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Dynamic Switching between Single- and Double-Axial Rotaxanes Manipulated by Charge and Bulkiness of Axle Termini

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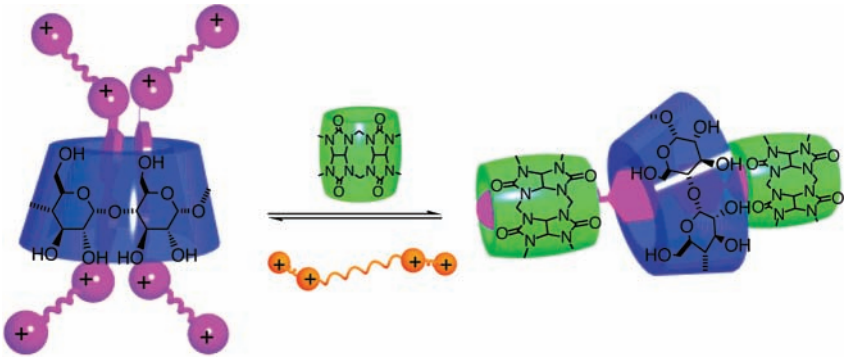
ABSTRACT



Twin-axial [3]pseudorotaxanes, in which two multicharged axles simultaneously thread through the γ-CD cavity, were formed for the first time in solution. The twin-axial [3]pseudorotaxane was converted exclusively to a CB [6]-stoppered [4]pseudorotaxane by the addition of CB[6] but regenerated from the [4]pseudorotaxane by the addition of spermine, implementing an unprecedented switching of single/twin-axial rotaxanation.

The design and construction of functional rotaxanes have received much attention in recent years.[1] Shuttling of the wheel component along the axle, controlled by external stimuli such as temperature, pH, ion, photon, and electron,[2] renders rotaxanes a promising element of molecular devices and machines.[3] Here we demonstrate that one of the axles in a twin-axial [3]pseudorotaxane can be moved in and out of the wheel by changing the electronic and steric nature of

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the axle termini to implement an unprecedented *switching of rotaxanation*.

Cyclodextrins (CDs), macrocyclic oligosaccharides possessing versatile binding abilities in aqueous solution,[4] were employed as wheel components for rotaxanation[5] with axles **1**−**6** (Figure 1). Addition of α- or *β*-CD to aqueous solutions

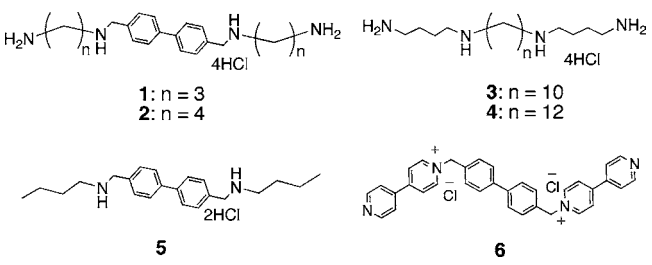

Figure 1. Axle molecules.

of **1**−**6** resulted in broadening or splitting of the NMR signals of the axle protons which appeared at lower field (Figure 2, spectra b and c). This result indicates that each molecule forms the corresponding [2]pseudorotaxane **7** that relatively slowly equilibrates with free α- or *β*-CD by the electrostatic trapping mechanism proposed by Harada et al.[5c] Unexpectedly, twin-axial [3]pseudorotaxanes **8**, in which two axles are interlocked with one wheel, were formed upon addition of *γ*-CD to aqueous solutions of **1** and **2**. As shown in Figure 2d, discrete sets of peaks assignable to interlocked **2** appear at higher fields with accompanying strong NOE correlations with the interior protons of *γ*-CD (see Figures S1 and S2 in the Supporting Information).[6] The stoichiometry of **2**/*γ*-CD in **8** was determined as 2:1 by integrating the relevant NMR signals.

Although the *γ*-CD cavity is well-known to have an ability to simultaneously accommodate two guests,[7] the first [3]rotaxanes with two axles sterically interlocked onto one *γ*-CD have been synthesized very recently by Anderson et al.[8a] Stoddart et al. have reported pseudorotaxanes comprising

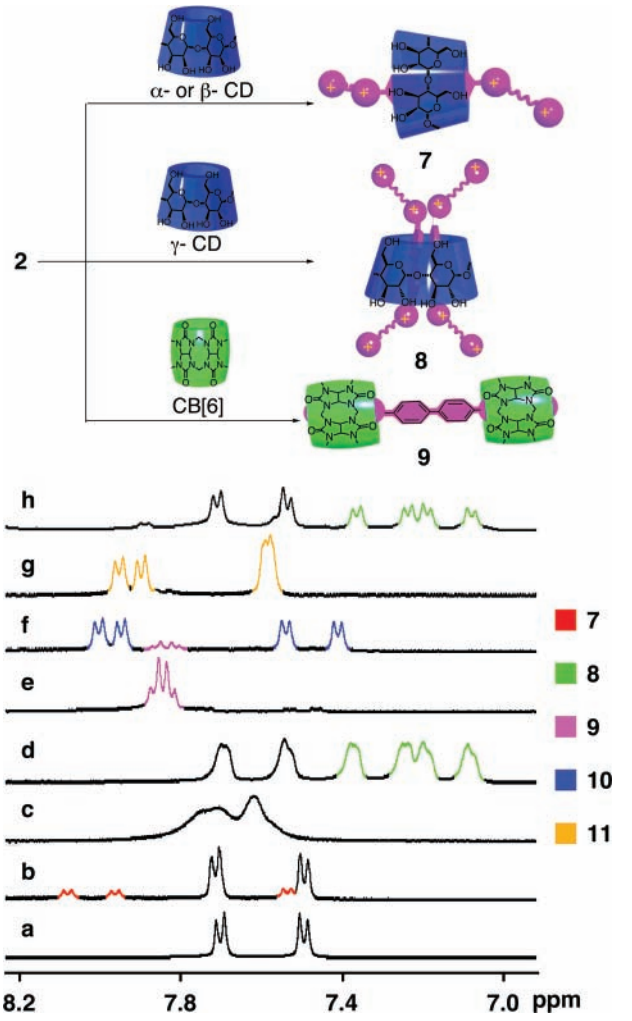

Figure 2. ^{1}H NMR spectra of equilibrated D_2O solutions of (a) 10 mM **2**, (b) 10 mM **2** + 80 mM α-CD, (c) 10 mM **2** + 10 mM *β*-CD, (d) 10 mM **2** + 10 mM *γ*-CD, (e) 10 mM **2** + 20 mM CB[6], (f) 5 mM **2** + 5 mM *β*-CD + 10 mM CB[6], (g) 5 mM **2** + 5 mM *γ*-CD + 10 mM CB[6], and (h) solution g + 20 mM spermine hydrochloride.

two or more axles in the solid state, which form fast exchange complexes in solution.[8b] We were therefore encouraged to explore the detailed formation mechanism of these unprecedented twin-axial [3]pseudorotaxanes in solution. Crucially, axle **5** gave no [3]pseudorotaxane with *γ*-CD. [3]Pseudorotaxane **8** was readily dissembled by adding Na_2CO_3 but regenerated by adding DCl. These observations reveal that the origin of the [3]pseudorotaxane formation is electrostatic entrapping in nature. This is further supported by the fact that **6** forms a rapidly exchanging complex with *γ*-CD, while protonated **6** quantitatively yields a [3]pseudorotaxane (Figure S4).[6] In sharp contrast, *γ*-CD gave no pseudorotaxane with axle **3** or **4**, in which the charged groups are linked to a less bulky, flexible alkyl rod. These observations indicate that an elegant complementarity, or a critical balance, of the terminal charge, the rod geometry, and the cavity size contributes to the formation of twin-axial [3]pseudorotaxanes.

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Thus, the strong electrostatic repulsion between the charged termini located at the same portal prevents simultaneous dethreading of the axles from the CD cavity, while the sequential dethreading is impeded as the partner axle narrows the tunnel.

The simultaneous interlocking of two axles in the same macrocycle provides a compelling microenvironment to greatly promote the intimate interaction between axles, and therefore endow them with unique properties. Indeed, the formation of **8** leads to a pronounced bathochromic shift in UV−vis spectrum (Figure S6) and even strong excimer fluorescence[9] in solution ($\lambda_{max} = 364$ nm, $\tau = 21.4$ ns) for the covalently unbound biphenyls (Figures S7 and S8).

Treatment of **2** with 2 equiv of cucurbit[6]uril (CB[6]), a macrocyclic host with strong affinity to alkanediammoniums,[10] gave a dumbbell-shaped complex **9**. Intriguingly, when CB[6] was added to a 1:1 mixture of **2** and γ-CD, the proton signals of [3]pseudorotaxane **8** disappeared before sampling for NMR analysis (Figure 3), and instead signals

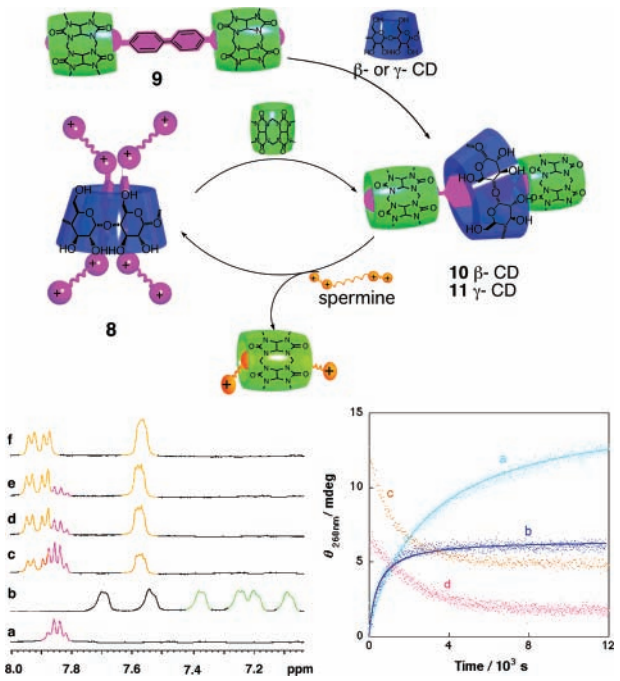

Figure 3. (Left) ^{1}H NMR spectra of (a) 10 mM **9**, (b) 10 mM **2** + 10 mM γ-CD, and time-dependent ^{1}H NMR spectral changes after adding 20 mM CB[6] to solution b: (c) 5 min, (d) 25 min, (e) 45 min, and (f) 8 h after the addition. (Right) Time-dependent circular dichroism intensities after adding (a) 0.7 mM β-CD, (b) 0.7 mM γ-CD to an aqueous solution of 0.7 mM **9**, and 3 mM spermine hydrochloride to (c) solution a after equilibration, and (d) solution b after equilibration. The solid lines show the results of curve fitting analysis, assuming the second-order kinetics.

assignable to a 55:45 mixture of **9** and CB[6]-stoppered [4]pseudorotaxane **11** emerged. Molecular model examinations suggest that dual CB[6] complexation with the diamine termini of **8** on the same side of γ-CD causes severe steric hindrance, and hence one of the axles in **8** is inevitably liberated upon complexation with CB[6], leading to the decomposition of the twin-axial pseudorotaxane structure. As shown in Figure 3c−f, the amount of **11** in the resultant mixture gradually grew at the expense of **9**, and eventually the equilibrium was reached after several hours to exclusively give **11** from the dynamic library of free and complexed species of **2**, γ-CD, and CB[6].

[4]Pseudorotaxanes **10** and **11** are efficiently formed in a dynamic manner by adding CDs to an aqueous solution of **9**. However, this rotaxanation obviously involves multistep equilibria consisting of decomplexation of CB[6] from **9**, threading of CDs, and stoppering with CB[6] (Chart S1),[6] since CB[6] is too bulky to pass through the CD cavity. We investigated the dynamic behavior of rotaxanation by circular dichroism (Figure 3, right) and ^{1}H NMR spectroscopy (Figure S14).[6] The observed rate constant (k_{obs}), determined by assuming the second-order kinetics, is much faster for **11** (3.07 M^{-1} s^{-1}) than for **10** (0.45 M^{-1} s^{-1}). This seems reasonable since γ-CD has a larger cavity and hence facilitates the charged termini to pass through.

The highly efficient [4]pseudorotaxane formation prompted us to further elucidate their complexation affinities. As shown in Table 1, the equilibrium constants for 1:1 complexation

Table 1. Association Constants of CDs with **2** and **9**

guest	α-CD	β-CD	γ-CD	
	K (M^{-1})	K (M^{-1})	K_1 (M^{-1})[a]	K_2 (M^{-1})[b]
2	2.5	600	18	320
9[c]	n.d.	15400	26900	

[a] For 1:1 complex formation. [b] For 1:2 host−guest complexation from 1:1 complex. [c] Determined by NMR measurement.

of **9** with β- and γ-CD, giving **10** and **11**, are strikingly larger than those for the complexation of **2** with the same hosts by factors of 26 and 1500, respectively. Such a dramatic enhancement of binding affinity due to the presence of CB[6] suggests that CD and CB[6] nicely cooperate to tightly hold the multicomponent entity together, for which the axle-promoted multipoint hydrogen-bonding interactions between the hydroxyl groups on the CD rims and the carbonyl groups of CB[6] are most likely to be responsible.

The chronologically regulated switching of rotaxanation with distinct strength of driving forces can be used for controlled entrapping or release of components in pseudorotaxanes and should enable this system to have wide potential applications, particularly in view of the versatile functions of CDs.[11] To exemplify this view, we propose a

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new strategy for swapping the axle of CD-rotaxanes on the basis of the above phenomena. As shown in Figure 4, the

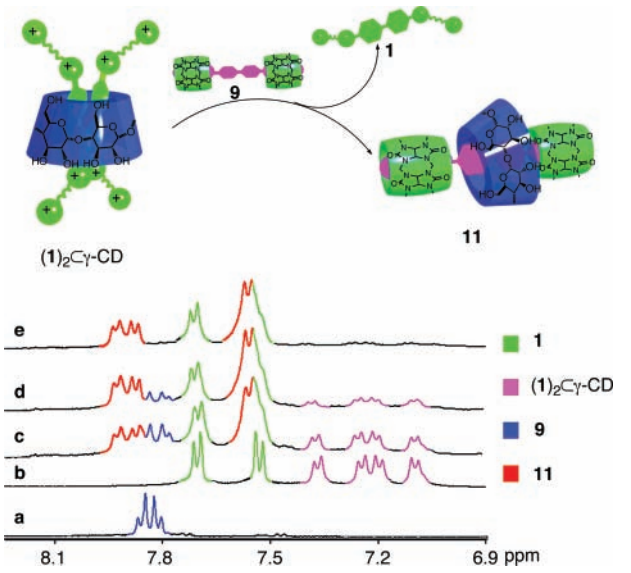

Figure 4. ^{1}H NMR spectra of D_2O solutions containing (a) 10 mM **9,** (b) 10 mM **1** + 10 mM γ-CD, and ^{1}H NMR spectra after adding 10 mM **9** to a mixture of 10 mM **1** and 10 mM γ-CD: (c) 25 min, (d) 60 min, and (e) 4 h after the addition.

addition of **9** to a mixture containing γ-CD and **1** led to a gradual increase of signals of the [4]pseudorotaxane **11** at the expense of the [3]pseudorotaxane $\mathbf{1}_2\subset\gamma$-CD and the dumbbell **9**. The switching from $\mathbf{1}_2\subset\gamma$-CD to **11** was accomplished after 4 h to give merely **11** and free **1**. Unlike the fast equilibrium normally observed in competitive complexation processes, **1** is allowed to be completely released from the CD cavity in a sustained manner. A distinct possibility stemming from this observation is to controllably release CD-encapsulated materials, or remove CDs from solution systems after they have been effected by adding solid absorbent loaded with the dumbbell **9**.

Conversely, the entrapped CD can be released from [3]pseudorotaxane by the treatment with spermine, whose binding affinity with CB[6] is 2 orders of magnitude higher than that of 1,4-butanediamine.[12] Thus, upon addition of spermine, the bulky stoppers in **11** can be dynamically removed to release the entrapped γ-CD (Figure 3) and regenerate [3]pseudorotaxane **8** (Figure 2h).

In summary, we have demonstrated for the first time the formation of twin-axial [3]pseudorotaxanes in solution. Adjusting the electrostatic and steric nature of the axle termini led to a chronological switching of rotaxanation between the twin-axial [3]pseudorotaxane and the CB[6]-stoppered [4]pseudorotaxane. This supramolecular rearrangement, being tunable by manipulating the external effectors, such as pH, CB[6], and spermine, offers attractive prospects for applications to dynamic devices and smart materials, as well as for controlled release and delivery.[13]

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Supporting Information Available: Synthesis and characterization data of **1**−**5**, the NMR, CD, UV−vis, and fluorescence spectra of pseudorotaxanes. This material is available free of charge via the Internet at http://pubs.acs.org.

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