Supplementary Materials

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NMR spectra of precursor platinum(II) complexes

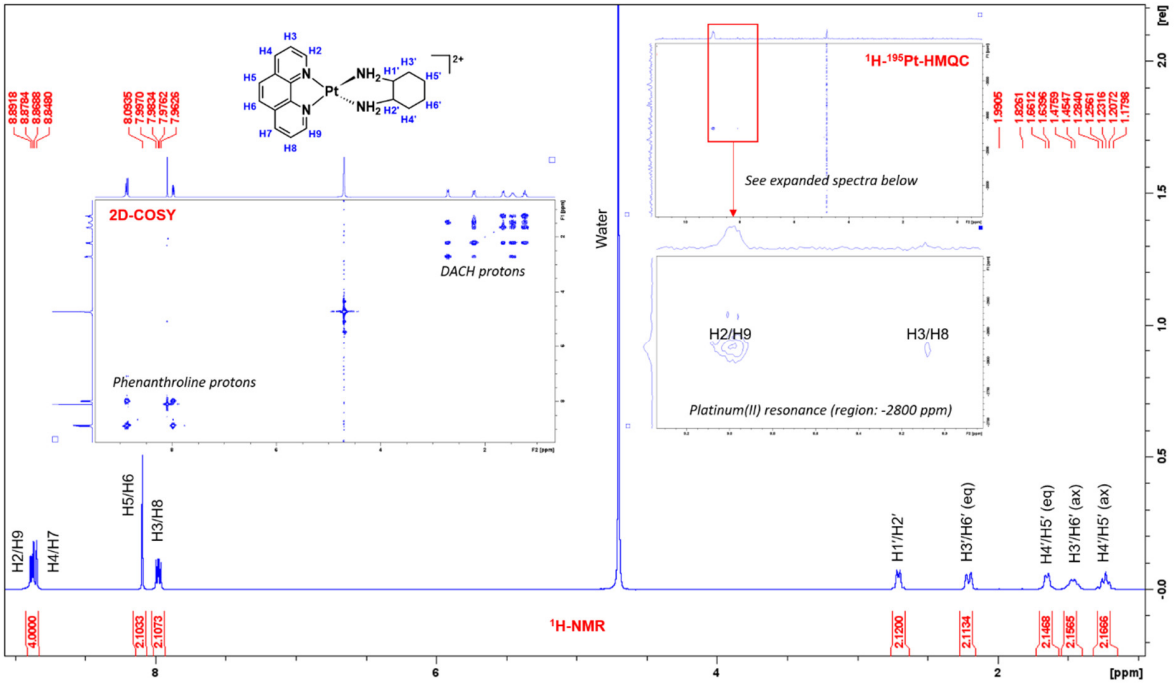

Figure S1: ^{1}H-NMR, 2D-COSY and ^{1}H-^{195}Pt-HMQC spectra of **PHEN*SS*** in D_2O obtained at 298 K. Inset: structure of **PHEN*SS*** with proton labeling system.

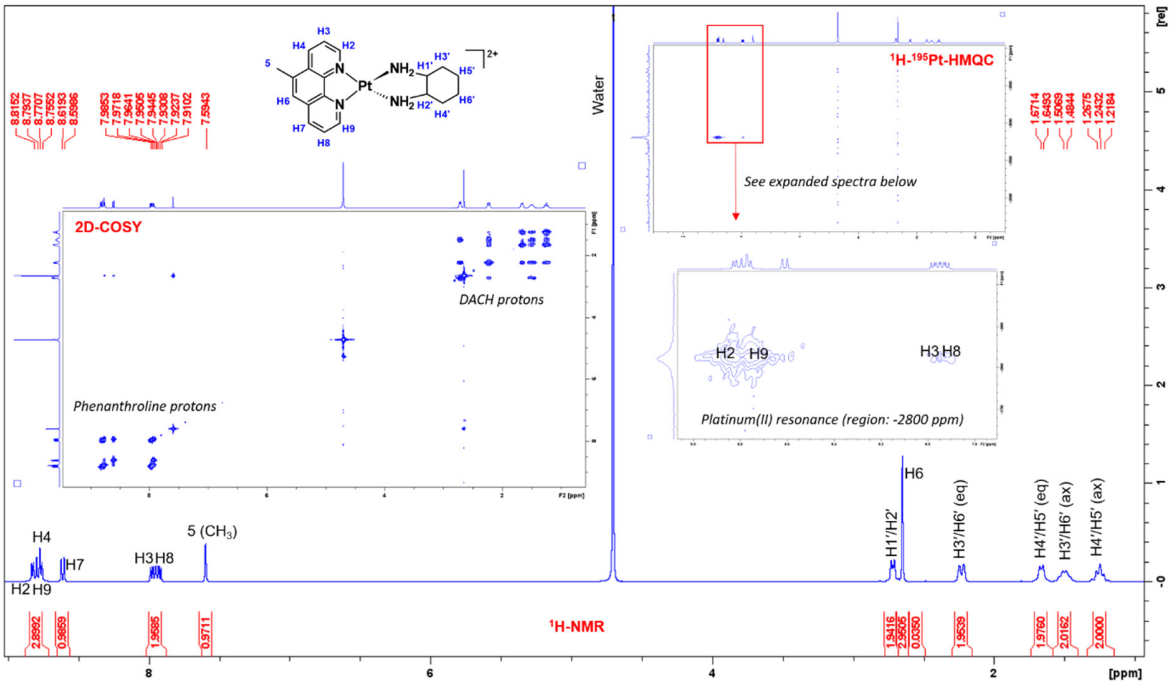

Figure S2: ^{1}H-NMR, 2D-COSY and ^{1}H-^{195}Pt-HMQC spectra of **5MESS** in D_2O obtained at 298 K. Inset: structure of **5MESS** with proton labeling system.

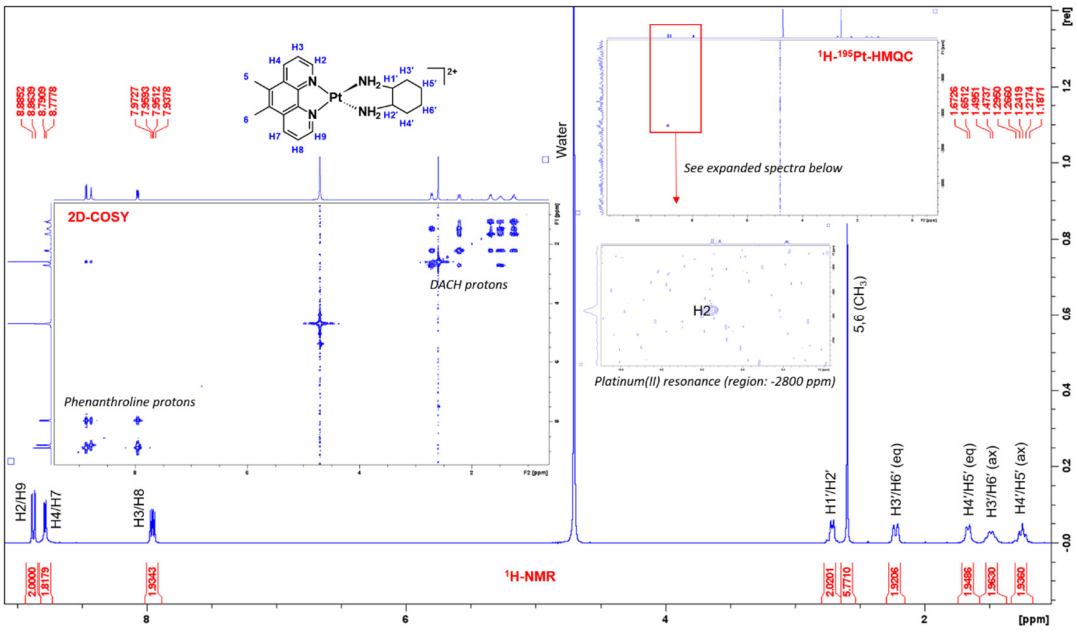

Figure S3: ^{1}H-NMR, 2D-COSY and ^{1}H-^{195}Pt-HMQC spectra of **56MESS** in D_2O obtained at 298 K. Inset: structure of **56MESS** with proton labeling system.

NMR spectra of precursor platinum(IV) dihydroxy complexes

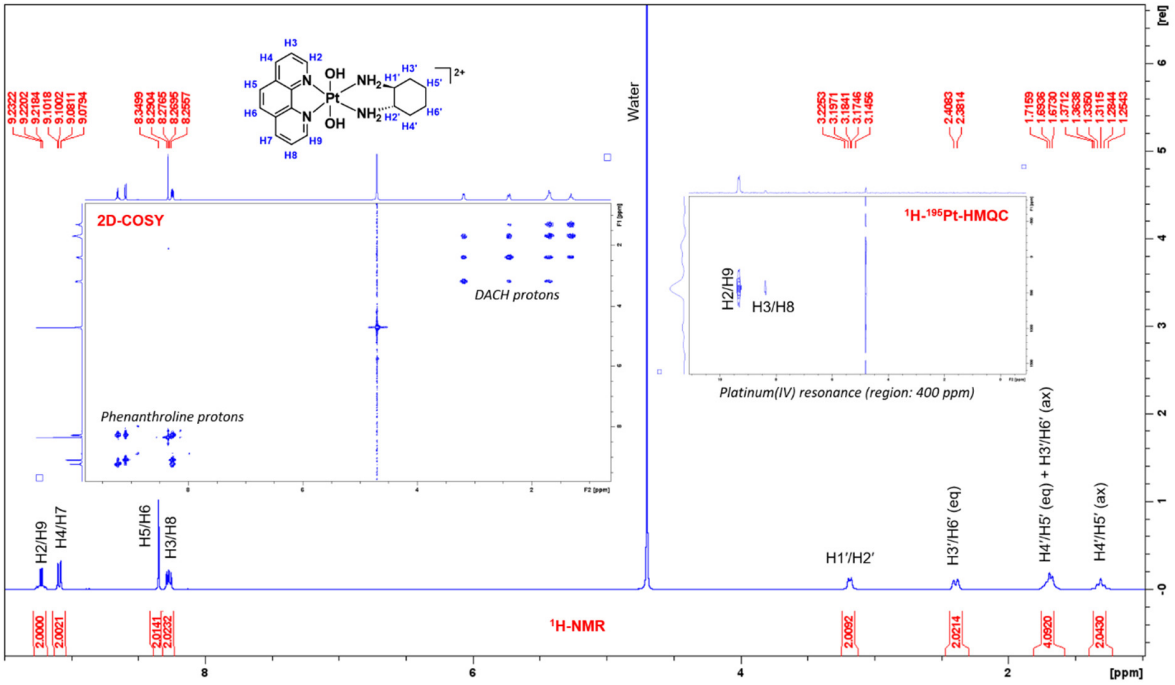

Figure S4: ^{1}H-NMR, 2D-COSY and ^{1}H-^{195}Pt-HMQC spectra of **PHEN*SS*(IV)(OH)$_2$** in D_2O obtained at 298 K. Inset: structure of **PHEN*SS*(IV)(OH)$_2$** with proton labeling system.

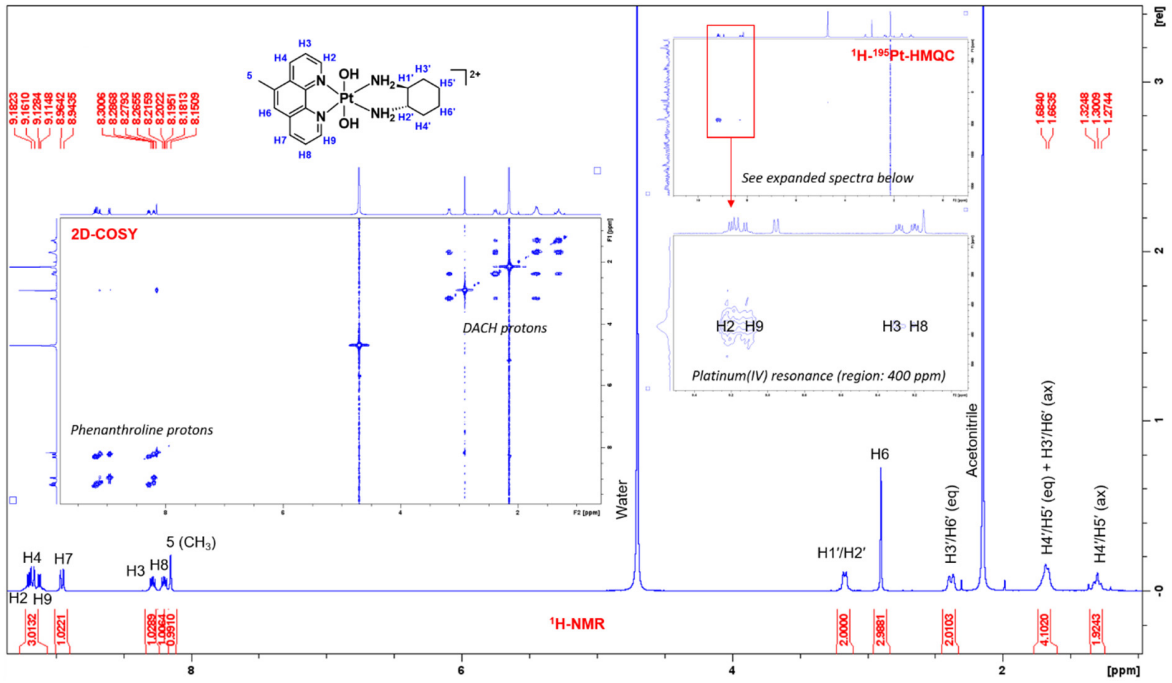

Figure S5: ^{1}H-NMR, 2D-COSY and ^{1}H-^{195}Pt-HMQC spectra of **5MES*S*(IV)(OH)$_2$** in D_2O obtained at 298 K. Inset: structure of **5MES*S*(IV)(OH)$_2$** with proton labeling system.

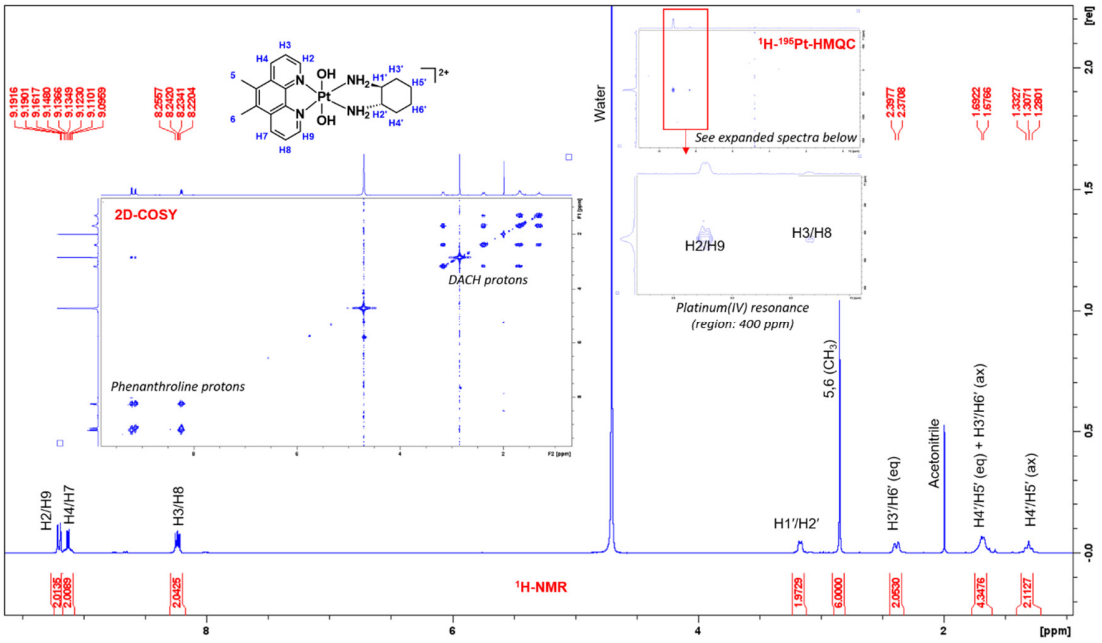

Figure S6: ^{1}H-NMR, 2D-COSY and ^{1}H-^{195}Pt-HMQC spectra of **56MES*S*(IV)(OH)$_2$** in D_2O obtained at 298 K. Inset: structure of **56MES*S*(IV)(OH)$_2$** with proton labeling system.

HPLC chromatogram of CLB anhydride

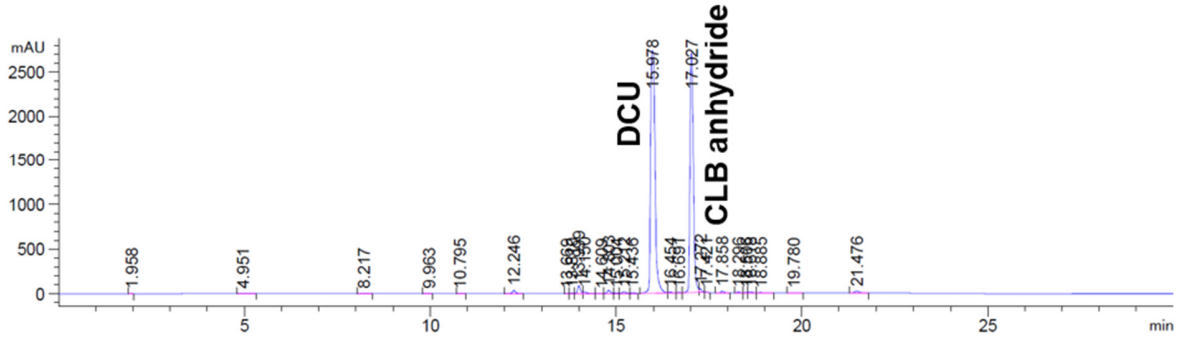

Figure S7: HPLC chromatogram of CLB anhydride (at 17 min) with DCU by-product (at 15.9 min), within the collection wavelength of 254 nm obtained at 298 K, by an Agilent ZORBAX RX-C_{18} column (100 × 4.6 mm, 3.5 µm pore size).

HPLC chromatograms of platinum(IV)-CLB complexes

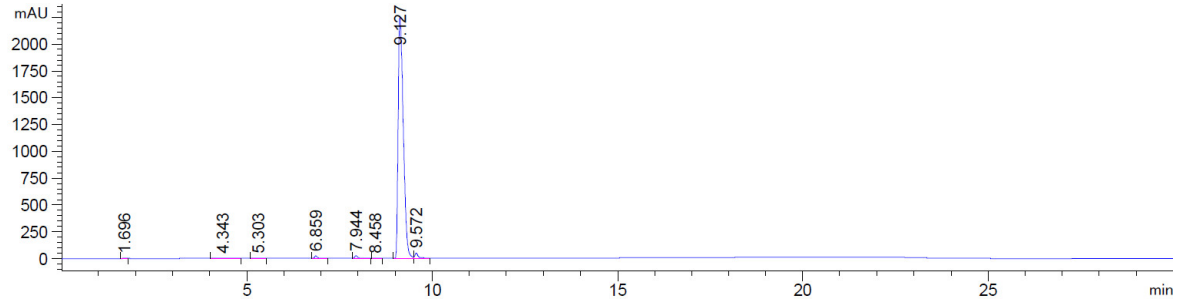

Figure S8: HPLC chromatogram of **PCLB** within the collection wavelength of 254 nm obtained at 298 K, by a Phenomenex Onyx™ Monolithic C_{18}-reverse phase column (100 × 4.6 mm, 5 µm pore size).

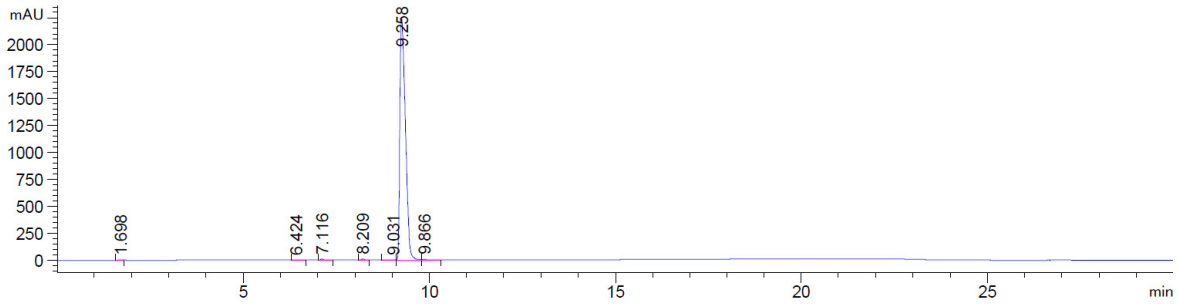

Figure S9: HPLC chromatogram of **5CLB** within the collection wavelength of 254 nm obtained at 298 K, by a Phenomenex Onyx™ Monolithic C_{18}-reverse phase column (100 × 4.6 mm, 5 μm pore size).

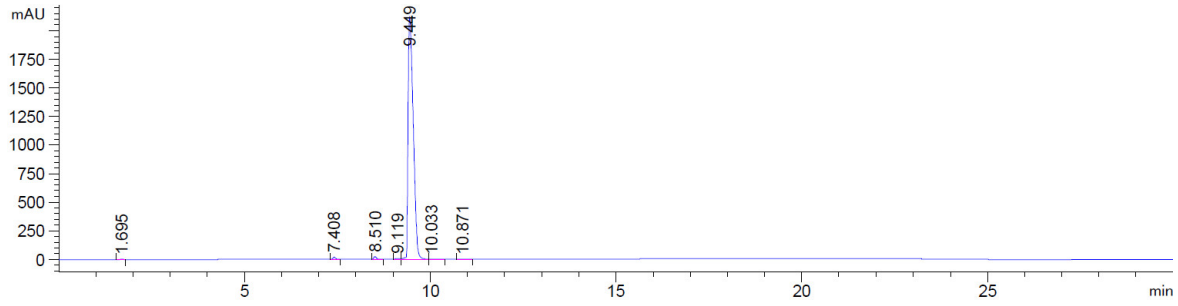

Figure S10: HPLC chromatogram of **56CLB** within the collection wavelength of 254 nm obtained at 298 K, by a Phenomenex Onyx™ Monolithic C_{18}-reverse phase column (100 × 4.6 mm, 5 μm pore size).

NMR spectra of platinum(IV)-CLB complexes

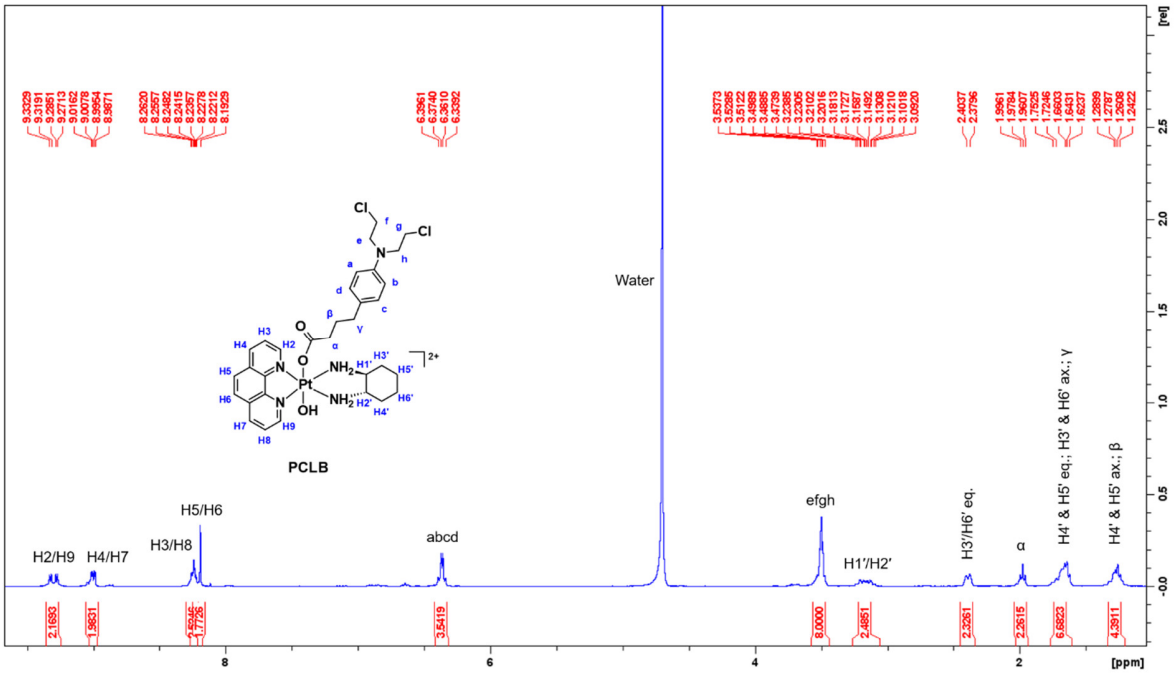

Figure S11: ^{1}H-NMR spectrum of **PCLB** in D_2O obtained at 298 K. Inset: structure of **PCLB** with proton labeling system.

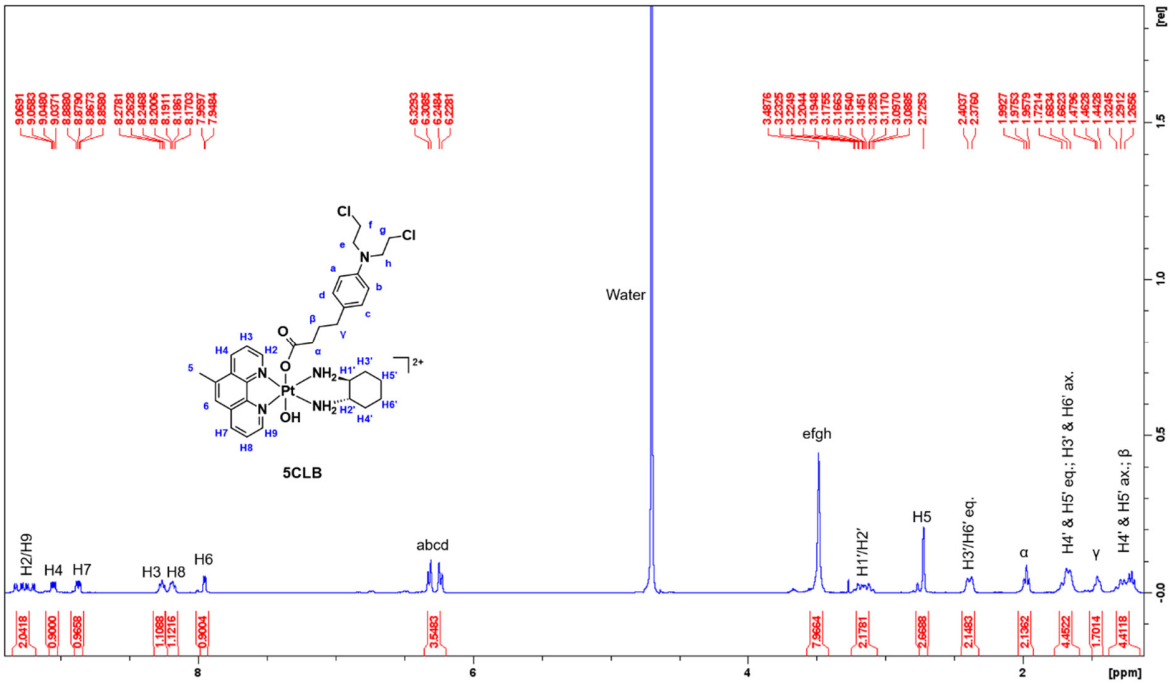

Figure S12: ^{1}H-NMR spectrum of **5CLB** in D_2O obtained at 298 K. Inset: structure of **5CLB** with proton labeling system.

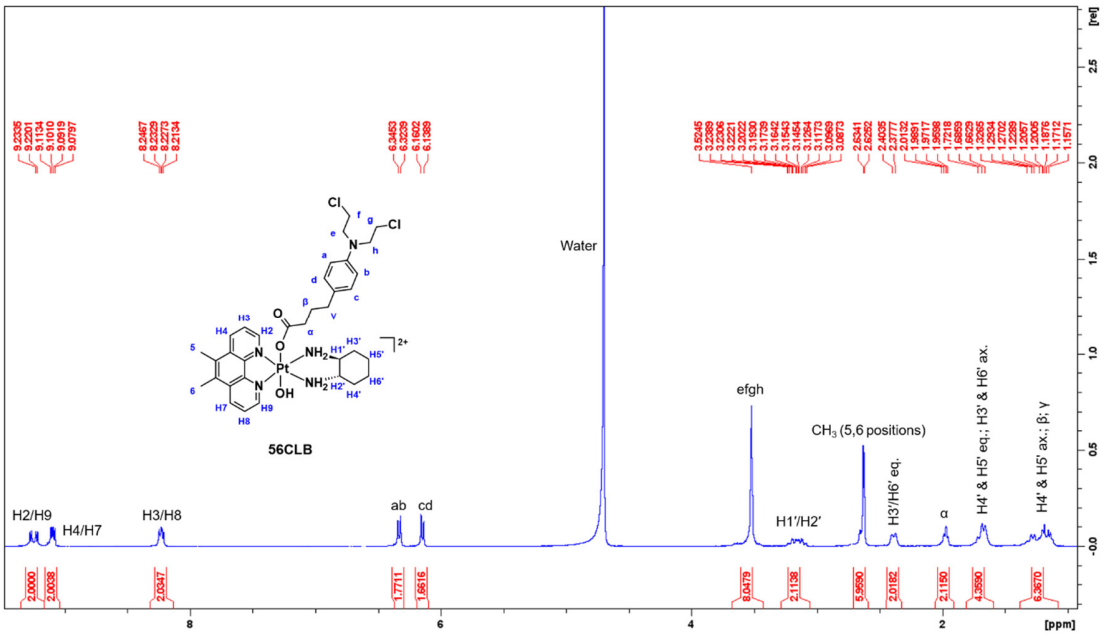

Figure S13: ^{1}H-NMR spectrum of **56CLB** in D_2O obtained at 298 K. Inset: structure of **56CLB** with proton labeling system.

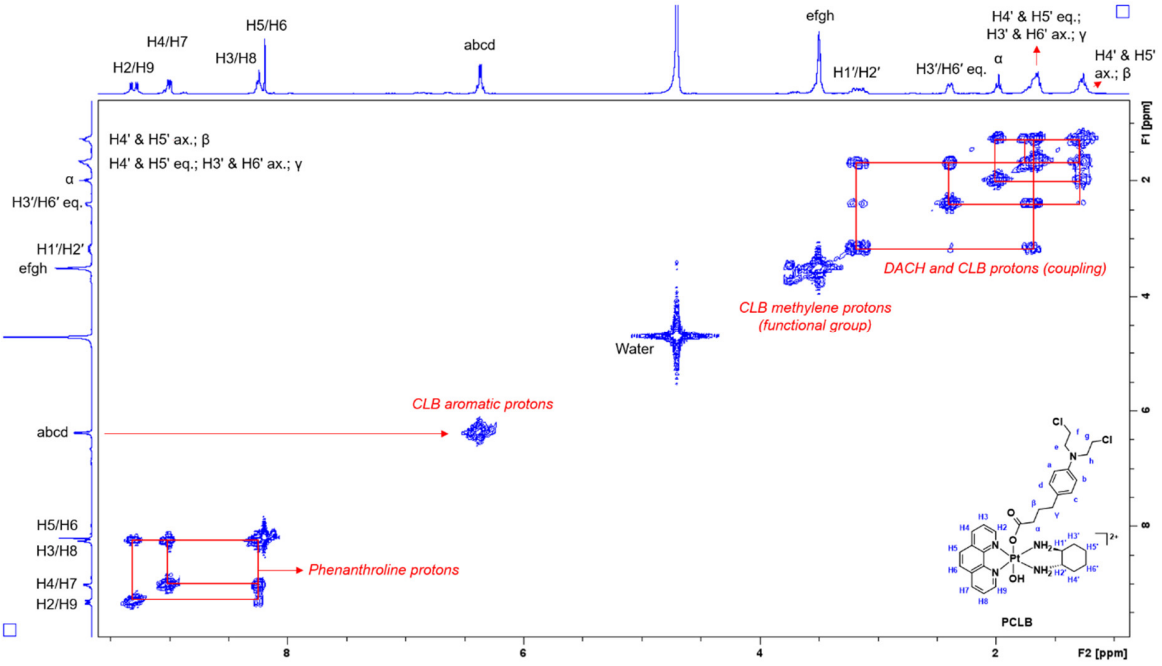

Figure S14: 2D-COSY spectrum of **PCLB** in D_2O obtained at 298 K. Inset: structure of **PCLB** with proton labeling system.

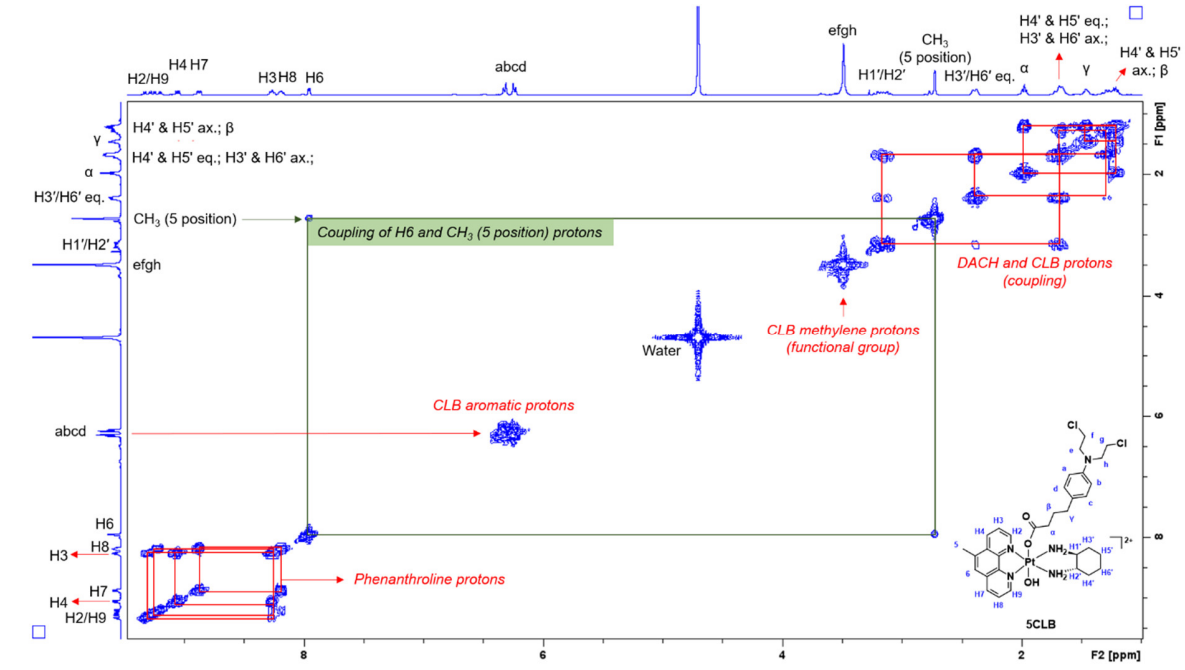

Figure S15: 2D-COSY spectrum of **5CLB** in D_2O obtained at 298 K. Inset: structure of **5CLB** with proton labeling system.

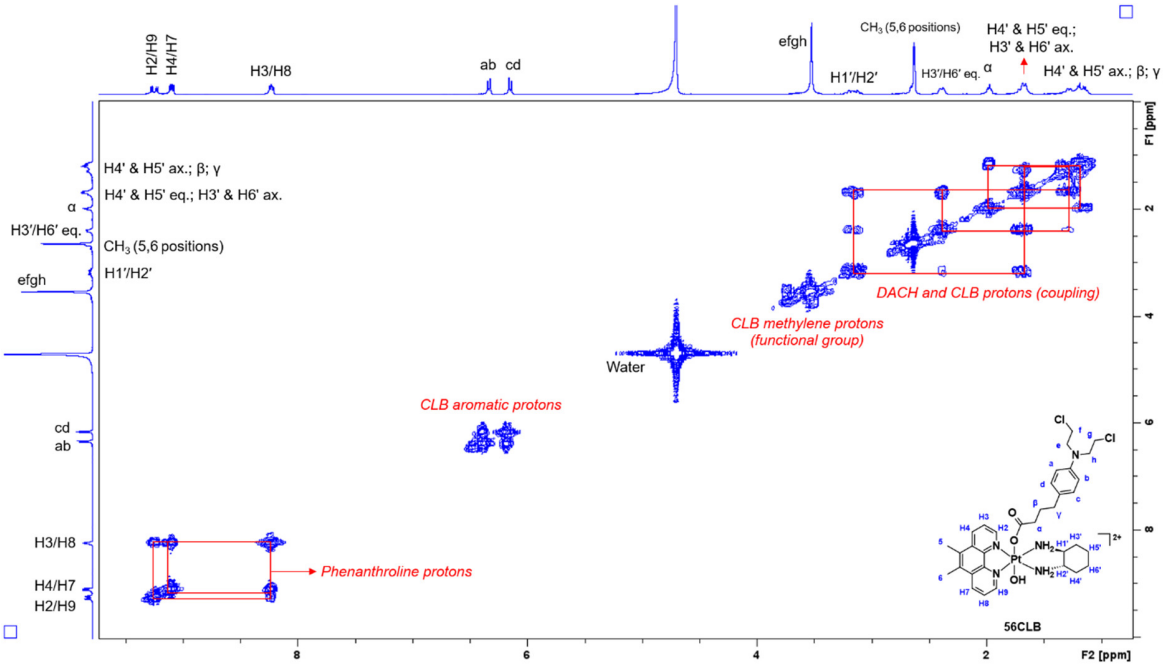

Figure S16: 2D-COSY spectrum of **56CLB** in D_2O obtained at 298 K. Inset: structure of **56CLB** with proton labeling system.

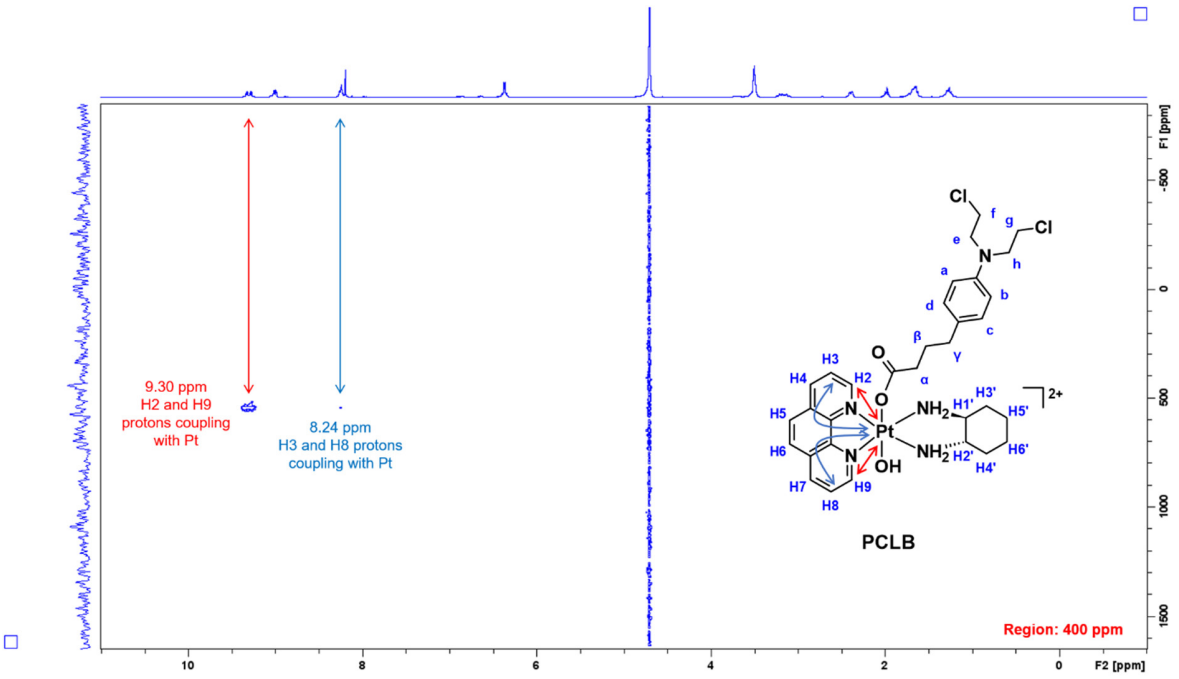

Figure S17: ^{1}H-^{195}Pt-HMQC spectrum of **PCLB** in D_2O obtained at 298 K. Region: 400 ppm. Inset: structure of **PCLB** with proton labelling system and arrows that indicate coupling.

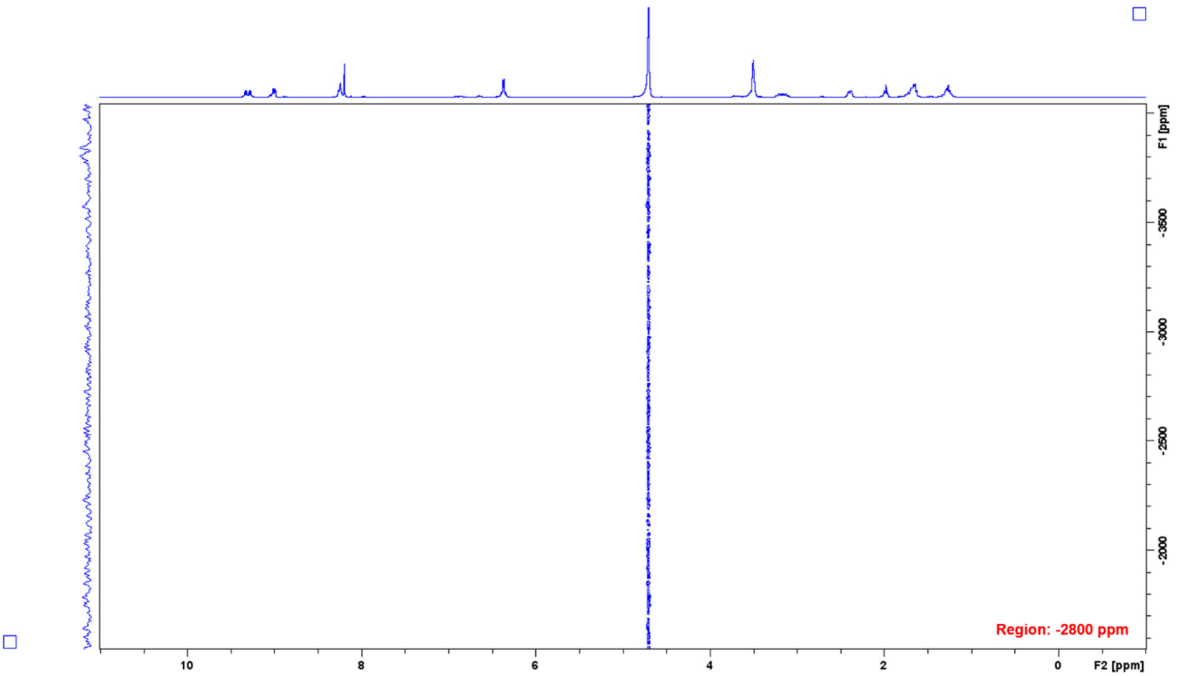

Figure S18: ^{1}H-^{195}Pt-HMQC spectrum of **PCLB** in D_2O obtained at 298 K. Region: -2800 ppm. Absence of platinum(II) resonance.

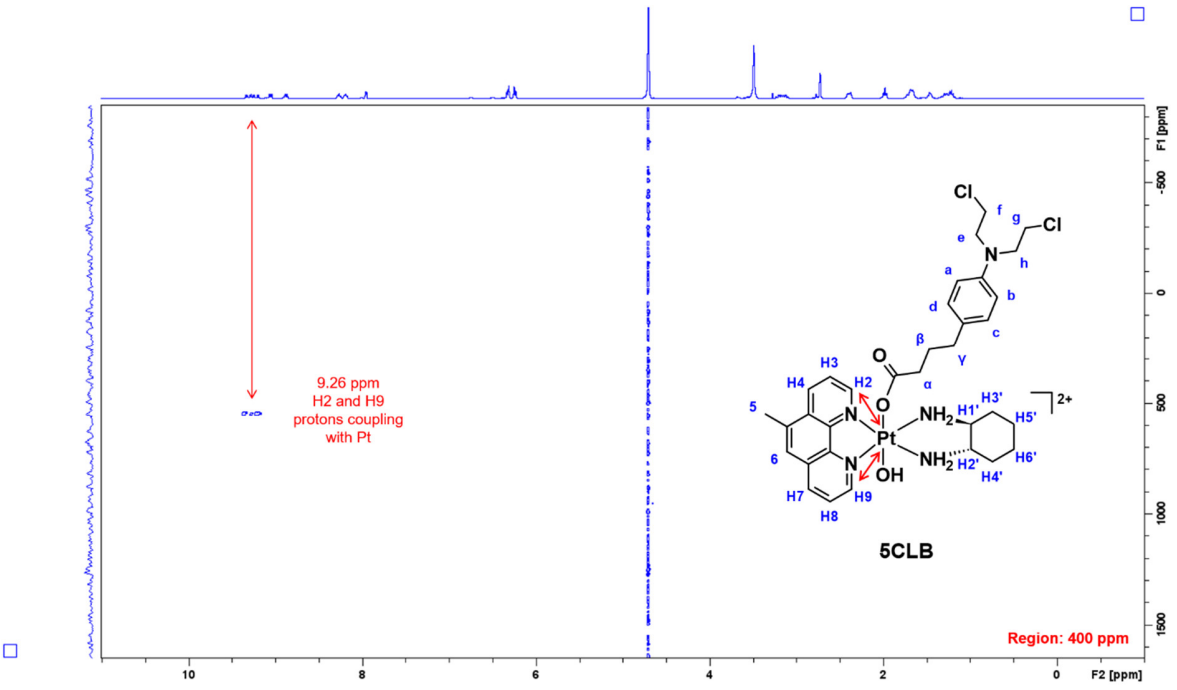

Figure S19: ^{1}H-^{195}Pt-HMQC spectrum of **5CLB** in D_2O obtained at 298 K. Region: 400 ppm. Inset: structure of **5CLB** with proton labelling system and arrow that indicate coupling.

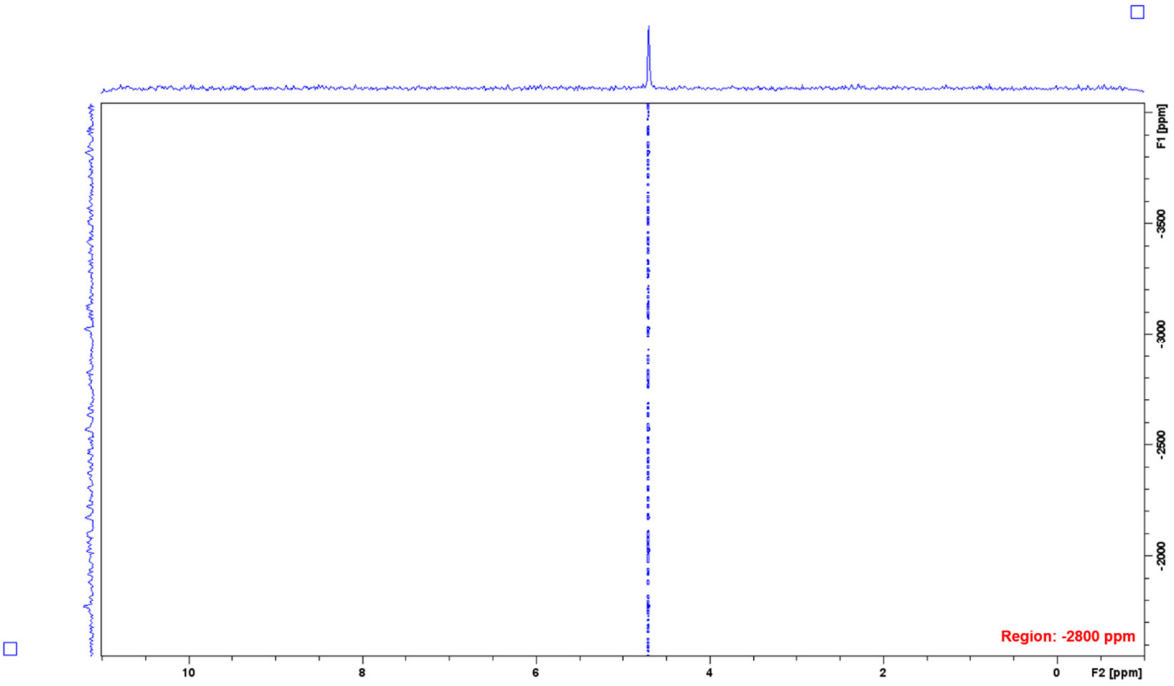

Figure S20: ^{1}H-^{195}Pt-HMQC spectrum of **5CLB** in D_2O obtained at 298 K. Region: -2800 ppm. Absence of platinum(II) resonance.

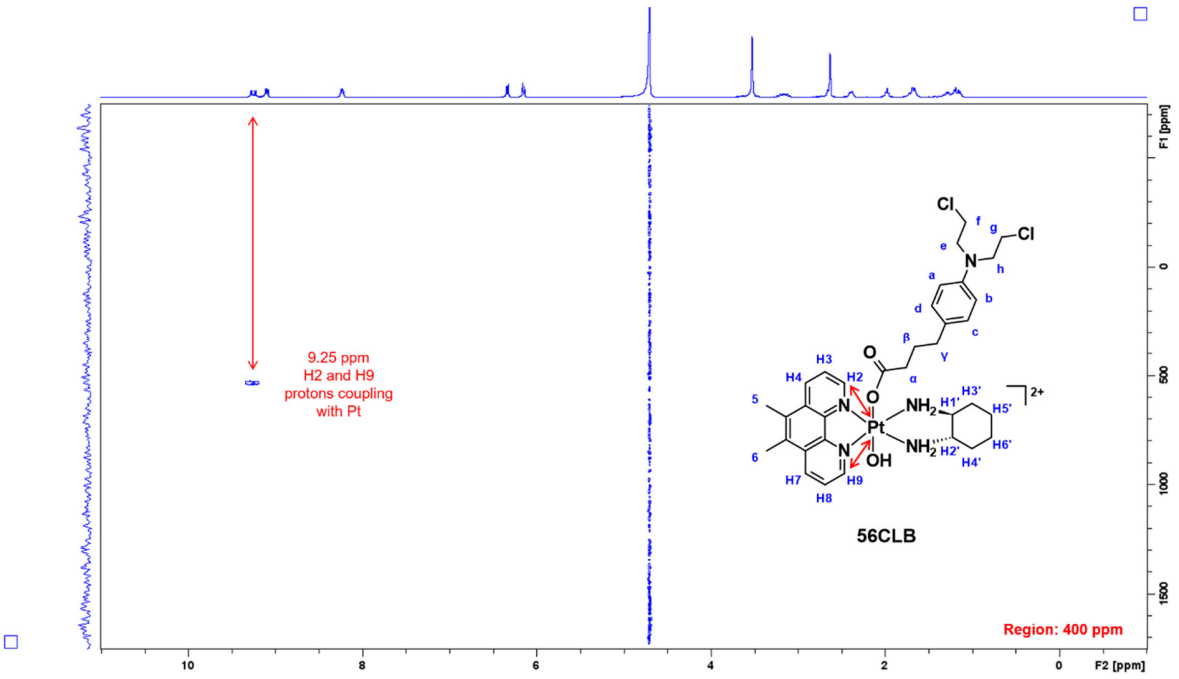

Figure S21: ^{1}H-^{195}Pt-HMQC spectrum of **56CLB** in D_2O obtained at 298 K. Region: 400 ppm. Inset: structure of **56CLB** with proton labelling system and arrows that indicate coupling.

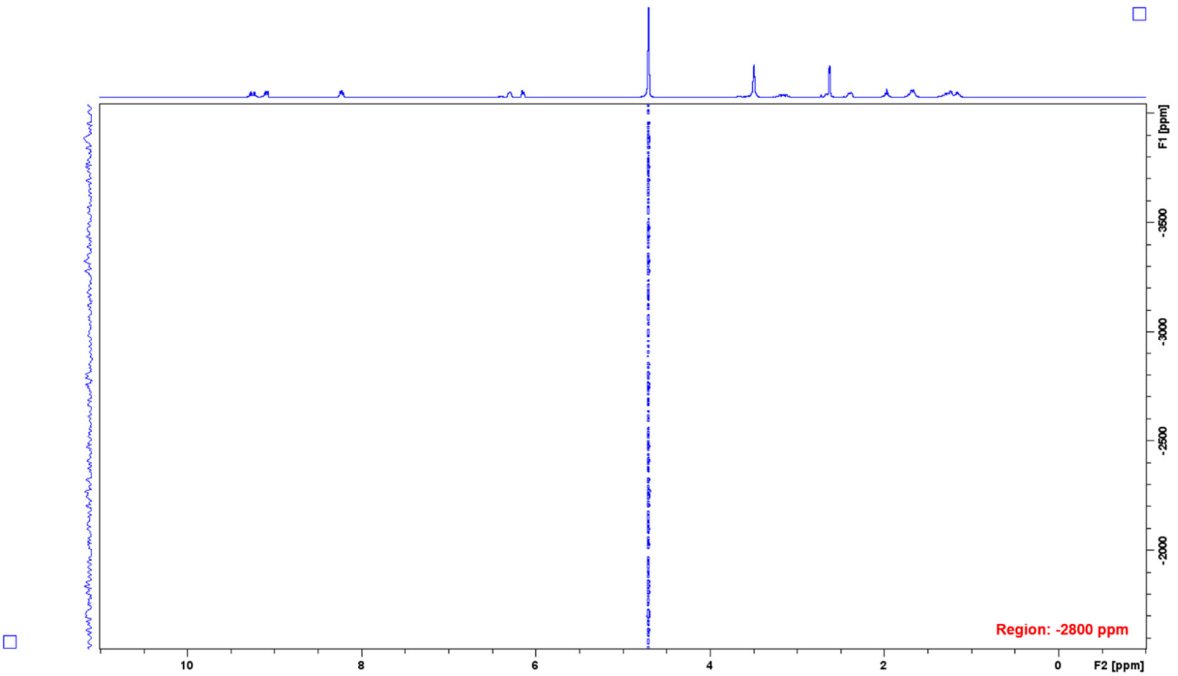

Figure S22: ^{1}H-^{195}Pt-HMQC spectrum of **56CLB** in D_2O obtained at 298 K. Region: -2800 ppm. Absence of platinum(II) resonance.

UV spectra of platinum(IV)-CLB complexes

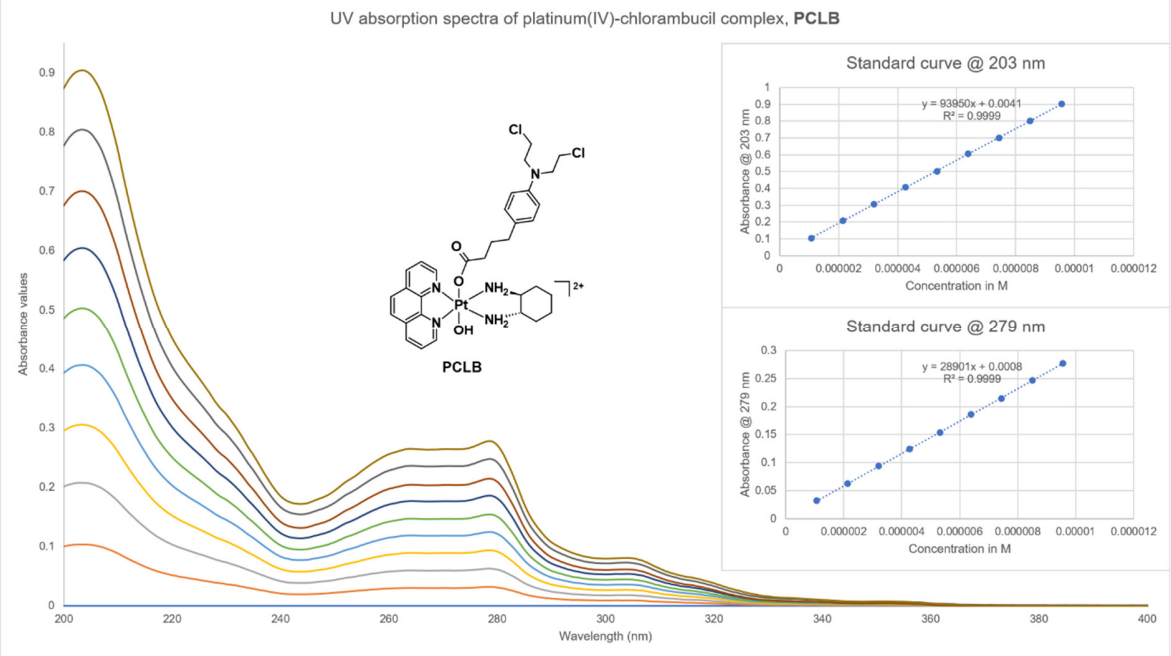

Figure S23: UV spectra of **PCLB** obtained at 298 K. Inset: structure of **PCLB** and generated plot curves within the wavelengths 203 and 279 nm at 298 K.

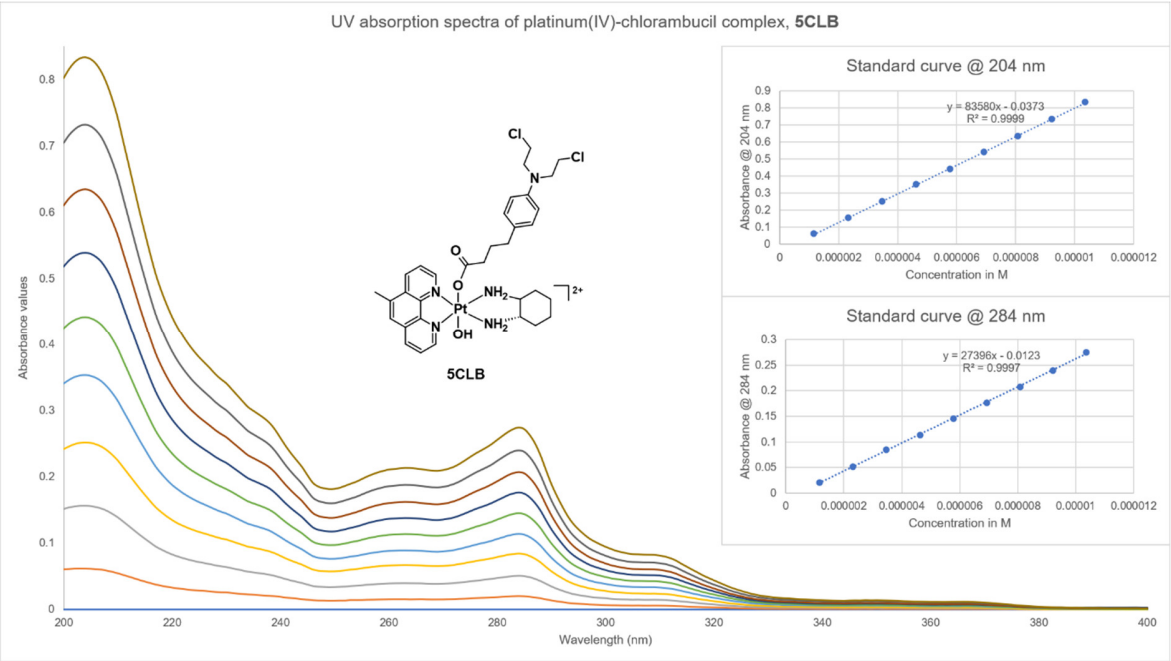

Figure S24: UV spectra of **5CLB** obtained at 298 K. Inset: structure of **5CLB** and generated plot curves within the wavelengths 204 and 284 nm at 298 K.

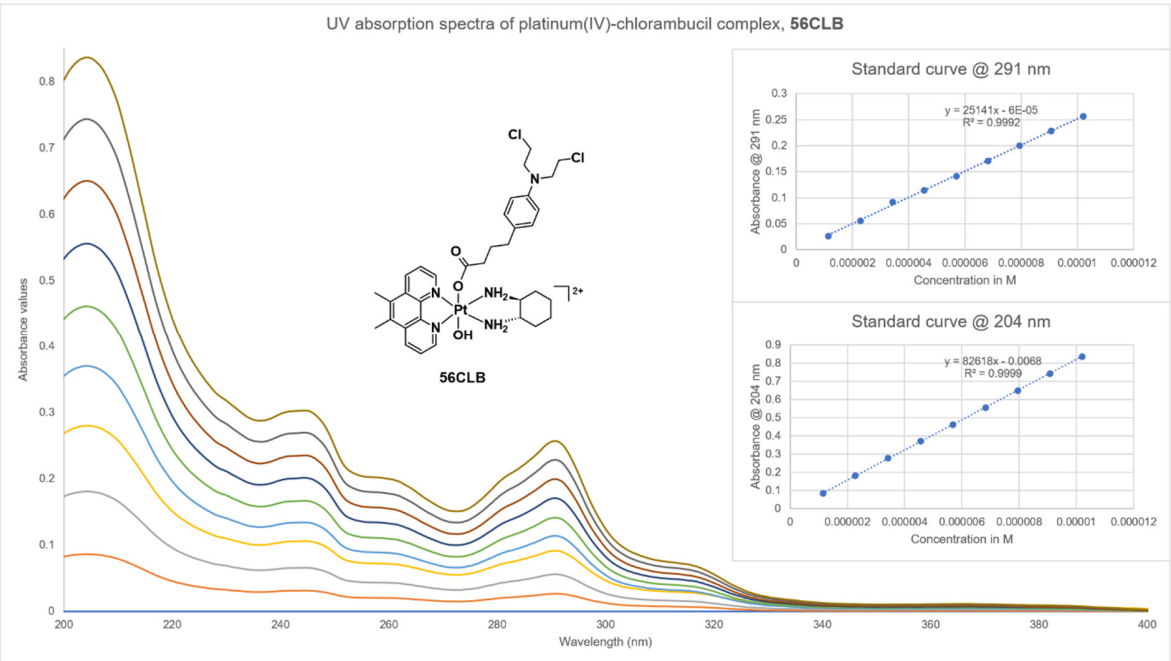

Figure S25: UV spectra of **56CLB** obtained at 298 K. Inset: structure of **56CLB** and generated plot curves within the wavelengths 204 and 291 nm at 298 K.

CD spectra of platinum(IV)-CLB complexes

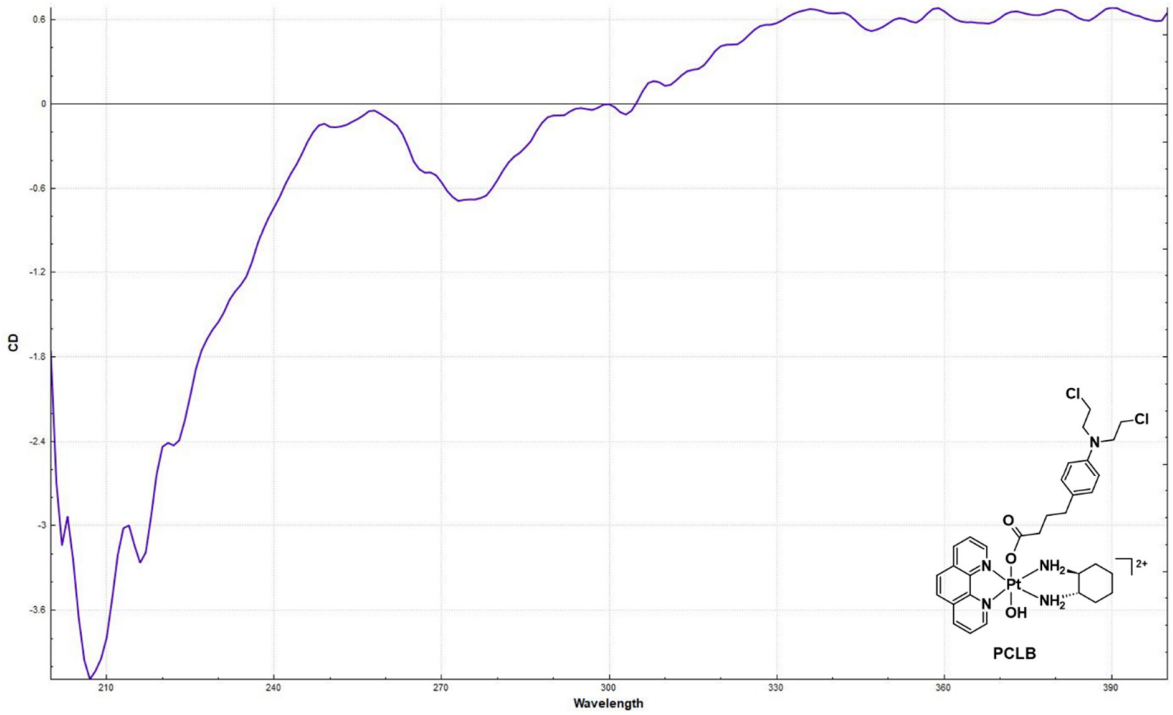

Figure S26: CD spectrum of **PCLB** in d.i.H_2O obtained at 298 K. Inset: structure of **PCLB**.

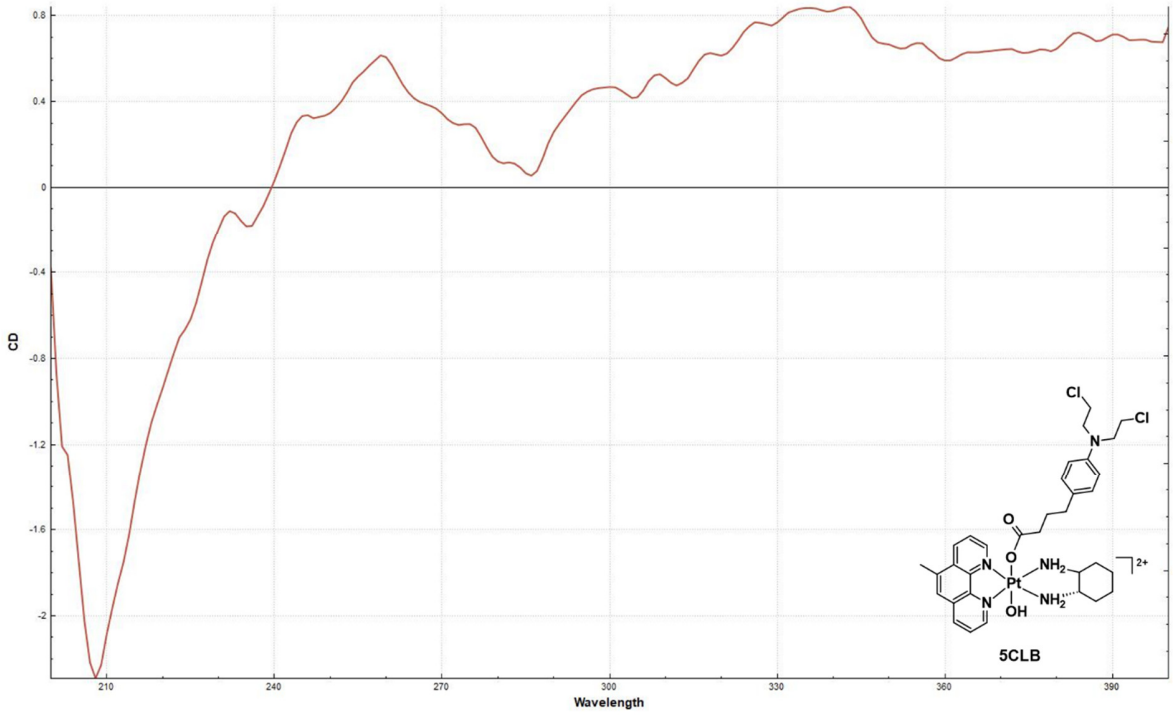

Figure S27: CD spectrum of **5CLB** in d.i.H_2O obtained at 298 K. Inset: structure of **5CLB**.

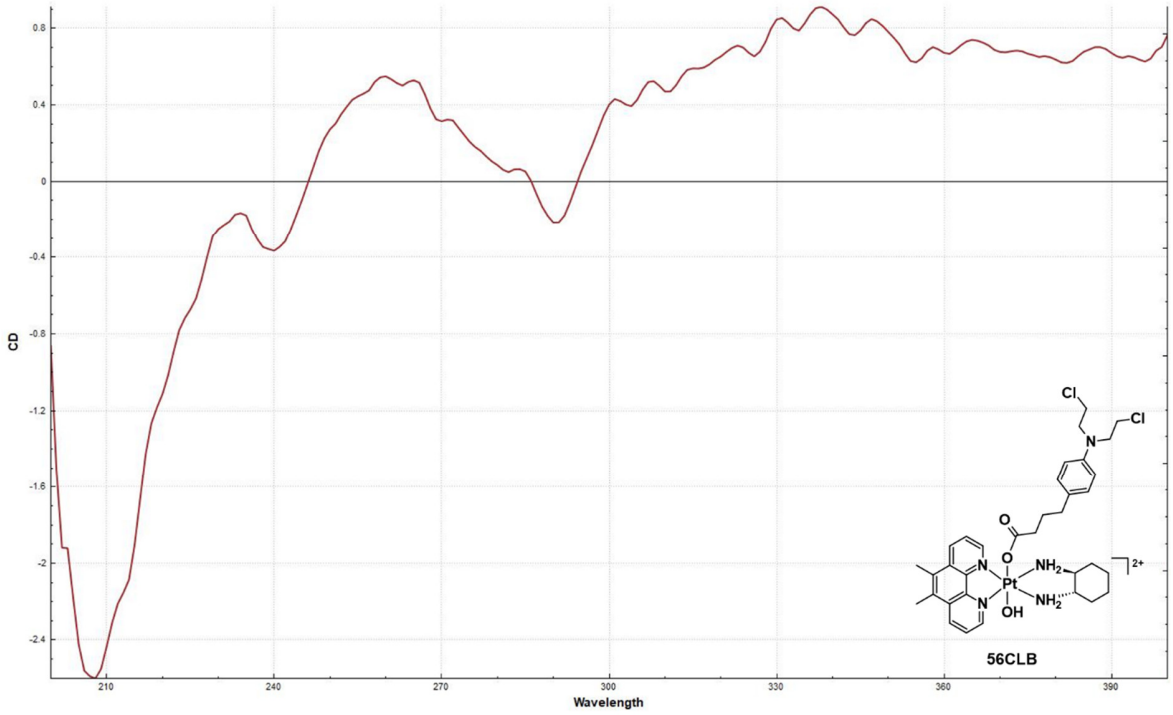

Figure S28: CD spectrum of **56CLB** in d.i.H_2O obtained at 298 K. Inset: structure of **56CLB**.

ESI-MS spectra of platinum(IV)-CLB complexes

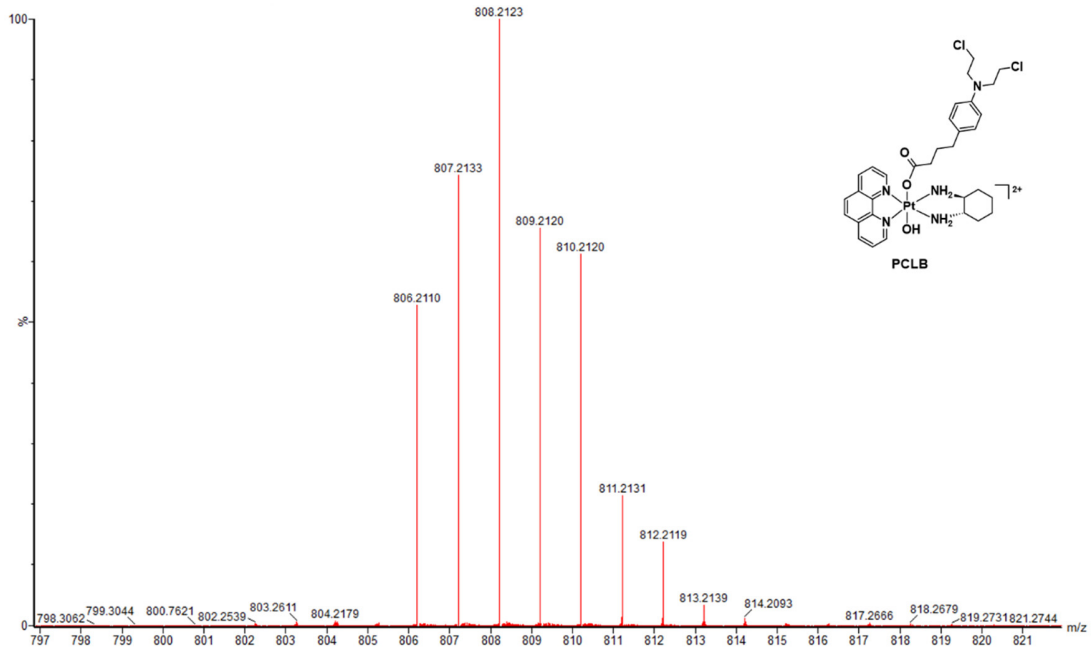

Figure S29: ESI-MS spectrum of **PCLB** in d.i.H_2O obtained at 298 K, using a Waters SYNAPT G2-Si quadruple time-of-flight (QTOF) HDMS. Inset: structure of **PCLB**.

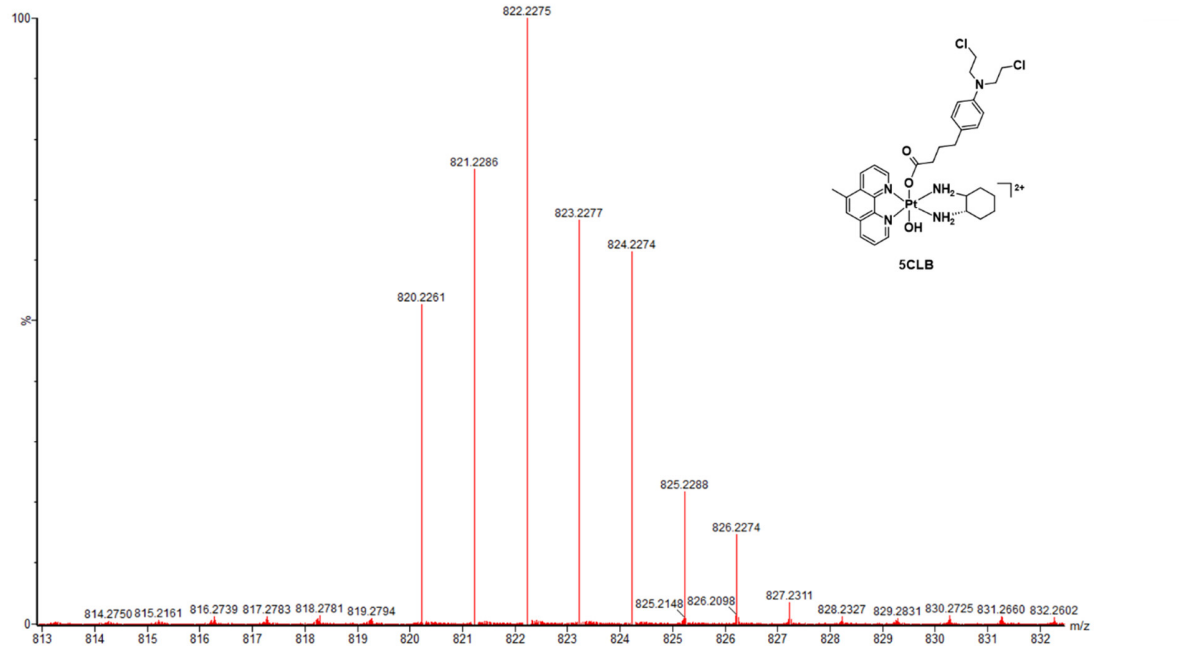

Figure S30: ESI-MS spectrum of **5CLB** in d.i.H_2O obtained at 298 K, using a Waters SYNAPT G2-Si quadruple time-of-flight (QTOF) HDMS. Inset: structure of **5CLB**.

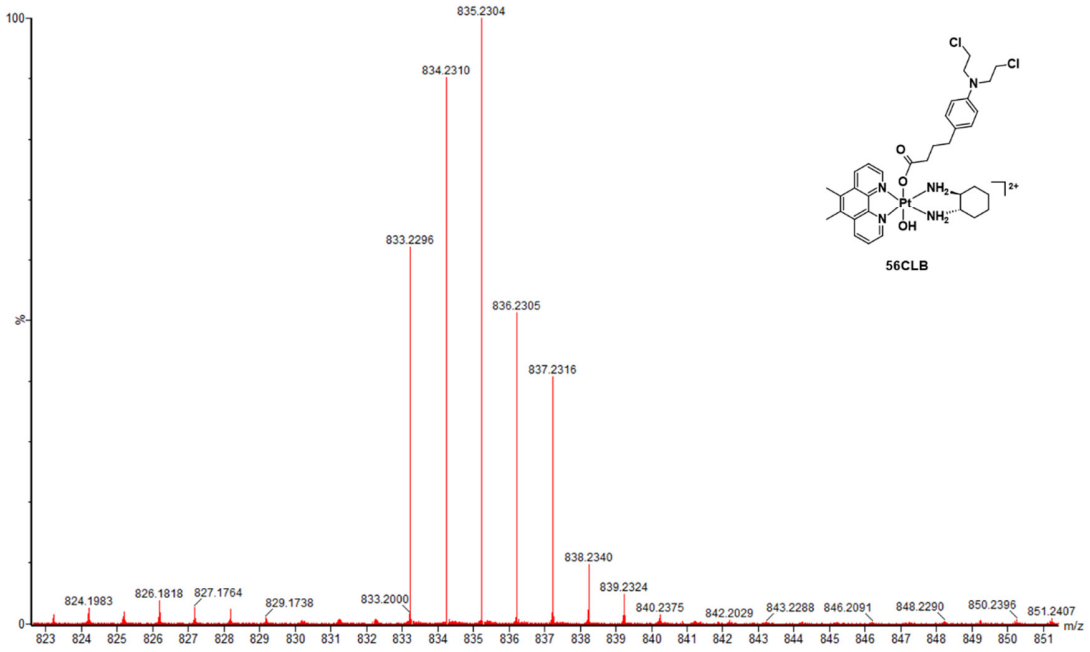

Figure S31: ESI-MS spectrum of **56CLB** in d.i.H_2O obtained at 298 K, using a Waters SYNAPT G2-Si quadruple time-of-flight (QTOF) HDMS. Inset: structure of **56CLB**.

Stability experiments

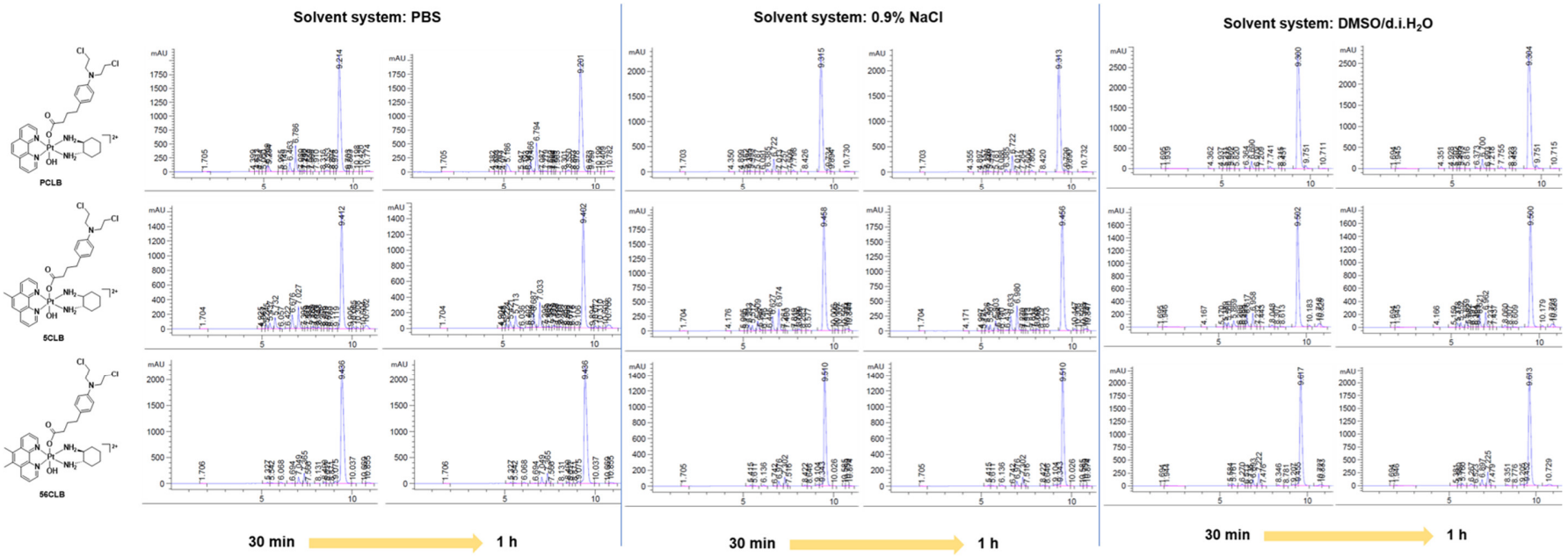

Figure S32: Combined HPLC chromatograms of **PCLB**, **5CLB** and **56CLB** in three solvent systems, obtained at 298 K. Inset: structures of **PCLB**, **5CLB** and **56CLB**.

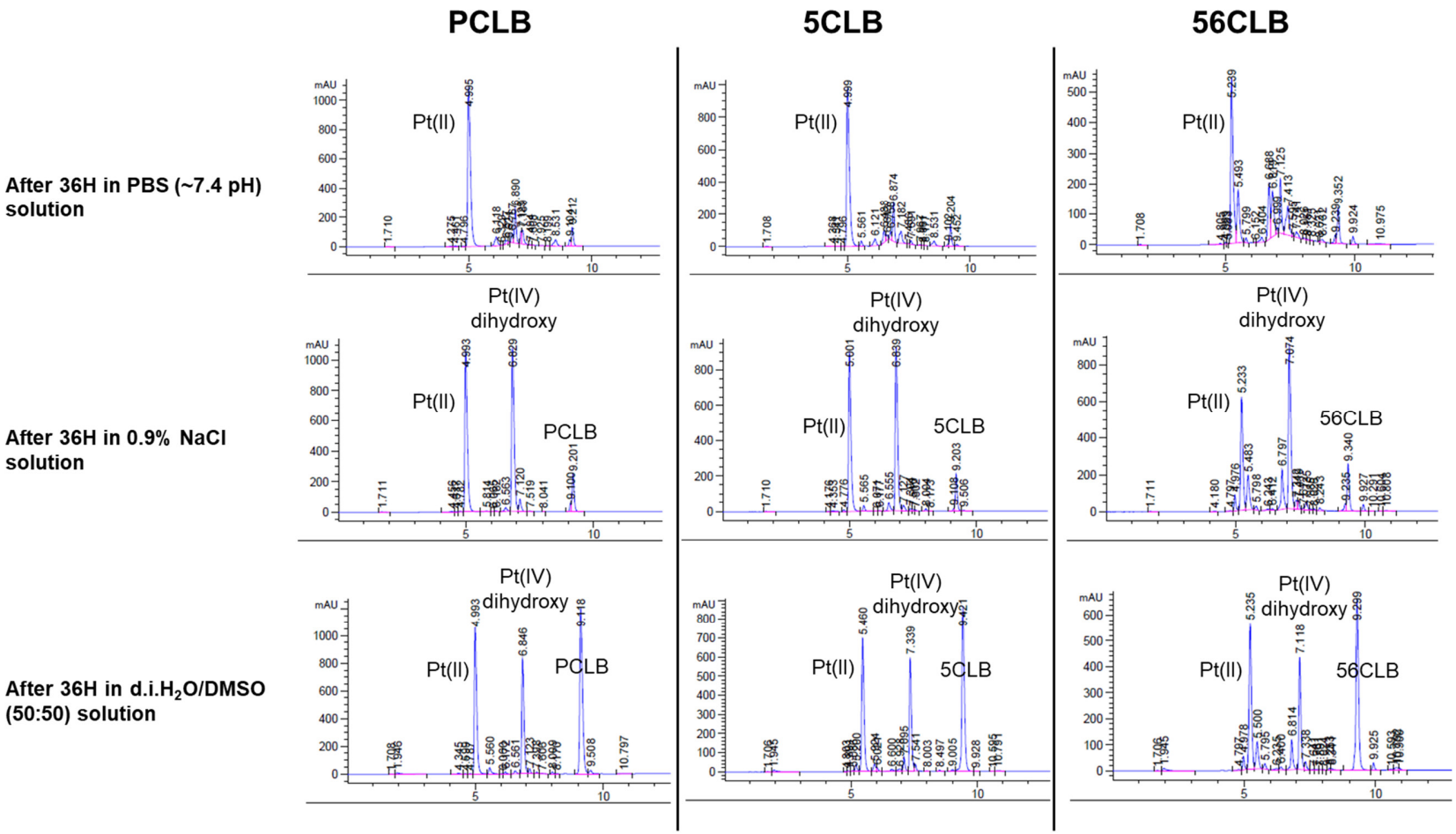

Figure S33: Combined HPLC chromatograms of **PCLB**, **5CLB** and **56CLB** in three solvent systems, obtained at 298 K at 36 h. Inset: structures of **PCLB**, **5CLB** and **56CLB**.

Lipophilicity

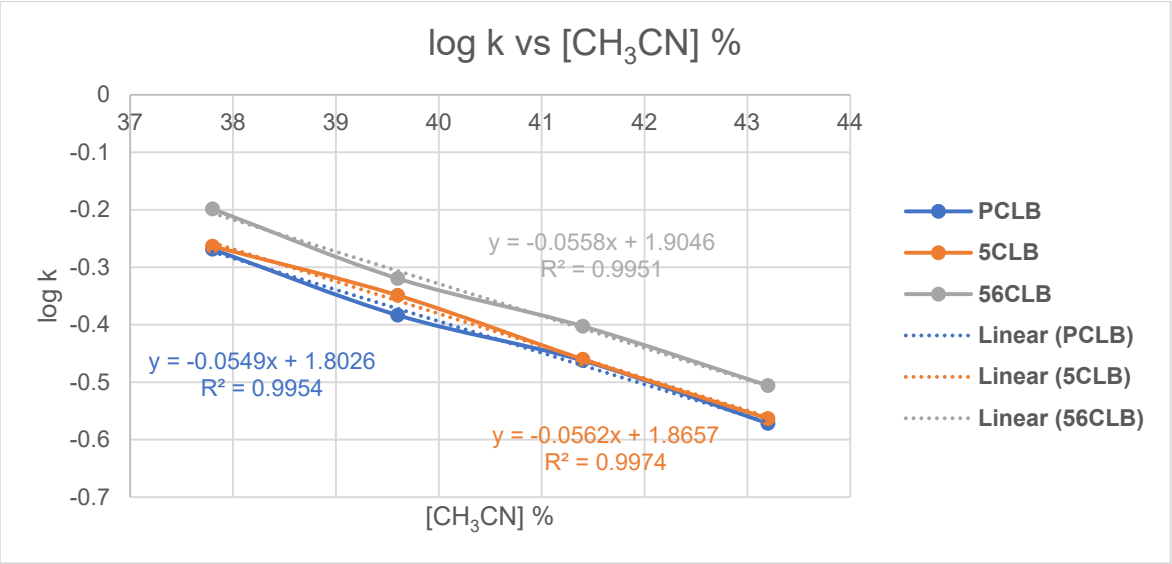

Figure S34: Generated plot curve of log k *versus* concentration of organic solvent, CH_3CN to determine the chromatographic lipophilicity index, log k_w of the platinum(IV)-CLB complexes.

Reduction reaction experiments

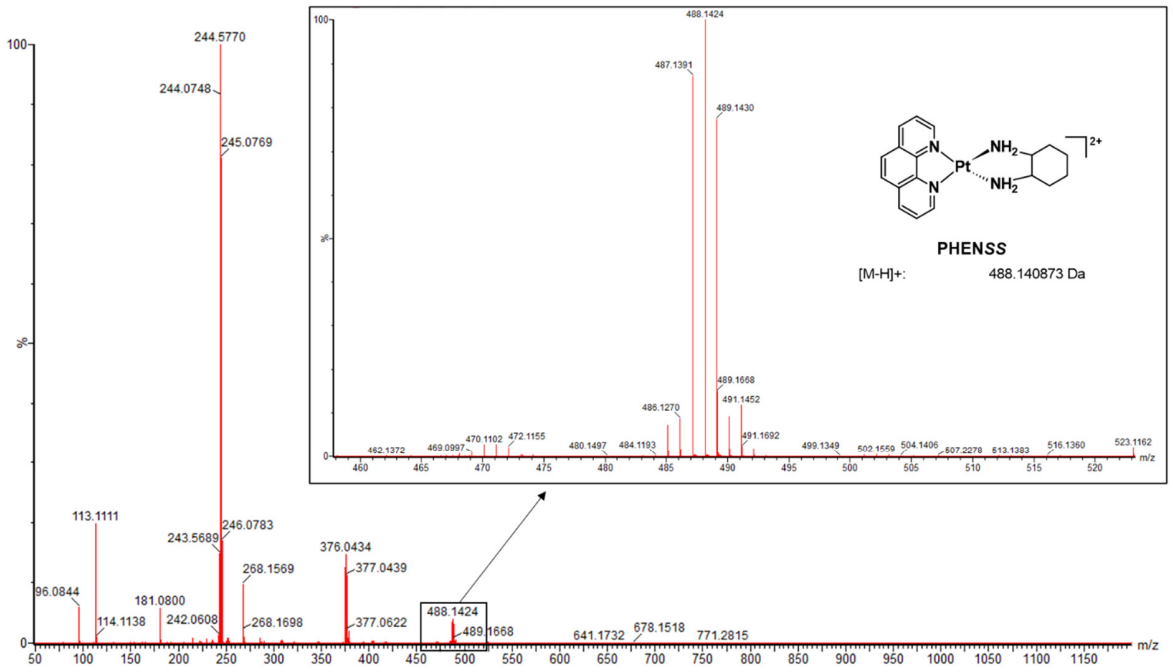

Figure S35: ESI-MS spectra of the reduced **PCLB** prodrug, highlighting the formation of the corresponding platinum(II) congener, **PHEN*SS***.

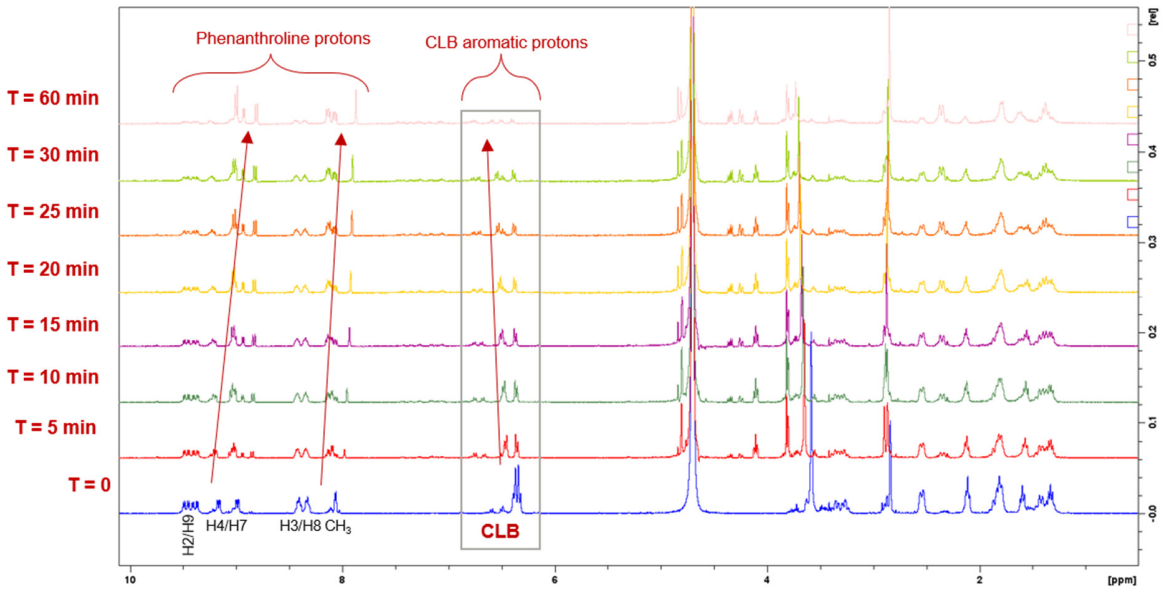

Figure S36: ^{1}H-NMR spectra of **5CLB** with PBS and AsA in D_2O at 310.15 K, in different time intervals, highlighting the movement of resonances from the phenanthroline protons and the aromatic protons of the CLB ligand. **T** represents time in min.

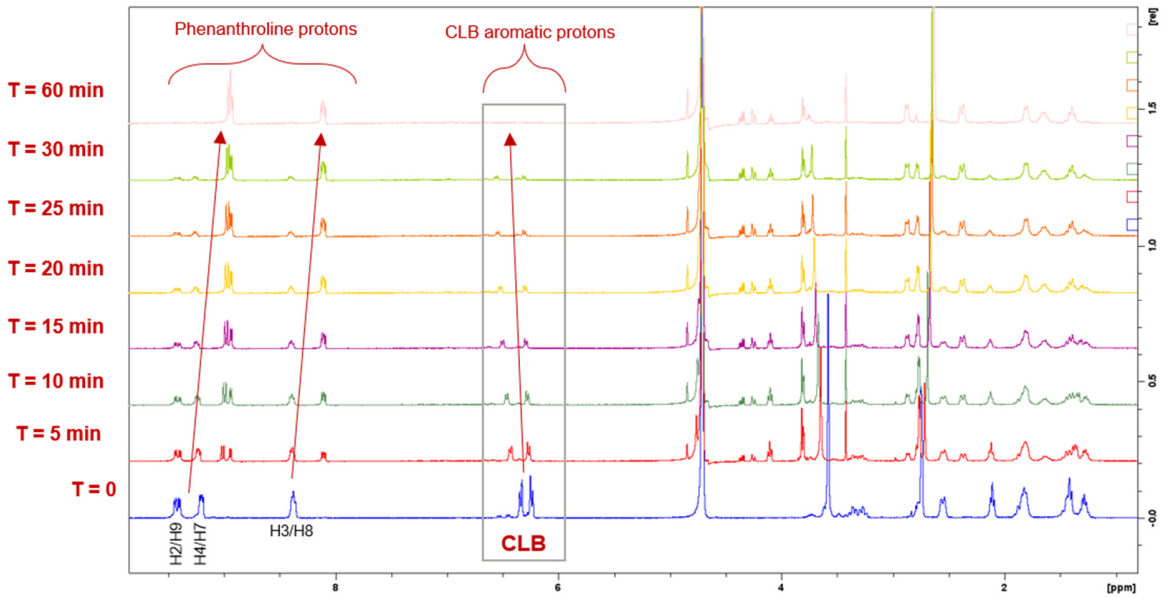

Figure S37: ^{1}H-NMR spectra of **56CLB** with PBS and AsA in D_2O at 310.15 K, in different time intervals, highlighting the movement of resonances from the phenanthroline protons and the aromatic protons of the CLB ligand. **T** represents time in min.

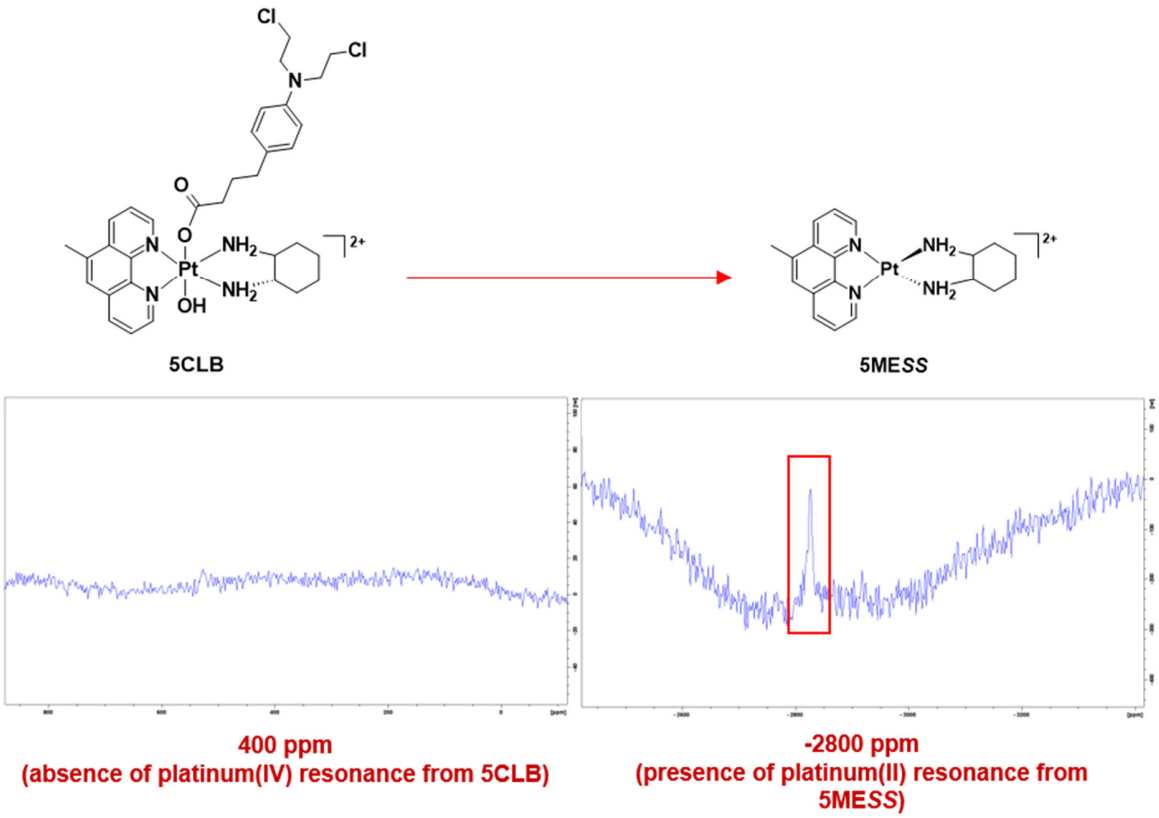

Figure S38: 1D-^{195}Pt NMR spectra of **5CLB** with PBS and AsA in D_2O at 310.15 K, within the regions of 400 and -2800 ppm, highlighting the complete reduction of the complex after 1 h. Above: Structures of **5CLB** and its platinum(II) scaffold, **5ME*SS***.

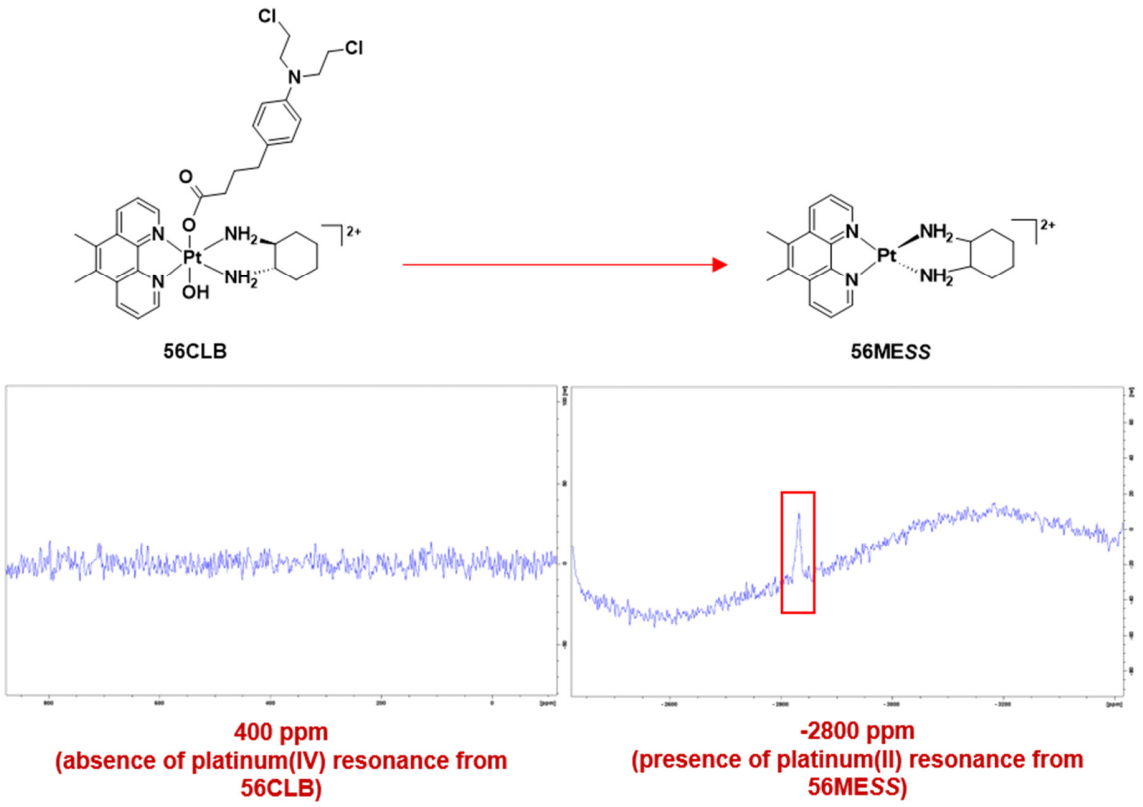

Figure S39: 1D-^{195}Pt NMR spectra of **56CLB** with PBS and AsA in D_2O at 310.15 K, within the regions of 400 and -2800 ppm, highlighting the complete reduction of the complex after 1 h. Above:Structures of **56CLB** and its platinum(II) scaffold, **56MES*S***.

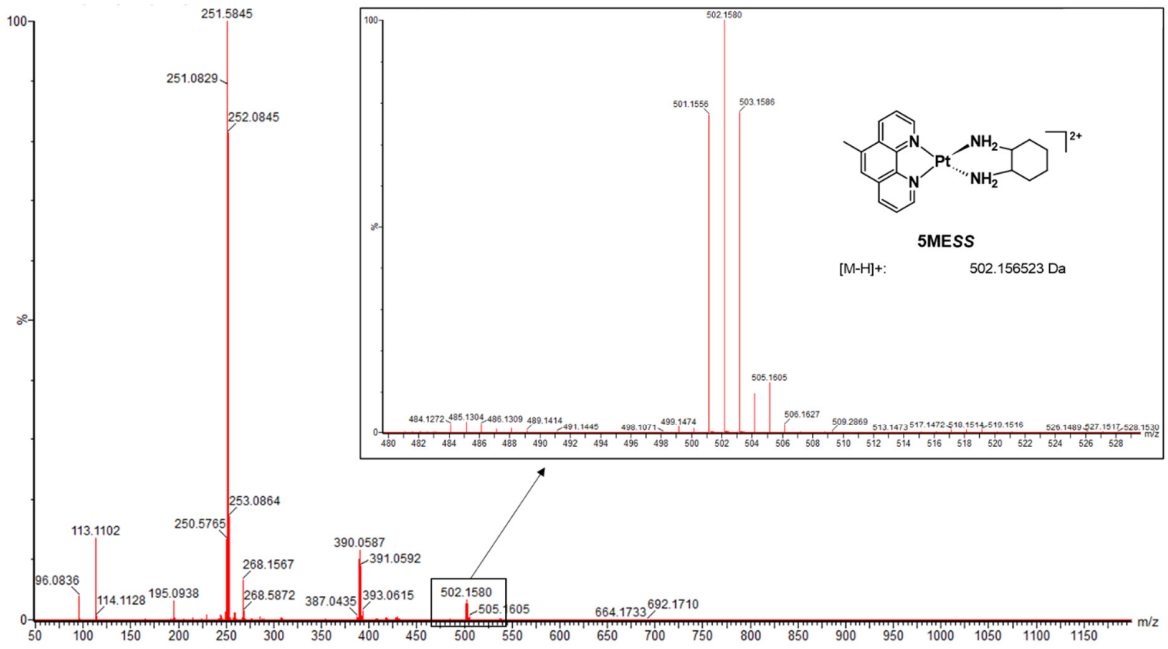

Figure S40: ESI-MS spectra of the reduced **5CLB** prodrug, highlighting the formation of the corresponding platinum(II) congener, **5MES*S***.

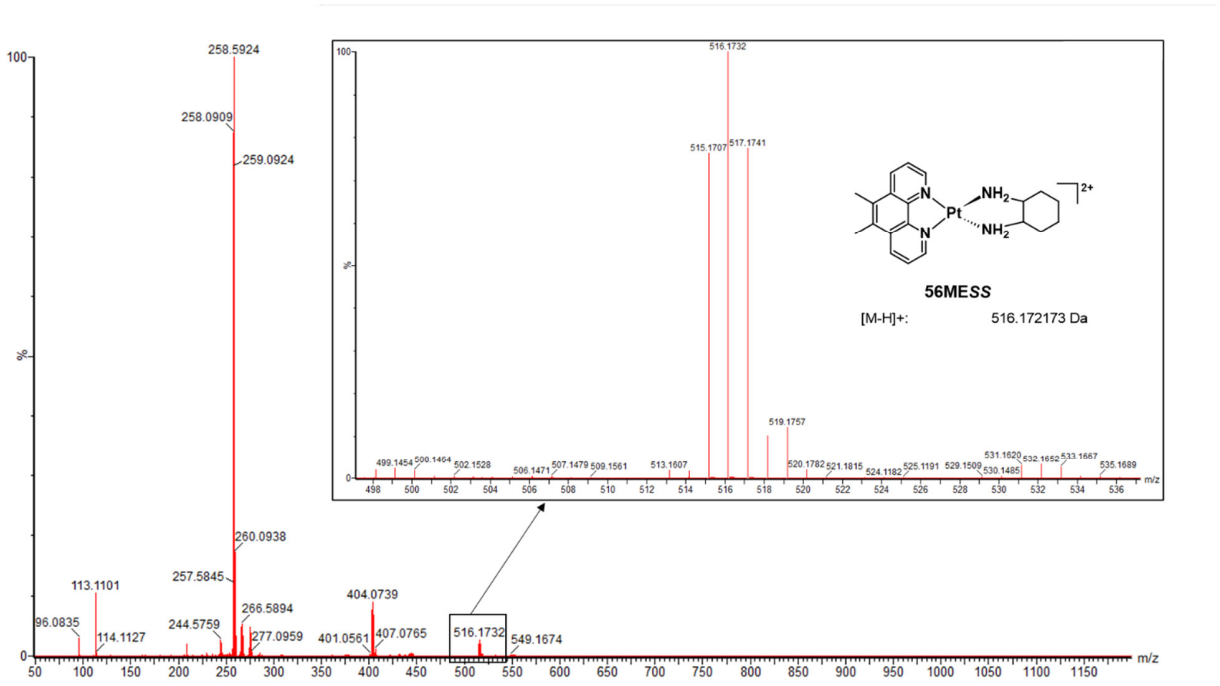

Figure S41: ESI-MS spectra of the reduced **56CLB** prodrug, highlighting the formation of the corresponding platinum(II) congener, **56ME*SS***.

ROS experiments

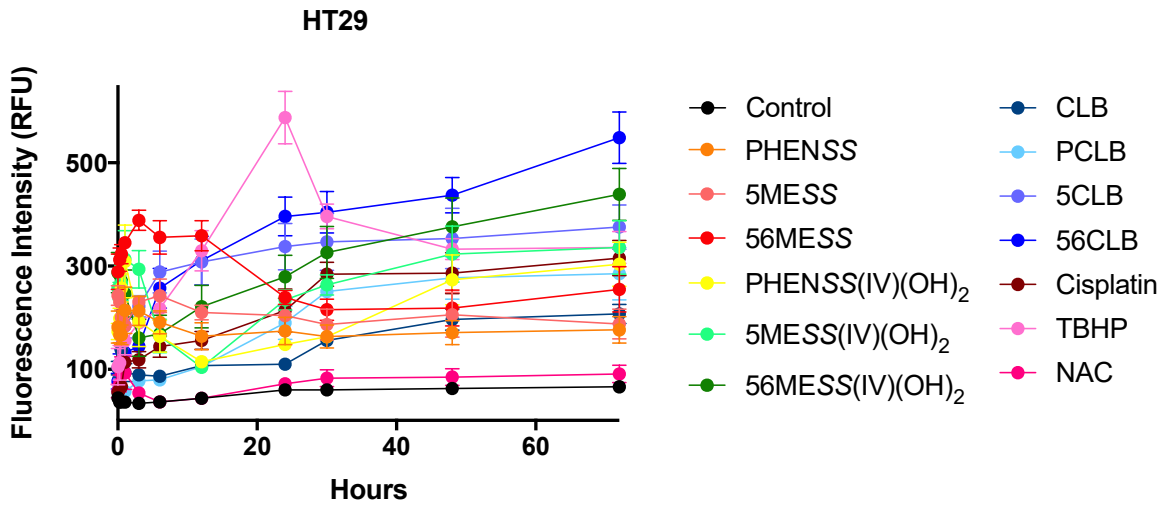

Figure S42: ROS production upon treatment with **PCLB**, **5CLB**, **56CLB**, cisplatin, together with precursor platinum(II) and (IV) scaffolds in HT29 colon cancer cell line at 0, 0.25, 0.5, 1, 3, 6, 12, 24, 48 and 72 h. TBHP: t-butyl hydroperoxide, NAC: *N*-acetylcysteine. Data points denote mean ± SEM. n = 3 from three independent experiments where samples were run in triplicates.