Electronic Supplementary Information

Control over Coordination Self-Assembly of Flexible, Multidentate Ligands by Stepwise Metal Coordination of Isopyrazole Subunits

Yoshiko Ashida, Yumehiro Manabe, Shota Yoshioka, Tomoki Yoneda, and Yasuhide Inokuma*

Table of contents

I. Reagents and Equipment

II. Synthesis and Characterization

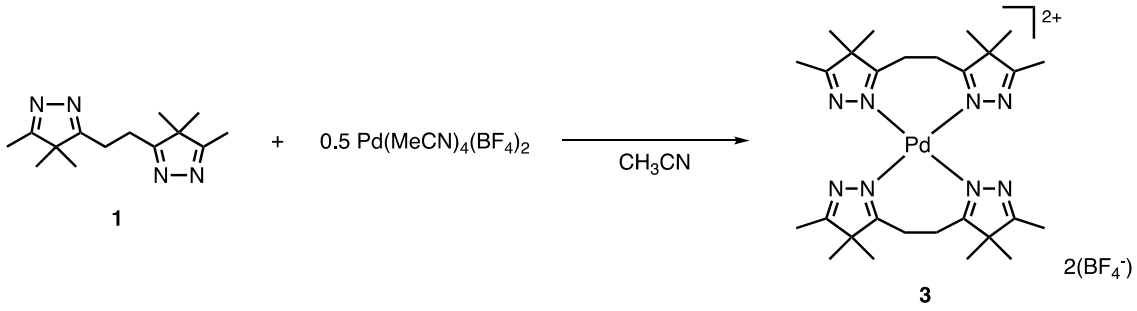
III. References

I. Reagents and Equipment

Solvents and reagents were purchased from WAKO Pure Chemical Industries Ltd., TCI Co., Ltd., or Sigma-Aldrich Co., and used without further purification. All the ^{1}H and ^{13}C and 2 dimensional NMR spectra were recorded using a JEOL JMN-ECS400 (400 MHz) or ECZ600 (600 MHz) spectrometers at 300 K and the chemical shifts are reported in parts per million (ppm) relative to solvent residual peak (δ = 1.94 ppm for ^{1}H and 1.32 ppm for ^{13}C) in CD_3CN. Simulation of ^{1}H NMR spectra for overlapping and multiply coupled system was performed using fast and accurate algorithm reported by Wist and co-workers[1]. ESI-TOF-MS spectra were recorded on a Thermo scientific Exactive spectrometer for organic compounds in CH_3CN. Infrared spectra were measured using a JASCO Co. FT/IR-4700. Elemental analysis was performed using a Exceter Analytical, Inc. CE440. Single crystal X-ray diffraction data were collected with Rigaku XtaLAB P200 diffractometer equipped with a PILATUS200K detector using multi-layer mirror (MoK_α radiation λ = 0.71073 Å or CuK_α radiation λ = 1.54184 Å) or a RAPID II diffractometer with an imaging plate detector using sealed tube MoK_α radiation. All structures were solved using a dual-space algorithm (SHELXT[2]) and refined using full-matrix least-squares method (SHELXL[3]). Isopyrazole ligands **1** and **2** were synthesized according to the reported procedure[4] and used for complexation with Pd ions as soon as synthesized. Since these compounds are hygroscopic, (if necessary) they should be stored in a desiccator.

II. Synthesis and Characterization

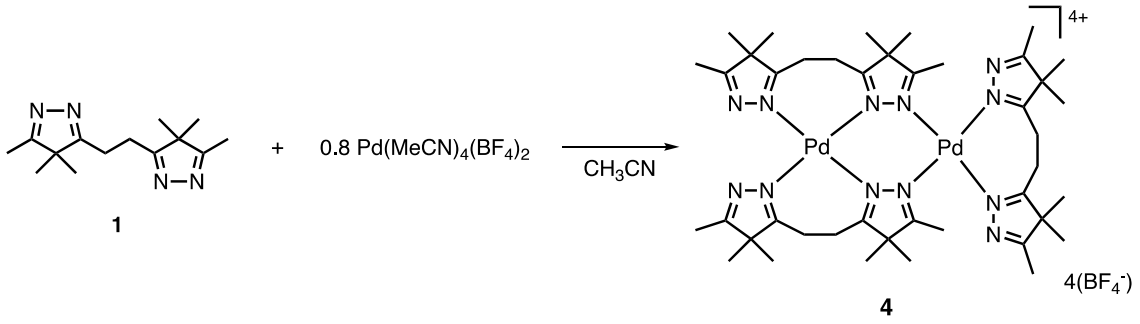
Synthesis of complex 3



In a 20 mL round-bottomed flask equipped with a reflux condenser, ligand **1** (50.0 mg, 203 μmol) and $[Pd(CH_3CN)_4](BF_4)_2$ (45.1 mg, 102 μmol) were dissolved in acetonitrile (3.4 mL). The solution was stirred at 60 °C with an oil bath for 1 h. After the solution was cooled to room temperature, the solution was analyzed by ^{1}H NMR spectroscopy and quantitative formation of complex **3** was confirmed. The product was precipitated as a pale yellow solid by addition of diethyl ether (6.0 mL) to the reaction solution. The precipitate was filtered with suction, washed with 3.0 mL of diethyl ether, and air-dried on a funnel to give complex **3** (56.3 mg) in 71% yield.

^{1}H NMR (400 MHz, CD_3CN, 298 K): δ 3.46 (br s, 8H, ethylene), 2.04 (s, 12H, terminal methyl), 1.26 (s, 24H, dimethylmethylene); ^{13}C NMR (100 MHz, CD_3CN, 298 K): δ 189.8, 184.9, 63.8, 23.1, 19.6, 12.0; HR-ESI-TOF MS: *m/z* = 299.1357 (calcd for $C_{28}H_{44}N_8Pd_1^{2+}$, $[M–2(BF_4^–)]^{2+}$, 299.1367); Elemental analysis (%): C, 42.95; H, 5.64; N, 14.28 (calcd. for $C_{28}H_{44}N_8PdB_2F_8$•$0.5H_2O$ (%): C, 43.02; H, 5.80; N, 14.33)

Synthesis of complex 4

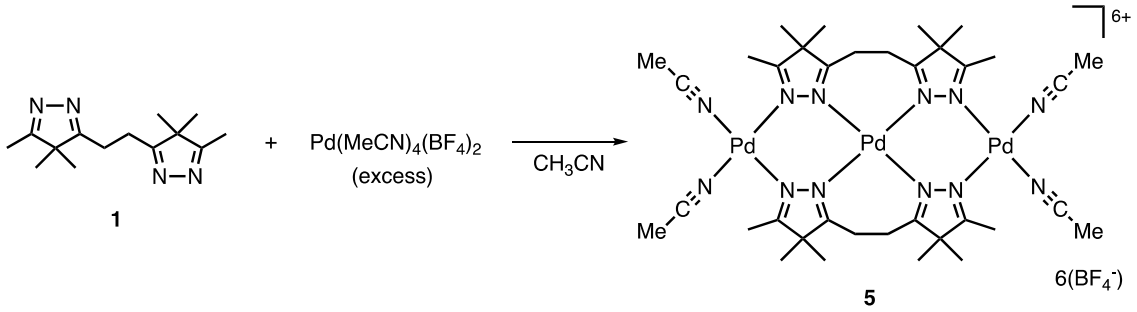


In a similar fashion to the synthesis of complex **3**, a solution of ligand **1** (50.0 mg, 203 μmol) and $Pd(CH_3CN)_4(BF_4)_2$ (72.0 mg, 162 μmol) in acetonitrile (3.4 mL) was stirred at 60 ºC for 1 h. After the solution was cooled to room temperature, dichloromethane (12.0 mL) was slowly added via a pipette, and the resulting solution was allowed to stand at room temperature for 12 h. Pale yellow crystals formed on the bottom of the flask. The crystals were collected by suction filtration, washed with dichloromethane (3.0 mL), and dried on a funnel to give complex **4**•1.5(CH_2Cl_2) (39.9 mg) in 46% yield.

^{1}H NMR (600 MHz, CD_3CN, 298 K): δ 4.58 (ddd, J = 15.0, 12.1, 4.8 Hz, 2H, ethylene), 3.79 (overlapped dt, 2H, ethylene), 3.74 (m, 2H, ethylene), 3.58 (dt, J = 15.0, 4.5 Hz, 2H, ethylene), 3.25 (overlapped ddd , 2H, ethylene), 3.18 (m, 2H, ethylene), 2.50 (s, 6H, terminal methyl), 2.17 (s, 6H, terminal methyl), 1.92 (s, 6H, terminal methyl), 1.43 (s, 6H, dimethylmethylene), 1.35 (s, 6H, dimethylmethylene), 1.34 (s, 6H, dimethylmethylene), 1.30 (s, 6H, dimethylmethylene), 1.28 (s, 6H, dimethylmethylene), 1.18 (s, 6H, dimethylmethylene); ^{13}C NMR (100 MHz, CD_3CN, 298 K): δ 195.1, 194.5, 193.5, 191.9, 186.9, 186.2, 66.5, 64.9, 63.6, 25.4, 23.2, 22.6, 21.9, 21.8, 20.3, 19.4, 19.2, 19.2, 15.2, 12.4, 12.3; HR-ESI-TOF MS: *m/z* = 346.4553 (calcd for $C_{42}H_{66}N_{12}Pd_2B_1F_4^{3+}$, $[M–3(BF_4^–)]^{3+}$, 346.4554); Elemental analysis (%): C, 36.59; H, 4.99; N, 12.09 (calcd. for $C_{42}H_{66}N_{12}Pd_2B_4F_{16}$•1.5$CH_2Cl_2$ (%): C, 36.63; H, 4.88; N, 11.78).

Note that complex **4** crystalized with 1.5 molecules of dichloromethane used as a crystallization solvent. Existence of dichloromethane was also confirmed by the NMR and X-ray analyses. The averaged formula was determined by elemental analysis.

Synthesis of complex 5



In a similar fashion to the synthesis of complex **3**, a solution of ligand **1** (100 mg, 406 μmol) and $Pd(CH_3CN)_4(BF_4)_2$ (721 mg, 1.62 mmol) in acetonitrile (6.8 mL) was stirred at 60 ºC for 1 h. After cooling the solution, pale yellow crystals formed in the flask were collected by filtration. The crystals were washed with acetonitrile (3.0 mL) and dried on a funnel to give complex **5** (181 mg) in 60% yield.

^{1}H NMR (400 MHz, CD_3CN, 298 K): δ 4.12 (m, 4H, ethylene), 3.25 (m, 4H, ethylene), 2.86 (s, 12H, terminal methyl), 1.96 (s, 12H, coordinated acetonitrile), 1.50 (s, 12H, dimethylmethylene), 1.46 (s, 12H, dimethylmethylene); ^{13}C NMR (100 MHz, CD_3CN, 298 K): δ 199.6, 196.5, 126.7, 67.1, 23.8, 23.5, 19.2, 16.8; HR-ESI-TOF MS: *m/z* = 412.0670 (calcd for $C_{36}H_{56}N_{12}$ $Pd_3B_3F_{12}^{3+}$, $[M–3(BF_4^-)]^{3+}$, 412.0665); Elemental analysis (%): C, 29.49; H, 3.66; N, 11.79 (calcd. for $C_{36}H_{56}N_{12}Pd_3B_6F_{24}$·$CH_3CN$ (%): C, 29.67; H, 3.87; N, 11.84). The signal intensity for coordinated acetonitrile at 1.96 ppm was gradually decreased because of slow exchange with NMR solvent (CD_3CN). Due to spectral overlap and ligand exchange with CD_3CN (that causes septet signal) during overnight measurement, the methyl carbon signal for complex **5** was not observed. Attempts to measure ^{13}C NMR spectrum of **5** in other conventional solvents were not successful because of low solubility.

ESI-TOF mass analysis

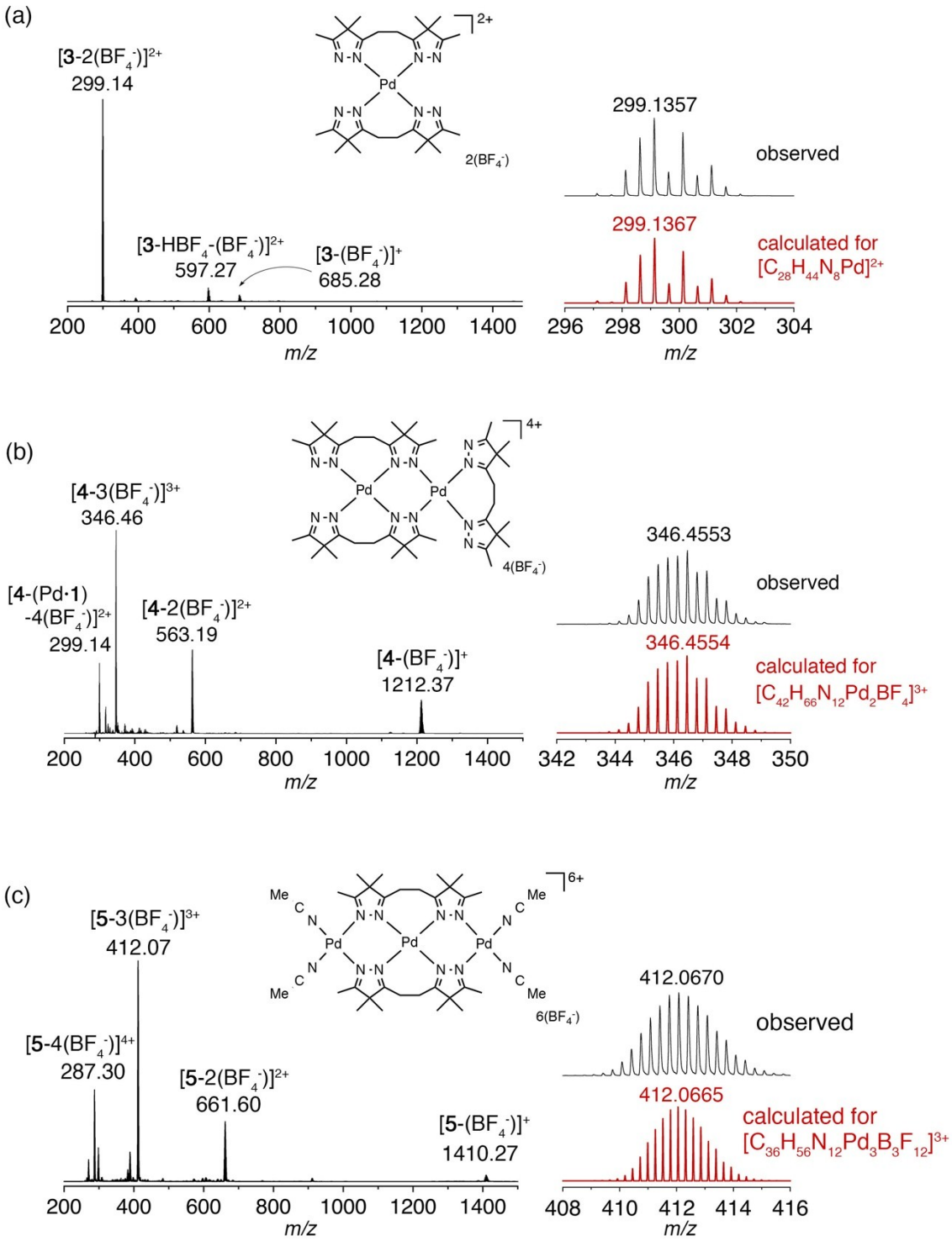


Figure S1. High-resolution ESI-TOF mass spectra of acetonitrile solutions of complexes (a) **3**, (b) **4** and (c) **5**.

NMR analysis

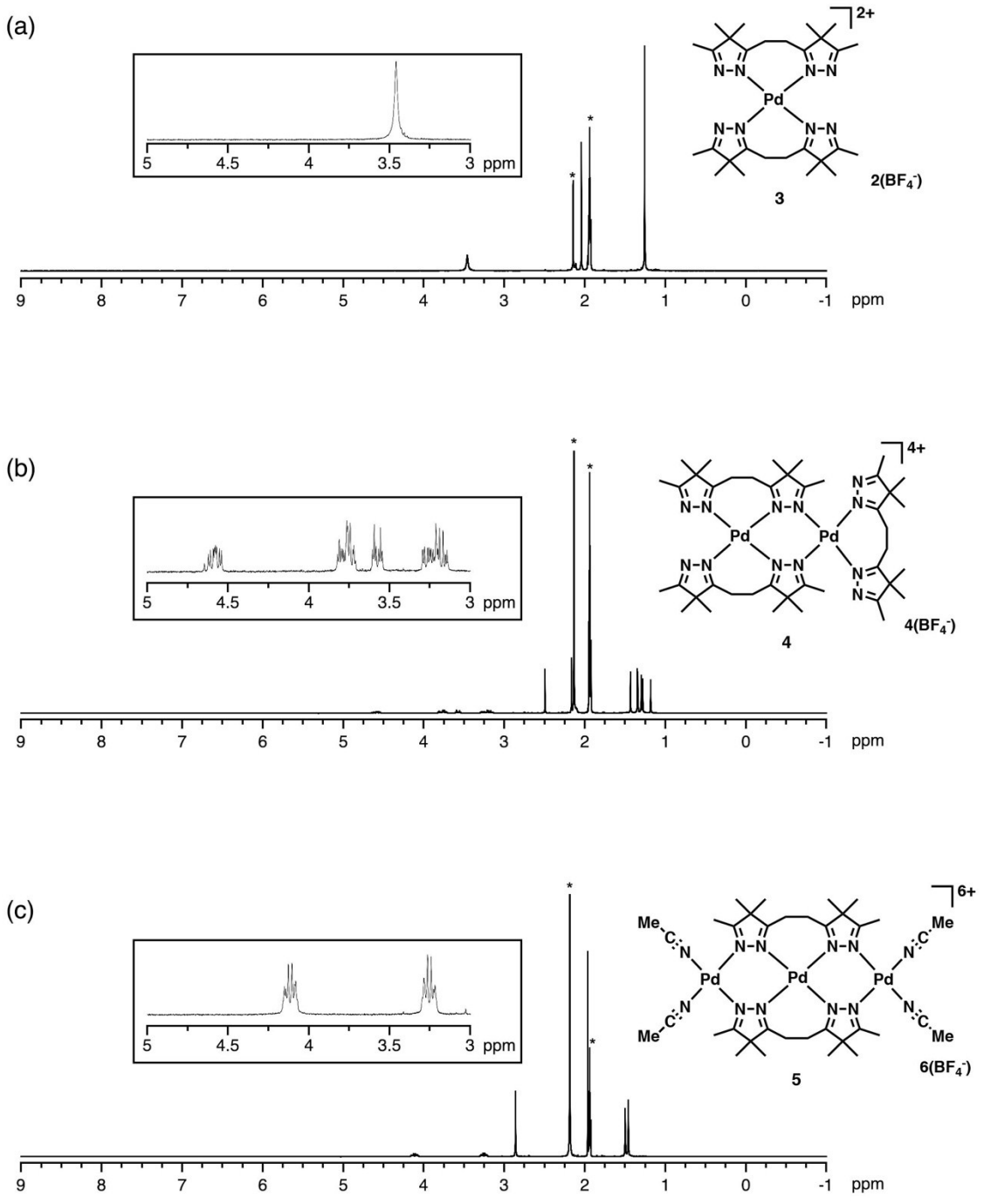


Figure S2. ^{1}H NMR (400 MHz) spectra of complexes (a) **3**, (b) **4**, and (c) **5** in acetonitrile-d_3. Insets show the magnified spectra at the ethylene proton region. Asterisks denote solvent (1.94 ppm) and water (2.13 ppm) signals.

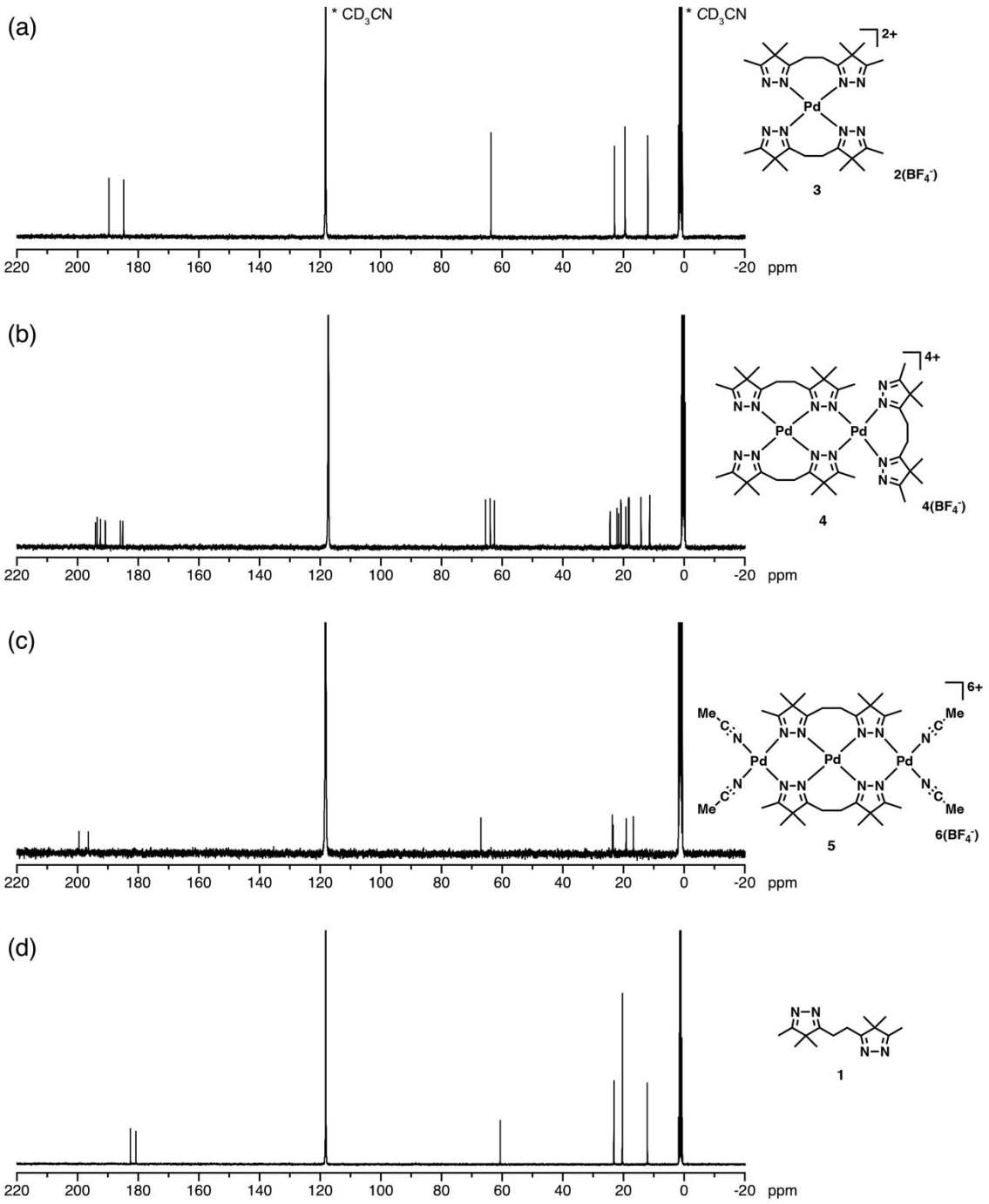


Figure S3. Comparison of the ^{13}C NMR spectra of complexes (a) **3**, (b) **4**, and (c) **5** with (d) ligand **1** in CD_3CN.

Titration analysis

To a 60 mM solution of ligand **1** in CD_3CN, $Pd(CH_3CN)_4(BF_4)_2$ was added in small portions. On each addition, the solution was heated to 60 ºC for 1 h and then ^1H NMR spectrum was measured at room temperature.

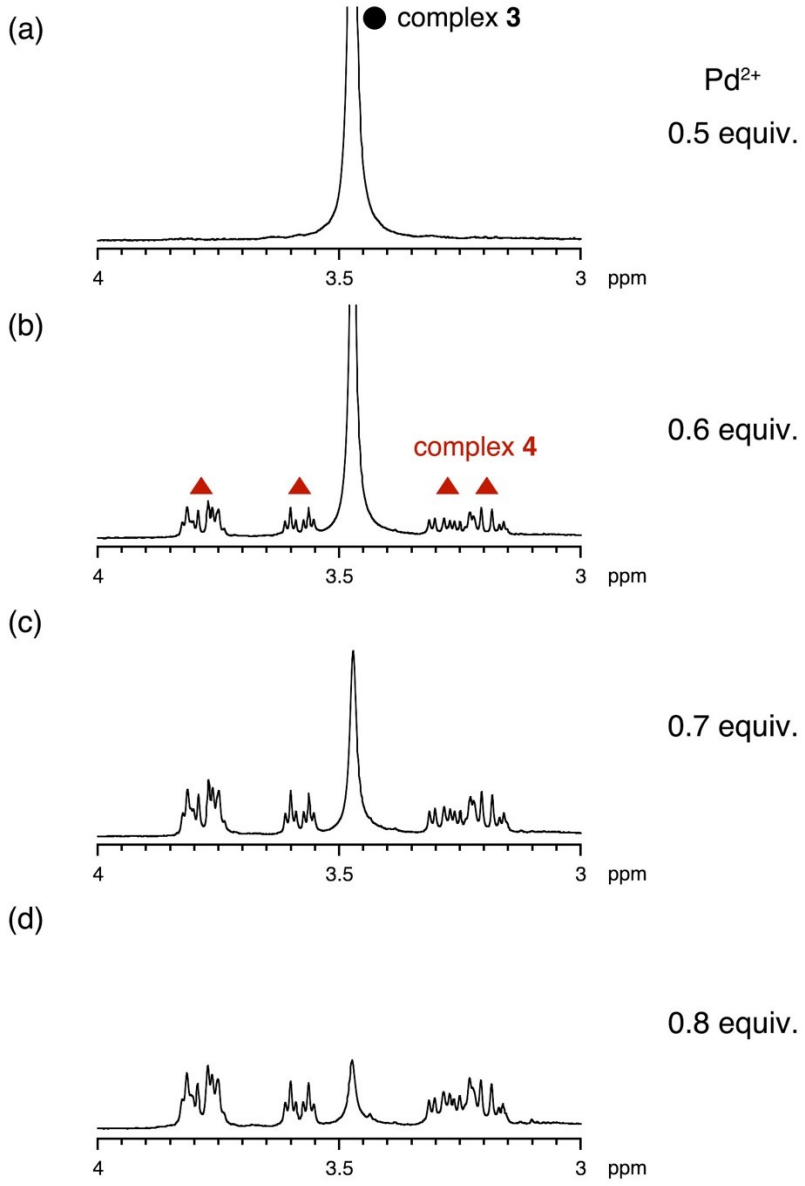


Figure S4. ^1H NMR spectra for the ethylene proton region in the presence of (a) 0.5, (b) 0.6, (c) 0.7, and (d) 0.8 equivalents of palladium ion to ligand **1**.

Conformation analysis for complex 4

Spectral simulation was carried out for the diastereotopically observed four protons of the ethylene bridge of ligand A in complex **4** (600 MHz; see Figure S2(b)) using following parameters.

	δ (ppm)	$J_{1\text{-}x}$	$J_{2\text{-}x}$	$J_{3\text{-}x}$
Proton 1	4.58	–	–	–
Proton 2	3.79	4.8	–	–
Proton 3	3.58	15.0	4.5	–
Proton 4	3.25	12.1	21.0	4.6

Line width for the simulation: 2.0 Hz

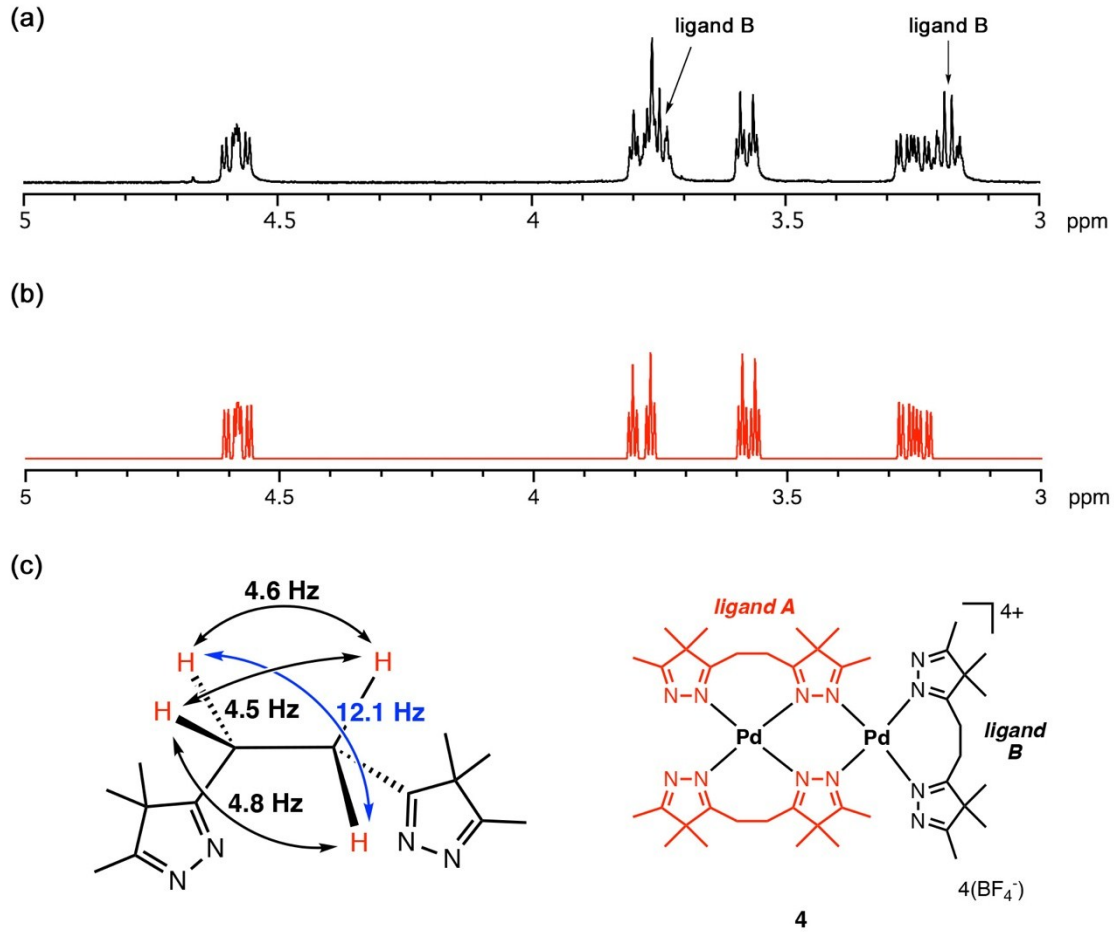


Figure S5. (a) Observed and (b) simulated spectra of the ethylene proton signals for ligand A of complex **4**. (c) A gauche conformation that matches with the vicinal coupling correlation of ligand A.[5]

Single crystal X-ray diffraction analysis

Crystallographic data for complex 3

Single crystals of complex **3** for X-ray analysis were grown by slow evaporation of the solvent of an acetonitrile solution of **3** (30 mM) over 5 d at room temperature.

$[(C_{28}H_{44}N_8Pd)\bullet(BF_4)_2]$, M = 772.73, crystal size: 0.20 × 0.20 × 0.08 mm^3, Triclinic, space group P-1, a = 6.5374(2) Å, b = 12.2580(3) Å, c = 21.5616(5) Å, α = 88.574(2)º, β = 85.328(2)º, γ = 85.018(2)º , V = 1715.33(8) Å^3 , Z = 2, T = 123(2) K, μ = 0.617 mm^{-1}, D_{calc} = 1.496 g/cm^3, 2.548º ≤ θ ≤ 29.497º, 6594 unique reflections out of 7871 with $I > 2\sigma(I)$, GOF = 1.045, R_1 = 0.0318 and wR_2 = 0.0827 for all data. CCDC deposit number: 1875329.

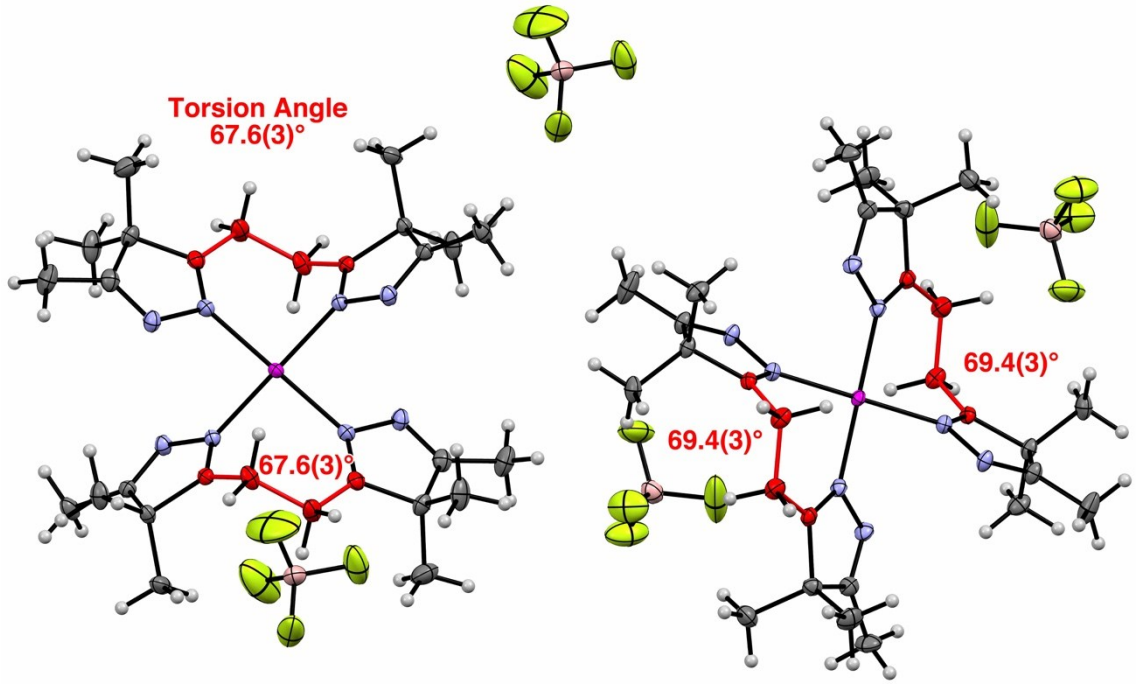


Figure S6. Two crystallographically inequivalent molecules of complex **3** observed in the unit cell. The torsion angle of each ethylene unit is represented in red.

Crystallographic data for complex 4

Single crystals of complex **4** for X-ray analysis were grown by vapor diffusion of dichloromethane into a reaction solution.

$[(C_{42}H_{66}N_{12}Pd_2)\bullet(BF_4)_4\bullet 2.616(CH_2Cl_2)\ \bullet 0.692O]$, M = 755.27, crystal size: 0.20 × 0.20 × 0.13 mm^3, Orthorhombic, space group *Ama*2, a = 25.6757(6) Å, b = 21.3064(6) Å, c = 11.7797(3) Å, V = 6444.2(3) Å^3 , Z = 8, T = 123(2) K, μ = 0.839 mm^{-1}, D_{calc} = 1.557 g/cm^3, 1.912° ≤ θ ≤ 27.481°, 7069 unique reflections out of 7515 with $I > 2\sigma(I)$, GOF = 1.118, R_1 = 0.0561 and wR_2 = 0.1423 for all data. CCDC deposit number: 1875330.

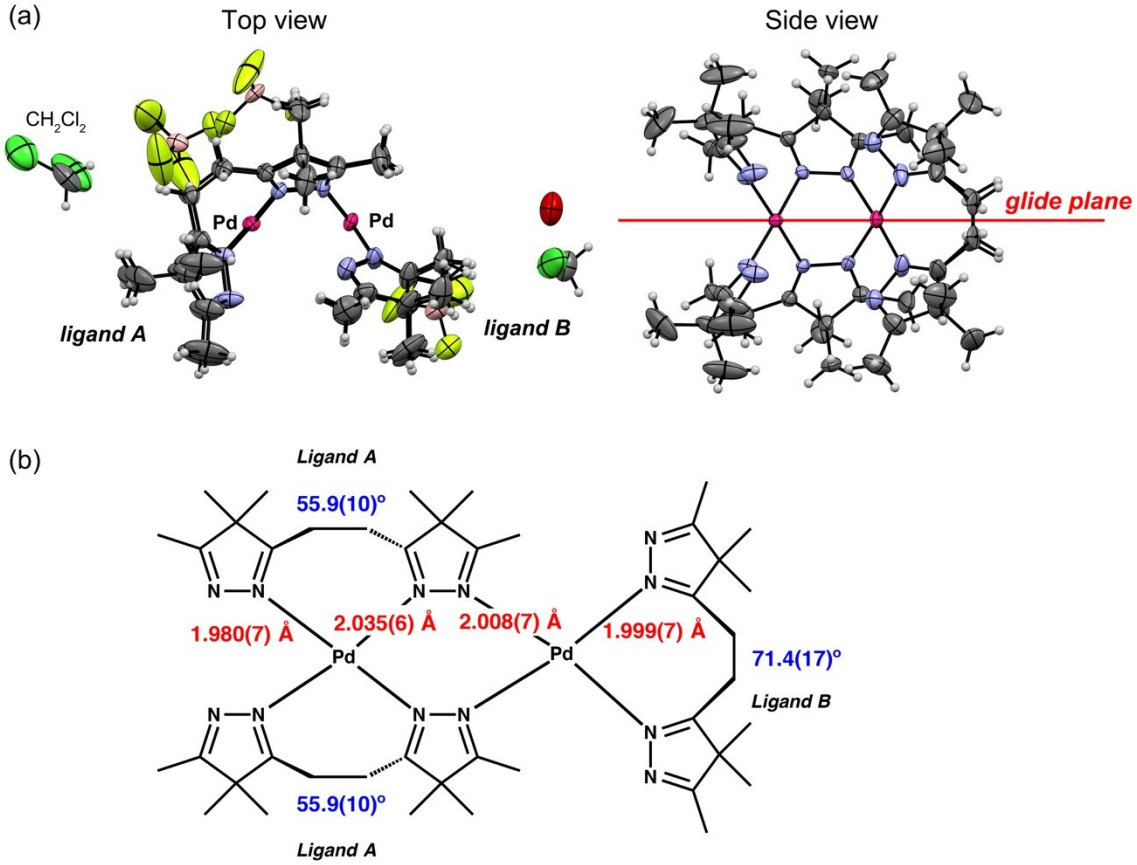


Figure S7. (a) Top and side views of the crystal structure of complex **4**. Two palladium ions are on the glide plane. The ethylene units for ligand B were solved using a disorder model. (b) Bond lengths for Pd–N (red) and torsion angles for the ethylene bridge (blue).

Crystallographic data for complex 5

Large-sized single crystals were obtained during the synthesis of complex **5** without stirring the solution.

$[(C_{36}H_{56}N_{12}Pd_3)\bullet(BF_4)_6\bullet 2(CH_3CN)]$, M = 789.55, crystal size: 0.17 × 0.14 × 0.06 mm^3, Monoclinic, space group $P2_1/m$, a = 11.60860(10) Å, b = 21.3061(2) Å, c = 12.43950(10) Å, β = 102.9090(10)º, V = 2998.95(5) Å^3 , Z = 4, T = 123(2) K, μ = 8.260 mm^{-1}, D_{calc} = 1.749 g/cm^3, 3.645º ≤ θ ≤ 74.020º, 5930 unique reflections out of 6091 with $I > 2\sigma(I)$, GOF = 1.086, R_1 = 0.0364 and wR_2 = 0.0997 for all data. CCDC deposit number: 1875331.

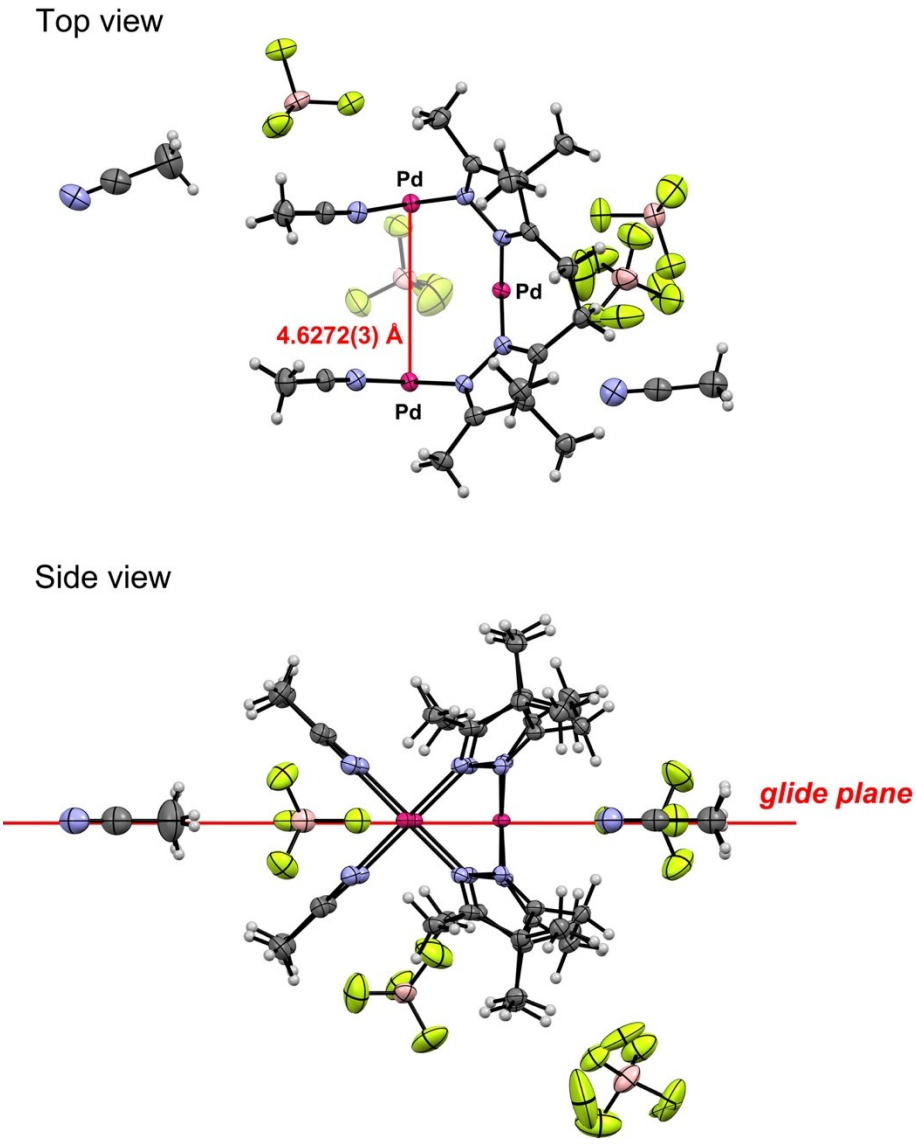
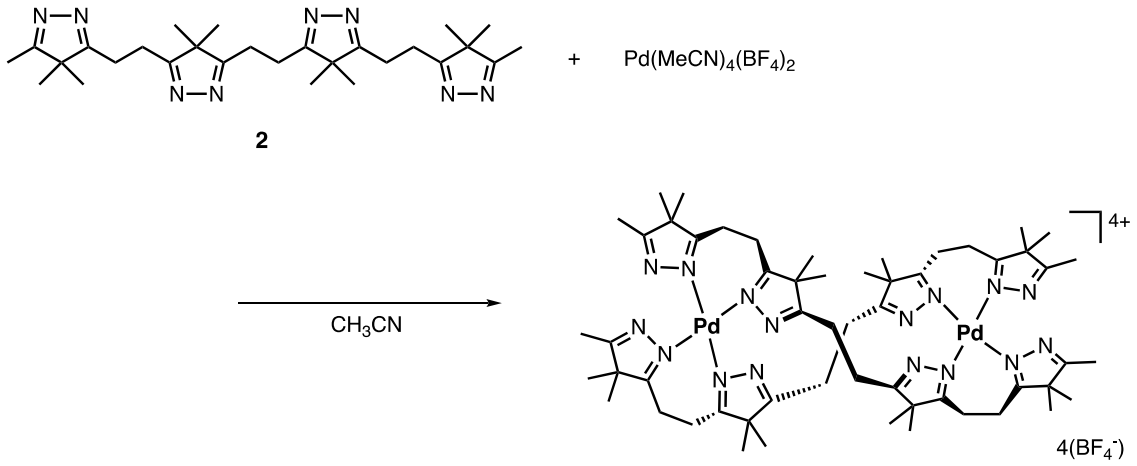


Figure S8. Top and side views of the crystal structure of complex **5**.

Synthesis of complex 6



In a 20 mL round bottomed flask equipped with a reflux condenser, ligand **2** (60.0 mg, 122 μmol) and $Pd(CH_3CN)_4(BF_4)_2$ (54.3 mg, 122 μmol) were dissolved in acetonitrile (2.0 mL). The solution was stirred at reflux for 24 h. After the solution was cooled to room temperature, the product was precipitated out from the solution by slow addition of ethyl acetate (4.0 mL). The precipitate was collected by suction filtration, washed with 2.0 mL of ethyl acetate, and air-dried on a funnel to give complex **6** (61.7 mg) in 66% yield.

^{1}H NMR (400 MHz, CD_3CN, 298 K): δ 3.96 (ddd, J = 15.9, 11.3, 4.2 Hz, 4H, terminal ethylene), 3.67 (ddd, J = 19.5, 6.2, 4.2 Hz, 4H, terminal ethylene), 3.34 (ddd, J = 15.9, 6.2, 4.1 Hz, 4H, terminal ethylene), 3.07 (overlapped ddd, 4H, terminal ethylene), 2.98 (m, 2H, central ethylene), 2.74 (m, 2H, central ethylene), 2.01 (s, 12H, terminal methyl), 1.26 (s, 12H, dimethylmethylene), 1.25 (s, 12H, dimethylmethylene), 1.24 (s, 12H, dimethylmethylene), 1.19 (s, 12H, dimethylmethylene); ^{13}C NMR (100 MHz, CD_3CN, 298 K): δ190.5, 189.1, 187.9, 184.7, 64.0, 63.4, 24.0, 22.5, 22.5, 21.3, 20.6, 19.0, 11.9; HR-ESI-TOF MS: m/z = 298.6278 (calcd. for $C_{56}H_{84}N_{16}Pd_2^{4+}$, $[M–4(BF_4^-)]^{4+}$, 298.6290); Elemental analysis (%): C, 42.27; H, 5.39; N, 13.86 (calcd. for $C_{56}H_{84}N_{16}Pd_2B_4F_{16}•3H_2O$ (%): C, 42.16; H, 5.69; N, 14.05)

Characterization of complex 6

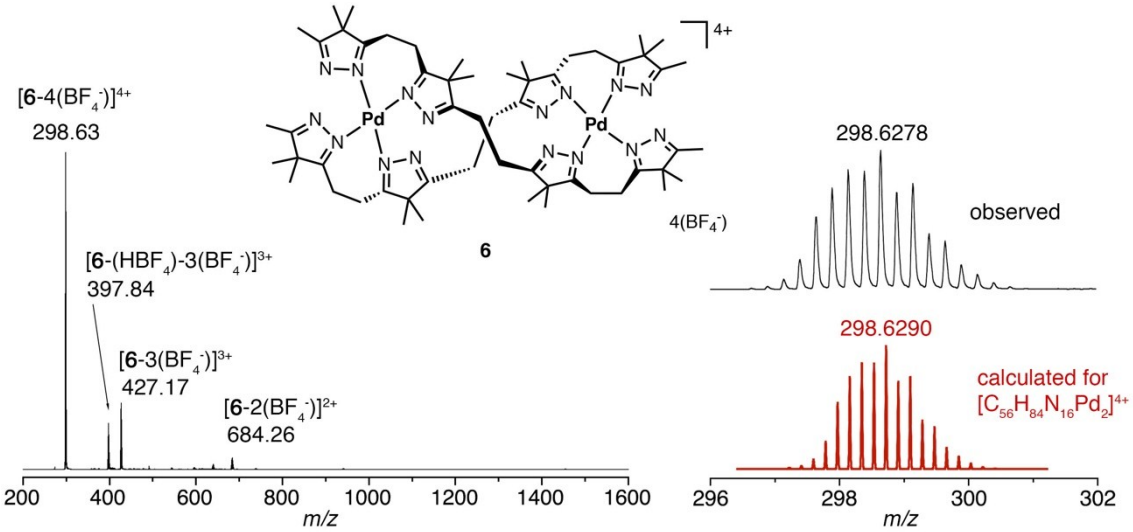


Figure S9. High-resolution ESI-TOF mass spectrum of complex **6**.

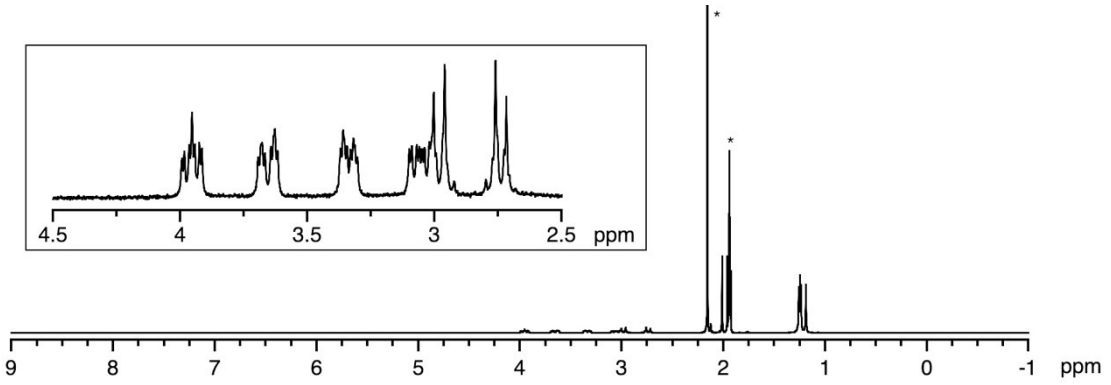


Figure S10. ^{1}H NMR spectrum of **6** in acetonitrile-d_3. Inset shows the magnified spectra at the ethylene proton region. Asterisks denote solvent and water signals.

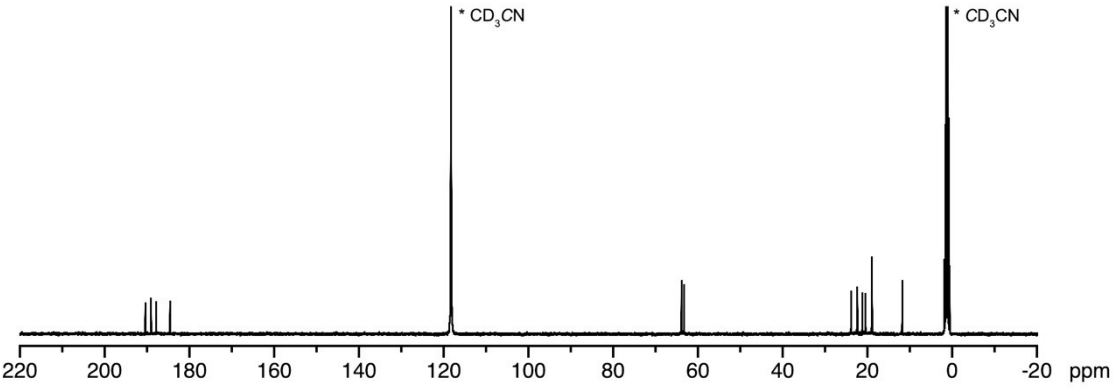


Figure S11. ^{13}C NMR spectrum of **6** in acetonitrile-d_3.

Conformation analysis for complex 6

In a similar manner to complex **4**, conformations of the terminal ethylene bridges in complex **6** were analyzed by NMR simulation (400 MHz) of four diastereotopic protons. Parameters used for the simulation are shown below.

	δ (ppm)	$J_{1\text{-}x}$	$J_{2\text{-}x}$	$J_{3\text{-}x}$
Proton 1	3.96	–	–	–
Proton 2	3.67	4.2	–	–
Proton 3	3.34	15.9	6.2	–
Proton 4	3.07	11.3	19.5	4.1

Line width for the simulation: 2.0 Hz

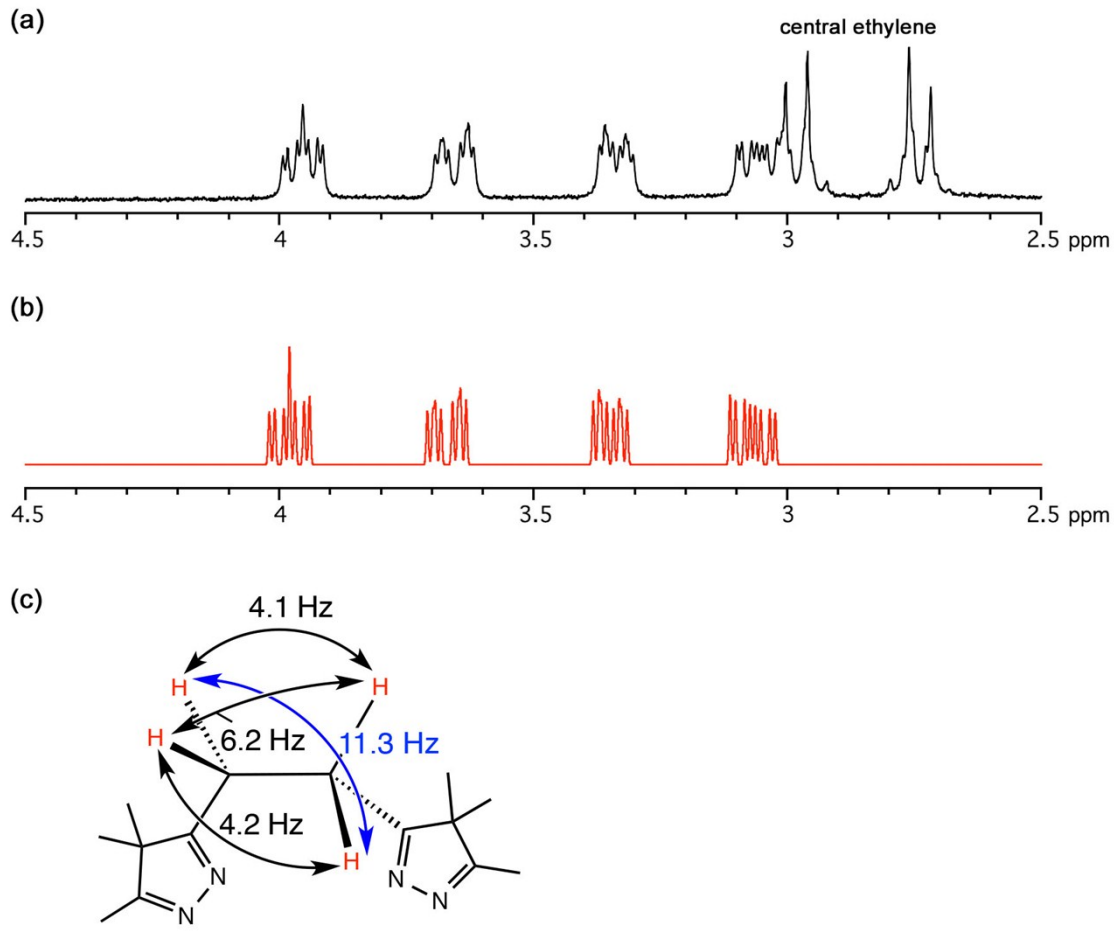


Figure S12. (a) Observed and (b) simulated spectra of the ethylene proton signals (shown in red) of complex **4**. (c) A gauche conformation that matches with the vicinal coupling correlation of the terminal ethylene bridge.[5]

Crystallographic data for complex 6

Single crystals for X-ray analysis were grown from an acetonitrile solution of **6** via vapor diffusion of ethyl acetate using a 5 mL vial.

$[(C_{56}H_{84}N_{16}Pd_2)\bullet(BF_4)_4\bullet 2.574(H_2O)]$, M = 1587.79, crystal size: 0.27 × 0.20 × 0.07 mm^3, Monoclinic, space group $P2_1/c$, a = 12.9729(3) Å, b = 14.3355(3) Å, c = 37.3886(7) Å, β = 91.940(2)º, V = 6949.3(3) $Å^3$, Z = 4, T = 123(2) K, μ = 0.614 mm^{-1} , D_{calc} = 1.518 g/cm^3, 2.406º ≤ θ ≤ 29.541º, 14071 unique reflections out of 16533 with $I > 2\sigma(I)$, GOF = 1.130, R_1 = 0.0472 and wR_2 = 0.0971 for all data. CCDC deposit number: 1875332.

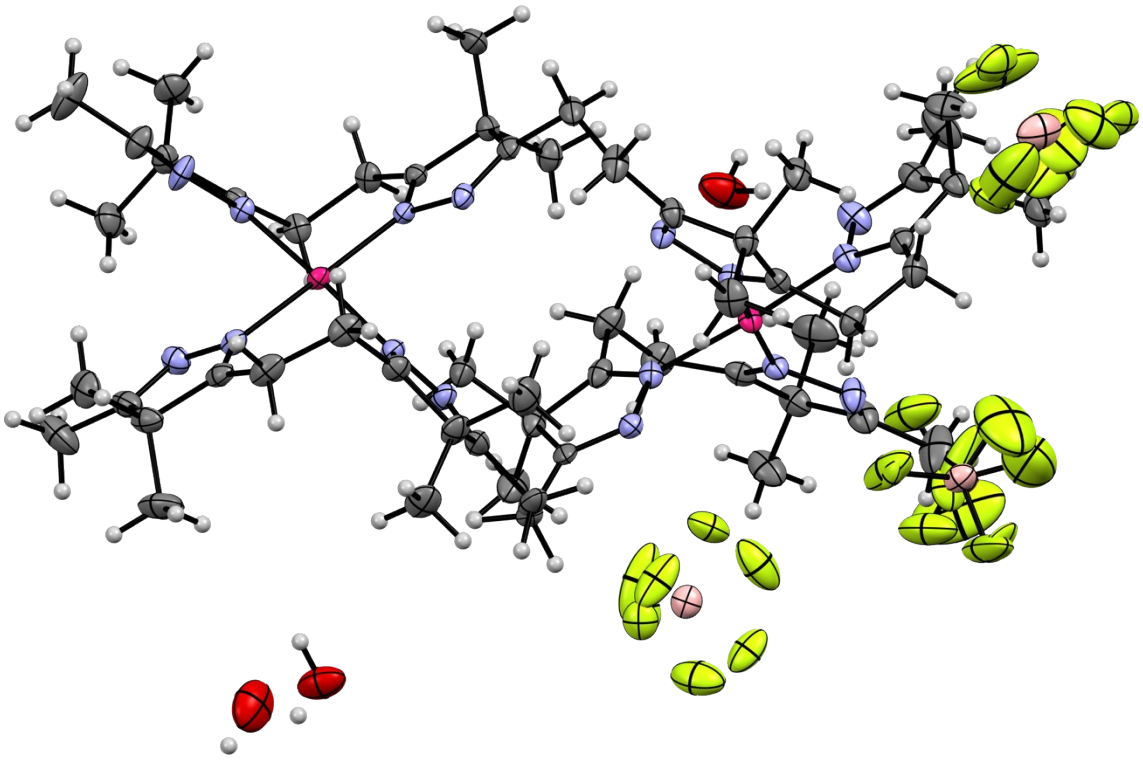


Figure S13. The asymmetric unit for the crystal structure of complex **6**.

III. References

[1] A. M. Castillo, L. Patiny, J. Wist, *J. Magn. Reson.*, 2011, **209**, 123-130.

[2] G. M. Sheldrick, *Acta Crystallogr. Sect. A*, 2015, **71**, 3-8.

[3] Sheldrick, G. M.; *Acta Crystallogr. Sect. C*, 2015, **71**,3-8.

[4] M. Uesaka, Y. Saito, S. Yoshioka, Y. Domoto, M. Fujita, Y. Inokuma, *Communications Chemistry*, 2018, **1**, article number 23.

[5] M. Karplus, *J. Am. Chem. Soc.*, 1963, **85**, 2870-2871.