The First [5]Supercyclodextrin Whose Cyclopentameric Array Is Held Only by a Mechanical Bond

Takahiro Kaneda,* Takashi Yamada, Tatsuhiko Fujimoto, and Yoshiteru Sakata
The Institute of Scientific and Industrial Research, Osaka University, 8-1 Mihogaoka, Ibaraki, Osaka 567-0047

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The first [5]supercyclodextrin **1s** whose nano-sized cyclopentameric array is held only by a mechanical bond was synthesized by the pentakis-azo coupling of a new hermaphrodite monomer **2** with 2-naphthol as a stopper, isolated by chromatography, and characterized by MS, 2D NMR, and vis spectral methods with the help of computer simulation.

We recently reported that the self-association of permethylated α-cyclodextrin(CD)-azobenzene dyads selectively forms face-to-face dimers or Janus [2]pseudorotaxanes in excellent yields.[1] After many attempts to construct much higher cyclic n-mers of CDs, [n]supercyclodextrins ([n]SCDs), we achieved the synthesis of the title compound by making use of a hermaphrodite monomer, where the host and guest parts are bridged by an ester linkage instead of an ether one like in the previous monomers,[1] and 2-naphthol as a stopper. The present [5]SCD, a type of unknown [c5]daisy chains,[2] has potential use as a fundamental framework for assembling molecular machines[3] since its nano-sized cyclopentameric array is held only by a mechanical bond. To date, only [3][4]- and two [2]SCDs[1c,5] have been isolated and [4]SCD[1b] as the highest member has existed only at equilibrium. We describe here the first [5]SCD **1s** which is also the highest homologue of the [n]SCD family.

A new hermaphrodite monomer α-CD$(OMe)_{17}$[6-O(CO-C_6H_4-*p*-N=N-C_6H_4-*p*-NH_2)][6] (**2**) was prepared in 85% yield by the reaction of 6-*O*-monotosyl permethylated α-CD[7] with 4-(4'-aminophenylazo)benzoic acid[8] in DMF. Subsequently, **2** was azo-coupled with 2-naphthol under usual conditions (2 mM of **2**). After purification of the reaction products by chromatography, we obtained a cyclic pentamer **1s**[6] as red film (15% yield) accompanied with the corresponding monomer **3**[6] (20%). The overall yield of the [5]SCD was 3% through the 4 steps from α-CD. The cyclic pentamer was found to be soluble in the usual organic solvents such as toluene and acetonitrile and showed a Na^+ adduct ion of $[M+Na]^+$ *m/e* 7955 corresponding to a five-fold stoppered pentamer $C_{380}H_{540}N_{20}O_{160}$ (MW: 7948) in its MALDI-TOFMS spectrum (MALDI = Matrix-Assisted Laser Desorption Ionization).

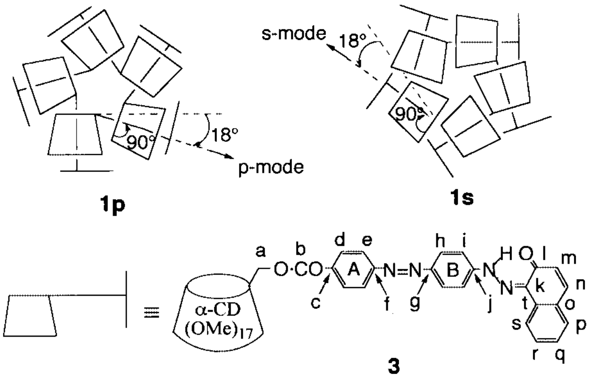

Figure 1. Two possible isomeric [5]supercyclodextrins **1p** and **1s** constructed from the perpendicular insertion of the guest parts from the primary (p-mode) and secondary faces (s-mode), respectively. In each isomer, the angle of 18 degrees between the plane of the primary face and the guest rod is required according to elementary geometry.

The ^1H NMR signals for the guest and stopper parts of **3** were assigned as the hydrazone tautomer[9] rather than the azo naphthol isomer as shown in Figure 2(a). The appearance of the NH proton at δ 16.37 and chemical shifts identical to those observed with Hp and Hr support the assignment as well as the finding of two correlations due to Hd–He and Hh–Hi.

It is noteworthy that the symmetry of the signal appearance in **1s** is as high as that in **3** (Figure 2(b)). This finding indicates that the cyclic pentamer belongs to the C_5 symmetry. A priori, there are two possible isomers **1p** and **1s** for its structure (Figure 1).

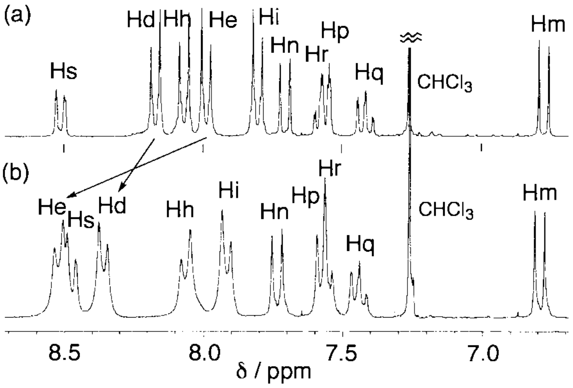

Figure 2. Aromatic region of 270 MHz ^1H NMR spectra of (a) **3** and (b) **1s** in $CDCl_3$.

We succeeded in the full assignment of the protons and carbons in the guest and stopper parts of **1s** on the basis of observations of pivotal correlation peaks due to Cd(δ 130.17)–Hd(8.36), Ha(4.63)–Ca(62.91), and NH(16.39)–Cj(146.86).[10] The HMQC technique revealed the chemical shifts of all of the vinyl protons (except for Hh and Hi) and sp^2-carbons with hydrogen, and HMBC revealed the rest (Hh and Hi and nine quaternary carbons). Therefore, the hypothetical cyclopentamerization of **3** to **1s** brought about the changes in the chemical shifts of Hd (+0.19 ppm), He (+0.50), Hh (+0.01), and Hi (+0.12). The largest down-field shift of 0.50 ppm indicated the proximity of He to α-1,4-glucosidic oxygen atoms according to "an empirical rule", which was derived from our previous works[1] and which leads to a down-field shift by ca. 0.55 ppm for such protons. Finally, the fact that the naphthol-stopper parts of **1s** and **3** showed the same

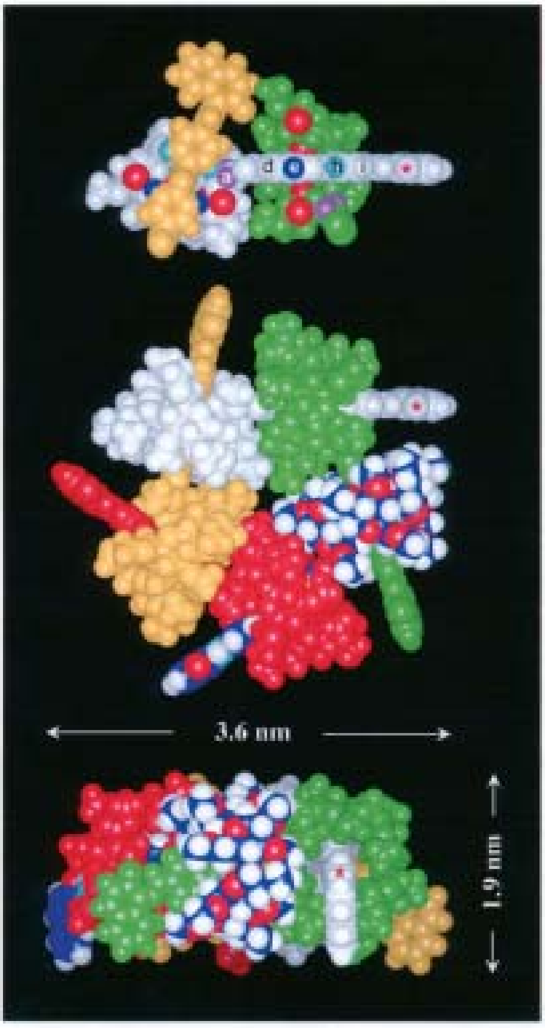

Figure 3. Computer-generated structures (CPK views) of **1s**. The monomer units are drawn monochromatically or with a color code: carbon, blue; hydrogen, white; nitrogen, yellow; oxygen, red. As a pivot, the hydrazone carbonyl oxygen of the naphthol-stopper is labeled with a red star mark. At the top view, the yellow guest part is shown by rotating 90 degrees, and Ha, He, Hh, and glucosidic oxygens are colored purple, blue, sky blue, and red, respectively.

spectral features strongly suggested that they are maintained outside of the CD cavities.

In order to compare the superiority of the isomeric structures **1p** and **1s**, molecular simulation[11] was carried out using the following three assumptions: (1) the CD skeletone of the host part is similar to that of a permethylated α-CD-p-nitrophenol complex[12]; (2) the guest rods are perpendicular to the faces of the hosts; and (3) the arrangement of the guest to the host in the same monomer is required by elementary geometry (Figure 1). Needless to say, He protons remained close to glucosidic oxygens as mentioned above. The resulting computer-generated structure for **1s** seemed to be rational (Figure 3). On the other hand, the corresponding structure for **1p** was found to have a serious steric repulsion between the primary rim of a CD moiety and the exterior wall of the neighboring CD providing the guest part. In addition to this superiority of **1s** over **1p**, it was found that NOE correlation due to Ha–Hh as observed by a NOESY experiment can be interpreted with **1s** as seen from the top view.

Consequently, we identified the present [5]SCD with the s-mode cycle **1s**. The chemical architecture has the following characteristics: (1) it is the first example of [n]SCDs constructed with s-mode insertion; (2) it enables the termination of a molecular hierarchy with α-D-glucopyranose as the bottom; (3) it is a nano-sized, condensed, and lipophilic pentagon with a diameter of 3.6 nm and a thickness of 1.9 nm. The pentagon, with ten aromatic rings of “A” and “B” that free-rotate fast on the NMR time scale, seems to be a nano-sized space station and it turned blue (λ_{max} 674 nm (log ε 5.28) in acetonitrile) from the original red (516 nm (5.31)) due to ionization to the corresponding azonaphtholate on encounter with a base as an alien.

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References and Notes

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6 **1s**: red film, mp 290–294 °C. Anal. Found: C, 53.58; H, 6.43; N, 3.21%. Calcd for $[C_{76}H_{108}N_4O_{32}]_5\cdot 6[CHCl_3]$: C, 53.51; H, 6.36; N, 3.23%. **2**: orange foam, mp 233–237 °C (dec). Anal. Found: C, 52.62; H, 6.96; N, 2.41%. Calcd for $C_{66}H_{103}N_3O_{31}\cdot 0.8\ [CHCl_3]$: C, 52.44; H, 6.84; N, 2.73%. TOFMS (m/z) 1460 $[M+Na]^+$. ^{1}H NMR (270 MHz, $CDCl_3$): δ 8.12 (d, J = 8.6 Hz, 2H), 7.90 (d, J = 8.6 Hz, 2H), 7.81 (d, J = 8.6 Hz, 2H), 6.74 (d, J = 8.6 Hz, 2H) for Ar–H. **3**: red film, mp 208–212 °C. Anal. Found: C, 54.08; H, 6.48; N, 3.26%. Calcd for $C_{76}H_{108}N_4O_{32}\cdot\ CHCl_3$: C, 54.11; H, 6.43; N, 3.28%. TOFMS (m/z) 1612 $[M+Na]^+$. The NMR data for **1s** and **3** will be reported elsewhere.

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