'Optimized Route' to Synthesis Isoelectronic and Isostructural Au(III)- and Pt(II)-NHC Complexes; Synthesis, Structure, Spectral Properties, Electrochemistry, and Molecular Docking Studies

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Supporting Information

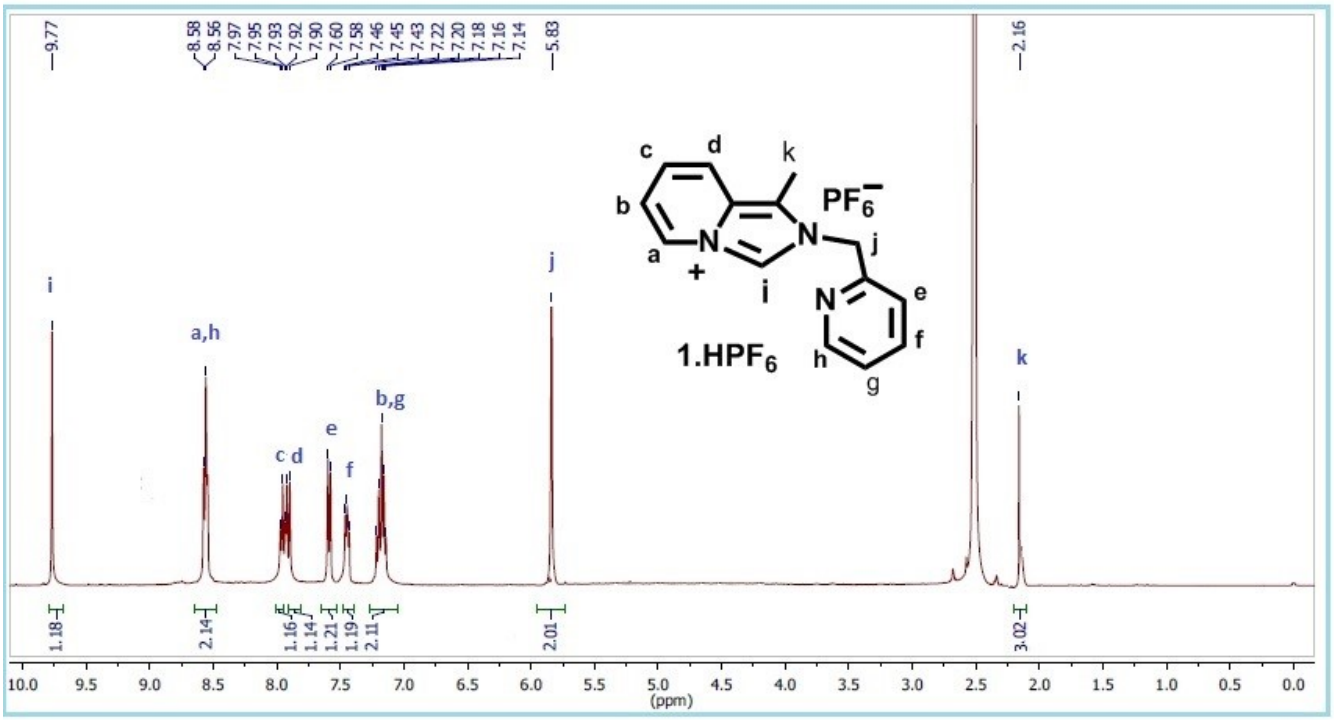


Figure S1.[1]H NMR spectrum of **1**.HPF6 in DMSO-d_6.

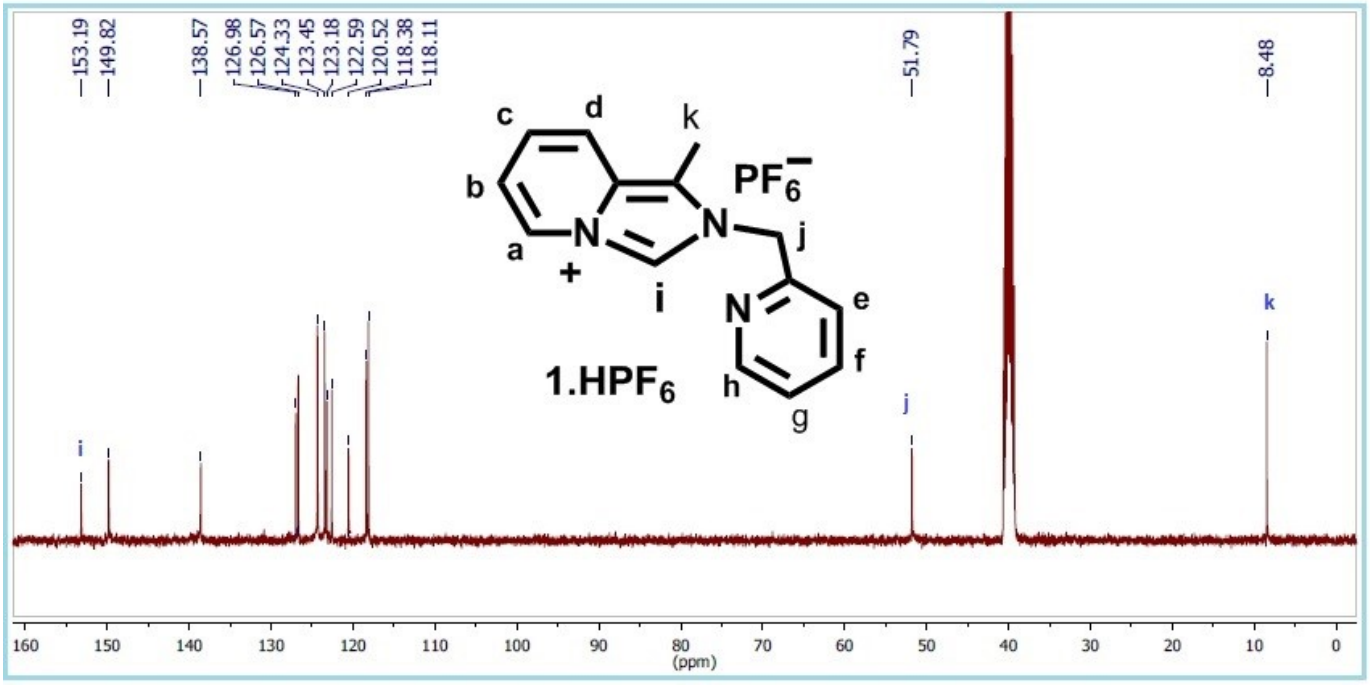


Figure S2.[13]C NMR spectrum of **1**.HPF6 in DMSO-d_6.

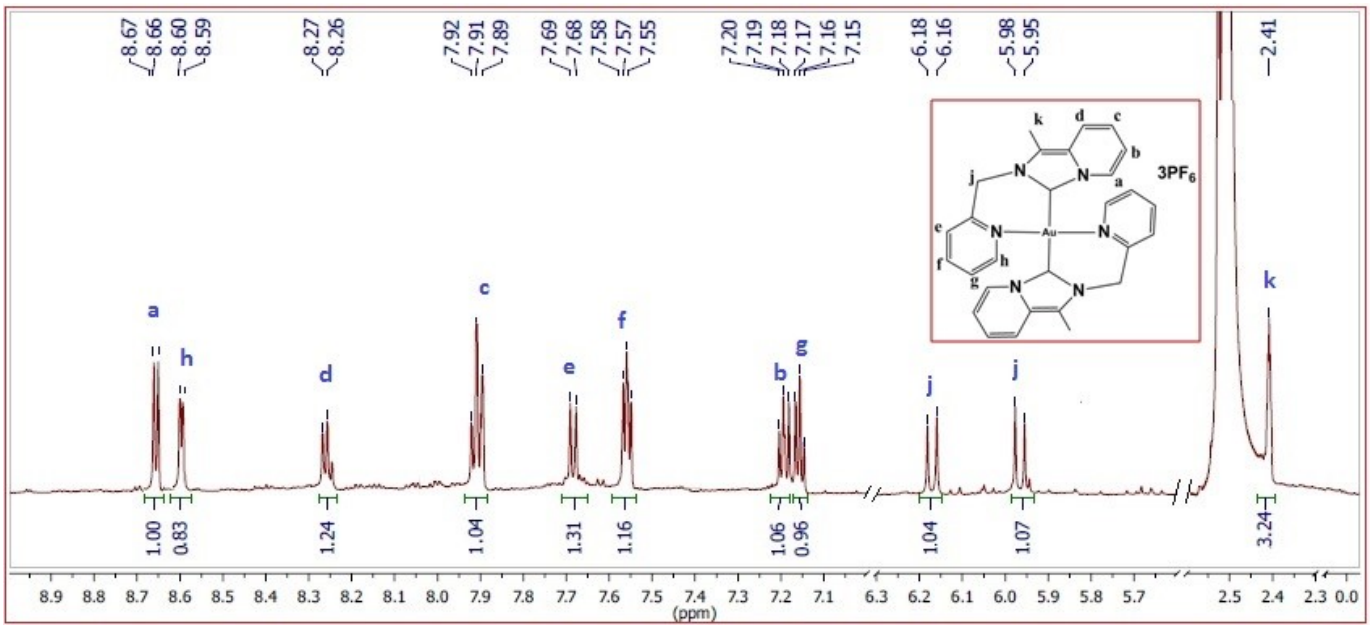


Figure S3.[1]H NMR spectrum of complex **2** in DMSO-d_6.

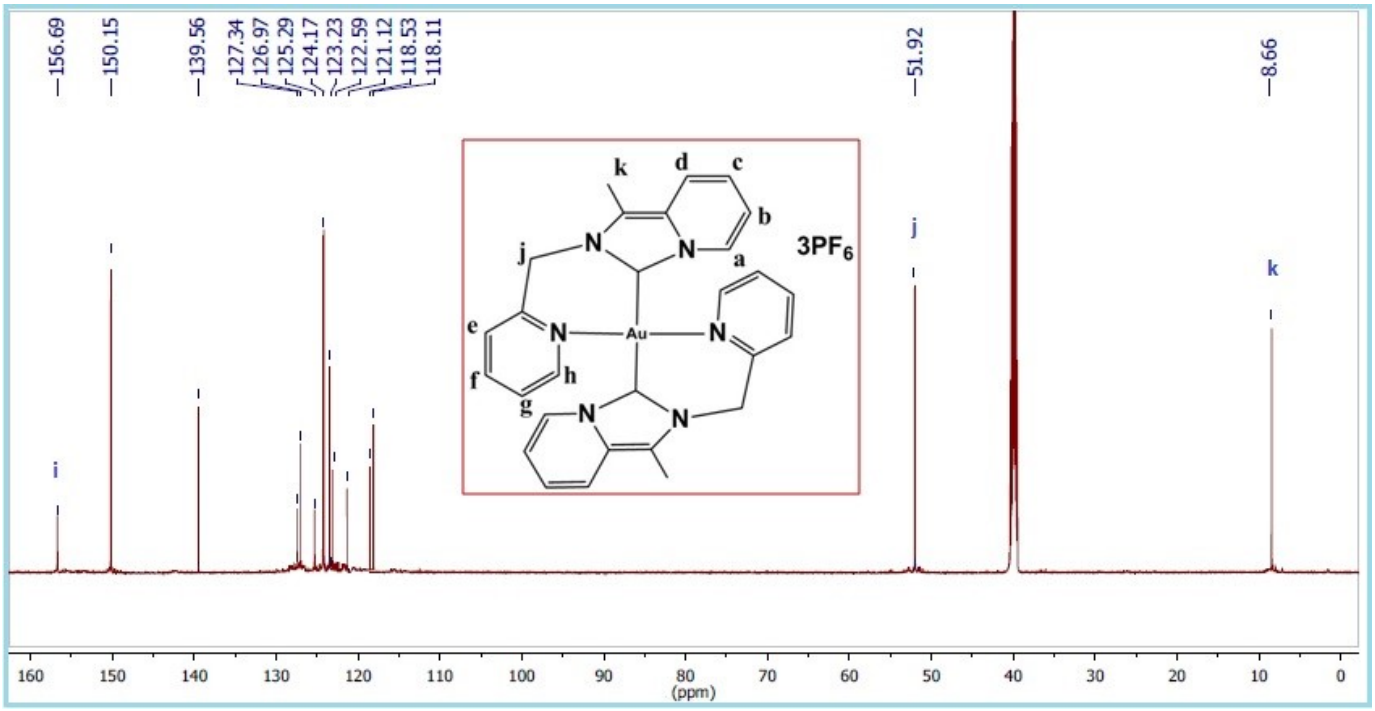


Figure S4.[13]C NMR spectrum of complex **2** in DMSO-d_6.

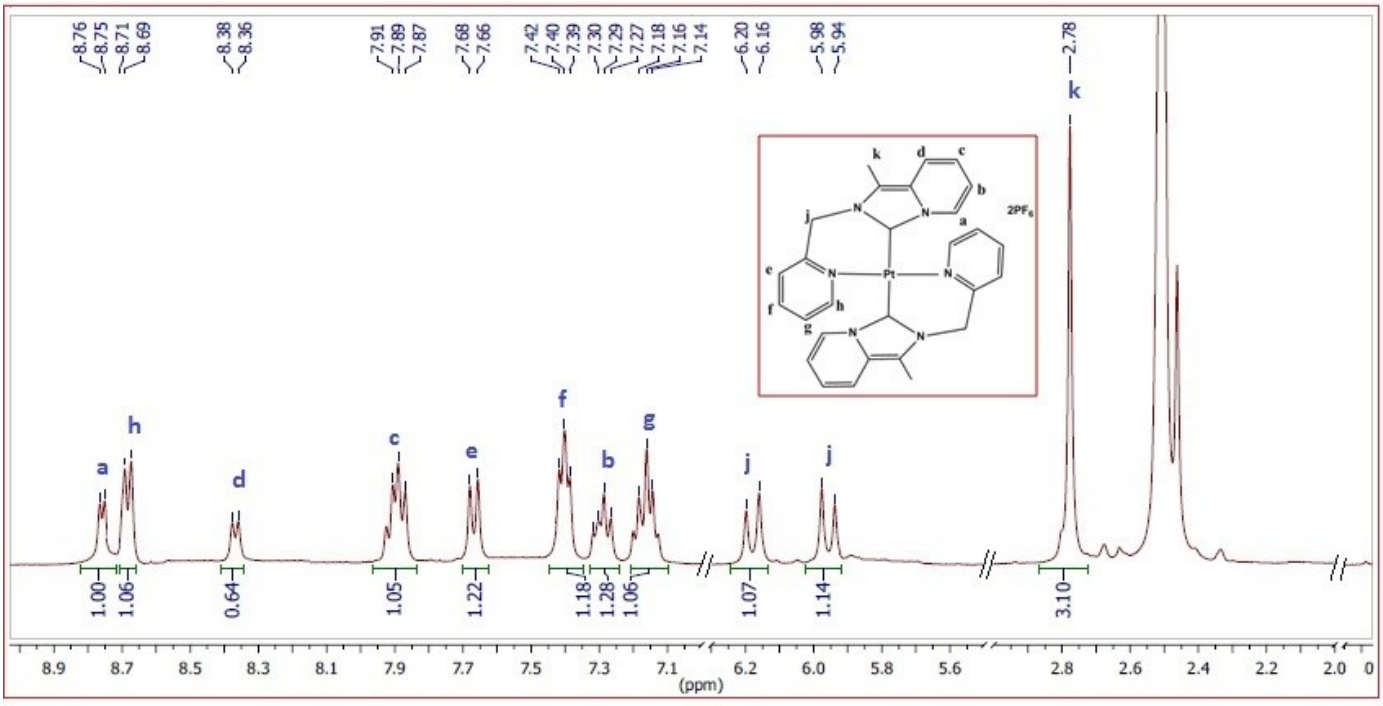


Figure S5.[1]H NMR spectrum of complex **3** in DMSO-d_6.

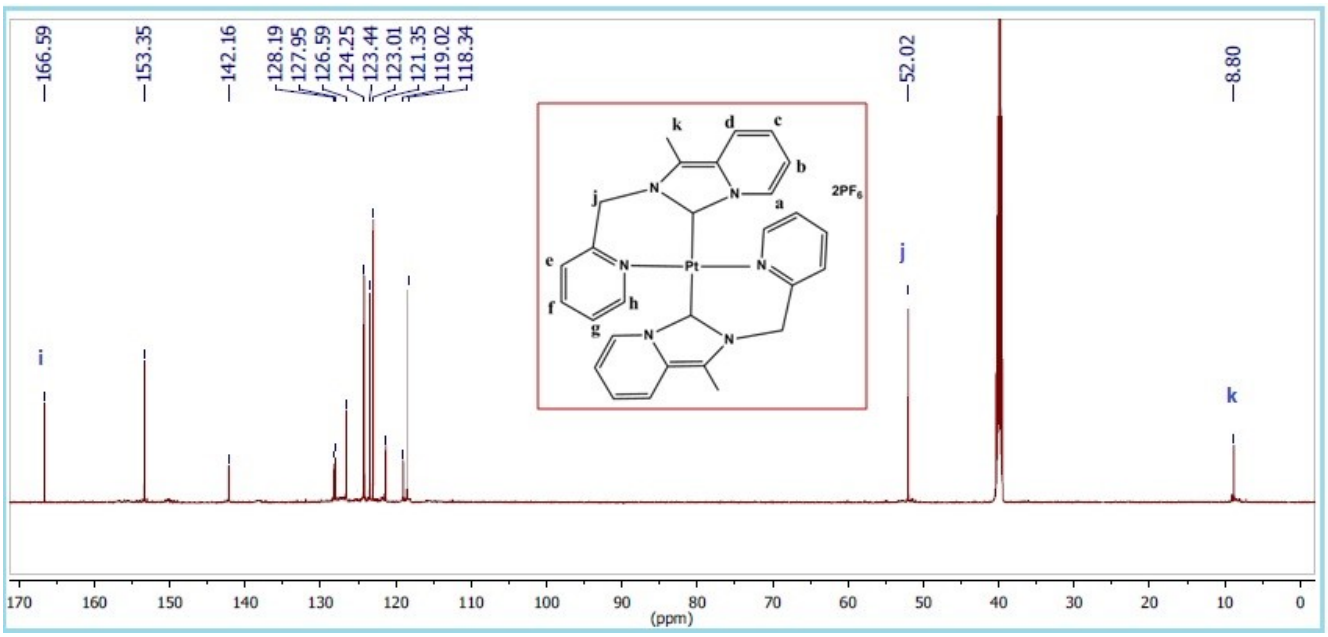


Figure S6.^{13}C NMR spectrum of complex **3** in DMSO-d_6.

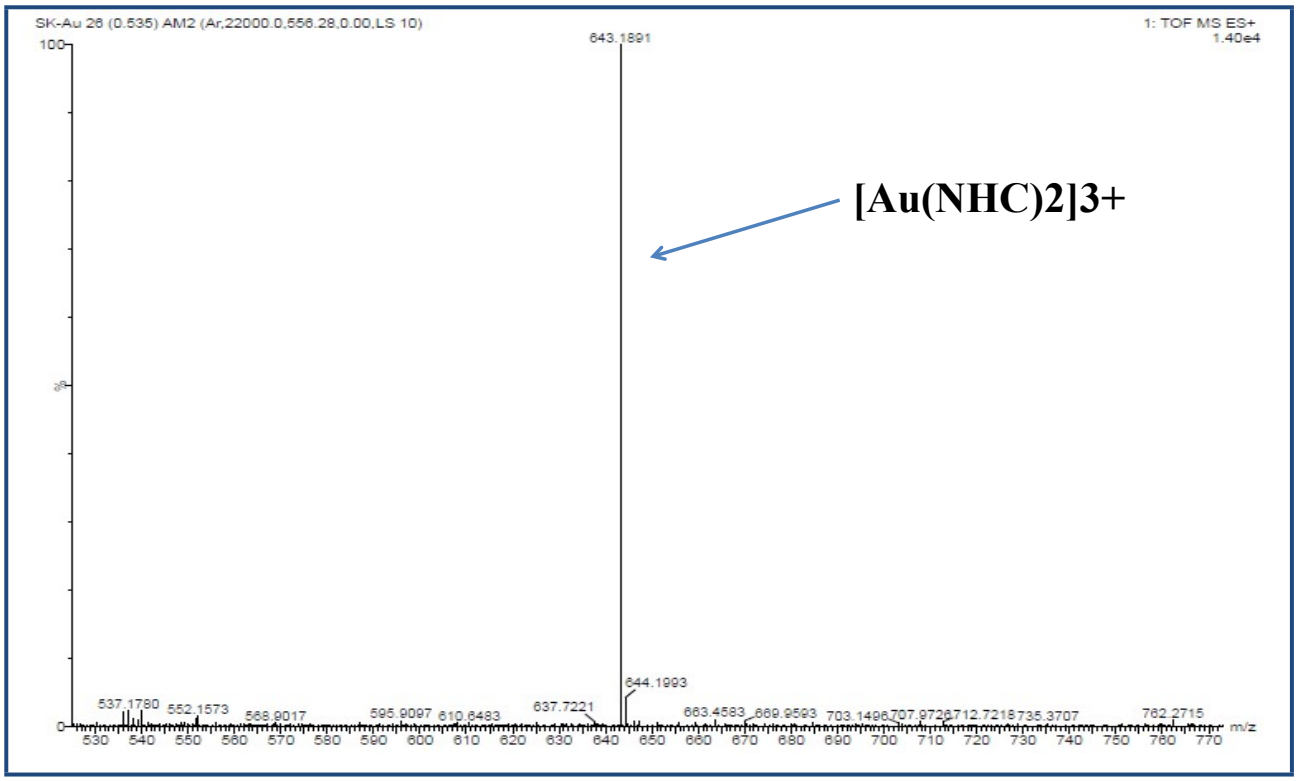


Figure S7.HRMass spectrum of complex **2**.

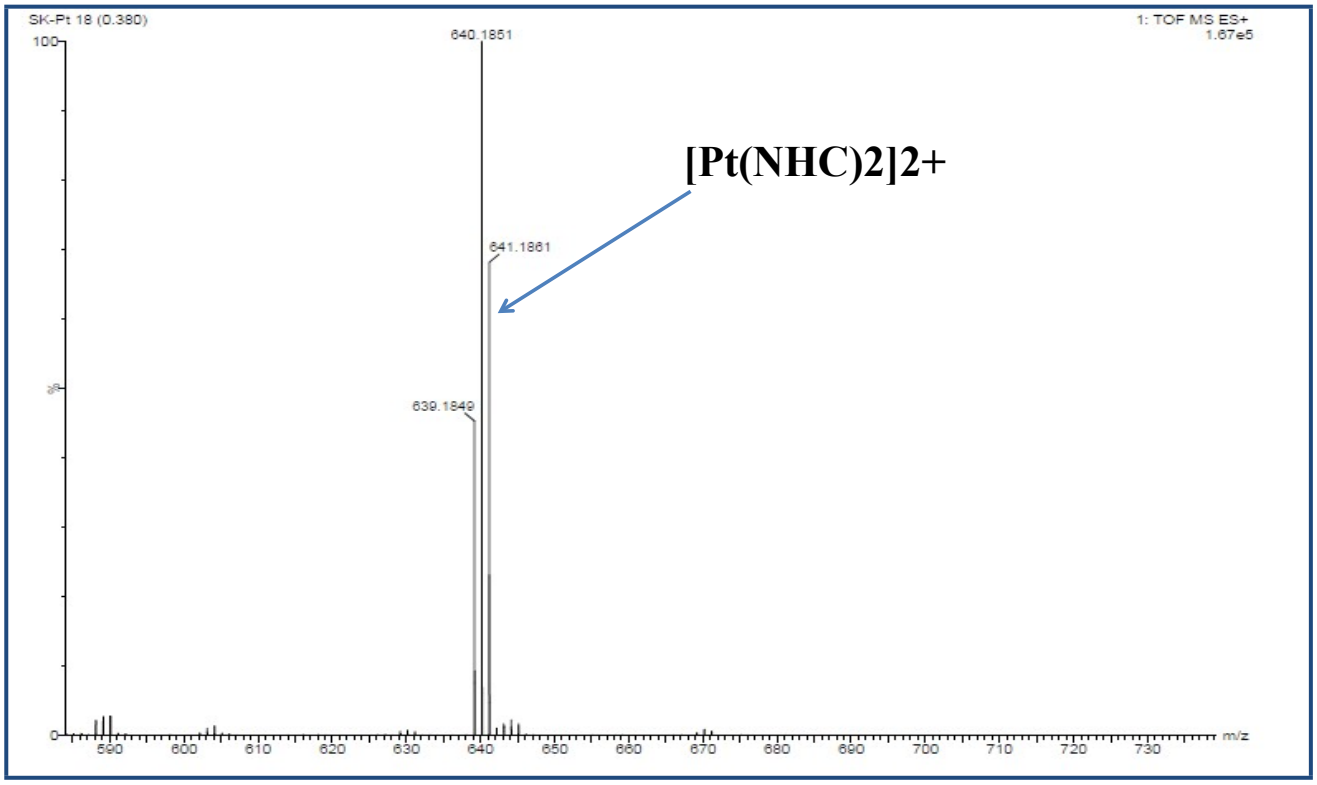


Figure S8.HRMass spectrum of complex **3**.

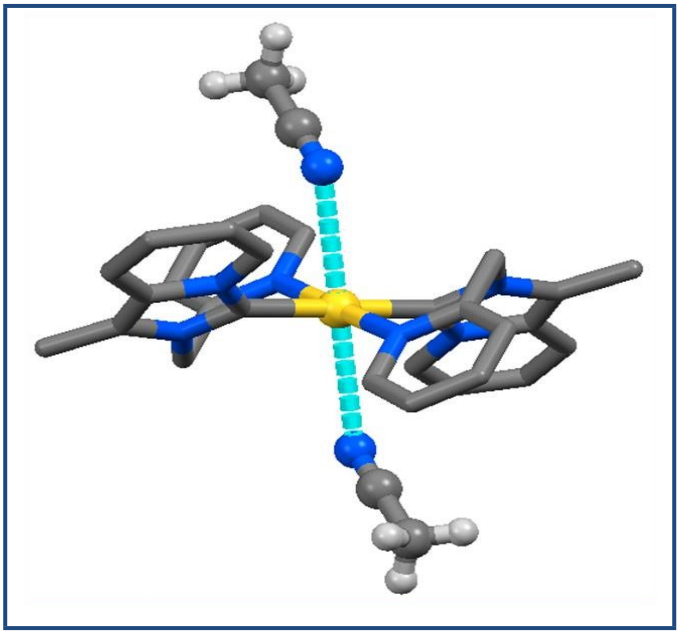


Figure S9. Distorted octahedral shape around Au(III) ion of complex **2**.

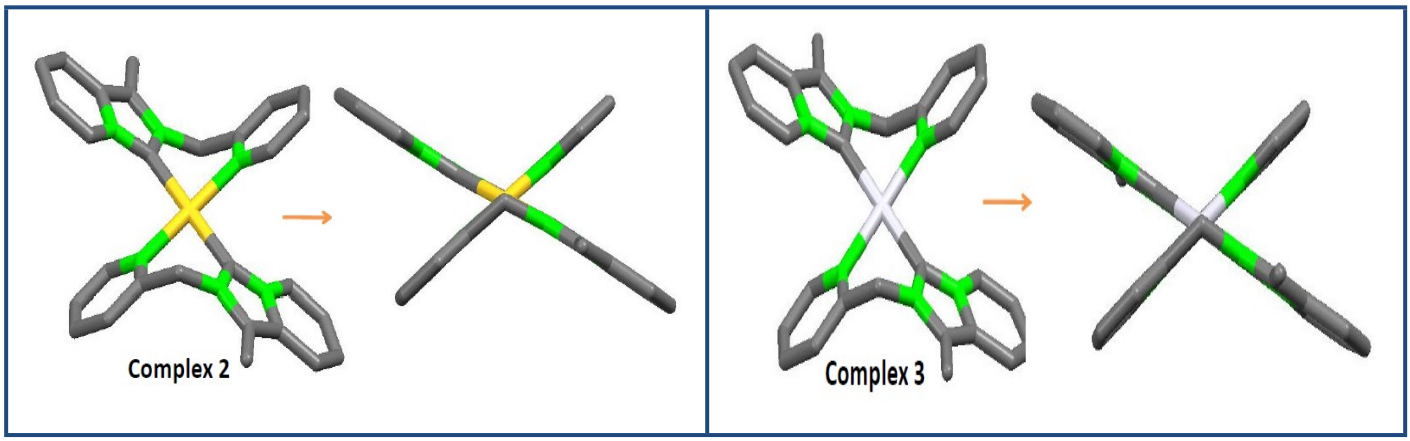


Figure S10. Butterfly like view of complex **2**(left) and complex **3** (right).

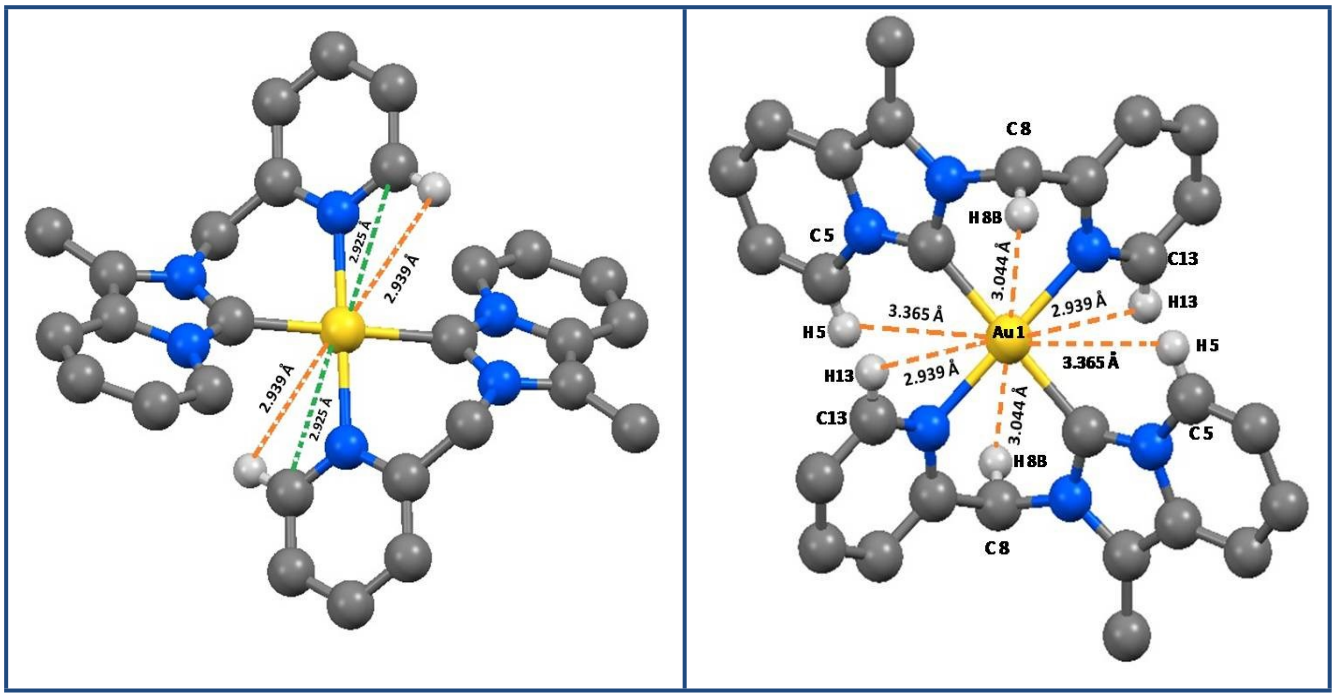


Figure S11. Various intramolecular Au(III)····H-C interactions present in complex **2.**

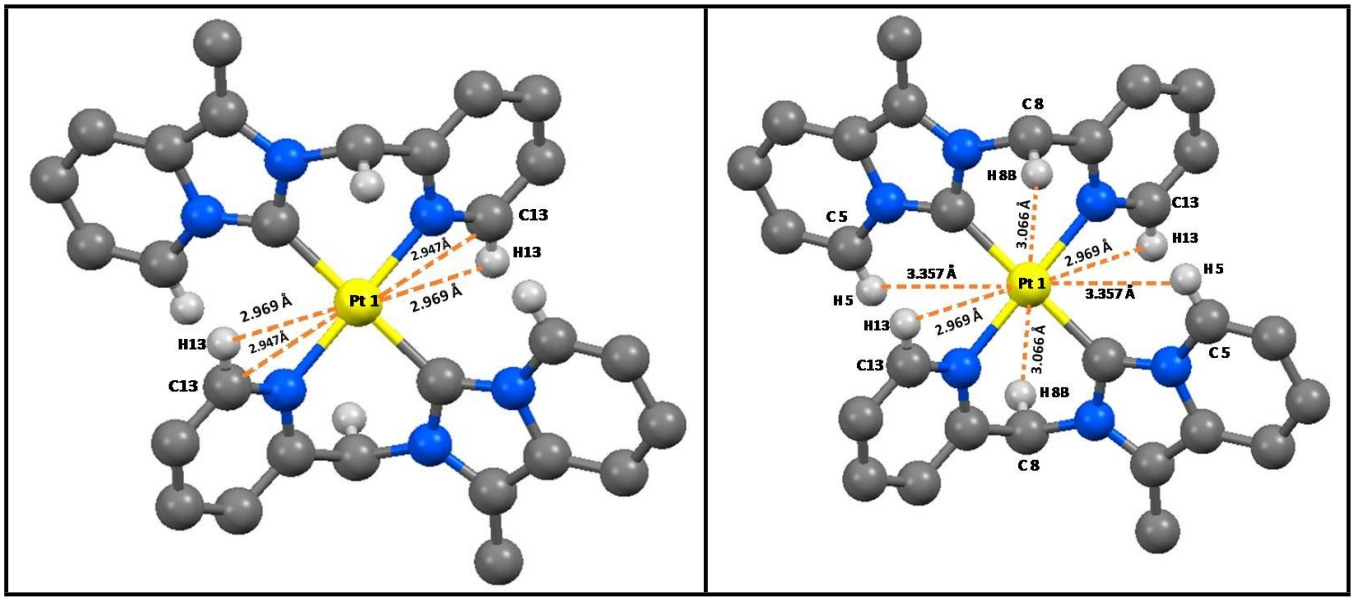


Figure S12. Various intramolecular Pt(II)····H-C interactions present in complex **3.**

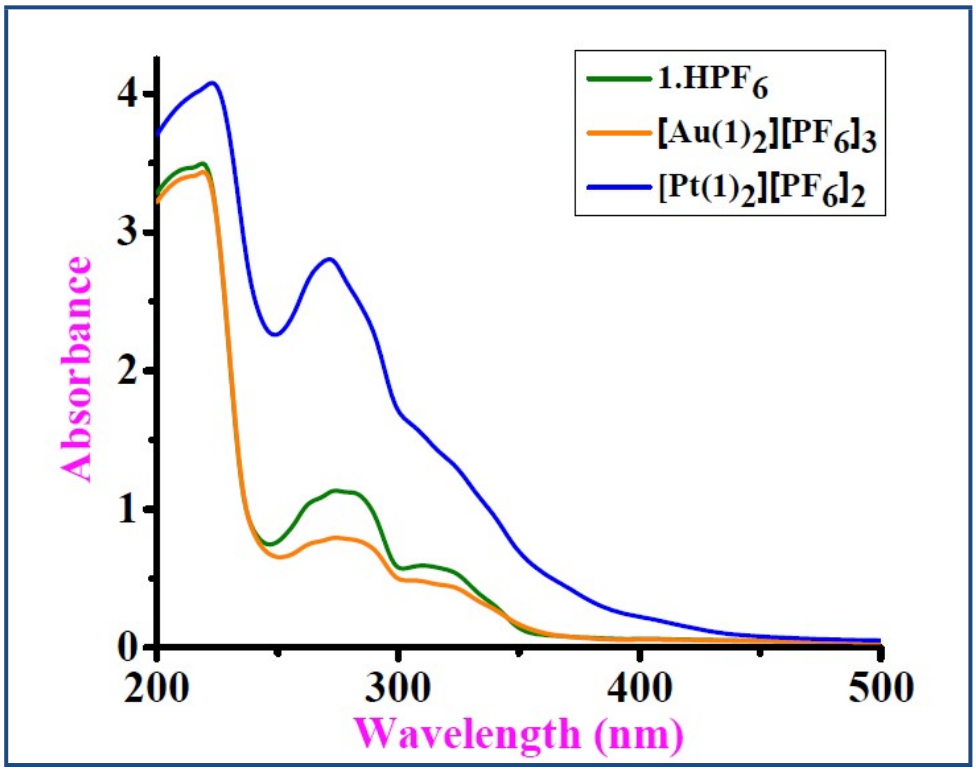


Figure S13. Absorption spectra of complexes **2** (Au-complex) and **3** (Pt-complex) and proligand **1**.HPF_6 studied in DCM solution at room temperature at 50 µM conc.

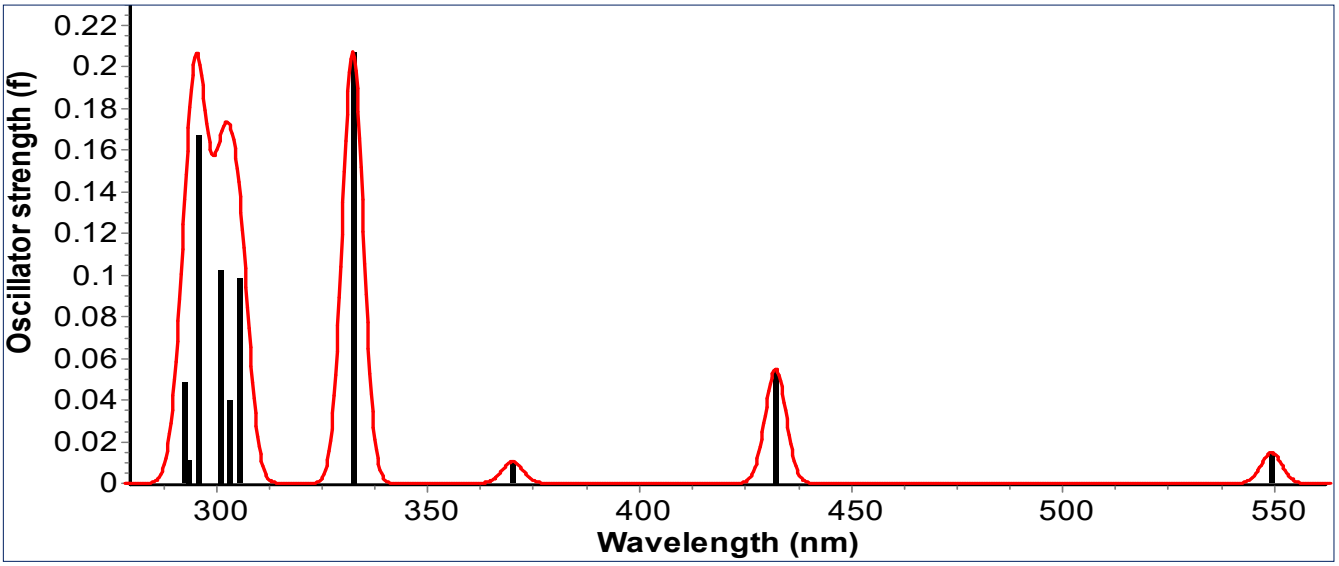


Figure S14.Simulated absorption spectra of Complex **2** in CH_3CN using TD-DFT Computation.

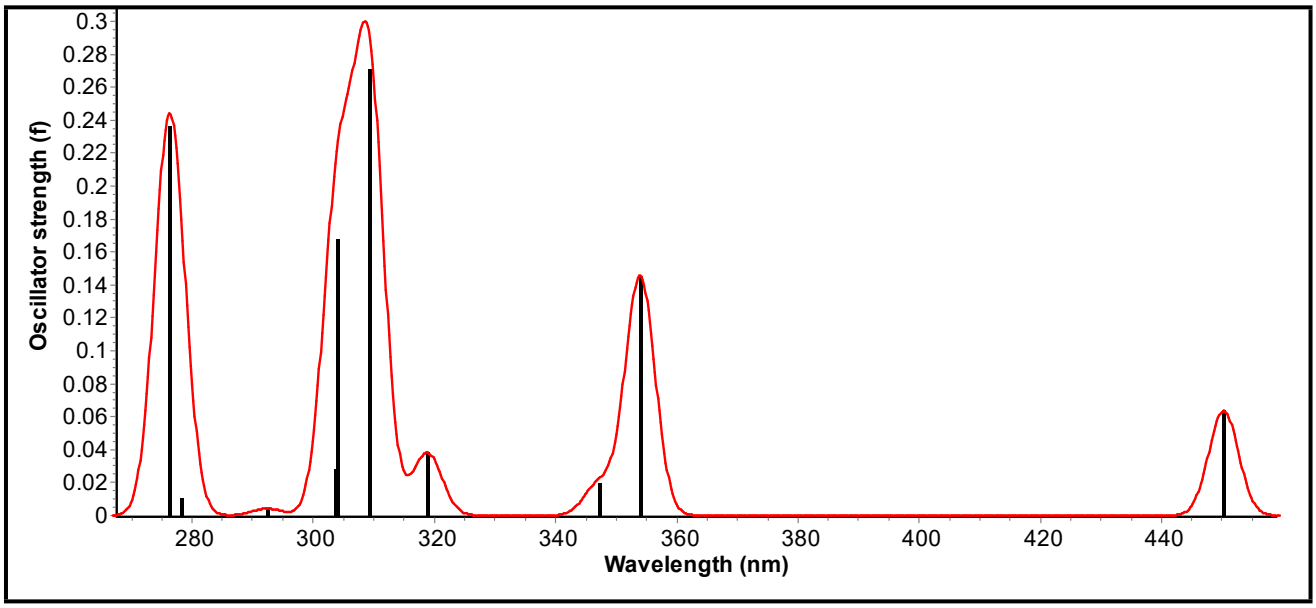


Figure S15.Simulated absorption spectra of Complex **3** in CH_3CN using TD-DFT Computation.

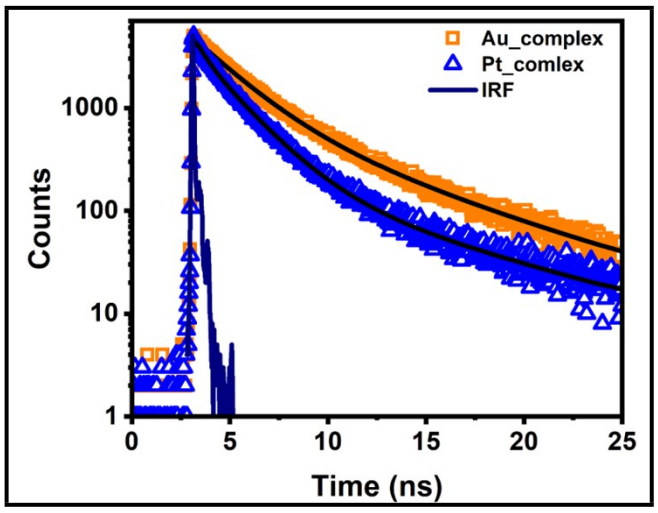


Figure S16. Time resolved fluorescence spectra of complex-**2** and **3** in dry CH_3CN solution with λ_{ex}= 340 nm. The solid navy-blue line represents the instrument response function (IRF) of the system.

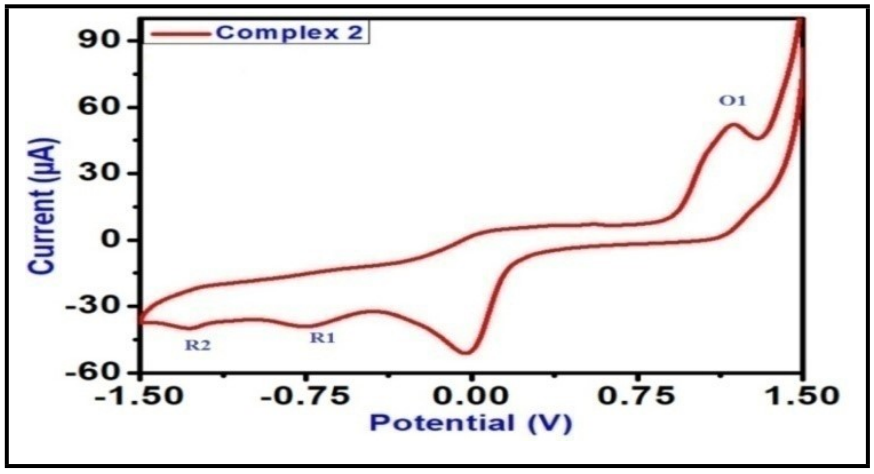


Figure S17.The cyclic voltammogram of complex **2** in dry acetonitrile at a 100 mVs^{-1} scan rate with Pt as the working electrode, Ag/AgCl as the reference electrode, and a 0.1(M) solution of $[N(Bu)_4]PF_6$ as the supporting electrolyte.

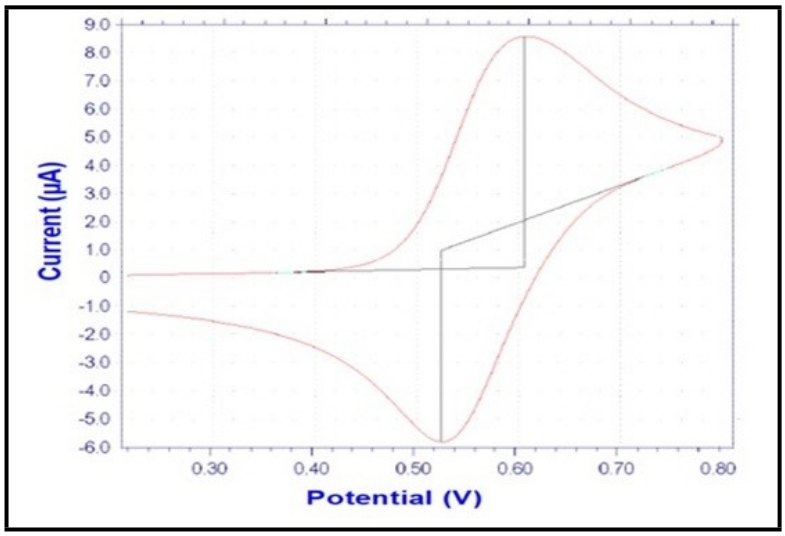


Figure S18. The cyclic voltammogram of **3** in dry acetonitrile at a 100 mVs^{-1} scan rate with Pt as the working electrode, Ag/AgCl as the reference electrode, and a 0.1(M) solution of $[N(Bu)_4]PF_6$ as the supporting electrolyte.

Table S1. Summary of X-Ray crystallographic data of **2** and **3**.

Complex parameters	**2**	**3**
Empirical formula	$C_{36}H_{38}N_{10}AuP_3F_{18}$	$C_{30}H_{29}N_7PtP_2F_{12}$
Formula weight	1242.64	972.63
Crystal system	Triclinic	Monoclinic
Space group	P -1	C 2/c
Temperature /K	295	100
a /Å	10.5186(13)	14.3168(16)
b / Å	11.1996(14)	20.207(2)
c / Å	11.4763(14)	12.3606(14)
α (°)	67.964(4)	90(4)
β (°)	89.955(4)	103.347(4)
γ (°)	69.998(4)	90(4)
Volume / $Å^3$	1164.9(3)	3479.2(7)
Z	1	4
Density / g cm^{-3}	1.771	1.857
Absorption coefficient(mm^{-1})	3.373	9.320
Theta range	2.628 to 25.460	7.304 to 76.747
Index ranges	-12<=h<=12, -13<=k<=13, -13<=l<=13	-16<=h<=17, -23<=k<=24, -13<=l<=13
Total / unique / obs. data	23197 /4295/4294	42953 /3355/3187
No. of Parameters	313	240
Final R indices [I>2sigma(I)]	R1 = 0.0287, wR2 = 0.0777	R1 = 0.0382, wR2 =0.1020
R indices (all data)	R1 = 0.0287, wR2 = 0.0777	R2 = 0.0396, wR2 =0.1034
GOF	1.039	1.149

Table S2. Selected bond lengths (Å) of various **M…H-C** interactions of complex **2** and **3**.

M···H/ M···C	**Complex 2 (Å) M= Au(III)**	**Complex 3 (Å) M= Pt(II)**
M(1)···H(13)	2.939	2.969
M(1)···H(8B)	3.044	3.066
M(1)···H(5)	3.365	3.357
Ave.	3.116	3.131
M(1)···C(13)	2.925	2.947
M(1)···C(8)	3.150	3.160
M(1)···C(5)	3.663	3.666
Ave.	3.246	3.258

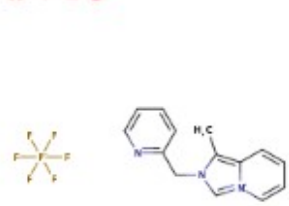
Table S3. Selected bond angles (°) of various **M…H-C** interactions of complex **2** and **3**.

C-H···M/ H-C···M	**Complex 2 M= Au(III)** (°)	**Complex 3 M= Pt(II)** (°)
C(13)-H(13)···M(1)	80.04	79.46
C(8)-H(8B)···M(1)	87.22	86.28
C(5)-H(5)···M(1)	101.34	101.46
Ave.	89.53	89.1
H(13)-C(13)···M(1)	81.71	82.05
H(8)-C(8B)···M(1)	74.86	75.49
H(5)-C(5)···M(1)	64.26	63.83
Ave.	73.61	73.79

Table S4. The docking results of NHC proligand (**1**.HPF_6), Complex **2** and Complex **3** with Human-DNA Topoisomerase (ID: 1t8i) are given in Kcal/mol.

compound	Binding free energy $\Delta G_{binding}$ (Kcal/mol)	vdW+H bond + dissolving energy ($\Delta G_{vdW+hb+desolv}$)	Electrostatic energy (ΔG_{elec})	Total internal energy (ΔG_{total})	Torsional free energy (ΔG_{tor})	Unbound system's energy (ΔG_{unb})	Estimated Inhibition Constant, Ki (micromolar)	Reference RMSD
Proligand **1**.HPF_6	-5.73	-6.33	-0.07	-0.15	+0.60	-0.15	62.55	31.60
Complex **2**	-6.94	-6.83	-0.11	+0.00	+0.00	+0.00	8.20	31.60
Complex-**3**	-7.26	-7.24	-0.02	+0.00	+0.00	+0.00	4.75	31.60

Table S5. Pharmacokinetic study parameters of proligand (**1**.HPF_6)



SMILES F[P-](F)(F)(F)(F)F.Cc1n(Cc2ccccn2)c[n+]2c1cccc2

Physicochemical Properties	
Formula	C14H14F6N3P
Molecular weight	369.25 g/mol
Num. heavy atoms	24
Num. arom. heavy atoms	15
Fraction Csp3	0.14
Num. rotatable bonds	2
Num. H-bond acceptors	7
Num. H-bond donors	0
Molar Refractivity	81.80
TPSA	35.51 Å²

Lipophilicity	
Log $P_{o/w}$ (iLOGP)	0.00
Log $P_{o/w}$ (XLOGP3)	6.16
Log $P_{o/w}$ (WLOGP)	7.88
Log $P_{o/w}$ (MLOGP)	2.41
Log $P_{o/w}$ (SILICOS-IT)	1.95
Consensus Log $P_{o/w}$	3.68

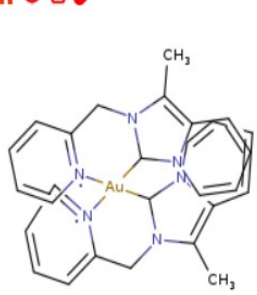
Water Solubility	
Log *S* (ESOL)	-6.34
Solubility	1.69e-04 mg/ml ; 4.56e-07 mol/l
Class	Poorly soluble
Log *S* (Ali)	-6.69
Solubility	7.55e-05 mg/ml ; 2.05e-07 mol/l
Class	Poorly soluble
Log *S* (SILICOS-IT)	-4.21
Solubility	2.29e-02 mg/ml ; 6.19e-05 mol/l
Class	Moderately soluble

Pharmacokinetics	
GI absorption	Low
BBB permeant	No
P-gp substrate	Yes
CYP1A2 inhibitor	Yes
CYP2C19 inhibitor	Yes
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	Yes
Log K_p (skin permeation)	-4.18 cm/s

Druglikeness	
Lipinski	Yes; 0 violation
Ghose	No; 1 violation: WLOGP>5.6
Veber	Yes
Egan	No; 1 violation: WLOGP>5.88
Muegge	No; 1 violation: XLOGP3>5
Bioavailability Score	0.55

Medicinal Chemistry	
PAINS	0 alert
Brenk	2 alerts: phosphor, quaternary_nitrogen_1
Leadlikeness	No; 2 violations: MW>350, XLOGP3>3.5
Synthetic accessibility	2.50

Table S6.Pharmacokinetic study parameters of complex **2**.



SMILES CC1=c2ccccn2C2N1Cc1ccccn1[Au]12C2N(Cc3n1cccc3)C(=c1n2ccccc1)C

Physicochemical Properties	
Formula	C28H28AuN6
Molecular weight	645.53 g/mol
Num. heavy atoms	35
Num. arom. heavy atoms	24
Fraction Csp3	0.21
Num. rotatable bonds	0
Num. H-bond acceptors	0
Num. H-bond donors	0
Molar Refractivity	141.57
TPSA	26.20 Å²

Lipophilicity	
Log $P_{o/w}$ (iLOGP)	0.00
Log $P_{o/w}$ (XLOGP3)	5.11
Log $P_{o/w}$ (WLOGP)	1.91
Log $P_{o/w}$ (MLOGP)	2.00
Log $P_{o/w}$ (SILICOS-IT)	-2.84
Consensus Log $P_{o/w}$	1.23

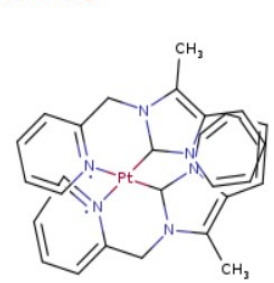
Water Solubility	
Log *S* (ESOL)	-7.57
Solubility	1.74e-05 mg/ml ; 2.70e-08 mol/l
Class	Poorly soluble
Log *S* (Ali)	-5.40
Solubility	2.55e-03 mg/ml ; 3.94e-06 mol/l
Class	Moderately soluble
Log *S* (SILICOS-IT)	-6.09
Solubility	5.19e-04 mg/ml ; 8.04e-07 mol/l
Class	Poorly soluble

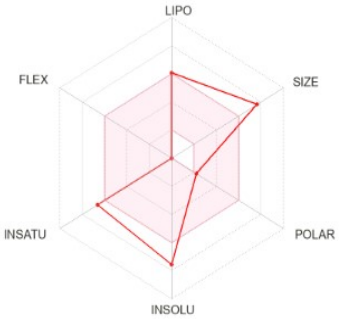
Pharmacokinetics	
GI absorption	High
BBB permeant	Yes
P-gp substrate	Yes
CYP1A2 inhibitor	Yes
CYP2C19 inhibitor	No
CYP2C9 inhibitor	Yes
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-6.61 cm/s

Druglikeness	
Lipinski	Yes; 1 violation: MW>500
Ghose	No; 2 violations: MW>480, MR>130
Veber	Yes
Egan	Yes
Muegge	No; 3 violations: MW>600, XLOGP3>5, #rings>7
Bioavailability Score	0.55

Medicinal Chemistry	
PAINS	0 alert
Brenk	0 alert
Leadlikeness	No; 2 violations: MW>350, XLOGP3>3.5
Synthetic accessibility	6.24

Table S7.Pharmacokinetic study parameters of complex **3**.





SMILES CC1=c2ccccn2C2N1Cc1ccccn1[Pt]12C2N(Cc3n1cccc3)C(=c1n2ccc c1)C

Physicochemical Properties	
Formula	C28H28N6Pt
Molecular weight	643.64 g/mol
Num. heavy atoms	35
Num. arom. heavy atoms	24
Fraction Csp3	0.21
Num. rotatable bonds	0
Num. H-bond acceptors	0
Num. H-bond donors	0
Molar Refractivity	141.57
TPSA	26.20 Å²

Lipophilicity	
Log $P_{o/w}$ (iLOGP)	0.00
Log $P_{o/w}$ (XLOGP3)	5.11
Log $P_{o/w}$ (WLOGP)	1.91
Log $P_{o/w}$ (MLOGP)	2.00
Log $P_{o/w}$ (SILICOS-IT)	-2.85
Consensus Log $P_{o/w}$	1.23

Water Solubility	
Log *S* (ESOL)	-7.56
Solubility	1.78e-05 mg/ml ; 2.77e-08 mol/l
Class	Poorly soluble
Log *S* (Ali)	-5.40
Solubility	2.54e-03 mg/ml ; 3.94e-06 mol/l
Class	Moderately soluble
Log *S* (SILICOS-IT)	-6.09
Solubility	5.22e-04 mg/ml ; 8.11e-07 mol/l
Class	Poorly soluble

Pharmacokinetics	
GI absorption	High
BBB permeant	Yes
P-gp substrate	Yes
CYP1A2 inhibitor	Yes
CYP2C19 inhibitor	No
CYP2C9 inhibitor	Yes
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Log K_p (skin permeation)	-6.60 cm/s

Druglikeness	
Lipinski	Yes; 1 violation: MW>500
Ghose	No; 2 violations: MW>480, MR>130
Veber	Yes
Egan	Yes
Muegge	No; 3 violations: MW>600, XLOGP3>5, #rings>7
Bioavailability Score	0.55

Medicinal Chemistry	
PAINS	0 alert
Brenk	0 alert
Leadlikeness	No; 2 violations: MW>350, XLOGP3>3.5
Synthetic accessibility	6.13