

## Synthesis and characterization of chiral catenanes based on rigid calix[4]arene

Yukihiro Okada,<sup>a,\*</sup> Zhihui Miao,<sup>b</sup> Miwa Akiba<sup>a</sup> and Jun Nishimura<sup>b,\*</sup>

<sup>a</sup>Department of Chemistry, Gunma University, Kiryu 376-8515, Japan

<sup>b</sup>Department of Nano-Material Systems, Gunma University, Kiryu 376-8515, Japan

Received 11 January 2006; revised 15 February 2006; accepted 16 February 2006

Available online 3 March 2006

**Abstract**—A new class of chiral calix[4]arene-based [2]catenanes was synthesized in excellent yields of 51–80%. They exhibit unique dynamic properties according to variable temperature NMR experiments. The enantiomeric pure (+)-catenane was prepared in 66% yield starting from (–)-calix[4]arene.

© 2006 Elsevier Ltd. All rights reserved.

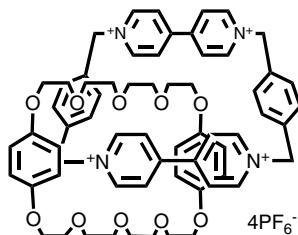
Catenanes,<sup>1</sup> which are basically formed by paraquat cyclophane structure like **1**,<sup>2</sup> have attracted much attention to their unique non-bonding structures and peculiar properties in supramolecular chemistry. Moreover, a catenane framework was made of host molecules attaching bipyridinium moiety, although only a few chiral catenanes were known so far.<sup>3–7</sup>

Rigid calix[4]arene analogs completely hold the cone conformation to take the face-to-face situation between functional groups even after the modification at their phenolic moieties.<sup>8–12</sup> Accordingly, they can be easily converted to chiral calixarenes and widely used as a platform for new functional molecules such as catenane and rotaxane.<sup>13,14</sup> Therefore, our research focuses on constructing the chiral calixarene-based catenanes,

using the effect of rigid framework maintaining donor–acceptor interaction between paraquat and crown ether moieties. In this letter, we would like to report the synthesis and characterization of new chiral calixarene-based catenanes.

The synthesis of catenanes **6** is shown in Scheme 1.<sup>3–5</sup> Hydroxyethers **3** were prepared from chiral calix[4]arene **2** (22 mM) by treatment with K<sub>2</sub>CO<sub>3</sub> (20 equiv) and  $\alpha,\omega$ -bromoalcohol having THP (20 equiv) in DMF/THF (7/3) at 90–100 °C for 24 h under N<sub>2</sub> and then pyridinium *p*-toluenesulfonate (2 equiv) in EtOH (50 mM) at 50–60 °C for 4 h in 68–92% yields. Bromides **4** were obtained with **3**, CBr<sub>4</sub> (4 equiv), and PPh<sub>3</sub> (4 equiv) in the minimum amount of THF (50 mM) at rt for 1 h in 72–83% yields. Pyridinium salts **5** were obtained with **4** and 4,4'-bipyridine (20 equiv) in CH<sub>3</sub>CN (25 mM) under reflux for 12 h in 74–98% yields.

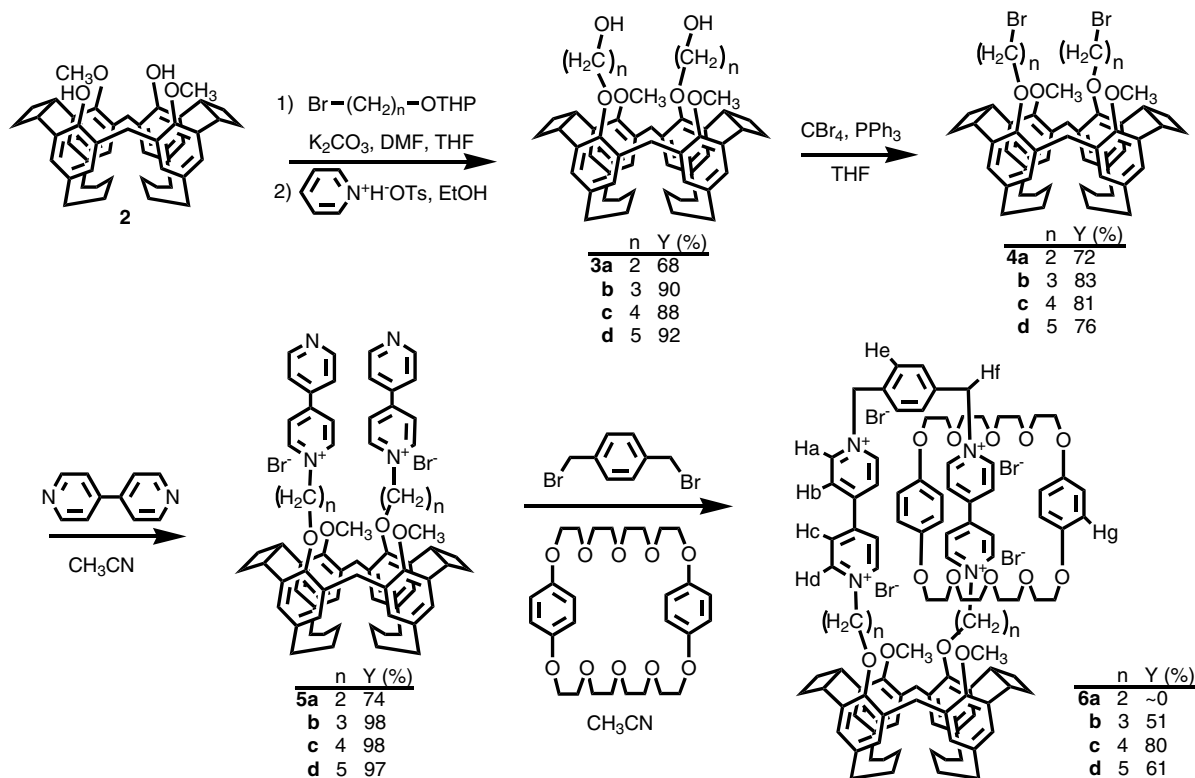
When catenation was firstly performed with **5b**,  $\alpha,\alpha'$ -di-bromo-*p*-xylene **7**, and bis-*p*-phenylene-34-crown-10 **8** in DMF as reported method, the desired product was obtained in meager yield.<sup>2,3</sup> Therefore, we examined what kind of intermediate in a mixture of **5b** and **8** was involved in CH<sub>3</sub>CN instead of DMF as a less polar solvent. Analyzing the mixture by <sup>1</sup>H NMR, the formation of *pseudo*-rotaxane was clearly recognized, so that catenane **6b** was prepared from **5b**, **7** (1.2 equiv), and **8** (5 equiv) in CH<sub>3</sub>CN (3.3 mM) at rt for 4 weeks. After alumina column chromatography (EtOH as an eluant), pure **6b** was isolated in 51% yield. Catenanes **6c** and **6d** were also obtained under the same conditions in



**1**

**Keywords:** Calixarene; Catenane; Enantiomer; Circular dichroism.

\* Corresponding authors. E-mail: [okada@chem.gunma-u.ac.jp](mailto:okada@chem.gunma-u.ac.jp)



Scheme 1.

excellent yields of 80% and 61%, respectively. Unfortunately, **6a** was not obtained as a pure compound, although its formation was confirmed by several spectroscopic analyses. Thus, these results clearly show that the chain length of the spacers did considerably govern the product yields.

The structures of calix[4]arene-based catenanes **6** obtained were mainly determined by  $^1\text{H}$  NMR and ESI mass spectroscopies.<sup>15</sup> The typical features of  $^1\text{H}$  NMR are as follows: (i) the methylene bridge protons between benzene rings of calixarene moiety appeared as two doublets at  $\delta$  3.00–3.04 ( $J = 13$  Hz) and  $\delta$  4.19–4.21 ( $J = 13$  Hz), typically showing cone structure with AB type splitting.<sup>10,14</sup> (ii) The aromatic protons of calixarene moiety showed the four sets of doublet at  $\delta$  6.78–7.21. (iii) The singlet peak of methoxy protons appeared at  $\delta$  3.22–3.48. (iv) The singlet peak of aromatic protons He for *p*-xylene moiety was located at  $\delta$  8.00–8.05. (v) The benzylic protons Hf of xylene moiety showed the doublet of doublet for **6b,c** and the singlet for **6d** at  $\delta$  5.98–6.10. (vi) The aromatic protons Ha, Hb, Hc, and Hd of 4,4'-bipyridinium units showed the four sets of doublet at  $\delta$  8.00–8.18, 8.06–8.20, 8.96–9.04, and 9.31–9.38, respectively, which were remarkably shift compared with those of pyridinium salts **5a–d** at  $\delta$  7.58–7.71, 8.30–8.38, 8.81–8.87, and 9.81–9.85. (vii) The singlet peak Hg of the aromatic protons of **8** shifted from  $\delta$  6.75 to  $\delta$  8.00–8.05 to a supramolecular situation. These results prove that products **6** include three components of calixarene, crown ether, and *p*-xylene units. Furthermore, ESI mass spectroscopy revealed the fragmentation of  $m/z = 594$  ( $\text{M}-3\text{Br}^-$ , int. 100%) for **6b**,

946 ( $\text{M}-2\text{Br}^-$ , int. 100%) for **6c**, and 440 ( $\text{M}-4\text{Br}^-$ , int. 94%) for **6d** to confirm their catenane structures.

The dynamic behavior of calixarene-based [2]catenanes **6** was observed by VT  $^1\text{H}$  NMR spectroscopy.<sup>2</sup> The movement of bipyridinium, crown ether, and *p*-xylene moieties was apparently recognized and its movement was different between **6b** and **d** and **6c** as shown in Figure 1. The typical features are as follows: (1) the Ha and Hb protons of pyridinium for **6b** and **6d** clearly show an up-field shift and they coalesce at 233–235 K. However, their Hc and Hd protons show little change under this condition. In contrast, all protons Ha–d of pyridinium for **6c** show an up-field shift and they coalesce at 241 K. (2) The He and Hf protons of **6** again show little change. (3) The Hg protons of **6** clearly show an up-field shift and they coalesce at 230 K. Accordingly, the crown ether of **6c** is nearly located, the center position over the four pyridinium rings, mainly the single bonding parts connecting the two pyridinium units, at low temperature. On the contrary, the crown ether of **6b** and **6d** predominantly is located between two pyridinium rings near *p*-xylene moiety. These results show that the donor–acceptor interaction at low temperature working in **6b** and **6d**, forces to hold the structure as a stable form in a certain way, while that of **6c** is in another. In fact, MM2 calculation demonstrated that two bipyridinium units approximately formed trapezoid structure for **6b** and **6d** to be close to each other in xylene leakage and parallel structure for **6c**.

The coalescence temperature ( $T_c = 233$ – $243$  K) of Ha protons for calixarene-based [2]catenanes **6** is nearly

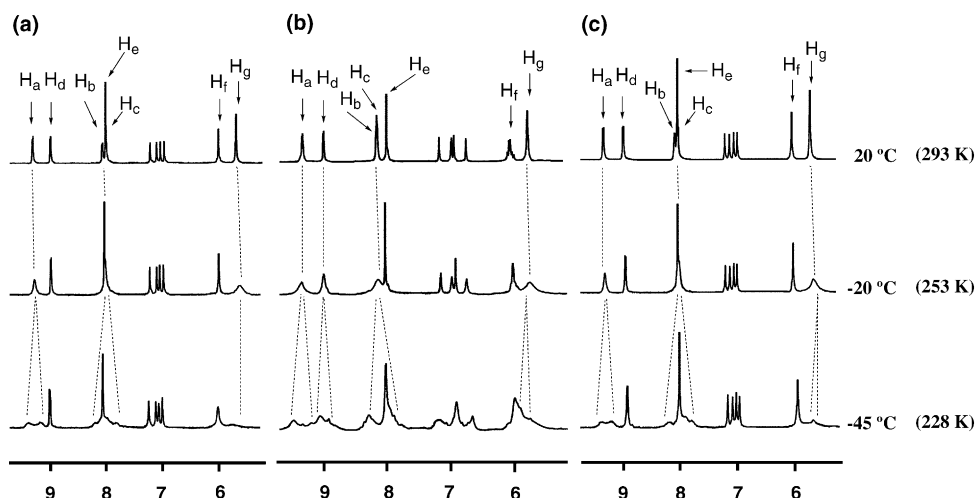


Figure 1. VT  $^1\text{H}$  NMR spectra of **6b** (a), **6c** (b), and **6d** (c) in  $\text{CD}_3\text{CN}$ .

equal, compared with that of paraquat-based [2]catenane **1**.<sup>2</sup> The  $T_c$  of Hg protons for **6** notably decreased ca. 110 K compared with that of **1**. Thus, calix[4]-arene-based [2]catenanes **6** have unique properties to be able to work at surrounding temperatures due to their more flexible structure than catenane **1**.

The enantiomer of catenane **6** was also successfully synthesized by using (–)-**2** isomer after HPLC chiral separation.<sup>14</sup> By proceeding through the same sequence depicted in Scheme 1, an enantiomeric pure catenane **6c** was obtained in excellent yield of 66% for the catenation step. Enantiomer **6c** in MeOH clearly shows a CD spectrum with (+)-sign at first Cotton as shown in Figure 2. In fact, specific rotation in MeOH at 20 °C was recorded,  $[\alpha]_D +23.9$ . Thus, we have successfully performed a first synthesis of enantiomeric pure catenane based on calixarene platform.

In conclusion, chiral calix[4]arene-based [2]catenanes **6** were obtained in excellent yields. They exhibited unique dynamic properties at surrounding temperatures. The enantiomeric pure catenane **6c** was also obtained from (–)-**2** in an excellent yield and assigned an (+)-isomer.

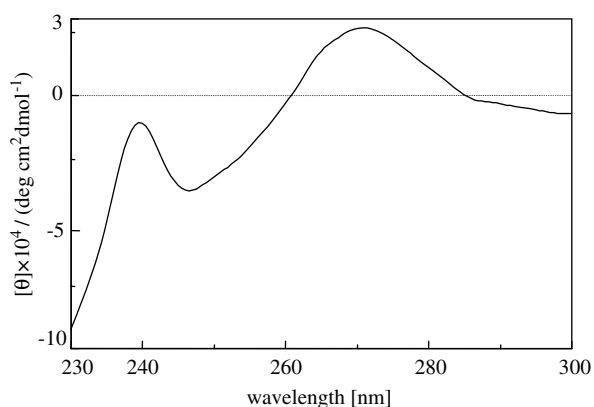


Figure 2. CD spectrum of enantiomer **6c** in MeOH.

Further investigations are now in progress and will be reported elsewhere.

#### Acknowledgments

This work was supported by grants from the Ministry of Education, Culture, Sports, Science, and Technology, Japan.

#### References and notes

1. *Molecular Catenanes, Rotaxanes, and Knots*; Sauvage, J.-P., Dietrich-Buchecker, C., Eds.; Wiley-VCH, 1999.
2. Anelli, P. L.; Ashton, P. R.; Ballardini, R.; Balzani, V.; Delgado, M.; Gandolfi, M. T.; Goodmow, T. T.; Kaifer, A. E.; Philp, D.; Pietraszkiewica, M.; Prodi, L.; Redington, M. V.; Slawin, A. M. A.; Spencer, N.; Stoddart, J. F.; Vicent, C.; Williams, D. J. *J. Am. Chem. Soc.* **1992**, *114*, 193.
3. Li, Z.-T.; Ji, G.-Z.; Yuan, S.-D.; Du, A.-L.; Ding, H.; Wei, M. *Tetrahedron Lett.* **1998**, *39*, 6517.
4. Li, Z.-T.; Ji, G.-Z.; Zhao, C.-X.; Yuan, S.-D.; Ding, H.; Huang, C.; Du, A.-L.; Wei, M. *J. Org. Chem.* **1999**, *64*, 3572.
5. Li, Z.-T.; Zhang, X.-L.; Lian, X.-D.; Yu, Y.-H.; Xia, Y.; Zhao, C.-X.; Chen, Z.; Lin, Z.-P.; Chen, H. *J. Org. Chem.* **2000**, *65*, 5136.
6. Vysotsky, M. O.; Bolte, M.; Thondorf, I.; Böhmer, V. *Chem. Eur. J.* **2003**, *9*, 3375.
7. Wang, L.; Vysotsky, M. O.; Bogdan, A.; Bolte, M.; Böhmer, V. *Science* **2004**, *304*, 1312.
8. *Calixarenes: A Versatile Class of Macrocyclic Compounds*; Vicens, J., Böhmer, V., Eds.; Kluwer: Dordrecht, 1991.
9. *Calixarenes 50th Anniversary*; Vicens, J., Asfari, Z., Harrowfield, J. M., Eds.; Kluwer: Dordrecht, 1994.
10. Okada, Y.; Ishii, F.; Kasai, Y.; Nishimura, J. *Chem. Lett.* **1992**, 755.
11. Okada, Y.; Ishii, F.; Kasai, Y.; Nishimura, J. *Tetrahedron Lett.* **1993**, *34*, 1971.
12. Okada, Y.; Kasai, Y.; Ishii, F.; Nishimura, J. *J. Chem. Soc., Chem. Commun.* **1993**, 976.
13. Okada, Y.; Mizutani, M.; Ishii, F.; Nishimura, J. *Tetrahedron Lett.* **1997**, *38*, 9013.

14. Okada, Y.; Mizutani, M.; Ishii, F.; Nishimura, J. *Enantiomer* **2002**, 7, 93.
15. Compd: Mp ( $^{\circ}\text{C}$ ); Anal. Calcd (Found); ESI-MS ( $m/z$ ); IR  $\nu$  ( $\text{cm}^{-1}$ );  $^1\text{H}$  NMR in  $\text{CD}_3\text{CN}$   $\delta$  (intensity, multiplicity,  $J$  in Hz). **6b**: 224–225; Calcd for  $\text{C}_{108}\text{H}_{126}\text{Br}_4\text{N}_4\text{O}_{14}\cdot 9\text{H}_2\text{O}$ : C, 59.34 (59.45); H, 6.65 (6.45); N, 2.56 (2.58); 932 ( $[\text{M}-2\text{Br}^-]^{2+}$ ), 594 ( $[\text{M}-3\text{Br}^-]^{3+}$ ), 426 ( $[\text{M}-4\text{Br}^-]^{4+}$ ); 2955, 1650, 1520, 1465, 1238, 1160, 1138, 1105, 1078, 962, 845, 805;  $-0.11$  (2H, m),  $0.71$  (2H, m),  $1.40$  (2H, m),  $1.55$  (2H, m),  $1.80$ – $2.10$  (12H, m),  $2.25$  (2H, m),  $2.33$  (2H, m),  $2.47$  (4H, m),  $2.58$  (4H, m),  $2.66$  (4H, m),  $3.04$  (2H, d, 13,  $\text{ArCH}_2\text{Ar}$ ),  $3.45$  (6H, s,  $\text{OCH}_3$ ),  $3.55$ – $3.92$  (32H, m,  $\text{OCH}_2\text{CH}_2\text{O}$ ),  $4.21$  (2H, d, 13,  $\text{ArCH}_2\text{Ar}$ ),  $4.40$  (2H, m, CH),  $4.51$  (2H, m, CH),  $4.83$  (4H, m,  $\text{NCH}_2\text{CH}_2\text{CH}_2$ ),  $5.67$  (8H, br s,  $\text{OC}_6\text{H}_4\text{O}$ ),  $6.02$  (4H, dd, 24, 13,  $\text{NCH}_2\text{Ar}$ ),  $6.96$  (2H, d, 1.8, ArH),  $7.03$  (2H, d, 1.8, ArH),  $7.10$  (2H, d, 1.8, ArH),  $7.21$  (2H, d, 1.8, ArH),  $8.04$  (4H, s),  $8.04$  (4H, d, 6.4),  $8.10$  (4H, d, 5.8),  $9.03$  (4H, d, 6.4),  $9.38$  (4H, d, 5.8). **6c**: 198–199; Calcd for  $\text{C}_{110}\text{H}_{130}\text{Br}_4\text{N}_4\text{O}_{14}\cdot 6\text{H}_2\text{O}$ : C, 61.16 (61.37); H, 6.64 (6.72); N, 2.59 (2.50); 946 ( $[\text{M}-2\text{Br}^-]^{2+}$ ), 604 ( $[\text{M}-3\text{Br}^-]^{3+}$ ), 433 ( $[\text{M}-4\text{Br}^-]^{4+}$ ); 2955, 1650, 1520, 1465, 1239, 1125, 1102, 1076, 960, 840, 800;  $0.09$  (2H, m),  $0.84$  (2H, m),  $1.28$  (4H, m),  $1.50$ – $2.20$  (16H, m),  $2.23$ – $2.73$  (16H, m),  $3.03$  (2H, d, 13,  $\text{ArCH}_2\text{Ar}$ ),  $3.22$  (6H, s,  $\text{OCH}_3$ ),  $3.40$ – $3.80$  (32H, m,  $\text{OCH}_2\text{CH}_2\text{O}$ ),  $4.13$  (2H, m, CH),  $4.19$  (2H, d, 13,  $\text{ArCH}_2\text{Ar}$ ),  $4.36$  (2H, m, CH),  $4.93$  (4H, m,  $\text{NCH}_2\text{CH}_2\text{CH}_2$ ),  $5.80$  (8H, br s,  $\text{OC}_6\text{H}_4\text{O}$ ),  $6.10$  (4H, dd, 26, 13,  $\text{NCH}_2\text{Ar}$ ),  $6.78$  (2H, d, 1.8, ArH),  $6.97$  (2H, d, 1.8, ArH),  $7.01$  (2H, d, 1.8, ArH),  $7.21$  (2H, d, 1.8, ArH),  $8.05$  (4H, s,  $\text{CH}_2\text{C}_6\text{H}_4\text{CH}_2$ ),  $8.18$  (4H, d, 6.4),  $8.20$  (4H, d, 6.1),  $9.04$  (4H, d, 6.4),  $9.38$  (4H, d, 6.1). **6d**: 220–221; Calcd for  $\text{C}_{112}\text{H}_{134}\text{Br}_4\text{N}_4\text{O}_{14}\cdot 6\text{H}_2\text{O}$ : C, 61.48 (61.67); H, 6.74 (6.58); N, 2.56 (2.58); 960 ( $[\text{M}-2\text{Br}^-]^{2+}$ ), 613 ( $[\text{M}-3\text{Br}^-]^{3+}$ ), 440 ( $[\text{M}-4\text{Br}^-]^{4+}$ ); 2952, 1648, 1520, 1465, 1238, 1159, 1128, 1105, 1079, 960, 840, 800;  $-0.08$  (2H, m),  $0.71$  (2H, m),  $1.21$ – $1.58$  (12H, m),  $1.74$ – $2.23$  (8H, m),  $2.29$ – $2.60$  (16H, m),  $2.70$  (4H, m),  $3.00$  (2H, d, 13,  $\text{ArCH}_2\text{Ar}$ ),  $3.48$  (6H, s,  $\text{OCH}_3$ ),  $3.51$ – $3.72$  (32H, m,  $\text{OCH}_2\text{CH}_2\text{O}$ ),  $4.20$  (2H, d, 13,  $\text{ArCH}_2\text{Ar}$ ),  $4.36$  (2H, m, CH),  $4.46$  (2H, m, CH),  $4.69$  (4H, m,  $\text{NCH}_2\text{CH}_2\text{-CH}_2\text{CH}_2\text{CH}_2$ ),  $5.65$  (8H, br s,  $\text{OC}_6\text{H}_4\text{O}$ ),  $5.98$  (4H, br s,  $\text{NCH}_2\text{Ar}$ ),  $6.95$  (2H, d, 1.8, ArH),  $7.00$  (2H, d, 1.8, ArH),  $7.08$  (2H, d, 1.8, ArH),  $7.17$  (2H, d, 1.8, ArH),  $8.00$  (4H, s),  $8.00$  (4H, d, 6.7),  $8.06$  (4H, d, 6.4),  $8.96$  (4H, d, 6.7),  $9.31$  (4H, d, 6.4).