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Self-assembled coordination cage derived from small-sized pyridinophane

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Abstract—The dithia[3.3]pyridinophane consisting of two pyridine rings has been found out to assume the *syn*-structure by the X-ray crystallography, meaning the two nitrogen atoms point in the same direction. From this cyclophane and cis-protected palladium(II), the self-assembled coordination molecular cage has been constructed.

The self-assembly between specific metal centers and selected pyridine-based ligands could give rise to well-defined discrete supramolecular architectures such as macrocycles, cages, tubes, and capsules.[1] On the other hand, cyclophanes known as bridged aromatic compounds have been intensively studied from various points of view for the last few decades.[2] Among them large-sized cyclophanes capable of forming an inner cavity have been playing a central role as synthetic receptors in molecular recognition.[3] On account of this background, large-sized cyclophanes represented by calixarenes[4] or resorcinarenes[5] have been employed as a component to create cavitand-based nanoscale cage via metal coordination. On the contrary, small-sized cyclophanes can be characterized by their aromatic components fixed in a forced proximity and their particular orientation. Considering their unique three-dimensional structure and conformational mobility, the small-sized cyclophanes possibly provide the fascinating supramolecular self-assembly upon coordination. However, to our best knowledge, there have been no reports on coordination-driven self-assembly from small-sized cyclophane components.

In our research on a series of cyclophanes we have shown that most of dithia[3.3]metacyclophanes tend to assume a *syn* conformation with two aromatic rings located in face-to-face orientation. This simple structure of the [3.3]metacyclophane system can be considered suitable for formation of self-assembled coordination cage. Taking the method developed by Fujita into account, the cyclophane should have several pyridine units. Thus, as a primary candidate we have focused on dithia[3.3](3,5)pyridinophane **1**. In this communication we will describe formation of a molecular cage based on the small-sized pyridinophane **1**.

Repeating the reported method[6] to prepare the pyridinophane **1** has resulted in poor yield. So we have modified this method to obtain the desired pyridinophane **1** in better yield. Direct chlorination of 3,5-lutidine with NCS gave a mixture of monochloromethyl and bis(chloromethyl)compounds. A pure 3,5-bis(chloromethyl) pyridine **2** could be successfully isolated by careful separation of the mixture employing a column chromatography. Subsequently 3,5-bis(mercaptomethyl)pyridine **3** was obtained by the conventional method from **2**. Cyclization of **2** and **3** using Cs_2CO_3 as a base under highly dilute condition afforded the desired pyridinophane **1**[7] in 45% yield (Scheme 1).

It should be critical to know the conformation of **1** in order to form a desired cage-shaped assembly based on the cyclophane compounds because they exhibit conformational variety. However, to our best knowledge the X-ray crystal analysis of **1** has never been done yet.

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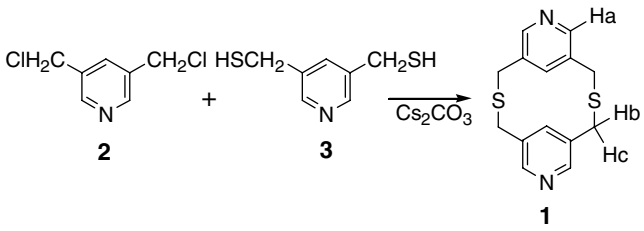


Scheme 1. Synthesis of the cyclophane **1**.

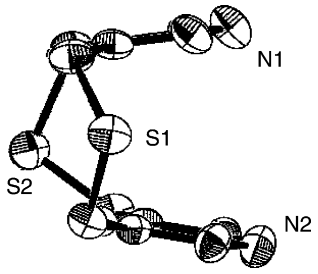


Figure 1. Single-crystal X-ray structure of **1**.

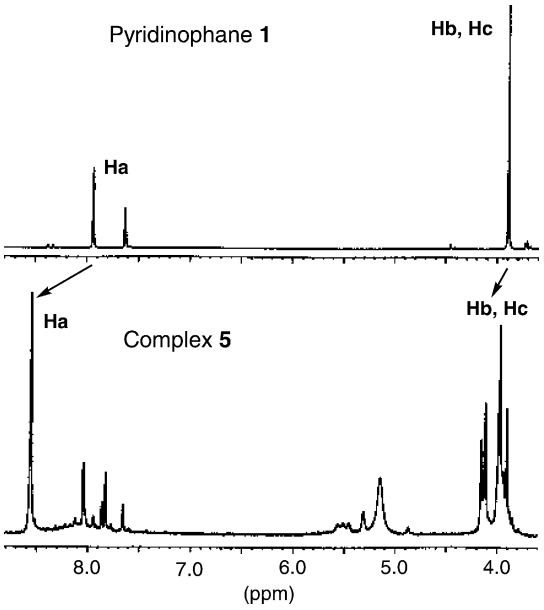


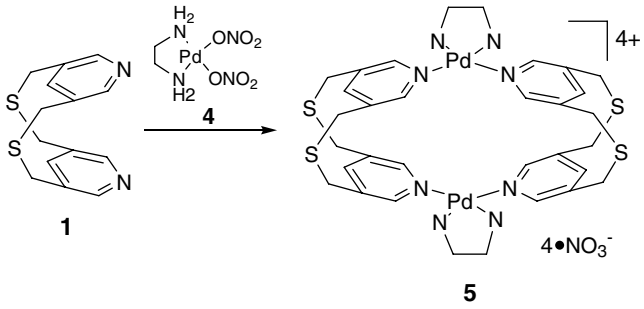
Figure 2. ^{1}H NMR spectra of **1** and **5** in DMSO-d_6 at 30 °C.

So we have carried out the analysis of the conformational structure of **1**.

As shown in Figure 1, the *syn* conformation was confirmed for **1** from the X-ray analysis.[†] A boat-chair shape observed for the bridging is very interesting, so details of conformational properties of **1** and related compounds will be discussed elsewhere.

The pyridinophane **1** and cis-protected palladium(II) complex (en)Pd(NO_3)$_2$ **4** were combined in 1:1 stoichiometry in water–methanol to afford the colorless powder **5** which was then washed with methanol (Scheme 2).

The ^{1}H NMR spectrum of the complex **5** in DMSO is shown in Figure 2 together with **1**. Upon complexation, some impurities have been produced. Although the pyridinophane **1** gives one singlet (δ 3.90) for bridge protons (Hb and Hc), in the spectrum of **5**, bridge protons appear as a set of doublets (δ 3.97, J 12 and δ 4.13, J 12). Such a spectral change is quite often observed with a decrease in temperature for these kinds of dithia[3.3]metacyclophanes.[8] This behavior can be explained by dynamic conformational changes of cyclophanes, meaning that a rapid ring inversion in the cyclophanes at higher temperature is suppressed to a great extent as the temperature is lowered. Thus, in this case flexibility of the pyridinophane **1** is considered to be depressed by complexation of the pyridine nitrogen with Pd.



Scheme 2. Formation of the cage structure **5** based on **1**.

This complexation is also supported by a downfield shift (from δ 7.94 to δ 8.55) of the proton (Ha) adjacent to the pyridine nitrogen. The formation of the cage structure shown in Scheme 2 might be expected from these NMR data.

It has been known the cold-spray ionization mass spectrum (CSI-MS)[9] is a powerful tool to obtain strong evidence for the formation of supramolecular structure. In order to dissolve **5** in acetonitrile the counter anion was replaced by PF_6^- to prepare the complex **6**. Further evidence for formation of cage structure was provided by the CSI-MS (Fig. 3) of **6** (PF_6^-), wherein the molecular ion peaks of **6** were observed at m/z 1316.7 $[\mathbf{6} - (PF_6^-)]^+$ (calcd 1316.75), 585.9 $[\mathbf{6} - (PF_6^-)_2]^{2+}$ (calcd 585.89), and 342.3 $[\mathbf{6} - (PF_6^-)_3]^{3+}$ (calcd 342.28). Although a small amount of the cage structure with other coordination (**1**:**4** = 4:4) was also detected in the CSI mass spectrum, the major component is the cage structure **5** shown in Scheme 2.

The molecular cage based on coordination of the cyclophane compound to the metal could provide novel possibilities for the field of supramolecular architecture since cyclophane components have various unique characteristics such as conformational diversity, trans-

[†] Crystal data for **1**: $C_{14}H_{14}N_2S_2$, $M = 274.40$, monoclinic, $a = 12.412(1)$, $b = 16.403(2)$, $c = 6.3676(9)$ Å, $\beta = 92.49(1)°$, $U = 1295.2(3)$ Å^3, $T = 293$ K, space group $P2_1/n$ (no. 14), $Z = 4$, $D_c = 1.407$ g/cm^{-3}, μ(CuKα) = 3.566 cm^{-1}, 3142 reflections measured, 220 parameters refined, $R1 = 0.0590$ (for 2940 reflections with $I > 3.0\sigma(I)$), $wR2 = 0.1680$ (for all data). CCDC 278767. Crystallographic data in cif format (Ref. CCDC 278767) can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

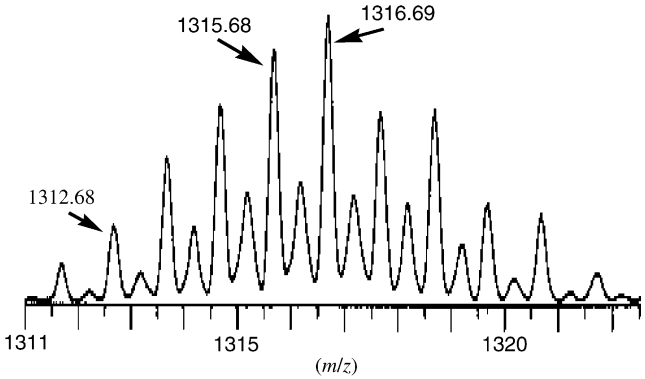


Figure 3. Cold-spray ionization mass spectrum of **6**.

annular π electronic interaction, molecular recognition and so on. Studies on cage formation from various cyclophanes with exclusive molar ratio are currently underway in our laboratory.

References and notes

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