Supplementary Information for

High-efficient Synthesis of Covalent Porphyrinic Cages via DABCO-templated Imine Condensation Reactions

Huimin Ding,[a] Xiangshi Meng,[a] Xu Cui,[a] Yihui Yang,[a] Tailin Zhou,[a] Caixing Wang,[a] Matthias Zeller[b] and Cheng Wang*[a]

[a] Key Laboratory of Biomedical Polymers (Ministry of Education), College of Chemistry and Molecular Sciences, Wuhan University, Wuhan 430072, China

[b] Department of Chemistry, Youngstown State University, One University Plaza, Youngstown, Ohio, USA

*E-mail address: chengwang@whu.edu.cn

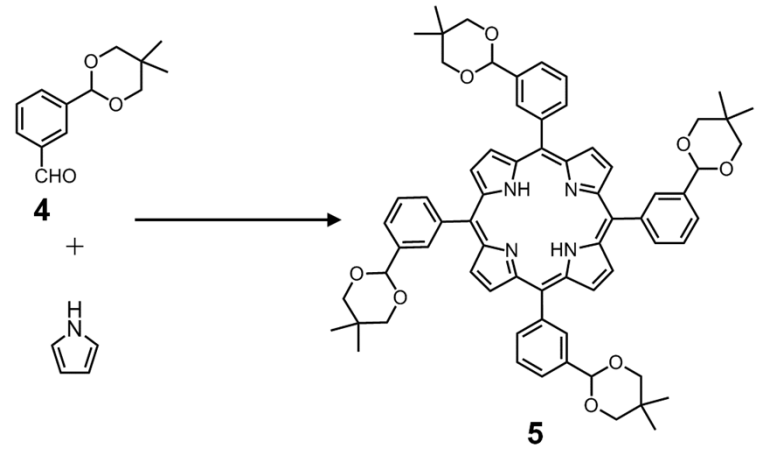
1. General Methods

Toluene, dichloromethane, chloroform, tetrahydrofuran, sulfuric acid, N, N-dimethylformamide (DMF), pyrrole, trifluoroacetic acid (TFA), *p*-chloranil, 1,4-diazabicyclo [2.2.2.] octane (DABCO), ethylenediamine and propane diamine were purchased from Acros. Dehydrated solvents were obtained after treating solvents with standard procedures. Neopentyl glycol, *p*-toluene sulfonic acid (TsOH) and 3-bromobenzaldehyde were purchased from TCI. Zinc acetate dihydrate and *n*-BuLi was purchased from Aladdin. Compound **4** was prepared according to the literature.[S1]

NMR spectra were measured on Bruker Fourier 300 M and 500 M spectrometer. Chemical shifts are quoted as parts per million (ppm) relative to residual $CHCl_3$ at δ=7.26 ppm. High resolution MALDI–TOF data was collected on a Bruker Solarix instrument. The X-ray crystal data for cage-**1** were collected at 298 K at the Beijing Synchrotron Radiation Facility, beam line station 3W1A equipped with a MarCCD-165 detector. The structures were solved by direct methods. CCDC 1013794 contains crystallographic data for this paper.

2. Chemical synthesis

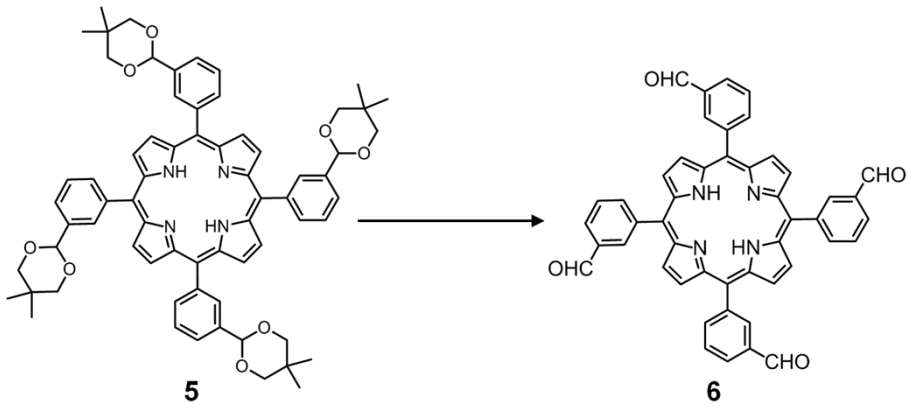
Scheme S1 Synthesis of compound **5**



Compound 5: Compound **4** (2.2 g, 10 mmol) and fresh distilled pyrrole (0.69 mL, 11 mmol) were dissolved in dry CH_2Cl_2 (700 mL) and purged with nitrogen for 30 min., upon which TFA (0.77 mL, 10 mmol) was added. The resulting solution was stirred at room temperature for 2 h, and *p*-chloranil (1.84 g, 3.2 mmol) was added to the resulting

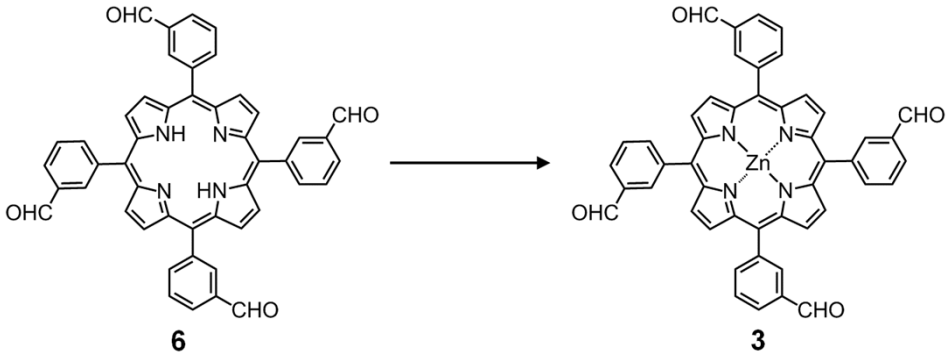
mixture, which was further stirred overnight. The reaction mixture was filtered through a silica gel pad, followed by washing with CH_2Cl_2 until the filtrate appeared colorless. The filtrate was then concentrated under vacuum, and the residue was purified by flash column chromatography [SiO_2 : CH_2Cl_2 / EtOAc (50 : 1)]. Compound **5** was isolated as a purple solid, which was further purified by recrystallization from $CHCl_3$/methanol (0.41 g, yield, 15%). ^{1}H NMR (300 MHz, $CDCl_3$, 298 K, ppm): δ = 8.83 (s, 8H), 8.33 (s, 4H), 8.18 (s, 4H), 7.98 (d, *J* = 7.9 Hz, 4H), 7.77 (t, *J* = 7.7 Hz, 4H), 5.67 (s, 4H), 3.87–3.72 (m, 16H), 1.34 (s, 12H), 0.82 (s, 12H), -2.85 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$, 298K, ppm): δ = 142.5, 137.5, 135.4, 132.9, 127.2, 125.9, 120.2, 102.4, 78.2, 30.7, 23.6, 22.3. MALDI-TOF MS: calcd for $C_{68}H_{70}N_4O_8$ *m/z* =1071.52719 $[M+H]^+$; found: *m/z* = 1071.5257 $[M+H]^+$.

Scheme S2 Synthesis of compound **6**



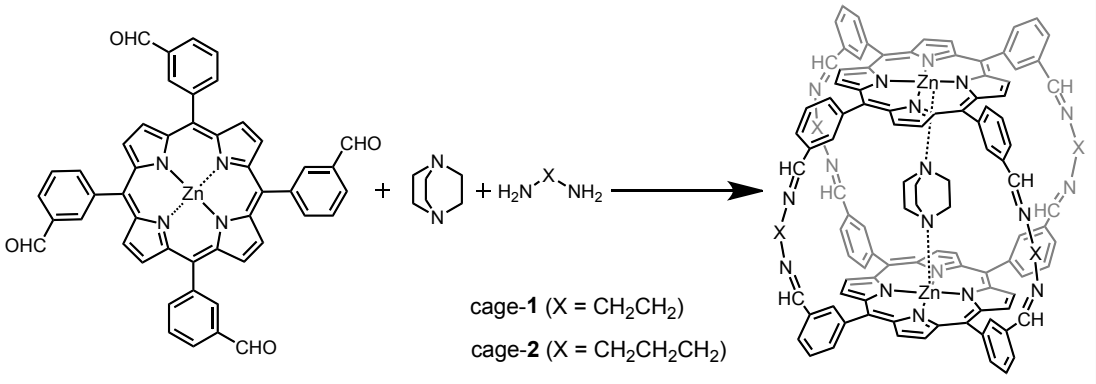
Compound 6: A stirred solution of compound **5** (0.4 g, 0.37 mmol) in $CHCl_3$: H_2SO_4 (9 M) (1:1, 40 mL) was heated at reflux for 3 d. After cooling down to room temperature, H_2O (50 mL) was added. The solution was extracted with CH_2Cl_2 (3×50 mL), and the combined extracts were washed with aqueous 10% NaOH (2×20 ml) and brine (3×50 mL), then dried over Na_2SO_4. After that, the solvents were evaporated under reduced pressure and compound **6** was isolated as a purple solid (0.26 g, yield, 95%). ^{1}H NMR (300 MHz, $CDCl_3$, 298 K, ppm): δ = 10.33 (s, 4H), 8.81 (s, 8H), 8.72 (s, 4H), 8.51 (d, *J* = 7.6 Hz, 4H), 8.36 (d, *J* = 7.8 Hz, 4H), 7.97 (t, *J* = 7.7 Hz, 4H), -2.77 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$, 298 K, ppm): δ = 192.8, 143.2, 140.1, 135.4, 131.8, 129.5, 128.0, 119.3. MALDI-TOF MS: calcd for $C_{48}H_{30}N_4O_4$ *m/z* = 726.22671 $[M]^+$; found *m/z* = 726.22916 $[M]^+$.

Scheme S3 Synthesis of compound **3**



Compound 3: $Zn(AcO)_2 \cdot 2H_2O$ (1.1g , 5.0 mmol) and compound **6** (0.2 g, 0.27 mmol) were added to a flask containing $CHCl_3$ (20 mL) and DMF (10 mL) and then heated at 80 °C for 4 h. After cooling down to room temperature, the solvents were concentrated to a small volume under reduced pressure. After that, H_2O (50 mL) was added. The purple precipitate was filtered, washed with H_2O (50 mL × 3), and dried under vacuum. Compound **3** was isolated as a purple powder (0.21 g, yield, 96%). ^{1}H NMR (400 MHz, $CDCl_3$, 298 K, ppm): δ = 10.22 (s, 4H), 8.89 (s, 8H), 8.67 (s, 4H), 8.48–8.40 (m, 4H), 8.31 (d, *J* = 7.6 Hz, 4H), 7.95 (t, *J* = 7.6 Hz, 4H).^{13}C NMR (75 MHz, $CDCl_3$, 298 K, ppm): δ =190.3, 150.4, 143.9, 140.0, 135.0, 132.5, 129.1, 127.8, 120.0, 107.3. MALDI-TOF MS: calcd for $C_{48}H_{28}N_4O_4Zn$ *m/z* = 788.14020 $[M]^+$; found *m/z* = 788.14237 $[M]^+$.

Scheme S4 Synthesis of cage-**1** and cage-**2**



Cage-1: Compound **3** (50 mg, 0.063 mmol), DABCO (3.5 mg, 0.031 mmol) and ethylene diamine (7.9 mg, 0.13 mmol) were dissolved in $CHCl_3$ (25 mL). The resulting mixture was left at room temperature for 24 h without stirring. After that, the solution was added drop wise into cool ether (200 mL) and purple solids precipitated out. The solvents were evaporated under reduced pressure and cage-**1** was obtained

quantitatively as a purple solid. ^{1}H NMR (500 MHz, $CDCl_3$, 298 K, ppm): δ = 8.83 (s, 8H), 8.75 (s, 8H), 8.49 (s, 16H), 7.87 (d, *J* = 7.6 Hz, 8H), 7.64 (d, *J* = 7.6 Hz, 8H), 7.51 (t, *J* = 7.6 Hz, 8H), 4.19 (d, *J* = 12.4 Hz, 16H), -4.58 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$, 298 K, ppm): δ = 163.6, 150.1, 143.9, 138.2, 134.7, 132.2, 128.9, 126.5, 120.1, 63.2, 39.2, 29.7. MALDI-TOF MS: calcd for $C_{110}H_{84}N_{18}Zn_2$: *m/z* = 1672.47088 [*M*-DABCO]$^+$; Found *m/z* = 1672.47081 [*M*-DABCO]$^+$.

Cage-2: Following the same procedure, cage-**2** was obtained quantitatively as a purple solid. ^{1}H NMR (500 MHz, $CDCl_3$, 298 K, ppm): δ = 8.56 (s, 8H), 8.43 (d, *J* = 7.7 Hz, 4H), 8.34 (s, 4H), 7.88–7.84 (m, 8H), 7.65 (t, *J* = 7.6 Hz, 4H), 3.83 (s, 8H), 2.50 (s, 4H), -4.61 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$, 298 K, ppm): δ = 162.1, 150.1, 143.4, 136. 9, 135.1, 134.5, 131.9, 127.5, 125.4, 120.1, 57.6, 39.1, 29.8. MALDI-TOF MS: calcd for $C_{114}H_{92}N_{18}Zn_2$: *m/z* = 1728.53348 [*M*-DABCO]$^+$; Found: *m/z* = 1728.53283 [*M*-DABCO]$^+$.

3. The tracing of cage formation

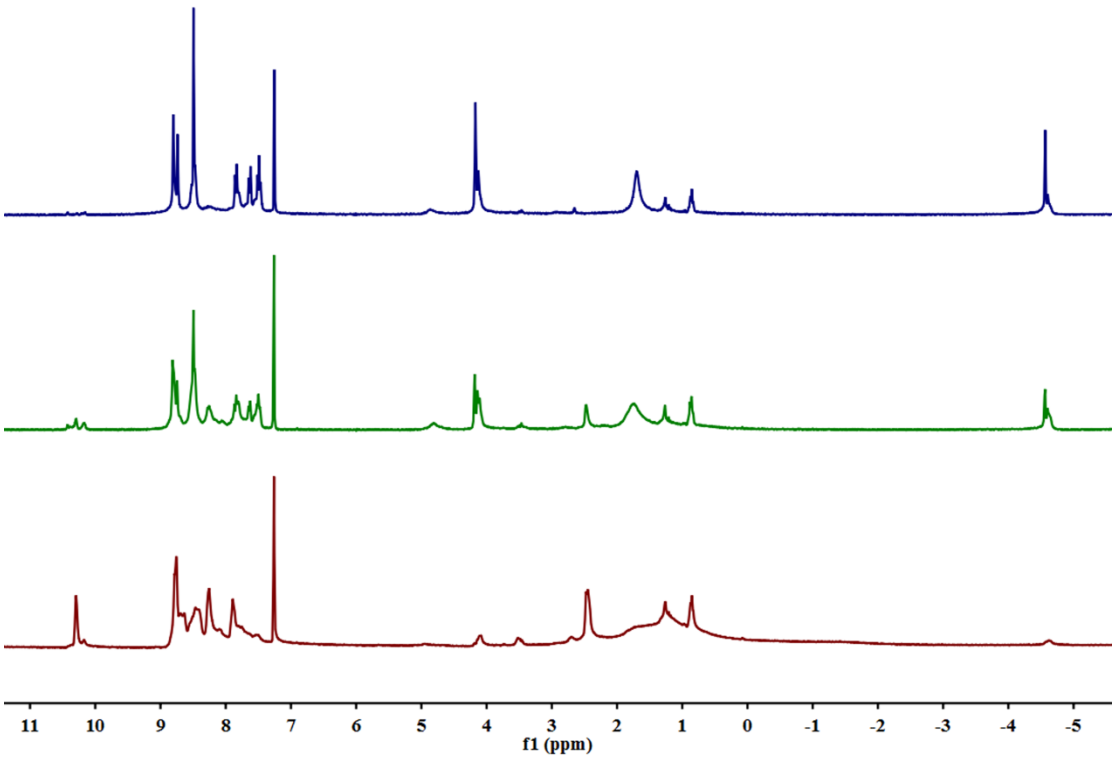


Fig. S1 Dynamic covalent formation of cage-**1** monitored by ^{1}H NMR spectroscopy (300 MHz, 298 K, $CDCl_3$) with different time (red: 1 h; green: 6 h; blue: 24 h).

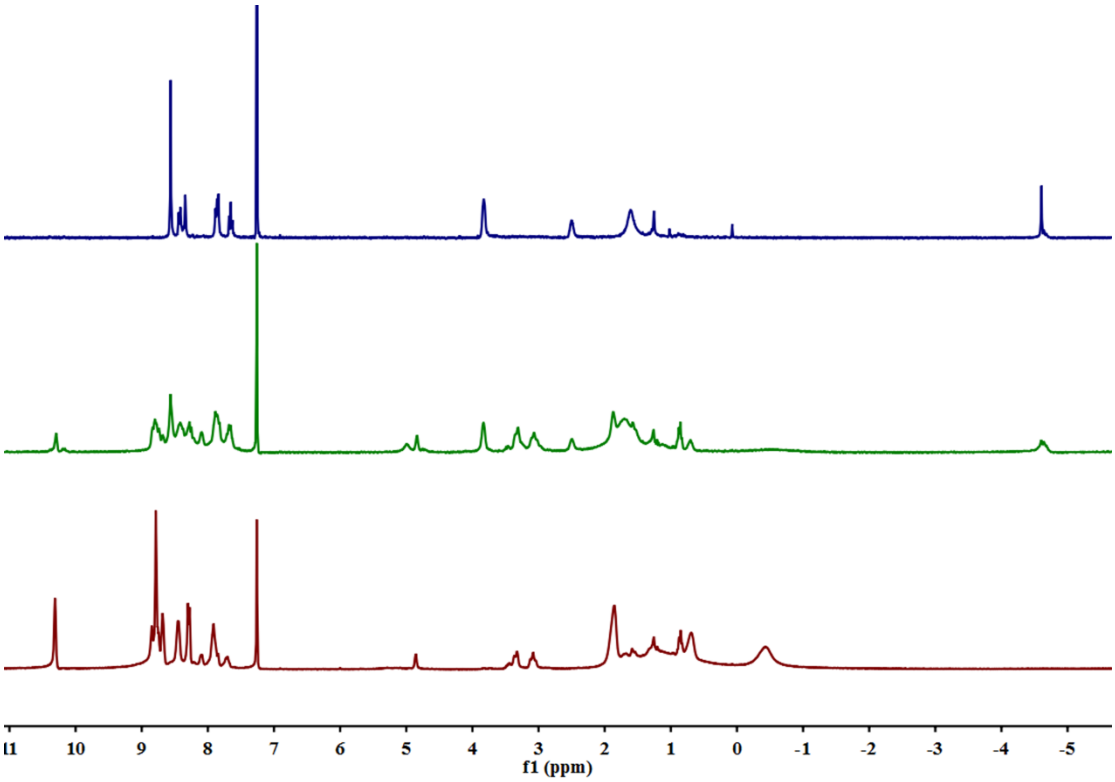


Fig. S2 Dynamic covalent formation of cage-**2** monitored by ^{1}H NMR spectroscopy (300 MHz, 298 K, $CDCl_3$) with different time (red: 1 h; green: 6 h; blue: 24 h).

4. Compound characterizations for cage-1 and cage-2

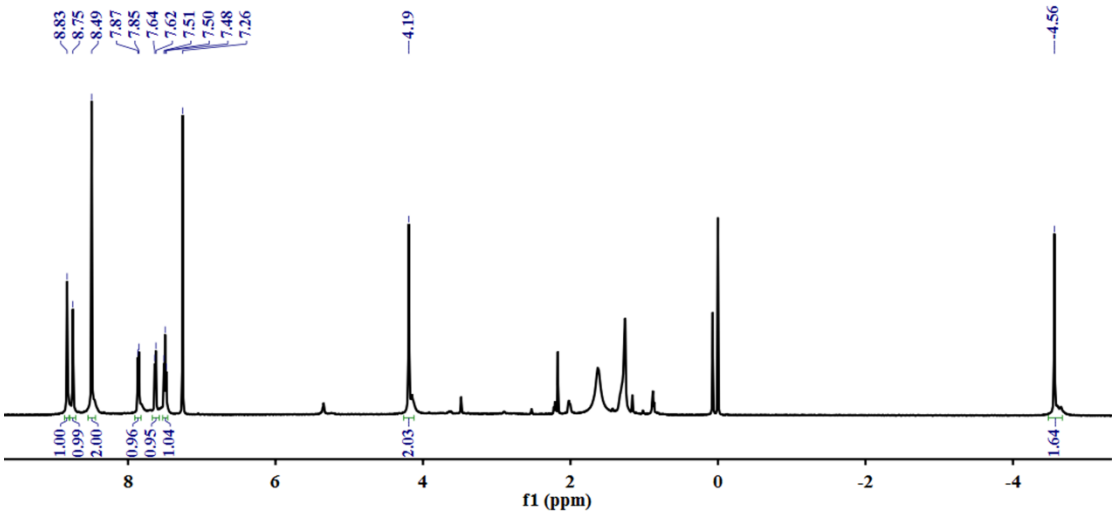


Fig. S3 ^{1}H NMR spectrum (500 MHz, 298 K, $CDCl_3$) of cage-**1**.

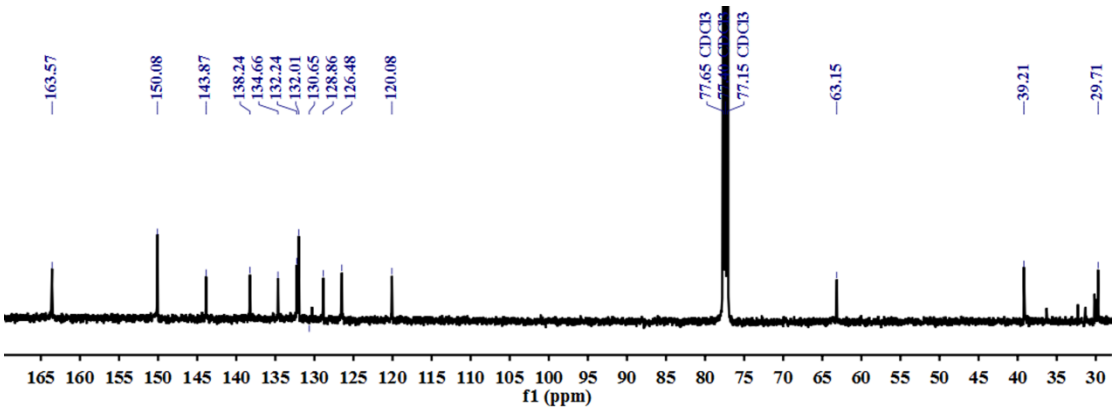


Fig. S4 ^{13}C NMR spectrum (125 MHz, 298 K, $CDCl_3$) of cage-**1**.

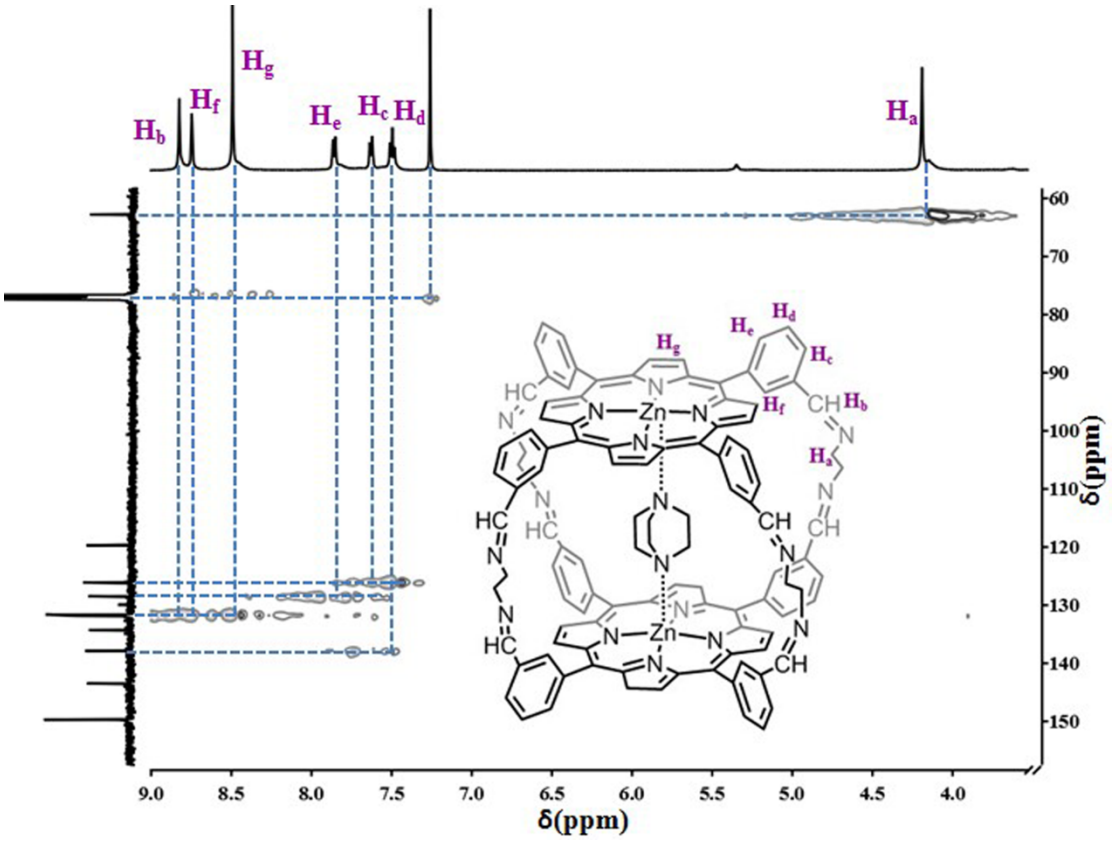


Fig. S4 HSQC NMR spectrum (500 MHz, 298 K, $CDCl_3$) of cage-**1**.

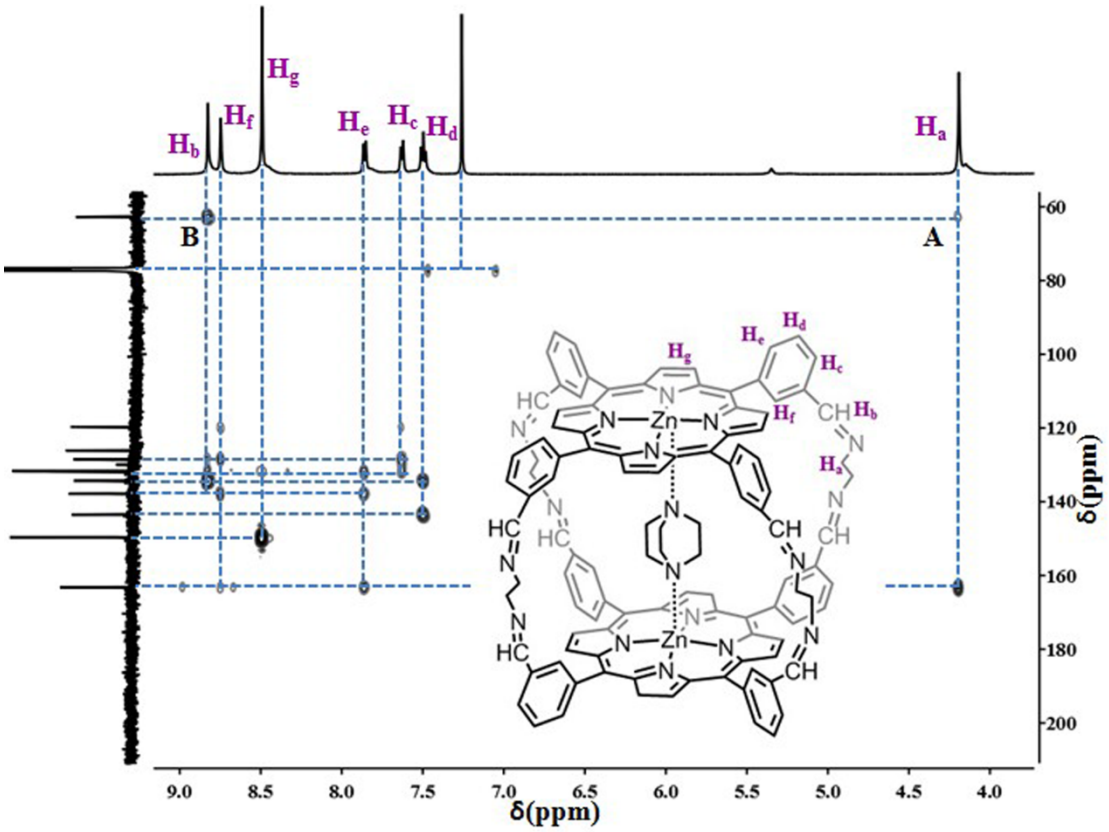


Fig. S5 HMBC NMR spectrum (500 MHz, 298 K, $CDCl_3$) of cage-**1**.

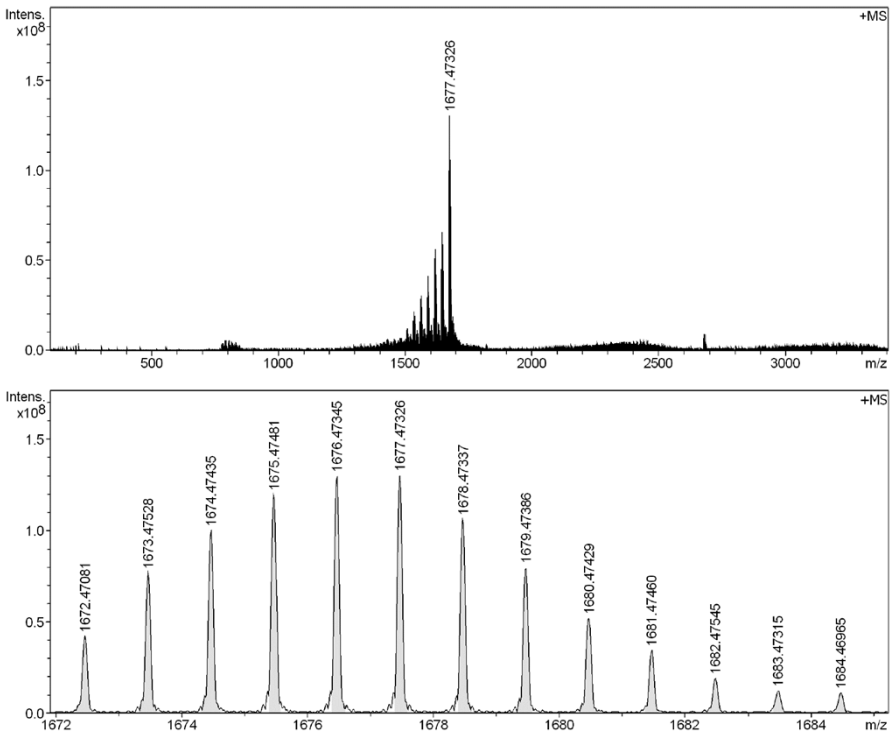


Fig. S6 HR-MALDI–TOF spectrum of cage-**1**.

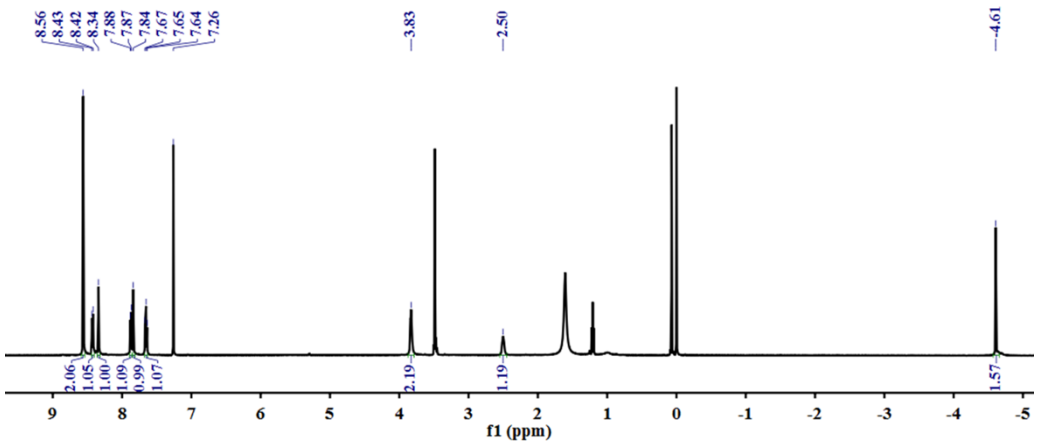


Fig. S7 ^{1}H NMR spectrum (500 MHz, 298 K, $CDCl_3$) of cage-**2**.

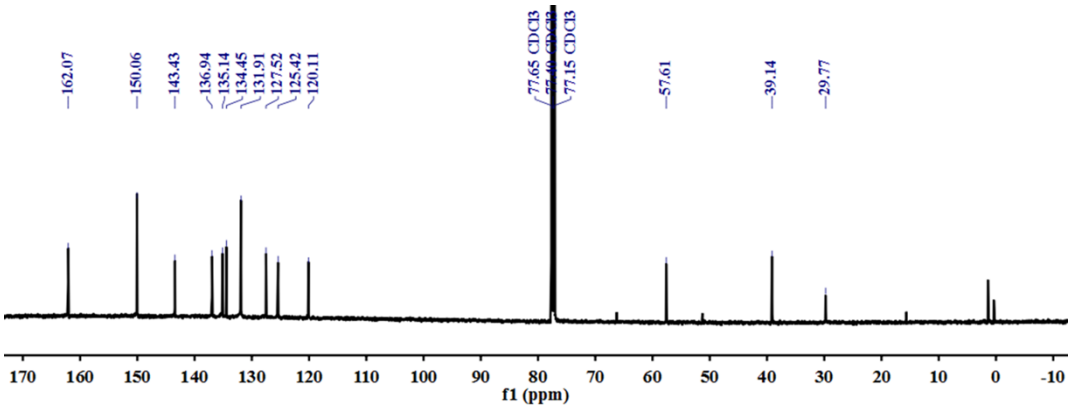


Fig. S8 ^{13}C NMR spectrum (125 MHz, 298 K, $CDCl_3$) of cage-**2**.

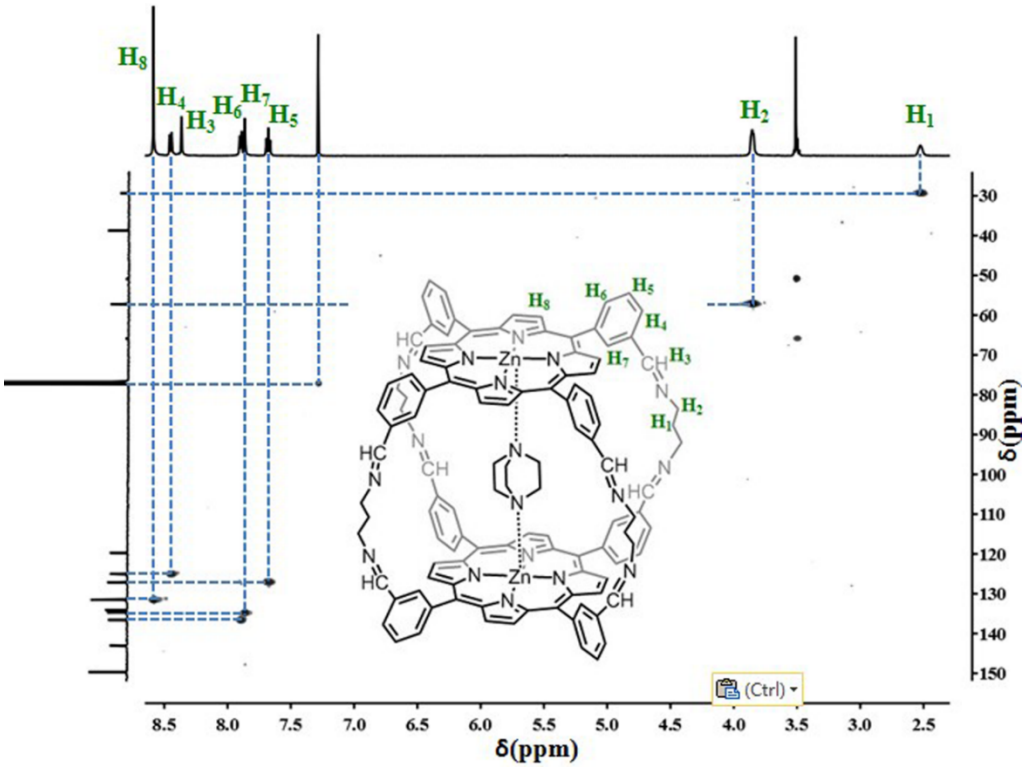


Fig. S9 HSQC-NMR spectrum (500 MHz, 298 K, $CDCl_3$) of cage-**2**.

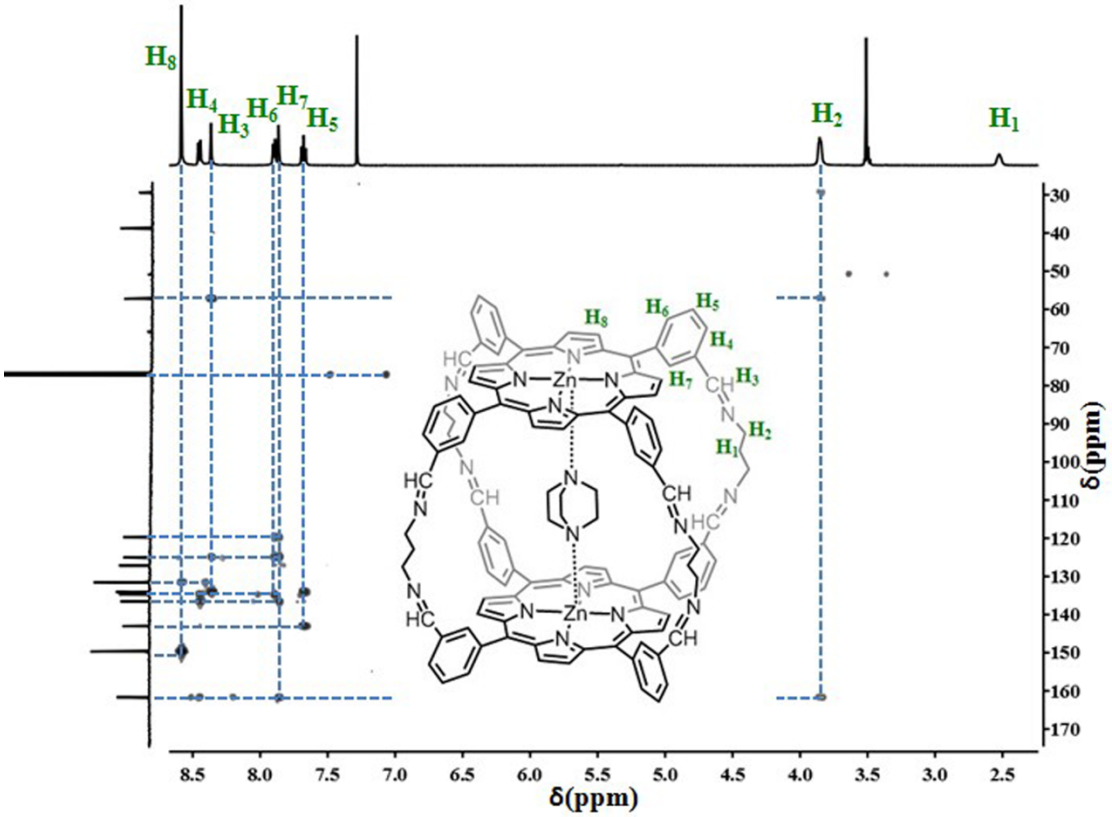


Fig. S10 HMBC-NMR spectrum (500 MHz, 298 K, $CDCl_3$) of cage-**2**.

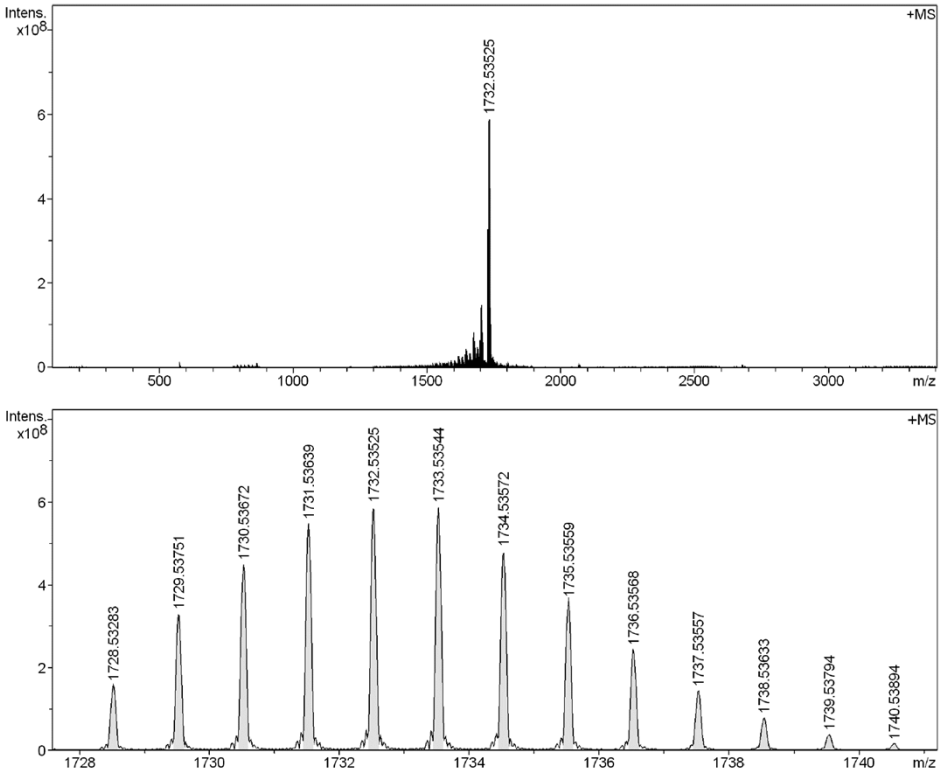


Fig. S11 HR-MALDI–TOF spectrum of cage-**2**.

5. X-Ray Crystallography

Data Collection for Cage-1: A dark red block crystal, having the approximate dimensions of 0.45 × 0.30 × 0.20 mm, was mounted using oil on a glass fiber. All measurements were made at the Beijing Synchrotron Radiation Facility, beam line station 3W1A equipped with a MarCCD-165 detector (the monochrome X-ray source is produced by an accelerator and selected by a double crystal monochromator, λ = 0.8001Å). Scattering factors for the wavelength of 0.8001 Å for use in Shelxl2013 were calculated for all elements using the program WCROMER[S2] and were implemented in Shelxl2013 using DISP commands.

The void space between and within the main molecules is filled with a mixture of diisopropyl ether and chloroform solvate molecules. Chloroform molecules are disordered and partially occupied, and diisopropyl ether molecules are not resolved beside the chloroform molecules, and they were omitted from the refinement. The disorder of the solvent molecules induces disorder of the ethylene diamine bridging units in the molecule. The DABCO molecules were found to be disordered and were modelled in two positions with 50% occupancies.

Chloroform molecules were refined as disordered over either two or four positions. Occupancies of individual moieties at one site were not constrained to sum up to 100%. Disordered chloroform molecules were restrained to have similar geometries, and ADPs of neighboring bonded atoms were restrained to be similar.

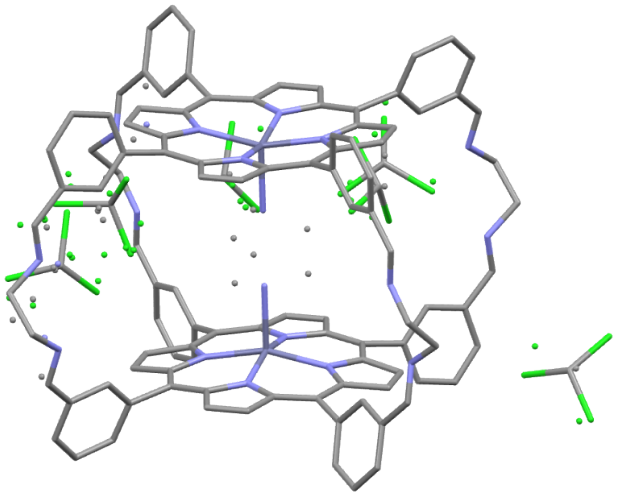


Fig. S12 The crystal structure of cage-**1**.

Table S1. Crystal Data and Structure Refinement for Cage-**1**

Empirical formula	$C_{110}\,H_{84}\,N_{18}\,Zn_2 \cdot 8.79CHCl_3$
Formula weight	2838.46
Temperature	293(2) K
Wavelength	0.8001Å
Crystal system, space group	monoclinic, $P2_1/n$
Unit cell dimensions	a = 18.058(4) Å
	b = 17.549(4) Å, β = 100.90(3)°
	c = 21.217(4) Å
Volume, V	6602(2)Å^3
Z, Calculated density	2, 1.428 g·cm^{-3}
Absorption coefficient	1.312 mm^{-1}
F(000)	2880.1
Crystal size	0.45 × 0.30 × 0.20 mm
Theta range for data collection	0.45 to 28.44º
Limiting indices	$-21 \le h \le 21$, $-20 \le k \le 0$, $-25 \le l \le 25$
Reflections collected / unique	84794 / 11629 [R_{int} = 0.0197]
Completeness to theta = 28.447	99.7 %
Absorption correction	none
Data / restraints / parameters	11629/496/1171
Goodness-of-fit on F^2	1.063
Final R indices [$I > 2\sigma(I)$]	R_1 = 0.0524, wR_2 = 0.1508
R indices (all data)	R_1 = 0.0607, wR_2 = 0.1575
Largest diff. peak and hole	+0.616 and –0.399 e·Å^{-3}

5. ^{1}H and ^{13}C NMR spectra for compound 3, 5, 6

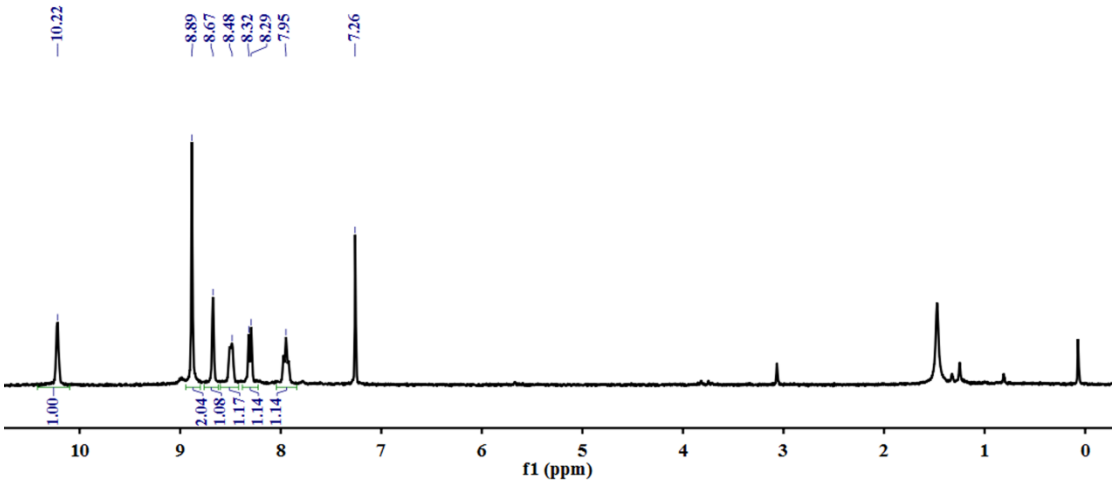


Fig. S13 ^{1}H NMR spectrum (300 MHz, 298 K, $CDCl_3$) of compound **3**.

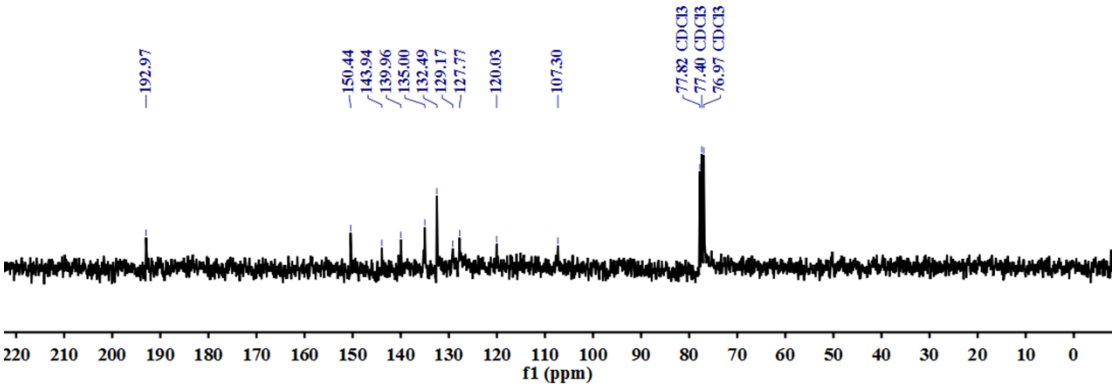


Fig. S14 ^{13}C NMR spectrum (75 MHz, 298 K, $CDCl_3$) of compound **3**.

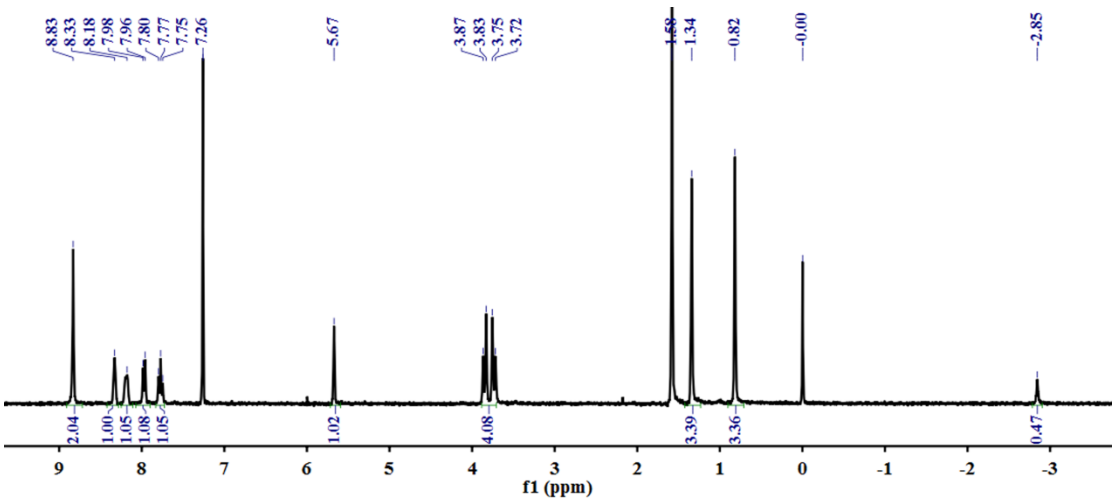


Fig. S15 ^{1}H NMR spectrum (300 MHz, 298 K, $CDCl_3$) of compound **5**.

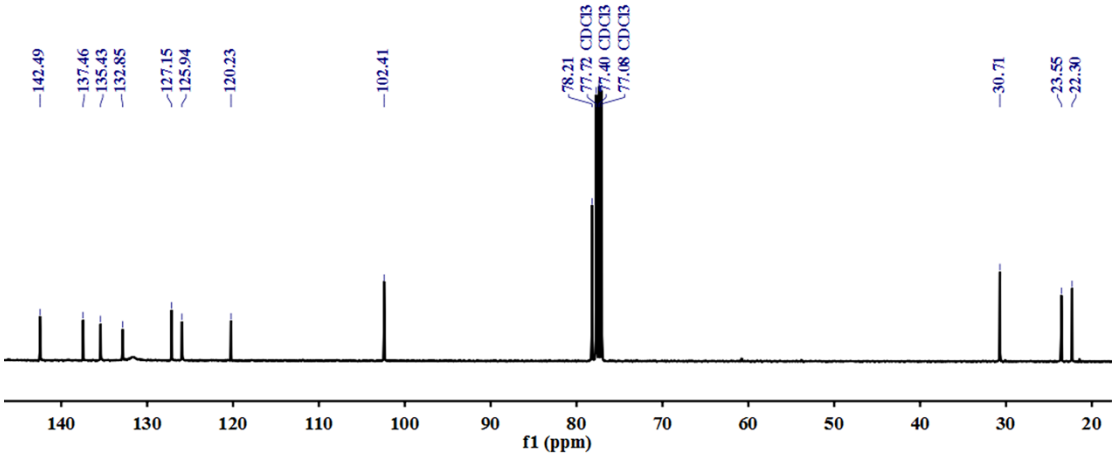


Fig. S16 ^{13}C NMR spectrum (75 MHz, 298 K, $CDCl_3$) of compound **5**.

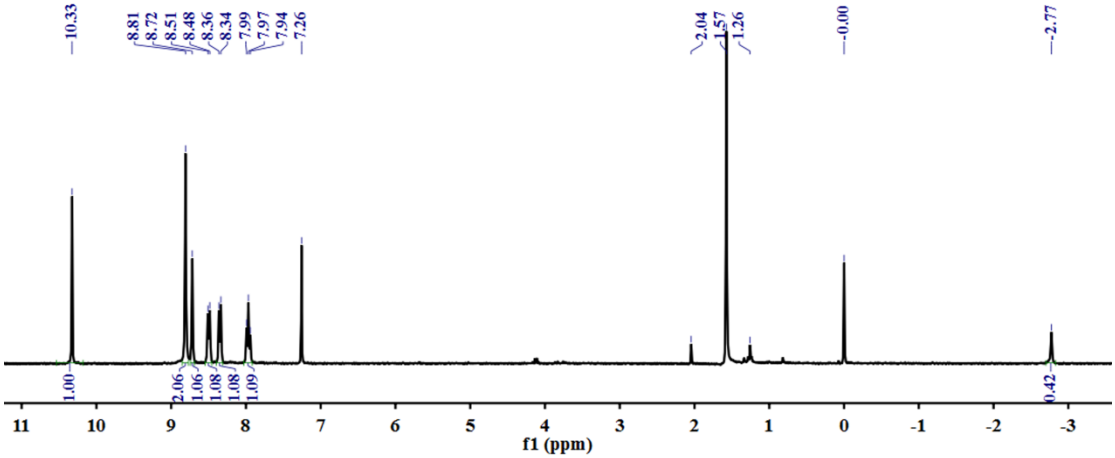


Fig. S17 ^{1}H NMR spectrum (300 MHz, 298 K, $CDCl_3$) of compound **6**.

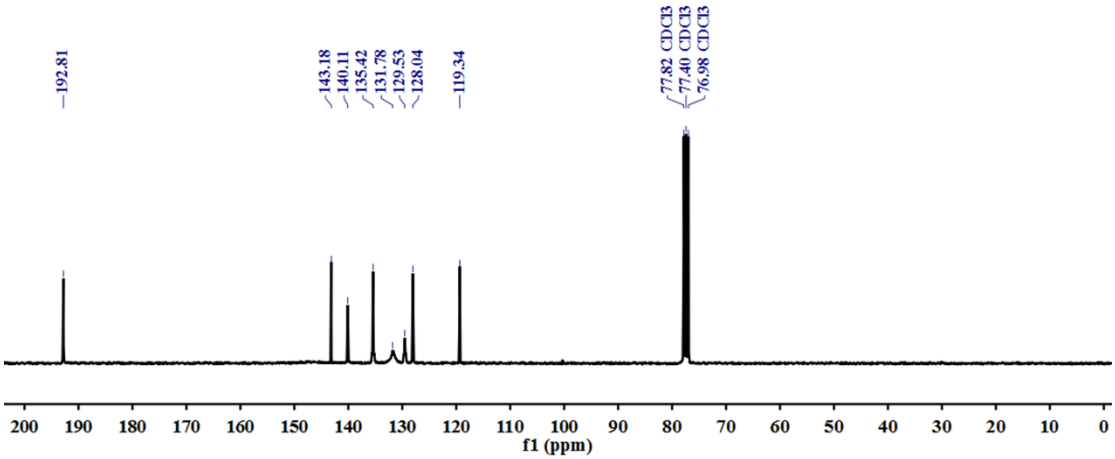


Fig. S18 ^{13}C NMR spectrum (75 MHz, 298 K, $CDCl_3$) of compound **6**.

Reference

S1 J. S. Lindsey, I. C. Schreiman, H. C. Hsu, P. C. Kearney and A. M. Marguerettaz, *J. Org. Chem*.1987, **52**, 827–836.

S2 L. Kissel and R. H. Pratt, *Acta Cryst.* 1990, A**46**, 170–175.