

## Exploring substitution effects on the potential dominant conformations of NBF derivatives leading to functional conversion at the mu opioid receptor

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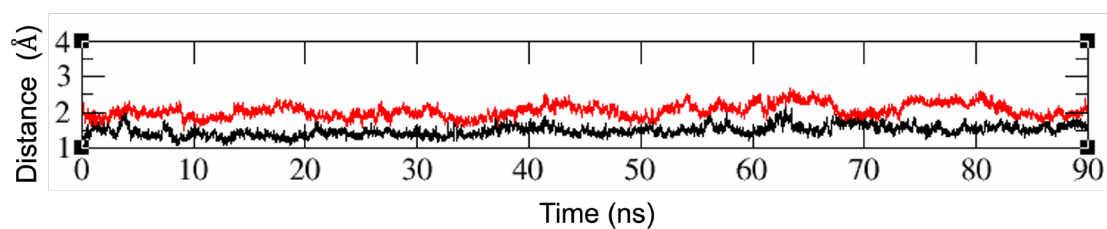


Figure S1. Root Mean Square Deviations (RMSD) of backbone atoms of the protein during the MD simulation; red represents Compound **3** bound to the inactive MOR, and black represents Compound **9** bound to the active MOR.

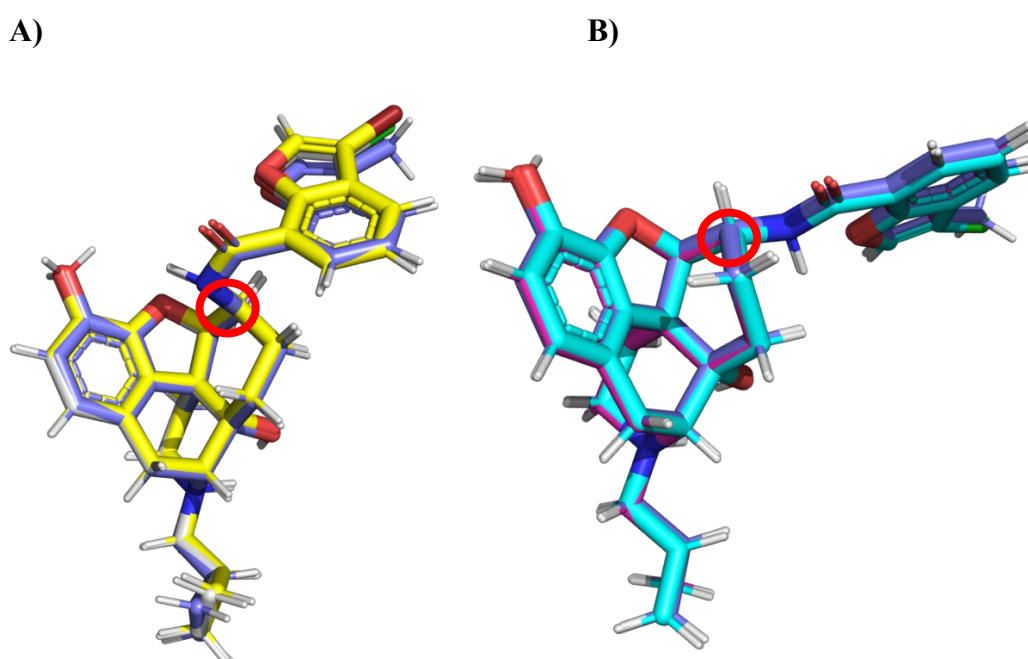
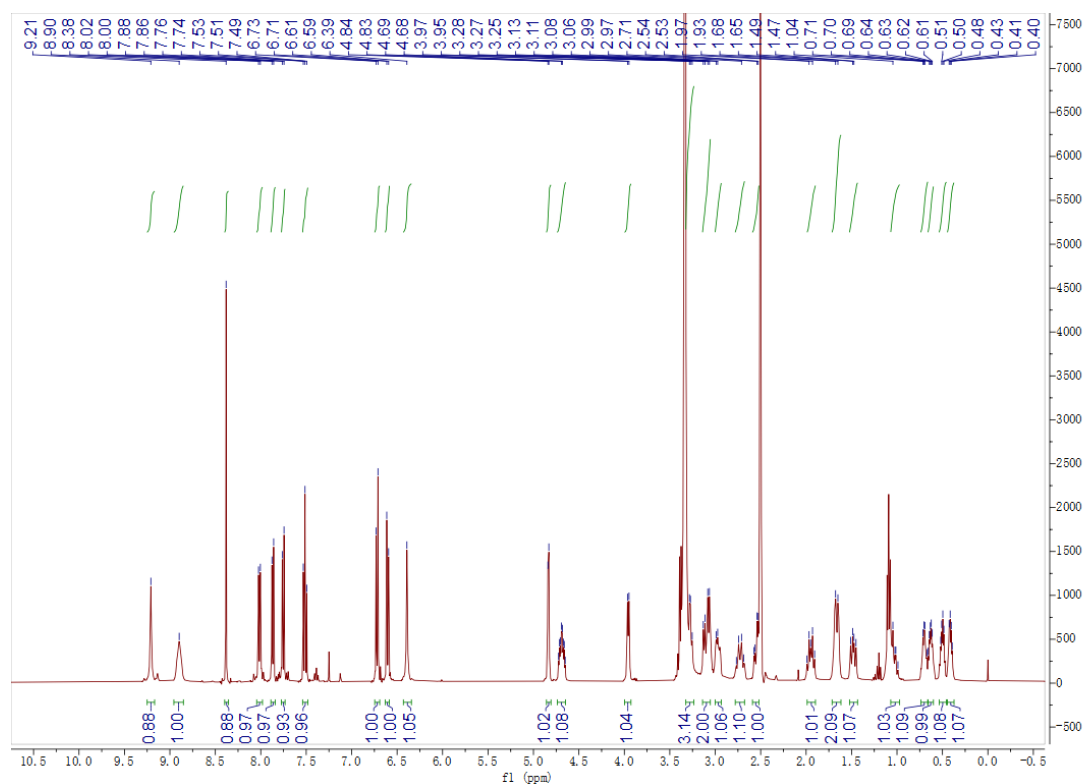


Figure S2. 3D structures of chair conformation of compounds 2,3,4 and boat conformation of compounds 8,9,10 at the C6. A) compounds 2,3,4 showing the chair conformation of C6 B) compounds 8,9,10 after docking showing the boat conformation at the C6. Carbon atoms: **2**, **8**, (Magenta); **3**, **9**, (cyan); **4**, **10** (blue); oxygen atoms (red); nitrogen atoms (blue).

Compound **2**



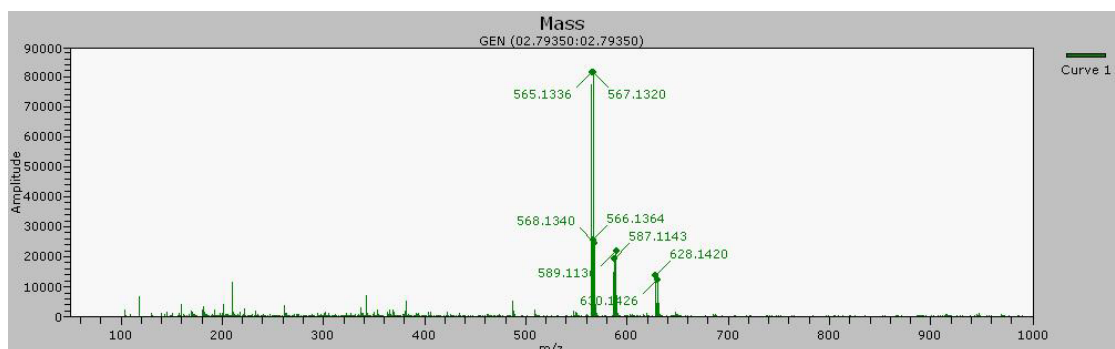
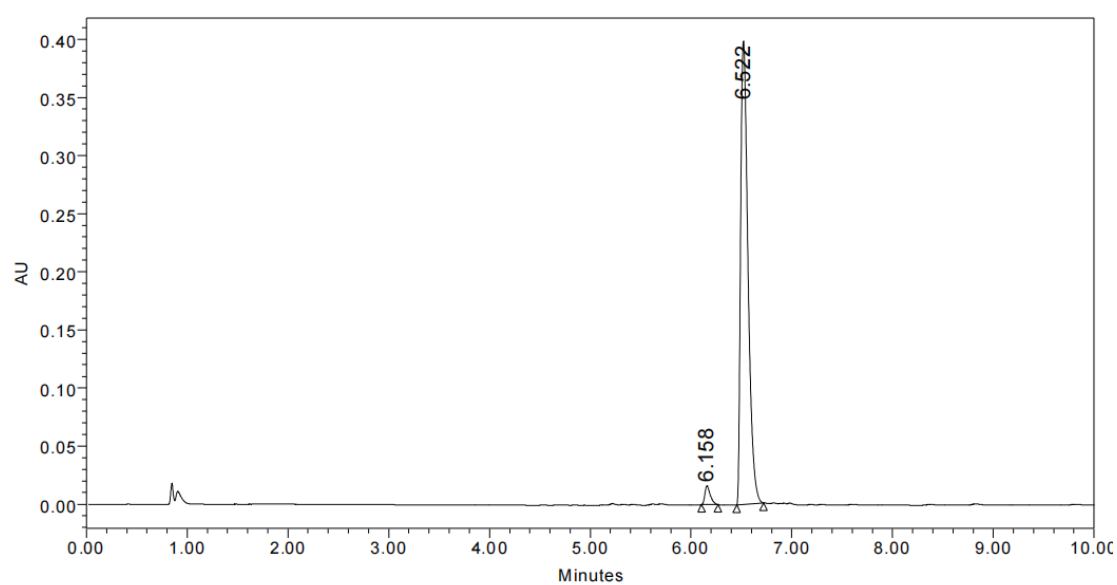


Figure S5. HRMS



	RT	Area	% Area	Height
1	6.158	60094	2.90	16157
2	6.522	2014323	97.10	398472

Figure S6. HPLC

Compound **3**

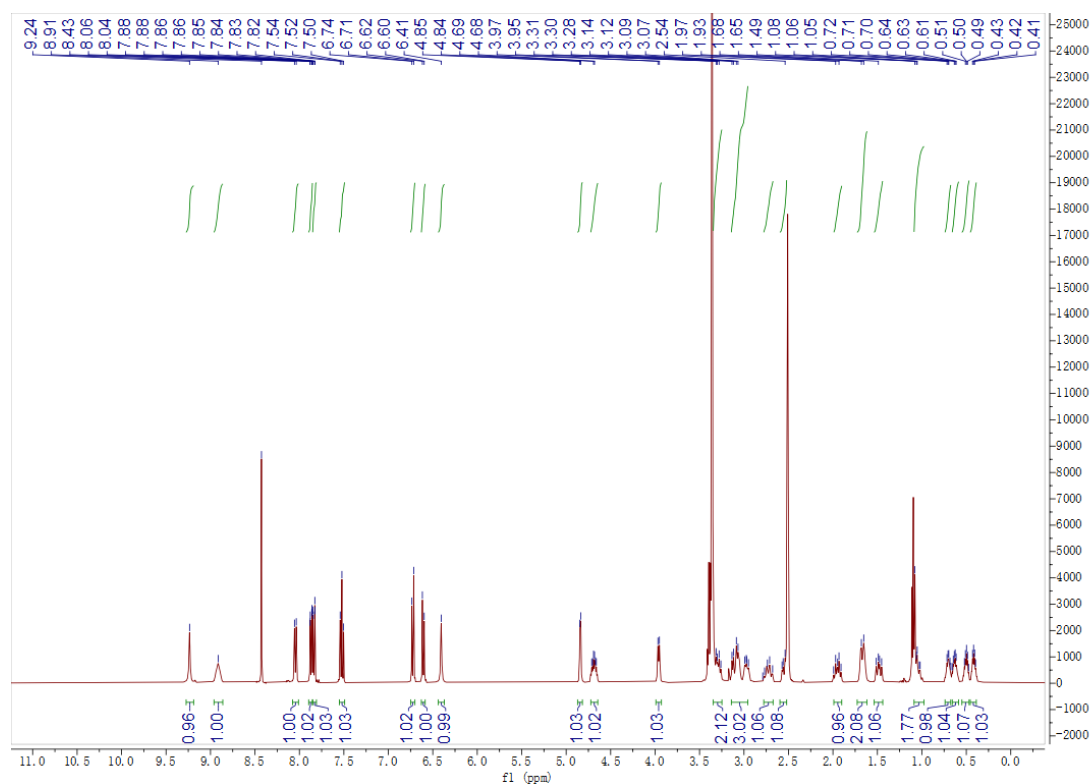


Figure S7. <sup>1</sup>H NMR (400M HZ, DMSO-*d*<sub>6</sub>)

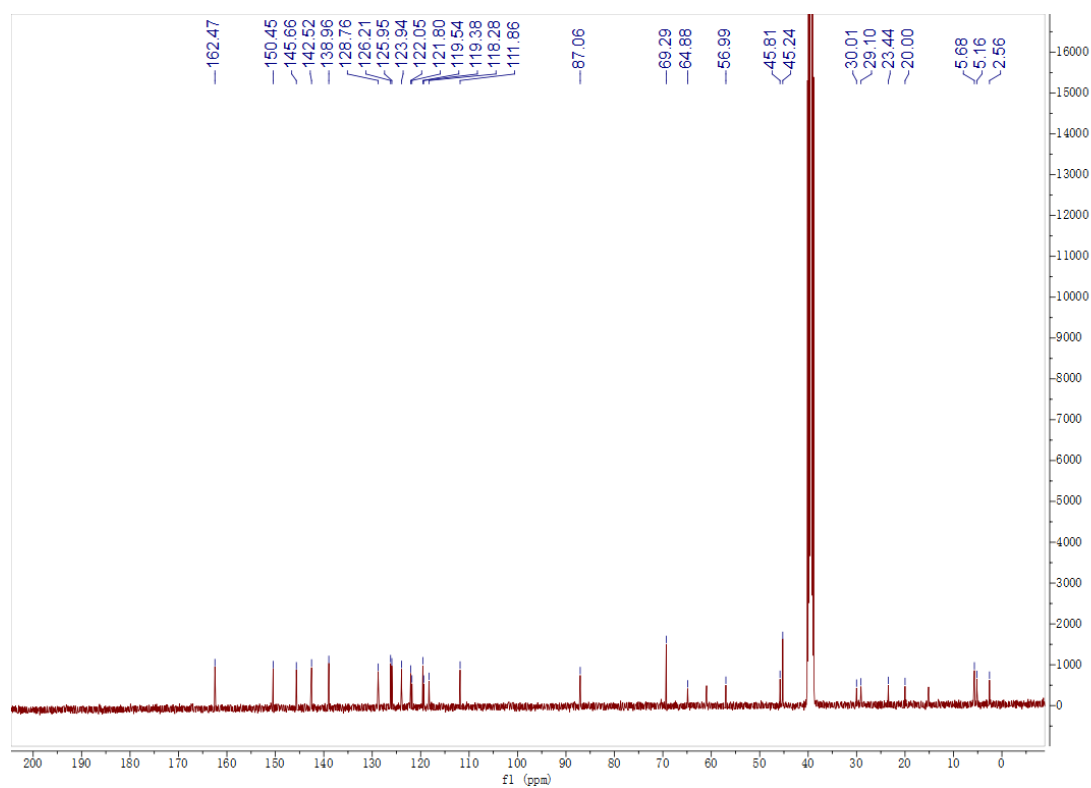


Figure S8. <sup>13</sup>C NMR (100M HZ, DMSO-*d*<sub>6</sub>)

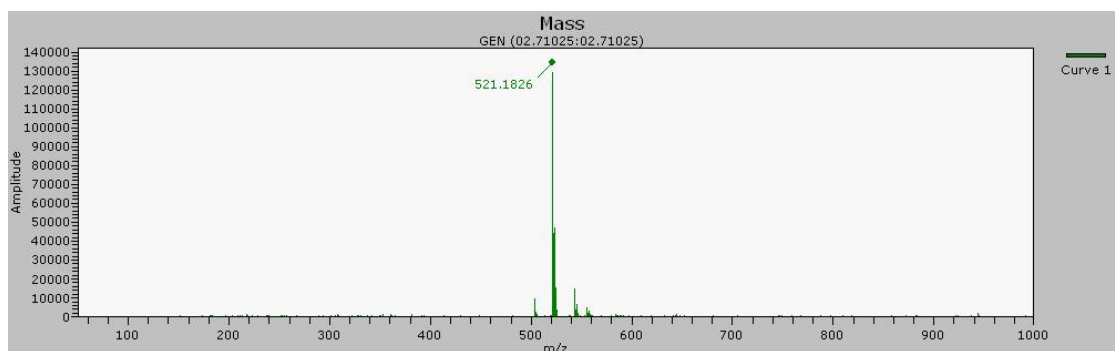
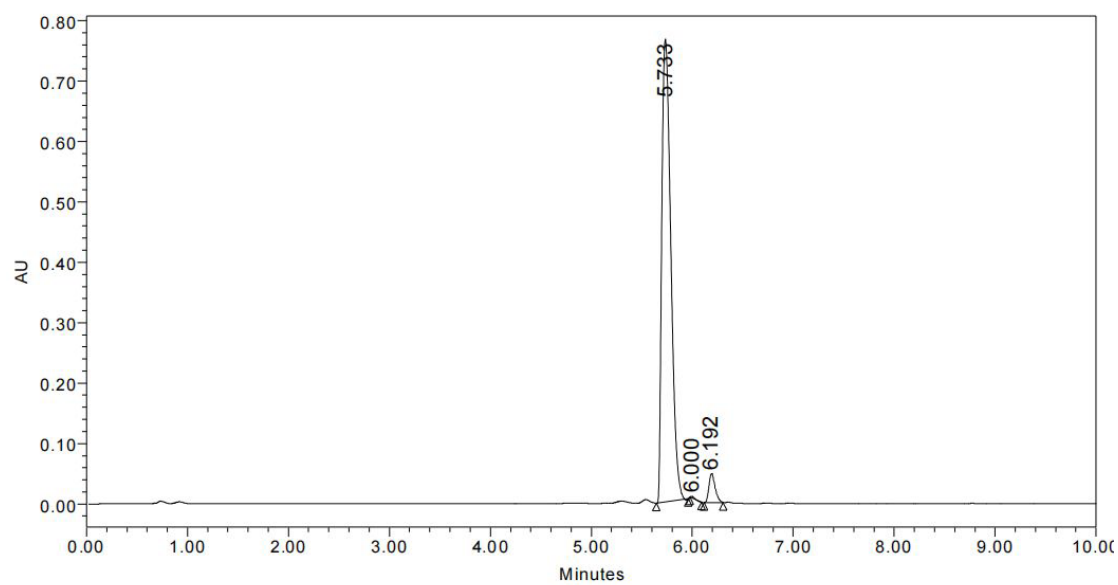


Figure S9. HRMS



	RT	Area	% Area	Height
1	5.733	4721477	95.65	765719
2	6.000	8826	0.18	3176
3	6.192	206088	4.17	48273

Figure S10. HPLC

Compound 4

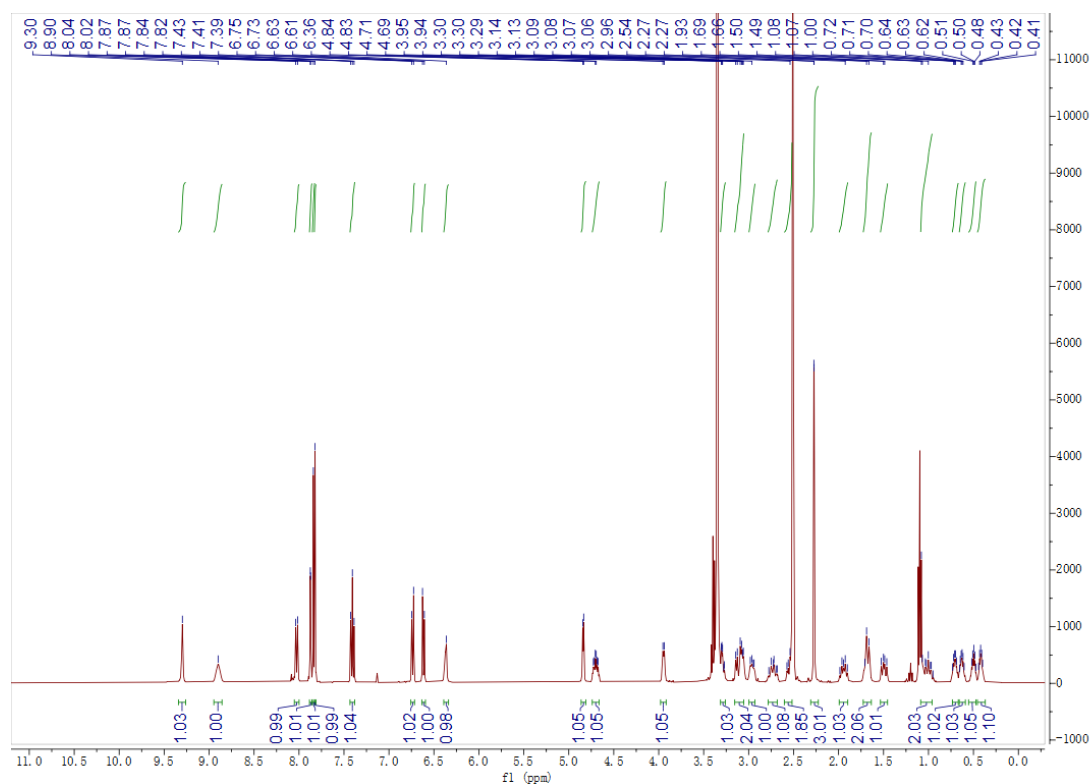


Figure S11. <sup>1</sup>H NMR (400M HZ, DMSO-*d*<sub>6</sub>)

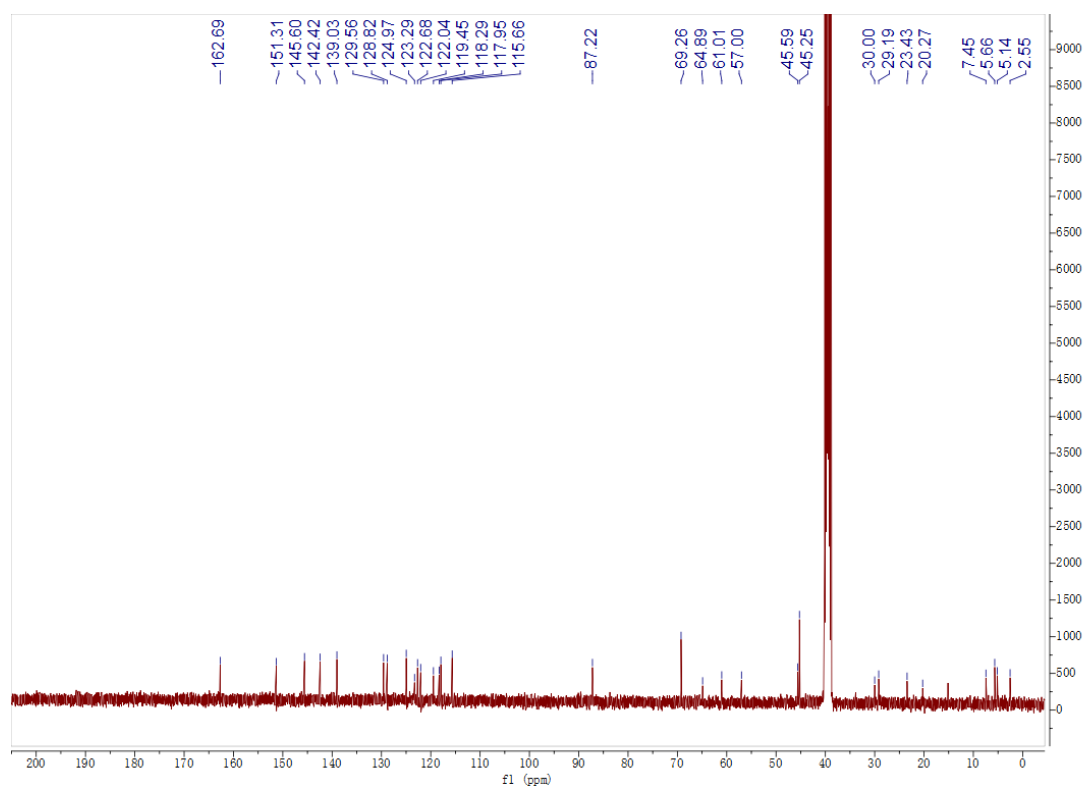


Figure S12. <sup>13</sup>C NMR (100M HZ, DMSO-*d*<sub>6</sub>)

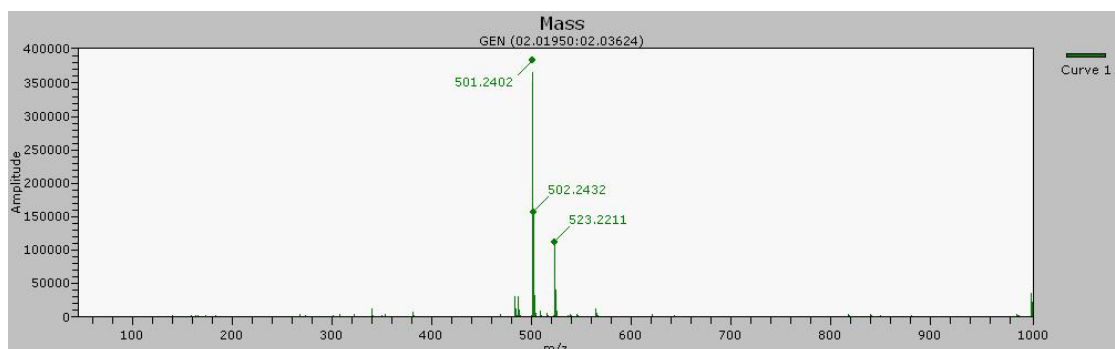
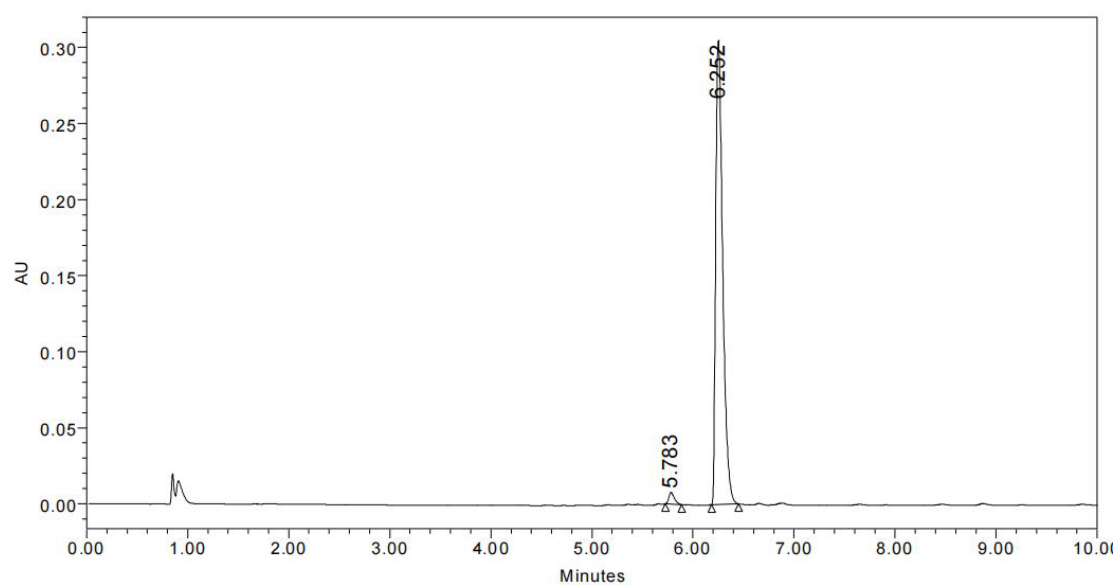


Figure S13. HRMS



	RT	Area	% Area	Height
1	5.783	28744	1.92	7634
2	6.252	1469221	98.08	304936

Figure S14. HPLC



Compound **5**

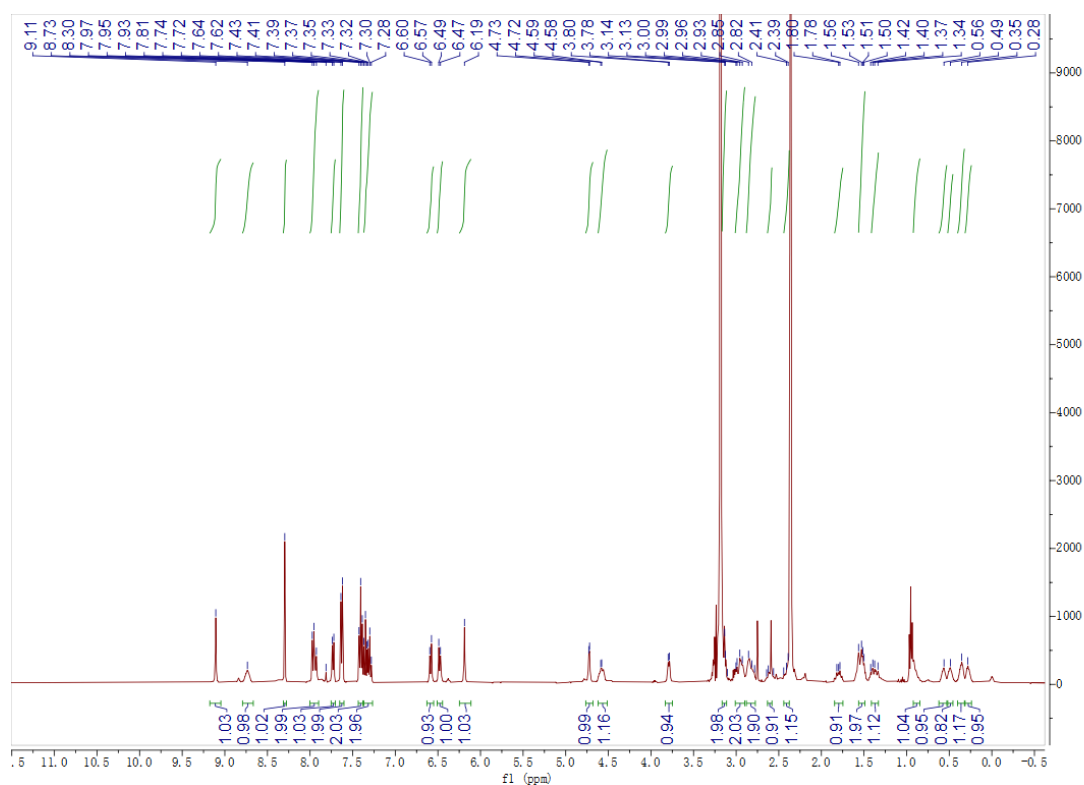


Figure S15. <sup>1</sup>H NMR (400M HZ, DMSO-*d*<sub>6</sub>)

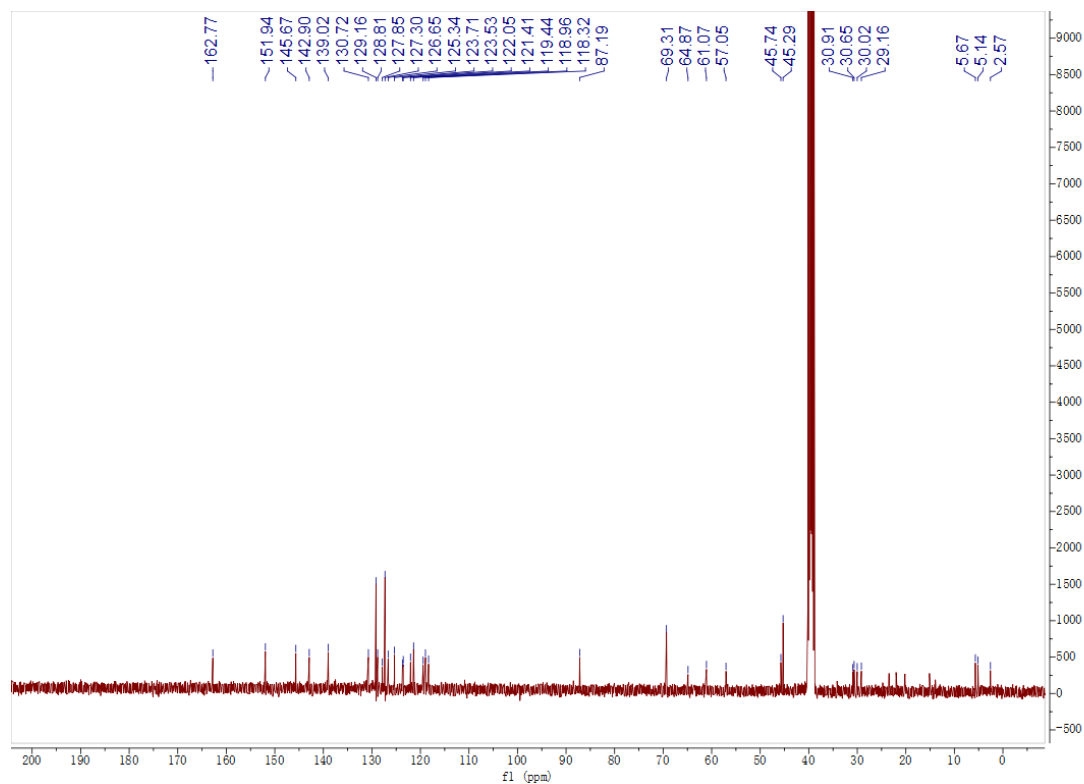


Figure S16. <sup>13</sup>C NMR (100M HZ, DMSO-*d*<sub>6</sub>)

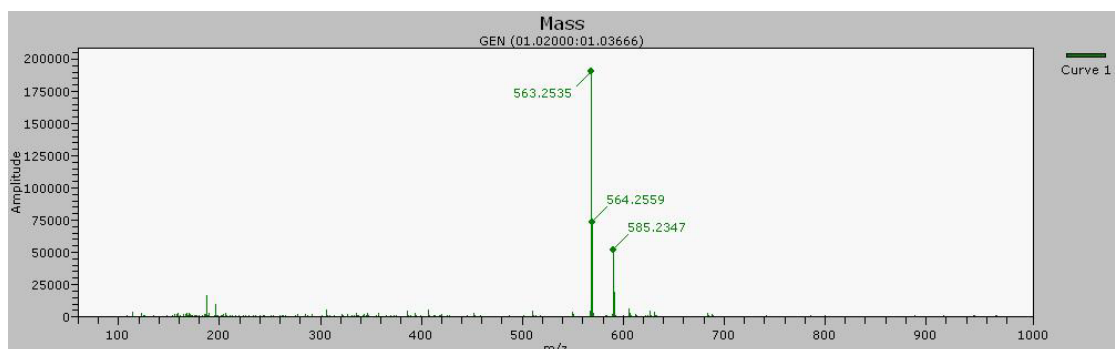
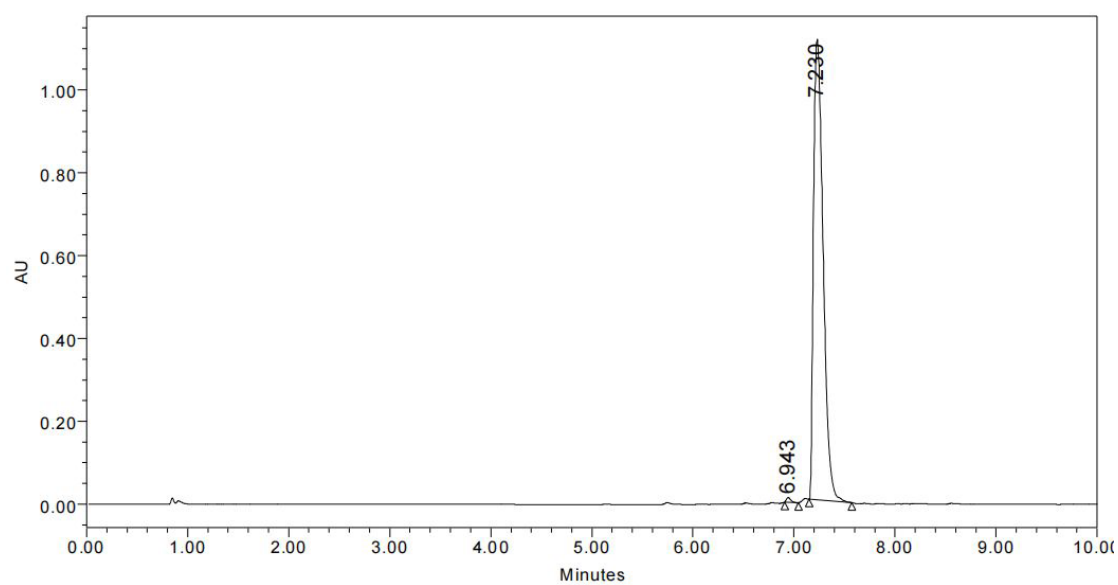


Figure S17. HRMS



	RT	Area	% Area	Height
1	6.943	34262	0.46	11432
2	7.230	7365314	99.54	1111619

Figure S18. HPLC

# Compound 6

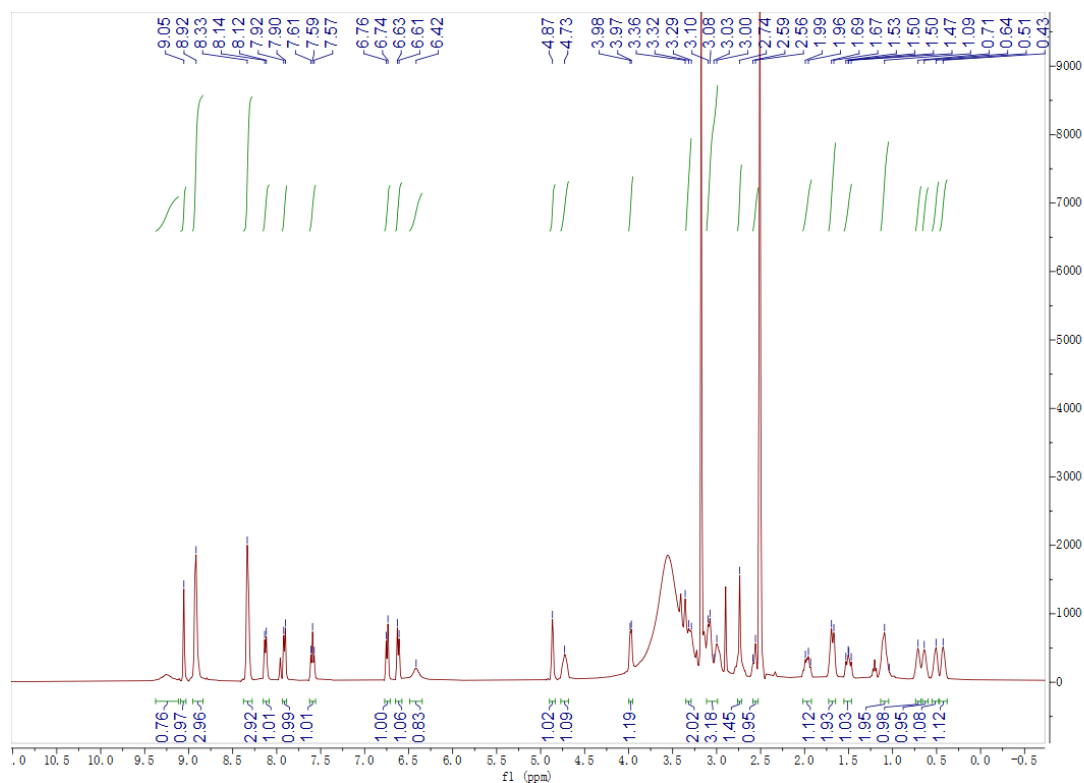


Figure S19. <sup>1</sup>H NMR (400M HZ, DMSO-*d*<sub>6</sub>)

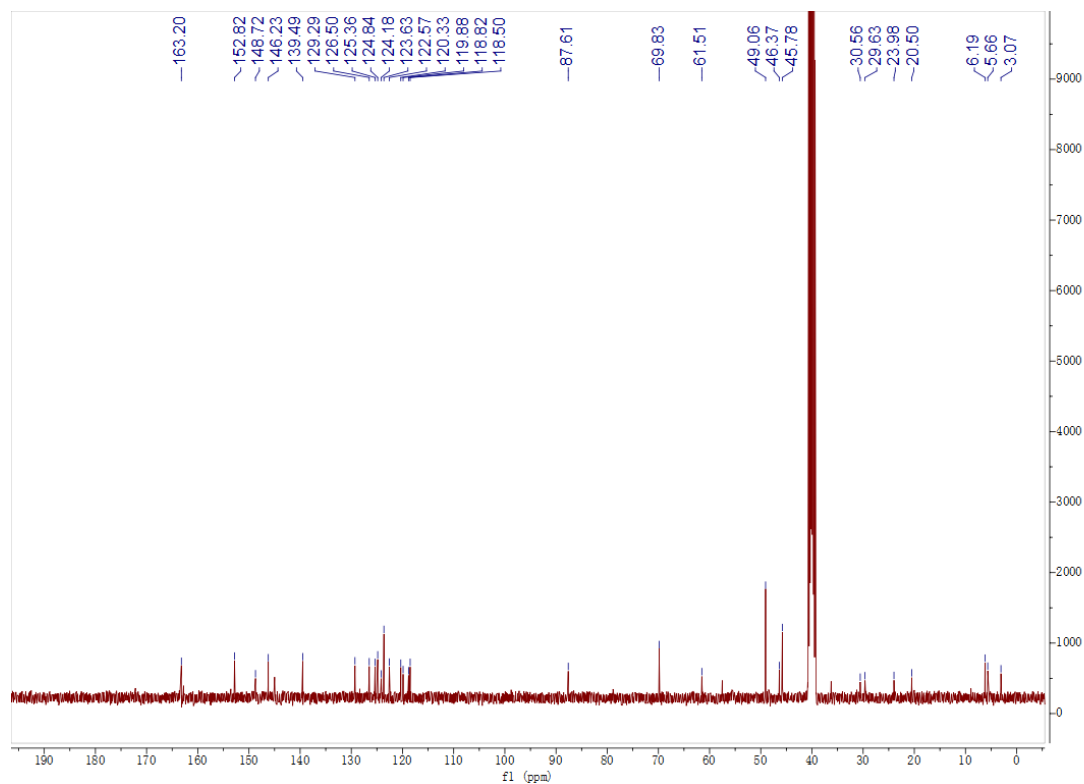


Figure S20. <sup>13</sup>C NMR (100M HZ, DMSO-*d*<sub>6</sub>)

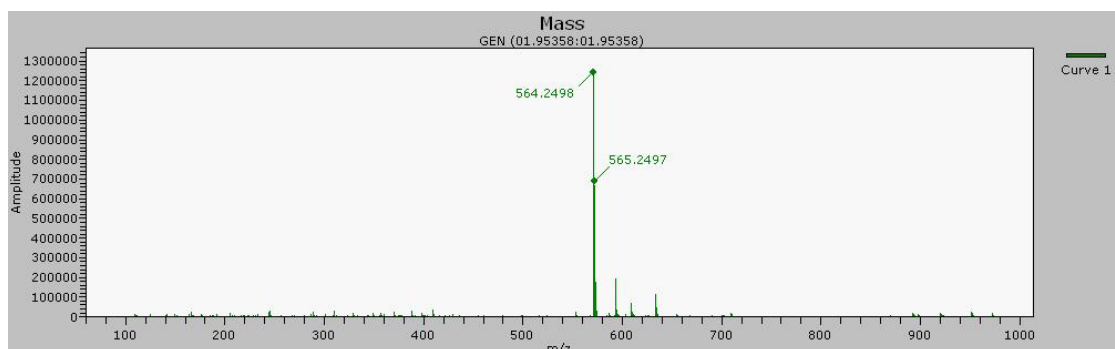
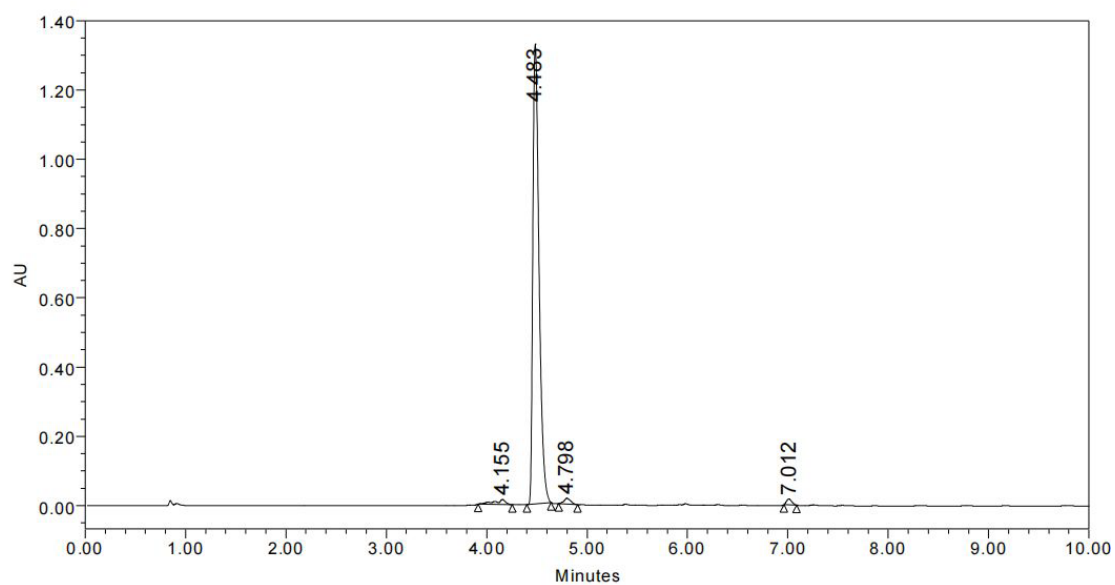


Figure S21. HRMS



	RT	Area	% Area	Height
1	4.155	112582	1.90	14765
2	4.483	5672182	95.62	1327658
3	4.798	83626	1.41	17408
4	7.012	63386	1.07	17135

Figure S22. HPLC

# Compound 8

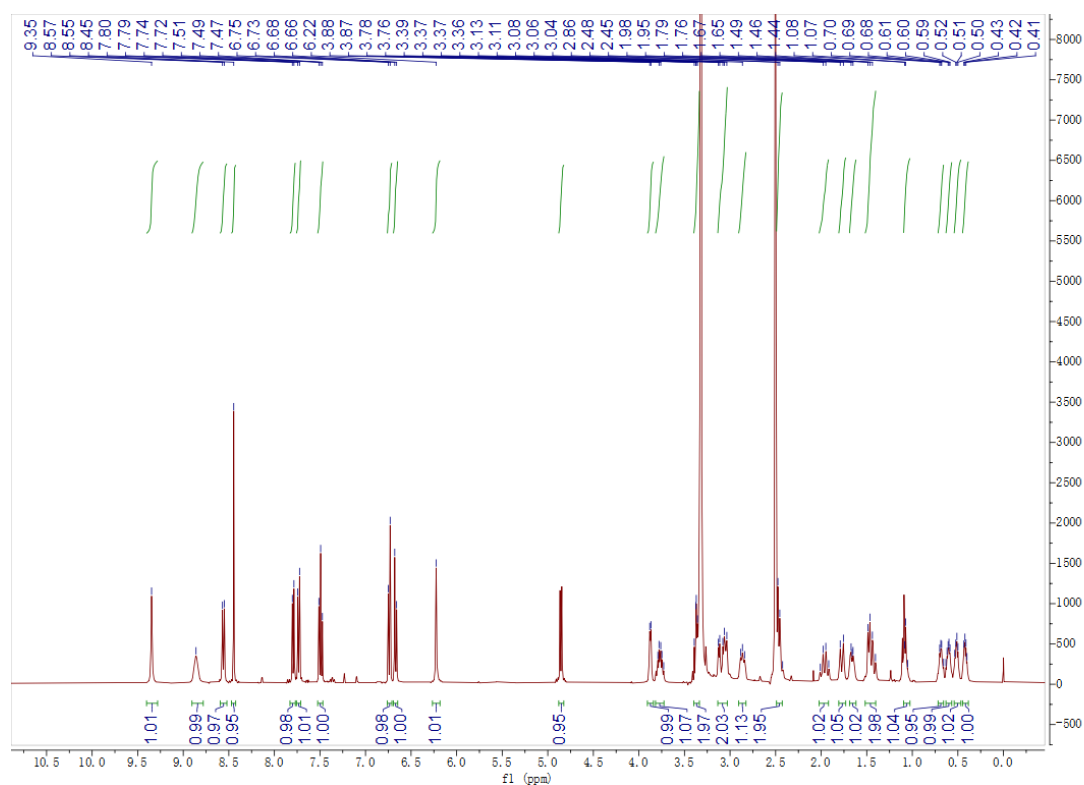


Figure S23. <sup>1</sup>H NMR (400M HZ, DMSO-*d*<sub>6</sub>)

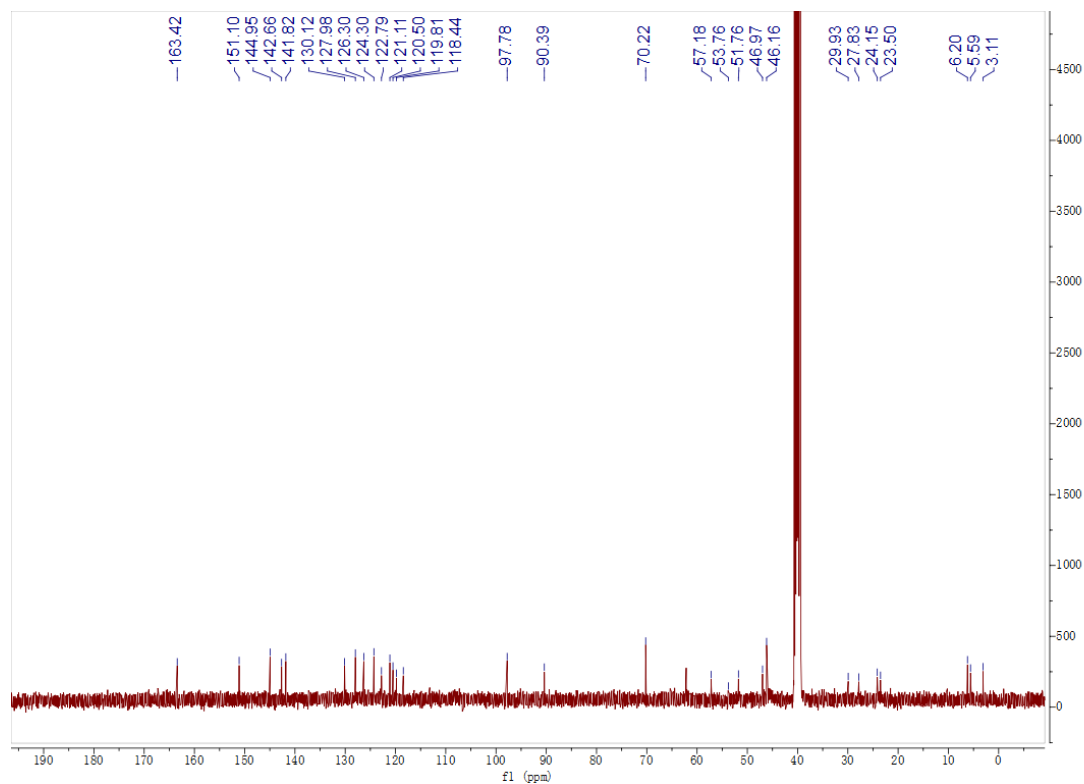


Figure S24. <sup>13</sup>C NMR (100M HZ, DMSO-*d*<sub>6</sub>)

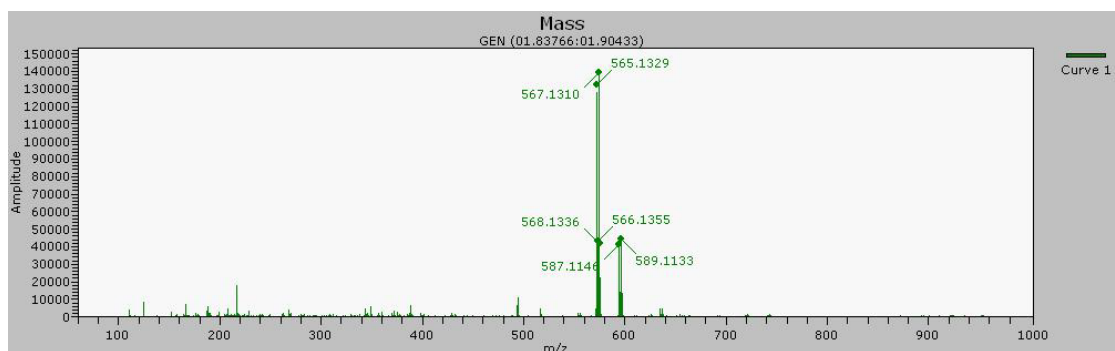
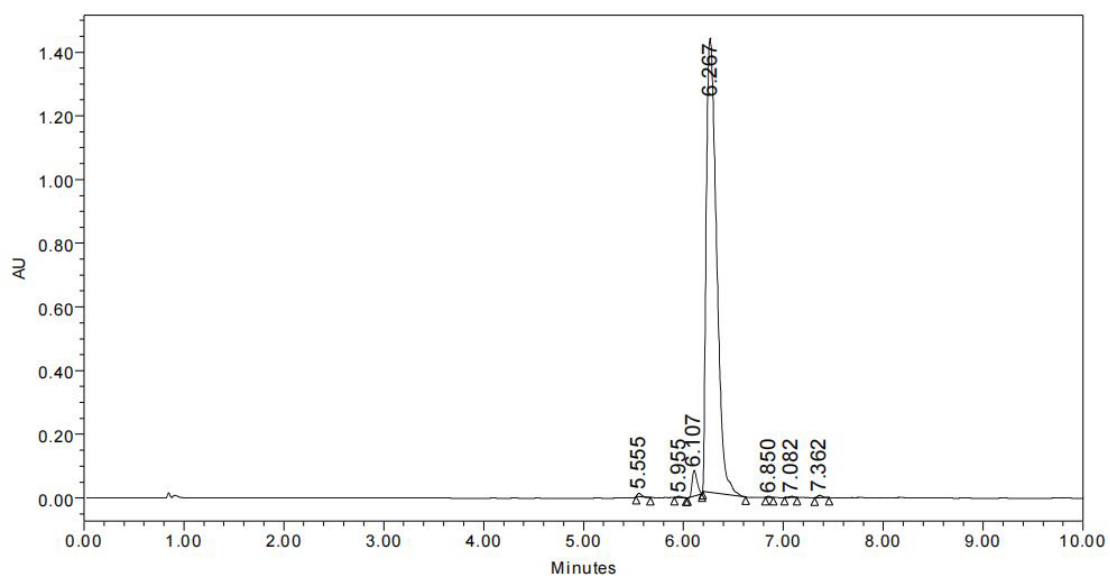


Figure S25. HRMS



	RT	Area	% Area	Height
1	5.555	31573	0.30	10674
2	5.955	14341	0.14	4543
3	6.107	275753	2.60	80349
4	6.267	10224016	96.56	1426337
5	6.850	6668	0.06	2702
6	7.082	9959	0.09	3185
7	7.362	26177	0.25	7338

Figure S26. HPLC

# Compound 9

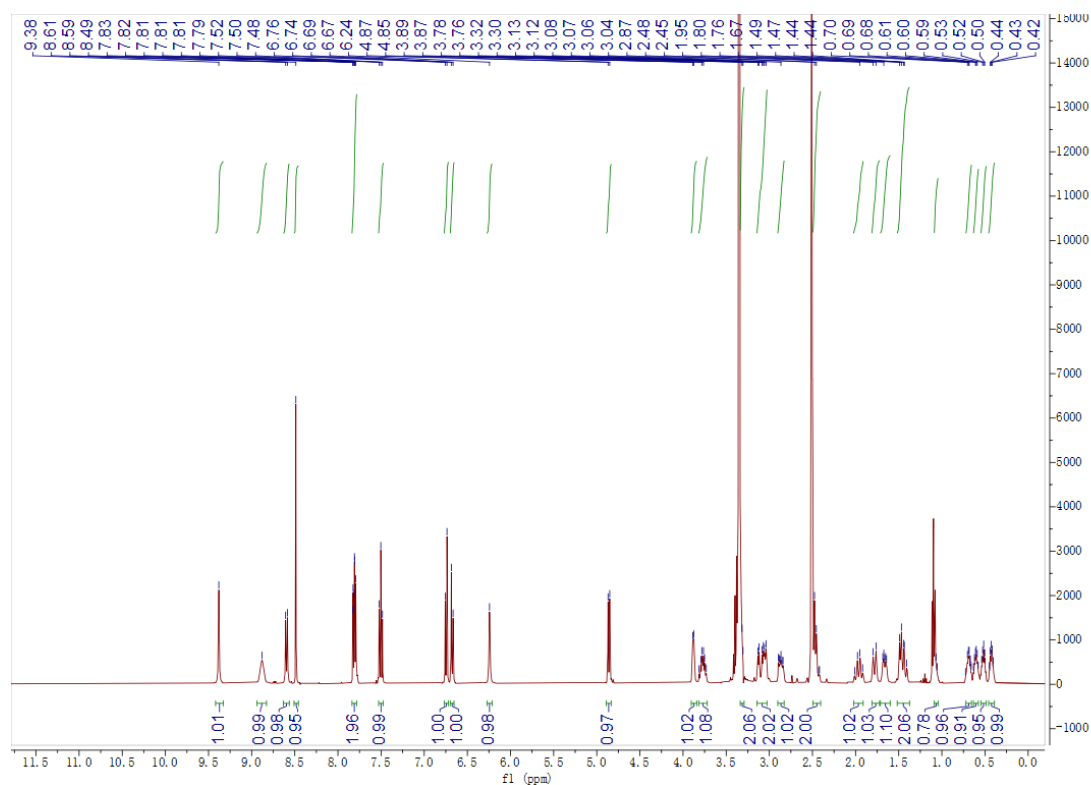


Figure S27. <sup>1</sup>H NMR (400M HZ, DMSO-*d*<sub>6</sub>)

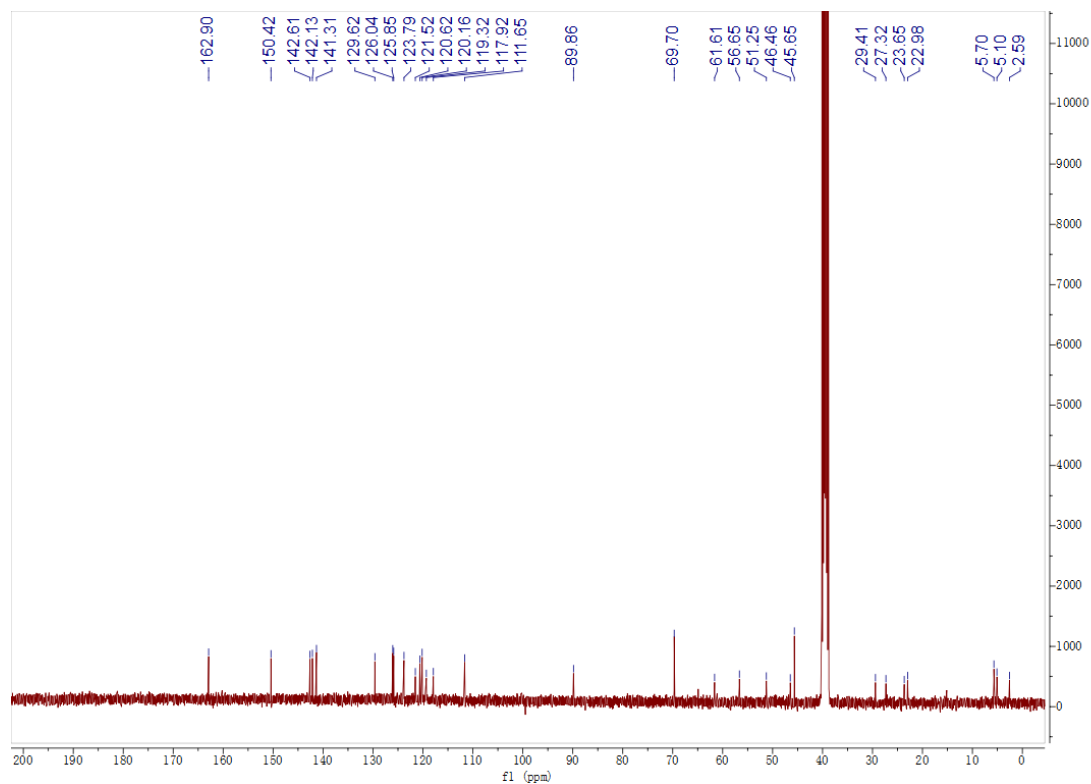


Figure S28. <sup>13</sup>C NMR (100M HZ, DMSO-*d*<sub>6</sub>)

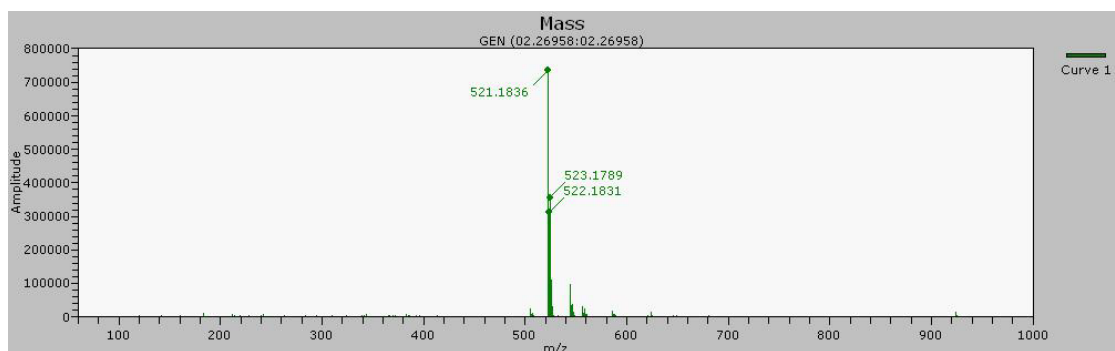
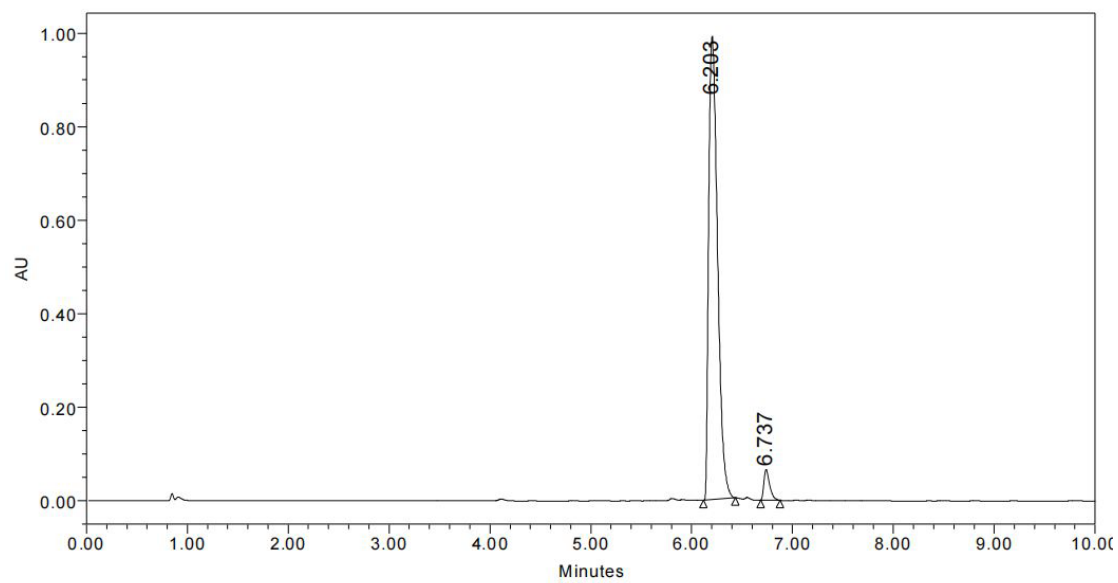


Figure S29. HRMS



	RT	Area	% Area	Height
1	6.203	6070714	95.95	991148
2	6.737	256524	4.05	65518

Figure S30. HPLC



# Compound 10

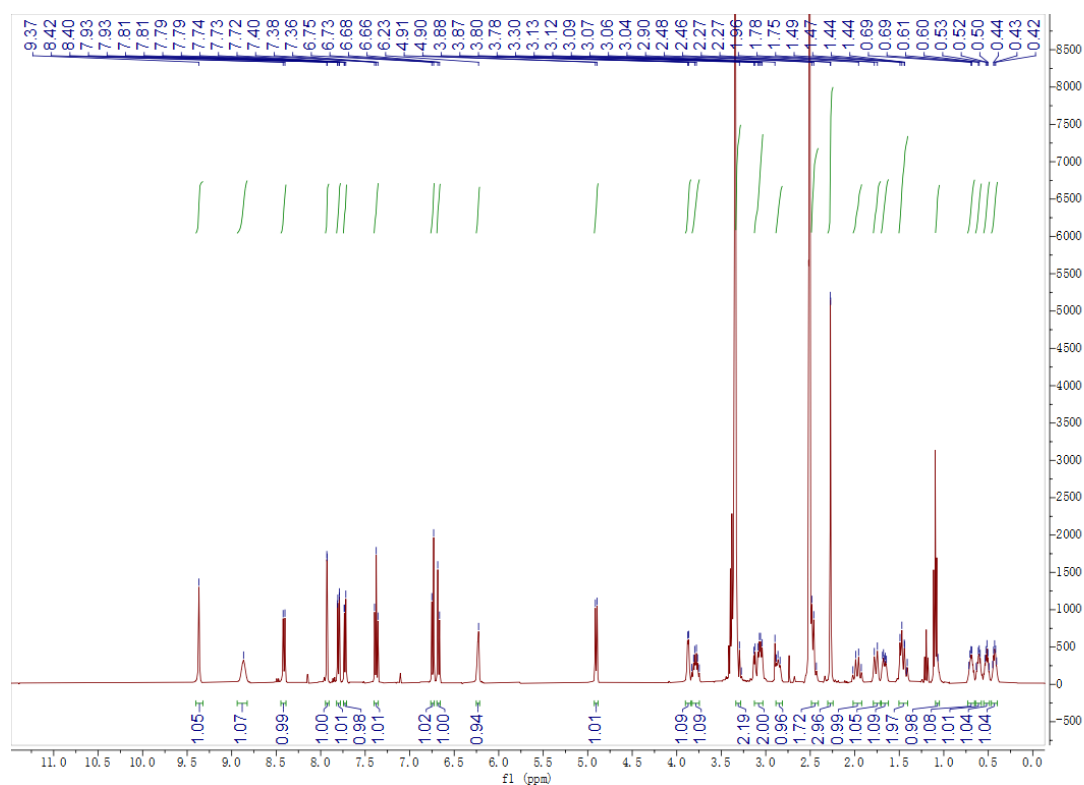


Figure S31. <sup>1</sup>H NMR (400M HZ, DMSO-*d*<sub>6</sub>)

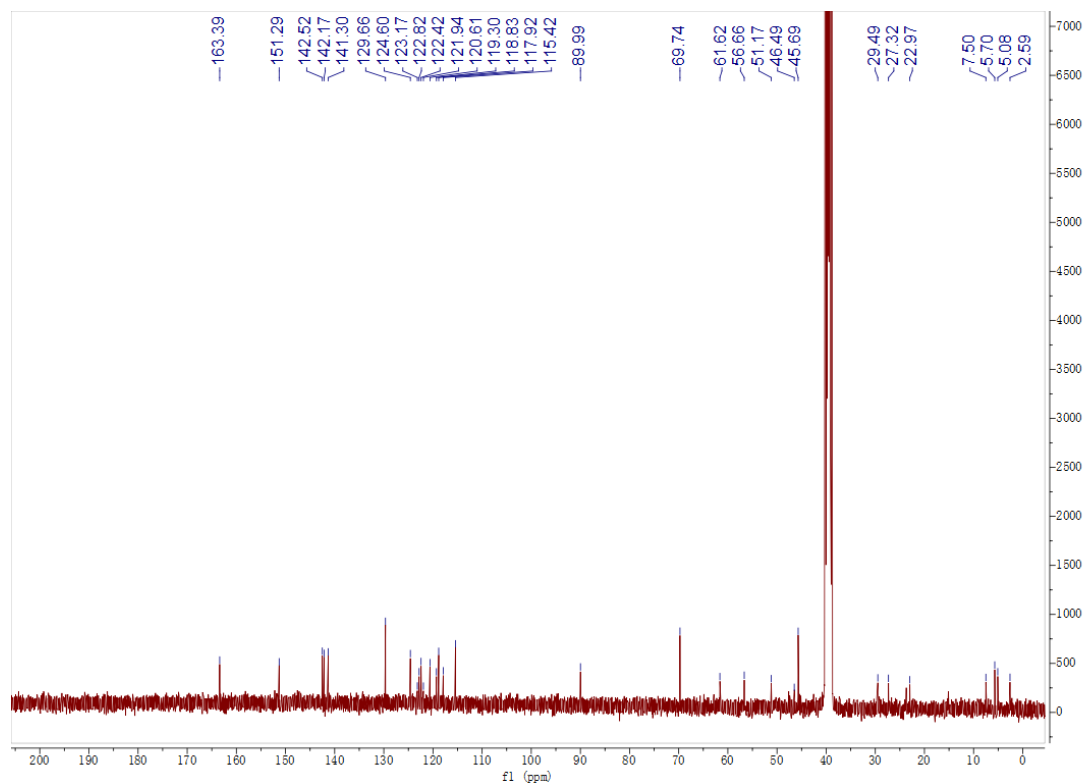


Figure S32. <sup>13</sup>C NMR (100M HZ, DMSO-*d*<sub>6</sub>)

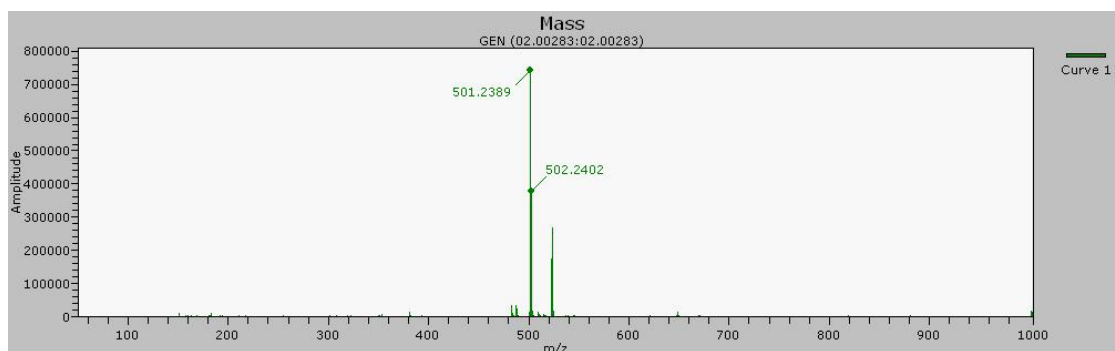
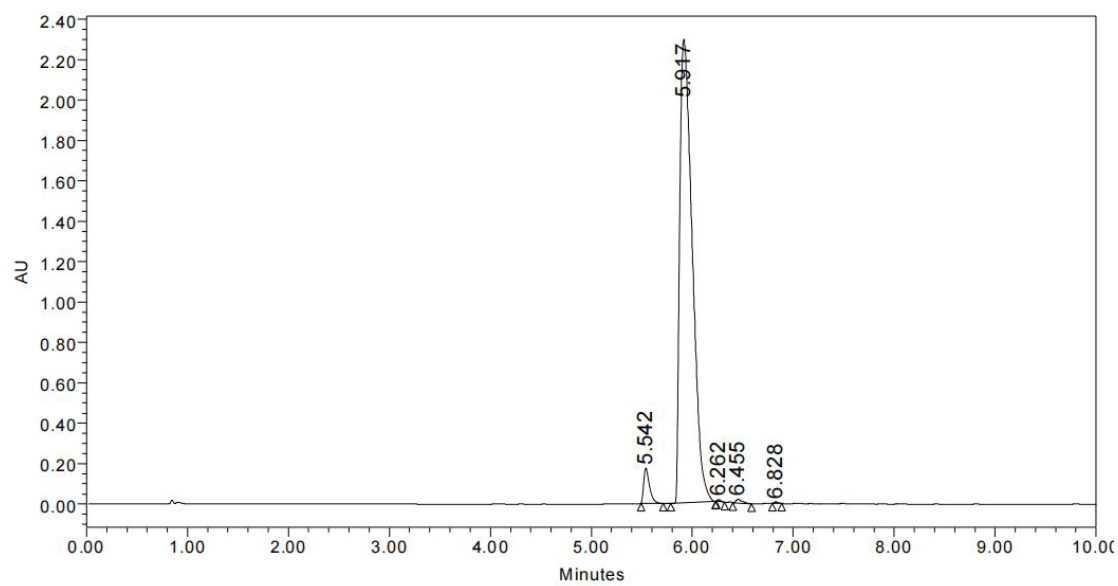


Figure S33. HRMS



	RT	Area	% Area	Height
1	5.542	689199	3.35	172916
2	5.917	19796948	96.09	2292401
3	6.262	18062	0.09	7176
4	6.455	76934	0.37	18244
5	6.828	20685	0.10	7019

Figure S34. HPLC

# Compound 11

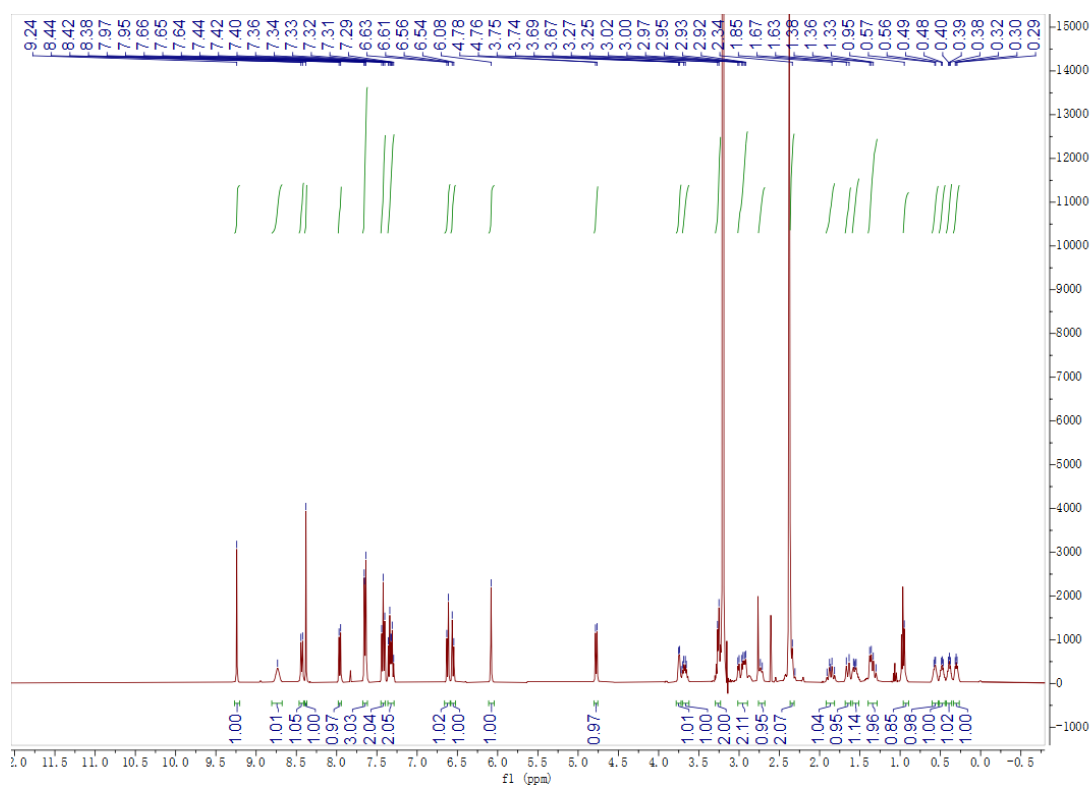


Figure S35. <sup>1</sup>H NMR (400M HZ, DMSO-*d*<sub>6</sub>)

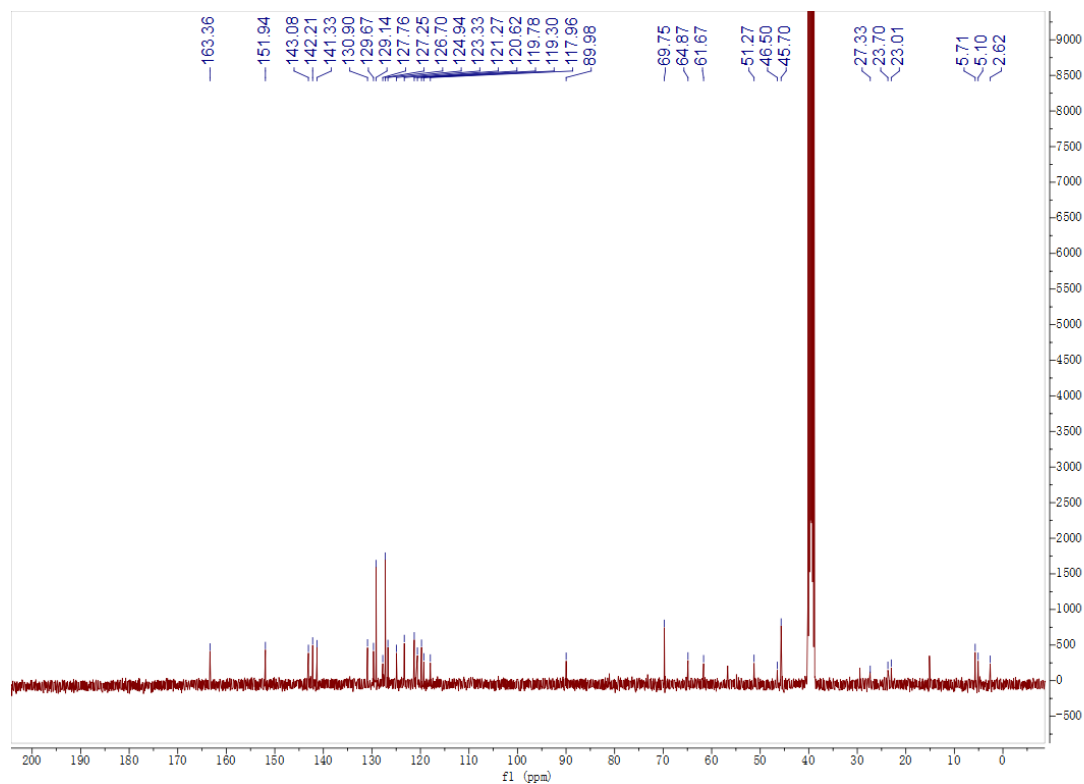


Figure S36. <sup>13</sup>C NMR (100M HZ, DMSO-*d*<sub>6</sub>)

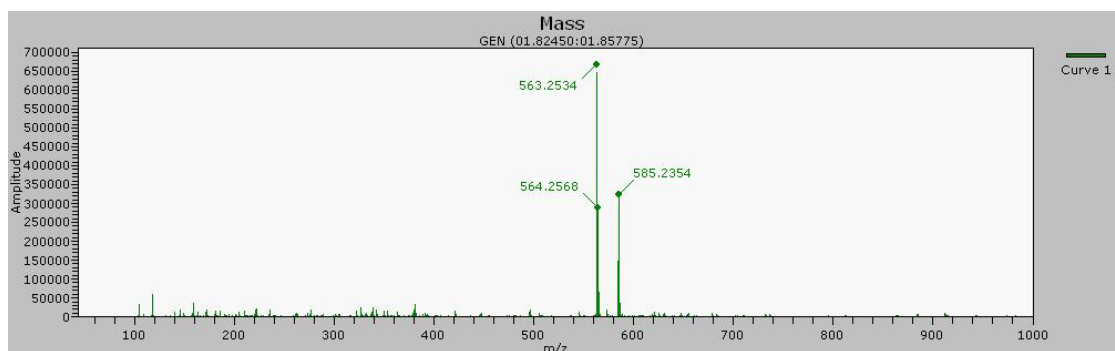
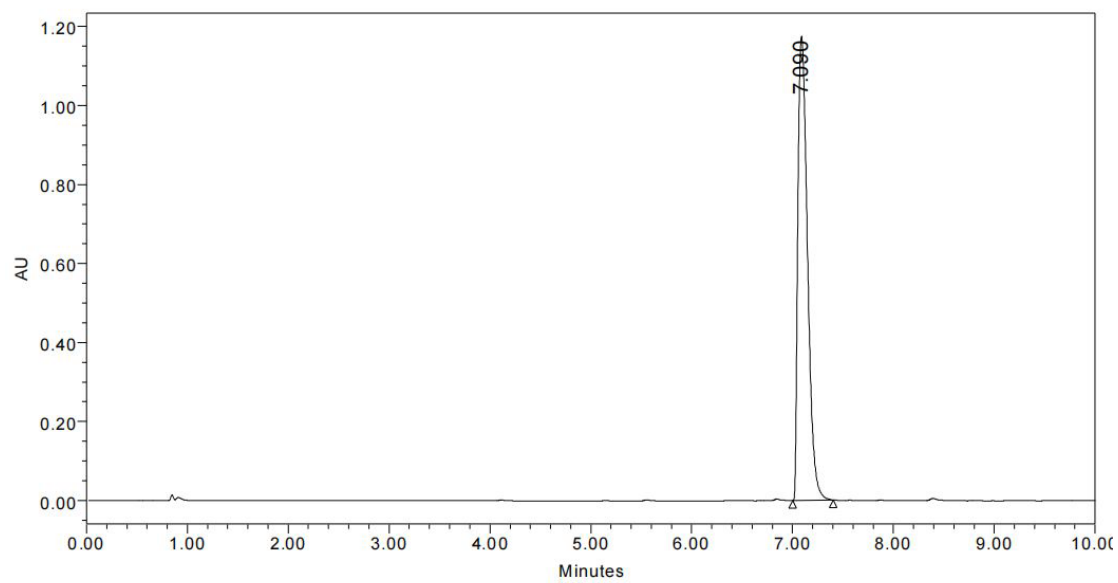


Figure S37. HRMS



	RT	Area	% Area	Height
1	7.090	7788976	100.00	1174598

Figure S38. HPLC

# Compound 12

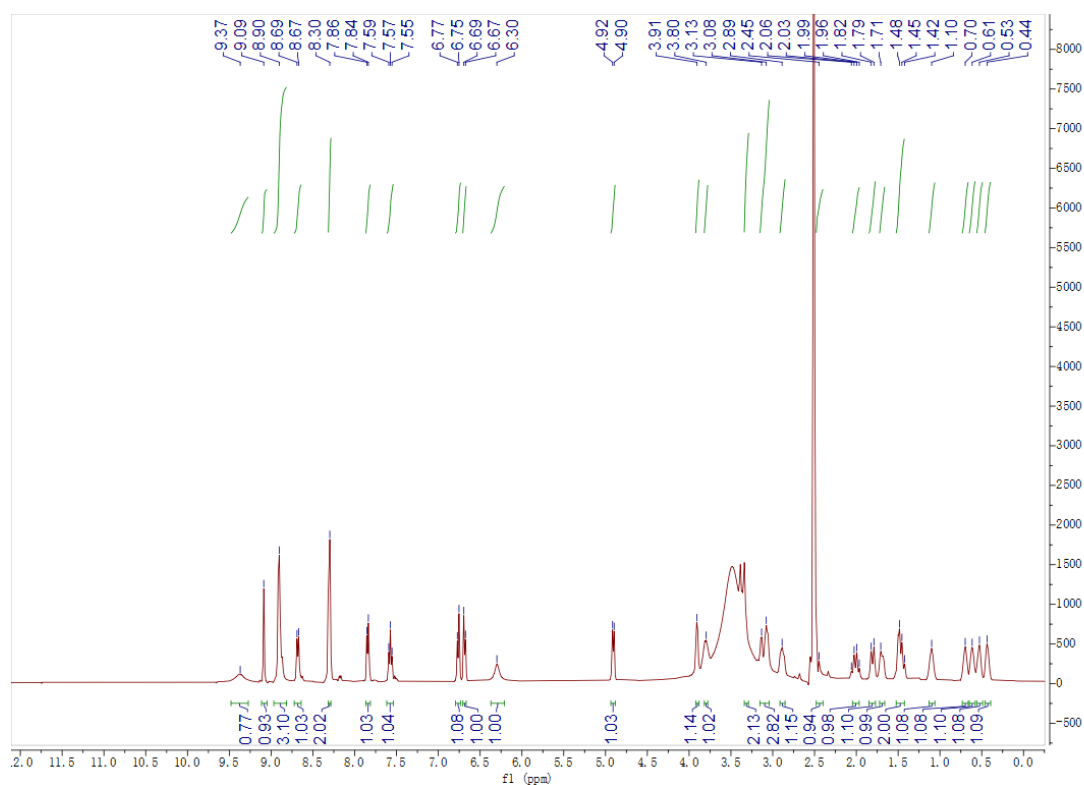


Figure S39. <sup>1</sup>H NMR (400M HZ, DMSO-*d*<sub>6</sub>)

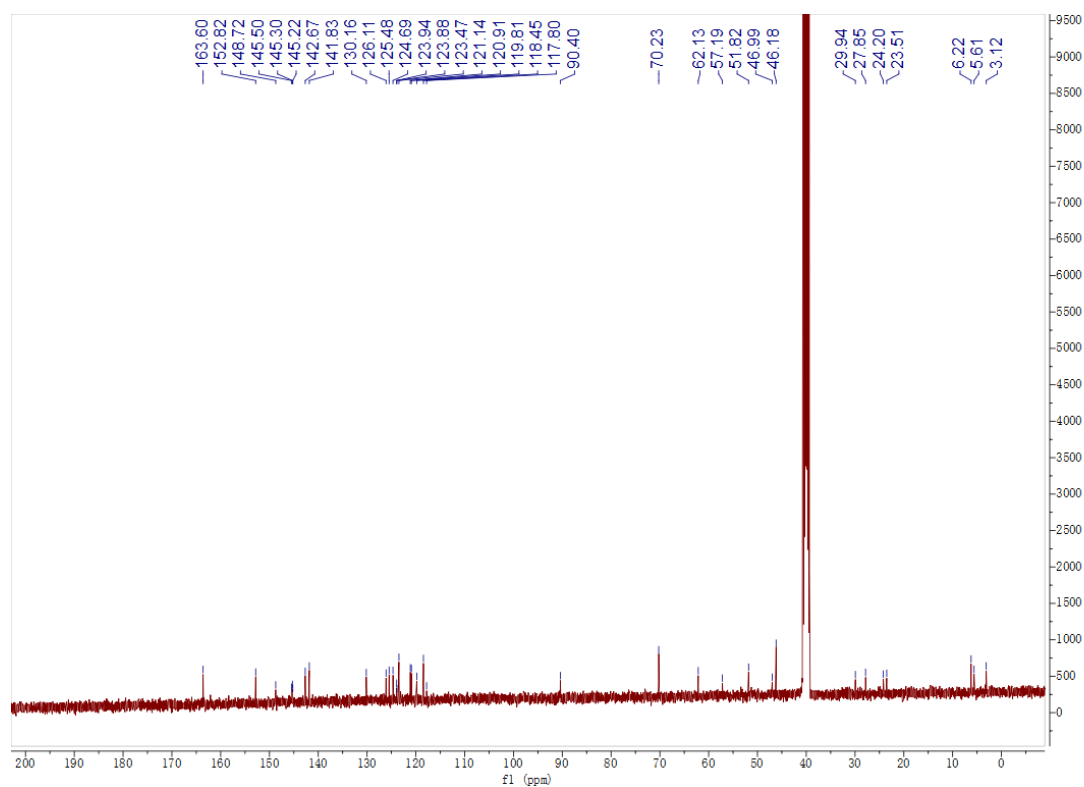


Figure S40. <sup>13</sup>C NMR (100M HZ, DMSO-*d*<sub>6</sub>)

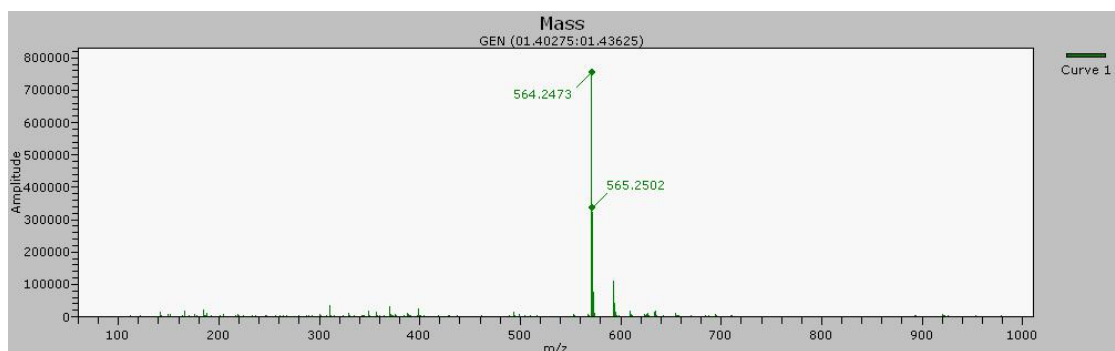
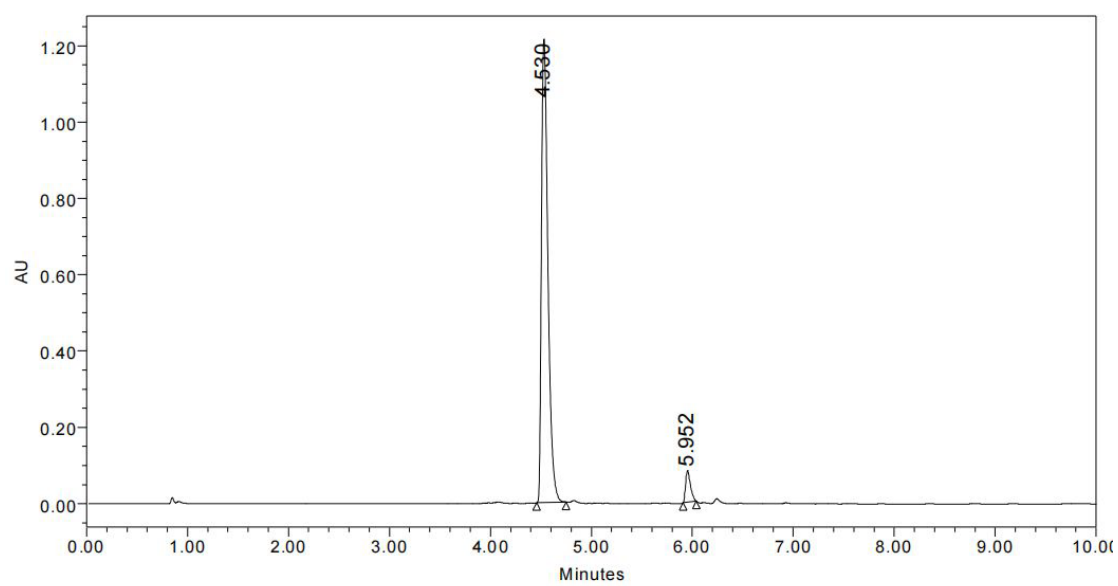


Figure S41. HRMS



	RT	Area	% Area	Height
1	4.530	5378630	95.15	1214480
2	5.952	274253	4.85	82062

Figure S42. HPLC