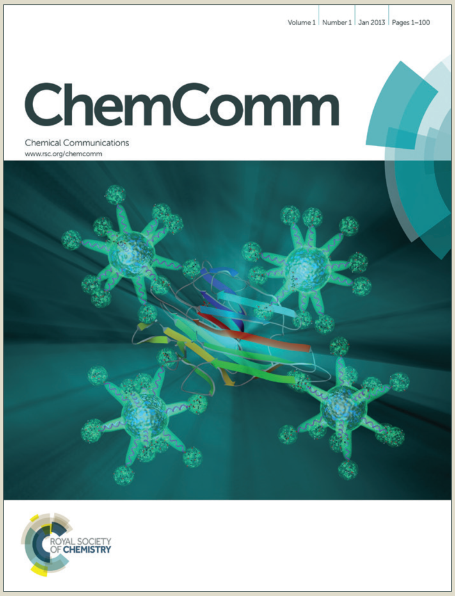
ChemComm

Accepted Manuscript



ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/chemcomm

ChemComm

Cite this: DOI: 10.1039/c0xx00000x

www.rsc.org/xxxxxx

ARTICLE TYPE

Diastereoselective Synthesis of a [2]Catenane from a Pillar[5]arene and a Pyridinium Derivative

Keisuke Kitajima, Tomoki Ogoshi* and Tada-aki Yamagishi

Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX

DOI: 10.1039/b000000x

We synthesized a new [2]catenane composed of a pillar[5]arene ring and pyridinium derivative using ring-closing metathesis.

Mechanically interlocked molecules (MIMs) are architectures of two or more connected, but not directly bonded components. These molecules have attracted much attention in recent years for potential applications in nanotechnology and as molecular machines.[1,2] Various types of MIMs such as rotaxanes,[1-5] polyrotaxanes,[2,6] catenanes,[7-12] and polycatenanes[13] have been reported. Among them, the synthesis of catenanes, which comprise two or more macrocycles, is difficult because the cyclization step must be performed under high-dilution conditions to favour cyclization and suppress linear chain extension. However, formation of pseudorotaxane structure is also disfavoured under high-dilution conditions and strong interactions must be used to construct catenanes such as donor-acceptor interactions,[8,9] hydrogen bonding,[10] metal-ligand coordination[11] and hydrophobic effects.[12]

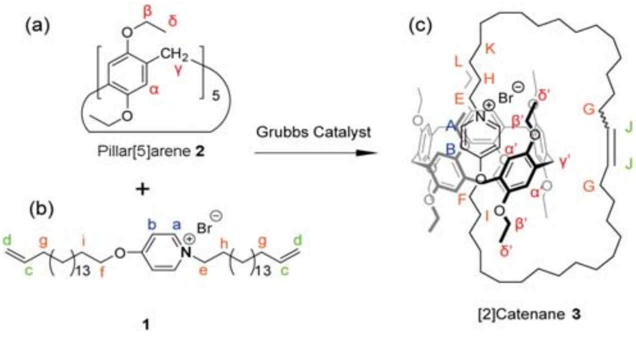


Fig. 1 Synthesis of (c) [2]catenane **3** from (a) pillar[5]arene **2** and (b) a pyridinium salt **1**.

Pillar[5]arenes (**Fig. 1a**), were first reported by our group in 2008,[14] and are cyclic pentamers composed of electron-donating dialkoxybenzene units connected by methylene bridges at the para-positions.[3-6,14-17] Pillar[5]arenes form very stable complexes with electron poor molecules such as pyridinium salts.[3,4,6,14-17] The association constants of such complexes are generally greater than 10^3 M^{-1}. In this study, we synthesized a pillar[5]arene-based [2]catenane (**Fig. 1c**) making use of the strong host-guest complex formation between a pyridinium salt and pillar[5]arene.

A pyridinium salt **1** bearing alkene groups at opposite ends of the molecule was prepared (**Fig. 1b**, synthetic procedure is shown in ESI). The ^{1}H NMR spectra of **1** and a mixture of **1** and per-ethylated pillar[5]arene **2** were measured (ESI, **Fig. S5**). Upon addition of pillar[5]arene **2** to **1**, the proton signals of **1** including the pyridinium (peaks a and b) and methylene (peak e) signals shifted upfield. This indicates the formation of a stable [2]pseudorotaxanebetween **1** and **2** [association constant: K = (1.76 ± 0.19) × 10^3 M^{-1}], and the presence of the pyridinium and methylene groups of **1** in the cavity of **2**. Ring-closing metathesis reaction was carried out to synthesize the [2]catenane **3**. Grubbs first generation catalyst was added to the mixture of **2** and **1** in

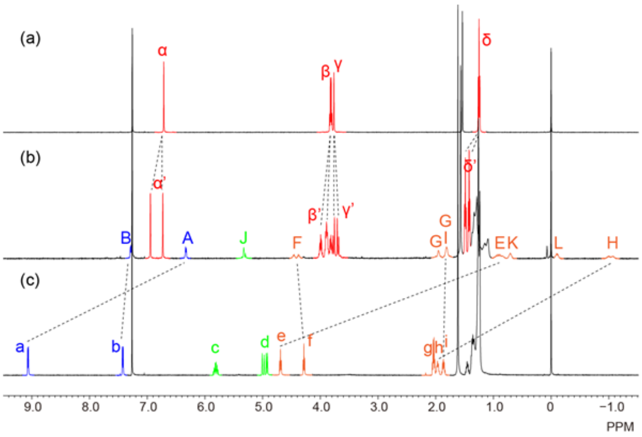


Fig. 2 ^{1}H NMR spectra of (a) **2**, (b) **3** and (c) **1** in $CDCl_3$ at 25 °C.

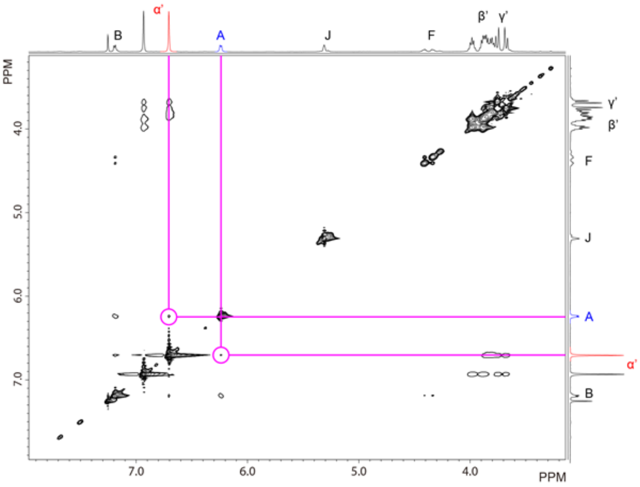


Fig. 3 2D ROESY analysis of **3** in $CDCl_3$ at 25 °C .

chloroform, and the reaction mixture was stirred at 25°C for 24 h (**Fig. 1**). As the first attempt, 3 equiv. of **2** was added to a 5 M solution of **1**. However, the isolated products by silica gel column chromatography was not [2]catenane **3**. This was due to the polymerization reaction between axles **1**. To avoid the polymerization reaction, the high dilution condition for the catenation was performed. In the dilute concentration of **1** (0.5 mM) with excess **2** (100 equiv. of **1**), the pillar[5]arene-based [2]catenane **3** was isolated by silica gel column chromatography in moderate yield (24%). The structure of **3** was confirmed by ^{1}H, ^{13}C, 2D NMR and high resolution mass spectrometry (HRMS). The HRMS of **3** featured a peak at *m*/*z* = 1459.0432, corresponding to the molecular ion with loss of a Br^- anion. **Fig. 2b** shows the ^{1}H NMR spectrum of **3**. Signals from the alkene protons (peaks c and d) of **1** disappeared, and the appearance of a new signal (peak J), indicated completion of the ring-closing metathesis reaction. Compared with **1** (**Fig. 2c**), the proton signals from **3** were shifted upfield including the pyridinium (peaks A and B) and methylene (peaks E and H) signals. This indicates that **2** interacted with the pyridinium and methylene groups of **1**. These signals were shifted further upfield than those of the [2]pseudorotaxane because **2** is mechanically interlocked into the pyridinium wheel of **3**. **Fig. 3** shows a 2D ROESY NMR spectrum of **3**. Correlation between the proton signals from the phenyl proton (peak α') of **2** and pyridinium proton (peak A) of **1** (**Fig. 3**) indicates that **2** was located near the pyridinium moiety of **1**. These results confirmed the successful synthesis of [2]catenane **3**.

One of the features of pillar[5]arenes that differs from traditional macrocycles is their various conformations in solution, caused by the rotation of alkoxybenzene units.[4,17,18] The units rotate around the methylene bridges as the axis; thus pillar[5]arene has eight conformers, as shown in **Fig. 4**: four diastereomers × two enantiomers: (*pS*, *pS*, *pS*, *pS*, *pS*), (*pR*, *pR*, *pR*, *pR*, *pR*), (*pR*, *pS*, *pS*, *pS*, *pS*), (*pS*, *pR*, *pR*, *pR*, *pR*), (*pR*, *pR*, *pS*, *pS*, *pS*), (*pS*, *pS*, *pR*, *pR*, *pR*), (*pR*, *pR*, *pS*, *pR*, *pS*), and (*pS*, *pS*, *pR*, *pS*, *pR*). These conformers are interconverted by rotation of the units at 25°C in solution.[17,18]

Two singlet peaks (peaks α') from the aromatic protons of **2** were observed in the ^{1}H NMR spectrum of **3** (**Fig. 2b**). However, the aromatic proton signals of pristine pillar[5]arene **2** appeared as one singlet (peak α, **Fig. 2a**) because of its symmetrical structure. This behaviour is the same as that observed in the pillar[5]arene-based [2]rotaxane **3** featuring a nonsymmetrical axle.[4] The aromatic proton signals of the upper and lower rims of **2** become distinct. The aromatic protons signals of the pillar[5]arene **2** ring in **3** features two singlet peaks with equal area. This suggests that the structure of **2**in **3** is highly symmetric and stereoregular. Considering the eight possible conformers of [2]catenane **3**, the product was obtained as a racemic mixture of [2]catenane **3** consisting of (*pS*, *pS*, *pS*, *pS*, *pS*) and (*pR*, *pR*, *pR*, *pR*, *pR*) forms of **2**. Other possible conformers of [2]catenane **3** were not formed (**Fig. 4**). These results indicate that catenation between **1** and **2** is diastereoselective, which may be attributed to the fact that (*pS*, *pS*, *pS*, *pS*, *pS*)-**2** and (*pR*, *pR*, *pR*, *pR*, *pR*)-**2** conformers have lower energy and possess a larger cavity than the other conformers. These two conformers likely possess cavities large enough to thread onto **1**, whereas the other conformers may not.

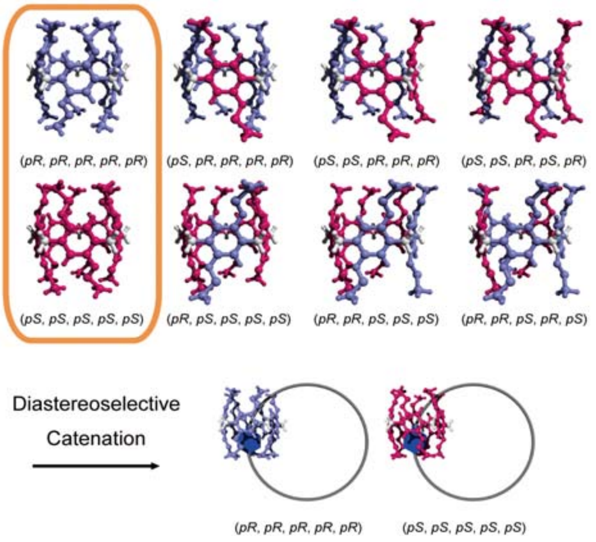


Fig. 4 Diastereoselective catenation.

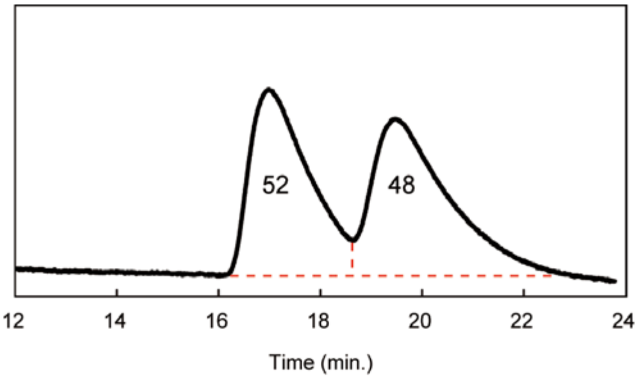


Fig. 5 Chiral HPLC trace of [2]catenane **3**. Column, Daicel CHIRALPAK IA (2.1 × 150 mm); eluent, hexane/ ethyl acetate / trifluoroacetic acid = 94.9/5/0.1 (v/v/v) at 1 ml/min.

To further investigate the planar chirality of [2]catenane **3**, chiral HPLC measurements were performed (**Fig. 5**). Upon injection of **3** onto an appropriate chiral HPLC column, two peaks of equal area were observed, indicating that [2]catenane **3** was racemic, i.e. a 1:1 mixture of [2]catenanes with one of the pyridinium cycles threaded through one (*pS*, *pS*, *pS*, *pS*, *pS*)-pillar[5]arene and the other one through the (*pR*, *pR*, *pR*, *pR*, *pR*)-pillar[5]arene wheel. These results are the same as those of a pillar[5]arene-based rotaxane,[4] indicating immobilized conformation of pillar[5]arene units in [2]catenane **3**. From the computationally generated energy-minimized molecular model of [2]catenane **3** (**Fig. S6**), the alkyl chain of the pyridinium wheel in **3** is tightly included in cavity of **2**. This also support immobilization of the conformation of the pillar[5]arene units in **3**.

In summary, we report the first synthesis of a pillar[5]arene-based [2]catenane **3**. So far, synthesis of [2]catenanes composed of typical macrocycles including cyclodextrins[1,12] and calixarenes[9] have been reported. However, to the best of our knowledge, this is the first example of a synthesis of a pillar[n]arene-based [2]catenane, although other pillar[n]arene-based MIMs such as rotaxanes[3-5] and polyrotaxane[6] have been reported. The synthesis of pillar[5]arene-based [2]catenane **3** is a starting point for achieving planar chiral high-order catenanes consisting of pillar[n]arene wheels.

This work was supported by a Grant-in-Aid (WAKATE A-25708022) from the ministry of Education, Culture, Sports, Science and Technology, Japan.

Notes and references

Graduate School of Natural Science and Technology, Kanazawa University, Kakuma-machi, Kanazawa 920-1192, Japan. Fax: +81 762344800; Tel: +81 762344775; E-mail: ogoshi@se.kanazawa-u.ac.jp

† Electronic Supplementary Information (ESI) available: Experimental section, characterization data and ^{1}H NMR spectrum of a mixture of **1** and pillar[5]arene and ^{1}H NMR titration. See DOI: 10.1039/b000000x/

1 S. A. Nepogodiev and J. F. Stoddart, *Chem. Rev.*, 1998, **98**, 1959.

2 A. Harada, *Acc. Chem. Res.*, 2001, **34**, 456; G. Wenz, B. H. Han and A. Müller, *Chem. Rev.*, 2006, **106**, 782; A. Harada, A. Hashidzume, H. Yamaguchi and Y. Takashima, *Chem. Rev.*, 2009, **109**, 5974; A. Harada, J. Li and M Kamachi, *Nature*, 1992, **356**, 325.

3 T. Ogoshi, D. Yamafuji, T. Yamagishi and A. M. Brouwer, *Chem. Commun.*, 2013, **49**, 5468; T. Ogoshi, D. Yamafuji, T. Aoki and T. Yamagishi, *Chem. Commun.*, 2012, **48**, 6842.

4 T. Ogoshi, D. Yamafuji, T. Aoki, K. Kitajima, T. Yamagishi, Y. Hayashi and S. Kawauchi, *Chem. Eur. J.*, 2012, **18**, 7493.

5 C. Ke, N. L. Strutt, H. Li, X. Hou, K. J. Hartlieb, P. R. McGonigal, Z. Ma, J. Iehl, C. L. Stern, C. Cheng, Z. Zhu, N. A. Vermeulen, T. J. Meade, Y. Y. Botros and J. F. Stoddart, *J. Am. Chem. Soc.*, 2013, **135**, 17019; N. L. Strutt, R. S. Forgan, J. M. Spruell, Y. Y. Botros and J. F. Stoddart, *J. Am. Chem. Soc.*, 2011, **133**, 5668; T. Ogoshi, T. Aoki, R. Shiga, R. Iizuka, S. Ueda, K. Demachi, D. Yamafuji, H. Kayama and T. Yamagishi, *J. Am. Chem. Soc.*, 2012, **134**, 20322.

6 T. Ogoshi, Y. Nishida, T. Yamagishi, Y. Nakamoto, *Macromolecules*, 2010, **43**, 7068.

7 E. Wasserman, *J. Am. Chem. Soc.*, 1960, **82**, 4433; J. P. Sauvage, *Acc. Chem. Res.*, 1990, **23**, 319; M. Fujita, *Acc. Chem. Res.*, 1999, **32**, 53.

8 W. Q. Deng, A. H. Flood , J. F. Stoddart and W. A. Goddard III, *J. Am. Chem. Soc.*, 2005, **127**, 15994; S. A. Vignon, J. Wong, H. R. Tseng and J. F. Stoddart, *Org. Lett.*, 2004, **6**, 1095; O. Š. Miljanić, W. R. Dichtel, S. Mortezaei and J. F. Stoddart, *Org. Lett.*, 2006, **8**, 1095; S. Grunder, P. L. McGrier, A. C. Whalley, M. M. Boyle, C. Stern and J. F. Stoddart, *J. Am. Chem. Soc.*, 2013, **135**, 17691.

9 C. Gaeta, C. Talotta, S. Mirra, L. Margarucci, A. Casapullo and P. Neri, *Org. Lett.*, 2013, **15**, 116.

10 M. K. Chung, P. S. White, S. J. Lee, M. L. Waters and M. R. Gagné, *J. Am. Chem. Soc.*, 2012, **134**, 11415.

11 A. Theil, C. Mauve, M. T. Adeline, A. Marinetti and J. P. Sauvage, *Angew. Chem. Int. Ed.*, 2006, **45**, 2104; J. F. Ayme, J. Lux, J. P. Sauvage and A. Sour, *Chem. Eur. J.*, 2012, **18**, 5565.

12 C. W. Lim, S. Sakamoto, K. Yamaguchi and J. I. Hong, *Org. Lett.*, 2004, **6**, 1079.

13 Z. Niu and H. W. Gibson, *Chem. Rev.*, 2009, **109**, 6024.

14 T. Ogoshi, S. Kanai, S. Fujinami, T. Yamagishi and Y. Nakamoto, *J. Am. Chem. Soc.*, 2008, **130**, 5022.

15 Reviews: T. Ogoshi, *J. Incl. Phenom. Macrocycl. Chem.*, 2012, **72**, 247; P. J. Cragg and K. Sharma, *Chem. Soc. Rev.*, 2012, **41**, 597; M. Xue, Y. Yang, X. Chi, Z. Zhang and F. Huang, *Acc. Chem. Res.*, 2012, **45**, 1294; T. Ogoshi and T. Yamagishi, *Bull. Chem. Soc. Jpn.*, 2013, **86**, 312; T. Ogoshi and T. Yamagishi, *Eur. J. Org. Chem.*, 2013, 2961.

16 T. Ogoshi, S. Tanaka, T. Yamagishi and Y. Nakamoto, *Chem. Lett.*, 2011, **40**, 96; C. Li, Q. Xu, J. Li, F. Yao and X. Jia, *Org. Biomol. Chem.*, 2010, **8**, 1568; X. Shu, S. Chen, J. Li, Z. Chen, L. Weng and X. Jia, *Chem. Commun.*, 2012, **48**, 2967; T. Ogoshi, R. Shiga and T. Yamagishi, *J. Am. Chem. Soc.*, 2012, **134**, 4577.

17 T. Ogoshi, K. Kitajima, T. Aoki, T. Yamagishi and Y. Nakamoto, *Phys. Chem. Lett.*, 2010, **1**, 817.

18 T. Ogoshi, K. Kitajima, T. Aoki, S. Fujinami, T. Yamagishi and Y. Nakamoto, *J. Org. Chem.* 2010, **75**, 3268.