Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Supporting Information

Luminescent Covalent organic cages with a C_3-symmetric structure for effective enantioseparation

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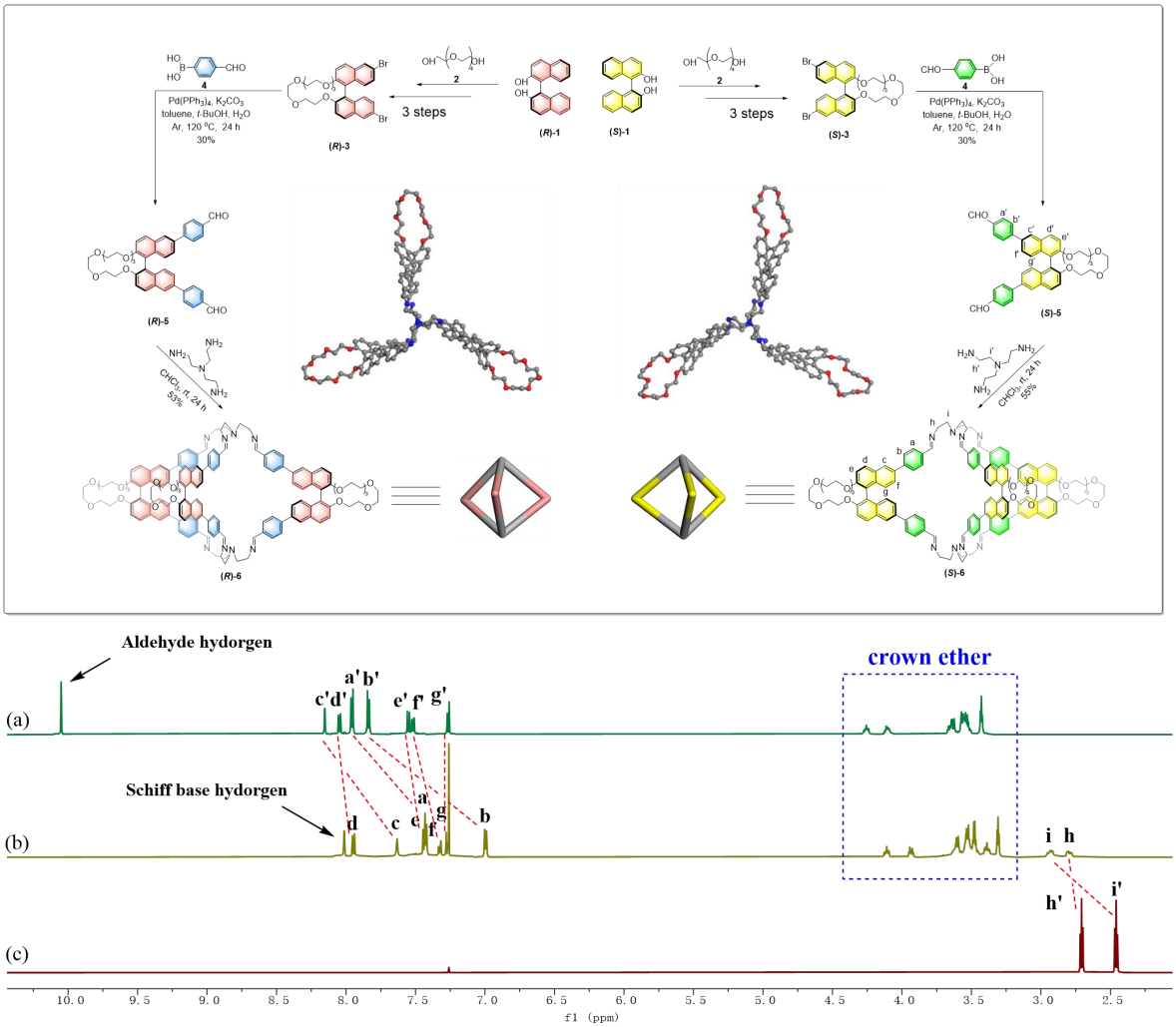
1. Materials and Methods.

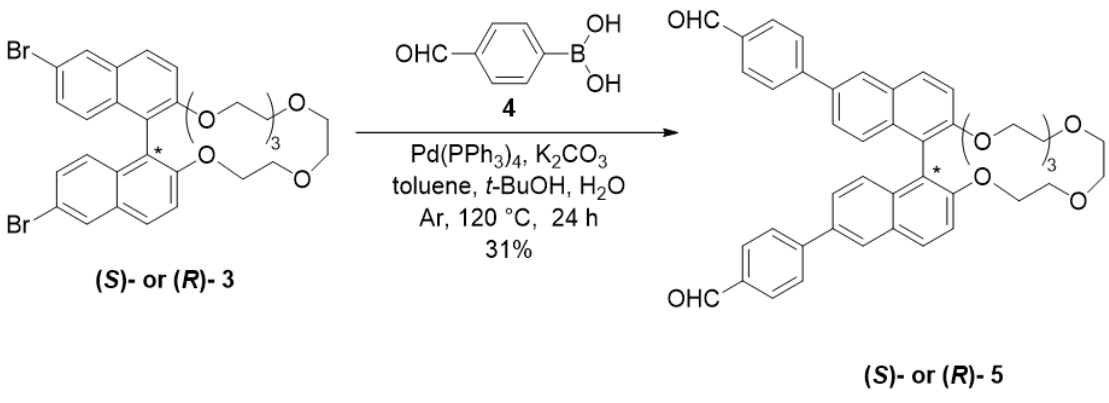
All reagents were purchased from Sigma-Aldrich, Shanghai, China, Fisher, Shanghai, China, Across, Shanghai, China, and Alfa Aesar, Tianjin, China, and they were used without further purification. Tetrahydrofuran (THF) was dried over sodium metal and freshly distilled under nitrogen atmosphere prior to use. All air-sensitive reactions were carried out under inert N_2 atmosphere. Column chromatography was conducted using SiO_2 (VWR, 40-60 μm, 60 Å) and the separated products were visualized by UV light. NMR spectra data were recorded on a 600 MHz Bruker NMR spectrometer in $CDCl_3$ with TMS as the reference. Emission spectra in the liquid state were recorded on a Horiba-FluoroMax-4 spectrofluorometer, HORIBA, Edison, NJ, USA. Circular dichroism (CD) spectra were recorded on Applied Photophysics Chirascan circular dichroism chiroptical spectrometer at room temperature. After adding solution of chiral cages in $CHCl_3$ (c = 0.1 mM) to the sample cell (l = 0.5 mm), the CD data were then recorded in a wavelength range of 240−400 nm. ESI-MS of cages was recorded with a Waters Synapt G2-Si mass spectrometer, USA and the experiments were performed with a Waters Q-Tof Micro MS/MS high-resolution mass, USA, spectrometer in ESI mode.The instrument used in the mass spectrometry experiment of compound **5** is Agilent 1290/InfinityII6546, Singapore. The data is recorded by Qualitative Analysis 10.0. The Fourier Transform Infrared FT-IR spectra were recorded on a Spectrum TWO FT-IR spectrophotometer, PerkinElmer, Llantrisant, UK.

2. Synthesis of chiral binol cages.



Scheme 1. Synthesis of chiral organic cages from binol, and ^{1}H NMR (600 MHz, $CDCl_3$, 22 °C) spectra of compound **(*S*)-5** (a), compound **(*S*)-6** (b), tri(2-aminoethyl)amine (c).

2.1 Synthesis of (*S*)- and (*R*)-5[1].

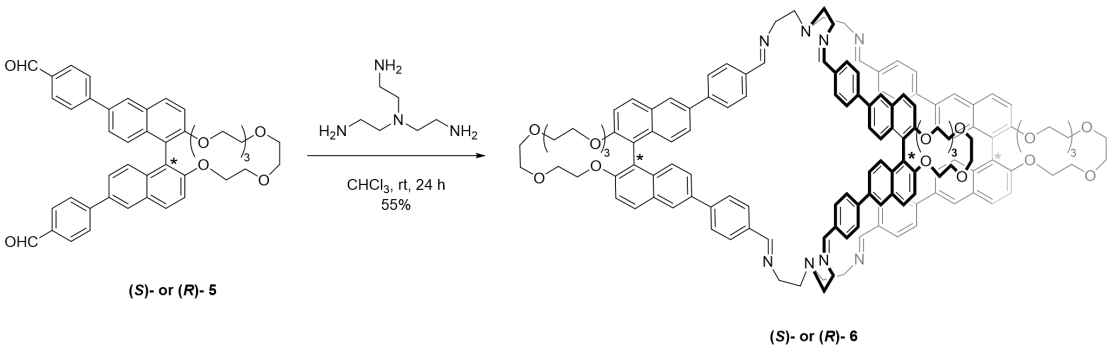


Compound **(*S*)-** or **(*R*)-3** (367 mg, 0.569 mmol), 4-formylphenylboronic acid (342 mg, 2.28 mmol), $Pd(PPh_3)_4$ (111.94 mg, 0.093 mmol) and K_2CO_3 (787.57 mg, 5.7 mmol) were added to a solution (15 mL) of toluene, *t*-BuOH and H_2O (3:1:1, V:V:V) under argon atmosphere. The reaction mixture was stirred at 120 °C for 24 h. Upon completion of reaction, the solvent was removed in vacuum, and the residue was added to 100 mL of CH_2Cl_2 and washed by water. The organic layer was dried over Na_2SO_4, concentrated and purified by silica column chromatography (CH_2Cl_2:CH_3OH = 200:1, v:v) to afford the product **5** as pale yellow solid.

(*S*)-5 (118.81 mg, 30% yield) ^{1}H NMR (600 MHz, Chloroform-*d*) δ (ppm) 10.06 (s, 2H), 8.16 (d, J = 1.9 Hz, 2H), 8.05 (d, J = 9.0 Hz, 2H), 7.98 – 7.96 (m, 4H), 7.86 – 7.83 (m, 4H), 7.57 – 7.52 (m, 4H), 7.27 (s, 2H), 4.28 – 4.24 (m, 2H), 4.13 – 4.10 (m, 2H), 3.68 – 3.63 (m, 4H), 3.58 – 3.51 (m, 8H), 3.43 (t, J = 4.4 Hz, 4H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ (ppm) 191.87, 155.24, 147.11, 135.03, 134.74, 133.86, 130.34, 129.99, 129.46, 127.61, 126.67, 126.29, 125.55, 120.09, 116.63, 70.91, 70.69, 70.63, 69.80.

(*R*)-5 (122.77 mg, 31% yield) ^{1}H NMR (600 MHz, Chloroform-*d*) δ (ppm) 10.06 (s, 2H), 8.16 (d, J = 1.9 Hz, 2H), 8.05 (d, J = 9.0 Hz, 2H), 8.00 – 7.94 (m, 4H), 7.90 – 7.82 (m, 4H), 7.60 – 7.50 (m, 4H), 7.27 (s, 2H), 4.28 – 4.24 (m, 2H), 4.13 – 4.10 (m, 2H), 3.64 (d, J = 9.6 Hz, 4H), 3.59 – 3.51 (m, 8H), 3.44 (d, J = 5.1 Hz, 4H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ (ppm) 191.87, 155.23, 147.11, 135.02, 134.73, 133.86, 130.34, 129.99, 129.46, 127.61, 126.67, 126.29, 125.55, 120.08, 116.63, 70.91, 70.69, 70.63, 69.80.

2.2 Synthesis of (*S*)- and (*R*)-6[1].



A solution of tris(2-aminoethyl)amine (373 μL, 0.086 mmol, 0.2 M in chloroform) was added dropwise into a solution of **(*S*)-** or **(*R*)-5** (71 mg, 0.1mmol) in 20 mL of chloroform. After the reaction mixture was stirred at 25 ºC for 24 h, the mixture was poured into 50 mL of methanol. The precipitate was filtered and dried under vacuum to afford **(*S*)-** or **(*R*)-6** as a white solid.

(*S*)-6 (42.45 mg, 55% yield) ^{1}H NMR (600 MHz, Chloroform-*d*) δ (ppm) 8.01 (s, 6H), 7.95 (d, *J* = 8.9 Hz, 6H), 7.63 (s, 6H), 7.43 (dd, *J* = 8.5, 6.4 Hz, 18H), 7.33 (dd, *J* = 8.6, 1.9 Hz, 6H), 7.27 (d, *J* = 8.7 Hz, 6H), 6.99 (d, *J* = 7.8 Hz, 12H), 4.14 – 4.09 (m, 6H), 3.94 (dt, *J* = 10.8, 4.3 Hz, 6H), 3.63 – 3.59 (m, 12H), 3.54 – 3.52 (m, 16H), 3.48 (q, *J* = 4.1 Hz, 12H), 3.41 – 3.37 (m, 8H), 3.31 (t, *J* = 4.3 Hz, 12H), 2.96 – 2.91 (m, 6H), 2.80 (dd, *J* = 13.2, 6.2 Hz, 6H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ (ppm) 161.14, 154.70, 144.12, 136.47, 135.03, 133.42, 129.52, 129.49, 128.67, 127.84, 126.17, 125.72, 120.25, 116.57, 70.82, 70.66, 70.58, 69.77, 69.70, 59.95, 56.71.

(*R*)-6 (41 mg, 53% yield) ^{1}H NMR (600 MHz, Chloroform-*d*) δ (ppm) 8.01 (s, 6H), 7.95 (d, *J* = 8.9 Hz, 6H), 7.63 (s, 6H), 7.43 (t, *J* = 7.9 Hz, 18H), 7.32 (d, *J* = 8.6 Hz, 6H), 7.28 (d, *J* = 8.7 Hz, 6H), 6.99 (d, *J* = 7.7 Hz, 12H), 4.13 -4.10 (m, 6H), 3.94 (dt, *J* = 10.0, 4.3 Hz, 6H), 3.61 -3.59 (m, 12H), 3.55 – 3.52 (m, 16H), 3.48 (q, *J* = 4.0 Hz, 12H), 3.41 -3.37 (m, 8H), 3.31 (t, *J* = 4.3 Hz, 12H), 2.93 (t, *J* = 11.0 Hz, 6H), 2.80 (dd, *J* = 13.6, 6.2 Hz, 6H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ (ppm) 161.14, 154.70, 144.12, 136.47, 135.03, 133.42, 129.52, 129.49, 128.67, 127.84, 126.17, 125.72, 120.25, 116.57, 70.82, 70.66, 70.58, 69.77, 69.70, 59.95, 56.71.

2.3 NMR and ESI-MS spectra of the compounds.

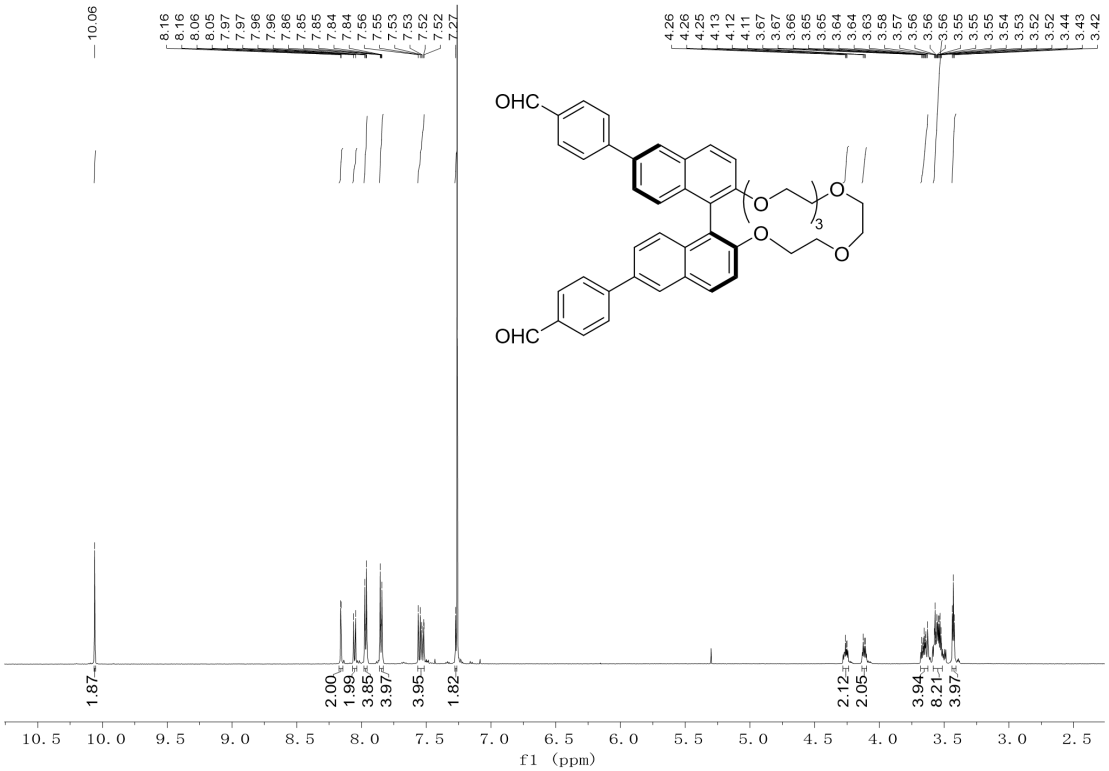


Figure S1 ^{1}H NMR spectrum of **(*S*)-5** in $CDCl_3$ at 298 K.

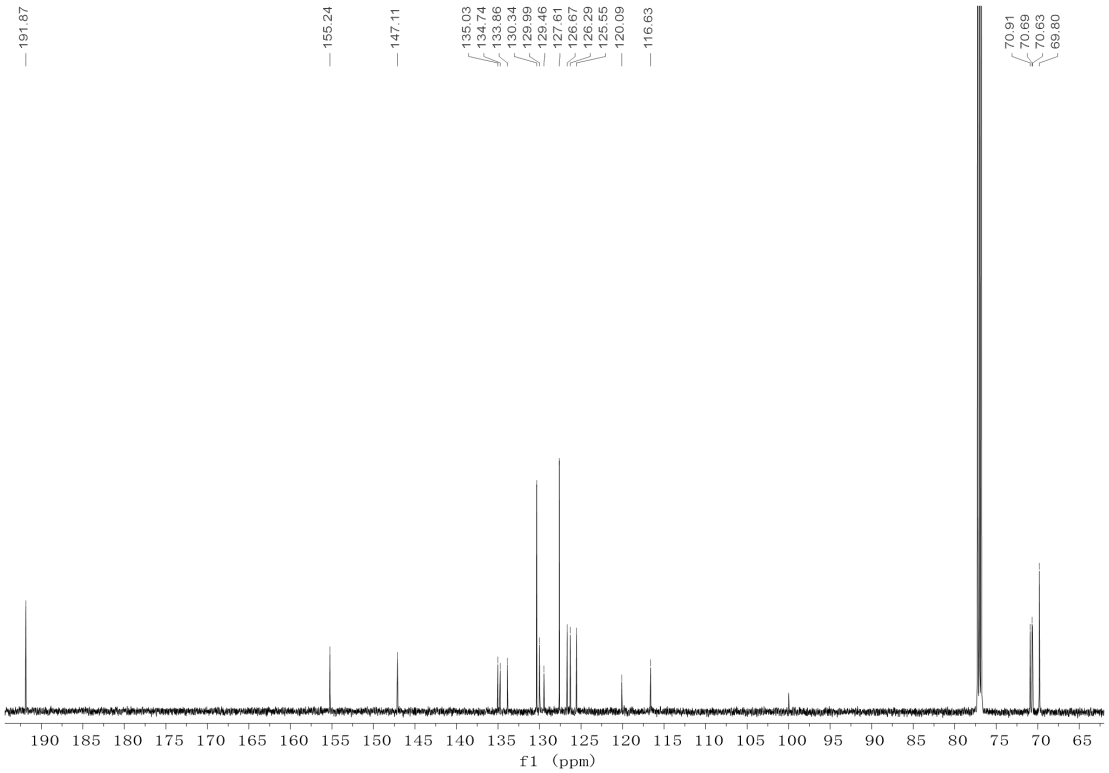


Figure S2 ^{13}C NMR spectrum of **(*S*)-5** in $CDCl_3$ at 298 K.

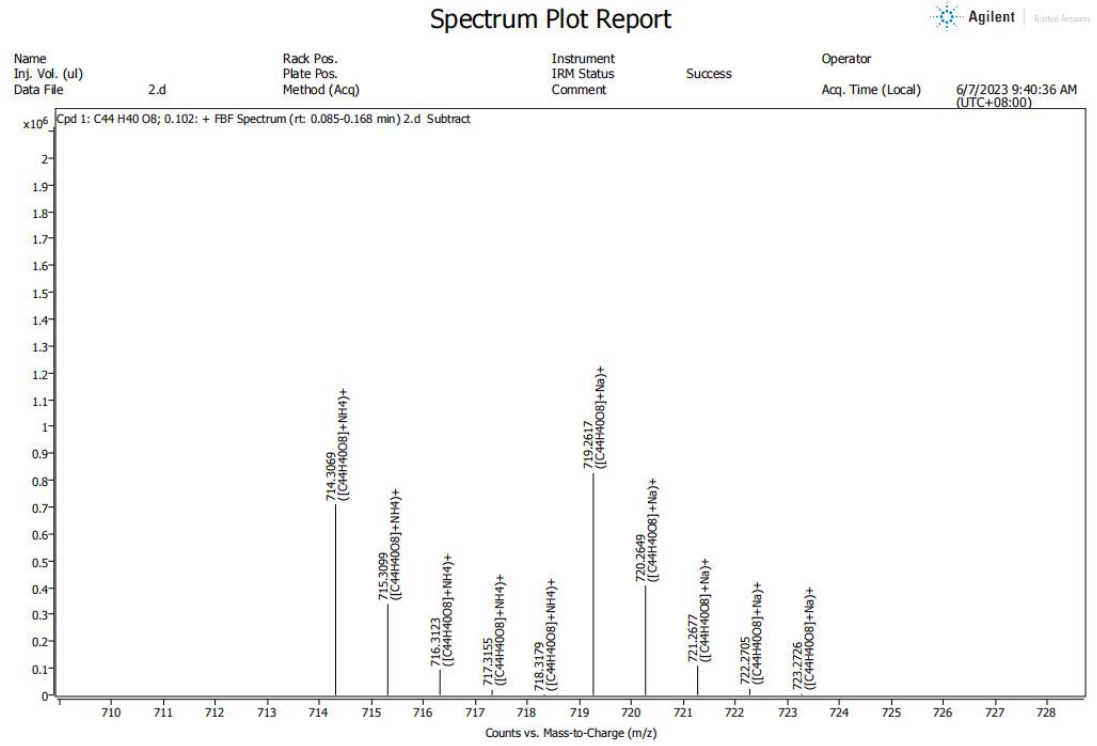


Figure S3 ESI-HRMS (Q-TOF) spectrum of **(*S*)-5**. ESI-HRMS (Q-TOF) (*m/z*) Calcd. for [**(*S*)-5** + NH_4]$^+$:714.3067; Found: 714.3069. Calcd. for [**(*S*)-5** + Na]$^+$: 719.2621; Found:719.2617.

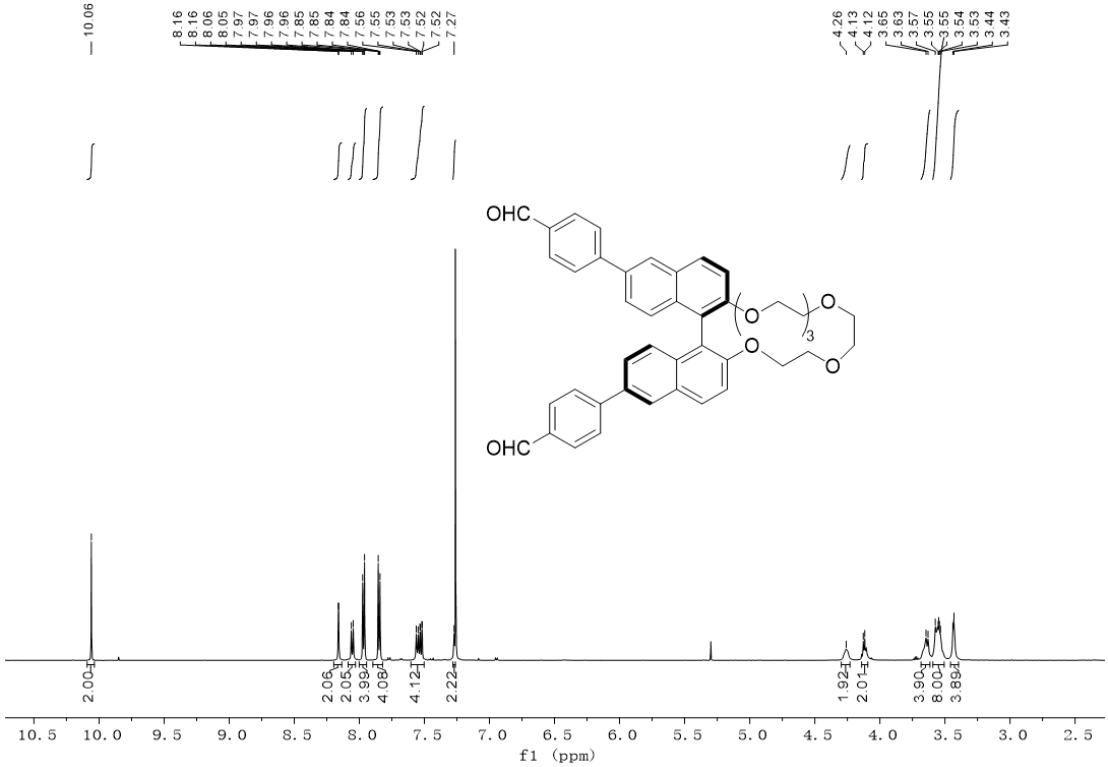


Figure S4 ^{1}H NMR spectrum of **(*R*)-5** in $CDCl_3$ at 298 K.

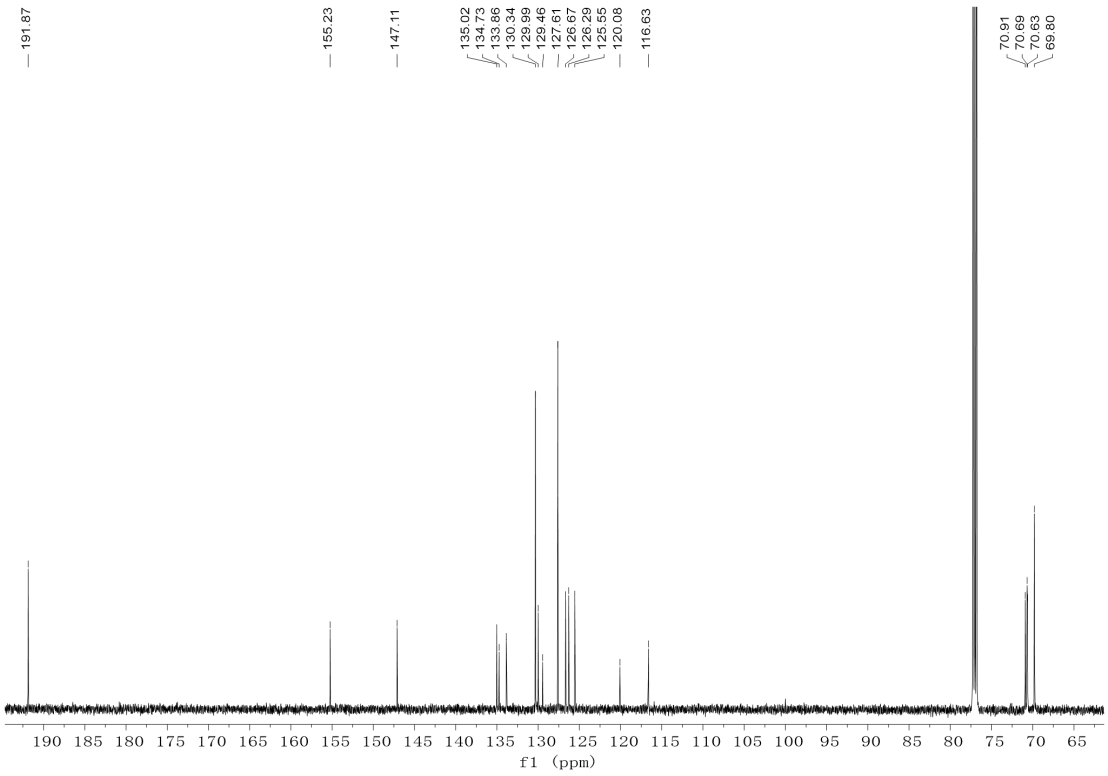


Figure S5 ^{13}C NMR spectrum of **(*R*)-5** in $CDCl_3$ at 298 K.

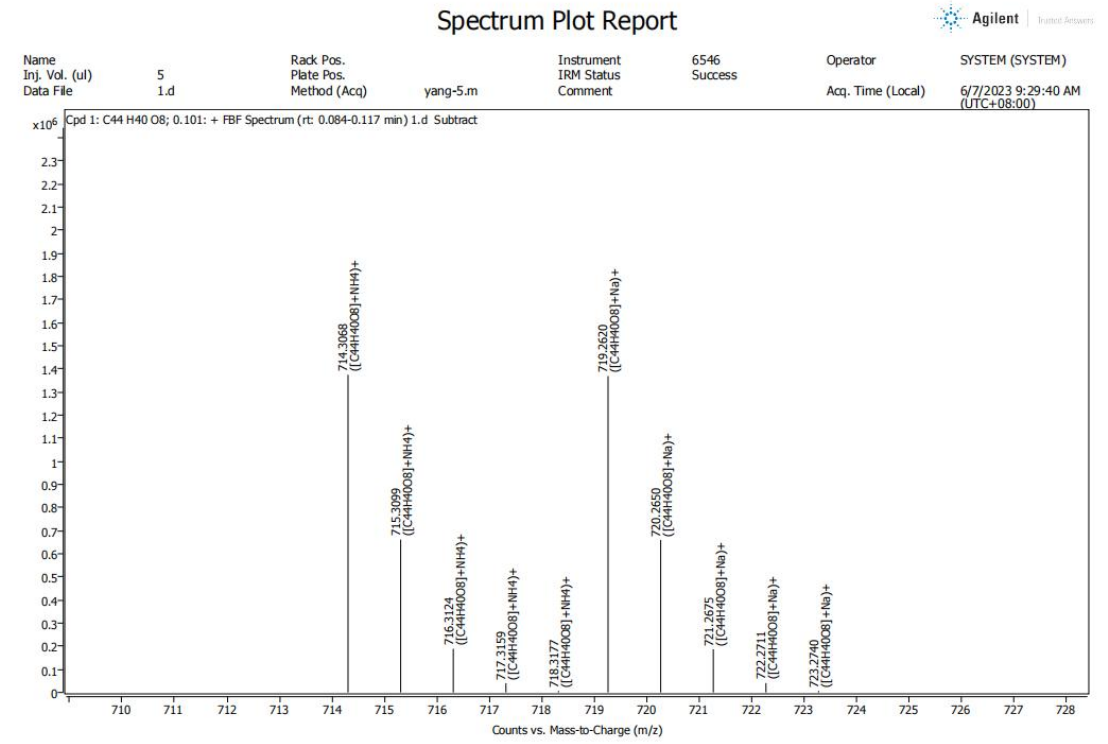


Figure S6 ESI-HRMS (Q-TOF) spectrum of **(*R*)-5**. ESI-HRMS (Q-TOF) (*m/z*) Calcd. for [**(*R*)-5** + NH_4]$^+$:714.3067; Found: 714.3068. Calcd. for [**(*R*)-5** + Na]$^+$: 719.2621; Found:719.2620.

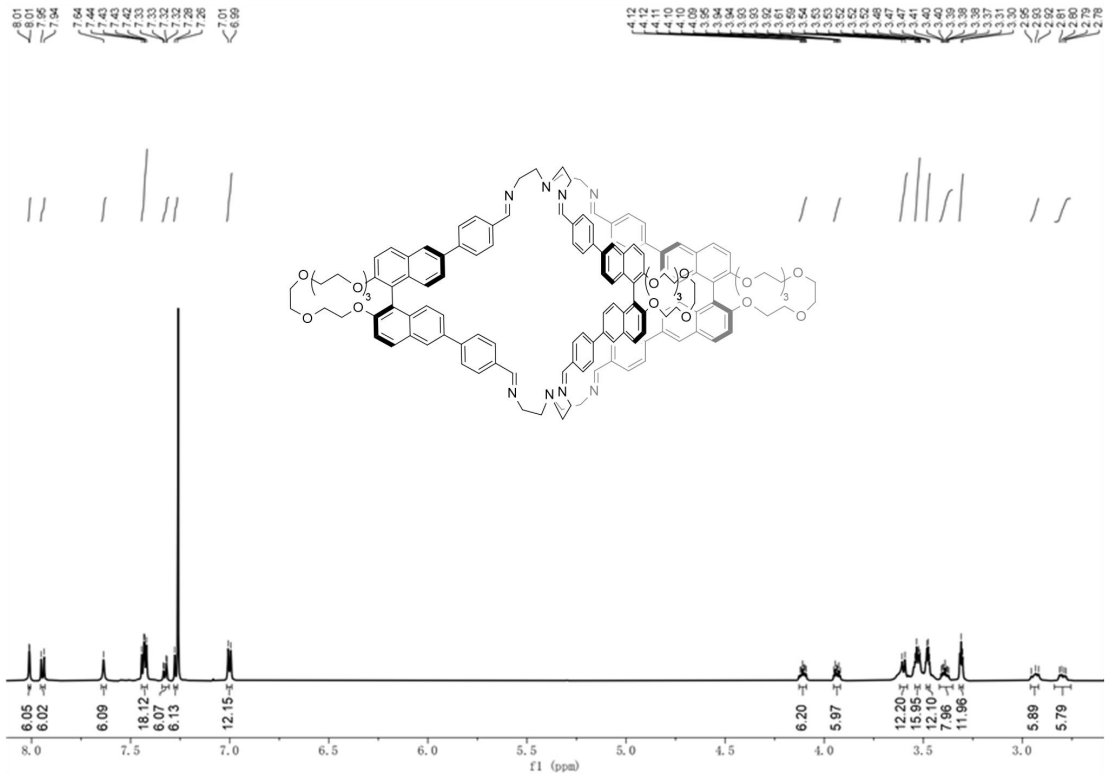


Figure S7 ^{1}H NMR spectrum of **(*S*)-6** in $CDCl_3$ at 298 K.

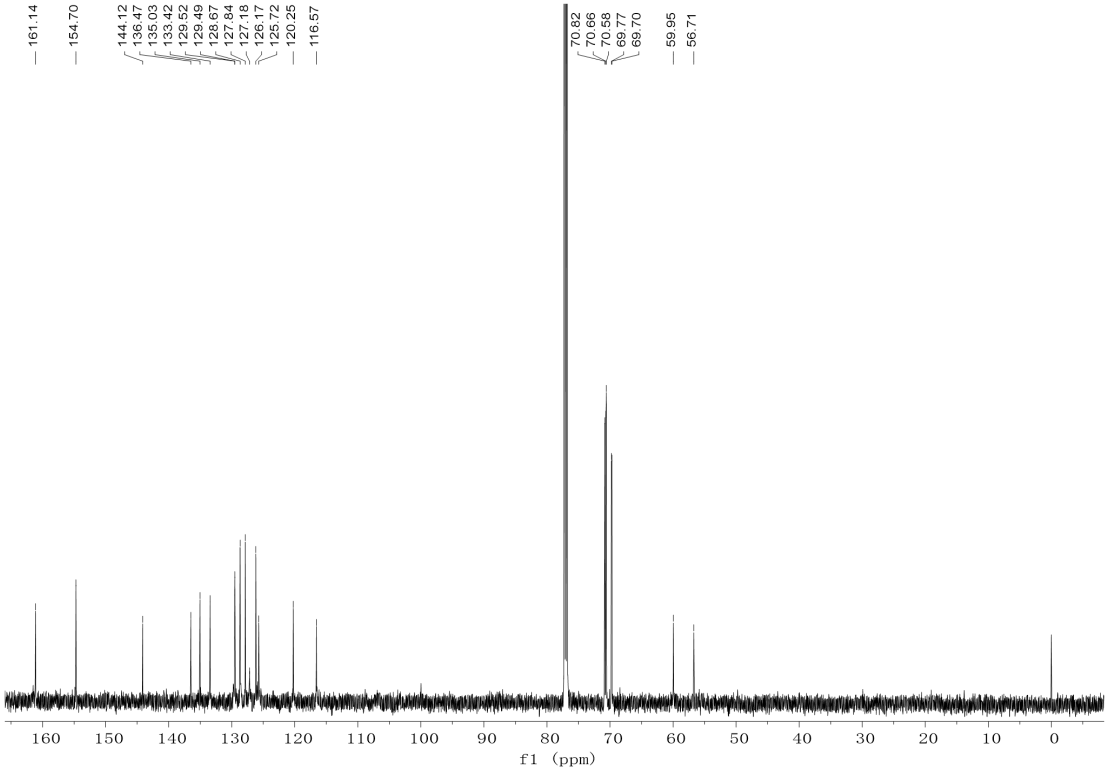


Figure S8 ^{13}C NMR spectrum of **(*S*)-6** in $CDCl_3$ at 298 K.

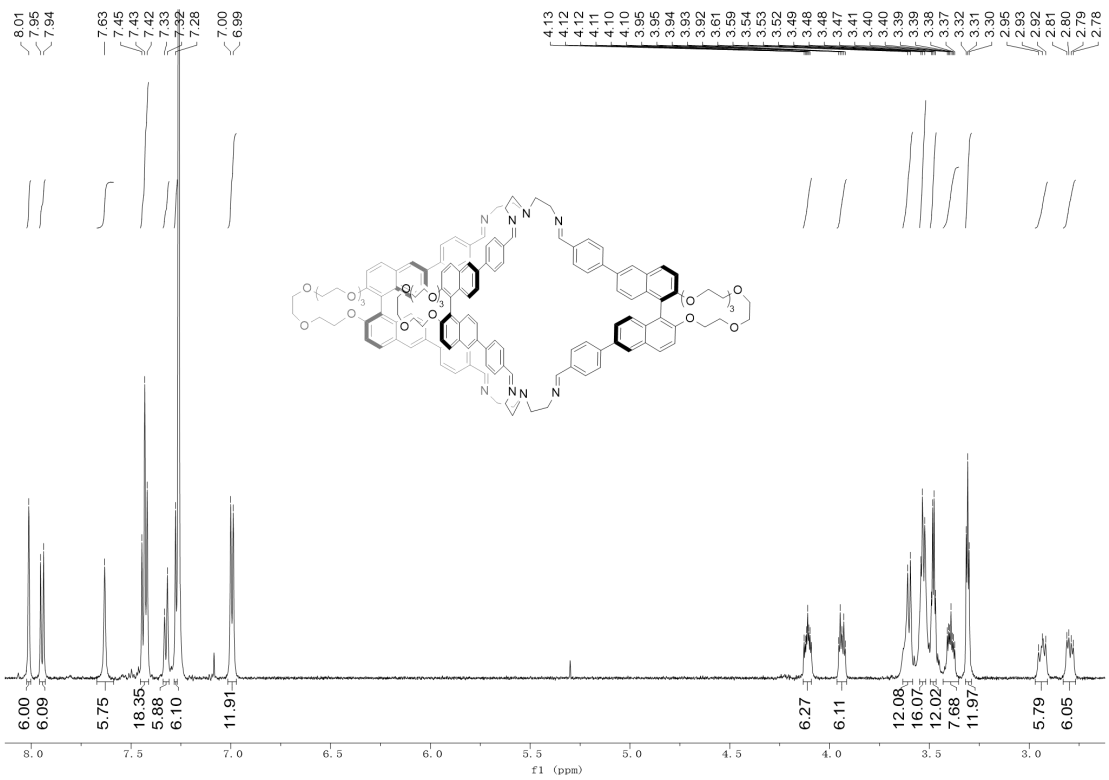


Figure S9 ^{1}H NMR spectrum of **(*R*)-6** in $CDCl_3$ at 298 K.

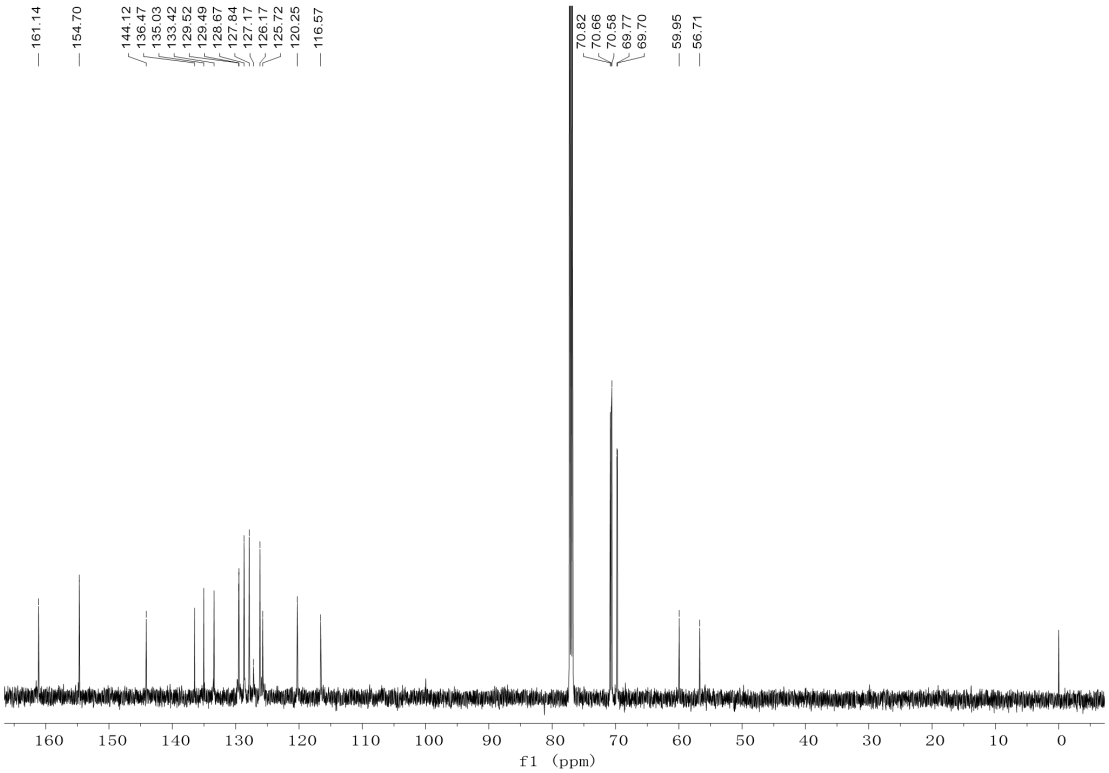


Figure S10 ^{13}C NMR spectrum of **(*R*)-6** in $CDCl_3$ at 298 K.

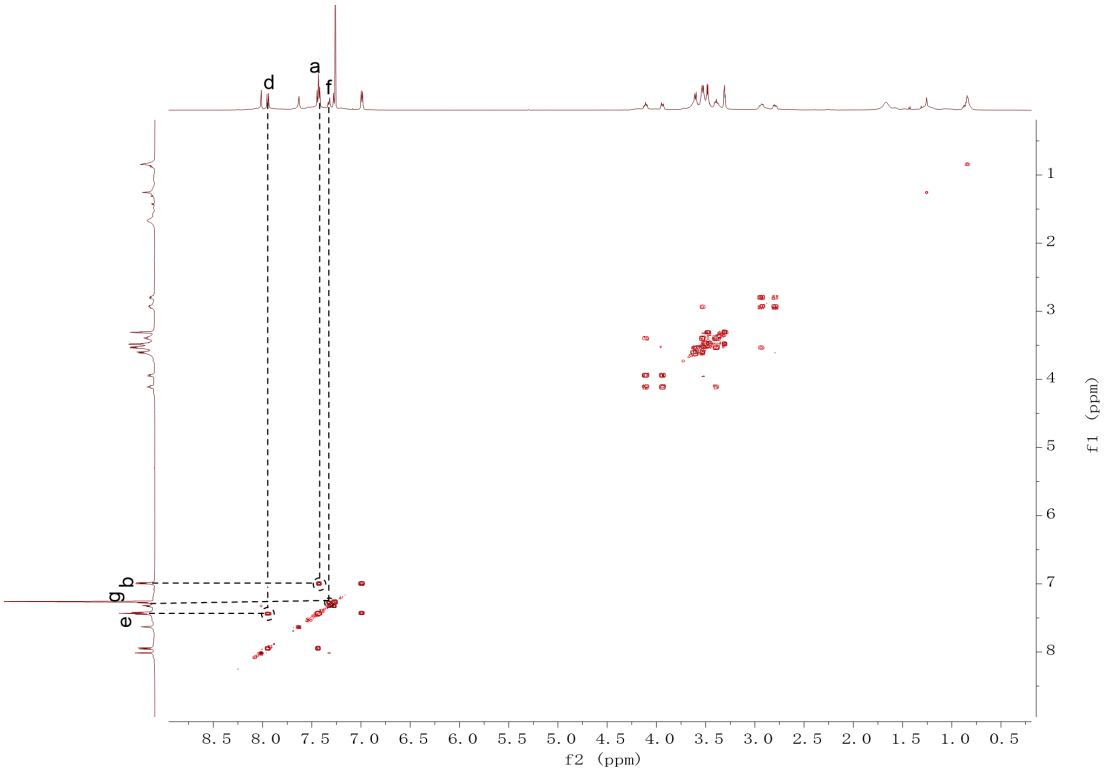


Figure S11 ^{1}H-^{1}H COSY spectra of **(*S*)-6** in $CDCl_3$ at 298 K.

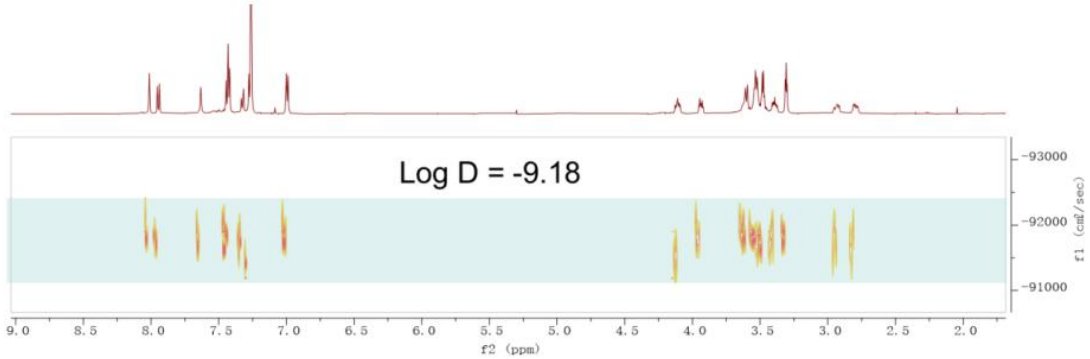


Figure S12 DOSY spectrum of **(*S*)-6** in $CDCl_3$ at 298 K.

In Stokes-Einstein equation,

$$D = \frac{Tk_B}{6\pi\eta r}$$

which was applied to estimate the dynamic radius for the **Cage**. D is diffusion coefficient obtained from DOSY spectrum, k_B is Boltzmann constant, T is temperature, Solvent viscosity η tested to be 0.57 mPa•s, and r is the estimated dynamic radius.

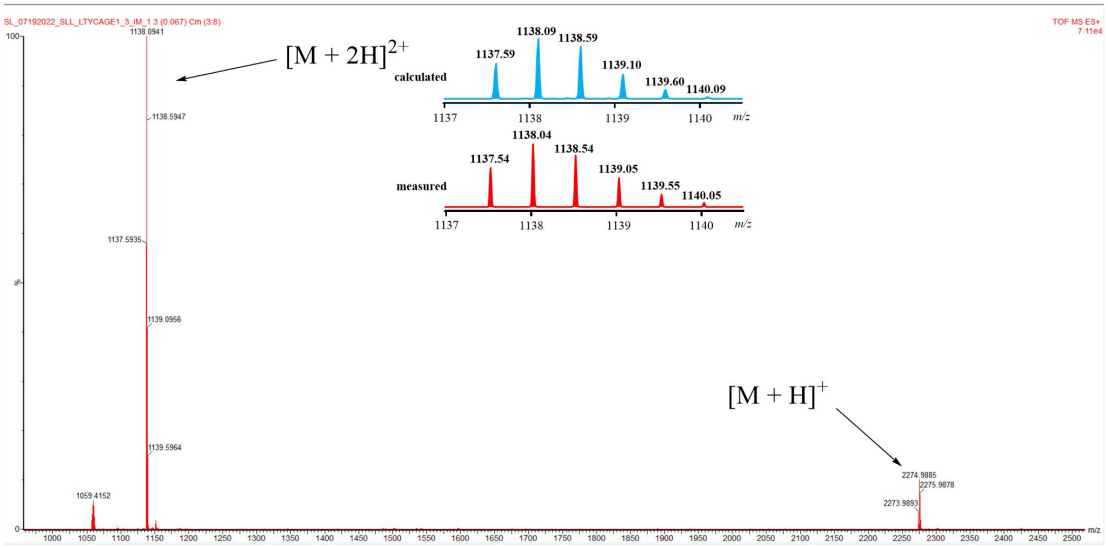


Figure S13 ESI-MS spectrum of **(*S*)-6**. Mass peak at *m/z* 1138.0941 for $[M+2H]^{2+}$was zoomed in to compare with the calculated mass.

2.4 UV-vis and CD spectra of cage..

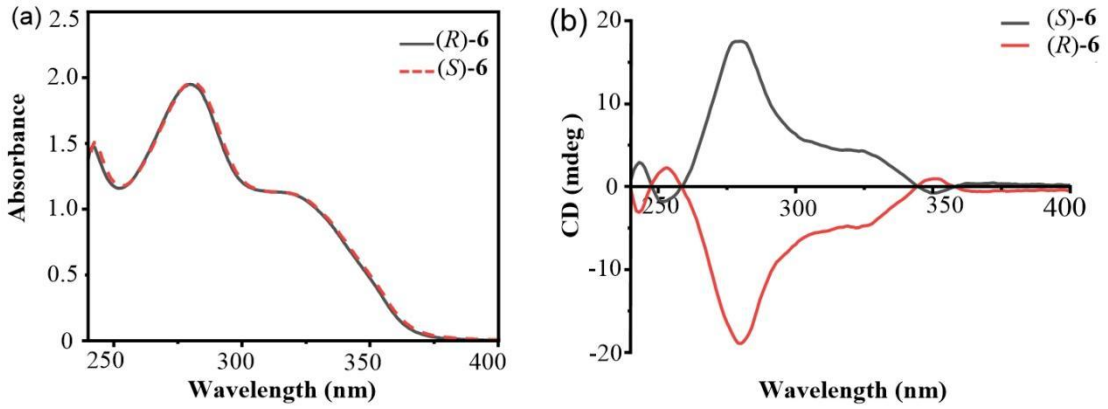


Figure S14. (a) The UV-vis spectra of **(*R*)-6** and **(*S*)-6** in $CDCl_3$ (c = 0.01 mM); (b) CD spectra of **(*R*)-6** and **(*S*)-6** in $CDCl_3$ (c = 0.1 mM).

3.NMR spectra of host-guest interaction.

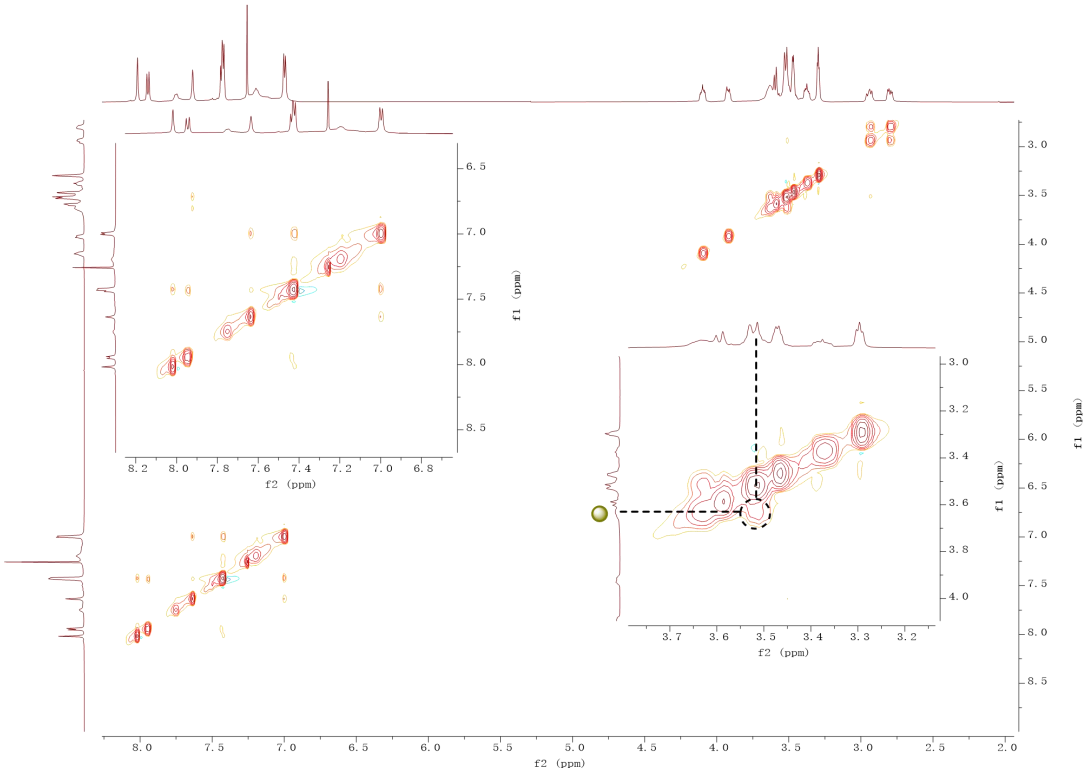


Figure S15. NOESY spectra of **(*R*)-6** +1 equiv (*S*)-binam.

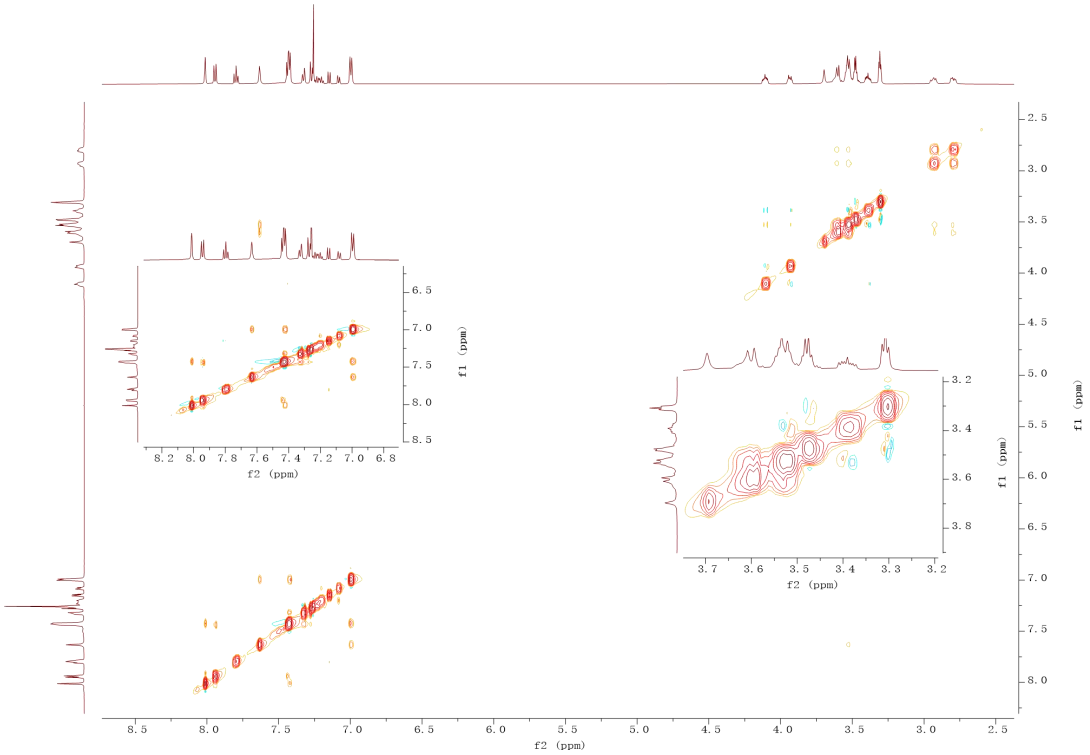


Figure S16. NOESY spectra of **(*R*)-6** +1 equiv (*R*)-binam.

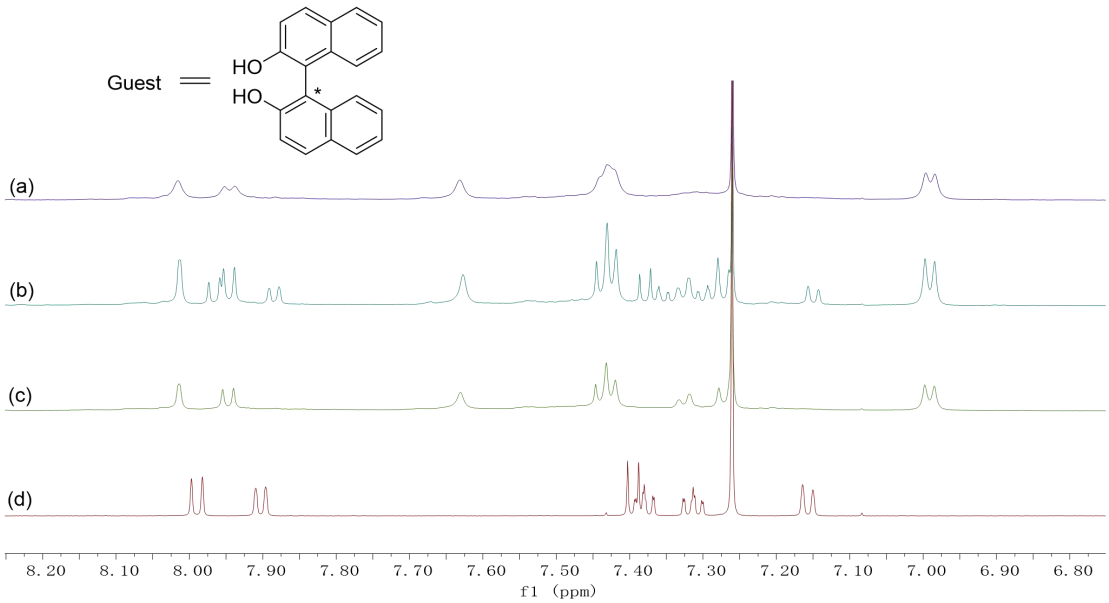


Figure S17 ^{1}H NMR spectra of **(*R*)-6** +1 equiv (*S*)-binol (a), **(*R*)-6** +1 equiv (*R*)-binol (b), **(*R*)-6** (c) and binol (d) in $CDCl_3$ at 298 K.

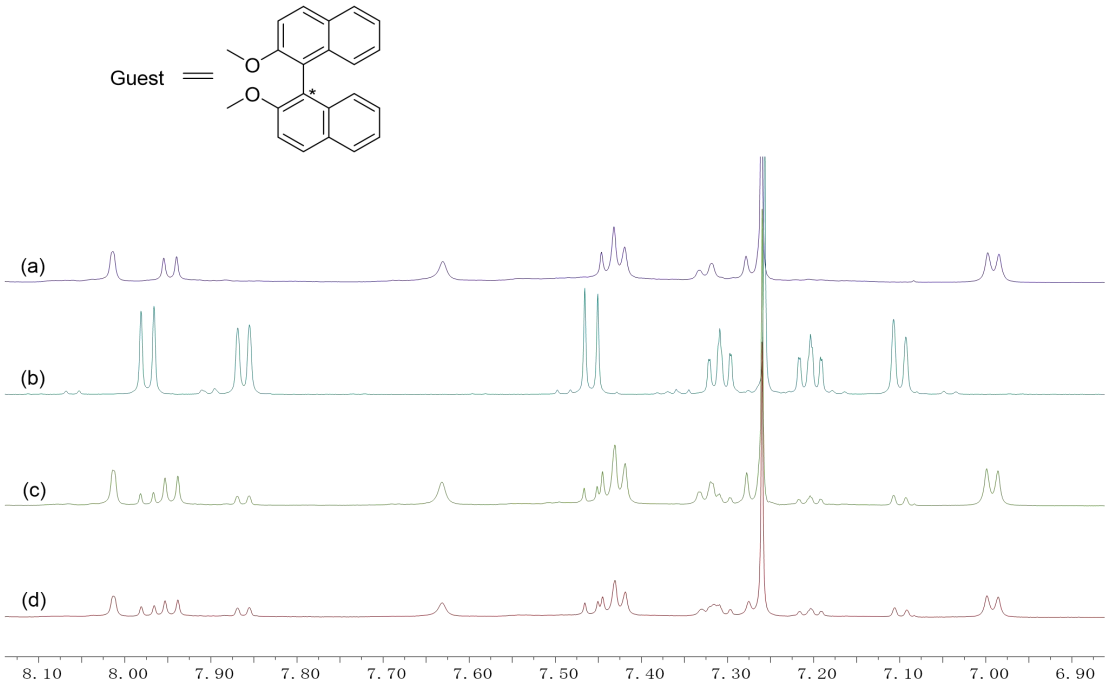


Figure S18 ^{1}H NMR spectra of **(*R*)-6** (a), *rac*- 2,2'-dimethoxy-1,1'-binaphthalene (b), **(*R*)-6** +1 equiv (*R*)- 2,2'-dimethoxy-1,1'-binaphthalene (c) and **(*R*)-6** +1 equiv (*S*)-2,2'-dimethoxy-1,1'-binaphthalene (d) in $CDCl_3$ at 298 K.

4.Chiral resolution of guest molecules by (*R*)-6.

4.1 Chiral resolution result for different time.

(*R*)-6 (6 mg, 0.003 mmol) and *rac*-binam (0.75mg 0.003 mmol) were added to 1.5 mL of $CHCL_3$, stirred at room temperature. Upon completion of reaction, the mixture was concentrated in vacuo. The solid was extracted with diethyl ether to get the solution of free guest molecules. The solution was concentrated in vacuo. Then, additional covalent cage were incorporated into the resulting product. Finally, chloroform was added to dissolve the mixture. *rac*-binam was separated two times and then the solution was centrifuged and enantiomeric excess (*ee*) value was determined by chiral HPLC. (Chiralcel AS-H column, isopropanol/hexane =15:85; flow rate 1.0 mL/min).

4.2 Chiral resolution result for different guest molecules.

(1) *rac*-binol

(*R*)-6 (6 mg, 0.003 mmol) and *rac*-binol (0.75mg 0.003 mmol) were added to 1.5 mL of $CHCL_3$, stirred at room temperature for 2 h. Upon completion of reaction, the mixture was concentrated in vacuo. The solid was extracted with diethyl ether to get the solution of free guest molecules. The solution was concentrated in vacuo. Then, additional covalent cage were incorporated into the resulting product. Finally, chloroform was added to dissolve the mixture. *rac*-binol was separated three times and then the solution was centrifuged and enantiomeric excess (*ee*) value was determined by chiral HPLC. (Chiralcel AS-H column, isopropanol/hexane =15:85; flow rate 1.0 mL/min).

(2) *rac*-6-Br-binol

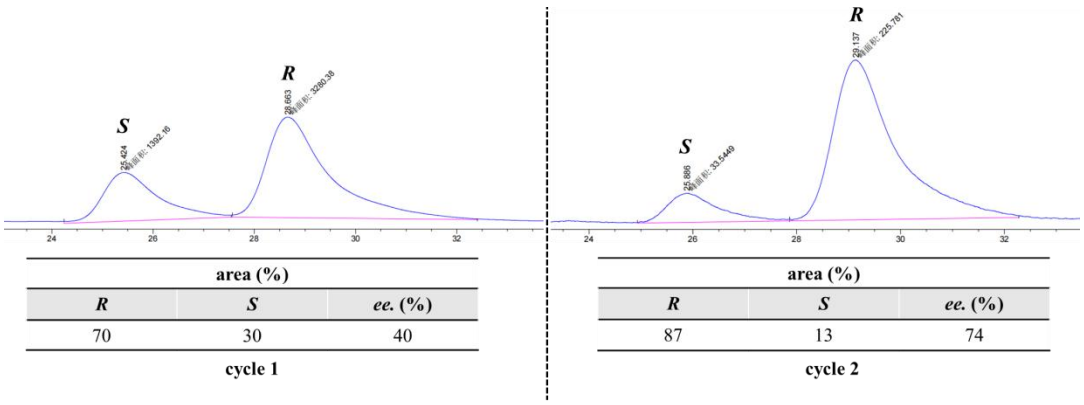
(*R*)-6 (6 mg, 0.003 mmol) and *rac*-6-Br-binol (1.17mg 0.003 mmol) were added to 1.5 mL of $CHCL_3$, stirred at room temperature for 2 h. Upon completion of reaction, the mixture was concentrated in vacuo. The solid was extracted with diethyl ether to get the solution of free guest molecules. The solution was centrifuged and enantiomeric excess (*ee*) value was determined by chiral HPLC. (Chiralcel AS-H column, isopropanol/hexane =10:90; flow rate 1.0 mL/min).

(3) *rac*-3-phenyl-binol

(*R*)-6 (6 mg, 0.003 mmol) and *rac*-3-phenyl-binol (1.16mg 0.003 mmol) were added to 1.5 mL of $CHCL_3$, stirred at room temperature for 2 h. Upon completion of reaction, the mixture was concentrated in vacuo. The solid was extracted with diethyl ether to get the solution of free guest molecules. The solution was centrifuged and enantiomeric excess (*ee*) value was determined by chiral HPLC. (Chiralcel OD-H column, isopropanol/hexane = 10:90; flow rate 1.0 mL/min).

(4) *rac*-sprioidol

(*R*)-6 (6 mg, 0.003 mmol) and *rac*-sprioidol (0.67mg 0.003 mmol) were added to 1.5 mL of $CHCL_3$, stirred at room temperature for 2 h. Upon completion of reaction, the mixture was concentrated in vacuo. The solid was extracted with diethyl ether to get the solution of free guest molecules. The solution was centrifuged and enantiomeric excess (*ee*) value was determined by chiral HPLC. (Chiralcel AD-H column, isopropanol/hexane = 20:80; flow rate 1.0 mL/min).



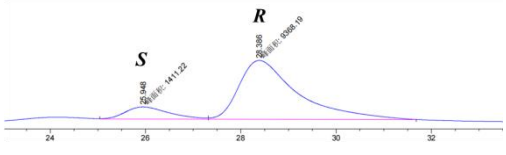
area (%)		
R	*S*	*ee.* (%)
70	30	40

cycle 1

area (%)		
R	*S*	*ee.* (%)
87	13	74

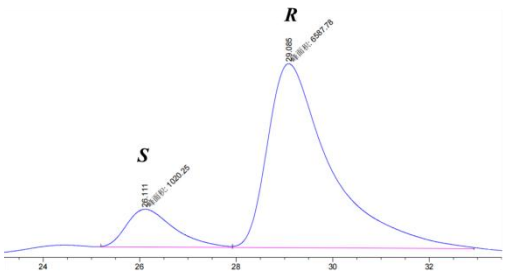
cycle 2

Figure S19 Successive enantioseparation results of (±)-binam after two hours of reaction.



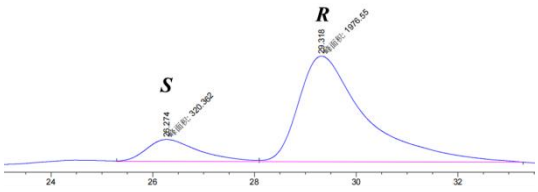
area (%)		
R	*S*	*ee.* (%)
87	13	74

Figure S20 Successive enantioseparation results of (±)-binam after 4 h of reaction.



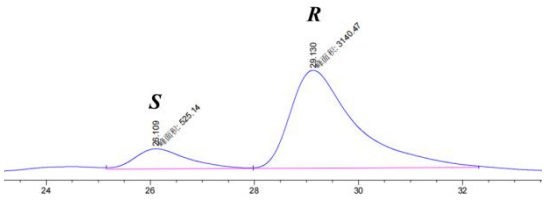
area (%)		
R	***S***	***ee.* (%)**
87	13	74

Figure S21 Successive enantioseparation results of (±)-binam after 6 h of reaction.



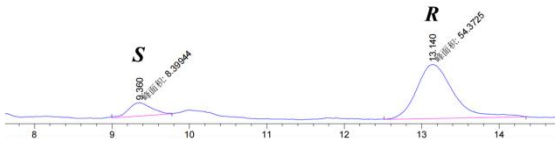
area (%)		
R	***S***	***ee.* (%)**
86	14	72

Figure S22 Successive enantioseparation results of (±)-binam after 8 h of reaction.



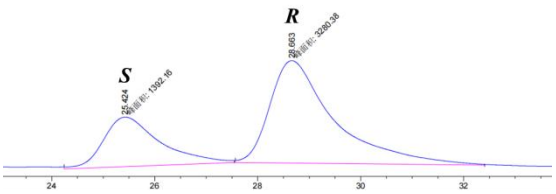
area (%)		
R	***S***	***ee.* (%)**
86	14	72

Figure S23 Successive enantioseparation results of (±)-binam after 12 h of reaction.



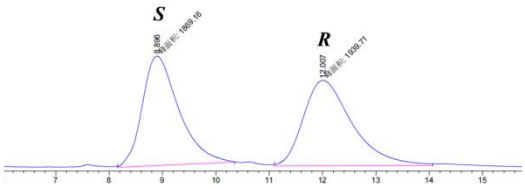
area (%)		
R	***S***	***ee.* (%)**
87	13	74

Figure S24 Successive enantioseparation results of (±)-binol



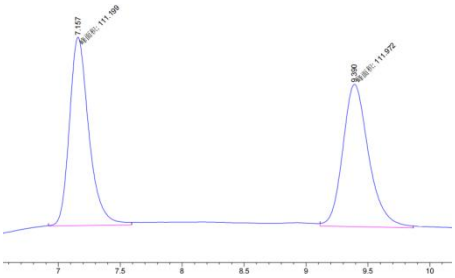
area (%)		
R	***S***	***ee.* (%)**
63	37	26

Figure S25 Enantioseparation results of (±)-6-Br-binol.



area (%)		
R	***S***	***ee.* (%)**
51	49	2

Figure S26 Enantioseparation results of (±)-3-phenyl-binol.



area (%)		
R	***S***	***ee.* (%)**
50	50	0

Figure S27 Enantioseparation results of (±)sprioidol.

4. References.

[1] Li, T., Ding L., Kang Y., Hao X.Q., Guo Y., Shi L., Song M.P. *Chem. Synth*. 2023, **3,** 45.