Supplementary Information for

Deuteration enhances catalyst lifetime in palladium-catalysed alcohol oxidation

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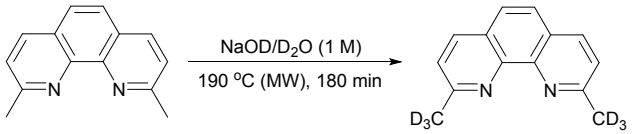
General Information

All solvents used for syntheses, extractions and filtrations were of commercial grade, and used without further purification. Reagents were purchased from Sigma-Aldrich, TCI and Merck, and used without further purification.

Microwave assisted syntheses were conducted in a CEM Discover Explorer Hybrid microwave.
^{1}H-, ^{13}C- and ^{19}F-NMR spectra were recorded on a Varian AMX400 (400 MHz, 101 MHz and 376 MHz respectively) using $CDCl_3$, CD_3CN or DMSO-d_6 as solvent. Chemical shift values are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: δ 7.26 for ^{1}H, δ 77.3 for ^{13}C; CD_3CN: δ 1.94 for ^{1}H, δ 118.3 for ^{13}C; DMSO-d_6: δ 2.50 for ^{1}H, δ 39.5 for ^{13}C). Data are reported as follows: chemical shifts (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants J (Hz), and integration.
GC-MS measurements were performed with an HP 6890 series gas chromatography system equipped with a HP 5973 mass sensitive detector. GC measurements were made using a Shimadzu GC 2014 gas chromatograph system bearing a AT5 column (Grace Alltech) and FID detection.
High Resolution Mass Spectrometry (HR-MS) measurements were performed with a Thermo Scientific LTQ OribitrapXL spectrometer.

General procedure for synthesis of ligand 2,9-bis(methyl-d_3)-1,10-phenanthroline (9-d_6)



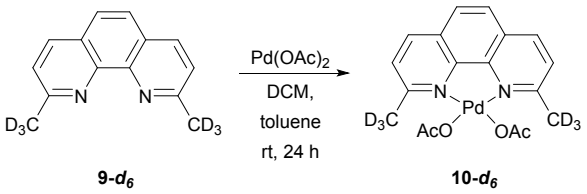
9 **9-d_6**

Neocuproine (**9**, 2.4 mmol, 500 mg) and 1 M NaOD/D_2O (15 mL) were placed in a 40 mL pressure-resistant glass ampoule. The ampoule was sealed with a silicone cap and placed into a microwave reactor and subjected to continuous irradiation with stirring at 190 °C for 180 min. The reaction mixture was then allowed to cool to room temperature, followed by filtration of the produced white precipitation by vacuum filtration. The separated product **9-d_6** was washed with water several times and dried

under vacuum. Yield: 470 mg (2.19 mmol, 92%). The degree of deuteration was 99%; determined by ^{1}H-NMR using the residual solvent peak ($CDCl_3$) as internal standard.

General procedures for synthesis of complexes, 10-*d*$_6$, 11-*d*$_6$

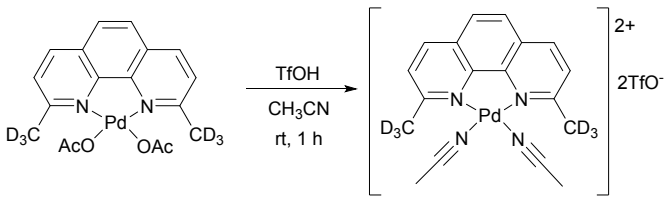
- **Synthesis of (2,9-bis(methyl-*d*$_3$)-1,10-phenanthroline)Pd(OAc)$_2$ (10-*d*$_6$)**



9-*d*$_6$ **10-*d*$_6$**

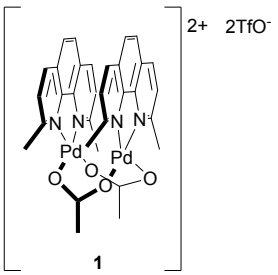
A solution of 2,9-bis(methyl-*d*$_3$)-1,10-phenanthroline (**9-*d*$_6$**) (1.89 mmol, 400 mg) in anhydrous CH_2Cl_2 (7 mL) was added to a solution of $Pd(OAc)_2$ (1.72 mmol, 385 mg) in anhydrous toluene (35 mL) at room temperature under nitrogen. The mixture was stirred overnight and pentane was added to precipitate the complex. Solids were filtered off, washed with acetone and dried under vacuum to give **10-*d*$_6$** as a dark yellow solid (660 mg, 1.5 mmol, 87% yield).

Synthesis of (2,9-bis(methyl-*d*$_3$)-1,10-phenanthroline)Pd(MeCN)$_2$(OTf)$_2$ (11-*d*$_6$)



10-*d*$_6$ **11-*d*$_6$**

To a slurry of **10-*d*$_6$** (2.5 mmol, 1.1 g) in anhydrous acetonitrile (5 mL) was added a solution of triflic acid (6.2 mmol, 550 µL) in anhydrous acetonitrile (0.33 M, 19 mL) at room temperature under nitrogen. The mixture was stirred for 1 h and diethyl ether was added to precipitate the complex. Solids were filtered off and dried under vacuum to give **11-*d*$_6$** as a light yellow solid (1.62 g, 2.31 mmol, 93% yield).



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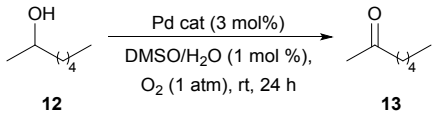
The complex [(neocuproine)Pd(OAc)]$_2$[OTf]$_2$ (**1**) was prepared and crystallized according to the literature procedure. [1]

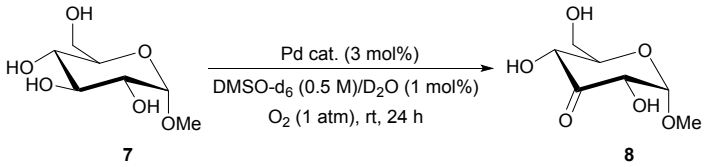
General protocol for aerobic oxidation of 2-heptanol (12)



To a 20 mL vial with magnetic stirrer were added **10-*d*$_6$** (26.32 mg, 0.06 mmol), **11-*d*$_6$** (42.06 mg, 0.06 mmol), DMSO (0.5 M, 4 mL) and H_2O (1 mol%, 10 µL). The mixture was vigorously stirred at room temperature until the Pd complexes had dissolved completely.

To two different 20 mL vials, equipped with magnetic stirrers, were added in each one Pd catalyst solution (2 mL, 3 mol%) and 2-heptanol (**12**) (142 µL, 1 mmol). The reaction mixtures were vigorously stirred at room temperature under a balloon of oxygen. During the reactions, aliquots were taken, quenched by dilution into ethyl acetate, and subjected to GC analysis to determine the conversion of **12**.

General protocol for aerobic oxidation of methyl-α-D-glucopyranoside (7)



To a 20 mL vial with magnetic stirrer were added **10-*d*$_6$** (32.91 mg, 0.075 mmol), **11-*d*$_6$** (52.58 mg, 0.075 mmol), DMSO-d_6 (0.5 M, 5 mL) and D_2O (1 mol%, 12 µL). The mixture was vigorously stirred at room temperature until the Pd complexes had dissolved completely.

To two different 20 mL vials, equipped with magnetic stirrers, were added in each one methyl-α-D-glucopyranoside (**7**) (243 mg, 1.25 mmol) and Pd catalyst solution (2.5 mL, 3 mol%). The reaction mixtures were vigorously stirred at room temperature under a balloon of oxygen. During the reactions, aliquots were taken, quenched by dilution into DMSO-d_6, and subjected to ^{1}H-NMR analysis to determine the conversion of **7**.

Determination of reaction progress

The reaction progress in the aerobic oxidation of both the substrates, 2-heptanol (**12**) and methyl-α-D-glucopyranoside (**7**), was determined using a ratiometric method, shown by the following equation:

$$\% \text{ conversion} = [\text{area}_{\text{substrate}} / (\text{area}_{\text{product}} + \text{area}_{\text{substrate}})] \times 100$$

This equation is valid because:

1) 2-heptanol (and methyl-α-D-glucopyranoside) is converted selectively to 2-heptanone (or methyl-α-D-ribo-hexapyranoside-3-ulose);

2) equimolar amounts of 2-heptanol and 2-heptanone produce the same FID response in GC-MS. In cases where the secondary alcohol and its corresponding ketone produce different detector responses, it is necessary to account for this using a response factor.

Reaction progress curves with indicated standard deviations

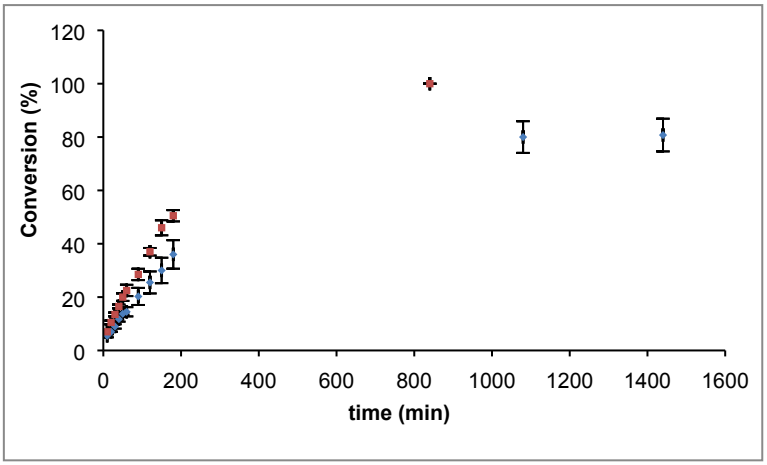


Figure S1 Reaction progress curves for the aerobic oxidation of 2-heptanol (**12**) with catalyst **1-*d*$_{12}$** in DMSO (♦) and in DMSO/H_2O (1 mol% with respect to DMSO) (■) at room temperature. Reactions were carried out in quadruplo and the mean conversion and the standard deviation are plotted.

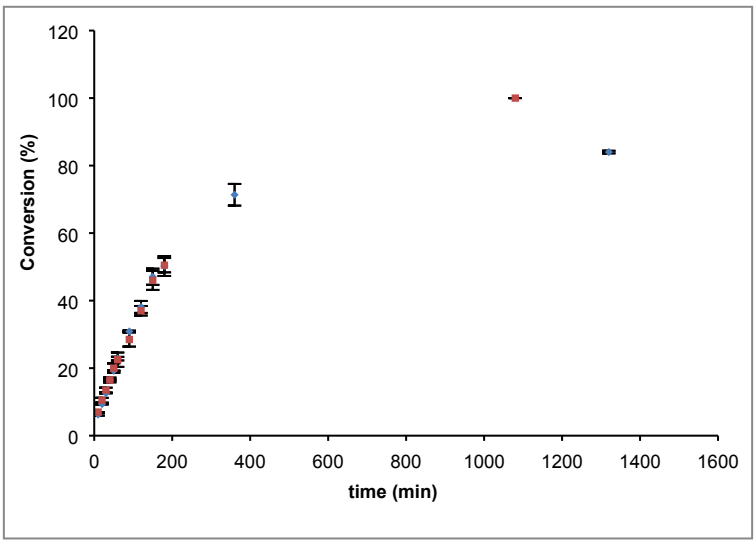


Figure S2 Reaction progress curves for the aerobic oxidation of 2-heptanol (**12**) with catalysts **1-*d*$_{12}$** (■) and **1** (♦) in DMSO/H_2O (1 mol% with respect to DMSO) at room temperature. Reactions were carried out in duplo and the mean conversion and the standard deviation are plotted.

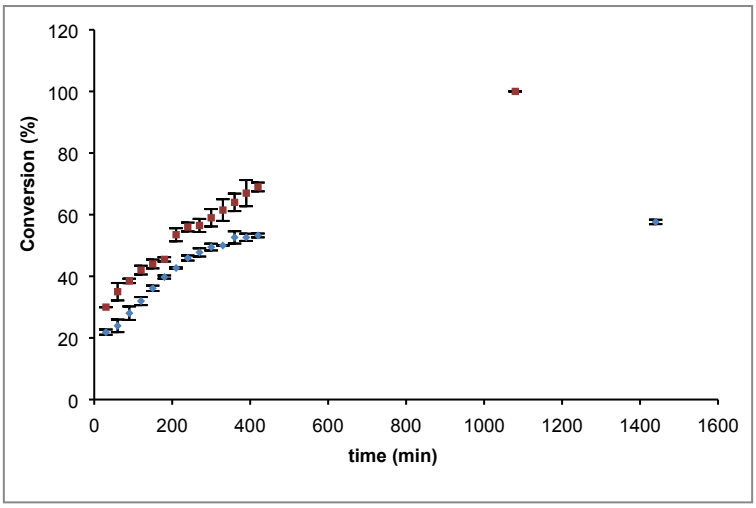


Figure S3 Reaction progress curves for the oxidation of glucopyranoside (**7**) with catalyst **1-*d*$_{12}$** (■) and **1** (♦) in DMSO-d_6/D_2O (1 mol% with respect to DMSO) at room temperature. Reactions have been carried out in duplo and the mean conversion is plotted.

Interpolation of reaction progress curves for determination of initial TOF

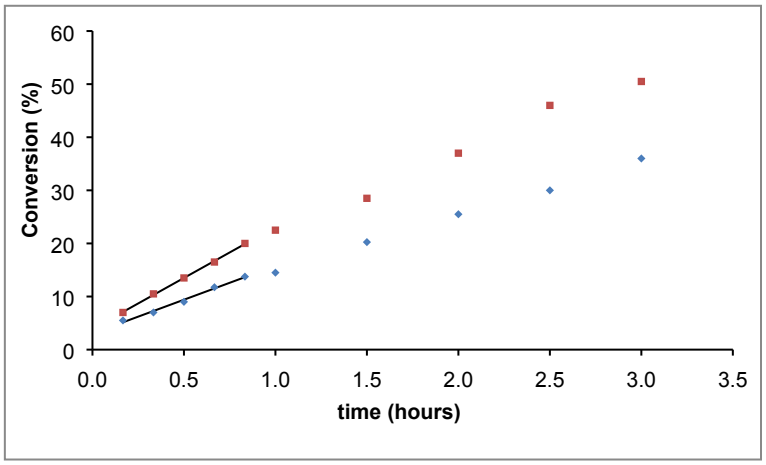


Figure S4 Interpolation of reaction progress curves for the aerobic oxidation of 2-heptanol (**12**) with catalyst **1-*d*$_{12}$** in DMSO (♦) and in DMSO/H_2O (1 mol%) (■) at room temperature.

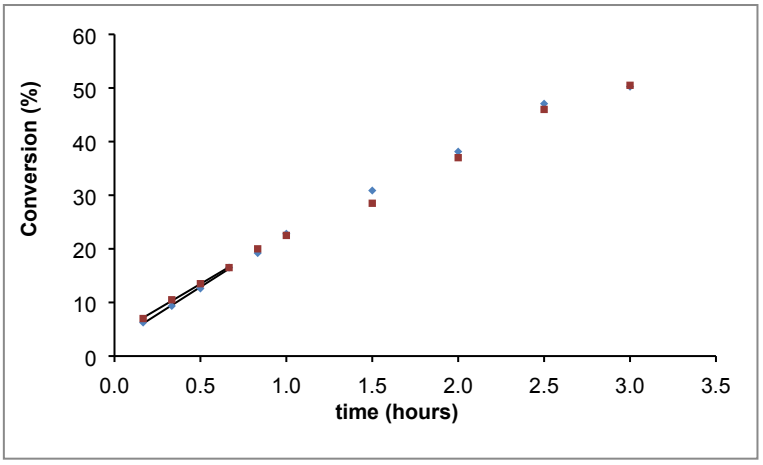


Figure S5 Interpolation of reaction progress curves for the aerobic oxidation of 2-heptanol (**12**) with catalysts **1-*d*$_{12}$** (■) and **1** (♦) in DMSO/H_2O (1 mol%) at room temperature.

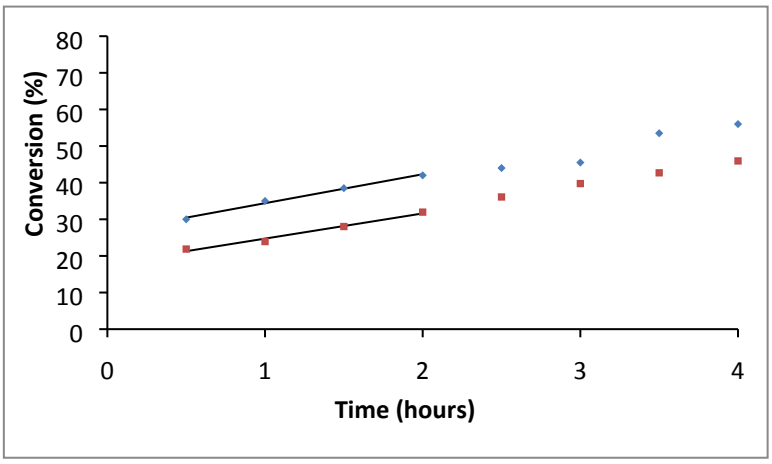
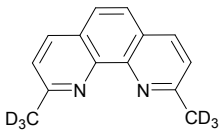


Figure S6 Interpolation of the reaction progress curves for the oxidation of glucopyranoside (**7**) with catalyst **1-*d*$_{12}$** (■) and **1** (♦) in DMSO-d_6/D_2O (1 mol%) at room temperature.

Characterization data of ligand (9-*d*$_6$)

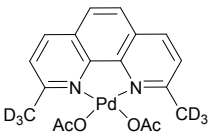
2,9-bis(methyl-*d*$_3$)-1,10-phenanthroline



Off-white solid; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.11 (d, *J* = 8.2 Hz, 2H), 7.69 (s, 2H), 7.48 (d, *J* = 8.2 Hz, 2H); **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 159.1, 145.2, 136.1, 126.7, 125.3, 123.3, 25.0; **HRMS (ESI+)** Calcd. for $C_{14}H_6D_6N_2$ ([M + H]$^+$): 215.145, found: 215.145 (100%); **elemental analysis** calculated (%) for $C_{14}H_6D_6N_2$ (214.30): C 78.47, H (corrected for deuterium) 2.82, N 13.07; found: C 78.58, H 2.81, N 13.31.

Characterization data of complexes 10-*d*$_6$, and 11-*d*$_6$

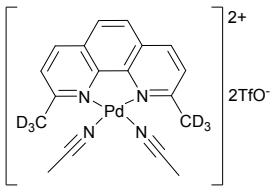
(2,9-bis(methyl-*d*$_3$)-1,10-phenanthroline)Pd(OAc)$_2$ (10-*d*$_6$)



Pale brown solid; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.37 (d, *J* = 8.4 Hz, 2H), 7.86 (s, 2H), 7.41 (d, *J* = 8.4 Hz, 2H), 2.05 (s, 6H, 2C*H*$_3$COO$^-$); **^{13}C NMR** (101

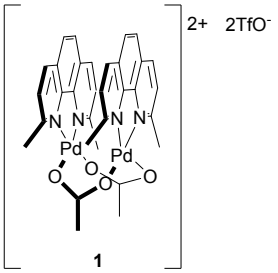
MHz, Chloroform-*d*) δ 178.56, 165.21, 147.26, 138.56, 127.98, 126.81, 126.48, 23.09; **HRMS (ESI+)** Calcd. for $C_{18}H_{12}D_6N_2O_4Pd$ ([M + H]$^+$): 439.075, found ([M - CH_3COO^- + H]$^+$): 379.054 (100%), ([M - $2CH_3COO^-$ + H]$^+$): 320.041 (28%); **elemental analysis** calculated (%) for $C_{18}H_{12}D_6N_2O_4Pd$ (438.81): C 49.27, H (corrected for deuterium) 2.76, N 6.48, found: C 49.57, H 3.08, N 6.89.

(2,9-bis(methyl-*d*$_3$)-1,10-phenanthroline)Pd(CH_3CN)$_2$(OTf)$_2$ (11-*d*$_6$)



Pale yellow solid; **^{1}H NMR** (400 MHz, Acetonitrile-*d*$_3$) δ 8.69 (d, *J* = 8.4 Hz, 2H), 8.08 (s, 2H), 7.78 (d, *J* = 8.4 Hz, 2H); **^{1}H NMR** (400 MHz, DMSO-*d*$_6$) δ 8.87 (d, *J* = 8.3 Hz, 1H), 8.79 (d, *J* = 8.4 Hz, 1H), 8.28 (s, 1H), 8.16 (s, 1H), 7.96 (d, *J* = 8.3 Hz, 1H), 7.89 (d, *J* = 8.3 Hz, 1H), 2.06 (s, 6H, 2C*H*$_3$CN); **^{13}C NMR** (101 MHz, DMSO-*d*$_6$) δ 164.75, 163.18, 144.95, 140.15, 128.88, 128.54, 127.47, 127.22, 127.07, 126.72, 125.54, 122.34, 119.13, 118.13, 115.93, 1.19; **^{19}F NMR** (376 MHz, Acetonitrile-*d*$_3$): δ -79.30 (s); **HRMS (ESI+)** Calcd. for $C_{20}H_{12}D_6F_6N_4O_6Pd^{2+}S_2$ ([M + H]$^+$): 701.006, found ([M - $2CH_3CN$ - $2CF_3SO_3^-$ + H]$^+$): 321.048 (100%), ([M - $CF_3SO_3^-$ - $2CH_3CN$]): 468.992 (34%); As acetonitrile slowly evaporated from the complex even at low temperature, a correct elemental analysis could not be obtained. This has been noted before, see ref 1.

[(2,9-Dimethyl-1,10-phenanthroline)Pd(*μ*-OAc)]$_2$(OTf)$_2$ (1)



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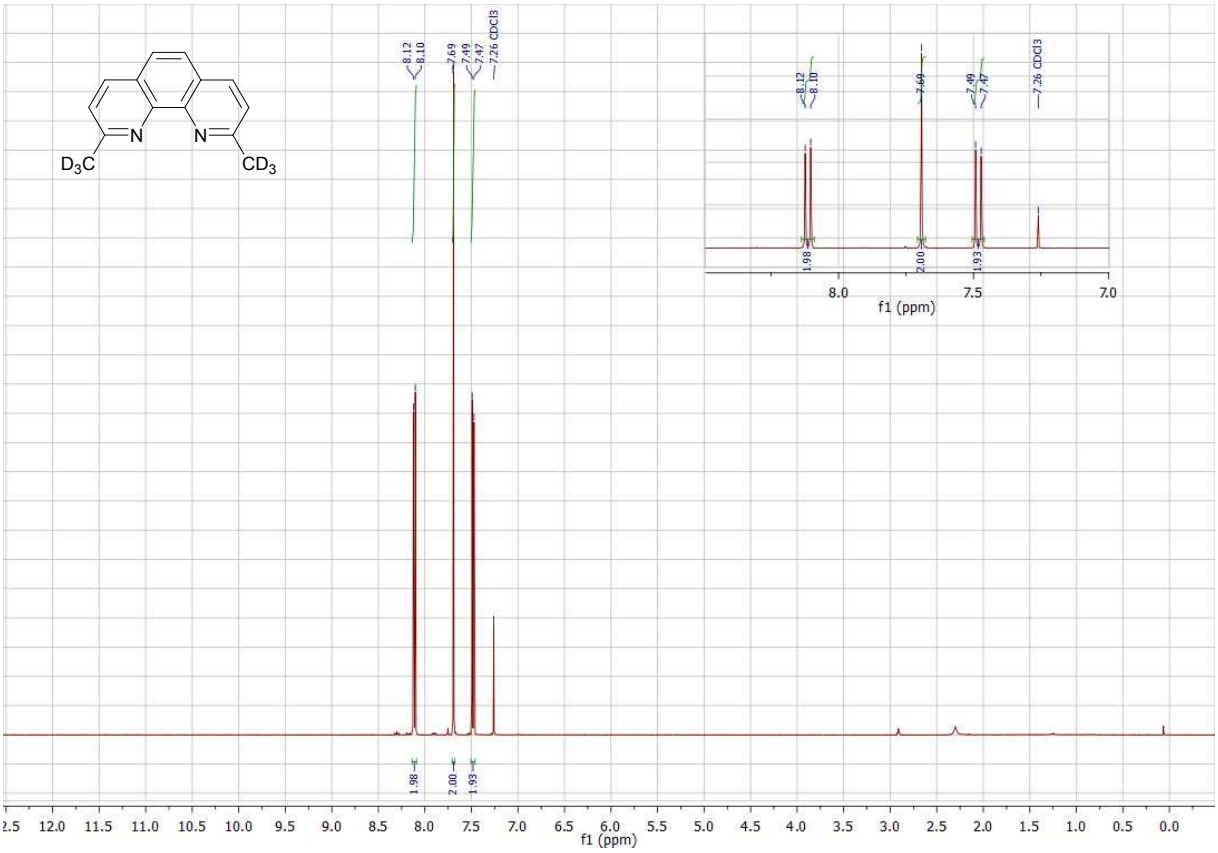
Characterization matches literature. Purity confirmed by element analysis.[1]

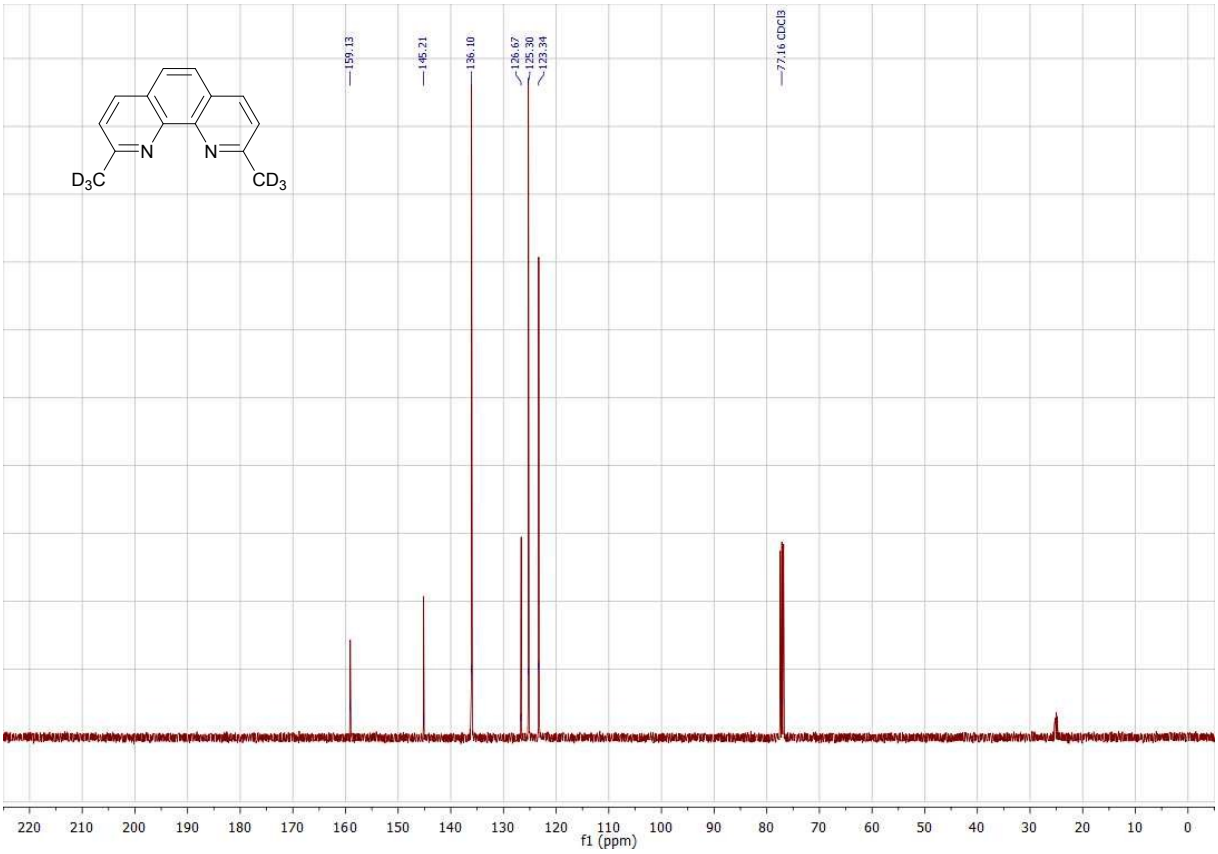
Elemental analysis calculated (%) for $C_{34}H_{30}F_6N_4O_{10}Pd_2S_2$ (1045.582): C 39.06, H 2.89, N 5.36, found: C 38.97, H 2.87, N 5.57

NMR spectra

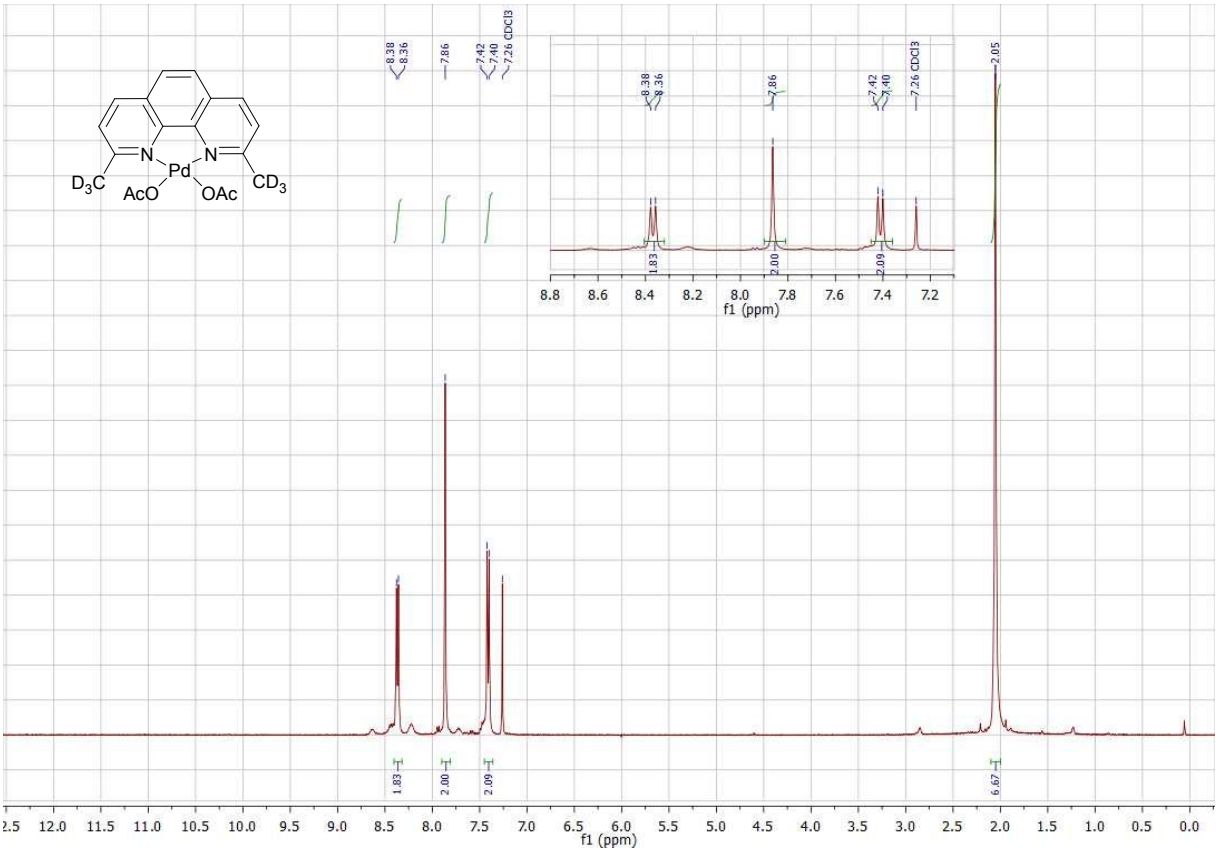
^{1}H NMR - 9-*d*$_6$ (400 MHz, Chloroform-*d*)



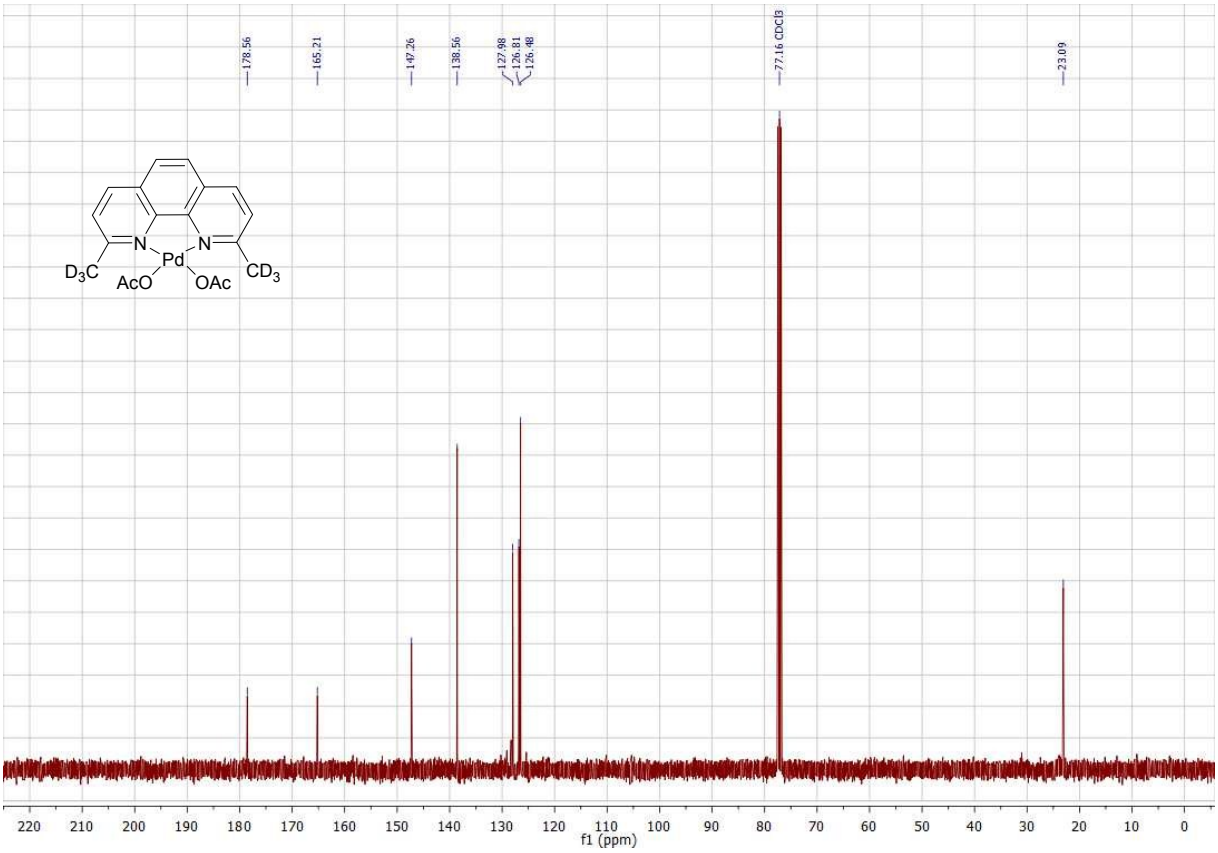
^{13}C NMR - 9-*d*$_6$ (101 MHz, Chloroform-*d*)



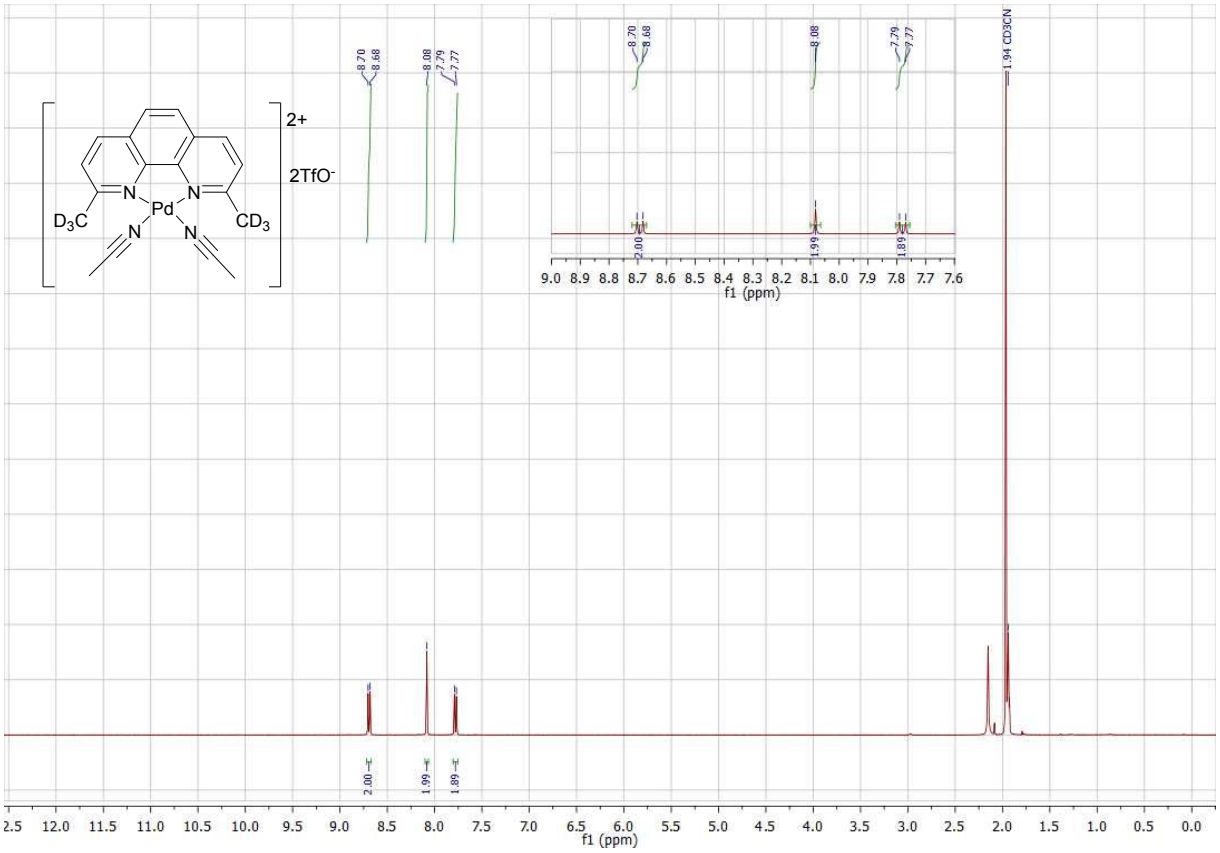
^{1}H NMR - 10-*d*$_6$ (400 MHz, Chloroform-*d*)



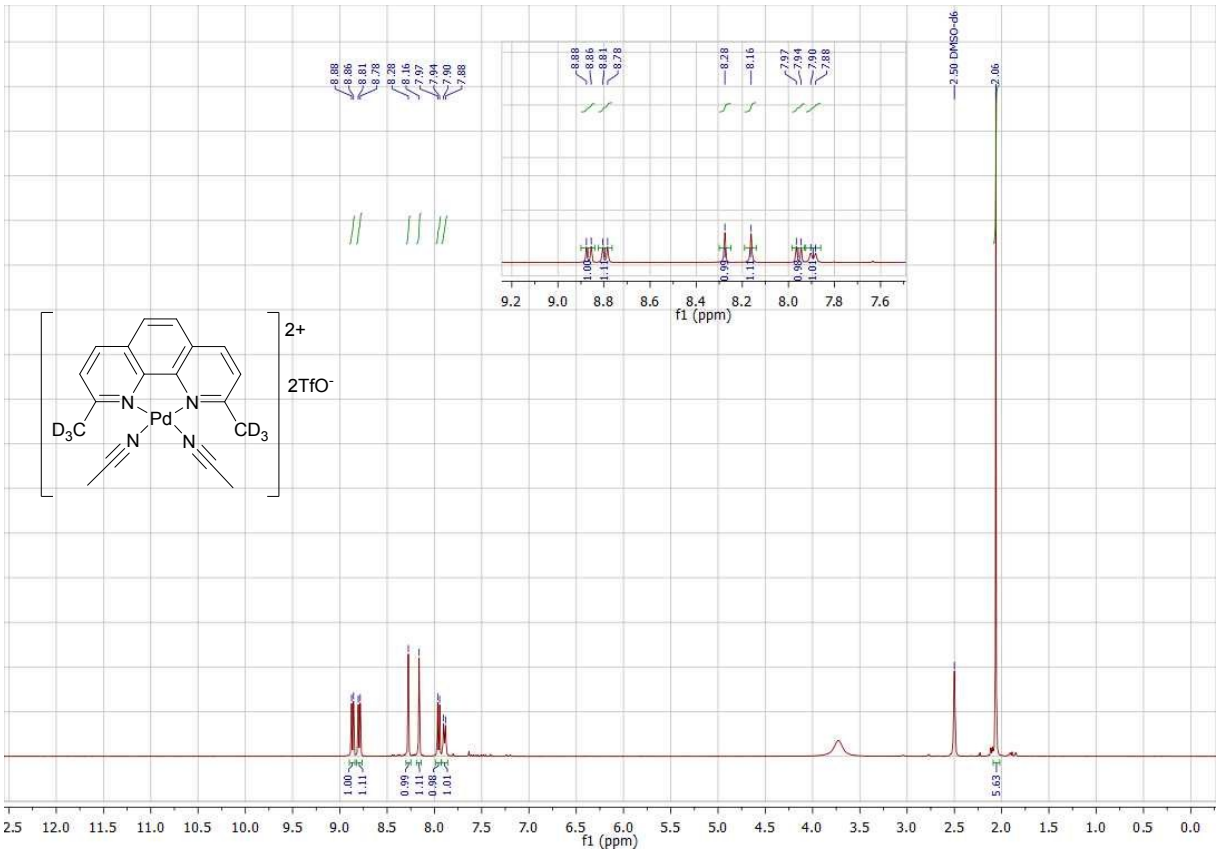
^{13}C NMR - 10-*d*$_6$ (101 MHz, Chloroform-*d*)



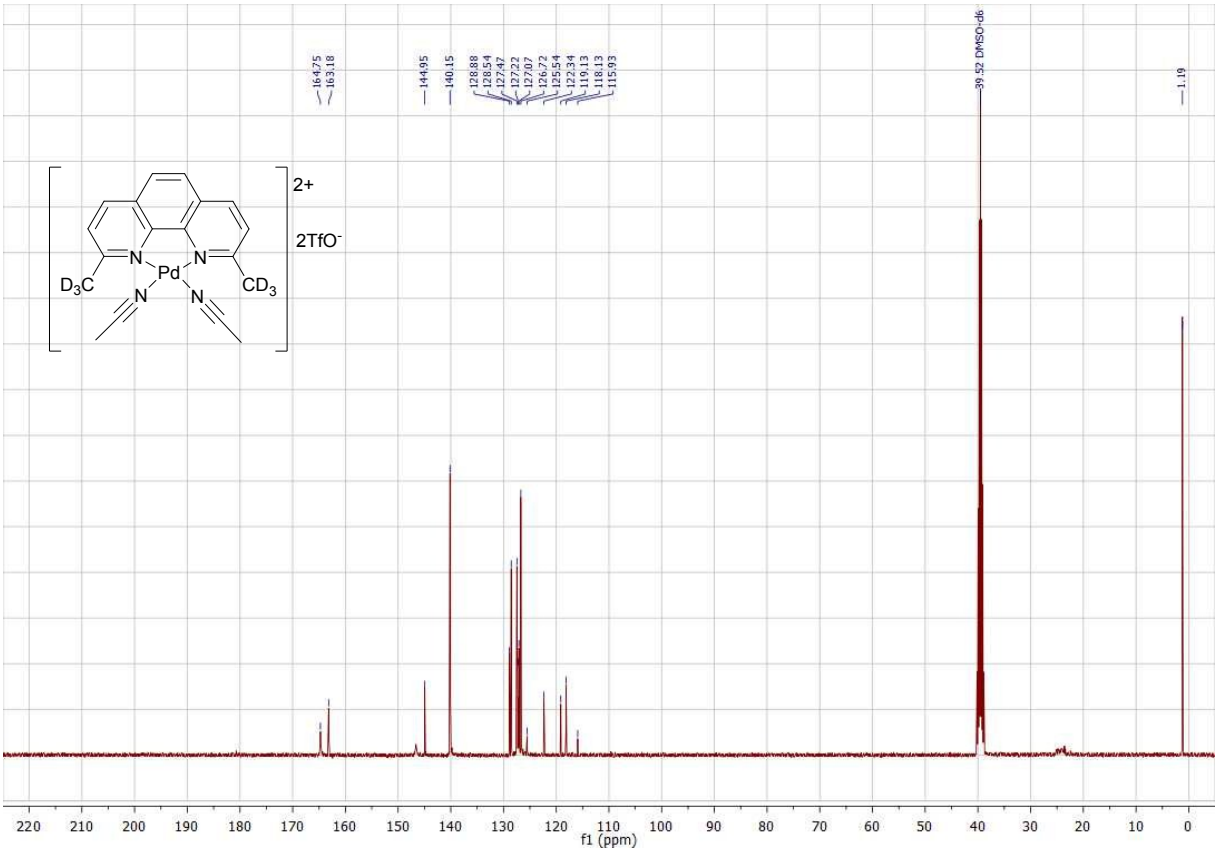
^{1}H NMR - 11-*d*$_6$ (400 MHz, Acetonitrile-d_3)



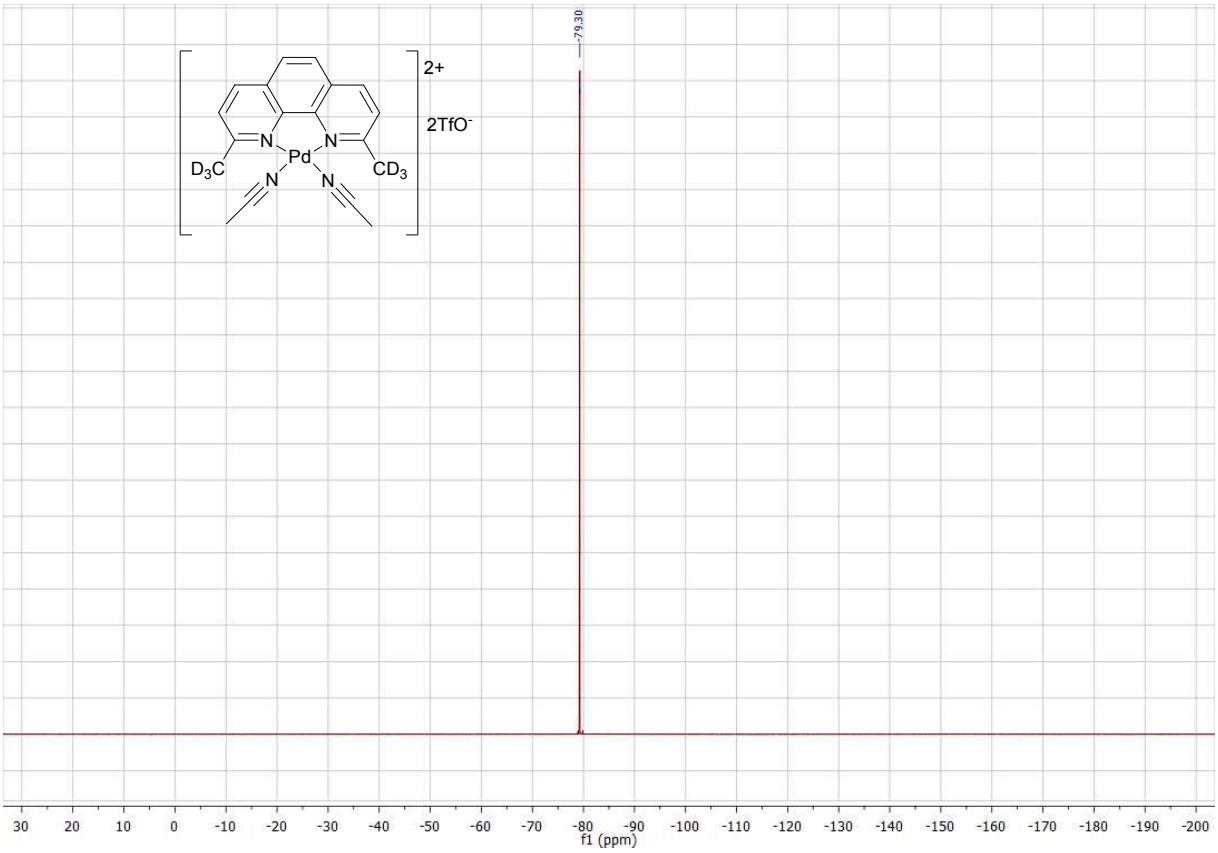
^{1}H NMR - 11-*d*$_6$ (400 MHz, DMSO-d_6)



^{13}C NMR - 11-*d*$_6$ (101 MHz, DMSO-*d*$_6$)



^{19}F NMR - 11-*d*$_6$ (376 MHz, Acetonitrile-*d*$_3$)



References

1) N. R. Conley, L. A. Labios, D. M. Pearson, C. C. L. McCrory and R. M. Waymouth, *Organometallics*, **2007**, *26*, 5447.