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Homo- and Hetero-[3]Rotaxanes with Two π-Systems Clasped in a Single Macrocycle

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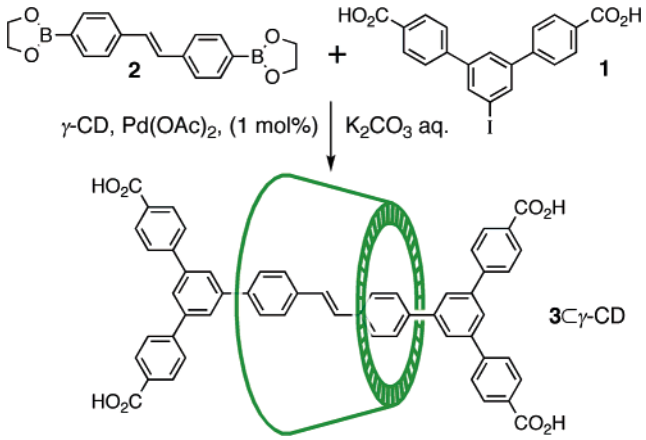
Rotaxane formation is a versatile approach to the encapsulation of dyes: a dumbbell-shaped dye, locked inside the cavity of a macrocycle, is shielded from the external environment leading to desirable changes in the properties, such as enhanced chemical stability and enhanced fluorescence efficiency.[1,2] Here we extend this concept to systems in which two π-systems are threaded through the same macrocycle to generate a [3]rotaxane. Although numerous rotaxanes have been synthesized,[3] to the best of our knowledge there are no previous examples of [3]rotaxanes consisting of two dumbbells threaded through the same macrocycle. It is well-known that large macrocycles such as γ-cyclodextrin, γ-CD,[4,5] cucurbit-[8]uril,[6] and crown ethers[5] can accommodate two threaded guests, but these labile inclusion complexes have not previously been elaborated into rotaxanes. This [3]rotaxane architecture provides a way of encapsulating an aggregate of two π-systems, which may be the same or different, even when such aggregates do not form in free solution. Here we report the synthesis of a hetero-[3]rotaxane with one stilbene and one cyanine dye threaded through the macrocycle, which exhibits quantitative energy transfer between the two encapsulated guests.

The synthesis of a [3]rotaxane with two dumbbells threaded through the same macrocycle requires the use of a large macrocycle, which in turn requires the use of very bulky stopper groups to prevent unthreading. We chose γ-CD as the macrocycle and iodoterphenylenedicarboxylic acid **1** as the stopper. Suzuki coupling of this stopper with stilbene diboronicacid **2** in the presence of excess aqueous γ-CD gave the [2]rotaxane **3**$\subset\gamma$-CD in 17% yield (Scheme 1).[2] The calculated van der Waals surface of this [2]rotaxane (Figure 1a) shows that it has a substantial cavity, and UV−vis titrations reveal that it has a phenomenal affinity for hydrophobic guests in aqueous solution. For example [2]rotaxane **3**$\subset\gamma$-CD binds cyanine dye **4a** with an association constant of 1.0 $\pm$ 0.2 $\times$ 10^5 M^{-1}, whereas the binding constant of native γ-CD

Scheme 1. Synthesis of [2]Rotaxane **3**$\subset\gamma$-CD by Suzuki Coupling



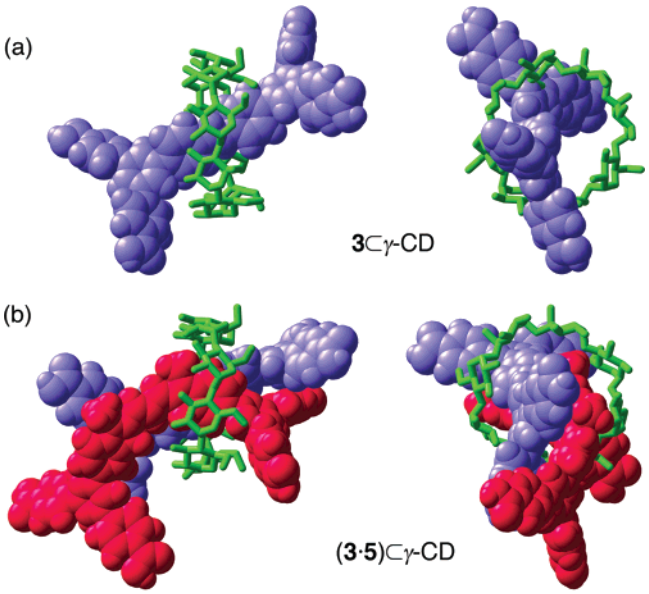
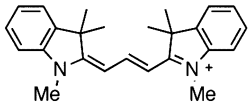


Figure 1. Orthogonal views of calculated structures of [2]rotaxane **3**$\subset\gamma$-CD (a) and [3]rotaxane (**3**·**5**)$\subset\gamma$-CD (b). The stilbene dumbbell **3** is shown in blue and the cyanine dumbbell **5** is shown in red.

under the same conditions is 87 $\pm$ 15 M^{-1}; β-CD binds even more weakly (K < 20 M^{-1}), and α-CD shows no detectable complexation with **4a**. The presence of the stilbene π-system in **3**$\subset\gamma$-CD adds a hydrophobic floor to the cavity of the cyclodextrin, leading to a 1000-fold increase in its affinity for suitably shaped guests. The threaded dumbbell also acts as a reporter, amplifying the spectroscopic changes associated with binding.



4a

The strong affinity of [2]rotaxane **3**$\subset\gamma$-CD for cyanine dye **4a** suggested that it would be possible to synthesize a hetero-[3]-rotaxane (**3**·**5**)$\subset\gamma$-CD by using the cyanine boronic acid **4b** and stopper **1** in a second round of Suzuki coupling (Scheme 2). Use of a slight excess of **1** and **4b** resulted in quantitative conversion of **3**$\subset\gamma$-CD to (**3**·**5**)$\subset\gamma$-CD, as monitored by HPLC, and the [3]-rotaxane was isolated in 18% yield. Similarly Suzuki coupling of **1** and **2** in the presence of **3**$\subset\gamma$-CD gave the stilbene−stilbene homo-[3]rotaxane **3**$_2\subset\gamma$-CD (87% yield). The cyanine dye [2]-rotaxane **5**$\subset\gamma$-CD was also synthesized from **1**, **4b**, and γ-CD, although in poor yield (11% conversion by HPLC; 2% isolated yield). In both cases, [3]rotaxane synthesis is remarkably efficient because the threaded stilbene favors the threading of a second guest, and (**3**·**5**)$\subset\gamma$-CD is easier to synthesize than **5**$\subset\gamma$-CD.

The ^{1}H NMR spectrum of (**3**·**5**)$\subset\gamma$-CD was assigned using COSY, NOESY, ROESY, and HSQC techniques. The pattern of

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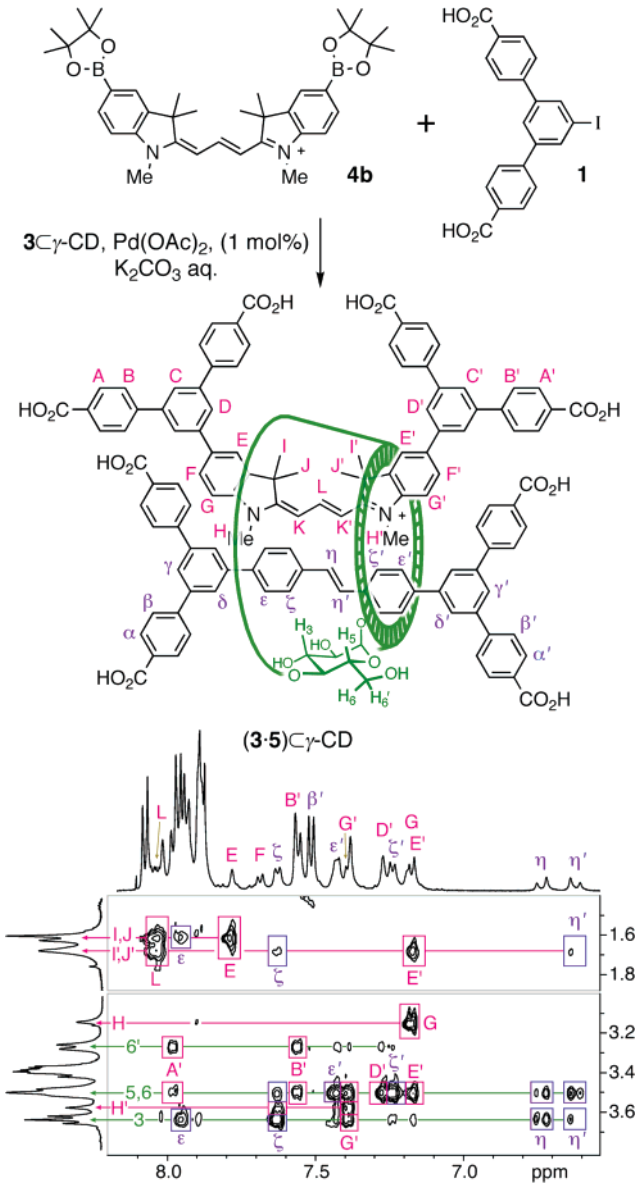
Scheme 2. Synthesis of (**3**·**5**)⊂γ-CD, Showing Part of the ^{1}H NMR ROESY Spectrum of the [3]Rotaxane (d_6-DMSO, 500 MHz, 343 K)



NOEs between the three components (Scheme 2) shows that one end of the cyanine dye resides near the narrow 5/6-rim of the cyclodextrin. Thus protons H5/6 of the γ-CD show NOEs to protons A′, B′, D′, E′, G′, I′, and J′ at one end of the cyanine dye **5**, while H3 at the other rim of the γ-CD shows NOEs to G′, I′, J′, I, and J which are near the same end of the dye. The stilbene component **3** is more centrally located on the cyclodextrin, and both central stilbene protons η and η' show NOEs to H3 and H5/6 of the γ-CD. The observation of NOEs from proton ζ of the stilbene to protons I′/J′ and H′ confirms this off-set arrangement.

The absorption and emission spectra of (**3**·**5**)⊂γ-CD are compared with those of the two analogous [2]rotaxanes **3**⊂γ-CD and **5**⊂γ-CD in Figure 2. The ground-state interaction between the two chromophores in (**3**·**5**)⊂γ-CD appears to be weak; the shapes of the absorption and emission bands are almost identical, although all the bands are shifted to longer wavelength by about 10 nm in

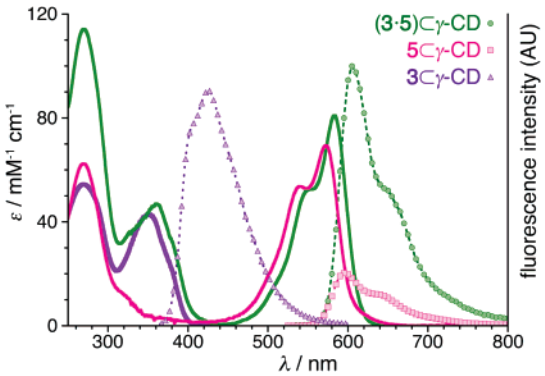


Figure 2. Absorption and fluorescence spectra of rotaxanes **3**⊂γ-CD (blue), **5**⊂γ-CD (red), and (**3**·**5**)⊂γ-CD (green) in aqueous sodium phosphate buffer (pH 11.4). The areas of the fluorescence spectra (dotted lines) are scaled in proportion to the fluorescence quantum yields.

the [3]rotaxane. However excitation of the stilbene component of (**3**·**5**)⊂γ-CD results in quantitative energy transfer to the cyanine dye, and emission from the cyanine, as demonstrated by the lack of stilbene-type emission at 430 nm when (**3**·**5**)⊂γ-CD is excited at 350 nm and by the fact that the excitation spectrum of (**3**·**5**)⊂γ-CD is superimposable with its absorption spectrum (see Supporting Information). The fluorescence quantum yield of the [3]rotaxane (**3**·**5**)⊂γ-CD ($\Phi_f = 0.56$) is substantially higher than that of the [2]rotaxane **5**⊂γ-CD ($\Phi_f = 0.12$) presumably because of restricted conformational freedom

In conclusion, the high affinities of [2]rotaxanes such as **3**⊂γ-CD and **5**⊂γ-CD for a second threaded guest provides an efficient route to [3]rotaxane synthesis. It should be possible to synthesize a variety of homo- and hetero-[3]rotaxanes and polyrotaxanes using this chemistry. The binding behavior of **3**⊂γ-CD and **5**⊂γ-CD also suggests that they may be useful in sensors.

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Supporting Information Available: Details of synthesis, UV−vis titrations, 2D NMR analysis, and fluorescence spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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