Electronic Supplementary Material (ESI) for Dalton Transactions

Self-Assembled Palladium(II) "Click" Cages: Synthesis, Structural Modification and Stability.

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1 Experimental

1.1 General.

Unless otherwise stated, all reagents were purchased from commercial sources and used without further purification. Solvents were laboratory reagent grade with the following exception: dry acetonitrile were obtained by passing the solvent through an activated alumina column on a PureSolv TM solvent purification system (Innovative Technologies Inc., MA). Petrol refers to the fraction of petroleum ether boiling in the range 40-60°C. All melting points were determined using a Sanyo Gallenkamp apparatus and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on either a 400 MHz Varian 400 MR or a Varian 500 MHz VNMRS spectrometer at 298 K. Chemical shifts are reported in parts per million (ppm) and referenced to residual solvent peaks ($CDCl_3$: ^{1}H δ 7.26 ppm, ^{13}C δ 77.16 ppm; CD_3CN: ^{1}H δ 1.94 ppm, ^{13}C δ 1.32, 118.26 ppm; d_6-DMSO: ^{1}H δ 2.50 ppm, ^{13}C δ 39.51 ppm). Coupling constants (J) are reported in Hertz (Hz). Standard abbreviations indicating multiplicity were used as follows: m = multiplet, quint. = quintet, q = quartet, t = triplet, d = doublet, s = singlet. IR spectra were recorded on a Bruker ALPHA FT-IR spectrometer with an attached ALPHA-P measurement module. Microanalyses were performed at the Campbell Microanalytical Laboratory at the University of Otago. Electrospray mass spectra (ESMS) were collected on a Bruker micro-TOF-Q spectrometer. 1-Bromomethyl-4-methylcarboxybenzene,[1] **1a**[2], **1b**[2], **4a**[3] and **4b**[3] were prepared according to the literature procedures.

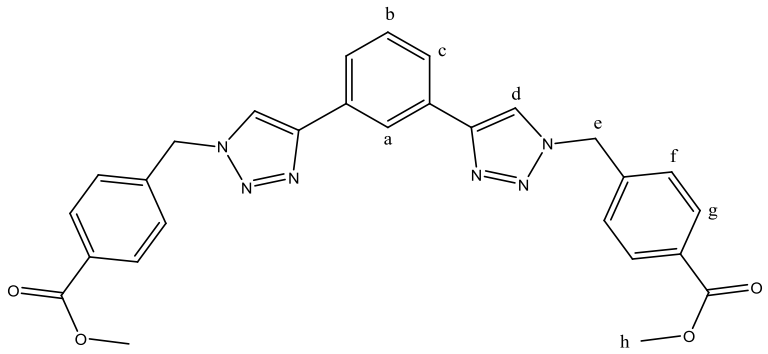
Safety Note: Sodium azide is extremely toxic and appropriate care should be taken. As low molecular weight organic azides are potential explosives, care must be taken during their handling. Generally, when the total number of carbon (C) plus oxygen (O) atoms is less than the total number of nitrogen atoms (N) by a ratio of three, i.e., (C+O)/N< 3, the compound is considered as an explosive hazard. A standard PVC blast shield was used when necessary. Additionally, copper azides and acetylides are explosive when dry, and their traces should be removed before the CuAAC reaction products are dried. This is achieved by pouring the crude reaction mixture into 100 mL of aqueous EDTA/NH_4OH.

1.2 Experimental Procedures

1.2.1 Synthesis of the 1,2,3-Triazole Ligands.

General Method.

The following general procedure was used for the synthesis of triazole ligands **1a-1d, 2a** and **3a**. Sodium azide (2.4 equiv.), sodium ascorbate (1 equiv.) and $CuSO_4 \cdot 5H_2O$ (0.4 equiv.) were added to a stirred solution of the appropriate bromide (2.2 equiv.) in DMF/H_2O (15 mL, 4:1). The appropriate dialkyne (1 equiv.) was added and the reaction mixture was stirred at room temperature for 20 h. The crude mixture was then quenched by stirring in aqueous EDTA/NH_4OH (100 mL, 1M) and the resulting white solid was isolated by filtration. The solid was dissolved in CH_2Cl_2 (100 mL) and was washed with H_2O (3 x 50 mL) and brine (3 x 50 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure to give the crude product which, if necessary, was further purified by chromatography.

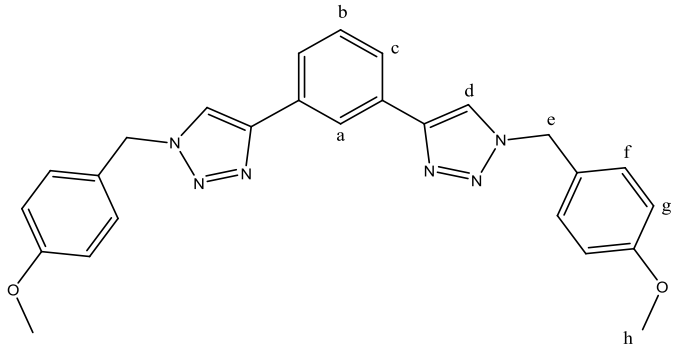


4,4′-benzene-1,3-diylbis[1-(4-methylbenzoate)-1*H*-1,2,3-triazole]

1c

Ligand **1c** was synthesized from 1,3-diethynylbenzene (0.315 g, 2.49 mmol, 0.332 ml, 1 equiv.) and 1-bromomethyl-4-methylcarboxybenzene (1.20 g, 5.24 mmol, 2.1 equiv.) using the general procedure outlined above. The crude white product was further purified by chromatography (9:1 CH_2Cl_2/acetone) yielding the ligand **1c** as a fluffy white solid. Yield: 1.00 g (79%). Mp: 203-205 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.21 (t, J = 1.7 Hz, 1H, H_a), 8.08-8.04 (m, 4H, H_g), 7.80 (dd, J = 7.8, 1.7 Hz, 2H, H_c), 7.77 (s, 2H, H_d), 7.46 (t, J = 7.8 Hz, 1H, H_b), 7.36 (d, J = 8.3 Hz, 4H, H_f), 5.64 (s, 4H, H_e), 3.92 (s, 6H, H_h); ^{13}C NMR (500 MHz, $CDCl_3$) δ: 166.6, 148.3, 139.6, 131.2, 130.9, 130.7, 129.7, 128.1, 125.7, 123.1, 120.1, 54.1,

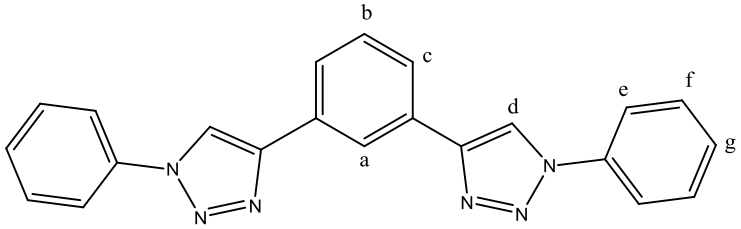
52.5; IR: ν (cm^{-1}) 3128, 2954, 2923, 1708, 1612, 1433, 1415, 1279, 1180, 1105, 1044, 1018, 790, 758, 692; HRESI-MS (MeOH): *m/z* = 509.1940 $[M+H]^+$ (calc. for $C_{28}H_{25}N_6O_4$ 509.1932 $[M+H]^+$); *Anal*. Calc. for $C_{28}H_{24}N_6O_4$: C, 66.13; H, 4.76; N, 16.53. Found: C, 66.19; H, 4.73; N, 16.63.



4,4′-benzene-1,3-diylbis[1-(4-methylbenzoate)-1*H*-1,2,3-triazole]

1d

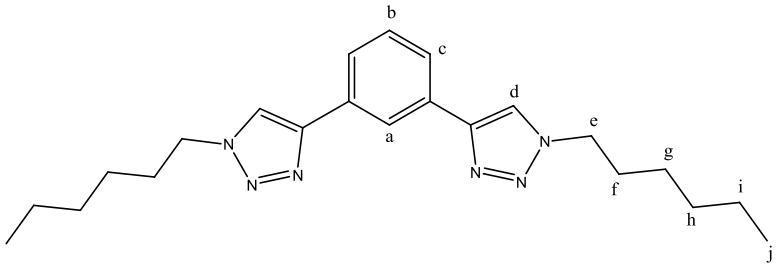
Ligand **1d** was synthesized from 1,3-diethynylbenzene (0.378 g, 0.398 mL, 3.00 mmol, 1 equiv.) and 1-bromomethyl-4-methylcarboxybenzene (1.03 g, 0.895 ml, 6.59 mmol, 2.2 equiv.) using the procedure outlined in Section 1.2.1. After stirring in aqueous EDTA/NH_4OH, a white precipitate formed. The solid was collected by filtration then dissolved in CH_2Cl_2 and was washed with H_2O (3 x 50 mL) and brine (3 x 50 mL) and dried over $MgSO_4$. The solvent was removed under vacuum to give a white solid. Yield: 1.157 g (85%). X-ray quality crystals were obtained by vapour diffusion of Et_2O into a $CHCl_3$ solution of **1d**. Mp: 133 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (t, *J* = 1.5 Hz, 1H, H_a), 7.76 (dd, *J* = 7.8, 1.7 Hz, 2H, H_c), 7.68 (s, 2H, H_d), 7.42 (t, *J* = 7.8 Hz, 1H, H_b), 7.31 – 7.27 (m, 4H, H_f), 6.95 – 6.87 (m, 4H, H_g), 5.50 (s, 4H, H_e), 3.82 (d, *J* = 1.2 Hz, 6H, H_h); ^{13}C NMR (500 MHz, $CDCl_3$) δ: 160.2, 148.0, 131.3, 130.0, 129.6, 126.7, 125.5, 123.0, 119.8, 114.8, 55.6, 54.1; IR: ν (cm^{-1}) 3278, 3125, 2965, 2936, 1609, 1511, 1443, 1244, 1202, 1024, 816, 766, 744, 654; HRESI-MS (MeOH): *m/z* = 475.1848 $[M+Na]^+$ (calc. for $C_{26}H_{24}N_6NaO_2$ 475.1853 $[M+Na]^+$); *Anal*. Calc. for $C_{26}H_{24}N_6O_2$: C, 69.01; H, 5.35; N, 18.57. Found: C, 68.80; H, 5.32; N, 18.80%.



4,4′-benzene-1,3-diylbis(1-phenyl-1*H*-1,2,3-triazole)

1e

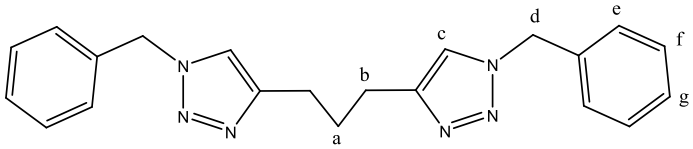
Sodium azide (1.92 g, 29.5 mmol, 14.4 equiv.) and copper(I) chloride (0.162 g, 1.6 mmol, 0.8 equiv.) were dissolved in dry methanol (50 mL). Phenylboronic acid (3.00 g, 24.6 mmol, 12 equiv.) was added and the reaction mixture was refluxed for 6 h. The reaction mixture was cooled to room temperature and $CuSO_4 \cdot 5H_2O$ (0.256 g, 1.0 mmol, 0.5 equiv.), ascorbic acid (0.361 g, 2.1 mmol, 1 equiv.), sodium carbonate (0.239 g, 2.3 mmol, 1.1 equiv.), 1,3-diethynyl benzene (0.259 g, 2.1 mmol, 1 equiv.) and water (4 mL) were added. The resulting reaction mixture was stirred for 20 h at room temperature. CH_2Cl_2 (150 mL) and aqueous EDTA/NH_4OH (150 mL, 1M) were added to the mixture and stirred vigorously for 30 mins. The organic layer was washed with water (2 x 75 mL) and NaCl (2 x 75 mL) then dried with $MgSO_4$. The solvent was removed under vacuum to give the crude product as a white solid. This was further purified by chromatography (silica gel, 9:1 CH_2Cl_2/acetone) to give an off-white solid. Yield: 0.345 g (45%). Mp: 168-170°C; ^{1}H NMR (400 MHz, CD_3CN) δ: 8.76 (s, 2H, H_d), 8.58 (t, J = 1.6 Hz, 1H, H_a), 7.97 (dd, J = 7.7, 1.8 Hz, 2H, H_c), 7.92-7.89 (m, 4H, H_e), 7.65-7.61 (m, 5H, $H_{b,f}$), 7.55-7.51 (m, 2H, H_g); ^{13}C NMR (500 MHz, CD_3CN) δ: 148.0, 137.1, 130.9, 129.8, 129.6, 128.9, 125.7, 123.1, 120.5, 118.0; IR: ν (cm^{-1}) 3124, 1595, 1501, 1466, 1402, 1232, 1037, 985, 897, 791, 760, 749, 680; HRESI-MS (MeOH): *m/z* = 365.1483 $[M+H]^+$ (calc. for $C_{22}H_{17}N_6$ 365.1509 $[M+H]^+$); *Anal*. Calc. for $C_{22}H_{16}N_6 \bullet 0.25(H_2O)$: C, 71.63; H, 4.51; N, 22.78; Found: C, 71.74; H, 4.49; N, 22.56%.



4,4′-benzene-1,3-diylbis(1-hexyl-1*H*-1,2,3-triazole)

1f

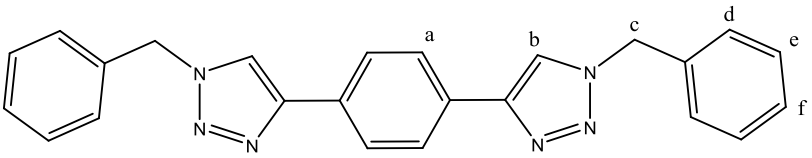
Sodium azide (0.429 g, 6.6 mmol, 2.2 equiv.), sodium iodide (0.440 g, 2.9 mmol, 0.95 equiv.) and 1-bromohexane (1.04 g, 6.3 mmol, 2.1 equiv.) were added to a 35 mL CEM microwave vessel, dissolved in DMF/H_2O (15 mL, 4:1) and irradiated (CEM microwave reactor, 250W) at 125°C for 45 mins. The reaction mixture was cooled to room temperature and 1,3-diethynyl benzene (0.378 g, 3.0 mmol, 1 equiv.), sodium ascorbate (0.528 g, 3.0 mmol, 1 equiv.) and $CuSO_4 \cdot 5H_2O$ (0.374 g, 1.5 mmol, 0.5 equiv.) were added and the resulting suspension was stirred at room temperature for 20 h. The mixture was quenched with aqueous EDTA/NH_4OH (100 mL, 1M) and extracted into CH_2Cl_2 (3 x 50 mL). The organic extract was then washed with H_2O (3 x 50 mL) and NH_4Cl (3 x 50 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure to give the crude product which was further purified by chromatography (silica gel, 8:2 CH_2Cl_2/acetone) to give a white solid. Yield: 0.968 g (86%). Mp: 88-89°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.29 (t, J = 16 Hz, 2H, H_d), 7.86-7.81 (m, 3H, $H_{a,c}$), 7.48 (t, J = 7.8 Hz, 1H, H_b), 4.41 (t, J = 7.2 Hz, 4H, H_e), 2.01-1.91 (m, 4H, H_f), 1.40-1.23 (m, 12H, H_{g-i}), 0.93-0.85 (m, 6H, H_j); ^{13}C NMR (500 MHz, $CDCl_3$) δ: 147.6, 131.5, 129.6, 125.5, 123.0, 119.9, 50.7, 31.4, 30.5, 26.4, 22.6, 14.2; IR: ν (cm^{-1}) 3121, 2954, 2923, 2857, 1462, 1222, 1050, 973, 877, 785, 684; HRESI-MS (MeOH): *m/z* = 381.2752 $[M+H]^+$ (calc. for $C_{22}H_{33}N_6$ 381.2761 $[M+H]^+$); *Anal*. Calc. for $C_{22}H_{32}N_6$: C, 69.44; H, 8.48; N, 22.09. Found: C, 69.50; H, 8.46; N, 22.46%.



4,4′-propane-1,3-diylbis(1-benzyl-1*H*-1,2,3-triazole)

2a

Ligand **2a** was synthesized from 1,6-heptadiyne (0.564 g, 0.7 mL, 6.12 mmol, 1 equiv.) and benzyl bromide (2.12 g, 1.54 mL, 12.84 mmol, 2.1 equiv.) using the general procedure outlined in section 1.2.1. The white precipitate which formed after treatment with aqueous EDTA/NH_4OH was collected by filtration, washed well with ether and petrol and dried under high vacuum. This white solid was used without further purification. Yield: 2.15 g (93%). Mp: 121-122°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.32-7.26 (m, 6H, $H_{c,e}$), 7.20-7.16 (m, 6H, $H_{f,g}$), 5.42 (s, 4H, H_d), 2.67 (t, J = 7.6 Hz, 4H, H_b), 1.95 (dq, J = 15.1, 7.6 Hz, 2H, H_a); ^{13}C NMR (500 MHz, $CDCl_3$) δ: 147.9, 134.9, 129.0, 128.6, 122.0, 121.0, 54.0, 29.0, 24.9; IR: ν (cm^{-1}) 3059, 2952, 2921, 2854, 1493, 1453, 1306, 1210, 1054, 1028, 868, 722, 694; HRESI-MS (MeOH): *m/z* = 381.1781 $[M+Na]^+$ (calc. for $C_{21}H_{22}N_6Na$ 381.1798 $[M+Na]^+$);. *Anal.* Calc. for $C_{21}H_{22}N_6$: C, 70.37; H, 6.19; N, 23.45. Found: C, 70.10; H, 6.26; N, 23.18%.

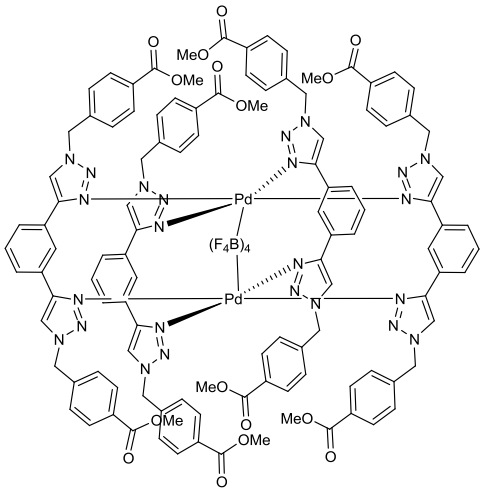


4,4′-benzene-1,4-diylbis(1-benzyl-1*H*-1,2,3-triazole)

3a

Ligand **3a** was synthesized from 1,4-diethynyl benzene (0.630 g, 4.99 mmol, 1 equiv.) and benzyl bromide (1.88 g, 10.99 mmol, 2.2 equiv.) using the using the general procedure outlined above. The white precipitate which formed after treatment with aqueous EDTA/NH_4OH was collected by filtration, washed well with ether and petrol and dried under high vacuum. Yield: 1.745 g (89%). Mp: >230°C; ^{1}H NMR (400 MHz, d_6-DMSO) δ: 8.67 (s, 2H, H_b), 7.92 (s, 4H, H_a), 7.42-7.32 (m, 10H, H_{d-f}), 5.65 (s, 4H, H_c); ^{13}C NMR (500 MHz, d_6-DMSO) δ: 146.3, 135.9, 130.1, 128.8, 128.1, 127.9, 125.6, 121.6, 53.0; IR: ν (cm^{-1}) 3118, 1493, 1453, 1433, 1306, 1222, 1052, 976, 852, 819, 730, 690; HRESI-MS (MeOH): *m/z* = 415.1609 $[M+Na]^+$ (calc. for $C_{24}H_{20}N_6Na$ 415.1642 $[M+Na]^+$); *Anal*. Calc. for $C_{24}H_{20}N_6 \bullet 0.25(H_2O)$: C, 72.62; H, 5.21; N, 21.17. Found: C, 72.65; H, 5.11; N, 21.60%.

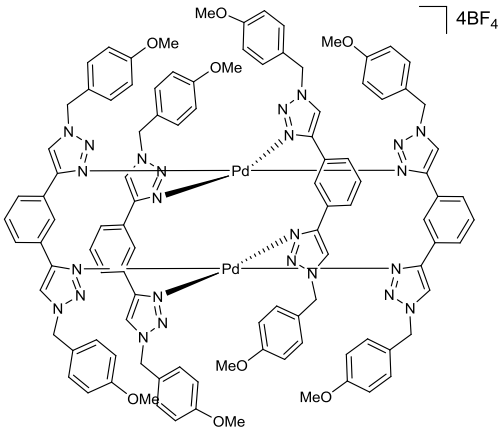
1.2 Palladium(II) "click" cages.



$[Pd_2(\mathbf{1c})_4](BF_4)_4$

4c

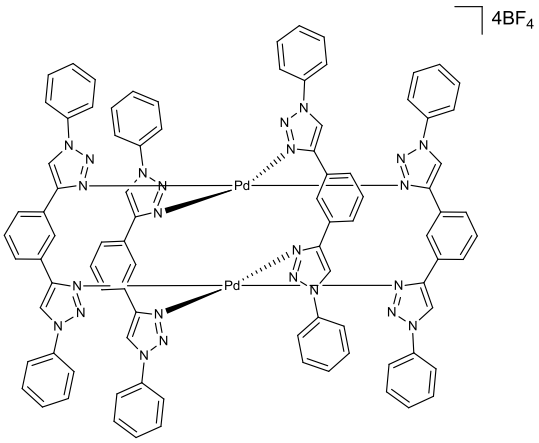
Ligand **1c** (0.102 g, 0.2 mmol, 2 equiv.) and $[Pd(CH_3CN)_4](BF_4)_2$ (0.044 g, 0.1 mmol, 1 equiv.) were stirred in dry acetonitrile for 30 min. The solution was then filtered through cotton wool and left to vapour diffuse with ether for 1 week. The resulting precipitate was collected by filtration and washed with ether and petrol to give **4c** as an off-white solid. Yield: 0.097g (76%). Mp: 208-209°C; ^{1}H NMR (400 MHz, CD_3CN) δ: 9.83 (t, J = 1.7 Hz, 4H, H_a), 7.92 (d, J = 8.7 Hz, 24H, $H_{d,g}$), 7.22 – 7.13 (m, 16H, H_f), 6.91 (t, J = 7.9 Hz, 4H, H_b), 6.63 (dd, J = 7.9, 1.7 Hz, 8H, H_c), 5.34 (s, 16H, H_e), 3.93 (s, 24H, H_h); ^{13}C NMR (500 MHz, CD_3CN) δ: 167.5, 147.4, 138.6, 132.7, 132.1, 131.3, 131.2, 130.6, 127.6, 126.5, 122.0, 56.7, 53.5; IR: ν (cm^{-1}) 3047, 1712, 1613, 1566, 1433, 1189, 969, 739, 671; HRESI-MS (CH_3CN): *m/z* = 509.2 $[\mathbf{1c}+H]^+$ (calc. for $C_{28}H_{25}N_6O_4$ 509.2); 613.1 $[Pd(\mathbf{1c}-H)]^+$ (calc. for $C_{28}H_{23}N_6O_4Pd$ 613.1); 777.9 $[Pd_2(\mathbf{1c})_4](BF_4)_3^+$ (calc. for $C_{112}H_{96}BF_4N_{24}O_{16}Pd_2$ 777.9); 1210.3 $[Pd_2(\mathbf{1c})_4](BF_4)_2^{2+}$ (calc. for $C_{112}H_{96}B_2F_8N_{24}O_{16}Pd_2$ 1210.3); *Anal*. Calc. for $C_{112}H_{96}B_4F_{16}N_{24}O_{16}Pd_2$●4($H_2O$): C, 50.45; H, 3.93; N, 12.61. Found: C, 50.38; H, 3.76; N, 12.72%.



$[Pd_2(\mathbf{1d})_4](BF_4)_4$

4d

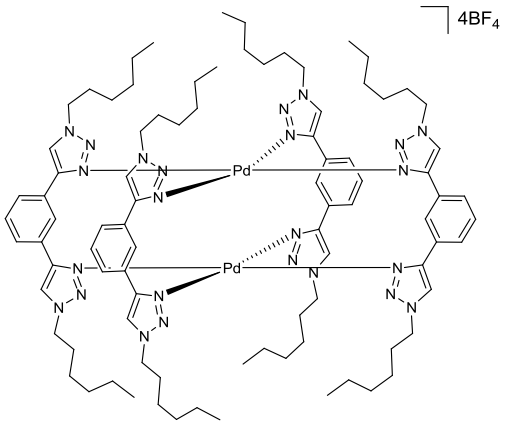
Ligand **1d** (0.090 g, 0.2 mmol, 2 equiv.) and $[Pd(CH_3CN)_4](BF_4)_2$ (0.044 g, 0.1 mmol, 1 equiv.) were stirred in dry acetonitrile for 30 min. The solution was then filtered through cotton wool and left to vapour diffuse with ether for 1 week. The resulting precipitate was collected by filtration and washed with ether and petrol to give **4d** as cream solid. Yield: 0.094 g (80%). Mp: >227 °C; ^{1}H NMR (400 MHz, CD_3CN) δ: 9.83 (t, J = 1.6 Hz, 4H, H_a), 7.81 (s, 8H, H_d), 7.03-6.99 (m, 16H, H_f), 6.89 (d, J = 7.7 Hz, 4H, H_b), 6.87-6.83 (m, 16H, H_g), 6.53 (dd, J = 7.9, 1.7 Hz, 8H, H_c), 5.19 (s, 16H, H_e), 3.82 (s, 24H, H_h); ^{13}C NMR (500 MHz, CD_3CN) δ: 161.5, 146.9, 131.7, 131.4, 130.6, 126.4, 126.1, 125.6, 121.7, 115.3, 56.4, 56.2; IR: ν (cm^{-1}) 3150, 1609, 1514, 1251, 1019, 785, 689, 557, 521; HRESI-MS (CH_3CN): *m/z* = 453.2 $[\mathbf{1d}+H]^+$ (calc. for $C_{26}H_{25}N_6O_2$ 453.2 $[\mathbf{1d}+H]^+$); 1098.3 $[M-(BF_4)_2]^{2+}$ (calc. for $C_{104}H_{96}B_2F_8N_{24}O_8Pd_2$ 1098.3 $[M-(BF_4)_2]^{2+}$); 2262.6 $[M-BF_4]^+$ (calc. for $C_{104}H_{96}B_3F_{12}N_{24}O_8Pd_2$ 2262.6 $[M-BF_4]^+$); *Anal*. Calc. for $C_{104}H_{96}B_4F_{16}N_{24}O_8Pd_2$: C, 52.70; H, 4.08; N, 14.18. Found: C, 52.64; H, 4.00; N, 14.26%.



$[Pd_2(\mathbf{1e})_4](BF_4)_4$

4e

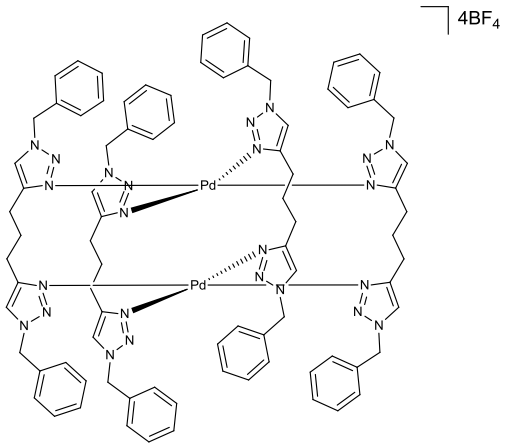
Ligand **1e** (0.072 g, 0.198 mmol, 2 equiv.) and $[Pd(CH_3CN)_4](BF_4)_2$ (0.044 g, 0.099 mmol, 1 equiv.) were stirred in dry acetonitrile (10 mL) for 1 h. The solution was then filtered through cotton wool and and the solvent removed under reduced pressure. The resulting yellow solid was dissolved in acetone (10 mL) and left to vapour diffuse with ether for 1 week. The resulting precipitate was collected by filtration and washed with ether and petrol to give **4e** as an off-white/yellow solid. Yield: 0.095 g (95%). Mp: >229°C; ^{1}H NMR (400 MHz, CD_3CN) δ: 10.63 (t, J = 1.3 Hz,4H, H_a), 8.53 (s, 8H, H_d), 7.60-7.51 (m, 40H, $H_{e,f,g}$), 7.33 (dd, J = 7.8, 1.5 Hz, 8H, H_c), 7.19 (dd, J = 7.4, 8.4 Hz, 4H, H_b); ^{13}C NMR (500 MHz, CD_3CN) δ: 148.0, 135.9, 132.3, 131.7, 131.3, 126.4, 126.1, 123.2, 121.6, 118.3; IR: ν (cm^{-1}) 3620, 3340, 3147, 1500, 1469, 1050, 800, 760, 686; HRESI-MS (CH_3CN): *m/z* = 922.2 $[M\text{-}2(BF_4)]^{2+}$ (calc. for $C_{88}H_{64}B_2F_8N_{24}Pd_2$ 922.2 $[M\text{-}2(BF_4)]^{2+}$); 1930.4 $[M\text{-}(BF_4)]^+$ (calc. for $C_{88}H_{64}B_3F_{12}N_{24}Pd_2$ 1930.4 $[M\text{-}(BF_4)]^+$);)]$^+$); *Anal*. Calc. for $C_{88}H_{64}B_4F_{16}N_{24}Pd_2\bullet5(H_2O)$: C, 50.15; H, 3.54; N, 15.95. Found: C, 49.86; H, 3.36; N, 16.07%.



$[Pd_2(\mathbf{1f})_4](BF_4)_4$

4f

Ligand **1f** (0.038 g, 0.1 mmol, 2 equiv.) and $[Pd(CH_3CN)_4](BF_4)_2$ (0.022 g, 0.05 mmol, 1 equiv.) were heated at 70 °C for 16 h. The solution was then filtered through cotton wool and left to vapour diffuse with ether for 1 week. The resulting precipitate was collected by filtration and washed with ether and petrol to give **4f** as cream solid. Yield: 0.040 g (76%). Mp: 215 °C (decomp.); ^{1}H NMR (400 MHz, CD_3CN) δ: 10.23 (s, 4H, H_a), 8.01 (s, 8H, H_d), 7.44 – 7.34 (m, 4H, H_b), 7.34 – 7.26 (m, 8H, H_c), 4.10 (td, J = 7.3, 1.7 Hz, 16H, H_e), 1.63 – 1.47 (m, 16H, $H_{alkyl(f,g,h,i)}$), 1.36 – 1.16 (m, 32H, $H_{alkyl(f,g,h,i)}$), 1.09 (m, 16H, $H_{alkyl(f,g,h,i)}$), 0.89 (t, J = 6.8 Hz, 24H, H_j); ^{13}C NMR (500 MHz, CD_3CN) δ: 147.1, 131.9, 131.1, 127.3, 126.9, 122.5, 53.5, 31.6, 29.8, 26.3, 23.1, 14.1; IR: ν (cm^{-1}) 3141, 2954, 2927, 2859, 1620, 1567, 1546, 1465, 1411, 1358, 1312, 1284, 1232, 1178, 1122, 1048, 1030, 875, 839, 802, 727, 714, 695, 595, 521; HRESI-MS (CH_3CN): *m/z* = 381.3 $[\mathbf{1f}+H]^+$ (calc. for $C_{22}H_{33}N_6$ 381.3); 433.7 $[Pd_2(\mathbf{1f})_4]^{4+}$ (calc. for $C_{88}H_{128}N_{24}Pd_2$ 433.7); 607.3 $[Pd_2(\mathbf{1f})_4]BF_4^{3+}$ (calc. for $C_{99}H_{128}BF_4N_{24}Pd_2$ 607.3); 686.3 $[Pd_2(\mathbf{1f})_3HOH]^{2+}$ (calc. for $C_{66}H_{98}N_{18}OPd_2$ 686.3); 954.4 $[Pd_2(\mathbf{1f})_4](BF_4)_2^{2+}$ (calc. for $C_{88}H_{128}B_2F_8N_{24}Pd_2$ 954.4), 1994.9 $[Pd_2(\mathbf{1f})_4](BF_4)_2^{2+}$ (calc. for $C_{88}H_{128}B_2F_8N_{24}Pd_2$ 1994.9); *Anal*. Calc. for $C_{88}H_{128}B_4F_{16}N_{24}Pd_2\bullet1.5(H_2O)$: C, 50.11; H, 6.26; N, 15.94. Found: C, 49.92; H, 6.19; N, 16.25%.



$[Pd_2(\mathbf{2a})_4](BF_4)_4$

5a

Ligand **2a** (0.293 g, 0.8 mmol, 2 equiv.) and $[Pd(CH_3CN)_4](BF_4)_2$ (0.182 g, 0.4 mmol, 1 equiv.) were stirred in dry acetonitrile for 30 min. The solution was then filtered through cotton wool and left to vapour diffuse with ether for 1 week. The resulting precipitate was collected by filtration and washed with ether and petrol to give **5a** as an off-white solid. Yield: 99%. Mp: 126-128°C; ^{1}H NMR (400 MHz, CD_3CN) δ: 7.77 (s, 8H, H_c), 7.39-7.31 (m, 24H, $H_{f,g}$), 7.13 (d, J = 6.8, 16H, H_e), 5.38 (s, 16H, H_d), 3.24 (s, 24H, $H_{a,b}$); ^{13}C NMR (500 MHz, CD_3CN) δ: 150.2, 134.5, 130.1, 130.0, 129.4, 126.7, 118.3, 56.4; I.R.: ν (cm^{-1}) 3145, 1557, 1160, 1032, 821, 730; HRESI-MS (CH_3CN): *m/z* = 1906.5 $[M-(BF_4)]^+$ (calc. for $C_{84}H_{88}B_3F_{14}N_{24}Pd_2$ 1906.6 $[M-(BF_4)]^+$); *Anal*. Calc. for $C_{84}H_{88}B_4F_{16}N_{24}Pd_2 \bullet 0.5(H_2O)$: C, 50.37; H, 4.48; N, 16.78. Found: C, 50.30; H, 4.56; N, 16.94%.

2 ^{1}H NMR and DOSY spectra of the synthesized compounds

2.1 ^{1}H NMR Stacked Plots.

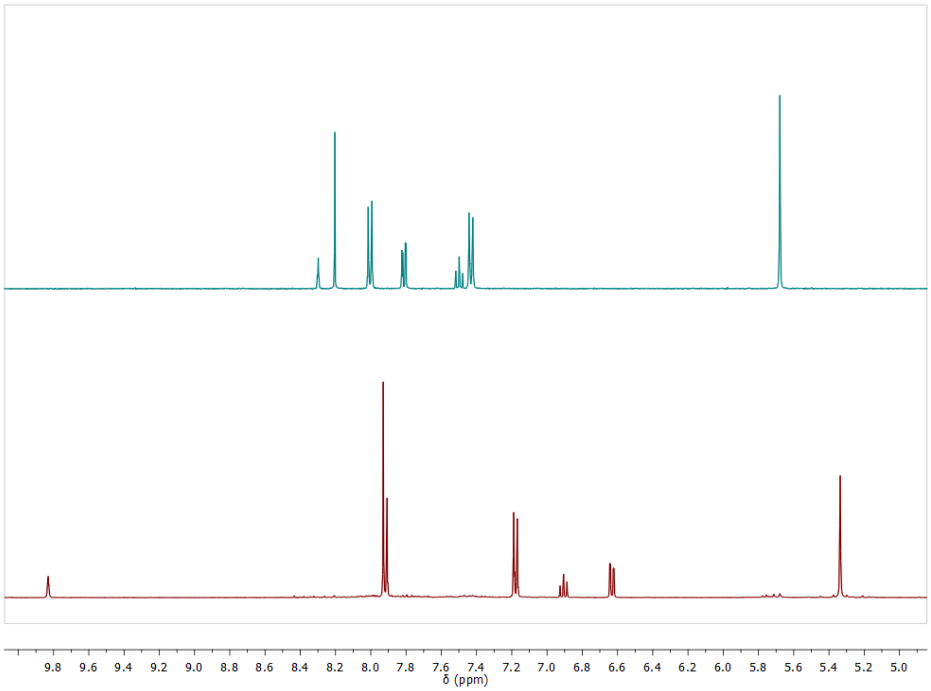


Figure S1 Partial ^{1}H NMR spectra (400 MHz, d_3-acetonitrile, 298 K) of the ligand **1c** (top) and the palladium cage complex **2c** (bottom).

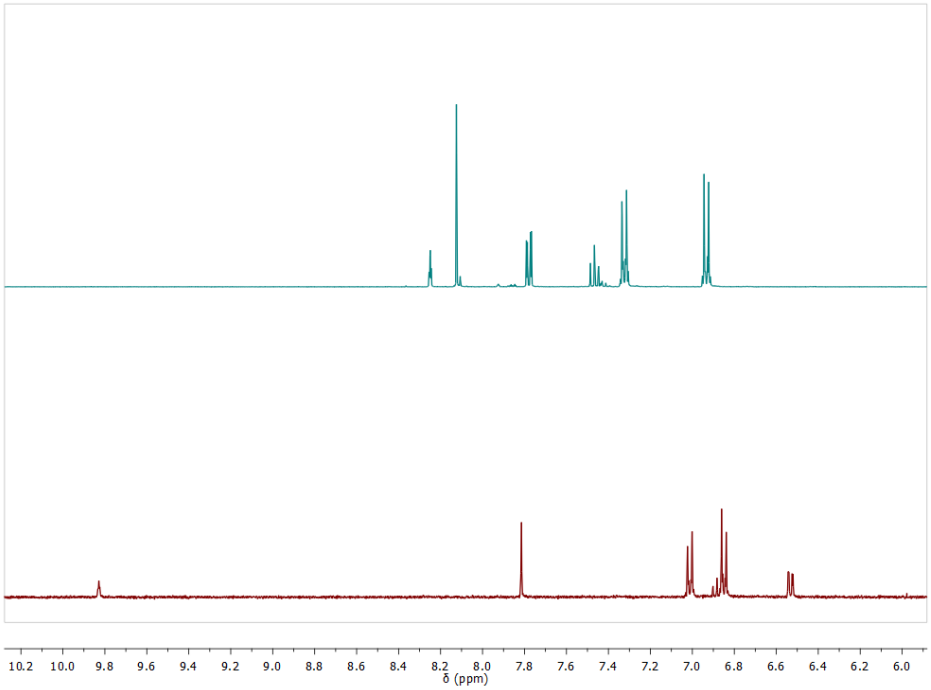


Figure S2 Partial ^{1}H NMR spectra (400 MHz, d_3-acetonitrile, 298 K) of the ligand **1d** (top) and the palladium cage complex **2d** (bottom).

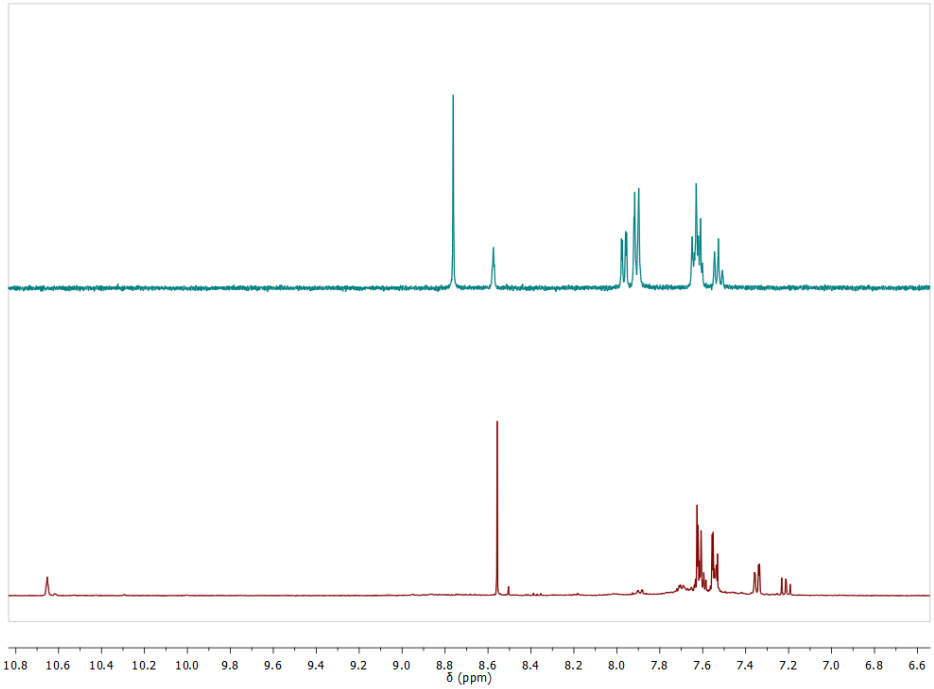


Figure S3 Partial ^{1}H NMR spectra (400 MHz, d_3-acetonitrile, 298 K) of the ligand **1e** (top) and the palladium cage complex **4e** (bottom).

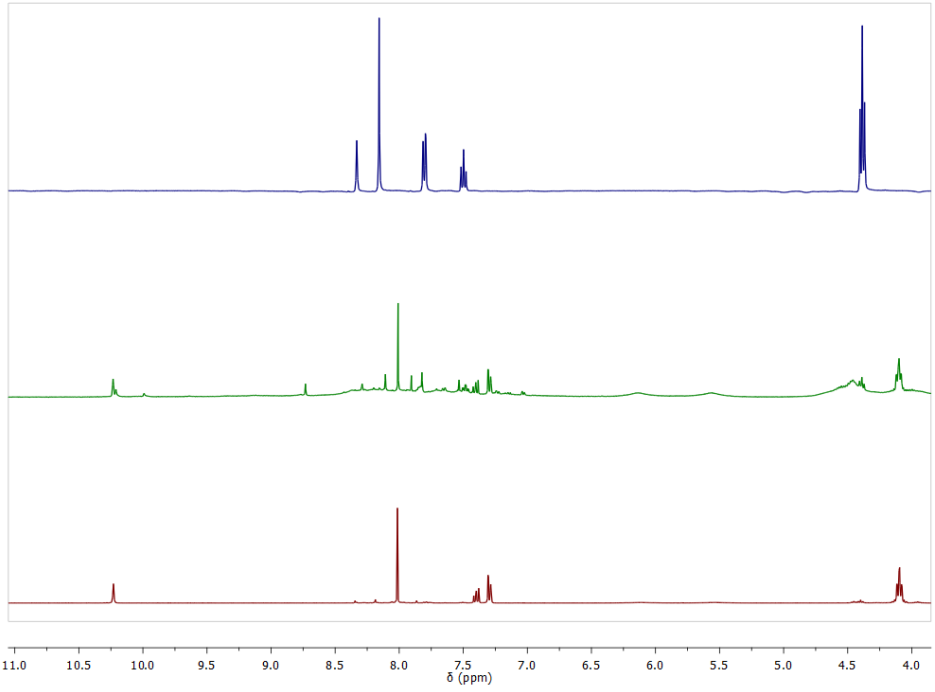


Figure S4 Partial ^{1}H NMR spectra (400 MHz, d_3-acetonitrile, 298 K) of the ligand **1f** (top), the reaction mixture formed from **1f** and $[Pd(CH_3CN)_4](BF_4)_2$ after 1h at RT (middle) and the palladium cage **4f** (bottom) obtained after heating the reaction mixture at 70 °C for 16 h.

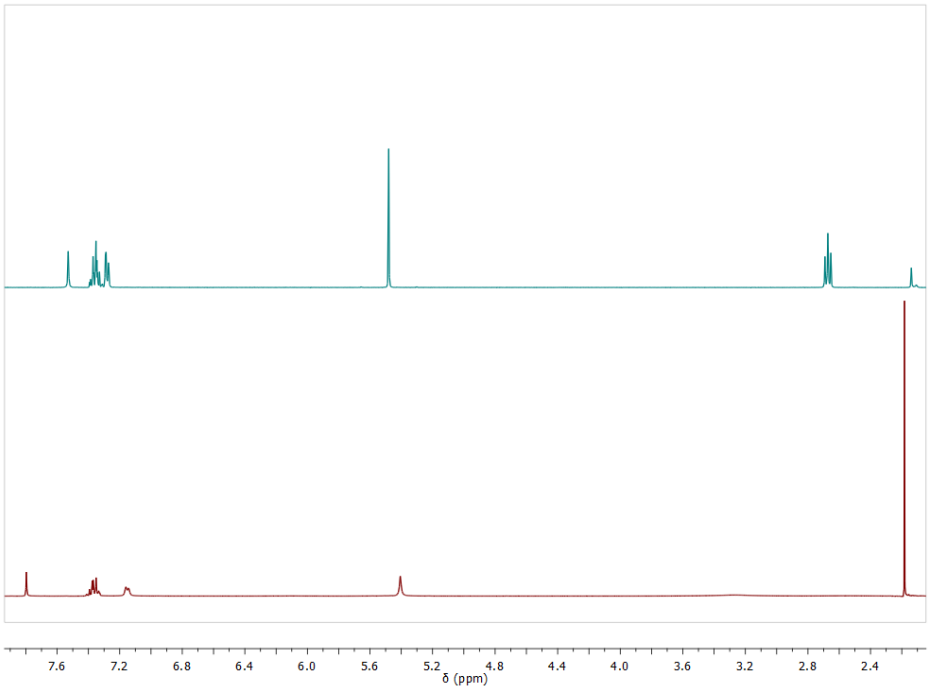


Figure S5 Partial ^{1}H NMR spectra (400 MHz, d_3-acetonitrile, 298 K) of the ligand **2a** (top) and the palladium cage complex **5a** (bottom).

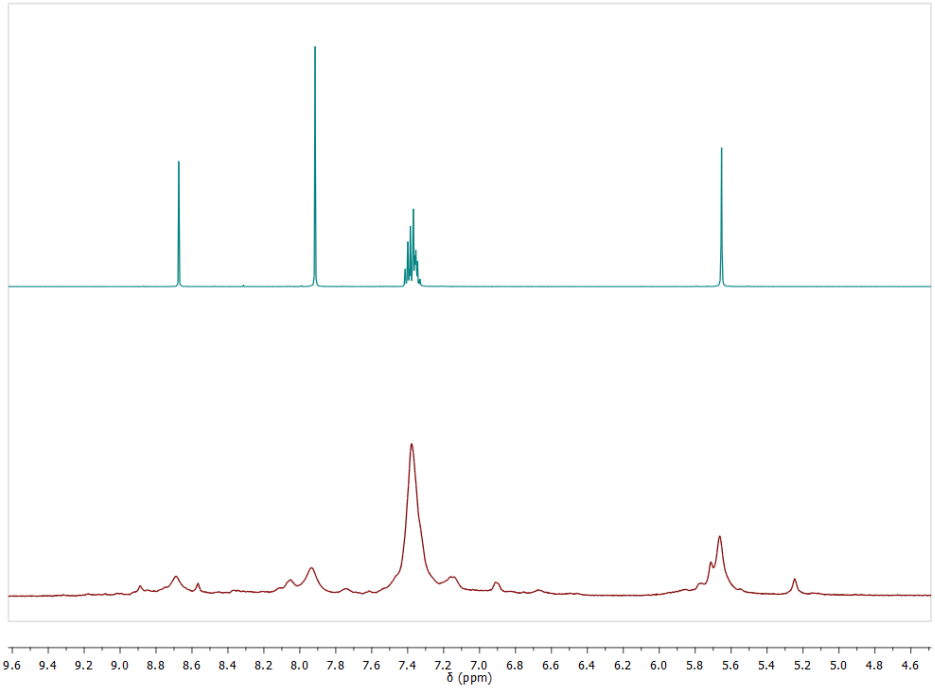
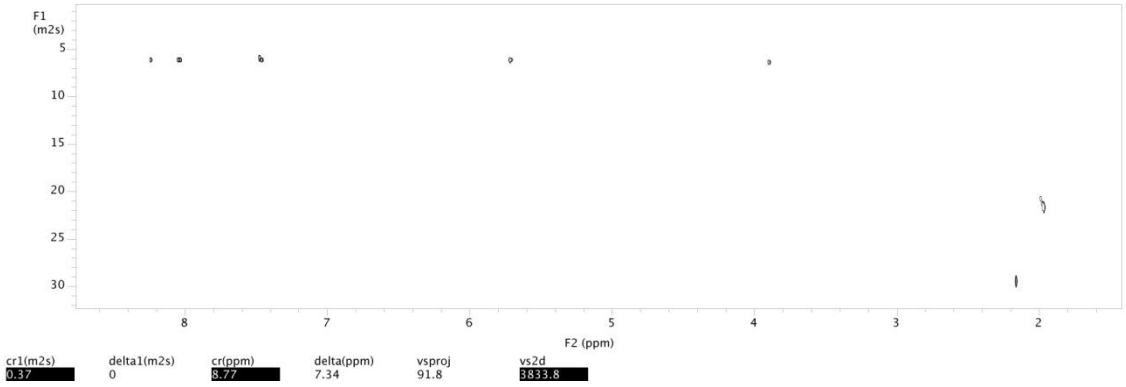


Figure S6 Partial ^{1}H NMR spectra (400 MHz, d_6-DMSO, 298 K) of the ligand **3a** (top) and the oligomeric reaction mixture **6a** (bottom).

2.2 DOSY NMR spectra of synthesized compounds



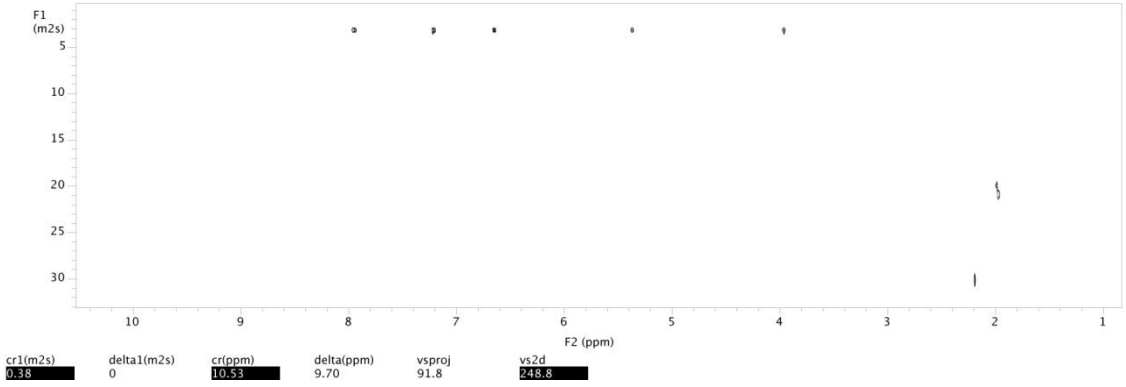


Figure S7 Partial DOSY NMR spectra (500 MHz, d_3-acetonitrile, 298 K) recorded for the ligand **1c** (top) and the palladium cage **2c** (bottom).

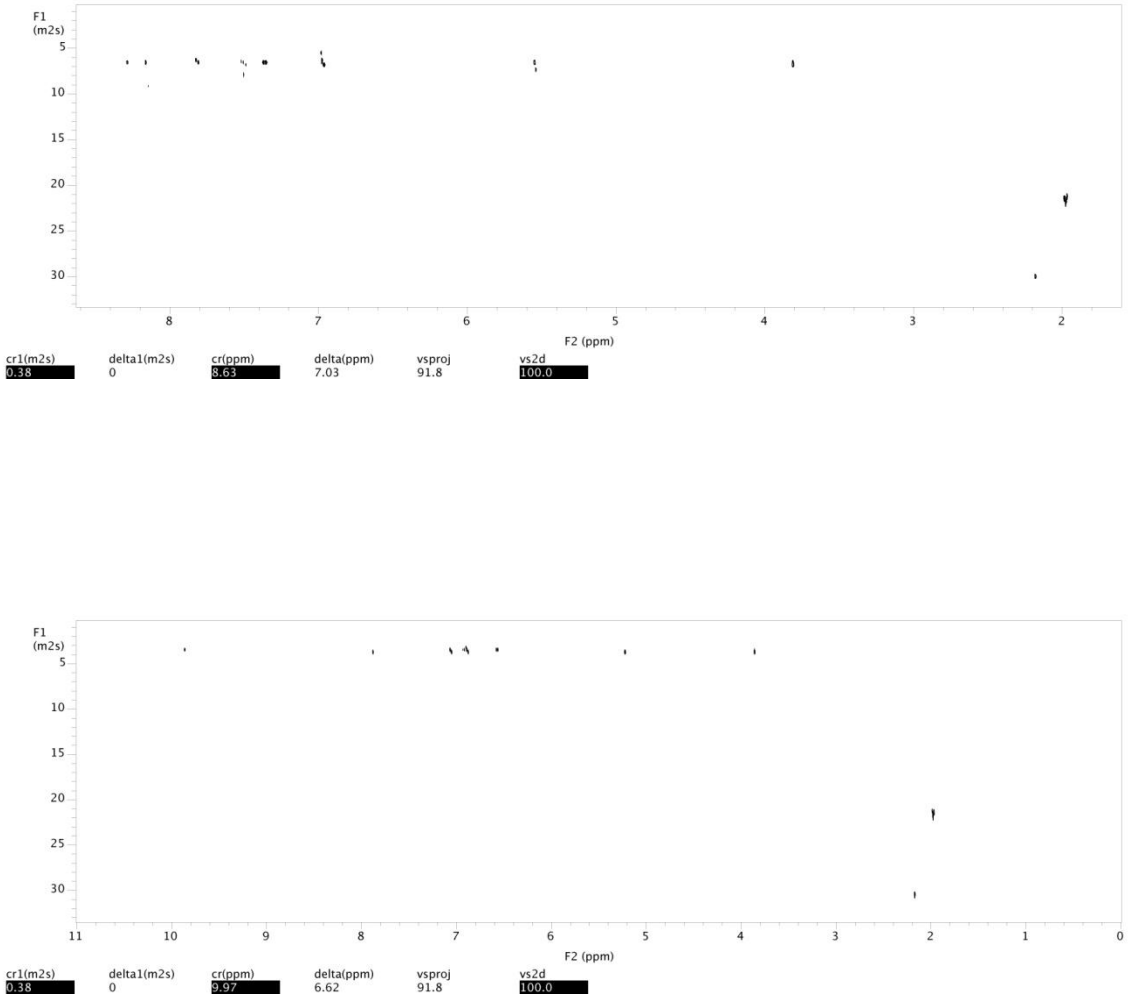


Figure S8 Partial DOSY NMR spectra (500 MHz, d_3-acetonitrile, 298 K) recorded for ligand **1d** (top) and the palladium cage **2d** (bottom).

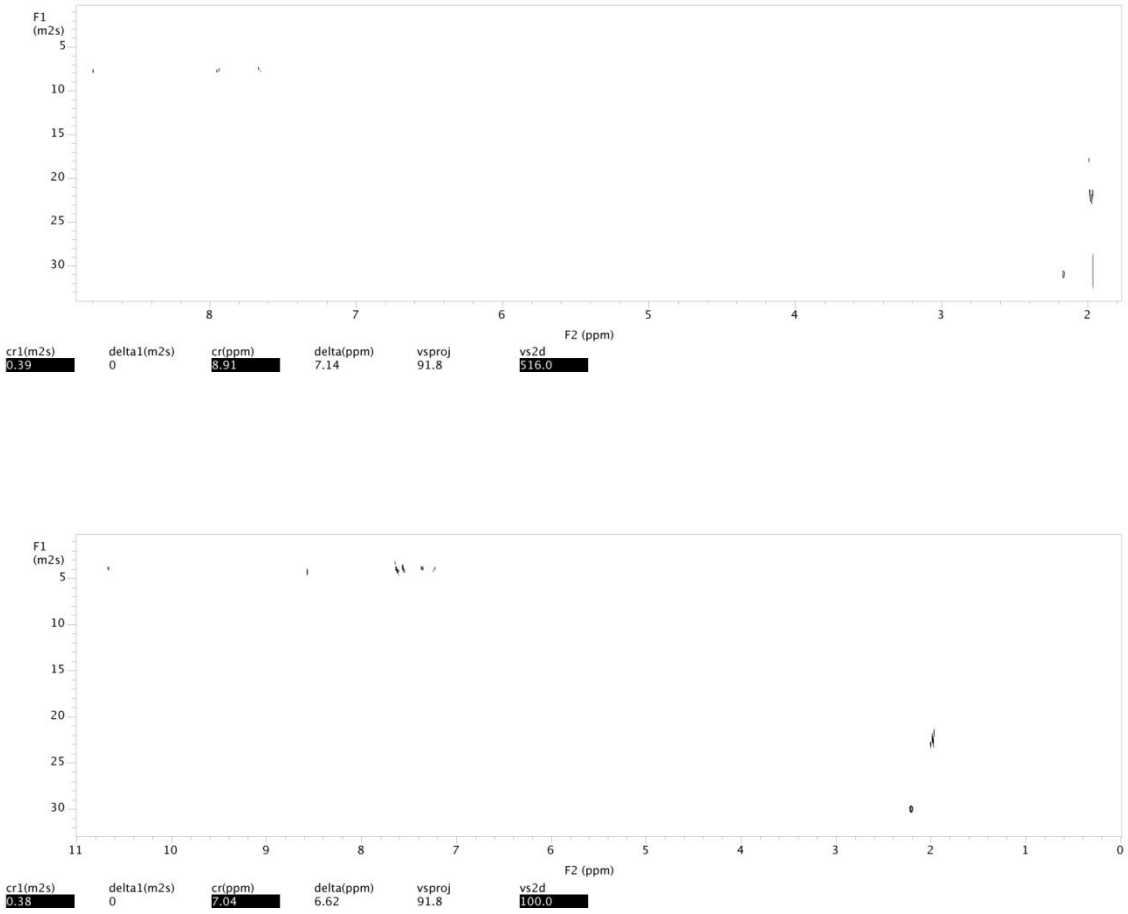


Figure S9 Partial DOSY NMR spectra (500 MHz, d_3-acetonitrile, 298 K) recorded for the ligand **1e** (top) and the palladium cage **4e** (bottom).

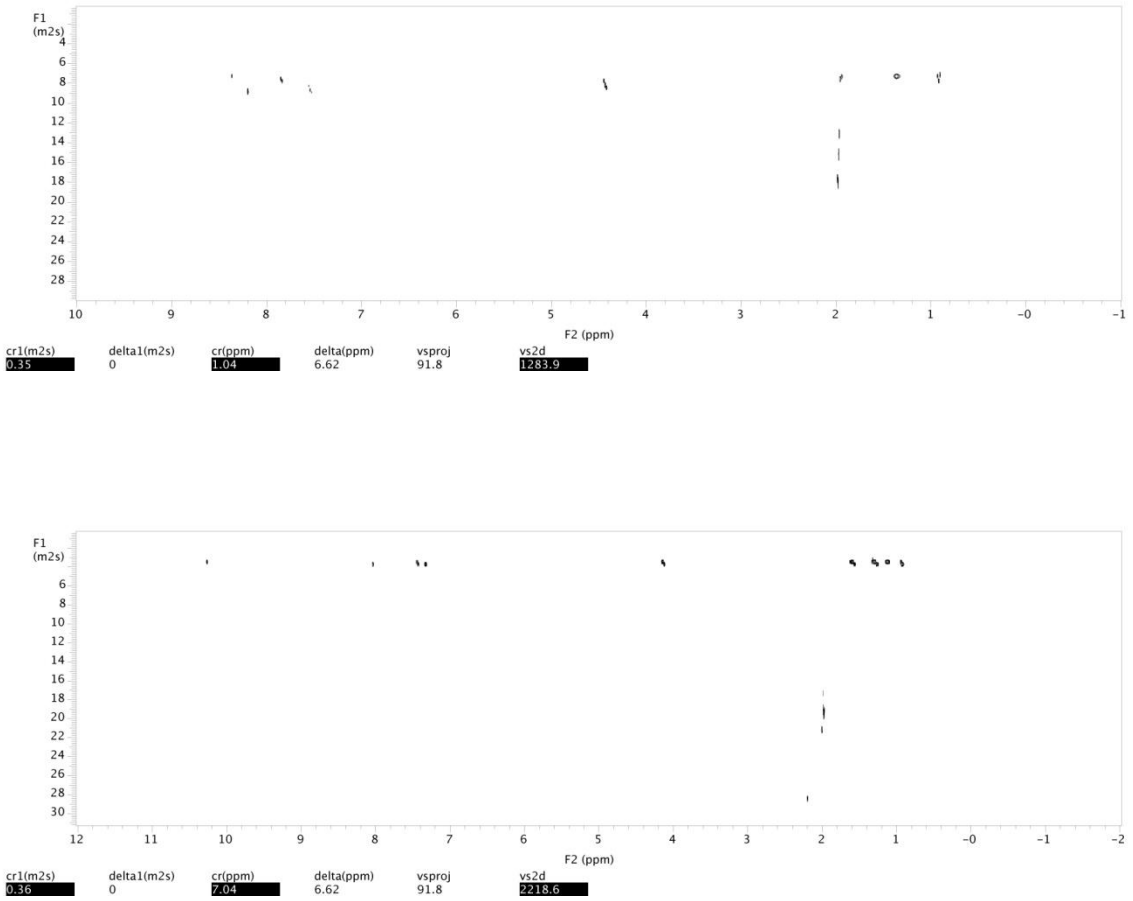


Figure S10 Partial DOSY NMR spectra (500 MHz, d_3-acetonitrile, 298 K) recorded for the ligand **1f** (top) and the palladium cage **4f** (bottom).

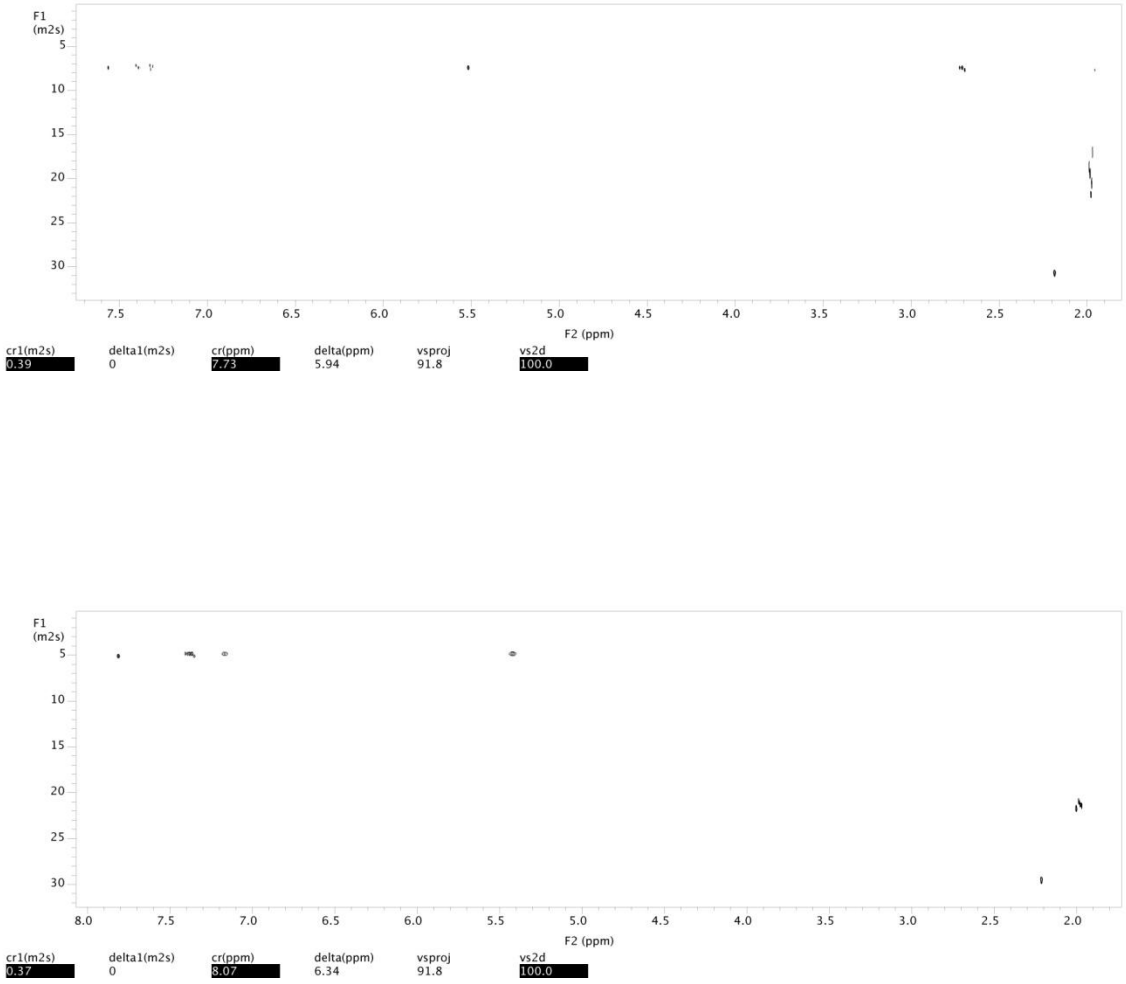


Figure S11 Partial DOSY NMR spectra (500 MHz, d_3-acetonitrile, 298 K) recorded for the ligand **2a** (top) and palladium cage **5a** (bottom).

3 Calculations

3.1 SPARTAN 08 molecular models of palladium(II) "click" cages compounds.

Geometry optimisations of all cage complexes were performed using MMFF in SPARTAN 08.

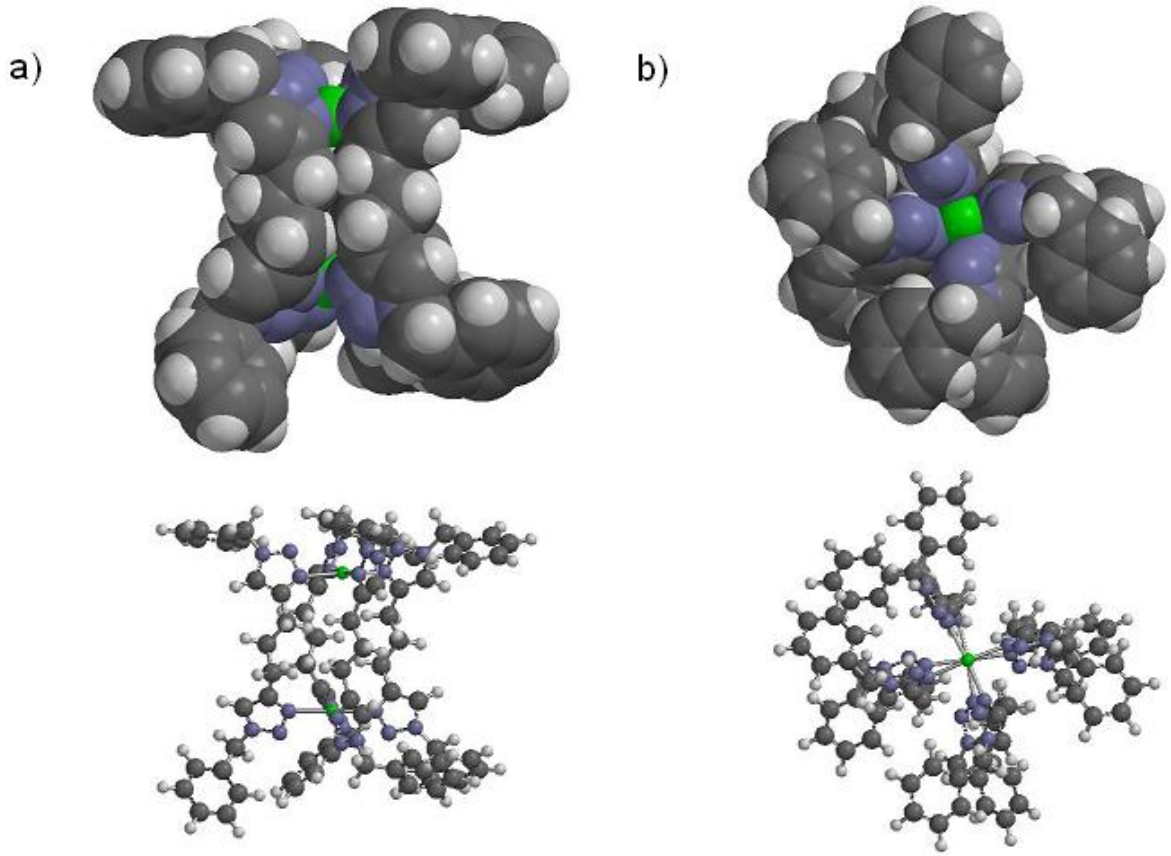


Figure S12 a) Side view and b) top view of a SPARTAN 08 (MMFF) molecular model of the palladium(II) cage complex **5a** (Spartan '08 for Windows, Wavefunction, Irvine, CA).

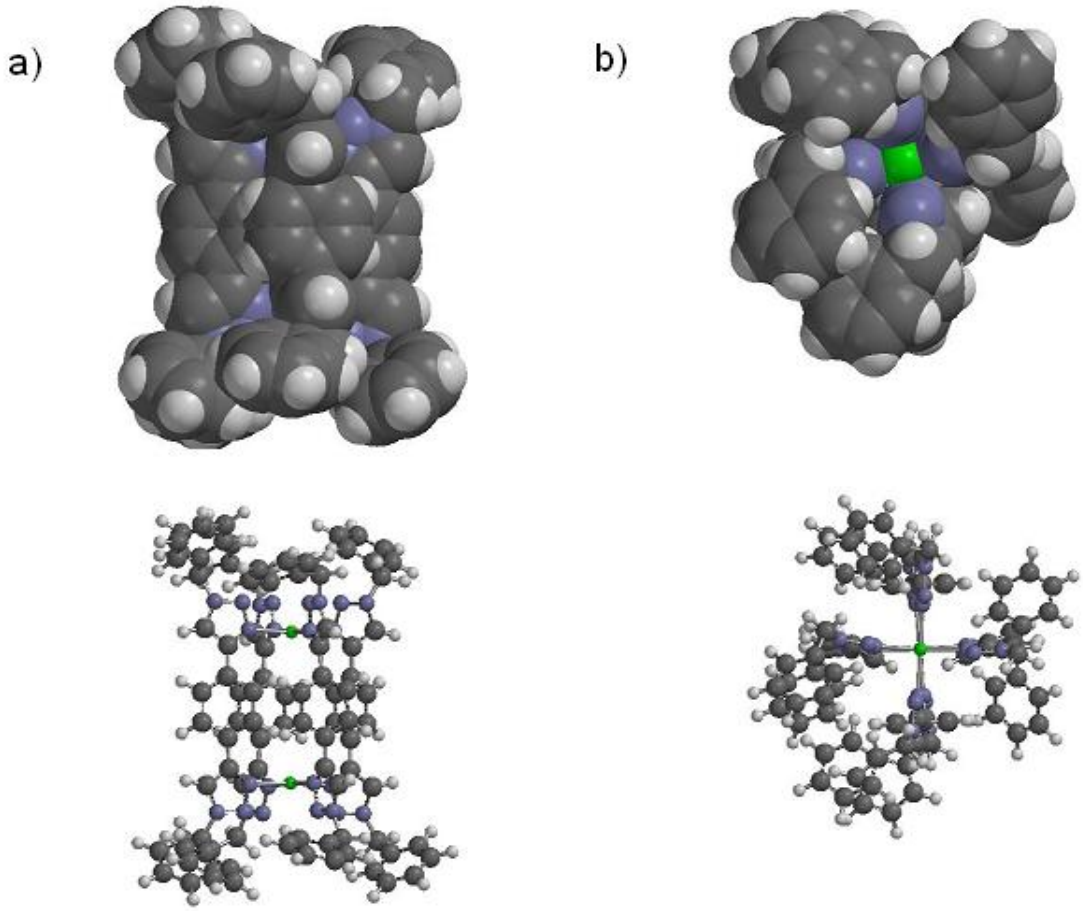


Figure S13 a) Side view and b) top view of a SPARTAN 08 (MMFF) molecular model of the palladium(II) cage complex **6a** (Spartan '08 for Windows, Wavefunction, Irvine, CA).

3.2. DFT computational procedures.

Geometry optimisations of all cage complexes were performed using density functional theory (DFT) with the B3LYP functional, a 3-21* basis set was used to describe the non-metal atoms and the central palladium ions was modelled with a LANL2DZ effective core potential. Ligands and other reactants/products were fully optimised within each particular functional-basis set combination. A solvent continuum model was used (polarised continuum model) with the parameters for acetonitrile used for the reaction field. No symmetry constraints were applied to any of the structures. Vibrational frequency calculations of the optimised geometries were completed to ensure convergence to the global minimum. Single point calculations (under tight convergence criteria) of the cage structures were made of the optimised

geometries with B3LYP//6-31g(d)/LANL2DZ and CAM-B3LYP//6-31g(d)/LANL2DZ combinations of functional and basis sets. All calculations were carried out using the Gaussian 09W computational Package. Structural diagrams of the complexes were generated using the GaussView 5.0.8W (Gaussian Inc.) software package.

Table 1. Calculated ΔH_{form} for the palladium(II) "click" cages (kJ mol^{-1})

	B3LYP/3-21G	B3LYP/6-31G(d)	CAM-B3LYP/6-31G(d)	B3LYP/6-31G(d)//ACN
4a	-572.72	293.77	391.07	**230.79**
4e	-466.82	325.67	448.78	**250.12**
4f	-299.32	371.34	472.14	**133.55**
6a'	505.33	533.13	533.01	**525.32**

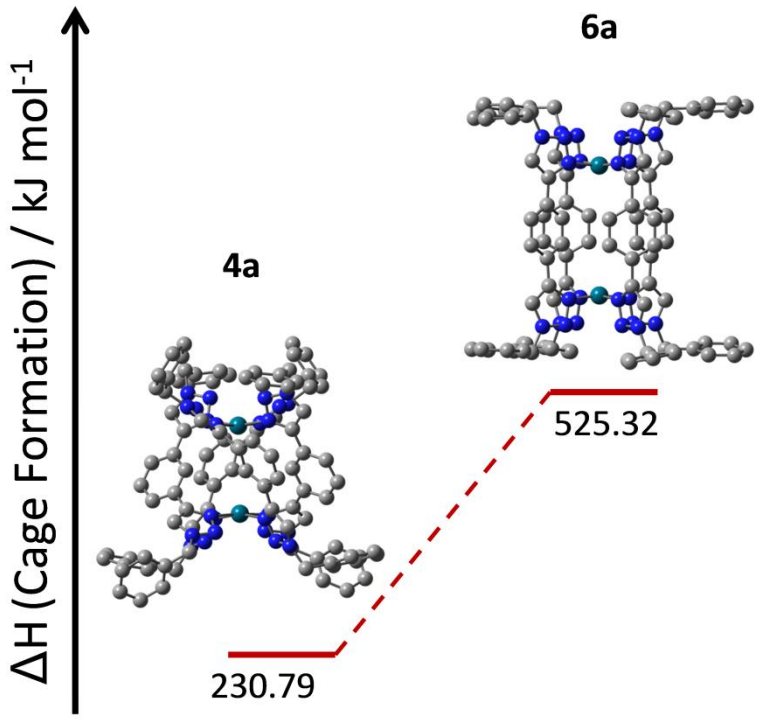


Figure S14 An energy diagram showing the calculated difference in ΔH_{form} for the isomeric dipalladium(II) "click" cages **4a** and **6a**. The cages are shown as ball-and-stick models.

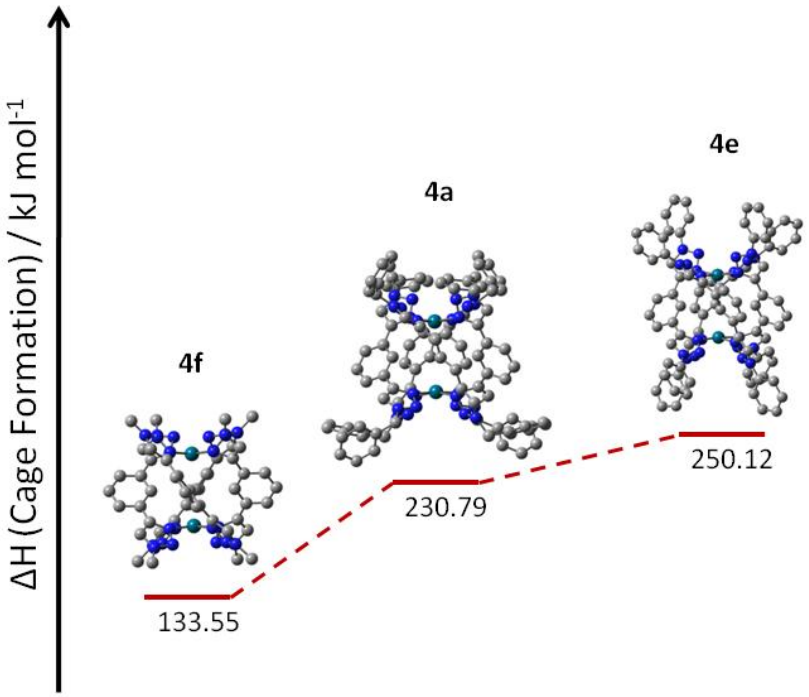


Figure S15 An energy diagram showing the calculated difference in ΔH_{form} for the alkyl (**4f**), benzyl (**4a**), and phenyl (**4e**) substituted dipalladium(II) "click" cages. The cages are shown as ball-and-stick models. In order to simplify the calculation the hexyl chain of the cage **4f** was modeled as a methyl group.

4 HR-ESMS spectra of the palladium/ligand product mixtures

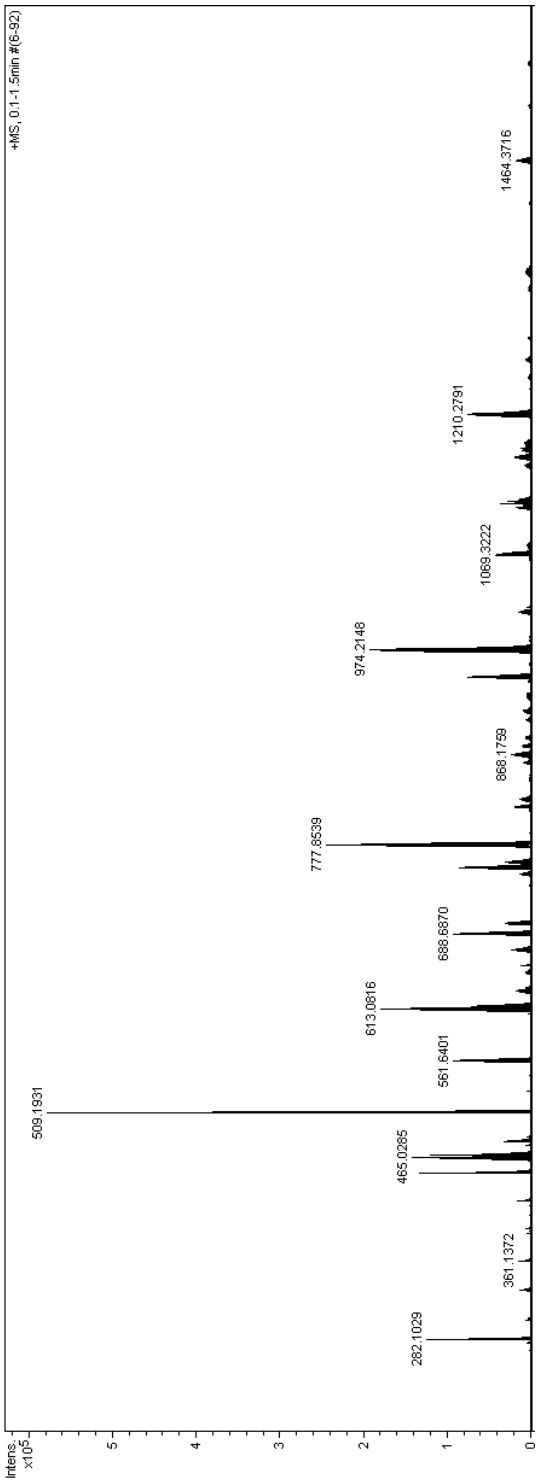


Figure S16 HRESI-MS (CH_3CN) of $[Pd_2(\mathbf{1c})_4](BF_4)_4$, **4c**: *m/z* = 509.2 $[\mathbf{1c}+H]^+$ (calc. for $C_{28}H_{25}N_6O_4$ 509.2); 613.1 $[Pd(\mathbf{1c}-H)]^+$ (calc. for $C_{28}H_{23}N_6O_4Pd$ 613.1); 777.9 $[Pd_2(\mathbf{1c})_4](BF_4)_3^+$ (calc. for $C_{112}H_{96}BF_4N_{24}O_{16}Pd_2$ 777.9); 1210.3 $[Pd_2(\mathbf{1c})_4](BF_4)_2^{2+}$ (calc. for $C_{112}H_{96}B_2F_8N_{24}O_{16}Pd_2$ 1210.3).

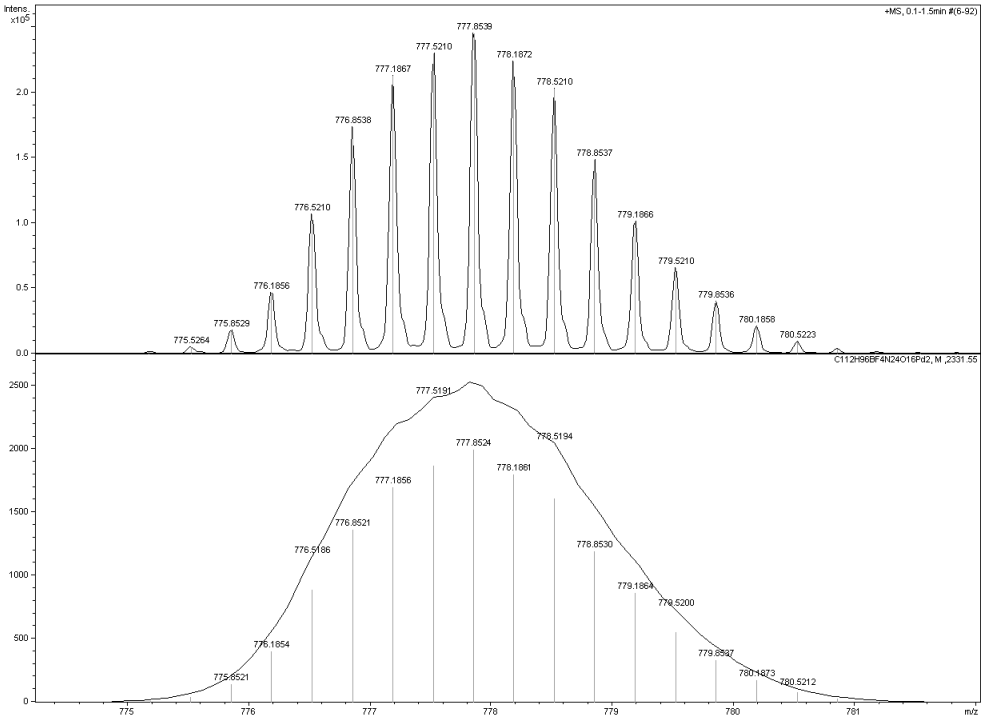


Figure S17 Observed (top) and calculated (bottom) isotopic distribution for the $[Pd_2(\mathbf{1c})_4](BF_4)^{3+}$ ion

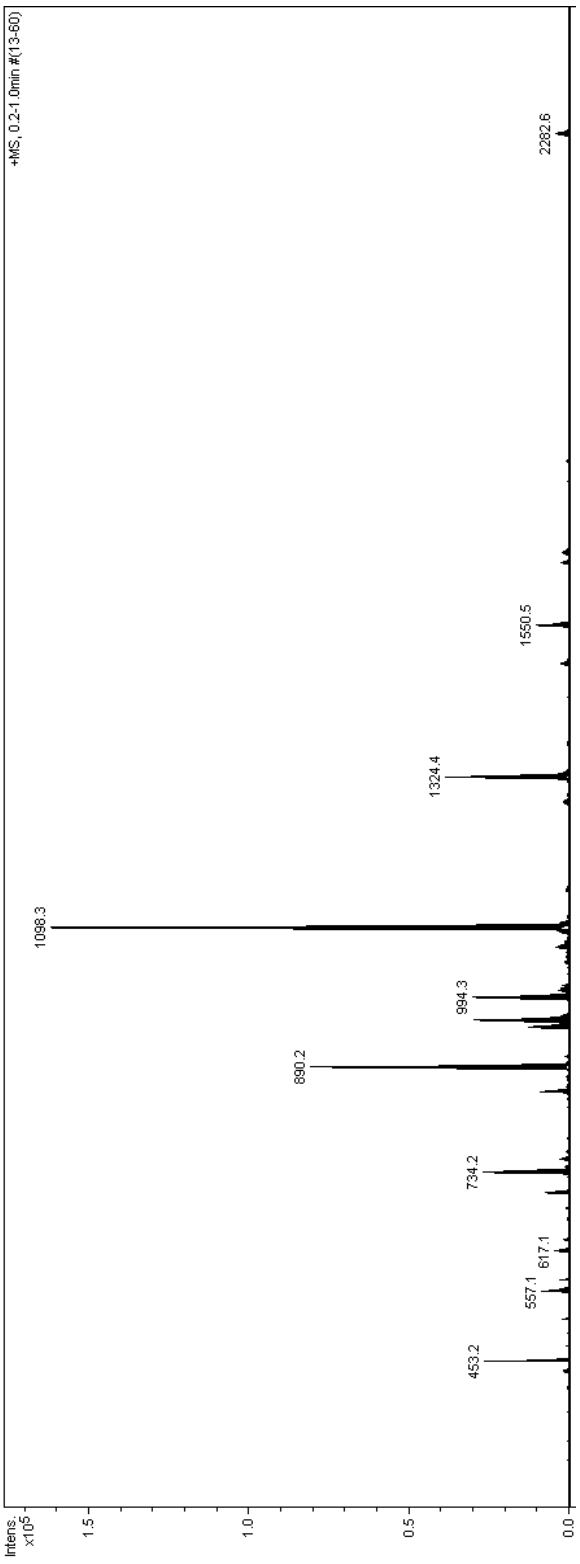


Figure S18 HRESI-MS (CH_3CN) of $[Pd_2(\mathbf{1d})_4](BF_4)_4$, **4d**: *m/z* = 453.2 $[\mathbf{1d}+H]^+$ (calc. for $C_{26}H_{25}N_6O_2$ 453.2); 890.2 $[Pd_2(\mathbf{1d})_3ClH](BF_4)_2^{2+}$ (calc. for $C_{78}H_{73}B_2ClF_8N_{24}O_8Pd_2$ 890.2); 1098.3 $[Pd_2(\mathbf{1d})_4](BF_4)_2^{2+}$ (calc. for $C_{104}H_{96}B_2F_8N_{24}O_8Pd_2$ 1098.3); 2262.6 $[Pd_2(\mathbf{1d})_4](BF_4)_3^{+}$ (calc. for $C_{104}H_{96}B_3F_{12}N_{24}O_8Pd_2$ 2262.6).

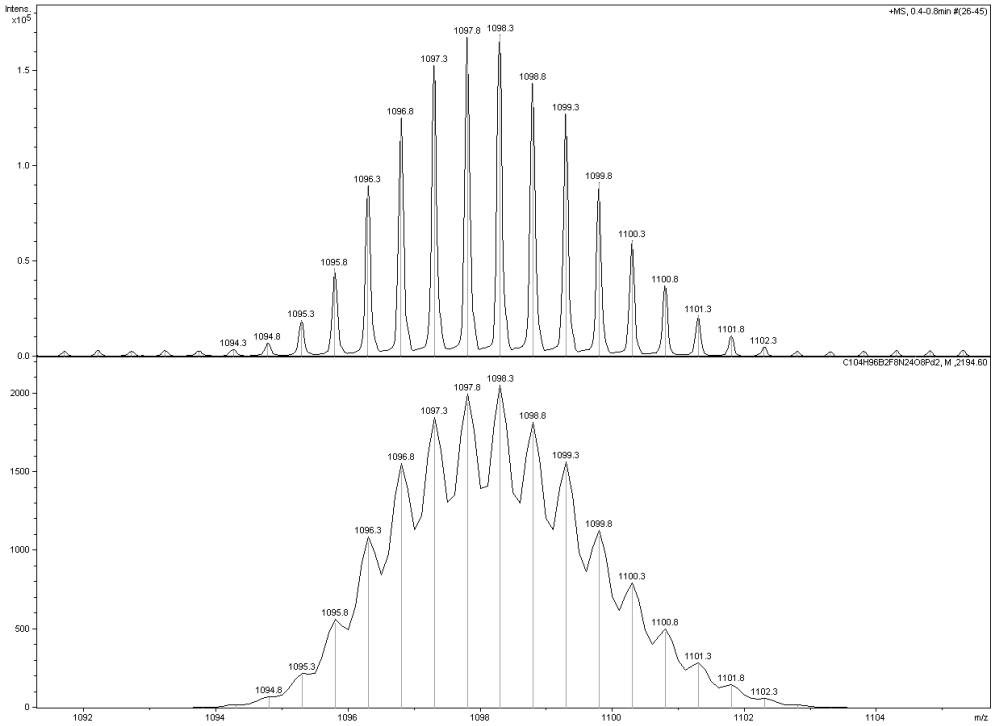


Figure S19 Observed (top) and calculated (bottom) isotopic distribution for the $[Pd_2(\mathbf{1d})_4](BF_4)_2^{2+}$ ion.

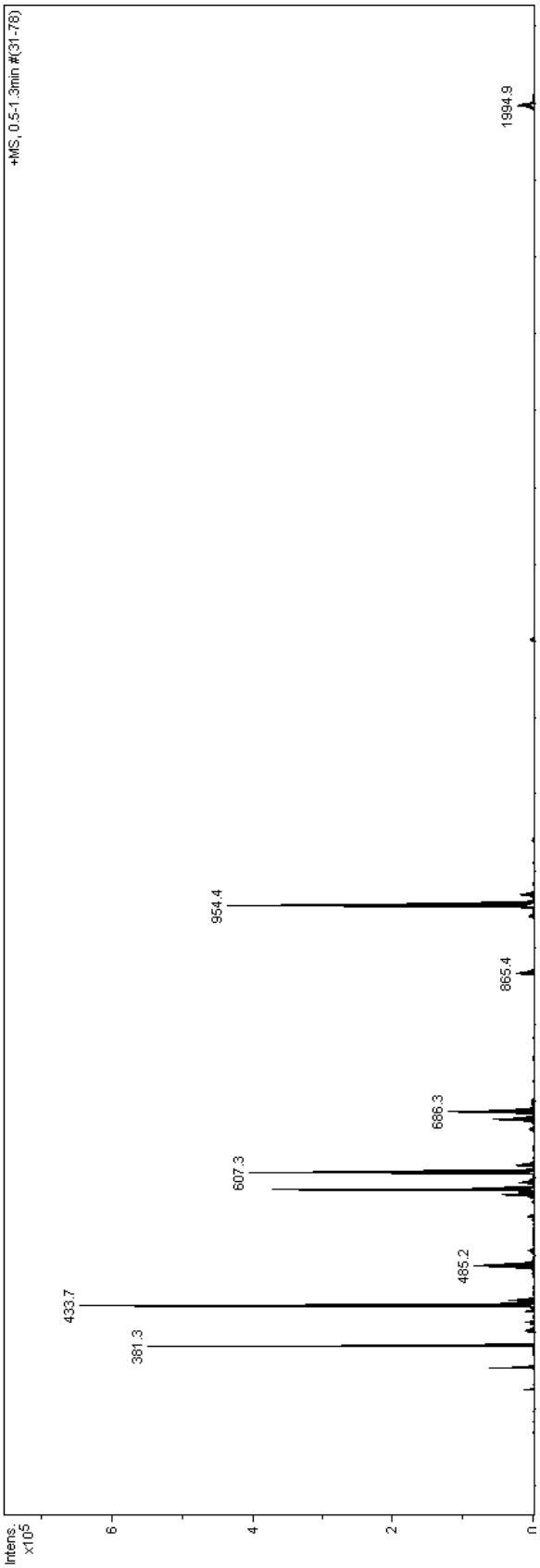


Figure S20 HRESI-MS (CH_3CN) $[Pd_2(\mathbf{1f})_4](BF_4)_4$, **4f**: *m/z* = 381.3 $[\mathbf{1f}+H]^+$ (calc. for $C_{22}H_{33}N_6$ 381.3); 433.7 $[Pd_2(\mathbf{1f})_4]^{4+}$ (calc. for $C_{88}H_{128}N_{24}Pd_2$ 433.7); 607.3 $[Pd_2(\mathbf{1f})_4]BF_4^{3+}$ (calc. for $C_{99}H_{128}BF_4N_{24}Pd_2$ 607.3); 686.3 $[Pd_2(\mathbf{1f})_3HOH]^{2+}$ (calc. for $C_{66}H_{98}N_{18}OPd_2$ 686.3); 954.4 $[Pd_2(\mathbf{1f})_4](BF_4)_2^{2+}$ (calc. for $C_{88}H_{128}B_2F_8N_{24}Pd_2$ 954.4); 1994.9 (calc. for $C_{88}H_{128}B_3F_{12}N_{24}Pd_2$ 1994.9).

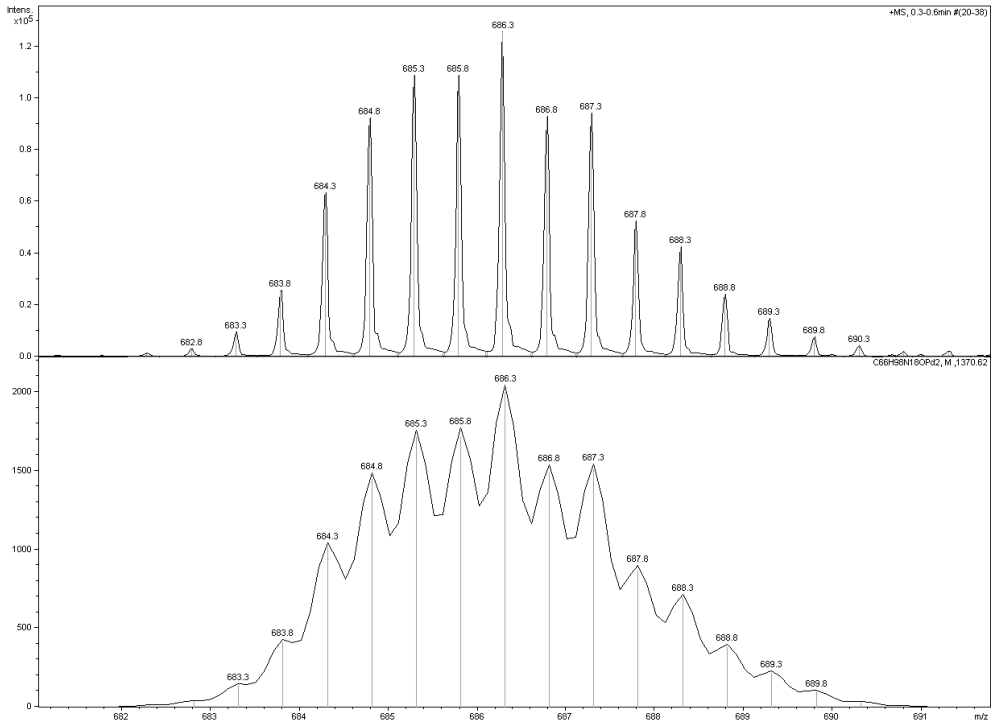


Figure S21 Observed (top) and calculated (bottom) isotopic distribution for the $[Pd_2(\mathbf{1f})_3HOH]^{2+}$ ion.

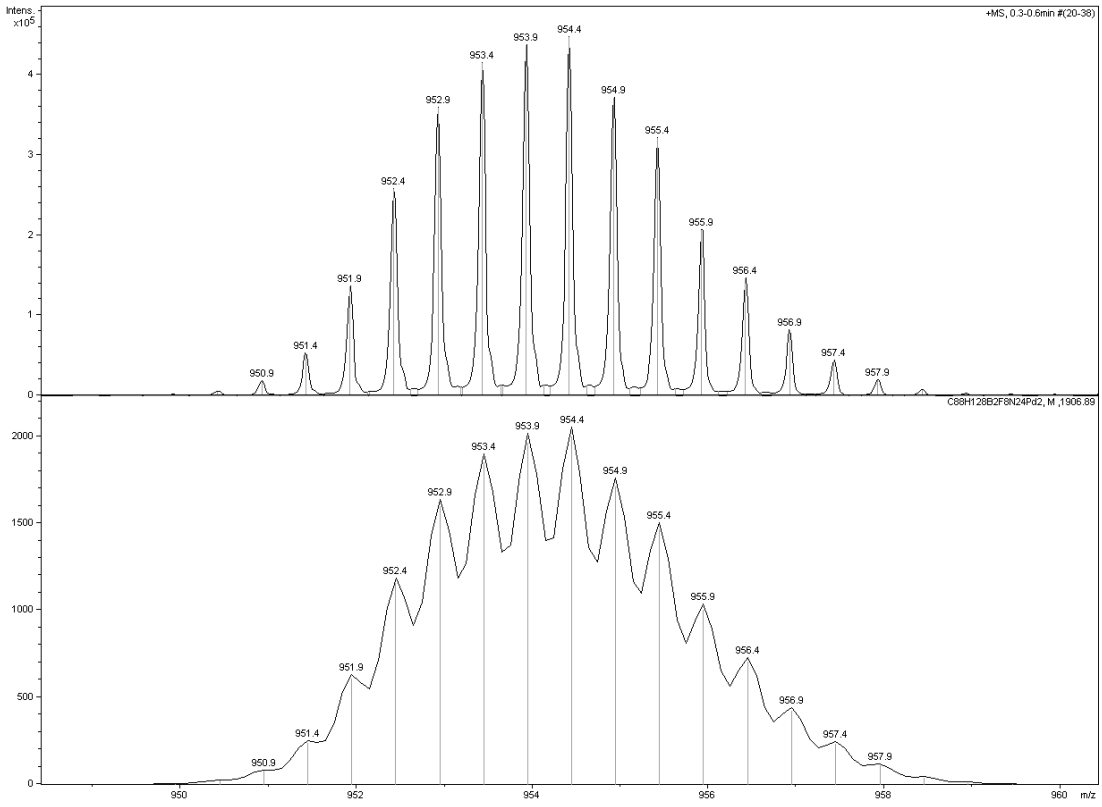


Figure S22 Observed (top) and calculated (bottom) isotopic distribution for the $[Pd_2(\mathbf{1f})_4](BF_4)_2^{2+}$ ion.

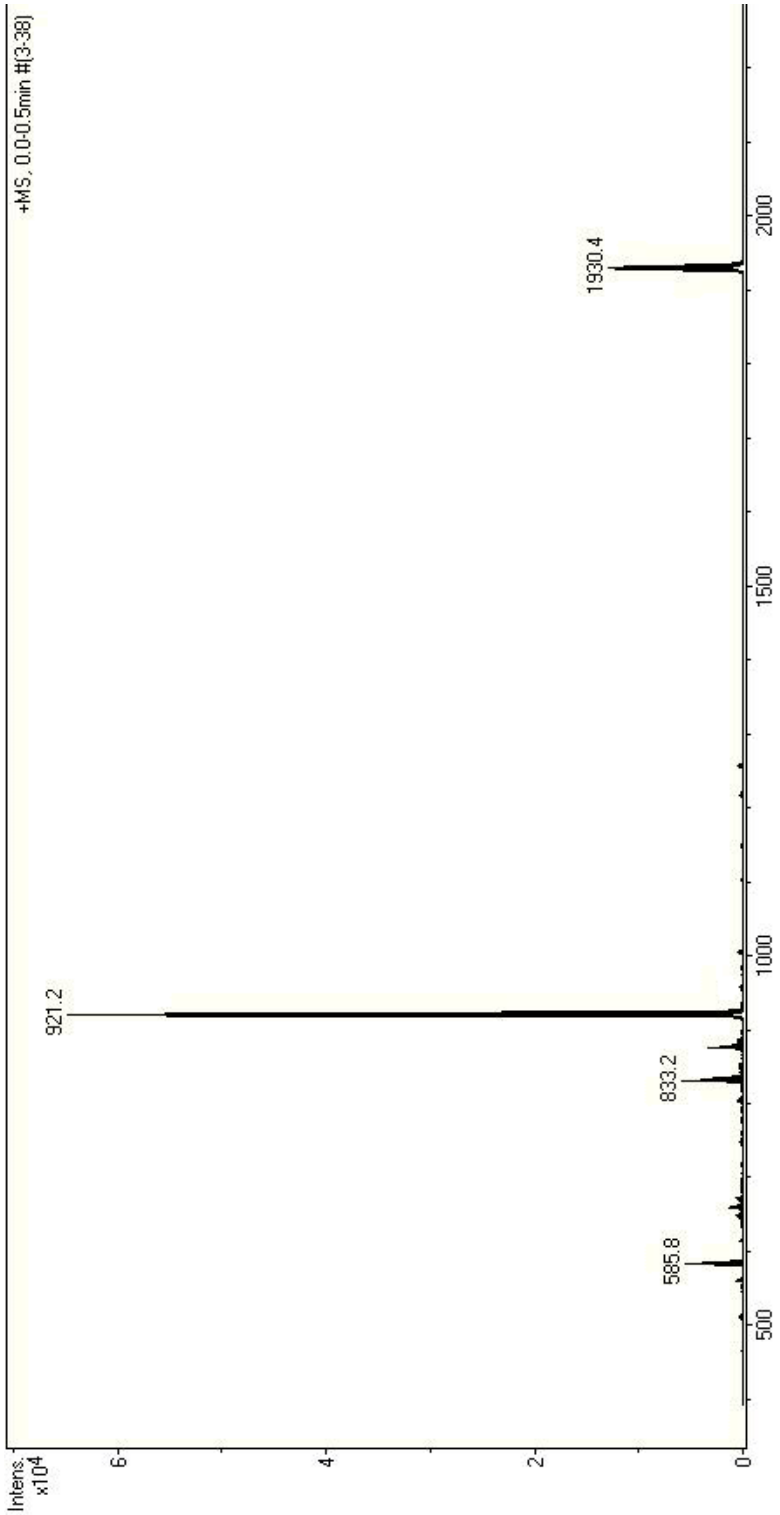


Figure S23 HRESI-MS (CH_3CN) of $[Pd_2(\mathbf{1e})_4](BF_4)_4$, **4e**: *m/z* = 922.2 $[Pd_2(\mathbf{1e})_4(BF_4)_2]^{2+}$ (calc. for $C_{88}H_{64}B_2F_8N_{24}Pd_2$ 922.2); 1930.4 $[Pd_2(\mathbf{1e})_4(BF_4)_3]^{+}$ (calc. for $C_{88}H_{64}B_3F_{12}N_{24}Pd_2$ 1930.4).

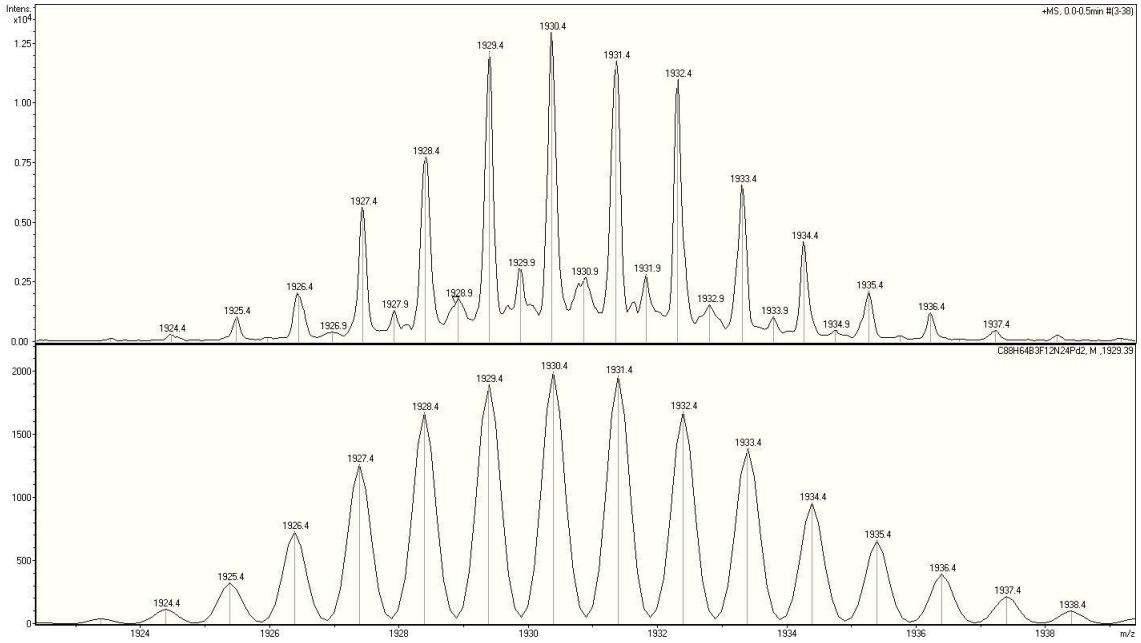


Figure S24 Observed (top) and calculated (bottom) isotopic distribution for the $[Pd_2(\mathbf{1e})_4](BF_4)_3^+$ ion.

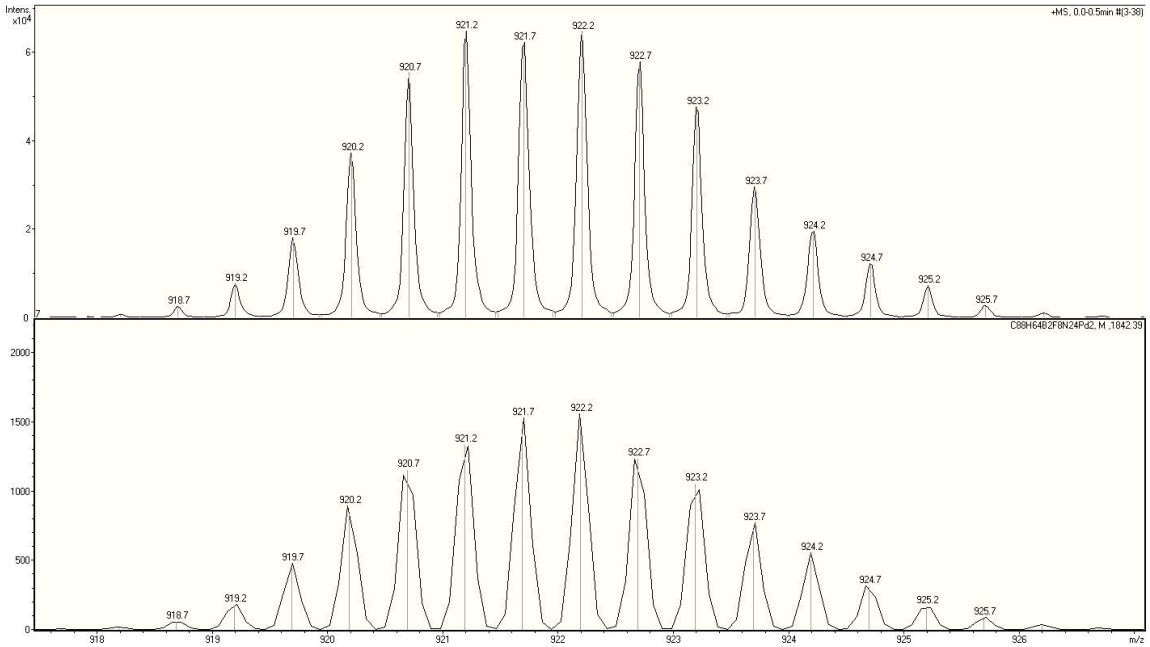


Figure S25 Observed (top) and calculated (bottom) isotopic distribution for the $[Pd_2(\mathbf{1e})_4](BF_4)_2^{2+}$ ion.

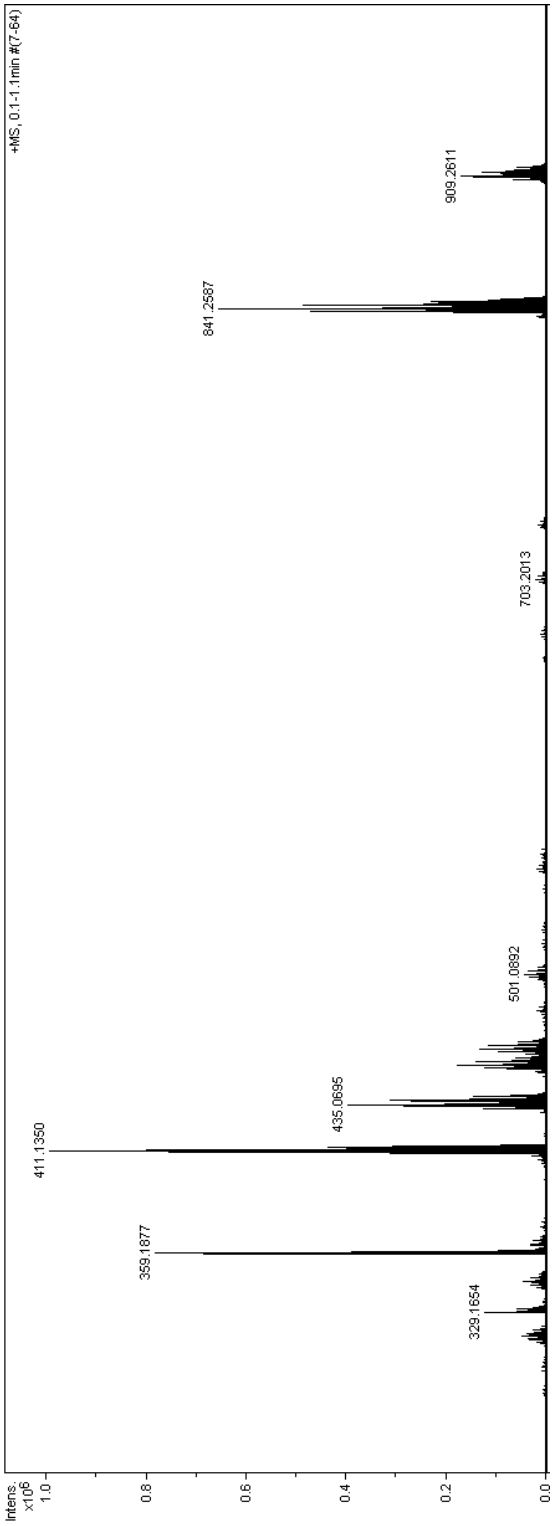


Figure S26 HRESI-MS (CH_3CN) of $[Pd_2(\mathbf{2a})_4](BF_4)_4$, **5a**: *m/z* = 359.2 $[\mathbf{2a}+H]^+$ (calc. for $C_{21}H_{23}N_6$ 359.2); 841.3 $[Pd(\mathbf{2a})(H_2O)H]^+$ (calc. for $C_{42}H_{47}N_{12}OPd$ 841.3); 909.3 $[Pd(\mathbf{2a})_2]BF_4^+$ (calc. for $C_{42}H_{44}BF_4N_{12}Pd$ 909.3); 1906.5 $[Pd_2(\mathbf{2a})_4](BF_4)_3^+$ (calc. for $C_{84}H_{88}B_3F_{12}N_{24}Pd_2$ 1906.6).

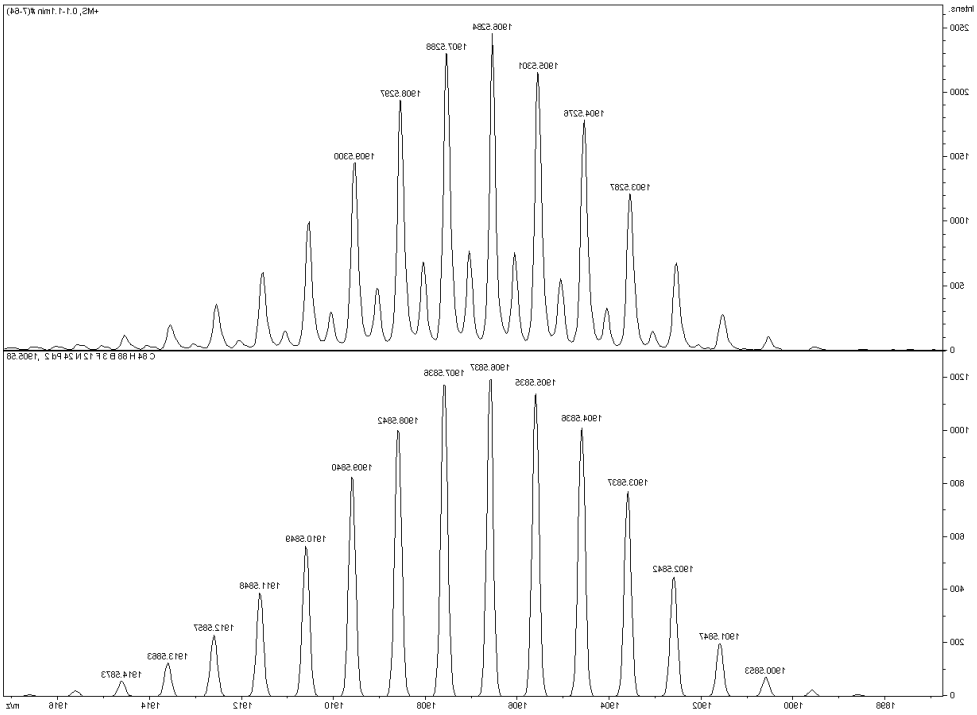


Figure S27 Observed (top) and calculated (bottom) isotopic distribution for the $[Pd_2(\mathbf{2a})_4(BF_4)_3]^+$ ion.

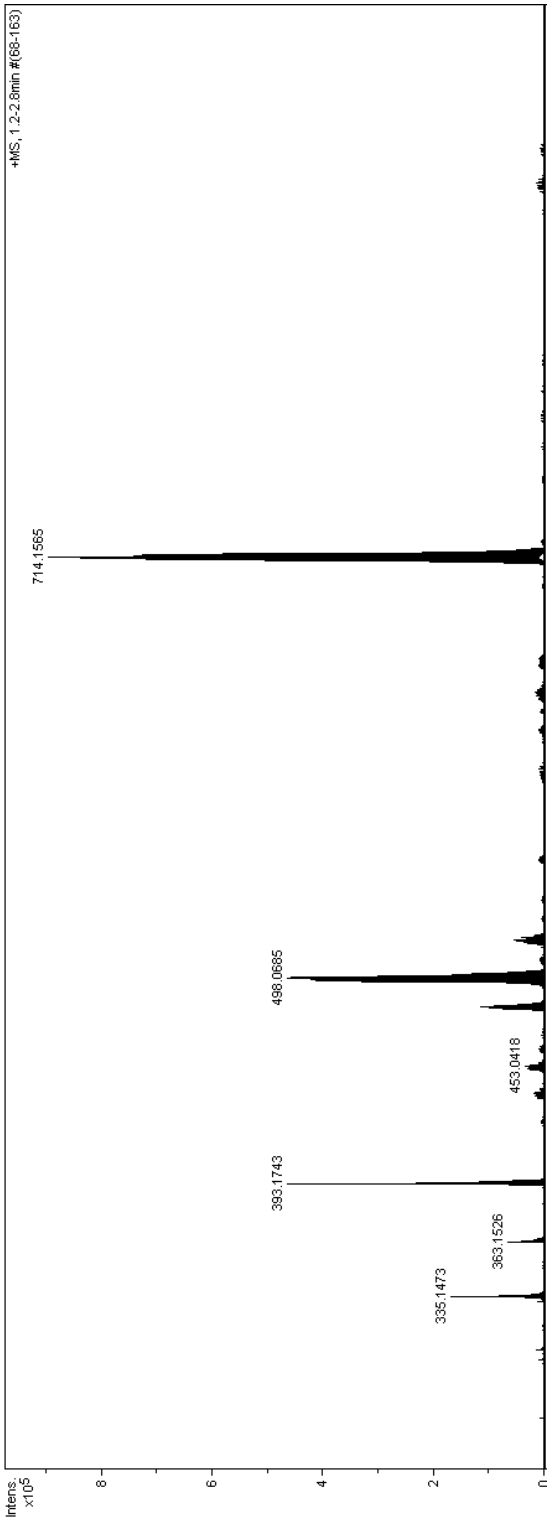


Figure S28 HRESI-MS (CH_3CN) of the product mixture formed from **3a** and $[Pd(CH_3CN)](BF_4)_2$: *m/z* = 393.2 $[\mathbf{3a}+H]^+$ (calc. for $C_{42}H_{21}N_6$ 393.2); 714.2 $[Pd_2(\mathbf{3a}\text{-}H)_3 H_2O](BF_4)_2.Na^{2+}$ (calc. for $C_{72}H_{59}N_{18}NaOPd_2$ 714.2).

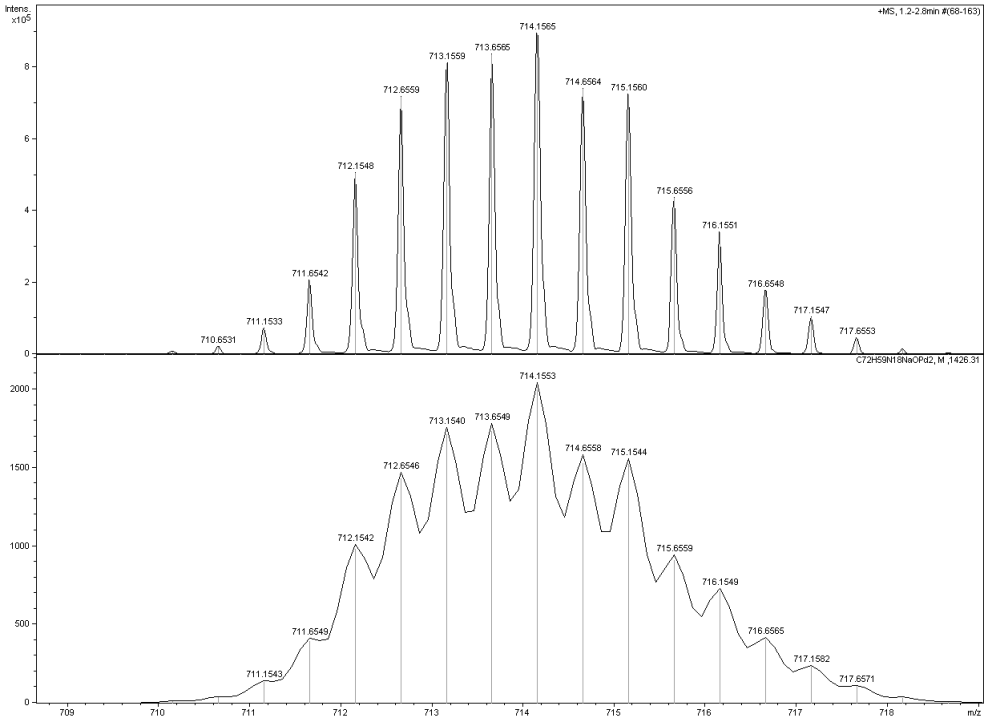


Figure S29 Observed (top) and calculated (bottom) isotopic distribution for the $[Pd_2(\mathbf{3a}\text{-}H)_3H_2O](BF_4)_2.Na^{2+}$ ion.

5 Crystallography.

5.1 X-ray data collection and refinement. X-ray data for **1d** and **4c** were recorded with a Bruker APEX II CCD diffractometer at 89(2) or 90(2) K using Mo Kα radiation (λ = 0.71073 Å). The structures were solved by direct methods using SIR97,[4] with the resulting Fourier maps revealing the location of all non-hydrogen atoms. Weighted full matrix refinement on F^2 was carried out using SHELXL-97[5] with all non-hydrogen atoms being refined anisotropically. The hydrogen atoms were included in calculated positions and were refined as riding atoms with individual (or group, if appropriate) isotropic displacement parameters.

In **4c** one of the BF_4^- counter ions was disordered over two sites. The B atom was refined with 100% occupancy but the F atoms of the BF_4^- anion were rotationally disordered. The F atoms were modelled satisfactorily in two different orientations (60:40)

about the B atom and all the atoms of the anion were refined anisotropically.

Following the location of the all the cage atoms and BF_4^- counter ions of **4c** in the ΔF map there was still residual electron density present within channels through the structure. Disappointingly, this residual electron density could not be satisfactorily modelled. The squeeze routine of the PLATON X-ray data refinement software package[6] was used to account for the contribution of these disordered solvent molecules. A total of 709 e were found in the void volume of the crystal, corresponding to 32 molecules of acetonitrile, the crystallisation solvent.

All ORTEP[7] diagrams have been drawn with 50% probability ellipsoids. Crystal data and collection parameters are given in Table 1. The CIF files CCDC 819052 (**1d**) and CCDC 819051 (**4c**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: (+44) 1223-336-033.

6. References

(1) Vassiliou, S.; Xeilari, M.; Yiotakis, A.; Grembecka, J.; Pawelczak, M.; Kafarski, P.; Mucha, A. *Bioorg. Med. Chem.* **2007**, *15*, 3187-3200.
(2) Gower, M. L.; Crowley, J. D. *Dalton Trans.* **2010**, *39*, 2371-2378.
(3) Crowley, J. D.; Gavey, E. L. *Dalton Trans.* **2010**, *39*, 4035-4037.
(4) Altomare, A.; Burla, M. C.; Camalli, M.; Cascarano, G. L.; Giacovazzo, C.; Guagliardi, A.; Moliterni, A. G. G.; Polidori, G.; Spagna, R. *J. Appl. Crystallogr.* **1999**, *32*, 115-119.
(5) Sheldrick, G. M. *Acta Crystallogr., Sect. A: Found. Crystallogr.* **2008**, *A64*, 112-122.
(6) Spek, A. L.; Utrecht University, 2000.
(7) Farrugia, L. J. *J. Appl. Crystallogr.* **1997**, *30*, 565.