Cyclobis(paraquat-*p*-phenylene)-Based [2]Catenanes Prepared by Kinetically Controlled Reactions Involving Alkynes

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Supporting Information

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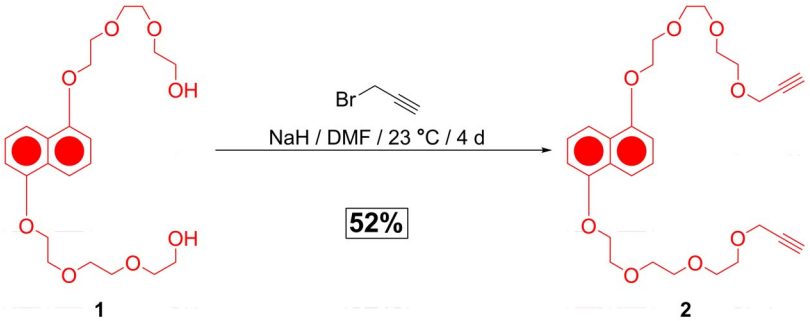
General Methods. All reagents were purchased from commercial suppliers (Aldrich or Fisher) and used without further purification. Cyclobis(paraquat-*p*-phenylene) hexafluorophosphate,[1] 1,5-bis[2-(2-(2-hydroxyethoxy)ethoxy)ethoxy]naphthalene,[2] and 1,1′-[1,4-phenylenebis(methylene)]bis-4,4′-bipyridinium hexafluorophosphate[3] were prepared according to literature procedures. Microwave-assisted reactions were performed in a CEM Discover System 908005, producing monochromatic microwave radiation with the frequency of 2455 MHz. Thin layer chromatography (TLC) was performed on silica gel 60 F_{254} (E. Merck). Column chromatography was performed on silica gel 60F (Merck 9385, 0.040–0.063 mm). Melting points were recorded on an Electrothermal 9100 instrument in open capillary tubes and are uncorrected. Nuclear magnetic resonance (NMR) spectra were recorded at 25 °C on a Bruker Avance 400 and 500 spectrometers, with working frequencies of 400 and 500 MHz for ^{1}H, and 100 and 125 MHz for ^{13}C nuclei respectively. Chemical shifts are reported in ppm relative to the signals corresponding to the residual non-deuterated solvents ($CDCl_3$: δ7.26 ppm, CD_3CN: δ1.93 ppm). All ^{13}C spectra were recorded with the simultaneous decoupling of proton nuclei. Fast atom bombardment mass spectra were obtained on a JEOL JMS-600H high resolution mass spectrometer equipped with a FAB probe.

Scheme S1. Synthesis of DNP Dialkyne Derivative **2**.

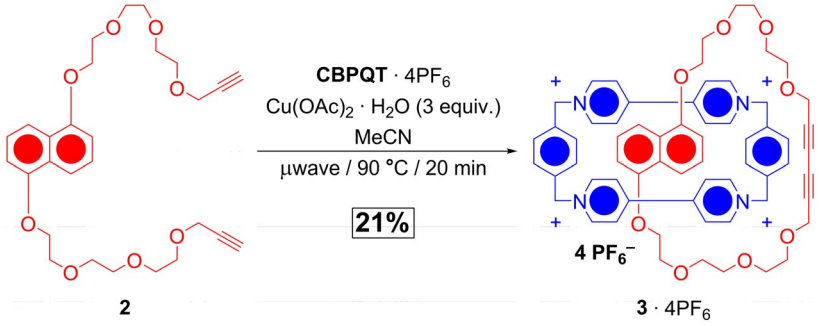


Preparation of 1,5-Bis(2-(2-(2-(prop-2-ynyloxy)ethoxy)ethoxy)ethoxy)naphthalene 2:

Solid NaH (362 mg, 15.1 mmol) was added to the solution of 1,5-bis[2-(2-(2-hydroxyethoxy)ethoxy)ethoxy]naphthalene[2] (**1**) (1.60 g, 3.78 mmol) in dry DMF (50 mL). The resulting suspension was stirred at 23 °C until the evolution of gas ceased (approx. 25

min). A solution of propargyl bromide in xylene (80% by weight, 4.20 mL, 37.8 mmol) was injected using a syringe. The mixture was stirred at 23 °C for 4 d, during which time it gradually turned brown. The reaction was stopped by the addition of MeOH, and the solvents were removed in vacuo. Crude brown oil was first filtered through a plug of silica, eluting with Me_2CO, and then subjected to chromatography on silica (hexane/EtOAc = 50/50) to provide **2** as a brown oil (0.98 g, 52%). **2**: MS (FAB+): *m/z* (rel intensity) = 502 (16%), 501 (48), 500 (M^+, 100), 460 (4), 433 (16), 419 (18). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.86 (d, ^3J (H,H) = 8.9 Hz, 2H, DNP aryl –H *p*-O), 7.34 (t, ^3J (H,H) = 8.2 Hz, 2H, DNP aryl –H *m*-O), 6.84 (d, ^3J (H,H) = 7.6 Hz, 2H, DNP aryl –H *o*-O), 4.29 (t, ^3J (H,H) = 4.9 Hz, 4H, DNP–OCH_2), 4.19 (d, ^4J (H,H) = 2.4 Hz, 4H, propargyl CH_2), 3.99 (t, ^3J (H,H) = 4.9 Hz, 4H), 3.81–3.79 (m, 4H), 3.71–3.68 (m, 8H), 2.41 (t, ^4J (H,H) = 2.4 Hz, 2H, ≡C–*H*). ^{13}C NMR (125 MHz, $CDCl_3$): δ 154.23, 126.67, 124.96, 114.51, 105.56, 79.56 (*C*≡C–H), 74.39 (C≡*C*–H), 70.88, 70.63, 70.37, 69.73, 69.02, 67.81, 58.29. HRMS Calcd for $C_{28}H_{36}O_8$: 500.2410. Found: 500.2425.

Scheme S2. Microwave-Assisted Synthesis of Catenane **3** · $4PF_6$.

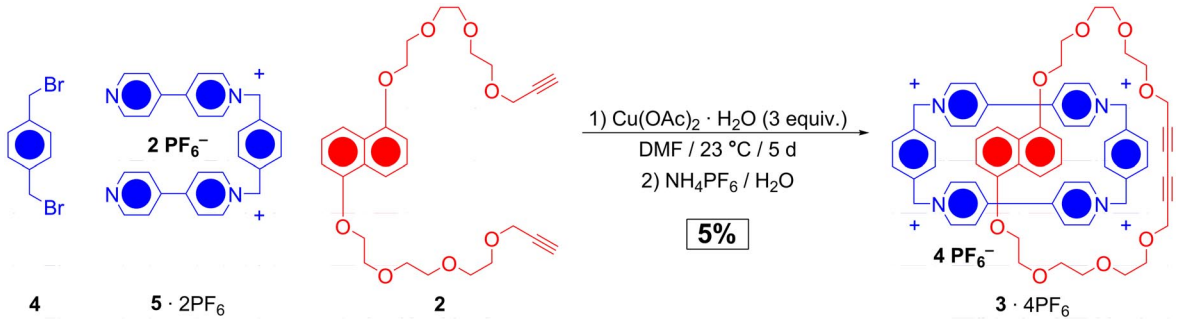


Microwave-Assisted Preparation of the [2]Catenane 3 · $4PF_6$:

The DNP derivative **2** (15.0 mg, 0.03 mmol), **CBPQT** · $4PF_6$ (10.0 mg, 0.009 mmol), and $Cu(OAc)_2 \cdot H_2O$ (8.0 mg, 0.04 mmol) were dissolved in MeCN (3.0 mL), forming a deep greenish-blue solution. The mixture was transferred into a 5 mL Intellivent thick-walled vial, sealed, and exposed to microwave irradiation for 20 min at 90 °C. After this time, a significant amount of black precipitate was observed in the reaction vial and the color of the solution changed to purple. The crude reaction mixture was filtered through silica,

eluting with a 1% solution of NH_4PF_6 in Me_2CO. The eluent was then treated with cold H_2O to precipitate a purple solid. This solid was purified by column chromatography, eluting first with EtOAc (to remove the uncharged species), then continuing with Me_2CO, and ending with 2% solution of NH_4PF_6 in Me_2CO. The purple band was collected and was again treated with cold H_2O, precipitating a purple solid. After air-drying, this material was identified as the [2]catenane **3** · $4PF_6$ (3.1 mg, 21%, mp 185 °C with decomp.). Performing the same reaction at 23 °C in a round-bottom flask for 4 d provided [2]catenane **3** · $4PF_6$ in 14% yield. Spectroscopic data collected for the two samples were identical. **3** · $4PF_6$: MS (FAB+): *m/z* (rel intensity) = 1453 ([**3** · $3PF_6$], 41%), 1308 ([**3** · $2PF_6$], 68), 1163 ([**3** · PF_6], 24), 955 ([**CBPQT** · $3PF_6$], 18), 810 ([**CBPQT** · $2PF_6$], 100), 665 ([**CBPQT** · PF_6], 58). ^{1}H NMR (500 MHz, CD_3CN): δ 9.07 (br s, 4H, α-$CBPQT^{4+}$ –H), 8.61 (d, ^3J (H,H) = 6.4 Hz, 4H, α-$CBPQT^{4+}$ –H), 8.03 (s, 4H, aryl-$CBPQT^{4+}$ –H), 7.94 (s, 4H, aryl-$CBPQT^{4+}$ –H), 7.42 (br d, ^3J (H,H) = 5.0 Hz, 4H, β-$CBPQT^{4+}$ –H), 7.23 (br d, ^3J (H,H) = 5.0 Hz, 4H, β-$CBPQT^{4+}$ –H), 6.27 (d, ^3J (H,H) = 7.6 Hz, 2H, DNP aryl –H *o*-O), 5.99 (t, ^3J (H,H) = 7.9 Hz, 2H, DNP aryl –H *m*-O), 5.71 (s, 8H, $CBPQT^{4+}$ benzyl H), 5.70 (s, 8H, $CBPQT^{4+}$ benzyl H), 4.31 (br s, 4H), 4.22 (br s, 4H), 4.02 (t, ^3J (H,H) = 4.0 Hz, 4H), 3.85 (br s, 4H), 3.69 (s, 4H, propargyl C*H*$_2$), 3.62 (br s, 4H), 3.29 (br s, 4H), 2.42 (d, ^3J (H,H) = 8.2 Hz, 2H, DNP aryl –H *p*-O). HRMS Calcd for $C_{64}H_{66}N_4O_8P_3F_{18}$ ([**3** · $3PF_6$]): 1453.381. Found: 1453.385.

Scheme S3. Synthesis of Catenane **3** · $4PF_6$ by Tandem Hetero-Catenation.

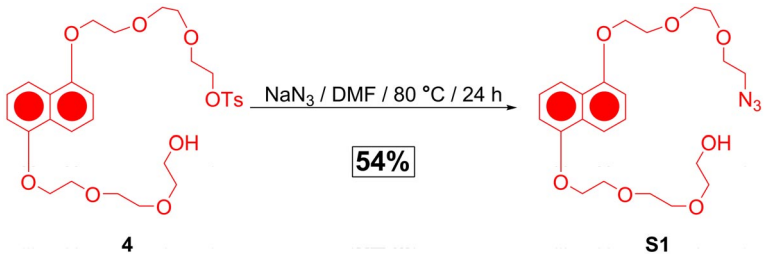


Preparation of the [2]Catenane 3 · $4PF_6$ by Tandem Hetero-Catenation:

The DNP derivative **2** (150 mg, 0.3 mmol), 1,4-bisbromomethylbenzene **4** (26.4 mg, 0.1 mmol), 1,1′-[1,4-phenylenebis(methylene)]bis-4,4′-bipyridinium hexafluorophosphate[3] **5** ·

$2PF_6$ (70.6 mg, 0.1 mmol), and $Cu(OAc)_2 \cdot H_2O$ (180 mg, 0.9 mmol) were combined in DMF (5.0 mL). The mixture was stirred at 23 °C for 5 d. During the course of reaction, the solution gradually changed color from brownish-yellow to purple, and precipitation was observed. After the completion of the reaction, the crude reaction mixture was filtered through a plug of silica (1% solution of NH_4PF_6 in Me_2CO) to provide a reddish-purple solution. The crude catenane was precipitated by the addition of H_2O. This chromatography-precipitation-filtration sequence was repeated two more times, to provide ultimately the [2]catenane **3** $\cdot 4PF_6$ as a purple solid (8.0 mg, 5%). Spectroscopic data for this material were identical to those obtained for the product isolated from the microwave-assisted reaction.

Scheme S4. Synthesis of DNP Azido Derivative **S1**.

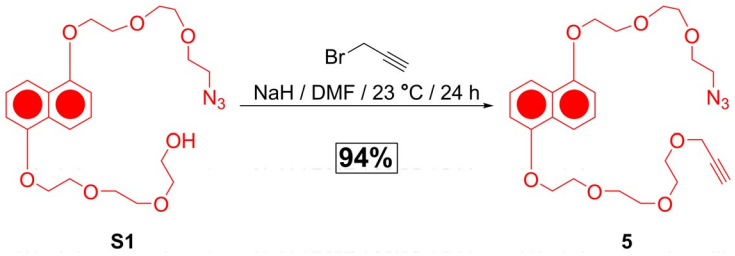


Preparation of 1-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)-5-(2-(2-(2-hydroxyethoxy)-ethoxy)ethoxy)naphthalene S1:

A solution of tosylate **4**[4] (120 mg, 0.207 mmol), and NaN_3 (27.0 mg, 0.415 mmol) in dry DMF (15 mL) was heated at 80 °C for 2 d. After cooling, the solution was diluted with H_2O (50 mL) and EtOAc (50 mL) was added. The layers were separated and the organic solution was washed with two portions of a saturated aqueous solution of NH_4Cl, followed by drying ($MgSO_4$). The crude product, obtained after the removal of the solvent, was subjected to chromatography on silica (EtOAc) to provide 51.0 mg of **S1** as a viscous orangish oil (55%). **S1**: MS (FAB+): *m/z* (rel intensity) = 449 (M^+, 100%), 422 (36), 317 (11). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.82 (d, ^3J (H,H) = 8.2 Hz, 1H, DNP aryl –H *p*-O), 7.81 (d, ^3J (H,H) = 8.2 Hz, 1H, DNP aryl –H *p*-O), 7.30 (t, ^3J (H,H) = 8.5 Hz, 1H, DNP aryl –H *m*-O), 7.29 (t, ^3J (H,H) = 8.5 Hz, 1H, DNP aryl –H *m*-O), 6.78 (d, ^3J (H,H) = 7.6

Hz, 1H, DNP aryl –H *o*-O), 6.77 (d, ^{3}J (H,H) = 7.6 Hz, 1H, DNP aryl –H *o*-O), 4.23–4.20 (m, 4H, DNP –OCH_2), 3.93–3.90 (m, 4H), 3.74–3.71 (m, 4H), 3.66–3.59 (m, 8H), 3.54 (t, ^{3}J (H,H) = 4.6 Hz, 2H), 3.29 (t, ^{3}J (H,H) = 4.9 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 154.18, 154.13, 126.61, 126.59, 124.99, 124.93, 114.49, 114.41, 105.52 (2C), 72.43, 70.85, 70.81, 70.57, 70.29, 69.91, 69.70, 69.62, 67.74, 67.70, 61.52, 50.50. HRMS Calcd for $C_{28}H_{36}O_8$: 500.2410. HRMS Calcd for $C_{22}H_{31}N_3O_7$: 449.2162. Found: 449.2171.

Scheme S5. Synthesis of DNP Azidoalkyne Derivative **5**.

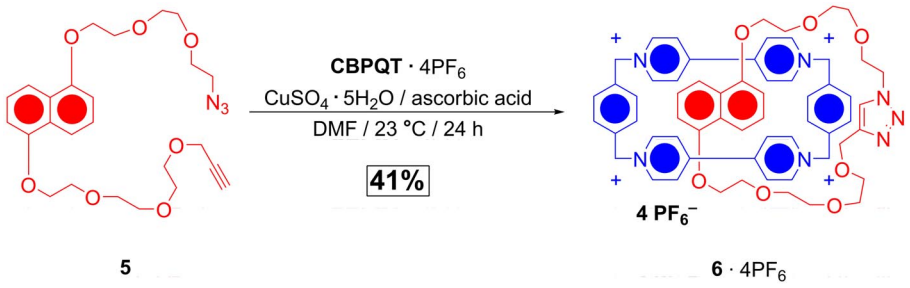


Preparation of 1-(2-(2-(2-azidoethoxy)ethoxy)ethoxy)-5-(2-(2-(2-(prop-2-ynyloxy)-ethoxy)ethoxy)ethoxy)naphthalene 5:

Solid NaH (5.0 mg, 0.208 mmol) was added to the solution of **S1** (45.0 mg, 0.100 mmol) in dry DMF (20 mL). The resulting suspension was stirred at 23 °C until the evolution of gas ceased (approx. 25 min). A solution of propargyl bromide in xylene (80% by weight, 56 µL, 0.5 mmol) was injected using a syringe. The mixture was stirred at 23 °C for 24 h, during which time it gradually turned brown. The reaction was stopped by the addition of MeOH, and the solvents were removed in vacuo. Crude brown oil was first filtered through a plug of silica, eluting with Me_2CO, and then subjected to chromatography on silica (hexane/EtOAc = 50/50) to provide **5** as a brown oil (46.0 g, 94%). **5**: MS (FAB+): *m/z* (rel intensity) = 526 ([M+K]$^+$, 25%), 487 (M$^+$, 100), 460 ([M–CH_2C≡CH]$^+$, 27), 288 (17). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.84 (d, ^{3}J (H,H) = 8.2 Hz, 2H, DNP aryl –H *p*-O), 7.31 (t, ^{3}J (H,H) = 8.2 Hz, 2H, DNP aryl –H *m*-O), 6.79 (d, ^{3}J (H,H) = 7.6 Hz, 2H, DNP aryl –H *o*-O), 4.22 (br t, ^{3}J (H,H) = 4.9 Hz, 4H, DNP –OCH_2), 4.14 (d, ^{4}J (H,H) = 2.4 Hz, 2H, propargyl CH_2), 3.92 (br t, ^{3}J (H,H) = 4.6 Hz, 4H), 3.75–3.73 (m, 4H), 3.65–3.59 (m, 8H), 3.29 (br t, ^{3}J (H,H) = 4.9 Hz, 4H), 2.43 (t, ^{4}J (H,H) = 2.4 Hz, 1H, ≡C–*H*). ^{13}C NMR (125

MHz, $CDCl_3$): δ 154.21, 154.19, 126.62 (2C), 124.98 (2C), 114.50, 114.44, 105.53 (2C), 79.60 (*C*≡C–H), 74.55 (C≡*C*–H), 70.85, 70.80, 70.57, 70.54, 70.30, 69.91, 69.71, 69.64, 68.96, 67.75 (2C), 58.22, 50.51. HRMS Calcd for $C_{25}H_{33}N_3O_7$: 487.2318. Found: 487.2324.

Scheme S6. Synthesis of Catenane **6** · $4PF_6$.



Preparation of the [2]Catenane 6 · $4PF_6$:

The DNP derivative **5** (24.0 mg, 0.05 mmol) and **CBPQT** · $4PF_6$ (55.0 mg, 0.05 mmol), were dissolved in 50 mL of DMF. Stock solutions of ascorbic acid (containing 0.88 mg, 0.005 mmol) and $CuSO_4 \cdot 5H_2O$ (containing 1.25 mg, 0.005 mmol) in DMF were diluted to 50 mL. Into this mixture, the solution of **5** and **CBPQT** · $4PF_6$ was dripped in over 5 h. After the addition was complete, the mixture was left to stir at 23 °C for 24 additional h. The solvent was removed in vacuo, and the crude purple solid was purified by column chromatography on silica (gradient elution: 1% → 5% solution of NH_4PF_6 in Me_2CO). Crude catenane **6** · $4PF_6$ was precipitated by the addition of water and filtered. This procedure was repeated twice, to yield a purple powder, containing **6** · $4PF_6$, contaminated with **CBPQT** · $4PF_6$ as minor fraction. This powder was washed with three portions of cold MeOH. Evaporation of the solvent from the combined wash solutions yielded pure **6** · $4PF_6$ as a purple solid, mp 190 °C with decomp. Yield: 32.0 mg (41%). **6** · $4PF_6$: MS (FAB+): *m/z* (rel intensity) = 1442 ([**6** · $3PF_6$], 50%), 1297 ([**6** · $2PF_6$], 100), 1152 ([**6** · PF_6], 36), 955 ([**CBPQT** · $3PF_6$], 20), 810 ([**CBPQT** · $2PF_6$], 92), 665 ([**CBPQT** · PF_6], 67). ^{1}H NMR (500 MHz, CD_3CN): δ 9.15 (d, ^3J (H,H) = 6.4 Hz, 1H, α-$CBPQT^{4+}$ –H), 8.86 (br s, 1H, α-$CBPQT^{4+}$ –H), 8.83 (d, ^3J (H,H) = 7.0 Hz, 1H, α-$CBPQT^{4+}$ –H), 8.73 (d, ^3J (H,H) = 6.4 Hz, 2H, α-$CBPQT^{4+}$ –H), 8.68 (d, ^3J (H,H) = 6.4 Hz, 1H, α-$CBPQT^{4+}$ –H),

8.65 (d, ^3J (H,H) = 6.4 Hz, 1H, α-CBPQT^{4+} –H), 8.51 (d, ^3J (H,H) = 6.4 Hz, 1H, α-CBPQT^{4+} –H), 8.17 (d, ^3J (H,H) = 6.1 Hz, 1H, β-CBPQT^{4+} –H), 7.99 (d, ^3J (H,H) = 6.1 Hz, 1H, β-CBPQT^{4+} –H), 7.97–7.92 (m, 6H, β-CBPQT^{4+} –H), 7.53 (br s, 1H, aryl-CBPQT^{4+} –H), 7.40 (br d, ^3J (H,H) = 6.1 Hz, 1H, aryl-CBPQT^{4+} –H), 7.37–7.17 (m, 5H, aryl-CBPQT^{4+} –H), 7.05 (s, 1H, triazole –H), 6.86 (br d, ^3J (H,H) = 6.1 Hz, 1H, aryl-CBPQT^{4+} –H), 6.33 (d, ^3J (H,H) = 7.9 Hz, 1H, DNP aryl –H *o*-O), 6.31 (d, ^3J (H,H) = 7.4 Hz, 1H, DNP aryl –H *o*-O), 5.97 (t, ^3J (H,H) = 7.6 Hz, 1H, DNP aryl –H *m*-O), 5.86 (t, ^3J (H,H) = 7.6 Hz, 1H, DNP aryl –H *m*-O), 5.74–5.55 (m, 8H, CBPQT^{4+} benzyl H), 4.56 (m, 2H), 4.33–3.51 (m, 24H), 2.32 (d, ^3J (H,H) = 7.9 Hz, 2H, DNP aryl –H *p*-O). HRMS Calcd for $C_{61}H_{65}N_7O_7P_2F_{12}$ ([**6** · $2PF_6$]): 1297.423. Found: 1297.426.

Characterization of the [2]Catenanes 3 · $4PF_6$ and 6 · $4PF_6$ by ^{1}H NMR Spectroscopy:

The ^{1}H NMR spectra (recorded in CD_3CN at 25 °C) of **3** · $4PF_6$ and **6** · $4PF_6$ are shown in Figure S1 with partial assignments.

References:

(1) Asakawa, M.; Dehaen, W.; L'abbé, G.; Menzer, S.; Nouwen, J.; Raymo, F. M.; Stoddart, J. F.; Williams, D. J. *J. Org. Chem.* **1996**, *61*, 9591–9595.

(2) Ashton, P. R.; Huff, J.; Menzer, S.; Parsons, I. W.; Preece, J. A.; Stoddart, J. F.; Tolley, M. S.; White, A. J. P.; Williams, D. J. *Chem. Eur. J.* **1996**, *2*, 31–44.

(3) Anelli, P. L.; Ashton, P. R.; Ballardini, R.; Balzani, V.; Delgado, M.; Gandolfi, M. T.; Goodnow, T. T.; Kaifer, A. E.; Philp, D.; Pietraszkiewicz, M.; Prodi, L.; Reddington, M. V.; Slawin, A. M. Z.; Spencer, N.; Stoddart, J. F.; Vicent, C.; Williams, D. J. *J. Am. Chem. Soc.* **1992**, *114*, 193–218.

(4) Liu, Y.; Saha, S.; Vignon, S. A.; Flood, A. H.; Stoddart, J. F. *Synthesis* **2005**, 3437–3455.

Figure S1. ^{1}H NMR Spectra of [2]Catenanes **3** · 4PF_6 and **6** · 4PF_6.