Electronic Supplementary Information

Reversing the ion transport selectivity through arm modification of artificial molecular hourglass

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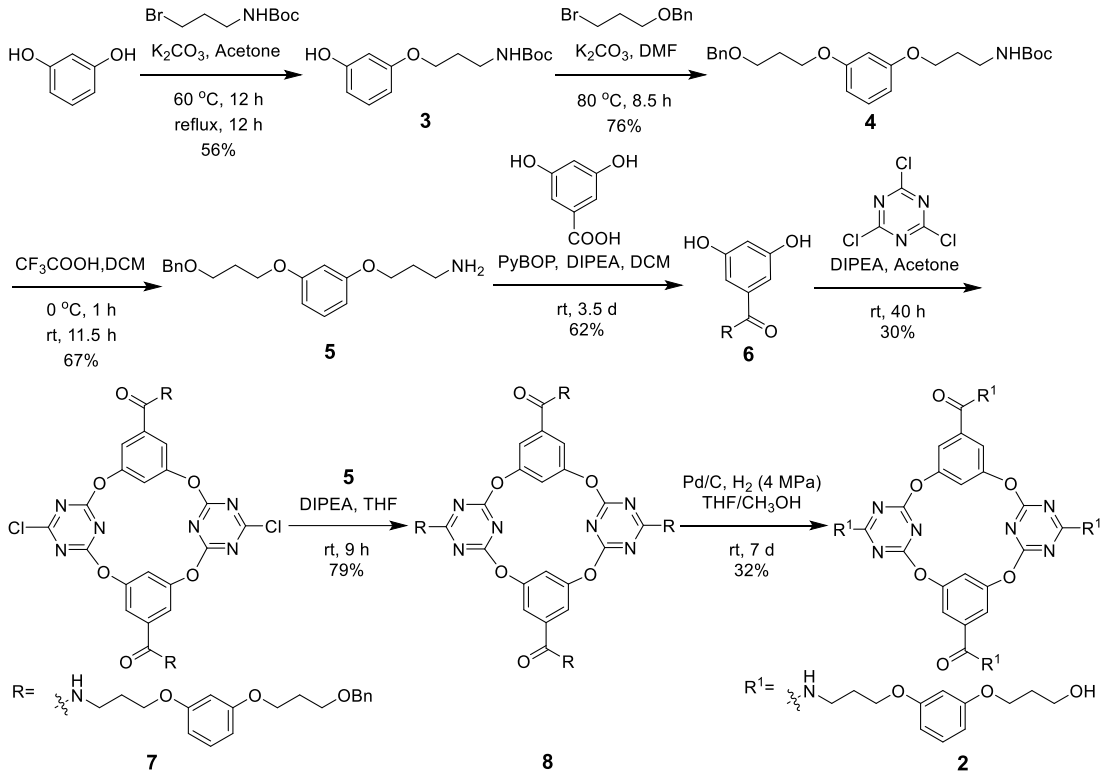
1. General information

Reagents for synthesis and analysis were purchased from J&K or Sigma-Aldrich. A Mini-Extruder used for vesicle preparation, egg yolk phosphatidylcholine (EYPC), and 1, 2-diphytanoyl-sn-glycero-3-phosphocholine (DPhPC) were purchased from Avanti Polar Lipids. ^{1}H and ^{13}C NMR spectra were recorded on Bruker 400 or 500 MHz NMR spectrometer. Chemical shifts are reported in ppm and referenced to tetramethylsilane (TMS) or the residual solvent resonance. Abbreviations are used in the description of NMR data as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, m = multiplet), coupling constant (*J*, Hz). Melting points are uncorrected. Infrared spectra were recorded on Nicolet-6700 FT-IR spectrometer. Mass spectra were obtained on Bruker APEX-2 (HRMS). Elemental analysis was recorded on Thermo Quest CE Instruments flash EA 1112 analyser. All anhydrous solvents were dried according to standard procedures prior to use. All other major chemicals were obtained from commercial sources and used without further purification.

2. Synthesis procedure



Compound 3: N-Boc-3-bromopropylamine (2.38 g, 10 mmol), acetone (60 mL), resorcinol (1.67 g, 15 mmol) and potassium carbonate (2.07 g, 15 mmol) were mixed in a flask. After heating at 60 ℃ for 12 h, the mixture was heated to reflux for another 12 h, and then cooled to room temperature. Acetone was removed by rotary evaporation. The residue was dissolved in water and extracted with ethyl acetate twice, the organic phase was washed with brine two times, and then dried with anhydrous sodium sulfate. After filtration and removal of organic solvent, the residue was chromatographed on a silica gel column (100-200 mesh) with a mixture of petroleum ether and acetone (10:1, v/v) as eluent. The obtain was recrystallized with dichloromethane and *n*-hexane to give pure compound **3** as a white solid (1.50 g, 56%). **3**: m.p. 163-164 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.10 (t, J = 8.1 Hz, 1H), 6.45 (td, J = 7.6, 2.3 Hz, 2H), 6.41 (t, J = 2.3 Hz, 1H), 4.83 (s, 1H), 3.96 (t, J = 6.0 Hz, 2H), 3.31 (t, J = 6.7 Hz, 2H), 1.94 (m, 2H), 1.45 (s, 9H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) δ 160.2, 157.4, 156.5, 130.2, 108.2, 106.8, 102.2, 79.8, 65.8, 38.3, 29.6, 28.6; IR (KBr) ν 3353, 2978, 2934, 1678, 1596, 1517, 1492, 1459, 1172, 1145 cm^{-1}; HRMS (ESI^{+}): *m/z* calc. for $[M+Na]^{+}$ ($C_{14}H_{21}NO_4Na^{+}$)

290.1368, found 290.1360. Anal. Calcd. for $C_{14}H_{21}NO_4$: C, 62.90; H, 7.92; N, 5.24. Found: C, 62.75; H, 7.92; N, 5.27.

Compound 4: 3 (2.94 g, 11 mmol), DMF (67 mL), benzyl 3-bromopropyl ether (2.57 g, 11 mmol) and potassium carbonate (2.28 g, 16.5 mmol) were mixed in a flask. The mixture was heated to 80 ℃ for 8.5 h, and then cooled to room temperature. DMF was removed by rotary evaporation. The residue was dissolved in water (100 mL) and extracted with ethyl acetate (3 × 50 mL), the organic phase was washed with brine (2 × 50 mL), and then dried with anhydrous sodium sulfate. After filtration and removal of organic solvent, the residue was chromatographed on a silica gel column (100-200 mesh) with a mixture of petroleum ether and ethyl acetate (5:1, v/v) as eluent to give pure compound **4** as a colorless viscous liquid (3.49 g, 76%). **4**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.36-7.26 (m, 5H), 7.16 (t, *J* = 8.2 Hz, 1H), 6.65-6.35 (m, 3H), 4.76 (s, 1H), 4.53 (s, 2H), 4.07 (t, *J* = 6.3 Hz, 2H), 3.99 (t, *J* = 6.0 Hz, 2H), 3.66 (t, *J* = 6.1 Hz, 2H), 3.31 (br s, 2H), 2.08 (quint, *J* = 6.2 Hz, 2H), 1.97 (quint, *J* = 6.3, 5.9 Hz, 2H), 1.45 (s, 9H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) δ 160.4, 160.1, 156.1, 138.5, 130.0, 128.5, 127.74, 127.69, 107.1, 106.7, 101.6, 79.4, 73.2, 67.0, 65.9, 65.0, 38.2, 29.9, 29.6, 28.6; IR (KBr) ν 3355, 2975, 2936, 2861, 1718, 1604, 1590, 1496 cm^{-1}; HRMS (ESI$^+$): *m/z* calc. for $[M+Na]^+$ ($C_{24}H_{33}NO_5Na^+$) 438.2256, found 438.2241. Anal. Calcd. for $C_{24}H_{33}NO_5$: C, 69.37; H, 8.00; N, 3.37. Found: C, 69.46; H, 8.16; N, 3.39.

Primary amine compound 5: Under ice bath, trifluoroacetic acid (6.66 mL) was added dropwise to the mixture of **4** (3.32 g, 8 mmol) and DCM (17 mL) within 1 h. Then the mixture reacted at room temperature for 11.5 h. DCM and trifluoroacetic acid were removed by rotary evaporation. The residue was dissolved in ethyl acetate (25 mL) and sodium carbonate aqueous solution (25 mL, 5%). The organic phase was washed with sodium carbonate aqueous solution (25 mL, 5%) and brine, and then dried with anhydrous sodium sulfate. After filtration and removal of organic solvent, the residue was chromatographed on a silica gel column (100-200 mesh) with a mixture of DCM and methanol (20:1, v/v) as eluent to give pure compound **5** as a oily liquid (1.70 g, 67%). **5**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.34-7.29 (m, 4H), 7.28-7.25 (m, 1H), 7.12 (t,

J = 8.6 Hz, 1H), 6.68-6.31 (m, 3H), 4.50 (s, 2H), 4.03 (dt, *J* = 11.3, 6.0 Hz, 4H), 3.63 (t, *J* = 6.2 Hz, 2H), 3.19 (t, *J* = 7.1 Hz, 2H), 2.21 (m, 2H), 2.05 (m, 2H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz) δ 160.3, 159.7, 138.5, 130.0, 128.5, 127.74, 127.69, 107.4, 106.9, 101.7, 73.2, 67.0, 65.3, 65.0, 38.1, 29.8, 27.8; IR (KBr) ν 2939, 2874, 1607, 1582, 1492, 1468 cm^{-1}; HRMS (ESI^+): *m/z* calc. for $[M+H]^+$ ($C_{19}H_{26}NO_3^+$) 316.1913, found 316.1897.

Resorcinol monomer 6: 5 (3.20 g, 10.14 mmol), DCM (40 mL), PyBOP (5.66 g, 10.65 mmol) and 3,5-dihydroxybenzoic acid (1.66 g, 10.65 mmol) were mixed in a flask. After stirring, DIPEA (2.65 g, 20.28 mmol) was added. Then the mixture reacted at room temperature for 3.5 d. After removal of organic solvent, the residue was chromatographed on a silica gel column (100-200 mesh) with a mixture of DCM and acetone (8:1, v/v) as eluent to give pure compound **6** as a light yellow viscous liquid (2.86 g, 62%). **6**: ^{1}H NMR (*d*$_6$-DMSO, 500 MHz) δ 9.41 (s, 2H), 8.30 (t, *J* = 5.6 Hz, 1H), 7.36-7.29 (m, 4H), 7.29-7.23 (m, 1H), 7.15 (t, *J* = 8.2 Hz, 1H), 6.67 (d, *J* = 2.2 Hz, 2H), 6.49 (dt, *J* = 8.2, 2.6 Hz, 2H), 6.46 (t, *J* = 2.3 Hz, 1H), 6.34 (t, *J* = 2.2 Hz, 1H), 4.47 (s, 2H), 4.00 (dt, *J* = 18.8, 6.3 Hz, 4H), 3.57 (t, *J* = 6.3 Hz, 2H), 3.35 (t, *J* = 6.2 Hz, 2H), 1.95 (m, 4H); $^{13}C\{^{1}H\}$ NMR (*d*$_6$-DMSO, 125 MHz) δ 166.5, 159.84, 159.79, 158.2, 138.5, 136.9, 129.9, 128.2, 127.4, 127.3, 106.8, 106.7, 105.4, 104.9, 101.1, 71.9, 66.3, 65.4, 64.5, 36.3, 29.1, 28.9; IR (KBr) ν 2953, 2931, 1643, 1591, 1539, 1492, 1451 cm^{-1}; HRMS (ESI^-): *m/z* calc. for $[M-H]^-$ ($C_{26}H_{28}NO_6^-$) 450.1917, found 450.1921; Anal. Calcd. for $C_{26}H_{29}NO_6+H_2O$: C, 66.51; H, 6.65; N, 2.98. Found: C, 66.46; H, 6.55; N, 3.05.

Macrocycle compound 7: 6 (1.14 g, 2.52 mmol), acetone (490 mL) and DIPEA (0.82 g, 6.30 mmol) were mixed in a flask. Under stirring, cyanuric chloride was added (0.47 g, 2.52 mmol), and the mixture reacted at room temperature for 40 h. After removal of organic solvent, the residue was chromatographed on a silica gel column (100-200 mesh) with a mixture of petroleum ether and ethyl acetate (3:2, v/v) as eluent to give pure compound **7** as a solid (427 mg, 30%). **7**: m.p. 88-89 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.32-7.29 (m, 7H), 7.28-7.24 (m, 1H), 7.17-7.04 (m, 6H), 6.90 (d, *J* = 5.3 Hz, 2H),

6.65 (t, J = 2.1 Hz, 2H), 6.50-6.39 (m, 6H), 4.50 (s, 4H), 4.10-3.99 (m, 8H), 3.66 (t, J = 6.1 Hz, 4H), 3.52 (quint, J = 6.1 Hz, 4H), 2.09 (m, 4H), 2.05-1.98 (m, 4H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 174.9, 172.2, 165.0, 160.4, 159.7, 151.6, 138.54, 138.47, 130.1, 128.5, 127.7, 127.7, 118.6, 118.4, 107.1, 106.9, 101.5, 73.1, 67.0, 66.8, 65.2, 38.8, 29.8, 28.5; IR (KBr) ν 3082, 2934, 2871, 1648, 1596, 1547, 1498, 1432 cm^{-1}; HRMS (ESI^+): *m/z* calc. for $[M+Na]^+$ ($C_{58}H_{54}N_8Cl_2O_{12}Na^+$) 1147.3136, found 1147.3133. Anal. Calcd. for $C_{58}H_{54}N_8O_{12}Cl_2$: C, 61.87; H, 4.83; N, 9.95. Found: C, 61.82; H, 4.86; N, 10.09.

Precursor compound 8: **7** (225 mg, 0.2 mmol), **5** (189 mg, 0.6 mmol), THF (30 mL) and DIPEA (209 mg, 1.6 mmol) were mixed in a flask, and reacted at room temperature for 9 h. After removal of organic solvent, the residue was chromatographed on a silica gel column (100-200 mesh) with a mixture of petroleum ether and ethyl acetate (2:3, v/v) as eluent to give pure compound **8** as a white solid (269 mg, 79%). **8**: m.p. 76-77 ^oC; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.31 (d, J = 4.2 Hz, 16H), 7.14 (dt, J = 13.1, 8.2 Hz, 8H), 6.72-6.57 (m, 4H), 6.54-6.38 (m, 12H), 6.32 (d, J = 6.3 Hz, 2H), 4.50 (s, 8H), 4.12-3.98 (m, 16H), 3.72 (quint, J = 6.3 Hz, 4H), 3.68-3.63 (m, 8H), 3.56-3.53 (m, 4H), 2.15-1.99 (m, 16H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 172.3, 171.3, 168.7, 165.9, 160.44, 160.39, 160.0, 159.8, 152.3, 152.2, 138.5, 137.3, 130.1, 128.5, 127.8, 127.7, 119.7, 118.2, 107.3, 107.2, 107.1, 107.0, 106.9, 106.8, 106.7, 101.7, 101.5, 73.17, 73.16, 67.1, 67.0, 66.8, 66.7, 66.6, 66.0, 65.1, 39.3, 38.5, 29.9, 29.0, 28.8; IR (KBr) ν 3030, 2923, 2874, 1602, 1580, 1547, 1492, 1435, 1388 cm^{-1}; HRMS (ESI^+): *m/z* calc. for $[M+Na]^+$ ($C_{96}H_{102}N_{10}O_{18}Na^+$) 1705.7271, found 1705.7286. Anal. Calcd. for $C_{96}H_{102}N_{10}O_{18}$: C, 68.47; H, 6.11; N, 8.32. Found: C, 68.49; H, 6.19; N, 8.17.

Artificial molecular hourglass 2: **8** (0.93 g, 0.55 mmol), THF (14 mL), methanol (5 mL) and 10% Pd/C (250 mg) were mixed in an autoclave. Under H_2 pressure (4 MPa), the mixture was stirred at room temperature for 7 d. The mixture was filtrated with siliceousearth and filtrate residue was washed with THF, the filtrate was concentrated. The residue was chromatographed on a silica gel column (100-200 mesh) with a mixture of petroleum ether and acetone (1:4, v/v) as eluent. The obtain was

recrystallized with acetone and *n*-hexane to give pure compound **2** as a white solid (233 mg, 32%). **2**: m.p. 103-104 °C; ^{1}H NMR (d_6-Acetone, 500 MHz) δ 7.82 (t, *J* = 5.8 Hz, 2H), 7.48 (t, *J* = 5.9 Hz, 2H), 7.36-7.32 (m, 4H), 7.18-7.07 (m, 4H), 6.96 (tt, *J* = 25.3, 2.1 Hz, 2H), 6.59-6.39 (m, 12H), 4.12 (t, *J* = 6.0 Hz, 4H), 4.10-4.02 (m, 12H), 3.74-3.68 (m, 12H), 3.68-3.64 (m, 3H), 3.63-3.49 (m, 6H), 2.17-2.10 (m, 4H), 1.94 (m, 8H); ^{13}C{^{1}H} NMR (d_6-Acetone, 125 MHz) δ 172.9 (d, *J* = 1.2 Hz), 172.2 (d, *J* = 1.9 Hz), 170.3, 165.8 (t, *J* = 5.5 Hz), 161.3 (d, *J* = 1.4 Hz), 161.2 (d, *J* = 3.1 Hz), 153.2 (t, *J* = 4.0 Hz), 137.9 (t, *J* = 3.5 Hz), 130.63, 130.60, 120.4 (t, *J* = 5.1 Hz), 118.3 (d, *J* = 5.9 Hz), 118.2 (d, *J* = 6.5 Hz), 107.60, 107.56, 107.51, 107.48, 102.1, 102.0, 66.4, 65.6 (d, *J* = 5.4 Hz), 59.1, 39.1, 37.9, 33.3; IR (KBr) ν 3355, 3191, 3011, 2923, 2846, 1660, 1645, 1634, 1582, 1544, 1468 cm^{-1}; HRMS (ESI^{+}): *m/z* calc. for [M+Na]$^{+}$ ($C_{68}H_{78}N_{10}O_{18}Na^{+}$) 1345.5388, found 1345.5387. Anal. Calcd. for $C_{68}H_{78}N_{10}O_{18}$: C, 61.71; H, 5.94; N, 10.58. Found: C, 61.72; H, 5.91; N, 10.41.

3. NMR titrations

^{1}H NMR titrations were performed in d_6-acetone at room temperature. The solutions of each guest were respectively prepared with the host solution of **2** (1×10^{-3} mol/L in d_6-acetone). Aliquots of guest solution were added directly to an NMR tube containing the host solution. All proton signals were referenced to the TMS or solvent residual peak. The association constants *K* were calculated by *Bindfit v0.5* (for this program, please see: http://app.supramolecular.org/bindfit/).

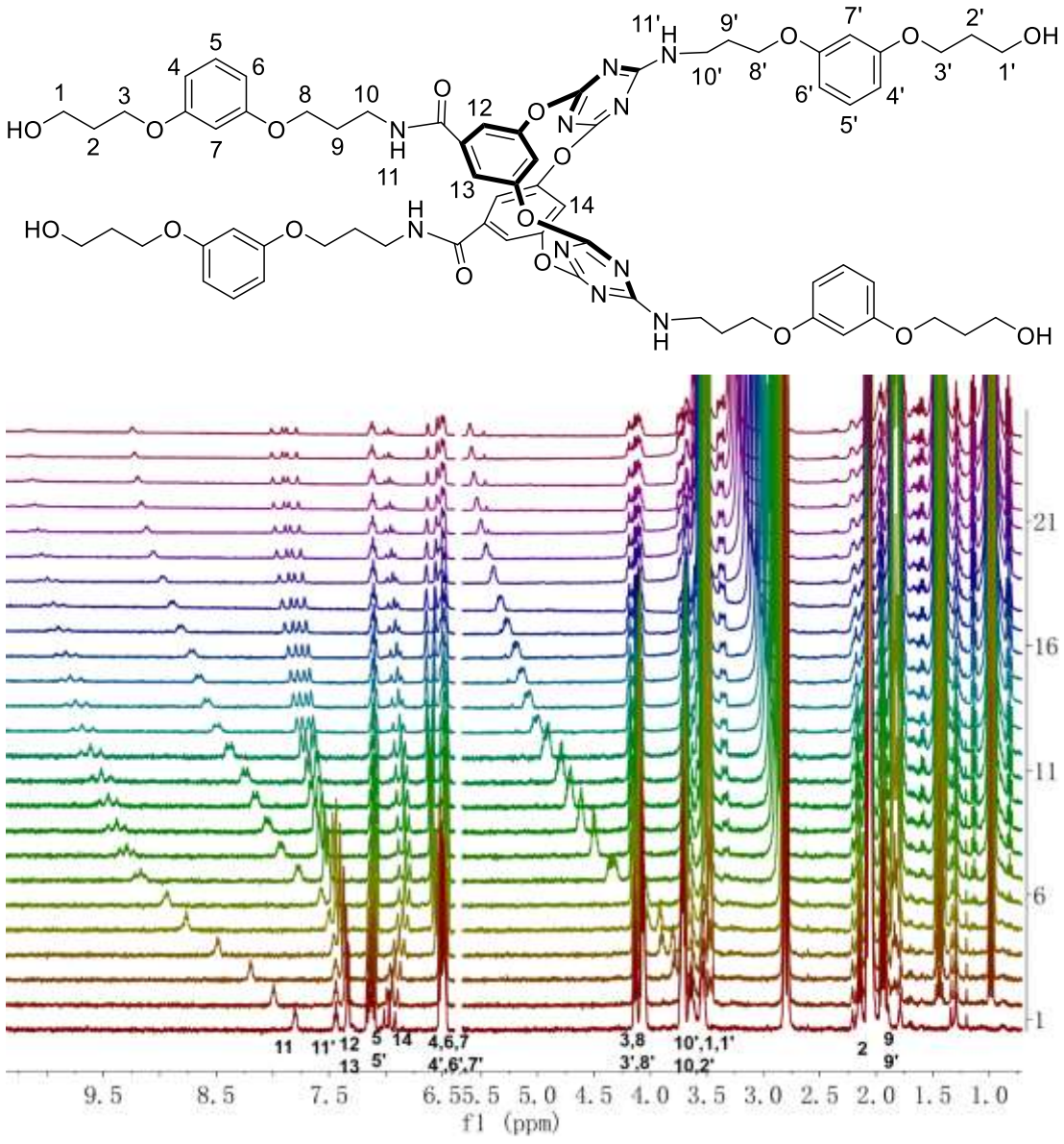


Figure S1. ^{1}H NMR titration of **2** (1×10^{-3} mol/L in d_6-acetone) upon addition of different amounts of tetrabutylammonium chloride (from bottom to top: 0, 0.4, 0.8, 1.5,

3.0, 5.0, 9.8, 14.6, 19.2, 23.8, 28.3, 37.0, 45.4, 53.6, 61.4, 69.0, 83.3, 96.8, 115.4, 142.8, 166.7, 187.5, 205.9, 222.2, 236.8 × 10^{-3} mol/L). For clarity, partial spectra are shown.

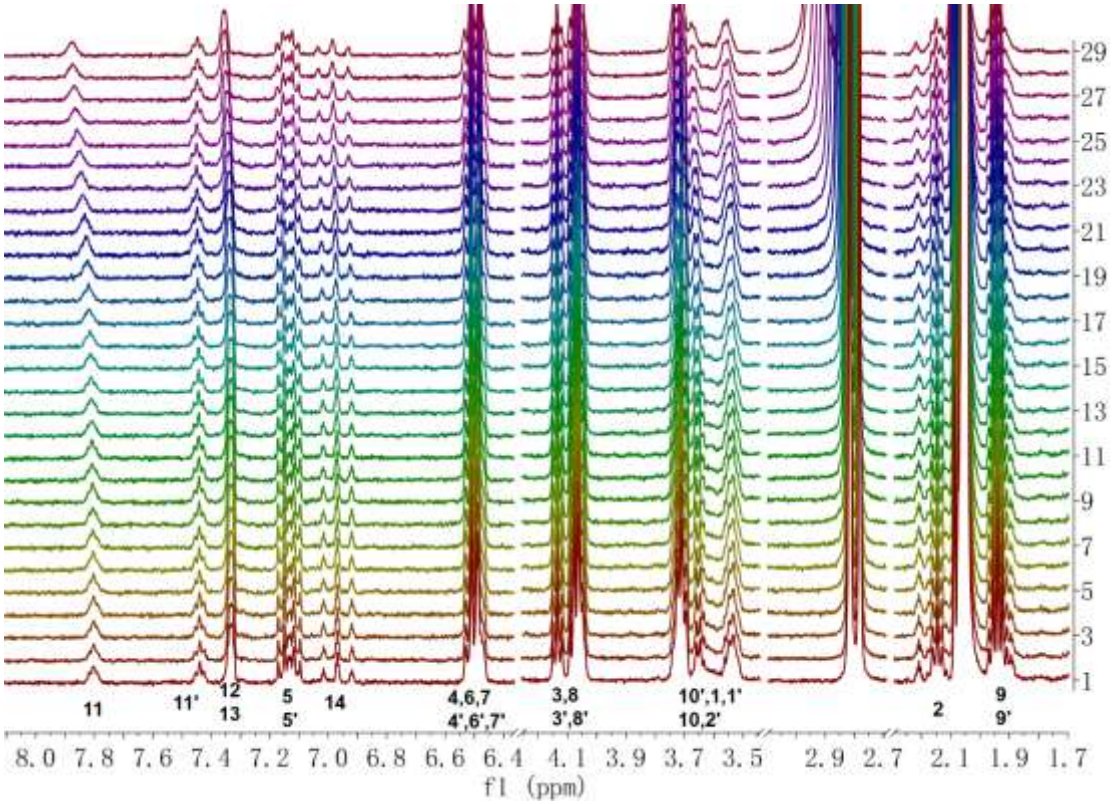


Figure S2. ^{1}H NMR titration of **2** (1 × 10^{-3} mol/L in d_6-acetone) upon addition of different amounts of KPF_6 (from bottom to top: 0, 0.2, 0.5, 0.8, 1.0, 1.5, 2.0, 3.0, 4.0, 5.0, 6.0, 7.0, 8.0, 10.0, 12.0, 14.9, 19.6, 24.3, 28.9, 37.8, 46.4, 62.7, 77.9, 92.1, 123.8, 151.1, 174.8, 213.9, 217.3 × 10^{-3} mol/L). For clarity, partial spectra are shown.

Table S1. Association constants K of **2** with $Bu_4N^+Cl^-$ and $K^+PF_6^-$ calculated by *Bindfit v0.5* with a host-guest stoichiometry of 1:2.

	$Bu_4N^+Cl^-$	$K^+PF_6^-$
K_1 (M^{-1})	1067.0 ± 28.8	242.9 ± 35.2
K_2 (M^{-1})	23.1 ± 0.2	4.2 ± 0.1

4. Ion transport assays in vesicles [S1-S3]

General preparation of Lucigenin containing EYPC vesicles. Egg yolk phosphatidylcholine (EYPC, 25 mg) was dissolved in EtOH/$CHCl_3$ (2 mL, v/v 1:1). The solution was evaporated under reduced pressure on a rotary evaporator (40 °C) to give a thin film, and the resulting thin film was dried under high vacuum for overnight to remove the residual solvent. The lipid film was hydrated in 1.0 mL buffer solution (10 mM HEPES + 100 mM $NaNO_3$ + 1 mM Lucigenin, pH = 7.0) for 20 mins at room temperature. The suspension was submitted to freeze-thaw for 5 cycles (with liquid nitrogen and 50 °C water bath, respectively), and high-pressure extrusion at room temperature (21 times extrusions through polycarbonate membrane with pore diameter of 100 nm). The vesicle suspension was separated from extravesicular Lucigenin dye by size exclusion chromatography (Sephadex G-50, mobile phase: 10 mM HEPES + 100 mM $NaNO_3$, pH = 7.0).

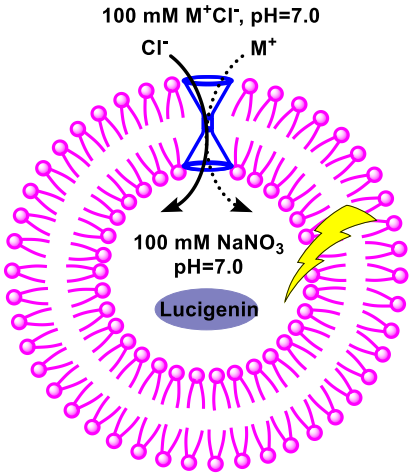


Figure S3. The schematic diagram of vesicle fluorescent assay.

Vesicle fluorescent assay. 50 μL Lucigenin- and $NaNO_3$-loaded EYPC vesicle solution was suspended in 1950 μL of the buffer solution (10 mM HEPES + 100 mM LiCl, NaCl, KCl, RbCl, or CsCl, pH = 7.0) and placed into a quartz cuvette at 25 °C. The intravesicular Lucigenin fluorescence intensity (I_t, λ_{ex} = 369 nm, λ_{em} = 505 nm) was measured over time. THF, DMF, or the solution of compound **2** in THF or DMF (25 μL) was added at t = 50 s (I_0), and then triton X-100 (25 μL, 10% in water) was

added at 500 s (I_∞). The fluorescent intensity I_t was normalized to fractional intensity I_f using equation (Eq. 1):

$$I_f = (I_t - I_\infty)/(I_0 - I_\infty) \qquad \text{(Eq. 1)}$$

Where I_0 is the fluorescent intensity before addition of THF, DMF, or compounds, and I_∞ is the fluorescent intensity after addition of triton X-100.

Evaluation of ion transport activity of 2 in different buffer solutions

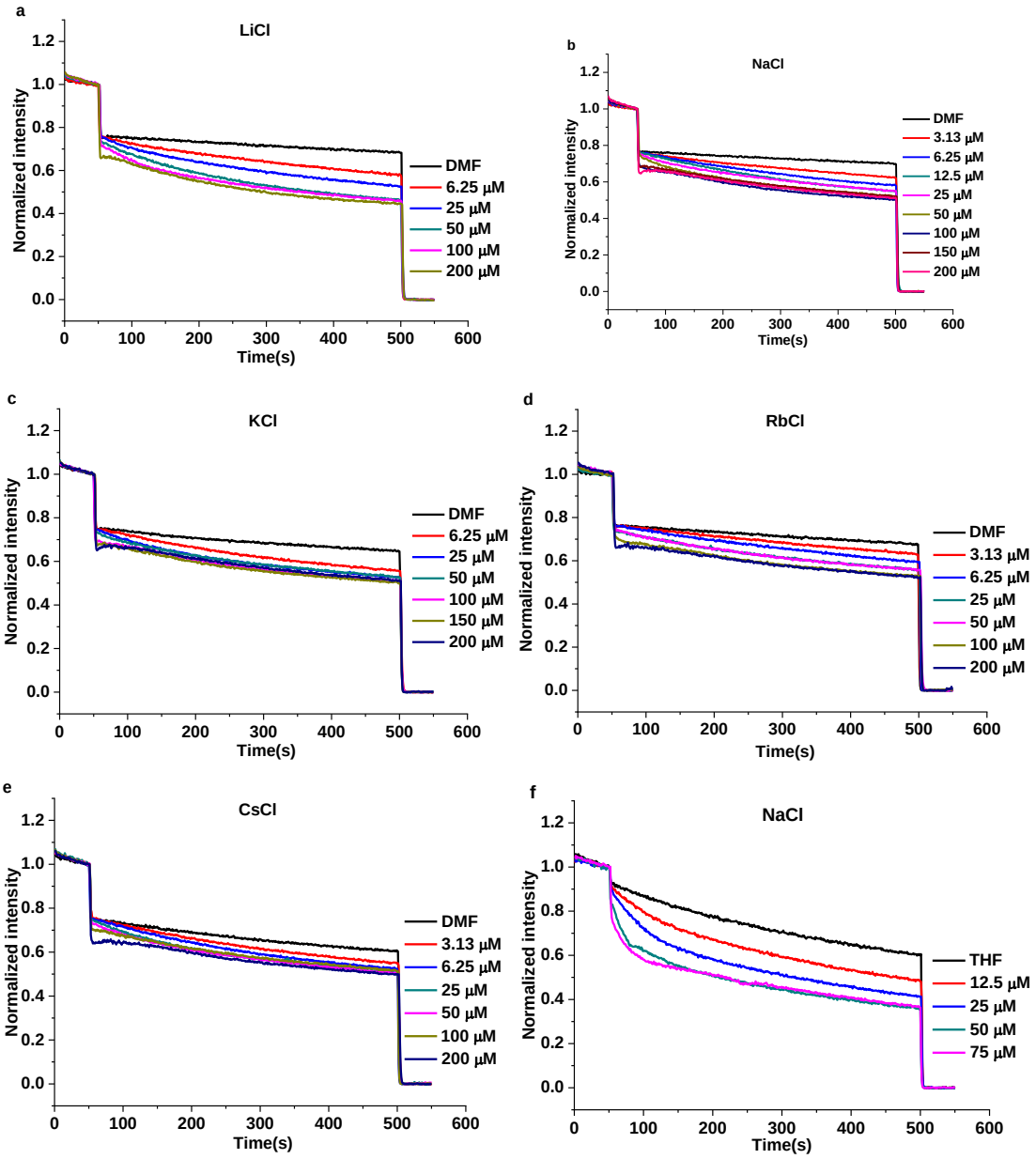


Figure S4. Evaluation of the ion transport activity of **2** in varied concentrations by vesicle fluorescent assay.

5. Planar lipid bilayer experiments[S1,S4]

The chloroform solution of 1,2-diphytanoyl-*sn*-glycero-3-phosphocholine (DPhPC, 25 mg/mL, 10 μL) was evaporated using nitrogen gas and dissolved in *n*-decane (25 μL). 0.5 μL of the *n*-decane solution was painted onto the aperture of the Delrin cup (diameter = 200 μm, Warner Instruments) and the *n*-decane was removed with nitrogen gas. In a traditional planar lipid bilayer conductance measurement experiment, the chamber (*cis* side) and the Delrin cup (*trans* side) were filled with 1.0 M KCl aqueous solution (1.0 mL). Ag-AgCl electrodes were placed into the two solutions with the *trans* side grounded. Planar lipid bilayer was formed by painting 0.5 μL of the above-mentioned *n*-decane solution around the pretreated aperture. The formation of planar lipid bilayer was confirmed by capacitance value ranging from 80 to 120 pF. THF or compound **2** in THF (1.0 μL) was added to the *cis* chamber to reach a final concentration around 10^{-6} M, and the solution was stirred for about five mins. Then the baseline and current signals were recorded at different holding potentials in a Faraday cage, amplified with BC-535 bilayer clamp amplifier (Warner Instruments), low-pass filtered with an 8-pole Bessel filter at 1 kHz (LPF-8, Warner Instruments), A-D converted (1550B, Axon Instruments), and sampled with a sample interval at 10 kHz by Clampex 10.6. The data were analyzed by Clampfit 10.6 with a digital filter at 100 Hz. All the measurements were performed at room temperature (*ca.* 25 °C).

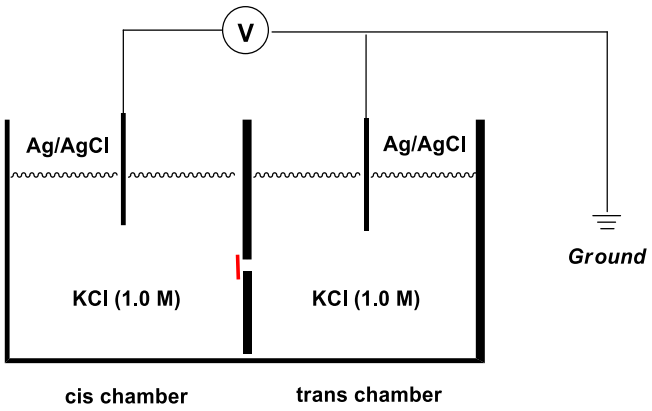
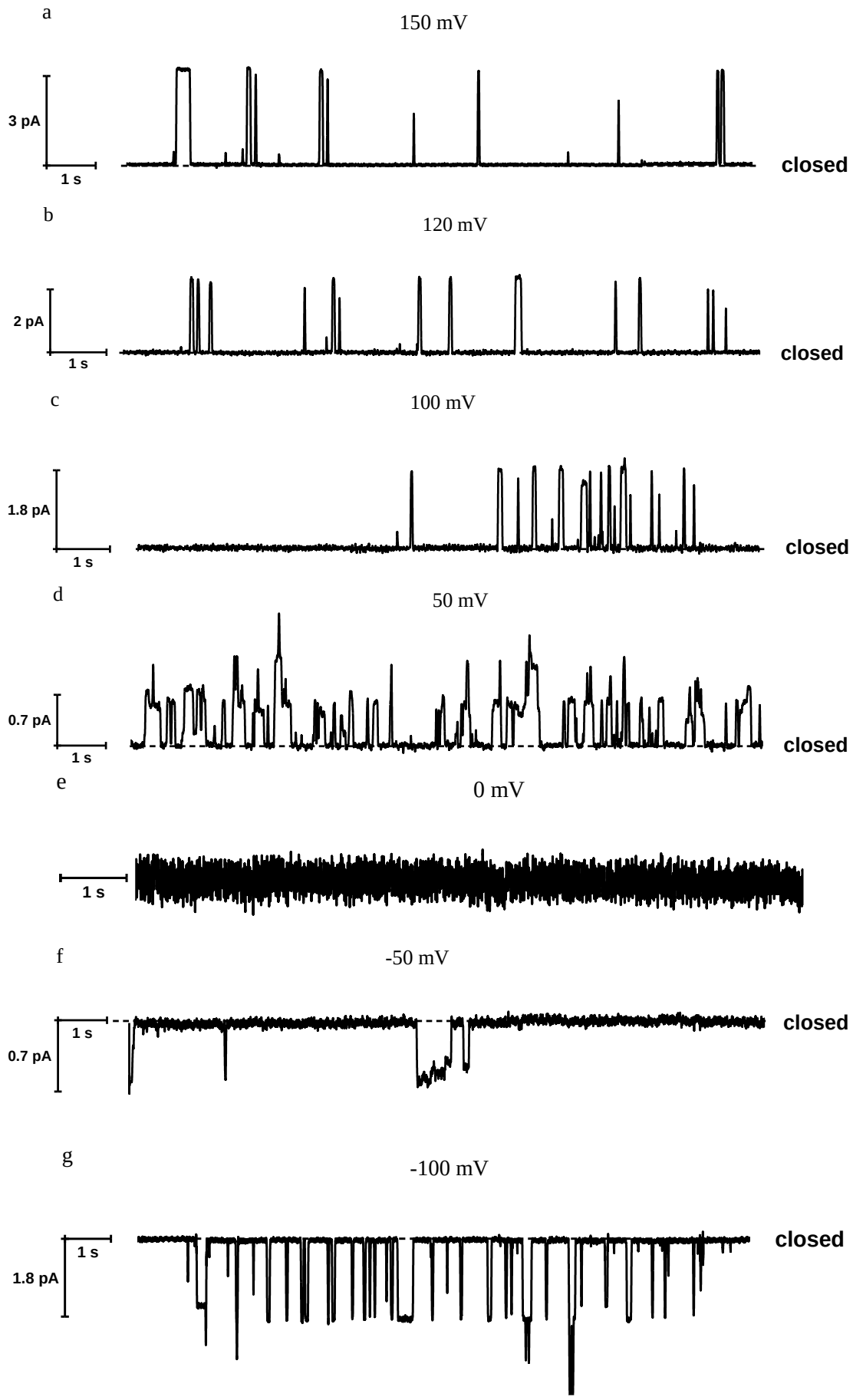


Figure S5. Schematic diagram of the planar lipid bilayer experiments. Experimental conditions: DPhPC in *n*-decane (10 mg/mL); *cis*/*trans* = 1.0 M/1.0 M KCl solution (1 mL/1 mL); applied voltages: −150 mV to 150 mV; addition: 1.0 μL THF solution of molecule **2** (1 mM), final concentration is 1.0 μM.


a
150 mV
3 pA
1 s
closed
b
120 mV
2 pA
1 s
closed
c
100 mV
1.8 pA
1 s
closed
d
50 mV
0.7 pA
1 s
closed
e
0 mV
1 s
f
-50 mV
1 s
0.7 pA
closed
g
-100 mV
1 s
1.8 pA
closed

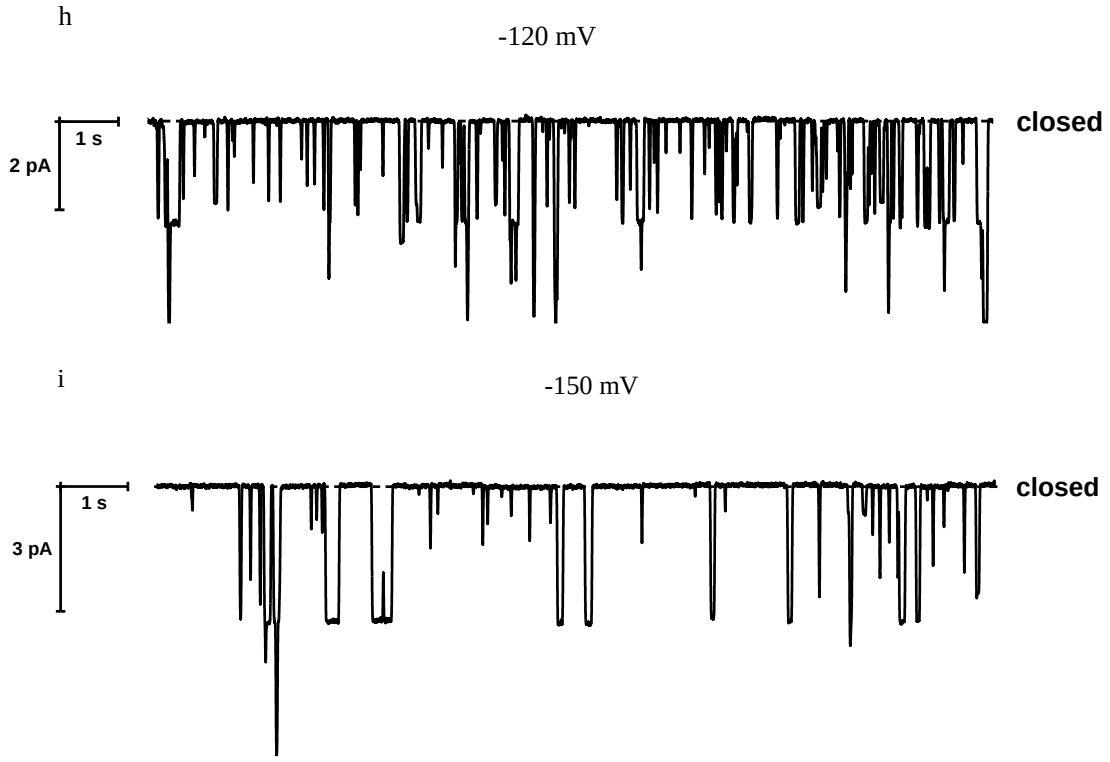
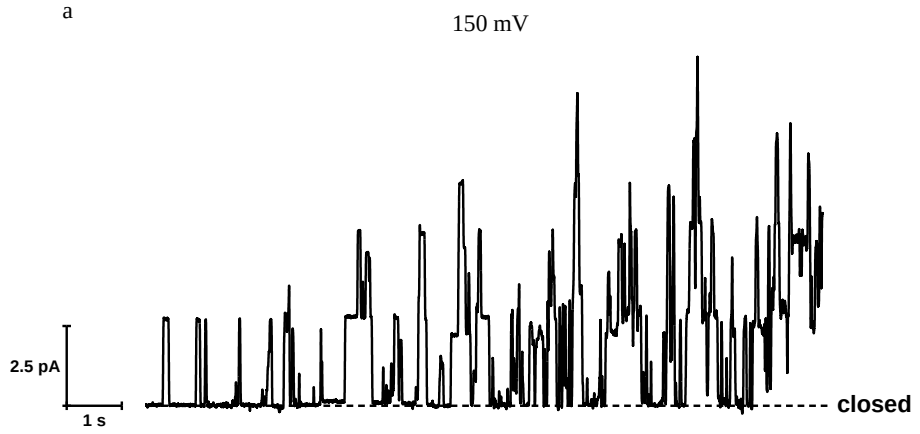
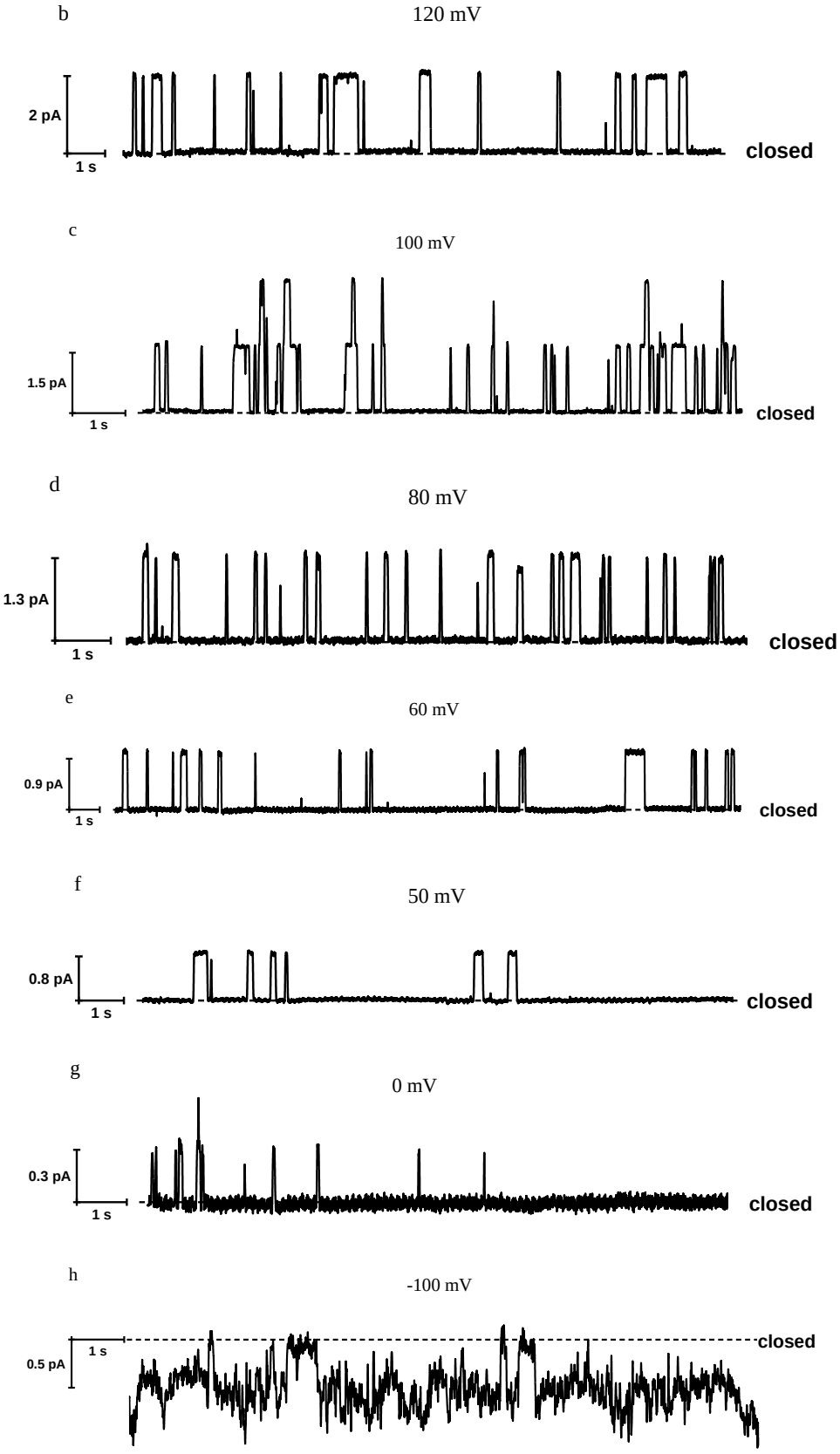


Figure S6. Current traces of molecule **2** at 150 mV (a), 120 mV (b), 100 mV (c), 50 mV (d), 0 mV (e), −50 mV (f), −100 mV (g), −120 mV (h), and −150 mV (i) in symmetrical KCl solutions (*cis*/*trans* = 1.0 M/1.0 M), final concentration is 1.0 μM.

Ion selectivity study by BLM experiments. Ion selectivity of **2** was studied in different *cis* chamber/*trans* chamber solutions: *cis*/*trans* = 1.0 M KCl/0.25 M KCl, *cis*/*trans* = 1.0 M KCl/1.0 M CsCl, *cis*/*trans* = 1.0 M KCl/1.0 M KBr, *cis*/*trans* = 1.0 M $MgCl_2$/0.25 M $MgCl_2$. Voltage changes between corresponding ranges. The final concentration of **2** is 1.0 μM.




b
120 mV
2 pA
1 s
closed
c
100 mV
1.5 pA
1 s
closed
d
80 mV
1.3 pA
1 s
closed
e
60 mV
0.9 pA
1 s
closed
f
50 mV
0.8 pA
1 s
closed
g
0 mV
0.3 pA
1 s
closed
h
-100 mV
1 s
0.5 pA
closed

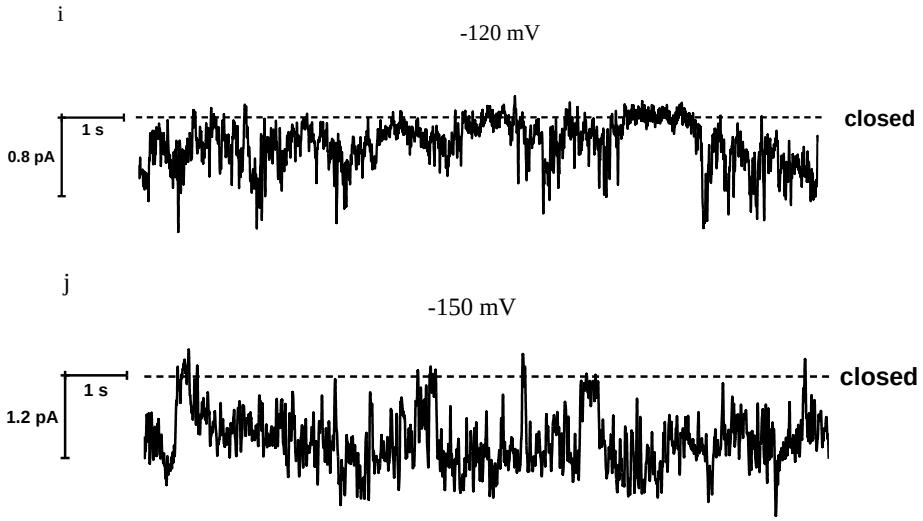


Figure S7. Current traces of molecule **2** at 150 mV (a), 120 mV (b), 100 mV (c), 80 mV (d), 60 mV (e), 50 mV (f), 0 mV (g), −100 mV (h), −120 mV (i), and −150 mV (j) in KCl solutions (*cis*/*trans* = 1.0 M KCl/0.25 M KCl).

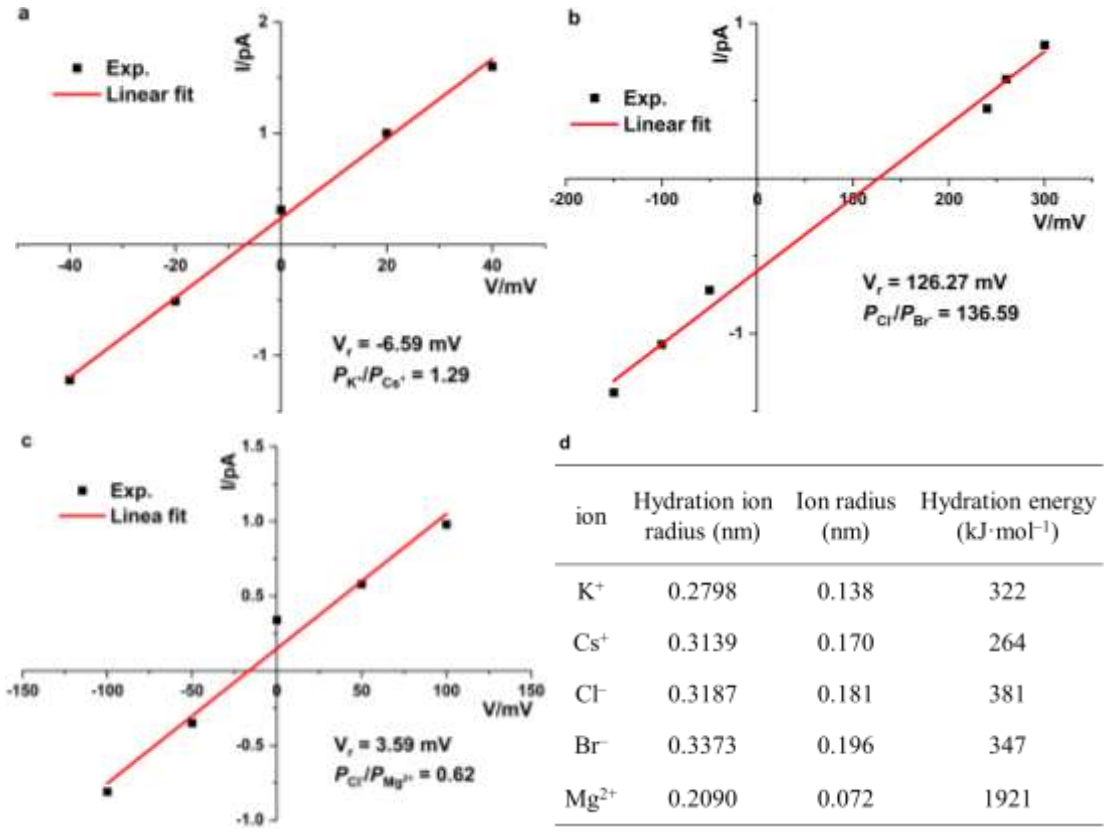
Table S2. Reversal potential V_r and permeability ratio P_{Cl^-}/P_{K^+} in *cis*/*trans* = 1.0 M/0.25 M KCl solution.

Entry	*cis*/*trans* = 1.0 M/0.25 M KCl	
	Reversal potential V_r (mV) [a]	P_{Cl^-}/P_{K^+} [b]
1	−7.74	0.60
2	−7.67	0.60
3	−9.28	0.54
4	−7.08	0.63
5	−11.47	0.46
6	−11.86	0.45
7	−3.55	0.79
8	−4.03	0.77

[a] obtained after correcting the potential caused by chloride concentration gradient; [b] calculated from the equation derived from Goldman-Hodgkin-Katz equation:

$$P_{Cl^-}/P_{K^+} = [a_{K,\,cis} - a_{K,\,trans}\exp(-V_rF/RT)]/[a_{Cl,\,cis}\exp(-V_rF/RT) - a_{Cl,\,trans}]$$

where $a_{K,\,cis}$ and $a_{K,\,trans}$ are activities of K^+ in the *cis* and *trans* chambers, $a_{Cl,\,cis}$ and $a_{Cl,\,trans}$ are activities of Cl^- in the *cis* and *trans* chambers.



d

ion	Hydration ion radius (nm)	Ion radius (nm)	Hydration energy ($kJ \cdot mol^{-1}$)
K^+	0.2798	0.138	322
Cs^+	0.3139	0.170	264
Cl^-	0.3187	0.181	381
Br^-	0.3373	0.196	347
Mg^{2+}	0.2090	0.072	1921

Figure S8. Ion selectivity of molecule **2**. (a) K^+/Cs^+ selectivity (*cis*/*trans* = 1.0 M KCl/1.0 M CsCl) and (b) Cl^-/Br^- selectivity (*cis*/*trans* = 1.0 M KCl/1.0 M KBr), the permeability ratios P_{K^+}/P_{Cs^+} and P_{Cl^-}/P_{Br^-} were calculated from the equation: $V_r = \{RTln(P_A*a_A/P_B*a_B)\}/zF$. (c) Cl^-/Mg^{2+} selectivity (*cis*/*trans* = 1.0 M $MgCl_2$/0.25 M $MgCl_2$), the permeability ratio $P_{Cl^-}/P_{Mg^{2+}}$ was calculated from the same equation as that for P_{Cl^-}/P_{K^+}. (d) The hydration ion radius and hydration energy of different ions.

6. Copies of ^{1}H and ^{13}C NMR spectra

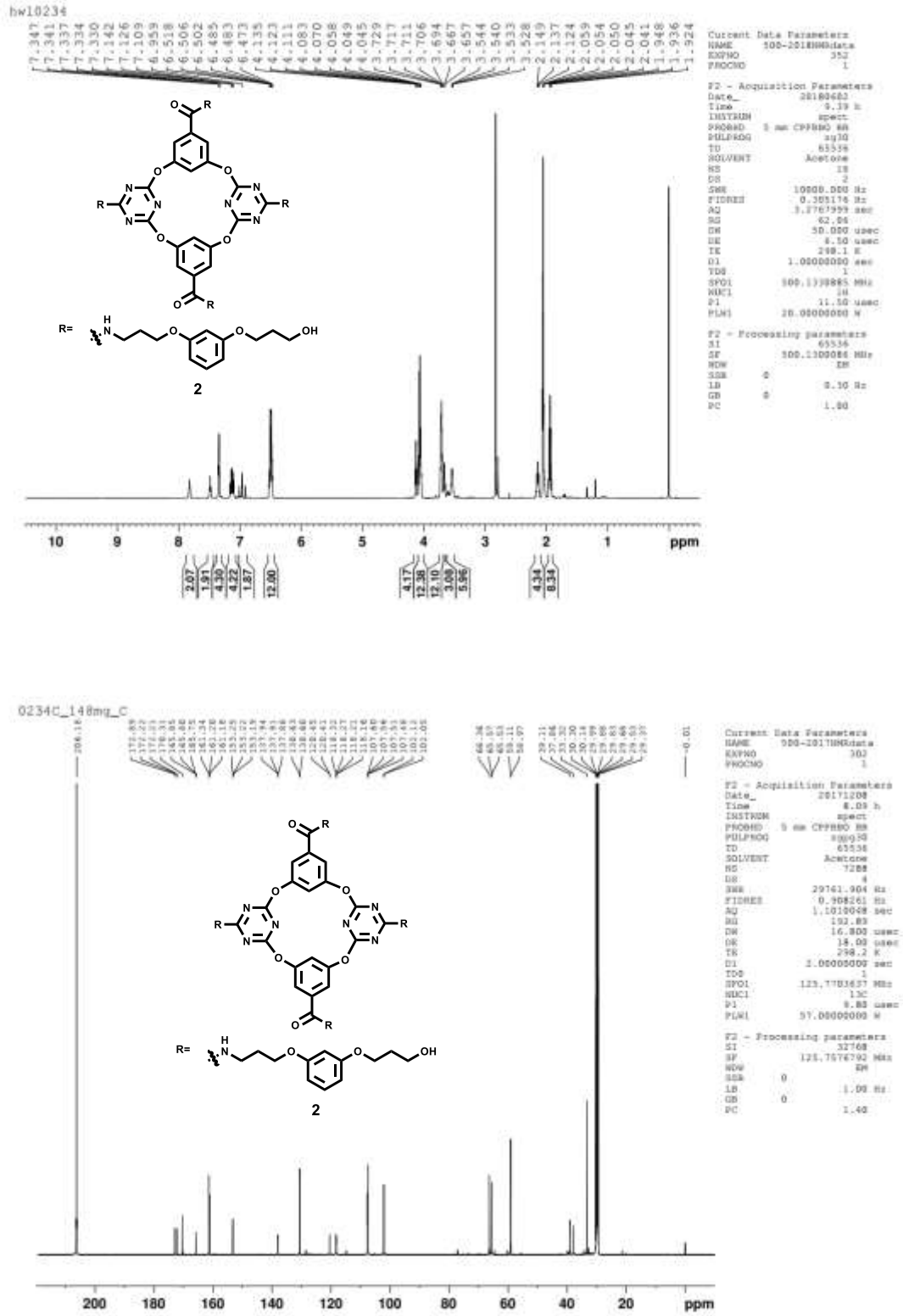


Figure S9. ^{1}H and ^{13}C NMR spectra of **2**.

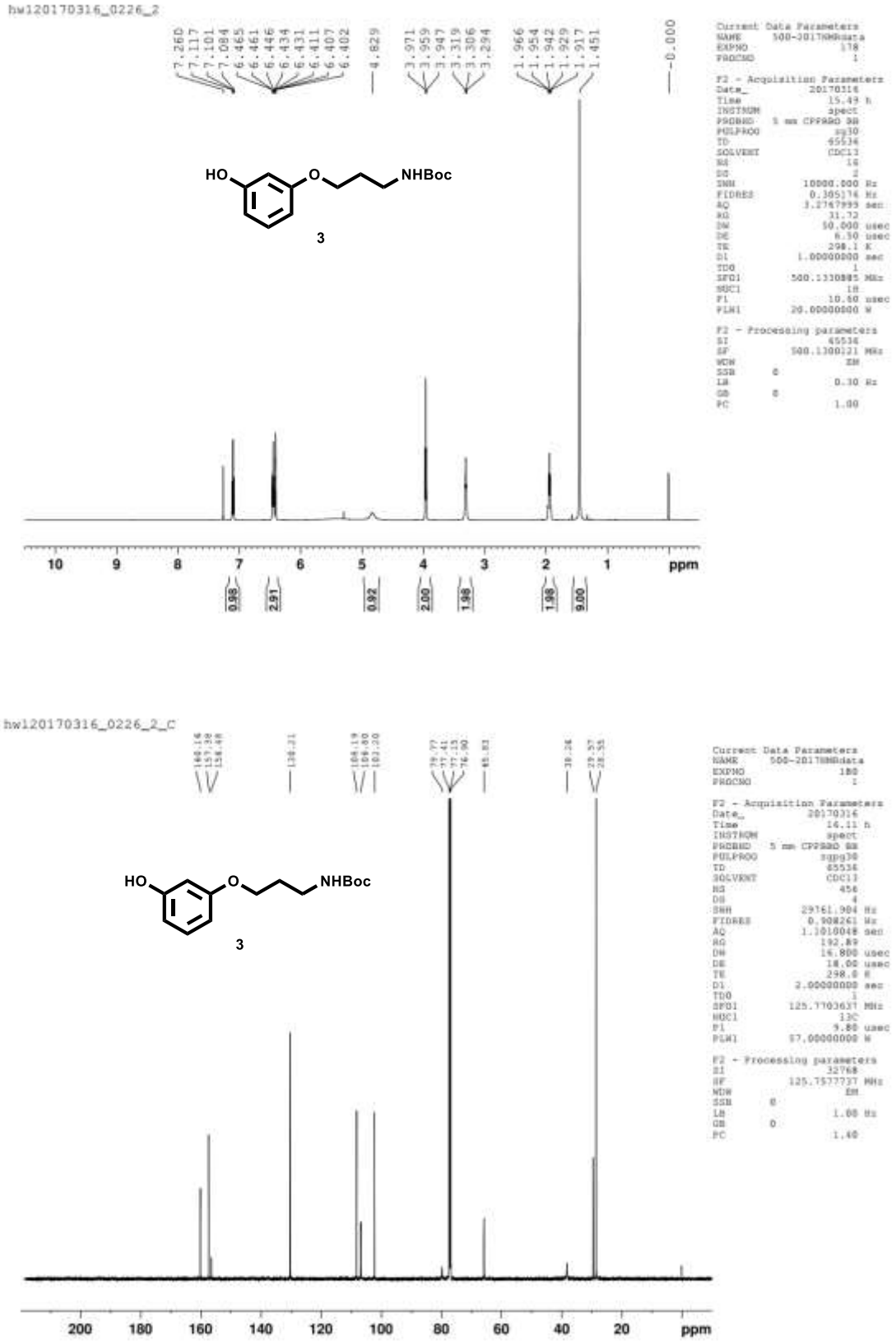


Figure S10. ^{1}H and ^{13}C NMR spectra of **3**.

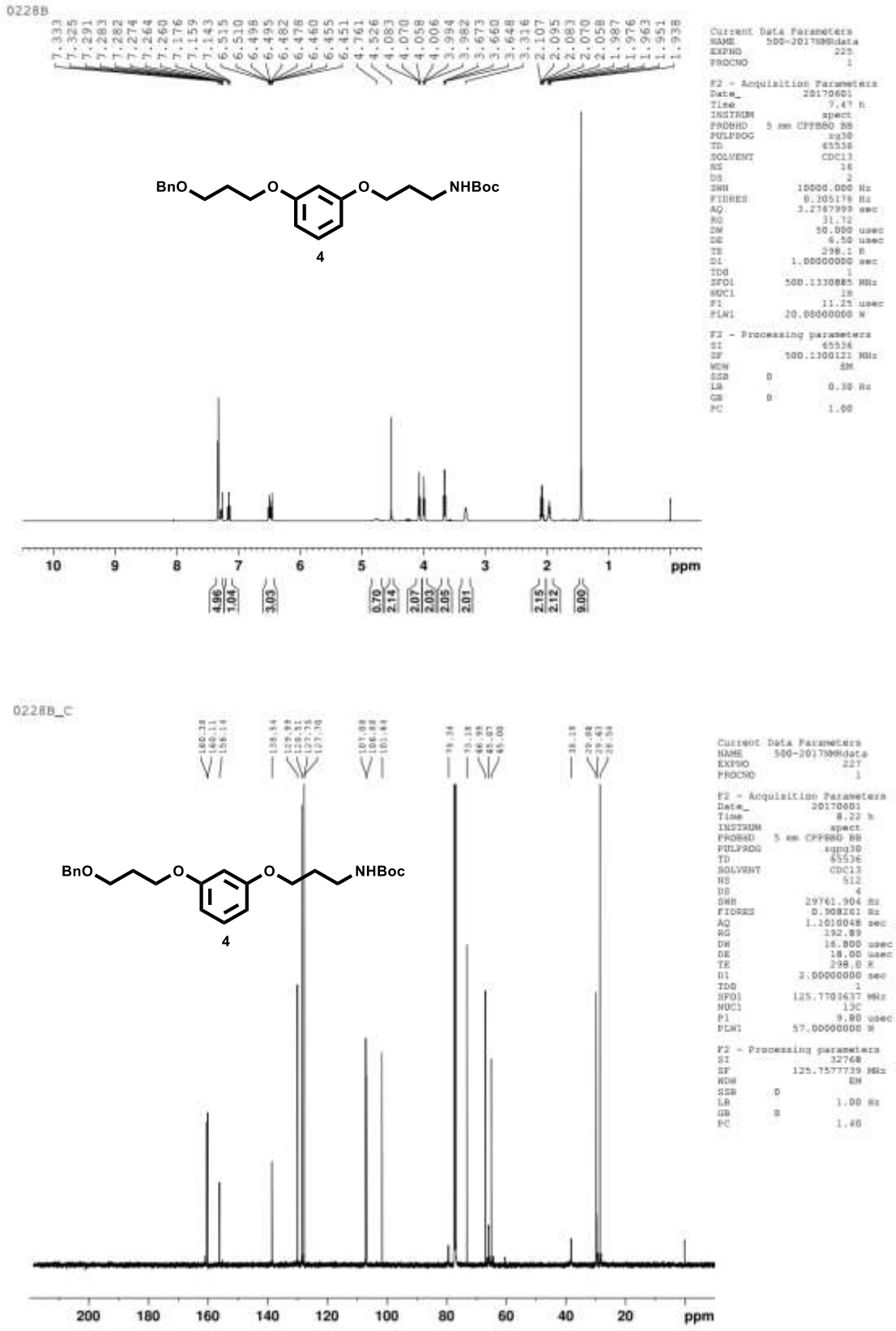


Figure S11. ^{1}H and ^{13}C NMR spectra of **4**.

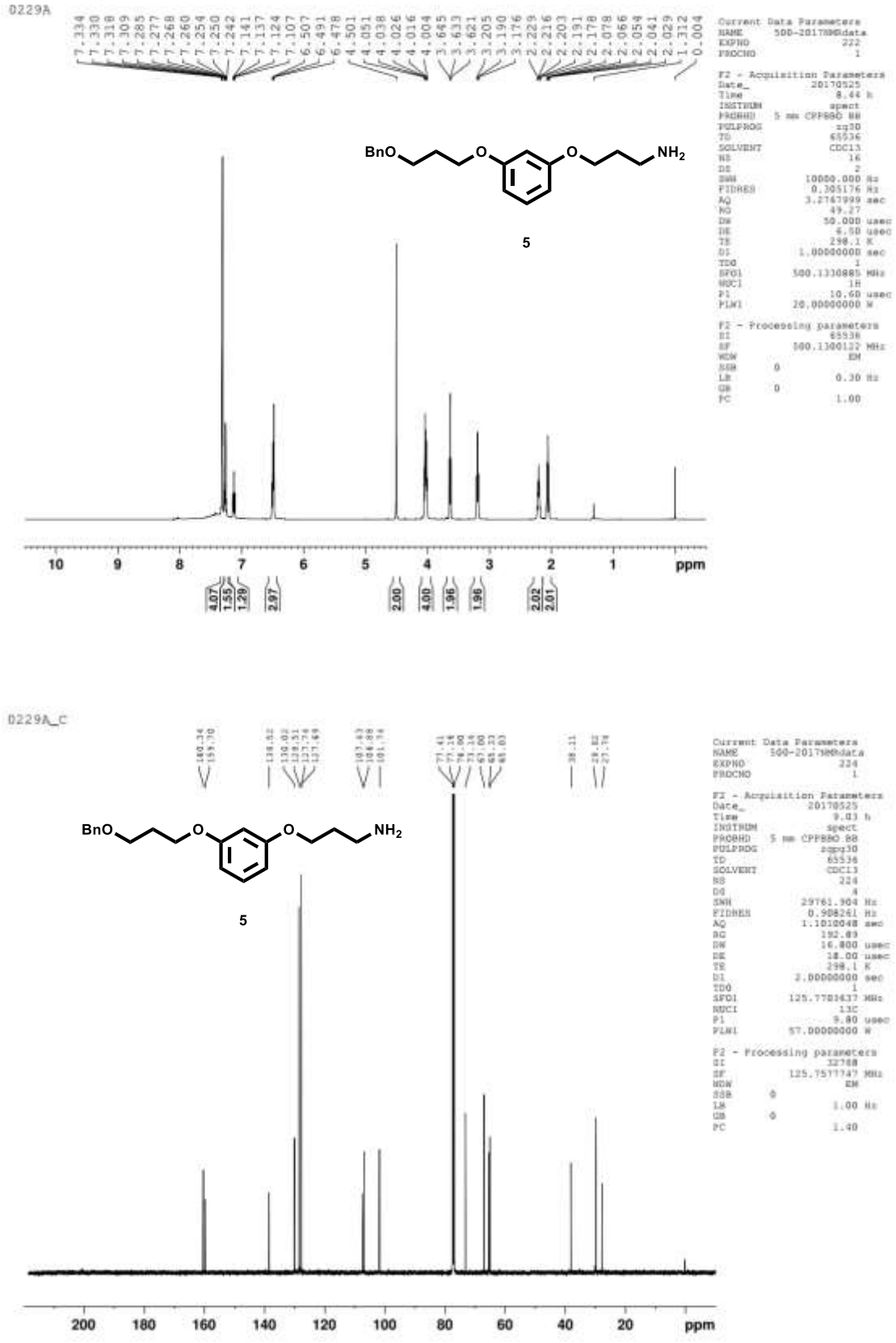


Figure S12. ^{1}H and ^{13}C NMR spectra of **5**.

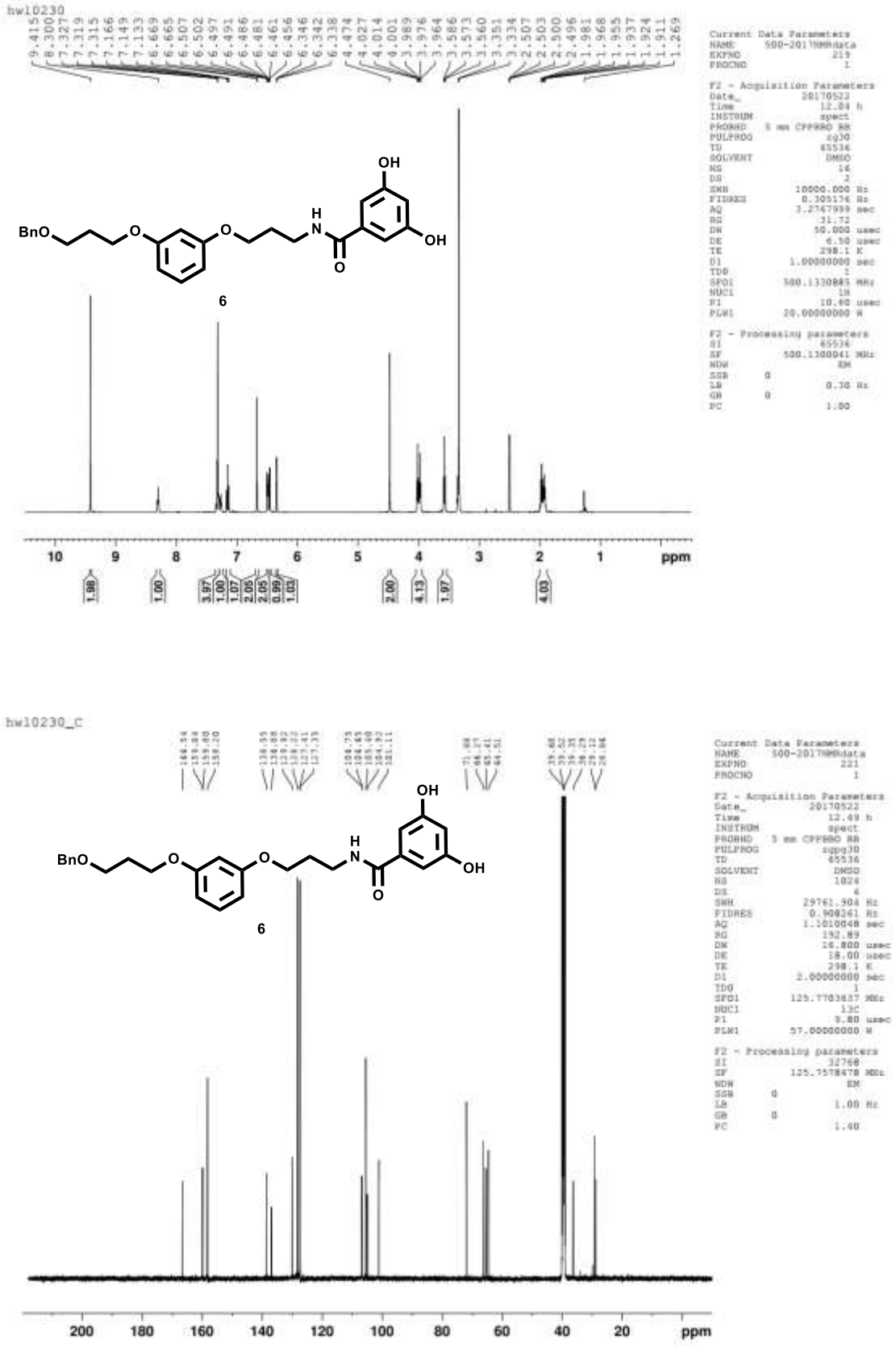


Figure S13. ^{1}H and ^{13}C NMR spectra of **6**.

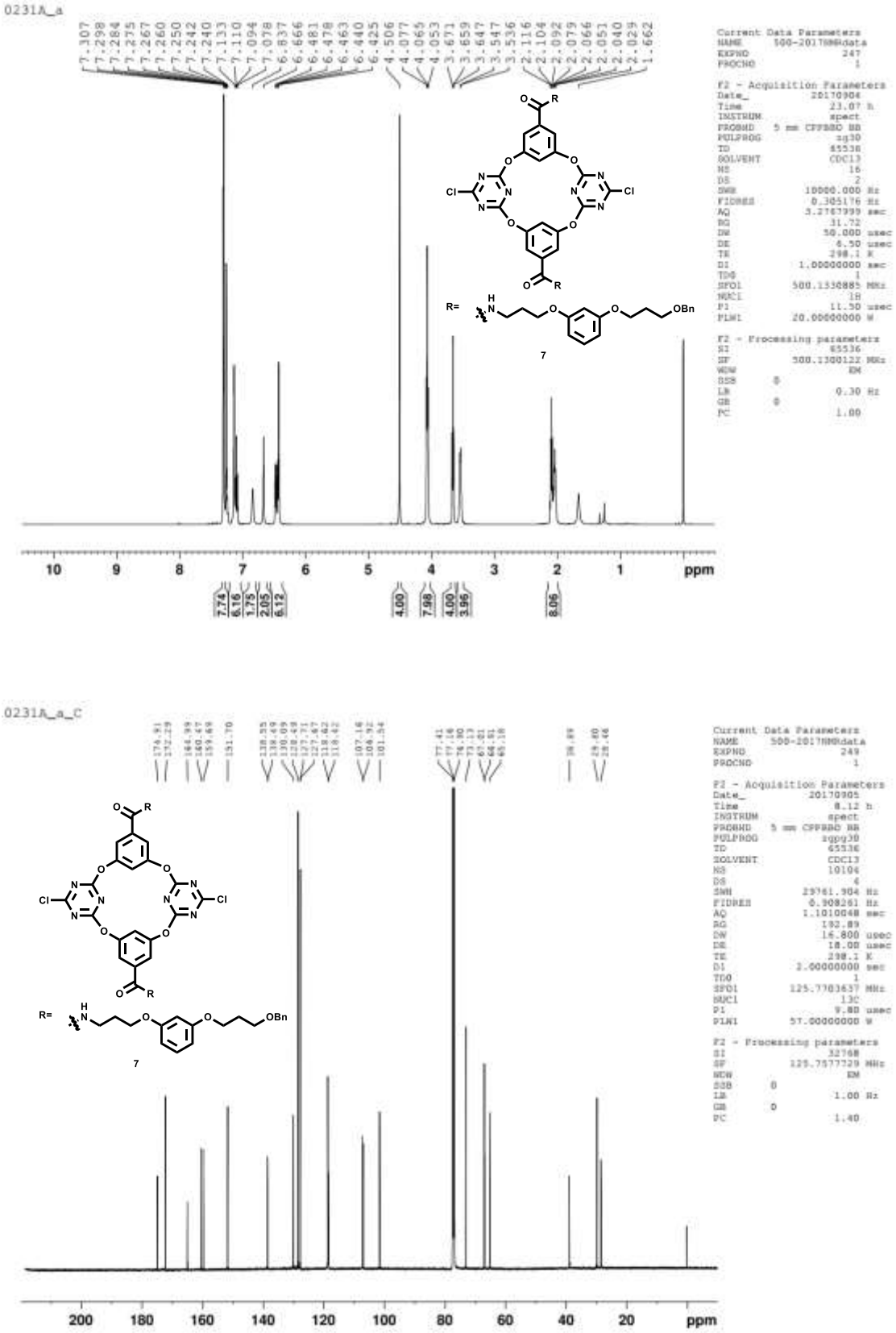
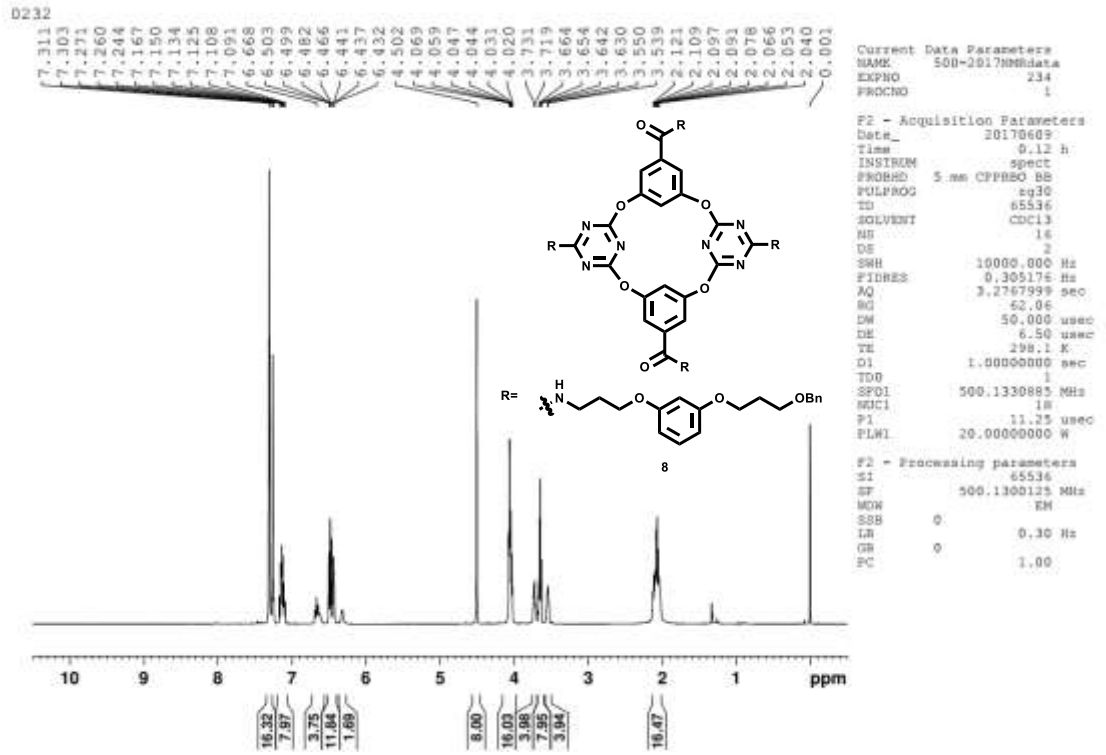


Figure S14. ^{1}H and ^{13}C NMR spectra of **7**.



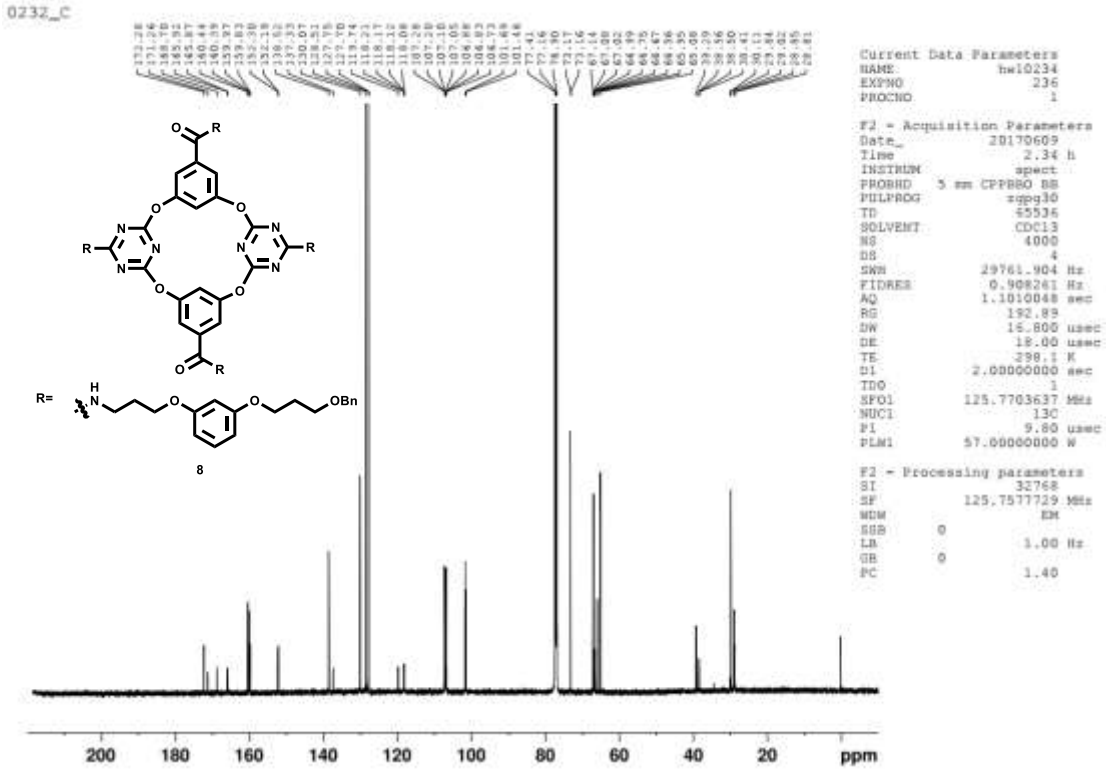


Figure S15. ^{1}H and ^{13}C NMR spectra of **8**.

7. References

[S1] W.-L. Huang, X.-D. Wang, Y.-F. Ao, Q.-Q. Wang and D.-X. Wang, *J. Am. Chem. Soc.*, 2020, **142**, 13273–13277.

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[S3] X.-D. Wang, S. Li, Y.-F. Ao, Q.-Q. Wang, Z.-T. Huang and D.-X. Wang, *Org. Biomol. Chem.*, 2016, **14**, 330–334.

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