

Pillar[5]arene derivatives with three different kinds of repeating units: first examples, crystal structures and selective preparation

Mingguang Pan, Min Xue*

Department of Chemistry, Zhejiang University, Hangzhou 310027, P. R. China

Fax: +86-571-8795-1895; Tel: +86-571-8795-3189; Email address: xuemin@zju.edu.cn.

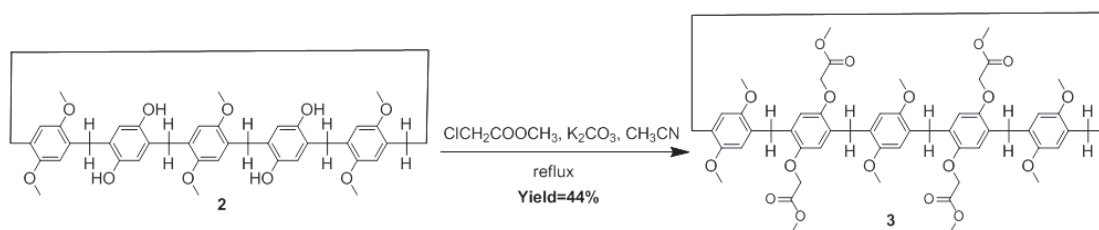
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1. Materials and Methods:

1^{S1} and **2**^{S2} were synthesized according to literature procedures. All reagents were commercially available and used as supplied without further purification. Solvents were either employed as purchased or dried according to procedures described in the literature. NMR spectra were recorded with a Bruker Advance DMX 400 spectrophotometer with use of the deuterated solvent as the lock and TMS as the internal reference. Low-resolution electrospray ionization (LRESI) mass spectra were obtained on a Bruker Esquire 3000 plus mass spectrometer (Bruker-Franzen Analytik GmbH Bremen, Germany) equipped with an ESI interface and an ion trap analyzer. High-resolution mass spectrometry experiments were performed with a Bruker Daltonics Apex III spectrometer or with a Bruker 7-Tesla FT-ICR mass spectrometer equipped with an electrospray source (Billerica, MA, USA). The melting points were collected on a SHPSIC WRS-2 automatic melting point apparatus.

2. Synthesis of **3**



A solution of **2** (1.00 g, 1.44 mmol) in acetonitrile (150 mL) was stirred in a 250 mL round-bottom flask, then potassium carbonate (2.01 g, 1.45 mmol) and methyl chloroacetate (1.56 g, 1.44 mmol) were added to the solution. The mixture was stirred under an atmosphere of nitrogen at reflux (83 °C) for 24 h. After the solid was filtered off, the solvent was removed. The residue was purified by column chromatography (eluent: petroleum ether/dichloromethane 3:1 → 0:1) to give **3** as a white solid (0.62 g, 44%). **3** M.p. 185.1–186.3 °C. The ¹H NMR spectrum of **3** is shown in Figure S1. ¹H NMR (400 MHz, CDCl₃, room temperature) δ (ppm): 6.85 (s, 2H), 6.83 (d, 4H), 6.71 (d, 4H), 4.53 (s, 4H), 4.52 (s, 4H), 3.77–3.79 (m, 10H), 3.73 (s, 6H), 3.70 (s, 6H), 3.66 (s, 6H), 3.32 (s, 6H), 3.12 (s, 6H). The ¹³C NMR spectrum of **3** is shown in Figure S2. ¹³C NMR (100 MHz, CDCl₃, room temperature) δ (ppm): 169.71, 169.96, 150.49, 150.38, 149.48, 149.25, 128.96, 128.82, 128.50, 127.82, 127.78, 114.70, 114.19, 113.90, 113.67, 65.98, 65.74, 55.72, 55.67, 51.62, 51.47, 29.73, 29.40, 29.28. The LRESI-MS of **3** is shown in Figure S3. LRESI-MS: *m/z* 1000.2 [M + NH₄]⁺

(100%), 1005.1 [M + Na]⁺ (25%). HRESI-MS: *m/z* calcd for [M] C₅₃H₅₈O₁₈Na⁺,
1005.3515, found 1005.3476, error 3.88 ppm.

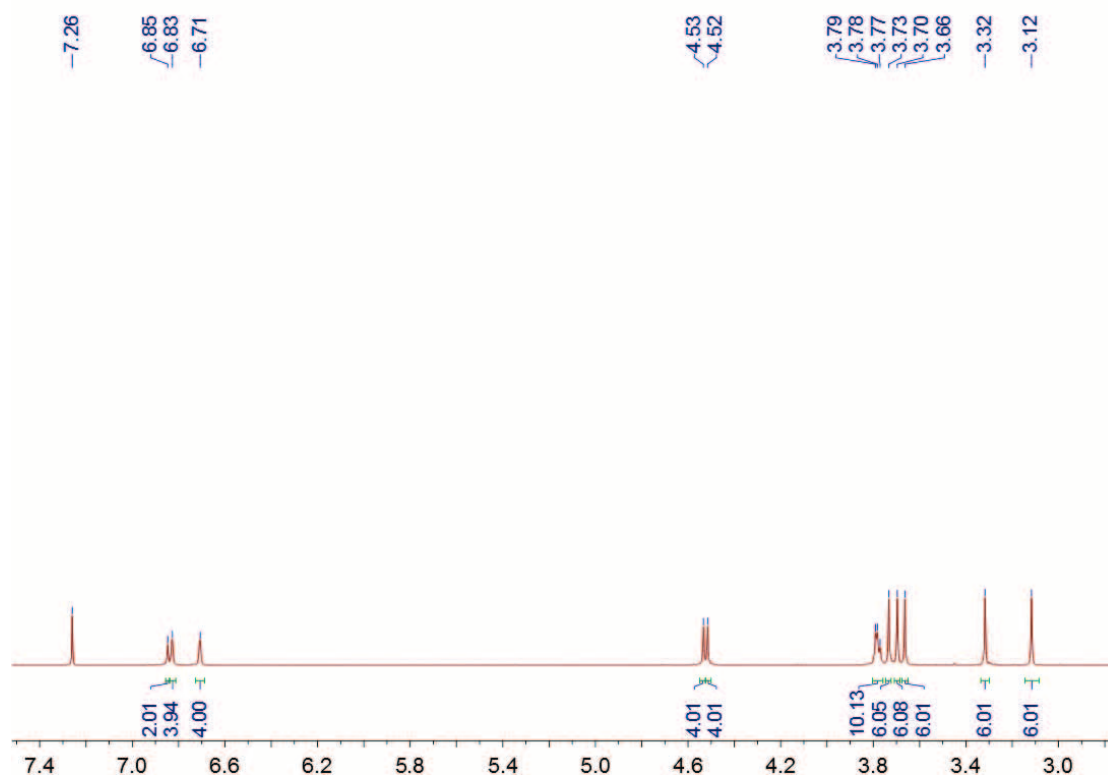


Fig. S1. ¹H NMR spectrum (400 MHz, CDCl₃, room temperature) of **3**.

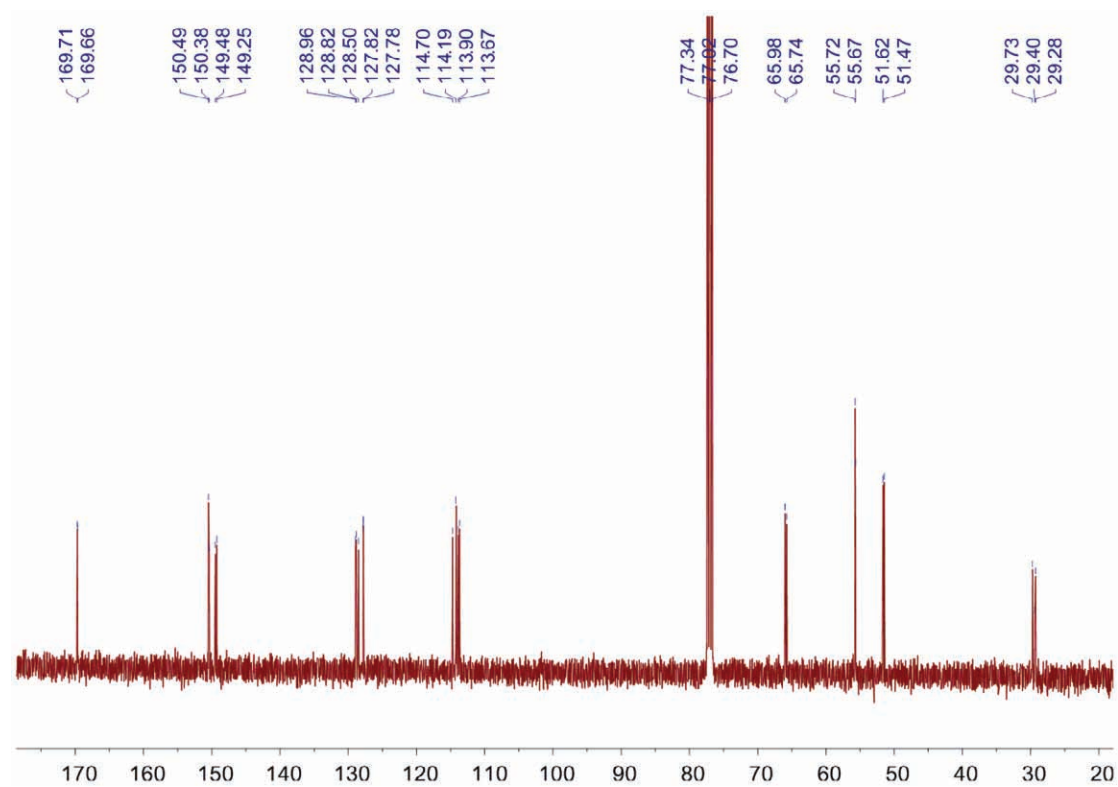


Fig. S2. ^{13}C NMR spectrum (100 MHz, CDCl_3 , room temperature) of **3**.

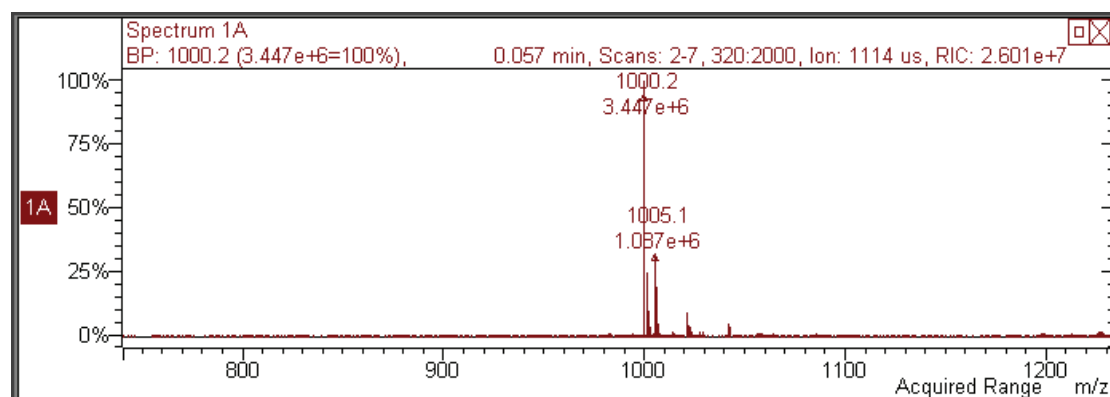
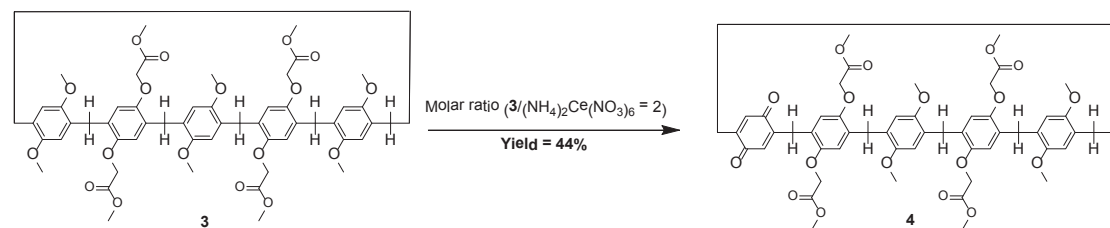


Fig. S3. Positive electrospray ionization mass spectrum of **3**.

3. Synthesis of **4**



Scheme S2. Synthesis of **4**.

A solution of **3** (1.10 g, 1.12 mmol) in THF (100 mL) was stirred in a 250 mL round-bottom flask while an aqueous solution $(\text{NH}_4)_2[\text{Ce}(\text{NO}_3)_6]$ (1.23 g, 2.24 mmol) was added dropwise. The mixture was stirred at 30 °C for 24 h. The organic solvent was removed, and the water layer was extracted with dichloromethane (3×50 mL). The combined organic layers were washed with water (100 mL) and saturated NaCl solution (100 mL) and then dried over anhydrous Na_2SO_4 . After being filtered and evaporated to dryness, the residue was purified by column chromatography on silica gel (petroleum ether/dichloromethane, v/v 5:1 \rightarrow 1:1; then ethyl acetate/petroleum ether/dichloromethane, $v/v/v$ 1:100/100 \rightarrow 2:100/100) to obtain **4** as a yellow red solid (0.36 g, 44 %) and also unchanged **3** (0.26 g). M.p. 80.8–82.0 °C. The ^1H NMR spectrum of **4** is shown in Figure S4. ^1H NMR (400 MHz, CDCl_3 , room temperature) δ (ppm): 7.02 (s, 1H), 7.00 (s, 1H), 6.86 (s, 1H), 6.81(s, 1H), 6.75 (s, 1H), 6.66 (br, 2H), 6.65 (s, 1H), 6.63 (br, 2H), 4.59 (s, 2H), 4.56 (br, 4H), 4.45 (s, 2H), 3.85 (s, 2H), 3.83 (d, 4H), 3.76 (s, 3H), 3.74 (s, 3H), 3.73 (s, 3H), 3.71 (br, 6H), 3.67 (s, 3H), 3.67 (s, 3H), 3.58 (br, 4H), 2.70 (s, 3H). The ^{13}C NMR spectrum of **4** is shown in Figure S5. ^{13}C NMR (100 MHz, CDCl_3 , room temperature) δ (ppm): 188.43, 188.39, 169.62, 169.58, 169.53, 169.13, 151.10, 150.58, 150.49, 150.44, 149.89, 149.39, 149.32, 149.14, 146.56, 146.08, 133.79, 133.23, 130.65, 128.48, 128.16, 127.86, 124.03, 123.66, 115.86, 114.72, 114.35, 114.07, 113.91, 113.85, 113.50, 66.55, 65.91, 65.82, 65.03, 55.92, 55.87, 55.80, 55.62, 51.94, 51.89, 51.25, 29.27, 29.17, 28.67, 28.17. The LRESI-MS of **4** is shown in Figure S6. LRESI-MS: m/z 975.3 $[\text{M} + \text{Na}]^+$ (100%). HRESI-MS: m/z calcd for $[\text{M}] \text{C}_{51}\text{H}_{52}\text{O}_{18}\text{Na}^+$, 975.3046, found 975.3048, error -0.21 ppm.

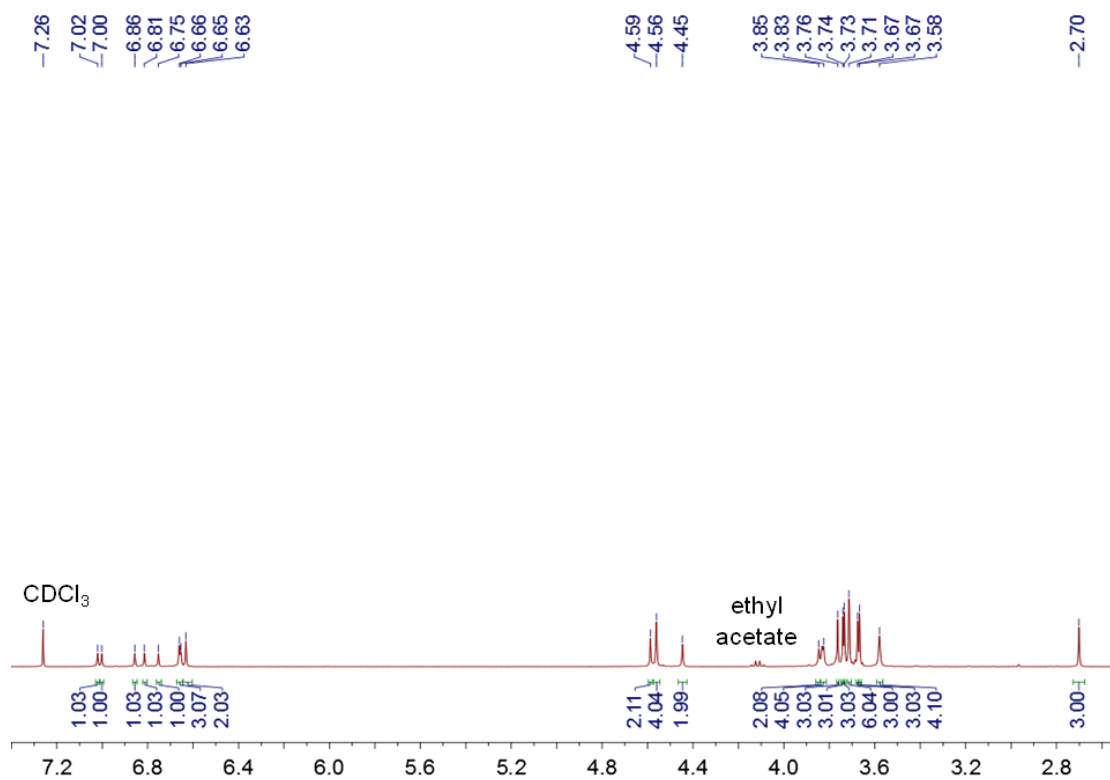


Fig. S4. ¹H NMR spectrum (400 MHz, CDCl₃, room temperature) of **4**.

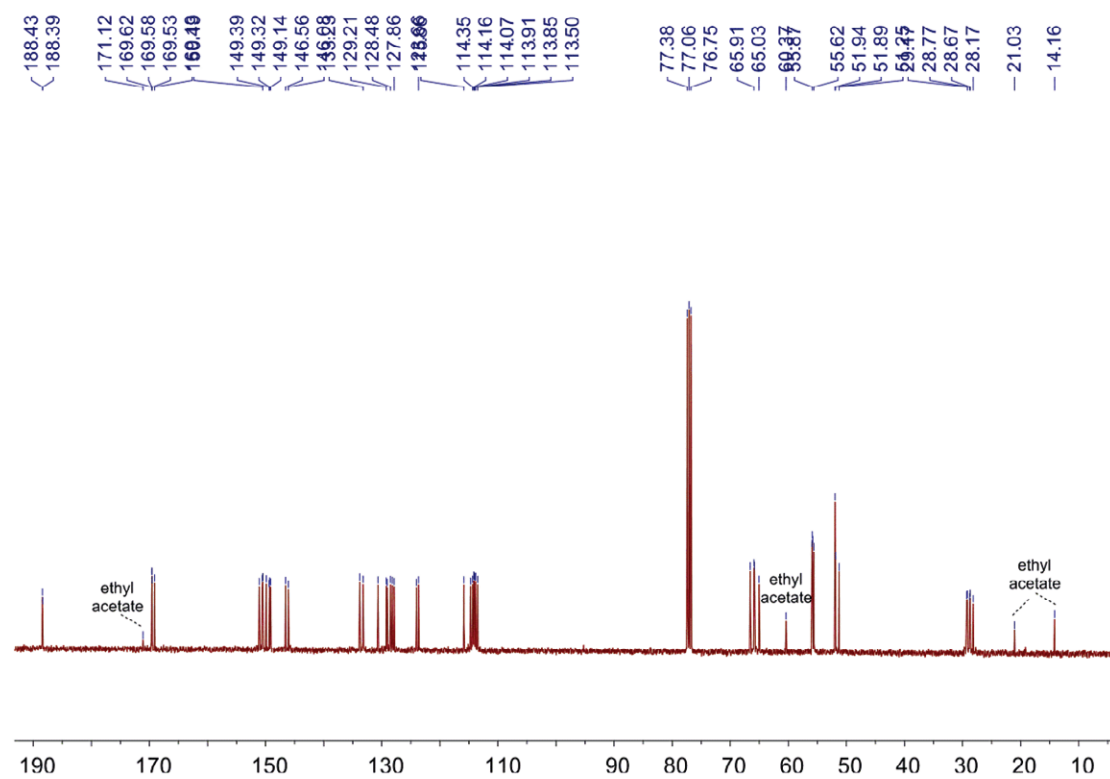


Fig. S5. ¹³C NMR spectrum (100 MHz, CDCl₃, room temperature) of **4**.

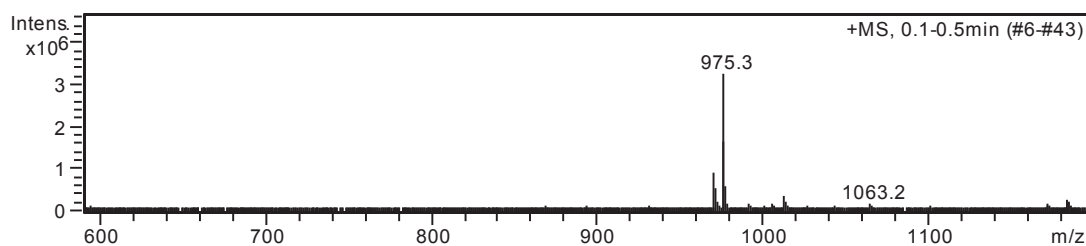
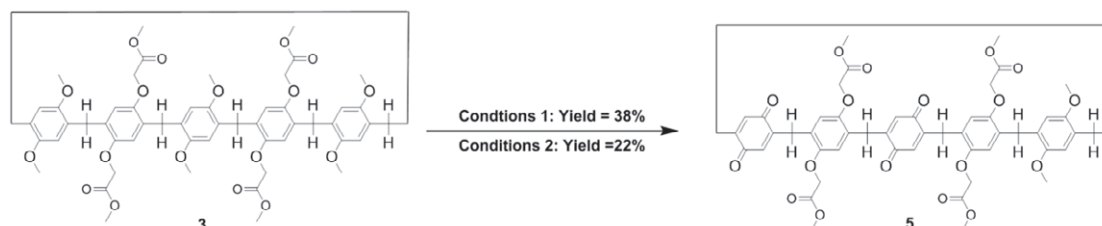


Fig. S6. Positive electrospray ionization mass spectrum of **4**.

4. Synthesis of **5**



Scheme S3. Synthesis of **5**.

Conditions 1: A solution of **3** (0.36 g, 0.37 mmol) in THF (30 mL) was stirred in a 50 mL round-bottom flask while an aqueous solution $(\text{NH}_4)_2[\text{Ce}(\text{NO}_3)_6]$ (1.21 g, 2.21 mmol) was added dropwise. The mixture was stirred at 20 °C for 24 h. The organic solvent was removed, and the water layer was extracted with dichloromethane (3×20 mL). The combined organic layers were washed with water (50 mL) and saturated NaCl solution (50 mL) and then dried over anhydrous Na_2SO_4 . After being filtered and evaporated to dryness, the residue was purified by column chromatography on silica gel (petroleum ether/dichloromethane, v/v 3:1 \rightarrow 0:1, then ethyl acetate/petroleum ether/dichloromethane, v/v/v 1:100/100 \rightarrow 5:100/100) to obtain **5** as a red solid (0.13 g, 38%).

Conditions 2: A solution of **3** (0.73 g, 0.74 mmol) in THF (75 mL) was stirred in a 150 mL round-bottom flask while an aqueous solution $(\text{NH}_4)_2[\text{Ce}(\text{NO}_3)_6]$ (1.22 g, 2.23 mmol) was added dropwise. The mixture was stirred at 30 °C for 24 h. The organic solvent was removed, and the water layer was extracted with dichloromethane (3×50 mL). The combined organic layers were washed with water (100 mL) and saturated NaCl solution (100 mL) and then dried over anhydrous Na_2SO_4 . After being filtered and evaporated to dryness, the residue was purified by chromatography on silica gel (petroleum ether/dichloromethane, v/v 3:1 \rightarrow 0:1, then ethyl

acetate/petroleum ether/dichloromethane, v/v/v 1:100/100 → 5:100/100) to obtain **4** as a yellow red solid (0.23 g, 32%) and **5** as a red solid (0.15 g, 22%).

5 M.p. 175.9–176.7 °C. The ^1H NMR spectrum of **5** is shown in Figure S7. ^1H NMR (400 MHz, CDCl_3 , room temperature) δ (ppm): 7.07 (s, 1H), 6.87 (s, 1H), 6.85 (s, 1H), 6.84 (s, 1H), 6.81 (s, 1H), 6.72 (s, 1H), 6.71 (s, 1H), 6.66 (s, 1H), 6.65 (s, 1H), 6.64 (s, 1H), 4.58 (s, 2H), 4.57 (s, 2H), 4.55 (s, 2H), 4.53 (s, 2H), 3.85 (s, 2H), 3.79 (s, 3H), 3.78 (s, 3H), 3.74 (s, 3H), 3.66 (br, 6H), 3.62 (s, 3H), 3.61 (s, 2H), 3.60 (s, 3H), 3.60 (s, 3H). The ^{13}C NMR spectrum of **5** is shown in Figure S8. ^{13}C NMR (100 MHz, CDCl_3 , room temperature) δ (ppm): 188.57, 188.48, 188.35, 169.28, 169.17, 169.04, 151.20, 150.31, 149.90, 149.79, 149.70, 149.09, 146.54, 146.02, 145.85, 145.76, 133.96, 133.86, 133.65, 133.16, 130.22, 128.89, 125.70, 125.59, 124.52, 123.83, 115.61, 115.10, 114.92, 114.31, 114.09, 113.72, 66.11, 65.71, 65.62, 65.46, 56.12, 55.69, 52.06, 52.00, 51.97, 29.71, 29.12, 27.95, 27.85, 27.76, 27.68. The LRESI-MS of **5** is shown in Figure S9. LRESIMS: m/z 945.2 $[\text{M} + \text{Na}]^+$ (100%). HRESI-MS: m/z calcd for $[\text{M}] \text{C}_{49}\text{H}_{46}\text{O}_{18}\text{Na}^+$, 945.2576, found 945.2541, error 3.78 ppm.

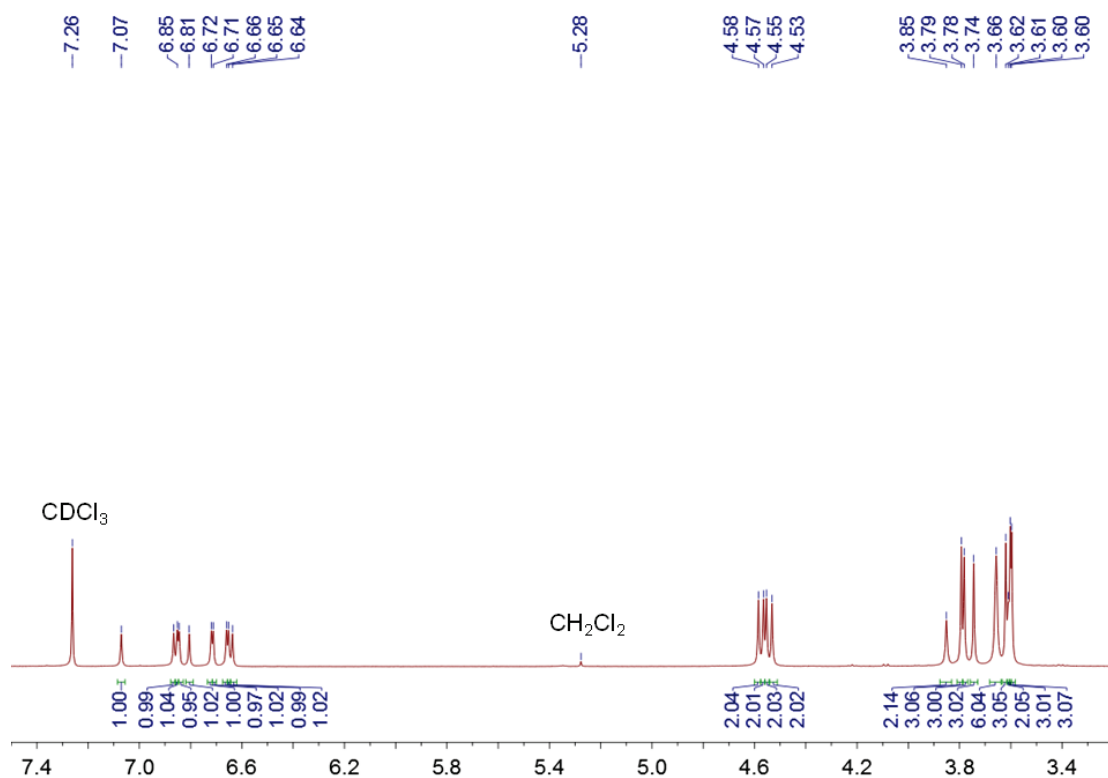


Fig. S7. ^1H NMR spectrum (400 MHz, CDCl_3 , room temperature) of **5**.

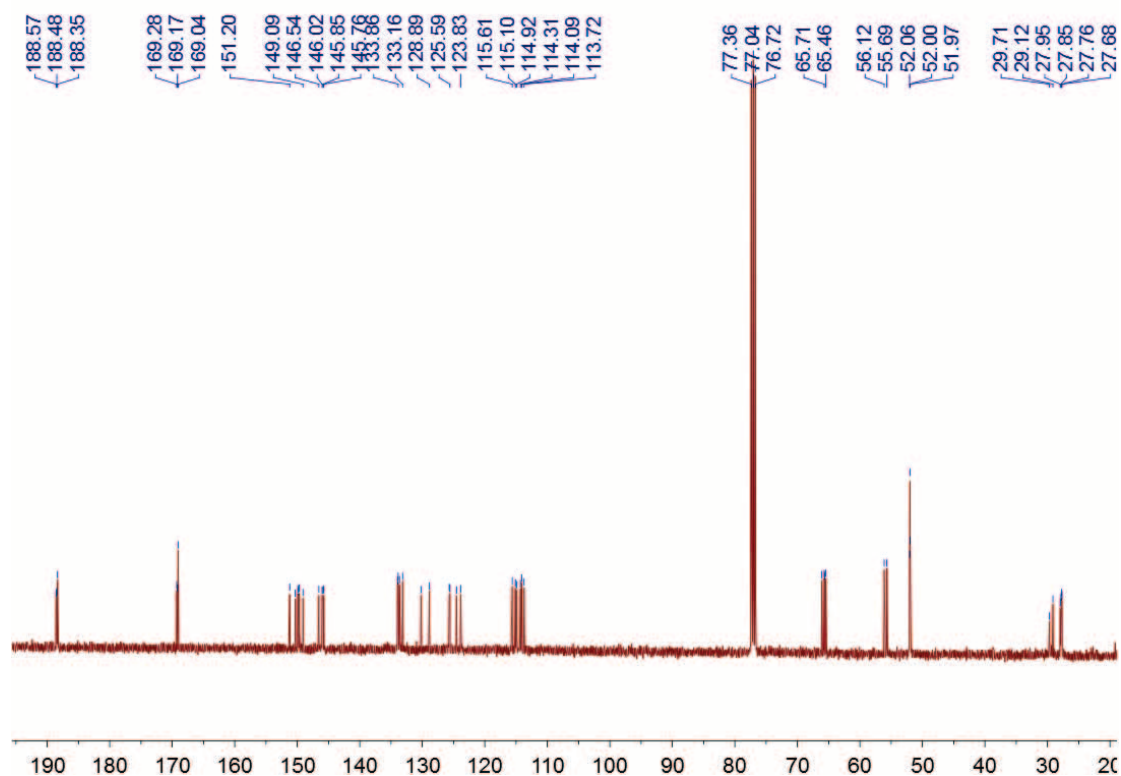


Fig. S8. ^{13}C NMR spectrum (100 MHz, CDCl_3 , room temperature) of **5**.

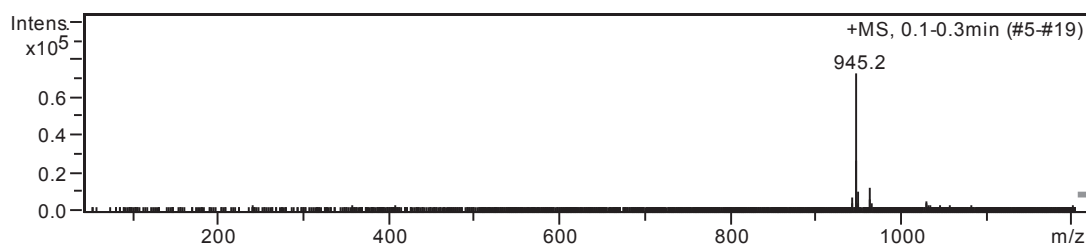
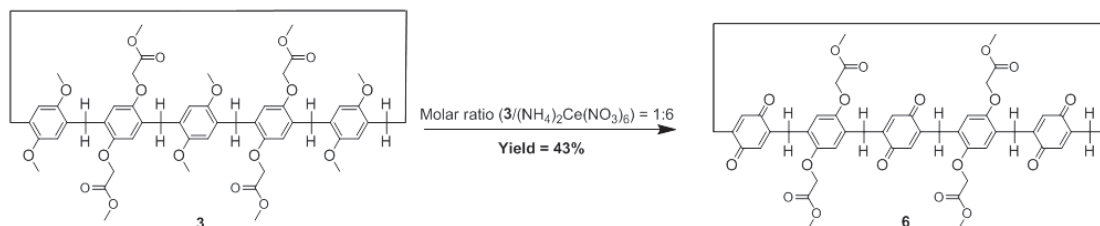


Fig. S9. Positive electrospray ionization mass spectrum of **5**.

5. Synthesis of **6**



Scheme S4. Synthesis of **6**.

A solution of **3** (2.46 g, 2.50 mmol) in THF (300 mL) was stirred in a 500 mL round-bottom flask while an aqueous solution of $(\text{NH}_4)_2[\text{Ce}(\text{NO}_3)_6]$ (8.03 g, 14.65 mmol) was added dropwise. The mixture was stirred at 30 °C for 24 h. The organic solvent was removed, and the water layer was extracted with dichloromethane (3×50

mL). The combined organic layers were washed with water (100 mL) and saturated NaCl solution (100 mL) and then dried over anhydrous Na₂SO₄. After being filtered and evaporated to dryness, the residue was purified by column chromatography on silica gel (petroleum ether/dichloromethane, v/v 2:1 → 0:1, then ethyl acetate/petroleum ether/dichloromethane, v/v/v 1:100/100 → 20:100/100) to obtain **6** as a red solid (0.96 g, 43%). M.p. 117.5–118.8 °C. The ¹H NMR spectrum of **6** is shown in Figure S10. ¹H NMR (400 MHz, CDCl₃, room temperature) δ (ppm): 7.03 (s, 2H), 6.93 (s, 2H), 6.70 (br, 4H), 6.62 (s, 2H), 4.57 (br, 8H), 3.76 (s, 6H), 3.75 (s, 6H), 3.69 (s, 4H), 3.68 (s, 4H), 3.47 (s, 2H). The ¹³C NMR spectrum of **6** is shown in Figure S11. ¹³C NMR (100 MHz, CDCl₃, room temperature) δ (ppm): 188.37, 187.67, 187.35, 168.93, 149.81, 149.71, 146.21, 145.95, 143.37, 135.09, 133.93, 133.78, 126.02, 125.36, 115.23, 114.96, 65.69, 65.67, 52.14, 28.17, 27.67, 25.66. The LRESI-MS of **6** is shown in Figure S12. LRESI-MS: *m/z* 915.0 [M + Na]⁺ (100%). HRESI-MS: *m/z* calcd for [M] C₄₇H₄₀O₁₈Na⁺, 915.2107, found 915.2098, error 0.91 ppm.

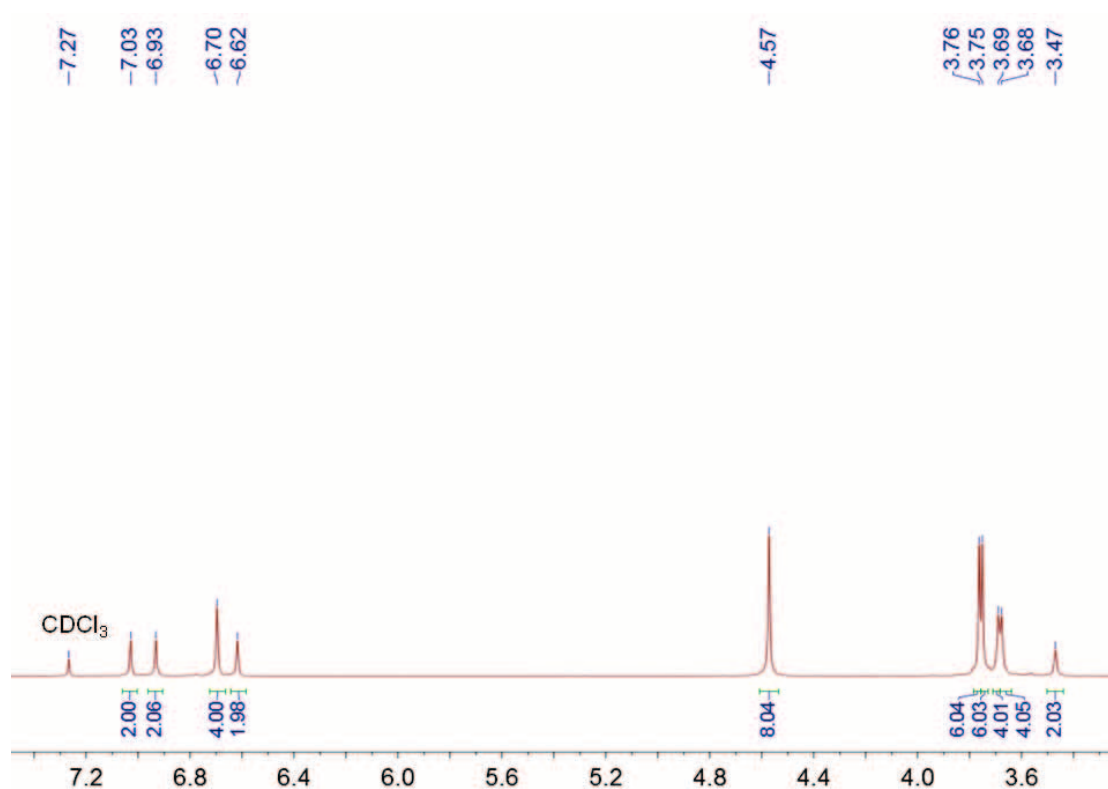


Fig. S10. ¹H NMR spectrum (400 MHz, CDCl₃, room temperature) of **6**.

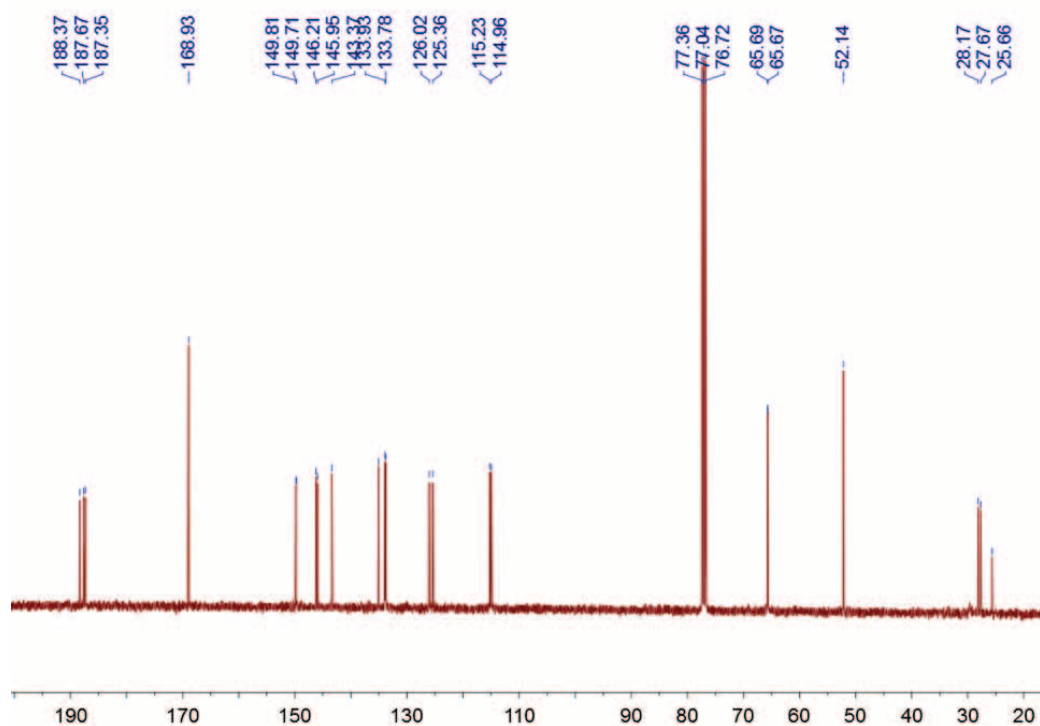


Fig. S11. ^{13}C NMR spectrum (100 MHz, CDCl_3 , room temperature) of **6**.

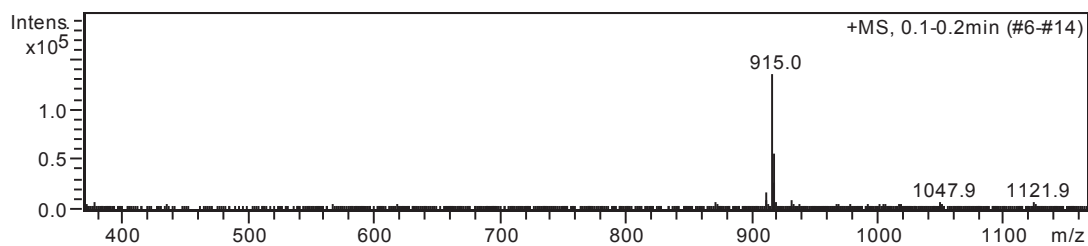
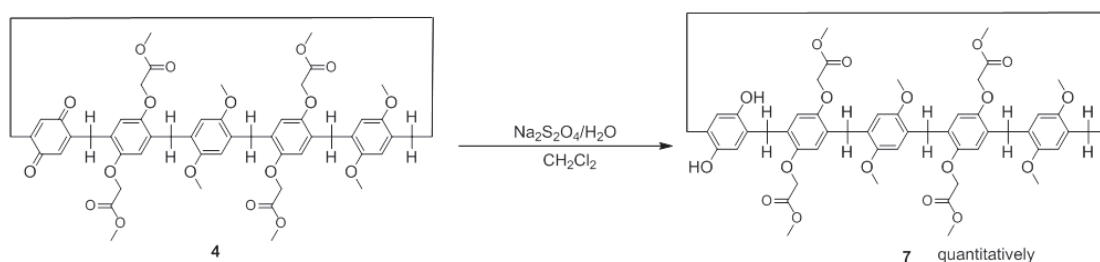


Fig. S12. Positive electrospray ionization mass spectrum of **6**.

6. Synthesis of **7**



Scheme S5. Synthesis of **7**.

A solution of **4** (0.21 g, 0.22 mmol) in CH_2Cl_2 (30 ml) was stirred in a 50 mL round-bottom flask while an aqueous solution of $\text{Na}_2\text{S}_2\text{O}_4$ (0.77 g, 4.42 mmol) was added. The mixture was stirred vigorously at room temperature for 1.0 h. The water

layer was extracted by CH_2Cl_2 (3×25 mL). The combined organic layers were washed with water (50 mL) and saturated NaCl solution (50 mL) and then dried over anhydrous Na_2SO_4 . After being filtered and evaporated to dryness, **7** was obtained as a white solid without further purification (0.21 g, 100%). Mp. 197.7–198.5°C. The ^1H NMR spectrum of **7** is shown in Figure S13. ^1H NMR (400 MHz, CDCl_3 , room temperature) δ (ppm): 7.12 (s, 1H), 7.07 (s, 1H), 6.93 (br, 1H), 6.82 (s, 1H), 6.75 (br, 2H), 6.63 (s, 1H), 6.58 (br, 2H), 6.54 (s, 1H), 6.52 (s, 1H), 4.60 (s, 2H), 4.57 (br, 4H), 4.51 (s, 2H), 3.85–3.67 (br, 22H), 3.49 (s, 3H), 3.47 (d, 6H), 3.37 (s, 3H). The ^{13}C NMR spectrum of **7** is shown in Figure S14. ^{13}C NMR (100 MHz, CDCl_3 , room temperature) δ (ppm): 169.67, 169.50, 169.32, 168.97, 151.67, 150.62, 150.40, 150.17, 149.38, 149.18, 148.17, 147.76, 147.36, 146.95, 130.14, 129.08, 128.86, 127.91, 127.42, 126.82, 126.17, 118.15, 117.74, 115.20, 114.73, 114.41, 114.30, 113.92, 113.87, 112.77, 66.02, 65.91, 65.83, 65.65, 56.47, 55.92, 55.81, 55.71, 52.04, 51.73, 51.68, 30.67, 30.00, 29.66, 29.52, 29.38. The LRESI-MS of **7** is shown in Figure S15. LRESI-MS: m/z 989.9 $[\text{M} + \text{Cl}]^-$ (100%). HRESI-MS: m/z calcd for $[\text{M}] \text{C}_{51}\text{H}_{54}\text{O}_{18}\text{Na}^+$, 977.3202, found 977.3163, error 4.01 ppm.

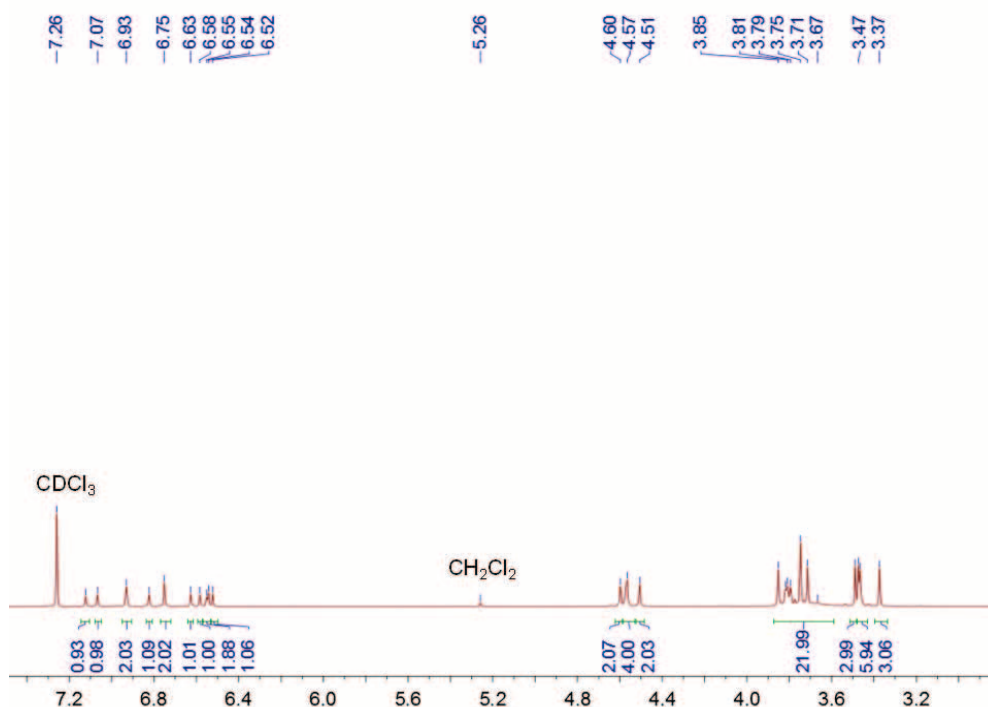


Fig. S13. ^1H NMR spectrum (400 MHz, CDCl_3 , room temperature) of **7**.

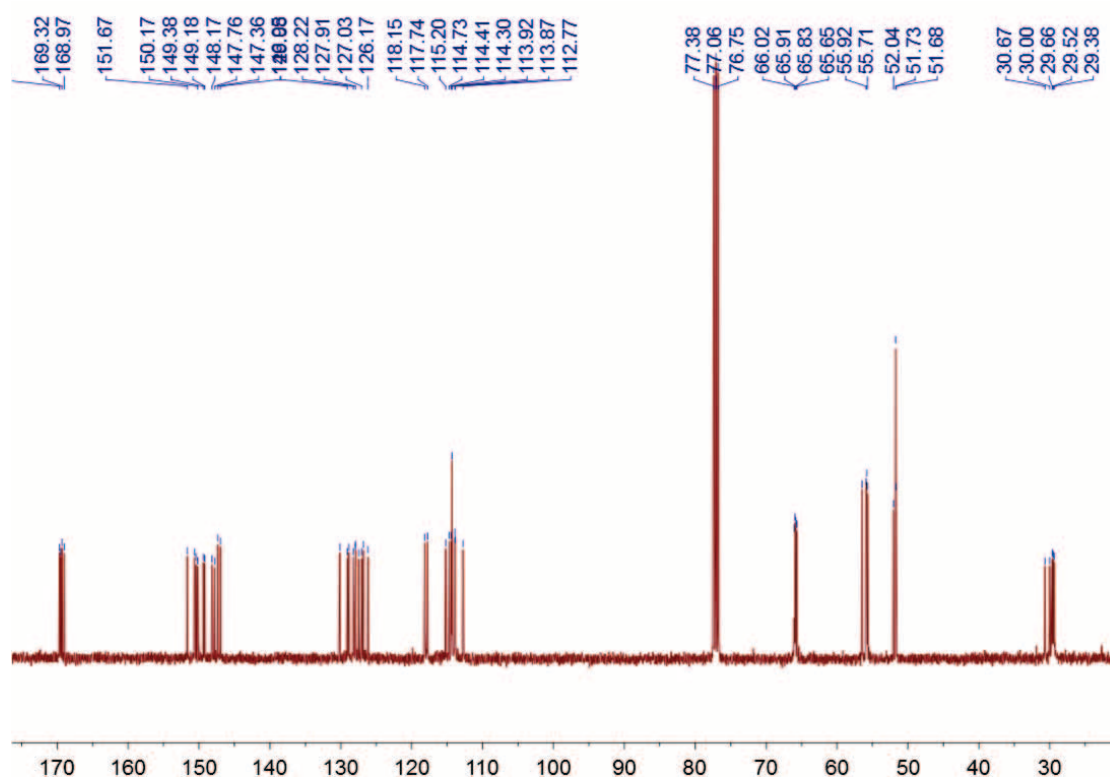


Fig. S14. ^{13}C NMR spectrum (100 MHz, CDCl_3 , room temperature) of **7**.

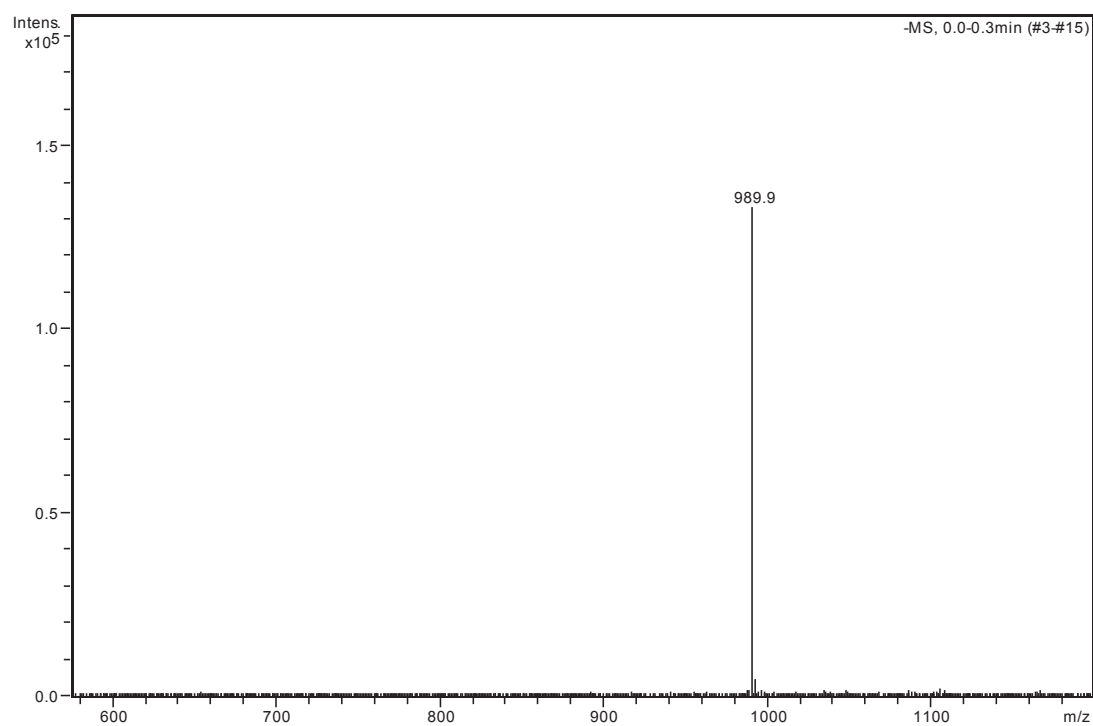


Fig. S15. Negative electrospray ionization mass spectrum of **7**.

7. X-ray crystal data of 3–7

Crystal data of **3**: colorless, $C_{57}H_{64}Cl_8O_{18}$, FW 1320.68, monoclinic, space group $C 2/c$, $a = 19.5855(4)$, $b = 15.4343(3)$, $c = 21.1972(4)$ Å, $\alpha = 90.00^\circ$, $\beta = 102.2746(19)^\circ$, $\gamma = 90.00^\circ$, $V = 6261.2(2)$ Å³, $Z = 4$, $D_c = 1.401$ g cm⁻³, $T = 170(2)$ K, $\mu = 3.869$ mm⁻¹, 28585 measured reflections, 5551 independent reflections, 326 parameters, 0 restraints, $F(000) = 2744$, $R_1 = 0.0610$, $wR_2 = 0.1486$ (all data), $R_1 = 0.0547$, $wR_2 = 0.1448$ [$I > 2\sigma(I)$], max. residual density $0.268e \cdot \text{Å}^{-3}$, and goodness-of-fit (F^2) = 1.034. CCDC 950515.

Crystal data of **4**: yellow, $C_{52}H_{54}Cl_2O_{18}$, FW 1037.85, orthorhombic, space group $P b c a$, $a = 21.1413(7)$, $b = 19.5241(7)$, $c = 24.0141(12)$ Å, $\alpha = 90.00^\circ$, $\beta = 90.00^\circ$, $\gamma = 90.00^\circ$, $V = 9912.2(7)$ Å³, $Z = 8$, $D_c = 1.391$ g cm⁻³, $T = 170(2)$ K, $\mu = 0.208$ mm⁻¹, 29984 measured reflections, 8735 independent reflections, 657 parameters, 12 restraints, $F(000) = 4352$, $R_1 = 0.1020$, $wR_2 = 0.1858$ (all data), $R_1 = 0.0643$, $wR_2 = 0.1617$ [$I > 2\sigma(I)$], max. residual density $0.813e \cdot \text{Å}^{-3}$, and goodness-of-fit (F^2) = 1.054. CCDC 950516.

Crystal data of **5**: red, $C_{51.50}H_{51.50}Cl_2O_{18.25}$, FW 1033.33, Triclinic, space group $P-1$, $a = 12.2090(11)$, $b = 12.3468(11)$, $c = 19.3418(17)$ Å, $\alpha = 84.024(7)^\circ$, $\beta = 87.960(7)^\circ$, $\gamma = 61.290(9)^\circ$, $V = 2542.9(4)$ Å³, $Z = 2$, $D_c = 1.350$ g cm⁻³, $T = 170(2)$ K, $\mu = 0.202$ mm⁻¹, 16173 measured reflections, 9255 independent reflections, 637 parameters, 48 restraints, $F(000) = 1081$, $R_1 = 0.1436$, $wR_2 = 0.2991$ (all data), $R_1 = 0.0903$, $wR_2 = 0.2604$ [$I > 2\sigma(I)$], max. residual density $0.798e \cdot \text{Å}^{-3}$, and goodness-of-fit (F^2) = 1.087. CCDC 950517.

Crystal data of **6**: red, $C_{49}H_{44}Cl_4O_{18}$, FW 1062.64, Triclinic, space group $P-1$, $a = 12.579(3)$, $b = 14.929(3)$, $c = 15.012(3)$ Å, $\alpha = 64.15(3)^\circ$, $\beta = 77.01(3)^\circ$, $\gamma = 73.74(3)^\circ$, $V = 2418.4(8)$ Å³, $Z = 2$, $D_c = 1.459$ g cm⁻³, $T = 93(2)$ K, $\mu = 0.322$ mm⁻¹, 19160 measured reflections, 8501 independent reflections, 645 parameters, 0 restraints, $F(000) = 1100$, $R_1 = 0.1746$, $wR_2 = 0.4015$ (all data), $R_1 = 0.1228$, $wR_2 = 0.3212$ [$I > 2\sigma(I)$], max. residual density $1.627e \cdot \text{Å}^{-3}$, and goodness-of-fit (F^2) = 1.418. CCDC 950518.

Crystal data of **7**: colorless, $C_{108}H_{119}Cl_8NO_{36}$, FW 2290.17, Triclinic, space group $P-1$, $a = 12.101(2)$, $b = 15.262(3)$, $c = 15.448(3)$ Å, $\alpha = 91.89(3)^\circ$, $\beta = 95.89(3)^\circ$, $\gamma = 101.88(3)^\circ$, $V = 2772.9(10)$ Å³, $Z = 1$, $D_c = 1.372$ g cm⁻³, $T = 93(2)$ K, $\mu = 0.286$ mm⁻¹, 21810 measured reflections, 9730 independent reflections, 705 parameters, 15 restraints, $F(000) = 1198$, $R_1 = 0.1475$, $wR_2 = 0.4225$ (all data), $R_1 = 0.1214$, $wR_2 = 0.3832$ [$I > 2\sigma(I)$], max. residual density $2.236e \cdot \text{Å}^{-3}$, and goodness-of-fit (F^2) = 1.752. CCDC 953388.

8. Crystal structure of 7

A single crystal of 7 was grown by vapor diffusion of isopropyl ether into a dichloromethane solution of 7 under an atmosphere of N₂ at room temperature.

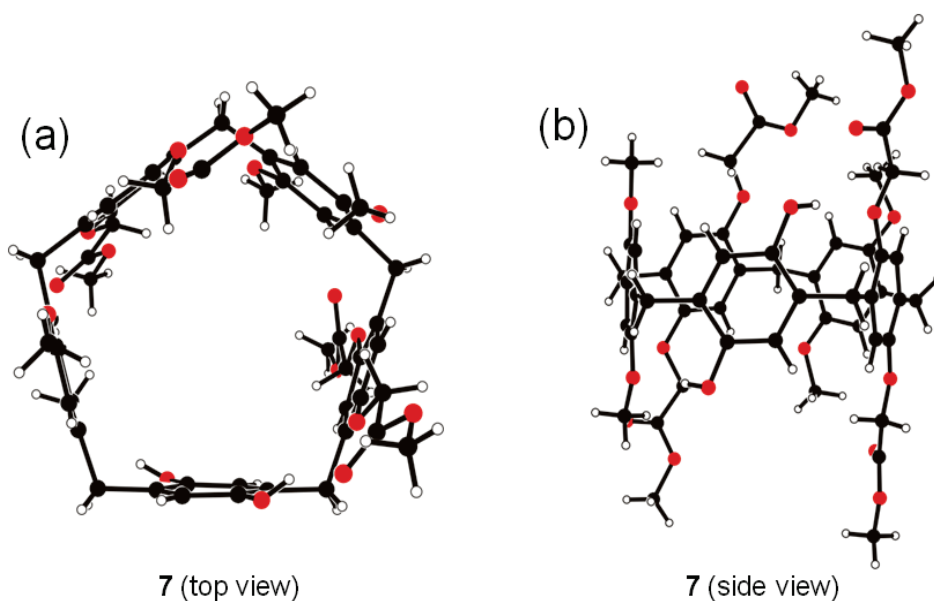


Fig. S16. Ball-and-stick views of the crystal structure of 7. Solvent molecules are omitted for clarity. C, black; H, white; O, red.

References:

- S1. G. Yu, M. Xue, Z. Zhang, J. Li, C. Han, F. Huang, *J. Am. Chem. Soc.*, 2012, **134**, 13248–13251.
- S2. M. Pan, M. Xue, *Eur. J. Org. Chem.*, 2013, 4787–4793.