# *Pseudo*-crown Ether-like Structure by Hydrogen-bonded Dimerization: A Water Complex With Bis(2'-hydroxyethyl) 2,6-Pyridinedicarboxylate in Solid, Solution, and Gas Phases

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**Dedicated to Professor Jerald S. Bradshaw**

Bis(2'-hydroxyethyl) 2,6-pyridinedicarboxylate (**1**) was prepared and the structure was characterized in solid (fourier transform-ir and X-ray analyses), in liquid ($^1$H and $^{13}$C nmr titrations), and in the gas-phase (fast atom bombardment (fab) and electron spray ionization (esi) ms). Two bis(2'-hydroxyethyl) 2,6-pyridinedicarboxylate molecules each with an included water molecule are bound together through hydrogen bonding to give a pseudo-macrocycle in the solid state and in chloroform solution. The fab and esi mass spectra also suggested that ligand **1** forms a dimer in the gas-phase.

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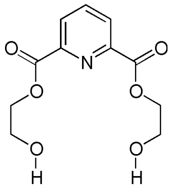
Many podands have been prepared and characterized as open-chain analogues of crown ether compounds [1]. Because the selectivities and complexation abilities of the podands are lower than comparable crown ether compounds, new kinds of the podands having functional groups at both ends have been prepared and their complexing abilities have been studied [2]. They form *pseudo*-cyclic structures by complexation with metal ions such as copper. Hydrogen bonding is another way to assemble and/or organize *pseudo*-cyclic ligating agents [3]. Although many examples of supramolecular structures organized by hydrogen bonding have been reported [1c], there is no report on the formation of *pseudo*-crown ether-like structures by the hydrogen bonded-dimerization of podands. Herein we report a podand that forms a *pseudo*-crown structure by hydrogen bonding.

New pyridine-containing podand **1** was prepared by treatment of 2,6-pyridinedicarboxylyl chloride with ethylene glycol in 78% yield. When ligand **1** was recrystallized from chloroform, a white amorphous solid of mp 116.0-118.0° was obtained. The structure of ligand **1** was confirmed by $^1$H nmr, ms, and elemental analysis. On the other hand, white plates of mp 77.0-79.0° were obtained when ligand **1** was recrystallized from water. As shown by the elemental analysis, the crystal contained one mole of water (**1**-$H_2O$).

To investigate the structures of ligands **1** and **1**-$H_2O$ in the solid state, solid-state fourie transform-ir (ftir) spectra were measured. Figure 1 shows the O-H stretching vibrations in the ir spectrum of **1** and **1**-$H_2O$. The O-H vibration of ligand **1** appears at 3363 cm$^{-1}$ as a broad absorption (dotted line). On the other hand, the O-H vibrations appear at 3419, 3304, 3215, and 3095 cm$^{-1}$ in the **1**-$H_2O$ (solid line). Usually, hydrogen-bonded O-H vibrations shift to lower frequency than that of free O-H vibrations [4]. Also, Dkhissi *et al.* reported [5] that hydrogen-bonded O-H stretching vibrations are observed at higher frequency than that of free O-H vibrations in pyridine-$H_2O$ complexes. Therefore, the vibration at 3419 cm$^{-1}$ is probably the N•••H-O vibration of an $H_2O$ that is hydrogen bonded with the N atom of pyridine unit. The other vibrations are probably the O-H vibrations of an end glycol O-H and $H_2O$ that form an O(ligand)•••H-O(water) or OH(ligand)•••O-H(water) hydrogen bond. In addition, there are some differences in the C-O absorption bands between ligand **1** and **1**-$H_2O$. The C=O stretching band at 1731 cm$^{-1}$ and the C-O stretching bands at 1250, 1176, and 1149 cm$^{-1}$ in ligand **1** shift to 1720, 1246, 1156, and 1143 cm$^{-1}$, respectively, in

Scheme



**1**

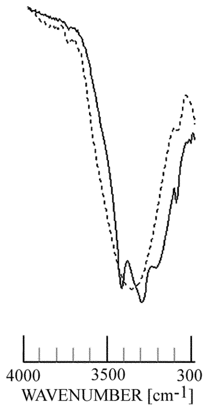


Figure 1. Ft-ir spectra of ligand **1** (dotted line) and **1**-$H_2O$ complex (solid line) for the O-H vibrations.

**1**-$H_2O$. These ir spectral data suggest that ligand **1** forms a complex with water by hydrogen bonding.

The structure of the **1**-$H_2O$ complex has been determined by X-ray analysis. Figure 2 shows the ORTEP [6] diagram of **1**-$H_2O$ complex. A water molecule (H17-O7-H18 or H17'-O7'-H18') is incorporated into a *pseudo*-cavity by hydrogen bonding of **1** wherein H17 bonds to N1, H1 to O7 and H18 to O6 (and a similar arrangement for H17' *etc.*). The N1-O7 (N1'-O7'), O5-O7 (O5'-O7'), O2-O7 (O2'-O7'), O6-O7 (O6'-O7'), and O1-O7 (O1'-O7') distances are 3.07, 2.92, 2.92, 2.78, and 2.68 Å, respectively. The ORTEP [6] diagram also suggests that ligand **1** forms a dimer using two hydrogen between H16 (H16') and O1' (O1) to give a 28-memberd *pseudo*-macrocyclic structure. The O6-O1' (O6'-O1) distance is 2.75 Å. These hydrogen bond lengths are comparable with those of water-crown ether complexes [7].

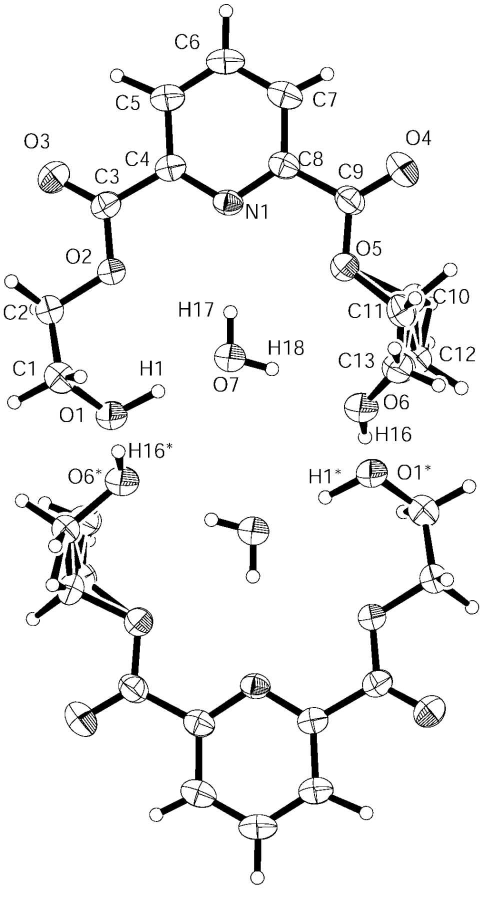


Figure 2. The ORTEP diagram of the **1**-$H_2O$ complex.

The structure of the water complex with **1** in solution was examined using $^1H$ and $^{13}C$ nmr titration experiments in deuteriochloroform (Table 1). Titration experiments were carried out by addition of 0.5, 1.0, 1.5 and 2.0 equiv. of water to ligand **1**, which is the water-free ligand. There are significant differences in the nmr signals of the aromatic protons between **1** and the water-included **1.** The signals for positions 3 and 4 protons in the pyridine ring shifted to lower field by 0.087 and 0.076 ppm, respectively, when water was added. These $^1H$ nmr chemical shift changes suggest that the conformation of the C=O carbonyl groups is fixed by complexation with the water molecule which would place these aromatic protons in the deshielding zone of the C=O groups.

Table 1

$^1H$ (250 MHz) and $^{13}C$ nmr (62.9 MHz) Spectral Data of Ligand **1** and Water-included **1** in Deuteriochloroform (313 K).

| | Ligand **1** | Water-included **1** [a] | *Δ* ppm [b] |
|---|---|---|---|
| $^1H$ nmr | | | |
| $H_3$ (pyridine) | 8.258 | 8.345 | +0.087 |
| $H_4$ (pyridine) | 7.961 | 8.037 | +0.076 |
| $H_{1'}$ (COOC$H_2$CH$_2$O) | 4.514 | 4.491 | -0.023 |
| $H_{2'}$ (COOCH$_2$C$H_2$O) | 3.991 | 3.977 | -0.014 |
| $^{13}C$ nmr | | | |
| $C_2$ (pyridine) | 148.33 | 148.19 | -0.14 |
| $C_3$ (pyridine) | 128.46 | 128.78 | +0.32 |
| $C_4$ (pyridine) | 138.69 | 138.92 | +0.23 |
| C=O | 164.65 | 164.58 | -0.07 |
| $C_{1'}$ (COO$C$H$_2$CH$_2$O) | 68.35 | 68.46 | -0.11 |
| $C_{2'}$ (COOCH$_2$$C$H$_2$O) | 60.66 | 60.44 | -0.22 |

[a] Conditions: [ligand **1**] = [water] = 0.01 mmole in deuteriochloroform. [b] Positive numbers show down-field shifts.

In the $^{13}C$ nmr spectra, remarkable chemical shift changes were observed in both the pyridine carbons ($C_3$: +0.32 ppm; $C_4$: +0.23 ppm) and the methylene carbons ($C_{1'}$: -0.11 ppm; $C_{2'}$: -0.22 ppm). The chemical shift changes in the $^{13}C$ nmr also suggested that the pyridine nitrogen and the oxygen atoms of the ester and end OH groups form hydrogen bonds with the water molecules in deuteriochloroform solution. Figures 3a and 3b show the selected titration curves of the water-induced $^1H$ and $^{13}C$ nmr spectra. All of these titration curves have an inflection point at [ligand **1**]/[water] = 1.0. Thus, the nmr titra-

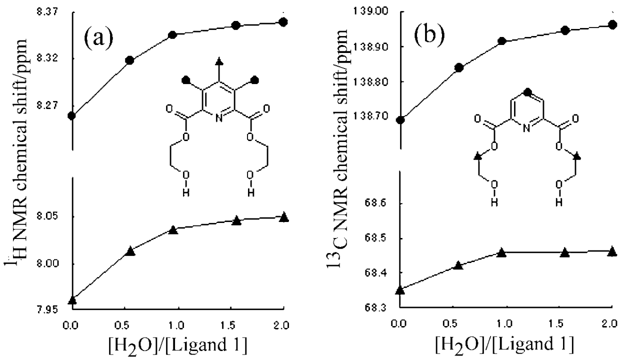


Figure 3. The water induced $^1H$ nmr (a) and $^{13}C$ nmr spectral changes (b) of ligand **1**.

tion experiments strongly suggest that ligand **1** forms a 1:1 complex with water in deuteriochloroform solution.

To see if ligand **1** forms a water complex and/or a *pseudo*-macrocyclic structure in the gas phase, the fast atom bombardment (fab) ionization mass was measured using *m*-nitrobenzylalcohol as a matrix (Figure 4). Ion peaks for $[M+H]^+$, $[M+H_2O+H]^+$, $[2M+H]^+$ were observed at 256 (100 %), 274 (10.7 %), and 511 (21.6 %), respectively. Also, ion peaks for $[M+Na]^+$ and $[2M+Na]^+$ were observed at 278 (56.1 %) and 533 (9.0 %), respectively.

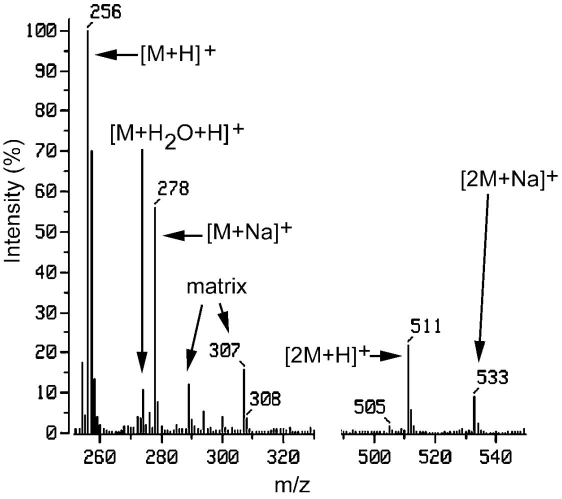


Figure 4. The fab mass spectra of the **1**-$H_2O$ complex.

The electron spray ionization (esi) mass is a recent technique to investigate structures of unstable complexes. Figure 5 shows observed ion peaks (a) and theoretical ion distributions (b) for dimerized ions of ligand **1** (water solution). Ion peaks for $[2M+H_2O]^+$ and $[2M+Na]^+$ were observed at 527.4 (49.9 %) and 532.3 (100 %), respectively in the esi mass spectrum. In addition, the observed ion peaks agree with the theoretical ion distributions. The fab and esi mass measurements suggest that ligand **1** does form the 1:1 complex with water and a dimer in the gas phase.

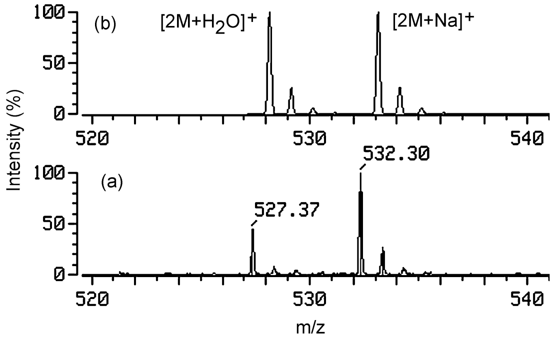


Figure 5. The esi mass spectra of ligand **1** (water solution) (a) and theoretical ion distributions (b).

Table 2

Crystal and Selected Experimental Data for **1**-$H_2O$ [a]

| | |
|---|---|
| Formula | $C_{11}H_{15}NO_7$ |
| *M* | 273.24 |
| Crystal system | monoclinic |
| Space group | $P2_1/c$ |
| *a*/Å | 9.410(3) |
| *b*/Å | 13.969(4) |
| *c*/Å | 9.785(2) |
| β/° | 90.48(2) |
| U/Å$^3$ | 1286.2(5) |
| *Z* | 4 |
| Dc/g cm$^{-3}$ | 1.411 |
| *F*(000) | 576.00 |
| μ(Mo-Kα)/cm$^{-1}$ | 1.19 |
| Crystal dimensions/mm | 1.00x0.50x0.50 |
| No. of reflections for unit cell deterimnation (2θ range)/° | 25 (28.0-29.9) |
| Scan width/° | 0.79+0.30tanθ |
| Limiting indices | $0 \leq h \leq 12$<br>$0 \leq k \leq 18$<br>$-12 \leq l \leq 12$ |
| No. reflections | |
| measured | 3267 |
| unique ($R_{int}$=) | 2959 (0.028) |
| used[all data], $N_o$ | 2950 |
| R | 0.082 |
| R*w* | 0.193 |
| R1 [I> 2.0σ(*I*)] | 0.059 |
| Goodness of fit | 1.47 |
| No. parameters, $N_p$ | 190 |
| Maximum shift/error in final cycle | 0.001 |
| Maximum, minimum peaks in final difference map/e Å$^{-3}$ | 0.44, -0.29 |
| $2\theta_{max}$ | 55° |

[a]Details in common: ω-2θ scan; $Rw=[\Sigma w(|Fo|-|Fc|)^2/\Sigma wFo^2]^{1/2}$, $R1 = \Sigma||Fo|-|Fc||/\Sigma|Fo|$, goodness of fit $[\Sigma w(|Fo|-|Fc|)^2/(N_o-N_p)]^{1/2}$.

In conclusion, we have demonstrated that ligand **1** forms a *pseudo*-crown ether-like structure in the solid state and in solution. Also, ligand **1** forms a 1:1 complex with water and a dimer in gas phase. Complexation studies of metal cations and organic guests by the new ligand are in progress.

## EXPERIMENTAL

$^1H$ and $^{13}C$ nmr spectra were measured in deuteriochloroform on a Brucker AC-250 (250 MHz) spectrometer. The ei, fab and esi mass measurements were perfomed using the Hitachi M80 (ei) and JEOL 600H (fab and esi) spectrometer. The ir spectra (potassium bromide disc) were recorded on a JASCO FT/IR-230 spectrometer.

### Preparation of Bis(2'-hydroxyethyl) 2,6-Pyridinedicarboxylate (1).

A mixture of thionyl chloride (5 ml) and 2,6-pyridinedicarboxylic acid (1.7 g, 10 mmole) was refluxed for 3 days under a nitrogen atmosphere. After the excess of thionyl chloride was removed, ethylene glycol (5 ml, 89 mmoles) was added and the mixture was heated for 2 days at 60°. The excess ethylene glycol

Table 3

Positional Parameters, B(eq) and Occupancy for **1**-$H_2O$.

| atom | x | y | z | B(eq) | occ. |
|---|---|---|---|---|---|
| O(1) | 0.5647(2) | 0.3126(2) | 0.5778(2) | 7.91(6) | 1.0000 |
| O(2) | 0.8648(1) | 0.2988(1) | 0.5377(2) | 5.16(4) | 1.0000 |
| O(3) | 1.0693(2) | 0.2528(1) | 0.6339(2) | 6.57(5) | 1.0000 |
| O(4) | 1.0524(2) | 0.5904(2) | 0.1047(2) | 7.64(6) | 1.0000 |
| O(5) | 0.8532(2) | 0.5291(1) | 0.1912(2) | 6.13(5) | 1.0000 |
| O(6) | 0.5595(2) | 0.5712(2) | 0.2301(2) | 8.00(6) | 1.0000 |
| O(7) | 0.6735(2) | 0.4181(1) | 0.3748(2) | 5.94(4) | 1.0000 |
| N(1) | 0.9992(2) | 0.4180(1) | 0.3657(2) | 3.97(4) | 1.0000 |
| C(1) | 0.6439(3) | 0.2269(2) | 0.5845(3) | 6.86(7) | 1.0000 |
| C(2) | 0.7898(3) | 0.2385(2) | 0.6344(3) | 6.00(6) | 1.0000 |
| C(3) | 1.0048(2) | 0.2992(2) | 0.5503(2) | 4.53(5) | 1.0000 |
| C(4) | 1.0773(2) | 0.3627(2) | 0.4501(2) | 4.14(4) | 1.0000 |
| C(5) | 1.2246(2) | 0.3615(2) | 0.4514(3) | 5.21(6) | 1.0000 |
| C(6) | 1.2957(2) | 0.4187(2) | 0.3615(3) | 6.05(7) | 1.0000 |
| C(7) | 1.2195(3) | 0.4761(2) | 0.2747(3) | 5.57(6) | 1.0000 |
| C(8) | 1.0722(2) | 0.4738(2) | 0.2795(2) | 4.37(5) | 1.0000 |
| C(9) | 0.9925(2) | 0.5371(2) | 0.1829(2) | 4.98(5) | 1.0000 |
| C(10) | 0.780(1) | 0.6068(8) | 0.115(1) | 6.7(3) | 0.5000 |
| C(11) | 0.754(1) | 0.5721(8) | 0.088(1) | 6.2(3) | 0.5000 |
| C(12) | 0.6571(5) | 0.6371(4) | 0.1615(5) | 5.0(1) | 0.5000 |
| C(13) | 0.6345(7) | 0.5719(6) | 0.1019(7) | 7.4(2) | 0.5000 |
| H(1) | 0.6103 | 0.3535 | 0.4969 | 8.9 | 1.0000 |
| H(2) | 0.5971 | 0.1855 | 0.6614 | 8.9 | 1.0000 |
| H(3) | 0.6384 | 0.2051 | 0.4748 | 8.9 | 1.0000 |
| H(4) | 0.7989 | 0.2695 | 0.7372 | 8.9 | 1.0000 |
| H(5) | 0.8499 | 0.1750 | 0.6393 | 8.9 | 1.0000 |
| H(6) | 1.2762 | 0.3137 | 0.5271 | 8.9 | 1.0000 |
| H(7) | 1.4017 | 0.4219 | 0.3608 | 8.9 | 1.0000 |
| H(8) | 1.2605 | 0.5212 | 0.2164 | 8.9 | 1.0000 |
| H(9) | 0.7753 | 0.6720 | 0.1782 | 8.8 | 0.5000 |
| H(10) | 0.8350 | 0.6168 | 0.0041 | 8.8 | 1.0000 |
| H(11) | 0.7742 | 0.5519 | 0.0023 | 8.8 | 0.5000 |
| H(12) | 0.6973 | 0.6956 | 0.2357 | 8.8 | 0.5000 |
| H(13) | 0.5927 | 0.6782 | 0.0960 | 8.8 | 0.5000 |
| H(14) | 0.6686 | 0.5174 | 0.0099 | 8.8 | 0.5000 |
| H(15) | 0.5936 | 0.6043 | 0.0318 | 8.8 | 0.5000 |
| H(16) | 0.5006 | 0.5985 | 0.2724 | 8.9 | 1.0000 |
| H(17) | 0.7687 | 0.4201 | 0.3728 | 8.9 | 1.0000 |
| H(18) | 0.6470 | 0.4679 | 0.3300 | 8.9 | 1.0000 |

was removed under reduced pressure (22 Torr.), and the residual oil was purified by column chromatography (silica-gel, chloroform:ethanol = 10:1 as an eluent). Ligand **1** (2.0 g, 78%) was isolated as a white amorphous solid (recrystallized from chloroform), mp 116-118°; $^1$H nmr: $\delta$ 8.36 (d, *J* = 7.8 Hz, 2H), 8,05 (t, *J* = 7.8 Hz, 1H), 4.51 (t, *J* = 4.4 Hz, 4H), 3.99 (t, *J* = 4.4 Hz, 4H), 3.71 (s, 2H); ms: ei (m/z, 20 eV) 256 ($M^+$+1, 0.3 %); $^{13}$C nmr: $\delta$ 164.6, 148.3, 138.7, 128.5, 68.4, and 60.7.

*Anal*. Calcd. for $C_{11}H_{13}NO_6$: C, 51.77; H, 5.13; N, 5.49. Found: C, 51.66; H, 5.13; N, 5.43.

When ligand **1** was recrystallized from water, **1**-$H_2O$ was obtained. *Anal*. Calcd. for $C_{11}H_{15}NO_7 \bullet H_2O$: C, 48.35; H, 5.53; N, 5.13. Found: C, 48.41; H, 5.54; N, 5.05.

## Crystallography.

The crystallographic and experimental data are listed in Tables 2. Each of the single crystals was mounted in a glass capillary. All measurements were made at 298 K on a Rigaku AFC5S four-circle diffract meter with graphite-monochromated Mo K$\alpha$ radiation (0.71069 Å) and a 12kW rotating-anode generator. Cell contacts and an orientation matrix for data collection were obtained from a least-squares refinement. The data were collected using the $\omega$-2$\theta$ scan technique to an above maximum 2$\theta$ value of 55.0°. All intensities were corrected for Lorentz and polarization effects. The structure was solved by direct methods (SIR 92) [8]. The non-hydrogen atoms were refined anisotropically. The coordinates of all hydrogen atoms except the hydrogen atoms of the phenolic OH group were calculated at ideal positions and were refined (Table 3). Neutral atom scattering factors were taken from Cromer and Weber [9]. Anomalous dispersion effects were included in Fc [10]; the values for $\Delta f'$ and $\Delta f''$ were those of Creagh and McAuley [11]. The values for the mass attenuation coefficients are those of Creagh and Hubbell [12]. All calculations were made using the Texsan$^{TM}$ crystallographic software package of Molecular Structure Coropration [13].

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