Supporting Information for

Mono- and Di-bromo Platinum(IV) Prodrugs via Oxidative Bromination: Synthesis, Characterization, and Cytotoxicity

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Contents

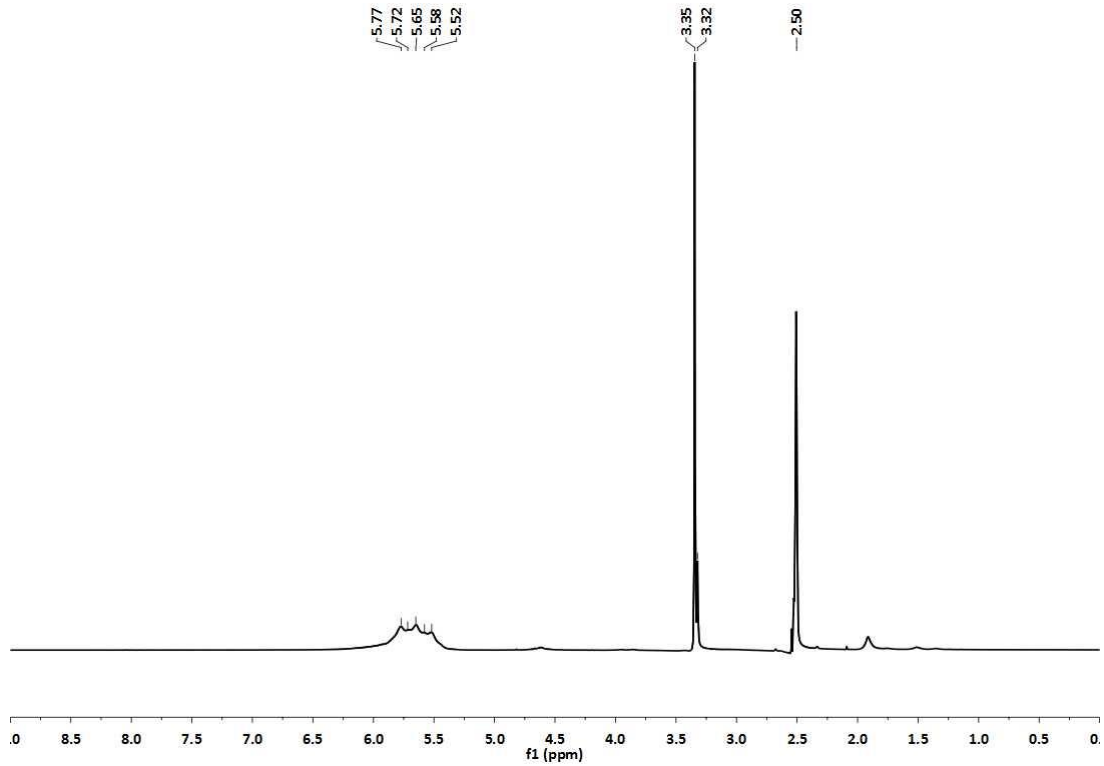

Figure S1. ^{1}H NMR spectrum of **1** in DMSO-d_6.

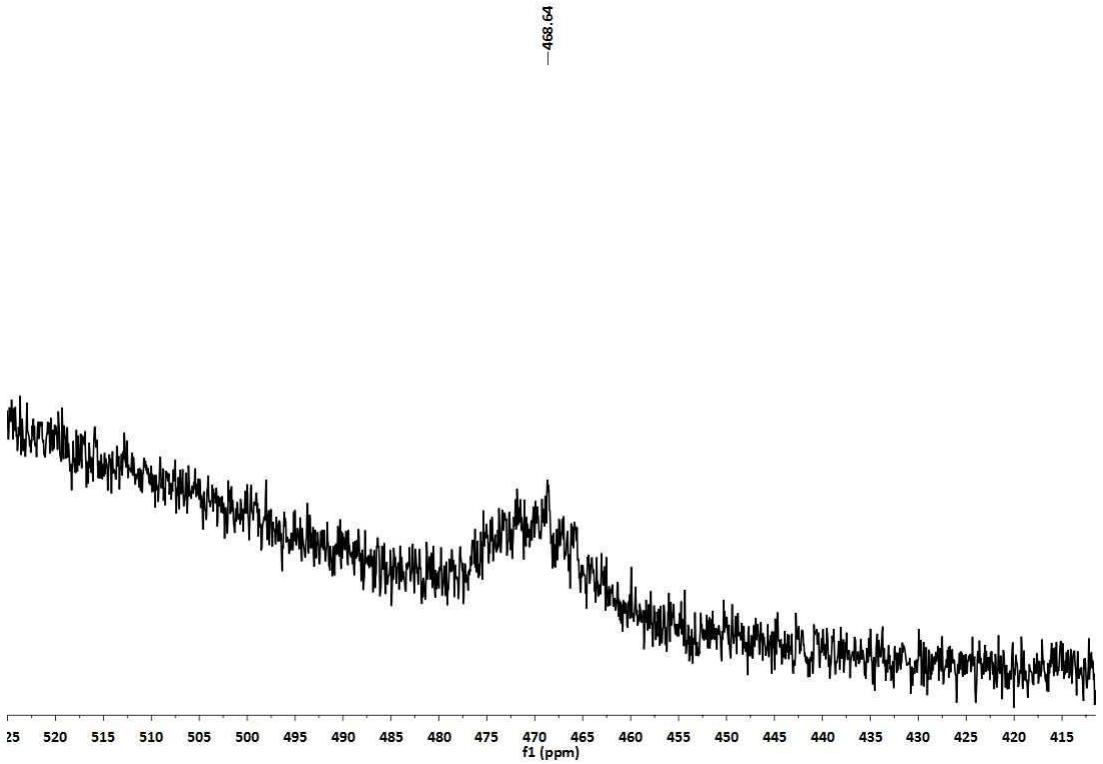

Figure S2. ^{195}Pt NMR spectrum of **1** in DMSO-d_6.

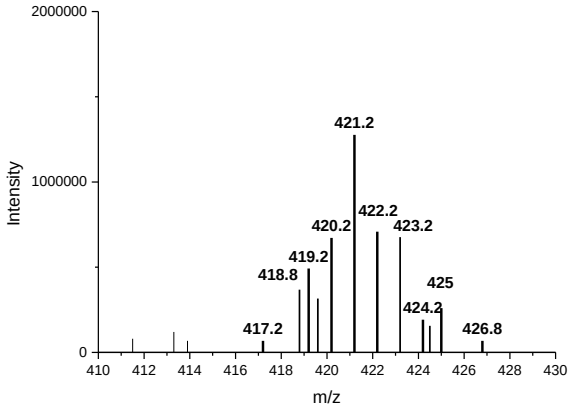

Figure S3. ESI-MS spectrum of **1**.

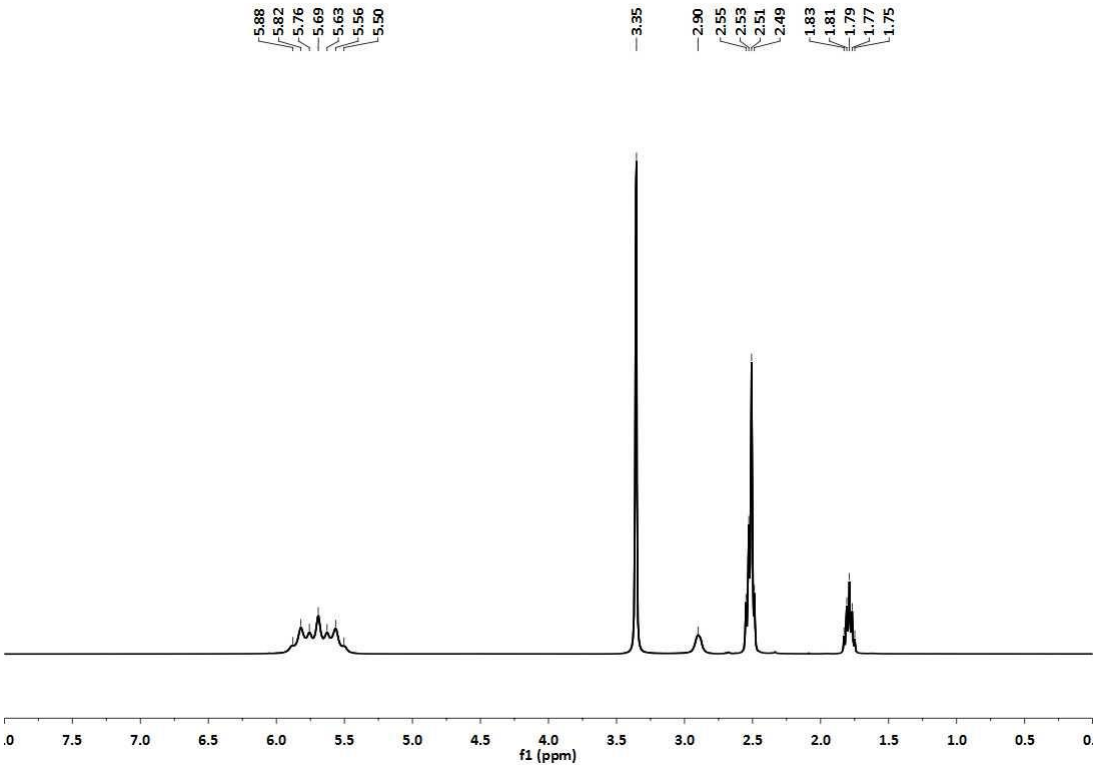

Figure S4. ^{1}H NMR spectrum of **2** in DMSO-d_6.

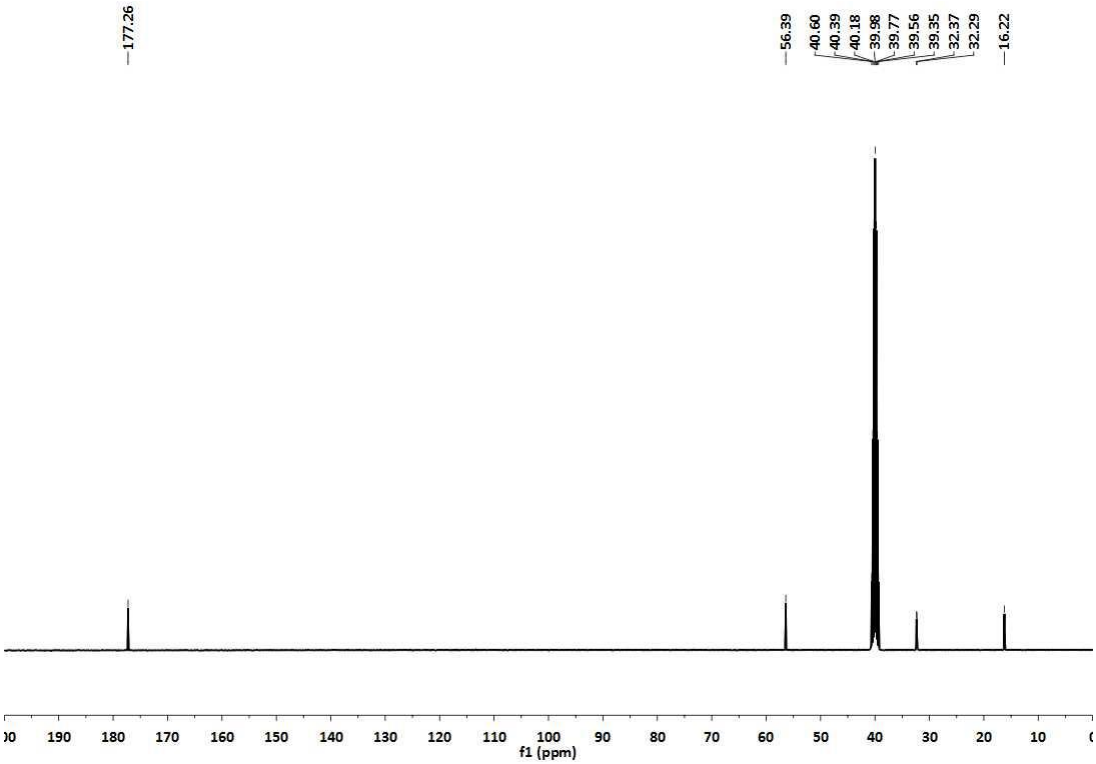

Figure S5. ^{13}C NMR spectrum of **2** in DMSO-d_6.

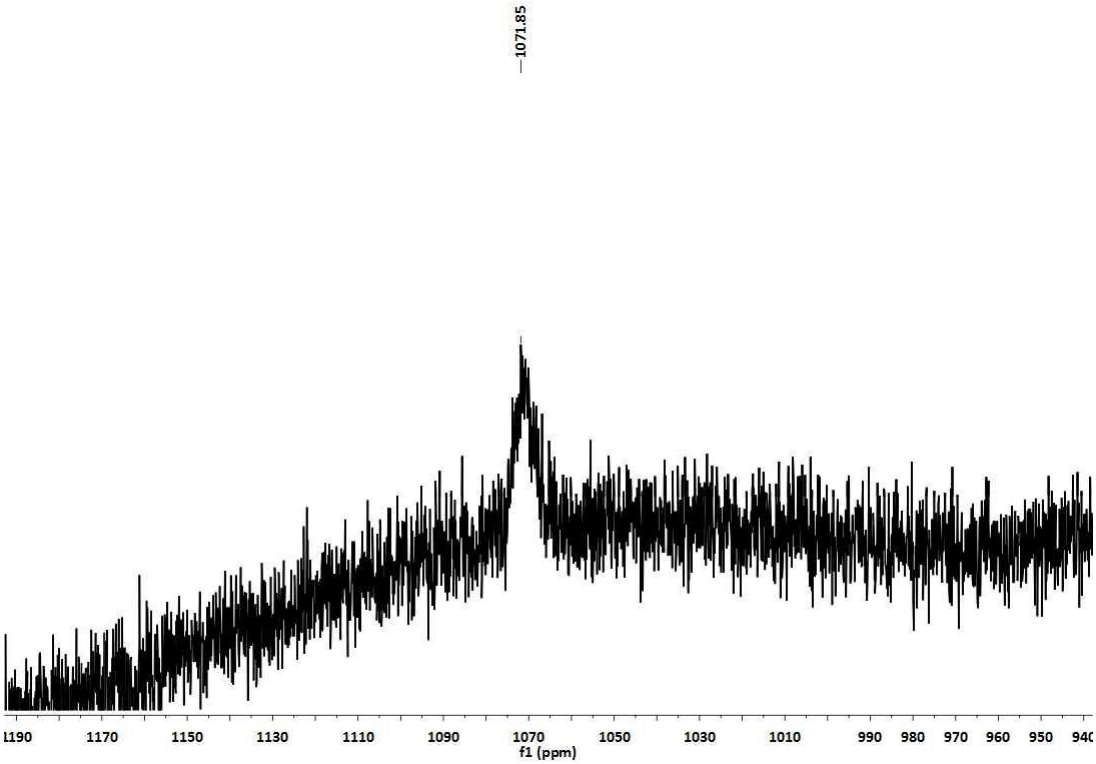

Figure S6. ^{195}Pt NMR spectrum of **2** in DMSO-d_6.

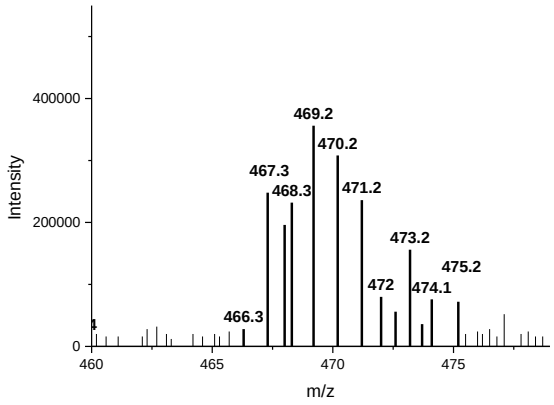

Figure S7. ESI-MS spectrum of **2**.

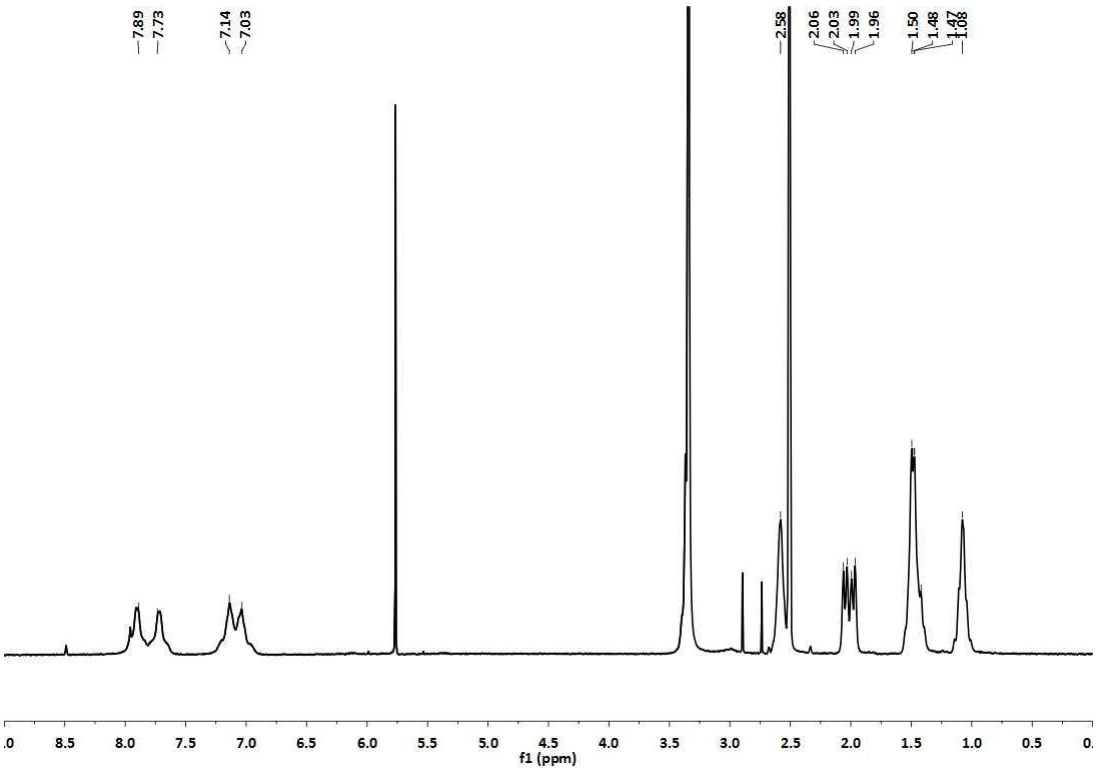

Figure S8. ^{1}H NMR spectrum of **3** in DMSO-d_6.

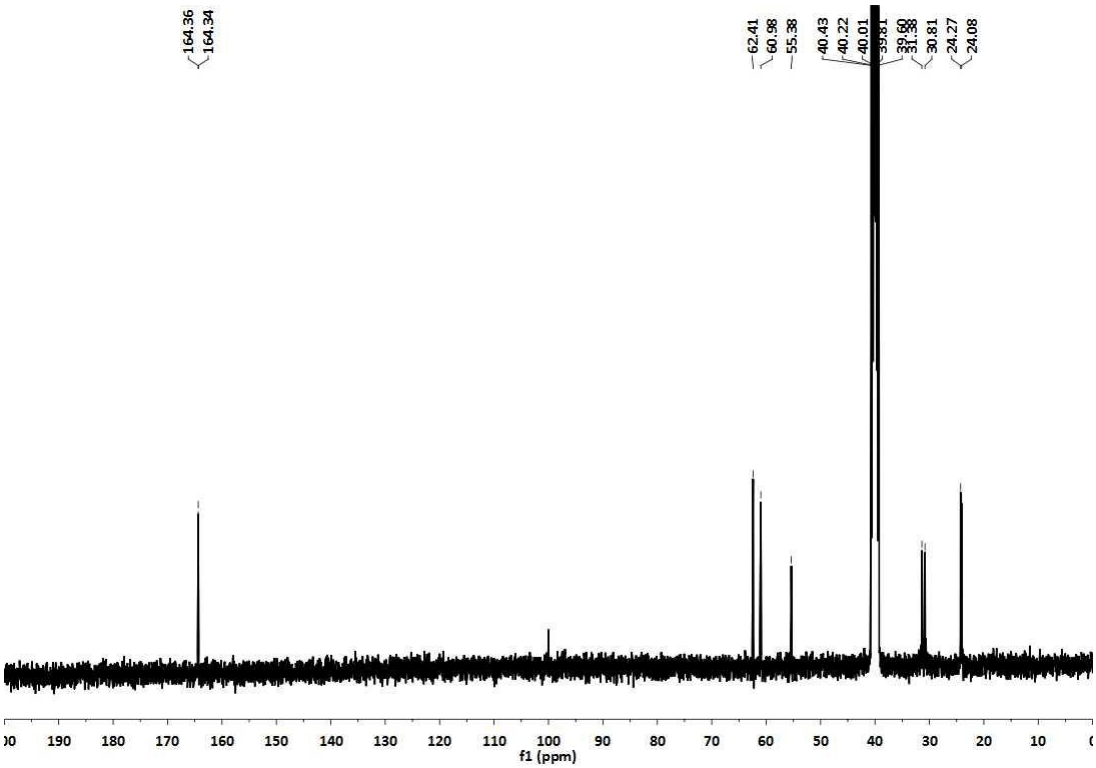

Figure S9. ^{13}C NMR spectrum of **3** in DMSO-d_6.

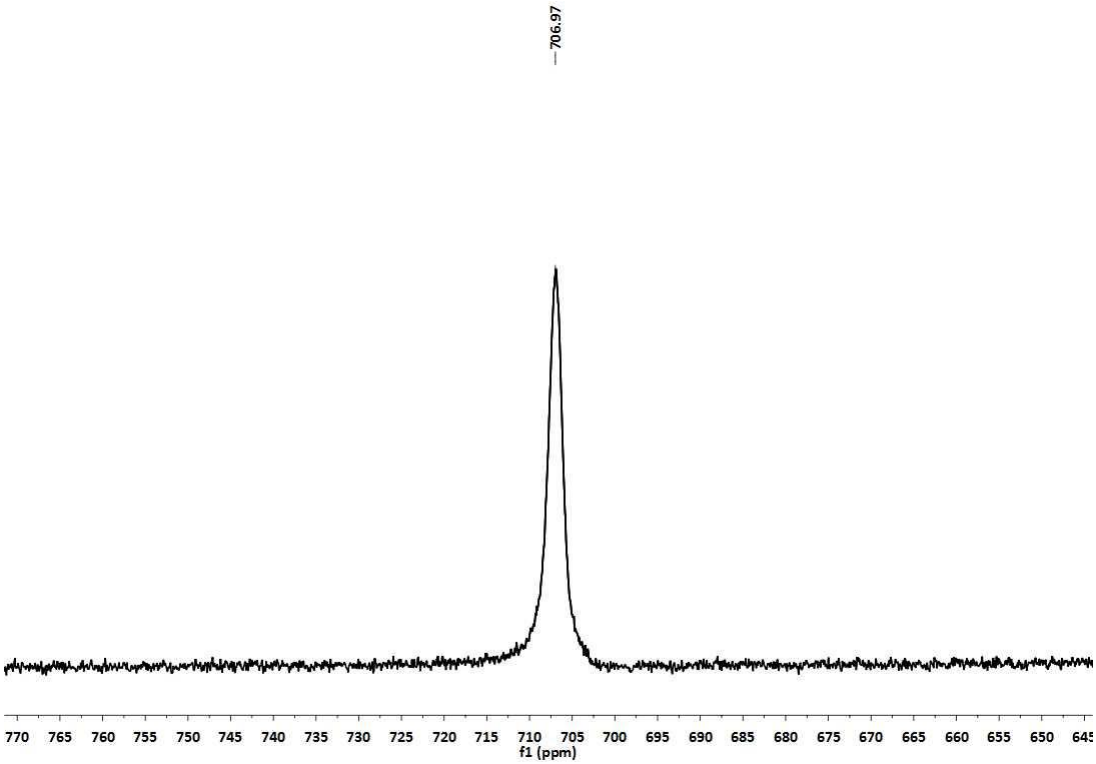

Figure S10. ^{195}Pt NMR spectrum of **3** in DMSO-d_6.

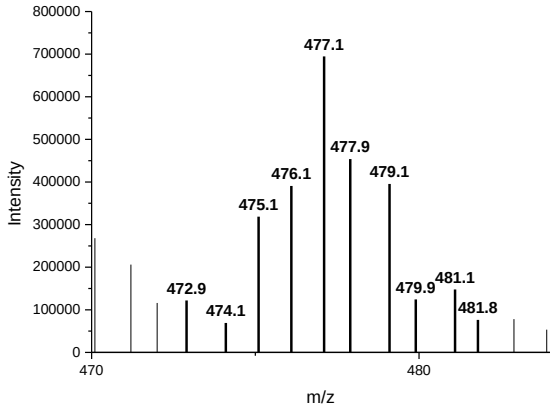

Figure S11. ESI-MS spectrum of **3**.

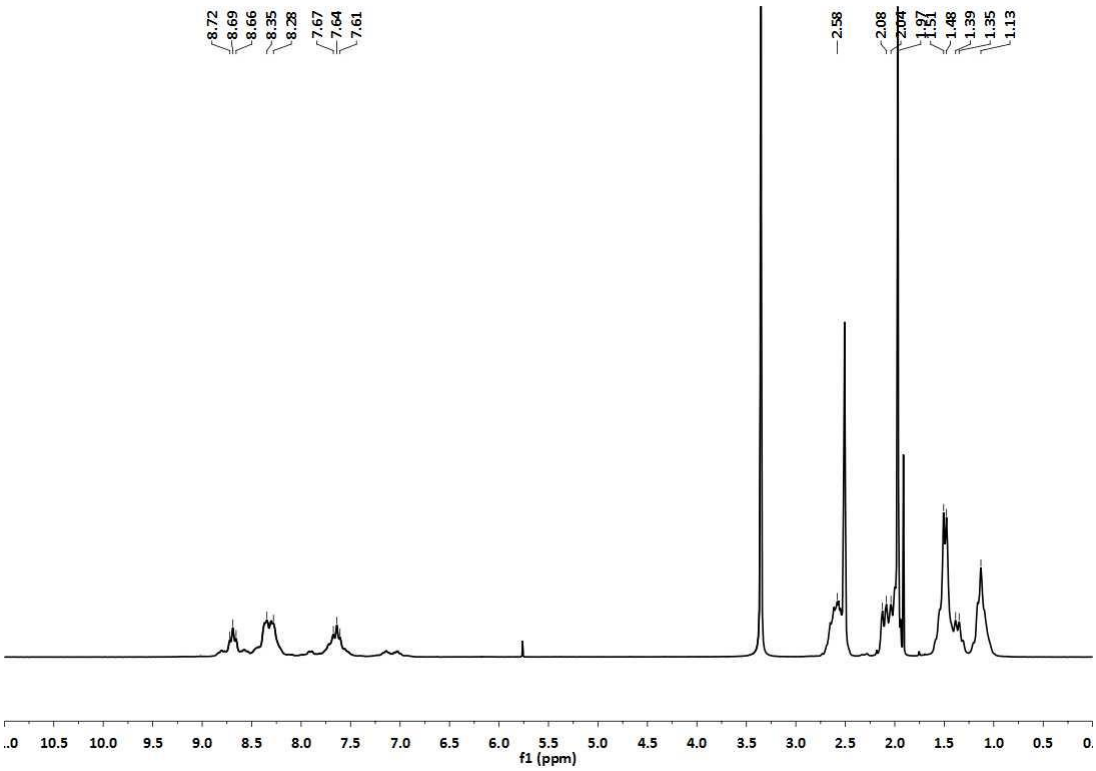

Figure S12. ^{1}H NMR spectrum of **4** in DMSO-d_6.

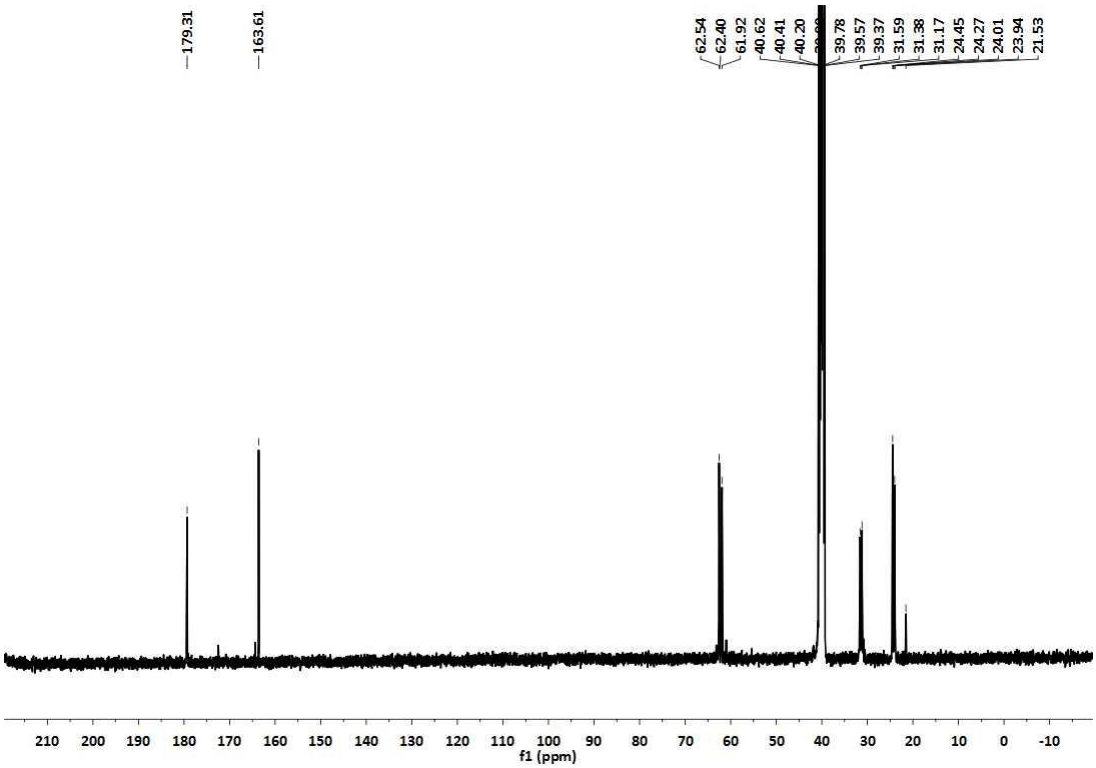

Figure S13. ^{13}C NMR spectrum of **4** in DMSO-d_6.

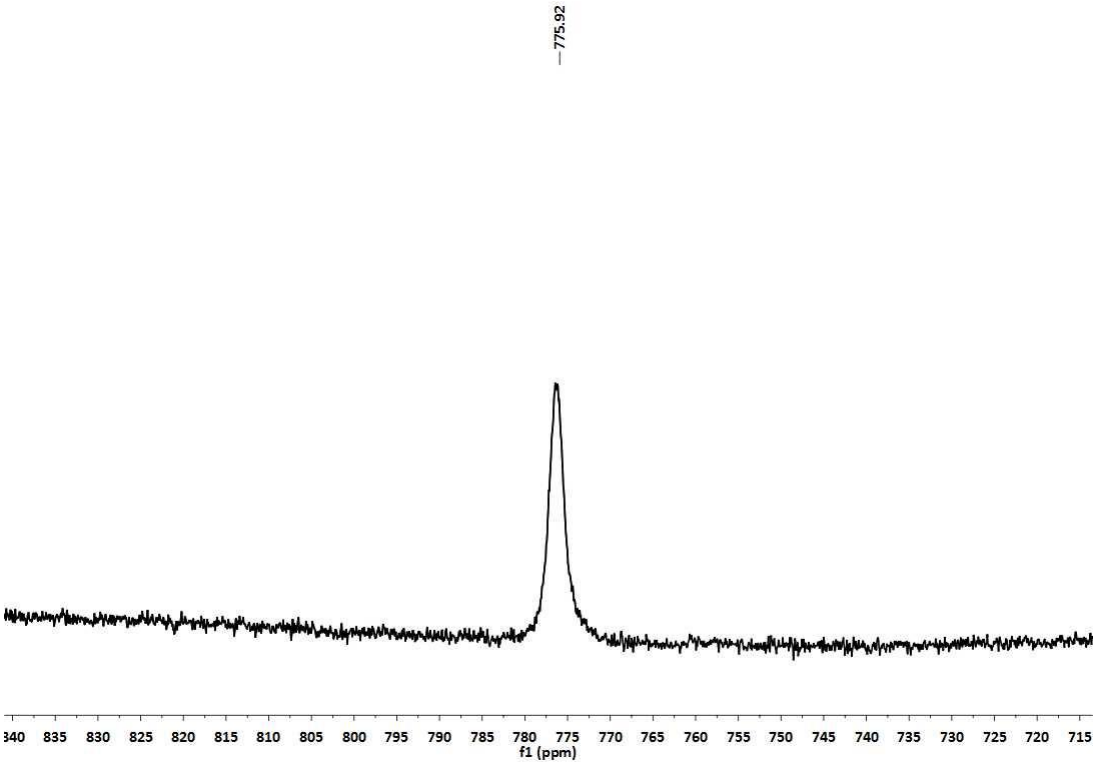

Figure S14. ^{195}Pt NMR spectrum of **4** in DMSO-d_6.

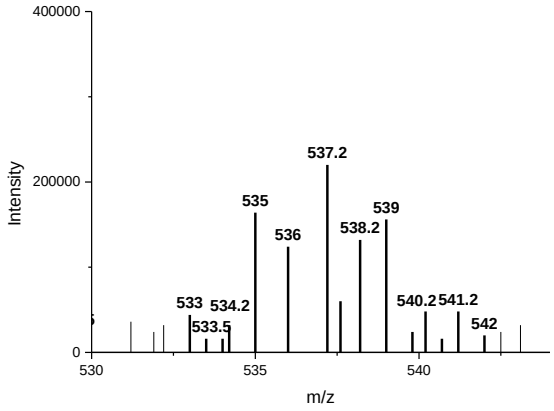

Figure S15. ESI-MS spectrum of **4**.

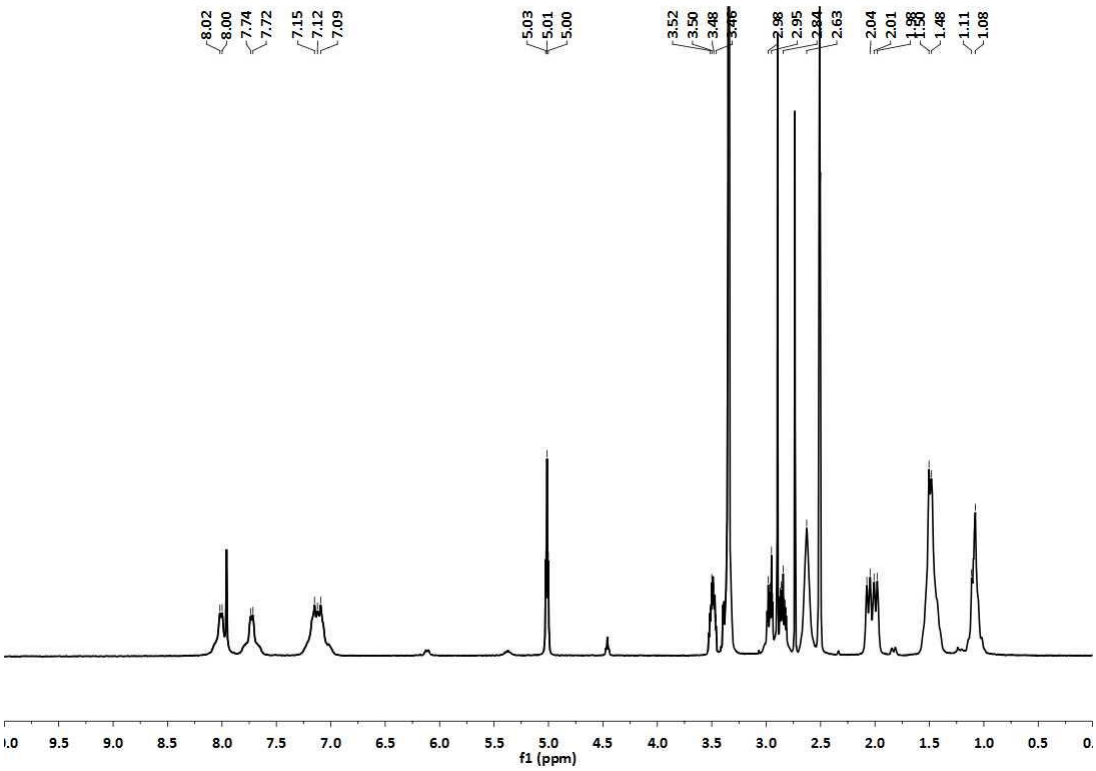

Figure S16. ^{1}H NMR spectrum of **5** in DMSO-d_6.

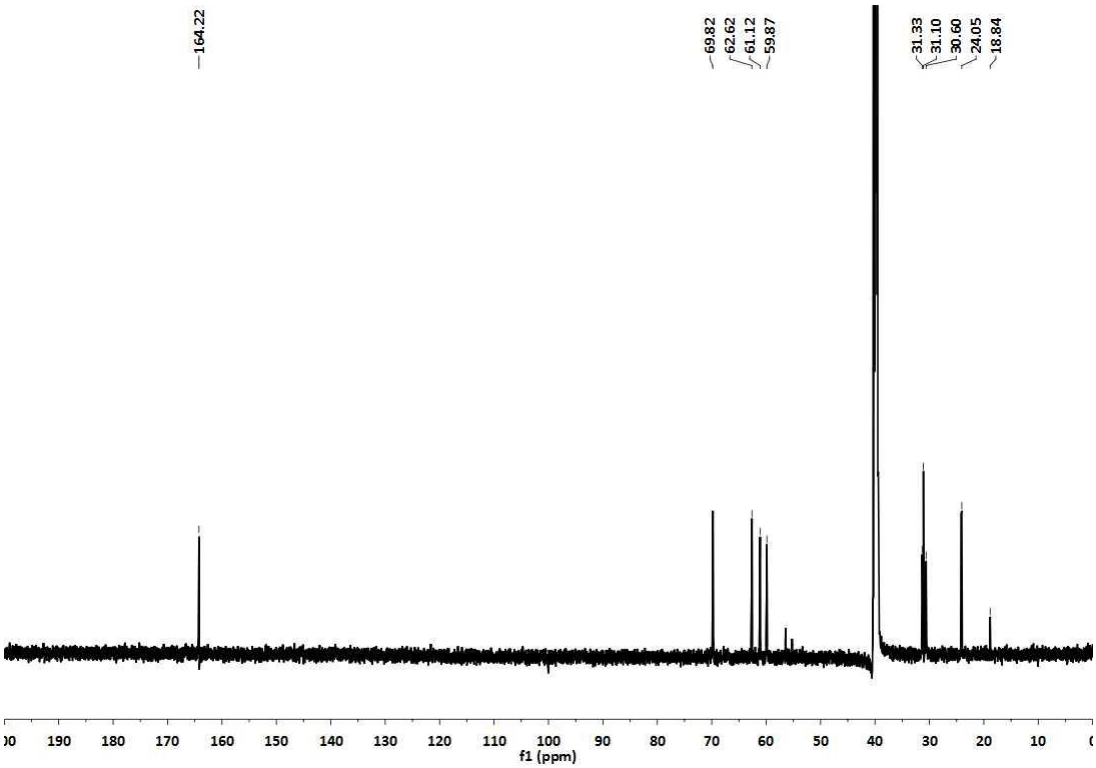

Figure S17. ^{13}C NMR spectrum of **5** in DMSO-d_6.

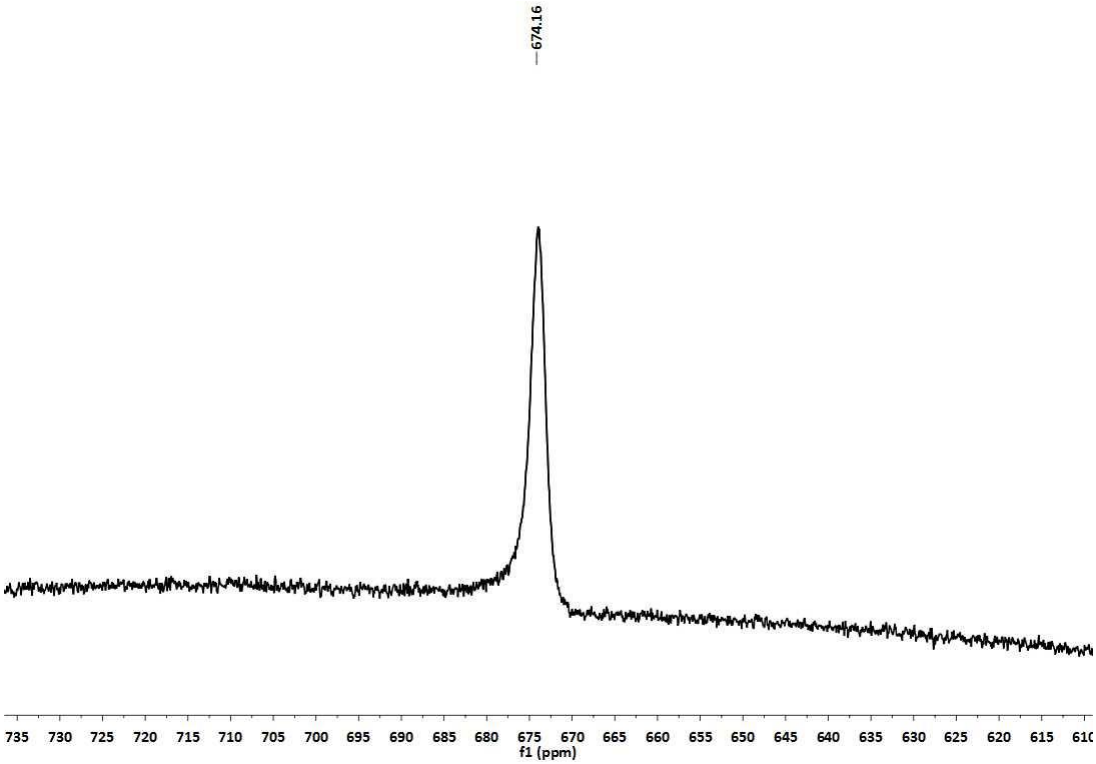

Figure S18. ^{195}Pt NMR spectrum of **5** in DMSO-d_6.

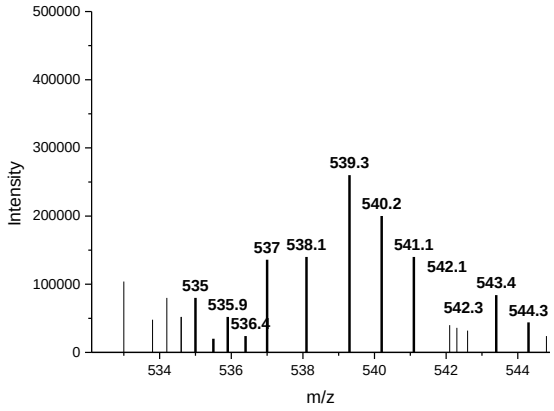

Figure S19. ESI-MS spectrum of **5**.

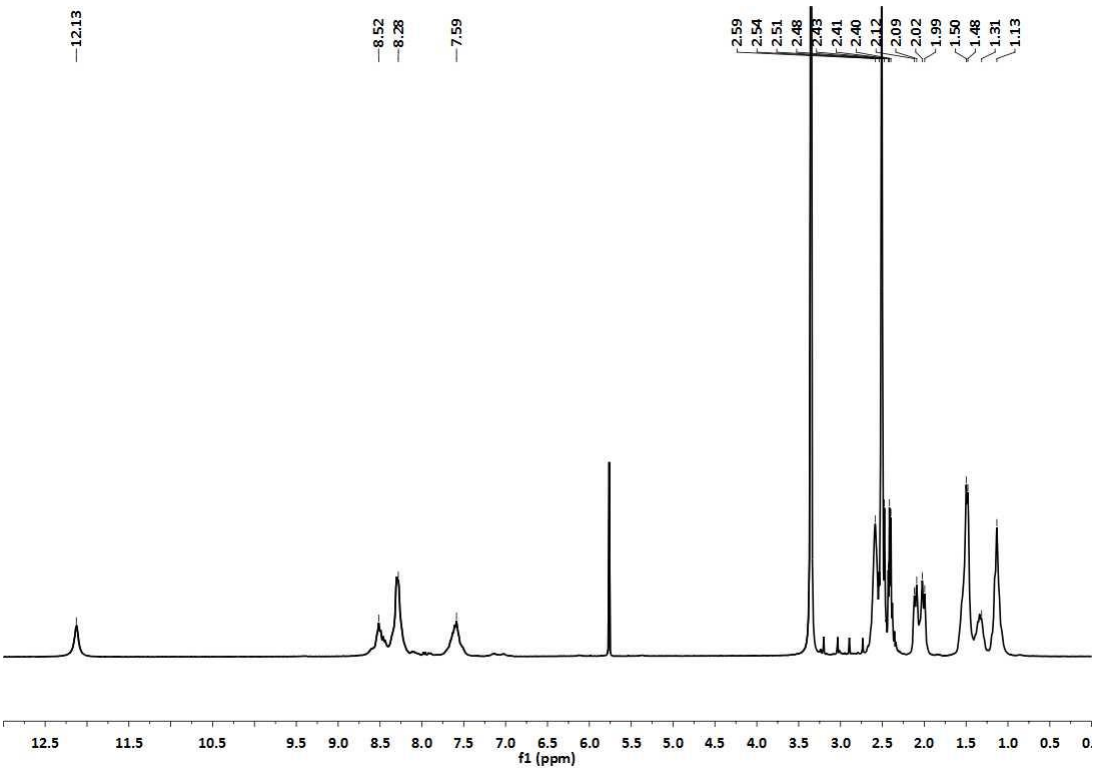

Figure S20. ^{1}H NMR spectrum of **6** in DMSO-d_6.

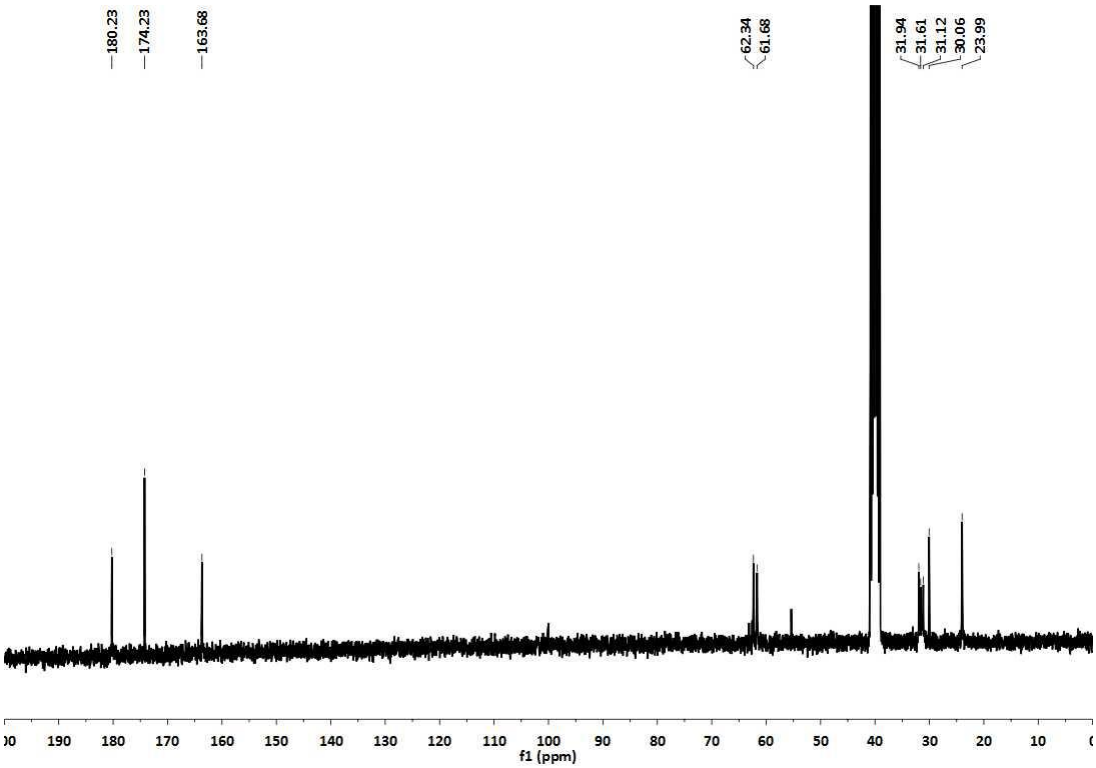

Figure S21. ^{13}C NMR spectrum of **6** in DMSO-d_6.

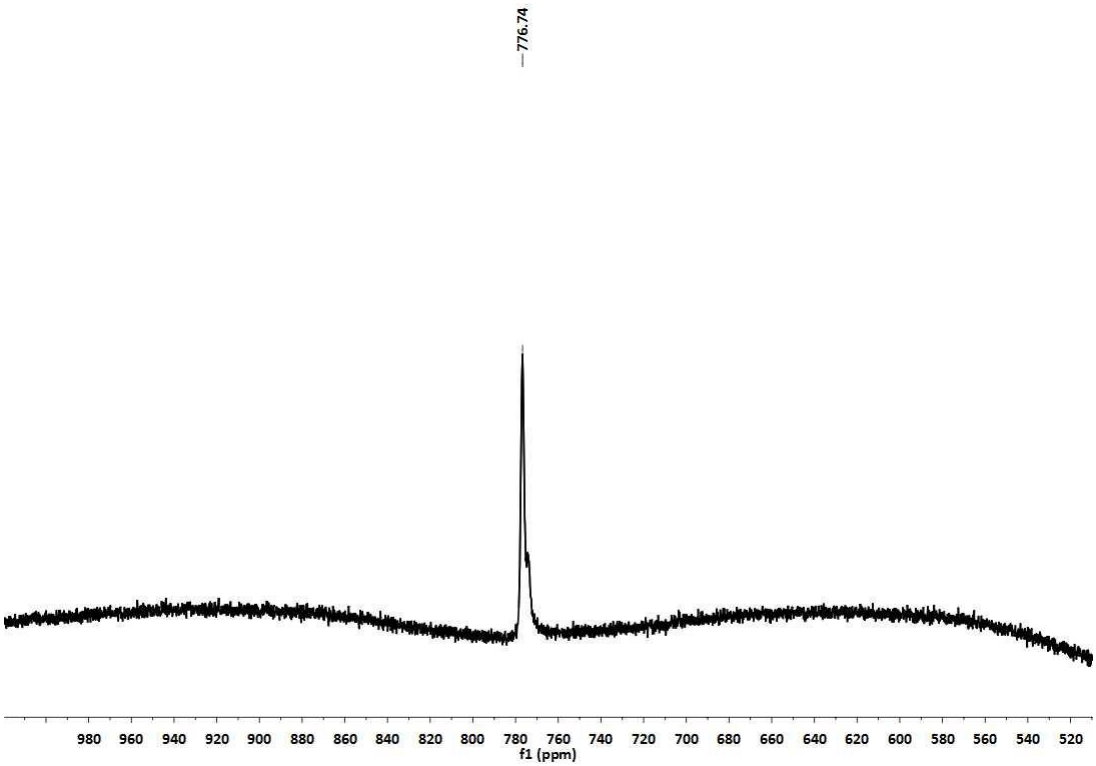

Figure S22. ^{195}Pt NMR spectrum of **6** in DMSO-d_6.

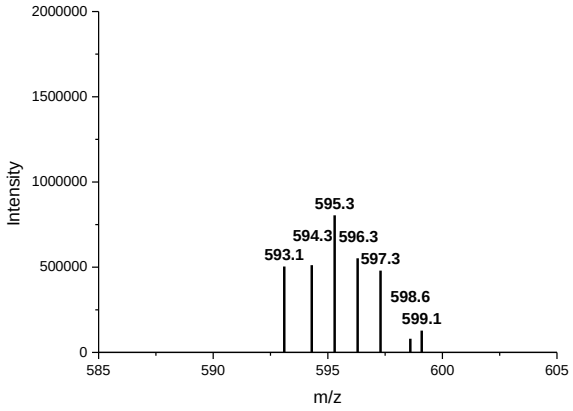

Figure S23. ESI-MS spectrum of **6**.

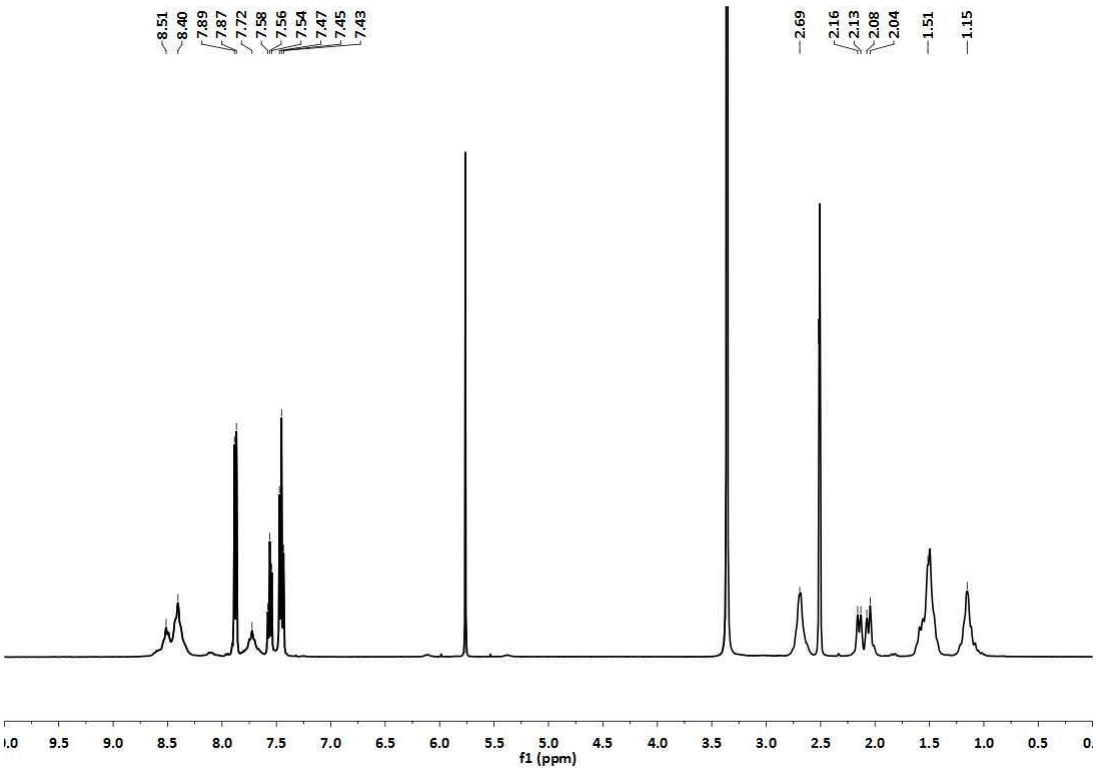

Figure S24. ^{1}H NMR spectrum of **7** in DMSO-d_6.

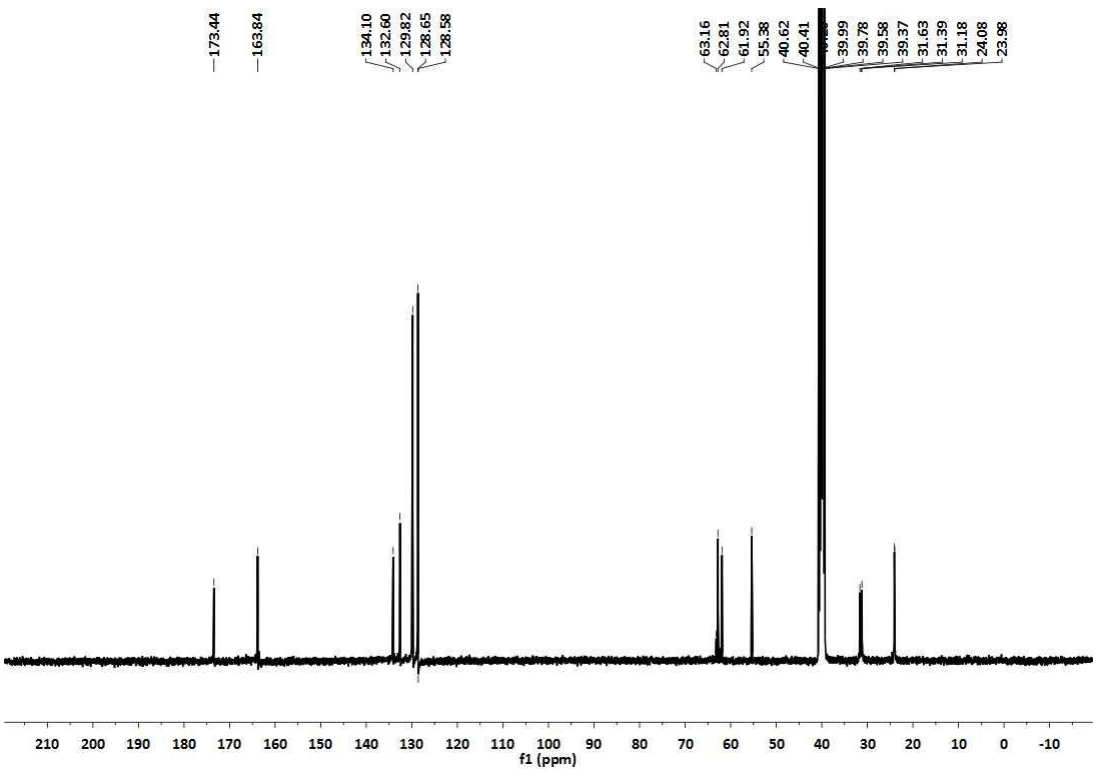

Figure S25. ^{13}C NMR spectrum of **7** in DMSO-d_6.

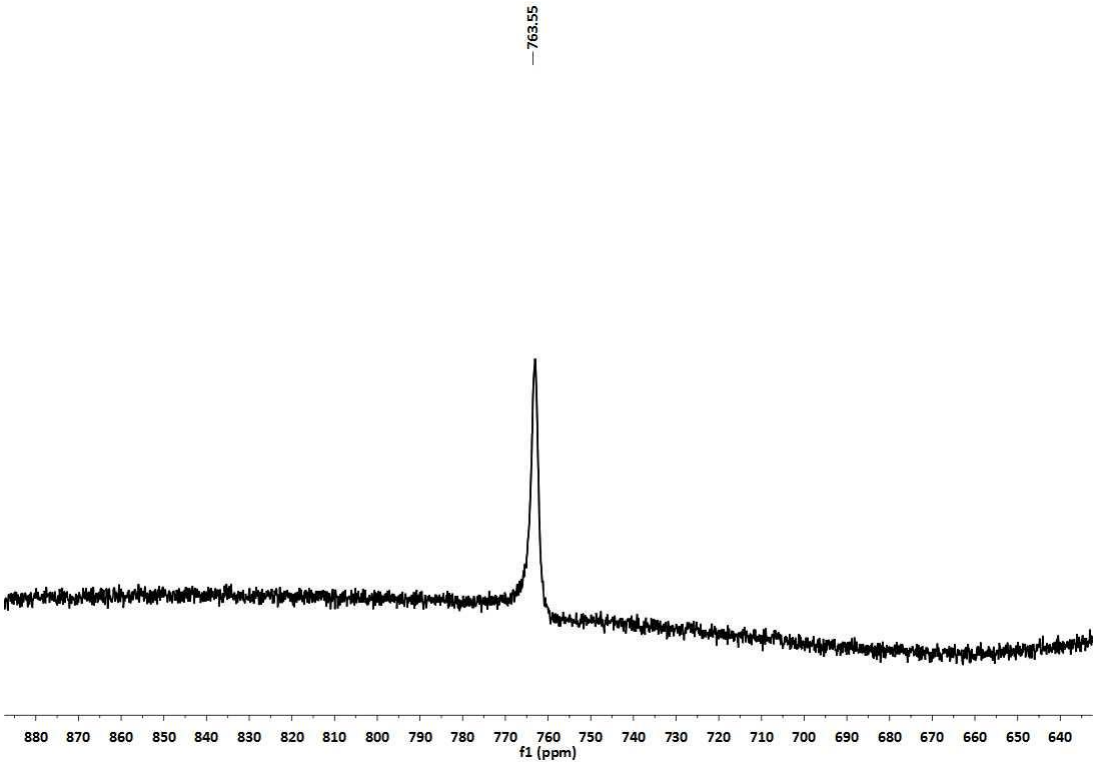

Figure S26. ^{195}Pt NMR spectrum of **7** in DMSO-d_6.

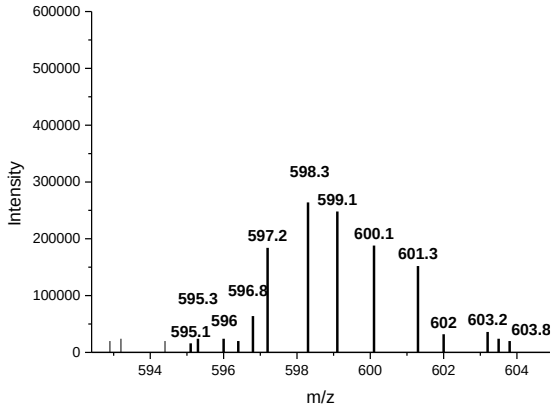

Figure S27. ESI-MS spectrum of **7**.

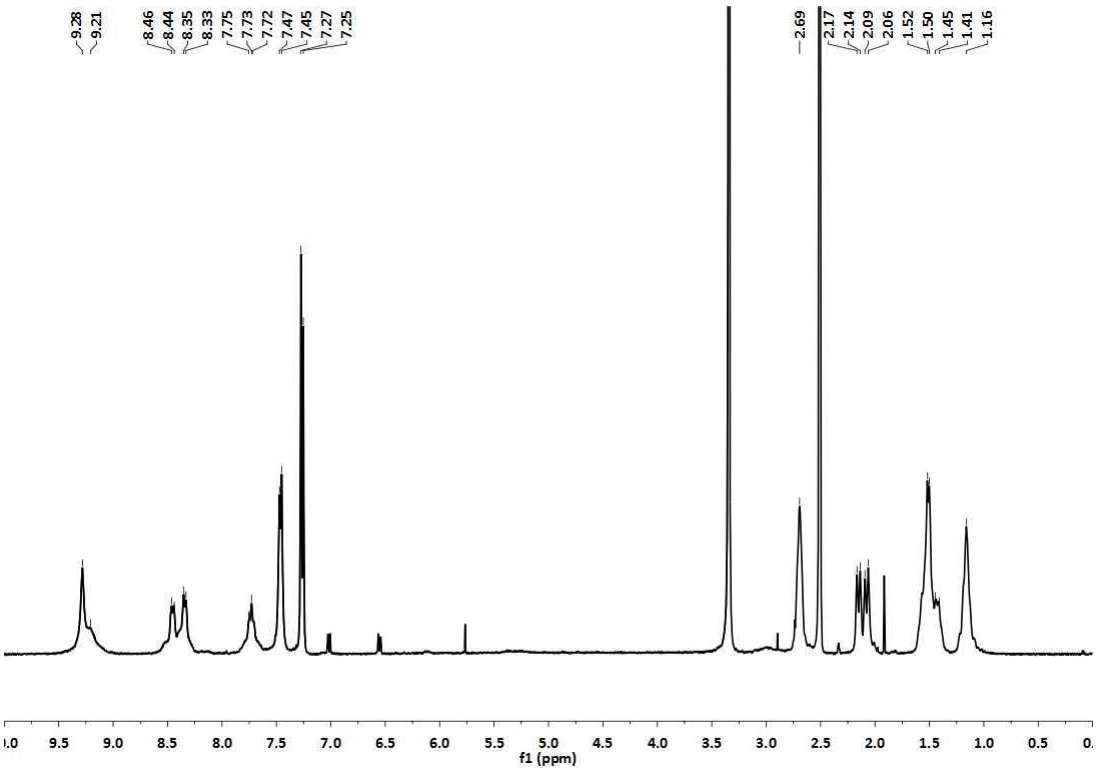

Figure S28. ^{1}H NMR spectrum of **8** in DMSO-d_6.

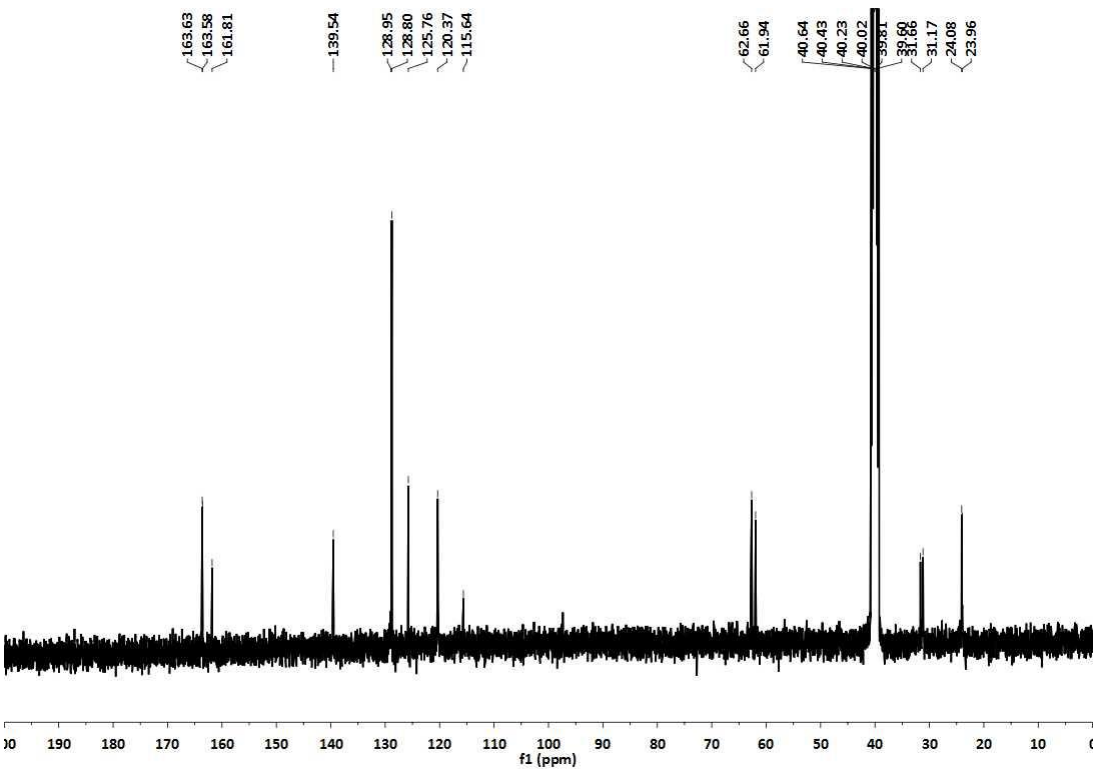

Figure S29. ^{13}C NMR spectrum of **8** in DMSO-d_6.

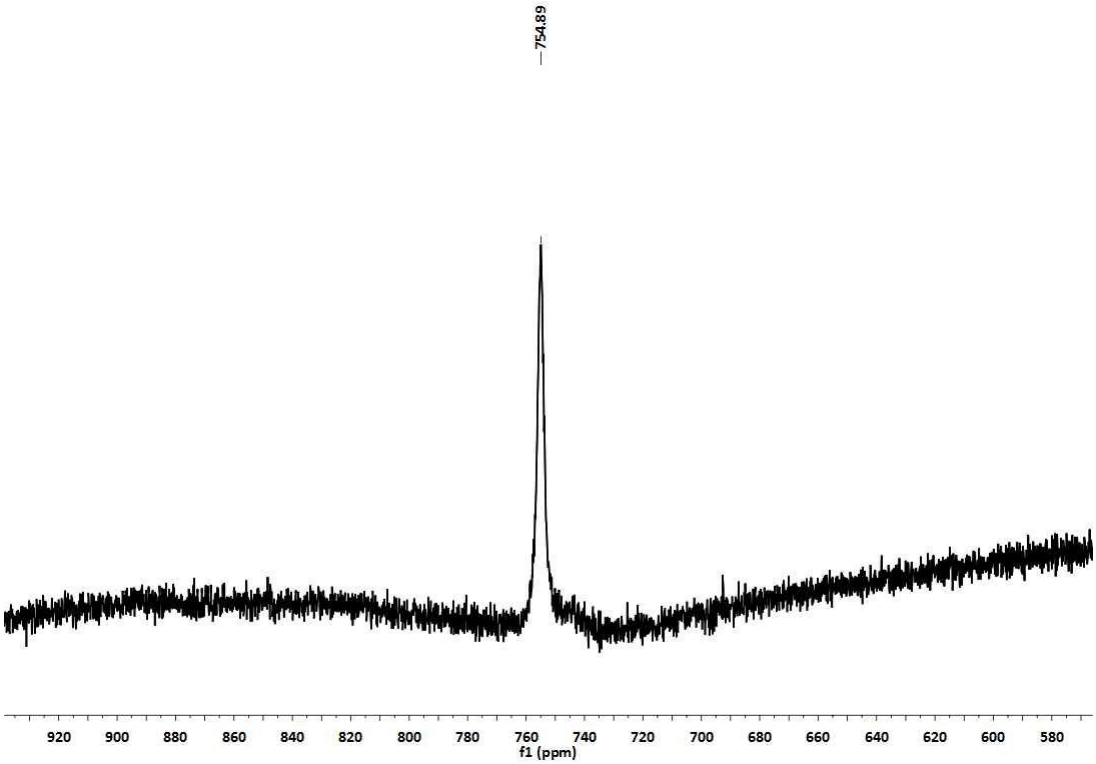

Figure S30. ^{195}Pt NMR spectrum of **8** in DMSO-d_6.

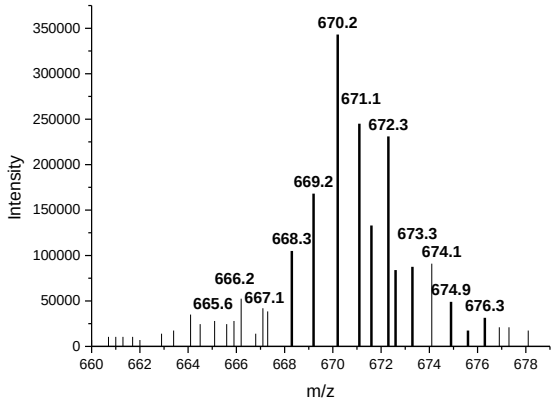

Figure S31. ESI-MS spectrum of **8**.

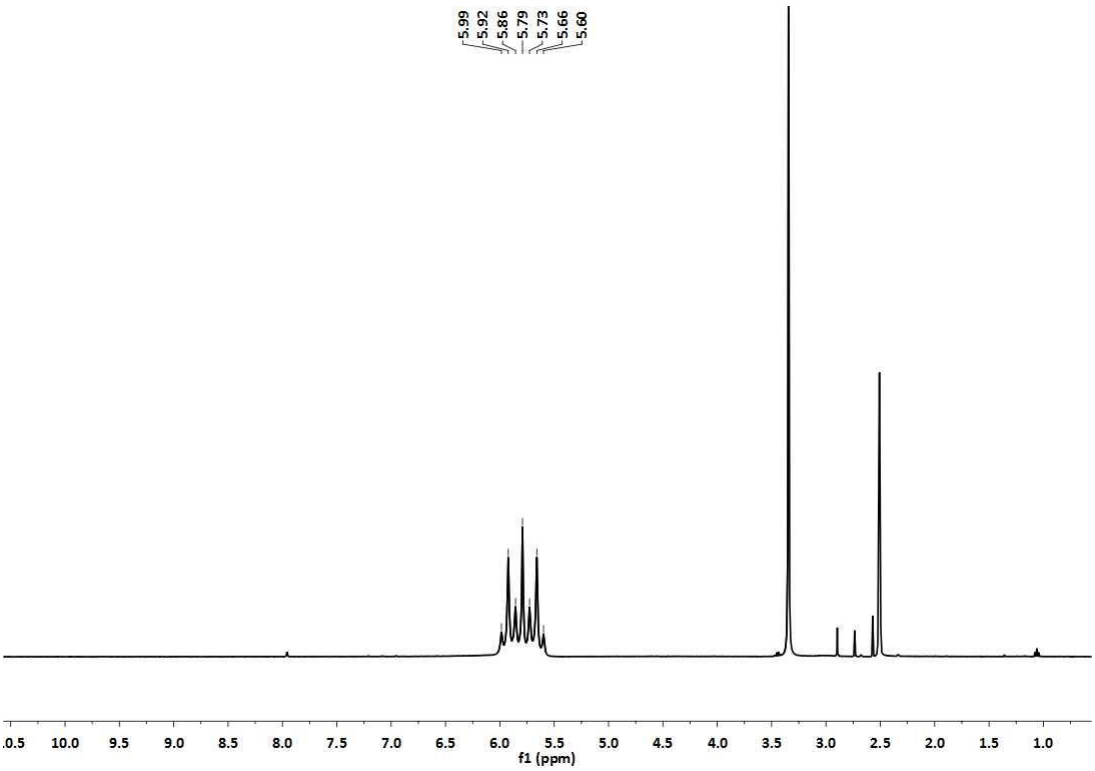

Figure S32. ^{1}H NMR spectrum of **9** in DMSO-d_6.

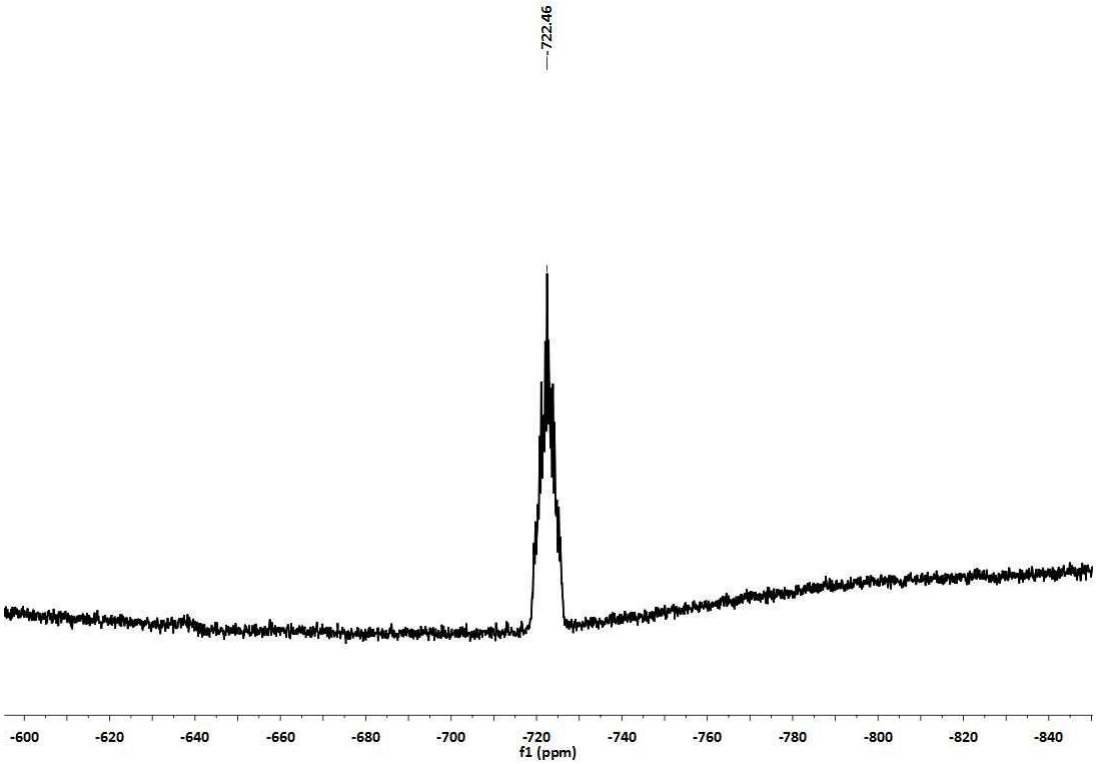

Figure S33. ^{195}Pt NMR spectrum of **9** in DMSO-d_6.

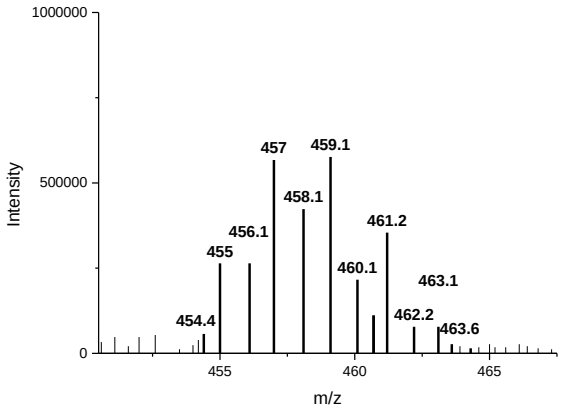

Figure S34. ESI-MS spectrum of **9**.

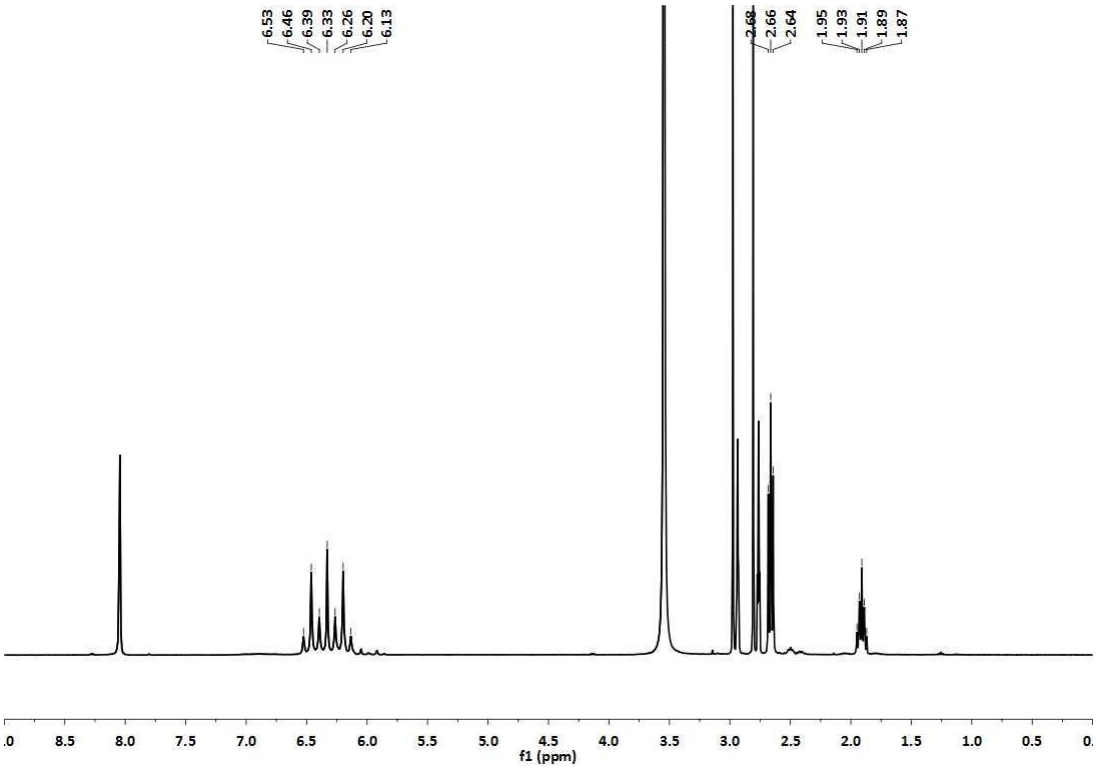

Figure S35. ^{1}H NMR spectrum of **10** in DMF-d_7.

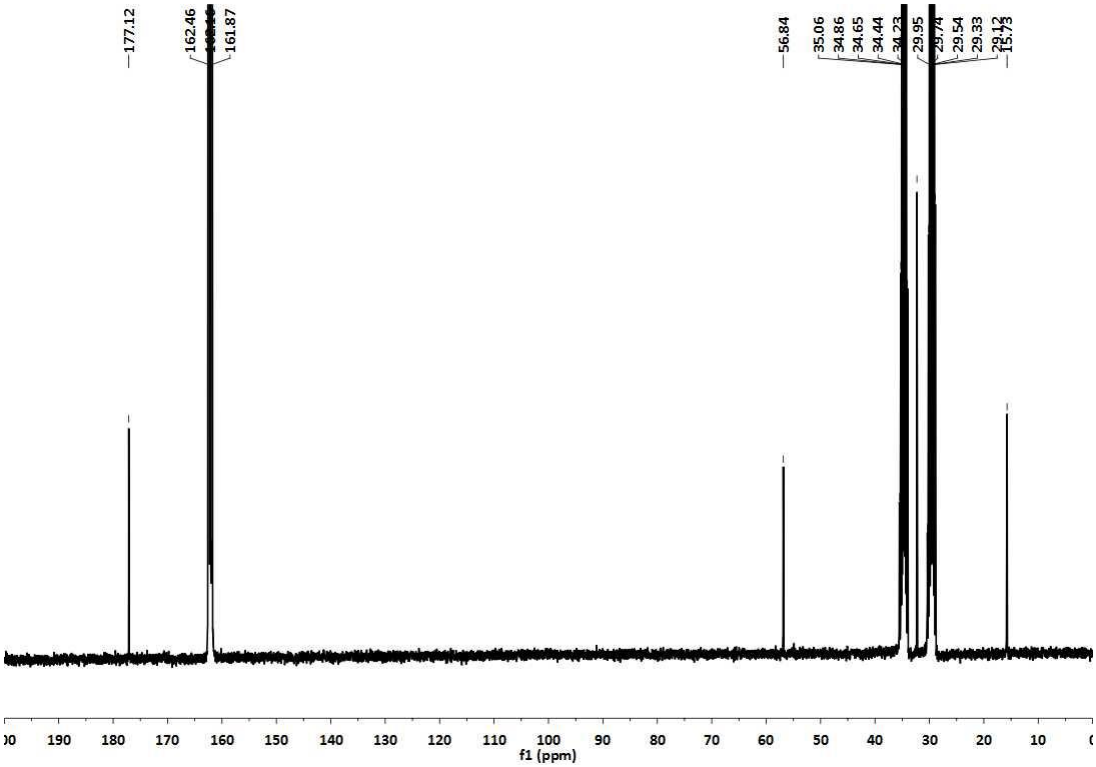

Figure S36. ^{13}C NMR spectrum of **10** in DMF-d_7.

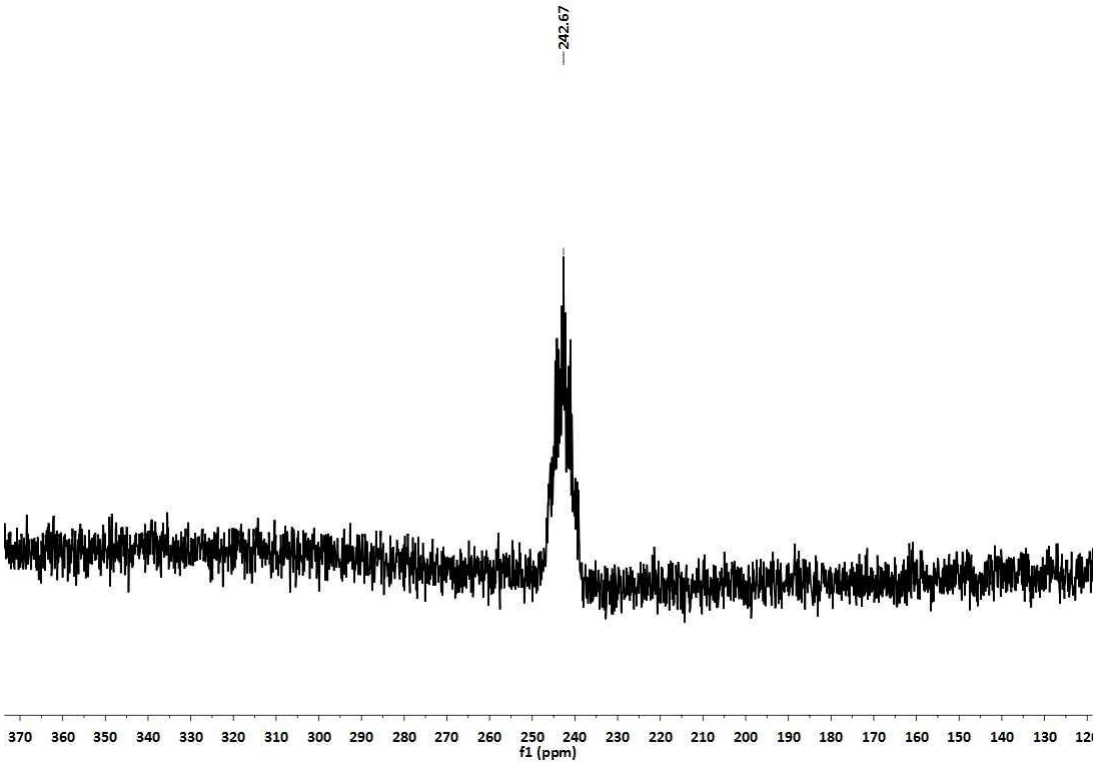

Figure S37. ^{195}Pt NMR spectrum of **10** in DMSO-d_6.

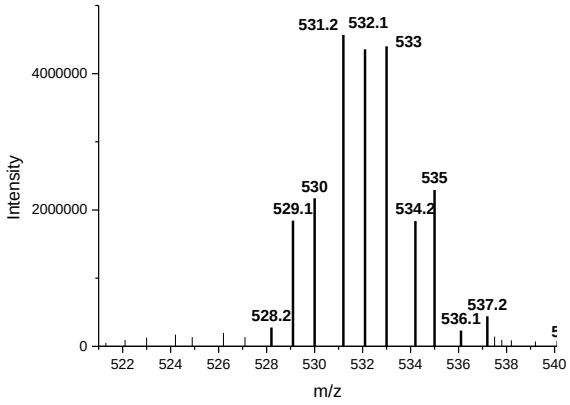

Figure S38. ESI-MS spectrum of **10**.

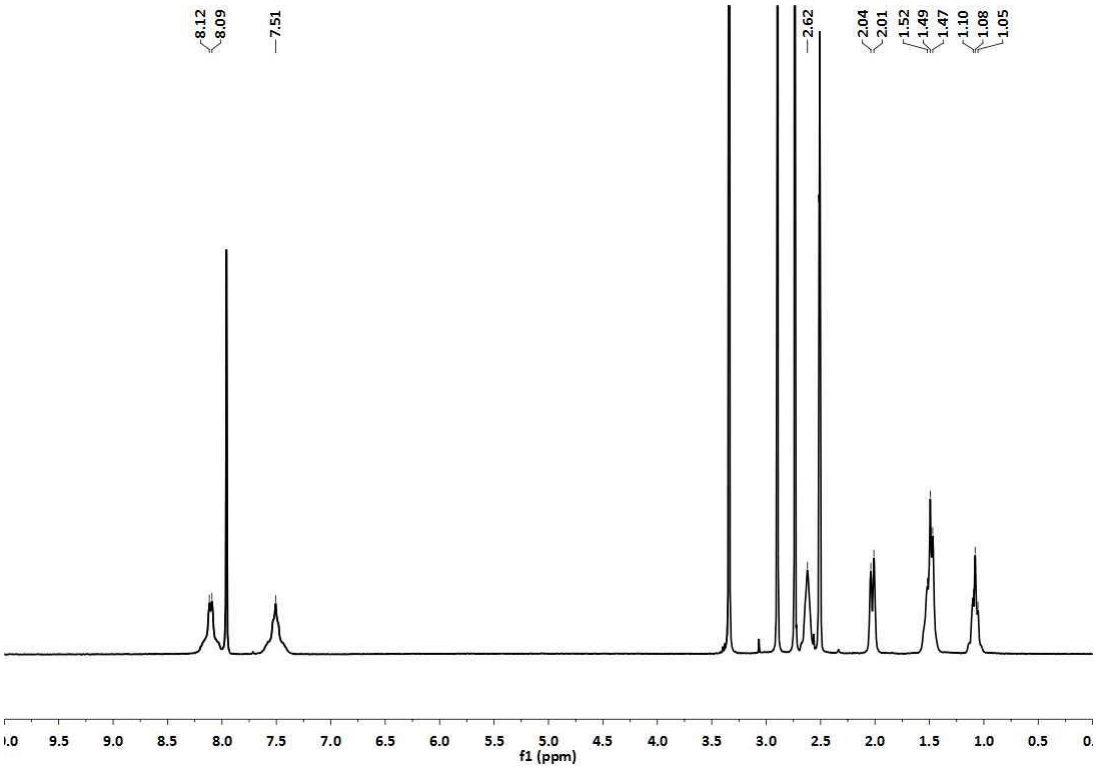

Figure S39. ^{1}H NMR spectrum of **11** in DMSO-d_6.

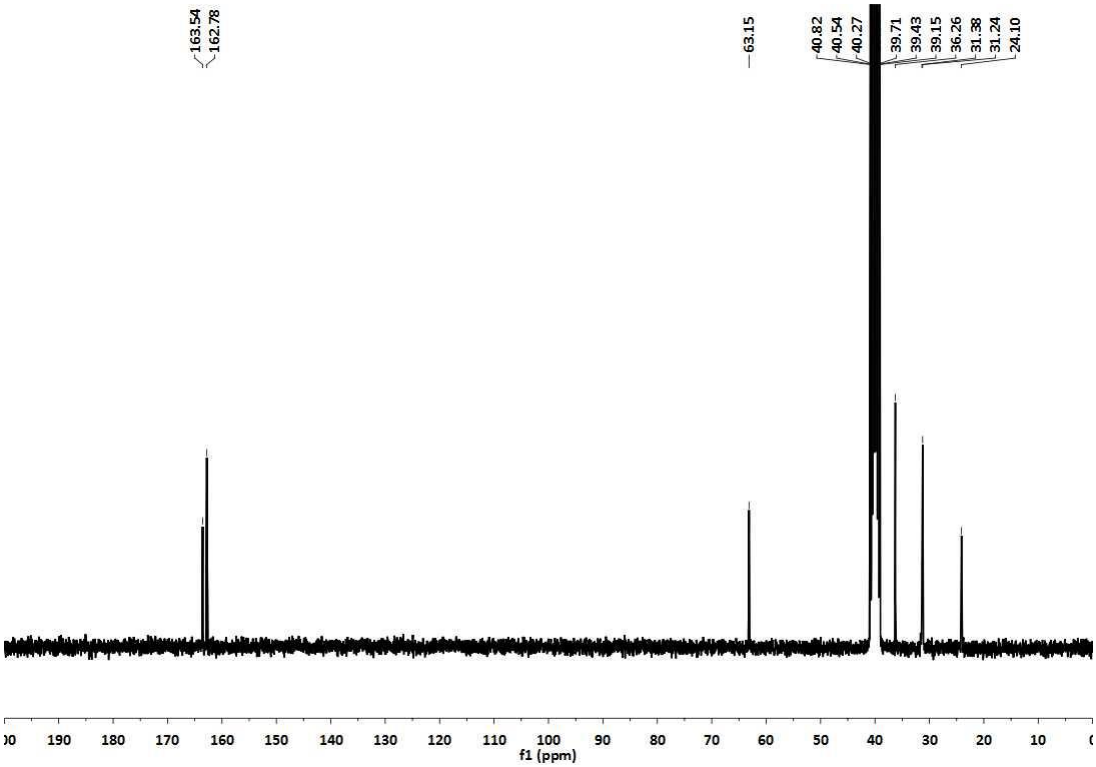

Figure S40. ^{13}C NMR spectrum of **11** in DMSO-d_6.

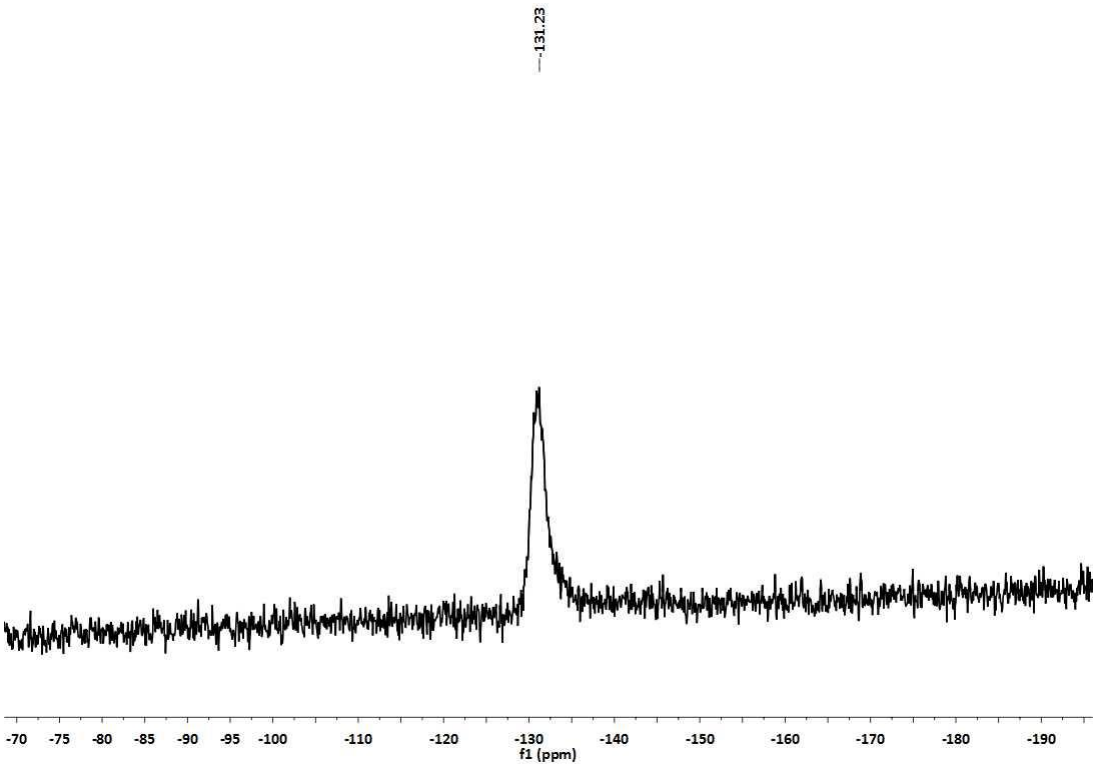

Figure S41. ^{195}Pt NMR spectrum of **11** in DMSO-d_6.

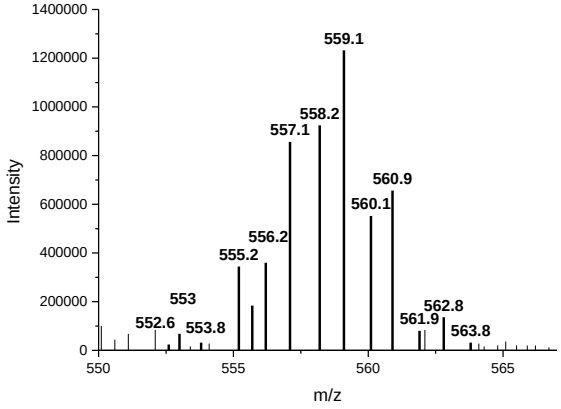

Figure S42. ESI-MS spectrum of **11**.

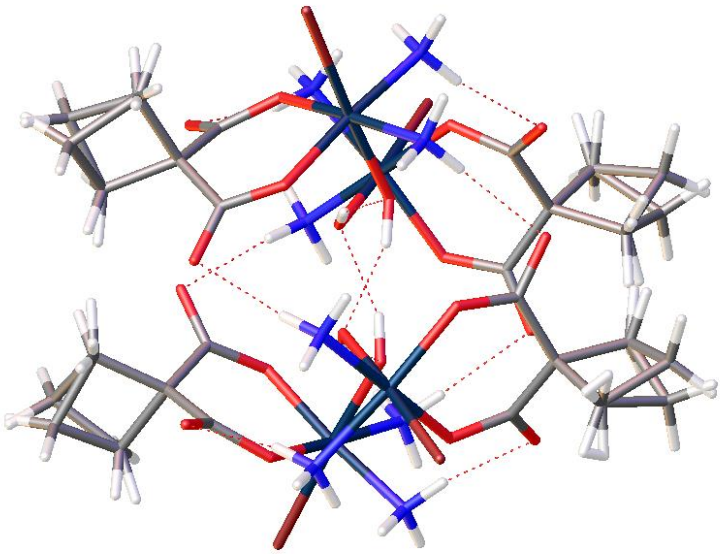

Figure S43. Packing diagram of compound **2** shows the intermolecular interactions in the crystal. The hydrogen bonds are indicated by red dot lines. DMF solvents were omitted for clarity.

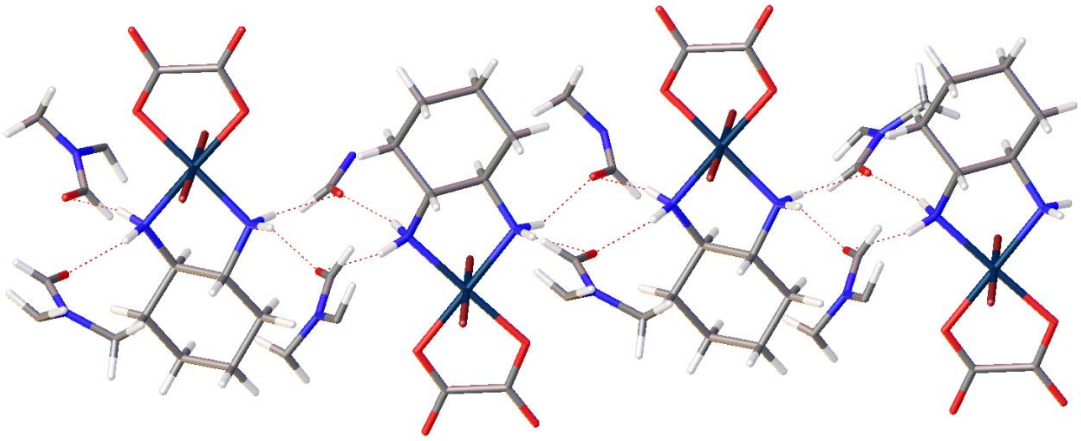

Figure S44. Packing diagram of compound **11** shows the intermolecular interactions in the crystal. The hydrogen bonds are indicated by red dot lines.

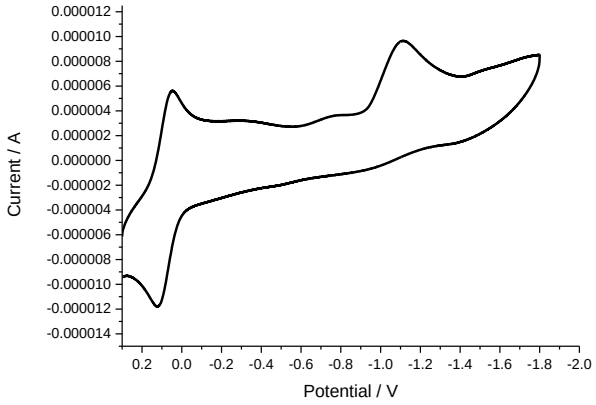

Figure S45. Cyclic voltammetry of compound **2** with ferrocene as an internal reference

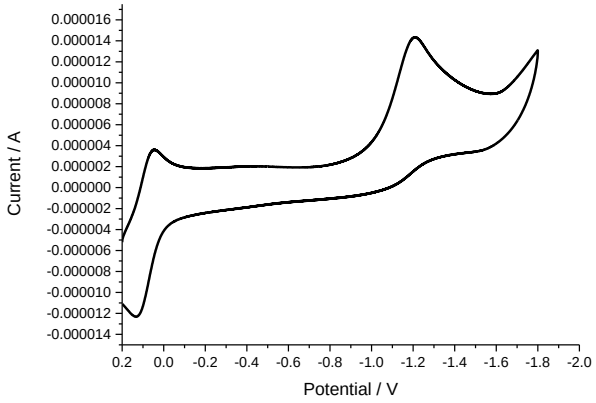

Figure S46. Cyclic voltammetry of compound **3** with ferrocene as an internal reference

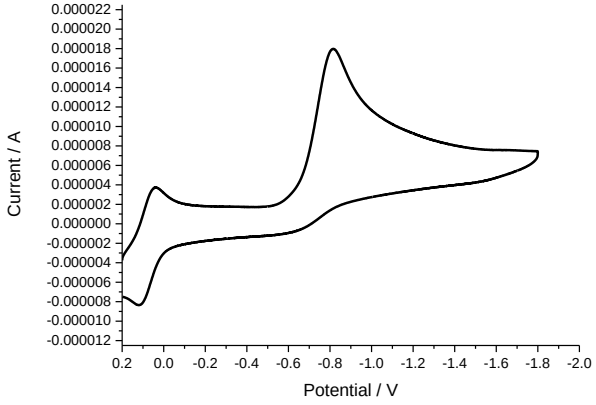

Figure S47. Cyclic voltammetry of compound **6** with ferrocene as an internal reference

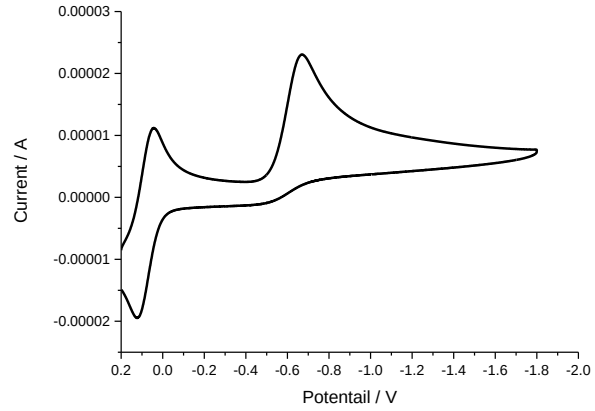

Figure S48. Cyclic voltammetry of compound **9** with ferrocene as an internal reference

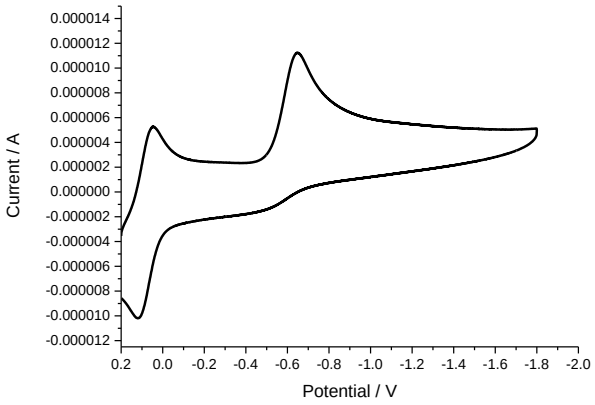

Figure S49. Cyclic voltammetry of compound **10** with ferrocene as an internal reference

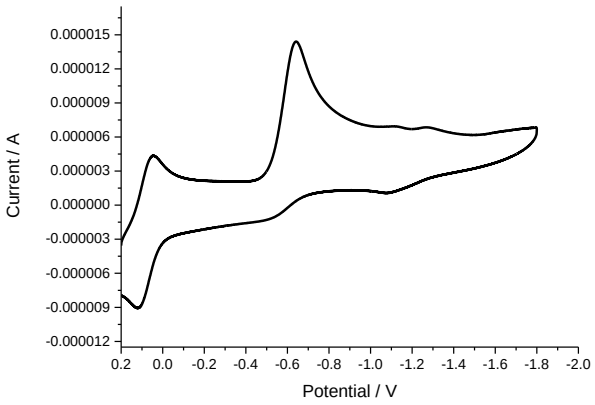

Figure S50. Cyclic voltammetry of compound **11** with ferrocene as an internal reference

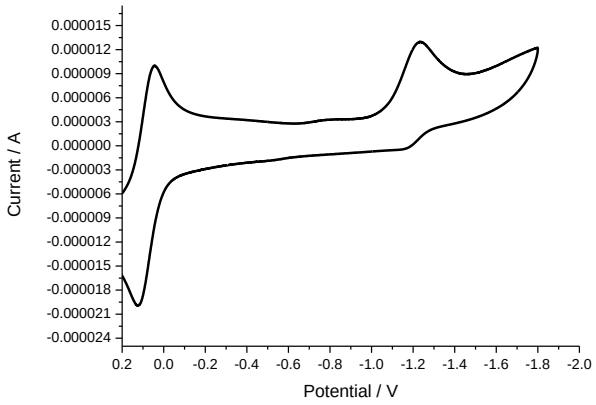

Figure S51. Cyclic voltammetry of compound **13** with ferrocene as an internal reference

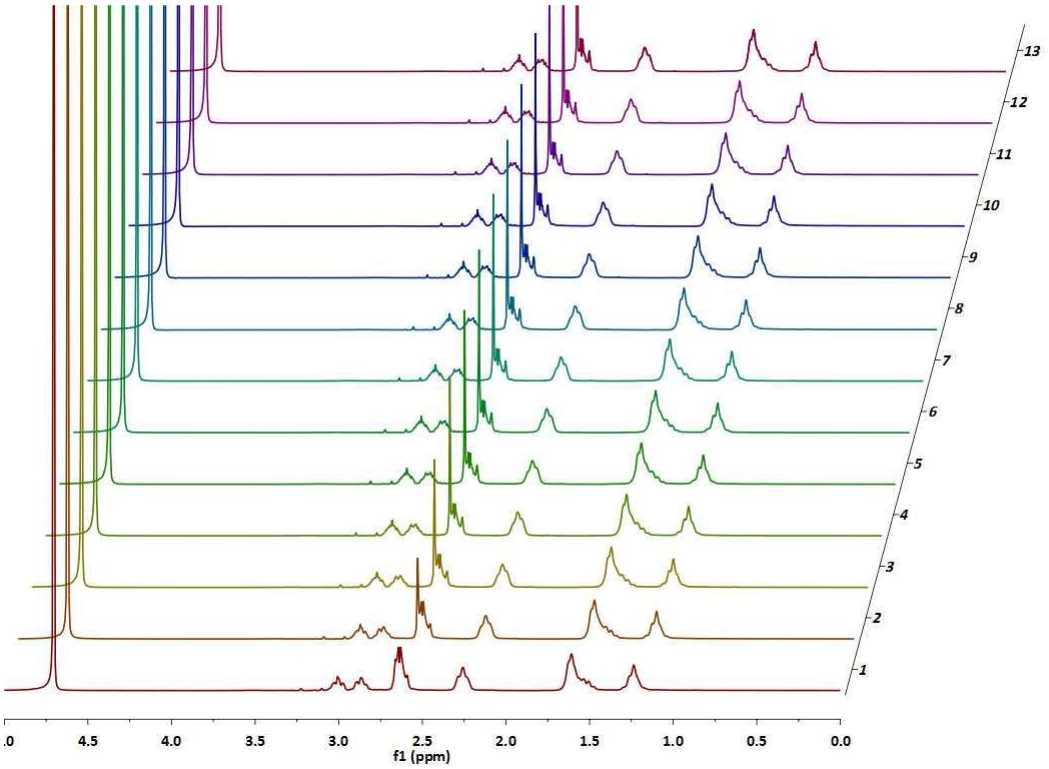

Figure S52. Hydrolysis of compound **6** in D_2O. Compound **6** was dissolved in D_2O and its stability was monitored by ^1H NMR every 30 min.

Table S1. Crystal data and structure refinement for compounds **2** and **11**

Identification code	**2**	**11**
Empirical formula	$C_9H_{20}BrN_3O_6Pt$	$C_{14}H_{28}Br_2N_4O_6Pt$
Formula weight	541.28	703.28
Temperature/K	193(2)	193(2)
Crystal system	tetragonal	orthorhombic
Space group	$I4_1/amd$	$P2_12_12_1$
a/Å	16.87350(10)	9.9096(3)
b/Å	16.87350(10)	13.3318(4)
c/Å	24.1091(2)	17.2606(6)
α/°	90	90
β/°	90	90
γ/°	90	90
Volume/Å^3	6864.22(8)	2280.35(13)
Z	16	4
ρ_{calc}g/cm^3	2.095	2.049
μ/mm^{-1}	18.266	15.926
F(000)	4096	1344
Crystal size/mm^3	0.36 × 0.25 × 0.19	0.24 × 0.21 × 0.02
Radiation	CuKα (λ = 1.54178)	CuKα (λ = 1.54178)
2Θ range for data collection/°	6.4 to 143.38	8.38 to 134
Index ranges	-20 ≤ h ≤ 19, -17 ≤ k ≤ 14, -29 ≤ l ≤ 26	-11 ≤ h ≤ 11, -15 ≤ k ≤ 15, -20 ≤ l ≤ 15
Reflections collected	6681	11661
Independent reflections	1769 [R_{int} = 0.0212]	3873 [R_{int} = 0.0598]
Data/restraints/parameters	1769/16/131	3873/24/268
Goodness-of-fit on F^2	1.158	1.069
Final R indexes [I>=2σ (I)]	R_1 = 0.0365, wR_2 = 0.1124	R_1 = 0.0336, wR_2 = 0.0894
Final R indexes [all data]	R_1 = 0.0384, wR_2 = 0.1144	R_1 = 0.0352, wR_2 = 0.0908
Largest diff. peak/hole / e Å^{-3}	1.08/-1.48	1.52/-1.35

Table S2. Selected bond lengths (A˚) and angles (°) for compound **2**

Bond lengths		**Bond angles**	
Pt-Br1	2.4675(12)	O3-Pt-O1	87.2(6)
Pt-O1	1.988(5)	O3-Pt-N1	85.5(8)
Pt-O2	2.014(17)	O1-Pt-N1	83.3(6)
Pt-O3	1.986(18)	O3-Pt-O2	95.5(3)
Pt-N1	2.005(17)	O1-Pt-O2	89.1(6)
Pt-N2	2.037(16)	N1-Pt-O2	172.3(8)
		O3-PtN-2	177.1(8)
		O1-Pt-N2	91.0(6)
		N1-Pt-N2	92.1(6)
		O2-Pt-N2	86.7(8)
		O3-Pt-Br1	92.1(6)
		O1-Pt-Br1	175.91(12)
		N1-Pt-Br1	92.6(6)
		O2-Pt-Br1	95.0(6)
		N2-Pt-Br1	89.6(6)

Tables S3. Selected bond lengths (A˚) and angles (°) for compound **11**

Bond lengths		**Bond angles**	
Pt-Br1	2.4590(6)	N2-Pt-O2	95.4(2)
Pt-Br2	2.4415(6)	N2-Pt-N1	83.42(18)
Pt-O1	2.050(6)	O2-Pt-N1	178.7(2)
Pt-O2	2.044(6)	N2-Pt-O1	179.0(2)
Pt-N1	2.050(5)	O2-Pt-O1	84.8(2)
Pt-N2	2.033(5)	N1-Pt-O1	96.4(3)
		N2-Pt-Br2	88.78(16)
		O2-Pt-Br2	89.04(17)
		N1-Pt-Br2	91.60(16)
		O1-Pt-Br2	90.28(17)
		N2-Pt-Br1	92.33(15)
		O2-Pt-Br1	90.21(17)
		N1-Pt-Br1	89.18(16)
		O1-Pt-Br1	88.61(17)
		Br2-Pt-Br1	178.71(2)