

Supporting Information

Selecting Reactions and Reactants using a Switchable Rotaxane Organocatalyst with Two Different Active Sites

Jack Beswick,^a Victor Blanco,^a Guillaume De Bo,^a David A. Leigh,^{a*} Urszula Lewandowska,^a Bartosz Lewandowski,^a and Kenji Mishirot^a

School of Chemistry, University of Manchester, Oxford Road, Manchester, M13 9PL
(UK)

* E-mail: david.leigh@manchester.ac.uk
Homepage: <http://www.catenane.net>

Table of Contents

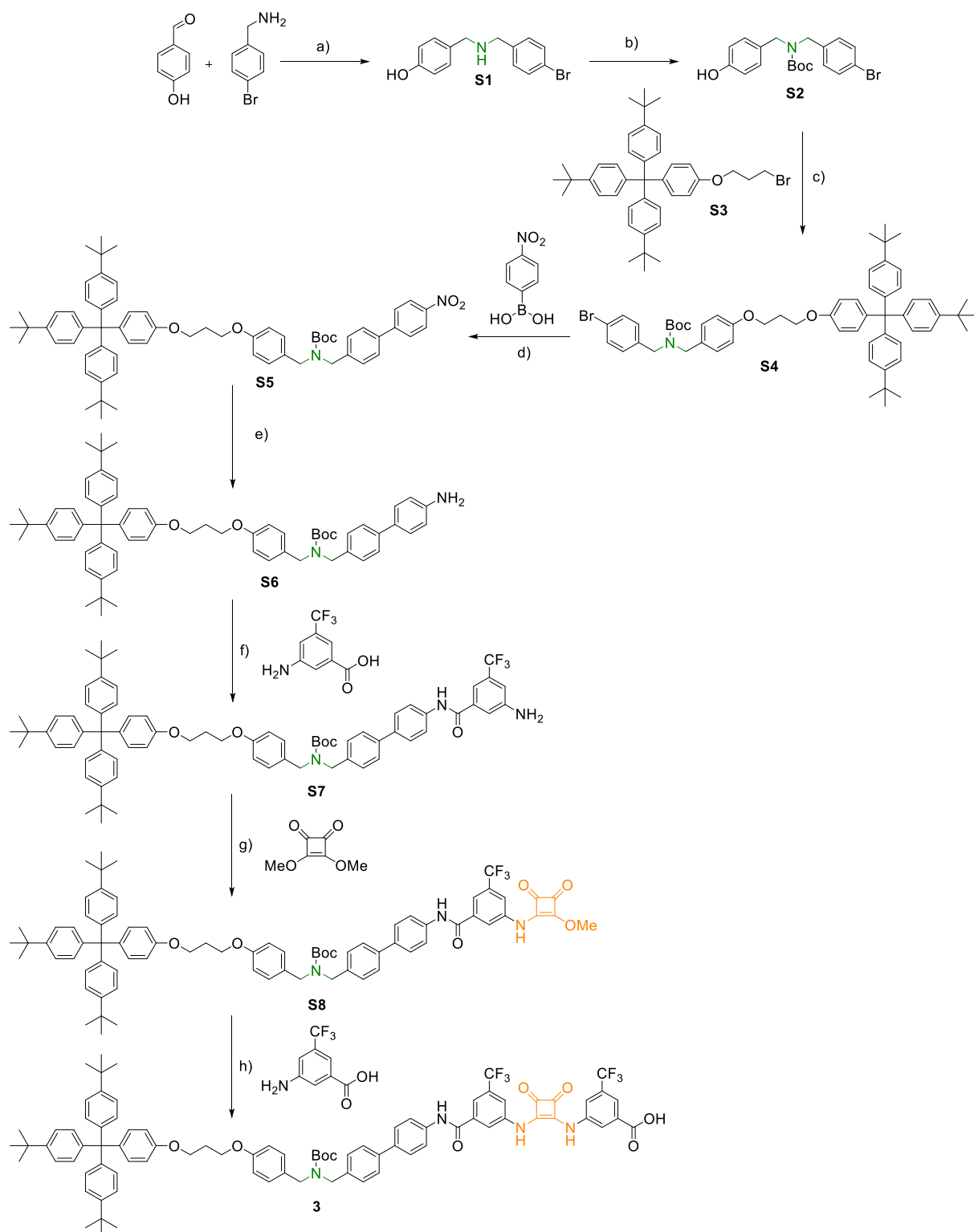
1. Experimental Section.....	S3
1.1. General Methods	S3
1.2. Synthesis Overview	S4
1.3. Synthetic Procedures and Characterization Details.....	S7
1.4. ¹ H NMR spectra for selected compounds	S18
2. Additional Supporting Figures	S22
3. References and notes	S23

1. Experimental Section

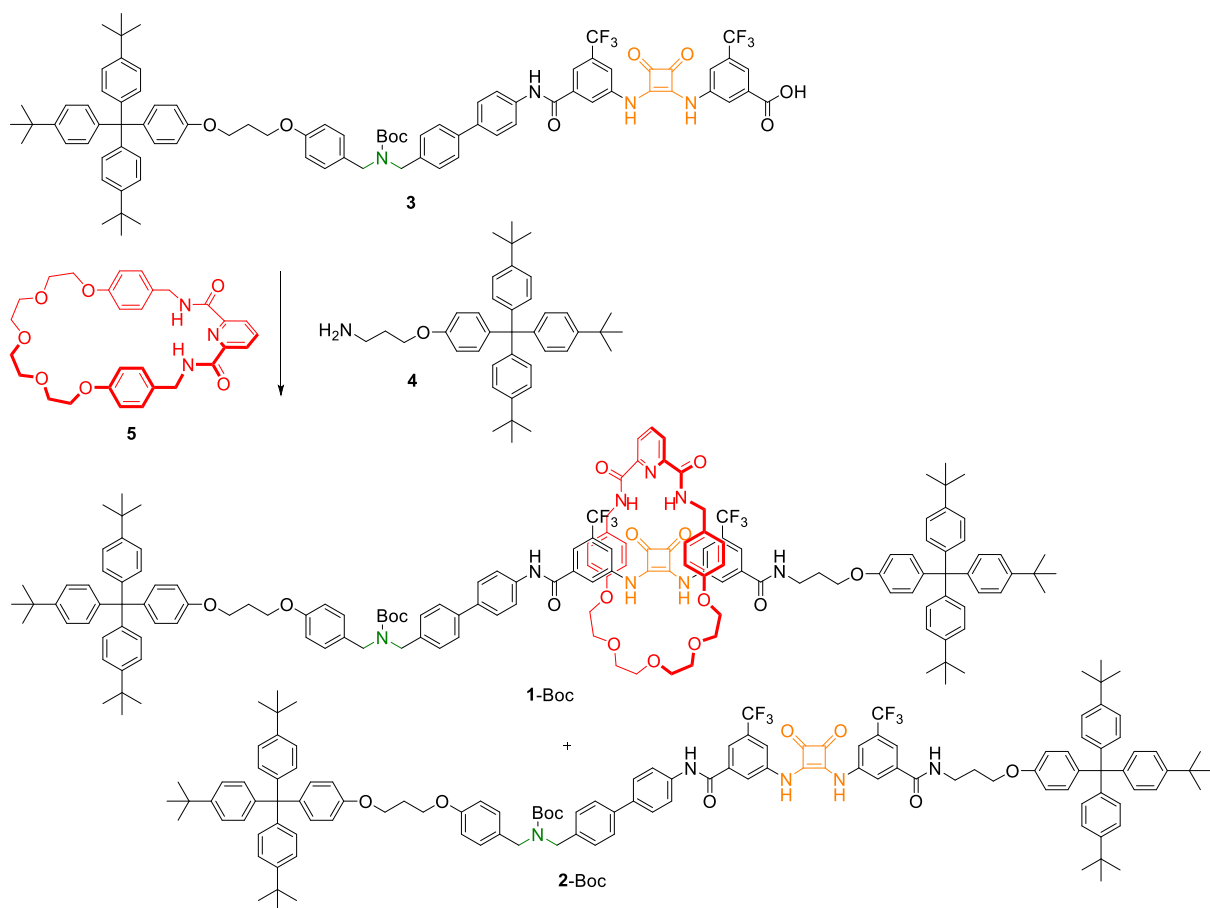
1.1. General Methods

Unless stated otherwise, all reagents and solvents were purchased from Aldrich Chemicals and used without further purification. 4-[*tris*-(4-*tert*-butylphenyl)methyl]phenol (**S8**)¹ and compounds **S3**,² **5**³ and **10**⁴ were prepared according to literature procedures. Dry THF was obtained by passing the solvent (HPLC grade) through an activated alumina column on a Phoenix SDS solvent drying system (JC Meyer Solvent Systems, CA, USA). Dry MeOH and dry DMF were purchased from Sigma-Aldrich. Peptide grade DMF was purchased from Applied Biosystems. Column chromatography was carried out using Aldrich Si 60 (particle size 40-63 μm) as the stationary phase, and TLC was performed on precoated silica gel plates (0.25 mm thick, 60 F₂₅₄, Merck, Germany) and observed under UV light. NMR spectra were recorded on a Bruker Avance III 400 or a Bruker Avance III (equipped with a cryoprobe) instrument with an Oxford AS600 magnet. Chemical shifts are reported in parts per million (ppm) from high to low frequency and referenced to the residual solvent resonance. Coupling constants (*J*) are reported in hertz (Hz). Standard abbreviations indicating multiplicity were used as follows: s = singlet, d = doublet, t = triplet, q = quartet, quin = quintuplet, m = multiplet, br = broad. ¹H assignments were made using 2D NMR methods (COSY, HSQC, HMBC). Melting points (M. p.) were determined using a Büchi M-565 apparatus and are reported uncorrected. Low resolution ESI mass spectrometry was performed with a Thermo Scientific LCQ Fleet mass spectrometer. High resolution ESI (electrospray ionization) mass spectrometry was carried out by the mass spectrometry services at the University of Manchester.

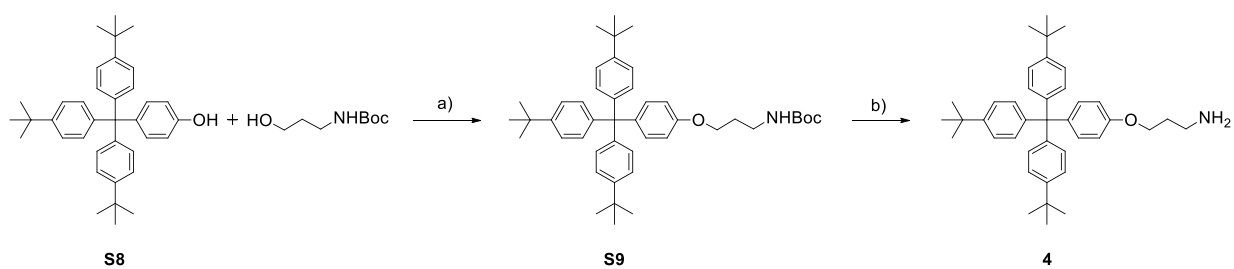
1.2. Synthesis Overview



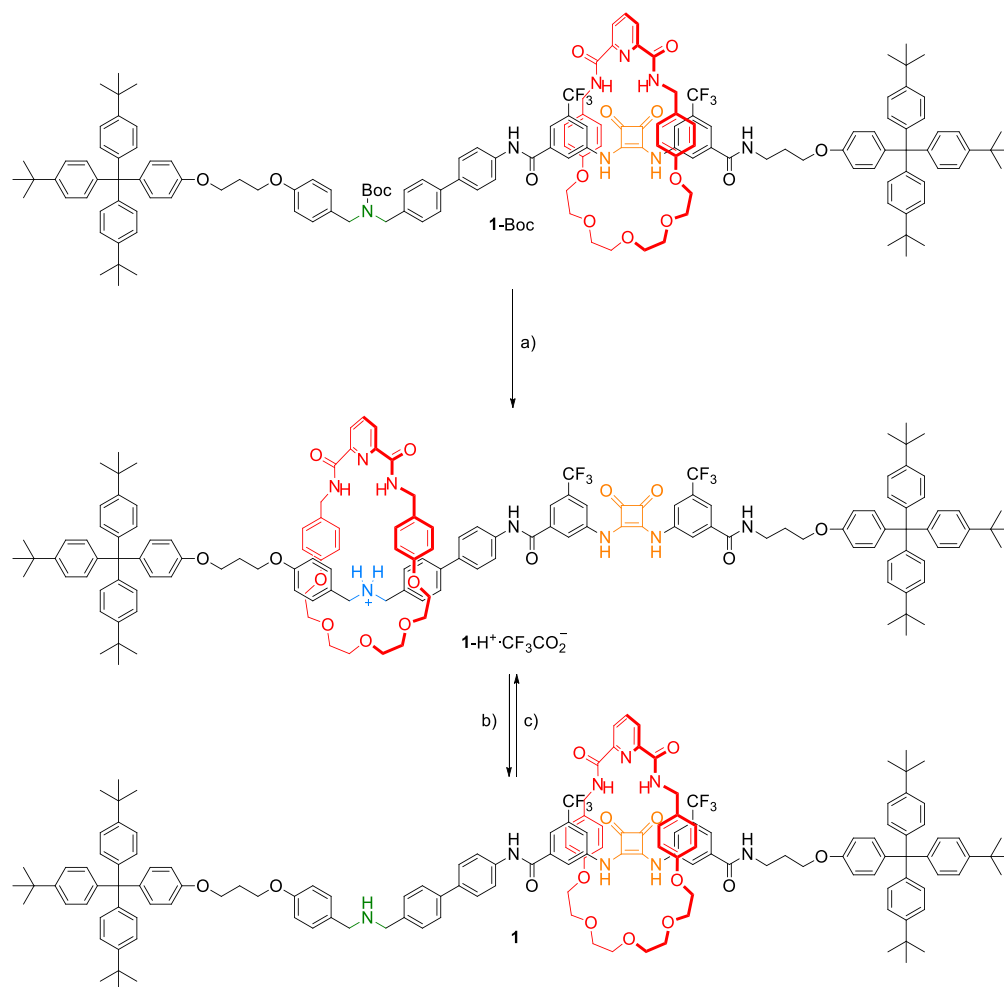
Scheme S1. Synthesis of compound **3**. Reagents and conditions: a) i) MeOH, RT, O/N; ii) NaBH₄, THF/MeOH, RT, O/N, 89%. b) Boc₂O, Et₃N, MeOH, RT, O/N, 84%. c) Cs₂CO₃, DMF, KI, 80 °C, 3 d, 85%. d) Pd(PPh₃)₄, Na₂CO₃, THF/H₂O, 75 °C, O/N, 90%. e) H₂, Pd(OH)₂/C, K₂CO₃, THF, RT, 5 h, 95%. f) EDCl, HOBT, THF/CHCl₃, RT, 2 d, 69% g) CH₂Cl₂/MeOH, RT, 2 d, 94%. h) Zn(OTf)₂, Toluene/DMF, 105 °C, O/N, 25%.



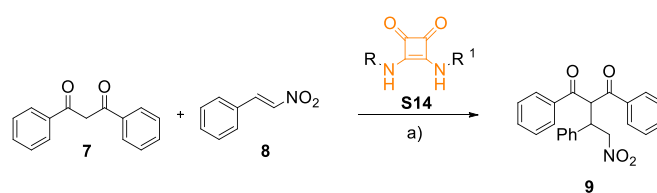
Scheme S2: Synthesis of rotaxane **1-Boc**. Reagents and conditions: PyBroP, DIPEA, CH₂Cl₂/THF/CH₃CN, RT, O/N, 47% (**1-Boc**), 46% (**2-Boc**).



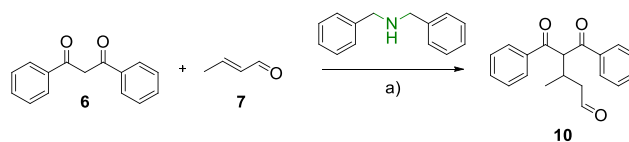
Scheme S3. Synthesis of amine functionalized stopper **4**. Reagents and conditions: a) PPh₃, DIAD, THF, RT, 12 h, 85%. b) CF₃CO₂H, CH₂Cl₂, RT, 4 h, 95%.



Scheme S4. Synthesis of rotaxane **1** and acid/base switching of the position of the macrocycle. Reagents and conditions: a) $\text{CF}_3\text{CO}_2\text{H}$, CH_2Cl_2 , RT, 1.5 h, quant. b) $\text{NaOH}_{(\text{aq})}$ 2M, CH_2Cl_2 , RT, 1 h, quant. c) $\text{CF}_3\text{CO}_2\text{H}$, CH_2Cl_2 , RT, 30 min, quant.



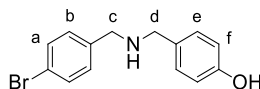
Scheme S5. Synthesis of compound **9**. Reagents and conditions: a) NaOAc , CH_2Cl_2 , RT, 16 h, 70%.



Scheme S6. Synthesis of compound **10**.⁴ Reagents and conditions: a) CH_2Cl_2 , RT, 48 h, 70%.

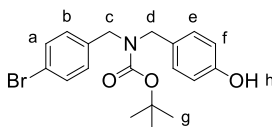
1.3. Synthetic Procedures and Characterization Details

Synthesis of S1



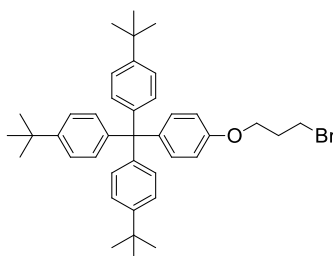
A solution of 4-hydroxybenzaldehyde (0.66 g, 5.37 mmol, 1.00 equiv.) and 4-bromobenzylamine (0.68 mL, 5.37 mmol, 1.00 equiv.) in dry MeOH (20 mL) was stirred overnight at room temperature under a N₂ atmosphere. The white precipitate formed was filtered and dissolved in THF/MeOH (1:3, 100 mL). To the resulting solution, NaBH₄ (0.609 g, 16.3 mmol, 3.00 equiv.) was added and the mixture was stirred overnight at room temperature under N₂. NH₄Cl_{aq(sat)} (25 mL) was added and the organic solvents were removed under reduced pressure. The resulting mixture was extracted with EtOAc (3 × 150 mL). The combined organic extracts were washed with brine (200 mL), dried with MgSO₄ and concentrated under reduced pressure to afford **S1** (1.40 g, 89%) as a pale brown solid. M. p. 142–143 °C. ¹H NMR (400 MHz, CD₃OD) δ: 7.57 (d, *J* = 8.4 Hz, 2H, H_a), 7.38 (d, *J* = 8.5 Hz, 2H, H_b), 7.28 (d, *J* = 8.5 Hz, 2H, H_e), 6.83 (d, *J* = 8.4 Hz, 2H, H_f), 4.05 (s, 2H, H_c), 4.01 (s, 2H, H_d). ¹³C NMR (100 MHz, CD₃OD) δ: 159.43, 133.90, 133.15, 132.65, 132.24, 124.89, 123.98, 116.75, 52.20, 51.39. HRMS (ESI⁺): *m/z* = 292.0336 [M+H]⁺ (calcd. 292.0332 for C₁₄H₁₅NOBr).

Synthesis of S2



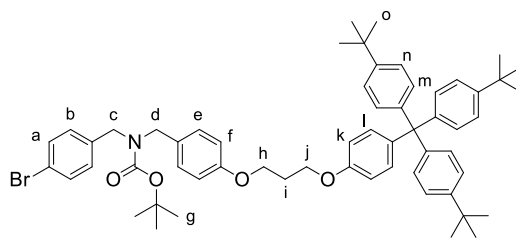
A solution of **S1** (1.38 g, 4.72 mmol, 1.00 equiv.), Boc₂O (1.29 g, 5.90 mmol, 1.25 equiv.) and Et₃N (10 mL) in MeOH (80 mL) was stirred overnight at room temperature. Water (30 mL) was added and the MeOH was removed under reduced pressure. The resulting mixture was extracted with CH₂Cl₂ (3 × 100 mL). The combined organic extracts were washed with water (150 mL), NaHCO_{3(sat)} (150 mL), water (150 mL) and dried with MgSO₄. The solvent was removed under reduced pressure to yield **S2** (1.55 g, 84%) as a yellow oil which crystallized after several days. M. p. 122–123 °C. ¹H NMR (600 MHz, CDCl₃) δ: 7.44 (d, *J* = 7.9 Hz, 2H, H_a), 7.04 (br m, 4H, H_{b+e}), 6.78 (br, 2H, H_f), 5.79 (s, 1H, H_h), 4.33–4.24 (m, 4H, H_{c+d}), 1.50 (m, 9H, H_g). ¹³C NMR (150 MHz, CDCl₃) δ: 156.24, 156.14, 155.39, 137.23, 136.99, 131.74, 129.79, 129.14, 121.59, 121.22, 121.11, 115.60, 80.69, 49.00, 48.83, 48.31, 28.60, 27.84.⁵ HRMS (ESI⁺): *m/z* = 414.0682 [M+Na]⁺ (calcd. 414.0675 for C₁₉H₂₂NO₃BrNa).

Synthesis of S3



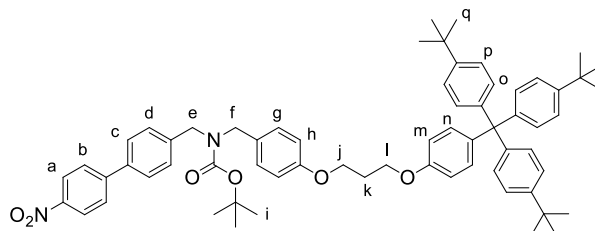
Synthesised according to a literature procedure.²

Synthesis of S4



A mixture of **S2** (1.40 g, 3.57 mmol, 1.50 equiv.), **S3** (1.49 g, 2.38 mmol, 1.00 equiv.), Cs₂CO₃ (5.82 g, 17.85 mmol, 7.50 equiv.) and a catalytic amount of KI in dry DMF (50 mL) was stirred at 80 °C for 3 d under N₂. The solvent was removed under reduced pressure and the residue was partitioned between CH₂Cl₂ (750 mL) and water (100 mL). The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (2 × 60 mL). The combined organic extracts were dried with MgSO₄ and the solvent removed under reduced pressure. Column chromatography (SiO₂, petrol ether/CH₂Cl₂ 2:1) of the residue gave **S4** (1.90 g, 85%) as a colourless solid. M. p. 85–86 °C. ¹H NMR (600 MHz, CDCl₃) δ: 7.43 (d, *J* = 8.0 Hz, 2H, H_a), 7.23 (d, *J* = 8.2 Hz, 6H, H_n), 7.08 (m, 12H, H_{b+e+m+l}), 6.86 (d, *J* = 8.2 Hz, 2H, H_f), 6.78 (d, *J* = 8.5 Hz, 2H, H_k), 4.39–4.20 (br m, 4H, H_{c+d}), 4.14 (m, 4H, H_{h+j}), 2.25 (quin, *J* = 6.1 Hz, 2H, H_i), 1.49 (m, 9H, H_g), 1.30 (s, 27H, H_o). ¹³C NMR (150 MHz, CDCl₃) δ: 158.37, 156.74, 156.01, 148.42, 144.25, 139.80, 137.22, 132.39, 131.71, 130.84, 129.87, 129.57, 129.17, 128.93, 124.17, 114.66, 113.06, 80.36, 64.63, 64.28, 63.17, 48.92, 48.67, 48.26, 34.43, 31.52, 29.47, 28.60. HRMS (ESI⁺): *m/z* = 953.4831 [M+NH₄]⁺ (calcd. 953.4826 for C₅₉H₇₄N₂O₄Br).

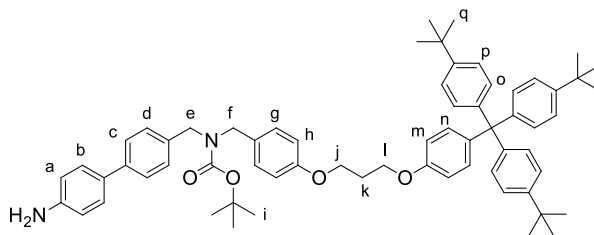
Synthesis of S5



A solution of **S4** (1.89 g, 2.02 mmol, 1.00 equiv.) and 4-nitrophenylboronic acid (0.35 g, 2.12 mmol, 1.05 equiv) in THF/water (1:1, 300 mL) was purged with N₂ for 40 min. Pd(PPh₃)₄ (0.23 g, 0.20 mmol, 0.10 equiv) and Na₂CO₃ (1.28 g, 12.12 mmol, 6.00 equiv.) were added and the resulting mixture was stirred overnight at 75 °C under a N₂ atmosphere. CH₂Cl₂ (250 mL) was added and the layers separated. The aqueous layer was extracted with CH₂Cl₂ (2 × 100 mL) and the combined organic extracts were dried with MgSO₄ and concentrated under reduced pressure. The residue was purified by column chromatography (SiO₂, CH₂Cl₂/petrol ether 7:3 to CH₂Cl₂) to afford **S5** (1.78 g, 90%) as a yellow solid. M. p. 111–112 °C. ¹H NMR (600 MHz, CDCl₃) δ: 8.30 (d, *J* = 7.6 Hz, 2H, H_a), 7.73 (d, *J* = 8.2 Hz, 2H, H_b), 7.59 (d, *J* = 7.5 Hz, 2H, H_c), 7.40–7.27 (br, 2H, H_d), 7.23 (d, *J* = 6.8 Hz, 6H, H_p), 7.15 (br, 2H, H_g), 7.08 (m, 8H, H_{n+o}), 6.88 (d, *J* = 7.4 Hz, 2H, H_h), 6.78 (d, *J* = 7.8 Hz, 2H, H_m), 4.38 (br m, 4H, H_{e+f}), 4.15 (m, 4H, H_{j+i}), 2.25 (quin, *J* = 6.2 Hz, 2H, H_k), 1.52 (m, 9H, H_i), 1.30 (s, 27H, H_q). ¹³C NMR (150 MHz, CDCl₃) δ: 158.39, 156.73, 156.08, 148.42, 147.39, 147.15, 144.25, 139.82, 139.32, 137.75, 132.40, 130.83, 129.94, 129.59, 128.95, 128.79, 128.26, 127.80, 127.67,

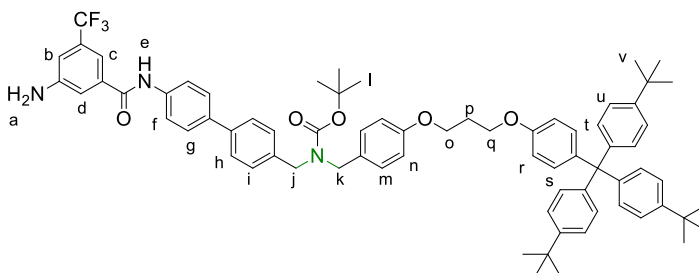
124.28, 124.18, 114.67, 113.06, 80.37, 64.64, 64.27, 63.17, 49.10, 48.67, 48.52, 34.43, 31.52, 29.48, 28.62. LRMS (ESI⁺): $m/z = 996.0$ [M+NH₄]⁺ (calcd. 996.6 for C₆₅H₇₈N₃O₆).

Synthesis of S6



A solution of **S5** (1.70 g, 1.74 mmol, 1.00 equiv.) in THF (120 mL) was purged with N₂ for 20 min. Pd(OH)₂/C (0.17 g, 10%w/w) and K₂CO₃ (1.20 g, 8.68 mmol, 5.00 equiv) were added and the resulting mixture was stirred under a H₂ atmosphere at room temperature for 5 h. The resulting mixture was filtered through a pad of Celite® and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (SiO₂, CH₂Cl₂ to CH₂Cl₂/EtOAc 95:5) to yield **S6** (1.57 g, 95%) as a white solid. M. p. 105–106 °C. ¹H NMR (600 MHz, CDCl₃) δ: 7.49 (d, $J = 8.1$ Hz, 2H, H_e), 7.43 (d, $J = 8.3$ Hz, 2H, H_b), 7.23 (d, $J = 8.5$ Hz, 6H, H_p), 7.21–7.10 (br, 4H, H_{d+g}), 7.09 (m, 8H, H_{n+o}), 6.87 (d, $J = 8.5$ Hz, 2H, H_h), 6.83 (d, $J = 8.3$ Hz, 2H, H_a), 6.78 (d, $J = 8.9$ Hz, 2H, H_m), 4.35 (br, 4H, H_{e+f}), 4.14 (m, 4H, H_{j+l}), 2.26 (quin, $J = 6.1$ Hz, 2H, H_k), 1.51 (s, 9H, H_i), 1.30 (s, 27H, H_q). ¹³C NMR (150 MHz, CDCl₃) δ: 158.28, 156.76, 156.13, 148.42, 144.63, 144.51, 144.26, 140.07, 139.78, 136.25, 132.39, 130.85, 130.22, 129.58, 128.96, 128.57, 128.10, 127.98, 126.64, 124.17, 116.18, 114.61, 113.07, 80.13, 64.62, 64.31, 63.17, 48.77, 48.37, 34.43, 31.53, 29.49, 28.65. LRMS (ESI⁺): $m/z = 949.3$ [M+H]⁺ (calcd. 949.6 for C₆₅H₇₇N₂O₄).

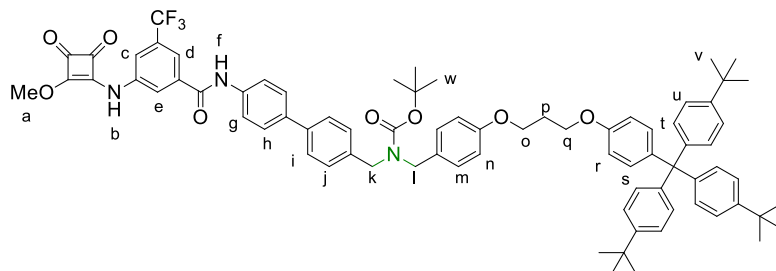
Synthesis of S7



To a solution of **S6** (0.40 g, 0.42 mmol, 1.00 equiv.) and 3-amino-5-trifluoromethylbenzenecarboxylic acid (87 mg, 0.42 mmol, 1.00 equiv.) in THF/CHCl₃ (3:1, 8 mL), HOBT (71 mg, 0.46 mmol, 1.10 equiv.) and EDCI (89 mg, 0.46 mmol, 1.10 equiv.) were added and the resulting mixture was stirred at room temperature for 2 d, under a N₂ atmosphere. The solvent was removed under reduced pressure and the residue was purified by column chromatography (SiO₂, CH₂Cl₂/EtOAc 95:5) to yield **S7** (0.33 g, 69%) as a pale brown solid. ¹H NMR (600 MHz, CDCl₃) δ: 7.79 (s, 1H, H_e), 7.71 (d, $J = 8.7$ Hz, 2H, H_f), 7.62 (d, $J = 8.3$ Hz, 2H, H_g), 7.55 (d, $J = 8.0$ Hz, 2H, H_o), 7.38 (s, 1H, H_{c/d}), 7.37 (s, 1H, H_{c/d}), 7.29 (m, 2H, H_i), 7.22 (d, $J = 8.5$ Hz, 6H, H_u), 7.20–7.10 (m, 2H, H_m), 7.10–7.06 (m, 8H, H_{s+t}), 7.06 (s, 1H, H_b), 6.87 (d, $J = 8.5$ Hz, 2H, H_n), 6.78 (d, $J = 8.8$ Hz, 2H, H_r), 4.36 (m, 4H, H_{j+k}), 4.14 (m, 4H, H_{o+q}), 2.25 (quin, $J = 5.9$ Hz, 2H, H_p), 1.51 (s, 9H, H_i), 1.29 (s, 27H, H_v). ¹³C NMR (150 MHz,

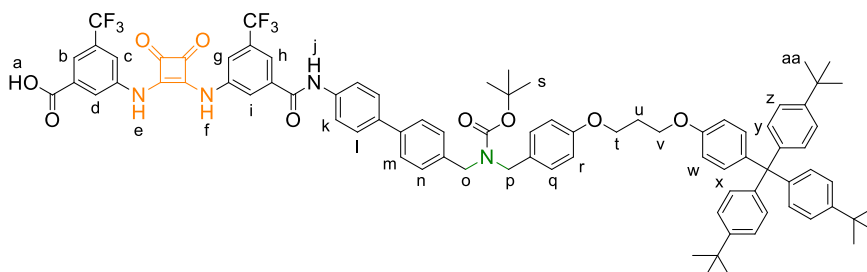
CDCl₃) δ : 164.75, 158.33, 156.76, 156.15, 148.43, 147.64, 144.27, 139.80, 139.41, 137.11, 132.40 (q, $J = 32.5$ Hz), 132.39, 130.84, 130.14, 129.59, 128.97, 128.62, 128.06, 127.78, 127.11, 124.60 (q, $J = 272.6$ Hz), 124.18, 120.74, 120.64, 116.86, 114.64, 114.40, 113.08, 112.71, 80.24, 64.64, 64.32, 63.18, 48.85, 48.49, 34.44, 31.52, 29.49, 28.65. LRMS (ESI⁻): $m/z = 1170.7$ [M+Cl]⁻ (calcd. 1170.6 for C₇₃H₈₀F₃N₃O₅Cl).

Synthesis of S8



A mixture of **S7** (0.13 g, 0.12 mmol, 1.00 equiv.), 3,4-dimethoxycyclobut-3-ene-1,2-dione (33 mg, 0.23 mmol, 2.00 equiv.) and zinc triflate (17 mg, 0.048 mmol, 0.40 equiv.) in CH₂Cl₂/MeOH (1:1, 3 mL) was stirred at room temperature for 2 d, under a N₂ atmosphere. The resulting mixture was concentrated under reduced pressure and the residue purified by column chromatography (SiO₂, CH₂Cl₂/EtOAc 95:5 to 85:15) to afford **S8** (0.14 g, 94%) as a pale yellow solid. ¹H NMR (600 MHz, CD₃COCD₃) δ : 9.87 (s, 1H, H_f), 8.33 (s, 1H, H_e), 8.10 (s, 1H, H_c), 8.04 (s, 1H, H_d), 7.93 (d, $J = 8.7$ Hz, 2H, H_g), 7.69 (d, $J = 8.6$ Hz, 2H, H_n), 7.64 (d, $J = 7.8$ Hz, 2H, H_i), 7.34 (m, 2H, H_j), 7.29 (d, $J = 8.6$ Hz, 6H, H_u), 7.21 (m, 2H, H_m), 7.12 (d, $J = 8.5$ Hz, 6H, H_t), 7.08 (d, $J = 8.8$ Hz, 2H, H_s), 6.93 (d, $J = 8.1$ Hz, 2H, H_n), 6.84 (d, $J = 8.9$ Hz, 2H, H_r), 4.50 (s, 3H, H_a), 4.46–4.30 (m, 4H, H_{l+k}), 4.17 (m, 4H, H_{o+q}), 2.23 (quin, $J = 6.2$ Hz, 2H, H_p), 1.49 (s, 9H, H_w), 1.29 (s, 27H, H_v). ¹³C NMR (150 MHz, CD₃COCD₃) δ : 188.20, 185.55, 180.65, 170.21, 164.40, 159.21, 157.81, 156.32, 149.10, 145.23, 140.56, 140.23, 140.04, 139.22, 139.13, 138.58, 138.55, 137.24, 132.79, 132.12 (q, $J = 32.6$ Hz), 131.40, 131.20, 130.12, 129.76, 129.23, 128.89, 127.91, 127.47, 125.03, 124.70 (q, $J = 272.6$ Hz), 122.93, 121.46, 121.37, 119.57, 119.31, 115.31, 114.02, 80.10, 65.17, 65.01, 63.86, 61.50, 49.59, 49.18, 34.83, 31.64, 30.05, 28.60. LRMS (ESI⁻): $m/z = 1244.7$ [M-H]⁻ (calcd. 1244.6 for C₇₈H₈₁F₃N₃O₈).

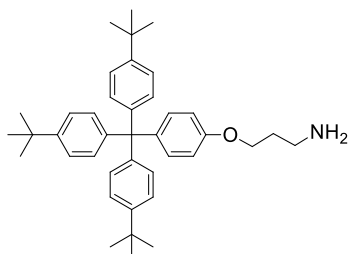
Synthesis of 3



A solution of **S8** (50 mg, 0.040 mmol), 3-amino-5-trifluoromethyl-benzenecarboxylic acid (12 mg, 0.06 mmol) and Zn(OTf)₂ (4.4 mg, 0.012 mmol) in a dry Toluene/DMF mixture (20:1, 3.65 mL) was stirred at 105 °C overnight. The solvent was removed under reduced

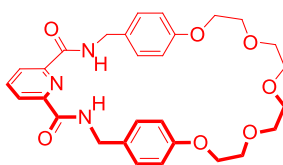
pressure and the residue was purified by preparative thin layer chromatography (SiO₂, CH₂Cl₂:MeOH 92:8) to yield **3** (14 mg, 25%) as a pale yellow solid. ¹H NMR (600 MHz, CD₃COCD₃) δ: 13.38 (s, 1H, H_a), 10.83 (s, 1H, H_{eff}), 10.21 (m, 2H, H_{eff+Ar}), 8.96 (s, 1H, H_{Ar}), 8.78 (s, 1H, H_{Ar}), 8.47 (s, 1H, H_{Ar}), 8.38 (s, 1H, H_{Ar}), 8.30 (d, *J* = 8.2 Hz, 2H, H_k), 7.99 (s, 1H, H_{Ar}), 7.72 (d, *J* = 8.1 Hz, 2H, H_l), 7.68 (d, *J* = 7.8 Hz, 2H, H_m), 7.37 (br, 2H, H_n), 7.31 (d, *J* = 8.2 Hz, 6H, H_z), 7.25 (br, 2H, H_q), 7.12 (d, *J* = 8.2 Hz, 6H, H_y), 7.09 (d, *J* = 8.6 Hz, 2H, H_x), 6.96 (d, *J* = 8.1 Hz, 2H, H_r), 6.87 (d, *J* = 8.5 Hz, 2H, H_w), 4.53–4.31 (m, 4H, H_{o+p}), 4.20 (m, 4H, H_{t+v}), 2.25 (quin, *J* = 5.9 Hz, 2H, H_u), 1.51 (s, 9H, H_s), 1.30 (s, 27H, H_{aa}). ¹³C NMR (150 MHz, CD₃COCD₃) δ: 183.49, 182.63, 170.26, 167.63, 167.39, 164.06, 159.22, 157.85, 156.35, 149.11, 145.26, 142.67, 142.06, 140.87, 140.37, 140.23, 139.92, 138.22, 136.94, 136.75, 132.79, 132.54, 131.40, 131.32, 130.21, 129.82, 129.29, 128.95, 127.85, 127.48, 126.39, 126.08, 125.05, 124.59, 124.28, 123.76, 122.59, 122.01, 121.23, 121.15, 118.78, 118.35, 117.92, 115.32, 114.05, 80.07, 65.18, 65.05, 63.87, 49.15, 34.85, 31.64, 29.65,⁶ 28.62. LRMS (ESI⁻): *m/z* = 1417.8 [M-H]⁻ (calcd. 1417.6 for C₈₅H₈₃F₆N₄O₉).

Synthesis of 4



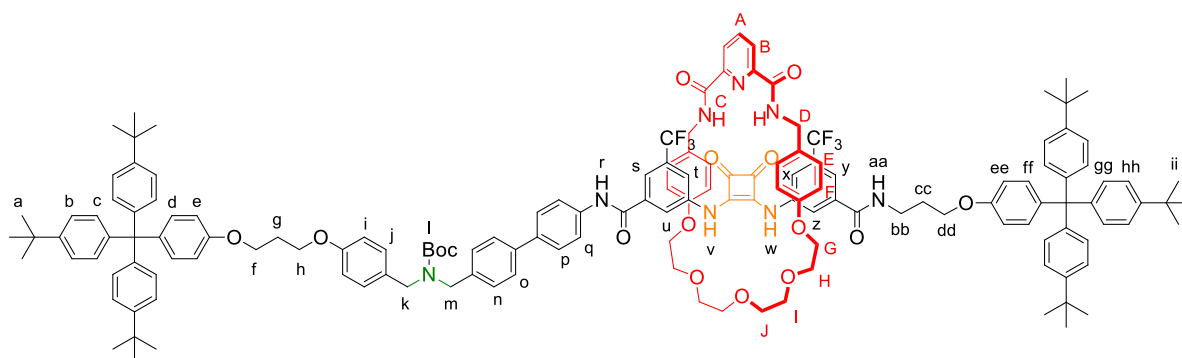
To a solution of **S9** (1.11 g, 1.68 mmol, 1.00 equiv.) in CH₂Cl₂ (9.5 mL), CF₃CO₂H (2.5 mL) was added dropwise. The resulting mixture was stirred in an open flask for 4 h. NaHCO_{3(aq)}(sat) was added in portions until pH > 9. The mixture was extracted with CH₂Cl₂ (3 × 15 mL). The combined organic extracts were washed with H₂O (20 mL) and brine (20 mL) and dried with MgSO₄. The solvent was removed under reduced pressure to afford **4** (0.90 g, 95%) as a white solid. The characterization data are in agreement with those previously reported.⁷

Synthesis of 5



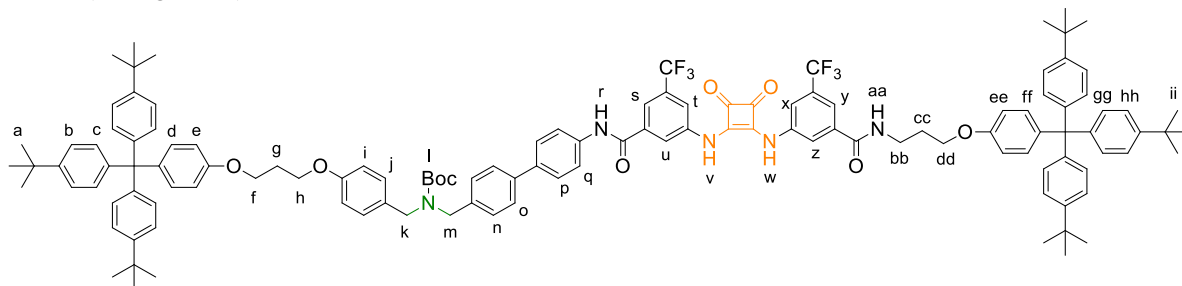
Synthesized according to a literature procedure.³

Synthesis of 1-Boc and 2-Boc



3 (30.0 mg, 0.021 mmol, 1.00 equiv), **5** (26.0 mg, 0.050 mmol, 2.35 equiv.) and **4** (30 mg, 0.055 mmol, 2.60 equiv) were dissolved in a mixture of CH₂Cl₂/THF/CH₃CN (60:35:5, 3.6 mL). The solution was stirred under N₂ atmosphere, at room temperature for 1 h after which PyBroP (20.0 mg, 0.043 mmol, 2.00 equiv.) and *N,N*-diisopropylethylamine (10 μL, 0.050 mmol, 2.35 equiv.) were added and the mixture stirred at room temperature for additional 20 h. The solvents were removed under reduced pressure and the crude was purified by column chromatography (SiO₂, CH₂Cl₂:MeOH 98:2) to afford **1-Boc** (25 mg, 47%) as a colourless solid. ¹H NMR (600 MHz, CD₂Cl₂) δ: 10.23 (s, 1H, H_{v/w}), 10.13 (s, 1H, H_{v/w}), 9.15 (t, *J* = 5.7 Hz, 2H, H_C), 8.55 (s, 1H, H_r), 8.44 (d, *J* = 7.8 Hz, 2H, H_B), 8.40 (s, 1H, H_{s/u}), 8.13 (s, 1H, H_{y/z}), 8.08 (t, *J* = 7.9 Hz, 1H, H_A), 8.04 (s, 1H, H_{s/u}), 7.95 (s, 1H, H_x), 7.80 (s, 2H, H_{t+y/z}), 7.78 (d, *J* = 8.5 Hz, 2H, H_q), 7.62 (m, 4H, H_{o+p}), 7.38–7.33 (m, 2H, H_n), 7.32–7.26 (m, 12H, H_{b+hh}), 7.24–7.17 (m, 16H, H_{c+gg+d+ff+j}), 6.94 (t, *J* = 7.9 Hz, 6H, H_{i+E}), 6.85 (d, *J* = 3.3 Hz, 2H, H_{e/ee}), 6.84 (d, *J* = 3.3 Hz, 2H, H_{e/ee}), 6.30 (d, *J* = 8.4 Hz, 4H, H_F), 4.56–4.45 (m, 4H, H_D), 4.41 (m, 4H, H_{k+m}), 4.19 (m, 4H, H_{f+h}), 4.13 (t, *J* = 5.7 Hz, 2H, H_{dd}), 3.90–3.80 (m, 16H, H_{G+H+I+J}), 3.68 (q, *J* = 6.3 Hz, 2H, H_{bb}), 2.28 (quin, *J* = 6.1 Hz, 2H, H_g), 2.13 (quin, *J* = 6.3 Hz, 2H, H_{cc}), 1.55 (s, 9H, H_l), 1.34 (s, 27H, H_{a/ii}), 1.33 (s, 27H, H_{a/ii}). ¹³C NMR (150 MHz, CD₂Cl₂) δ: 181.81, 181.45, 165.14, 163.80, 163.71, 163.31, 158.24, 157.27, 156.73, 156.44, 155.79, 149.43, 148.44, 148.38, 144.50, 144.46, 140.13, 139.73, 139.58, 139.36, 139.11, 138.34, 137.35, 137.04, 136.98, 131.98, 131.88, 130.99, 130.38, 130.34, 129.94, 127.53, 126.82, 124.66, 124.31, 124.28, 122.68, 120.43, 120.13, 120.02, 119.27, 118.19, 117.73, 114.41, 113.71, 113.15, 113.12, 79.80, 70.74, 70.51, 70.20, 66.91, 66.22, 64.51, 64.34, 63.09, 63.08, 48.84, 48.35, 42.88, 42.75, 38.29, 34.18, 31.59, 31.07, 30.94, 29.32, 28.95, 28.19.

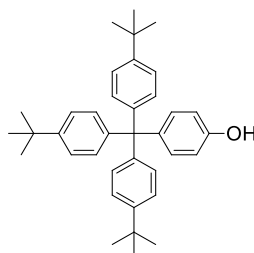
2-Boc (19 mg, 46%) was also isolated as a colourless solid.



¹H NMR (600 MHz, CD₃COCD₃) δ: 10.11 (s, 1H, H_{v/w}), 9.87 (s, 1H, H_{v/w}), 8.30 (s, 1H, H_{Ar}), 8.23 (s, 1H, H_{Ar}), 8.20 (s, 3H, H_{Ar}), 7.98–7.87 (m, 2H, H_q), 7.82 (s, 1H, H_{Ar}), 7.64 (dd, *J* = 15.9,

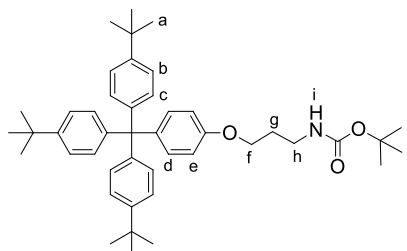
7.9 Hz, 4H, H_{o+p}), 7.36–7.27 (m, 14H, H_{b+n+hh}), 7.26–7.19 (m, 2H, H_j), 7.14 (m, 12H, H_{c+gg}), 7.11–7.07 (m, 4H, H_{d+ff}), 6.95 (d, $J = 8.2$ Hz, 2H, H_i), 6.86 (d, $J = 8.8$ Hz, 2H, $H_{e/ee}$), 6.80 (d, $J = 8.4$ Hz, 2H, $H_{e/ee}$), 4.39 (m, 4H, H_{k+m}), 4.25–4.15 (m, 4H, H_{f+h}), 4.06 (t, $J = 6.0$ Hz, 2H, H_{dd}), 3.69 – 3.56 (m, 2H, H_{bb}), 2.25 (quin, $J = 6.2$ Hz, 2H, H_g), 1.51 (s, 9H, H_l), 1.31 (s, 27H, $H_{a/ii}$), 1.30 (s, 27H, $H_{a/ii}$). ^{13}C NMR (150 MHz, CD_3COCD_3) δ : 182.76, 182.71, 166.08, 165.91, 164.83, 158.36, 156.97, 156.95, 155.46, 148.25, 148.20, 144.41, 144.39, 140.23, 140.03, 139.37, 139.31, 139.21, 138.31, 137.43, 137.13, 136.34, 131.94, 131.88, 130.55, 130.52, 130.35, 129.30, 128.91, 128.34, 128.01, 127.01, 126.63, 124.76, 124.61, 124.19, 122.95, 122.91, 121.63, 121.36, 120.59, 118.26, 117.95, 117.80, 114.46, 113.17, 113.12, 79.22, 65.13, 64.31, 64.16, 63.00, 48.69, 48.28, 36.97, 33.97, 31.42, 27.75. LRMS (ESI^+): $m/z = 1980.8$ $[\text{M}+\text{NH}_4]^+$ (calcd. 1980.0 for $\text{C}_{125}\text{H}_{137}\text{F}_6\text{N}_6\text{O}_9$).

Synthesis of S8

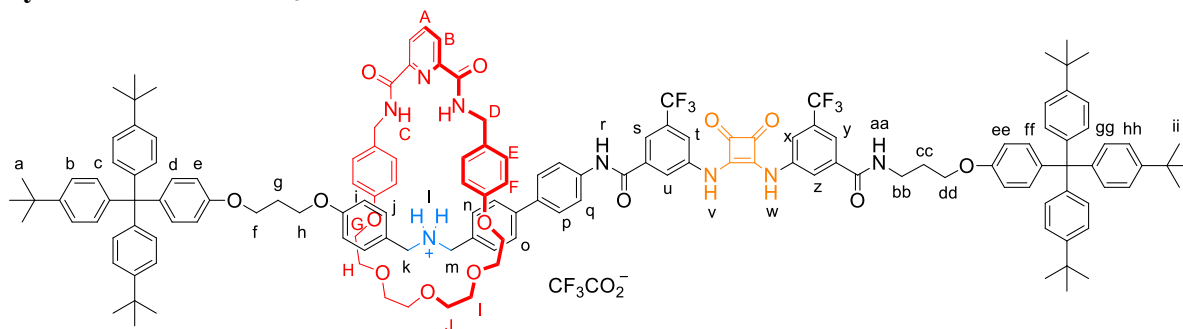


Synthesised according to a literature procedure.¹

Synthesis of S9



To a solution of **S8** (1.00 g, 1.98 mmol, 1.00 equiv.) in dry THF (20 mL), *tert*-butyl-3-hydroxypropylcarbamate (0.69 g, 3.96 mmol, 2.00 equiv.) and PPh_3 (1.04 g, 3.96 mmol, 2.00 equiv.) were added and the resulting mixture was cooled in a water-ice bath. DIAD (0.80 g, 3.96 mmol, 2.00 equiv.) was added and the resulting mixture was stirred overnight at room temperature under a N_2 atmosphere. The solvent was removed under reduced pressure and the crude mixture was dissolved in CH_2Cl_2 (3 mL). MeOH (100 mL) was added and the colourless precipitate formed was filtered off and dried under vacuum to give **S9** (1.11 g, 1.68 mmol, 85%) as a colourless solid. M. p. 126–127 °C. ^1H NMR (600 MHz, CDCl_3) δ : 7.23 (d, $J = 8.2$ Hz, 6H, H_b), 7.08 (d, $J = 8.3$ Hz, 8H, H_{c+d}), 6.76 (d, $J = 8.5$ Hz, 2H, H_e), 4.79 (s, 1H, H_i), 4.00 (t, $J = 5.9$ Hz, 2H, H_j), 3.35–3.28 (m, 2H, H_h), 2.00–1.92 (m, 2H, H_g), 1.44 (s, 9H, H_l), 1.30 (s, 27H, H_a). ^{13}C NMR (150 MHz, CDCl_3) δ : 156.66, 156.14, 148.43, 144.24, 139.89, 132.39, 130.84, 124.18, 113.04, 79.32, 65.87, 63.17, 38.34, 34.44, 31.53, 29.66, 28.56. HRMS (ESI^+): $m/z = 684.4391$ $[\text{M}+\text{Na}]^+$ (calcd. 684.4387 for $\text{C}_{45}\text{H}_{59}\text{NO}_3\text{Na}$).

Synthesis of $1\text{-H}^+\cdot\text{CF}_3\text{CO}_2^-$ Procedure A: From **1-Boc**

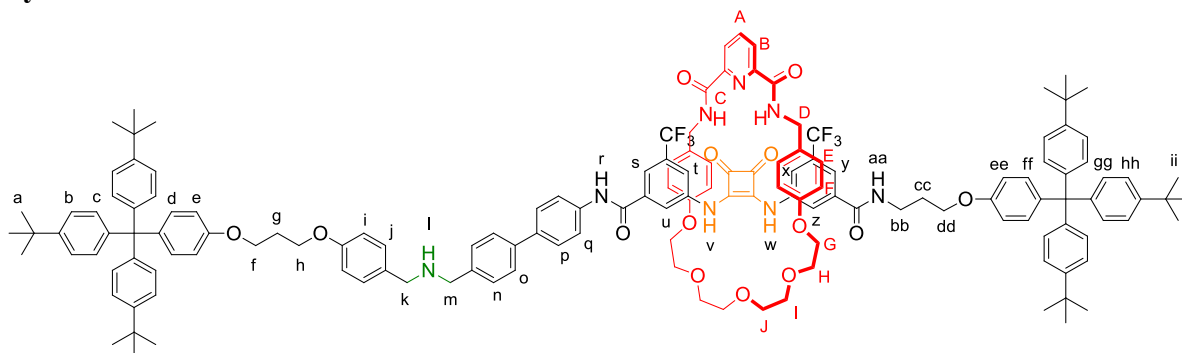
Rotaxane **1-Boc** (25.0 mg, 0.010 mmol, 1.00 equiv.) was dissolved in CH_2Cl_2 (1.0 mL). $\text{CF}_3\text{CO}_2\text{H}$ (0.25 mL) was added and the mixture was stirred at room temperature for 90 min. The solvents were removed under reduced pressure to yield $1\text{-H}^+\cdot\text{CF}_3\text{CO}_2^-$ (25 mg, quant.) as a solid which was used in the next step without further purification.

Procedure B: From **1**

1 (22 mg, 0.092 mmol, 1.00 equiv.) was dissolved in CH_2Cl_2 (1.0 mL). $\text{CF}_3\text{CO}_2\text{H}$ (10 μL , 0.13 mmol, 1.4 equiv.) was added and the mixture was stirred at room temperature for 30 min. The solvents were removed under reduced pressure to yield $1\text{-H}^+\cdot\text{CF}_3\text{CO}_2^-$ (23 mg, 0.092 mmol, quant.) as a solid.

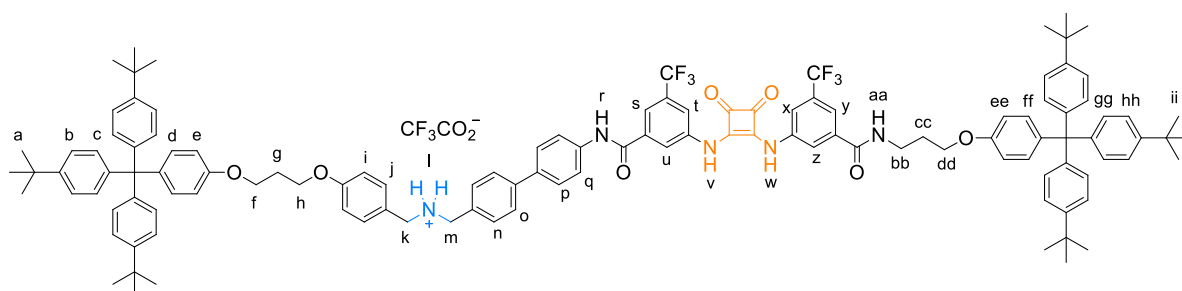
^1H NMR (600 MHz, CD_2Cl_2) δ : 10.22 (s, 1H, $\text{H}_{v/w}$), 10.11 (s, 1H, $\text{H}_{v/w}$), 9.14 (t, $J = 5.8$ Hz, 2H, H_C), 8.53 (s, 1H, H_r), 8.43 (d, $J = 7.8$ Hz, 2H, H_B), 8.40 (s, 1H, $\text{H}_{s/u}$), 8.13 (s, 1H, $\text{H}_{y/z}$), 8.08 (t, $J = 7.9$ Hz, 1H, H_A), 8.03 (s, 1H, $\text{H}_{s/u}$), 7.94 (s, 1H, H_x), 7.80 (s, 2H, $\text{H}_{t+y/z}$), 7.79–7.75 (m, 2H, H_q), 7.62 (dd, $J = 8.1, 4.8$ Hz, 4H, H_{o+p}), 7.48 (d, $J = 7.8$ Hz, 2H, H_n), 7.33–7.26 (m, 14H, H_{b+hh+j}), 7.24–7.17 (m, 16H, $\text{H}_{c+gg+d+ff}$), 6.93 (dd, $J = 11.3, 8.1$ Hz, 6H, H_{i+E}), 6.88–6.81 (m, 4H, H_{e+ee}), 6.30 (d, $J = 8.1$ Hz, 4H, H_F), 4.51 (t, $J = 5.9$ Hz, 4H, H_D), 4.18 (m, 4H, H_{f+h}), 4.13 (t, $J = 5.7$ Hz, 2H, H_{dd}), 3.90 – 3.81 (m, 18H, $\text{H}_{k/m+G+H+I+J}$), 3.80 (s, 2H, $\text{H}_{k/m}$), 3.67 (m, 2H, H_{bb}), 2.28 (quin, $J = 6.1$ Hz, 2H, H_g), 2.13 (quin, $J = 6.4$ Hz, 2H, H_{cc}), 1.34 (s, 27H, $\text{H}_{a/ii}$), 1.33 (s, 27H, $\text{H}_{a/ii}$). ^{13}C NMR (150 MHz, CD_2Cl_2) δ : 181.82, 181.44, 165.28, 164.55, 163.87, 163.55, 159.92, 157.33, 156.64, 156.43, 149.26, 148.38, 148.36, 144.47, 144.46, 141.36, 140.13, 139.77, 139.58, 139.36, 138.43, 136.97, 136.93, 136.01, 131.97, 131.89, 131.52, 130.37, 130.34, 129.92, 128.96, 128.86, 128.83, 128.68, 128.54, 128.34, 127.49, 127.27, 124.78, 124.31, 124.28, 122.67, 120.39, 120.32, 119.15, 118.13, 117.90, 117.84, 114.96, 113.74, 113.11, 70.73, 70.47, 70.17, 66.91, 66.24, 64.59, 64.16, 63.09, 63.07, 46.08, 42.98, 42.36, 38.35, 34.18, 31.94, 31.92, 31.07, 30.63, 29.70, 29.16.

Synthesis of 1



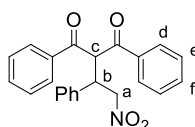
$1\text{-H}^+\cdot\text{CF}_3\text{CO}_2^-$ (25 mg, 0.010 mmol, 1.00 equiv) was dissolved in CH_2Cl_2 (2.0 mL). $\text{NaOH}_{(\text{aq})}$ 2M (2.0 mL) was added and the mixture was stirred at room temperature for 1 h. The layers were separated and the organic phase was dried with MgSO_4 , filtered and the solvent removed under reduced pressure to yield **1** (22 mg, 92%) as a colourless oil which was used without further purification.

Synthesis of $2\text{-H}^+\cdot\text{CF}_3\text{CO}_2^-$



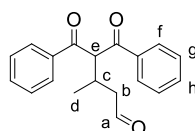
The free thread **2-Boc** (19 mg, 0.010 mmol, 1.00 equiv.) was dissolved in CH_2Cl_2 (1 mL). $\text{CF}_3\text{CO}_2\text{H}$ (0.25 mL) was then added and the mixture was stirred at room temperature for 90 min. The mixture was concentrated to afford $2\text{-H}^+\cdot\text{CF}_3\text{CO}_2^-$ (19 mg, quant.) as a solid which was used in the next step without further purification. ^1H NMR (600 MHz, CD_3COCD_3) δ : 9.74 (br s, 2H, $\text{H}_{v/w}$), 8.87 (s, 1H, H_s), 8.57 (s, 1H, H_y), 8.44 (s, 1H, $\text{H}_{t/x}$), 8.22 (s, 1H, $\text{H}_{t/x}$), 7.99 (d, $J = 8.5$ Hz, 2H, H_q), 7.94 (s, 1H, H_u), 7.86 (s, 1H, H_z), 7.68 (d, $J = 8.0$ Hz, 2H, H_n), 7.62 (d, $J = 8.7$ Hz, 2H, H_p), 7.59 (dd, $J = 8.5, 6.7$ Hz, 4H, H_{o+j}), 7.34–7.28 (m, 12H, H_{b+hh}), 7.15–7.10 (m, 12H, H_{c+gg}), 7.09 (d, $J = 8.8$ Hz, 4H, H_{d+ff}), 7.02 (d, $J = 8.6$ Hz, 2H, H_i), 6.86 (d, $J = 8.9$ Hz, 2H, $\text{H}_{e/ee}$), 6.83 (d, $J = 8.9$ Hz, 2H, $\text{H}_{e/ee}$), 4.59 (s, 2H, $\text{H}_{k/m}$), 4.52 (s, 2H, $\text{H}_{k/m}$), 4.22 (t, $J = 6.2$ Hz, 2H, $\text{H}_{f/h}$), 4.15 (m, 4H, $\text{H}_{f/h+dd}$), 3.70 (t, $J = 6.8$ Hz, 2H, H_{bb}), 2.24 (quin, $J = 6.1$ Hz, 3H, H_g), 2.19–2.13 (m, 2H, H_{cc}), 1.31 (s, 27H, $\text{H}_{a/ii}$), 1.29 (s, 29H, $\text{H}_{a/ii}$). ^{13}C NMR (150 MHz, CD_3COCD_3) δ : 181.88, 181.79, 165.81, 165.50, 163.03, 159.89, 157.02, 156.92, 148.28, 148.21, 144.40, 144.36, 141.09, 140.72, 140.61, 139.42, 139.36, 139.06, 136.94, 136.47, 134.65, 131.95, 131.92, 131.72, 130.78, 130.55, 130.52, 130.08, 128.87, 128.15, 126.78, 126.65, 125.23, 124.97, 124.87, 124.17, 123.46, 121.33, 121.01, 120.16, 118.31, 117.55, 117.38, 114.81, 113.18, 113.14, 65.16, 64.51, 64.07, 63.01, 50.89, 50.77, 36.97, 33.96, 30.80, 30.76.

Synthesis of 9



To a solution of *trans*- β -nitrostyrene (**8**) (74.6 mg, 0.50 mmol, 2.00 equiv.), 1,3-diphenylpropane-1,3-dione (**6**) (56.0 mg, 0.25 mmol, 1.00 equiv.) and **S14** (25.7 mg, 0.025 mmol, 0.10 equiv) in CH₂Cl₂/isopropanol (5:1, 0.6 mL), sodium acetate (4.0 mg, 0.05 mmol, 0.20 equiv.) was added and the mixture was stirred O/N at room temperature. The solvents were removed under reduced pressure and the crude residue was purified by column chromatography (SiO₂, petrol ether/EtOAc, 8:2) to yield **9** (65 mg, 70%) as a colourless solid. Characterisation data in agreement with previously reported compound.⁸ ¹H NMR (600 MHz, CDCl₃) δ : 7.86 (dd, $J = 8.3, 1.3$ Hz, 2H, H_{d/d'}), 7.78 (dd, $J = 8.3, 1.3$ Hz, 2H, H_{d/d'}), 7.55 (t, $J = 7.4$ Hz, 1H, H_{ff'}), 7.51 (t, $J = 7.4$ Hz, 1H, H_{ff'}), 7.41–7.35 (m, 4H, H_{e+e'}), 7.25–7.15 (m, 5H, H_{Ar}), 5.84 (d, $J = 8.0$ Hz, 1H, H_c), 5.00 (d, $J = 6.8$ Hz, 2H, H_a), 4.62 (q, $J = 7.1$ Hz, 1H, H_b).

Synthesis of 10



Synthesised according to a literature procedure.⁴

General procedure for catalytic tests

The catalyst (2.8 μ mol, 0.05 equiv., 7 mg in case of **1**-H⁺·CF₃CO₂⁻, 6.7 mg in case of **1**, 3 mg in case of **S14**), *trans*- β -nitrostyrene (8.9 mg, 60 μ mol, 1.00 equiv.), crotonaldehyde (10 μ L, 120 μ mol, 2.00 equiv.) and 1,3-diphenylpropane-1,3-dione (13.3 mg, 60 μ mol, 1.00 equiv.) were dissolved in CH₂Cl₂ (0.12 mL) (with **1**, **1**-H⁺·CF₃CO₂⁻ or **2**-H⁺·CF₃CO₂⁻). Sodium acetate (0.5 mg, 6.0 μ mol, 0.1 equiv.) was added and the mixture was stirred at room temperature. The progress of the reaction was monitored by taking 5 μ L aliquots of the mixture, diluting by 0.5 mL of CDCl₃ and analysing by ¹H NMR spectroscopy.

1.4. ^1H NMR spectra for selected compounds

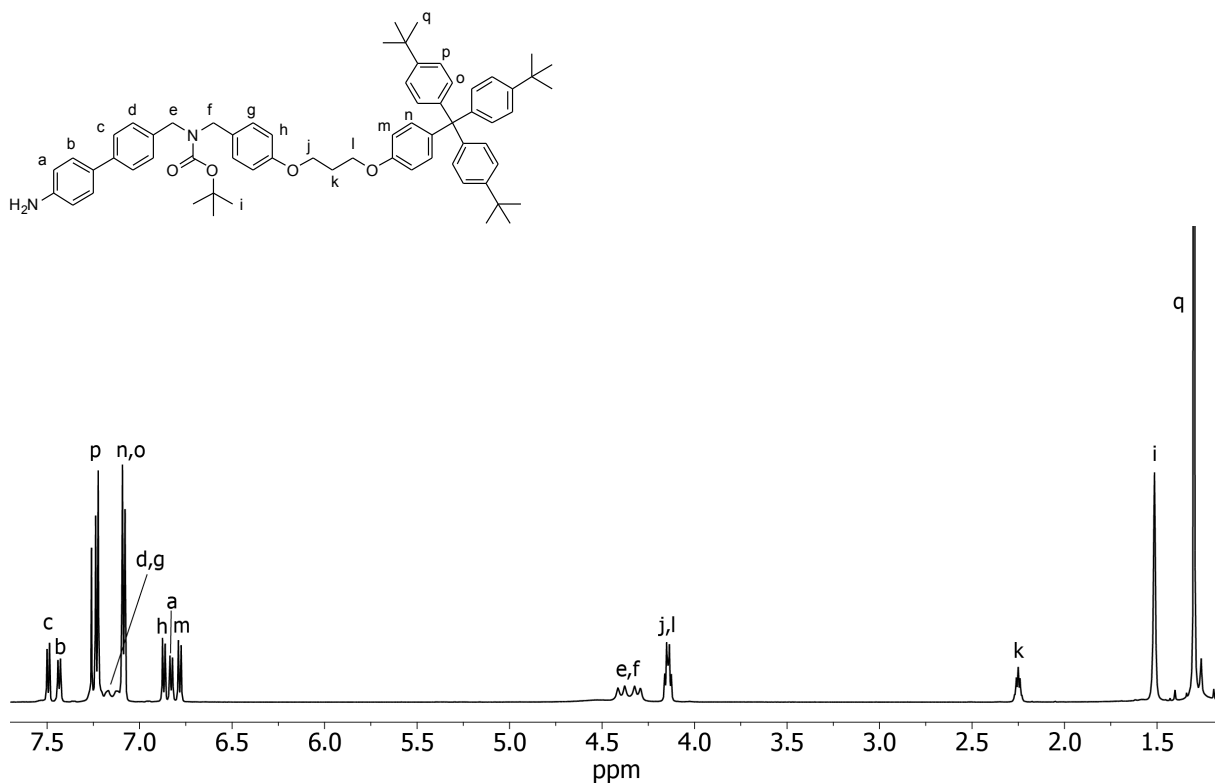


Figure S1. ^1H NMR spectrum (600 MHz, CDCl_3) of compound S6.

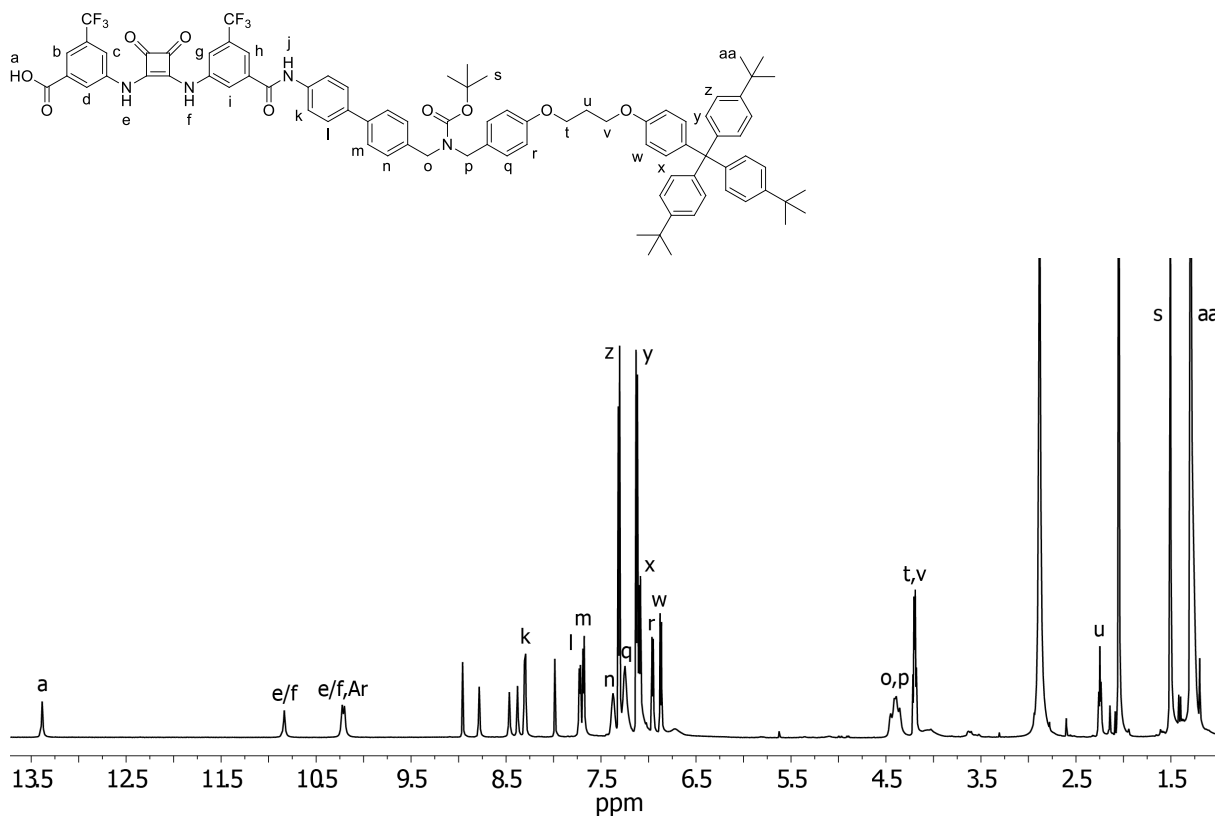


Figure S2. ^1H NMR spectrum (600 MHz, CD_3COCD_3) of compound 3.

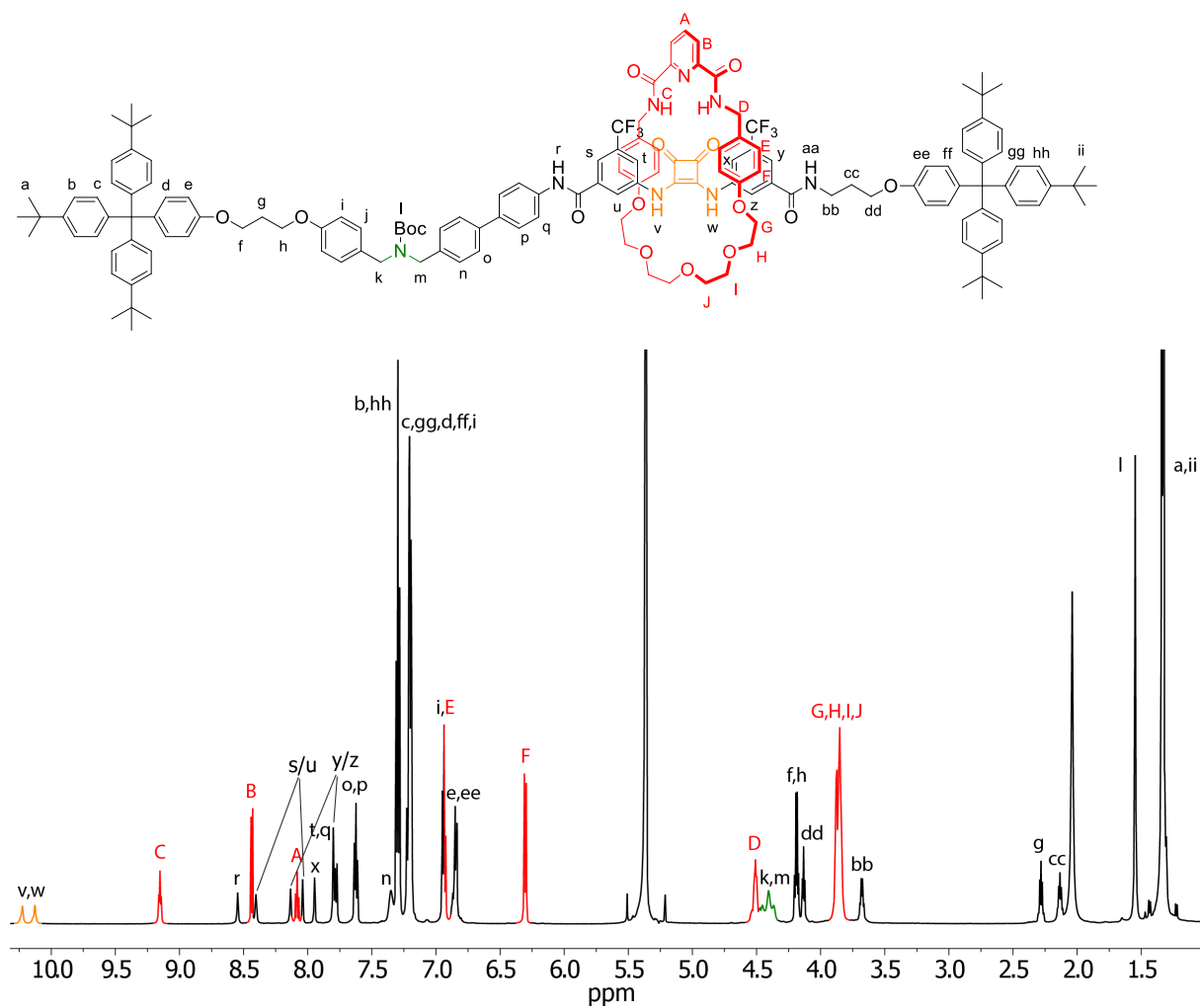


Figure S3. ¹H NMR spectrum (600 MHz, CD₂Cl₂) of compound 1-Boc.

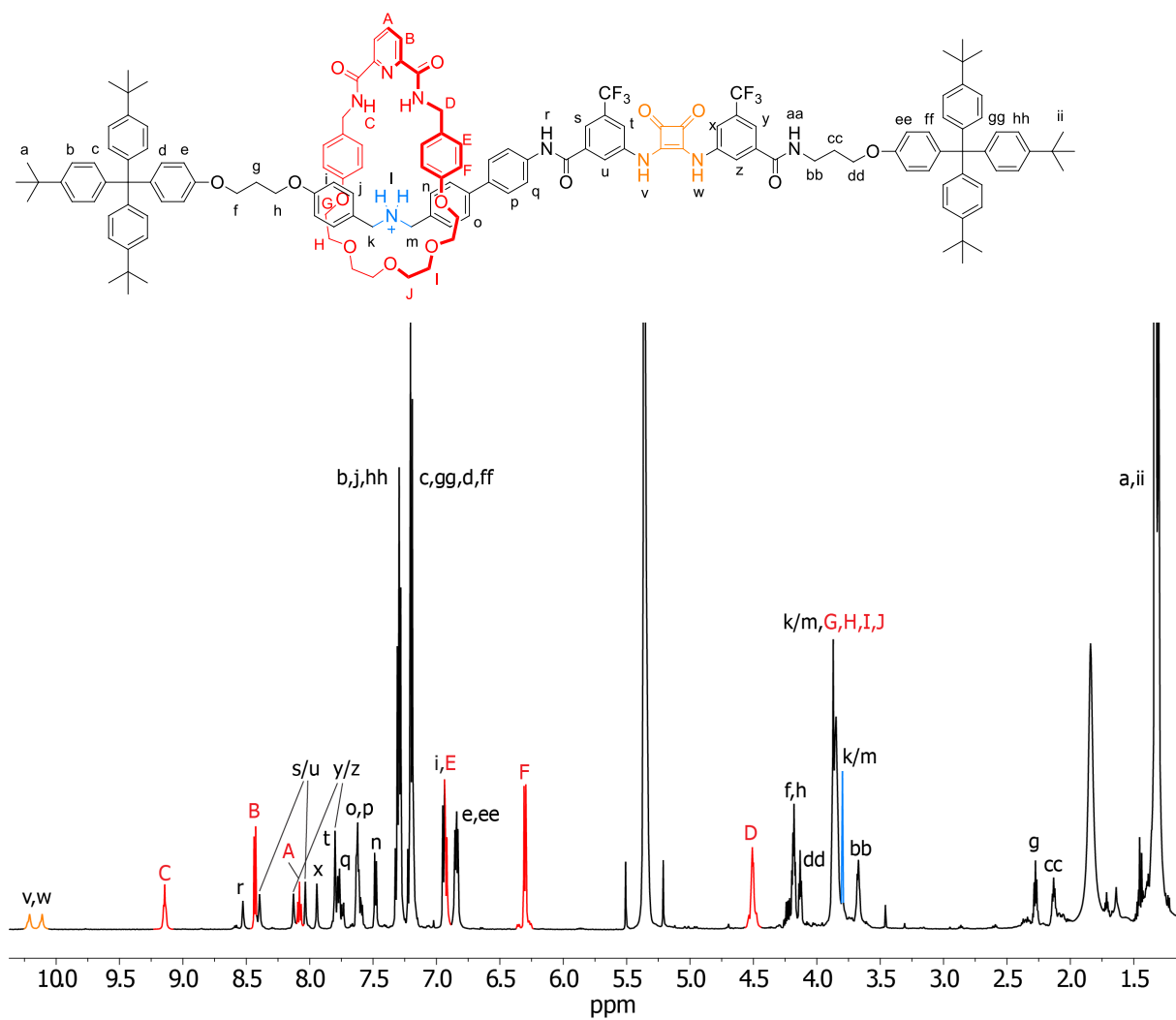


Figure S4. ¹H NMR spectrum (600 MHz, CD₂Cl₂) of compound **1-H⁺·CF₃CO₂⁻**.

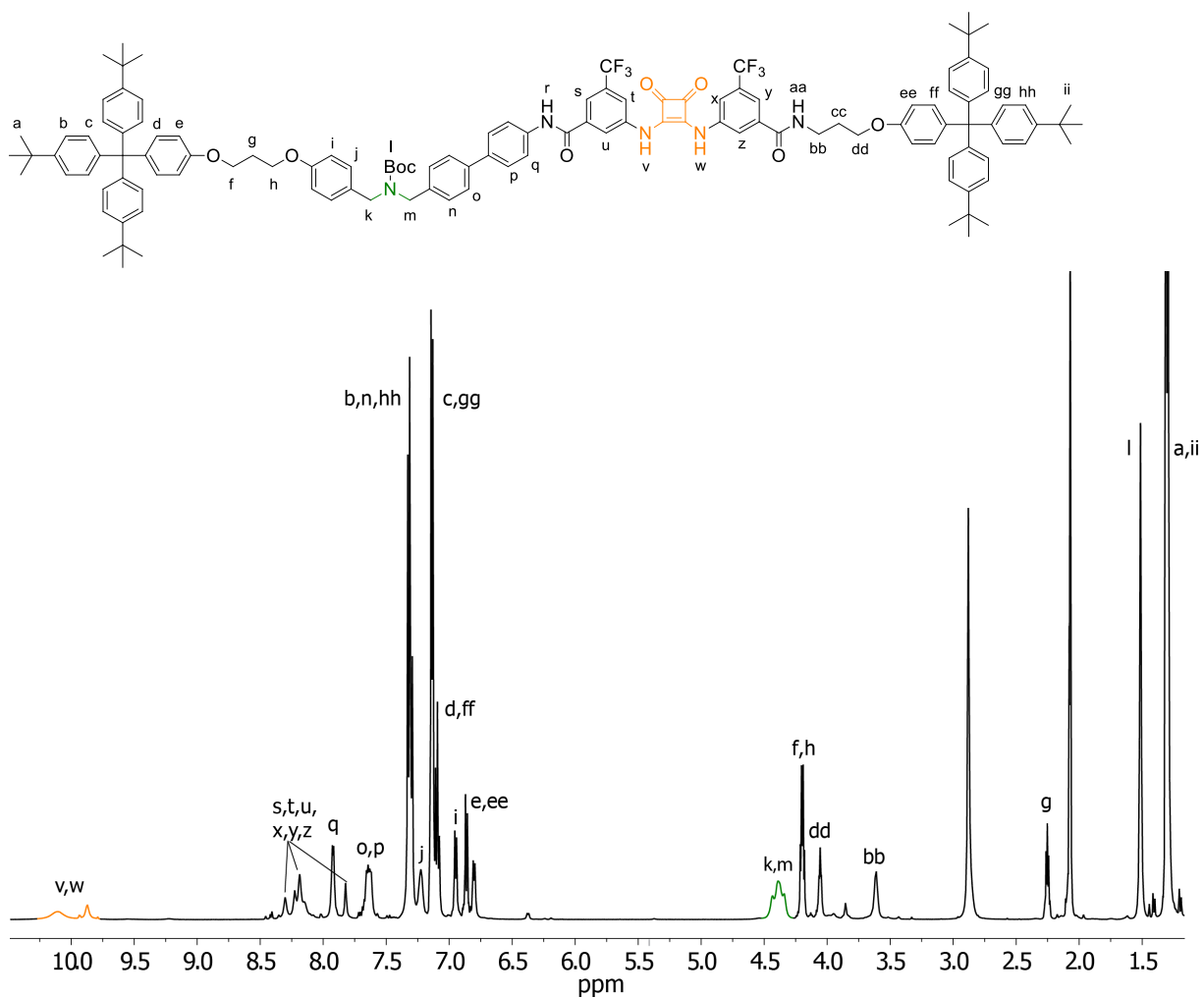


Figure S5. ^1H NMR spectrum (600 MHz, CD_3COCD_3) of compound 2-Boc.

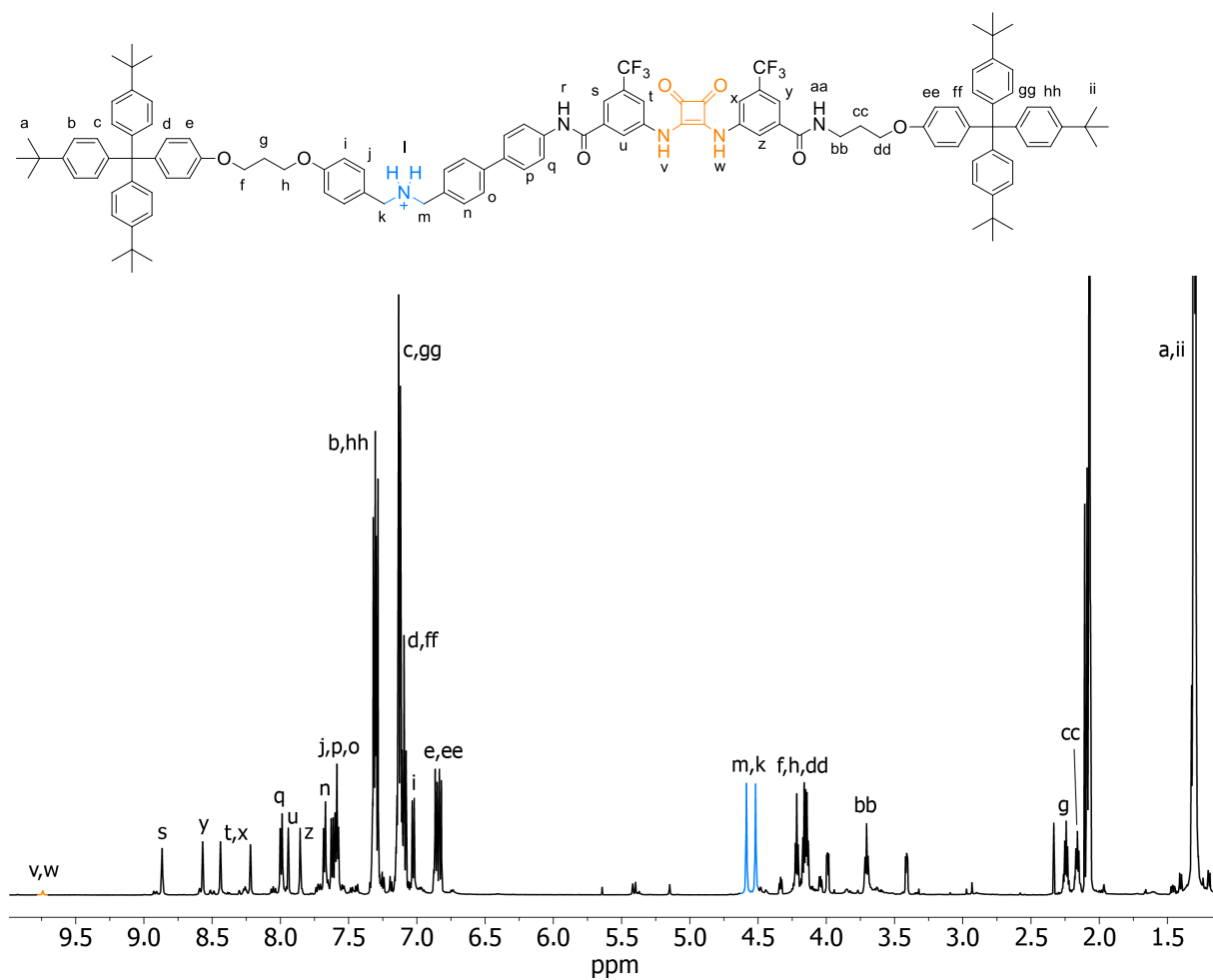


Figure S6. ¹H NMR spectrum (600 MHz, CD₃COCD₃) of compound 2-H⁺·CF₃CO₂⁻

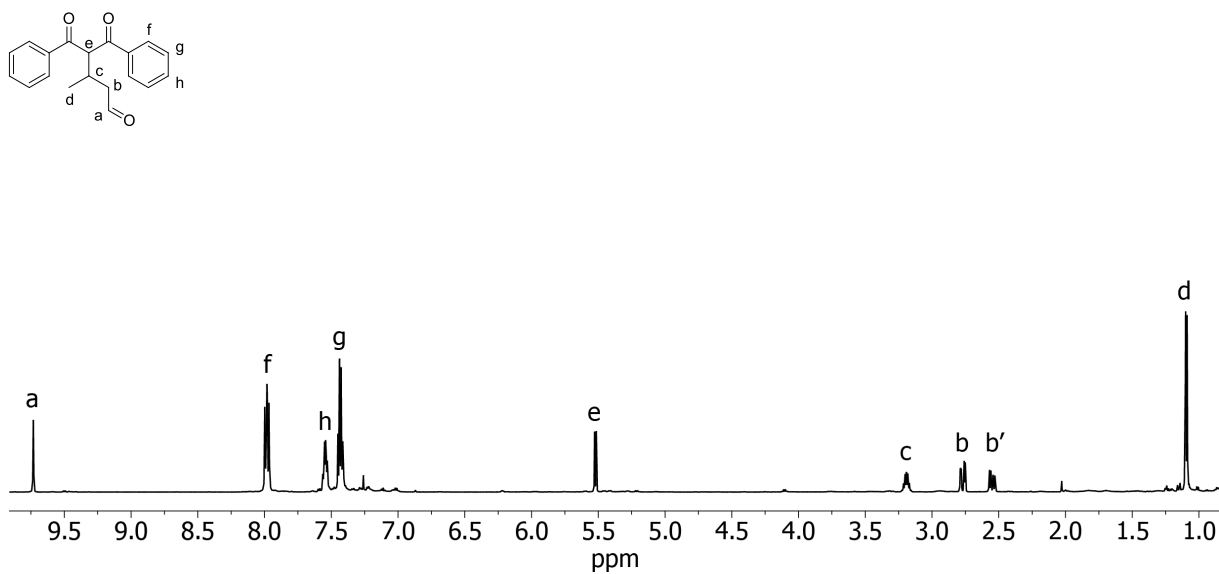


Figure S7. ¹H NMR spectrum (600 MHz, CDCl₃) of compound 10.

2. Additional Supporting Figures

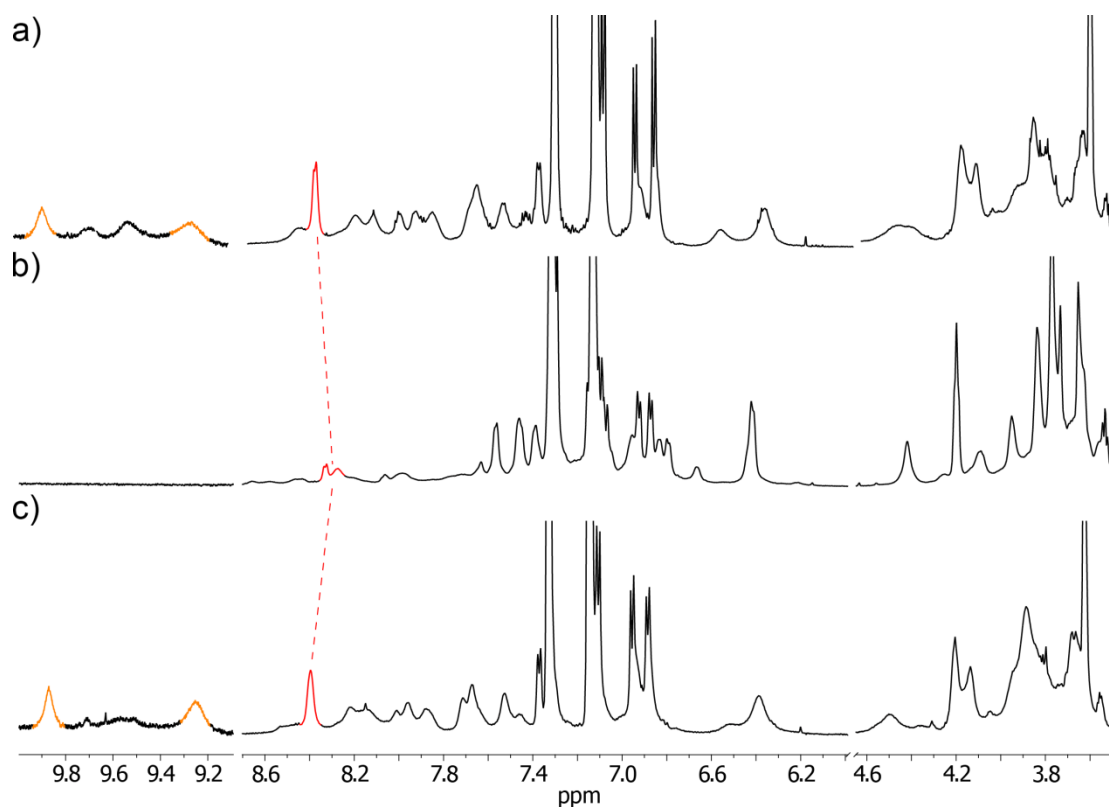


Figure S8. Partial ^1H NMR spectrum (600 MHz, CD_3COCD_3) of the reversible switching between a) $\mathbf{1}\text{-H}^+\text{-CF}_3\text{CO}_2^-$, b) $\mathbf{1}$, c) $\mathbf{1}\text{-H}^+\text{-CF}_3\text{CO}_2^-$, using 2M $\text{NaOH}_{(\text{aq})}$ (from a to b) and $\text{CF}_3\text{CO}_2\text{H}$ (from b to c). The region between $\delta = 9.2$ ppm and $\delta = 9.9$ ppm is shown at x8 increased intensity in comparison with the signals below $\delta = 8.6$ ppm

3. References and notes

- 1 H. W. Gibson, S. H. Lee, P. T. Engen, P. Lecavalier, J. Sze, Y. X. Shen, M. Bheda, *J. Org. Chem.* 1993, **58**, 3748.
- 2 J. D. Crowley, K. D. Hänni, A.-L. Lee, D. A. Leigh, *J. Am. Chem. Soc.* 2007, **129**, 12092.
- 3 M. J. Barrell, D. A. Leigh, P. J. Lusby, A. M. Z. Slawin, *Angew. Chem. Int. Ed.* 2008, **47**, 8036.
- 4 V. Blanco, D. A. Leigh, V. Marcos, J. A. Morales-Serna, A. L. Nussbaumer, *J. Am. Chem. Soc.* 2014, **136**, 4905; V. Blanco, D. A. Leigh, U. Lewandowska, B. Lewandowski, V. Marcos, *J. Am. Chem. Soc.* 2014, **136**, 15775.
- 5 The large number of ^{13}C signals observed is due to the different rotamers that arise from the slow rotation on the NMR timescale of the Boc protecting group.
- 6 Signal located under one of the residual peaks of the solvent and identified in the HSQC spectrum.
- 7 H. Zheng, W. Zhou, J. Lv, X. Yin, Y. Li, H. Liu, Y. Li, *Chem.—Eur. J.* 2009, **15**, 13253.
- 8 P. Kotrusz, S. Toma, H.-G. Schmalz, A. Adler, *Eur. J. Org. Chem.* 2004, 1577.