

# Versatile Formation of [2]Catenane and [2]Pseudorotaxane Structures; Threading and Noncovalent Stopping by a Self-Assembled Macrocyclic

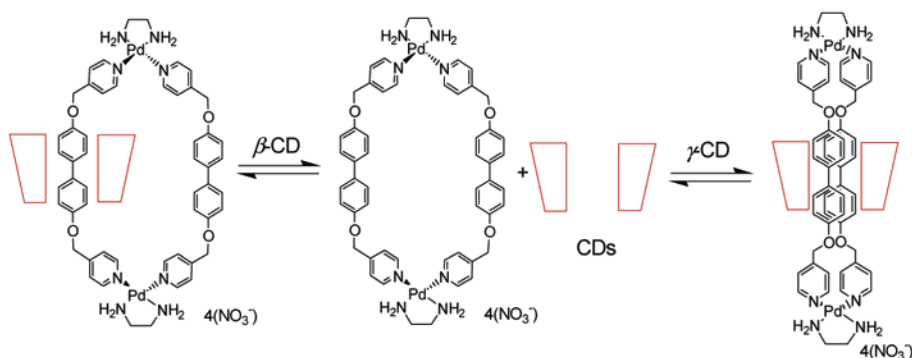
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## ABSTRACT



A self-assembled dimeric macrocycle between 4,4'-bis(4-pyridylmethoxy)biphenyl (L) and (en)Pd(NO<sub>3</sub>)<sub>2</sub> was constructed, and its interactions with cyclodextrins of different cavity size resulted in the formation of [2]catenane and [2]pseudorotaxane systems, respectively. The structures were identified by 1D and 2D NMR spectroscopy and cold spray ionization mass (CSI-MS) spectrometry.

Recently, linear motors such as myosin and kinesin and rotary motors such as bacterial flagellum and F<sub>1</sub>-ATPase have come to be recognized as distinctive examples of molecular motors found in biological systems.<sup>1</sup> Supramolecular chemistry has been extensively applied to mimic molecular devices in biological systems by aiding the creation of interlocked molecules with precise structures in high yields. Interlocked molecules<sup>2</sup> such as catenanes,<sup>3</sup> rotaxanes,<sup>4</sup> and knots<sup>5</sup> have

been studied as potential candidates for molecular devices, and there have been extensive synthetic approaches directed toward the development of molecular devices. Herein we report on new controllable systems that are composed of  $\beta$ -

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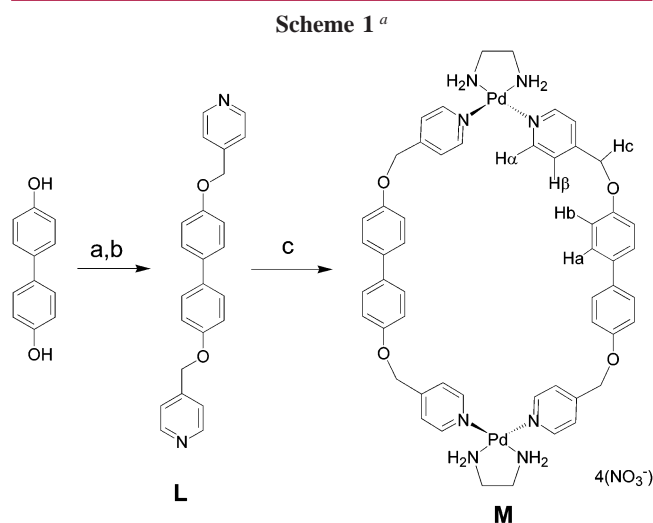
(1) (a) Special Issues-Movement: Molecular to Robotic. *Science* **2000**, 288, 79. (b) Howard, J. *Nature* **1997**, 389, 561. (c) Mooseker, M. S.; Cheney, R. E. *Annu. Rev. Cell Dev. Biol.* **1995**, 11, 633. (d) Barton, N. R.; Goldstein, L. S. B. *Proc. Natl. Acad. Sci. U.S.A.* **1996**, 93, 1735. (e) Rayment, I.; Holden, H. M.; Whittaker, M.; Yohn, C.; Lorenz, M.; Holmes, K. C.; Milligan, R. A. *Science* **1993**, 261, 58. (f) Noji, H.; Yasuda, R.; Yoshida, M.; Kinosita, K., Jr. *Nature* **1997**, 386, 299. (e) Allison, W. S. *Acc. Chem. Res.* **1998**, 31, 819.

(2) (a) Schill, G. *Catenanes, Rotaxanes, and Knots*; Academic: New York, 1971. (b) Cram, D. J.; Cram, J. M. In *Container Molecules and their Guests*; Stoddart, J. F., Ed.; RSC: Cambridge, 1994. (c) Amabilino, D. B.; Stoddart, J. F. *Chem. Rev.* **1995**, 95, 2725. (d) Hubin, T. J.; Kolchinski, A. G.; Vance, A. L.; Busch, D. H. *Adv. Supramol. Chem.* **1999**, 5, 237. (e) *Molecular Catenanes, Rotaxanes and Knots*; Sauvage, J.-P., Dietrich-Buchecker, C., Eds.; VCH-Wiley: Weinheim, 1999.

(3) (a) Leigh, D. A.; Murphy, A.; Smart, J. P.; Deleuze, M. S.; Zerbetto, F. *J. Am. Chem. Soc.* **1998**, 120, 6458. (b) Andrievsky, A.; Ahuis, F.; Sessler, J. L.; Vögtle, F.; Gudat, D.; Moini, M. *J. Am. Chem. Soc.* **1998**, 120, 9712. (c) Balzani, V.; Credi, A.; Langford, S. J.; Raymo, F. M.; Stoddart, J. F.; Venturi, M. *J. Am. Chem. Soc.* **2000**, 122, 3542.

(4) (a) Ashton, P. R.; Baxter, I.; Fyfe, M. C. T.; Raymo, F. M.; Spencer, N.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *J. Am. Chem. Soc.* **1998**, 120, 2297. (b) Brouwer, A. M.; Frochet, C.; Gatti, F. G.; Leigh, D. A.; Mottier, L.; Paolucci, F.; Roffia, S.; Wurple, G. W. *H. Science* **2001**, 291, 2124. (c) Kawaguchi, Y.; Harada, A. *J. Am. Chem. Soc.* **2000**, 122, 3797.

or  $\gamma$ -cyclodextrin (CD) and a macrocyclic complex (**M**) self-assembled by **L** and Pd(en) moieties. Depending on the cavity size of the CDs, this controllable system produces either rotaxane or catenane structures. Whereas the combination of  $\beta$ -CD and **M** leads to the formation of a [2]catenane structure, the combination of  $\gamma$ -CD and **M** results in a novel pseudorotaxane structure. As one component of the system, **M** was prepared by treating **L** with (en)Pd(NO<sub>3</sub>)<sub>2</sub> as shown in Scheme 1.<sup>6</sup>



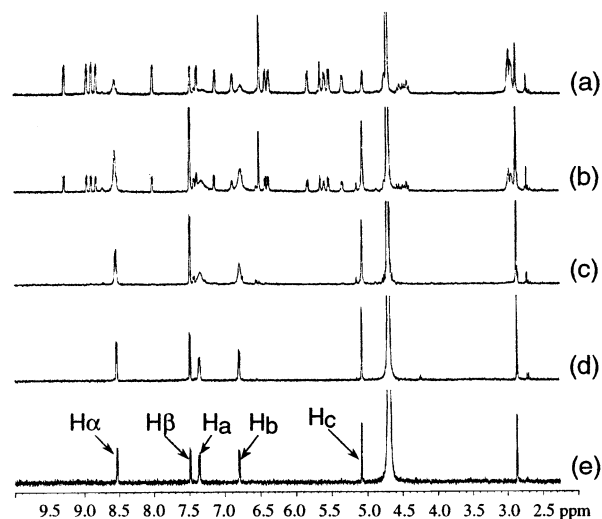
<sup>a</sup> (a) 60% NaH, DMF; (b) 4-(chloromethyl)pyridine hydrochloride, DMF; (c) (en)Pd(NO<sub>3</sub>)<sub>2</sub>, MeOH/H<sub>2</sub>O.

Because several self-assembled systems constructed by Pd(II) ions and ligand molecules having pyridine moieties in D<sub>2</sub>O have shown guest-induced or concentration-dependent reorganization behavior,<sup>7</sup> we performed <sup>1</sup>H NMR measurements at various concentrations in D<sub>2</sub>O to investigate the structure of **M** as a function of the concentration. Self-assembly of **L** and (en)Pd(NO<sub>3</sub>)<sub>2</sub> showed concentration-dependent behavior as expected. <sup>1</sup>H NMR spectra (Figure 1a) revealed the self-assembled structures of oligomers or multicomponents at relatively high concentrations (> 2 mM). Lowering the concentration gradually led to single sets of signals in <sup>1</sup>H NMR spectra, which are presumably derived from a dimeric structure (**M**). At concentrations lower than 1 mM, <sup>1</sup>H NMR spectra (Figure 1d,e) revealed the formation of a self-assembled dimeric structure as a dominant species, which was confirmed by cold spray ionization mass spec-

(5) (a) Rapenne, G.; Dietrich-Buchecker, C. O.; Sauvage, J.-P. *J. Am. Chem. Soc.* **1999**, *121*, 994. (b) Ashton, P. R.; Matthews, O. A.; Menzer, S.; Raymo, F. M.; Spencer, N.; Stoddart, J. F.; Williams, D. J. *Liebigs Ann. Chem.* **1997**, 2485. (c) Meyer, M.; Albrecht-Gary, A. M.; Dietrich-Buchecker, C. O.; Sauvage, J.-P. *J. Am. Chem. Soc.* **1997**, *119*, 4599.

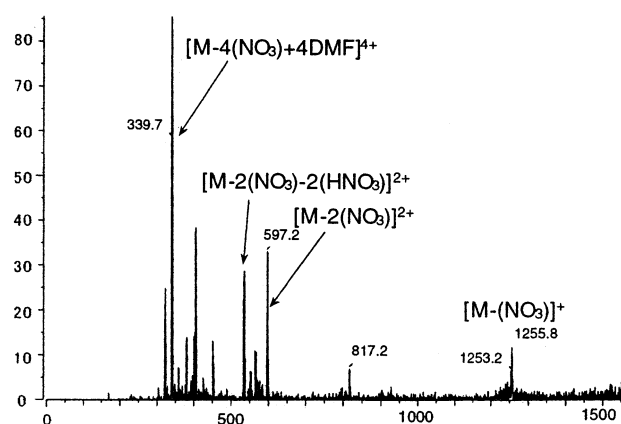
(6) The macrocyclic Pd(II) complexes were prepared by mixing the complex (en)Pd(NO<sub>3</sub>)<sub>2</sub> in H<sub>2</sub>O and equimolar amounts of **L** in MeOH, followed by the removal of solvents.

(7) (a) Fujita, M.; Sasaki, O.; Mitsuhashi, T.; Fujita, T.; Yazaki, J.; Yamaguichi, K.; Ogura, K. *Chem. Commun.* **1996**, 1635. (b) Lee, S. B.; Hwang, S.; Chung, D. S.; Yun, H.; Hong, J.-I. *Tetrahedron Lett.* **1998**, *39*, 873. (c) Ma, G.; Jung, Y. S.; Chung, D. S.; Hong, J.-I. *Tetrahedron Lett.* **1999**, *40*, 531.



**Figure 1.** Concentration-dependent <sup>1</sup>H NMR spectra (500 MHz) of **M** in D<sub>2</sub>O: (a) 4, (b) 2, (c) 1, (d) 0.3, and (e) 0.1 mM. See Scheme 1 for proton labeling.

trometry (CSI-MS). The CSI-MS spectrum shows fragments of the dinuclear Pd complex **M** (Figure 2).<sup>8</sup>



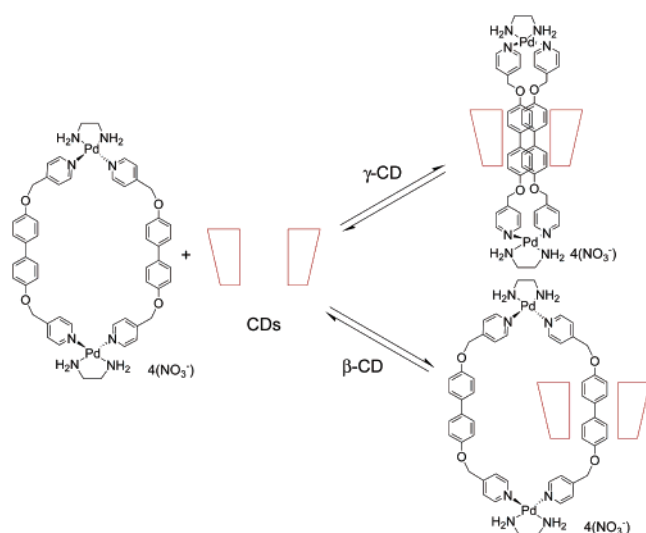
**Figure 2.** CSI-MS spectrum of the dinuclear Pd(II) complex **M**.

It has been known for many years that the cavity of  $\gamma$ -CD is sufficiently large to contain two aromatic residues simultaneously.<sup>9</sup> Therefore, we expected that the formation of a [2]pseudorotaxane would be possible upon addition of  $\gamma$ -CD to **M** (Scheme 2). Subsequently, the quantitative formation of a rotaxane-like structure between **M** and  $\gamma$ -CD was observed in the <sup>1</sup>H NMR spectra (Figure 3). The <sup>1</sup>H NMR spectrum clearly shows one set of newly emerging signals for the rotaxane-like structure (Figure 3b–e), which indicates that the equilibrium kinetics between pseudoro-

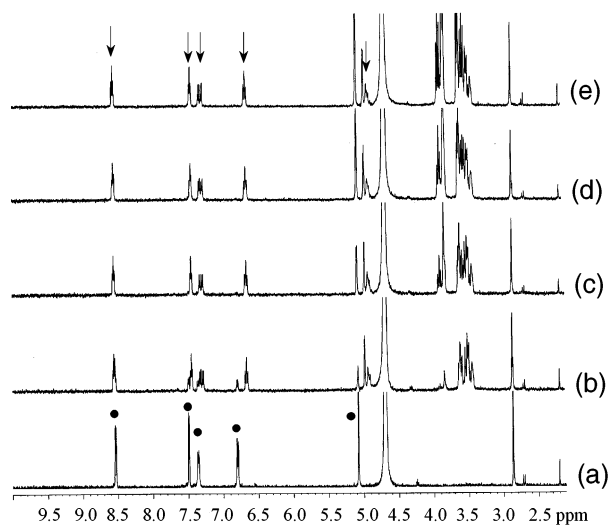
(8) **M** is dissolved in aqueous DMF solution.

(9) Kobayashi, N.; Ueno, A.; Osa, T. *J. Chem. Soc., Chem. Commun.* **1981**, 340.

Scheme 2



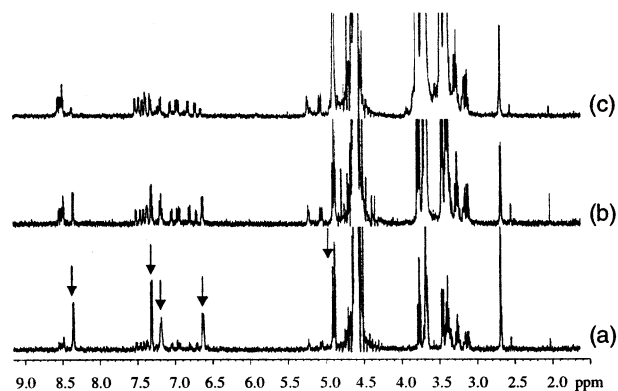
taxane and free ring **M** are slow, at 500 MHz, on the  $^1\text{H}$  NMR time scale.



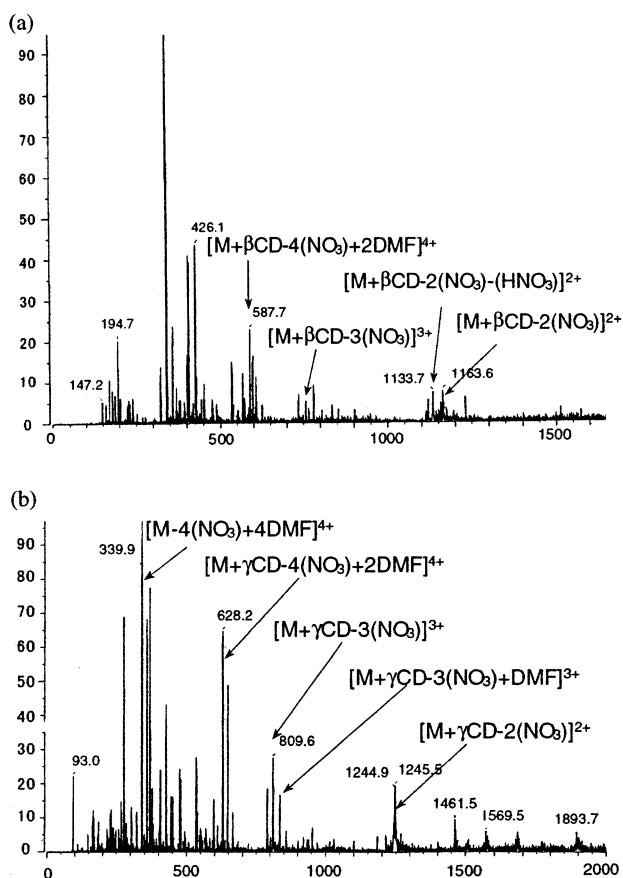
**Figure 3.**  $^1\text{H}$  NMR spectra (500 MHz) showing the formation of a pseudorotaxane ( $\downarrow$ ) by the addition of  $\gamma$ -CD to **M** ( $\bullet$ , 0.3 mM) in  $\text{D}_2\text{O}$ , according to the equivalents of  $\gamma$ -CD added: (a) 0, (b) 0.6, (c) 1.2, (d) 1.8, and (e) 2.8 equiv.

In the  $^1\text{H}$  NMR spectra, the signals corresponding to the new components appear upfield under the influence of the chiral  $\gamma$ -CD ring, indicating that both biphenyl moieties are accommodated in the cavity of  $\gamma$ -CD and interact with each other. However, since the large cavity of  $\gamma$ -CD might enable  $\gamma$ -CD to circumrotate along the macrocycle ring **M** without interfering with a Pd(en) moiety, the formation of catenanes could also be expected as in the case of  $\beta$ -CD (Scheme 2). To examine the possibility of a catenane formation in the self-assembly of **M** and  $\gamma$ -CD, a bulky ancillary ligand (1,2-

diaminocyclohexane) was used instead of ethylenediamine (en) on the Pd center to prevent the circumrotation of  $\gamma$ -CD. If the spectrum due to 2:2:1 assembly of (1,2-diaminocyclohexane)Pd(NO<sub>3</sub>)<sub>2</sub>, **L**, and  $\gamma$ -CD is different from that of 2:2:1 assembly of (en)Pd(NO<sub>3</sub>)<sub>2</sub>, **L**, and  $\gamma$ -CD, the self-assembled structure between **M** and  $\gamma$ -CD would be a catenane. However, if both spectra remain the same, the self-assembled structure would be a rotaxane. We observed exactly the same  $^1\text{H}$  NMR spectrum as in the case of the formation of an interlocked molecule by use of a Pd(en) moiety.<sup>10</sup> This indicates that the self-assembly of **M** and  $\gamma$ -CD should generate a rotaxane as shown in Scheme 2. Analysis of 2D ROESY spectra of the self-assembled structure<sup>10</sup> also clearly shows that the biphenyl groups of **M** are included in the cavity of  $\gamma$ -CD, in which the cross-peaks arise from intercomponent through-space correlations between the biphenyl protons ( $\text{H}_a$  and  $\text{H}_b$ ) and the inner cavity protons of  $\gamma$ -CD ( $\text{H}-3$  and  $\text{H}-5$ ). The stoichiometry of the rotaxane-like structure is shown to be 1:1, from the relative integration ratio of the protons of **M** to those of  $\gamma$ -CD ( $\text{H}-1$ ). The formation of this rotaxane-like structure was also supported by the CSI-MS spectrum.<sup>8</sup> The isotope patterns correspond to the related molecular ions (Figure 5b).<sup>10</sup> However, excimer emission peaks expected from the two biphenyl moieties inside the  $\gamma$ -CD cavity cannot be clearly located because of the spectral overlap with the Pd(II) emission peak in the same region. It is known that most rotaxanes have been constructed by the combination of a single rod and macrocycles. We believe that this is the first example of a dual rod-threaded [2]pseudorotaxane (similar to a ring-in-ring complex)<sup>11a-d</sup> formed by the self-assembly of the macrocyclic complex **M** and  $\gamma$ -CD in  $\text{D}_2\text{O}$  in which the dual rod<sup>12</sup> derives from **M** and Pd(en) moieties. Although the Pd(II) complexes prepared at 2 mM concentrations exist not as a single dimeric species (**M**) but as oligomers or multicomponents, addition of  $\gamma$ -CD to the 1:1 mixture of **L** and (en)Pd(NO<sub>3</sub>)<sub>2</sub> at 2 mM concentration led to the spontaneous and quantitative formation of a rotaxane-like structure.<sup>11e-g</sup> As the amount of  $\gamma$ -CD increases, the newly



**Figure 4.**  $^1\text{H}$  NMR spectra (500 MHz) showing the formation of [2]catenane structure by the addition of  $\beta$ -CD to **M** ( $\downarrow$ , 0.5 mM) in  $\text{D}_2\text{O}$ , according to the equivalents of  $\beta$ -CD added: (a) 2, (b) 8, and (c) 20 equiv.



**Figure 5.** CSI-MS spectrum of (a) [2]catenane and (b) [2]pseudorotaxane by the self-assembly of **M** and  $\beta$ -CD or  $\gamma$ -CD, respectively.

manifested signals of the  $^1\text{H}$  NMR spectra correspond to the same signals as those of the  $^1\text{H}$  NMR spectra observed at

(10) Spectral data can be found in Supporting Information.

(11) (a) Chiu, S.-H.; Pease, A. P.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *Angew. Chem., Int. Ed.* **2002**, *41*, 270. (b) Schmittel, M.; Ganz, A.; Fenske, D. *Org. Lett.* **2002**, *4*, 2289. (c) Kim, S.-Y.; Jung, L.-S.; Lee, E.; Kim, J.; Sakamoto, S.; Yamaguchi, K.; Kim, K. *Angew. Chem., Int. Ed.* **2002**, *41*, 270. (d) Jeppesen, J. O.; Vignon, S. A.; Stoddart, J. F. *Chem. Eur. J.* **2003**, *9*, 4611. (e) Ballardini, R.; Balzani, V.; Di Fabio, A.; Gandolfi, M. T.; Becher, J.; Lau, J.; Nielson, M. B.; Stoddart, J. F. *New J. Chem.* **2001**, *25*, 293. (f) McArdle, C. P.; Vittal, J. J.; Puddephatt, R. J. *Angew. Chem., Int. Ed.* **2000**, *39*, 3819. (g) Horn, M.; Ihringer, J.; Glink, P. T.; Stoddart, J. F. *Chem. Eur. J.* **2003**, *9*, 4046.

(12) (a) Harada, A.; Li, J.; Kamachi, M. *Nature* **1994**, *370*, 126. (b) Wylie, R. S.; Macartney, D. H. *J. Am. Chem. Soc.* **1992**, *114*, 3136. (c) Rao, T. V.; Lawrence, D. S. *J. Am. Chem. Soc.* **1990**, *112*, 2440.

0.3 mM concentrations (Figure 3), indicating the specific formation of a  $\gamma$ -CD-based [2]pseudorotaxane.<sup>10</sup>

The cavity of  $\beta$ -CD is structured to accommodate only one biphenyl group. Therefore, the formation of a catenane structure was observed, as shown in Scheme 2. When 2 equiv of  $\beta$ -CD was added to a solution of **M** in  $\text{D}_2\text{O}$  (0.5 mM) (Figure 4a), signals of a new component, which was expected to be the [2]catenane structure, began to appear in the  $^1\text{H}$  NMR spectrum. With an increase of the molar concentration of  $\beta$ -CD, complicated signals of a new component were observed. Because the (en)Pd moiety region of a macrocycle prevents the circumrotation of  $\beta$ -CD along the macrocycle ring **M**, the signals of **M** in the inside cavity of  $\beta$ -CD become magnetically nonequivalent to the signals in the outside cavity upon the formation of a catenane structure, which results in four different sets of signals in the  $^1\text{H}$  NMR spectrum of a catenated macrocycle.

The structure of [2]catenane in solution was confirmed from HH COSY and NOE studies.<sup>10</sup> The formation of the [2]catenane structure was also supported by the CSI-MS spectrum.<sup>8</sup> The isotope patterns correspond to the related molecular ions (Figure 5a).<sup>10</sup>

In both [2]pseudorotaxane and [2]catenane structures, the movement of CDs around the Pd(II) center seems to have a high energy barrier due to electrostatic and steric criteria.

In summary, we have demonstrated that the self-assembly of the macrocyclic ring **M** and  $\gamma$ -CD or  $\beta$ -CD in  $\text{D}_2\text{O}$  results in the formation of [2]pseudorotaxane and [2]catenane structures, respectively, depending on the cavity size of CDs. Extension of this work toward the development of polyrotaxanes and switching devices using the rotaxane structure as new scaffolds is underway.

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**Supporting Information Available:** Selected spectral data ( $^1\text{H}$  NMR, HH COSY, 2D ROESY, 2D NOESY, 1D NOE, and CSI-MS spectra) for compounds **M**, [2]catenane, and [2]pseudorotaxane structures, and  $^1\text{H}$  NMR spectra upon addition of  $\gamma$ -CD to the 1:1 mixture of **L** and (en)Pd(NO<sub>3</sub>)<sub>2</sub> or (1,2-diaminocyclohexane)Pd(NO<sub>3</sub>)<sub>2</sub> at 2 and 0.1 mM concentrations, respectively. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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