Supporting Information

Synthesis, characterization and antiproliferative evaluation of Pt(II) and Pd(II) complexes with a thiazine-pyridine derivative ligand

Silvia Gutiérrez-Tarriño[1,#], Javier Espino[2,#,*], Francisco Luna-Giles[1], José A. Pariente[2], Ana B. Rodríguez[2], Emilio Viñuelas-Zahínos[1,*]

[1] *Department of Organic and Inorganic Chemistry (Chemistry of Coordination Research Group), Faculty of Science, University of Extremadura, Badajoz, Spain;*

[2] *Department of Physiology (Neuroimmunophysiology and Chrononutrition Research Group), Faculty of Science, University of Extremadura, Badajoz, Spain;*

 # Both authors contributed equally.

** Correspondence: emilvin@unex.es, (E.V.-Z.); jespino@unex.es, (J.E.)*

This manuscript is in Memoriam of Prof. Álvaro Bernalte García, Group Leader of the Coordination Chemistry Research Group

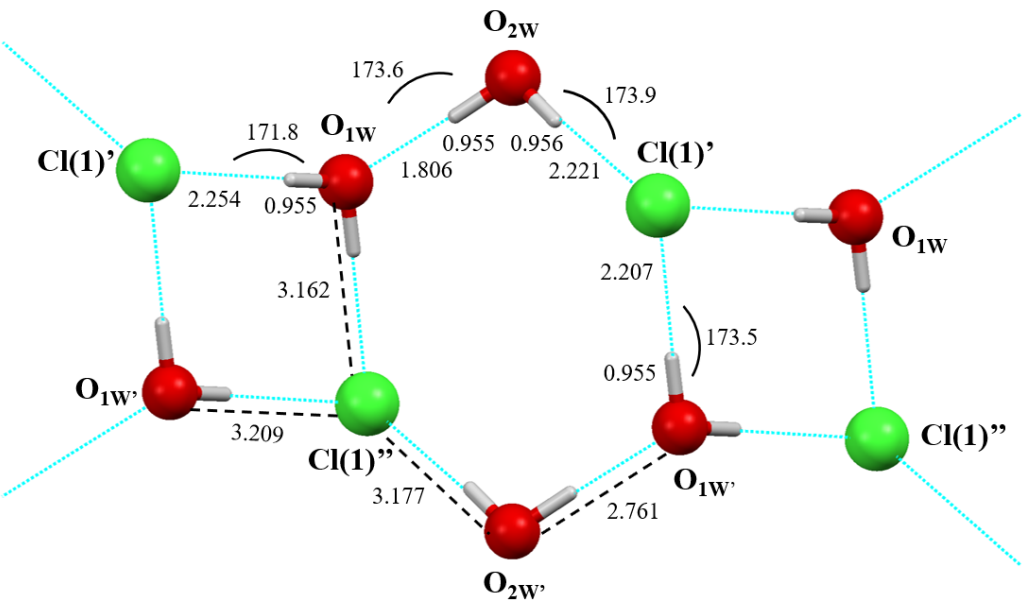


Figure S1. Structural parameters of $\{[(H_2O)_5Cl_3]^{3-}\}_n$ tapes in PyTzHCl·2H_2O.

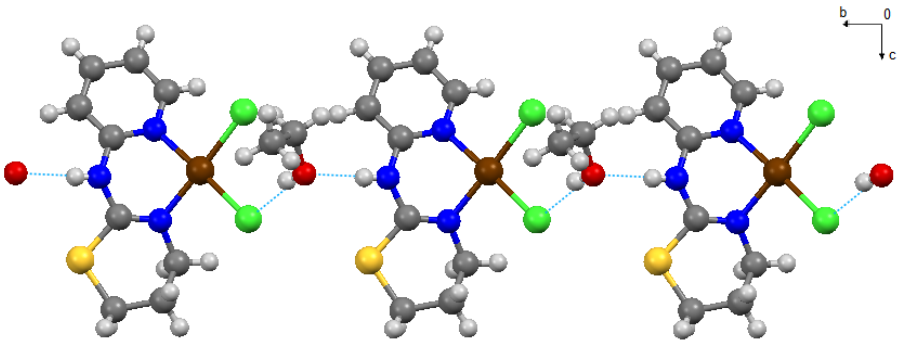


Figure S2. Supramolecular arrangement in PtPyTz stabilized by intramolecular hydrogen-bonds.

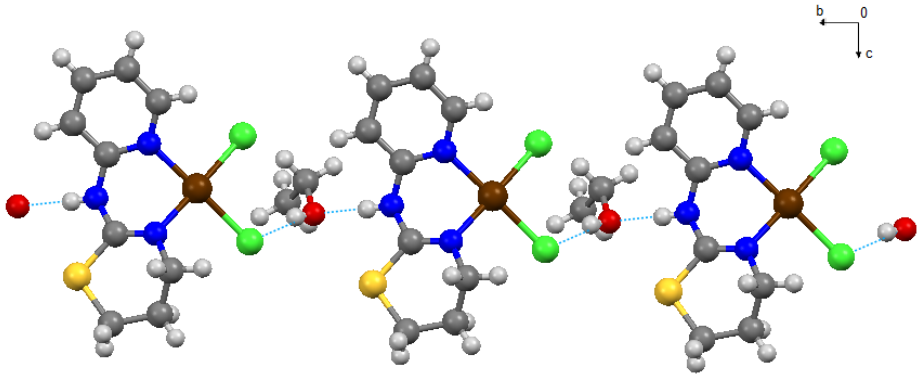
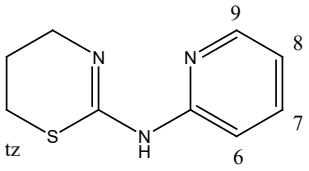


Figure S3. Supramolecular arrangement in PdPyTz stabilized by intramolecular hydrogen-bonds.

Table S1. ^{1}H NMR spectral data for PyTz and its Pt(II) and Pd(II) complexes in DMF-d_7 solvent.



Compound	N-H	H(9)	H(7)	H(8)	H(6)	N-CH_2 (tz)	S-CH_2(tz)	CH_2 (tz)
PyTz	11.31	8.17	7.63	6.95	6.86	3.56	3.12	2.05
PtPyTz	11.20	9.01	8.06	7.23	7.39	4.02	3.30	2.09
PdPyTz	11.33	8.75	8.06	7.29	7.41	3.85	3.29	2.05

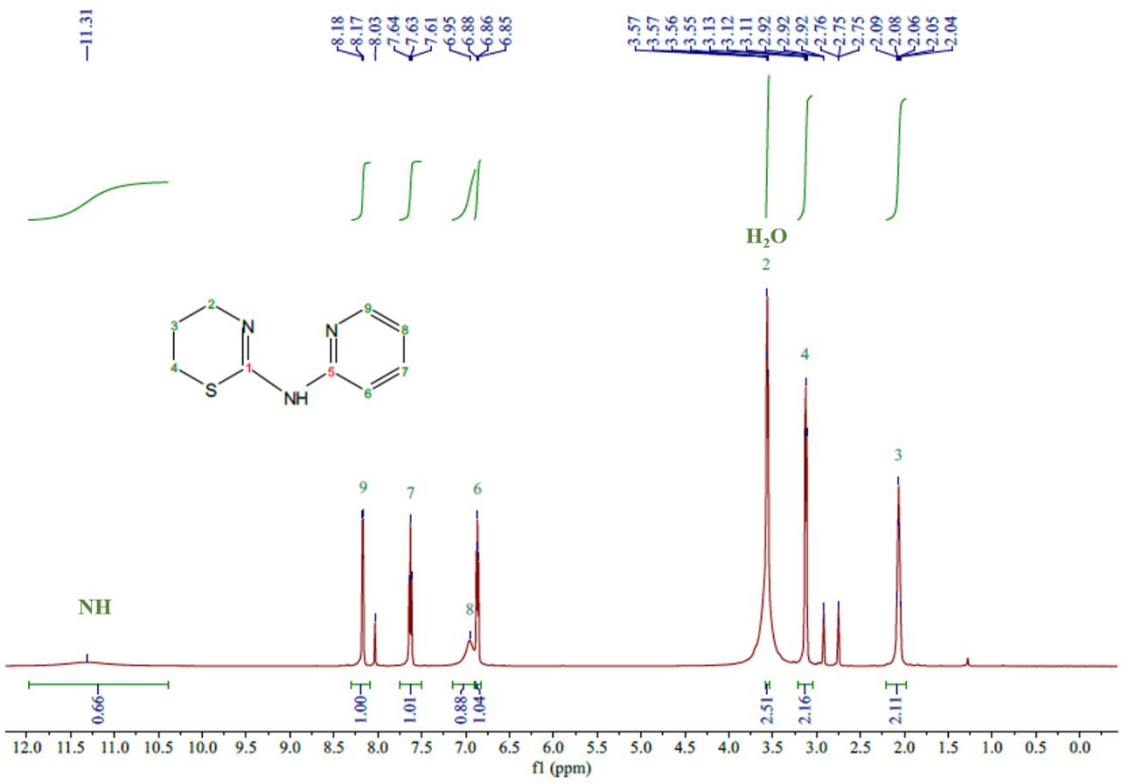


Figure S4. ^{1}H NMR spectrum of PyTz in DMF-d_7.

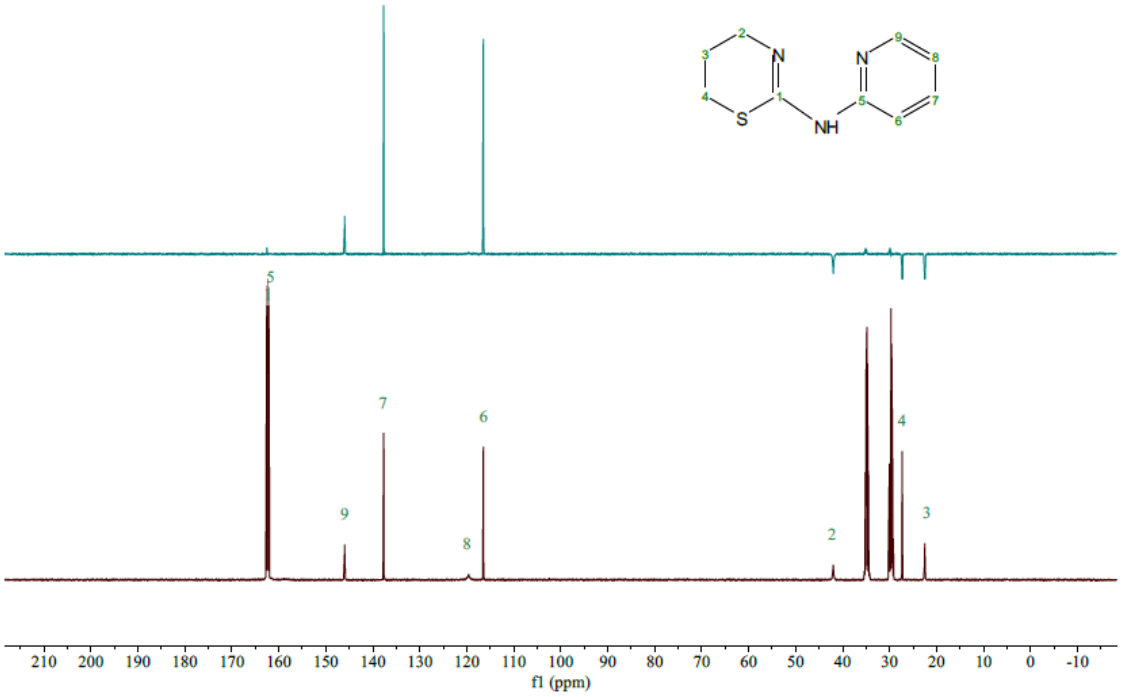


Figure S5. ^{13}C NMR spectrum of PyTz in DMF-d_7.

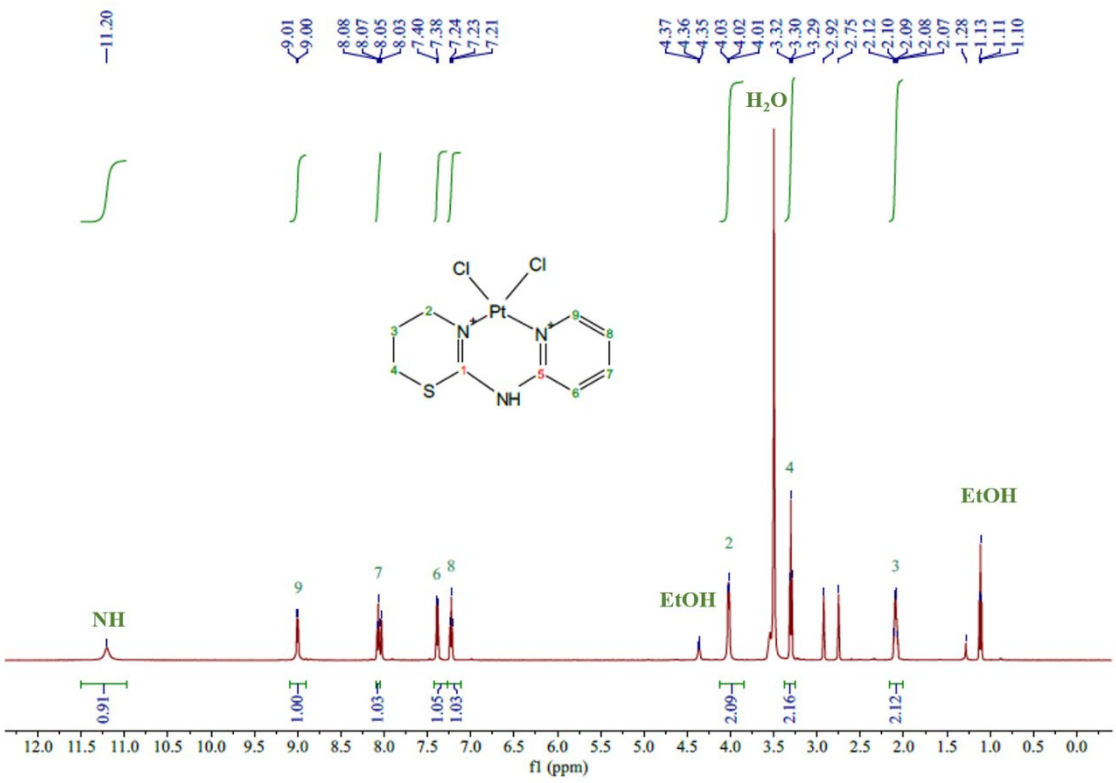


Figure S6. ^{1}H NMR spectrum of PtPyTz in DMF-d_7.

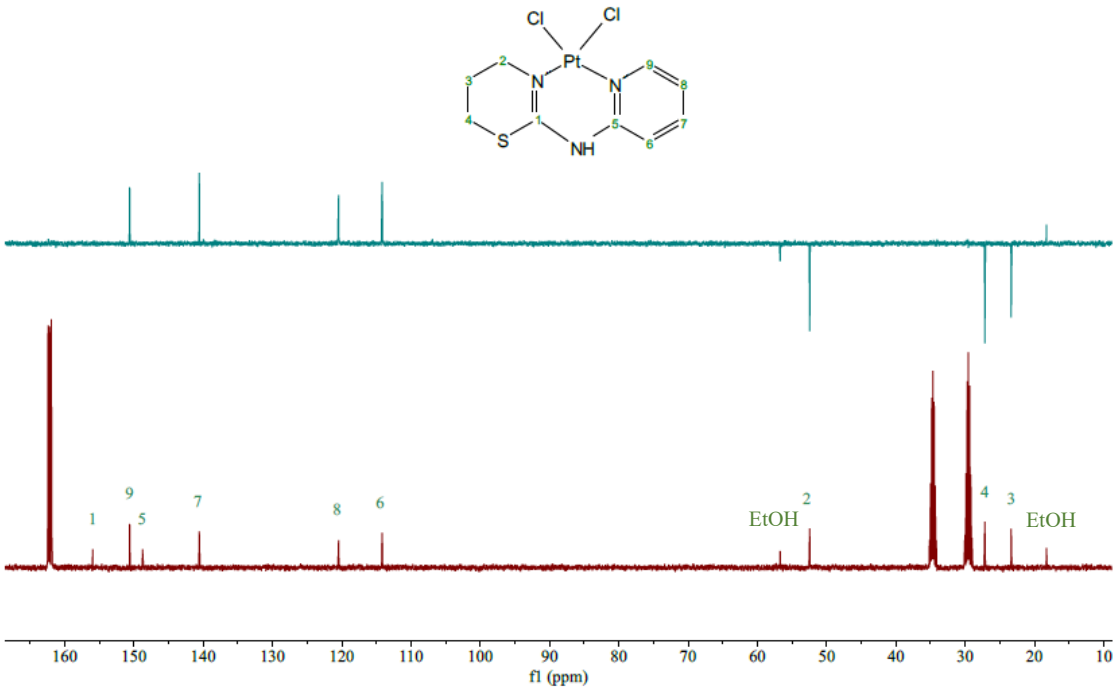


Figure S7. ^{13}C NMR spectrum of PtPyTz in DMF-d_7.

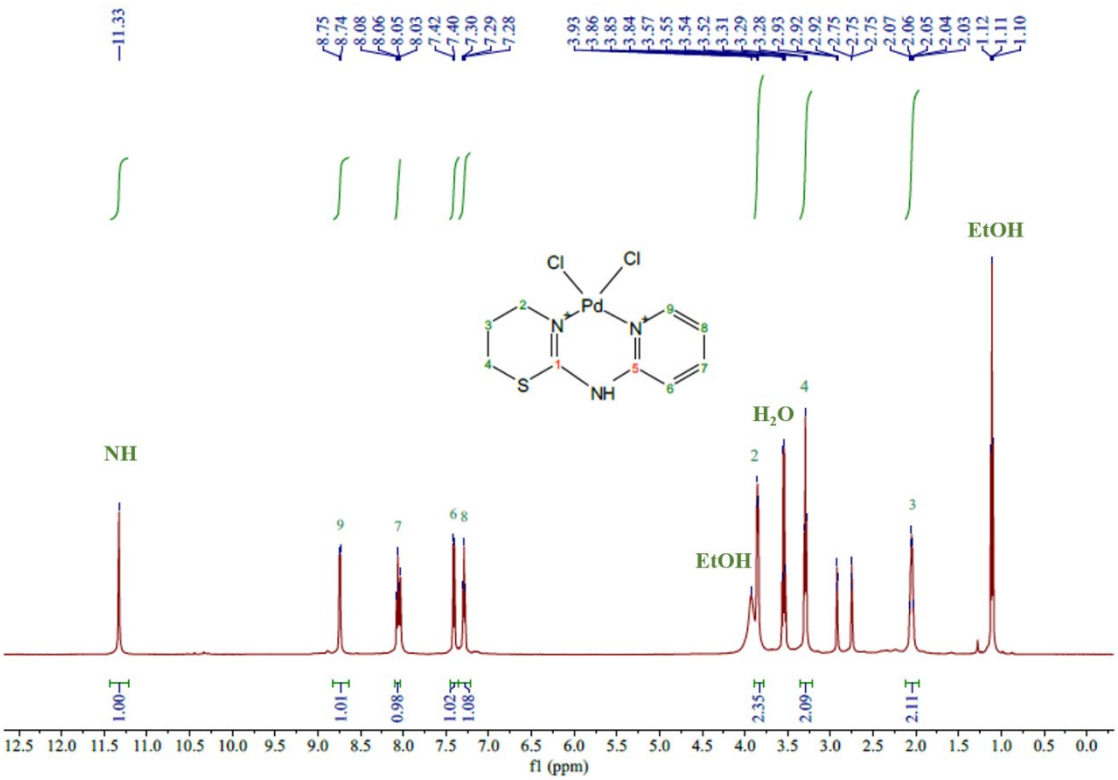


Figure S8. ^{1}H NMR spectrum of PdPyTz in DMF-d_7.

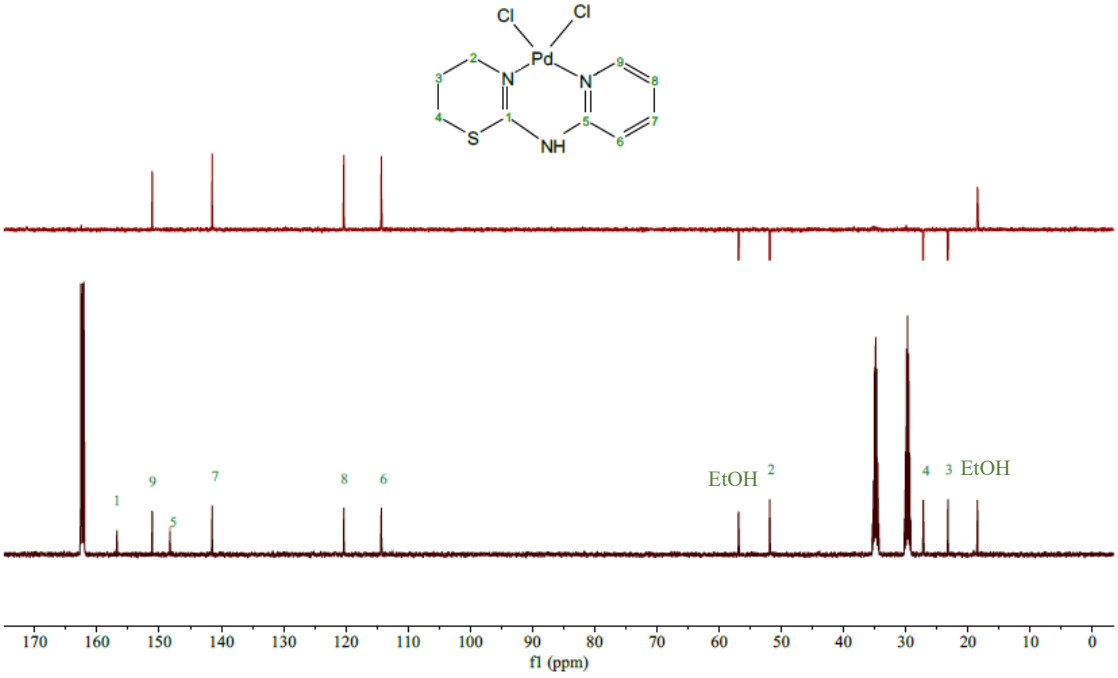


Figure S9. ^{13}C NMR spectrum of PdPyTz in DMF-d_7.

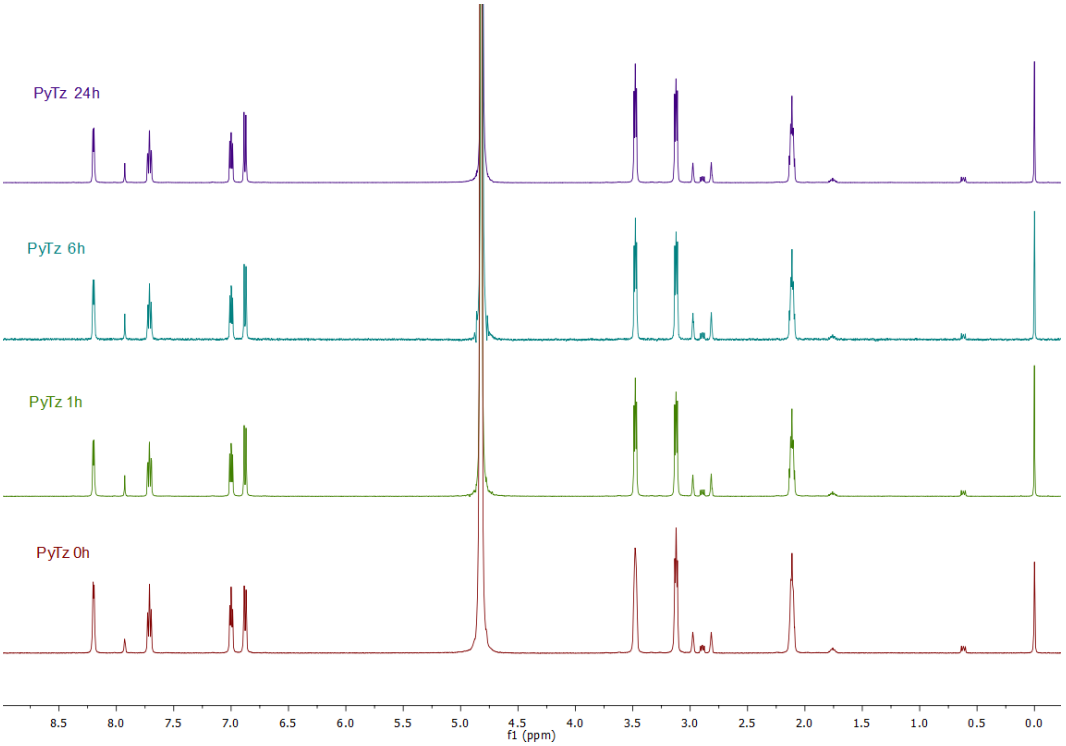


Figure S10. ^{1}H NMR spectrum of PyTz in D_2O:DMF-d_7 (11:1 ratio) after preparation (red), 1 hour (green), 6 hours (blue), 24 hours (purple).

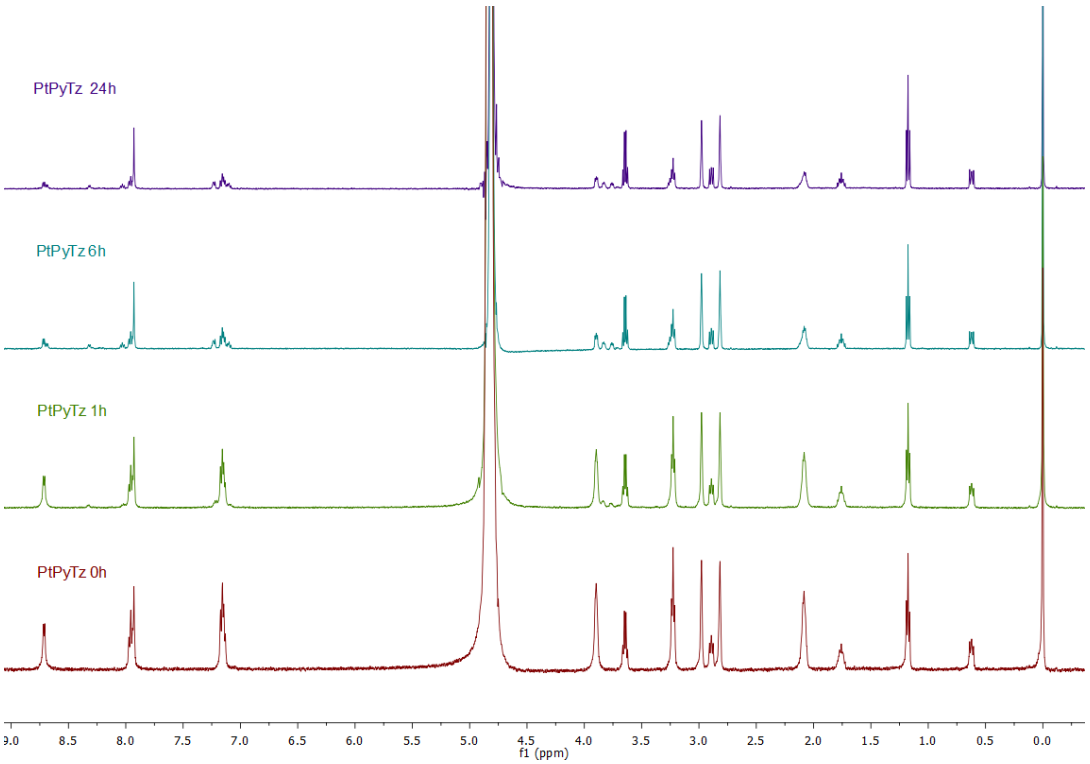


Figure S11. ^{1}H NMR spectrum of PtPyTz in D_2O:DMF-d_7 (11:1 ratio) after preparation (red), 1 hour (green), 6 hours (blue), 24 hours (purple).

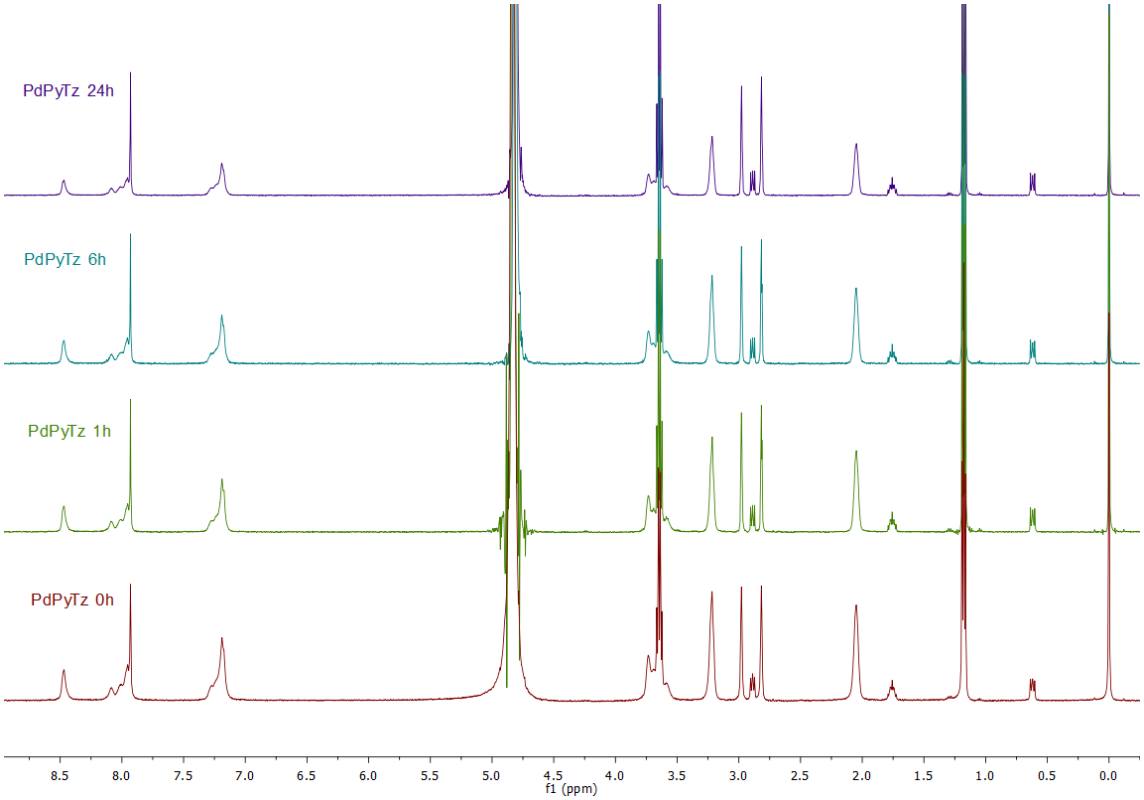


Figure S12. ^{1}H NMR spectrum of PdPyTz in D_2O:DMF-d_7 (11:1 ratio) after preparation (red), 1 hour (green), 6 hours (blue), 24 hours (purple).

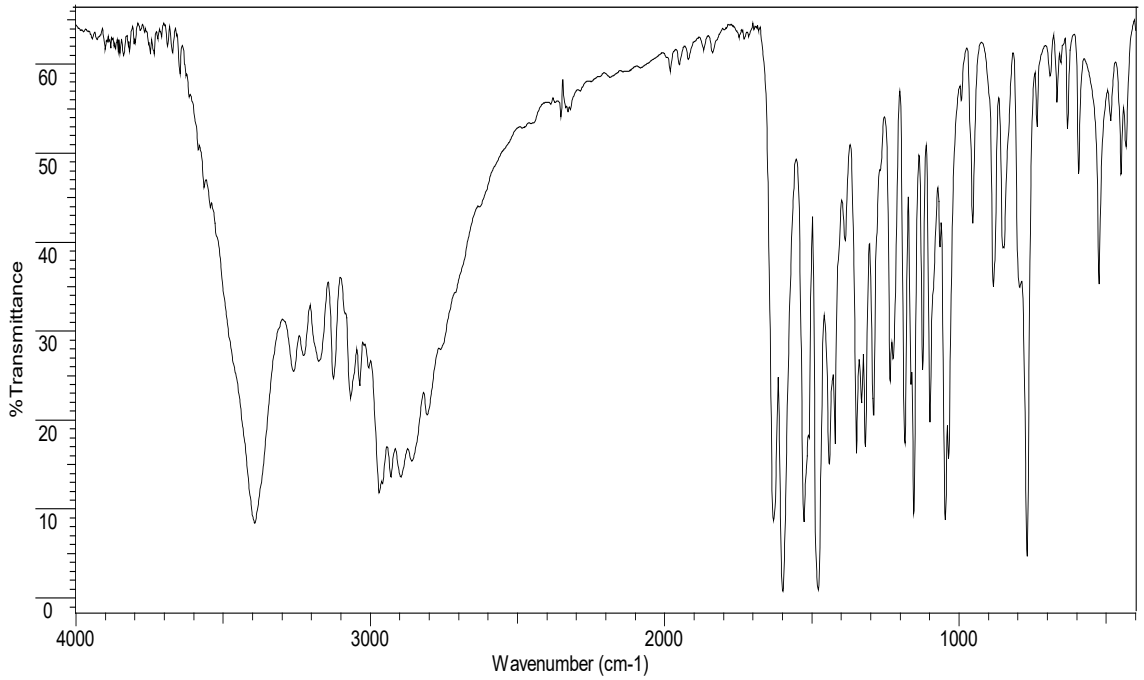


Figure S13. FTIR spectrum of PtPyTz between 4000-400 cm^{-1}.

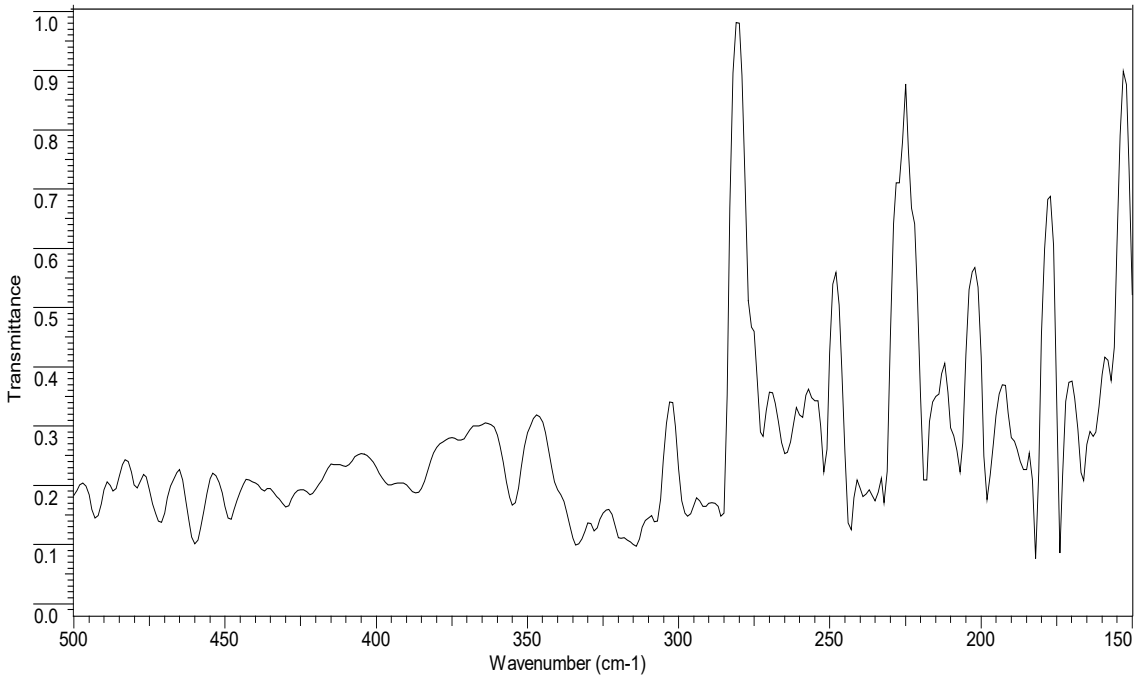


Figure S14. FTIR spectrum of PtPyTz between 500-150 cm^{-1}.

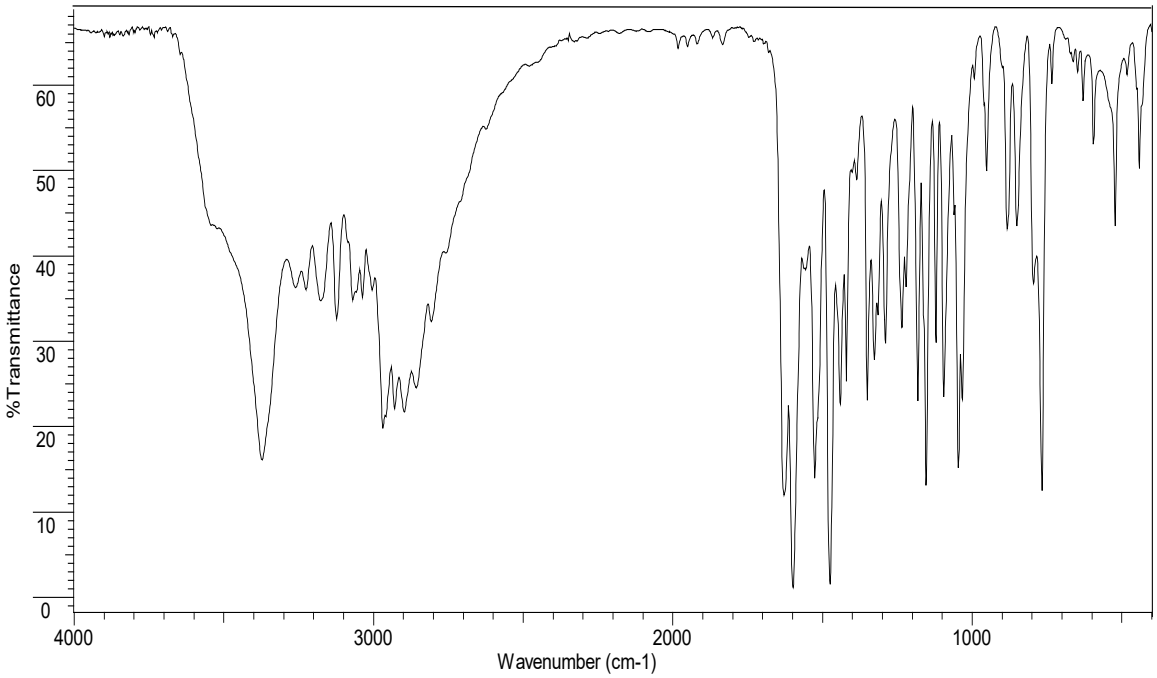


Figure S15. FTIR spectrum of PdPyTz between 4000-400 cm^{-1}.

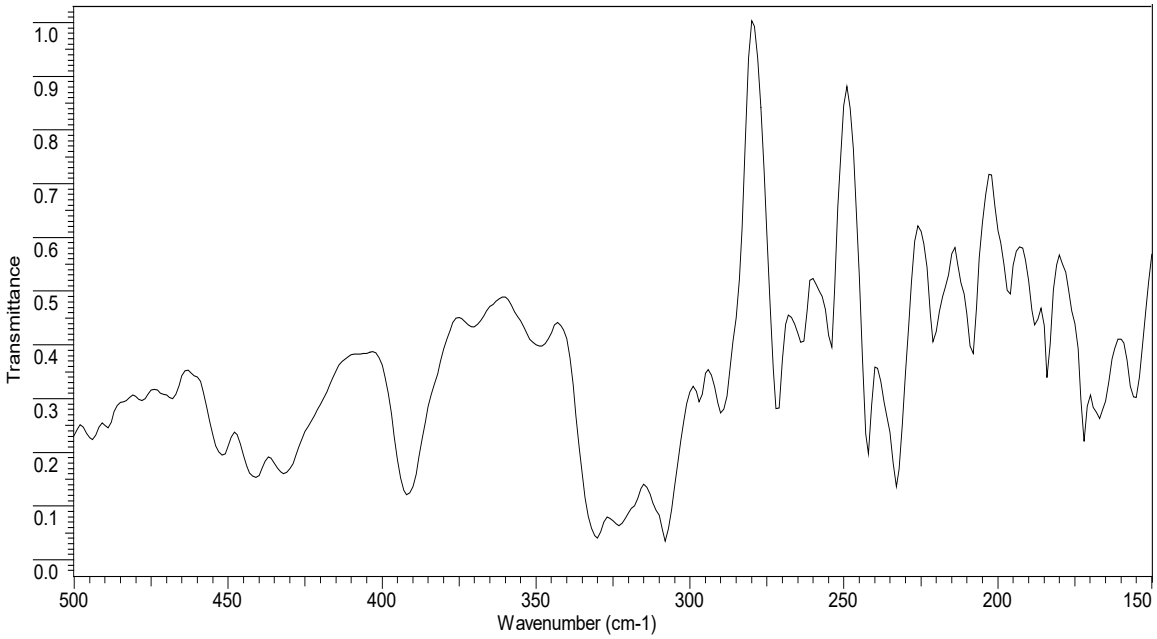


Figure S16. FTIR spectrum of PdPyTz between 500-150 cm^{-1}.

Table S2. ADME properties factor of the synthesized compounds.

	PyTz	**PtPyTz**	**PdPyTz**
Mw(g/mol)	193.27	459.25	370.59
TPSA[1]	62.58	54.62	54.62
Log$P_{o/w}$[2]	1.54	1.59	1.48
LogS[3]	-2.10	-4.69	-4.41
Rotable bonds	2	0	0
GI Absorption[4]	High	High	High
BBB permeant[4]	Yes	Yes	Yes
Lipinski violiations[5]	0	0	0
PAINS alerts[6]	0	0	0

1. Topological Polar Surface Area calculated from: Etrl, P.; Rohde, B.; Selzer, P. Fast calculation of molecular polar surface area as a sum of fragment-based contributions and its application to the prediction of drug transport properties. J. Med. Chem. **2000**, *43*, 3714–3717. 2.

2. Consensus Log $P_{o/w}$ average of 5 prediction methods.

3. ESOL topological method implemented from Delaney, J. S. Prediction of aqueous solubility and partition coefficient optimized by a genetic algorithm based descriptor selection method. J. Chem. Inf. Model. **2004**, *44*, 1000-1005.

4. Saina, A.; Zoete, V. A BOILED-Egg to predict gastrointestinal absorption and brain penetration of small molecules. Chem. Med. Chem. **2016**, *11*, 1117-1121.

5. Lipinski, C. A.; Lombardo, F.; Dominy, B. W.; Feeney, P. J. Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. Adv. Drug Deliv. Rev. **2001**, *46*, 3-26.

6. Baell, J.B.; Holloway G. A. New substructure filters for removal of pan assay interference compounds (PAINS) from screening libraries and for their exclusion in bioassays. J. Med. Chem. **2010**, *53*, 2719-2740.