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Daisy Chain Necklace: Tri[2]rotaxane Containing Cyclodextrins

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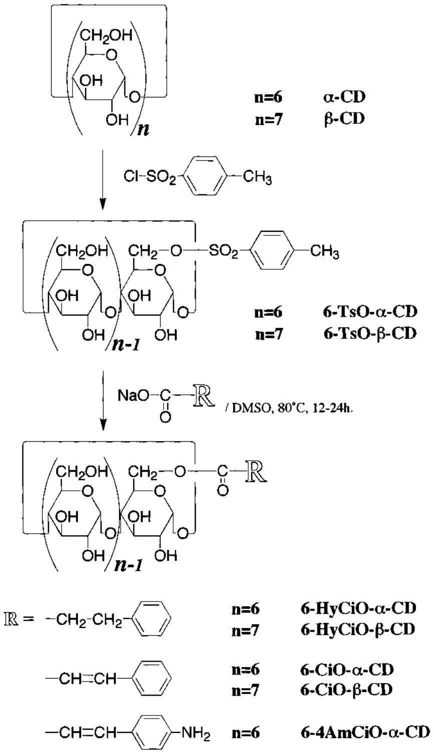
Recently, much attention has been focused on design and synthesis of interlocked molecules, such as rotaxanes and catenanes, because of their unique structures and properties.[1] Host−guest interactions are used for efficient preparation of such interlocked molecules. When a guest group is covalently attached to a cyclic host, the molecule may form an intramolecular complex[2] or intermolecular complexes[3] to give supramolecular polymers. When supramolecular polymers are treated with bulky stopper groups, they may form poly[2]rotaxanes, daisy chains.[4] Now we found that a cyclodextrin derivative which has a cinnamoyl group as a guest part on the 6-position of cyclodextrin forms an oligomeric supramolecular structure in aqueous solutions and that the supramolecular structure could be stabilized by attaching bulky stoppers to give the cyclic trimer of [2]rotaxane, daisy chain necklace.

We chose cyclodextrin (CD) as a cyclic host and a phenyl group as a guest moiety because a phenyl group is suitable for fitting in a cyclodextrin cavity. However, benzoyl CD did not form supramolecular polymers.[5] This result suggests that some spacer groups are required for efficient formation of intermolecular complexes. Therefore, we tested a hydrocinnamoyl group as a guest moiety. However, 6-hydrocinnamoyl *β*-CD (6-HyCi-*β*-CD) formed an intramolecular complex and 6-HyCiO-α-CD gave only weak intermolecular complexes. So we have decided to use cinnamoyl derivatives as a guest because cinnamoyl derivatives have a rigid carbon−carbon double bond. The synthetic route is shown in Scheme 1.

Scheme 1



6-Cynnamoyl *β*-CD (6-CiO-*β*-CD) is sparingly soluble in water, although most of 6-substituted *β*-CDs are soluble. However, 6-CiO-*β*-CD is solubilized in water on the addition of *p*-iodoaniline or *p*-iodophenol which can be included in a *β*-CD cavity. These results suggest that 6-CiO-*β*-CD forms supramolecular polymers in the solid state. The X-ray powder pattern of 6-CiO-*β*-CD is very similar to that of the complex between *β*-CD and ethyl cinnamate,[6] in which *β*-CDs form a layer structure. In contrast, 6-CiO-α-CD is soluble in water. The ^{1}H NMR spectra of 6-CiO-α-CD in D_2O are similar to those of methyl cinnamate (a model compound) in the presence of α-CD, indicating that a cinnamoyl group is included in the α-CD cavity. The ^{1}H NMR spectra are dependent on the concentration, although those in DMSO-d_6 are independent of concentration. The ROESY spectra of 6-CiO-α-CD in D_2O showed NOE between phenyl signals and the inner protons of CD. These results indicate that 6-CiO-α-CD forms intermolecular complexes in D_2O solutions.

Therefore, we measured the molecular weight of 6-CiO-α-CD using vapor pressure osmometry (VPO) at various concentrations. Figure 1 shows the results of the VPO measurements of the CD and their derivatives at various concentrations at 40 °C in D_2O. Although α-CD showed no concentration dependency of the molecular weight, 6-CiO-α-CD showed concentration dependence. The molecular weight increased with increase in the concentrations and the molecular weight reached saturation at about 3000. This result suggests that 6-CiO-α-CD forms a trimer. 6-4-AminoCiO-α-CD (6-4AmCiO-α-CD) showed a similar result, although the molecular weight observed by VPO and the ^{1}H NMR spectra of the starting tosyl α-CD are independent of the concentrations. At higher temperature (at 70 °C) the molecular weight observed is lower than that observed at lower temperature (at 40 °C). Supramolecular polymeric structures have been reported in the solid states of *β*-CD having a guest moiety by X-ray studies.[7] To the best of our knowledge, there have been no reports on the formation of supramolecular polymers of CD derivatives in aqueous solutions, although there have been a few reports in which dimeric complexes have been suggested in aqueous solutions.[8]

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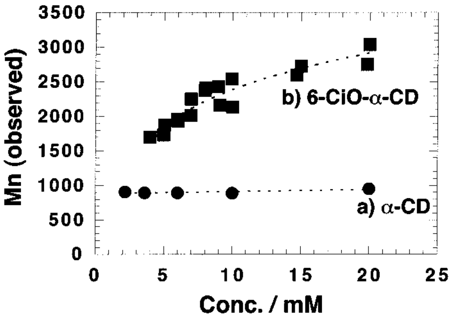
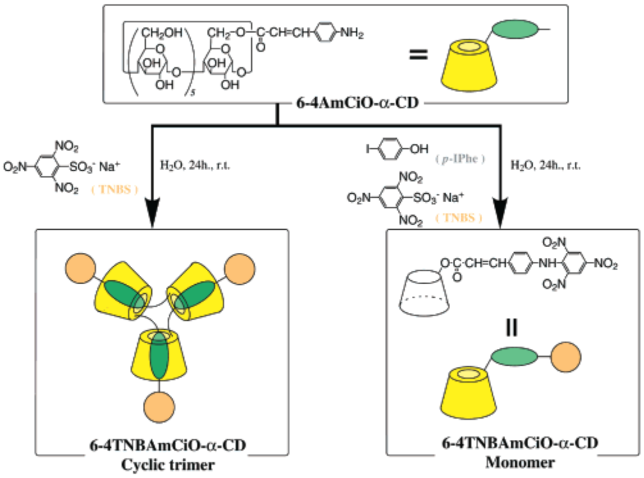


Figure 1. Effects of the concentrations on the molecular weight of α-CD (a, ●) and 6-CiO-α-CD (b, ■) observed by VPO in water at 40 °C.

Scheme 2



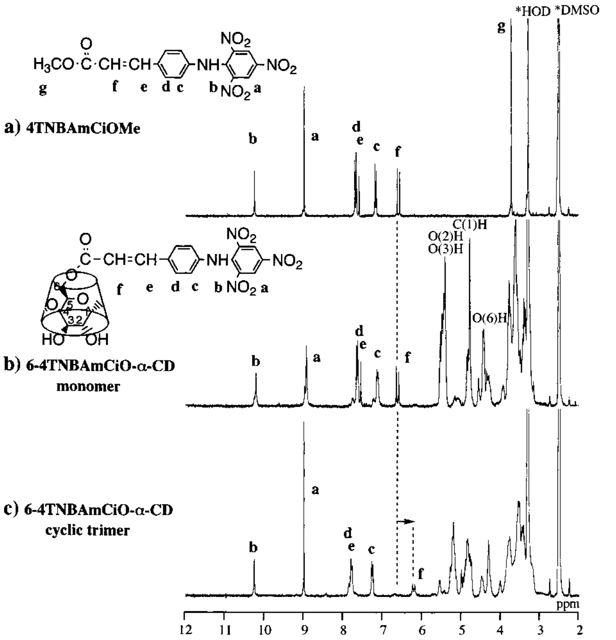


Figure 2. ^{1}H NMR spectra of 4TNBAmCiOMe (a), 6-4TNBAmCiO-α-CD monomer (b), and 6-4TNBAmCiO-α-CD cyclic trimer (c) in D_2O at 30 °C.

When 6-4AmCiO-α-CD (40 mM) was treated with 2 M excess 2,4,6-trinitrobenzenesulfonic acid sodium salt (TNBS) as bulky stoppers in aqueous solutions (Scheme 2), the solution became turbid and the product was obtained as a precipitate. The ^{1}H NMR and TOF mass spectra showed that the crude product is mainly a cyclic trimer with a small amount of cyclic dimer and monomer. The product was purified by column chromatography on DIAION HP20 followed by chromatography on TOYOPEARL HW-40. The product was characterized by UV−visible absorption, FT IR, ^{1}H NMR, ^{13}C NMR, 2D ROESY spectra, and MALDI TOF mass spectra.[9] The ^{1}H NMR spectra showed that the product does not have a nonincluded cinnamoyl group and that each peak is broadened (Figure 2). These results indicate that the product is a polymer or a cyclic compound. Therefore, we measured the MALDI TOF mass spectra and found a signal with the mass of the cyclic trimer, 4009 (trimer + Na$^+$), and no peaks due to dimers or higher aggregates. This result clearly showed that the product is a cyclic trimer. When the reaction was carried out in the presence of 3 M excess of *p*-iodophenol, the product is only the monomer, 6-4-TNBAmCiO-α-CD (Scheme 2). These results indicate that *p*-iodophenol inhibited the formation of self-assembling supramolecular structures. The ROESY spectrum of the cyclic trimer shows cross-peaks between phenyl protons close to an amino group and secondary hydroxyl groups (O(2)H), indicating that a trinitrophenyl group is located at the secondary hydroxyl group side. A proposed structure of cyclic trimer (a daisy chain necklace) isolated is shown in Scheme 2.

Detailed structures and their dynamic aspects are now being investigated and the results will be published later.

Supporting Information Available: Experimental details (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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[9] Cyclic trimer: *cyclo*-tri[mono-6-O-{4-(*N*-2,4,6-trinitrobenzamino)cinnamoyl}-α-CD] (*cyclo*[6−4TNBAmCiO-α-CD]3). Yield: 38%. ^{1}H NMR (DMSO-d_6, 270 MHz): δ 10.26 (s, 1H, Ph−N*H*−Ph), 8.99 (s, 2H, H of trinitrophenyl), 7.85−7.78 (3H, Ph−CH=, and 2-H of phenyl), 7.25 (d, J = 7.6 Hz, 2H, 3-H of phenyl), 6.20 (d, J = 15.8 Hz, 1H, =C*H*−CO−), 5.54−5.12 (m, 12H, O(2)H and O(3)H of α-CD), 5.00−4.26 (m, 13H, C(1)H, O(6)H, and C(6′)H of α-CD), 4.01−3.25 (m, overlaps with HOD, C(2-6)H of α-CD); IR (KBr, cm^{-1}): 3394 (vs, ν_{OH}), 2932 (vs, ν_{CH}), 1715 (s, $\nu_{C=O}$), 1338 (s, $\nu_{(C=O)-O}$), 1151, 1076, 1029 (vs, ν_{C-O}). MALDI-TOF-MS 4009 [cyclic trimer + Na]$^+$; Anal. Calcd for $(C_{51}H_{68}N_4O_{37})_3 \cdot 17H_2O$: C, 42.80; H, 5.59; N, 3.91. Found: C, 42.44; H, 5.09; N, 3.89.