Two 2:3 copillar[5]arene constitutional isomers: syntheses, crystal structures and host-guest complexation of their derivatives with dicarboxylic acid sodium salts in water

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Electronic Supplementary Information (26 pages)

1. Materials and methods

1,4-Bis(4-bromobutoxy)benzene (DBB) **1**[S1] and sodium dodecanedioate **6**[S2] and **7**[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 or a Bruker Advance DMX 500 spectrophotometer with use of the deuterated solvent as the lock and the residual solvent or 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. Microcalorimetric experiments were obtained on a thermostated and fully computer-operated isothermal calorimetry (VP-ITC) instrument, purchased from Microcal Inc., Northampton, MA.

*2. ^{1}H NMR spectra of guests **6** and **7***

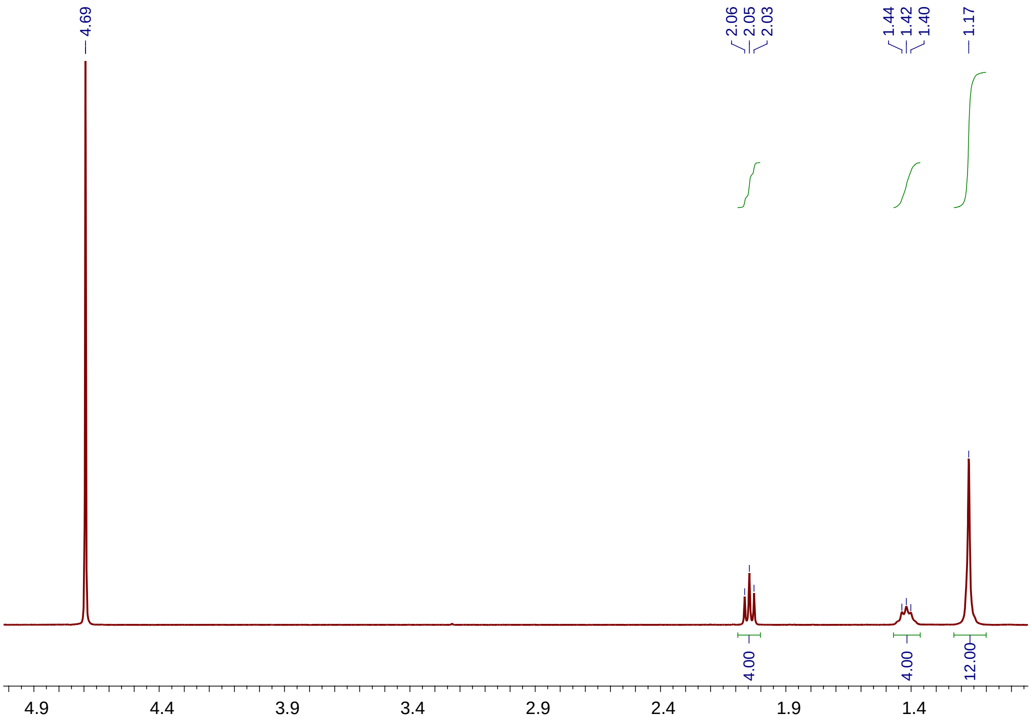


Figure S1. ^{1}H NMR spectrum (400 MHz, D_2O, 20 °C) of **6**.

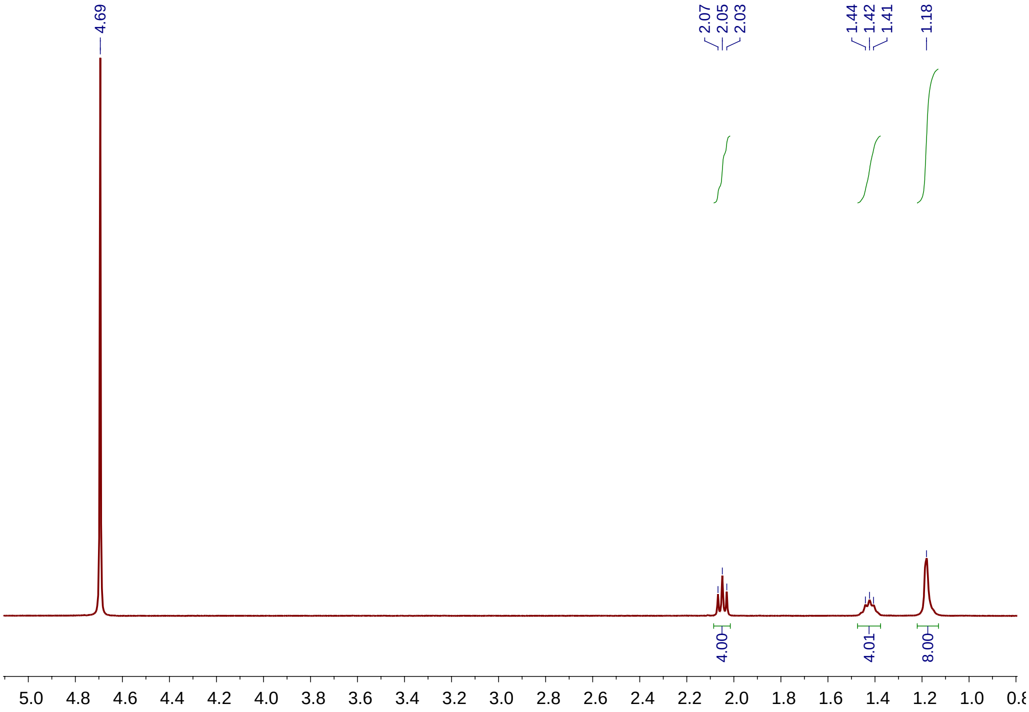
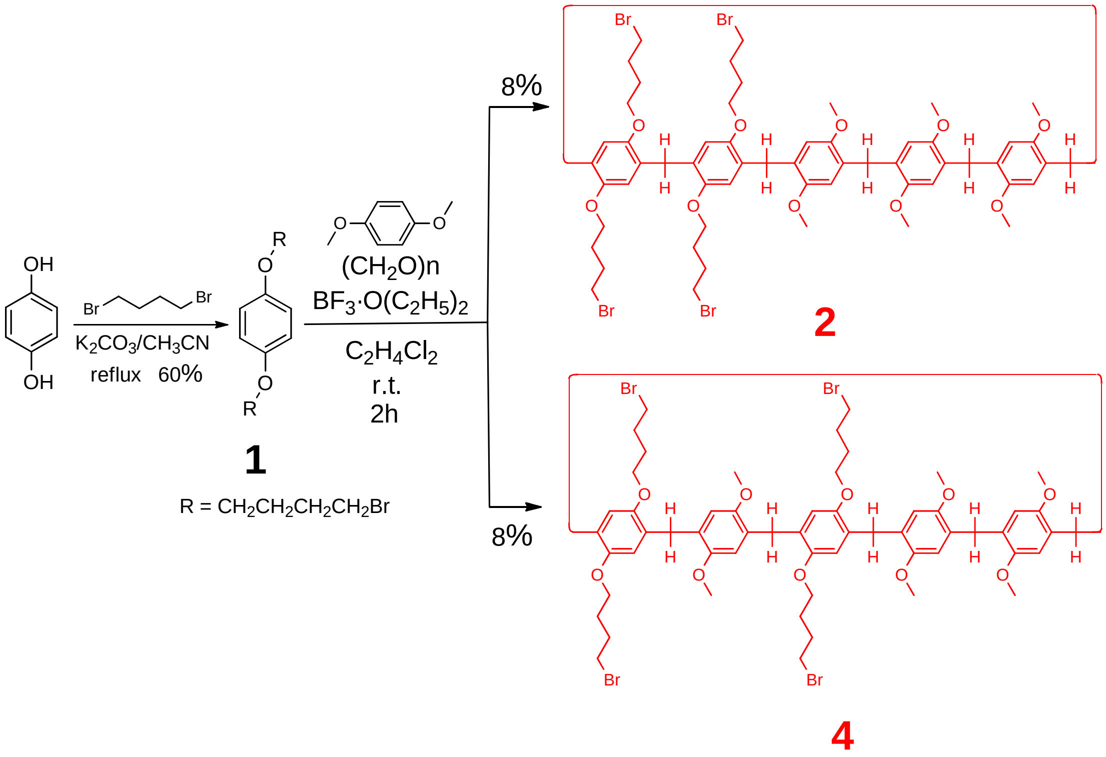


Figure S2. ^{1}H NMR spectrum (400 MHz, D_2O, 20 °C) of **7**.

3. *Syntheses of copillar[5]arenes **2** and **4***



A mixture of **1** (3.80 g, 5.00 mmol), 1,4-dimethoxybenzene (2.76 g, 20.0 mmol), 1,2-dichloroethane (150 mL) and paraformaldehyde (0.775 g, 25.0 mmol) was added into a 100 mL round-bottom flask under nitrogen atmosphere. Then $BF_3{\cdot}O(C_2H_5)_2$ (3.10 mL, 25.0 mmol) was injected. After the mixture was stirred at room temperature for 2 h, the solvent was evaporated by rotary evaporation. The resultant residue was dissolved in CH_2Cl_2 (100 mL) and washed twice with deionized water (75 mL). The organic layer was dried over anhydrous Na_2SO_4 and evaporated to afford the crude product, which was isolated by flash column chromatography using petroleum ether/dichloromethane (10:1) as the eluent. The fractions containing the product were combined and concentrated under vacuum to give copillar[5]arenes **2** (0.67 g, 8%) and **4** (0.67 g, 8%) as white solids, mp 144.2−146.3 °C and 161.3−162.7 °C, respectively. ^{1}H NMR (400 MHz, $CDCl_3$, room temperature) δ (ppm) for **2**: 6.73–6.82 (m, 10H), 3.83–3.85 (m, 8H), 3.66–3.78 (m, 28H), 3.29–3.32 (m, 8H), 1.88–1.91 (m, 8H), 1.78–1.80 (m, 8H). ^{13}C NMR (100 MHz, $CDCl_3$, 22 °C) δ (ppm) for **2**: 150.6, 150.5, 149.8, 149.7, 128.3, 128.2, 128.0, 127.9, 115.0, 114.9, 114.0, 113.8, 113.6, 67.4, 67.3, 55.9, 55.8, 55.7, 33.5, 29.7, 29.4, 29.3, 28.3. Low-resolution ESI-MS for **2**: *m*/*z* 1257.6 (100%) $[M + Na]^+$. HR ESI-MS for **2**: *m*/*z* calcd for $[M + CH_3OH + Na]^+$ $C_{58}H_{74}Br_4NaO_{11}$ 1285.1862; found 1285.1974; error 8.7 ppm. ^1H NMR (400 MHz, $CDCl_3$, room temperature) δ (ppm) for **4**: 6.90–6.91 (m, 6H), 6.85 (d, 4H, $J = 4.0$ Hz), 3.93–3.97 (m, 8H), 3.78–3.81 (m, 28H), 3.49–3.52 (m, 8H), 2.08–2.18 (m, 8H). 1.95–2.05 (m, 8H). ^{13}C NMR (100 MHz, $CDCl_3$, 22 °C) δ (ppm) for **4**: 150.2, 150.1, 149.3, 149.2, 128.1, 128.0, 127.9, 113.7, 113.5, 113.2, 112.9, 66.8, 66.7, 55.5, 55.4, 39.7, 33.8, 33.7, 29.7, 29.3, 29.2, 28.9, 28.4. Low-resolution ESI-MS for **4**: *m*/*z* 1257.4 (70%) $[M + Na]^+$. HR ESI-MS for **4**: *m*/*z* calcd for $[M + CH_3CH_2OH + NH_4]^+$ $C_{59}H_{80}Br_4NO_{11}$ 1294.2465; found 1294.2344; error −9.3 ppm.

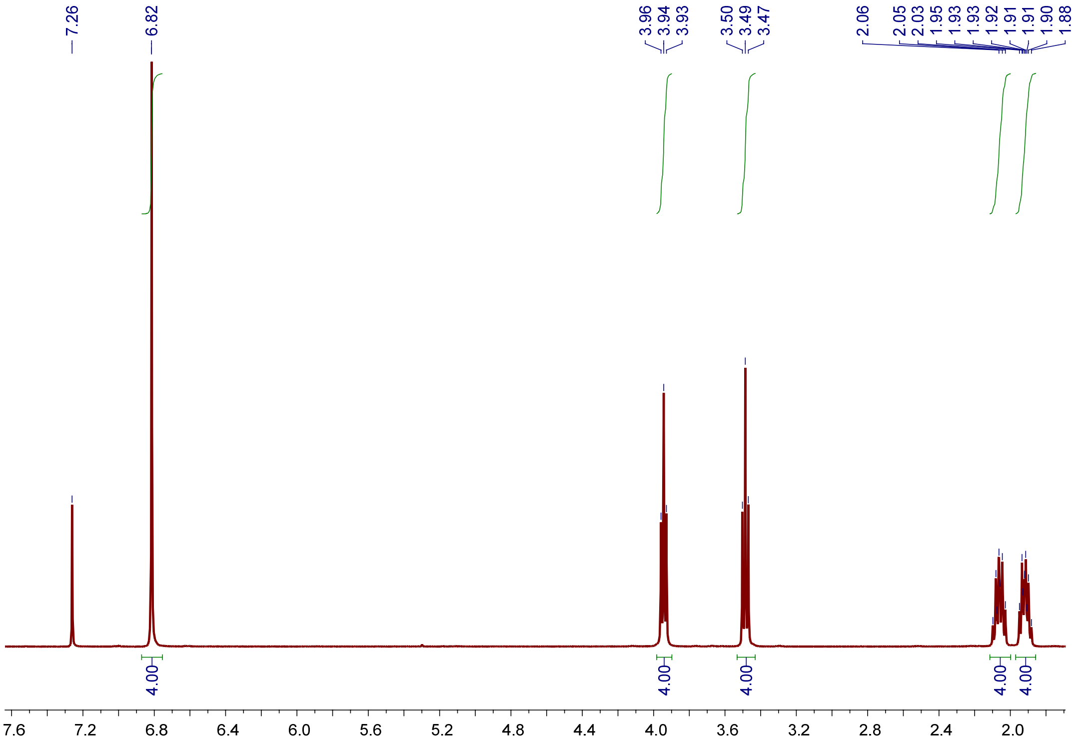


Figure S3. ^1H NMR spectrum (400 MHz, $CDCl_3$, 20 °C) of **1**.

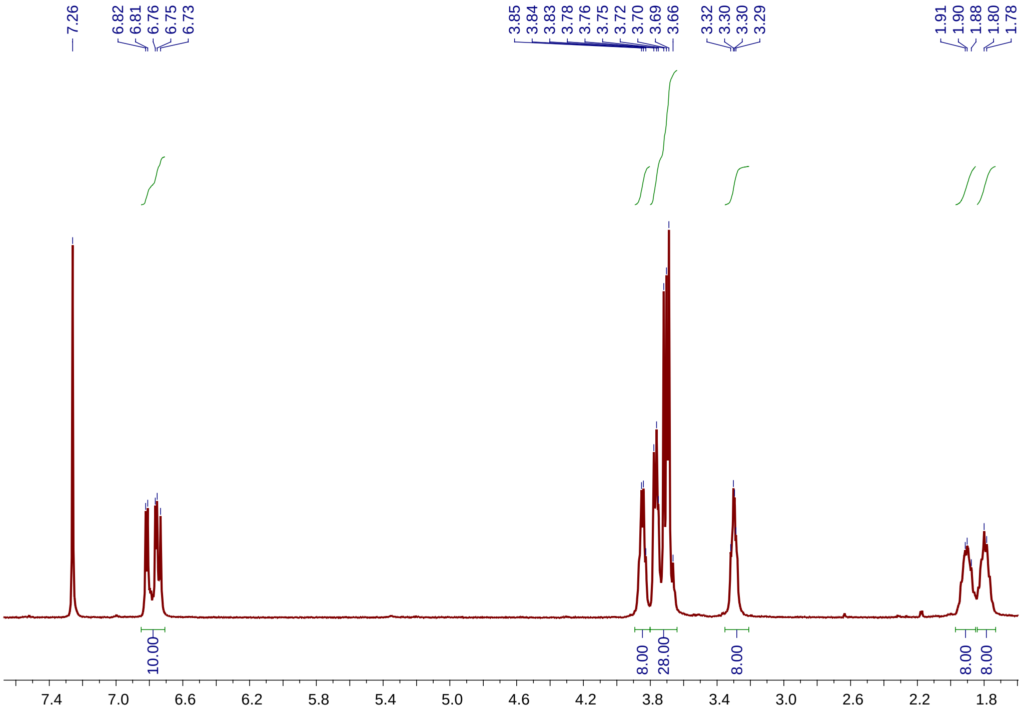


Figure S4. ^{1}H NMR spectrum (400 MHz, $CDCl_3$, 20 °C) of **2**.

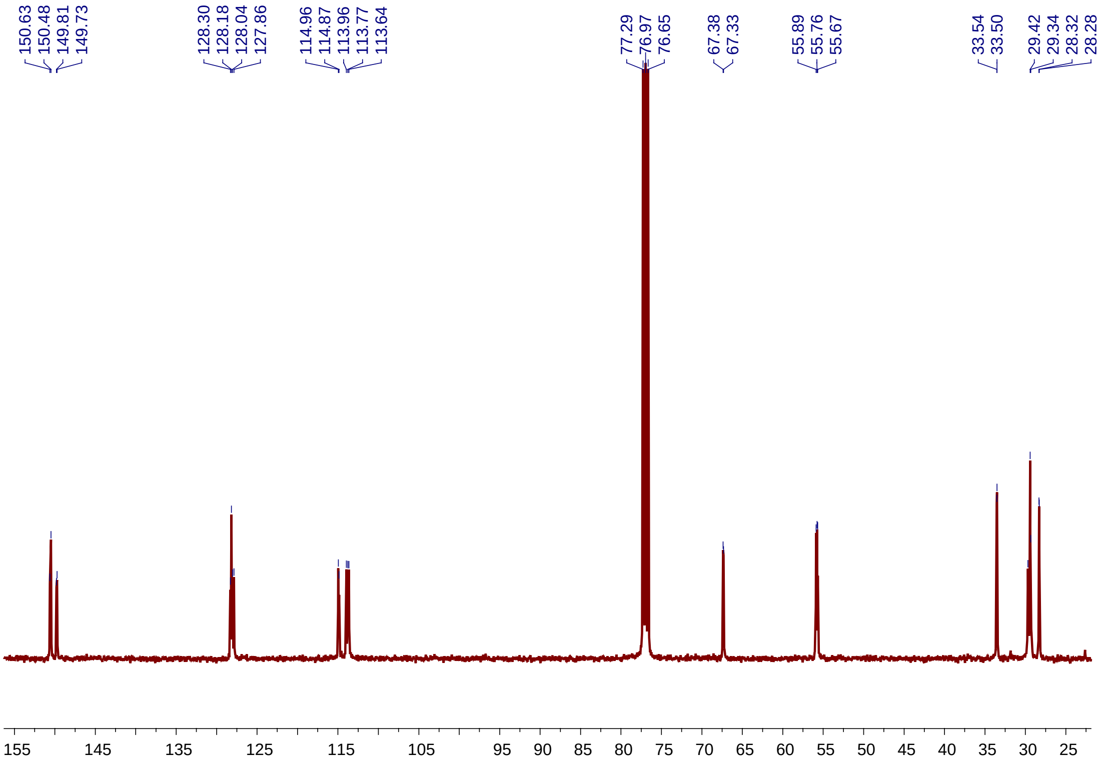


Figure S5. ^{13}C NMR spectrum (100 MHz, $CDCl_3$, 20 °C) of **2**.

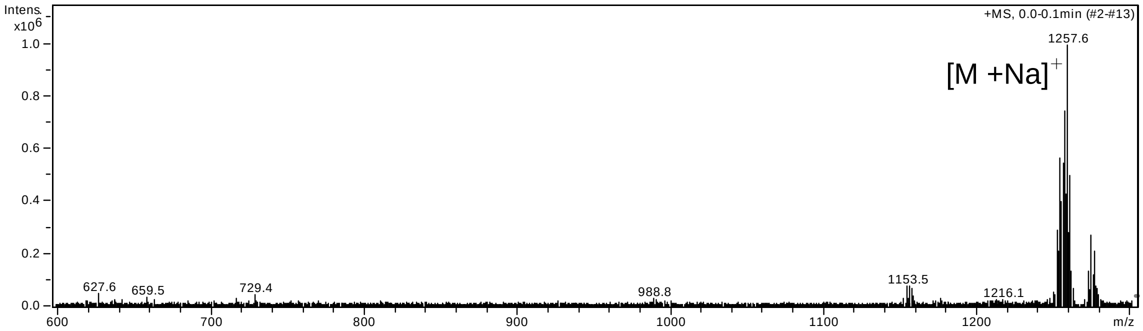


Figure S6. Positive electrospray ionization mass spectrum of **2**.

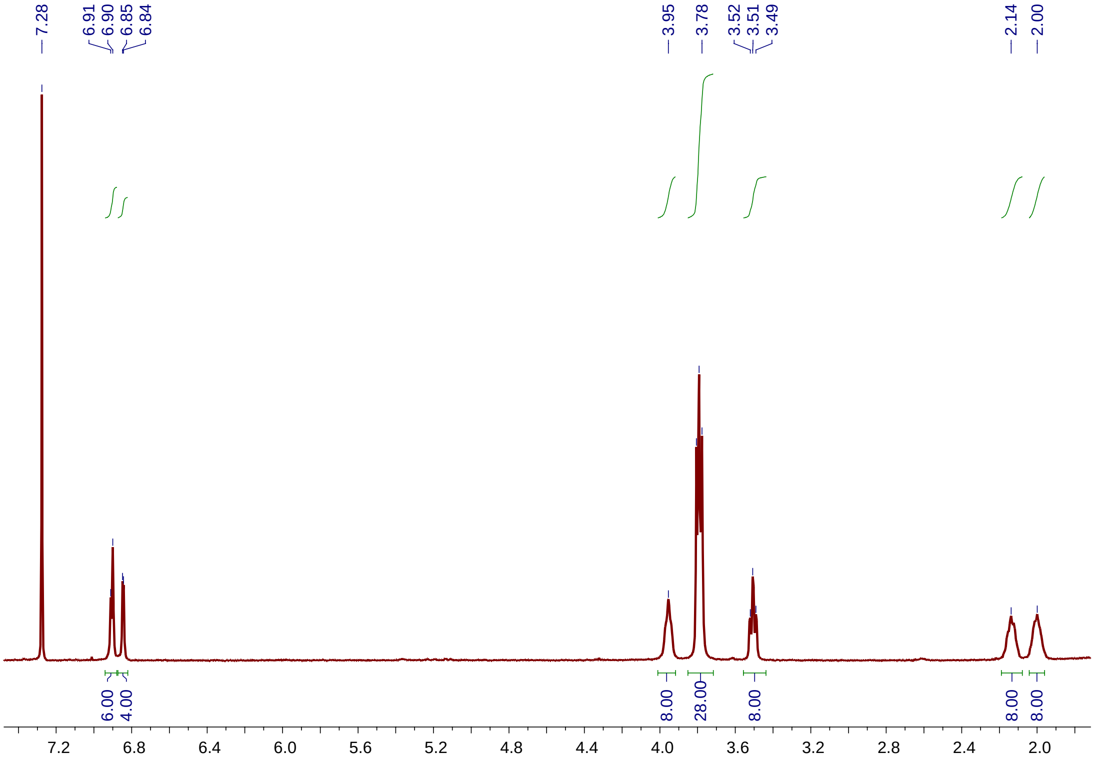


Figure S7. ^{1}H NMR spectrum (400 MHz, CDCl$_3$, 20 °C) of **4**.

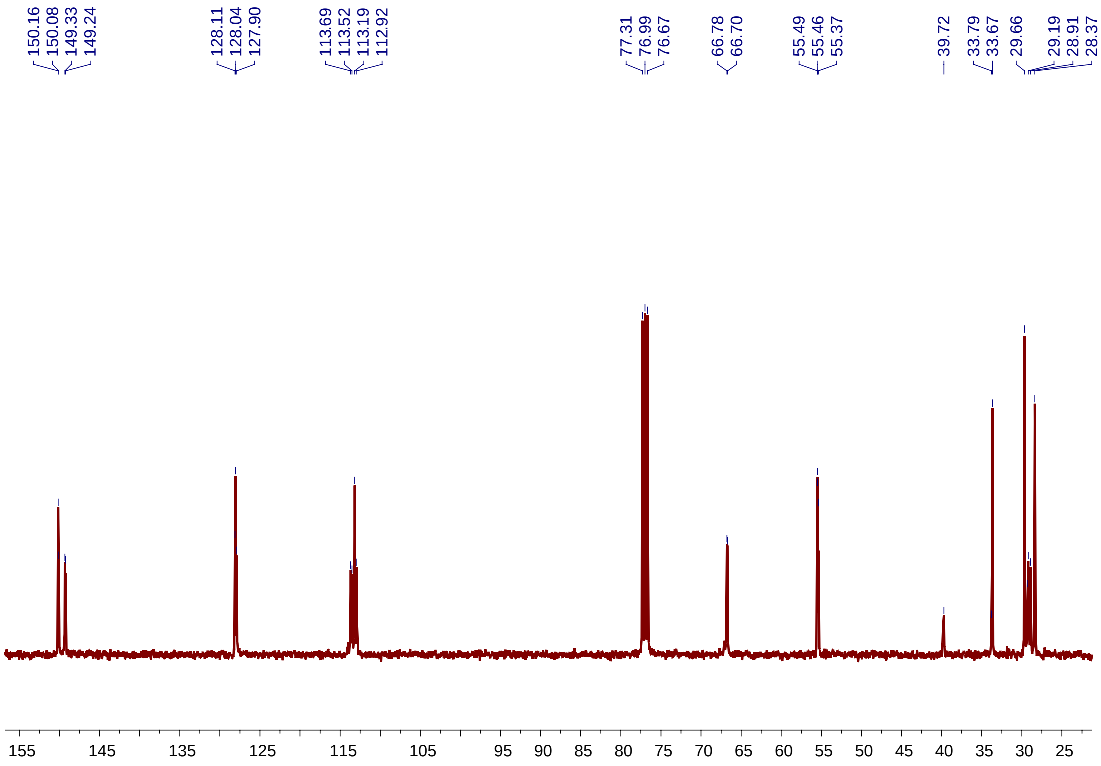


Figure S8. ^{13}C NMR spectrum (100 MHz, $CDCl_3$, 20 °C) of **4**.

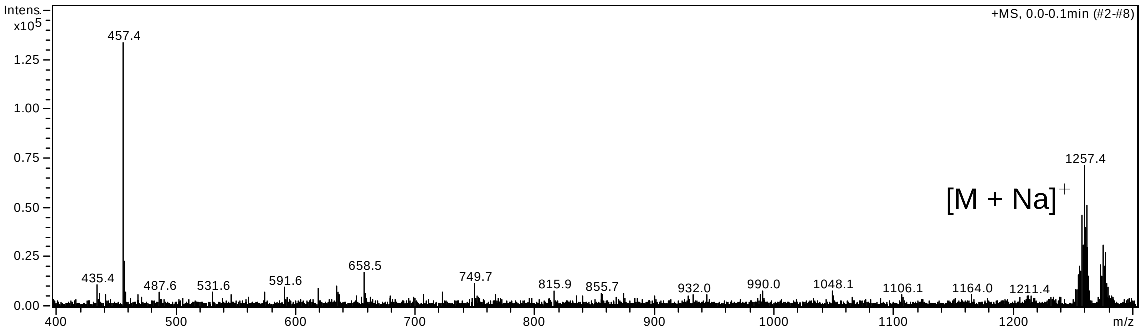


Figure S9. Positive electrospray ionization mass spectrum of **4**.

*4. Syntheses of copillar[5]arenes **3** and **5***

Compounds **2** or **4** (100 mg, 0.0680 mmol) and trimethylamine (33% in methanol, 50 mL) were added to methanol (10 mL). The solution was refluxed overnight. Then the solvent was removed by evaporation to obtain **3** (120 mg, 100%) and **5** (120 mg, 100%) as colorless solids, mp: 159.5−161.9 °C and 174.2−175.2 °C, respectively. ^{1}H NMR (400 MHz, D_2O, room temperature) δ (ppm) for **3**: 6.30–6.89 (m, 10H), 3.64–3.83 (m, 28H), 3.24–3.44 (m, 16H), 2.88–3.15 (m, 36H), 1.63–1.89 (m, 16H). ^{13}C NMR (125 MHz, CD_3SOCD_3, 22 °C) δ (ppm) for **3**: 149.9, 149.2, 149.1, 128.0, 127.9, 127.6, 114.3, 67.3, 67.1, 64.8, 59.1, 55.6, 52.1, 28.9, 26.3, 26.2, 19,3, 19.1. Low-resolution ESI-MS for **3**: *m*/*z* 656.3 (100%) $[M - 2Br]^{2+}$. HR ESI-MS for **3** *m*/*z* calcd for $[M - 2Br]^{2+}$ $C_{69}H_{106}Br_2N_4O_{10}$ 655.3134; found 655.3105; error –4.4 ppm. ^1H NMR (400 MHz, D_2O, room temperature) δ (ppm) for **5**: 6.47–6.84 (m, 10H), 3.55–3.72 (m, 24H), 3.20–3.37 (m, 26H), 3.01–3.12 (m, 36H), 1.65–1.86 (m, 16H). ^{13}C NMR (125 MHz, CD_3SOCD_3, 22 °C) δ (ppm) for **5**: 154.0, 149.6, 128.5, 128.4, 128.1, 114.8, 113.9, 66.8, 66.7, 65.5, 56.2, 56.1, 52.6, 31.2, 29.4, 26.8, 23.6, 19.7, 19.0, 14.0. Low-resolution ESI-MS for **5**: *m*/*z* 655.4 (100%) $[M - 2Br]^{2+}$. HR ESI-MS for **5** *m*/*z* calcd for $[M - 3Br]^{3+}$ $C_{69}H_{106}BrN_4O_{10}$ 409.9025; found 409.8992; error –8.1 ppm.

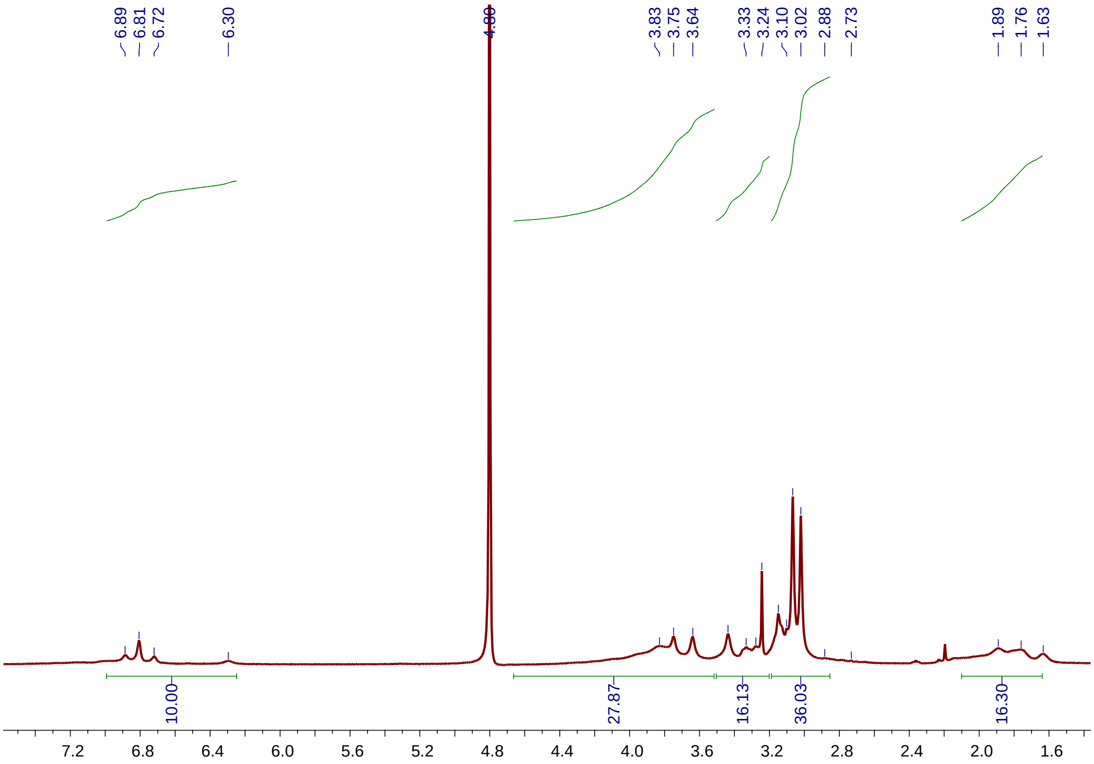


Figure S10. ^1H NMR spectrum (400 MHz, D_2O, 20 °C) of **3**.

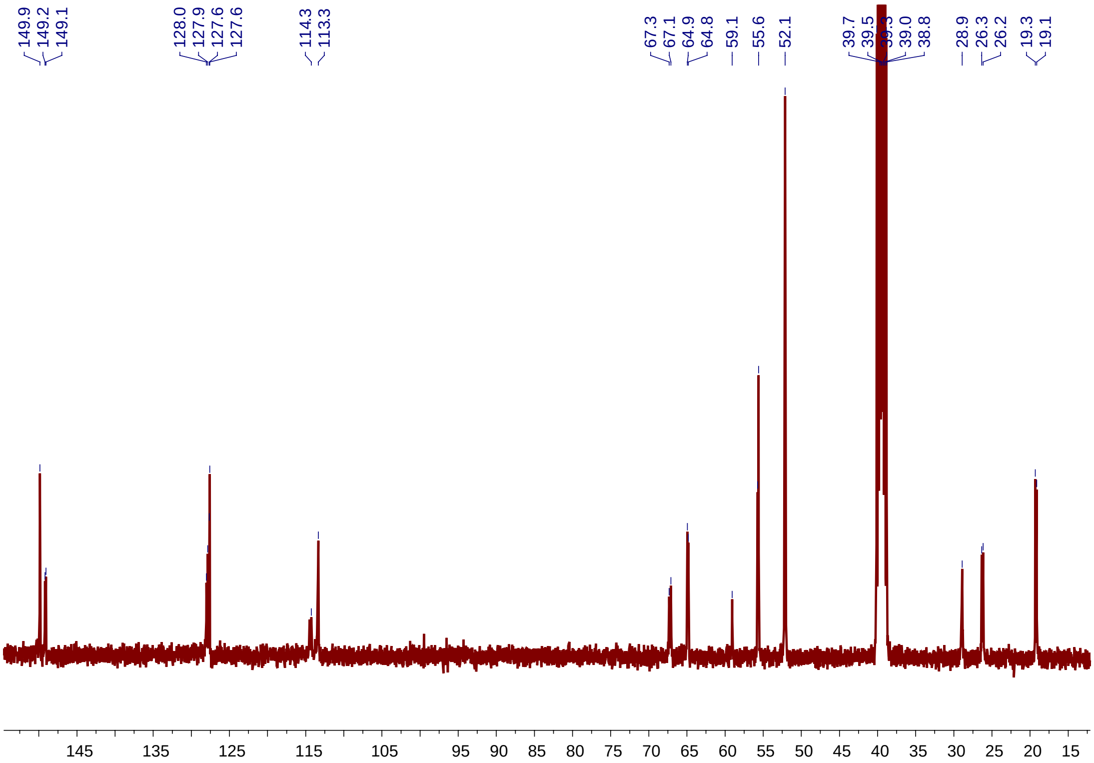


Figure S11. ^{13}C NMR spectrum (125 MHz, CD_3SOCD_3, 20 °C) of **3**.

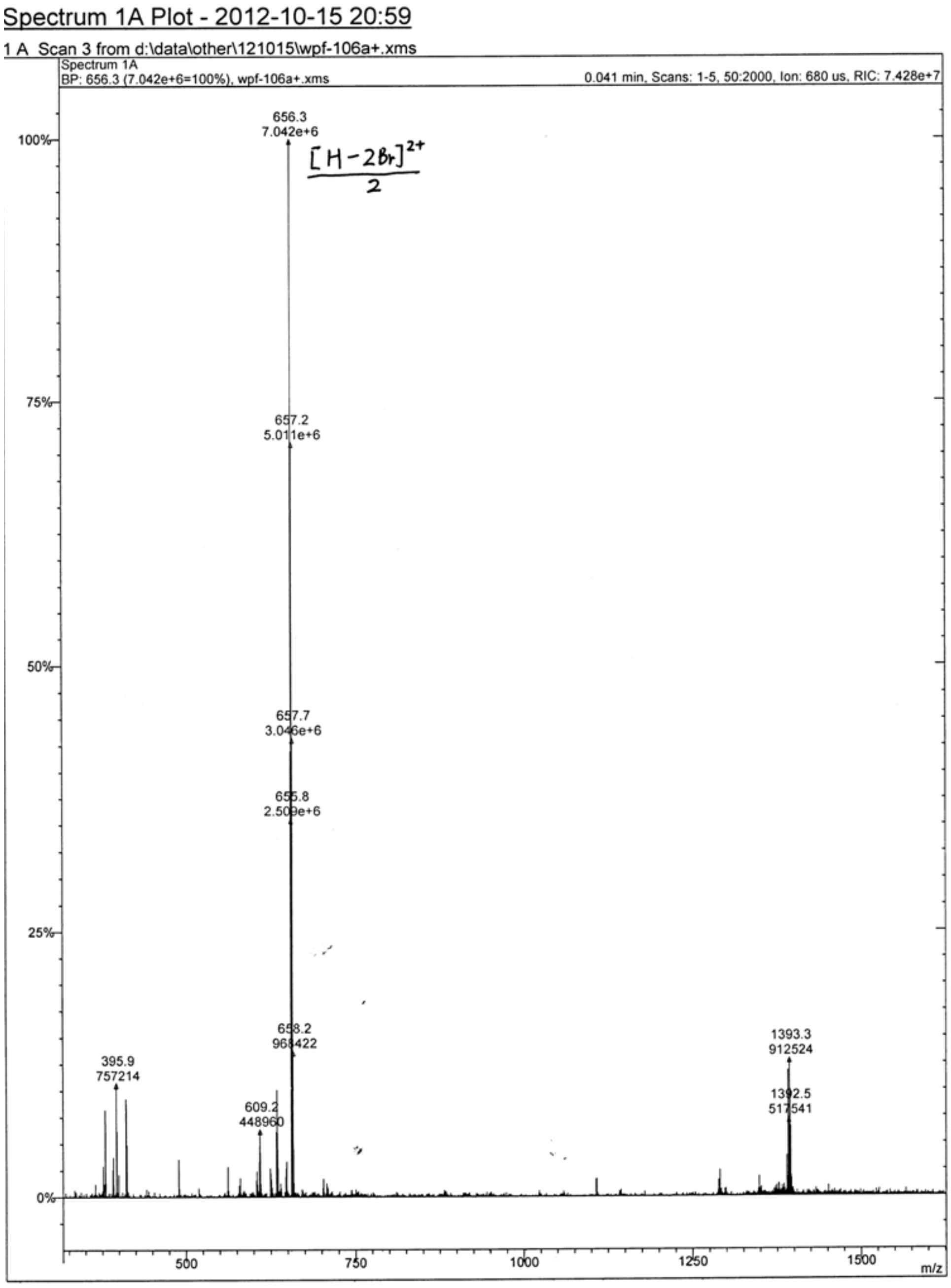


Figure S12. Positive electrospray ionization mass spectrum of **3**.

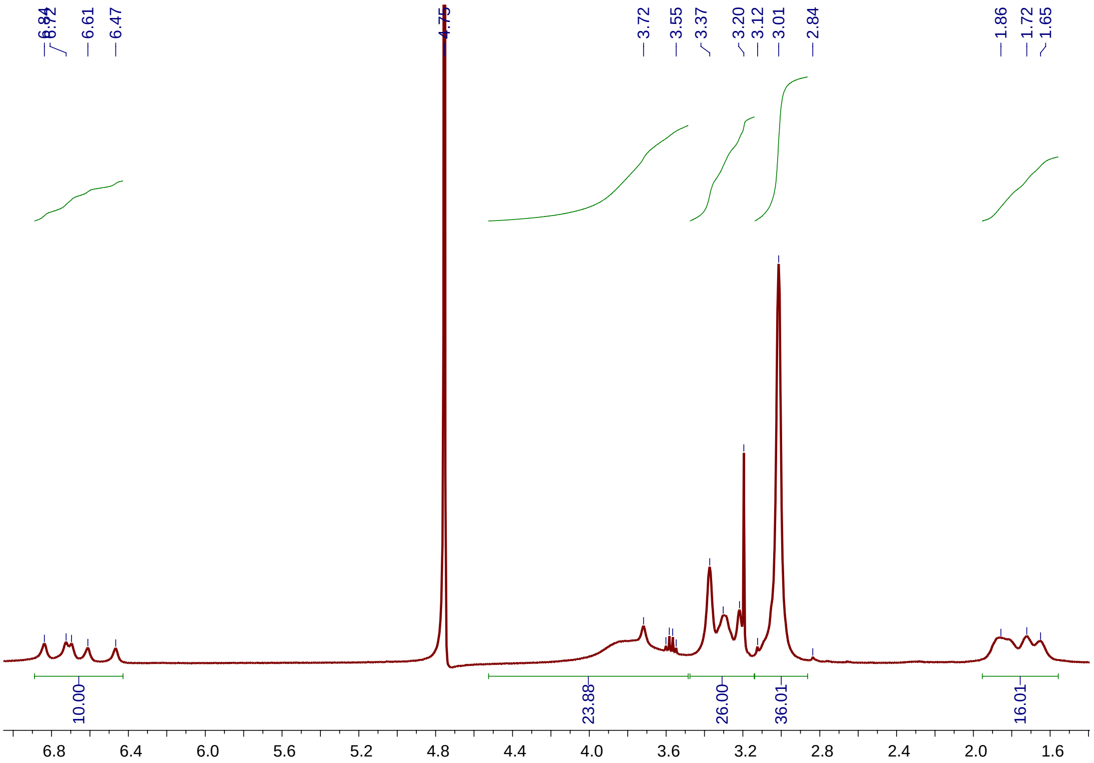


Figure S13. ^{1}H NMR spectrum (400 MHz, D_2O, 20 °C) of **5**.

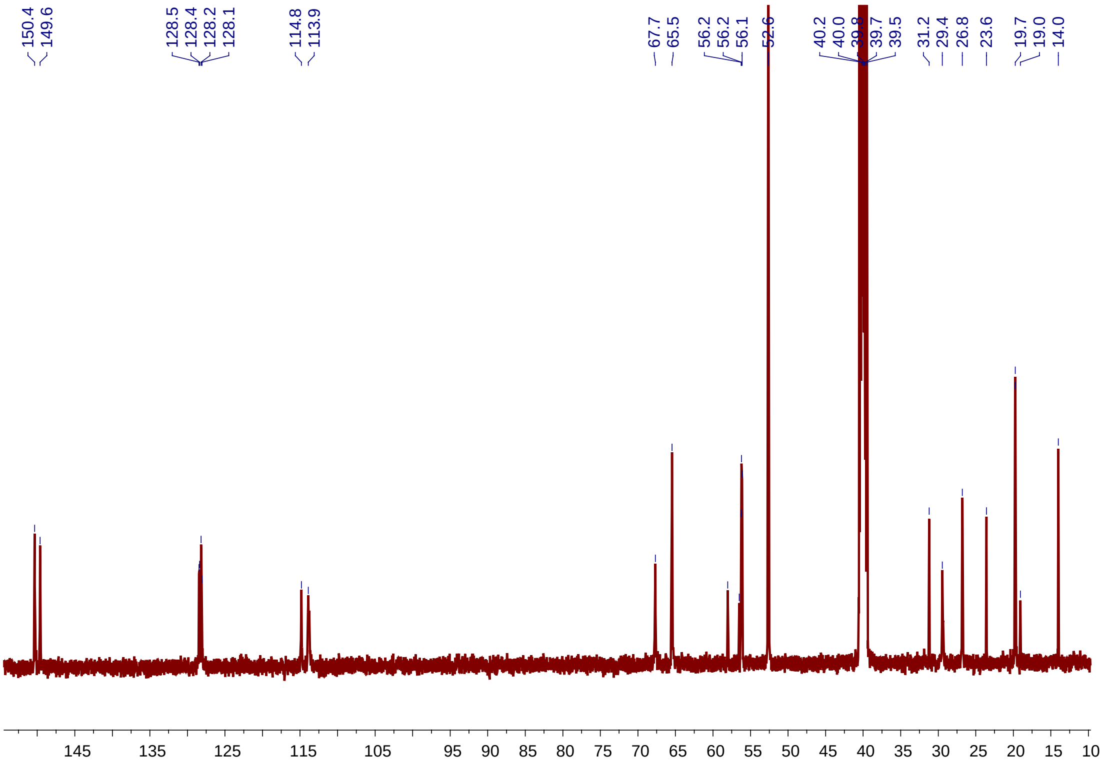


Figure S14. ^{13}C NMR spectrum (125 MHz, CD_3SOCD_3, 20 °C) of **5**.

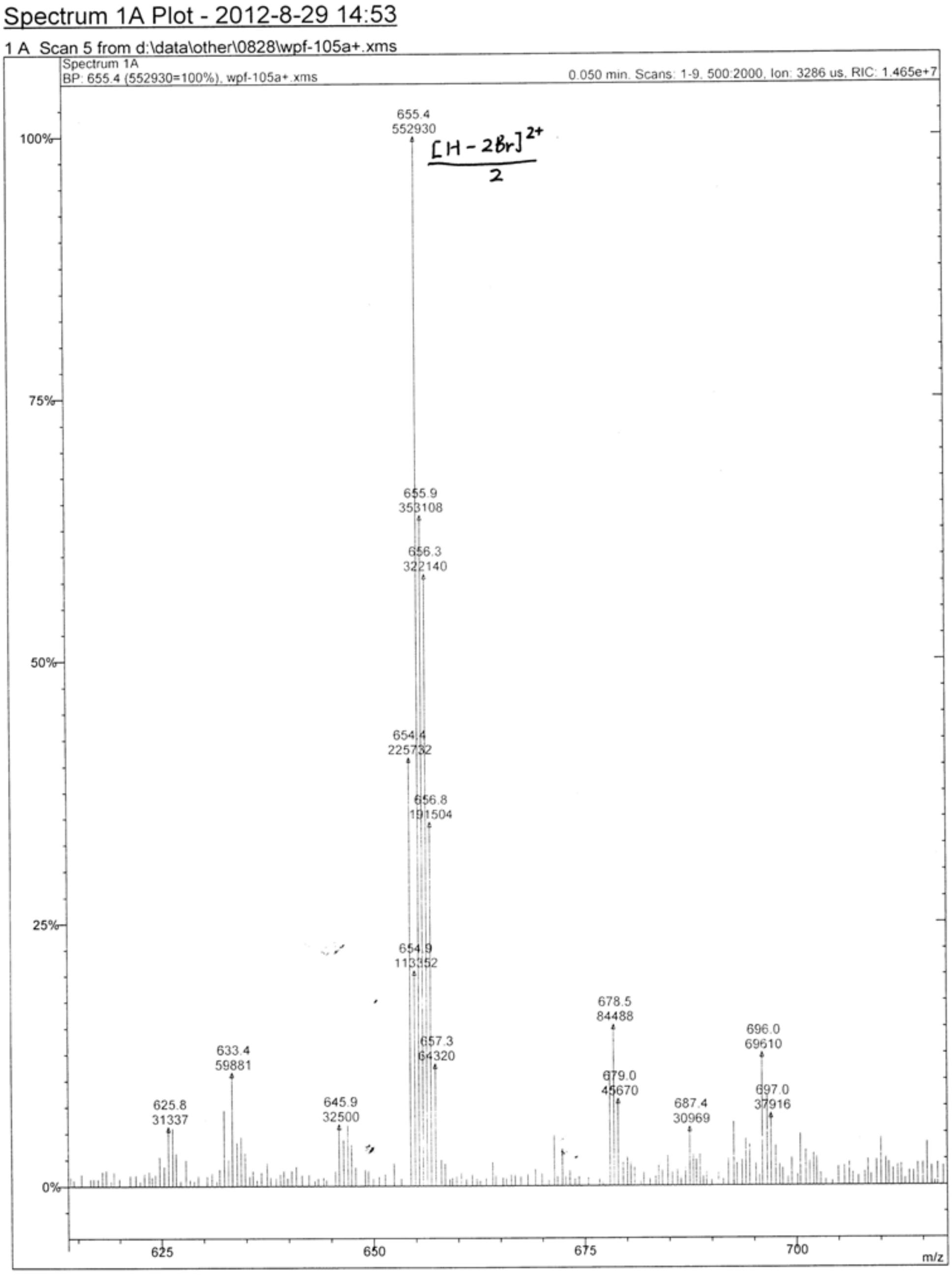


Figure S15. Positive electrospray ionization mass spectrum of **5**.

*5. Partial ^{1}H NMR and ^{13}C NMR spectra of constitutional isomers **2** and **4***

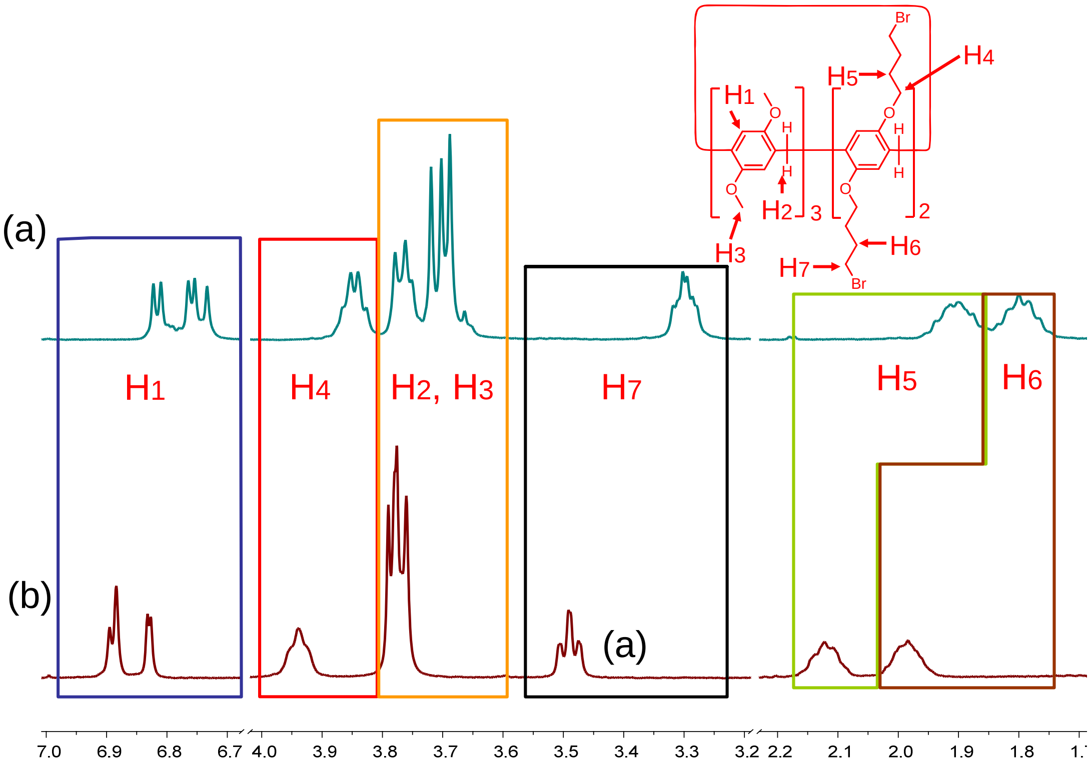


Figure S16. Partial ^{1}H NMR spectra (400 MHz, CDCl$_3$, 20 °C) of the two isomers: (a) **2**; (b) **4**.

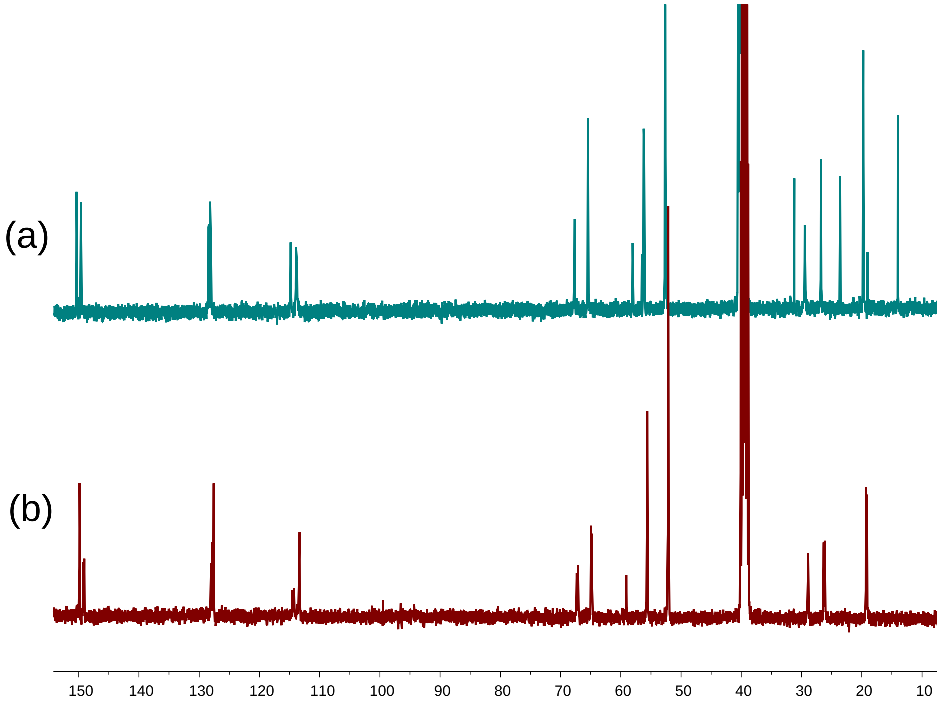


Figure S17. ^{13}C NMR spectra (500 MHz, CD$_3$SOCD$_3$, 20 °C) of the two isomers: (a) **2**; (b) **4**.

*6. Complexation studies of **3⊐6**, **3⊐7**, **5⊐6**, and **5⊐7***

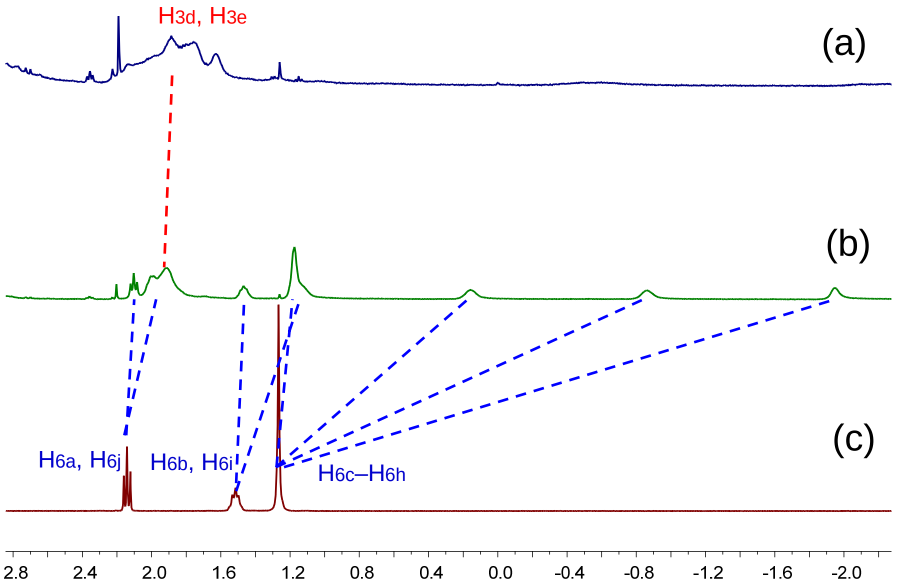


Figure S18. ^{1}H NMR spectra (400 MHz, D_2O, 20 °C): (a) **3** (10.0 mM); (b) an equimolar mixture of **3** (10.0 mM) and **6** (10.0 mM); (c) **6** (10.0 mM).

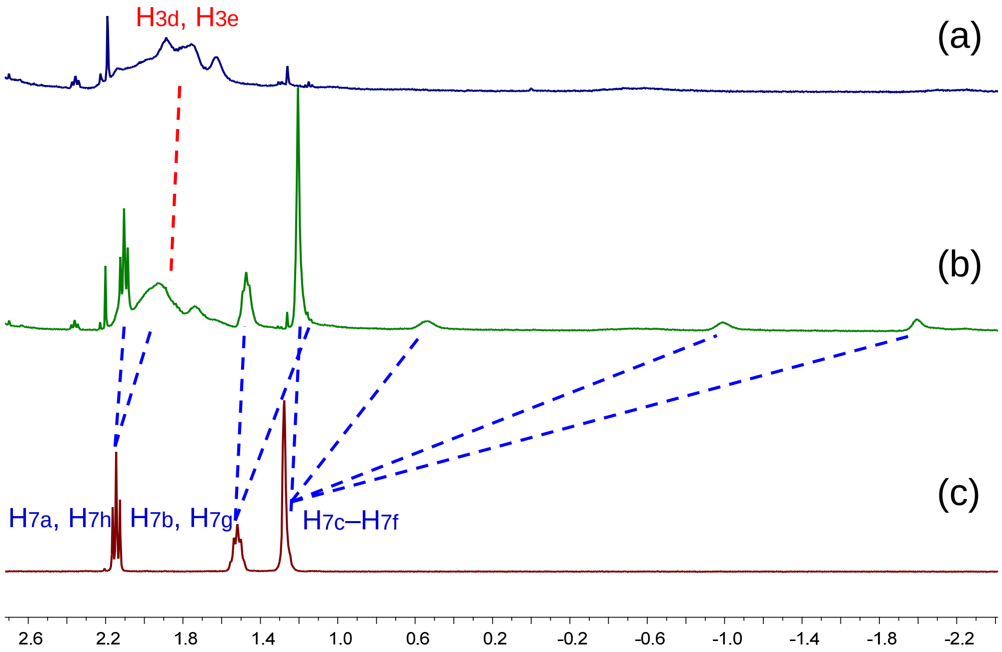


Figure S19. ^{1}H NMR spectra (400 MHz, D_2O, 20 °C): (a) **3** (10.0 mM); (b) an equimolar mixture of **3** (10.0 mM) and **7** (10.0 mM); (c) **7** (10.0 mM).

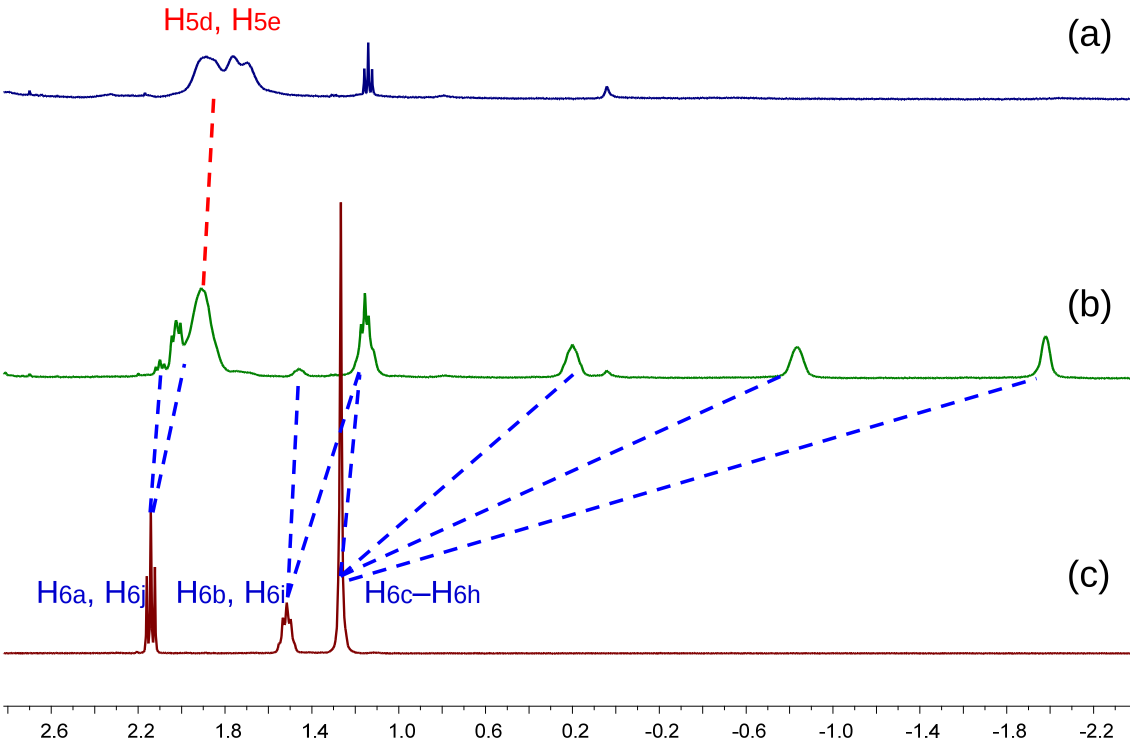


Figure S20. ^{1}H NMR spectra (400 MHz, D_2O, 20 °C): (a) **5** (10.0 mM); (b) an equimolar mixture of **5** (10.0 mM) and **6** (10.0 mM); (c) **6** (10.0 mM).

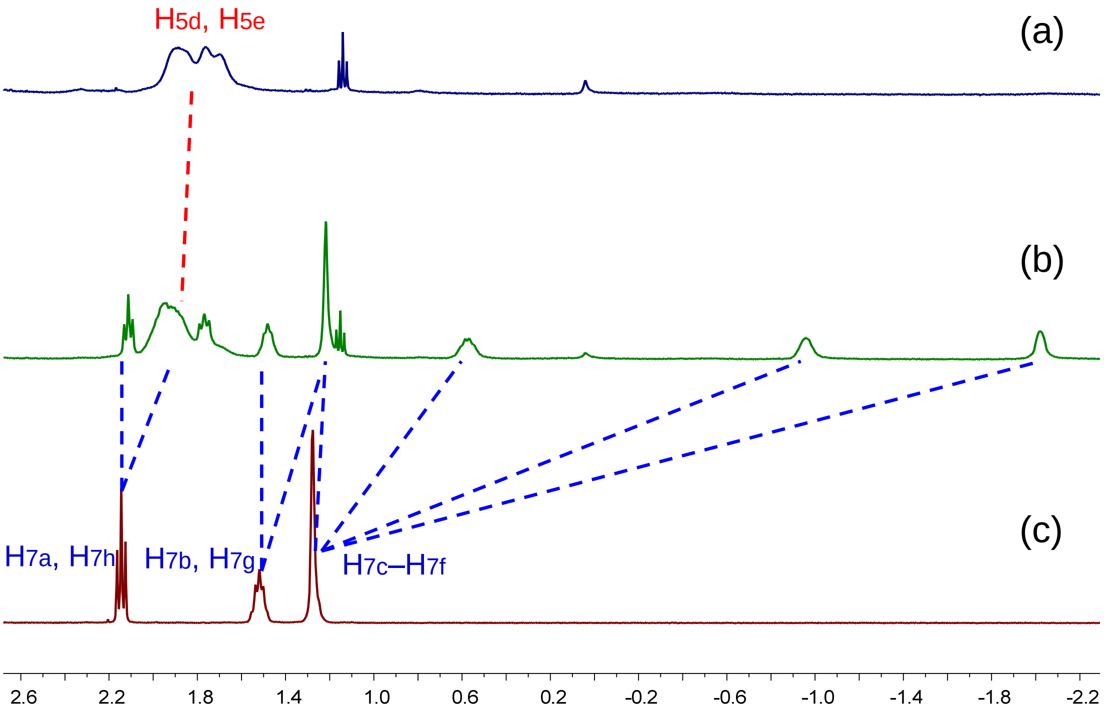
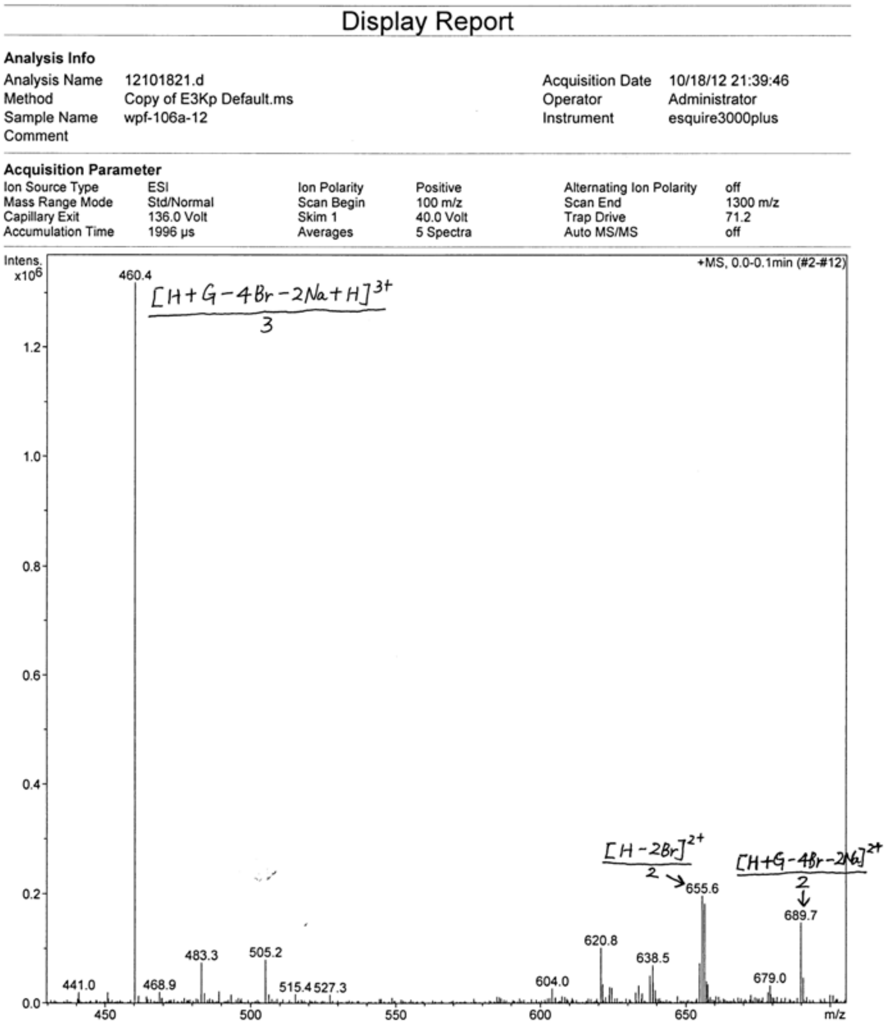


Figure S21. ^{1}H NMR spectra (400 MHz, D_2O, 20 °C): (a) **5** (10.0 mM); (b) an equimolar mixture of **5** (10.0 mM) and **7** (10.0 mM); (c) **7** (10.0 mM).

7. *LR ESI-MS studies of* ***3⊃6****,* ***3⊃7****,* ***5⊃6****, and* ***5⊃7***



Display Report

Analysis Info

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Comment			

Acquisition Parameter

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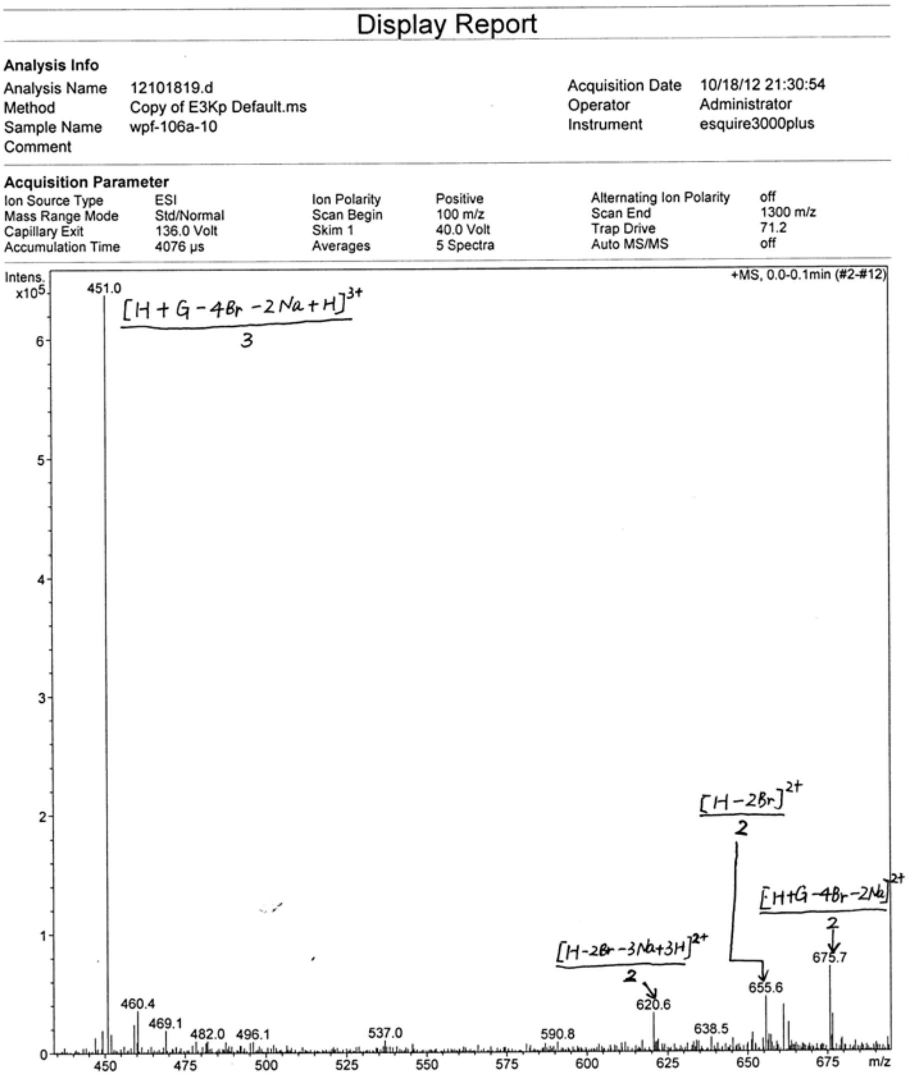
Figure S22. Electrospray ionization mass spectra of equimolar aqueous solutions of **3** with **6**.



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Comment			

Acquisition Parameter

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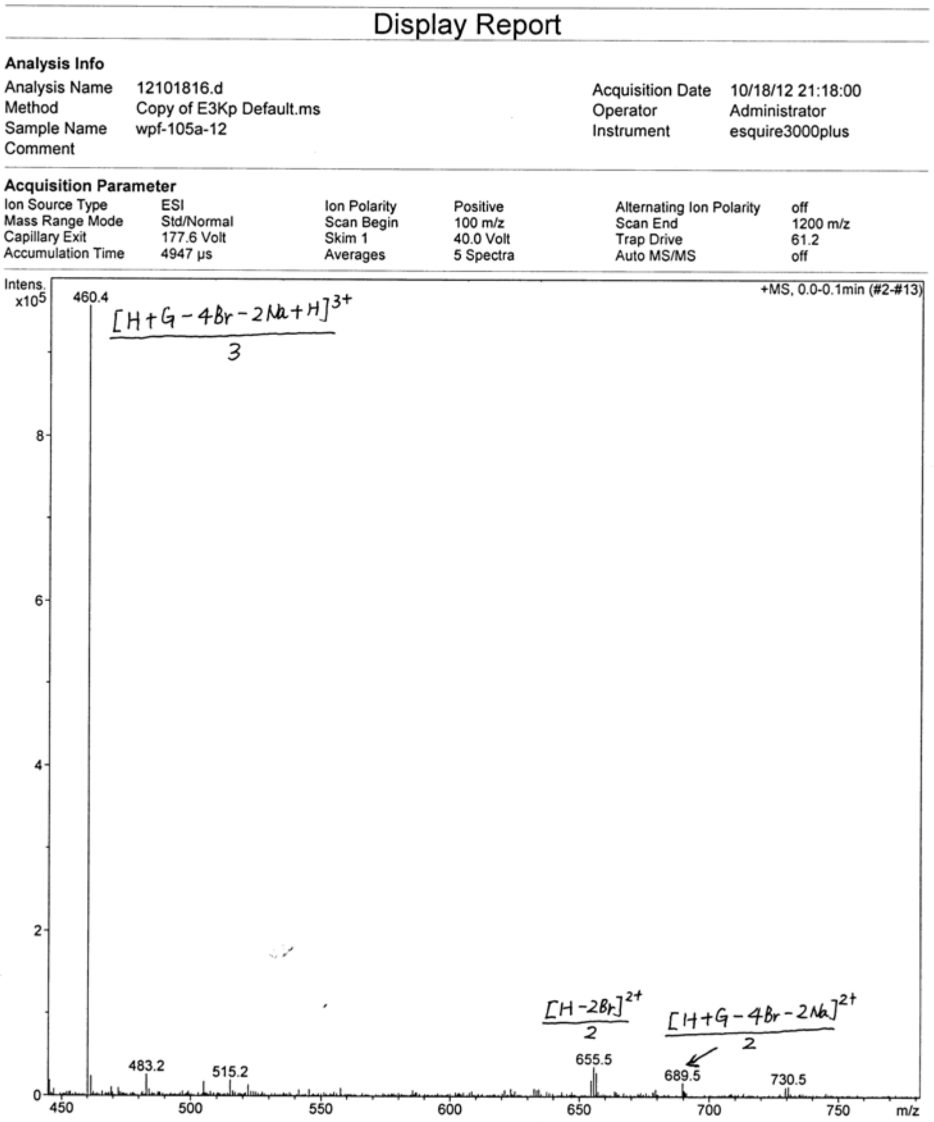
Figure S23. Electrospray ionization mass spectra of equimolar aqueous solutions of **3** with **7**.



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Comment			

Acquisition Parameter

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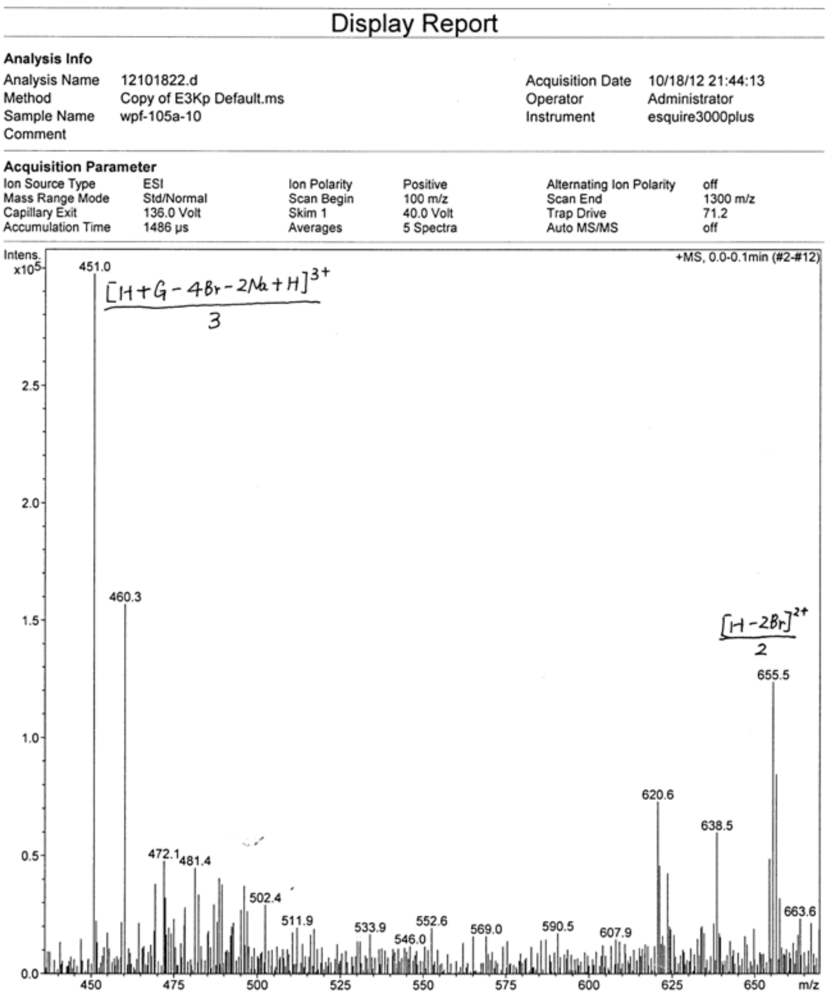
Capillary Exit	177.6 Volt	Skim 1	40.0 Volt	Trap Drive	61.2
Accumulation Time	4947 µs	Averages	5 Spectra	Auto MS/MS	off

Figure S24. Electrospray ionization mass spectra of equimolar aqueous solutions of **5** with **6**.



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Analysis Info

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Sample Name	wpf-105a-10	Instrument	esquire3000plus
Comment			

Acquisition Parameter

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Capillary Exit	136.0 Volt	Skim 1	40.0 Volt	Trap Drive	71.2
Accumulation Time	1486 µs	Averages	5 Spectra	Auto MS/MS	off

Figure S25. Electrospray ionization mass spectra of equimolar aqueous solutions of **5** with **7**.

8. *NOESY NMR analysis of* ***3⊃6***

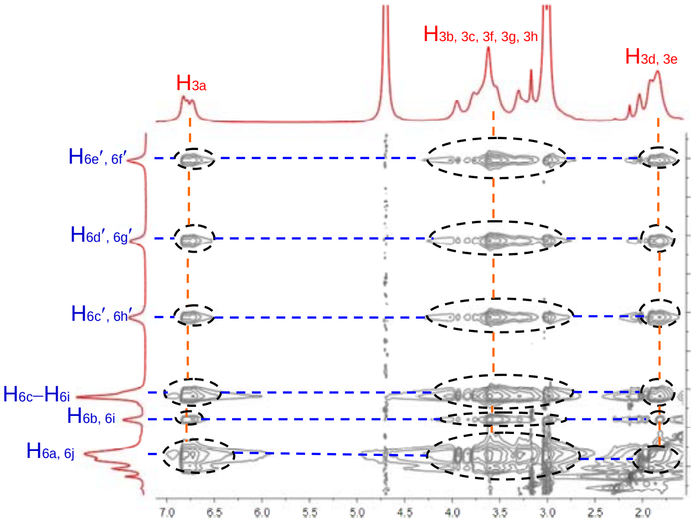


Figure S26. Partial NOESY NMR analysis of **3⊃6** (15.0 mM) in D_2O with a mixing time of 800 ms (500 MHz, 20 °C). The prime ′ in the spectrum denotes the complexed species.

9. *COSY NMR analysis of* ***3⊃6***

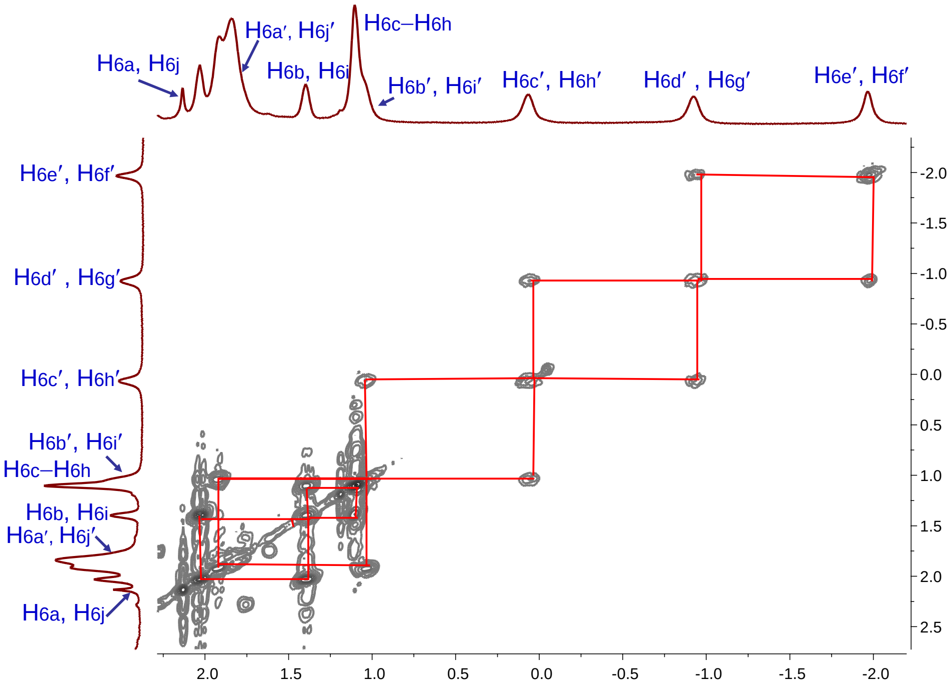


Figure S27. Partial COSY spectrum (500 MHz, D_2O, 20 °C) of **3** (15.0 mM) and **6** (15.0 mM). The prime ′ in the spectrum denotes the complexed species.

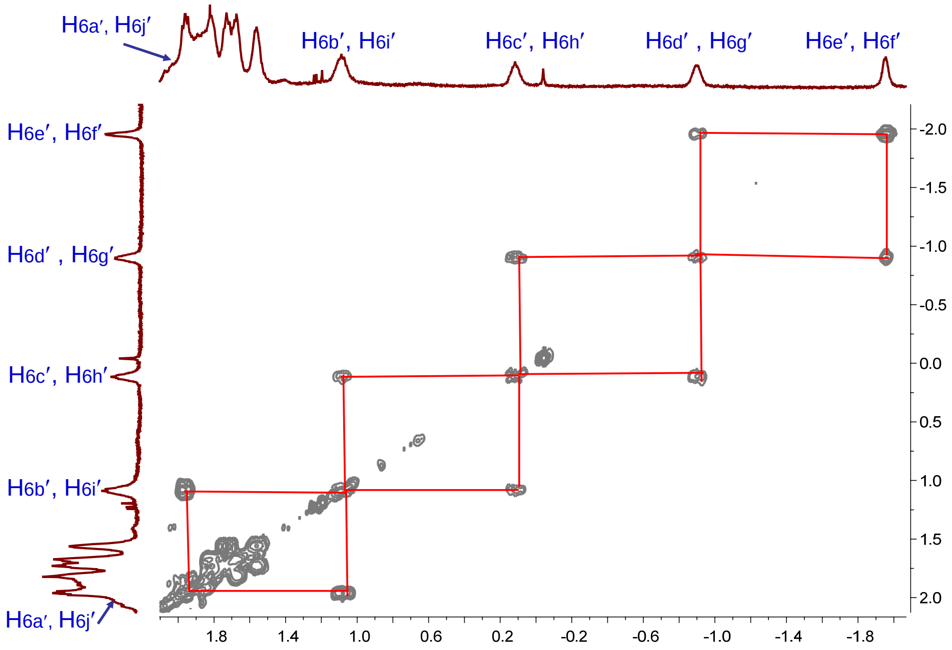


Figure S28. Partial COSY spectrum (500 MHz, D_2O, 20 °C) of **3** (5.00 mM) and **6** (1.00 mM). The prime ′ in the spectrum denotes the complexed species. From the 2D COSY characterization, the signals from the alkyl chain of the guest can be identified clearly.

10. ITC experiments of ***3⊃7***, ***5⊃6***, *and* ***5⊃7***

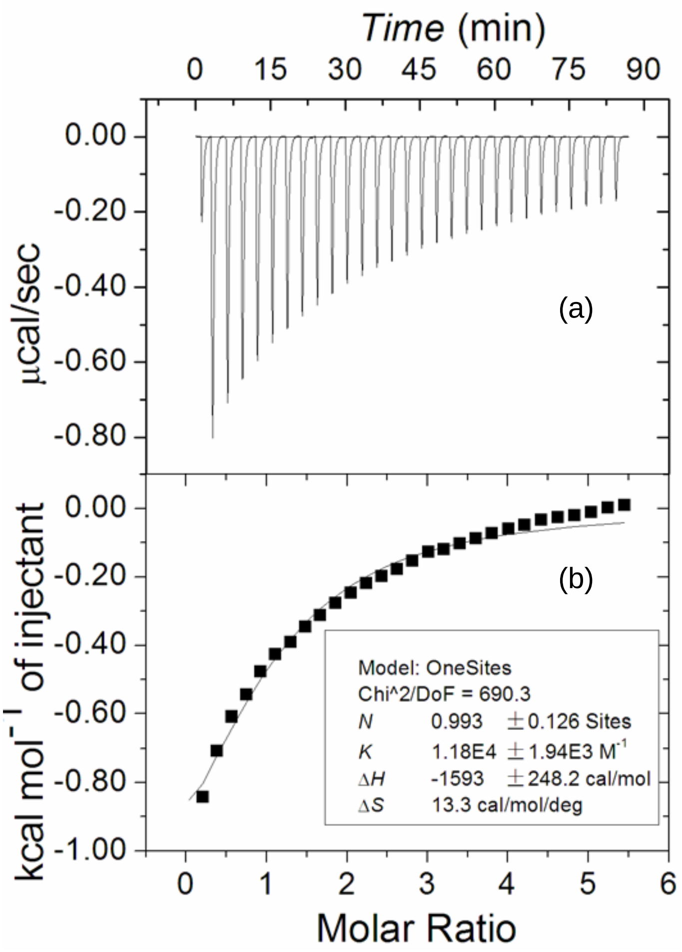


Figure S29. Microcalorimetric titration of **3** with **7** in water (pH = 7.0) at 298.15 K. (a) Raw ITC data for 29 sequential injections (10 µL per injection) of a **7** solution (2.50 mM) into a **3** solution (0.100 mM). (b) Net reaction heat obtained from the integration of the calorimetric traces.

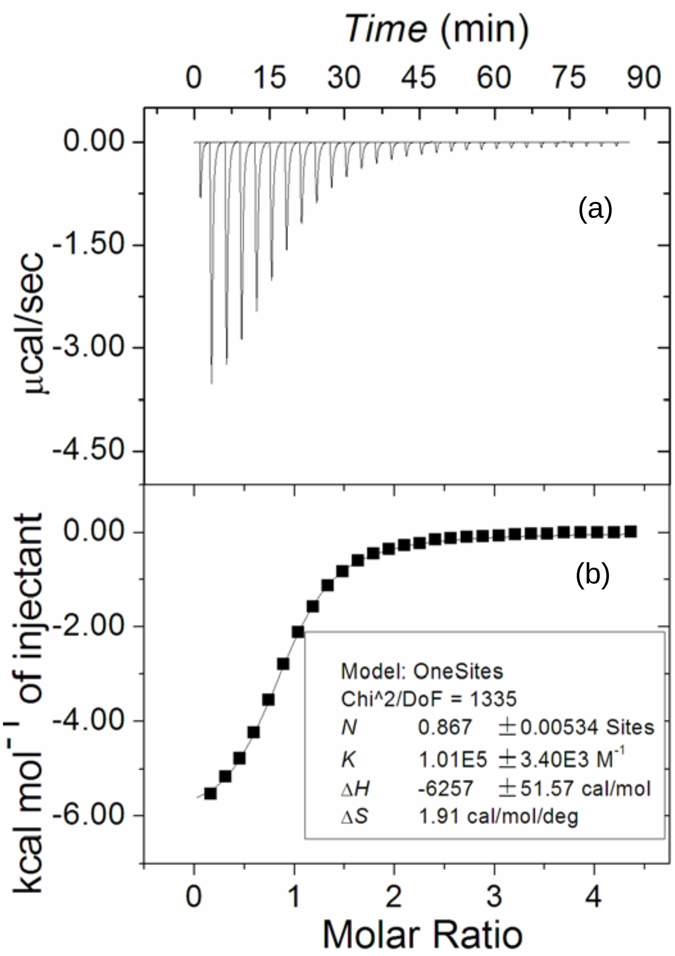


Figure S30. Microcalorimetric titration of **5** with **6** in water (pH = 7.0) at 298.15 K. (a) Raw ITC data for 29 sequential injections (10 μL per injection) of a **6** solution (2.00 mM) into a **5** solution (0.100 mM). (b) Net reaction heat obtained from the integration of the calorimetric traces.

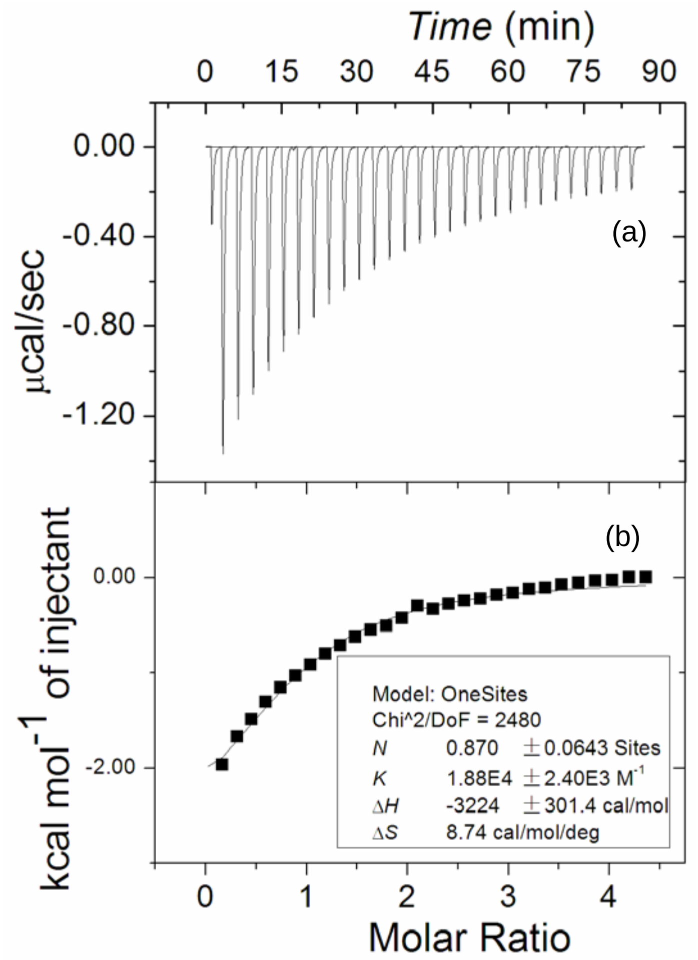


Figure S31. Microcalorimetric titration of **5** with **7** in water (pH = 7.0) at 298.15 K. (a) Raw ITC data for 29 sequential injections (10 µL per injection) of a **7** solution (2.00 mM) into a **5** solution (0.100 mM). (b) Net reaction heat obtained from the integration of the calorimetric traces.

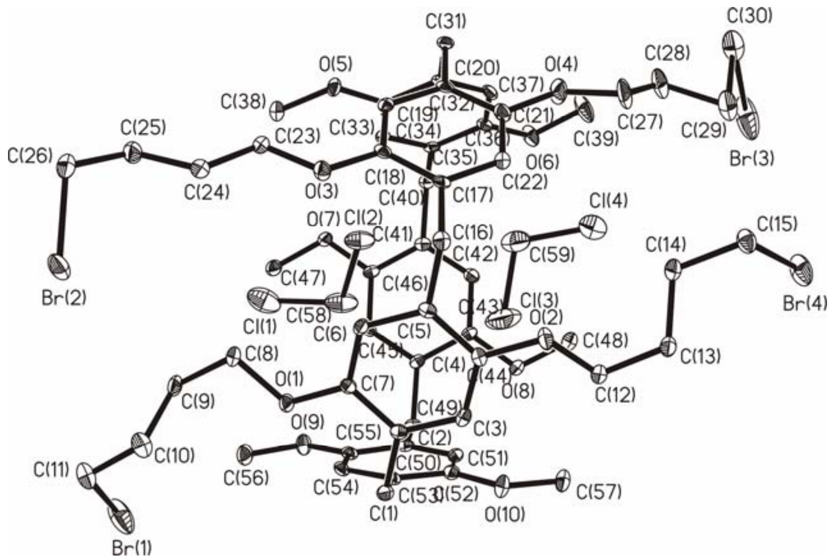
11. X-ray crystal data of ***2*** *and* ***4***

Crystal data of **2**: block, colorless, 0.35 × 0.28 × 0.26 mm^3, $C_{59}H_{74}Br_4Cl_4O_{10}$, *FW* 1404.63, monoclinic, space group *P* 21/c, $a = 26.1413(9)$, $b = 11.8492(6)$, $c = 21.3437(9)$ Å, $\alpha = 90.00°$, $\beta = 109.625(4)°$, $\gamma = 90.00°$, $V = 6227.2(5)$ Å^3, $Z = 4$, $D_c = 1.498$ g cm^{-3}, $T = 140(2)$ K, $\mu = 2.811$ mm^{-1}, 11362 measured reflections, 7713 independent reflections, 725 parameters, 150 restraints, $F(000) = 2864$, $R_1 = 0.1042$, $wR_1 = 0.1642$ (all data), $R_2 = 0.0652$, $wR_2 = 0.1439$ $[I > 2\sigma(I)]$, max. residual density 2.427 e•Å^{-3}, and goodness-of-fit (F^2) = 1.025. CCDC 910572.

Crystal data of **4**: block, colorless, 0.35 × 0.32 × 0.28 mm^3, $C_{59}H_{76}Br_4O_{11}Cl_2$, *FW* 1351.74, triclinic, space group *P*–1, $a = 11.9824(10)$, $b = 15.2216(9)$, $c = 16.9837(12)$ Å, $\alpha = 78.725(6)°$, $\beta = 79.801(7)°$, $\gamma = 89.345(6)°$, $V = 2989.0(4)$ Å^3, $Z = 2$, $D_c = 1.372$ g cm^{-3}, $T = 293(2)$ K, $\mu = 3.708$ mm^{-1}, 10133 measured reflections, 7644 independent reflections, 647 parameters, 96 restraints, $F(000) = 1384$, $R_1 = 0.1622$, $wR_1 = 0.4075$ (all data), $R_2 = 0.1452$, $wR_2 = 0.3816$ $[I > 2\sigma(I)]$, max. residual density 2.631 e•Å^{-3}, and goodness-of-fit (F^2) = 1.579. CCDC 910571.

12. ORTEP diagrams for ***2*** *and* ***4***

(a)



(b)

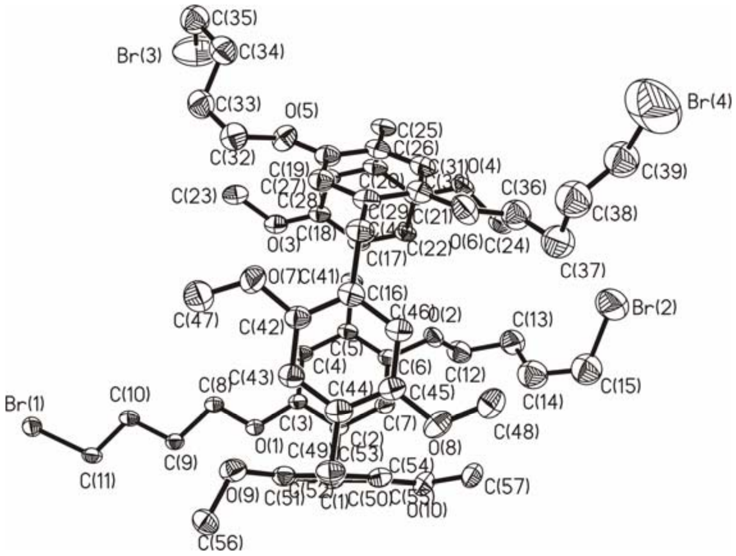


Figure S32. ORTEP diagrams for the two copillar[5]arenes: (a) **2**; (b) **4**.

References:

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