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Switching from *altro*- α -Cyclodextrin Dimer to *pseudo*[1]Rotaxane Dimer through Tumbling

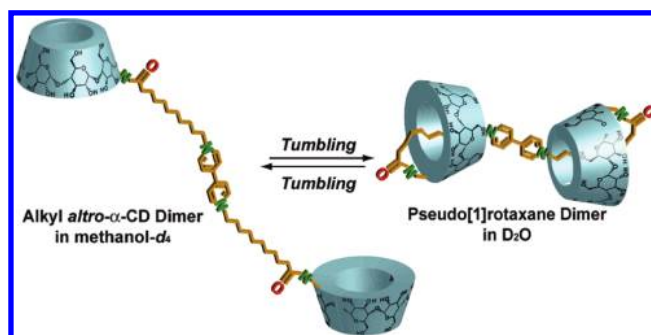
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Received January 23, 2010

ABSTRACT



An alkyl *altro*- α -CD dimer was converted to the *pseudo*[1]rotaxane dimer through tumbling of the altropyranose unit of *altro*- α -CD in D₂O. The tumbling of the altropyranose unit was found to be a rotational vibration with $1.18 \times 10^{-3} \text{ s}^{-1}$ at 293 K. The activation free energy ($\Delta G_{288\text{K}}^\ddagger$) for the conformational change from an alkyl *altro*- α -CD dimer to *pseudo*[1]rotaxane dimer was 88.0 kJ mol⁻¹, which corresponds to the breakage of the hydrogen bond network for the tumbling of an altropyranose unit.

The development of supramolecular chemistry has resulted in the discovery of various host molecules having specific functions.¹ Crown ethers, calix[*n*]arenes, calixresorcinarenes, and cyclodextrins (CDs) are widely known to be typical host molecules.² Although calixresorcinarene and CD have stable cyclic structures, calix[*n*]arene shows a core-inverted core transition.^{3–6} In contrast, it has long been thought that not only unmodified CDs but also monosubstituted CDs have stable cyclic structures and do not demonstrate tumbling

behavior. Permethylated CDs only allow tumbling of glucopyranose residues due to lack of a hydrogen bond network.^{7–10} In our report of the crystal structure of 3-stilbene amide- α -CD, we found the presence of hydrogen bonding between an altropyranose unit and glucopyranose unit, and we did not observe tumbling behavior with this molecule.¹¹ We predicted that an altropyranose unit of an

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altro- α -CD might rotate around the axis of an $\alpha(1,4)$ bond as a result of the weak conformational restriction by hydrogen bonds if flexible alkyl chains were linked to the altropyranose unit. We now report the formation of a *pseudo*[1]rotaxane dimer from an *altro*- α -CD dimer by using tumbling of an altropyranose unit.

The alkyl *altro*- α -CD dimer with a decamethylene (C10) linker and viologen unit was prepared from a 3-NH₂- α -CD¹⁴ bearing an altropyranose residue. To distinguish the decamethylene protons of the *altro*- α -CD side from that of the viologen side, the viologen unit was introduced to an alkyl *altro*- α -CD dimer. Figure 1a,b shows the ¹H NMR spectra

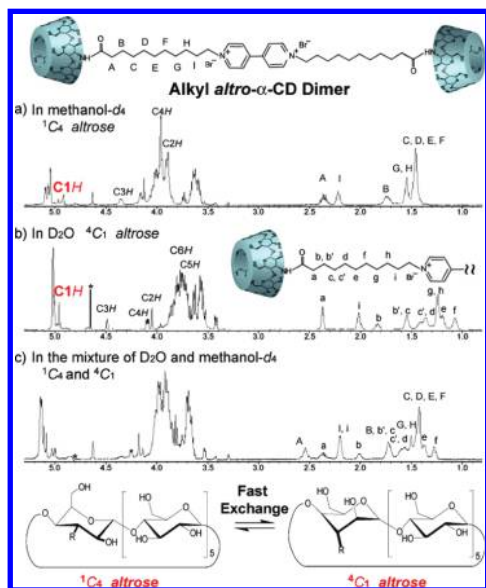


Figure 1. ¹H NMR spectra (CD part and alkyl part) of the alkyl α -CD dimer in methanol-*d*₄ (1 mM) at 35 °C (a), in D₂O (1 mM) (b), and in a mixture of methanol-*d*₄ and D₂O (c) at 30 °C. *: HOD.

of the alkyl *altro*- α -CD dimer in CD₃OD and D₂O, respectively. Protons of the altropyranose unit exhibited a distinctive coupling constant ($J_{1,2} = 6.0$ Hz at C₁H) in CD₃OD, whereas the altropyranose unit in D₂O exhibited a different coupling constant ($J_{1,2} = 1.6$ Hz at C₁H). One characteristic of an altropyranose group is that the ¹C₄ and ⁴C₁ conformations show characteristic coupling constants (¹C₄, $J = 5-7$ Hz at C₁H; ⁴C₁, $J = 1-2$ Hz at C₁H) in ¹H NMR spectroscopy.¹² There is *pseudo* rotational conversion between the ⁴C₁ and ¹C₄ conformations due to their flexible

frame. The ⁴C₁ ↔ ¹C₄ conformational change is fast on the NMR time scale. The altropyranose unit of the alkyl *altro*- α -CD dimer in CD₃OD was found to form the ¹C₄ conformation, and that in D₂O formed the ⁴C₁ conformation. The ¹H NMR spectrum in a mixed solvent of D₂O and CD₃OD exhibited two species that exist in equilibrium. These results indicate that the conformational change of the alkyl *altro*- α -CD dimer depends on solvent polarity.

To clarify the relationship between the conformation of the altropyranose residue and the supramolecular structure of the alkyl *altro*- α -CD dimer, 2D ROESY (or NOESY) NMR were measured in D₂O and in a mixture of D₂O and CD₃OD. In the ¹H NMR spectrum in D₂O, protons of the alkyl chains of the alkyl *altro*- α -CD dimer exhibited splitting to form an inclusion complex with alkyl chains. Figure 2

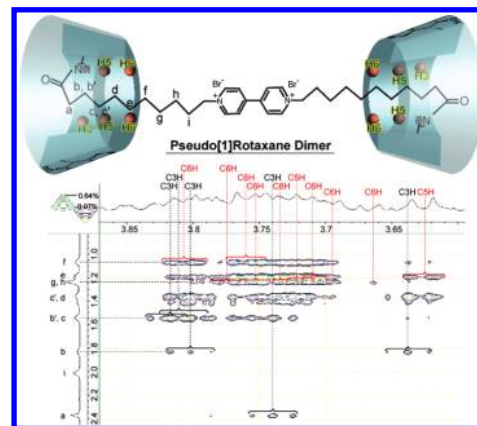


Figure 2. Partial 2D ROESY NMR (CD part and alkyl part) spectrum of the alkyl *altro*- α -CD dimer in D₂O (1 mM) at 30 °C (mixing time = 200 ms) and proposed structure of the alkyl *altro*- α -CD dimer in water from the ROESY spectrum.

shows that methylene groups e and f in the vicinity of the bipyridinium group showed ROE correlations to the C₅H and C₆H around the narrow rim of *altro*- α -CD, whereas methylene groups a, b, and c adjacent to the *altro*- α -CD unit showed weak correlations. C₃H at the wider rim of *altro*- α -CD clearly correlated to the alkyl protons a, b, and c. These results indicate that the alkyl chain surprisingly penetrated the *altro*- α -CD cavity in D₂O and the narrow rim of the *altro*- α -CD faced the bipyridyl group. The alkyl *altro*- α -CD dimer changed to the *pseudo*[1]rotaxane dimer in D₂O.

We thought that the alkyl *altro*- α -CD dimer with the ¹C₄ altropyranose unit would not form the penetrating structure but that the dimer with the ⁴C₁ altropyranose unit would form it. To observe correlation peaks between the protons of the *altro*- α -CD with a ¹C₄ altropyranose residue and alkyl protons, we chose the mixed solvent because the protons derived from ¹C₄ and ⁴C₁ conformations were independently observed in the mixed solvent. As shown in Figure 3, the protons of the ⁴C₁ altropyranose unit showed correlation peaks to alkyl protons, whereas the protons of the ¹C₄ altropyranose unit showed no correlation peaks to the alkyl protons. This result indicates that the alkyl *altro*- α -CD dimer with the ¹C₄ altropyranose unit does

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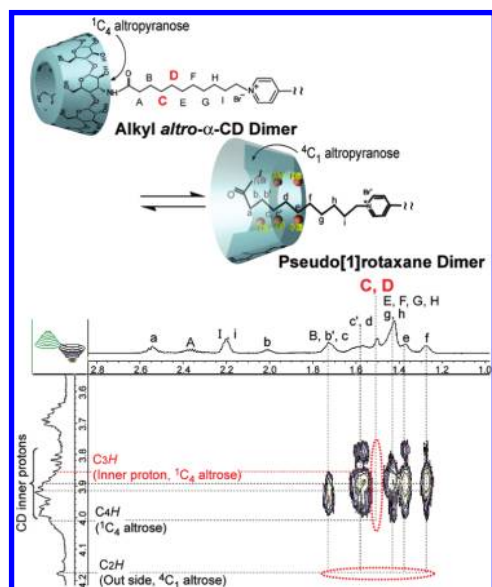


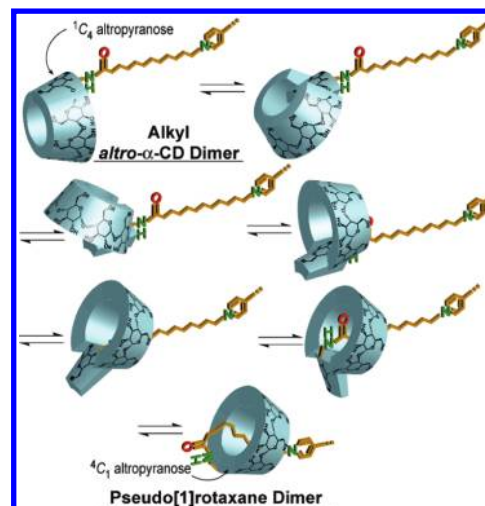
Figure 3. Partial 2D NOESY NMR (CD part and alkyl part) spectrum of the alkyl *altro*- α -CD dimer in the mixed solvent of D₂O and CD₃OD (1 mM) at 30 °C (mixing time = 800 ms).

not form the penetrating structure, whereas that with the 4C_1 altropyranose unit does form it.

We propose the following possible mechanisms for the formation of the penetrating structure: (1) pulling the alkyl chain into the *altro*- α -CD cavity, (2) threading from another *altro*- α -CD end group, or (3) tumbling of the altropyranose unit with a substituent. Hypotheses (1) and (2) are unlikely because these actions are physically impossible and do not coincide with the results of the ROE correlations. The results of the NMR studies suggest that the alkyl *altro*- α -CD dimer formed the *pseudo*[1]rotaxane dimer via tumbling of the altropyranose residue (Scheme 1).

To examine the kinetics of the alkyl *altro*- α -CD dimer, the activation free energy (ΔG^\ddagger) for the conformational change of the alkyl *altro*- α -CD dimer was determined by using the Eyring equation. When this process is assumed to be a two-site exchange, the ΔG^\ddagger_{288K} value for the conformational change from the alkyl *altro*- α -CD dimer to the *pseudo*[1]rotaxane dimer was calculated to be 88.0 kJ mol⁻¹ by using a single exponential fitting (see Figure S6 in Supporting Information). The calculated ΔG^\ddagger value for tumbling of the altropyranose residue is slightly higher than the reported value for calix[4]arene tumbling.¹³ In D₂O, the preferred conformation was one in which the alkyl chains in the alkyl *altro*- α -CD dimer were included in the *altro*- α -CD cavities to form the *pseudo*[1]rotaxane dimer. The conformational change from 4C_1 to 1C_4 is fast on the NMR time scale. When there are no hydrogen bonds between an altropyranose unit and glucopyranose unit, the altropyranose unit seems to be capable of easily tumbling.^{9,10} Therefore, the main energetic barrier for the conformational change of the alkyl *altro*- α -CD dimer is the breakage of the hydrogen

Scheme 1. Formation of the *pseudo*[1]Rotaxane Dimer from the Alkyl *altro*- α -CD Dimer via Tumbling of an Altropyranose Unit



bond network to permit the tumbling process. The tumbling of an altropyranose unit was found to be a rotation with a period of $6.58 \times 10^{-4} \text{ s}^{-1}$ at 288 K and the ΔG° value at 288 K was found to be -8.1 kJ mol^{-1} . These results indicate that an enthalpy gain occurred and that the conformational change of an altropyranose residue contributes to the stabilization of the *pseudo*[1]rotaxane dimer.

In conclusion, we have succeeded in forming a *pseudo*[1]rotaxane dimer through tumbling. We initially thought that the alkyl *altro*- α -CD dimer would change conformation by pulling the alkyl chain into the CD cavity. However, the results of 2D ROESY did not support this hypothesis. A 3-stilbene amide- α -CD with a rigid guest group could not form a self-inclusion complex and was shown to form a double threaded dimer in aqueous solution.¹¹ In contrast, the alkyl *altro*- α -CD dimer, which has long and flexible alkyl chains, formed the self-inclusion complex easily in aqueous solution. The alkyl *altro*- α -CD dimer reels the decamethylene chain into the cavity of the *altro*- α -CD end groups to form the *pseudo*[1]rotaxane dimer.

Acknowledgment. The authors thank Mr. S. Adachi and H. Okuda (Osaka University) for their support with 2D-NMR experiments. This work was supported by the “Core Research for Evolutional Science and Technology” program of the Japan Science and Technology Agency, Japan.

Supporting Information Available: Selected NMR data (variable temperature NMR and time-resolved NMR spectrometry, 2D gCOSY, TOCSY, ROESY, 2D NOESY, gHSQC) and Eyring plots. This material is available free of charge via the Internet at <http://pubs.acs.org>.

OL1001736

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