on an Enraf-Nonius CAD4 automatic diffractometer. Scan rates varied from 0.26 to 5.0 deg. min.$^{-1}$ in order to measure all significant data with approximately equal precision. Corrections for background, Lorentz, and polarization effects were made; no absorption correction was necessary. The structure was solved by direct methods (MULTAN 78)[7] and refined by least squares (SHELX)[8] techniques, treating nonhydrogen atoms anisotropically and fixing hydrogen atoms in calculated positions. Atomic positions and thermal parameters are given in the supplementary material.

Figure 1 illustrates the *in*-*in* configuration of cryptand **2**; in contrast with the planar nitrogen configuration previously reported for **1**. The surprising structural aspect of **2** is the relative orientations of the pyridine rings. While the plane normals of two of the pyridine rings, point toward the center of the molecule, *the third pyridine ring is located within the cavity*! The center of the molecule is occupied by a pyridine 4-hydrogen atom, which lies within 1Å of the midpoint between the two bridgehead nitrogen atoms. Whereas, in cryptand **1**, linkage to the aromatic ring is *cis* to the nitrogen atom with the N-C-O-C torsion angle near zero, such a linkage in cryptand **2**, described by torsion angles equivalent to N(4)-C(19)-C(20)-O(4), is in all cases within 30° of the *trans* configuration. The low symmetry of **2** and the presence of different conformations for each of its three bridging chains attests to its greater flexibility versus **1**.

Distances and angles compare quite well with corresponding values found for cryptand **1**, except for the bridgehead C-N-C angle, which has a normal value (114.0°). No unusual bond distances or angles are present, and no unusually short intramolecular contacts exist.

In accordance with the X-ray crystal structure, variable temperature NMR studies of **2** suggest that, at least in solution (CDCl_3 or C_6D_6-CD_2Cl_2), the three pyridine rings are equivalent and freely rotating and that, on the average, one of the pyridine rings *is included in the cavity*.

A rapidly rotating structure of this type with average C_3 symmetry is indicated by low-temperature NMR studies. Although, coalesence of the pyridine H_4 occurs at -78°C, $\Delta G^{\ddagger}$ cannot be calculated because the sample freezes before the peaks reappear.

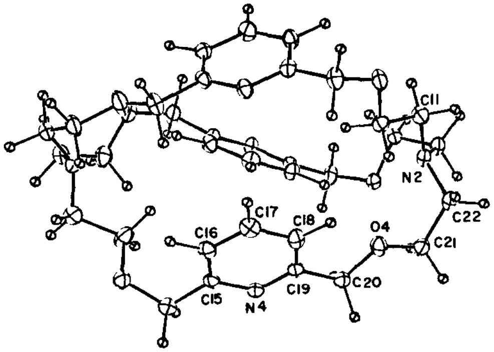

Figure 1. Distances and angles averaged over chemically equivalent bonds are: N4-C19 1.344, C18-C19 1.379, C18-C17 1.385, C19-C20 1.517, O4-C21 1.421, C21-C22 1.511, C22-N2 1.459 Å; C15-N4-C19 116.6°, C16-C17-C18 119.4°, C17-C18-C19 118.2°, C18-C19-N4 123.9°, N4-C19-C20 114.6°, C18-C19-C20 121.8°, C19-C20-O4 111.1°, C20-O4-C21 112.8°, O4-C21-C22 107.3°, C21-C22-N4 111.6°, C22-N2-C11 114.0°. Standard deviations in individual values are 0.004-0.006Å and 0.4-0.6 degrees.

As determined from related studies[9], the unfolding of 2 on displacement of the inner pyridine moiety by a solvent molecule precludes metal ion inclusion. Complexes of 2 with $CoCl_2$ and $CuCl_2$ have been prepared and elemental analysis and limited spectral data indicate that in both cases there are two metal atoms associated with each cryptand molecule. Studies are currently in progress to ascertain the role of solvent prior to metal ion inclusion[10] and the location of the metal ion(s) in the resultant cryptates.

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