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pH-Responsive Movement of Cucurbit[7]uril in a Diblock Polypseudorotaxane Containing Dimethyl *β*-Cyclodextrin and Cucurbit[7]uril

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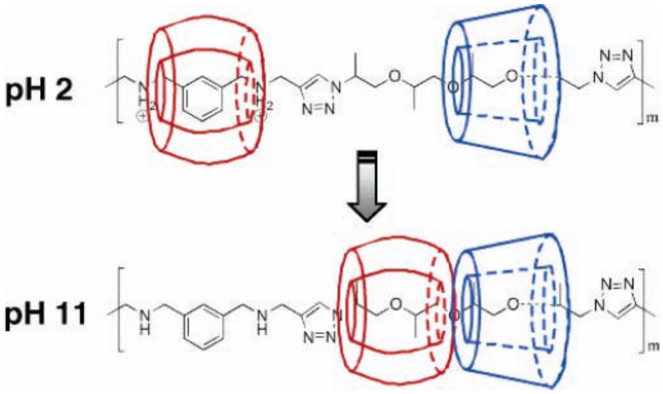
ABSTRACT



A polypseudorotaxane consisting of cucurbit[7]uril (CB[7])/*N*,*N*′-(3-phenylenebis(methylene)dipropargylamine (PMPA), [2]pseudorotaxane, and 2,6-*O*-dimethyl *β*-cyclodextrin (DM-*β*-CD)/α,*ω*-bisazidopropylene glycol 400 [2]pseudorotaxane was synthesized using the “click” reaction. The polypseudorotaxane structure was maintained in aqueous solution over a wide range of pH values with the DM-*β*-CD units contributing to increased solubilization of the polypseudorotaxane without dethreading. The pH-responsive movement of the CB[7] units in the polypseudorotaxane was also observed.

Polypseudorotaxanes consisting of cyclic molecules and a linear polymeric chain are widely used components in functional supramolecular materials.[1] Cyclodextrins (CDs), 1,4-linked cyclic oligomers of anhydroglucopyranose, are one

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[1] (1) Recent review: (a) Wenz, G.; Han, B. H.; Muller, A. *Chem. Rev.* **2006**, in press. (b) Lee, J. W.; Samal, S.; Selvapalam, N.; Kim, H. J.; Kim, K. *Acc. Chem. Res.* **2003**, *36*, 621−630.

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type of cyclic molecule that has been utilized to prepare complexes with linear polymers,[2] star-shaped polymers,[3] and single-walled carbon nanotubes.[4] Yui and co-workers have observed polypseudorotaxane formation between CDs and such polycations as poly(ϵ-lysine)[5] and linear poly(ethylene imine).[6] The CDs in these polypseudorotaxanes can be discharged into the medium when amine groups on the polymeric chain are protonated, thus demonstrating that the CD molecules can move along the polycations using the repulsive force between the hydrophobic CD cavities and the positively charged guest polymer backbone.

Cucurbit[*n*]uril (CB, $n = 5-8$), a macrocycle comprising glycoluril units that has a hydrophobic cavity and polar carbonyl groups surrounding the portals, can also be used as a polypseudorotaxane precursor for CDs in many research fields.[1b] In contrast to CDs, CBs are only soluble in strongly acidic aqueous media, such that CB[6] and CB[7] form very stable inclusion complexes with protonated diaminoalkanes and methyl viologen, respectively.[7] Water-soluble polypseudorotaxanes of CB[6] and polyviologen have also been prepared using the hydrophobic and dipole−charge interactions between the cationic polymer and CB units.[8] Steinke et al. have recently reported a synthetic method for preparing CB-based polypseudorotaxanes by utilizing a 1,3-dipolar cycloaddition reaction between azide and alkyne units within the cavities of CB[6].[9] Recently, Inoue et al. reported a unique ternary complex between CB[6], CDs, and dihexaammonium;[10] however, acidic conditions are required for its formation due to poor CB solubility in nonacidic media. To achieve our goal of producing a multifunctional supramolecular material that is stable in solution, it is essential to maintain good water solubility without dethreading either the CD or CB units over a wide range of pH. In this study, we synthesized a diblock polypseudorotaxane consisting of two independent inclusion complexes, CB[7]/*N*,*N*′-(3-phenylenebis(methylene)dipropargylamine (PMPA) and 2,6-*O*-dimethyl β-CD (DM-β-CD)/α,ω-bisazidopropylene glycol 400 (PPG-N_3, M_n of PPG = 400) [2]pseudorotaxanes, using Cu(I)-catalyzed Huisgen [2 + 3] dipolar cycloaddition (also known as "click" reaction). The pH-responsive properties of this polypseudorotaxane were investigated at pH 2 and 11 to determine whether the CB[7] units move in response to pH changes in a manner similar to that observed for CD−polycation polypseudorotaxanes.[5,6]

The [2]pseudorotaxane precursors, PMPA and PPG-N_3 (Figure 1), were synthesized according to previously reported methods with some modifications.[9b,11,12] PMPA was mixed with CB[7] (PMPA:CB[7] = 1:1.3) in D_2O at pH 5, and the [2]pseudorotaxane formation was monitored by ^{1}H NMR and MALDI-TOF mass spectrometry. The ^{1}H NMR spectra of PMPA display aromatic signals ($\delta = 7.5-7.4$) that are split into three peaks and shifted to higher field ($\delta = 7.0$, 6.7, and 6.0) upon rotaxanation.[12] Accompanying the change in the ^{1}H NMR spectra is the appearance of a base peak in the MALDI-TOF mass spectrum at $m/z = 1377.7$, indicating 1:1 complexation of PMPA and CB[7].[12] PPG-N_3 and DM-β-CD, dissolved together in water at pH 7 (PPG-N_3:DM-β-CD = 1:1), also produced ^{1}H NMR spectra with split signals for the PPG methyl resonance ($\delta = 1.1-0.9$).[12] Cross-peaks between the C(3)H protons of DM-β-CD and the PPG methyl group were observed in the 2D-ROESY NMR spectra, further supporting the conclusion that DM-β-CD is threaded onto PPG-N_3.[12]

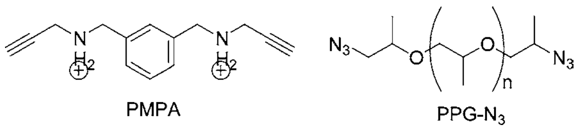
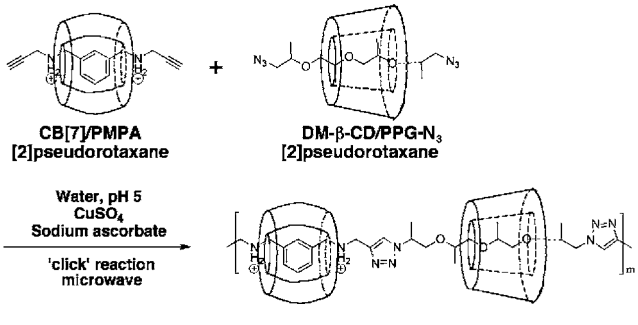


Figure 1. Structures of the PMPA and PPG-N_3 diblock precursors.

The two [2]pseudorotaxane subunits (PMPA:CB[7] = 1:1.1 and PPG-N_3:DM-β-CD = 1:1.8) were co-dissolved in water at pH 5. $CuSO_4$ and sodium ascorbate solutions were then added, producing a yellow reaction mixture due to Cu(II) reduction. The mixture was vigorously shaken and heated in a microwave for 30 min to accelerate the "click" reaction (Scheme 1). The polypseudorotaxane product was characterized by ^{1}H NMR spectra in D_2O at pH 2 after purification by dialysis against water at pH 5. Signals attributable to CB[7], DM-β-CD, the PMPA phenylene

Scheme 1. "Click" Polymerization of Two Different [2]Pseudorotaxane Blocks



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group, and PPG were all observed. The alkynyl peak of PMPA ($\delta = 2.9$) had notably disappeared, whereas a new peak attributed to the triazole group was observed at $\delta = 8.2$ (Figure 2). These results indicate that the "click" reaction between the two [2]pseudorotaxanes proceeded successfully. Threading of CB[7] and DM-β-CD onto the polymer backbone was confirmed by the ^{1}H NMR and 2D-ROESY NMR. The aromatic PMPA signals were still split in the ^{1}H NMR spectrum after the reaction (Figure 2), indicating that the PMPA phenylene groups were still included in the cavity of the CB[7] units. The 2D-ROESY NMR spectra also displayed cross-peaks between the C(3)H of DM-β-CD and the PPG methyl groups (Figure 3). Taken together, these results suggest that the isolated product is a polypseudorotaxane containing both CB[7] and DM-β-CD units.

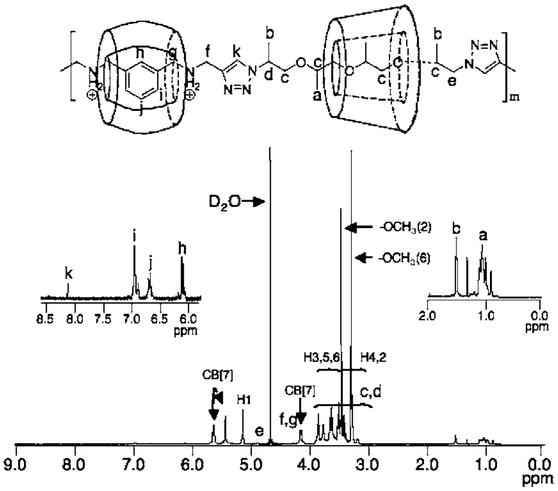

Figure 2. ^{1}H NMR spectrum of the polypseudorotaxane synthesized via "click" reaction in D_2O at pH 2.

MALDI-TOF mass spectrometry was performed to further characterize the polypseudorotaxane product. Detectable peaks were seen in the range of *m*/*z* 2368−24 444, with an interpeak spacing of 1100−1200. Since the molecular weight of CB[7] and DM-β-CD are 1163 and 1331, respectively, the peak spacing values were smaller than that of each intact [2]pseudorotaxane precursor block. Although these spacing values was not identified, the number of combined [2]pseudorotaxane units were estimated to be ≤18. The CB[7]:PMPA and DM-β-CD:PPG stoichiometries were calculated to be 1:1 and 1:1.7, respectively, based on ^{1}H NMR integration. Since these ratios were similar to the feed ratio of each host and guest, "click" polymerization using two different kinds of [2]pseudorotaxane precursors can proceed successfully without dethreading either the CB[7] or DM-β-CD subunits. In other words, the "click" polymerization makes it possible to maintain water solubility of the polypseudorotaxane.

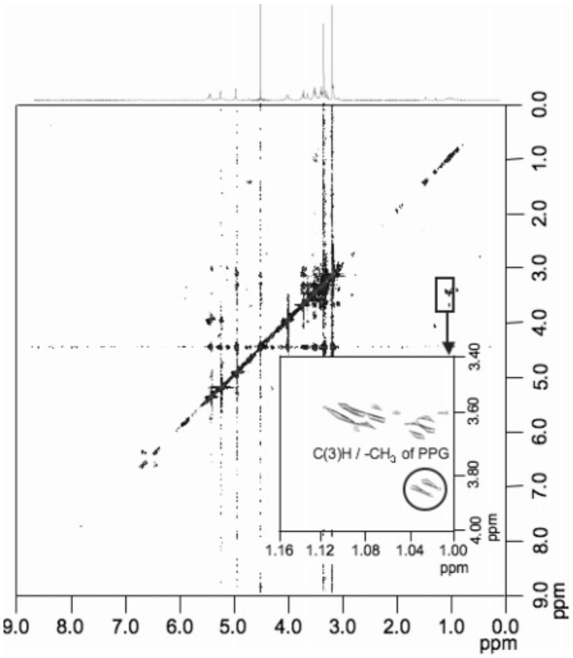

Figure 3. Two-dimensional-ROESY NMR spectrum of the polypseudorotaxane in D_2O at pH 2.

The CB[7] units in the polypseudorotaxane are located over the phenylene group in water at pH 2 (Figure 2) due to hydrophobic and charge−dipole interactions,[8] whereas the DM-β-CD units are located over the PPG units. These results show that the polypseudorotaxane structure is maintained in acidic aqueous media even in the absence of terminal endcaps. This raises the question of how deprotonation of the PMPA secondary amines may affect the position and retention of both CB[7] and DM-β-CD. To establish the location of CB[7] and DM-β-CD at high pH, the ^{1}H NMR spectrum was recorded at pH 11 and compared with the

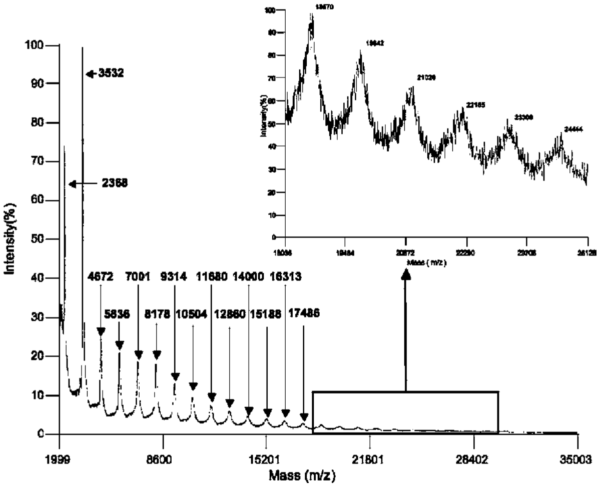

Figure 4. MALDI-TOF mass spectrum of the polypseudorotaxane.

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[12] See Supporting Information.

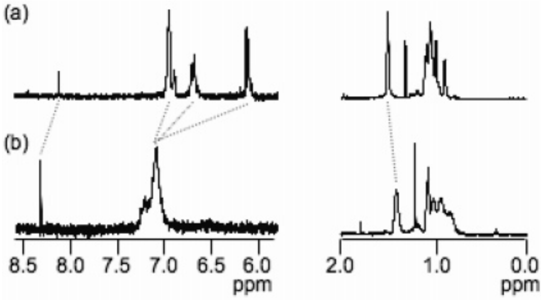

Figure 5. ^{1}H NMR spectrum of the "click" polypseudorotaxane at pH 2 (a) and 11 (b).

spectrum at pH 2 (Figure 5). At pH 11, a broad peak attributed to the phenylene group was observed at $\delta = 7.3-7.0$ compared to the three split peaks observed at pH 2 ($\delta =$ 7.0, 6.7, and 6.2) (Figure 5a and b). The triazole C(5)H signal was shifted to lower field ($\delta = 8.1$ and 8.3 at pH 2 and 11, respectively). Inspection of the PPG resonances indicated that the signal assigned to the methyl group next to the triazole group was also shifted to higher field ($\delta = 1.6$ and 1.4 at pH 2 and 11, respectively). In addition, the peaks attributed to the other PPG methyl groups were slightly broadened and shifted toward higher field. On the basis of these findings, we propose that the CB[7] units move toward the PPG units near the triazole group when the PMPA unit is deprotonated; however, the DM-β-CD units remains located on the PPG block regardless of pH. This conclusion is supported by the results of 2D-ROESY NMR at pH 11; these spectra display the same cross-peaks between the C(3)H proton of DM-β-CD and the methyl peak of PPG as were observed at pH 2.[12] Thus, it is clear that the polypseudorotaxane structure is maintained in both alkaline and acidic media. Given the properties of the CB[7]/PMPA precursor, it is a remarkable finding that the diblock polypseudorotaxane produced by the "click" reaction is soluble in D_2O and retains its rotaxanated structure even under alkaline conditions where the CB[7]/PMPA interaction is destroyed. Indeed, a polypseudorotaxane having only CB[7] units prepared by the same "click" polymerization method displayed extremely low solubility at pH 11 (data not shown). The DM-β-CD/PPG units, therefore, play an important role in this material by increasing the solubility of the polypseudorotaxane under alkaline conditions and serving as a noncovalent blocking group that enables the pH-responsive movement and retention of CB[7] across a wide range of pHs (Figure 6).

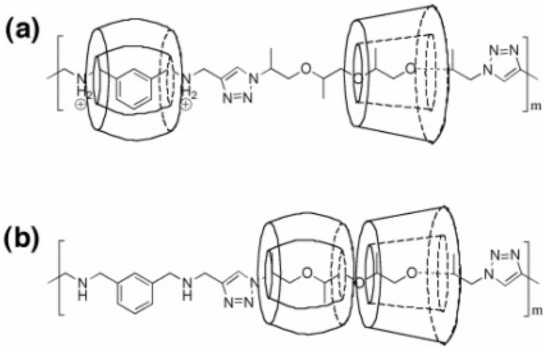

Figure 6. Proposed location of CB[7] and DM-β-CD at pH 2 (a) and 11 (b).

In conclusion, a polypseudorotaxane having both CB[7] and DM-β-CD units was synthesized using the "click" reaction. The polypseudorotaxane produced is soluble in water at pH 11, retains both the CB[7] and DM-β-CD units on the guest polymer without dethreading and enables the movement of the CB[7] units along the guest polymer in response to pH.

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Supporting Information Available: Experimental methods, ^{1}H NMR spectra of PMPA, PPG-N_3, [2]pseudorotaxanes, MALDI-TOF mass spectrum of CB[7]/PMPA−[2]pseudorotaxane, and 2D-ROESY NMR spectrum of polypseudorotaxane at pH 11. This material is available free of charge via the Internet at http://pubs.acs.org.

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