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Supplementary Information

A Pyrazolate Osmium(VI) Nitride Exhibits Anticancer Activity Through Modulating Protein Homeostasis in HepG2 Cells

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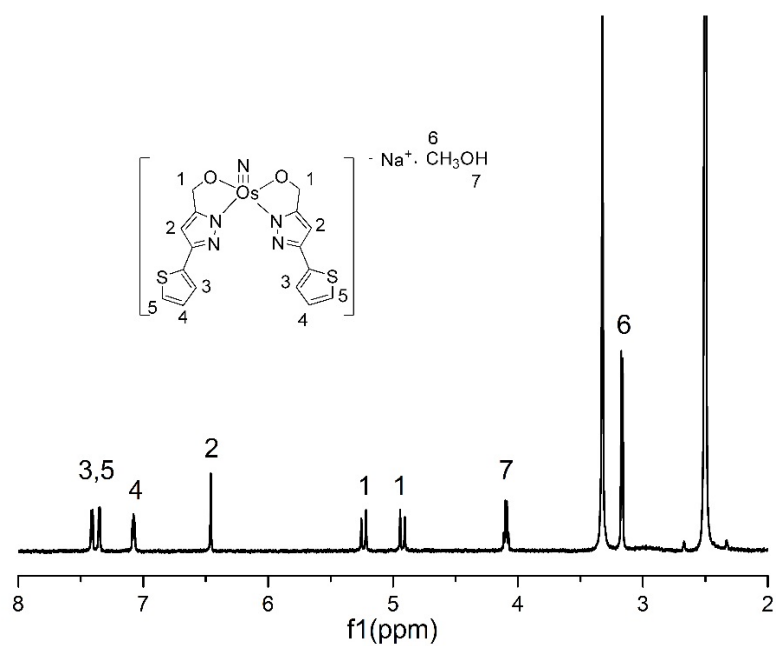


Figure S1. The ^1H NMR spectrogram of $\text{Na}[\text{Os}^{\text{VI}}(\text{N})(\text{tpm})_2]$ in d_6 -DMSO.

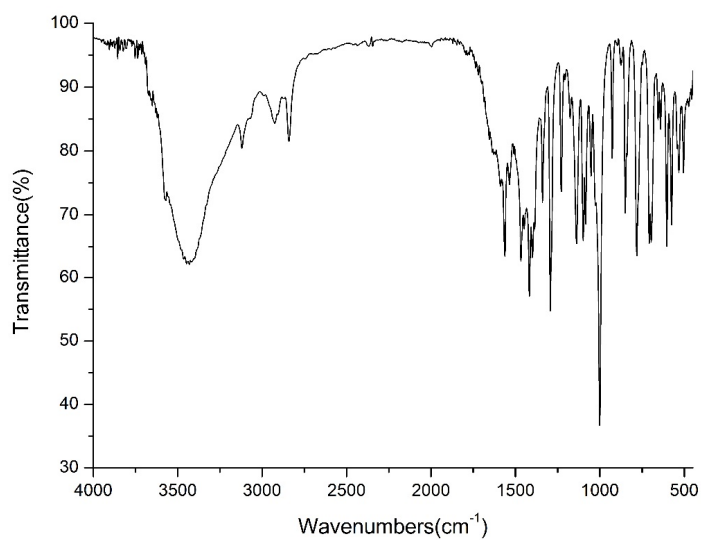


Figure S2. The IR spectrogram of $\text{Na}[\text{Os}^{\text{VI}}(\text{N})(\text{tpm})_2]$.

Table S1 Crystal data and structure refinements for **Na[Os^{VI}(N)(tpm)₂]**

	Na[Os^{VI}(N)(tpm)₂]
Formula	C ₁₇ H ₁₆ N ₅ NaO ₃ OsS ₂
Mr.	615.66
Crystal system	Orthorhombic
Space group	<i>P</i> 2 ₁ 2 ₁ 2 ₁
Temp (K)	293(2)
a (Å)	7.52480(10)
b (Å)	13.9934(3)
c (Å)	18.9699(3)
α (°)	90
β (°)	90
γ (°)	90
V (Å ³)	1997.48(6)
Z	4
D _c (g·cm ⁻³)	2.047
no. of reflns	4617
no. of unique	3330
data collected	3.93 to 74.54
unique refl.(R _{int})	0.0283
GOF on F ²	1.086
R ₁ [I ≥ 2σ(I)] ^a	0.0374
wR ₂ [I ≥ 2σ(I)] ^b	0.1018
R ₁ [all data]	0.0381
wR ₂ [all data]	0.1022
Flack parameter	0.33(2)

^aR₁ = Σ || F_o | - | F_c | | / Σ | F_o |. ^b wR₂ = [Σ[w(F_o² - F_c²)²] / Σw(F_o²)²]^{1/2}, where w = 1/[w²(F_o)² + (aP)² + bP] and P = (F_o² + 2F_c²)/3.

Table S2 Selected bond lengths (Å) and angles (°) for **Na[Os^{VI}(N)(tpm)₂]**.

Os(1)-O(1)	1.965(7)	Os(1)-O(2)	1.956(8)	Os(1)-N(1)	2.000(8)
Os(1)-N(3)	2.006(8)	Os(1)-N(5)	1.649(9)	Na(1)-O(1)#2	2.493(9)
Na(1)-O(2)#2	2.388(9)	Na(1)-O(3)	2.116(7)	Na(1)-N(2)	2.463(9)
Na(1)-N(4)	2.511(10)				
O(2)-Os(1)-O(1)	82.3(3)	O(2)-Os(1)-N(1)	143.5(4)	O(2)-Os(1)-N(3)	80.0(4)
O(1)-Os(1)-N(1)	79.5(3)	O(1)-Os(1)-N(3)	144.0(3)	N(1)-Os(1)-N(3)	96.8(3)
N(5)-Os(1)-O(2)	109.9(5)	N(5)-Os(1)-O(1)	109.3(4)	N(5)-Os(1)-N(1)	106.0(4)
N(5)-Os(1)-N(3)	106.1(4)	O(2)#2-Na(1)-O(1)#2	63.8(3)	O(2)#2-Na(1)-N(4)	109.2(3)
O(2)#2-Na(1)-N(2)	168.9(4)	O(1)#2-Na(1)-N(4)	171.3(3)	N(2)-Na(1)-O(1)#2	106.7(3)
N(2)-Na(1)-N(4)	79.7(3)	O(3)-Na(1)-O(2)#2	114.4(3)	O(3)-Na(1)-O(1)#2	115.9(3)
O(3)-Na(1)-N(4)	71.2(3)	O(3)-Na(1)-N(2)	74.4(3)		
Os(1)-O(2)-Na(1)#1	109.1(4)	Os(1)-O(1)-Na(1)#1	104.8(3)		

Symmetry transformations used to generate equivalent atoms: #1 x-1, y, z #2 x+1, y, z

Table S1 The Na content of **Na[Os^{VI}(N)(tpm)₂]** detected by ICP-MS.

Sample weight	Calculated content of Na (mg)	Measured content of Na (mg)
2.52mg	0.0993	0.09725
4.86mg	0.1915	0.16975

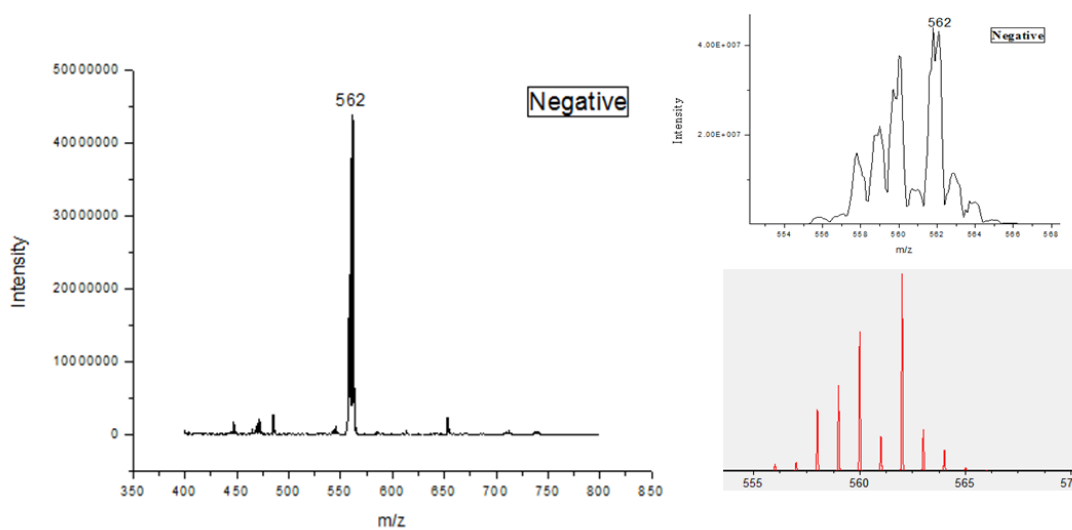


Figure S3. The ESI-MS spectra of $\text{Na}[\text{Os}^{\text{VI}}(\text{N})(\text{tpm})_2]$ in MeOH, acquired in negative ion mode. Insets right show the experimental (black) and simulated (red) isotopic patterns for the peak at m/z 562.

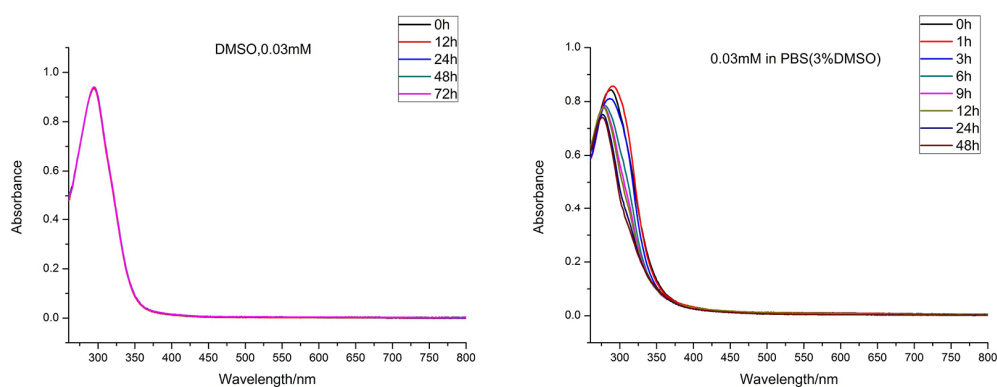


Figure S4. The stability of $\text{Na}[\text{Os}^{\text{VI}}(\text{N})(\text{tpm})_2]$ ($30\mu\text{M}$) in DMSO and in PBS (3% DMSO). ($T=298\text{K}$, path length=1cm)

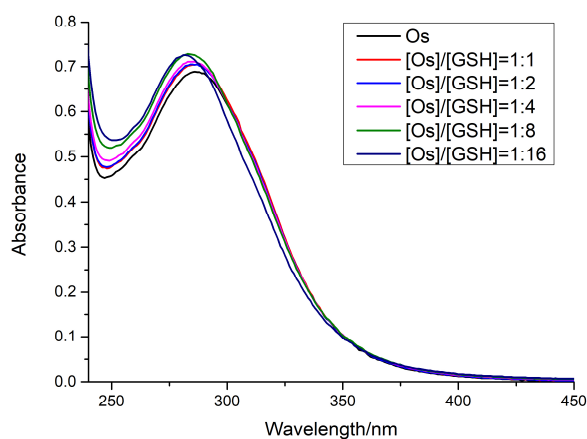


Figure S5. The stability of $\text{Na}[\text{Os}^{\text{VI}}(\text{N})(\text{tpm})_2]$ ($30\mu\text{M}$) with different concentration of GSH in PBS (3% DMSO). Os represents $\text{Na}[\text{Os}^{\text{VI}}(\text{N})(\text{tpm})_2]$. (T=298K, path length=1 cm)

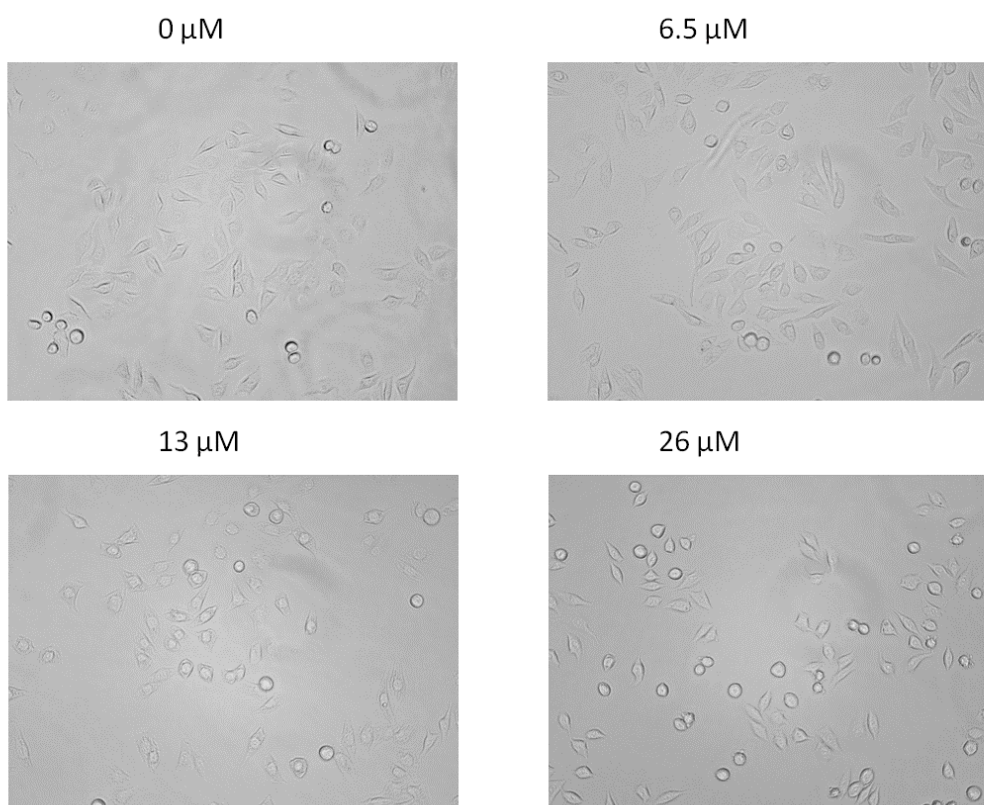


Figure S6. Effects of different concentrations of $\text{Na}[\text{Os}^{\text{VI}}(\text{N})(\text{tpm})_2]$ on the morphology of HepG2 cells at 3 h.

Table S4 Abbreviations in the main text.

Abbreviations	Explanations
INTS3	Integrator Complex Subunit 3
hSSB1	human ssDNA binding protein SSB1
SMARCA1	SWI/SNF Related, Matrix Associated, Actin Dependent Regulator Of Chromatin, Subfamily A, Member 1
DDB	Damage Specific DNA Binding Protein 2
TYMS	Thymidylate Synthetase
HCC	hepatic cell carcinoma
TOP2A	topoisomerase II α
NER	Nucleotide Excision Repair
PAQR3	Progestin And AdipoQ Receptor Family Member 3
LRH-1	Liver receptor homolog-1
LSF/TFCP2	Transcription factor CP2
GCLM	Glutamate-Cysteine Ligase Modifier Subunit
GCLC	glutamate-cysteine ligase catalytic subunit
EPRE	electrophile response element
KYNU	Kynureninase or L-kynurenine hydrolase
PLP	Pyridoxal5-phosphatemonohydrate
Kyn	kynurenine
Ant	anthranilic acid
CCCP	carbonyl cyanide m-chlorophenylhydrazine
DCFH-DA	2'-7'-dichlorofluorescein diacetate
ROS	Reactive oxygen species
MMP	Mitochondrial membrane potential
JC-1	5,5',6,6'-tetrachloro-1,1'-3,3'-tetraethyl-benzimidazolylcarbocyanine iodide
GSH	glutathione
caspase	cysteiny aspartate specific proteinase
PARP1	poly-(ADP-ribose)-polymerase-1
Cl-PARP1	Cleaved poly-(ADP-ribose)-polymerase-1
Cl-caspase 3	Cleaved cysteiny aspartate specific proteinase 3
Cl-caspase 9	Cleaved cysteiny aspartate specific proteinase 9
p-CDC2	Phosphorylation cell division cycle 2