Application of the anthraquinone drug rhein as axial ligand in bifunctional Pt(IV) complexes to obtain antiproliferative agents against human glioblastoma cells

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SUPPLEMENTARY MATERIAL

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Figures S8-S13 ESI-MS, ^{1}H, ^{13}C, ^{195}Pt, [^{1}H, ^{1}H] COSY and [^{1}H, ^{13}C] HSQC NMR spectra of **2**.

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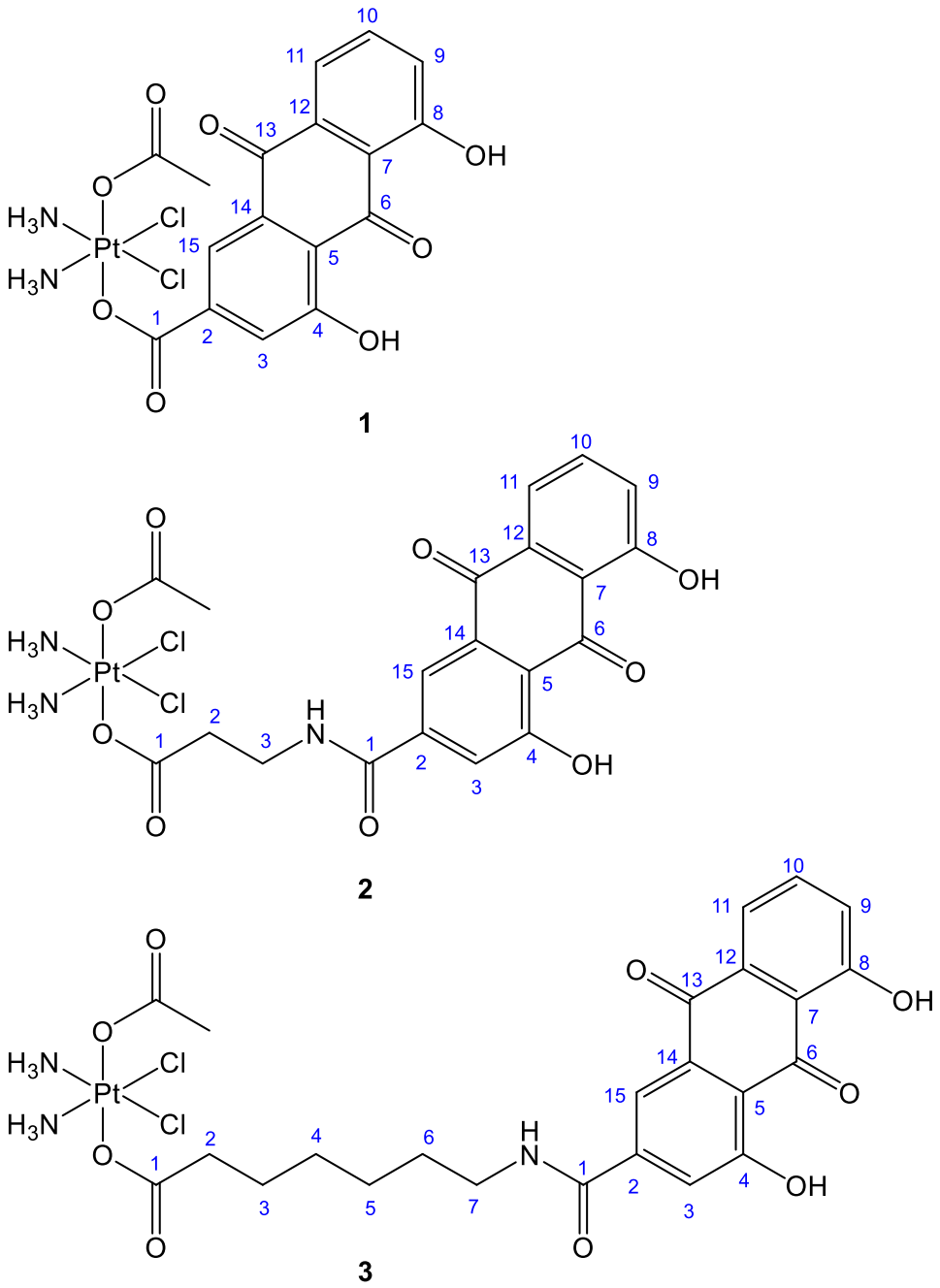

Figure S1. Sketch of the compounds under investigation and numbering scheme for NMR assignment used in the characterization of the complexes (see Experimental section). The assignment includes numbers and codes for the different portions of the molecules: Ac = acetate, AH = 7-aminoheptanoic acid, βA = β-alanine, R = **rhein**.

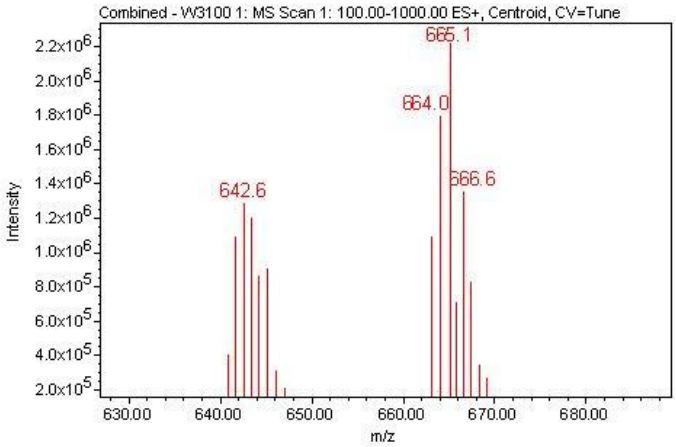

Figure S2. ESI-MS of **1**.

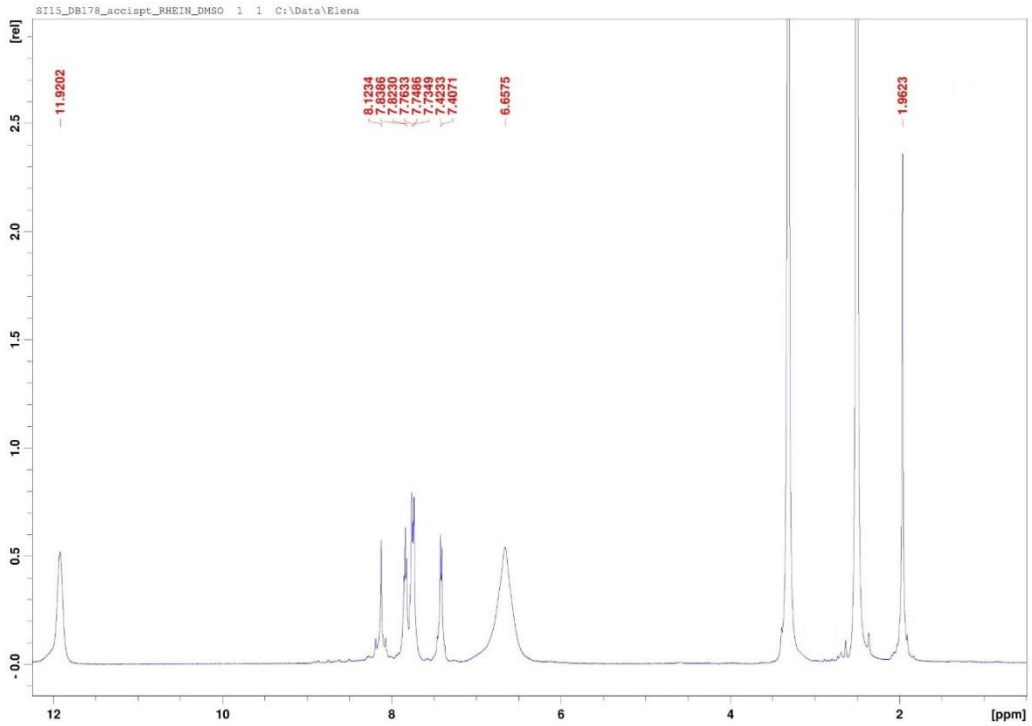

Figure S3. ^{1}H NMR spectrum of **1** (in DMSO-d6).

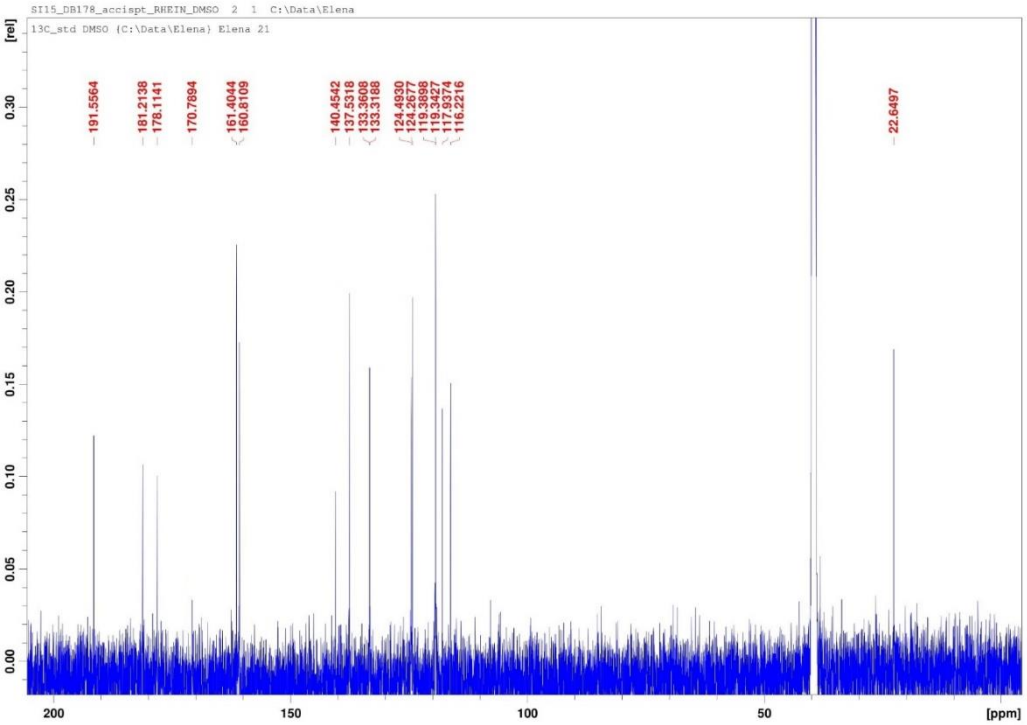

Figure S4. ^{13}C NMR spectrum of **1** (in DMSO-d6).

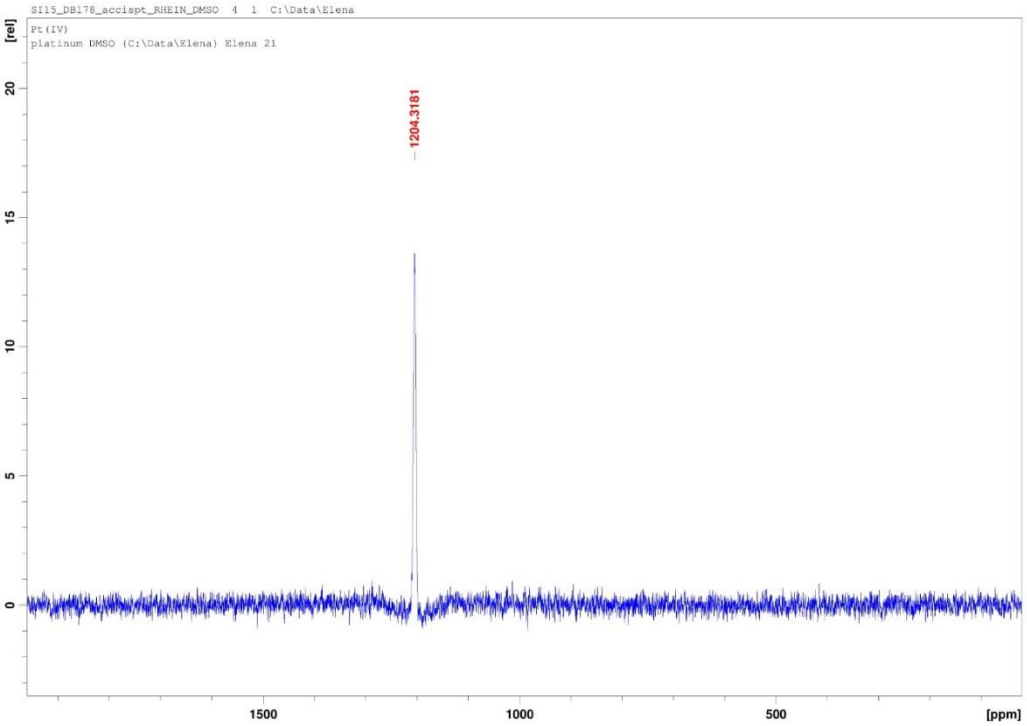

Figure S5. ^{195}Pt NMR spectrum of **1** (in DMSO-d6).

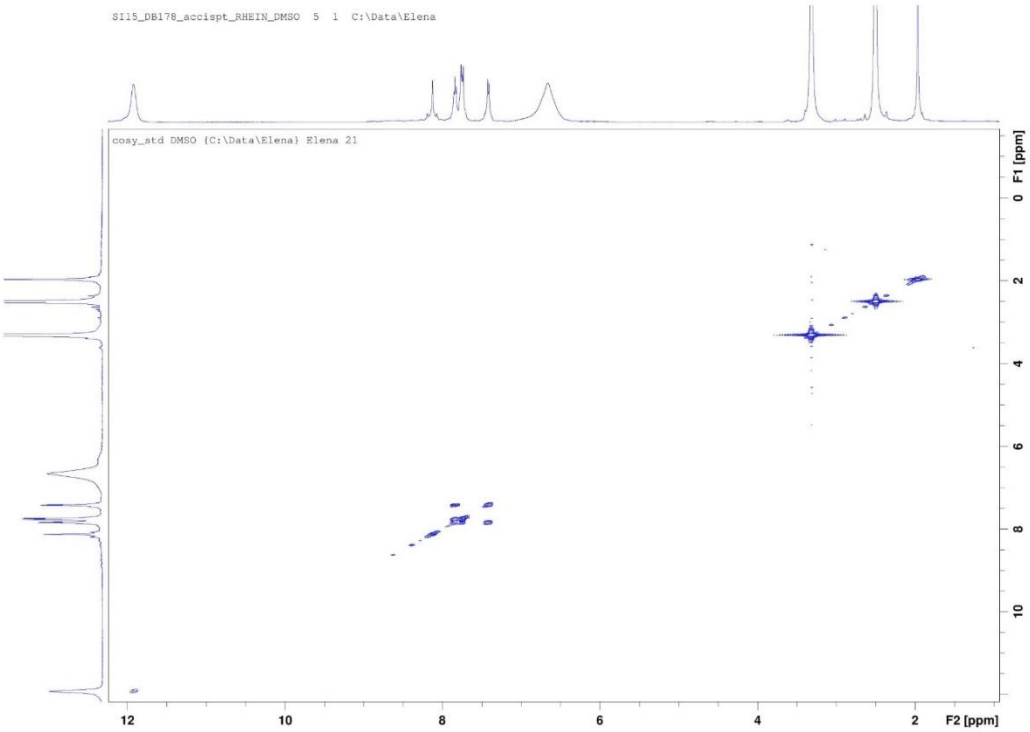

Figure S6. [^{1}H, ^{1}H] COSY NMR spectrum of **1** (in DMSO-d6).

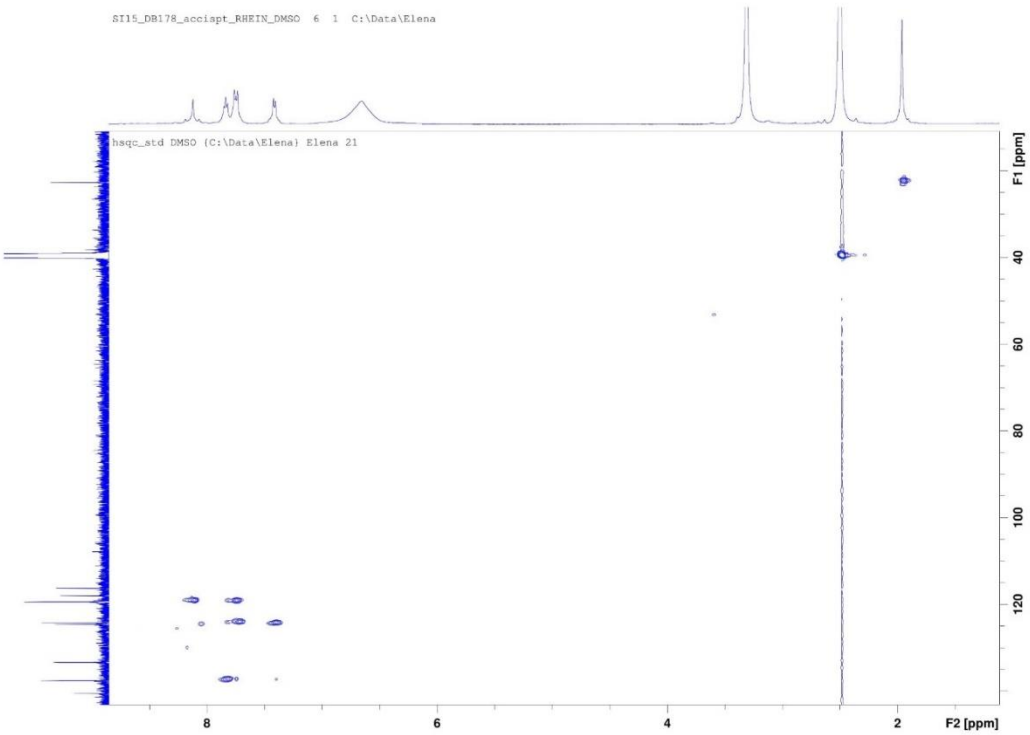

Figure S7. [^{1}H, ^{13}C] HSQC NMR spectrum of **1** (in DMSO-d6).

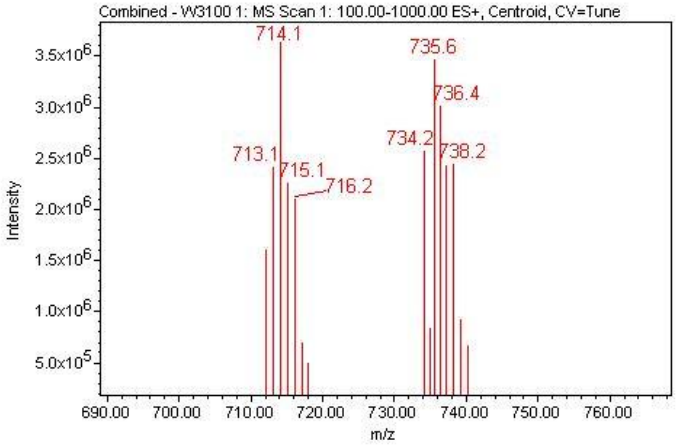

Figure S8. ESI-MS spectrum of **2**.

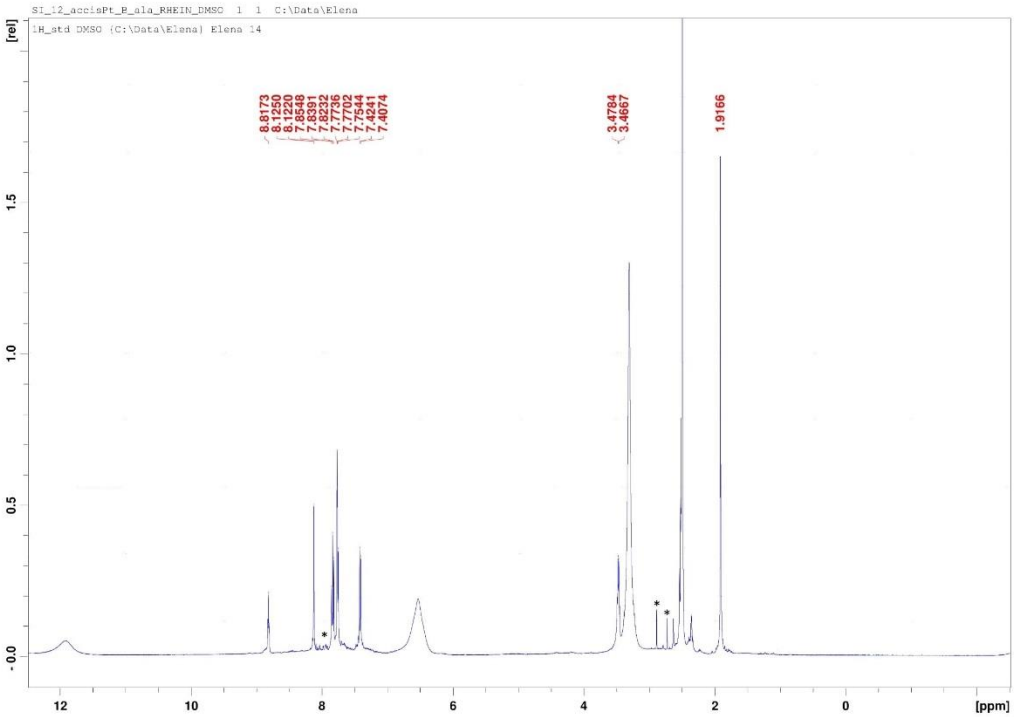

Figure S9. ^{1}H NMR spectrum of **2** (in DMSO-d6). The signals of residual *N*,*N*-dimethylformamide are also visible (*).

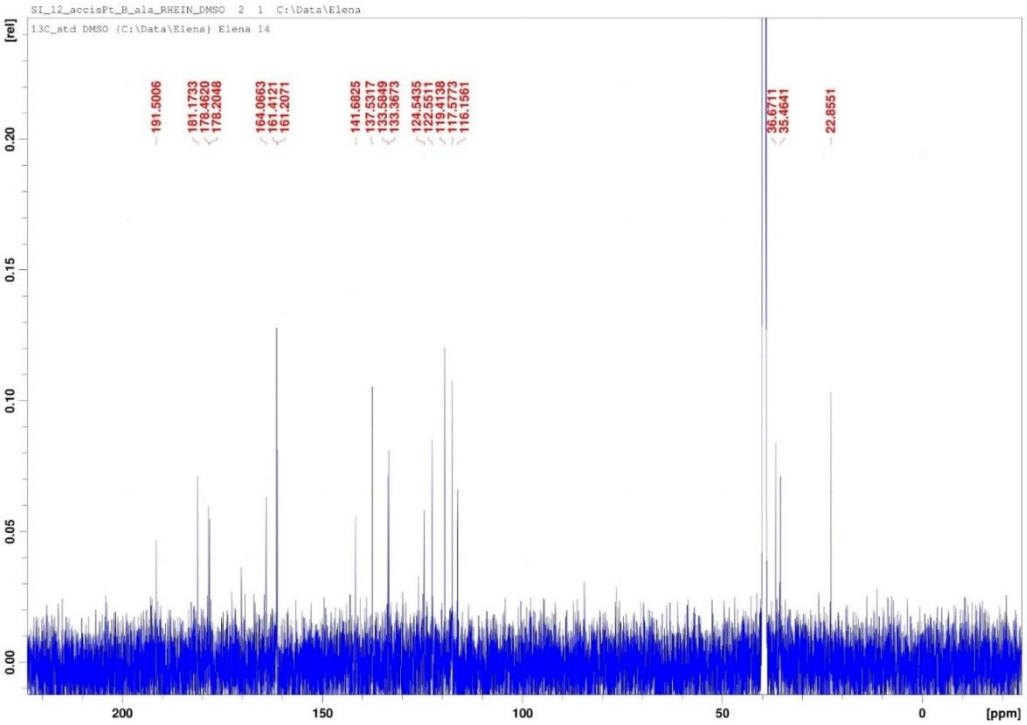

Figure S10. ^{13}C NMR spectrum of **2** (in DMSO-d6).

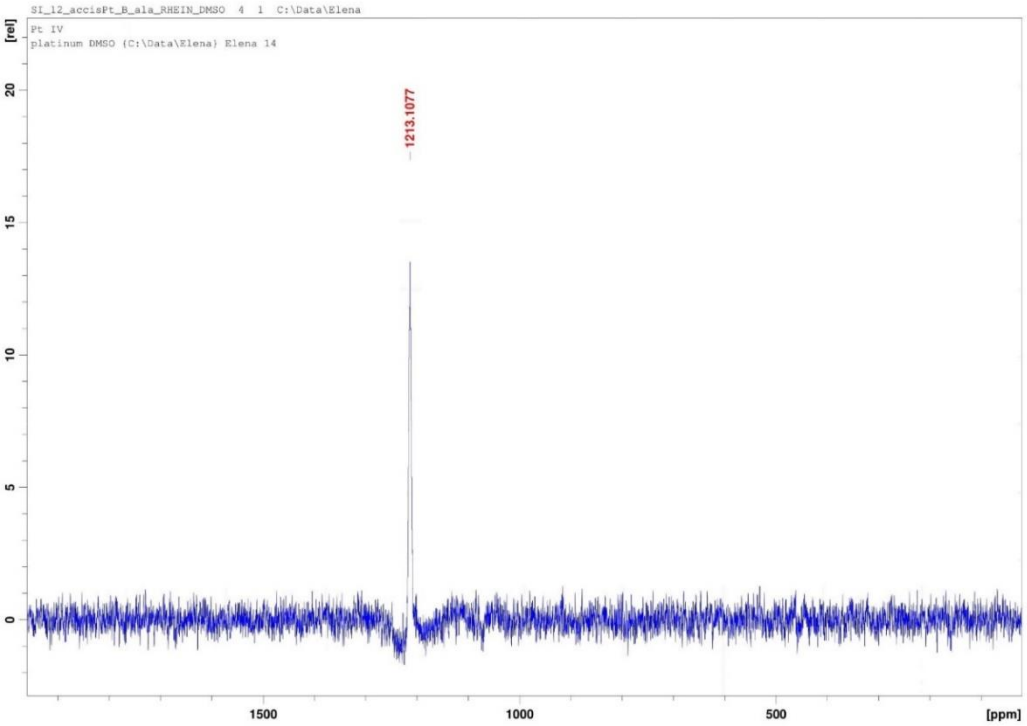

Figure S11. ^{195}Pt NMR spectrum of **2** (in DMSO-d6).

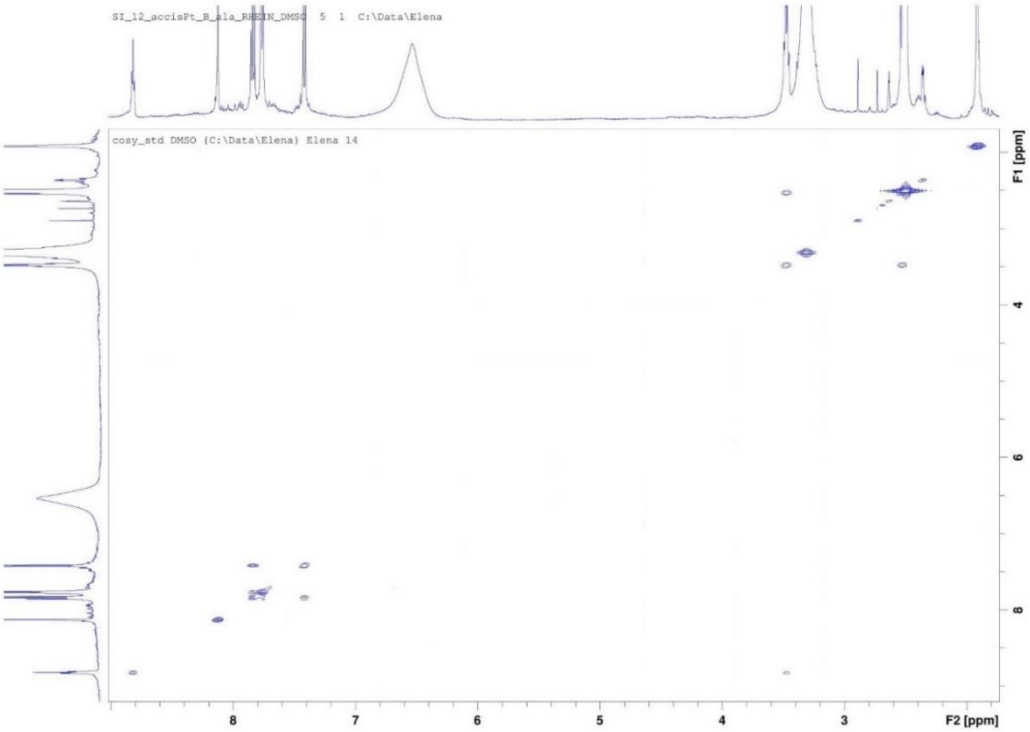

Figure S12. [^{1}H, ^{1}H] COSY NMR spectrum of **2** (in DMSO-d6).

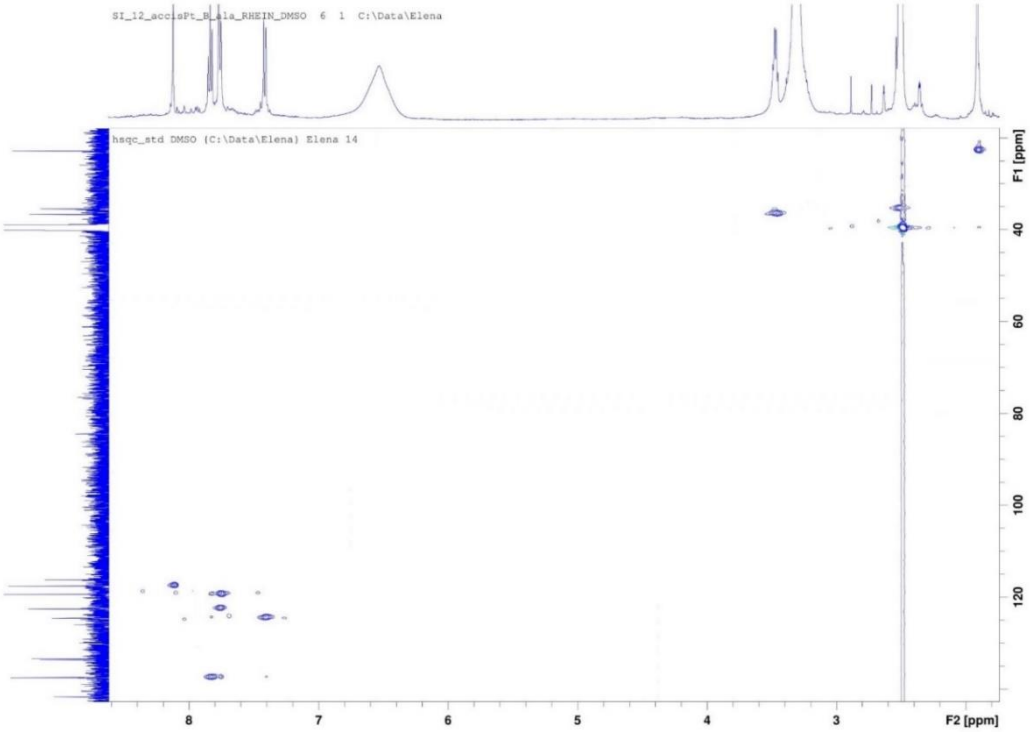

Figure S13. [^{1}H, ^{13}C] HSQC NMR spectrum of **2** (in DMSO-d6).

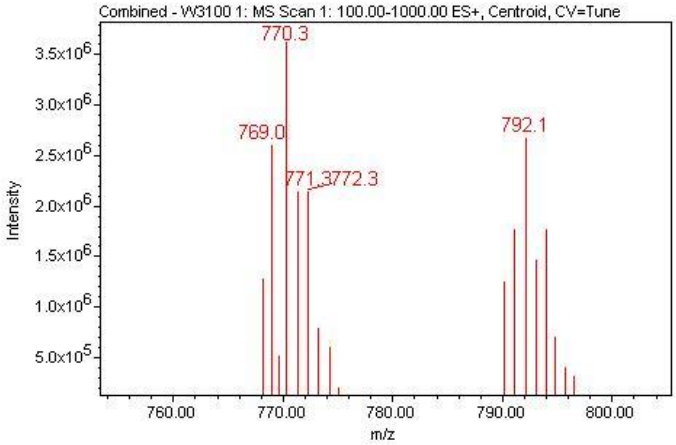

Figure S14. ESI-MS spectrum of **3** (in DMSO-d6).

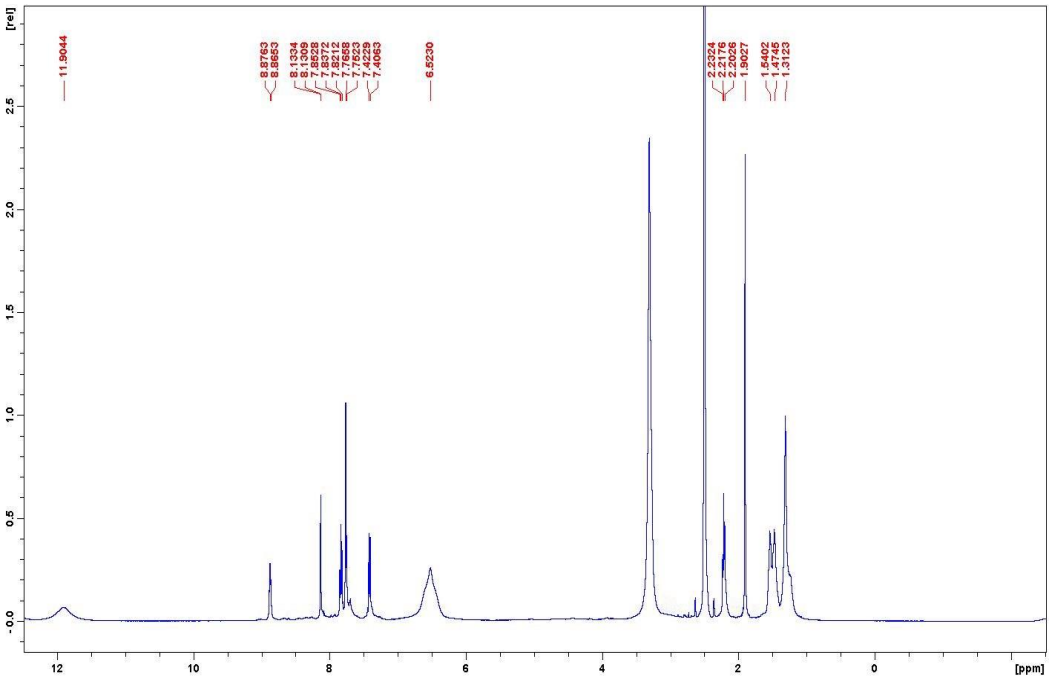

Figure S15. ^{1}H NMR spectrum of **3** (in DMSO-d6).

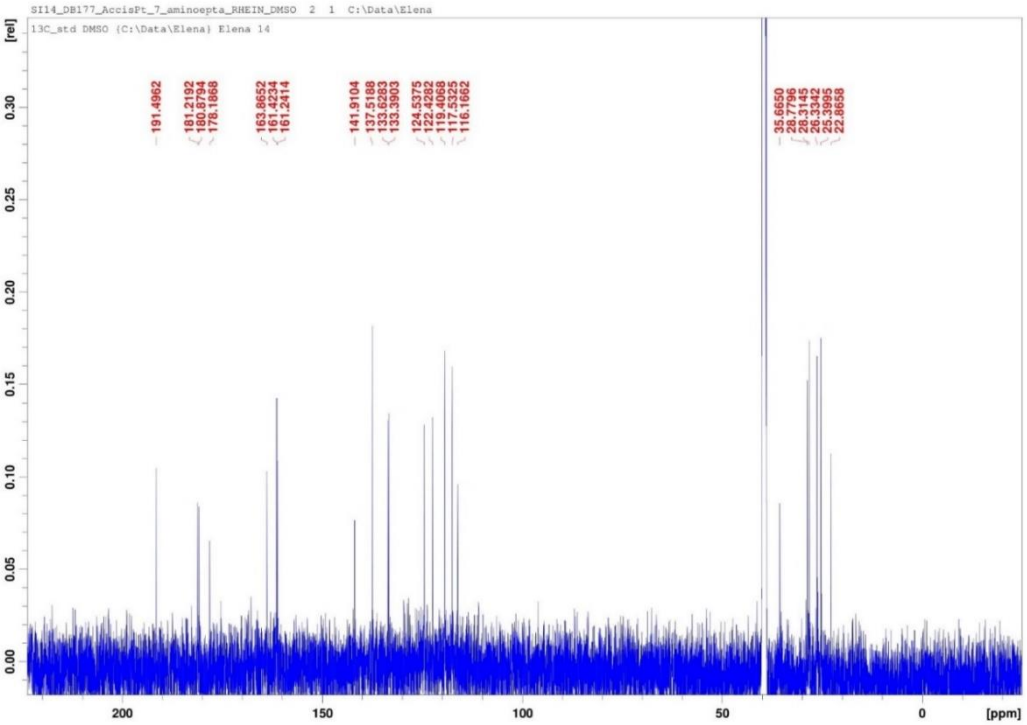

Figure S16. ^{13}C NMR spectrum of **3** (in DMSO-d6).

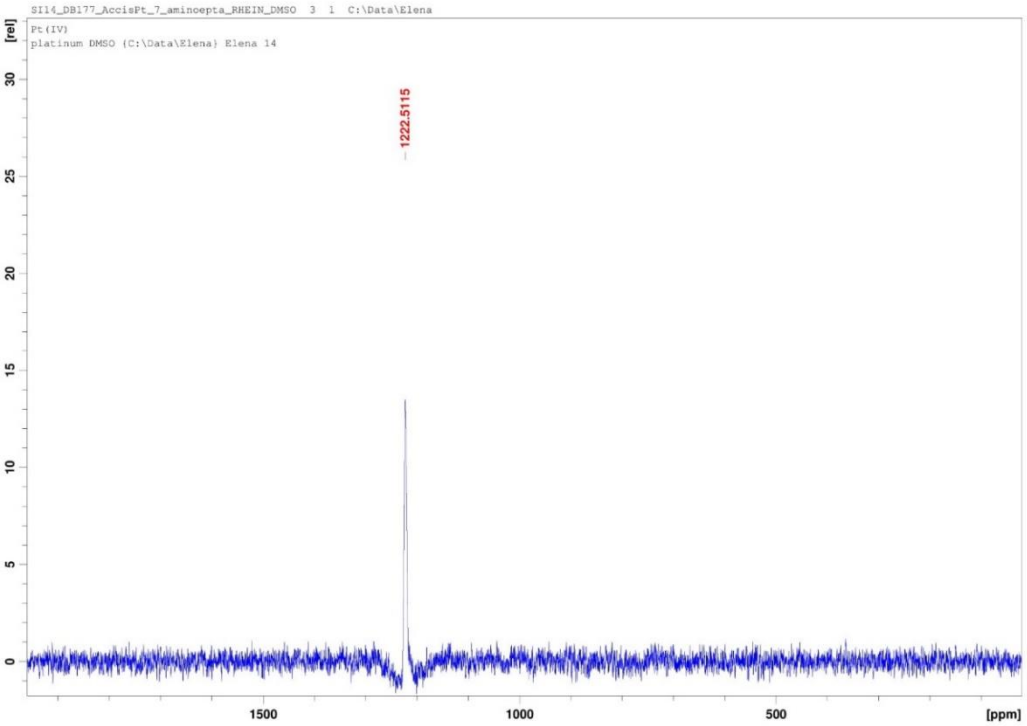

Figure S17. ^{195}Pt NMR spectrum of **3** (in DMSO-d6).

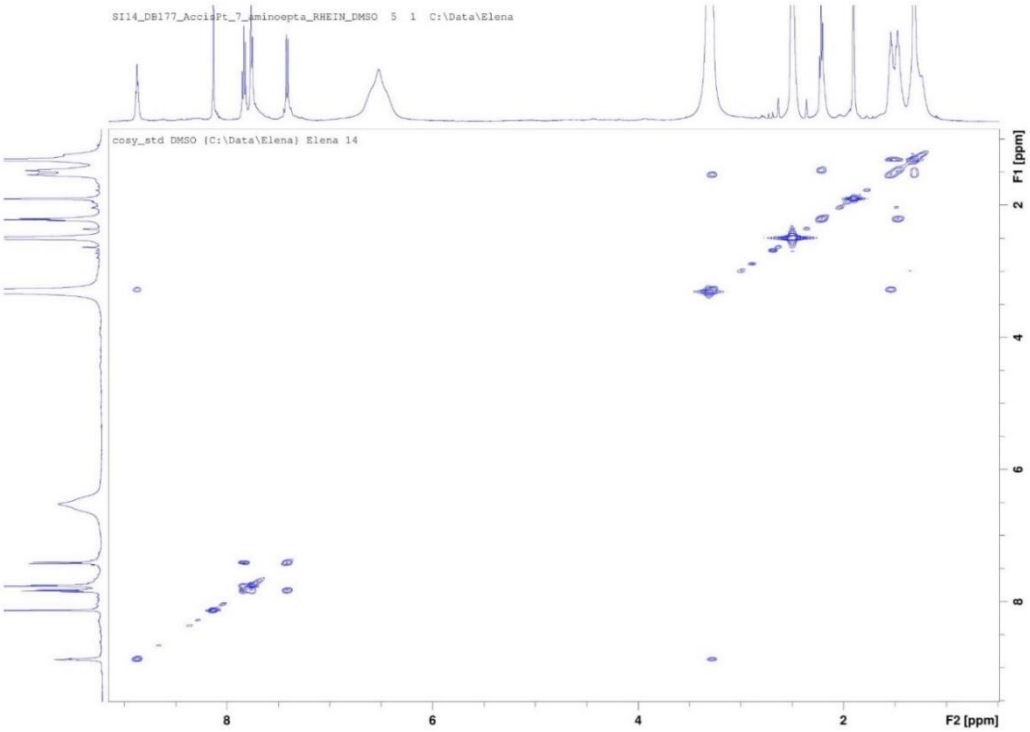

Figure S18. [^{1}H, ^{1}H] COSY NMR spectrum of **3** (in DMSO-d6).

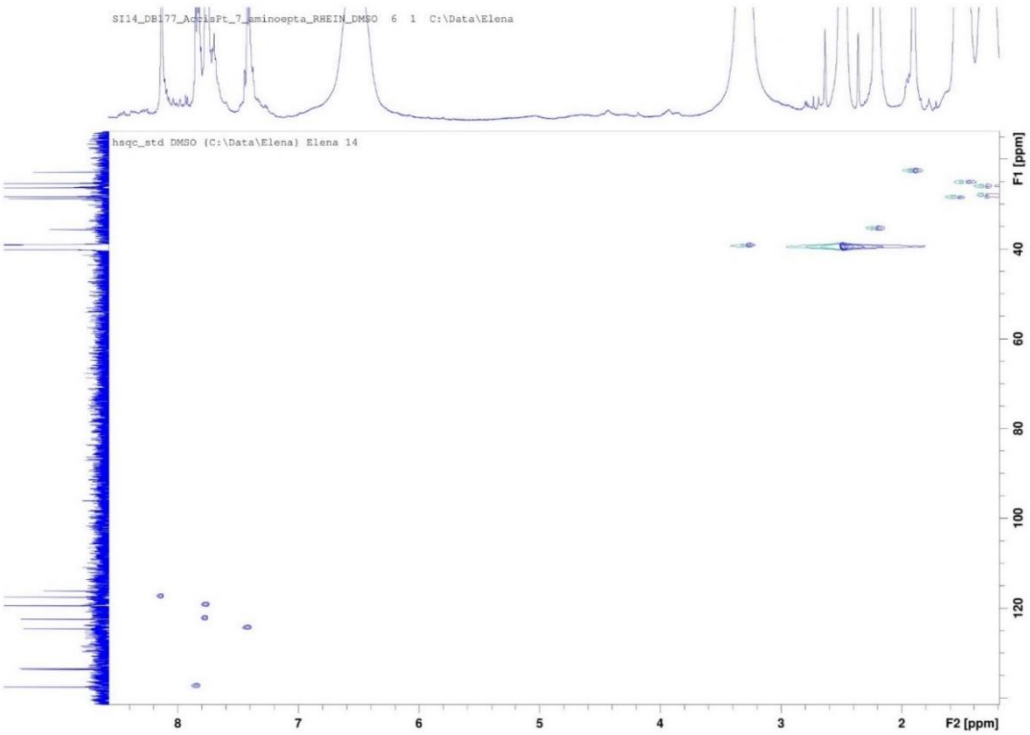

Figure S19. [^{1}H, ^{13}C] HSQC NMR spectrum of **3** (in DMSO-d6).

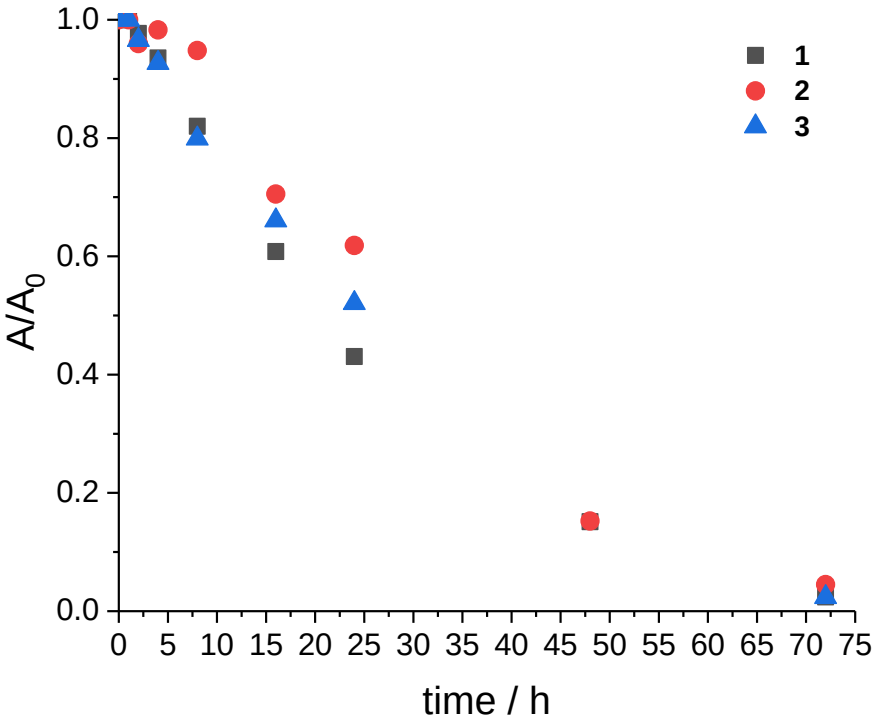

Figure S20. Solution behavior of the **1-3** complexes in RPMI 1640 cell culture medium with CH_3OH as cosolvent (10% v/v); final [Pt] = 0.1 mM. The reaction was monitored at 37 °C for 72 h by measuring the area of the RP-HPLC chromatographic peaks of the Pt complexes at the different time points (A). Data are normalized *vs.* the area at t = 0 (A_0).

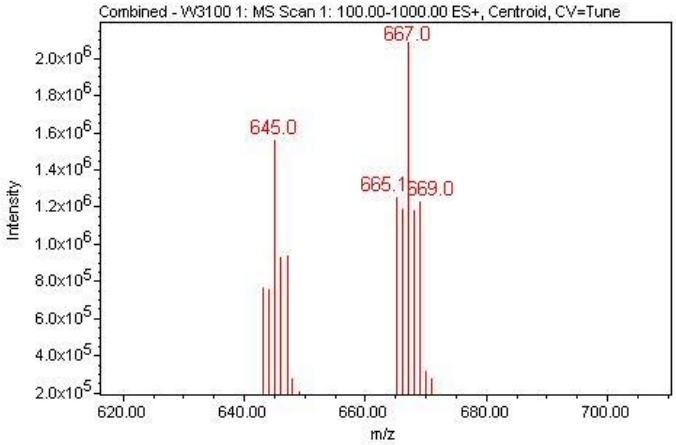

Figure S21. ESI MS spectrum of **^{15}N-1**.

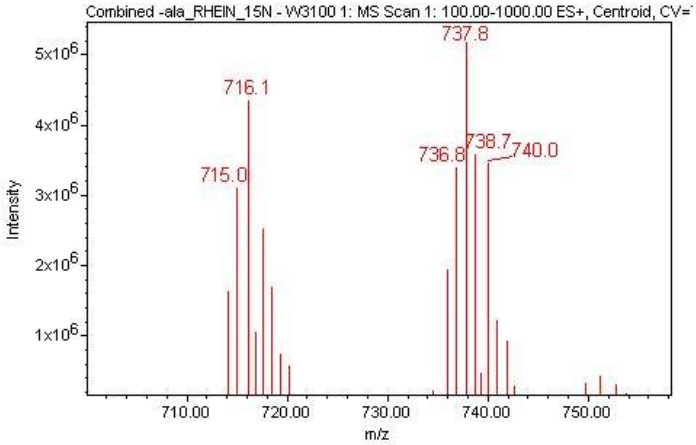

Figure S22. ESI MS spectrum of **^{15}N-2**.

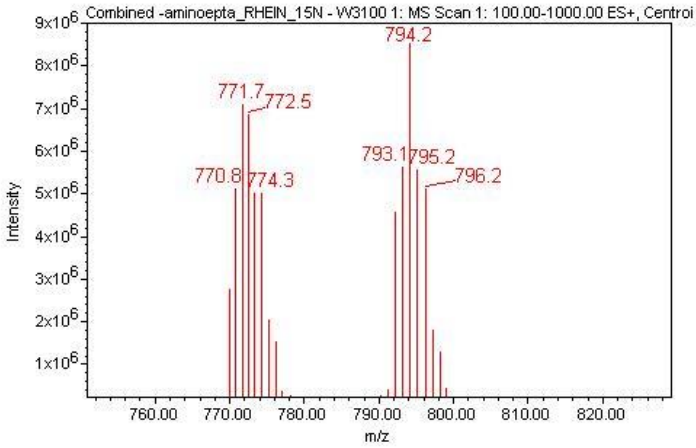

Figure S23. ESI MS spectrum of **^{15}N-3**.

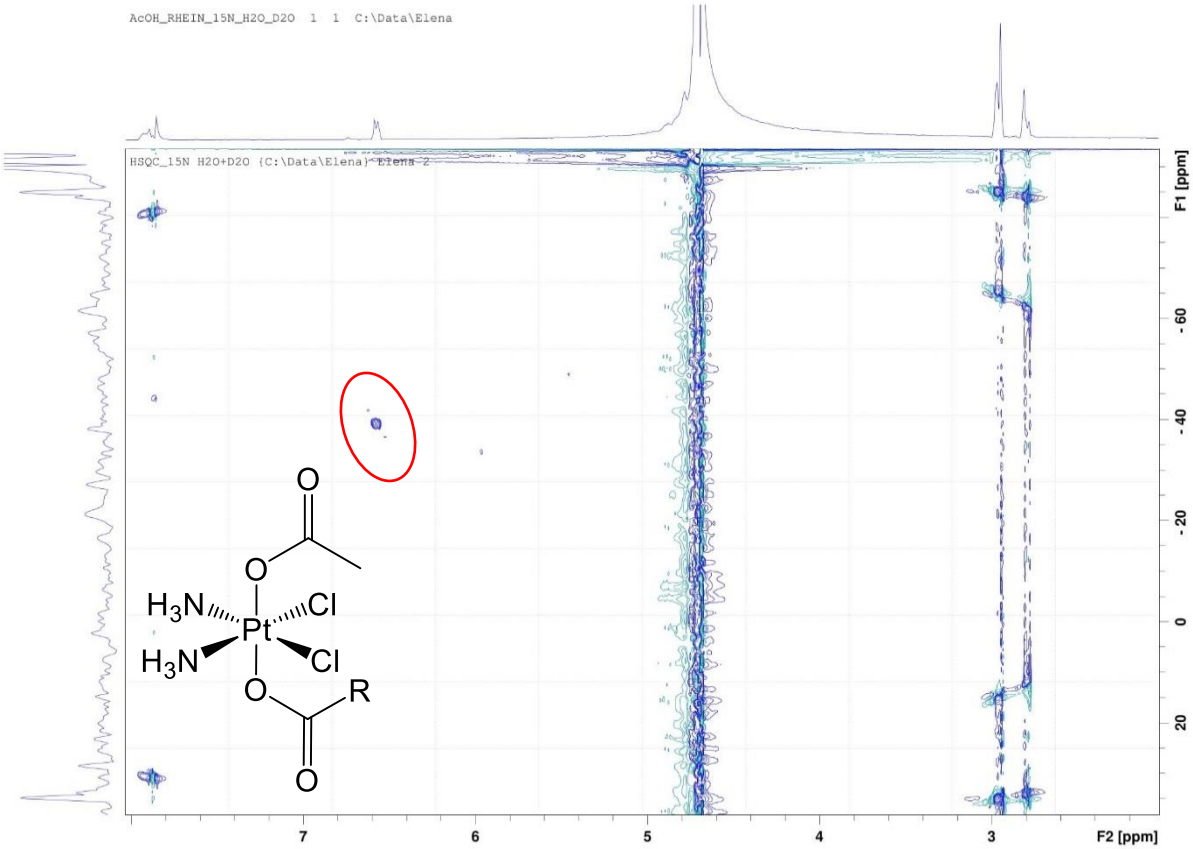

Figure S24. [^{1}H, ^{15}N] HSQC NMR spectrum of **^{15}N-1** (in DMF/D_2O/H_2O).

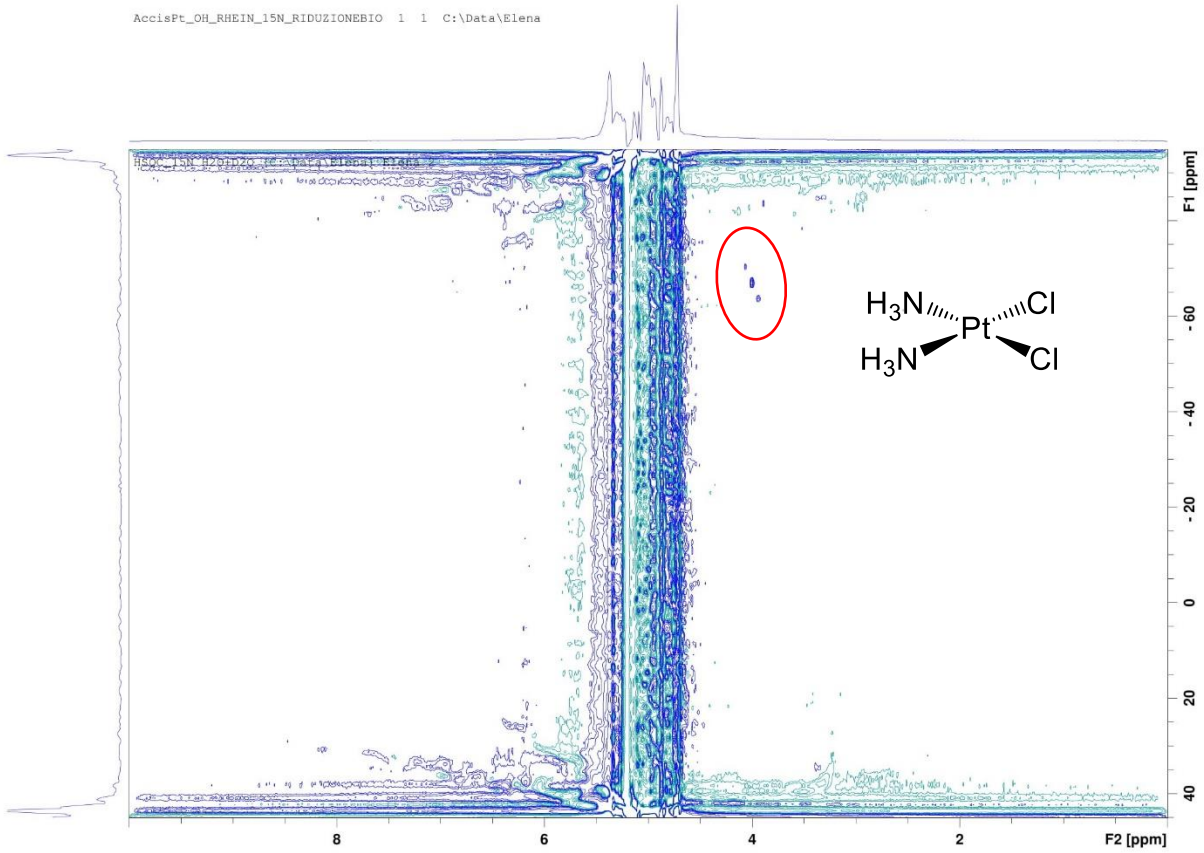

Figure S25. [^{1}H, ^{15}N] HSQC NMR spectrum of **^{15}N-1** upon reduction with cytosol.

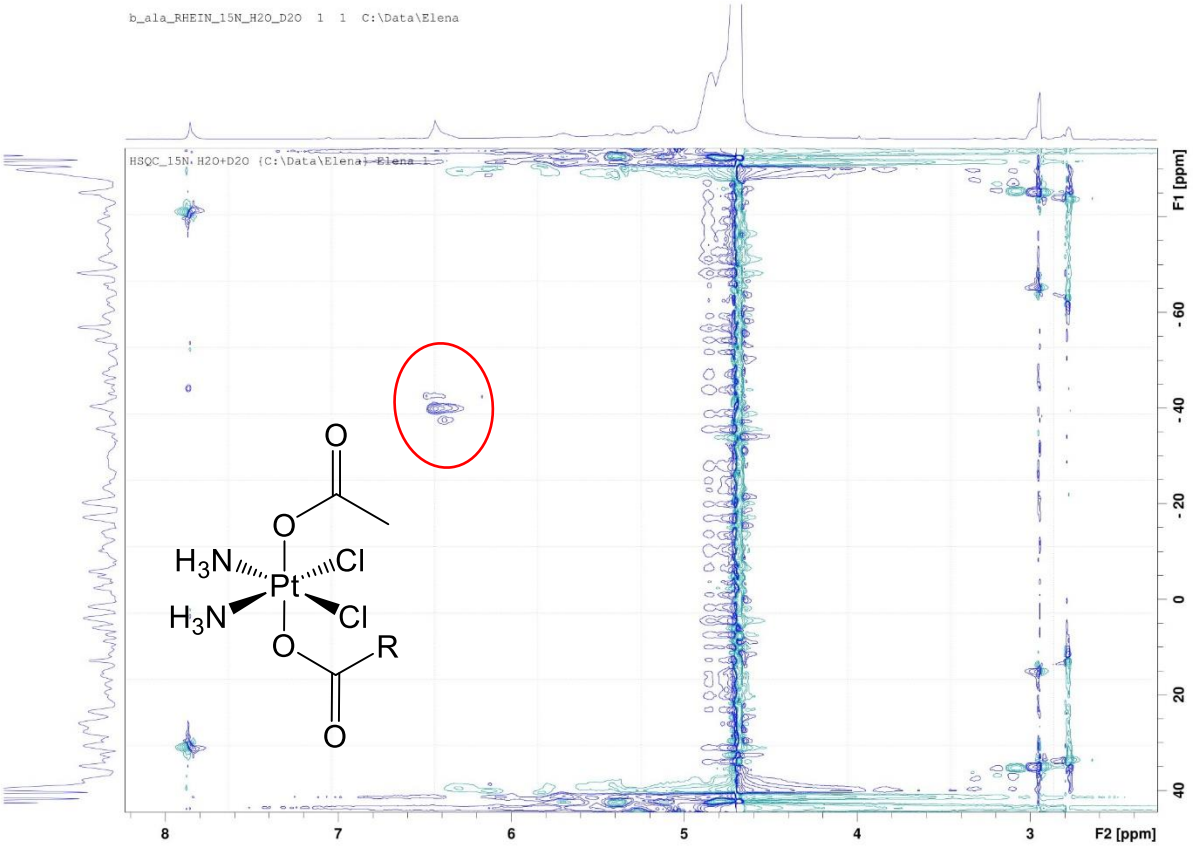

Figure S26. [^{1}H, ^{15}N] HSQC NMR spectrum of **^{15}N-2** (in DMF/D_2O/H_2O).

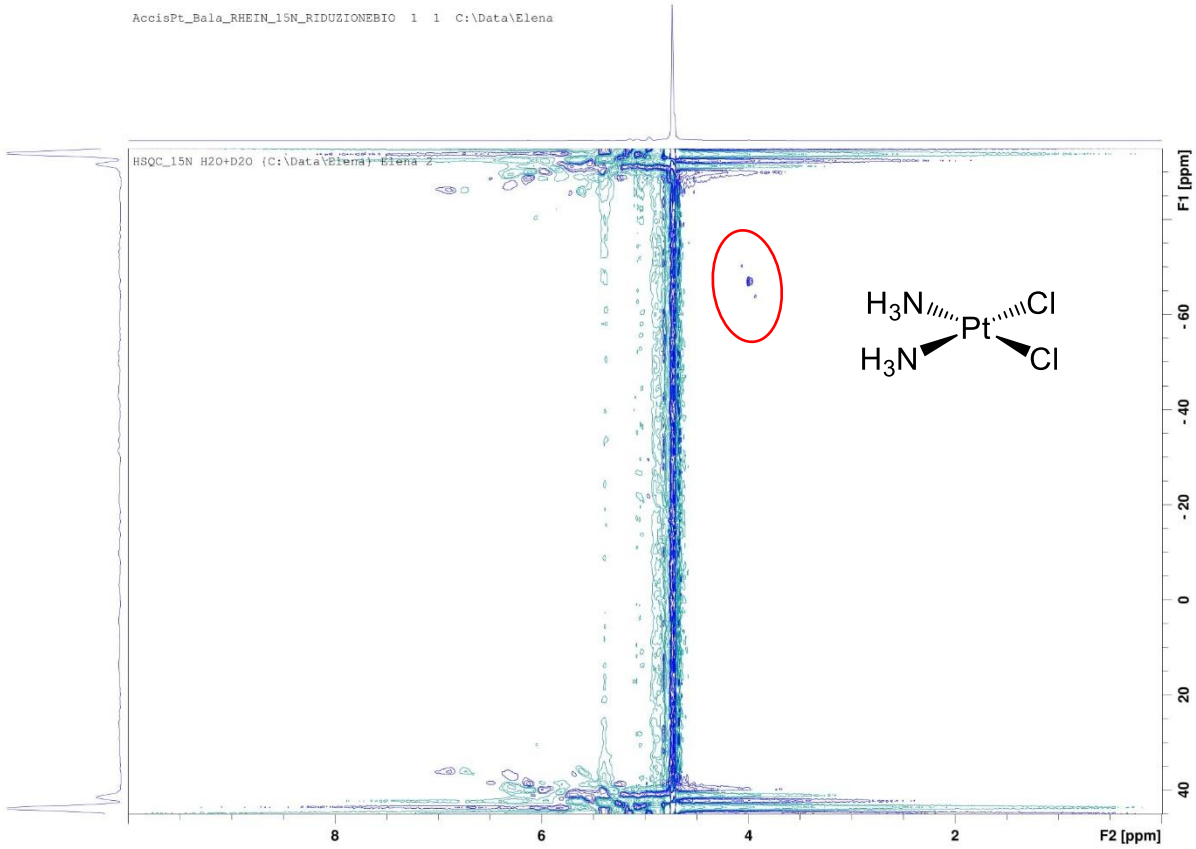

Figure S27. [^{1}H, ^{15}N] HSQC NMR spectrum of **^{15}N-2** upon reduction with cytosol.

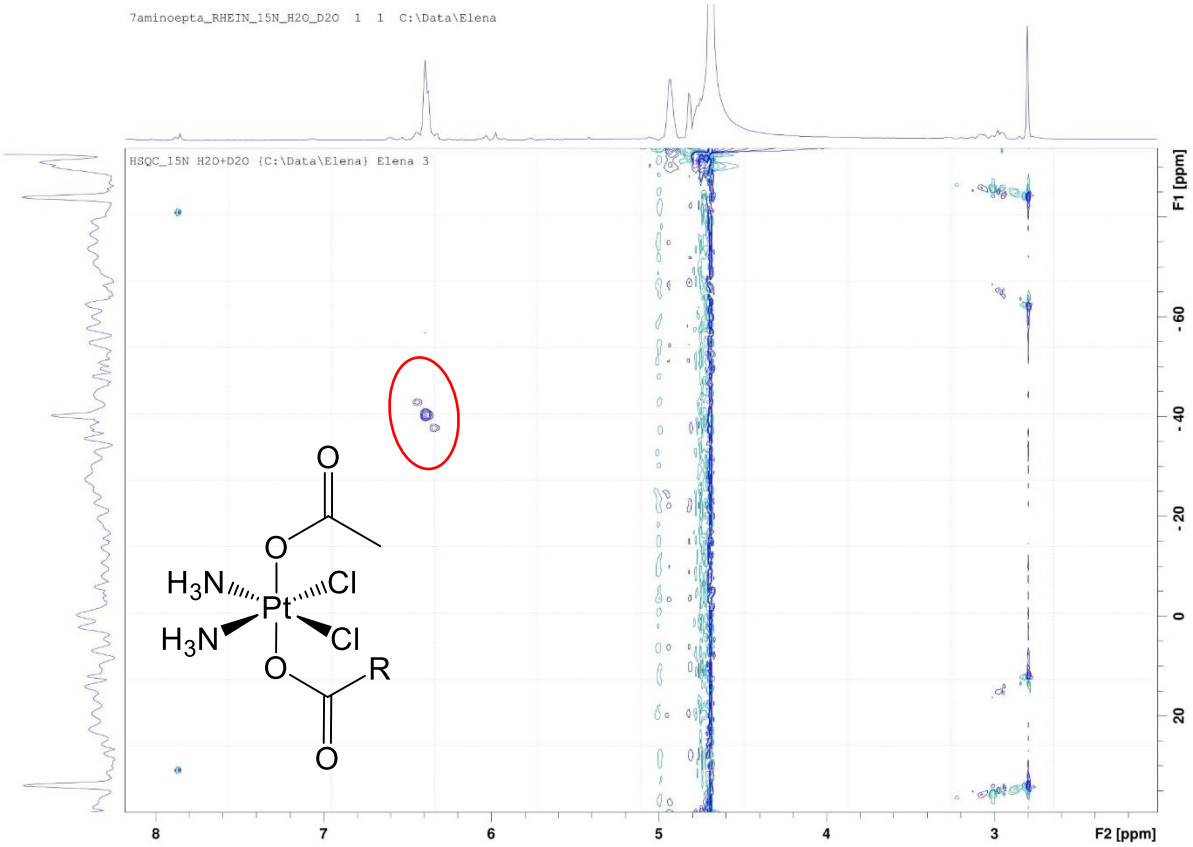

Figure S28. [^{1}H, ^{15}N] HSQC NMR spectrum of **^{15}N-3** (in DMF/D_2O/H_2O).

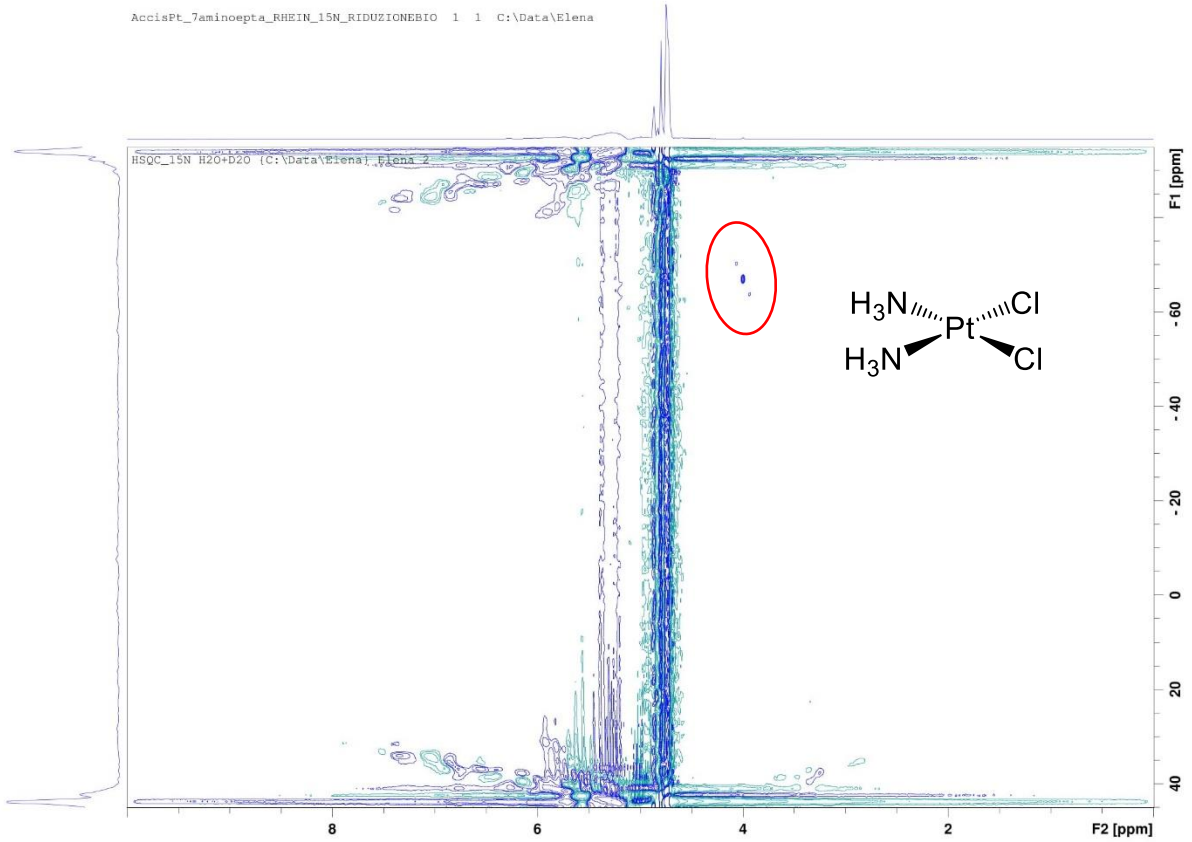

Figure S29. [^{1}H, ^{15}N] HSQC NMR spectrum of **^{15}N-3** upon reduction with cytosol.