

# A chiral molecular bowl containing three ferrocenes: synthesis and its efficiency in an optical resolution of 1,1'-bi-2-naphthol†

Bog Ki Hong, In Su Lee, Dong Mok Shin and Young Keun Chung\*

School of Chemistry, Center for Molecular Catalysis, Seoul National University, Seoul 151-747, Korea

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**Condensation reaction of 1,1'-ferrocenedicarboxaldehyde with (1*R*,2*R*)-1,2-diaminocyclohexane affords a novel bowl-shaped macrocycle with a chiral concave cavity which exhibits a remarkable ability as a host material for the enantioselective enclathration of 1,1'-bi-2-naphthol.**

The design and study of new macrocyclic species is one of the most active and interesting areas in the field of supramolecular chemistry because of their exploitable properties such as molecular recognition, sensing, and catalysis.<sup>1</sup> During the past several years, a variety of polygonal structures have been successfully designed and synthesized through the self-assembly process based on coordination or condensation reactions between molecular components.<sup>2</sup> Employing redox- or photo-active metal components in the construction of macrocycles is an attractive prospect in the context of selective sensing for the specific guest species *via* electrochemical or optical methodologies.<sup>3</sup> Recently, some works indicated that chiral molecular triangles and squares containing metal fragments could be used for asymmetric catalysis and chiral sensing.<sup>4</sup> Ferrocenyl compounds have been one of the most popular metal-containing building blocks in supramolecular synthesis and many macrocycles have been derived from them.<sup>5</sup> However, just a handful of ferrocenyl triangles have been synthesized.<sup>6</sup> Moreover, there has only been one chiral example reported to date.<sup>6a</sup>

In this respect, our recent research has been focused on the construction of new chiral macrocyclic triangles from ferrocenyl components in the hope of generating novel functionalities. Herein we communicate a facile synthetic route for chiral ferrocenyl triangles and its application to an effective resolution of 1,1'-bi-2-naphthol.

1,1'-Ferrocenedicarboxaldehyde (**1**) was reacted with (1*R*,2*R*)-1,2-diaminocyclohexane ((1*R*,2*R*)-**2**) in dichloromethane in the presence of a molecular sieve at room temperature for one day. After the solution was filtered, the filtrate was concentrated and precipitated by addition of excess diethyl ether (Scheme 1).<sup>7</sup> Powdered solids (*R*)-**3** were obtained in high yields. The <sup>1</sup>H and <sup>13</sup>C NMR, HRMS, and elemental analysis revealed the occurrence of a [3 + 3] assembly and the formation of a macrocyclic complex with the formulation of [–N=CH–C<sub>5</sub>H<sub>4</sub>FeC<sub>5</sub>H<sub>4</sub>–CH=N–C<sub>6</sub>H<sub>10</sub>–]<sub>3</sub>. Numerous attempts to produce single crystals with an X-ray diffraction quality failed. Thus, a structural analysis of the

macrocyclic complex could not be carried out. However, the circular dichroism (CD) spectra of (*R*)-**3** and (*S*)-**3** show that the macrocycles are chiral (Fig. 1).

In an endeavour to find out its utility, an enantioselective enclathration of **3** with 1,1'-bi-2-naphthol (**4**) was attempted.<sup>8</sup> Enantiopure **4** is an extremely useful backbone from which a variety of powerful, chiral ligands can be accessed which are widely used in asymmetric catalysis.<sup>9</sup> Thus, the optical resolution of its racemate has been the subject of numerous works of research.<sup>10</sup> When (*R*)-**3** and (*R*)-**4** were dissolved together in CHCl<sub>3</sub> and diethyl ether was layered onto the solution, orange block-like crystals were gradually grown at the interface of the two solutions over a period of a few days. Formation of 1:1 co-crystals of (*R*)-**3**·(*R*)-**4** was confirmed by <sup>1</sup>H NMR and X-ray crystallographic analyses. The X-ray structural determination of (*R*)-**3**·(*R*)-**4** reveals the assembly of macrocycles of (*R*)-**3** and (*R*)-**4** molecules into a one-dimensional tubular-helical structure with a hydrogen-bond mediated by water molecules (Fig. 2).<sup>†</sup> A Schiff-base molecular bowl was formed by the [3 + 3] condensation reaction of **1** and (1*R*,2*R*)-**2** around the pseudo-C<sub>3</sub> axis and the chiral concave cavity was formed with a rim diameter of 3.6 Å and a depth of 4.7 Å. To the best of our knowledge, no structures like this have been reported

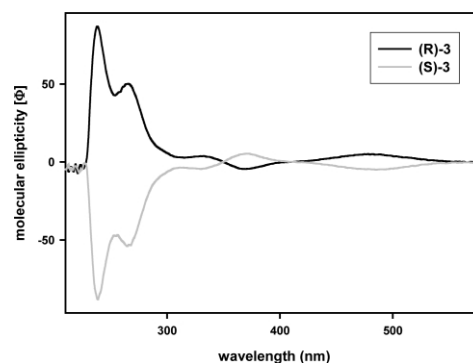
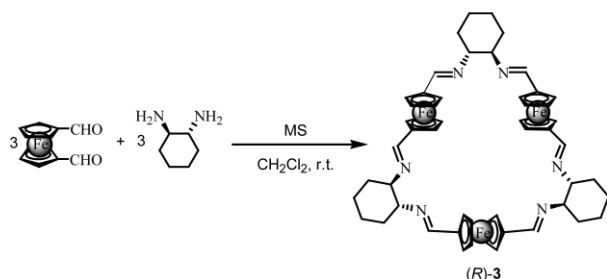


Fig. 1 CD spectra of **3** in CH<sub>2</sub>Cl<sub>2</sub> at a concentration of 2 × 10<sup>−5</sup> M.



Scheme 1 Synthesis of ferrocenyl-[3+3] macrocycle.

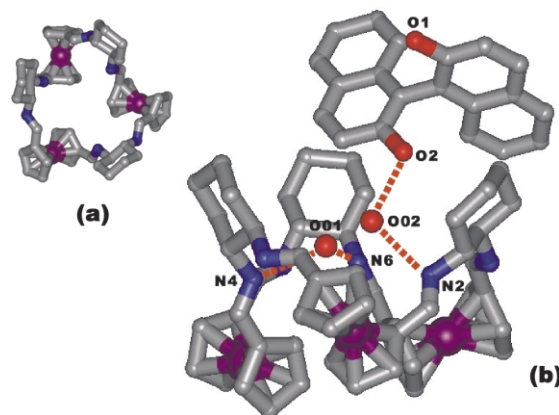


Fig. 2 (a) Top view of (*R*)-**3** found in (*R*)-**3**·(*R*)-**4**, (b) side view of (*R*)-**3**·(*R*)-**4**. Hydrogen atoms and solvent molecules are omitted for clarity. Hydrogen bondings are shown as red dot lines.

† Electronic supplementary information (ESI) available: synthesis, NMR, HRMS, and elemental analysis of compounds. See <http://www.rsc.org/suppdata/cc/b3/b316520e/>

among ferrocenyl compounds. In the crystal, two water molecules occupy the cavity of (*R*)-**3** and cause the hydrogen bonding with (*R*)-**3** and (*R*)-**4** to extend a one-dimensional hydrogen bonding network. Solvent molecules, chloroform and diethyl ether, are present in the crystal lattice without additional hydrogen bonding interactions. When the same procedure was applied to (*R*)-**3** and (*S*)-**4**, a growth of crystals was not observed within a week and a small amount of (*R*)-**3** itself was solidified from the solution after several weeks. This means that the formation of a hydrogen-bonding network and packing into the co-crystal with (*R*)-**3** is favored just for (*R*)-**4**. Therefore, it was expected that (*R*)-**3** should be able to function as a host for an optical resolution of ( $\pm$ )-**4** through an enclathration process. Thus, a resolution was carried out by dissolving (*R*)-**3** and ( $\pm$ )-**4** together in  $\text{CHCl}_3$  and laying diethyl ether onto the solution, followed by standing it at room temperature. After a few days, a solidification of 1:1 co-crystals of (*R*)-**3**-(*R*)-**4'** along with a small quantity of microcrystals of (*R*)-**3** was observed. X-ray crystallography analysis shows that the crystals of (*R*)-**3**-(*R*)-**4'** consist of a hydrogen bonding chain almost equivalent to that of (*R*)-**3**-(*R*)-**4**, but contain less solvent molecules. The resulting solids are readily dissolved in  $\text{CH}_2\text{Cl}_2$  and (*R*)-**3** can be recovered by addition of an excess amount of diethyl ether. Thus, enantio-enriched (*R*)-**4** is obtained from the mother liquor. In the course of the study of the resolution efficiency, the best result was given by layering 5 mL of diethyl ether onto the 1 mL  $\text{CHCl}_3$  solution of 50 mg (0.052 mmol) of (*R*)-**3** and 30 mg (0.10 mmol) of ( $\pm$ )-**4**. After two days, 60 mg of solids were formed. 13 mg (0.045 mmol, 86% yield) of enantiomerically pure (*R*)-**4** was obtained and 45 mg (0.046 mmol, 90% yield) of (*R*)-**3** was recovered from them. The optical purity of resolved (*R*)-**4** was monitored to be over 99% by HPLC analysis. Enantioselective enclathration of (*S*)-**4** using (*S*)-**3** showed almost the same behavior as (*R*)-**3** to (*R*)-**4**, which means that **3** is a highly effective host for chiral resolution of 1,1'-bi-2-naphthol.

In order to extend our strategy of [3+3] cyclization, a diamine such as (1*R*,2*R*)-1,2-diphenylethylenediamine was reacted with **1** to give **5** (73% yield). An X-ray structural determination of **5** shows that **5** has quite a similar structure to **1** with a rim diameter of 2.6 Å and a depth of 4.6 Å (Fig. 3).

In conclusion, we have demonstrated the synthesis of a novel bowl-shaped chiral macrocyclic compound with a ferrocenyl moiety through a concise condensation reaction. Furthermore, we have also demonstrated its remarkable efficiency in the optical resolution of 1,1'-bi-2-naphthol via an enclathration process. Research for the further improvement of the resolution efficiency, especially in large-scale processes, is currently in progress.

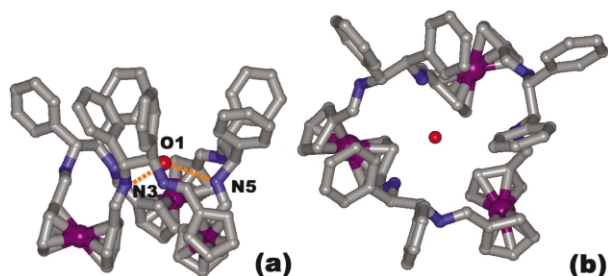
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## Notes and references

† Single crystal data for (*R*)-**3**-(*R*)-**4**:  $\text{C}_{80}\text{H}_{90.50}\text{Cl}_{5.50}\text{Fe}_3\text{N}_6\text{O}_5$  (293K).  $M_w = 1578.61$ , orthorhombic, space group  $P2_12_12_1$ ,  $a = 15.5300(2)$ ,  $b = 21.4870(2)$ ,  $c = 26.6130(2)$  Å,  $V = 8880.57(17)$  Å<sup>3</sup>,  $Z = 4$ ,  $\rho_{\text{calc.}} = 1.181$  g cm<sup>-3</sup>, total reflections collected 15088, unique 9728 ( $R_{\text{int}} = 0.1344$ ), GOF = 1.006,  $R_1 = 0.0960$ ,  $R_w = 0.1810$  ( $I > 2\sigma(I)$ ); Elemental Anal.(Calcd.) for (*R*)-**3**-(*R*)-**4**·0.5 $\text{CHCl}_3$ : C, 66.45(66.64); H, 6.13(5.89); N, 6.04(6.26). (*R*)-**3**-(*R*)-**4'**:  $\text{C}_{75}\text{H}_{80}\text{Fe}_3\text{N}_6\text{O}_4$  (293K).  $M_w = 1283.01$ , orthorhombic, space group  $P2_12_12_1$ ,  $a = 13.5860(10)$  Å,  $b = 20.4300(10)$ ,  $c = 25.7270(10)$  Å,  $V = 7140.8(7)$  Å<sup>3</sup>,  $Z = 4$ ,  $\rho_{\text{calc.}} = 1.272$  g cm<sup>-3</sup>, total reflections collected 15803, unique 15803 ( $R_{\text{int}} = 0.0000$ ), GOF = 1.008,  $R_1 = 0.0546$ ,  $R_w = 0.1087$  ( $I > 2\sigma(I)$ ); Elemental Anal.(Calcd.) for (*R*)-**3**-(*R*)-**4'**: C, 65.84(65.85); H, 6.11(5.89); N, 6.06(6.14). (*R*)-**5**:  $\text{C}_{79}\text{H}_{70}\text{Cl}_2\text{Fe}_3\text{N}_6\text{O}_1$  (293K).  $M_w = 1357.86$ , orthorhombic, space group  $P2_12_12_1$ ,  $a = 11.8360(2)$ ,  $b = 16.4830(3)$ ,  $c = 34.7660(5)$  Å,  $V = 6782.60(19)$  Å<sup>3</sup>,  $Z = 4$ ,  $\rho_{\text{calc.}} = 1.330$  g cm<sup>-3</sup>, total reflections collected 25476, unique 12861 ( $R_{\text{int}} = 0.0908$ ), GOF = 0.964,  $R_1 = 0.0521$ ,  $R_w = 0.0665$  ( $I > 2\sigma(I)$ ); Elemental Anal.(Calcd.) for (*R*)-**5**: C, 74.34(74.65); H, 5.38(5.30); N, 6.64(6.70). Crystallographic data (excluding structure factors) for (*R*)-**3**-(*R*)-**4**, (*R*)-**3**-(*R*)-**4'** and (*R*)-**5** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 227311, 227312 and 227313, respectively. See <http://www.rsc.org/suppdata/cc/b3/b316520e/> for crystallographic data in .cif or other electronic format.

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**Fig. 3** An X-ray structure of **5**; side view (a), top view (b). Hydrogen atoms and  $\text{CH}_2\text{Cl}_2$  are omitted for clarity. One water molecule is included inside the bowl, making hydrogen bonds (red dot lines) with N3 and N5.