Electronic Supplementary Material (ESI) for Inorganic Chemistry Frontiers.

Supporting Information for

Discoveries from a Phenanthroline-based Dynamic Combinatorial Library: Catenane from Copper(I) or Copper(II) Template?

*King-Lung Tong, Chi-Chung Yee, Yuen Cheong Tse and Ho Yu Au-Yeung**

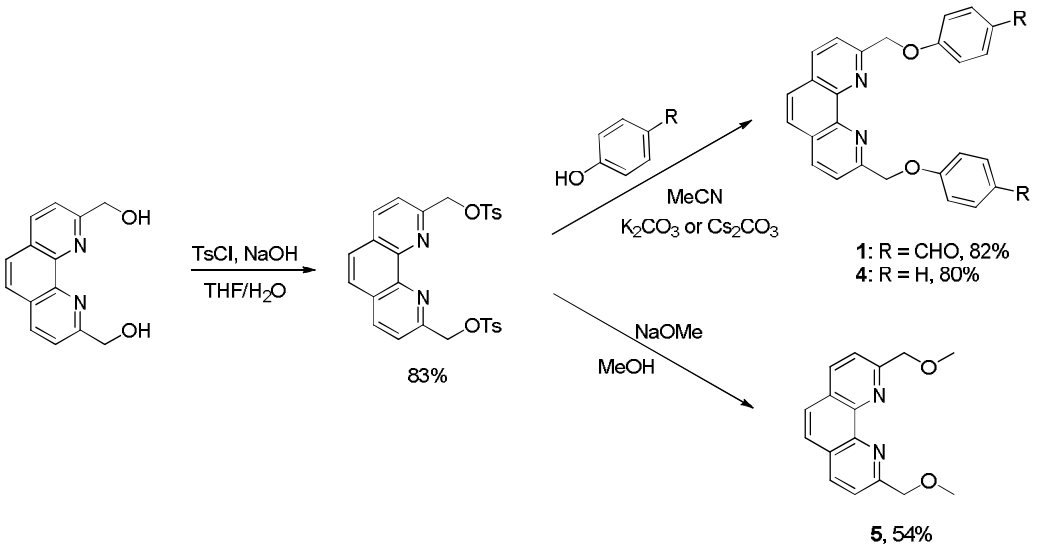
Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong, PRC

Email: hoyuay@hku.hk

Table of content

1. Synthesis

General. All reagents purchased from commercial suppliers (Aldrich, Dkmchem and J & K) were used without further purification. Solvents for synthesis were of analytical grade (ACI Labscan and Arkonic Scientific). Phen-OH,[1] L-Met-OMe,[2] tetraethylene glycol ditosylate,[3] DN-OTs,[4] cyclo*bis*paraquat(*p*-phenylene) ($CBPQT^{4+}$)[5] were synthesized according to literature procedures. Thin layer chromatography (TLC) was performed on silica gel 60 F254 (Merck, Germany, Aluminium sheet) and column chromatography was carried out on silica gel 60F (Silicycle, Canada). LCMS analyses were carried out using a Waters-Alliance e2695 system coupled to a 2489 UV/Vis detector and a QDa MS detector. NMR spectra were recorded on Brucker DPX spectrometers with working frequencies of 300 MHz and 400 MHz for ^{1}H and 100 MHz for ^{13}C, respectively. Unless stated otherwise, chemical shifts are reported in ppm and referenced to solvent residues ($CDCl_3$: ŭ = 7.26 ppm, D_2O: ŭ = 4.79 ppm, CD_3CN: ŭ = 1.94 ppm and $(CD_3)_2SO$: ŭ = 2.50 ppm). UV-Vis spectra were recorded by a Perkin Elmer 19 UV/Vis spectrophotometer. MS/MS experiments were performed on a Finnigan LCQ mass spectrometer. Simulation of isotopic patterns were conducted on IsoPro, version 3.1.



Scheme S1

Synthesis of Phen-OTs. To a suspension of **Phen-OH** (1.18 g, 4.9 mmol) in THF (6 mL) was added a solution of NaOH (0.59 g, 14.7 mmol) in water (5 mL). The mixture was cooled to 0 ^{o}C and a THF solution of TsCl (2.33 g, 12.3 mmol, 30 mL) was added over 2 hr. The reaction mixture was stirred for another 1 hr at room temperature before iced water (10 mL) was added. The resulting aqueous solution was extracted with CH_2Cl_2 (3 × 30 mL). The organic fractions were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated to afford a brown oil.

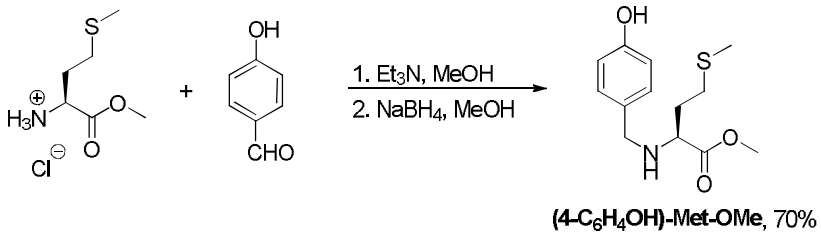
The crude material was purified by a silica column (ethyl acetate/hexanes = 2:1) to give the product as a white solid. Yield = 2.23 g, 83%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) ŭ: 8.30 (d, *J* = 8.4 Hz, 2 H), 7.89ï 7.84 (m, 6 H), 7.81 (s, 2 H), 7.36ī 7.33 (d, *J* = 8.4 Hz, 4 H), 5.50 (s, 4 H), 2.43 (s, 6 H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 298 K) ŭ: 154.9, 145.4, 144.9, 137.7, 132.6, 130.1, 128.7, 128.3, 126.9, 121.3, 72.5, 21.8. ESI-MS: 571.4 $[M+Na]^+$.

Synthesis of 1. A mixture of **Phen-OTs** (0.84 g, 1.5 mmol), 4-hydroxybenzaldehyde (0.56 g, 4.6 mmol) and K_2CO_3 (0.98 g, 7.1 mmol) in CH_3CN (50 mL) was heated to reflux for overnight. Solvents were removed using a rotary evaporator. The residue was partitioned between CH_2Cl_2 (40 mL) and water (20 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated to afford a yellow solid. Purification by a silica column (CH_2Cl_2/MeOH = 20:1) gave the product as a white solid. Yield = 0.55 g, 82%. ^{1}H NMR (300 MHz, $CDCl_3$, 298 K) ŭ: 9.91 (s, 2 H), 8.35 (d, *J* = 8.4 Hz, 2 H), 7.94 (d, *J* = 8.1 Hz, 2 H), 7.89ï 7.86 (m, 6 H), 7.19 (d, *J* = 8.7 Hz, 4 H), 5.73 (s, 4 H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 298 K) ŭ: 190.2, 162.7, 156.6, 144.6, 136.8, 131.5, 129.9, 127.9, 126.0, 120.4, 114.7, 71.1. ESI-MS: 471.4 $[M+Na]^+$.

Synthesis of 4. To a suspension of **Phen-OTs** (0.57 g, 1.0 mmol) in MeCN (40 mL) was added phenol (0.22 g, 2.3 mmol) and Cs_2CO_3 (1.4 g, 4.2 mmol). The mixture was heated to reflux for 3 days. Volatiles were removed by a rotary evaporator. The residue was partitioned between CH_2Cl_2 (50 mL) and 2 M aq. NaOH (50 mL). The organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic solution was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated to afford the product as a white solid. Yield: 0.31 g, 80%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) ŭ: 8.26 (d, *J* = 8 Hz, 2 H), 7.98 (d, *J* = 8.4 Hz, 2 H), 7.76 (s, 2 H), 7.40ī 7.36 (m, 4 H), 7.17ī 7.15 (m, 4 H), 7.07ī 7.03 (m, 2 H), 5.73 (s, 4 H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 298 K) ŭ: 158.3, 158.1, 145.0, 136.9, 129.5, 128.0, 126.1, 121.1, 120.7, 114.7, 71.1. ESI-MS: 415.5 $[M+Na]^+$.

Synthesis of 5. To a suspension of **Phen-OTs** (0.31 g, 0.56 mmol) in MeCN (40 ml) was added a sodium methoxide solution in methanol (20 ml) prepared by dissolving sodium (0.2 g, 8.7 mmol) in methanol (20 ml) under argon. The yellow mixture was heated to reflux for 2 days. Volatiles were removed by a rotary evaporator. The solid residue was partitioned between $CHCl_3$ (50 ml) and 2 M aq. NaOH (50 ml). The organic phase was separated, and the aqueous phase was extracted with $CHCl_3$ (3 × 20 ml). The combined organic solution was washed with brine and dried over anhydrous $MgSO_4$. Volatiles were removed by a rotary evaporator to give the product as an orange oil. Yield: 81 mg, 54%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) ŭ: 8.25 (d, *J* = 8.4 Hz, 2 H), 7.81 (d, *J* = 8.4 Hz, 2 H), 7.75 (s, 2 H), 4.99 (s, 4 H), 3.54 (s, 6 H). ^{13}C{^{1}H} NMR (100 MHz,

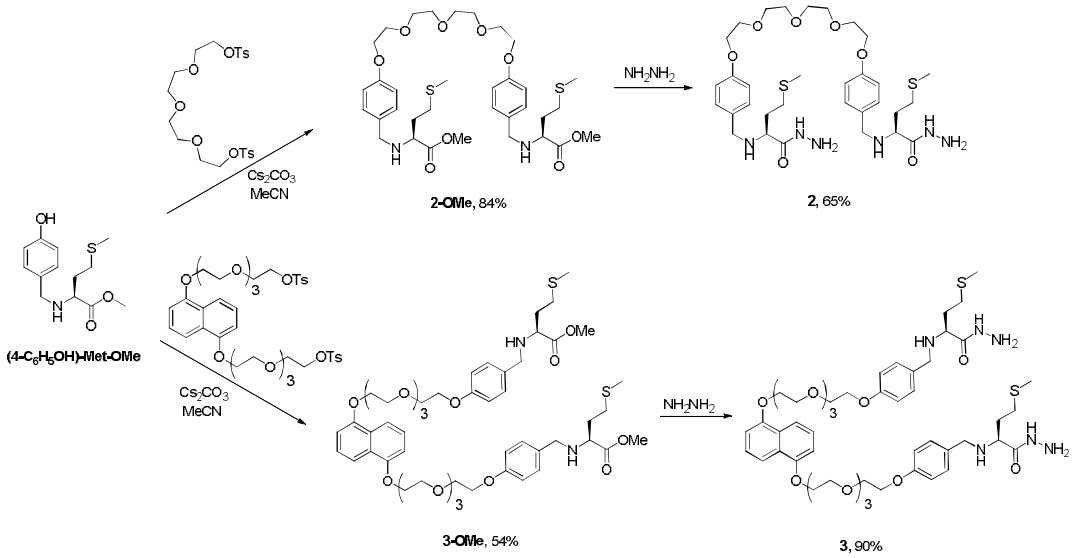
$CDCl_3$, 298 K) ŭ: 159.6, 145.1, 137.0, 128.1, 126.2, 120.8, 76.1, 59.0, 29.8. ESI-MS: 291.3 $[M+Na]^+$.



(4-C_6H_4OH)-Met-OMe, 70%

Scheme S2

Synthesis of (4-C_6H_4OH)-Met-OMe. A solution of L-Met-OMe hydrochloride (1.6 g, 8 mmol) and Et_3N (1.2 mL, 8 mmol) in MeOH (50 mL) was stirred at room temperature for 30 min and 4-hydroxybenzaldehyde (1.2 g, 9.6 mmol) was added. The reaction mixture was stirred at room temperature for overnight. The mixture was cooled at 0°C and $NaBH_4$ (1.3 g, 33.6 mmol) was added in portions. The mixture was stirred for another 30 min at room temperature. Solvents were removed under reduced pressure and the residue was partitioned in water (80 mL) and Et_2O (80 mL). The organic layer was separated, washed with brine, dried over $MgSO_4$ and concentrated to afford a colourless oily liquid. Yield = 1.51 g, 70%. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) ŭ: 7.16 (d, *J* = 8.4 Hz, 2 H), 6.74 (d, *J* = 8.4 Hz, 2 H), 3.74 (s, 3 H), 3.64 (dd, *J* = 54 Hz, *J* = 12.8 Hz, 2 H), 3.41 (dd, *J* = 2 Hz, *J* = 5.6 Hz, 1 H), 2.60ī 2.56 (m, 2 H), 2.07 (s, 3 H), 1.99ī 1.90 (m, 1 H), 1.89ī 1.80 (m, 1 H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$ 298 K) ŭ: 175.4, 155.6, 130.2, 129.7, 115.5, 59.3, 52.0, 51.5, 32.3, 30.2, 15.1. ESI-MS: 270.3 $[M+H]^+$.



Scheme S3

Synthesis of 2-OMe. A mixture of **(4-C_6H_4OH)-Met-OMe** (590 mg, 2.2 mmol), tetraethylene glycol ditosylate (500 mg, 1 mmol) and Cs_2CO_3 (1.3 g, 4 mmol) in CH_3CN (50 mL) was heated to reflux for one day. The resulting solution was filtered and concentrated. The residue was partitioned between water (40 mL) and CH_2Cl_2 (40 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated to afford a brown oily liquid. Yield = 0.59 g, 84%. ^{1}H NMR (300 MHz, $CDCl_3$, 298 K) ŭ: 7.20 (d, *J* = 8.4 Hz, 4 H), 6.84 (d, *J* = 8.1 Hz, 4 H), 4.09 (t, *J* = 4.8 Hz, 4 H), 3.83 (t, *J* = 4.8 Hz, 4 H), 3.71ï 3.52 (m, 18 H), 3.37 (dd, *J* = 1.5 Hz, *J* = 5.7 Hz, 2 H), 2.65ī 2.50 (m, 4 H), 2.06 (s, 6 H), 1.96ī 1.75 (m, 4 H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$ 298 K) ŭ: 175.4, 157.8, 131.9, 129.2, 114.3, 70.6, 70.5, 69.5, 67.3, 59.2, 51.6, 51.3, 32.7, 30.4, 15.2. ESI-MS: 719.4 $[M+Na]^+$.

Synthesis of 2. To a solution of **2-OMe** (590 mg, 0.84 mmol) in MeOH (20 mL) was added hydrazine monohydrate (5 mL). The mixture was heated to reflux for overnight. The solvent was removed by a rotary evaporator. The residue was partitioned between water (40 mL) and CH_2Cl_2 (40 mL). The organic layer was separated, dried over $MgSO_4$, filtered and concentrated to afford a pale yellow oily liquid. Yield = 0.38 g, 65%. ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) ŭ: 8.40 (s, 2 H), 7.05 (d, *J* = 8.4 Hz, 4 H), 6.72 (d, *J* = 8.4 Hz, 4 H), 3.95 (t, *J* = 4.8 Hz, 4 H), 3.69 (t, *J* = 4.8 Hz, 4 H), 3.56ï 3.40 (m, 12 H), 3.12 (dd, *J* = 1.6 Hz, *J* = 5.6 Hz, 2 H), 2.39 (t, *J* = 7.2 Hz, 4 H), 1.91 (s, 6 H), 1.85ī 1.77 (m, 2 H), 1.74ī 1.66 (m, 2 H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$ 298 K) ŭ: 173.6, 157.4, 131.3, 128.8, 114.0, 70.2, 70.0, 69.1, 66.9, 59.4, 51.1, 32.1, 30.0, 14.8. ESI-MS: 719.6 $[M+Na]^+$.

Synthesis of 3-OMe. A solution mixture of **(4-C_6H_4OH)-Met-OMe** (300 mg, 1.1 mmol), Cs_2CO_3 (650 mg, 2.0 mmol) and **DN-OTs** (410 mg, 0.5 mmol) in CH_3CN (50 mL) was heated to reflux for one day. The reaction mixture was filtered and concentrated *in vacuo*. The residue was partitioned between CH_2Cl_2 (100 mL) and H_2O (100 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated to give a pale yellow oily liquid, which was purified by a silica column (ethyl acetate) to afford a pale yellow liquid. Yield = 270 mg, 54%. ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) ŭ: 7.86 (d, *J* = 11.6 Hz, 2 H), 7.33 (t, *J* = 10.6 Hz, 2 H), 7.20 (d, *J* = 11.6 Hz, 4 H), 6.86ï 6.81 (m, 6 H), 4.29 (t, *J* = 6.4 Hz, 4 H), 4.08 (t, *J* = 6.4 Hz, 4 H), 3.99 (t, *J* = 6.4 Hz, 4 H), 3.84ï 3.79 (m, 8 H), 3.73ï 3.53 (m, 22 H), 3.38 (dd, *J* = 3.2 Hz, *J* = 7.2 Hz, 2 H), 2.65ï 2.53 (m, 4 H), 2.07 (s, 6 H), 1.95ī 1.88 (m, 2 H), 1.86ī 1.78 (m, 2 H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$ 298 K) ŭ: 175.5, 157.8, 154.2, 132.0, 129.3, 126.7, 125.0, 114.5, 114.4, 105.6, 70.9, 70.7, 70.6, 70.6, 69.7, 69.6, 67.9, 67.3, 59.3, 51.7, 51.4, 32.8, 30.5, 15.3. ESI-MS: 1037.4 $[M+Na]^+$.

Synthesis of 3. To a solution of **3-OMe** (200 mg, 0.19 mmol) in MeOH (20 mL) was added hydrazine monohydrate (5 mL). The mixture was heated to reflux for overnight. The solvent was removed. The residue was partitioned between water (40 mL) and CH_2Cl_2 (40 mL). The organic layer was separated, dried over $MgSO_4$, filtered and concentrated to afford an off-white solid. Yield = 0.17 g, 90%. ^{1}H NMR ($CDCl_3$, 400 MHz, 298 K) ŭ: 7.84 (d, *J* = 8.4 Hz, 2 H), 7.32 (t, *J* = 8 Hz, 2 H), 7.15 (d, *J* = 8.4 Hz, 4 H), 6.85ï 6.80 (m, 6 H), 4.27 (t, *J* = 5 Hz, 4 H), 4.06 (t, *J* = 4.8 Hz, 4 H), 3.97 (t, *J* = 4.8 Hz, 4 H), 3.82ï 3.78 (m, 8 H), 3.71ï 3.55 (m, 16 H), 3.26 (dd, *J* = 2 Hz, *J* = 5.4 Hz, 2 H), 2.65ï 2.53 (dt, *J* = 2.4 Hz, *J* = 7.2 Hz, 4 H), 2.06 (s, 6 H), 2.02ī 1.95 (m, 2 H), 1.88ī 1.79 (m, 2 H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$ 298 K) ŭ: 174.2, 158.2, 154.4, 131.7, 129.4, 126.8, 125.2, 114.7, 114.7, 105.8, 71.0, 70.9, 70.8, 70.8, 69.9, 69.8, 68.0, 67.5, 60.4, 52.1, 32.6, 30.7, 15.5. ESI-MS: 1037.5 $[M+Na]^+$.

Isolation of M1, C1·Cu$^+$ and C2·Cu$^+$ for MS/MS and ^{1}H NMR analysis. For further characterization of **M1**, **C1·Cu$^+$** and **C2·Cu$^+$**, larger scale (*ca.* 5ï 40 ml) DCLs of the respective building blocks were prepared as described below. The pure products could be isolated from the DCL by preparative HPLC using a SunFire C18 column (10 μm, 4.6 × 250 mm) using elution profiles as described below. Alternatively, the products can also be purified by flash column chromatography. The library solutions were first neutralized with Et_3N. Solvents were removed and the residue was diluted by CH_2Cl_2 and washed twice with saturated $NaHCO_3$ solution. The organic fraction was dried by $MgSO_4$, filtered, concentrated and purified by silica columns (CH_2Cl_2/MeOH/Et_3N = 100:5:1). **M1**: 98 mg from 40 ml DCL, 45%; **C1·Cu$^+$**: 15 mg from 6 ml DCL, 44%; **C2·Cu$^+$**: 3 mg from 4 ml DCL, 52%.

Self-assembly of C3·Cu$^+$. A mixture of **1** (68 mg, 0.15 mmol) and $Cu(CH_3CN)_4PF_6$ (28 mg, 0.075 mmol) in $CHCl_3$/MeCN (v/v 7:3, 7.5 mL) was heated to reflux for 30 mins, followed by addition of 4,9-dioxa-1,12-dodecanediamine (31 mg, 0.15 mmol) in $CHCl_3$/MeCN (v/v 7:3, 7.5 mL). The dark red solution was heated to reflux for overnight. The solution was cooled to 0^{o}C and $NaBH_4$ (23 mg, 0.6 mmol) was added in portions. The resulting solution was stirred at room temperature for 2 hr. Solvents were removed by a rotary evaporator and the residue was partitioned between CH_2Cl_2 (30 mL) and 2M NaOH (10 mL). The organic fraction was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The organic fractions were combined, dried over $MgSO_4$ and filtered. HPLC analysis of the filtrate showed **C3·Cu**$^+$ corresponds to 70% of the assembly material. A pure sample of **C3·Cu**$^+$ was obtained by preparative HPLC. Of the 90 mL of the filtrate, a total of 6 mL was injected onto the preparative column and 4 mg of **C3·Cu**$^+$ was obtained (isolated yield = 58%). On the other hand, using $CuCl_2{\cdot}2H_2O$ as the template under the same assembly condition yielded **C3·Cu**$^+$ in 15%. ^{1}H NMR (400 MHz, D_2O, 298 K) ŭ: 8.55 (d, *J* = 8.1 Hz, 4 H), 8.06 (d, *J* = 8.1 Hz, 4 H), 7.91 (s, 4 H), 6.63 (d, *J* = 8.5 Hz, 8 H), 6.03 (d, *J* = 8.5 Hz, 8 H), 5.02 (s, 8 H), 3.91 (s, 8 H), 3.72 (m, 16 H), 3.07 (t, *J* = 7.2 Hz, 8 H), 2.07 (m, 8H), 1.82 (m, 8 H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 298 K) ŭ: 158.1, 153.6, 143.3, 138.2, 130.8, 129.1, 126.9, 126.5, 122.7, 113.5, 71.3, 71.1, 68.4, 49.7, 44.9, 26.0, 25.6. ESI-MS: 1303.6 $[M\text{-}PF_6]^+$.

Demetallation of catenated species. The metal free catenanes (**C1**, **C2** and **C3**) were obtained by treating solutions of the purified samples with excess NaCN. Colourless solutions were resulted indicating the successful decomplexation of Cu^+ from phenanthroline coordination. The metal-free catenanes were extracted from the colourless aqueous solutions with CH_2Cl_2 (3 × 10 mL), which was analyzed by ESI-MS showing the corresponding *m/z* at 1132.3 [**C1**+2Na]$^{2+}$, 1450.3 [**C2**+2Na]$^{2+}$ and 1263.6 [**C3**+Na]$^+$ respectively.

2. NMR

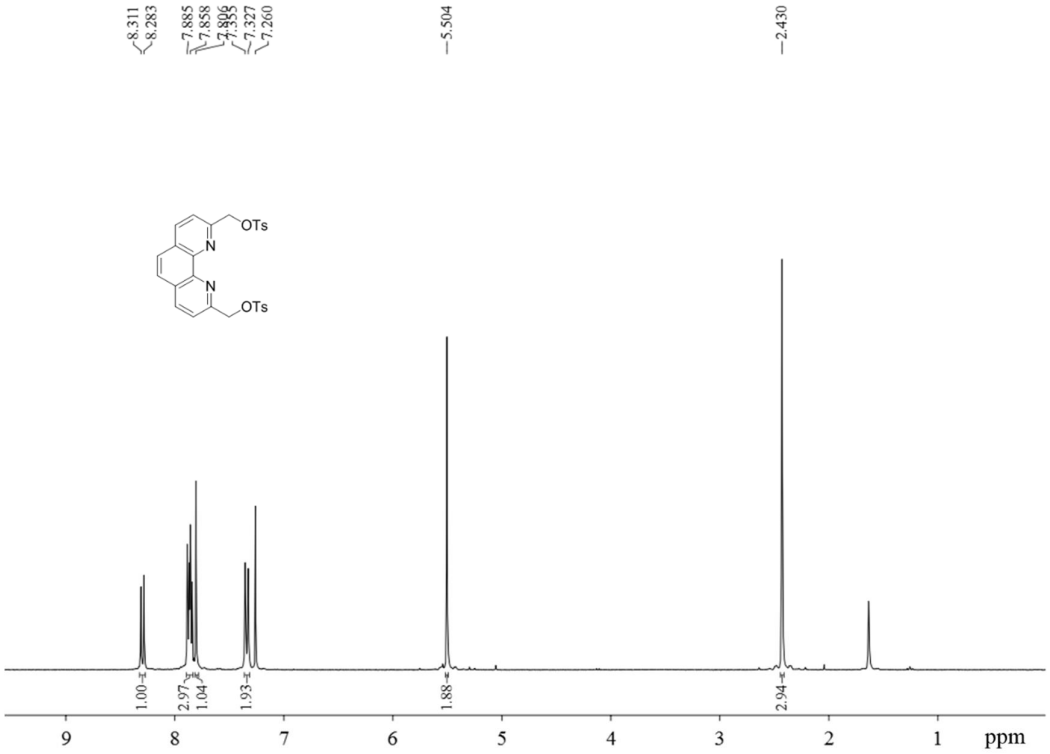


Figure S1. ^{1}H NMR (300 MHz, $CDCl_3$, 298 K) of **Phen-OTs**.

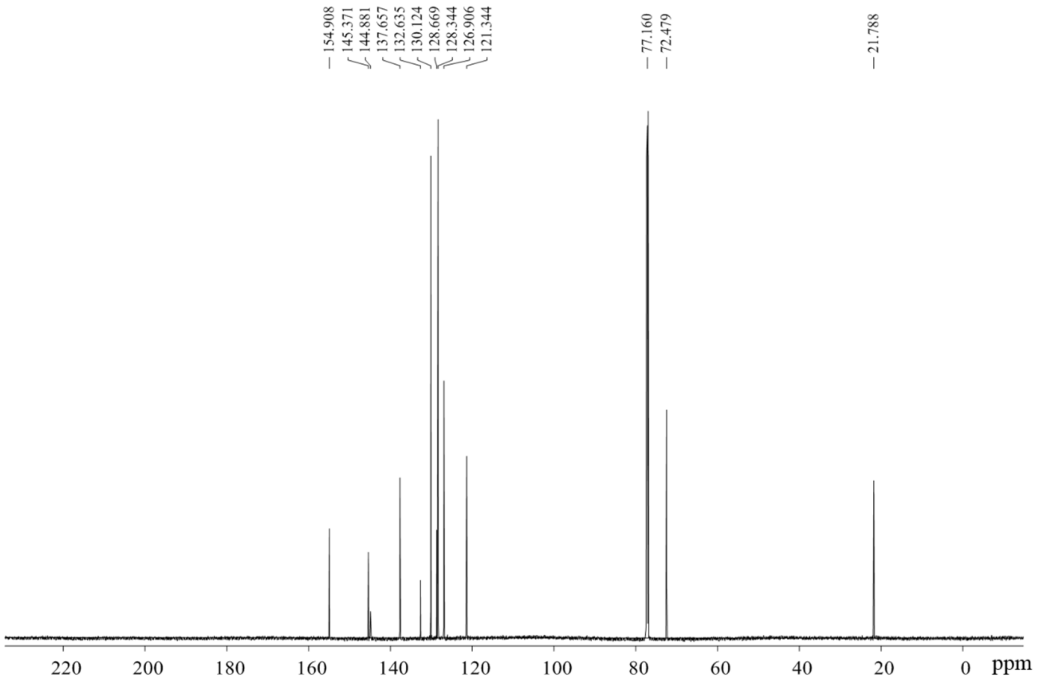


Figure S2. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, 298 K) of **Phen-OTs.**

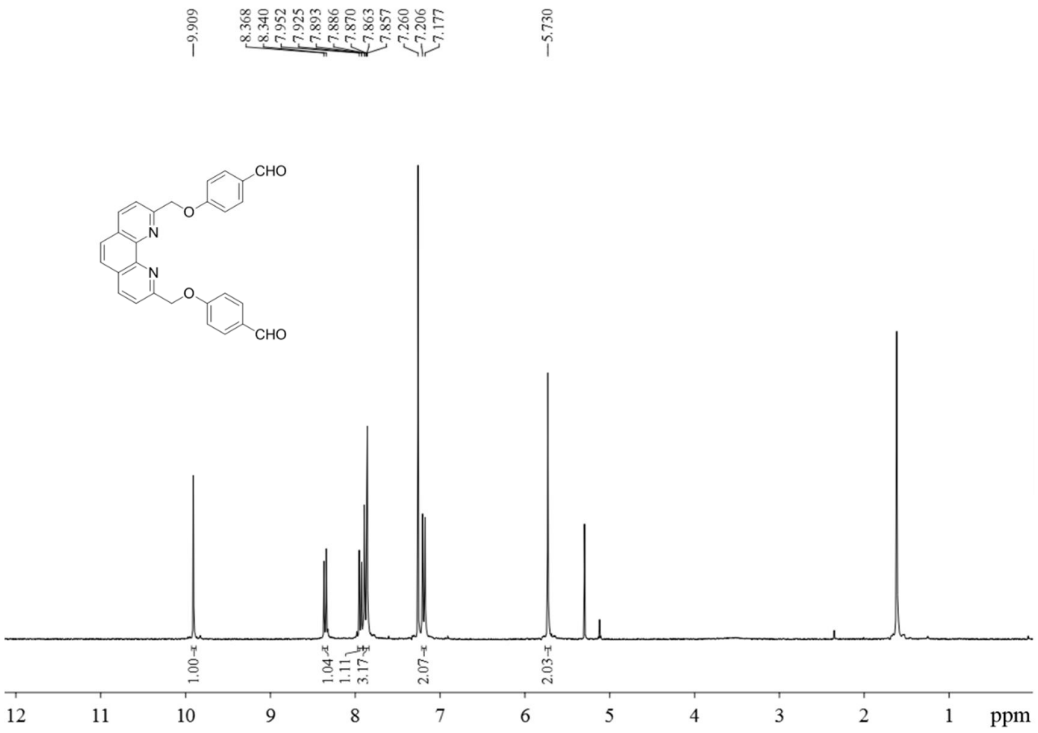


Figure S3. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) of **1**.

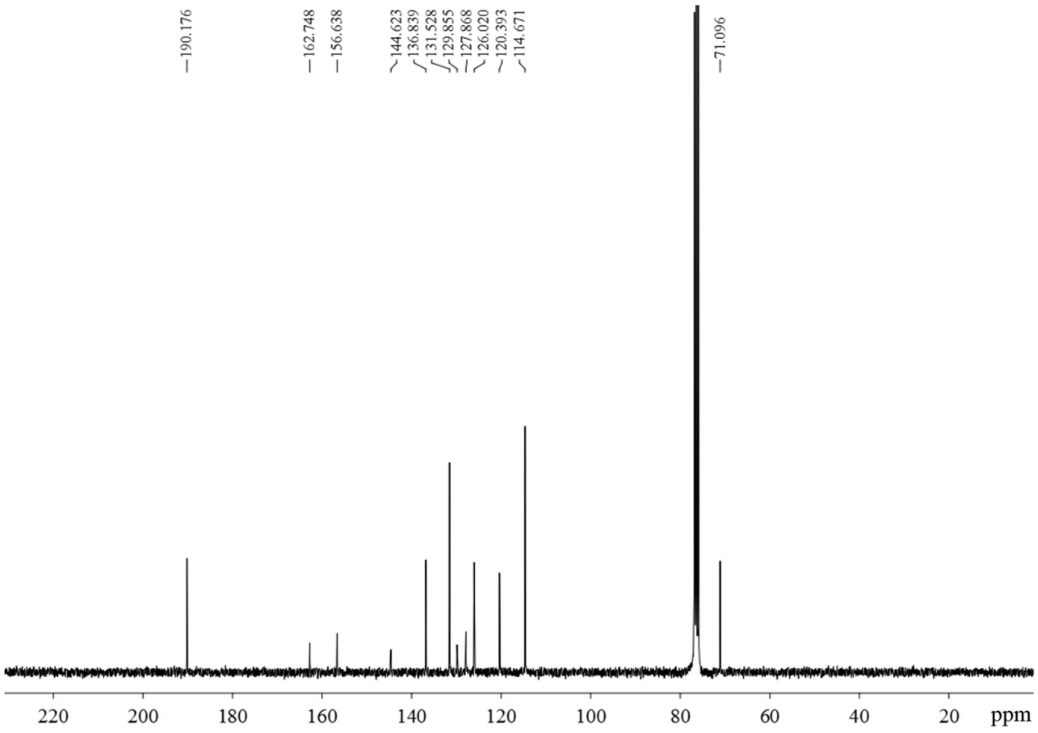


Figure S4. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, 298 K) of **1**.

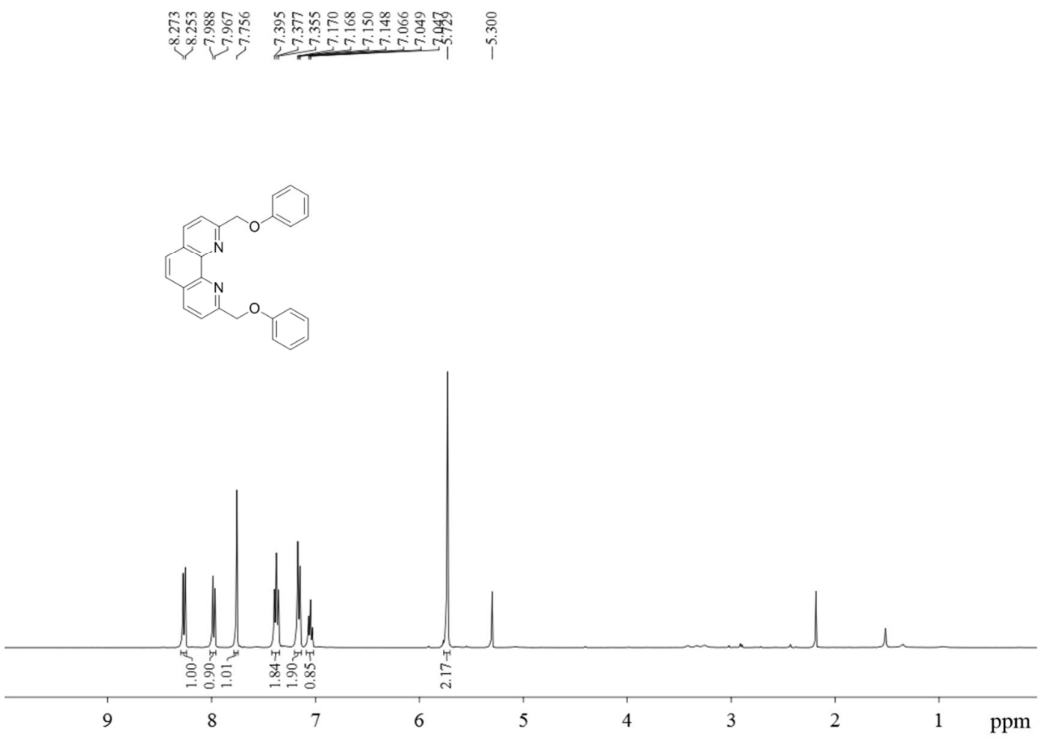


Figure S5. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) of **4**.

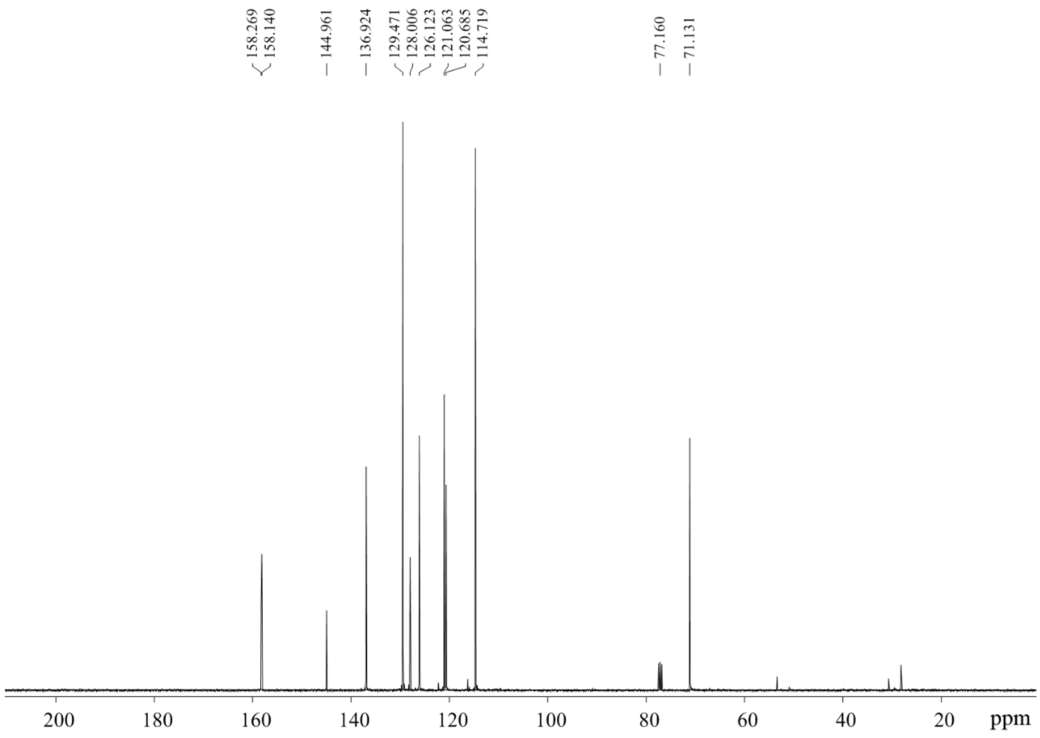


Figure S6. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, 298 K) of **4**.

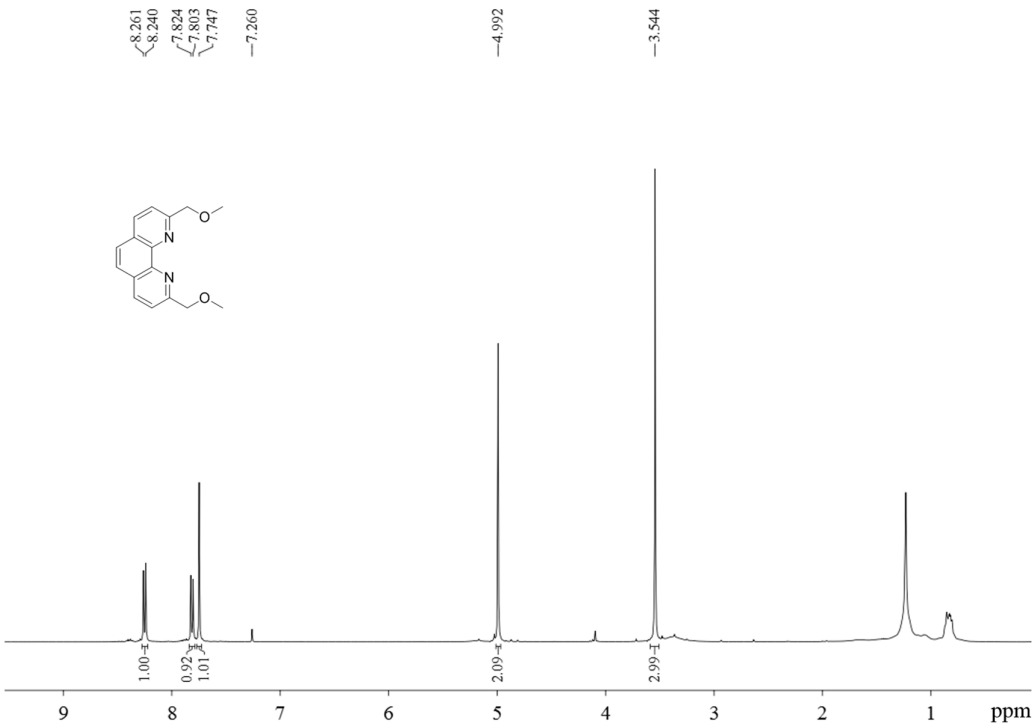


Figure S7. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) of **5**.

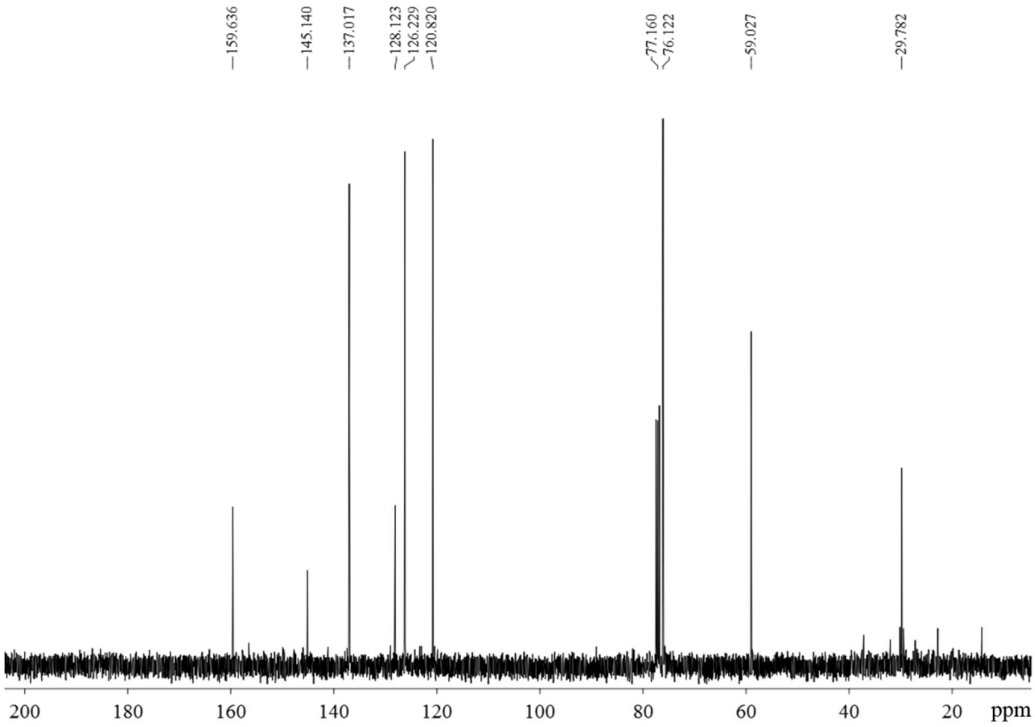


Figure S8. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, 298 K) of **5**.

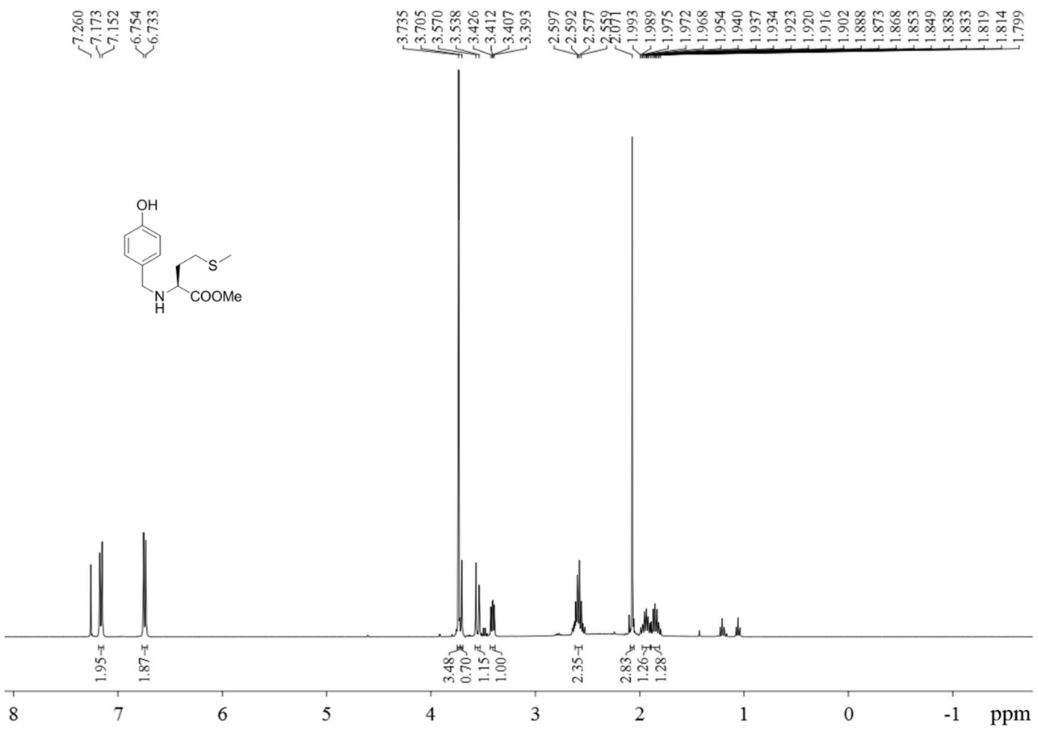


Figure S9. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) of **(4-C_6H_4OH)-Met-OMe**.

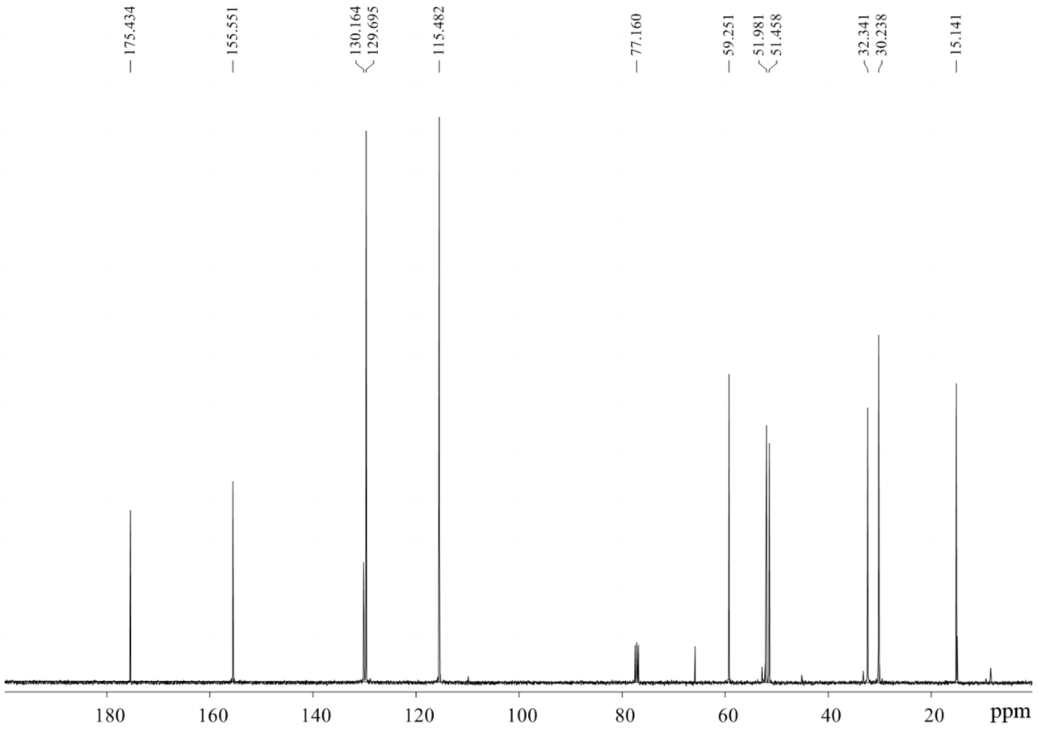


Figure S10. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, 298 K) of **(4-C_6H_4OH)-Met-OMe**.

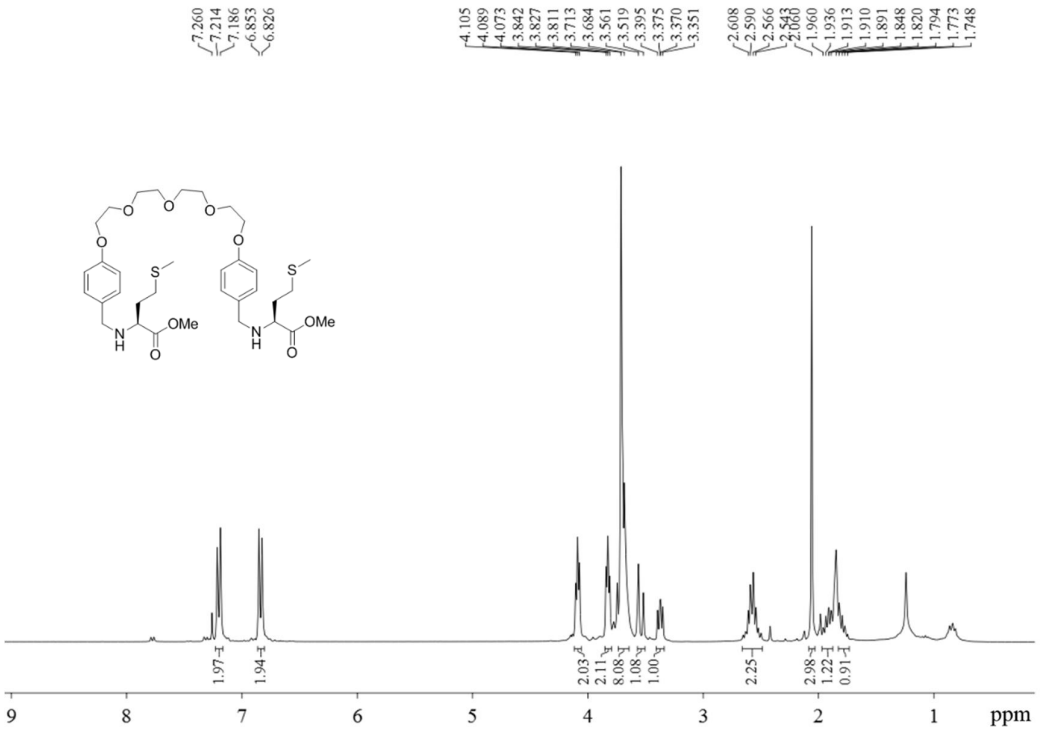


Figure S11. ^{1}H NMR (300 MHz, $CDCl_3$, 298 K) of **2-OMe**.

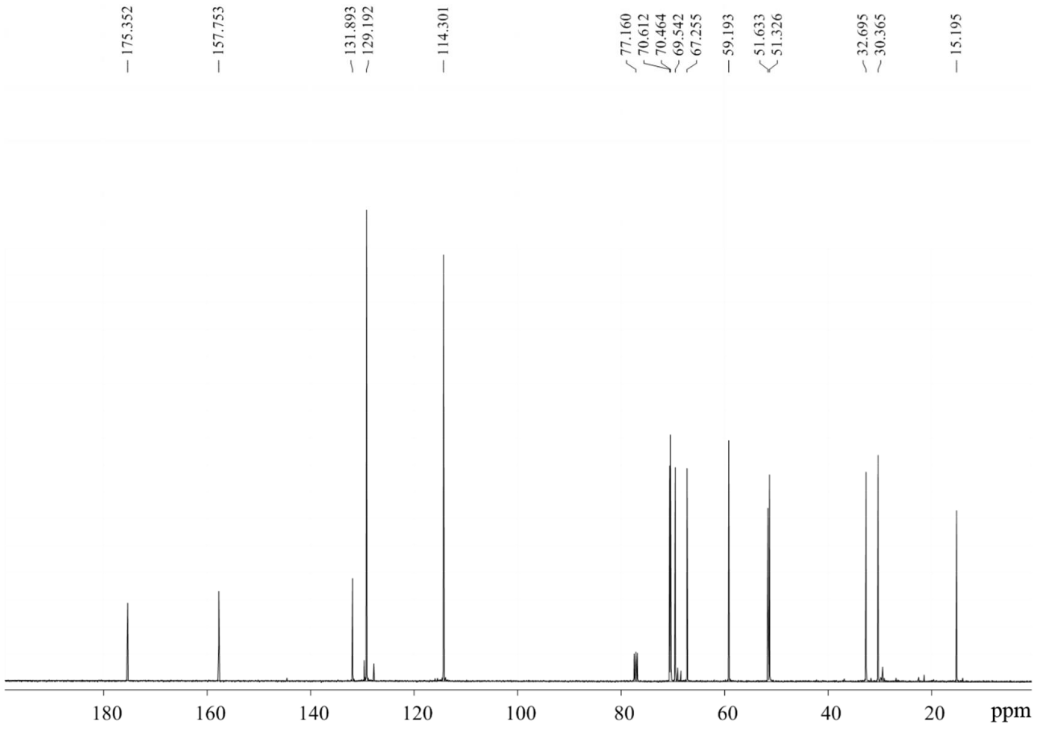


Figure S12. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, 298 K) of **2-OMe**.

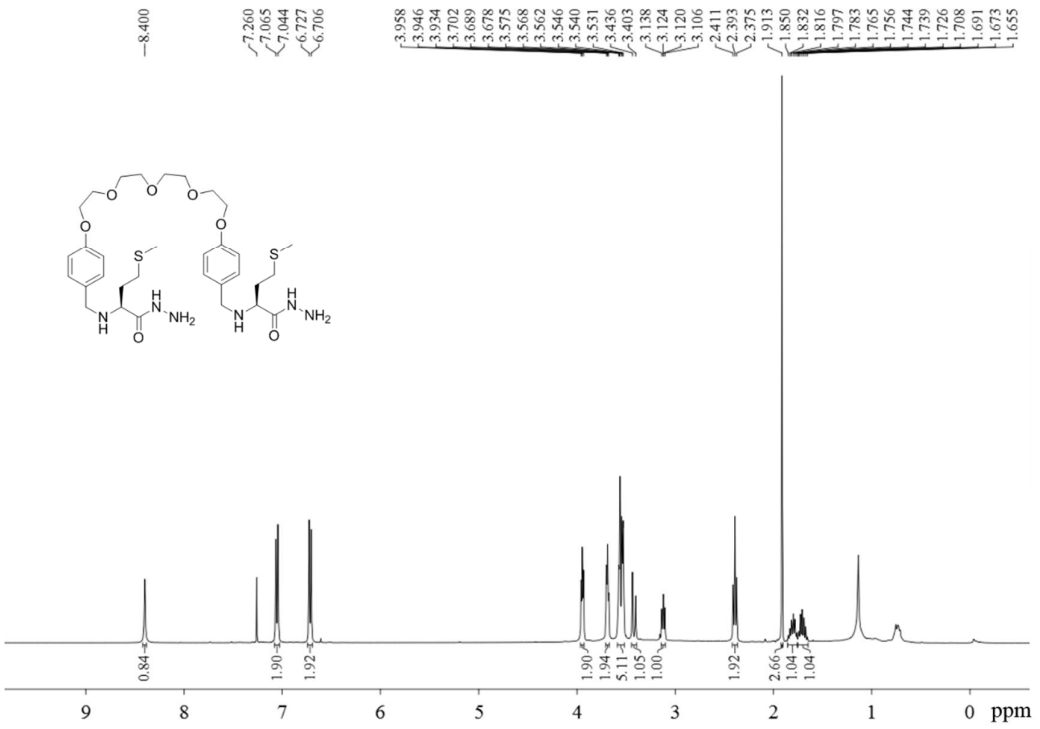


Figure S13. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) of **2**.

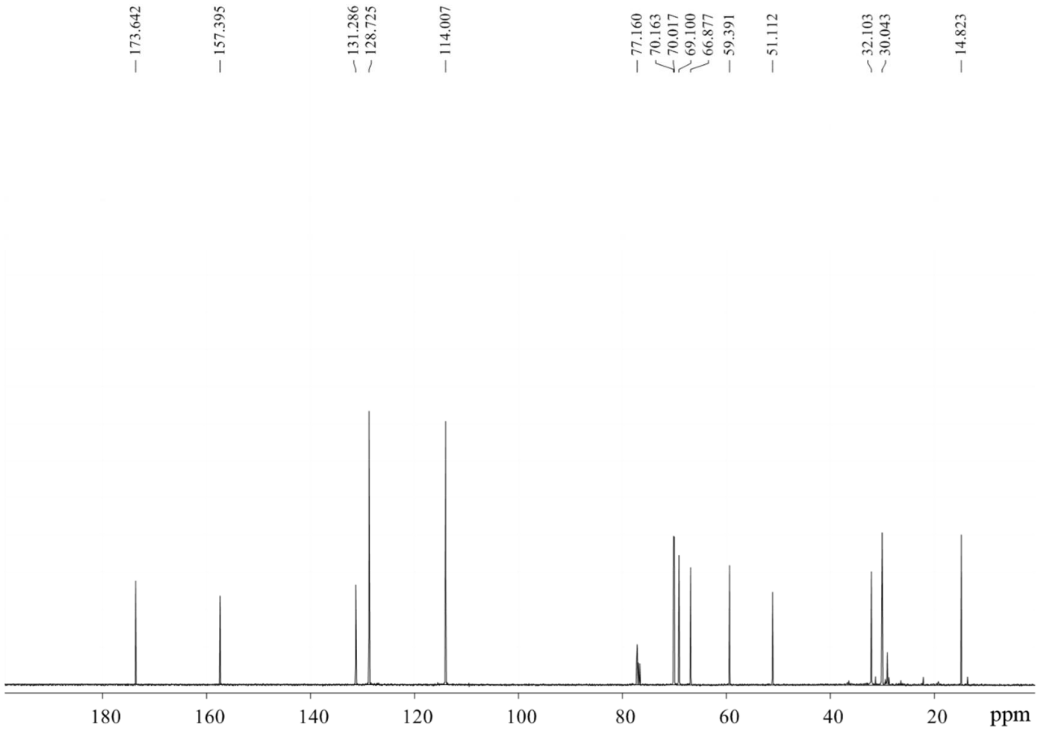


Figure S14. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, 298 K) of **2**.

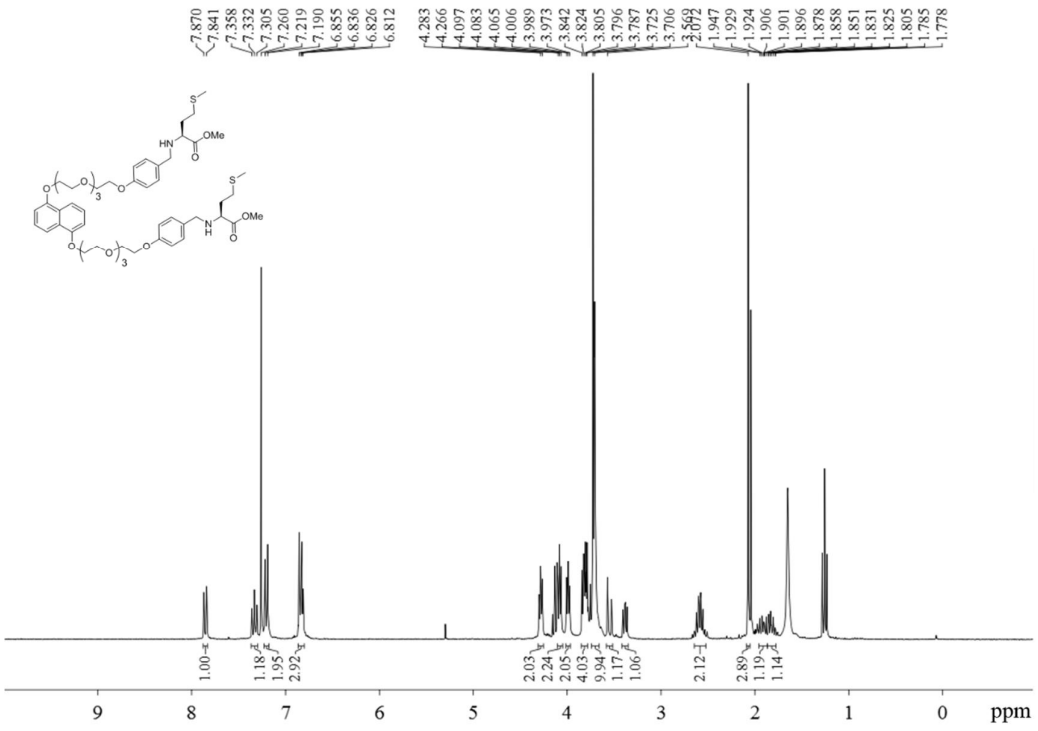


Figure S15. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) of **3-OMe**.

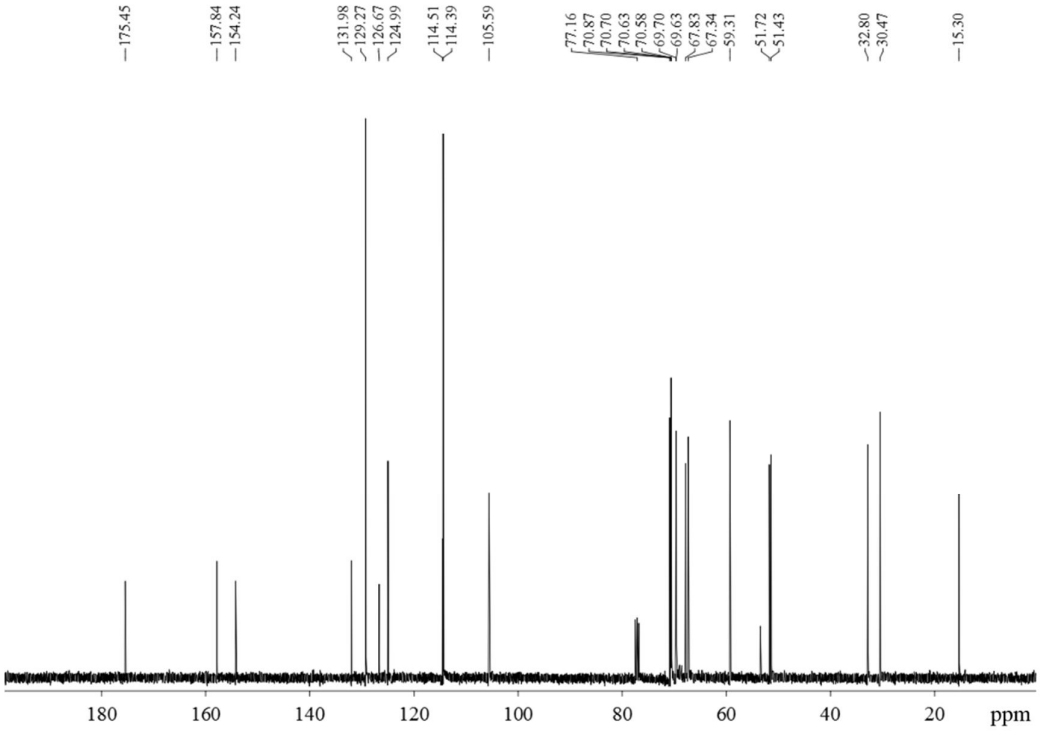


Figure S16. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, 298 K) of **3-OMe**.

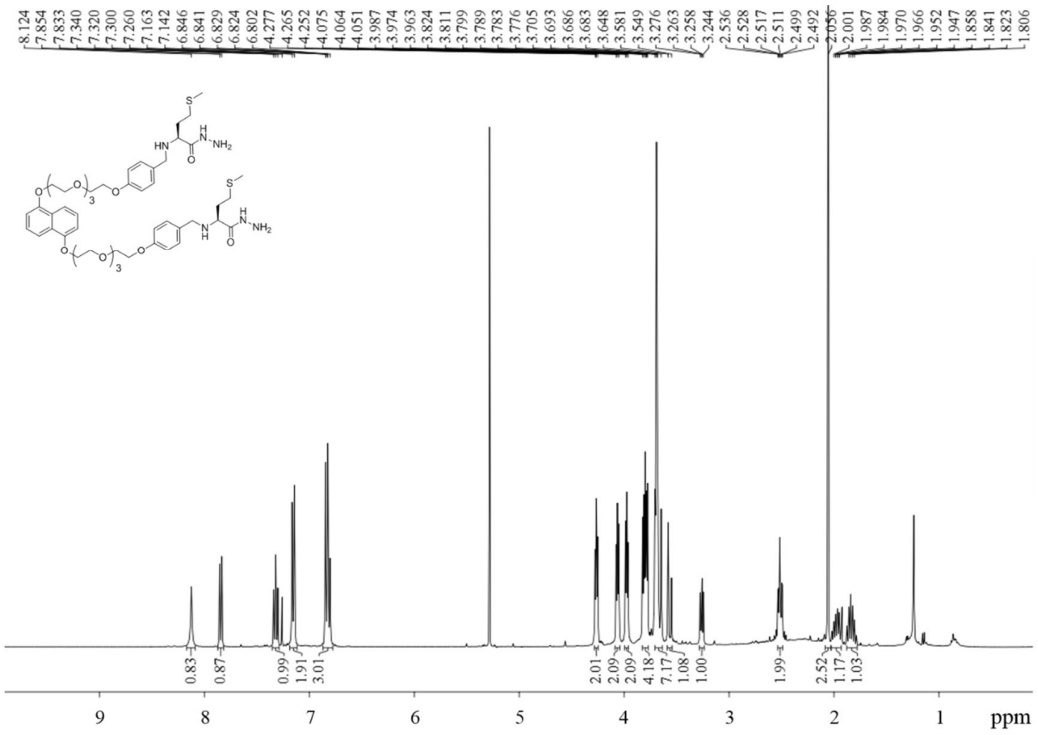


Figure S17. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) of **3**.

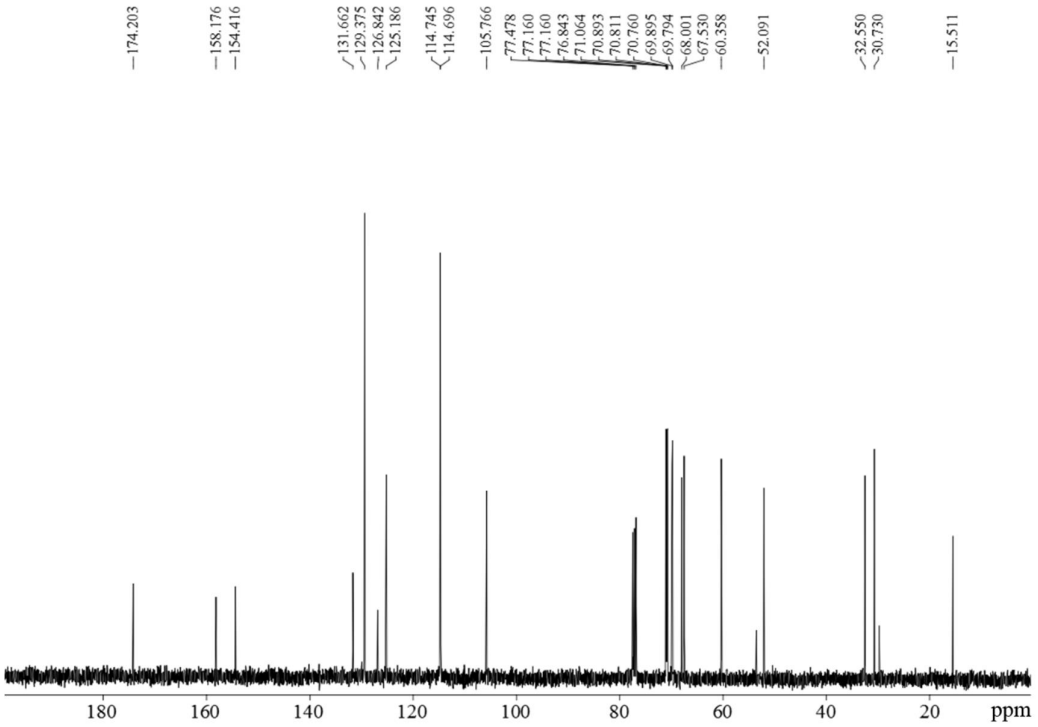


Figure S18. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, 298 K) of **3**.

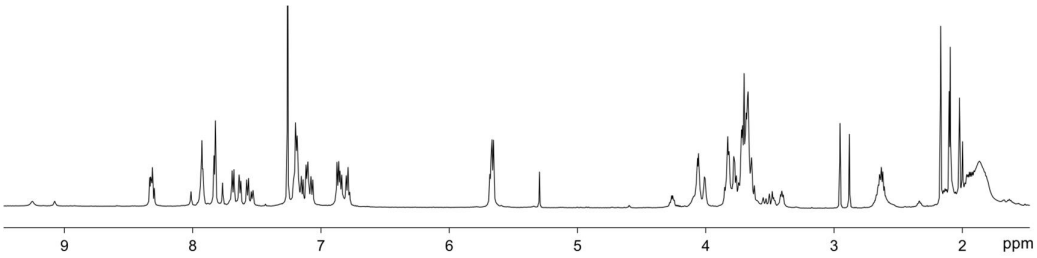


Figure S19. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) of **M1**.

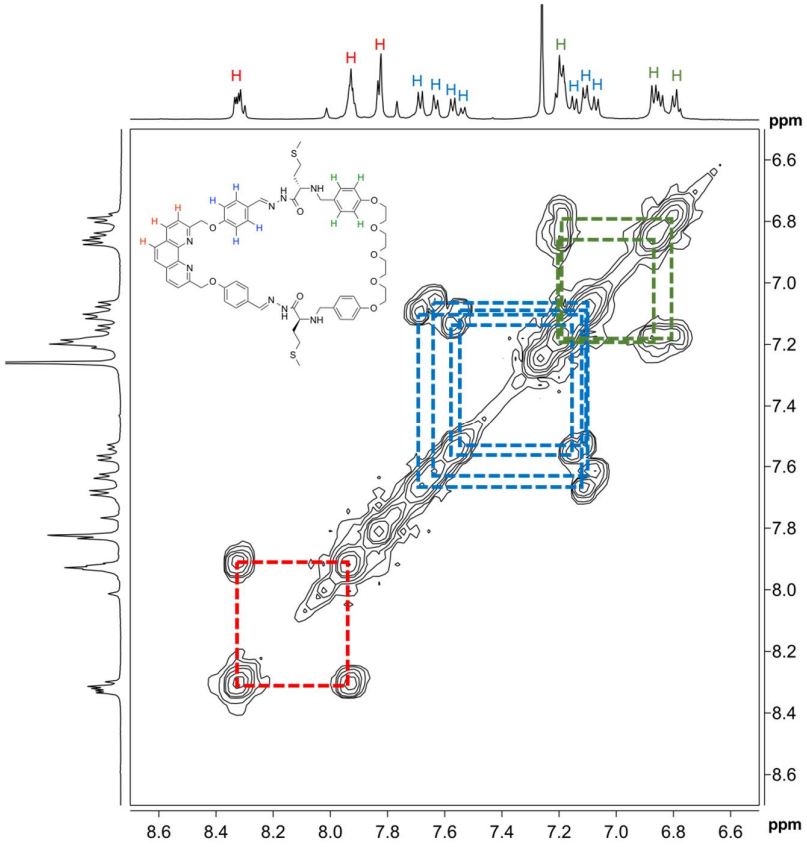


Figure S20. Partial COSY (400 MHz, $CDCl_3$, 298 K) spectrum of **M1**.

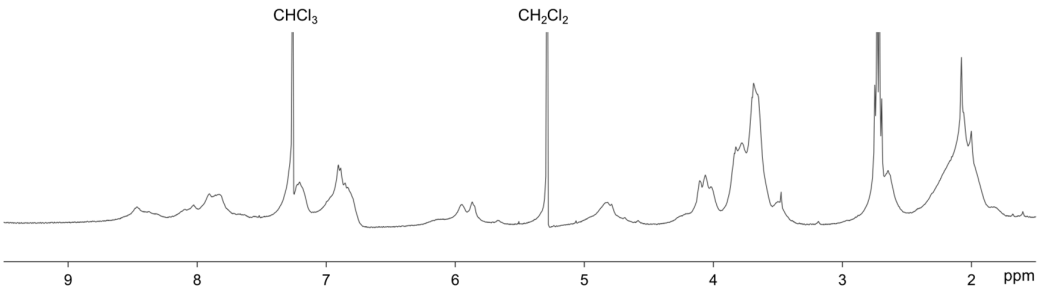


Figure S21. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) of **C1·Cu**$^{+}$.

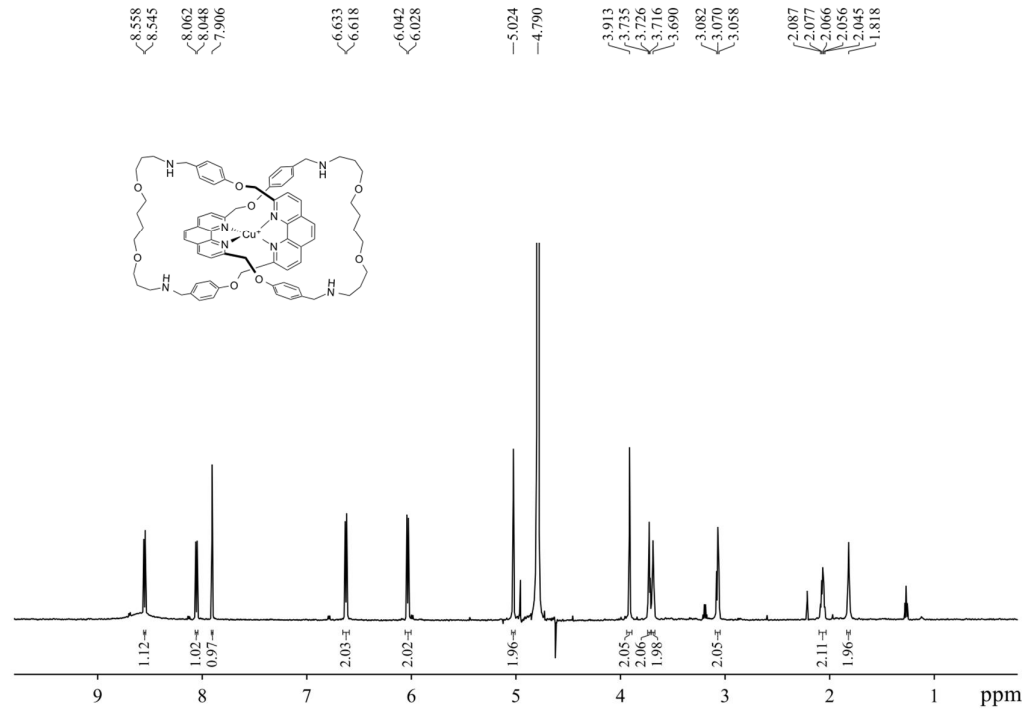


Figure S22. ^{1}H NMR (400 MHz, D_2O, 298 K) of **C3·Cu^{+}**.

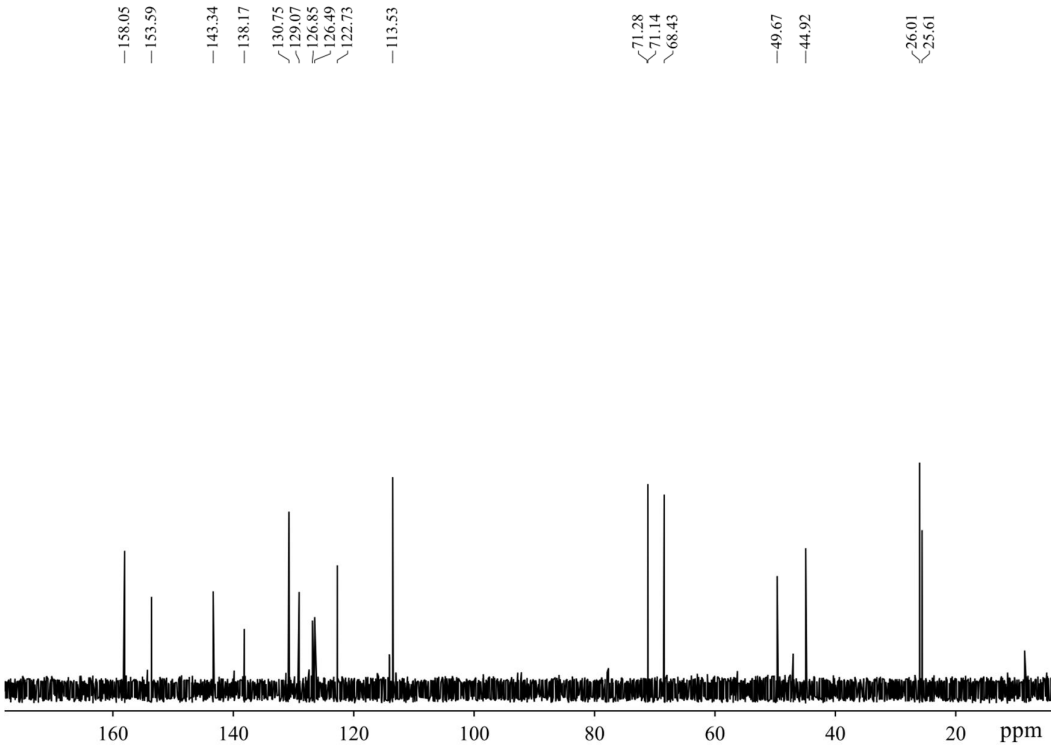


Figure S23. ^{13}C{^{1}H} NMR (100 MHz, D_2O, 298 K) of **C3·Cu^{+}**.

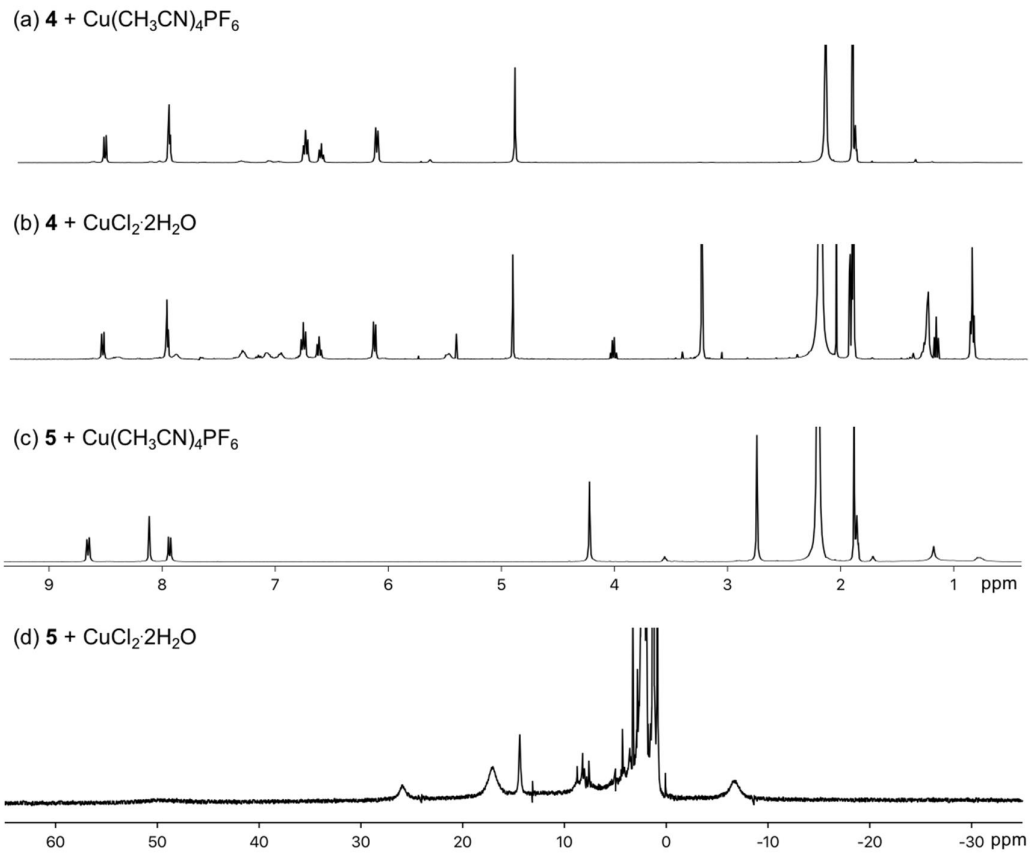


Figure S24. ^{1}H NMR (400 MHz, CD_3CN, 298 K) of a 2:1 complex from (a) **4** and $Cu(CH_3CN)_4PF_6$; (b) **4** and $CuCl_2{\cdot}2H_2O$; (c) **5** and $Cu(CH_3CN)_4PF_6$; and (d) **5** and $CuCl_2{\cdot}2H_2O$.

3. DCL Setup and Analysis

$CHCl_3$ and MeOH were of analytical grade and distilled over CaH_2 and 3Å molecular sieve before use. Metal salts (LiCl, NaCl, KCl, $MgCl_2 \cdot 6H_2O$, $Al(NO_3)_3 \cdot 9H_2O$, $CaCl_2 \cdot 6H_2O$, $MnCl_2 \cdot 6H_2O$, $FeCl_2 \cdot 4H_2O$, $FeCl_3 \cdot 6H_2O$, $CoCl_2 \cdot 6H_2O$, $NiCl_2 \cdot 6H_2O$, CuI, $CuCl_2 \cdot 2H_2O$, $ZnCl_2$, $CdCl_2$, $Ce(NO_3)_3 \cdot 6H_2O$ and $Er(NO_3)_3 \cdot 6H_2O$) were from commercial suppliers (Aldrich, Alfa Aesar, Dkmchem and Strem) and used as received. Stock solutions of template metal salt were prepared at 50 mM in MeOH. Stock solution of $CBPQT^{4+}$ was prepared at 100 mM in MeCN.

DCLs were prepared by dissolving an equimolar mixture of the building blocks in $CHCl_3$/MeOH/TFA (10:10:1) at 0.1 mM, 1 mM or 5 mM each of the building blocks. Metal templates were introduced to the DCLs by adding a corresponding amount of the 50 mM stock solutions of the metal salt to the library in a final volume of 1 mL. For DCLs templated by $CBPQT^{4+}$, the macrocycle was added as a 100 mM stock solution to the library in a final volume of 1 mL. The libraries were stirred in closed capped vials at room temperature for 3 days before HPLC/LCMS analysis.

HPLC and LCMS analyses were carried out using a Waters-Alliance e2695 system coupled to a 2489 UV/Vis detector and a QDa MS detector. HPLC grade water (Scharlau), MeCN (Arkonic Scientific) and formic acid (Fluka) were used without purification. Analytical HPLC analyses were performed by injecting 5 εL of the library solution onto an XBridge analytical column (C18, 3.5 εm particle size, 2.1 × 50 mm). Elutions were performed at a flow rate of 0.6 mL/min at room temperature with gradient elution profiles as described below. UV/Vis absorbance was monitored at 285 nm.

Table S1. Elution profile for Method 1.

Time/min	Water (with 0.05% formic acid)	MeCN
0	95%	5%
1	95%	5%
10	5%	95%
10.5	0%	100%
13.5	0%	100%

Table S2. Elution profile for Method 2.

Time/min	Water (with 0.05% formic acid)	MeCN (with 0.05% formic acid)
0	95%	5%
1	95%	5%
7.5	5%	95%
7.6	0%	100%
9.5	0%	100%

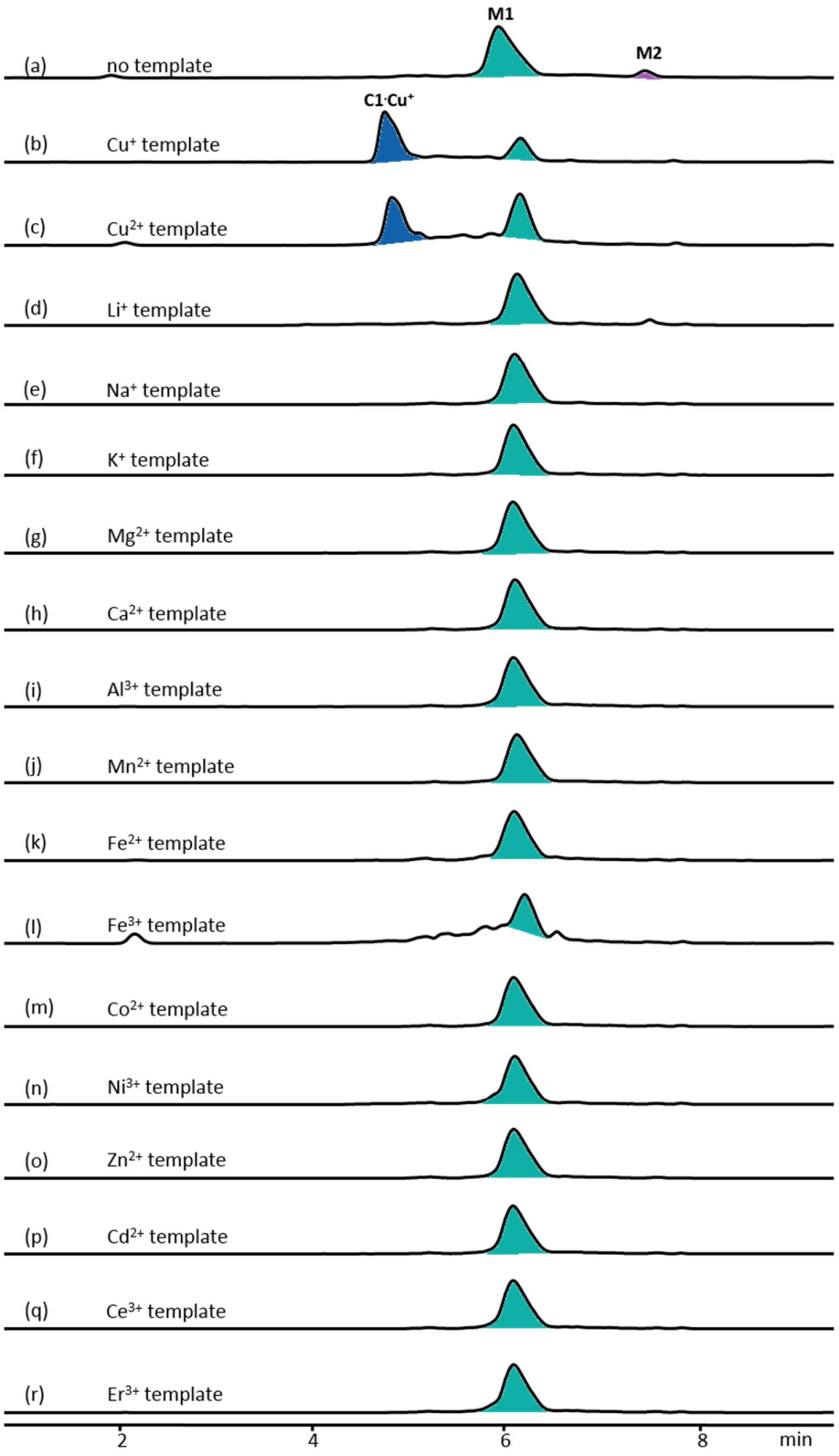


Figure S25. HPLC chromatograms (Method 1) of DCLs from **1** and **2** (1 mM each) in (a) the absence of template, and (b to r) the presence of 0.5 mM of metal templates.

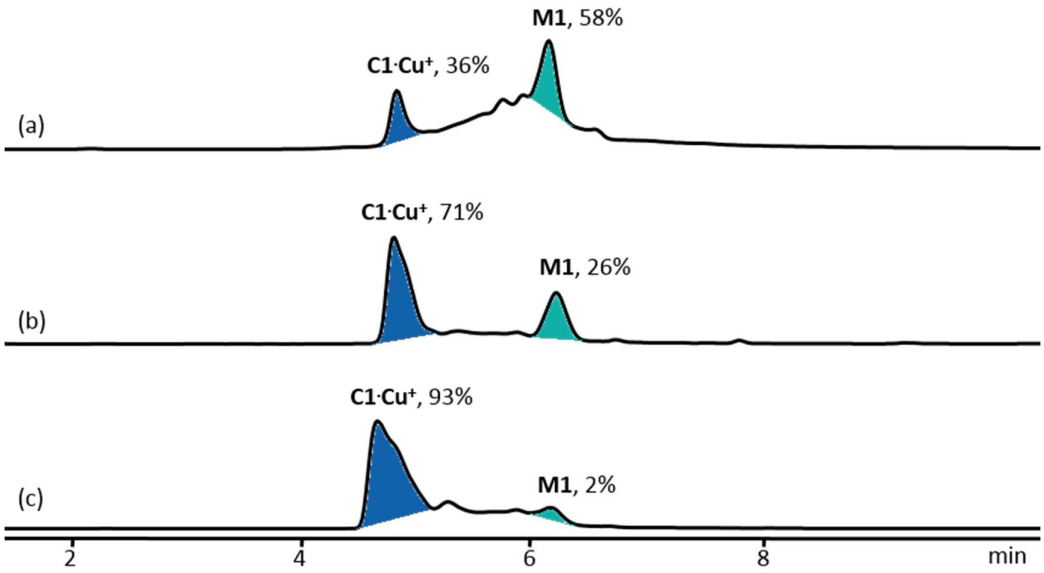


Figure S26. HPLC chromatograms (Method 1) of DCLs from **1** and **2** at (a) 0.1 mM, (b) 1 mM and (c) 5 mM each in the presence of 0.5 eq. of Cu^{+} (0.05 mM, 0.5 mM and 2.5 mM) with respect to **1**.

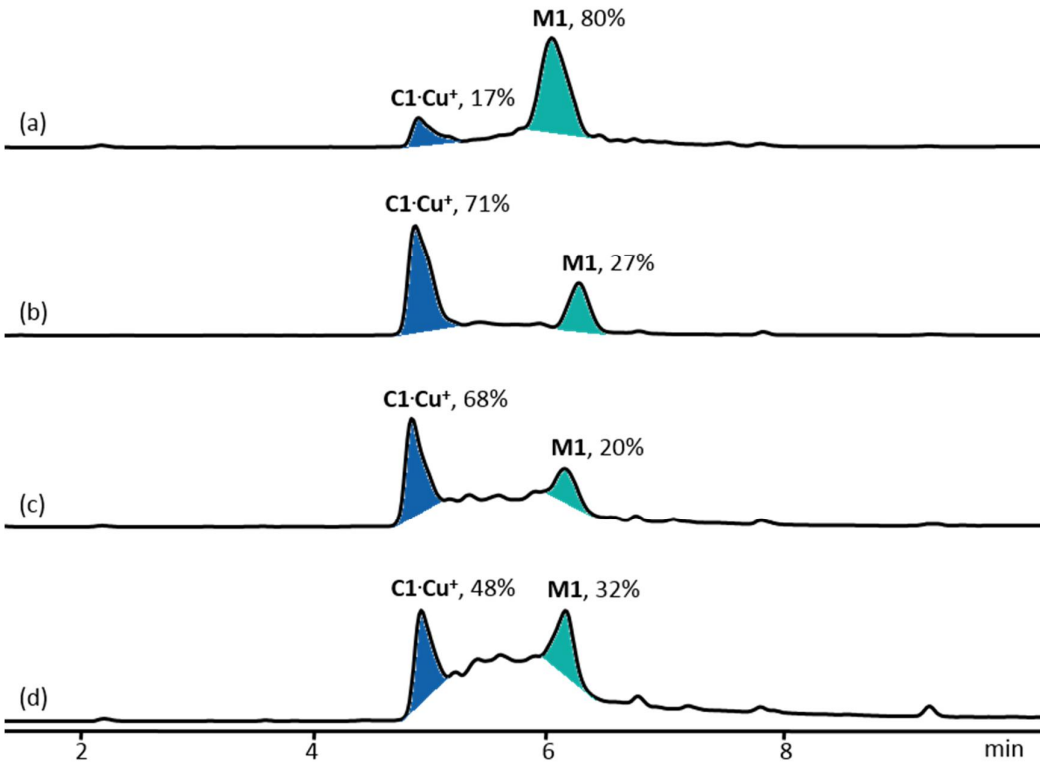


Figure S27. HPLC chromatograms (Method 1) of DCLs from 1 mM each of **1** and **2** in the presence of (a) 0.1 mM, (b) 0.5 mM, (c) 1 mM and (d) 2 mM of Cu^{+}**.**

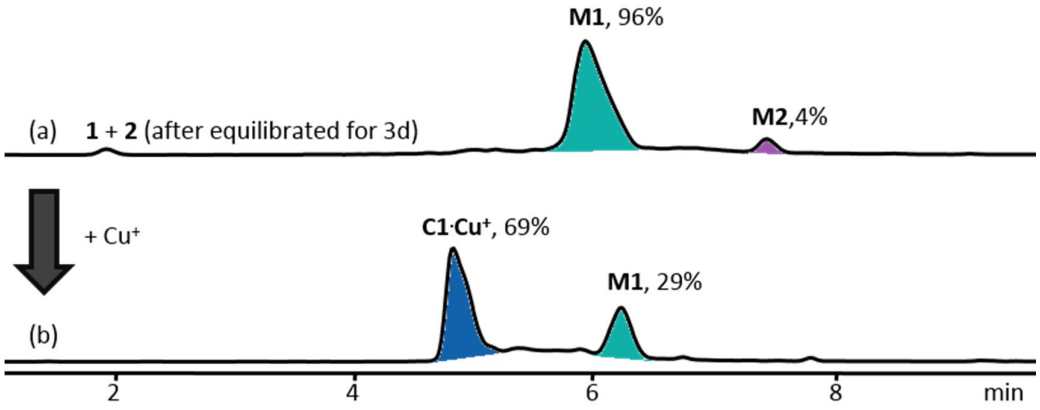
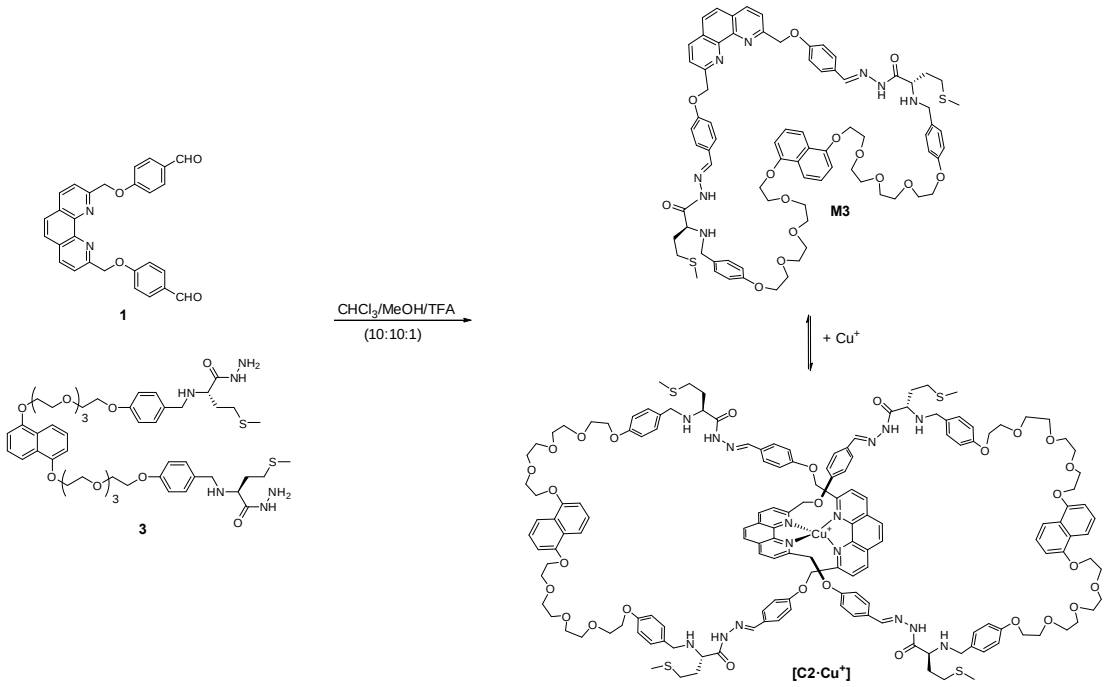


Figure S28. HPLC chromatograms (Method 1) of DCLs of 1 mM each of **1** and **2** (a) after 3 days of its preparation; and (b) after subsequent addition of Cu^{+} in a final concentration of 0.5 mM.



Scheme S4. Generation of DCL from building blocks **1** and **3**.

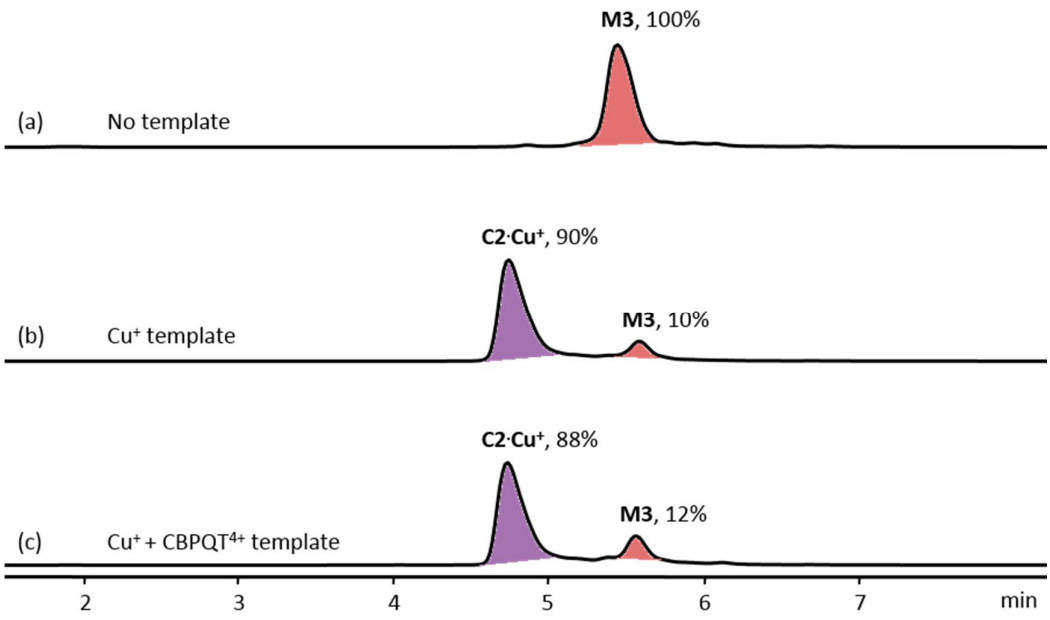


Figure S29. HPLC chromatograms (Method 2) of DCLs of 1 mM each of **1** and **3** in (a) the absence of template, and in the presence of (b) 0.5 mM of Cu^{+} and (c) 0.5 mM of Cu^{+} and 1 mM $CBPQT^{4+}$.

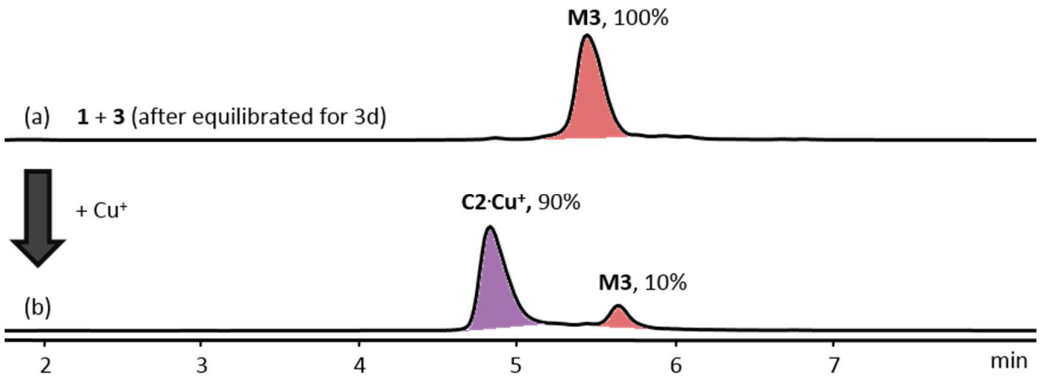


Figure S30. HPLC chromatograms (Method 2) of DCLs of 1 mM each of **1** and **3** (a) after 3 days of its preparation; and (b) after subsequent addition of Cu^{+} in a final concentration of 0.5 mM.

4. ESI-MS

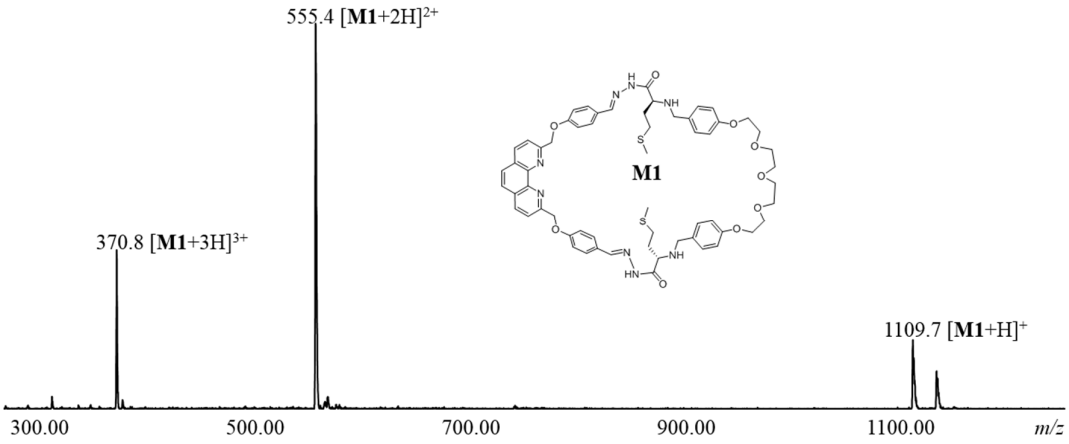


Figure S31. ESI-MS (+ve) spectrum of **M1**.

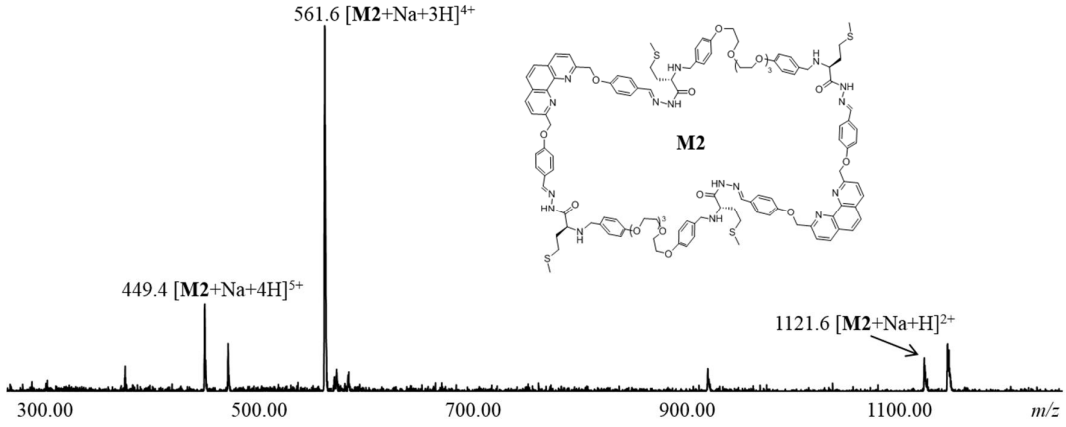


Figure S32. ESI-MS (+ve) spectrum of **M2**.

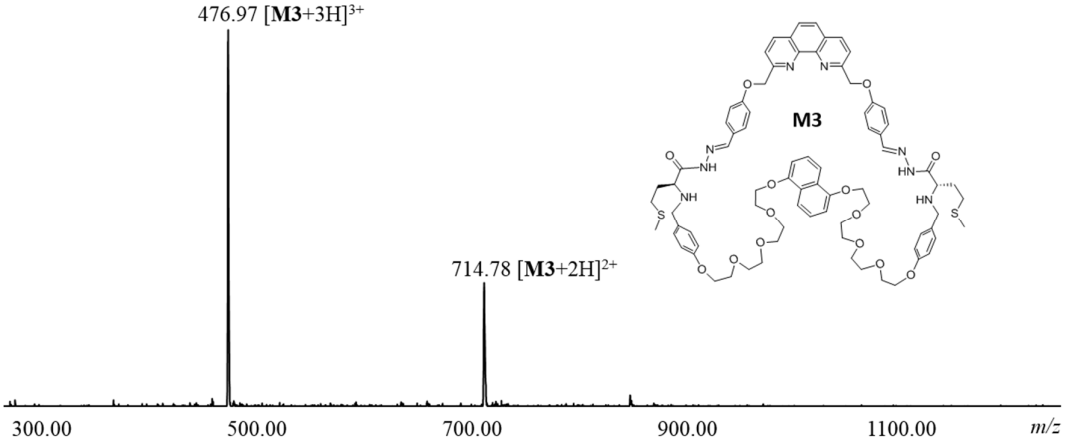


Figure S33. ESI-MS (+ve) spectrum of **M3**.

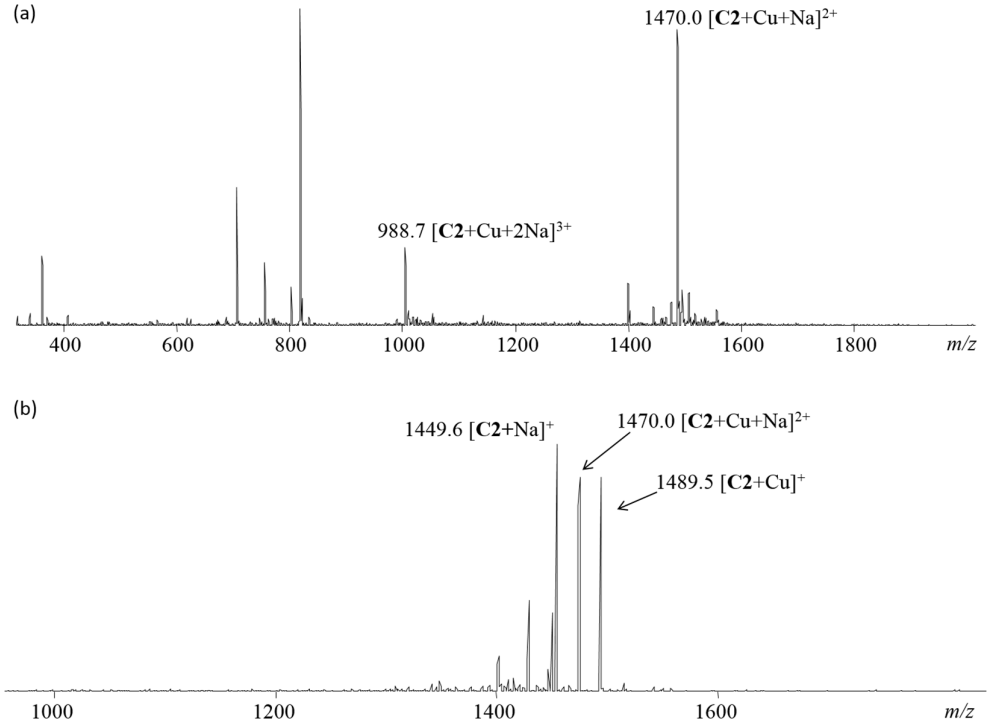


Figure S34. (a) ESI-MS spectrum of **C2·Cu**$^{+}$. (b) MS/MS spectrum of **C2·Cu**$^{+}$ from the fragmentation of peak at *m/z* = 1470.0.

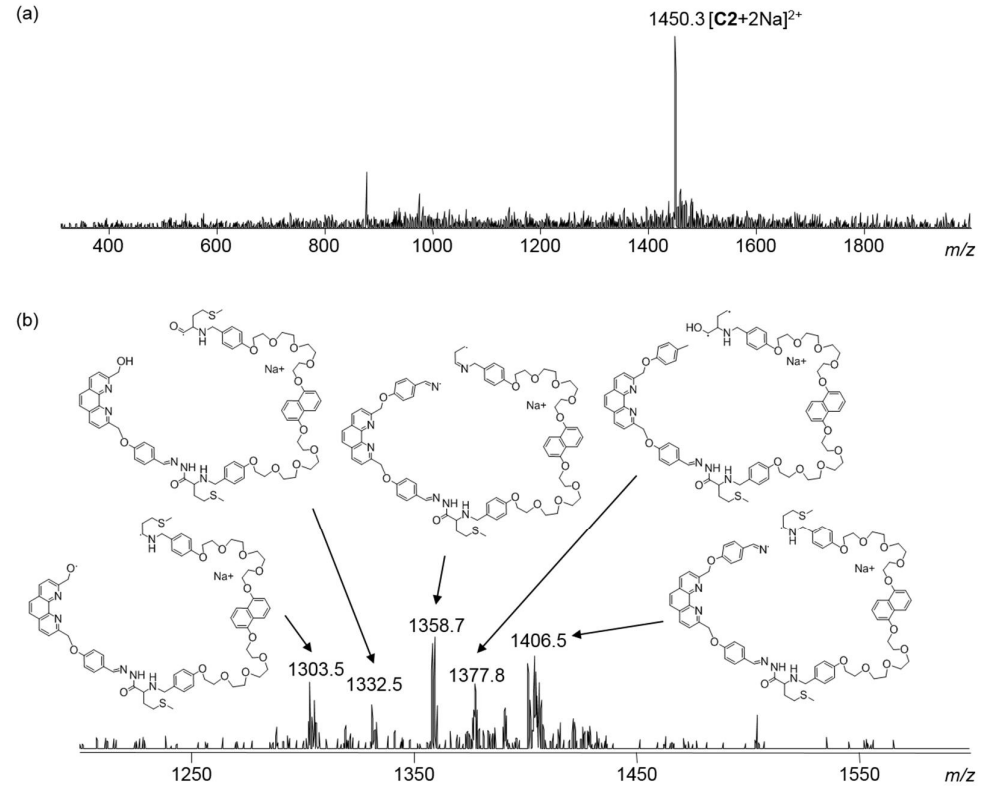


Figure S35. (a) ESI-MS spectrum of **C2** (b) MS/MS spectrum of **C2** from the fragmentation of peak at *m/z* = 1450.3.

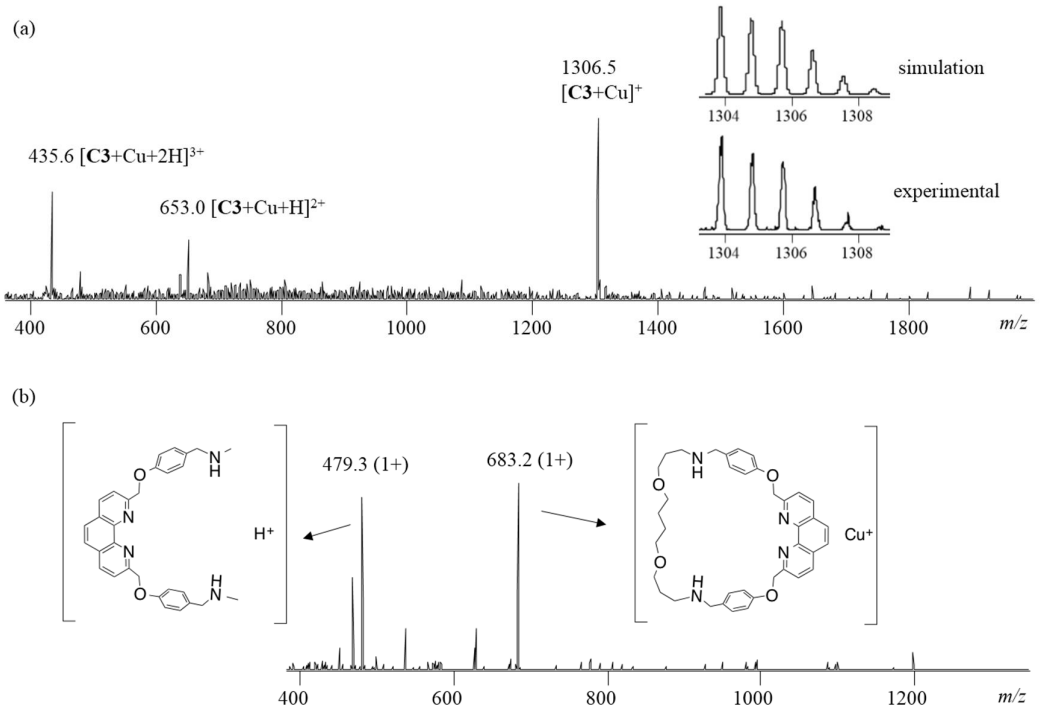


Figure S36. (a) ESI-MS spectrum of **C3·Cu**$^{+}$, expanded view of the peak at *m/z* = 1306.5 is shown in the inset; (b) MS/MS spectrum of **C3·Cu**$^{+}$ from the fragmentation of peak at *m/z* = 1306.5.

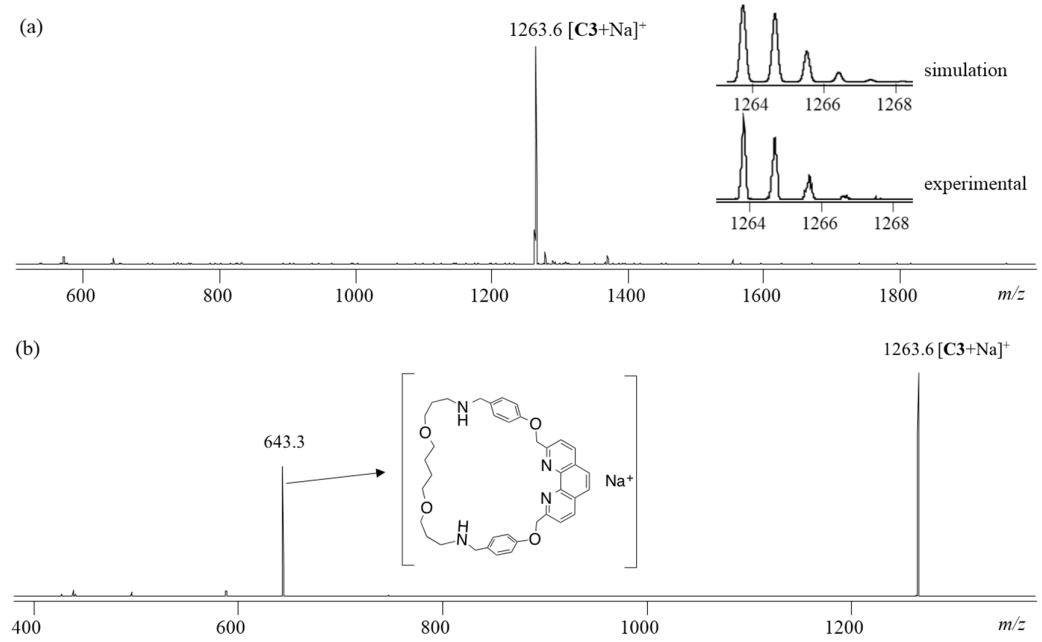


Figure S37. (a) ESI-MS spectrum of **C3**, expanded view of the peak at *m/z* = 1263.6 is shown in the inset; (b) MS/MS spectrum of **C3** from the fragmentation of peak at *m/z* = 1263.6.

5. *X-Ray Diffraction Analysis*

Compound		$[Cu(\mathbf{4})_2]PF_6$		$[Cu(\mathbf{5})Cl_2]$	
Empirical formula		$C_{52}H_{40}CuF_6N_4O_4P$		$C_{16}H_{16}Cl_2CuN_2O_2$	
Formula weight		993.39		402.75	
Temperature / K		301(2)		300(2)	
Wavelength / Å		0.71073		0.71073	
Crystal system		Triclinic		Triclinic	
Space group		P-1		P-1	
Unit cell dimension					
a / Å	Ŭ/ degree	12.8662(4)	107.7890(10)	8.4793(3)	89.7970(10)
b / Å	ɓ / degree	12.9465(4)	98.4350(10)	8.9464(3)	85.5580(10)
c / Å	ɔ / degree	15.7376(5)	110.0870(10)	11.1491(4)	74.3700(10)
Volume / Å^3		2249.57(12)		811.91(5)	
Z		2		2	
Density (calcd) / Mgm^{-3}		1.467		1.647	
Absorption coeff. / mm^{-1}		0.598		1.683	
F(000)		1020		410	
Crystal size / mm^3		0.084 x 0.173 x 0.329		0.132 x 0.175 x 0.344	
ɗ range for data collection		2.55 to 25.02°		2.94 to 25.03°	
Index ranges		-15<=h<=15		-10<=h<=10	
		-15<=k<=15		-10<=k<=10	
		-18<=l<=18		-13<=l<=13	
Reflection collected		42659		26210	
Independent reflections		7947 [R(int) = 0.1031]		2858[R(int)=0.0725]	
Completeness to ɗ		ɗ = 25.02, 99.9 %		ɗ = 25.03, 99.9 %	
Absorption correction		Multi-scan		Multi-scan	
Max. and min. transmission		0.9510 and 0.8270		0.8080 and 0.5950	
Refinement method		Full-matrix least-squares on F^2		Full-matrix least-squares on F^2	
Data/ restraints / parameters		7947 / 0 / 613		2858 / 0 / 210	
Goodness-of-fit on F^2		1.035		1.081	
Final R indices [I Ó2σ(I)]		R1 = 0.0477, wR2 = 0.1224		R1 = 0.0280, wR2 = 0.0791	
R indices (all data)		R1 = 0.0668, wR2 = 0.1328		R1 = 0.0306, wR2 = 0.0808	
Largest diff. peak and hole		0.620 and -0.417 eÅ^{-3}		0.608 and -0.496 eÅ^{-3}	

The X-ray intensity data were measured on a *PHOTON100 CMOS* detector system equipped with a compact optics monochromator and a Mo KŬmicrofocus IεS (ə = 0.71073 Å). The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The structure was solved and refined using the Bruker SHELXTL Software Package.

6. References

1. G. R. Newkome, G. E. Kiefer, W. E. Puckett and T. Vreeland, *J. Org. Chem.*, 1983, **48**, 5112.
2. A. K. Jain, A. Paul, B. Maji, K. Muniyappa and S. Bhattacharya, *J. Med. Chem.*, 2012, **55**, 2981.
3. A. Mirzahosseini and B. Noszál, *J. Pharma. Biomed. Ana.*, 2014, **95**, 184.
4. P. R. Ashton, J. Huff, S. Menzer, I. W. Parsons, J. A. Preece, J. F. Stoddart, M. S. Tolley, A. J. P. White and D. J. Williams, *Chem. Eur. J.*, 1996, **2**, 31.
5. M. Asakawa, W. Dehaen, G. Lôabbé, S. Menzer, J. Nouwen, F. M. Raymo, J. F. Stoddart and D. J. Williams, *J. Org. Chem.,* 1996, **61**, 9591.