

Supporting Information

Design, synthesis and structure-activity relationship analysis of the dibenzodiazepinone derivatives against osimertinib resistant NSCLC

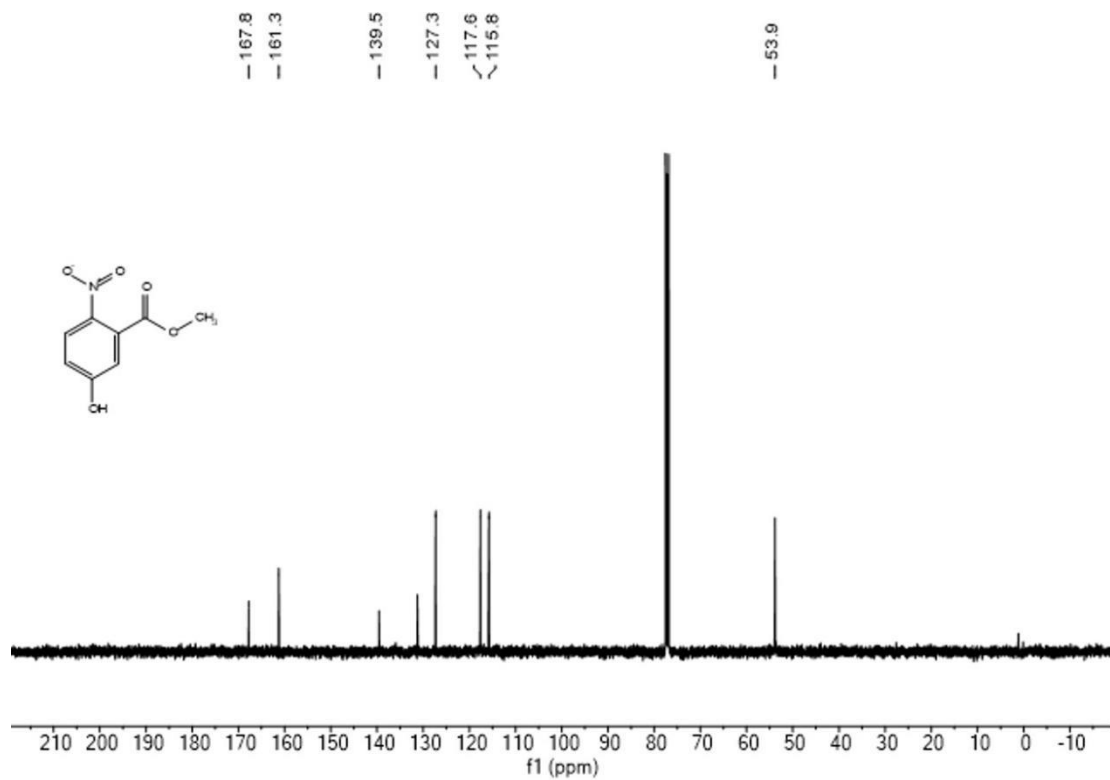
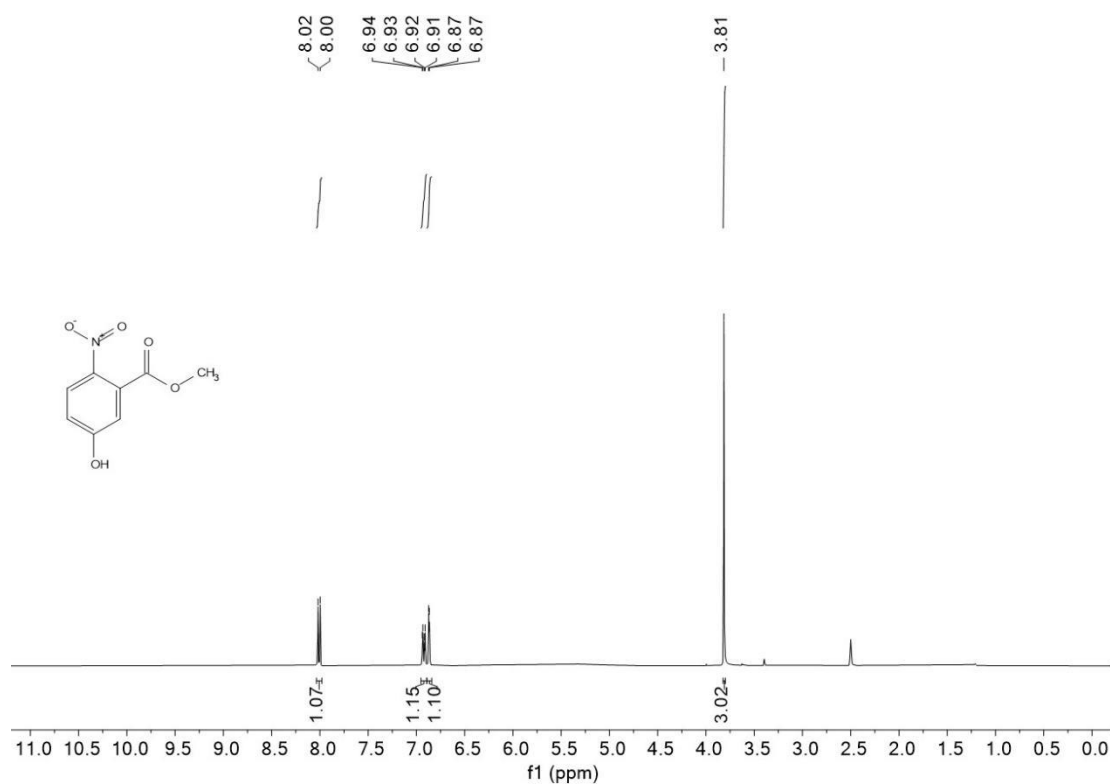
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1. NMR spectra of the intermediates and the final target compounds.



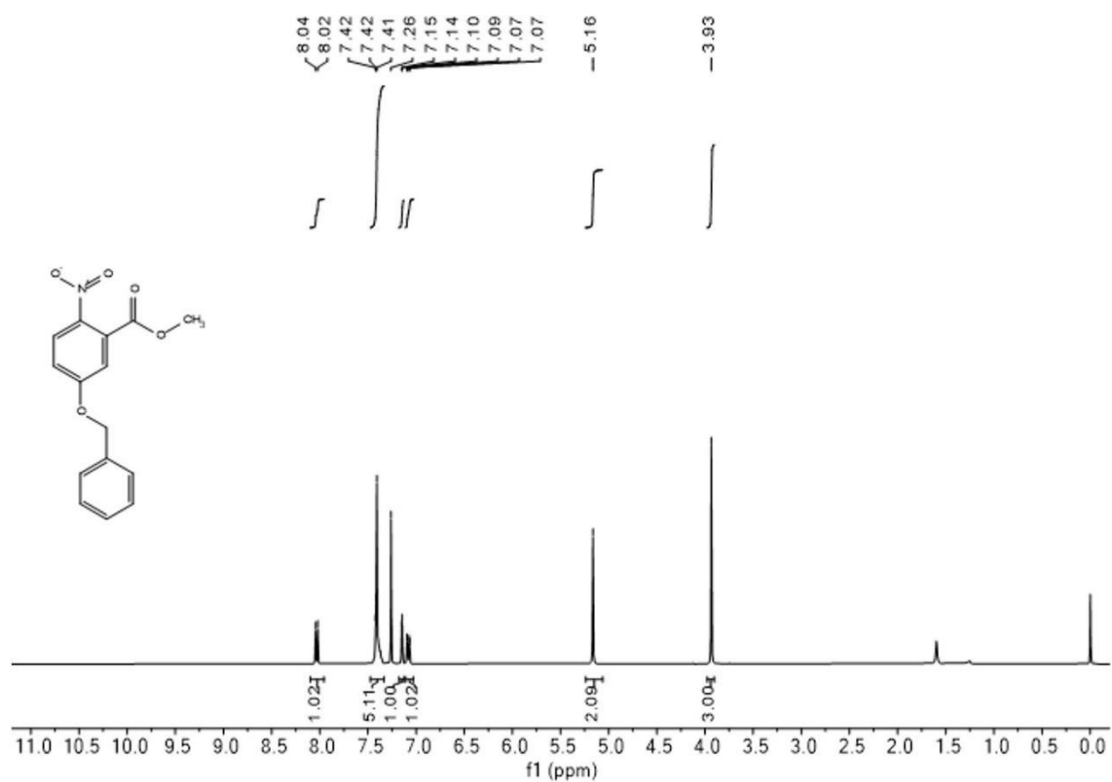


Figure S3. ¹H NMR (400 MHz, CDCl₃) spectrum of compound S3.

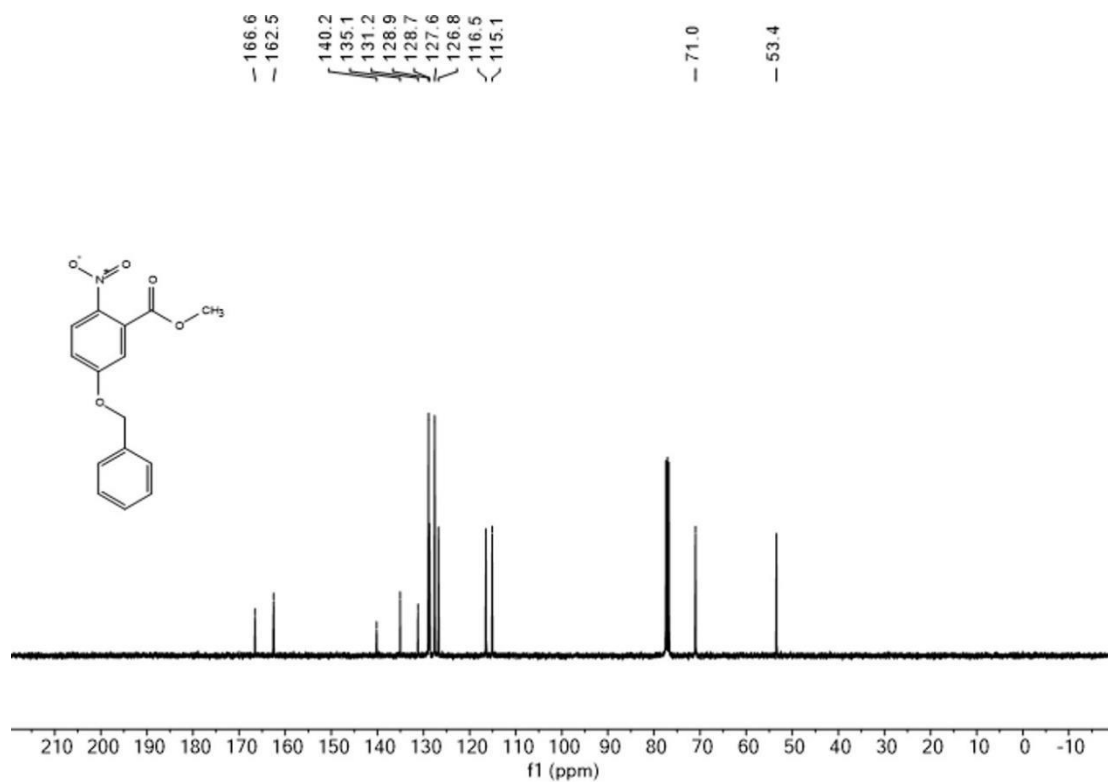


Figure S4. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound S3.

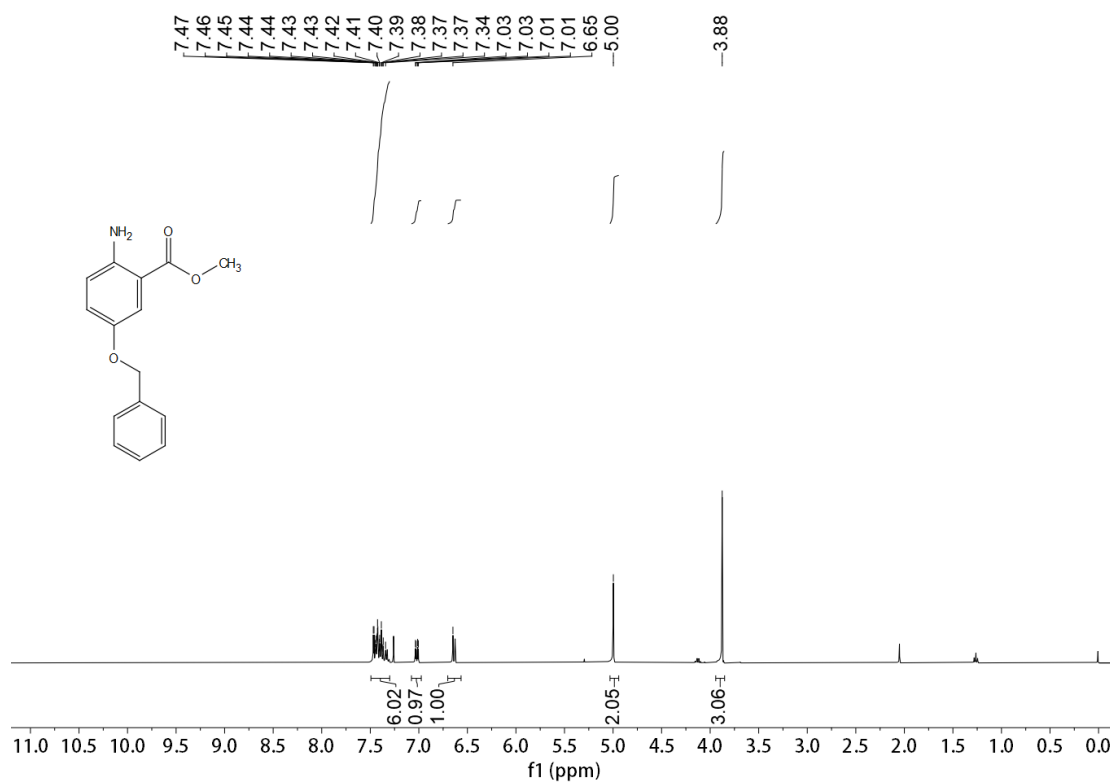


Figure S5. ¹H NMR (400 MHz, CDCl₃) spectrum of compound S4.

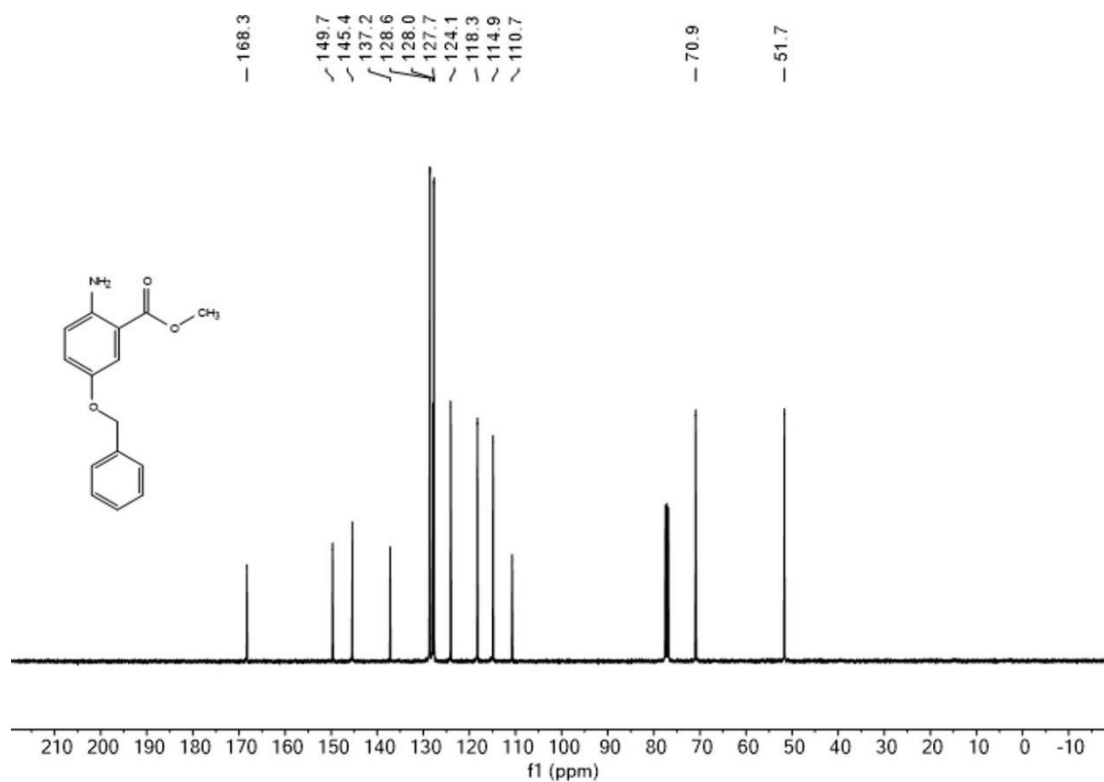


Figure S6. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound S4.

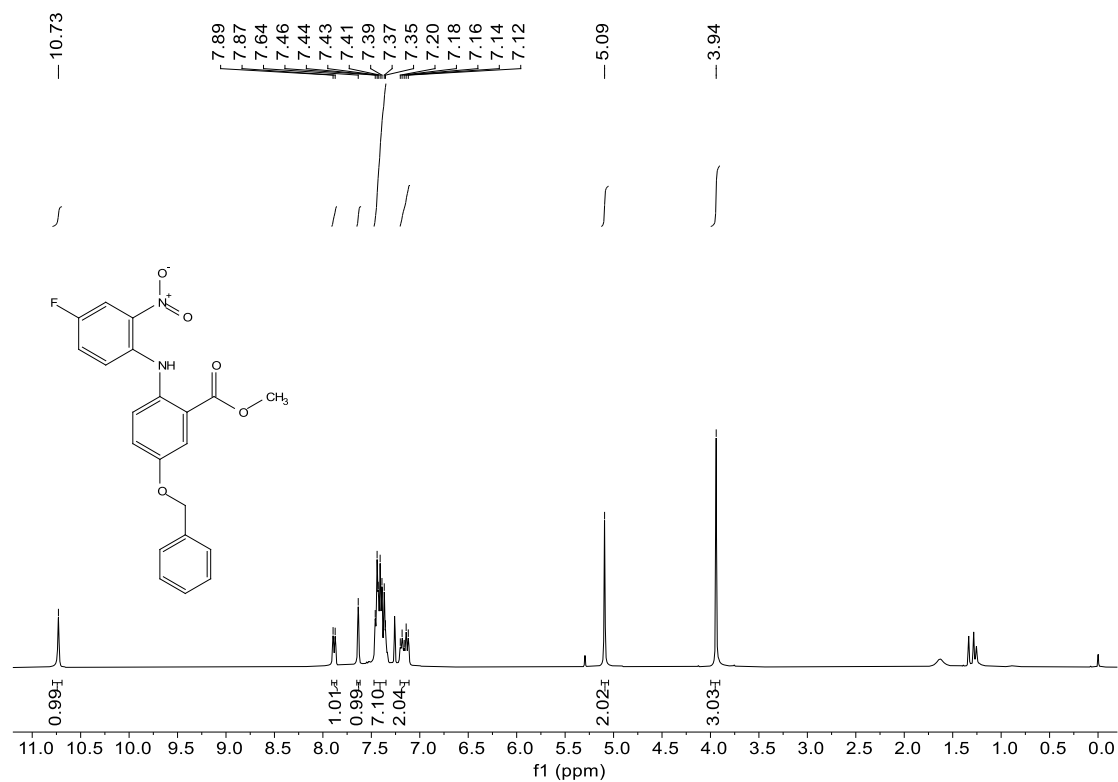


Figure S7. ¹H NMR (400 MHz, CDCl₃) spectrum of compound S5.

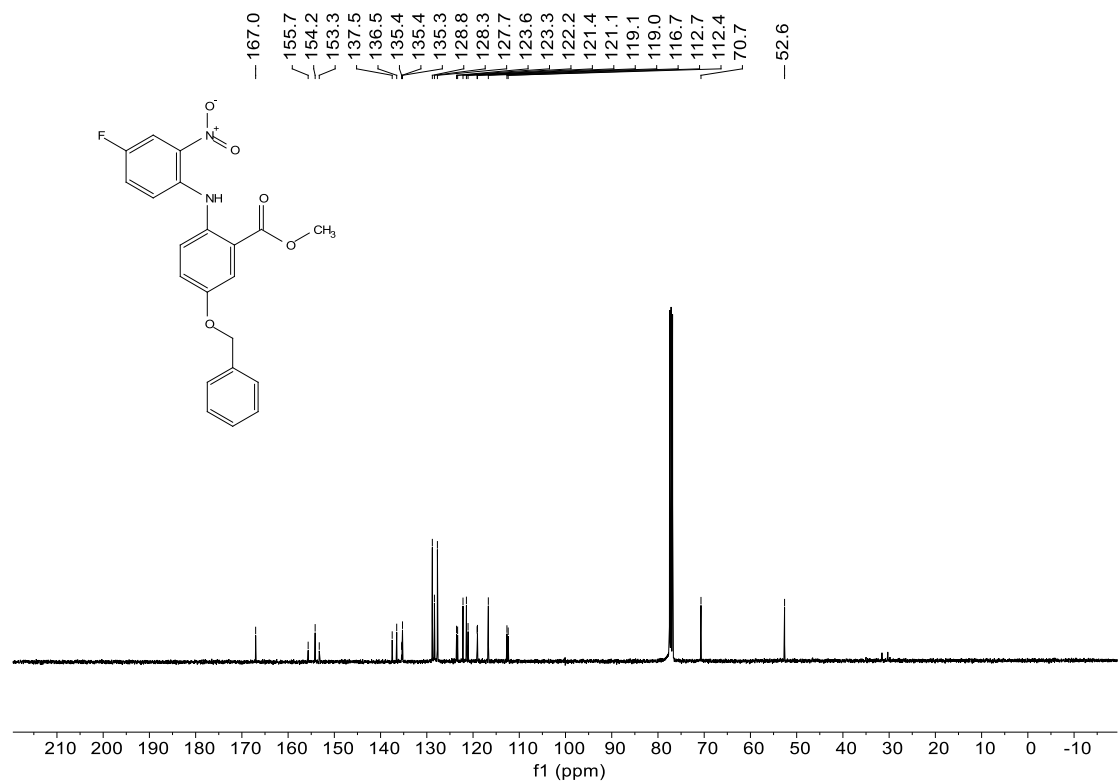


Figure S8. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound S5.

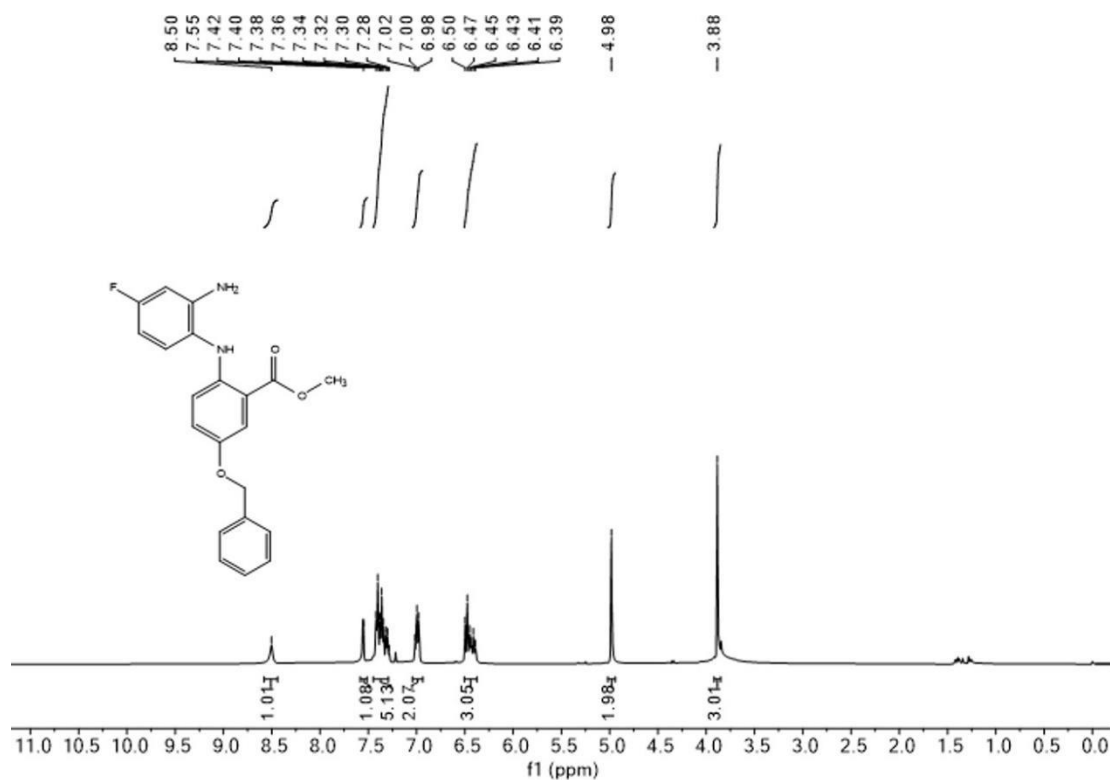


Figure S9. ¹H NMR (400 MHz, CDCl₃) spectrum of compound S6.

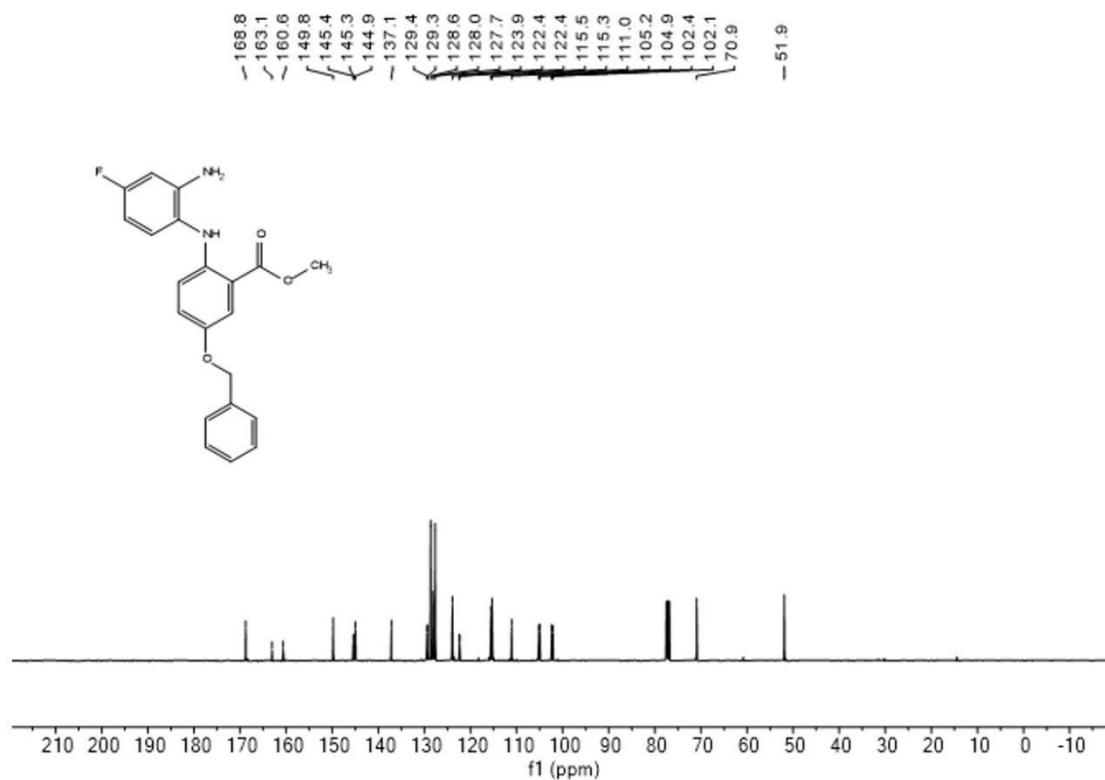


Figure S10. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound S6.

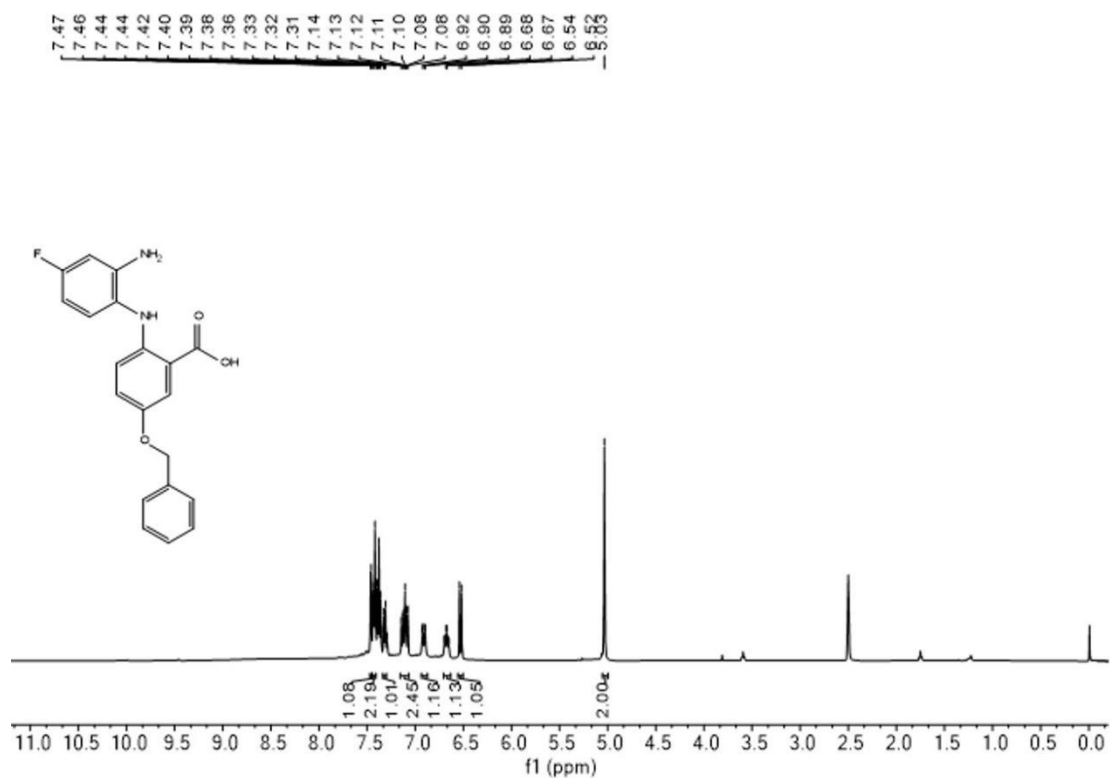


Figure S11. ¹H NMR (400 MHz, DMSO-*d*₆) spectrum of compound S7.

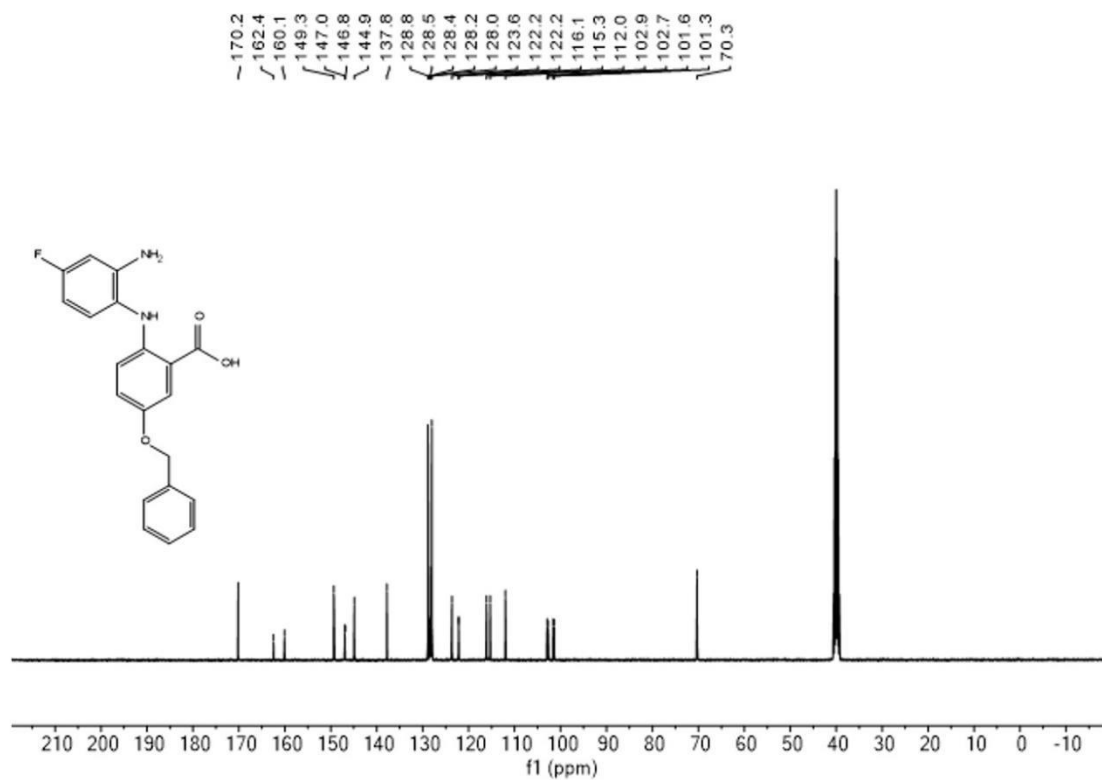


Figure S12. ¹³C NMR (101 MHz, DMSO-*d*₆) spectrum of compound S7.

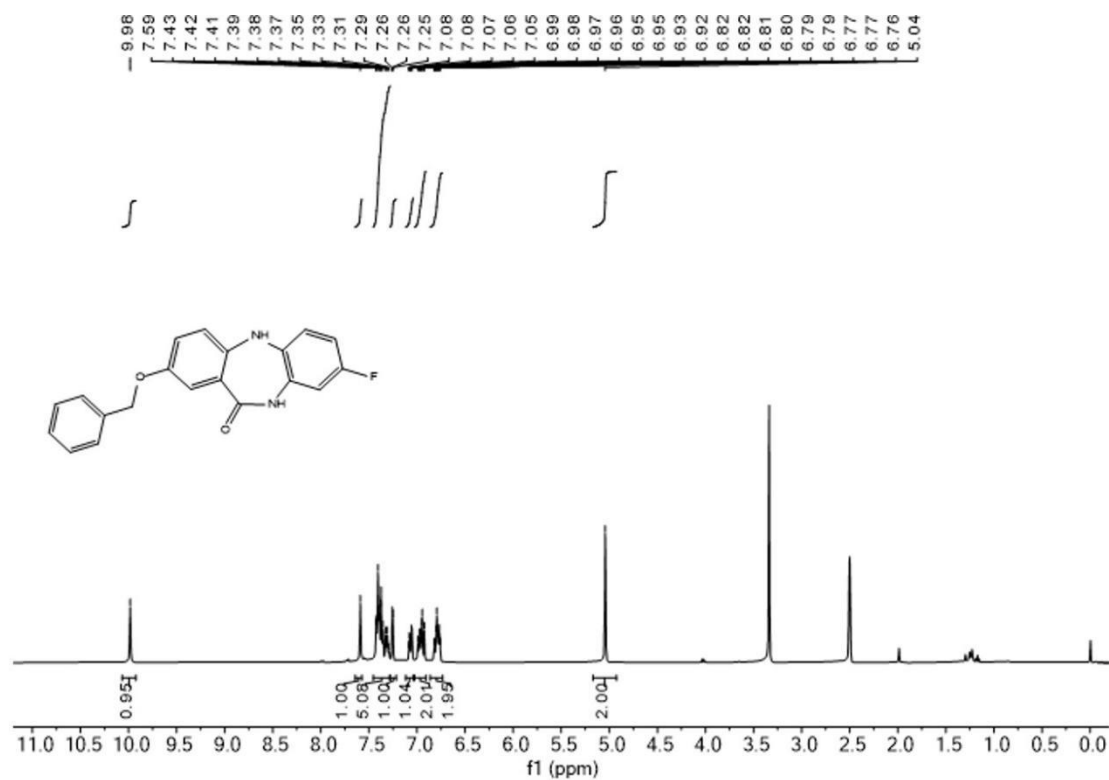


Figure S13. ¹H NMR (400 MHz, DMSO-*d*₆) spectrum of compound **S8**.

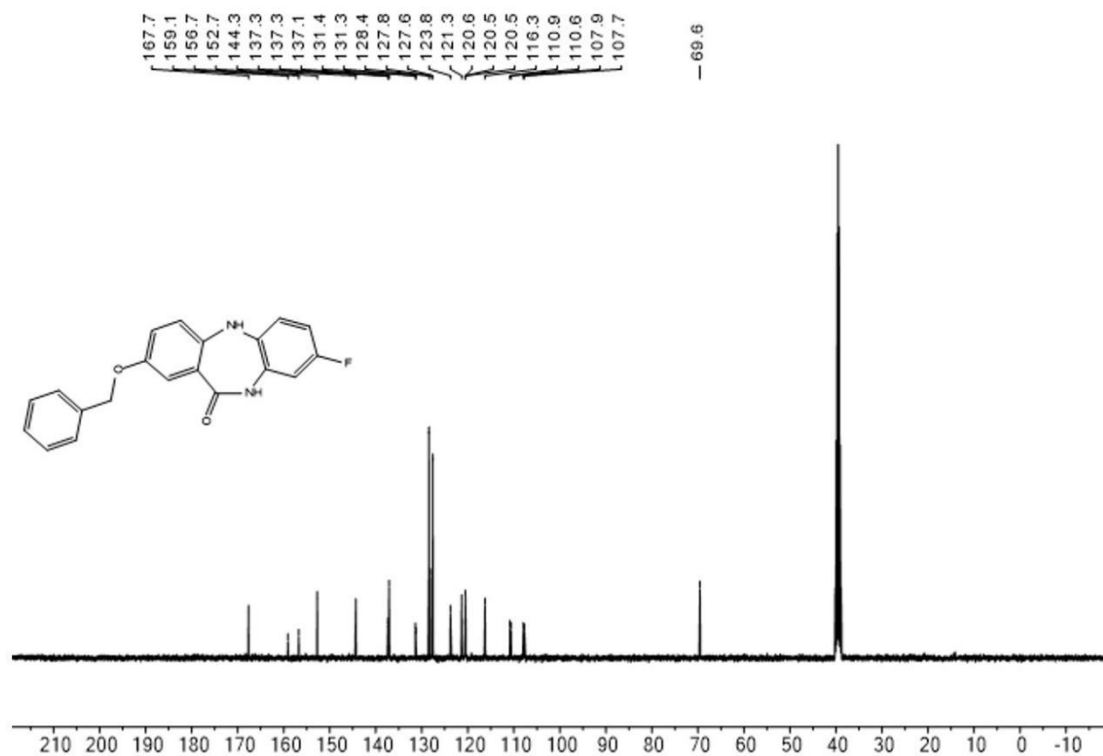


Figure S14. ¹³C NMR (101 MHz, DMSO-*d*₆) spectrum of compound **S8**.

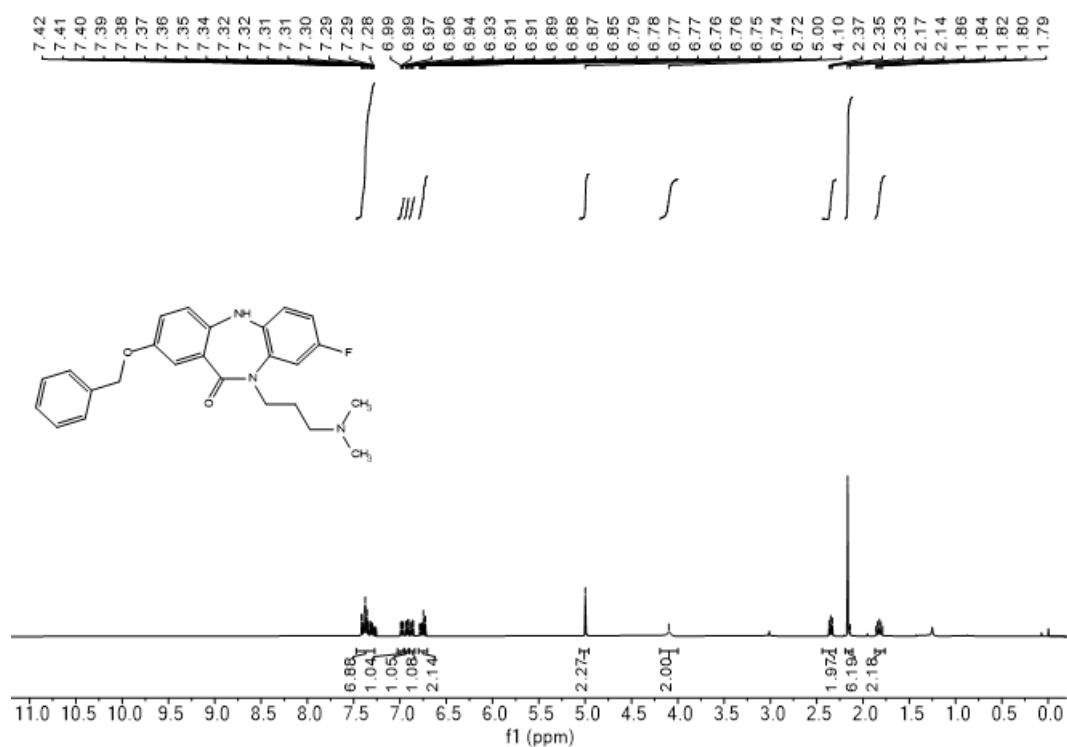


Figure S15. ¹H NMR (400 MHz, CDCl₃) spectrum of compound 1.

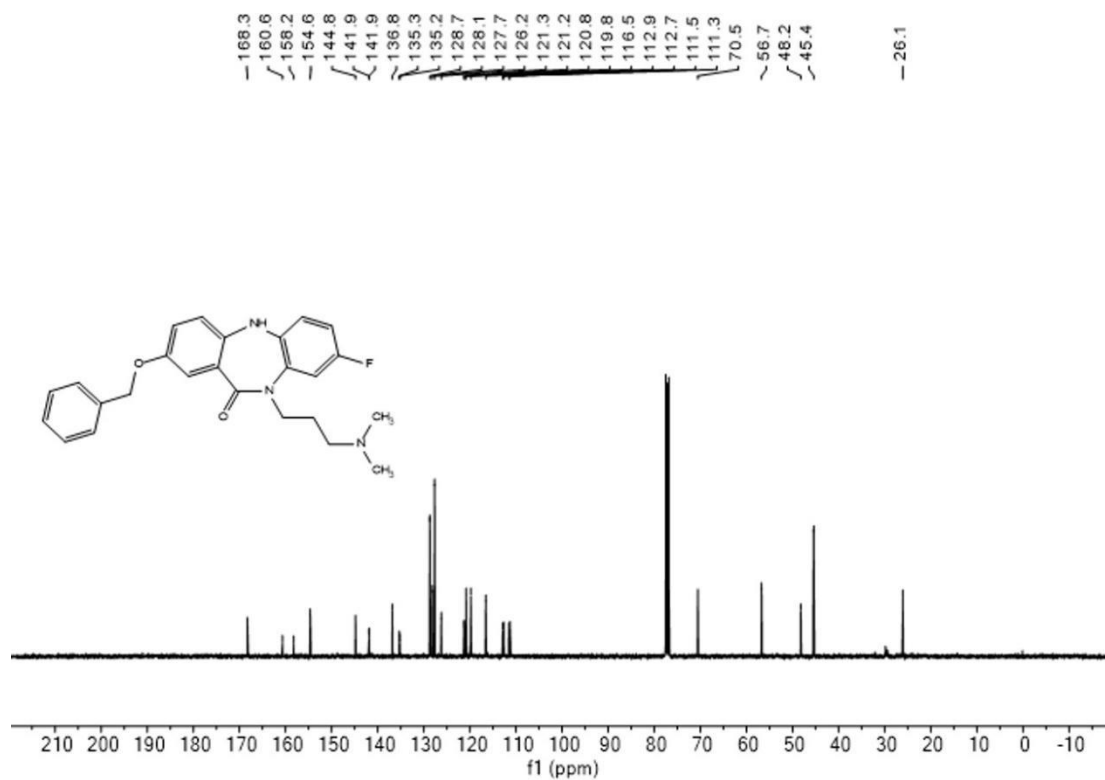


Figure S16. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound 1.

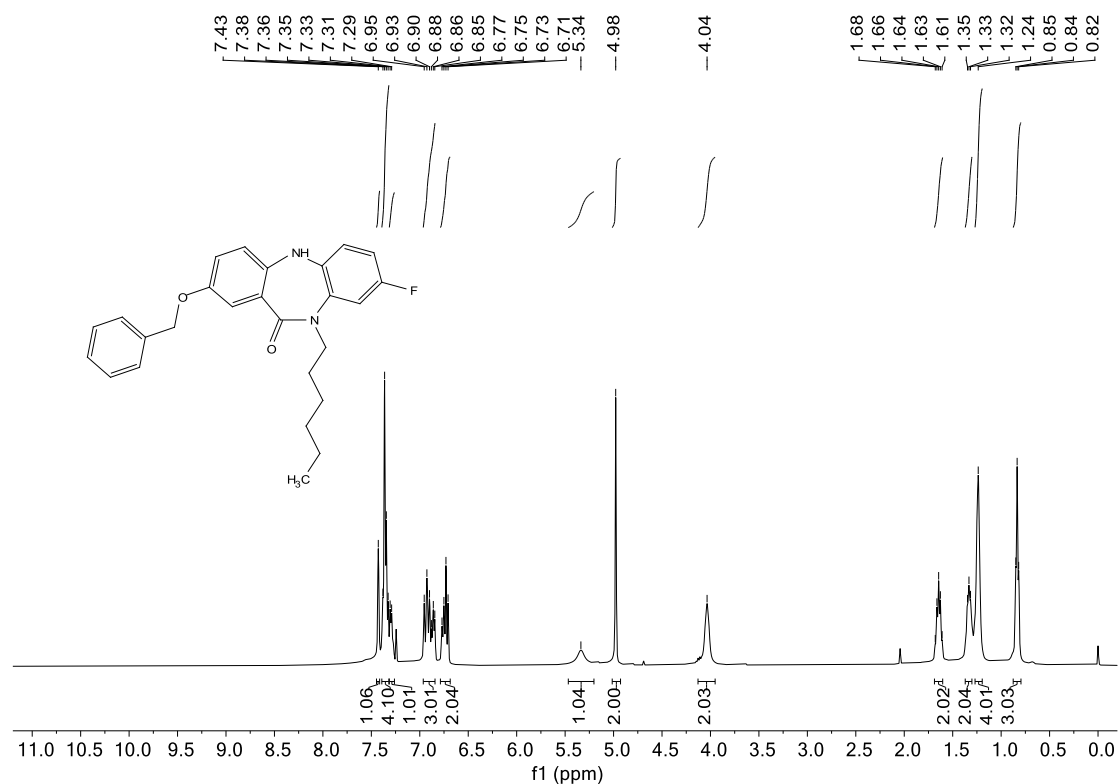


Figure S17. ¹H NMR (400 MHz, CDCl₃) spectrum of compound 2.

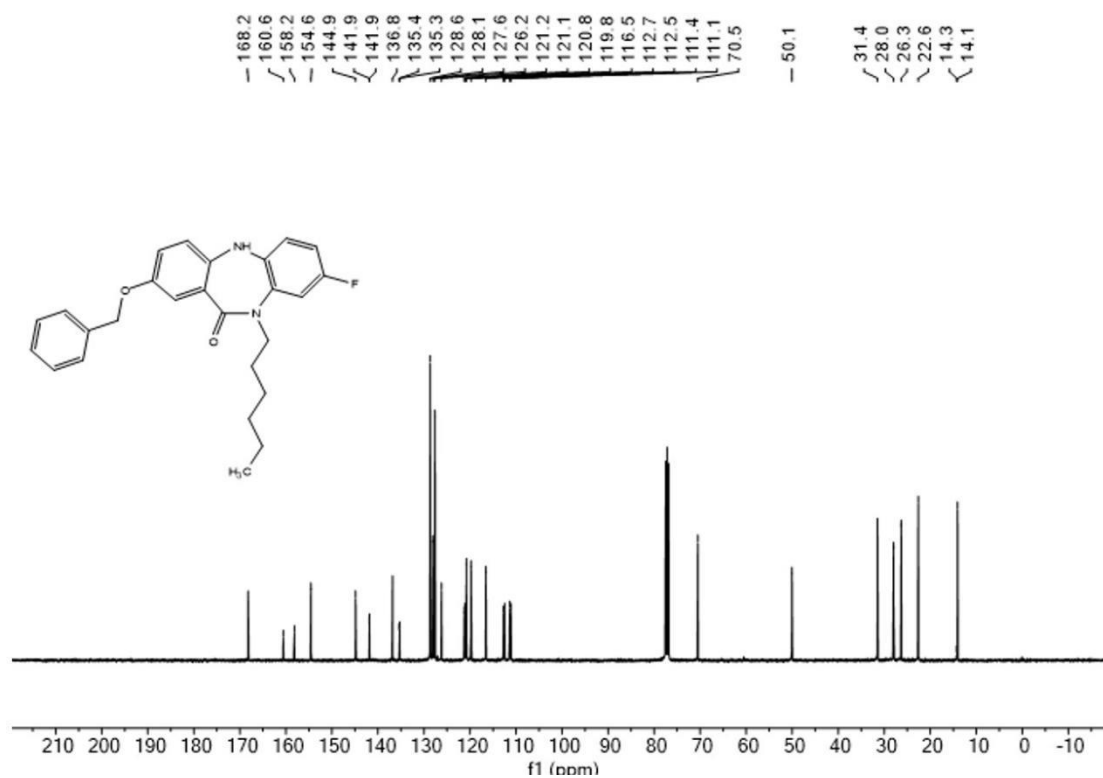


Figure S18. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound 2.

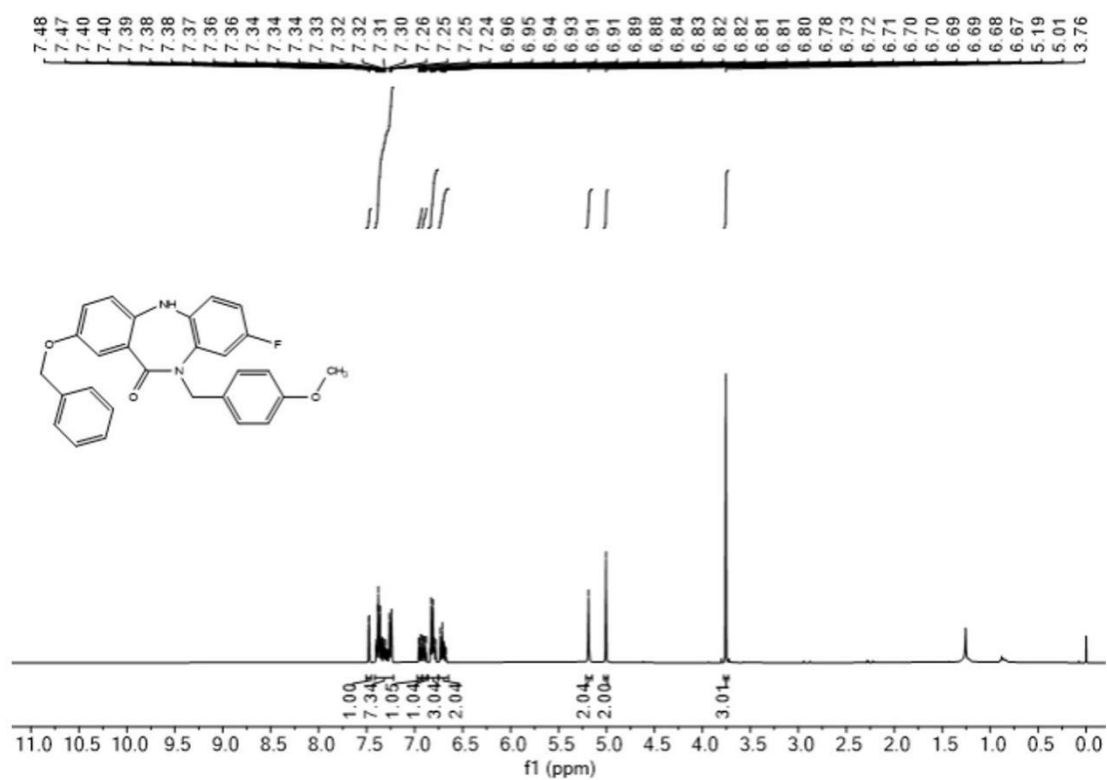


Figure S19. ¹H NMR (400 MHz, CDCl₃) spectrum of compound 3.

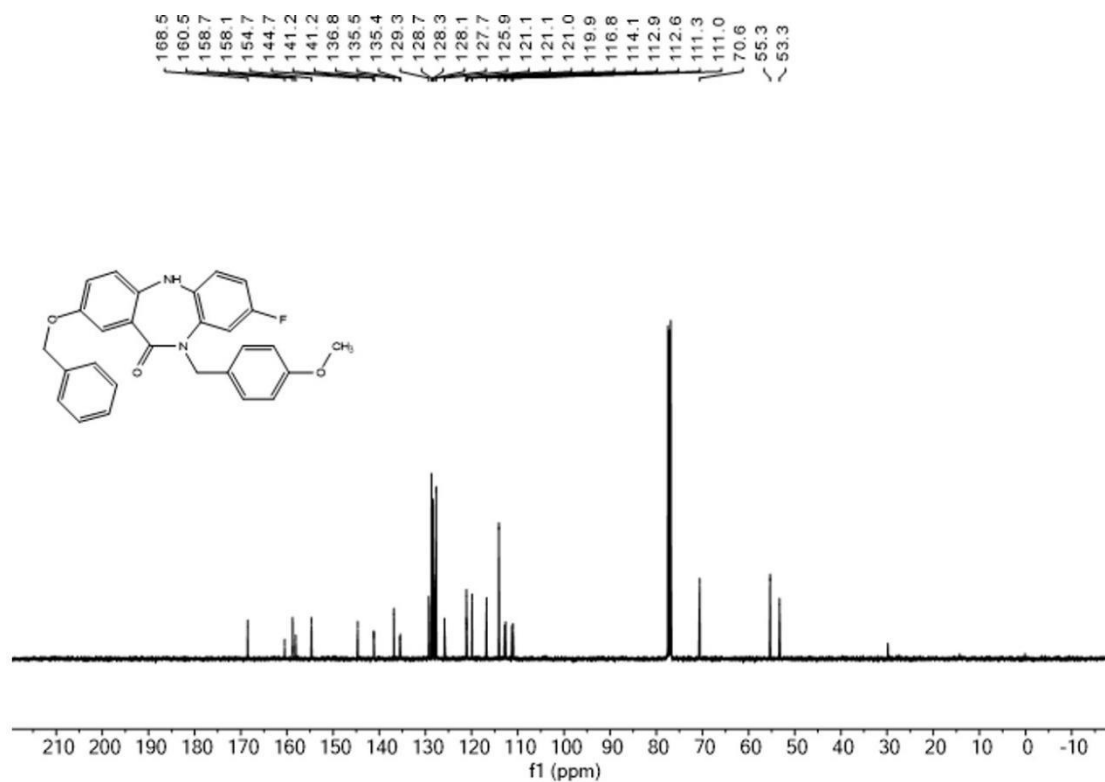


Figure S20. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound 3.

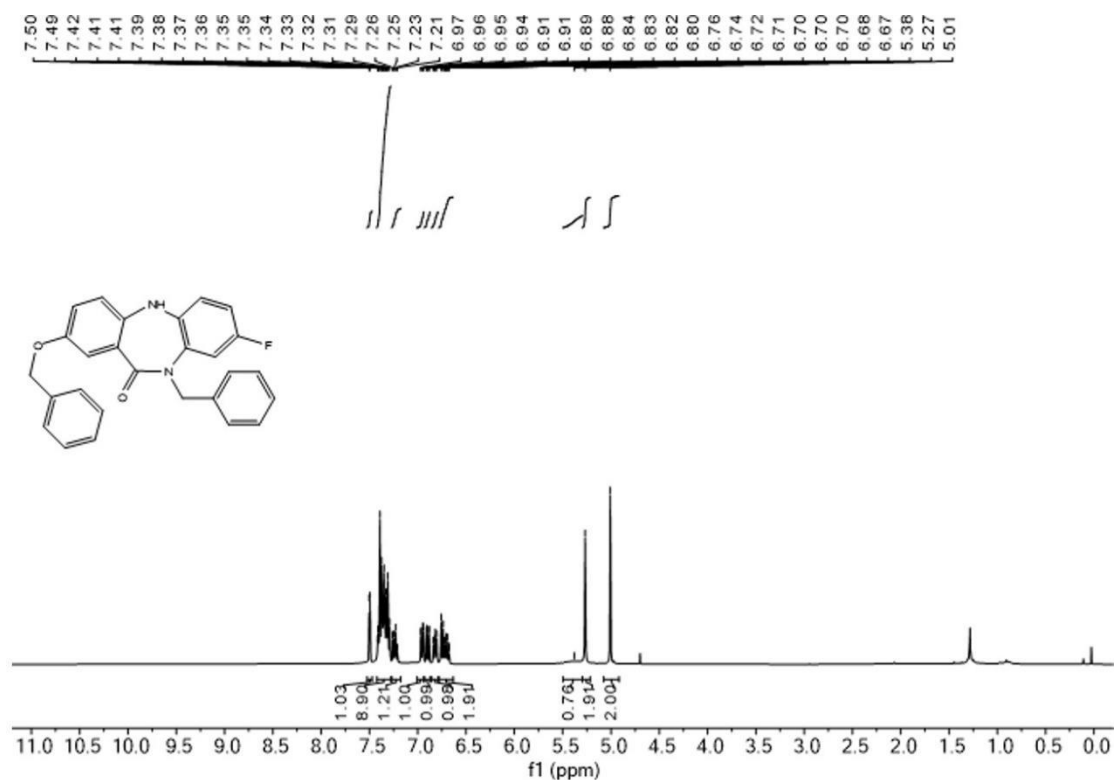


Figure S21. ¹H NMR (400 MHz, CDCl₃) spectrum of compound 4.

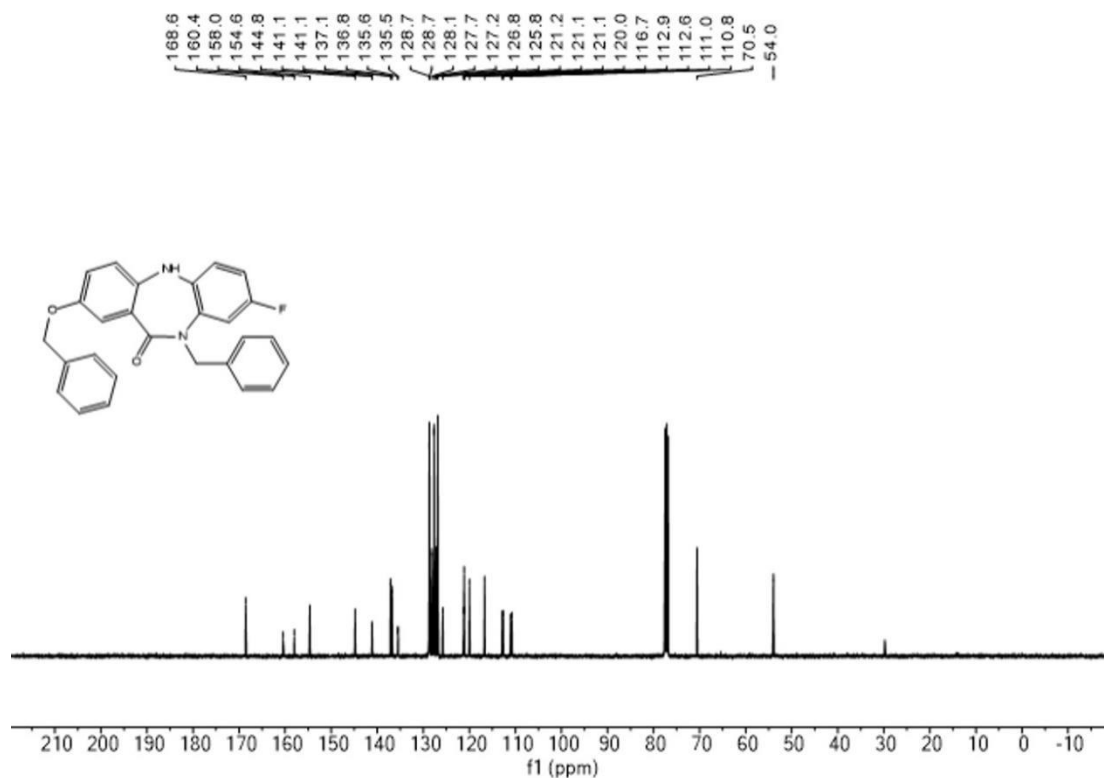


Figure S22. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound 4.

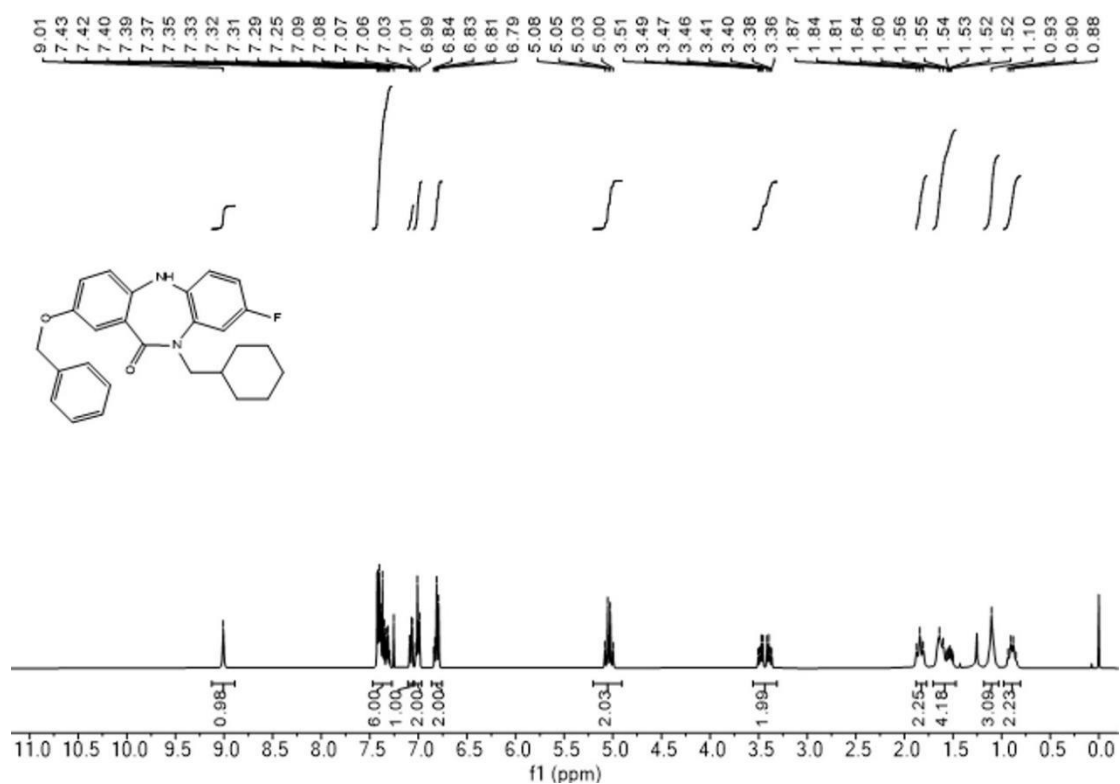


Figure S23. ¹H NMR (400 MHz, CDCl₃) spectrum of compound 5.

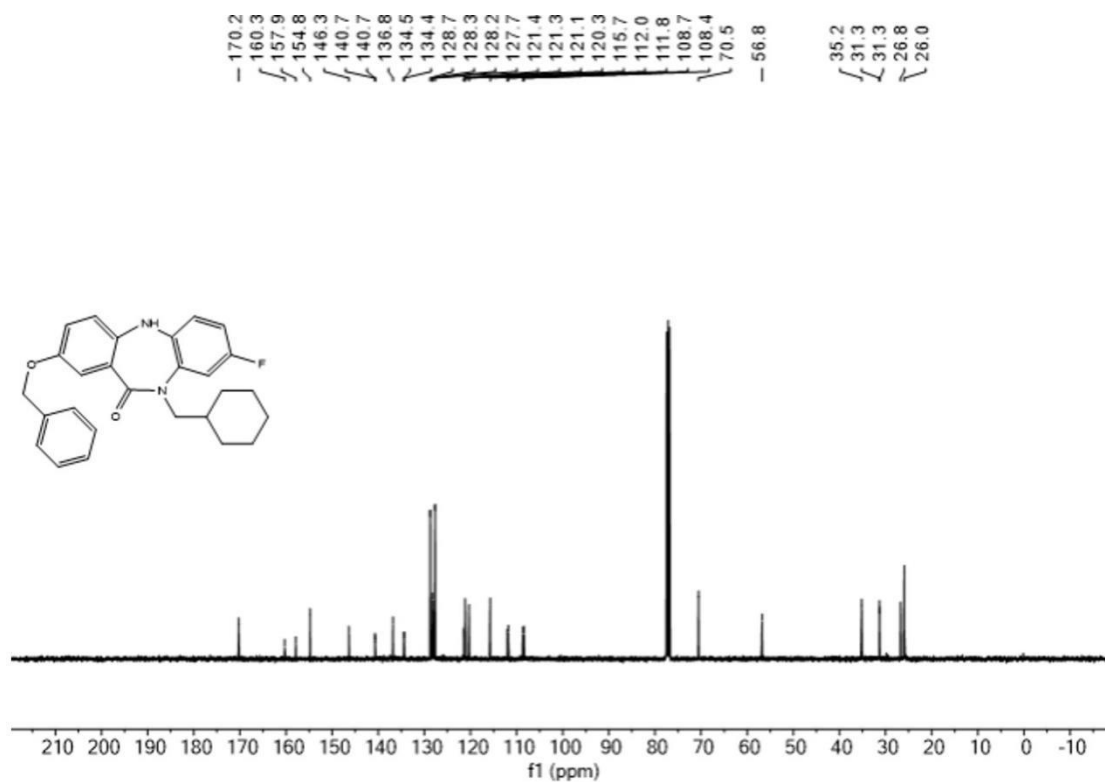


Figure S24. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound 5.

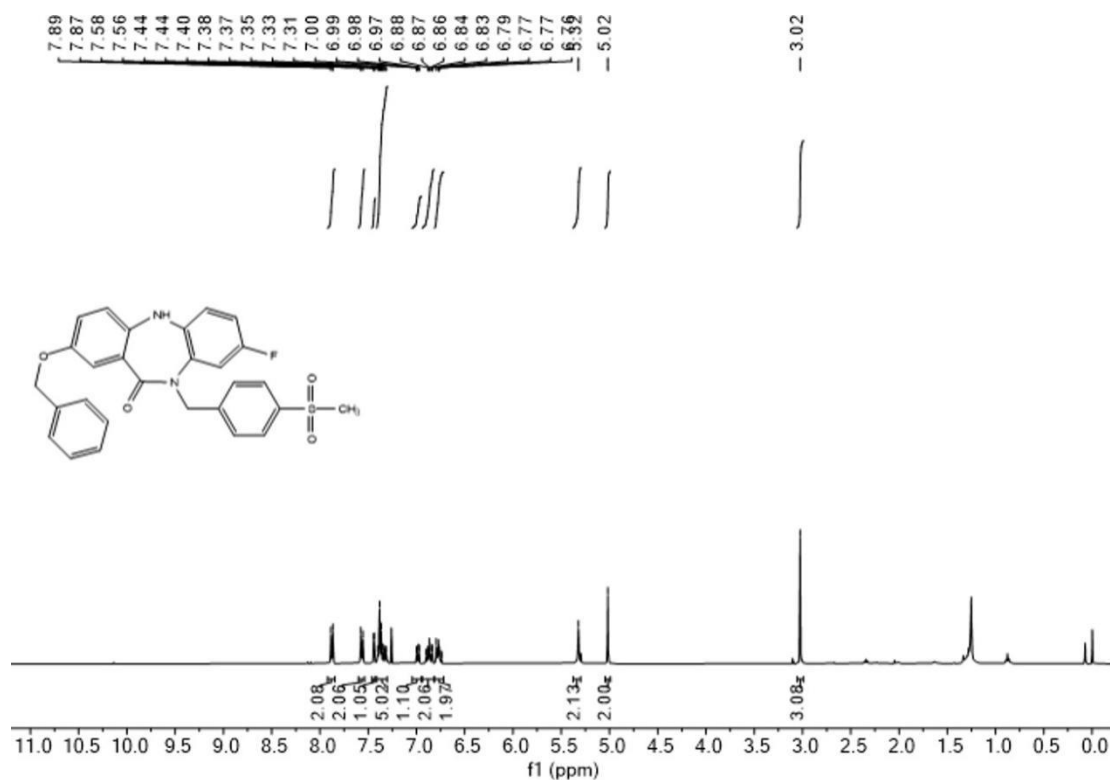


Figure S25. ¹H NMR (400 MHz, CDCl₃) spectrum of compound 6.

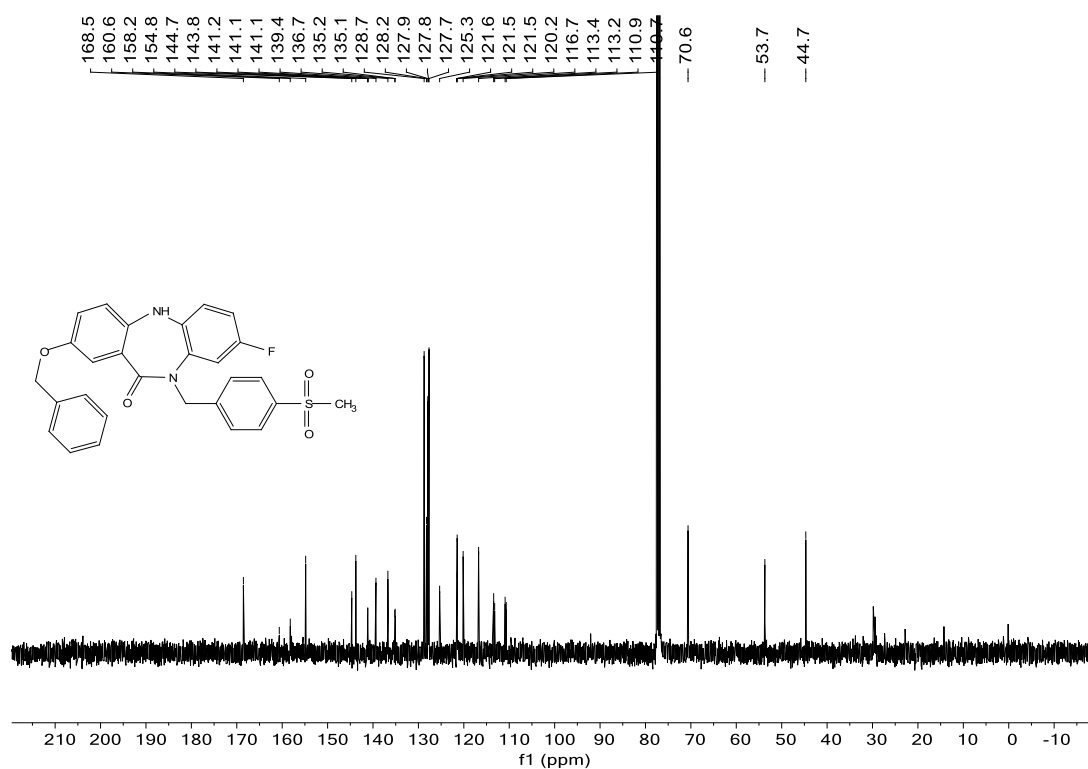


Figure S26. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound 6.

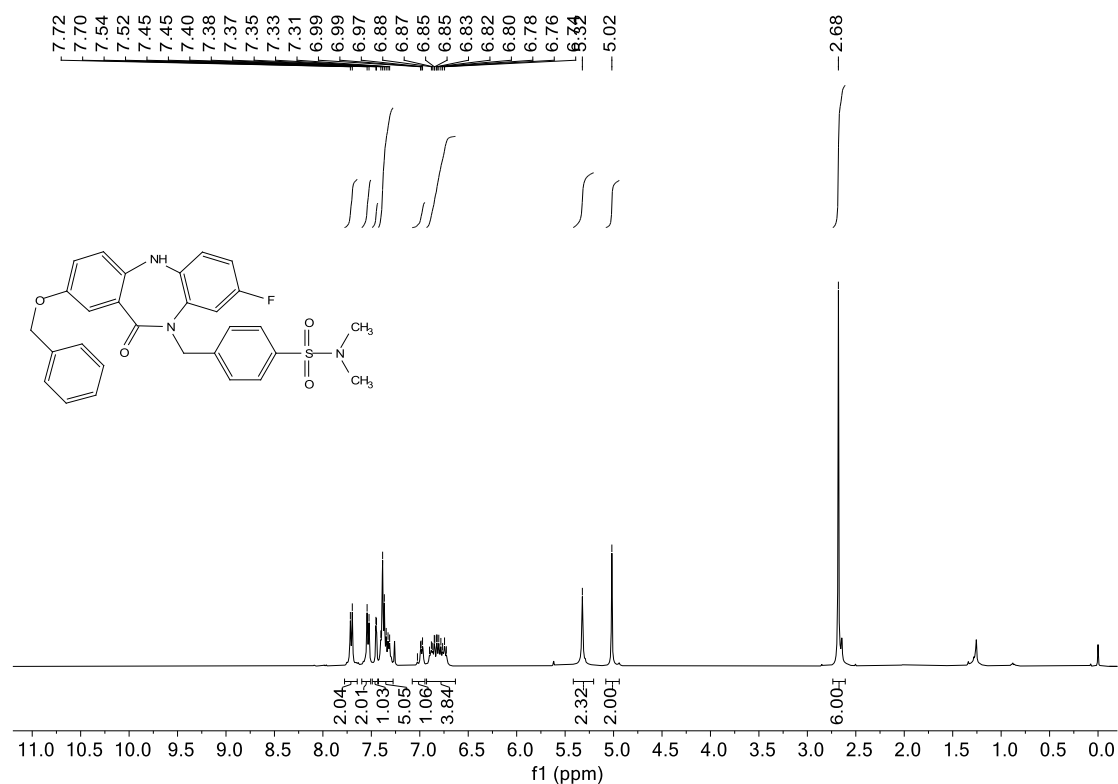


Figure S27. ¹H NMR (400 MHz, CDCl₃) spectrum of compound 7.

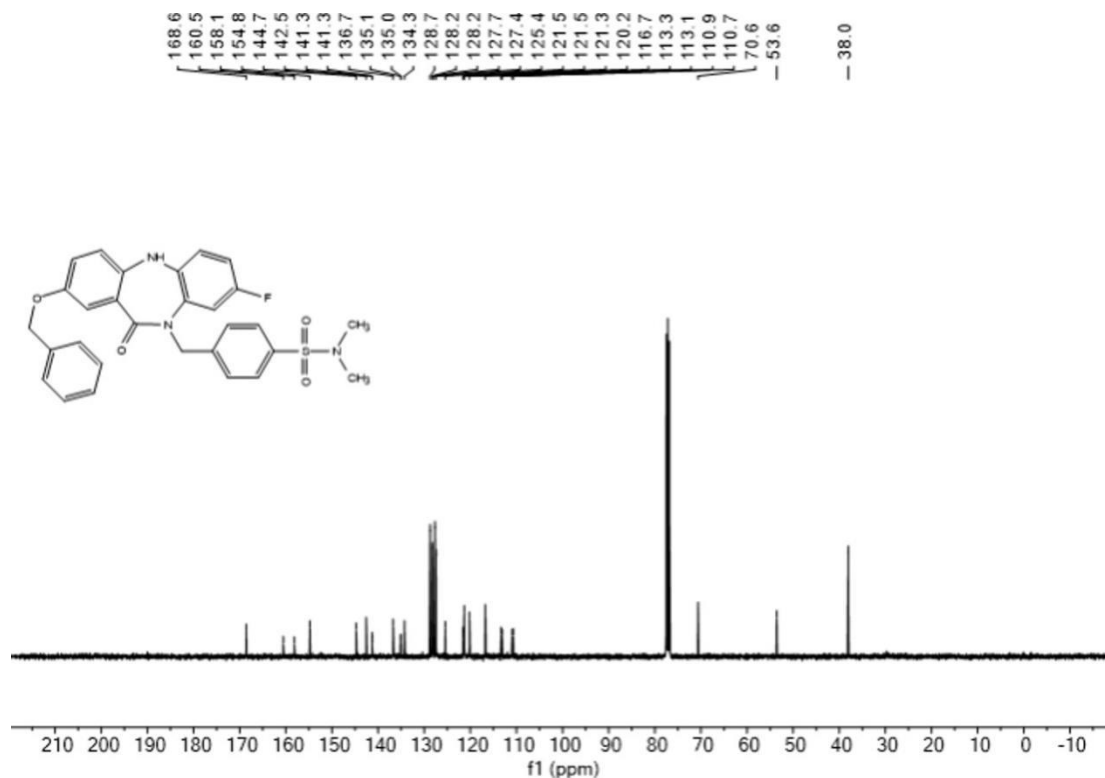


Figure S28. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound 7.

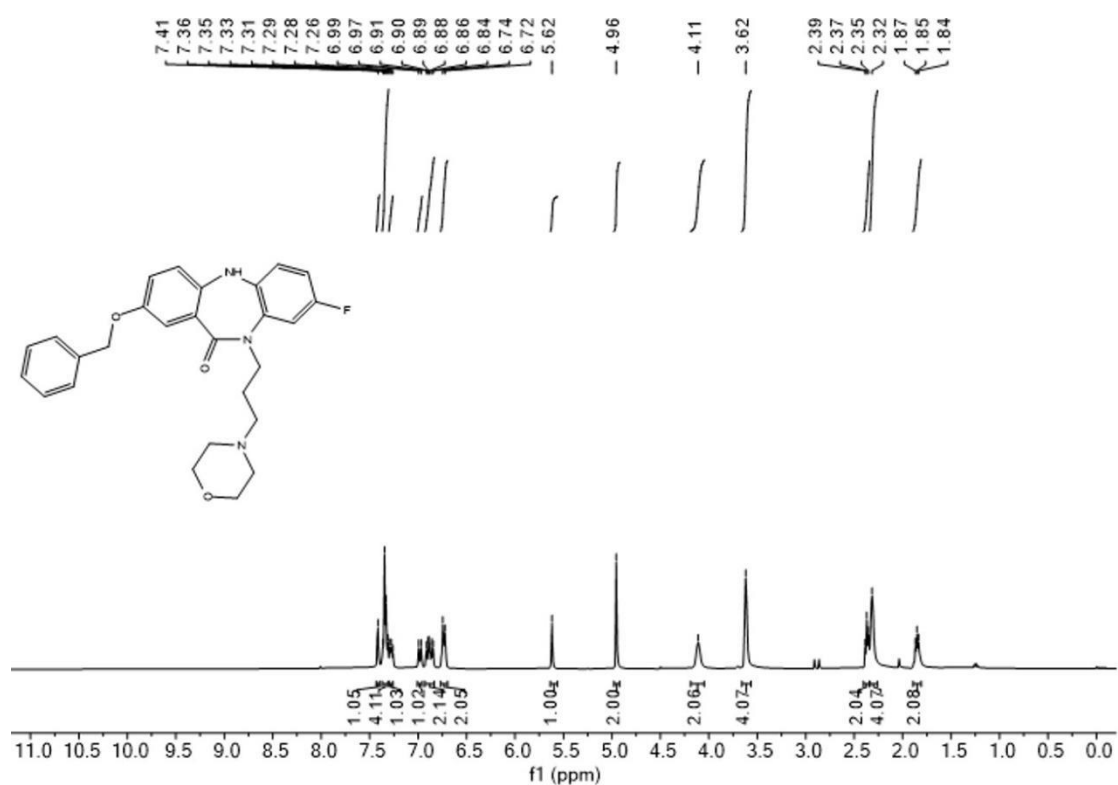


Figure S29. ¹H NMR (400 MHz, CDCl₃) spectrum of compound 8.

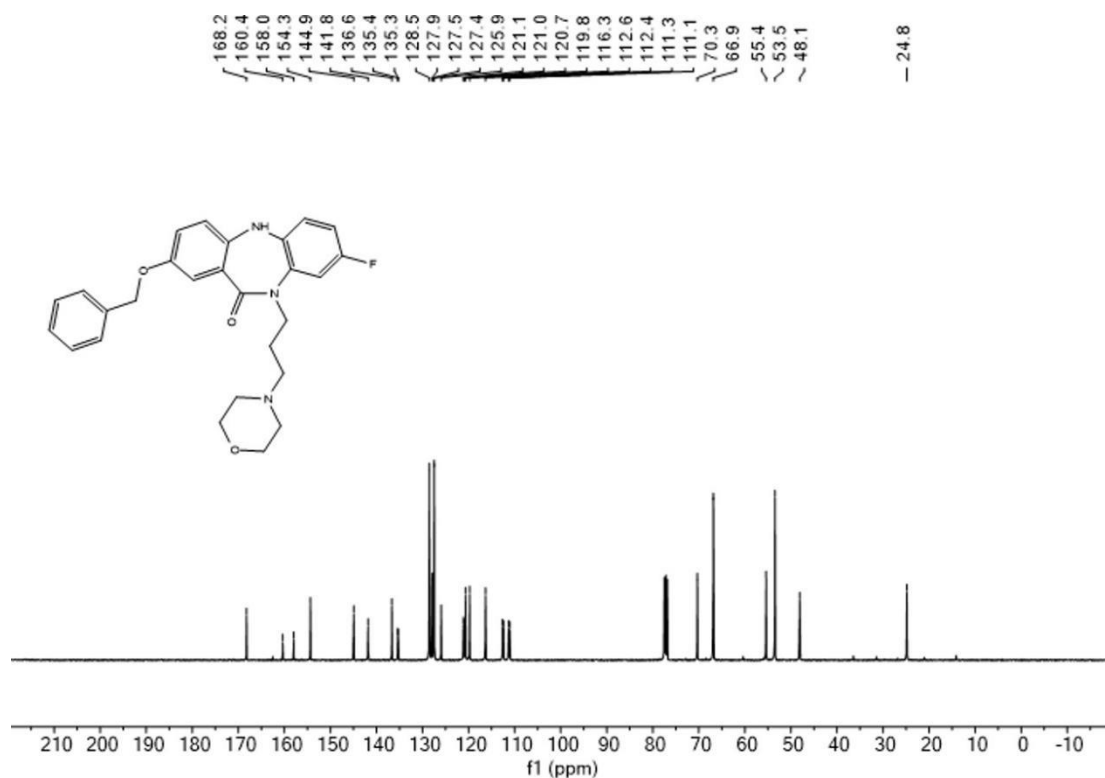


Figure S30. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound 8.

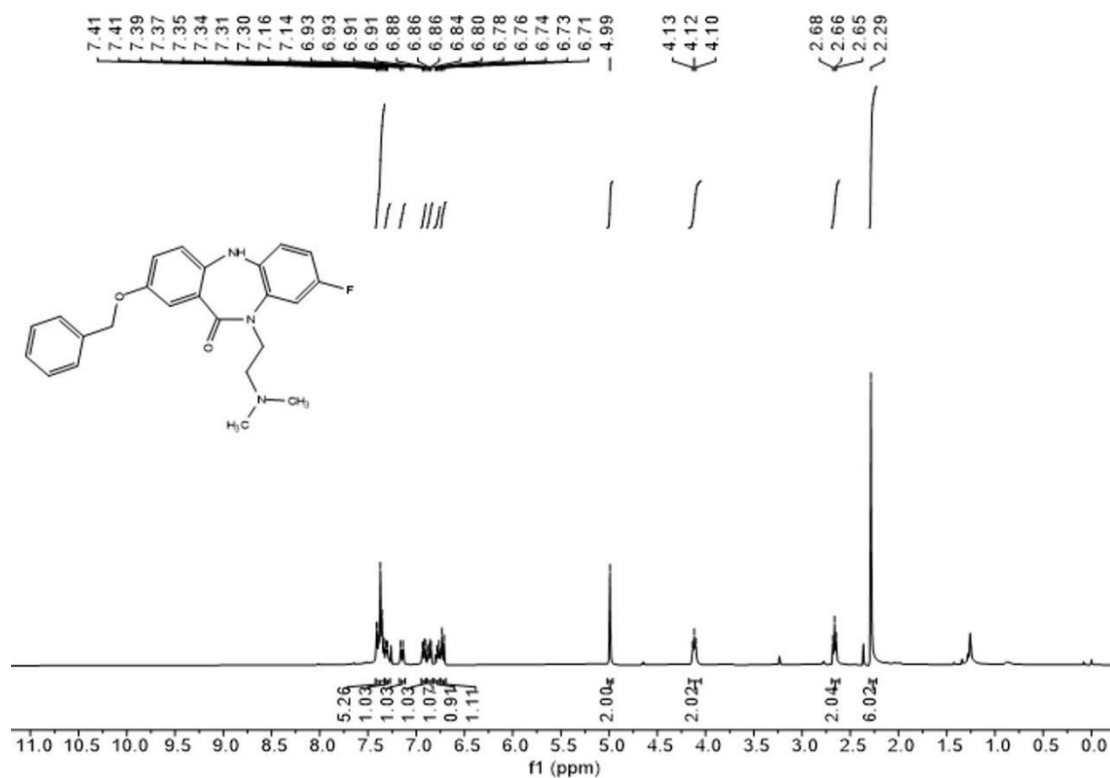


Figure S31. ¹H NMR (400 MHz, CDCl₃) spectrum of compound 9.

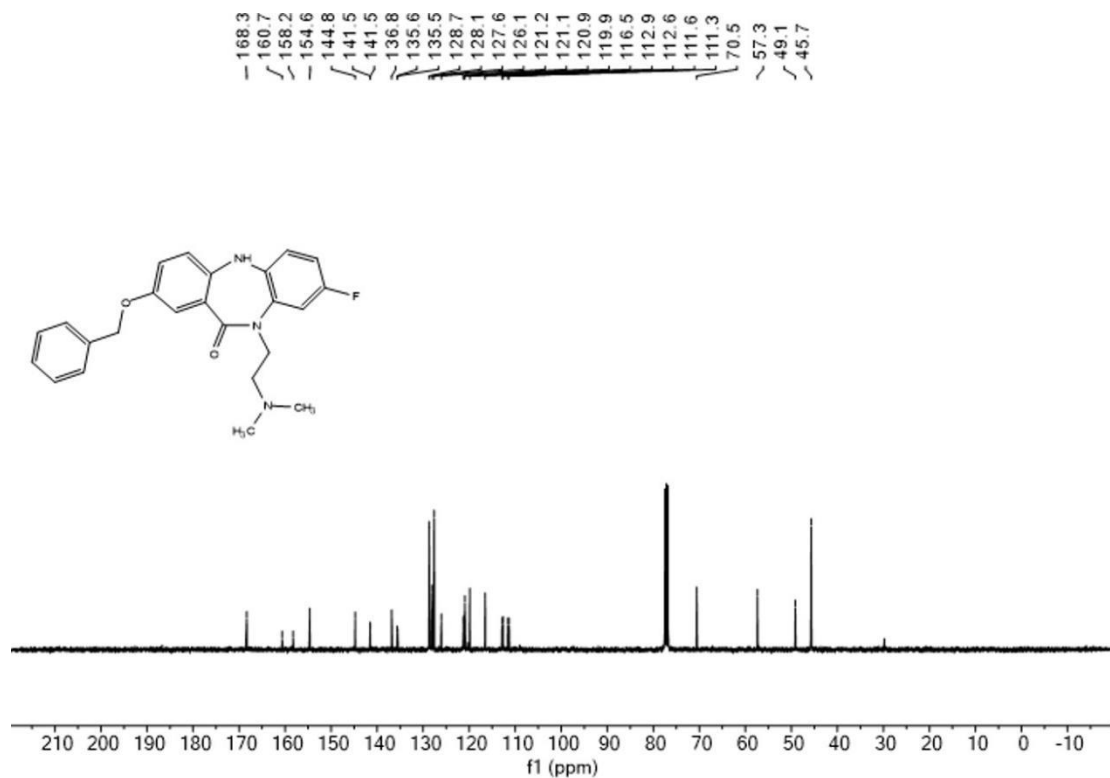


Figure S32. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound 9.

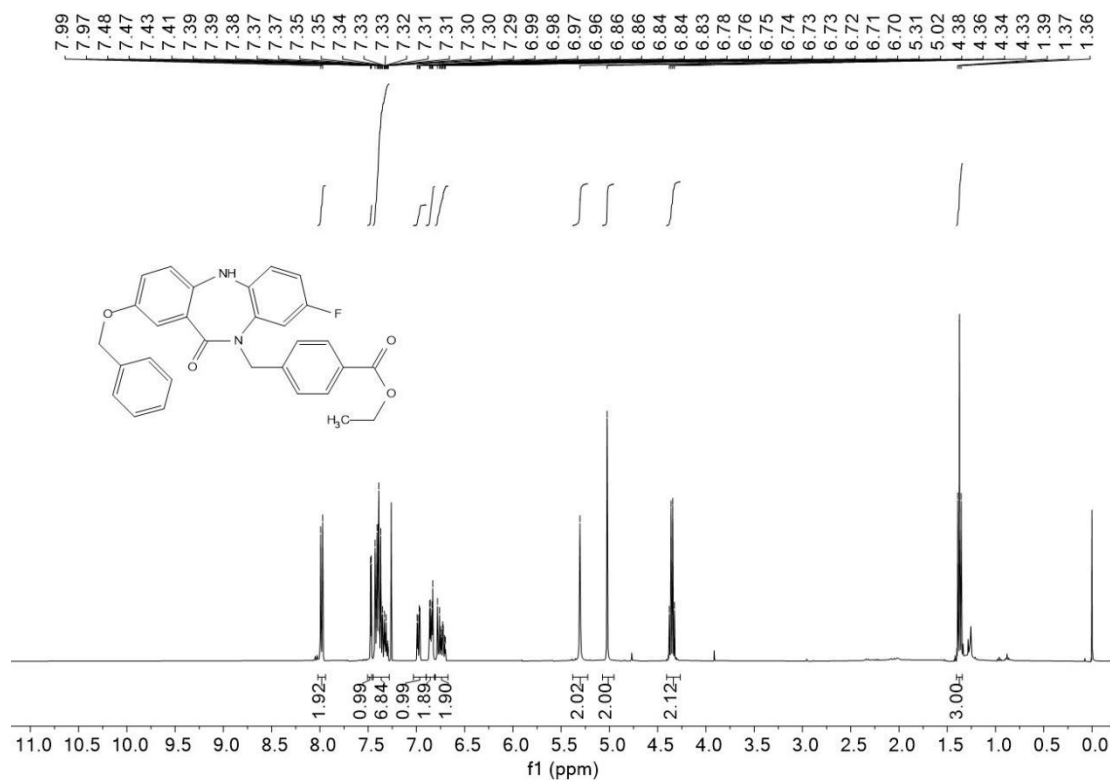


Figure S33. ¹H NMR (400 MHz, CDCl₃) spectrum of compound **10**.

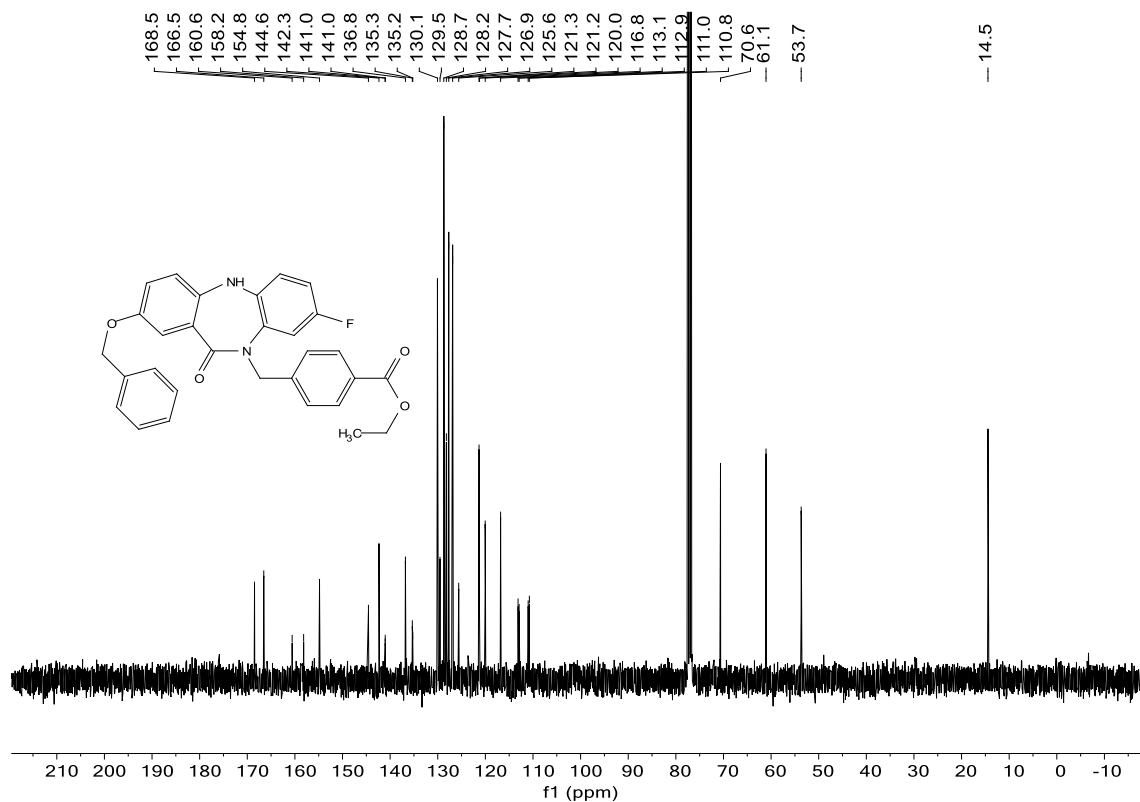


Figure S34. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound **10**.

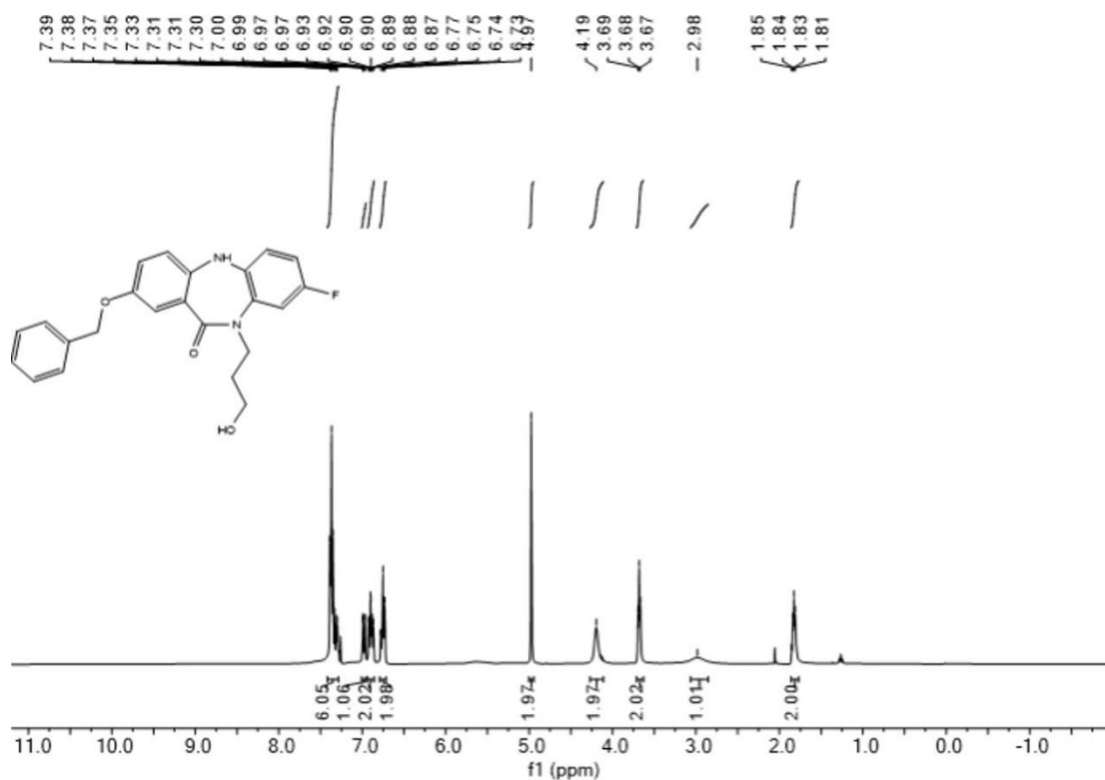


Figure S35. ¹H NMR (400 MHz, CDCl₃) spectrum of compound 11.

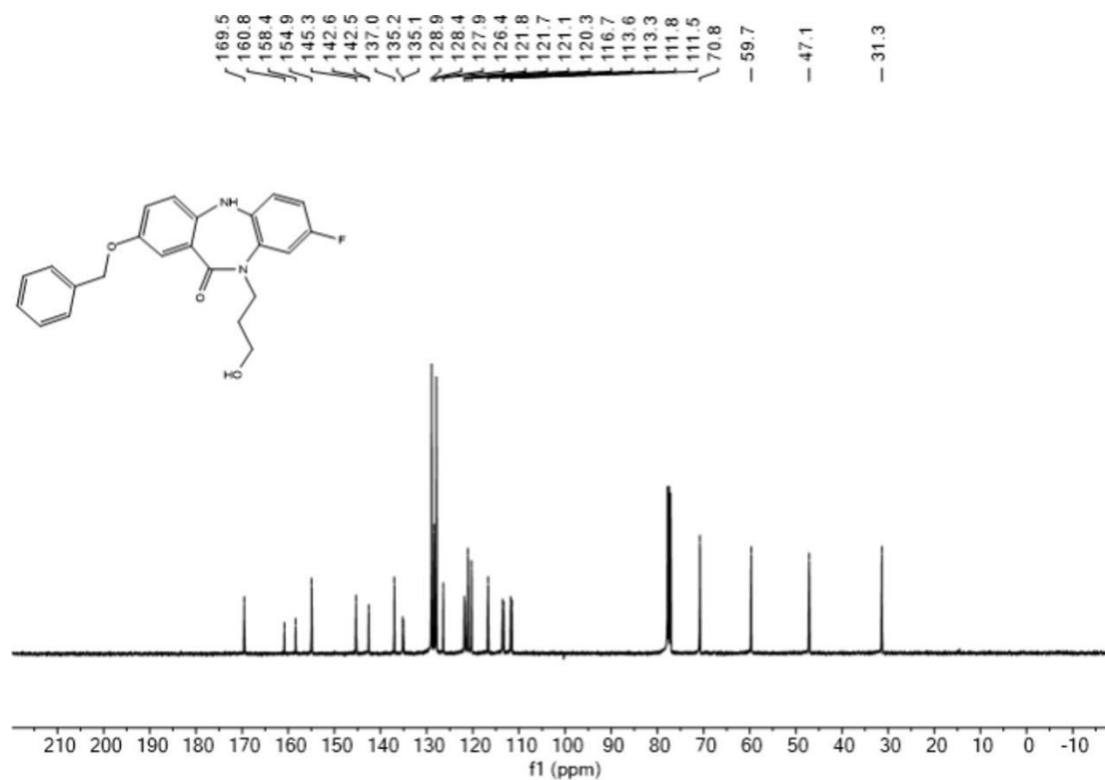


Figure S36. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound 11.

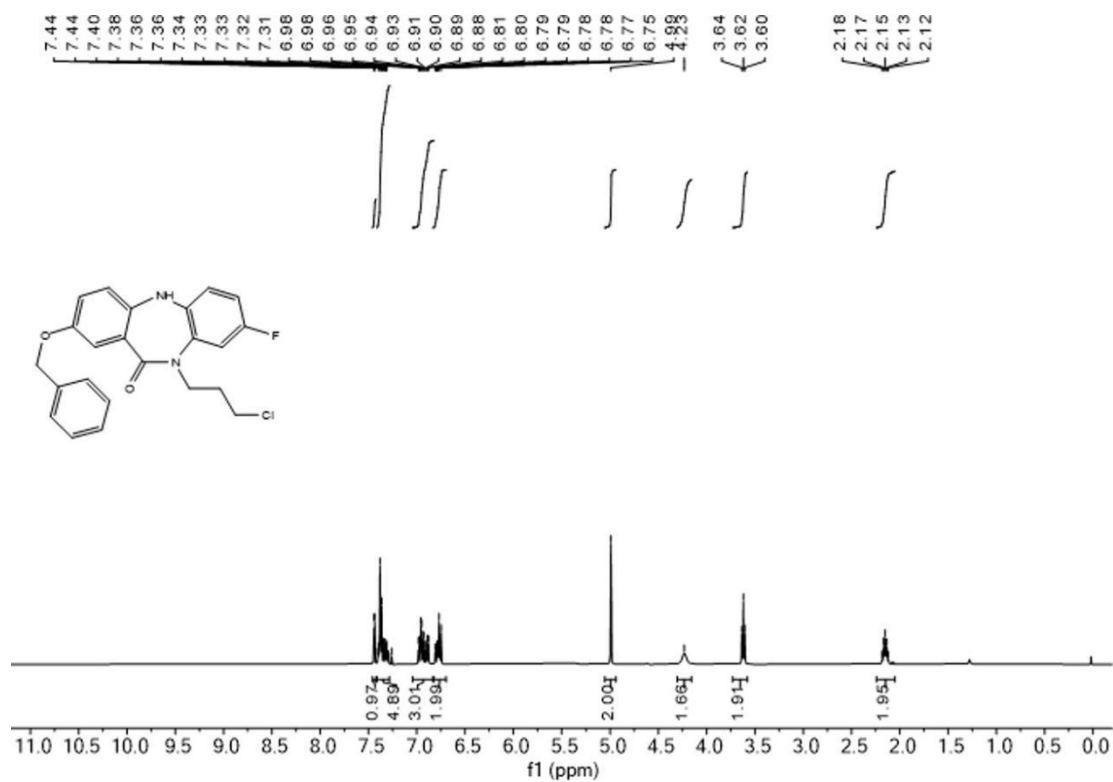


Figure S37. ¹H NMR (400 MHz, CDCl₃) spectrum of compound 12.

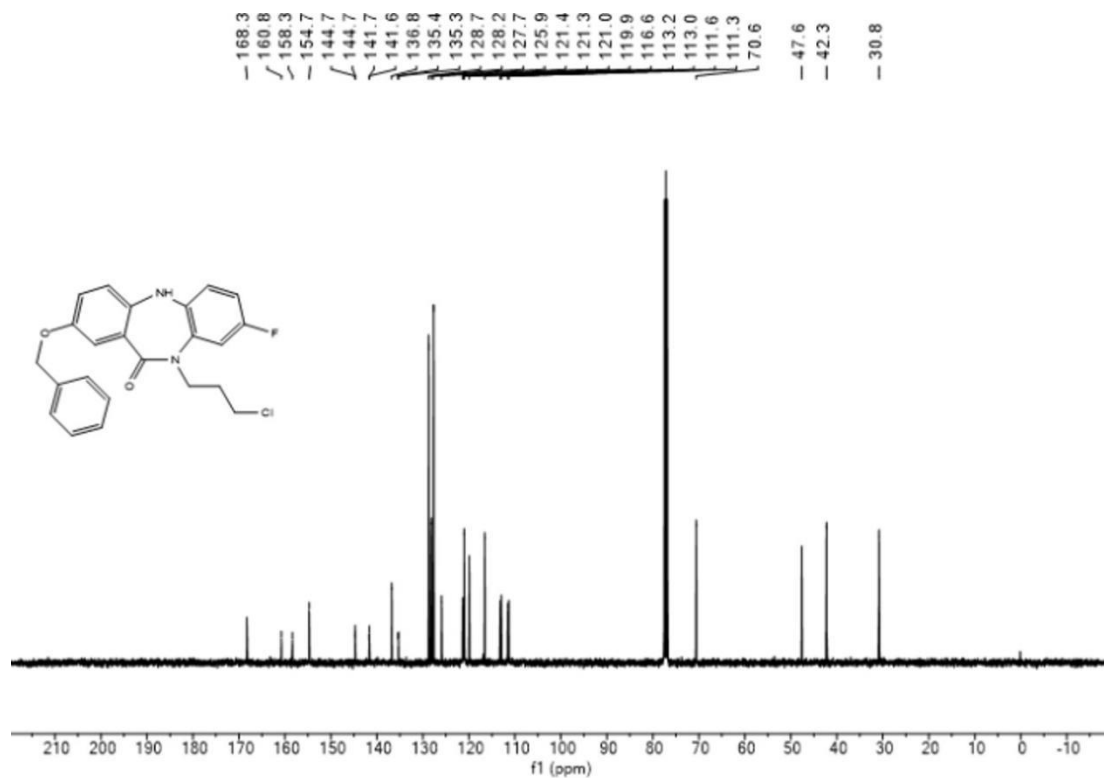


Figure S38. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound 12.

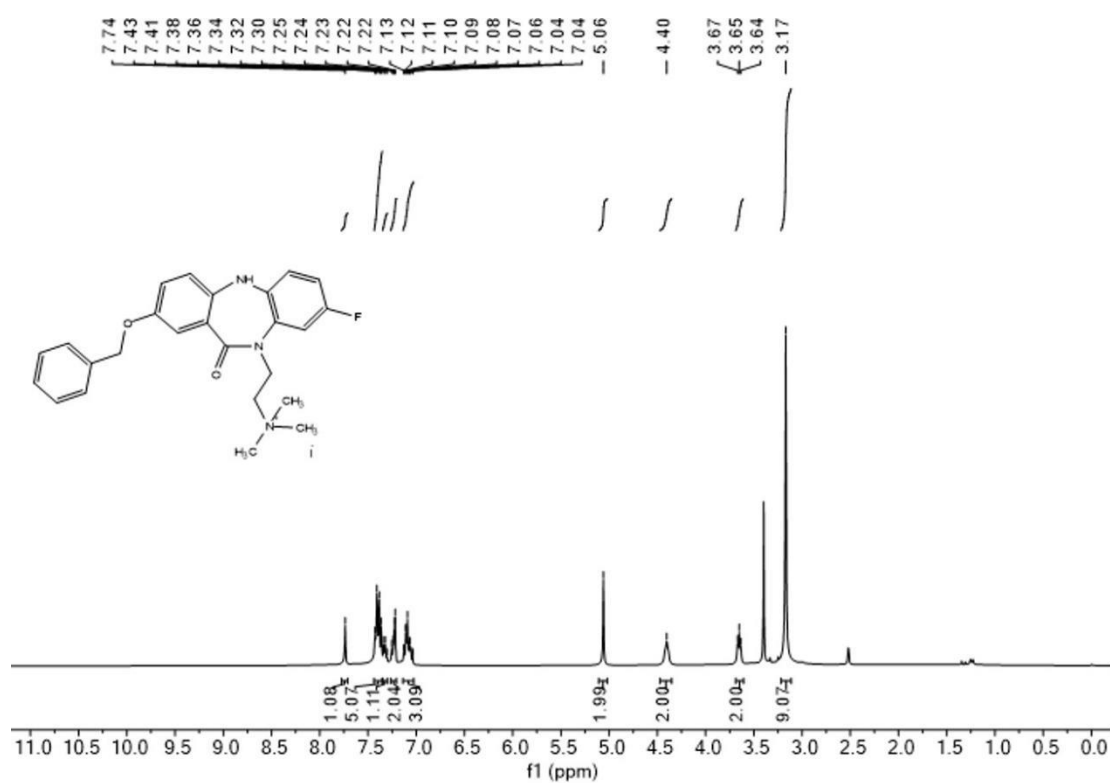


Figure S39. ¹H NMR (400 MHz, DMSO-*d*₆) spectrum of compound **13**.

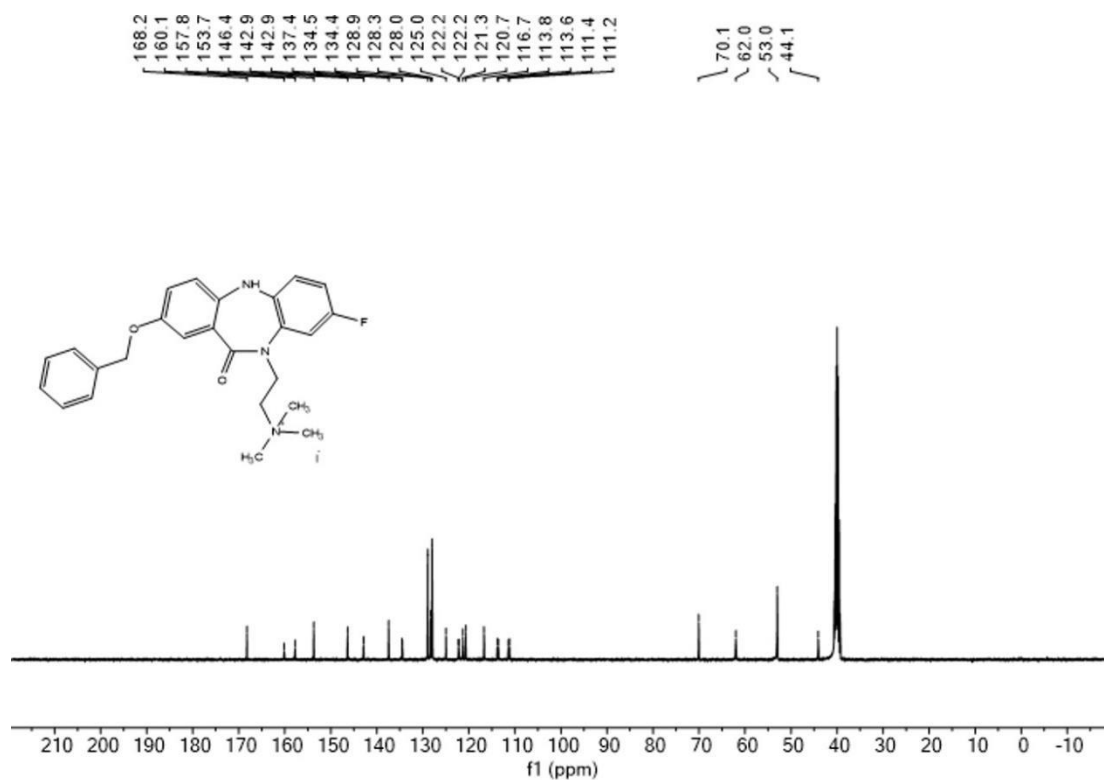


Figure S40. ¹³C NMR (101 MHz, DMSO-*d*₆) spectrum of compound **13**.

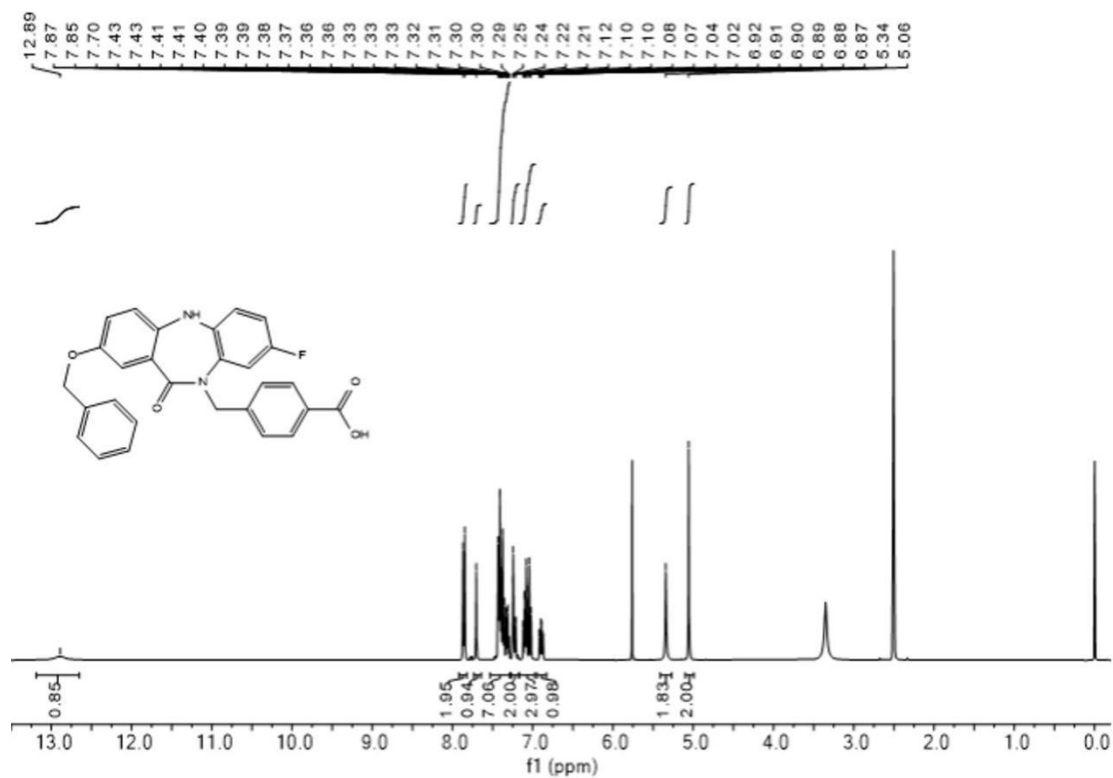


Figure S41. ¹H NMR (400 MHz, DMSO-*d*₆) spectrum of compound 14.

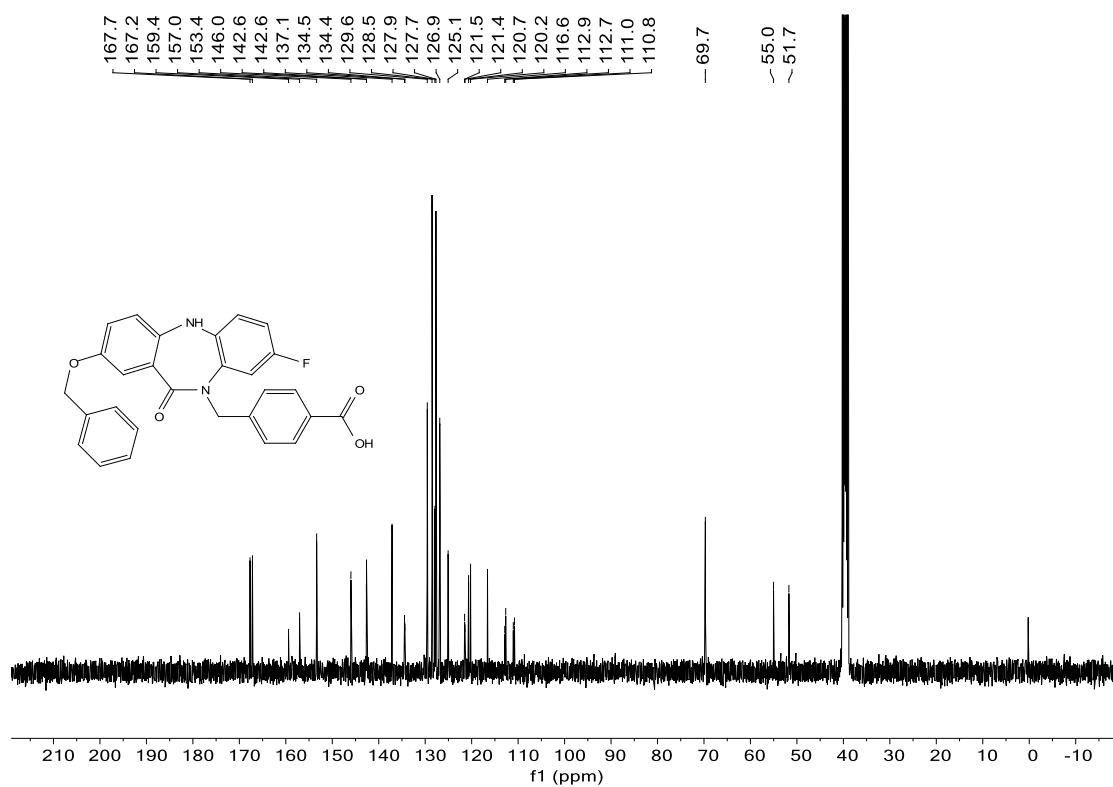


Figure S42. ¹³C NMR (101 MHz, DMSO-*d*₆) spectrum of compound 14.

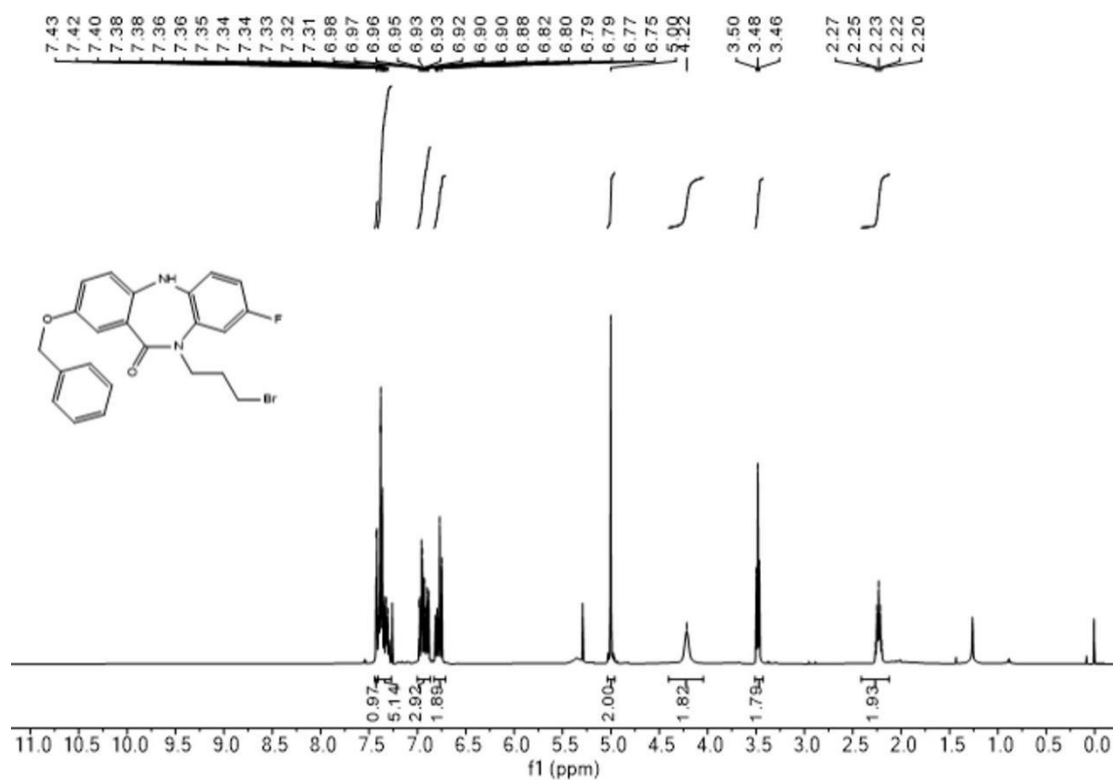


Figure S43. ¹H NMR (400 MHz, CDCl₃) spectrum of compound 15.

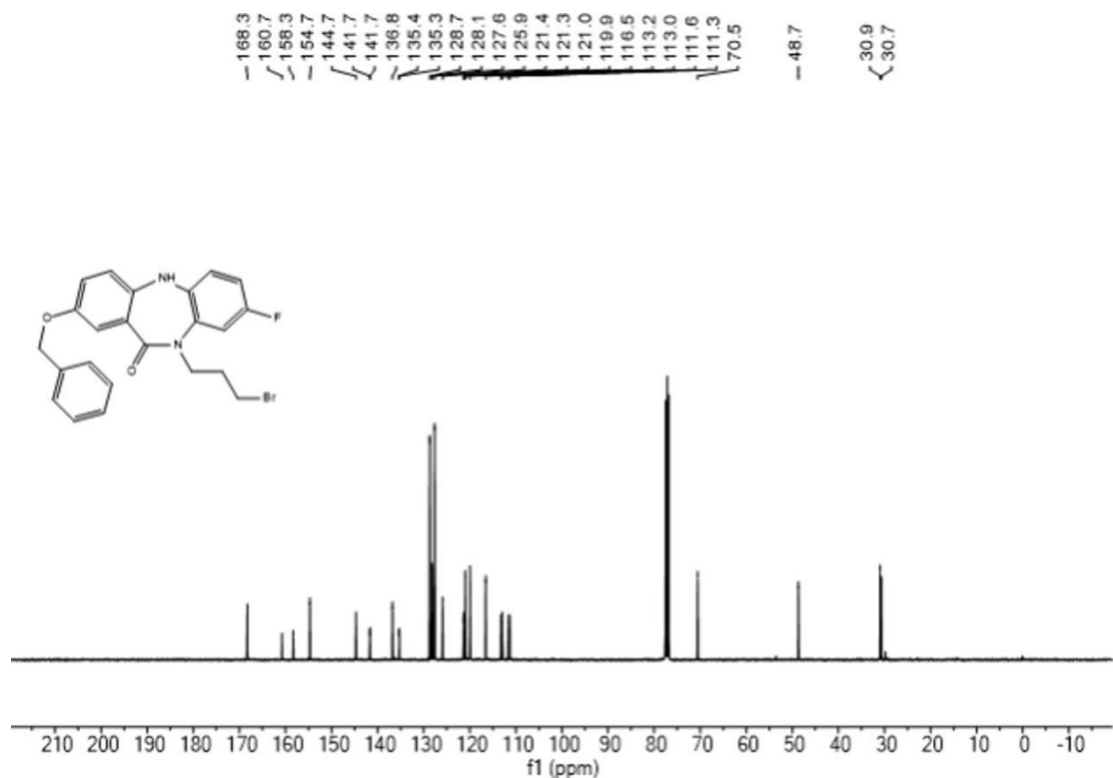


Figure S44. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound 15.

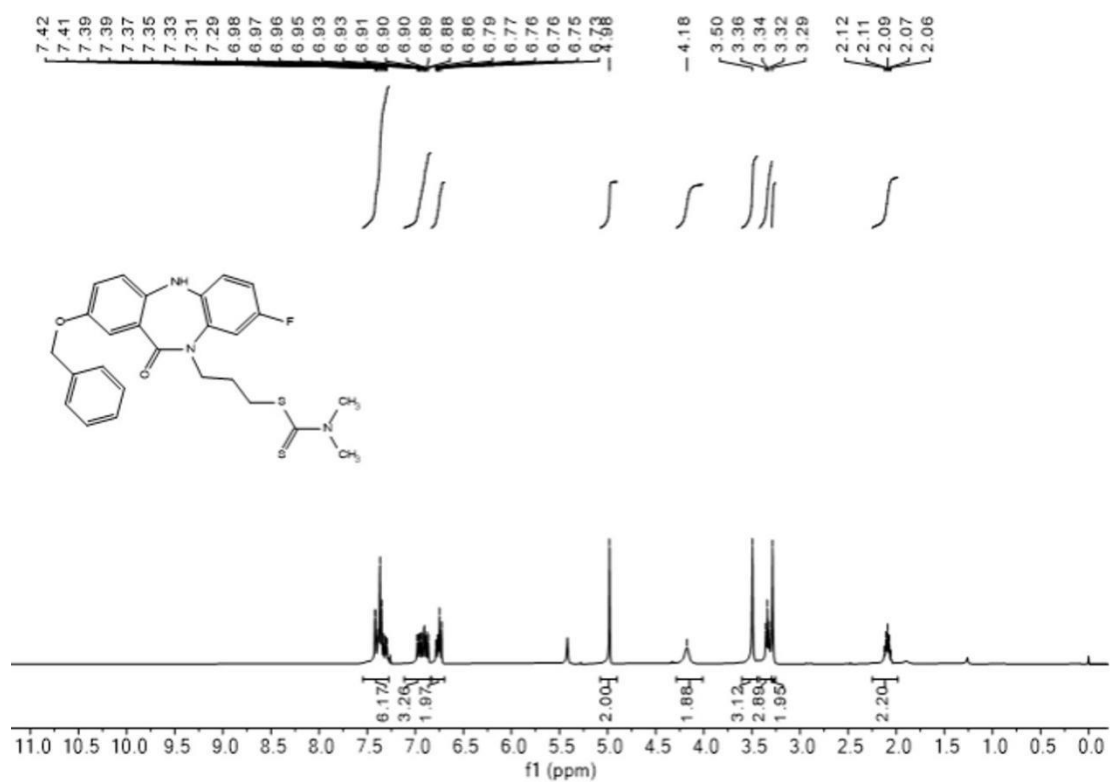


Figure S45. ¹H NMR (400 MHz, CDCl₃) spectrum of compound **16**.

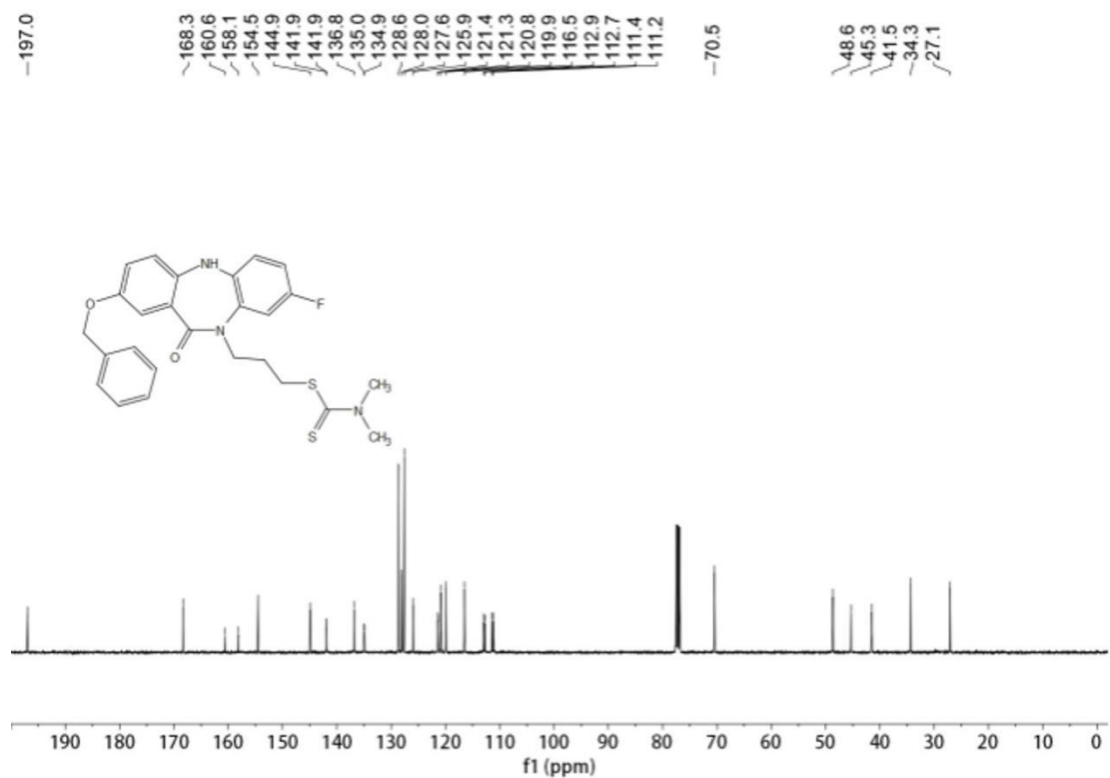


Figure S46. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound **16**.

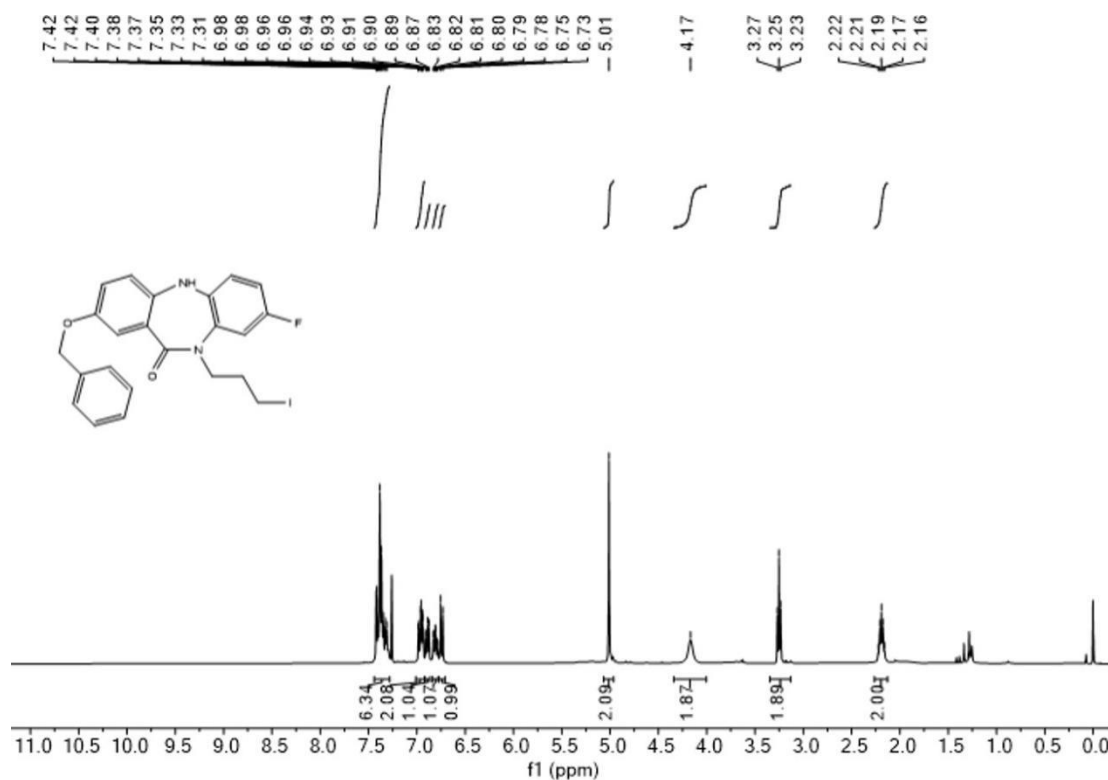


Figure S47. ¹H NMR (400 MHz, CDCl₃) spectrum of compound 17.

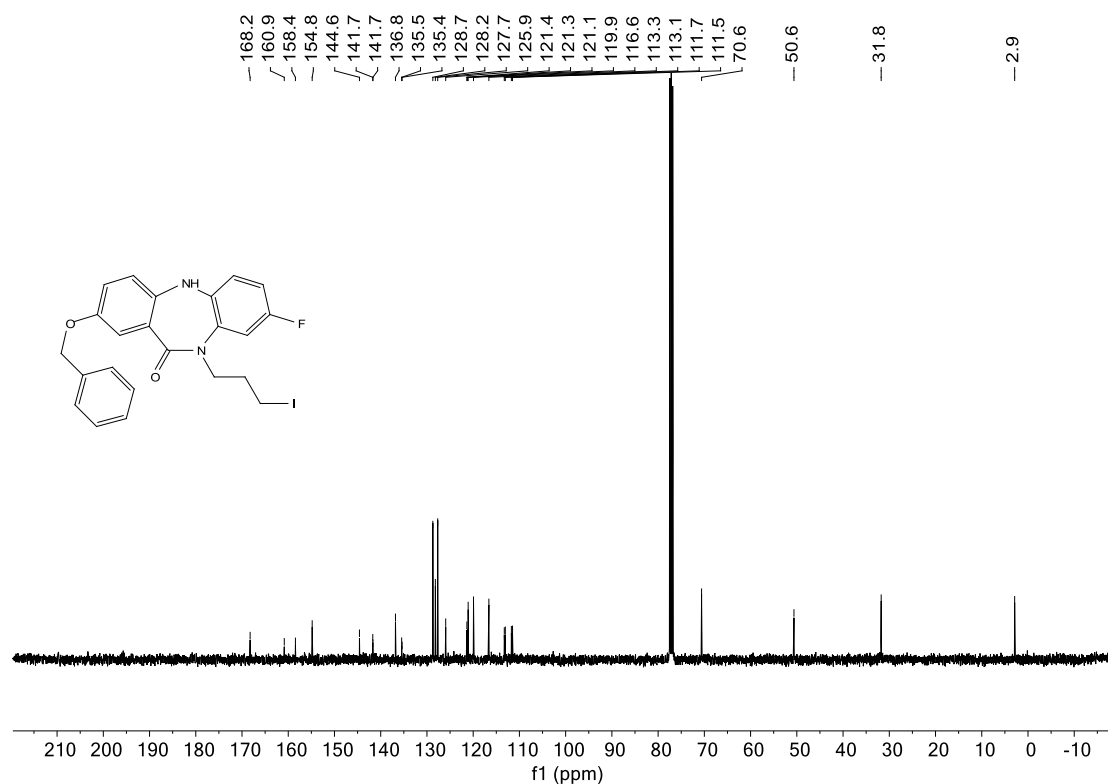


Figure S48. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound 17.

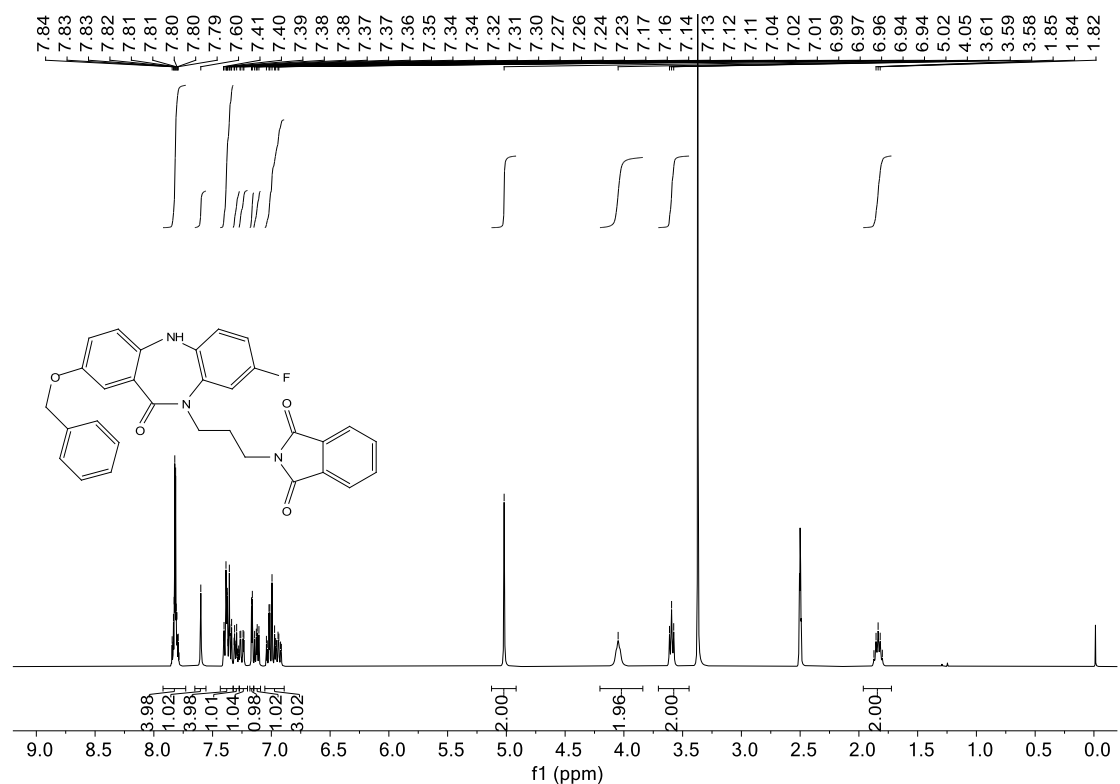


Figure S49. ¹H NMR (400 MHz, DMSO-*d*₆) spectrum of compound S9.

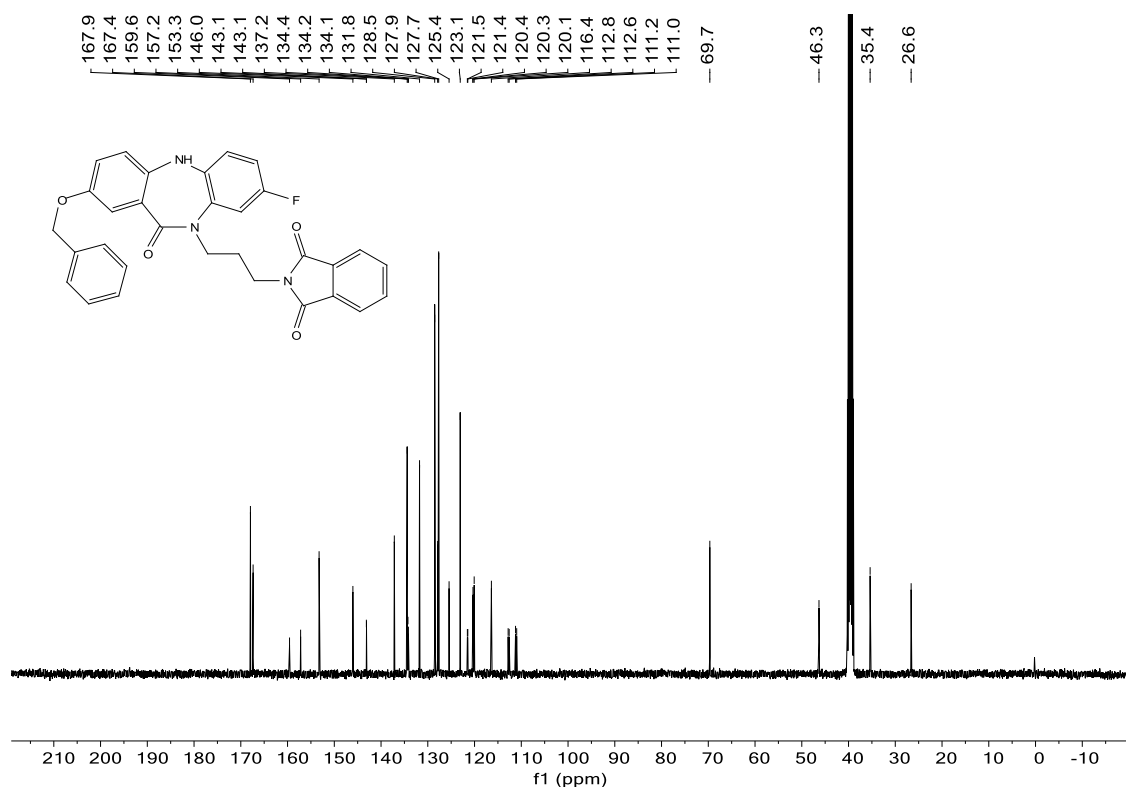


Figure S50. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound S9.

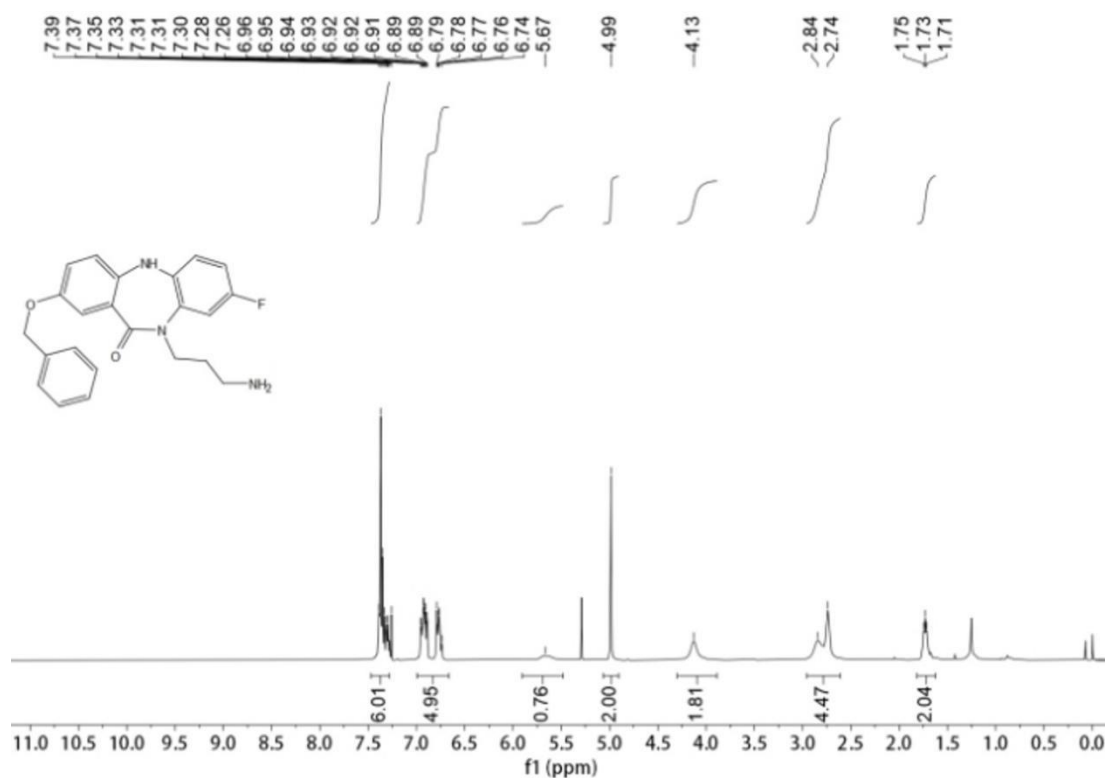


Figure S51 ¹H NMR (400 MHz, CDCl₃) spectrum of compound 18.

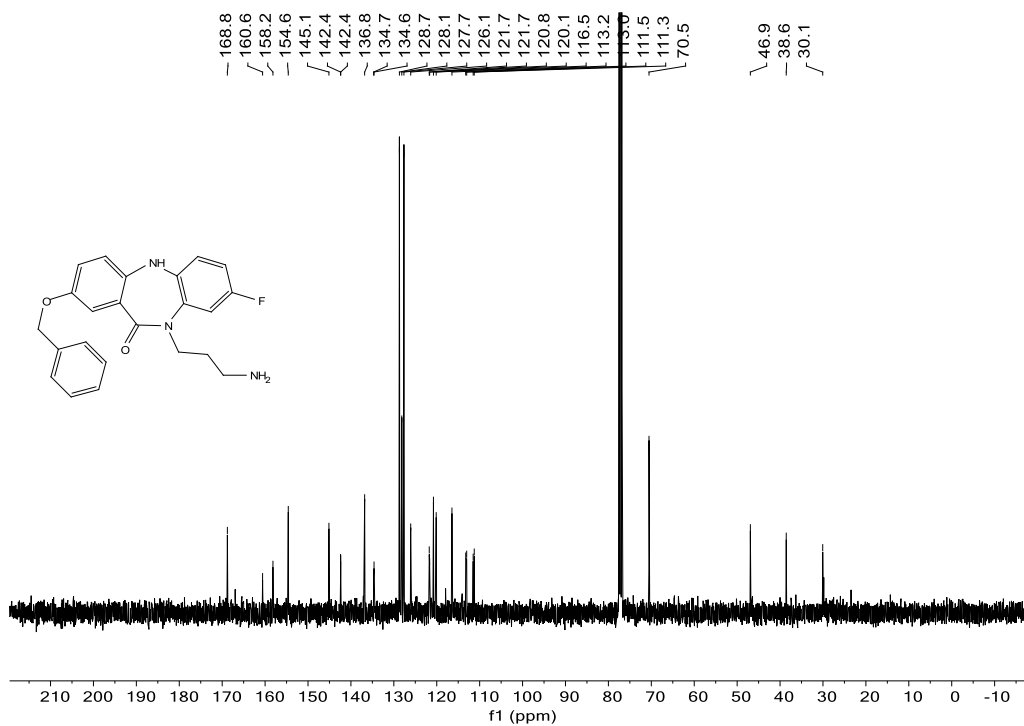


Figure S52. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound 18.

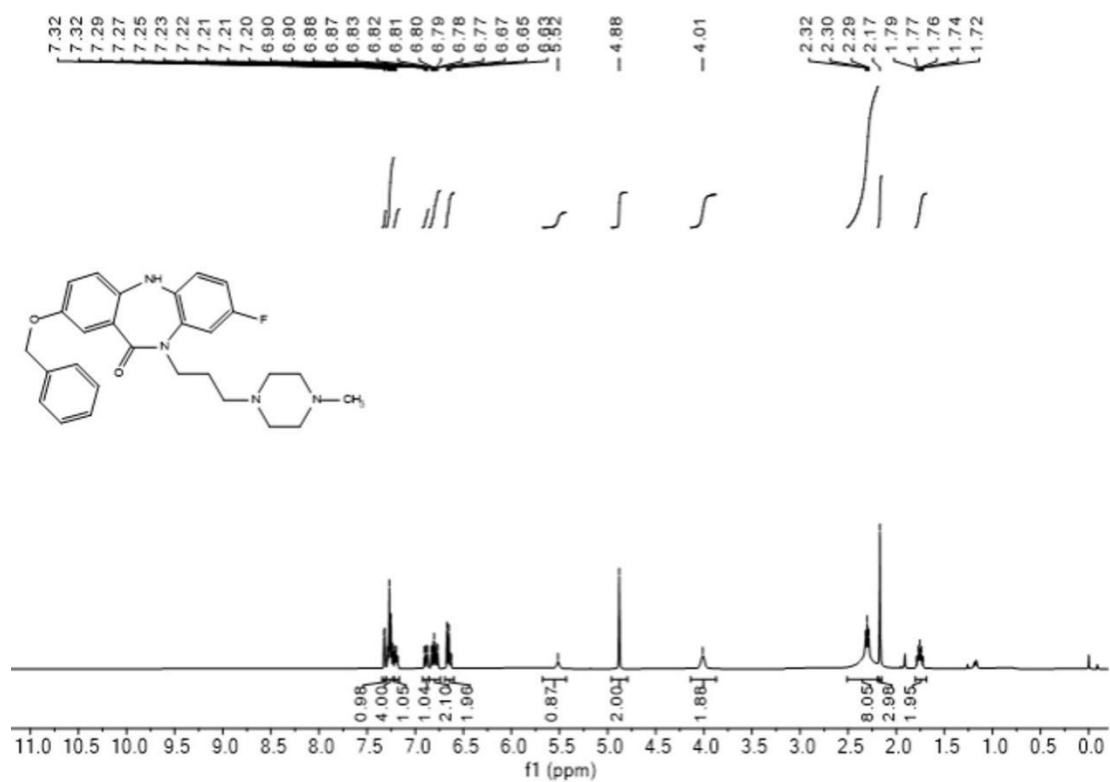


Figure S55. ¹H NMR (400 MHz, CDCl₃) spectrum of compound 20.

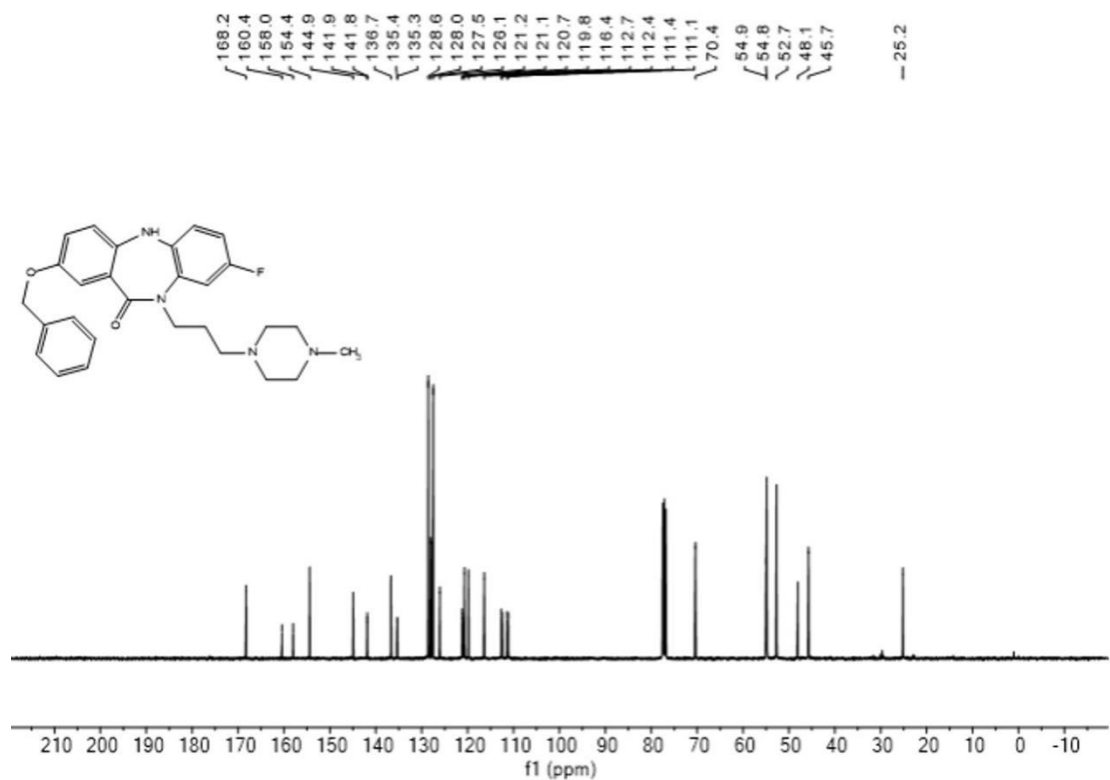


Figure S56 ¹³C NMR (101 MHz, CDCl₃) spectrum of compound 20.

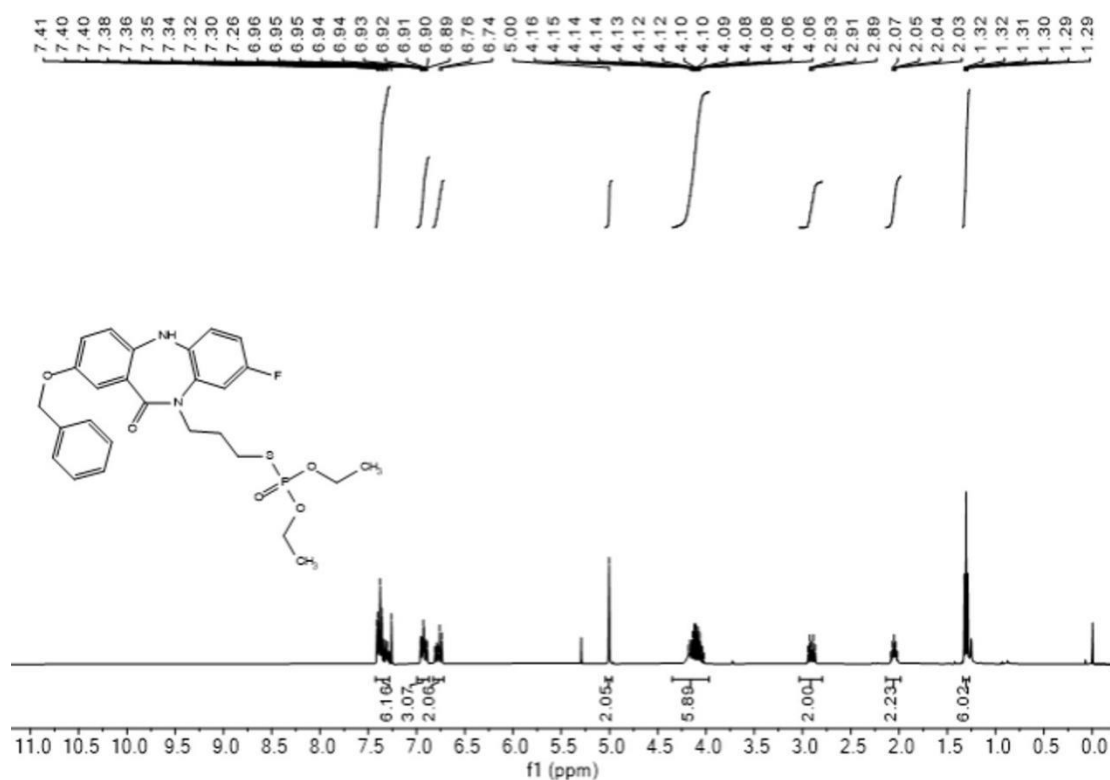


Figure S57. ¹H NMR (400 MHz, CDCl₃) spectrum of compound 21.

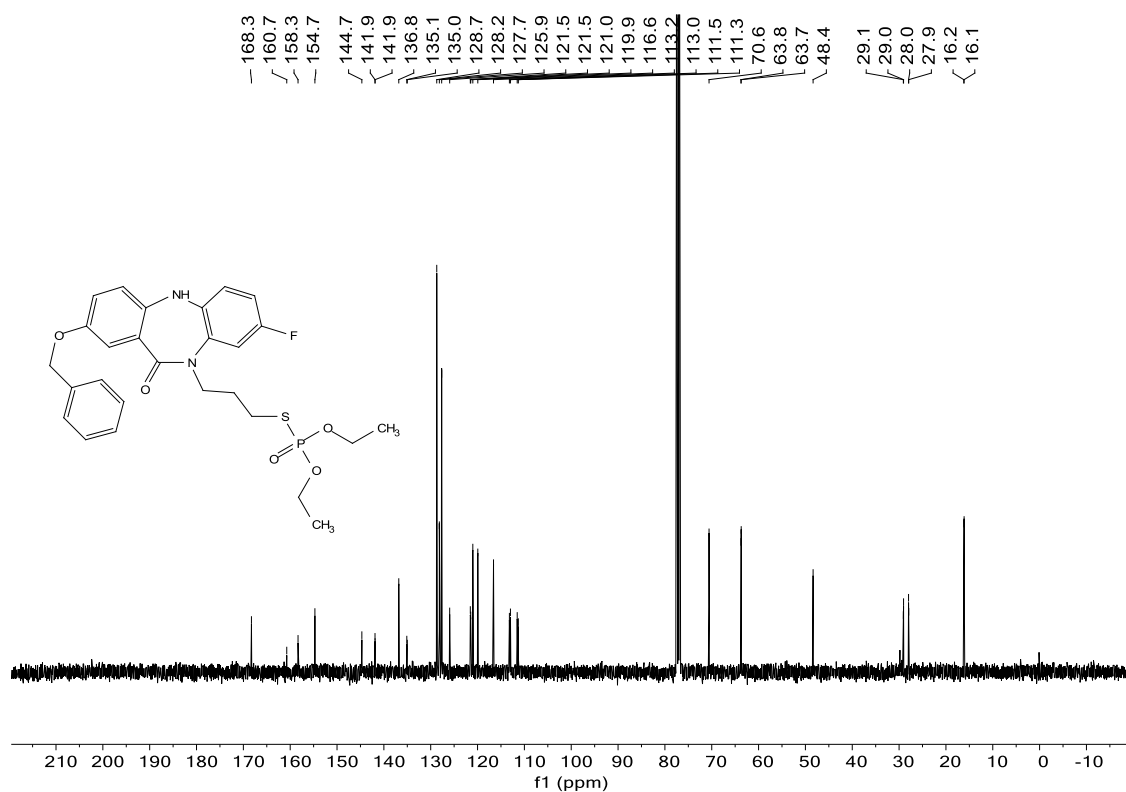


Figure S58. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound 21.

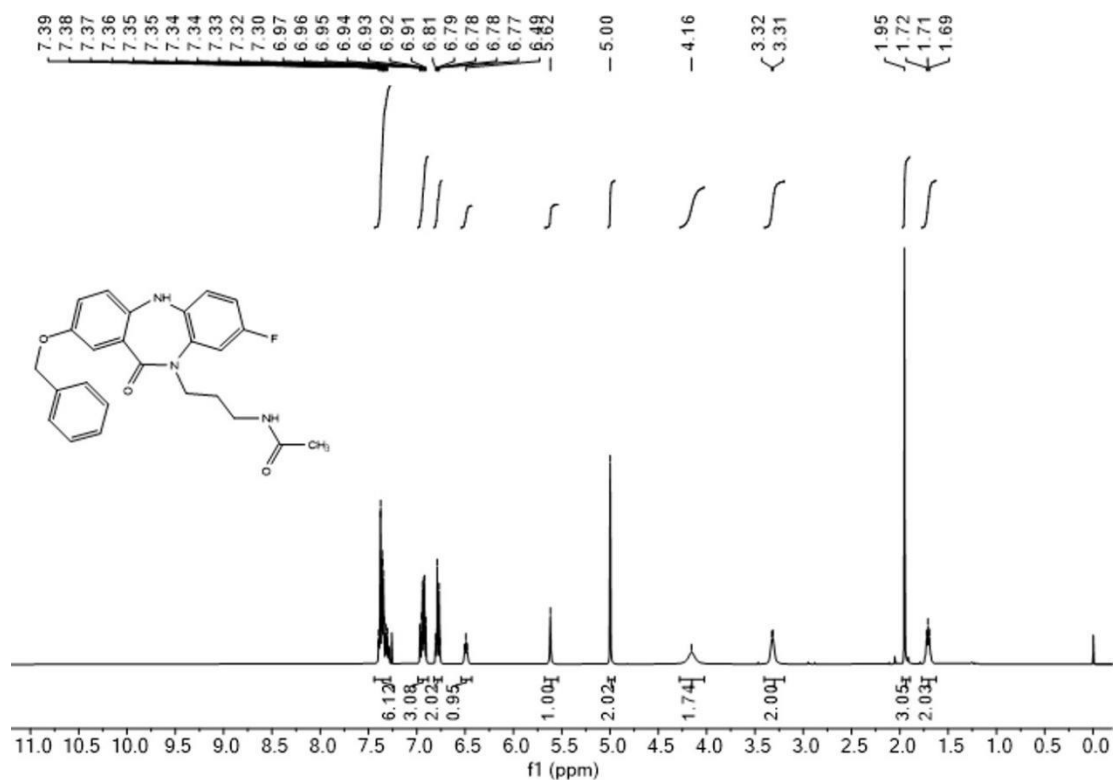


Figure S59. ¹H NMR (400 MHz, CDCl₃) spectrum of compound 22.

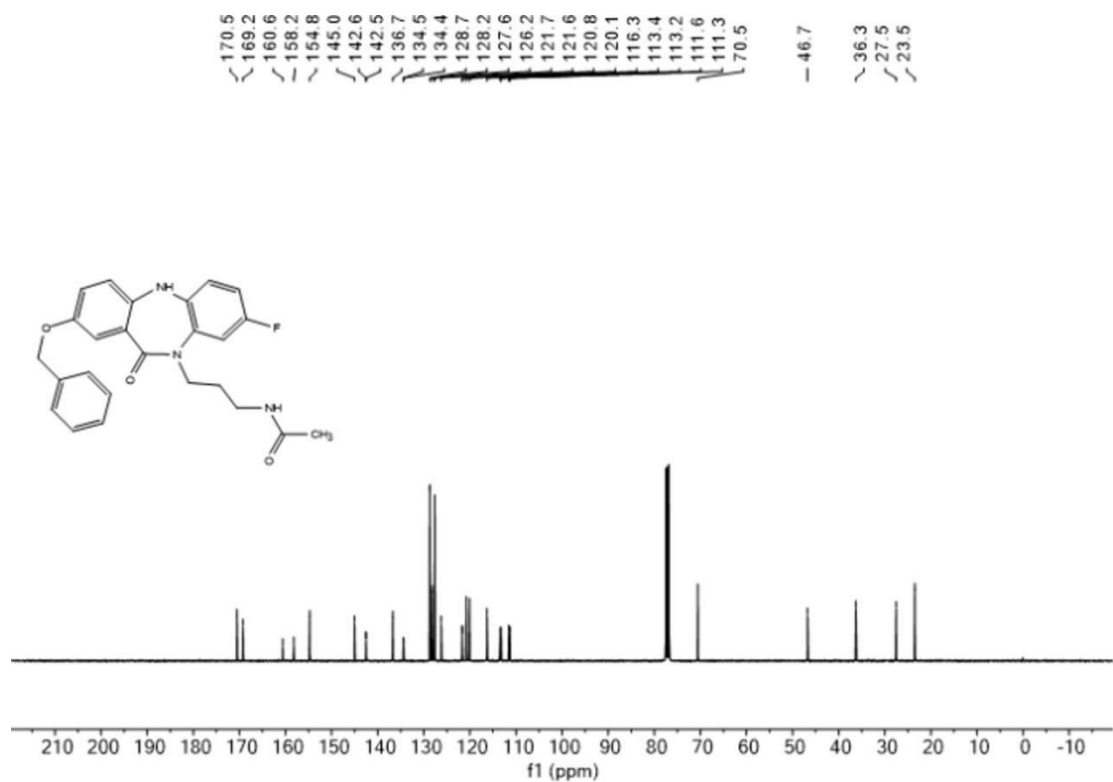


Figure S60. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound 22.

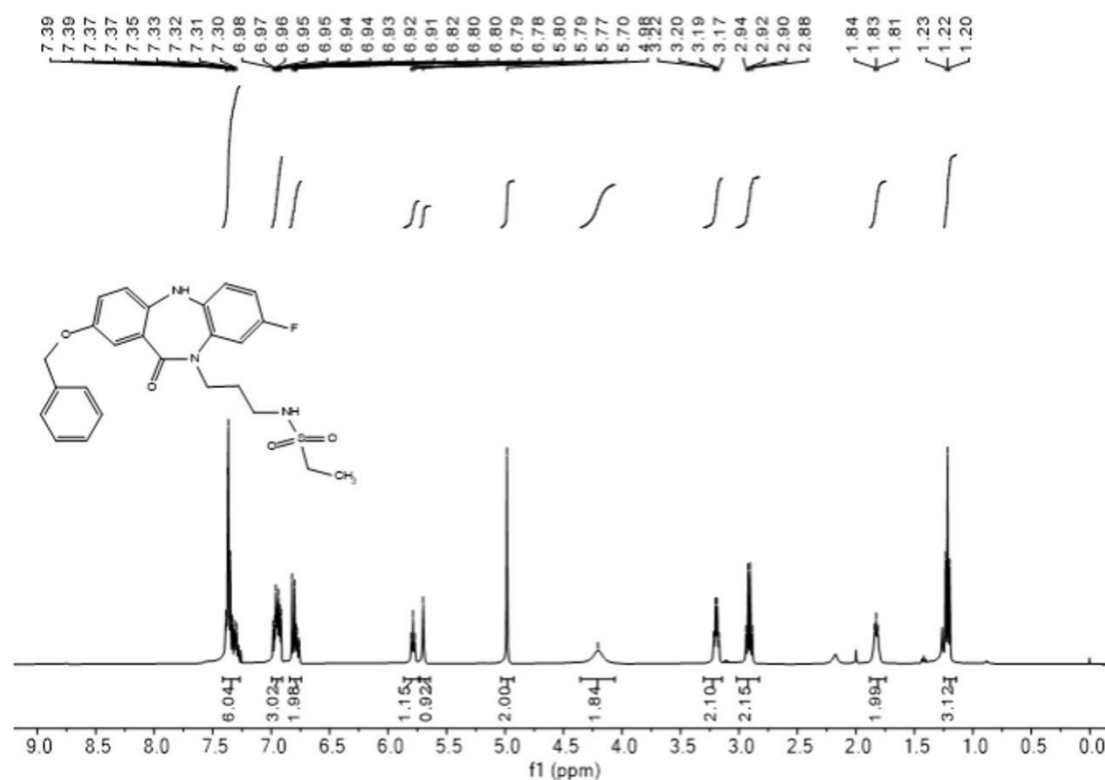


Figure S61. ¹H NMR (400 MHz, CDCl₃) spectrum of compound **23**.

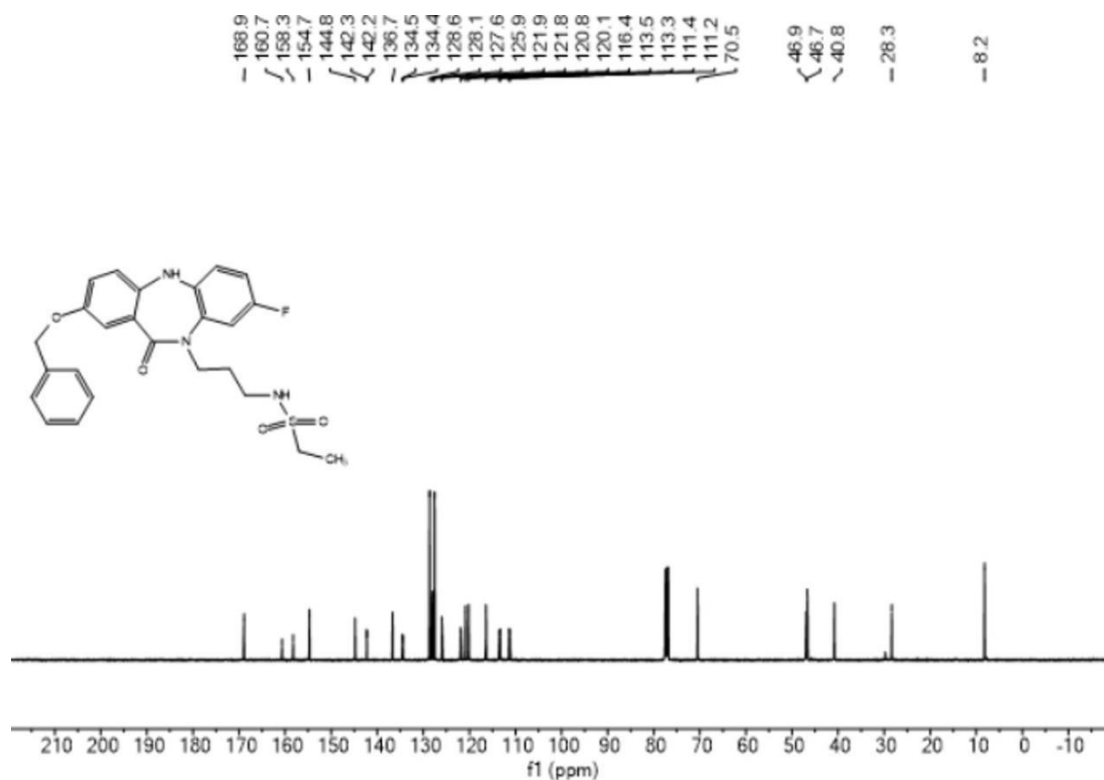


Figure S62. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound **23**.

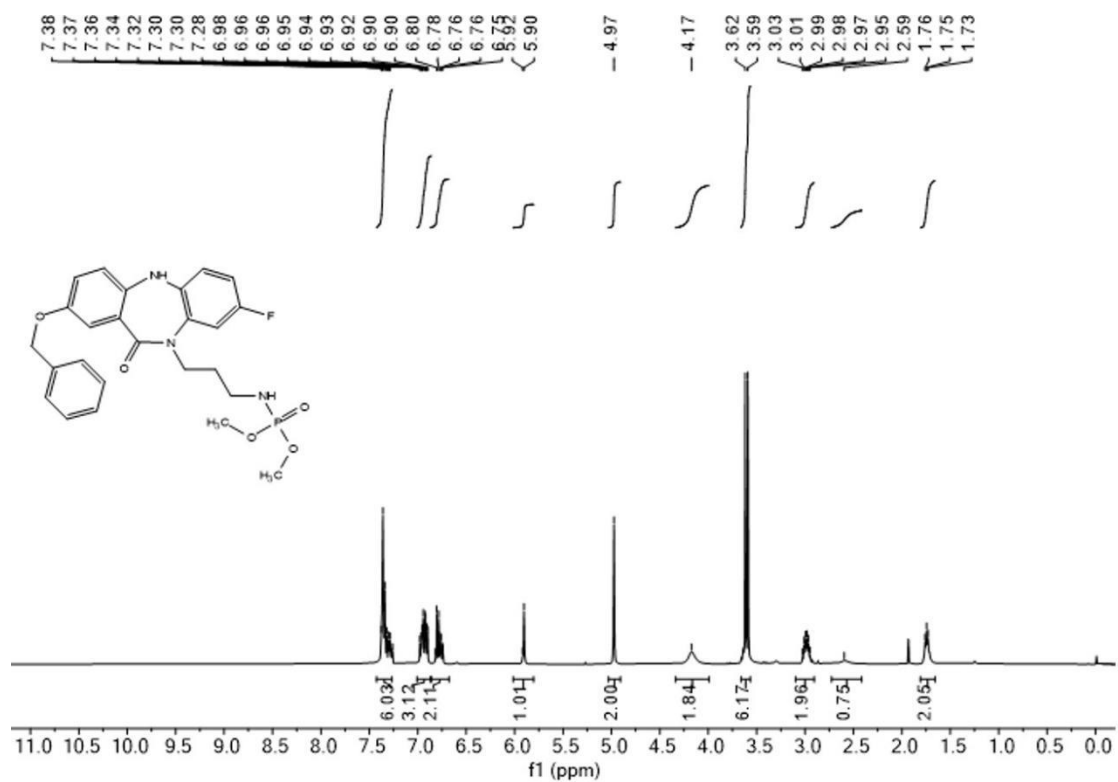


Figure S63. ¹H NMR (400 MHz, CDCl₃) spectrum of compound 24.

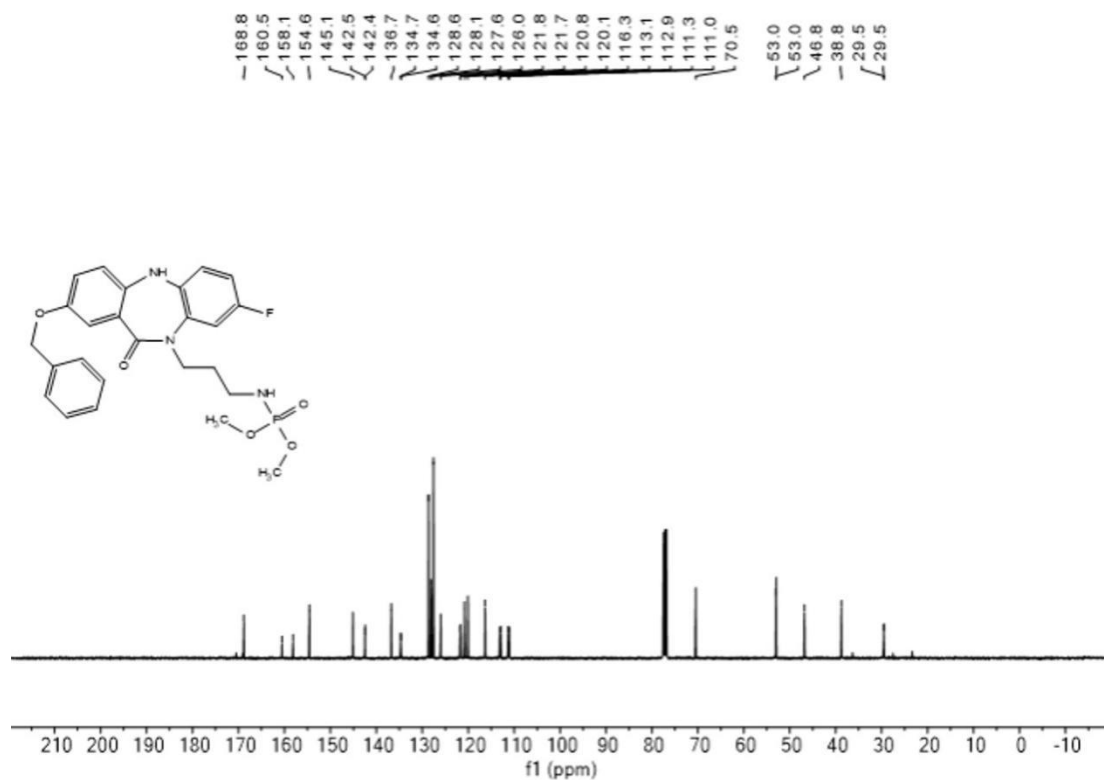


Figure S64. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound 24.

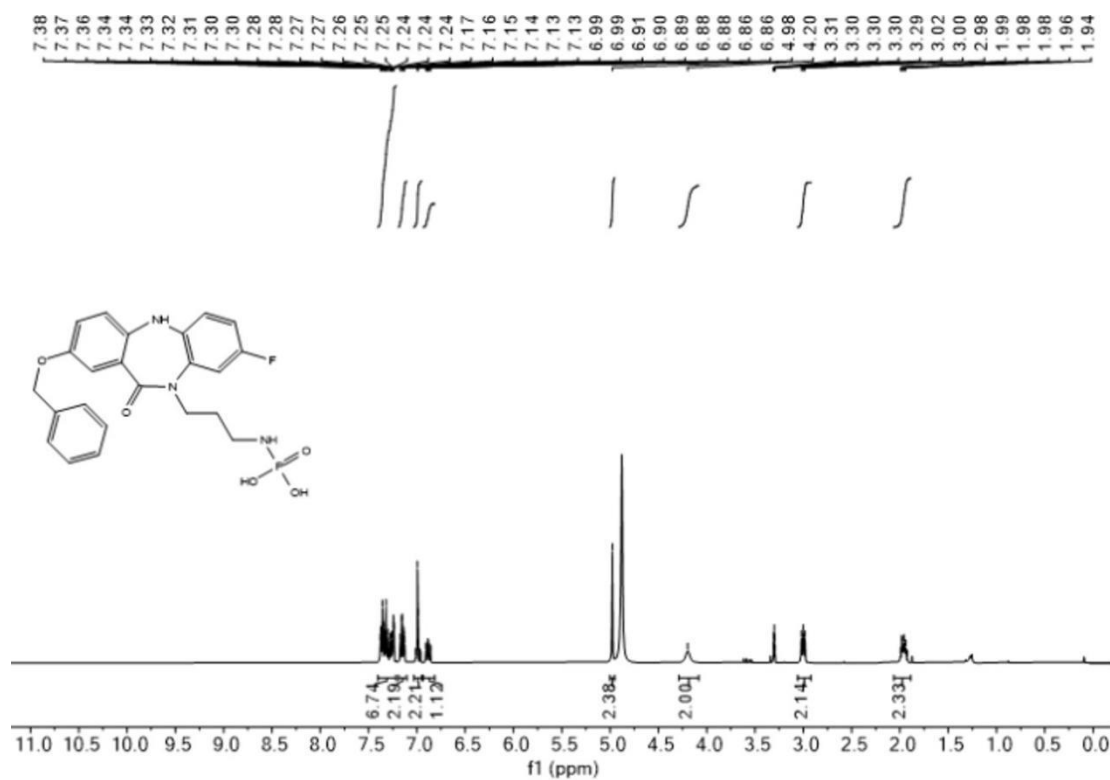


Figure S65. ¹H NMR (400 MHz, CDCl₃) spectrum of compound 25.

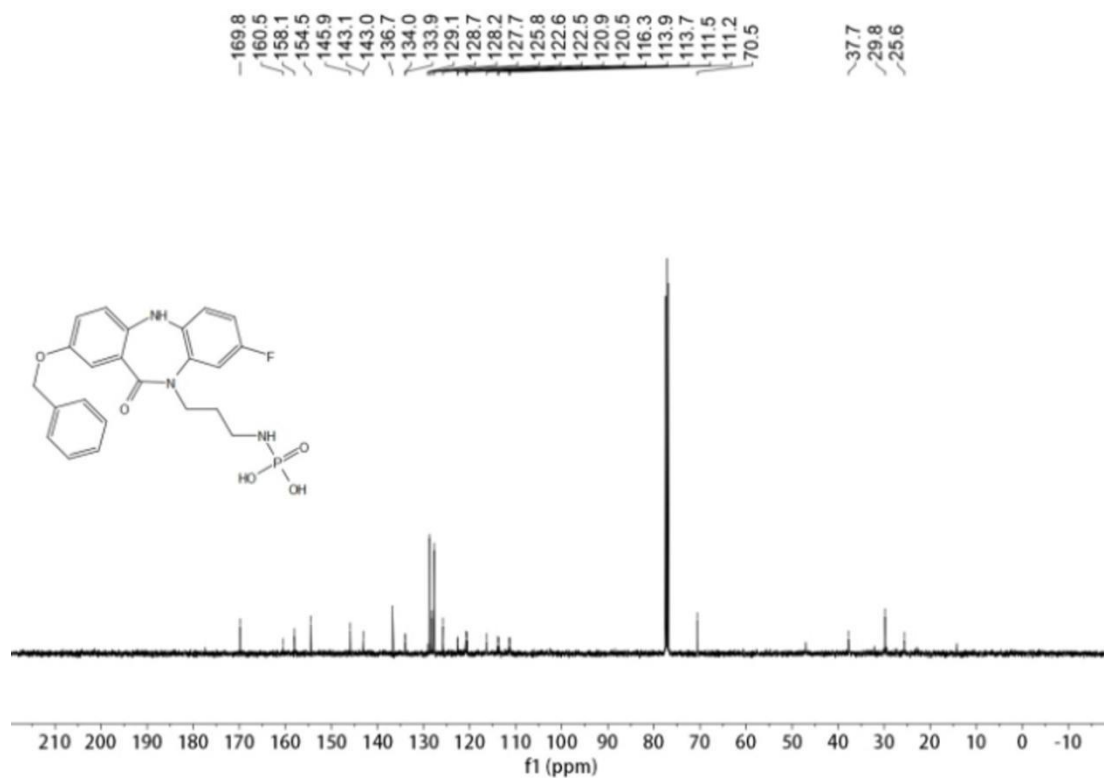


Figure S66. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound 25.

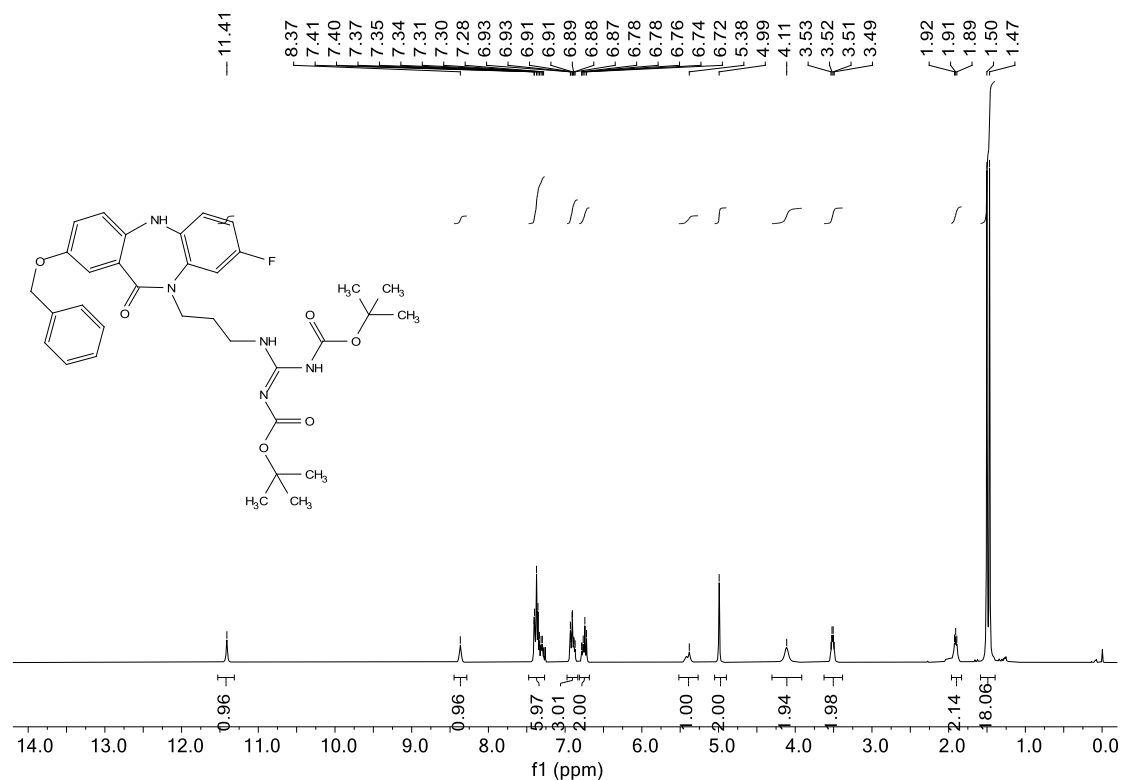


Figure S67. ¹H NMR (400 MHz, CDCl₃) spectrum of compound S10.

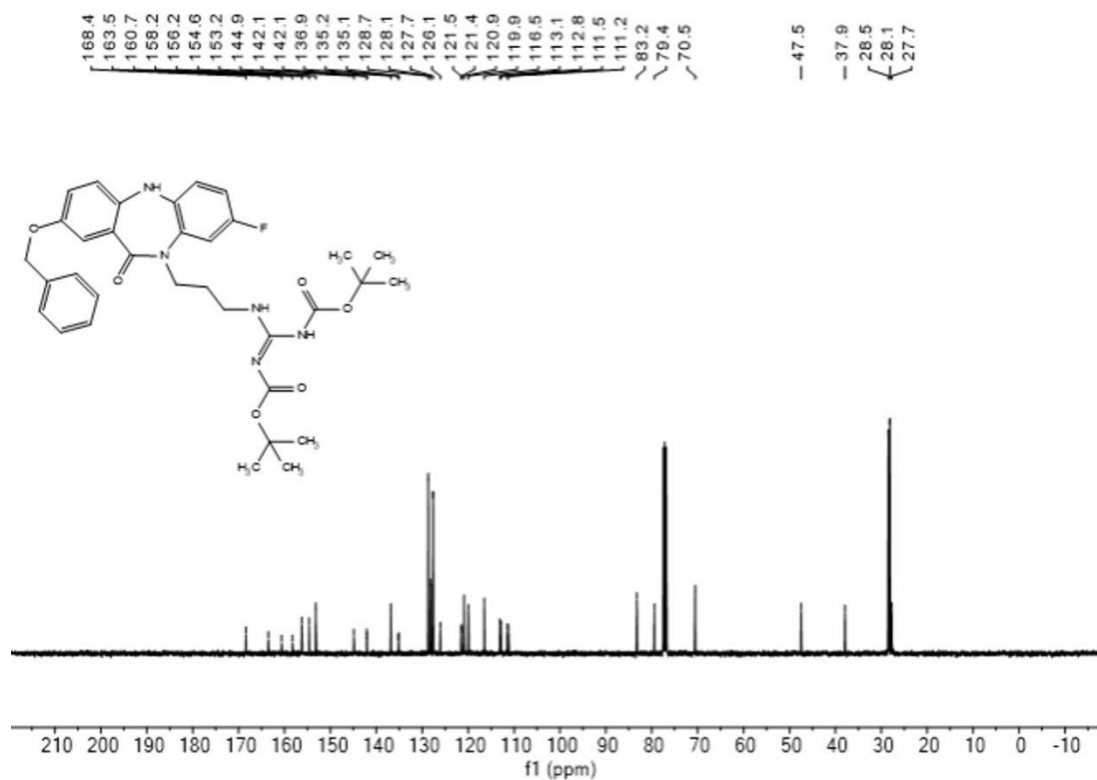


Figure S68. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound S10.

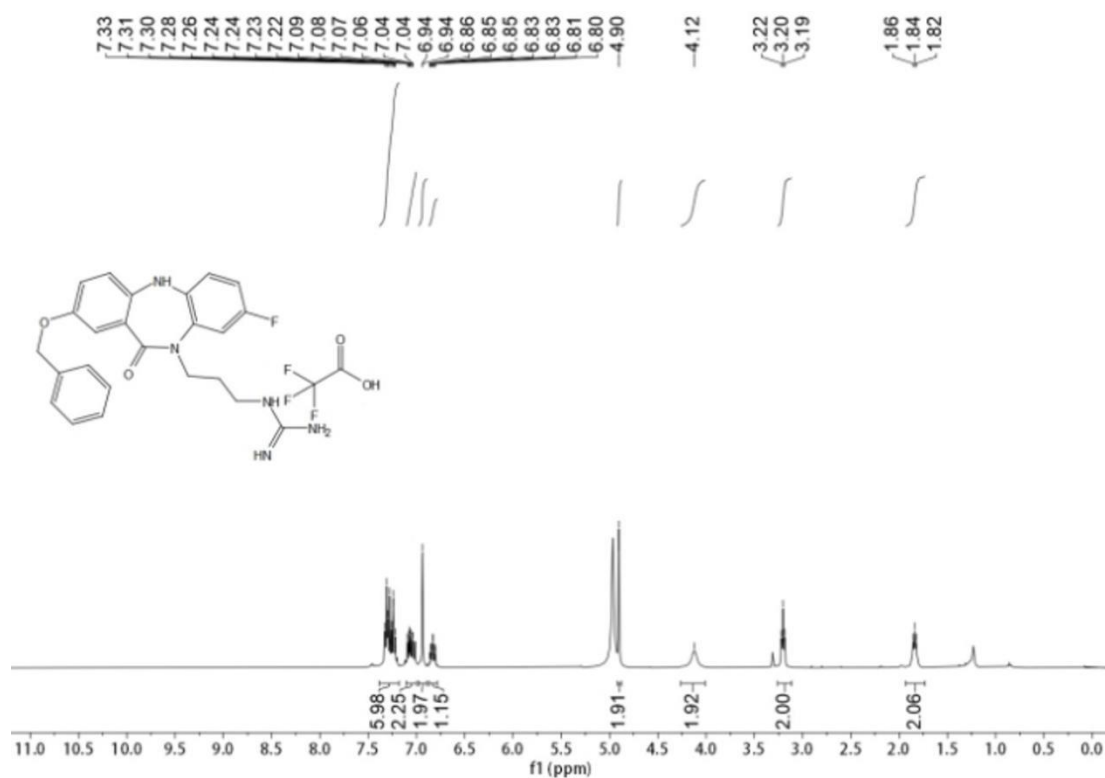


Figure S69. ¹H NMR (400 MHz, CD₃OD) spectrum of compound 26.

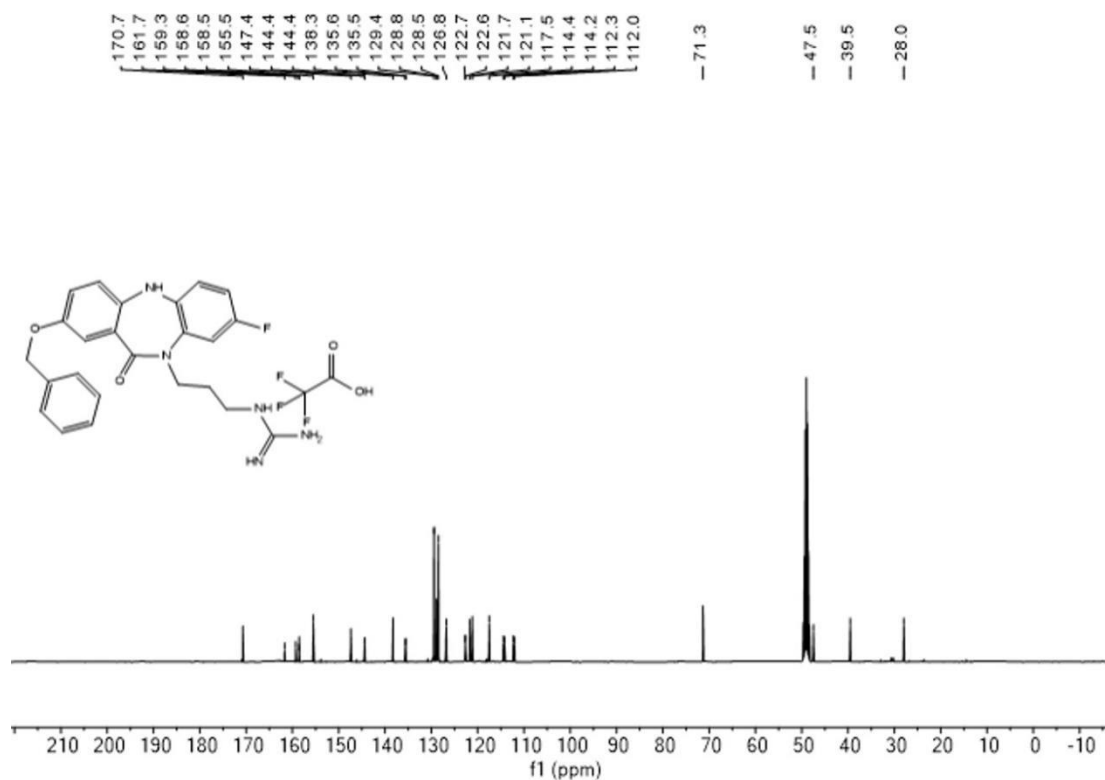


Figure S70. ¹³C NMR (101 MHz, CD₃OD) spectrum of compound 26.

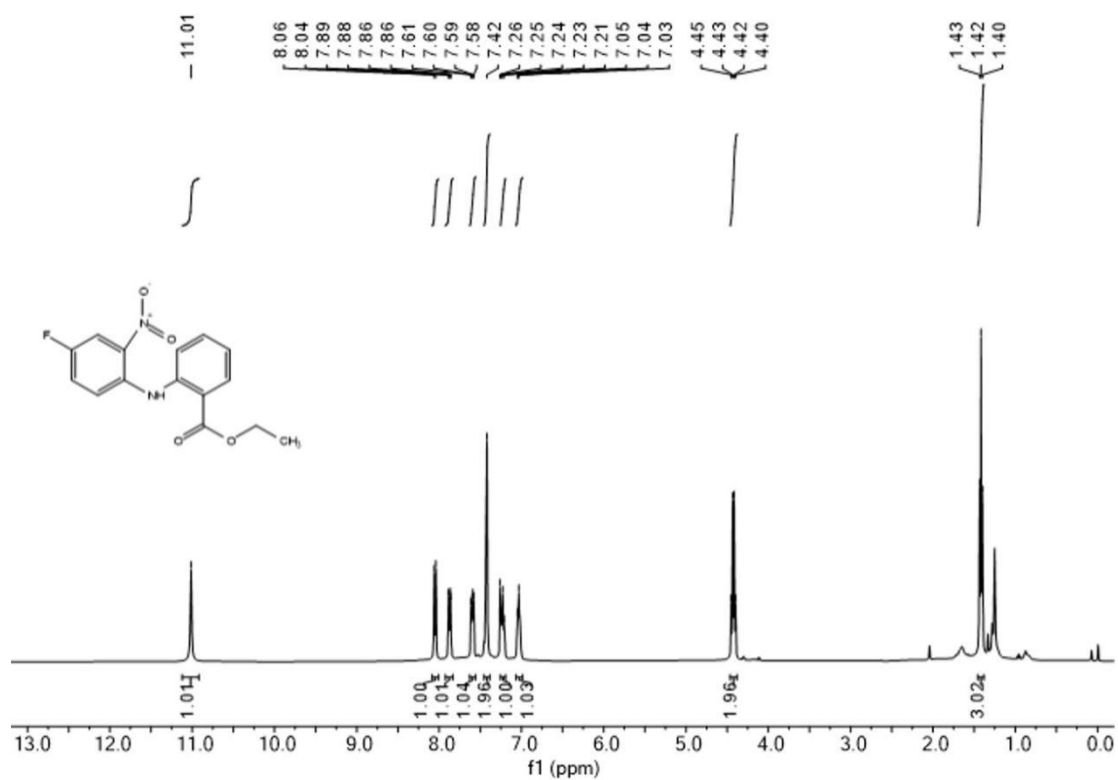


Figure S71. ¹H NMR (400 MHz, CDCl₃) spectrum of compound S12.

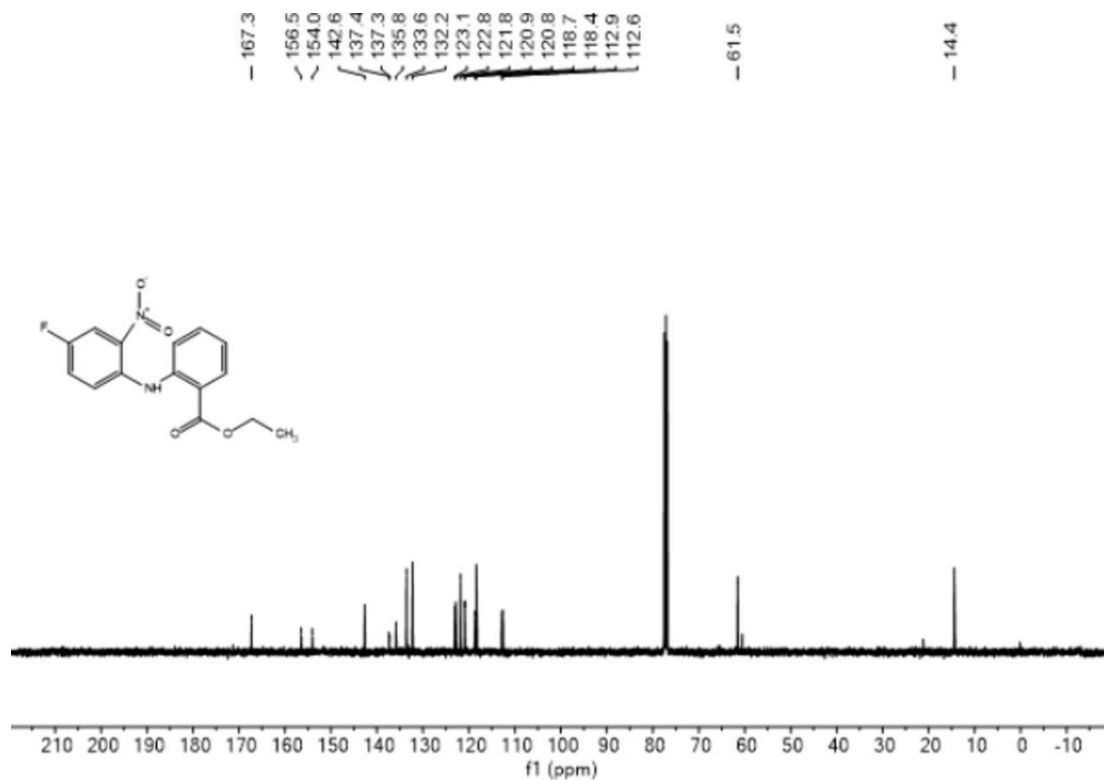


Figure S72. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound S12.

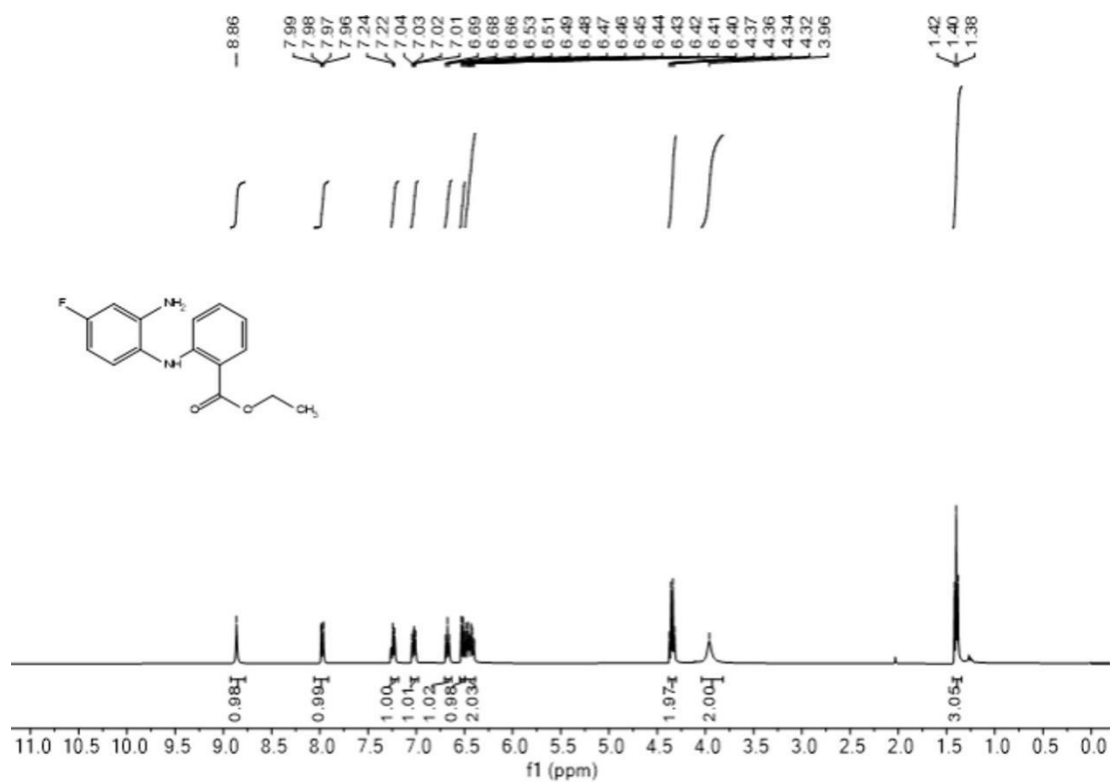


Figure S73. ¹H NMR (400 MHz, CDCl₃) spectrum of compound S13.

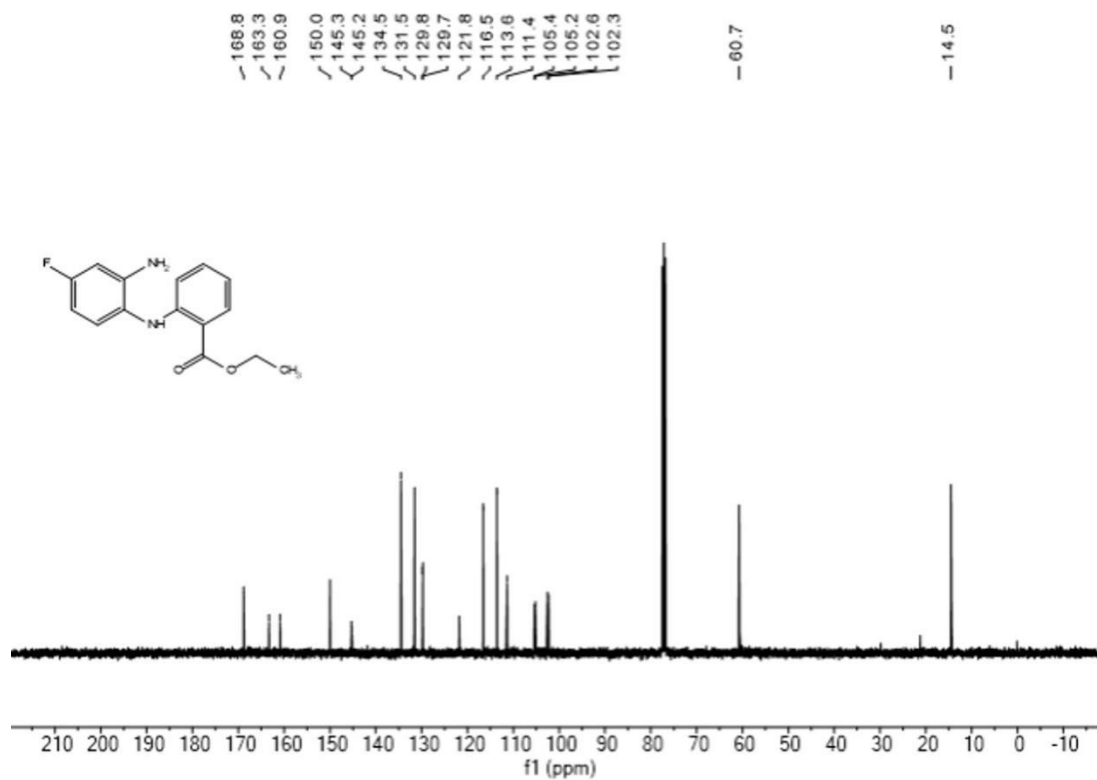


Figure S74. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound S13.

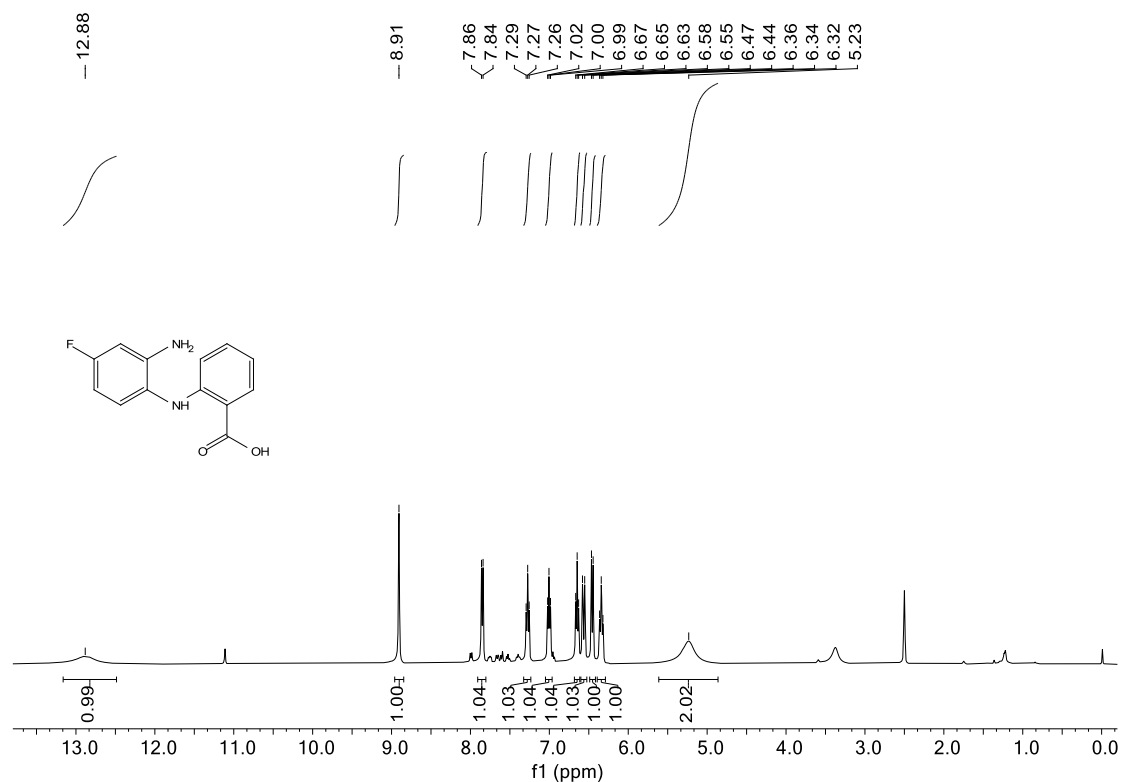


Figure S75. ¹H NMR (400 MHz, DMSO-*d*₆) spectrum of compound S14.

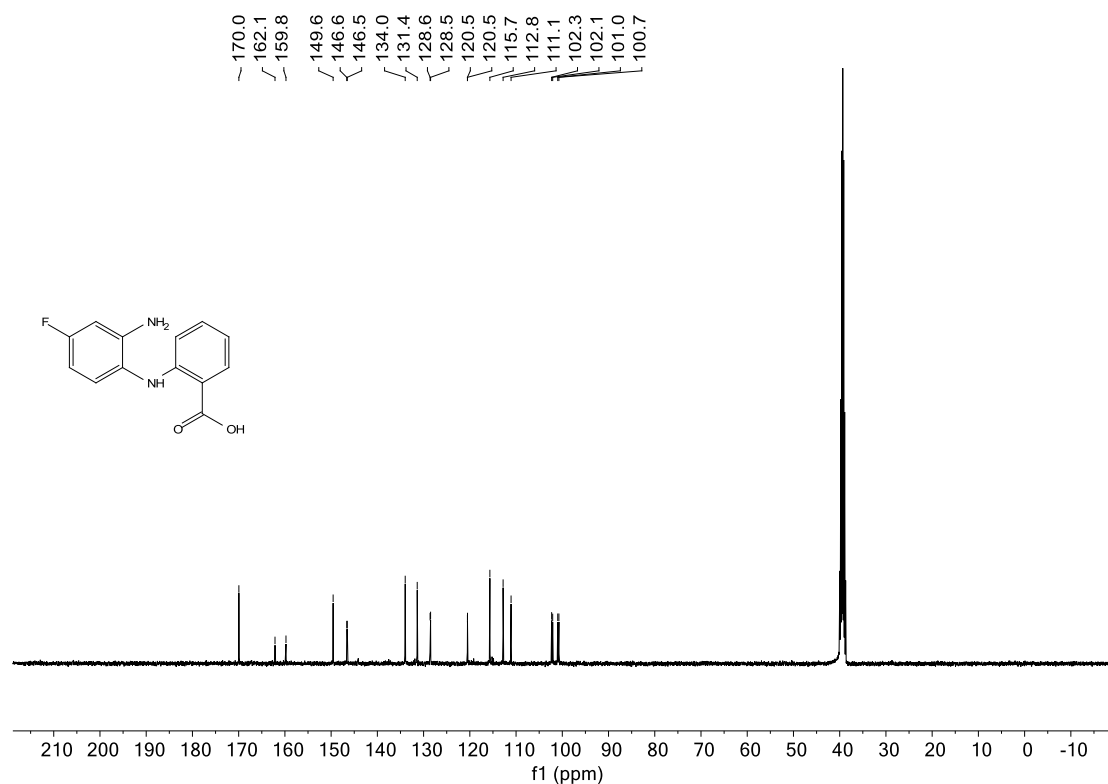


Figure S76. ¹³C NMR (101 MHz, DMSO-*d*₆) spectrum of compound S14.

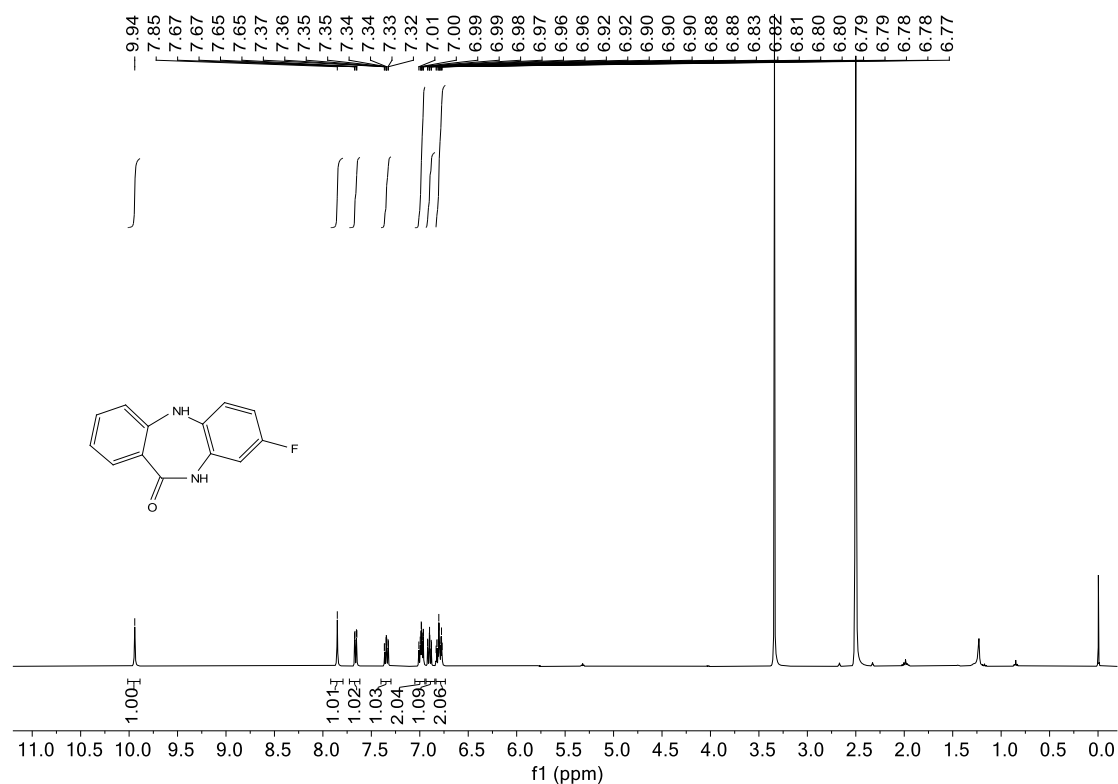


Figure S77. ¹H NMR (400 MHz, DMSO-*d*₆) spectrum of compound S15.

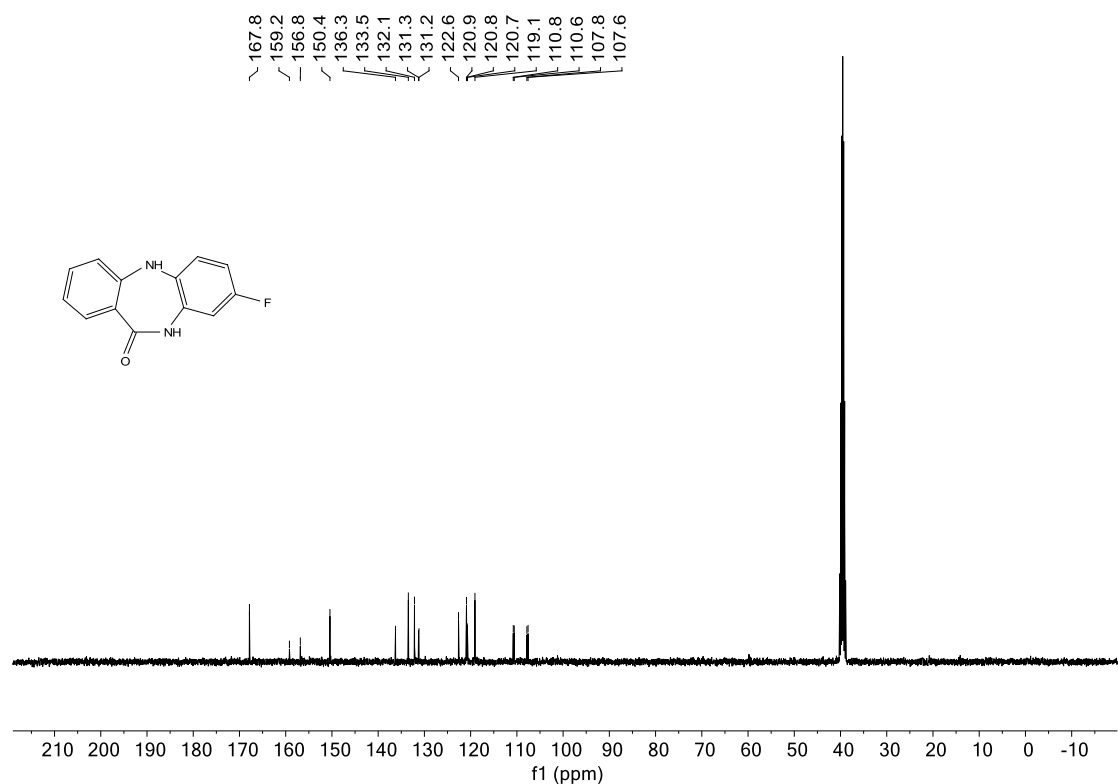


Figure S78 ¹³C NMR (101 MHz, DMSO-*d*₆) spectrum of compound S15.

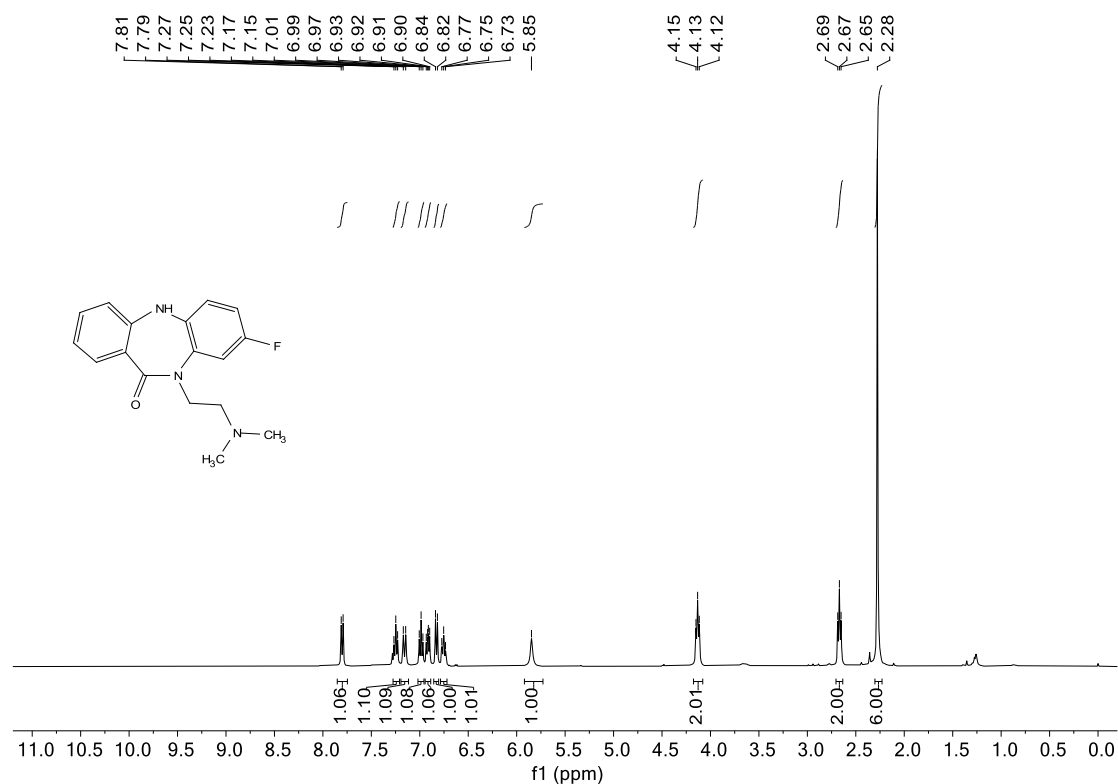


Figure S79. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound 27.

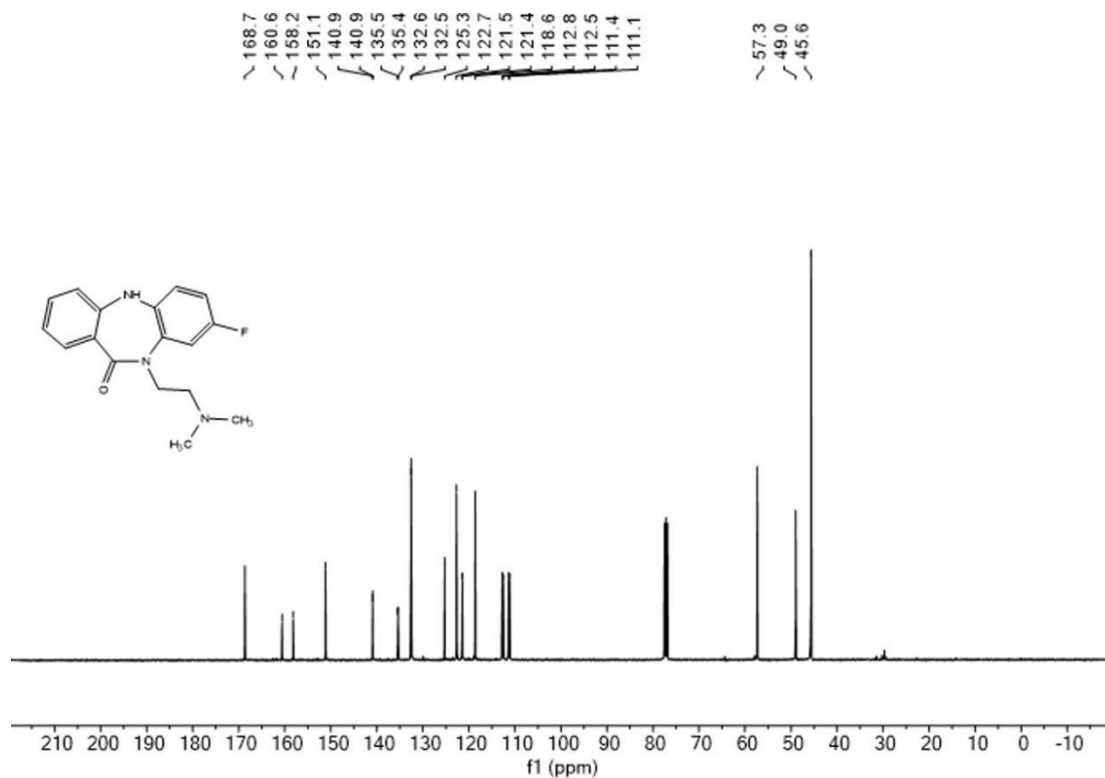


Figure S80. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound 27.

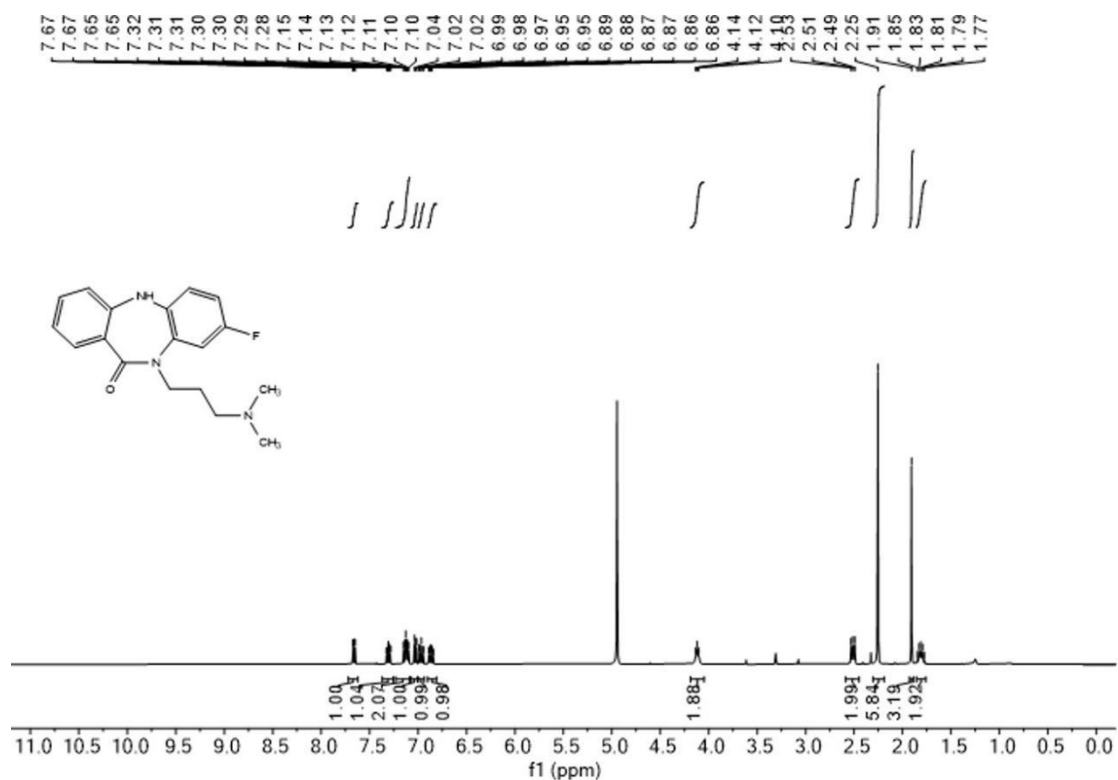


Figure S81. ¹H NMR (400 MHz, CD₃OD) spectrum of compound **28**.

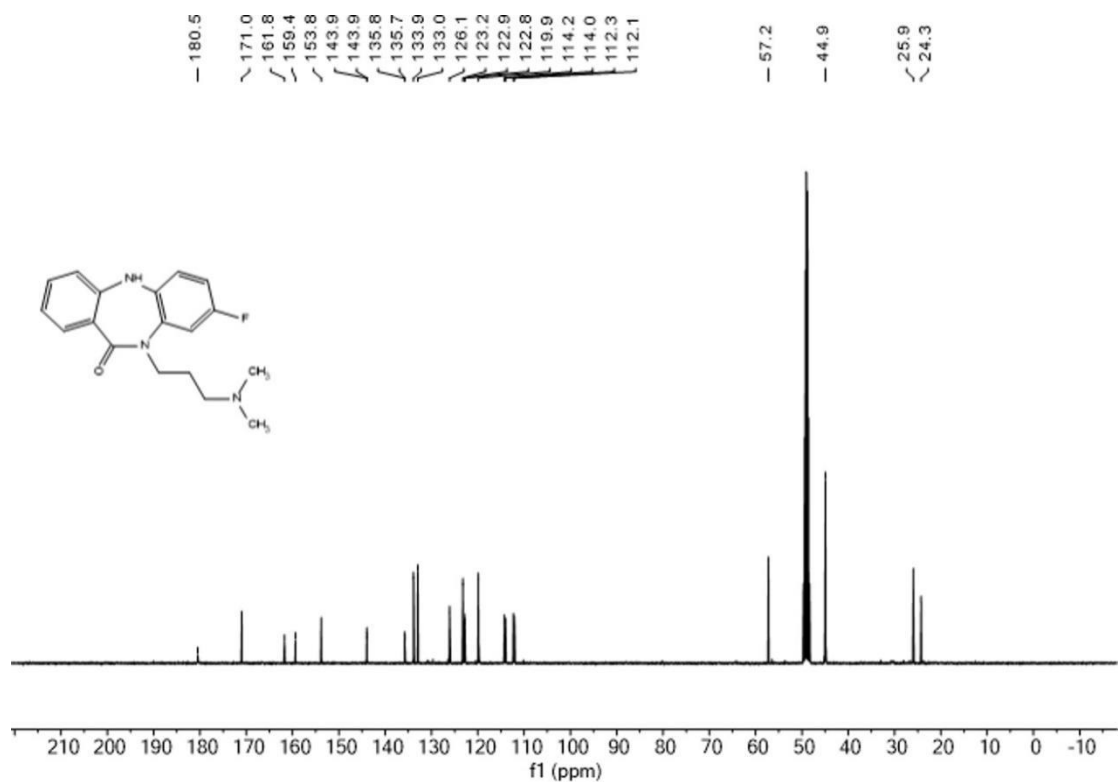


Figure S82. ¹³C NMR (101 MHz, CD₃OD) spectrum of compound **28**.

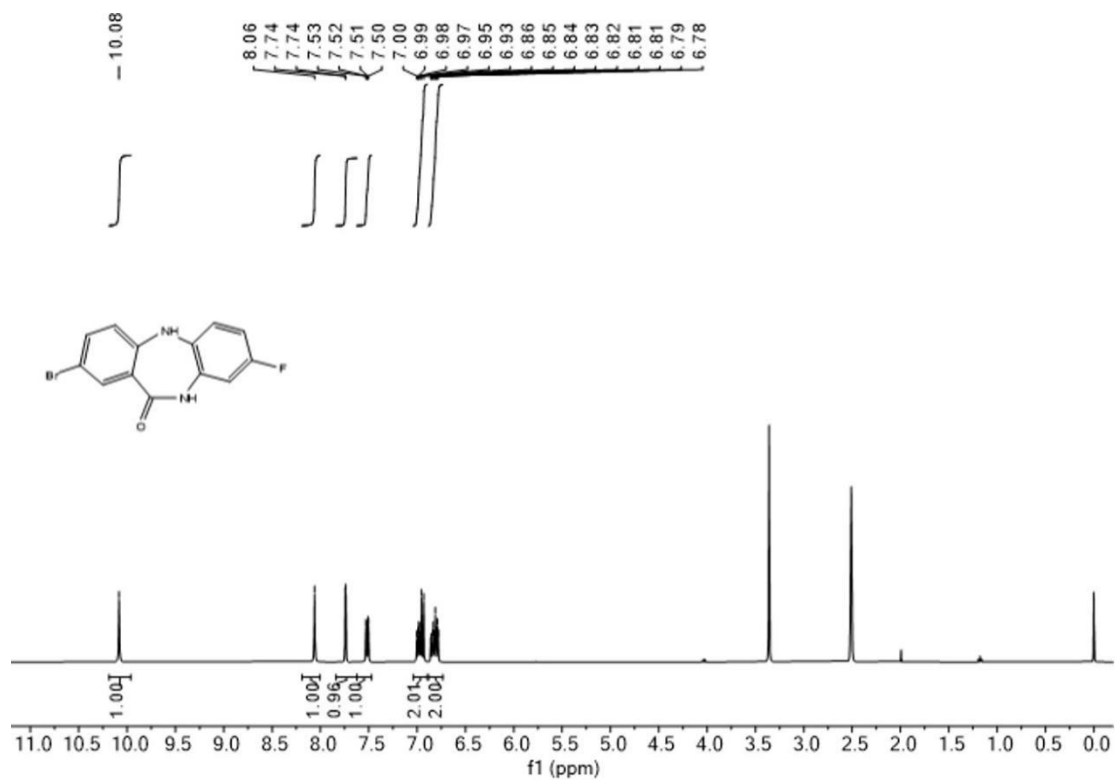


Figure S83. ¹H NMR (400 MHz, DMSO-*d*₆) spectrum of compound S16.

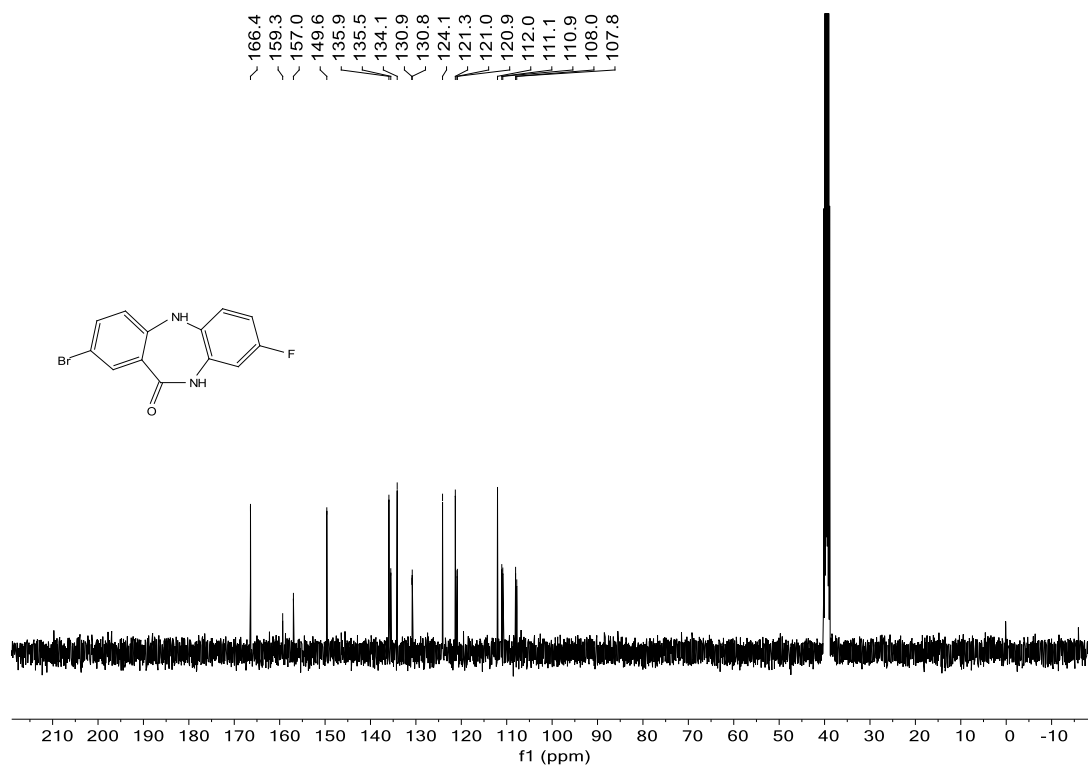


Figure S84. ¹³C NMR (101 MHz, DMSO-*d*₆) spectrum of compound S16.

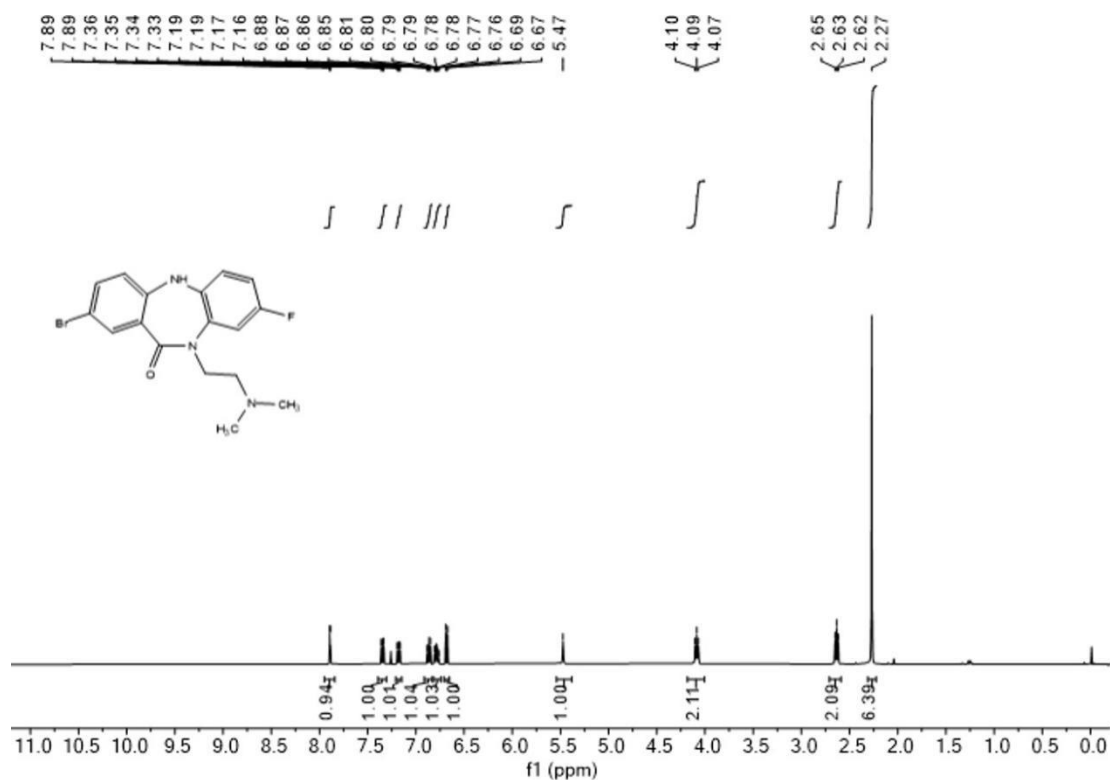


Figure S85. ¹H NMR (400 MHz, CDCl₃) spectrum of compound S17.

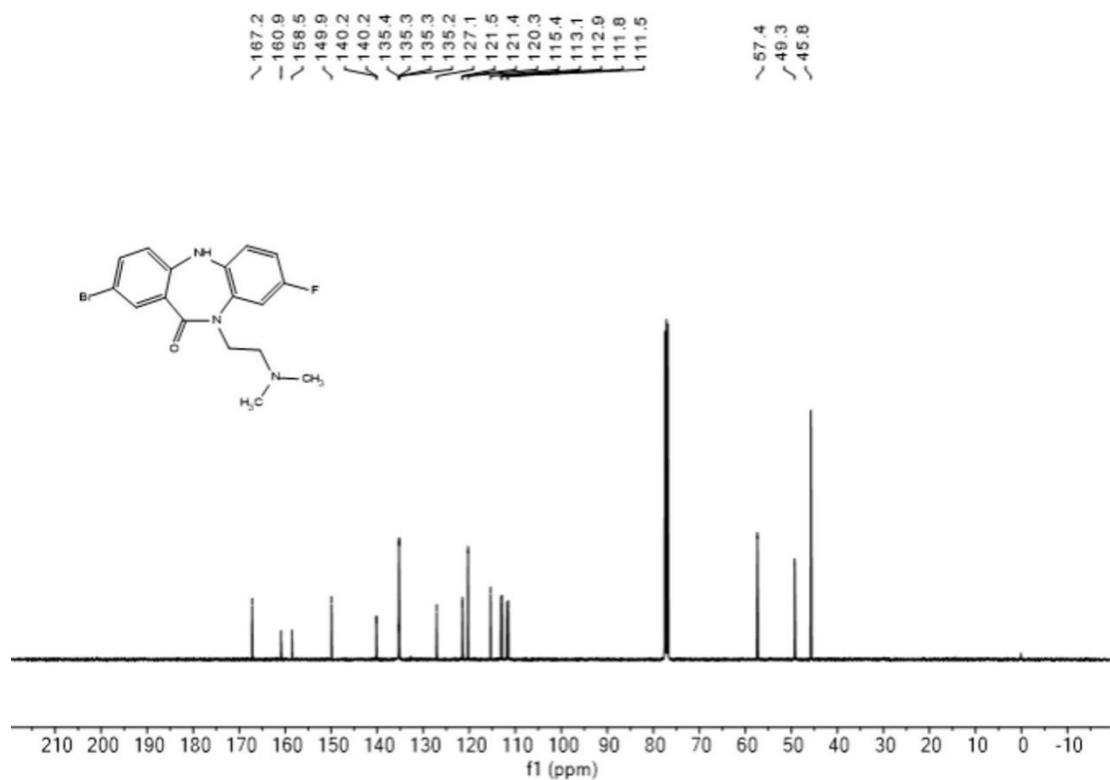


Figure S86. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound S17.

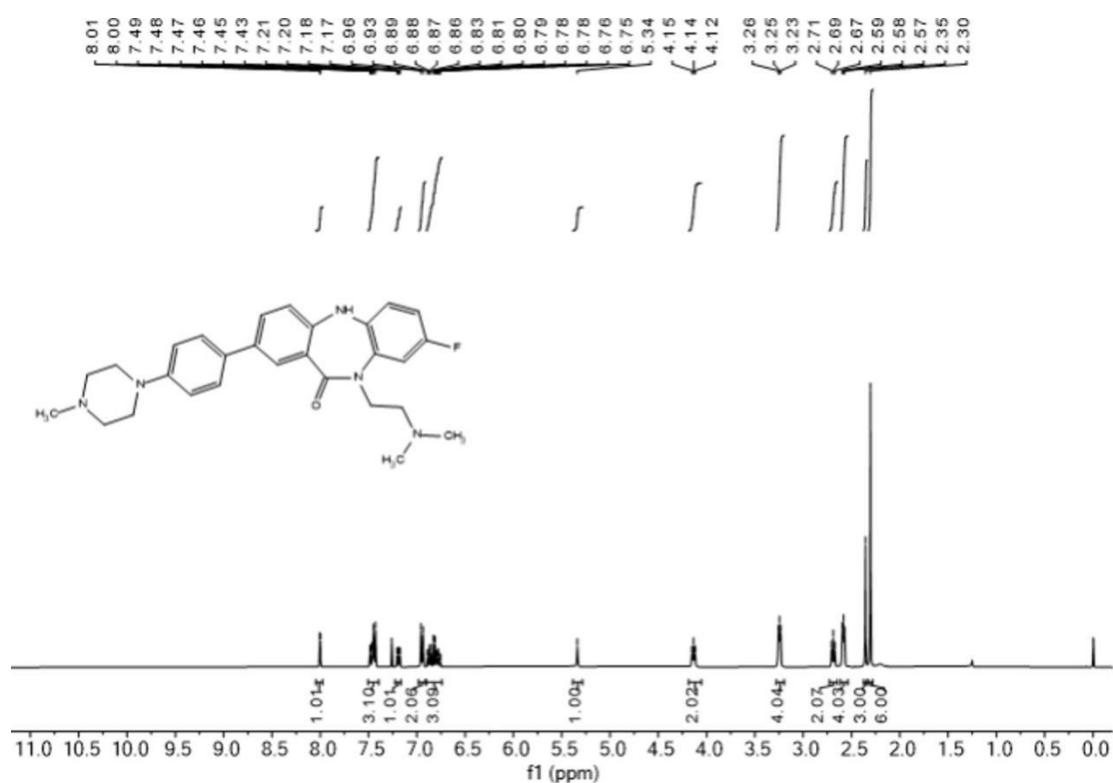


Figure S87. ¹H NMR (400 MHz, CDCl₃) spectrum of compound 29.

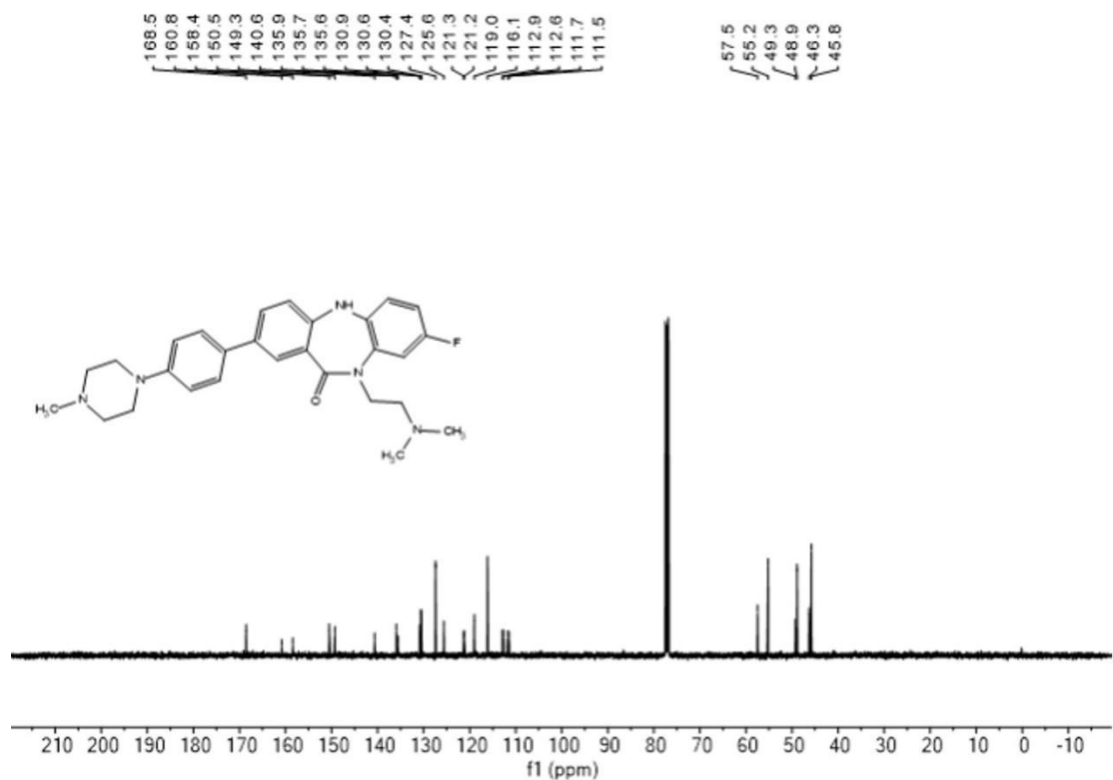


Figure S88. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound 29.

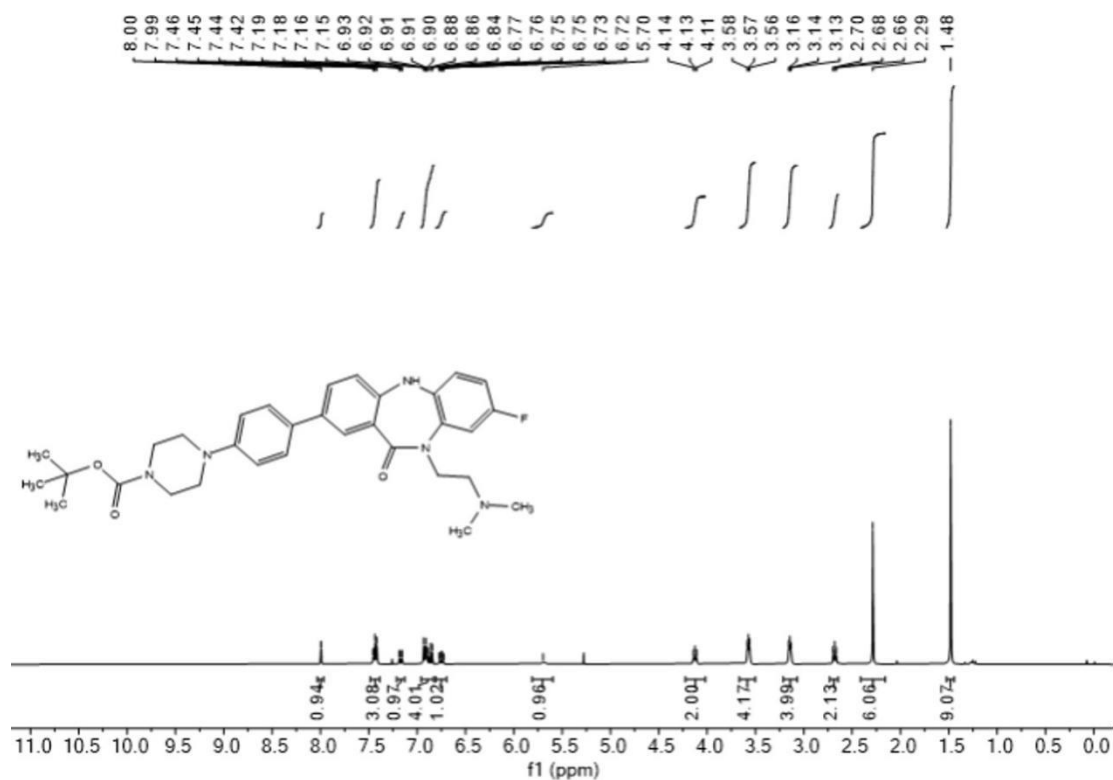


Figure S89. ^1H NMR (400 MHz, CDCl_3) spectrum of compound S18.

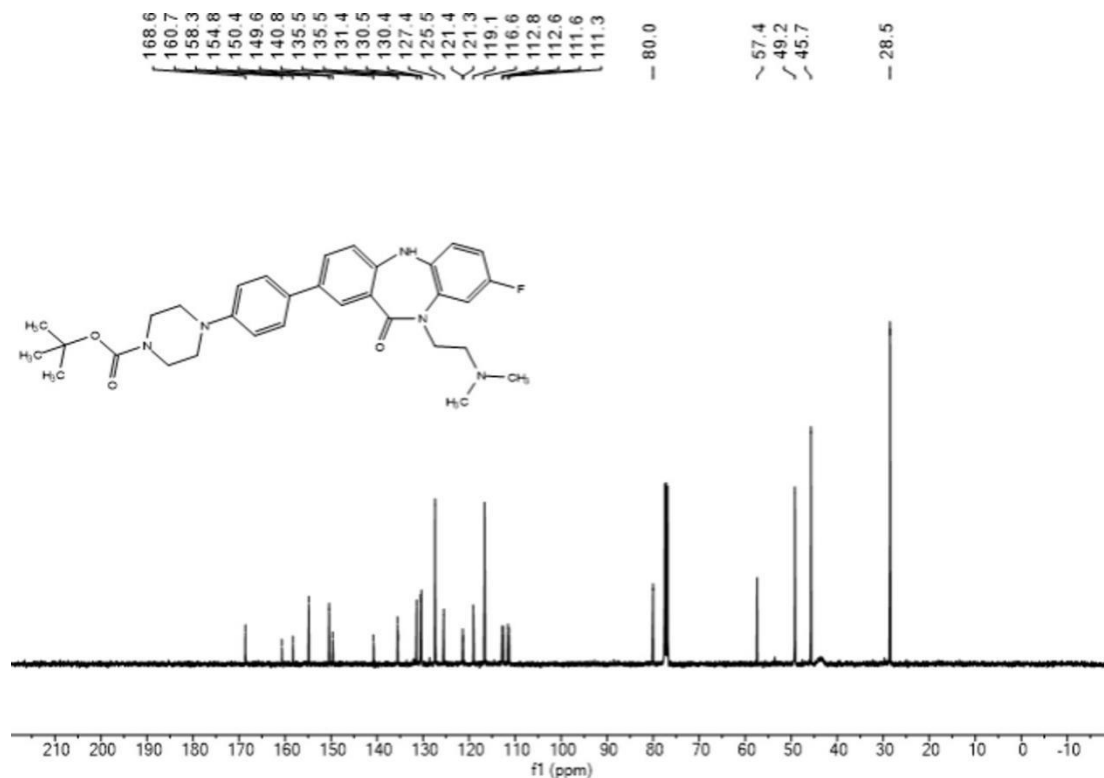


Figure S90. ^{13}C NMR (101 MHz, CDCl_3) spectrum of compound S18.

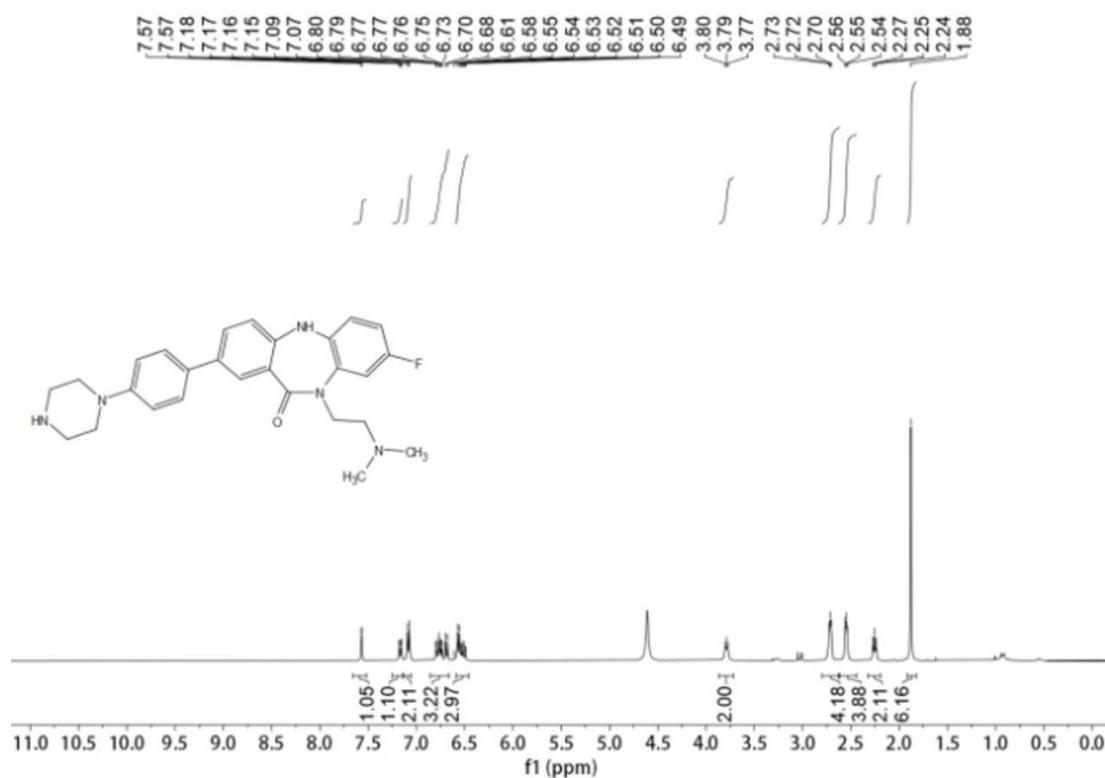


Figure S91. ¹H NMR (400 MHz, CD₃OD) spectrum of compound 30.

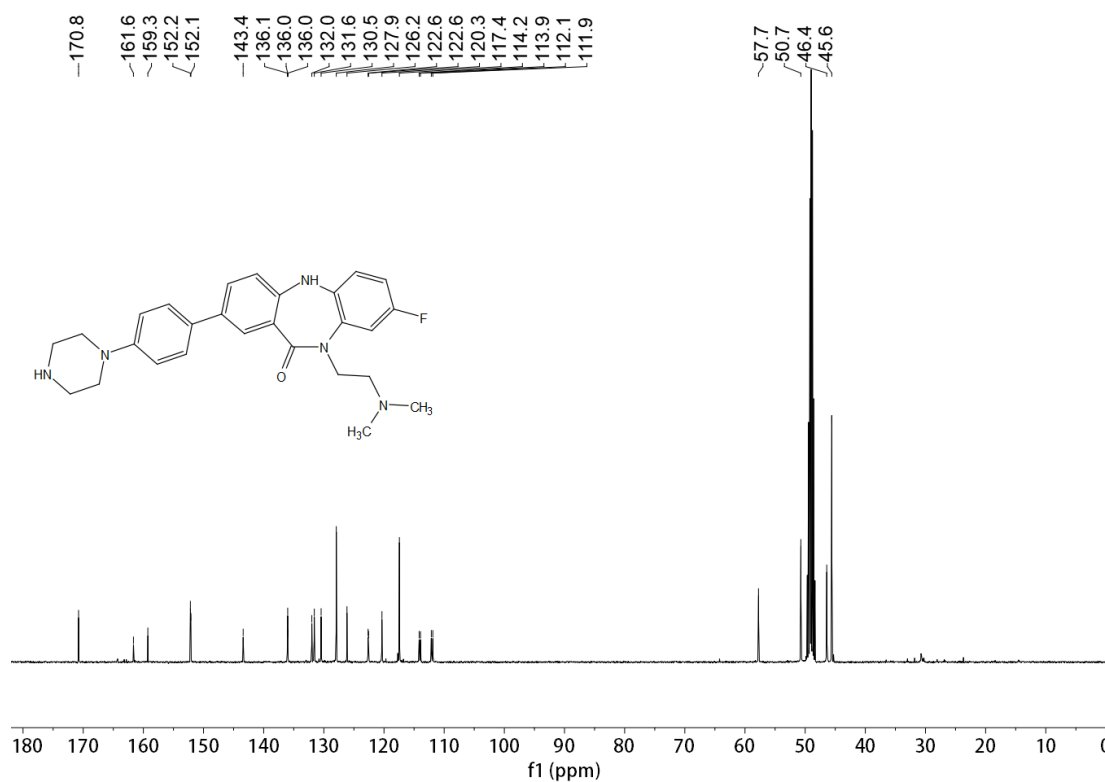


Figure S92. ¹³C NMR (101 MHz, CD₃OD) spectrum of compound 30.

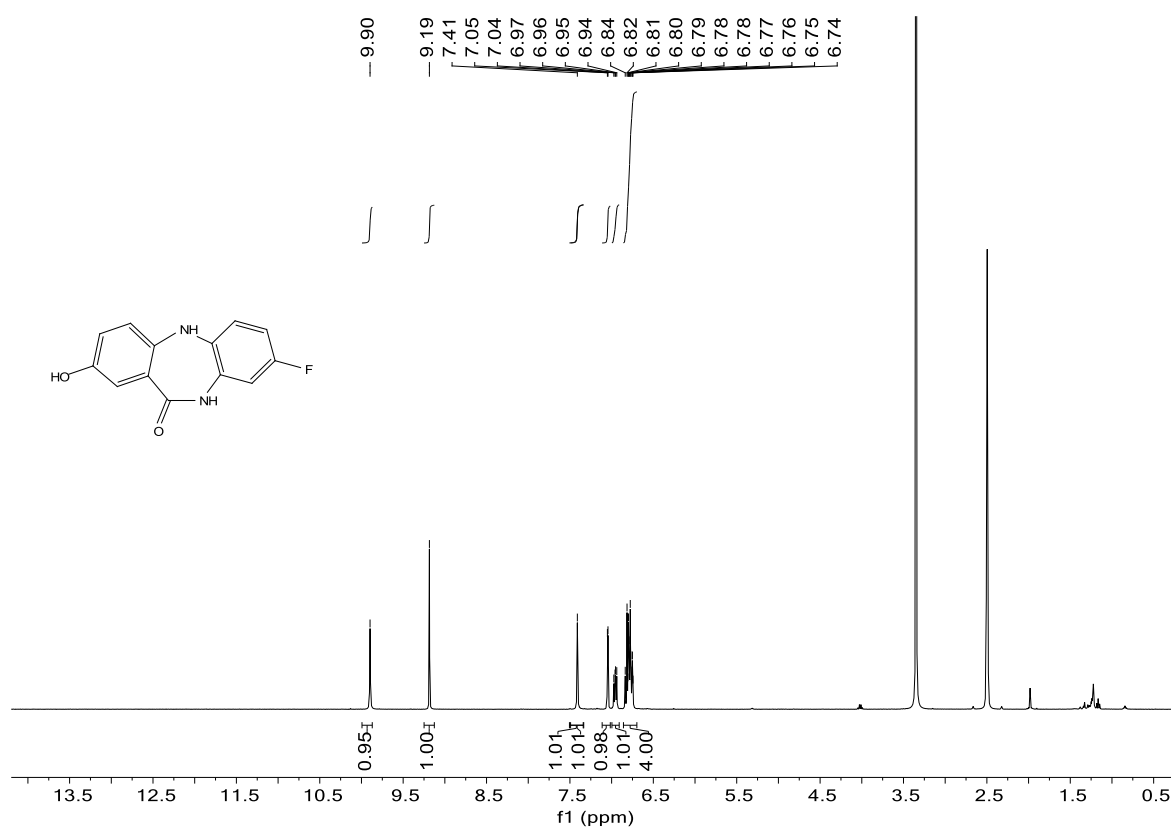


Figure S93. ¹H NMR (400 MHz, DMSO-*d*₆) spectrum of compound S19.

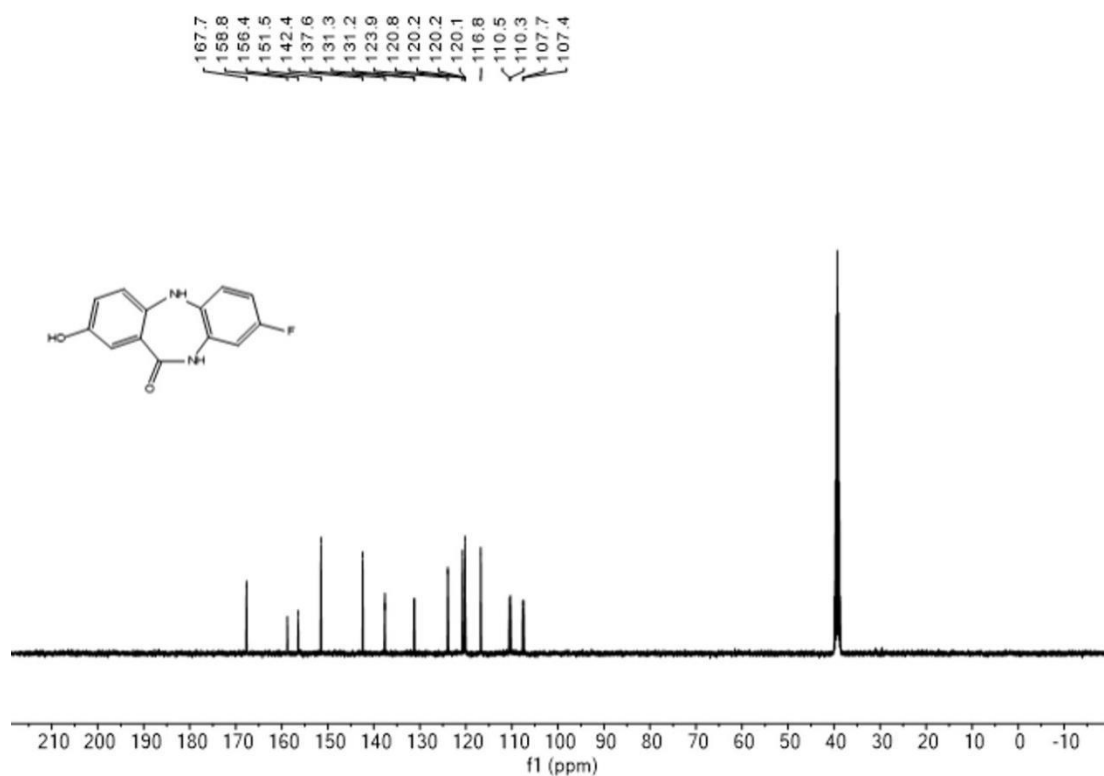


Figure S94. ¹³C NMR (101 MHz, DMSO-*d*₆) spectrum of compound S19.

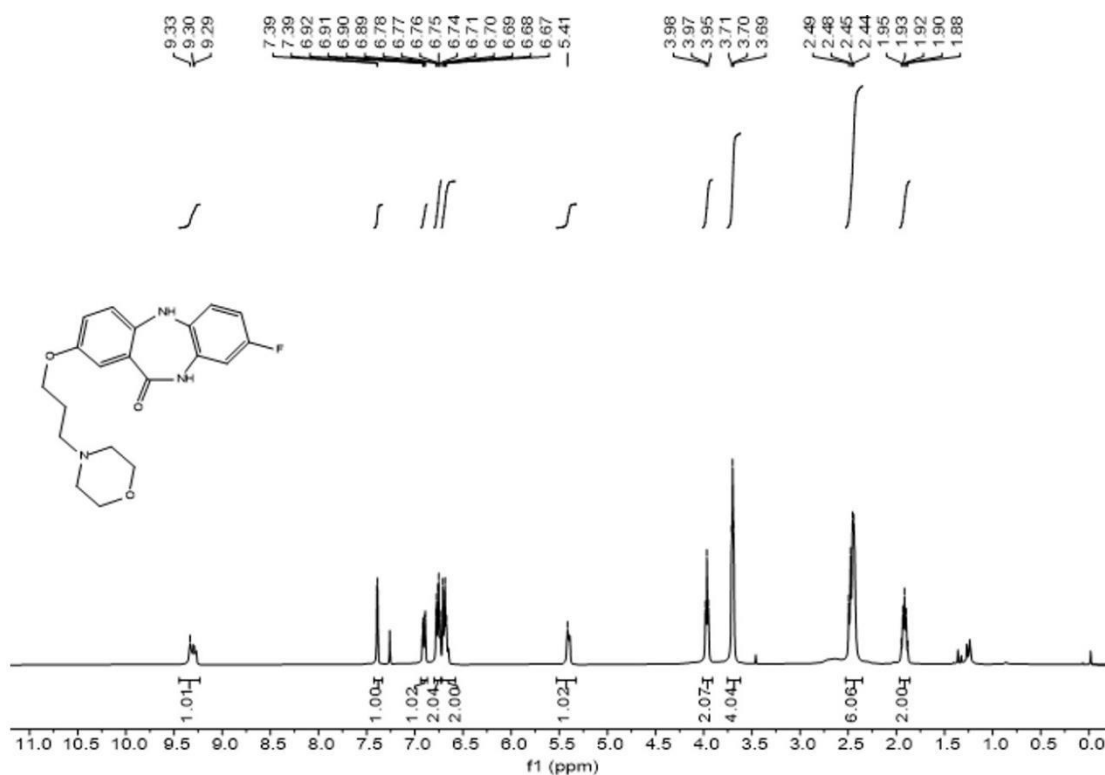


Figure S95. ¹H NMR (400 MHz, CDCl₃) spectrum of compound S20.

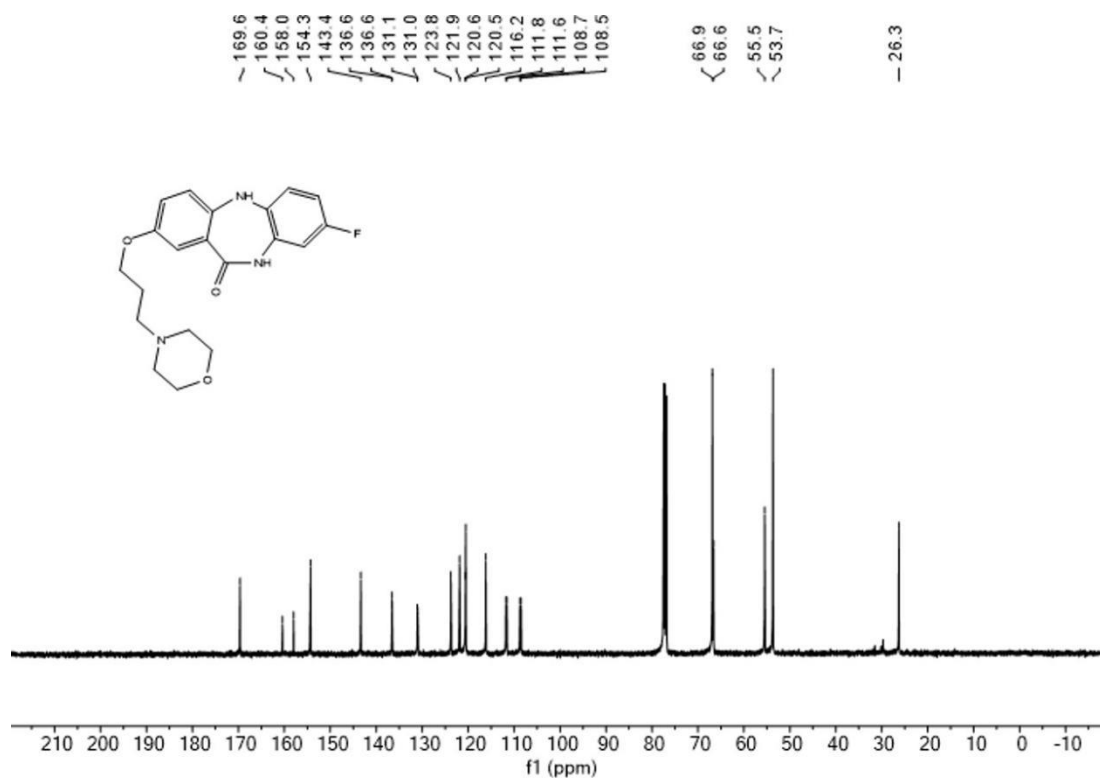


Figure S96. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound S20.

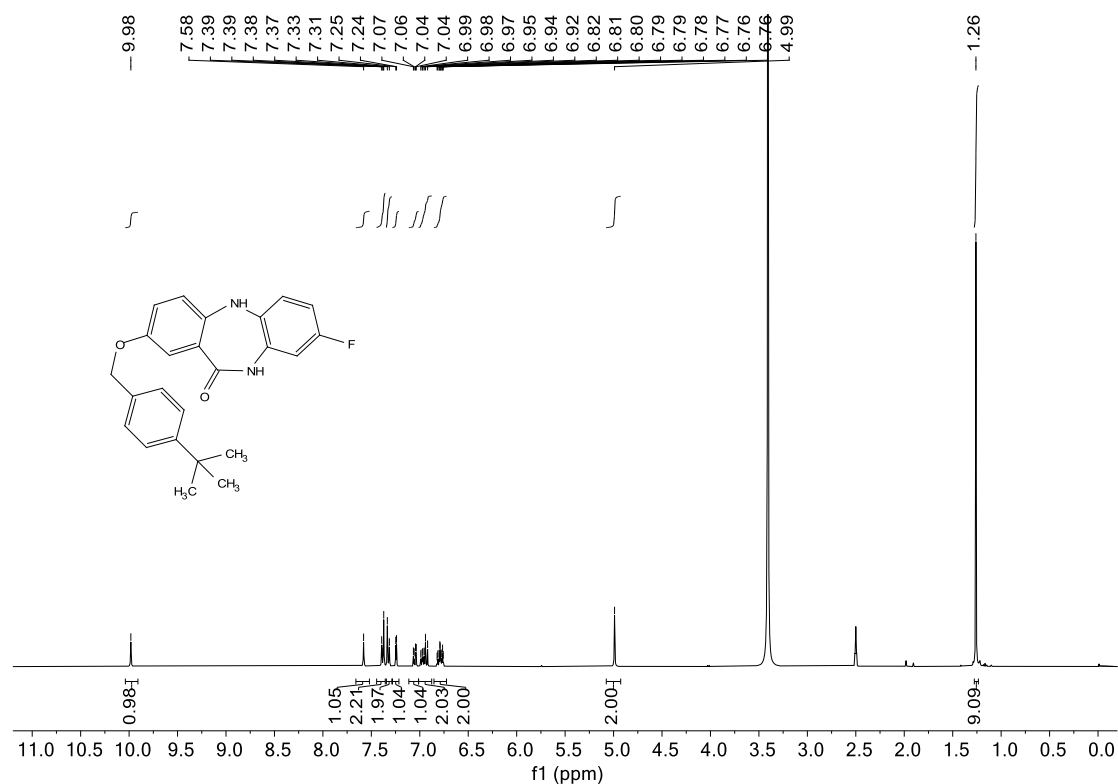


Figure S97. ¹H NMR (400 MHz, CDCl₃) spectrum of compound S21.

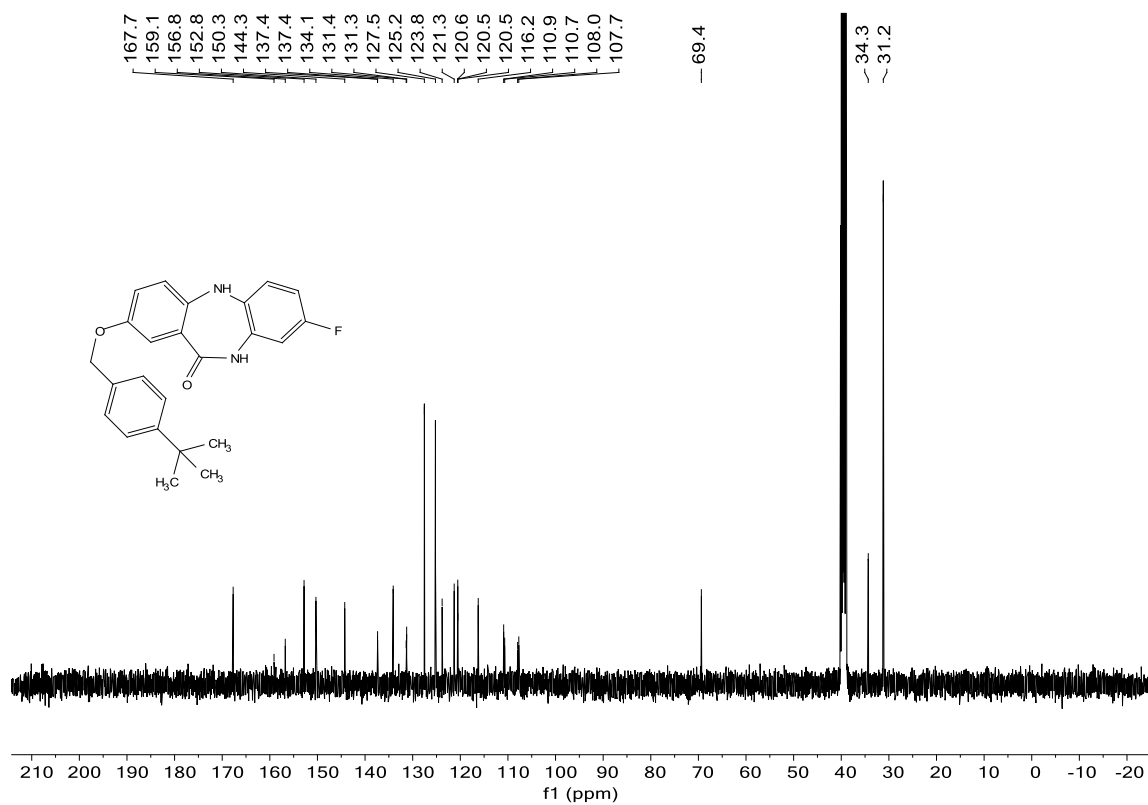


Figure S98. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound S21.

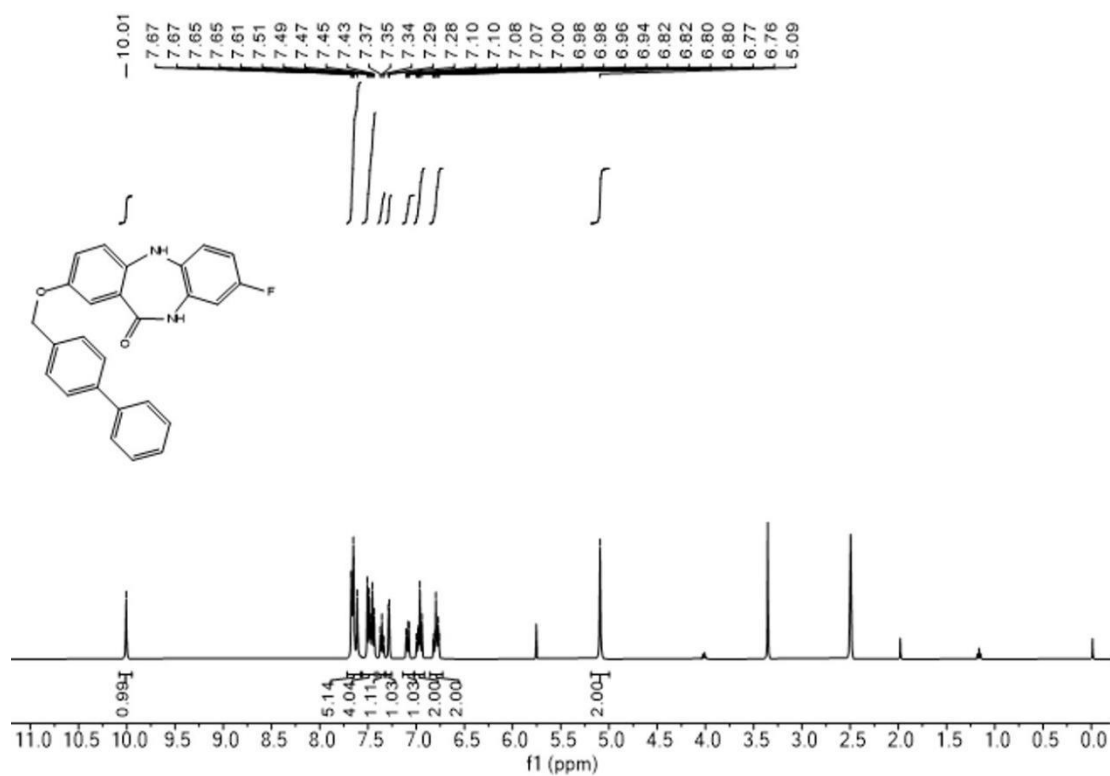


Figure S99. ¹H NMR (400 MHz, DMSO-*d*₆) spectrum of compound S22.

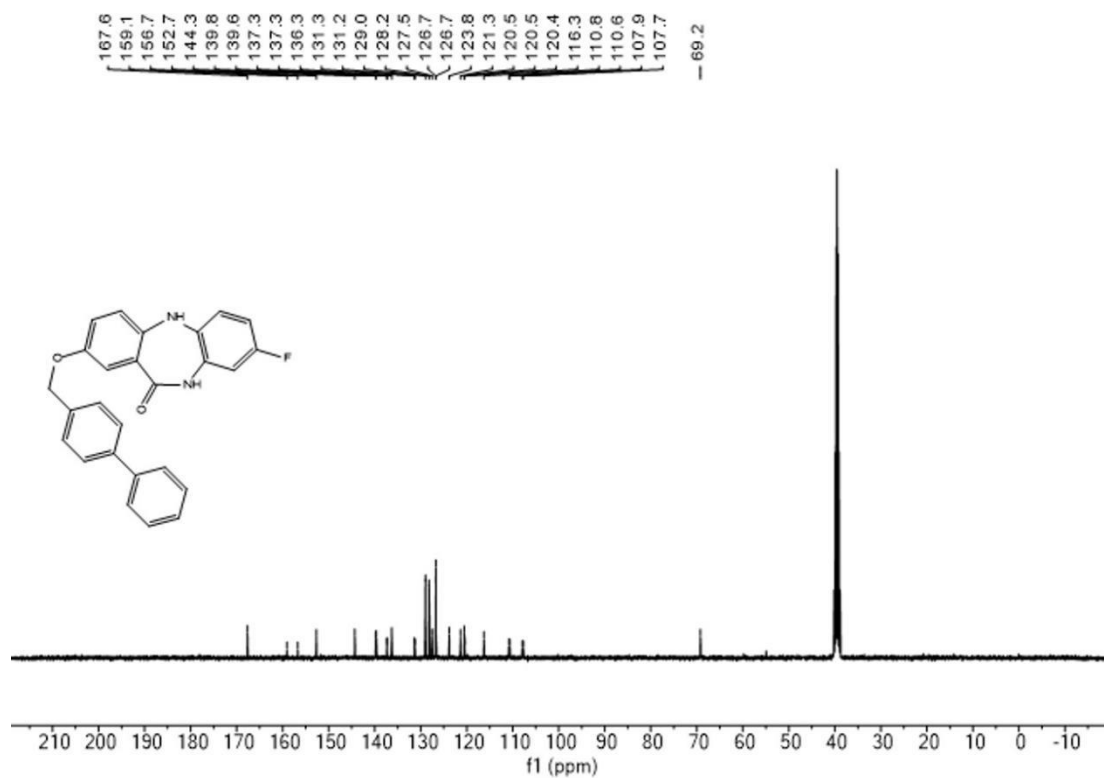


Figure S100. ¹³C NMR (101 MHz, DMSO-*d*₆) spectrum of compound S22.

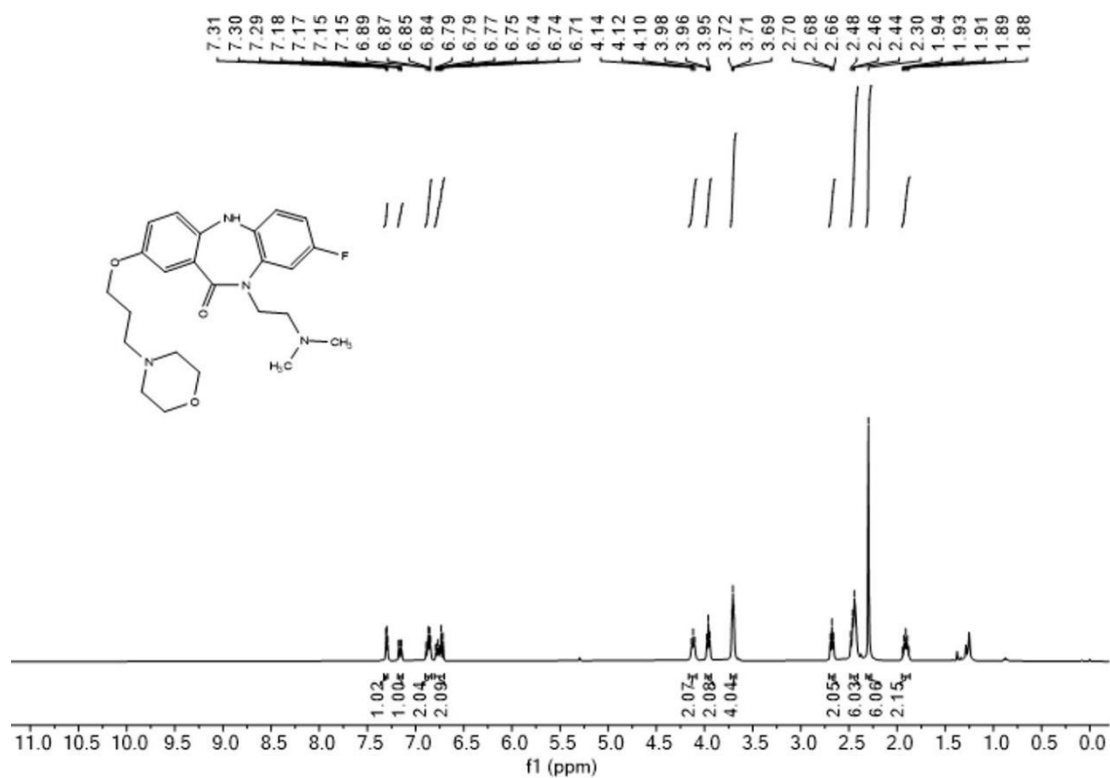


Figure S101. ¹H NMR (400 MHz, CDCl₃) spectrum of compound **31**.

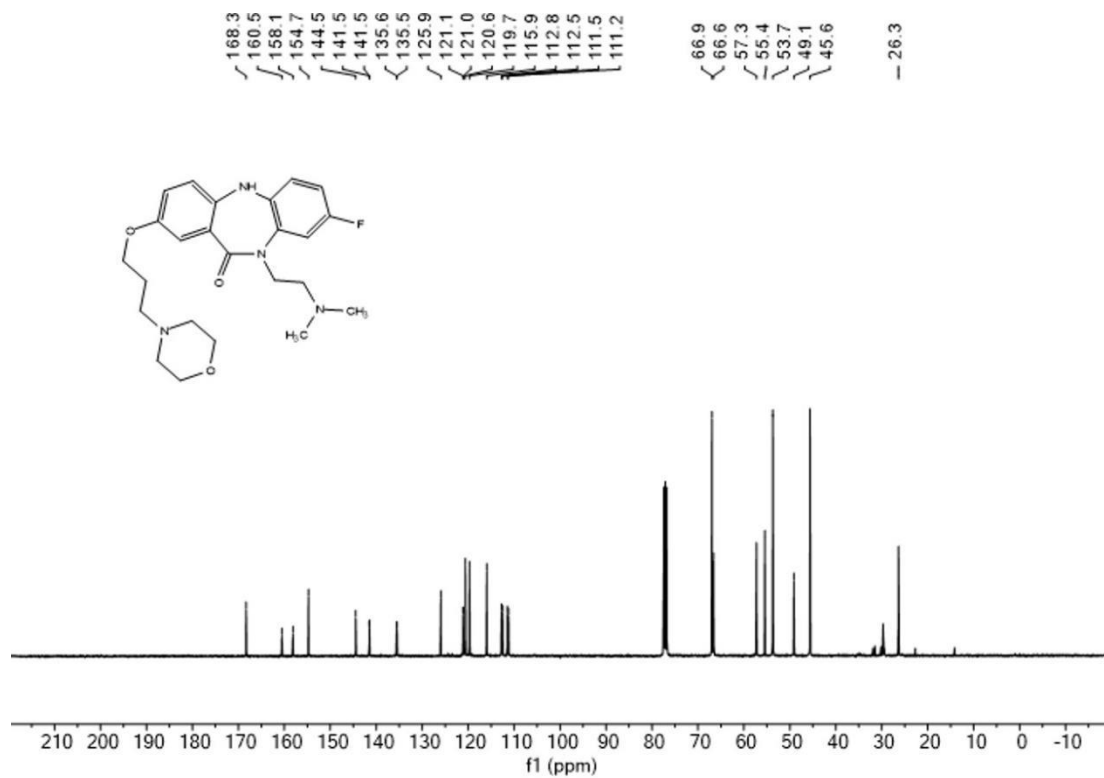


Figure S102. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound **31**.

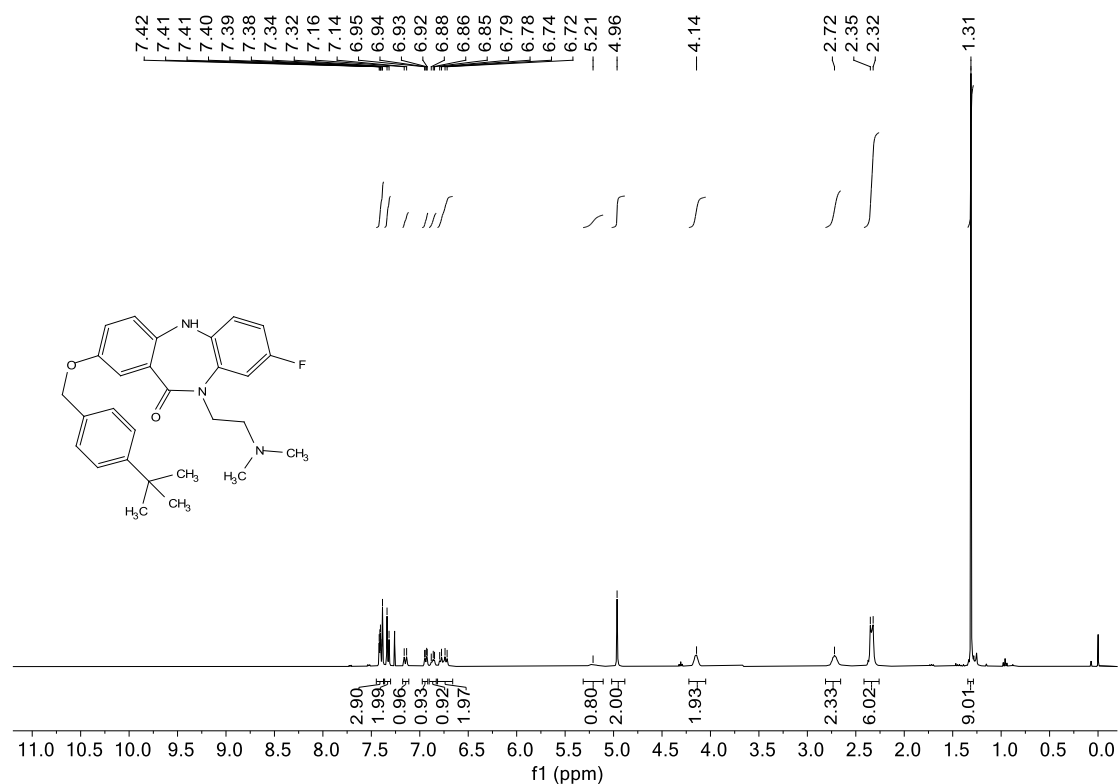


Figure S103. ¹H NMR (400 MHz, CDCl₃) spectrum of compound **32**.

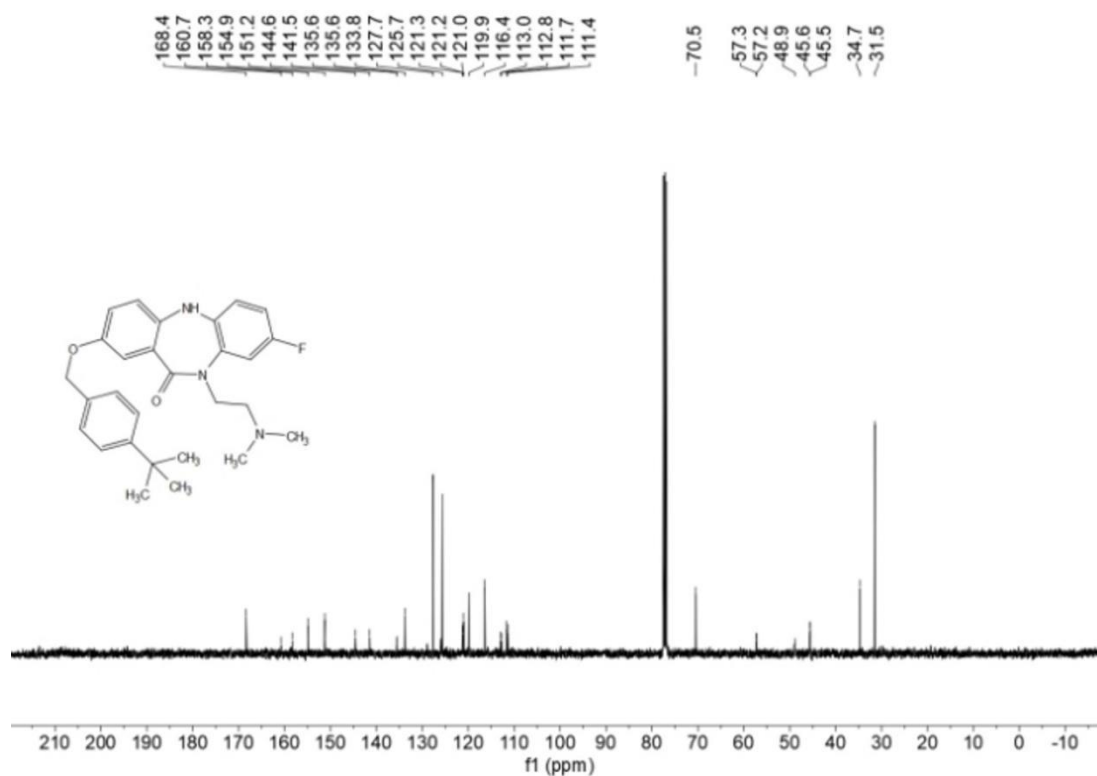


Figure S104. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound **32**.

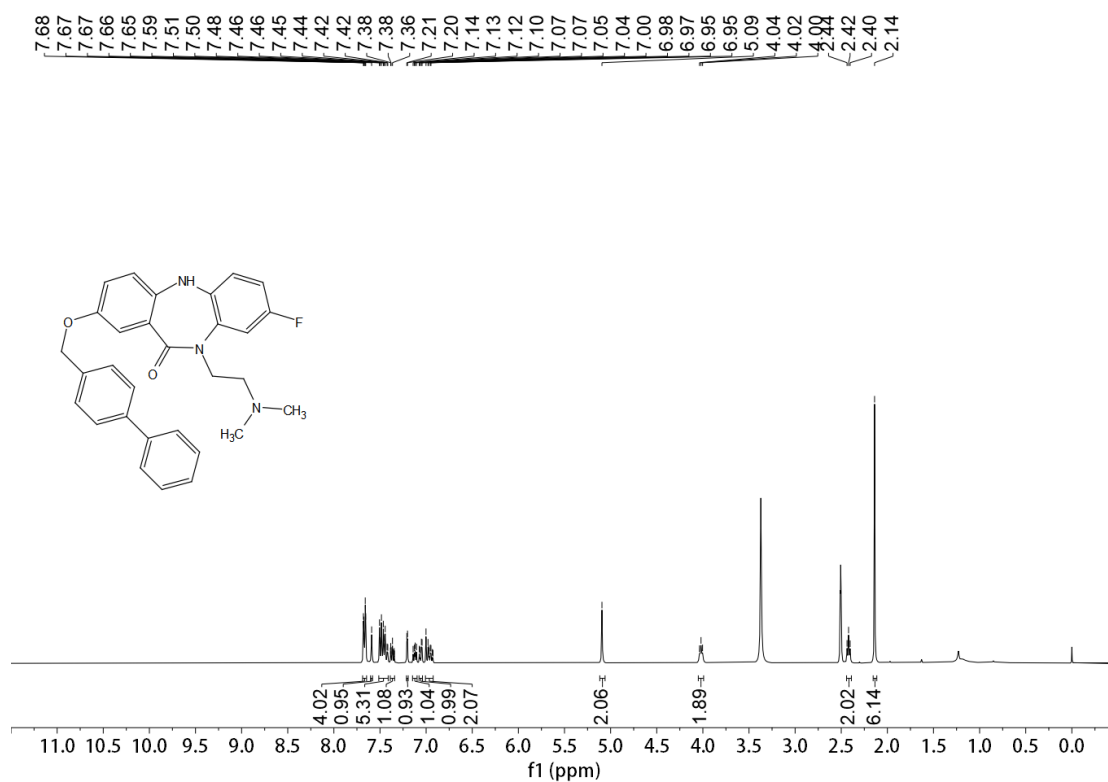


Figure S105. ¹H NMR (400 MHz, DMSO-*d*₆) spectrum of compound 33.

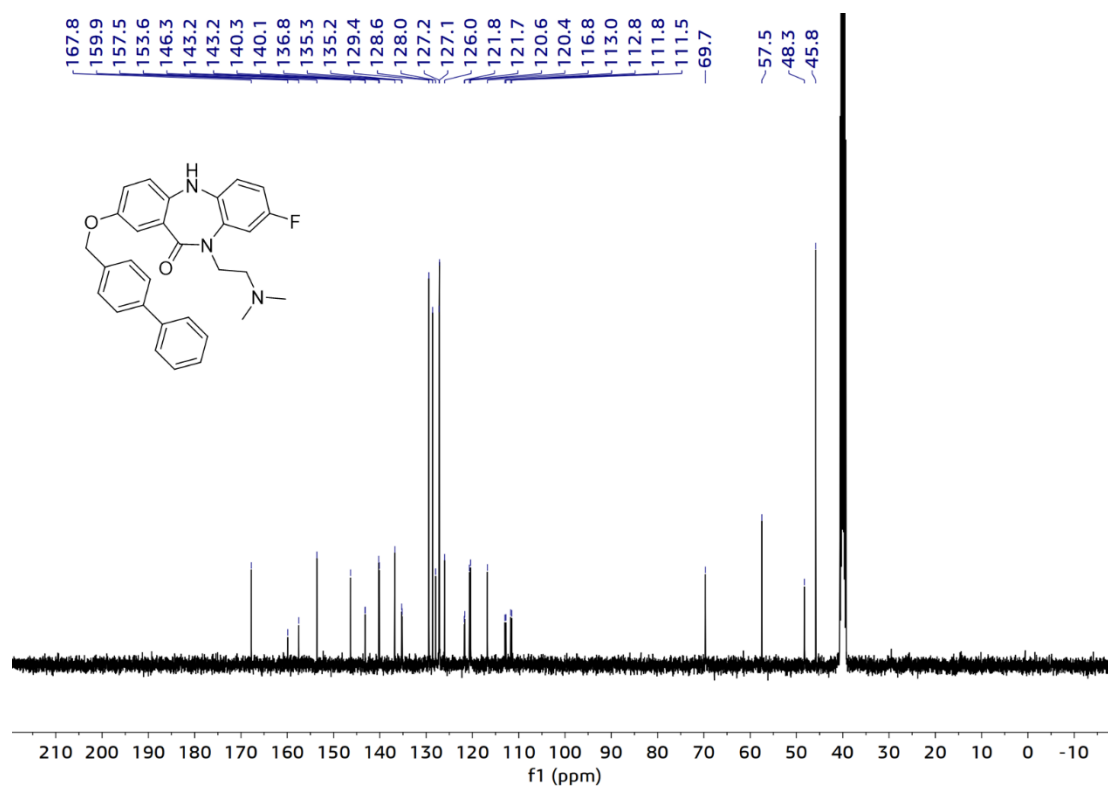


Figure S106. ¹³C NMR (101 MHz, DMSO-*d*₆) spectrum of compound 33.

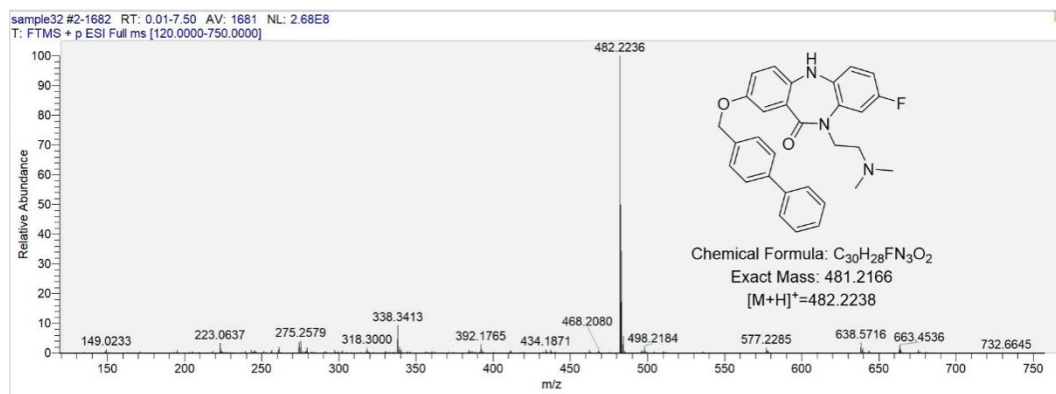


Figure S107. ESI-TOF mass spectrum of compound **33**.

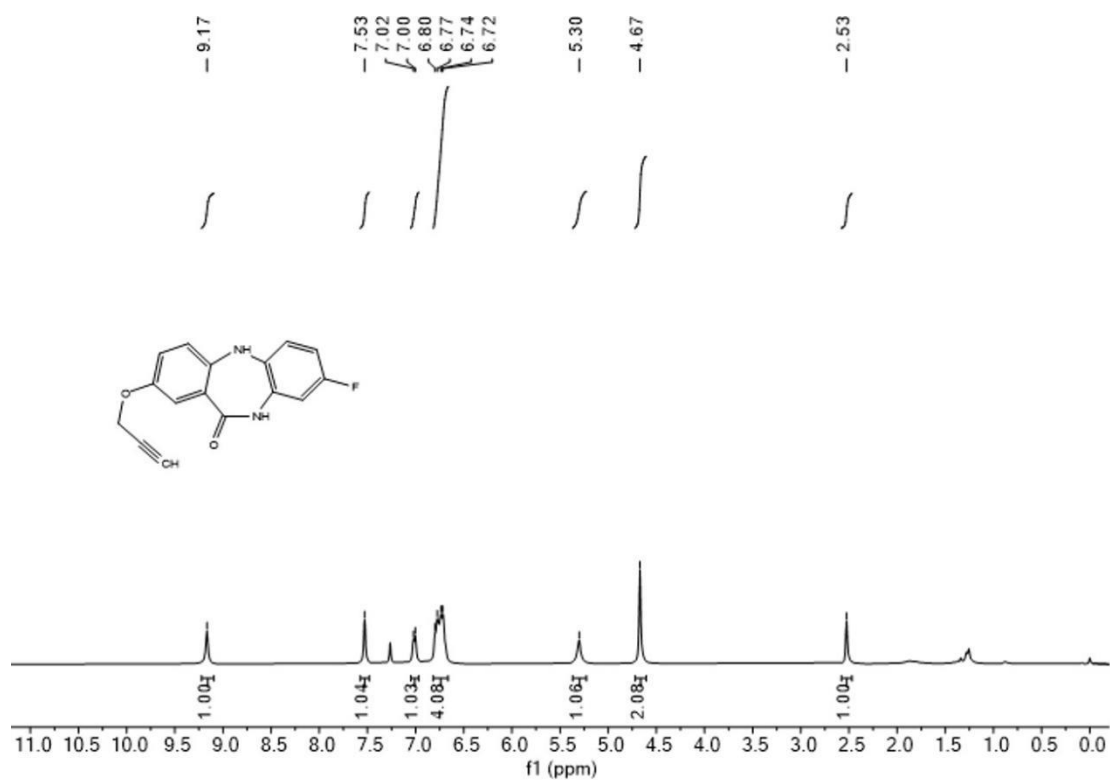


Figure S108. 1H NMR (400 MHz, $CDCl_3$) spectrum of compound **S23**.

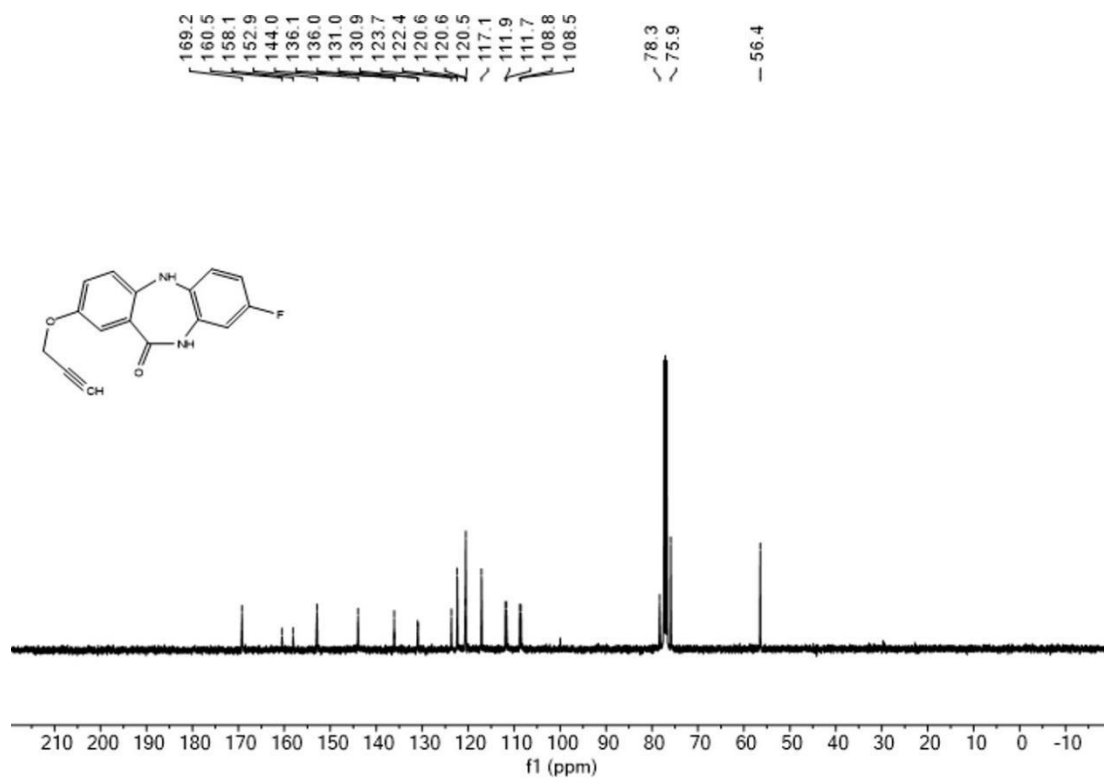


Figure S109. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound S23.

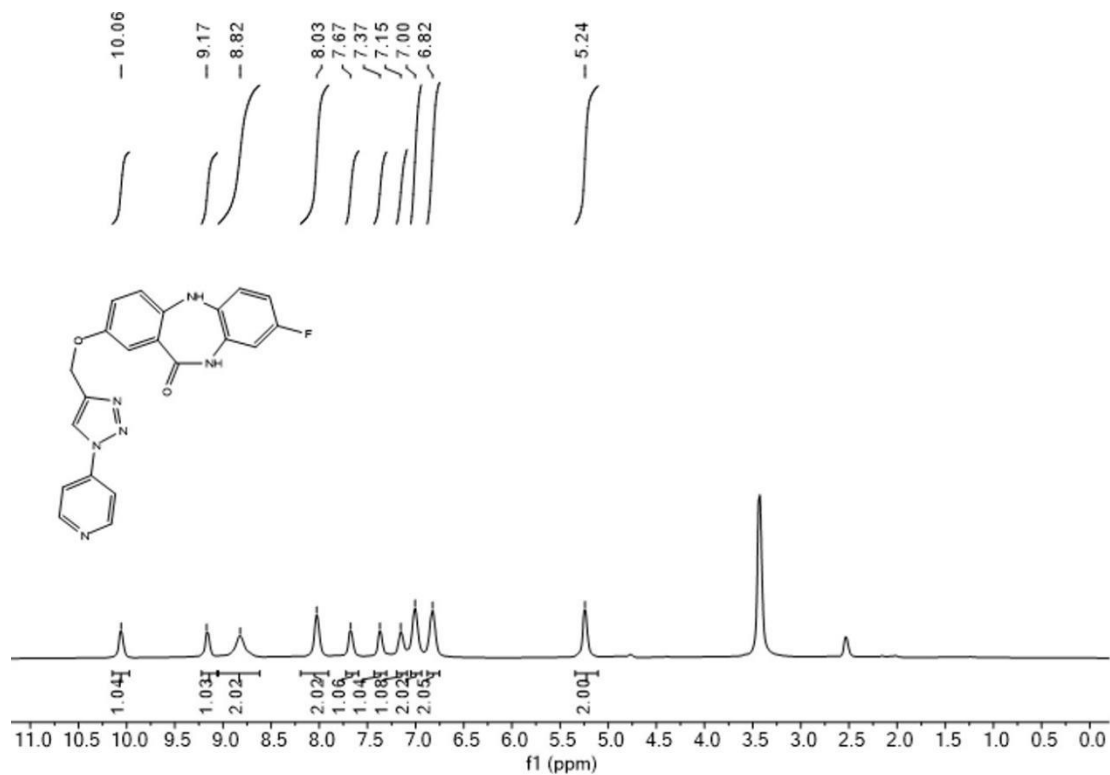


Figure S110. ¹H NMR (400 MHz, DMSO-*d*₆) spectrum of compound S24.

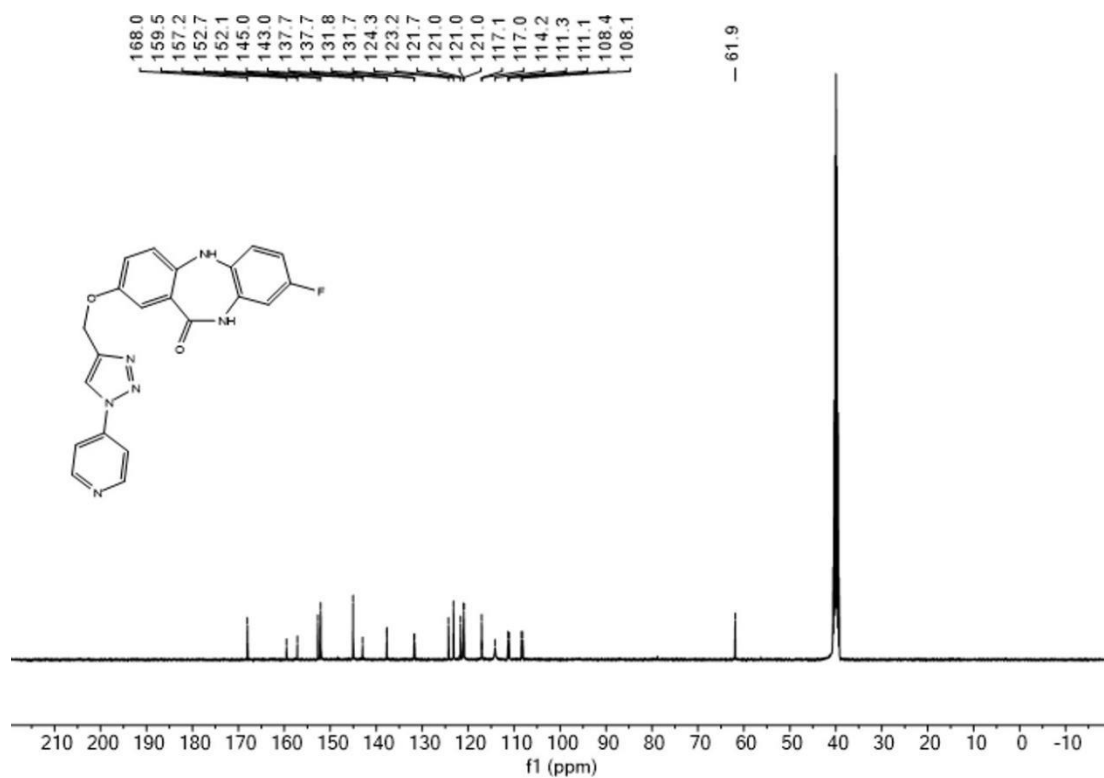


Figure S111. ¹³C NMR (101 MHz, DMSO-*d*₆) spectrum of compound S24.

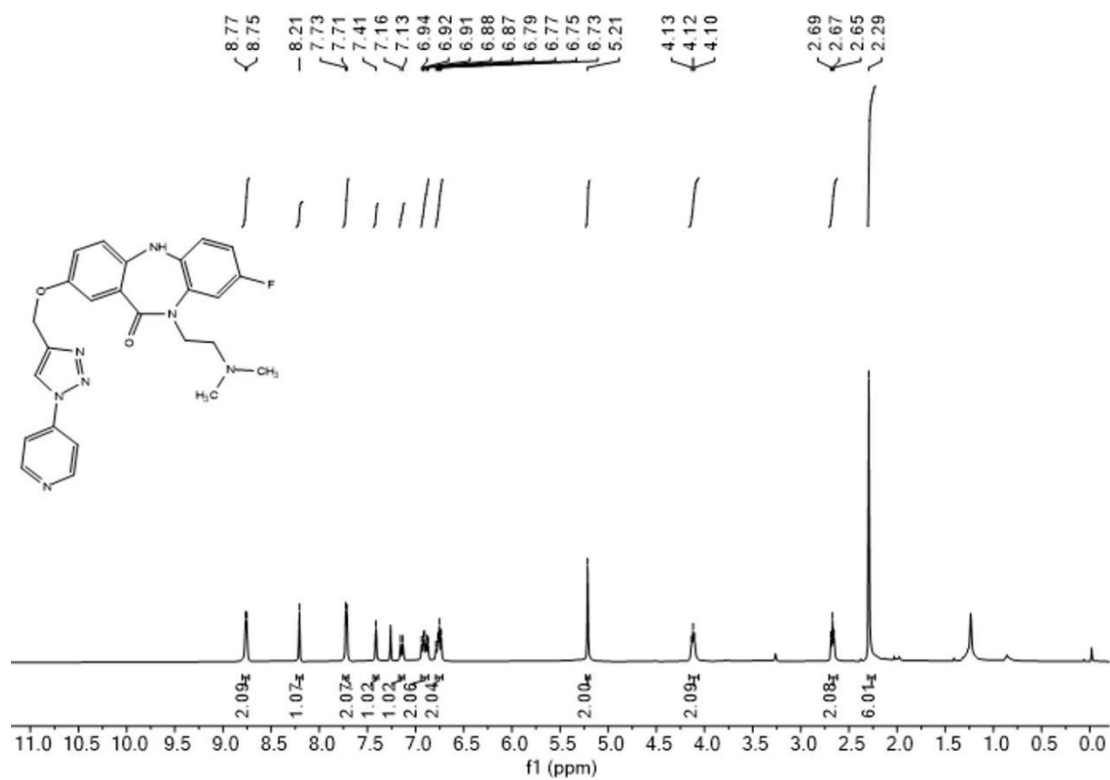


Figure S112. ¹H NMR (400 MHz, CDCl₃) spectrum of compound 34.

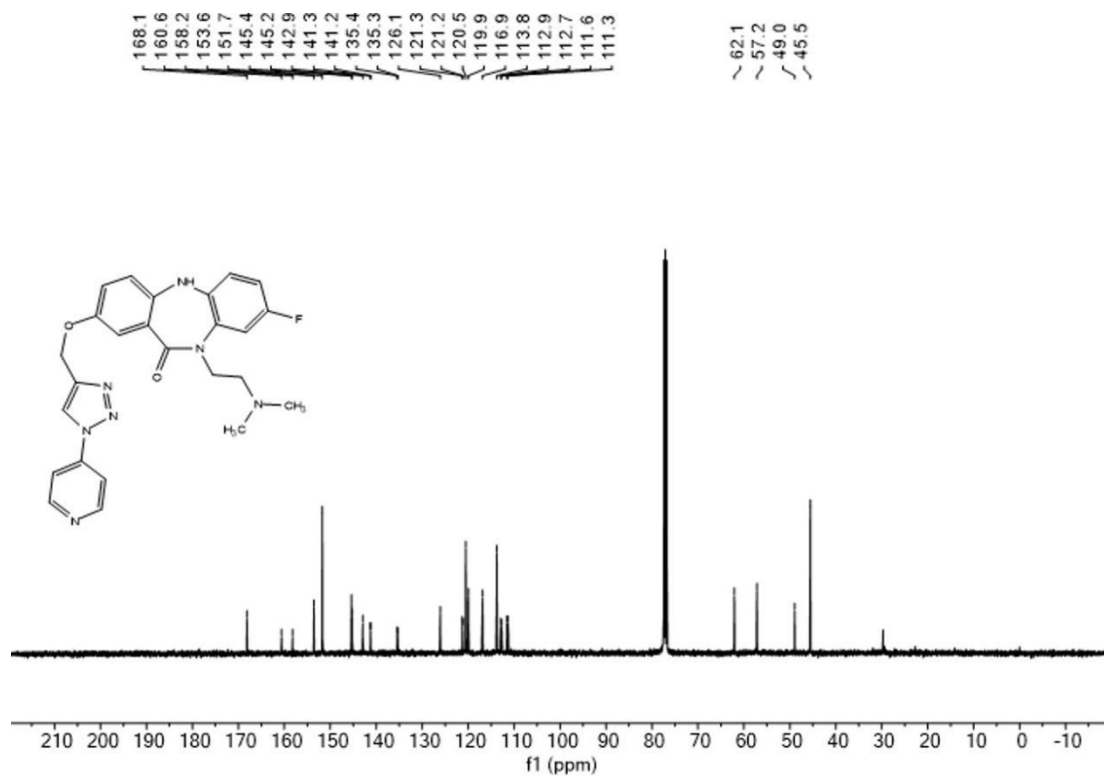


Figure S113. ^{13}C NMR (101 MHz, CDCl_3) spectrum of compound **34**.

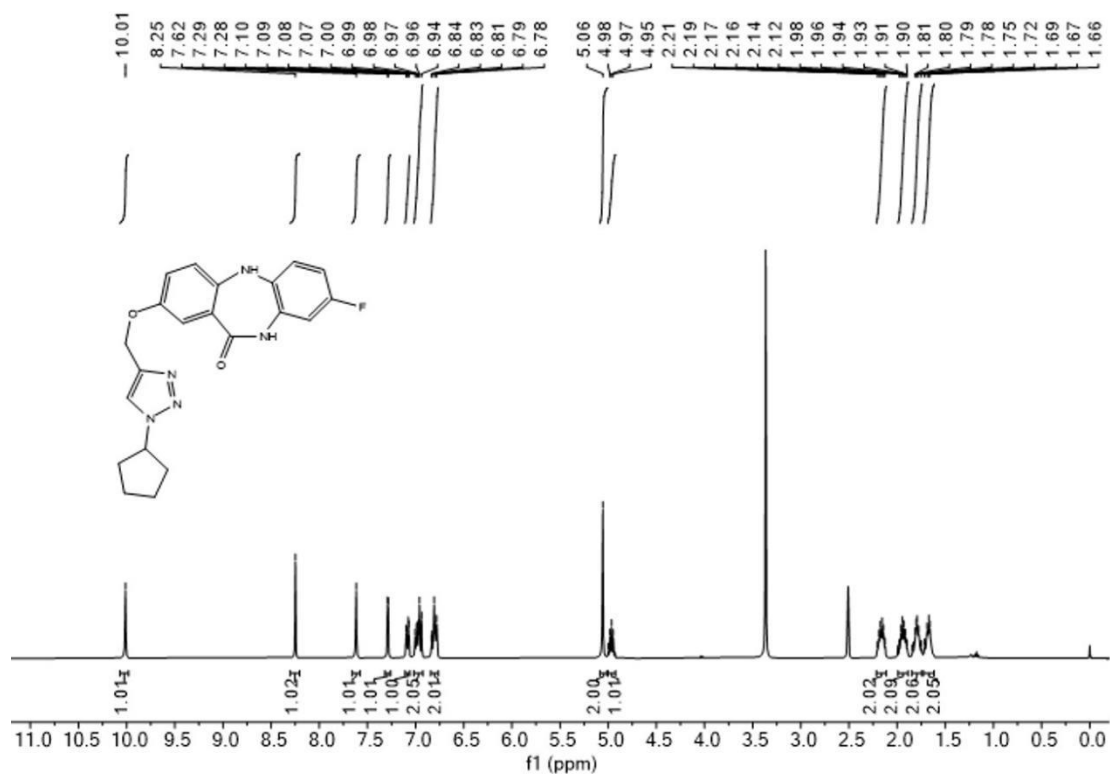


Figure S114. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) spectrum of compound **S25**.

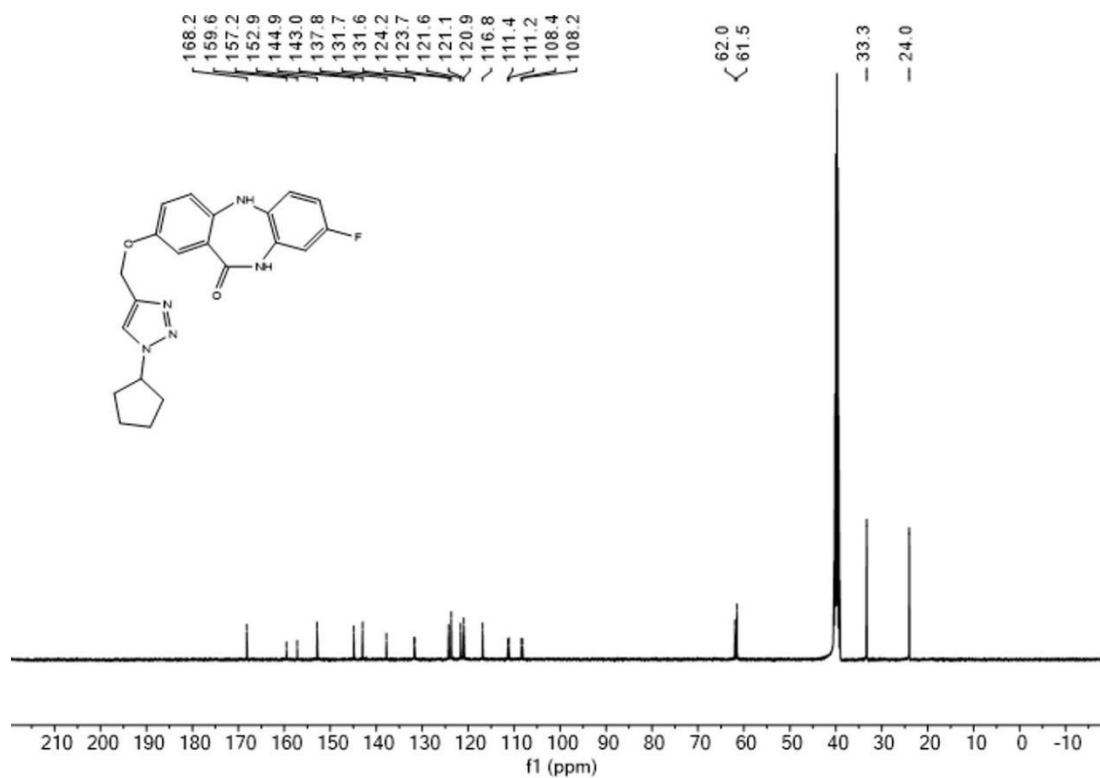


Figure S115. ¹³C NMR (101 MHz, DMSO-*d*₆) spectrum of compound **S25**.

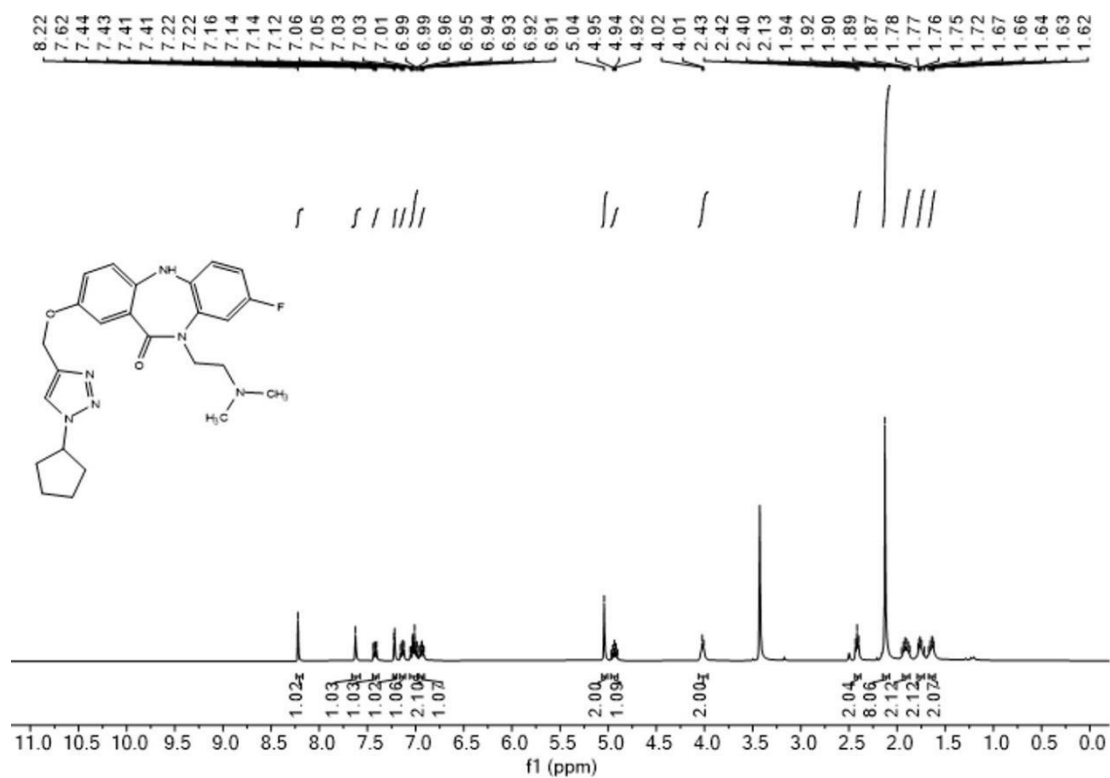


Figure S116. ¹H NMR (400 MHz, DMSO-*d*₆) spectrum of compound **35**.

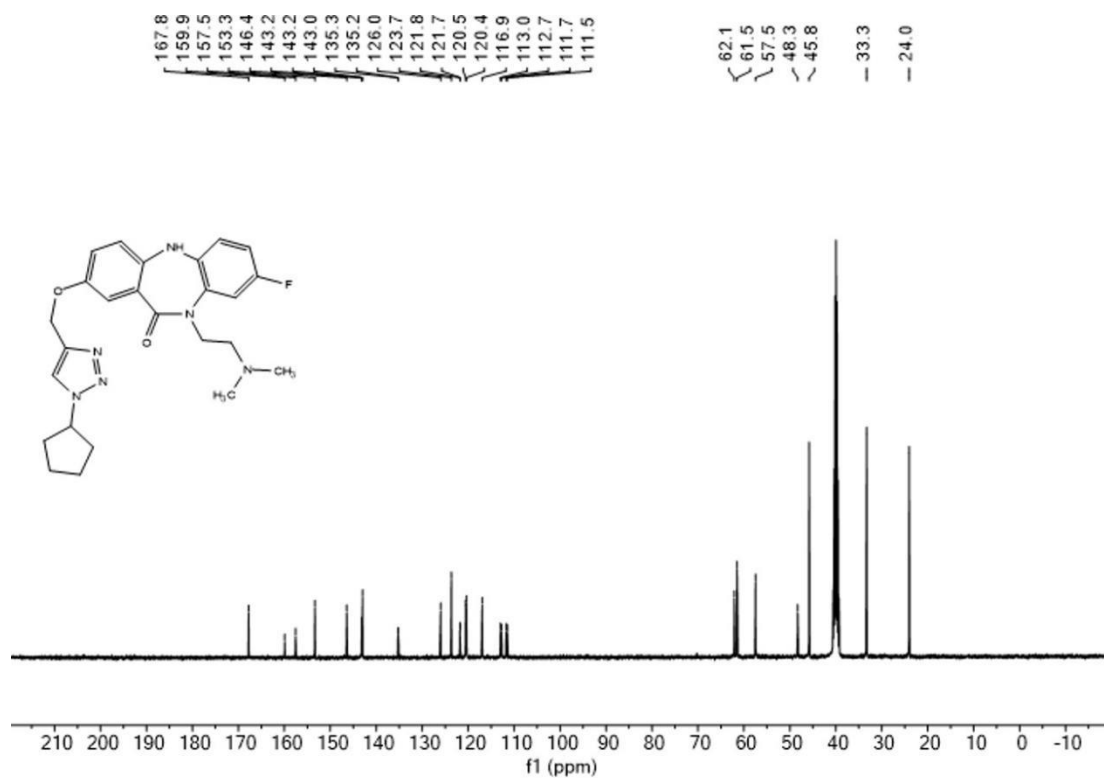


Figure S117. ¹³C NMR (101 MHz, DMSO-*d*₆) spectrum of compound **35**.

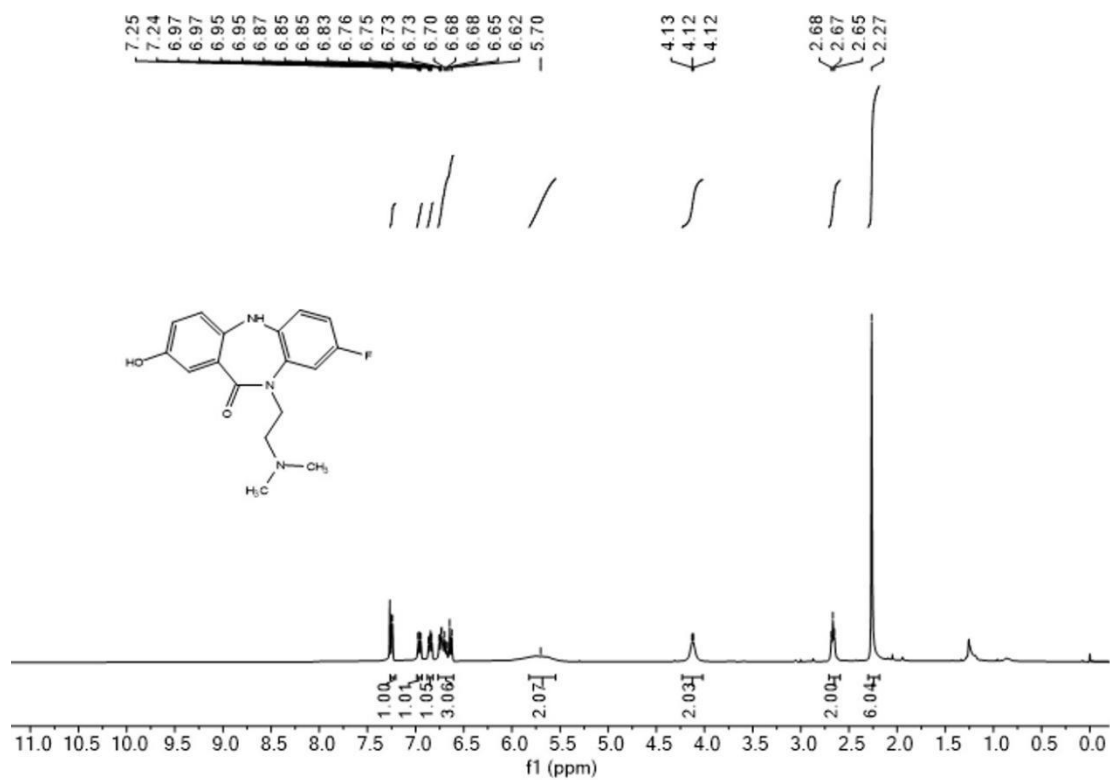


Figure S118. ¹H NMR (400 MHz, CDCl₃) spectrum of compound **S26**.

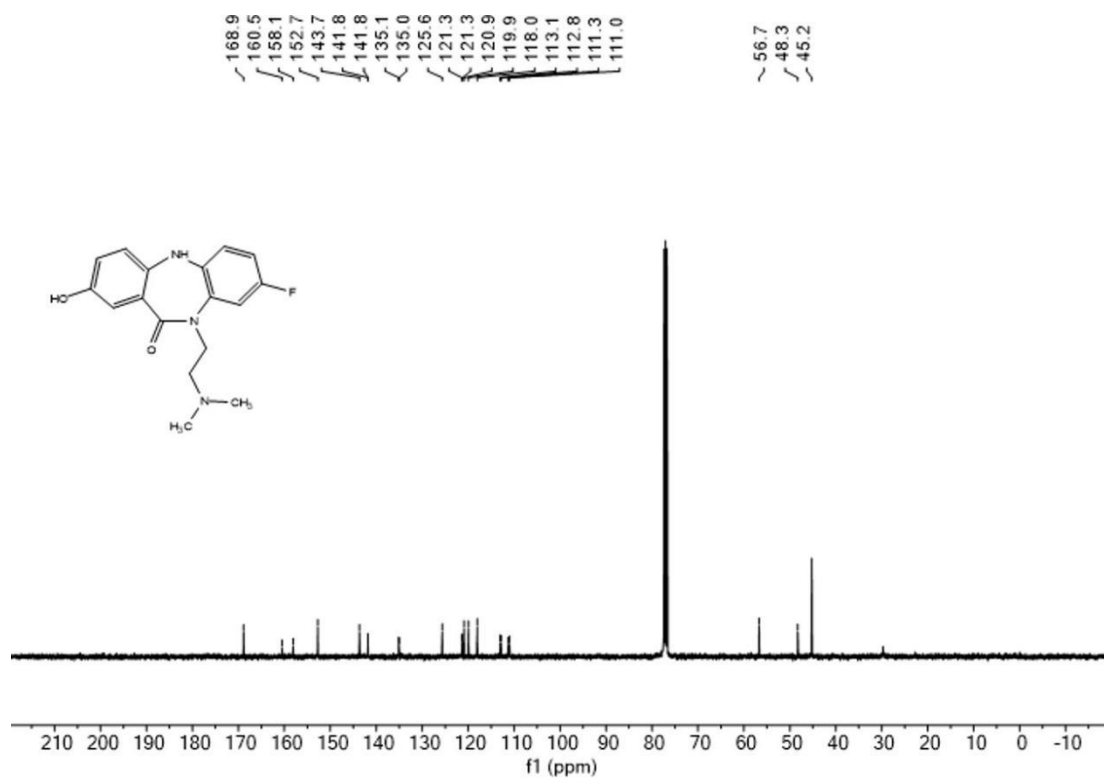


Figure S119. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound S26.

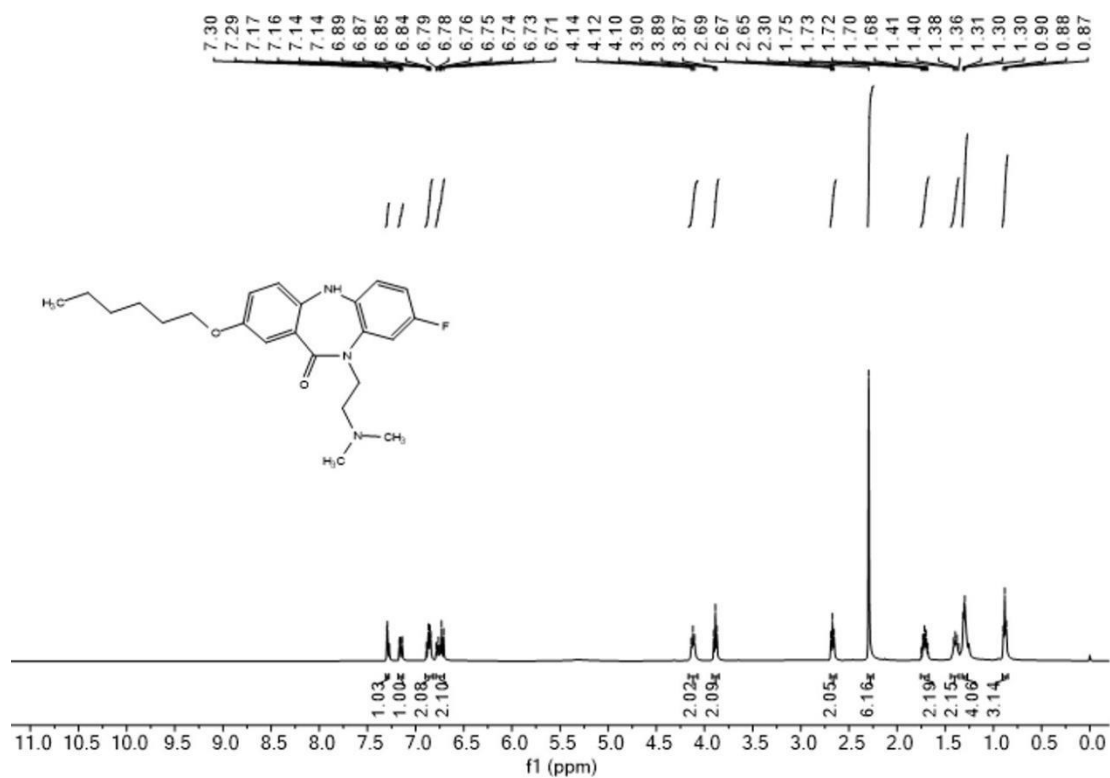


Figure S120. ¹H NMR (400 MHz, CDCl₃) spectrum of compound 36.

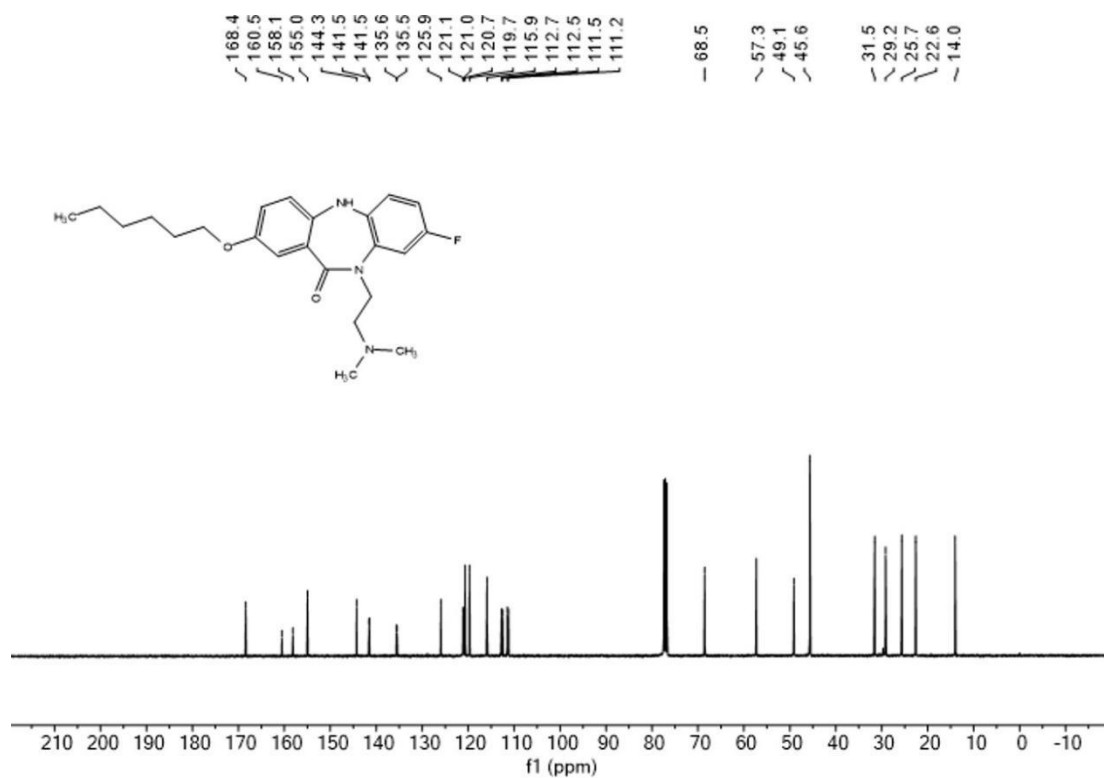


Figure S121. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound **36**.

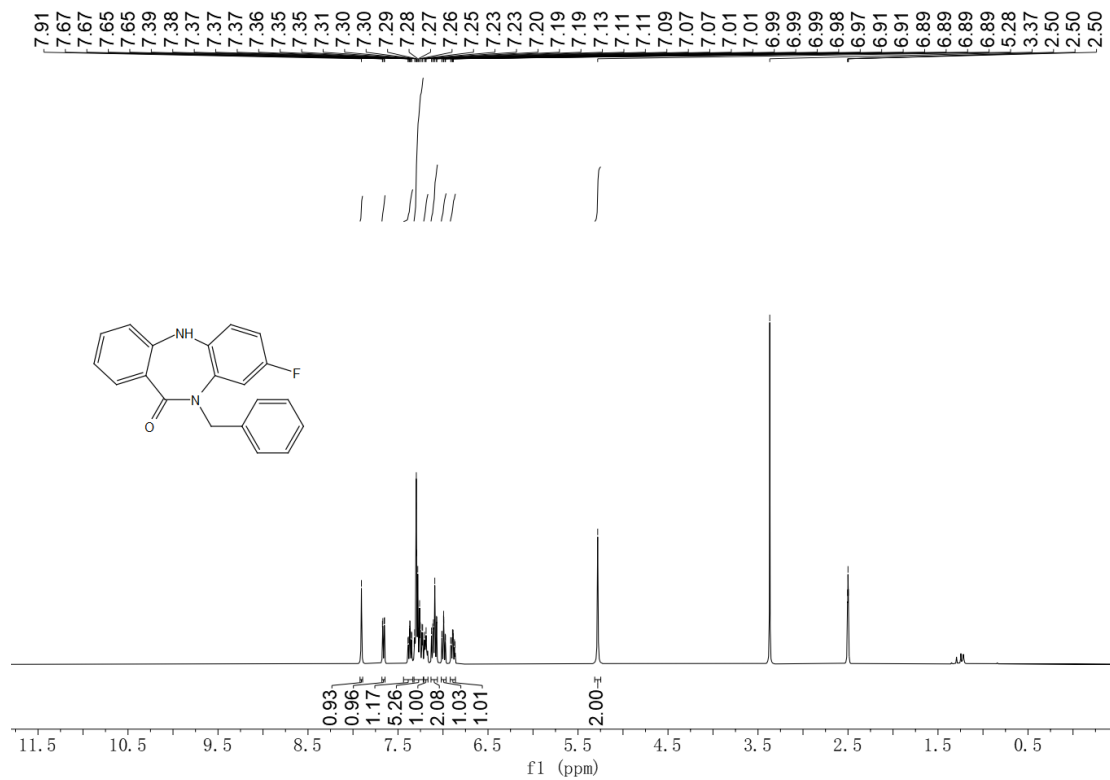


Figure S122. ¹H NMR (400 MHz, DMSO-*d*₆) spectrum of compound **DDC4002**.

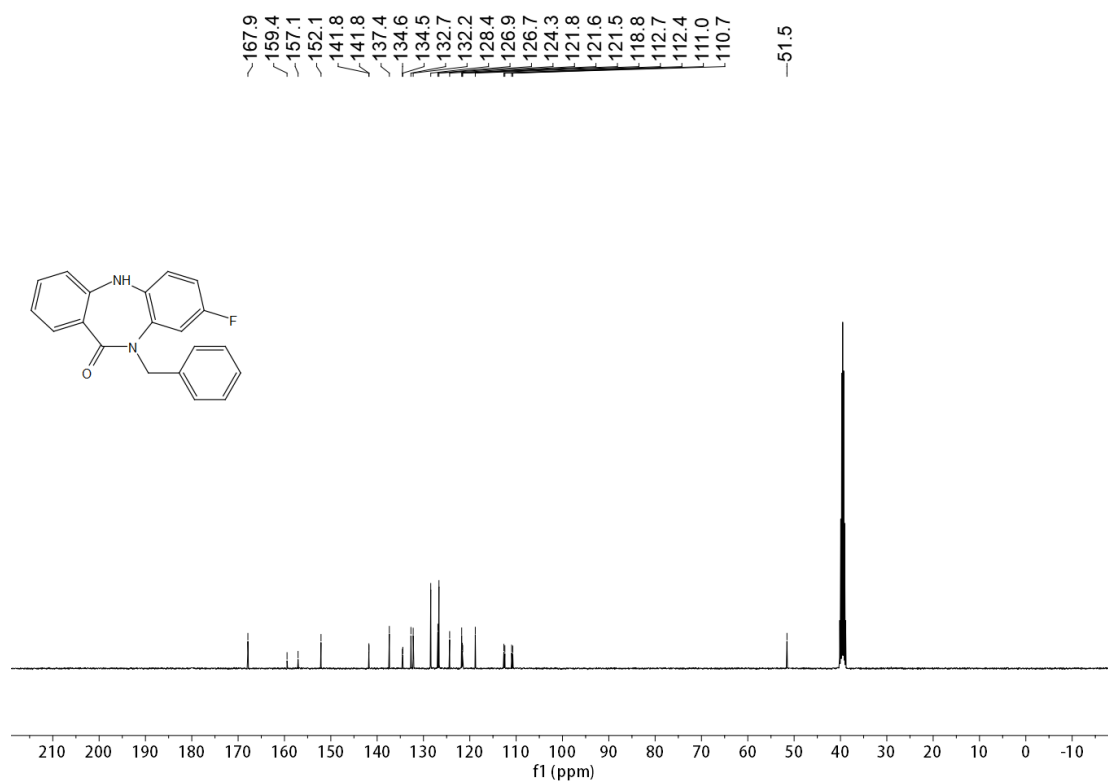


Figure **S123**. ¹³C NMR (101 MHz, DMSO-*d*₆) spectrum of compound **DDC4002**.

2. HPLC chromatogram of the compound 33.

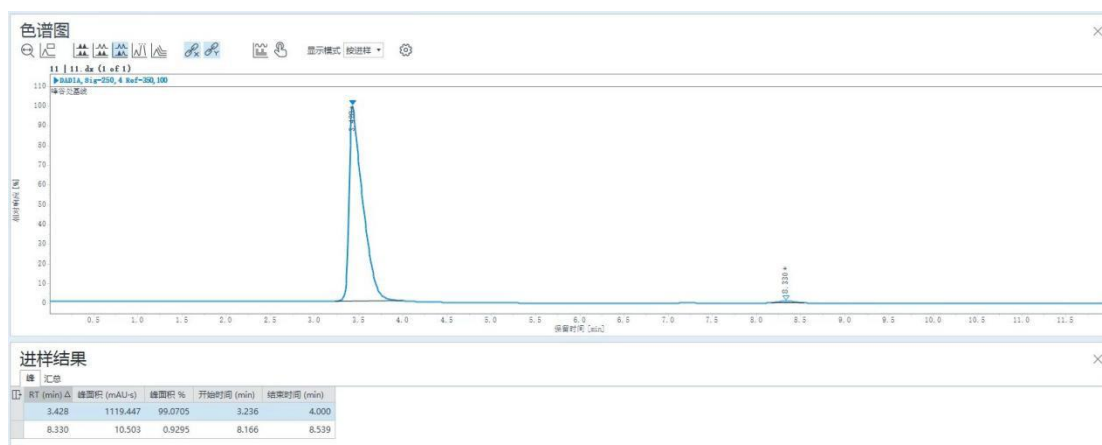
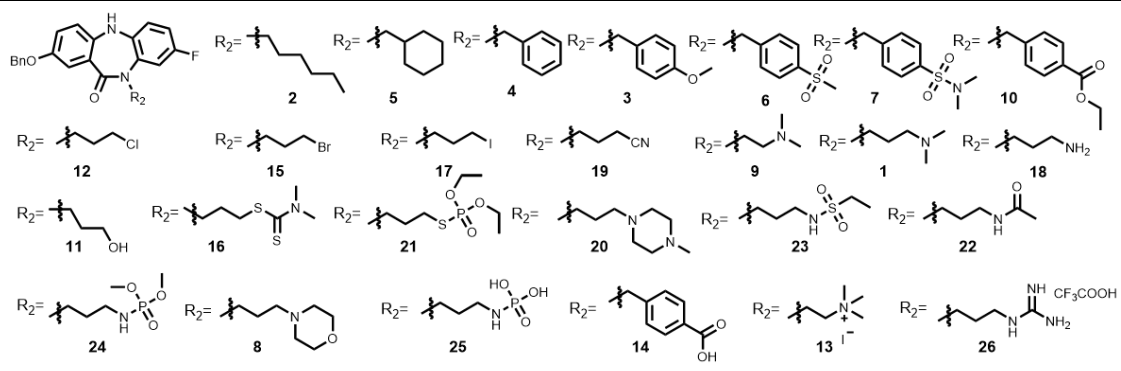


Figure S124. HPLC chromatogram of the compound **33** (mobile phase, MeOH : water = 90 :10; flow rate, 1 mL/min; detection wavelength, 250 nm).

3. Inhibitory activities (%) of target compounds against NSCLC cells.

Table S1. Inhibitory activities (%) of compounds **1-26** against NSCLC cells.

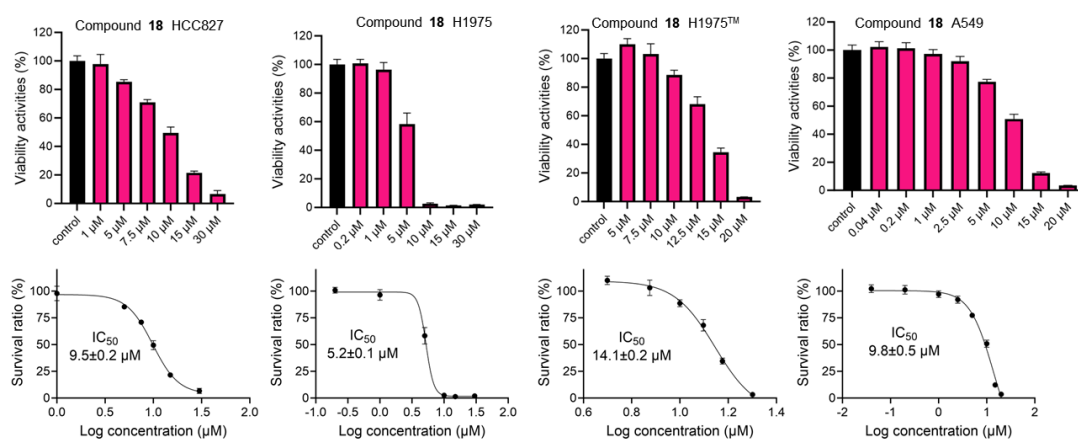
									
Entry	Compound	HCC827 (48 h)		H1975 (48 h)		H1975 TM (72 h)		A549 (48 h)	
		10 μ M	1 μ M	10 μ M	1 μ M	10 μ M	1 μ M	30 μ M	10 μ M
1	2	NA	NA	8.1 $\pm$ 4.2	NA	NA	NA	16.6 $\pm$ 1.7	12.9 $\pm$ 1.9
2	5	65.3 $\pm$ 2.0	50.2 $\pm$ 1.7	40.2 $\pm$ 9.7	30.7 $\pm$ 6.7	17.9 $\pm$ 4.7	NA	17.8 $\pm$ 3.9	10.9 $\pm$ 2.1
3	4	47.3 $\pm$ 4.0	26.8 $\pm$ 3.4	58.1 $\pm$ 3.2	27.8 $\pm$ 2.7	30.6 $\pm$ 3.3	5.4 $\pm$ 5.6	25.3 $\pm$ 3.1	22.6 $\pm$ 1.0
4	3	NA	NA	51.7 $\pm$ 2.0	22.2 $\pm$ 4.6	13.0 $\pm$ 9.0	NA	6.9 $\pm$ 3.9	2.8 $\pm$ 3.3
5	6	18.4 $\pm$ 1.7	NA	NA	NA	NA	NA	17.3 $\pm$ 0.4	15.1 $\pm$ 1
6	7	NA	NA	NA	NA	8.6 $\pm$ 2.7	5.5 $\pm$ 2.1	9.2 $\pm$ 0.9	3.4 $\pm$ 2.2
7	10	NA	NA	NA	NA	NA	NA	8.9 $\pm$ 2.4	7.2 $\pm$ 1.9
8	12	65.1 $\pm$ 0.6	7.8 $\pm$ 9.9	55.5 $\pm$ 5.3	18.5 $\pm$ 9.4	NA	NA	32.4 $\pm$ 3.6	8.0 $\pm$ 2.4
9	15	NA	NA	NA	NA	NA	NA	25.1 $\pm$ 1.9	11.2 $\pm$ 1.2
10	17	42.2 $\pm$ 2.6	14.0 $\pm$ 12.5	12.6 $\pm$ 2.8	NA	6.2 $\pm$ 3.3	NA	33.4 $\pm$ 0.8	17.2 $\pm$ 1.5
11	19	NA	NA	50.4 $\pm$ 2.1	18.6 $\pm$ 5.9	NA	NA	33.4 $\pm$ 1.2	4.9 $\pm$ 1
12	9	52.8 $\pm$ 4.9	6.4 $\pm$ 2.2	56.7 $\pm$ 3	28.3 $\pm$ 2.1	NA	NA	45.3 $\pm$ 3.3	23 $\pm$ 0.9
13	1	49.1 $\pm$ 4	31.8 $\pm$ 6.6	23.6 $\pm$ 2.9	NA	NA	NA	38.6 $\pm$ 2.8	17.7 $\pm$ 1.1
14	18	72.5 $\pm$ 3.2	33.8 $\pm$ 7.7	97.9 $\pm$ 0.2	3.6 $\pm$ 4	51.2 $\pm$ 1.2	NA	97.7 $\pm$ 0.1	54.0 $\pm$ 1.8
15	11	18.9 $\pm$ 3.5	NA	49 $\pm$ 2.3	18.2 $\pm$ 2	NA	NA	25.0 $\pm$ 3.4	14.4 $\pm$ 1.6
16	16	NA	NA	32.0 $\pm$ 0.8	9.7 $\pm$ 3.0	NA	NA	11.0 $\pm$ 2.7	9.8 $\pm$ 2.2
17	21	20.3 $\pm$ 3.1	5.6 $\pm$ 4.6	58.0 $\pm$ 2.8	6.7 $\pm$ 3.7	NA	NA	34.4 $\pm$ 1.5	27.0 $\pm$ 2.3
18	20	30.5 $\pm$ 0.5	8.7 $\pm$ 2.0	55.5 $\pm$ 1.3	4.4 $\pm$ 2.7	19.7 $\pm$ 4.5	NA	95.5 $\pm$ 0.2	35.0 $\pm$ 1.5
19	23	NA	NA	33.2 $\pm$ 3.2	16.6 $\pm$ 0.8	NA	NA	24.6 $\pm$ 8.7	9.6 $\pm$ 0.6
20	22	NA	NA	47.7 $\pm$ 1.7	18.5 $\pm$ 3.1	22.9 $\pm$ 1.1	NA	34.5 $\pm$ 2.5	11.9 $\pm$ 2.6
21	24	NA	NA	11.7 $\pm$ 6.9	3.3 $\pm$ 2.2	3.3 $\pm$ 3.9	3.7 $\pm$ 1.3	20.8 $\pm$ 4.5	7.2 $\pm$ 2.9
22	8	NA	NA	40.4 $\pm$ 0.5	19.2 $\pm$ 0.8	NA	NA	48.8 $\pm$ 1.2	26.5 $\pm$ 1.9
23	25	67.8 $\pm$ 1.2	33.9 $\pm$ 0.7	50.3 $\pm$ 6.3	14.6 $\pm$ 4.1	12.4 $\pm$ 5.6	NA	97.9 $\pm$ 0.1	44.7 $\pm$ 1.2
24	14	66.1 $\pm$ 3.1	43.9 $\pm$ 5.0	71.7 $\pm$ 4.1	13.0 $\pm$ 4.0	NA	NA	19.8 $\pm$ 3.3	10.0 $\pm$ 3.2
25	13	11.2 $\pm$ 5.2	NA	43.6 $\pm$ 1.9	15.2 $\pm$ 3.4	NA	NA	14.2 $\pm$ 1.5	6.2 $\pm$ 1.8
26	26	9.0 $\pm$ 5.1	1.6 $\pm$ 8.5	49.7 $\pm$ 1.8	20.3 $\pm$ 3.8	NA	NA	33.7 $\pm$ 2.8	18.2 $\pm$ 0.7
27	Osimertinib	91.2 $\pm$ 1.0	66.4 $\pm$ 4.2	96.0 $\pm$ 1.1	57.9 $\pm$ 2.1	93.3 $\pm$ 1.4	NA	96.8 $\pm$ 0.2	57.2 $\pm$ 1.8

NA indicates that it does not affect cell proliferation.

Table S2. Inhibitory activities (%) of compounds **1**, **9**, **27-36** against NSCLC cells.

 1 R₁ = R₂ = 27 R₁ = H R₂ = 28 R₁ = H R₂ = 9 R₁ = R₂ = 32 R₁ = R₂ = 33 R₁ = R₂ = 34 R₁ = R₂ = 35 R₁ = R₂ = 36 R₁ = R₂ = 31 R₁ = R₂ = 29 R₁ = R₂ = 30 R₁ = R₂ =									
Entry	Compound	HCC827 (48 h)		H1975 (48 h)		H1975 TM (72 h)		A549 (48 h)	
		10 μ M	1 μ M	10 μ M	1 μ M	10 μ M	1 μ M	30 μ M	10 μ M
1	27	NA	NA	44.7 $\pm$ 4.4	25.2 $\pm$ 2.5	13.2 $\pm$ 2.5	13.2 $\pm$ 0.5	22.8 $\pm$ 5.5	9.2 $\pm$ 3.0
2	28	7.3 $\pm$ 2.9	NA	35.3 $\pm$ 1.47	22.4 $\pm$ 0.6	NA	NA	18.2 $\pm$ 3.4	8.8 $\pm$ 1.0
3	9	52.8 $\pm$ 4.9	6.4 $\pm$ 2.2	56.7 $\pm$ 3.0	28.3 $\pm$ 2.1	NA	NA	45.3 $\pm$ 3.3	23.0 $\pm$ 0.9
4	1	49.1 $\pm$ 4.0	31.8 $\pm$ 6.6	23.6 $\pm$ 2.9	NA	NA	NA	38.6 $\pm$ 2.8	17.7 $\pm$ 1.1
5	32	72.4 $\pm$ 2.8	10.6 $\pm$ 3.0	57.9 $\pm$ 3.2	37.8 $\pm$ 2.1	59 $\pm$ 4.9	24.7 $\pm$ 3.4	27.2 $\pm$ 0.9	NA
6	33	91.7 $\pm$ 0.9	30.9 $\pm$ 5.4	91.1 $\pm$ 0.4	37.0 $\pm$ 5.4	95.9 $\pm$ 0.6	23.4 $\pm$ 0.7	96.7 $\pm$ 1.0	44.8 $\pm$ 1.2
7	34	NA	NA	48.2 $\pm$ 6.0	22.7 $\pm$ 2.9	NA	NA	9.1 $\pm$ 3.5	1.6 $\pm$ 2.5
8	35	35.7 $\pm$ 8.6	3.3 $\pm$ 8.2	41.3 $\pm$ 2.9	15.1 $\pm$ 3.5	NA	NA	10.3 $\pm$ 2.9	2.3 $\pm$ 2.6
9	36	25.7 $\pm$ 1.4	NA	36.5 $\pm$ 2.2	17.7 $\pm$ 3.1	NA	NA	95.9 $\pm$ 0.3	27.8 $\pm$ 2.7
10	31	33.9 $\pm$ 5.4	NA	59.3 $\pm$ 4.2	15.0 $\pm$ 4.2	17.5 $\pm$ 5.7	16.4 $\pm$ 4.3	11.0 $\pm$ 3.1	NA
11	29	67.8 $\pm$ 1.2	33.9 $\pm$ 0.7	80.0 $\pm$ 0.8	27.2 $\pm$ 0.9	30.8 $\pm$ 6.3	17.3 $\pm$ 8.8	97.8 $\pm$ 0.1	33.3 $\pm$ 2.3
12	30	75.3 $\pm$ 0.4	50.5 $\pm$ 2.4	67.4 $\pm$ 0.4	NA	31.6 $\pm$ 9.6	7.2 $\pm$ 6.2	97.4 $\pm$ 0.3	47.8 $\pm$ 4.1
13	Osimertinib	91.2 $\pm$ 1.0	66.4 $\pm$ 4.2	96.0 $\pm$ 1.1	57.9 $\pm$ 2.1	93.3 $\pm$ 1.4	NA	96.8 $\pm$ 0.2	57.2 $\pm$ 1.8

NA indicates that it does not affect cell proliferation.

**Figure S125.** Inhibitory activities (IC₅₀, μ M) of compound **18** against NSCLC cells.

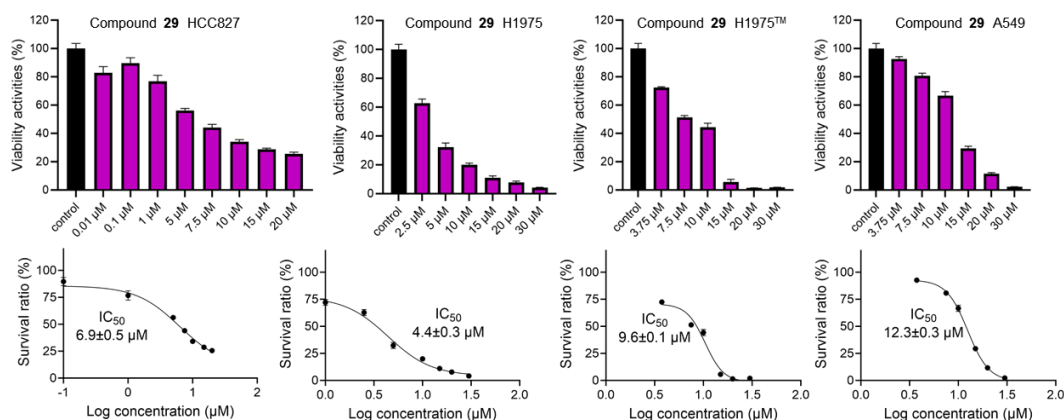


Figure S126. Inhibitory activities (IC₅₀, μM) of compound **29** against NSCLC cells.

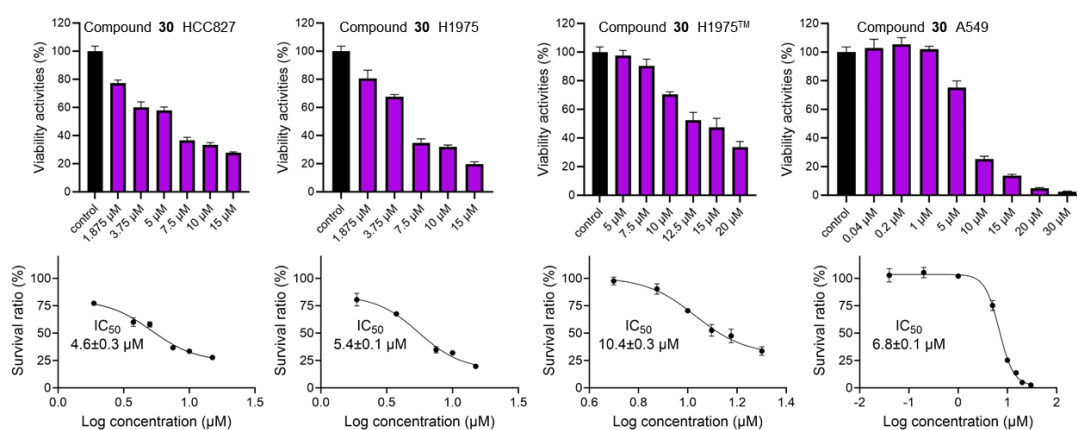


Figure S127. Inhibitory activities (IC₅₀, μM) of compound **30** against NSCLC cells.

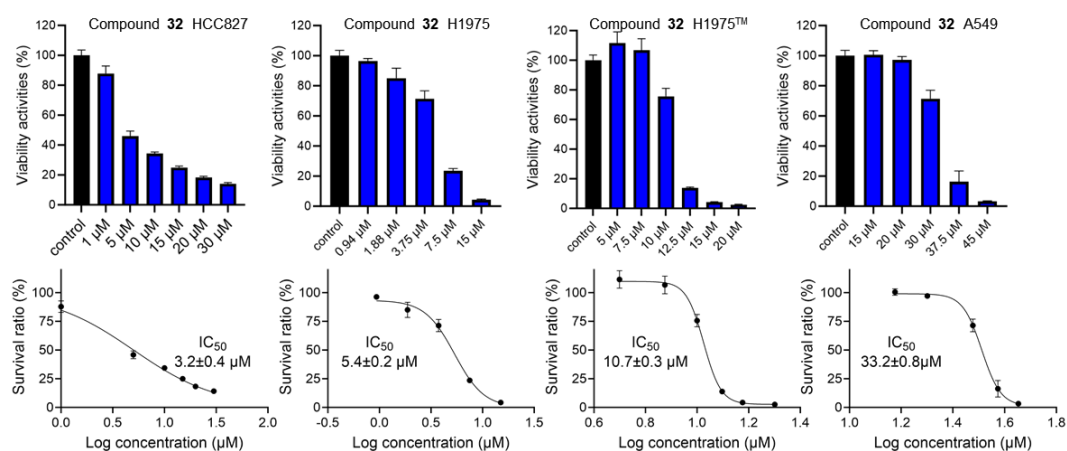


Figure S128. Inhibitory activities (IC₅₀, μM) of compound **32** against NSCLC cells.

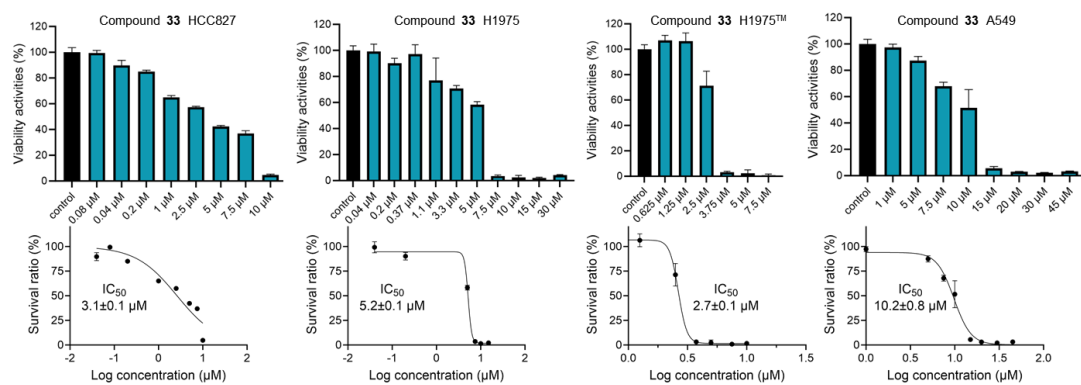


Figure S129. Inhibitory activities (IC₅₀, μM) of compound **33** against NSCLC cells.

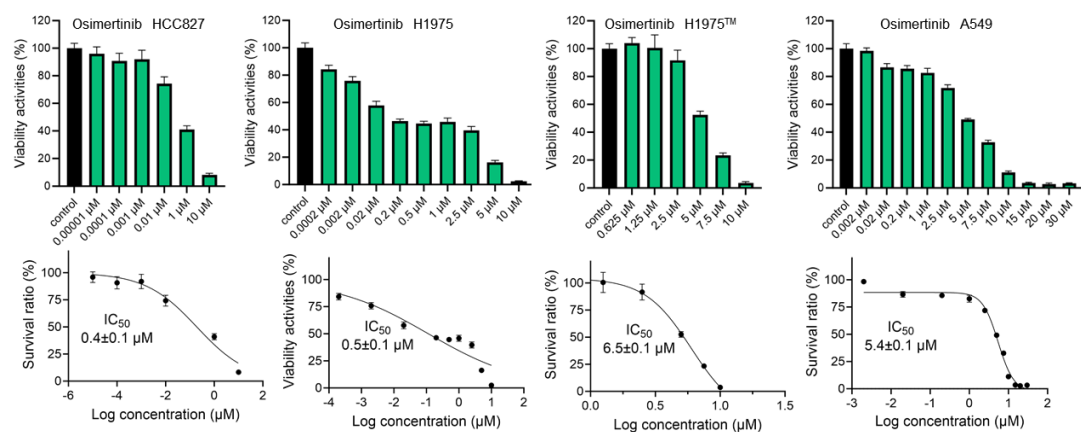


Figure S130. Inhibitory activities (IC₅₀, μM) of Osimertinib against NSCLC cells.

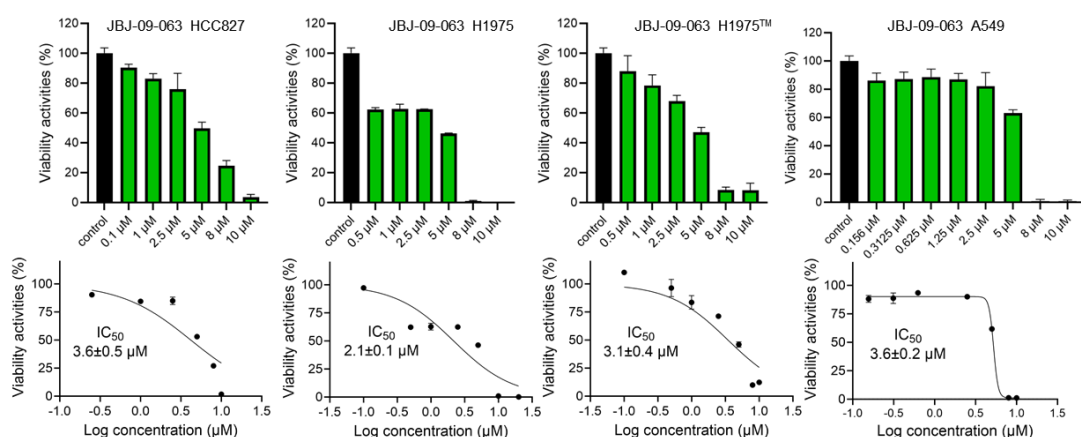


Figure S131. Inhibitory activities (IC₅₀, μM) of JBJ-09-063 against NSCLC cells.

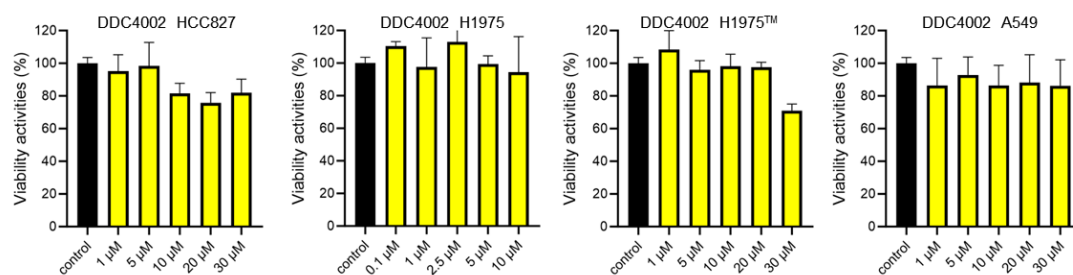
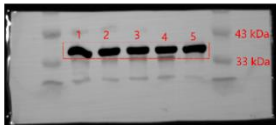
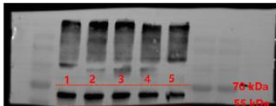
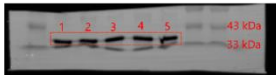
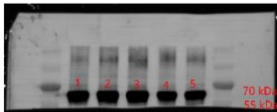
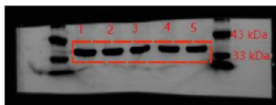
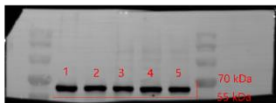
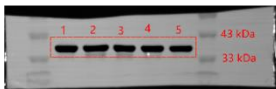
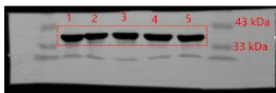


Figure S132. Inhibitory activities of DDC4002 against NSCLC cells.

4. WB's Raw Data

33				Osimertinib
1	2	3	4	5
DMSO	2 μ M	6 μ M	10 μ M	10 μ M
Figure 1a-AKT(60 kDa) -repeat 1		Figure 1a-GAPDH(36 kDa) -repeat 1		
				
Figure 1a-AKT(60 kDa) -repeat 2		Figure 1a-GAPDH(36 kDa) -repeat 2		
				
Figure 1a-AKT(60 kDa) -repeat 3		Figure 1a-GAPDH(36 kDa) -repeat 3		
				
Figure 1a-AKT(60 kDa) -repeat 4		Figure 1a-GAPDH(36 kDa) -repeat 4		
				
Figure 1a-AKT(60 kDa) -repeat 5		Figure 1a-GAPDH(36 kDa) -repeat 5		
				

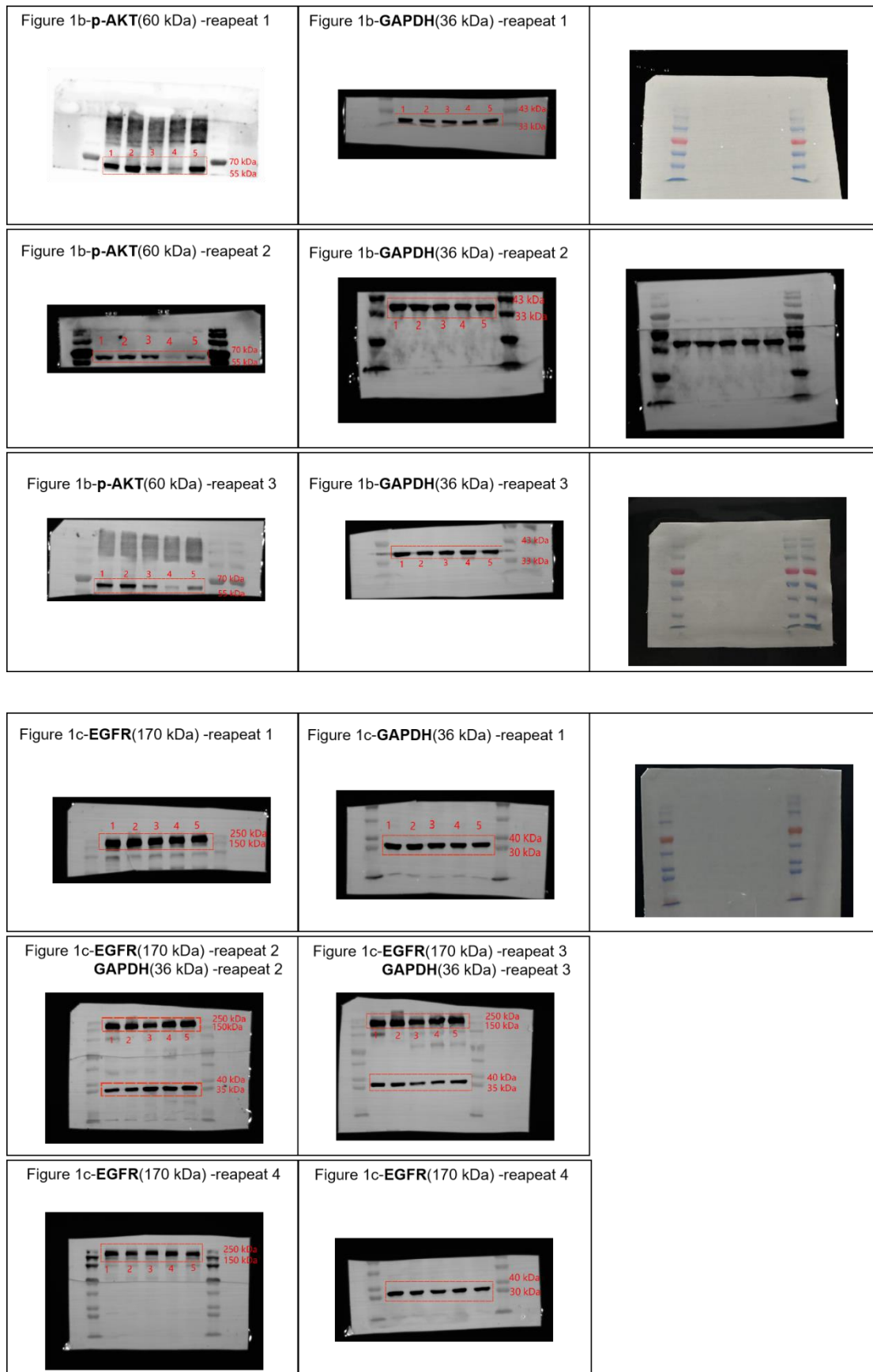


Figure 1d-**p-EGFR**(170 kDa) -repeat 1
GAPDH(36 kDa) -repeat 1

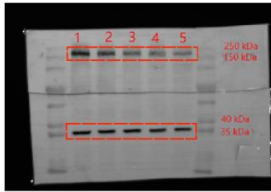


Figure 1d-**p-EGFR**(170 kDa) -repeat 1
GAPDH(36 kDa) -repeat 1

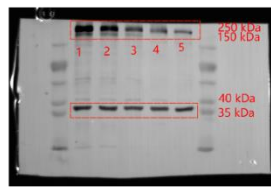


Figure 1d-**p-EGFR**(170 kDa) -repeat 3
GAPDH(36 kDa) -repeat 3

