Supporting Information

Heterotrimetallic Double Cavity Cages: Syntheses and Selective Guest Binding

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Contents

1 Experimental Procedures ........................................................................................................ 2
  1.1 General .......................................................................................................................... 2
  1.2 Synthesis of 1\[^4\] ....................................................................................................... 3
  1.3 Synthesis of 2 ............................................................................................................... 4
  1.4 Synthesis of 3 ............................................................................................................... 5
  1.5 Synthesis of 4\[^5\] ..................................................................................................... 6
  1.6 Synthesis of L1 .......................................................................................................... 7
  1.7 Synthesis of L2 .......................................................................................................... 8
  1.8 Synthesis of DC1 ...................................................................................................... 9
  1.9 Synthesis of DC2 ...................................................................................................... 11
  1.10 1H DOSY NMR data ............................................................................................... 14

2 HPLC ..................................................................................................................................... 16

3 Quantifying by-product formation .................................................................................... 17

4 Guest binding .................................................................................................................... 19
  4.1 2,6-Diaminoanthraquinone (DAQ) .............................................................................. 19
  4.2 5-Fluorouracil (5-FU) binding in DC1 and DC2 .......................................................... 21
    4.2.1 5-Fluorouracil binding in DC1 ............................................................................. 22
    4.2.2 5-Fluorouracil binding in DC2 ........................................................................... 24
  4.3 Host-guest chemistry of monocavity structures ............................................................ 26
    4.3.1 5-Fluorouracil binding in MC ............................................................................. 26
    4.3.2 Cisplatin binding to MC .................................................................................... 27
    4.3.3 5-Fluorouracil binding to [Pd\(_2\)(2,6-bis(pyridin-3-ylethynyl)pyridine)\(_4\)](BF\(_4\))\(_4\) 28
  4.4 Segregated Host-Guest Chemistry .............................................................................. 28

5 X-ray crystallography ........................................................................................................... Error! Bookmark not defined.

6 References .......................................................................................................................... 32
1 Experimental Procedures

1.1 General

All reagents were purchased from commercial sources and used without further purification. 3,5-Bis(trimethylsilyl)ethynylpyridine,[1] [Pt(3-pyridylcarboxyaldehyde)4](BF4)2 (Ptppyald),[2] the Pd(II)/Pt(II) monocavity cage (MC)[2] and [Pd2(2,6-bis(pyridin-3-ylethynyl)pyridine)4](BF4)4[3] were synthesized using previously established methods. TLC plates (200 µm thickness) and silica gel (40 – 63 µm) were purchased from Silicycle. The solvents used were laboratory reagent grade unless specified otherwise. Petroleum ether refers to the fraction of petrol boiling in the range of 40-60 °C. Abbreviated solvents and reagents include acetonitrile (CH3CN), dichloromethane (DCM), dimethylformamide (DMF), dimethylsulfoxide (DMSO), ethylenediaminetetraacetic acid (EDTA), methanol (MeOH) tetrahydrofuran (THF), triethylamine (TEA). 0.1 M Ammonium hydroxide/ ethylenediaminetetraacetic acid (NH4OH/EDTA) solution was made up by mixing 30 g EDTA with 900 mL water and 100 mL NH4OH. 1H and 13C{1H} NMR spectra were collected using either a 400 MHz Varian/Agilent 400-MR or a Varian 500 MHz AR spectrometer. Chemical shifts (δ) are reported in parts per million (ppm) and referenced to residual solvent peaks (CDCl3: 1H δ, 7.26 ppm, 13C δ, 77.16 ppm; CD3CN: 1H δ, 1.94 ppm, 13C δ, 1.32 & 118.26 ppm; [D8]DMSO: 1H δ, 2.50 ppm, 13C δ, 39.52 ppm). Coupling constants (J) are reported in Hertz (Hz). Standard abbreviations indicating multiplicity were used as follows: m = multiplet, sex = sextet, quin = quintet, q = quartet, t = triplet, dt = doublet of triplets, d = doublet, dd = doublet of doublets, s = singlet, dtd = doublet of triplets of doublets, ddd = doublet of doublets of doublets, dq = doublet of quartets. 1H DOSY NMR spectra were obtained using a Bruker Advance 400 MHz NMR spectrometer and processed on MestReNova 14.2.2 using the peak fit method. All proton assignments were carried out using data from COSY, NOESY (ROESY) and if required model compounds. ESI-mass spectra (ESIMS) were collected using either a Bruker microTOF-Q spectrometer or a Shimadzu LCMS-9030 spectrometer. ESIMS data of metal complexes were obtained using either pseudo coldspray or coldspray conditions (nebulizer and heating gasses cooled to room temperature or -10 °C, respectively. Microanalyses were conducted at the Campbell Microanalytical Laboratory at the University of Otago.

Synthetic scheme showing the synthesis of L1

\[ \text{Scheme S1 Synthesis of L1 (i) CuI, [Pd(PPh3)2Cl2], TEA, THF, 60 °C for 16 h (ii) K2CO3, MeOH, 1 h (iii) CuI, [Pd(PPh3)4], TEA, THF, 80 °C for 16 h.} \]
Synthetic scheme showing the synthesis of L2

Scheme S2 Synthesis of L1

1.2 Synthesis of 1\[^{[4]}\]

3-iodoaniline (2.31 g, 10.6 mmol) and ethynyltrimethylsilane (3.01 mL, 21.1 mmol) were added to degassed TEA:THF (1:1 v/v, 6.00 mL) under Ar in a sealed tube. Then copper(I) iodide (0.201 g, 1.05 mmol) and bis(triphenylphosphine)palladium(II) dichloride (0.186 g, 0.263 mmol) were added as solids and the reaction mixture was heated at 60 °C for 16 h. The solvents were removed under vacuum to yield the crude residue as a brown oil. The residue was dissolved in CHCl₃ (150 mL) and the solution washed with EDTA/NH₄OH (0.10 M, 150 mL), water (150 mL) and then brine (150 mL). The organic layer was separated and dried over Na₂SO₄. The solvent was then removed under vacuum to afford the crude product as a brown oil. The product was purified by column chromatography (silica, 1:0 – 0:1 petroleum ether/CHCl₃ gradient) to yield pure 1 as a colourless oil (1.58 g, 79%). ^{1}H NMR (400 MHz, 298 K, CDCl₃) δ, 7.08 (t, J = 7.7 Hz, 1H, Hc), 6.88 (dt, J = 7.7, 1.2 Hz, 1H, Hb), 6.80 (dd, J = 2.6, 1.8 Hz, 1H, Ha), 6.64 (ddd, J = 8.1, 2.4, 1.0 Hz, 1H, Hb), 3.72 (s, 2H, Hf). ^{13}C NMR (100 MHz, 298 K, CDCl₃) δ, 146.22, 129.30, 123.94, 122.60, 118.36, 115.72, 105.50, 93.57, 0.15. ESIMS: (MeOH) m/z = 190.1037 [M + H]^+ (calc. for C₁₁H₁₆NSi, 190.1047).
1.3 Synthesis of 2

1 (1.20 g, 6.34 mmol) and sodium carbonate (3.50 g, 25.4 mmol) were combined in MeOH (80 mL) and stirred at RT for 30 min. The resulting mixture was filtered through celite and the solvent removed under vacuum. The crude mixture was dissolved in DCM (10 mL) and passed through a silica plug (DCM). The solvent was removed under vacuum to afford a colourless oil. The resulting oil was combined with 3,5-dibromopyridine (5.40 g, 22.8 mmol) in a deoxygenated TEA:THF solution (1:3 v/v, 235 mL) under Ar. Copper(I) iodide (0.108 g, 0.574 mmol) and bis(triphenylphosphine)palladium(II) dichloride (0.120 g, 0.169 mmol) were added as solids and the resulting mixture was heated at 80 °C for 16 hours. The solvent was removed under vacuum and the resulting residue was dissolved in DCM and washed with EDTA/NH₄OH (0.10 M, 200 mL) and finally brine (200 mL). The organic layer was collected and dried over MgSO₄. The solvent was removed under vacuum to give the crude product as a brown oil. The crude product was purified by column chromatography (silica, 1:0 – 0.8:0.2 petroleum ether/ethyl acetate gradient) to yield pure 2 as an off-white solid (0.708 g, 45%). ¹H NMR (400 MHz, 298 K, CDCl₃) δ, 8.63 (d, J = 1.8 Hz, 1H, H₅), 8.58 (d, J = 2.3 Hz, 1H, H₄), 7.93 (t, J = 2.0 Hz, 1H, H₆), 7.14 (t, J = 7.8 Hz, 1H, H₃), 6.92 (dt, J = 7.6, 1.2 Hz, 1H, H₂), 6.83 (dd, J = 2.4, 1.5 Hz, 1H, H₁), 6.69 (ddd, J = 8.1, 2.4, 1.0 Hz, 1H, H₀), 3.71 (s, 2H, H₇). ¹³C NMR (100 MHz, 298 K, CDCl₃) δ, 150.37, 149.73, 146.56, 140.80, 129.62, 122.84, 122.32, 122.18, 120.23, 117.92, 116.30, 94.46, 83.98. ESIMS: (CH₃CN) m/z = 273.0037 [M + H]+ (calc. for C₁₃H₁₀N₂Br, 273.0022).
1.4 Synthesis of 3

2 (0.600 g, 2.20 mmol) was added to a deoxygenated solution of TEA:THF (1:1 v/v, 6 mL) under Ar in a sealed tube. Then copper(I) iodide (0.041 g, 0.220 mmol), tetrakis(triphenylphosphine)palladium(0) (0.025 g, 0.022 mmol) and ethynyltrimethylsilane (0.782 mL, 5.49 mmol) were added to the deoxygenated solution and the resulting mixture was heated at 80 °C for 16 h. The solvent was removed under vacuum and the residue was dissolved in DCM (50 mL), washed with EDTA/NH₄OH (0.10 M, 75 mL), water (75 mL) and brine (75 mL). The organic layer was collected and dried over MgSO₄. The solvent was removed under vacuum and the crude product obtained purified by column chromatography (silica, DCM) to give pure 3 as a brown oil (0.388 g, 60%). ¹H NMR (400 MHz, 298 K, CDCl₃) δ, 8.63 (d, J = 2.0 Hz, 1H, Hg/h), 8.58 (d, J = 2.0 Hz, 1H, Hg/h), 7.85 (t, J = 2.0 Hz, 1H, Hf), 7.14 (t, J = 7.3 Hz, 1H, Hc), 6.92 (dt, J = 7.6, 1.2 Hz, 1H, Hb), 6.93 (s, 2H, Hb), 6.83 (t, J = 1.9 Hz, 1H, Ha), 6.68 (ddd, J = 8.1, 2.4, 1.0 Hz, 1H, Ha), 3.61 (s, 2H, Ha), 0.25 (s, 9H, Hi). ¹³C NMR (100 MHz, 298 K, CDCl₃) δ, 151.09, 151.03, 146.52, 141.11, 129.53, 123.04, 122.20, 120.23, 120.02, 117.86, 116.08, 100.78, 99.16, 93.67, 84.60, -0.40. Anal. calc. for C₁₈H₁₈N₂Si·0.2CHCl₃ C, 69.55; H, 5.84; N, 8.91% Found C, 69.65; H, 6.18; N, 9.30%. ESIMS: (MeOH) m/z = 291.1300 [M + H]⁺ (calc. for C₁₈H₁₈N₂Si, 291.1312).
1.5 Synthesis of 4

3-Ethynylpyridine (0.796 g, 7.72 mmol) and 2,6-dibromopyridine (7.31 g, 30.9 mmol) were added to a degassed solution of TEA:THF (1:3 v/v, 285 mL) under Ar. Then copper(I) iodide (0.147 g, 0.772 mmol) and bis(triphenylphosphine)palladium(II) dichloride (0.163 g, 0.232 mmol) were added as solids to the reaction mixture and heated at 80 °C for 16 h. The solvent was removed under vacuum and the crude residue was dissolved in DCM (150 mL) and washed with EDTA/NH4OH (0.10 M, 150 mL), water (150 mL) and finally brine (150 mL). The organic layer was collected and dried over MgSO4. The crude mixture was purified by column chromatography (silica, 1:0 – 0:1 DCM/ethyl acetate gradient) to give pure 4 as an off-white solid (1.09 g, 54%). 1H NMR (400 MHz, 298 K, CDCl3) δ, 8.82 (d, J = 1.0 Hz, 1H, Ha), 8.60 (dd, J = 4.9, 1.7 Hz, 1H, Hb), 7.87 (dt, J = 7.9, 1.9 Hz, 1H, Hd), 7.56 (t, J = 7.7 Hz, 1H, Hf), 7.52 – 7.45 (m, 2H, He,g), 7.31 (ddd, J = 7.9, 4.9, 0.9 Hz, 1H, Hc). 13C NMR (100 MHz, 298 K, CDCl3) δ, 152.78, 149.66, 143.37, 142.11, 139.09, 138.55, 128.07, 126.29, 123.26, 119.20, 90.52, 87.26. ESIMS: (MeOH) m/z = 258.9860 [M + H]⁺ (calc. for C12H8N2Br, 258.9865).
Figure S8 $^{13}$C($^1$H) NMR spectrum (100 MHz, CDCl$_3$, 298 K) of 4.

1.6 Synthesis of L1

3,5-Bis(trimethylsilyl)ethynylpyridine (0.686 g, 2.52 mmol) and potassium carbonate (1.39 g, 10.1 mmol) were combined in MeOH (32 mL) and stirred at RT for 1 h. The resulting mixture was filtered through celite and the solvent was removed under vacuum. The product was dissolved in DCM and passed through a silica plug (DCM). The solvent was then removed under vacuum. The resulting compound was combined with 3-iodoaniline (1.03 g, 4.72 mmol) in degassed TEA:THF (1:1 v/v, 3 mL) under Ar in a sealed tube. Then copper(I) iodide (0.045 g, 0.24 mmol) and tetrakis(triphenylphosphine)palladium(0) (0.027 g, 0.024 mmol) were added as solids and the reaction mixture was heated at 80 °C for 16 h. The solvent was removed under vacuum to yield a brown oil which was dissolved in CHCl$_3$ (200 mL) and washed with EDTA/NH$_4$OH (0.10 M, 150 mL), water (150 mL) and finally brine (150 mL). The organic layer was separated and dried over MgSO$_4$. The solvent was removed under vacuum and the crude product was purified by column chromatography (silica, 1:0 – 0:1 CHCl$_3$/CH$_3$CN gradient) to yield pure L1 as a brown solid (0.267 g, 36%). $^1$H NMR (400 MHz, 298 K, [D$_6$]DMSO) $\delta$, 8.70 (d, $J$ = 2.1 Hz, 2H, H$_f$), 8.10 (t, $J$ = 7.8 Hz, 2H, H$_e$), 7.08 (t, $J$ = 2.1 Hz, 1H, H$_g$), 6.76 (t, $J$ = 1.9 Hz, 2H, H$_h$), 6.72 (dt, $J$ = 7.6, 1.3 Hz, 2H, H$_e$), 6.64 (ddd, $J$ = 8.1, 2.3, 1.0 Hz, 2H, H$_b$), 5.32 (s, 4H, H$_a$). $^{13}$C NMR (100 MHz, 298 K, [D$_6$]DMSO) $\delta$, 150.95, 149.35, 140.59, 129.77, 122.08, 120.05, 119.45, 116.63, 115.64, 94.53, 84.36. Anal. calc. for C$_{21}$H$_{15}$N$_3$·0.3H$_2$O C, 80.13; H, 5.00; N, 13.35%. Found C, 79.59; H, 4.95; N, 13.84. ESIMS: (MeOH) $m/z$ = 310.1323 [M + H]$^+$ (calc. for C$_{21}$H$_{15}$N$_3$, 310.1339).

Figure S9 $^1$H NMR spectrum (400 MHz, [D$_6$]DMSO, 298 K) of L1.
1.7 Synthesis of L2

3 (0.300 g, 1.03 mmol) and sodium carbonate (0.438 g, 4.13 mmol) were combined in MeOH (13 mL) and stirred at RT for 30 min. The resulting mixture was filtered through celite and the solvent was removed under vacuum. The reaction mixture was dissolved in DCM (5 mL) and passed through a silica plug (DCM). The solvent was removed under vacuum and the resulting product (a colourless oil) was combined with 4 (0.223 g, 0.859 mmol) in deoxygenated diisopropylamine:THF (1:1 v/v, 4 mL) under Ar in a sealed tube. Then copper(I) iodide (16 mg, 0.084 mmol) and tetrakis(triphenylphosphine)palladium(0) (30 mg, 0.036 mmol) were added as solids and the mixture was heated at 80 °C for 16 h. The solvent was removed under vacuum and the solid residue was dissolved in DCM (50 mL) and washed with EDTA/NH₄OH (0.10 M, 75 mL), water (75 mL) and finally brine (75 mL). The organic layer was separated and dried over MgSO₄. The solvent was removed under vacuum to afford a brown solid. The solid was purified by column chromatography (silica, 1:0-0:1 DCM/ethyl acetate gradient) and the brown band collected. The solvent was removed under vacuum and the resulting brown solid purified by recrystallisation from hot ethyl acetate. The resulting solid was collected by vacuum filtration and washed with ethyl acetate (5 mL) to yield pure L2 as a colourless solid (0.140 g, 41%).

1H NMR (400 MHz, 298 K. [D₆]DMSO) δ, 8.82 (m, 3H, Hₐ,i,j), 8.66 (d, J = 4.6 Hz, 1H, Hₙ), 8.23 (s, 1H, Hₗ), 8.08 (d, J = 8.0 Hz, 1H, Hₖ), 7.80 (t, J = 7.8 Hz, 1H, Hₙ), 7.76 (m, 2H, Hₐ,g), 7.53 (dd, J = 7.9, 4.9 Hz, 1H, Hₜ), 7.09 (t, J = 7.8 Hz, 1H, Hₗ), 6.77 (t, J = 1.9 Hz, 1H, Hₙ), 6.73 (d, J = 7.5 Hz, 1H, Hₖ), 6.65 (d, J = 8.0 Hz, 1H, Hₗ), 5.31 (s, 2H, H₀). 13C NMR (100 MHz, [D₆]DMSO) δ, 151.97, 151.50, 150.86, 149.79, 148.90, 142.35, 142.15, 140.70, 139.05, 137.91, 129.30, 127.52, 127.47, 123.72, 121.54, 119.73, 119.01, 118.26, 118.23, 116.19, 115.25, 94.35, 91.43, 90.85, 85.83, 84.92, 83.72. ESIMS: (CH₃CN): m/z = 397.1453 [M + H]+ (calc. for C₂₇H₁₇N₄, 397.1448), 419.1261 [M + Na]+ (calc. for C₂₇H₁₆N₄Na, 419.1267), 815.2630 [2M + Na]+ (calc. for C₅₄H₃₂N₈Na₂Na, 815.2642).
1.8 Synthesis of DC1

**L1** (0.267 g, 0.863 mmol), Ptppy (0.344 g, 0.432 mmol) and [Pd(CH₃CN)₄](BF₄)₂ (0.096 g, 0.22 mmol) were dissolved in DMSO (5 mL) and stirred at RT for 5.5 h. Ethyl acetate (20 mL) was then added to the solution and the resulting precipitate was collected by filtration. The precipitate was washed with ethyl acetate (20 mL) and diethyl ether (20 mL) to yield DC1 as a colourless solid (0.612 g, 95%). ¹H NMR (400 MHz, [D₆]DMSO) δ, 9.55 (d, J = 1.8 Hz, 8H, Hₐ), 9.91-9.71 (m, 16H, Hₖ), 8.97 (s, 8H, Hₜ), 8.63 (d, J = 8.0 Hz, 8H, Hₔ), 8.58 (s, 4H, Hᵢ), 7.94 (t, J = 6.9 Hz, 8H, Hₜ), 7.85 (s, 4H, Hᵢ), 7.68 – 7.51 (m, 24H, Hₙ,ₙ,ₙ,ₙₙ). ¹³C NMR (125 MHz, [D₆]DMSO) δ, 157.75, 153.81, 152.75, 151.55, 149.50, 144.82, 139.25, 134.90, 131.12, 128.44, 125.33, 123.33, 122.55, 121.67, 95.19, 84.15. Anal. calc. for C₁₃₂H₈₄B₆F₂₄N₂₀PdPt₂•5DMSO C, 50.79; H, 3.42; N, 8.34%. Found C, 50.50; H, 3.24; N, 8.48%. ESIMS: (CH₃CN) m/z = 496.3030 [M – 6BF₄ + Cl]⁵⁺ (calc. for C₁₃₂H₈₄N₂₀PdPt₂Cl, 496.30421), 499.9063 [M – 6BF₄ + Cl + H₂O]⁵⁺ (calc. for C₁₃₂H₈₆N₂₀OPdPt₂Cl, 499.9063), 502.7095 [M – 6BF₄ + Cl + CH₃OH]⁵⁺ (calc. for C₁₃₄H₈₆N₂₀OPdPt₂Cl, 502.7095), 505.5100 [M – 5BF₄]⁷⁺ (calc. for C₁₃₄H₈₄N₂₀PdPt₂BF₄Cl, 506.5112), 642.1297 [M – 5BF₄ + Cl]⁷⁺ (calc. for C₁₃₂H₈₄N₂₀PdPt₂BF₄Cl, 642.1313).
Figure S13: $^1$H NMR spectrum (400 MHz, [D$_6$]DMSO, 298 K) of DC1.

Figure S14: $^{13}$C($^1$H) NMR spectrum (125 MHz, [D$_6$]DMSO, 298 K) of DC1.

Figure S15: $^1$H NMR spectrum (400 MHz, CD$_3$CN, 298 K) of DC1.
1.9 Synthesis of DC2

\[ \text{L}^2 \text{ (0.030 g, 0.076 mmol), } \text{Pt}_{\text{pyald}} \text{ (0.015 g, 0.019 mmol) and } [\text{Pd(}\text{CH}_3\text{CN})_4](\text{BF}_4)_2 \text{ (0.017 g, 0.038 mmol) were dissolved in } [\text{D}_6]\text{DMSO (750 }\mu\text{L). The reaction mixture was heated at } 50^\circ\text{C for } 10 \text{ h. After cooling to ambient temperature, ethyl acetate (20 mL) was added to the solution and the resulting precipitated was collected by vacuum filtration. The precipitate was washed with DCM (10 mL) and diethyl ether (10 mL) to yield DC2 as a tan solid (0.047 g, 87%).} \]

^1H NMR (400 MHz, [D₆]DMSO) δ 9.74 (d, J = 1.8 Hz, 4H, Hᵢ/j), 9.63 (s, 4H, Hₐ), 9.48 (s, 4H, Hᵢ/j), 9.37 – 9.32 (m, 8H, Hᵢ/r), 9.30 (s, 4H, Hₛ), 8.96 (s, 4H, Hₒ), 8.68 – 8.58 (m, 8H, Hₕ,p), 8.33 (d, J = 8.0 Hz, 4H, Hᵢ), 8.03 (t, J = 7.8 Hz, 4H, Hᵢ), 7.93 (dd, J = 8.2, 6.1 Hz, 4H, Hᵢ/j), 7.86 – 7.78 (m, 16H, Hᵥᵥᵥᵥ), 7.58 – 7.50 (m, 12H, Hₙ,m,n). ^13C NMR (100 MHz, [D₆]DMSO) δ 171.96, 158.18, 154.22, 153.87, 153.61, 153.51, 152.94, 152.72, 151.55, 150.01, 145.68, 143.91, 142.46, 142.31, 139.32, 138.84, 135.34, 131.44, 130.97, 129.40, 128.80, 127.79, 126.24, 123.43,
122.91, 122.09, 121.98, 118.49, 95.74, 94.45, 93.75, 84.48, 84.27, 83.79. Anal. calc. for C\textsubscript{132}H\textsubscript{76}B\textsubscript{6}F\textsubscript{24}N\textsubscript{20}Pd\textsubscript{2}Pt\textcdot 3.5DCM C, 51.37; H, 2.64; N, 8.84%. Found C, 51.39; H, 2.34; N, 9.07%. ESIMS: (CH\textsubscript{3}CN) \textit{m/z} = 391.5733 [\textit{M} – 6BF\textsubscript{4}]\textsuperscript{6+} (calc. for C\textsubscript{132}H\textsubscript{76}N\textsubscript{20}Pd\textsubscript{2}Pt, 391.5716), 477.0814 [\textit{M} – 6BF\textsubscript{4} + Cl]\textsuperscript{5+} (calc. for C\textsubscript{132}H\textsubscript{76}N\textsubscript{20}Pd\textsubscript{2}PtCl, 477.0797), 619.3581 [\textit{M} – 6BF\textsubscript{4} + Cl + F + CH\textsubscript{3}CN + CH\textsubscript{3}OH]\textsuperscript{4+} (calc. for C\textsubscript{135}H\textsubscript{83}N\textsubscript{21}OPdPt\textsubscript{2}ClF, 619.3626).

Figure S17 ¹H NMR spectrum (400 MHz, [D\textsubscript{6}]DMSO, 298 K) of DC\textsubscript{2}.

Figure S18 ¹³C{¹H} NMR spectrum (100 MHz, [D\textsubscript{6}]DMSO, 298 K) of DC\textsubscript{2}.

Figure S19 ¹H NMR spectrum (400 MHz, CD\textsubscript{3}CN, 298 K) of DC\textsubscript{2}.
Figure S20: ESIMS (CH3CN) of DC2.

Figure S21: Stacked partial ¹H NMR spectra (400 MHz, [D₆]DMSO, 298 K) of a) L2, b) DC2, and c) Ptpyald.
1.10 $^1$H DOSY NMR data

**Figure S22** Partial $^1$H NMR and corresponding DOSY NMR spectra for Pt$_{pyald}$ (400 MHz, CD$_3$CN, 298 K).

**Figure S23** Partial $^1$H NMR and corresponding DOSY NMR spectra for L1 (400 MHz, CD$_3$CN, 298 K).

**Figure S24** Partial $^1$H NMR and corresponding DOSY NMR spectra for DC1 (400 MHz, CD$_3$CN, 298 K).
Figure S25 Partial $^1$H NMR and corresponding DOSY NMR spectra for DC2 (400 MHz, CD$_3$CN, 298 K).

Figure S26 Partial $^1$H NMR and corresponding DOSY NMR spectra for the monocavity (MC)$^{[2]}$ cage (400 MHz, CD$_3$CN, 298 K).

Table S1 Diffusion coefficients as obtained via $^1$H DOSY NMR experiments (400 MHz, CD$_3$CN, 298 K).

| Species | Molecular Weight (g mol$^{-1}$) | Diffusion Coefficient ($\times 10^{-10}$ m$^2$ s$^{-1}$) |
|---------|--------------------------------|------------------------------------------------------|
| DC1     | 2966.67                        | 4.50                                                 |
| DC2     | 2870.95                        | 4.55                                                 |
| MC      | 1743.00                        | 5.55                                                 |
| L1      | 309.37                         | 11.8                                                 |
| L2      | 396.44                         | -                                                   |
| Pt$_{pyald}$ | 797.13                      | 8.10                                                 |
Figure S27 Plot of log(D) against log(Mw) for L1, Pt_{pyald}, MC, DC1 and DC2 (400 MHz, CD\textsubscript{3}CN, 298 K, units D: \( \times 10^{-10} \text{m}^2 \text{s}^{-1} \), M\textsubscript{w}: g mol\textsuperscript{-1}).

2 HPLC

HPLC grade CH\textsubscript{3}CN was purchased from Merck Chemicals. MilliQ grade water (H\textsubscript{2}O) was obtained from a Millipore purification system. HPLC grade trifluoroacetic acid (TFA) was purchased from Scharlau. HPLC analyses were conducted using analytical RP-HPLC (Shimadzu LC-20AD equipped with an SPD-20A UV detector [210 and 254 nm] and a Shimadzu ELSD-LTII Low Temperature Evaporative Light Scattering Detector) using a Phenomenex Prodigy 5 \textmu m ODS-3 100 Å column (C-18, 5 \textmu m, 3 x 250 mm) at 0.5 mL/min, heated to 40 °C. The solvent system for all LC purposes was a mixture of A (0.05% TFA in H\textsubscript{2}O) and B (CH\textsubscript{3}CN). RP-HPLC (10% to 100% B over 12.5 min, then 100% B for 2.5 min), t\textsubscript{R} = 21 min. Samples were prepared in HPLC grade CH\textsubscript{3}CN (1 mg/mL).
3 Quantification of the amounts of DC1 and DC2 formed in the assembly reactions

DC1 and DC2 were synthesised at a series of concentrations (20 mM, 10 mM, 5 mM and 2 mM) in [D₆]DMSO (500 µL) in the presence of a tert-butanol internal standard (1 eq. to the theoretical DC cage product). DC1 systems were left at RT for 10 h and DC2 systems were heated at 50 °C for 10 h. ¹H NMR spectra were collected after these time periods for all samples. The formation of the cage in solution was quantified by comparing proton signals to that of the tert-butanol internal standard. The experimental data for DC1 and DC2 suggested that the amount of cage formed in solution compared to the tert-butanol internal standard remained the same across all concentration. A yield was calculated by comparing the experimental ratio to the theoretical ratio. A calculated yield of 64% for DC1 and 79% for DC2 was determined. ¹H NMR spectra were again obtained after 30 days in solution at RT and the ratio of standard to cage peaks appeared unchanged.
Figure S29 Stacked partial $^1$H NMR spectra ([D$_6$]DMSO, 298 K, 400 MHz) showing the formation of DC1 at different concentrations.

Figure S30 Stacked partial $^1$H NMR spectra ([D$_6$]DMSO, 298 K, 400 MHz) showing the formation of DC1 at different concentrations after 30 days in solution.

Figure S31 Stacked partial $^1$H NMR spectra ([D$_6$]DMSO, 298 K, 400 MHz) showing the formation of DC2 at different concentrations.
Figure S32 Stacked partial $^1$H NMR spectra ([D$_6$]DMSO, 298 K, 400 MHz) showing the formation of DC2 at different concentrations after 30 days in solution.

4 Guest binding

4.1 2,6-Diaminoanthraquinone (DAQ)

2,6-Diaminoanthraquinone (0.33 mg, 1.4 µmol) was added to a solution of DC1 (1.02 mg, 0.348 µmol) or DC2 (1.00 mg, 0.348 µmol) in [D$_6$]DMSO (700 µL). The binding was monitored using $^1$H NMR spectroscopy.

Figure S33 Stacked partial $^1$H NMR spectra (400 MHz, [D$_6$]DMSO, 298 K) of a) DC1, b) DC1 + DAQ, and c) DAQ.
Figure S34 Stacked partial $^1$H NMR spectra (400 MHz, [D$_6$]DMSO, 298 K) of a) DC2, b) DC2 + DAQ, and c) DAQ.

Figure S35 ESIMS (CH$_3$CN) of a DC1 – DAQ mixture (1:2).
4.2 5-Fluorouracil (5-FU) binding to DC1 and DC2

5-Fluorouracil guest binding studies were carried out in CD$_3$CN using tetrakis(trimethylsilyl)silane as a standard (0.10 µmol). Stock solutions of DC1 (1.48 mg, 1 mL) or DC2 (0.57 mg, 1 mL) (including the by-products) were prepared in CD$_3$CN and the undissolved impurities were removed by centrifugation. Half of the cage stock solution (0.5 mL) was taken and combined with solid 5-fluorouracil (50 eq) to give the guest stock solution. The remaining host stock solution was added to an NMR tube to which varying aliquots of the guest stock were added (5 – 50 µL). The resulting solutions with different host-guest stoichiometries were examined using $^1$H NMR spectroscopy and the final concentrations of host/guest were determined by integration of peaks and comparison to the standard used. Using this procedure, the concentration of the host remained the same throughout the titration experiment. Association constants were obtained using Bindfit (supramolecular.org) by curve fitting the shifts of proton signals against mole ratio of guest relative to host.$^{[6]}$ The titration experiments were repeated in triplicates and an average binding constant is reported. Data for 5-fluorouracil binding within DC1 was fitted to 1:2 host/guest binding models. The model presenting the lowest errors, root mean square and covariances were assumed to be the most accurate. The binding constants for the statistical model provided binding constants with the least error and was therefore the model used to determine the binding constants of 5-fluorouracil binding within DC1 ($K_1 = 1260 \pm 20$ M$^{-1}$, $K_2 = 315 \pm 5$ M$^{-1}$). The binding of 5-
fluorouracil in DC2 was fitted to a 1:1 host-guest mixture to give an average binding constant of $210 \pm 3 \text{ M}^{-1}$.

### 4.2.1 5-Fluorouracil binding to DC1

![ESIMS (CH$_3$CN) of a DC1 – 5-fluorouracil (5-FU) mixture.](image)

**Figure S37** ESIMS (CH$_3$CN) of a DC1 – 5-fluorouracil (5-FU) mixture.
Figure S38 Stacked partial $^1$H NMR spectra (CD$_3$CN, 500 MHz, 298 K) of 5-fluorouracil titrated into a solution of DC1.

Figure S39 $^1$H NMR spectroscopy (CD$_3$CN, 500 MHz, 298 K) titration curves of DC1 with 5-fluorouracil monitored by the shifts of protons $H_a$, $H_k$ and $H_i$. One of three titration sets is shown.
Table S2 Binding constants (K), root mean squared (RMS) and covariances calculated from fitting the different 1:2 host/guest binding models for the titration of 5-fluorouracil with DC1 (CD3CN). The obtained values are averages of three different titration data sets.

| Model          | Average $K_1$ (M⁻¹) | Average $K_2$ (M⁻¹) | RMS         | Covariances |
|----------------|----------------------|----------------------|-------------|-------------|
| No Restraints  | 1500 ± 200           | 350 ± 20             | 1.45 × 10⁻³ | 9.61 × 10⁻⁴ |
| Non-cooperative| 1420 ± 20            | 355 ± 5              | 1.49 × 10⁻³ | 1.85 × 10⁻³ |
| Additive       | 1250 ± 90            | 450 ± 30             | 1.31 × 10⁻³ | 5.28 × 10⁻⁴ |
| Statistical    | 1260 ± 20            | 315 ± 4              | 1.33 × 10⁻³ | 5.46 × 10⁻⁴ |

4.2.2 5-Fluorouracil binding in DC2

Figure S40 ESIMS (CH₃CN) of a DC2 – 5-FU mixture (1:2).
Figure S41 Stacked partial $^1$H NMR spectra (CD$_3$CN, 500 MHz, 298 K) of 5-fluorouracil titrated into a solution of DC2.

Figure S42 $^1$H NMR spectroscopy (CD$_3$CN, 500 MHz, 298 K) titration curves of DC2 with 5-fluorouracil, monitored by the shifts of protons $H_s$, $H_i$, $H_j$ and $H_n$. One of three titration sets.
4.3 Host-guest chemistry of monocavity structures

4.3.1 5-Fluorouracil binding in MC

5-Fluorouracil guest binding studies within MC were carried out in CD$_3$CN. A stock solution of MC (1.00 mL, 0.50 mM) was prepared. Half of the MC (0.50 mL, 0.50 mM) stock solution was added to solid 5-fluorouracil (0.005 mmol) giving a 1:10 host-guest stock solution. Then varying amounts of the host-guest stock solution (either 5, 25, 50 and 150 μL) were titrated into the MC (0.50 mL, 0.50 mM) stock solution to give a series of different host-guest stoichiometries that were examined using $^1$H NMR spectroscopy. Using this procedure, the concentration of MC was maintained at 0.50 mM throughout the titration experiment. Association constants were obtained by analysis of the resulting titration using a 1:1 host:guest stoichiometry with Bindfit (supramolecular.org). An average of three binding constants was calculated to give $K_a = 283 \pm 5$ M$^{-1}$ in CH$_3$CN.

![Figure S43 Stacked partial $^1$H NMR spectra (400 MHz, CD$_3$CN, 298 K) of 5-fluorouracil titrated into a solution of MC.](image-url)
Figure S44 One of three $^1$H NMR spectroscopy (400 MHz, CD$_3$CN, 298 K) titration curves of MC with 5-fluorouracil, tracking the shift of protons H$_a$ and H$_m$.

Table S3 Binding constants of 5-fluorouracil in MC, DC1, and DC2 (400 MHz, CD$_3$CN, 298 K).

| Host (H) | Guest (G) | H:G | $K_1$ (M$^{-1}$) | $K_2$ (M$^{-1}$) |
|----------|-----------|-----|-----------------|-----------------|
| MC       | 5-FU      | 1:1 | 283 ± 5         | -              |
| DC1      | 5-FU      | 1:2 | 1260 ± 20       | 315 ± 5         |
| DC2      | 5-FU      | 1:1 | 210 ± 3         | -              |

4.3.2 Cisplatin binding (CP) to MC

MC (0.5 µmol, 1.0 mM) and cisplatin (1.0 µmol) were combined in CD$_3$CN (500 µL) in an NMR tube. A $^1$H NMR (400 MHz, 298 K) spectrum of the resulting solution was obtained. The spectrum of the mixture was compared to that of the host and the guest to check for a shift in peaks, suggestive of guest binding. No complexation induced shifts consistent with guest binding were observed.

Figure S45 Stacked partial $^1$H NMR spectra (400 MHz, CD$_3$CN, 298 K) of a) MC and b) after addition of 2 eq. CP.
4.3.3 5-Fluorouracil binding to $[\text{Pd}_2(2,6\text{-bis(pyridin-3-ylethynyl)pyridine})_4](\text{BF}_4)_4$

$[\text{Pd}_2(2,6\text{-bis(pyridin-3-ylethynyl)pyridine})_4](\text{BF}_4)_4\text{[3]}$ (0.5 µmol, 1.0 mM) and 5-fluorouracil (1.5 µmol) were combined in CD$_3$CN (500 µL) in an NMR tube. A $^1$H NMR (400 MHz, 298 K) spectrum of the resulting host-guest mixture was obtained. The spectrum of the mixture was compared to that of the host and the guest to check for a shift in peaks. No complexation induced shifts consistent with guest binding were observed.

![Diagram of $[\text{Pd}_2(2,6\text{-bis(pyridin-3-ylethynyl)pyridine})_4](\text{BF}_4)_4\text{[3]}$](image)

**Figure S46** Stacked partial $^1$H NMR spectra (400 MHz, CD$_3$CN, 298 K) of a) $[\text{Pd}_2(2,6\text{-bis(pyridin-3-ylethynyl)pyridine})_4](\text{BF}_4)_4\text{[3]}$, b) + 3 eq. 5-FU, and c) 5-FU.

4.4 Segregated Host-Guest Chemistry

Segregated guest binding studies within DC2 were tested using 5-fluorouracil and cisplatin. 5-Fluorouracil (0.065 mg, 0.50 µmol) was added as a solid to a solution of DC2 (1.4 mg, 0.50 µmol) in CD$_3$CN (0.750 mL). A $^1$H NMR spectrum of the solution was obtained. To this solution, cisplatin (0.30 mg, 1.00 µmol) was added as a solid and another $^1$H NMR spectrum was recorded. In addition, a second study was conducted where solid cisplatin (0.30 mg, 1.00 µmol) was first added to a solution of DC2 (1.44 mg, 0.50 µmol) in CD$_3$CN (0.750 mL) and a $^1$H NMR spectrum was obtained. Following from this, 5-FU was added as a solid (0.065 mg, 0.50 µmol) to the solution and a second $^1$H NMR spectrum was measured.
Figure S47 Stacked partial $^1$H NMR spectra (CD$_3$CN, 400 MHz, 298 K) of DC2 followed by the addition of 5-FU and then the addition of CP.

Figure S48 Stacked partial $^1$H NMR spectra (CD$_3$CN, 400 MHz, 298 K) of DC2 followed by the addition of CP and then the addition of 5-FU.
5 Molecular Modelling/Computations

All MMFF models were obtained using SPARTAN 16®. The structures were energy minimized to give the optimized models. The MMFF molecular models initially generated in SPARTAN 16®[8] were then optimised at the GFN2-xtb level of theory using the XTB program.[9] Standard settings were used, with a DMSO implicit solvent field, at 298 K. The .xyz files for the different models are available as supporting information.

6 X-ray crystallography

X-ray data were collected at 100 K on an Agilent Technologies Supernova system using Mo Kα or Cu Kα radiation with exposures over 1.0°, and data were treated using CrysAlisPro software.[10] The structures were solved using SHELXT and weighted full-matrix refinement on F² was carried out using SHELXL-97[11] both running within the OLEX2-v1.2.9 package.[12] All non-hydrogen atoms were refined anisotropically. Hydrogen atoms attached to carbons were placed in calculated positions and refined using a riding model. Ellipsoids are shown at 50% probability level.

CCDC# 2129018. Vapour diffusion of ethyl acetate into a concentrated solution of [(DAQ)₂⊂DC1] in DMSO, resulted in the formation of orange, needle-shaped crystals of [(DAQ)₂⊂DC1]. The structure was solved in the monoclinic space group I2/m and refined to an R₁ value of 8.38%. The asymmetric unit contains one ligand, a quarter palladium, a half platinum and half a DAQ guest with two half carbonyl groups. The rest of the cage was generated through rotation and inversion across the palladium and a reflection across a mirror plane passing through the platinum and palladium. The rest of the DAQ molecule was generated through a reflection across a mirror plane passing through the carbonyl groups. There was disorder in the 2-fold rotation axis perpendicular to the carbonyl groups of the DAQ molecule which solved to have two amine groups with half occupancy. The FLAT command was used on the pyridine ring coordinated to the platinum centre. Crystal packing effects presented one DAQ molecule in each cavity of DC1. A “solvent mask” (with the OLEX2-v1.2.9 package) was applied to resolve diffused electron density, where a void consisting of 609.9 electrons was measured which was attributed to six BF₄⁻ counteranions and eight DMSO solvent molecules.

Figure S49 Mercury ellipsoid plot of the asymmetric unit of [(DAQ)₂⊂DC1]. Ellipsoids are shown at the 50% probability level. Color scheme: carbon = grey, hydrogen = white, nitrogen = blue, oxygen = red, palladium = purple, platinum = pink.
| Identification Code  | [(DAQ)$_2$⊂DC1] |
|----------------------|------------------|
| CCDC#                | 2129018          |
| Empirical formula    | C$_{40}$H$_{25}$N$_6$O$\text{Pd}_{0.25}$Pt$_{0.5}$ |
| Formula weight       | 729.80           |
| Temperature/K        | 100.02(12)       |
| Crystal system       | Monoclinic       |
| Space group          | I2/m             |
| a/Å                  | 12.1550(9)       |
| b/Å                  | 16.953(3)        |
| c/Å                  | 52.829(4)        |
| α°                   | 90               |
| β°                   | 90.761(7)        |
| γ°                   | 90               |
| Volume/Å$^3$         | 10885(2)         |
| Z                    | 8                |
| $\rho_{\text{calc}}$ g/cm$^3$ | 0.891 |
| μ/mm$^{-1}$          | 1.405            |
| F(000)               | 2924.0           |
| Crystal size/mm$^3$  | 0.395 × 0.159 × 0.076 |
| Radiation            | MoKα (λ = 71073) |
| 2Θ range for data collection/° | 6.9 to 48.812 |
| Index ranges         | -14 ≤ h ≤ 14, -18 ≤ k ≤ 19, -57 ≤ l ≤ 61 |
| Reflections collected| 33431            |
| Independent reflections| 9185 [R$_{\text{int}}$ = 0.1200, R$_{\text{sigma}}$ = 0.1290] |
| Data/restraints/parameters | 9185/927/449 |
| Goodness-of-fit on $F^2$ | 0.965 |
| Final R indexes [I≥2σ(I)] | R$_1$ = 0.0838, wR$_2$ = 0.2173 |
| Final R indexes [all data] | R$_1$ = 0.1234, wR$_2$ = 0.2490 |
| Largest diff. peak/hole / e Å$^{-3}$ | 0.88/-1.03 |
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