

Discovery of Novel Diarylamide *N*-Containing Heterocyclic Derivatives as New Tubulin Polymerization Inhibitors with Anti-Cancer Activity

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¹H NMR of compound 15a

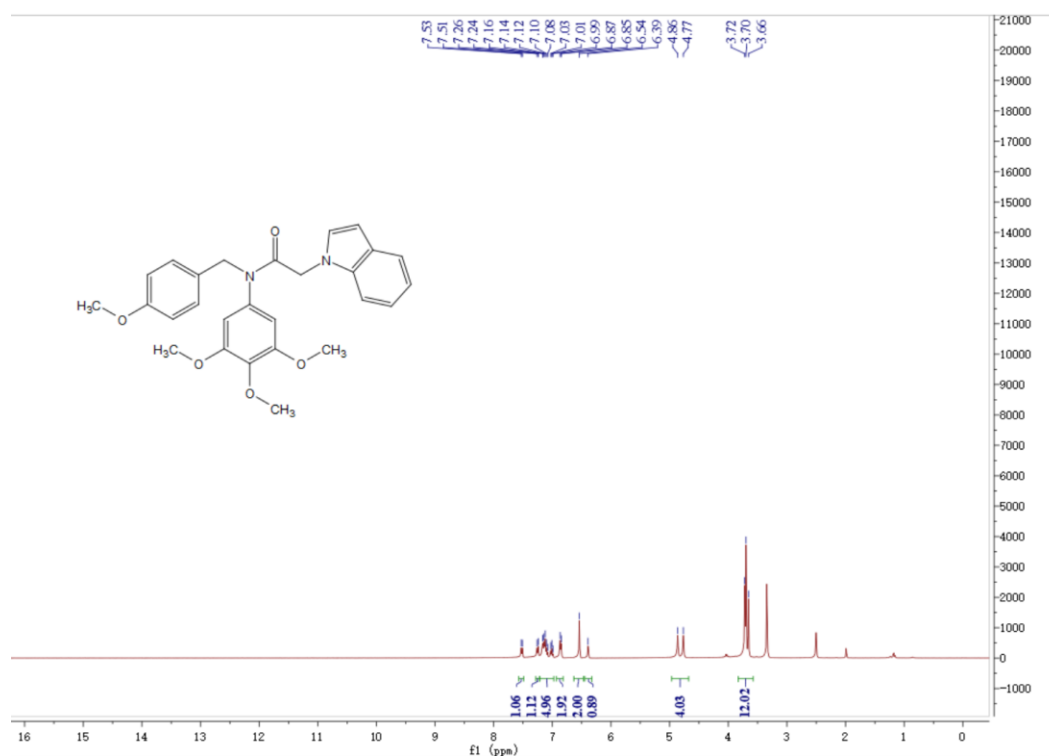


Fig. S1. ¹H NMR spectrum of compound 15a (400 MHz, DMSO-*d*₆)

^{13}C NMR of compound **15a**

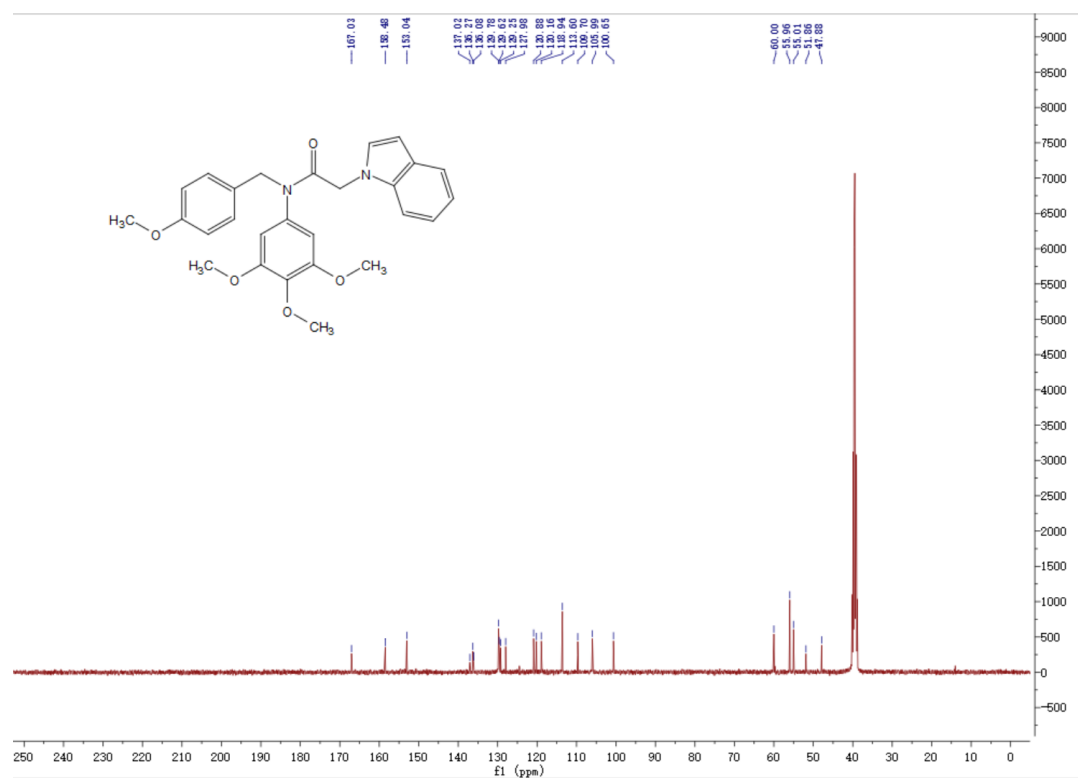


Fig. S2. ^{13}C NMR spectrum of compound **15a** (400 MHz, $\text{DMSO-}d_6$)

HRMS of compound 15a

MOYO-223

18-Jul-2019

LHM-7597 9 (0.155) AM (Cen,4, 80.00, Ht,5000.0,0.00,1.00); Sm (Mn, 2x3.00); Cm (1:15)

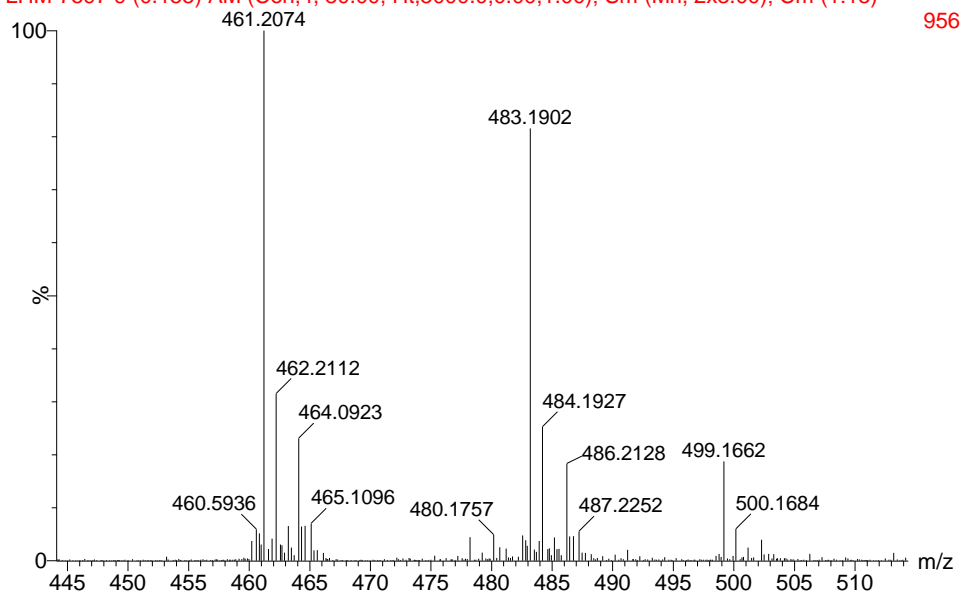


Fig. S3. HRMS spectrum of compound 15a

¹H NMR of compound 15b

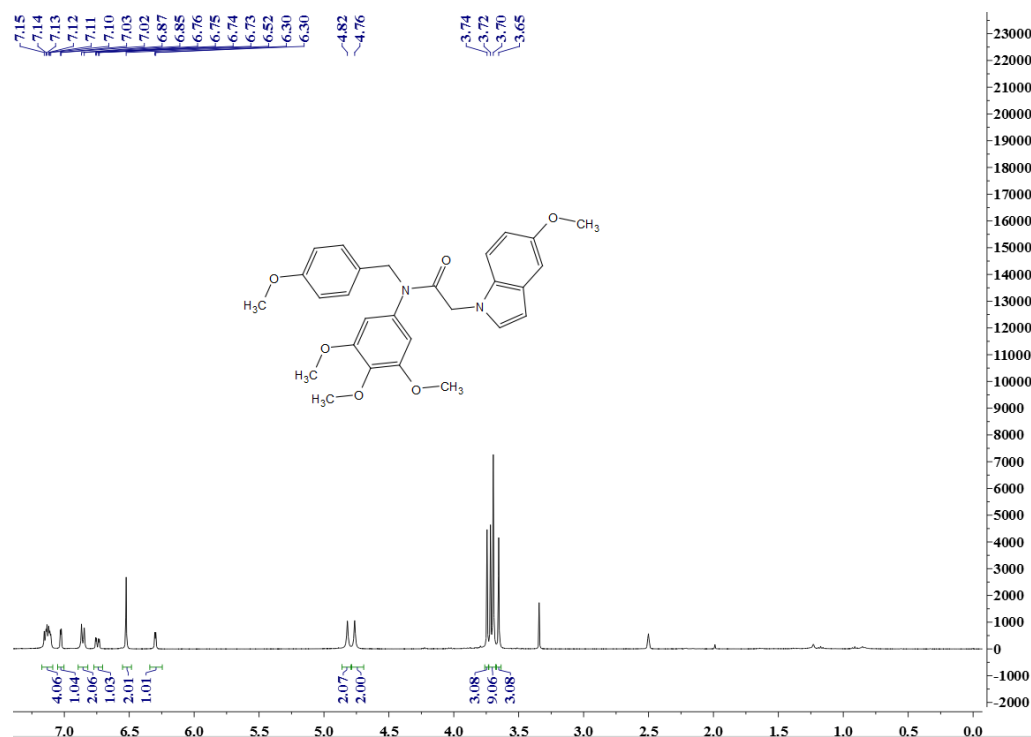


Fig. S4. ¹H NMR spectrum of compound **15b** (400 MHz, DMSO-*d*₆)

^{13}C NMR of compound **15b**

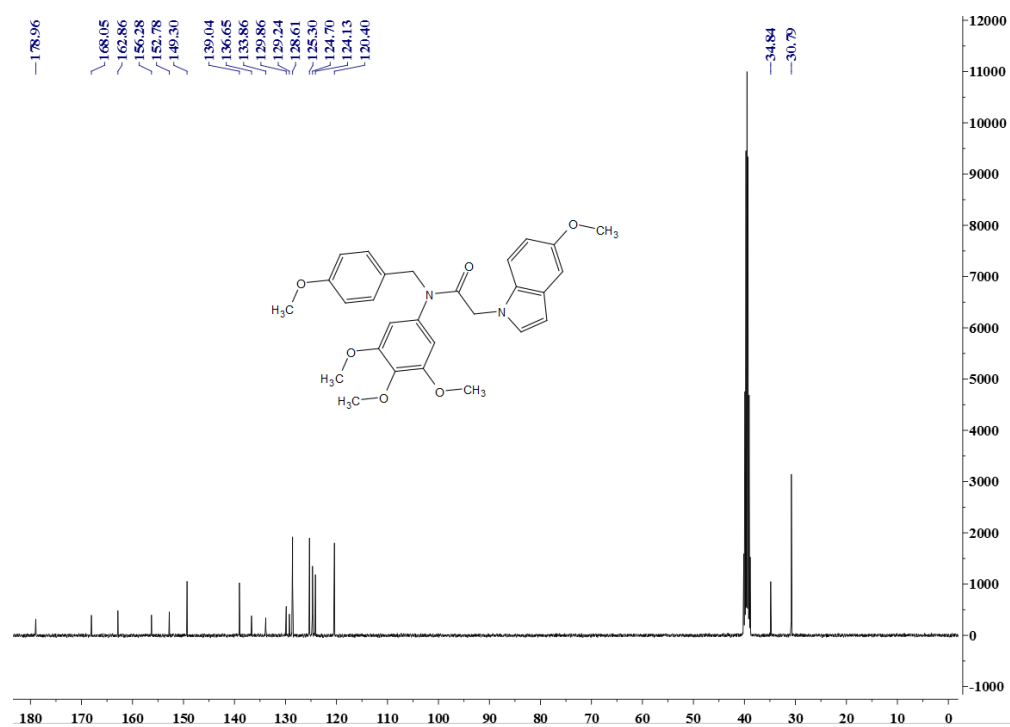


Fig. S5. ^{13}C NMR spectrum of compound **15b** (400 MHz, DMSO- d_6)

^1H NMR of compound **15c**

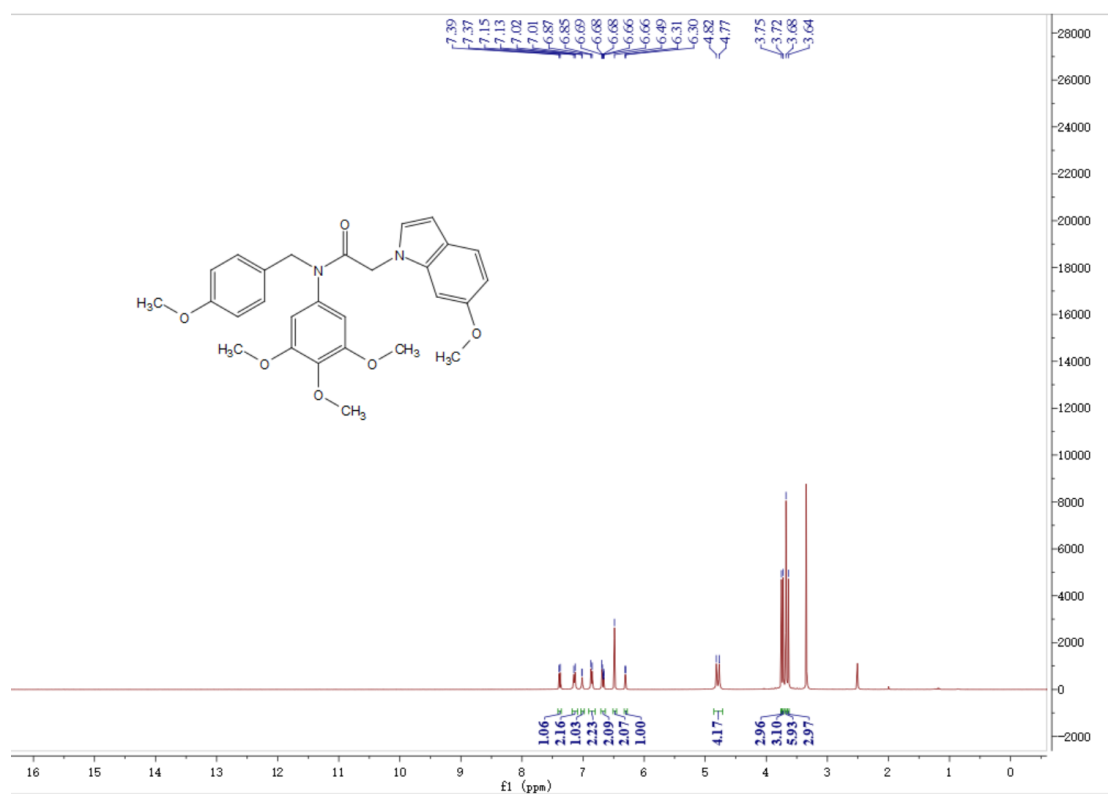


Fig. S6. ^1H NMR spectrum of compound **15c** (400 MHz, $\text{DMSO-}d_6$)

¹³C NMR of compound **15c**

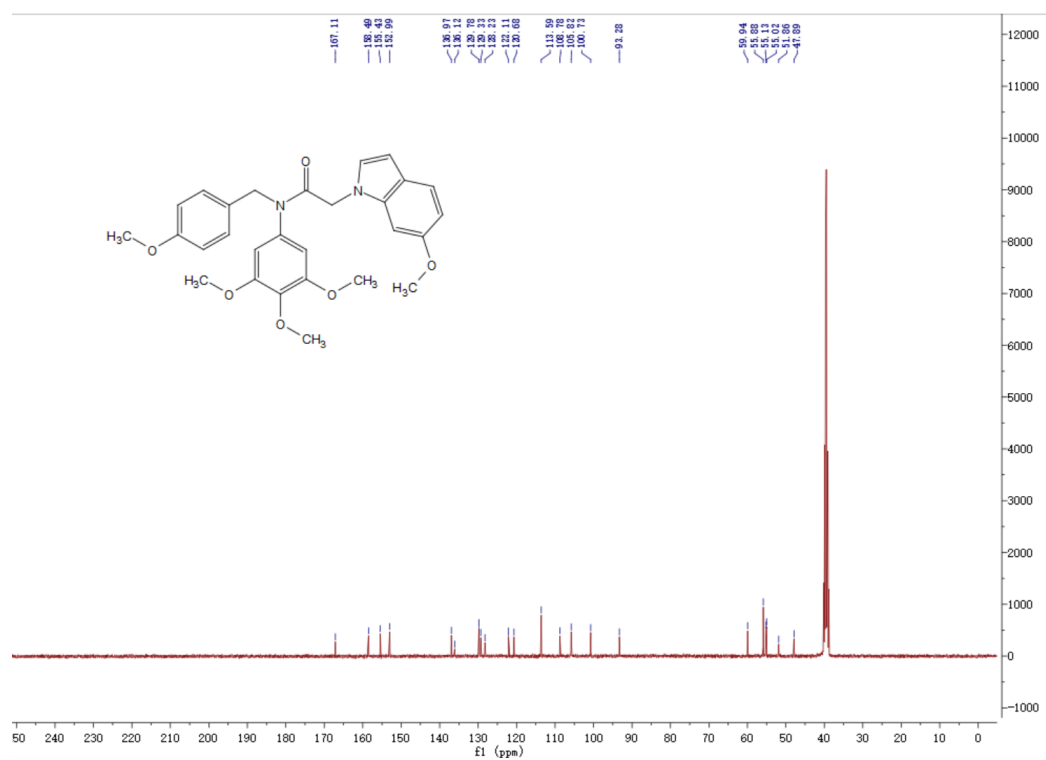


Fig. S7. ¹³C NMR spectrum of compound **15c** (400 MHz, DMSO-*d*₆)

HRMS of compound **15c**

MOYO-208

18-Jul-2019

LHM-7596 4 (0.069) AM (Cen,4, 80.00, Ht,5000.0,0.00,1.00); Sm (Mn, 2x3.00); Cm (1:14)

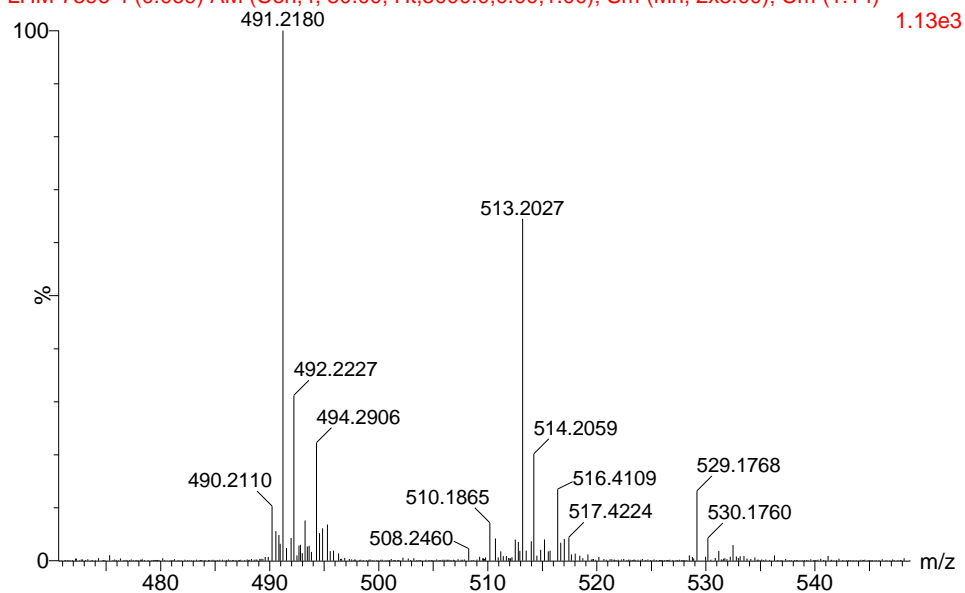


Fig. S8. HRMS spectrum of compound **15c**

¹H NMR of compound 15d

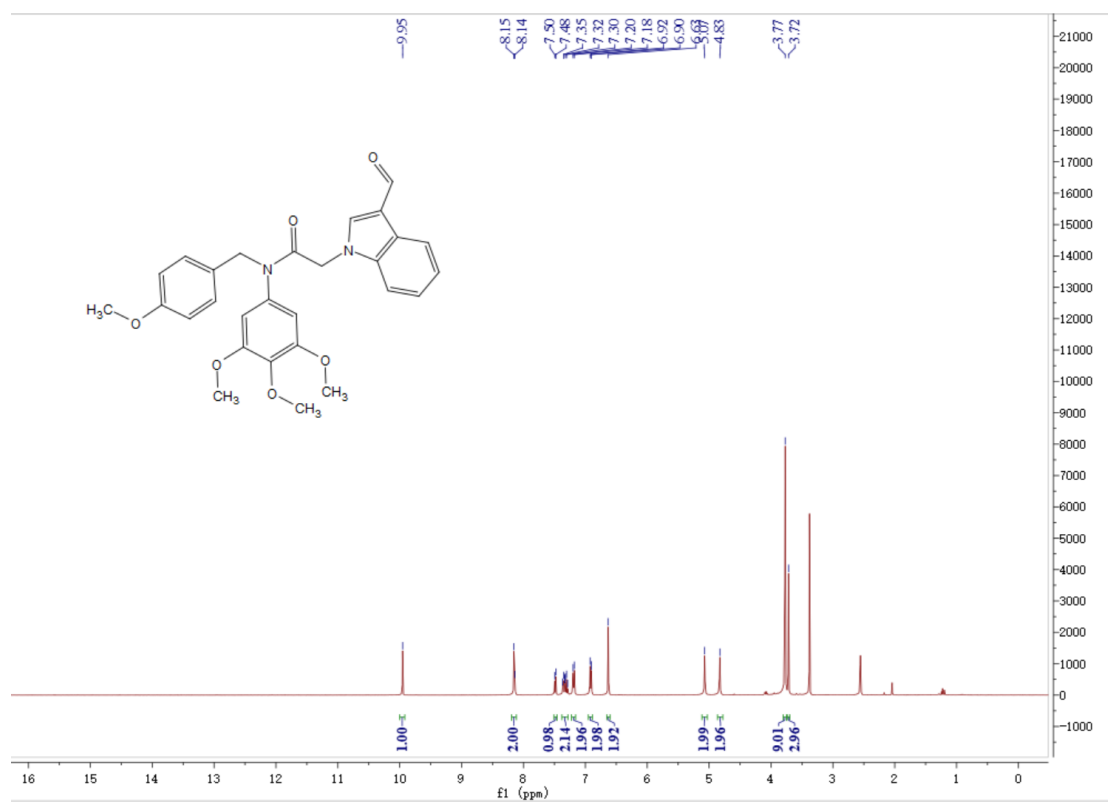
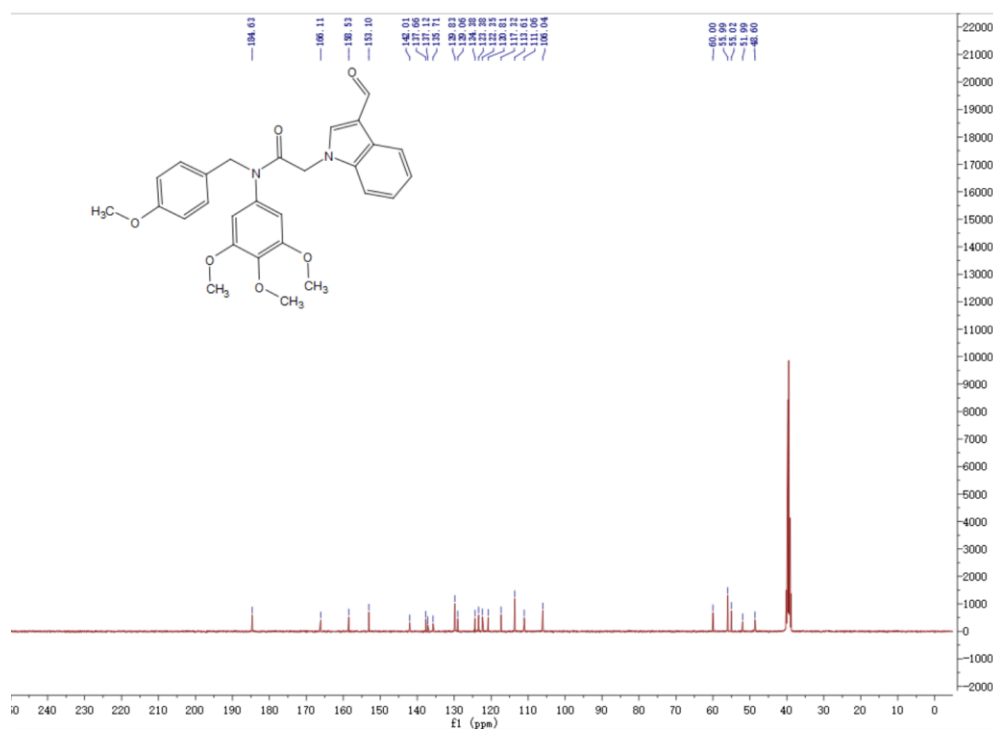


Fig. S9. ¹H NMR spectrum of compound 15d (400 MHz, DMSO-*d*₆)

^{13}C NMR of compound **15d**



HRMS of compound 15d

MOYO-183

18-Jul-2019

LHM-7594 4 (0.069) AM (Cen,4, 80.00, Ht,5000.0,0.00,1.00); Sm (Mn, 2x3.00); Cm (1:22)

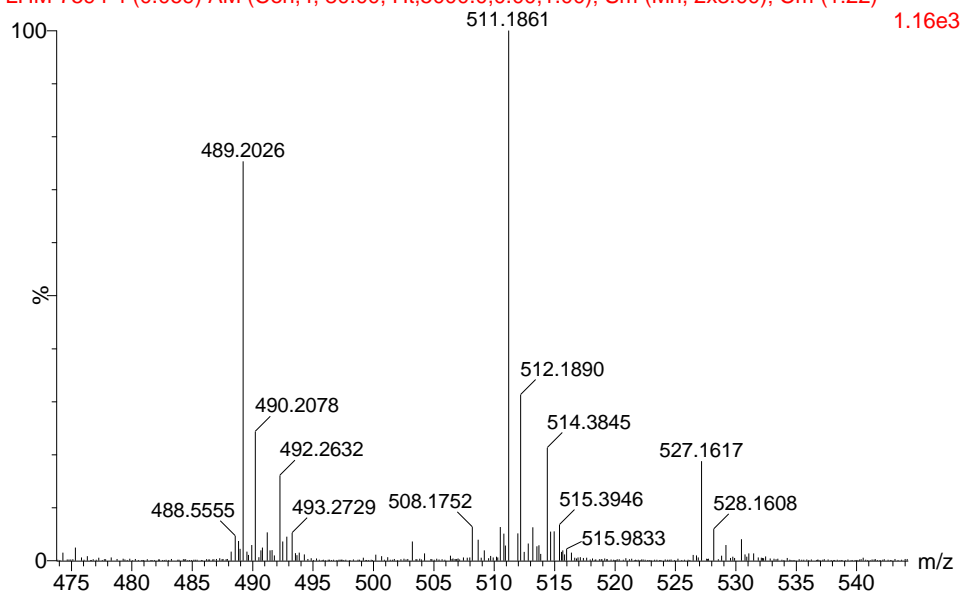


Fig. S11. HRMS spectrum of compound 15d

^1H NMR of compound **15e**

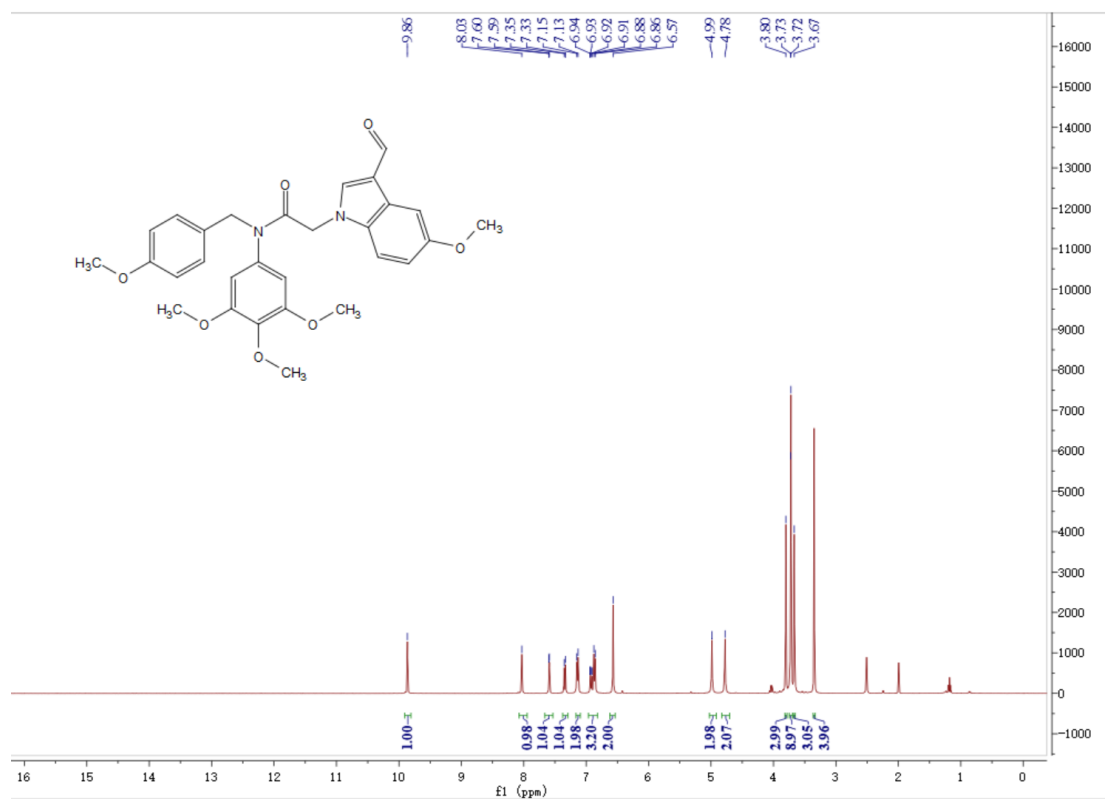


Fig. S12. ^1H NMR spectrum of compound **15e** (400 MHz, $\text{DMSO}-d_6$)

^{13}C NMR of compound **15e**

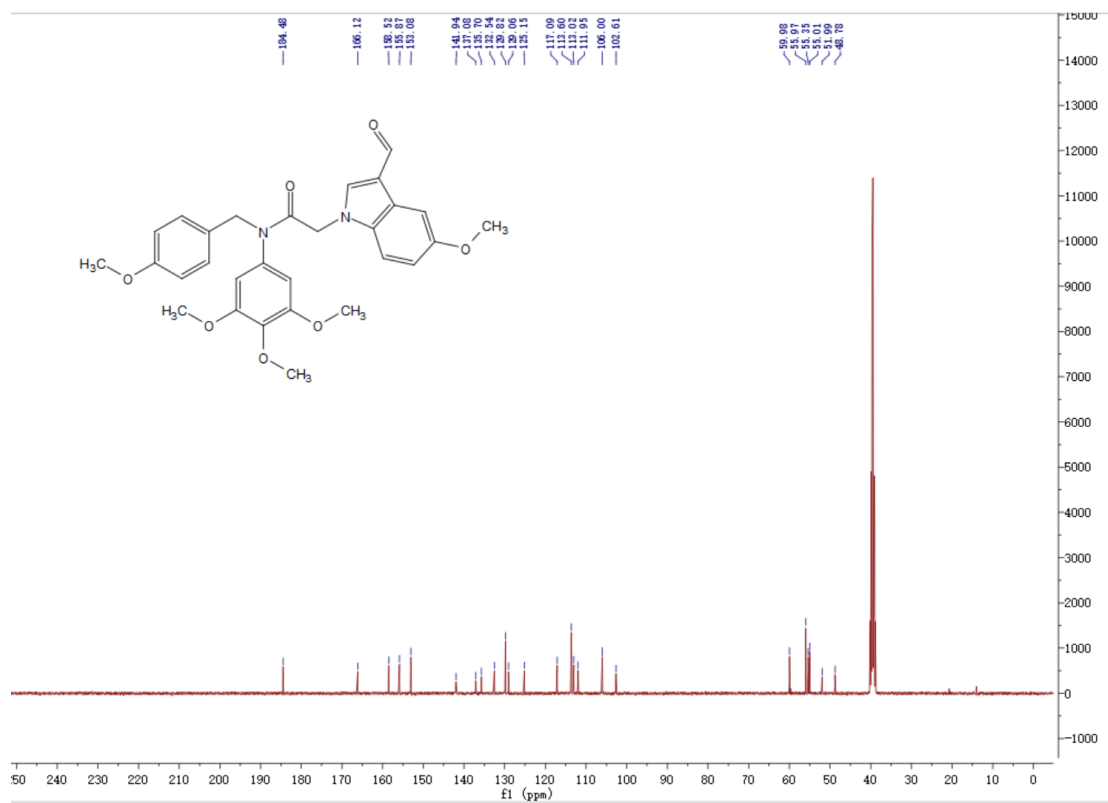


Fig. S13. ^{13}C NMR spectrum of compound **15e** (400 MHz, DMSO- d_6)

HRMS of compound 15e

MOYO-206

18-Jul-2019

LHM-7595 25 (0.434) AM (Cen,4, 80.00, Ht,5000.0,0.00,1.00); Sm (Mn, 2x3.00); Cm (1:26)

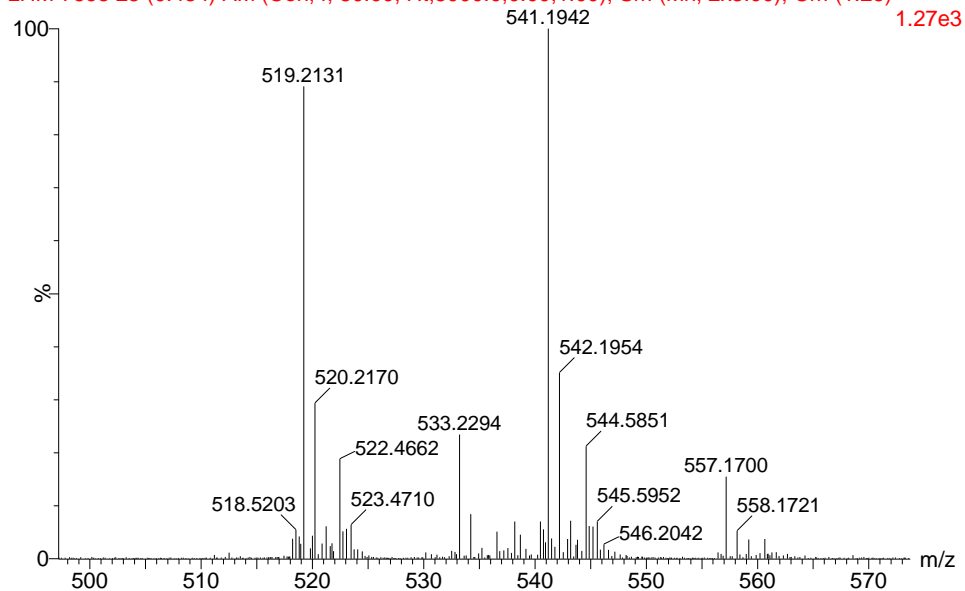


Fig. S14. HRMS spectrum of compound 15e

¹H NMR of compound 15f

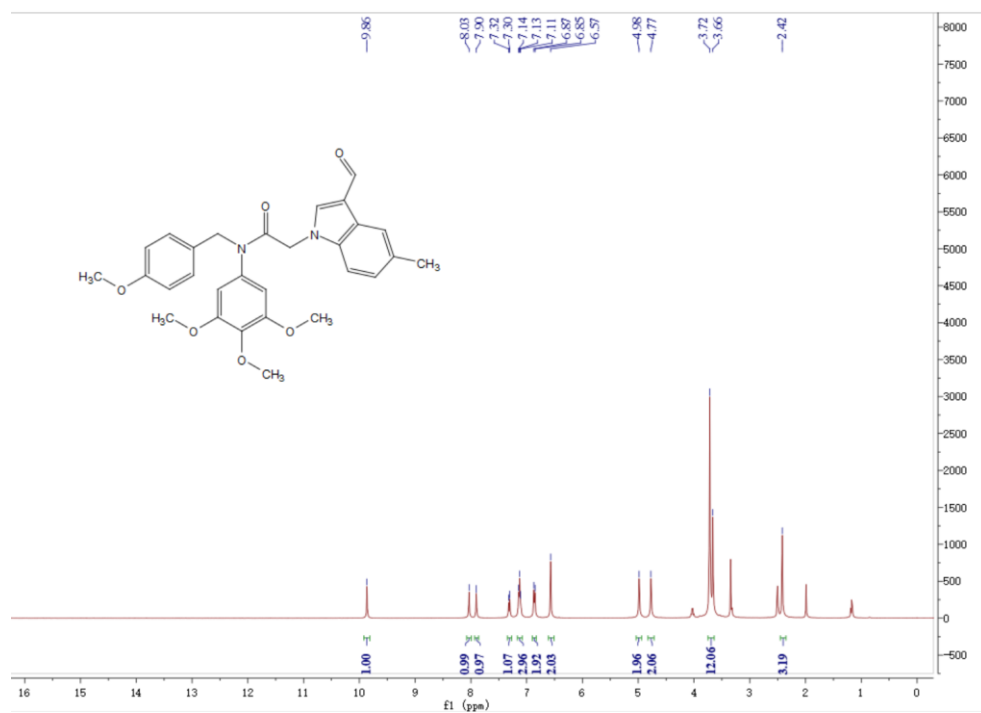


Fig. S15. ¹H NMR spectrum of compound **15f** (400 MHz, DMSO-*d*₆)

^{13}C NMR of compound **15f**

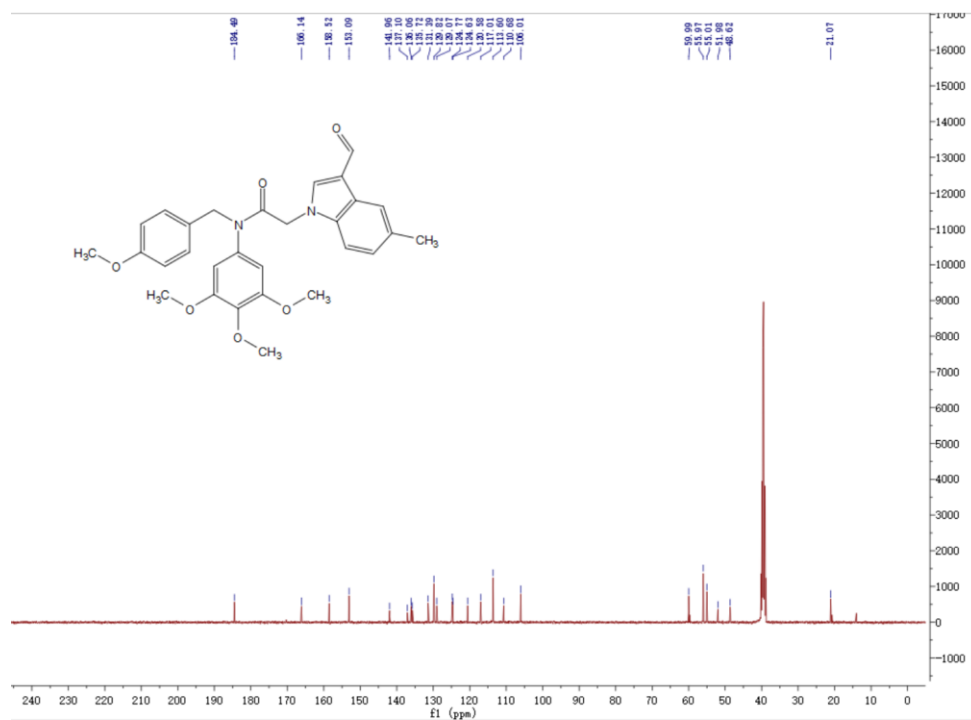


Fig. S16. ^{13}C NMR spectrum of compound **15f** (400 MHz, $\text{DMSO-}d_6$)

HRMS of compound 15f

MOYO-224

18-Jul-2019

LHM-7598 4 (0.069) AM (Cen,4, 80.00, Ht,5000.0,0.00,1.00); Sm (Mn, 2x3.00); Cm (1:22)

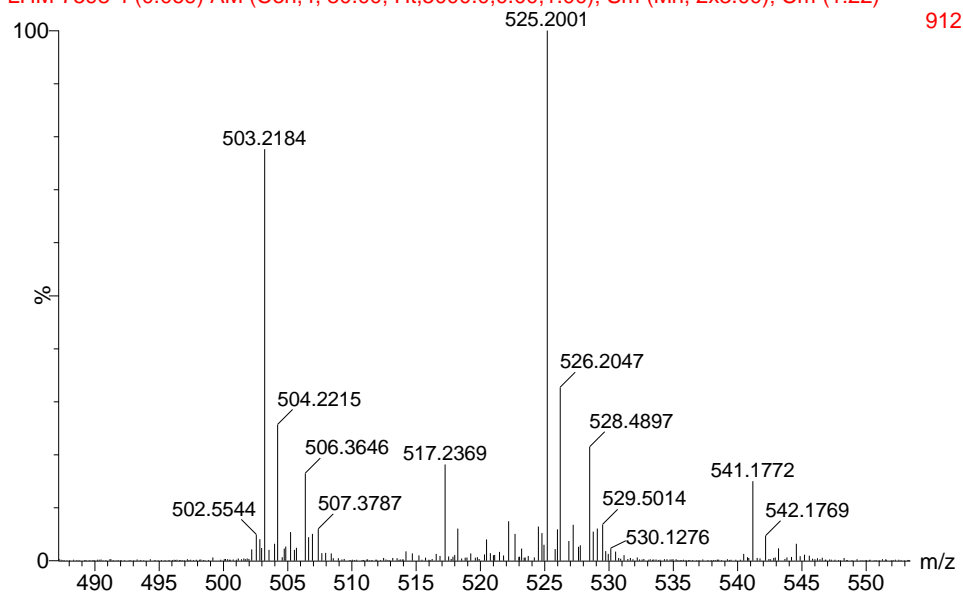


Fig. S17. HRMS spectrum of compound 15f

Chemical structure of compound 10: COc1ccc(cc1)CN(C(=O)CN2C=CC(=C(C=C2)Br)C3=CC(OC)=C(OC)C=C3)C4=CC(OC)=C(OC)C=C4

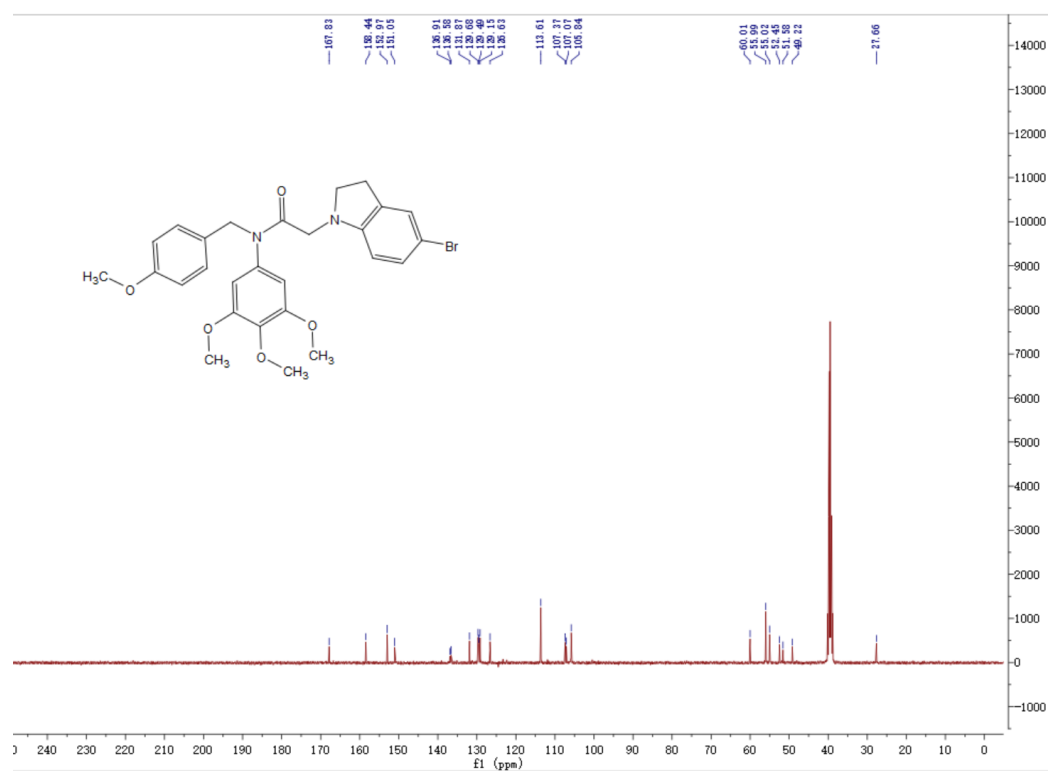
¹H NMR spectrum (CDCl₃) of compound 10. The x-axis represents the chemical shift in ppm (δ), ranging from 12.5 to 0.0. The y-axis represents the intensity, ranging from 0 to 60,000. The spectrum shows several peaks, with integration values provided below the baseline.

Integration values (from left to right): 4.00, 1.99, 1.91, 0.89, 2.00, 1.94, 2.02, 2.01, 2.11, 1.91.

Chemical shifts (δ) listed at the top: 7.13, 7.11, 7.09, 7.08, 7.01, 6.91, 6.81, 6.80, 6.73, 6.71, 4.75, 3.89, 3.72, 3.71, 3.67, 3.64, 3.49, 3.47, 3.40, 3.39, 3.38, 3.38, 3.38.

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¹³C NMR of compound 15g



HRMS of compound 15g

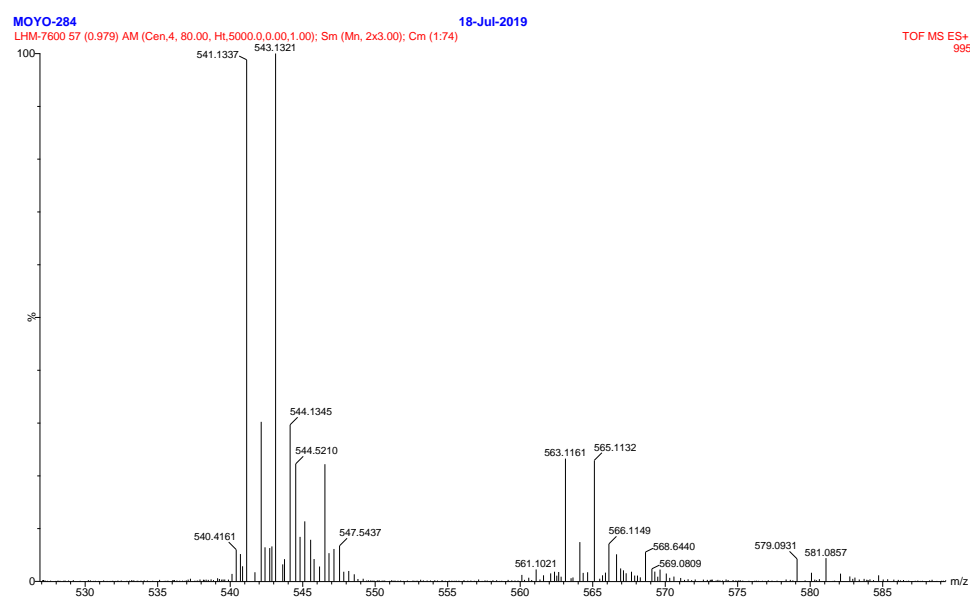
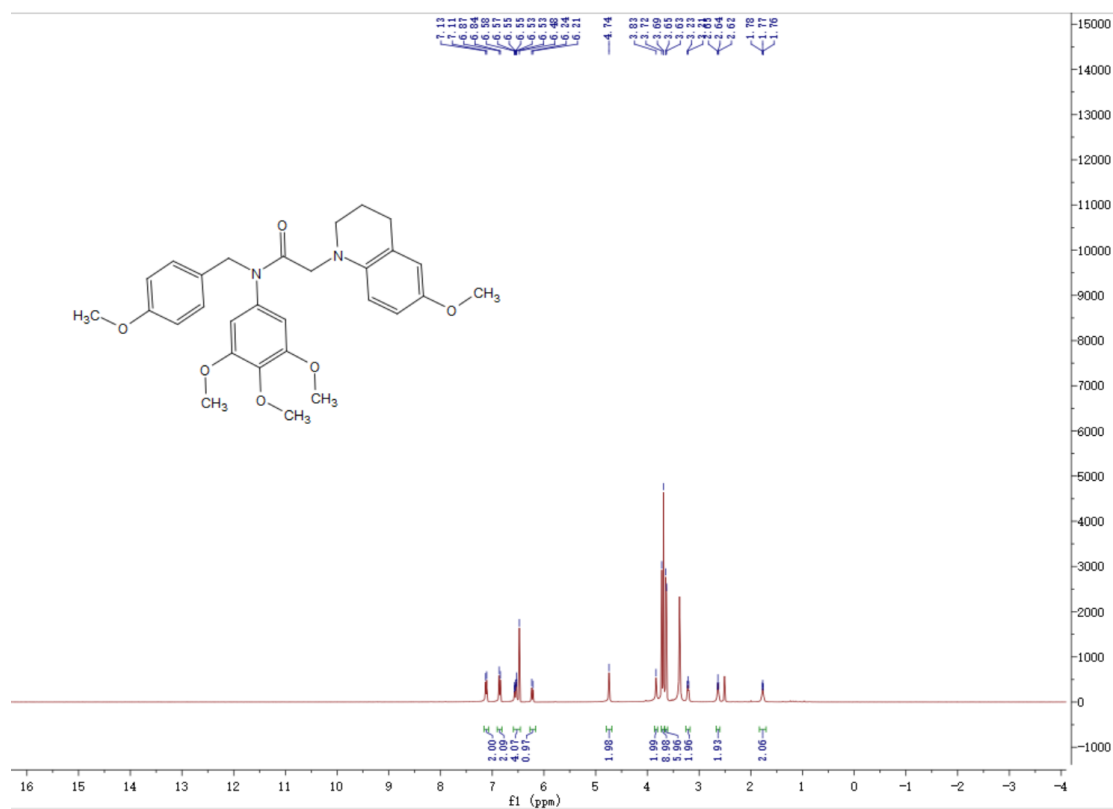


Fig. S20. HRMS spectrum of compound 15g

¹H NMR of compound 15h



^{13}C NMR of compound **15h**

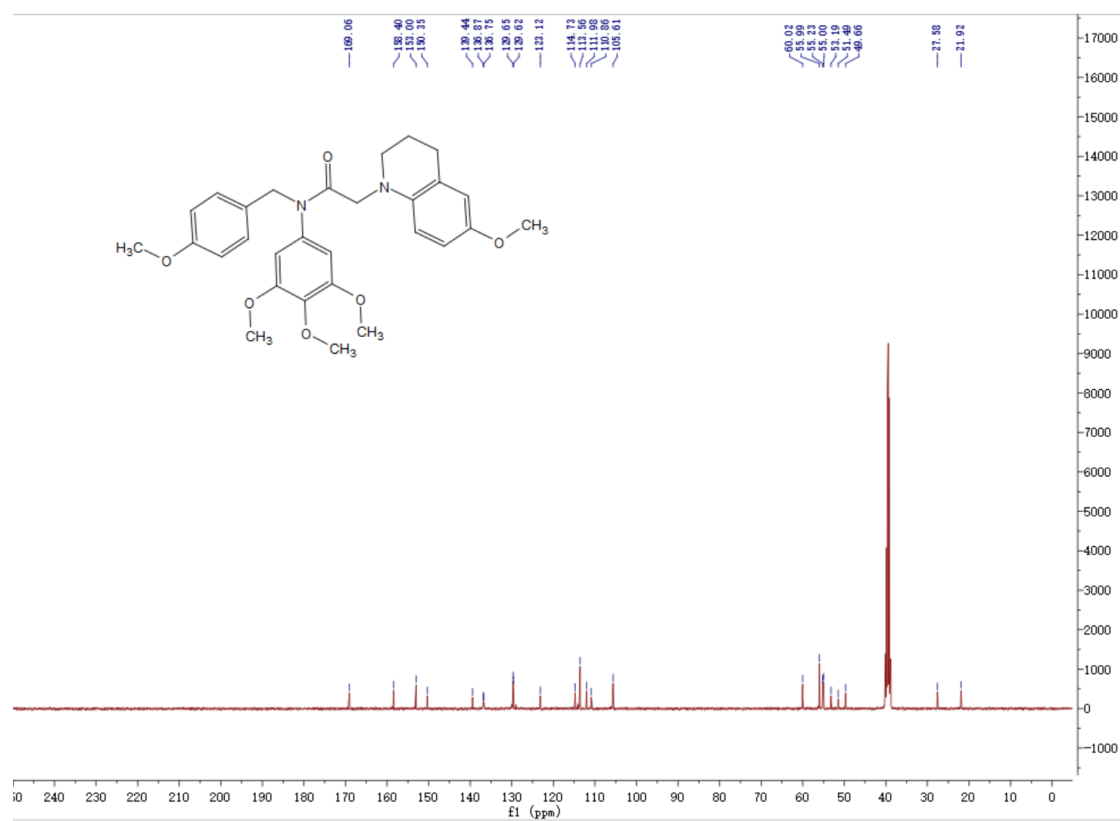


Fig. S22. ^{13}C NMR spectrum of compound **15h** (400 MHz, $\text{DMSO}-d_6$)

HRMS of compound 15h

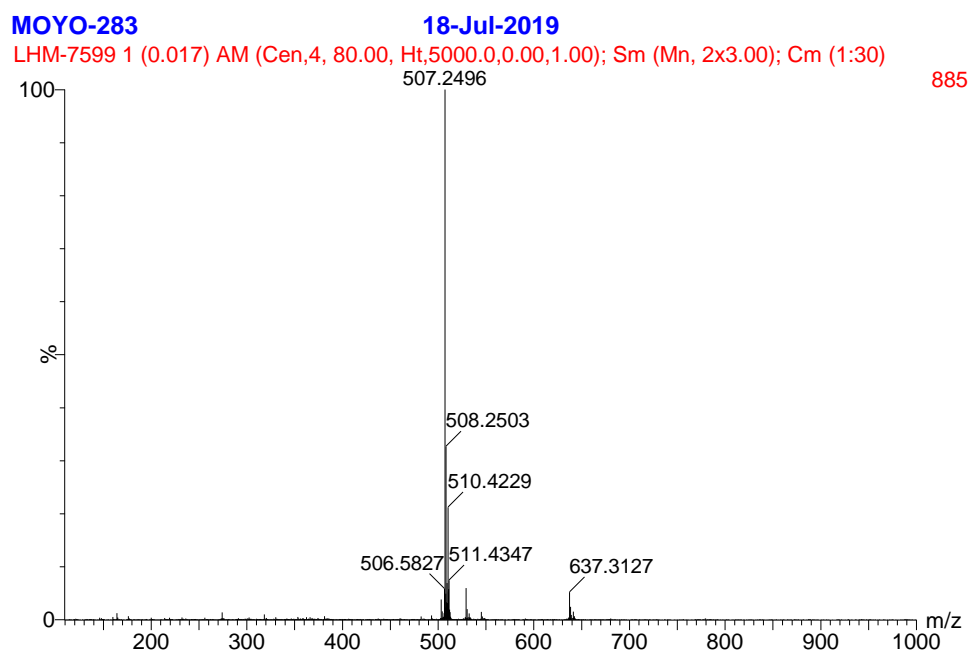


Fig. S23. HRMS spectrum of compound 15g

¹H NMR of compound 19a

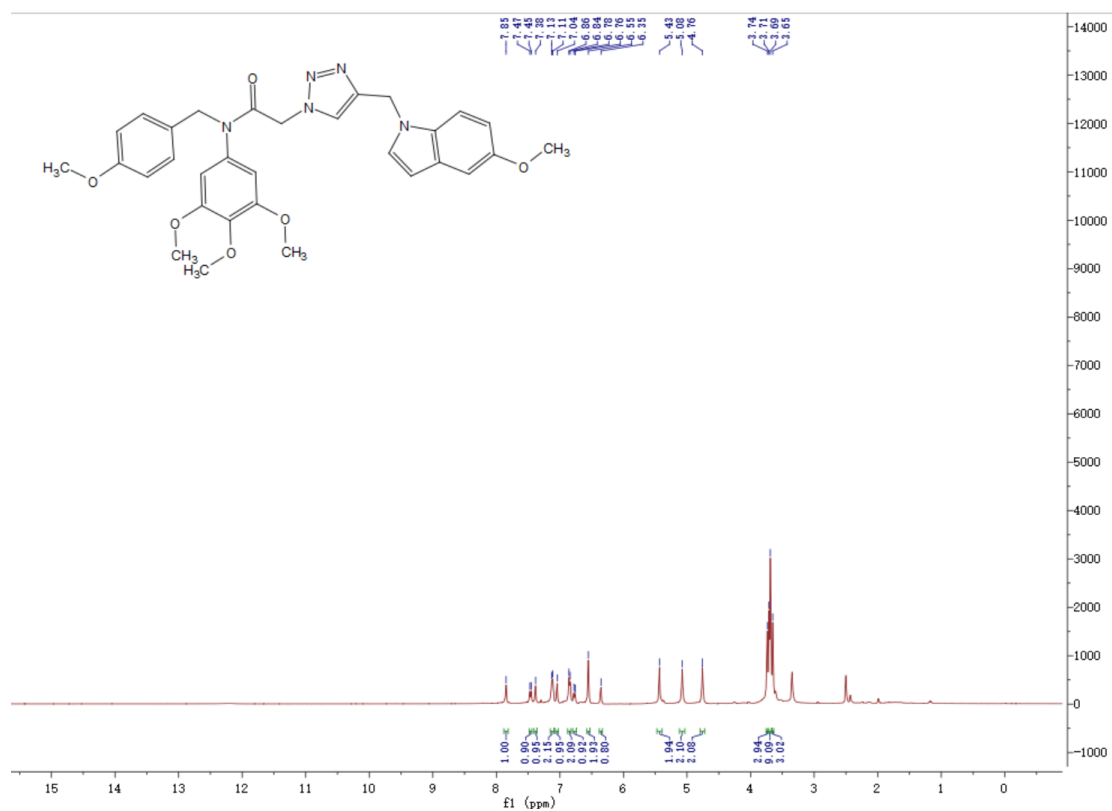


Fig. S24. ¹H NMR spectrum of compound 19a (400 MHz, DMSO-*d*₆)

¹³C NMR of compound 19a

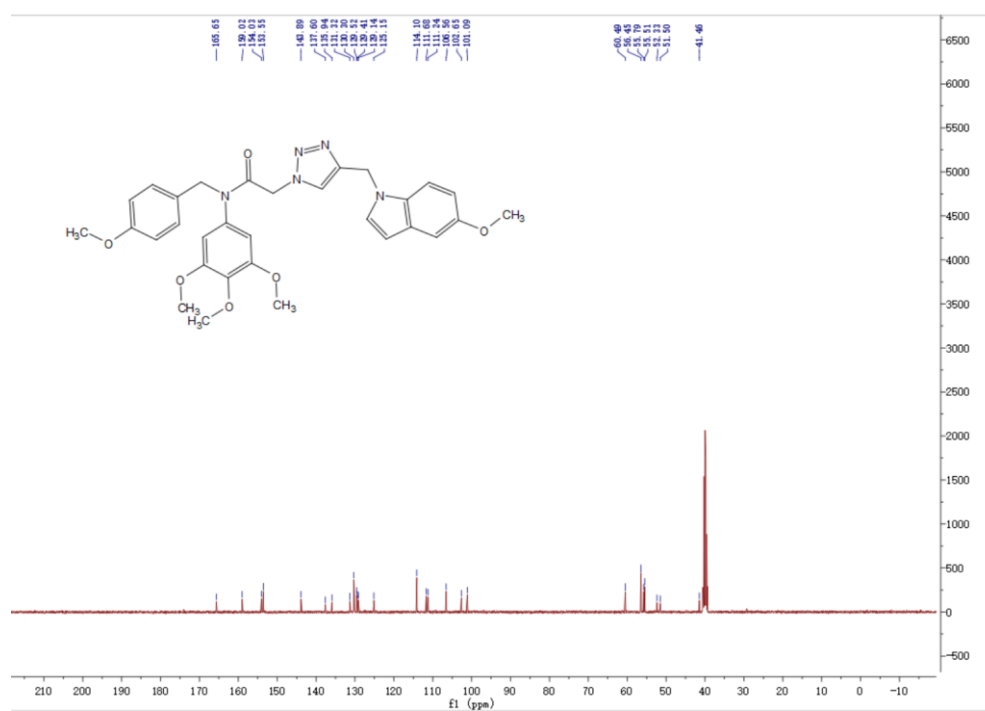


Fig. S25. ^{13}C NMR spectrum of compound **19a** (400 MHz, DMSO-*d*6)

HRMS of compound 19a

MOYO-402

18-Jul-2019

LHM-7624 26 (0.451) AM (Cen,4, 80.00, Ht,5000.0,0.00,1.00); Sm (Mn, 2x3.00); Cm (1:27)

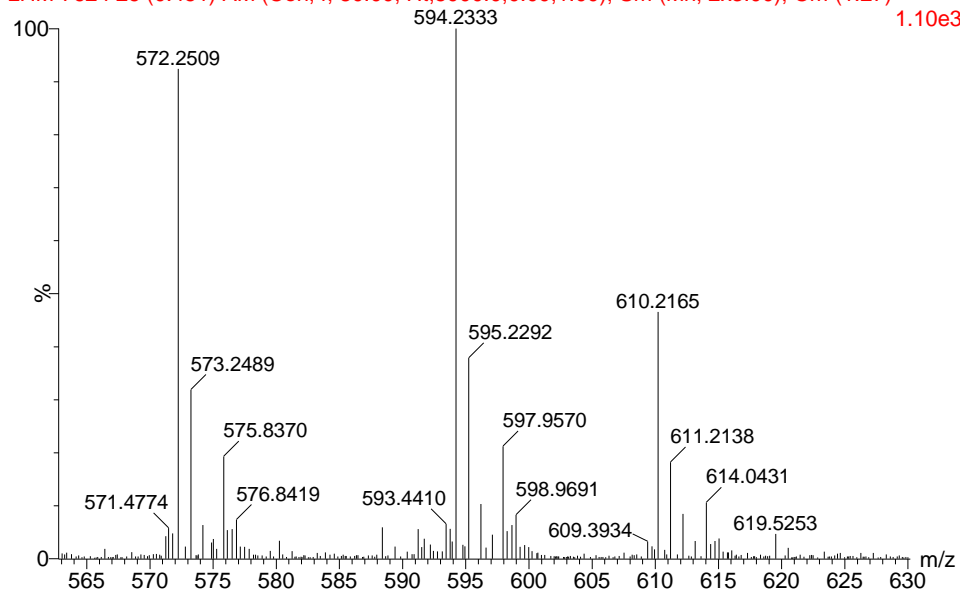


Fig. S26. HRMS spectrum of compound 19a

^1H NMR of compound **19b**

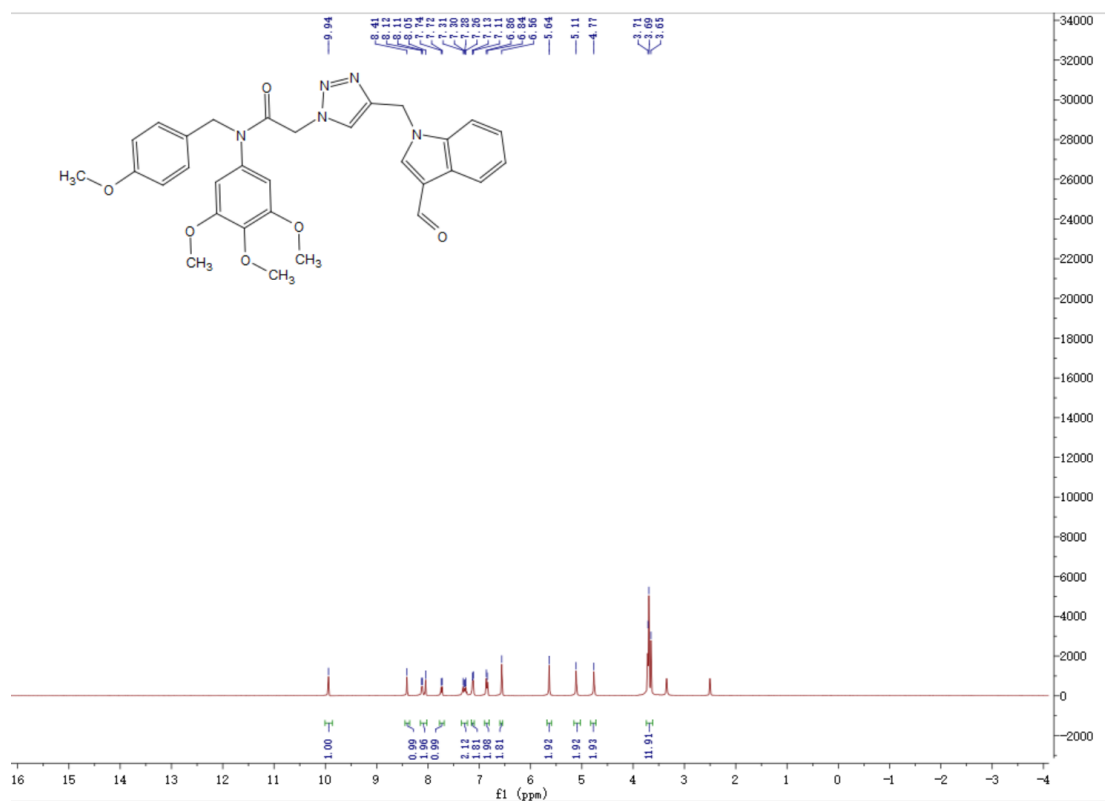


Fig. S27. ^1H NMR spectrum of compound **19b** (400 MHz, $\text{DMSO-}d_6$)

¹³C NMR of compound **19b**

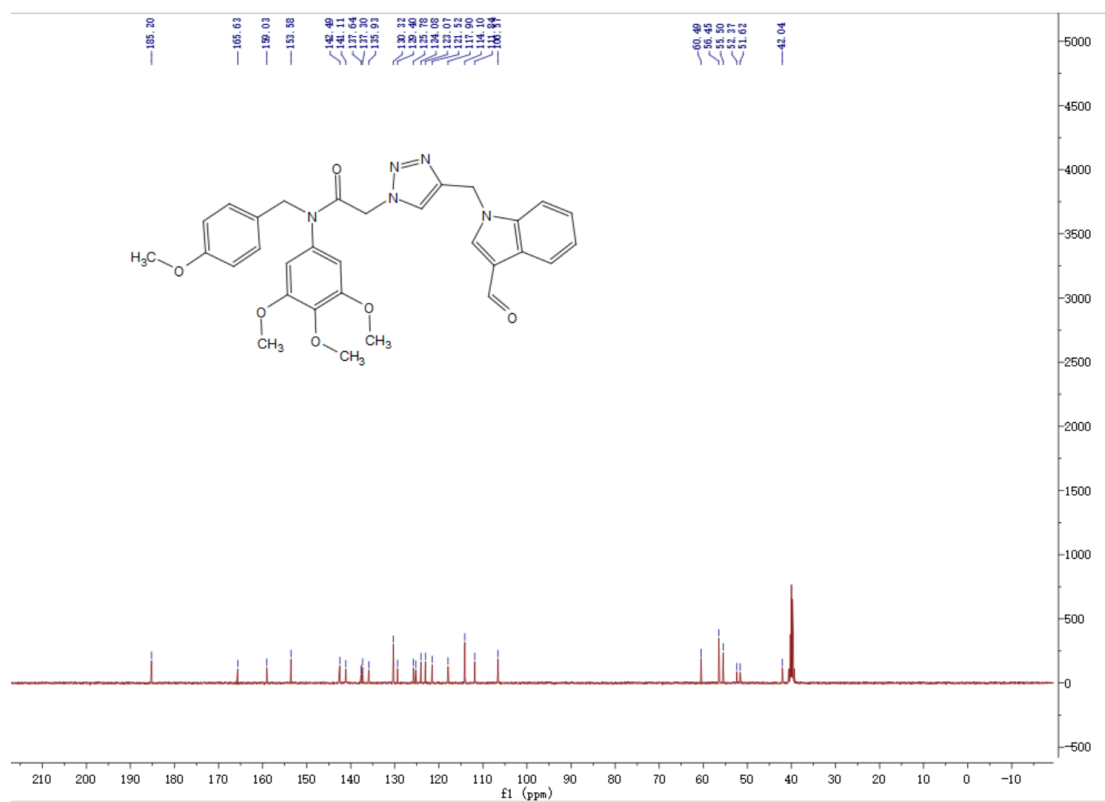


Fig. S28. ¹³C NMR spectrum of compound **19b** (400 MHz, DMSO-*d*₆)

HRMS of compound 19b

MOYO-404

18-Jul-2019

LHM-7626 6 (0.103) AM (Cen,4, 80.00, Ht,5000.0,0.00,1.00); Sm (Mn, 2x3.00); Cm (1:23)

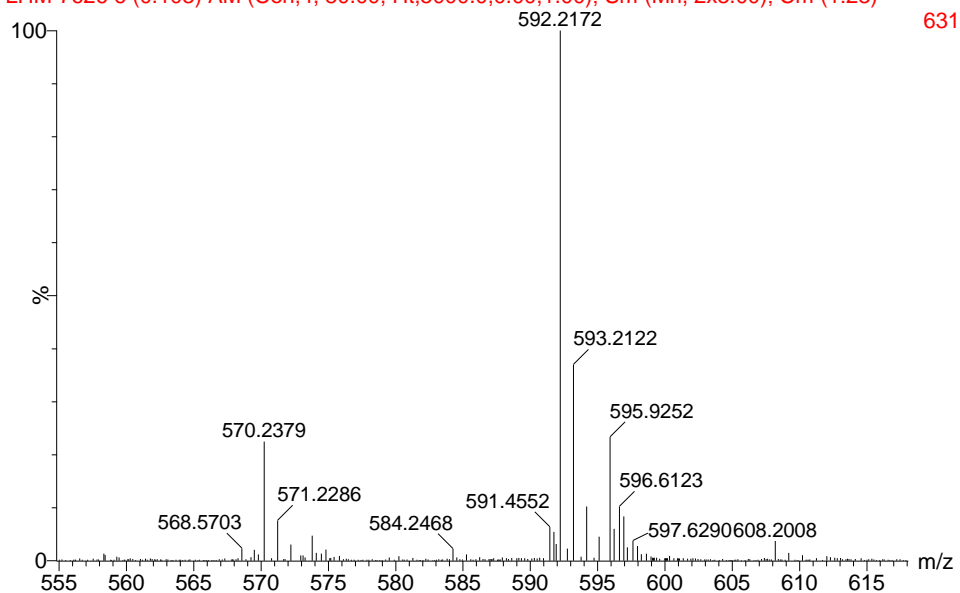


Fig. S29. HRMS spectrum of compound 19b

¹H NMR of compound 19c

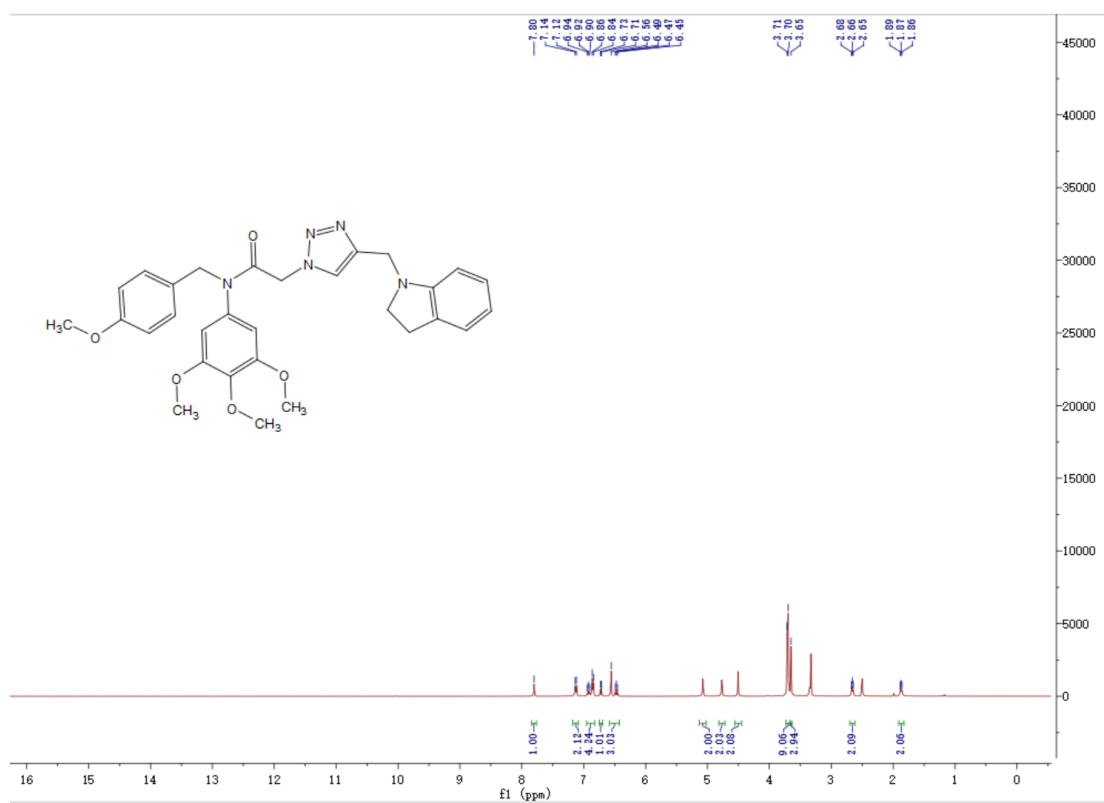


Fig. S30. ¹³C NMR spectrum of compound 19c (400 MHz, DMSO-d₆)

¹³C NMR of compound **19c**

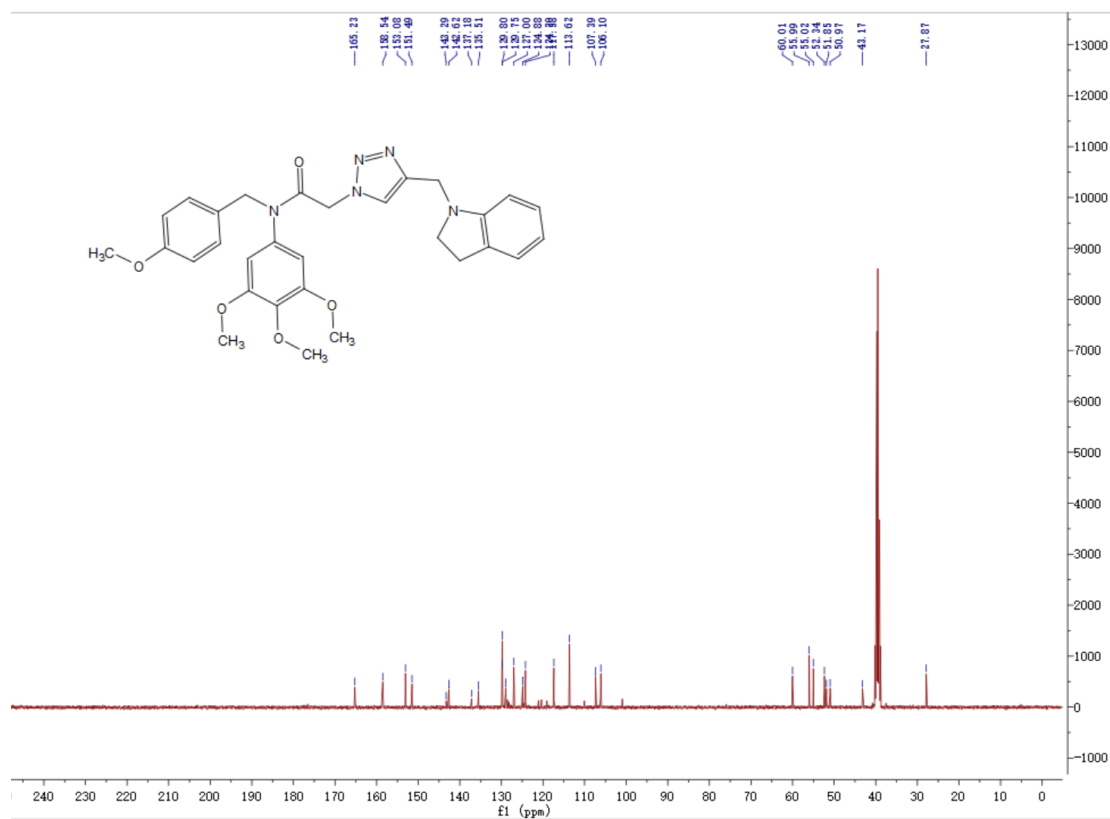


Fig. S31. ¹³C NMR spectrum of compound **19c** (400 MHz, DMSO-*d*₆)

HRMS of compound 19c

MOYO-273

18-Jul-2019

LHM-7620 8 (0.139) AM (Cen,4, 80.00, Ht,5000.0,0.00,1.00); Sm (Mn, 2x3.00); Cm (1:19)

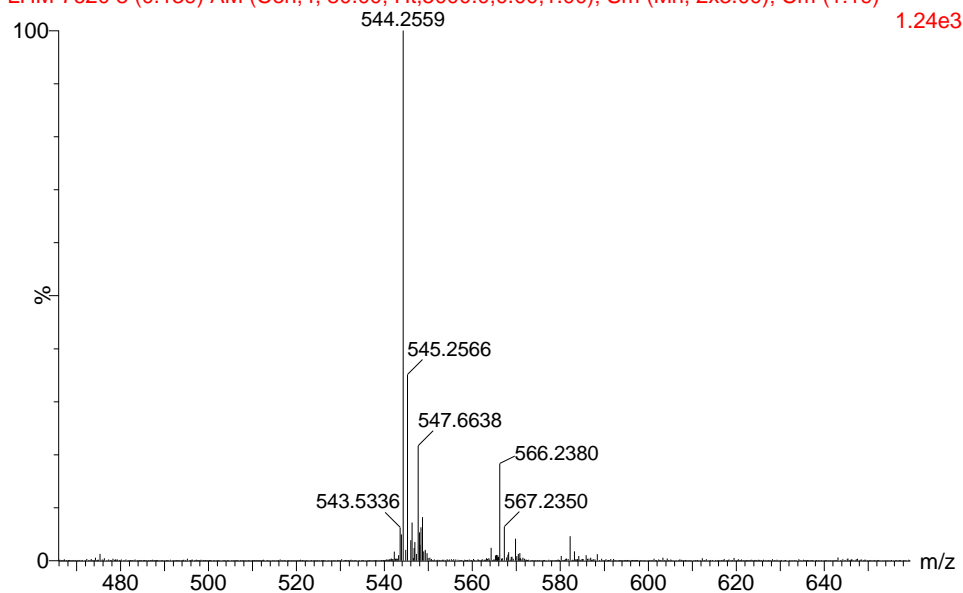


Fig. S32. HRMS spectrum of compound 19c

Chemical structure of compound 10: COc1ccc(cc1)CN(C(=O)CN2C=NC=C2Cc3ccccc3C)C4=CC(OC)=C(OC)C=C4

¹H NMR spectrum (CDCl₃) of compound 10. The x-axis represents the chemical shift in ppm (δ), ranging from 0.5 to 8.5. The y-axis represents the intensity in arbitrary units, ranging from -2000 to 24000. The spectrum shows several peaks corresponding to the protons in the molecule. Integration values are provided below the baseline, and chemical shift values are listed above the peaks.

Chemical Shift (ppm)	Integration
~7.78	0.94
~7.13	2.17
~7.07	2.00
~6.96	2.15
~6.52	3.98
~5.07	2.00
~4.77	2.01
~4.76	1.00
~4.54	0.99
~4.50	
~4.27	
~4.23	
~3.71	8.91
~3.70	2.68
~3.65	
~3.05	0.99
~2.71	
~2.70	
~2.65	
~2.05	
~2.01	
~1.99	
~1.32	3.00
~1.30	

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^{13}C NMR of compound **19d**

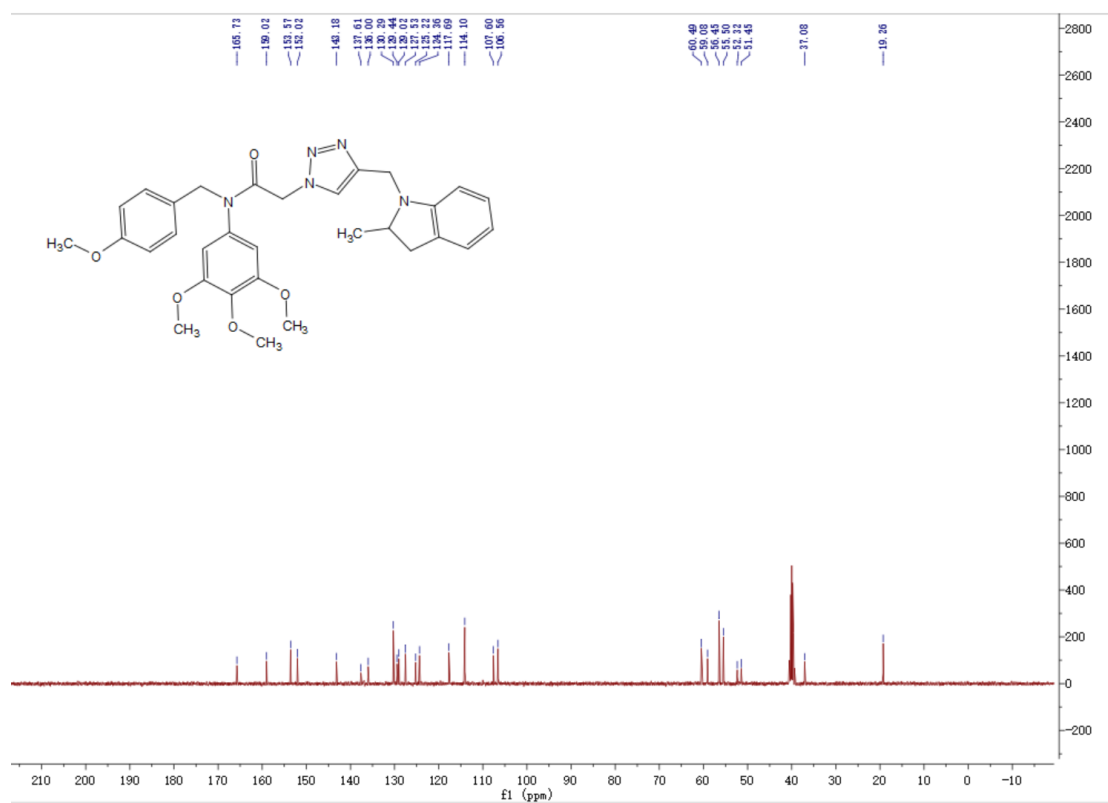


Fig. S34. ^{13}C NMR spectrum of compound **19d** (400 MHz, DMSO- d_6)

HRMS of compound 19d

MOYO-294

18-Jul-2019

LHM-7622 17 (0.295) AM (Cen,4, 80.00, Ht,5000.0,0.00,1.00); Sm (Mn, 2x3.00); Cm (1:22)

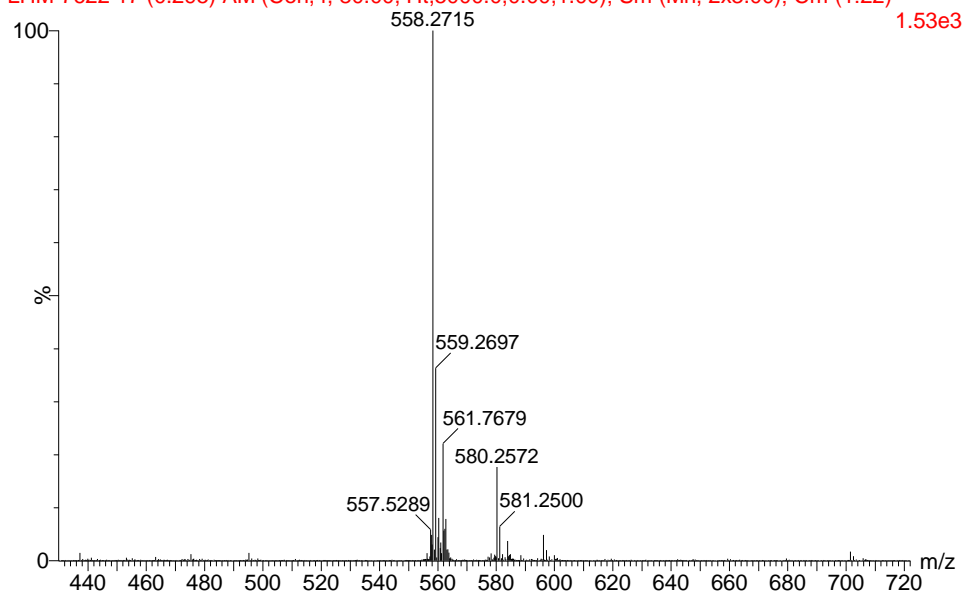


Fig. S35. HRMS spectrum of compound 19d

¹H NMR of compound 19e

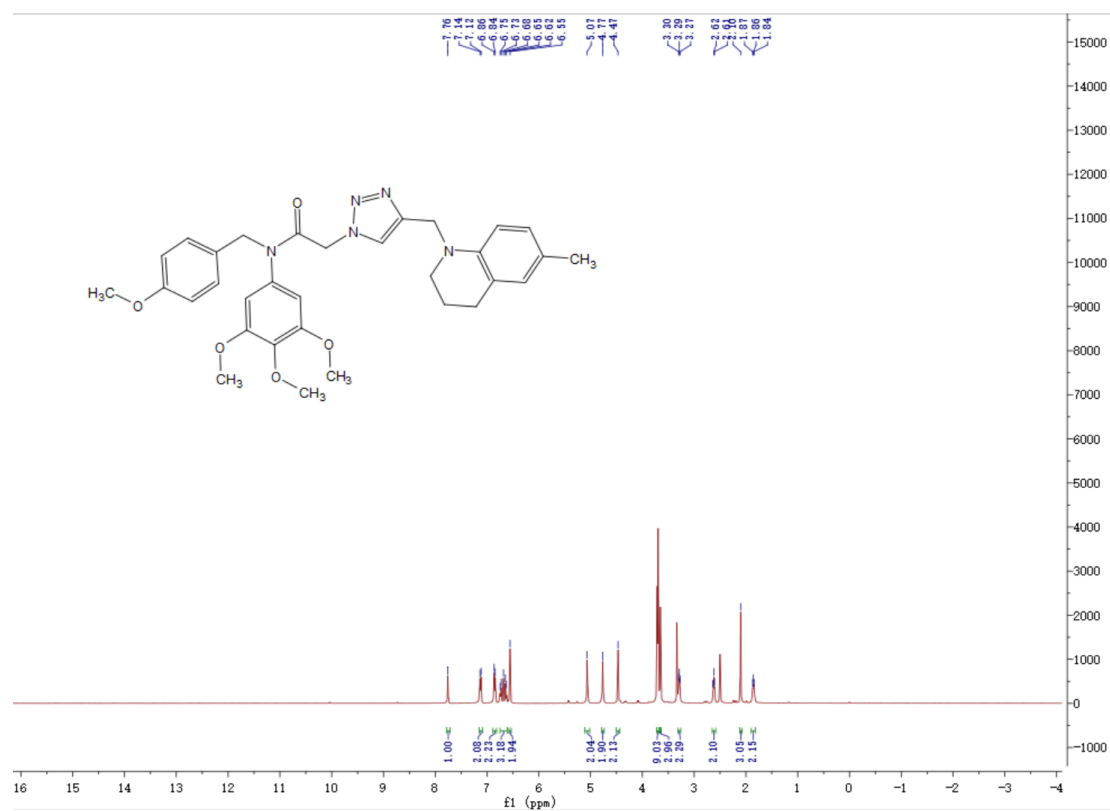


Fig. S36. ¹H NMR spectrum of compound 19e (400 MHz, DMSO-*d*₆)

¹³C NMR of compound **19e**

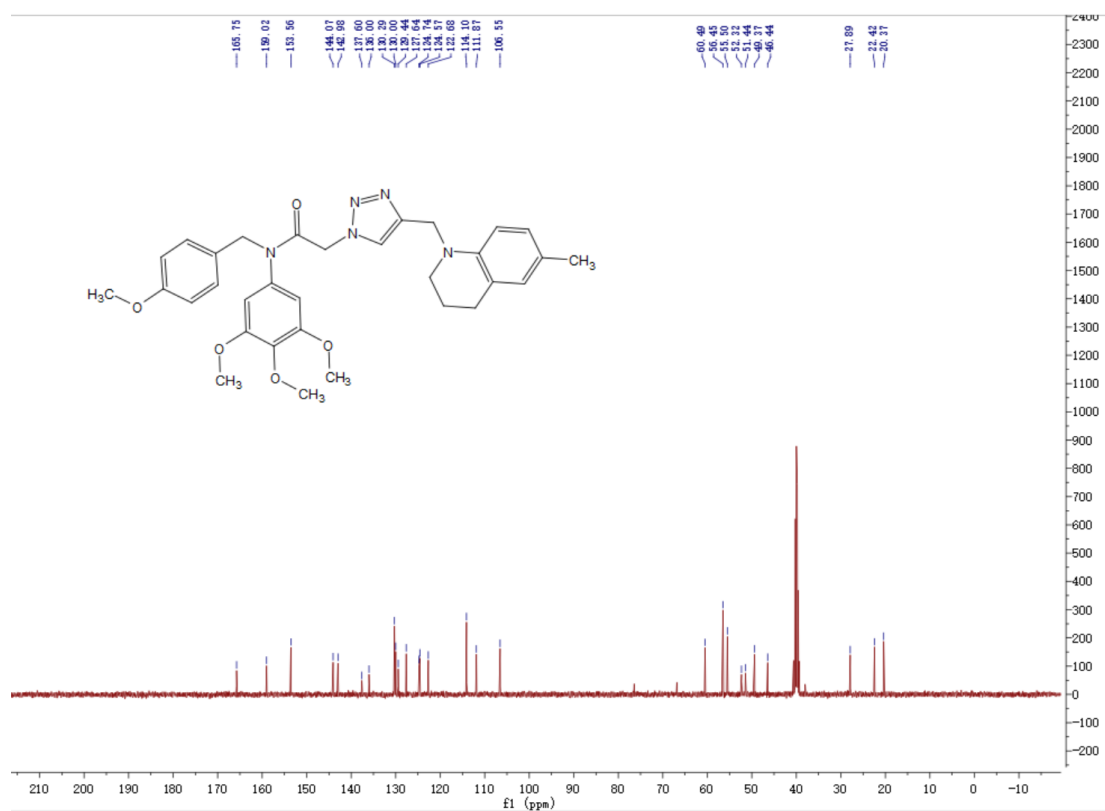


Fig. S37. ¹³C NMR spectrum of compound **19e** (400 MHz, DMSO-*d*₆)

HRMS of compound 19e

MOYO-405

18-Jul-2019

LHM-7627 24 (0.412) AM (Cen,4, 80.00, Ht,5000.0,0.00,1.00); Sm (Mn, 2x3.00); Cm (1:26)

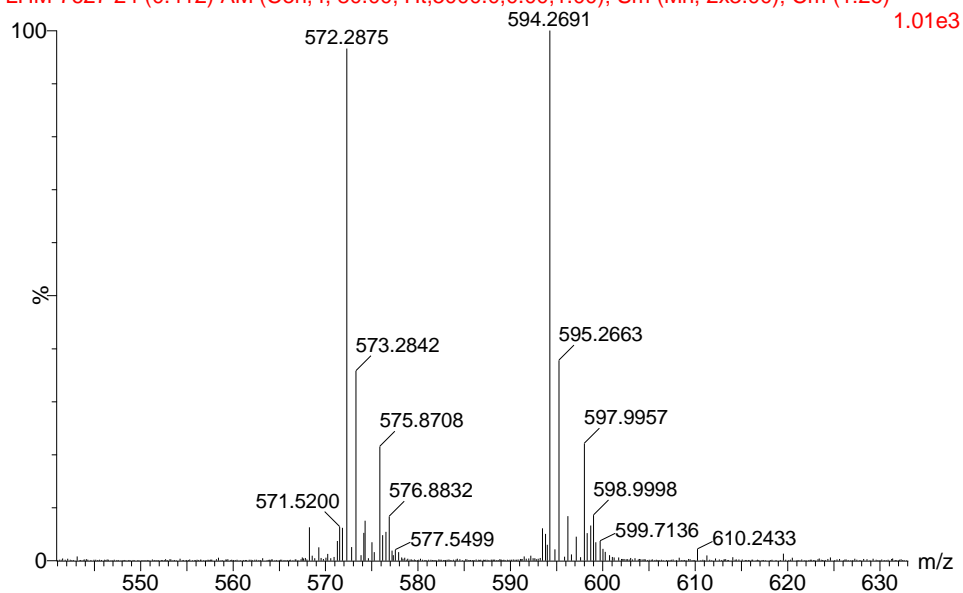


Fig. S38. HRMS spectrum of compound 19g