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Supporting Information

Facile Synthetic Routes to Bridge-Functionalised Calix[4]arenes

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Supporting information here includes:

- General experimental details.
- General crystallographic details.
- Syntheses and analyses of **2 – 4**, **5A – B**, **5D** and **6**.
- Crystallographic details relating to the CIF files also available.
- Ellipsoid plots of crystal structures included in this paper.

General experimental details

Compound **1** was synthesised according to literature procedure.[S1] All starting materials were purchased from Aldrich and used as supplied.

General crystallographic details

Single crystal X-ray diffraction data were collected as follows:

- For **2**, on a Rigaku SuperNova Diffractometer operating at 120(2) K with Mo-Ka radiation (λ = 0.71073 Å) and an Atlas detector.
- For **3**, on a Bruker Apex II CCD diffractometer operating at 173(2) K with synchrotron radiation (λ = 0.7749 Å).
- For **4**, **5A**, **5B**, **5D** and **6**, on a Bruker Apex II CCD diffractometer operating at 100(2) K with synchrotron radiation (λ = 0.7288 Å).

Details for structure refinement in each case are listed below with other analytical data.

Syntheses and analyses of 2 – 4, 5A – B, 5D and 6.

Synthesis of 5,11,17,23-tetra-tert-butyl-2,8,14,20-tetrakis(pent-2-ene-1,4-dione)-25,26,27,28-tetramethoxycalix[4]arene, 2: Compound **1** (1.805 g) and mCPBA (2.403 g) in DCM (60 mL) was stirred at room temp. under N_2 for 18 hours. A white precipitate formed overnight which was removed by filtration and washed with DCM. The filtrate was washed once with Na_2SO_3 (aq) (50 mL), $NaHCO_3$ (aq) (50 mL) and finally with water (50 mL). The organic phase was collected and dried over $MgSO_4$ before removal of solvent under reduced pressure. The crude product was purified by column chromatography (3:2 EtOAc/PET) to yield 0.659 g (34%) of pure product. ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 1.05 (s, 36 H), 2.36 (s, 12 H), 3.86 (s, 12 H), 5.83 (s, 4 H), 6.31 (d, J=11.98 Hz, 4 H), 6.52 (d, J=11.98 Hz, 4 H), 6.82 (s, 8 H). ^{13}C NMR (100.6 MHz, CDCl3): δ ppm 201.5, 199.9, 154.9, 146.0, 139.0, 133.1, 130.8, 125.3, 62.1, 51.2, 34.2, 31.2, 29.6. ESI-MS: 1111.6 $[M+Na]^+$. **Crystal Data (CCDC 2126914):** $C_{146}H_{175}N_5O_{24}$ (*M* =2383.90 g/mol), tetragonal, space group *P*4*bm* (no. 100), *a* = 25.0238(7) Å, *c* = 10.8155(6) Å, *V* = 6772.6(5) Å^3, *Z* = 2, *T* = 120.01(10) K, μ(Mo Kα) = 0.079 mm^{-1}, *Dcalc* = 1.169 g/cm^3, 73696 reflections measured (5.87° ≤ 2Θ ≤ 53.992°), 7480 unique (R_{int} = 0.0831, R_{sigma} = 0.0440) which were used in all calculations. The final R_1 was 0.0520 (I > 2σ(I)) and wR_2 was 0.1046 (all data).

Synthesis of 5,11,17,23-tetra-tert-butyl-2,8,14,20- tetrakis(pentane-1,4-dione)-25,26,27,28-tetramethoxycalix[4]arene, 3:
Compound **1** (0.999 g) in acetic acid (300 mL), water (120 mL) and conc. sulfuric acid (20 mL) was heated at reflux for 20 hours. The green solution was cooled to room temp. before extraction with chloroform (3 x 100 mL). The combined organic phase was washed with water (3 x 100 mL), then dried over $MgSO_4$ before the solvent was removed under reduced pressure. The crude solid was purified by column chromatography (3:2 $CHCl_3$/EtOAc) to yield 0.566 g (53%) of pure product. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.73 (s, 8H), 5.84 (s, 4H), 3.91 (s, 12H), 2.93 (dd, J = 7.2, 5.1 Hz, 4H), 2.80 (dd, J = 7.2, 5.1 Hz, 4H), 2.19 (s, 12H), 1.03 (s, 36H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ ppm 208.76, 207.37, 155.20, 145.85, 131.60, 124.99, 62.51, 51.64, 37.87,

36.70, 34.50, 31.66, 30.31. ESI-MS: 1119.6, $[M+Na]^+$. **Crystal Data (CCDC 2126915):** $C_{68}H_{88}O_{12}$ (*M* =1097.38 g/mol), monoclinic, space group $P2_1/c$ (no. 14), *a* = 13.0103(6) Å, *b* = 19.7417(9) Å, *c* = 24.1171(10) Å, *β* = 91.046(2)°, *V* = 6193.3(5) Å^3, *Z* = 4, *T* = 173(2) K, μ(Synchrotron) = 0.095 mm^{-1}, *Dcalc* = 1.177 g/cm^3, 80335 reflections measured (2.906° ≤ 2Θ ≤ 67.264°), 18907 unique (R_{int} = 0.0780, R_{sigma} = 0.0718) which were used in all calculations. The final R_1 was 0.0629 (I > 2σ(I)) and wR_2 was 0.1856 (all data).

Synthesis of 5,11,17,23-tetra-tert-butyl-2,8,14,20-tetrakis(3-methylpyridazine)-25,26,27,28-tetramethoxycalix[4]arene, 4: Compound **2** (0.501 g) and hydrazine hydrate (1.0 mL) in acetic acid (120 mL) were heated at reflux overnight. Water (100 mL) was added to the brown solution prior to extraction with $CHCl_3$ (3 x 100 mL). The combined organic phase was washed with water (3 x 100 mL) before being dried over $MgSO_4$. Solvent was removed under reduced pressure and the crude was purified by column chromatography (9:1 EtOAc/MeOH) to yield 0.329 g (67%) of pure product. ^{1}H NMR (300 MHz, CD_2Cl_2): δ ppm 0.99 (s, 36 H) 2.69 (s, 12 H) 3.85 (s, 12 H) 6.54 (s, 4 H) 6.78 (s, 8 H) 7.29 (d, *J*=8.80 Hz, 4 H) 7.53 (d, *J*=8.44 Hz, 4 H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ ppm 162.17, 157.69, 155.19, 145.12, 134.60, 127.03, 126.43, 124.70, 62.13, 34.16, 31.37, 22.03. ESI-MS: 1095.6, $[M+Na]^+$. **Crystal Data (CCDC 2126916):** $C_{68}H_{80}N_8O_4$ (*M* =1073.40 g/mol), orthorhombic, space group *Pnma* (no. 62), *a* = 10.9501(4) Å, *b* = 21.9386(8) Å, *c* = 25.0173(9) Å, *V* = 6009.9(4) Å^3, *Z* = 4, *T* = 100(2) K, μ(Synchrotron) = 0.078 mm^{-1}, *Dcalc* = 1.186 g/cm^3, 57612 reflections measured (2.532° ≤ 2Θ ≤ 52.138°), 5651 unique (R_{int} = 0.0540, R_{sigma} = 0.0332) which were used in all calculations. The final R_1 was 0.0615 (I > 2σ(I)) and wR_2 was 0.1955 (all data).

Synthesis of 5,11,17,23-tetra-tert-butyl-2,8,14,20-tetrakis(2-methyl-1H-pyrrole) 25,26,27,28-tetramethoxycalix[4]arene, 5A: Compound **3** (0.402 g) and ammonium acetate (1.008 g) in acetic acid (50 mL) was heated at reflux for 4 hours. After this time the reaction mixture was poured into water (~50 mL). This was then extracted with $CHCl_3$ (3 x 40 mL). The organic phase was then washed once with 1M NaOH solution (40 mL) and twice with water (2 x 40 mL). The combined organic phase was dried over $MgSO_4$ before removal of the solvent under reduced pressure to yield 0.390 g of crude product. The crude solid was purified by column chromatography (9:1 $CHCl_3$/EtOAc) to yield 0.258 g (69%) of pure product. ^{1}H NMR (400 MHz, CDCl3): d ppm 1.01 (s, 36 H), 2.26 (s, 12 H), 3.87 (s, 12 H), 5.82 (d, *J* =1.96 Hz, 8 H), 6.02 (s, 4 H), 6.81 (s, 8 H), 7.68 (br. s, 4 H). ^{13}C NMR (100.6 MHz, CDCl3): δ ppm 154.9, 145.0, 135.4, 132.1, 126.4, 123.9, 108.4, 105.5, 62.1, 37.2, 34.1, 31.3, 13.1. ESI-MS: 1043.6, $[M+Na]^+$. **Crystal Data (CCDC 2126917):** $C_{70}H_{92}N_4O_6$ (*M* =1085.47 g/mol), monoclinic, space group $P2_1/c$ (no. 14), *a* = 16.9126(11) Å, *b* = 24.2434(15) Å, *c* = 15.1940(11) Å, *β* = 90.126(3)°, *V* = 6229.8(7) Å^3, *Z* = 4, *T* = 100(2) K, μ(Synchrotron) = 0.076 mm^{-1}, *Dcalc* = 1.157 g/cm^3, 85343 reflections measured (3.692° ≤ 2Θ ≤ 52.388°), 11523 unique (R_{int} = 0.0618, R_{sigma} = 0.0424) which were used in all calculations. The final R_1 was 0.0533 (I > 2σ(I)) and wR_2 was 0.1495 (all data).

Synthesis of 5,11,17,23-tetra-tert-butyl-2,8,14,20-tetrakis(1-phenyl-2-methyl-1H-pyrrole)-25,26,27,28-tetramethoxycalix[4]arene, 5B: Toluene (30 mL), aniline (0.25 mL) and *p*-toluenesulfonic acid (0.0050 g) were added to compound **3** (0.200 g) and the mixture heated at reflux for 24 hours. The cloudy yellow mixture was cooled to room temp. before the solvent was removed under reduced pressure. The yellow solid was dissolved in chloroform and filtered to yield 0.132 g (55%) of white product. ^{1}H NMR (400 MHz, CDCl3): δ ppm 0.89 (s, 18

H), 1.22 (s, 18 H), 1.98 (s, 12 H), 2.49 (s, 6 H), 3.35 (s, 6 H), 5.42 (s, 4 H), 5.93 (d, *J*=3.30 Hz, 4 H), 5.99 (d, *J*=3.42 Hz, 4 H), 6.42 (s, 4 H), 6.68 - 6.75 (m, 4 H), 6.75 (s, 4 H), 7.16 - 7.27 (m, 8 H), 7.32 - 7.37 (m, 4 H), 7.38 - 7.45 (m, 4 H). ^{13}C NMR (100.6 MHz, CDCl3): δ ppm 153.7, 153.1, 144.2, 143.2, 139.5, 137.4, 134.0, 132.6, 129.1, 128.4, 127.1, 124.6, 122.3, 109.3, 105.6, 62.1, 58.5, 36.1, 34.2, 33.7, 31.7, 31.2, 13.1. ESI-MS: 1347.8, $[M+Na]^+$. **Crystal Data (CCDC 2126918):** $C_{92}H_{100}N_4O_4$ (*M* =1325.75 g/mol), monoclinic, space group *P*2/*n* (no. 13), *a* = 16.383(11) Å, *b* = 11.516(7) Å, *c* = 21.907(15) Å, *β* = 113.553(17)°, *V* = 3789(4) Å^3, *Z* = 2, *T* = 100(2) K, μ(Synchrotron) = 0.073 mm^{-1}, *Dcalc* = 1.162 g/cm^3, 3967 reflections measured (2.726° ≤ 2Θ ≤ 42.846°), 3967 unique (R_{sigma} = 0.0454) which were used in all calculations. The final R_1 was 0.0628 (I > 2σ(I)) and wR_2 was 0.1791 (all data).

Synthesis of 5,11,17,23-tetra-tert-butyl-2,8,14,20-tetrakis(3-(2-methyl-1H-pyrrole)pyridine)-25,26,27,28-tetramethoxycalix[4]arene, 5D: Toluene (50 mL) was added to compound **3** (1.021 g), 3-aminopyridine (0.717 g) and *p*-toluenesulfonic acid (0.099 g) and the mixture heated at reflux for 7 days. The yellow solution was cooled to room temp. before the solvent was removed under reduced pressure. The solid was then dissolved in chloroform (50 mL) before it was washed with water (3 x 50 mL). The organic phase was dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (9:1 DCM/MeOH) to yield 0.345 g (28%) of brown product. ^{1}H NMR (400 MHz, $C_2D_2Cl_4$): δ ppm: 0.85 (br. s, 18 H), 1.19 (s, 18 H), 1.98 (s, 12 H), 2.41 (br. s, 6 H), 3.40 (s, 6 H), 5.32 (br. s, 4 H), 5.94 (br. s, 4 H), 5.99 (br. s, 4 H), 6.38 (br. s, 4 H), 6.67 (br. s, 4 H), 6.98 (br. s, 2 H), 7.39 (br. s, 4 H), 7.57 (br. s, 2 H), 8.00 (br. s, 2 H), 8.44 (br. s, 2 H), 8.64 (br. s, 4 H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ ppm 153.7, 153.3, 151.2, 150.2, 148.8, 144.9, 143.7, 137.1, 136.0, 134.0, 132.1, 129.8, 125.7, 122.6, 110.1, 106.5, 62.2, 58.8, 36.2, 34.4, 33.8, 31.7, 31.2, 13.1. ESI-MS: 1351.8, $[M+Na]^+$. **Crystal Data (CCDC 2126919):** $C_{88}H_{96}N_8O_4$ (*M* =1329.72 g/mol), monoclinic, space group *P*2/*c* (no. 13), *a* = 16.153(9) Å, *b* = 11.480(6) Å, *c* = 21.506(12) Å, *β* = 109.163(9)°, *V* = 3767(4) Å^3, *Z* = 2, *T* = 100(2) K, μ(Synchrotron) = 0.075 mm^{-1}, *Dcalc* = 1.172 g/cm^3, 5337 reflections measured (2.738° ≤ 2Θ ≤ 47.876°), 5337 unique (R_{sigma} = 0.0473) which were used in all calculations. The final R_1 was 0.0581 (I > 2σ(I)) and wR_2 was 0.1598 (all data).

Synthesis of 5,11,17,23-tetra-tert-butyl-2,8,14,20-tetrakis(3-methylpyridazine)-25,26,27,28-trihydroxycalix[4]arene, 6: Compound, 4 (0.350 g) was dissolved in dry DCM (10 mL) under N_2 in a Schlenk flask. The solution was cooled to -78°C using dry ice/acetone before adding 1M BBr_3 in DCM (6.52 mL 6.52 mmol, 20 equivalents) very slowly. Immediately, a solid precipitates. The reaction mixture was stirred at -78°C for 1 hour before it was warmed to RT and stirred for 24h. The brown solution was quenched with water (50 mL) before pouring into a separating funnel. Any residue still in Schlenk flask was dissolved in DCM and added to the aqueous solution. Solution was extracted with DCM and the combined organic phases washed with water (3 x 30 mL). The organic phase was dried over $MgSO_4$ and the solvent was removed under reduced pressure to afford a brown solid (0.265 g). The procedure was then repeated using the crude product and purified via gradient column chromatography (100% $CHCl_3$ → 9:1 $CHCl_3$ in 1% increments). The columned product was then washed with cold ACN to afford 5,11,17,23-tetra-tert-butyl-2,8,14,20-tetrakis(3-methylpyridazine)-25,26,27,28-trihydroxycalix[4]arene as an off white powder (0.018 g, 5 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.60 (br. s, 4H), 7.42 (d, *J* = 8.5 Hz, 4H), 7.33 (d, *J* = 8.5 Hz, 4H), 6.91 (br. s, 8H), 5.55 (s, 4H),

2.72 (s, 12H), 1.06 (s, 36H). ^{13}C NMR (100.6 MHz, CDCl3): δ ppm 162.44, 157.15, 150.34, 138.04, 127.52, 127.34, 127.26, 51.73, 32.71, 30.58, 30.43, 30.36, 28.69, 20.91. ESI-MS: 1039.5 $[M+Na]^+$. **Crystal Data (CCDC 2126920):** $C_{64}H_{72}N_8O_4$ (*M* =1017.29 g/mol), tetragonal, space group *I*-4 (no. 82), *a* = 12.0951(5) Å, *c* = 22.4894(10) Å, *V* = 3290.0(3) Å^3, *Z* = 2, *T* = 100(2) K, μ(Synchrotron) = 0.068 mm^{-1}, *Dcalc* = 1.027 g/cm^3, 42098 reflections measured (3.92° ≤ 2Θ ≤ 52.224°), 3026 unique (R_{int} = 0.0526, R_{sigma} = 0.0294) which were used in all calculations. The final R_1 was 0.0534 (I > 2σ(I)) and wR_2 was 0.1523 (all data).

Ellipsoid Plots

Hydrogen atoms omitted for clarity. Colour code, C – grey, N – blue, O – red. Figures not to scale.

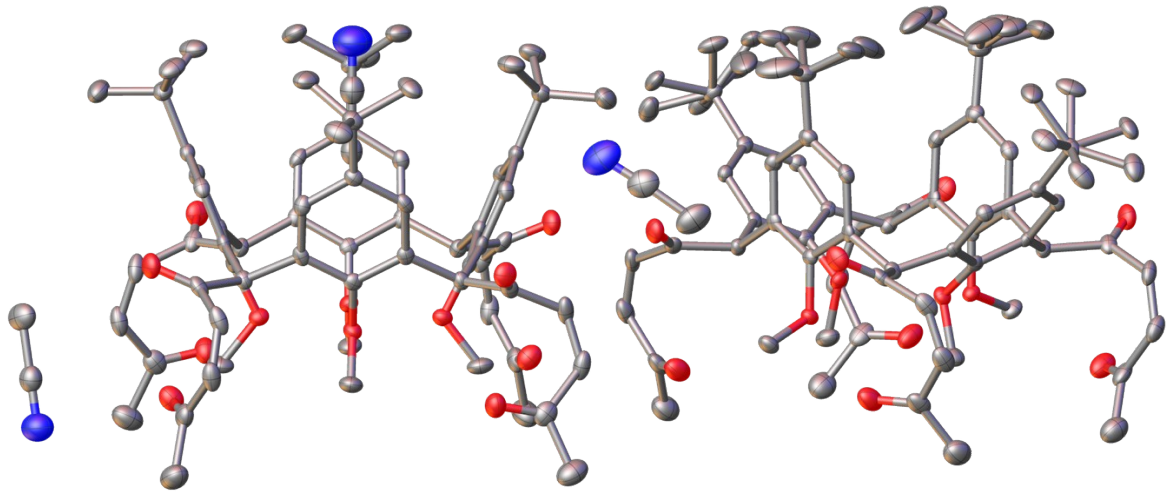

Figure S1. Ellipsoid plot of **2** drawn at 50% probability.

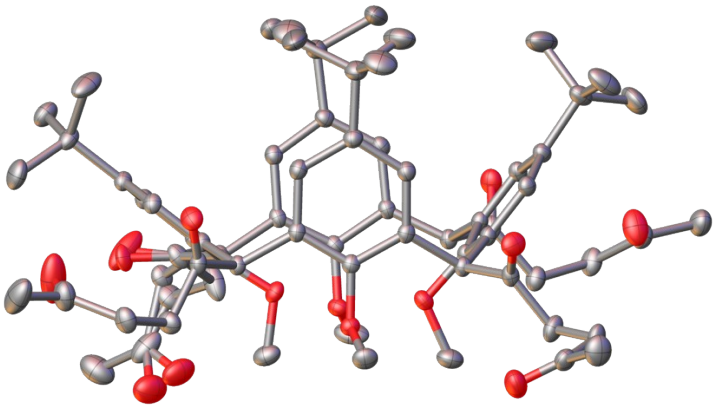

Figure S2. Ellipsoid plot of **3** drawn at 50% probability.

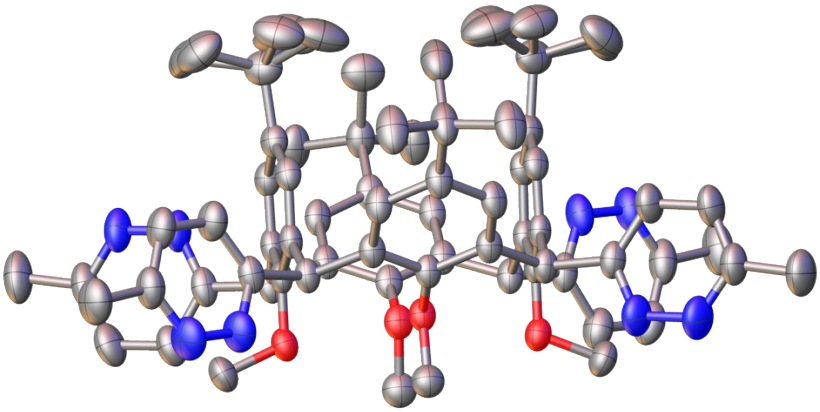

Figure S3. Ellipsoid plot of **4** drawn at 50% probability.

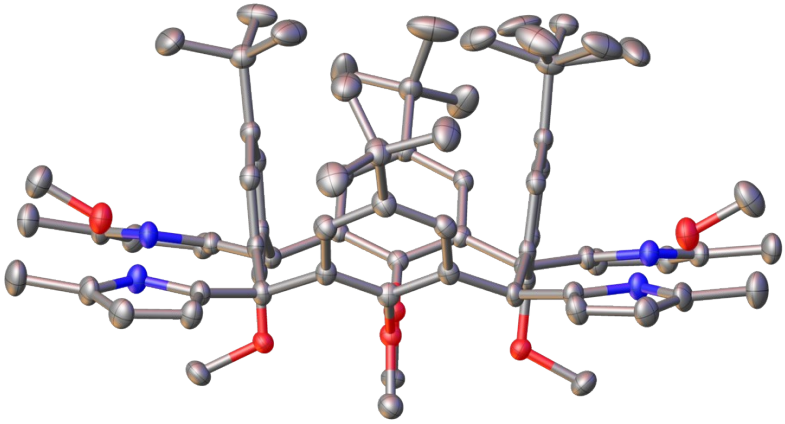

Figure S4. Ellipsoid plot of **5A** drawn at 50% probability.

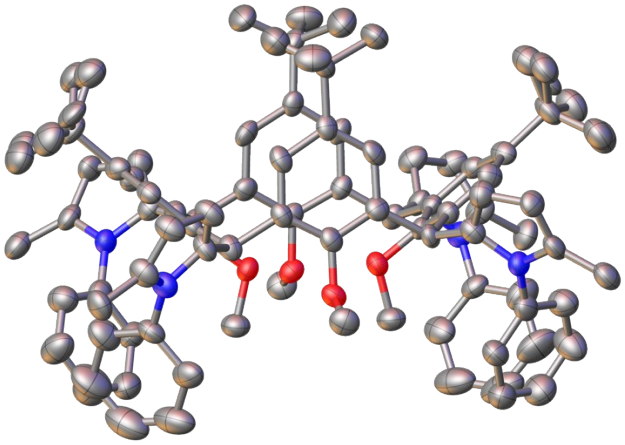

Figure S5. Ellipsoid plot of **5B** drawn at 50% probability.

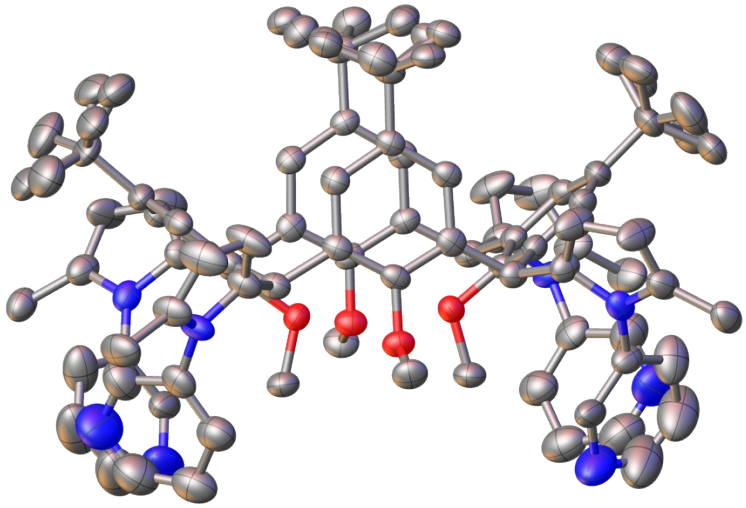

Figure S6. Ellipsoid plot of **5D** drawn at 50% probability.

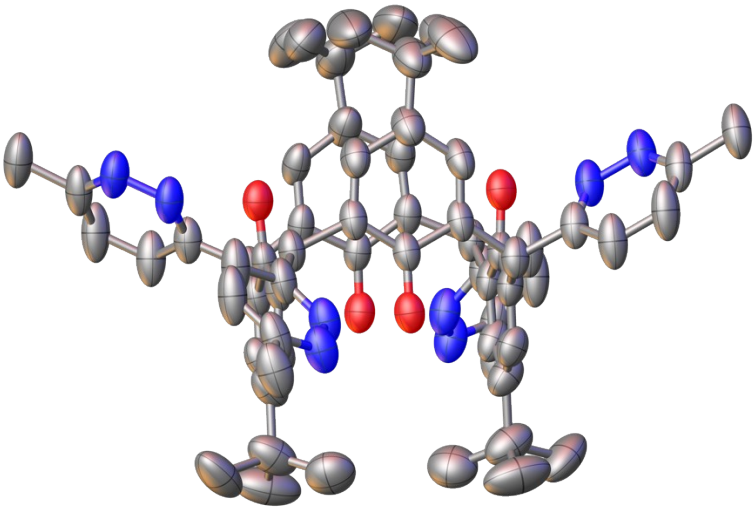

Figure S7. Ellipsoid plot of **6** drawn at 50% probability.

References

S1 I. Columbus and S. E. Biali, *Org. Lett.*, 2007, **9**, 2927–2929.