

## Supplementary Information For:

### A Ru(II)-arene Complex With Promising Anti-A $\beta$ Activity

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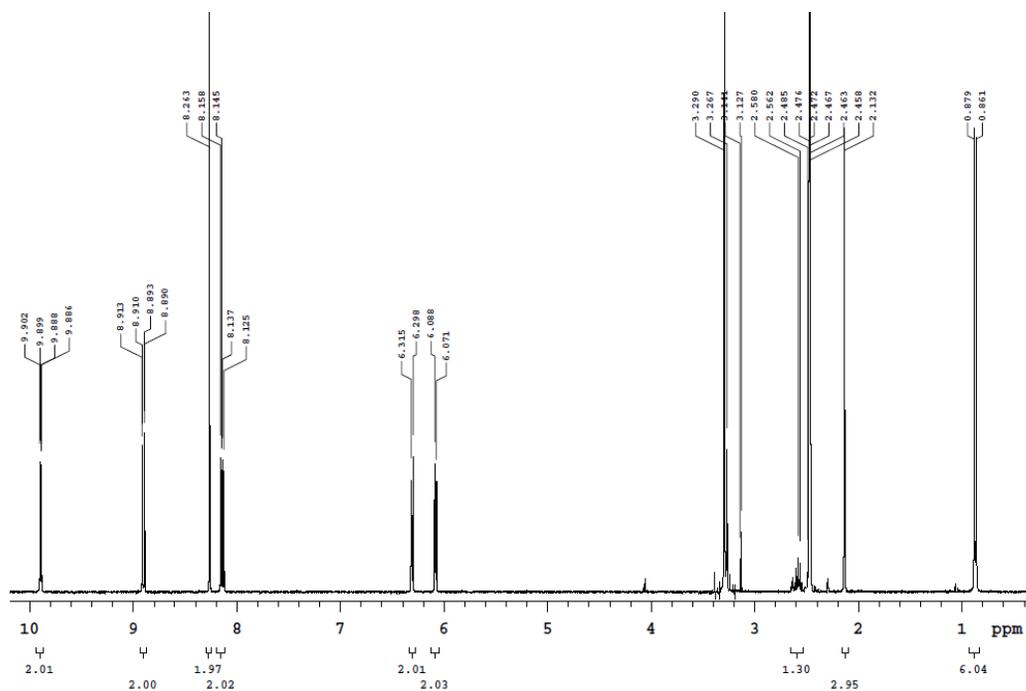


Figure S1.  $^1\text{H}$  NMR spectrum of complex RuP in DMSO- $\text{D}_6$ .

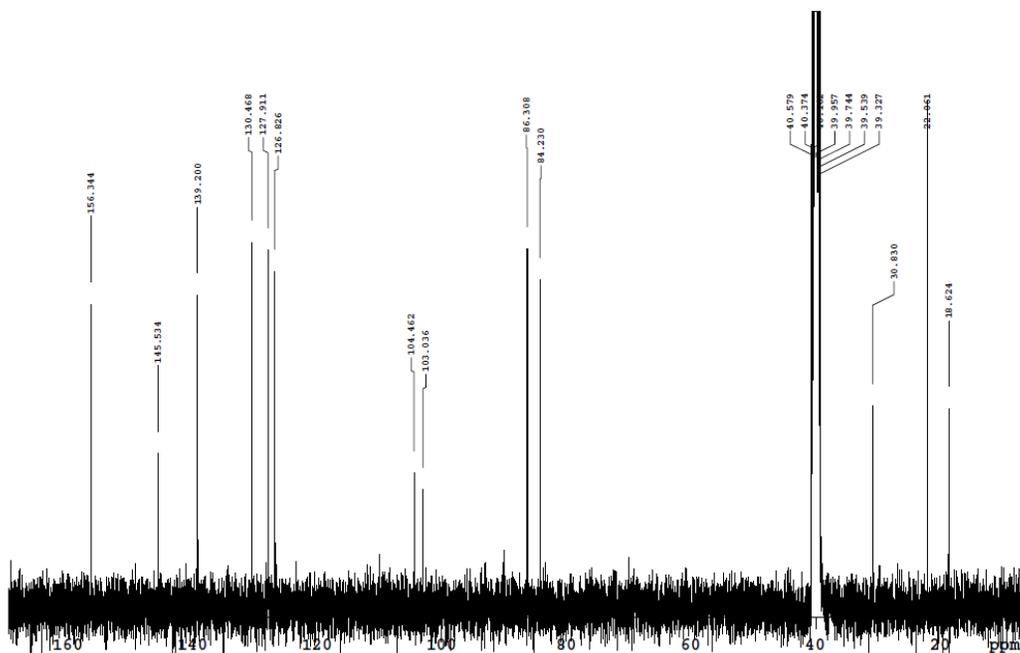


Figure S2.  $^{13}\text{C}$  NMR spectrum of complex RuP in DMSO- $\text{D}_6$ .

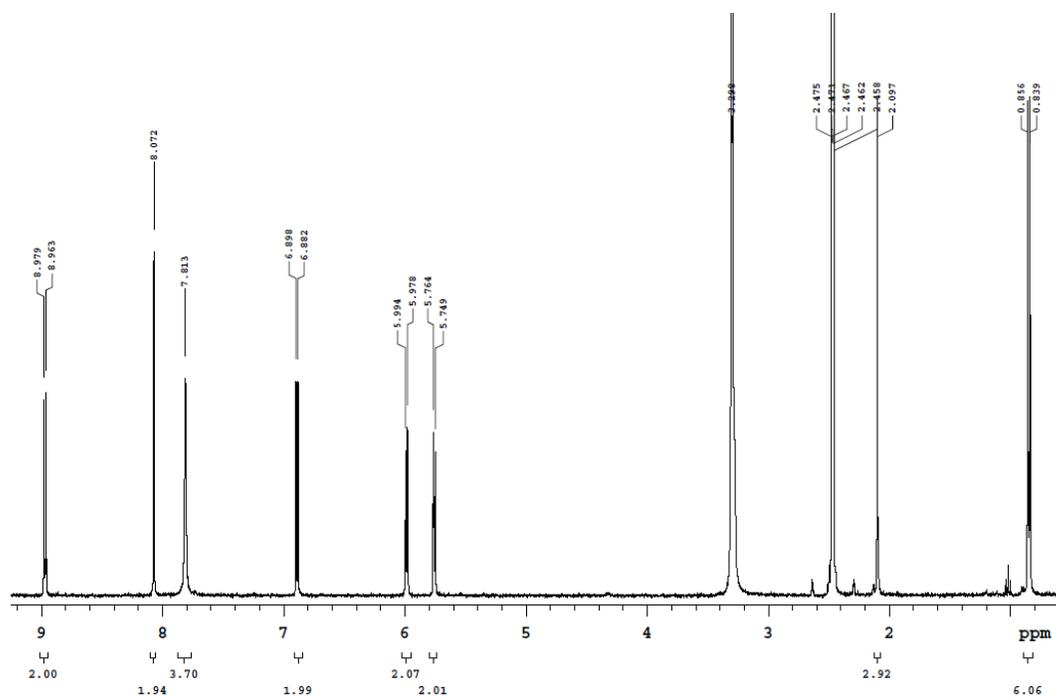


Figure S3.  $^1\text{H}$  NMR spectrum of complex **RuPA** in  $\text{DMSO-D}_6$ .

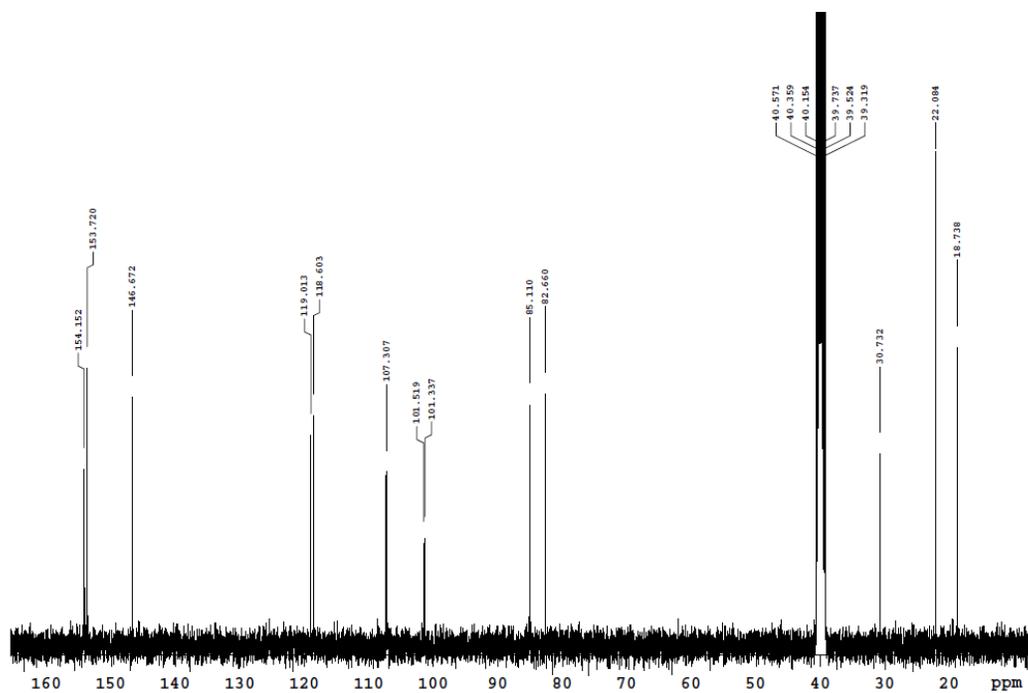
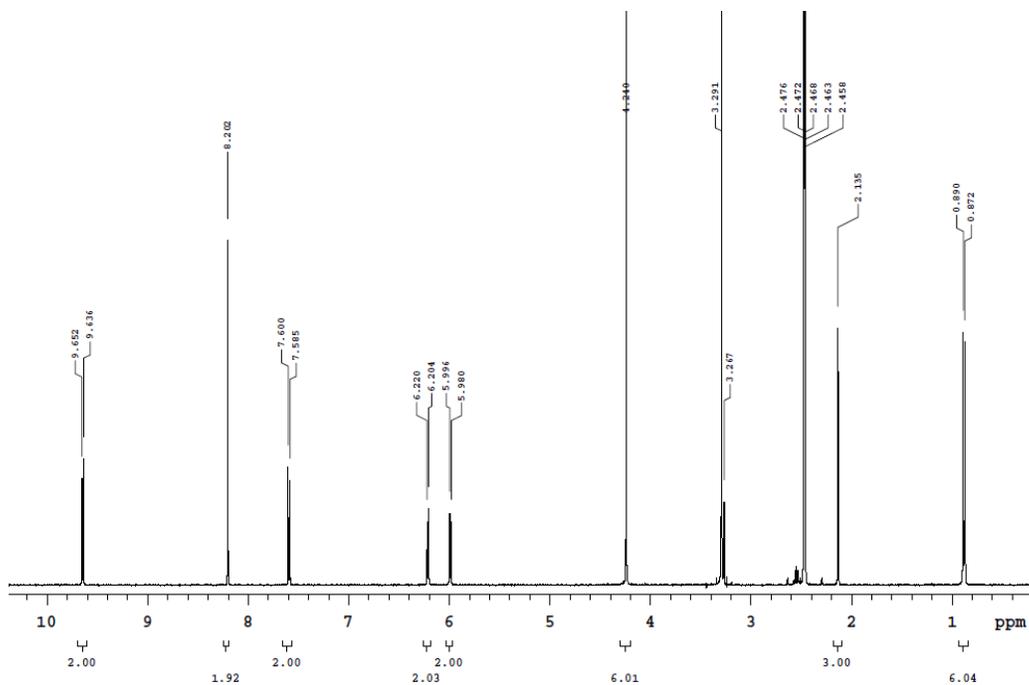
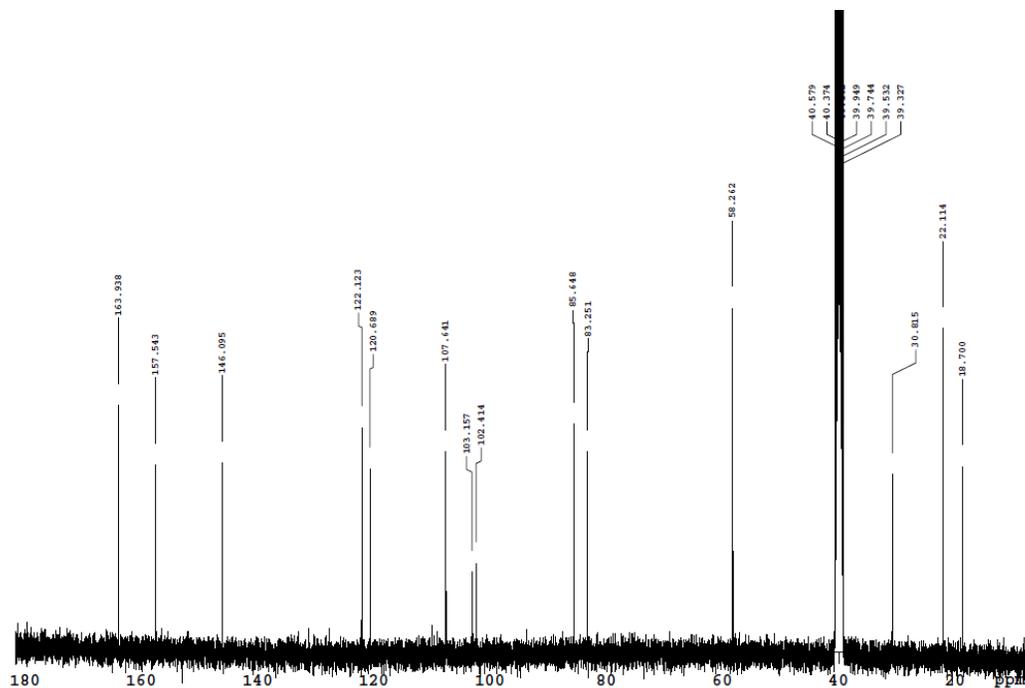


Figure S4.  $^{13}\text{C}$  NMR spectrum of complex **RuPA** in  $\text{DMSO-D}_6$ .



**Figure S5.**  $^1\text{H}$  NMR spectrum of complex **RuPMeO** in  $\text{DMSO-D}_6$ .



**Figure S6.**  $^{13}\text{C}$  NMR spectrum of complex **RuPMeO** in  $\text{DMSO-D}_6$ .

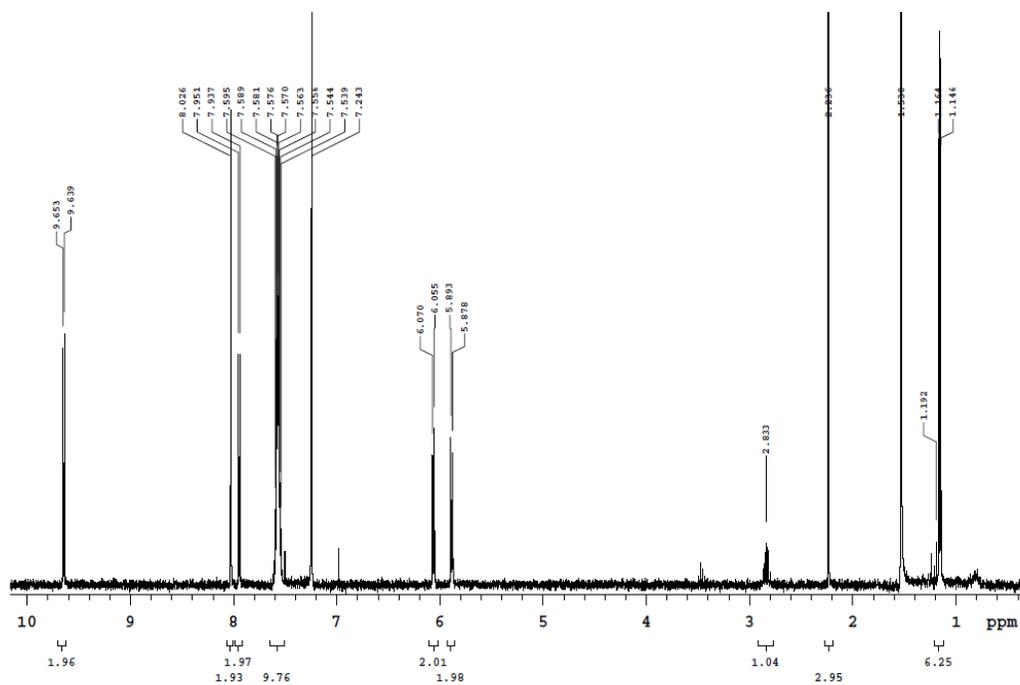


Figure S7.  $^1\text{H}$  NMR spectrum of complex **RuPPh** in  $\text{CDCl}_3$ .

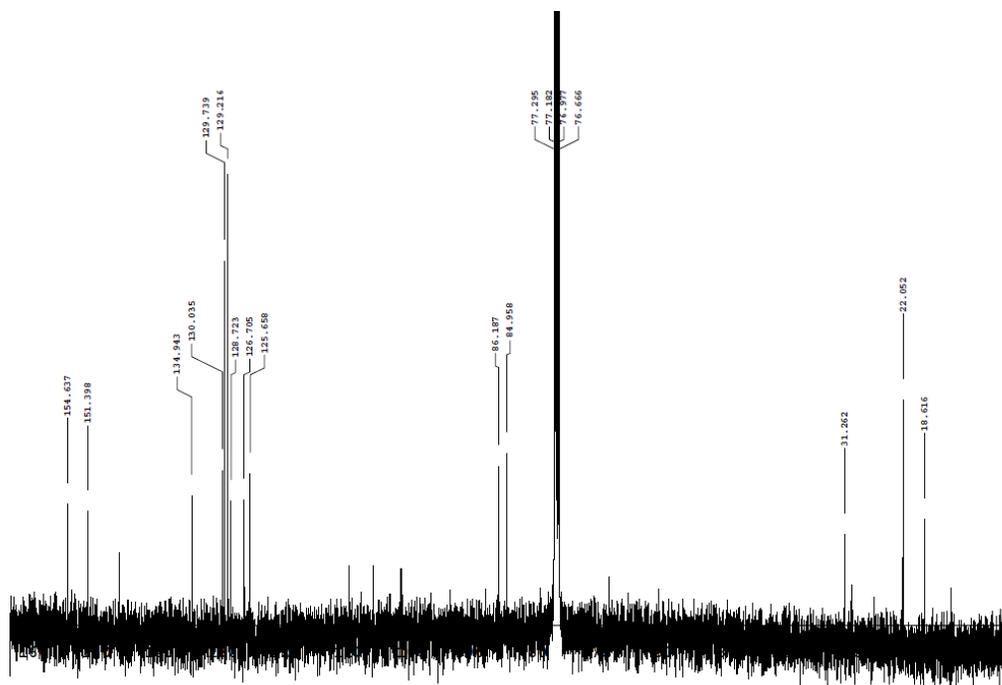


Figure S8.  $^{13}\text{C}$  NMR spectrum of complex **RuPPh** in  $\text{CDCl}_3$ .

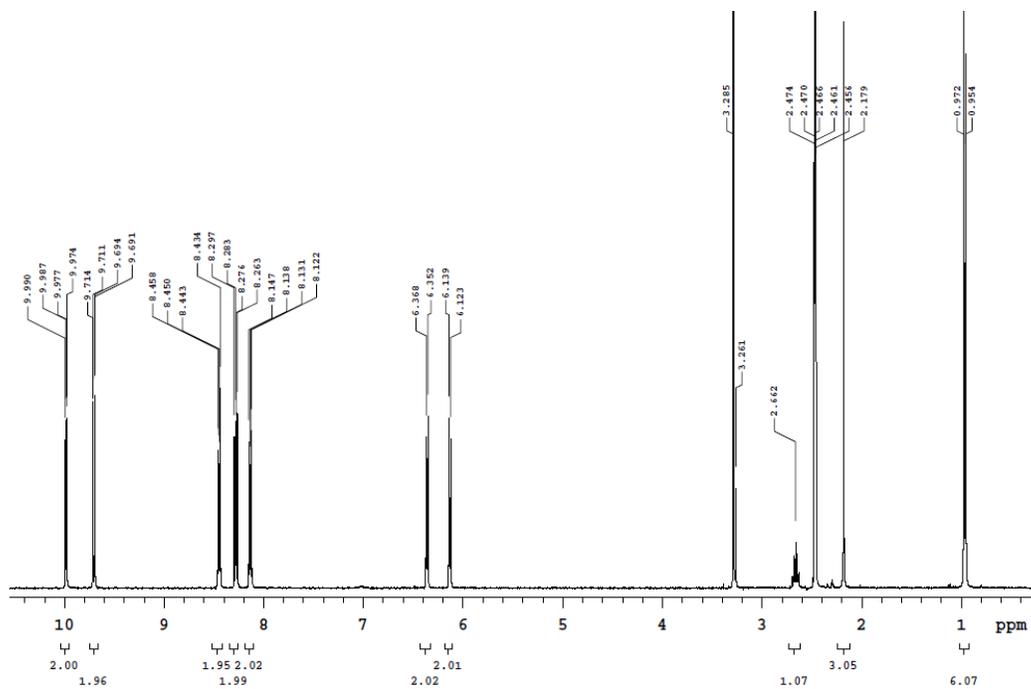


Figure S9.  $^1\text{H}$  NMR spectrum of complex **RuDppz** in  $\text{DMSO-D}_6$ .

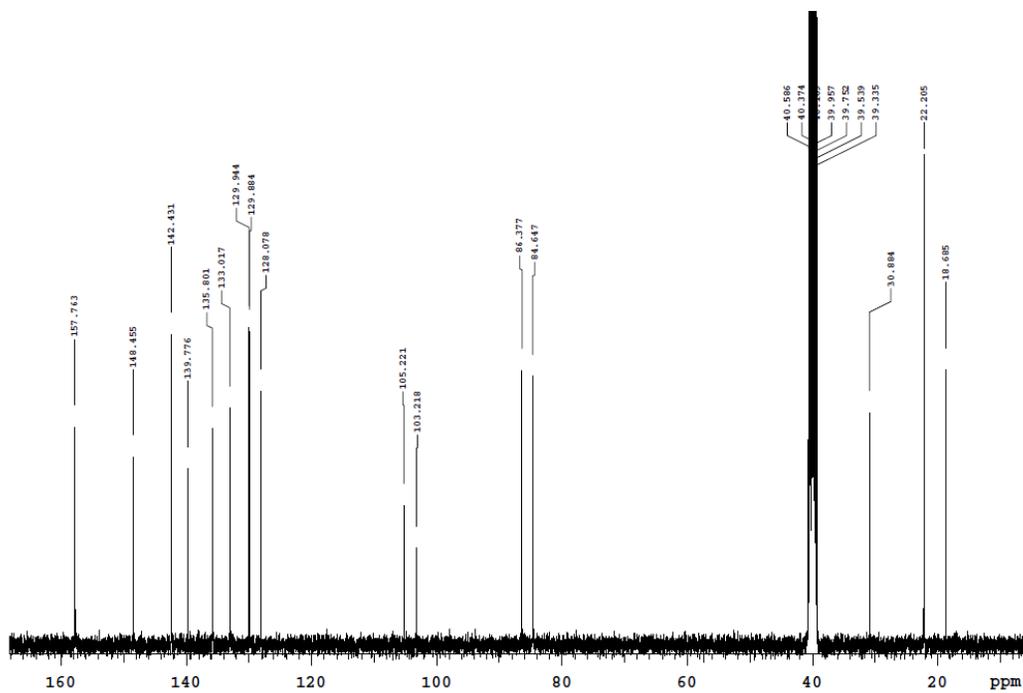
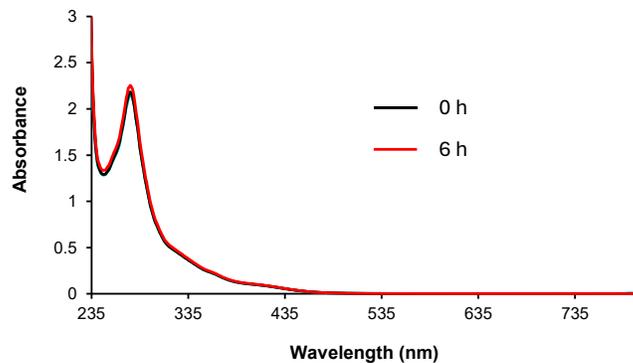
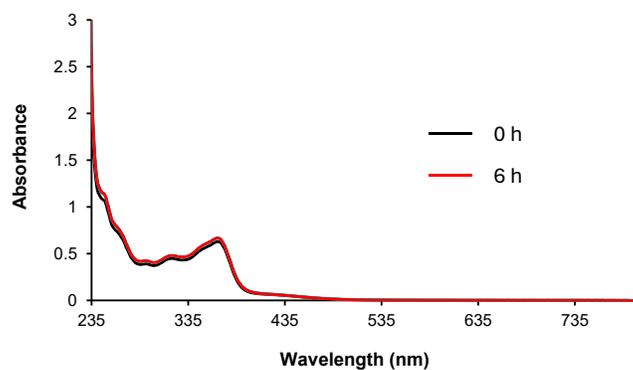


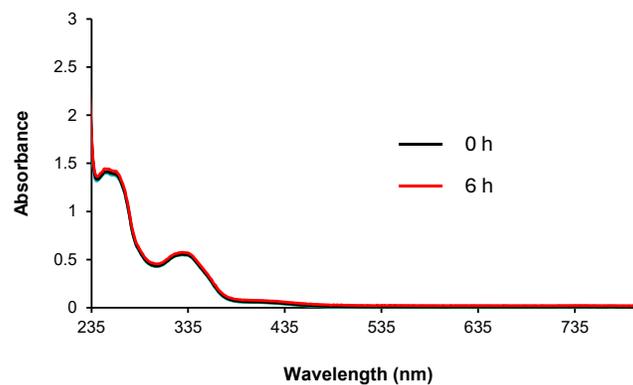
Figure S10.  $^{13}\text{C}$  NMR spectrum of complex **RuDppz** in  $\text{DMSO-D}_6$ .



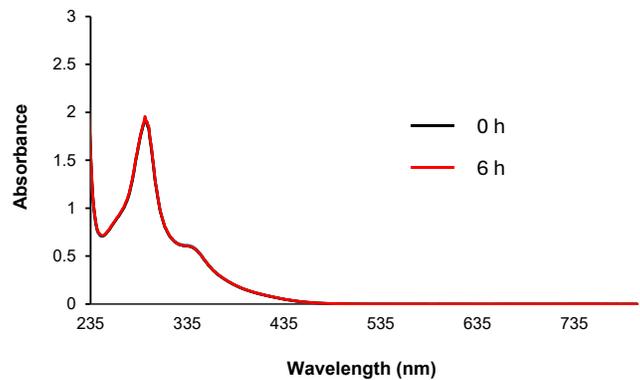
**Figure S11.** UV-Vis spectra of complex **RuP** (100 μM) incubated in PBS (pH 7.4) at 37 °C for up to 6 hours.



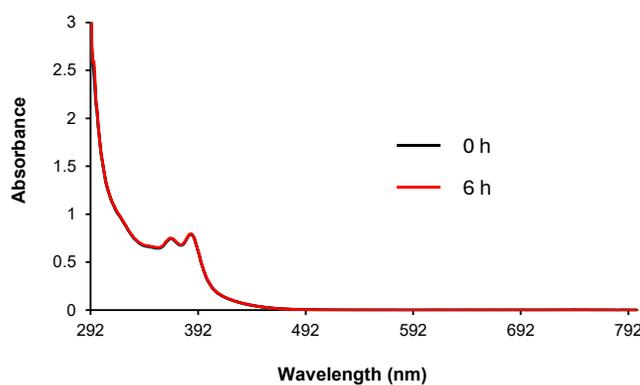
**Figure S12.** UV-Vis spectra of complex **RuPA** (100 μM) incubated in PBS (pH 7.4) at 37 °C for up to 6 hours.



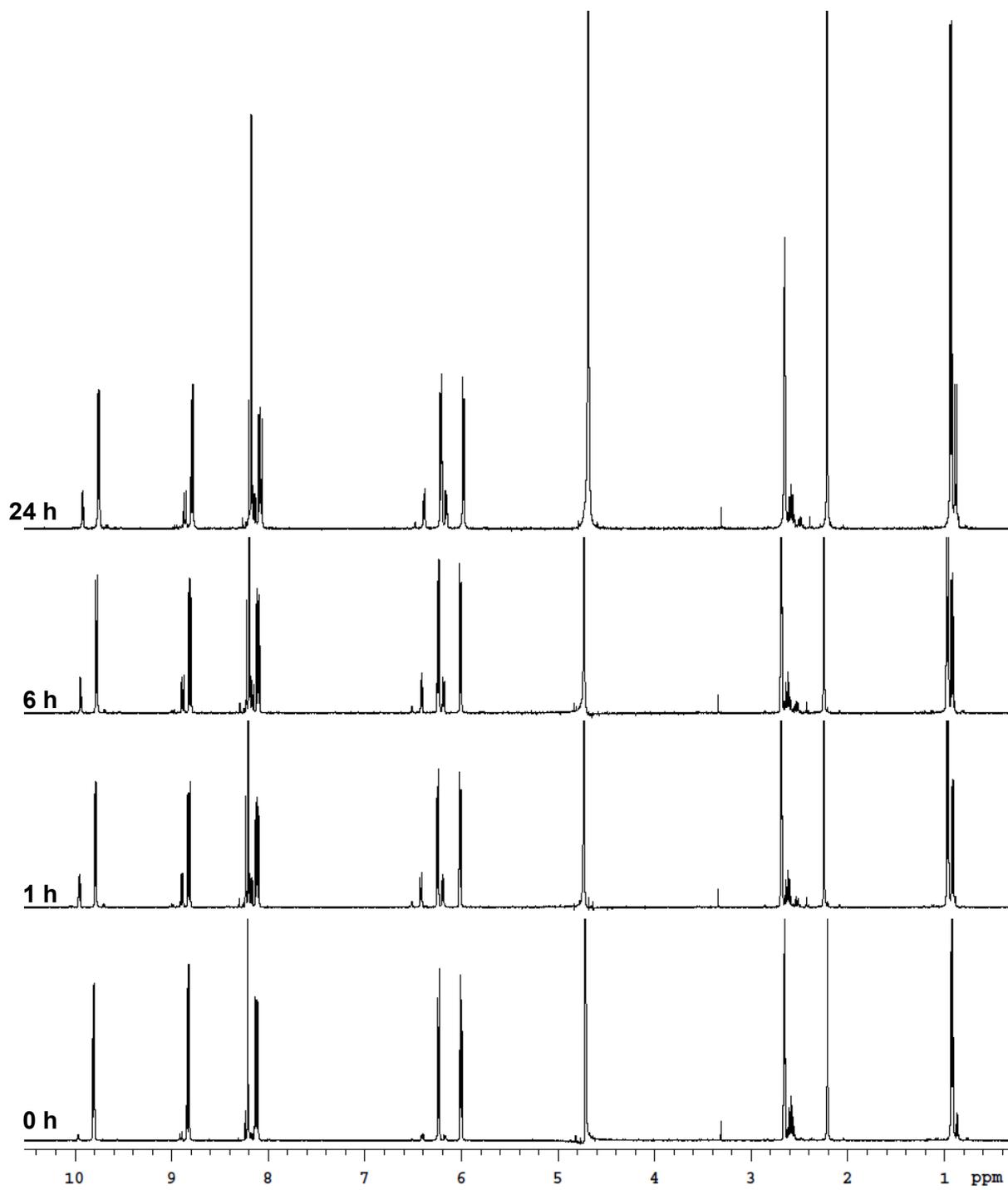
**Figure S13.** UV-Vis spectra of complex **RuPMeO** (100 μM) incubated in PBS (pH 7.4) at 37 °C for up to 6 hours.



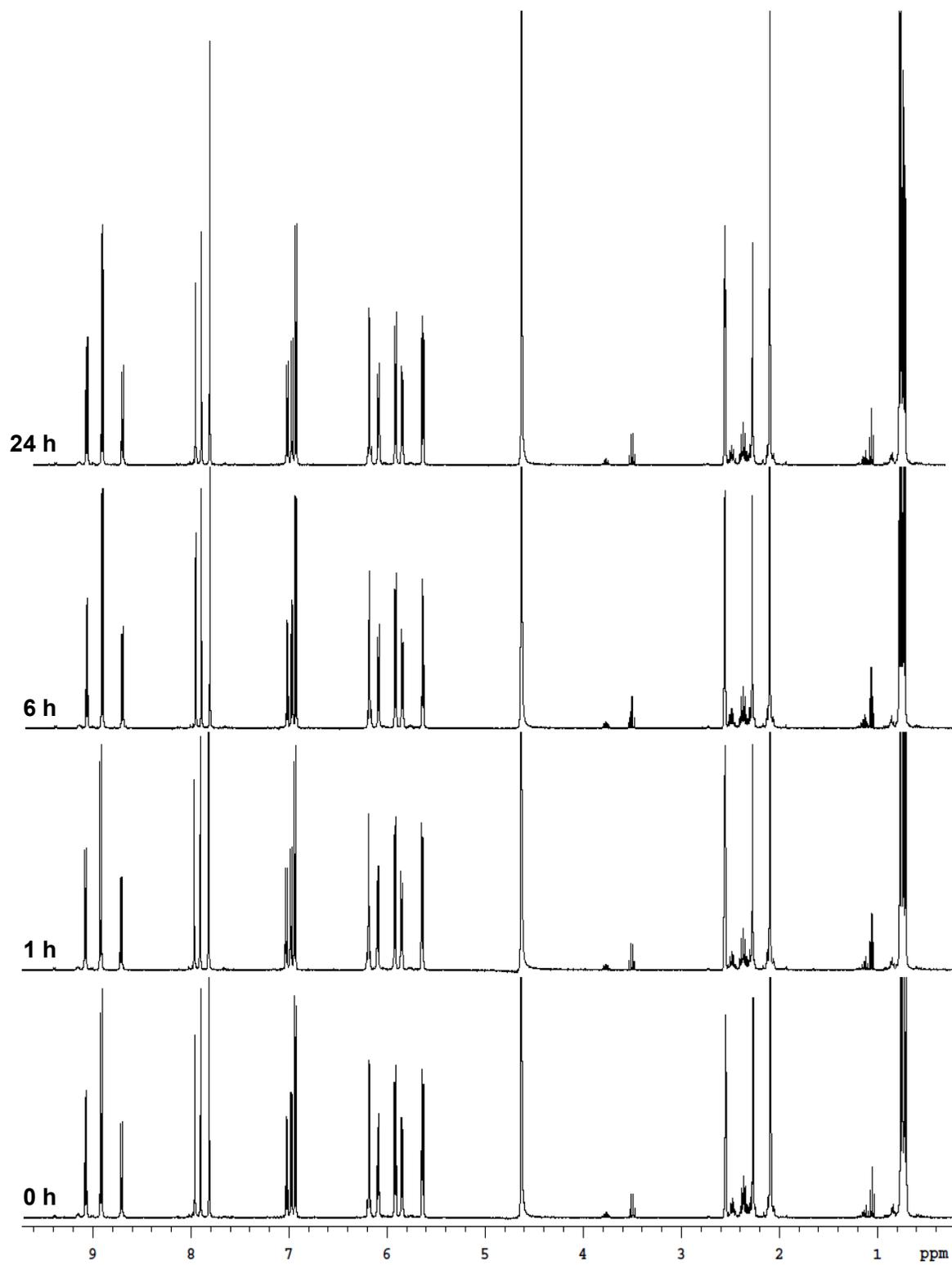
**Figure S14.** UV-Vis spectra of complex **RuPPh** (100  $\mu\text{M}$ ) incubated in PBS (pH 7.4) at 37  $^{\circ}\text{C}$  for up to 6 hours.



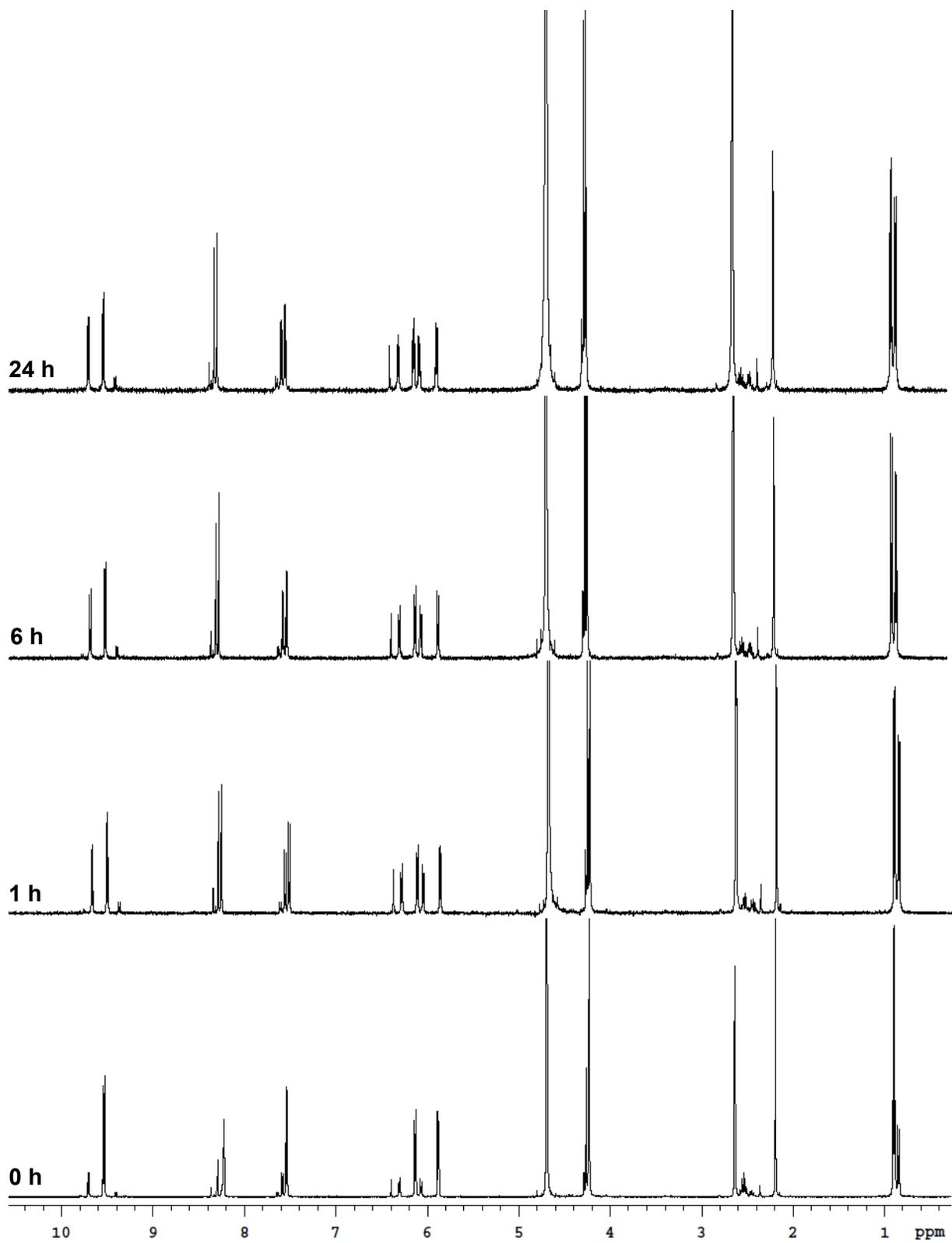
**Figure S15.** UV-Vis spectra of complex **RuDppz** (100  $\mu\text{M}$ ) incubated in PBS (pH 7.4) at 37  $^{\circ}\text{C}$  for up to 6 hours.



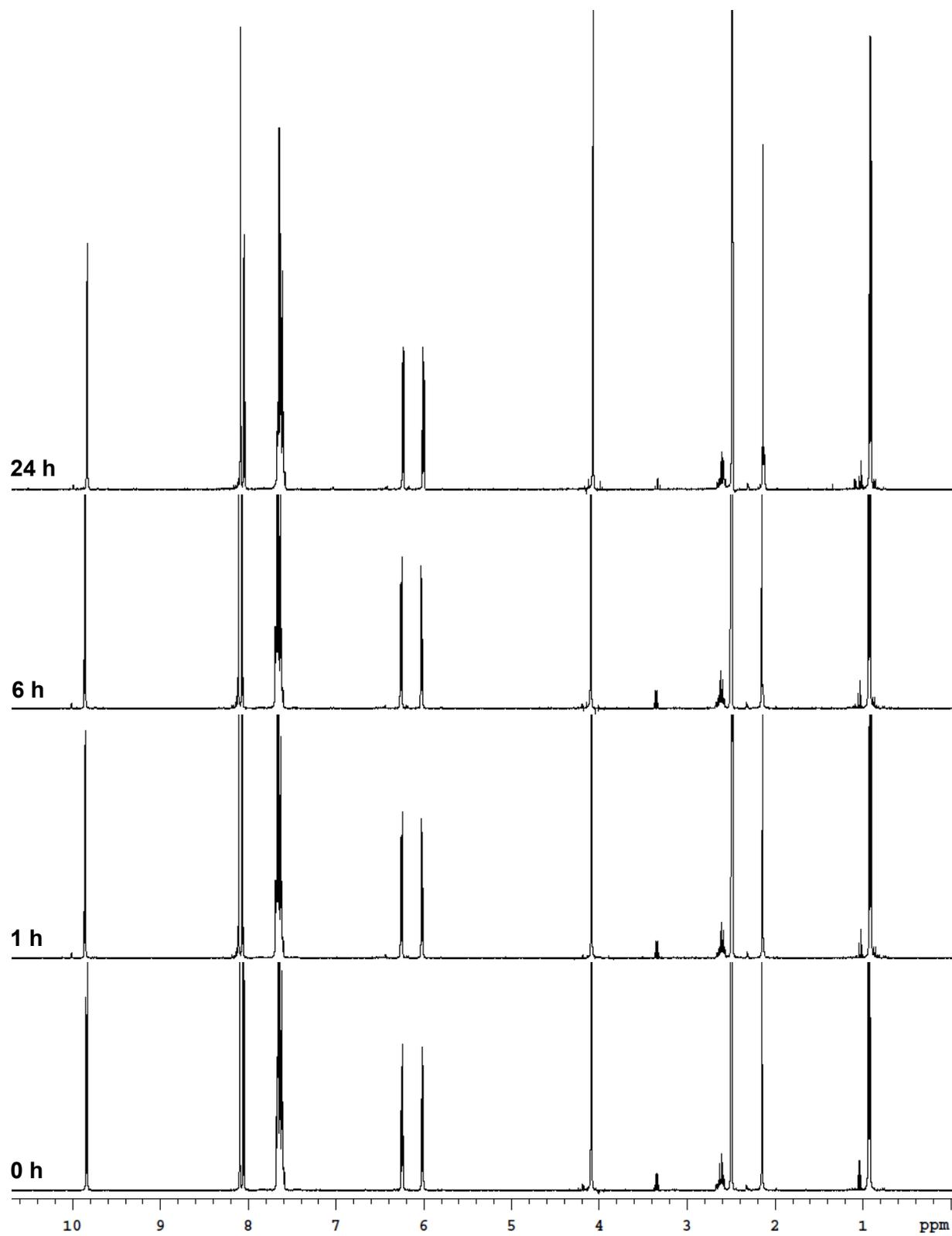
**Figure S16.** <sup>1</sup>H NMR spectrum of complex **RuP** in 33% DMSO-D<sub>6</sub> and D<sub>2</sub>O over 24 hours.



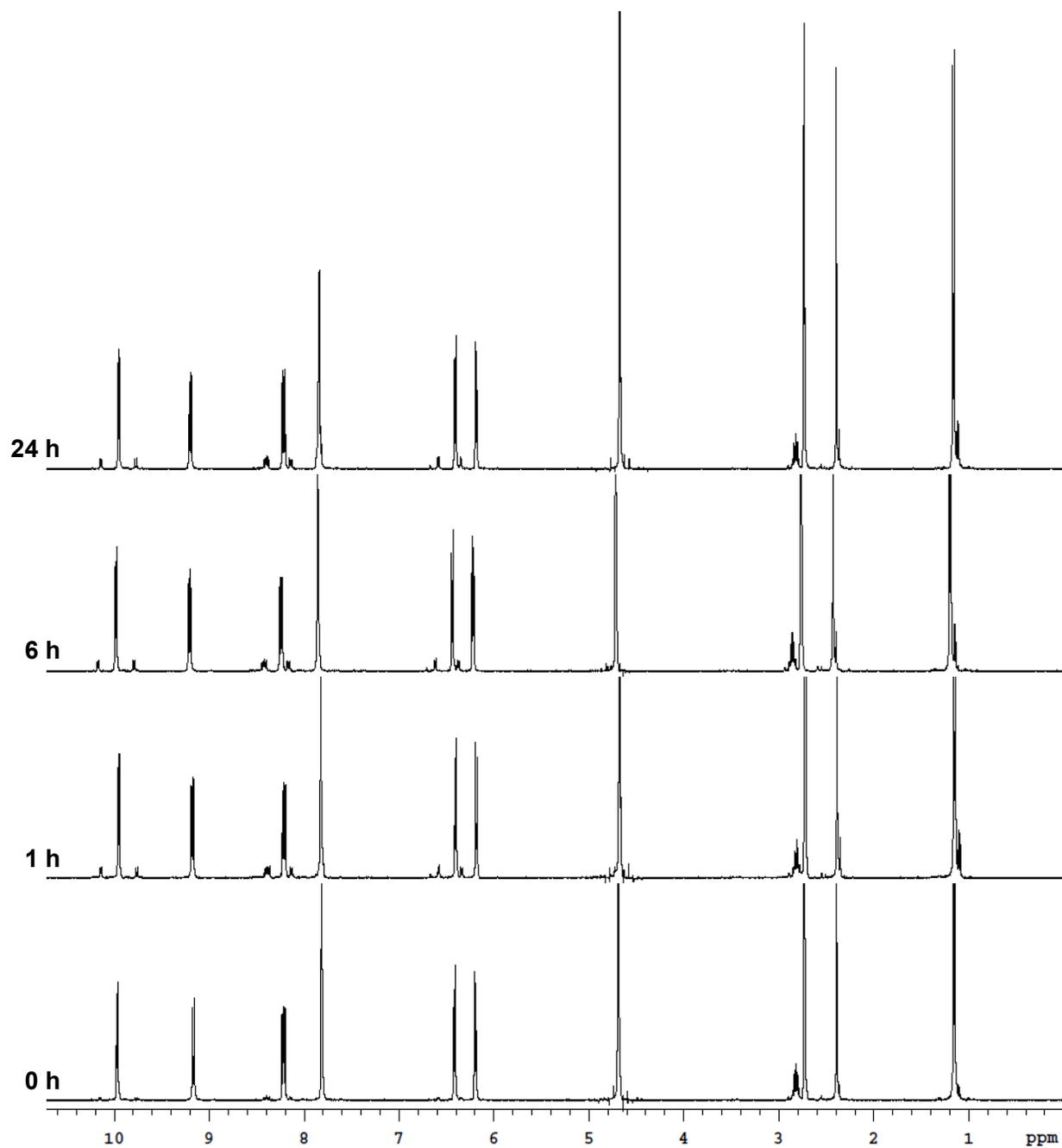
**Figure S17.** <sup>1</sup>H NMR spectrum of complex **RuPA** in 33% DMSO-D<sub>6</sub> and D<sub>2</sub>O over 24 hours.



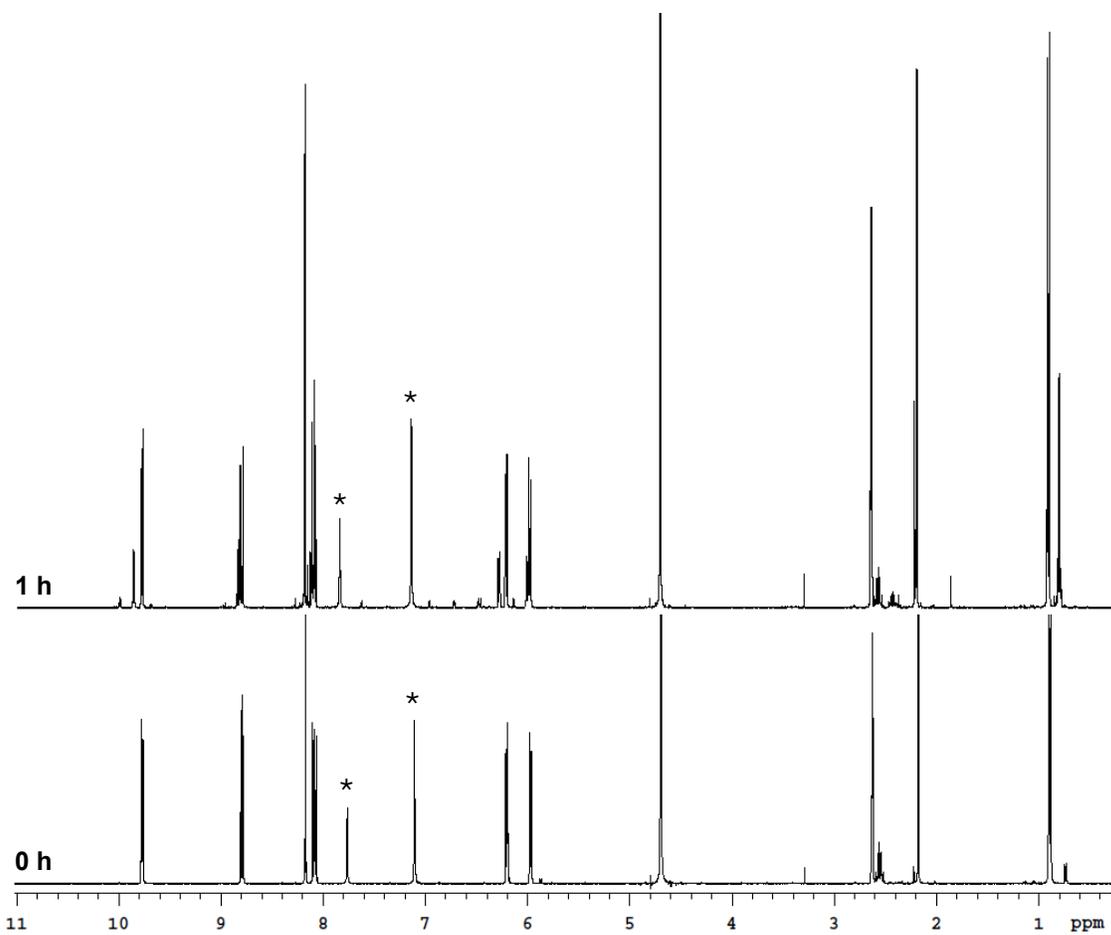
**Figure S18.** <sup>1</sup>H NMR spectrum of complex **RuPMeO** in 33% DMSO-D<sub>6</sub> and D<sub>2</sub>O over 24 hours.



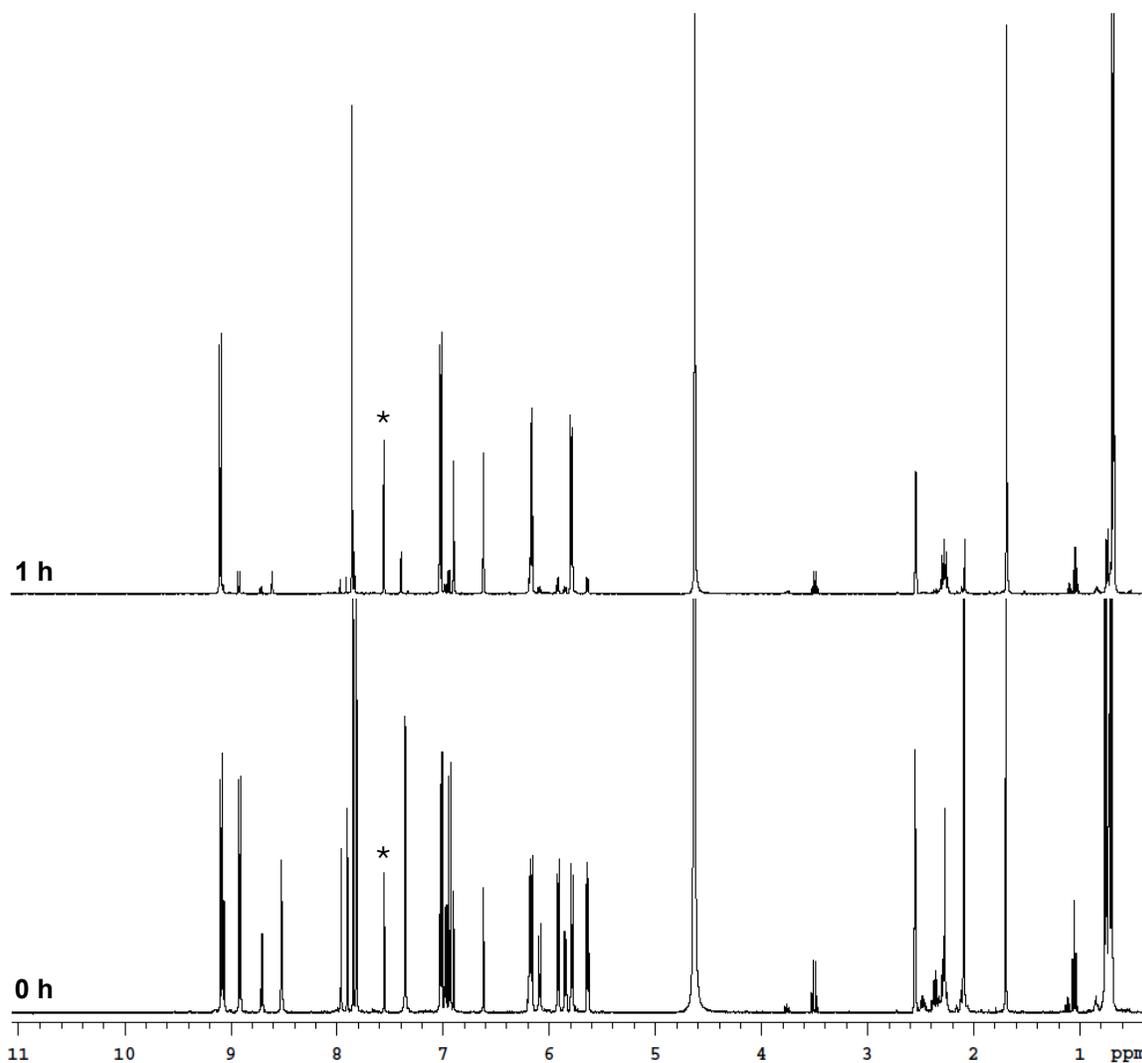
**Figure S19.** <sup>1</sup>H NMR spectrum of complex **RuPPh** in 75% DMSO-D<sub>6</sub> and D<sub>2</sub>O over 24 hours.



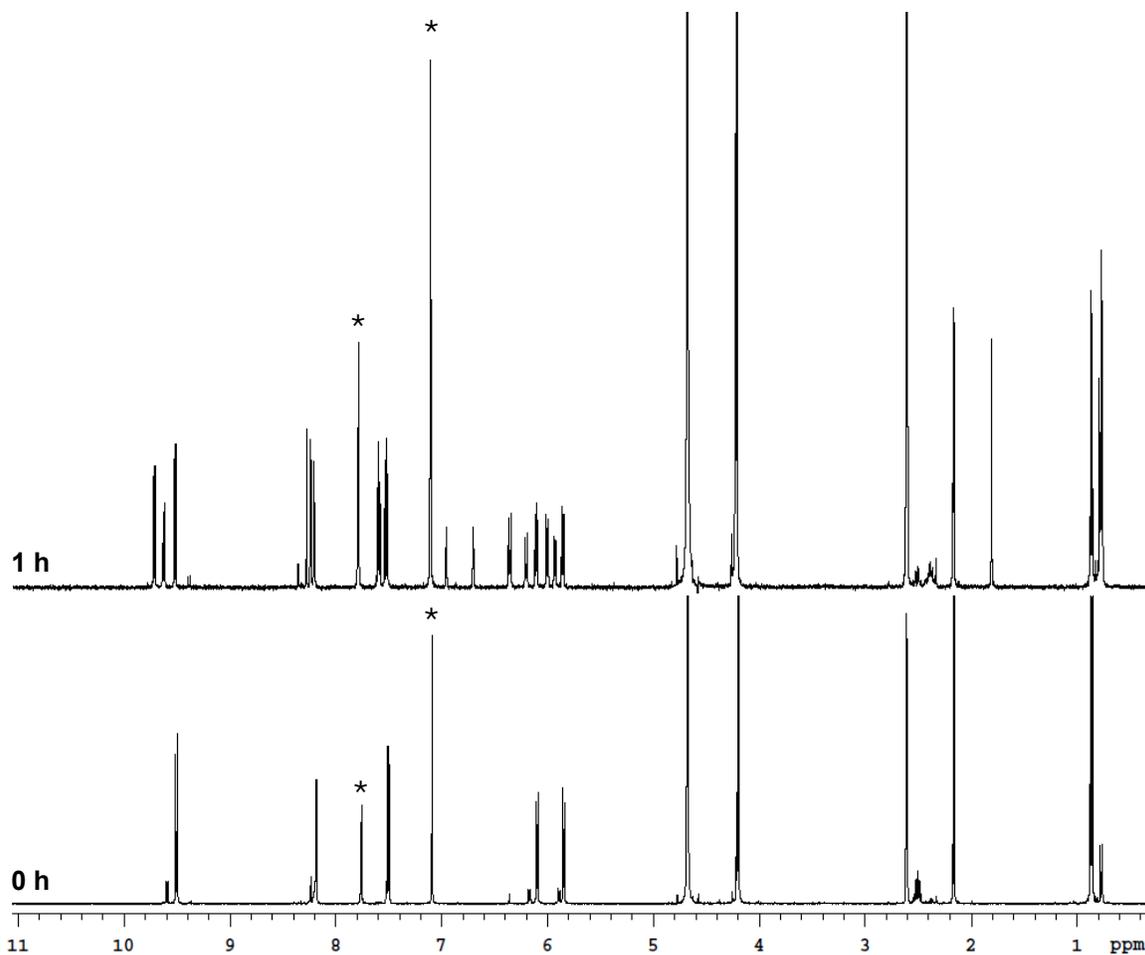
**Figure S20.** <sup>1</sup>H NMR spectrum of complex **RuDppz** in 50% DMSO-D<sub>6</sub> and D<sub>2</sub>O over 24 hours.



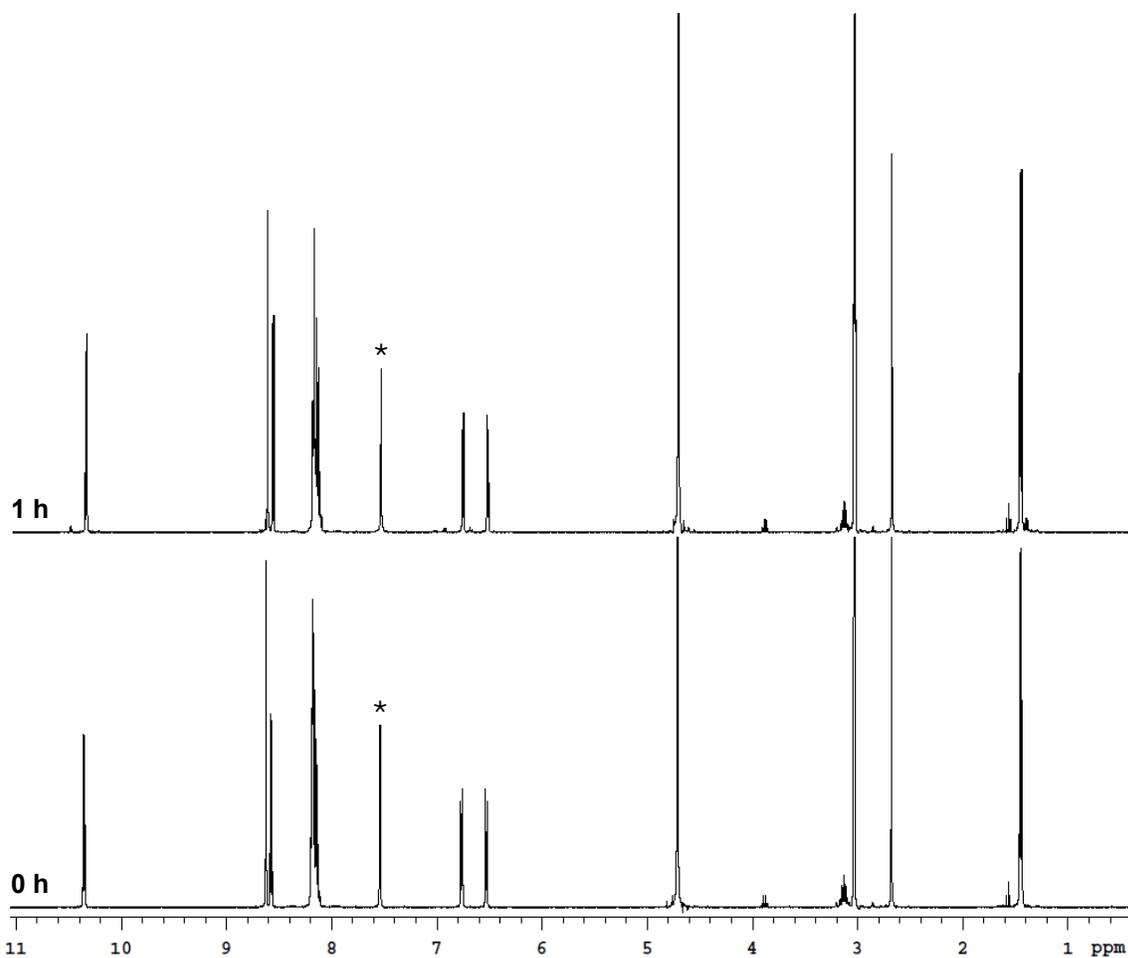
**Figure S21.** <sup>1</sup>H NMR spectra in 33% DMSO-D<sub>6</sub> and D<sub>2</sub>O of complex **RuP** (18 mM) with imidazole (18 mM). The bottom spectrum is immediately after mixing, while the top is after 1 hour of incubation at 37 °C. The free imidazole peaks are marked with an asterisk (\*).



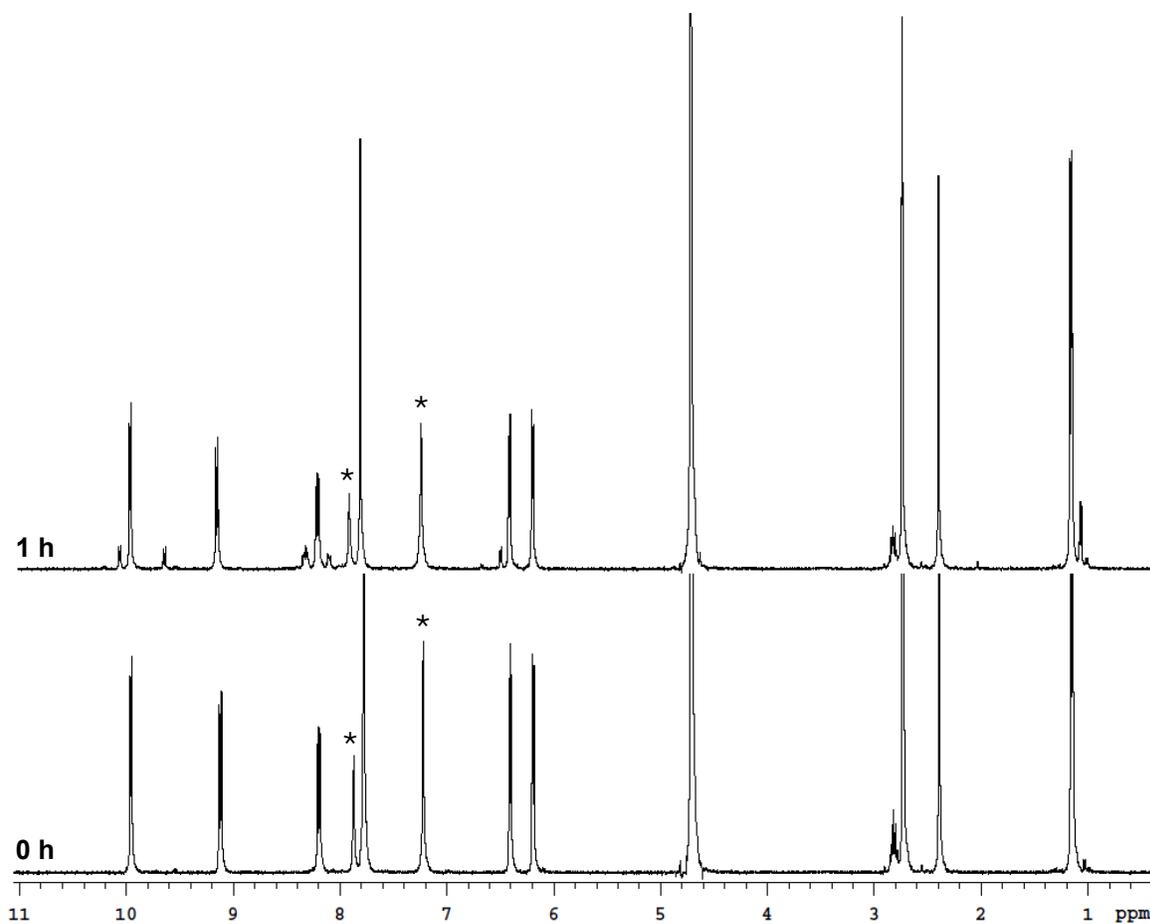
**Figure S22.**  $^1\text{H}$  NMR spectra in 33%  $\text{DMSO-D}_6$  and  $\text{D}_2\text{O}$  of complex **RuPA** (18 mM) with imidazole (18 mM). The bottom spectrum is immediately after mixing, while the top is after 1 hour of incubation at 37 °C. The free visible imidazole peak is marked with an asterisk (\*).



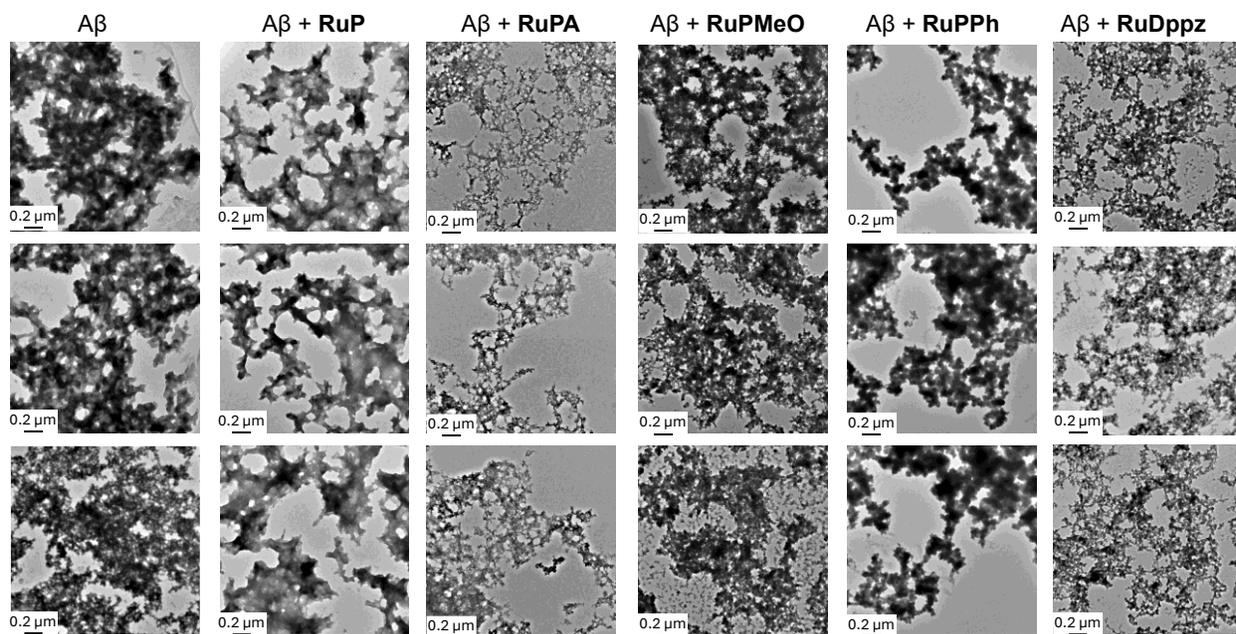
**Figure S23.** <sup>1</sup>H NMR spectra in 33% DMSO-D<sub>6</sub> and D<sub>2</sub>O of complex **RuPMeO** (18 mM) with imidazole (18 mM). The bottom spectrum is immediately after mixing, while the top is after 1 hour of incubation at 37 °C. The free imidazole peaks are marked with an asterisk (\*).



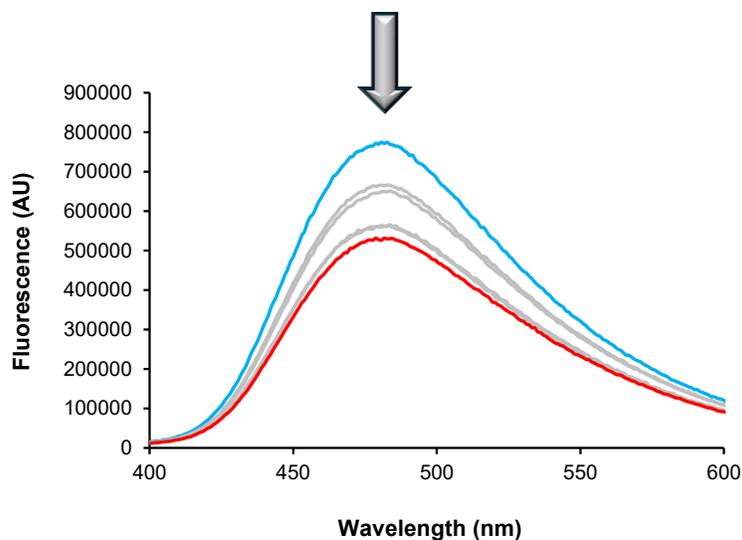
**Figure S24.** <sup>1</sup>H NMR spectra in 75% DMSO-D<sub>6</sub> and D<sub>2</sub>O of complex **RuPPh** (18 mM) with imidazole (18 mM). The bottom spectrum is immediately after mixing, while the top is after 1 hour of incubation at 37 °C. The free visible imidazole peak is marked with an asterisk (\*).



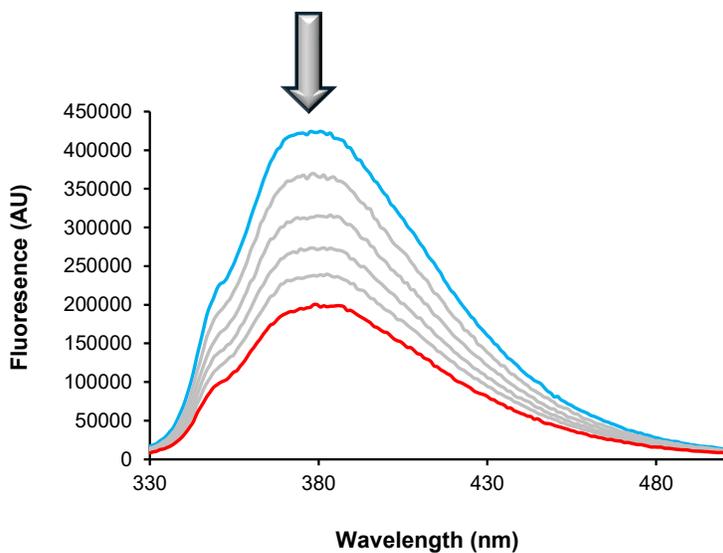
**Figure S25.** <sup>1</sup>H NMR spectra in 33% DMSO-D<sub>6</sub> and D<sub>2</sub>O of complex **RuDppz** (18 mM) with imidazole (18 mM). The bottom spectrum is immediately after mixing, while the top is after 1 hour of incubation at 37 °C. The free imidazole peaks are marked with an asterisk (\*).



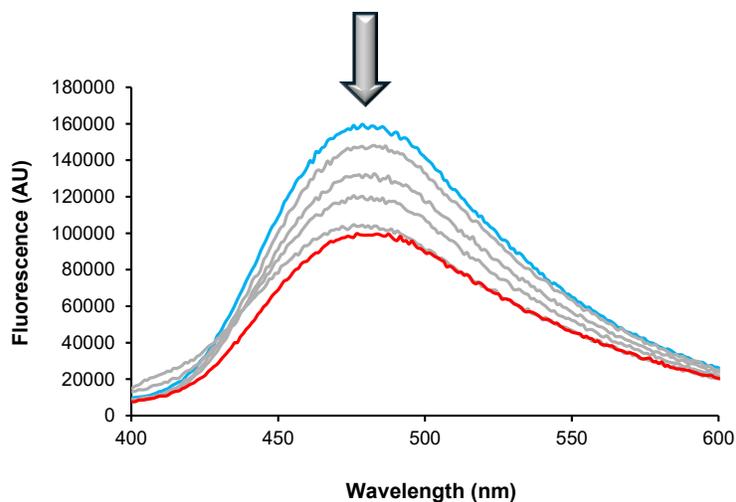
**Figure S26.** Additional TEM images collected for all of the Ru complexes with  $A\beta_{40}$  from the DLS filtrates. Scale bars are provided within each image.



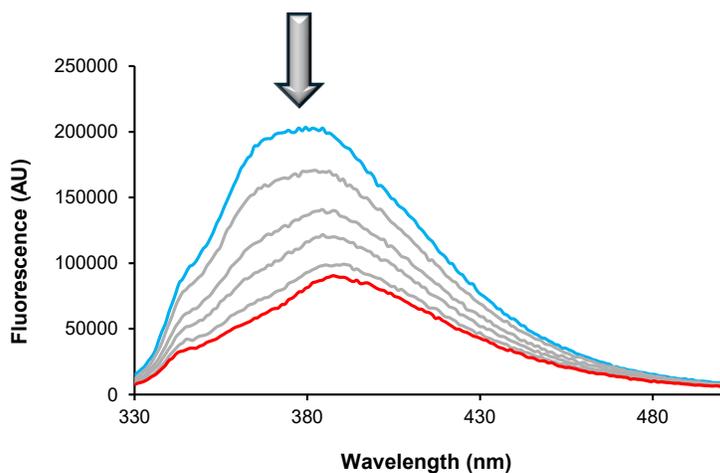
**Figure S27.** Fluorescence emission spectra at various Ru-HSA ratios by the titration of HSA-DG (1:1) with **RuP**. Experimental conditions:  $\lambda_{\text{ex}} = 330 \text{ nm}$ ,  $\lambda_{\text{em}} = 350\text{-}600 \text{ nm}$ ,  $[\text{HSA}] = [\text{DG}] = 2.5 \mu\text{M}$ ,  $[\text{Ru}] = 0$  (blue line), 12.5, 25, 32.5, 50, and 62.5  $\mu\text{M}$  (red line), in PBS (pH 7.4).



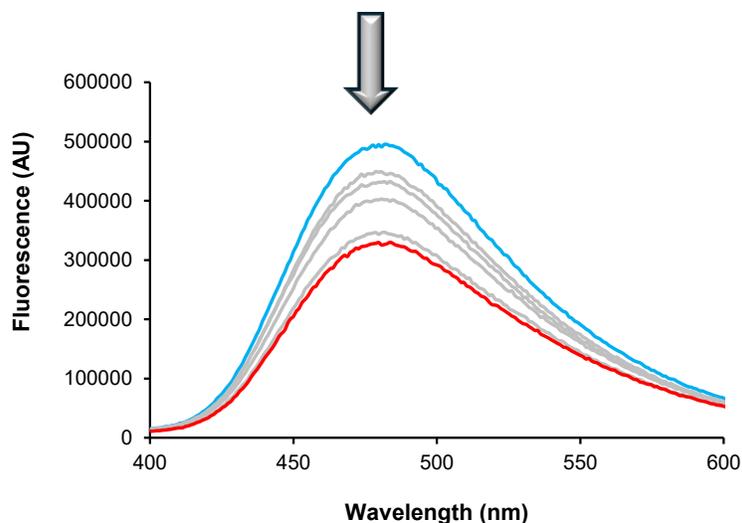
**Figure S28.** Fluorescence emission spectra at various Ru-HSA ratios by the titration of HSA-WF (1:1) with **RuP**. Experimental conditions:  $\lambda_{\text{ex}} = 295 \text{ nm}$ ,  $\lambda_{\text{em}} = 330\text{-}500 \text{ nm}$ ,  $[\text{HSA}] = [\text{WF}] = 2.5 \mu\text{M}$ ,  $[\text{Ru}] = 0$  (blue line), 5, 10, 15, 20, and 25  $\mu\text{M}$  (red line), in PBS (pH 7.4).



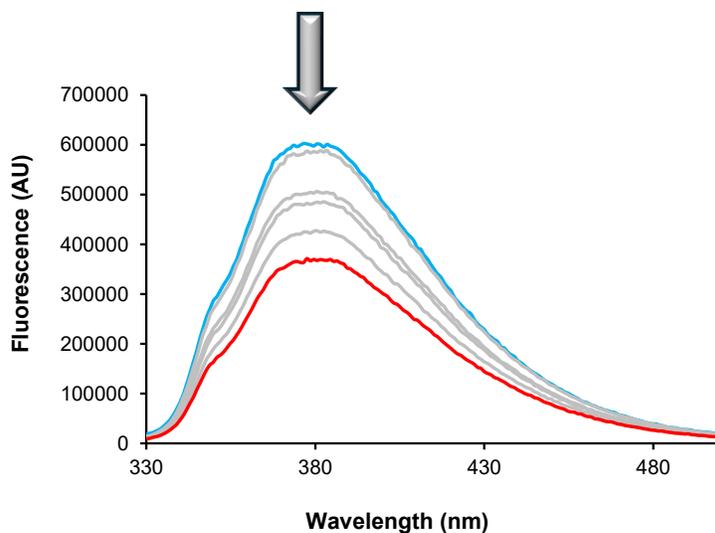
**Figure S29.** Fluorescence emission spectra at various Ru-HSA ratios by the titration of HSA-DG (1:1) with **RuPA**. Experimental conditions:  $\lambda_{\text{ex}} = 330$  nm,  $\lambda_{\text{em}} = 350\text{-}600$  nm,  $[\text{HSA}] = [\text{DG}] = 2.5$   $\mu\text{M}$ ,  $[\text{Ru}] = 0$  (blue line), 12.5, 25, 32.5, 50, and 62.5  $\mu\text{M}$  (red line), in PBS (pH 7.4).



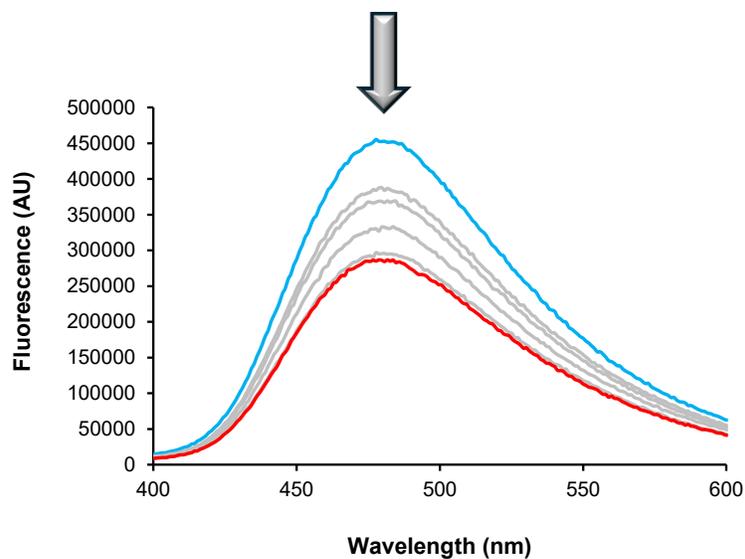
**Figure S30.** Fluorescence emission spectra at various Ru-HSA ratios by the titration of HSA-WF (1:1) with **RuPA**. Experimental conditions:  $\lambda_{\text{ex}} = 295$  nm,  $\lambda_{\text{em}} = 330\text{-}500$  nm,  $[\text{HSA}] = [\text{WF}] = 2.5$   $\mu\text{M}$ ,  $[\text{Ru}] = 0$  (blue line), 12.5, 25, 32.5, 50, and 62.5  $\mu\text{M}$  (red line), in PBS (pH 7.4).



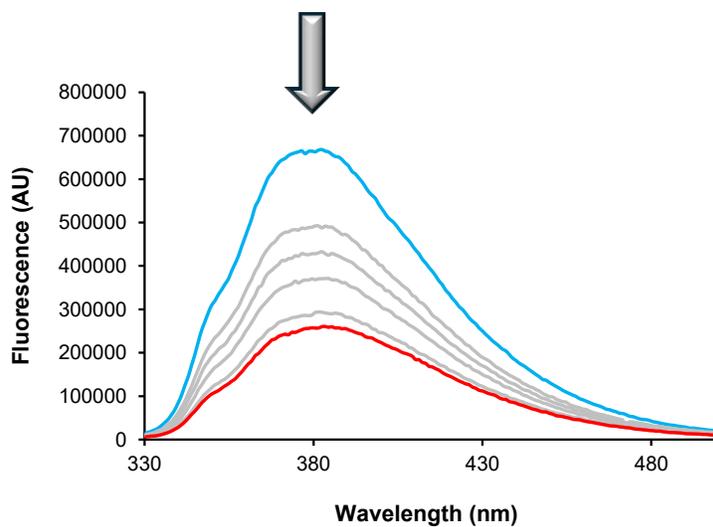
**Figure S31.** Fluorescence emission spectra at various Ru-HSA ratios by the titration of HSA-DG (1:1) with **RuBMeO**. Experimental conditions:  $\lambda_{\text{ex}} = 330$  nm,  $\lambda_{\text{em}} = 350\text{-}600$  nm,  $[\text{HSA}] = [\text{DG}] = 2.5$   $\mu\text{M}$ ,  $[\text{Ru}] = 0$  (blue line), 12.5, 25, 32.5, 50, and 62.5  $\mu\text{M}$  (red line), in PBS (pH 7.4).



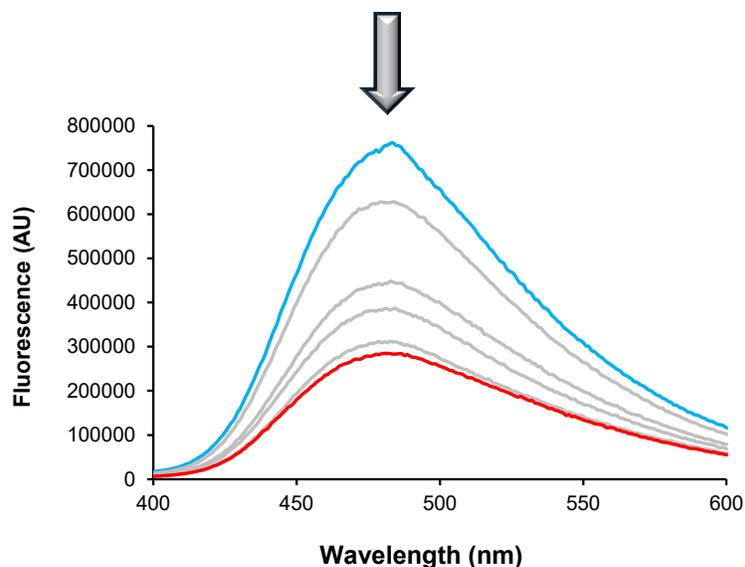
**Figure S32.** Fluorescence emission spectra at various Ru-HSA ratios by the titration of HSA-WF (1:1) with **RuBMeO**. Experimental conditions:  $\lambda_{\text{ex}} = 295$  nm,  $\lambda_{\text{em}} = 330\text{-}500$  nm,  $[\text{HSA}] = [\text{WF}] = 2.5$   $\mu\text{M}$ ,  $[\text{Ru}] = 0$  (blue line), 12.5, 25, 32.5, 50, and 62.5  $\mu\text{M}$  (red line), in PBS (pH 7.4).



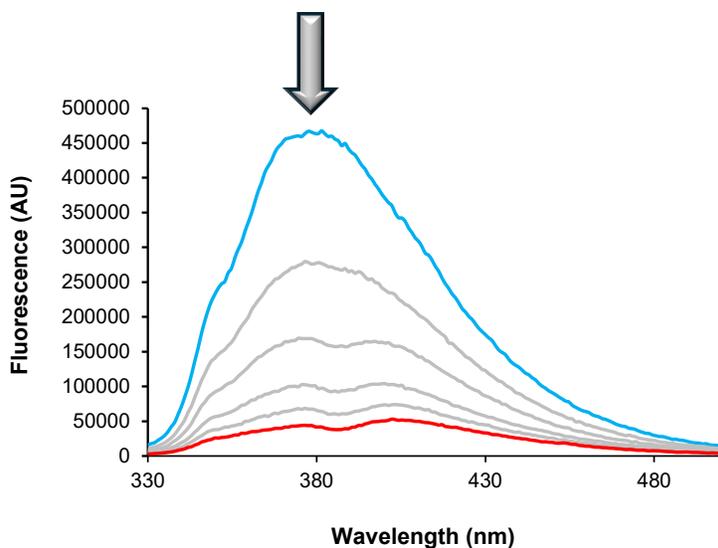
**Figure S33.** Fluorescence emission spectra at various Ru-HSA ratios by the titration of HSA-DG (1:1) with **RuPPh**. Experimental conditions:  $\lambda_{\text{ex}} = 330$  nm,  $\lambda_{\text{em}} = 350\text{-}600$  nm,  $[\text{HSA}] = [\text{DG}] = 2.5$   $\mu\text{M}$ ,  $[\text{Ru}] = 0$  (blue line), 12.5, 25, 32.5, 50, and 62.5  $\mu\text{M}$  (red line), in PBS (pH 7.4).



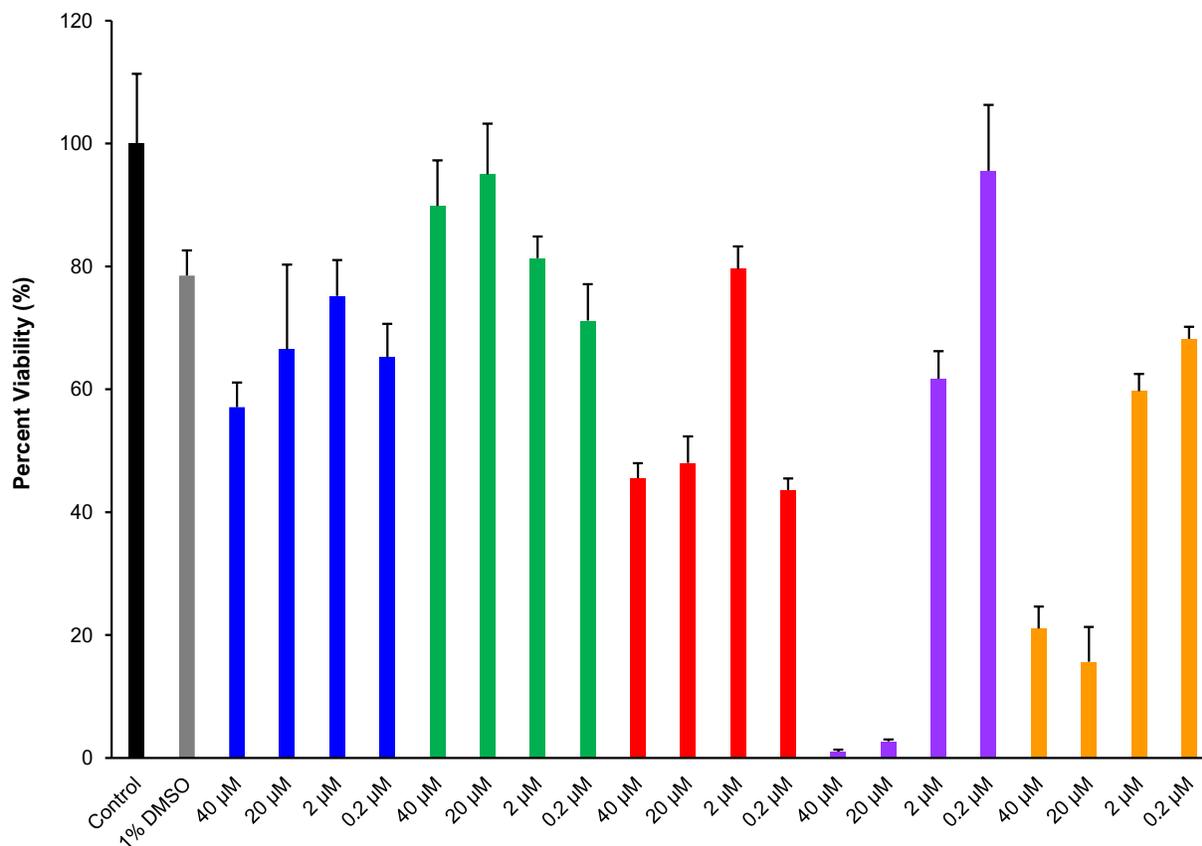
**Figure S34.** Fluorescence emission spectra at various Ru-HSA ratios by the titration of HSA-WF (1:1) with **RuPPh**. Experimental conditions:  $\lambda_{\text{ex}} = 295$  nm,  $\lambda_{\text{em}} = 330\text{-}500$  nm,  $[\text{HSA}] = [\text{WF}] = 2.5$   $\mu\text{M}$ ,  $[\text{Ru}] = 0$  (blue line), 12.5, 25, 32.5, 50, and 62.5  $\mu\text{M}$  (red line), in PBS (pH 7.4).



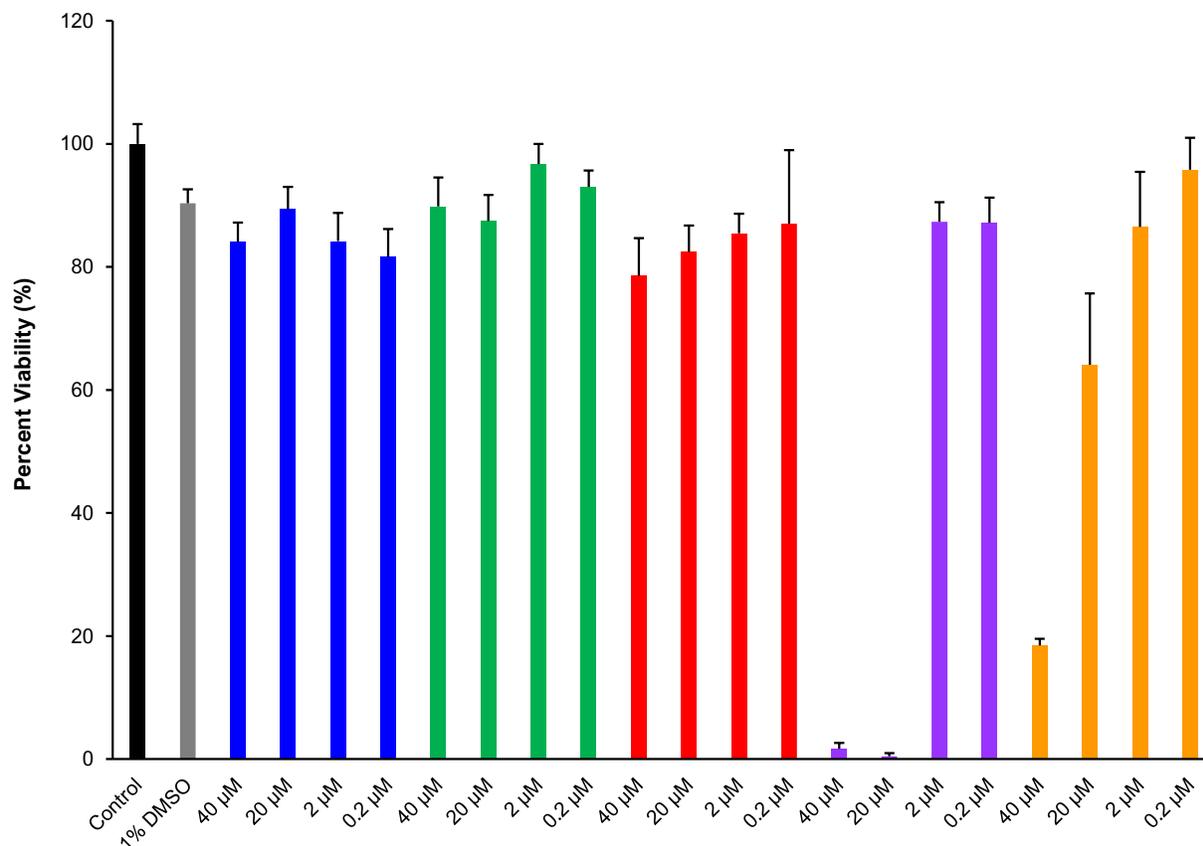
**Figure S35.** Fluorescence emission spectra at various Ru-HSA ratios by the titration of HSA-DG (1:1) with **RuDppz**. Experimental conditions:  $\lambda_{\text{ex}} = 330 \text{ nm}$ ,  $\lambda_{\text{em}} = 350\text{-}600 \text{ nm}$ ,  $[\text{HSA}] = [\text{DG}] = 2.5 \text{ }\mu\text{M}$ ,  $[\text{Ru}] = 0$  (blue line), 12.5, 25, 32.5, 50, and 62.5  $\mu\text{M}$  (red line), in PBS (pH 7.4).



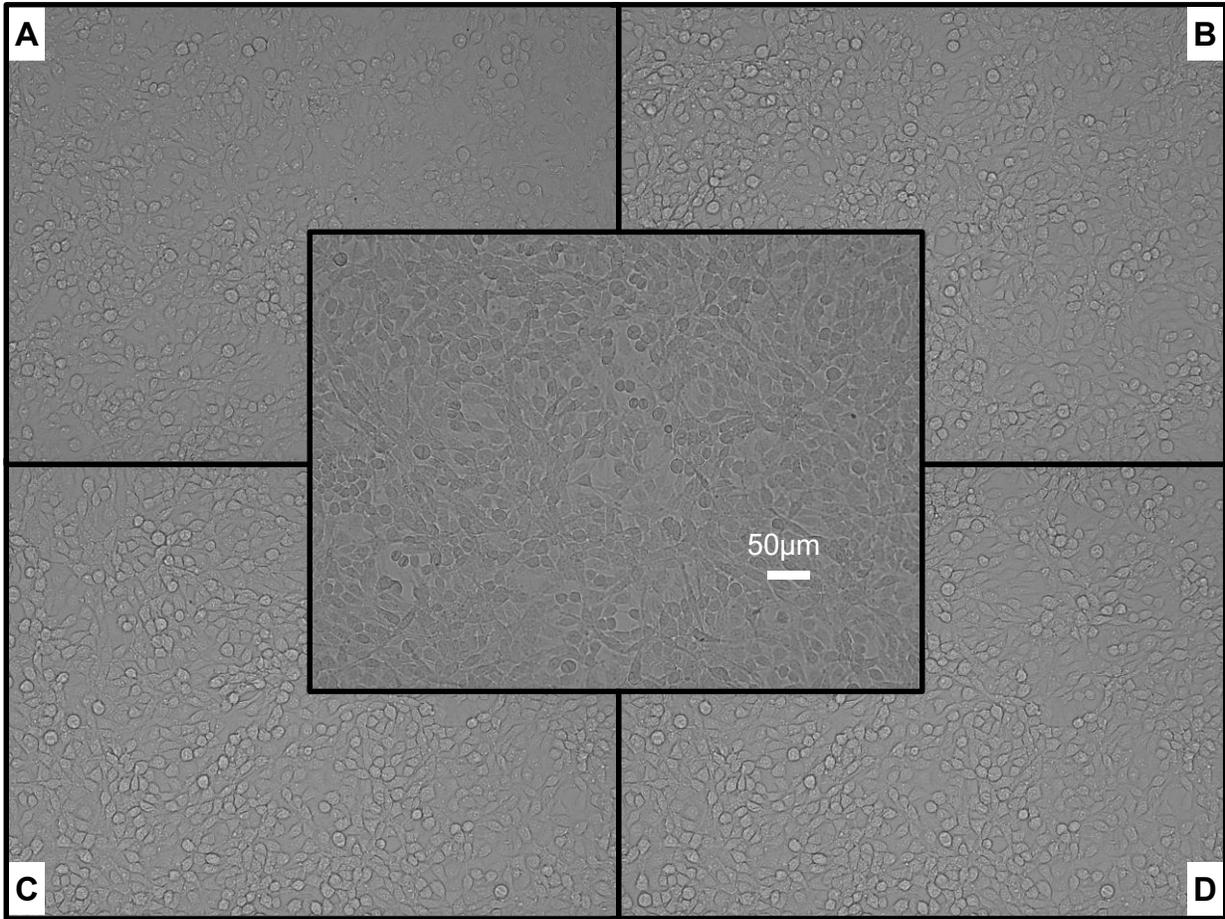
**Figure S36.** Fluorescence emission spectra at various Ru-HSA ratios by the titration of HSA-WF (1:1) with **RuDppz**. Experimental conditions:  $\lambda_{\text{ex}} = 295 \text{ nm}$ ,  $\lambda_{\text{em}} = 330\text{-}500 \text{ nm}$ ,  $[\text{HSA}] = [\text{WF}] = 2.5 \text{ }\mu\text{M}$ ,  $[\text{Ru}] = 0$  (blue line), 12.5, 25, 32.5, 50, and 62.5  $\mu\text{M}$  (red line), in PBS (pH 7.4).



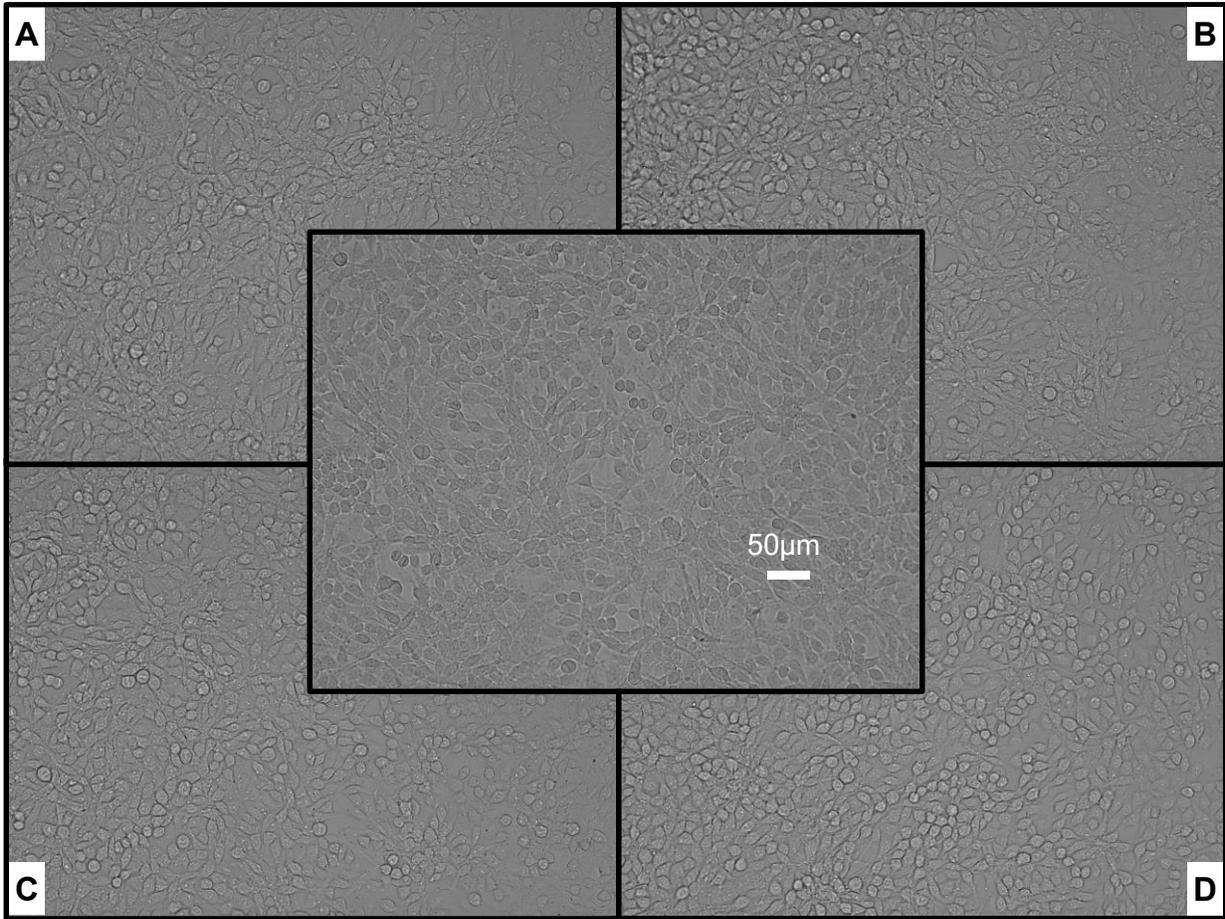
**Figure S37.** Cell viability of C6 cells as determined by MTT following incubation with the respective Ru complexes, where untreated cells are black, 1% DMSO is gray, **RuP** is blue, **RuPA** is green, **RuPMeO** is red, **RuPPh** is purple, and **RuDppz** is orange.



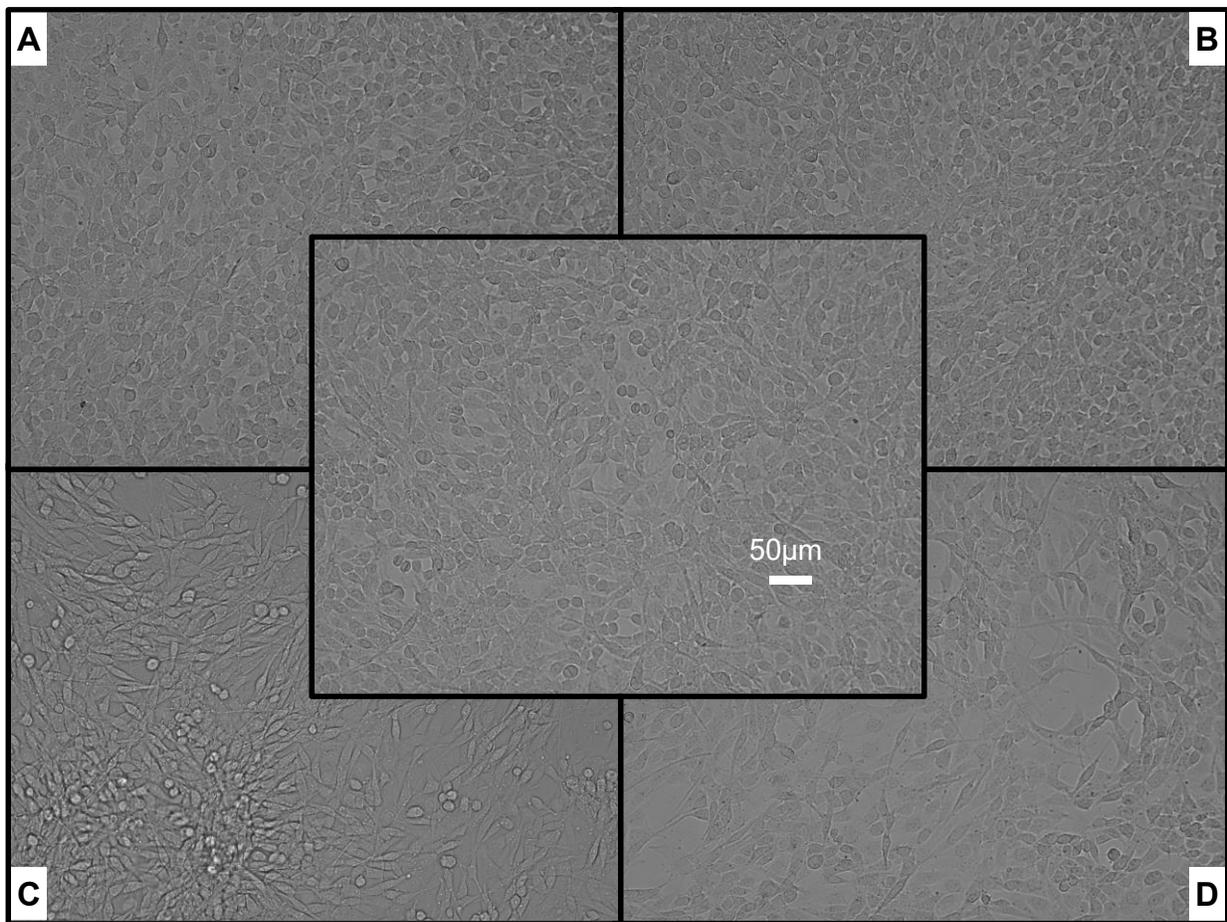
**Figure S38.** Cell viability of P12 cells as determined by MTT following incubation with the respective Ru complexes, where untreated cells are black, 1% DMSO is gray, **RuP** is blue, **RuPA** is green, **RuPMeO** is red, **RuPPh** is purple, and **RuDppz** is orange.



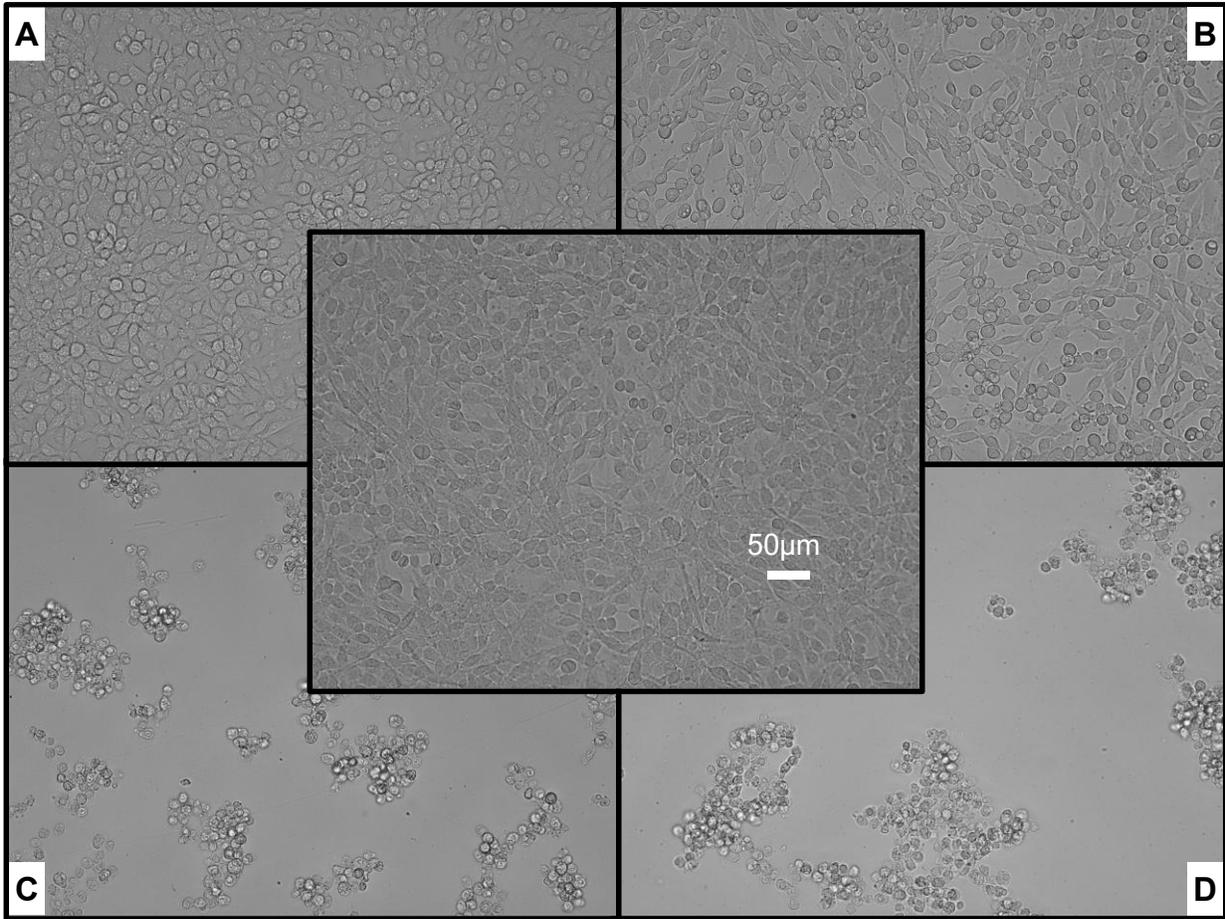
**Figure S39.** Confocal images of the C6 cells following 24 hours of incubation with **RuP** at (A) 0.2 μM, (B) 2 μM, (C) 20 μM, and (D) 40 μM. Central image are DMSO control cells.



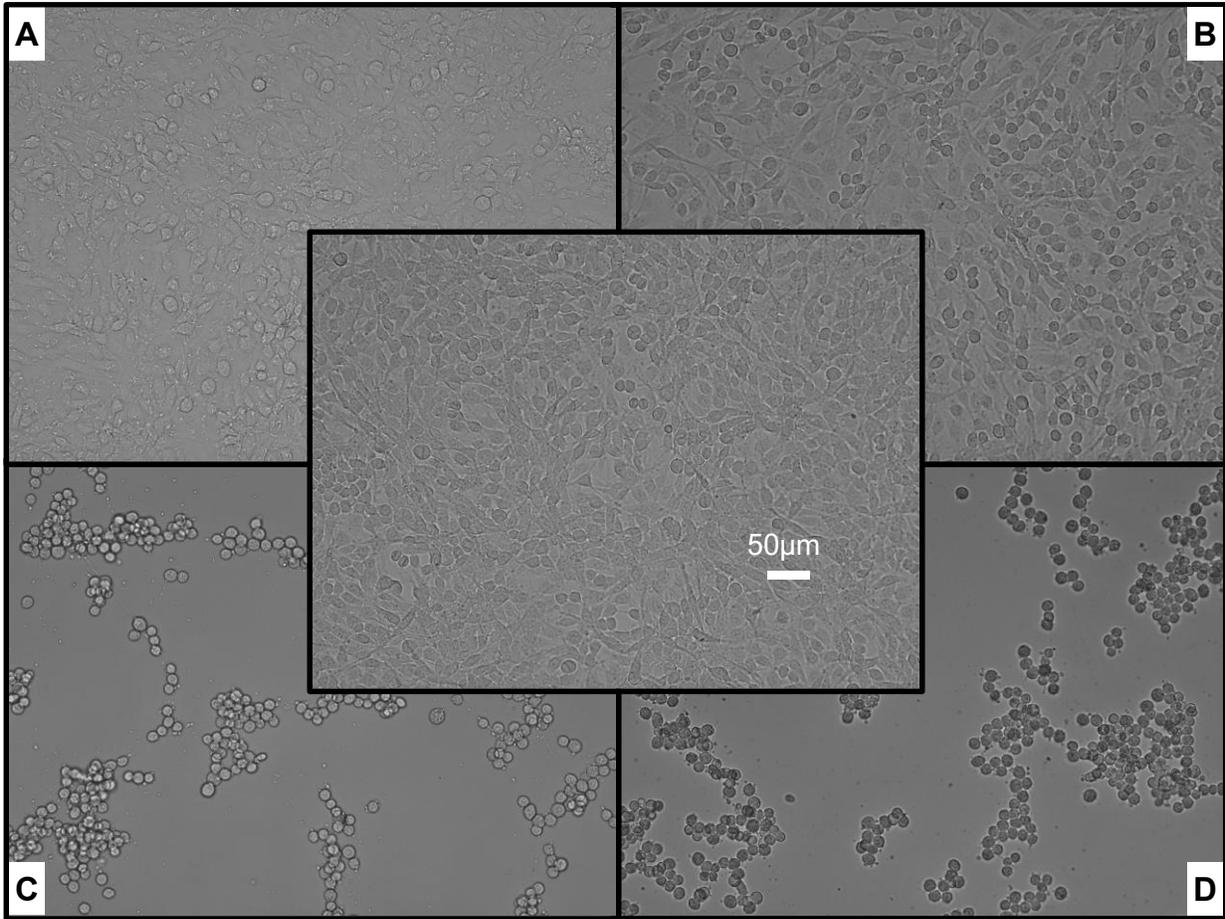
**Figure S40.** Confocal images of the C6 cells following 24 hours of incubation with **RuPA** at (A) 0.2 μM, (B) 2 μM, (C) 20 μM, and (D) 40 μM. Central image are DMSO control cells.



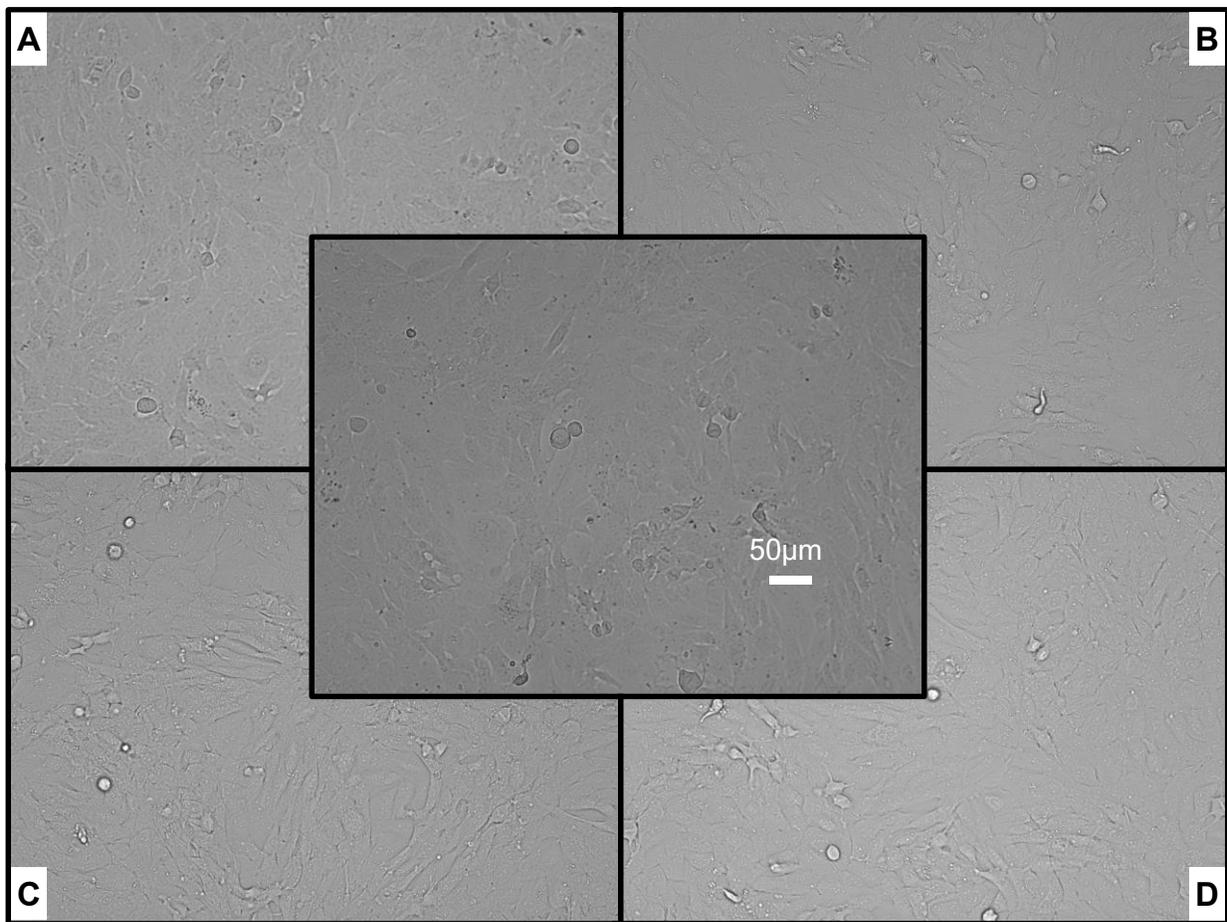
**Figure S41.** Confocal images of the C6 cells following 24 hours of incubation with **RuPMeO** at (A) 0.2 μM, (B) 2 μM, (C) 20 μM, and (D) 40 μM. Central image are DMSO control cells.



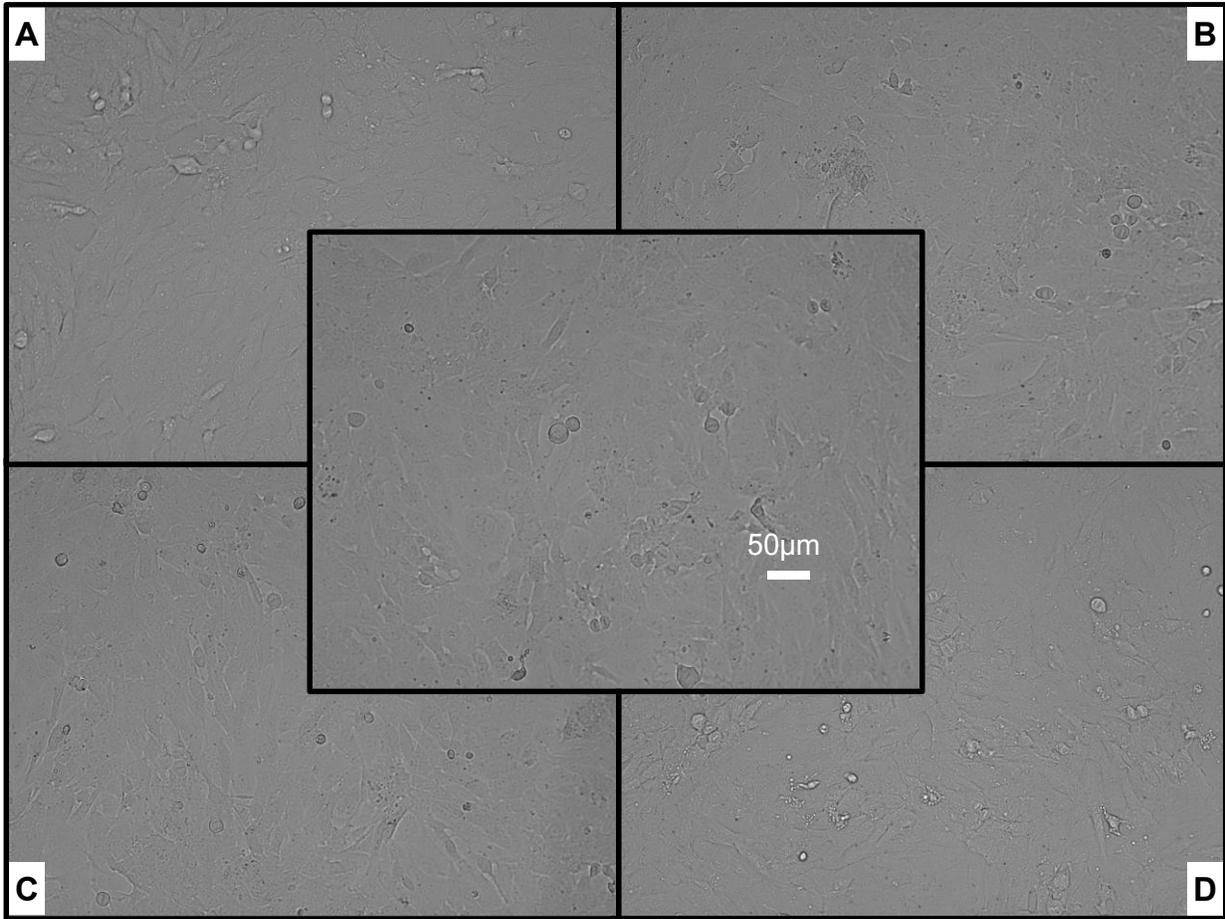
**Figure S42.** Confocal images of the C6 cells following 24 hours of incubation with **RuPPh** at (A) 0.2µM, (B) 2µM, (C) 20µM, and (D) 40µM. Central image are DMSO control cells.



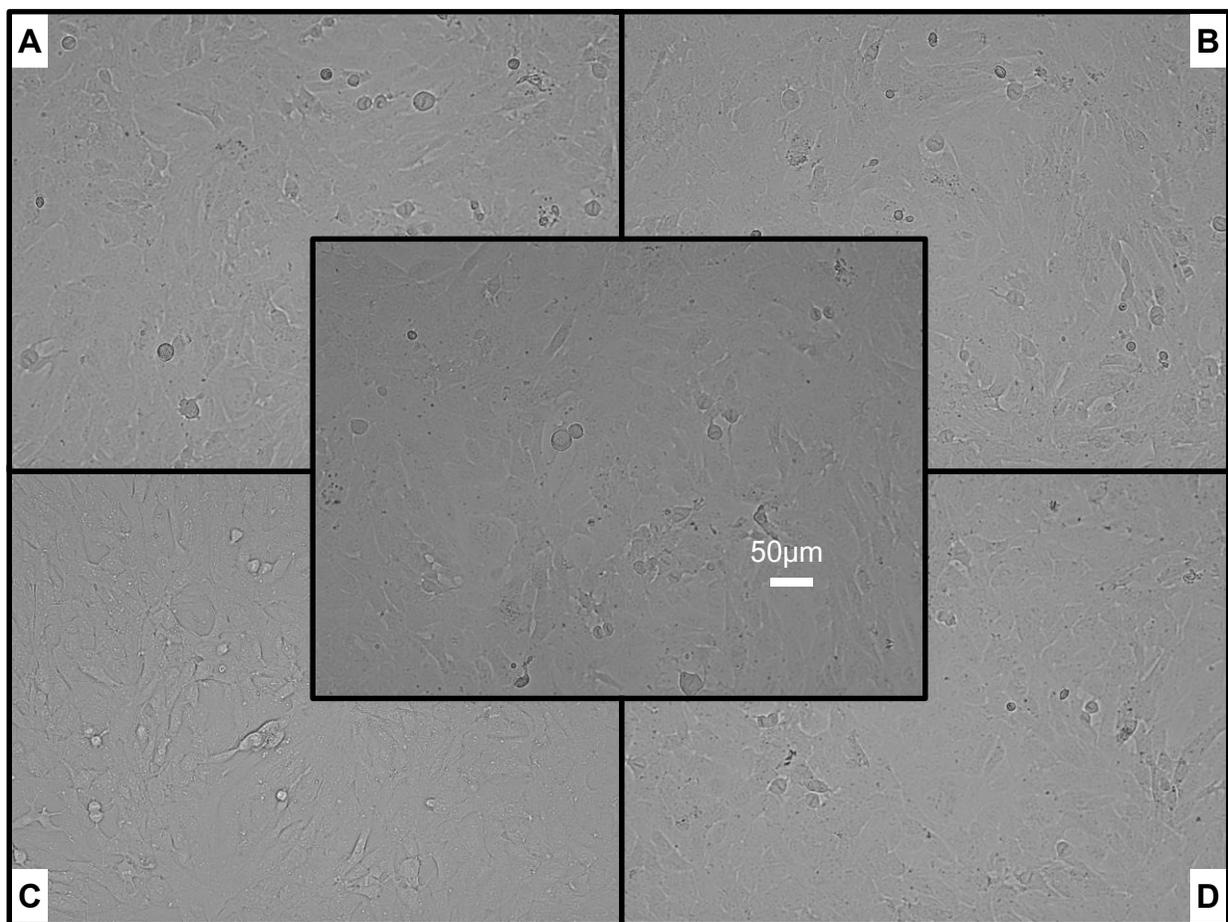
**Figure S43.** Confocal images of the C6 cells following 24 hours of incubation with **RuDppz** at (A) 0.2µM, (B) 2µM, (C) 20µM, and (D) 40µM. Central image are DMSO control cells.



**Figure S44.** Confocal images of the PC12 cells following 24 hours of incubation with **RuP** at (A) 0.2µM, (B) 2µM, (C) 20µM, and (D) 40µM. Central image are DMSO control cells.



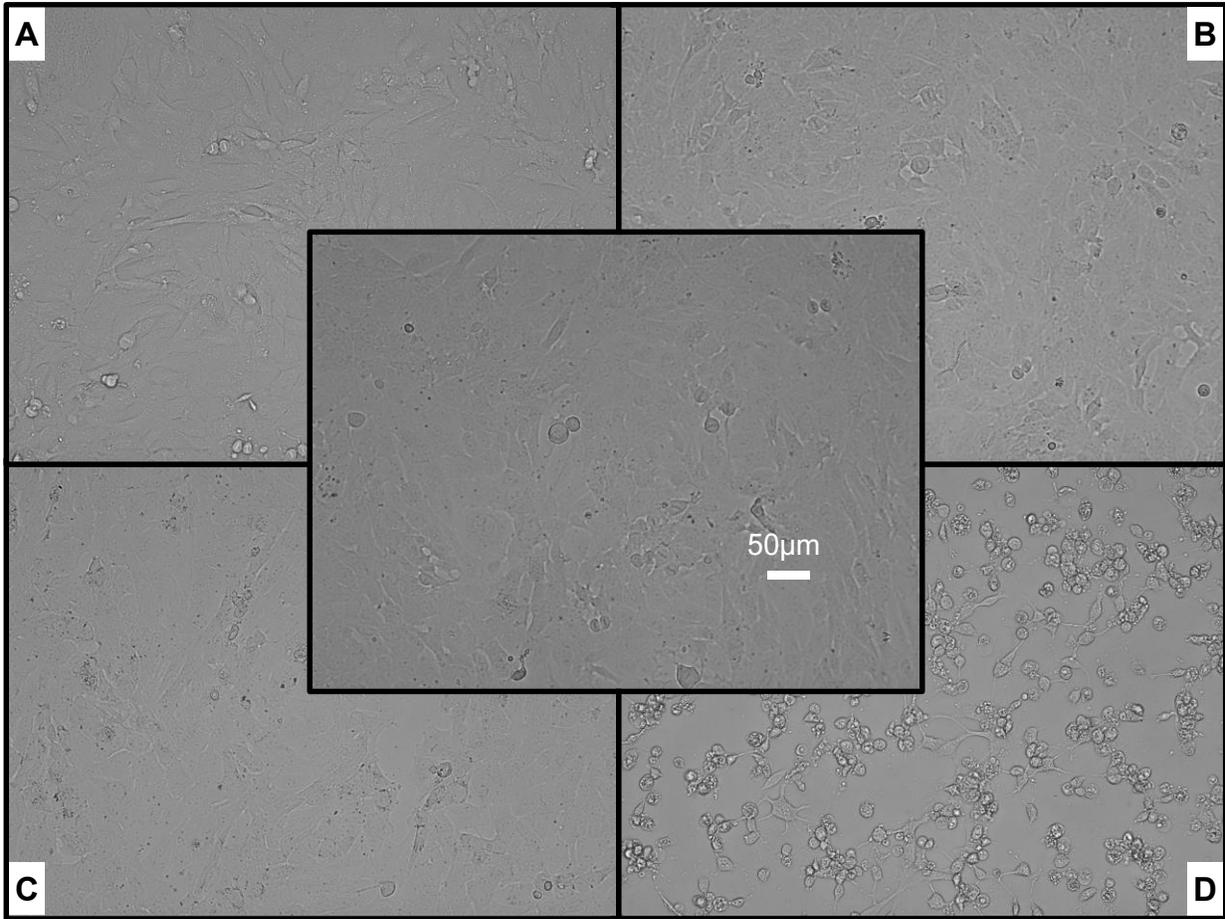
**Figure S45.** Confocal images of the PC12 cells following 24 hours of incubation with **RuPA** at (A) 0.2µM, (B) 2µM, (C) 20µM, and (D) 40µM. Central image are DMSO control cells.



**Figure S46.** Confocal images of the PC12 cells following 24 hours of incubation with **RuPMeO** at (A) 0.2µM, (B) 2µM, (C) 20µM, and (D) 40µM. Central image are DMSO control cells.



**Figure S47.** Confocal images of the PC12 cells following 24 hours of incubation with **RuPPH** at (A) 0.2µM, (B) 2µM, (C) 20µM, and (D) 40µM. Central image are DMSO control cells.



**Figure S48.** Confocal images of the PC12 cells following 24 hours of incubation with **RuDppz** at (A) 0.2 μM, (B) 2 μM, (C) 20 μM, and (D) 40 μM. Central image are DMSO control cells.

**Table S1.** Crystal data and structure refinement for **RuPA**.

CCDC Number	2489851	
Empirical formula	C <sub>22</sub> H <sub>28.19</sub> Cl F <sub>6</sub> N <sub>4</sub> O <sub>2.10</sub> P Ru	
Formula weight	663.77	
Temperature	99.99(10) K	
Wavelength	1.54184 Å	
Crystal system	triclinic	
Space group	<i>P</i> -1	
Unit cell dimensions	<i>a</i> = 7.09210(10) Å	<i>a</i> = 103.4700(10)°
	<i>b</i> = 12.31010(10) Å	<i>b</i> = 93.5520(10)°
	<i>c</i> = 15.07760(10) Å	<i>g</i> = 95.8310(10)°
Volume	1268.51(2) Å <sup>3</sup>	
<i>Z</i>	2	
Density (calculated)	1.738 Mg/m <sup>3</sup>	
Absorption coefficient	7.242 mm <sup>-1</sup>	
<i>F</i> (000)	670	
Crystal color, morphology	yellow-orange, plate	
Crystal size	0.173 x 0.109 x 0.028 mm <sup>3</sup>	
Theta range for data collection	3.026 to 80.114°	
Index ranges	-8 ≤ <i>h</i> ≤ 9, -15 ≤ <i>k</i> ≤ 14, -18 ≤ <i>l</i> ≤ 19	
Reflections collected	42850	
Independent reflections	5429 [ <i>R</i> (int) = 0.0476]	
Observed reflections	5328	
Completeness to theta = 74.504°	99.8%	
Absorption correction	Multi-scan	
Max. and min. transmission	1.00000 and 0.65087	
Refinement method	Full-matrix least-squares on <i>F</i> <sup>2</sup>	
Data / restraints / parameters	5429 / 0 / 383	
Goodness-of-fit on <i>F</i> <sup>2</sup>	1.044	
Final <i>R</i> indices [ <i>I</i> > 2σ( <i>I</i> )]	<i>R</i> 1 = 0.0289, <i>wR</i> 2 = 0.0693	
<i>R</i> indices (all data)	<i>R</i> 1 = 0.0293, <i>wR</i> 2 = 0.0696	
Extinction coefficient	0.00121(9)	
Largest diff. peak and hole	0.851 and -0.673 e.Å <sup>-3</sup>	

**Table S2.** Crystal data and structure refinement for **RuPMeO**.

CCDC Number	2449928
Empirical formula	C <sub>24</sub> H <sub>26</sub> Cl F <sub>6</sub> N <sub>2</sub> O <sub>2</sub> P Ru
Formula weight	655.96
Temperature	100.00(10) K
Wavelength	1.54184 Å
Crystal system	orthorhombic
Space group	<i>Pbca</i>
Unit cell dimensions	$a = 14.44500(10) \text{ \AA}$ $a = 90^\circ$ $b = 14.88420(10) \text{ \AA}$ $b = 90^\circ$ $c = 23.39920(10) \text{ \AA}$ $c = 90^\circ$
Volume	5030.88(5) Å <sup>3</sup>
Z	8
Density (calculated)	1.732 Mg/m <sup>3</sup>
Absorption coefficient	7.273 mm <sup>-1</sup>
<i>F</i> (000)	2640
Crystal color, morphology	yellow-orange, block
Crystal size	0.153 x 0.127 x 0.074 mm <sup>3</sup>
Theta range for data collection	3.778 to 80.159°
Index ranges	-18 ≤ <i>h</i> ≤ 15, -18 ≤ <i>k</i> ≤ 18, -29 ≤ <i>l</i> ≤ 26
Reflections collected	44968
Independent reflections	5403 [ <i>R</i> (int) = 0.0386]
Observed reflections	5069
Completeness to theta = 74.504°	99.9%
Absorption correction	Multi-scan
Max. and min. transmission	1.00000 and 0.76175
Refinement method	Full-matrix least-squares on <i>F</i> <sup>2</sup>
Data / restraints / parameters	5403 / 0 / 340
Goodness-of-fit on <i>F</i> <sup>2</sup>	1.095
Final <i>R</i> indices [ <i>I</i> > 2σ( <i>I</i> )]	<i>R</i> 1 = 0.0286, <i>wR</i> 2 = 0.0778
<i>R</i> indices (all data)	<i>R</i> 1 = 0.0305, <i>wR</i> 2 = 0.0791
Extinction coefficient	0.000057(14)
Largest diff. peak and hole	0.536 and -0.675 e.Å <sup>-3</sup>