

Construction of a Homooxacalix[3]arene-based Dimeric Capsule Cross-linked by a Pd(II)-pyridine Interaction

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Homooxacalix[3]arenes bearing 4-pyridyl groups at the 7,15,23-positions formed a dimeric complex with Pd(II). Only when the homooxacalix[3]arene was preorganized to a cone conformation, a dimeric molecular capsule with D_{3h} symmetry was yielded. Mass spectral studies established that CD_2Cl_2 is included in this cavity.

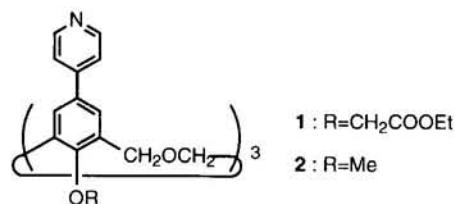
Calix[n]arenes feature a half-bowl-shaped architecture. This structural characteristic has tempted us to design a mid-air molecular capsule from two calix[n]arenes by binding two upper rim edges through "adhesive" functional groups. An early example was already reported in 1991 in which the disulfide groups were utilized for the cross-link.¹ However, the inclusion properties were estimated only qualitatively because of its synthetic difficulty.¹ It was later shown that such a bis-calix[n]arene-based molecular capsule can be created according to a self-assembly manner utilizing the hydrogen-bonding interaction, but direct evidence for guest inclusion was not obtained in solution probably because of the exchange rates faster than the NMR time-scale.^{2,3} In 1995, Rebek et al. demonstrated that calix[4]arene bearing four urea groups on the upper rim can dimerize owing to the formation of complementary hydrogen-bonds and included guests are detectable by NMR spectroscopy.⁴ Reinhoudt et al. found, after a long-termed synthetic effort, that a covalently-linked calix[4]arene-resorcin[4]arene conjugate provides a closed inner cavity which can include small guest molecules.⁵

Here, it occurred to us that the utilization of a coordination bond has been an escaped idea, for Fujita et al.⁶ and Stang et al.⁷ have shown a number of examples that the coordination bond is very useful for the construction of self-assembled supramolecular structures. We thus designed compounds **1** and **2**: the molecular modeling with MOPAC ver.6 suggests that when two cone-homooxacalix[3]arenes form an edge-to-edge dimer, pendant pyridines are exactly arranged at a right angle. This angle is particularly favorable to the cross-link by Pd(II).^{6,7} ¹H NMR and mass spectroscopic studies have shown that in **1** two homooxacalix[3]arenes dimerize in the presence of three equivalents of Pd(II) ($Ph_2PCH_2CH_2PPh_2\cdot(OTf)_2$) (**3**) and the dimeric capsule can include small molecules.⁸

Compound **1** was synthesized from 7,15,23-tribromo-25,26,27-tris[(ethoxycarbonyl)methoxy]-2,3,10,11,18,19-hexahomo-3,11,19-trioxacalix[3]arene⁹ and diethyl-4-pyridylborane in dimethylethylene glycol in the presence of $Pd(PPh_3)_4$ and CsF (yield 30%, mp 171.3–172.5 °C). 7,15,23-Tribromo-25,26,27-trimethoxy-2,3,10,11,18,19-hexahomo-3,11,19-trioxacalix[3]arene was prepared from 7,15,23-tribromo-2,3,10,11,18,19-hexahomo-3,11,19-trioxacalix[3]arene-25,26,27-triol⁹ by the reaction with MeI in

acetone in the presence of Cs_2CO_3 (yield 93%, mp 84.9–85.2 °C) and then converted to compound **2** by the similar method (yield 35%, mp 96.7–98.4 °C). Both products were identified by IR and ¹H NMR spectral evidence and elemental analyses. The largest difference between **1** and **2** is that **1** is immobilized to a cone whereas **2** is conformationally still mobile.¹⁰

When **1** and **3** were mixed in CD_2Cl_2 , the simple ¹H NMR splitting pattern was obtained only for the $[1]:[3] = 2:3$ ratio (Figure 1A). When the ratio was higher or lower than this value, the ¹H NMR spectra gave additional peaks and became very complicated (e.g., Figure 1B). Careful examination of Figure 1A reveals that all peaks can be assigned to a single phenyl unit, indicating that the 2:3 complex has a D_{3h} -symmetrical structure (for the assignment see Figure 2). It is known that in cone-calix[n]arenes the chemical shift difference ($\Delta\delta$) in the geminal coupling of the $ArCH_2Ar$ methylene protons is useful as a measure for the phenyl unit inclination: the larger the $\Delta\delta$, the more the phenyl units stand up.¹¹ Our recent study suggests, however, that this correlation is rather inverted in cone-homooxacalix[3]arenes.⁹ The $\Delta\delta$ (0.30 ppm) in the $ArCH_2O$ methylene protons (4.62 and 4.92 ppm) in **1** is enlarged to 0.58 ppm in those of the 2:3 complexes (4.41 and 4.99 ppm). This change implies that the phenyl units are more flattened for the pyridyl nitrogens to fully interact with Pd(II). The similar D_{3h} -symmetrical ¹H NMR spectra were also obtained in $CDCl_3$, $CDCl_2CDCl_2$, and $CD_2Cl_2:CD_3OD = 7.5:1.0$ (v/v). On the other hand, the spectra became complicated in $DMF-d_7$ and $DMSO-d_6$ even though the mole ratio of **1**:**3** is maintained to 2:3.



In contrast, when conformationally-mobile **2** was mixed with **3** in CD_2Cl_2 , the ¹H NMR spectrum at $[2]:[3] = 2:3$ (Figure 1C) was simpler than those at other ratios. However, the peaks were significantly broadened. Since partial-cone-**2** is energetically more stable than cone-**2** (partial-cone/cone = 5.1/1.0 at -80 °C in CD_2Cl_2 where the peak splitting is observable), the formation of the cone-shaped dimer from **2** and **3** accompanies an additional energy loss or even though such a dimer is formed, it still retains some molecular motion which causes the line broadening in ¹H NMR spectroscopy. Hence, clear evidence for the formation of the dimeric capsule was not obtained from the **2** + **3** system. The difference suggests that

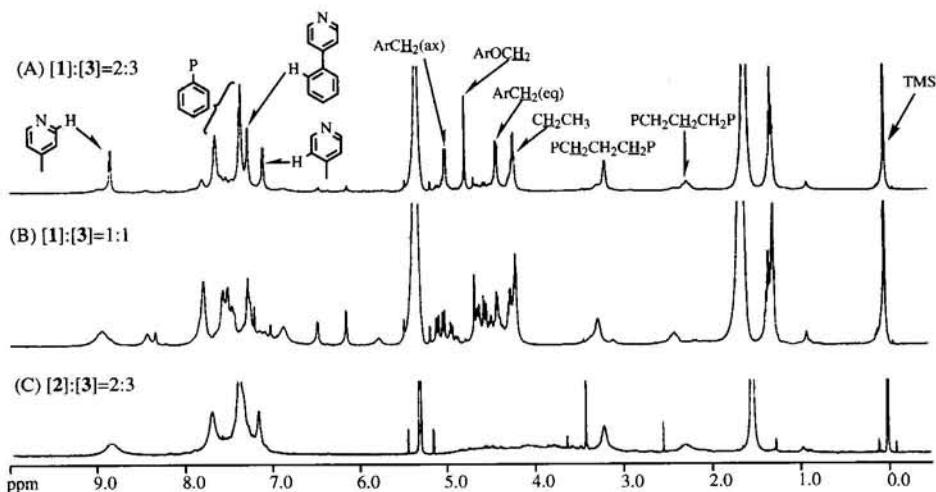


Figure 1. ^1H -NMR spectra (600 MHz) of (A) $[1]:[3] = 2:3$, (B) $[1]:[3] = 1:1$, and (C) $[2]:[3] = 2:3$ in CD_2Cl_2 at 25°C . [1] and [2] were maintained constant ($1.33 \times 10^{-3} \text{ mol}\cdot\text{dm}^{-3}$).

preorganization of homooxacalix[3]arene in a cone conformation is a prerequisite for the construction of the D_{3h} -symmetrical capsule according to a self-assembly manner.

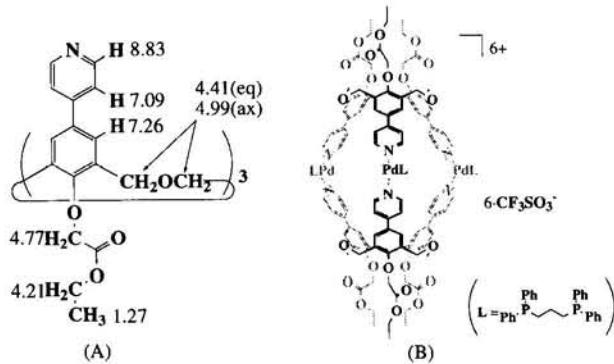


Figure 2. Assignment of the protons in the $[1]:[3] = 2:3$ complex (A) and the proposed dimeric structure (B).

The vapor pressure osmometry of **1** and **3** (in a 2:3 ratio) in CH_2Cl_2 gave the MW of 4227 ± 390 . This value is commensurate with the dimer (theoretical MW, 4246.92). The formation of the dimeric capsule was also supported by mass spectrometry (ESI, the measurable molecular weight < 3000). When a CD_2Cl_2 solution containing **1** and **3** in a 2:3 ratio was subjected, one strong peak and a relatively weak peak appeared at 1975 [$\text{m/z} = (\text{M}-2\text{TfO}^-)/2$] and 1266 [$\text{m/z} = (\text{M}-3\text{TfO}^-)/3$], which were both assignable to the dimer ($\text{M} = 4242$).¹² For the sample solution containing **1** and **3** in a 1:1 ratio, on the other hand, a strong peak and a very weak peak assignable to the 1:1 complex ($\text{M} = 1713$) and the 1:2 complex ($\text{M} = 2529$) appeared at 1564 [$\text{m/z} = (\text{M}-\text{TfO}^-)$] and 2383 [$\text{m/z} = (\text{M}-\text{TfO}^-)$], respectively. For the sample solution containing **1** and **3** in a 1:3 ratio, all peaks assignable to the 1:1, 1:2 and 2:3 complexes were observable. These mass spectral data shows that the dimer formation is highly dependent upon the ratio of **1** and **3**.

Very interestingly, the peak 1975 obtained from the CD_2Cl_2 solution containing **1** and **3** in a 2:3 ratio accompanied a relatively weak peak at 2060 and the intensity was always correlated with that of 1975. This peak can be accounted for by

$\text{m/z} = [(\text{M}-2\text{TfO}^-) + 2\text{CD}_2\text{Cl}_2]/2$.¹² The finding indicates that the dimer capsule includes two CD_2Cl_2 molecules or the dimer structure is constructable by filling two CD_2Cl_2 molecules inside the cavity.

In conclusion, the present study has demonstrated that the Pd(II)-pyridine interaction is useful to create a novel capsule-like molecule by dimerization of homooxacalix[3]arene derivatives. Through this study, it was shown that the capsule formation based on the self-assembly manner requires the favorable preorganization of building-blocks, the strict pyridine-Pd(II)-pyridine angle, the strict concentration ratio, and the proper solvent choice. Further study is currently continued in this laboratory.

References and Notes

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- 8 More recently, an Italian group reported that a resorcin[4]arene bearing cyano groups can dimerize in the presence of Pd(II), but this coordination bond is not so stable as the Pd(II)-pyridine bond: P. Jacobozzi and E. Dalcanale, *Angew. Chem. Int. Ed. Engl.*, **36**, 613 (1997).
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- 12 Although these species are multicharged ions and should give the peaks with 0.33 or 0.5 increment for the isotope species, they are not clearly detected because of the line-broadening in the mass spectra.