Electronic Supplementary Material (ESI) for Inorganic Chemistry Frontiers.

Seratrodast Platinum(IV) Hybrids Efficiently Inhibit Cancer-related Thrombosis and Metastasis Phenotype *In Vitro* and *In Vivo*

Xue-Qing Song[†,*], Yi-Xin Ding[†], Yu-Hang Zhang, Qing Xu, Xiaofeng Xie, Yali Song, and Longfei Li*

College of Pharmacy, Key Laboratory of Pharmaceutical Quality Control of Hebei Province, Key Laboratory of Medicinal Chemistry and Molecular Diagnosis of Ministry of Education, Hebei University, Baoding 071002, Hebei, P. R. China.

*Corresponding author:

E-mail address: sxqing@hbu.edu.cn (X.-Q. Song)

E-mail address: lilongfei@hbu.edu.cn (L.L.)

[†]These authors contributed equally.

List of Contents Pages

Figures and Tables

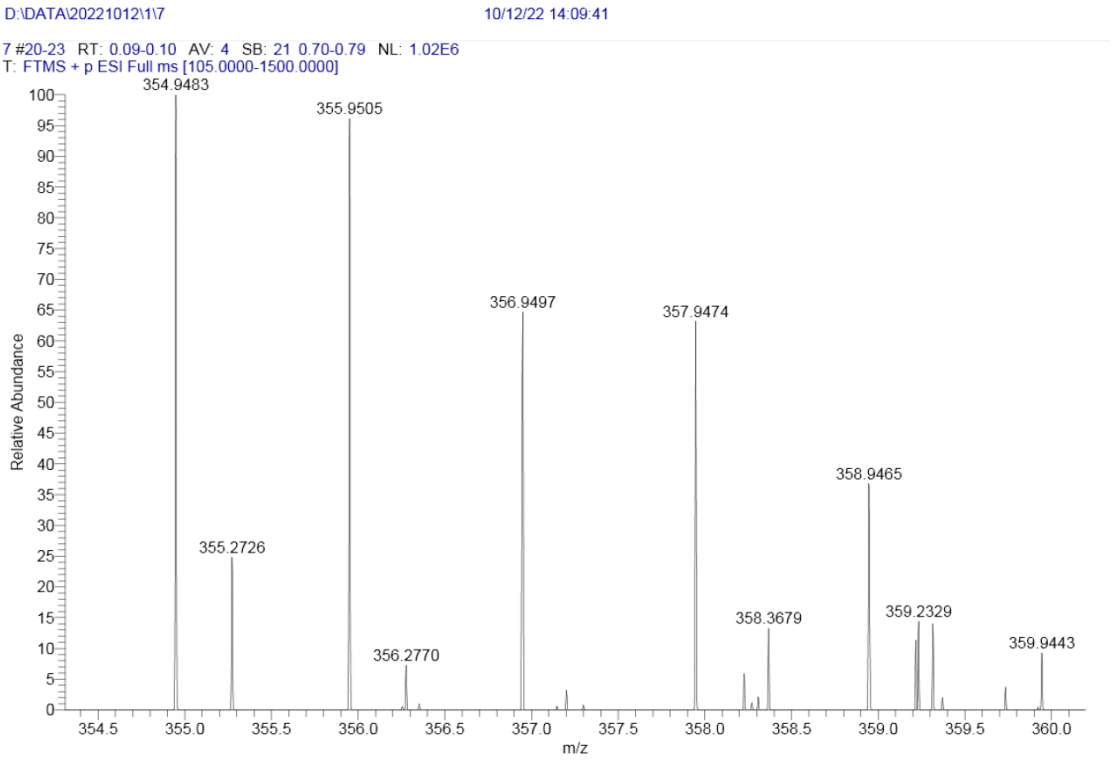


Figure S1. FTMS spectrum of **1** in methanol.

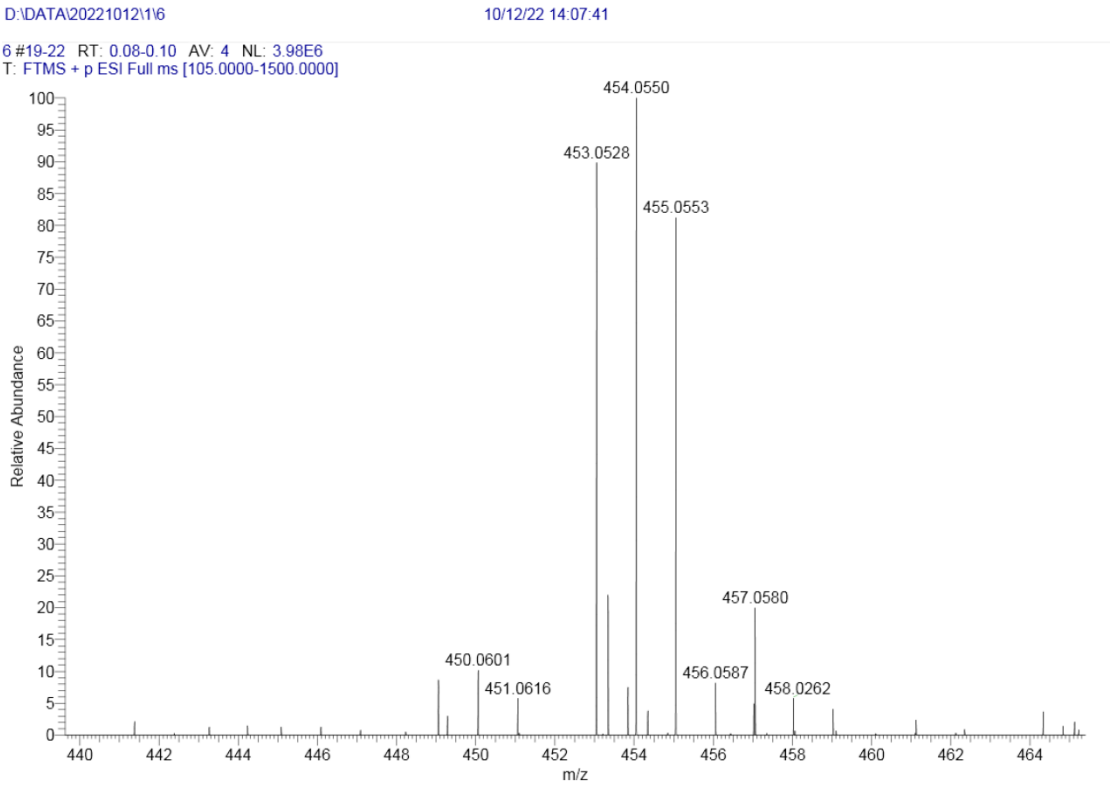


Figure S2. FTMS spectrum of **2** in methanol.

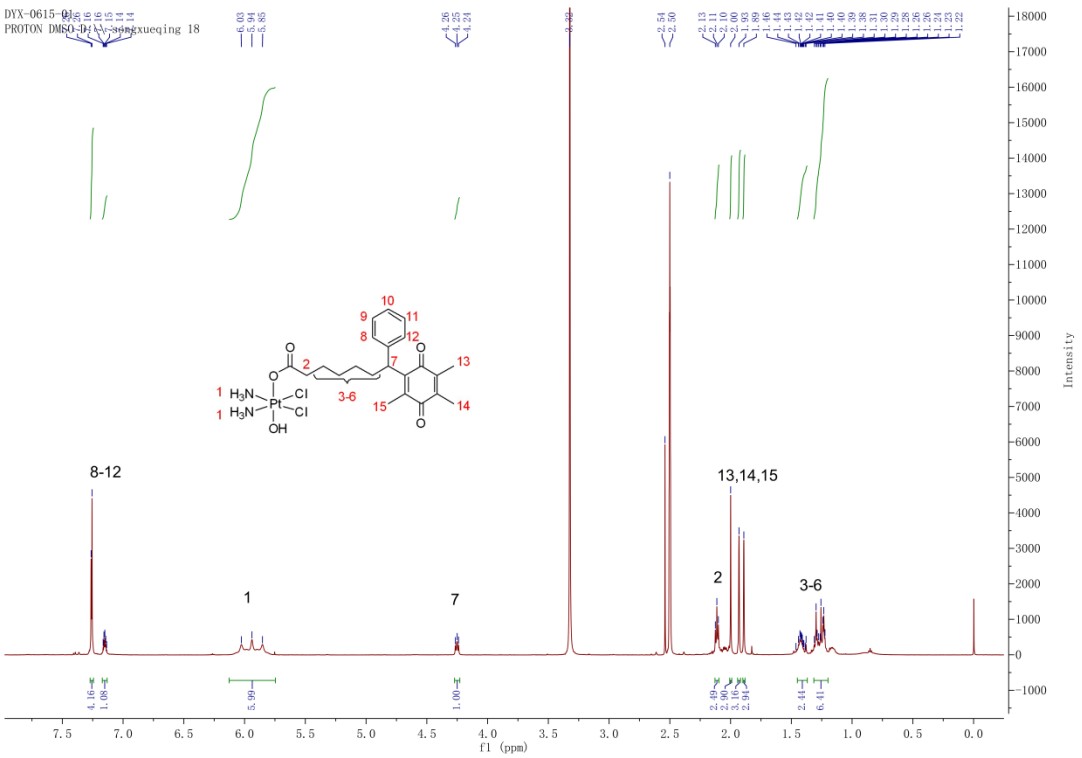


Figure S3. ^{1}H-NMR spectrum of **3** in DMSO-d_6.

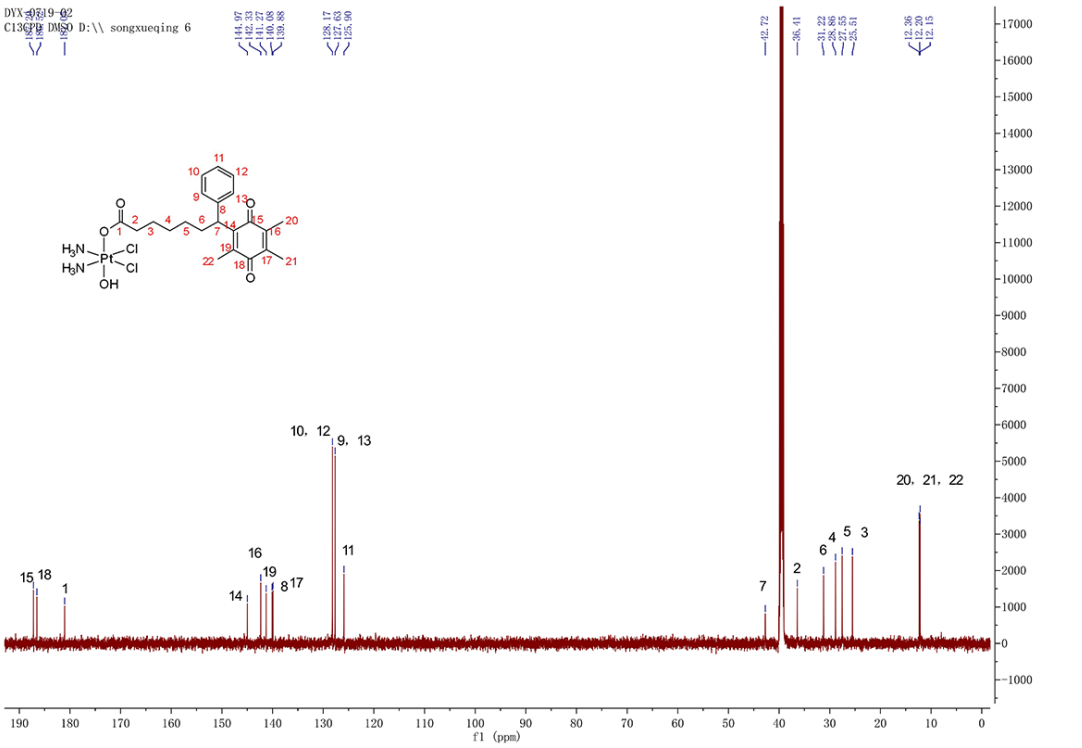
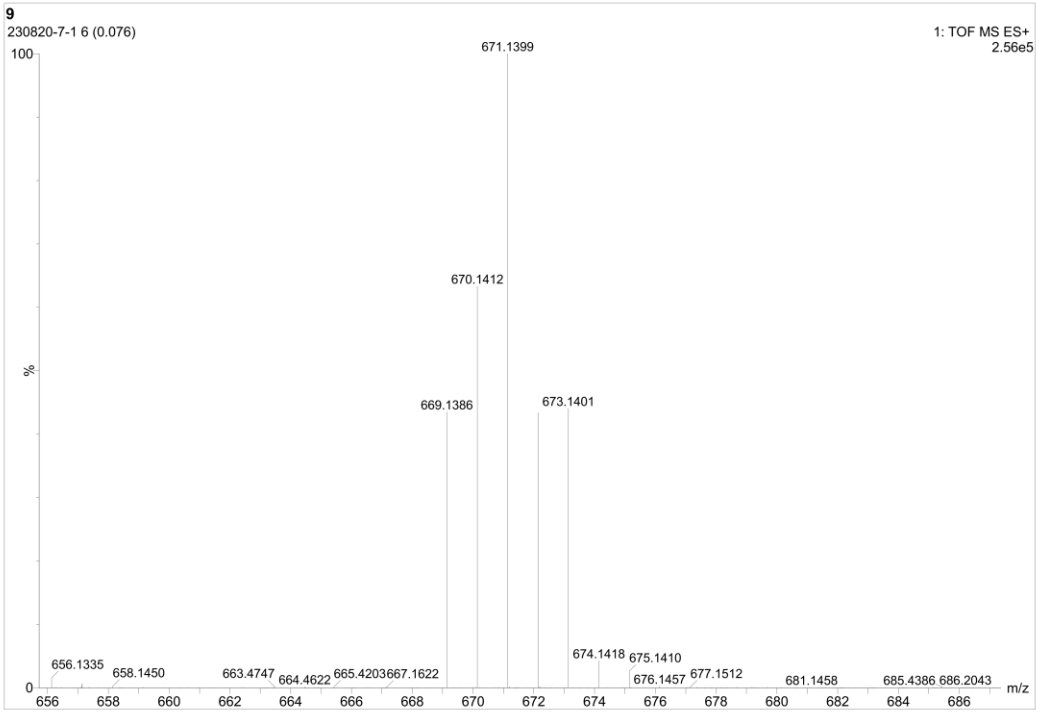
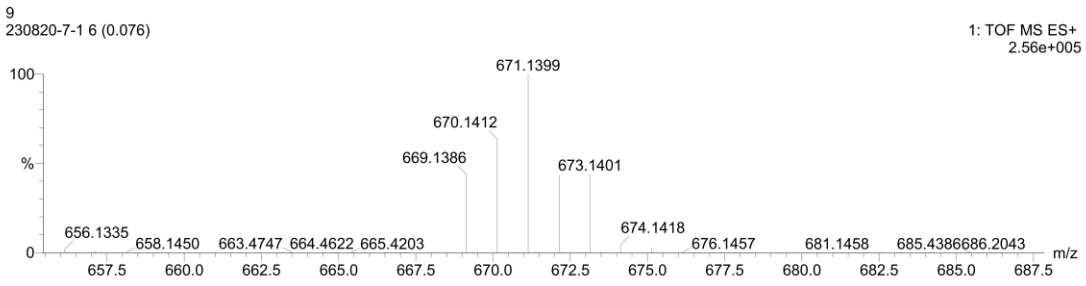


Figure S4. ^{13}C-NMR spectrum of **3** in DMSO-d_6.

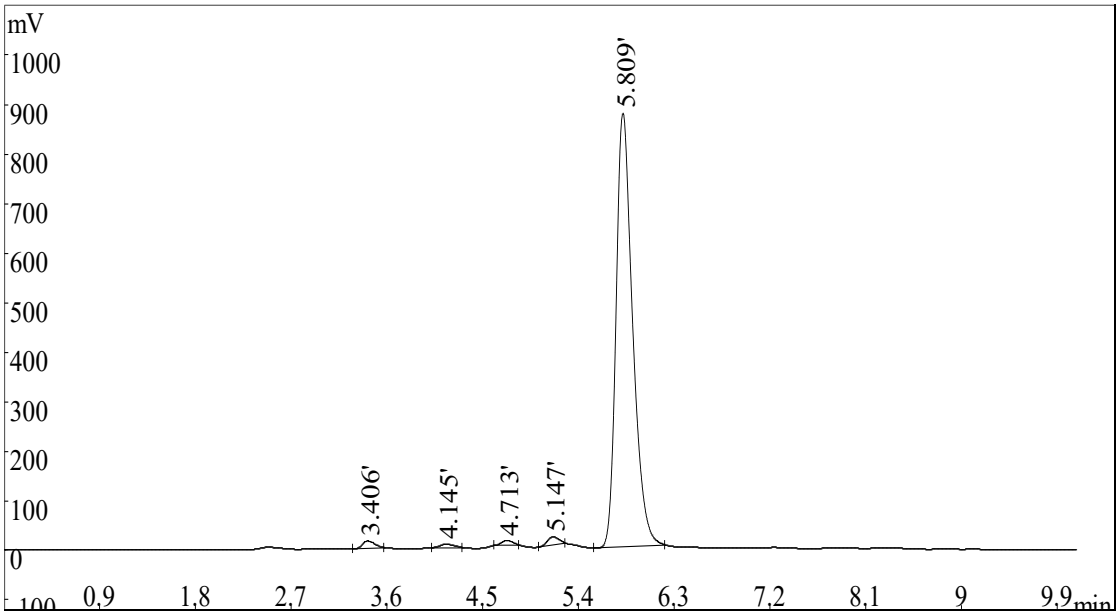


Monoisotopic Mass, Even Electron Ions
1301 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 22-22 H: 33-33 N: 0-100 O: 0-100 Cl: 1-4 Pt: 1-1



Minimum:				-1.5				
Maximum:		5.0	20.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
670.1412	670.1414	-0.2	-0.3	7.5	218.4	n/a	n/a	C22 H33 N2 O5 Cl2 Pt

Figure S5. HRMS spectrum of **3** in methanol. The measured m/z is 670.1412 and the calculated m/z is 670.1414.



No.	Retention time	Peak area	Concentration (%)
1	3.406	116590	1.23
2	4.145	60734	0.6405
3	4.713	70118	0.7395
4	5.147	122210	1.289
5	5.809	9112587	96.10

Figure S6. HPLC characterization of **3**.

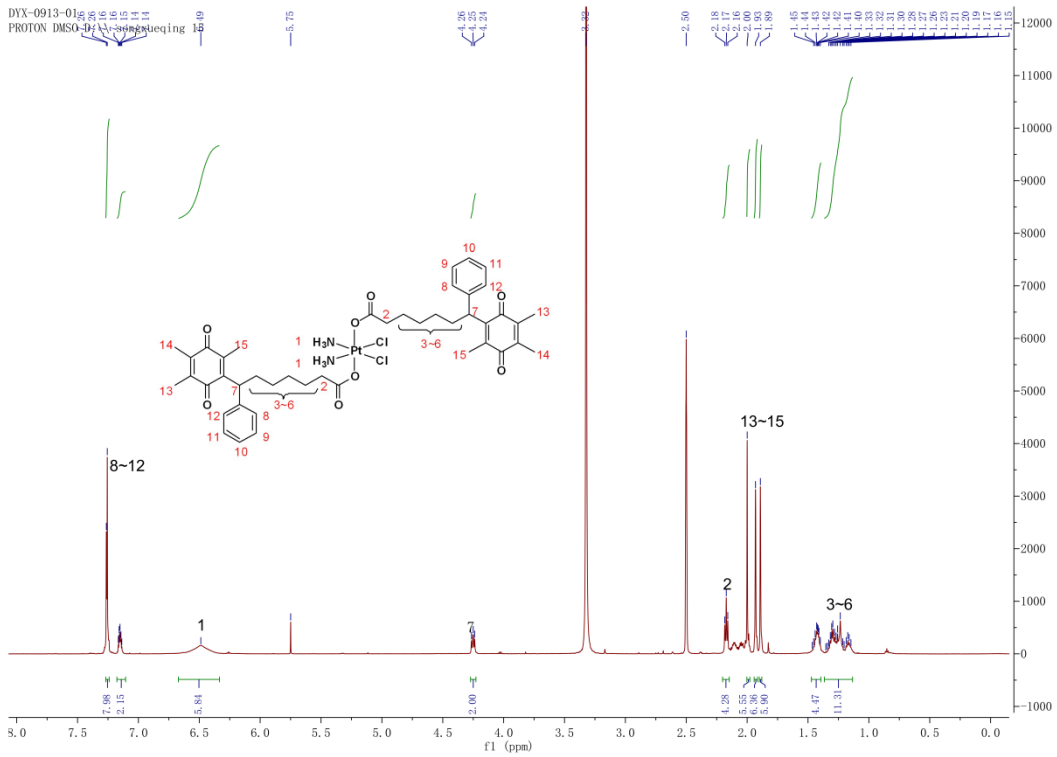


Figure S7. ^{1}H-NMR spectrum of **4** in DMSO-d_6.

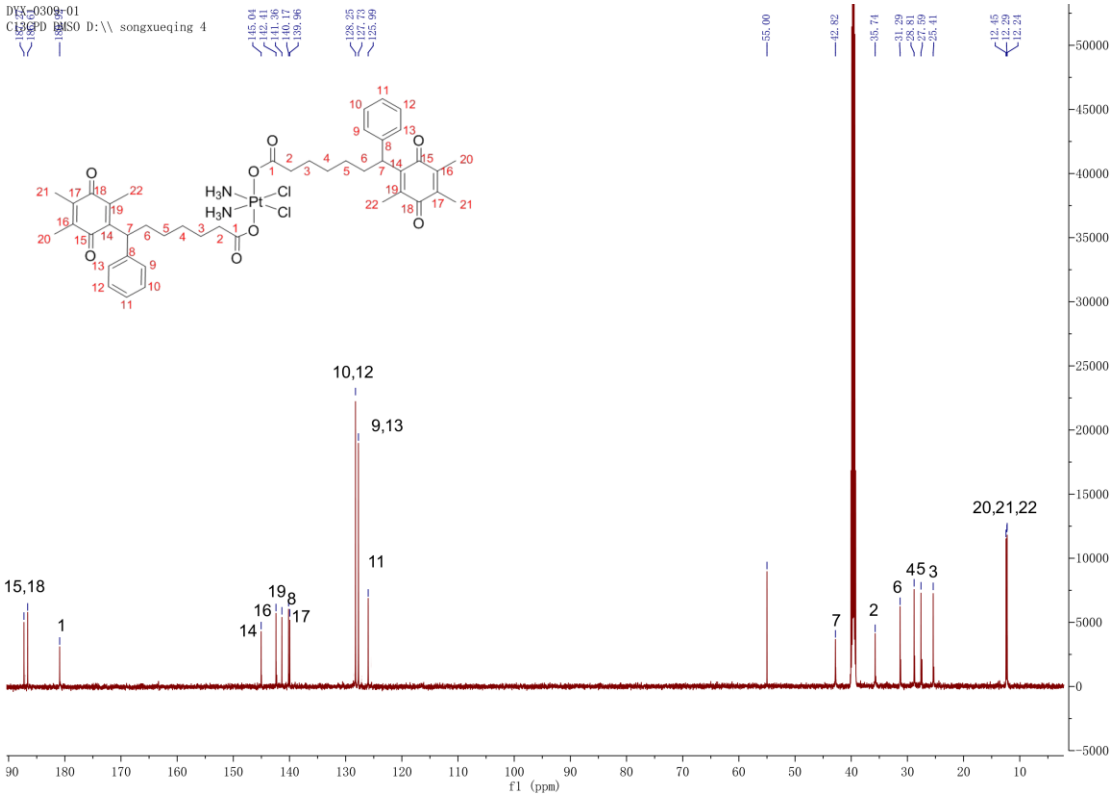
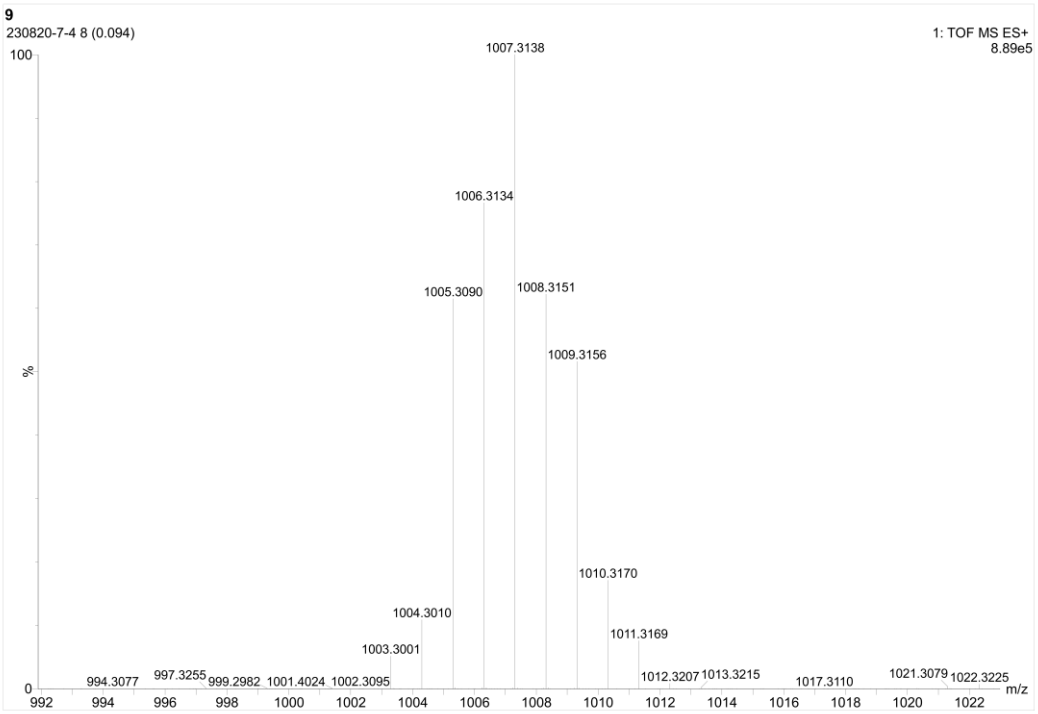


Figure S8. ^{13}C-NMR spectrum of **4** in DMSO-d_6.



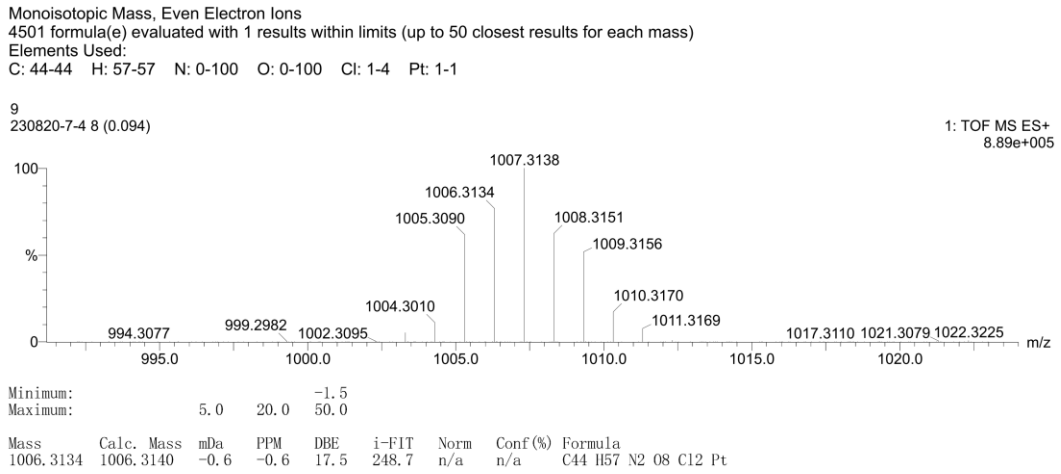
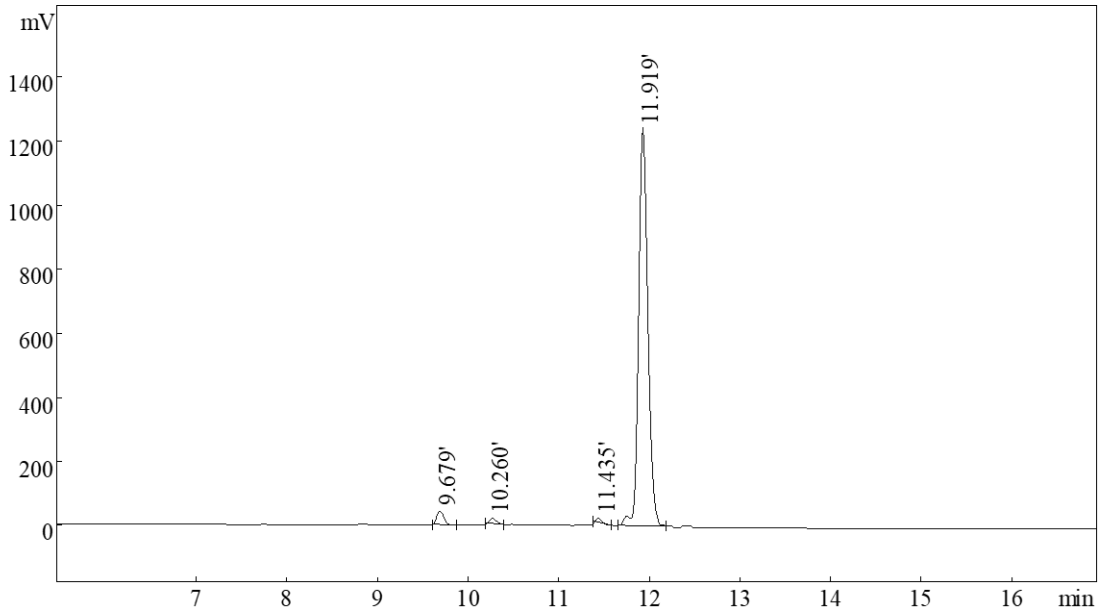


Figure S9. HRMS spectrum of compound **4** in methanol. The measured m/z is 1006.3134 and the calculated m/z is 1006.3140.



No.	Retention time	Peak area	Concentration (%)
1	9.679	248113	2.667
2	10.260	102695	1.104
3	11.435	76567	0.8231
4	11.919	8874211	95.41

Figure S10. HPLC characterization of **4**.

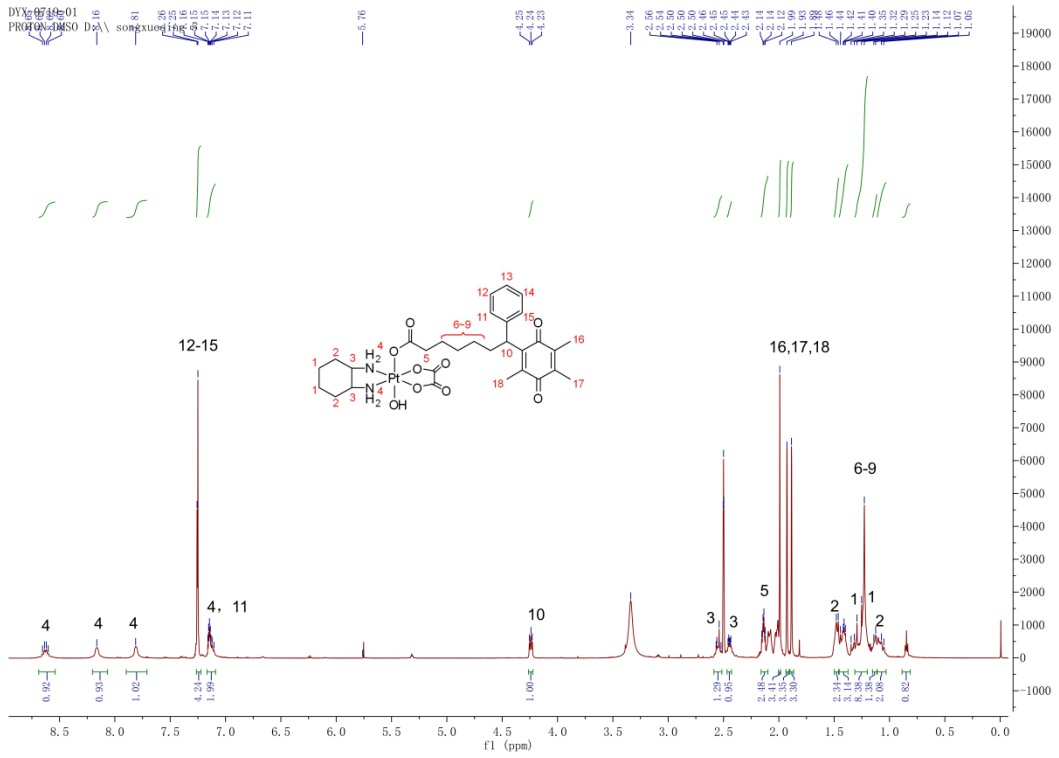


Figure S11. ^{1}H-NMR spectrum of **5** in DMSO-d_6.

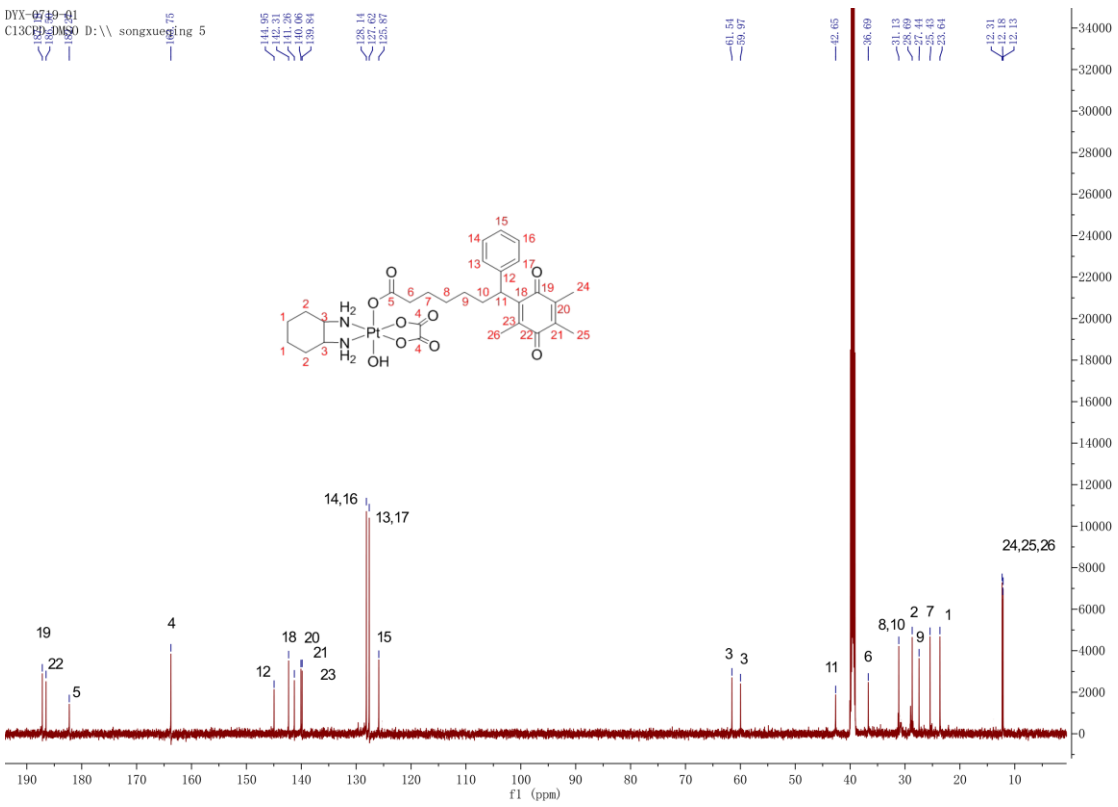
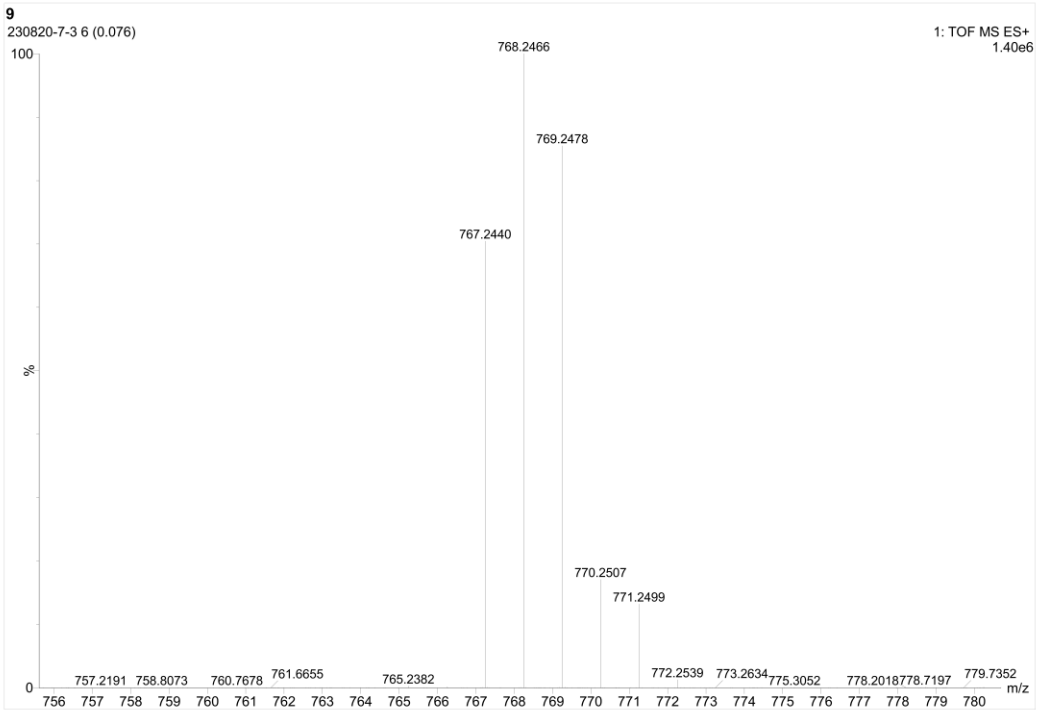
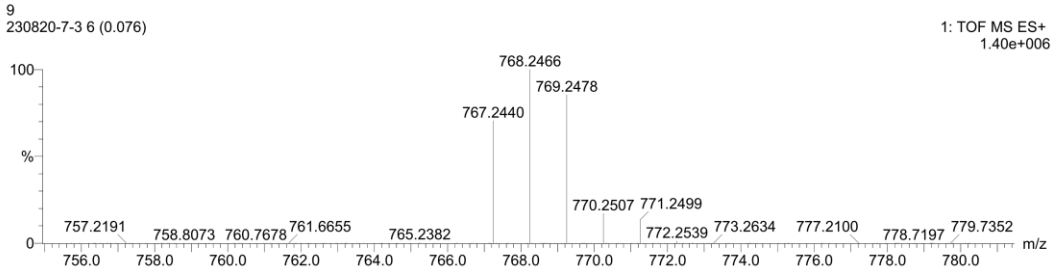


Figure S12. ^{13}C-NMR spectrum of **5** in DMSO-d_6.

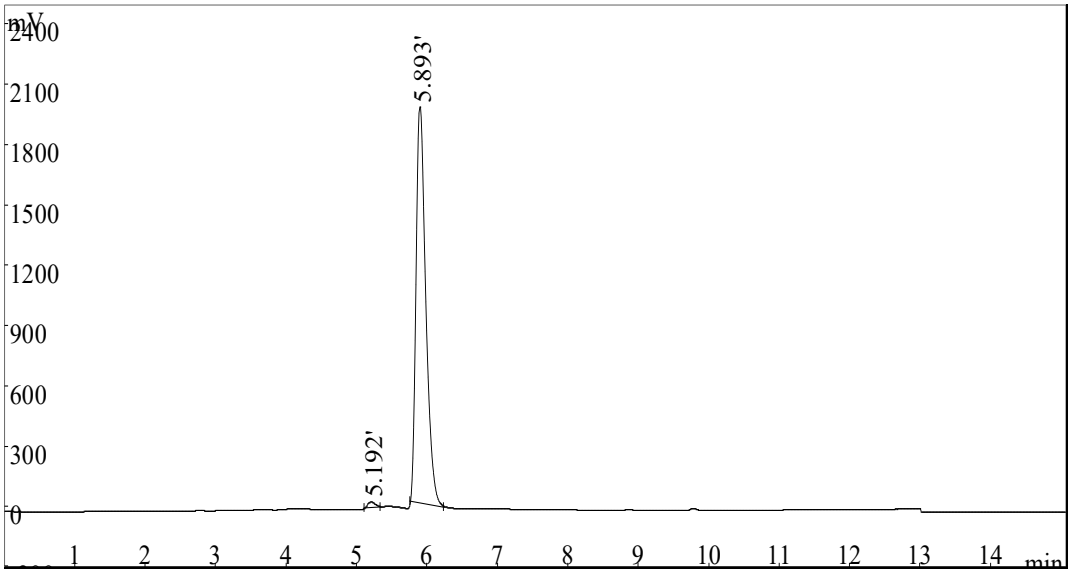


Monoisotopic Mass, Even Electron Ions
683 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 30-30 H: 41-41 N: 0-100 O: 0-100 Pt: 1-1



Minimum:				-1.5				
Maximum:		5.0	20.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
768.2466	768.2460	0.6	0.8	12.5	313.2	n/a	n/a	C30 H41 N2 O9 Pt

Figure S13. HRMS spectrum of **5** in methanol. The measured m/z is 768.2466 and the calculated m/z is 768.2460.



No.	Retention time	Peak area	Concentration (%)
1	5.192	186190	1.039
2	5.893	17739307	98.96

Figure S14. HPLC characterization of **5**.

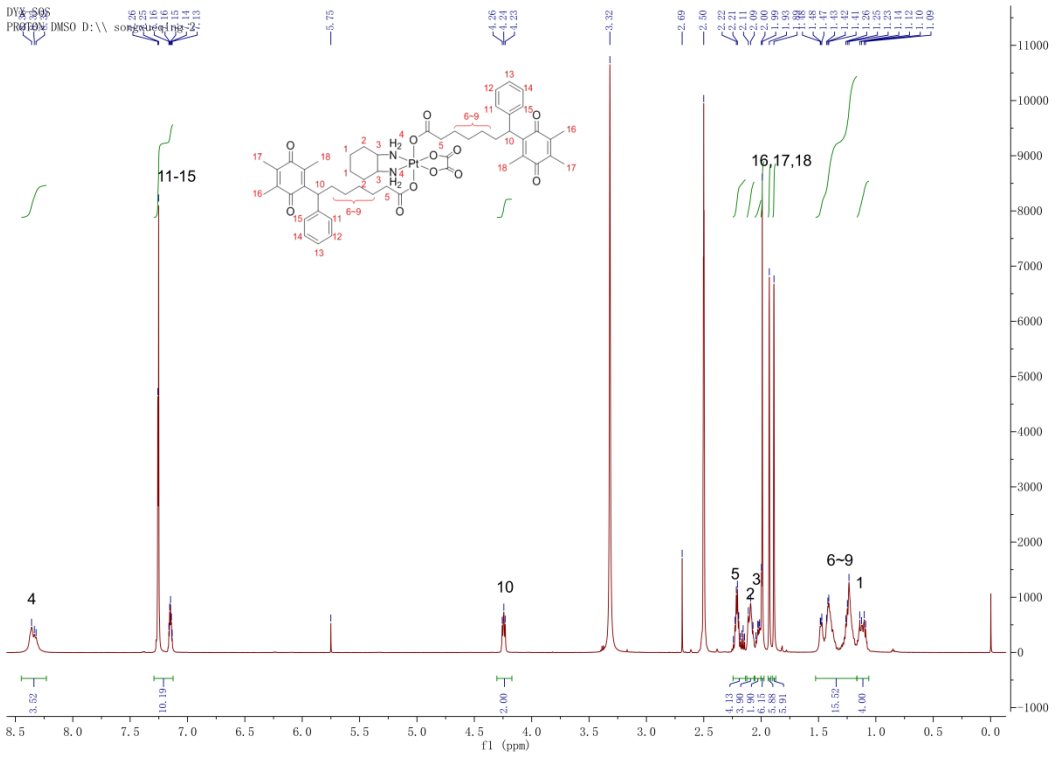


Figure S15. ^{1}H-NMR spectrum of **6** in DMSO-d_6.

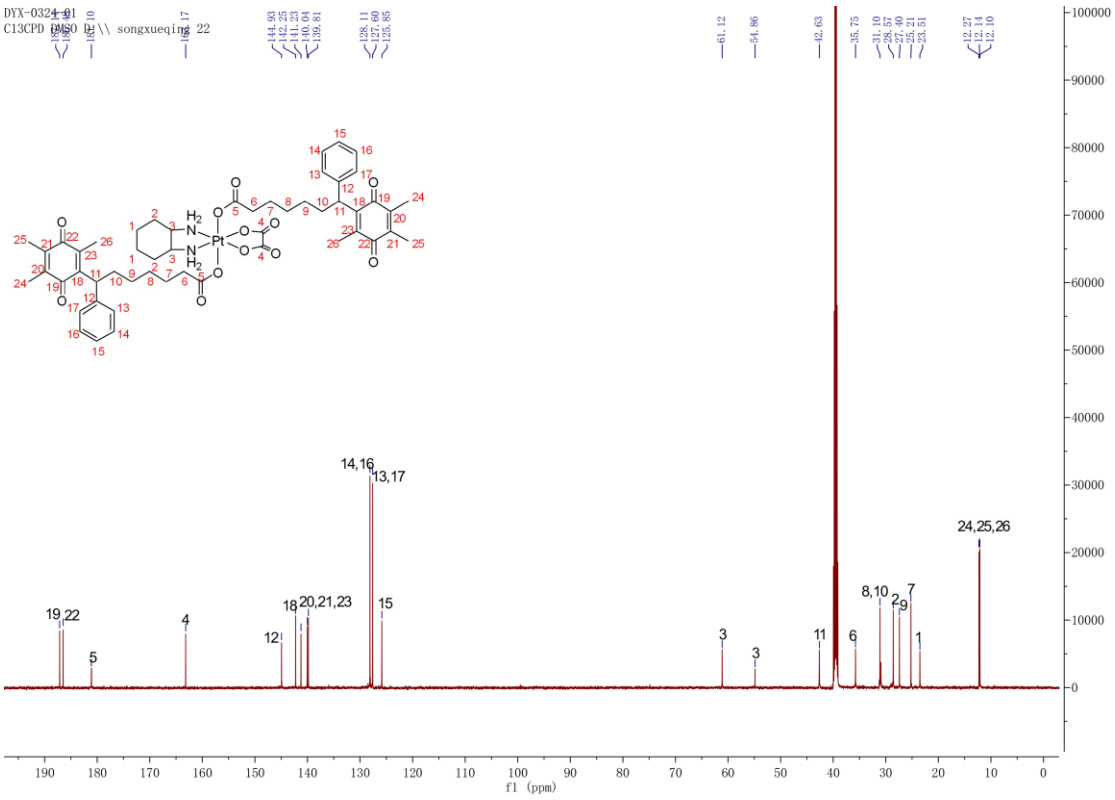
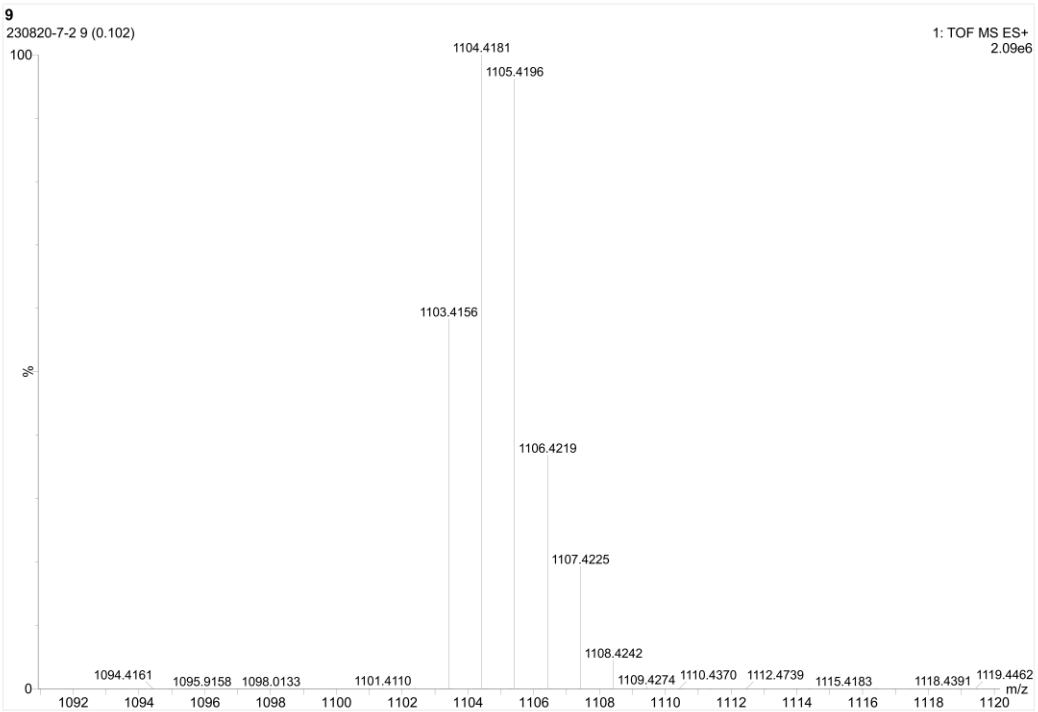


Figure S16. ^{13}C-NMR spectrum of **6** in DMSO-d_6.



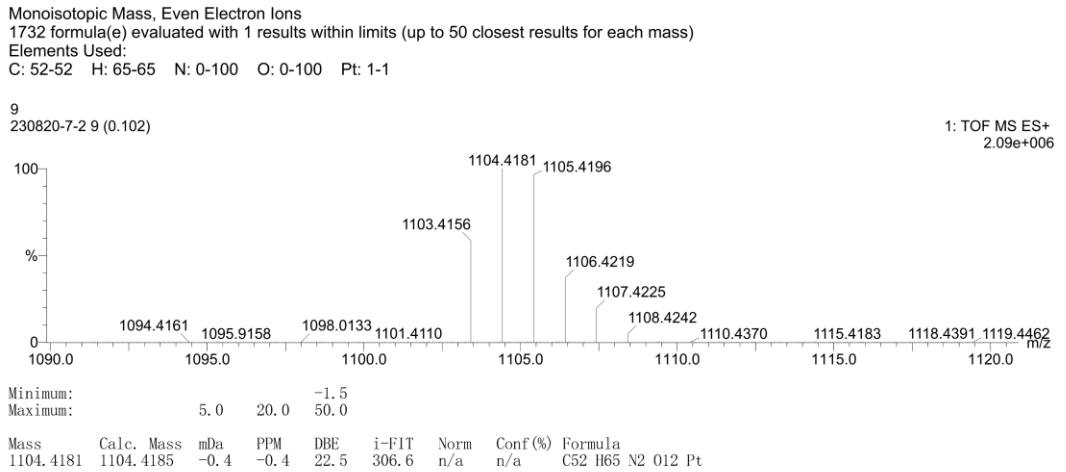
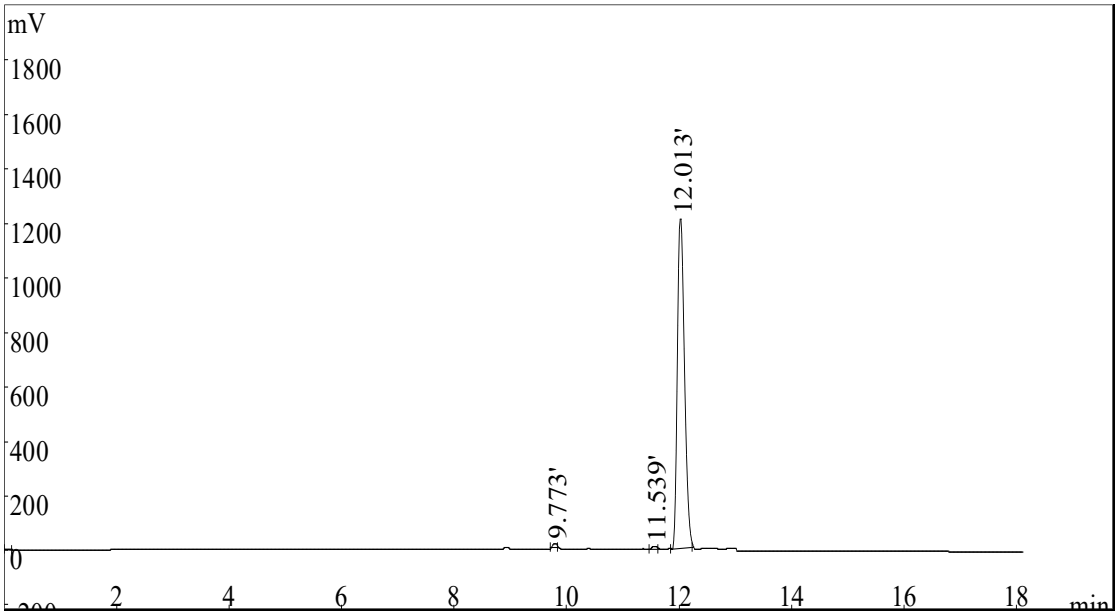


Figure S17. HRMS spectrum of **6** in methanol. The measured m/z is 1104.4181 and the calculated m/z is 1104.4185.



No.	Retention time	Peak area	Concentration (%)
1	9.773	74619	0.753
2	11.539	60322	0.6087
3	12.013	9774331	98.64

Figure S18. HPLC characterization of **6**.

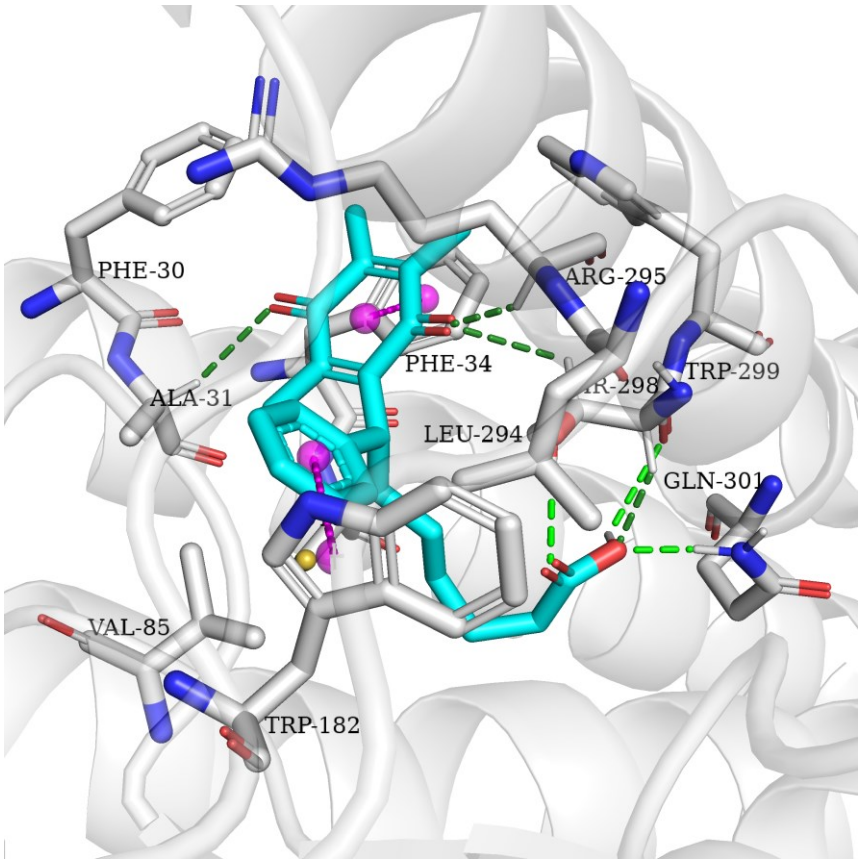


Figure S19. The binding modes of SRT with TXA2R. The hydrogen interactions are in green dashed lines, the carbon hydrogen interactions are in forest dashed lines, and the Pi−Pi interactions and Pi−Cation interactions are in magenta dashed line. All the hydrogens are omitted except that on the heavy atoms that can form hydrogen bond interactions. The hydrophobic interactions are not presented.

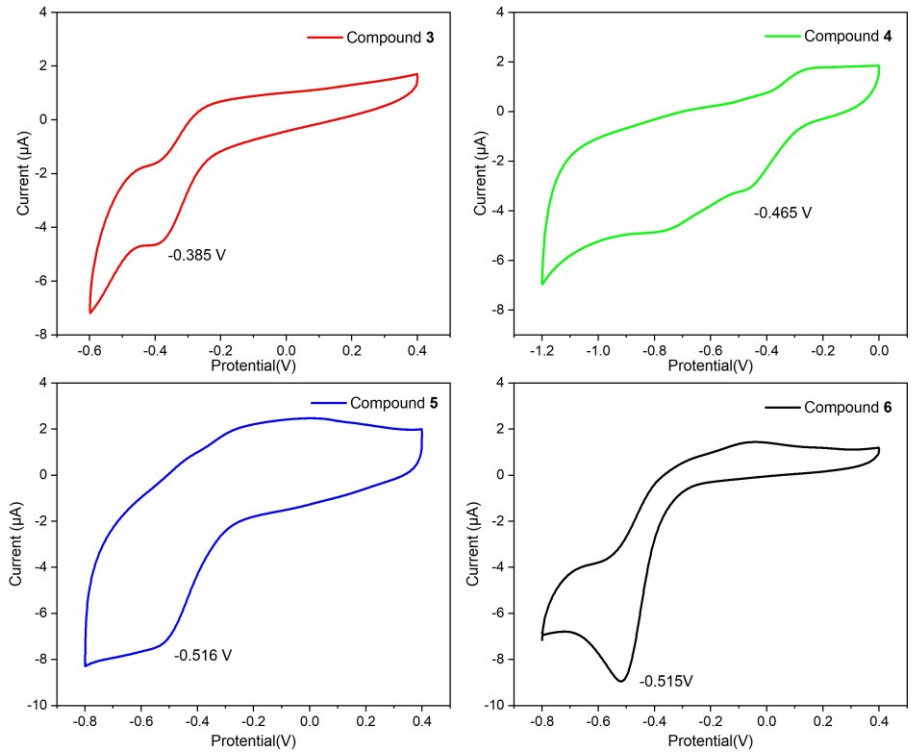


Figure S20. Cyclic voltammograms of Pt(IV) complexes **3**–**6** recorded at a glassy carbon electrode in PBS buffer (DMF : PBS = 1:20, pH = 7.4) containing 0.1 M KCl as supporting electrolyte and 0.1 mM Pt(IV) complex.

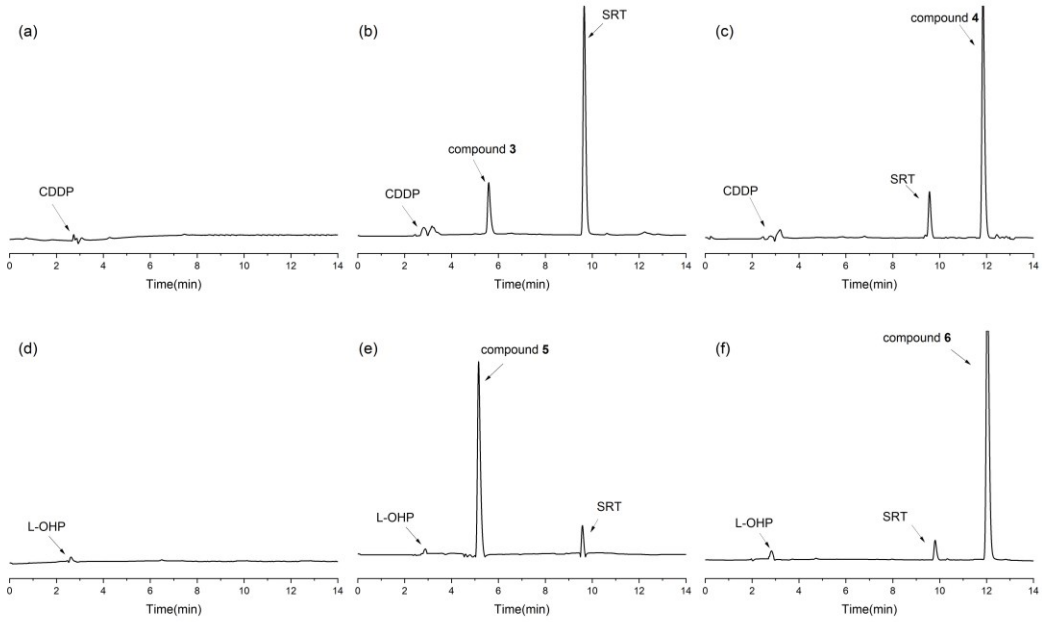


Figure S21. The HPLC of CDDP (a) and L-OHP (d) in DMSO. The reduction of compounds **3–6** with GSH in H_2O at 37°C for 24 h in dark. (b) Compound **3**. (c) Compound **4**. (e) Compound **5**. (f) Compound **6**.

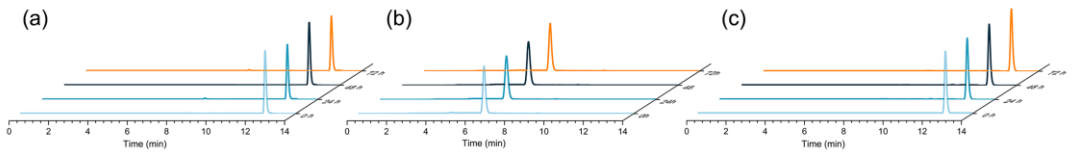


Figure S22. Stability of compounds **4**–**6** at 37°C in PBS/DMF (3:1, v/v, pH 7.4) for 0, 6, 12, 24 and 48 h in the dark. (a) Stability of compound **4**. (b) Stability of compound **5**. (c) Stability of compound **6**.

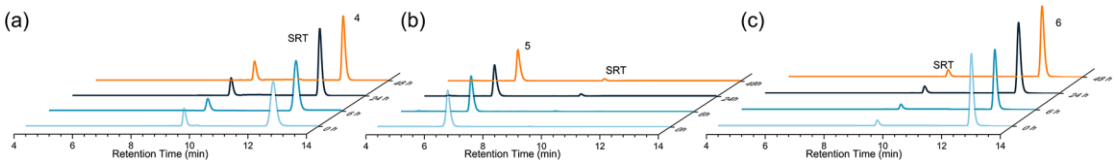


Figure S23. Reduction of compounds **4–6** with GSH in PBS at 37°C for 0, 6, 24 and 48 h in the dark. (a) Reduction of compound **4**. (b) Reduction of compound **5**. (c) Reduction of compound **6**.

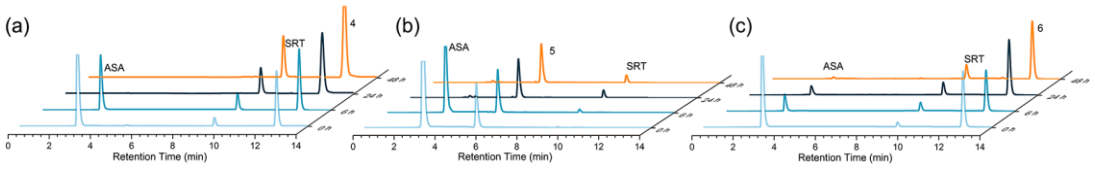


Figure S24. Reduction of compounds **4–6** with AsA in PBS at 37°C for 0, 6, 24 and 48 h in the dark. (a) Reduction of compound **4**. (b) Reduction of compound **5**. (c) Reduction of compound **6**.

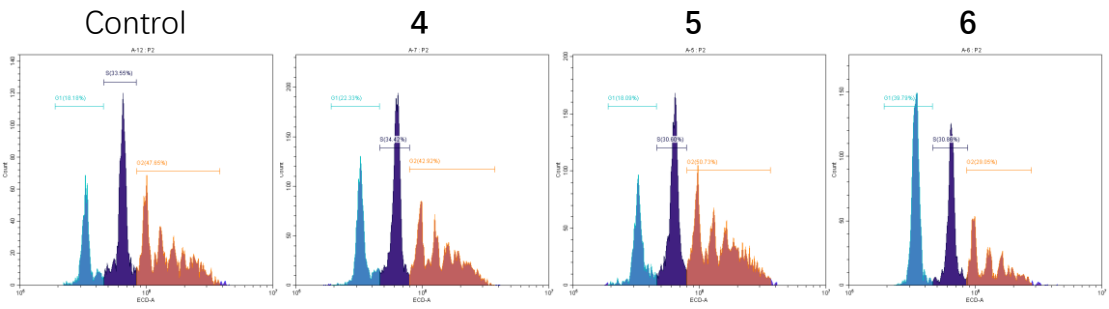


Figure S25. DNA contents were detected by flow cytometry.

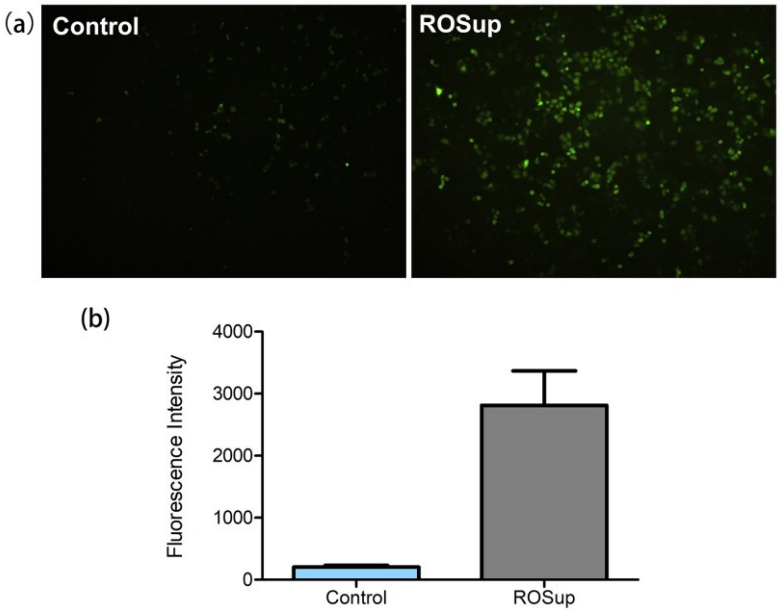


Figure S26. (a) Fluorescent images of ROS detected by DFCH-DA probe in control and ROSup. (b) Statistics of fluorescence intensity.

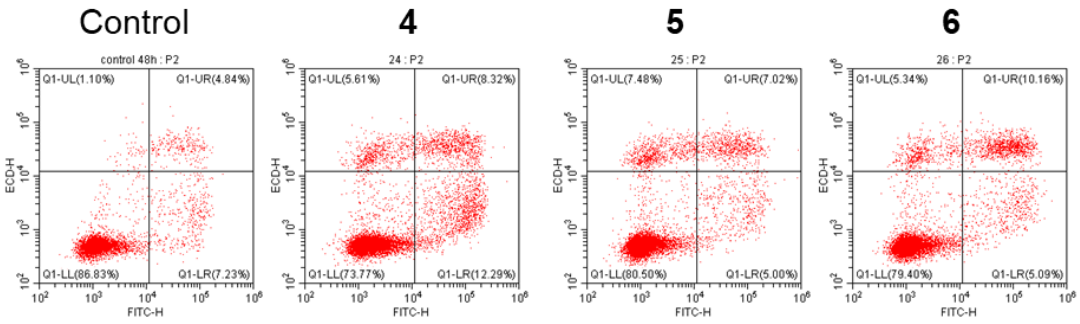


Figure S27. Annexin V-FITC/PI double staining detected by flow cytometry (all 5 μM) for 48 h.

Table S1. Effects of compounds on clotting time.

Compounds	Dose (mg/mL)	Clotting time (s)
PBS	-	214.00 ± 7.94
ADP	4	174.00 ± 22.34
Ozagrel	4	331.3 ± 30.67**
SRT	4	253.00 ± 39.36
CDDP	4	233.67 ± 44.74
Compound **3**-I	4	538.00 ± 20.42
Compound **3**-II	0.4	308.00 ± 53.11
Compound **3**-III	0.04	241.33 ± 26.35