Electronic Supplementary Material (ESI) for Dalton Transactions.

Electronic Supporting Information

Novel cis-[(NHC)^1(NHC)^2(L)Cl]platinum(II) complexes – synthesis, structures, and anticancer activities

Tobias Rehm,[a] Matthias Rothemund,[a] Julienne K. Muenzner,[a] Awal Noor,[b] Rhett Kempe,[b] and Rainer Schobert[a]

[a]*Organic Chemistry Laboratory, University Bayreuth, Universitaetsstrasse 30, 95440 Bayreuth.*

E-mail: Rainer.Schobert@uni-bayreuth.de

[b]Lehrstuhl fuer Anorganische Chemie II (Catalyst Design), University Bayreuth, Universitaetsstrasse 30, 95440 Bayreuth.

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General information

All chemicals and reagents were purchased from Sigma Aldrich, Alfa Aesar or ABCR and were used without further purification. Melting points are uncorrected; NMR spectra were run on a 500 MHz spectrometer; chemical shifts are given in ppm (δ) and referenced relative to the internal solvent signal; ^{195}Pt NMR shifts are quoted relative to Ξ(^{195}Pt) = 21.496784 MHz, K_2PtCl_4 was used as external standard (δ ^{195}Pt = -1612.81); mass spectra: direct inlet, EI, 70 eV; X-Ray diffractometers: STOE-IPDS II and STOE-STADIVARI. *N*-methyl- and *N*-benzylimidazolium salts were prepared based on literature procedures[1-4] and complex **1b** was prepared analogously to **1a**[5] as described herein.

Synthesis and characterization of imidazolium chlorides and complex 1b

General procedure:

Imidazole (1eq) and the respective benzyl chloride (2.1 eq) in acetonitrile (10 mL/mmol) were treated with K_2CO_3 (1.2 eq) and the resulting mixture was heated to 70 °C for 3-5 days. After filtration the solvent was evaporated in vacuo and the residue was washed several times with Et_2O.

Synthesis of 1,3-dibenzylimidazolium chloride:[1]

Imidazole (100 mg, 1.47 mmol), benzyl chloride (355 µL) and K_2CO_3 (244 mg) in acetonitrile (15 mL) for 72 h gave 333 mg (80%) of a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 5.43 (4 H, s), 7.17 - 7.24 (6 H, m), 7.33 - 7.42 (6 H, m), 10.85 (1 H, s).

Synthesis of 1,3-di(4-methoxybenzyl)imidazolium chloride:

Imidazole (100 mg, 1.47 mmol), 4-methoxybenzyl chloride (417 µL) and K_2CO_3 (244 mg) in acetonitrile (15 mL) for 72 h gave 500 mg (99%) of a pale yellow gum. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.74 (6 H, s), 5.43 (4 H, s), 6.84 (4 H, d, J=8.9 Hz), 7.22 (2 H, s), 7.39 (4 H, d, J=8.9 Hz), 10.98 (1 H, s).

Synthesis of 1,3-di(4-fluorobenzyl)imidazolium chloride:[2]

Imidazole (50 mg, 0.735 mmol), 4-fluorobenzyl chloride (182 µL) and K_2CO_3 (122 mg) in acetonitrile (7.5 mL) for 72 h gave 165 mg (70%) of a yellow gum. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 5.51 (4 H, s), 7.00 (2 H, tt, *J*=8.7, 2.6 Hz), 7.34 (2 H, s), 7.49 (1 H, dd, *J*=8.7, 5.0 Hz), 11.02 (1 H, br. s.).

Synthesis of 1,3-di(3,5-dimethoxybenzyl)imidazolium chloride:[3]

Imidazole (50 mg, 0.735 mmol), 3,5-dimethoxybenzyl chloride (288 mg) and K_2CO_3 (122 mg) in acetonitrile (7.5 mL) for 5 d gave 205 mg (69%) of an orange gum. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.73 (12 H, s), 5.39 (4 H, s), 6.39 (2 H, t, J=2.3 Hz), 6.56 (4 H, d, J=2.3 Hz), 7.18 (2 H, s), 11.20 (1 H, s).

Synthesis of 1-benzyl-3-methylimidazolium chloride:[4]

Methylimidazole (60 mg, 0.735 mmol) and benzyl chloride (100 µL, 0.882 mmol) in acetonitrile (5 mL) were heated to 70 °C for 72 h. After evaporation of the solvent in vacuo the residue was washed several times with Et_2O to yield 132 mg (86%) of a pale yellow gum. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.98 (3 H, s), 5.54 (2 H, s), 7.29 - 7.34 (3 H, m), 7.37 (1 H, t, *J*=1.7 Hz), 7.41 - 7.46 (2 H, m), 7.51 (1 H, t, *J*=1.7 Hz), 10.51 (1 H, s).

Synthesis of *trans*-[dichlorido-bis(1,3-di(4-methoxybenzyl)imidazol-2-ylidene)]platinum(II) (**1b**):[5]

A solution of 1,3-di(4-methoxybenzyl)imidazolium chloride (60 mg, 0.154 mmol) in CH_2Cl_2 was treated with silver(I) oxide (18 mg, 77 µmol), and the resulting mixture was stirred at room temperature for 24 h. Then K_2PtCl_4 (32 mg, 77 µmol) was added and the reaction was allowed to stir for additional 24 h. The suspension was filtered, the filtrate was concentrated in vacuo, and the residue was recrystallized from CH_2Cl_2/hexane. Yield 38 mg (56%) white crystals of m.p. 194 °C (decomp.). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.76 (12 H, s), 5.74 (8 H, s), 6.63 (4 H, s), 6.83 (8 H, d, J=8.5 Hz), 7.43 (8 H, d, J=8.5 Hz); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 53.0, 55.2, 114.0, 120.1, 128.6, 129.9, 159.3, 167.2 (NHC). EI-MS: *m/z* 883 (M^+, 5%), 847 (12, -Cl), 810 (35,-2x Cl), 501 (17), 308 (23), 241 (28), 121 (100).

Table S 1: X-ray structural data of platinum carbene complexes **5a**,**d**,**h** and **8a**

	5a (CCDC1481381)	**5d** (CCDC1481378)	**5h** (CCDC1481379)	**8a** (CCDC1481380)
Empirical formula	$C_{34}H_{32}Cl_2N_4Pt$	$C_{34}H_{28}Cl_2F_2N_4Pt$	$C_{39}H_{42}Cl_4N_4O_4Pt$	$C_{53}H_{53}Cl_4N_4O_2PPt$
Formula weight	762.62	796.59	967.65	1145.85
Temperature	133 K	133 K	133 K	133 K
Wavelength	0.71069 Å	0.71069 Å	0.71069 Å	0.71069 Å
Crystal system	monoclinic	monoclinic	monoclinic	triclinic
Space group	$P2_1/c$	C2/c	$P2_1/c$	P-1
Unit cell dimensions	a = 7.5380(3) Å b = 33.6480(12) Å c = 12.1810(5) Å α = γ = 90° β = 95.951(3)°	a = 15.6790(6) Å b = 14.1220(6) Å c = 15.1390(8) Å α = γ = 90° β = 113.895(5)°	a = 11.1330(4) Å b = 29.7780(14) Å c = 12.1160(4) Å α = γ = 90° β = 101.539(3)°	a = 11.4460(4) Å b = 11.7520(4) Å c = 19.7120(8) Å α = 75.959(3)° β = 74.604 (3)° γ = 73.708(3)°
Volume	3072.9(2) $Å^3$	3064.8(3) $Å^3$	3935.5(3) $Å^3$	2412.88(16) $Å^3$
Z	4	4	4	2
Density (calcd)	1.648 Mg/m^3	1.726 Mg/m^3	1.633 Mg/m^3	1.577 Mg/m^3
Absorption coefficient	4.77 mm^{-1}	4.80 mm^{-1}	3.88 mm^{-1}	3.21 mm^{-1}
F(000)	1504	1560	1928	1152
Crystal size / mm	0.16 × 0.11 × 0.08	0.21 × 0.14 × 0.08	0.15 × 0.12 × 0.08	0.25 × 0.18 × 0.11
Theta range (data col.)	3.6–54.5°	4.1–53.1°	4.4–55.3°	3.7–53.2°
Index ranges	–9 ≤ h ≤ 9	–19 ≤ h ≤ 19	–7 ≤ h ≤ 13	–14 ≤ h ≤ 14
Index ranges	–42 ≤ k ≤ 0	–17 ≤ k ≤ 17	–36 ≤ k ≤ 36	–14 ≤ k ≤ 14
Index ranges	–15 ≤ l ≤ 15	–18 ≤ l ≤ 18	–14 ≤ l ≤ 14	–24 ≤ l ≤ 24
Reflections collected	12924	19249	23066	34049
Independent reflexes	6540 [R_{int}=0.040]	3070 [R_{int}=0.073]	7701 [R_{int}=0.069]	9655 [Rint=0.099]
Completeness to qmax	99.4%	99.4%	99.7%	98.9%
Absorption correction	numerical	numerical	numerical	numerical
Max / min transmission	0.740 / 0.454	0.506 / 0.248	0.848 / 0.652	0.712 / 0.424
Refinement method	Full–matrix least–squares on F^2	Full–matrix least–squares on F^2	Full–matrix least–squares on F^2	Full–matrix least–squares on F^2
Data / restraints / param	6540 / 0 / 370	3070 / 18 / 204	7701 / 18 / 475	9655 / 4 / 602
Goodness–of–fit on F^2	0.766	0.984	0.934	0.994
Final R indices	R_1 = 0.0276	R_1 = 0.0267	R_1 = 0.0575	R_1 = 0.0582
[I>2σ(I)]	wR_2 = 0.0601	wR_2 = 0.0639	wR_2 = 0.1494	wR_2 = 0.1538
R indices	R_1 = 0.0471	R_1 = 0.0350	R_1 = 0.0931	R_1 = 0.0794
(all data)	wR_2 = 0.0579	wR_2 = 0.0625	wR_2 = 0.1342	wR_2 = 0.1436
Largest diff. peak / hole	1.40/– 1.21 $eÅ^{-3}$	2.30/– 1.11 $eÅ^{-3}$	1.89/– 2.14 $eÅ^{-3}$	3.43/– 1.47 $eÅ^{-3}$

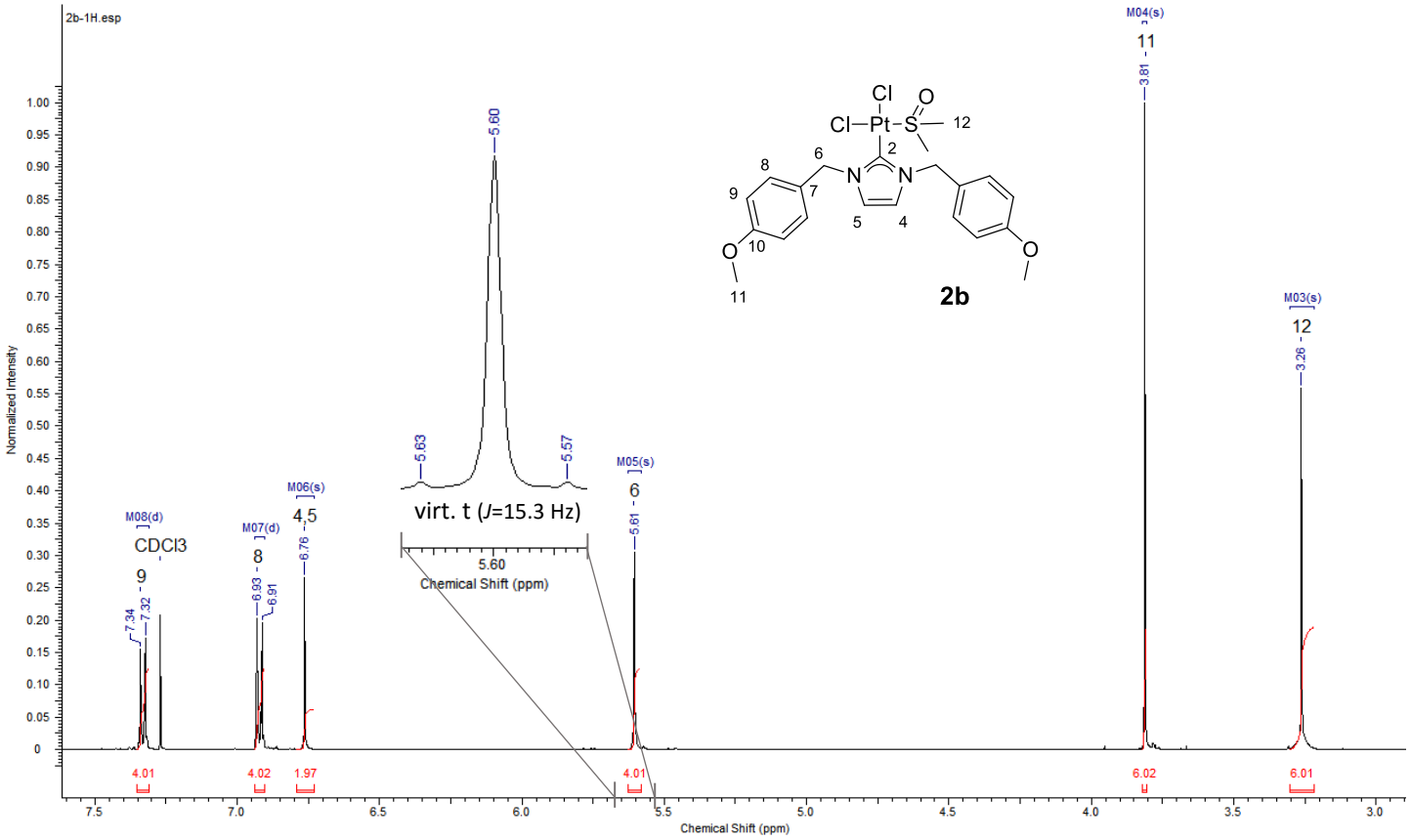

Fig. S 1: ^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of complex **2b**.

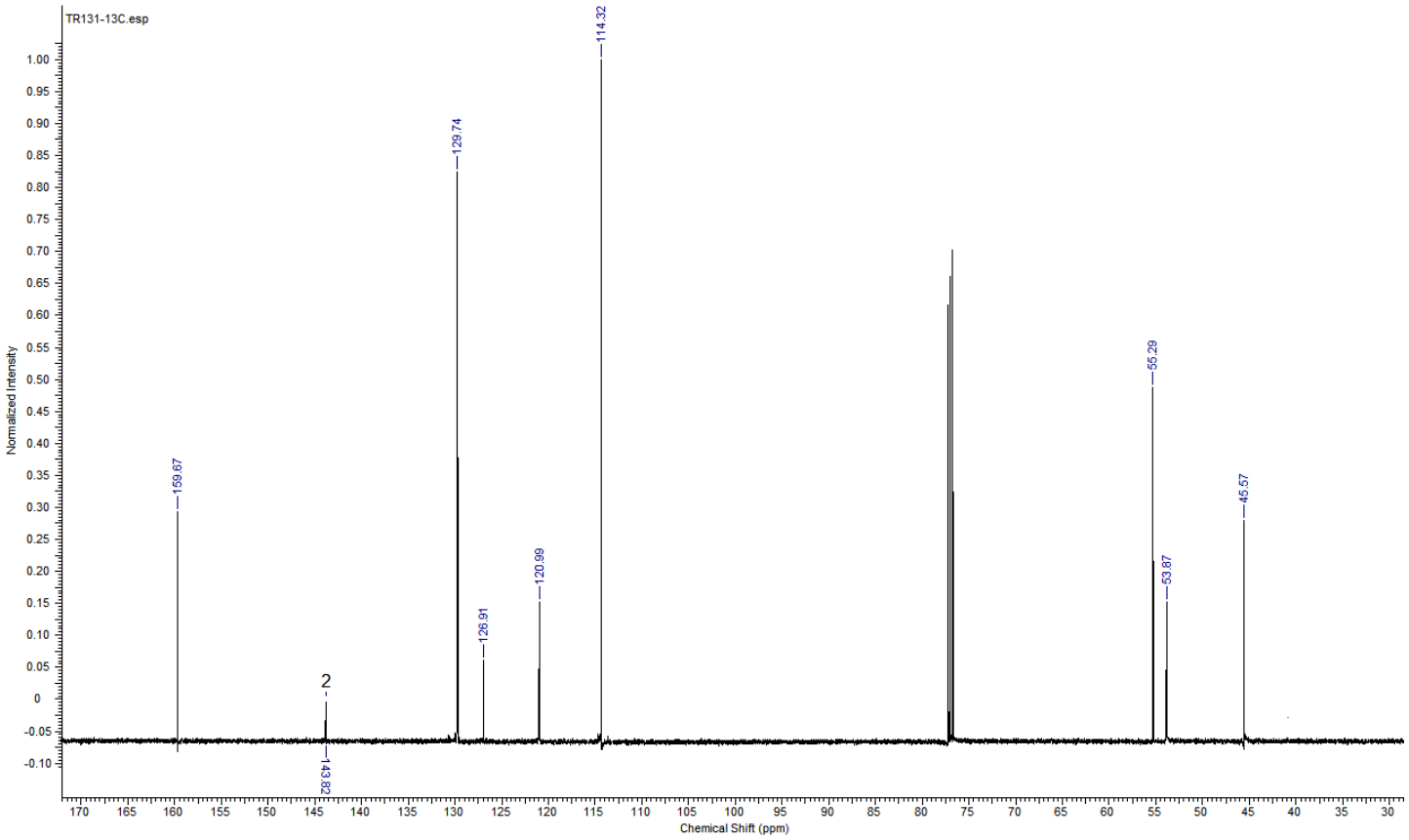

Fig. S 2: ^{13}C-NMR spectrum (126 MHz, $CDCl_3$) of complex **2b**.

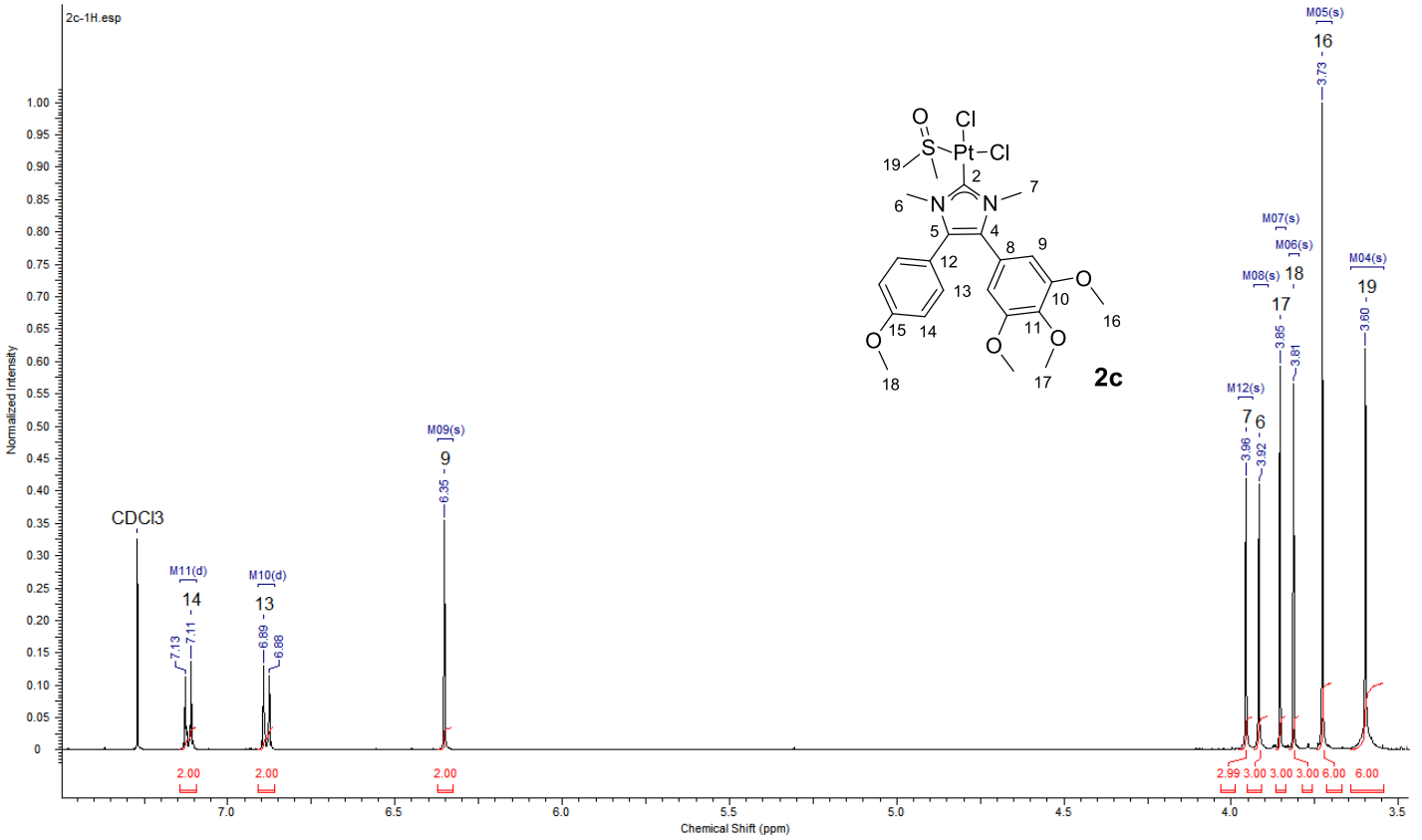

Fig. S 3: ^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of complex **2c**.

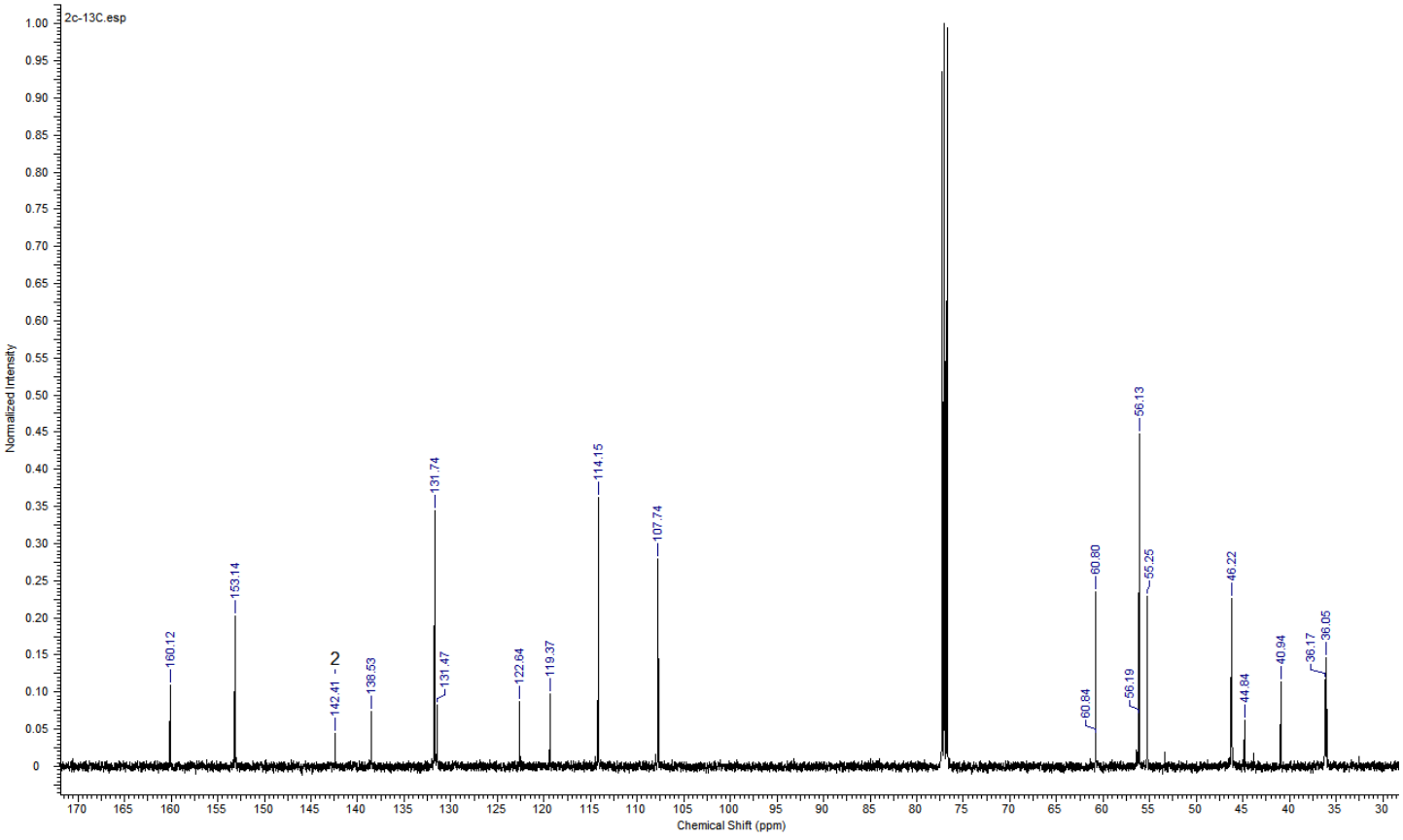

Fig. S 4: ^{13}C-NMR spectrum (126 MHz, $CDCl_3$) of complex **2c**.

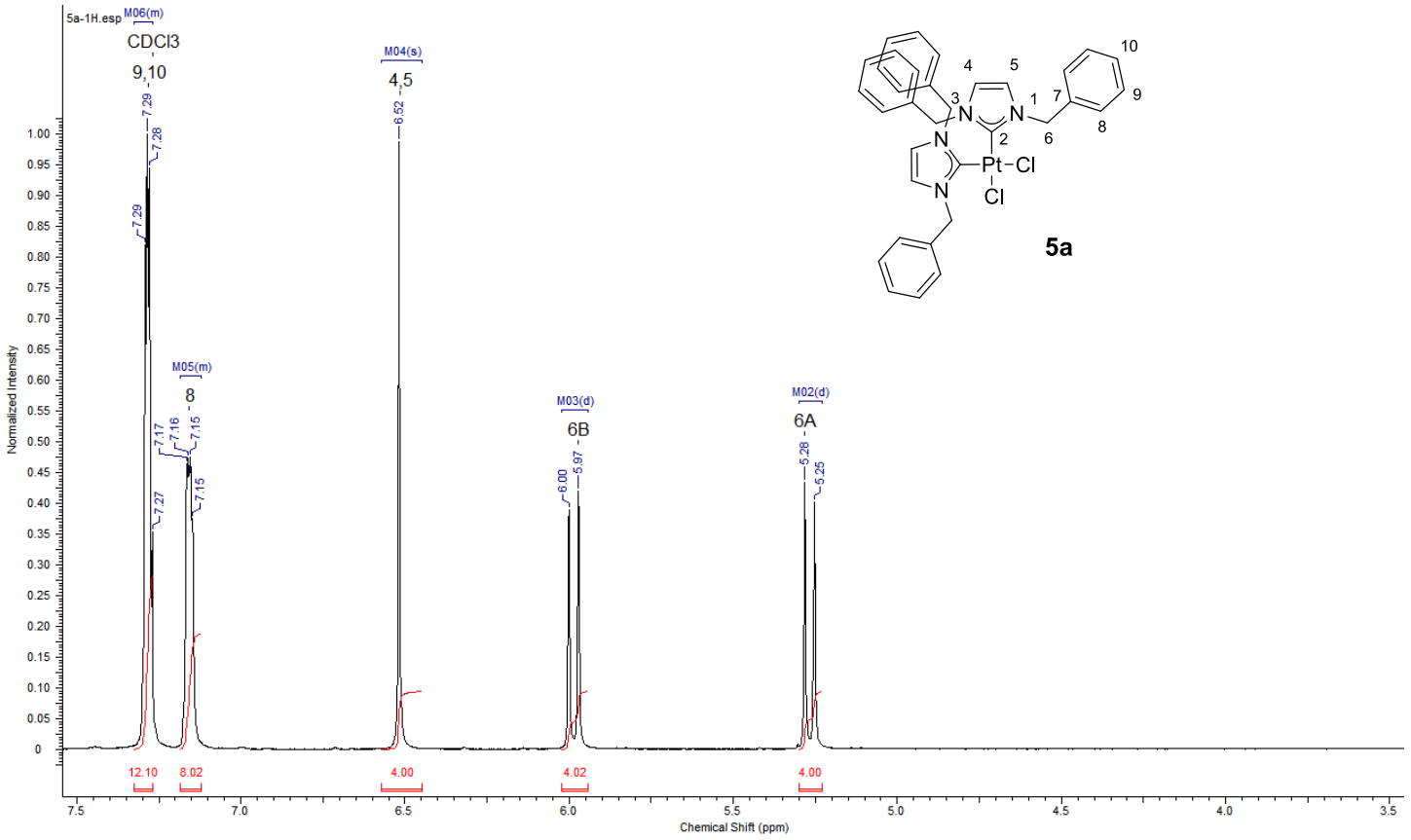

Fig. S5: ^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of complex **5a**.

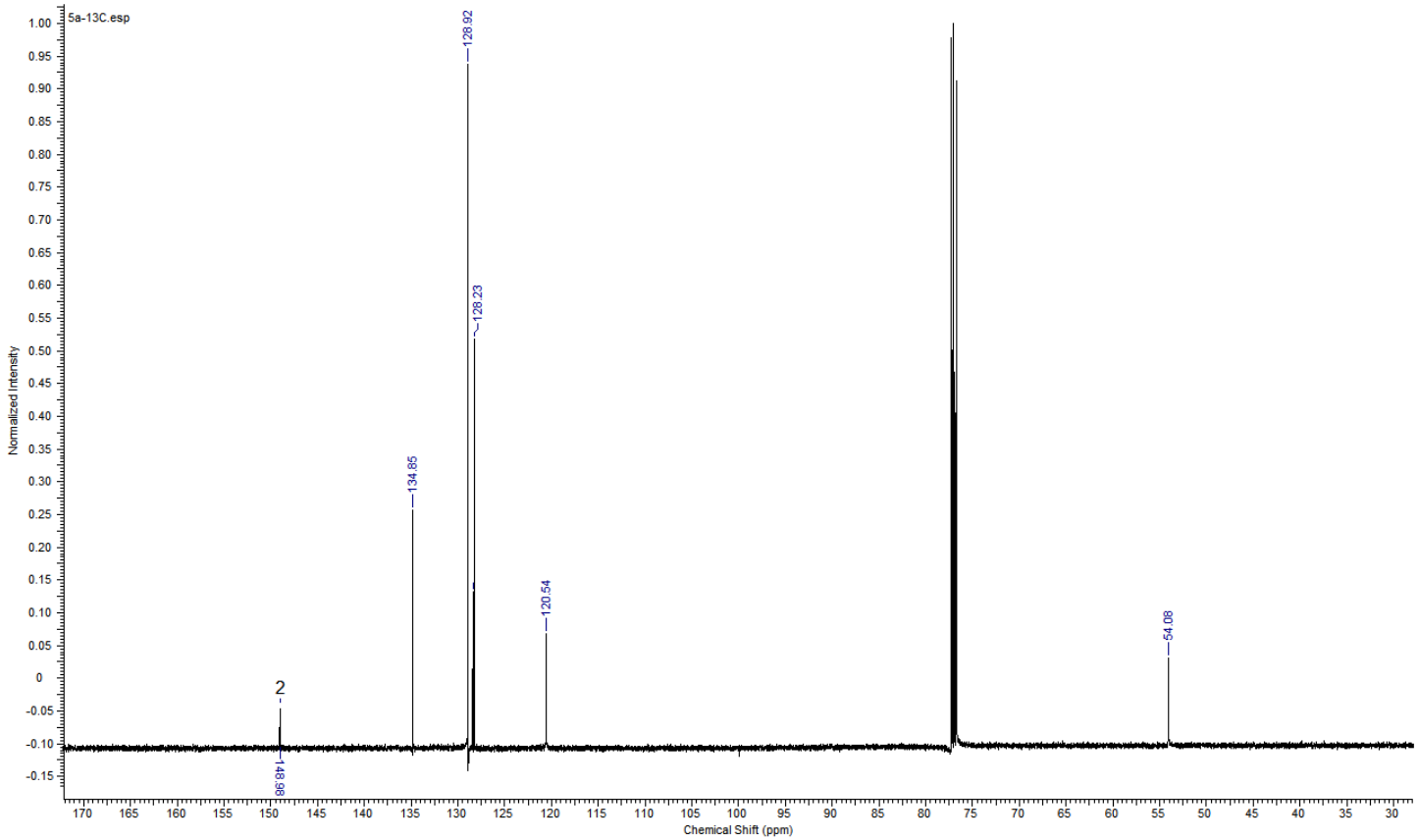

Fig. S 6: ^{13}C-NMR spectrum (126 MHz, $CDCl_3$) of complex **5a**.

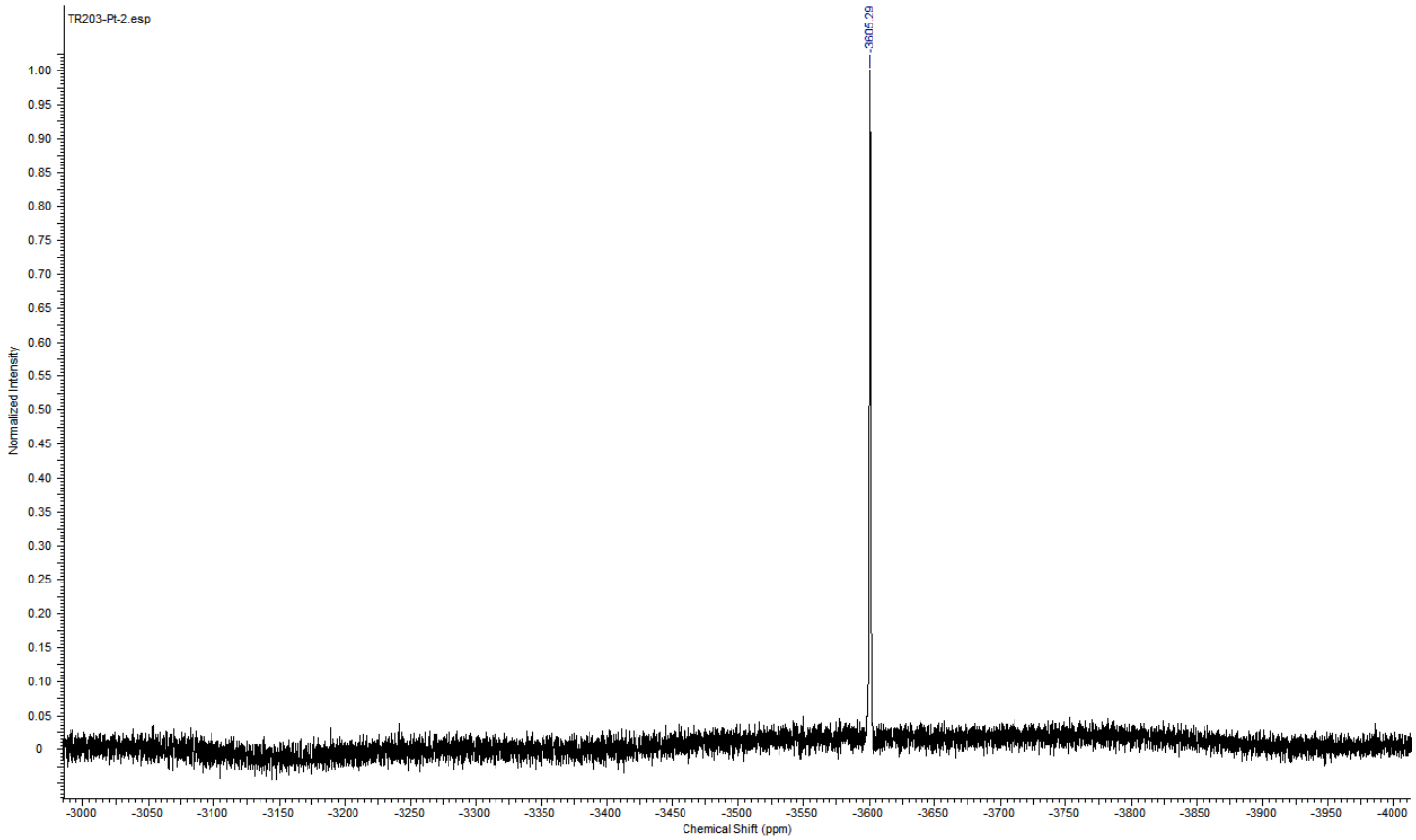

Fig. S 7: ^{195}Pt-NMR spectrum ($CDCl_3$) of complex **5a**.

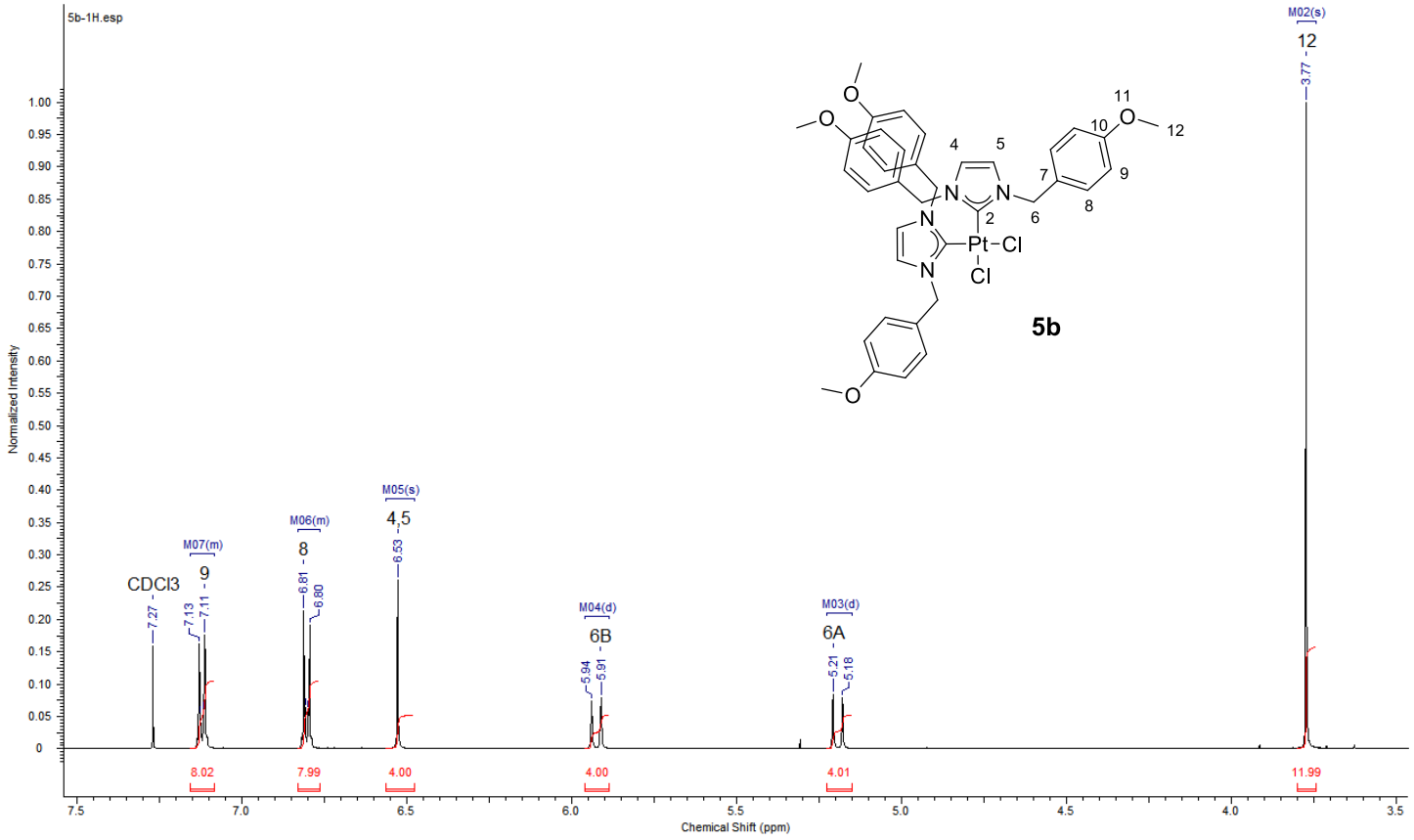

Fig. S8: ^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of complex **5b**.

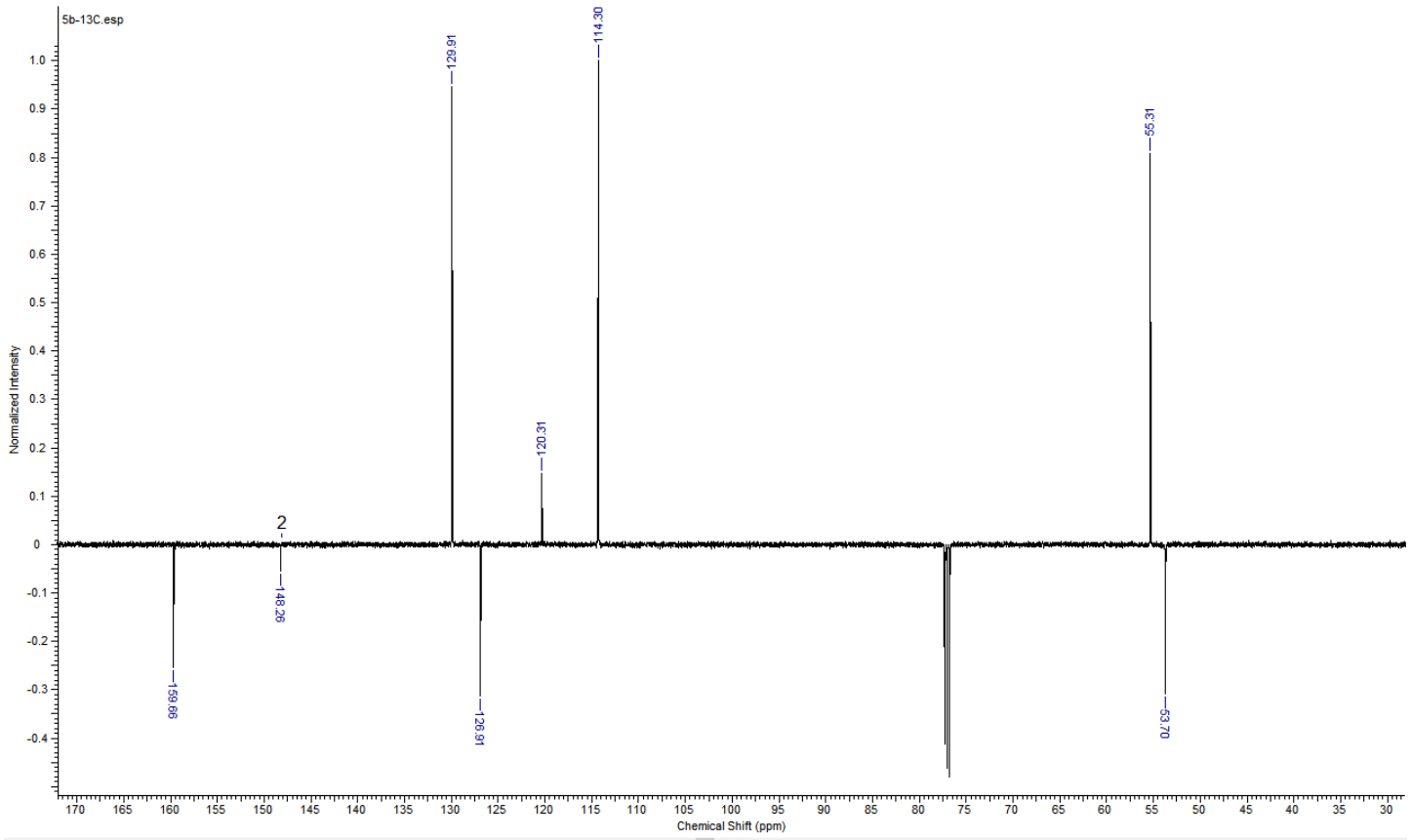

Fig. S 9: ^{13}C-ATP-NMR spectrum (126 MHz, $CDCl_3$) of complex **5b**.

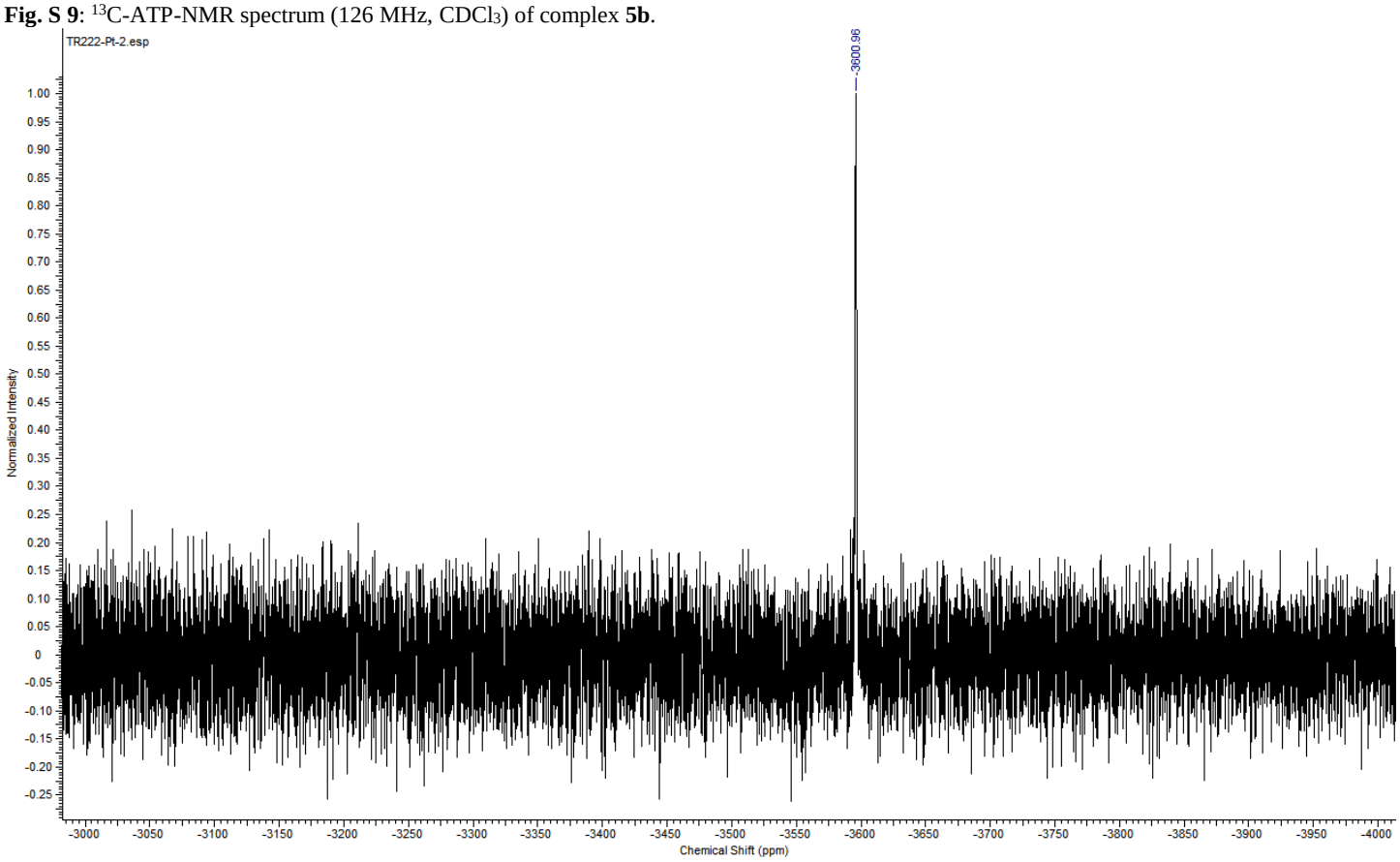

Fig. S 10: ^{195}Pt-NMR spectrum ($CDCl_3$) of complex **5b**.

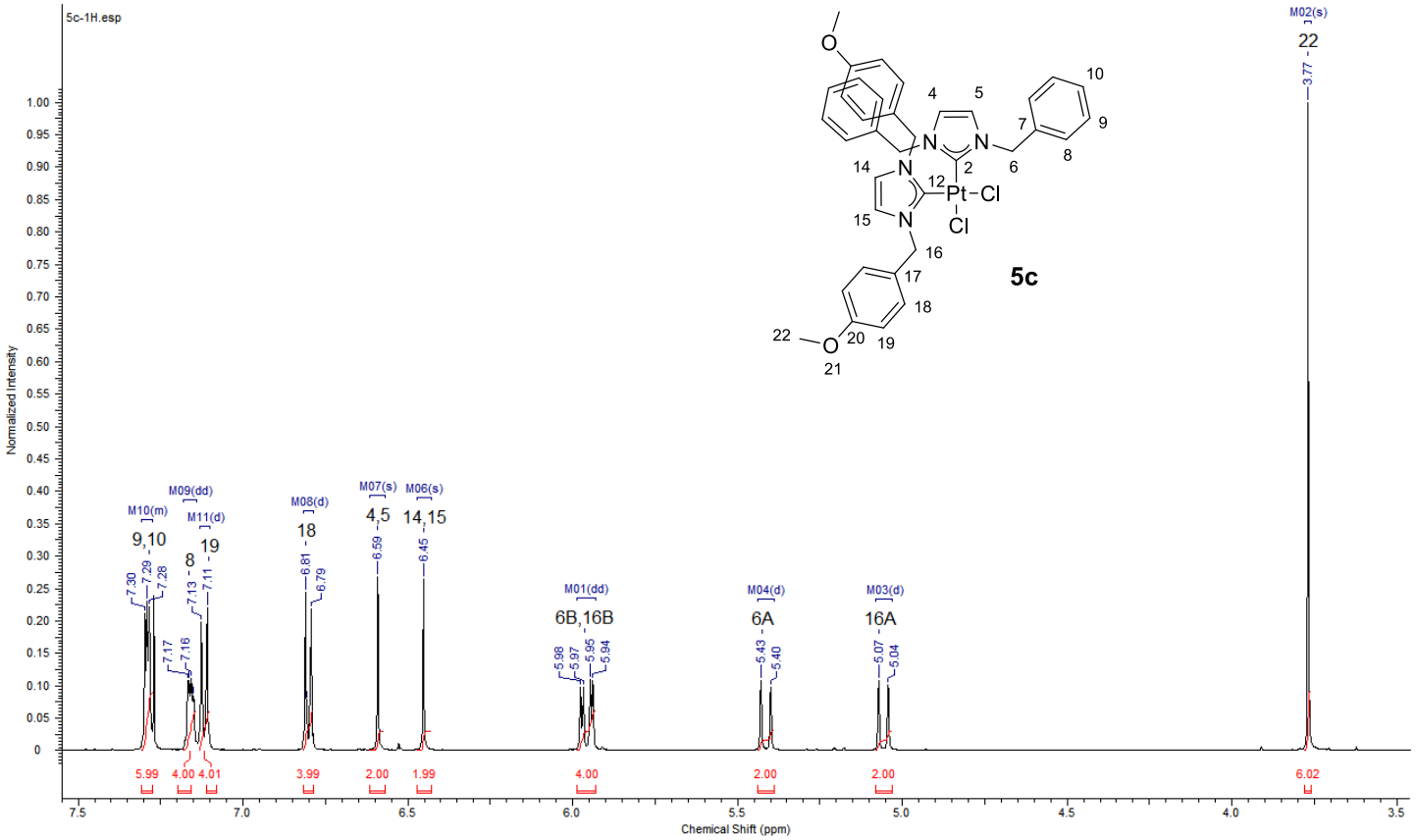

Fig. S11: ^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of complex **5c**.

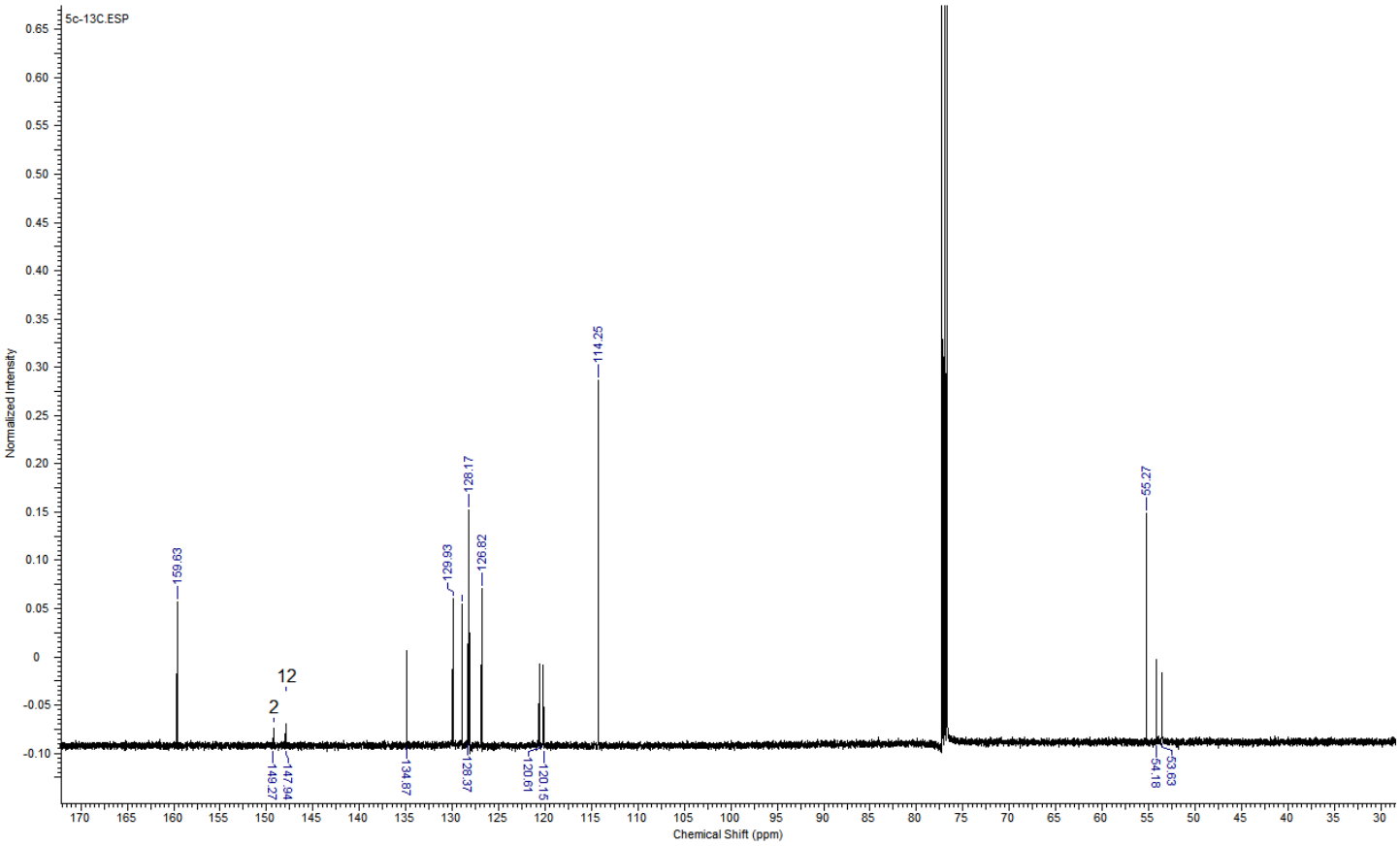

Fig. S 12: ^{13}C-NMR spectrum (126 MHz, $CDCl_3$) of complex **5c**.

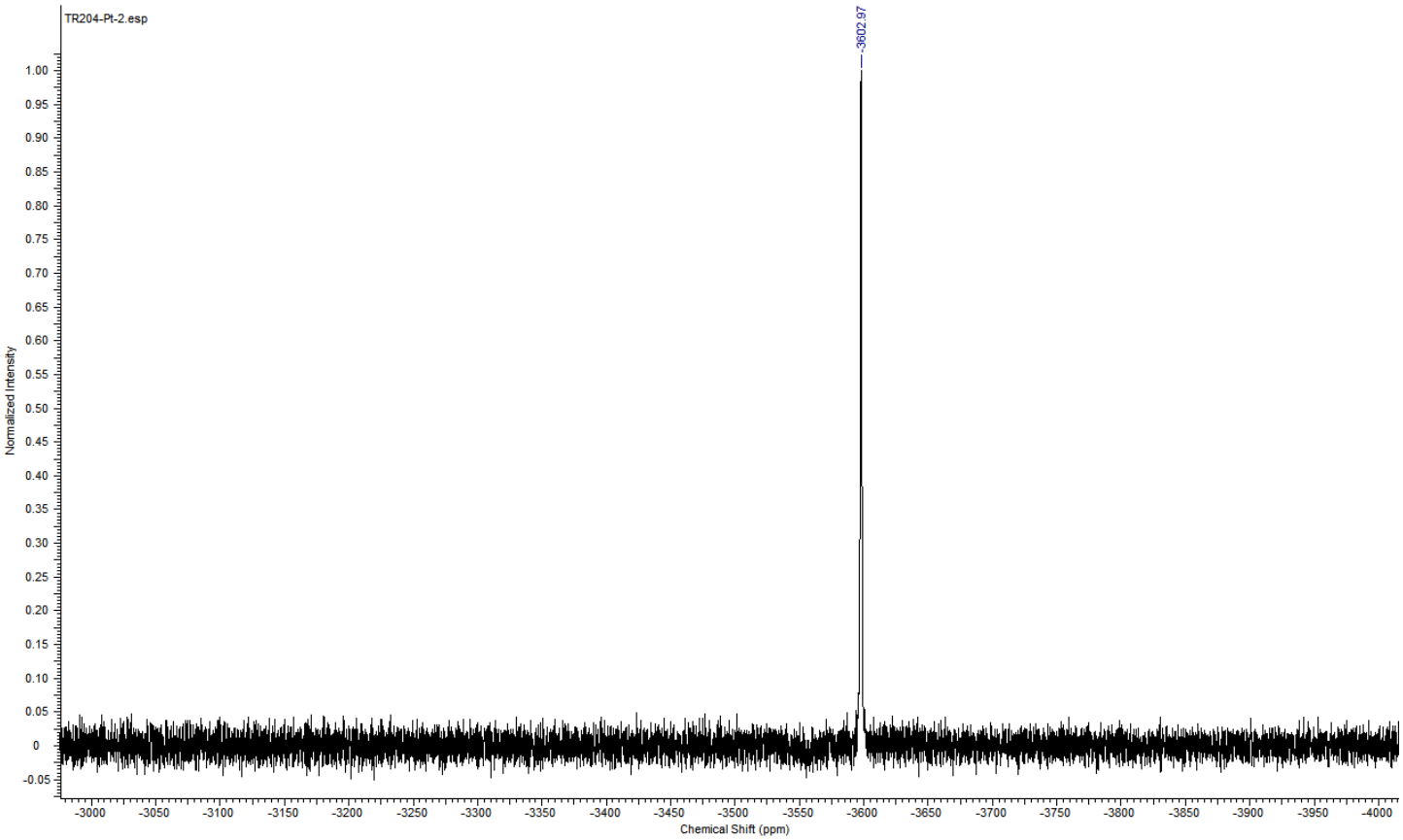

Fig. S 13: ^{195}Pt-NMR spectrum ($CDCl_3$) of complex **5c**.

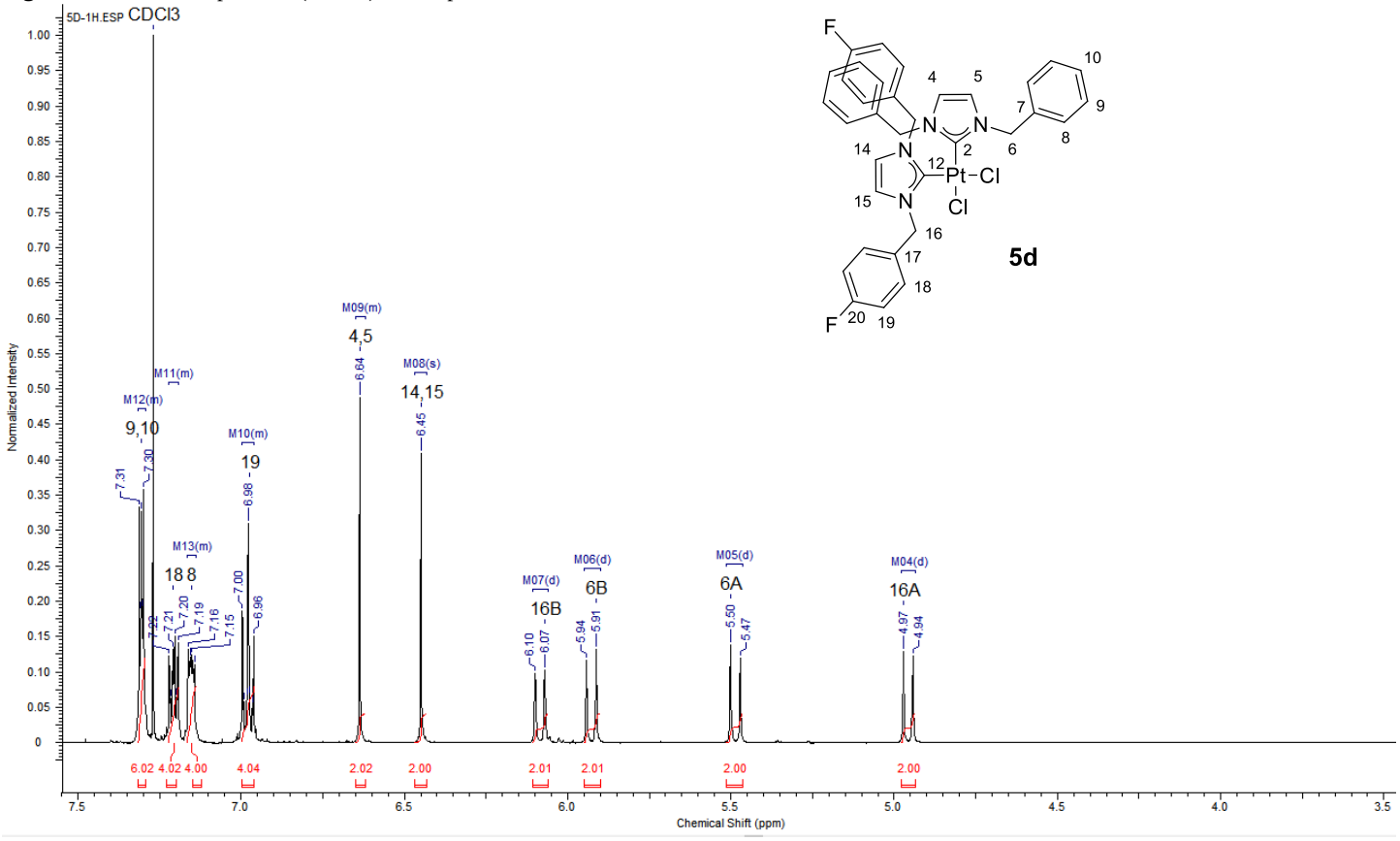

Fig. S14: ^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of complex **5d**.

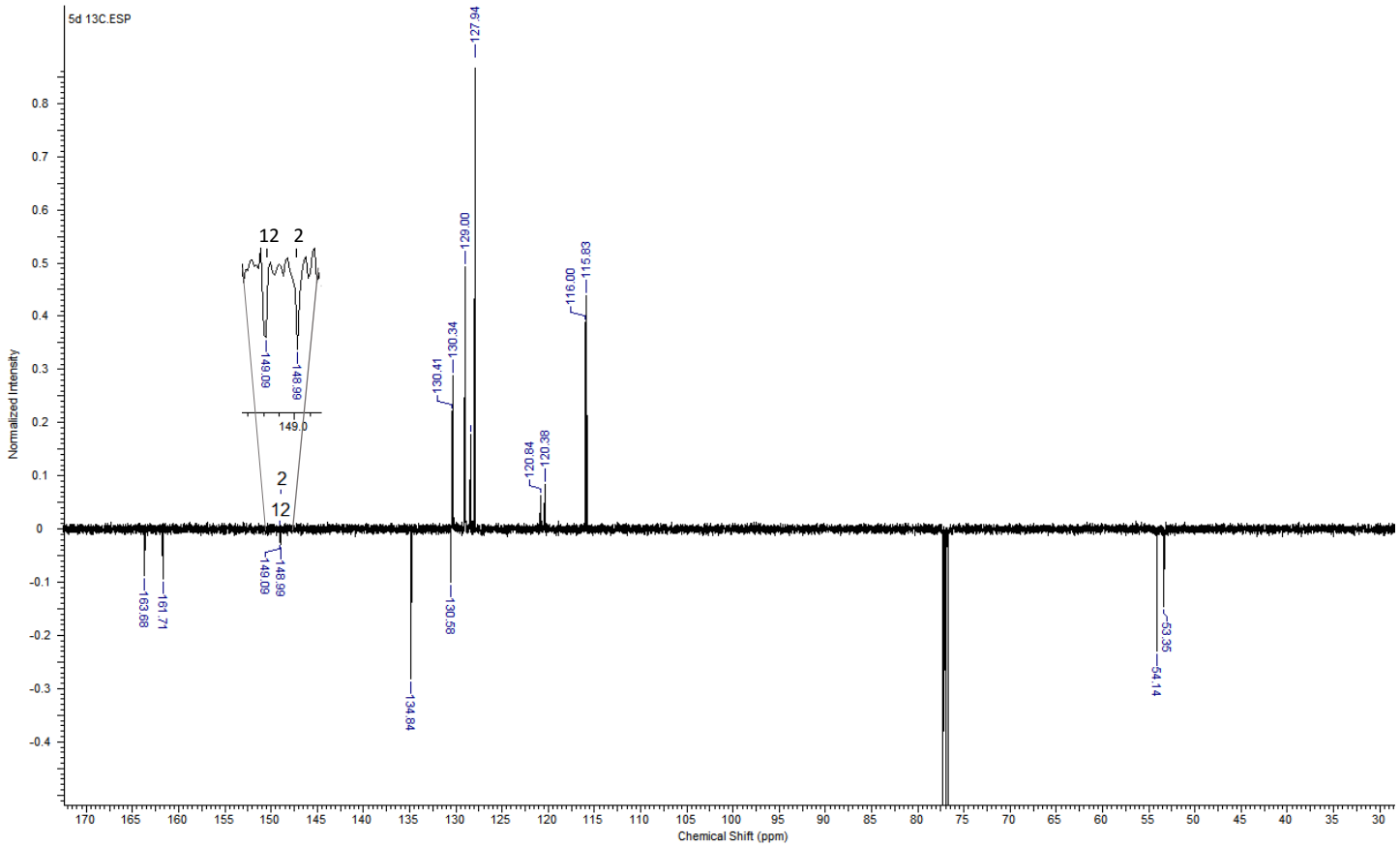

Fig. S 15: ^{13}C-ATP-NMR spectrum (126 MHz, $CDCl_3$) of complex **5d**.

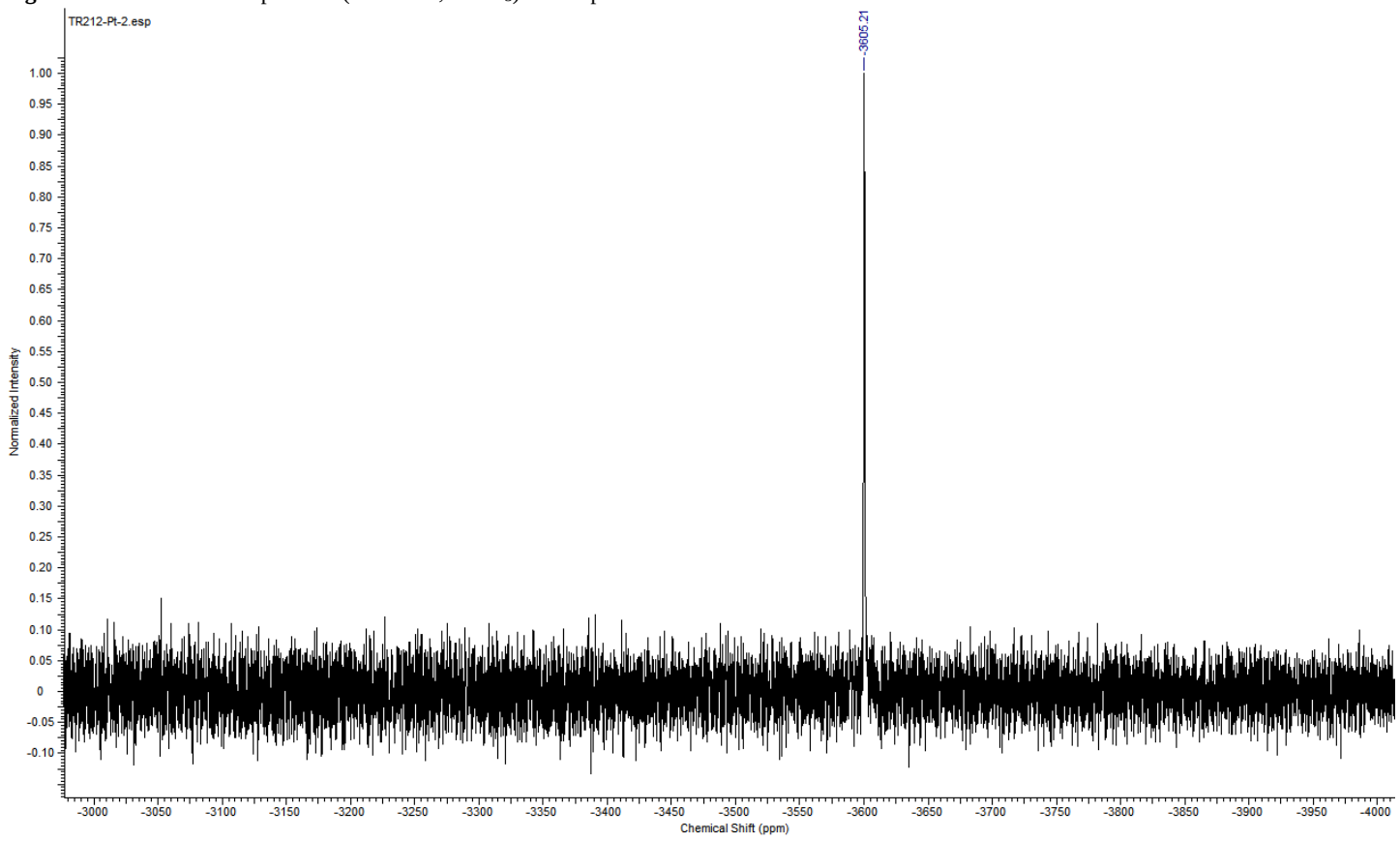

Fig. S 16: ^{195}Pt-NMR spectrum ($CDCl_3$) of complex **5d**.

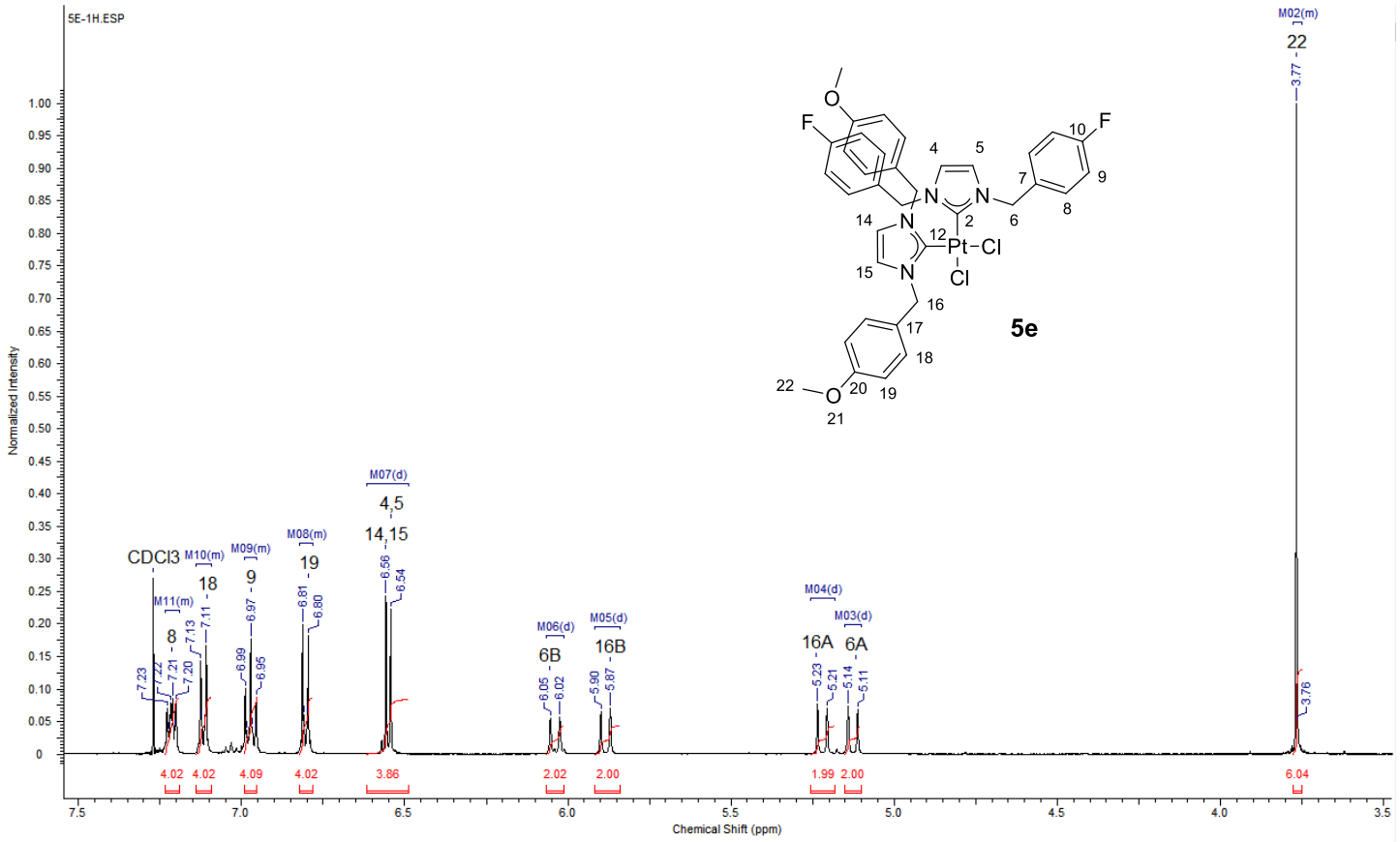

Fig. S17: ^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of complex **5e**.

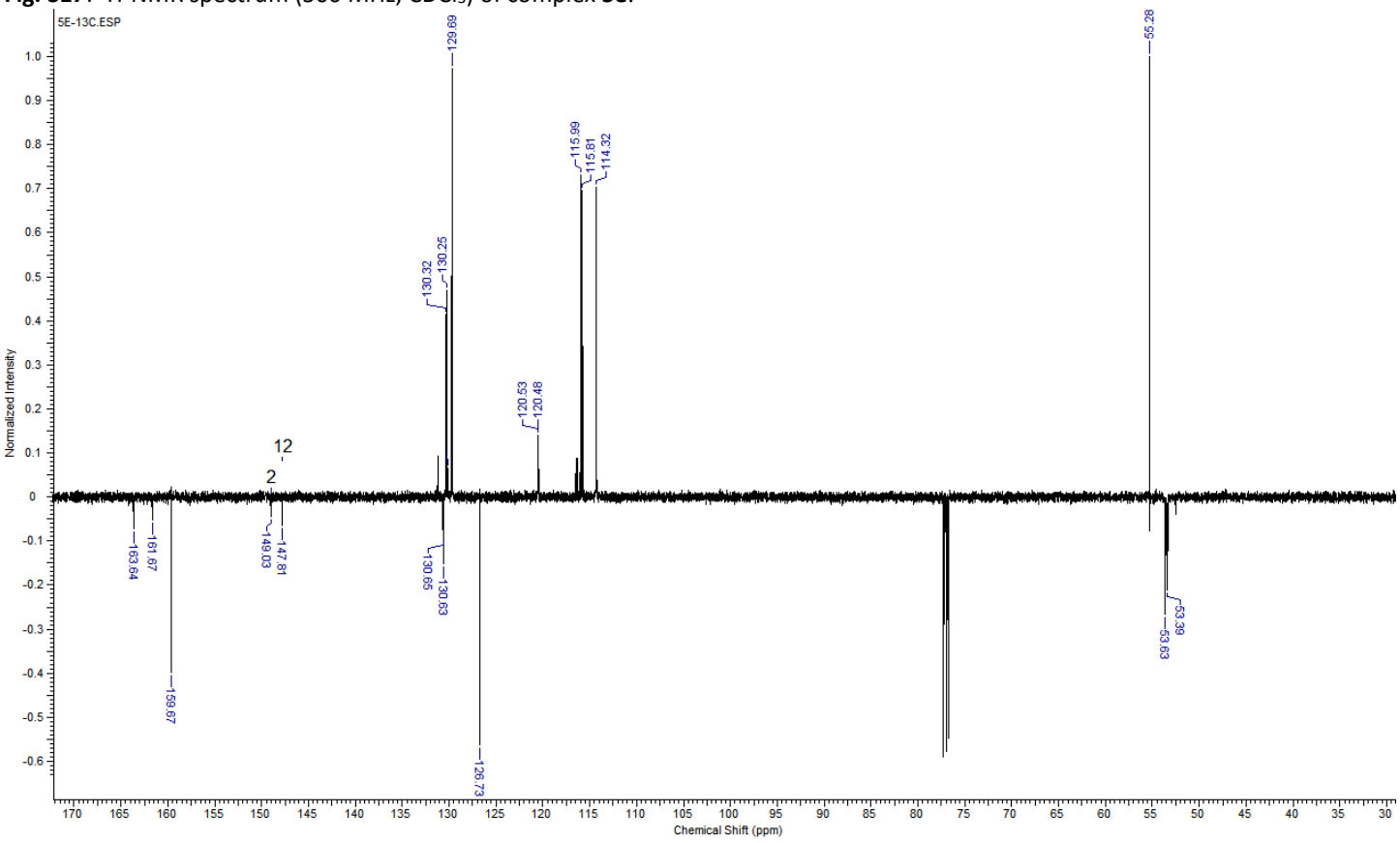

Fig. S 18: ^{13}C-ATP-NMR spectrum (126 MHz, $CDCl_3$) of complex **5e**.

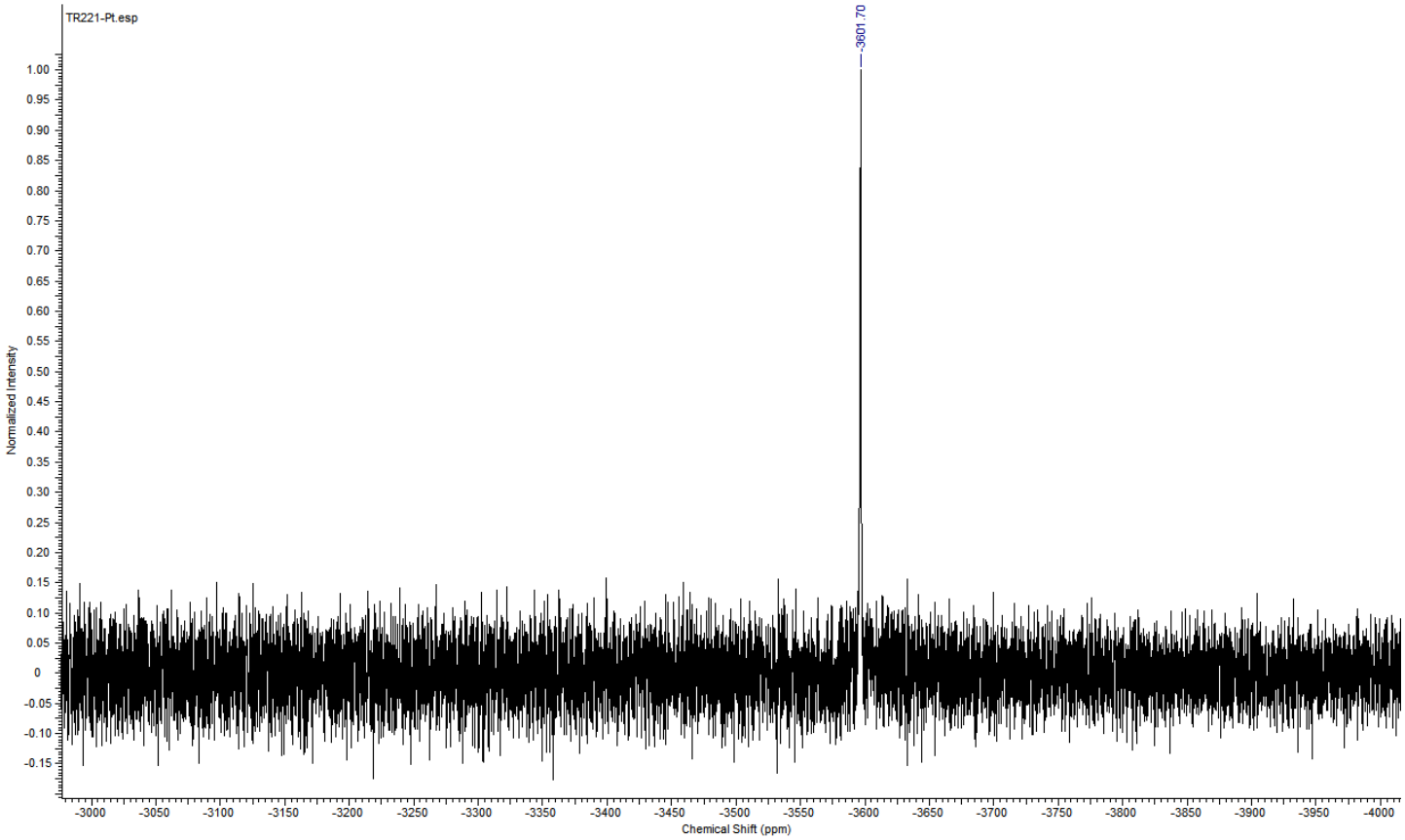

Fig. S 19: ^{195}Pt-NMR spectrum ($CDCl_3$) of complex **5e**.

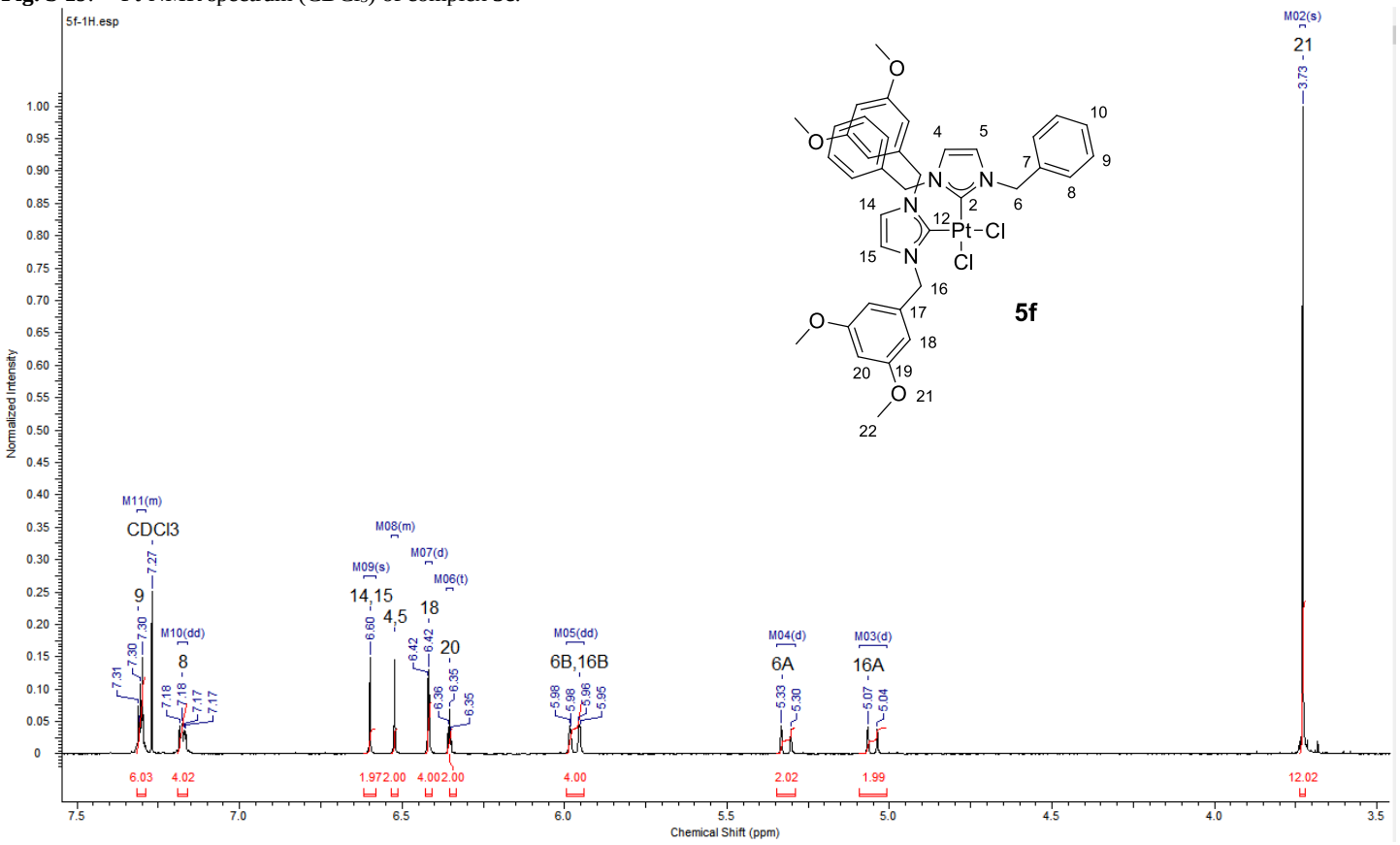

Fig. S20: ^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of complex **5f**.

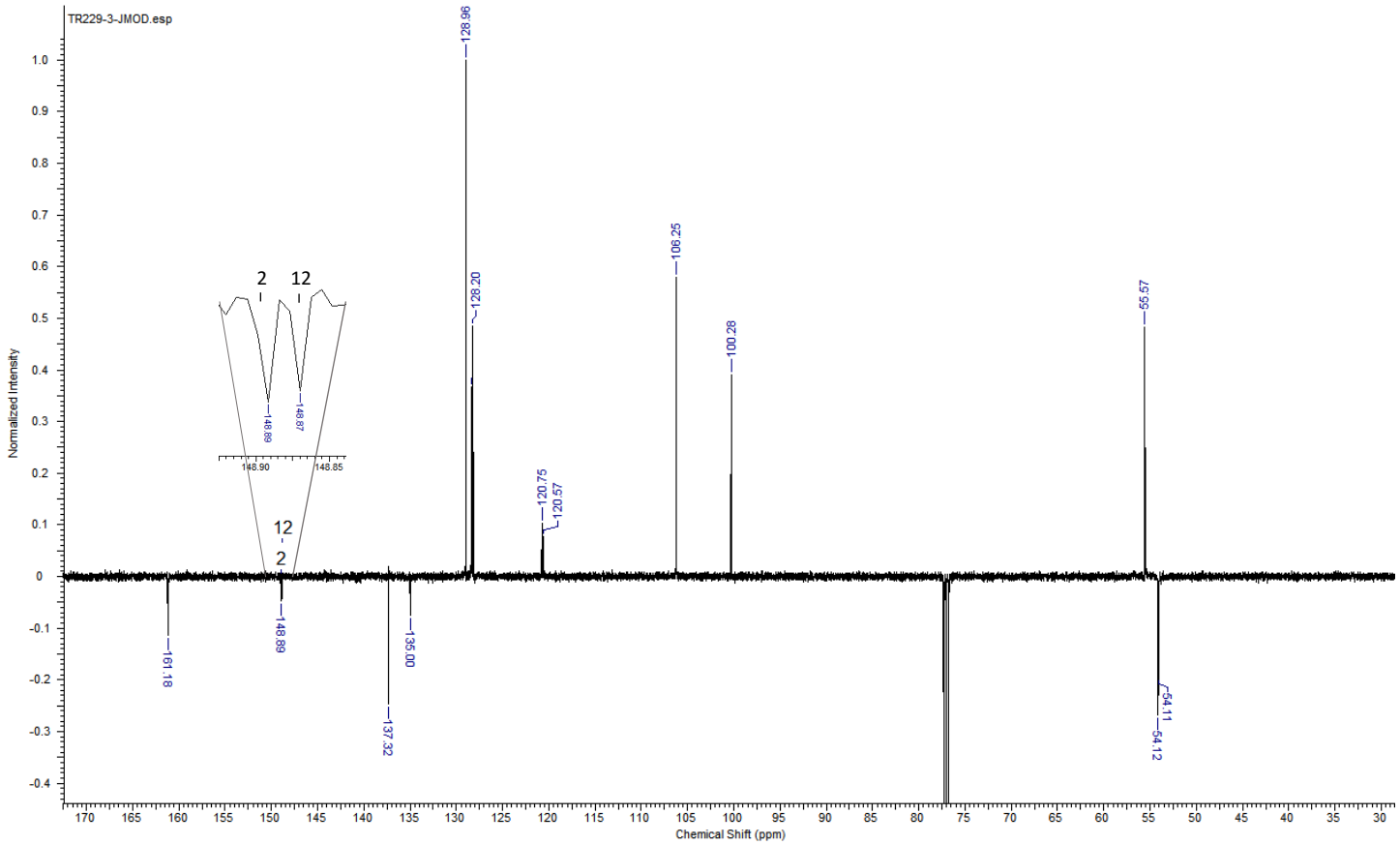

Fig. S 21: ^{13}C-ATP-NMR spectrum (126 MHz, $CDCl_3$) of complex **5f**.

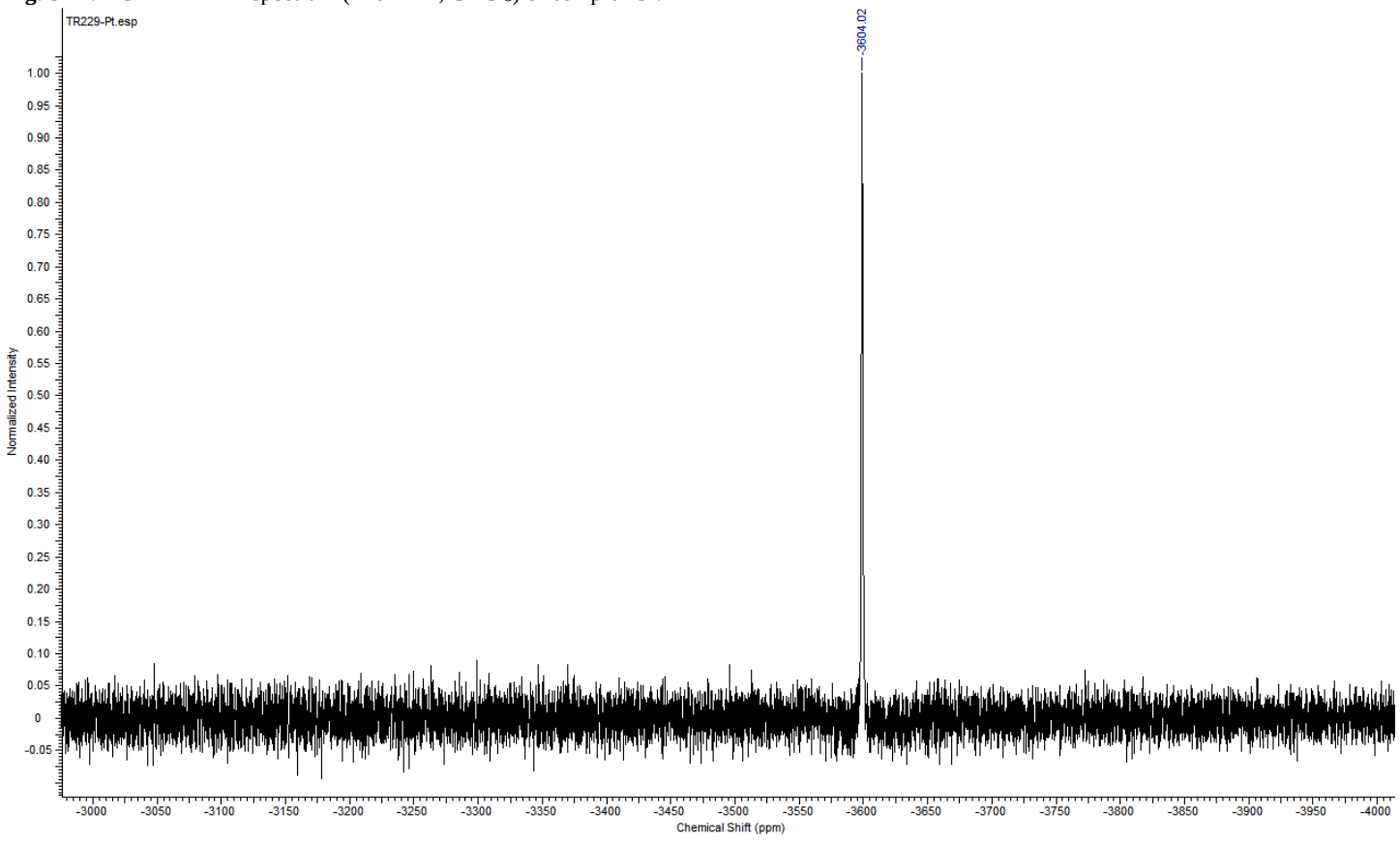

Fig. S 22: ^{195}Pt-NMR spectrum ($CDCl_3$) of complex **5f**.

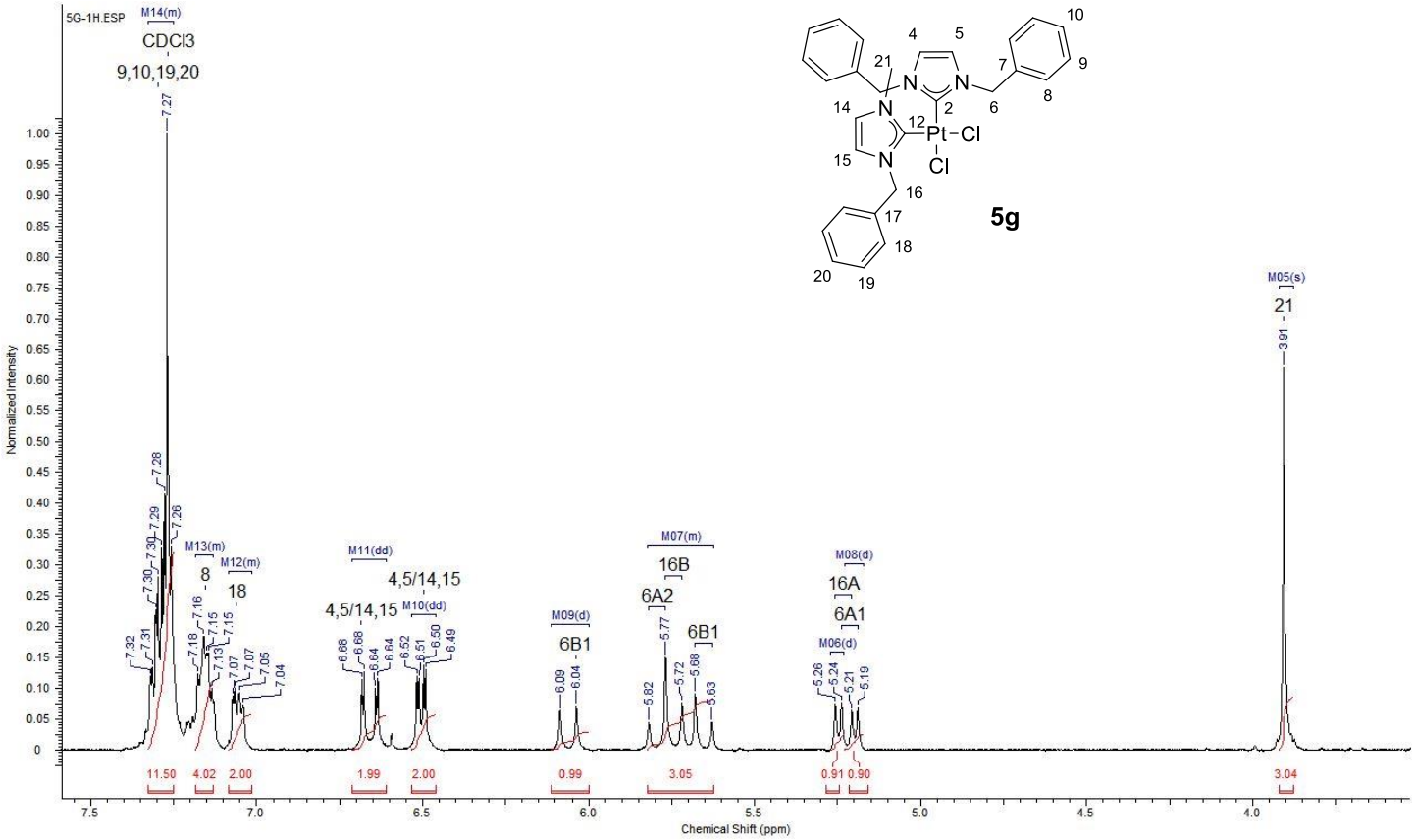

Fig. S23: ^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of complex **5g**.

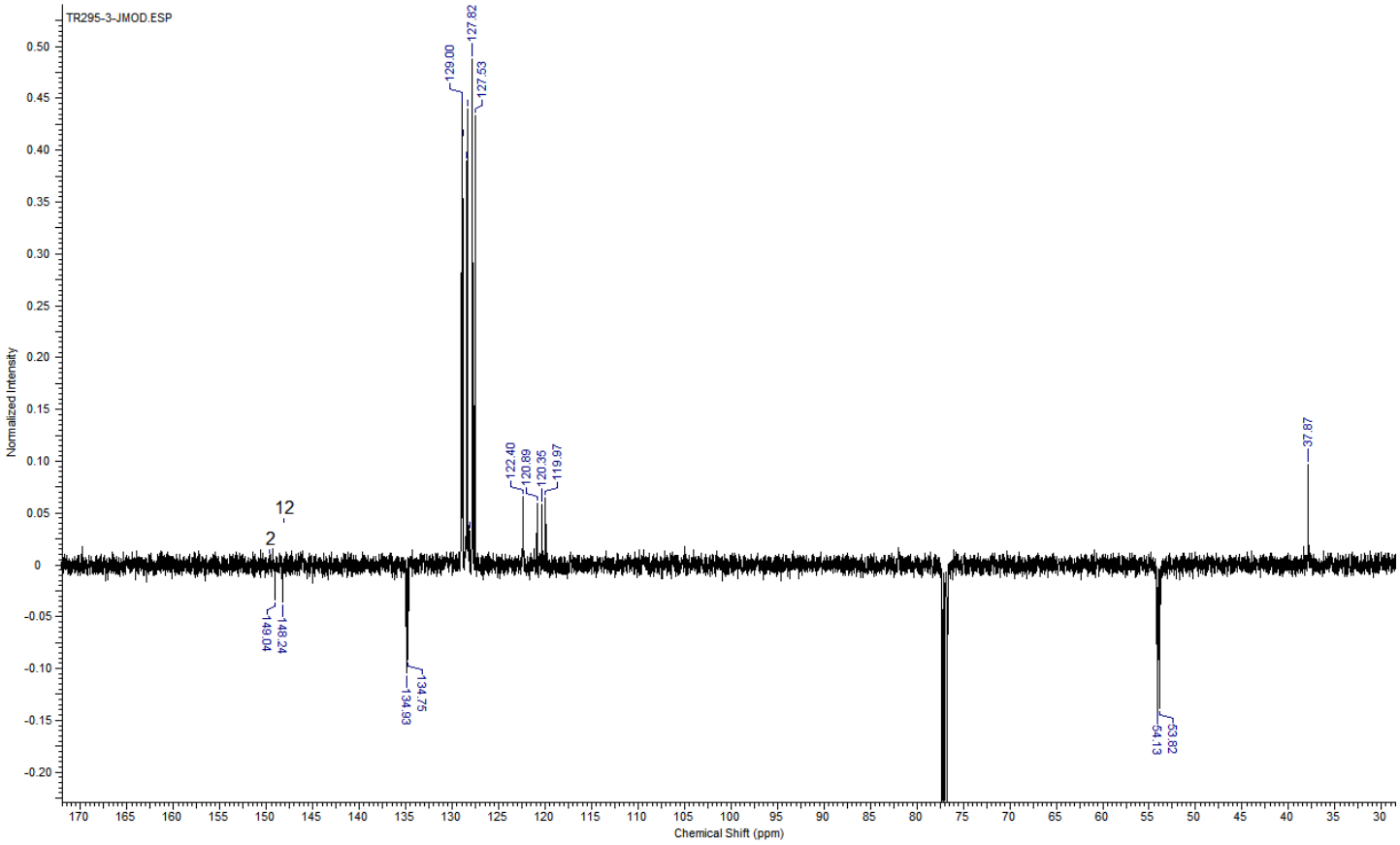

Fig. S 24: ^{13}C-ATP-NMR spectrum (126 MHz, $CDCl_3$) of complex **5g**.

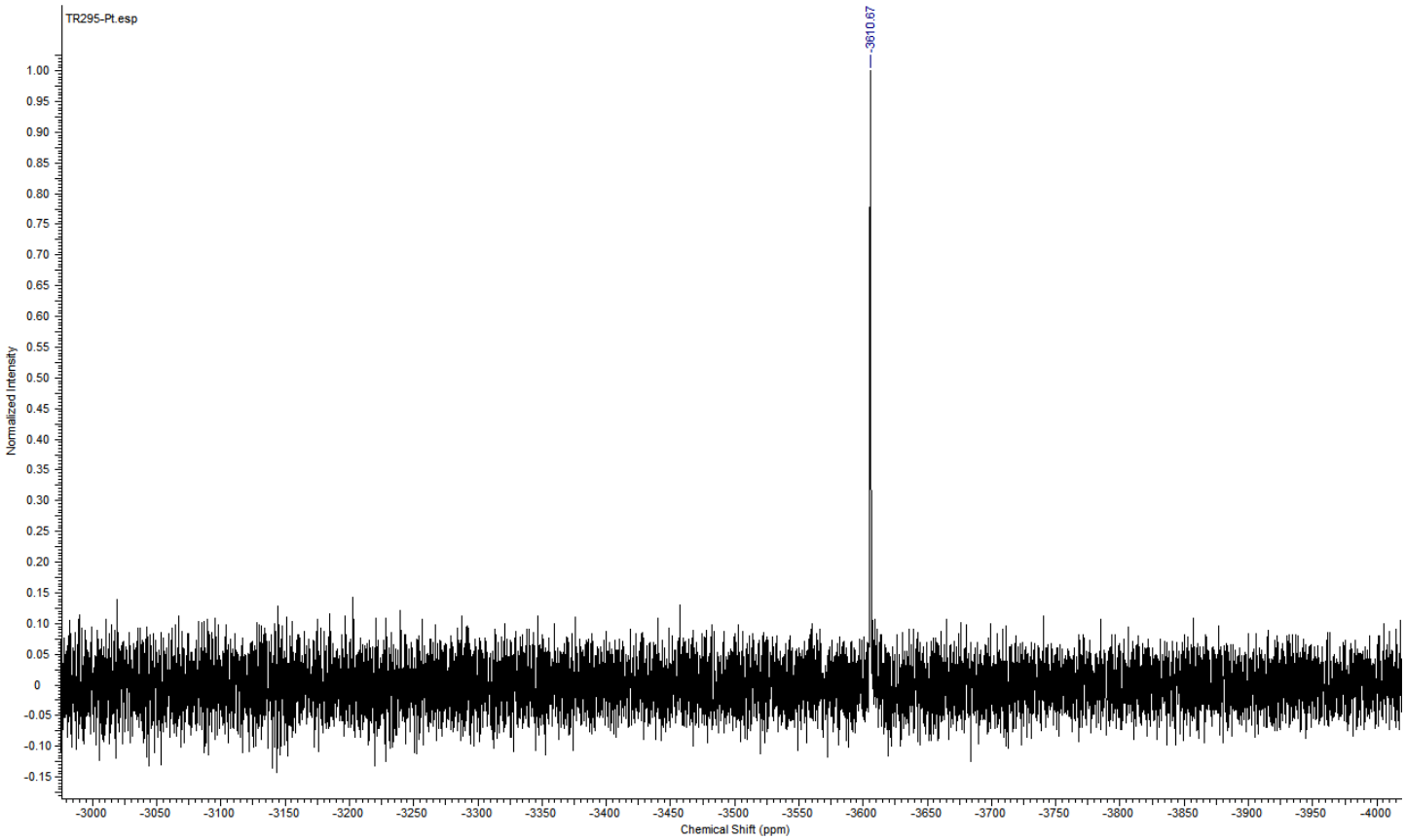

Fig. S 25: ^{195}Pt-NMR spectrum ($CDCl_3$) of complex **5g**.

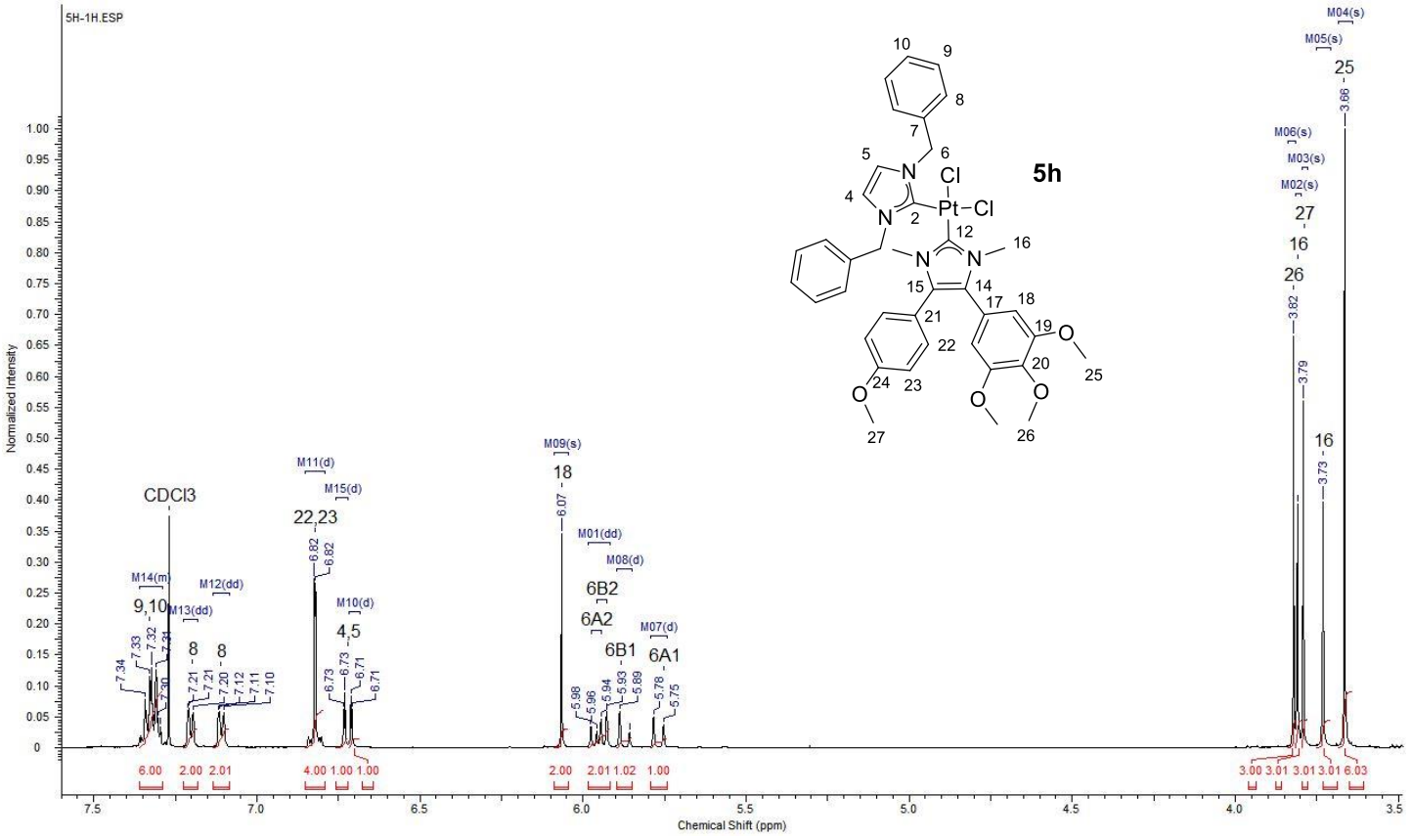

Fig. S26: ^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of complex **5h**.

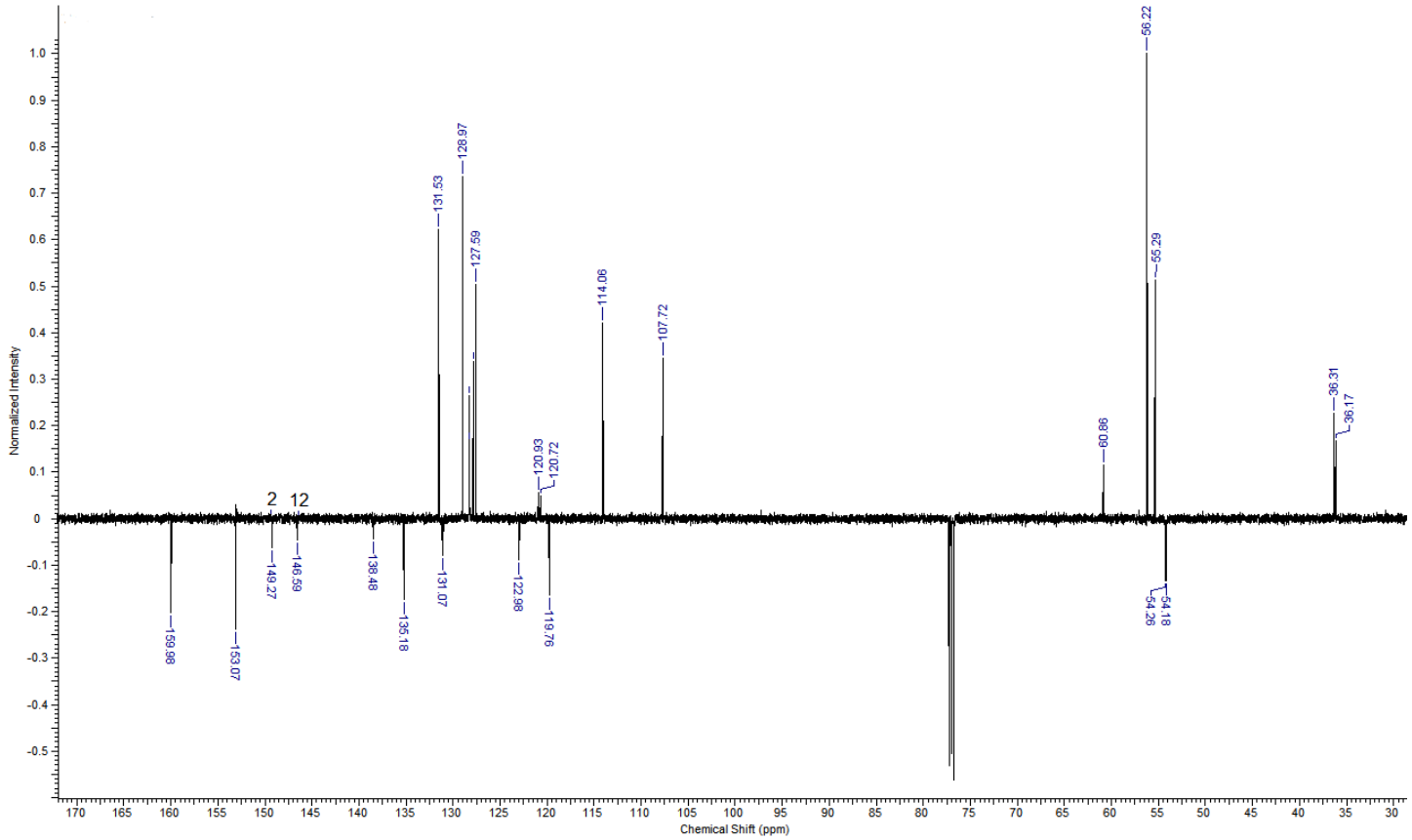

Fig. S 27: ^{13}C-ATP-NMR spectrum (126 MHz, $CDCl_3$) of complex **5h**.

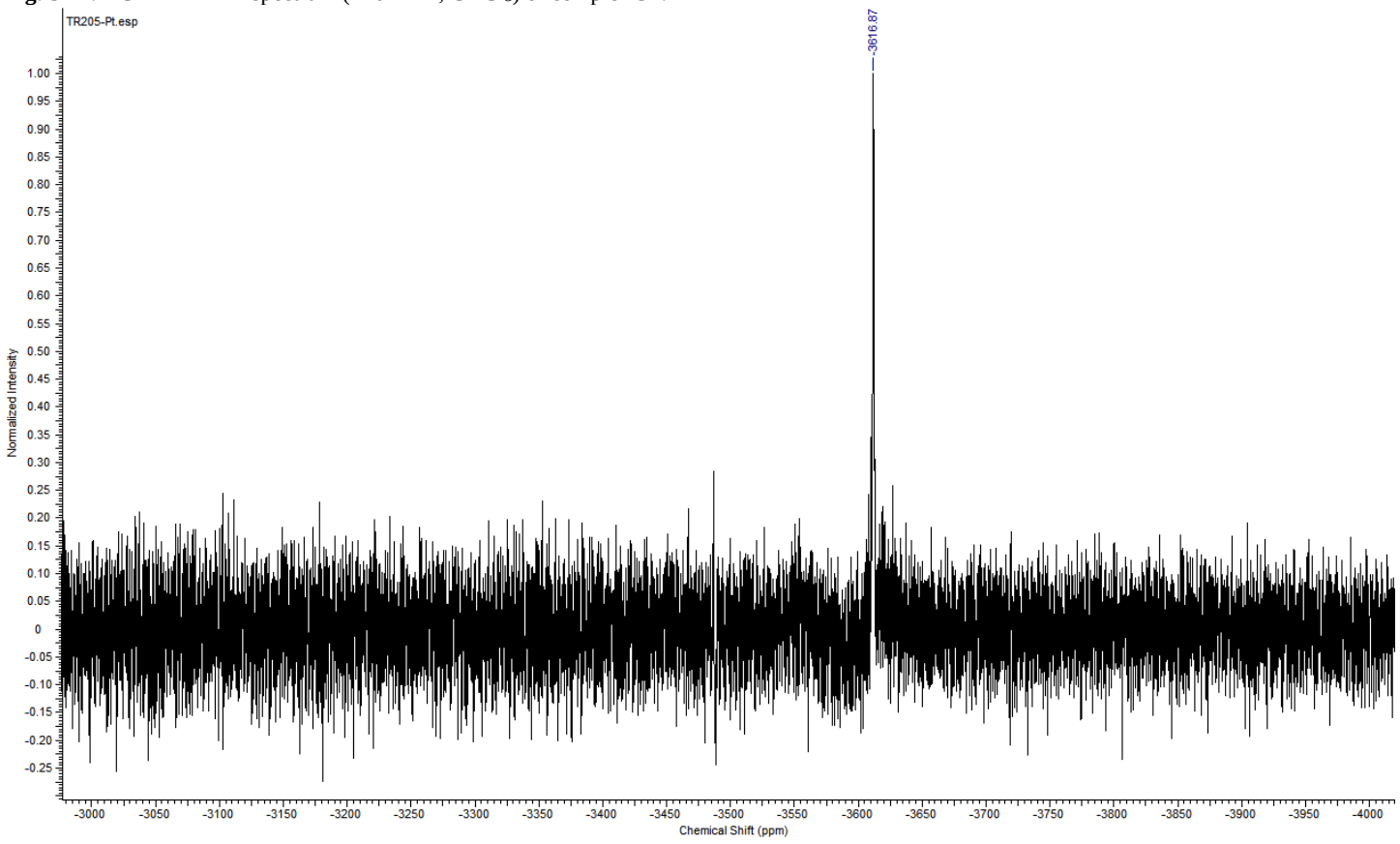

Fig. S 28: ^{195}Pt-NMR spectrum ($CDCl_3$) of complex **5h**.

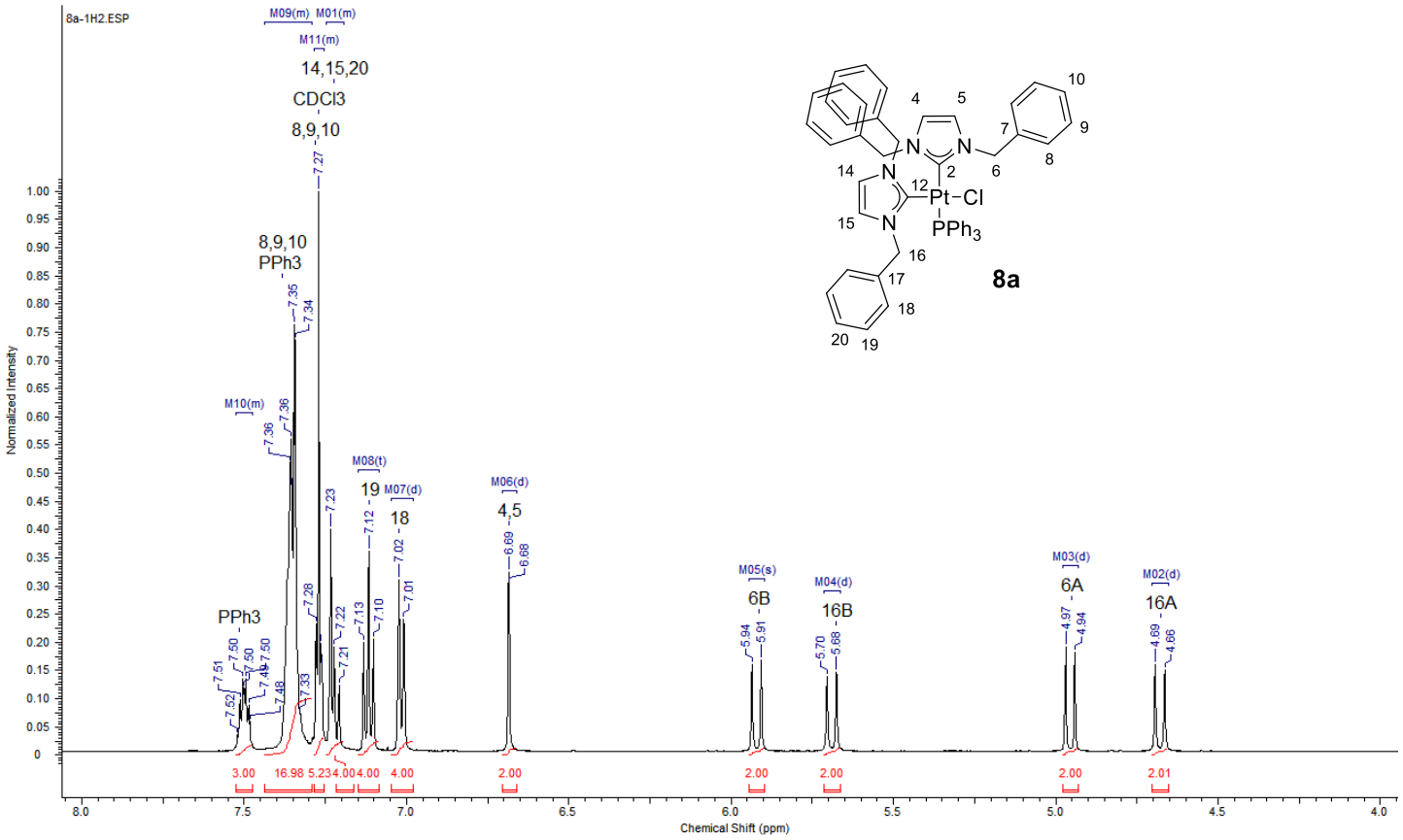

Fig. S 29: ^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of complex **8a**.

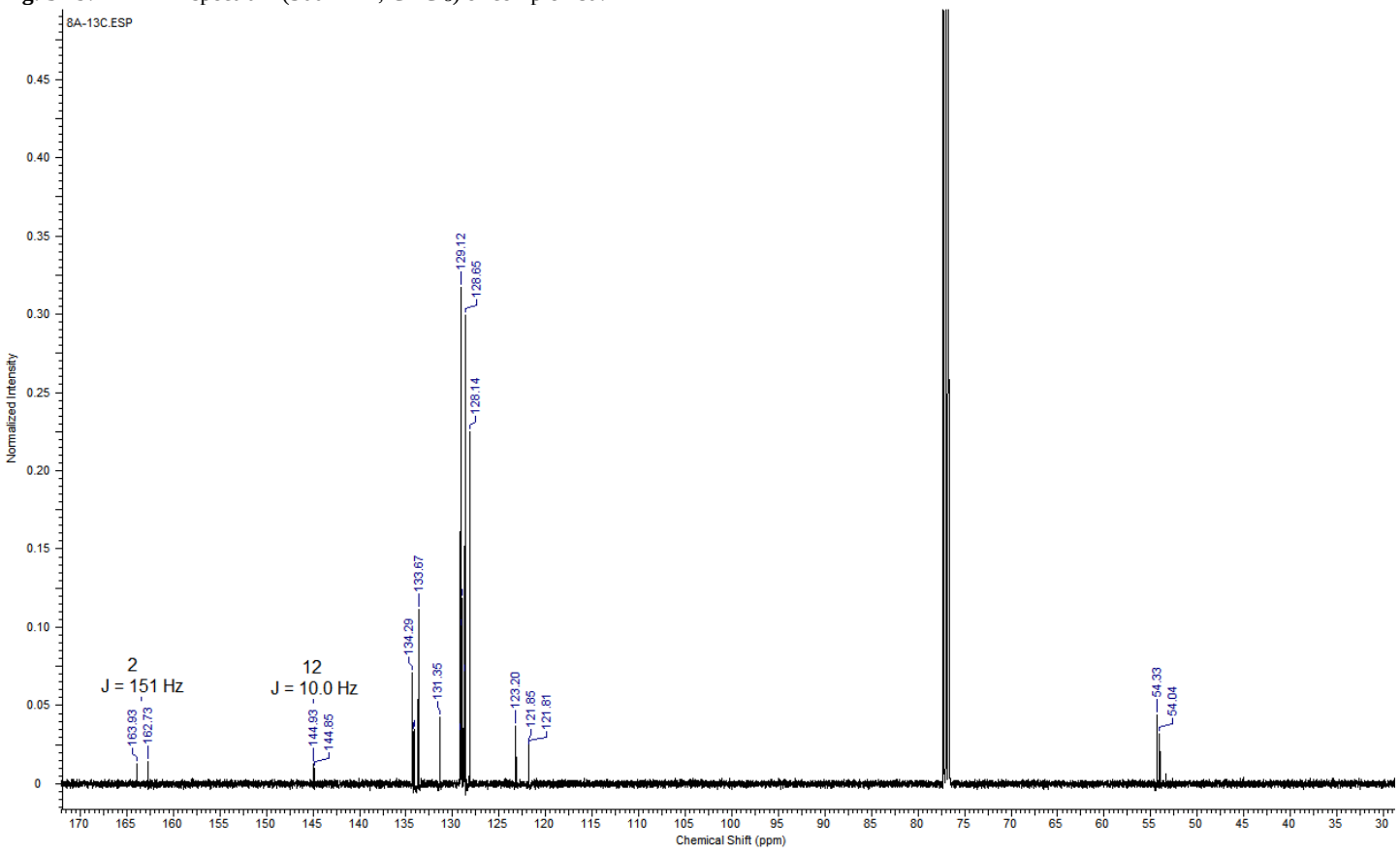

Fig. S 30: ^{13}C-NMR spectrum (126 MHz, $CDCl_3$) of complex **8a**.

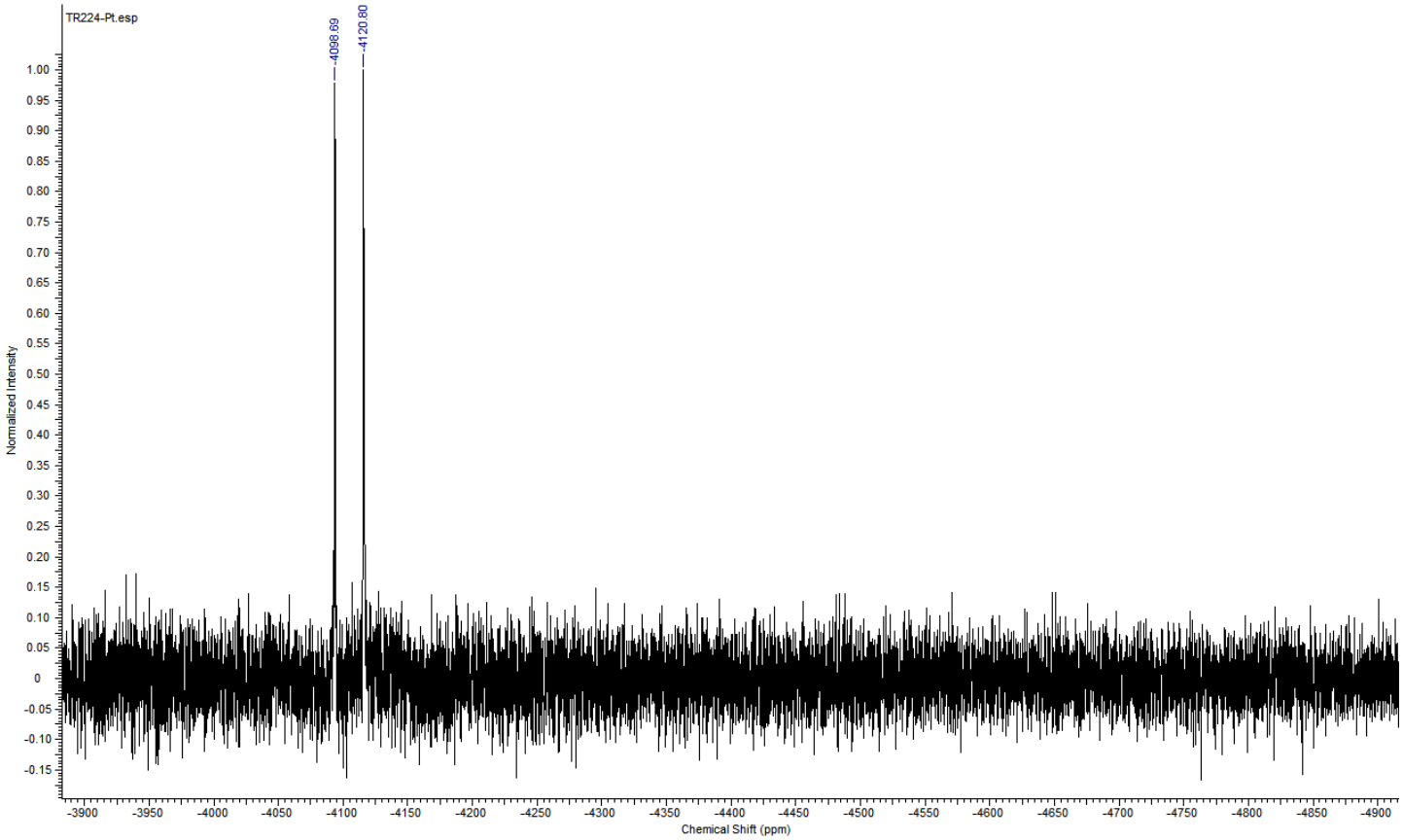

Fig. S 31: ^{195}Pt-NMR spectrum ($CDCl_3$) of complex **8a**.

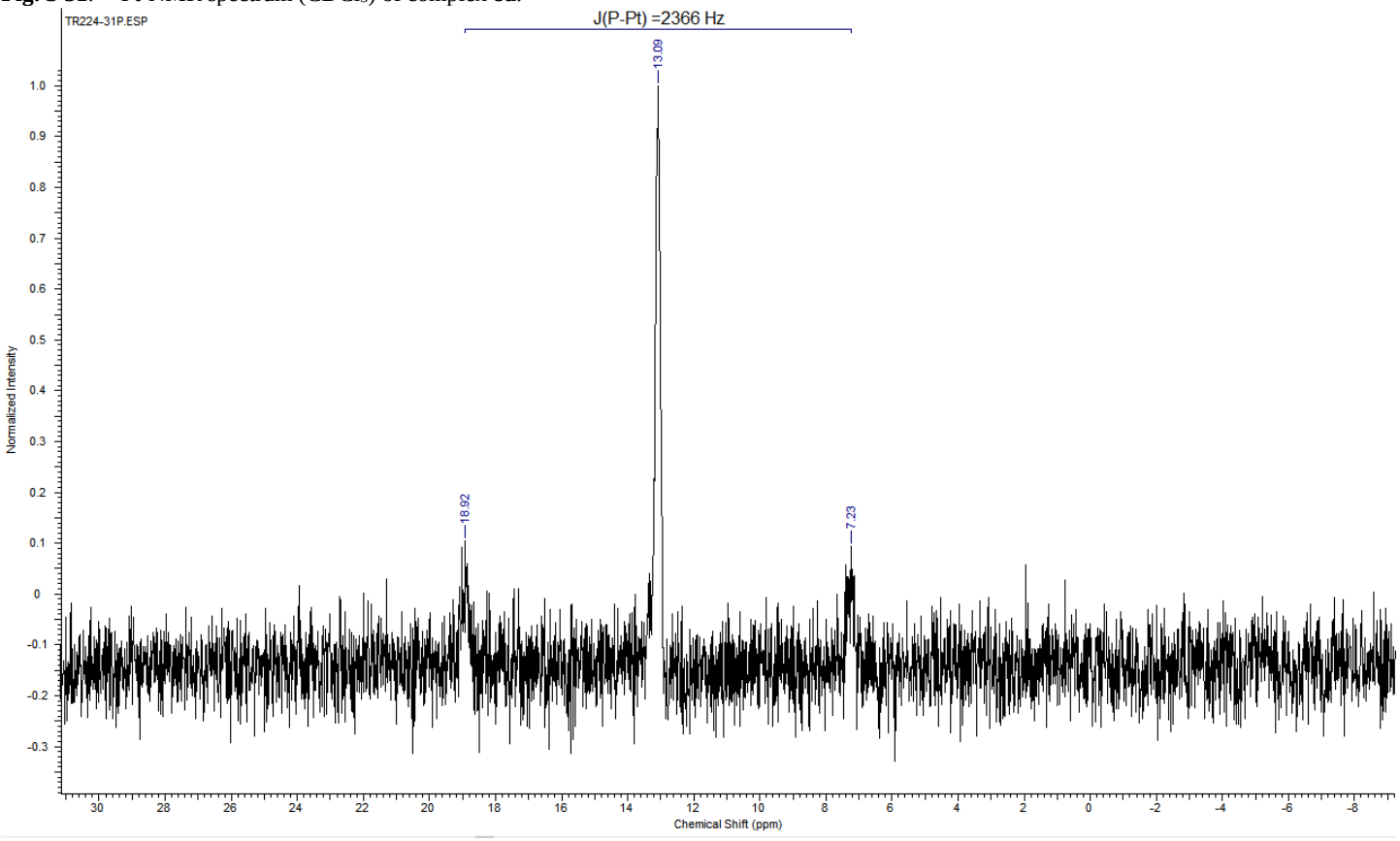

Fig. S 32: ^{31}P-NMR spectrum (202 MHz, $CDCl_3$) of complex **8a**.

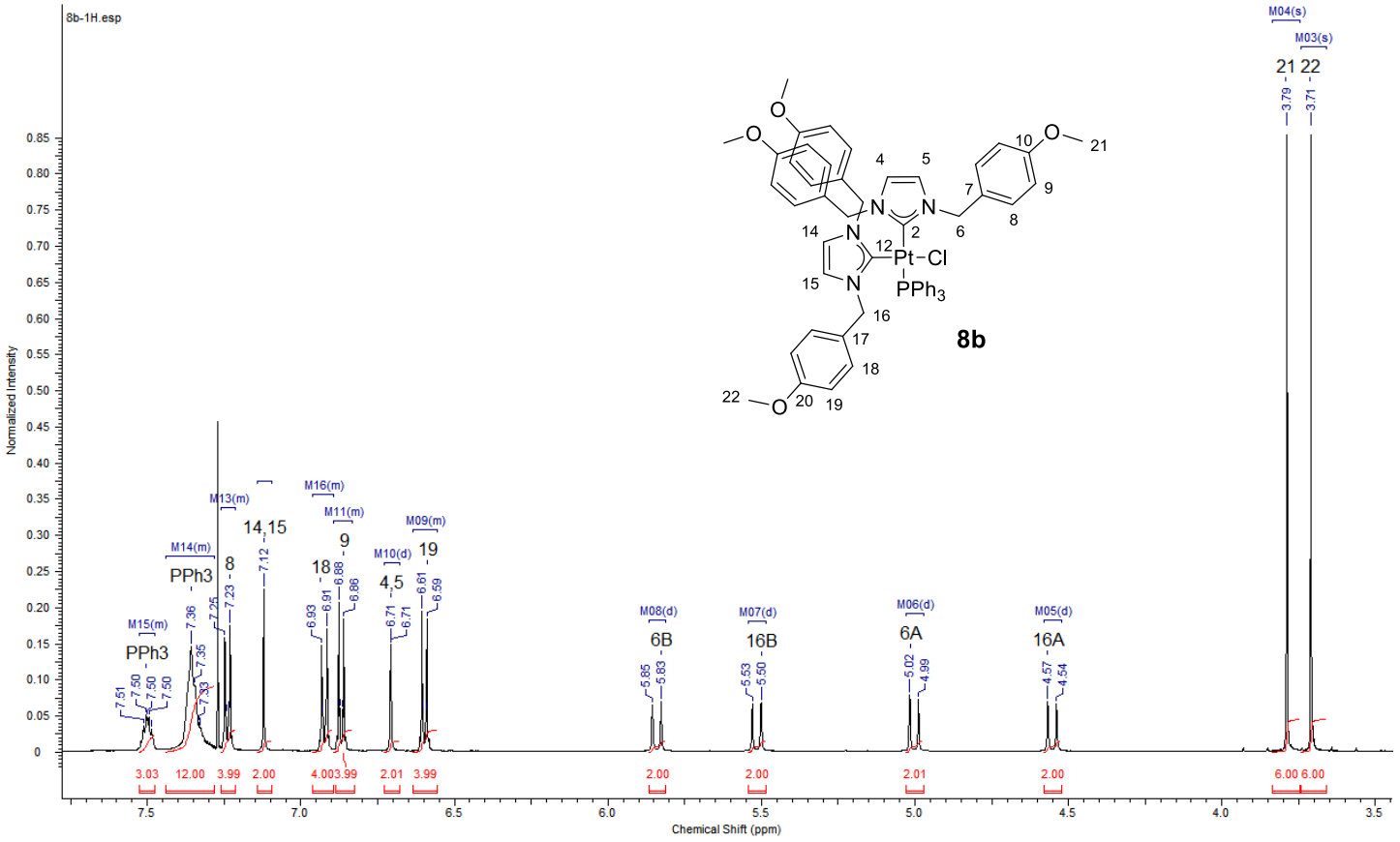

Fig. S 33: ^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of complex **8b**.

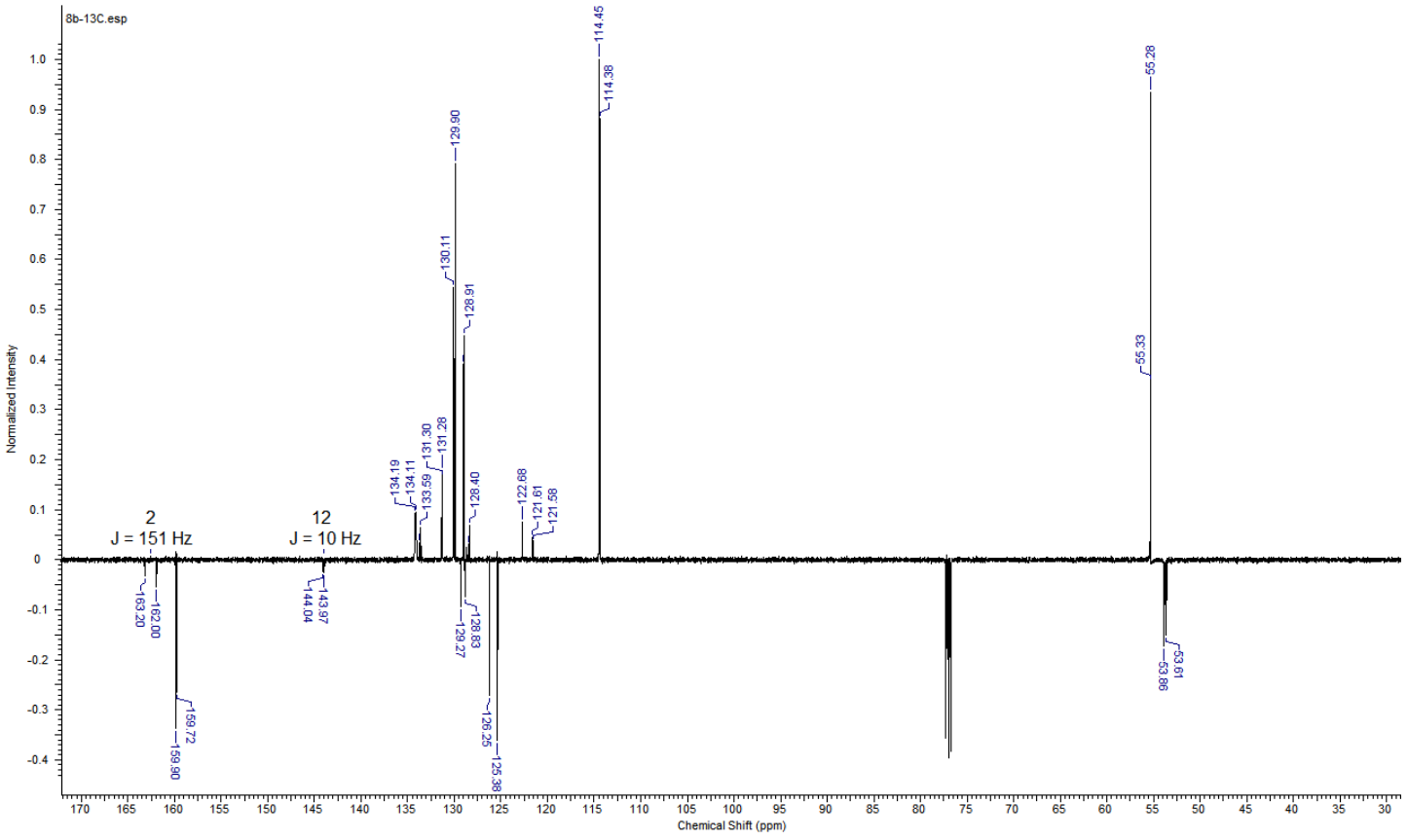

Fig. S 34: ^{13}C-ATP-NMR spectrum (126 MHz, $CDCl_3$) of complex **8b**.

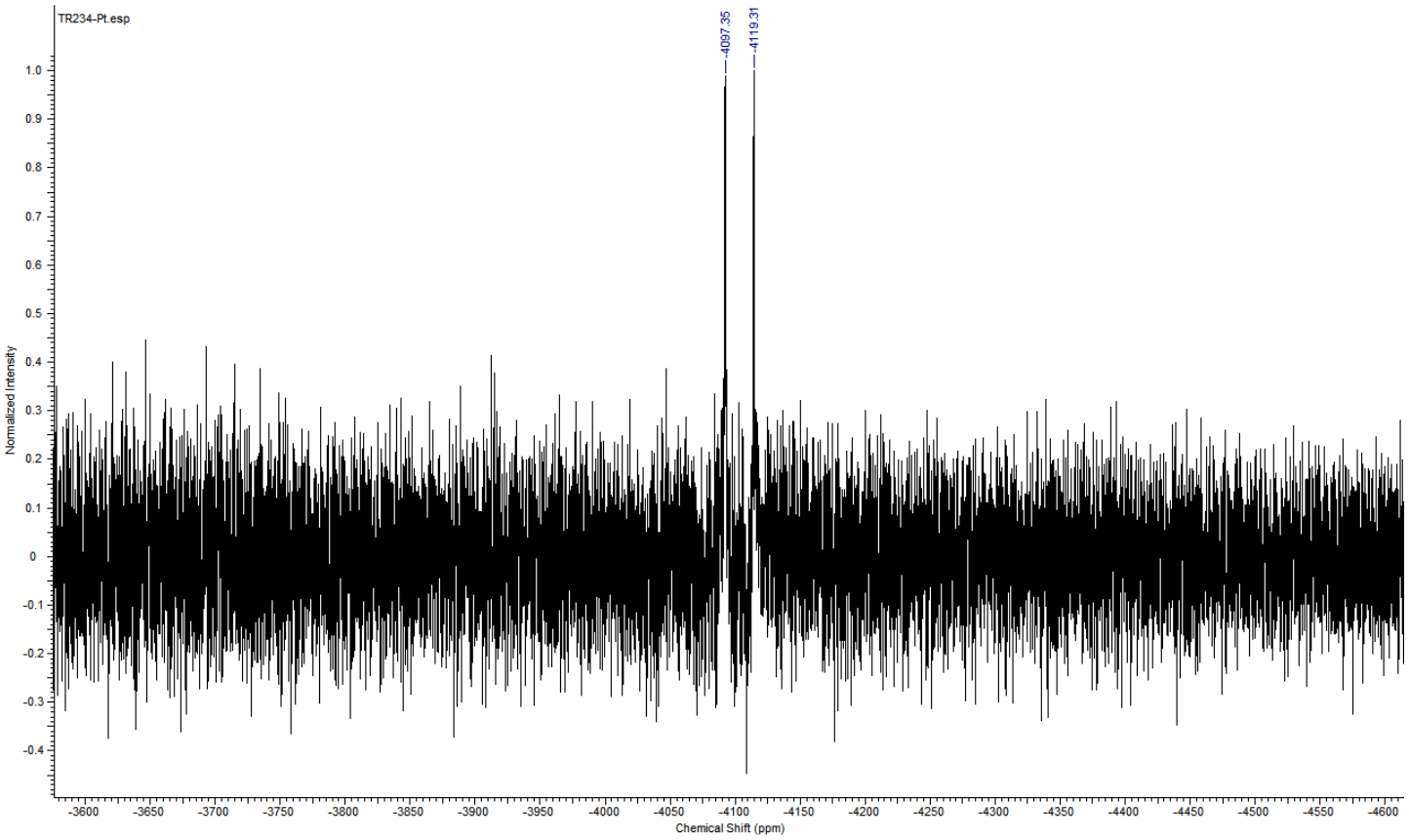

Fig. S 35: ^{195}Pt-NMR spectrum ($CDCl_3$) of complex **8b**.

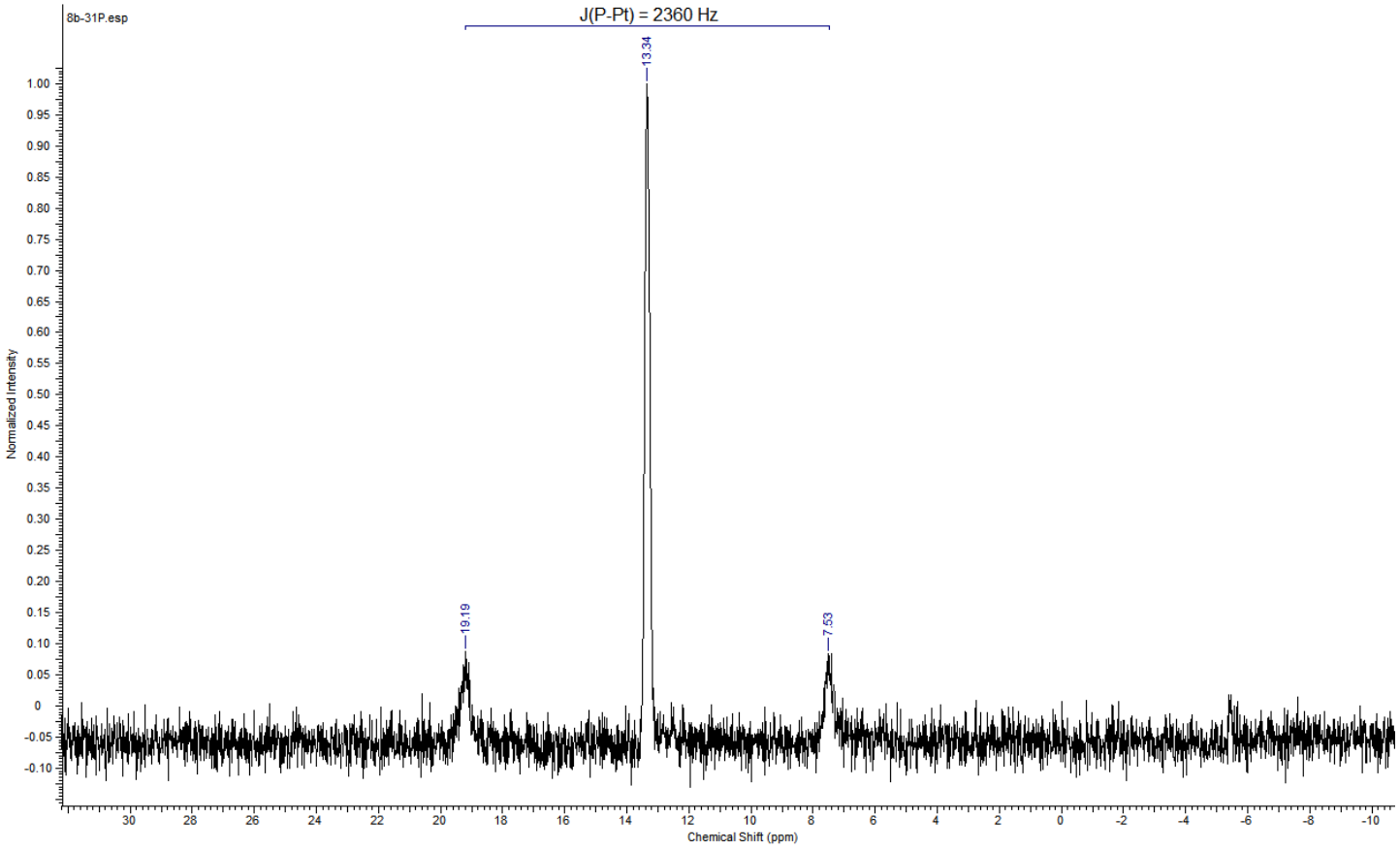

Fig. S 36: ^{31}P-NMR spectrum (202 MHz, $CDCl_3$) of complex **8b**.

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