Dendritic Phosphorescent Probes for Oxygen Imaging in Biological Systems

Supporting Information

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1. Materials and methods

All solvents and reagents were obtained from commercial sources and used as received. Pd porphyrins Pd-**1**-OBu and Pd-**1**-OH were synthesized as described previously.[1] Column chromatography was performed on Selecto™ silica gel (Fisher) or aluminum oxide (neutral, Brockmann I, ~150 mesh, 58Å). Preparative GPC was performed on S-X1 (Biorad) beads, using THF as a mobile phase, unless otherwise stated. ^{1}H and ^{13}C NMR spectra were recorded on a Brucker DPX-400 spectrometer. Mass-spectra were obtained on a MALDI-TOF Voyager-DE^{TM} RP BioSpectrometry workstation, using α-cyano-4-hydroxycinnamic acid as the matrix.

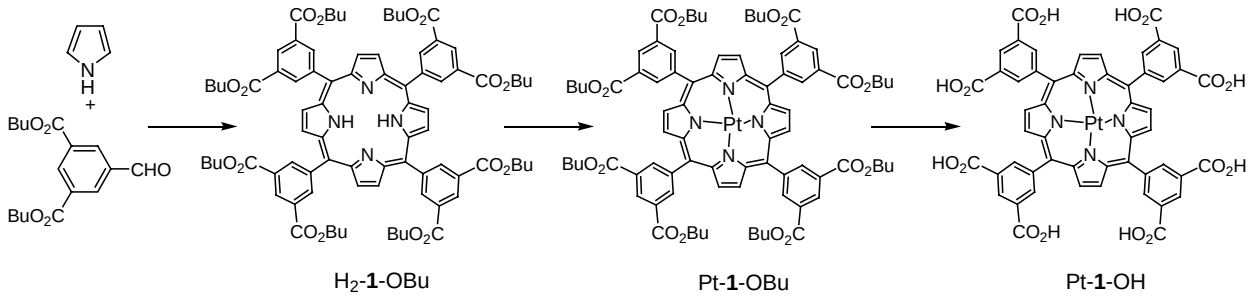
Quartz fluorometric cells (Starna, Inc, 1 cm optical path length) were used in optical experiments. Optical spectra were recorded on a Perkin-Elmer Lambda 35 UV-Vis spectrophotometer. Steady state fluorescence and phosphorescence measurements were performed on a SPEX Fluorolog-2 spectrofluorometer (Jobin-Yvon Horiba), equipped with an infra-red enhanced R2658P PMT (Hamamatsu). Emission spectra were obtained using solutions with absorption at the excitation maxima of approximately 0.05 OD. Quantum yields of emission of all the synthesized compounds were measured relative to the fluorescence of tetraphenylporphyrin (ϕ_{fl}=0.11 in deox. C_6H_6).[2]

The system for oxygen titrations was described previously.[1,3] Time resolved phosphorescence measurements were performed using an in house constructed phosphorometer,[4] modified for time domain operation. For phosphorescence measurements, solutions were deoxygenated by Ar bubbling (Airgas, Grade 5.5), while monitoring changes in phosphorescence lifetimes. Aqueous solutions were deoxygenated by glucose/glucose oxidase/catalase enzymatic system[5] or by prolonged purging by Ar.

2. Synthesis

2.1. Synthesis of core porphyrins

Regular (non-extended) porphyrins:



H_2-**1**-OBu Pt-**1**-OBu Pt-**1**-OH

H_2-1-OBu: Free base porphyrin H_2-**1**-OBu was prepared following the general procedure described by Lindsey *et al*.[6] A mixture of pyrrole (330 mg, 5 mmol) and 3,5-dibutoxycarbonylbenzaldehyde[7] (1.53 g, 5 mmol) in CH_2Cl_2 (500 ml) was bubbled with Ar for 10 min, then $BF_3{\cdot}Et_2O$ (71 mg, 0.5 mmol) was added. The reaction vessel was shaded from the ambient light and left to stir for 2 h at r.t. DDQ (0.85 g, 3.75 mmol) was added, and the mixture was left overnight under stirring. The resulting solution was evaporated to dryness and suspended in MeOH (100 ml). Precipitate was filtered off and chromatographed on neutral alumina (120g, CH_2Cl_2). The carmine-red band was collected, the solvent evaporated and the product was obtained as a red-brown powder. Yield: 576 mg, 33%.

^{1}H NMR ($CDCl_3$) δ 9.16 (t, J = 1.7 Hz, 4H), 9.06 (d, J = 1.7 Hz, 8H), 8.80 (s, 8H), 4.46 (m, 16H), 1.80 (m, 16H), 1.48 (m, 16H), 0.96 (t, J = 7.5 Hz, 24H).

^{13}C NMR ($CDCl_3$) δ 166.0, 142.5, 138.2, 131.6 (br), 131.1 (br), 129.8, 118.5, 65.6, 30.7, 19.2, 13.7.

MALDI-TOF (*m/z*): calcd. for $C_{84}H_{96}N_4O_{16}$: 1415.7, found: 1415.8, 1416.9 [M^+; $M+H^+$].

Pt-1-OBu: $PtCl_2{\cdot}2PhCN$ (707 mg, 1.5 mmol) was added to a boiling solution of H_2-**1**-OBu (707 mg, 0.5 mmol) in dry PhCN (300 ml), and the solution was refluxed under Ar until the conversion was complete (controlled by UV-Vis spectroscopy, typically around 5 h). To complete the conversion, an additional portion of $PtCl_2{\cdot}2PhCN$ (~200 mg) could be required. The reaction time and the required amount of $PtCl_2{\cdot}2PhCN$ were found to be dependent on the solvent (PhCN) purity.

The mixture was evaporated to dryness, and the residual solid was purified by column chromatografy on silicagel (200 g of silicagel, CH_2Cl_2, then CH_2Cl_2/THF 20/1). An orange band was collected, tghe solvent was evaporated, and the residual was precipitated from CH_2Cl_2 (30 ml) by addition of MeOH (150 ml). The precipitate was separated by centrifugation and dried in vacuum. The product was obtained as an orange powder. Yield:780 mg, 97%.

^{1}H NMR ($CDCl_3$) δ 9.13 (dt, J_1 = 1.6 Hz, J_2 = 0.4 Hz, 4H), 8.99 (dd, J_1 = 1.6 Hz, J_2 = 0.4 Hz, 8H), 8.69 (s, 8H), 4.44 (t, J = 6.6 Hz, 16H), 1.78 (m, 16H), 1.46 (m, 16H), 0.94 (t, J = 7.3 Hz, 24H).

^{13}C NMR ($CDCl_3$) δ 165.9, 141.7, 141.0, 137.6, 131.1, 130.5, 129.9, 120.7, 65.6, 30.7, 19.2, 13.7.

MALDI-TOF (*m/z*): calcd. for $C_{84}H_{92}N_4O_{16}Pt$: 1608.7, found: 1608.6 [M^+].

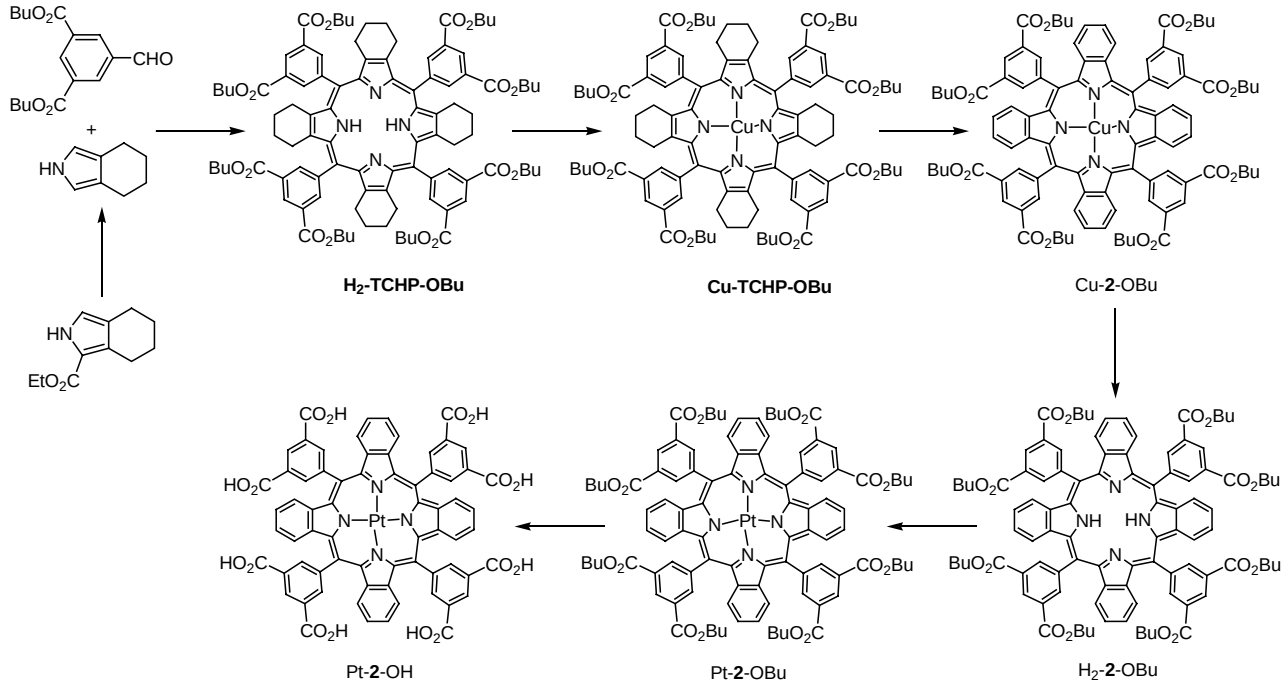
Pt-1-OH: Pt-**1**-OBu (300 mg, 0.187 mmol) was dissolved in THF (50ml). For complete reaction it is critically important to fully dissolve the ester before addition of the reagents. KOH (~500 mg), MeOH (5 ml) and water (0.5 ml) were added, and the mixture was stirred at r.t. until the insoluble potassium salt of the porphyrin-acid precipitated, leaving the supernatant colorless. The precipitate was decanted and

dissolved in water (30 ml). The solution was acidified with conc. HCl. The orange precipitate was washed with water and dried in vacuum. The product was obtained as orange powder. Yield: 210 mg, 97%.

^{1}H NMR (DMSO-d_6) δ 8.97 (t, J = 1.5 Hz, 4H), 8.88 (d, J = 1.4 Hz, 8H), 8.78 (s, 8H).

^{13}C NMR (DMSO-d_6) δ 166.9, 141.3, 140.9, 137.6, 131.6, 131.2, 130.4, 121.1.

Synthesis of tetrabenzoporphyrins and their Pt complexes:



H_2-TCHP-OBu: KOH (2.60 g, 46 mmol) was added to a solution of ethyl-4,5,6,7-tetrahydro-2*H*-isoindole-1-carboxylate (4.20 g, 21.8 mmol)[8] in ethylene glycol (60 ml), and the mixture was refluxed under Ar for 1 hour. The mixture was cooled to r.t. and poured into a mixture of water (100 ml) and CH_2Cl_2 (100 ml). The organic layer was separated, dried with Na_2SO_4, passed through a short silicagel column and diluted with CH_2Cl_2 to the total volume of 2L. 3,5-dibutoxycarbonylbenzaldehyde[7] (6.12 g, 4.4 mmol) was added, the solution was protected from the ambient light and bubbled with Ar for 15 min. $BF_3{\cdot}Et_2O$(0.62 g, 4.4 mmol) was added to the mixture, and it was stirred under Ar for 2 h. DDQ (5.00 g, 22 mmol) was added, and the stirring was continued overnight. The resulting dark-green mixture was reduced in volume to 1.3L, washed with saturated solution of Na_2SO_3 (2x250 ml), 10% Na_2CO_3 (250 ml), water (250 ml), 5% HCl (300 ml) and water (300 ml). The organic layer was dried over Na_2SO_4, and the solvent was removed in vacuum. The remaining material was chromatographed on alumina (400 g, CH_2Cl_2). The first brown and the first green bands were collected, and evaporated to dryness. The product was obtained as a brown solid. Yield: 2.84 g, 34%.

^{1}H NMR ($CDCl_3$) δ 9.05 (t, *J* = 1.6 Hz, 4H), 9.02 (d, *J* = 1.5 Hz, 8H), 4.48 (t, *J* = 6.7 Hz, 16H), 2.20 (br. s, 16H), 1.85 (m, 16H), 1.54 (m, 16H), 1.44 (br s, 16H), 1.00 (t, *J* = 7.3 Hz, 24H), -2.20 (br s, 2H).

^{13}C NMR ($CDCl_3$+HCl, 50^{o}C) δ 165.6, 143.9, 140.4, 135.7, 131.8, 131.5, 125.49, 116.3, 65.9, 30.8, 25.3, 22.4, 19.4, 13.6.

MALDI-TOF (*m/z*): calcd. for $C_{100}H_{118}N_4O_{16}$: 1632.0, found:1632.1 [M^+].

Cu-TCHP-OBu: H_2-**TCHP**-OBu (2.00 g, 1.23 mmol) and $Cu(OAc)_2{\cdot}2H_2O$ (2.66 g, 12.3 mmol) were dissolved in a mixture of $CHCl_3$ (700 ml) and MeOH (70 ml). The mixture was stirred for 2h, then washed with 10% AcOH (100ml), water (100ml), saturated $NaHCO_3$ (100 ml) and water (100 ml) again. The organic phase was dried over Na_2SO_4 and evaporated to dryness. The product was obtained as a dark-red powder. Yield: 2.05 g, 99%.

MALDI-TOF (*m/z*): calcd. for $C_{100}H_{116}CuN_4O_{16}$: 1693.6, found: 1692.8, 1693.8, 1694,8 1695.8 [M^+; $M+H^+$].

Cu-2-OBu: Cu-**TCHP**-OBu (2.00 g, 1.18 mmol) and DDQ (4.54 g, 20 mmol) were dissolved in 150 ml of dry THF and refluxed for 40 min. After cooling to r.t., the mixture was diluted with CH_2Cl_2 (200 ml) and washed with 10% Na_2SO_3 (2 x 100 ml), 10% Na_2CO_3 (100 ml) and water (100 ml). The organic phase was dried over Na_2SO_4 and evaporated to dryness. The residue was chromatographed on silicagel 100-200 mesh (100 g, CH_2Cl_2), and the fist green band was collected. The product was isolated as a deep green powder. Yield: 0.96 g, 46%.

MALDI-TOF (*m/z*): calcd. for $C_{100}H_{100}CuN_4O_{16}$: 1677.4, found: 1676.7, 1677.7, 1678.7, 1679.7 [M^+; $M+H^+$].

H_2-2-OBu: Cu-**2**-OBu (50 mg, 0.029 mmol) was dissolved in H_2SO_4 conc. (200 ml) and immediately poured onto crushed ice (300 g). The resulting solution was extracted with CH_2Cl_2 (2x200 ml), the organic phase was washed with water (200 ml), saturated $NaHCO_3$ (200 ml) and dried over Na_2SO_4. The solvent was removed in vacuum, and the product was purified on a short silica gel column (CH_2Cl_2-THF, 5:1). The product was obtained as a green solid. Yield: 37 mg, 77%.

^{1}H NMR ($CDCl_3$, 45^{o}C) δ 9.27 (t, *J* = 1.5 Hz, 4H), 9.20 (d, *J* = 1.5 Hz, 8H), 7.25 (br s, 8H), 7.07 (br s, 8H), 4.45 (t, *J* = 6.7 Hz, 16H), 1.80 (m, 16 H), 1.47 (m, 16H), 0.94 (t, *J* = 7.3 Hz, 24H).

^{13}C NMR ($CDCl_3$, 45^{o}C) δ 165.8, 142.5, 139.0, 132.1, 131.2, 126.6, 124.3, 114.1, 65.7, 30.8, 19.3, 13.7.

MALDI-TOF (*m/z*): calcd. for $C_{100}H_{102}N_4O_{16}$: 1615.9: found: 1615.2 [M^+].

Pt-2-OBu: Pt was inserted into H_2-**2**-OBu following the method described for Pt-**1**-OBu (*vide supra*) starting from $PtCl_2$x2PhCN (140 mg, 0.296 mmol) and H_2-**2**-OBu (100 mg, 0.062 mmol) in dry PhCN (50 ml). Yield: 103 mg, 92%.

^{1}H NMR ($CDCl_3$) δ 9.29 (t, *J* = 1.5 Hz, 4H), 9.11 (d, *J* = 1.5 Hz, 8H), 7.21 (m, 8H), 6.94 (m, 8H), 4.42 (t, *J* = 6.7 Hz, 16H), 1.77 (m, 16H), 1.44 (m, 16H), 0.92 (t, *J* = 7.5 Hz, 24H).

^{13}C NMR ($CDCl_3$) δ 165.8, 142.1, 138.2, 137.3, 136.0, 132.2, 131.5, 126.1, 124.0, 116.6, 65.7, 30.6, 19.2, 13.7.

MALDI-TOF (*m/z*): calcd. for $C_{100}H_{100}N_4O_{16}Pt$: 1808.9, found: 1809.1, 1810.1, 1811.1 [$M+H^+$].

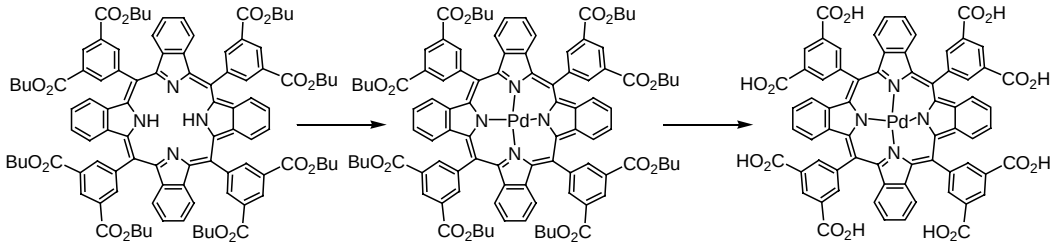
Pt-2-OH: The butyl ester groups on Pt-**2**-OBu were hydrolyzed following the procedure described for Pt-**1**-OBu. The product was isolated as deep emerald powder. Yield: 95%.

^{1}H NMR (DMSO-d_6) δ 9.11 (m, 4H), 9.04 (t, *J* = 1.3 Hz, 8H), 7.36 (m, 8H), 6.92 (m, 8H), 3.37 (br s, 8H).

^{13}C NMR (DMSO-d_6) δ 167.1, 142.0, 138.3, 137.4, 136.0, 133.4, 131.8, 127.2, 124.2, 117.3.

MALDI-TOF (*m/z*): calcd. for $C_{68}H_{36}N_4O_{16}Pt$: 1360.1, found: 1359.5 [M^+].

Synthesis of Pd tetrabenzoporphyrins:



H_2-**2**-OBu Pd-**2**-OBu Pd-**2**-OH

Pd-2-OBu: $PdCl_2$ (22 mg, 0.124 mmol) was added to a solution of H_2-**2**-OBu (50 mg, 0.031 mmol) in dry PhCN (20 ml), and the resulting mixture was refluxed under Ar until the conversion was complete (controlled by UV-Vis spectroscopy, typically 1h). The mixture was evaporated to dryness, and the residual solid was purified by column chromatografy on silicagel (30 g of silica, CH_2Cl_2, then CH_2Cl_2/THF 20/1). The green band was collected, the solvent was evaporated in vacuum and the residual precipitated from CH_2Cl_2 (3 ml) by addition of MeOH (12 ml). The precipitate was separated by centrifugation and dried in vacuum. Pd-**2**-OBu was obtained as a green powder. Yield: 50 mg, 95%.

^{1}H NMR ($CDCl_3$) δ 9.30 (t, *J* = 1.7 Hz, 4H), 9.12 (d, *J* = 1.7 Hz, 8H), 7.22 (m, 8H), 6.99 (m, 8H), 4.43 (t, *J* = 6.7 Hz, 16H), 1.79 (m, 16H), 1.45 (m, 16H), 0.93 (t, *J* = 7.5 Hz, 24H).

^{13}C NMR ($CDCl_3$) δ 165.8, 142.4, 138.5, 138.5, 137.9, 132.3, 131.4, 126.0, 123.9, 116.4, 65.7, 30.8, 19.3, 13.7.

MALDI-TOF (*m/z*): calcd. for $C_{100}H_{100}N_4O_{16}Pd$: 1720.3, found:1720.0, 1721.0, 1722.0, 1723.0 [M^+; $M+H^+$].

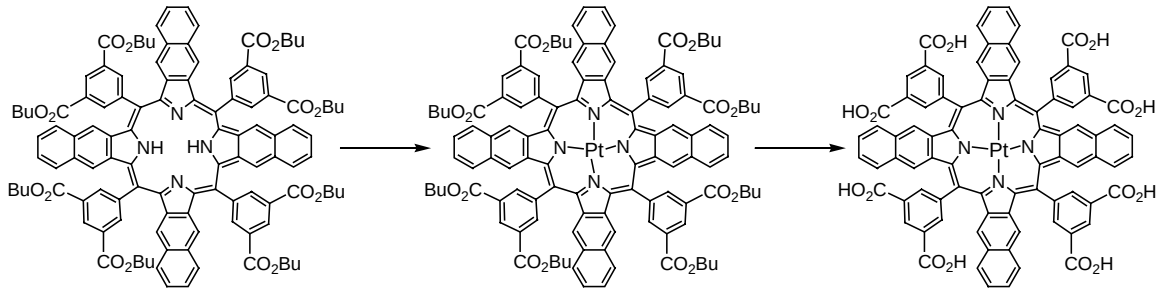
Pd-2-OH: The butyl ester groups on Pd-**2**-OBu were hydrolyzed following the procedure described for Pt-**2**-OBu. Yield: 95%.

^{1}H NMR (DMSO-d_6) δ 9.11 (t, *J* = 1.7 Hz, 4H), 8.98 (d, *J* = 1.7 Hz, 8H), 7.32 (m, 8H), 7.02 (m, 8H), 3.01 (br s, 8H).

^{13}C NMR (DMSO-d_6) δ 165.7, 141.0, 137.2, 137.1, 136.8, 132.4, 130.3, 125.6, 122.8, 115.7.

MALDI-TOF (*m/z*): calcd. for $C_{68}H_{36}N_4O_{16}Pd$: 1271.5, found:1271.4; 1272.4; 1273.4;1275.4 [M^+;$M+H^+$].

Synthesis of Pt tetranaphthoporphyrins:



H_2-**3**-OBu Pt-**3**-OBu Pt-**3**-OH

Pt-3-OBu: Pt-**3**-OBu was obtained as a deep green powder according to method described for Pt-**1**-OBu starting from $PtCl_2$·2PhCN (85 mg, 0.18 mmol) and H_2-**3**-OBu[7] (109 mg, 0.06 mmol) in dry PhCN (60 ml). Yield: 102 mg, 85%.

^{1}H NMR (DMF-d_7, 100°C) δ 9.57 (t, *J* = 1.7 Hz, 4H); 9.43 (d, *J* = 1.7 Hz, 8H); 7.85 (m, 8H); 7.81 (br s, 8H); 7.71 (m, 8H); 4.61 (t, *J* = 6.5 Hz, 16H), 1.91 (m, 16H); 1.55 (m, 16H); 1.02 (t, *J* = 7.5 Hz, 24H).

^{13}C NMR (DMF-d_7, 110°C) δ 165.8, 141.0, 139.0, 136.3, 135.6, 134.1, 131.6, 131.3, 129.2, 127.1, 121.0, 116.0, 65.9, 31.1, 19.4, 13.4.

MALDI-TOF (*m/z*): calcd. for $C_{116}H_{108}N_4O_{16}Pt$: 2009.2, found: 2011.8 [$M+H^+$].

Pt-3-OH: Pt-**3**-OBu (100 mg, 0.05 mmol) was dissolved in pyridine (30 ml) and Me_4NOH (1 ml of 1% solution in MeOH) was added to the mixture. The mixture was stirred for 10 min, the resulting green

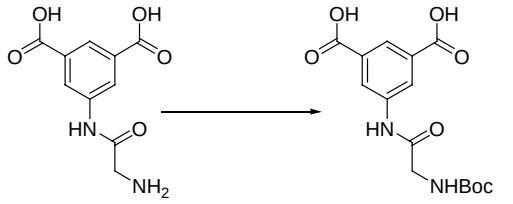
slurry was separated by centrifugation, and the solvents were removed in vacuum. Water (15 ml) was added to the remaining green solid, which dissolved immediately, forming a deep green solution. The target porphyrin-acid was precipitated upon acidification of the solution with HCl conc. The resulting green powder was washed two times with cold water by way of suspension/centrifugation and dried in vacuum. Yield: 72 mg, 92%.

^{1}H NMR (DMF-d_7, 80^{o}C) δ 9.47 (t, *J* = 1.7 Hz, 4H), 9.28 (d, *J* = 1.7 Hz, 8H), 7.71 (m, 8H), 7.66 (s, 8H), 7.56 (m, 8H), 3.40 (br s, 8H).

^{13}C NMR (DMF-d_7, 80^{o}C) δ 167.2, 143.0, 139.0, 136.5, 135.8, 134.8, 132.1, 131.7, 129.5, 127.4, 124.1, 116.5.

MALDI-TOF (*m/z*): calcd. for $C_{84}H_{44}N_4O_{16}Pt$: 1560.3, found: 1562.9 [M+H$^+$].

2.2. Synthesis of dendrons

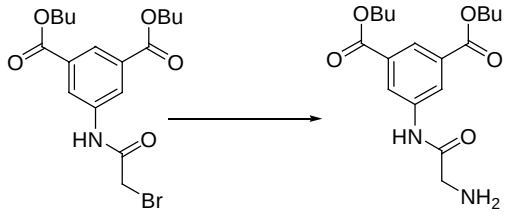


H_2N-AG^1-OH **BocNH-AG^1-OH**
4

<u>BocNH-AG^1-OH (4):</u> 3,5-Dicarboxylphenyl glycineamide[9] (9.52 g, 40 mmol) and NaOH (3.20 g, 80 mmol) were dissolved in water (80 ml). The solution was cooled in an ice bath, and Boc_2O (9.52 g, 44 mmol) in dioxane (40 ml) was added in one portion. The resulting slurry was vigorously stirred for 2 days at room temperature, yielding a homogeneous solution. It was washed with Et_2O (100 ml), the aqueous layer was separated and acidified with citric acid (10% in water). The supernatant was decanted, and the remaining semi-solid substance completely solidified upon addition of CH_2Cl_2 (100 ml). It was filtered off, washed with water (50 ml), MeOH (50 ml) and dried in vacuum. The product was isolated as a white powder. Yield: 6.12 g, 43%.

^{1}H NMR (DMSO-d_6) δ 10.42 (s, 1H), 8.44 (d, *J* = 1.2 Hz, 2H), 8.17 (t, *J* = 1.2 Hz, 1H); 7.04 (t, *J* = 5.4 Hz, 1H), 3.76 (d, *J* = 6.2 Hz, 2H), 3.47 (br s, 2H), 1.41 (s, 9H).

^{13}C NMR (DMSO-d_6) δ 168.8, 166.4, 155.9, 139.5, 131.78, 124.5, 123.5, 78.1, 43.9, 28.2.



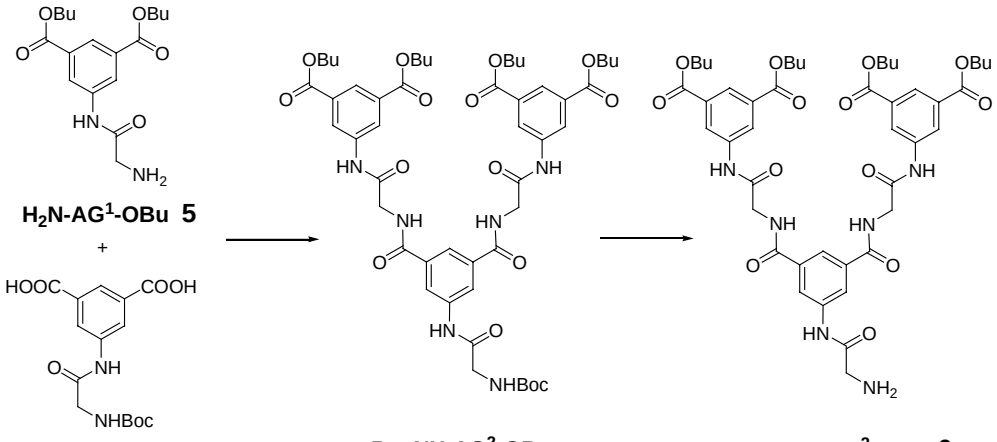
H_2N-AG^1-OBu
5

<u>H_2N-AG^1-OBu (5):</u> Dibutoxycarbonylphenyl bromoacetyleamide[9] (20.7 g, 50 mmol) was dissolved in THF (150 ml), and the solution was added dropwise to a rapidly stirred solution of NH_3 in MeOH (saturated, 500 ml) at 0°C. The mixture was kept under stirred for 4 h, and the solvent and the excess of ammonia were removed on a rotary evaporator. It is critically important to avoid heating of the reaction mixture above 30°C. Even though evaporation of the alcohol can take longer time without heating, elevated temperatures sharply decreases the yield and become purification very complicated.

The resulting yellow oil was treated with a mixture of EtOAc and hexane (1:1, 100 ml), resulting the formation of white solid, which was collected and dissolved in a mixture of water (50 ml) and EtOAc (200 ml). The product does not dissolve in water and neither does it dissolve in EtOAc; however, it readily dissolves in the mixture of water and EtOAc! The organic layer was separated, dried briefly over Na_2SO_4 (prolonged drying may lead to precipitation) and the solvent was removed in vacuum. The product was obtained in the form of a colorless foam-like solid. Yield: 12.3 g, 70%.

^{1}H NMR (DMSO-d_6) δ 11.03 (br s, 1H), 8.48 (d, J = 1.2 Hz, 2H), 8.21 (br s, 2H), 8.14 (t, J = 1.5 Hz, 1H); 4.26 (t, J = 6.4 Hz, 4H), 3.86 (s, 2H), 1.66 (m, 4H), 1.39 (m, 4H), 0.90 (t, J = 7.4 Hz, 6H).

^{13}C NMR (DMSO-d_6) δ 165.6, 164.7, 139.2, 131.1, 124.5, 123.5, 64.9, 41.2, 30.2, 18.8, 13.6.



H_2N-AG^1-OBu 5 + **$BocNH$-AG^1-OH 4**

$BocNH$-AG^2-OBu

H_2N-AG^2-OBu 6

Boc·NH-AG^2-OBu: Boc-protected 3,5-dicarboxylphenyl glycineamide (3.38 g, 10 mmol) and CDMT (2-chloro-4,6-dimethoxy-1,3,5-triazine) (4.38 g, 25 mmol) were dissolved in dry DMF (100 ml). The flask was sealed with rubber septa, and the solution was stirred on an ice bath for 15 min, after which NMM (N-methylmorpholine) (4.04 g, 40 mmol) was added in one portion. The resulting mixture was stirred on an ice bath for 1h, warmed up to r.t. and stirred for 15 min. 3,5-Dibutoxycarbonylphenyl glycineamide (7.35 g, 21 mmol) was added to the resulting yellow suspension in one portion, and the mixture was stirred overnight. The mixture was poured into ice-cold water (300 ml) under vigorous stirring. The resulting precipitate was collected by filtration, washed with water (2 x 50 ml), rapidly washed with MeOH (50 ml) and dried in vacuum. Yield: 8.95 g, 89%.

^{1}H NMR (DMSO-d$_6$) δ 10.52(s, 2H); 10.22(s, 1H); 8.89(t, *J* = 5.7 Hz, 2H); 8.52(s, 4H); 8.28(s, 2H); 8.18(s, 2H); 8.15(s, 1H); 7.03(t, *J* = 5.3 Hz, 1H); 4.31 (t, *J* = 6.5 Hz, 8H); 4.16 (d. *J* = 5.3 Hz, 4H); 3.79 (d, *J* = 5.2 Hz, 2H); 1.77-1.63 (m, 8H); 1.49-1.32 (m, 8H); 1.41 (s, 9H); 0.91 (t, *J* = 7.4 Hz, 12H).

^{13}C NMR (DMSO-d$_6$) δ 168.5; 168.2; 166.2; 164.7; 155.8; 139.6; 139.1; 134.8; 130.9; 123.9123.5; 121.0; 120.7; 78.0; 64.8; 43.8; 43.4; 30.1; 28.1; 18.6; 13.4.

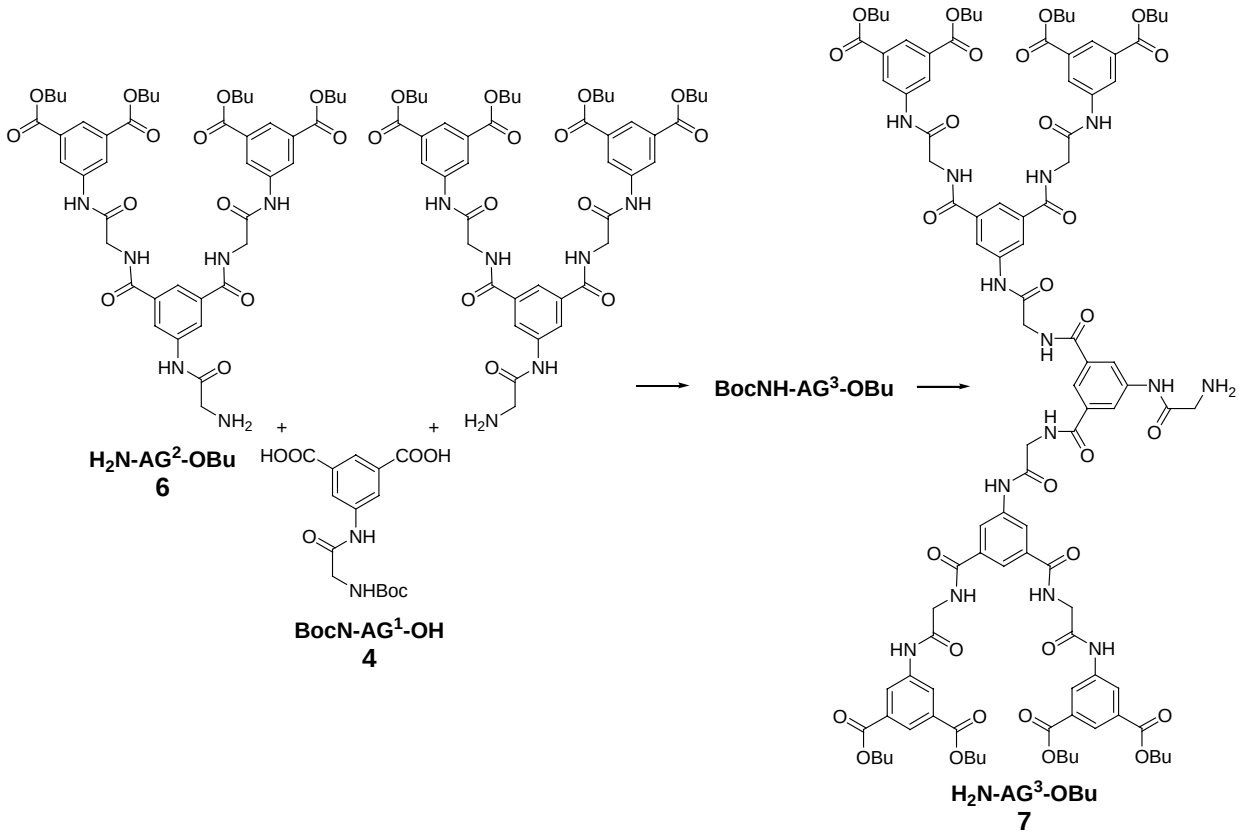
MALDI-TOF (*m/z*): calcd. for $C_{51}H_{66}N_6O_{16}$: 1019.1, found:1041.3 [M+Na$^+$], 1057.9 [M+K$^+$].

H_2N-AG^2-OBu (6): Boc·NH-AG^2-OBu (8.02 g, 8 mmol) was dissolved in trifluoroacetic acid (100 ml), the solution was kept for 1 h at r.t. and evaporated to dryness. The residual viscous oil solidified upon treatment with water (100 ml). The resulting solid was collected by filtration, washed with water (50 ml) and dried in vacuum. Yield: 7.65 g, 94%.

^{1}H NMR (DMSO-d$_6$) δ 10.78 (s, 1H), 10.59 (s, 2H), 8.93 (t, *J* = 5.4 Hz, 2H), 8.51 (d, *J* = 1.0 Hz, 4H), 8.28 (s, 2H), 2.26-8.21 (m, 3H), 8.18 (t, *J* = 1.6 Hz, 2H), 4.31 30 (t, *J* = 6.5 Hz, 8H), 4.17 30 (d, *J* = 5.4 Hz, 4H), 3.86 (s, 2H), 1.71 (m, 8H), 1.43 (m, 8H), 0.94 (t, *J* = 7.3 Hz, 12H).

^{13}C NMR (DMSO-d$_6$) δ 169.0, 166.8, 165.9, 165.5, 140.5, 139.1, 135.8, 131.7, 124.7, 124.2, 122.0, 121.9, 65.5, 44.1, 41.8, 30.9, 19.4, 14.2.

MALDI-TOF (*m/z*): calcd. for $C_{46}H_{58}N_6O_{13}$: 903.0, found: 922.2, 1805.5 [M+H_3O^+; 2M$^+$].



<u>BocNH-AG^3-OBu:</u> BocNH-AG^3-OBu was obtained from **5** (169 mg, 0.5 mmol) and **7** (1.03 g, 1 mmol) following the procedure described for BocNH-AG^2-OBu. Yield: 1.04 g, 98%.

^{1}H NMR (DMSO-d$_6$, 110^{o}C) δ 10.15 (br s, 4H), 10.00 (br s, 4H), 9.81 (br s, 4H), 8.45 (d, *J* = 1.6 Hz, 8H), 8.48-8.42 (br m, 7H), 8.26 (d, *J* = 1.5 Hz, 4H), 8.23 (d, *J* = 1.5 Hz, 2H), 8.18 (t, *J* = 1.6 Hz, 4H), 8.11 (t, *J* = 1.5 Hz, 2H), 8.10 (t, *J* = 1.5 Hz, 1H), 4.33 (t, *J* = 6.6 Hz, 16H), 4.18 (d, *J* = 5.6 Hz, 8H), 4.17 (d, *J* = 5.7 Hz, 4H), 3.79 (d, *J* = 6.0 Hz, 2H), 1.73 (m, 161.45 (m, 16*J* = 7.4 Hz, 24H).

^{13}C NMR (DMSO-d$_6$, 110^{o}C) δ 169.22, 169.18, 168.9, 168.7, 167.1, 167.1, 165.6, 140.4, 139.8, 136.0, 136.0, 132.0, 124.9, 124.7, 122.3, 122.2, 121.7, 121.6, 79.1, 65.5, 46.3, 45.2, 44.4, 31.0, 28.9, 19.3, 13.9.

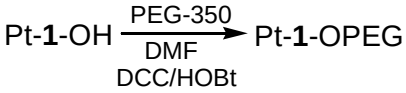
<u>NH$_2$-AG^3-OBu (7):</u> was obtained from BocNH-AG^3-OBu (1.00 g, 0.5 mmol) following the procedure described for the synthesis of **6**. Yield: 1.00 g, 99%.

^{1}H NMR (DMSO-d$_6$) δ 10.61 (s, 1H), 10.44 (s, 4H), 10.32 (s, 2H), 8.78 (s, 4H), 8.49 (d, *J* = 1.5 Hz, 8H), 8.28 (d, *J* = 1.3 Hz, 4H), 8.23 (d, *J* = 1.2 Hz, 2H), 8.19 (t, *J* = 1.2 Hz, 1H), 8.16 (t, *J* = 1.5 Hz, 4H), 8.14 (t, *J* = 1.3 Hz, 2H), 4.86 (br s, 2H), 4.30 (t, *J* = 6.5 Hz, 16H), 4.20-4.10 (m, 12H), 3.80 (br s, 2H), 1.70 (m, 16H), 1.42 (m, 16H), 0.93 (t, *J* = 7.3 Hz, 24H).

^{13}C NMR (DMSO-d_6) δ 168.8, 168.5, 166.8, 166.7, 165.3, 165.0, 140.3, 139.6, 138.8, 135.8, 135.4, 131.5, 124.5, 124.0, 123.1, 121.9, 121.7, 121.3, 65.3, 44.0, 41.6, 41.00, 30.7, 19.2, 14.00.

MALDI-TOF (*m/z*): calcd. for $C_{102}H_{122}N_{14}O_{29}$: 2008.0, found: 2030.6 [M+Na^+]; 2047.6 [M+Na^+]. Each peak was accompanied by a satellite with mass incremented by 552 units.

2.3. Synthesis of porphyrin-dendrimers

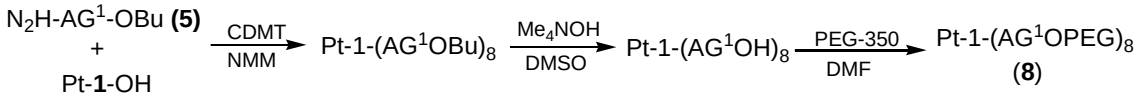


Pt-1-OPEG: was synthesized following the procedure described for **8**. Yield: 28%.

^{1}H NMR (DMSO-d_6) δ 8.99 (t, *J* = 1.5 Hz, 4H), 8.93 (d, *J* = 1.5 Hz, 8H), 8.77 (s, 8H), 4.6-3.0 (multiple peaks, ~270 H).

^{13}C NMR (DMSO-d_6) δ 164.6, 140.8, 140.2, 136.9, 130.8, 129.5, 129.3, 120.0, 71.0, 69.7, 69.6, 69.5, 69.5, 69.4, 68.0, 64.3, 30.1.

MALDI-TOF (*m/z*): calcd. for $C_{172}H_{268}N_4O_{72}Pt$: 3739.0, found: series of peaks with mass increment 44, normally distributed around 3778 Da. [M+K^+]



Pt-1-(AG^1OBu)$_8$: Pt-**1**-OH (46.4 mg, 0.04 mmol) and CDMT (2-chloro-4,6-dimethoxy-1,3,5-triazine) (0.07 g, 0.4 mmol) were dissolved in dry DMF (10 ml). The flask was sealed with rubber septa, and the solution was stirred on an ice bath for 15 min. NMM (N-methylmorpholine) (0.08 g, 0.8 mmol) was added in one portion, the resulting mixture was stirred on an ice bath for 1h, warmed up to r.t. and stirred for additional 15 min. 3,5-Dibutoxycarbonylphenyl glycineamide (140 mg, 0.4 mmol) was added to the resulting orange suspension in one portion, and the mixture was stirred overnight. It was poured into ice-cold water (20 ml), the precipitate was separated by centrifugation, washed with water (20 ml) and MeOH (20 ml) by suspension/centrifugation cycles and dried in vacuum. Pt-1-(AG^1OBu)$_8$ was isolated as an orange powder. Yield: 130 mg, 85%.

^{1}H NMR (DMSO-d_6) δ 10.45 (s, 8H), 9.23 (t, *J* = 5.7 Hz, 8H), 8.97 (t, *J* = 1.5 Hz, 4H), 8.90 (d, *J* = 1.5 Hz, 8H), 8.87 (s, 8H), 8.47 (d, *J* = 1.5 Hz, 16H), 8.12 (t, *J* = 1.6 Hz, 8H), 4.24 (t, *J* = 6.5 Hz, 32H), 4.17 (d, *J* = 5.3 Hz, 16H), 1.64 (m, 32H), 1.36 (m, 32H), 0.87 (t, *J* = 7.4 Hz, 48H).

^{13}C NMR (DMSO-d_6) δ 168.9, 167.0, 165.6, 141.4, 141.3, 140.4, 135.0, 134.1, 131.99, 131.95, 127.5, 124.9, 124.7, 122.0, 65.5, 44.6, 30.9, 19.3, 13.9.

MALDI-TOF (*m/z*): calcd. for $C_{196}H_{220}N_{20}O_{48}Pt$: 3819.0, found: 3819.0, 3841.0 [M^+; $M+Na^+$].

Pt-1-(AG^1-OH)$_8$: Pt-**1**-(AG^1-OBu)$_8$ (106 mg, 0.0277 mmol) was dissolved in DMSO (25 ml) and Me_4NOH (0.1 ml of 25% in MeOH) was added in one portion. The mixture was stirred for 20 min, diluted with water (25 ml) and acidified with HCl conc. The resulting suspension was centrifuged, the precipitate washed with water (20 ml), dissolved in NaOH aq. (pH~9), and left overnight. The solution was acidified with 0.1 HCl aq., the resulting suspension was centrifuged, the precipitate washed with water and dried in vacuum. Pt-**1**-(AG^1-OH)$_8$ was isolated as an orange powder. Yield: 72 mg, 89%.

^{1}H NMR (DMSO-d_6) δ 10.41 (s, 8H), 9.37 (s, 8H), 8.98 (s, 4H), 8.95 (s, 8H), 8.90 (s, 8H), 8.41 (s, 16H), 8.13 (s, 8H), 4.16 (s, 16H).

^{13}C NMR (DMSO-d_6) δ 168.2, 167.1, 166.1, 140.5, 140.4, 139.1, 134.5, 133.1, 132.8, 131.6, 127.0, 124.7, 123.5, 121.4, 43.7.

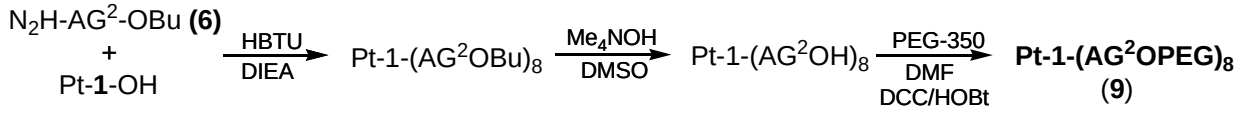
MALDI-TOF (*m/z*): calcd. for $C_{132}H_{92}N_{20}O_{48}Pt$: 2921.3, found: 3032.2 ($C_{132}H_{87}N_{20}O_{48}PtNa_5+H^+$); 3048.4 ($C_{132}H_{87}N_{20}O_{48}PtNa_4K+H^+$); 3060.5 ($C_{132}H_{88}N_{20}O_{48}PtNa_2K_2+H_3O^+$); 3076.0 ($C_{132}H_{85}N_{20}O_{48}PtNa_7+H^+$); 3090.3 ($C_{132}H_{86}N_{20}O_{48}PtNa_6+H_2O+H_3O^+$); 3098.4 ($C_{132}H_{85}N_{20}O_{48}PtNa_7+Na^+$).

Pt-1-(AG^1-OPEG)$_8$ (8): Pt-1-(AG^1-OH)$_8$ (73 mg, 0.025 mmol), DCC (dicyclohexylcarbodiimide) (0.206 g, 1 mmol), HOBt (1-hydroxybenzotriazole) (0.135 g, 1 mmol) were dissolved in dry DMF (1 ml), PEG350 (2 ml) and three drops of *sym*-collidine were added to the mixture, and it was left to react overnight. The resulting red mixture was poured into water (20 ml) and extracted with CH_2Cl_2 (2 x 20 ml). The organic phase was dried over Na_2SO_4 and evaporated in vacuum. The resulting viscous liquid was diluted with THF (2 ml), and Et_2O (25 ml) was added to yield a red oily precipitate, containing the target compound together with unreacted PEG350. The precipitate was collected by centrifugation. This dissolution-precipitation procedure was repeated three times. The product was obtained as a red viscous solid. Yield: 130 mg, ~60%.

^{1}H NMR (DMSO-d_6) δ 10.68 (s, 8H), 9.38 (s, 8H), 9.01 (s, 4H), 8.93 (s, 8H), 8.90 (s, 8H), 8.53 (s, 8H), 8.16 (s, 8H), 4.5-3.0 (multiple peaks, ~500H).

^{13}C NMR (DMSO-d_6) δ 168.0, 165.6, 164.3, 140.0, 139.4, 138.9, 133.9, 132.6, 131.1, 130.3, 126.6, 123.7, 123.3, 120.9, 70.8, 69.3, 67.8, 64.1, 57.5, 43.2.

MALDI-TOF spectrum showed two bell-shaped peaks centered around 8.0 and 15.2 kDa. Calculated $MW_{av.}$ 8.2 kDa.



Pt-1-(AG^{2}OBu)$_8$: Pt-**1**-OH (11.6 mg, 0.01 mmol) was dissolved in dry NMP (10 ml) at 140^{o}C during 10 min. Longer heating may lead to decomposition of the porphyrin. The solution was cooled to room temperature, 2-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU) (0.1 mmol, 38 mg) was added, and the mixture was stirred for 5 min. N,N-diisopropylethylamine (DIEA) (65 mg, 0.5 mmol) was added to the mixture in one portion by a syringe. This was immediately followed by addition of **6** (0.11 mmol, 110 mg) in dry NMP (2 ml), and the mixture was left overnight under stirring. The mixture was poured into aq. NaCl (3%, 20 ml), and the resulting precipitate was collected by centrifugation and washed with water (2x20 ml), MeOH (2x20 ml), and Et_2O by repetitive suspension/centrifugation. The crude product was dissolved in NMP (20 ml), and isothiocyanate immobilized on cross-linked polystyrene (Aldrich) was added (50 mg, 0.05 mmol). The mixture was stirred overnight. The resin was filtered trough a cotton clot, washed with NMP (2x10 ml), and the combined solutions containing the coupling product were poured into aq. NaCl (3%, 40 ml). The precipitate formed was collected by centrifugation and washed with water (2x20 ml), MeOH (2x20 ml), and Et_2O by repetitive suspension/centrifugation. The target porphyrin-dendrimer was isolated as red solid. Yield: 74 mg, 90%. Thus prepared compound contained ca. 10% of impurities (by mass). Further purification was performed by size exclusion chromatography on polystyrene beads (column: 100x5 cm, mobile phase – THF), collecting the front edge of the color band. Thus purified compound was obtained in 5-10% yield.

^{1}H NMR (DMSO-d$_6$, 100^{o}C) δ 10.16 (s, 16H), 10.08 (s, 8H), 8.96 (br s, 4H), 8.94 (br s, 8H), 8.85 (d, *J* = 1.5 Hz, 8H), 8.84 (s, 8H), 8.47 (t, *J* = 5.2 Hz, 16H), 8.42 (d, *J* = 1.6 Hz, 32H), 8.25 (d, *J* = 1.5 Hz, 16H), 8.14 (t, *J* = 1.6 Hz, 16H), 8.09 (t, *J* = 1.5 Hz, 8H), 4.27 (t, *J* = 6.5 Hz, 64H), 4.20 (d, *J* = 5.9 Hz, 16H), 4.12 (d, *J* = 5.7 Hz, 32H), 1.67 (m, 64H), 1.40 (m, 64H), 0.90 (t, *J* = 7.5 Hz, 96H).

^{13}C NMR (DMSO-d$_6$, 100^{o}C) δ 167.8, 167.6, 165.9, 165.8, 164.4, 140.2, 140.1, 139.3, 138.7, 134.7, 134.0, 133.0, 130.9, 130.7, 126.3, 123.7, 123.4, 121.2, 120.9, 120.5, 64.4, 43.3, 43.2, 29.8, 18.2, 12.9.

MALDI-TOF (*m/z*): calcd. for $C_{420}H_{476}N_{52}O_{112}Pt$: 8239.6, found: 8240.4 [M^++]; 8282.4 [$M+H_2O+Na^+$]. Each ion was accompanied by satellites with masses incremented by 554 mass units. The Intensities of the satellite peaks was dependent on instrument parameters (laser intensity, voltage).

NOTE: In the early experiments, before the coupling conditions were established, MALDI analyses of reaction mixtures revealed multiple peaks. The ratio between these peaks was found to be independent

of the ionization power and of the method used for the sample preparation, which suggested that the distribution was caused by the presence of imperfect dendrimers and not the fragmentation. In order to confirm this hypothesis, we performed two model experiments. The synthesis was carried out in the presence of either 2-fold excess of G2 dendron **7** or 2-fold excess of the core porphyrin (Pd-**3**-OH). The MALDI analysis showed two predictably different product distributions: in the case of the dendron excess - the distribution was enriched by peaks of higher molecular weight; whereas in the case of the excess of the porphyrin, peaks of lower molecular weight were predominant. Importantly, both distributions consisted of the peaks with the same masses, and only their ratios were different. We speculated that the synthesis in which the porphyrin was used in excess resulted in a mixture of imperfect dendrimers. The fact that we observed exactly the same peaks in the experiment where the dendron was present in excess suggests that the cause of the peak distribution (as opposed to the single peak, corresponding to octasubstituted porphyrin-dendrimer) was the incomplete reaction and not the ion fragmentation.

Pt-1-(AG^{2}OH)$_8$: Pt-**1**-(AG^{2}OH)$_8$ was obtained following the procedure described for Pt-**1**-(AG^{1}OH)$_8$, starting from crude Pt-**1**-(AG^2-OBu)$_8$, not treated with amine scavenging resin and not purified by chromatography. Yield: 208 mg, 81% (for coupling and hydrolysis combined)!

^{1}H NMR (DMSO-d$_6$, 100^{o}C) δ 10.17 (s, 8H), 10.13 (s, 16H), 9.01 (t, *J* = 5.4 Hz, 4H), 8.97 (broad s, 8H), 8.86 (d, *J* = 5.4 Hz, 8H), 8.55 (t, *J* = 4.3 Hz, 16H), 8.43 (s, 8H), 8.41 (s, 32H), 8.27 (s, 16H), 8.17 (s, 16H), 8.10 (s, 8H), broad 5.92 (s, 32H), 4.22 (d, *J* = 4.3 Hz, 16H), 4.13 (t, *J* = 5.4 Hz, 32H).

^{13}C NMR (DMSO-d$_6$,100^{o}C) δ 167.6, 167.5, 166.7, 166.0, 165.8, 140.1, 140.0, 138.9, 138.7, 134.7, 134.0, 133.0, 131.7, 130.9, 126.2, 124.3, 123.5, 121.1, 120.5, 115.2, 46.7, 43.3.

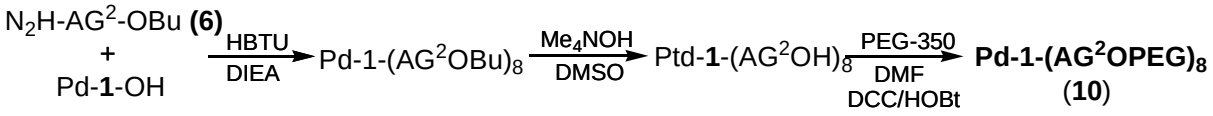
MALDI-TOF (*m/z*): calcd. for $C_{292}H_{220}N_{52}O_{112}Pt$: 6444.2, found: broad peak centered around 6466 [M+Na$^+$], accompanied by series of peaks with mass increment ~ 450. Intensity of satellites depends on instrument parameters.

Pt-1-(AG^2-OPEG)$_8$ (9): Pt-**1**-(AG^2-OPEG)$_8$ was obtained from Pt-**1**-(AG^{2}OH)$_8$ (50 mg, 0.0078 mmol) following the procedure described for **8**. Yield: 75 mg,~60%.

^{1}H NMR (DMSO-d$_6$) δ 10.32 (bs, 16H), 10.21 (bs, 8H), 9.05 (bs, 8H), 8.97 (bs, 4H), 8.87 (bs 16H), 8.59 (bs, 16H), 8.48 (bs, 32H), 8.29 (s, 16H), 8.17 (bs, 16H), 8.13 (bs, 8H), 4.5-3.0 (mult. overl. sign., ~1060H).

^{13}C NMR (DMSO-d$_6$) δ 167.8, 167.5, 165.9, 165.8, 164.4, 140.2, 139.4, 138.8, 134.7, 134.0, 131.0, 130.9, 130.5, 123.8, 123.6, 121.6, 121.0, 120.4, 70.9, 69.6, 69.5, 69.4, 69.2, 67.9, 67.9, 64.0, 57.6, 43.4, 43.2.

MALDI-TOF spectrum showed three broad bell-shaped peaks centered around 16.6; 33.2 and 49.8 kDa. Calculated $MW_{av.}$ 17.1 kDa.



The above reaction sequence was performed following the procedures described for Pt-**1**-AG^2-OBu/OH/OPEG (*vide supra*).

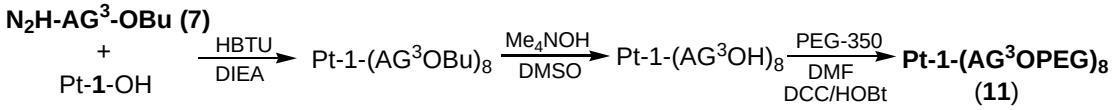
Pd-1-$(AG^2OH)_8$: Yield: 195 mg, 76% (for coupling and hydrolysis combined!)

^{1}H NMR (DMSO-d_6) δ 10.43 (bs, 24H), 9.35 (bs, 8H), 8.97 (broad s, 4H), 8.92 (bs, 32H), 8.43 (s, 32H), 8.27 (s, 16H), 8.13 (s, 16H), 8.10 (s, 8H), 4.17 (bs, 16H), 4.08 (bs, 32H).

Pd-1-$(AG^2$-OPEG$)_8$ (10): Yield: 373 mg,~72%.

^{1}H NMR (DMSO-d_6) δ 10.55 (bs, 16H), 10.44 (bs, 8H), 9.34 (bs, 8H), 8.98 (bs, 4H), 8.89 (bs 32H), 8.49 (bs, 32H), 8.29 (s, 16H), 8.14 (bs, 24H), 4.5-3.0 (mult. overl. sign., ~1060H).

MALDI-TOF spectrum showed broad bell-shaped peak centered around 16.2. Calculated $MW_{av.}$ 17.1 kDa.



The above reaction sequence was performed following the procedures described for Pt-**1**-AG^2-OBu/OH/OPEG (*vide supra*).

Pt-1-$(AG^3OBu)_8$: Yield: 498 mg, 73%.

MALDI-TOF (*m/z*): calcd. for $C_{868}H_{988}N_{116}O_{240}Pt$: 17080.8, found: 15095 [Pt-1-$(AG^3$-OBu$)_7$+Na^+] +17103 [M+Na^+]. Each peak is accompanied by set of at least eight peaks with mass increments of 551 units. The peaks are centered around mass of 16 kDa.

Pt-1-$(AG^3OH)_8$: Yield: 351 mg, 65% (for coupling and hydrolysis combined!)

Because of the high sample viscosity and low mobility of the dendritic branches, it was impossible to obtain a high resolution NMR spectrum even at elevated temperature. Nevertheless, the ratio of the peak intensities was in a good agreement with the expected molecular formula.

^{1}H NMR (DMSO-d_6, 100°C) δ 10.45 (bs, 52H), 9.5-7.9 (series of overlapped peaks, 228 H), 4.1-3.8 (series of overlapped peaks, 112 H).

^{13}C NMR (DMSO-d_6) δ 167.8, 167.6, 166.0, 165.9, 165.8, 139.1, 138.7, 134.5, 131.3, 124.2, 123.2, 120.6, 120.5, 43.1, 42.9 (all peaks are broadened).

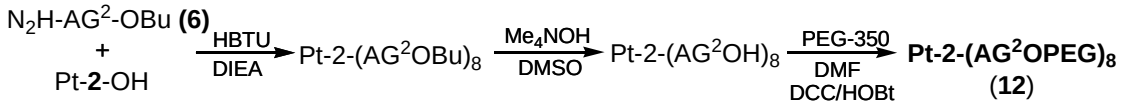
MALDI-TOF (*m/z*): calcd. for $C_{612}H_{476}N_{116}O_{240}Pt$: 13490.0, found: broad bell-shaped peak centered at 13.5 kDa.

Pt-1-(AG^{3}OPEG)$_8$ (11): 100 mg of Pt-1-(AG^{3}OH)$_8$ yield ~140 mg of Pt-**1**-(AG^{3}OPEG)$_8$,. Yield: ~55%.

^{1}H NMR (DMSO-d_6) δ 10.7-10.3 (set of broad overlapping peaks, 52H), 9.5-7.9 (set of broad overlapping peaks, 228H), 4.6-3.0 (set of broad overlapping peaks, ~2400H).

^{13}C NMR (DMSO-d_6) 168.3, 168.0, 166.3, 165.2, 164.7, 139.9, 139.2, 134.9, 130.7, 124.9, 124.1, 123.7, 121.1, 71.2, 69.7, 69.5, 68.2, 67.0, 64.5, 58.0, 43.4, 43.2.

MALDI-TOF spectrum showed a very broad low-intensity peak centered at 31.1 kDa. Calculated $MW_{av.}$ 33.7 kDa.



The above reaction sequence was performed following the procedures described for Pt-**1**-AG^2-OBu/OH/OPEG (*vide supra*).

Pt-2-(AG^{2}OBu)$_8$: Yield: 293 mg, 87% (prior to chromatographic purification)

^{1}H NMR (DMSO-d_6, 100°C) δ 10.16 (s, 16H), 10.12 (s, 8H), 9.16 (br s, 4H), 9.02 (t, J = 6.0 Hz, 8H), 8.96 (s, 8H), 8.46 (t, J = 6.0 Hz, 16H), 8.42 (d, J = 1.4 Hz, 32H), 8.26 (d, J = 1.0 Hz, 16H), 8.14 (t, J = 1.6 Hz, 16H), 8.09 (t, J = 1.4 Hz, 8H), 7.34 (m, 8H), 7.08 (m, 8H), 4.27 (t, J = 6.4 Hz, 64H), 4.20 (d, J = 4.9 Hz, 16H), 4.12 (d, J = 5.6 Hz, 32H), 1.67 (m, 64H), 1.40 (m, 64H), 0.90 (t, J = 7.5 Hz, 96H).

^{13}C NMR (DMSO-d_6, 100°C) δ 167.8, 167.5, 165.9, 165.4, 164.4, 140.5, 139.3, 138.7, 136.5, 135.2, 134.7, 133.9, 130.7, 130.5, 127.6, 126.0, 123.7, 123.4, 123.1, 121.0, 120.5, 116.8, 64.4, 43.3, 43.2, 29.8, 18.2, 12.9.

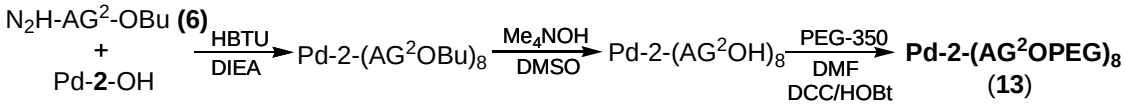
MALDI-TOF (*m/z*): calcd. for $C_{436}H_{484}N_{52}O_{112}Pt$: 8439.9, found: 8433.9 [M+H$^+$], 8462.2 [M+Na$^+$], 8478.8 [M+K$^+$]. Each ion is accompanied by a series of satellites with mass increments of 551 or 1102 mass units. The intensity of the satellite peaks were found to be dependent on the instrument parameters.

Pt-2-(AG^{2}OH)$_8$: Yield 215 mg, 81% (for coupling and hydrolysis combined!)

^{1}H NMR (DMSO-d$_6$, 80^{o}C) δ 10.24 (s, 8H), 10.19 (s, 16H), 9.17 (s, 8H), 9.15 (s, 4H), 8.98 (s, 8H), 8.61 (s, 16H), 8.41 (s, 32H), 8.27 (s, 16H), 8.16 (s, 16H), 8.11 (s, 8H), 7.37 (s, 8H), 7.08 (s, 8H), 4.20 (s, 16H), 4.13 (s, 32H).

Pt-2-(AG^{2}OPEG)$_8$ (12): Pt-**2**-(AG^{2}OPEG)$_8$ was obtained from Pt-**2**-(AG^2-OH)$_8$ (50 mg, 0.0078 mmol) following the procedure described for **8.** Yield: 75 mg,~60%.

^{1}H NMR (DMSO-d$_6$) δ 10.65-10.40 (m, 24H), 9.42 (bs, 8H), 9.20 (bs, 4H), 9.02 (bs 8H), 8.91 (bs, 16H), 8.49 (bs, 32H), 8.29 (s, 16H), 8.17 (bs, 24H), 7.40 (m, 8H), 7.02 (m, 8H), 4.5-3.0 (mult. overl. sign., ~1140H).



The above reaction sequence was performed following the procedures described for Pt-**1**-AG^2-OBu/OH/OPEG (*vide infra*).

Pd-2-(AG^{2}OBu)$_8$: Yield 307 mg, 92% (before chromatographic purification).

^{1}H NMR (DMSO-d$_6$, 100^{o}C) δ 10.25 (s, 16H), 10.21 (s, 8H), 9.17 (bs, 4H), 9.12 (bs, 8H), 8.97 (s, 8H), 8.50 (t, *J* = 5.5 Hz, 16H), 8.44 (d, *J* = 1.5 Hz, 32H), 8.27 (d, *J* = 1.0 Hz, 16H), 8.13 (t, *J* = 1.6 Hz, 16H), 8.10 (t, *J* = 1.4 Hz, 8H), 7.35 (m, 8H), 7.10 (m, 8H), 4.27 (t, *J* = 6.4 Hz, 64H), 4.20 (d, *J* = 4.9 Hz, 16H), 4.12 (d, *J* = 5.6 Hz, 32H), 1.67 (m, 64H), 1.40 (m, 64H), 0.90 (t, *J* = 7.5 Hz, 96H).

^{13}C NMR (DMSO-d$_6$, 100^{o}C) δ 167.8, 167.5, 165.9, 165.4, 164.4, 139.3, 138.7, 137.4, 136.9, 135.1, 134.7, 134.0, 131.0, 130.7, 127.6, 125.8, 123.7, 123.3, 121.0, 120.6, 120.5, 118.4, 64.4, 43.25, 43.2, 39.5, 29.8, 18.2, 12.9.

MALDI-TOF (*m/z*): calcd. for $C_{436}H_{484}N_{52}O_{112}Pd$: 8351.2, found: 8374.5 [M+Na$^+$]. The MI is accompanied by a set of satellites with masses incremented by 551, 1102, 1653 and 2204 mass units. The intensities of the satellites were found to be dependent on the instrument parameters.

Pd-2-(AG^{2}OH)$_8$: Yield 207 mg, 79% (for coupling and hydrolysis combined!)

^{1}H NMR (DMSO-d$_6$, 80^{o}C) δ 10.22 (s, 8H), 10.18 (s, 16H), 9.13 (bs, 4H), 9.05 (bs, 8H), 8.97 (bs, 8H), 8.59 (s, 16H), 8.41 (s, 32H), 8.27 (s, 16H), 8.15 (s, 16H), 8.13 (s, 8H), 7.38 (s, 8H), 7.11 (s, 8H), 4.21 (s, 16H), 4.13 (s, 32H).

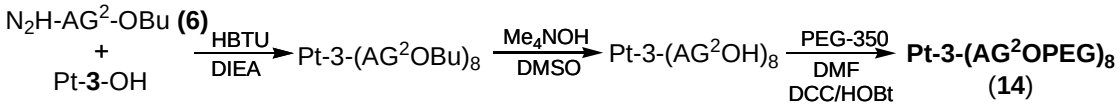
^{13}C NMR (DMSO-d$_6$, 80^{o}C) δ 167.7, 167.6, 167.5, 165.9, 165.4, 140.7, 139.0, 138.7, 138.6, 137.4, 136.9, 135.1, 134.7, 134.1, 131.5, 127.6, 125.9, 124.3, 123.5, 121.0, 120.5, 116.4, 43.23, 43.03.

MALDI-TOF (*m/z*): calcd. for $C_{308}H_{228}N_{52}O_{112}Pd$: 6555.8, found: broad peak 6657.6, $[C_{308}H_{223}N_{52}O_{112}PdNa_5 + H^+]$. The peak was accompanied by a series of satellites with mass incremented by 452 units. The intensities of the satellites were found to be dependent on the instrument parameters.

Pd-2-(AG^{2}OPEG)$_8$ (13): Pd-**2**-(AG^{2}OPEG)$_8$ was obtained from Pd-**2**-(AG^{2}OH)$_8$ (51 mg, 0.0078 mmol) following the procedure described for **8.** Yield: 75 mg, ~60%.

^{1}H NMR (DMSO-d$_6$) δ 10.58 (bs, 16H), 10.48 (bs, 8H), 9.5-8.0 (mult. overl. sign., ~108H), 4.5-3.0 (mult. overl. sign., ~1106H).

MALDI-TOF spectrum showed two broad bell-shaped peaks centered at 16.8 and 33.6 kDa. Calculated MW$_{av.}$ 17.2 kDa.



The above reaction sequence was performed following the procedures described for Pt-**1**-AG^2-OBu/OH/OPEG respectively.

Pt-3-(AG^{2}OBu)$_8$: Yield 314 mg, 91%.

^{1}H NMR (DMSO-d$_6$, 80^{o}C) δ 10.27 (s, 16H), 10.22 (s, 8H), 9.32 (br s, 4H), 9.17 (t, *J* = 5.6 Hz, 8H), 9.06 (s, 8H), 8.59 (t, *J* = 5.9 Hz, 16H), 8.45 (d, *J* = 1.4 Hz, 32H), 8.27 (s, 16H), 8.14 (s, 16H), 8.11 (s, 8H), 7.69 (m, 8H), 7.63 (s, 8H), 7.56 (m, 8H), 4.27 (t, *J* = 6.5 Hz, 64H), 4.19 (d, *J* = 4.0 Hz, 16H), 4.14 (d, *J* = 5.5 Hz, 32H), 1.67 (m, 64H), 1.40 (m, 64H), 0.90 (t, *J* = 7.5 Hz, 96H).

^{13}C NMR (DMSO-d$_6$, 100^{o}C) δ 167.8, 167.5, 165.9, 165.6, 164.4, 140.8, 139.3, 138.7, 136.1, 134.8, 134.7, 134.1, 134.0, 130.7, 130.1, 128.4, 127.6, 126.2, 123.7, 123.4, 123.0, 120.9, 120.5, 115.3, 64.3, 43.4, 43.2, 29.8, 18.2, 12.9.

MALDI-TOF (*m/z*): calcd. for $C_{452}H_{492}N_{52}O_{112}Pt$: 8640.1, found: 8662.3 [M+Na^+], 8679.3 [M+K^+]. Each ion is accompanied by a set of satellites with masses incremented by 551 and 1102 units. The intensities of the satellites were found to be dependent on the instrument parameters.

Pt-3-(AG^{2}OH): Yield 205 mg, 75% (coupling and hydrolysis combined!)

^{1}H NMR (DMSO-d_6, 100^{o}C) δ 10.21 (s, 8H), 10.18 (s, 16H), 9.30 (bs, 4H), 9.16 (bs, 8H), 9.04 (bs, 8H), 8.59 (s, 16H), 8.41 (s, 32H), 8.26 (s, 16H), 8.15 (s, 16H), 8.10 (s, 8H), 7.69 (m, 8H), 7.61 (s, 8H), 7.56 (m, 8H), 4.19 (s, 16H), 4.12 (s, 32H).

^{13}C NMR (DMSO-d_6, 80^{o}C) δ 167.7, 167.5, 167.2, 165.9, 165.7, 140.8 ,139.0, 138.8, 136.1, 134.8, 134.1, 134.1, 131.5, 130.1, 128.4, 127.7, 126.4, 124.3, 123.5, 123.0, 120.9, 120.6, 120.5, 115.4, 43.30, 43.35.

Pt-3-(AG^{2}OPEG)$_8$ (14): Pt-**3**-(AG^{2}OPEG)$_8$ was obtained from Pt-**3**-(AG^{2}OH)$_8$ (50 mg, 0.0078 mmol) following the procedure described for **8.** Yield: 85 mg,~65%.

^{1}H NMR (DMSO-d_6) δ 10.55 (bs, 16H), 10.48 (bs, 8H), 9.5-7.9 (mult. overl. sign., ~116H), 7.75-7.50 (m, 16H), 4.5-3.0 (mult. overl. sign., ~1050H).

3. X-ray structure determination for Pt-3-OBu (CCDC # 717606)

PtAr$_4$TNP, Ar=3,5-(BuO$_2$C)$_2$C$_6$H$_3$)

Compound Pt-**3**-OBu, $C_{122}H_{122}N_6O_{18}Pt$, crystallizes in the triclinic space group PT with a=14.8581(4)Å, b=19.7322(6)Å, c=20.2160(6)Å, α=62.8220(10)°, β=82.2930(10)°, γ=79.6520(10)°, V=5177.7(3)Å^3, Z=2 and d_{calc}=1.382 g/cm^3. X-ray intensity data were collected on a Rigaku Mercury CCD area detector employing graphite-monochromated Mo-K_α radiation (λ=0.71069 Å) at a temperature of 143K. Preliminary indexing was performed from a series of twelve 0.5° rotation images with exposures of 30 seconds. A total of 712 rotation images were collected with a crystal to detector distance of 35 mm, a 2θ swing angle of -12°, rotation widths of 0.5° and exposures of 30 seconds: scan no. 1 was a ϕ-scan from 135° to 315° at ω = 10° and χ = 20°; scan no. 2 was a ϕ-scan from 247.5° to 337.° at ω = 0° and χ = -30°; scan no. 3 was an ω-scan from -20° to 4° at χ = -90° and ϕ = 225°; scan no. 4 was an ω-scan from -20° to 2° at χ = -90° and ϕ = 45°; scan no. 5 was an ω-scan from -20° to 20° at χ = -90° and ϕ = 135°. Rotation images were processed using CrystalClear[10], producing a listing of unaveraged F^2 and σ(F^2) values which were then passed to the CrystalStructure[11] program package for further processing and structure solution on a Dell Pentium III computer. During integration of the rotation images, it was apparent that there were a number of extraneous diffraction spots, Data reduction was completed using the twinsolve module of

CrystalClear, which revealed that the crystal was twinned by a rotation of 180° around 01T . A type 5 HKL file was prepared and used during the final stages of refinement. A total of 69744 reflections were measured over the ranges $5.12 \leq 2\theta \leq 55.12$ °, $-19 \leq h \leq 19$, $-25 \leq k \leq 24$, $-25 \leq l \leq 25$ yielding 69744 unique reflections (R_{int} = 0.0256). The intensity data were corrected for Lorentz and polarization effects and for absorption using REQAB[12] (minimum and maximum transmission 0.911, 1.000).

The structure was solved by direct methods (SIR97[13]). Refinement was by full-matrix least squares based on F^2 using SHELXL-97[14]. All reflections were used during refinement (F^2's that were experimentally negative were replaced by $F^2 = 0$). The weighting scheme used was $w=1/[\sigma^2(F_o^2)+ 0.0219P^2 + 33.8378P]$ where $P = (F_o^2 + 2F_c^2)/3$. Non-hydrogen atoms were refined anisotropically and hydrogen atoms were refined using a "riding" model. Refinement converged to R_1=0.0553 and wR_2=0.1195 for 58024 reflections for which $F > 4\sigma(F)$ and R_1=0.0782, wR_2=0.1384 and GOF = 1.139 for all 69744 unique, non-zero reflections and 1326 variables[15]. The maximum Δ/σ in the final cycle of least squares was 0.090 and the two most prominent peaks in the final difference Fourier were +3.044 and -1.699 e/Å^3. The twinning parameter refined to a value of 0.117.

Table 1 lists cell information, data collection parameters, and refinement data. Final positional and equivalent isotropic thermal parameters are given in Table 2. Anisotropic thermal parameters are in Table 3. Tables 4. and 5. list bond distances and bond angles. Figure 1. is an ORTEP[16] representation of the molecule with 30% probability thermal ellipsoids displayed.

Table 1. Summary of Structure Determination of Pt-3-OBu

Formula:	$C_{122}H_{122}N_6O_{18}Pt$
Formula weight:	2155.35
Crystal class:	triclinic
Space group:	PT (#2)
Z	2
Cell constants:	
a	14.8581(4)Å
b	19.7322(6)Å
c	20.2160(6)Å
α	62.8220(10)°
β	82.2930(10)°
γ	79.6520(10)°
V	5177.7(3)Å^3
μ	14.29 cm^{-1}
crystal size, mm	0.35 x 0.30 x 0.26

D_{calc}	1.382 g/cm^3
F(000)	2236
Radiation:	Mo-K_α (λ=0.71069Å)
2θ range	5.12 – 55.12 °
hkl collected:	-19≤ h ≤19; -25≤ k ≤24; -25≤ l ≤25
No. reflections measured:	69744
No. unique reflections:	69744 (R_{int}=0.0256)
No. observed reflections	58024 (F>4σ)
No. reflections used in refinement	69744
No. parameters	1326
R indices (F>4σ)	R_1=0.0553
	wR_2=0.1195
R indices (all data)	R_1=0.0782
	wR_2=0.1384
GOF:	1.139
Final Difference Peaks, e/Å^3	+3.044, -1.699

4. Oxygen quenching plots

Example 1

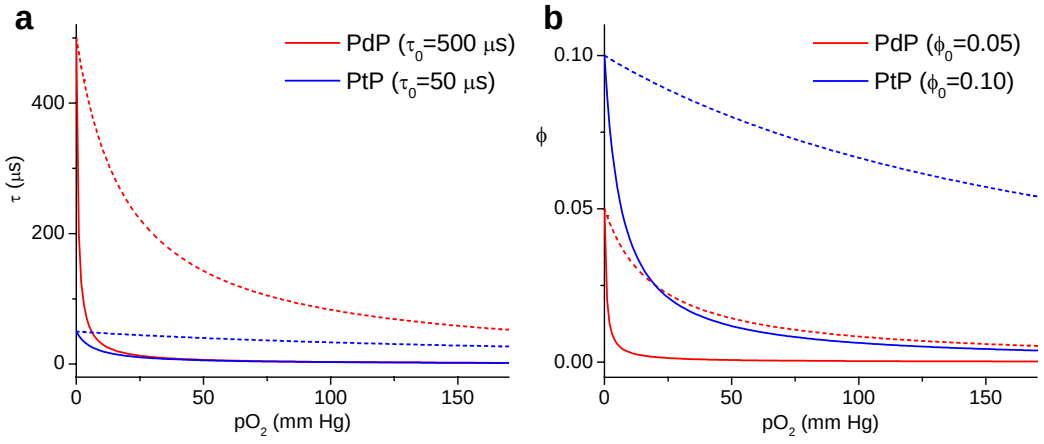
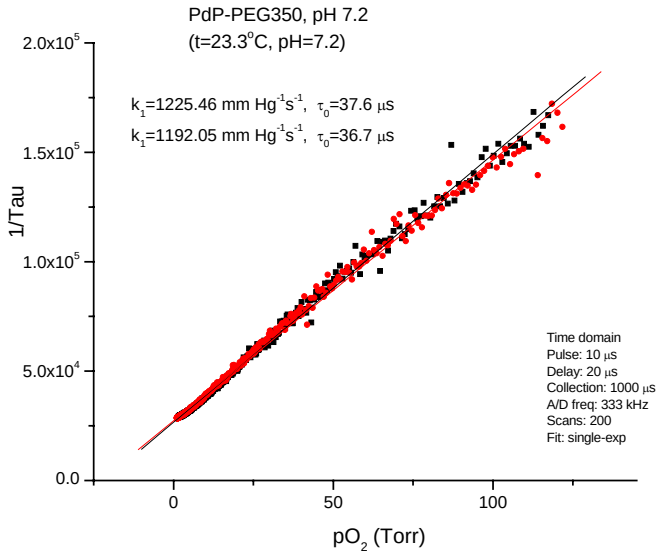


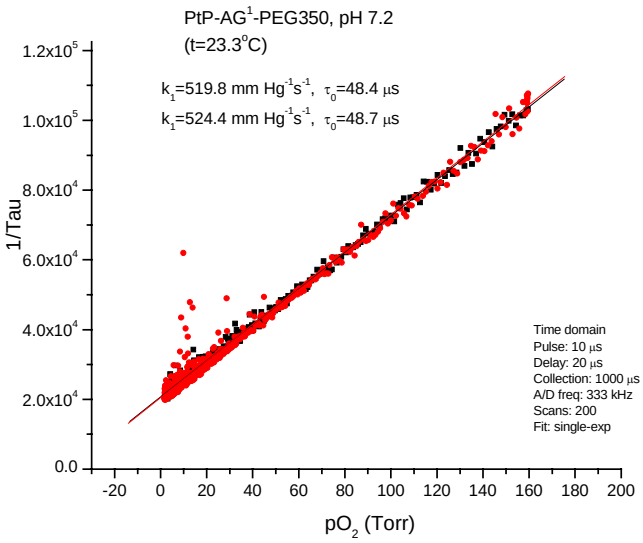
Figure 1. Dependencies of phosphorescence lifetimes (a) and quantum yields (b) for arbitrary Pd (red) and Pt (blue) porphyrins and two different quenching constants: k_q=3,000 mm Hg^{-1}s^{-1} (solid line) and k_q=100 mm Hg^{-1}s^{-1} (dashed line).

To illustrate how quenching constants k_q and lifetimes τ_0 affect the measurement, we consider two probes, PdP and PtP, representing arbitrary Pd and Pt porphyrins: τ_0(PdP)=500 μs, τ_0(PtP)=50 μs; ϕ_0(PdP)=0.05, ϕ_0(PtP)=0.10, where subscript "0" indicates pO_2=0 mm Hg. Graphs in Fig. 1 (above) show how the phosphorescence lifetimes (A) and quantum yields (B) of these probes change throughout the physiological pO_2 range.

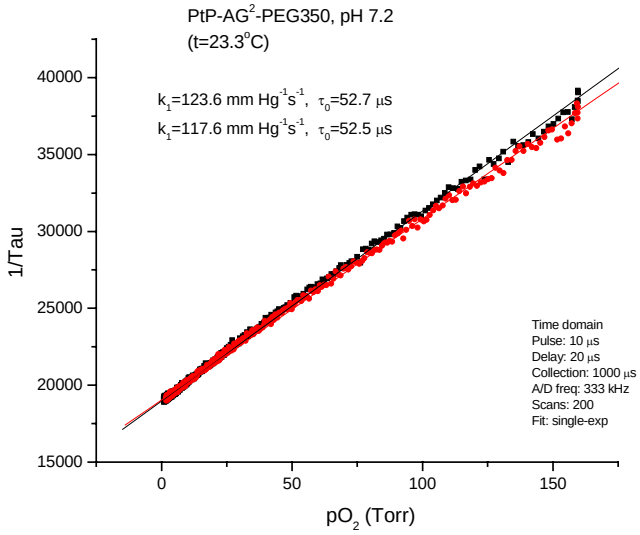
Pt-1-OPEG



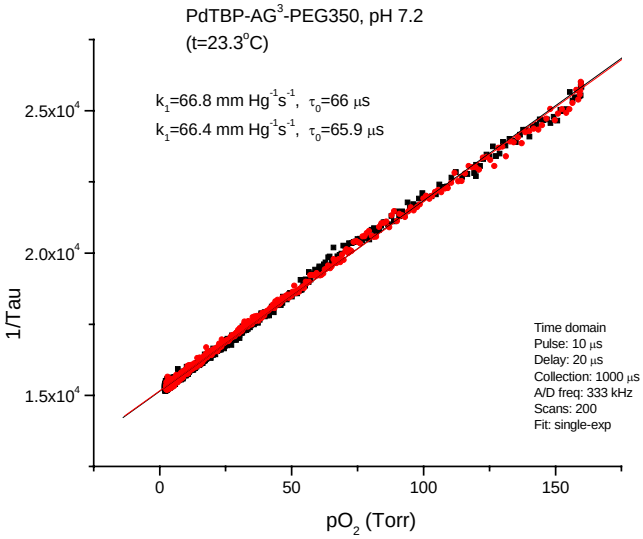
Pt-1-AG[1]OPEG (8)



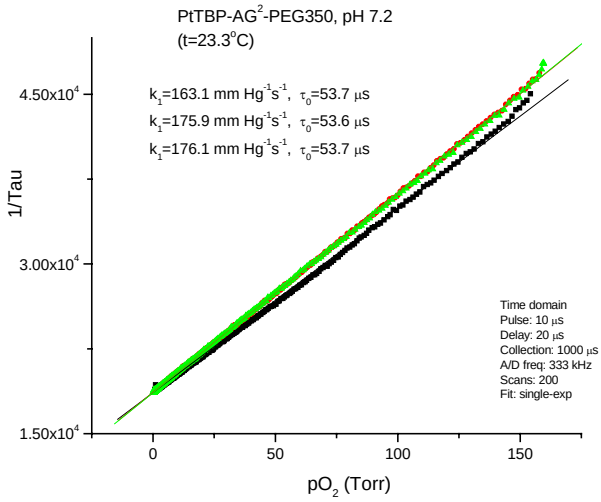
Pt-1-AG[2]OPEG (9)



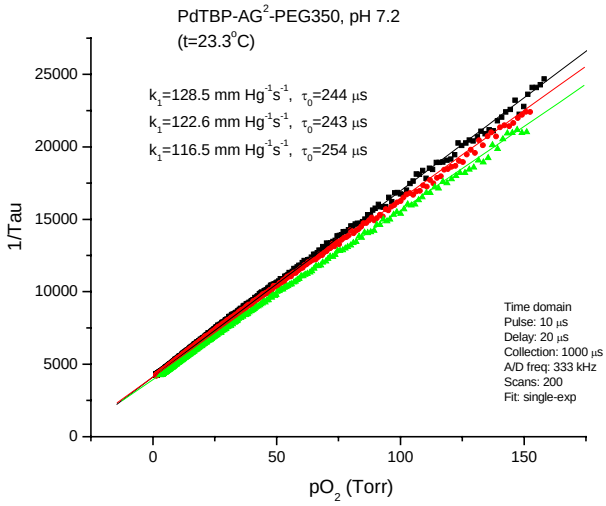
Pt-1-AG[3]OPEG (11)



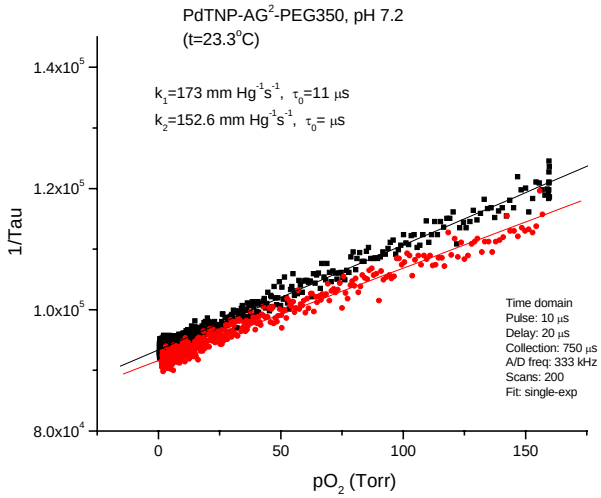
Pt-2-AG^{2}OPEG (12)



Pd-2-AG^{2}OPEG (13)



Pt-3-AG^{2}OPEG (14)



5. Biological imaging experiments

Sprague Dawley rats (250-320 g) were initially anesthetized with isoflurane and the femoral artery and vein were catheterized. Body temperature was maintained at 37±0.1 ^{o}C. Tracheotomy was performed and rats were ventilated with a mixture of air and oxygen. After completion of the surgery, isoflurane was discontinued and anesthesia was switched to alpha-chloralose (50 mg/kg intravenous bolus followed by 40 mg/(kg h) infusion). Imaging was performed through a 4 x 4 mm^2 closed cranial window on the parietal bone. The dura was removed and the cranial window was filled with 1.5% agarose and sealed with a microscope coverslip. An additional 1 mm^2 burr hole on the frontal bone was used to induce cortical spreading depression[17] by intracortical microinjection of KCl (10 µl, 1 M). Probe **10** was injected via the

femoral vein before imaging ($4x10^{-5}$ M blood concentration). All experimental procedures were approved by the Massachusetts General Hospital Subcommittee on Research Animal Care.

Imaging of pO_2 was performed with the thermoelectrically cooled camera (Imager QE, La Vision). The camera frame rate was synchronized with the triggering rate of the pulsed laser (10 Hz) used for excitation of phosphorescence (Brilliant, Big Sky Laser Technologies, 532 nm wavelength). The light from the pulsed laser was coupled into the multimode fiber and typically 5-10 mJ/cm^2 was delivered to the brain tissue at an angle of approximately 60 degrees with respect to the cranial window surface. The CCD exposure time was set to 50 μs. To obtain a two-dimensional map of cortical pO_2 a sequence of 24 frames was acquired with variable delay times with respect to the laser Q-switch opening. The calculation was performed by fitting the exponential decay lifetime τ of the phosphorescence intensity for each CCD pixel, followed by the conversion of phosphorescence lifetimes to the pO_2 values using a Stern-Volmer relationship. Single exponential decay of phosphorescence was assumed, and the fitting procedure was written in Matlab (MathWorks, Inc.) using a nonlinear least square fit with statistical weighting.

6. References

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15. $R_1 = \sum ||F_o| - |F_c|| / \sum |F_o|$

$wR_2 = \{ \sum w (F_o^2 - F_c^2)^2 / \sum w(F_o^2)^2 \}^{1/2}$

$GOF = \{ \sum w (F_o^2 - F_c^2)^2 / (n - p) \}^{1/2}$
where n = the number of reflections and p = the number of parameters refined.

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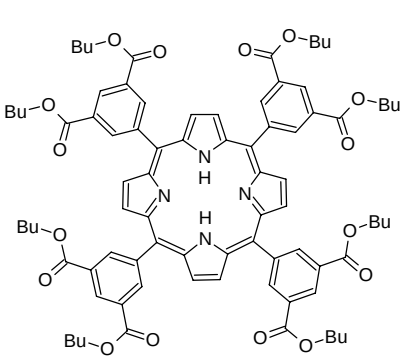
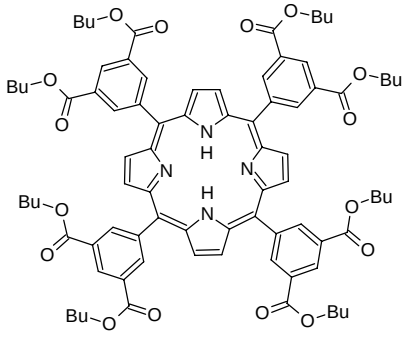
Spectra

H_2-1-OBu, ^1H

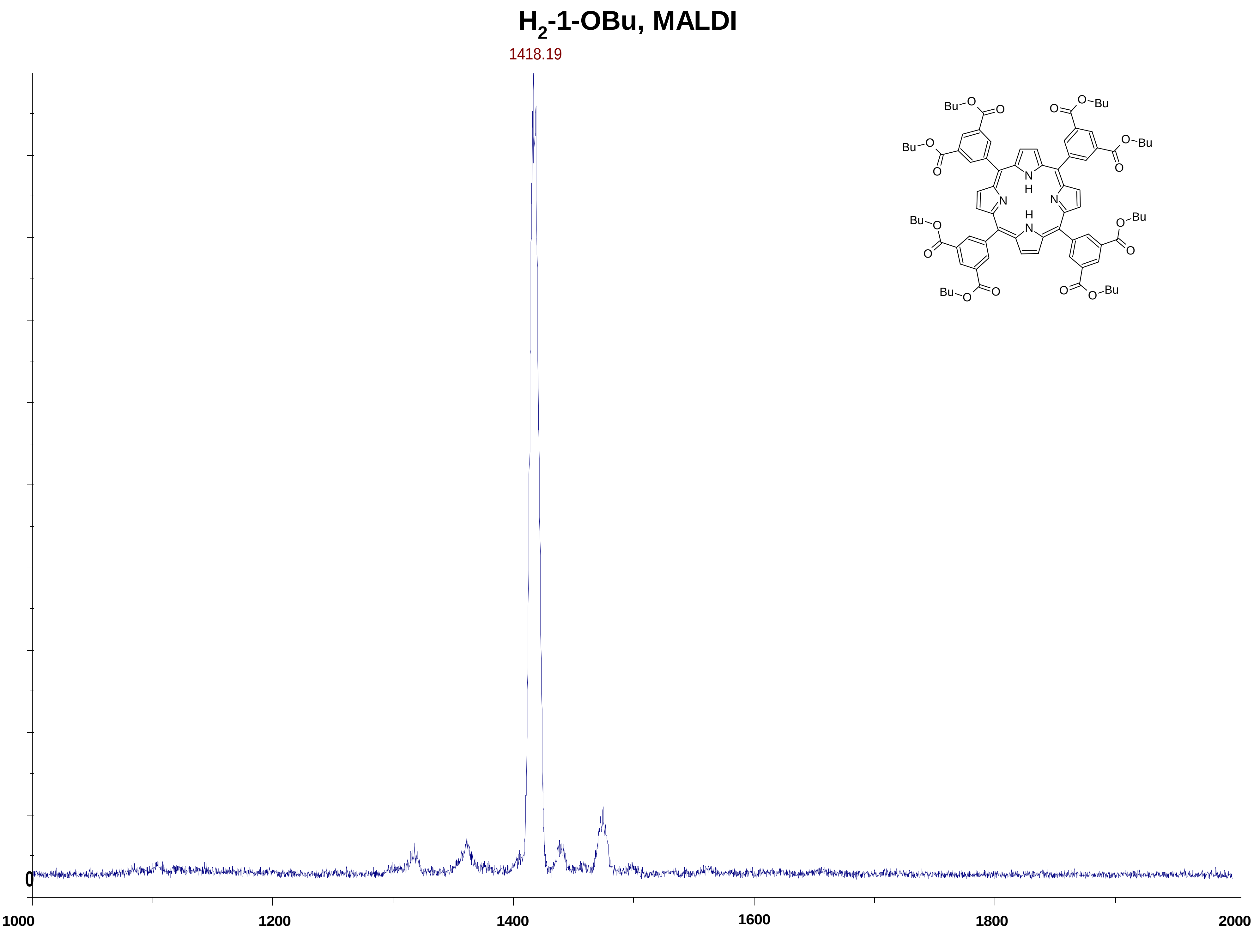


9.17
9.07
9.17
8.81
Chloroform-d
7.25
4.48
4.46
4.45
1.82
1.80
1.78
1.76
1.51
1.49
1.47
1.45
0.97
0.95
0.93
TMS
0.00
12.24
7.57
16.00
15.93
16.08
23.88
ppm

H_2-1-OBu, 1H

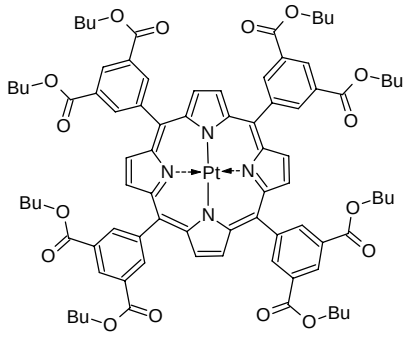


165.98
142.46
138.22
131.62
131.10
129.78
118.45
Chloroform-d
77.00
65.60
30.70
19.22
13.71
ppm



H2-1-OBu, MALDI
1418.19
0
1000
1200
1400
1600
1800
2000

Pt-1-OBu, ^{1}H

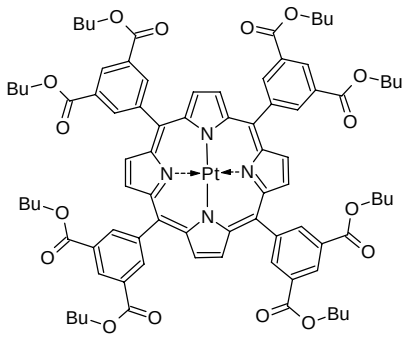


9.13
8.99
8.98
8.68
CDCl3
7.25
4.45
4.43
4.41
Water
1.80
1.79
1.77
1.75
1.73
1.48
1.47
1.45
1.43
0.95
0.93
0.91

7.70 7.93 16.00 16.05 16.01 23.70

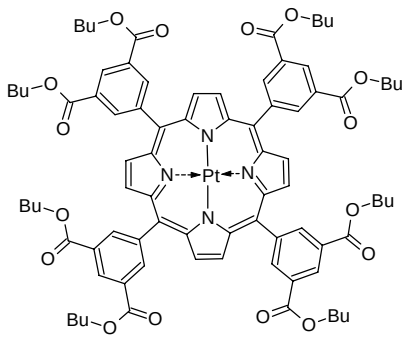
ppm

Pt-1-OBu, ^{13}C


Bu
O
O
N
Pt
N
N

165.90
141.65
140.96
137.63
131.10
129.91
120.70
Chloroform-d
65.61
30.69
19.22
13.71
ppm

Pt-1-OBu, MALDI

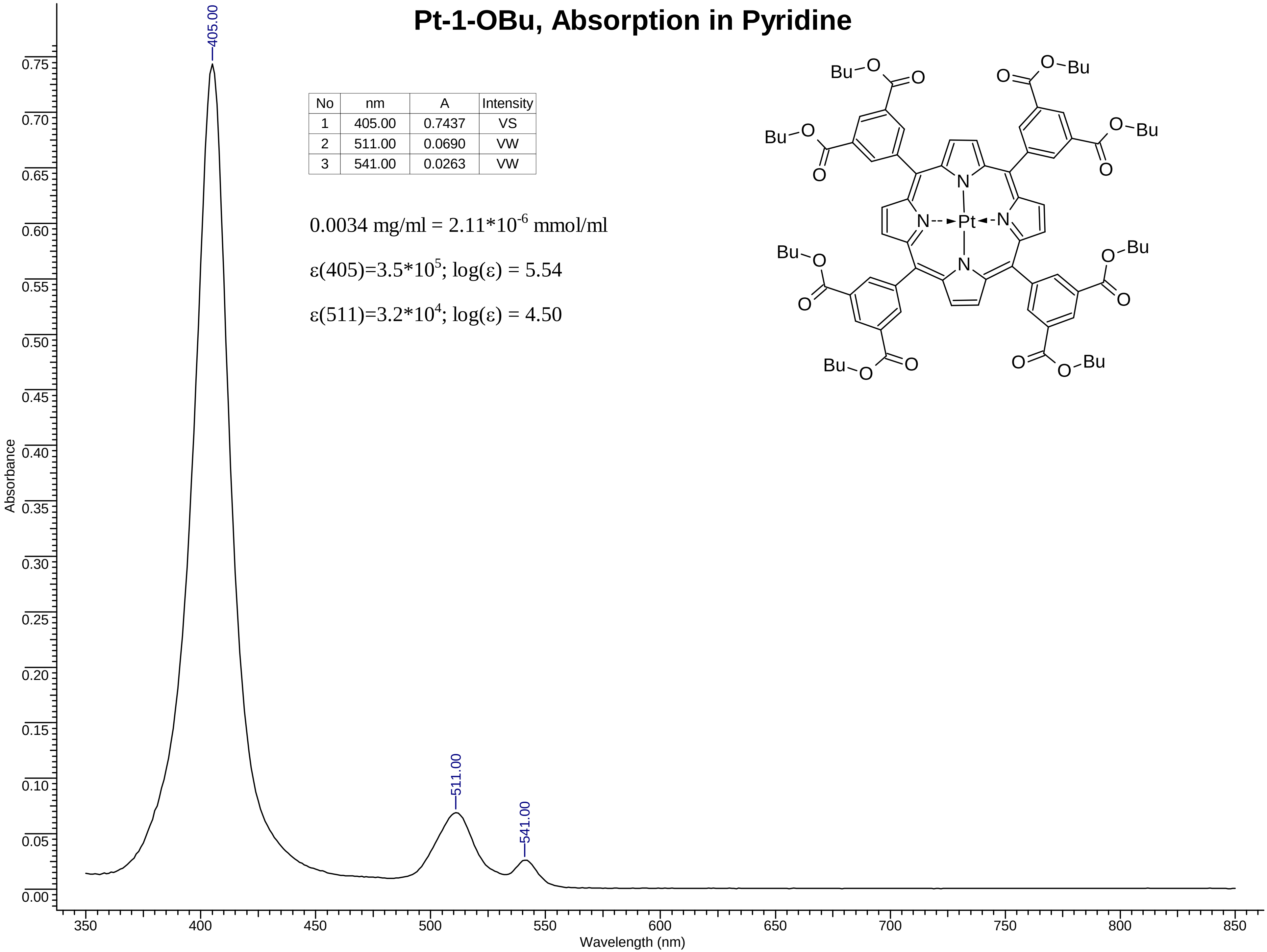


1608.62

1554.35

1000.0 1199.6 1399.2 Mass (m/z) 1598.8 1798.4 1998.0

Pt-1-OBu, Absorption in Pyridine



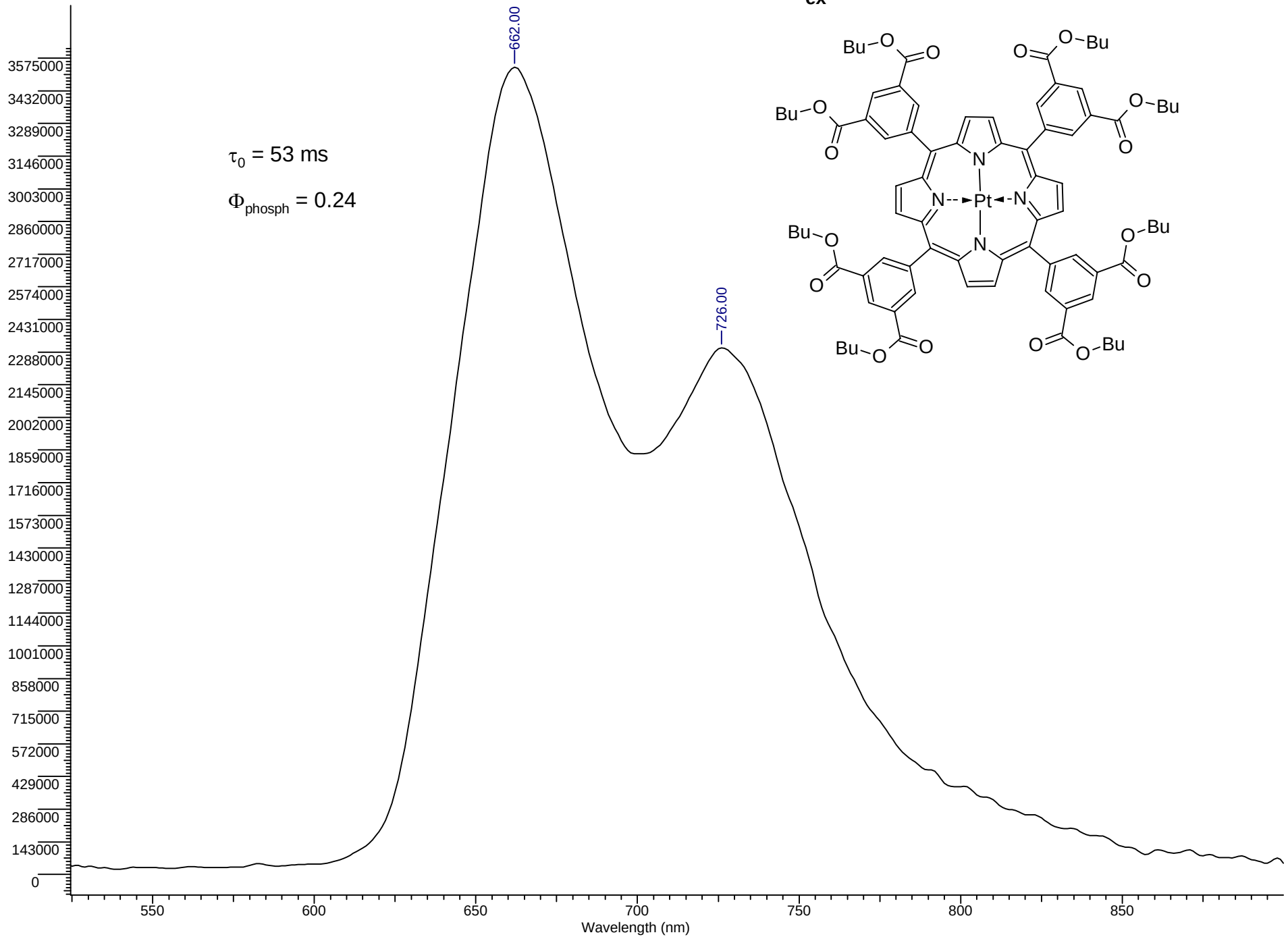
No	nm	A	Intensity
1	405.00	0.7437	VS
2	511.00	0.0690	VW
3	541.00	0.0263	VW

0.0034 mg/ml = $2.11*10^{-6}$ mmol/ml

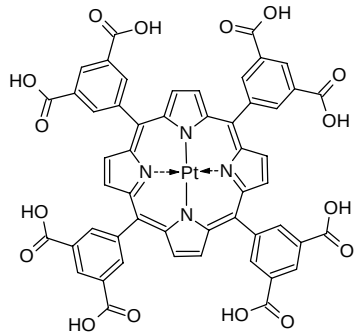
$\varepsilon(405)=3.5*10^5$; $\log(\varepsilon) = 5.54$

$\varepsilon(511)=3.2*10^4$; $\log(\varepsilon) = 4.50$

Pt-1-OBu, Emission in PhCN, λ_{ex}=515

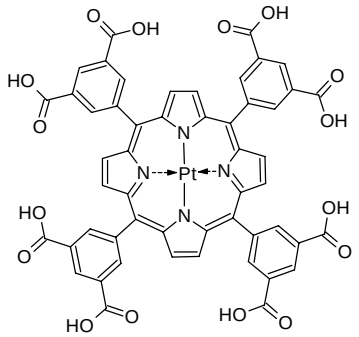


Pt-1-OH, ^{1}H

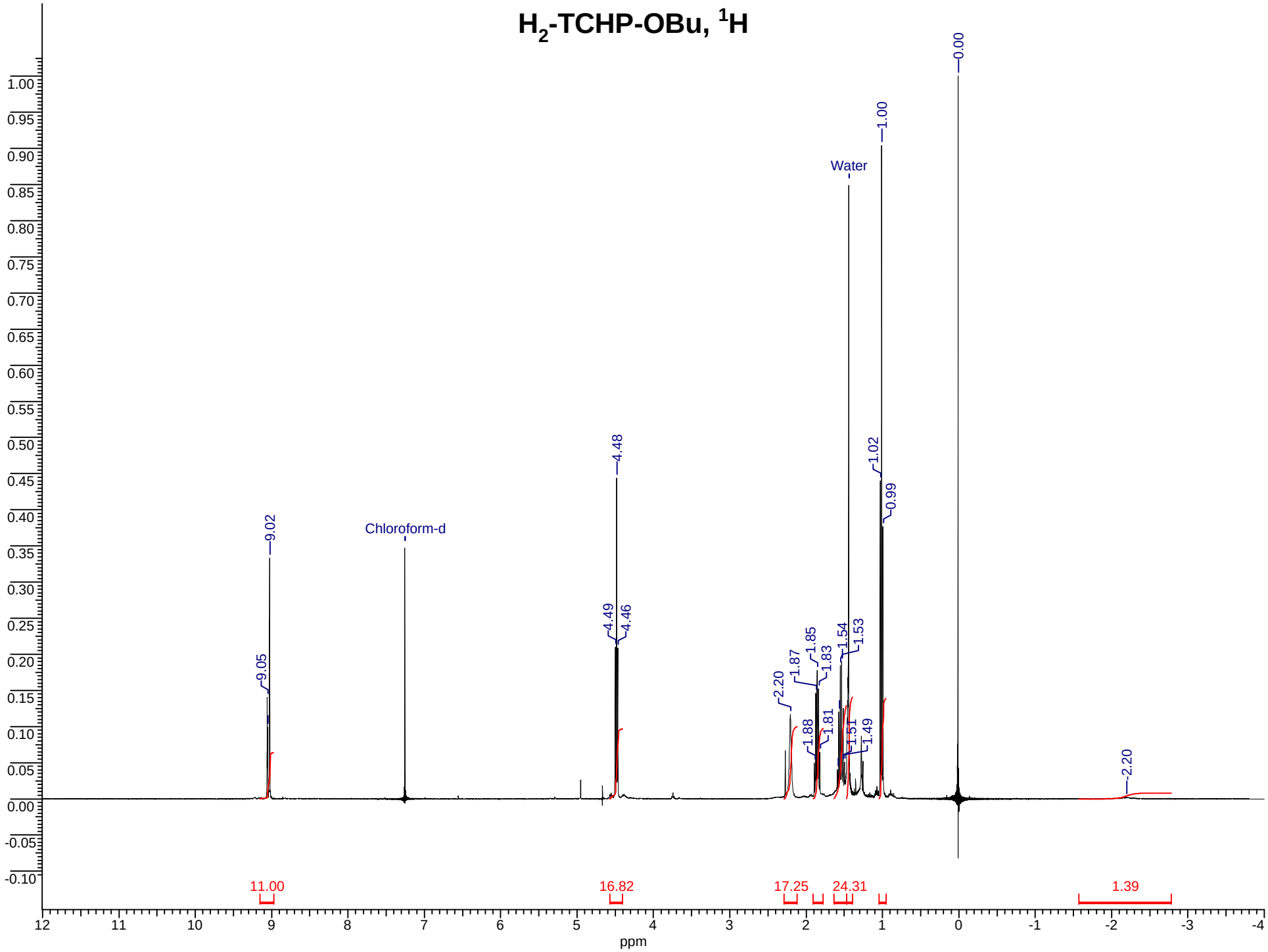

O
OH
HO
O
N
Pt
N
N
N
HO
O
OH
O
HO
O
OH
O
HO
O

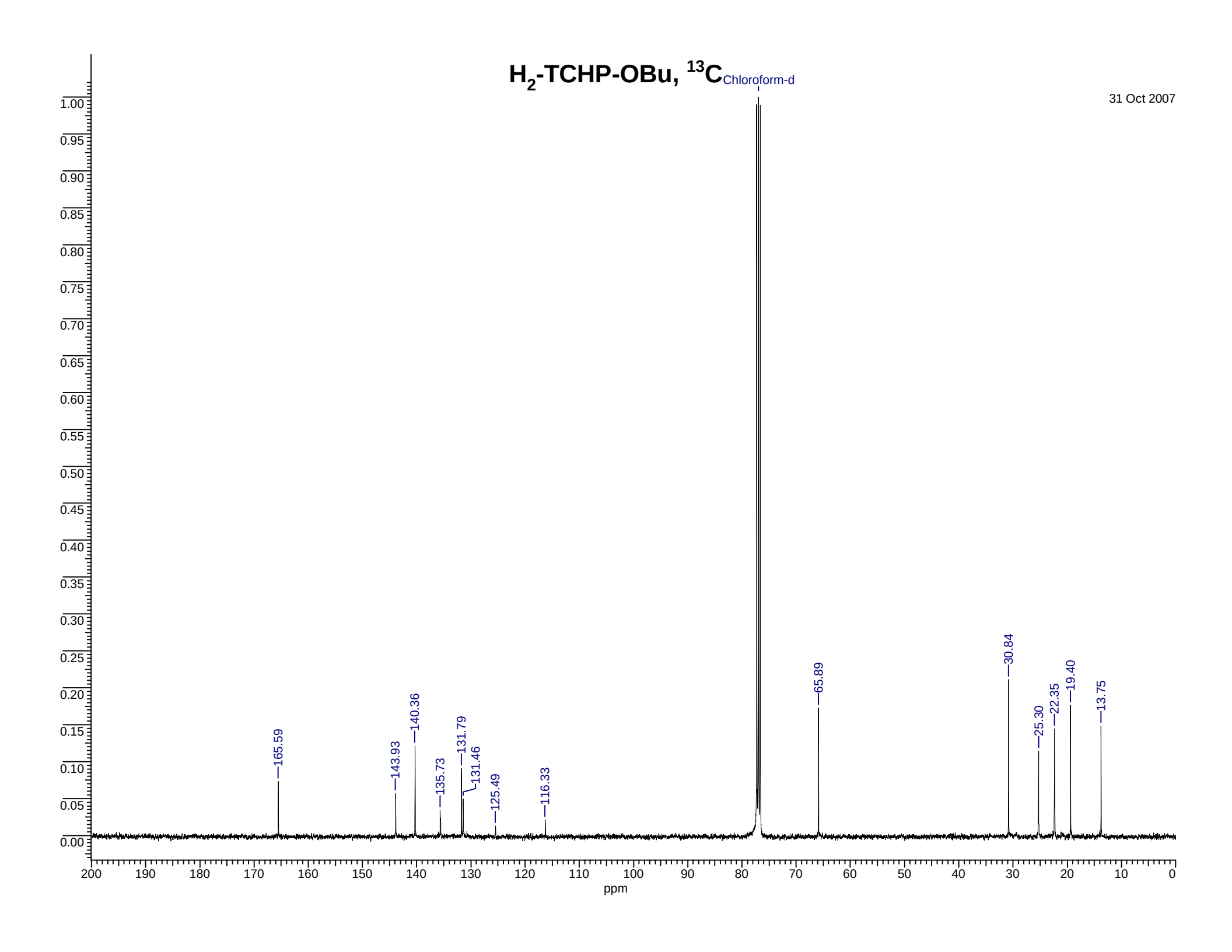
8.76
8.86
8.95
DMSO-d6
2.49
8.09
ppm

Pt-1-OH, ^{13}C

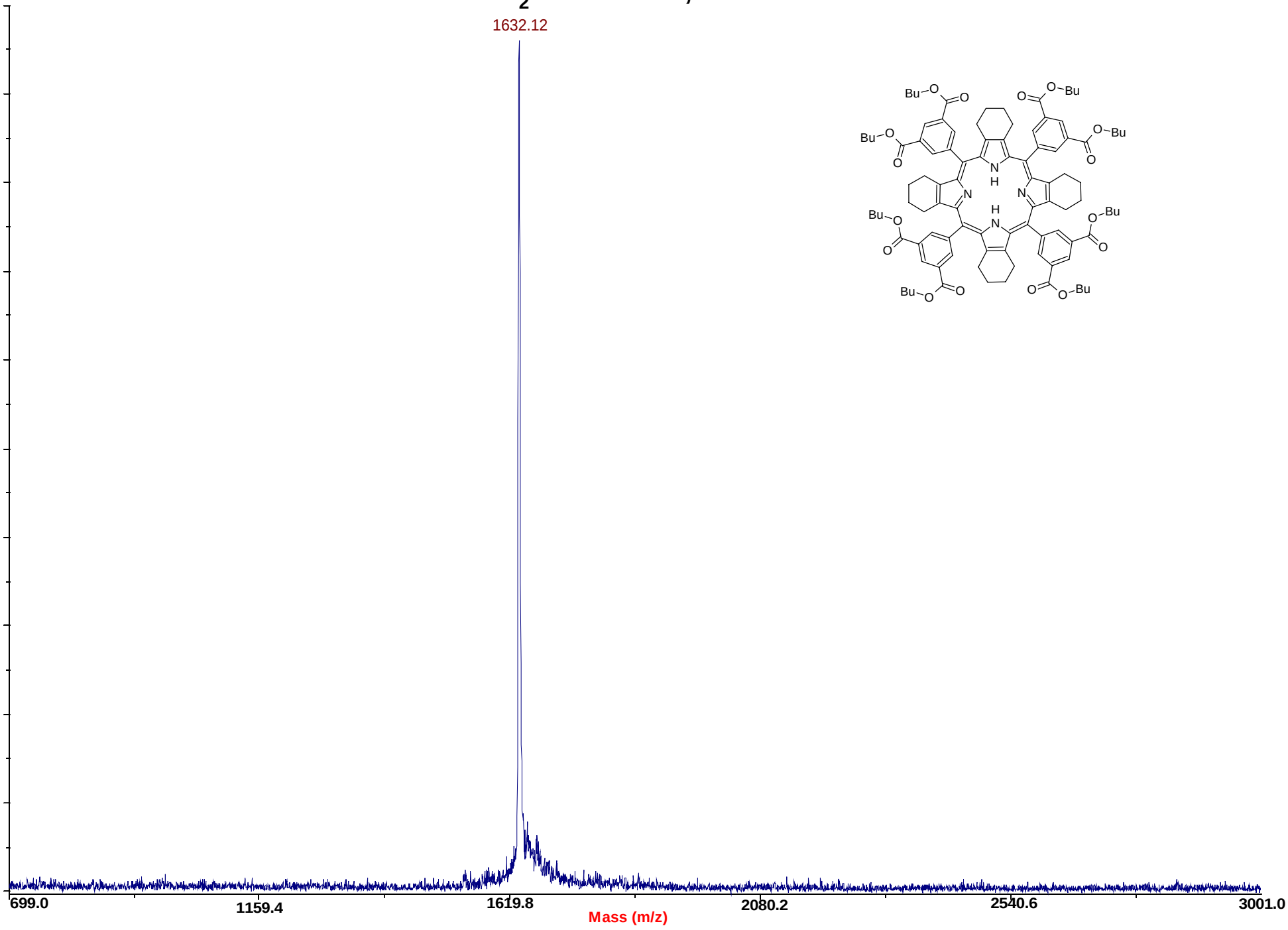

O
OH
HO
O
N
Pt
N
N
N
HO
O
OH
O
HO
O
HO
O
OH
O
HO
O

136.59
165.94
140.30
139.91
130.58
130.18
129.35
120.06
Spike
DMSO-d6
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
-0.05
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

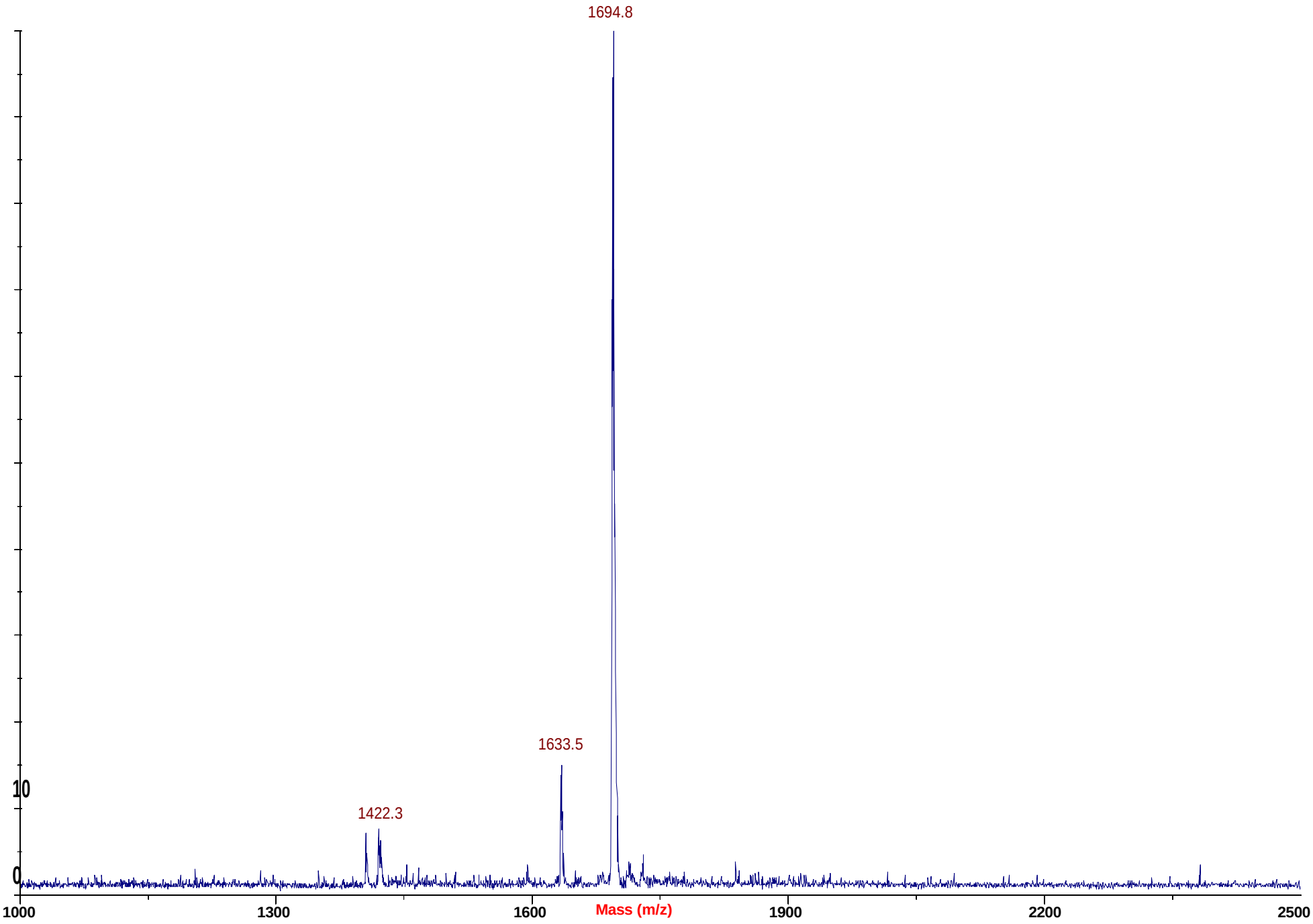

H2-TCHP-OBu, 1H
Water
Chloroform-d
9.05
9.02
4.49
4.48
4.46
2.20
1.88
1.87
1.85
1.83
1.81
1.54
1.53
1.51
1.49
1.02
1.00
0.99
0.00
2.20
11.00
16.82
17.25
24.31
1.39
ppm


H2-TCHP-OBu, 13C
Chloroform-d
31 Oct 2007
165.59
143.93
140.36
135.73
131.79
131.46
125.49
116.33
65.89
30.84
25.30
22.35
19.40
13.75
ppm

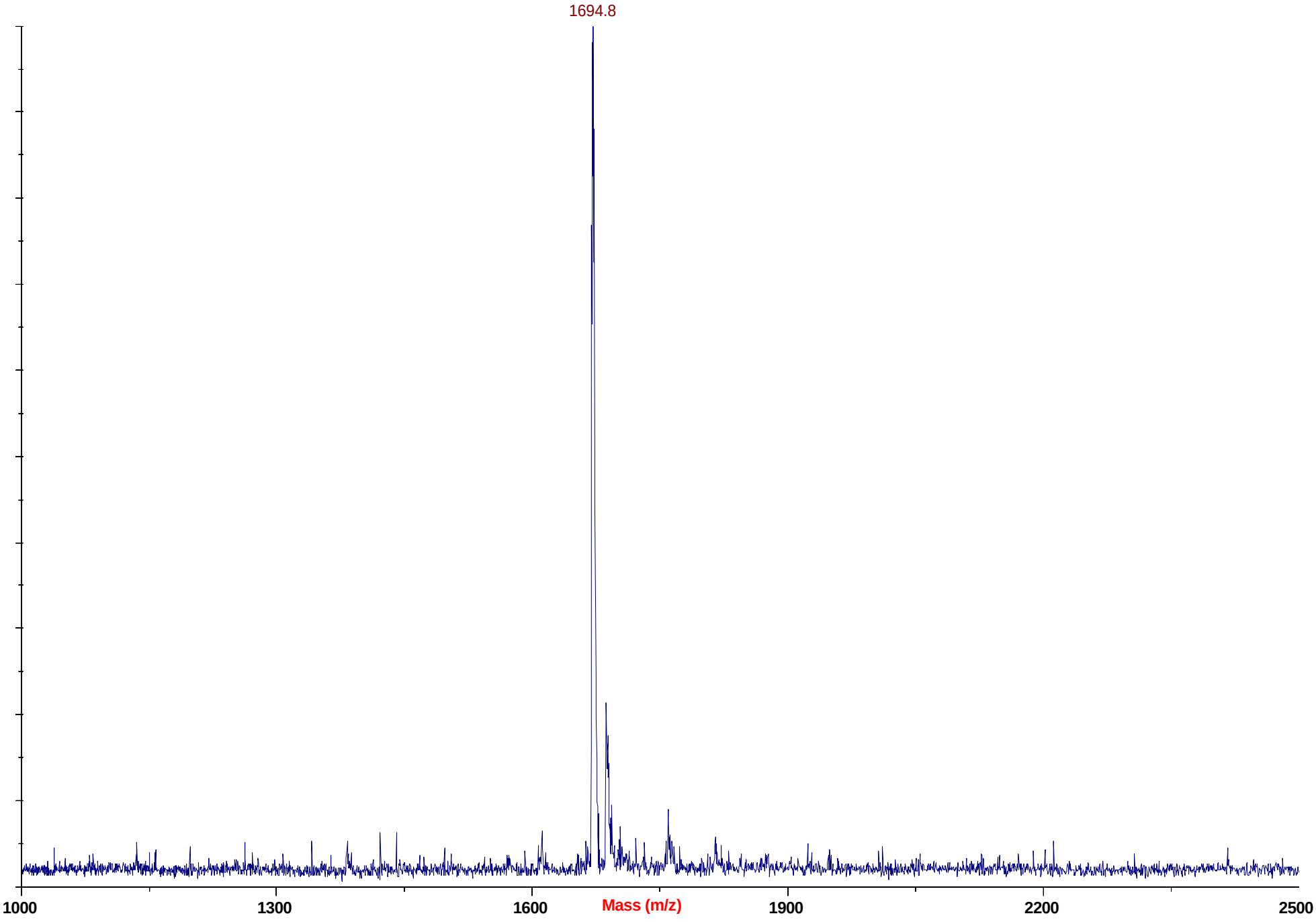
H_2-TCHP-OBu, MALDI



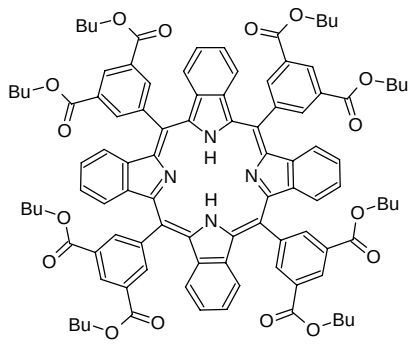
Cu-TCHP-OBu, MALDI



Cu-2-OBu, MALDI



H_2-2-OBu, ^1H

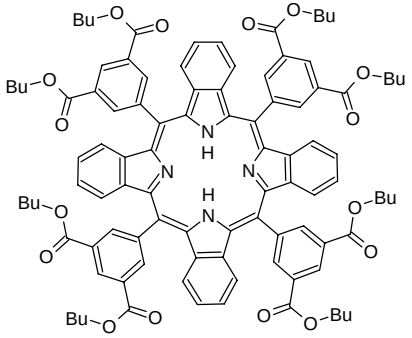


9.28
9.21
Chloroform-d
7.25
7.07
4.47
4.45
4.43
1.84
1.82
1.80
1.78
1.77
Water
1.47
1.46
1.44
1.42
0.96
0.94
0.92
-1.01

8.13
10.73
18.69
24.46
27.21
2.29

ppm

H_2-2-OBu, ^{13}C



Chloroform-d

65.69

30.76

19.27

13.68

165.83

142.54

139.04

132.05

131.24

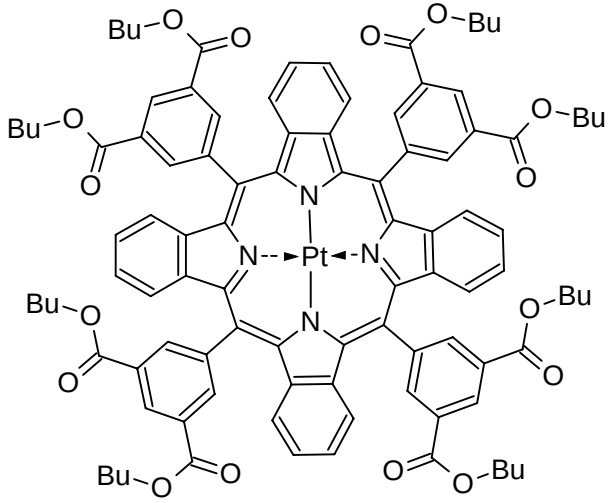
126.63

124.25

114.13

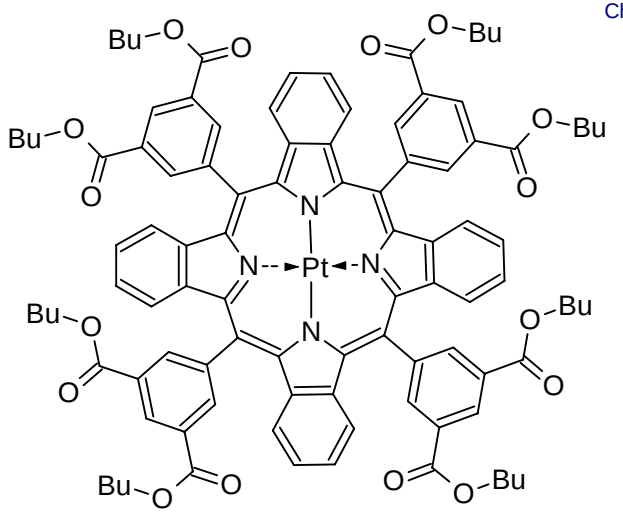
ppm

Pt-2-OBu, ^{1}H


Bu–O
O
O–Bu
N
Pt
N

9.29
9.11
Chloroform-d
7.25
7.21
6.96
6.95
6.94
6.93
4.44
4.42
4.41
Water
1.79
1.77
1.75
1.81
1.74
1.48
1.47
1.45
1.43
1.41
1.39
0.94
0.92
0.90
8.02
8.02
8.09
16.00
16.09
16.12
24.05
ppm

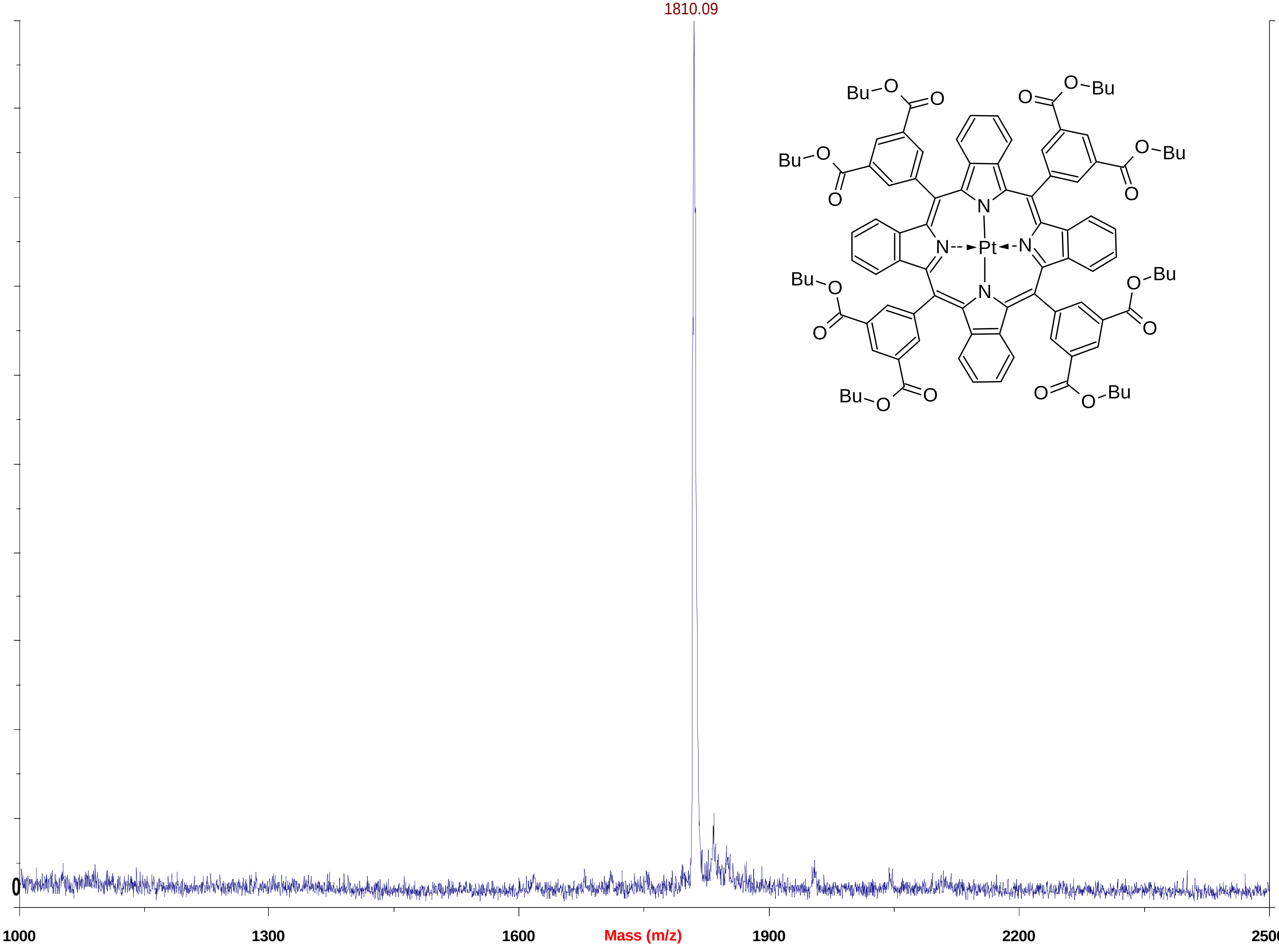
Pt-2-OBu, ^{13}C



Chloroform-d
77.00
30.62
65.74
19.23
13.73
138.23
126.13
123.95
132.18
131.47
165.75
142.07
137.30
136.03
116.60

ppm

Pt-2-OBu, MALDI



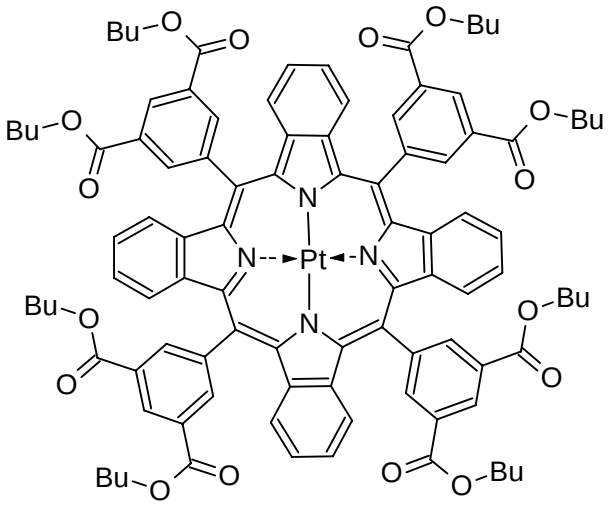
Pt-2-OBu, Absorption in Pyridine

No	nm	A	Intensity
1	432.00	0.5540	VS
2	570.00	0.0482	VW
3	621.00	0.3693	S

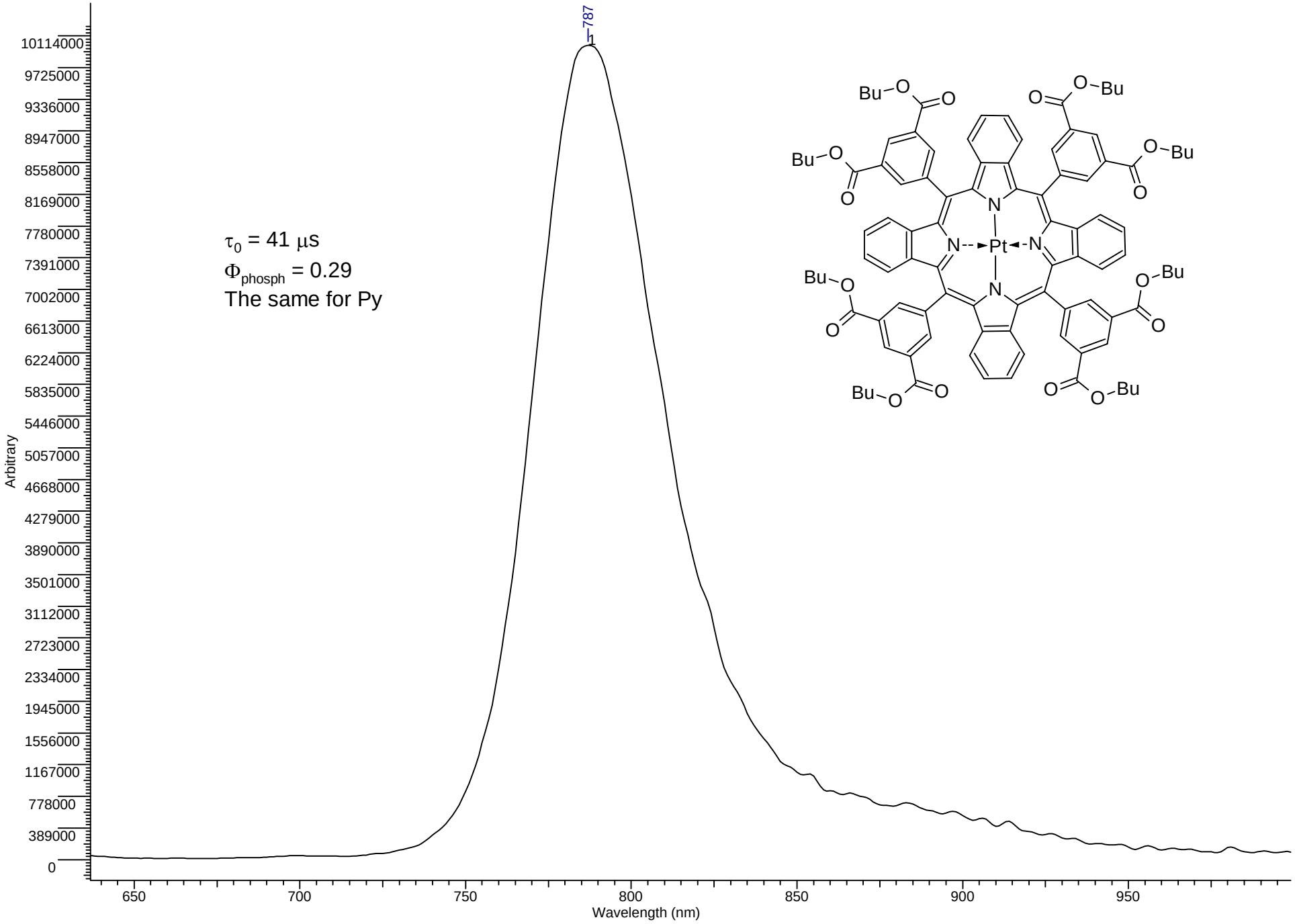
0.0058 mg/ml = $3.21*10^{-6}$ mmol/ml

$\varepsilon(432)=1.7*10^{5}$ log(ε) = 5.23

$\varepsilon(511)=1.1*10^{5}$ log(ε) = 5.00



Pt-2-OBu, Emission in PhCN, λ_{ex} = 621 nm

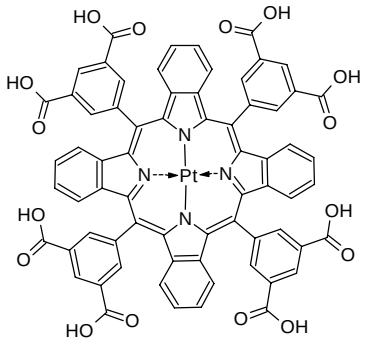


τ_0 = 41 μs

Φ_{phosph} = 0.29

The same for Py

Pt-2-OH, ^{1}H



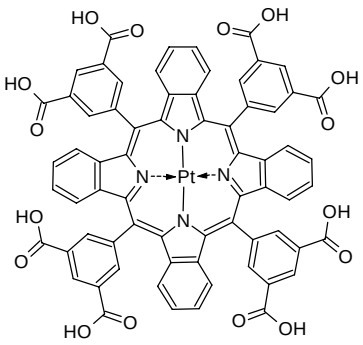
DMSO-d6

9.04
9.11
7.37
7.36
7.34
6.92
6.92
6.91
3.37
2.49

11.89
8.00
7.97
6.87

ppm

Pt-2-OH, ^{13}C



DMSO-d6

39.50

166.46

141.31

137.63

136.74

135.34

132.72

131.17

126.51

123.57

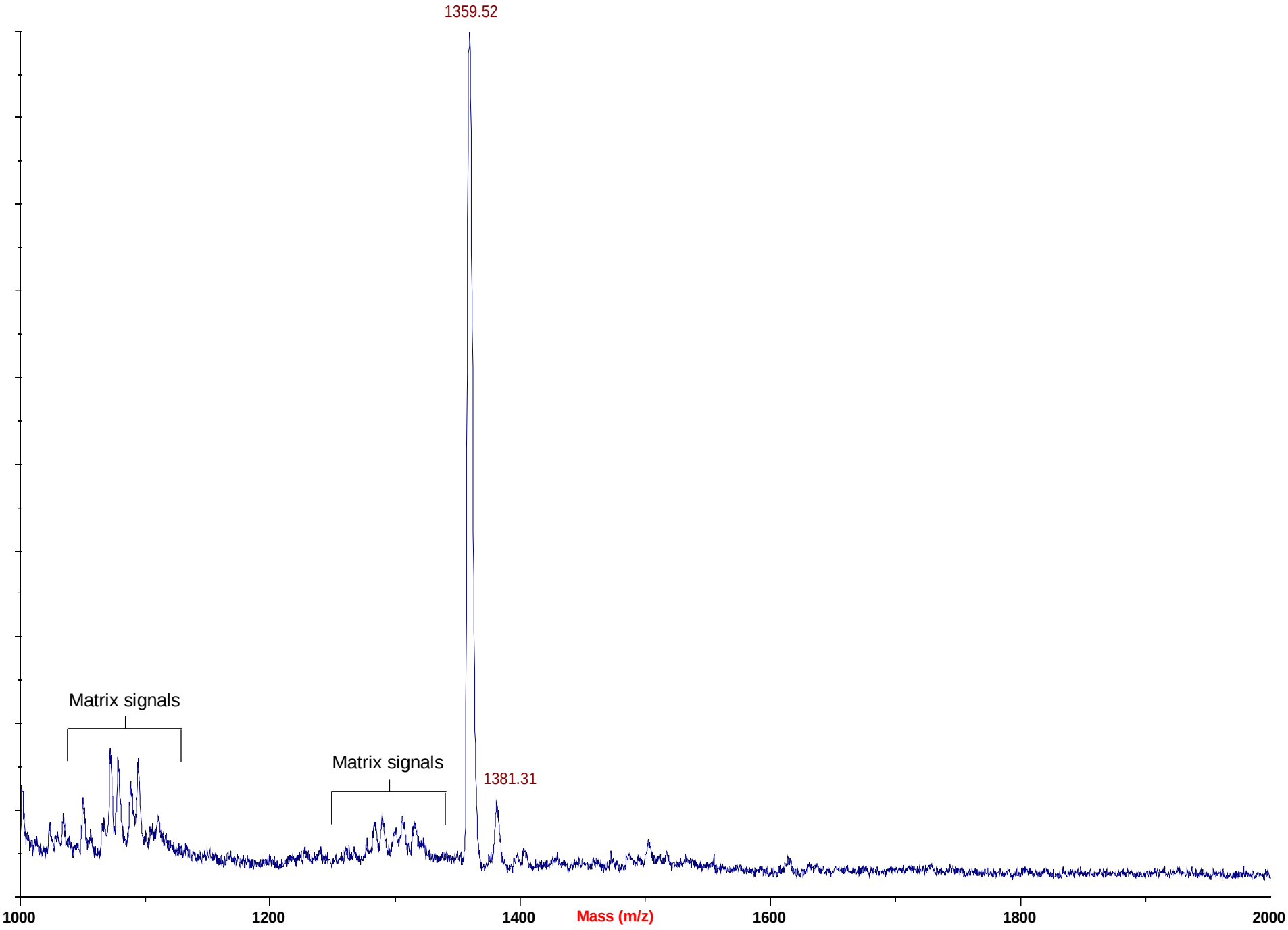
116.62

0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0.00
-0.01
-0.02

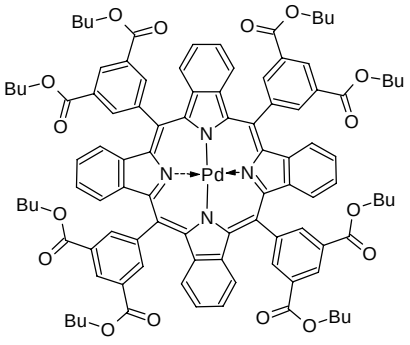
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

ppm

Pt-2-OH, MALDI

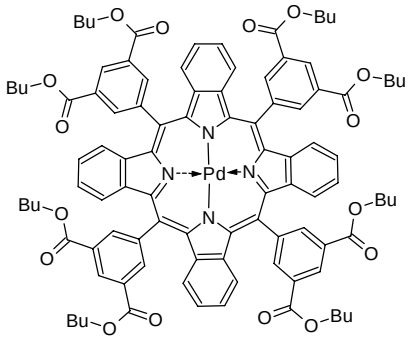

1359.52
Matrix signals
Matrix signals
1381.31
1000
1200
1400
Mass (m/z)
1600
1800
2000

Pd-2-OBu, ^{1}H


Bu–O
O
O–Bu
N
Pd
N
N

9.30
9.13
9.30
Chloroform-d
7.25
7.21
7.00
7.00
6.99
6.98
7.01
6.97
4.43
4.45
4.42
0.93
0.95
0.91
1.80
1.79
1.77
1.46
1.44
1.48
1.42
1.82
1.75
1.49
1.40
7.81
8.67
7.55
16.00
15.91
15.60
23.34
ppm

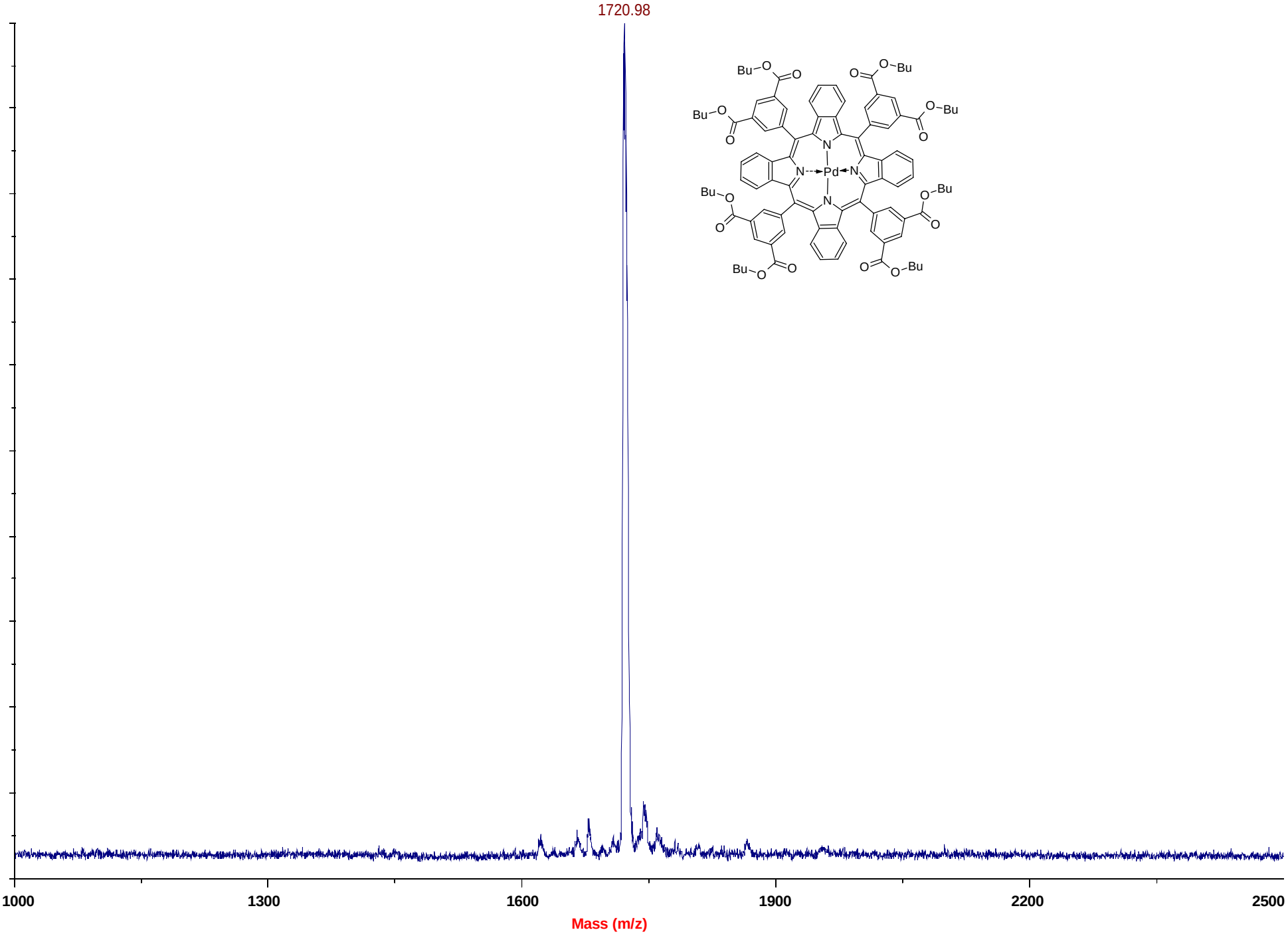
Pd-2-OBu, ^{13}C



65.69
30.76
19.27
13.67
Chloroform-d
138.53
126.00
123.87
132.28
131.36
137.91
165.75
142.41
116.36

ppm

Pd-2-OBu, MALDI



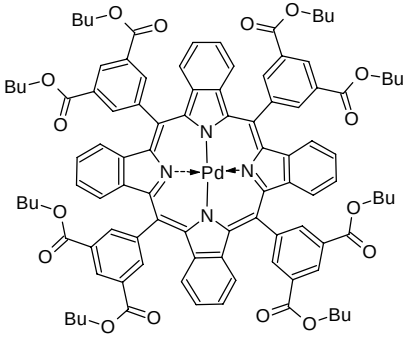
Pd-2-OBu, Absorption in Pyridine

No	nm	A	Intensity
1	419.00	0.1528	W
2	445.00	0.7840	VS
3	586.00	0.0404	VW
4	635.00	0.3130	M

0.0046 mg/ml = $2.67*10^{-6}$ mmol/ml

$\varepsilon(445)=2.9*10^{5}$ $\log(\varepsilon) = 5.46$

$\varepsilon(635)=1.1*10^{5}$ $\log(\varepsilon) = 5.00$

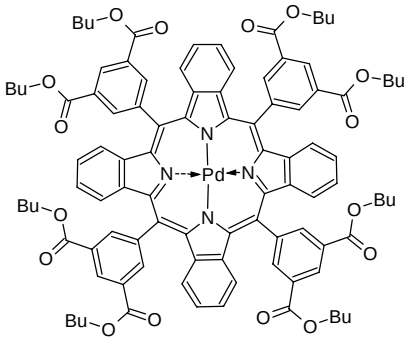


Pd-2-OBu, Emission in PhCN, λ_{exc} = 635 nm

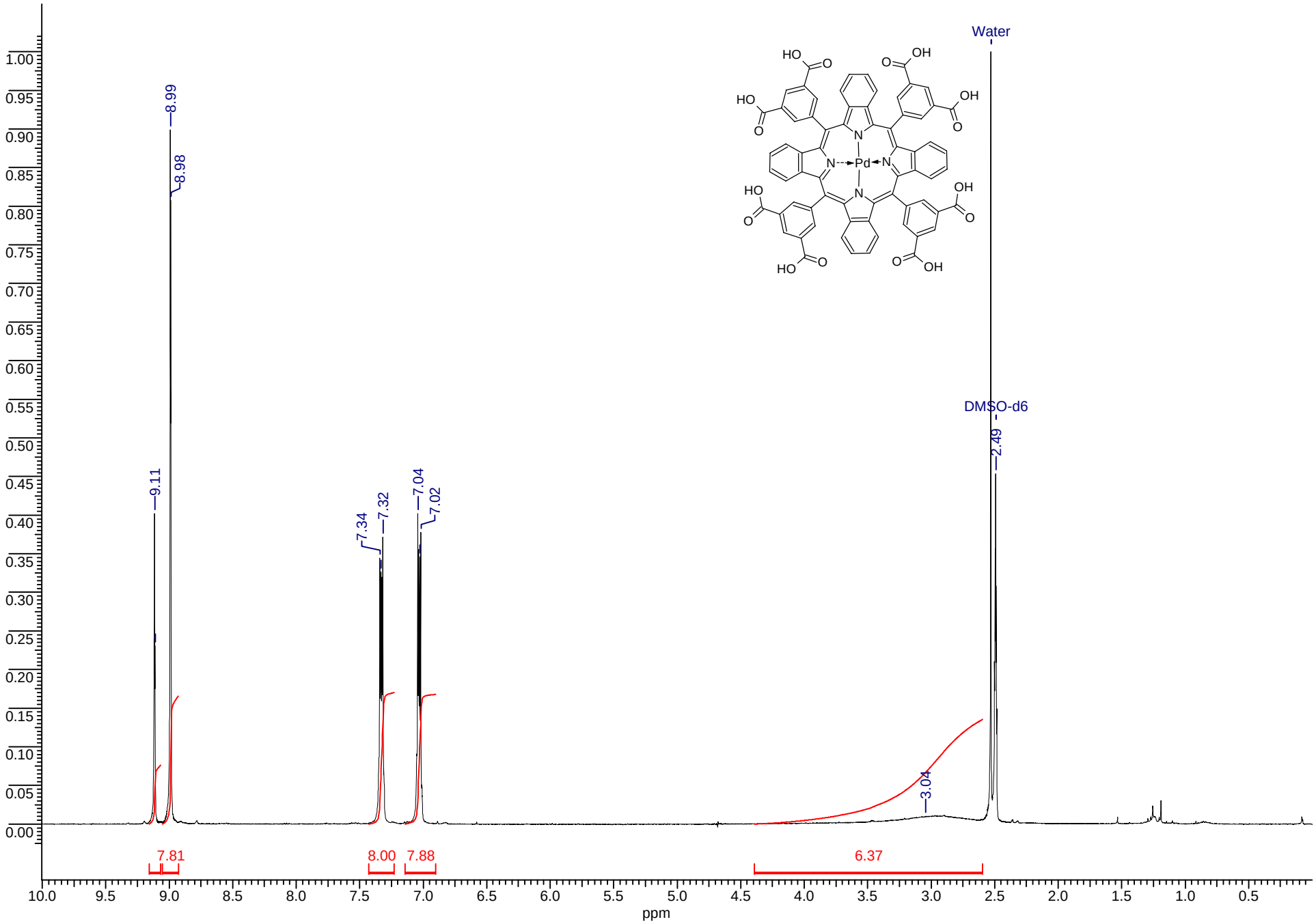
τ_0 = 210 μs

Φ_{phosph} = 0.08

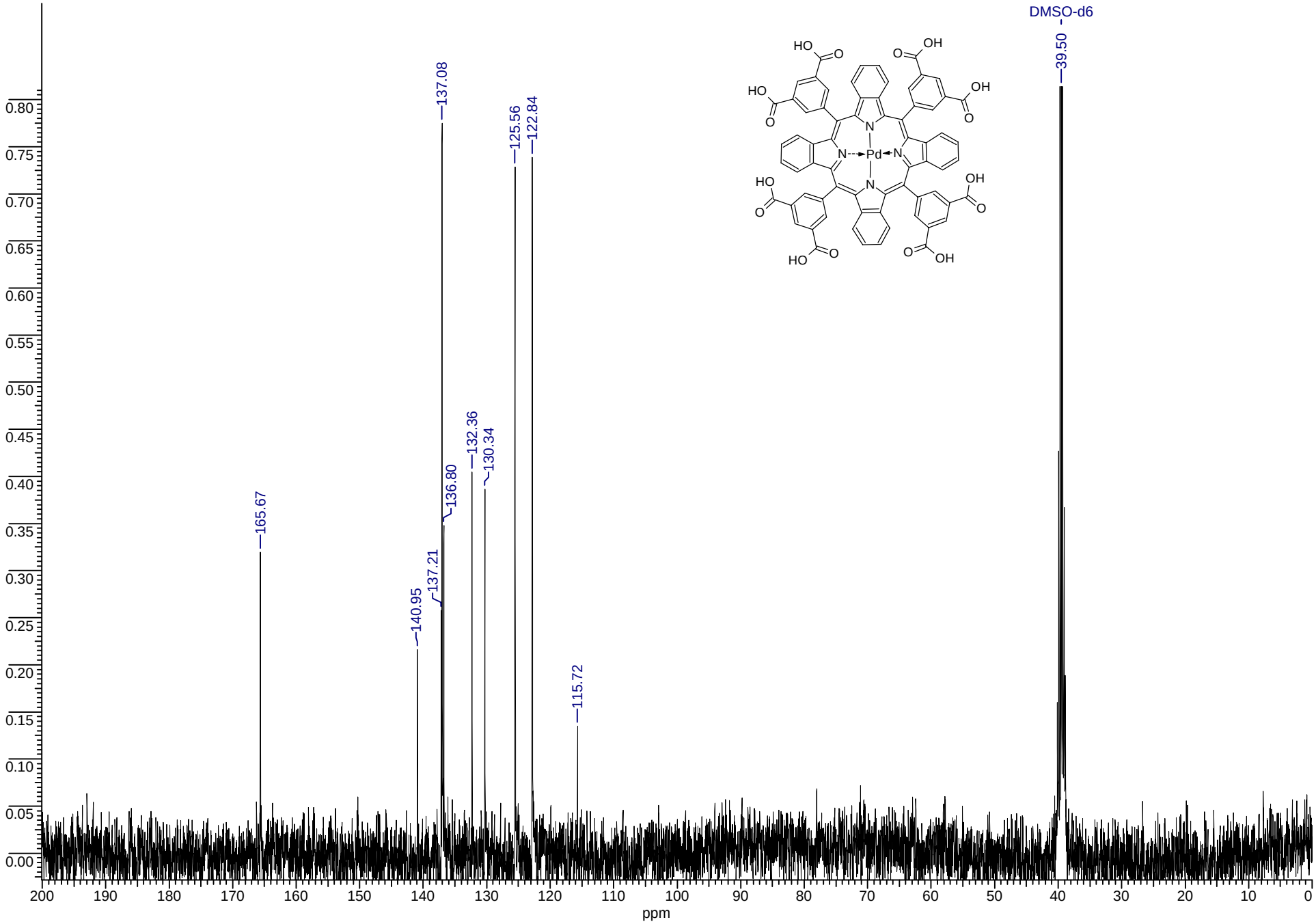
The same for Py



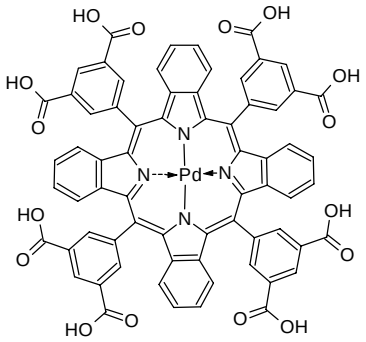
Pd-2-OH, ^{1}H


Water
DMSO-d6
9.11
8.99
8.98
7.34
7.32
7.04
7.02
2.49
3.04
7.81
8.00
7.88
6.37
ppm

Pd-2-OH, ^{13}C

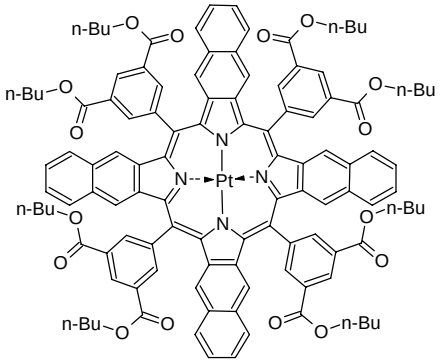

DMSO-d6
39.50
137.08
125.56
122.84
165.67
136.80
132.36
130.34
140.95
137.21
115.72
ppm

Pd-2-OH, MALDI


HO
O
O
OH
HO
O
O
OH
N
N
Pd
N
N
HO
O
O
OH
HO
O
O
OH

1271.38
1273.38
1275.40
1000
1300
1600
1900
2200
2500
Mass (m/z)

Pt-3-OBu, ^{1}H

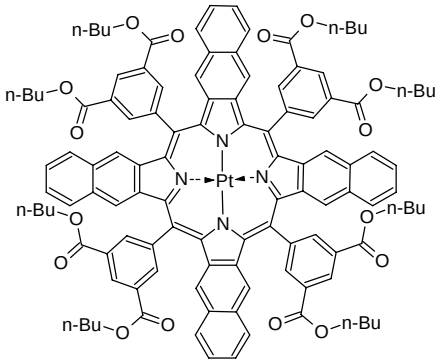


9.57
9.43
DMF-d7
7.86
7.85
7.84
7.72
7.71
7.70
4.62
4.61
4.59
Water
DMF-d7
DMF-d7
1.94
1.92
1.91
1.89
1.87
1.61
1.59
1.57
1.55
1.53
1.51
1.03
1.02
1.00

6.91
11.79
16.00
15.86
15.87
23.17

ppm

Pt-3-OBu, ^{13}C


n-Bu
O
N
Pt

DMF-d7
DMF-d7
DMF-d7
165.78
142.98
138.96
135.59
134.05
131.62
131.33
129.19
127.08
123.98
115.99
65.91
31.07
19.35
13.38
ppm

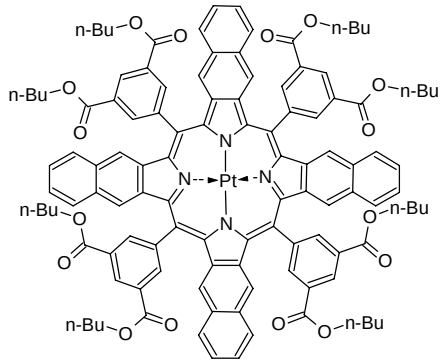
Pt-3-OBu, Absorption in Pyridine

No	nm	A	Intensity
1	442.00	0.4148	S
2	631.00	0.0789	W
3	699.00	0.5579	VS

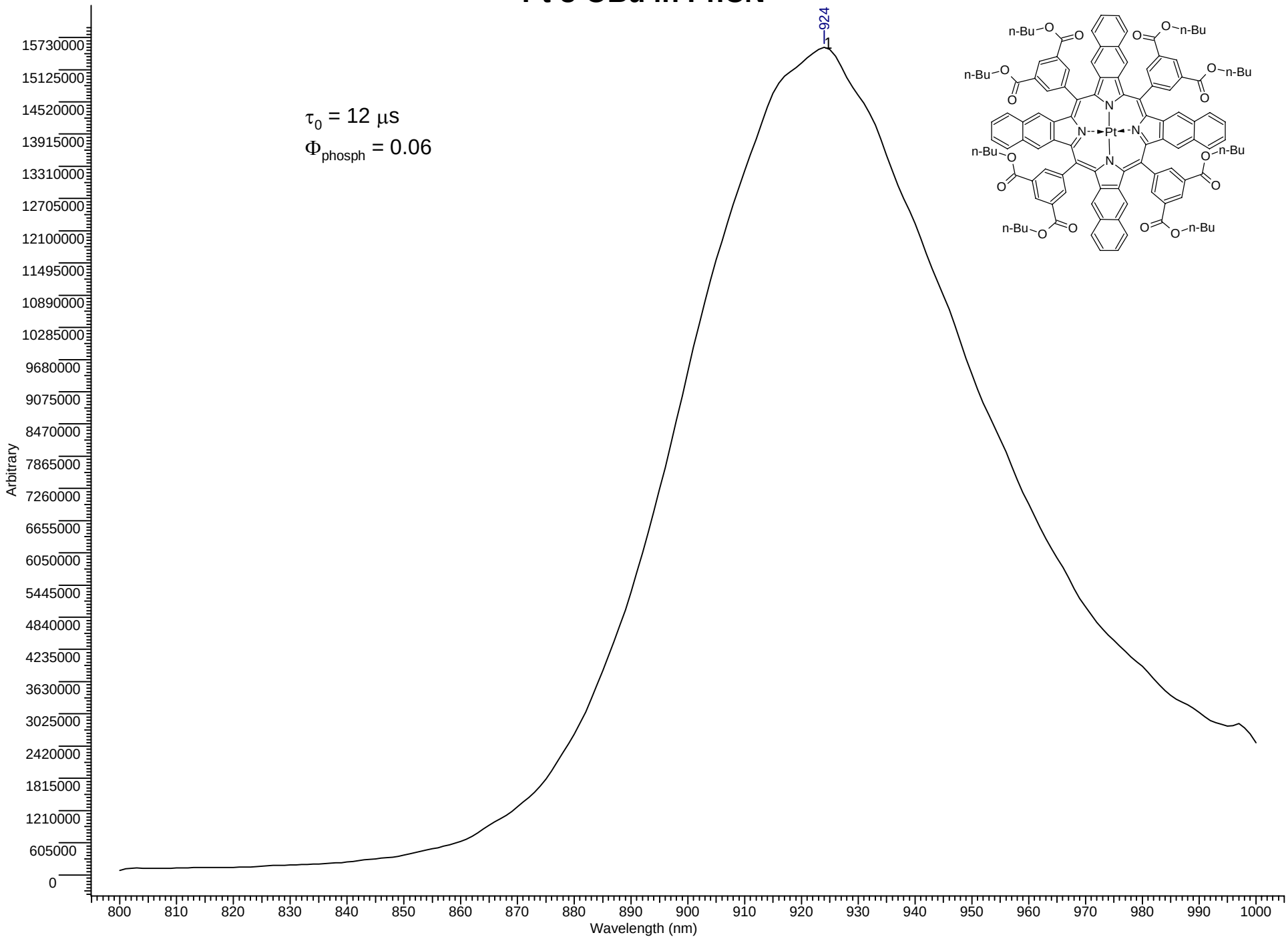
0.0059 mg/ml = $2.94*10^{-6}$ mmol/ml

$\varepsilon(442)=1.4*10^{5}$ $\log(\varepsilon) = 5.14$

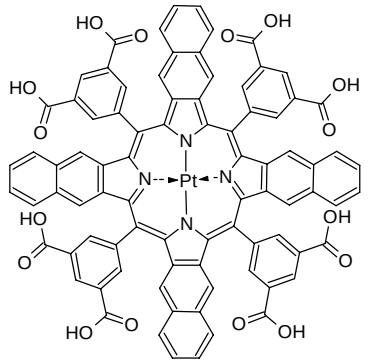
$\varepsilon(511)=1.9*10^{5}$ $\log(\varepsilon) = 5.28$



Pt-3-OBu in PhCN

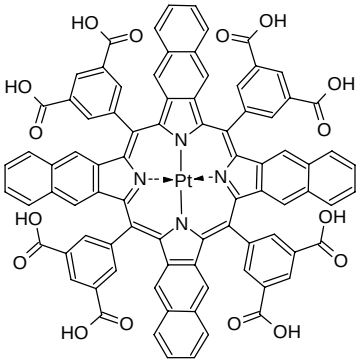


Pt-3-OH, ^{1}H


HO
O
OH
N
Pt
N
N
N

DMF-d7
8.01
9.47
9.28
7.71
7.71
7.66
7.57
7.57
7.55
3.40
Water
3.08
DMF-d7
DMF-d7
DMF
DMF
8.52
9.66
7.64
ppm

Pt-3-OH, ^{13}C

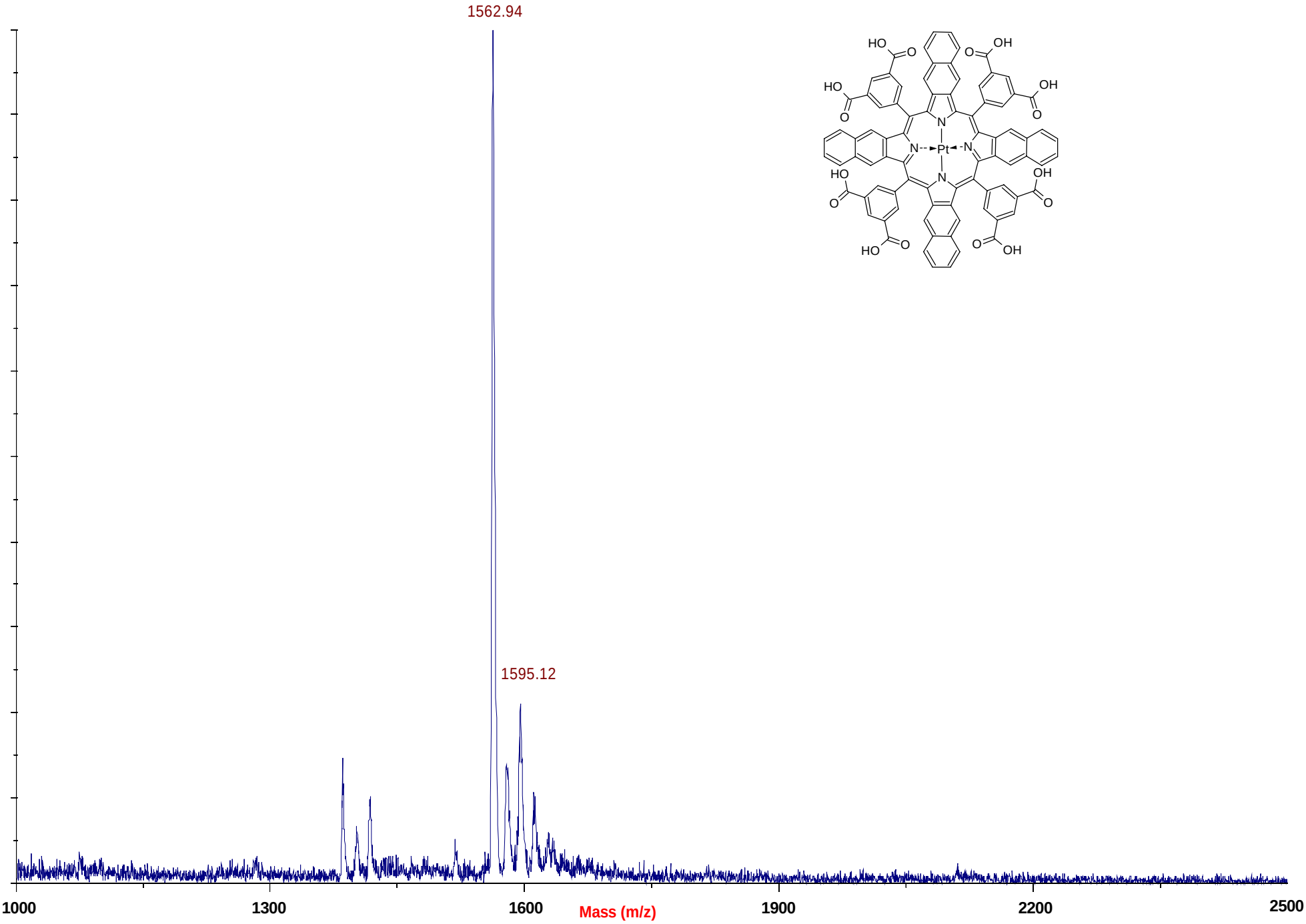


Dimethylformamid-d7

162.70
167.24
143.04
139.04
135.79
134.81
132.10
131.73
129.46
127.35
124.11
116.53
Spike

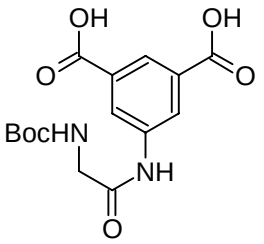
ppm

Pt-3-OH, MALDI

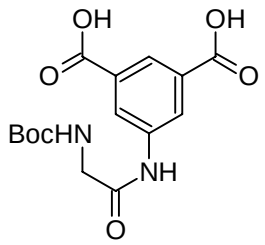

1562.94
1595.12
1000
1300
1600
1900
2200
2500
Mass (m/z)

HO
O
OH
O
HO
O
OH
O
N
N
Pt
N
N
HO
O
OH
O
HO
O
O
OH

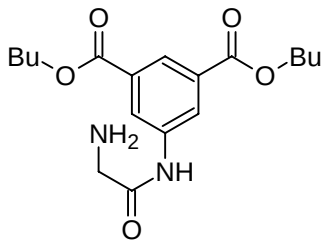
BocNH-AG[1]-OH (4), ^{1}H



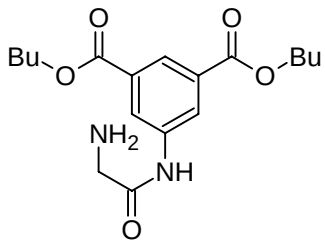
BocNH-AG^{1}-OH (4), ^{13}C



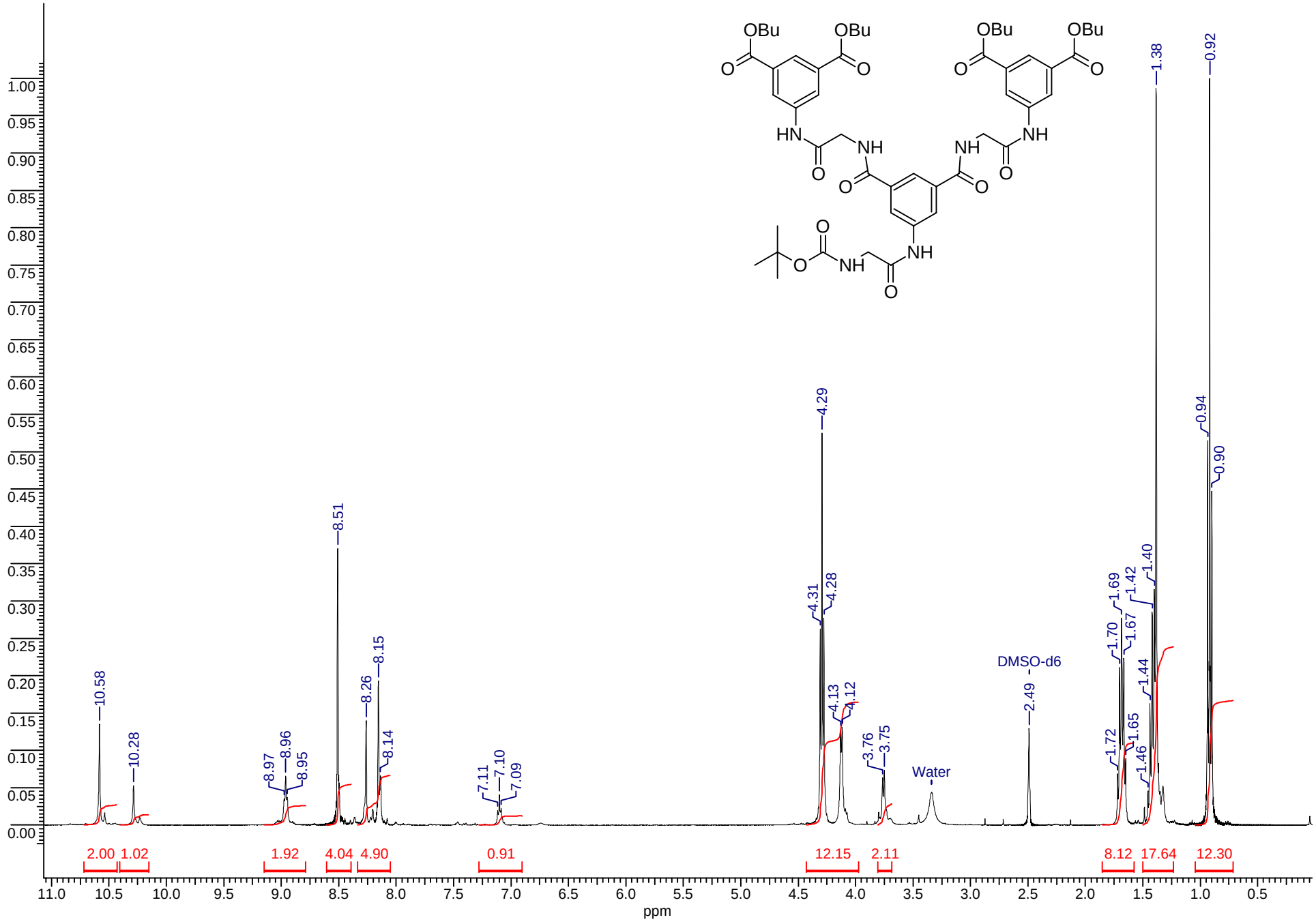
H_2N-AG^1-OBu (5), ^{1}H



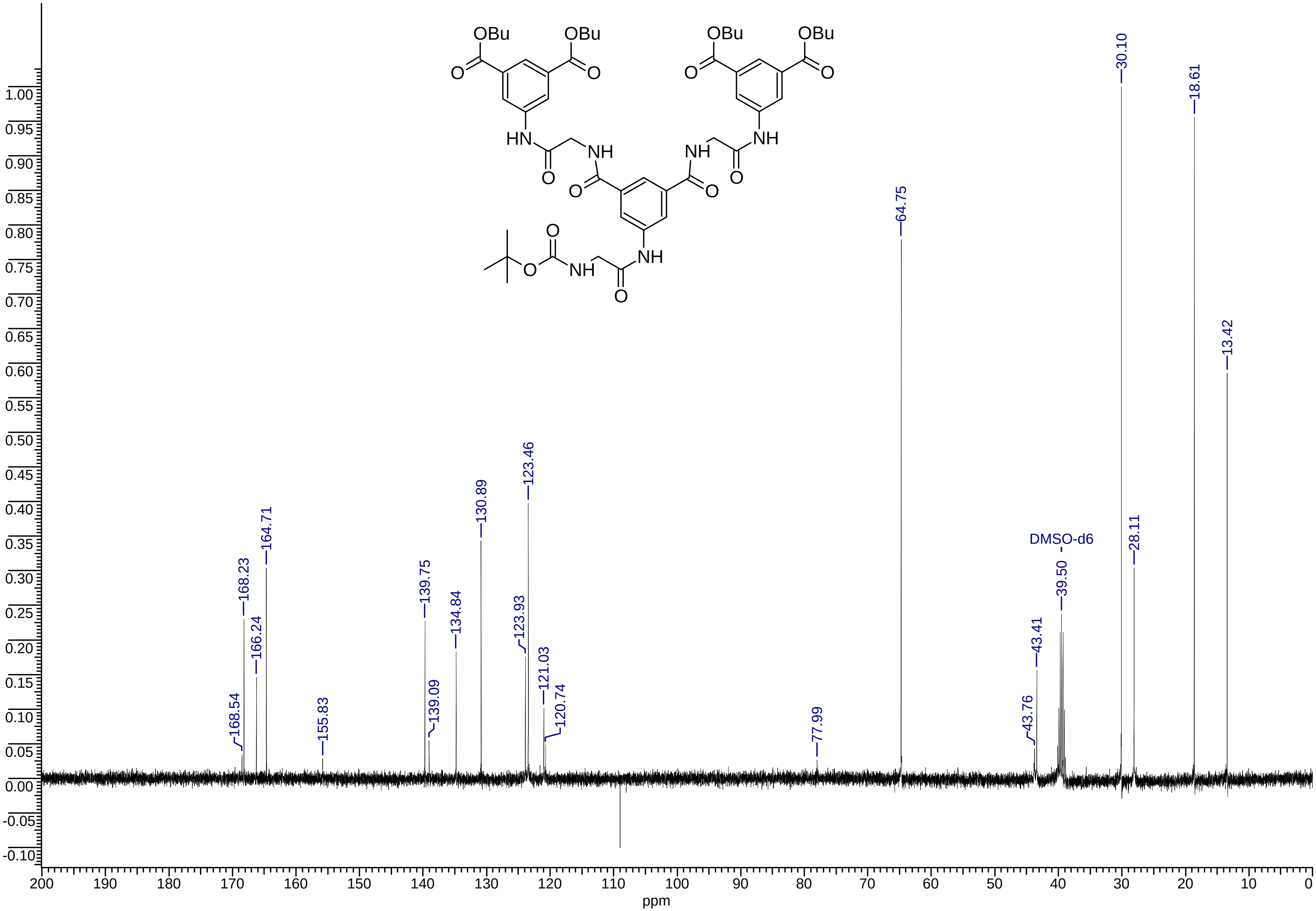
H_2N-AG[1]-OBu (5), ^{13}C



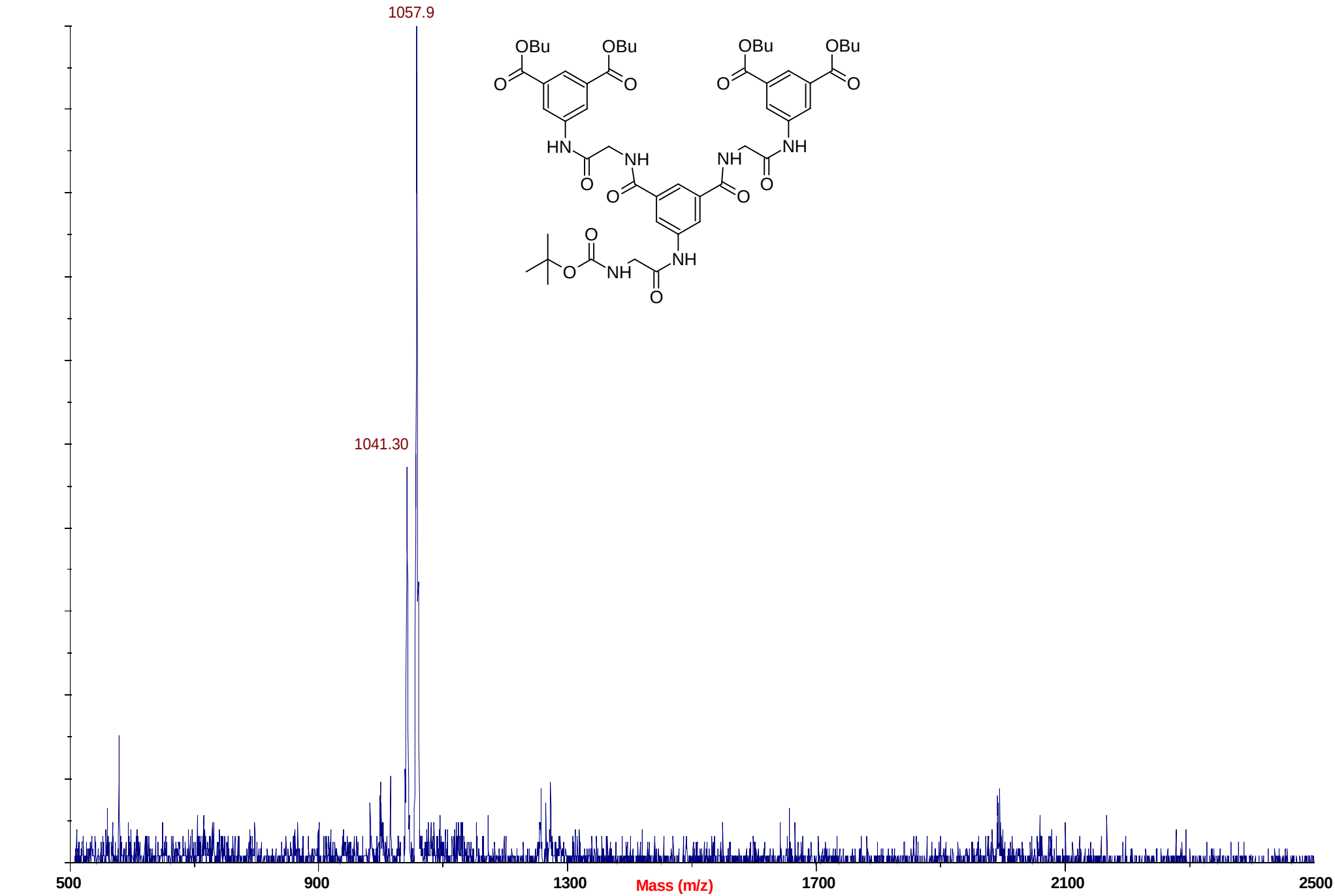
BocNH-AG^2-OBu, ^{1}H



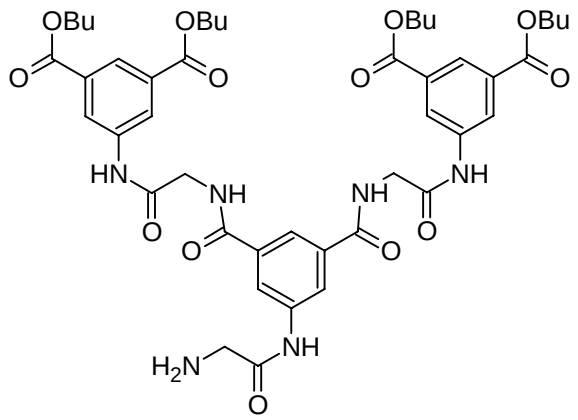
BocNH-AG^2-OBu, ^{13}H



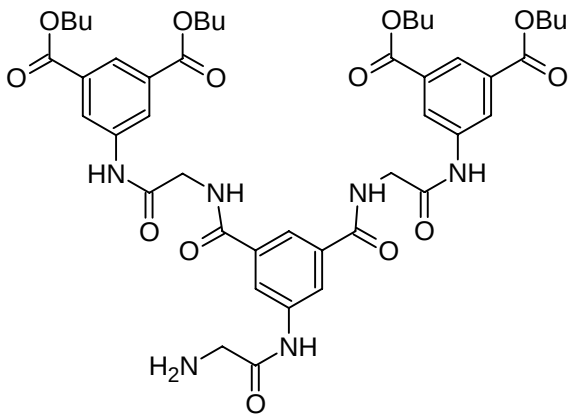
BocNH-AG^2-OBu, MALDI



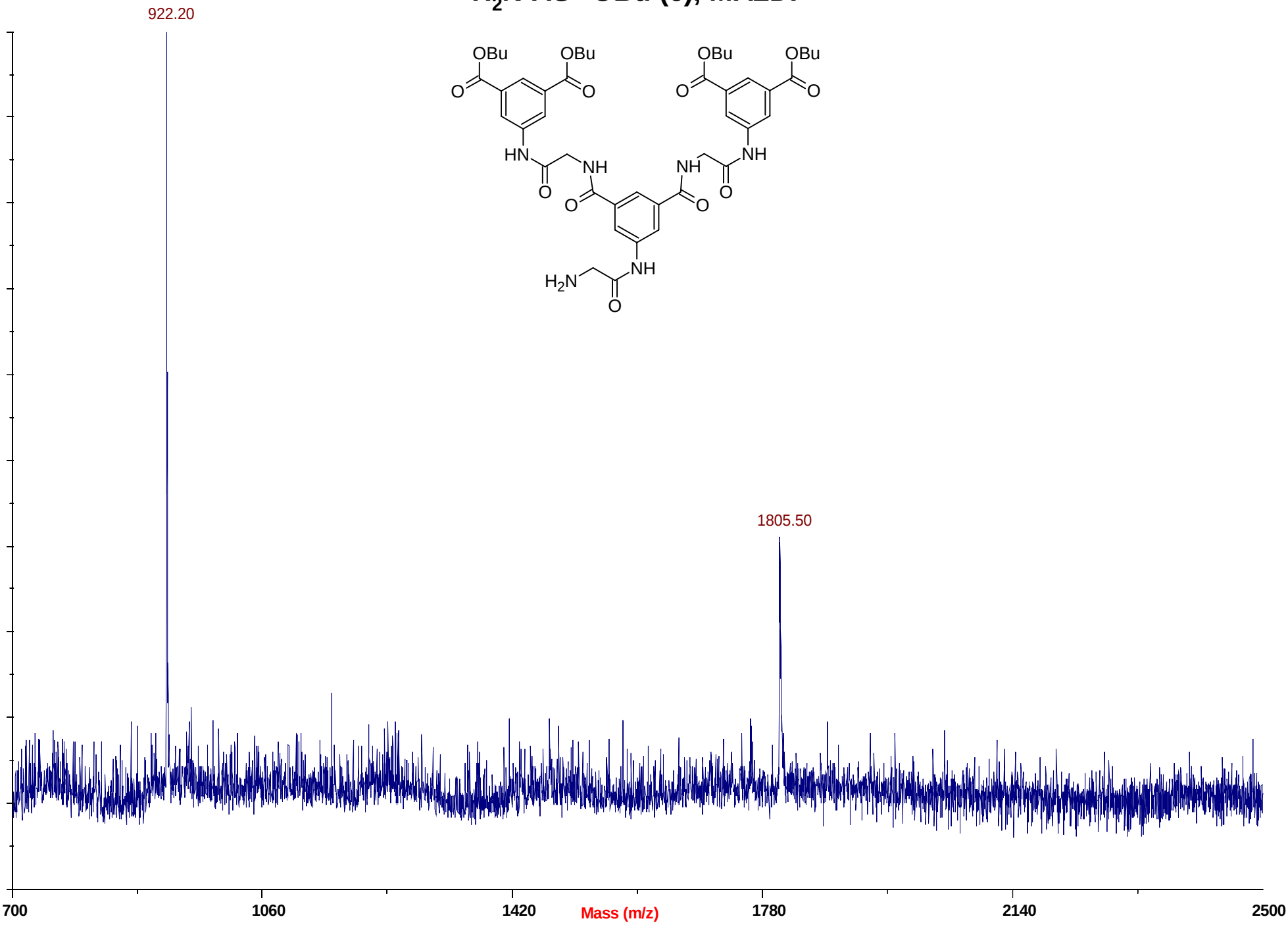
H_2N-AG^2-OBu (6), ^1H



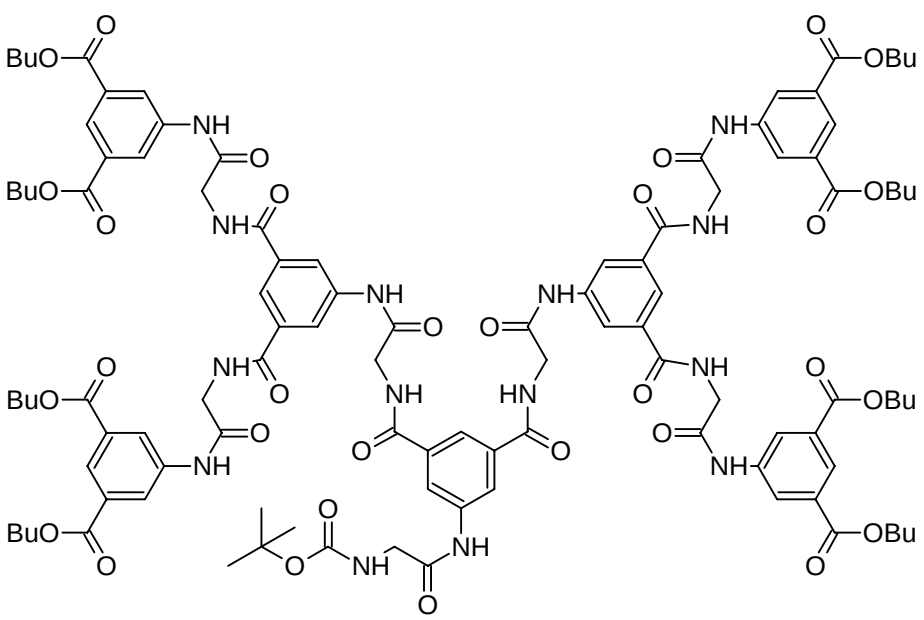
H_2N-AG^2-OBu (6), ^{13}C



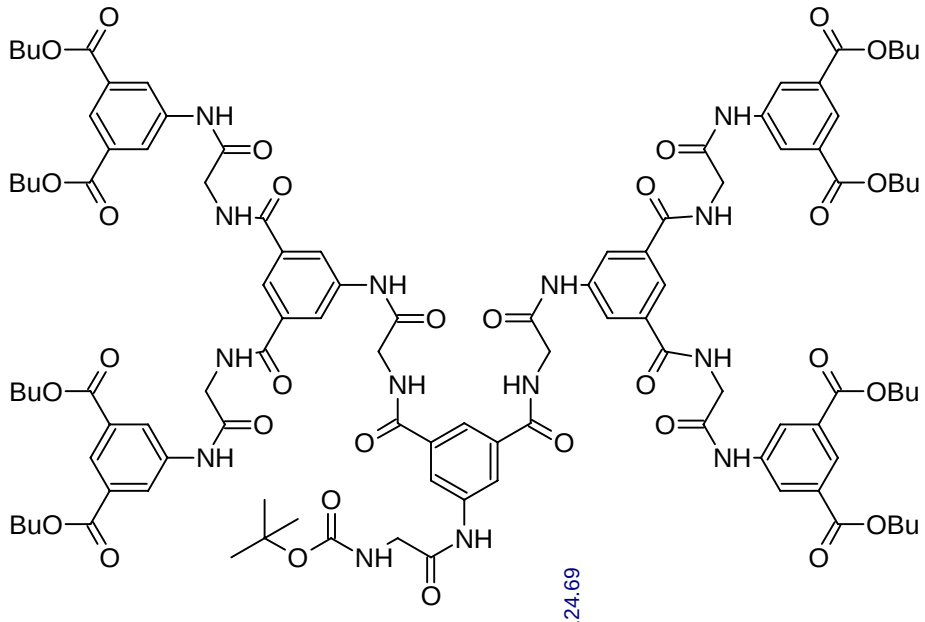
H_2N-AG^2-OBu (6), MALDI



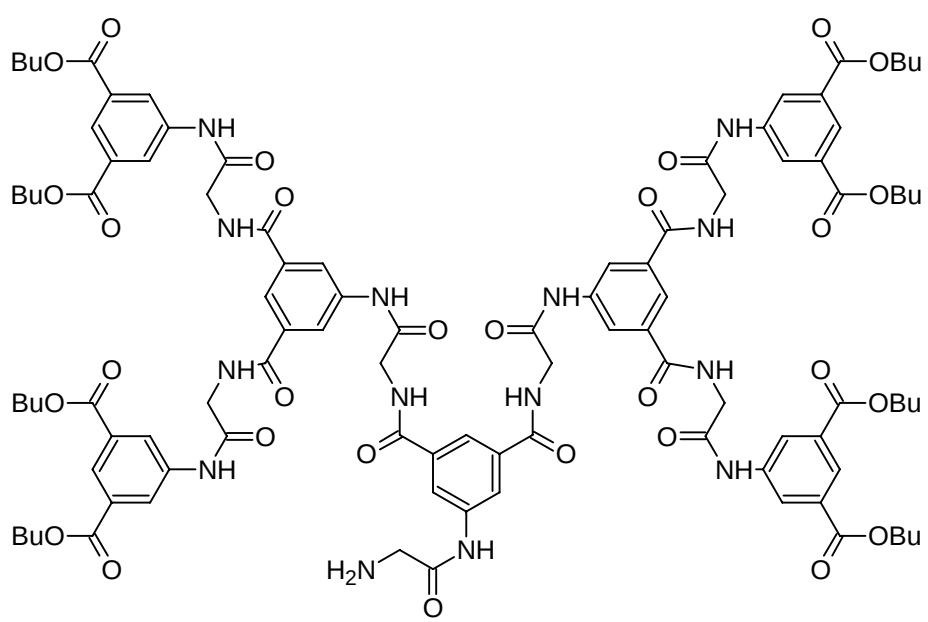
BocNH-AG^3-OBu, ^{1}H



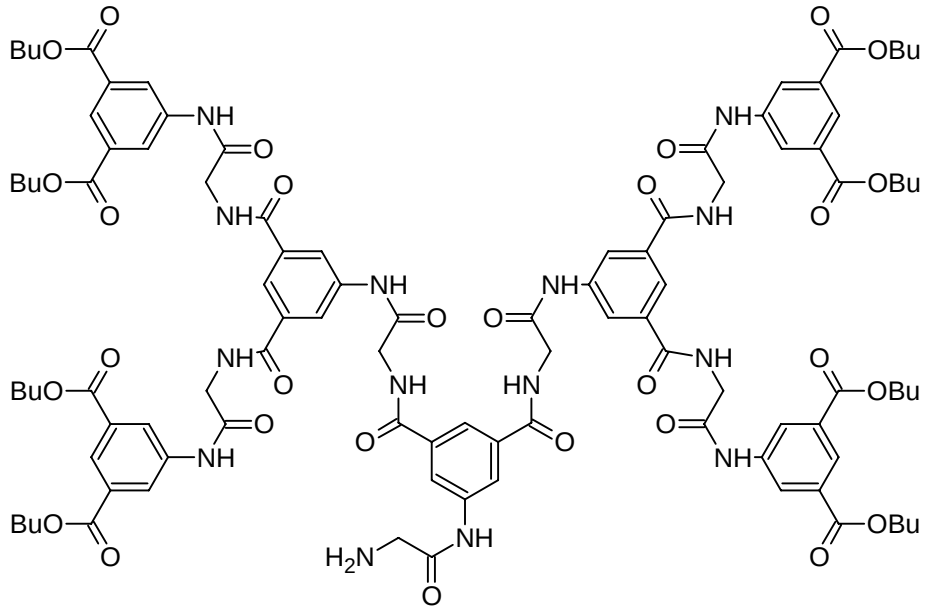
BocNH-AG^3-OBu, ^{13}C



H_2N-AG^3-OBu (7), ^1H



H_2N-AG^3-OBu (7), ^{13}C

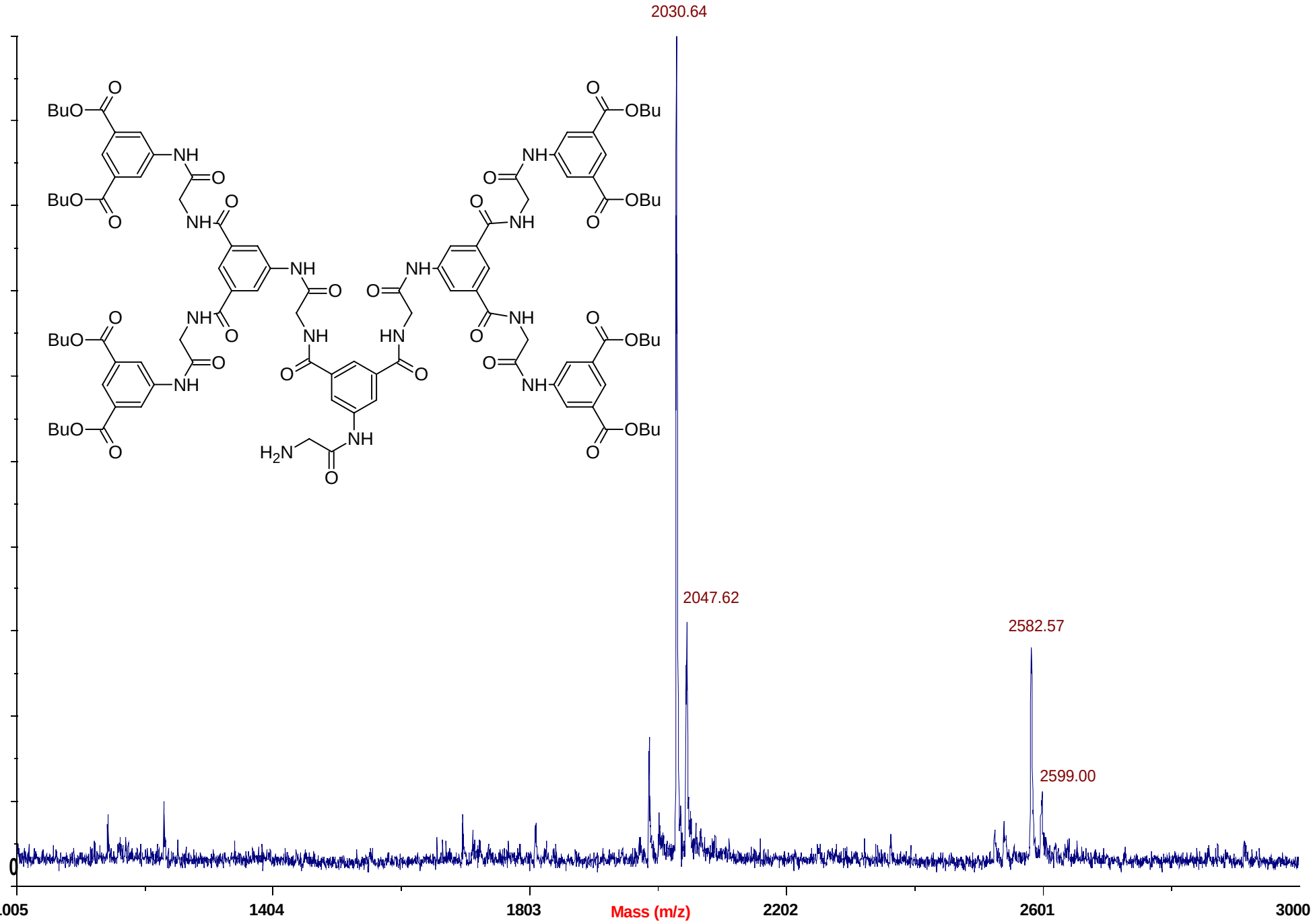


DMSO-d6

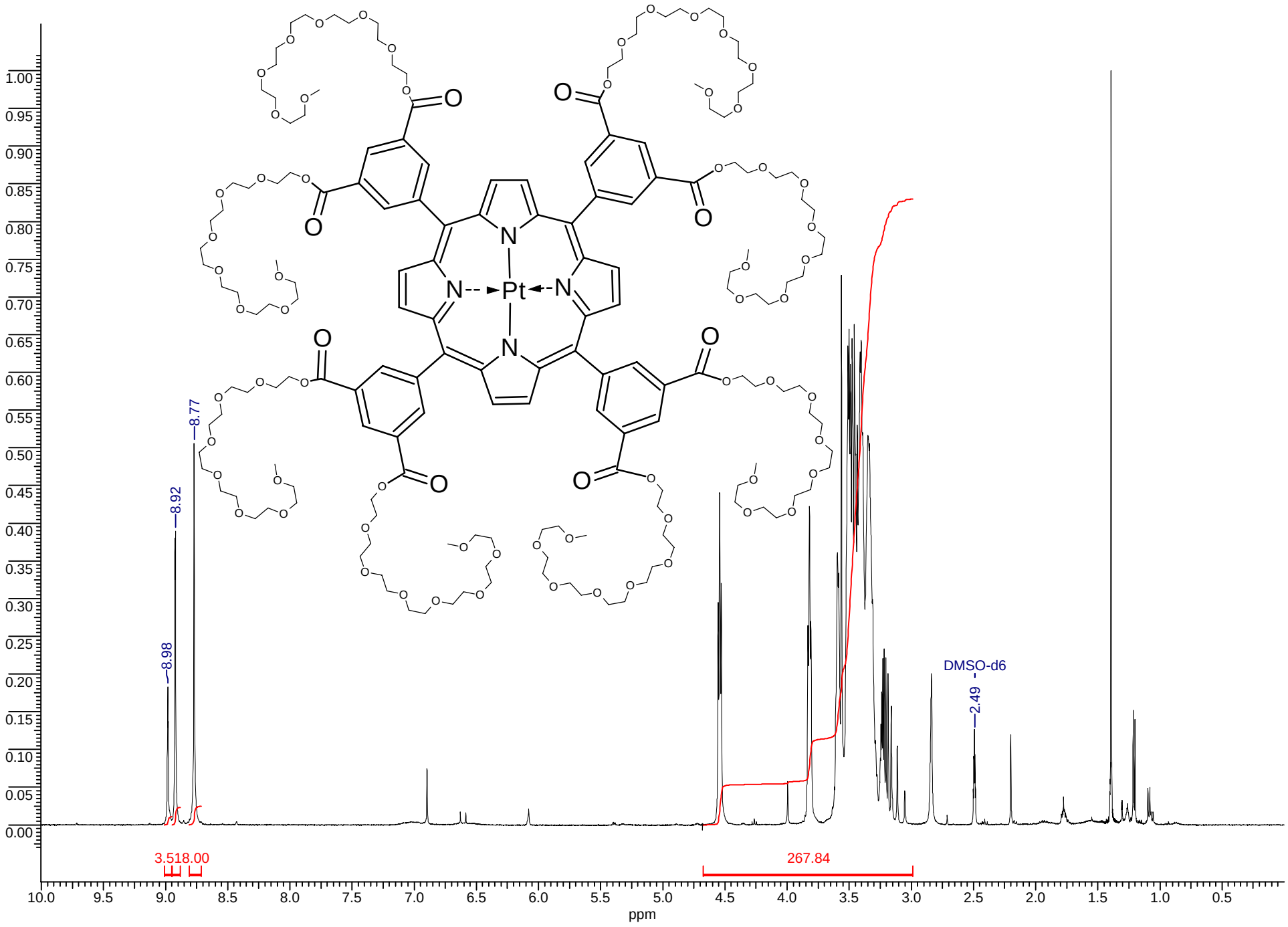
65.33
43.95
41.61
41.00
30.66
19.17
14.00
168.81
168.47
165.28
165.03
140.31
139.61
135.42
131.49
124.50
124.01
121.67
121.34

ppm

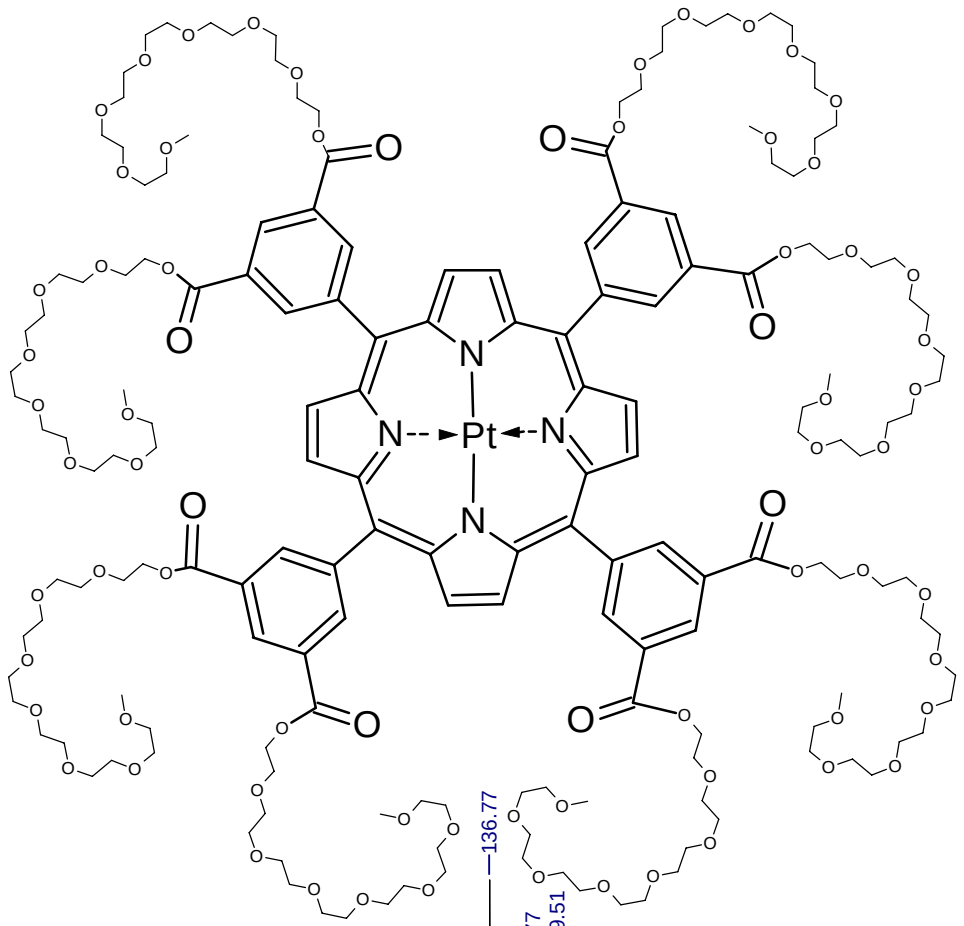
H_2N-AG^3-OBu (7), MALDI



Pt-1-OPEG, ^{1}H

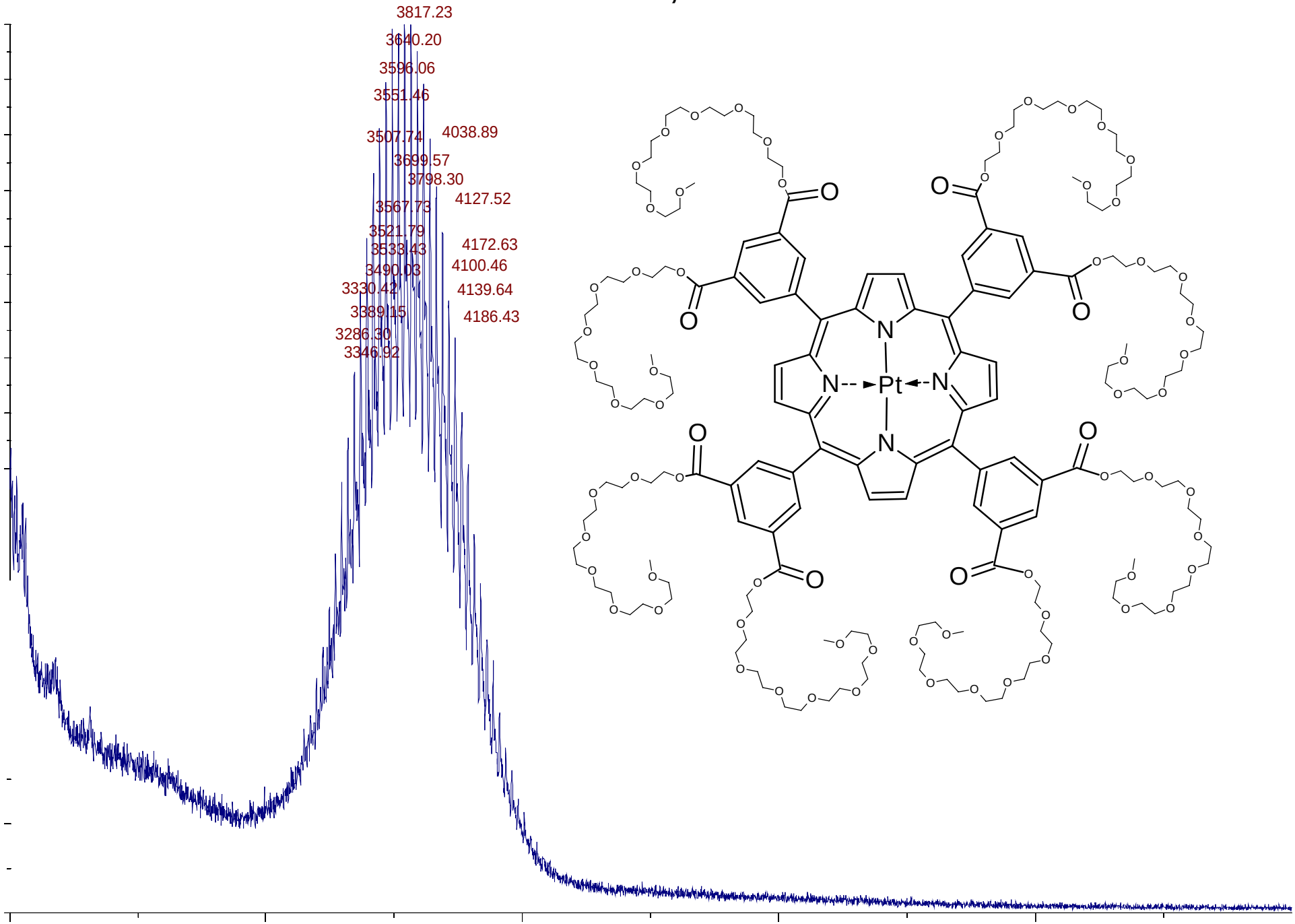


Pt-1-OPEG, ^{13}C

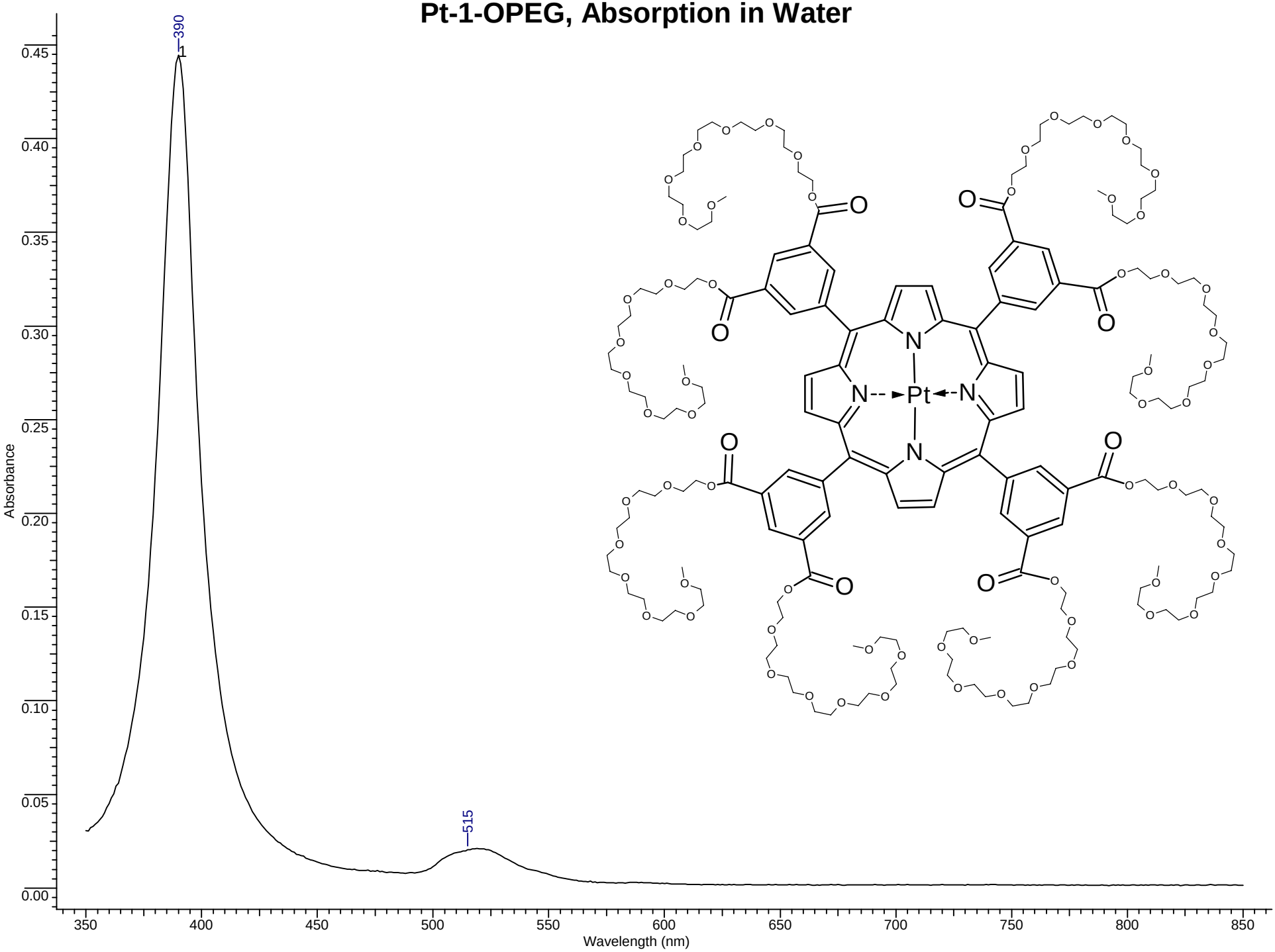

N
N
Pt
N
N
O

69.51
67.96
64.32
69.64
136.77
130.77
129.51
129.25
164.61
140.82
140.23
120.01
71.02
30.13
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
-0.05
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

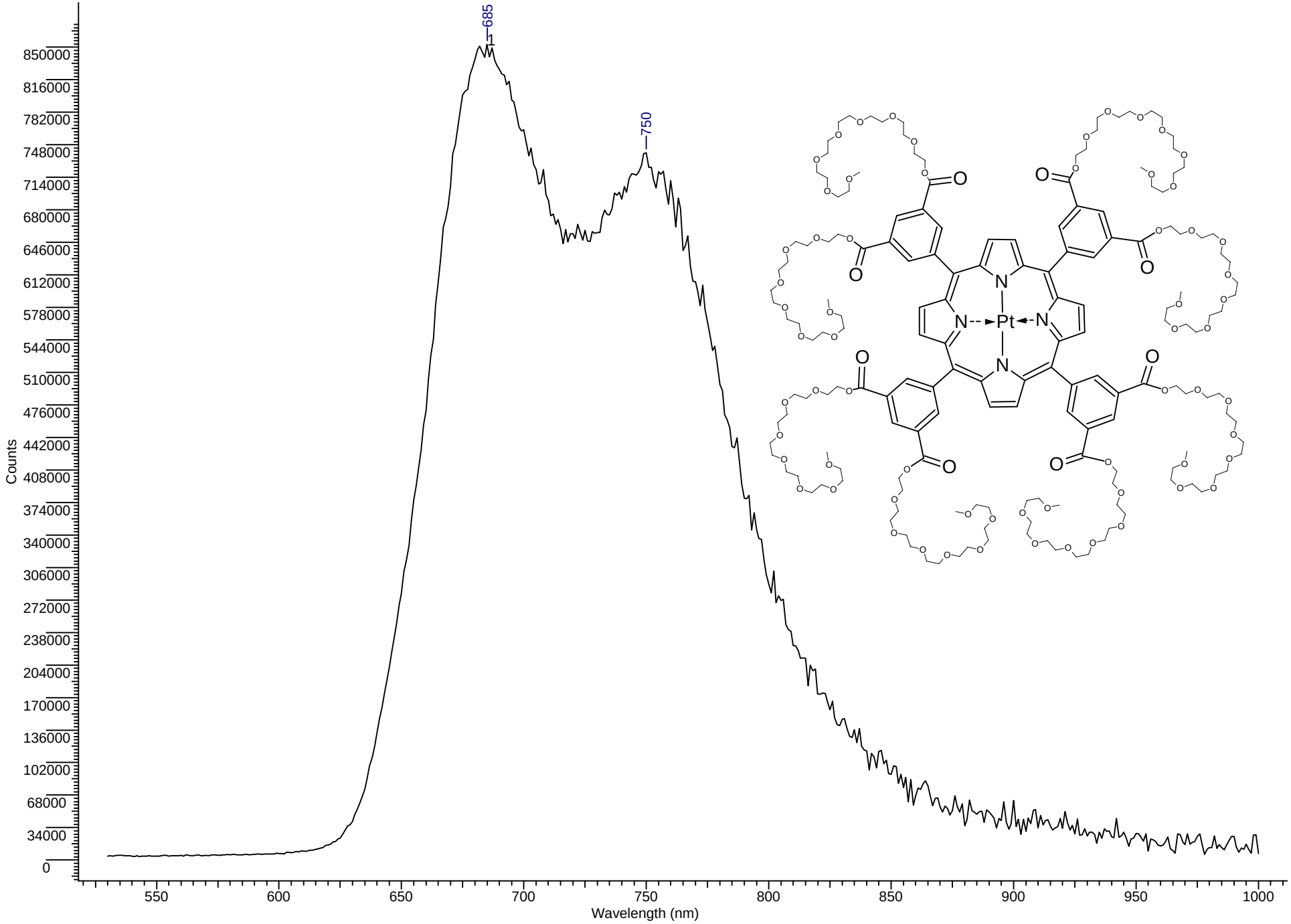
Pt-1-OPEG, MALDI



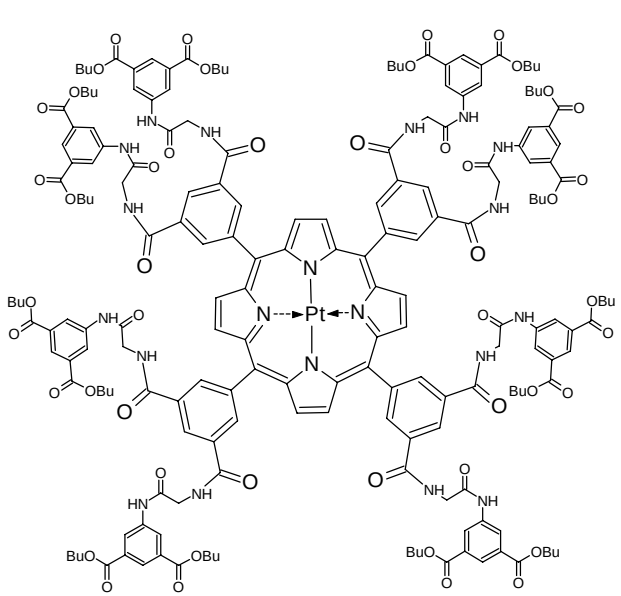
Pt-1-OPEG, Absorption in Water



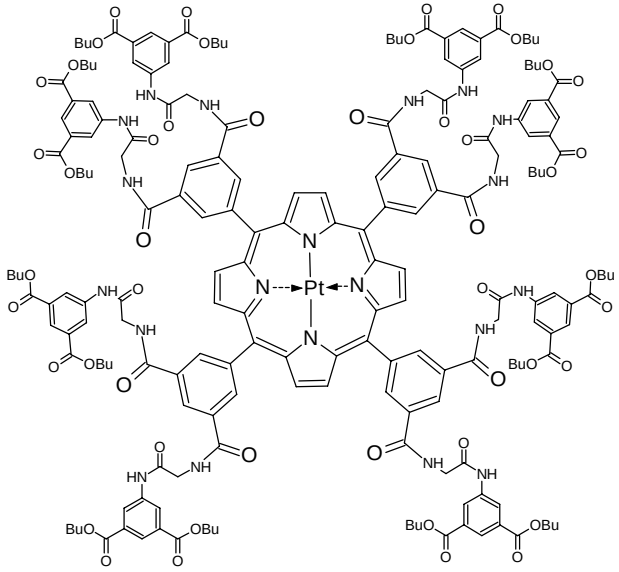
Pt-1-OPEG, Emission in deoxygenated water



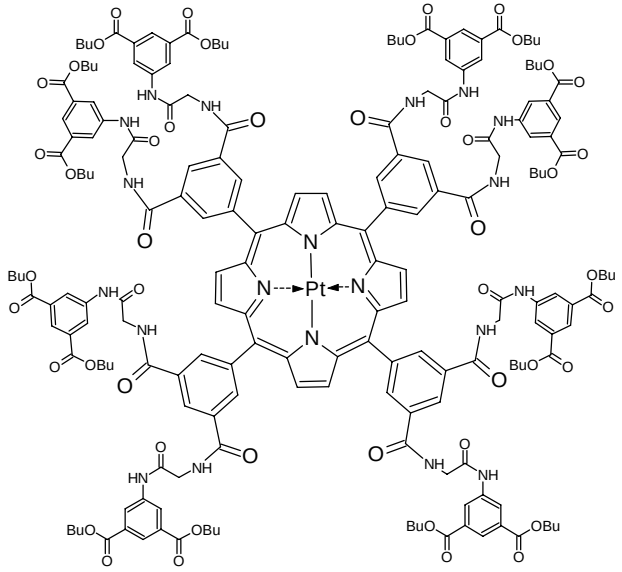
Pt-1-(AG^{1}OBu)$_{8}$, ^{1}H



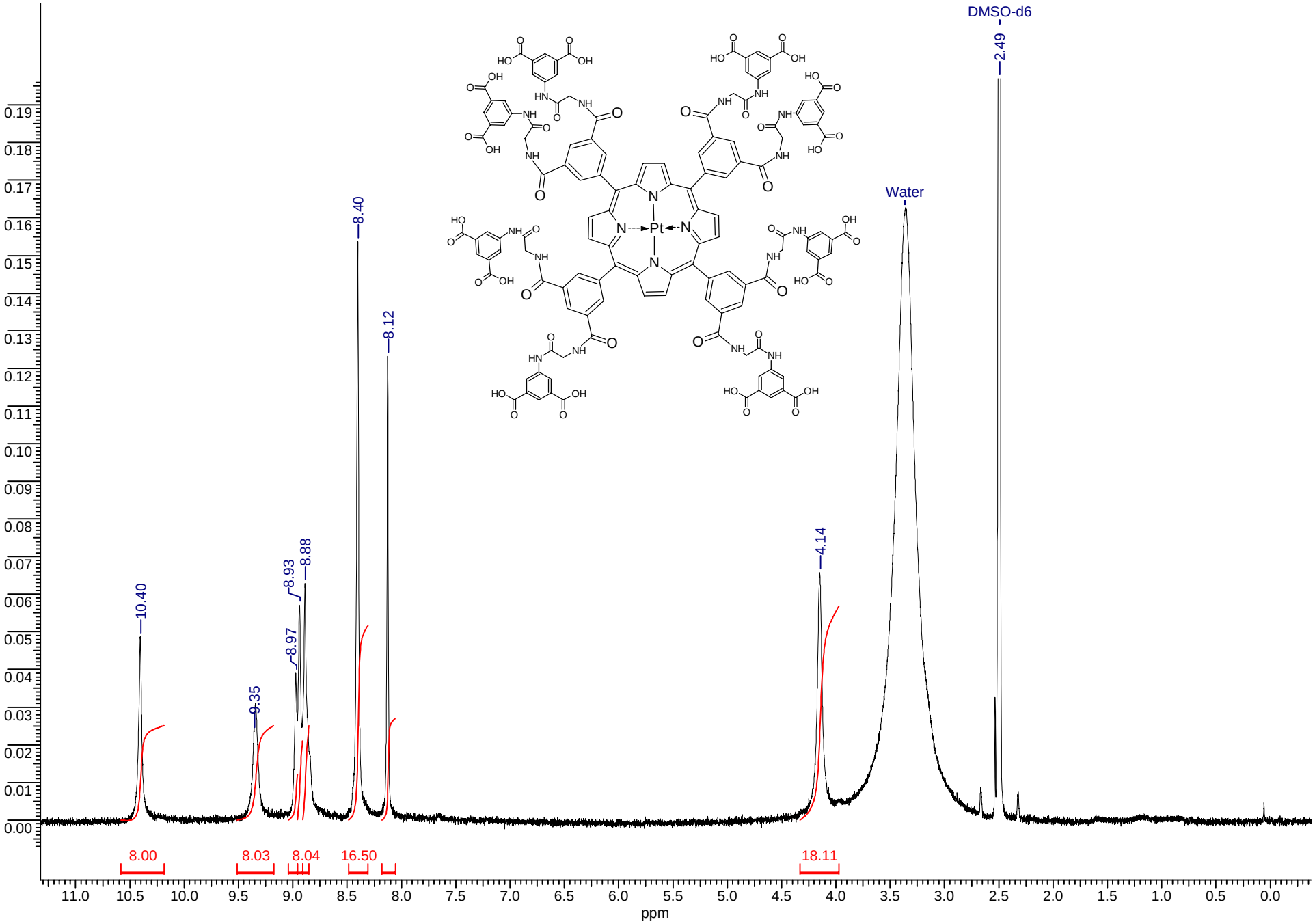
Pt-1-(AG^{1}OBu)$_{8}$, ^{13}C



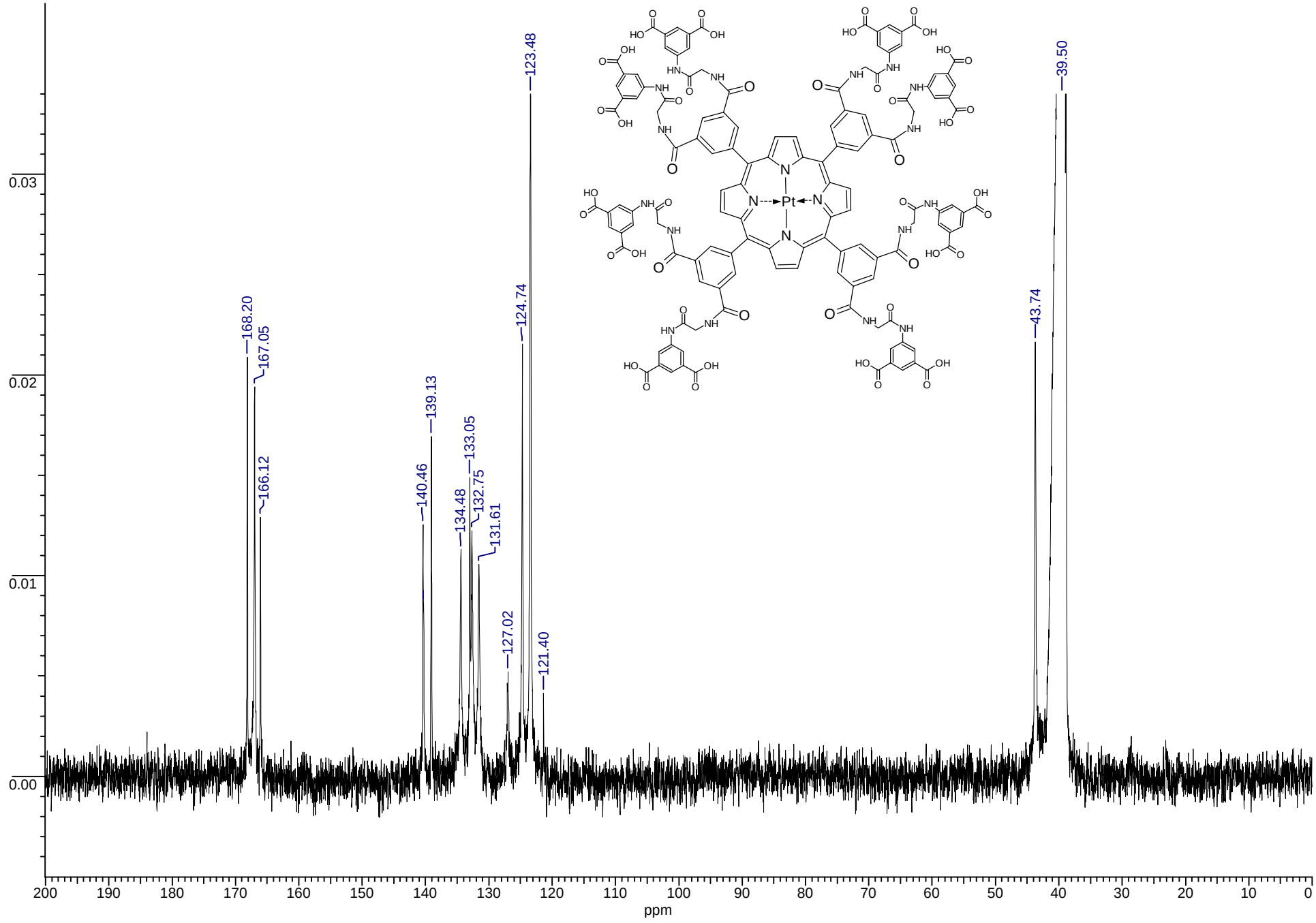
Pt-1-(AG^{1}OBu)$_{8}$, MALDI



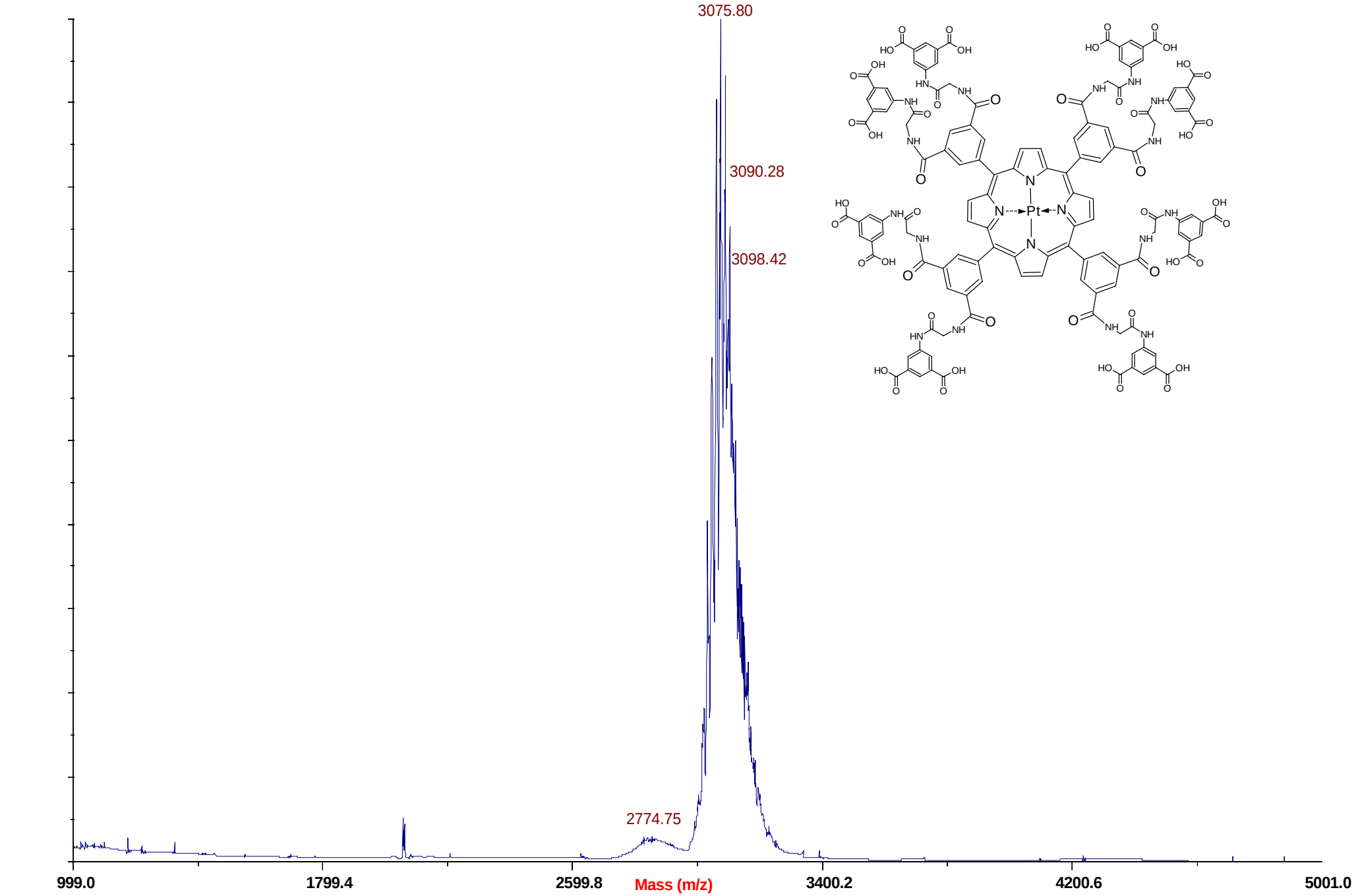
Pt-1-(AG^{1}OH)$_{8}$, ^{1}H



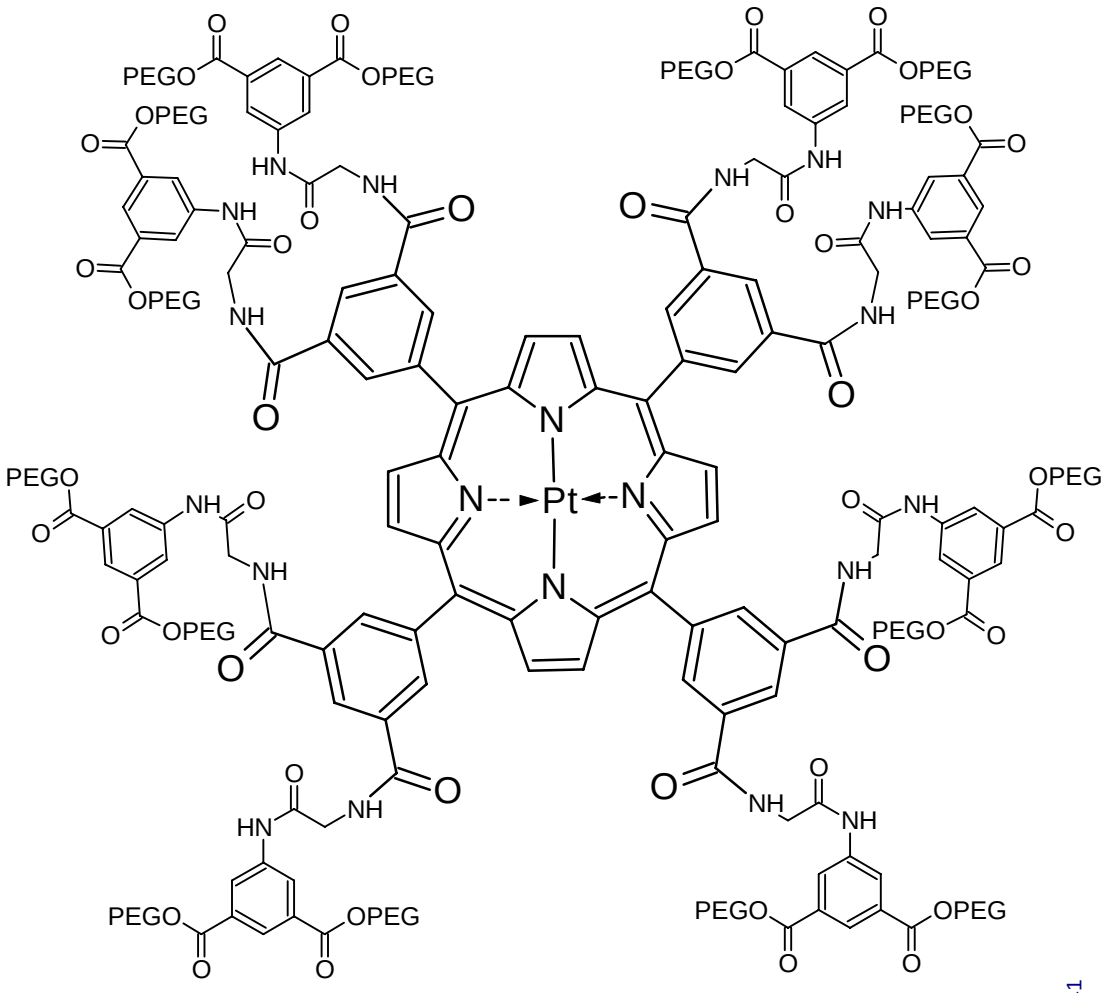
Pt-1-(AG^{1}OH)$_{8}$, ^{13}C



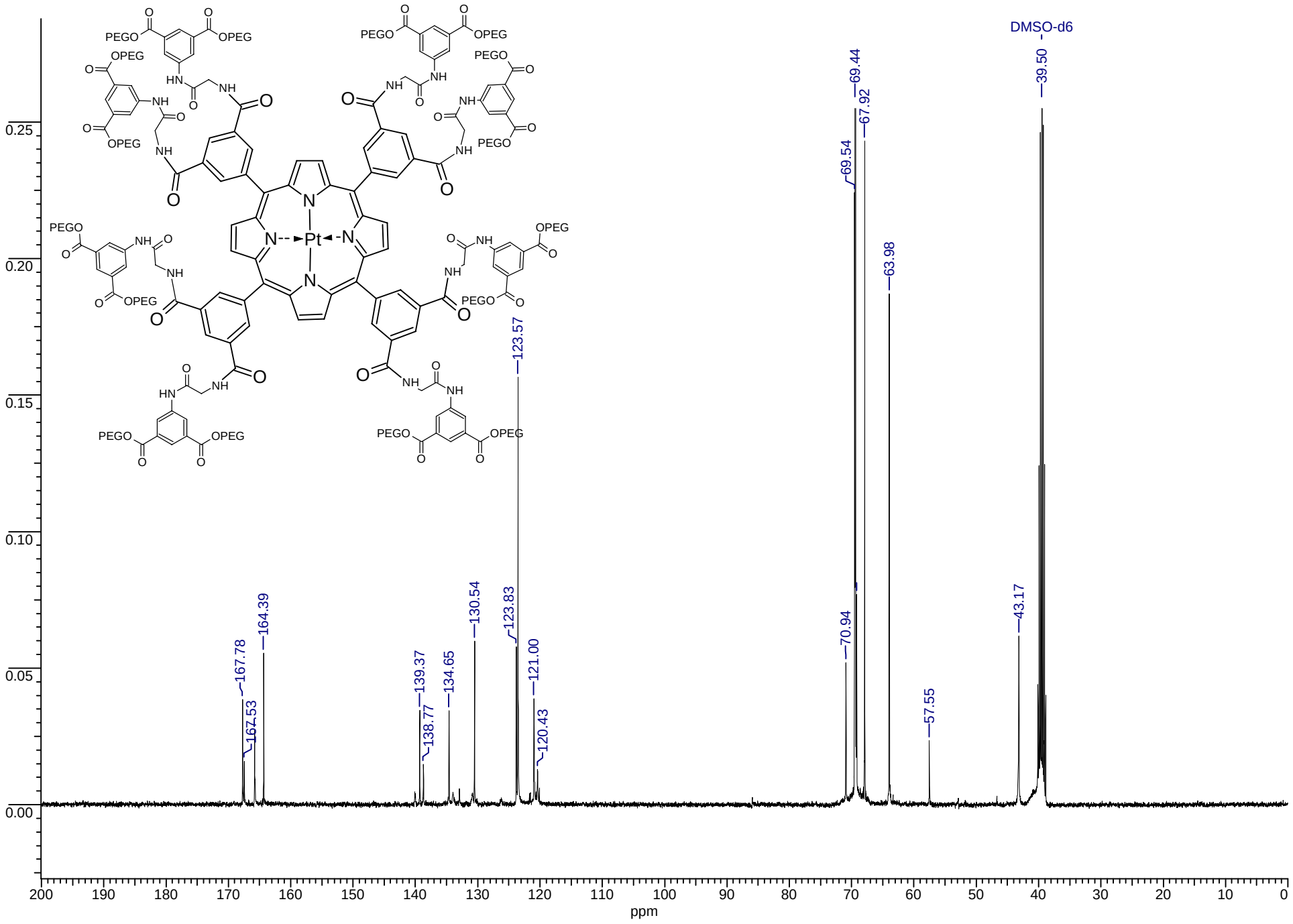
Pt-1-(AG^{1}-OH)$_{8}$, MALDI



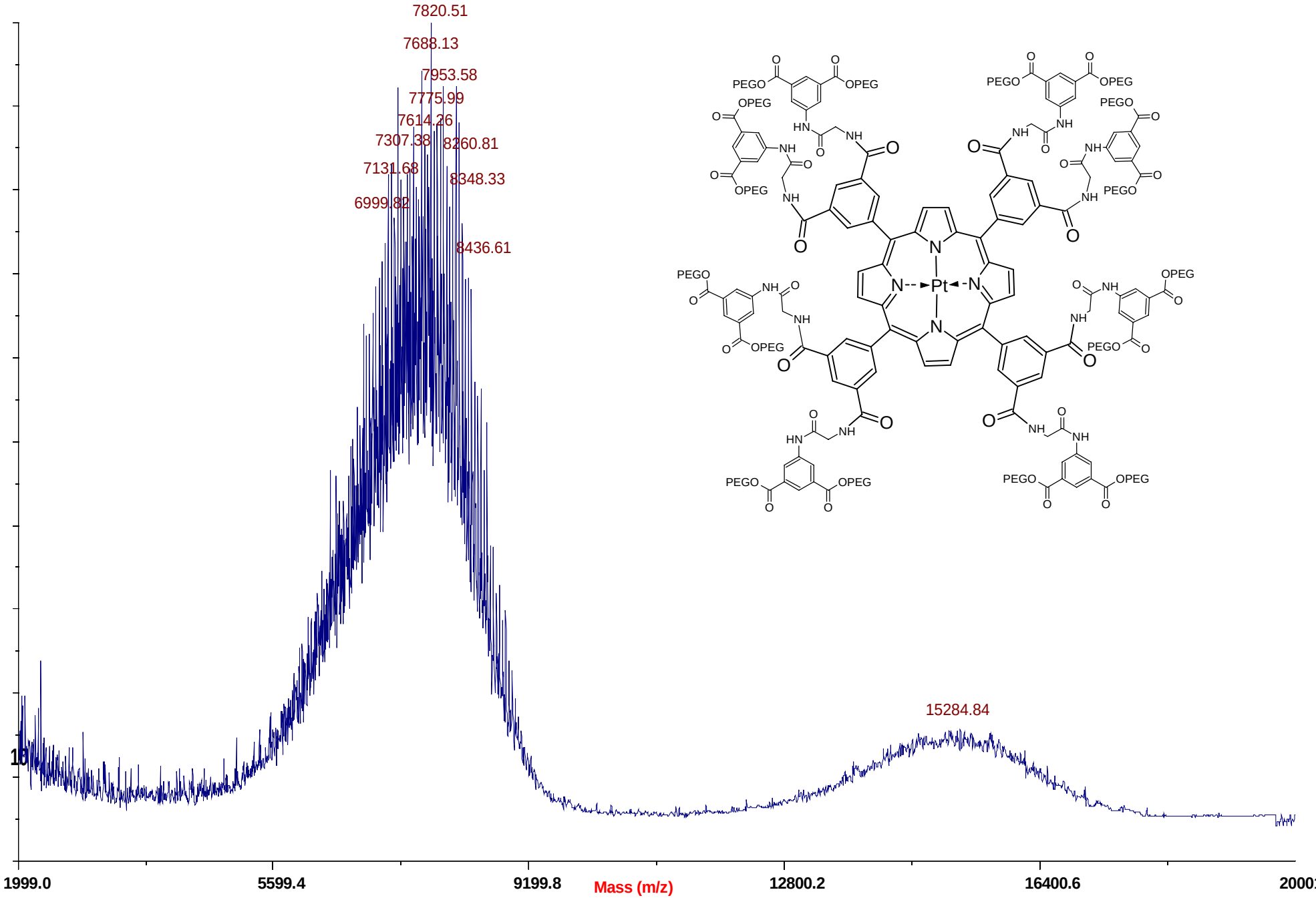
Pt-1-(AG^{1}OPEG)$_8$ (8), ^{1}H



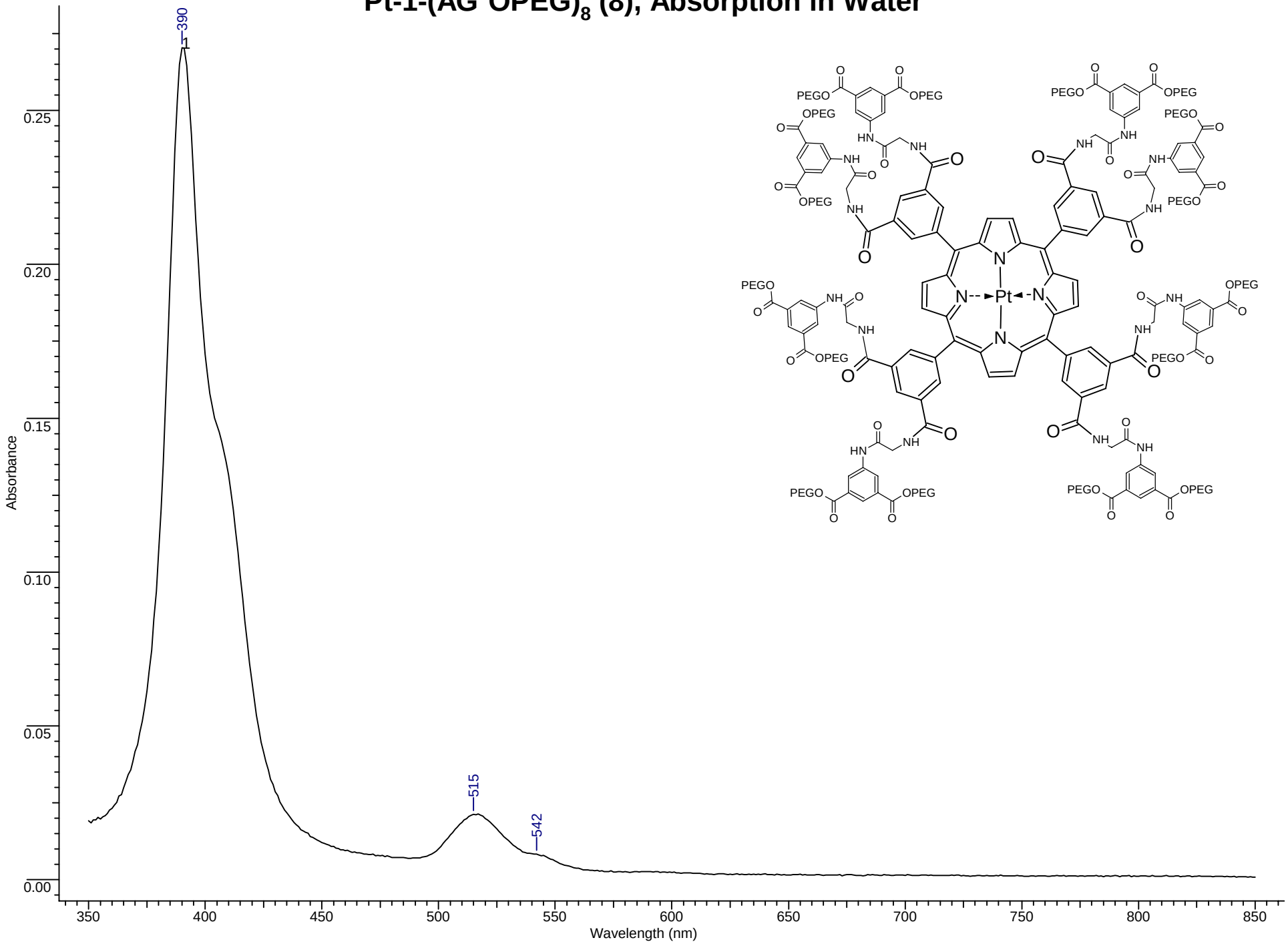
PtP-(AG^{1}-OPEG)$_{8}$ (8), ^{13}C



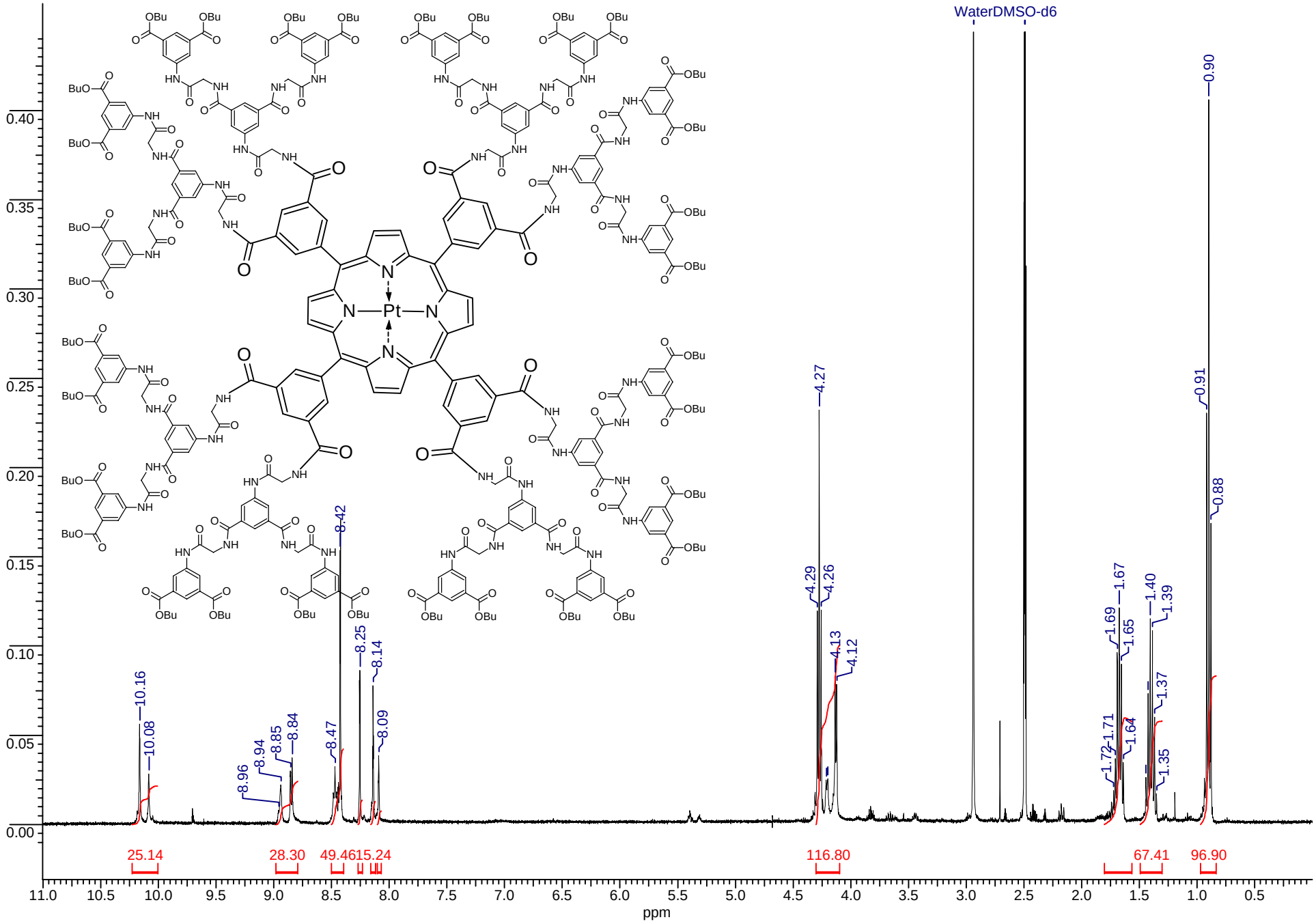
PtP-(AG^{1}-OPEG)$_{8}$ (8), MALDI



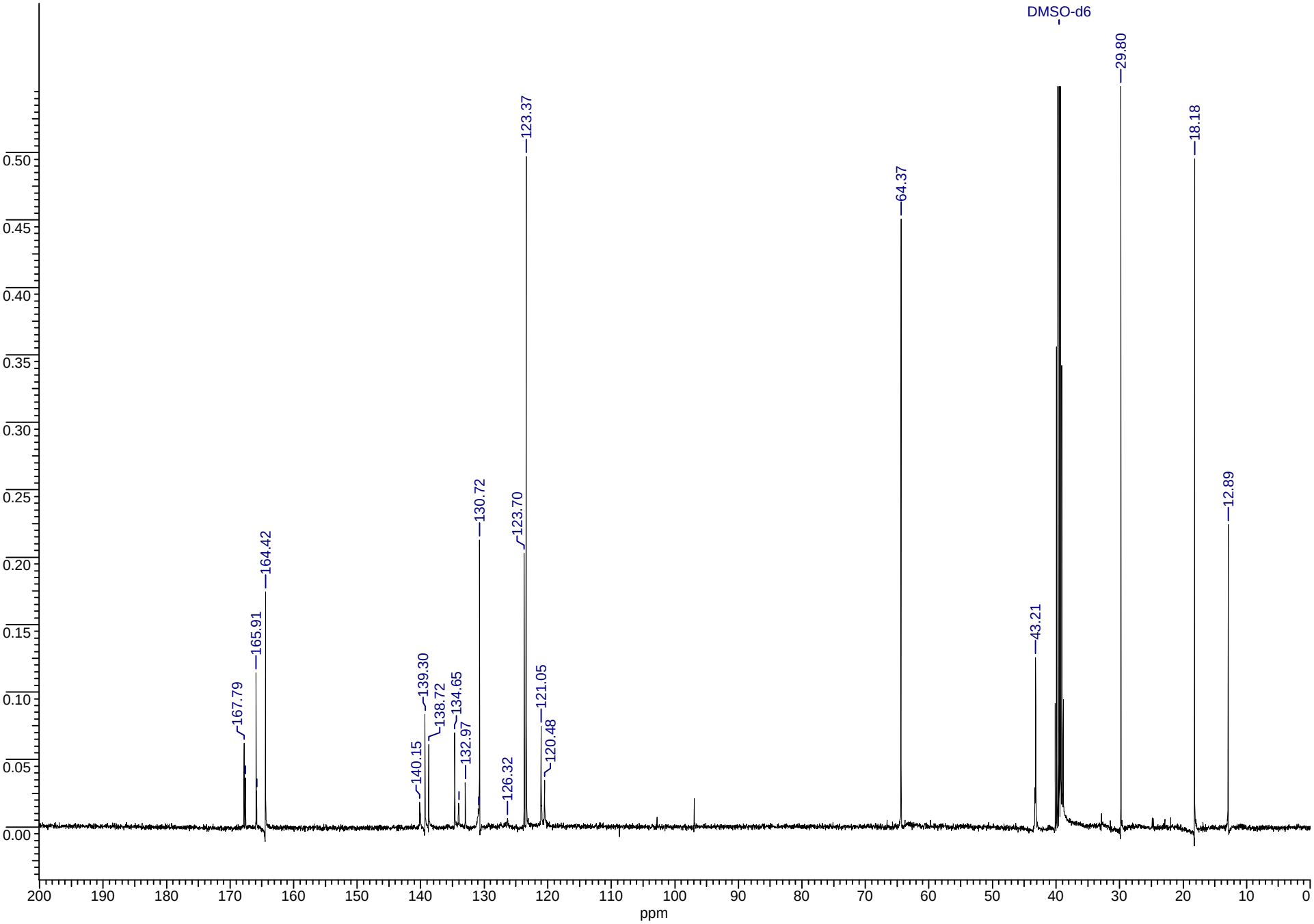
Pt-1-(AG^{1}OPEG)$_8$ (8), Absorption in Water



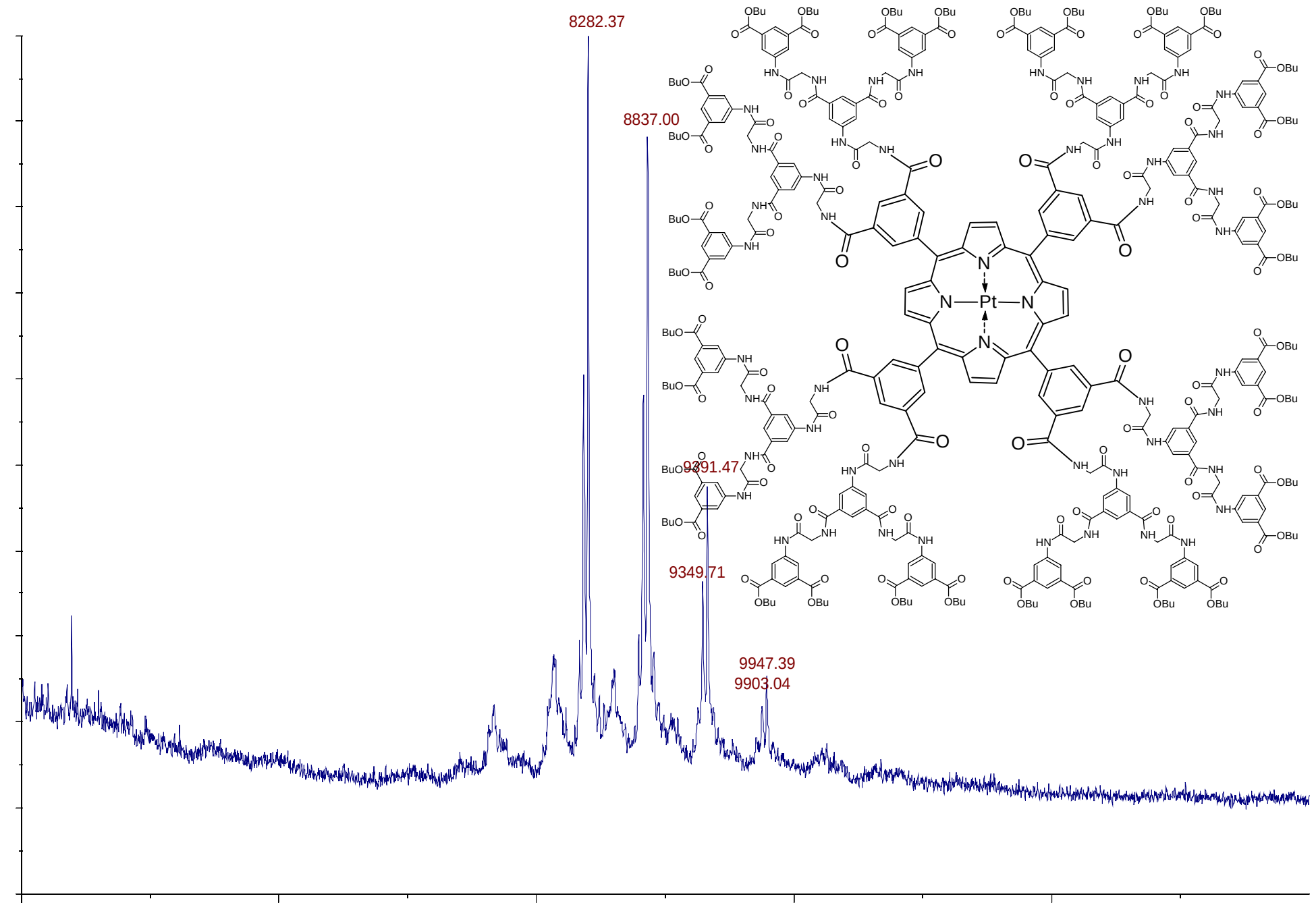
Pt-1-(AG^{2}OBu)$_8$, ^{1}H



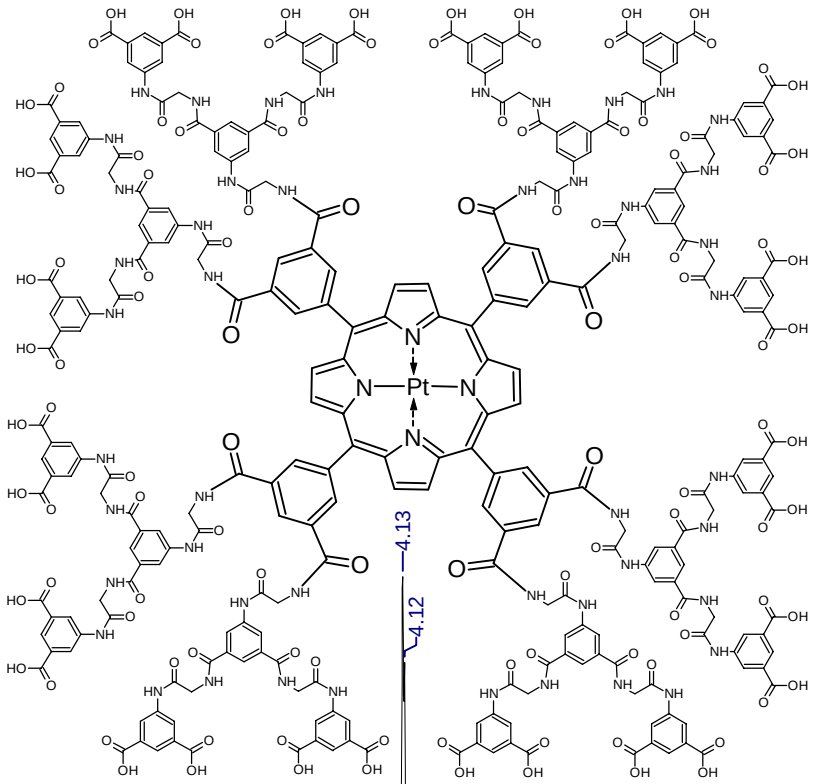
Pt-1-(AG^{2}OBu)$_8$, ^{13}C



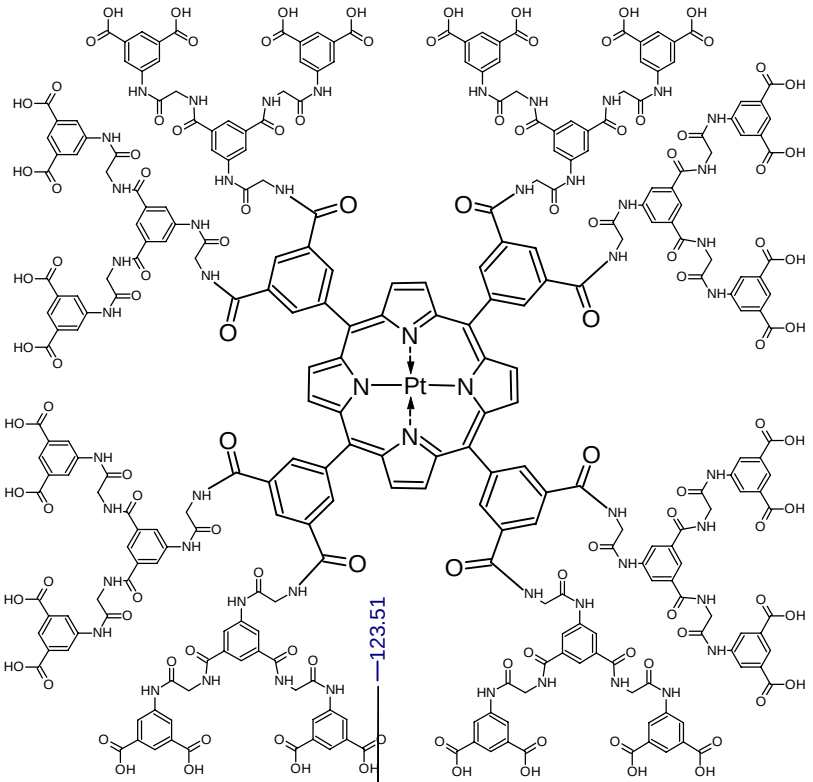
Pt-1-(AG^{2}OBu)$_8$, ^{13}C



Pt-1-(AG^2-OH)$_8$, ^{1}H



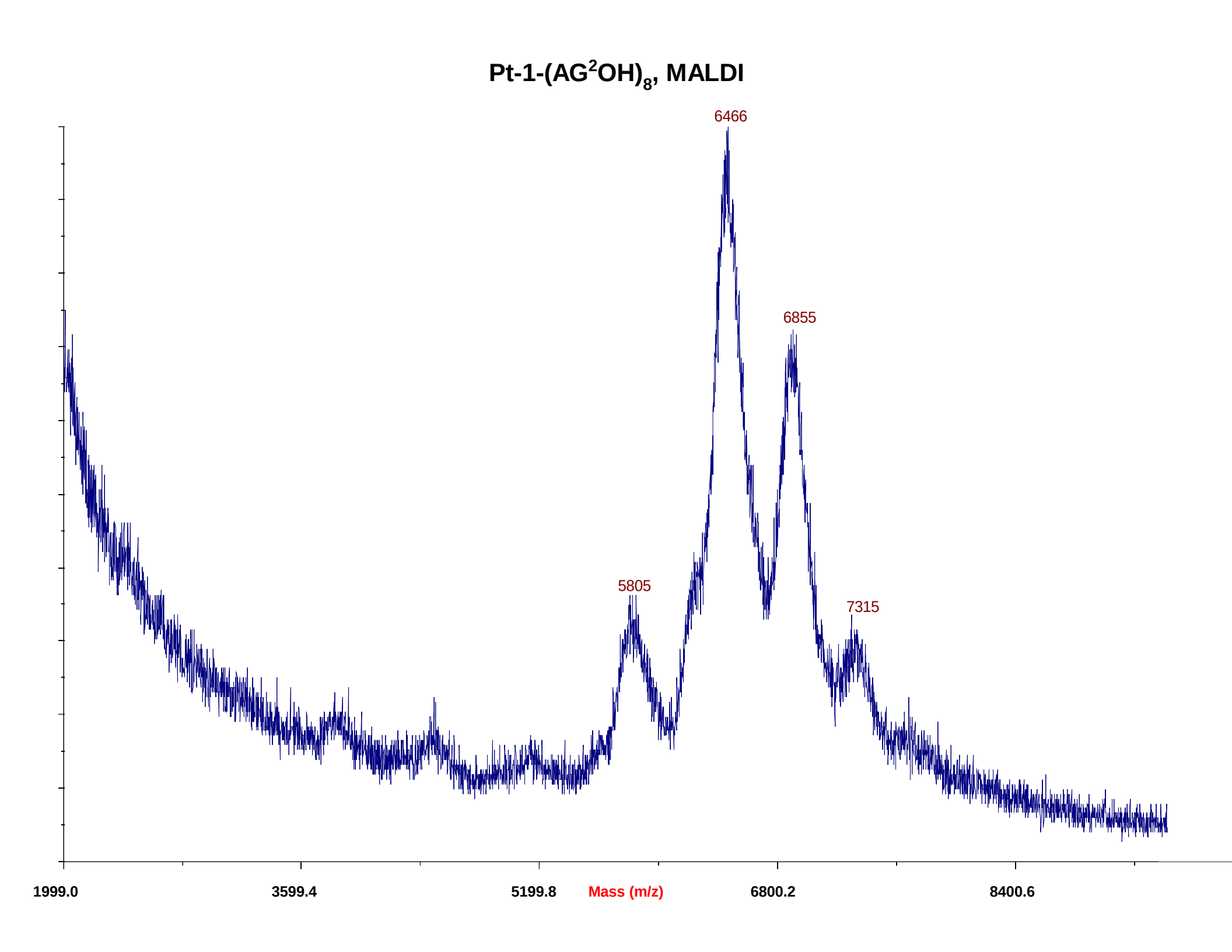
Pt-1-(AG^{2}OH)$_8$, ^{13}C



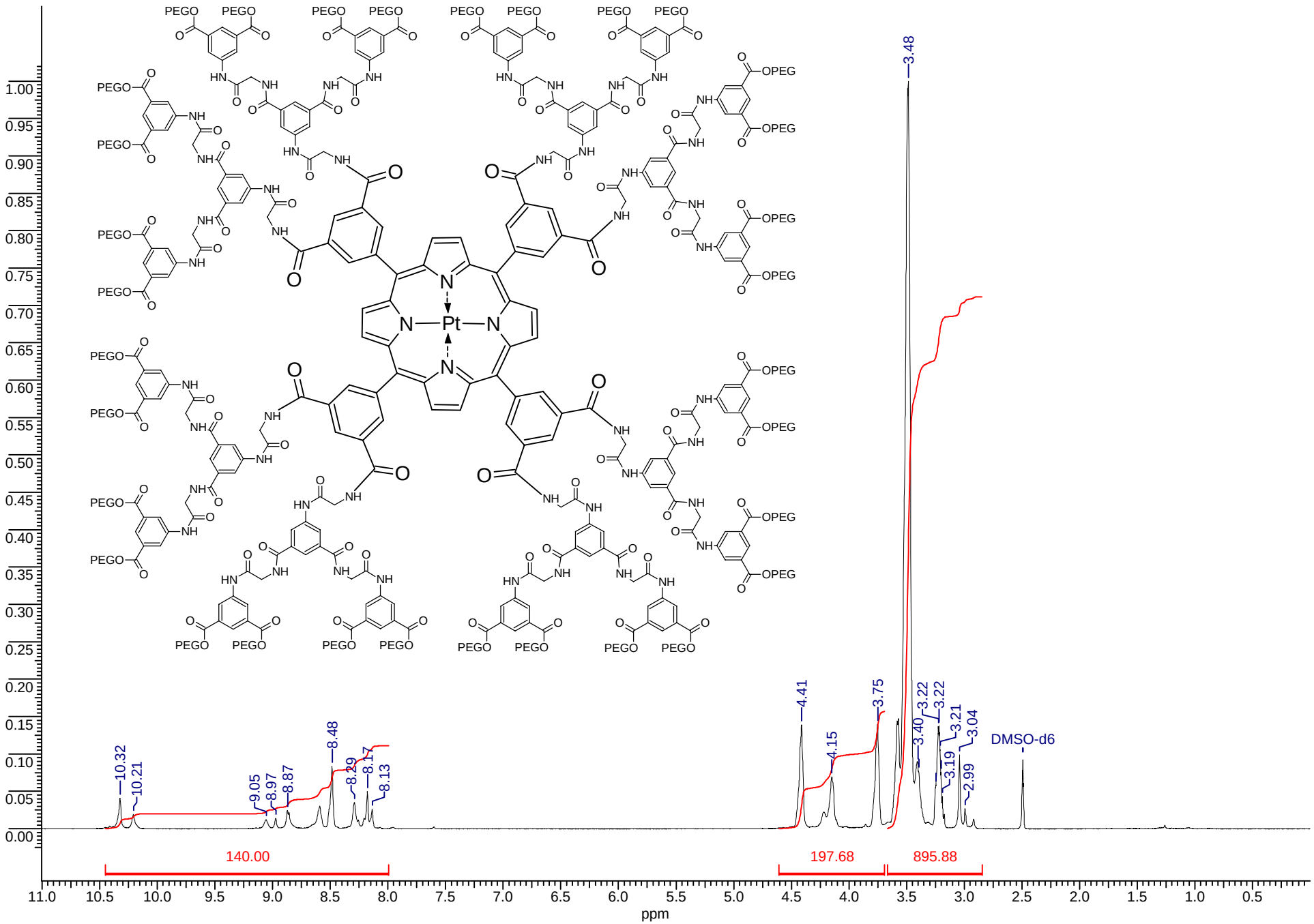
DMSO-d6

167.63
165.96
140.13
138.88
138.68
134.71
132.97
131.73
130.88
126.24
124.34
123.51
121.05
120.47
115.16
46.69
43.26

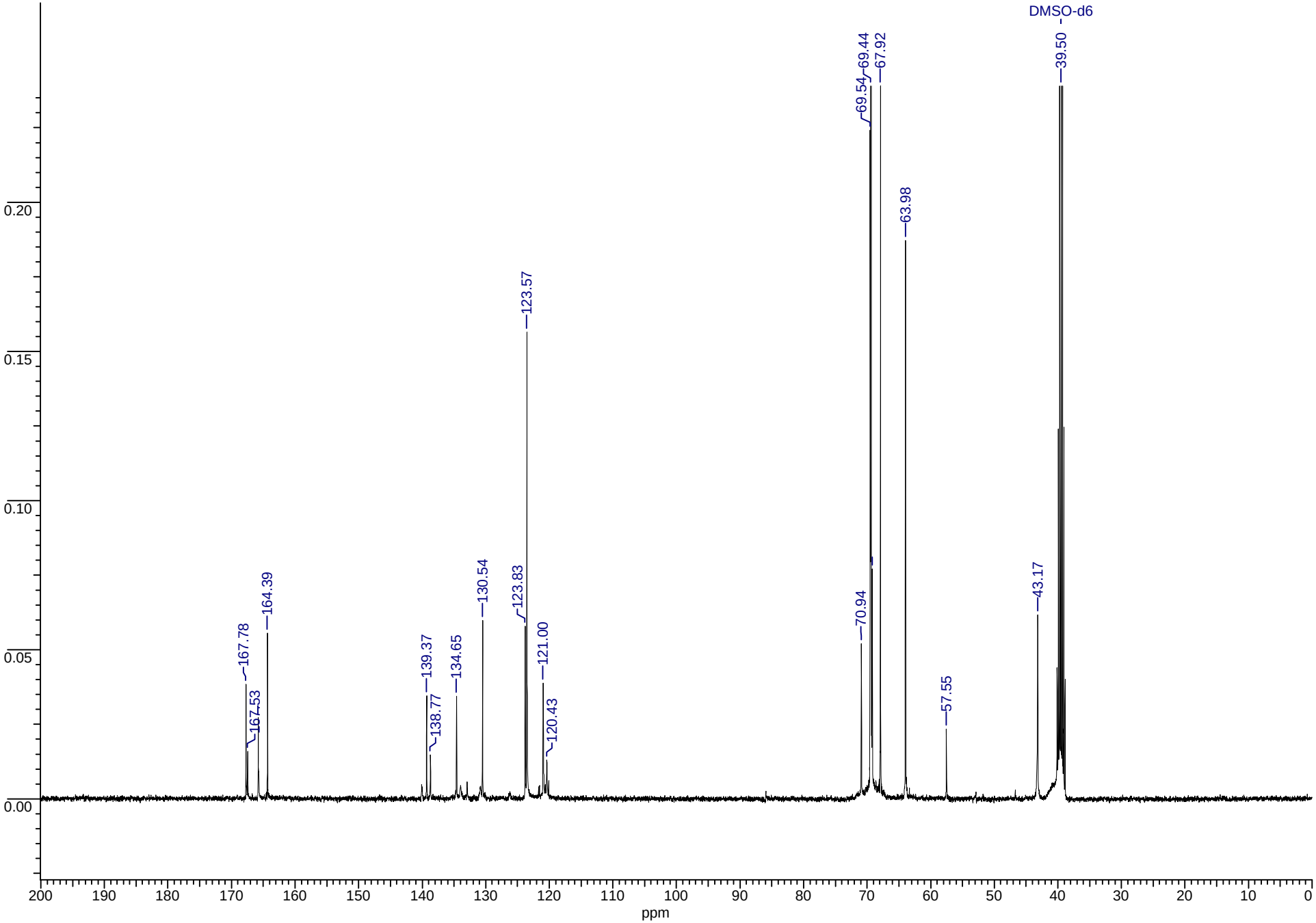
ppm


Pt-1-(AG2OH)8, MALDI
6466
6855
5805
7315
1999.0
3599.4
5199.8
Mass (m/z)
6800.2
8400.6

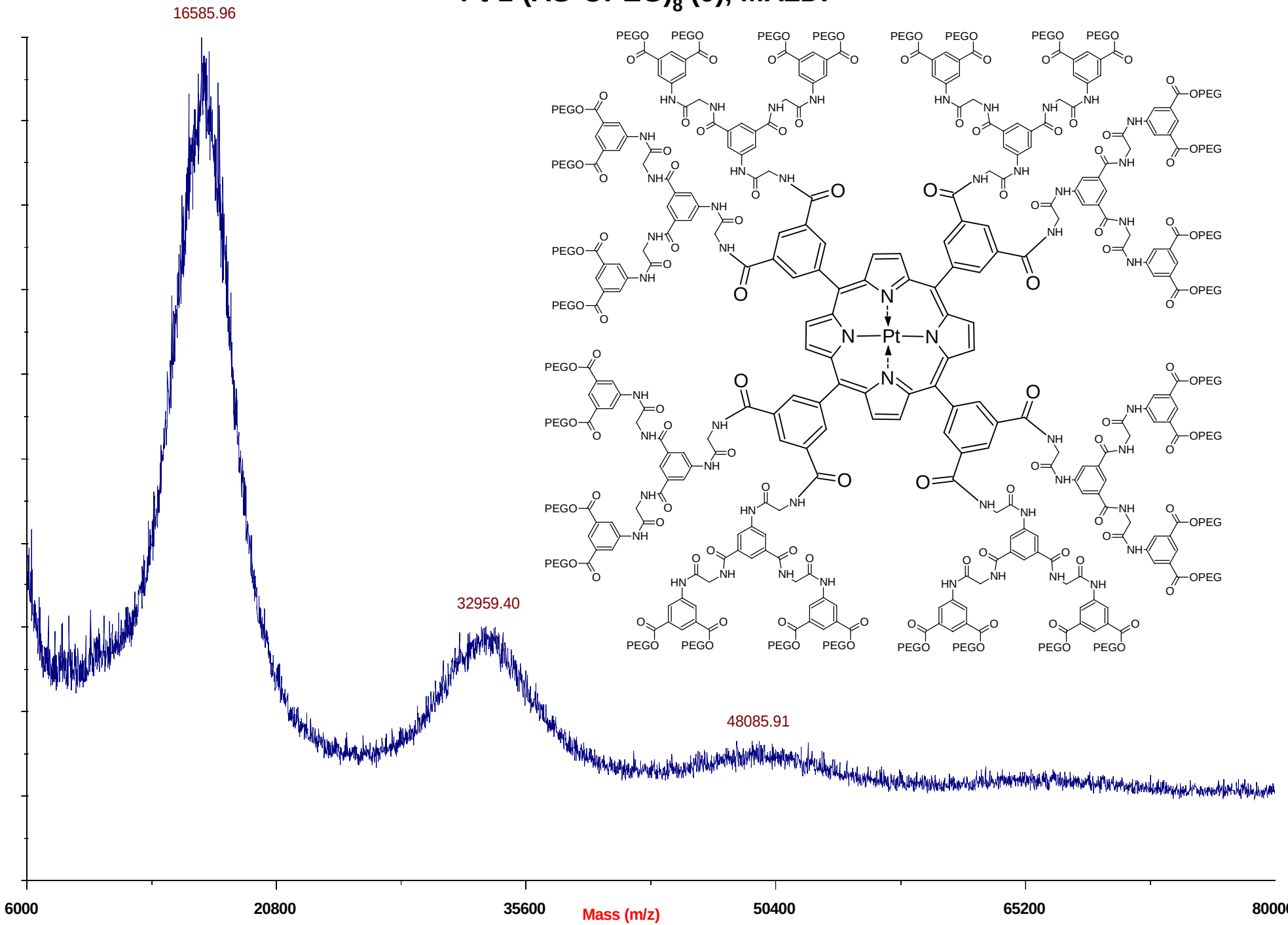
Pt-1-(AG^{2}OPEG)$_8$ (9), ^{1}H



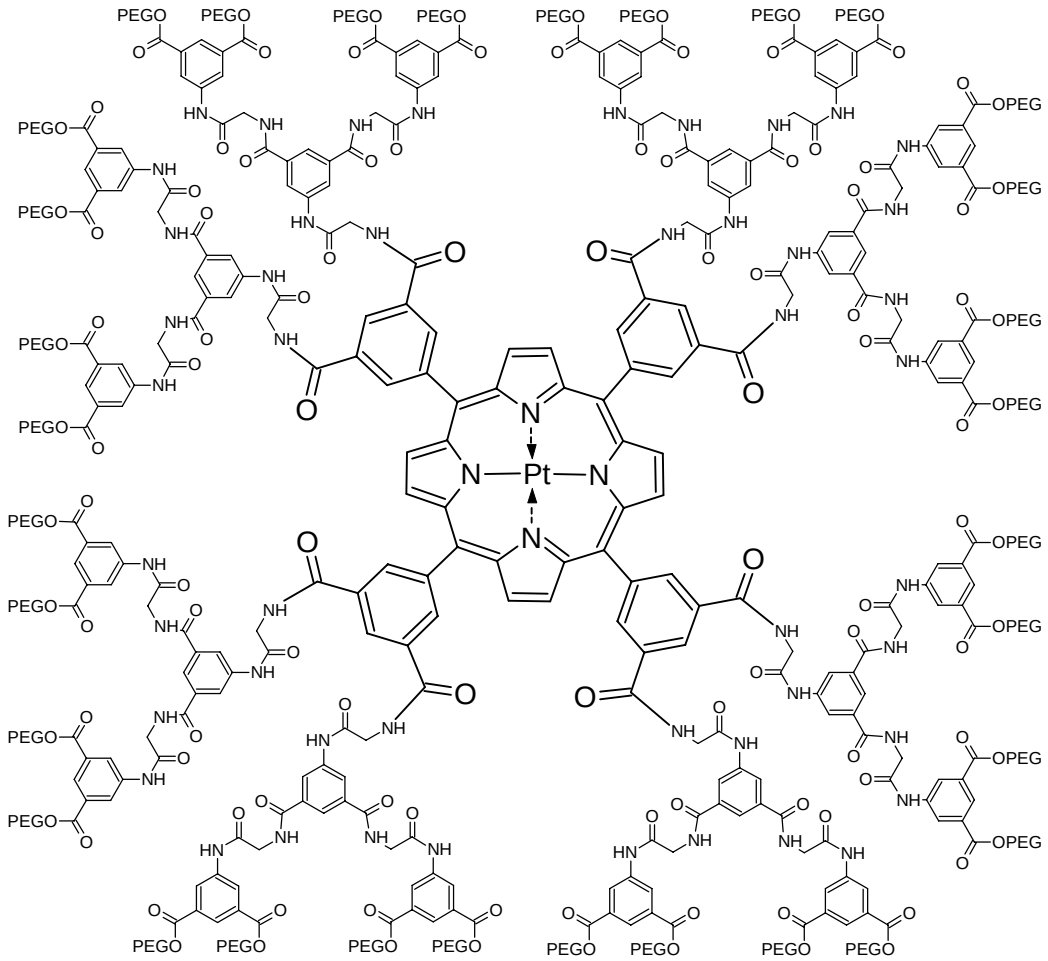
Pt-1-(AG^{2}OPEG)$_8$ (9), ^{13}C



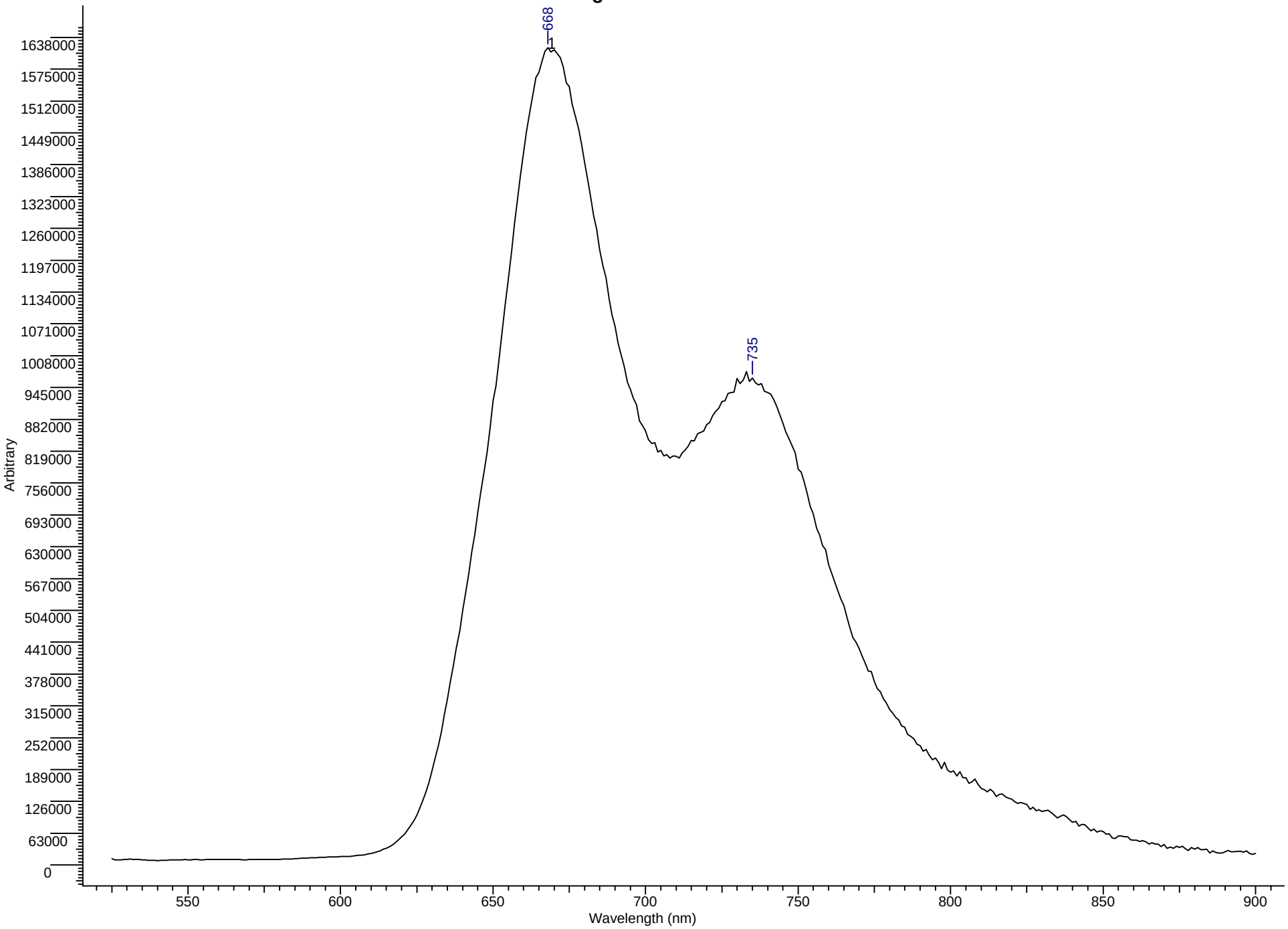
Pt-1-(AG^{2}OPEG)$_8$ (9), MALDI

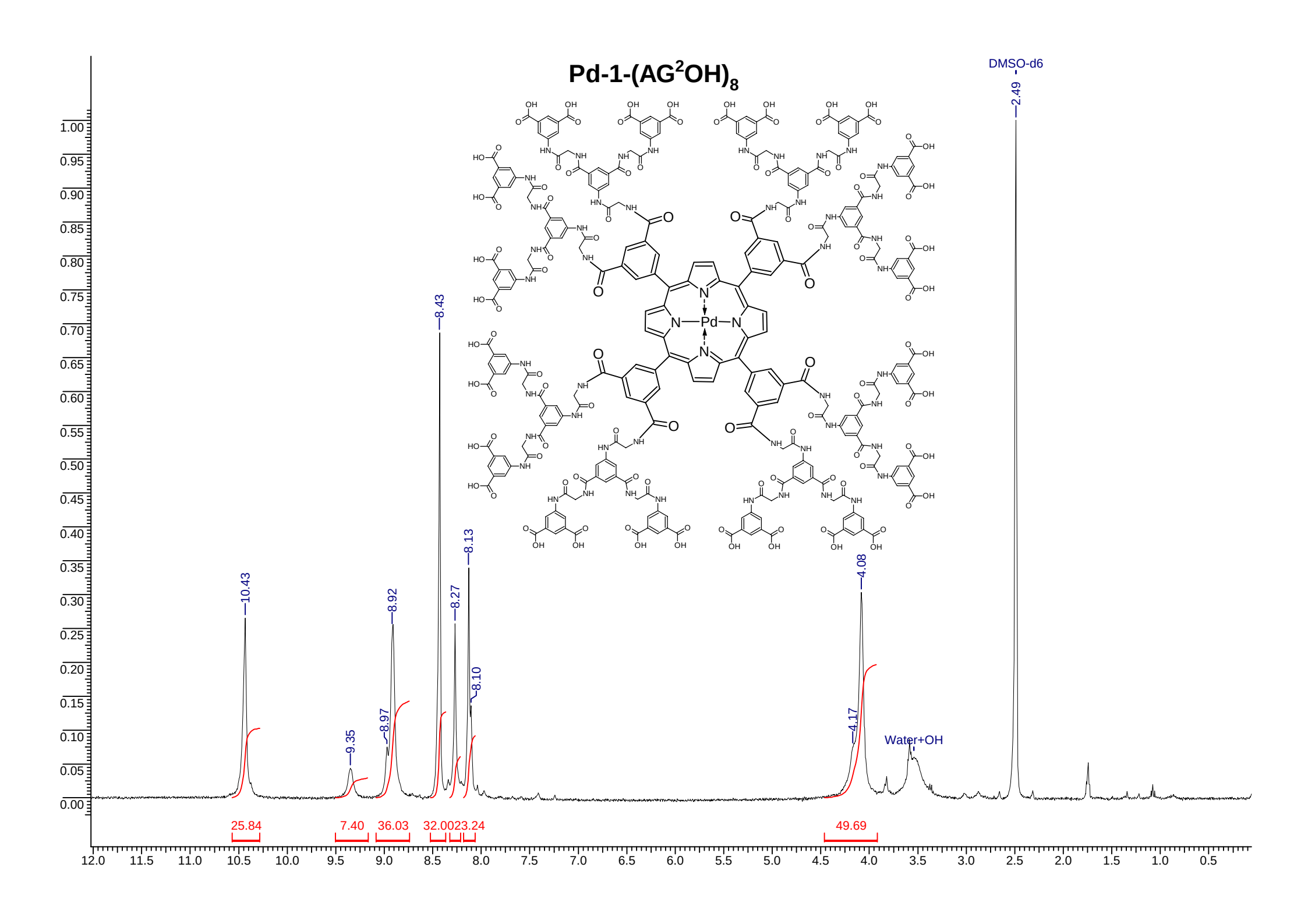


Pt-1-(AG^{2}OPEG)$_8$ (9), Absorption in Water

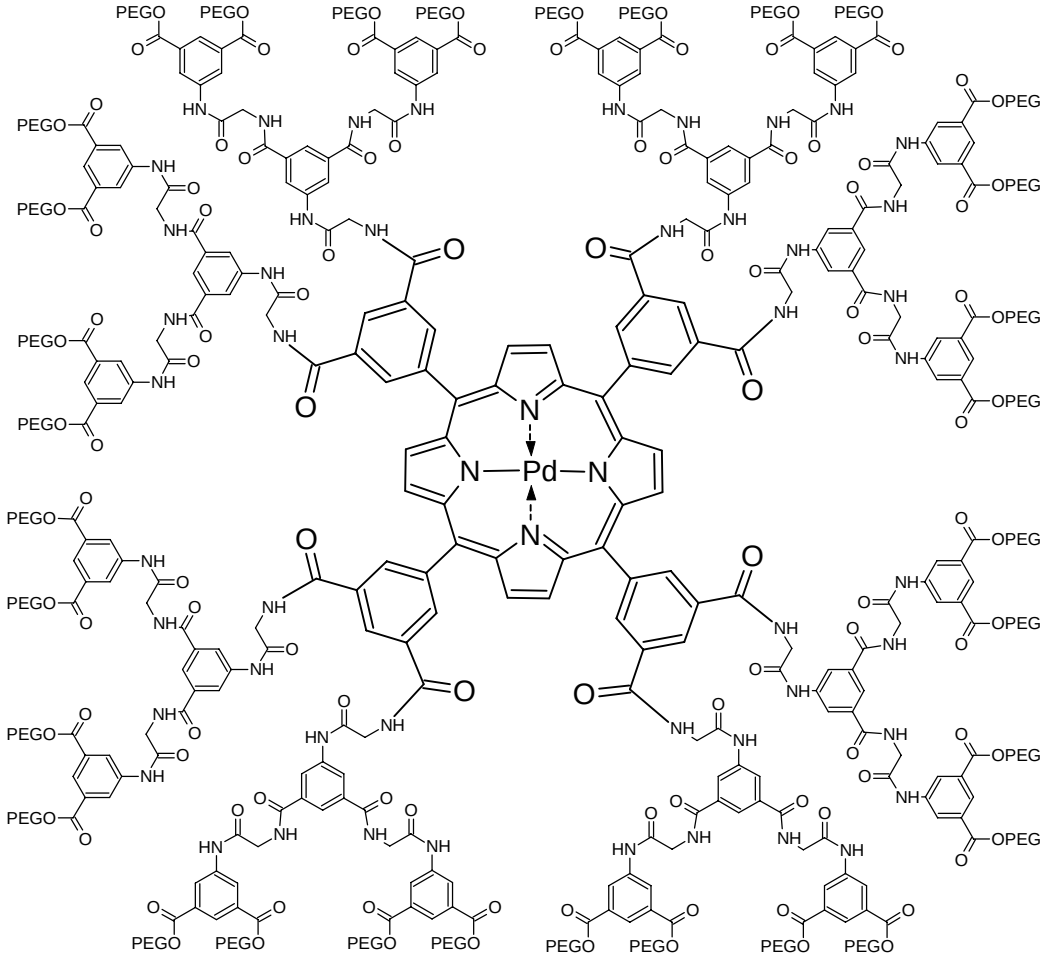


Pt-1-(AG^{2}OPEG)$_8$ (9), Emission in Water

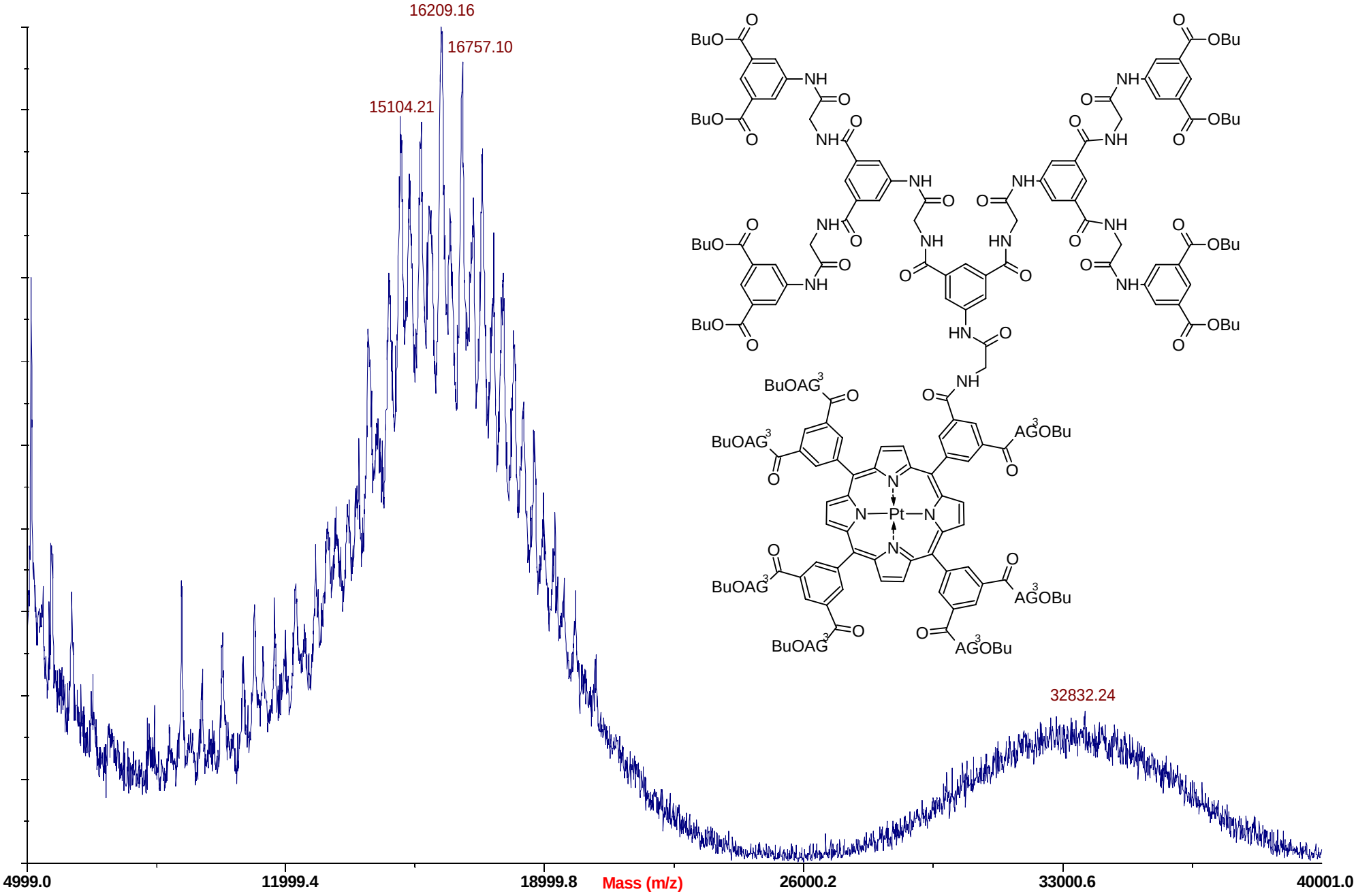



Pd-1-(AG2OH)8
DMSO-d6
2.49
10.43
9.35
8.97
8.92
8.43
8.27
8.13
8.10
4.17
4.08
Water+OH
25.84
7.40
36.03
32.00
23.24
49.69

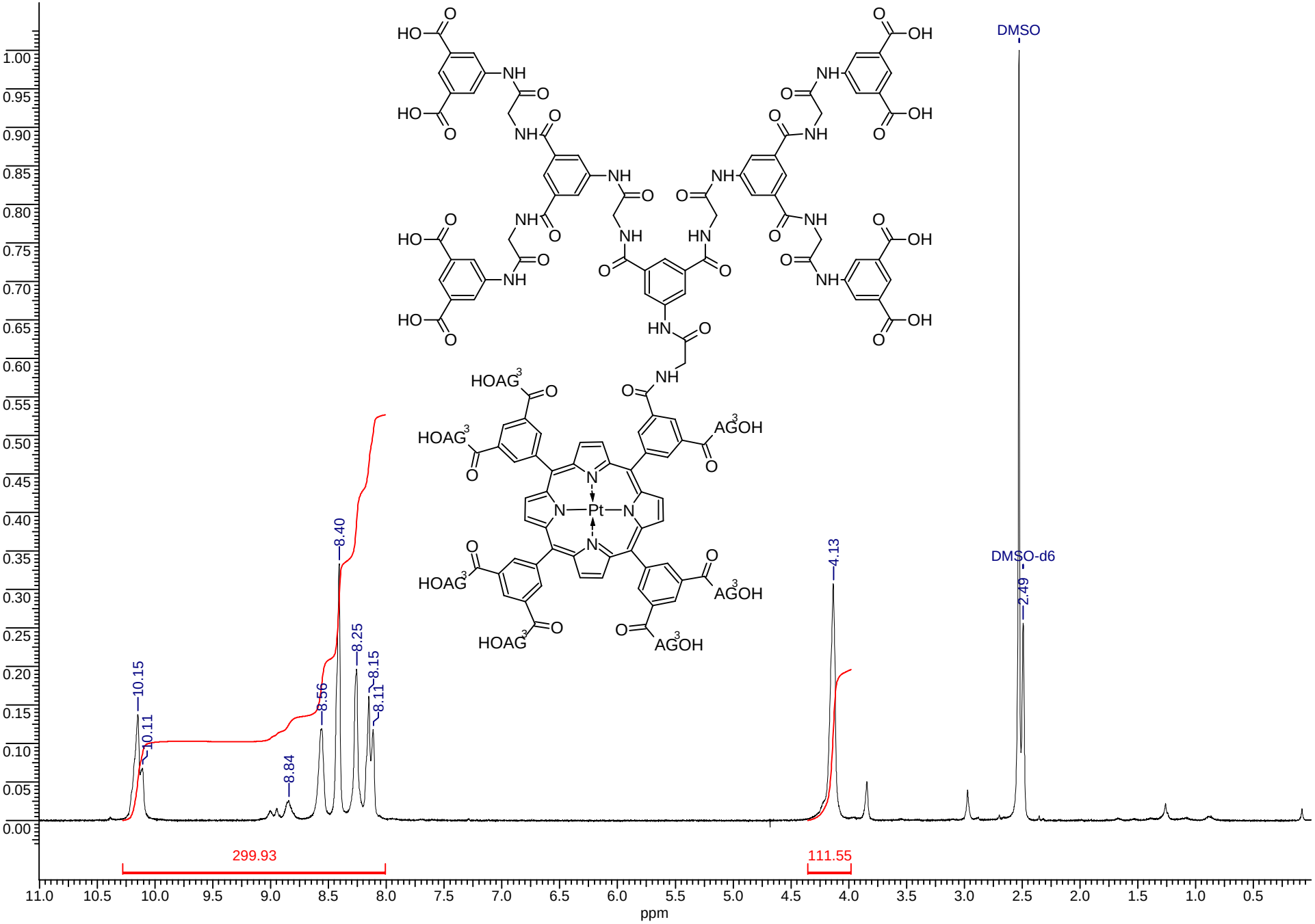
Pd-1-(AG^{2}OPEG)$_8$ (10)



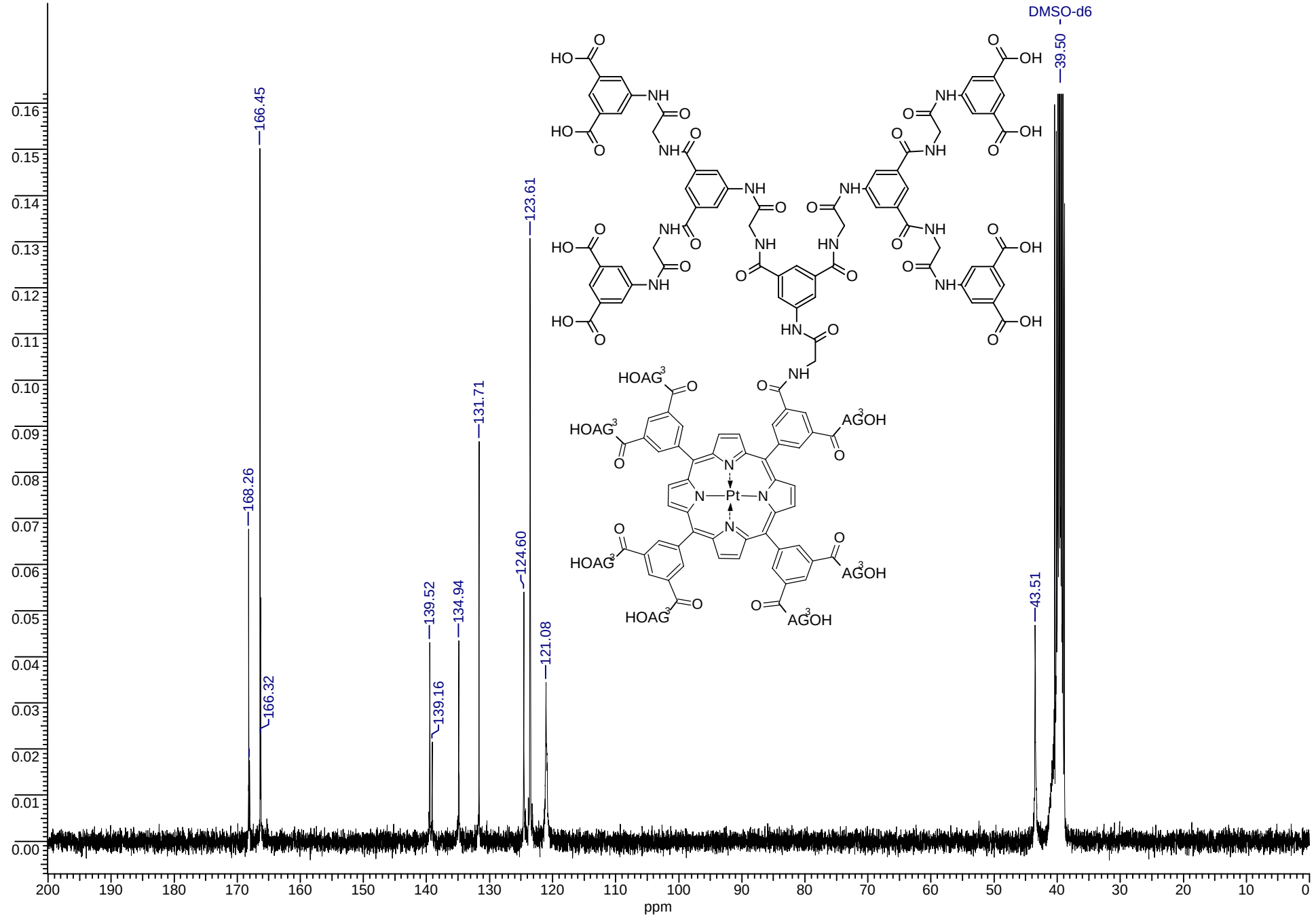
Pt-1-(AG^{3}OBu)$_8$, MALDI



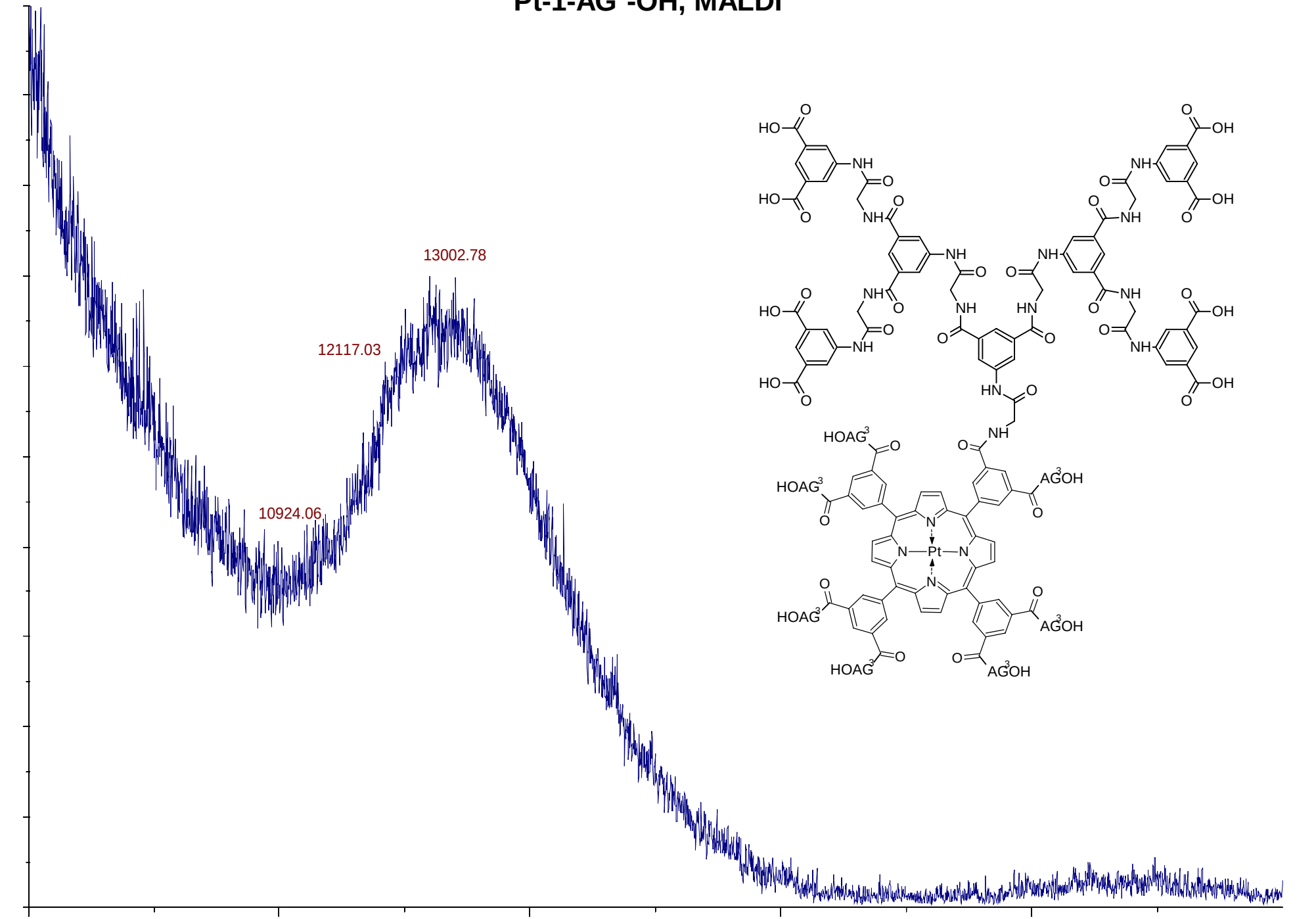
Pt-1-AG^3-OH, ^{1}H


DMSO
DMSO-d6
10.15
10.11
8.84
8.56
8.40
8.25
8.15
8.11
4.13
2.49
299.93
111.55
ppm

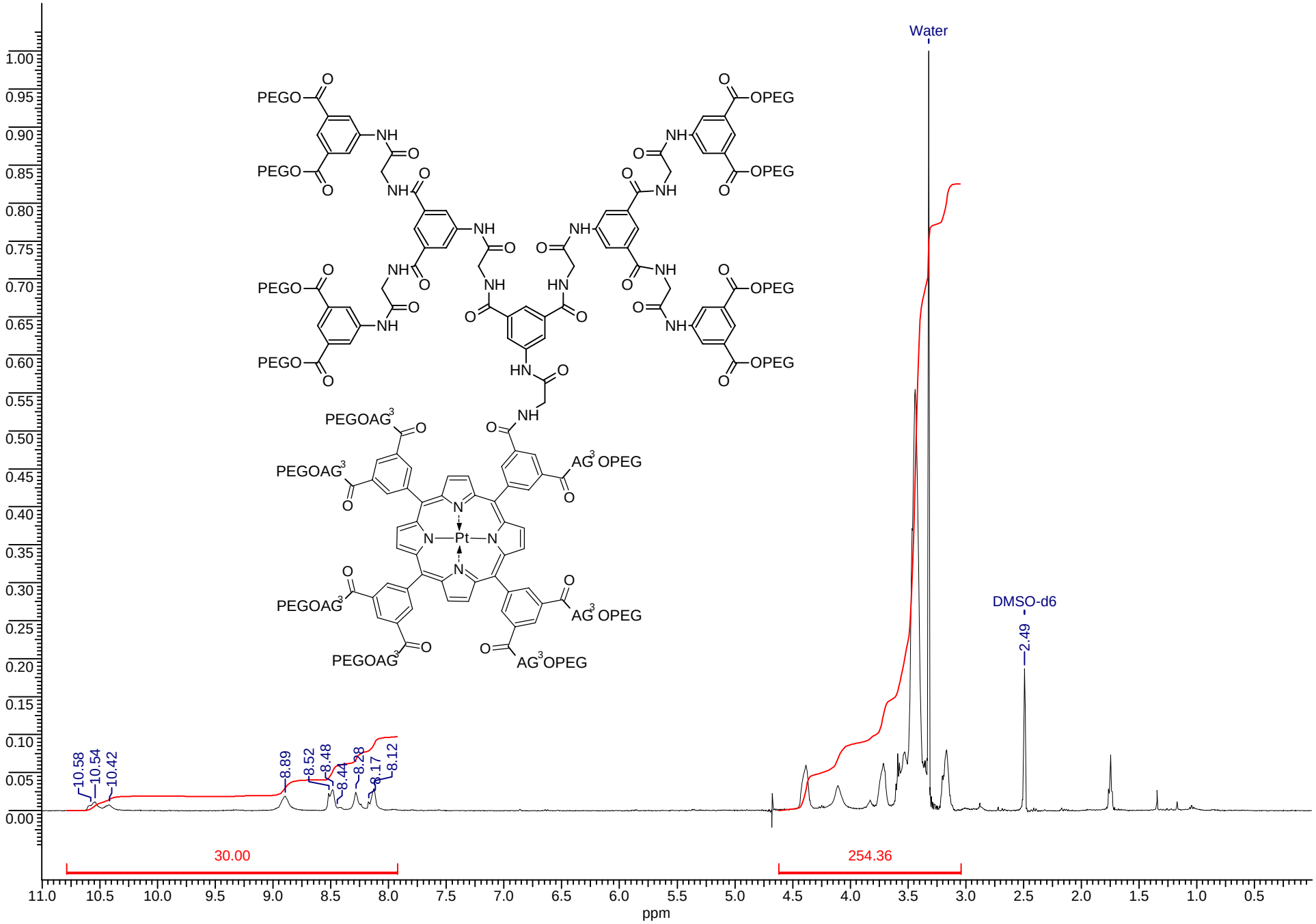
Pt-1-AG^3-OH, ^{13}C



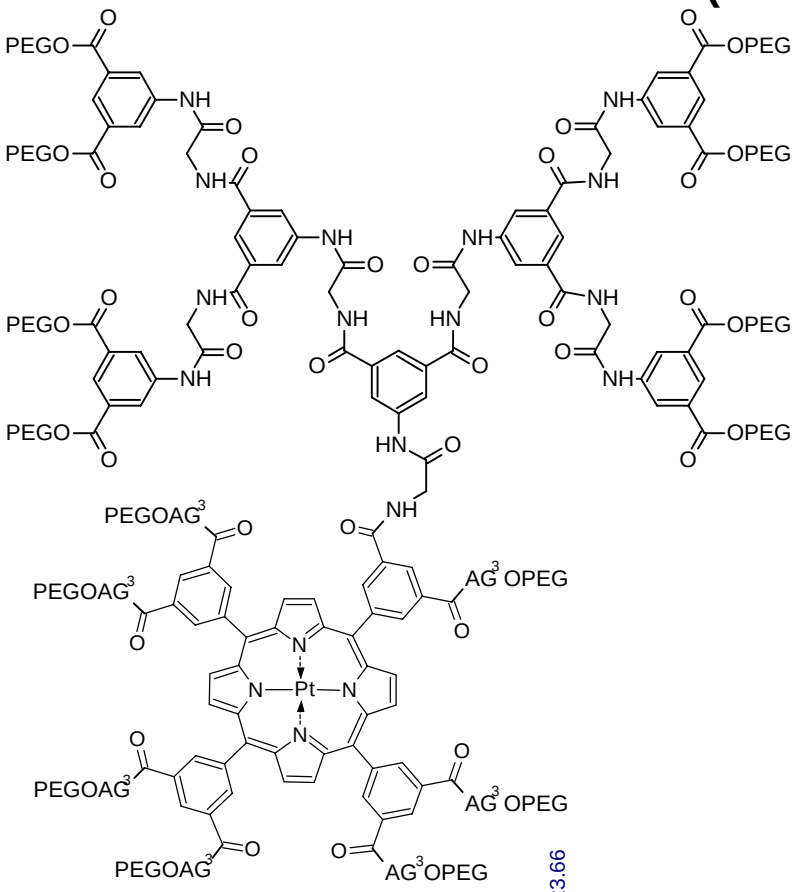
Pt-1-AG^3-OH, MALDI



Pt-1-(AG^3-OPEG)$_8$ (11), ^{1}H



Pt-1-(AG^3-OPEG)$_8$ (11), ^{13}C



DMSO-d6

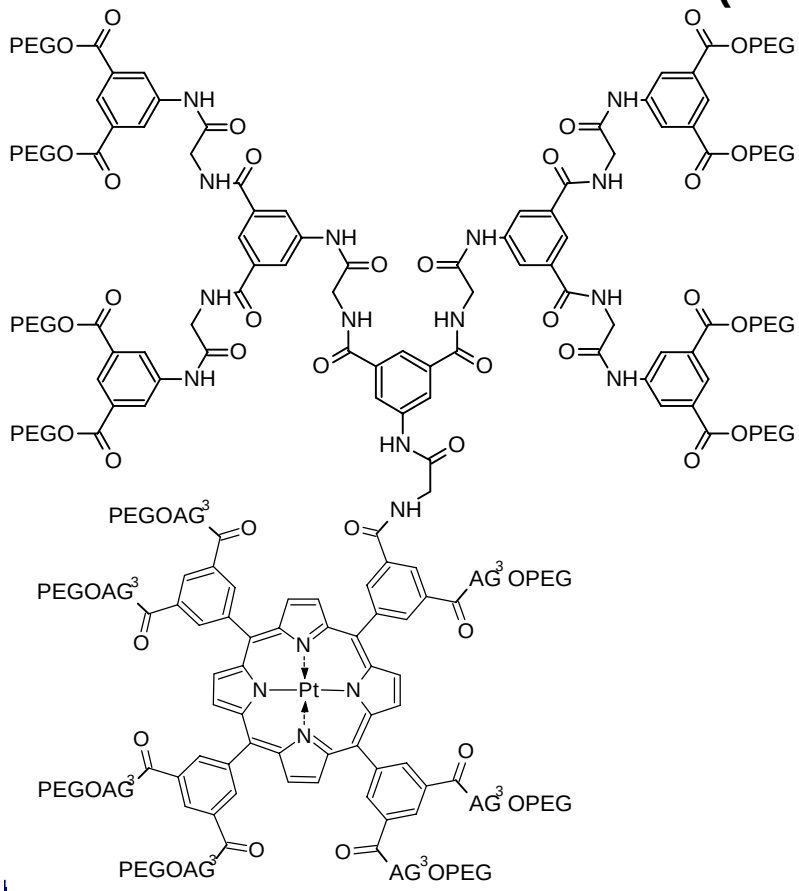
69.74
39.50
69.54
71.22
68.24
64.47
57.97
67.02
43.43
43.18
123.66
130.71
164.74
168.32
168.03
139.85
139.18
134.89
124.91
124.13
121.08

0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0.00
-0.01

180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

ppm

Pt-1-(AG^{3}OPEG)$_8$ (11), ^{13}C

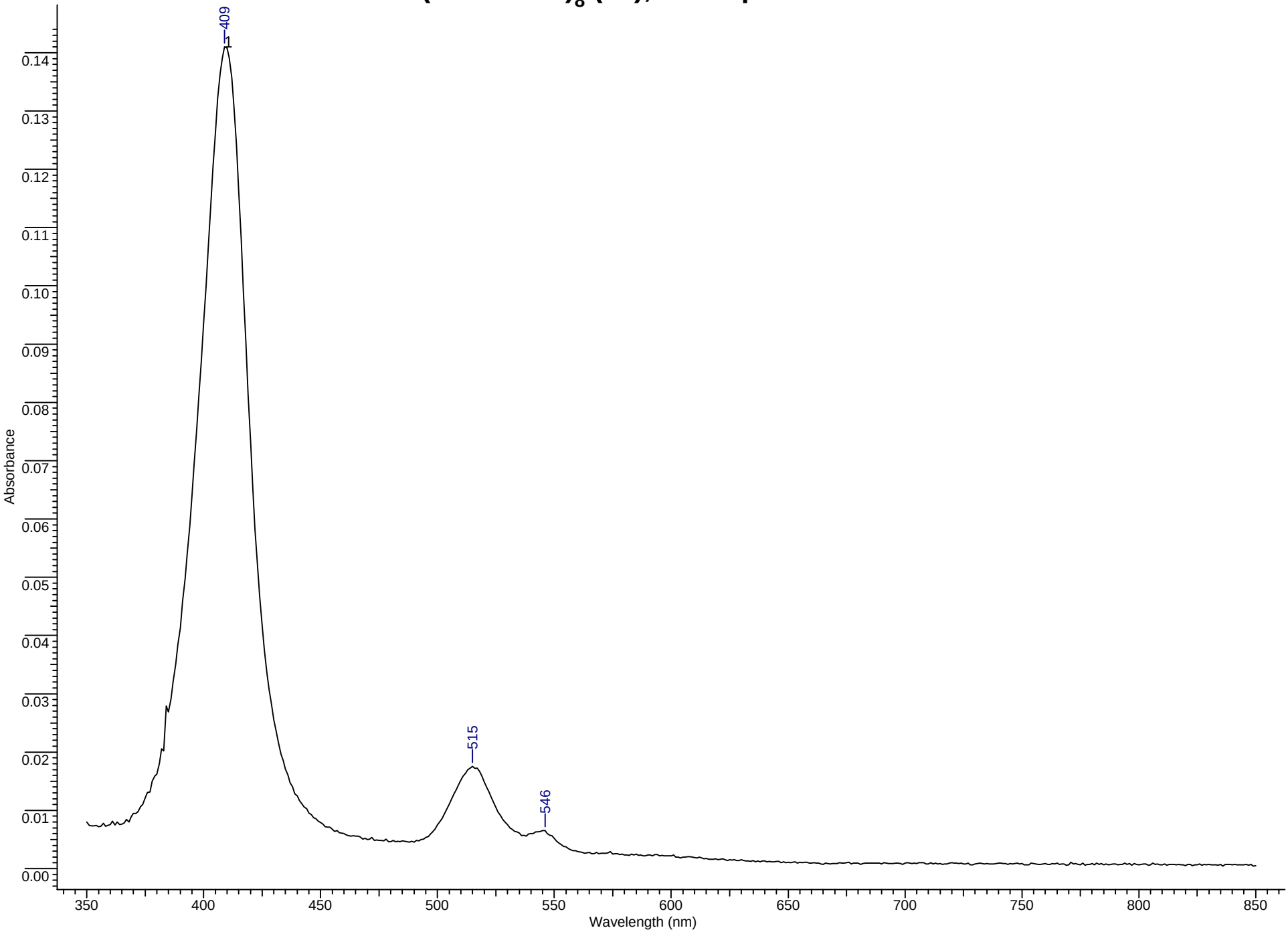


31 kDa

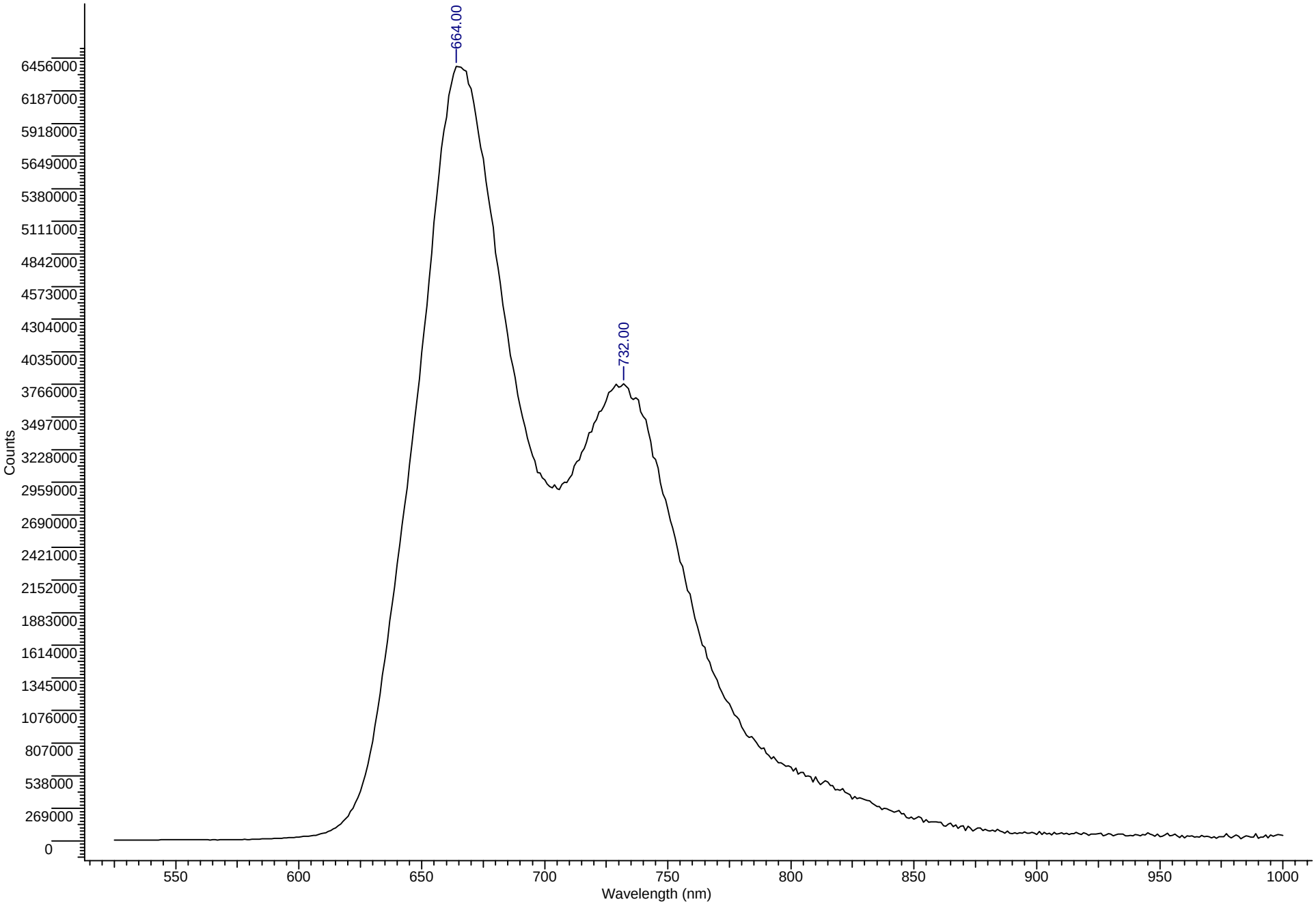
0

10100.0 28079.8 46059.6 Mass (m/z) 64039.4 82019.2 99999.0

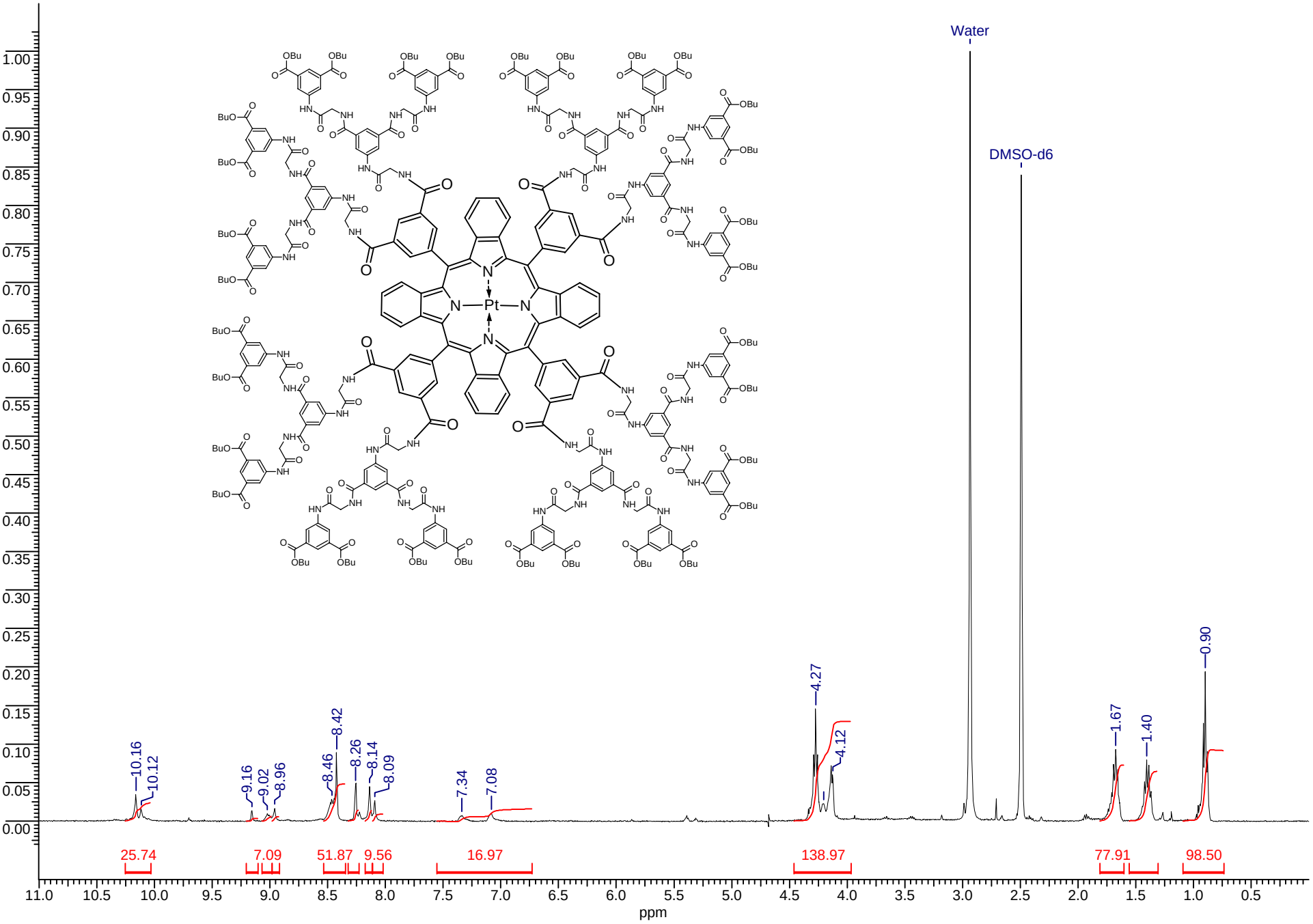
Pt-1-(AG^{3}OPEG)$_8$ (11), Absorption in water



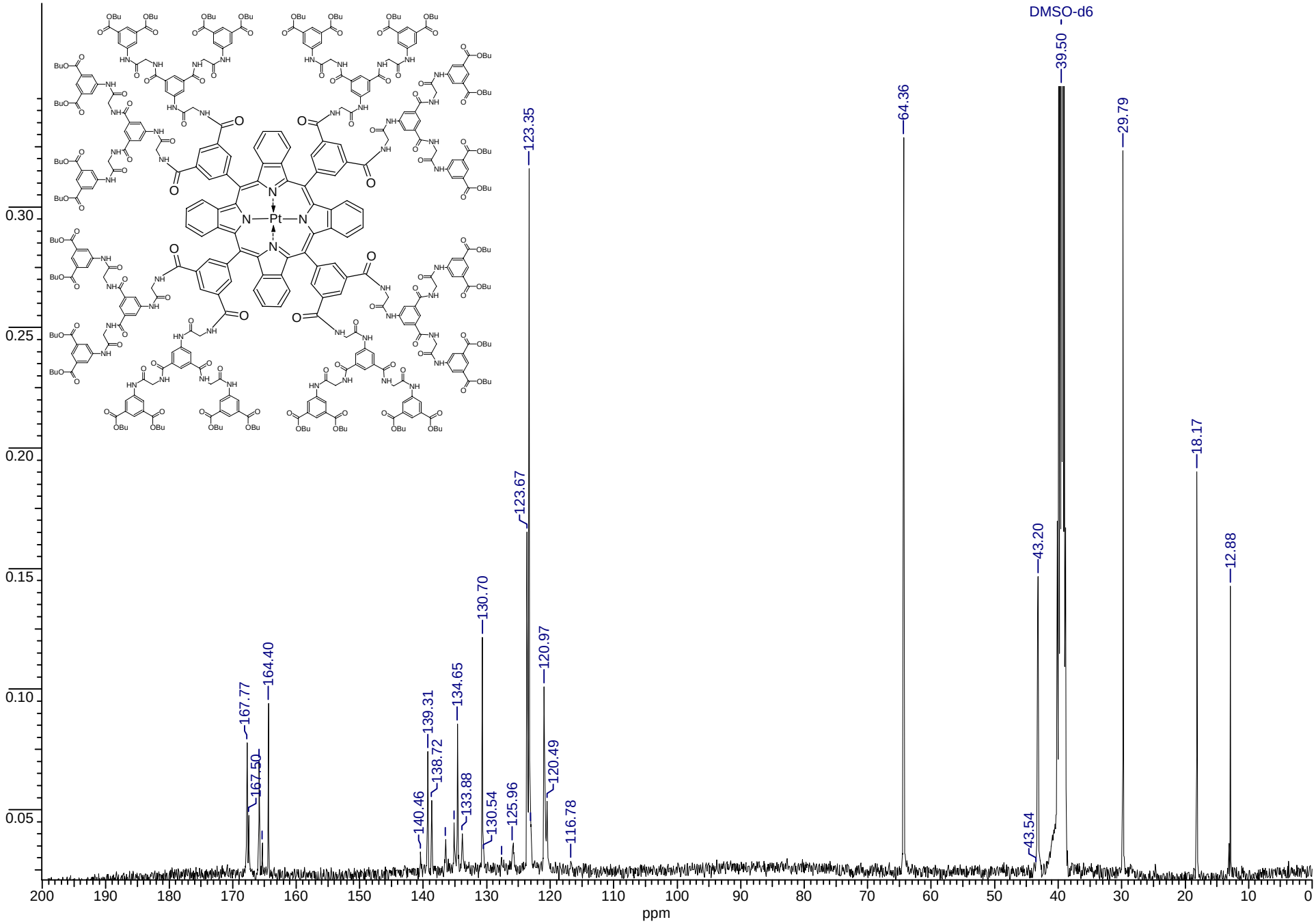
Pt-1-(AG^{3}OPEG)$_8$ (11), Emission in water



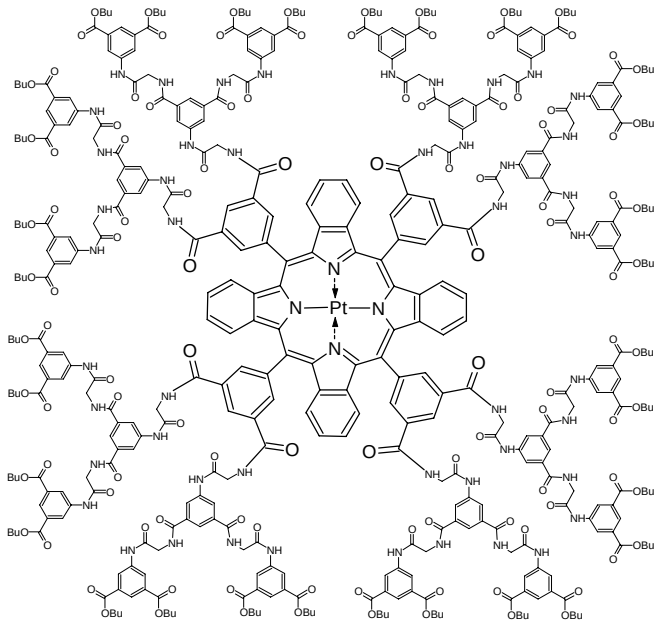
Pt-2-(AG^2-OBu)$_8$, ^{1}H



Pt-2-(AG^2-OBu)$_8$, ^{13}C



Pt-2-(AG^2-OBu)$_8$, ^{13}C



8478.83

8462.24

9029.44

8433.94

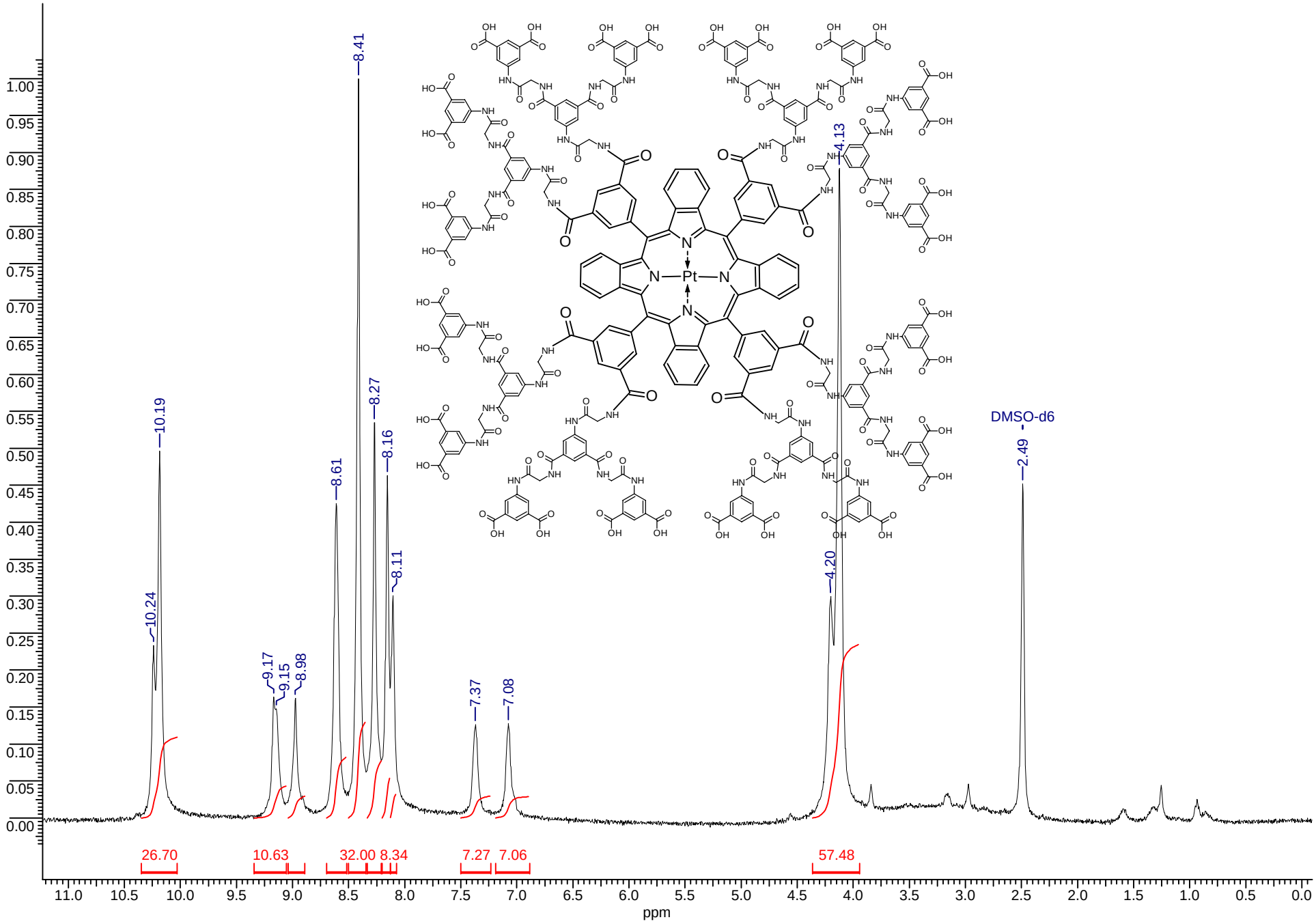
9013.21

8991.32

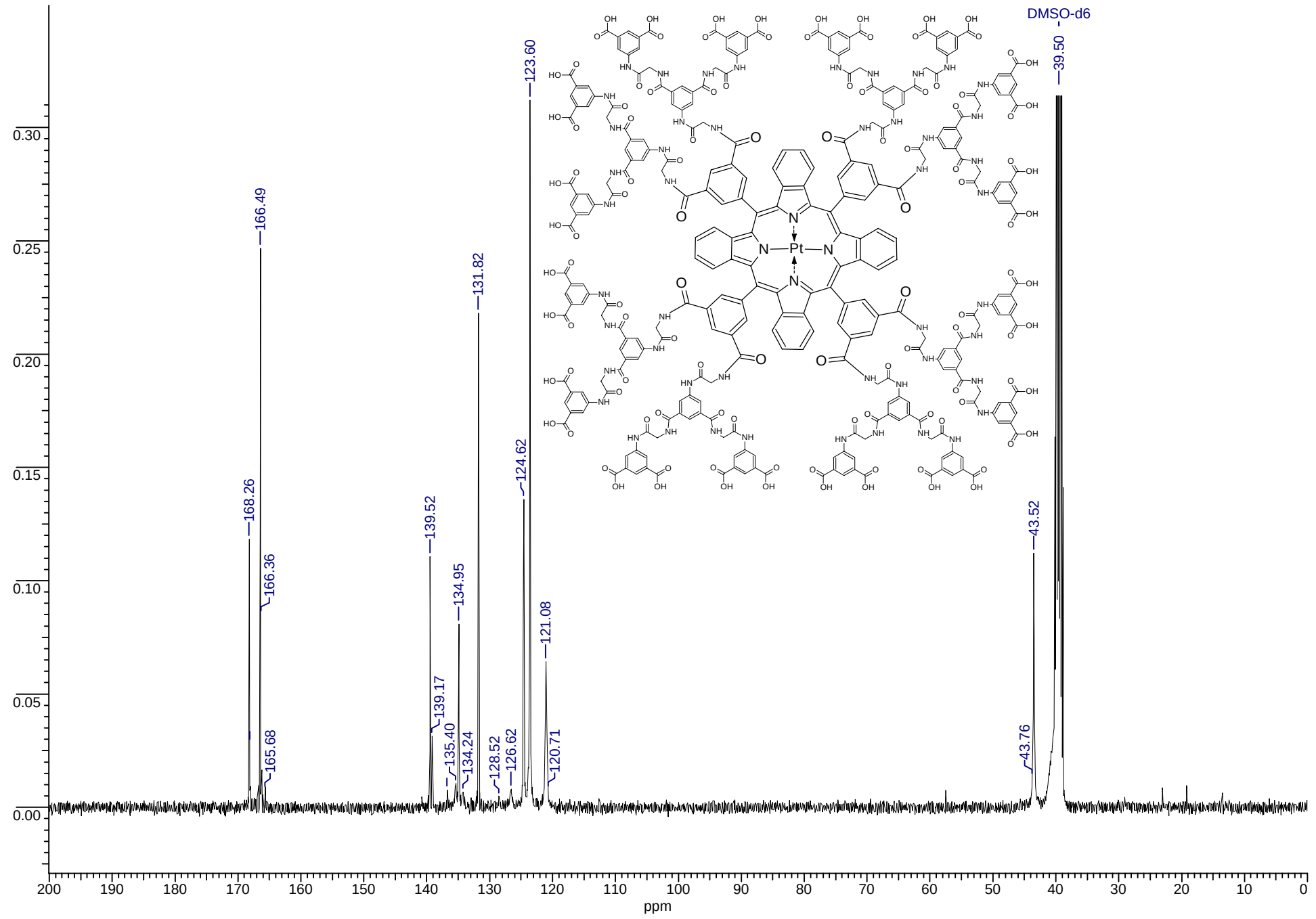
9582.48

3000 5400 7800 Mass (m/z) 10200 12600 15000

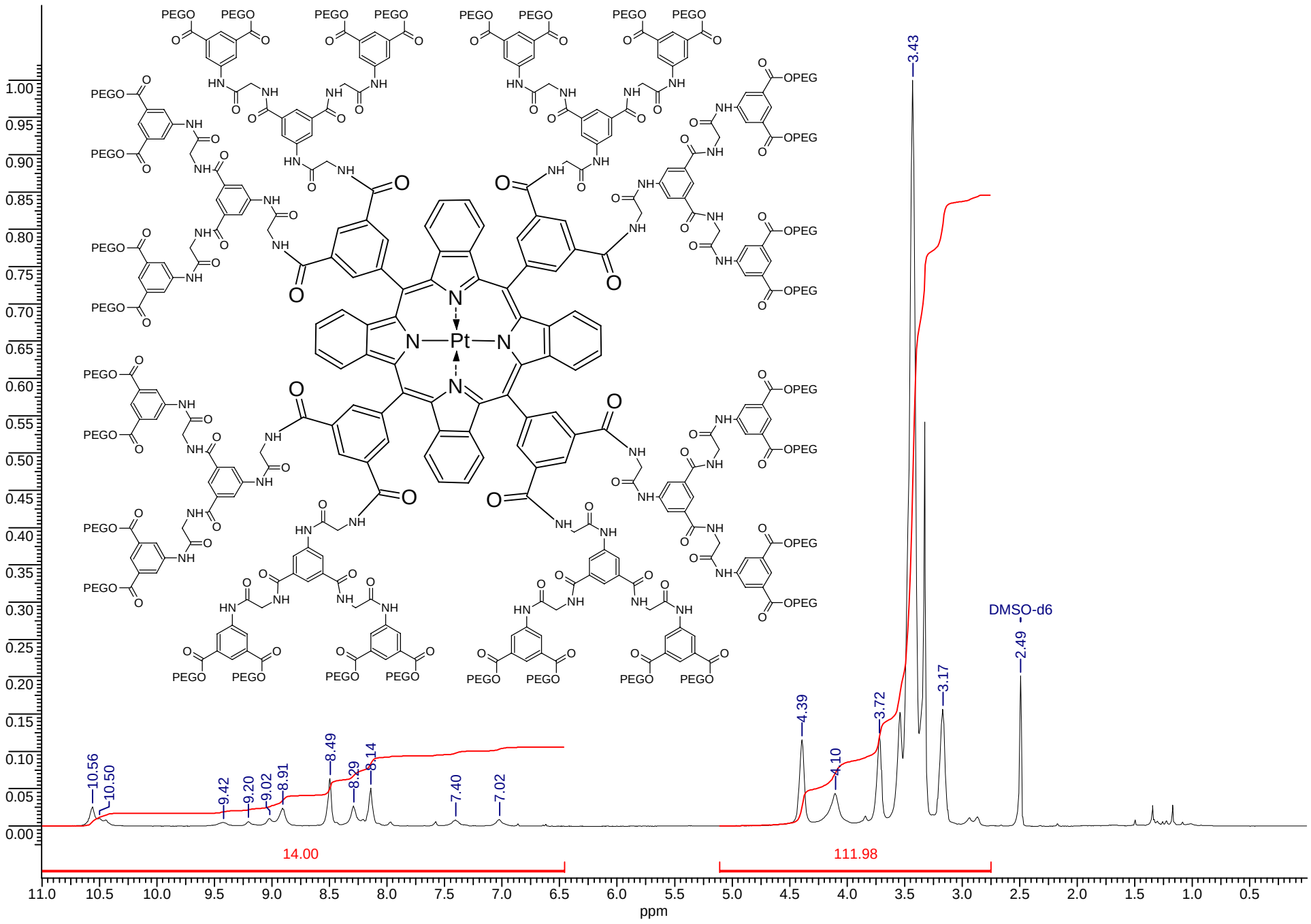
Pt-2-(AG^{2}OH)$_8$, ^{1}H



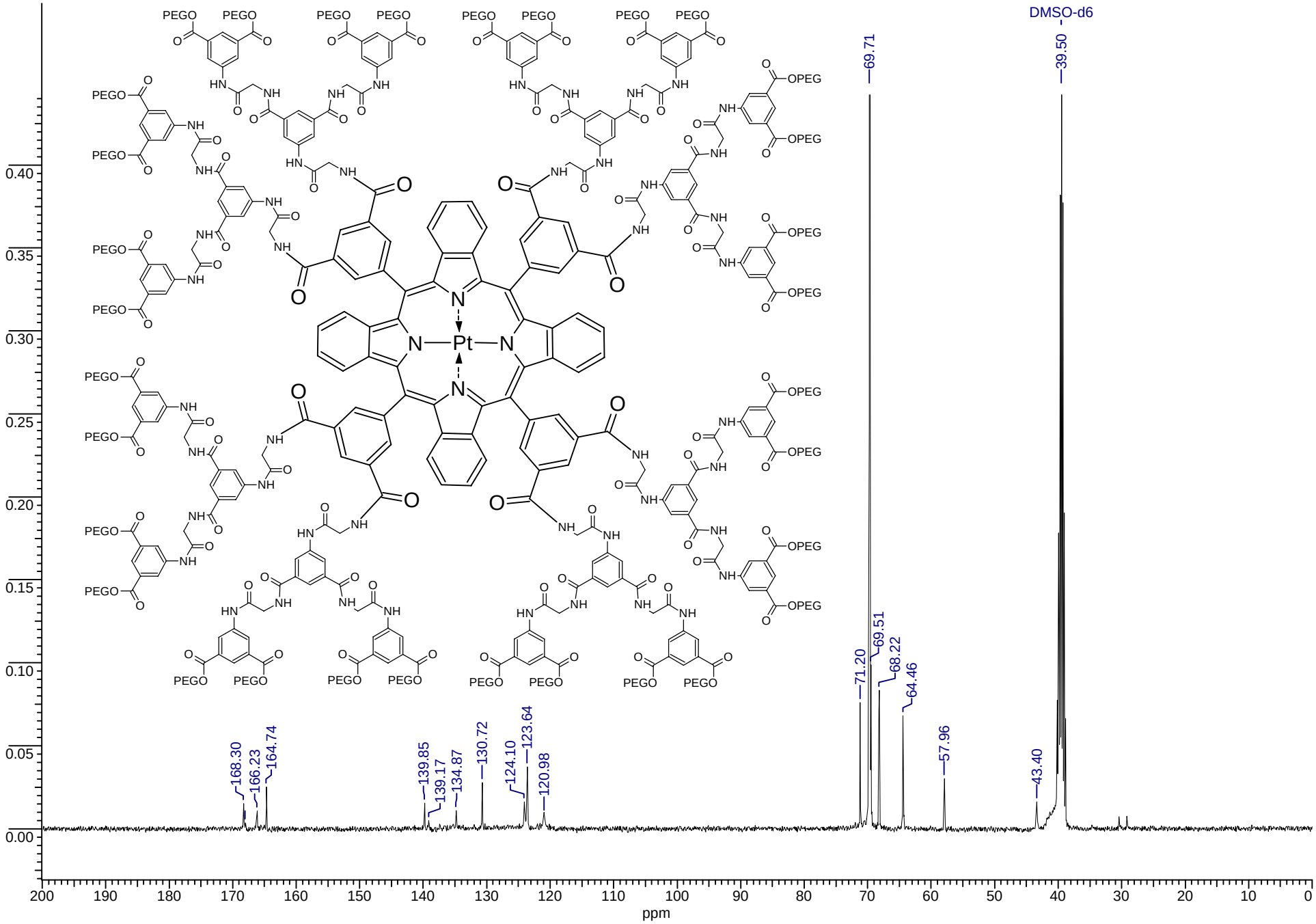
Pt-2-(AG^{2}OH)$_8$, ^{13}C



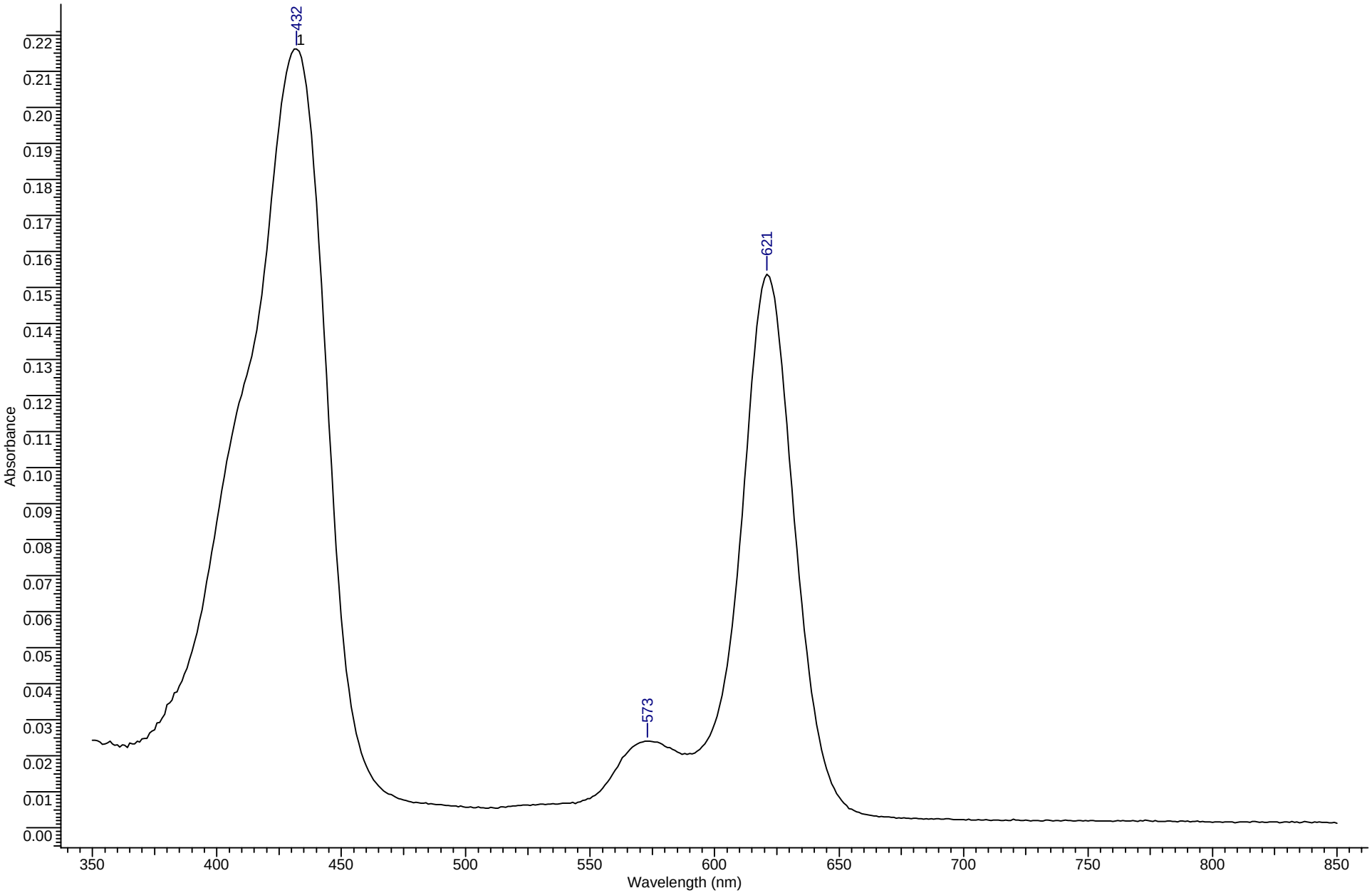
Pt-2-(AG^{2}OPEG)$_8$ (12), ^{1}H



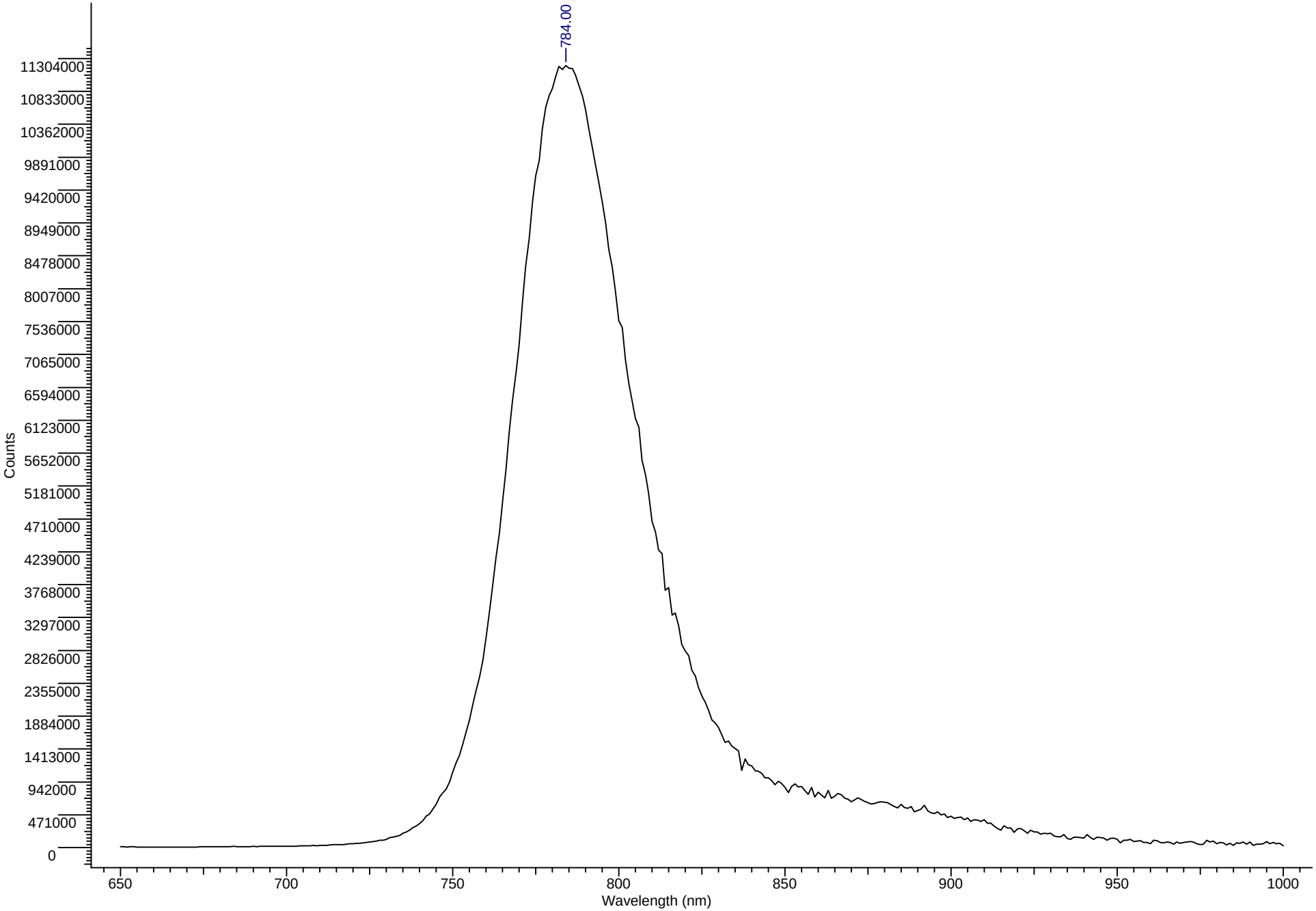
PtTBP-(AG^2-OPEG)$_8$ (12), ^{13}C



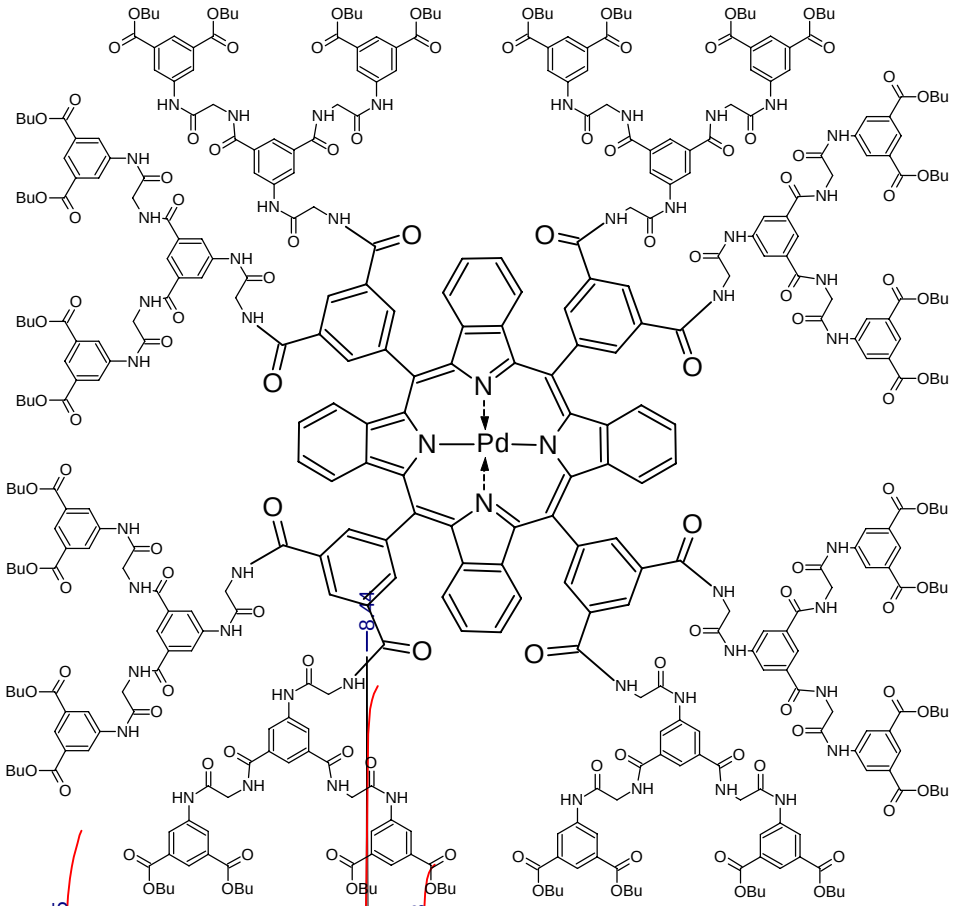
Pt-2-(AG^{2}OPEG)$_8$ (12), Absorption in Water



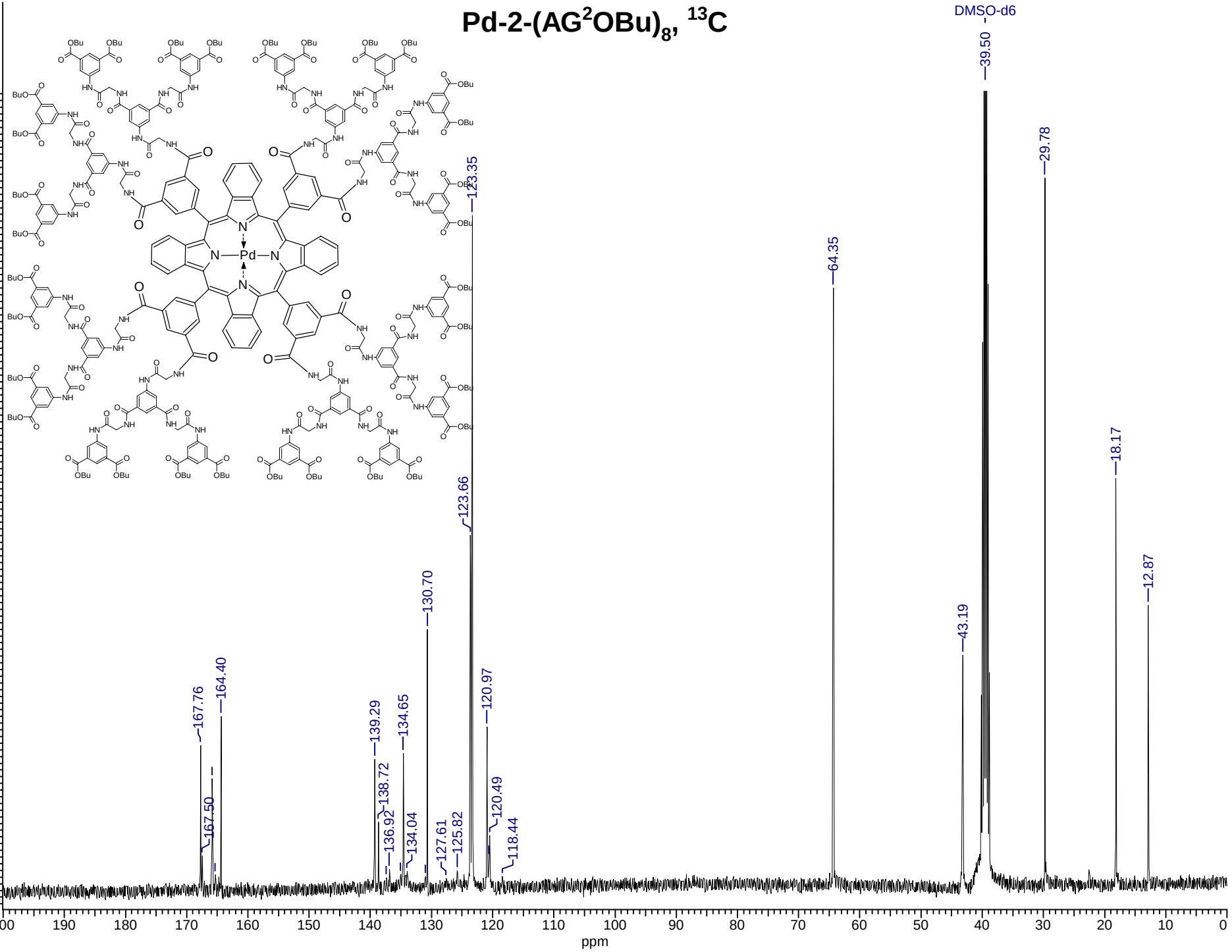
Pt-2-(AG^{2}OPEG)$_8$ (12), Emission in Water



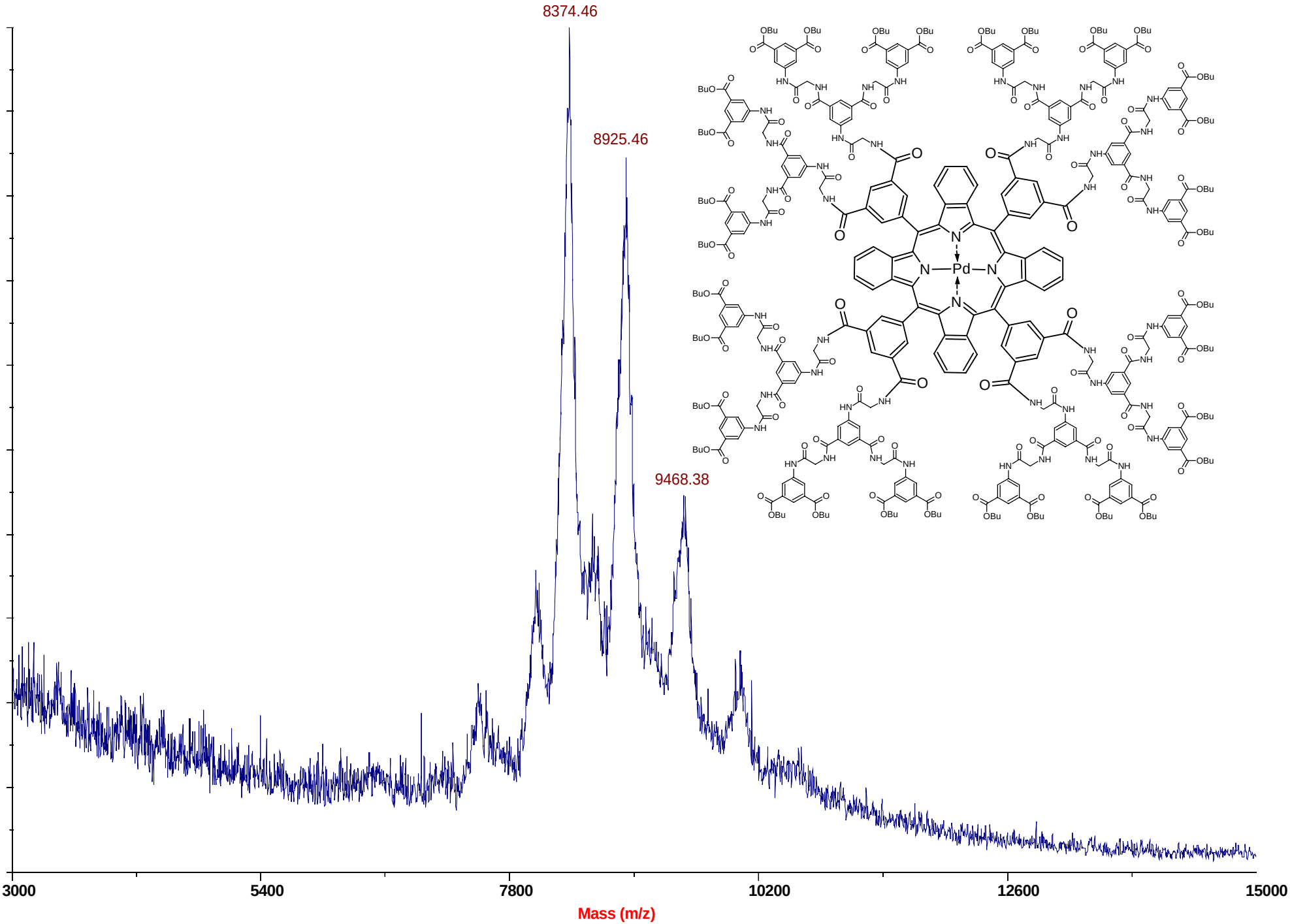
Pd-2-(AG^{2}OBu)$_8$, ^{1}H



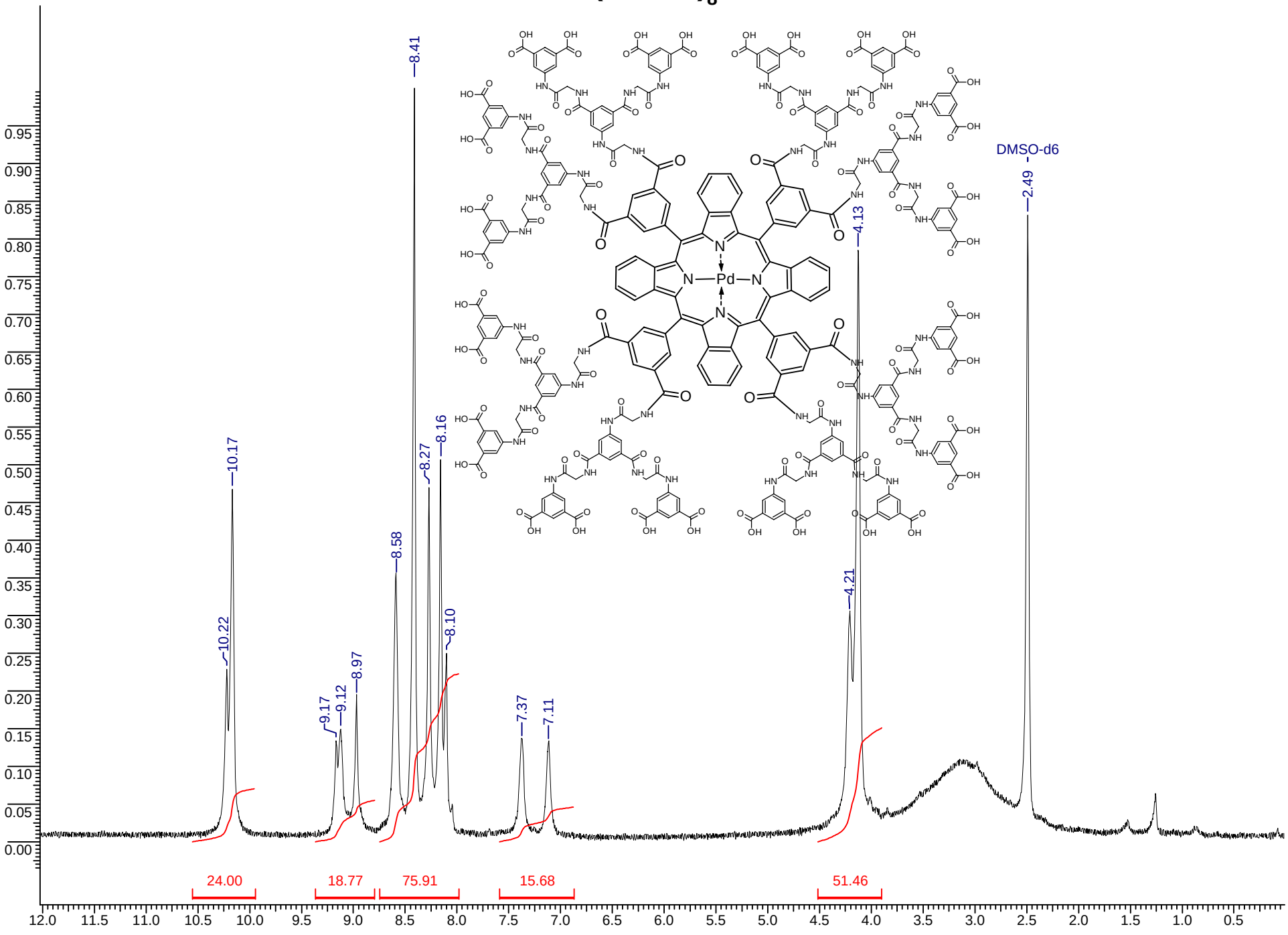
Pd-2-(AG^{2}OBu)$_8$, ^{13}C



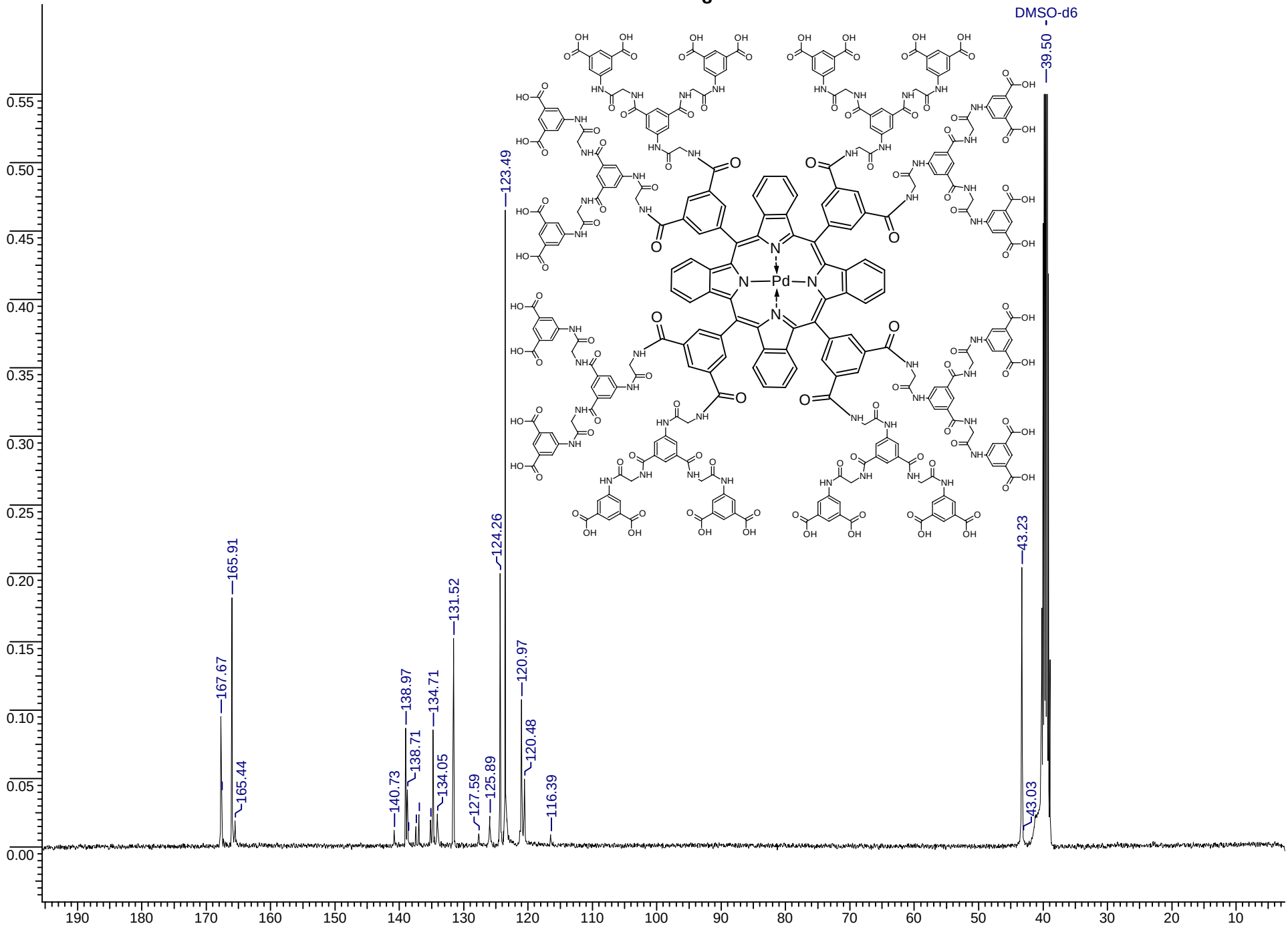
Pd-2-(AG^{2}OBu)$_8$, MALDI



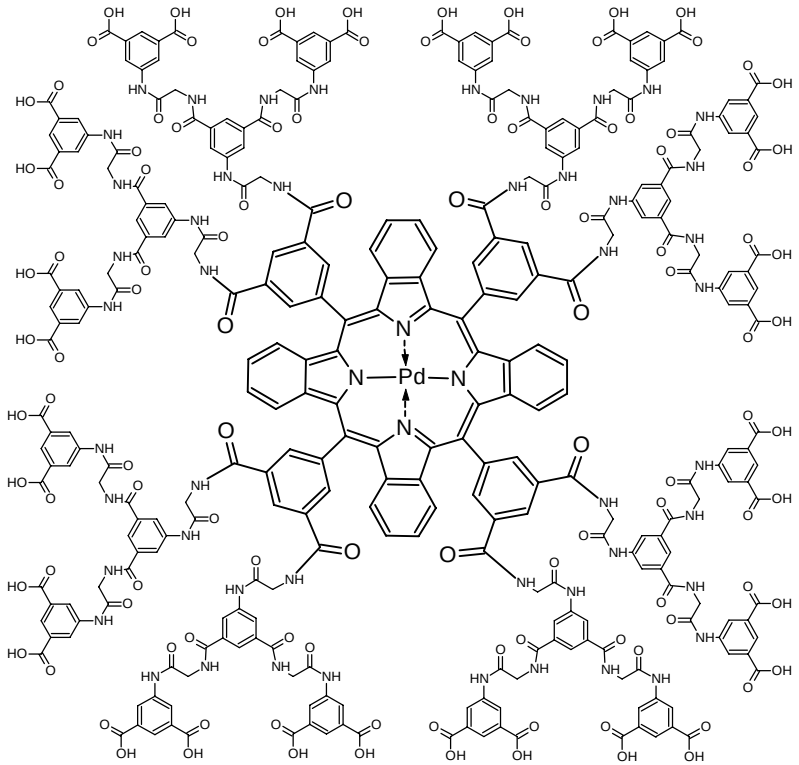
Pd-2-(AG^{2}OH)$_8$, ^{1}H



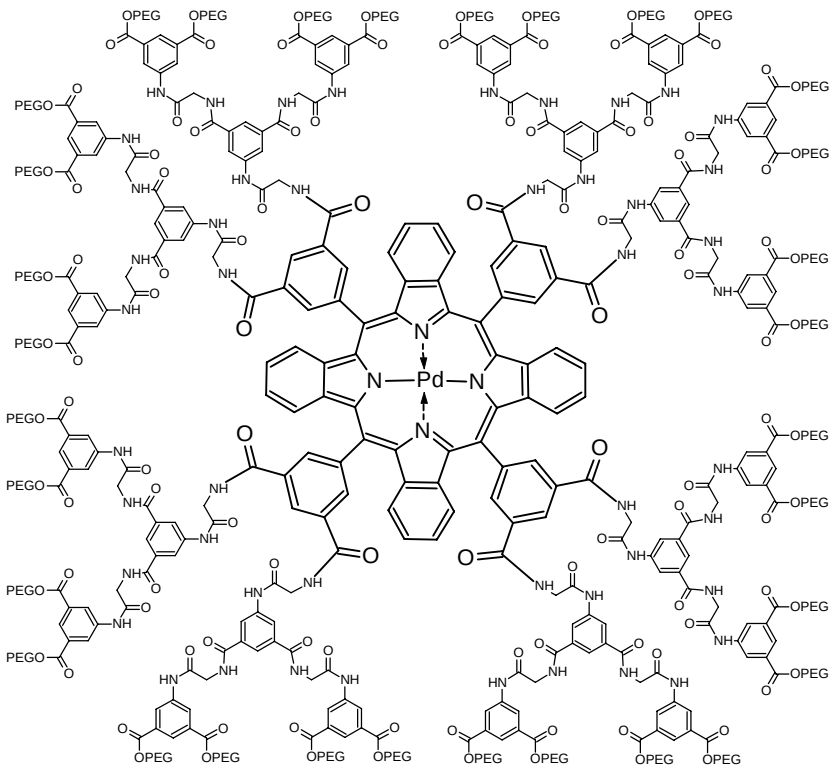
Pd-2-(AG^{2}OH)$_8$, ^{13}C



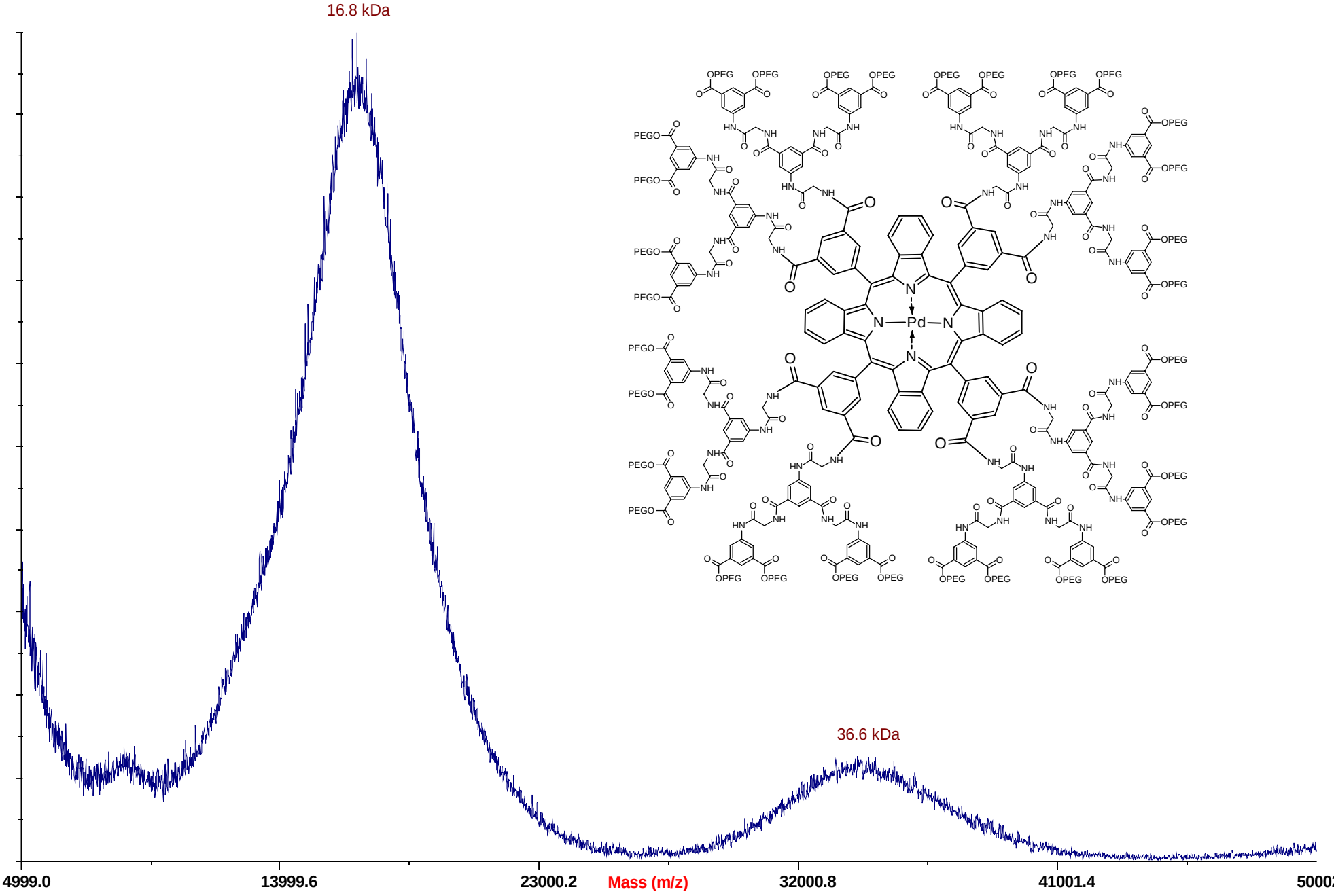
Pd-2-(AG^{2}OH)$_8$, ^{1}H



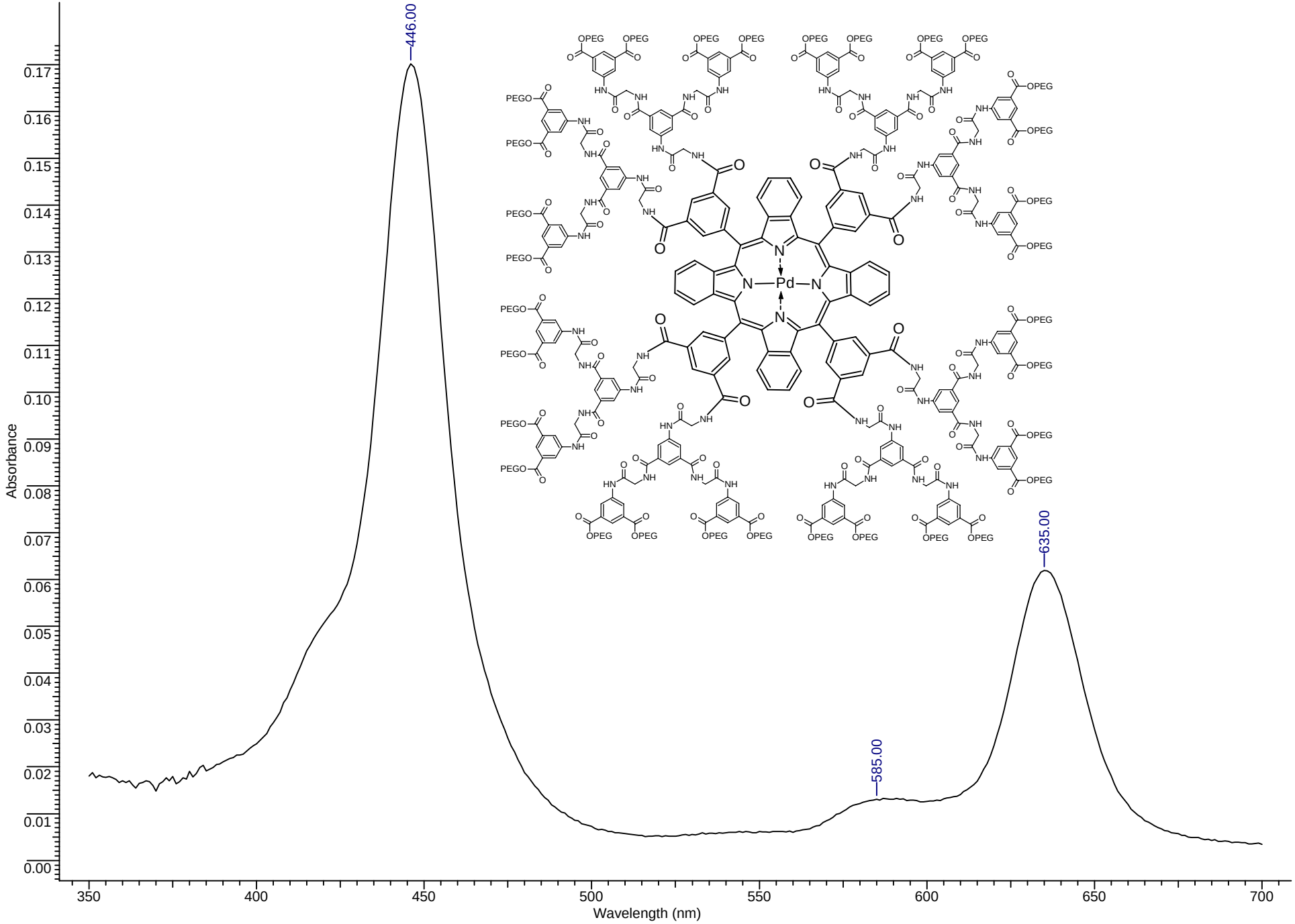
Pd-2-(AG^{2}OPEG)$_8$ (13), ^{1}H



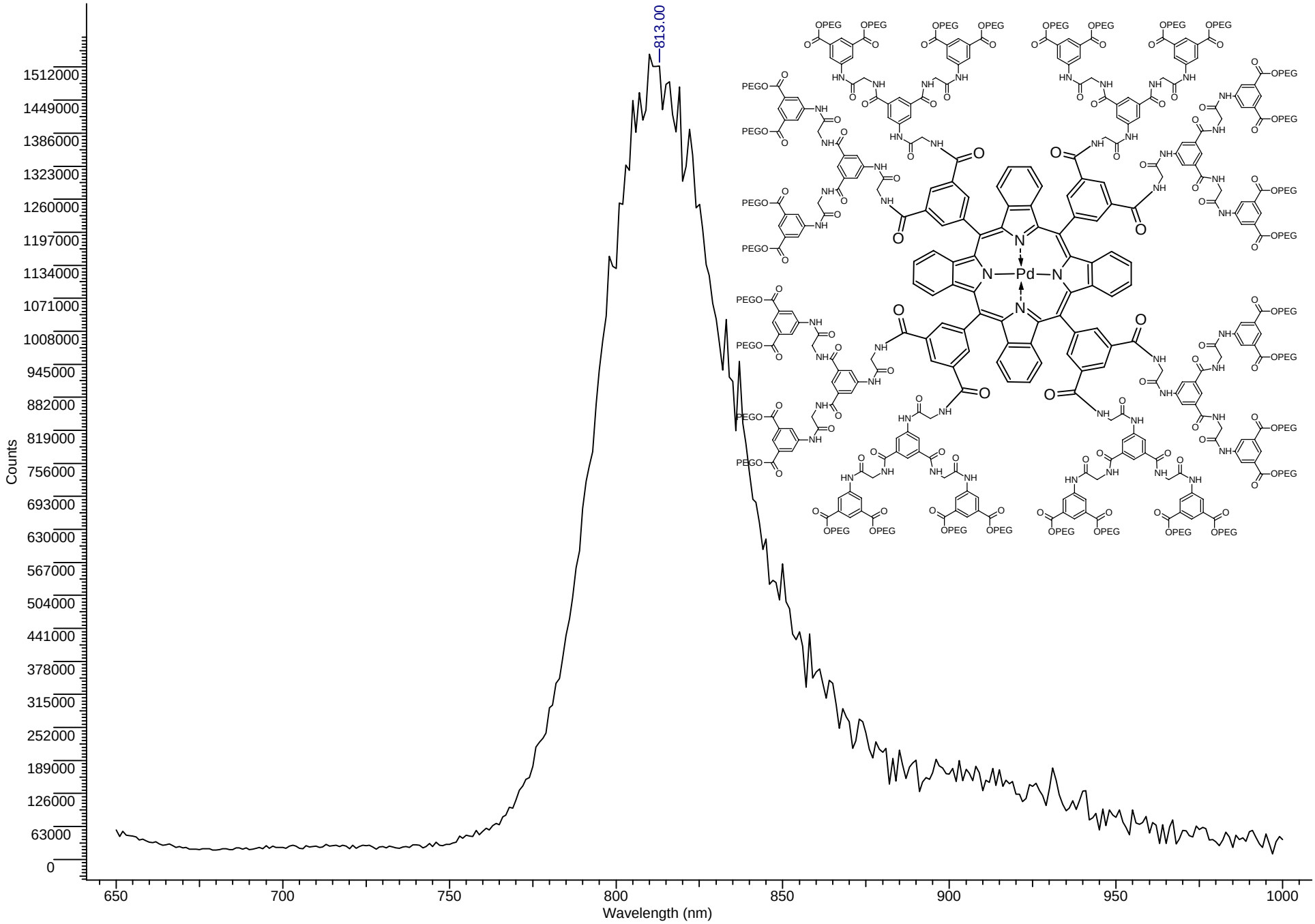
Pd-2-(AG^{2}OPEG)$_8$ (13), MALDI



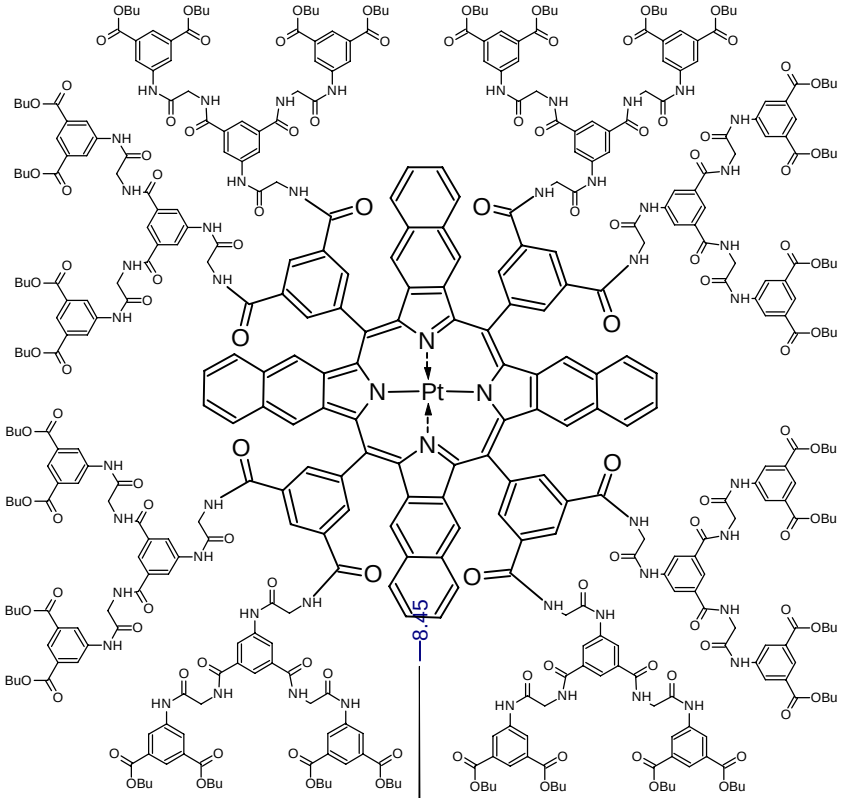
Pd-2-(AG^{2}OPEG)$_8$ (13), Absorption in water



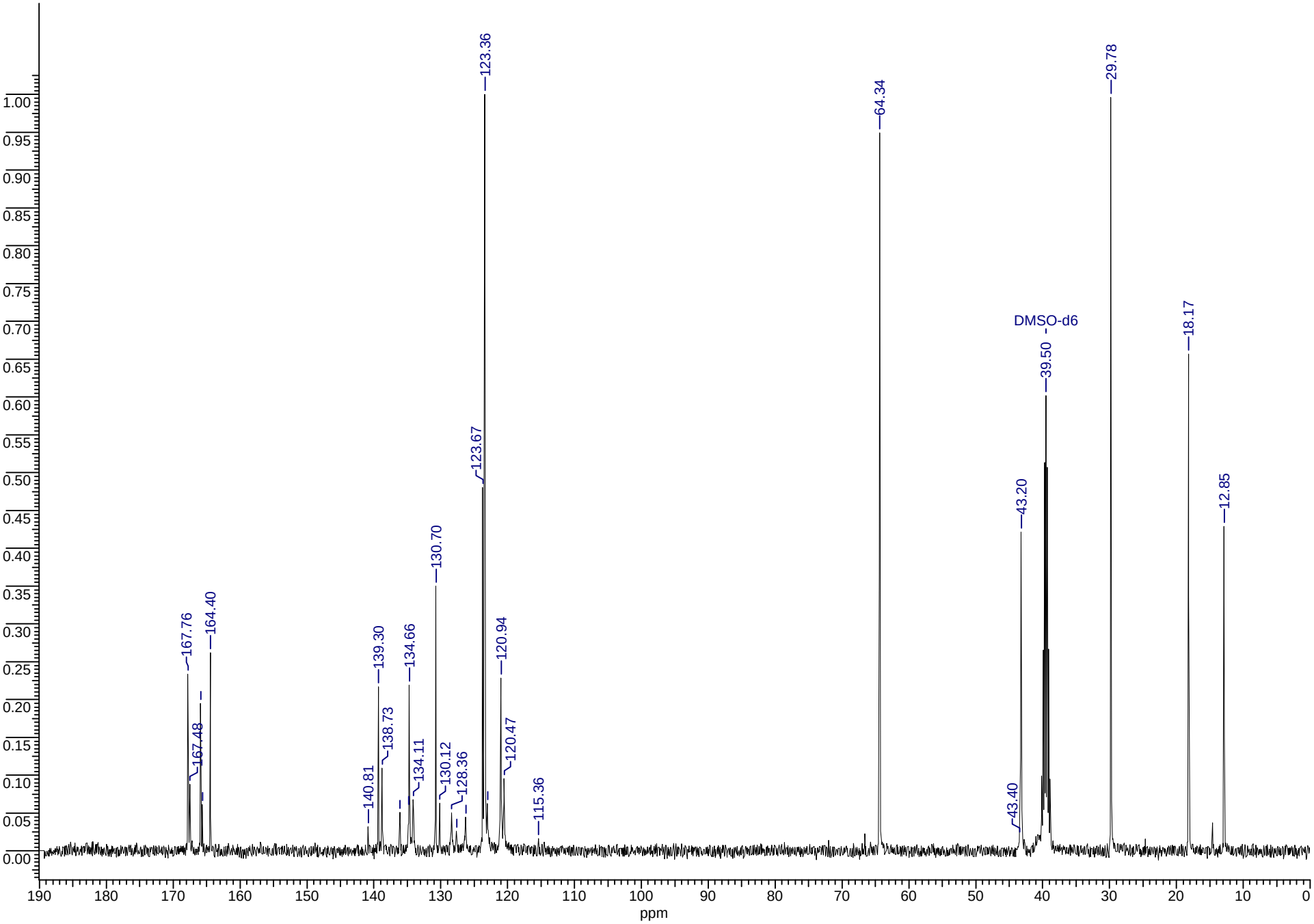
Pd-2-(AG^{2}OPEG)$_8$ (13), Emission in water



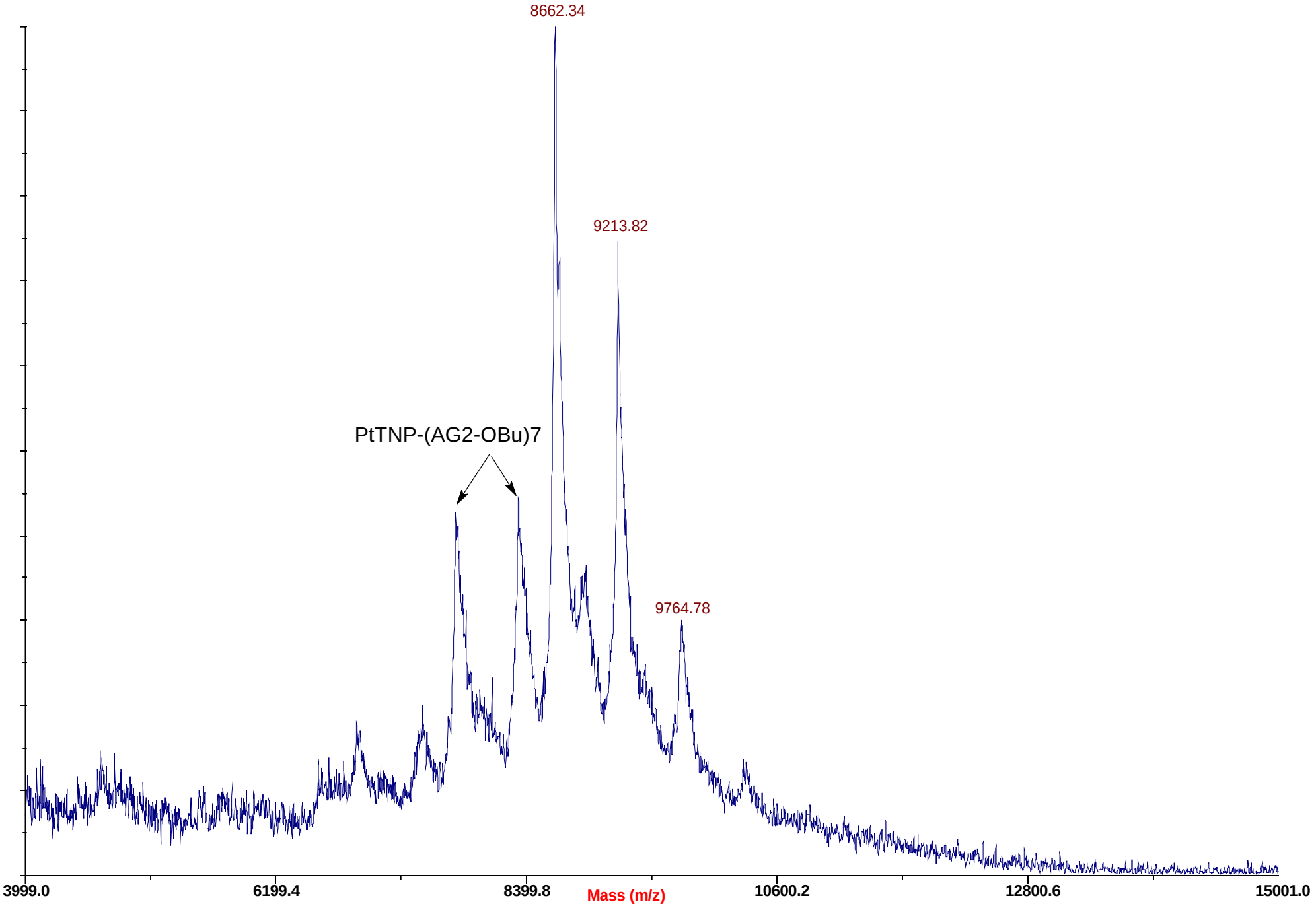
Pt-3-(AG^2-OBu)$_8$, ^{1}H



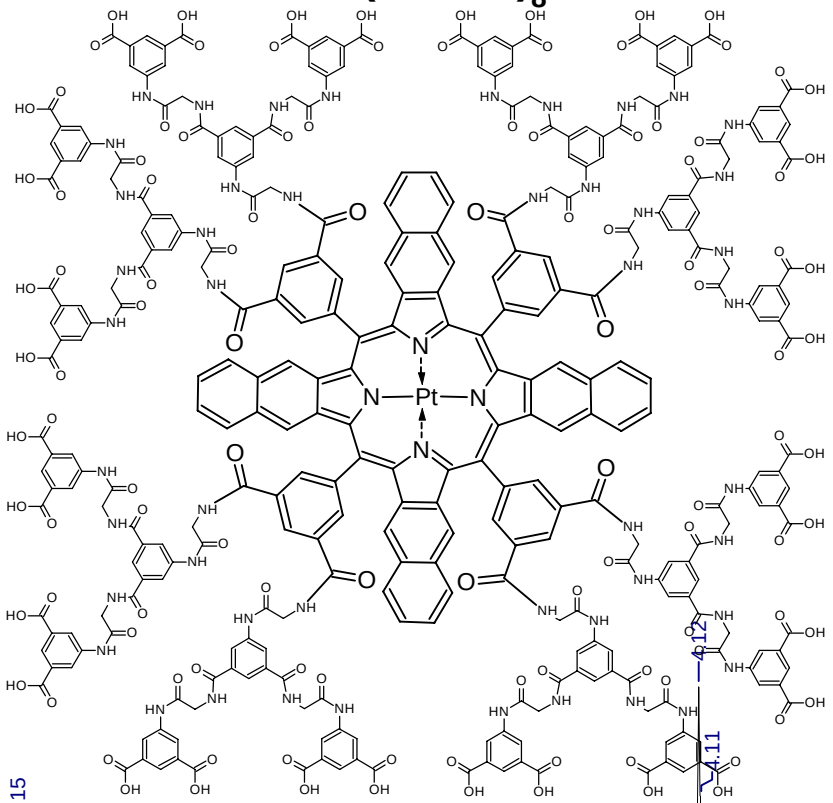
Pt-3-(AG^{2}OBu)$_8$, ^{13}C



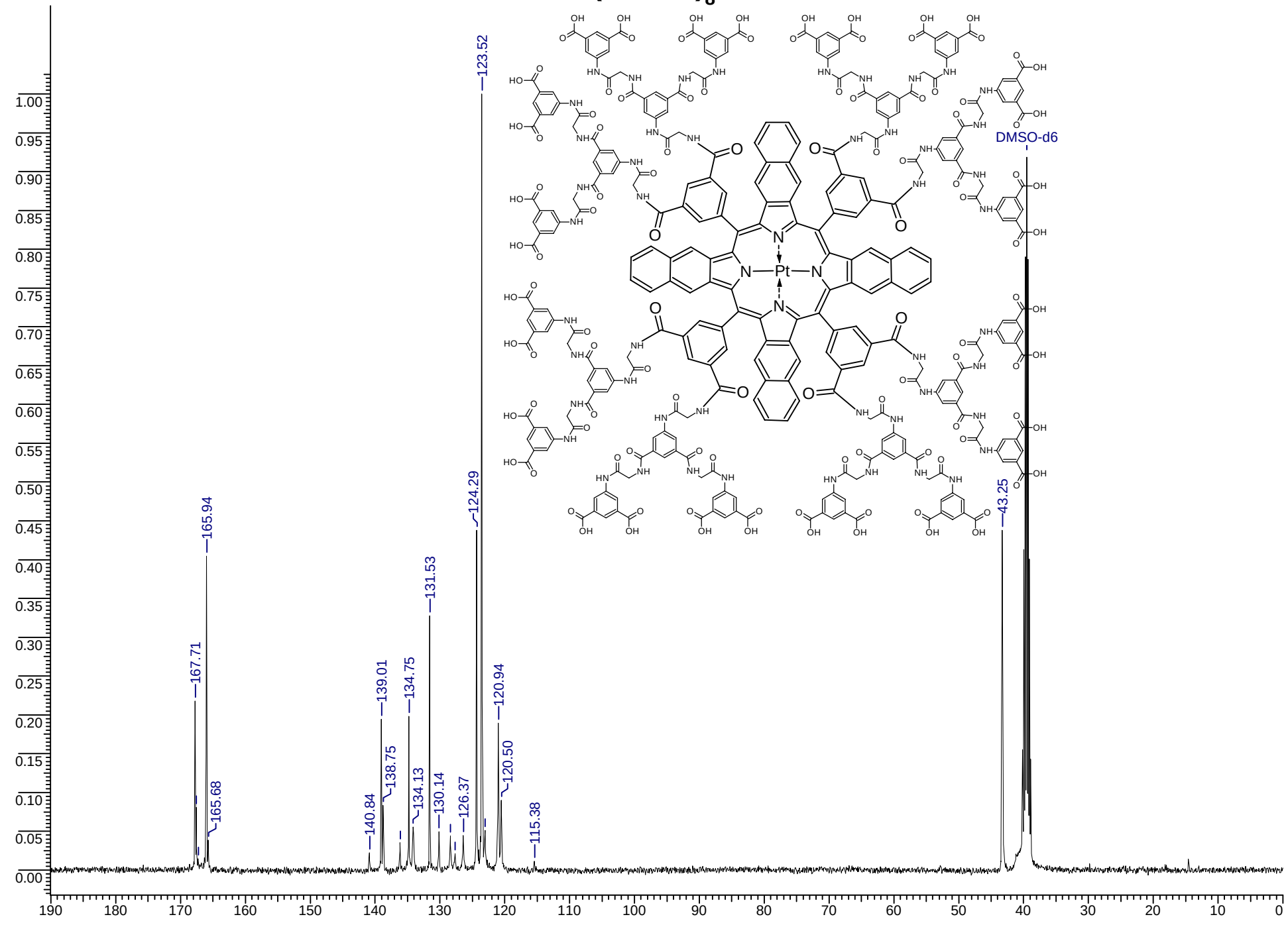
Pt-3-(AG^{2}OBu)$_8$, MALDI



Pt-3-(AG^{2}OH)$_8$ ^{1}H



Pt-3-(AG^{2}OH)$_8$ ^{13}C



Pt-3-(AG^{2}OPEG)$_8$ (15), ^{1}H