

Supporting Information for:

Development of Cytotoxic GW7604-Zeise's Salt Conjugates as Multitarget Compounds with Selectivity for Estrogen Receptor-Positive Tumor Cells

Patricia Grabher,[†] Paul Kapitza,^{*,†} Nikolas Hörmann,[†] Amelie Scherfler,[†] Martin Hermann,[#] Michael Zwerger,[§] Hristo P. Varbanov,[†] Brigitte Kircher,^{‡,¶} Daniel Baecker,^{*,ⁱ} and Ronald Gust^{*,†}

[†] Department of Pharmaceutical Chemistry, Institute of Pharmacy, Center for Molecular Biosciences Innsbruck, University of Innsbruck, Innrain 80/82, A-6020 Innsbruck.

[#] Department of Anesthesiology & Critical Care Medicine, Medical University Innsbruck, Anichstrasse 35, A-6020 Innsbruck.

[§] Department of Pharmacognosy, Institute of Pharmacy, Center for Molecular Biosciences Innsbruck, University of Innsbruck, Innrain 80/82, A-6020 Innsbruck.

[‡] Department of Internal Medicine V, Haematology & Oncology, Immunobiology and Stem Cell Laboratory, Medical University Innsbruck, Anichstrasse 35, A-6020 Innsbruck.

[¶] Tyrolean Cancer Research Institute, Innrain 66, A-6020 Innsbruck.

ⁱ Department of Pharmaceutical and Medicinal Chemistry, Institute of Pharmacy, Freie Universität Berlin, Königin-Luise-Straße 2+4, D-14195 Berlin.

Corresponding Authors:

Paul Kapitza (paul.kapitza@uibk.ac.at)

Daniel Baecker (d.baecker@fu-berlin.de)

Ronald Gust (gust.ronald@gmail.com)

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1. ^1H , ^{13}C , $^1\text{H}/^1\text{H}$ COSY, AND $^1\text{H}/^{13}\text{C}$ HSQC NMR SPECTRA OF THE GW7604-ALK-PTCL₃ COMPLEXES

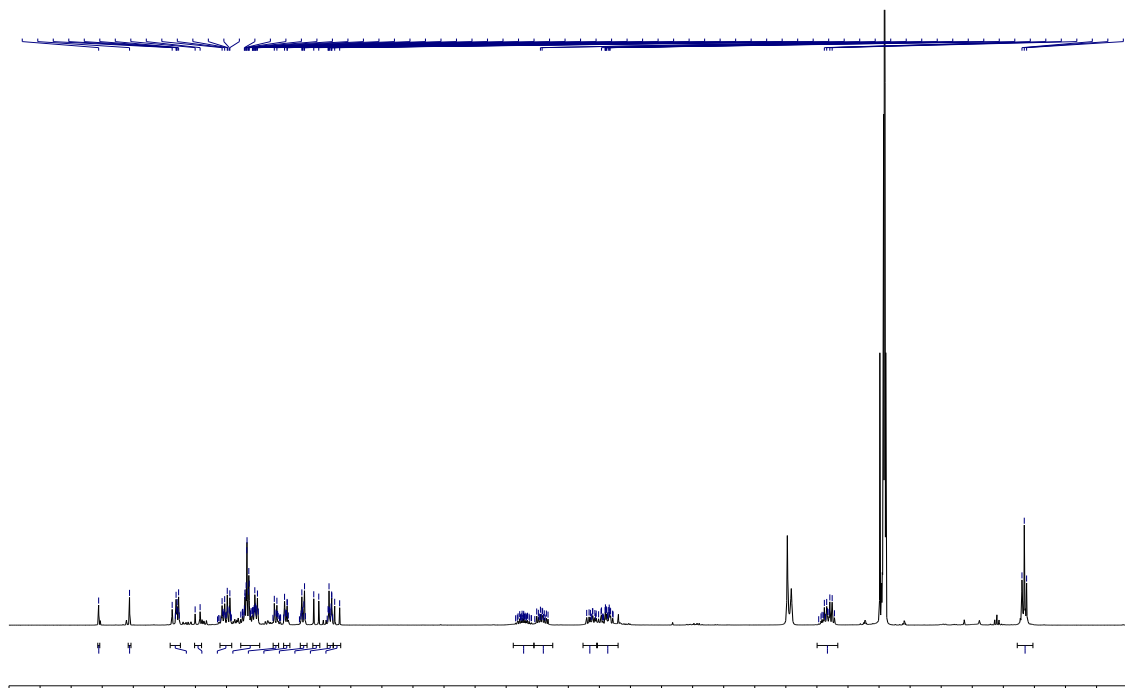


Figure S1. ^1H NMR (400 MHz) of GW7604-Prop-PtCl₃ in acetone-*d*₆

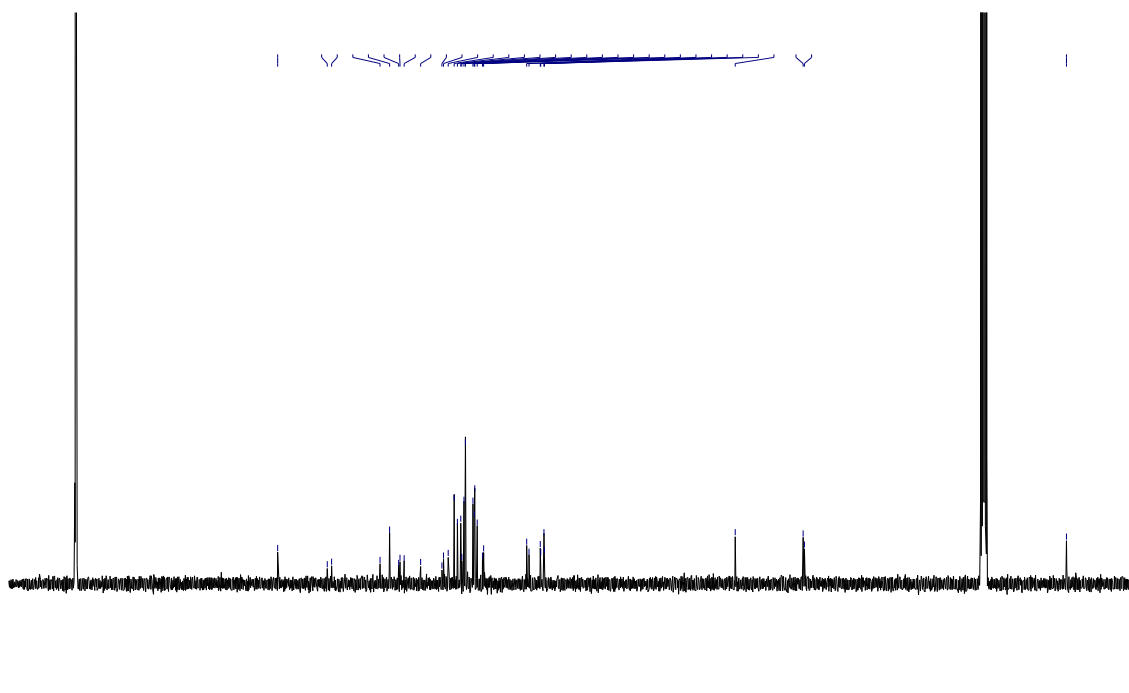


Figure S2. ^{13}C NMR (101 MHz) of GW7604-Prop-PtCl₃ in acetone-*d*₆.

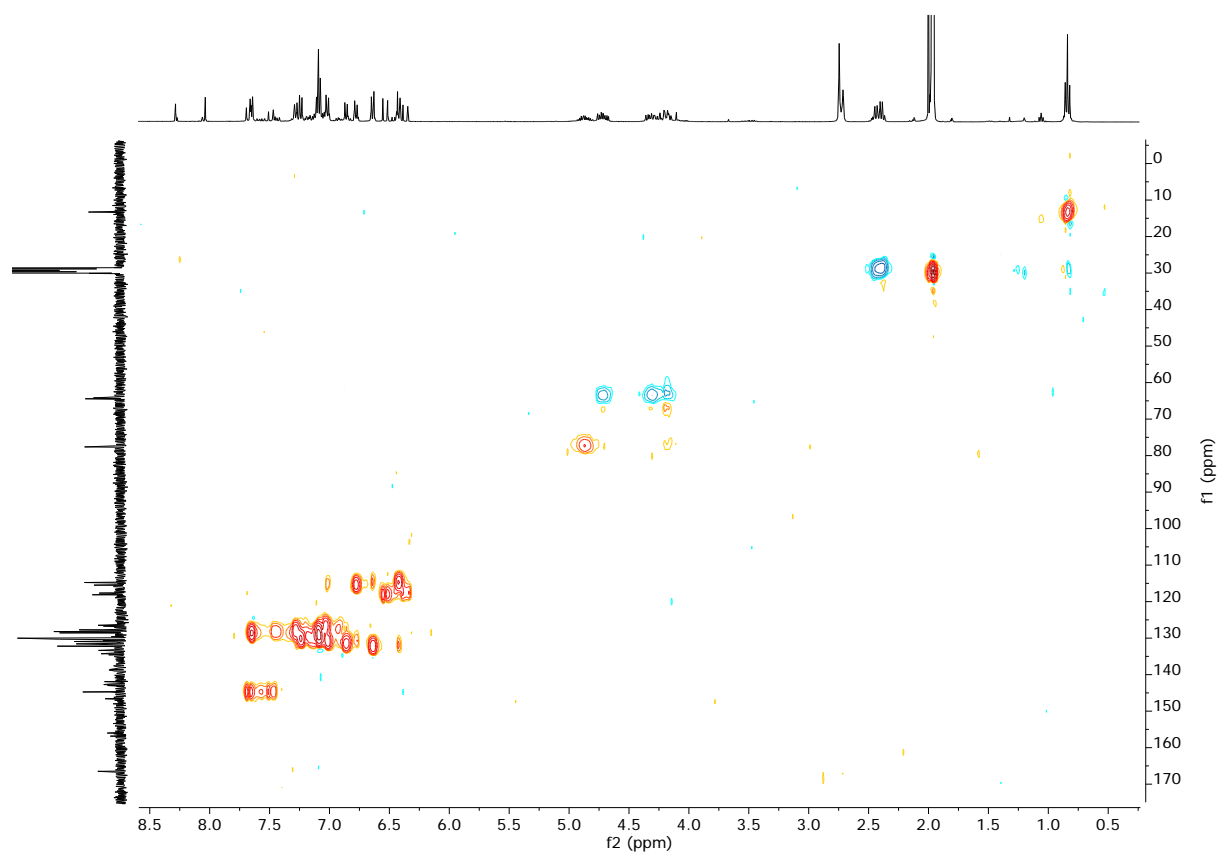


Figure S3. $^1\text{H}/^{13}\text{C}$ HSQC of GW7604-Prop-PtCl₃ in acetone-*d*₆

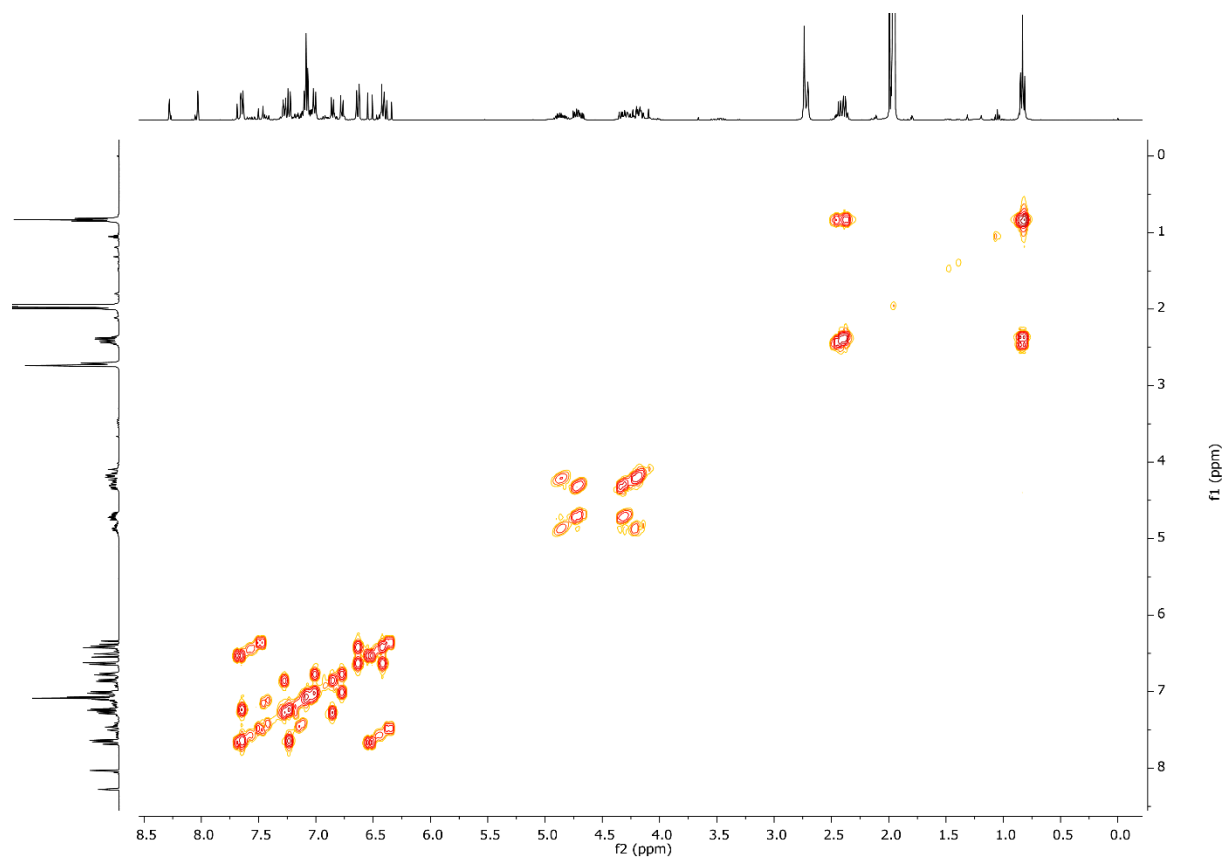


Figure S4. ^1H COSY of GW7604-Prop-PtCl₃ in acetone-*d*₆.

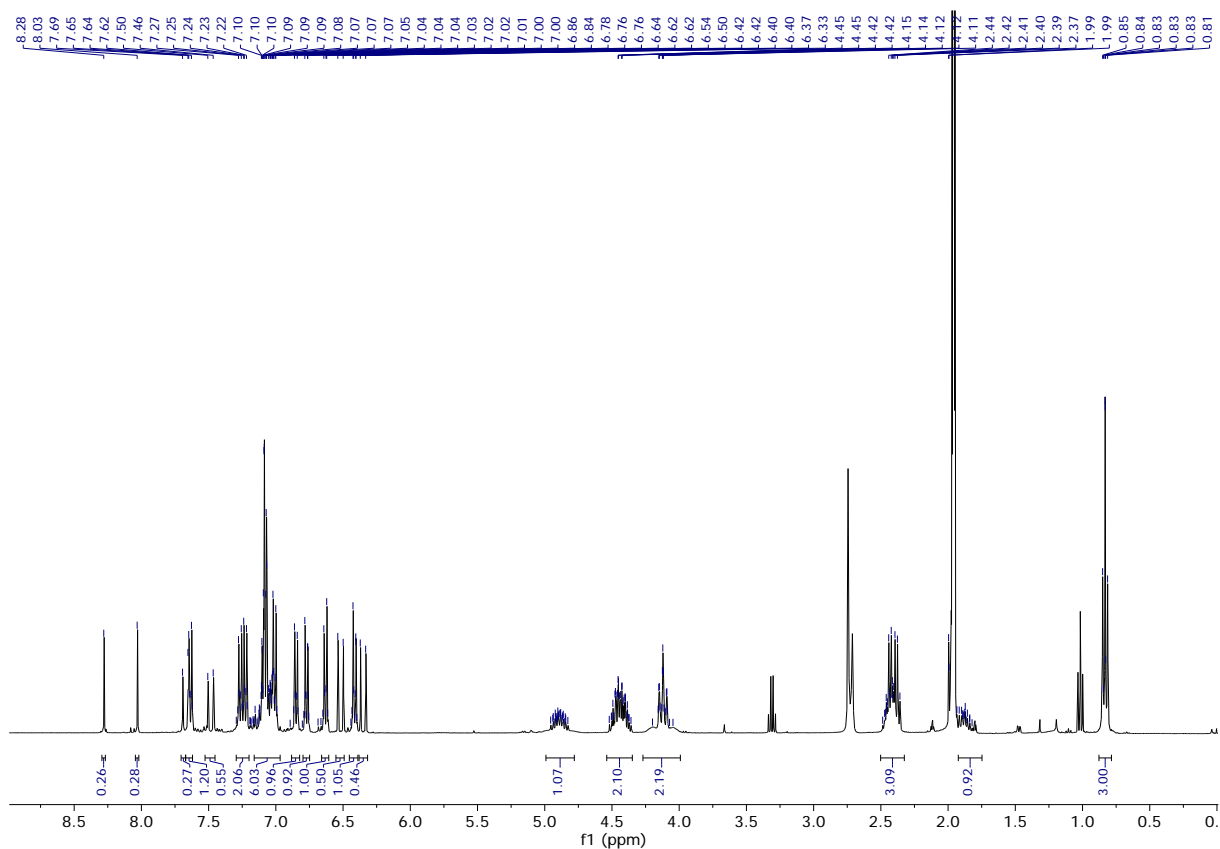


Figure S5. ^1H NMR (400 MHz) of the GW7604-But- PtCl_3 in acetone- d_6 .

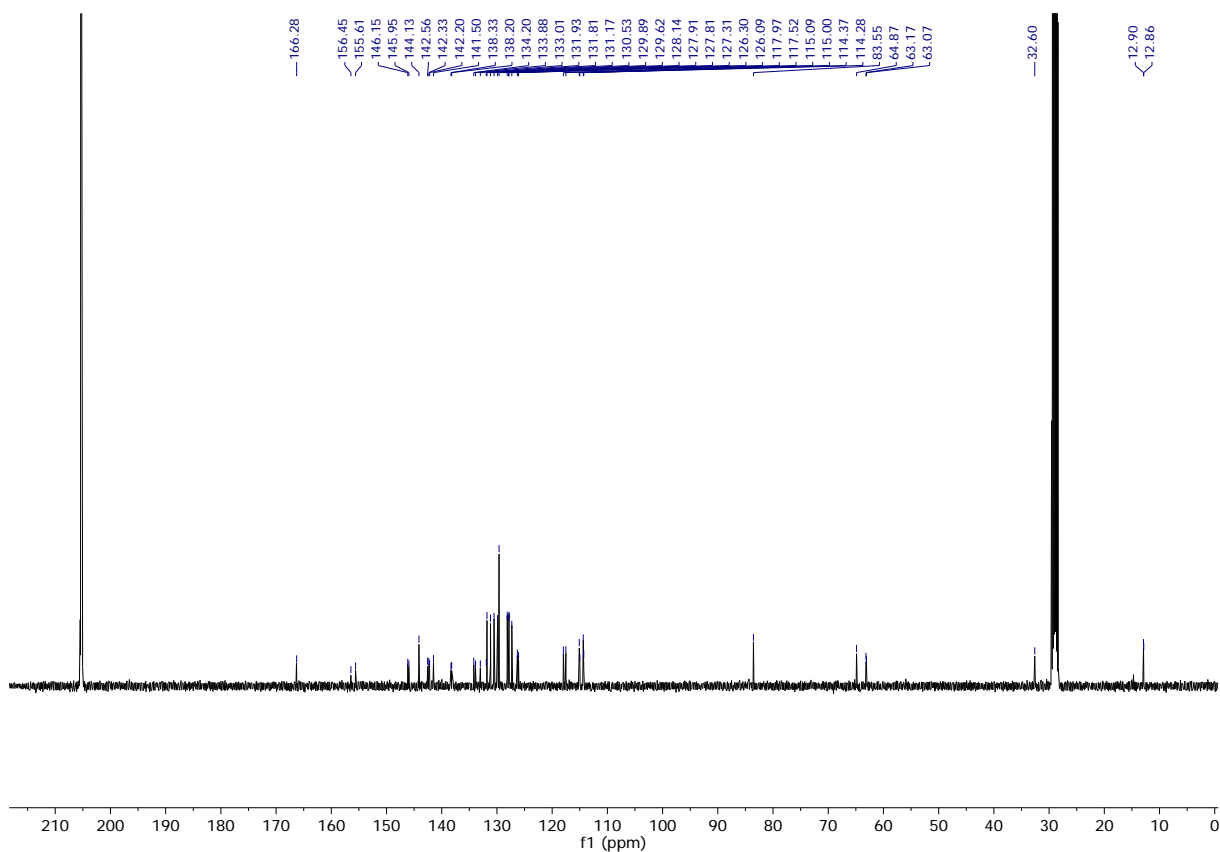


Figure S6. ^{13}C NMR (101 MHz) of GW7604-But- PtCl_3 in acetone- d_6 .

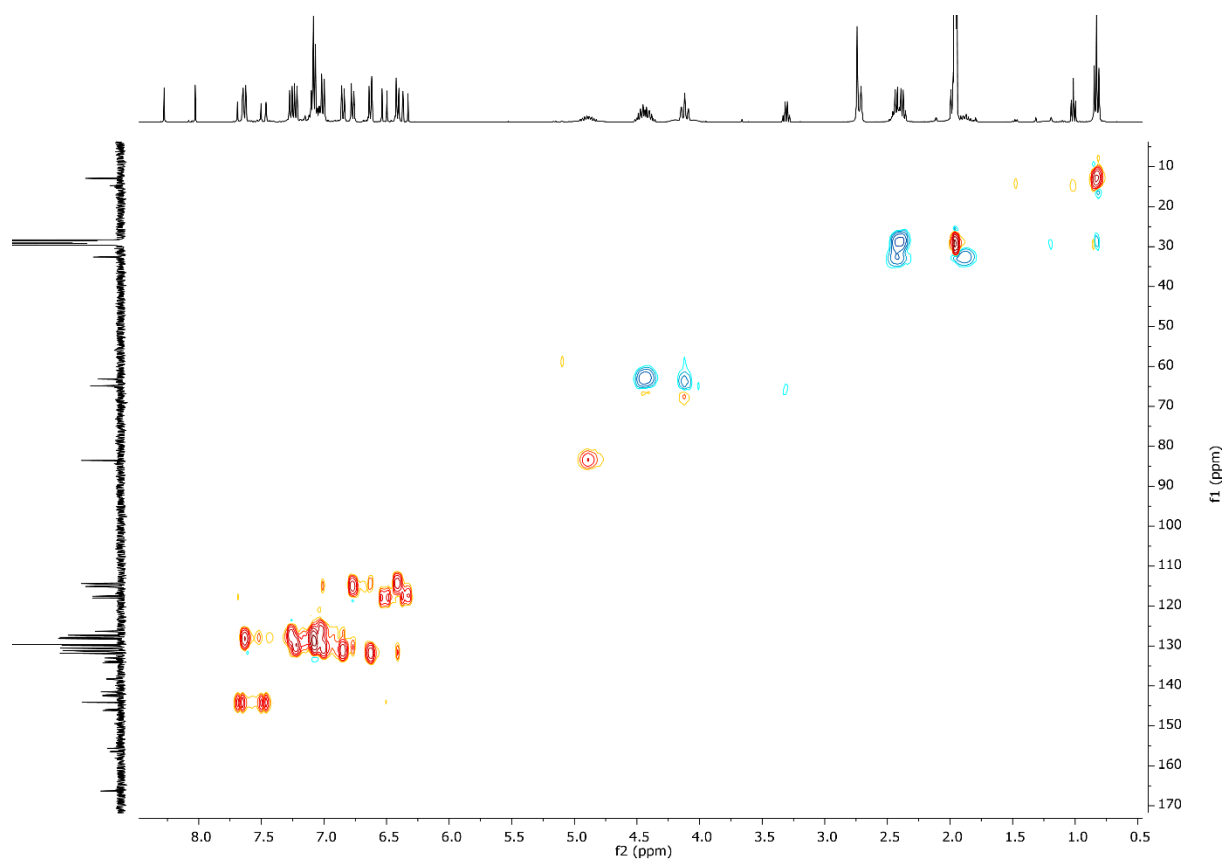


Figure S7. $^1\text{H}/^{13}\text{C}$ HSQC of GW7604-But-PtCl₃ in acetone-*d*₆.

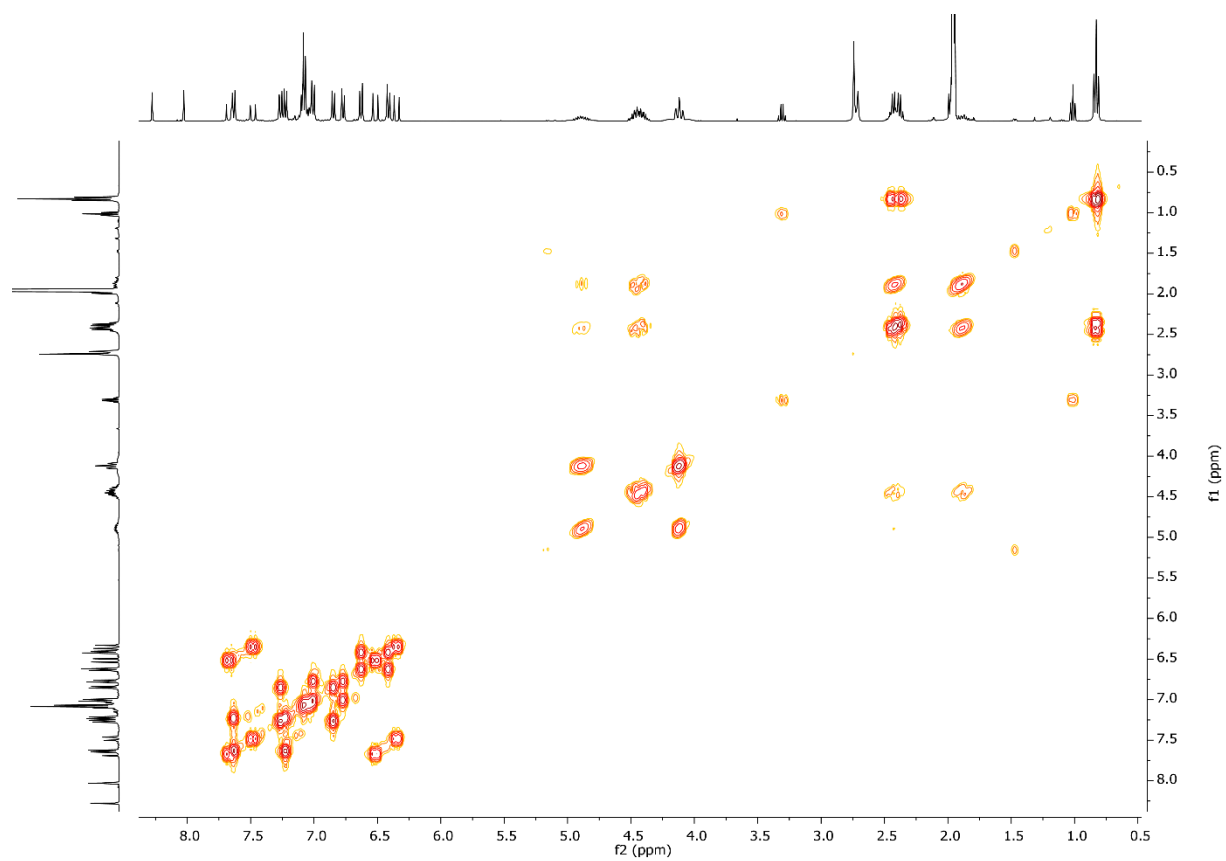


Figure S8. ^1H COSY of GW7604-But-PtCl₃ in acetone-*d*₆.

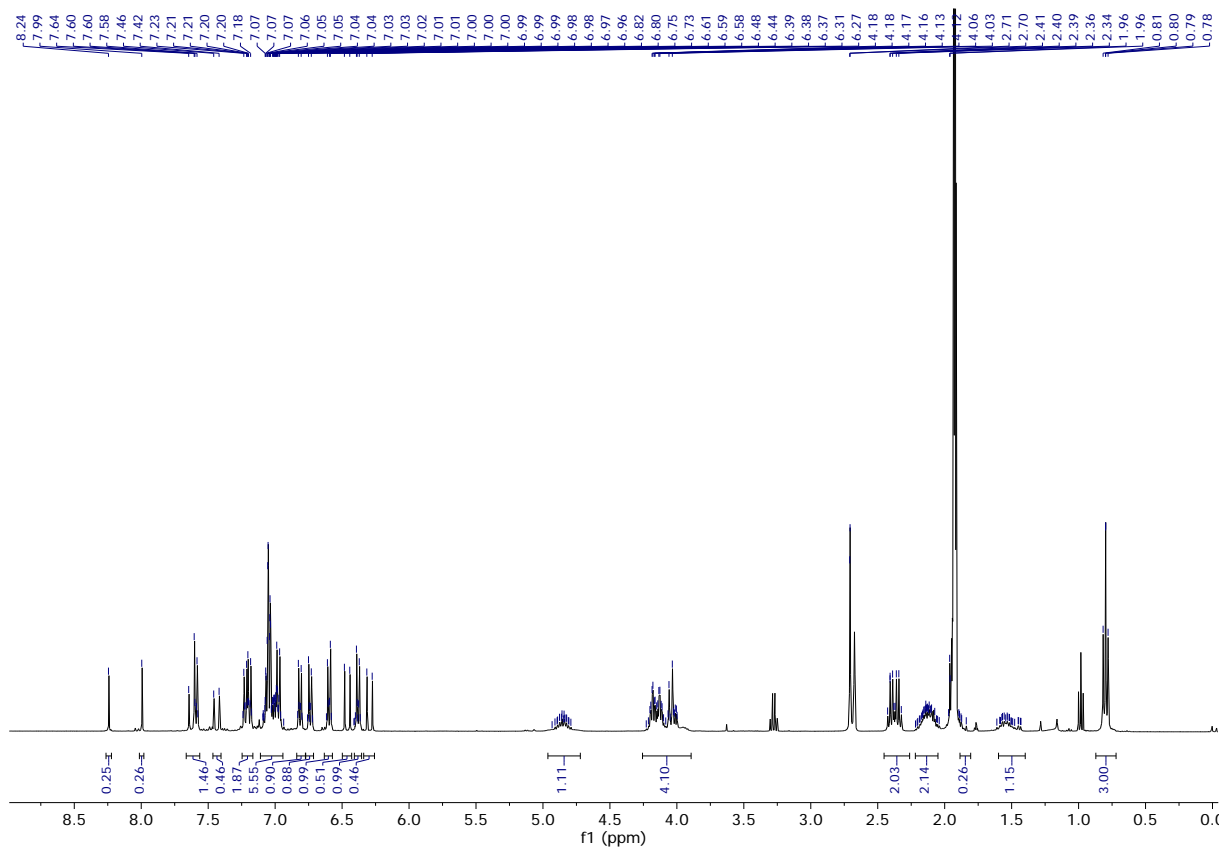


Figure S9. ^1H NMR (400 MHz) of GW7604-Pent-PtCl₃ in acetone-*d*₆.

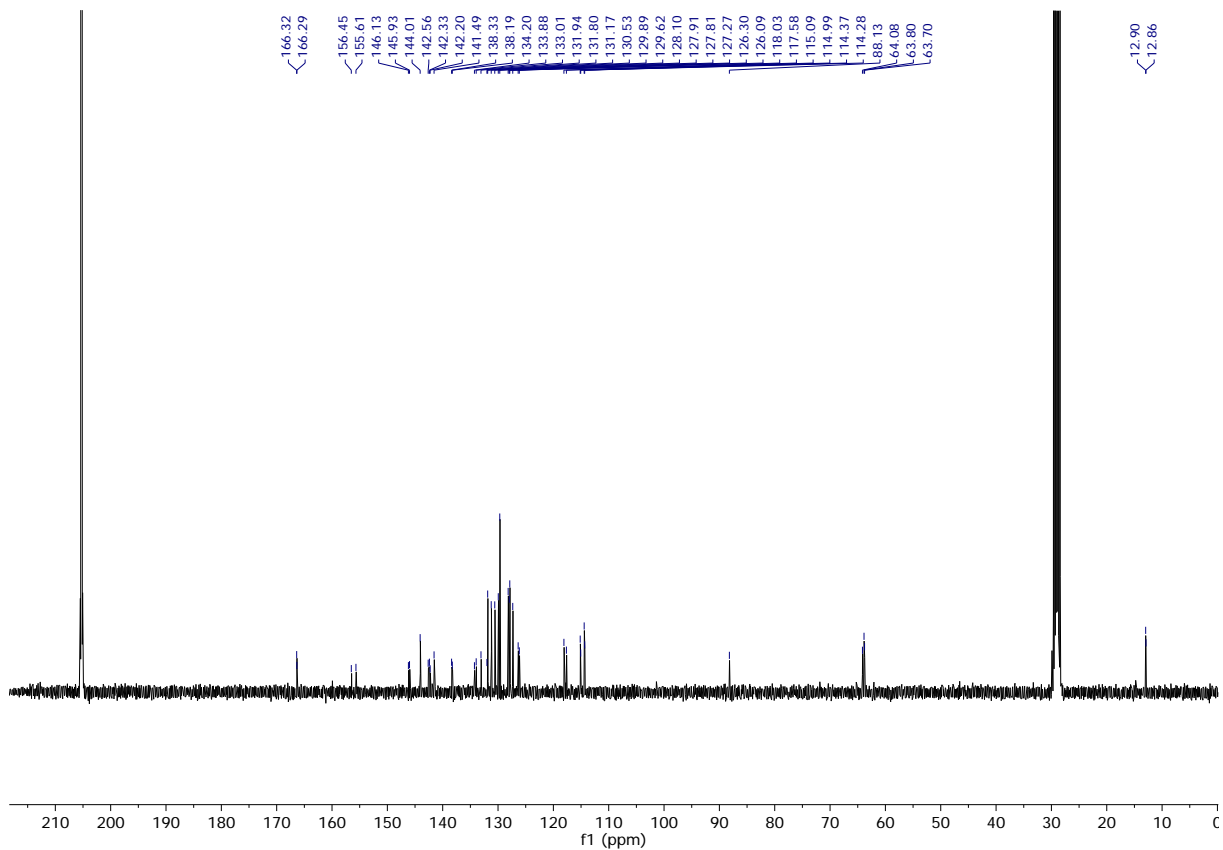


Figure S10. ^{13}C NMR (101 MHz) of GW7604-Pent-PtCl₃ in acetone-*d*₆.

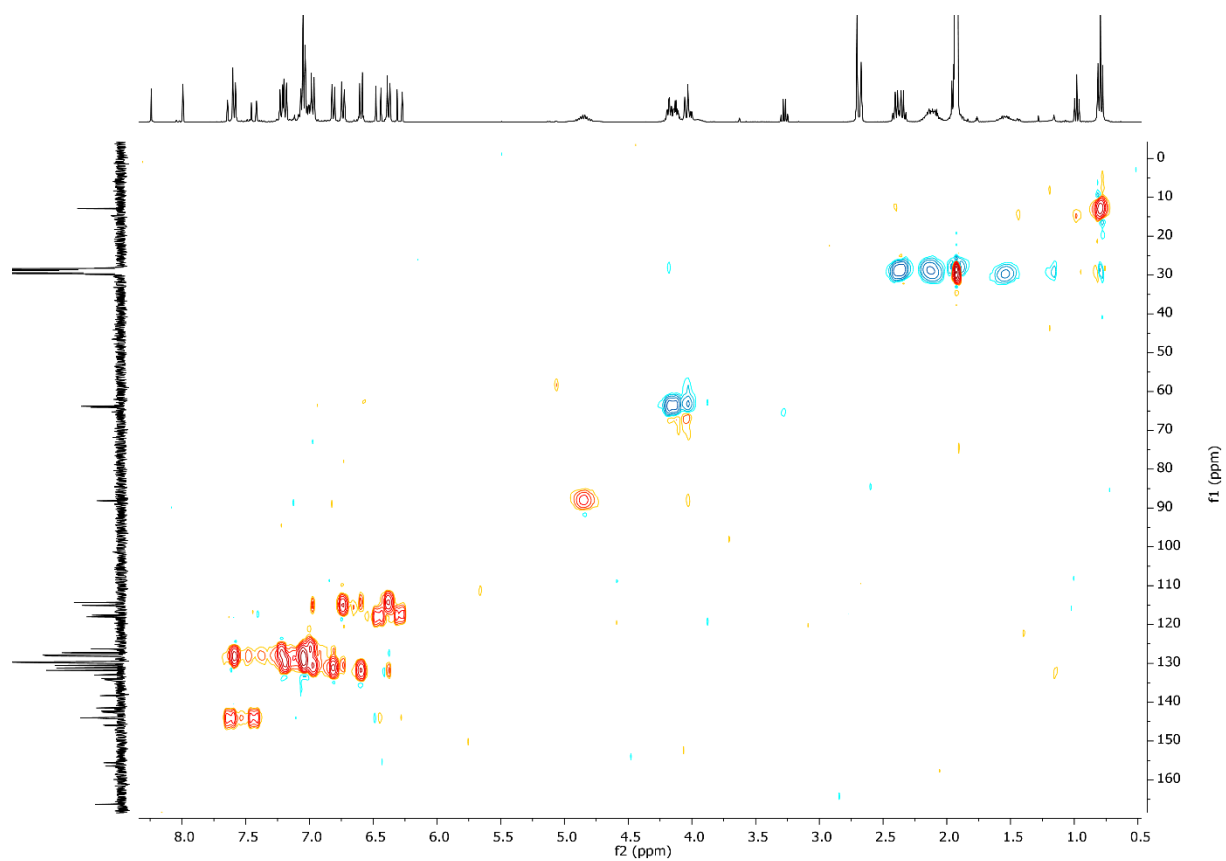


Figure S11. $^1\text{H}/^{13}\text{C}$ HSQC of the GW7604-Pent-PtCl₃ in acetone-*d*₆.

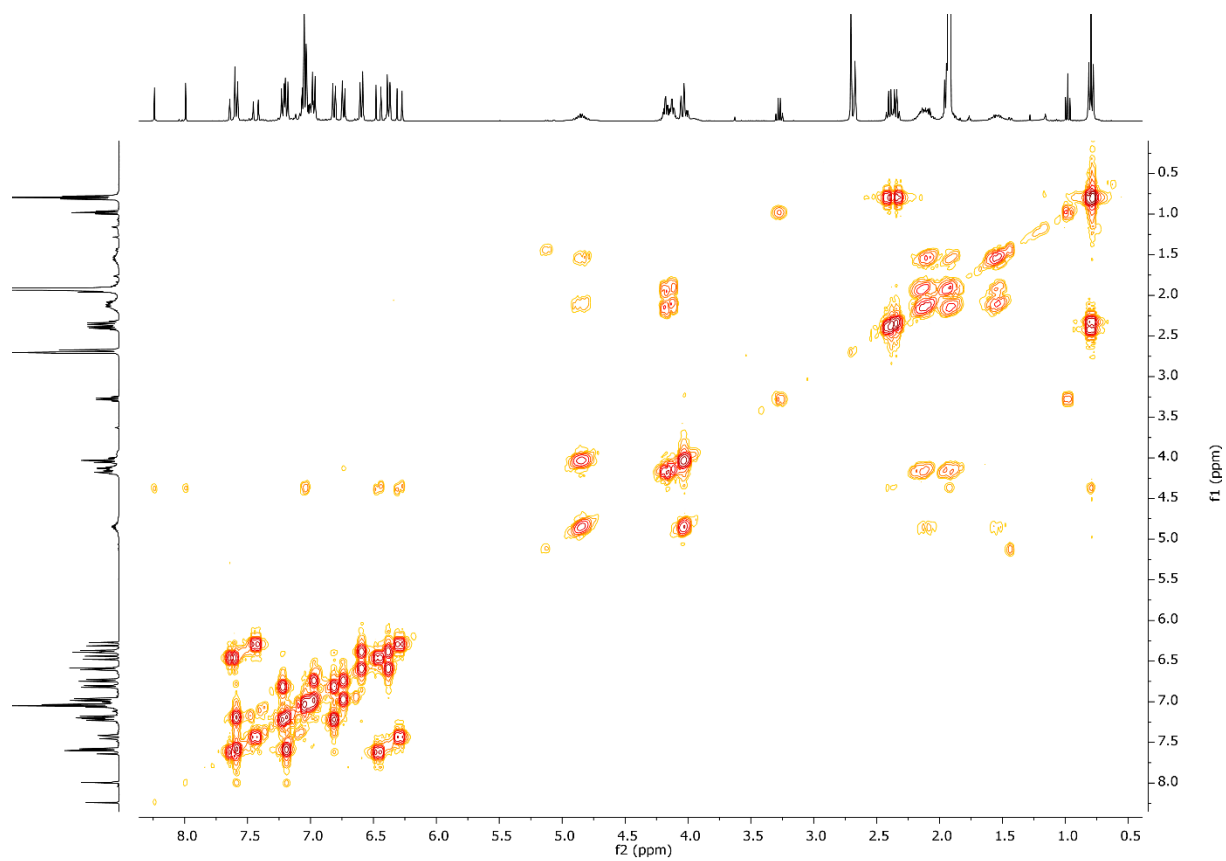


Figure S12. ^1H COSY of the GW7604-Pent-PtCl₃ in acetone-*d*₆.

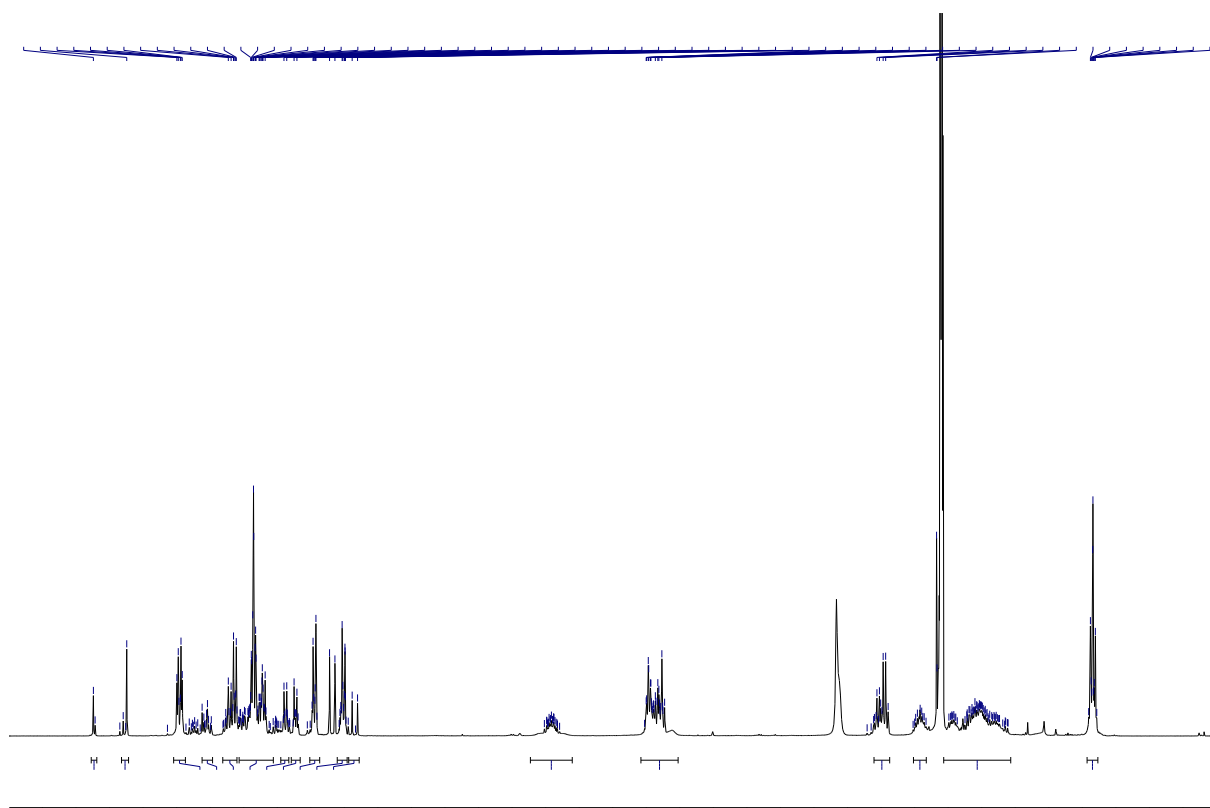


Figure S13. ^1H NMR (400 MHz) of GW7604-Hex-PtCl₃ in acetone-*d*₆.

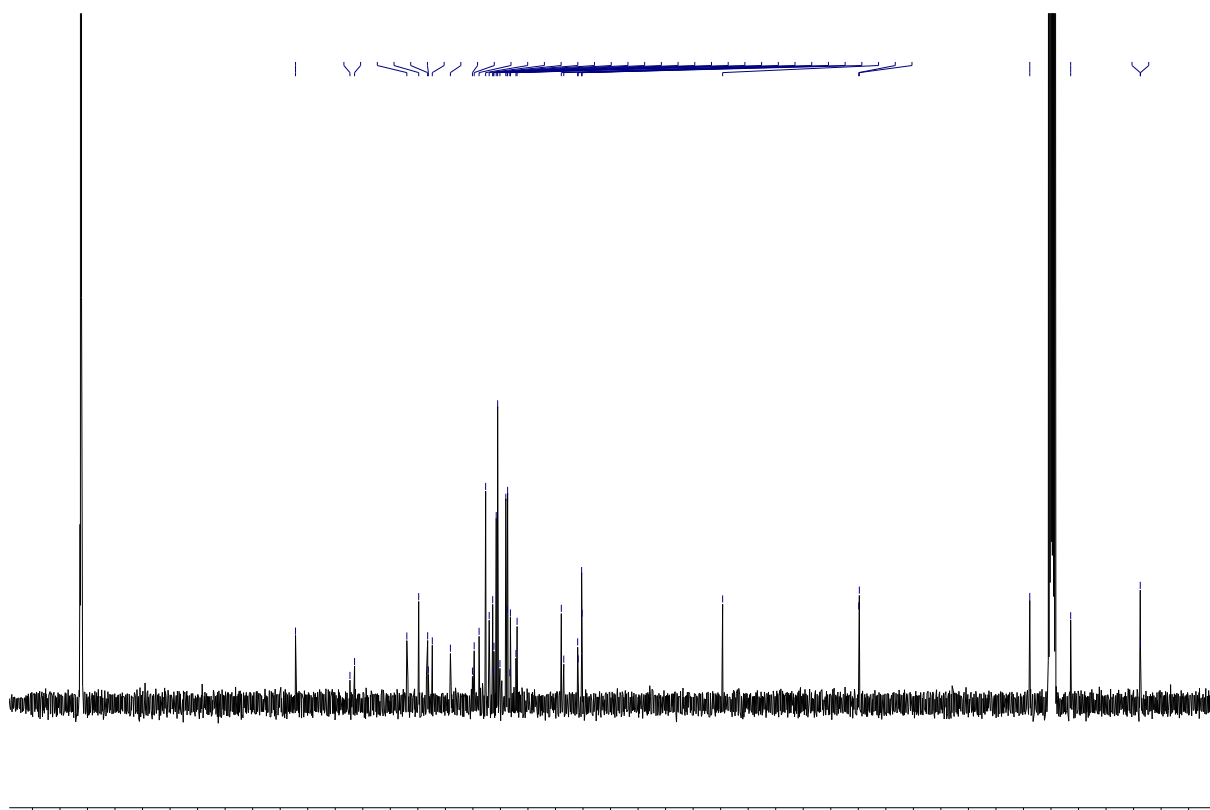


Figure S14. ^{13}C NMR (101 MHz) of GW7604-Hex-PtCl₃ in acetone-*d*₆.

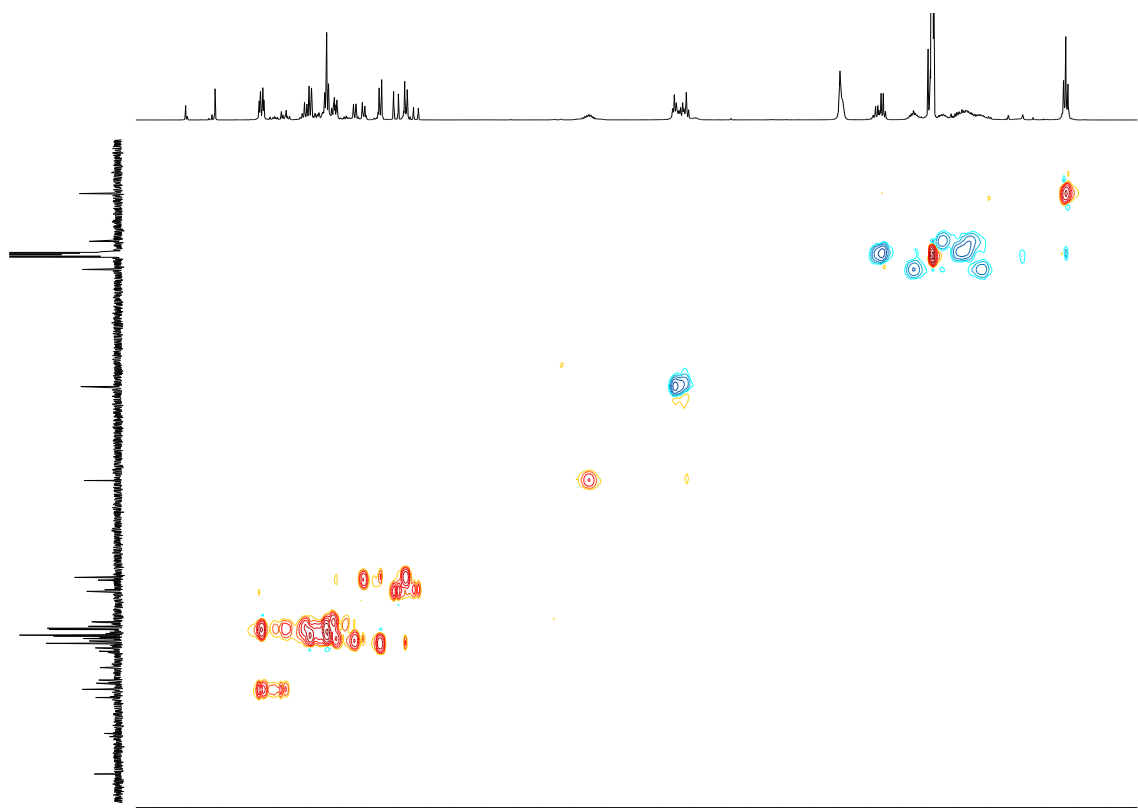


Figure S15. $^1\text{H}/^{13}\text{C}$ HSQC of GW7604-Hex-PtCl₃ in acetone-*d*₆.

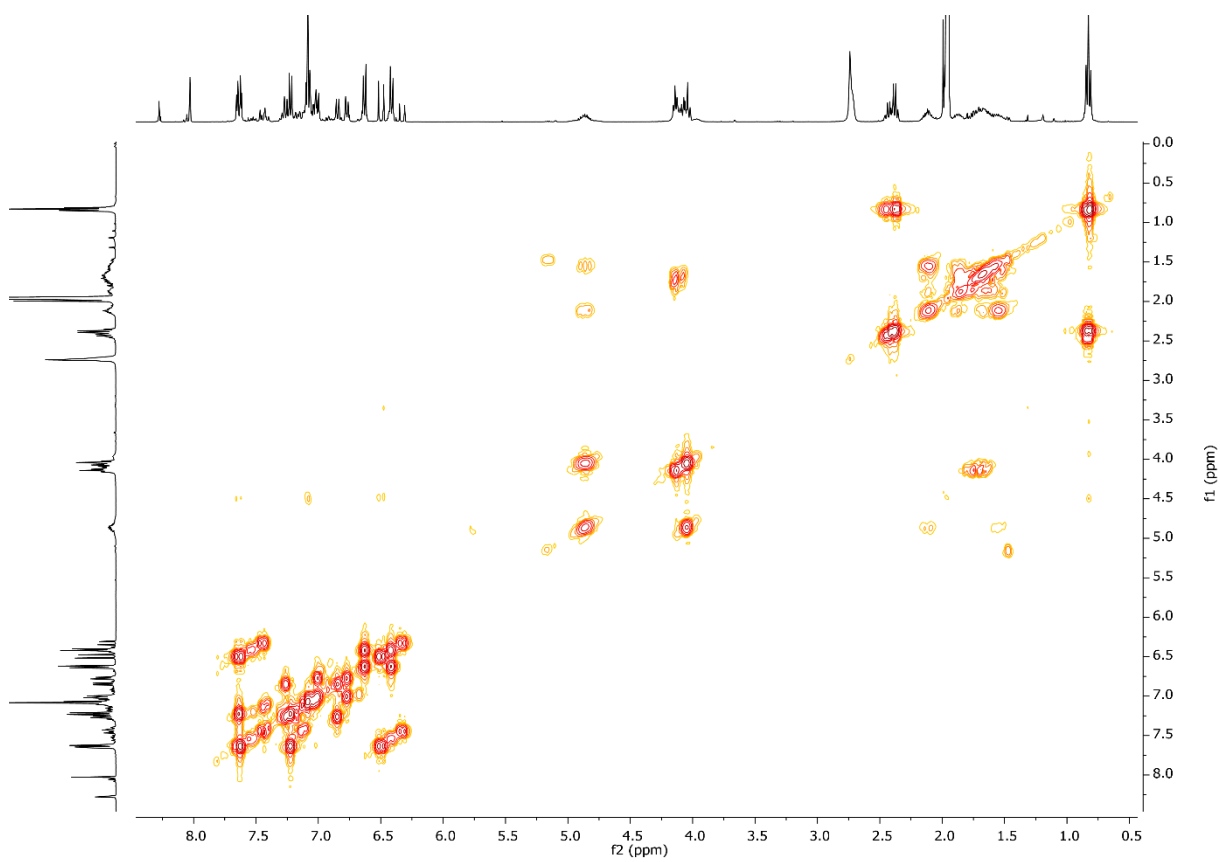


Figure S16. ^1H COSY of GW7604-Hex-PtCl₃ in acetone-*d*₆.

2. CONFORMATIONAL DESCRIPTION OF GW7604-BUT-PTCl₃ ISOMERS

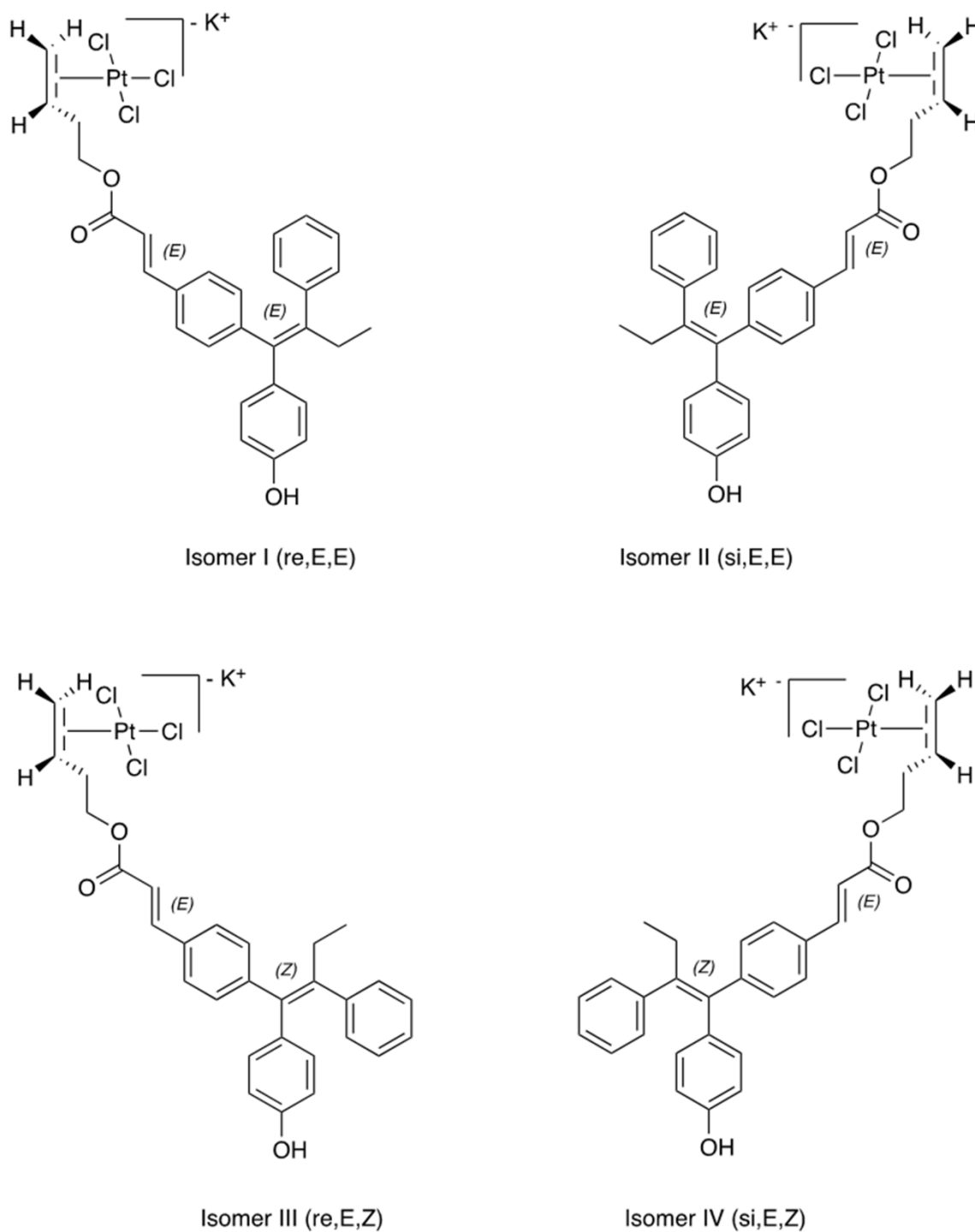


Figure S17. Conformational description of **GW7604-But-PtCl₃** isomers I and II as well as isomers III and IV are enantiomers. The enantiomeric pairs I/II and III/IV are diastereomeric to each other. They cause for instance two sets of Signals in the ¹H NMR spectrum (Figure 1).

3. NMR SPECTRA FROM STABILITY STUDIES IN ORGANIC SOLVENTS

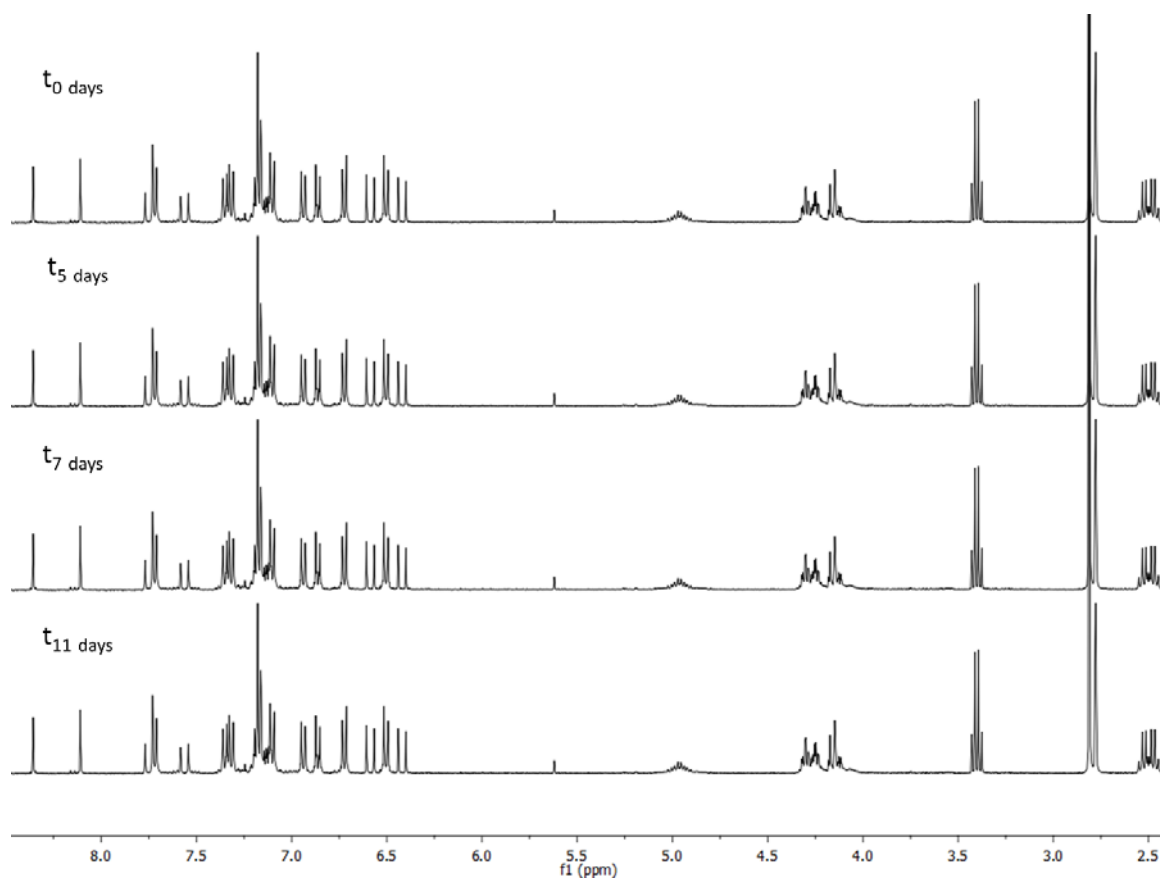


Figure S18. ^1H NMR (400 MHz) of GW7604-Pent-PtCl₃ in acetone-*d*₆.

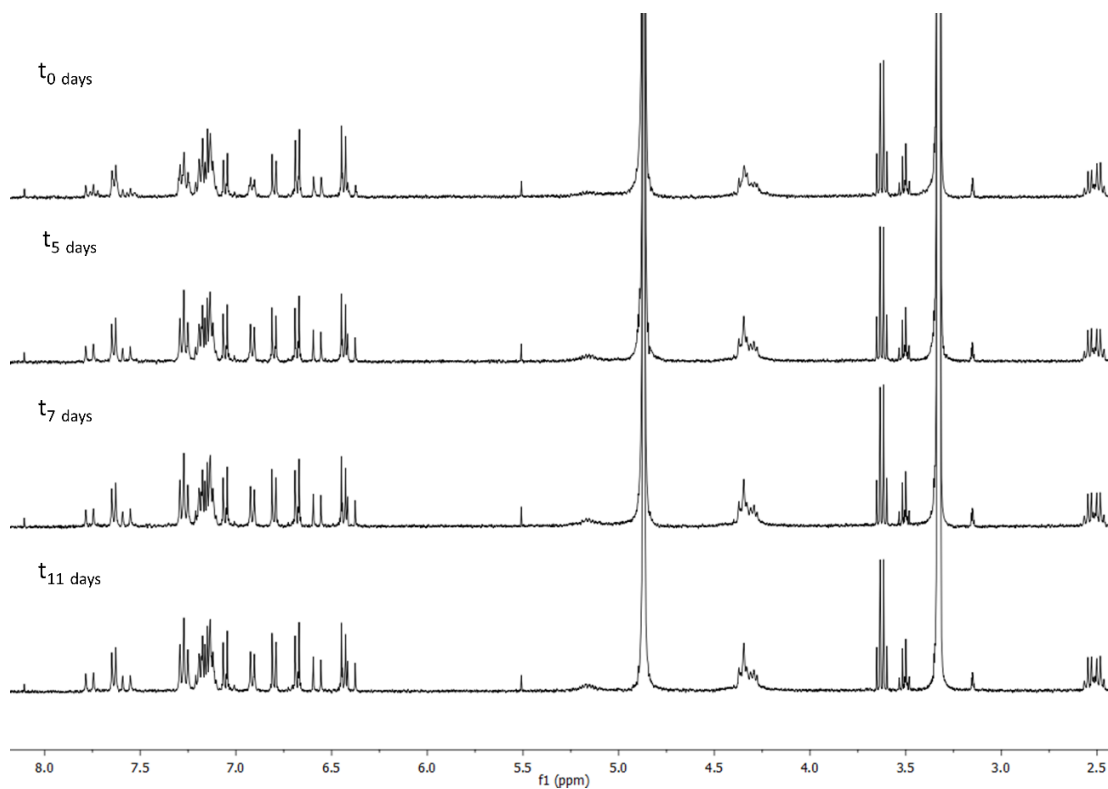


Figure S19. ^1H NMR (400 MHz) of GW7604-Pent-PtCl₃ in methanol-*d*₄.

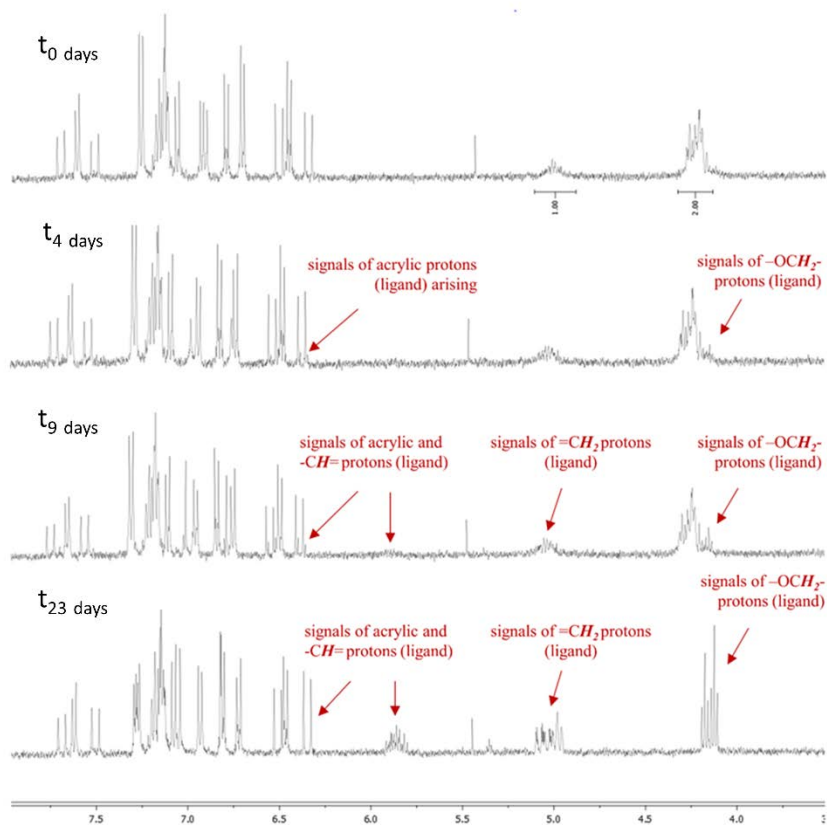


Figure S20. ^1H NMR (400 MHz) of GW7604-Pent-PtCl₃ in acetonitrile-*d*₃.

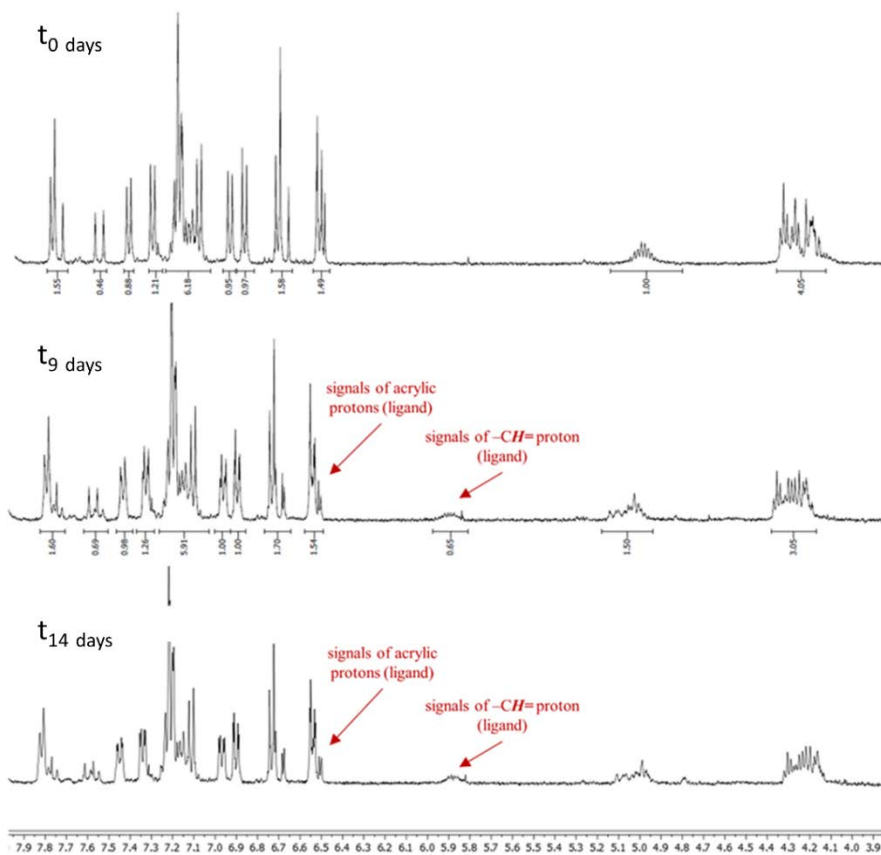


Figure S21. ^1H NMR (400 MHz) of GW7604-Pent-PtCl₃ in DMF-*d*₇.

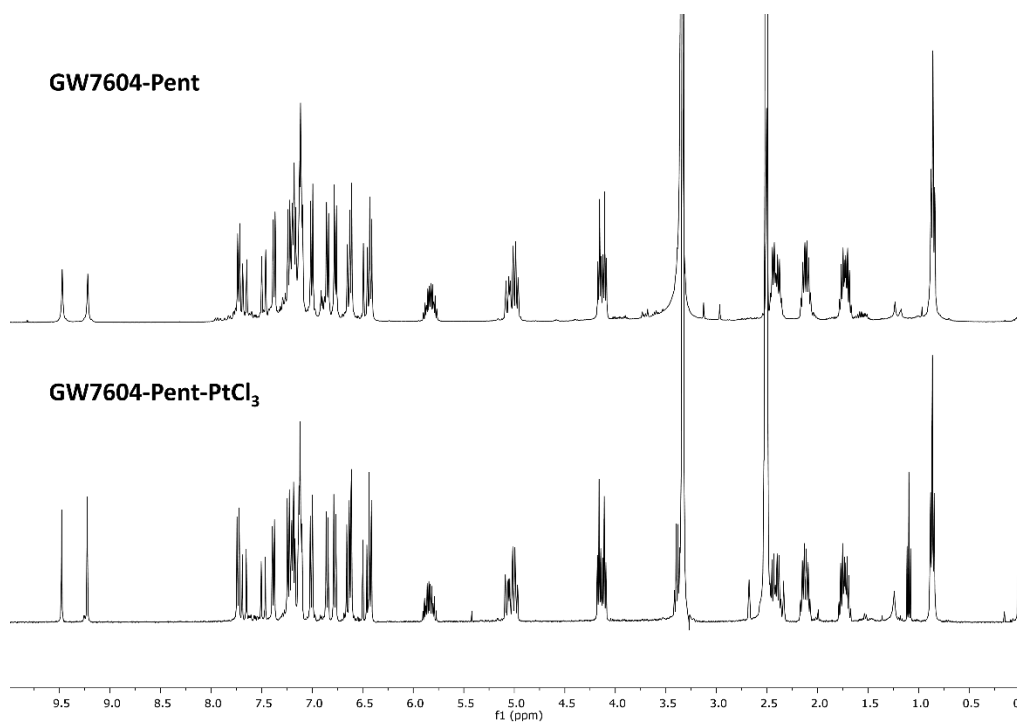


Figure S22. ^1H NMR spectra (400 MHz) of **GW7604-Pent** and **GW7604-Pent-PtCl₃** recorded in $\text{DMSO-}d_6$ after 5 min of incubation at rt. The spectrum of **GW7604-Pent-PtCl₃** contains traces of diethyl ether.

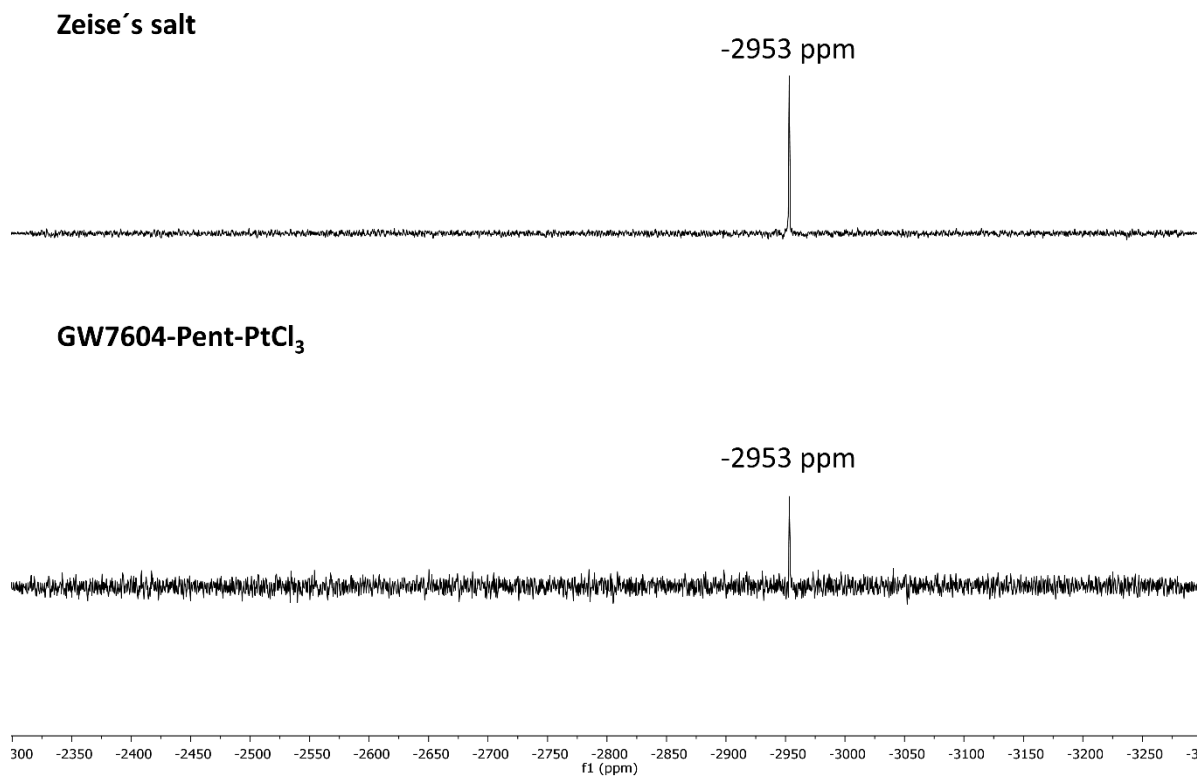


Figure S23. ^{195}Pt NMR spectra (86 MHz) of **Zeise's salt** and **GW7604-Pent-PtCl₃** recorded in $\text{DMSO-}d_6$ after 24 h of incubation at rt.

4. HPLC CHROMATOGRAMS OF THE GW7604-ALK-PtCl₃ COMPLEXES

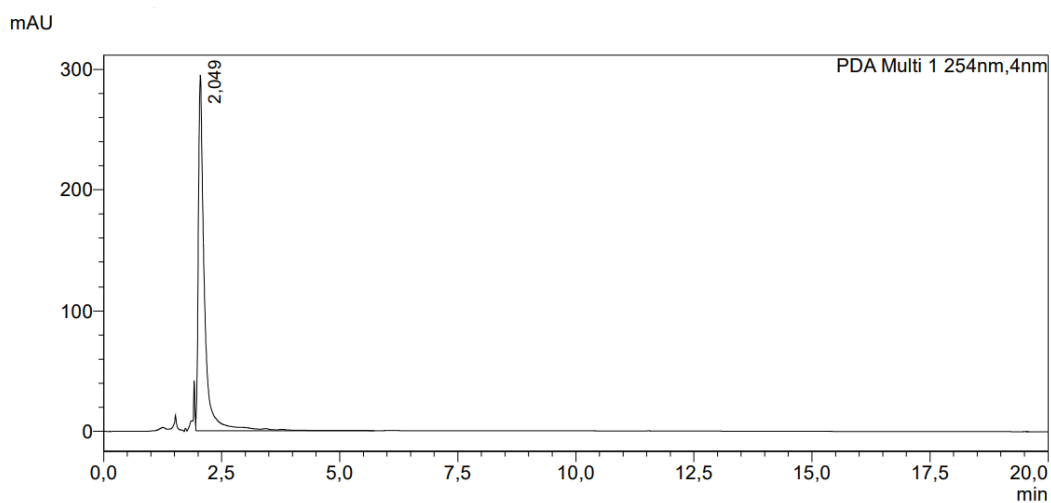


Figure S24. HPLC chromatogram of GW7604-Prop-PtCl₃.

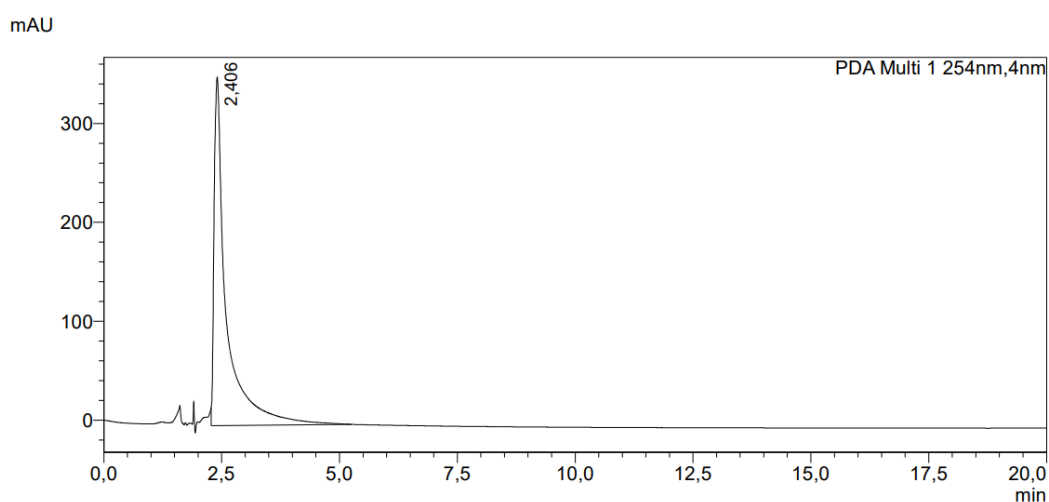


Figure S25. HPLC chromatogram of GW7604-But-PtCl₃.

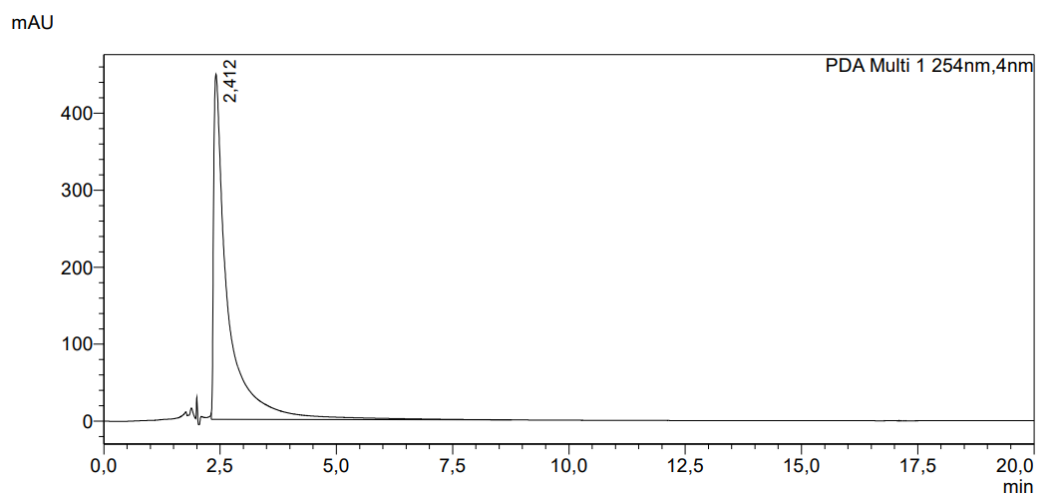


Figure S26. HPLC chromatogram of GW7604-Pent-PtCl₃.

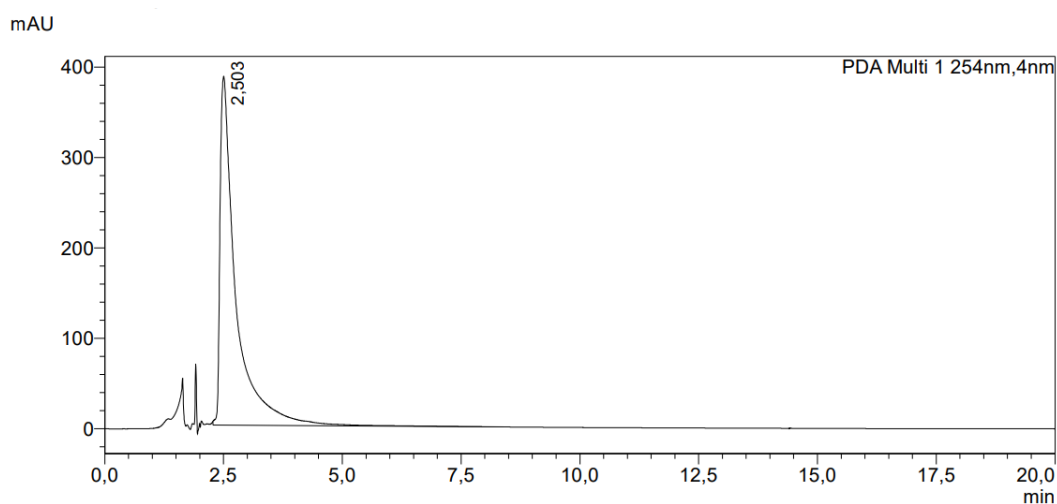


Figure S27. HPLC chromatogram of GW7604-Hex-PtCl₃.

5. MS SPECTRUM OF THE METHANOLIC EXTRACT FROM DMEM INCUBATED WITH GW7604-PENT-PTCL₃ AND THE CALCULATED ISOTOPIC DISTRIBUTION PATTERN FOR [GW7604-PENT-PT(ALA)(CH₃OH)]⁺

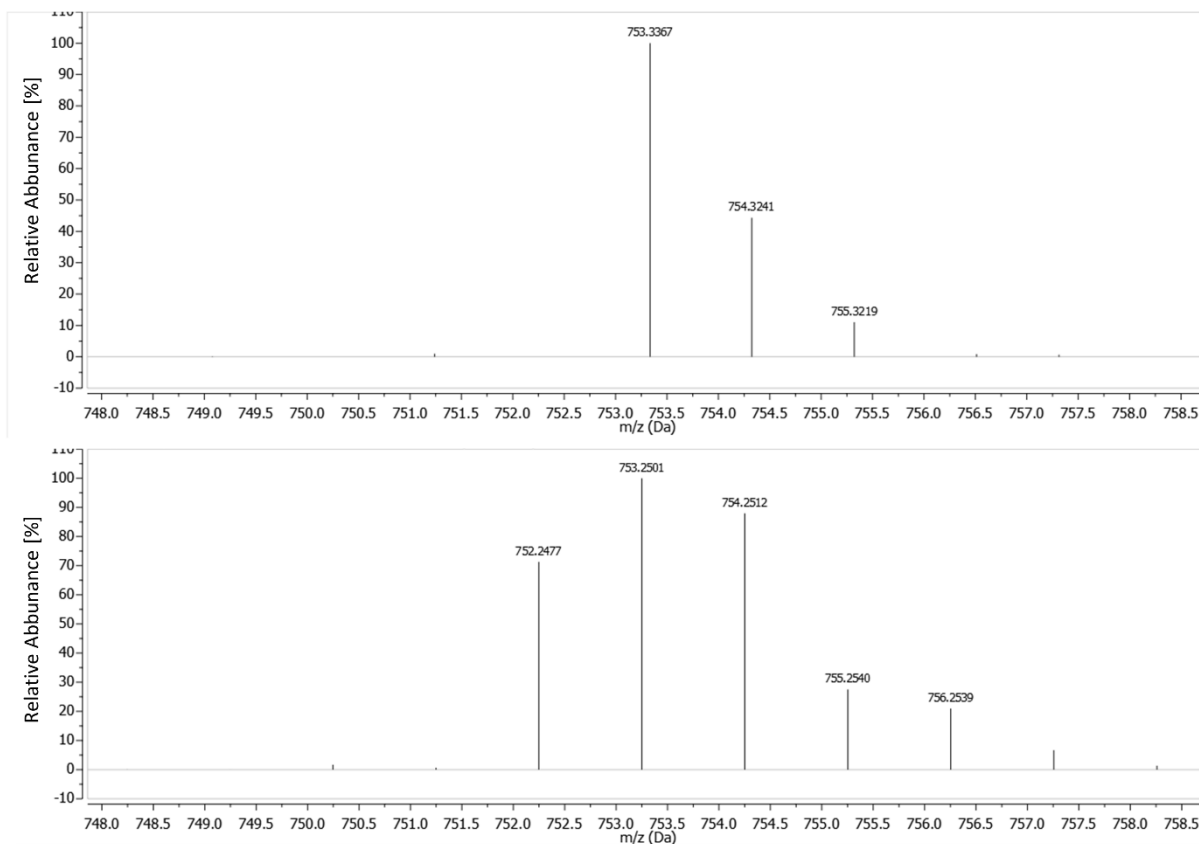


Figure S28. Comparison of the found (upper MS spectrum) with the MS spectrum (lower figure) calculated for the supposed adduct [GW7604-Pent-Pt(Ala)(CH₃OH)]⁺. Calculations were carried out with MestreNova v14.

6. ADDITIONAL ESI-HR-MS DATA FROM REACTIVITY STUDIES TOWARDS 5'-GUANOSIN MONOPHOSPHATE

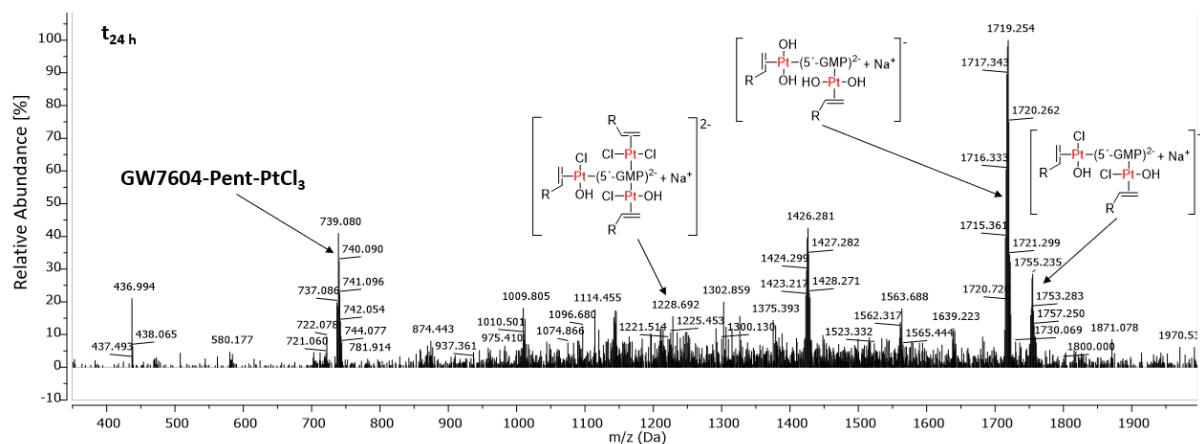


Figure S29. ESI-HR-MS spectrum in negative mode obtained from a mixture of **GW7604-Pent-PtCl₃** in MeOH and 5'-GMP in water (80/20, (v/v)) after 24 h incubation at rt; R-C=C: **GW7604-Pent**.

7. ADDITIONAL BIOLOGICAL DATA FOR TSA-201 AND MCF-7 CELLS

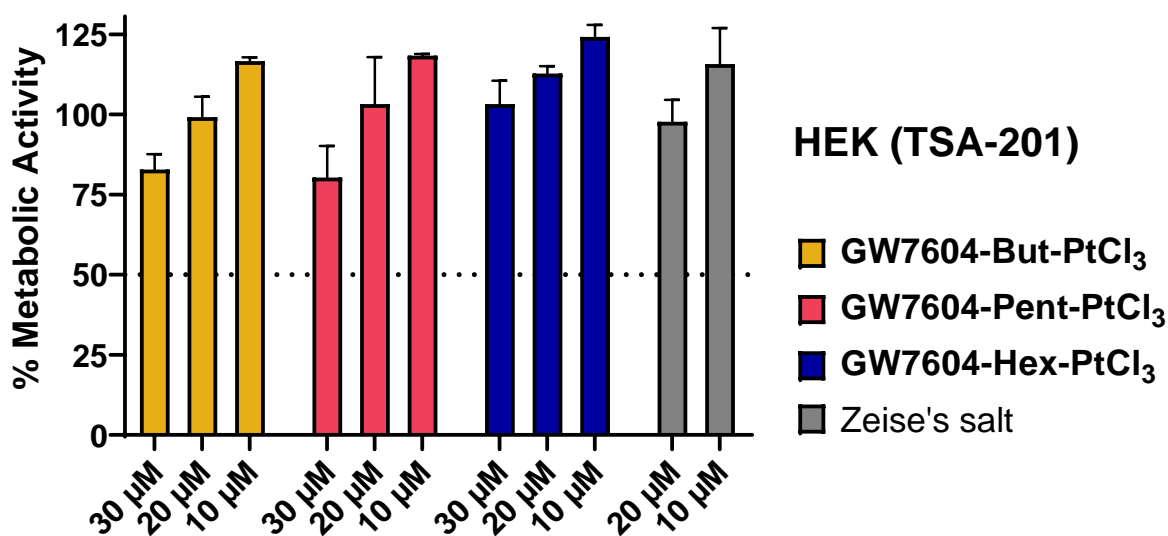


Figure S30. Investigation of metabolic activity in non-cancerous HEK (TSA-201) cells. Cells were incubated for 72 h. The reduction of metabolic activity was measured *via* an MTT assay as the mean of 3 independent experiments \pm SD.

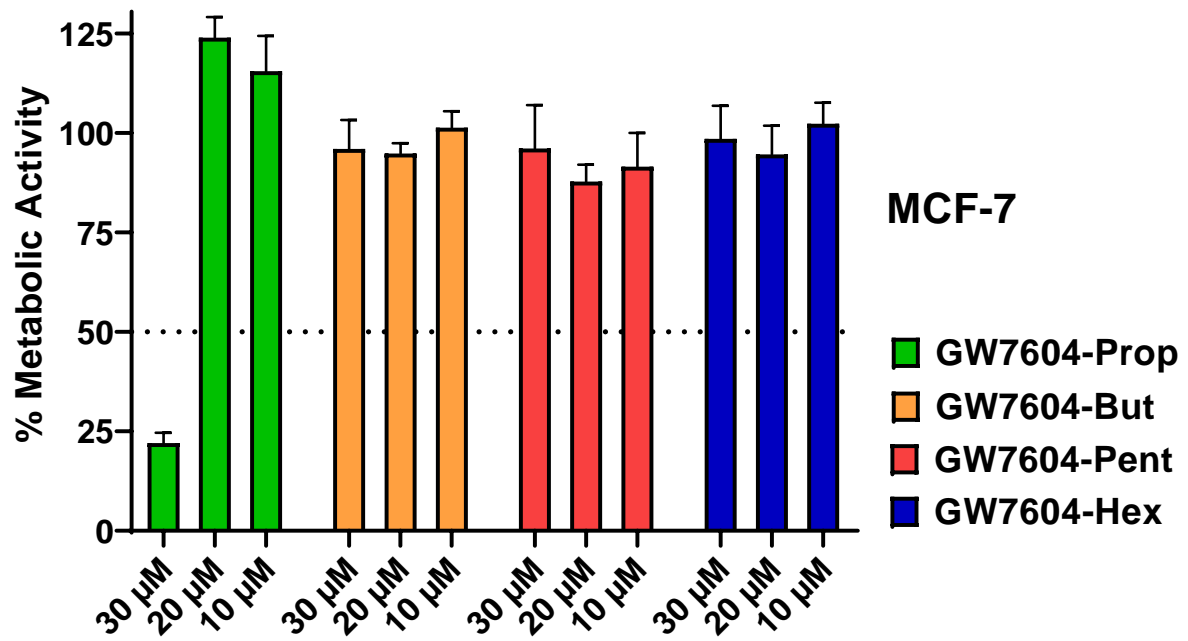


Figure S31. Investigation of metabolic activity in MCF-7 cells. Cells were incubated for 72 h. The reduction of metabolic activity was measured *via* an MTT assay as the mean of 3 independent experiments \pm SD.