

# Design, Synthesis and Characterisation of Chimeric Ruthenium(II)-Gold(I) Complexes showing enhanced cytotoxic properties.

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## Supplementary Information

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## 1. Crystallographic data for compound **1**

Crystals of **1** (red prisms with approximate dimensions 0.25 x 0.23 x 0.23 mm) were obtained from a solution of **1** in CH<sub>2</sub>Cl<sub>2</sub> and slow evaporation at RT to yield bright red crystals.

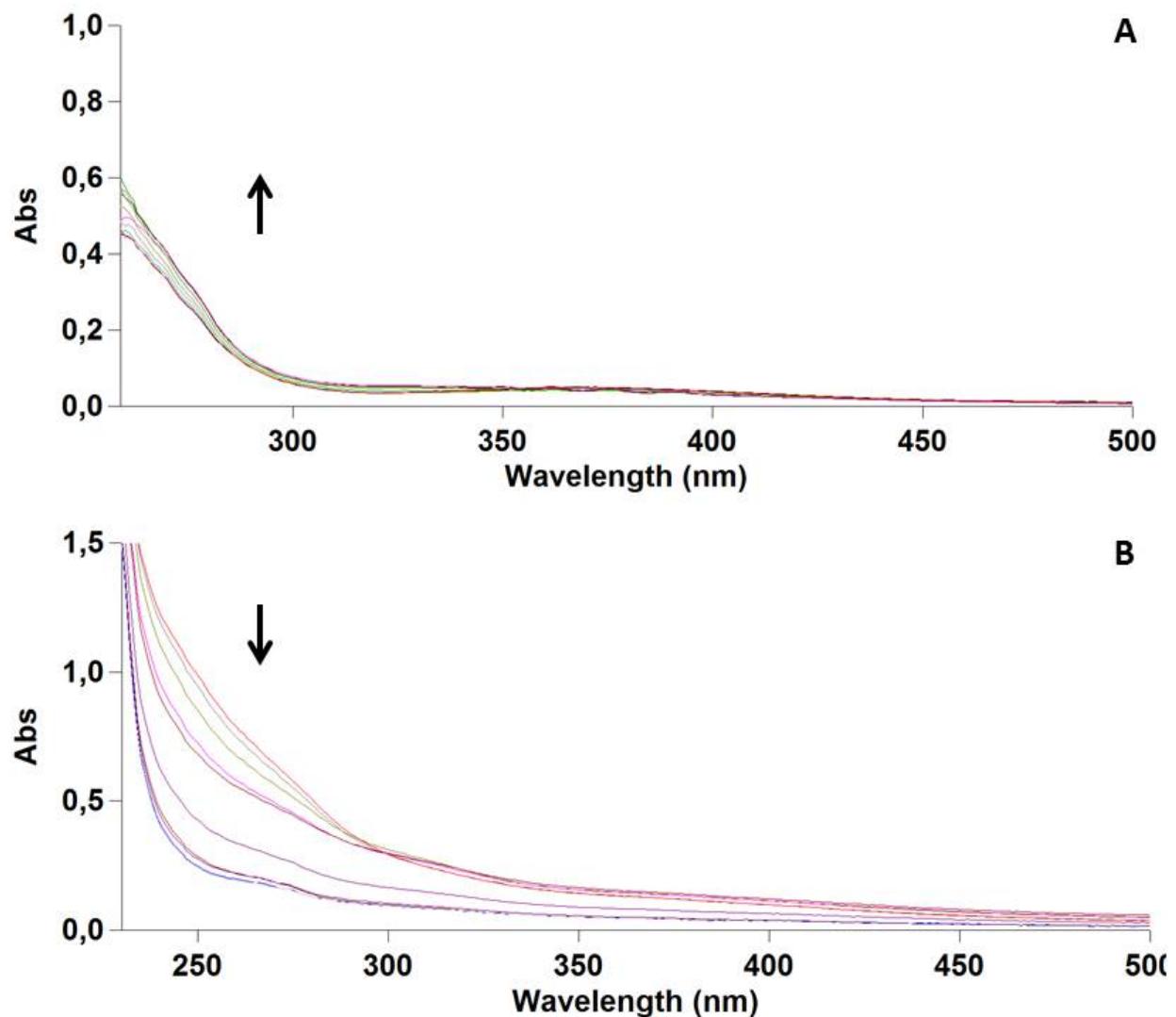
**Table S1.** Crystal data and structure refinement for compound **1**.

formula	C <sub>35</sub> H <sub>36</sub> AuCl <sub>3</sub> P <sub>2</sub> Ru
fw	923.01
T [K]	293
$\lambda$ (Mo <sub>Kα</sub> )[Å]	0.71069
crystal system	Monoclinic
space group	P 21/n
<i>a</i> [Å]	11.8959(4)
<i>b</i> [Å]	26.8401(6)
<i>c</i> [Å]	13.1736(5)
$\beta$ [°]	113.398(4)
V [Å] <sup>3</sup>	3860.3(2)
Z	4
D <sub>calcd</sub> (g cm <sup>-3</sup> )	1.661
$\mu$ (mm <sup>-1</sup> )	4.570
GOF	1.031
R <sub>1</sub> [ <i>I</i> > 2 $\sigma$ ]	0.1257
wR <sub>2</sub> (all data)	0.1931

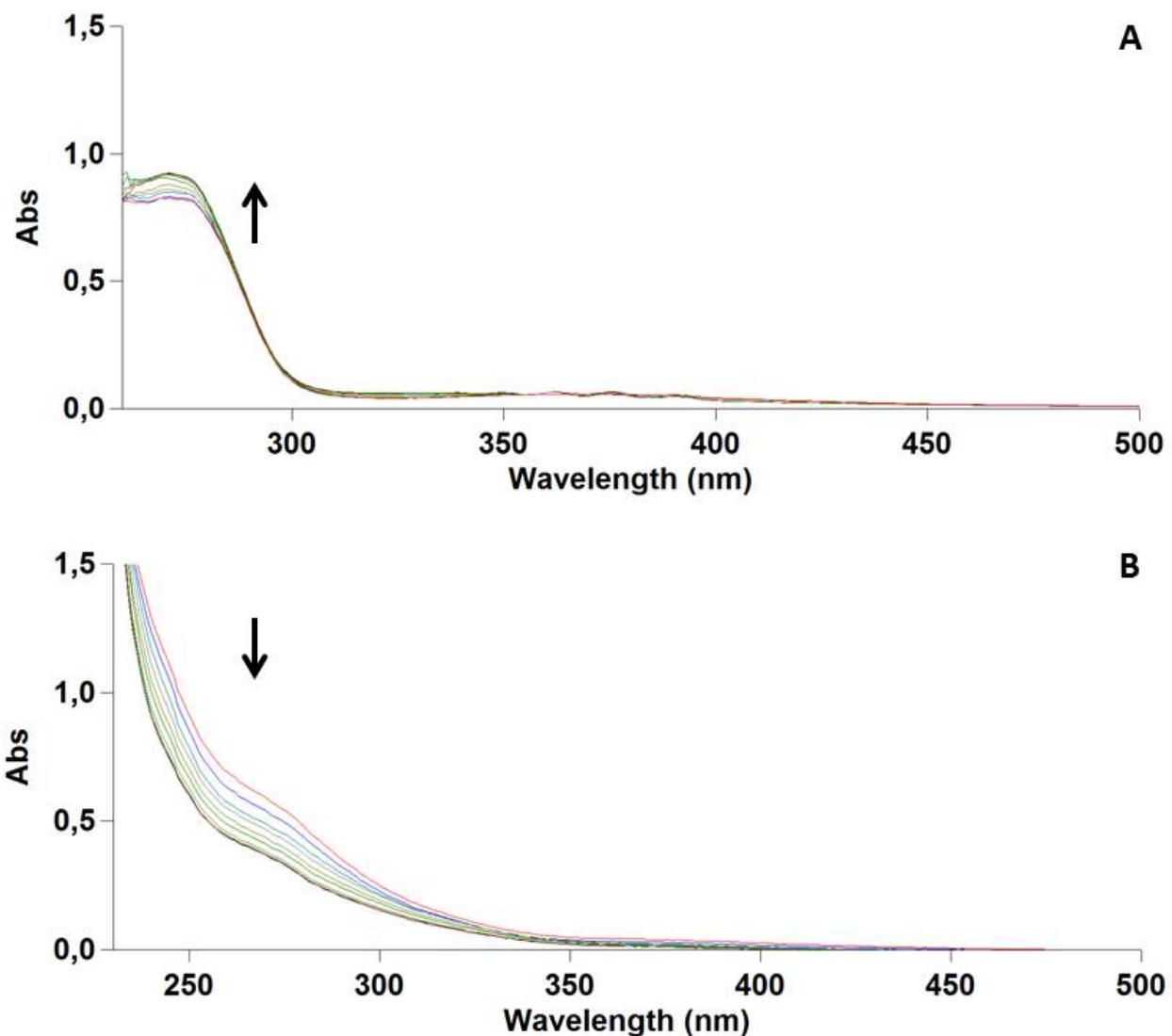
**Table S2.** Selected structural parameters of complex **1** obtained from X-ray single crystal diffraction studies. Bond lengths in Å and angles in °.

Ru(1)-C(1)	2.2121(9)	C(2)-Ru(1)-Cl(1)	153.96(7)
Ru(1)-C(2)	2.1873(9)	C(2)-Ru(1)-Cl(2)	117.89(8)
Ru(1)-C(3)	2.172(1)	C(2)-Ru(1)-P(1)	95.72(6)
Ru(1)-C(4)	2.182(1)	C(3)-Ru(1)-C(4)	37.23(3)
Ru(1)-C(5)	2.2067(9)	C(3)-Ru(1)-C(5)	66.70(3)
Ru(1)-C(6)	2.2217(9)	C(3)-Ru(1)-C(6)	78.49(4)
Ru(1)-Cl(1)	2.400(3)	C(3)-Ru(1)-Cl(1)	116.79(8)
Ru(1)-Cl(2)	2.416(4)	C(3)-Ru(1)-Cl(2)	155.06(9)
Ru(1)-P(1)	2.352(2)	C(3)-Ru(1)-P(1)	95.42(6)
Au(1)-Cl(3)	2.275(4)	C(4)-Ru(1)-C(5)	36.93(3)
Au(1)-P(2)	2.228(2)	C(4)-Ru(1)-C(6)	66.28(4)
		C(4)-Ru(1)-Cl(1)	90.67(8)
		C(4)-Ru(1)-Cl(2)	151.70(9)
C(1)-Ru(1)-C(2)	36.83(3)	C(4)-Ru(1)-P(1)	120.73(6)
C(1)-Ru(1)-C(3)	66.61(3)	C(5)-Ru(1)-C(6)	36.58(3)
C(1)-Ru(1)-C(4)	78.49(4)	C(5)-Ru(1)-Cl(1)	91.50(8)
C(1)-Ru(1)-C(5)	66.03(3)	C(5)-Ru(1)-Cl(2)	114.83(8)
C(1)-Ru(1)-C(6)	36.54(3)	C(5)-Ru(1)-P(1)	157.40(6)
C(1)-Ru(1)-Cl(1)	154.57(8)	C(6)-Ru(1)-Cl(1)	118.03(8)
C(1)-Ru(1)-Cl(2)	90.74(7)	C(6)-Ru(1)-Cl(2)	89.49(7)
C(1)-Ru(1)-P(1)	121.04(6)	C(6)-Ru(1)-P(1)	157.33(6)
C(2)-Ru(1)-C(3)	37.19(3)	Cl(1)-Ru(1)-Cl(2)	88.2(1)
C(2)-Ru(1)-C(4)	66.88(3)	Cl(1)-Ru(1)-P(1)	84.30(8)
C(2)-Ru(1)-C(5)	78.49(3)	Cl(2)-Ru(1)-P(1)	87.29(8)
C(2)-Ru(1)-C(6)	66.18(3)	P(2)-Au(1)-Cl(3)	177.88(9)

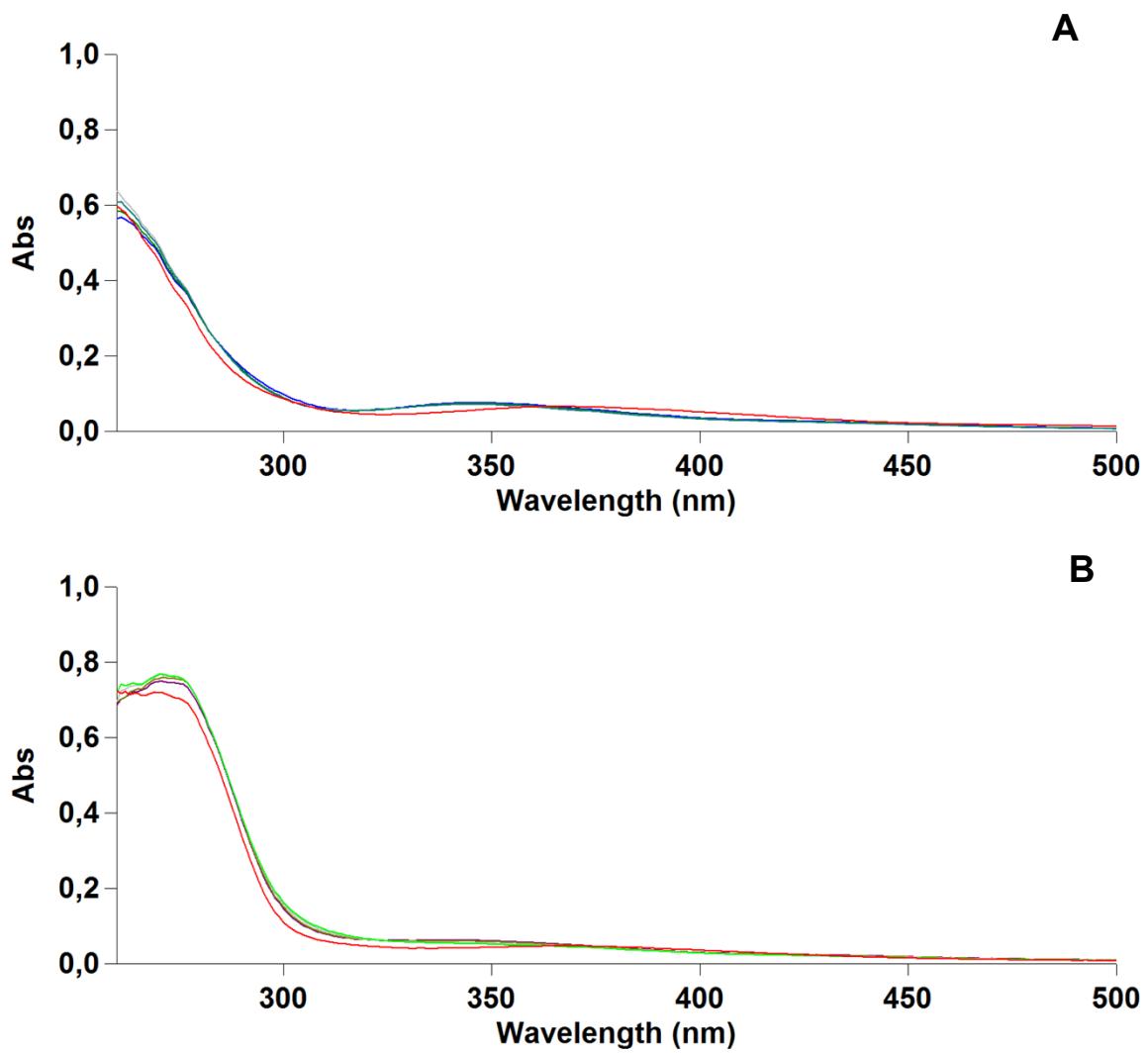
2. Time course UV-vis spectra



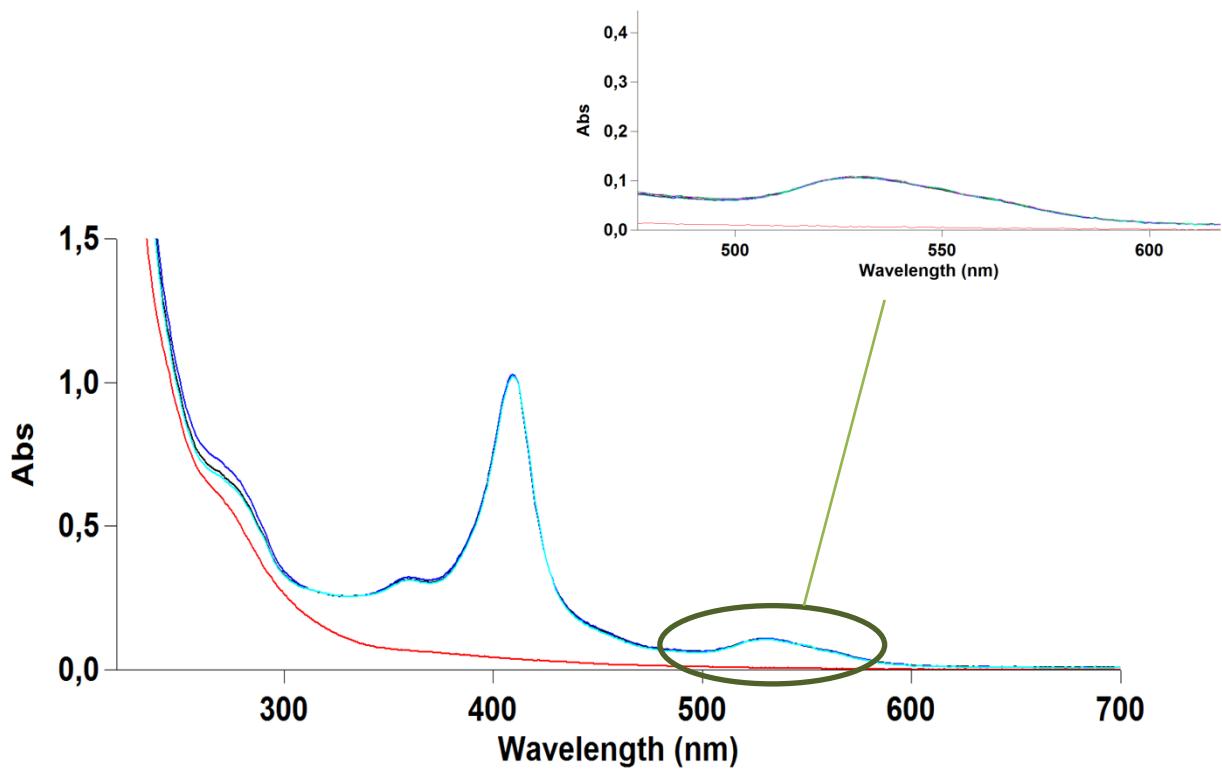
**Figure S1.** Time course UV-vis spectra compound **1** ( $10^{-5}$  M) dissolved in DMSO: (A) and ammonium acetate 20mM; (B) Over 72 h incubation.



**Figure S2.** Time course UV-vis spectra of compound **3** ( $10^{-5}$  M) dissolved in DMSO: (A) and ammonium acetate 20mM (B) Over 72 h incubation.

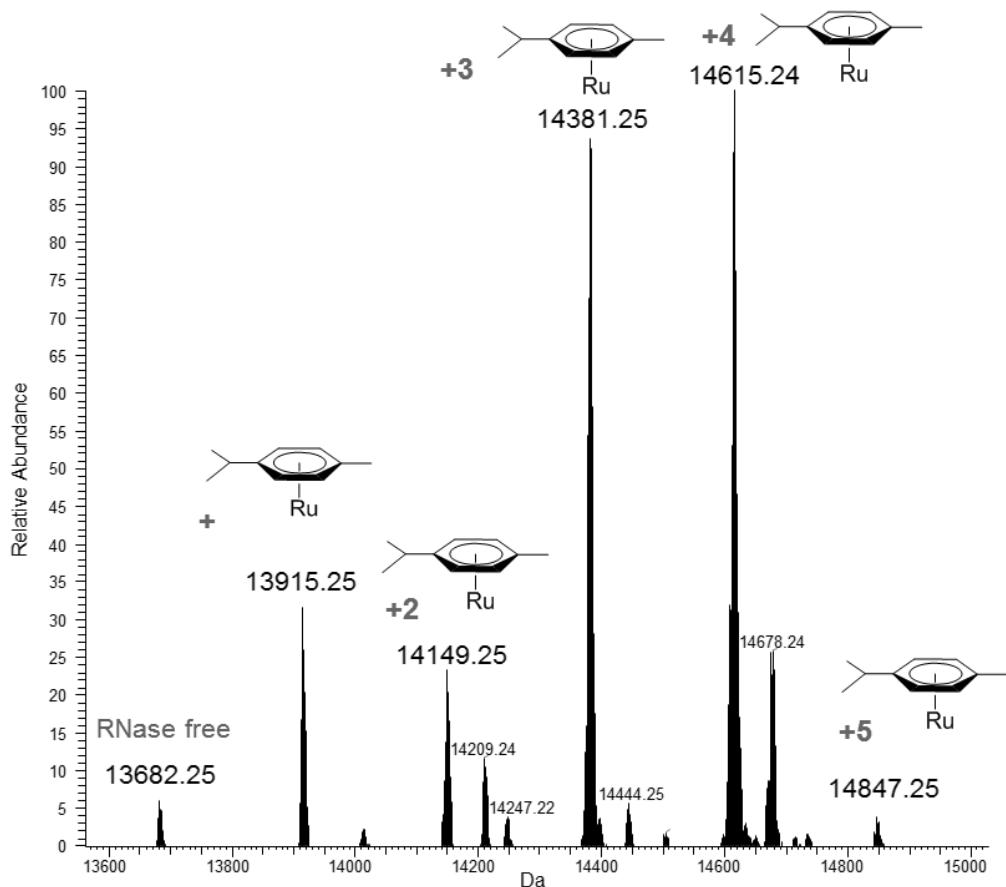


**Figure S3.** Time course UV-vis spectra of compound **1** (**A**) and compound **3** (**B**) dissolved in DMSO after addition of 10 equivalent  $\text{AgNO}_3$  over 2 h.



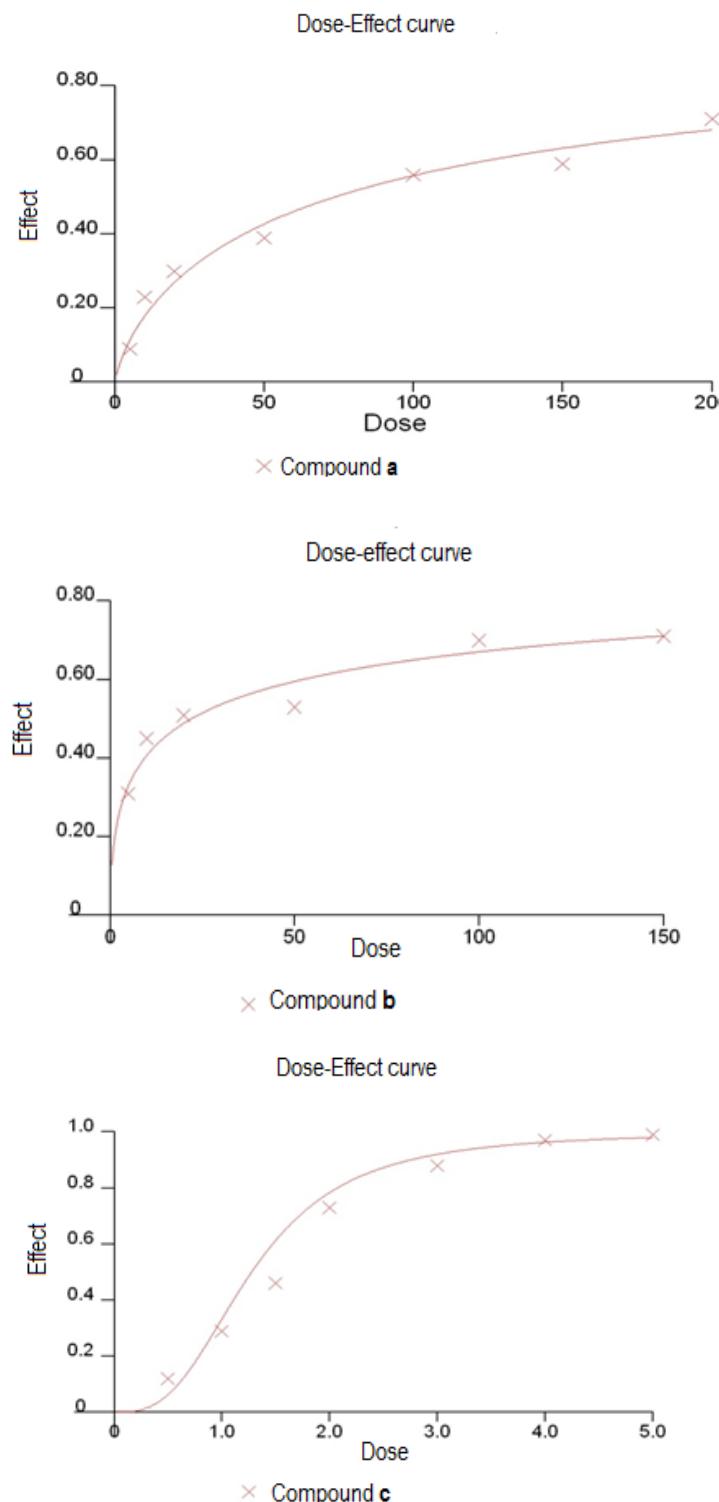
**Figure S4.** Time course UV-vis spectra of compound **1** and cytochrome c dissolved in ammonium acetate buffer over 24 h.

### 3. ESI Mass spectra



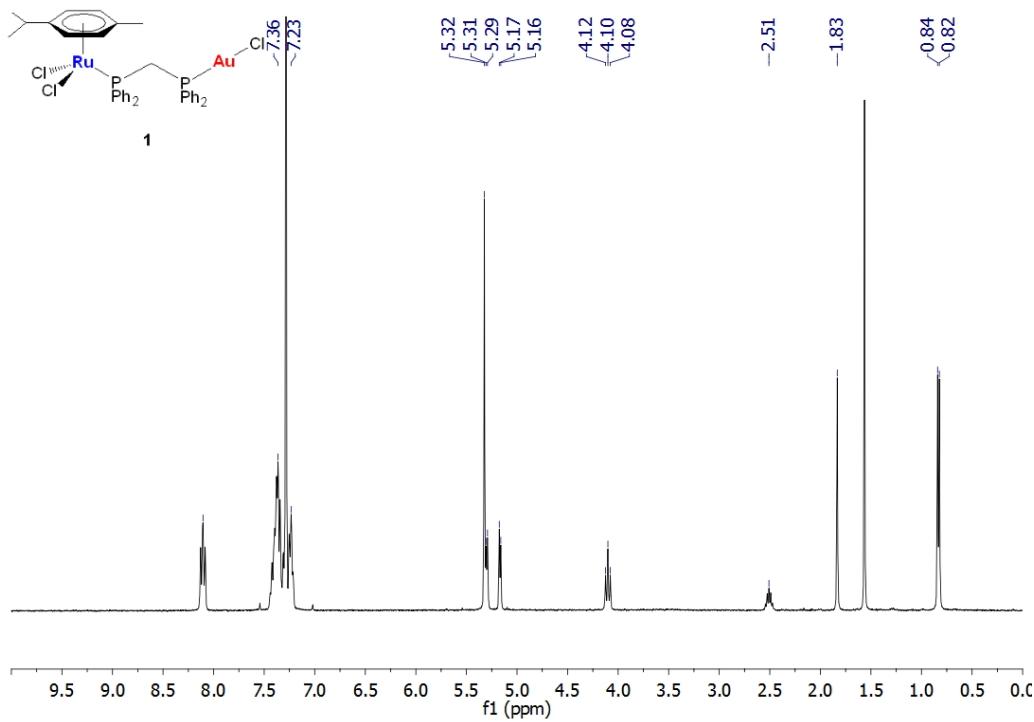
**Figure S5.** LTQ-Orbitrap ESI mass spectra of  $[\text{RuCl}(\mu\text{-Cl})(p\text{-cymene})]_2$  dissolved in 20 mM ammonium acetate buffer, pH 6.8 in the presence RNase. Protein concentration is  $10^{-4}$  M (with a metallodrug-protein molar ratio of 3:1).

#### 4. Cytotoxicity studies

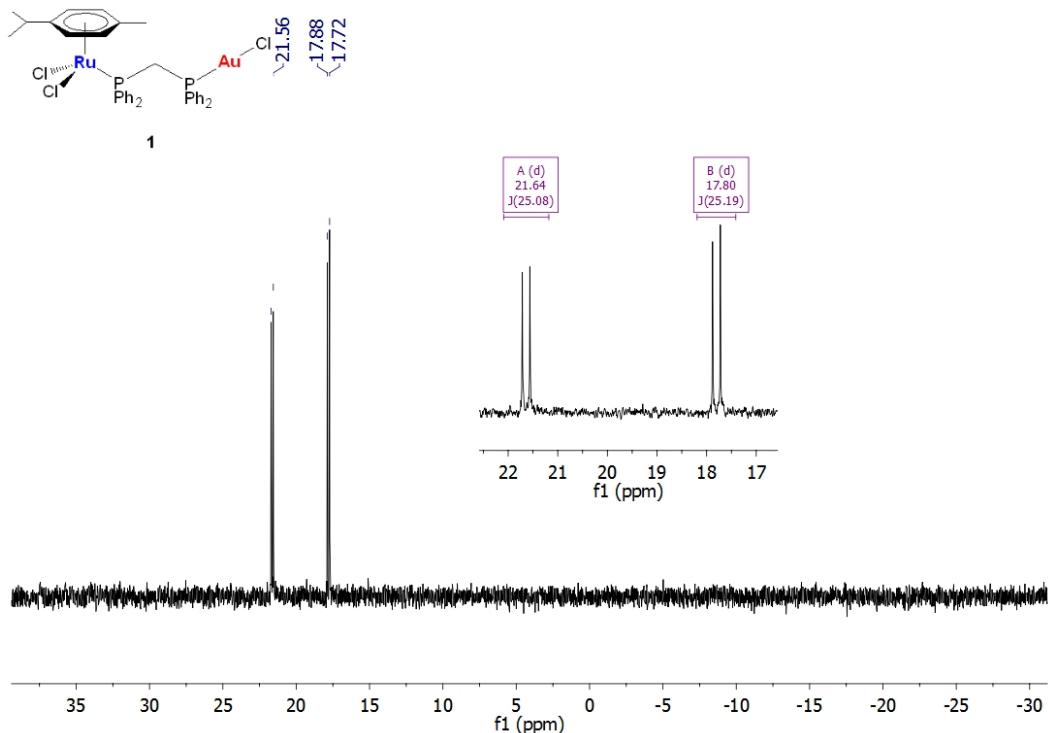


**Figure S6.** Dose/Effect curve for compound **a**, **b** and **c** against HCT116 cells(after 48 h of incubation) calculated by fitting the data points with a sigmoidal curve using Calcusyn software.

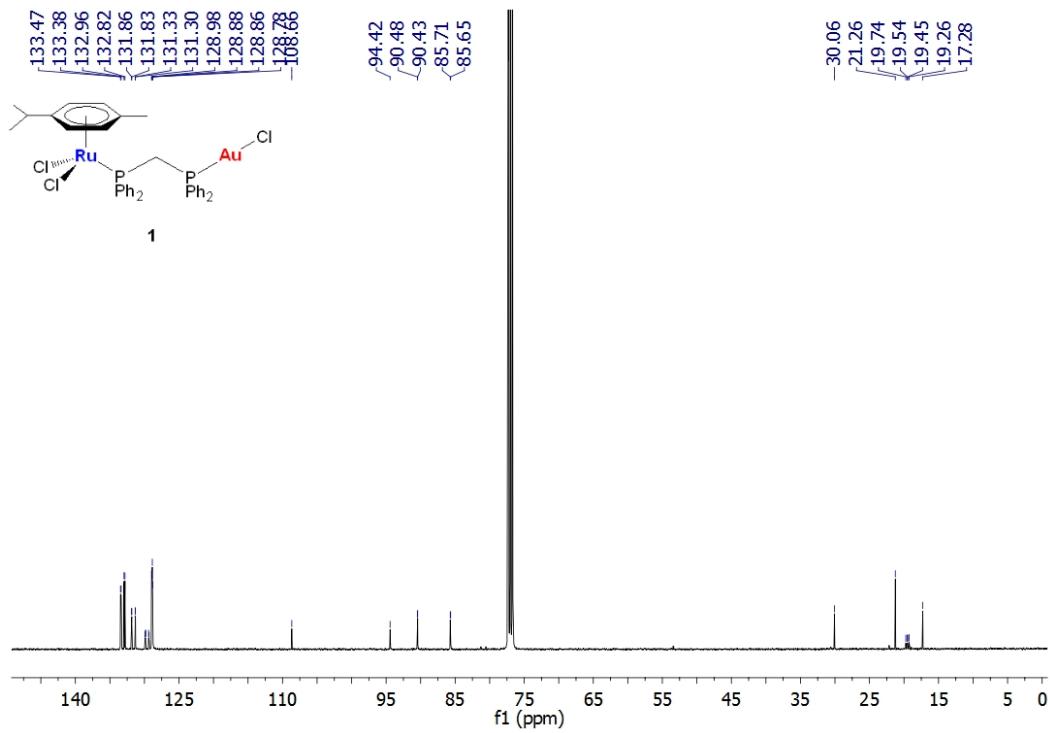
**5. NMR spectra of compound **1** and **3** in  $\text{CDCl}_3$**



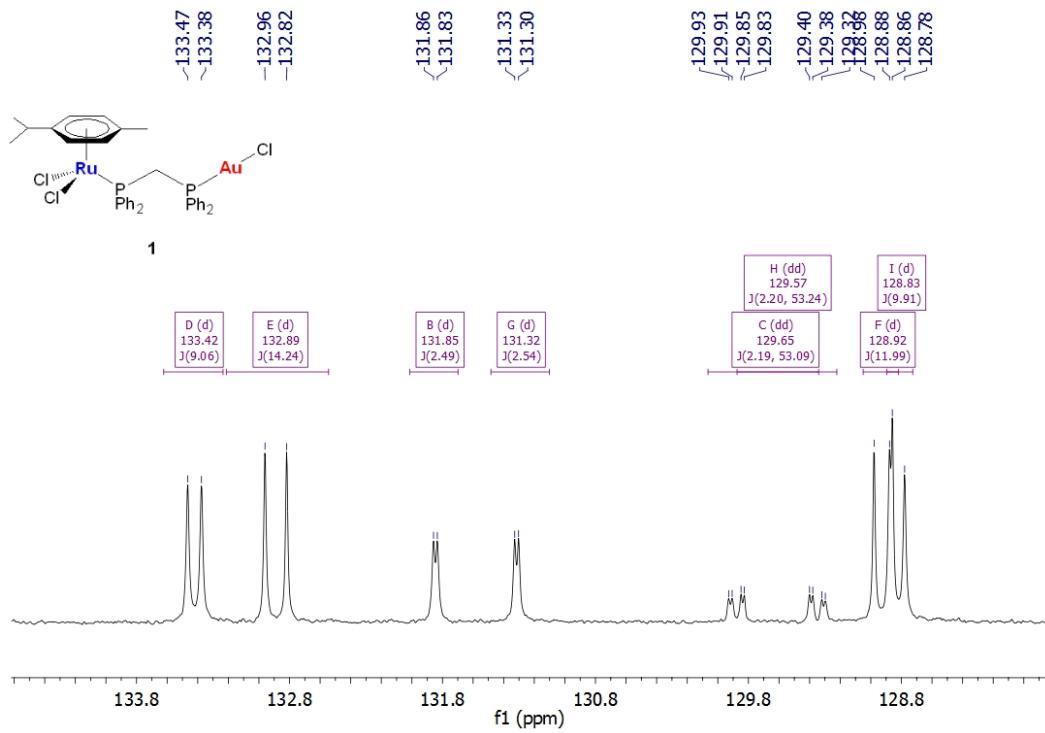
**Figure S7.**  $^1\text{H}$  NMR spectrum of compound **1** in  $\text{CDCl}_3$ .



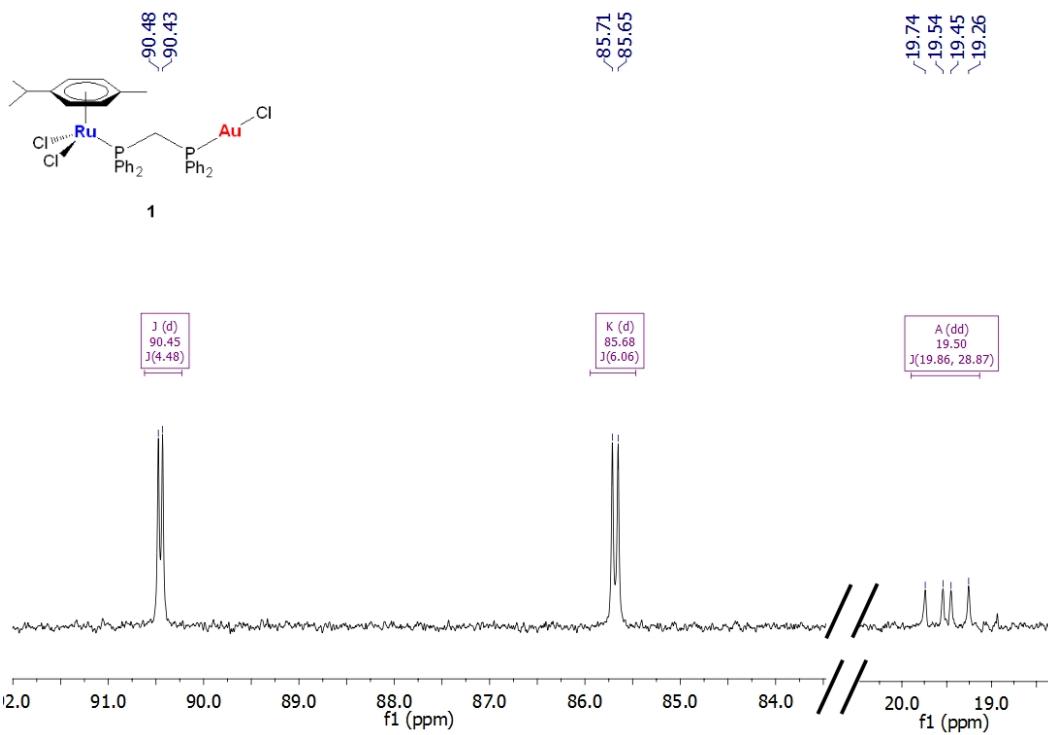
**Figure S8.**  $^{31}\text{P}\{^1\text{H}\}$  NMR spectrum of compound **1** in  $\text{CDCl}_3$ .



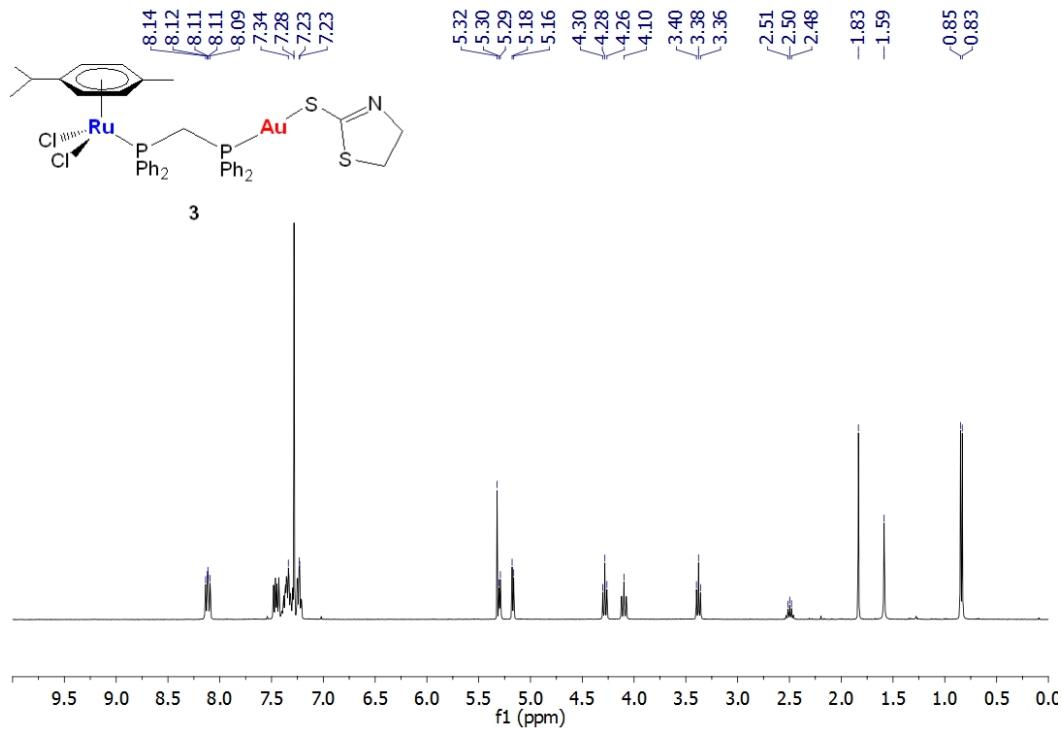
**Figure S9.**  $^{13}\text{C}\{\text{H}\}$  NMR spectrum of compound **1** in  $\text{CDCl}_3$ .



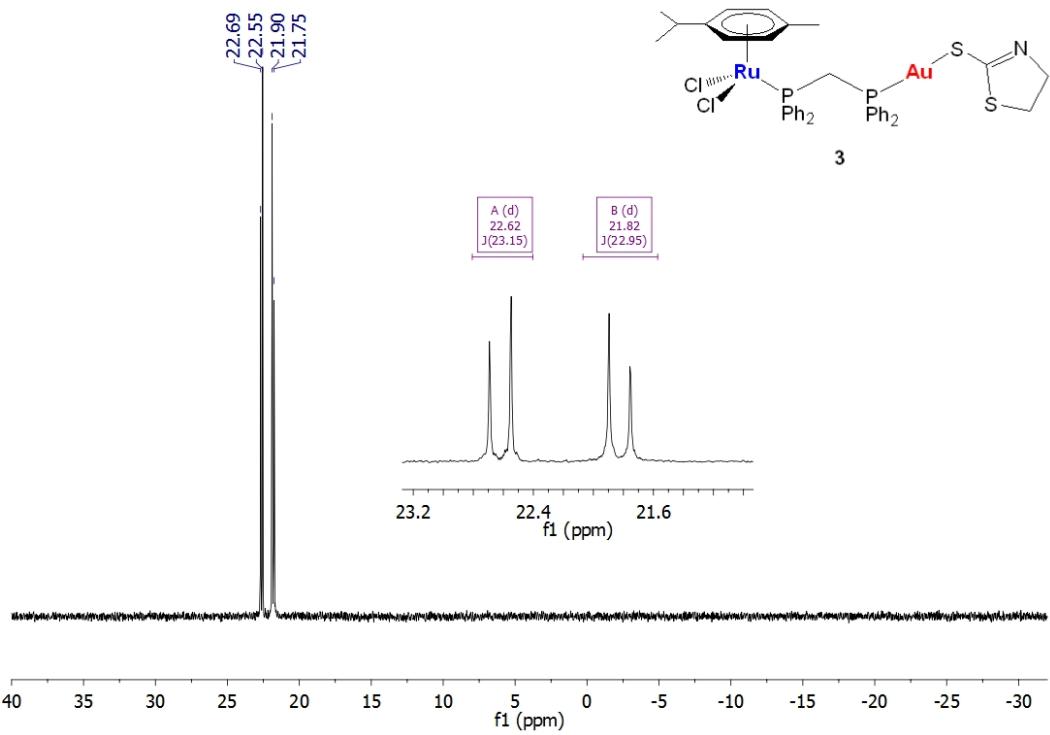
**Figure S10.** Magnification of aromatic region of  $^{13}\text{C}\{\text{H}\}$  NMR spectrum of compound **1** in  $\text{CDCl}_3$ .



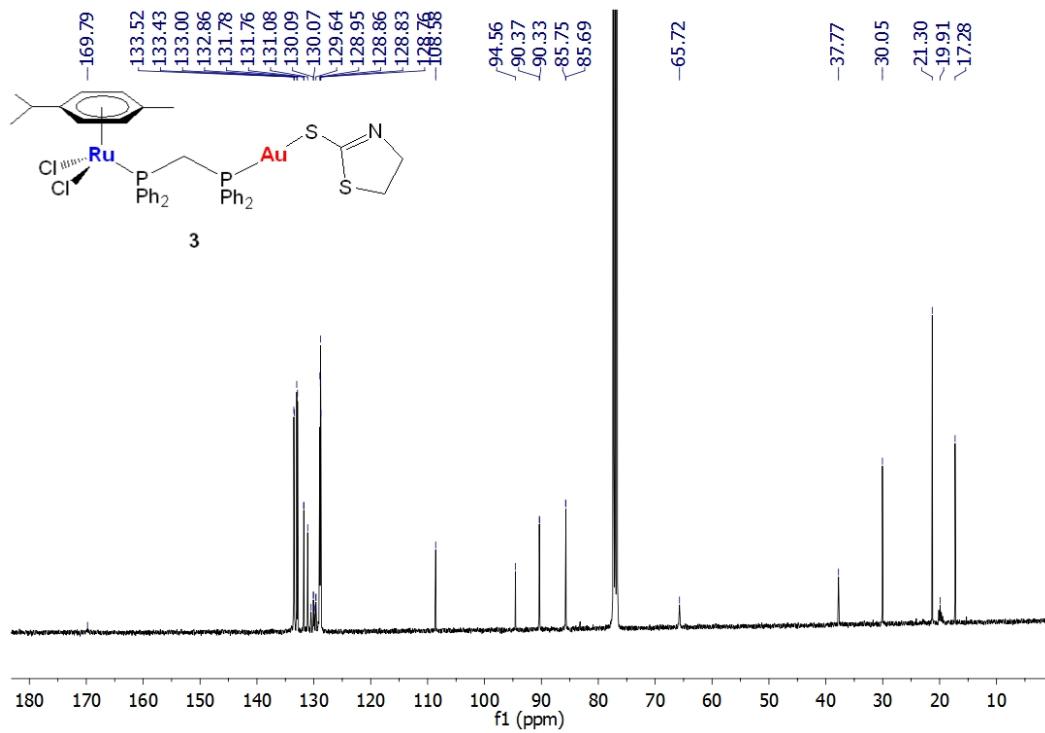
**Figure S11.** Magnification of two regions of  $^{13}\text{C}\{^1\text{H}\}$  NMR spectrum of compound **1** in  $\text{CDCl}_3$ .



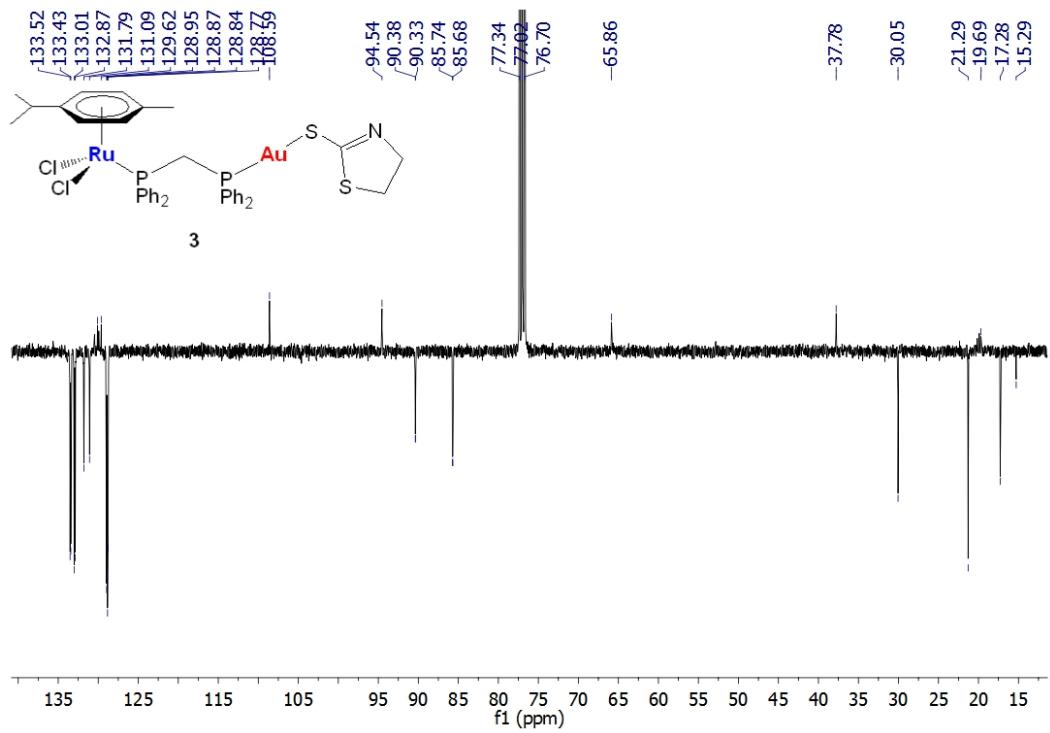
**Figure S12.**  $^1\text{H}$  NMR spectrum of compound **3** in  $\text{CDCl}_3$ .



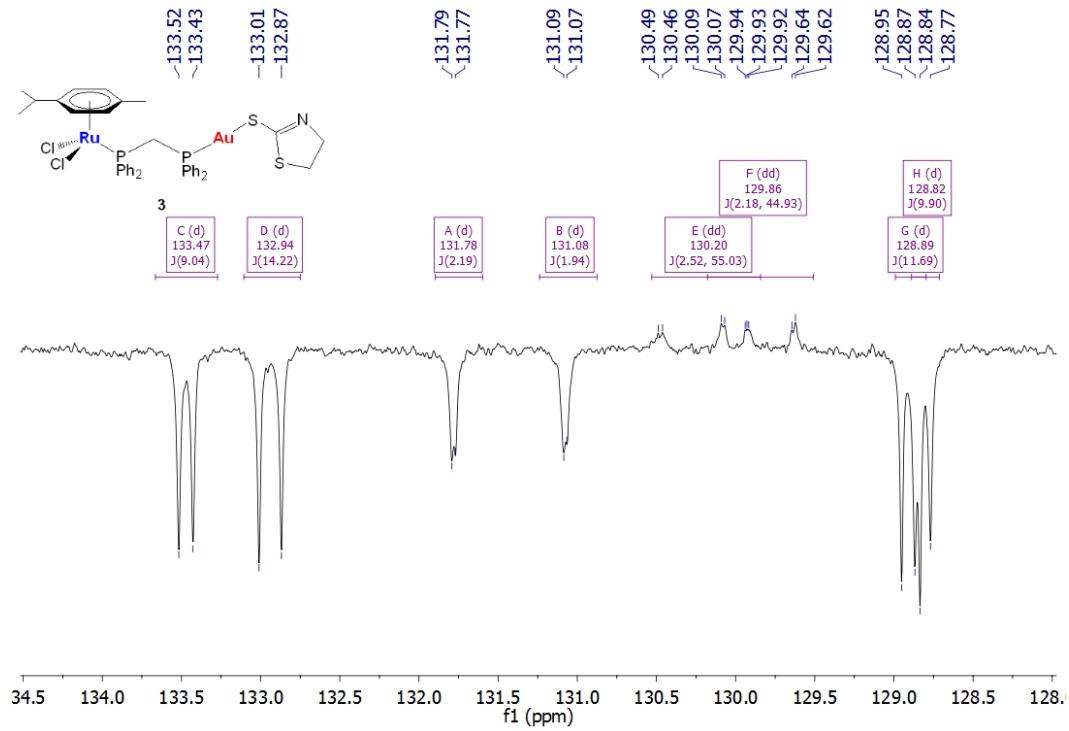
**Figure S13.**  $^{31}\text{P}\{\text{H}\}$  NMR spectrum of compound **3** in  $\text{CDCl}_3$ .



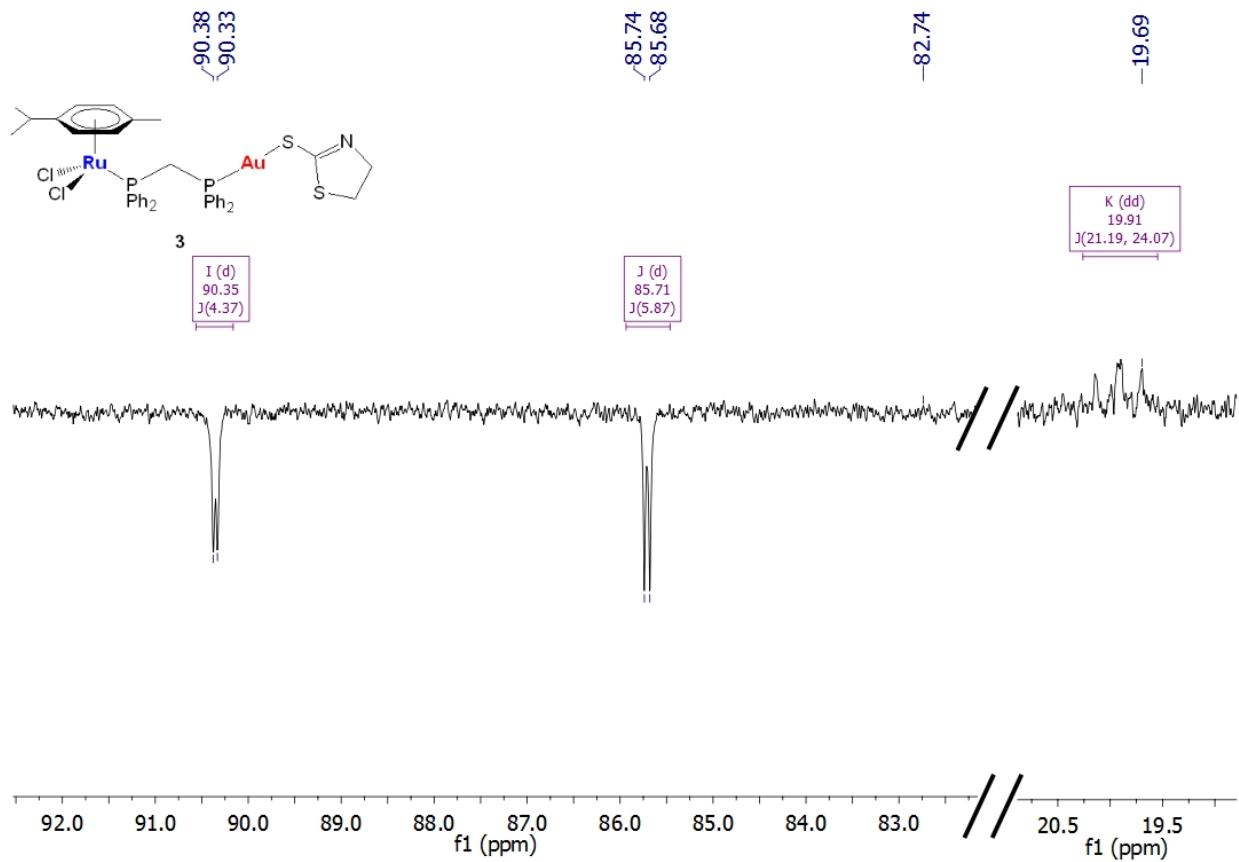
**Figure S14.**  $^{13}\text{C}\{\text{H}\}$  NMR spectrum of compound **3** in  $\text{CDCl}_3$ .



**Figure S15.**  $^{13}\text{C}\{^1\text{H}\}$ -ATP NMR spectrum of compound **3** in  $\text{CDCl}_3$ .

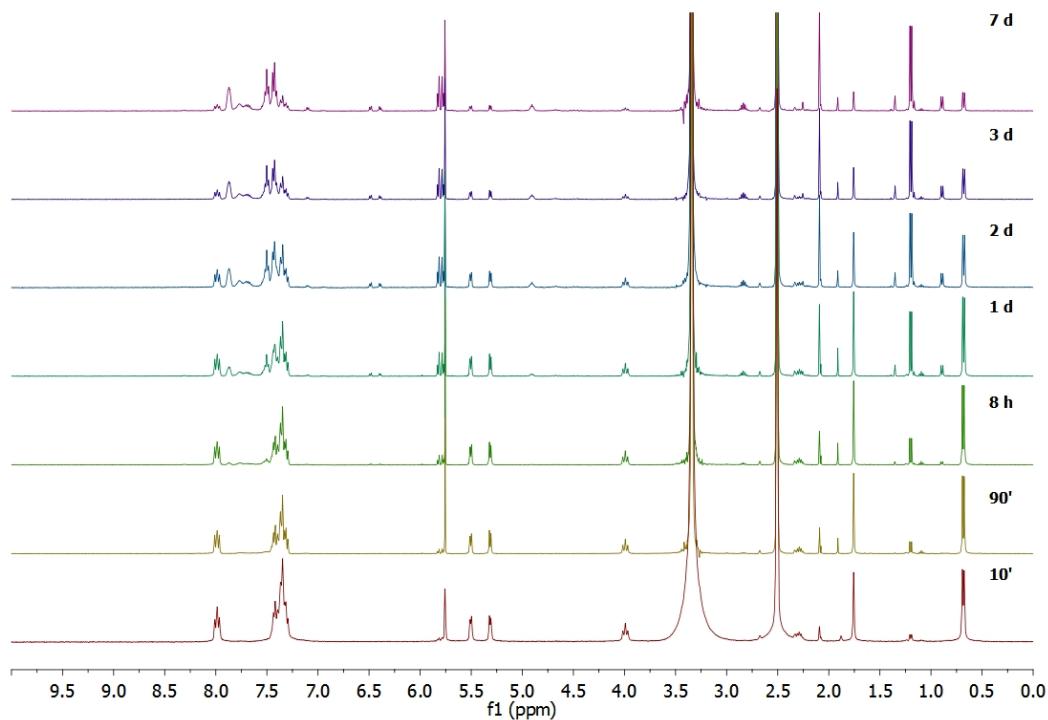


**Figure S16.** Magnification of aromatic region of  $^{13}\text{C}\{^1\text{H}\}$ -ATP NMR spectrum of compound **3** in  $\text{CDCl}_3$ .

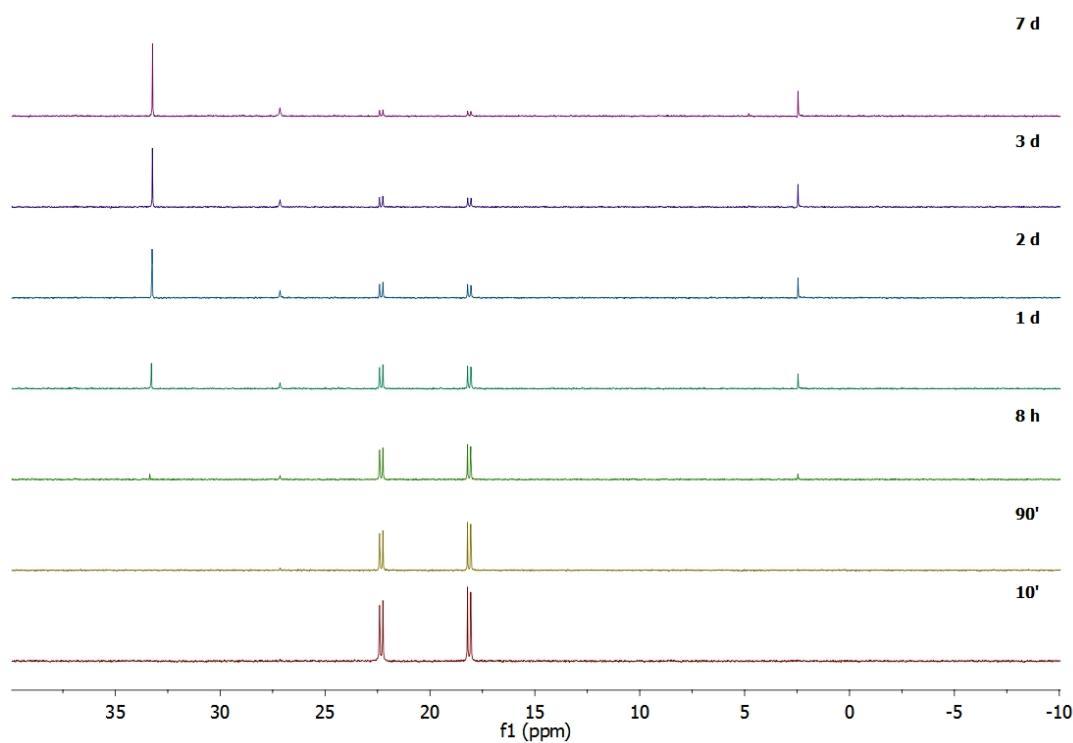


**Figure S17** Magnification of two regions of  $^{13}\text{C}\{^1\text{H}\}$ -ATP NMR spectrum of compound **3** in  $\text{CDCl}_3$ .

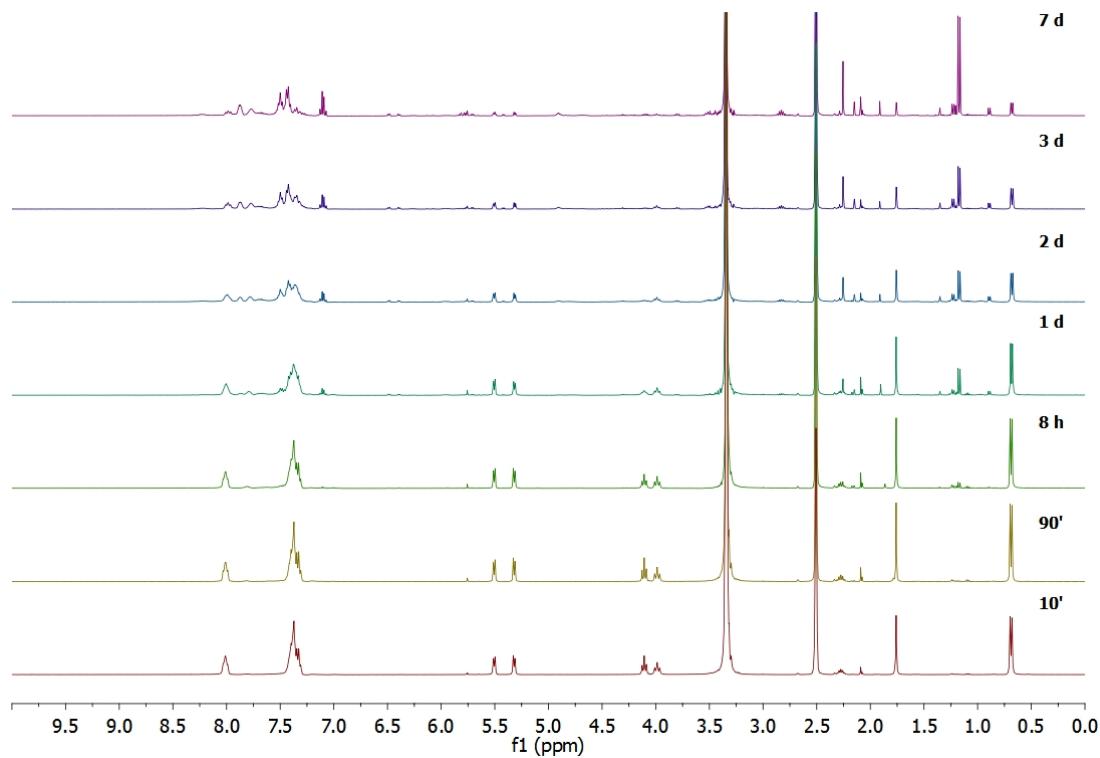
**6. Selected NMR spectra of decomposition of compounds **1** and **3** in DMSO-*d*<sub>6</sub>**



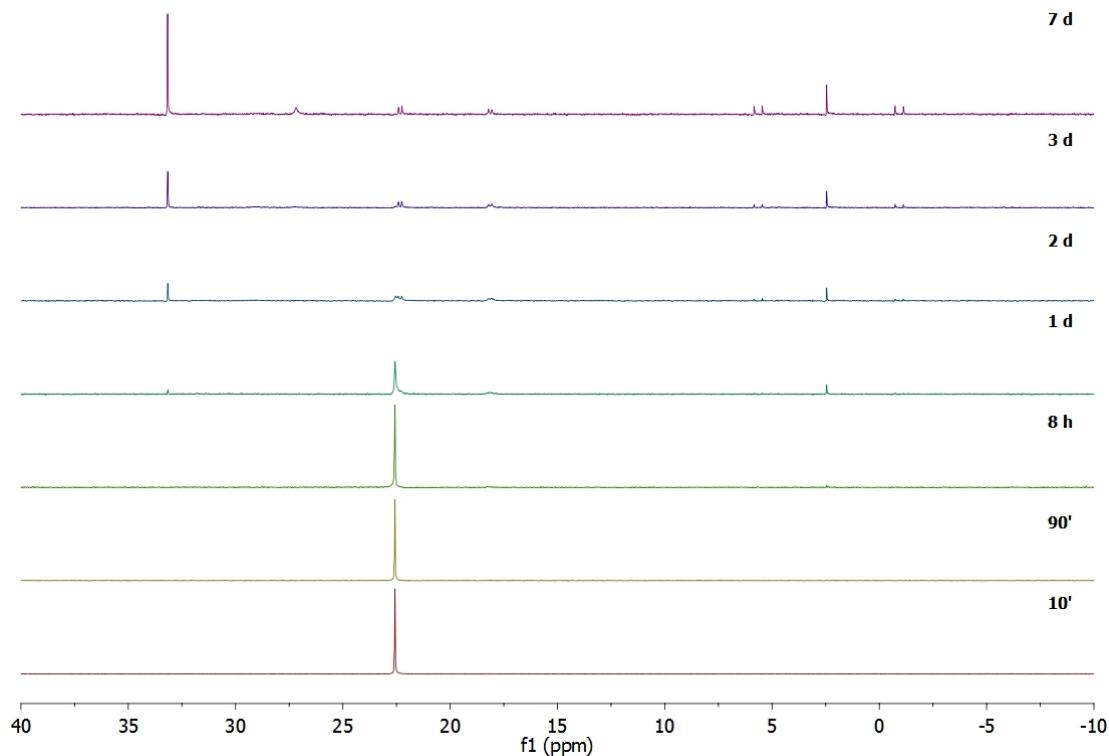
**Figure S18.** <sup>1</sup>H NMR spectrum in DMSO-*d*<sub>6</sub>. Decomposition of compound **1** over time.  $t_{1/2}=2\text{d}$ .



**Figure S19.** <sup>31</sup>P{<sup>1</sup>H} NMR spectrum in DMSO-*d*<sub>6</sub>. Decomposition of compound **1** over time.  $t_{1/2}=2\text{d}$ .

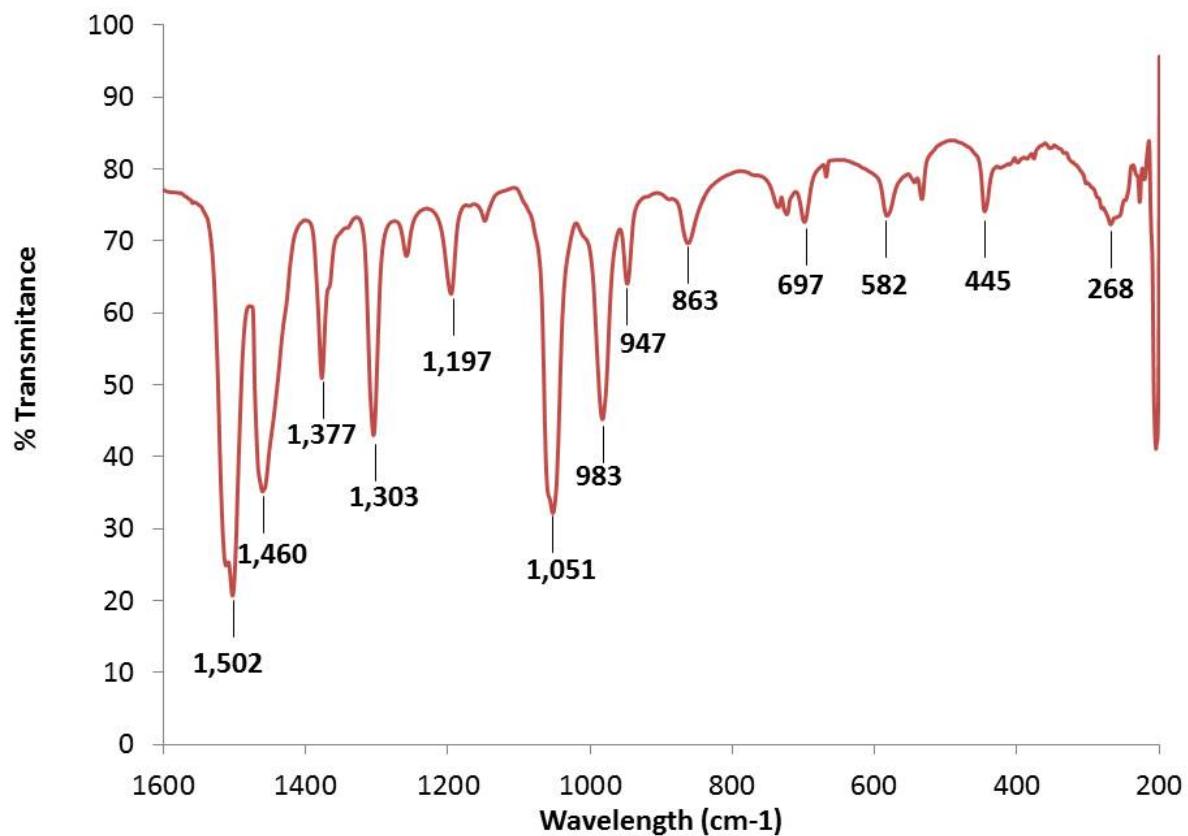


**Figure S20.**  $^1\text{H}$  NMR spectrum in  $\text{DMSO}-d_6$ . Decomposition of compound **3** over time.  $t_{1/2}=2\text{d}$ .



**Figure S21.**  $^{31}\text{P}\{\text{H}\}$  NMR spectrum in  $\text{DMSO}-d_6$ . Decomposition of compound **3** over time.  $t_{1/2}=2\text{d}$ .

7. IR spectrum of compound **2** in nujol



**Figure S22.** IR spectrum of compound **2** in a nujol mull.