

# Creation of Novel Chiral Cryptophanes by a Self-Assembling Method Utilizing a Pyridyl–Pd(II) Interaction

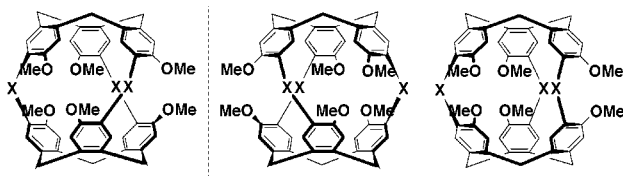
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## ABSTRACT



This Letter demonstrates the molecular design of novel self-assembled chiral cryptophanes. Mediated by square-planar Pd(II) complexes, racemic pyridyl cyclotrimeratrylene derivative *rac*-2 self-assembles into mixtures of racemic chiral cryptophanes and *meso* cryptophanes (1), which interconvert with each other, and the rates are remarkably enhanced by the addition of a slight excess of *rac*-2. On the other hand, optically resolved *P*-2 or *M*-2 self-assembles into the chiral cryptophane as the only product.

Metal-mediated self-assembly has proved to be a very effective methodology in constructing two- or three-dimensional supramolecular architectures,<sup>1</sup> such as macrocycles, molecular containers, tubular structures, interlocked and intertwined structures, and helicates, which are all useful in molecular or chiral recognition, host–guest chemistry, catalysis, and memory storage.<sup>2</sup> Despite the exciting results obtained so far, to construct predictable self-assembled structures is still a major challenge in the field of supra-

molecular chemistry. Bowl-shaped molecules such as calixarenes<sup>3</sup> and cyclotrimeratrylenes<sup>4</sup> have a particular advantage in the design of molecular capsules, for proper linking of only two these molecules can construct a molecular capsule.<sup>5</sup>

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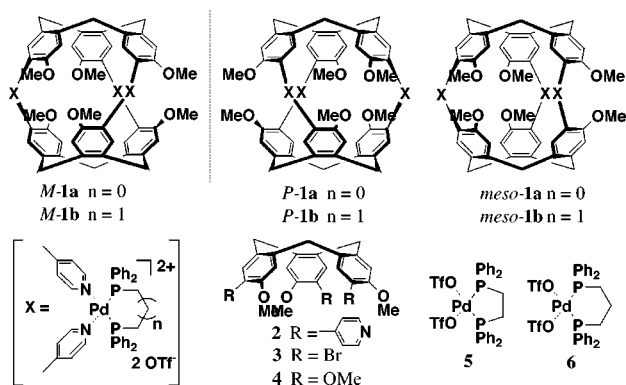
(4) Reviews on cyclotrimeratrylenes and cryptophanes: (a) Collet, A.; Dutasta, J.-P.; Lozach, B.; Canceill, J. *Top. Curr. Chem.* **1993**, *165*, 103. (b) Collet, A. *Tetrahedron* **1987**, *43*, 5725. (c) Collet, A. In *Comprehensive Supramolecular Chemistry*; Lehn, J.-M., Atwood, J. L., Davies, J. E. D., MacNicol, D. D., Vögtle, F., Series Eds.; Pergamon: New York, 1996; Vol. 2, pp 325–365. (d) Wytko, J. A.; Boudon, C.; Weiss, J.; Gross, M. *Inorg. Chem.* **1996**, *35*, 4469.

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It is known that when mediated by square-planar metal complexes, properly functionalized cyano- or pyridylcalix-arene analogues can dimerize into molecular capsules with predictable structures.<sup>6,7</sup> On the other hand, a number of covalently linked cryptophanes were reported and found capable of encapsulating guests ranging from single atoms to small and medium-sized neutral or ionic organic molecules.<sup>4–8</sup> More interestingly, chiral ethylene-bridged cryptophane enantioselectively complexes bromochlorofluoromethane and is useful in determining the absolute configuration of the guest.<sup>9</sup> These findings prompted us to design pyridyl cyclotrimeratrylene derivative **2** for construction of self-assembled chiral cryptophane **1**. The rigid bowl-shaped  $C_{3v}$  structure makes it impossible for **2** to chelate a metal complex intramolecularly, whereas the orientation of the pyridyl groups (the angle between the benzene plane and the  $C_3$  axis of a cyclotrimeratrylene crown is  $47 \pm 2^\circ$ ) makes **2** ready to self-assemble with square-planar metal complexes into cryptophane **1**.



Pyridyl cyclotrimeratrylene derivative **2** was synthesized by reacting **3**<sup>10</sup> with diethyl(4-pyridyl)borane<sup>11</sup> catalyzed by Pd(PPh<sub>3</sub>)<sub>4</sub> in the presence of CsF in refluxing DME. The *P* and *M* enantiomers<sup>12</sup> thus obtained were optically resolved in ca. 95% ee on a chiral HPLC column (Daicel Chiralcel OD-H, 1-propanol).

As shown in the <sup>1</sup>H NMR spectra (Figures 1B and 1C), mixing of (±)-**2** and **5** in a 2:3 ratio quantitatively affords a mixture of *meso*-**1a** and chiral (*P* and *M*)-**1a** within seconds.

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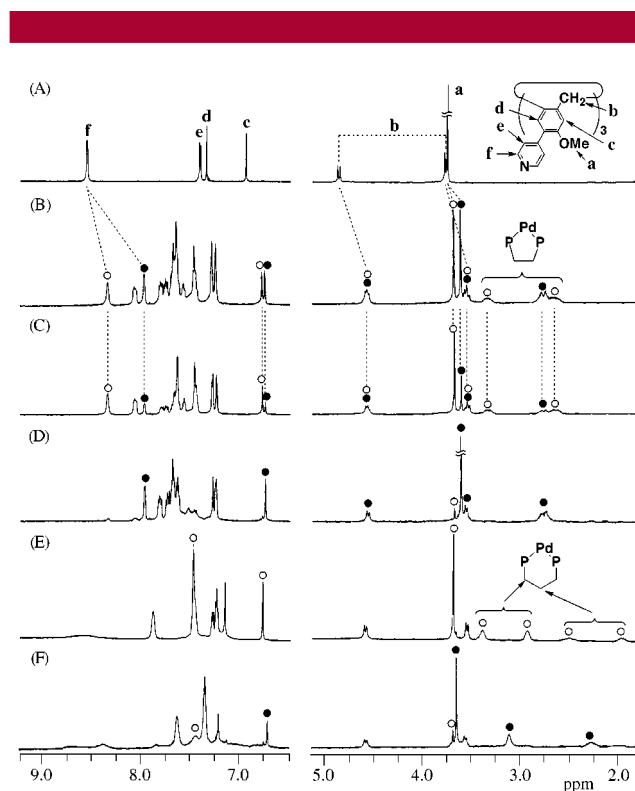
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It is easy to discriminate the signals for the *meso* and chiral isomers on the basis of the splitting pattern of the ethylene CH<sub>2</sub> protons in the diphosphine ligand. In syn-linked *meso*-**1a**, the two protons on the same carbon are diastereotopic: i.e., they experience on average a different magnetic environment, showing two sets of broad multiple peaks at 3.4 and 2.7 ppm. In anti-linked (*P* and *M*)-**1a**, the magnetic circumstances of the two protons experience a very similar chemical environment, showing only one set of broad multiple peaks at 2.8 ppm. In the mixture, the *meso*/(*P* and *M*) ratio increases very slowly from 1:1 to 2.5:1. Apparently, this phenomenon appears because the formation rates of the two kinds of isomers are comparable but *meso*-**1a** is thermodynamically more stable than (*P* and *M*)-**1a**. One can thus propose that when mediated by metal complex **5** an enantiomer of **2** forms a *meso* cryptophane when it meets a mirror enantiomer and forms a chiral cryptophane when it meets a same enantiomer.

Mixing of (±)-**2** with metal complex **6** instead of **5** gives similar results. The monitoring by <sup>1</sup>H NMR spectroscopy showed that at the beginning it gives a cryptophane mixture of *meso*-**1b** and (*P* and *M*)-**1b**. Unlike the equilibrium between *meso*-**1a** and (*P* and *M*)-**1a** with an equilibrium constant of 2.5:1, however, the ratio of (*P* and *M*)-**1b** decreases slowly until it almost disappears in the <sup>1</sup>H NMR spectrum (Figure 1E). This suggests that syn-linked *meso*-**1b** is much more stable than anti-linked (*P* and *M*)-**1b**,

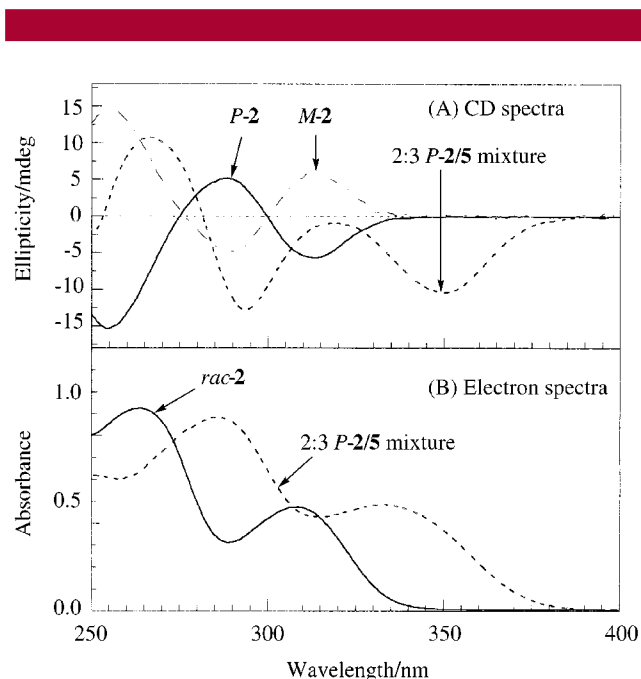


**Figure 1.** Partial 600 MHz <sup>1</sup>H NMR spectra of (A) **2**, (B) 2:3 **2**/**5** mixture (measured soon after mixing), (C) 2:3 **2**/**5** mixture (measured 9 days later after mixing), (D) 2:3 *P*-**2**/**5** mixture, (E) 2:3 **2**/**6** mixture (measured 9 days later after mixing), and (F) 2:3 *P*-**2**/**6** mixture in Cl<sub>2</sub>CDCDCl<sub>2</sub> at 25 °C: peaks marked with circles and black dots are assignable to chiral **1** and *meso*-**1**, respectively.

presumably because the former has a smaller N–Pd–N bond angle and thus there is less crowding between the pyridyl and diphenylphosphino groups attached to the Pd(II) than in the latter.

In an attempt to measure the equilibrium rate between the *meso* and chiral cryptophanes, we unexpectedly found that the presence of a slight excess of **2** greatly accelerates the interconversion rate. When the ratio of **2** and **5** is “exactly” 2:3, the equilibrium rate (*k*) between *meso*-**1a** and (*P* and *M*)-**1a** was estimated to be  $5 \times 10^{-6} \text{ s}^{-1}$ ,<sup>13</sup> which means that a minimal change can be observed within hours. In the presence of a 10% excess of **2**, however, the equilibrium is reached within 1 min ( $k > 1 \times 10^{-2} \text{ s}^{-1}$ ). In the case of *meso*-**1b** and (*P* and *M*)-**1b**, the chiral cryptophane converts to the *meso* one so rapidly that it cannot be observed by NMR spectroscopy in the presence of a 10% excess of **2**. These results provide a clue to understanding the mechanism of the interconversion. Presumably, one **2** molecule first adds to a cryptophane by replacing a pyridyl group on the pyridyl–Pd–pyridyl linkage, forming a trimeric intermediate, and finally replaces a whole **2** molecule from the cryptophane.

As shown by the <sup>1</sup>H NMR spectra (Figures 1D and 1F), mixing an optically resolved enantiomer of **2** with metal complexes **5** or **6** produces only chiral cryptophanes as predicted. The optical activities of the chiral cyclotrimeratrylene derivative **2** and the self-assembled cryptophane were measured by circular dichroism (CD) spectroscopy (Figure 2). Using the exciton model for cyclotrimeratrylenes,<sup>14</sup> the absolute configuration of the first HPLC fraction was



**Figure 2.** (A) CD spectra of (1) *P*-**2** (first fraction), (2) *M*-**2** (second fraction), and (3) 2:3 *P*-**2**/**5** mixture; (B) electron spectra of (4) **2** and (5) 2:3 **2**/**5** mixture in  $\text{Cl}_2\text{CHCHCl}_2$  at 25 °C.

assigned as *P*-**2** and the second fraction as *M*-**2** on the basis of the CD spectra.<sup>15</sup>

The structures of the self-assembled cryptophanes were further supported by coldspray ionization mass spectroscopy (CSI MS)<sup>16</sup> measurements in addition to the <sup>1</sup>H NMR spectra. The CSI MS spectrum of a 2:3 **2**/**5** mixture shows the strongest peaks at *m/z* 748.9, 1047.7, and 1647.5 for the species of (**1a** – 4OTf)<sup>4+</sup>, (**1a** – 3OTf)<sup>3+</sup>, and (**1a** – 2OTf)<sup>2+</sup>, respectively; the CSI MS spectrum of a 2:3 **2**/**6** mixture shows the strongest peaks at *m/z* 759.4, 1062.4, and 1668.0 for the species of (**1b** – 4OTf)<sup>4+</sup>, (**1b** – 3OTf)<sup>3+</sup>, and (**1b** – 2OTf)<sup>2+</sup>, respectively. Interestingly, the spectra also show obvious peaks at *m/z* 1752.7, 1118.8, 1732.2, and 1104.8 which are assignable to (**1b** – 2OTf +  $\text{Cl}_2\text{-CDCDCl}_2$ )<sup>2+</sup>, (**1b** – 3OTf +  $\text{Cl}_2\text{-CDCDCl}_2$ )<sup>3+</sup>, (**1a** – 2OTf +  $\text{Cl}_2\text{-CDCDCl}_2$ )<sup>2+</sup>, and (**1a** – 3OTf +  $\text{Cl}_2\text{-CDCDCl}_2$ )<sup>3+</sup>, respectively, indicating that the self-assembled cryptophanes form complexes with the solvent.

In conclusion, this Letter demonstrates novel self-assembled chiral cryptophanes and their dynamic interconversions. Mediated by square-planar Pd(II) complexes **5** or **6**, racemic pyridyl cyclotrimeratrylene derivative ( $\pm$ )-**2** self-assembles into mixtures of racemic chiral cryptophanes and *meso* cryptophanes, whose ratios are dependent on the structure of the metal complexes; optically resolved *P*-**2** or *M*-**2** self-assembles into a chiral cryptophane as the only product. We believe that these self-assembled chiral cryptophanes are useful not only as conventional hosts for chiral guest recognition but also as novel hosts which change the structure, the aggregation properties, and even the chirality in response to included guest molecules.

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**Supporting Information Available:** <sup>1</sup>H–<sup>1</sup>H COSY spectra and CSI MS spectra of **1a** and **1b**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(13) The rate is so sensitive to the amount of **2** that it is very difficult to get reproducible results.

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(15) To assign the configuration, it is necessary to know the relative magnitude of the spectroscopic moments (SM) of the pyridyl and methoxy groups in **2**. The SM is an empirical parameter for quantifying the influence of a substituent on the absorption intensities in aromatic compounds. Since  $\epsilon_{\text{max}}$  of **4** is 9300 at 292 nm<sup>13</sup> and  $\epsilon_{\text{max}}$  of **2** is 14000 at 310 nm in methanol, the SM of the pyridyl group is greater than that of the methoxy group.

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