

Disruption of lipid metabolism to induce ferroptosis by multifunctional fibrate-Pt(IV) prodrugs for cancer treatment

Peng Sun^{a,1}, Jia-Qian Wang^{a,1}, Qiang Xie^a, Xuan-Lin Ren^a, Xin Qiao^{a,*}, Jing-Yuan Xu^{a,b,*}

^a*Department of Chemical Biology, School of Pharmacy, Tianjin Medical University, Tianjin 300070, China.*

^b*Key Laboratory of Immune Microenvironment and Disease of the Ministry of Education, Tianjin Medical University, Tianjin 300070, China.*

*Corresponding author:

E-mail address: qiaoxin@tmu.edu.cn (X. Qiao), xujingyuan@tmu.edu.cn (Prof. J.-Y. Xu)

¹These authors contributed equally to this work.

Table of Contents

Fig. S1. ^1H -NMR spectrum of compound 1 in DMSO- <i>d</i> ₆	2
Fig. S2. ^{13}C -NMR spectrum of compound 1 in DMSO- <i>d</i> ₆	3
Fig. S3. HR-MS spectrum of compound 1	4
Fig. S4. Reverse-phase HPLC trace of compound 1	5
Fig. S5. ^1H -NMR spectrum of compound 2 in DMSO- <i>d</i> ₆	6
Fig. S6. ^{13}C -NMR spectrum of compound 2 in DMSO- <i>d</i> ₆	7
Fig. S7. HR-MS spectrum of compound 2	8
Fig. S8. Reverse-phase HPLC trace of compound 2	9
Fig. S9. ^1H -NMR spectrum of compound 3 in DMSO- <i>d</i> ₆	10
Fig. S10. ^{13}C -NMR spectrum of compound 3 in DMSO- <i>d</i> ₆	11
Fig. S11. HR-MS spectrum of compound 3	12
Fig. S12. Reverse-phase HPLC trace of compound 3	13
Fig. S13. ^1H -NMR spectrum of compound 4 in DMSO- <i>d</i> ₆	14
Fig. S14. ^{13}C -NMR spectrum of compound 4 in DMSO- <i>d</i> ₆	15
Fig. S15. HR-MS spectrum of compound 4	16
Fig. S16. Reverse-phase HPLC trace of compound 4	17
Fig. S17. Comparison of cell viability of A549 cells treated with different concentrations of compounds for 48 h.....	18
Fig. S18. Un-cropped western blotting images of Figure 8a.....	19
Fig. S19. Un-cropped western blotting images of Figure 8c.....	20
Fig. S20. Structure of 12C and protein expression of A549 cells treated with 5 μM compounds for 24 h	20

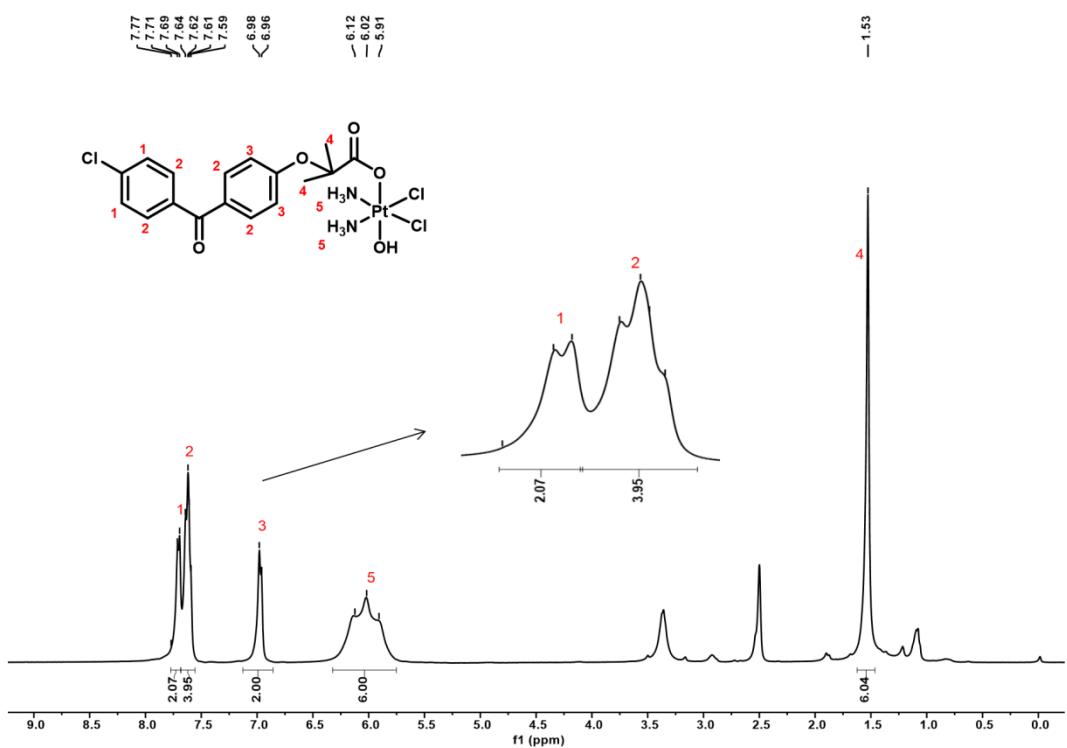


Fig. S1. ^1H -NMR spectrum of compound **1** in $\text{DMSO}-d_6$.

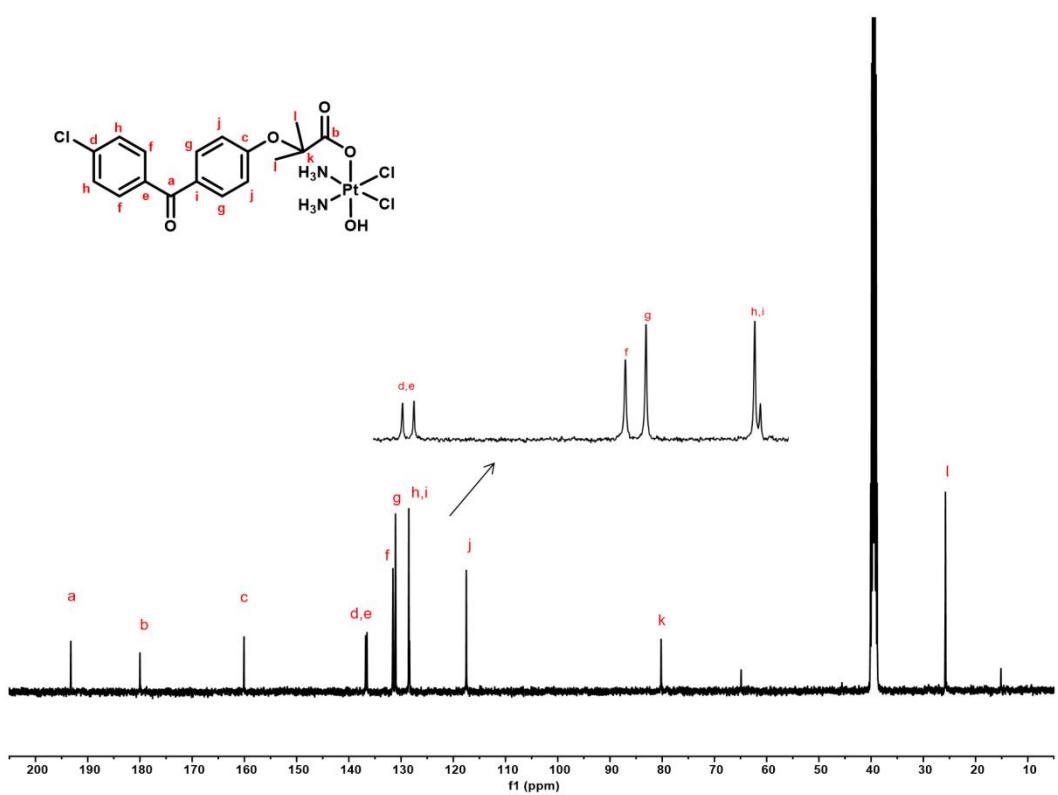


Fig. S2. ^{13}C -NMR spectrum of compound 1 in $\text{DMSO}-d_6$.

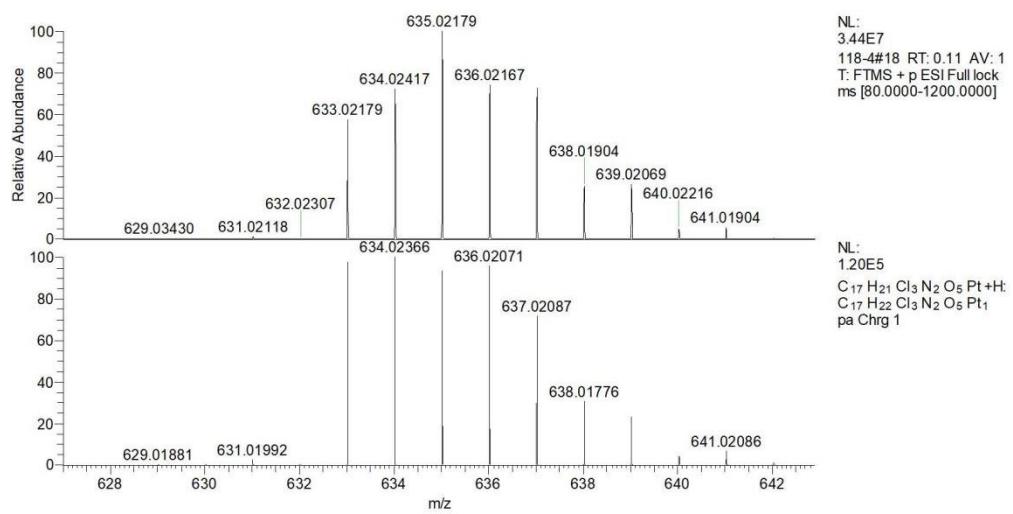
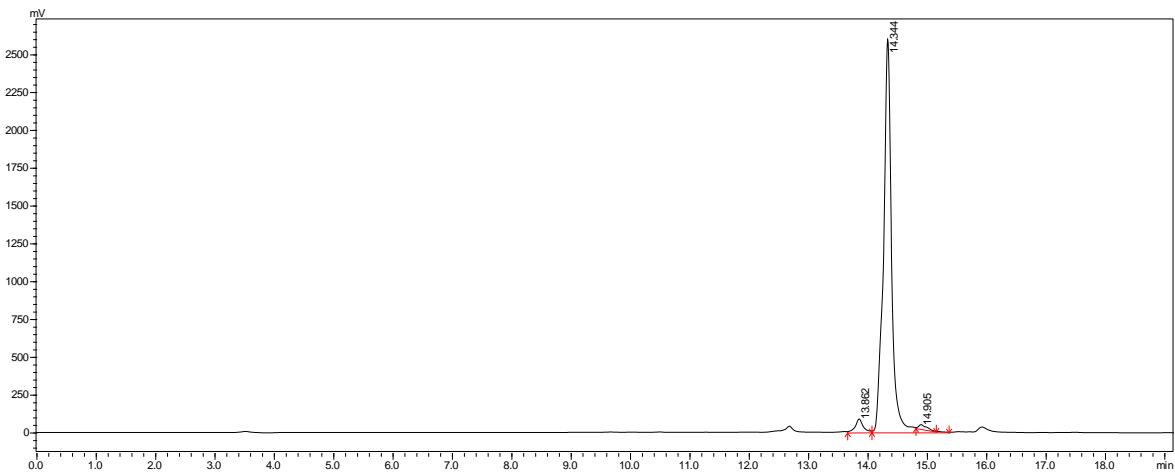


Fig. S3. HR-MS spectrum of compound 1.



	Retention	Peak area	Concentration
1	13.862	787449	3.049
2	14.344	24787777	95.985
3	14.905	249446	0.966
Total		25824673	100.000

Fig. S4. Reverse-phase HPLC trace of compound **1**.

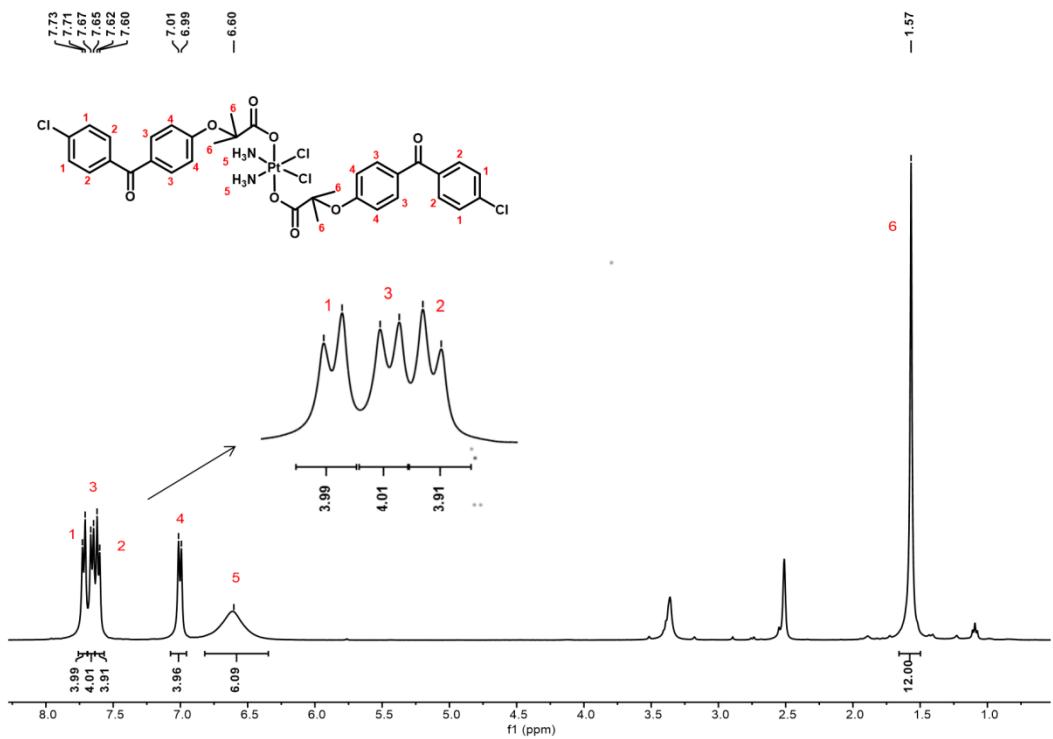


Fig. S5. ^1H -NMR spectrum of compound **2** in $\text{DMSO}-d_6$.

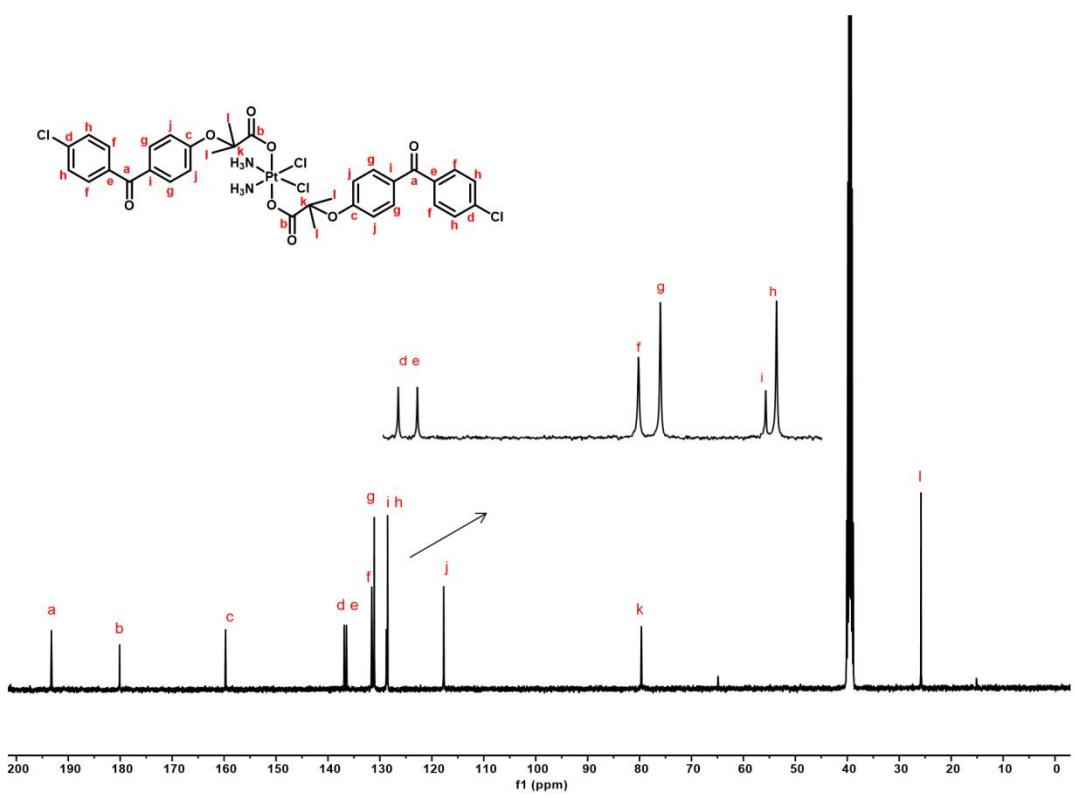


Fig. S6. ^{13}C -NMR spectrum of compound **2** in $\text{DMSO}-d_6$.

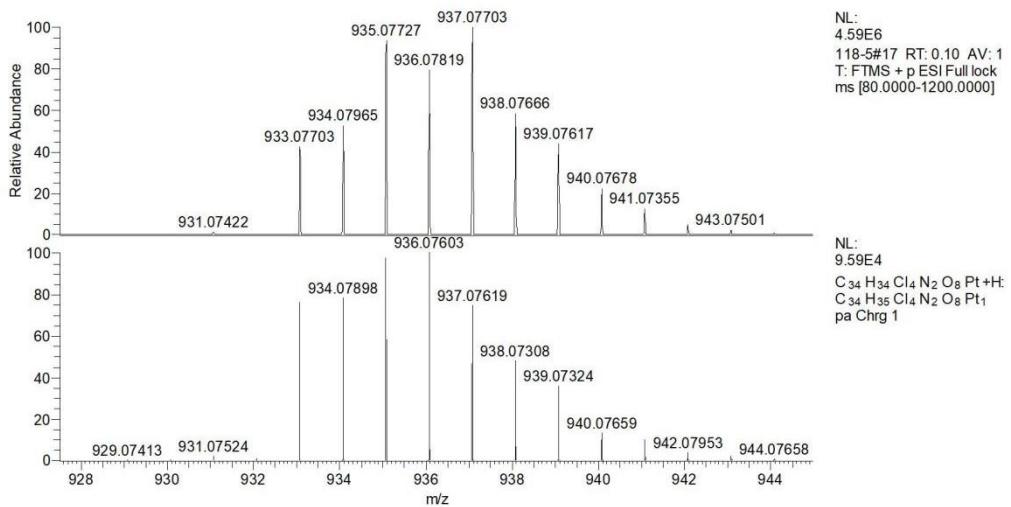
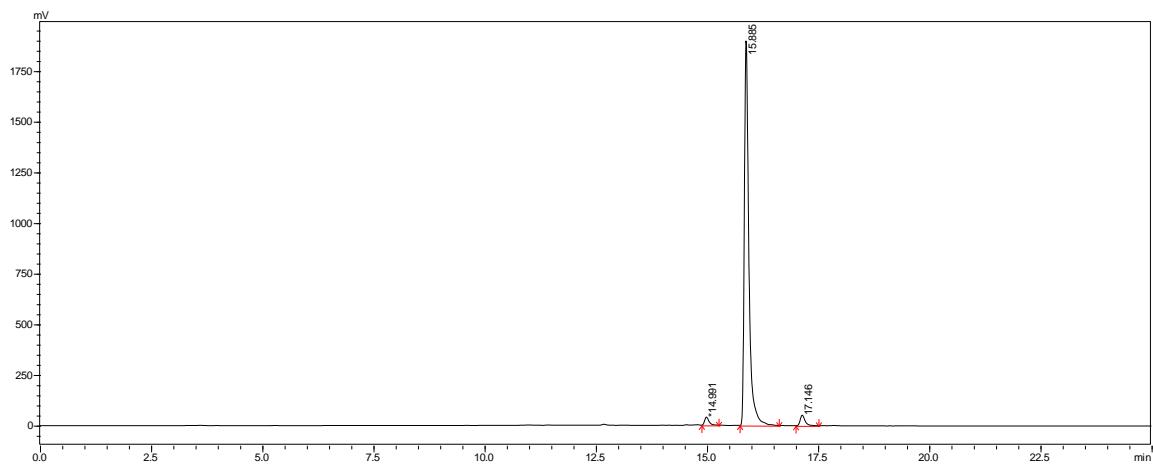


Fig. S7. HR-MS spectrum of compound 2.



	Retention	Peak area	Concentration
1	14.991	401243	1.523
2	15.885	25384642	96.376
3	17.146	553216	2.101
Total		26339101	100.000

Fig. S8. Reverse-phase HPLC trace of compound **2**.

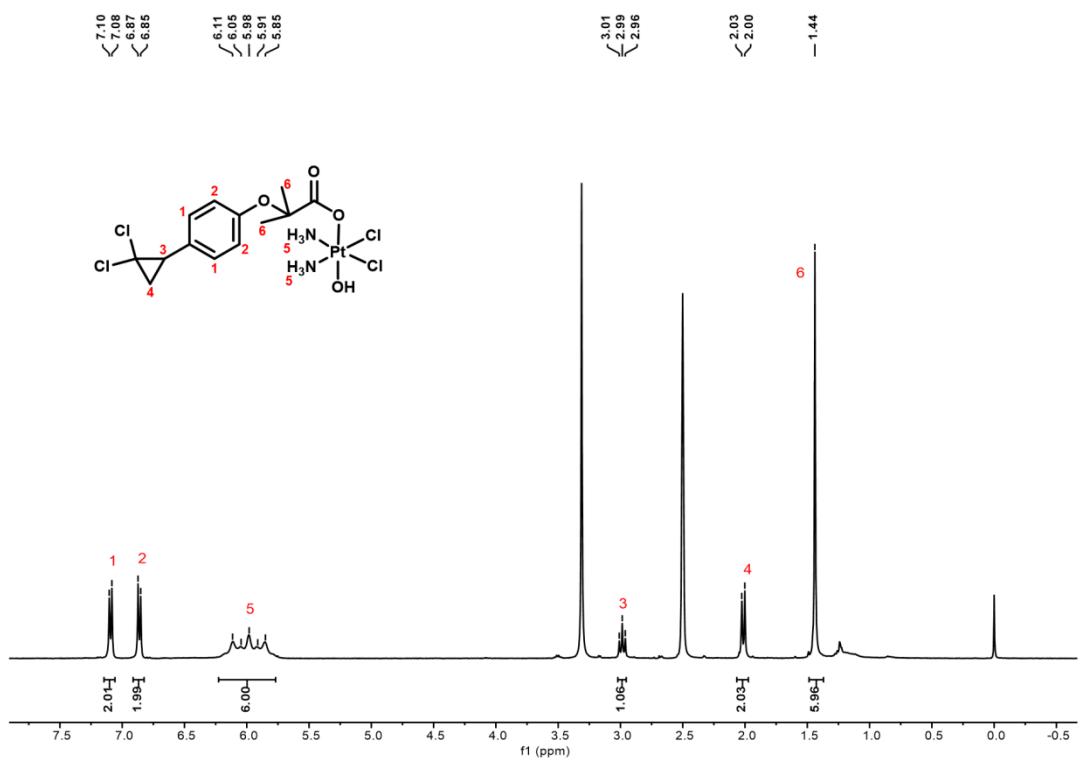


Fig. S9. ^1H -NMR spectrum of compound 3 in $\text{DMSO}-d_6$.

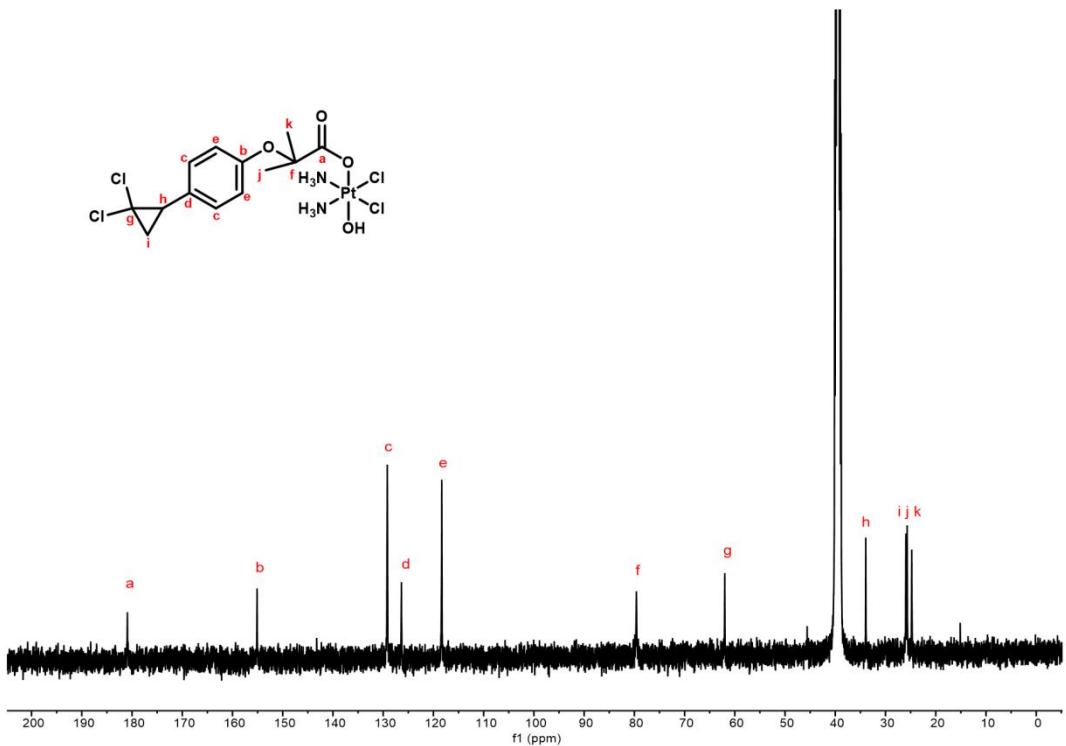


Fig. S10. ^{13}C -NMR spectrum of compound **3** in $\text{DMSO}-d_6$.

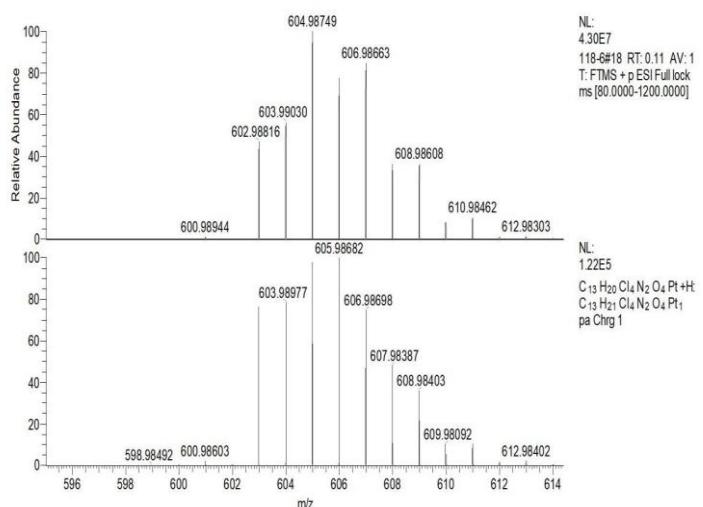
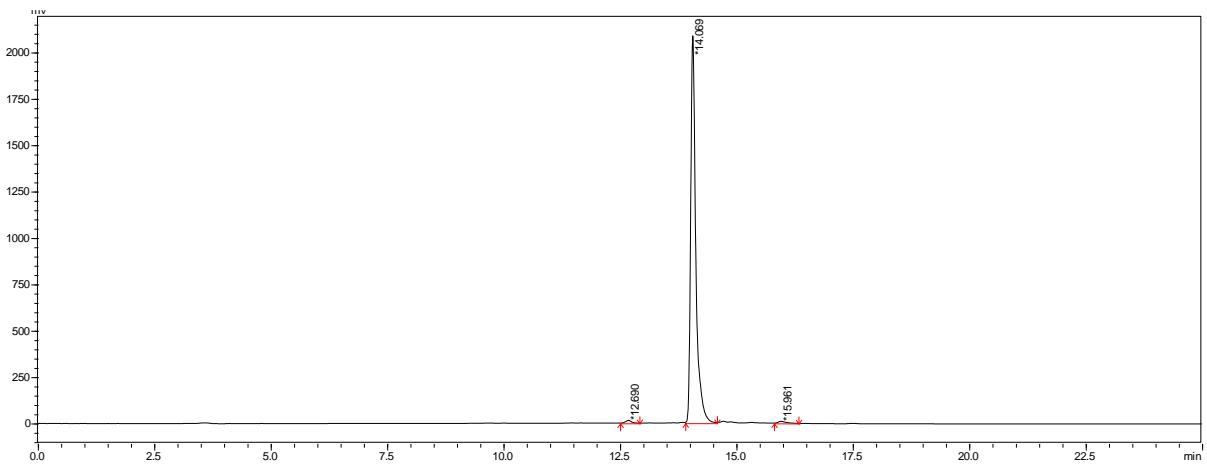


Fig. S11. HR-MS spectrum of compound 3.



	Retention	Peak area	Concentration
1	12.690	122730	0.756
2	14.069	15990395	98.563
3	15.961	110391	0.680
Total		16223516	100.000

Fig. S12. Reverse-phase HPLC trace of compound 3.

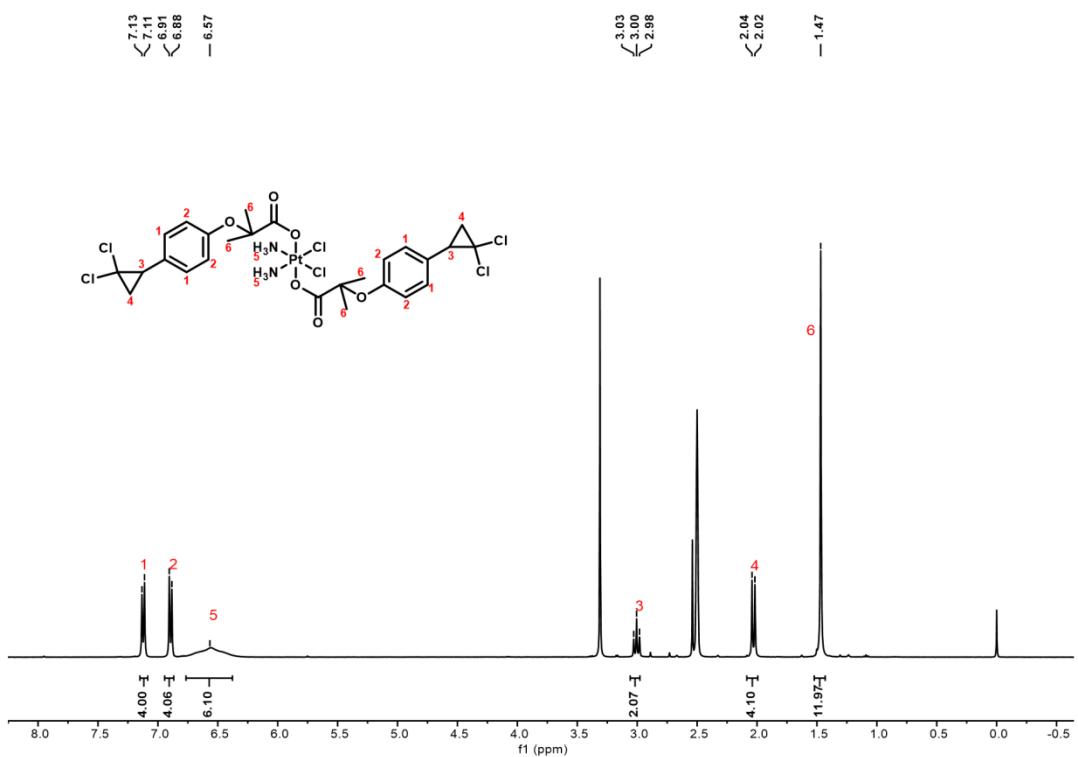


Fig. S13. ¹H-NMR spectrum of compound 4 in DMSO-*d*₆.

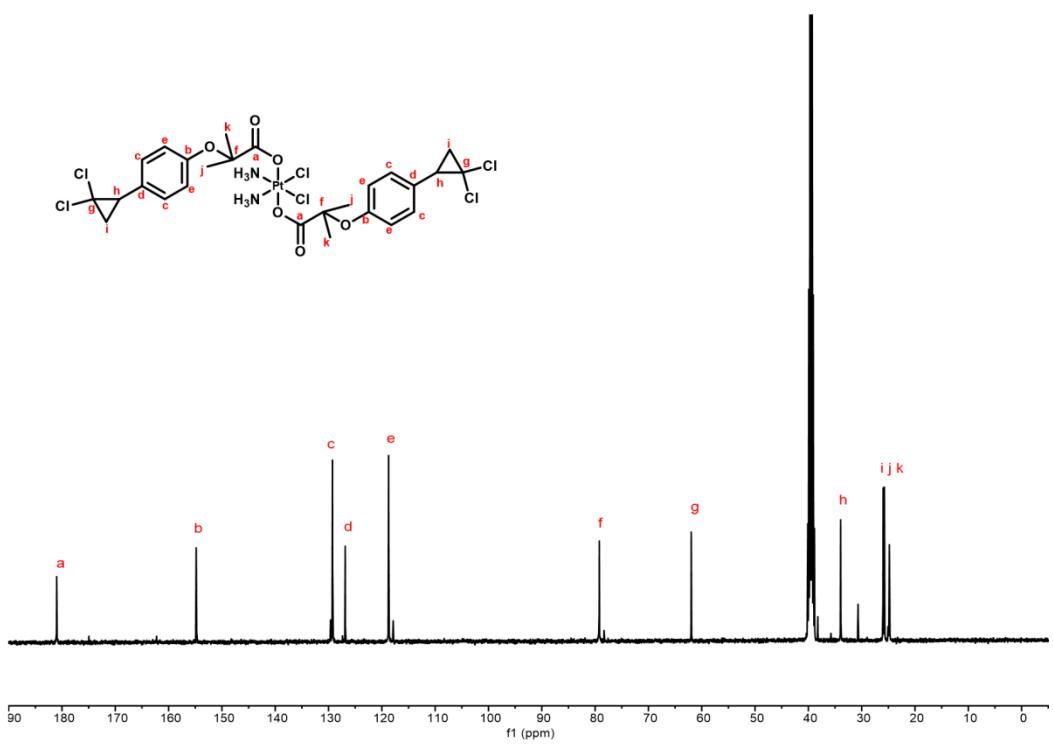


Fig. S14. ^{13}C -NMR spectrum of compound 4 in $\text{DMSO}-d_6$.

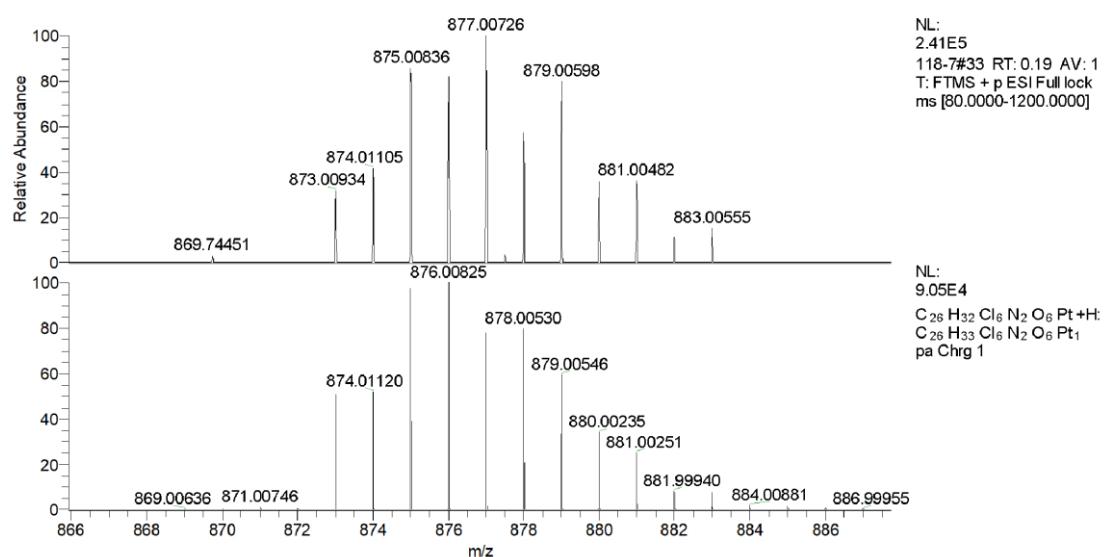
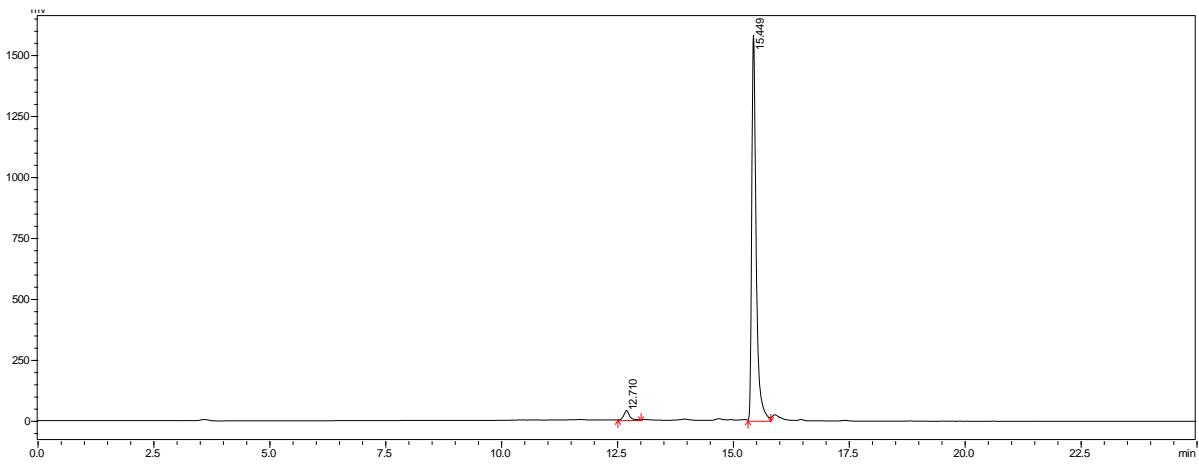


Fig. S15. HR-MS spectrum of compound 4.



	Retention	Peak area	Concentration
1	12.710	313928	2.902
2	15.4449	10501909	97.098
Total		10815836	100.000

Fig. S16. Reverse-phase HPLC trace of compound 4.

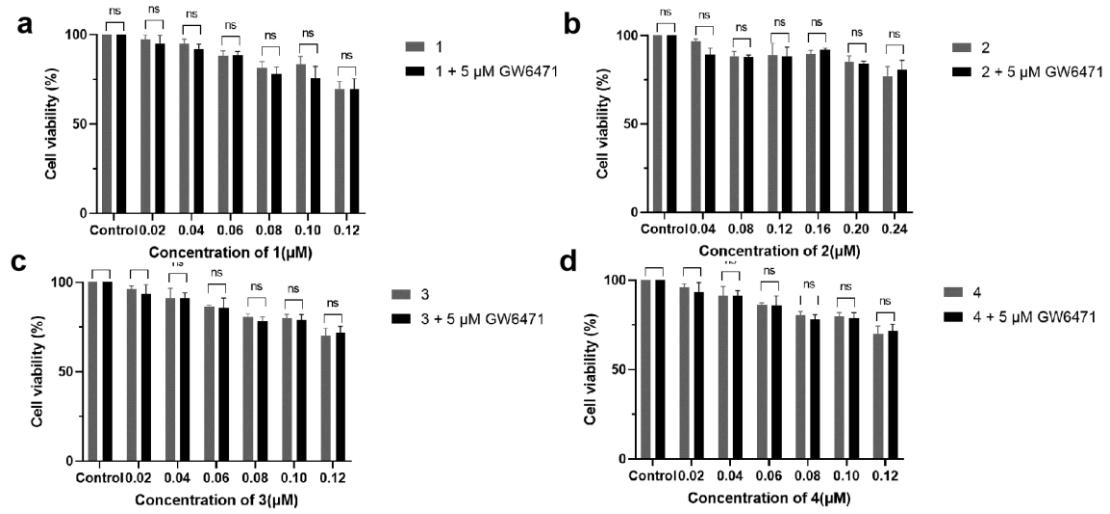


Fig. S17. Comparison of cell viability of A549 cells treated with different concentrations of compounds for 48 h.

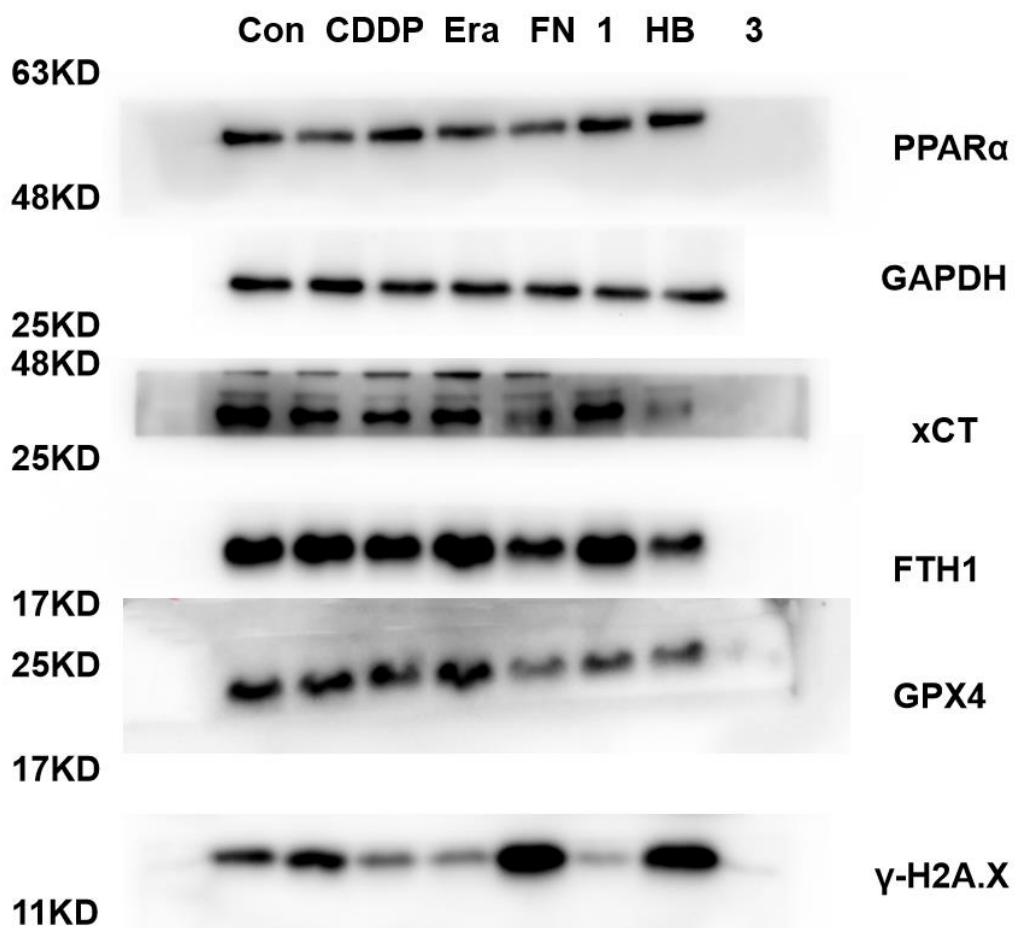


Fig. S18. Un-cropped western blotting images of Figure 8a.

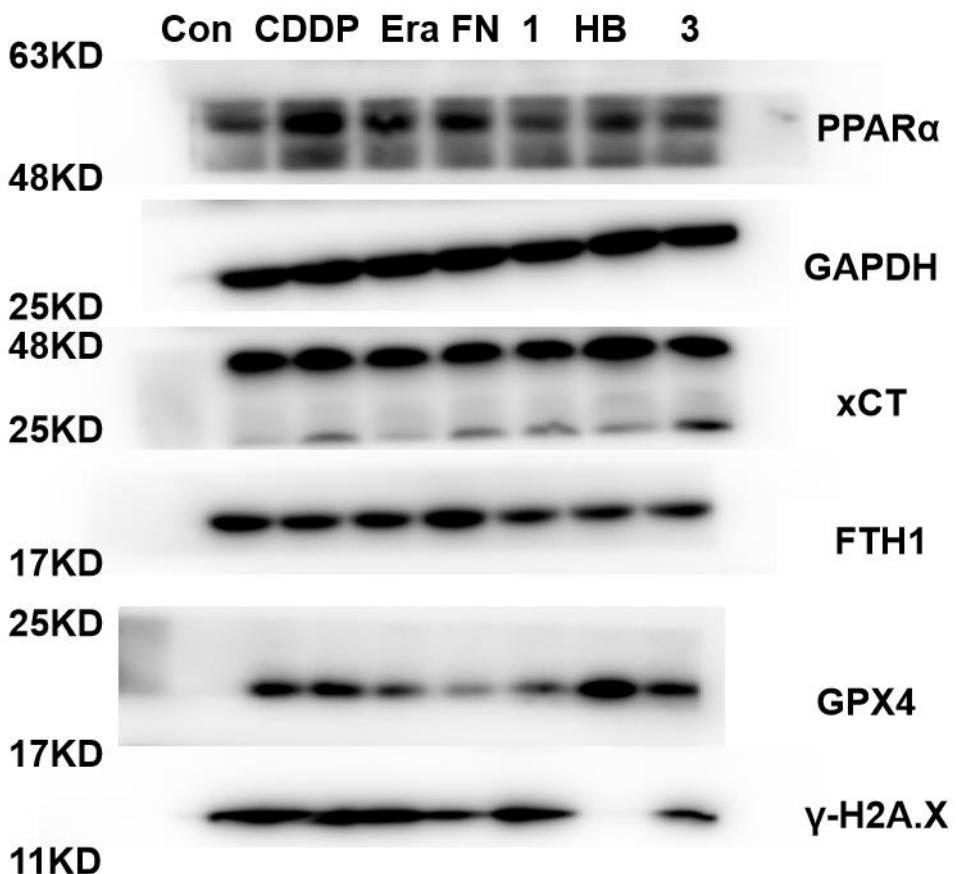


Fig. S19. Un-cropped western blotting images of Figure 8c.

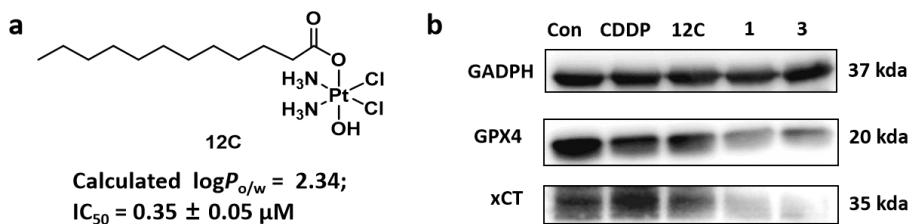


Fig. S20. (a) Chemical structure of compound **12C**. (b) Protein expression of A549 cells treated with 5 μM platinum compounds for 24 h.