Design, Synthesis and Anti-proliferative Activity of 3-Aryl-Evodiamines

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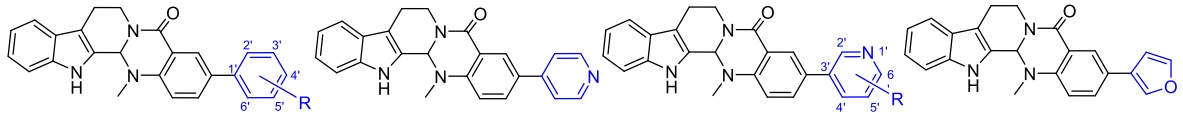
Content

Table 1. Antiproliferative activity of compounds



6a - 6z　　6aa　　6ab - 6ad　　6ae

Compounds	R	Inhibition rate (%) [a]		
		HCT116 [b]	4T1 [c]	HepG2 [b]
6a	H	33.0 ± 5.0	97.1 ± 1.1	39.0 ± 3.1
6b	4'-Me	51.3 ± 2.8	98.0 ± 0.9	61.7 ± 4.1
6c	3'-Me	70.1 ± 1.4	44.3 ± 2.3	39.3 ± 2.8
6d	4'-*i*Pr	22.8 ± 7.2	89.8 ± 1.8	45.4 ± 9.3
6e	4'-OMe	48.1 ± 3.9	82.7 ± 1.6	32.2 ± 3.9
6f	3',5'-OMe	43.7 ± 7.3	98.0 ± 1.7	3.0 ± 9.3
6g	4'-S-Me	69.4 ± 4.0	99.3 ± 0.4	55.3 ± 3.7
6h	3'-S-Me	64.3 ± 2.3	99.4 ± 0.8	14.9 ± 5.0
6i	2'-S-Me	31.4 ± 6.0	69.2 ± 3.2	2.3 ± 10.2
6j	4'-OH	43.6 ± 3.9	84.6 ± 2.0	32.4 ± 3.1
6k	4'-CO-NH_2	62.4 ± 2.6	52.5 ± 2.0	47.9 ± 2.7
6l	4'-Cl	32.6 ± 6.1	60.5 ± 3.9	10.9 ± 8.4
6m	3'-Cl	36.4 ± 6.9	44.8 ± 3.2	35.5 ± 2.6
6n	2'-Cl	97.6 ± 1.2	51.2 ± 6.7	97.8 ± 0.2
6o	4'-F	25.7 ± 4.5	34.9 ± 3.2	42.1 ± 6.4
6p	3',5'-F	37.8 ± 1.9	72.1 ± 3.1	20.4 ± 0.6
6q	4'-CF_3	51.2 ± 1.4	78.6 ± 1.7	28.0 ± 1.3
6r	3',5'-CF_3	73.2 ± 2.7	99.5 ± 0.9	70.4 ± 3.1
6s	4'-CN	96.3 ± 2.4	99.6 ± 1.8	88.3 ± 6.5
6t	4'-CH-CH_2	67.0 ± 4.6	94.1 ± 1.9	53.2 ± 3.2
6u	4'-CHO	62.5 ± 2.7	88.8 ± 1.9	42.2 ± 5.4
6v	4'-CO-Me	71.0 ± 1.5	98.8 ± 0.5	75.9 ± 3.1
6w	4'-CO-OMe	65.6 ± 0.5	95.4 ± 1.3	94.2 ± 1.2
6x	4'-CO-Ph	22.9 ± 3.5	65.6 ± 5.0	50.6 ± 2.1
6y	4'-SO_2-Me	88.2 ± 1.6	87.2 ± 1.1	61.2 ± 4.0
6z	4'-SO_2-*i*Pr	72.3 ± 2.1	93.1 ± 3.2	42.4 ± 4.4
6aa	—	6.7 ± 2.7	59.3 ± 7.1	19.9 ± 6.6
6ab	6'-OMe	44.5 ± 3.7	46.1 ± 2.8	23.7 ± 5.6
6ac	6'-Cl	74.9 ± 0.7	92.6 ± 1.2	73.8 ± 2.4
6ad	6'-F	70.2 ± 3.1	94.1 ± 1.2	87.5 ± 6.5
6ae	—	70.0 ± 2.8	36.8 ± 5.1	32.4 ± 2.1
Evodiamine	—	40.4 ± 1.7	35.5 ± 0.9	22.9 ± 1.0
Camptothecin	—	98.7 ± 0.3	41.5 ± 0.01	95.8 ± 0.9

[a] MTT method; the cells were incubated with the indicated compounds for 48 h (mean ± SD, n = 3); [b] Inhibition rate was tested at a concentration of 12.5 μM; [c] Inhibition rate was tested at a concentration of 25 μM.

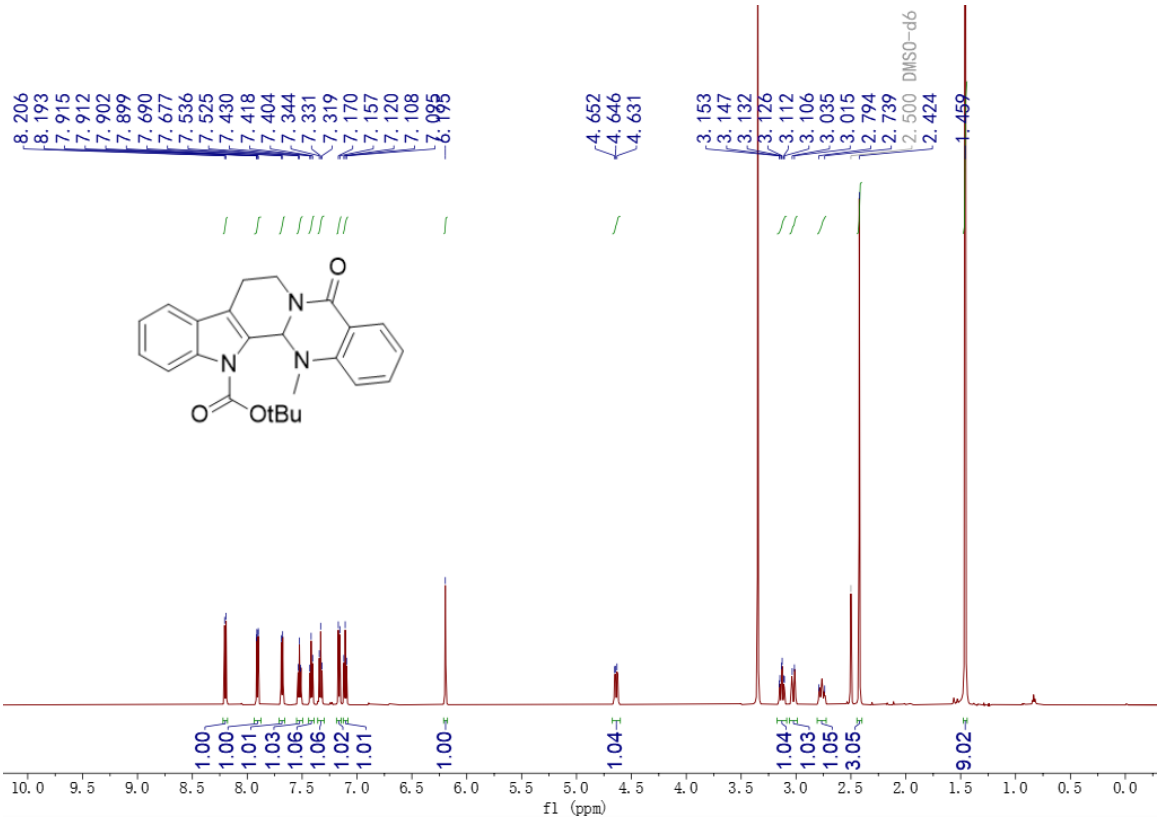


Figure 1. ^{1}H NMR spectrum of compound **2** (600 MHz, DMSO-d_6)

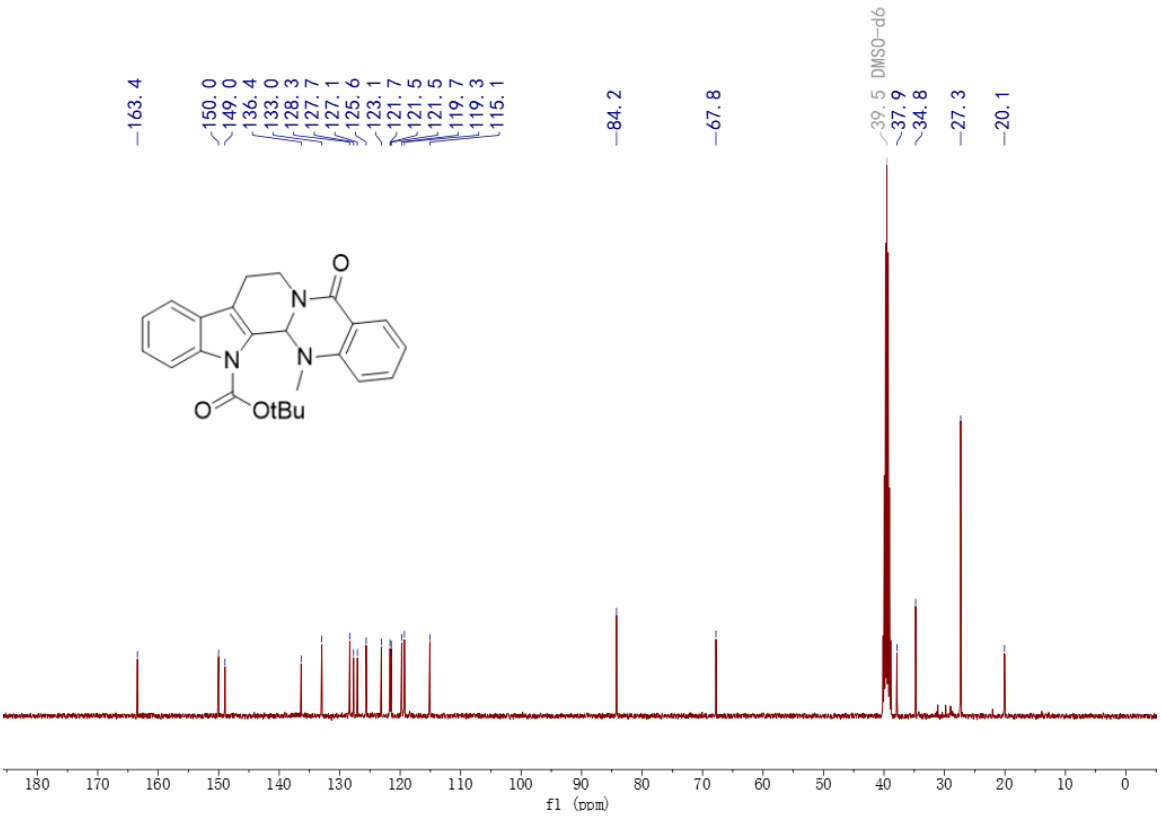


Figure 2. ^{13}C NMR spectrum of compound **2** (100 MHz, DMSO-d_6)

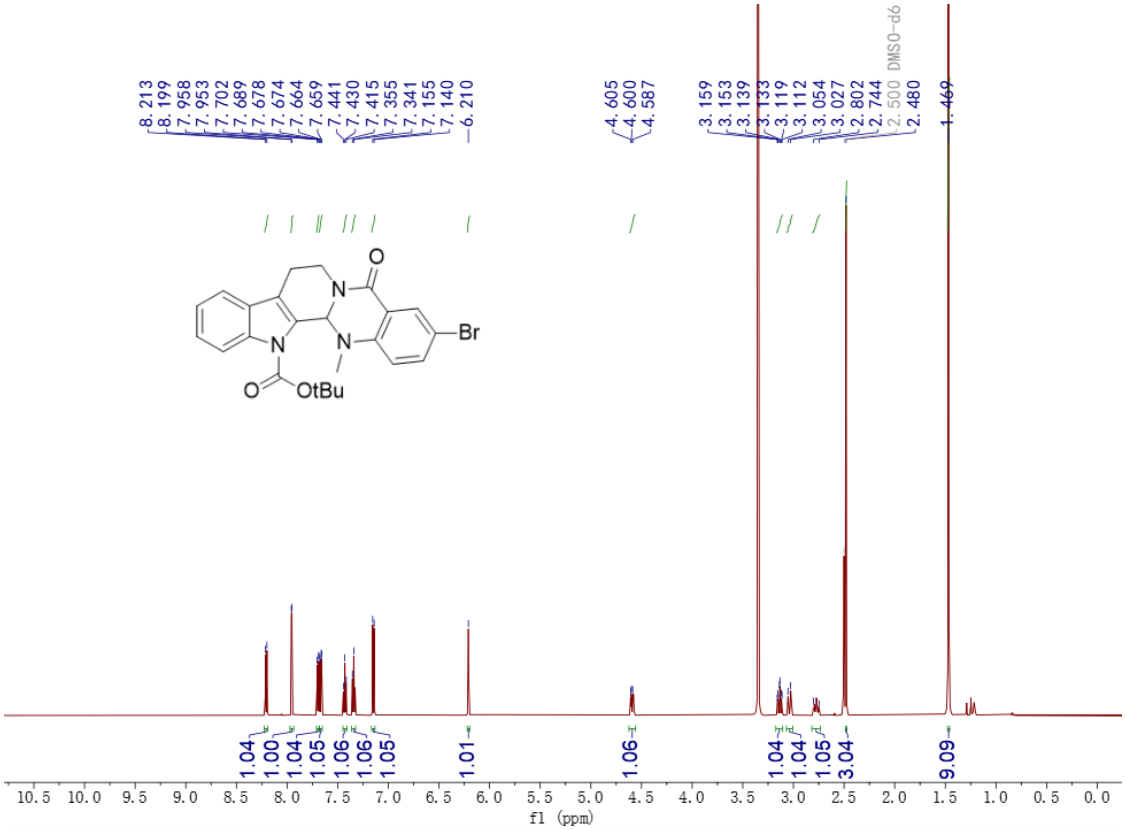


Figure 3. ^{1}H NMR spectrum of compound **3** (600 MHz, DMSO-d_6)

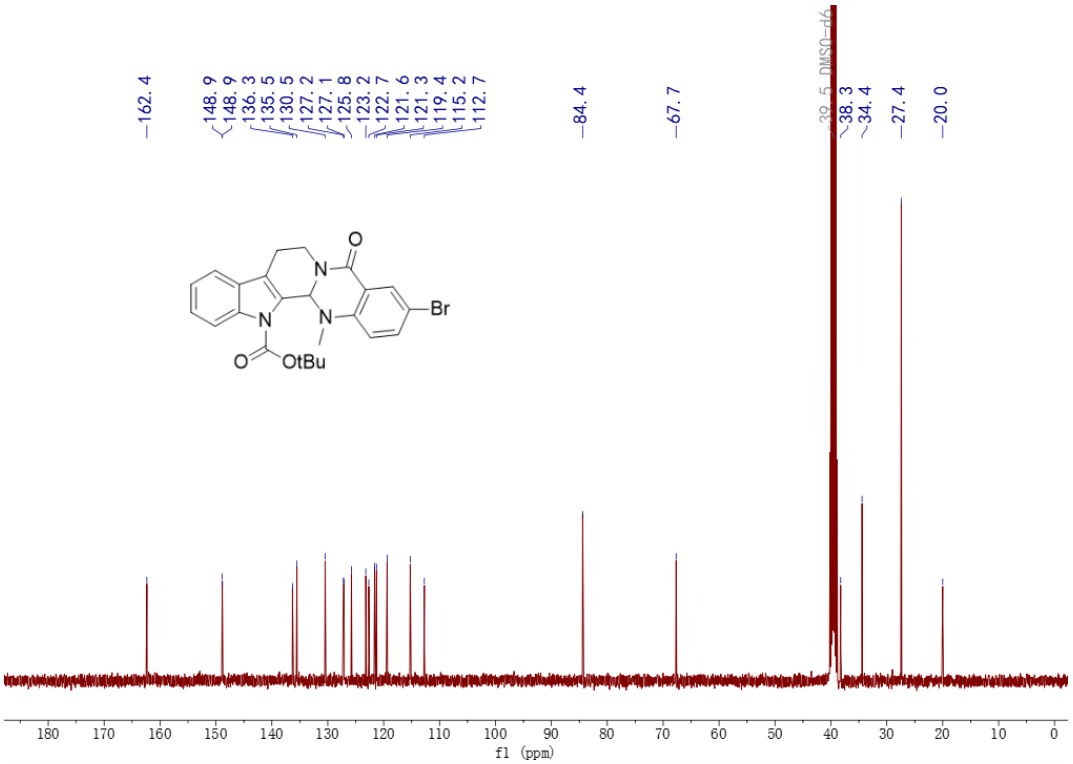


Figure 4. ^{13}C NMR spectrum of compound **3** (100 MHz, DMSO-d_6)

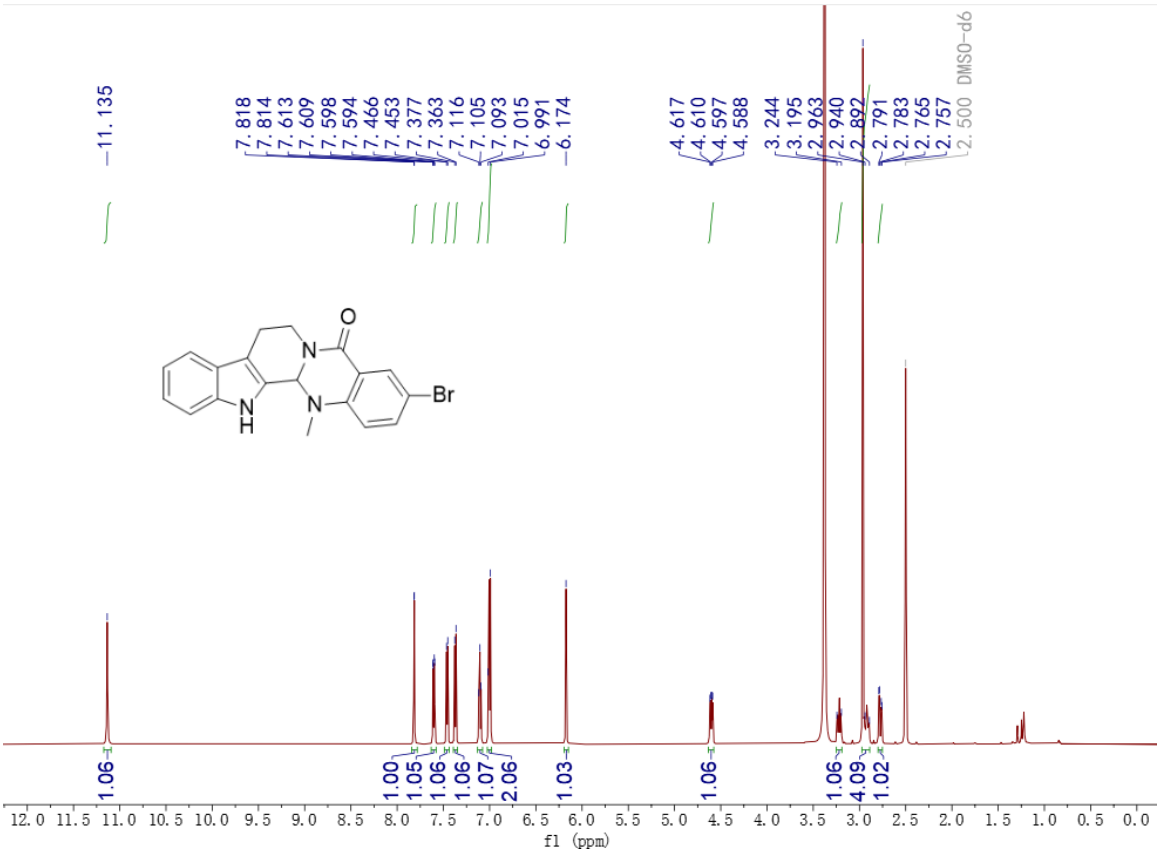


Figure 5. ^{1}H NMR spectrum of compound **4** (600 MHz, DMSO-d_6)

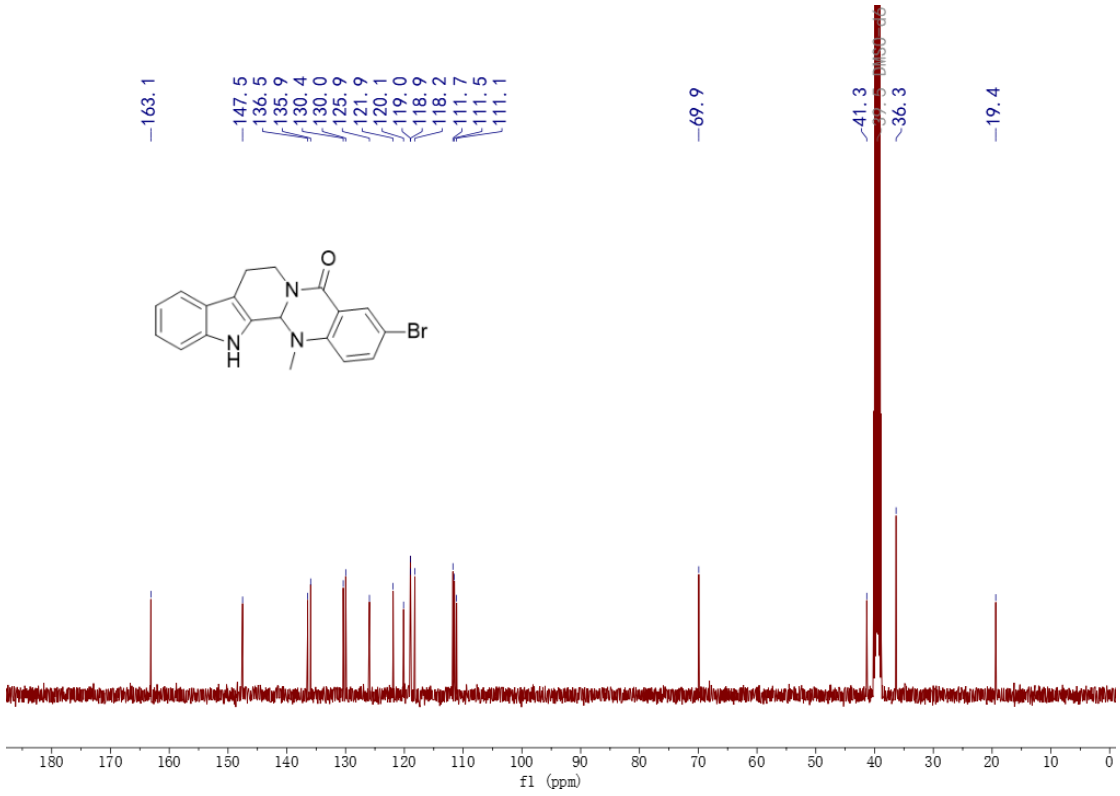


Figure 6. ^{13}C NMR spectrum of compound **4** (100 MHz, DMSO-d_6)

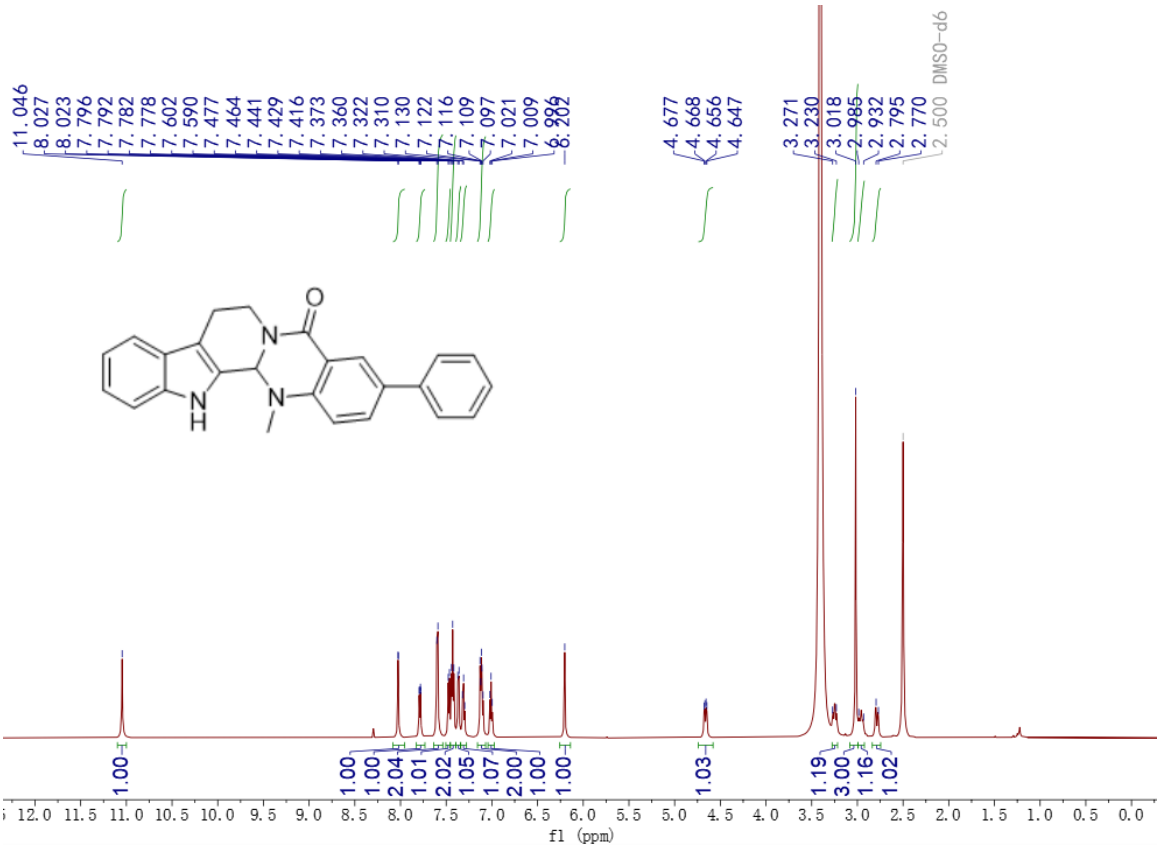


Figure 7. ^{1}H NMR spectrum of compound **6a** (600 MHz, DMSO-d_6)

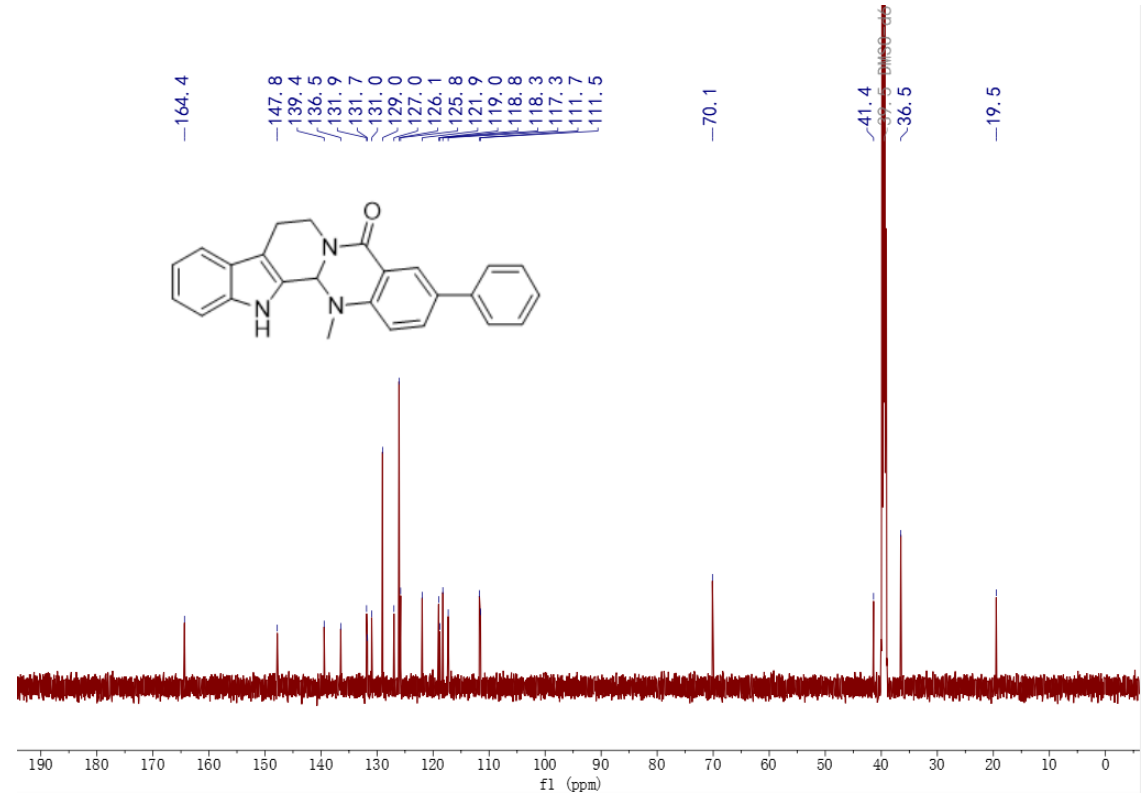


Figure 8. ^{13}C NMR spectrum of compound **6a** (100 MHz, DMSO-d_6)

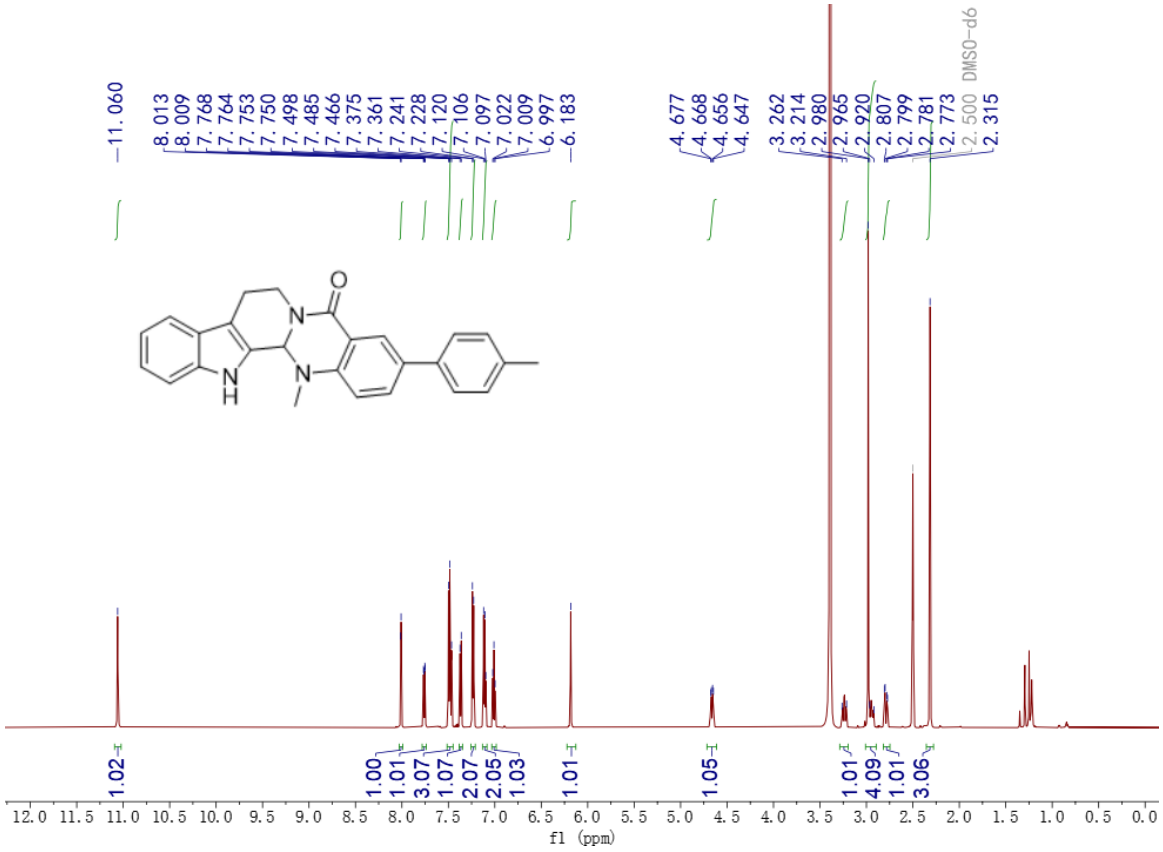


Figure 9. ^{1}H NMR spectrum of compound **6b** (600 MHz, DMSO-d_6)

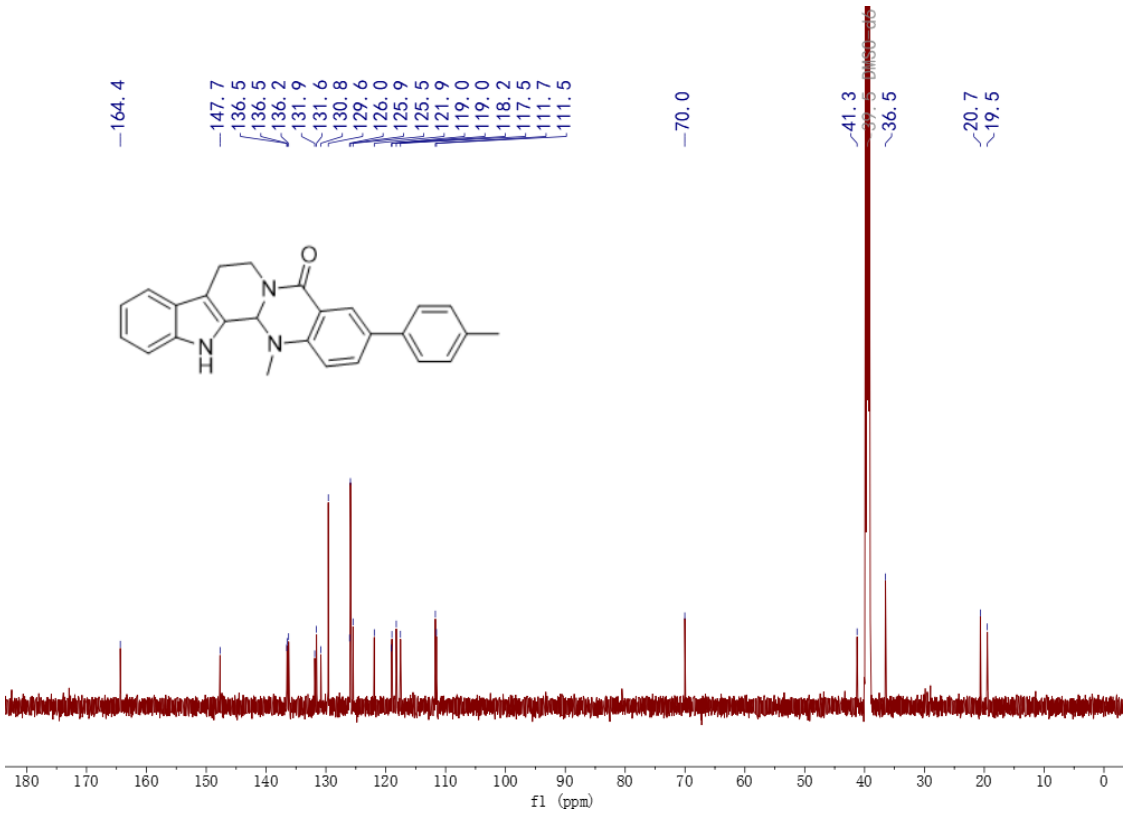


Figure 10. ^{13}C NMR spectrum of compound **6b** (100 MHz, DMSO-d_6)

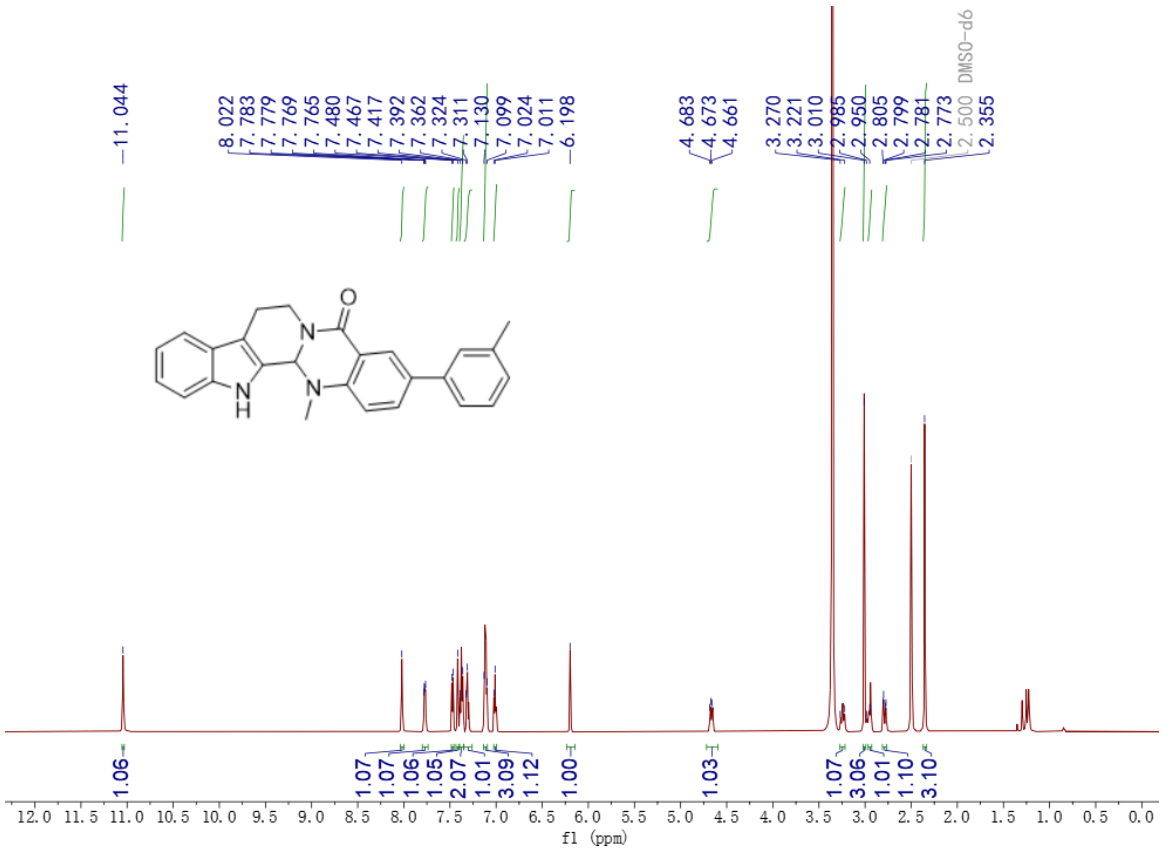


Figure 11. ^{1}H NMR spectrum of compound **6c** (600 MHz, DMSO-d_6)

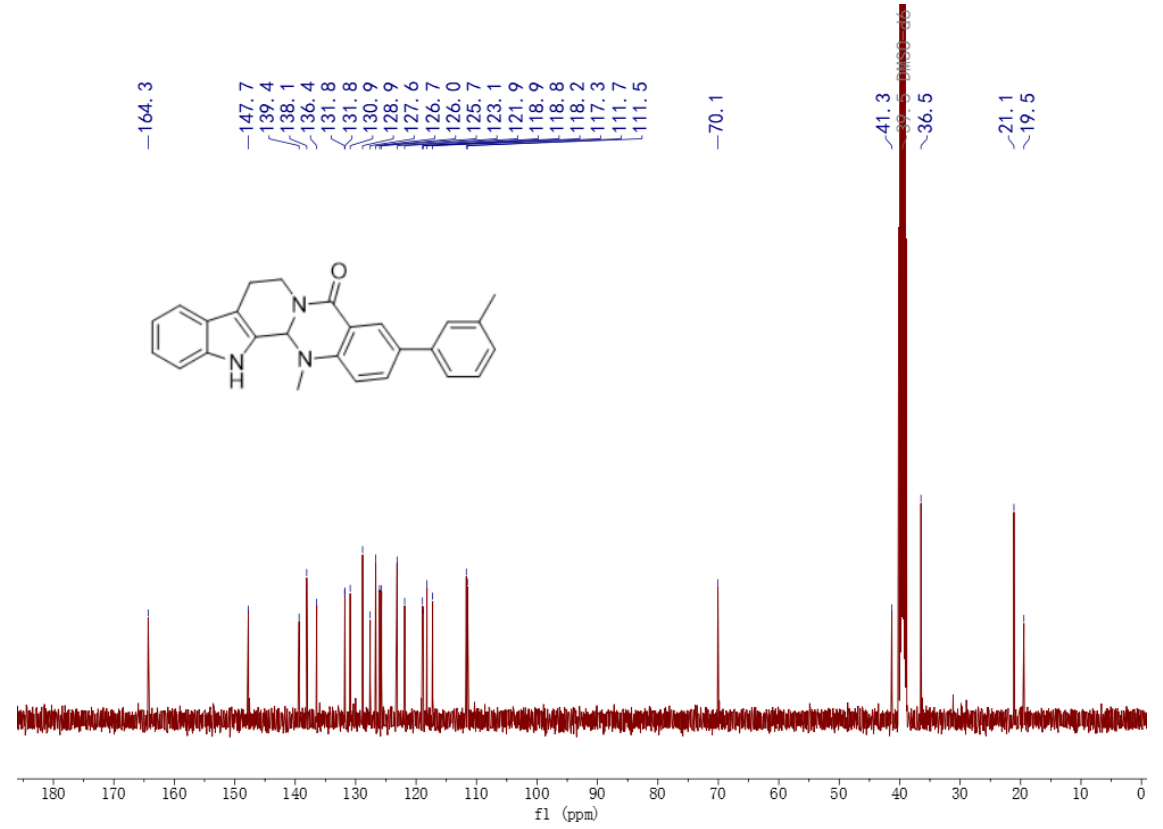


Figure 12. ^{13}C NMR spectrum of compound **6c** (150 MHz, DMSO-d_6)

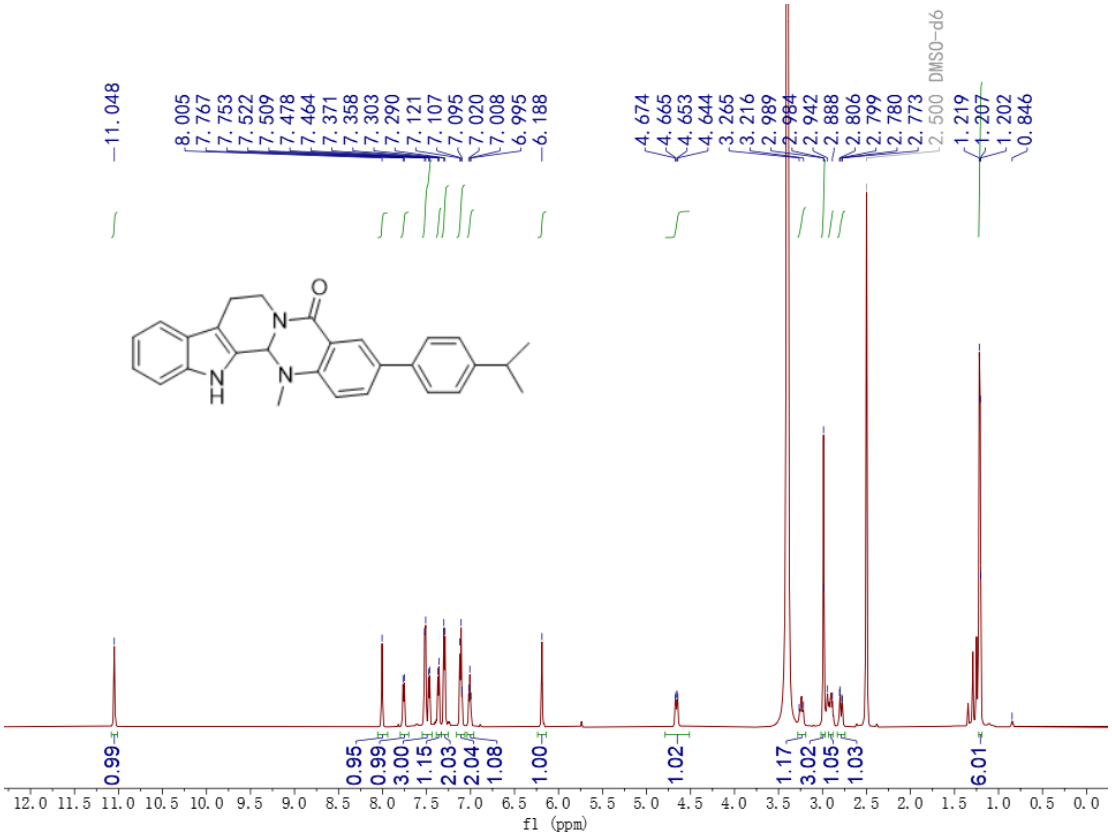


Figure 13. ^{1}H NMR spectrum of compound **6d** (600 MHz, DMSO-d_6)

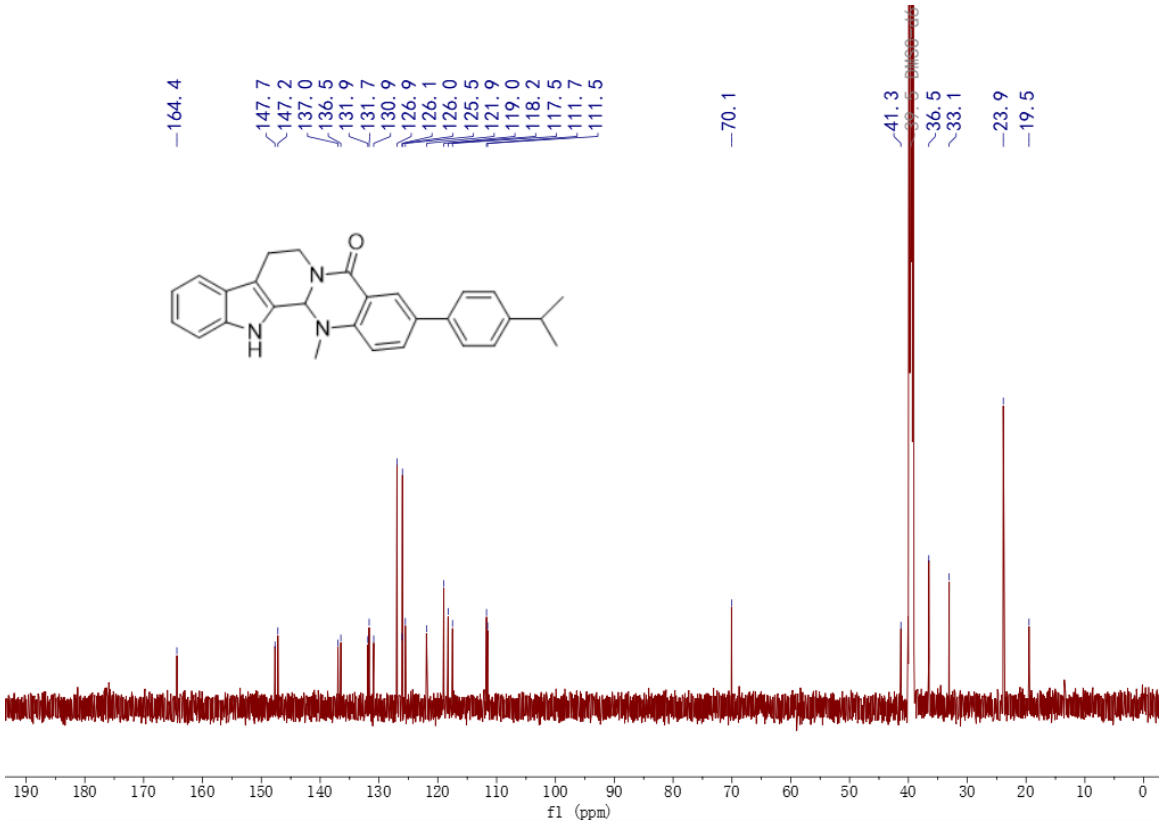


Figure 14. ^{13}C NMR spectrum of compound **6d** (100 MHz, DMSO-d_6)

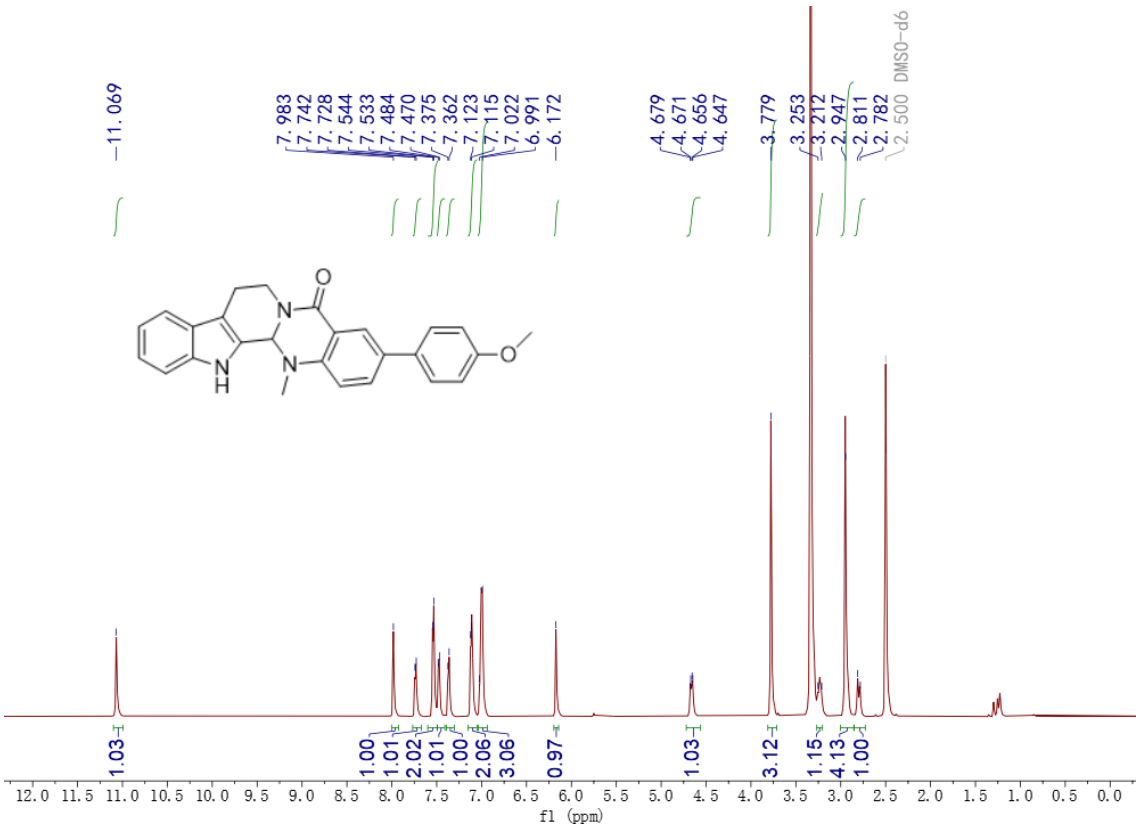


Figure 15. ^{1}H NMR spectrum of compound **6e** (600 MHz, DMSO-d_6)

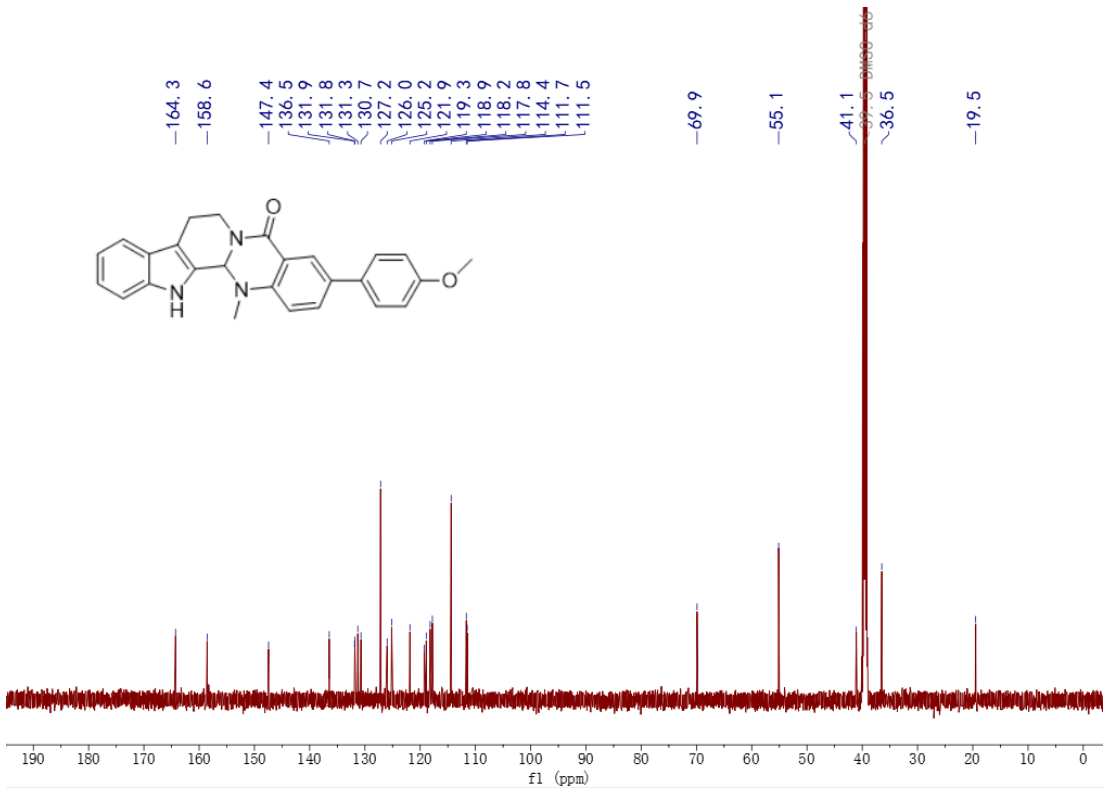


Figure 16. ^{13}C NMR spectrum of compound **6e** (100 MHz, DMSO-d_6)

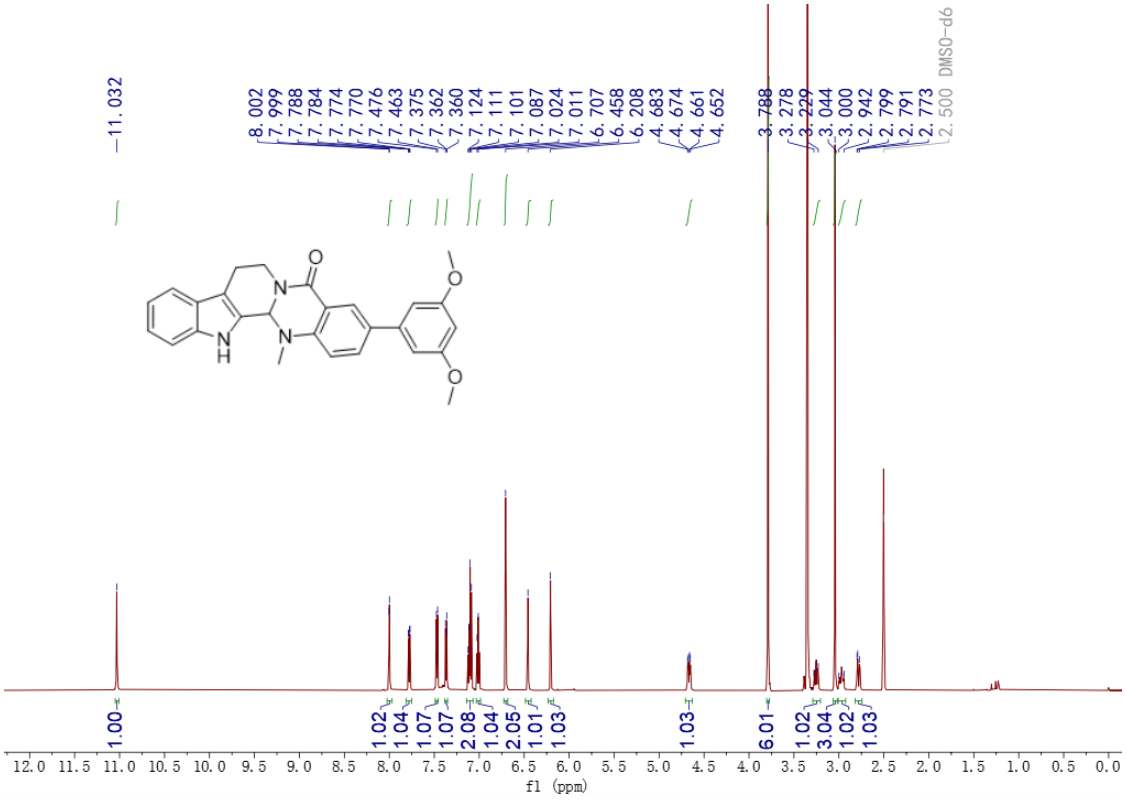


Figure 17. ^{1}H NMR spectrum of compound **6f** (600 MHz, DMSO-d_6)

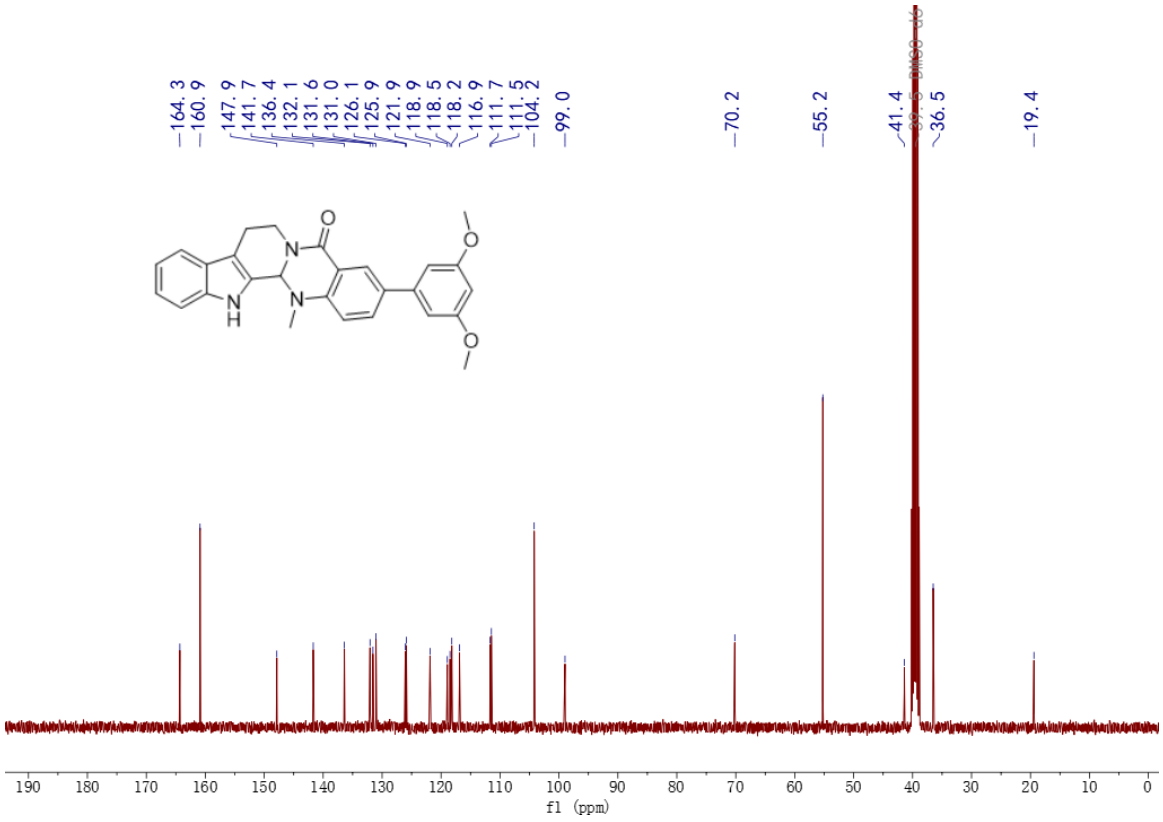


Figure 18. ^{13}C NMR spectrum of compound **6f** (100 MHz, DMSO-d_6)

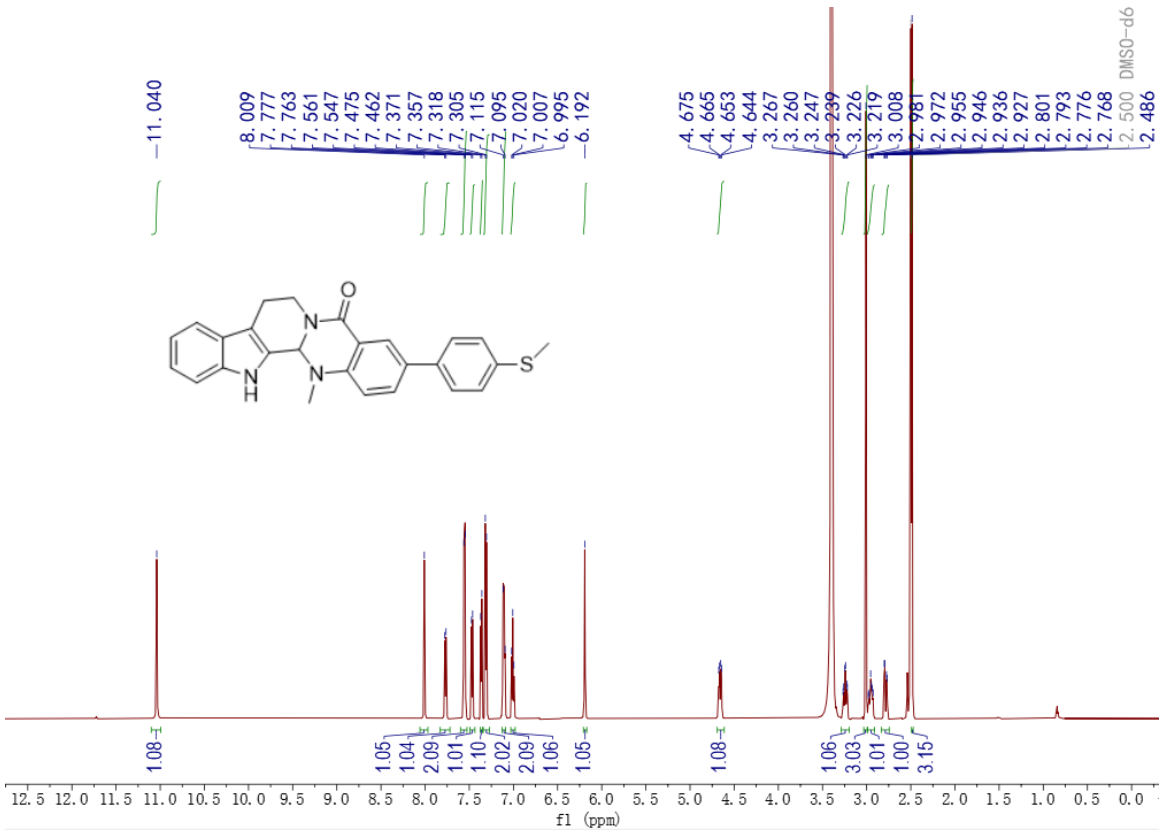


Figure 19. ^{1}H NMR spectrum of compound **6g** (600 MHz, DMSO-d_6)

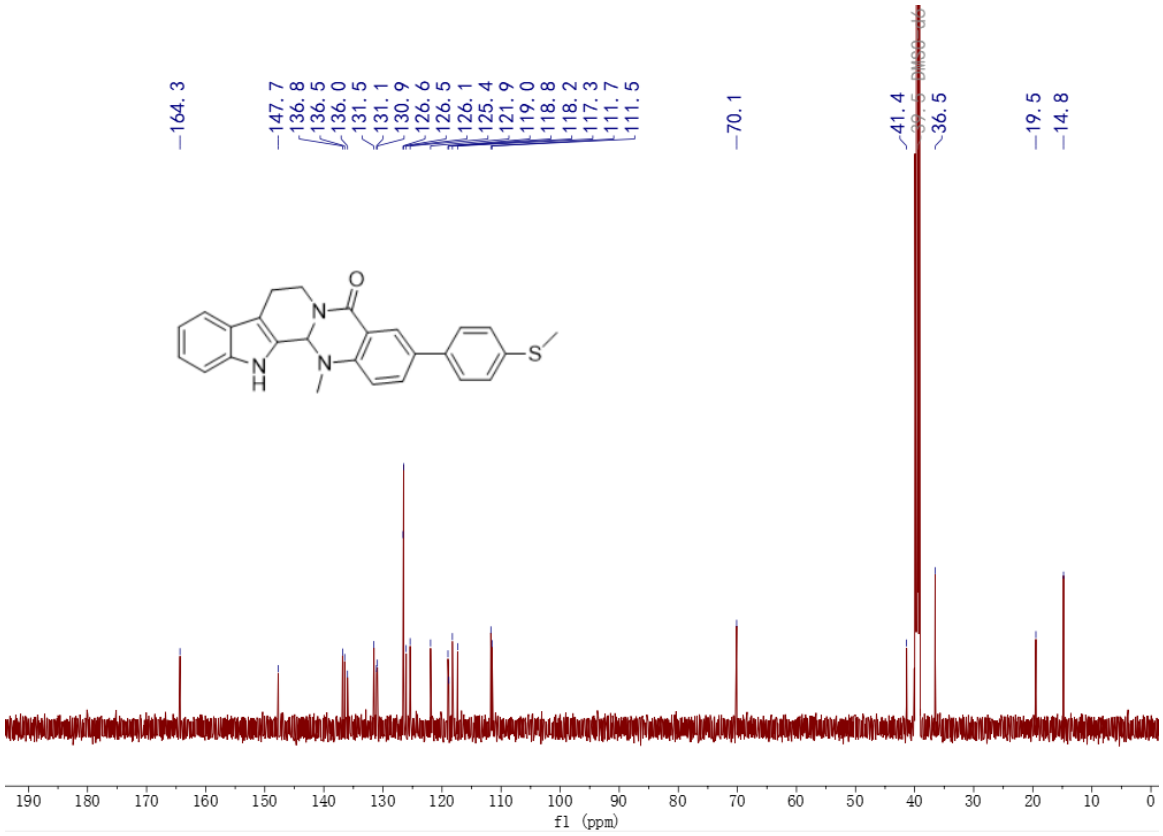


Figure 20. ^{13}C NMR spectrum of compound **6g** (100 MHz, DMSO-d_6)

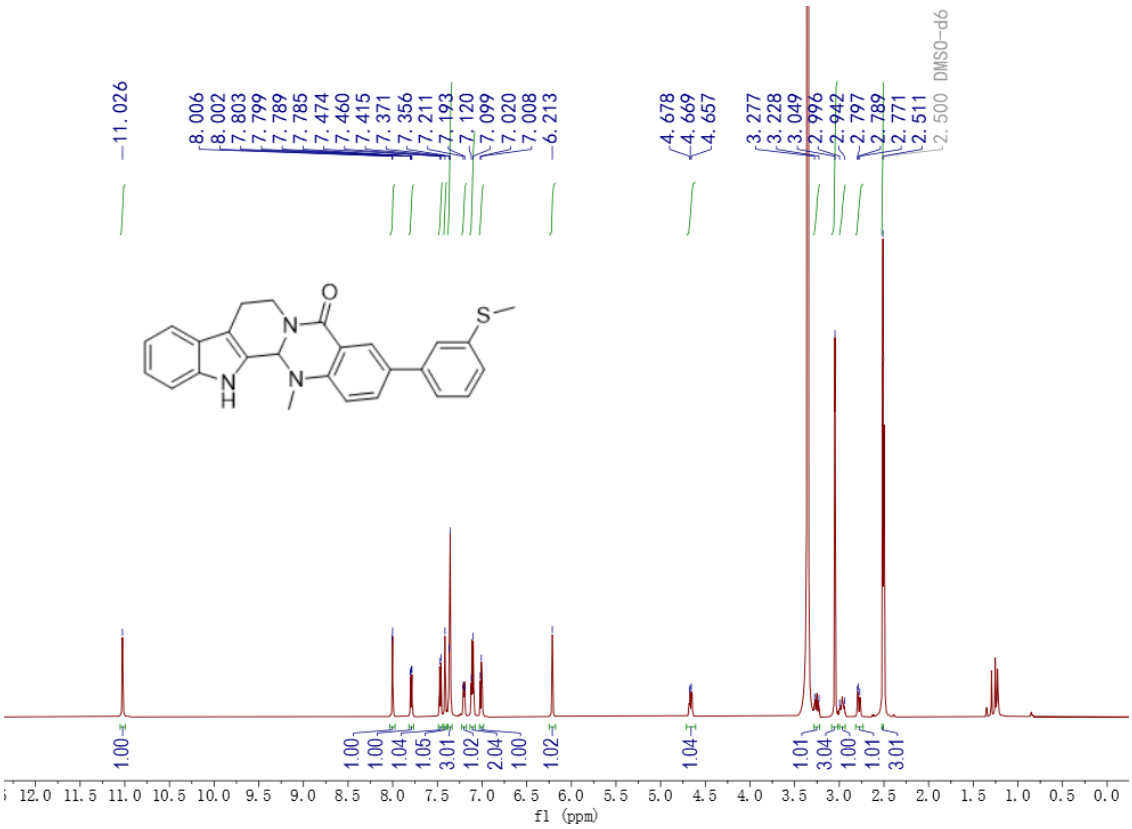


Figure 21. ^{1}H NMR spectrum of compound **6h** (600 MHz, DMSO-d_6)

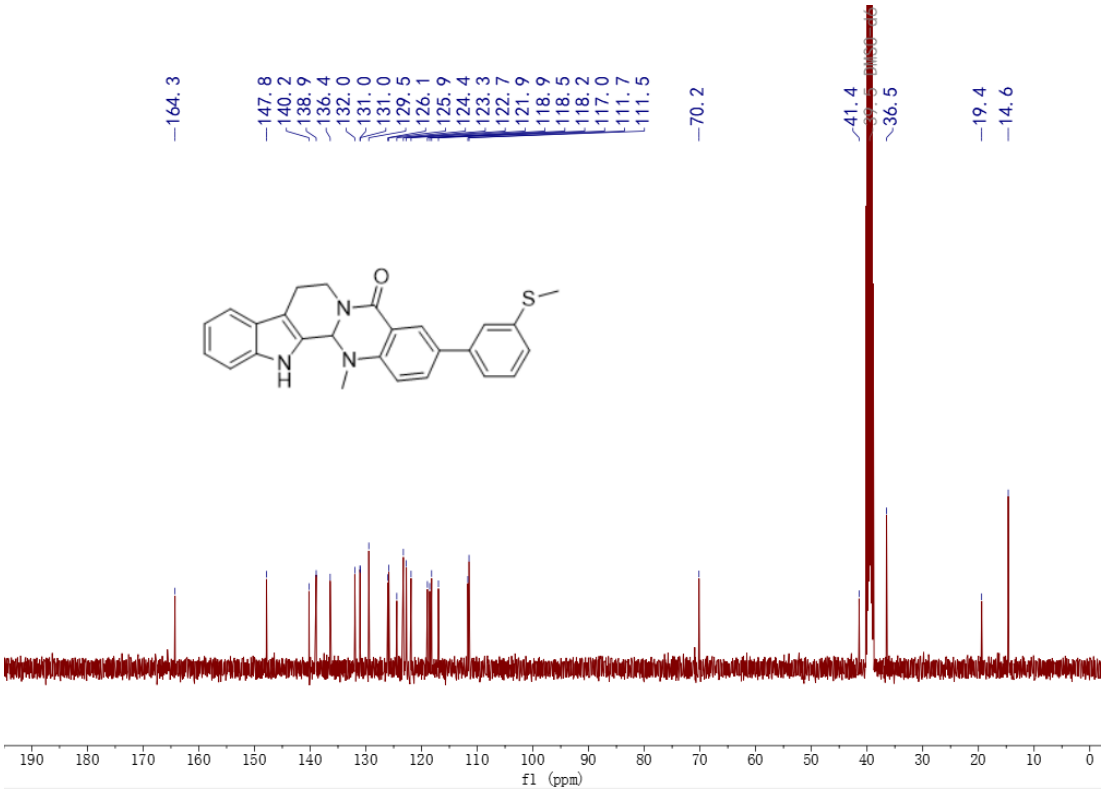


Figure 22. ^{13}C NMR spectrum of compound **6h** (150 MHz, DMSO-d_6)

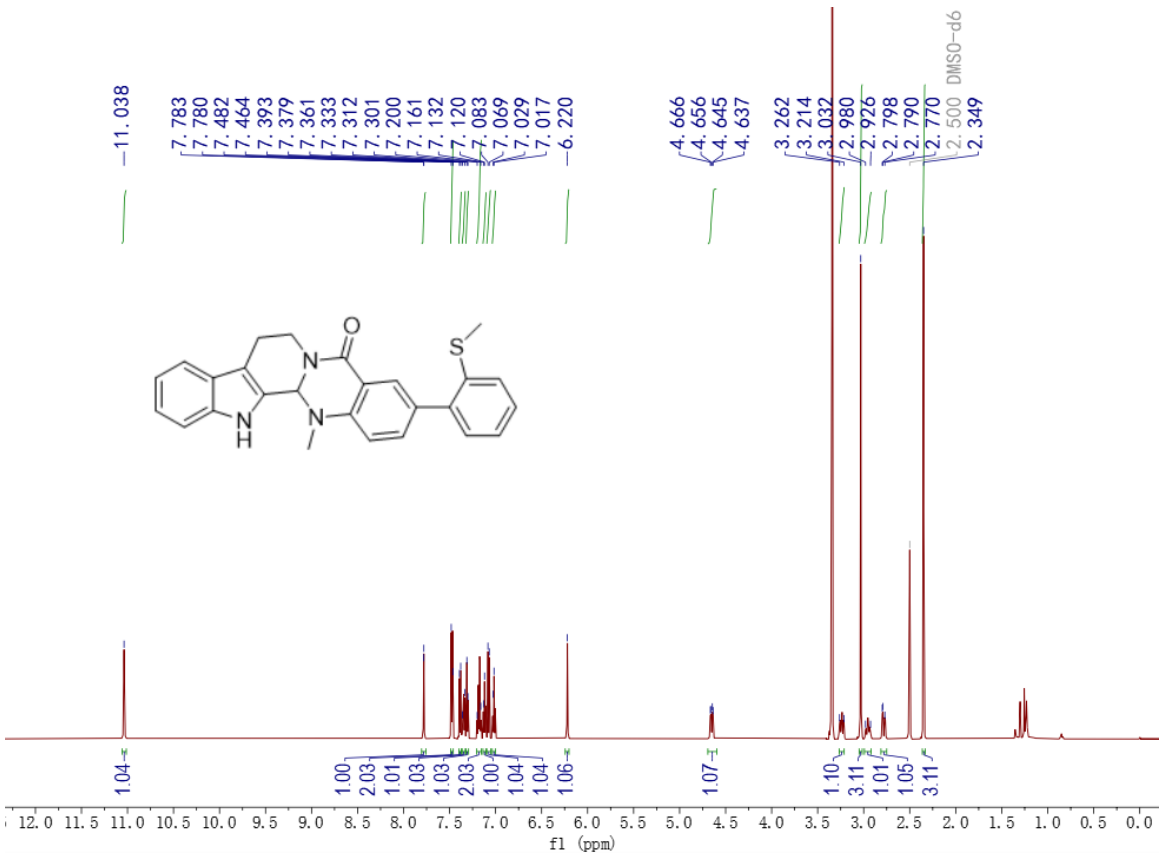


Figure 23. ^{1}H NMR spectrum of compound **6i** (600 MHz, DMSO-d_6)

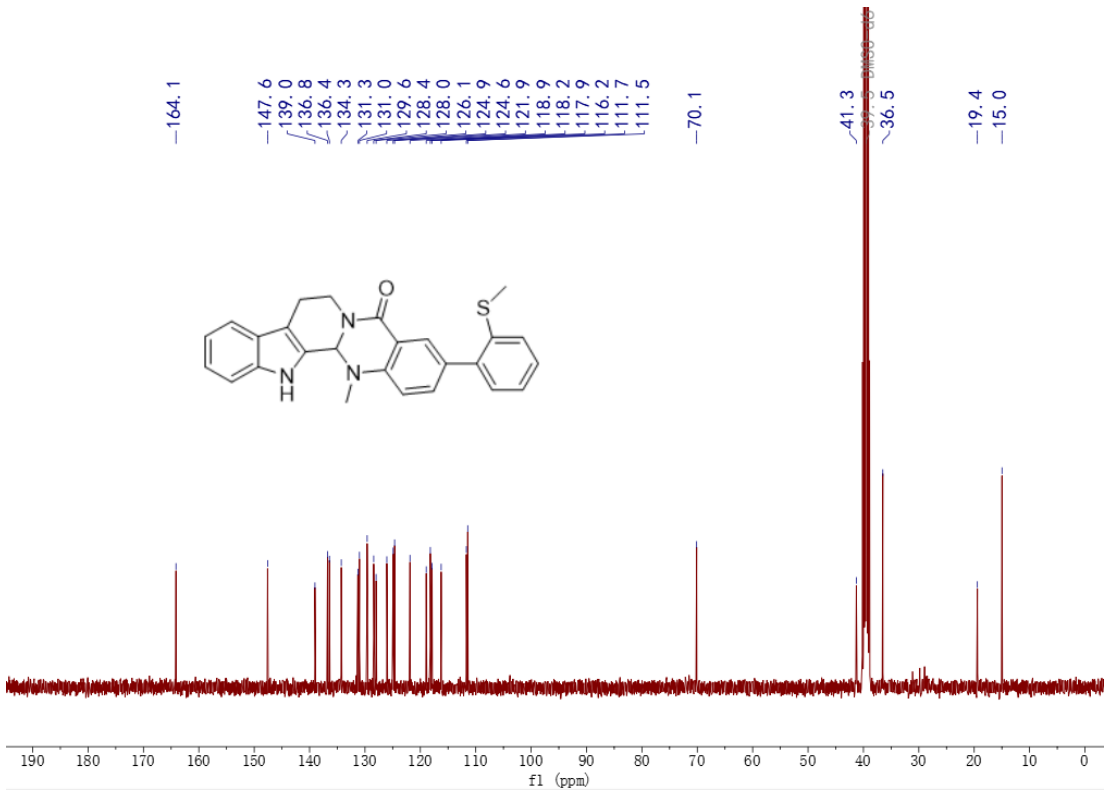


Figure 24. ^{13}C NMR spectrum of compound **6i** (150 MHz, DMSO-d_6)

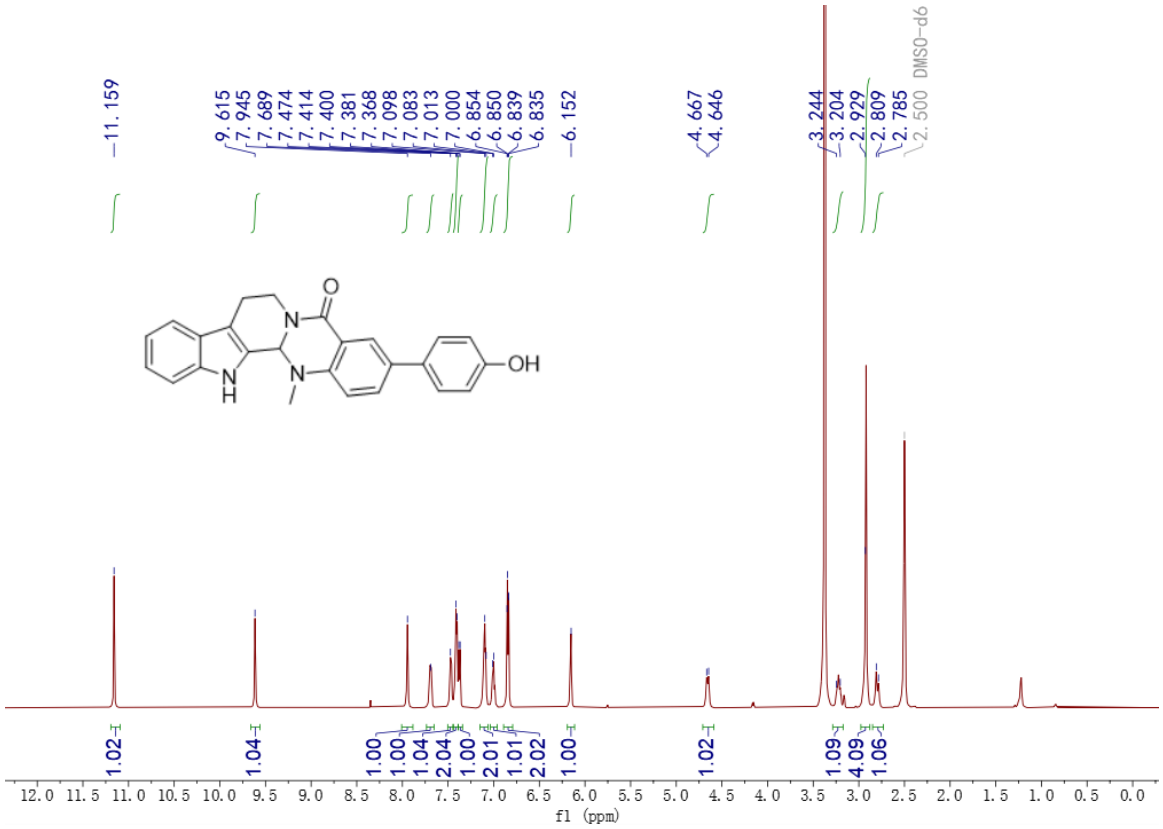


Figure 25. ^{1}H NMR spectrum of compound **6j** (600 MHz, DMSO-d_6)

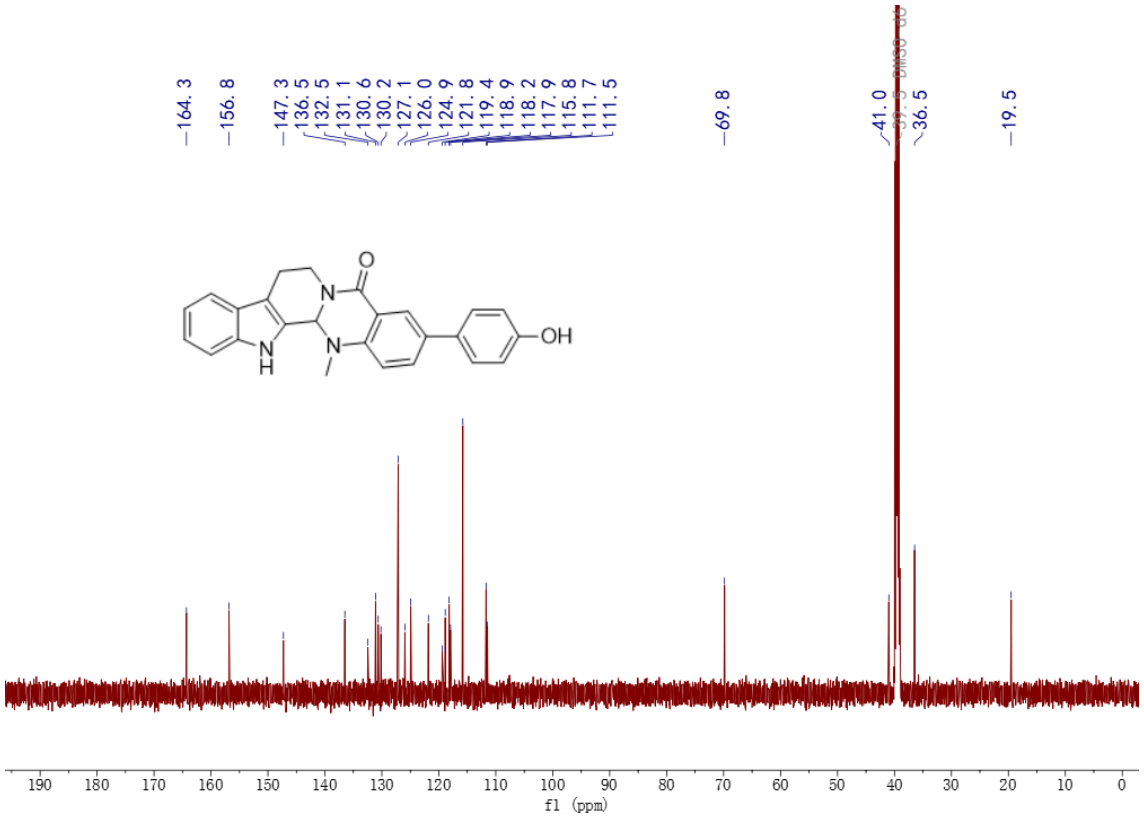


Figure 26. ^{13}C NMR spectrum of compound **6j** (150 MHz, DMSO-d_6)

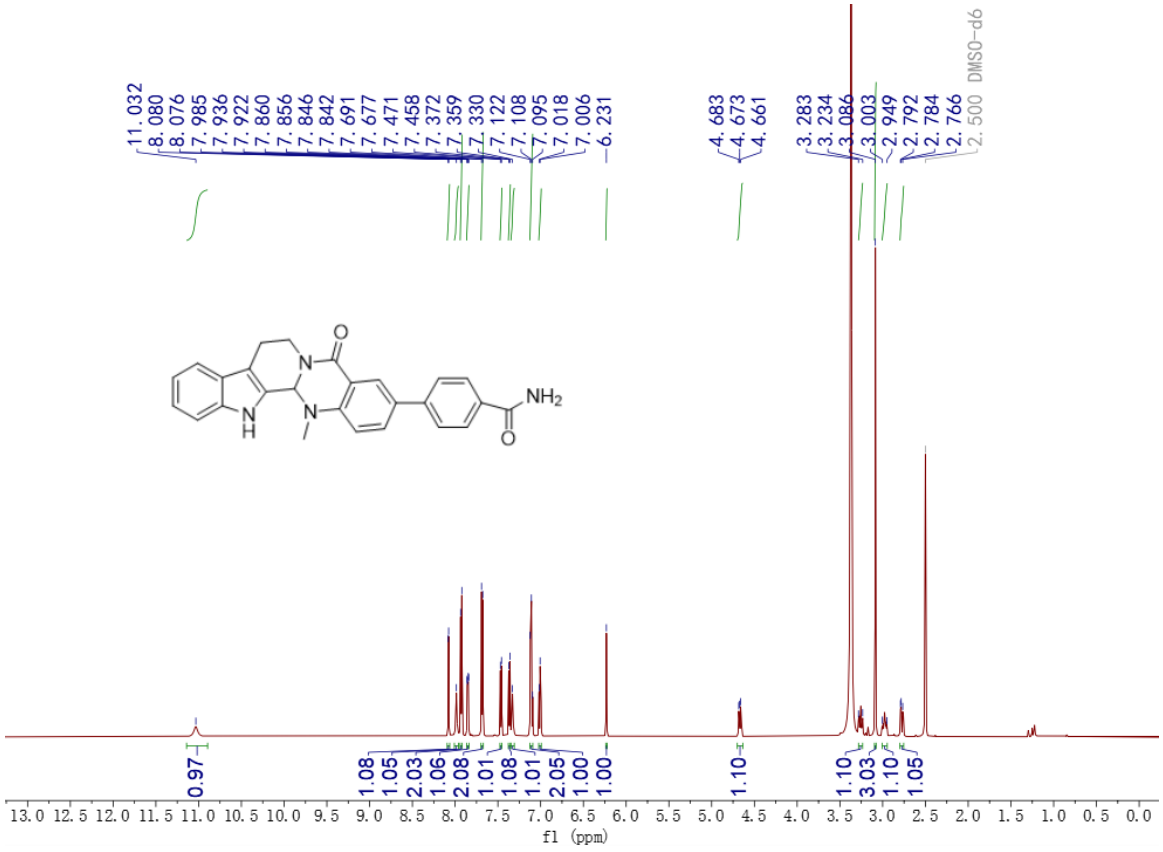


Figure 27. ^{1}H NMR spectrum of compound **6k** (600 MHz, DMSO-d_6)

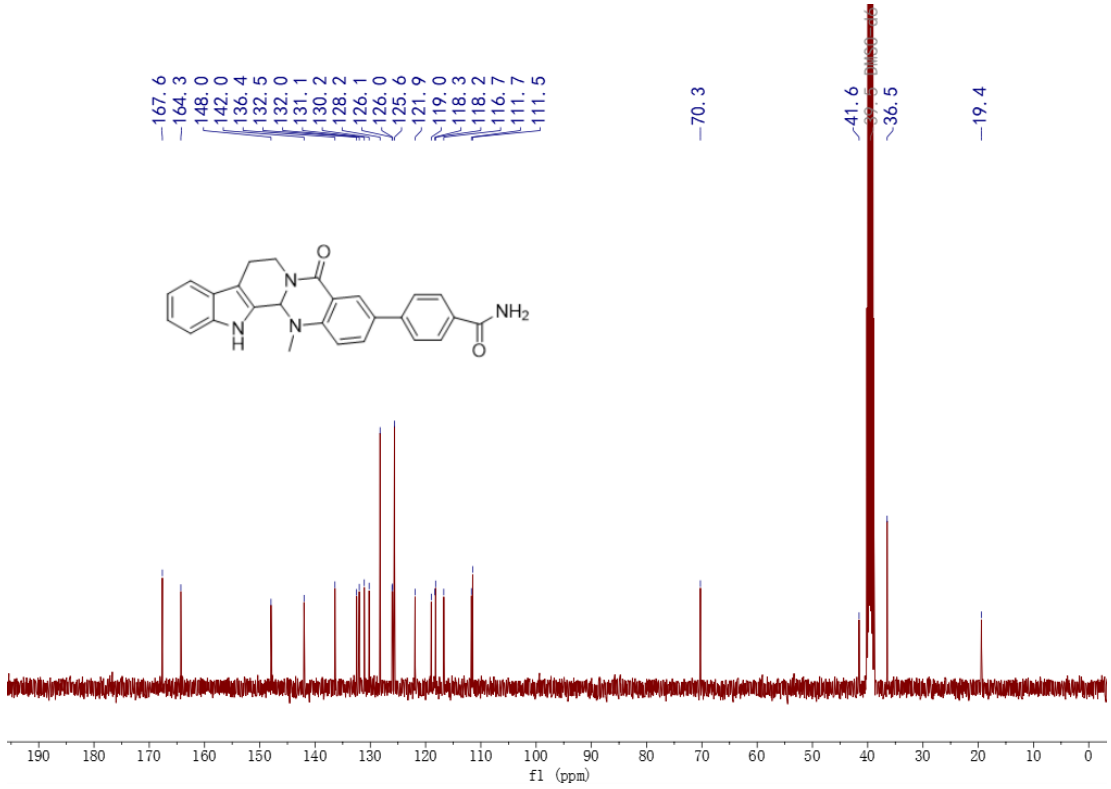


Figure 28. ^{13}C NMR spectrum of compound **6k** (100 MHz, DMSO-d_6)

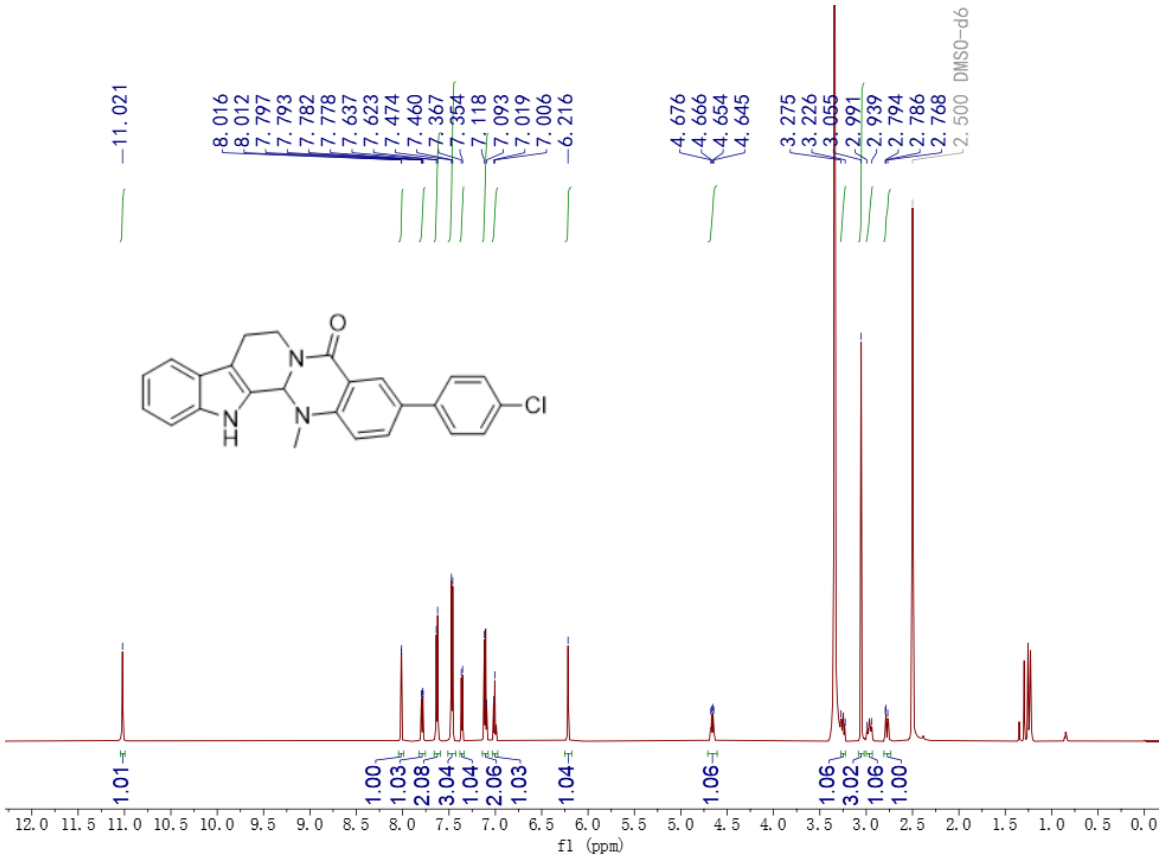


Figure 29. ^{1}H NMR spectrum of compound **6l** (600 MHz, DMSO-d_6)

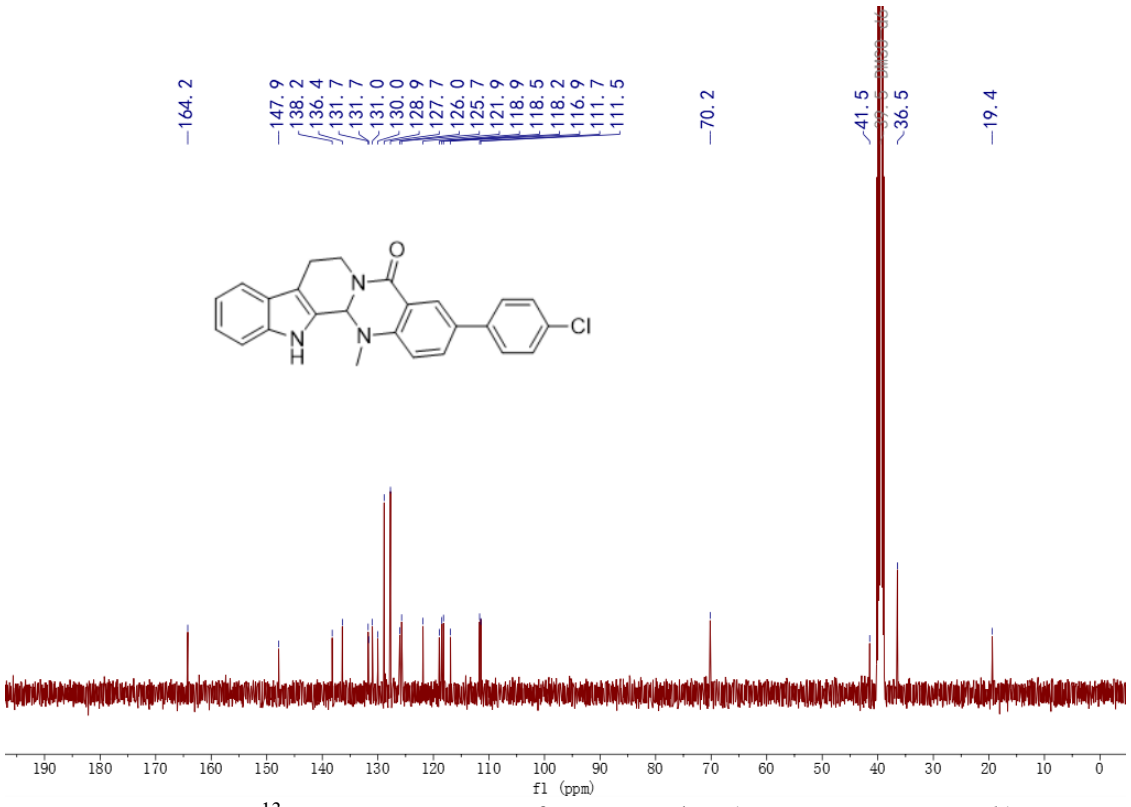


Figure 30. ^{13}C NMR spectrum of compound **6l** (100 MHz, DMSO-d_6)

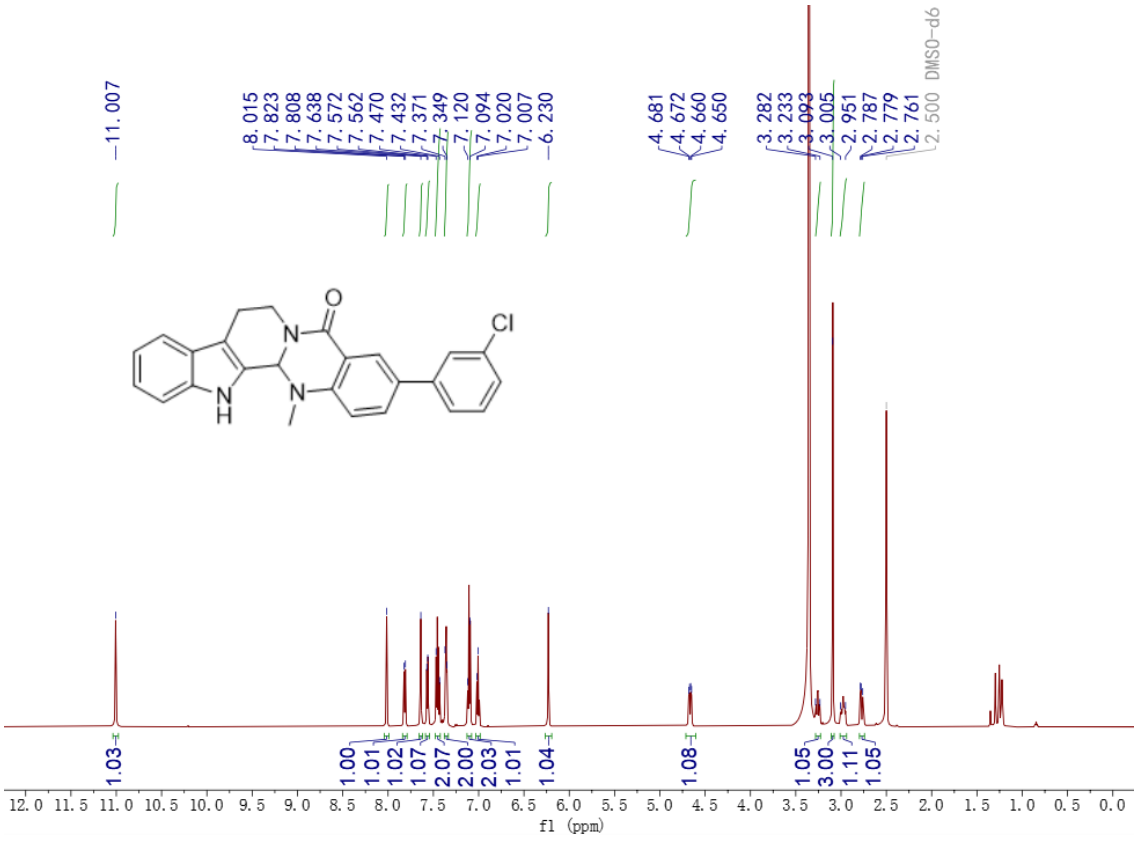


Figure 31. ^{1}H NMR spectrum of compound **6m** (600 MHz, DMSO-d_6)

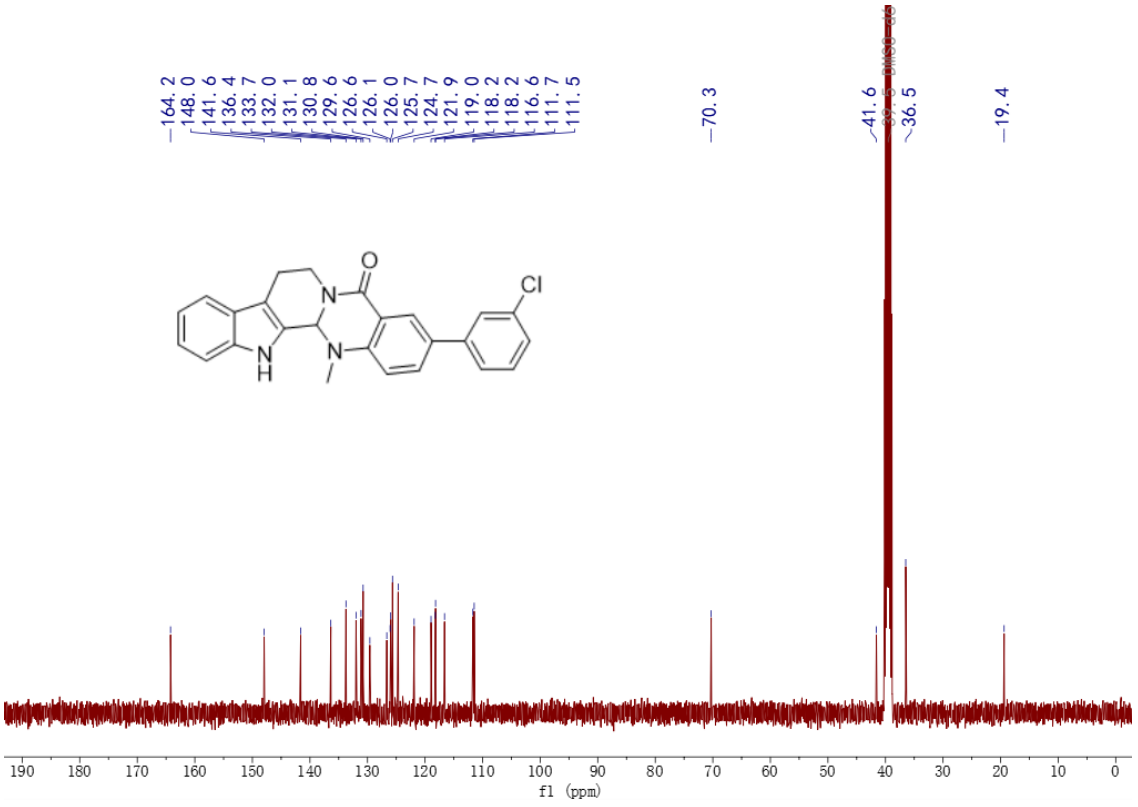


Figure 32. ^{13}C NMR spectrum of compound **6m** (150 MHz, DMSO-d_6)

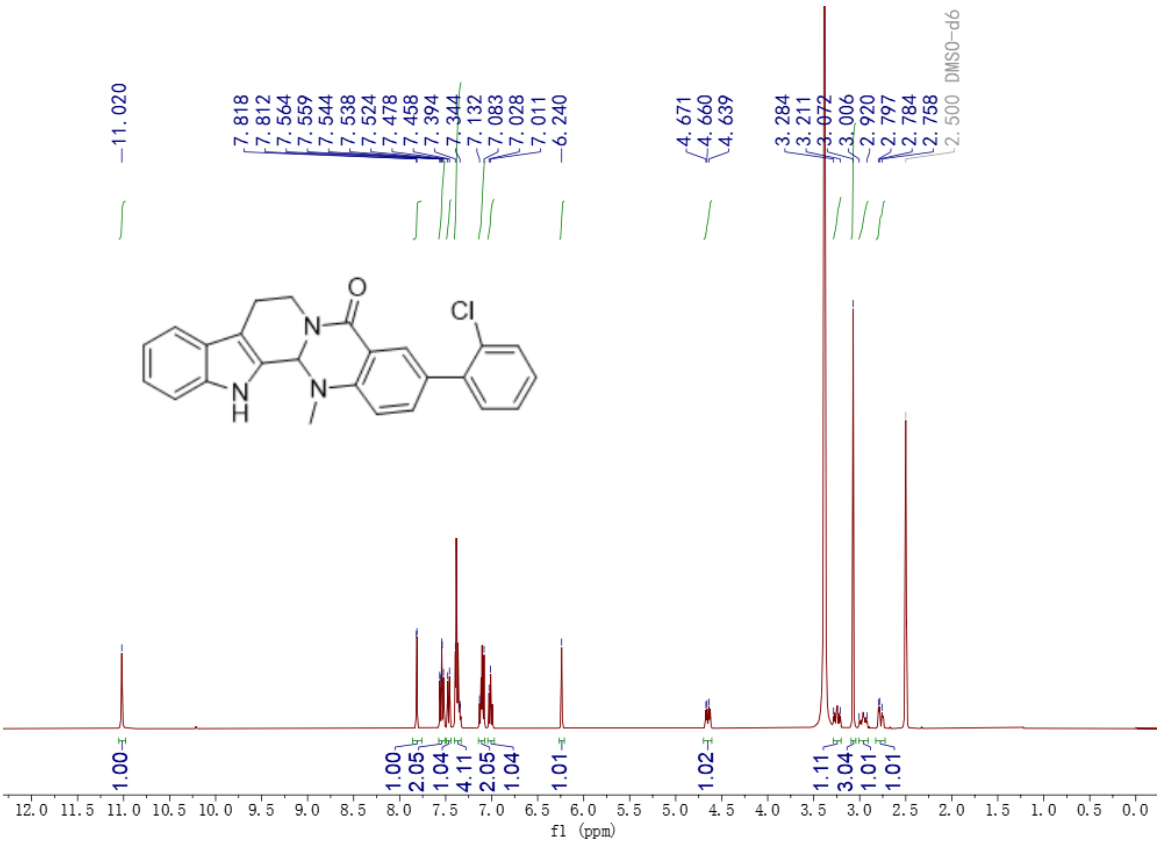


Figure 33. ^{1}H NMR spectrum of compound **6n** (400 MHz, DMSO-d_6)

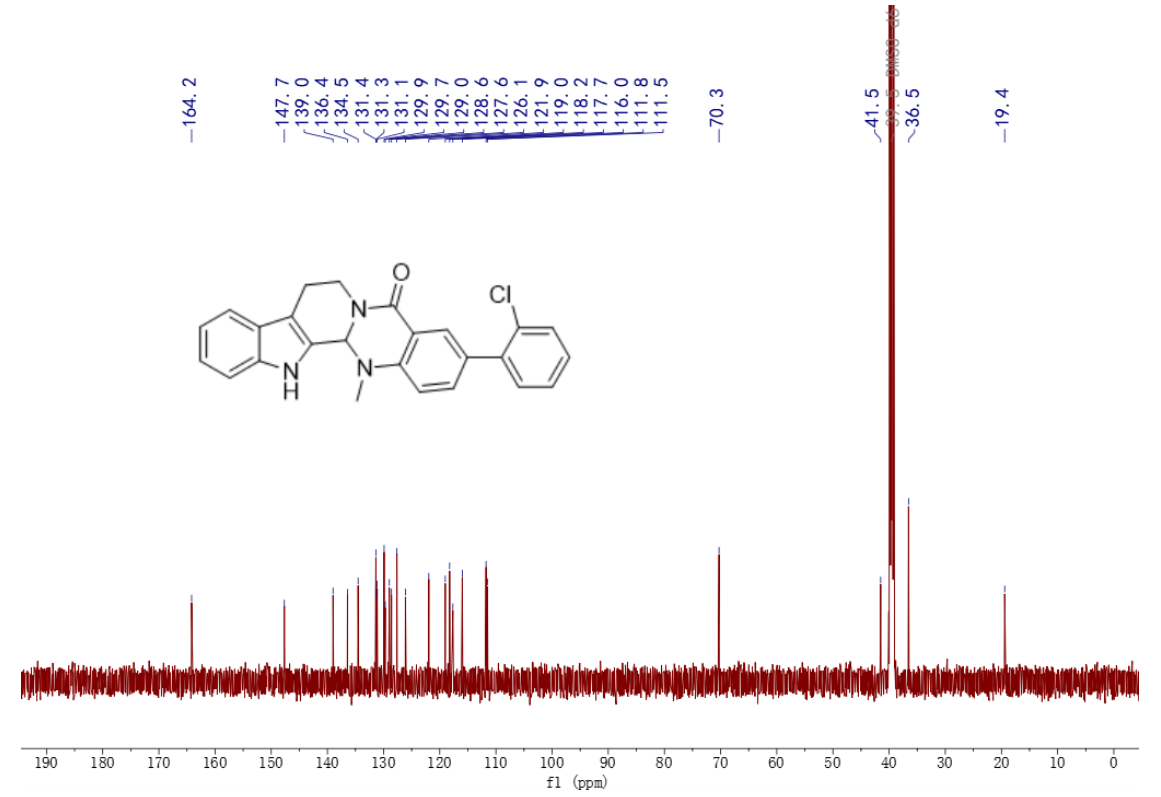


Figure 34. ^{13}C NMR spectrum of compound **6n** (150 MHz, DMSO-d_6)

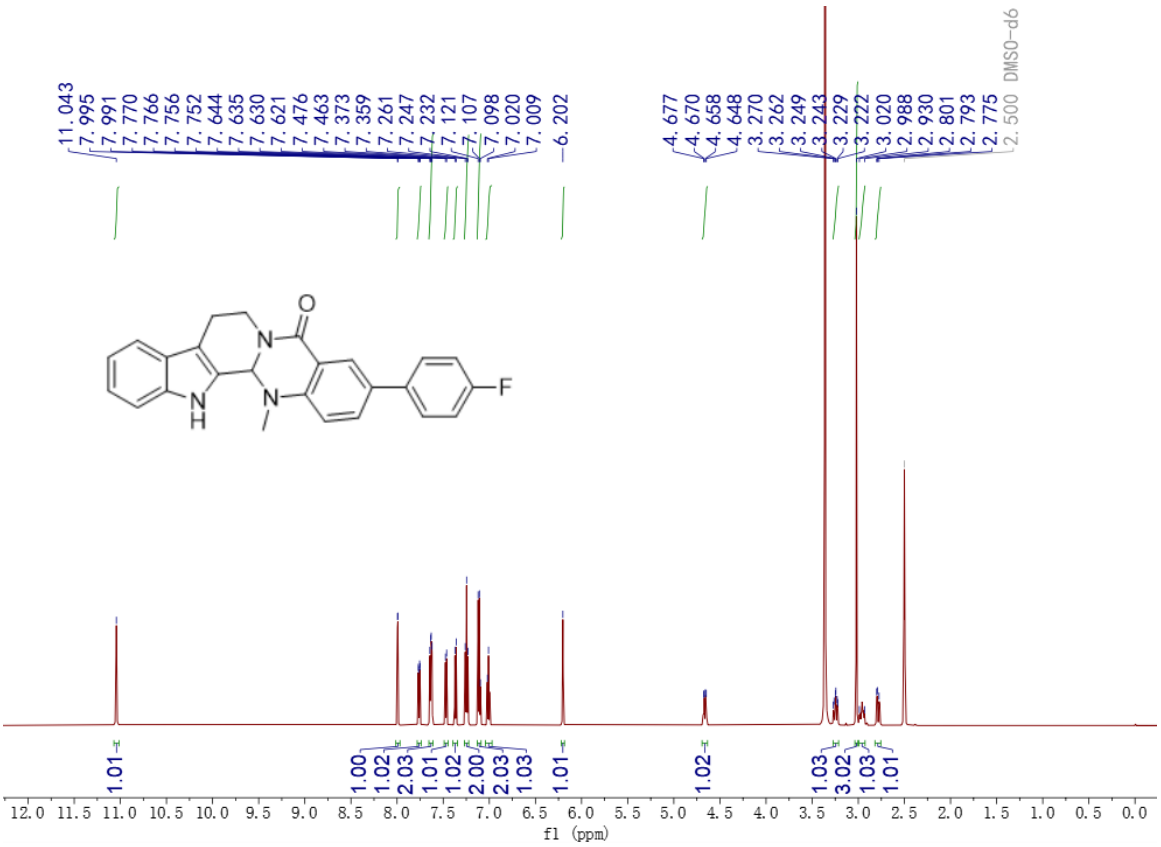


Figure 35. ^{1}H NMR spectrum of compound **6o** (600 MHz, DMSO-d_6)

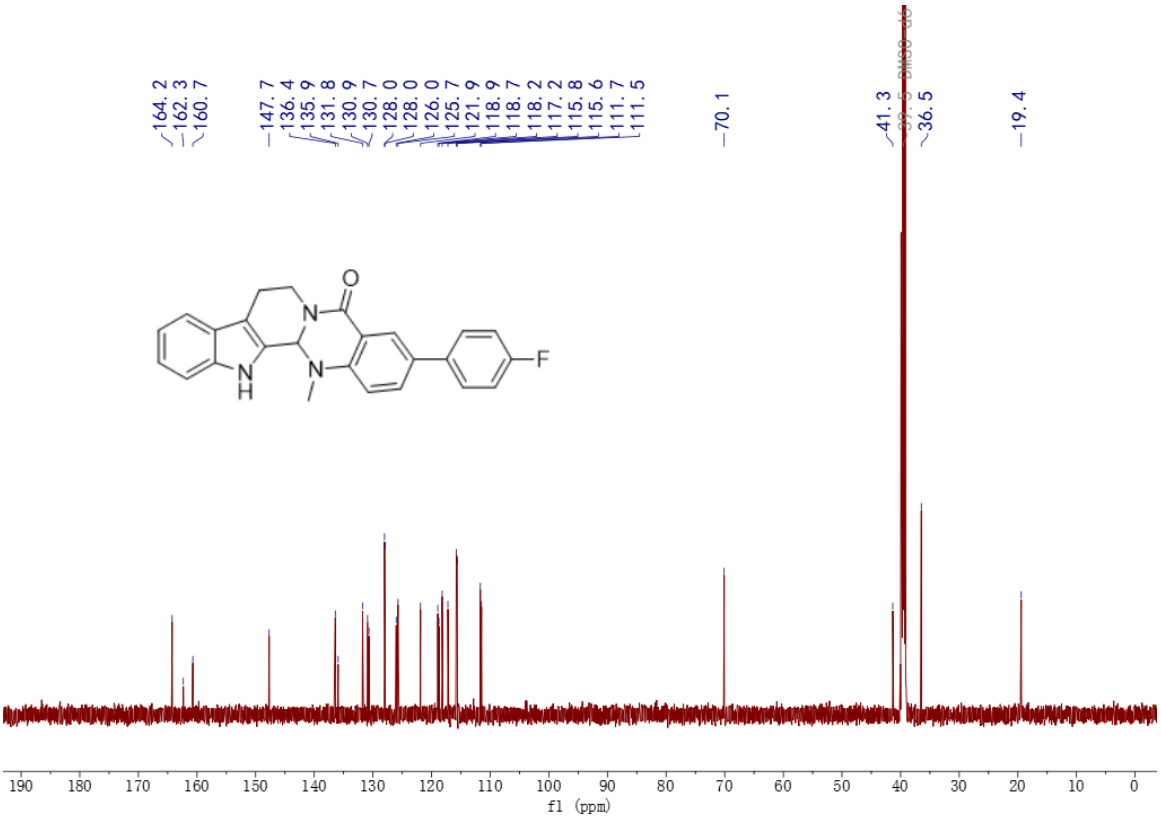


Figure 36. ^{13}C NMR spectrum of compound **6o** (150 MHz, DMSO-d_6)

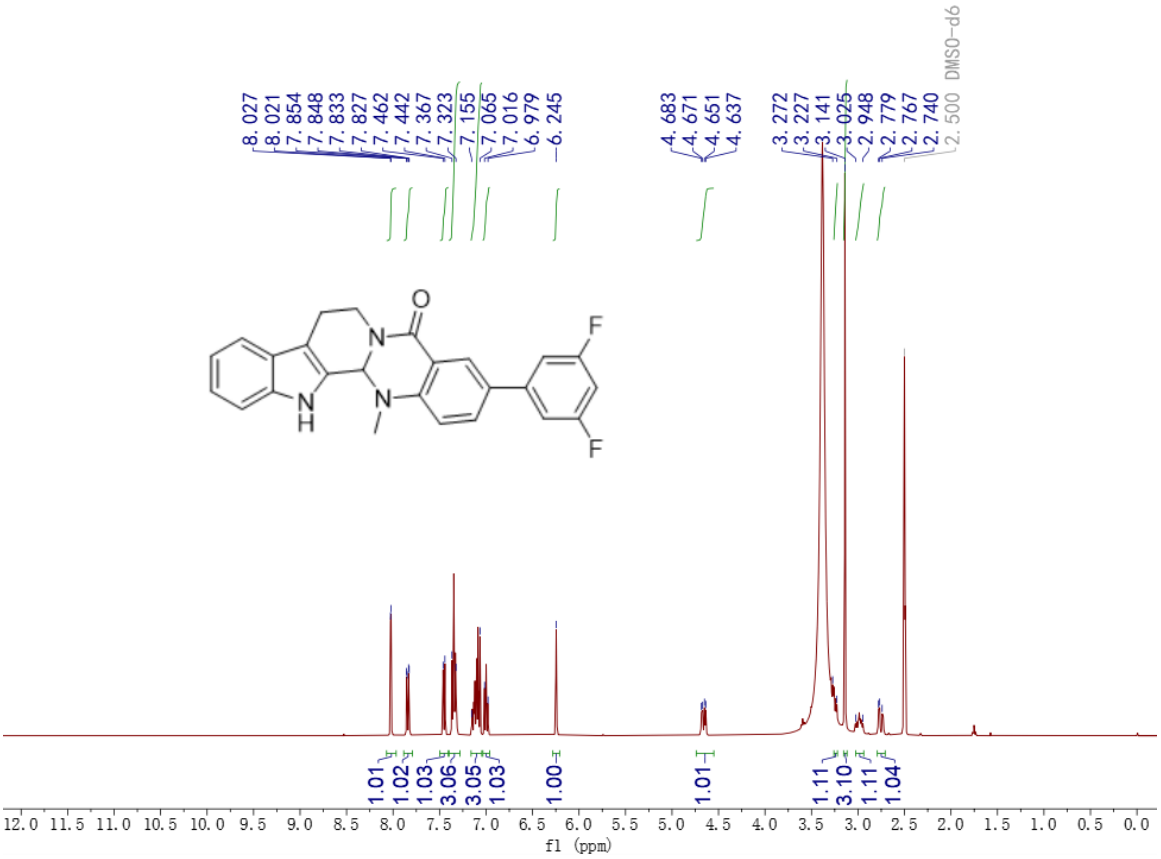


Figure 37. ^{1}H NMR spectrum of compound **6p** (400 MHz, DMSO-d_6)

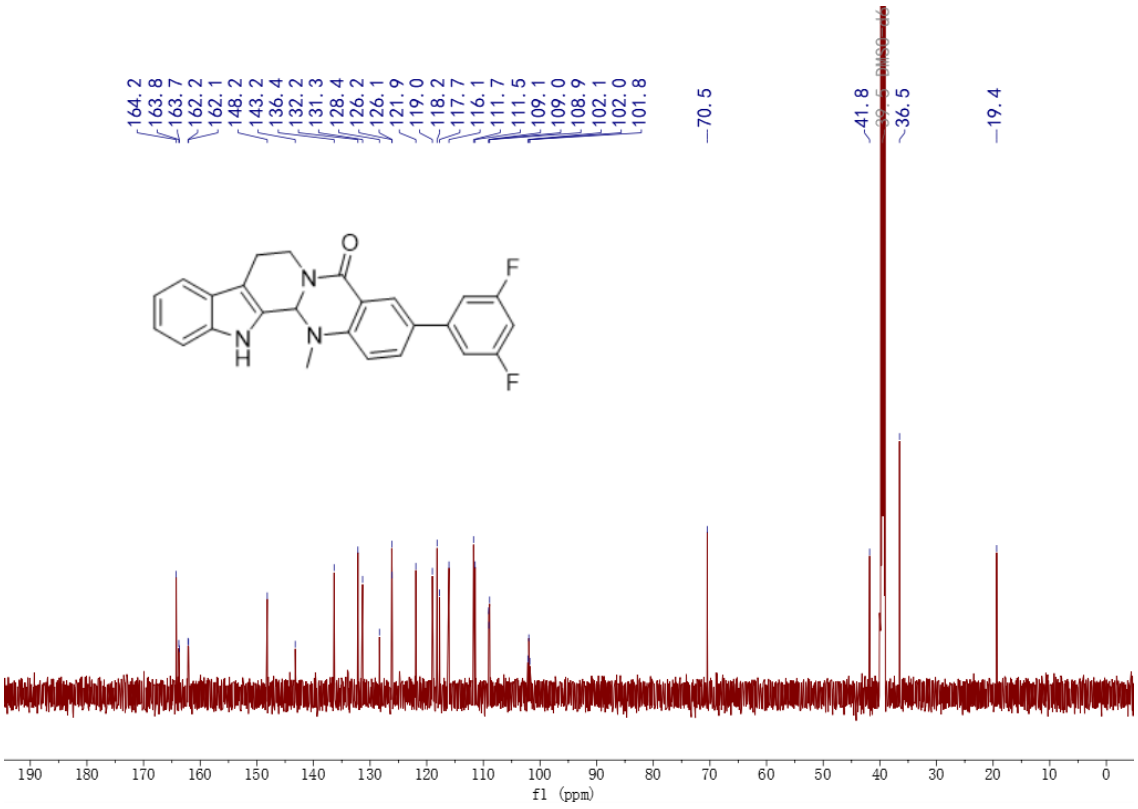


Figure 38. ^{13}C NMR spectrum of compound **6p** (150 MHz, DMSO-d_6)

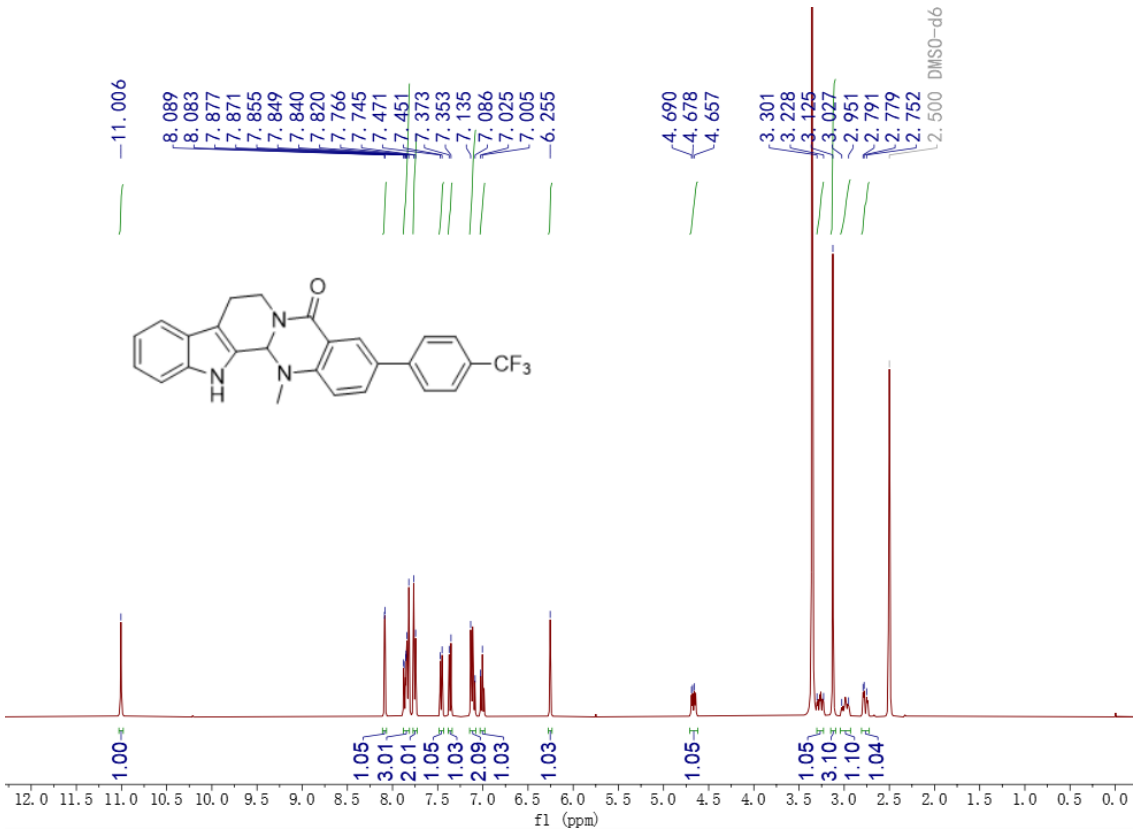


Figure 39. ^{1}H NMR spectrum of compound **6q** (400 MHz, DMSO-d_6)

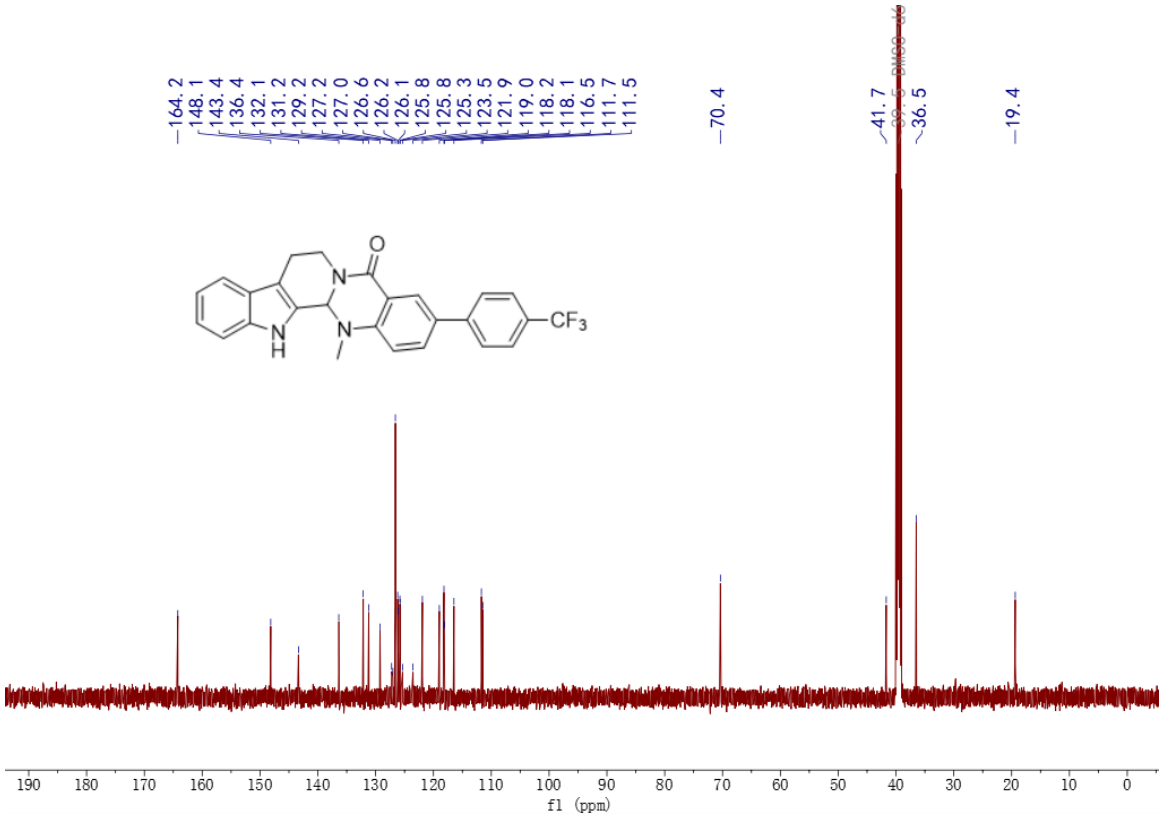


Figure 40. ^{13}C NMR spectrum of compound **6q** (150 MHz, DMSO-d_6)

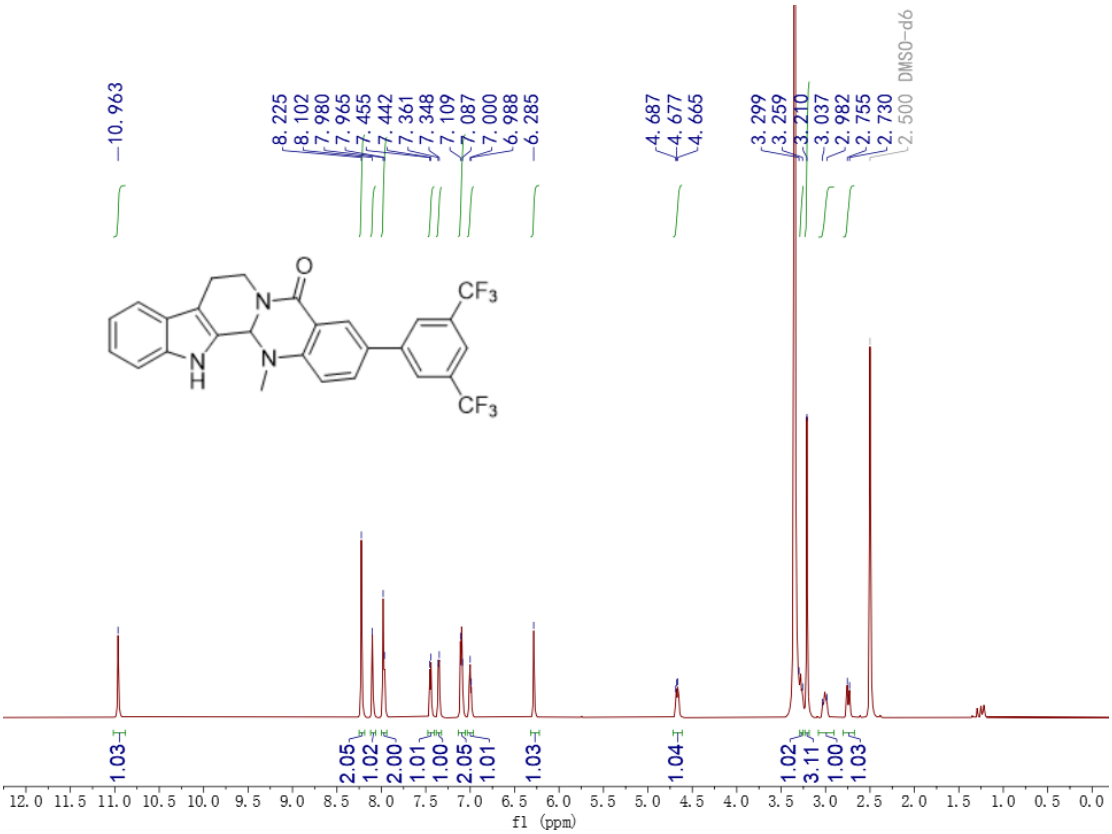


Figure 41. ^{1}H NMR spectrum of compound **6r** (600 MHz, DMSO-d_6)

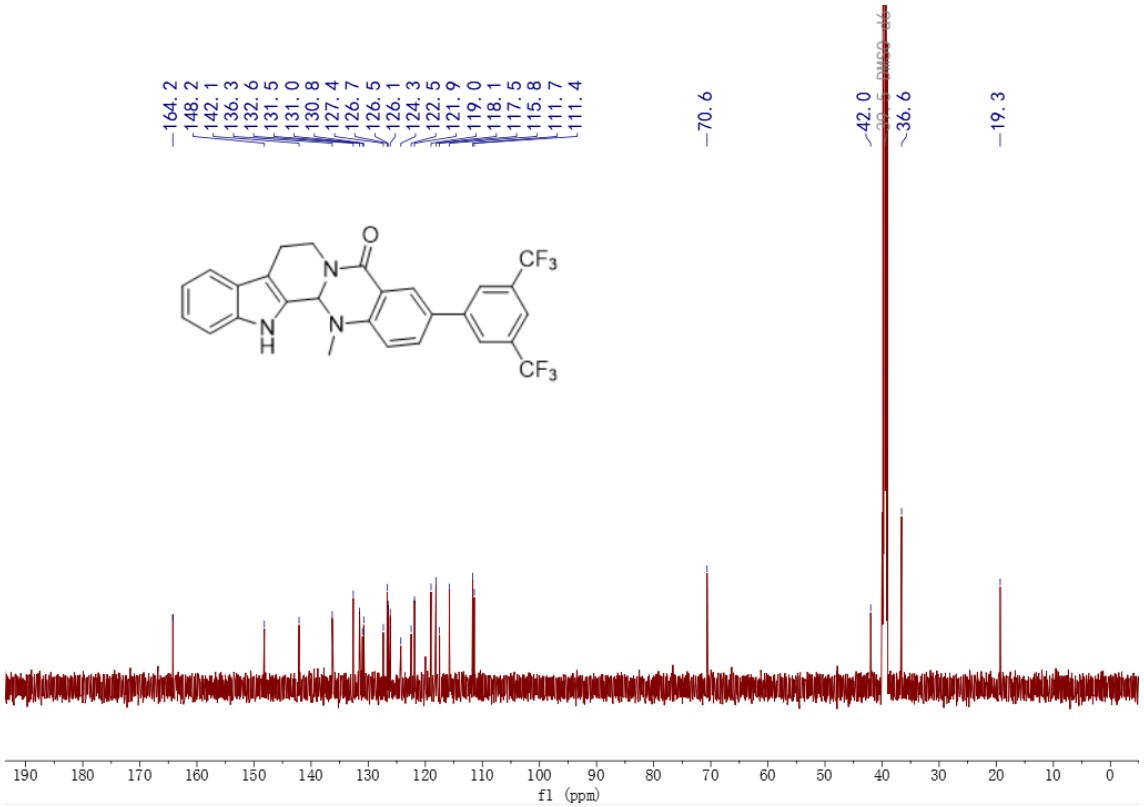


Figure 42. ^{13}C NMR spectrum of compound **6r** (150 MHz, DMSO-d_6)

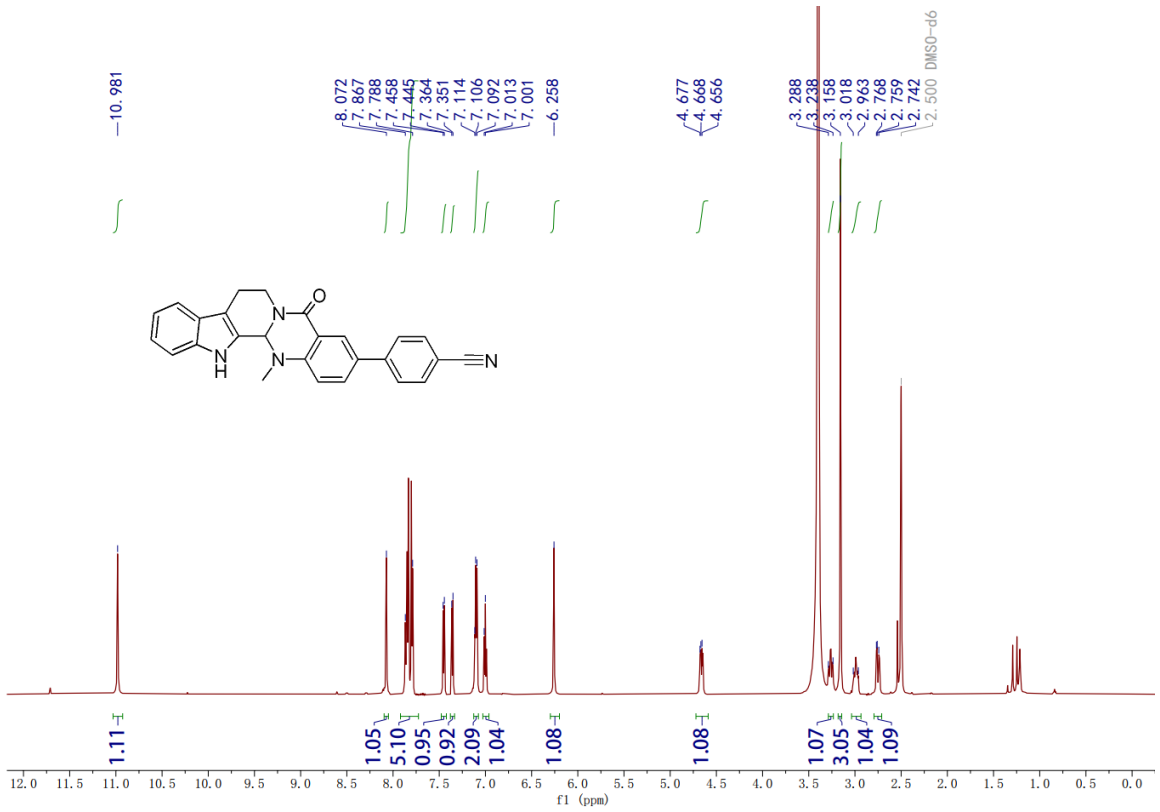


Figure 43. ^{1}H NMR spectrum of compound **6s** (600 MHz, DMSO-d_6)

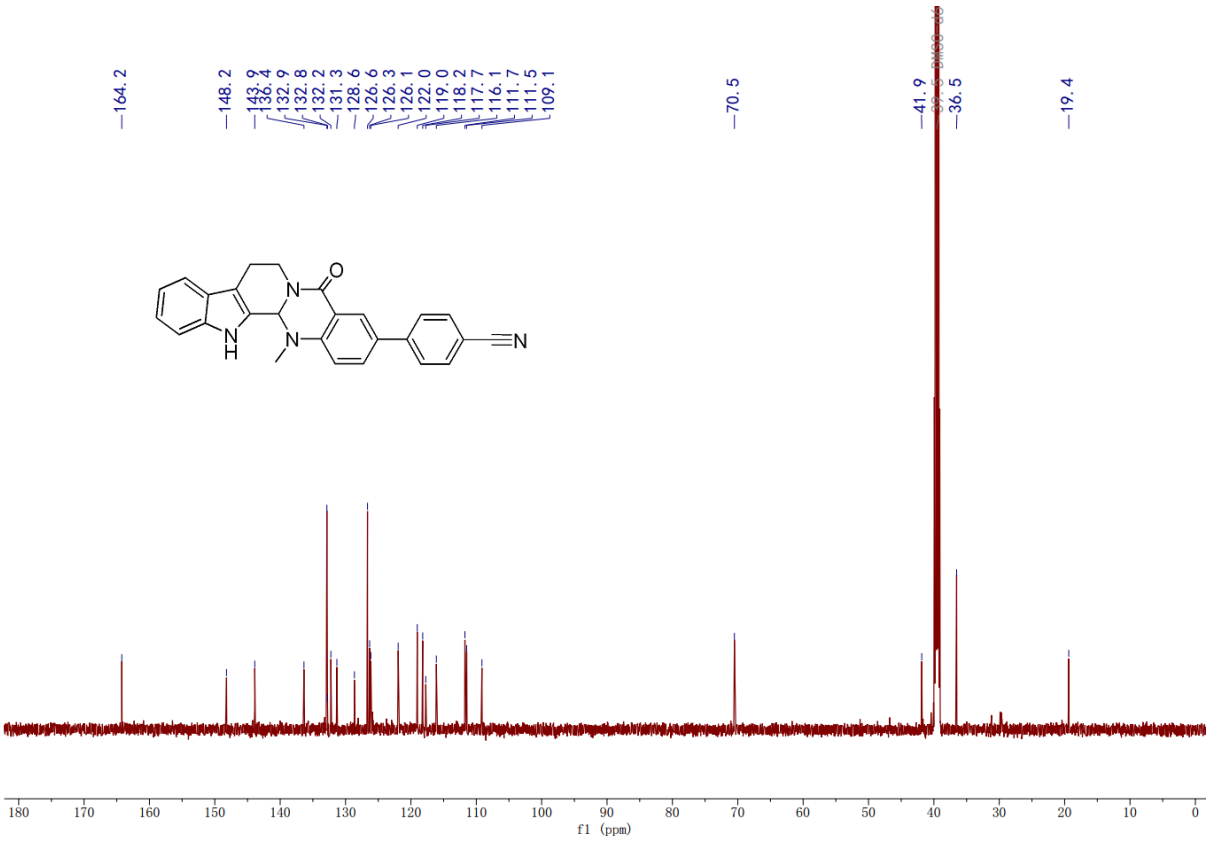


Figure 44. ^{13}C NMR spectrum of compound **6s** (100 MHz, DMSO-d_6)

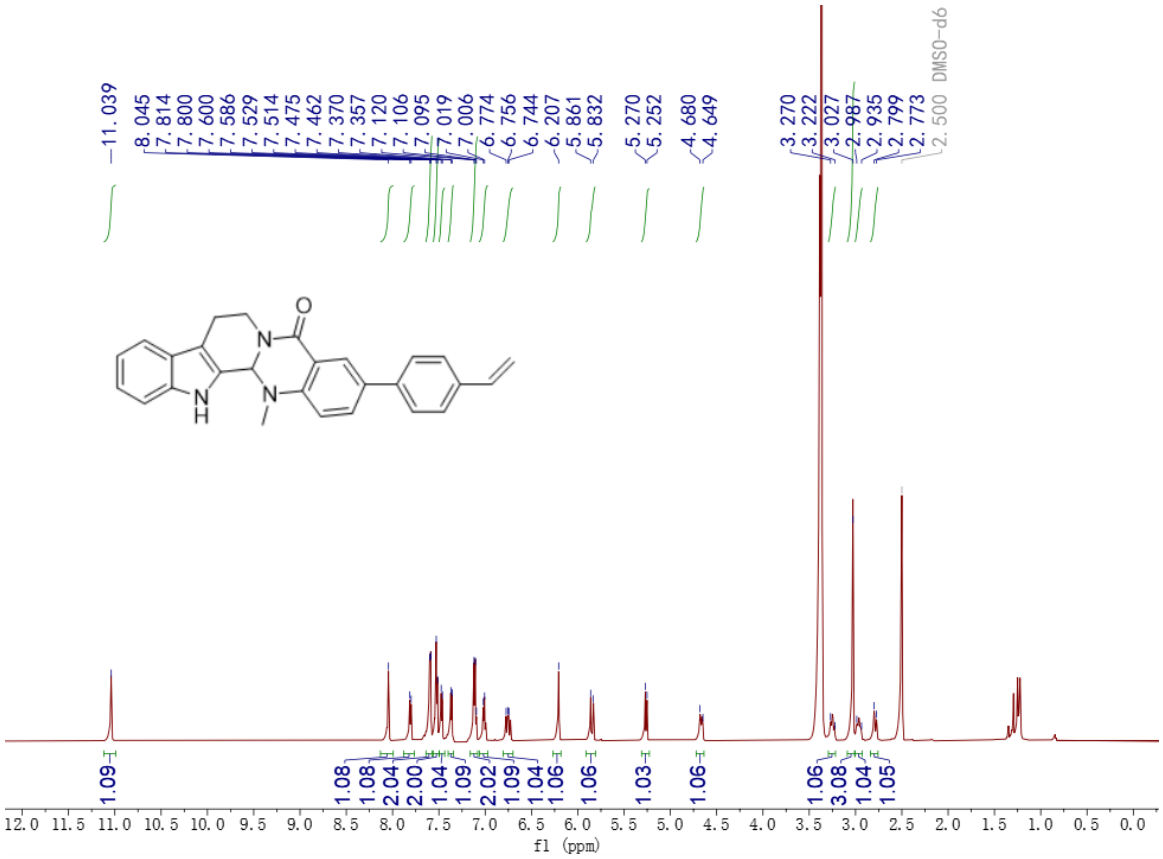


Figure 45. ^{1}H NMR spectrum of compound **6t** (600 MHz, DMSO-d_6)

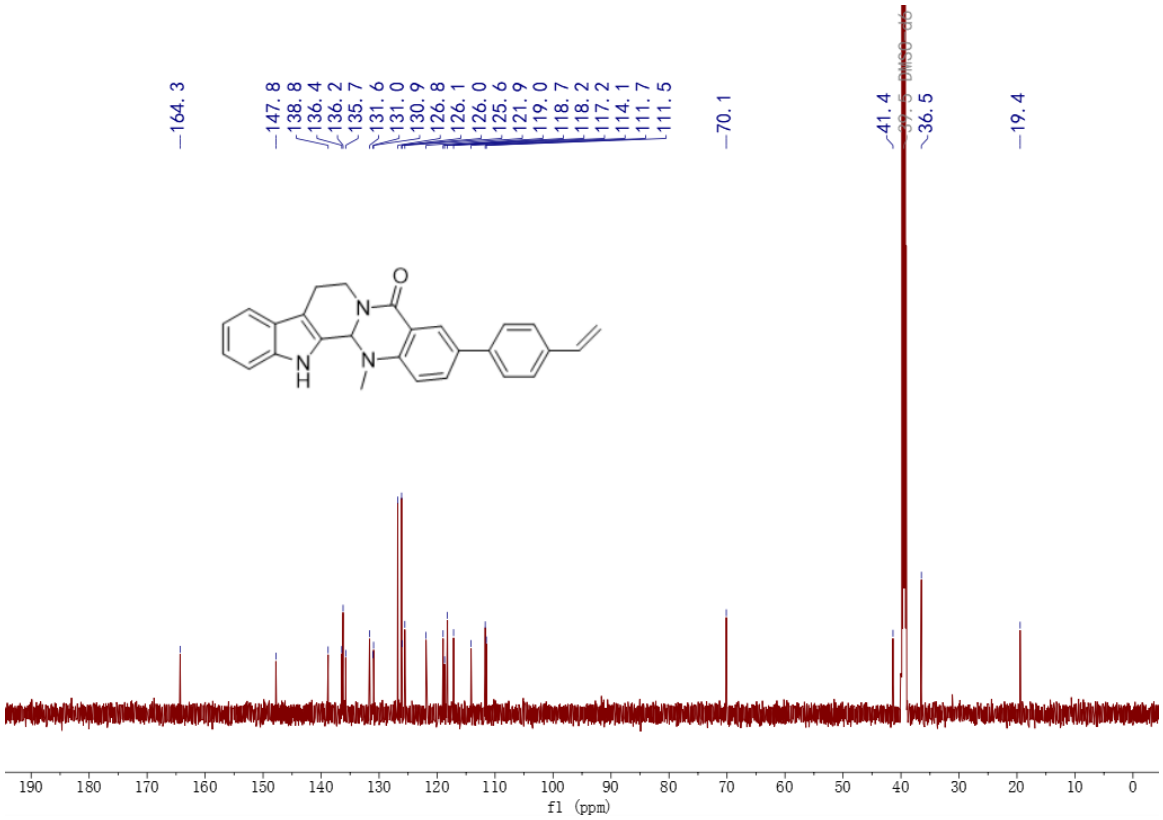


Figure 46. ^{13}C NMR spectrum of compound **6t** (100 MHz, DMSO-d_6)

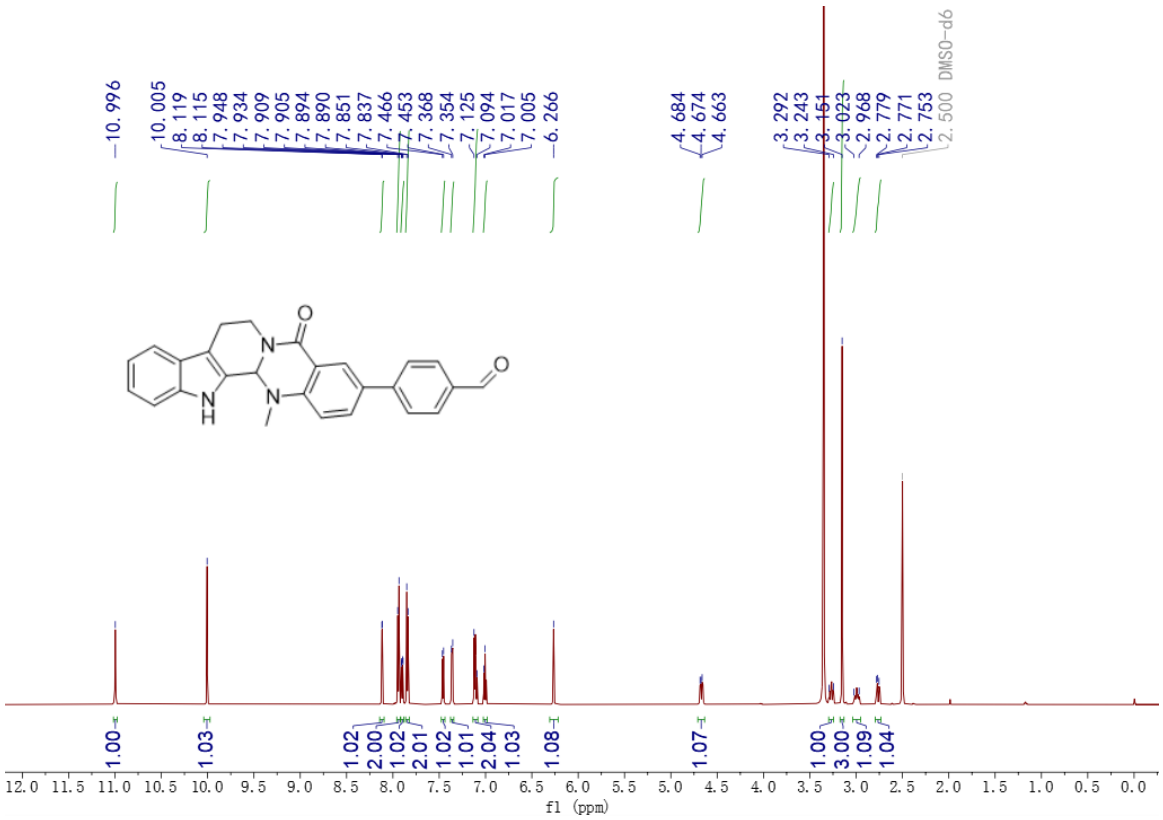


Figure 47. ^{1}H NMR spectrum of compound **6u** (600 MHz, DMSO-d_6)

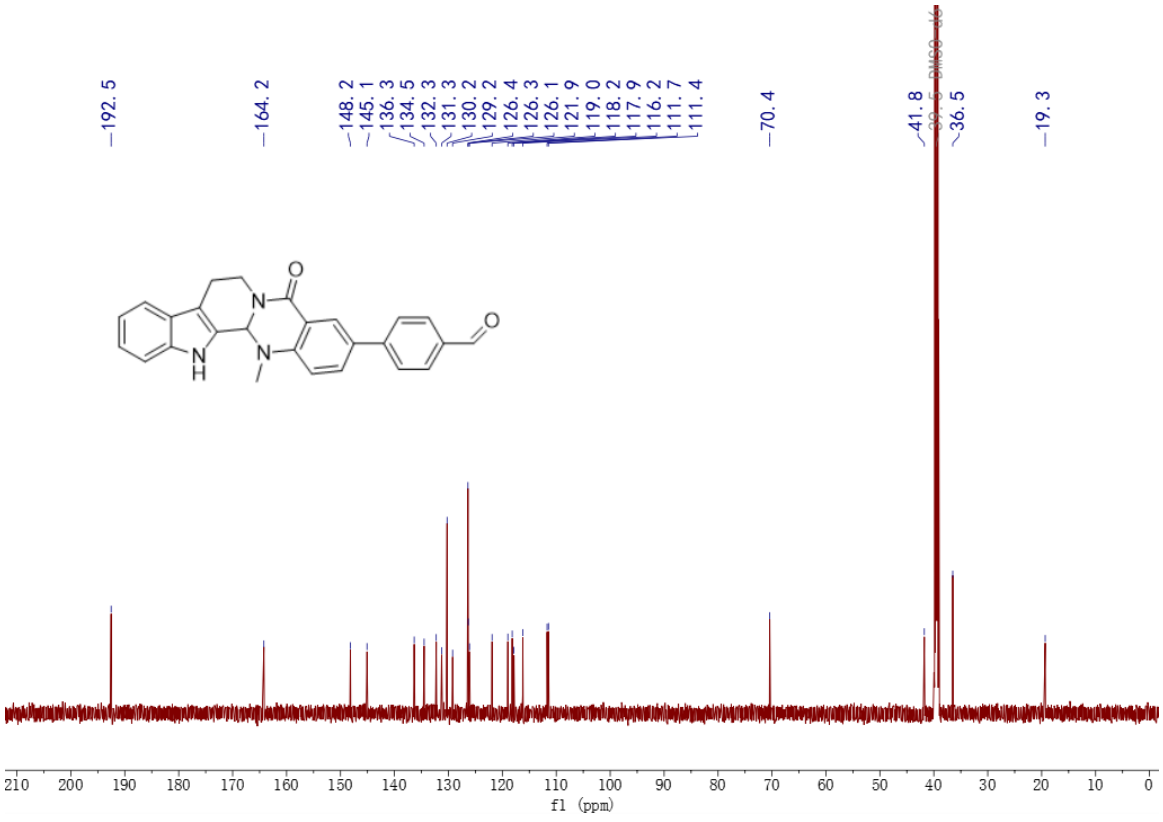


Figure 48. ^{13}C NMR spectrum of compound **6u** (150 MHz, DMSO-d_6)

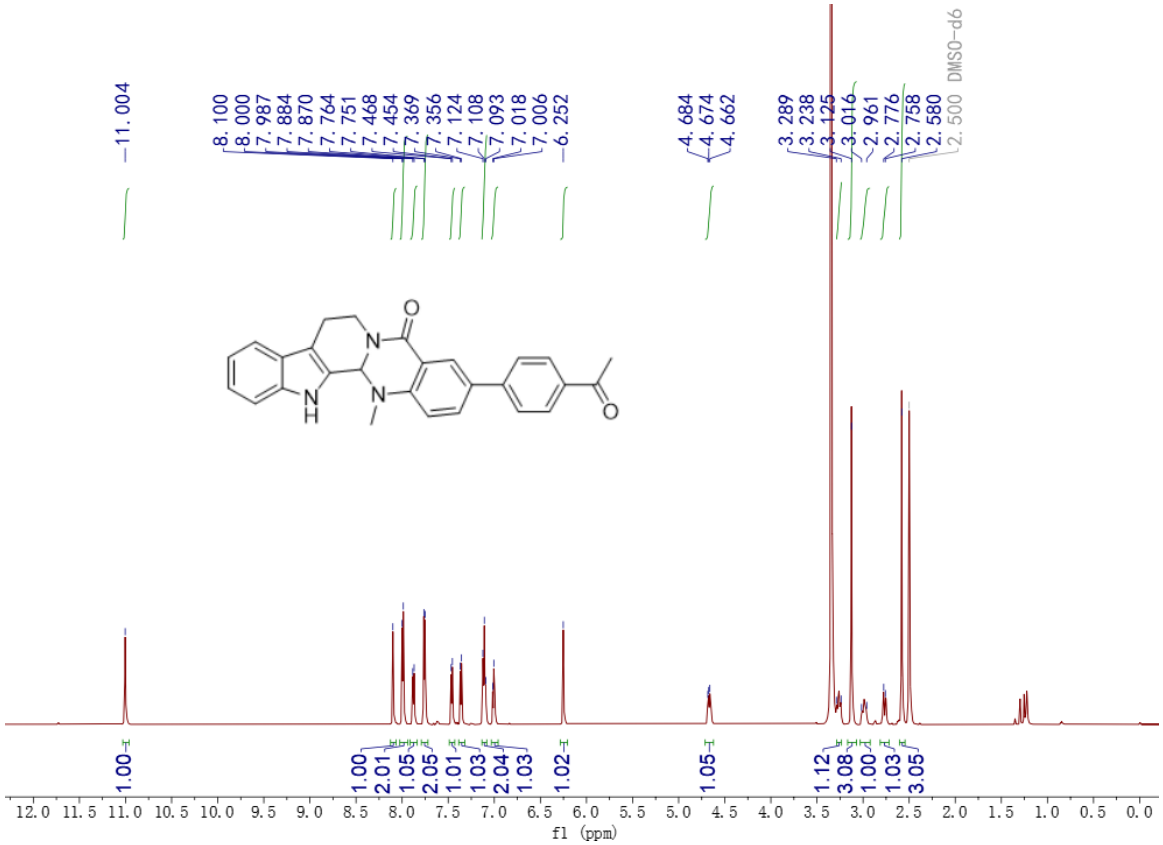


Figure 49. ^{1}H NMR spectrum of compound **6v** (600 MHz, DMSO-d_6)

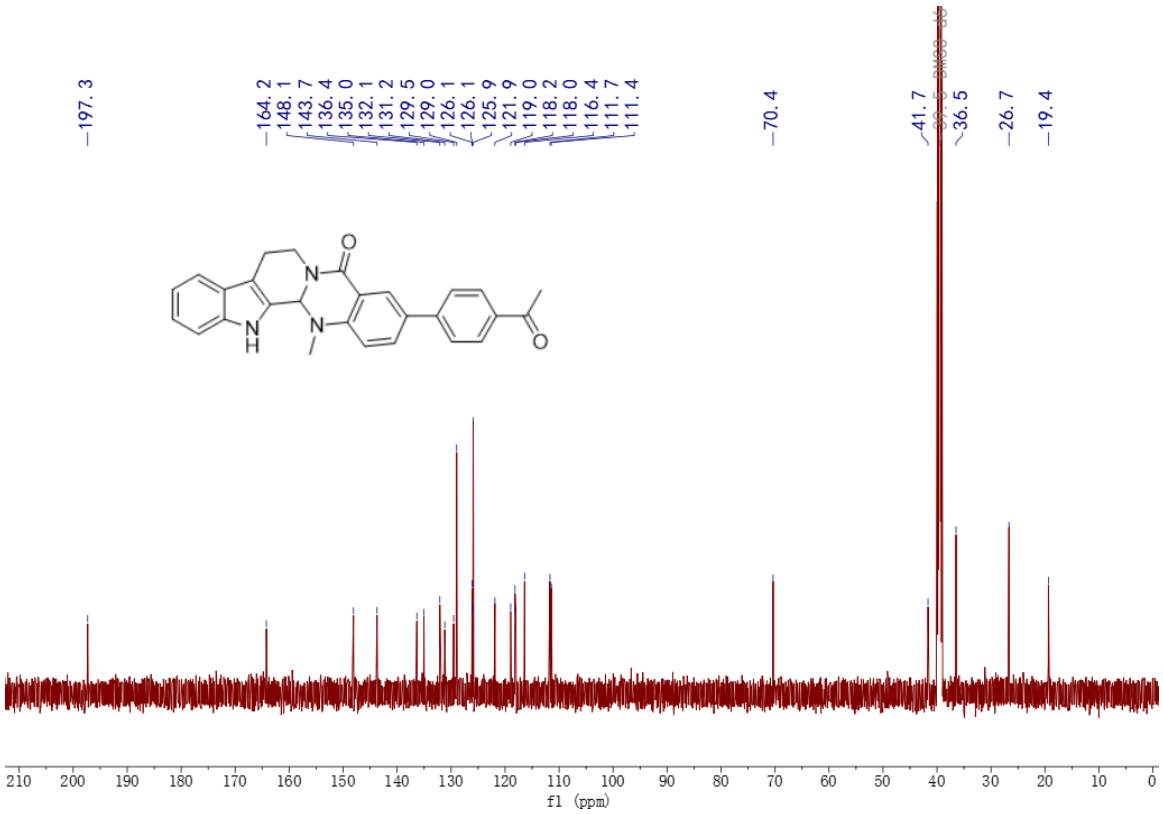


Figure 50. ^{13}C NMR spectrum of compound **6v** (100 MHz, DMSO-d_6)

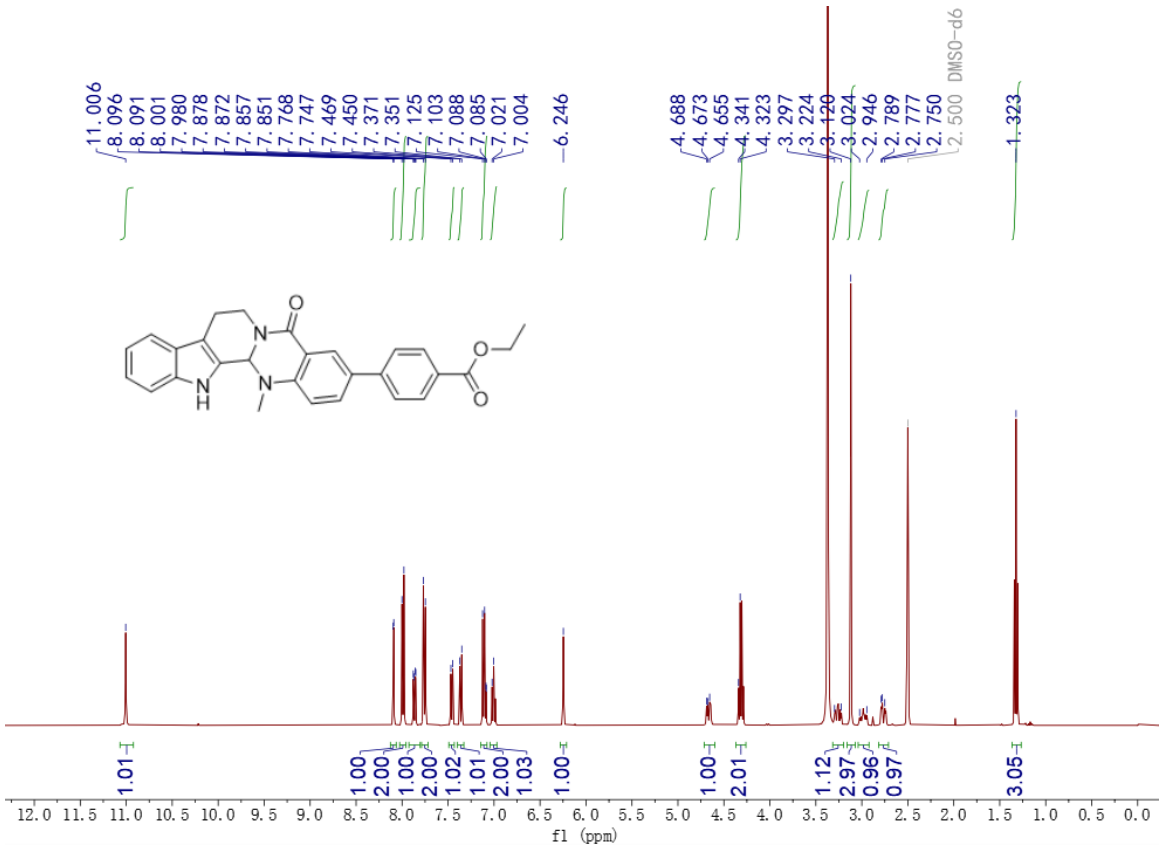


Figure 51. ^{1}H NMR spectrum of compound **6w** (400 MHz, DMSO-d_6)

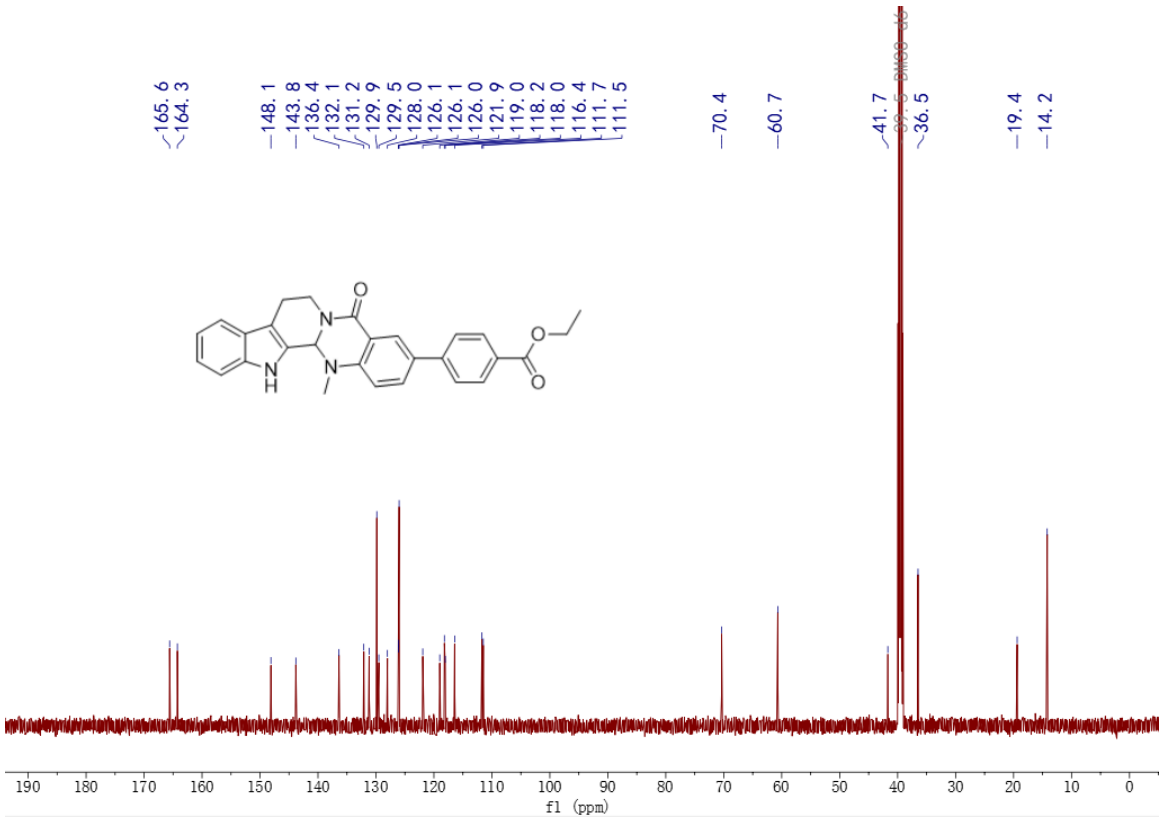


Figure 52. ^{13}C NMR spectrum of compound **6w** (150 MHz, DMSO-d_6)

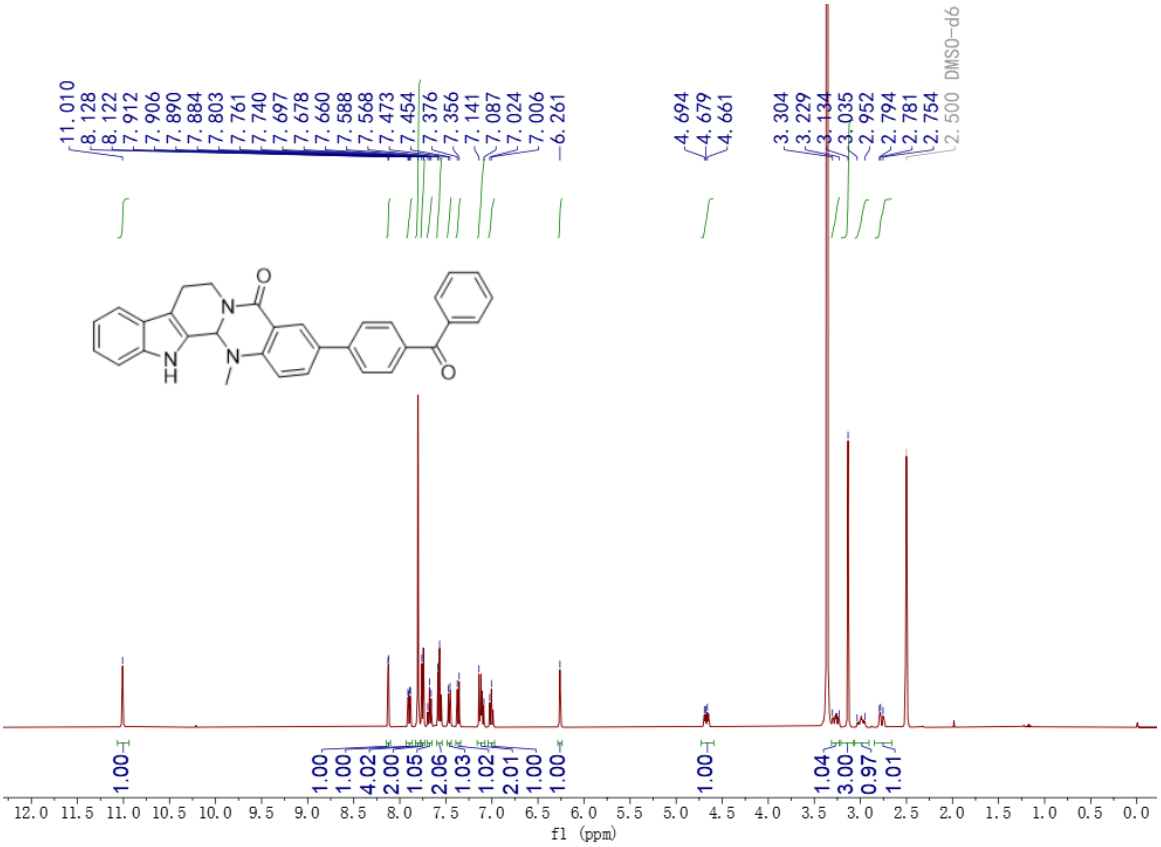


Figure 53. ^{1}H NMR spectrum of compound **6x** (400 MHz, DMSO-d_6)

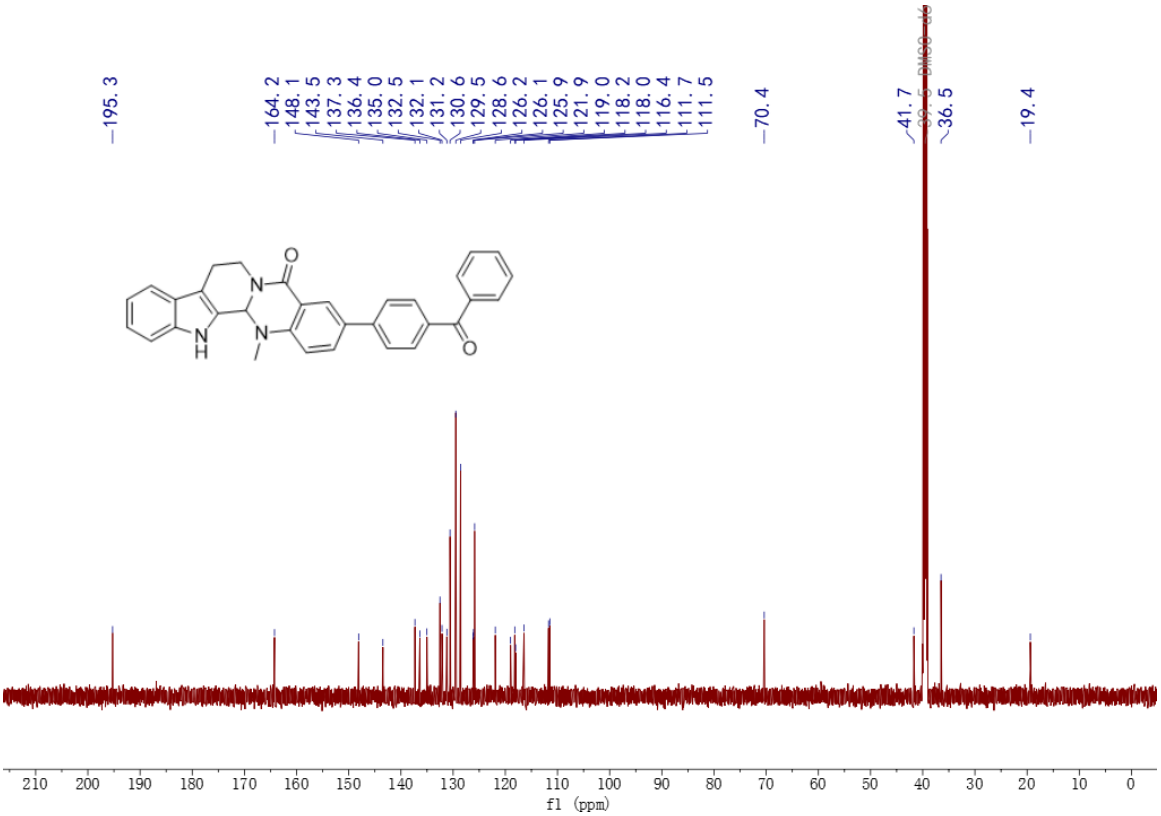


Figure 54. ^{13}C NMR spectrum of compound **6x** (150 MHz, DMSO-d_6)

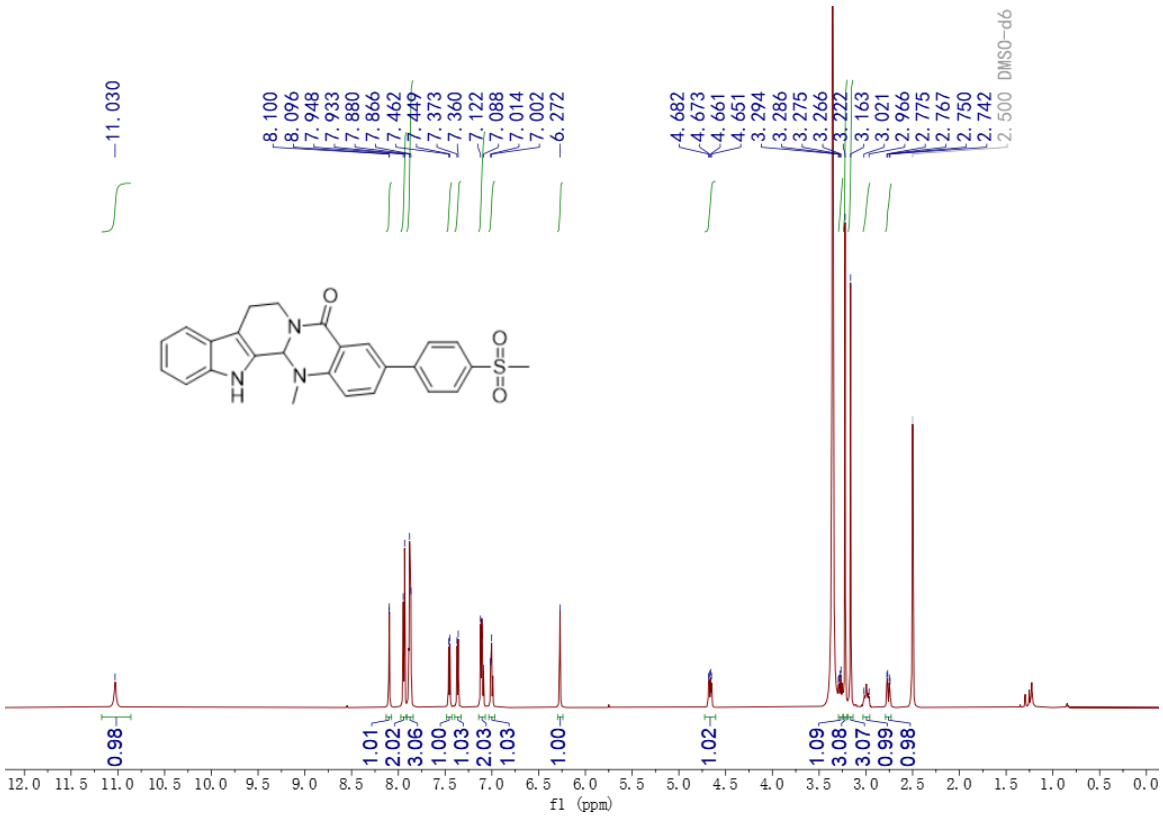


Figure 55. ^{1}H NMR spectrum of compound **6y** (600 MHz, DMSO-d_6)

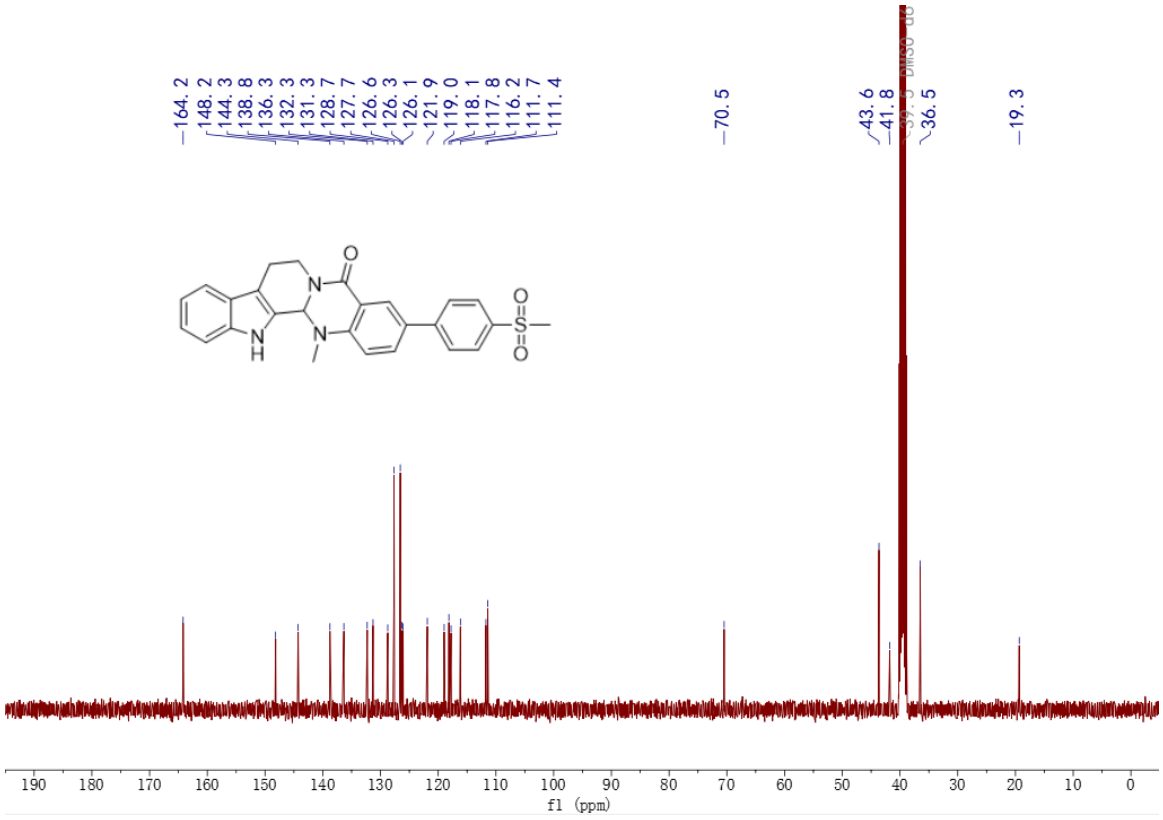


Figure 56. ^{13}C NMR spectrum of compound **6y** (100 MHz, DMSO-d_6)

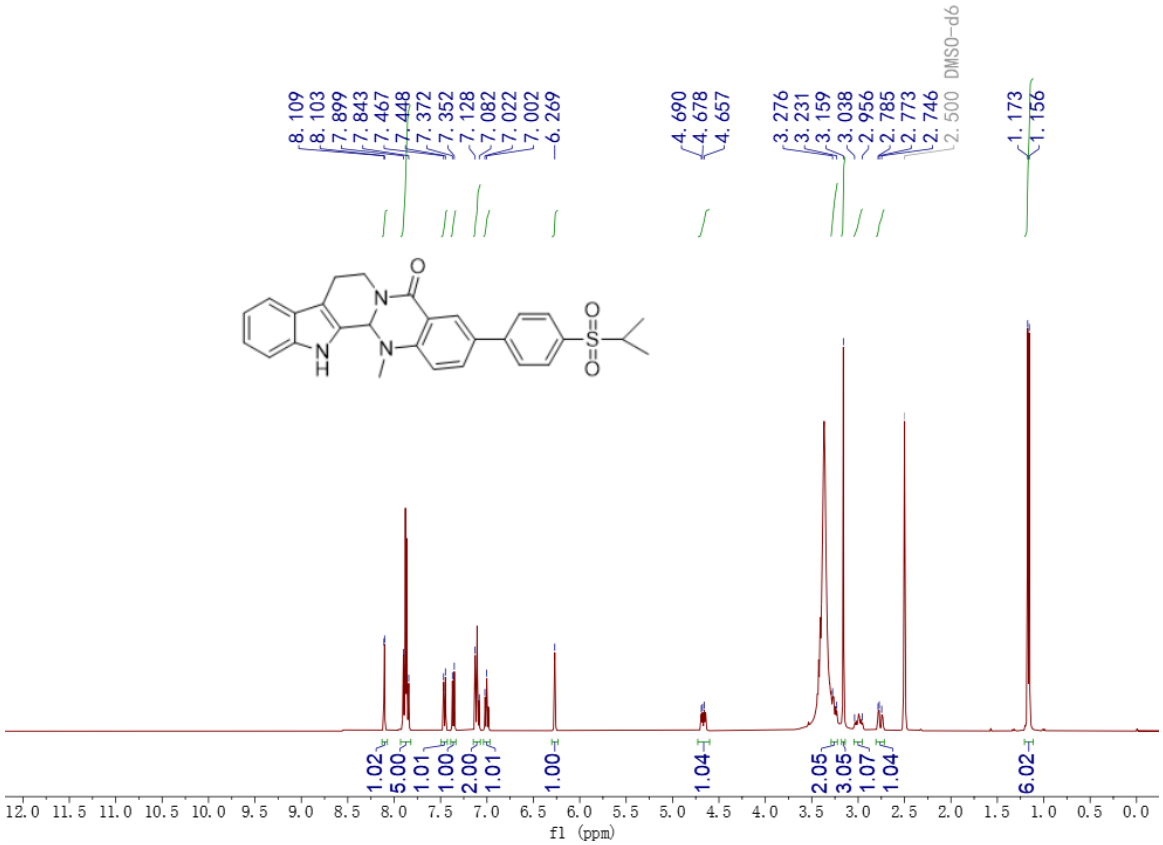


Figure 57. ^{1}H NMR spectrum of compound **6z** (400 MHz, DMSO-d_6)

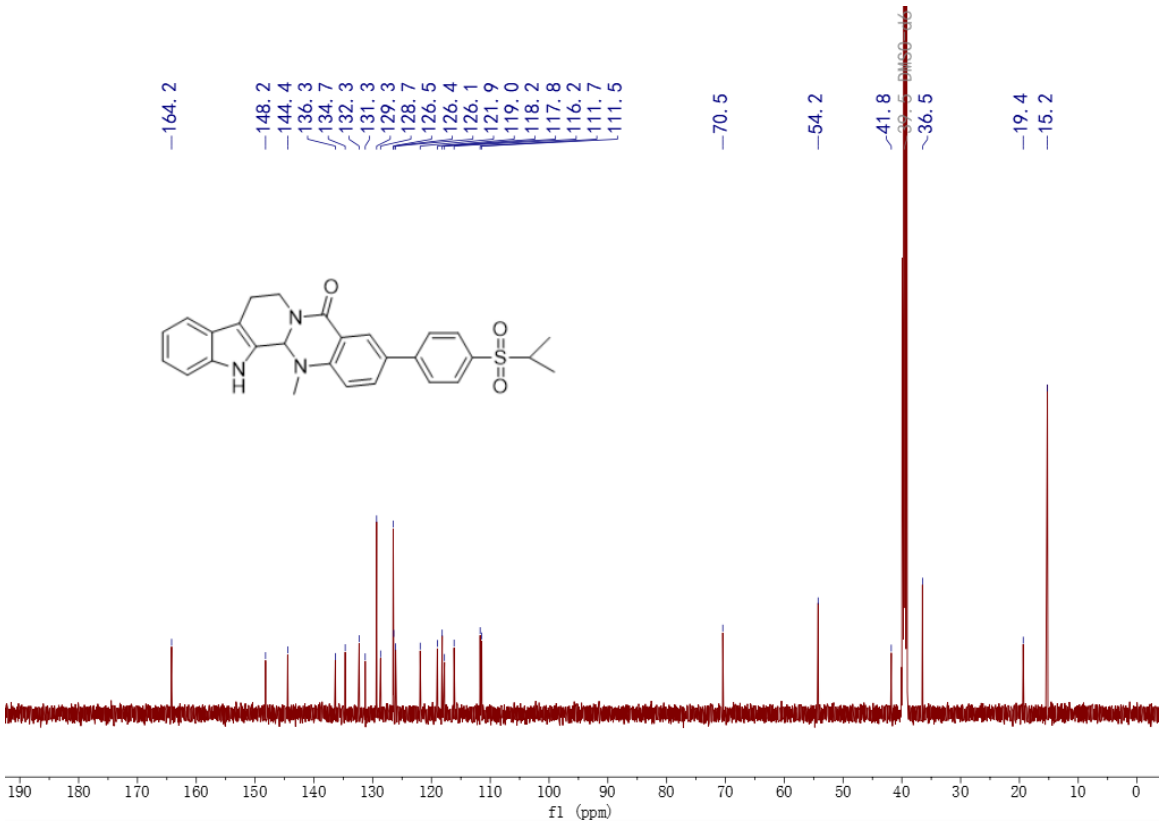


Figure 58. ^{13}C NMR spectrum of compound **6z** (150 MHz, DMSO-d_6)

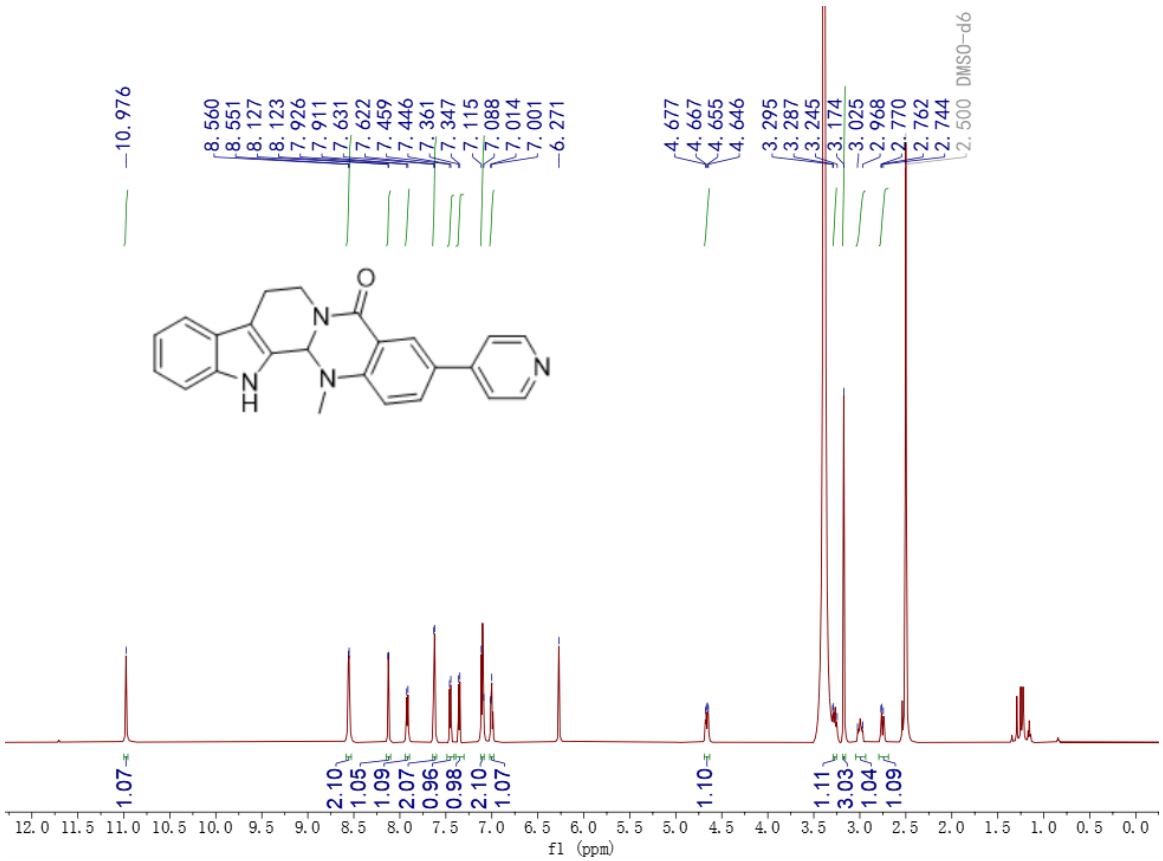


Figure 59. ^{1}H NMR spectrum of compound **6aa** (600 MHz, DMSO-d_6)

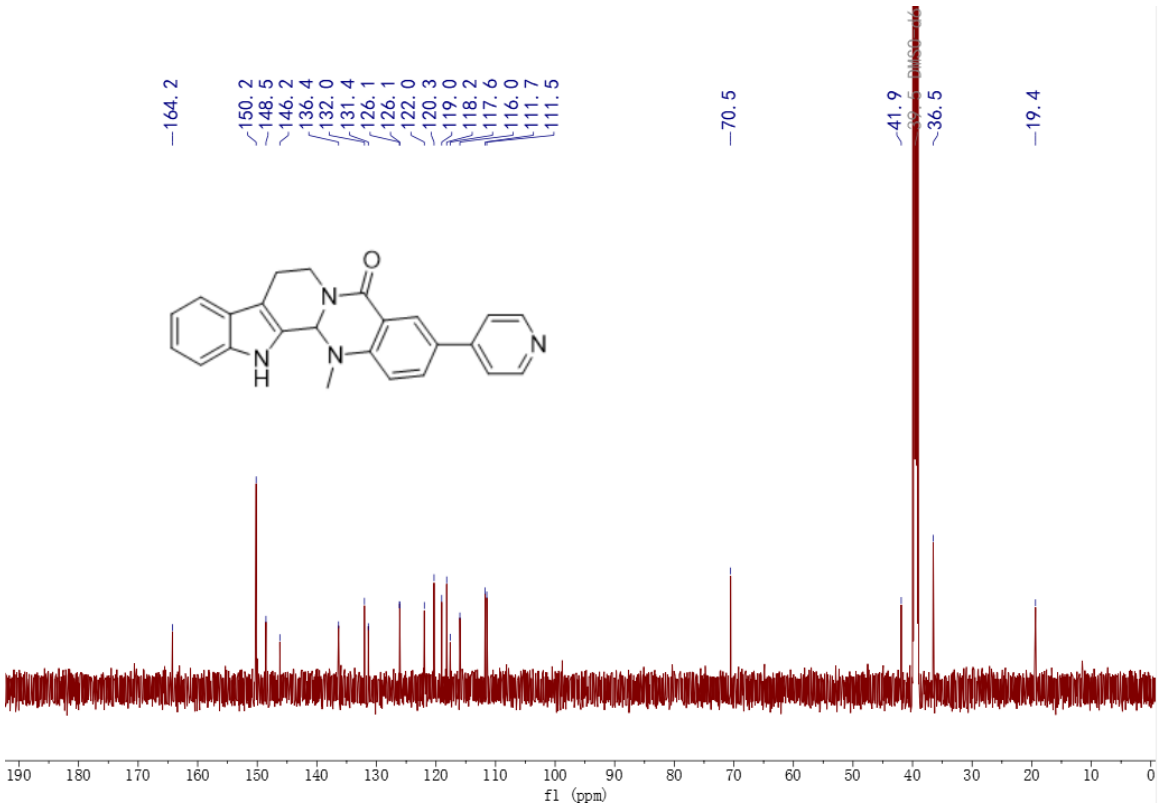


Figure 60. ^{13}C NMR spectrum of compound **6aa** (150 MHz, DMSO-d_6)

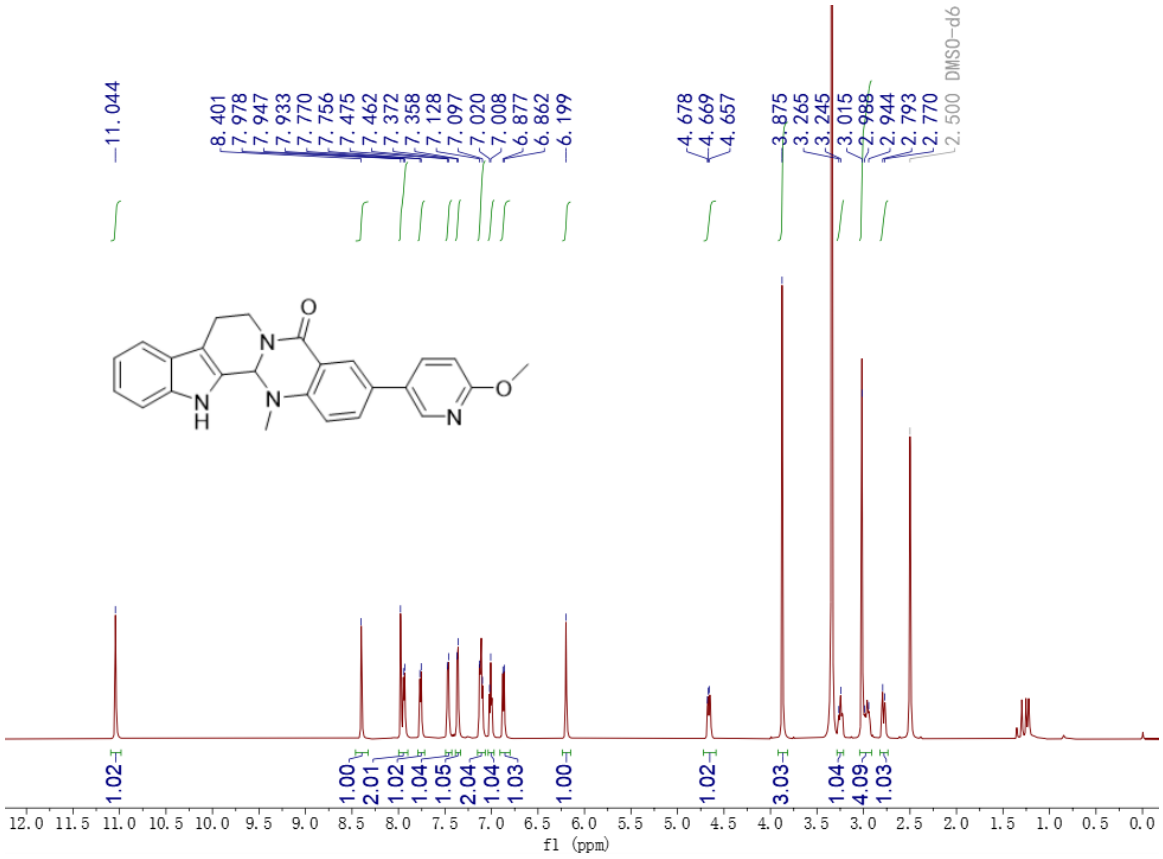


Figure 61. ^{1}H NMR spectrum of compound **6ab** (600 MHz, DMSO-d_6)

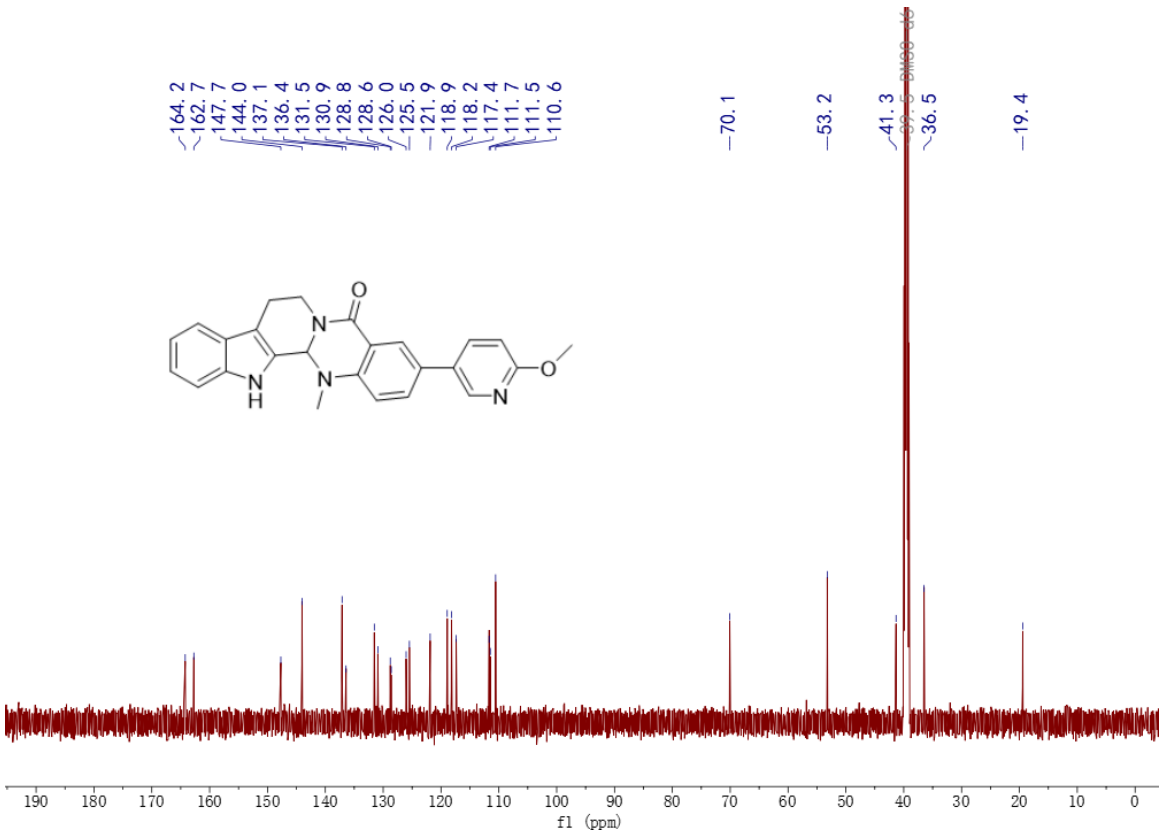


Figure 62. ^{13}C NMR spectrum of compound **6ab** (150 MHz, DMSO-d_6)

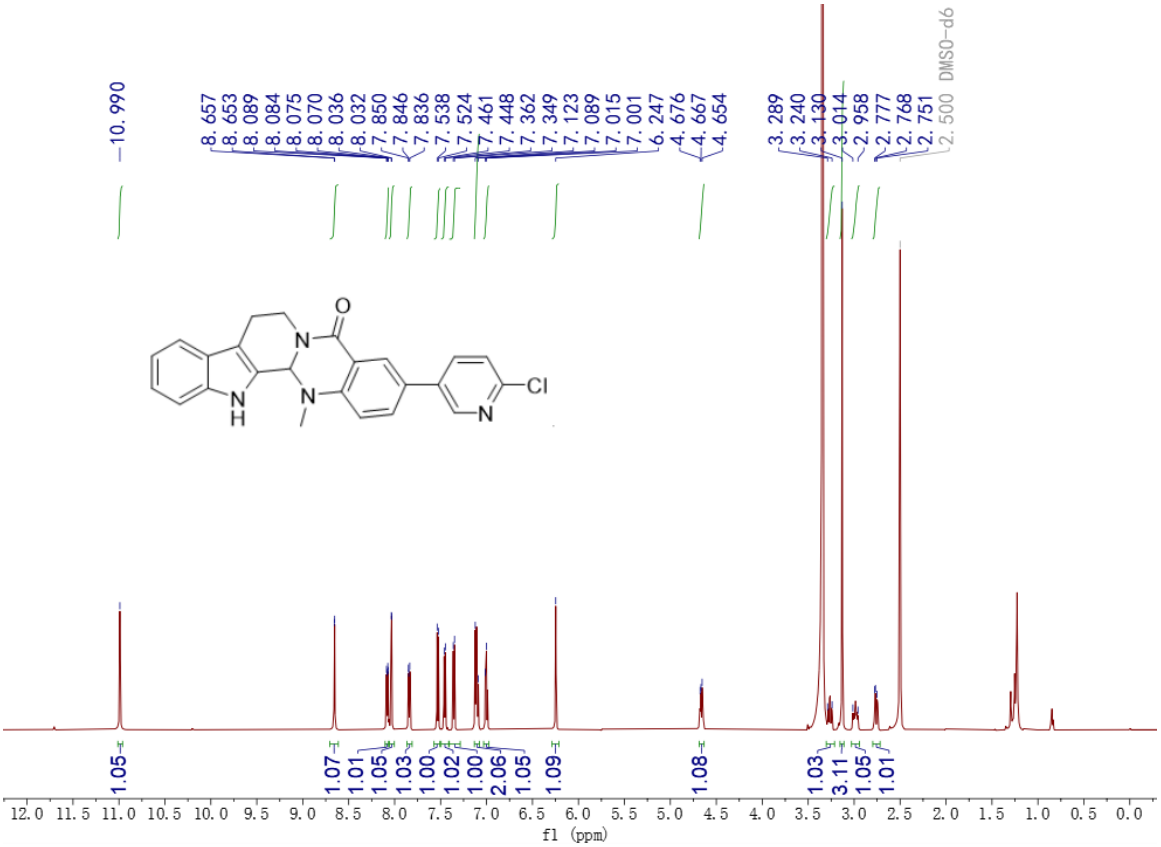


Figure 63. ^{1}H NMR spectrum of compound **6ac** (600 MHz, DMSO-d_6)

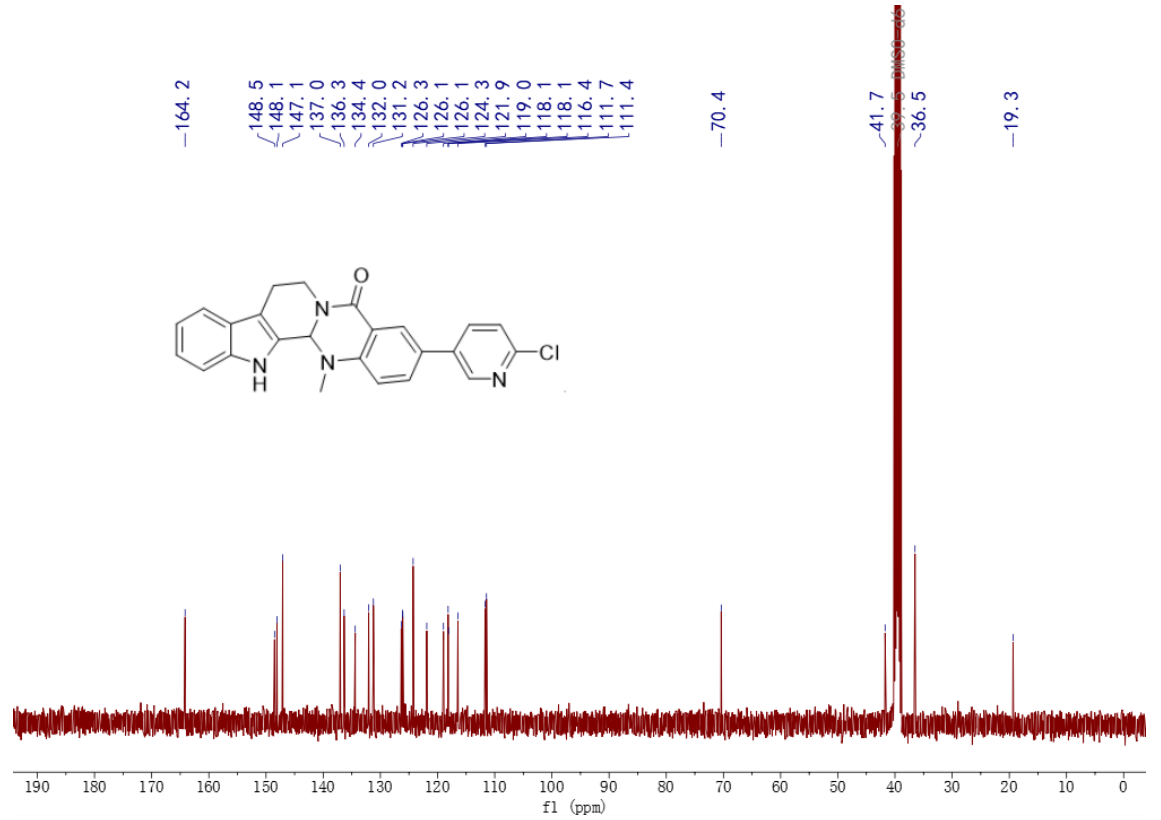


Figure 64. ^{13}C NMR spectrum of compound **6ac** (150 MHz, DMSO-d_6)

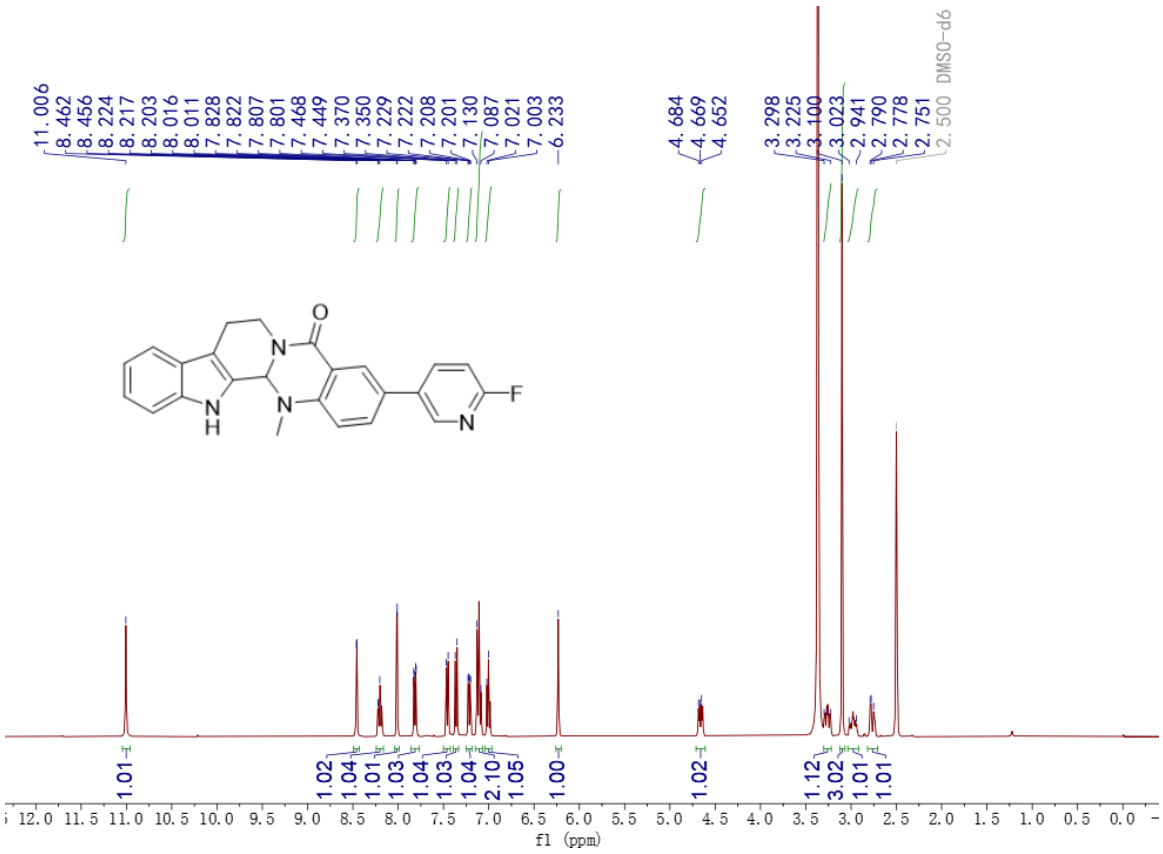


Figure 65. ^{1}H NMR spectrum of compound **6ad** (400 MHz, DMSO-d_6)

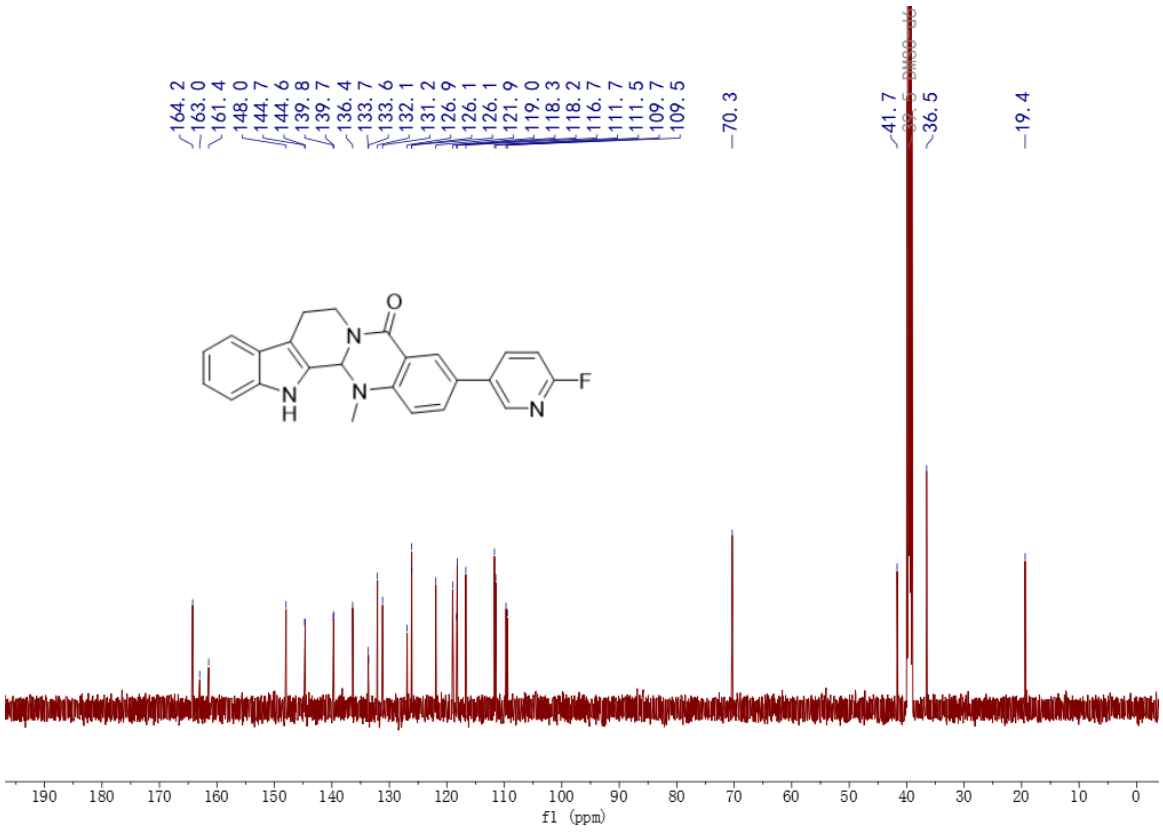


Figure 66. ^{13}C NMR spectrum of compound **6ad** (150 MHz, DMSO-d_6)

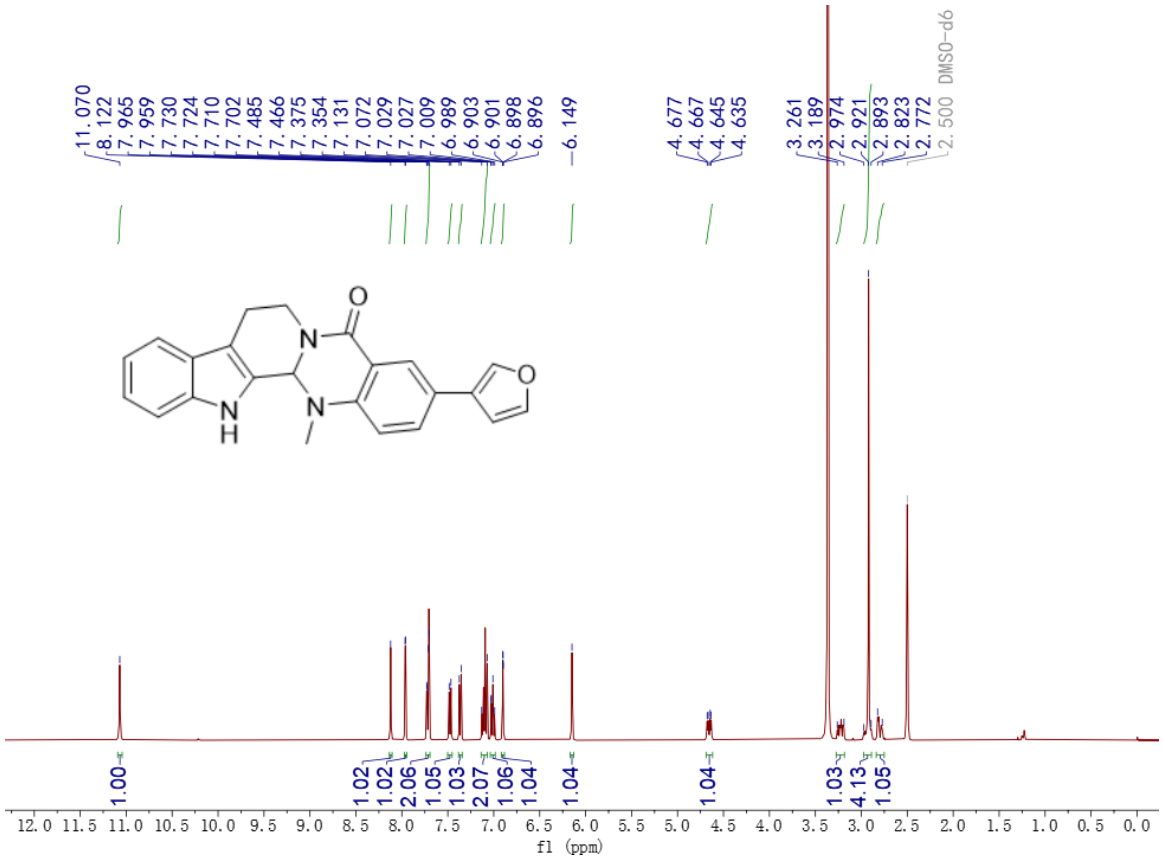


Figure 67. ^{1}H NMR spectrum of compound **6ae** (400 MHz, DMSO-d_6)

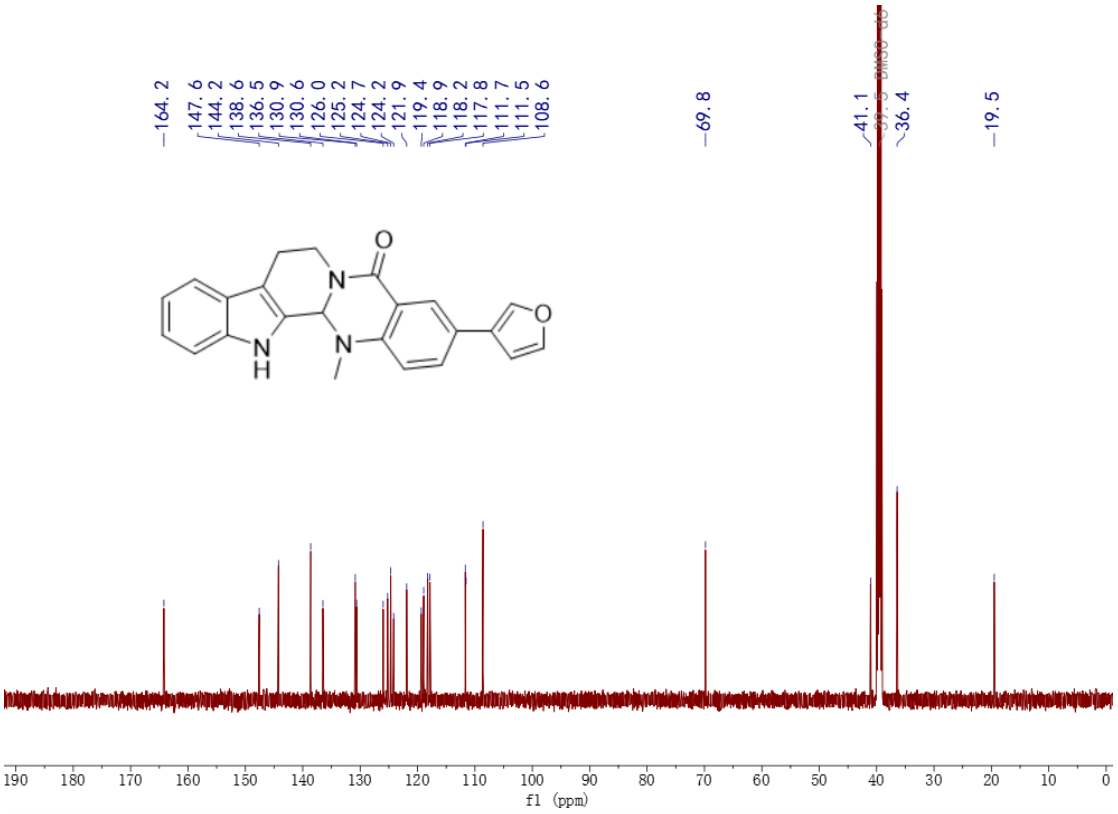


Figure 68. ^{13}C NMR spectrum of compound **6ae** (150 MHz, DMSO-d_6)