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An Hermaphrodite [2]Rotaxane: Preparation and Analysis of Structure

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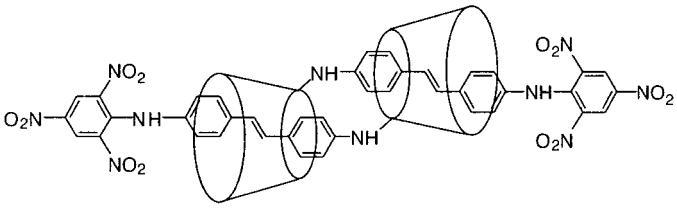
ABSTRACT



The pictured rotaxane is assembled in water by capping a substituted cyclodextrin composed of the wheel and axle components. The unusual dimeric structure of the rotaxane reflects the thermodynamics of the assembly process. In *N*,*N*-dimethylformamide, the corresponding monomer is the predominant product.

A few decades ago, interlocked molecules such as rotaxanes and catenanes existed only in the minds of some imaginative chemists.[1] Now, they are commonly used in supramolecular chemistry and are poised to become key components of the revolution in microelectronics and nanotechnology.[2,3] However, in order for their full potential to be realized, reliable and efficient methods are required for the design, synthesis, and characterization of a range of the interlocked species. The name rotaxane is derived from the Latin *rota* for wheel and *axis* for axle. Examples of rotaxanes composed of various types of molecular wheels and axles, in a range of combinations, have been reported.[3,4] Early last year, Stoddart et al.[5] described the synthesis of a new type of [2]rotaxane (**I**) consisting of a doubly capped symmetric dimer of a molecule possessing both a DB24C8 coronand and a dibenzylamine moiety. In recent months, there have been three other reports of the synthesis of *hermaphrodite* rotaxanes, from molecules possessing both the wheel and axle components, which form association complexes and are then capped to prevent dissociation.[6−8] The example reported by Sauvage and coworkers[6] involves a phenanthroline incorporated into a coronand as the wheel, another phenanthroline as the axle, and metal coordination to facilitate the assembly process to give a dimer (**I**). Harada et al.[7] used a cinnamoyl-substituted cyclodextrin to produce a rotaxane, which exists as a cyclic

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(1) For a discussion, see: van Gulick, N. *New J. Chem*. **1993**, *17*, 619−625, including the preceding pages which carry a preface to the van Gulick article by David, M. Walba (p 618) and foreword to this special issue devoted to Topology in Molecular Chemistry by Guest-Editor, Jean-Pierre Sauvage (p 617).

(2) (a) Balzani, V.; Gómez-López, M.; Stoddart, J. F. *Acc. Chem. Res*. **1998**, *31*, 405. (b) Sauvage, J.-P. *Acc. Chem. Res*. **1998**, *31*, 611. (c) Balzani, V.; Credi, A.; Raymo, F. M.; Stoddart, J. F. *Angew. Chem., Int. Ed*. **2000**, *39*, 3348.

(3) Easton, C. J.; Lincoln, S. F. In *Modified Cyclodextrins: Scaffolds and Templates for Supramolecular Chemistry*; Imperial College Press: London, 1999.

(4) (a) Dietrich-Buchecker, C. O.; Sauvage, J.-P. *Chem. Rev*. **1987**, *87*, 795. (b) Amabilino, D. B.; Stoddart, J. F. *Chem. Rev*. **1995**, *95*, 2725. (c) Nepogodiev, S. A.; Stoddart, J. F. *Chem. Rev*. **1998**, *98*, 1959. (d) Raymo, F. M.; Stoddart, J. F. *Chem. Rev*. **1999**, *99*, 1643. (e) *Molecular Catenanes, Rotaxanes and Knots: A Journey Through the World of Molecular Topology*; Sauvage, J.-P., Dietrich-Buchecker, C., Eds.; Wiley-VCH: Weinheim, 1999. (f) Wenz, G.; Wolf, F.; Wagner, M.; Kubik, S. *New J. Chem*. **1993**, *17*, 729. (g) Harada, A.; Li, J.; Kamachi, M. *J. Chem. Soc., Chem. Commun*. **1997**, 1413. (h) Vögtle, F.; Dünnwald, T.; Schmidt, T. *Acc. Chem. Res*. **1996**, *29*, 451. (i) Jäger, R.; Vögtle, F. *Angew. Chem., Int. Ed. Engl*. **1997**, *36*, 930.

(5) Rowan, S. J.; Cantrill, S. J.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *Org. Lett*. **2000**, *2*, 759.

(6) Jiménez, M. C.; Dietrich-Buchecker, C.; Sauvage, J.-P. *Angew. Chem., Int. Ed*. **2000**, *39*, 3284.

(7) Hoshino, T.; Miyauchi, M.; Kawaguchi, Y.; Yamaguchi, H.; Harada, A. *J. Am. Chem. Soc*. **2000**, *122*, 9876.

(8) Fujimoto, T.; Sakata, Y.; Kaneda, T. *J. Chem. Soc., Chem. Commun*. **2000**, 2143.

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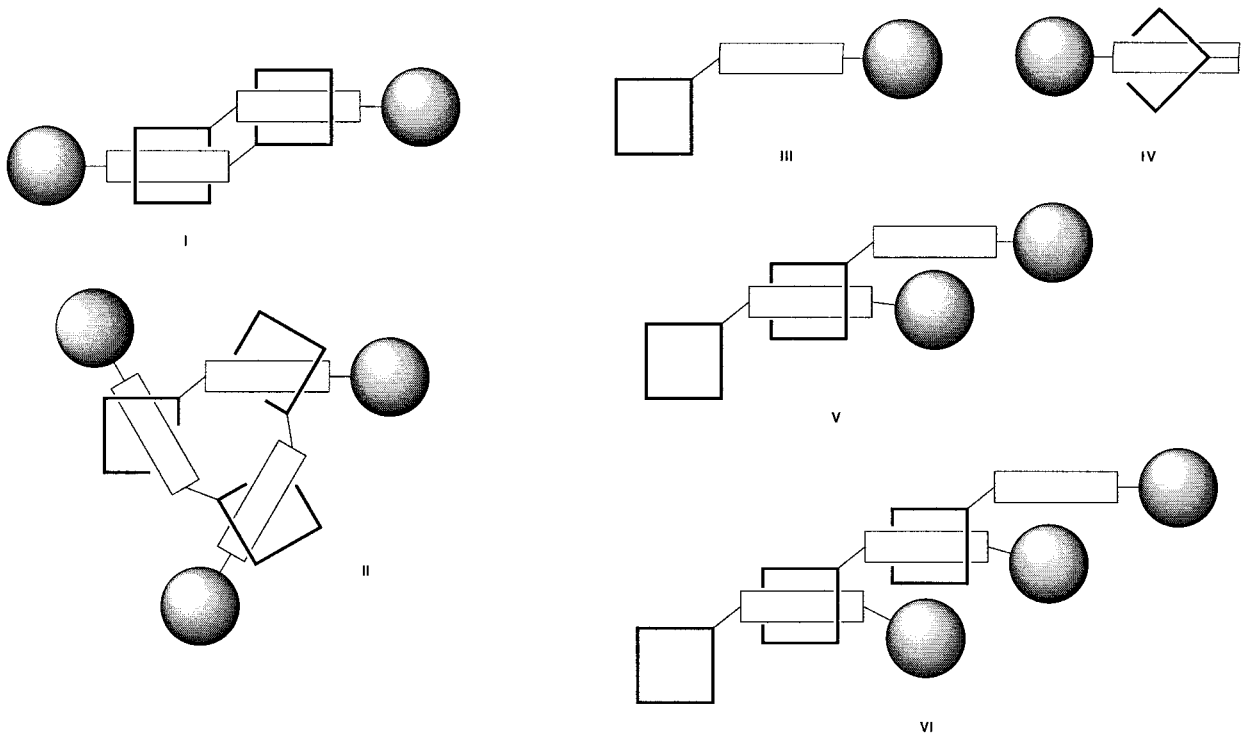
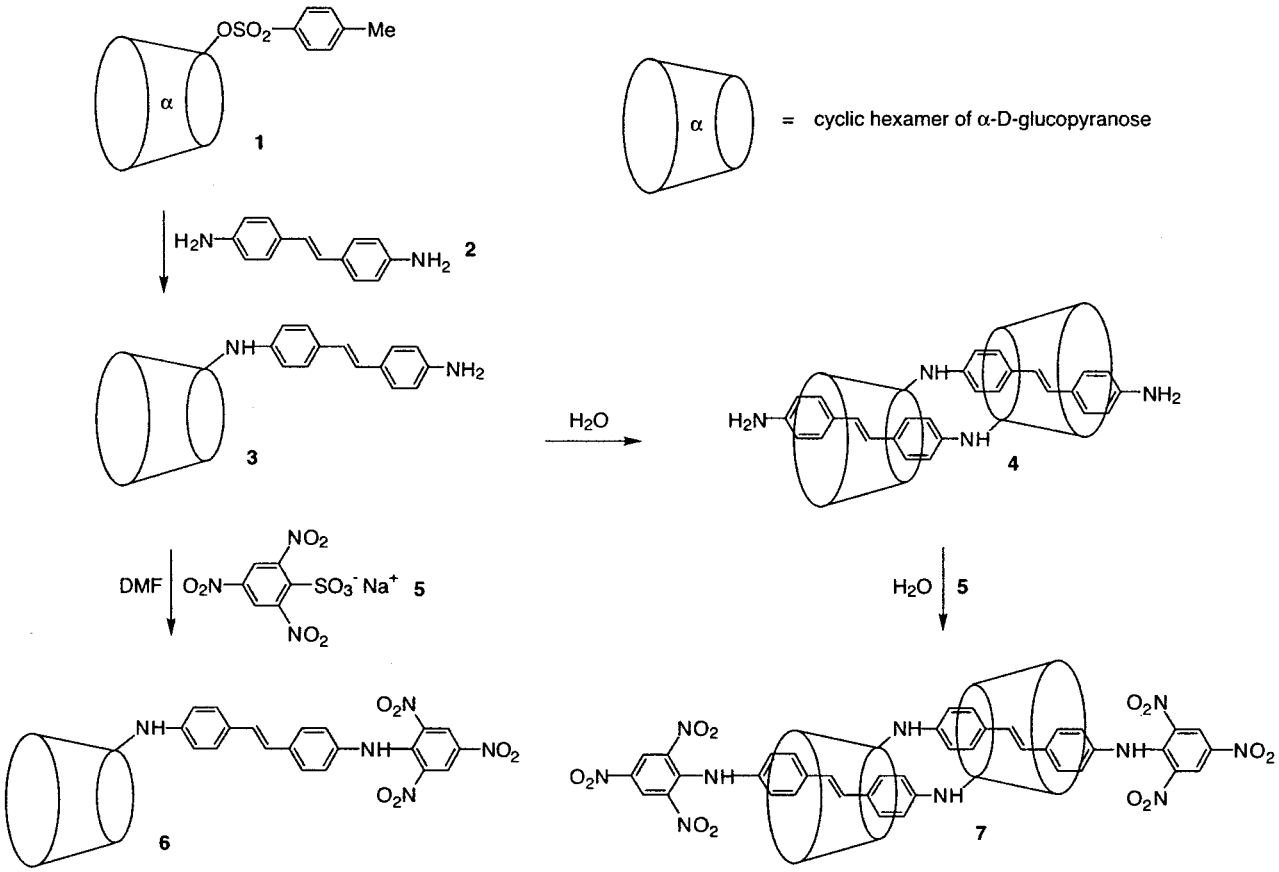


Figure 1.

Scheme 1



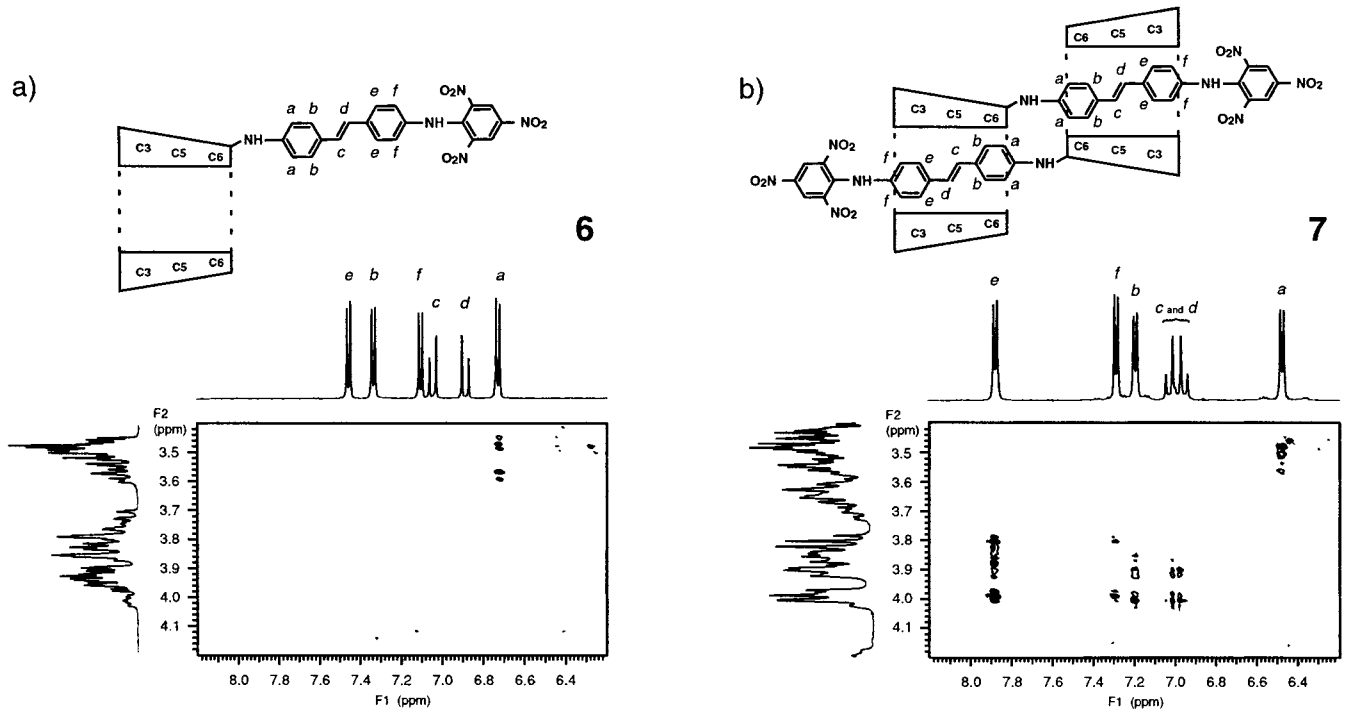


Figure 2. (a) Resonance assignments for the stilbene protons of monomer **6**, as determined using DQCOSY and ROESY NMR spectrometry, and a section of the 500 MHz ROESY NMR spectrum recorded in d_4-methanol with a mixing time of 250 ms. (b) Resonance assignments for the stilbene protons of the rotaxane **7**, as determined using DQCOSY and ROESY NMR spectrometry, and a section of the 500 MHz ROESY NMR spectrum recorded in d_4-methanol with a mixing time of 250 ms. For 500 MHz ROESY NMR spectra in a and b, resonances between δ 3.4 and 4.1 correspond to cyclodextrin protons.

trimer (**II**). In the work of Kaneda et al.,[8] a cyclodextrin was also used, but in this case a dimeric [2]rotaxane (**I**) was produced. These recent communications reflect an intense level of activity in the area and prompt us to describe our cyclodextrin-based contribution to the field.

In aqueous solution, (*E*)-4,4′-diaminostilbene **2** readily forms an inclusion complex with α-cyclodextrin. Earlier we exploited this observation to prepare [(*E*)-4,4′-bis(2,4,6-trinitrophenylamino)stilbene]-[α-cyclodextrin]-[rotaxane], by capping the stilbene **2** while complexed in α-cyclodextrin, through reaction with 2,4,6-trinitrobenzenesulfonate **5**.[9] With the stilbene moiety covalently bound to the cyclodextrin, capping could, in principle, give rise to a range of molecular structures such as **I**−**VI**, Figure 1. These possibilities were examined and the results are illustrated in Scheme 1. Substituted cyclodextrin **3** was prepared by treatment of tosylate **1**[10] with stilbene **2** and potassium iodide, in *N*-methylpyrrolidin-2-one.[11] At a concentration of 34 mM in aqueous carbonate buffer, **3** reacted with 2,4,6-trinitrobenzenesulfonate **5** to give rotaxane dimer **7** and monomer **6**, in a ratio of ca. 50:1. Dimer **7** was isolated by HPLC in 65% yield. By contrast, the analogous reaction in *N*,*N*-dimethylformamide, with cyclodextrin **3** at a concentration of 3.4 mM, afforded a mixture of monomer **6** and dimer **7**, in a ratio of ca. 25:1, from which monomer **6** was isolated by HPLC in 64% yield. Dimer **7** and monomer **6** were distinguished from each other and from stilbene **3**, tosylate **1**, and α-cyclodextrin by HPLC and TLC. Each was isolated as a single component which on TLC showed both the characteristic ultraviolet absorbance of a stilbene and the pink coloration of a cyclodextrin on exposure to acidic 1,3-dihydroxynaphthalene.

The dimeric nature of rotaxane **7** was established using MALDI-TOF mass spectroscopy, which showed a peak with *m*/*z* 2753 corresponding to the protonated molecular ion and no peaks attributable to higher oligomers. The symmetry of rotaxane **7** is reflected in the simplicity of the 1D ^{1}H NMR spectrum. The resonances corresponding to the protons of the stilbene moieties were assigned using DQCOSY and ROESY NMR spectrometry, and those assignments are shown in Figure 2b. The portion of the ROESY NMR spectrum illustrated in Figure 2b shows numerous nuclear Overhauser effect (NOE) interactions between the stilbene proton resonances and those of the cyclodextrin annulus protons (the latter between δ 3.4−4.1), consistent with the structure. By comparison, the MALDI-TOF mass spectrum of monomer **6** shows a peak with *m*/*z* 1377 corresponding to the protonated molecular ion and no peak corresponding

(9) Easton, C. J.; Lincoln, S. F.; Meyer, A. G.; Onagi, H. *J. Chem. Soc., Perkin Trans. 1* **1999**, 2501.

(10) Brown, S. E.; Coates, J. H.; Coghlan, D. R.; Easton, C. J.; van Eyk, S. J.; Janowski, W.; Lepore, A.; Lincoln, S. F.; Luo, Y.; May, B. L.; Schiesser, D. S.; Wang, P.; Williams, M. L. *Aust. J. Chem.* **1993**, *46*, 953.

(11) The method follows that reported for reactions of other amines with tosylate **1**: May, B. L.; Kean, S. D.; Easton, C. J.; Lincoln, S. F. *J. Chem. Soc., Perkin Trans. 1* **1997**, 3157.

to either a proton bound dimer (*m*/*z* 2753) or other higher oligomers. With this compound, only one of the stilbene proton resonances, assigned using DQCOSY and ROESY NMR spectrometry, shows NOE interactions with the resonances of the cyclodextrin annulus protons (Figure 2a). It is not practical to assign the cyclodextrin resonances to specific protons, due to the asymmetry of the annulus and the consequent complexity of this region of the spectrum. However, the cross-peaks in the ROESY spectrum are easily rationalized as being due to the Ha protons of the stilbene moiety and their proximity to the $C6^{A}$ protons of the cyclodextrin annulus.

The product distribution in the reactions of the substituted cyclodextrin **3** with sulfonate **5** may be attributed to complexation phenomena. Presumably, in aqueous solution, cyclodextrin **3** forms the symmetric inclusion complex **4**, where each hydrophobic stilbene moiety is included in the hydrophobic annulus of the other molecule.[12] Capping this species through reaction with sulfonate **5** then affords dimer **7** as the major product. A self-threaded species (**IV**) is not produced, probably because formation of the putative precursor self-inclusion complex is prevented by geometrical constraints. The absence of molecules with trimeric (**II**) and daisy chain[13] (**V** and **VI**) structures indicates that the corresponding inclusion complexes that would lead to these species are thermodynamically less stable than the symmetric dimer **4**, as would be expected.[3] In *N*,*N*-dimethylformamide and under the more dilute conditions used in that case, there is less tendency for inclusion complexes to form, with the result that the substituted cyclodextrin **3** instead reacts directly with sulfonate **5** to give mainly monomer **6**.

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Supporting Information Available: Experimental procedures and characterization for compounds **3**, **6**, and **7**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(12) Formation of a complex under these conditions is evident from 2D ^{1}H NMR spectroscopy, though it is not practical to assign the structure using this technique.

(13) Ashton, P. R.; Baxter, I.; Cantrill, S. J.; Fyfe, M. C. T.; Glink, P. T.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *Angew. Chem., Int. Ed.* **1998**, *37*, 1294.