Supplementary Materials

Design and synthesis of novel anti-proliferative emodin derivatives and studies on their cell cycle arrest, apoptosis pathway and migration

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Table S1. The apoptosis rates of HepG2 cells treated with different concentration compound **7a**.

Apoptosis stage	Apoptosis percentage (%)[a]			
	0 μM	2.5 μM	5 μM	10 μM
Early apoptosis	1.85 ± 0.13	2.91 ± 0.45	15.93 ± 0.76	37.73 ± 0.97
Late apoptosis	3.62 ± 0.07	3.69 ± 0.48	7.51 ± 0.68	14.63 ± 1.17
Overall apoptosis	5.47 ± 0.06	6.59 ± 0.93[b]	23.450 ± 1.07[c]	52.00 ± 1.41[c]

[a] Data are expressed as means ± SD of the percentages of apoptotic cells from three independent experiments.
[b] Statistical significance is determined by two-tailed Student t-test: $p < 0.01$.
[c] Statistical significance is determined by two-tailed Student t-test: $p < 0.001$.

Table S2. Western blot analysis effect of compound **7a** in HepG2 cells.

Antibody	Relative expression level[a]			
	0 μM	2.5 μM	5 μM	10 μM
Bax	1.011 ± 0.113	1.180 ± 0.046[b]	1.347 ± 0.081[c]	1.593 ± 0.112[d]
Bcl-2	1.052 ± 0.107	0.685 ± 0.025[d]	0.312 ± 0.012[d]	0.268 ± 0.022[d]
cytochrome c	1.023 ± 0.078	1.407 ± 0.015[d]	1.663 ± 0.110[d]	2.220 ± 0.387[d]
procaspase-3	1.106 ± 0.033	0.510 ± 0.132[d]	0.317 ± 0.031[d]	0.170 ± 0.053[d]
procaspase-9	1.050 ± 0.013	0.600 ± 0.082[d]	0.297 ± 0.058[d]	0.223 ± 0.029[d]
Full length procaspase-3	0.852 ± 0.019	0.78 ± 0.012[d]	0.220 ± 0.019[d]	0.152 ± 0.009[d]
Cleaved Caspase-3	0.045 ± 0.007	0.056 ± 0.011[d]	0.143 ± 0.013[d]	0.185 ± 0.026[d]

[a] Data are expressed as means ± SD of the percentages of apoptotic cells from three independent experiments.
[b] Statistical significance is determined by two-tailed Student t-test: $p < 0.05$.
[c] Statistical significance is determined by two-tailed Student t-test: $p < 0.01$.
[d] Statistical significance is determined by two-tailed Student t-test: $p < 0.001$.

Table S3. The statistical results of cell cycle distribution after treatment of compound **7a** in HepG2 cells.

Cell cycle stage	Cell cycle distribution (%)[a] in different concentrations			
	0 μM	0.25 μM	0.5 μM	1 μM
G0/G1	33.73 ± 1.93	44.18 ± 1.79[b]	56.49 ± 1.40[c]	63.96 ± 2.42[c]
S	48.10 ± 2.52	38.25 ± 1.65[b]	19.21 ± 1.33[c]	14.52 ± 1.43[c]
G2/M	18.30 ± 1.64	17.55 ± 0.90[d]	24.81 ± 1.79[d]	22.22 ± 1.16[d]

[a] Data are expressed as means ± SD of the percentages of apoptotic cells from three independent experiments.
[b] Statistical significance is determined by two-tailed Student t-test: $p < 0.05$.
[c] Statistical significance is determined by two-tailed Student t-test: $p < 0.001$.
[d] No significance.

Table S4. Compound **7a** inhibited migration of HepG2 cells.

Concentration	0 μM	0.25 μM	0.5 μM	1 μM
Inhibition (%)[a]	0	12.58 ± 1.69[b]	23.71 ± 0.59[b]	40.18 ± 2.92[b]

[a] Data are expressed as means ± SD of cell inhibitory rate (%) for the migration of HepG2 cells from three independent experiments.
[b] Statistical significance is determined by two-tailed Student t-test: $p < 0.001$.

NMR Spectra

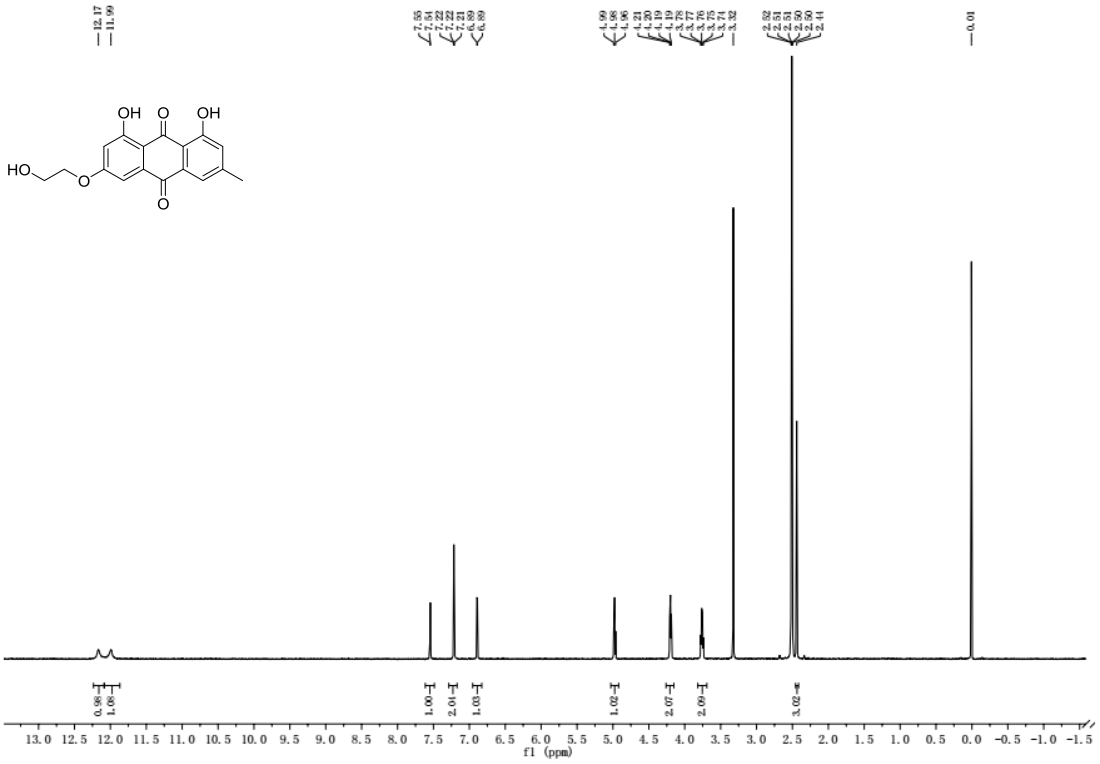

Figure S1. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **2**.

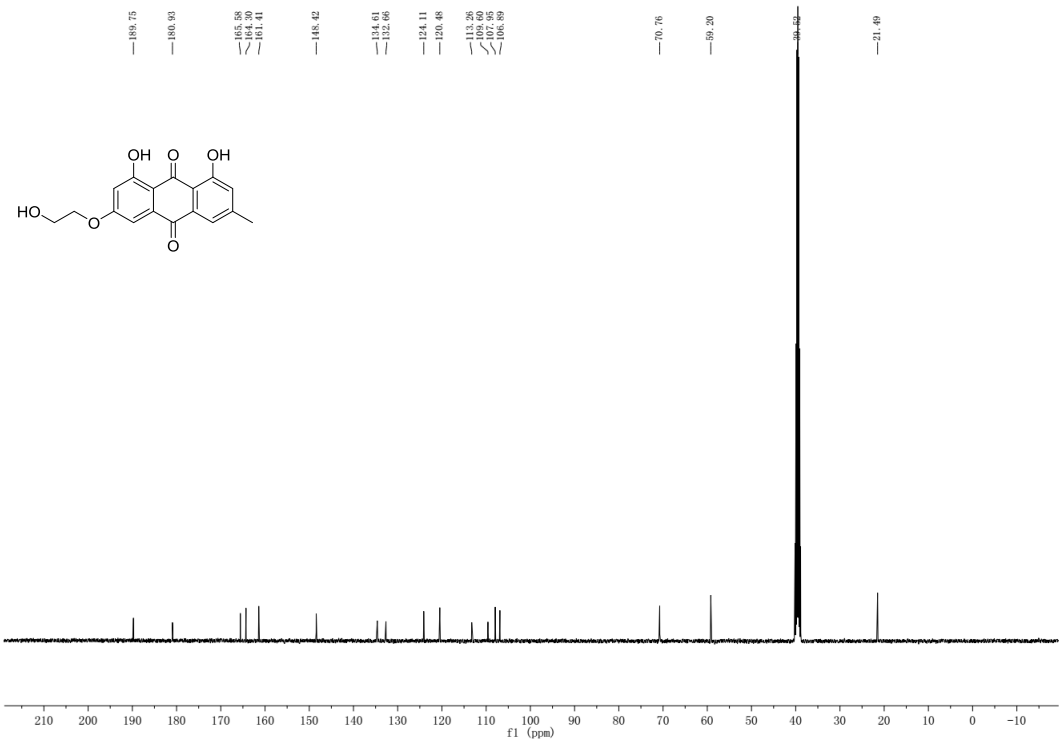

Figure S2. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **2**.

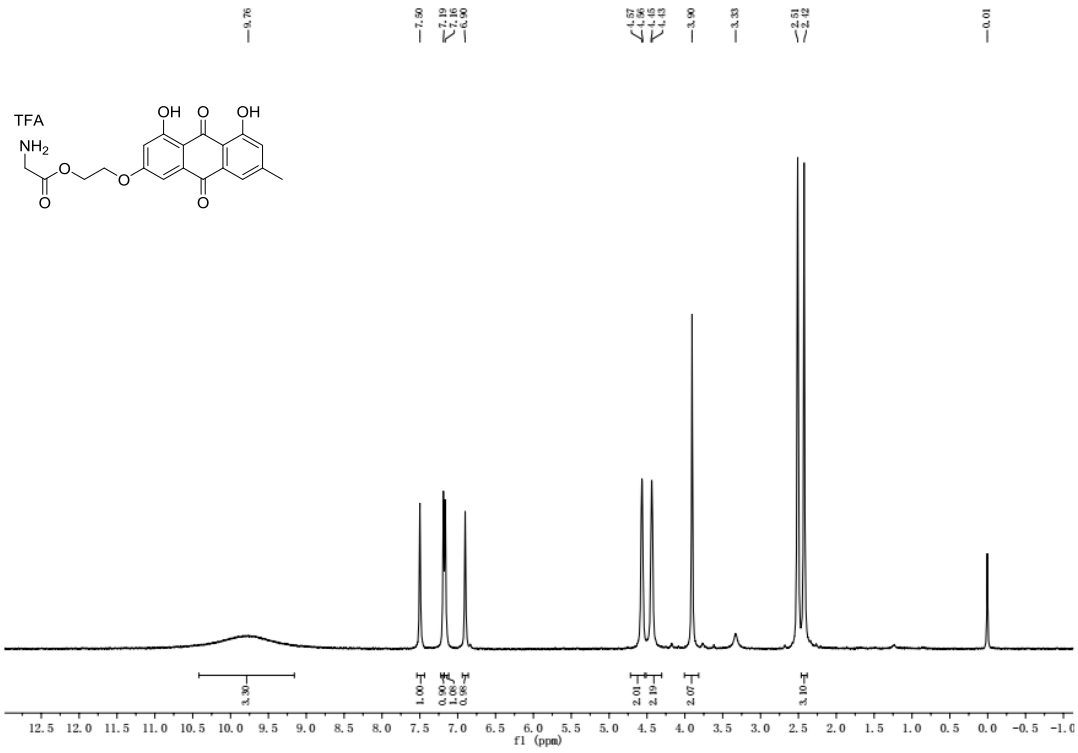

Figure S3. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **3a**.

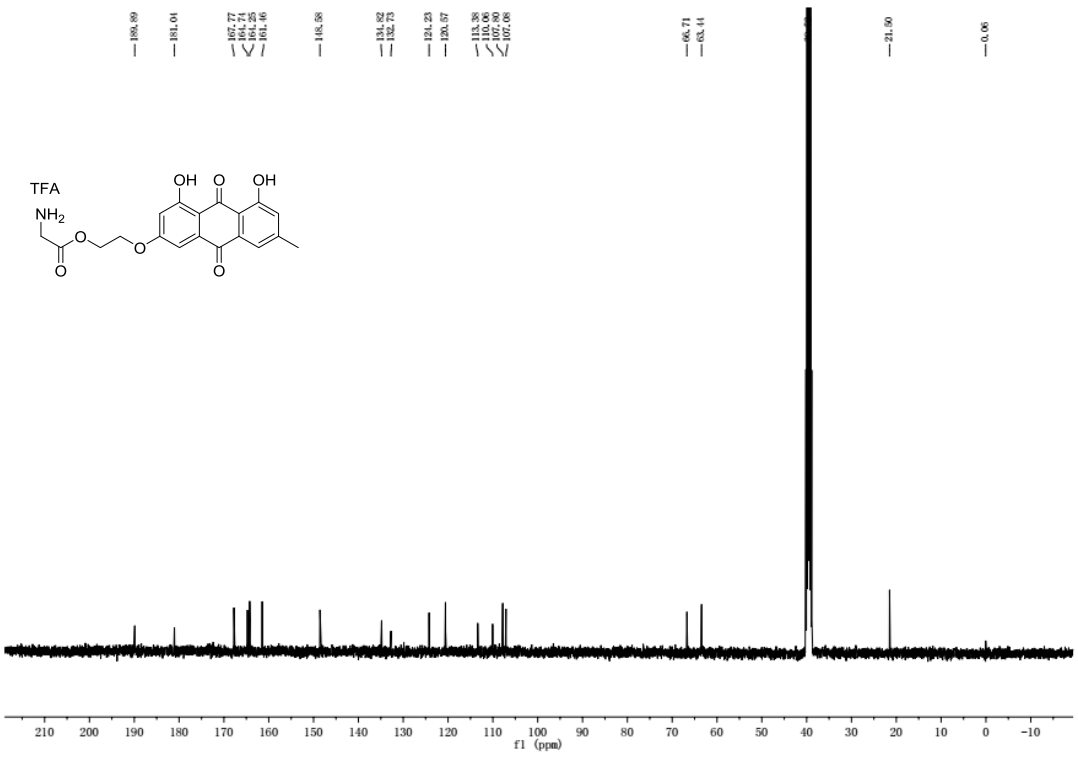

Figure S4. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **3a**.

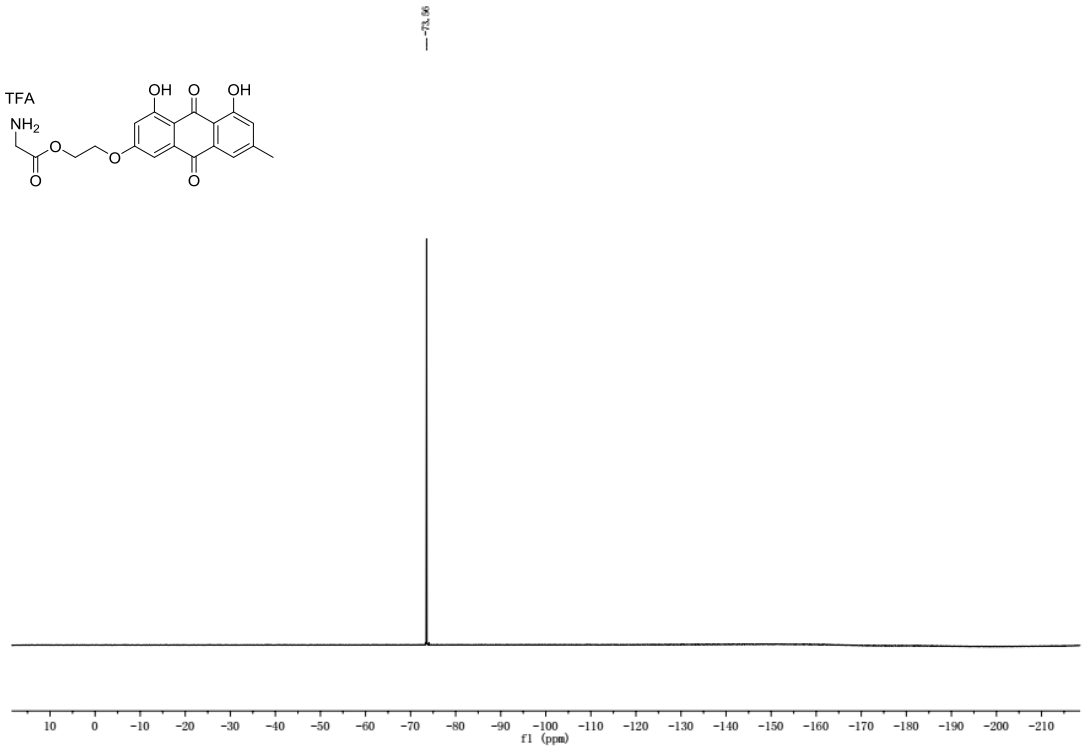

Figure S5. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **3a**.

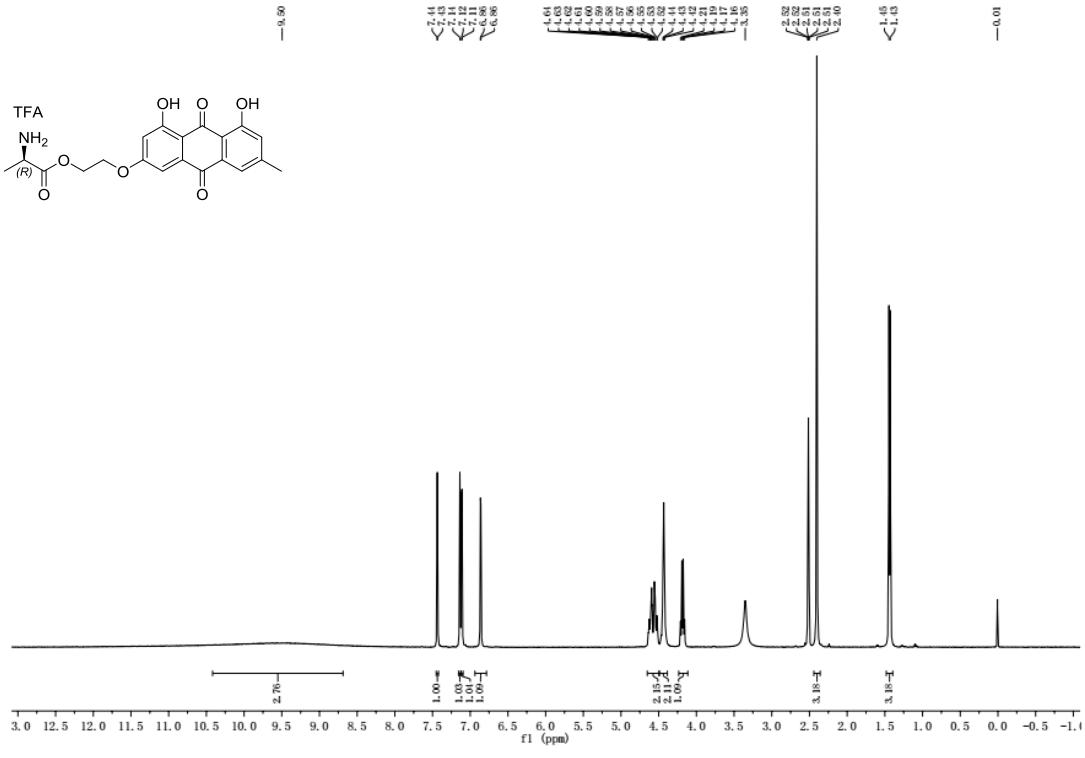

Figure S6. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **3b**.

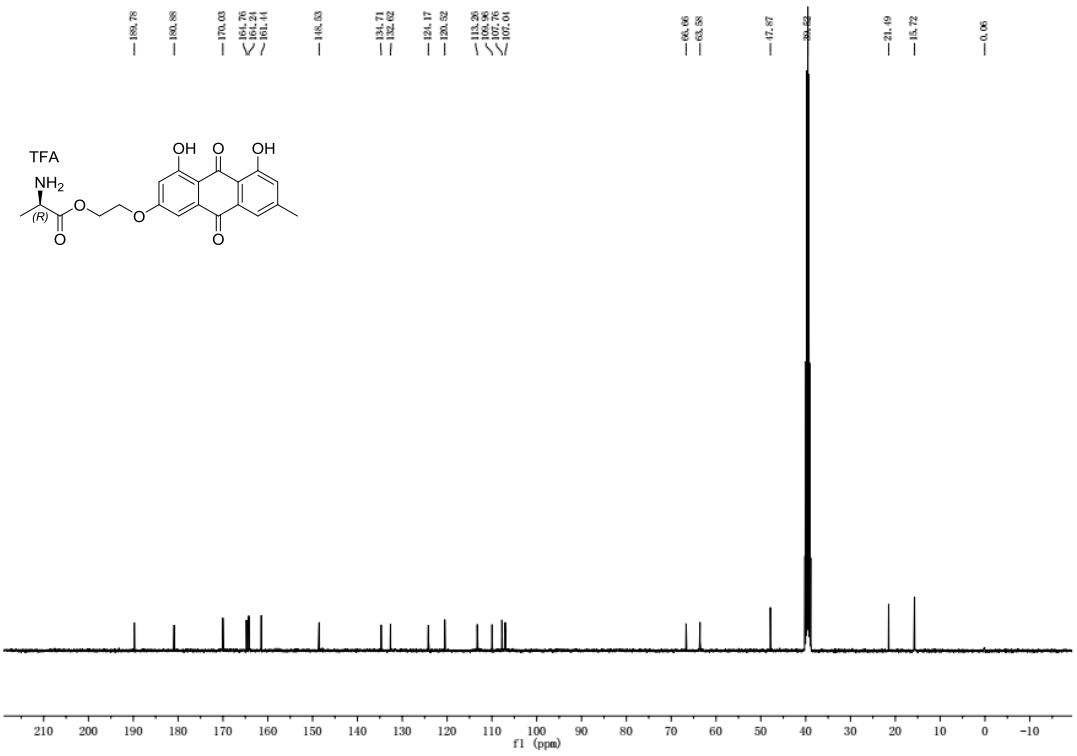

Figure S7. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **3b**.

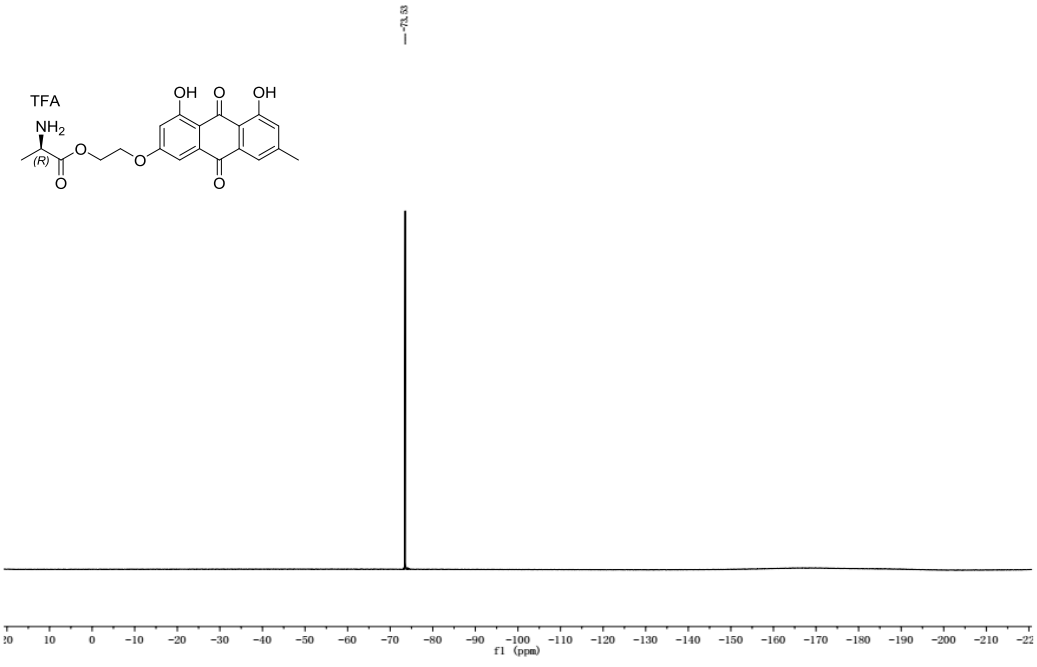

Figure S8. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **3b**.

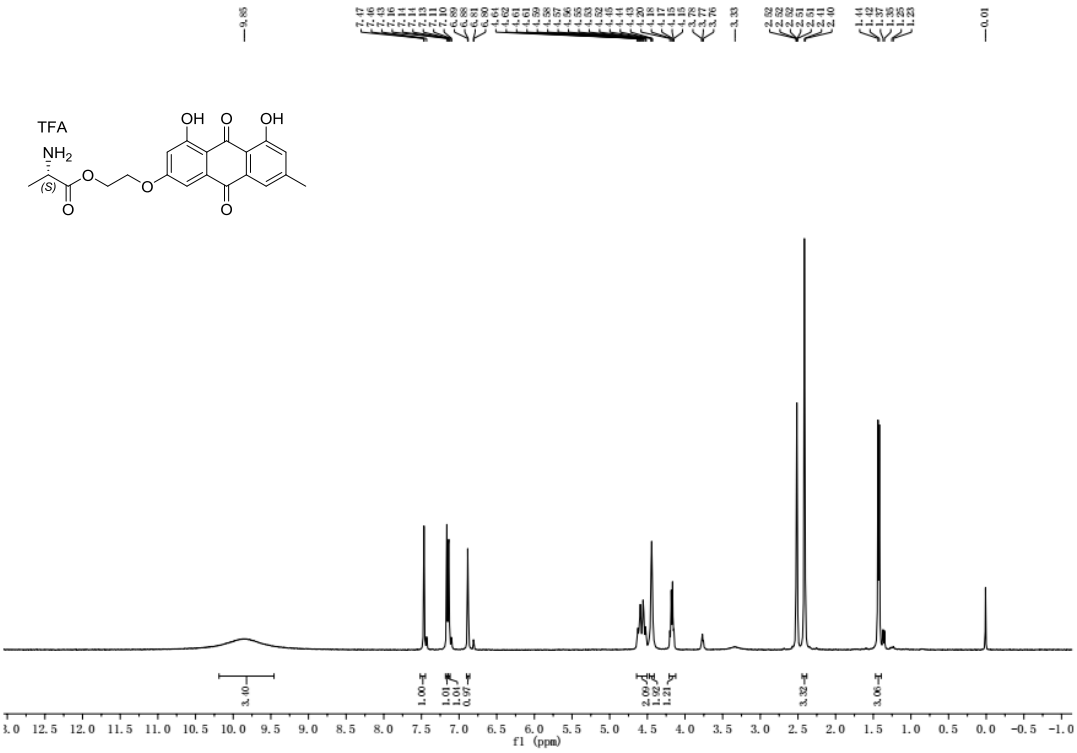

Figure S9. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **3c**.

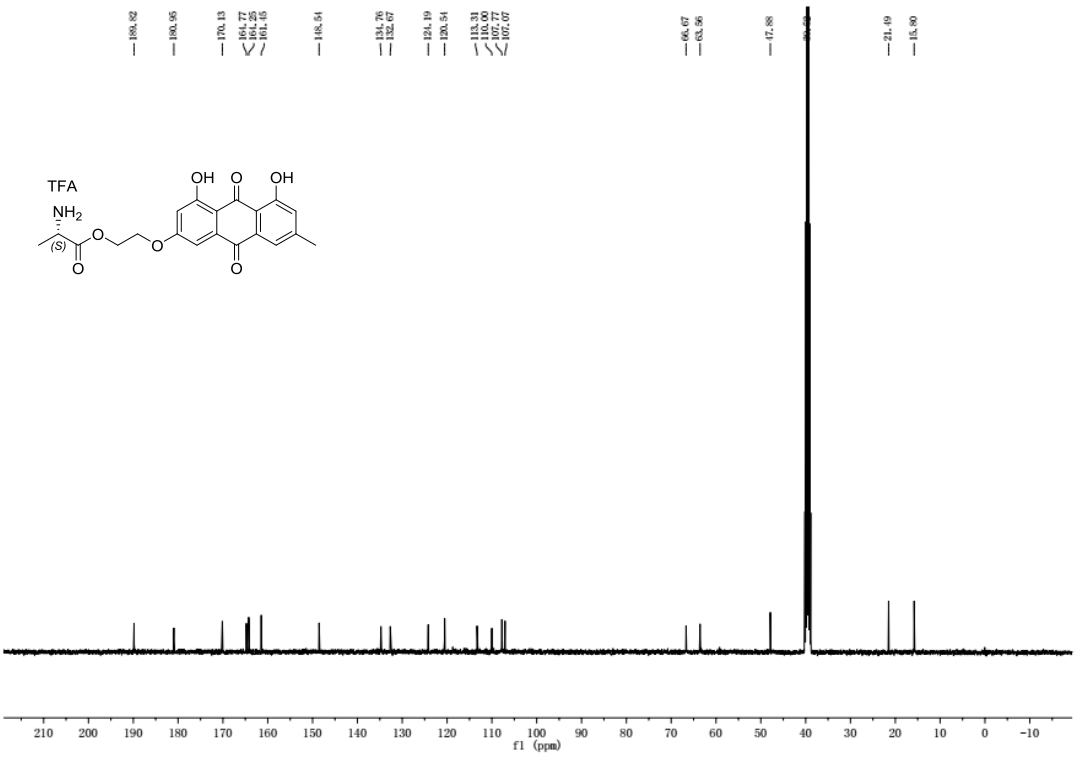

Figure S10. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **3c**.

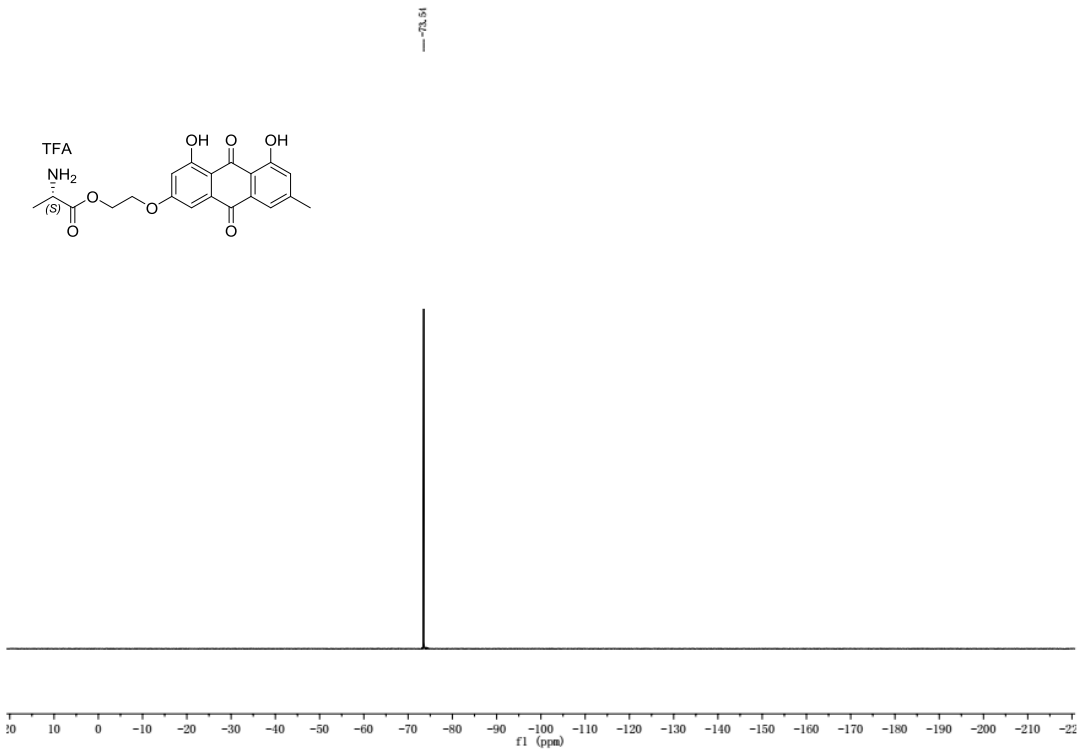

Figure S11. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **3c**.

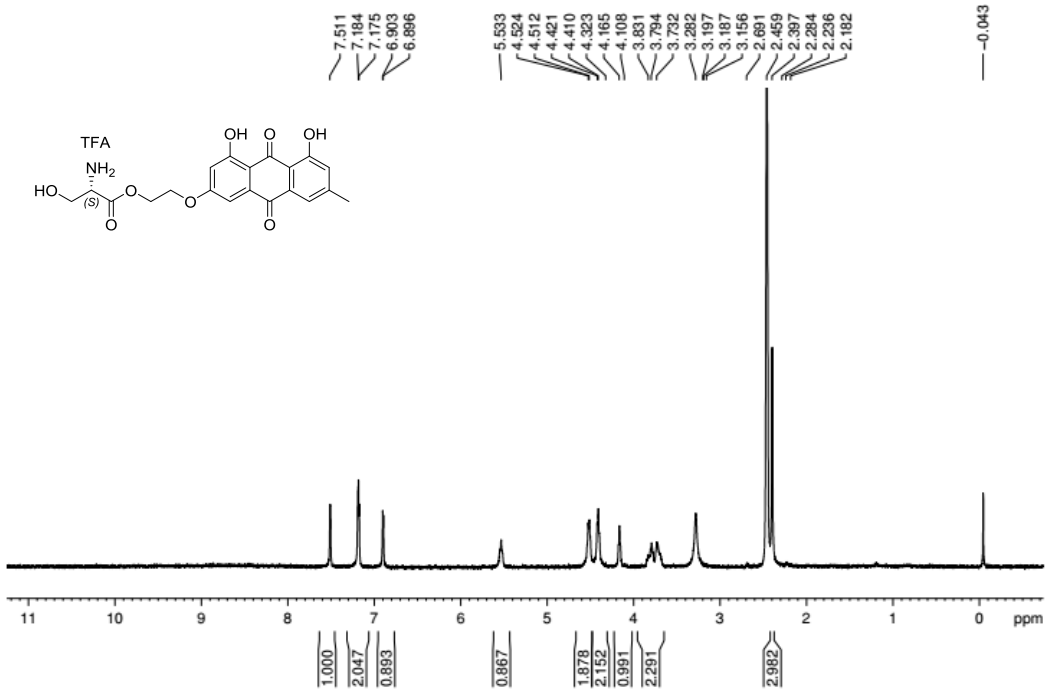

Figure S12. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **3d**.

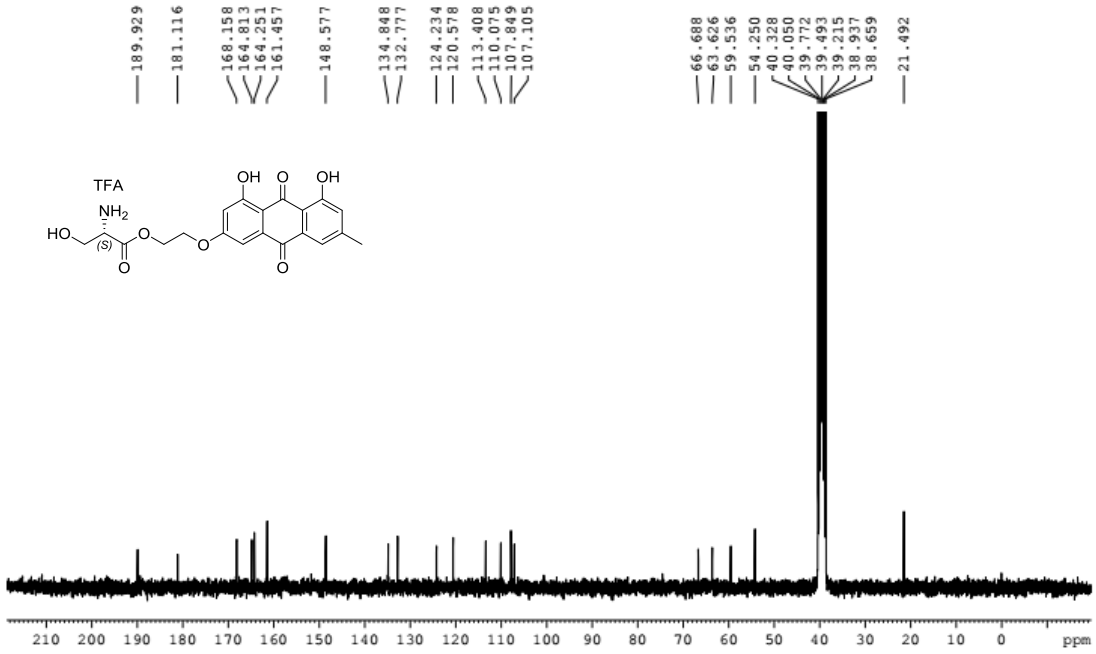

Figure S13. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **3d**.

Figure S14. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **3d**.

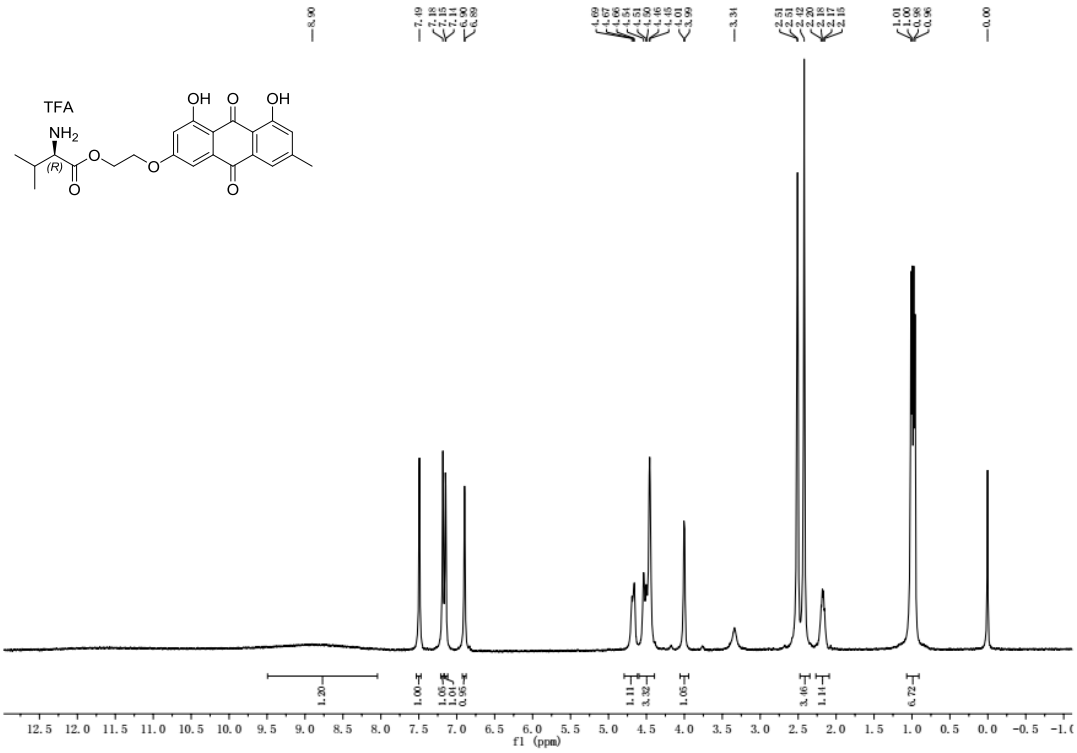

Figure S15. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **3e**.

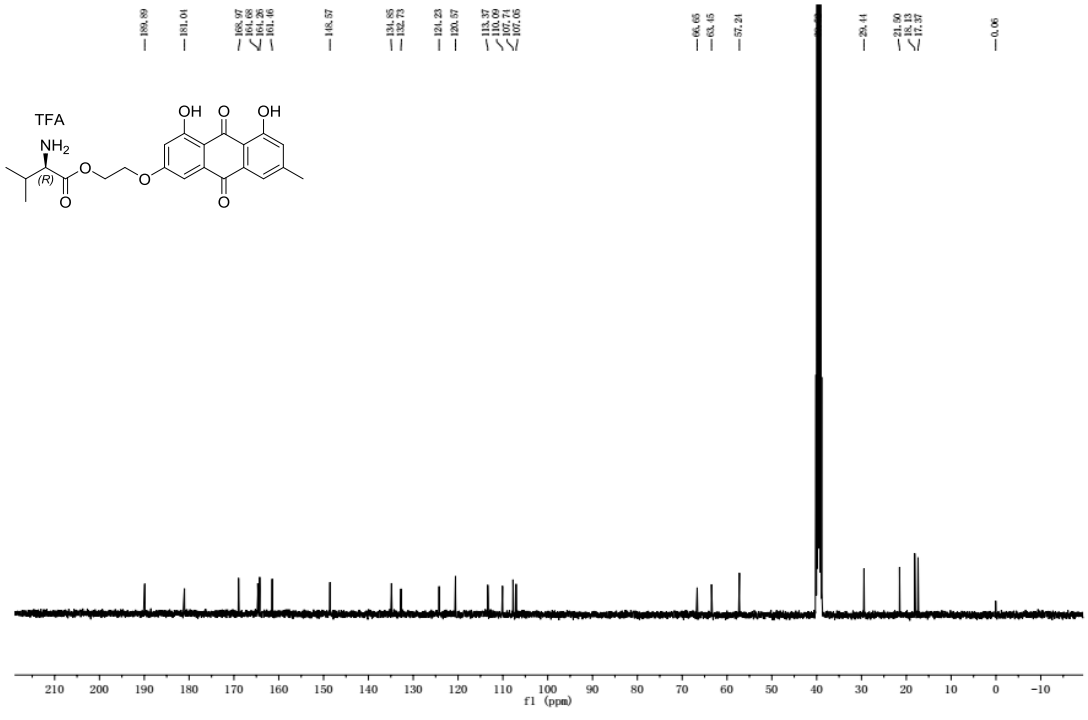

Figure S16. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **3e**.

Figure S17. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **3e**.

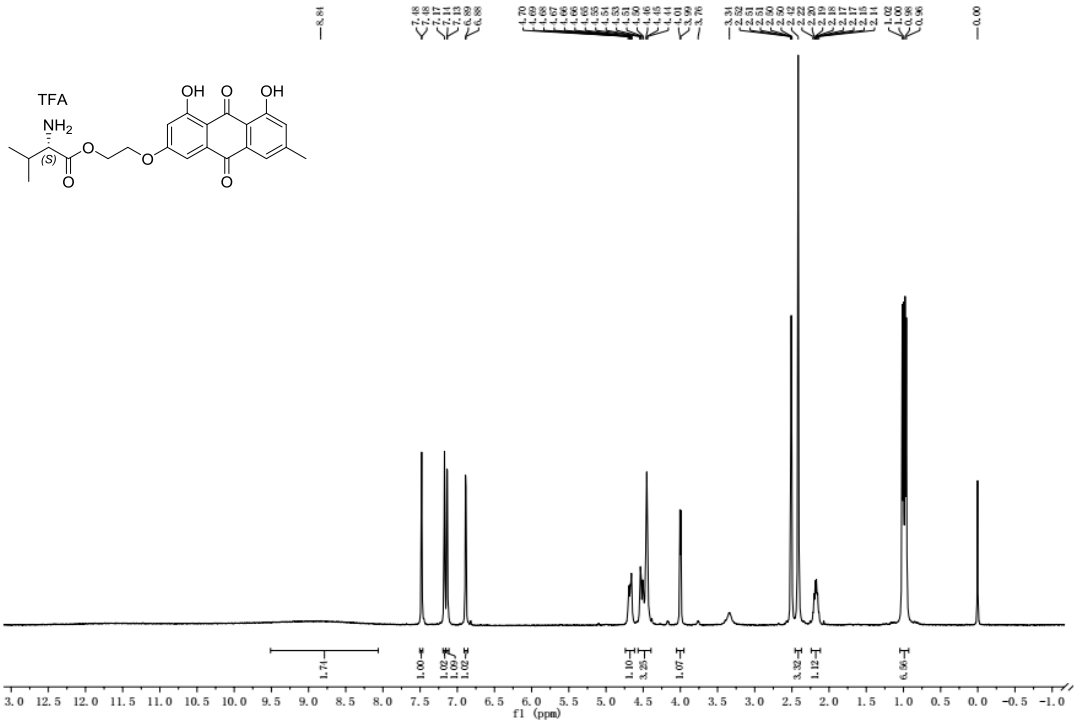

Figure S18. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **3f**.

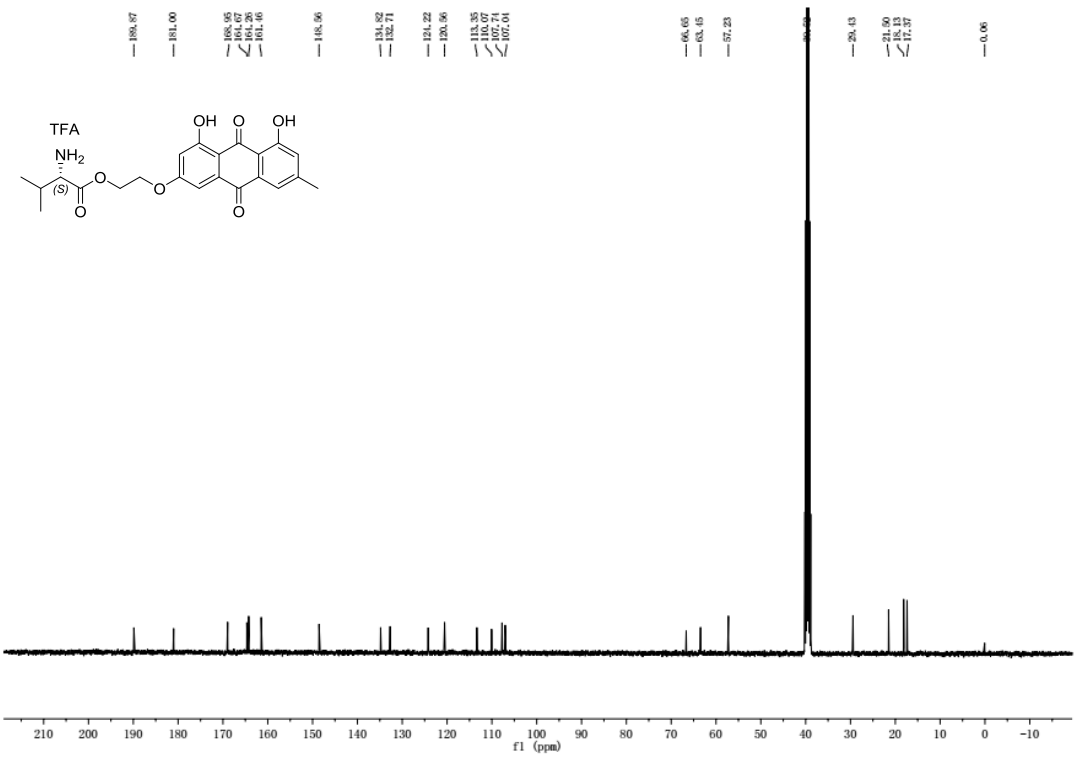

Figure S19. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **3f**.

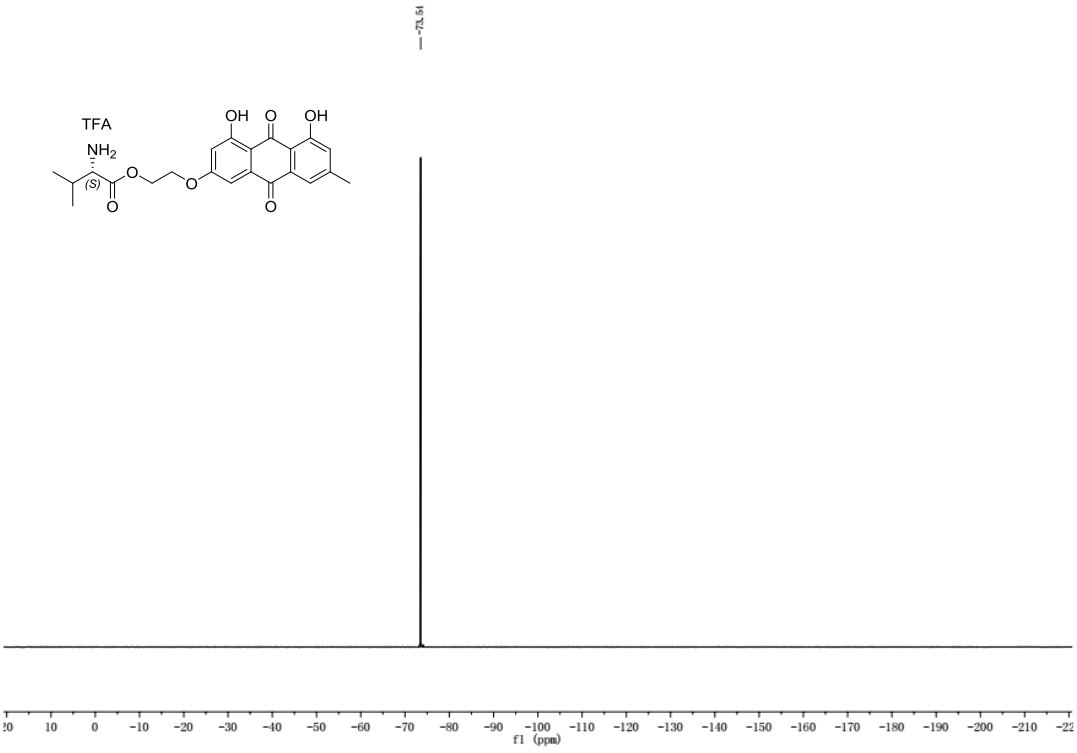

Figure S20. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **3f**.

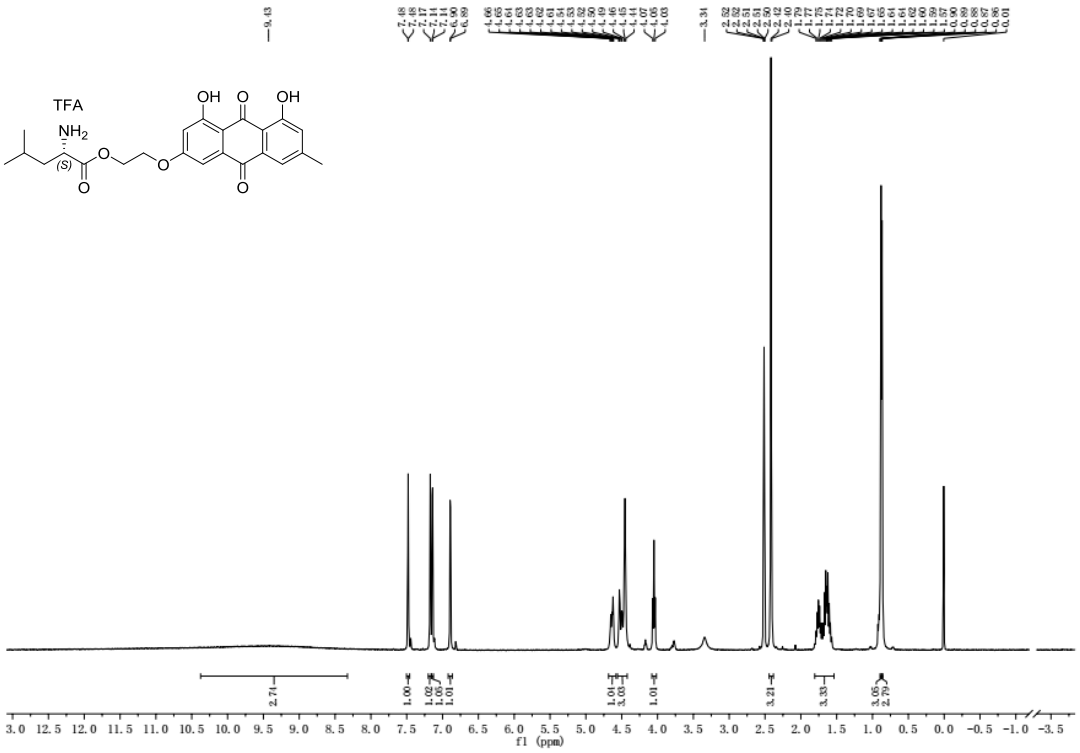

Figure S21. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **3g**.

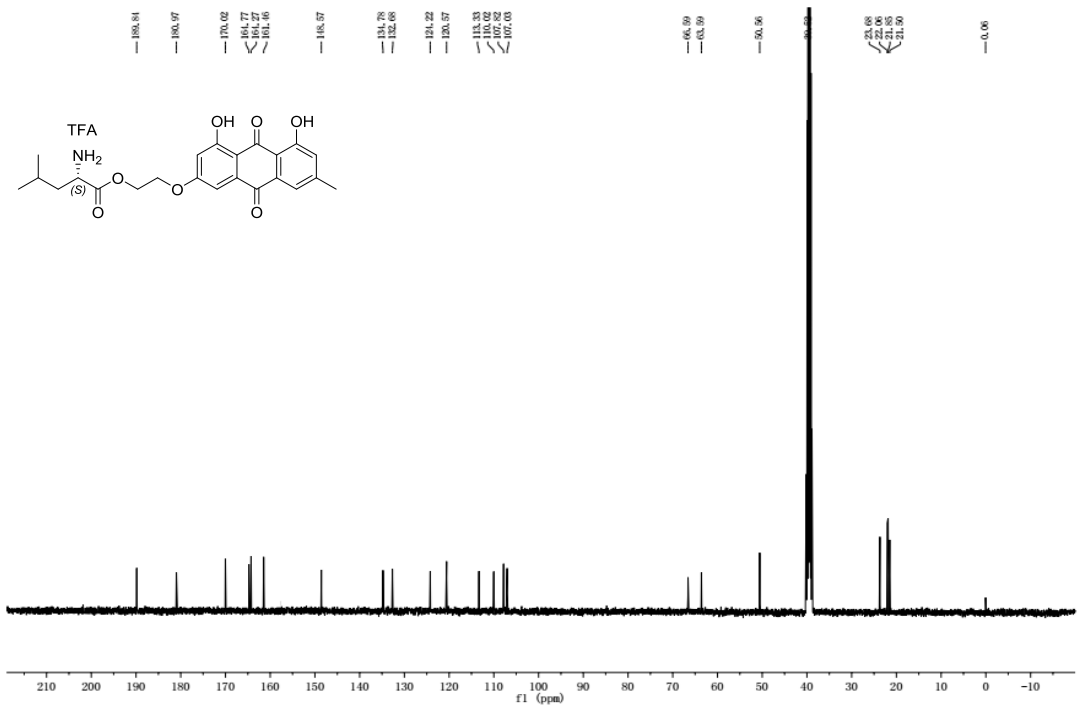

Figure S22. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **3g**.

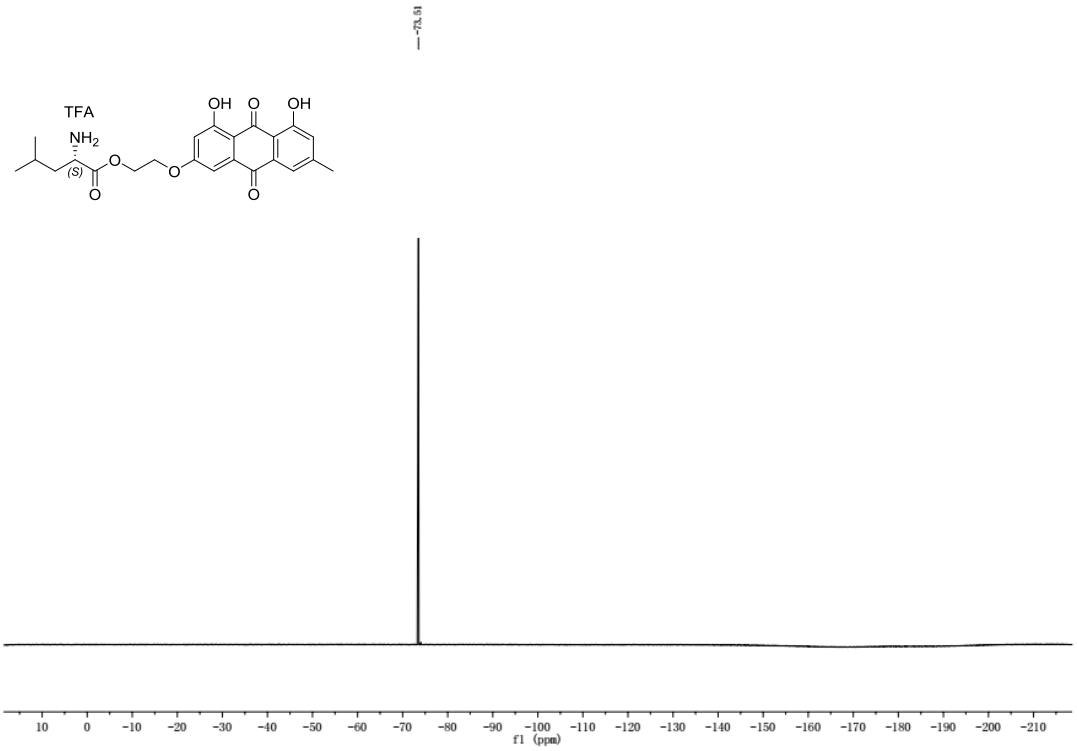

Figure S23. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **3g**.

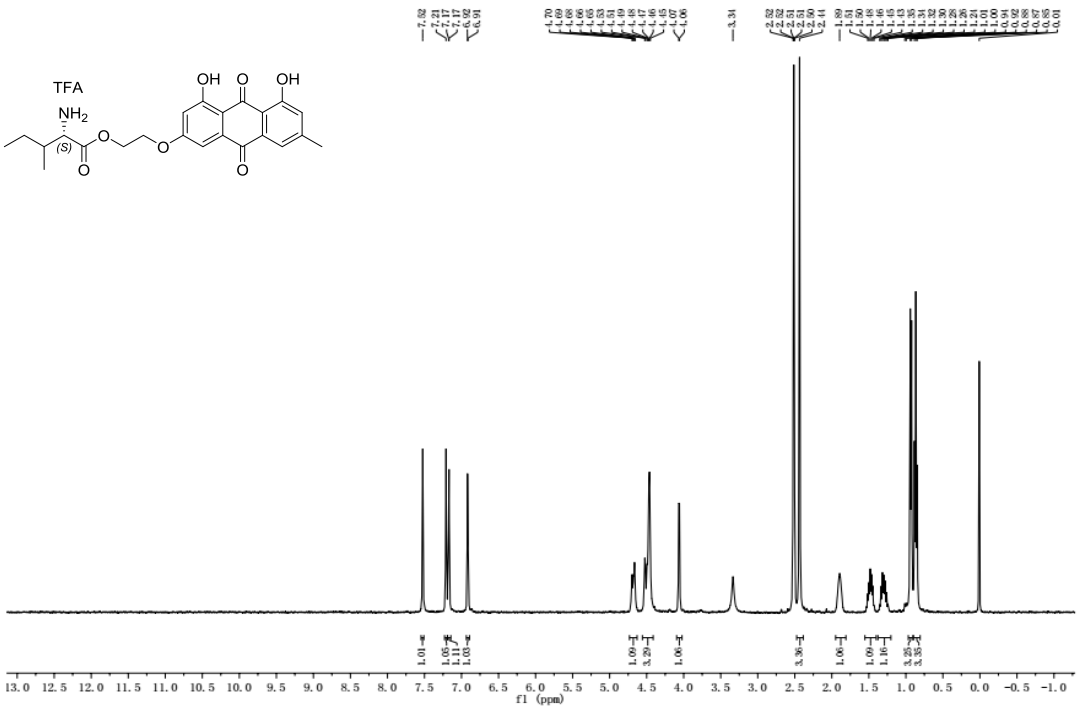

Figure S24. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **3h**.

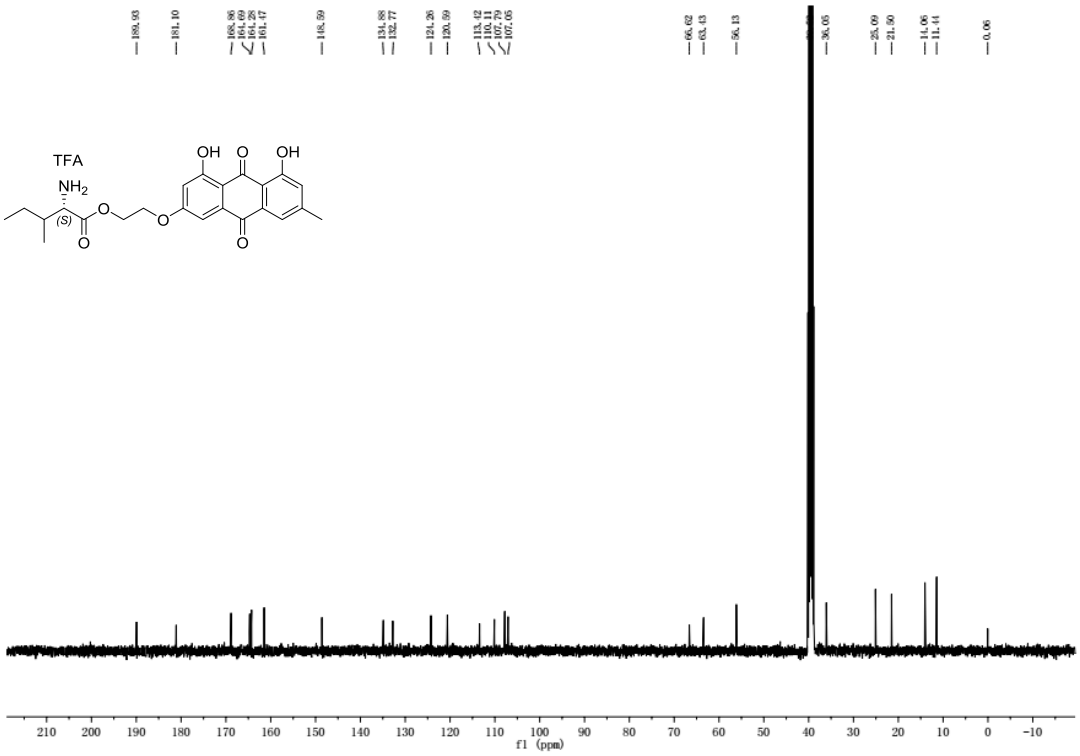

Figure S25. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **3h**.

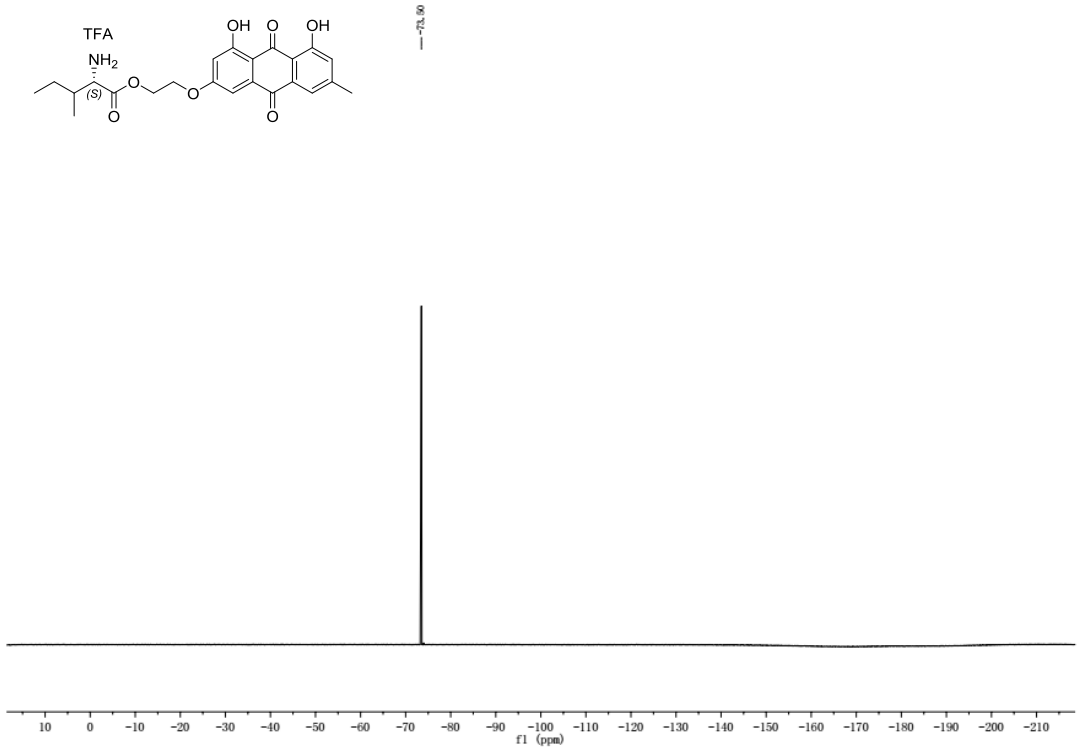

Figure S26. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **3h**.

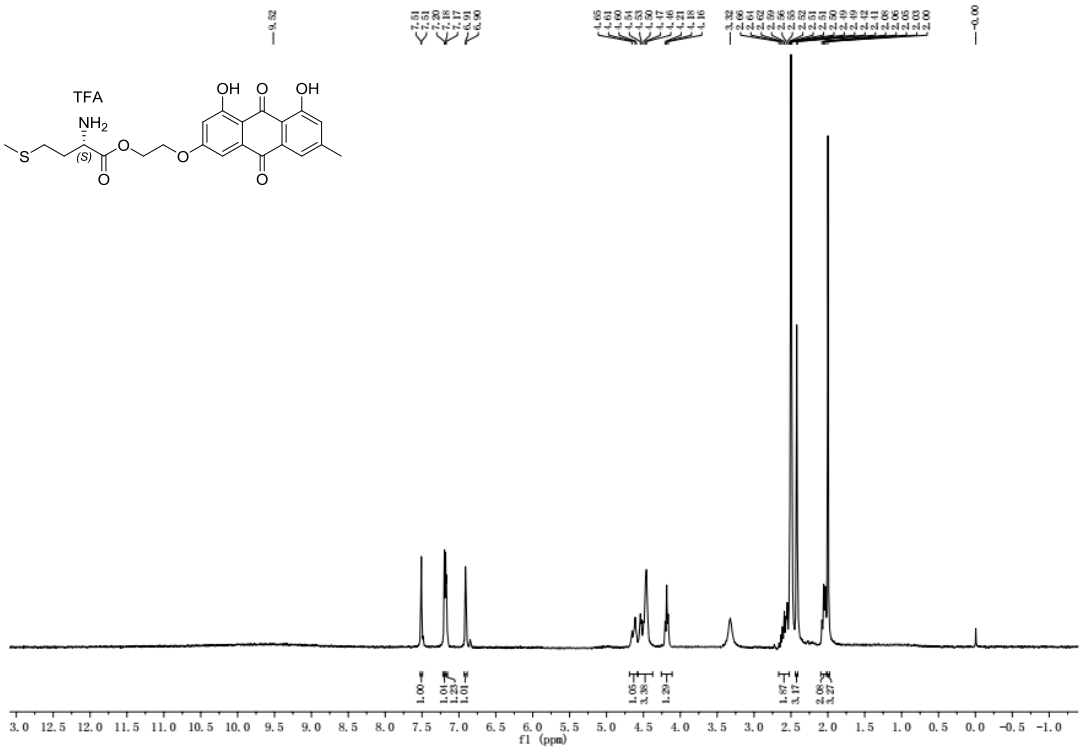

Figure S27. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **3i**.

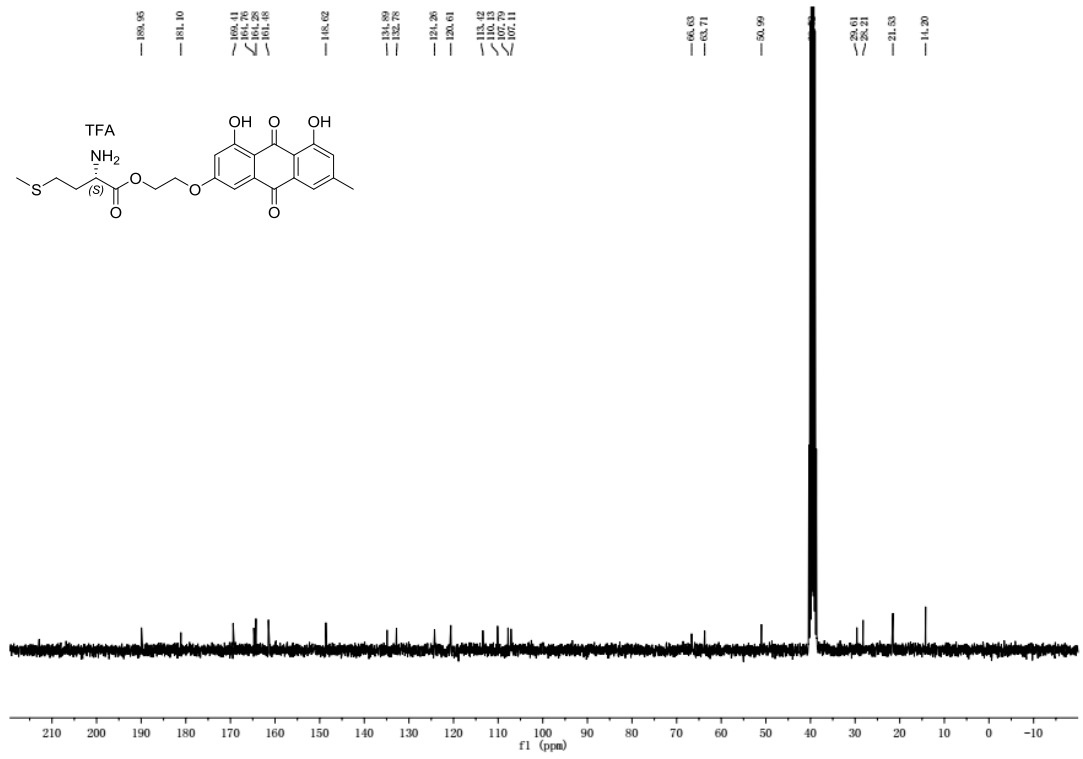

Figure S28. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **3i**

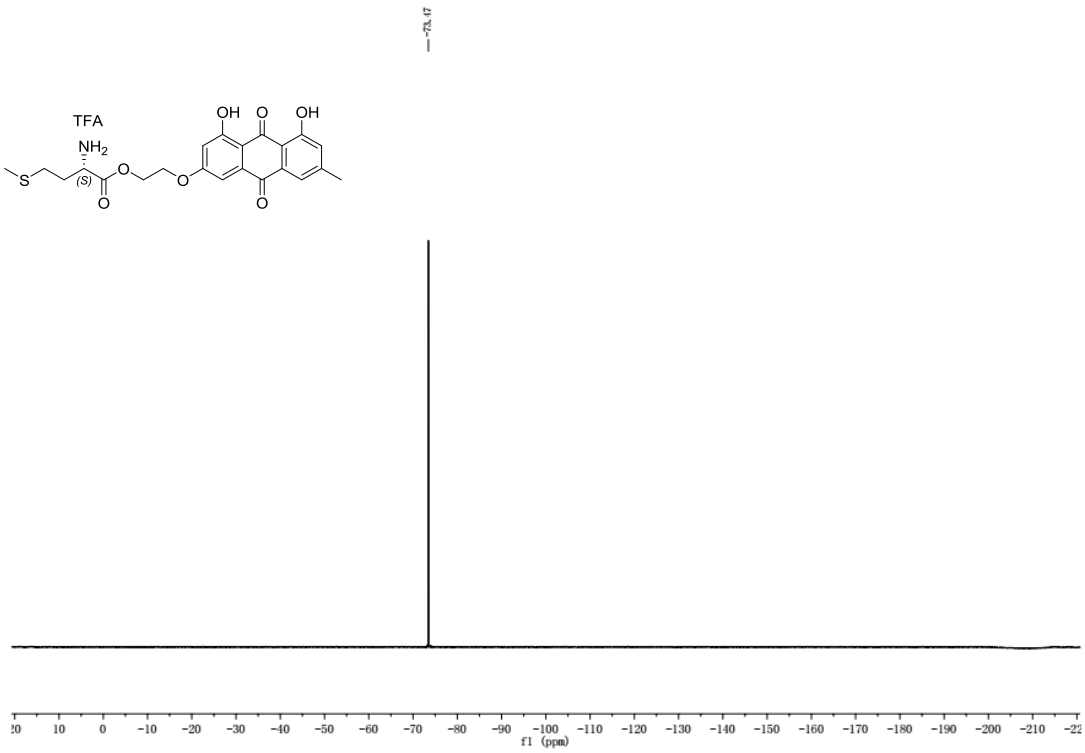

Figure S29. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **3i**.

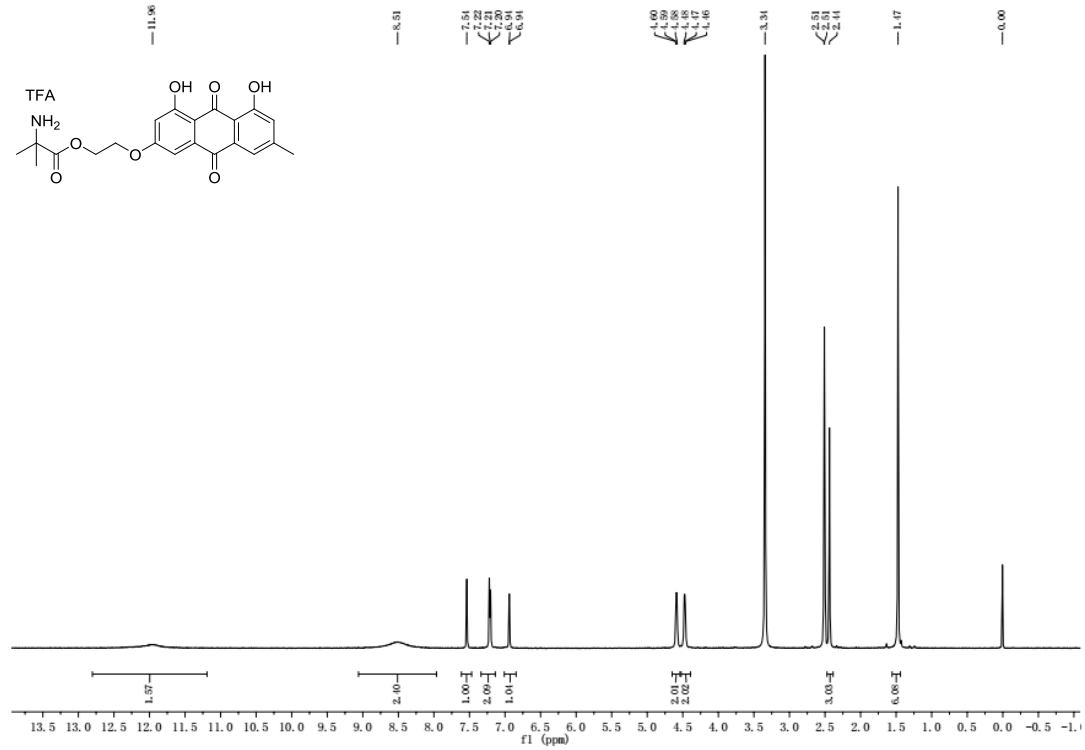

Figure S30. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **3j**.

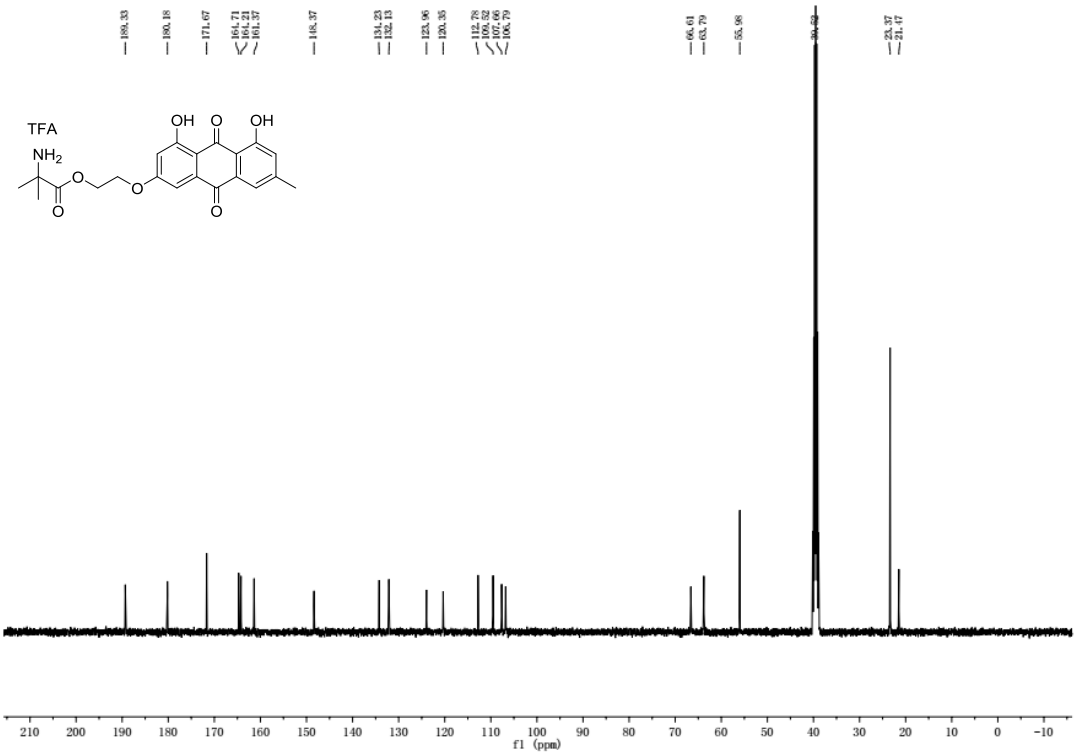

Figure S31. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **3j**.

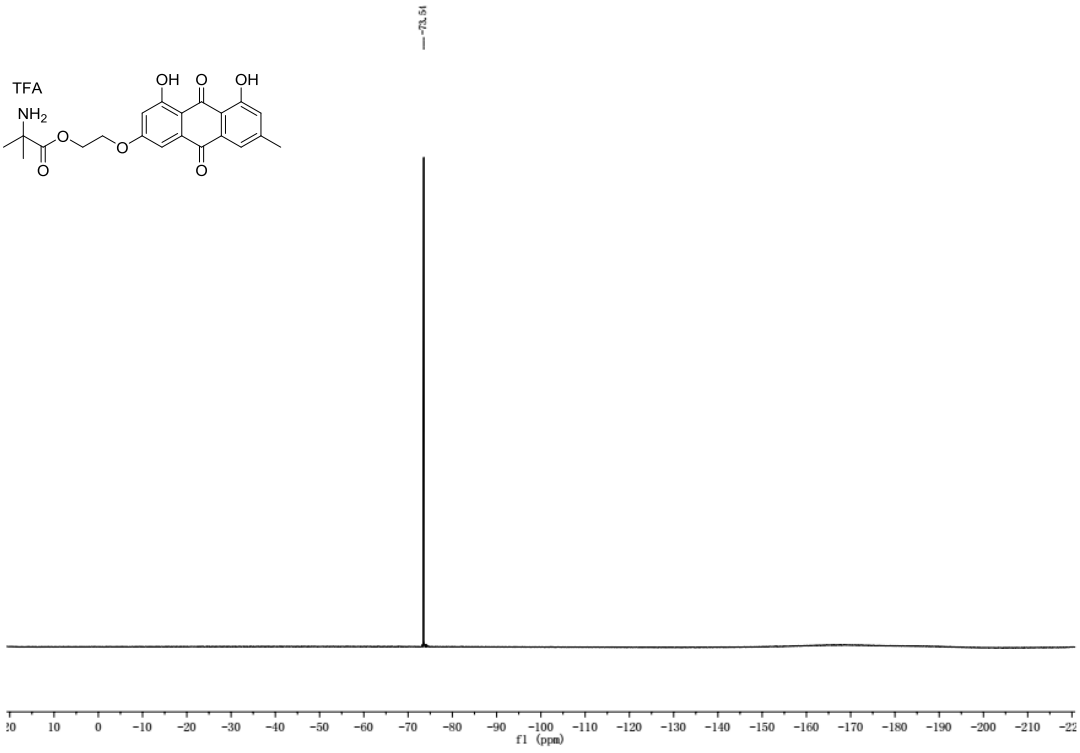

Figure S32. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **3j**.

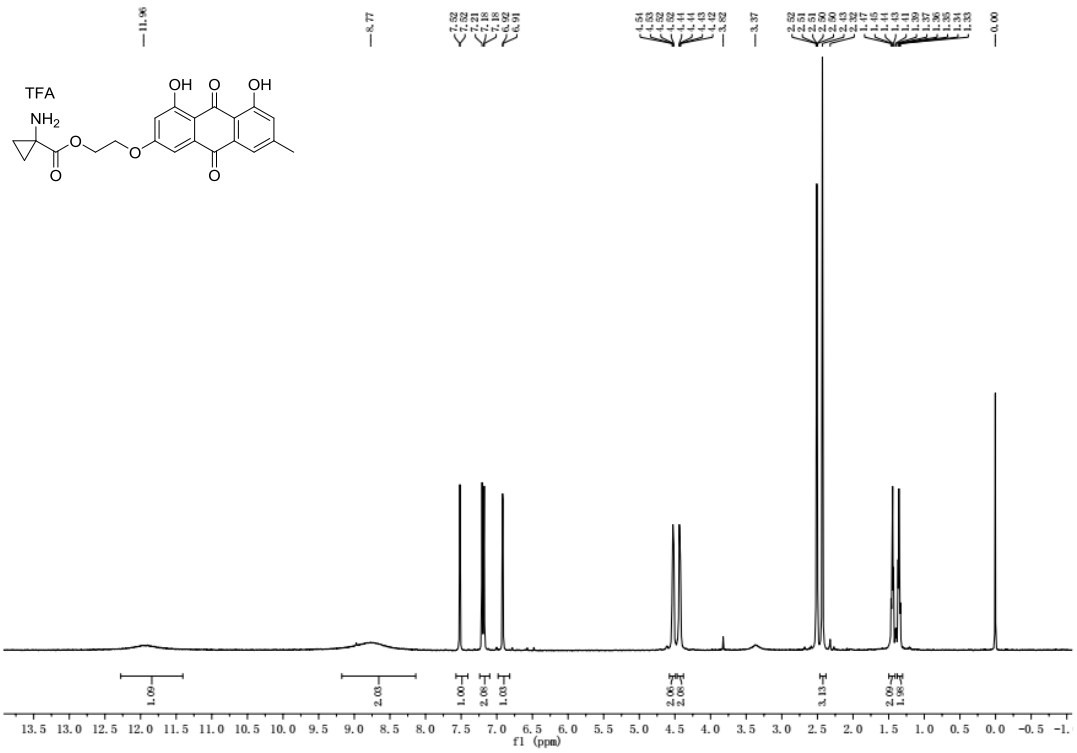

Figure S33. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **3k**.

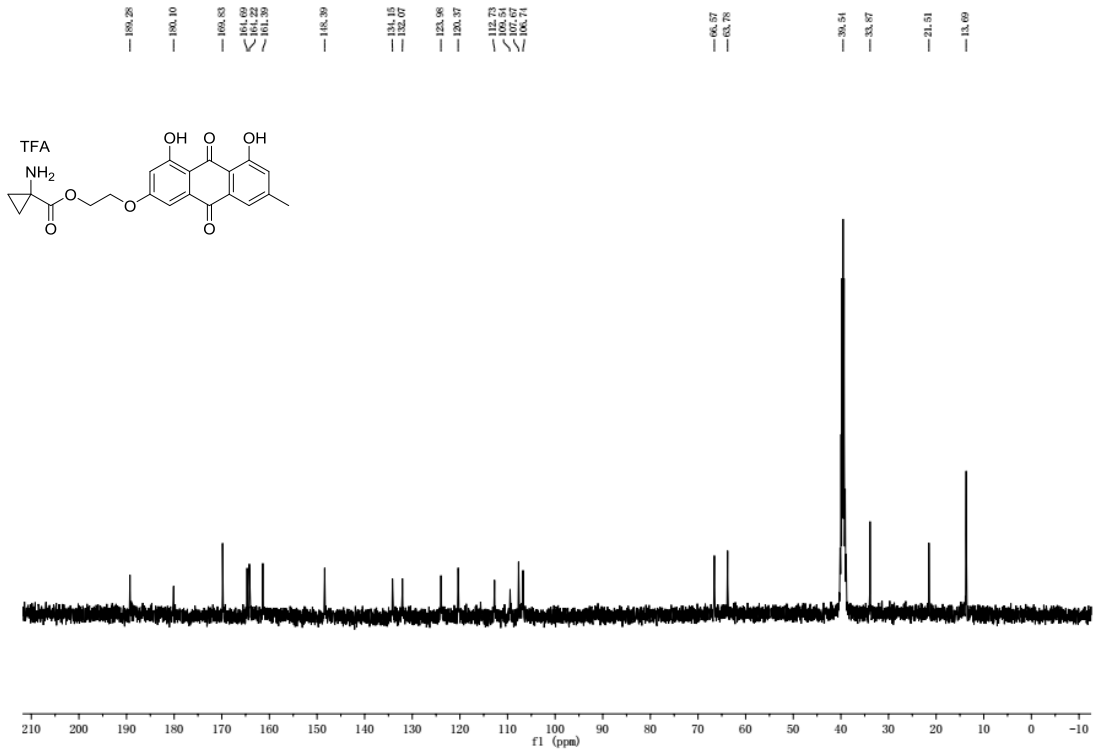

Figure S34. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **3k**.

Figure S35. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **3k**.

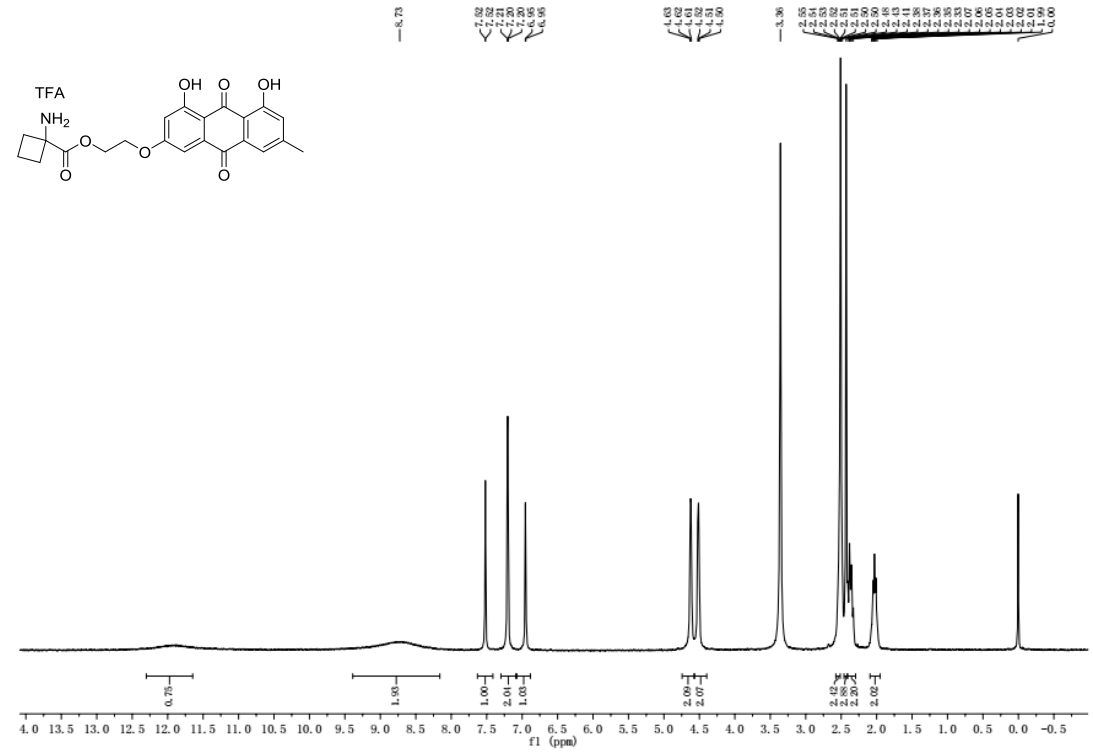

Figure S36. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **3l**.

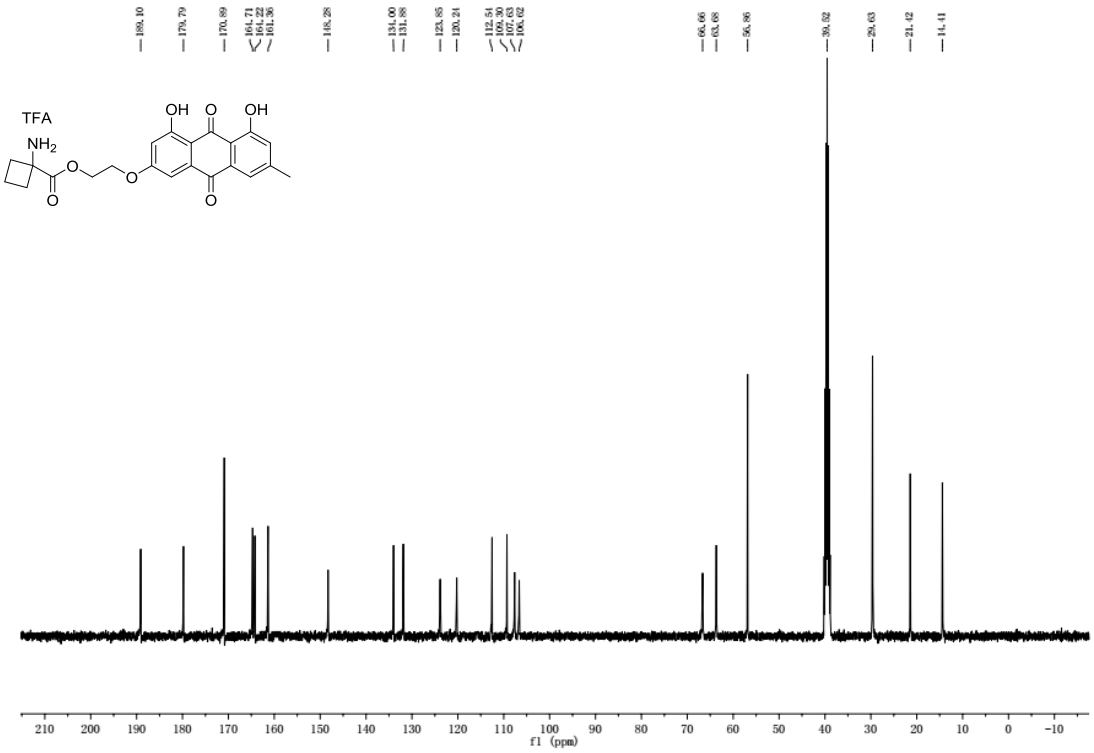

Figure S37. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **3l**.

Figure S38. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **3l**.

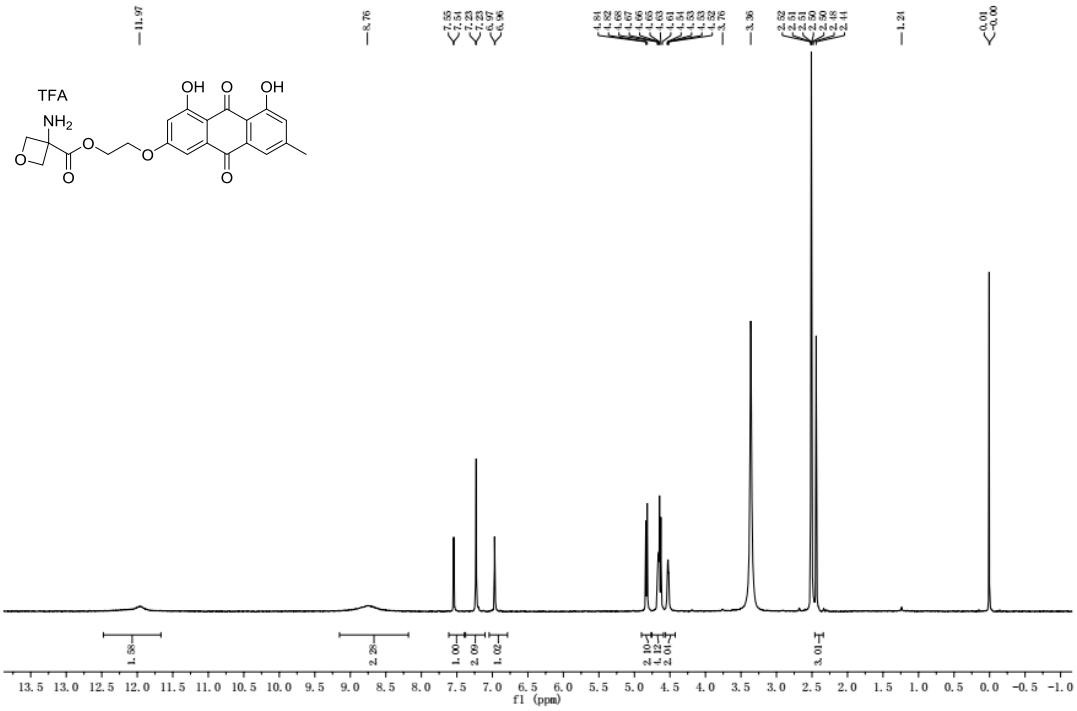

Figure S39. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **3m**.

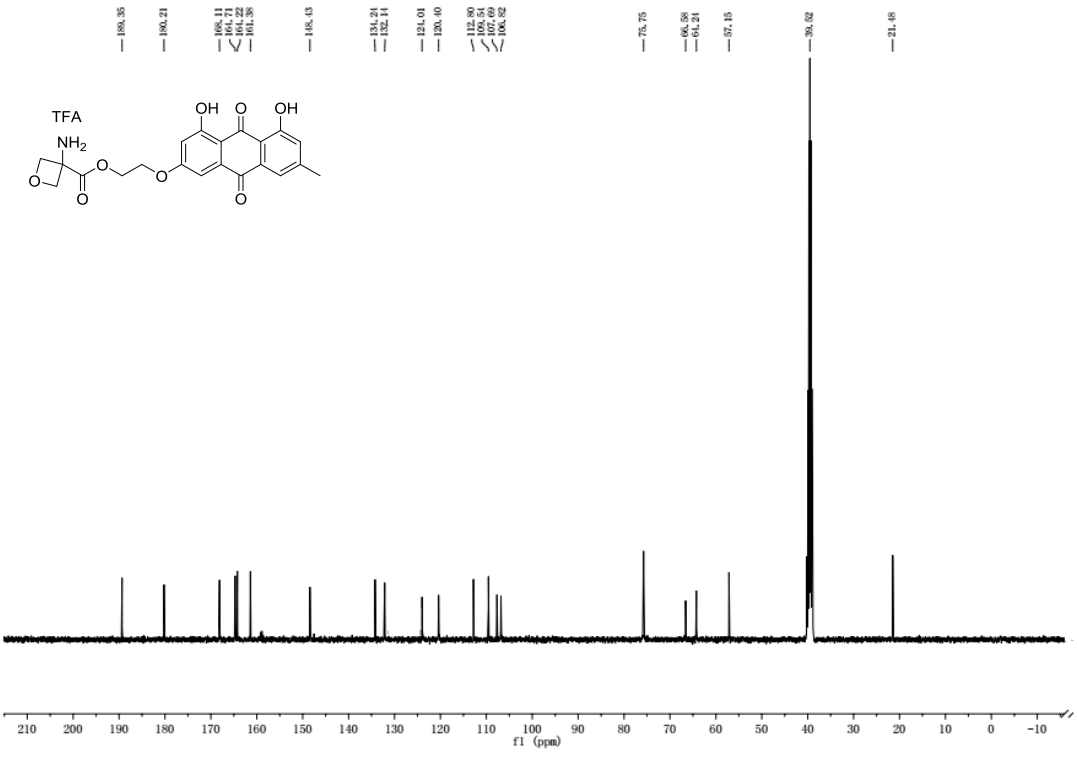

Figure S40. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **3m**.

Figure S41. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **3m**.

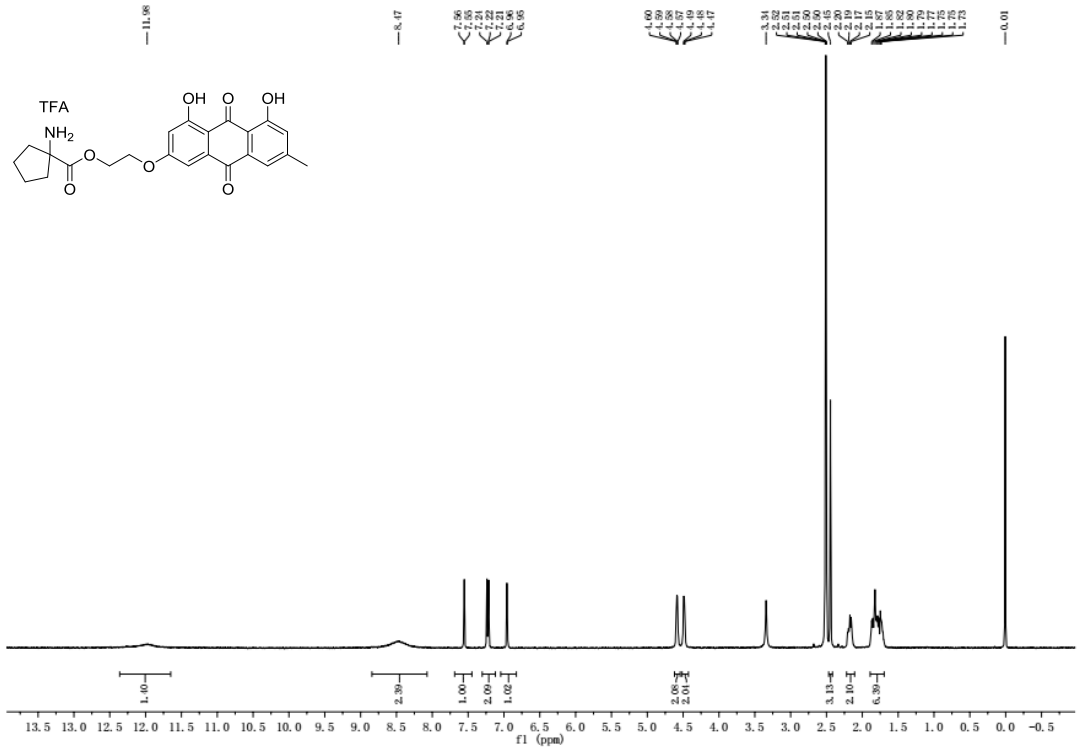

Figure S42. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **3n**.

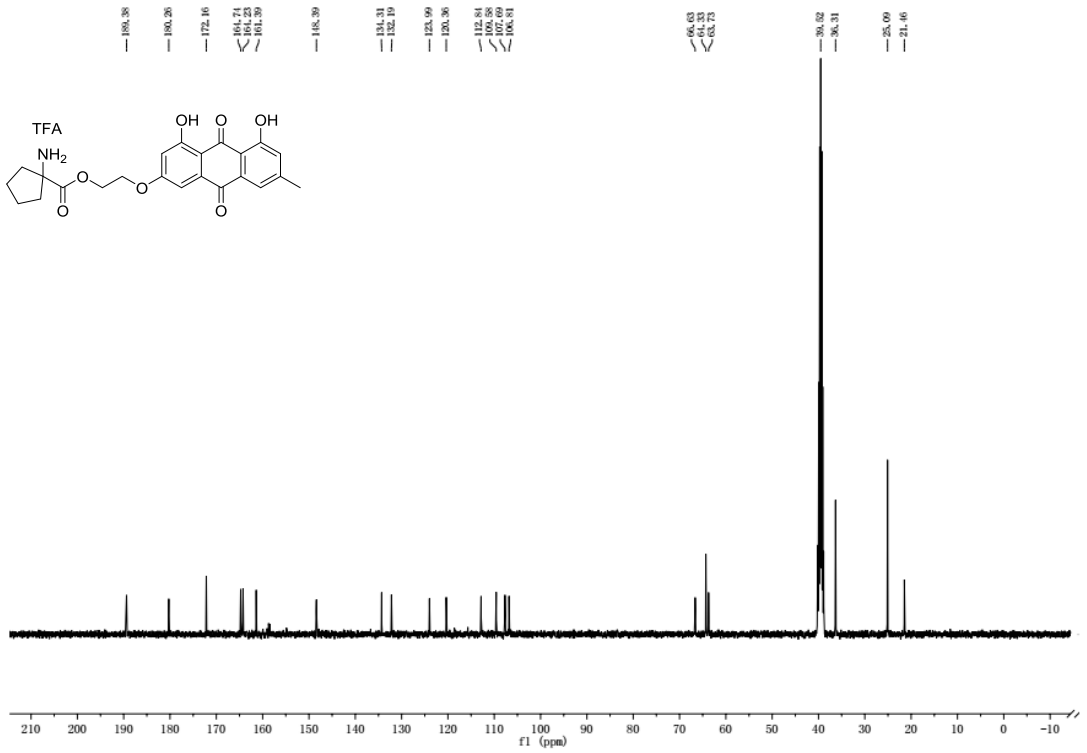

Figure S43. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **3n**.

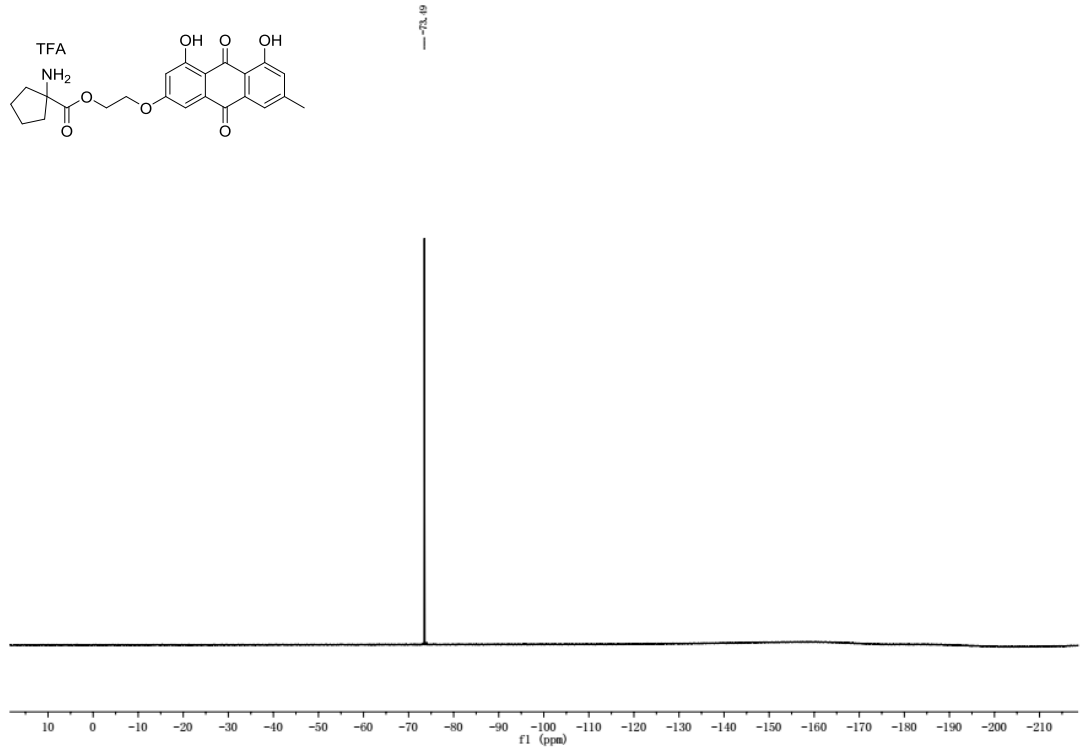

Figure S44. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **3n**.

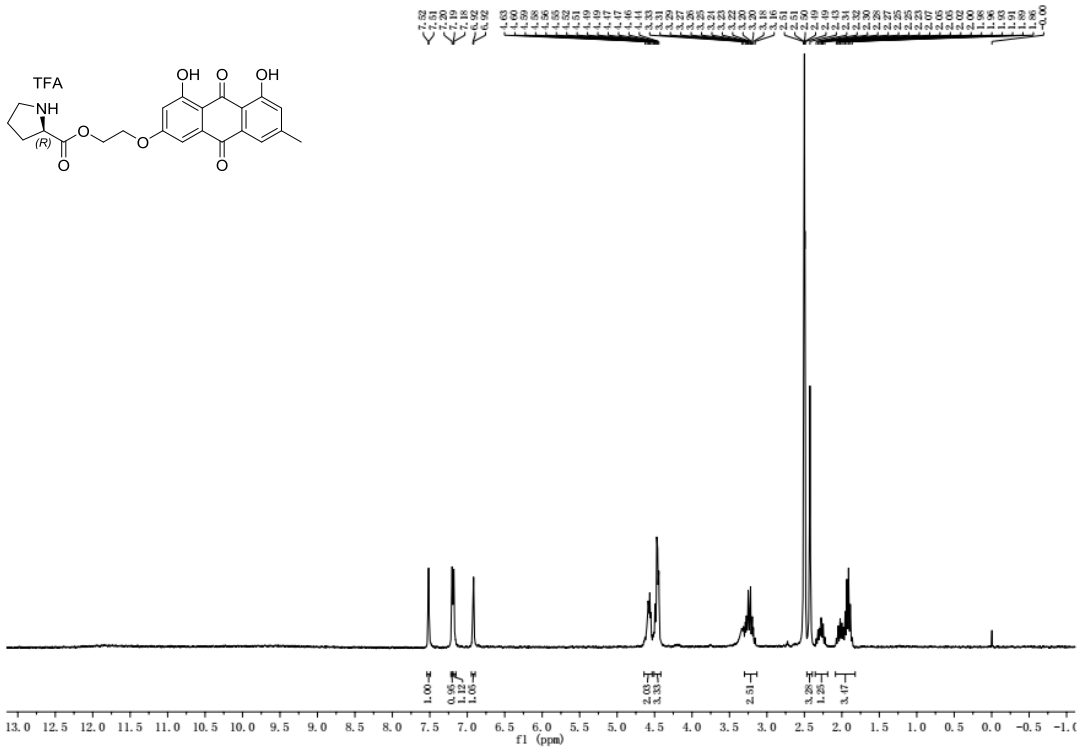

Figure S45. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **3o**.

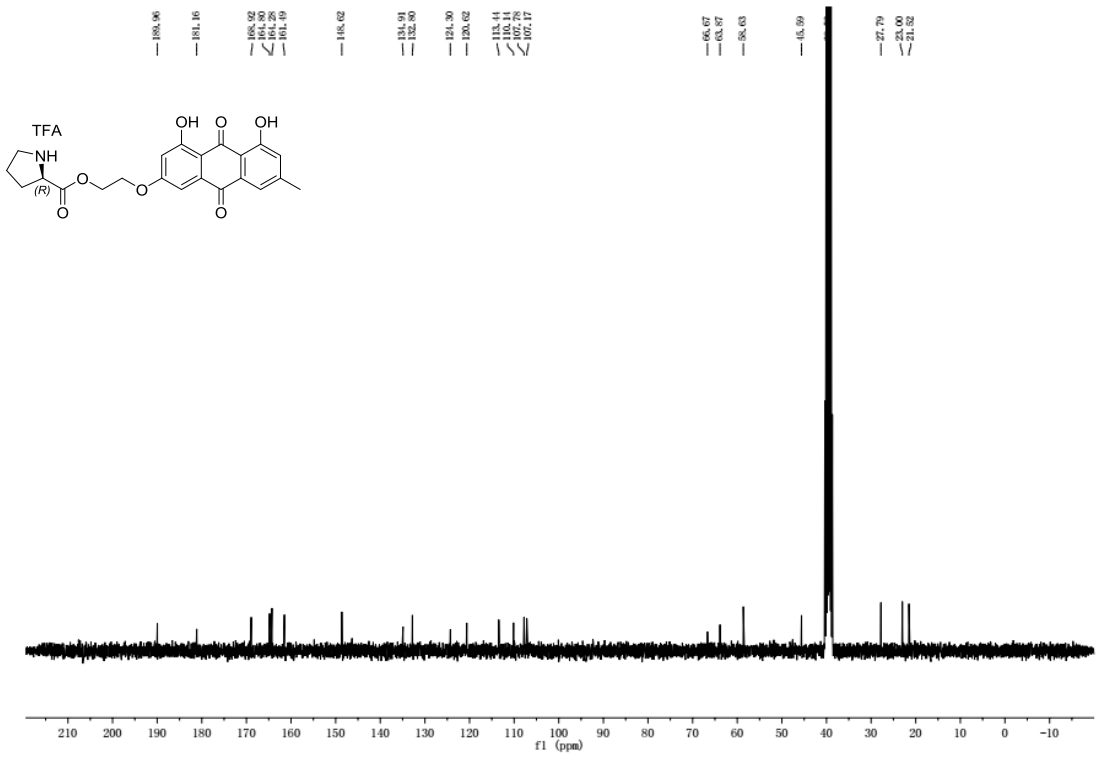

Figure S46. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **3o**.

Figure S47. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **3o**.

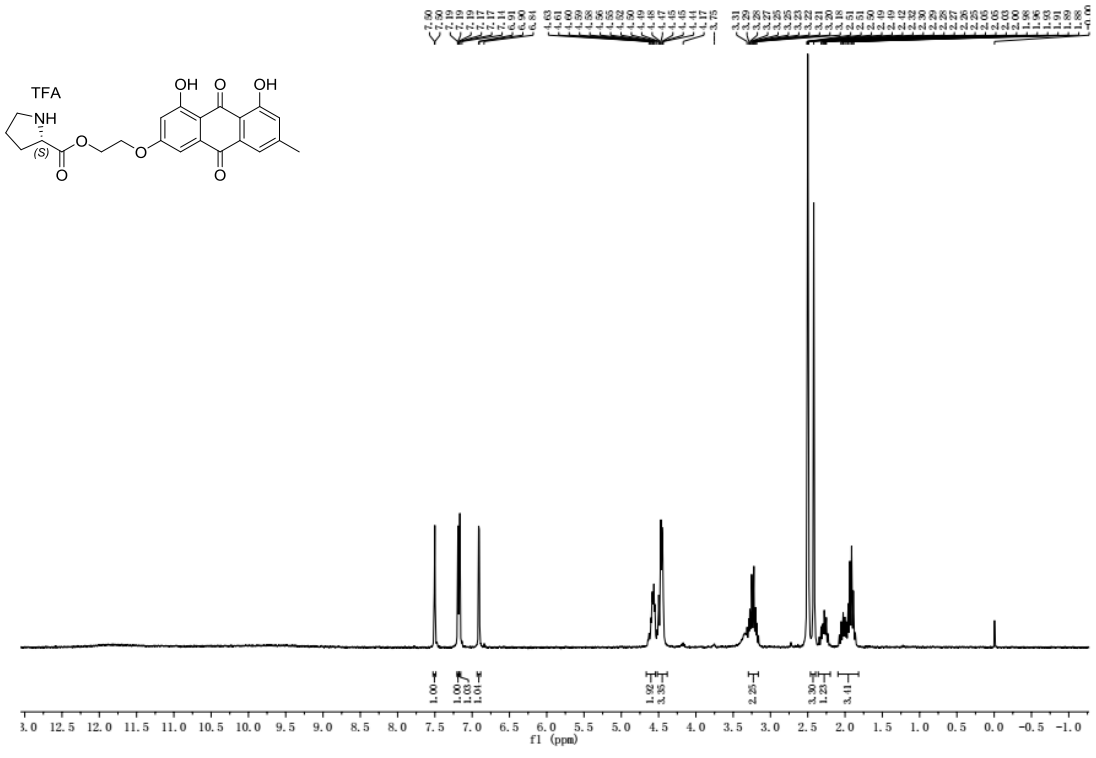

Figure S48. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **3p**.

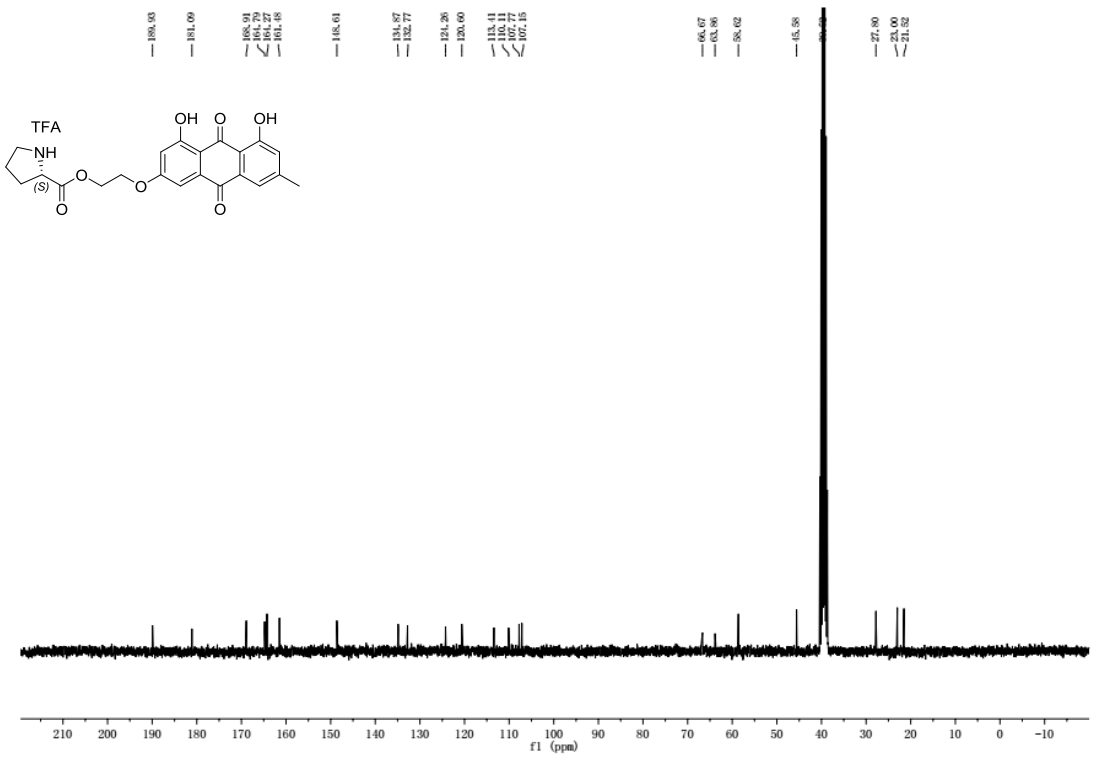

Figure S49. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **3p**.

Figure S50. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **3p**.

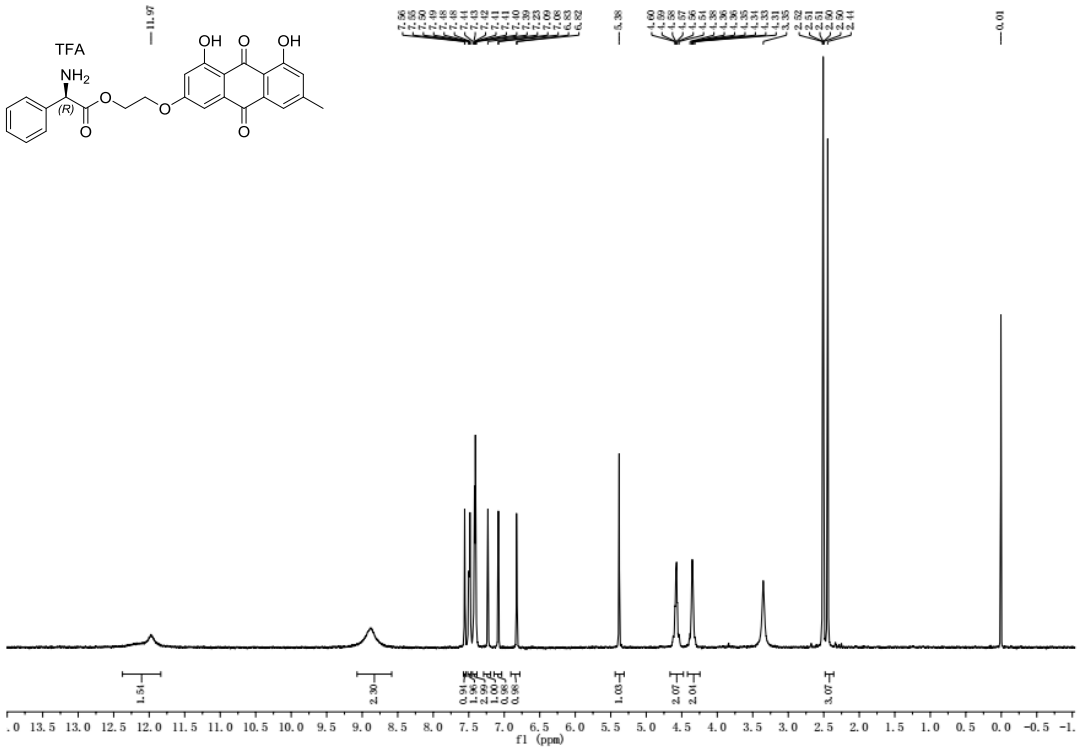

Figure S51. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **3q**.

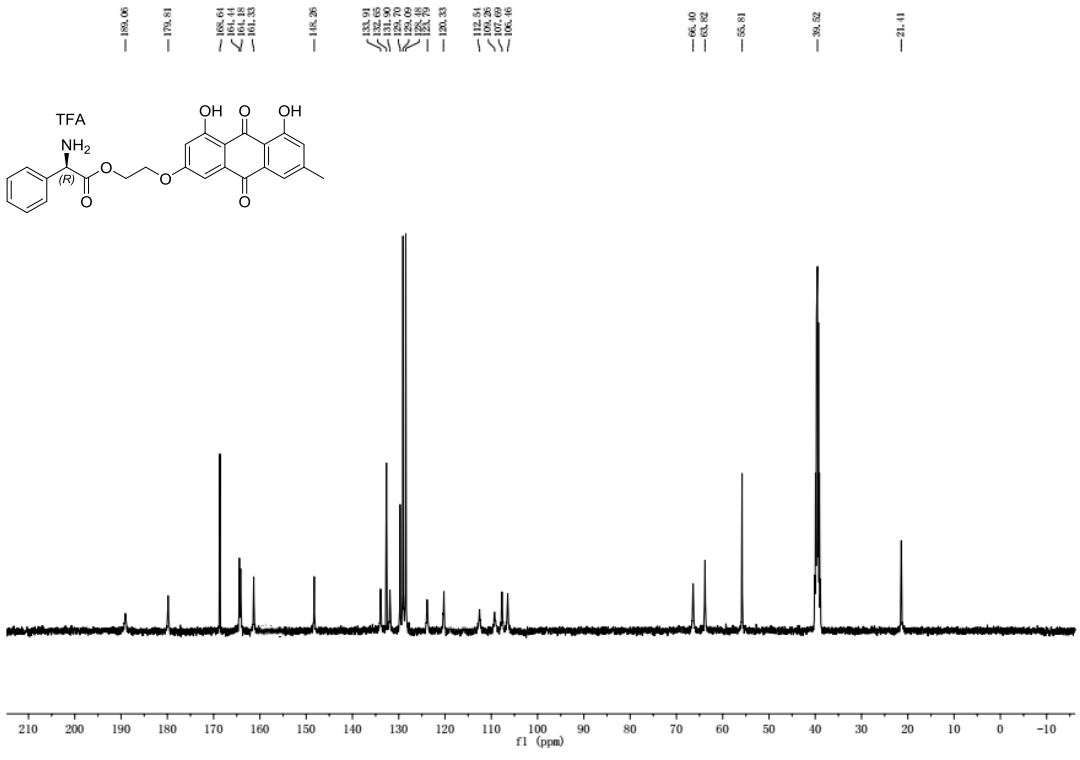

Figure S52. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **3q**.

Figure S53. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **3q**.

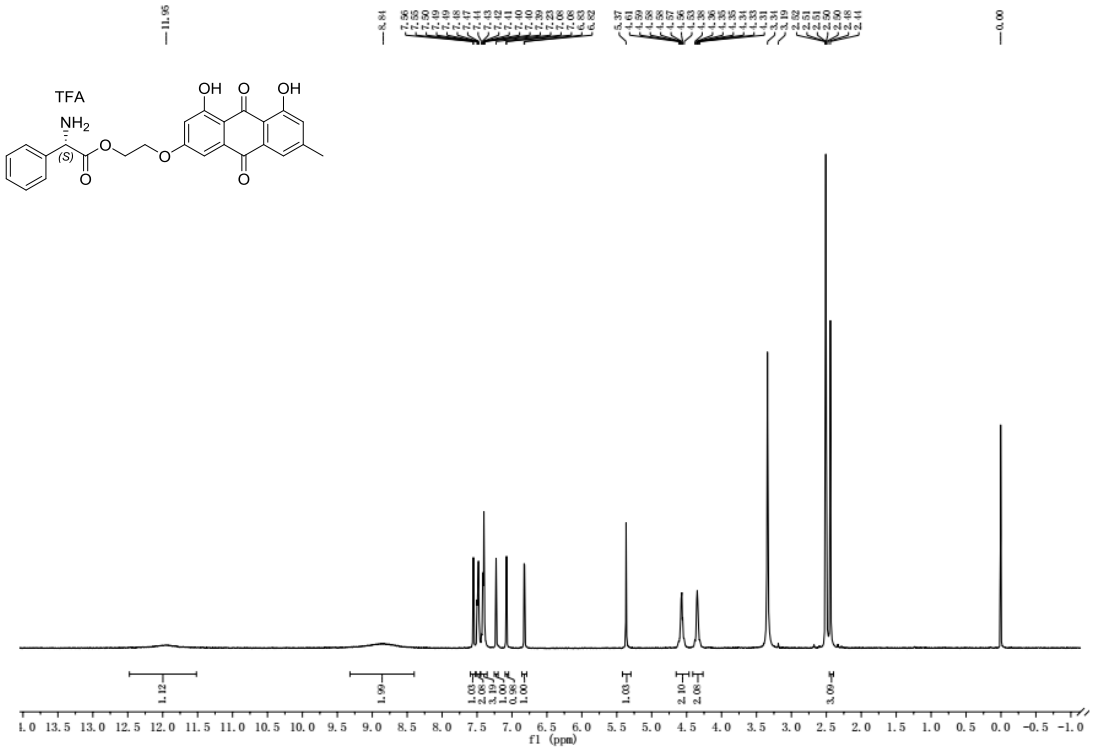

Figure S54. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **3r**.

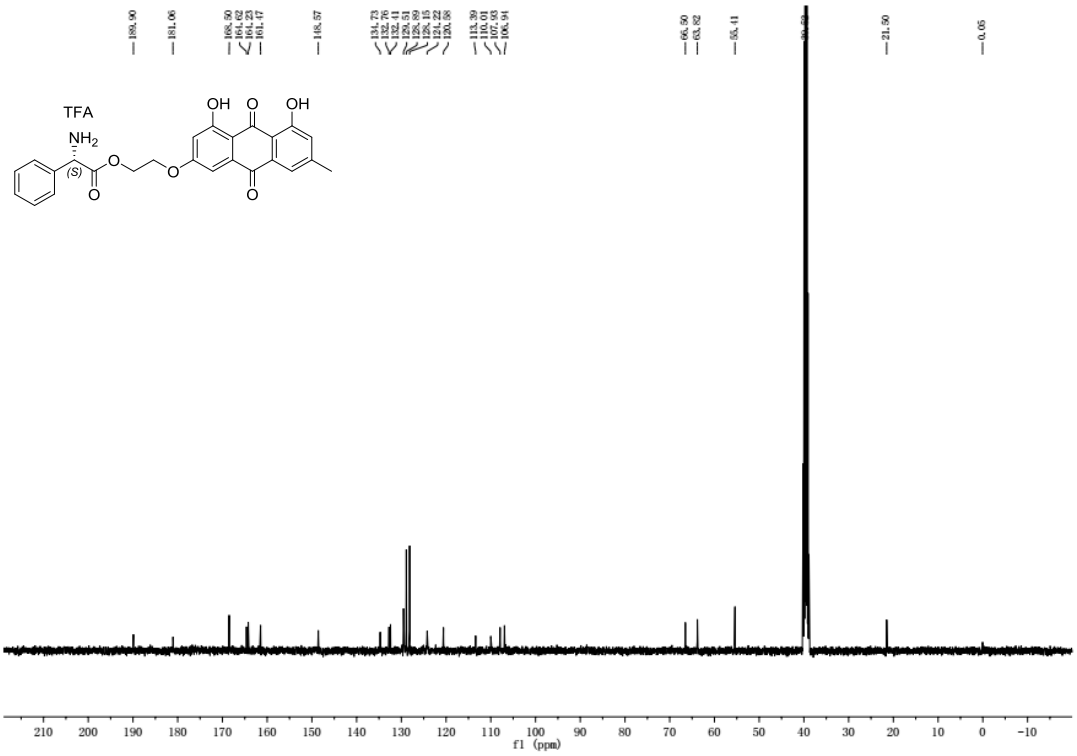

Figure S55. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **3r**.

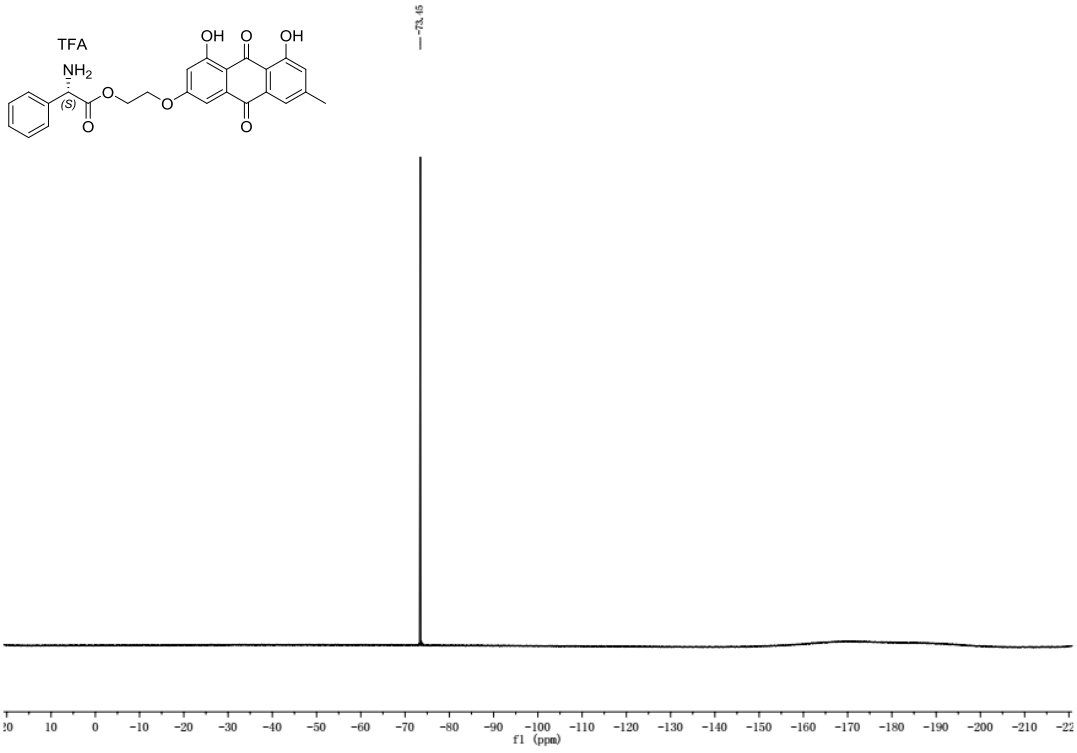

Figure S56. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **3r**.

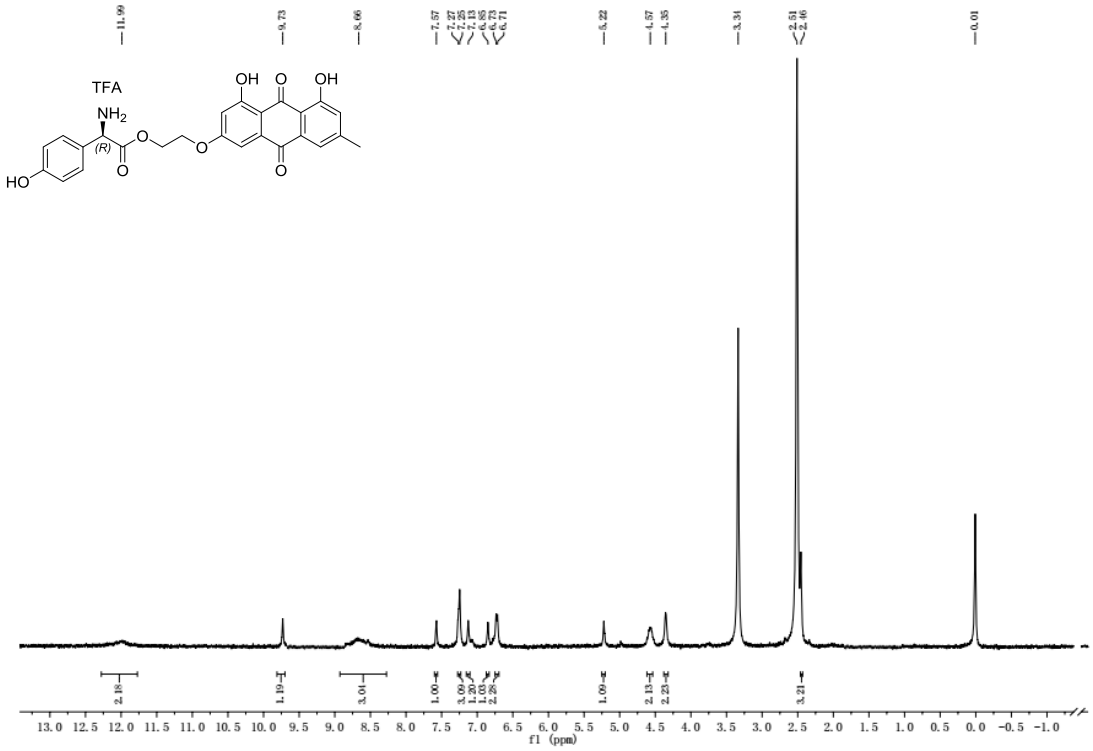

Figure S57. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **3s**.

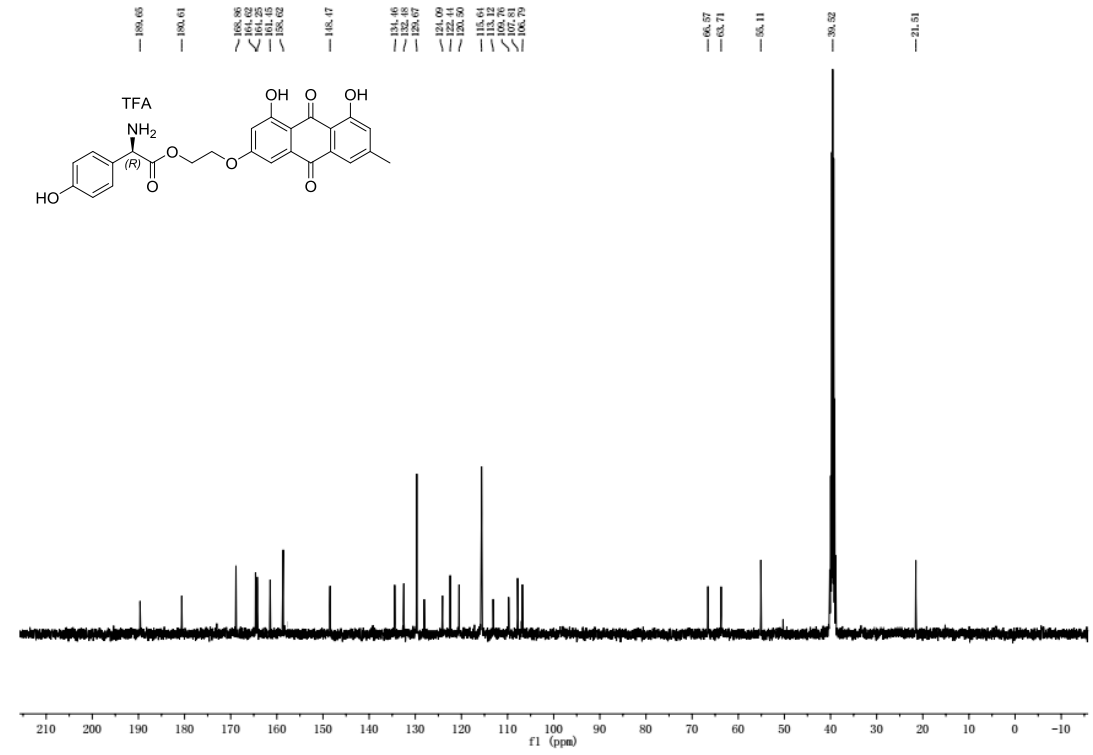

Figure S58. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **3s**.

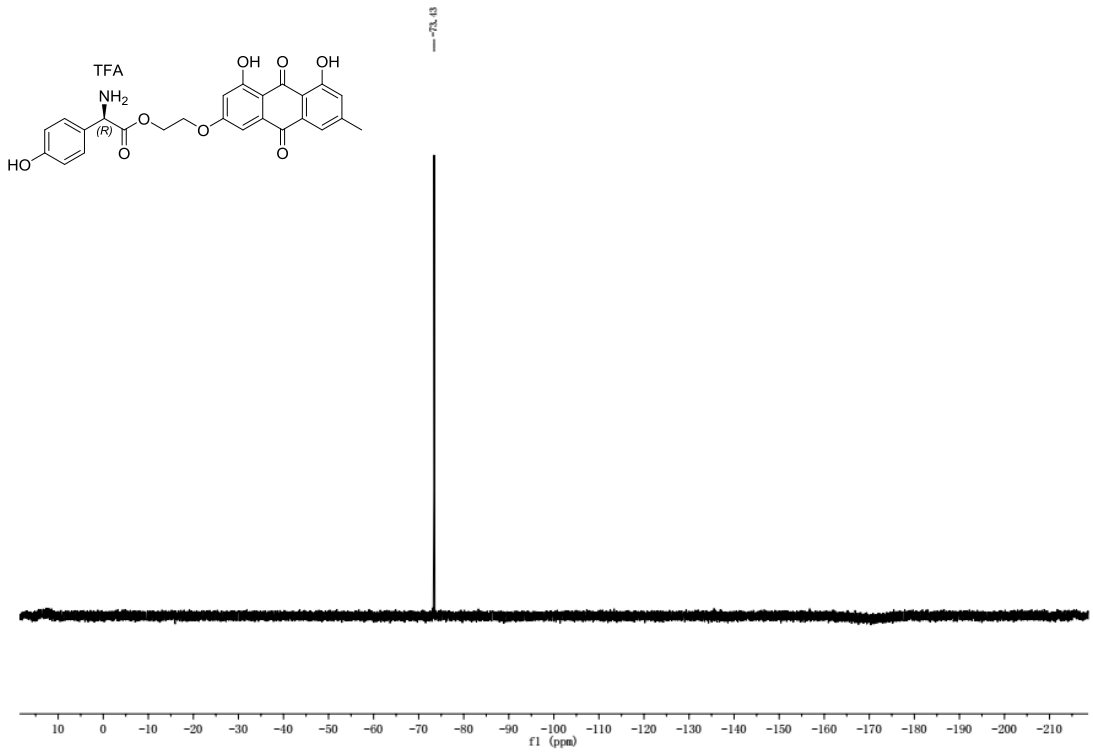

Figure S59. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **3s**.

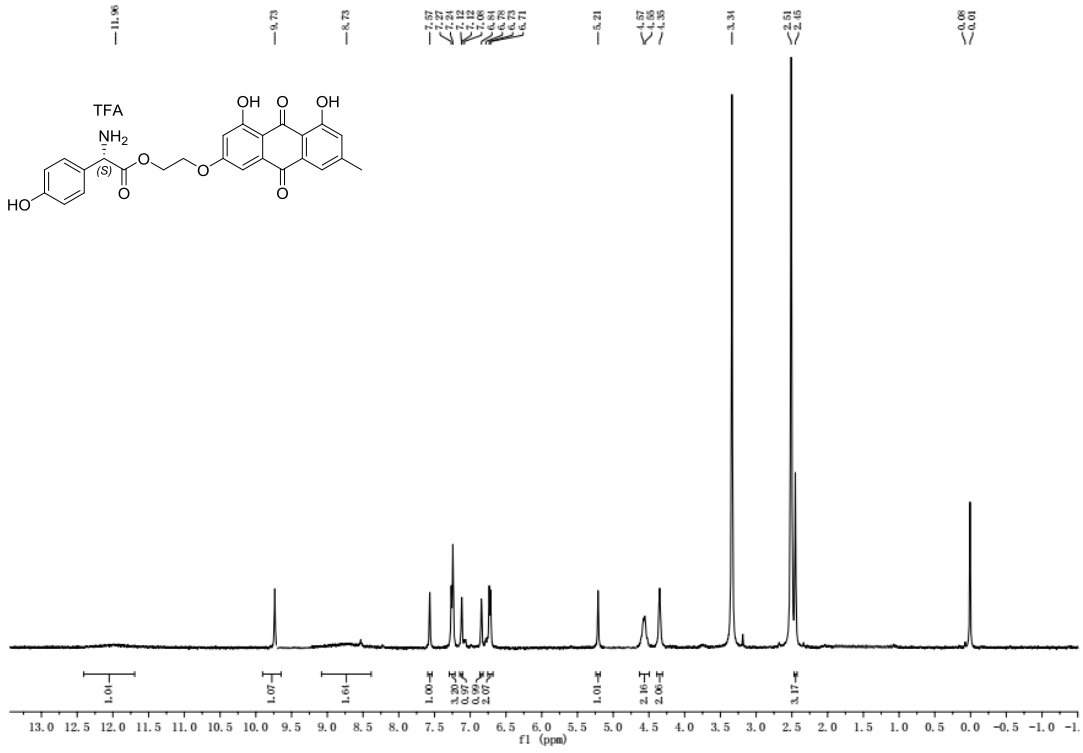

Figure S60. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **3t**.

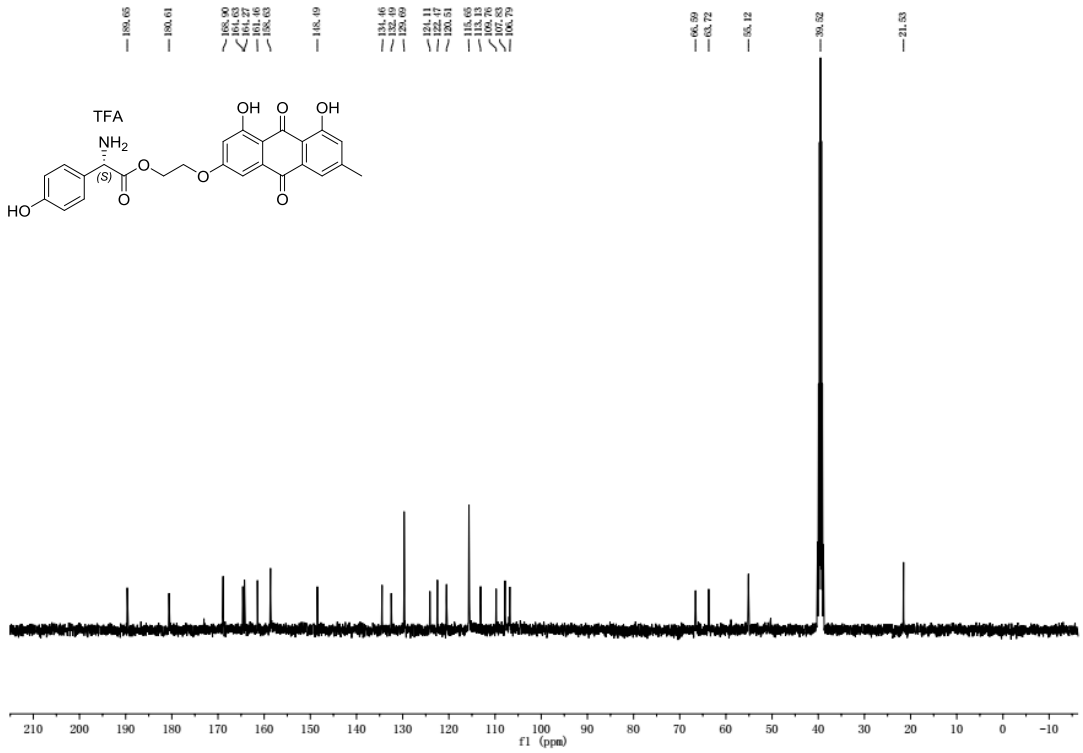

Figure S61. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **3t**.

Figure S62. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **3t**.

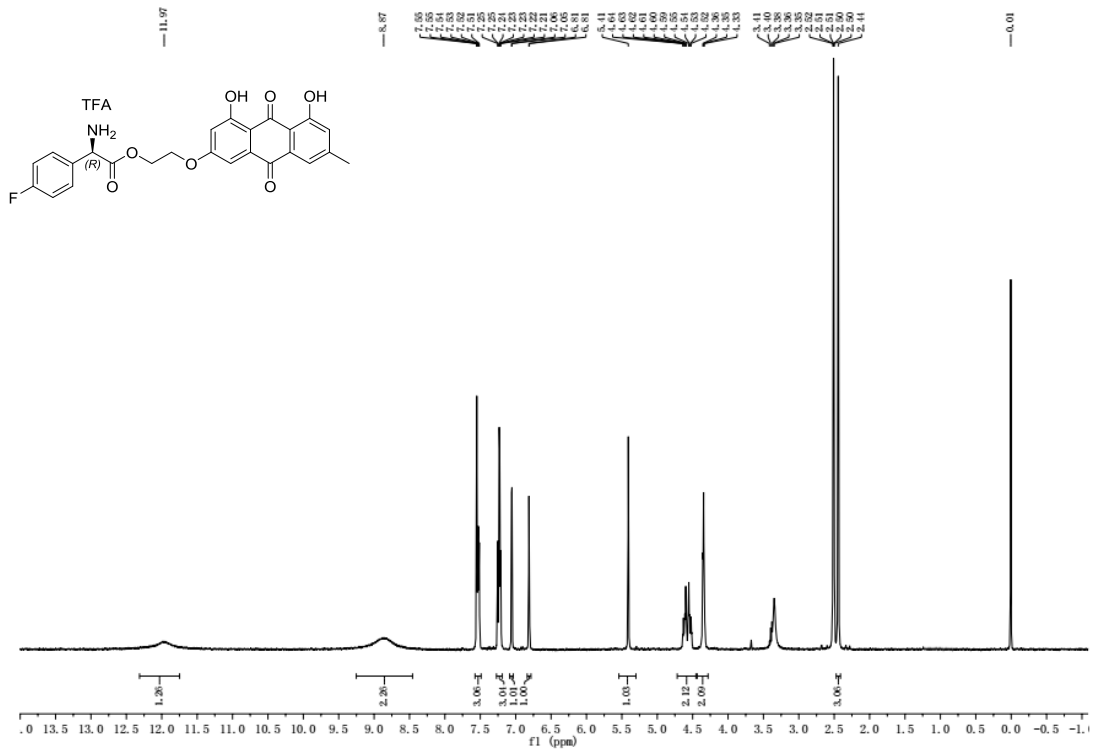

Figure S63. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **3u**.

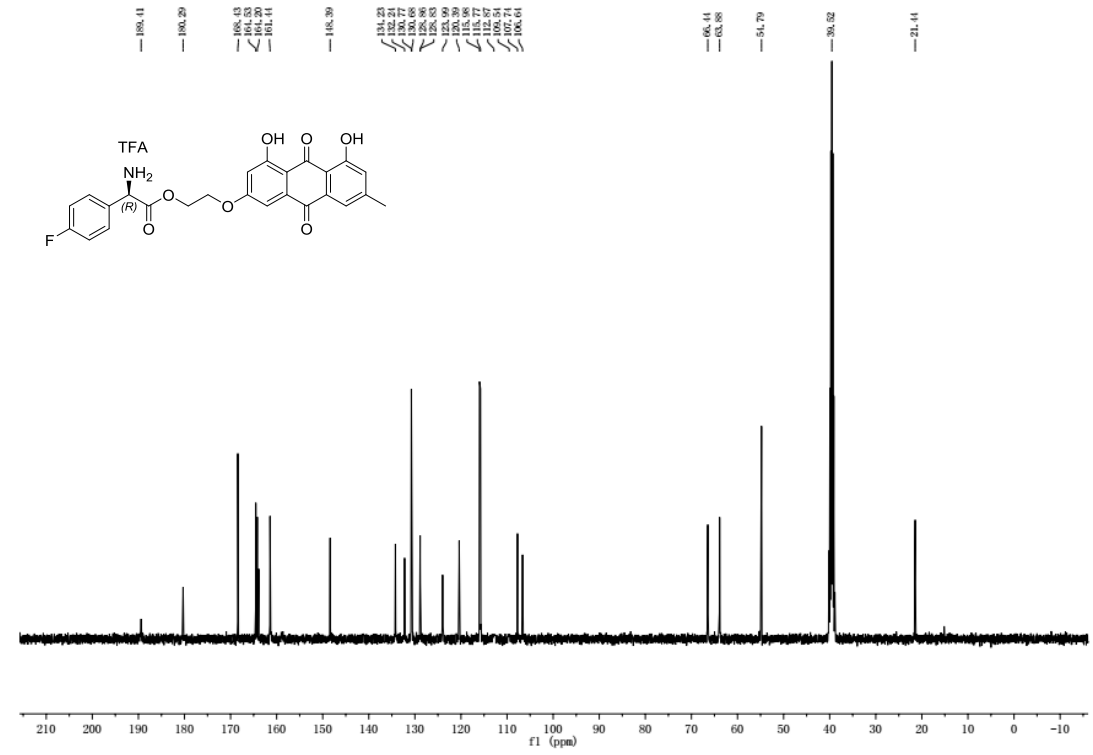

Figure S64. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **3u**.

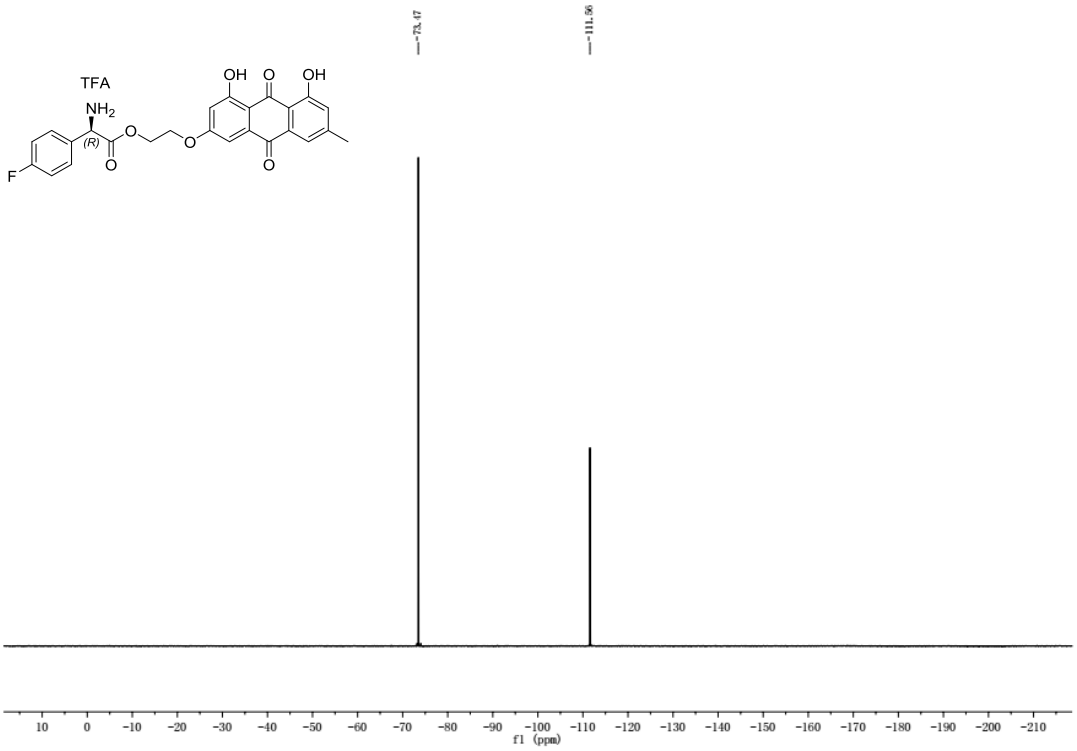

Figure S65. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **3u**.

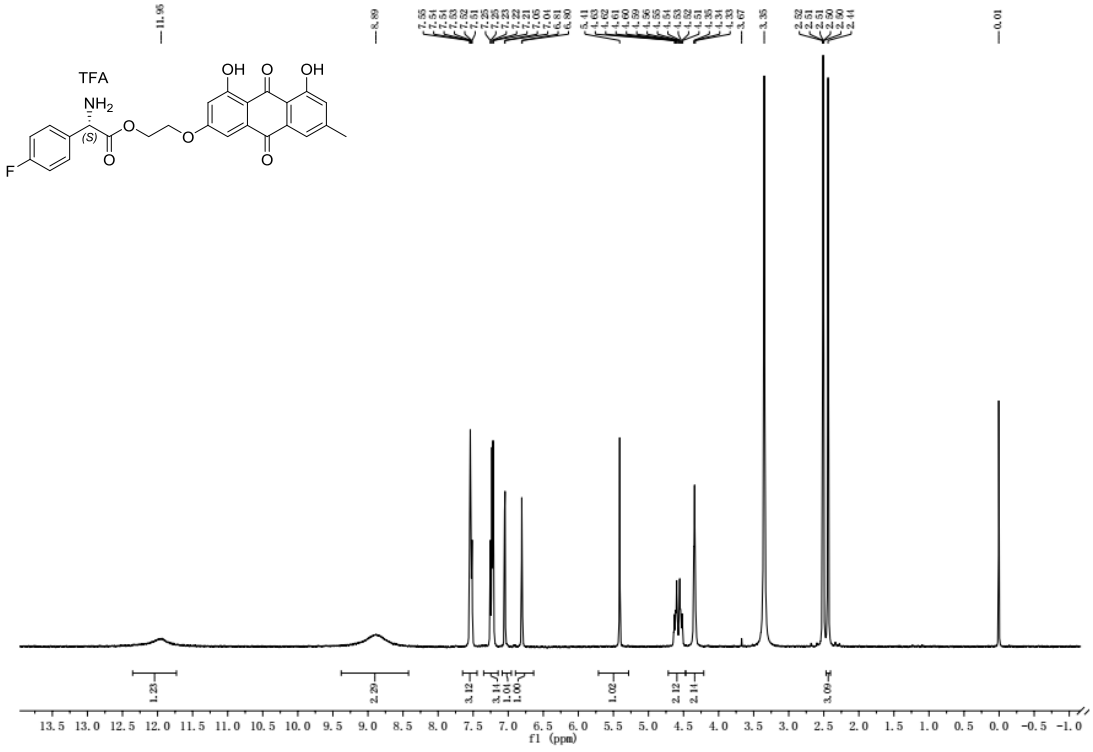

Figure S66. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **3v**.

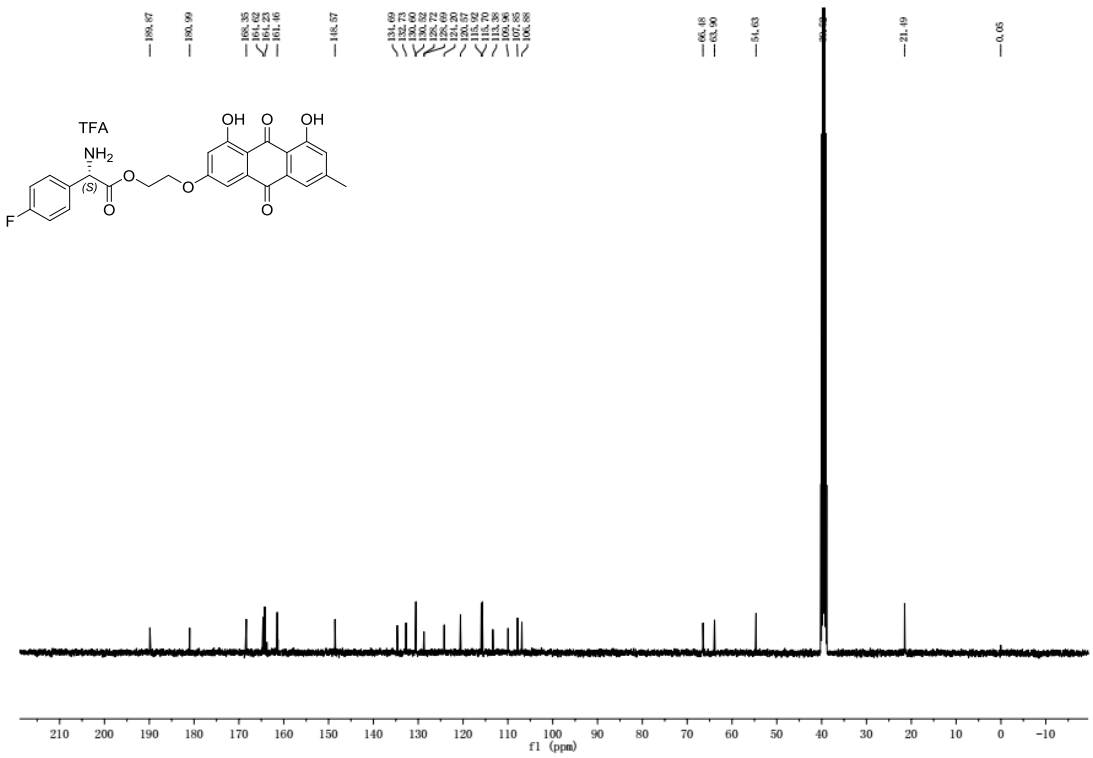

Figure S67. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **3v**.

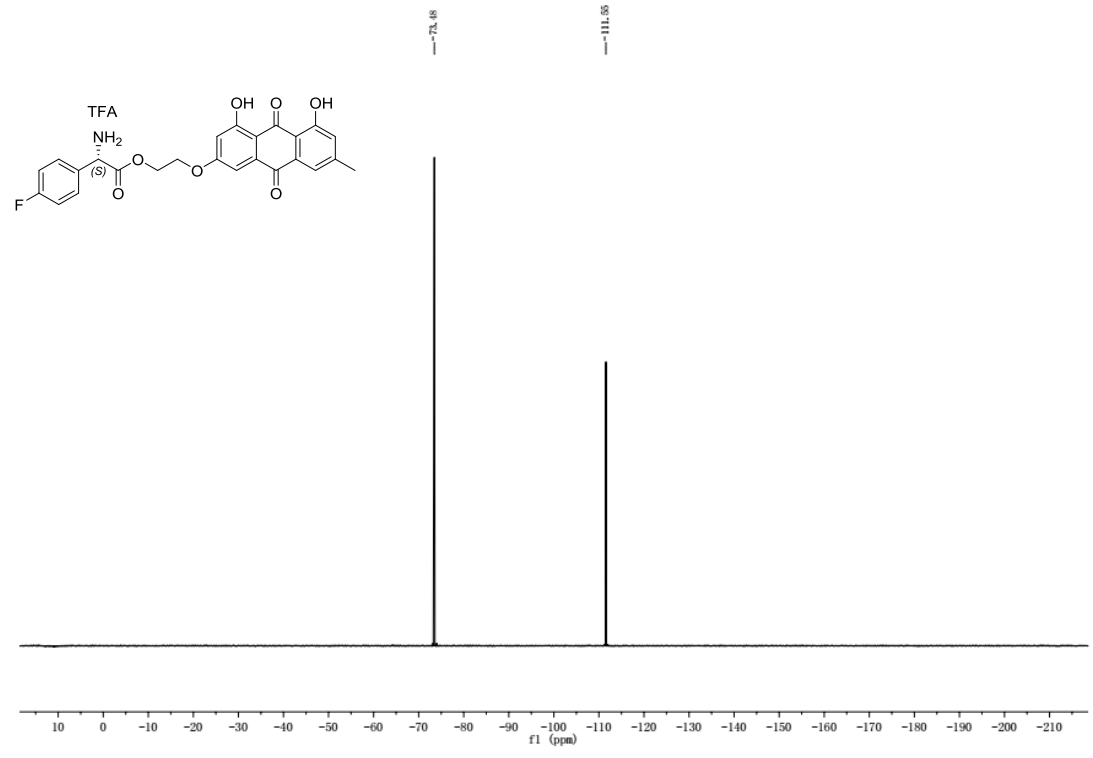

Figure S68. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **3v**.

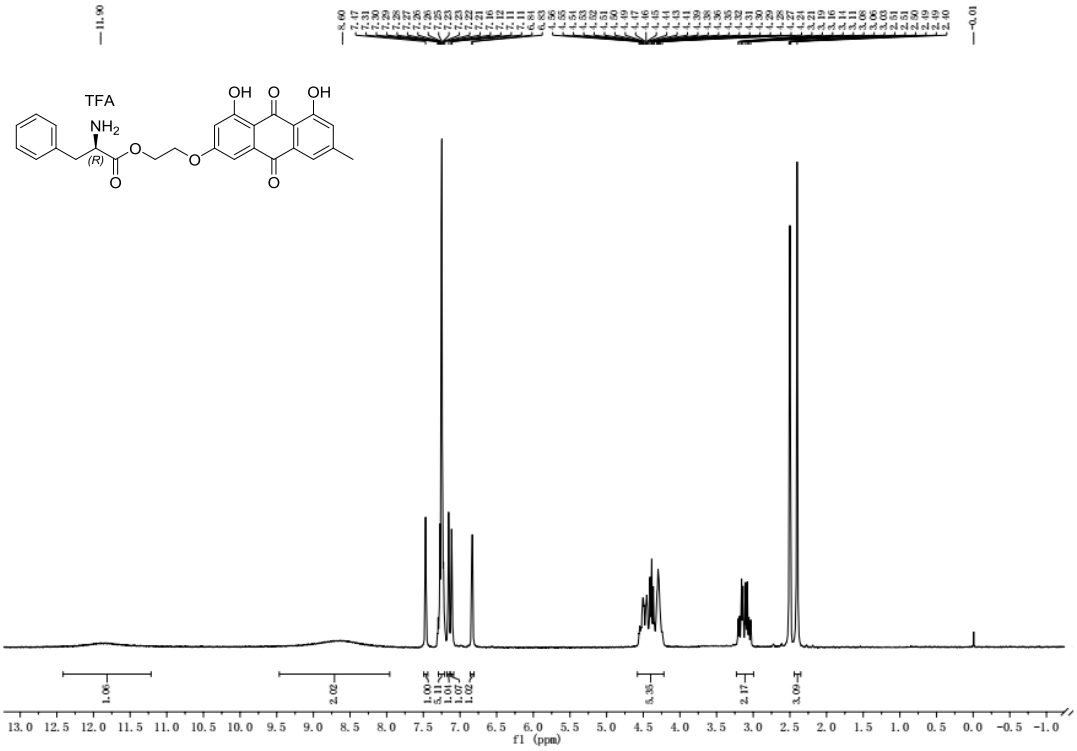

Figure S69. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **3w**.

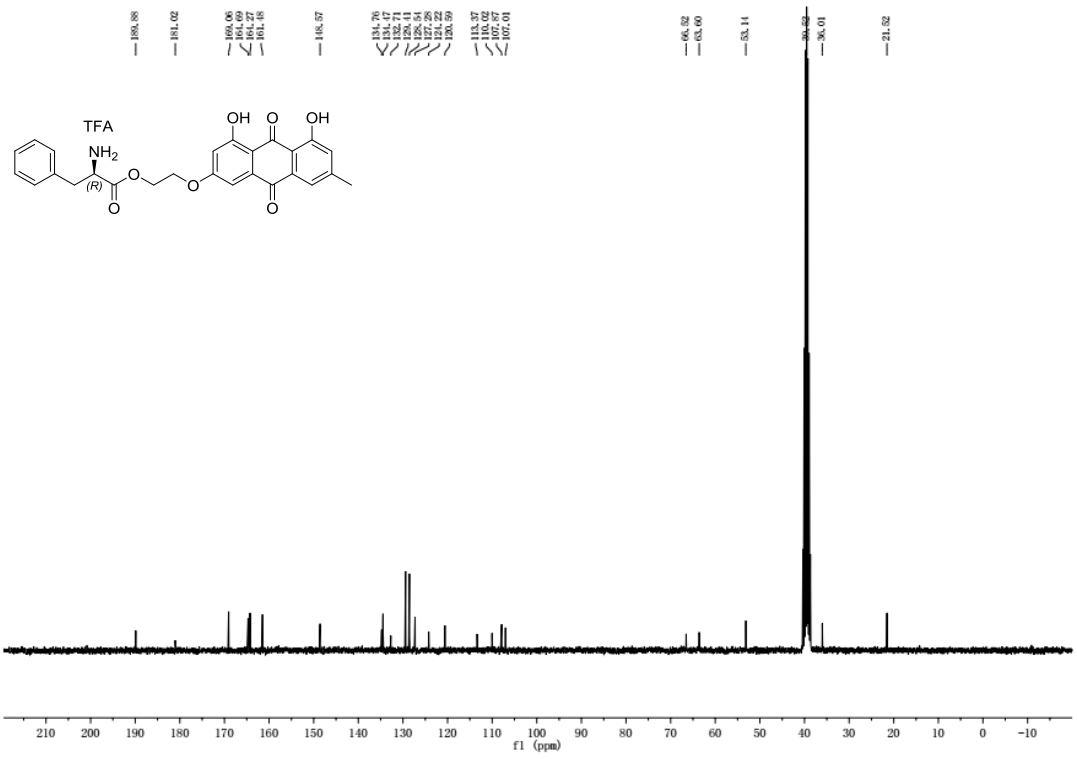

Figure S70. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **3w**.

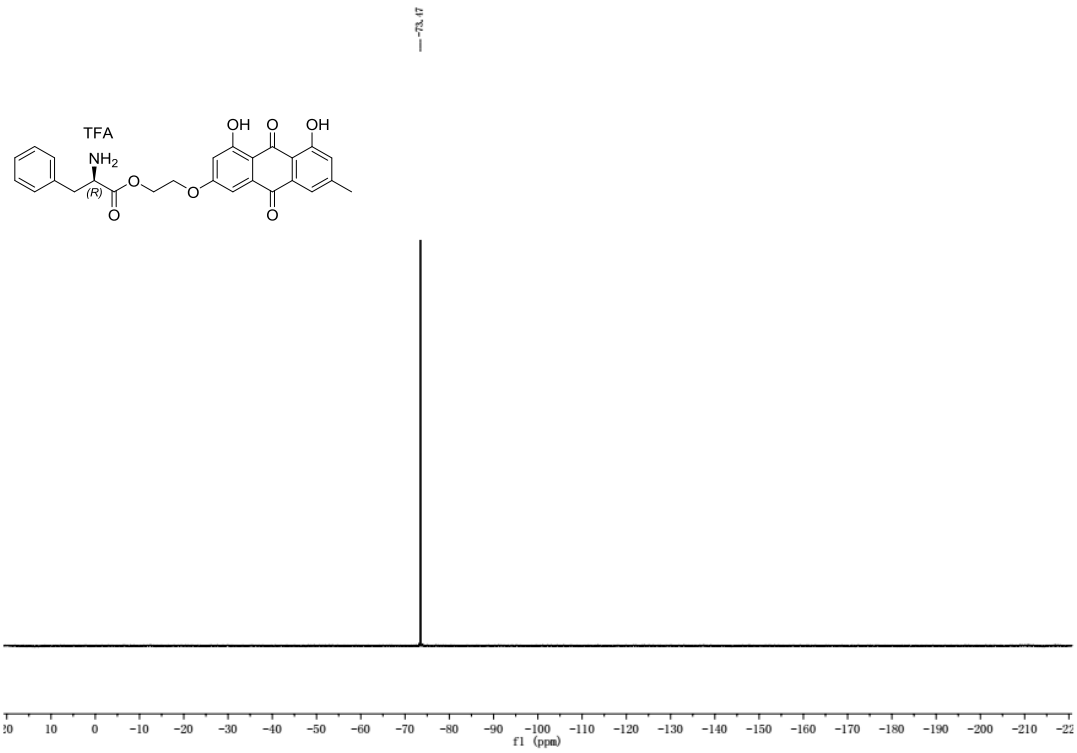

Figure S71. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **3w**.

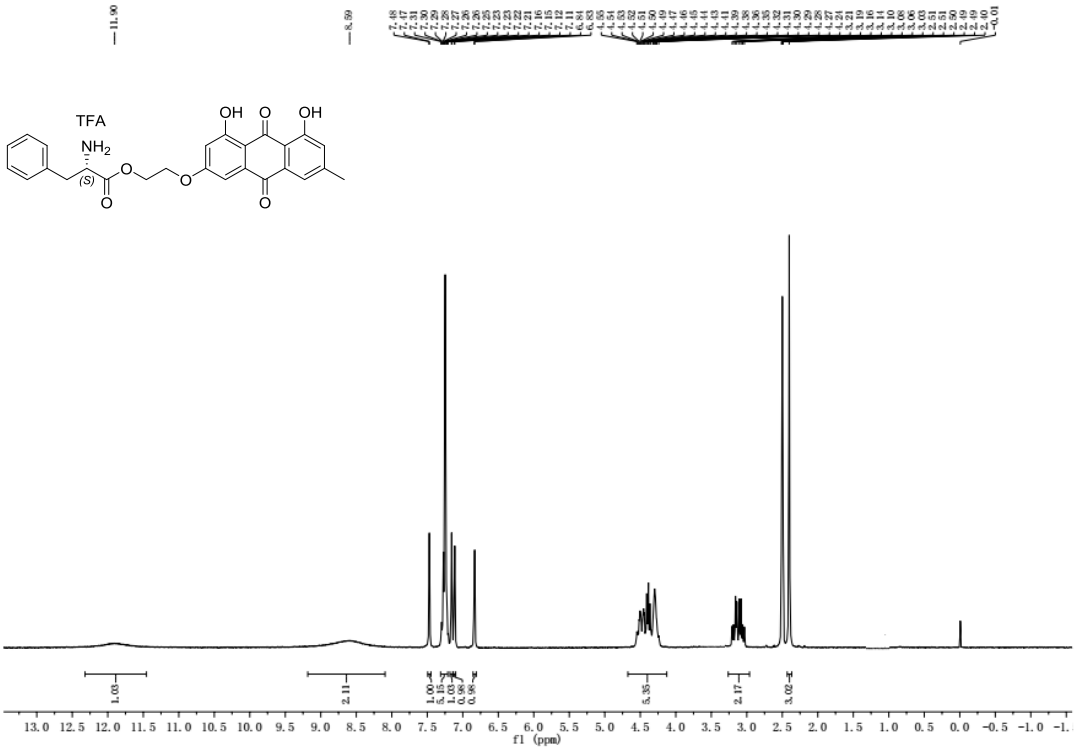

Figure S72. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **3x**.

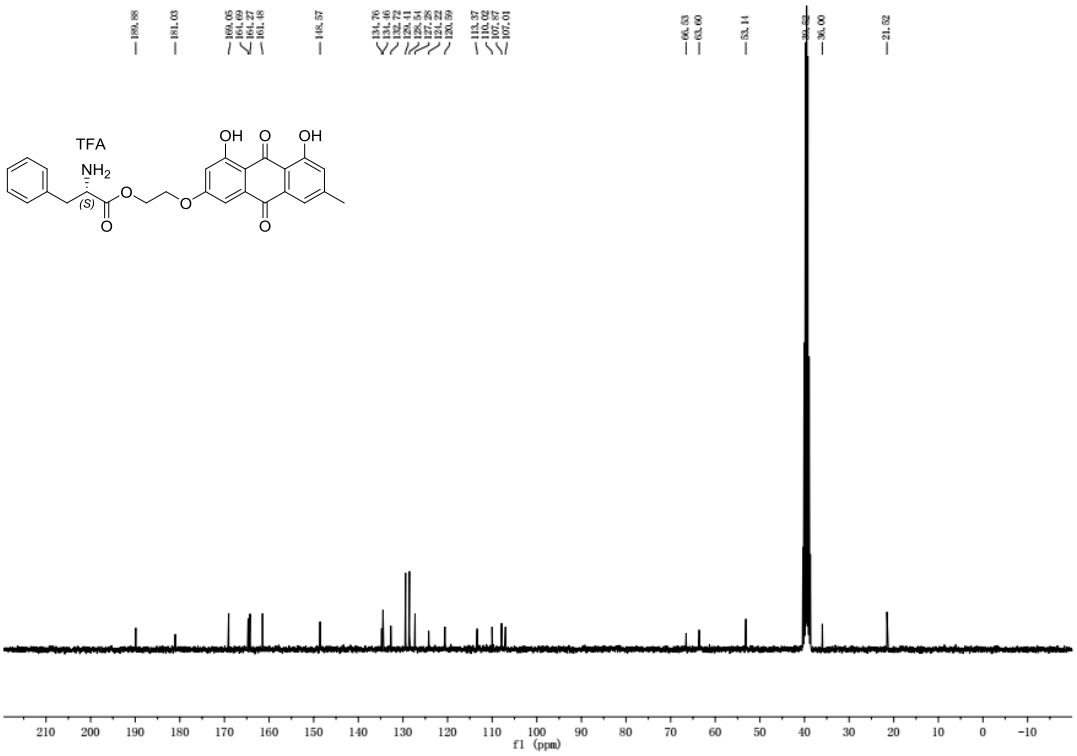

Figure S73. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **3x**.

Figure S74. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **3x**.

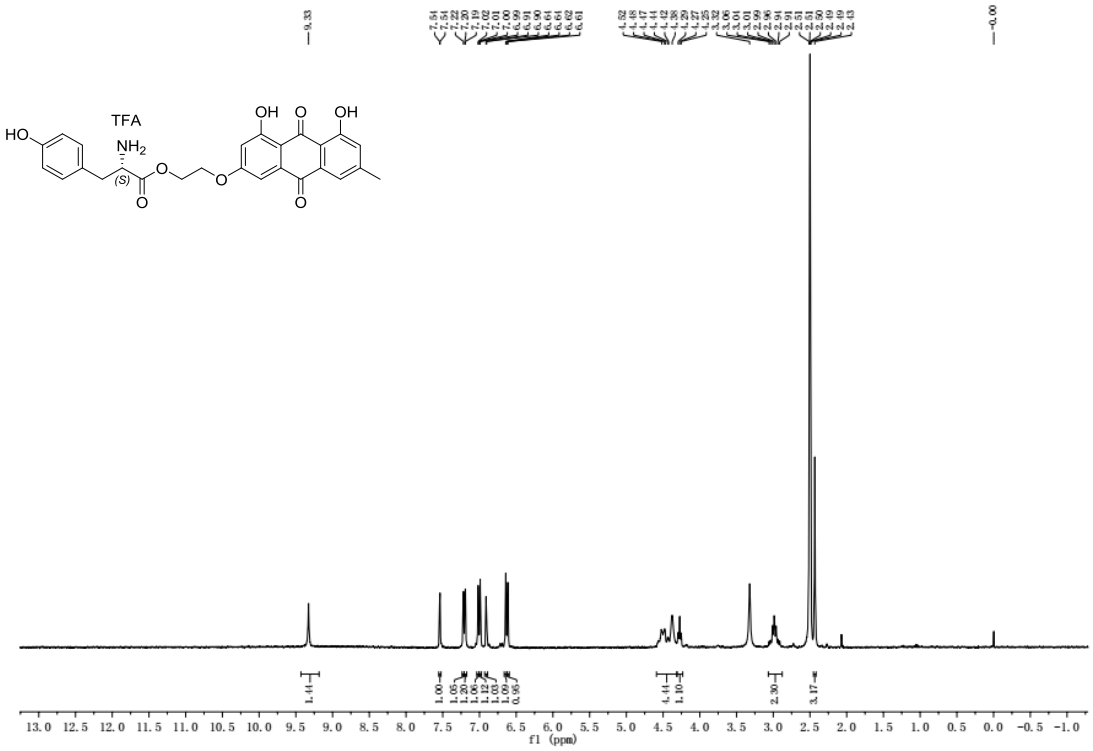

Figure S75. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **3y**.

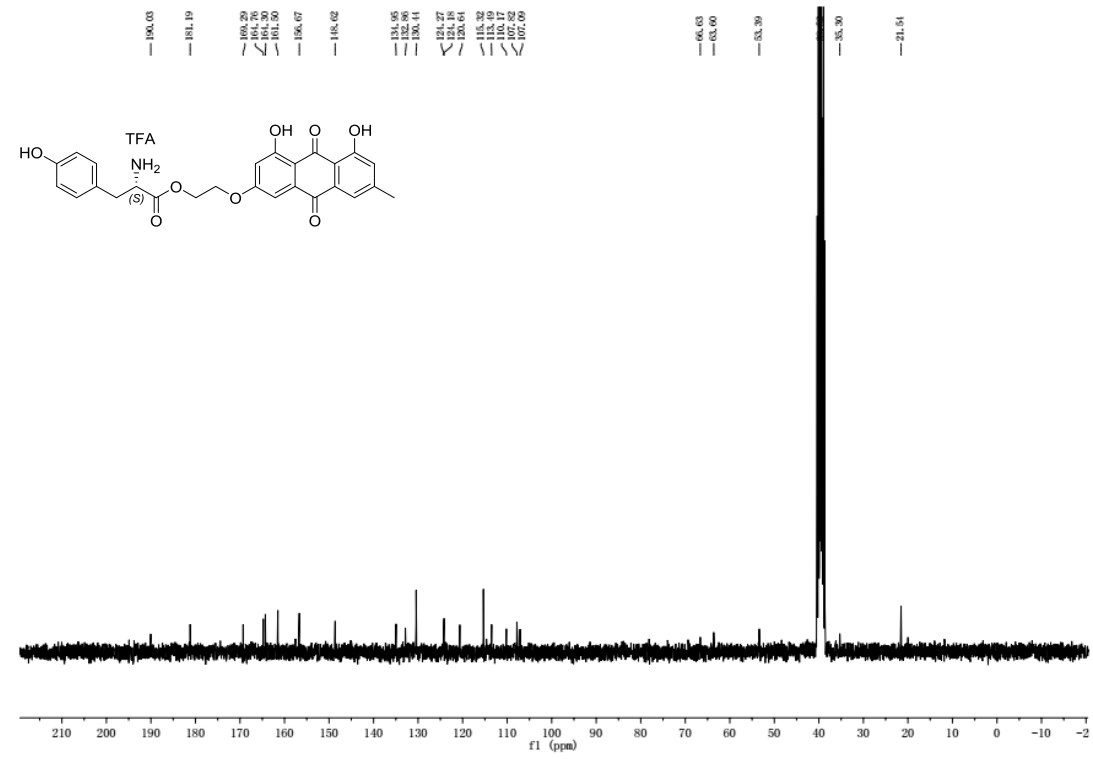

Figure S76. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **3y**.

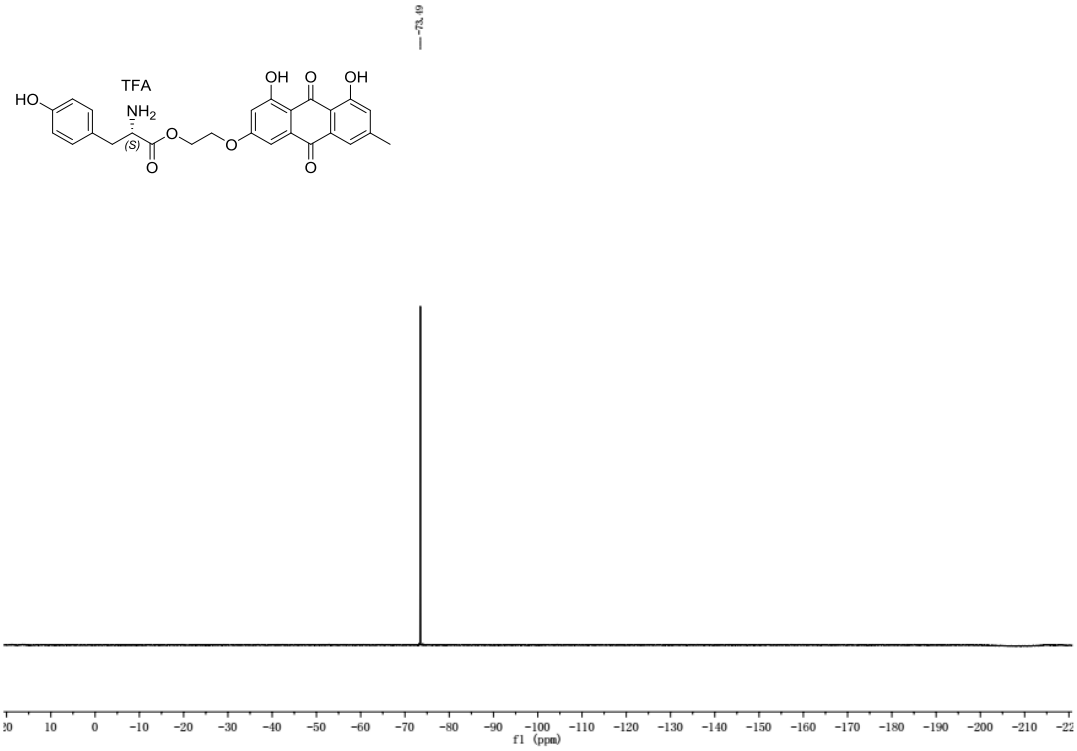

Figure S77. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **3y**.

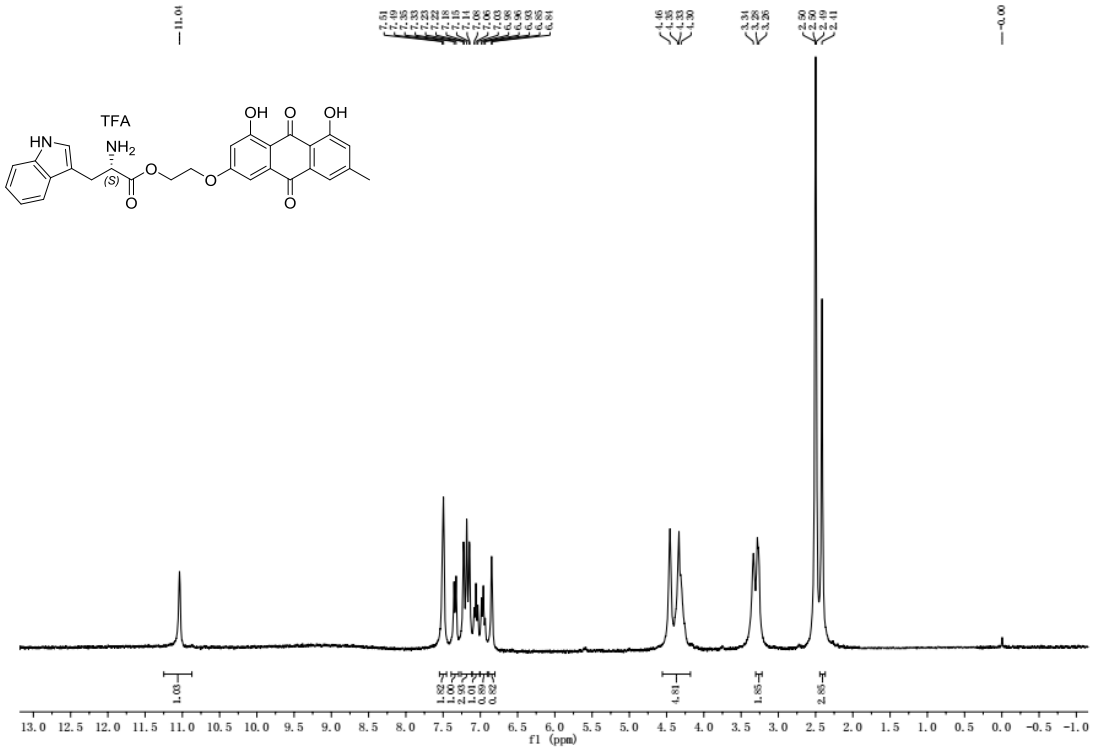

Figure S78. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **3z**.

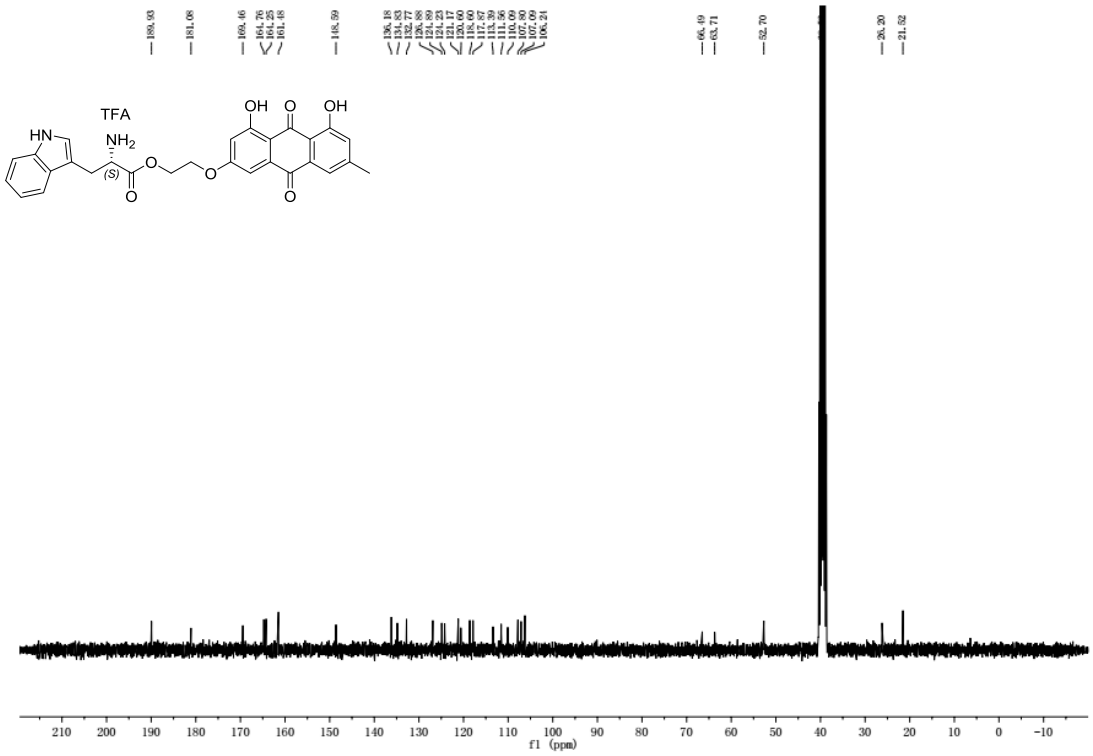

Figure S79. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **3z**.

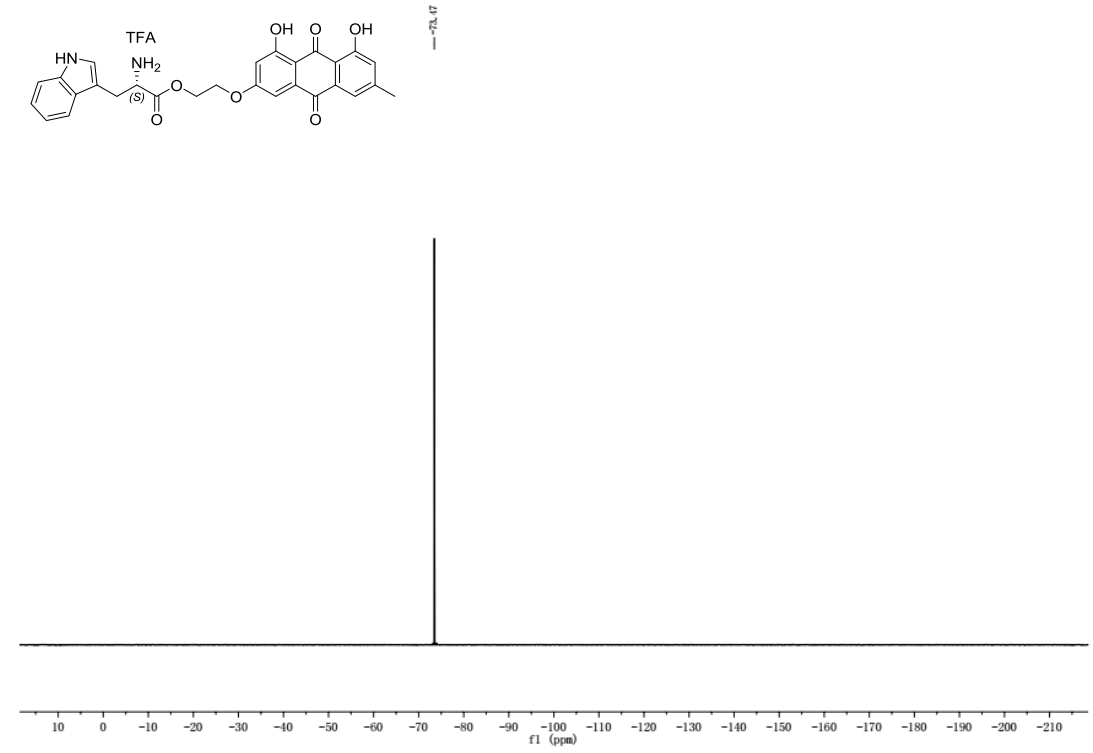

Figure S80. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **3z**.

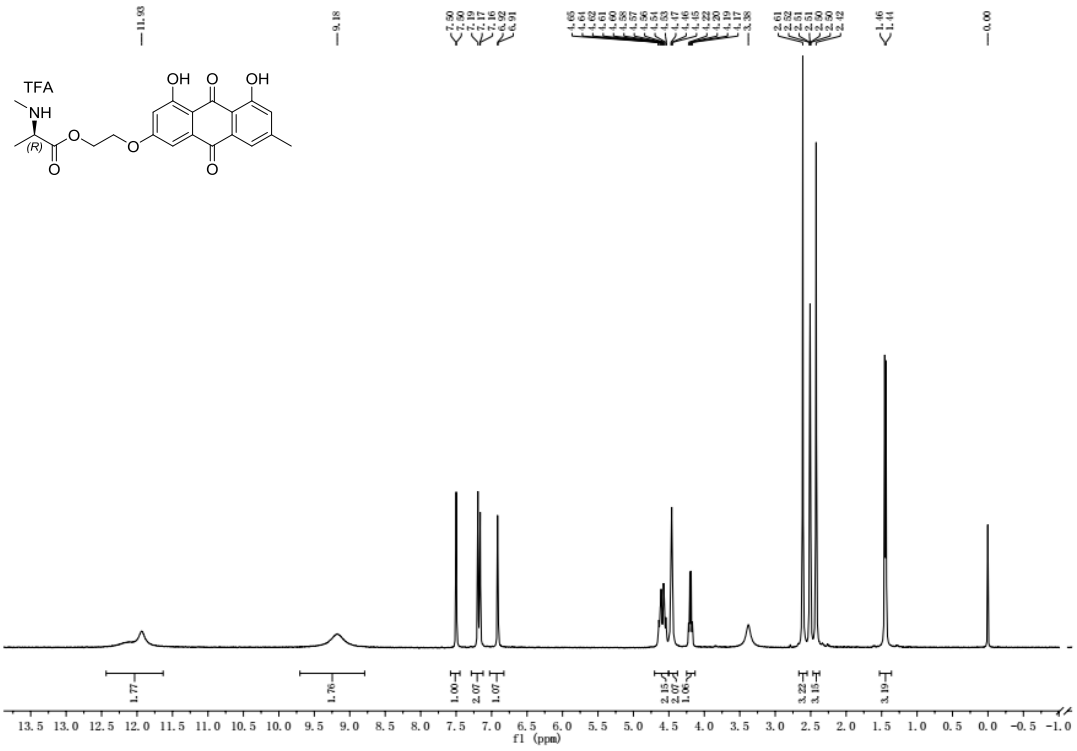

Figure S81. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **4a**.

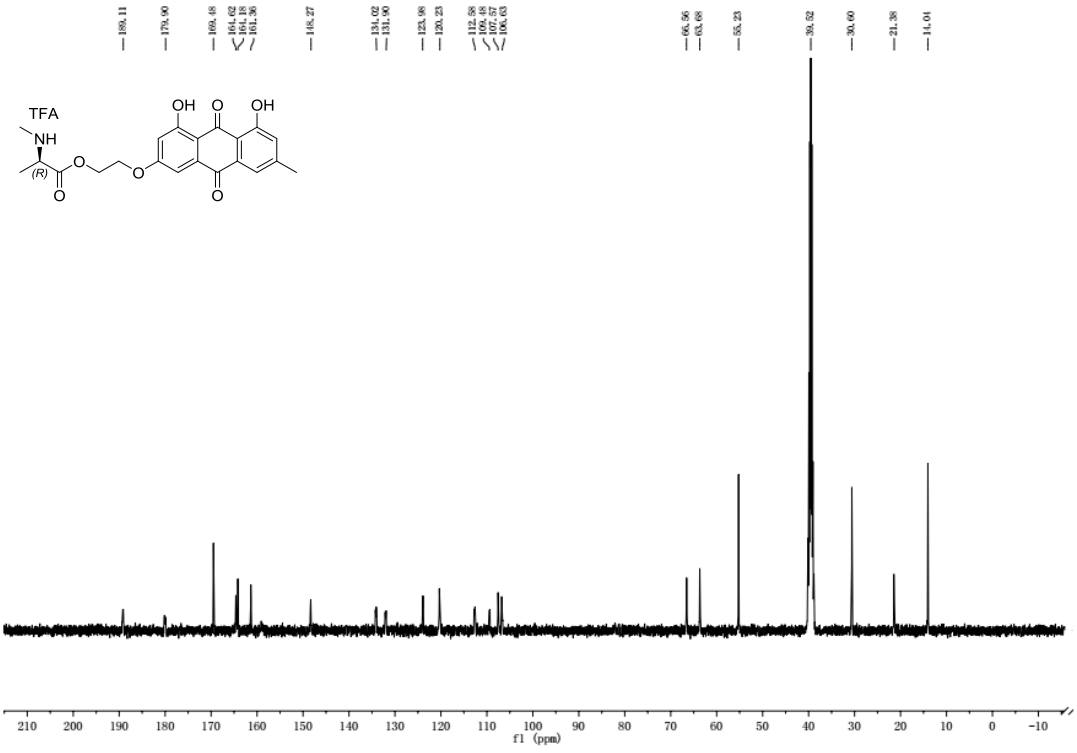

Figure S82. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **4a**.

Figure S83. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **4a**.

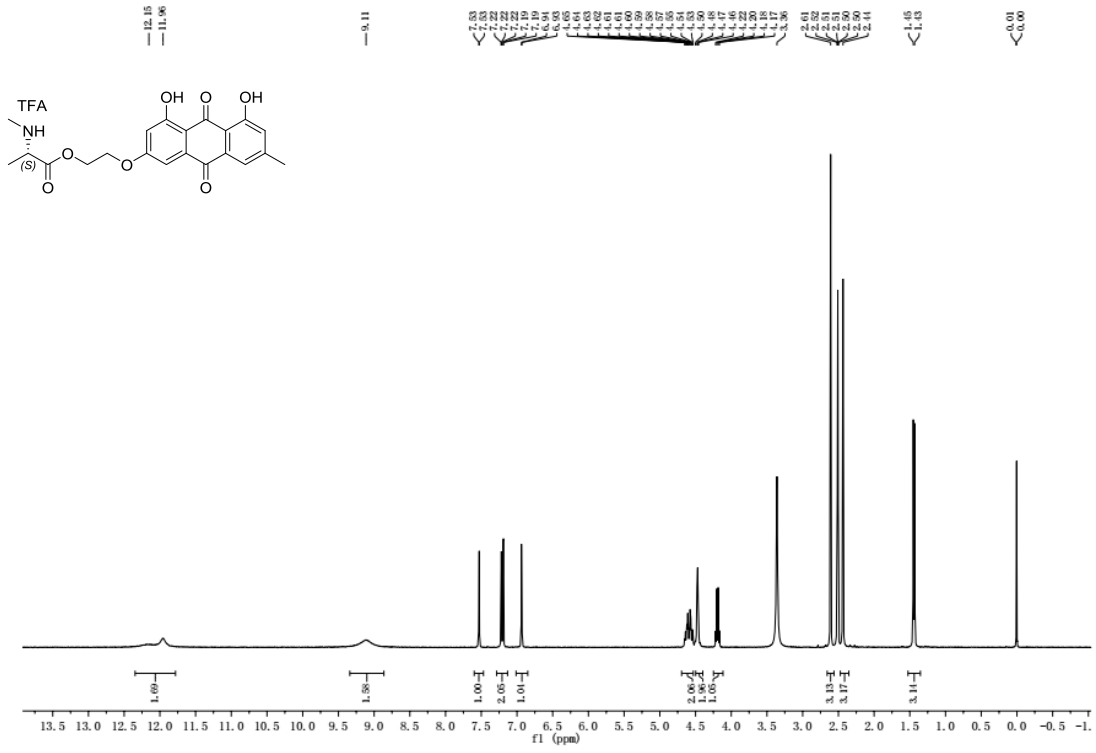

Figure S84. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **4b**.

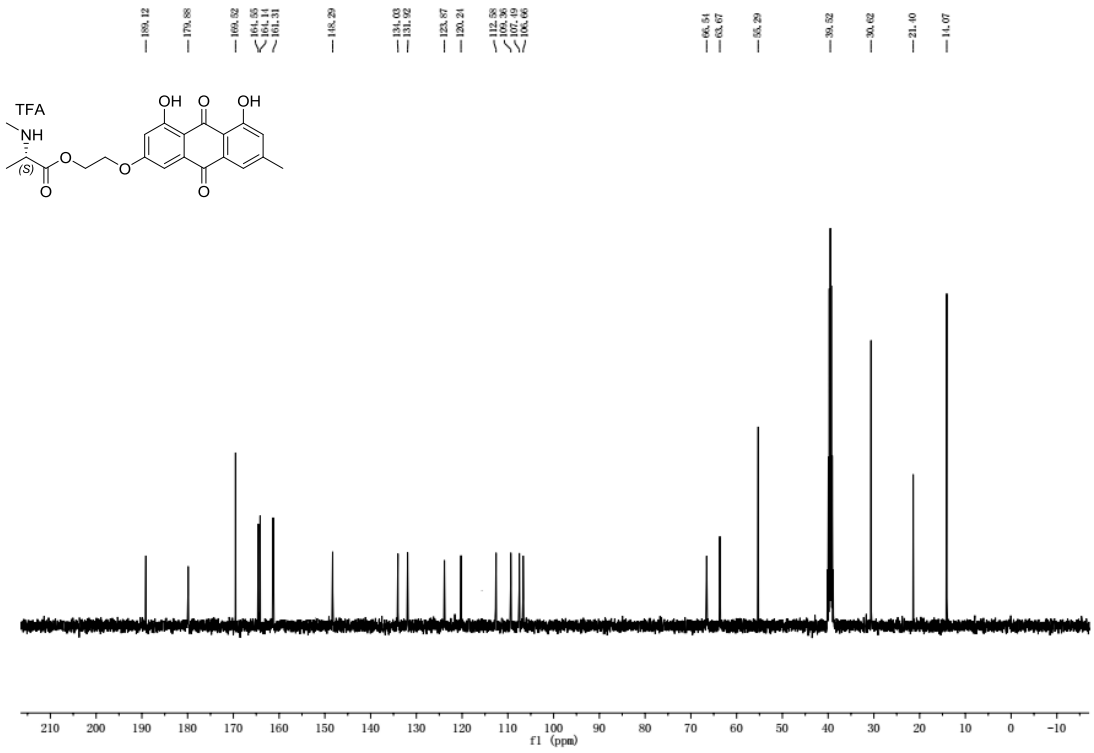

Figure S85. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **4b**.

Figure S86. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **4b**.

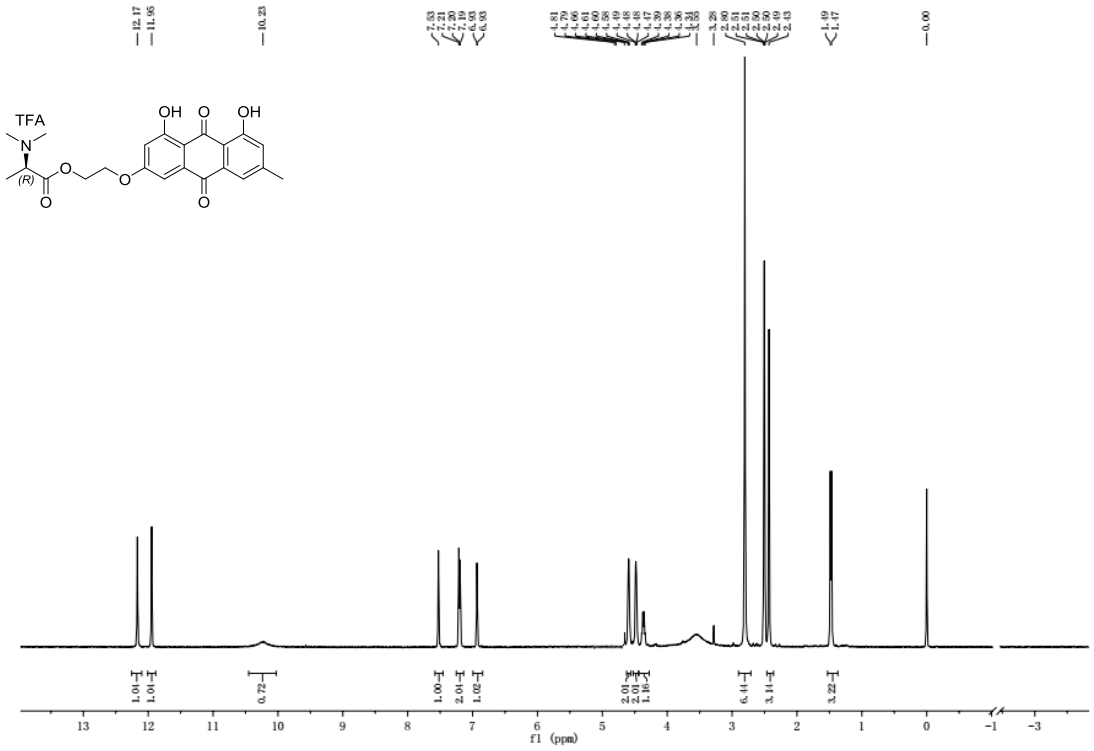

Figure S87. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **5a**.

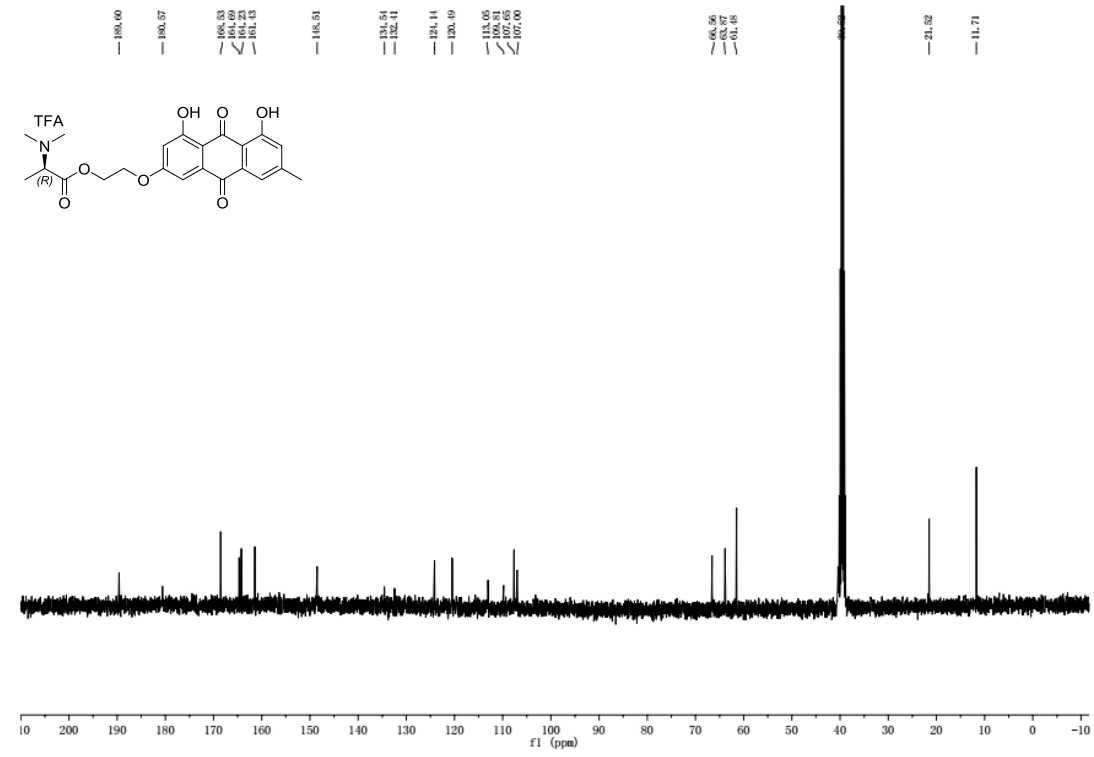

Figure S88. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **5a**.

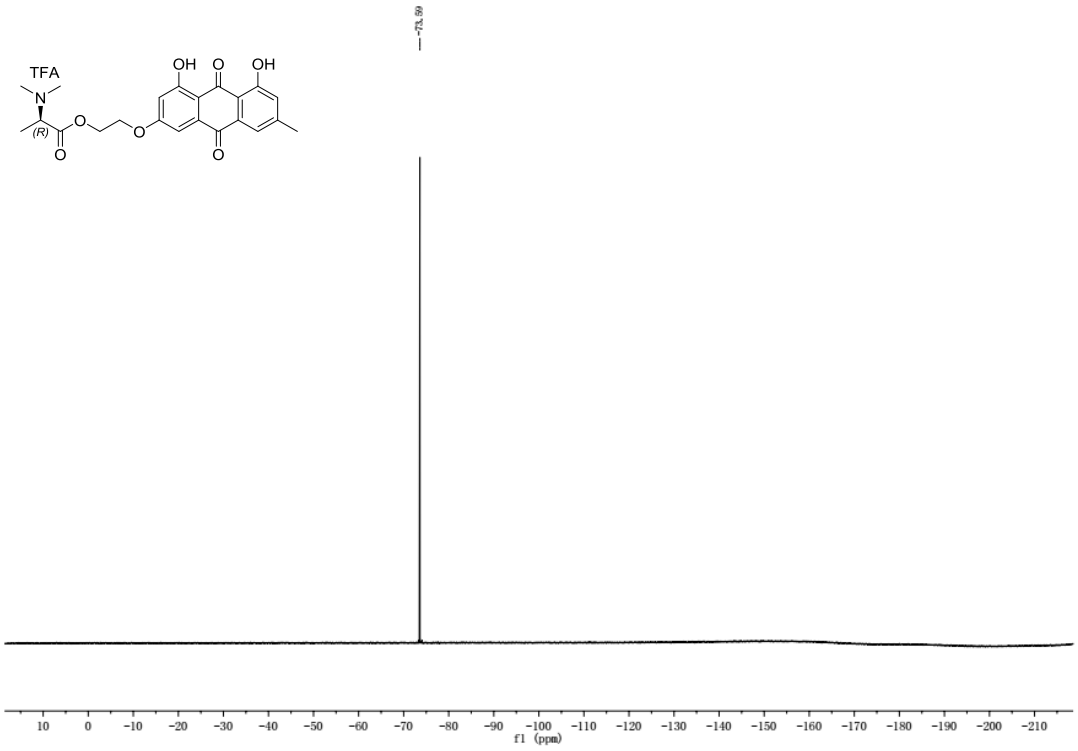

Figure S89. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **5a**.

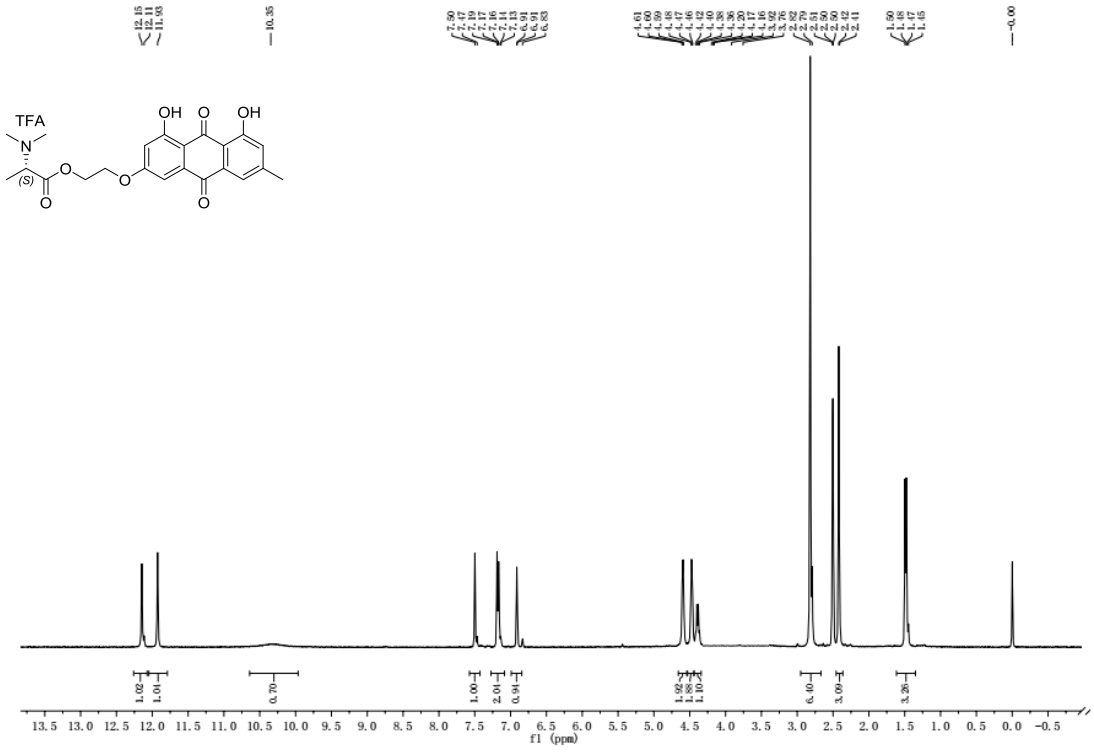

Figure S90. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **5b**.

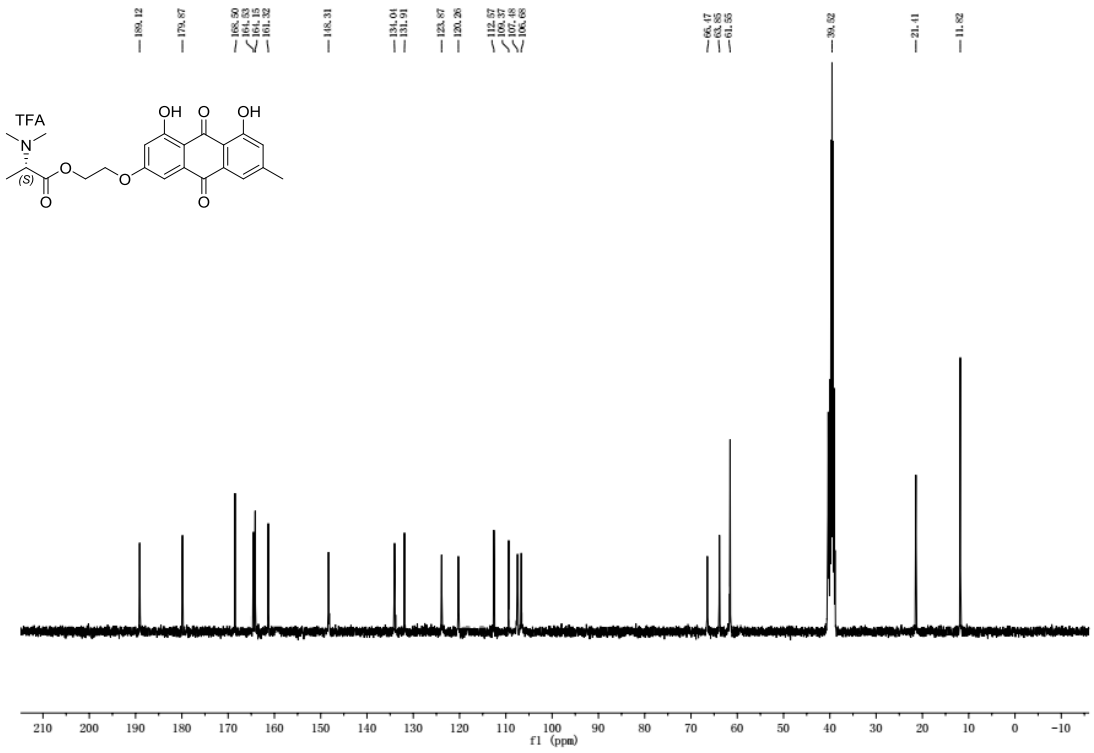

Figure S91. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **5b**.

Figure S92. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **5b**.

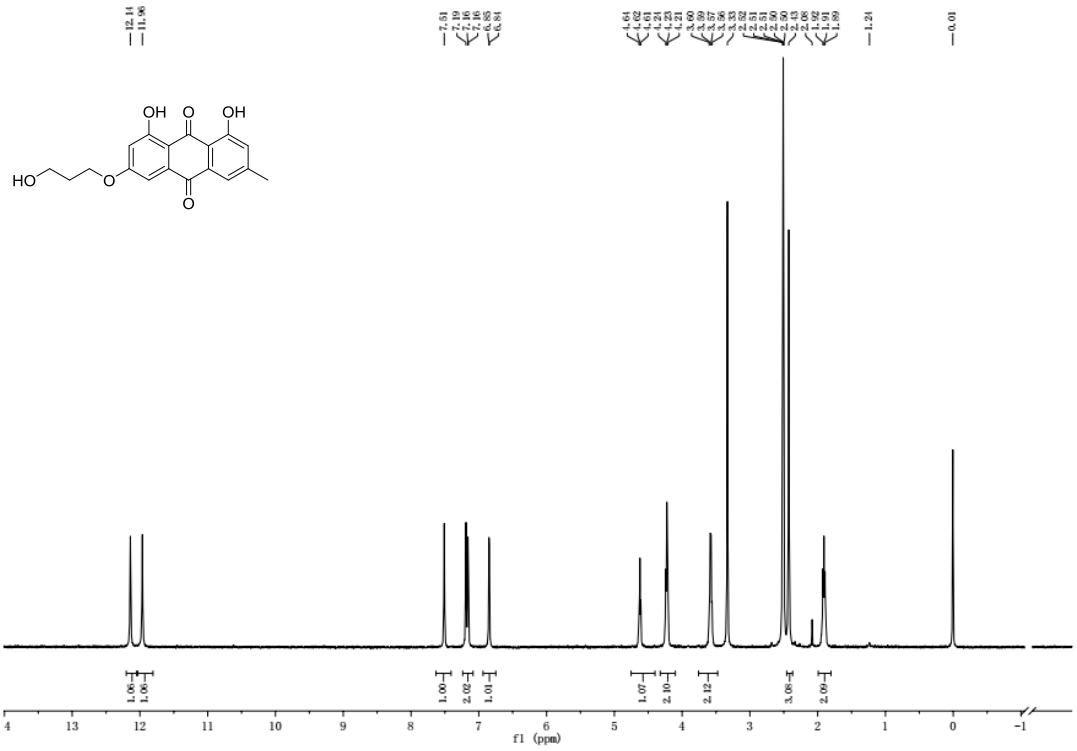

Figure S93. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **6a**.

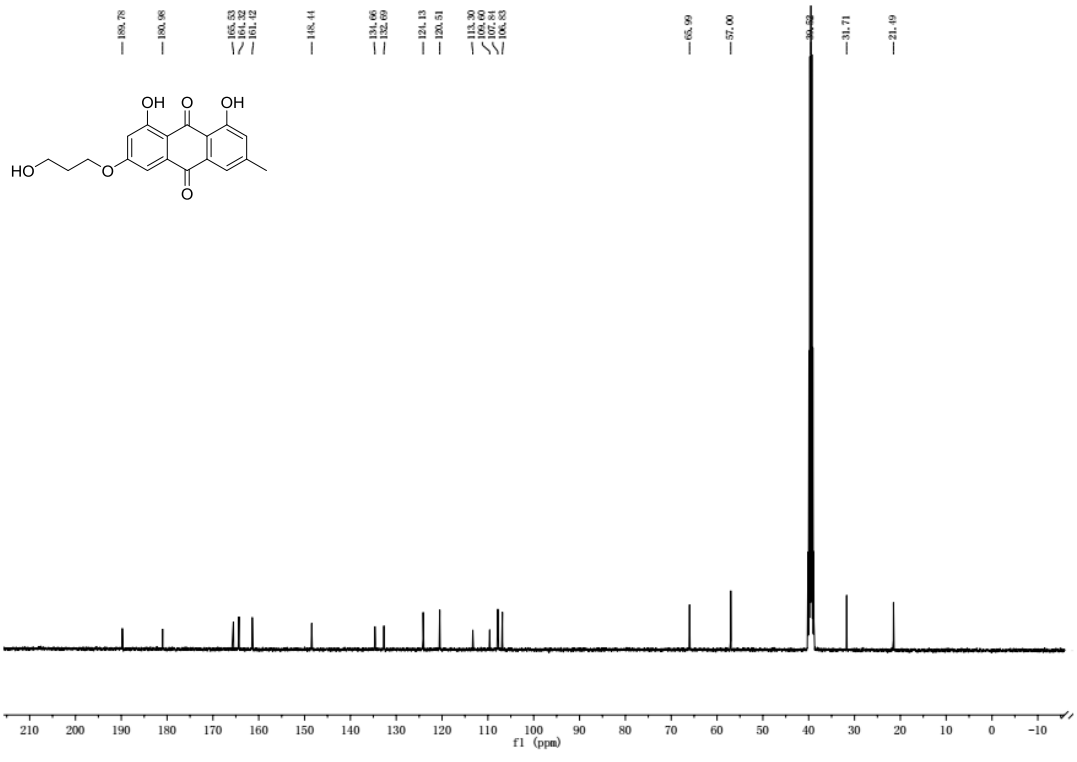

Figure S94. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **6a**.

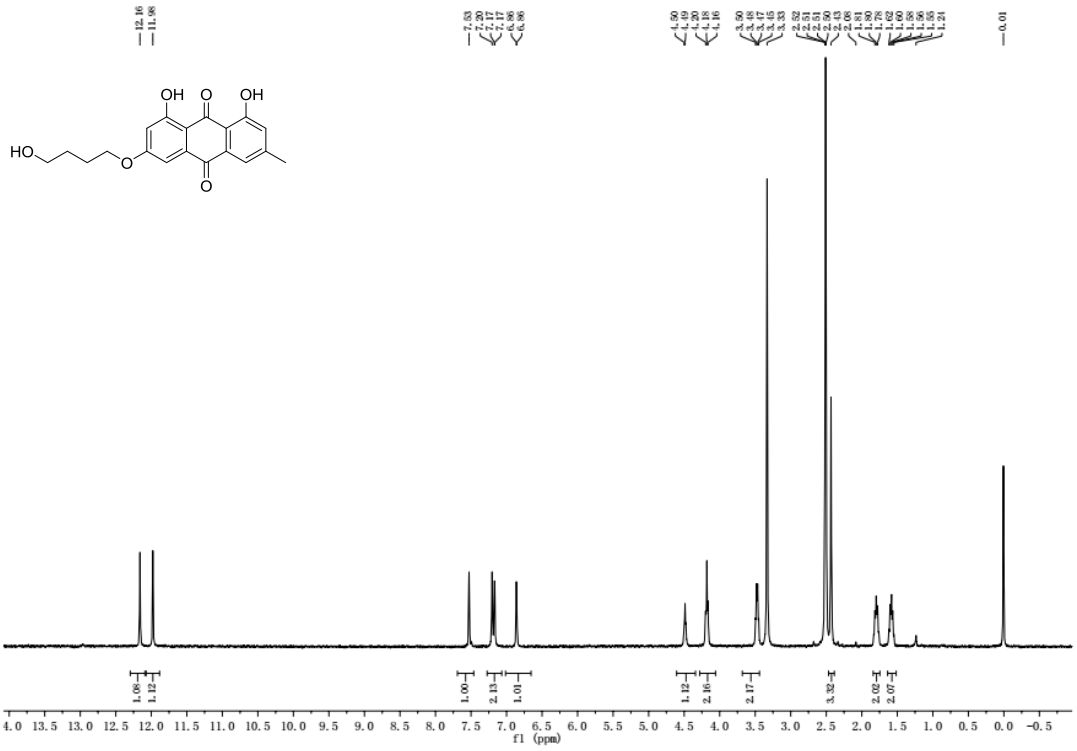

Figure S95. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **6b**.

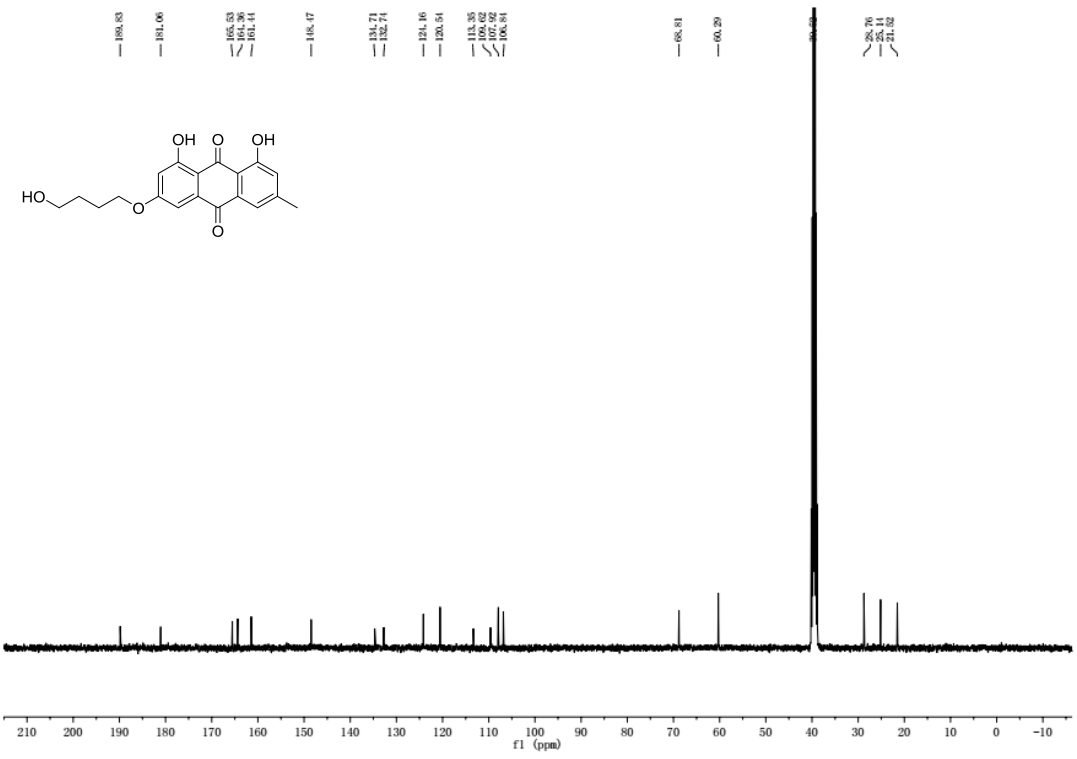

Figure S96. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **6b**.

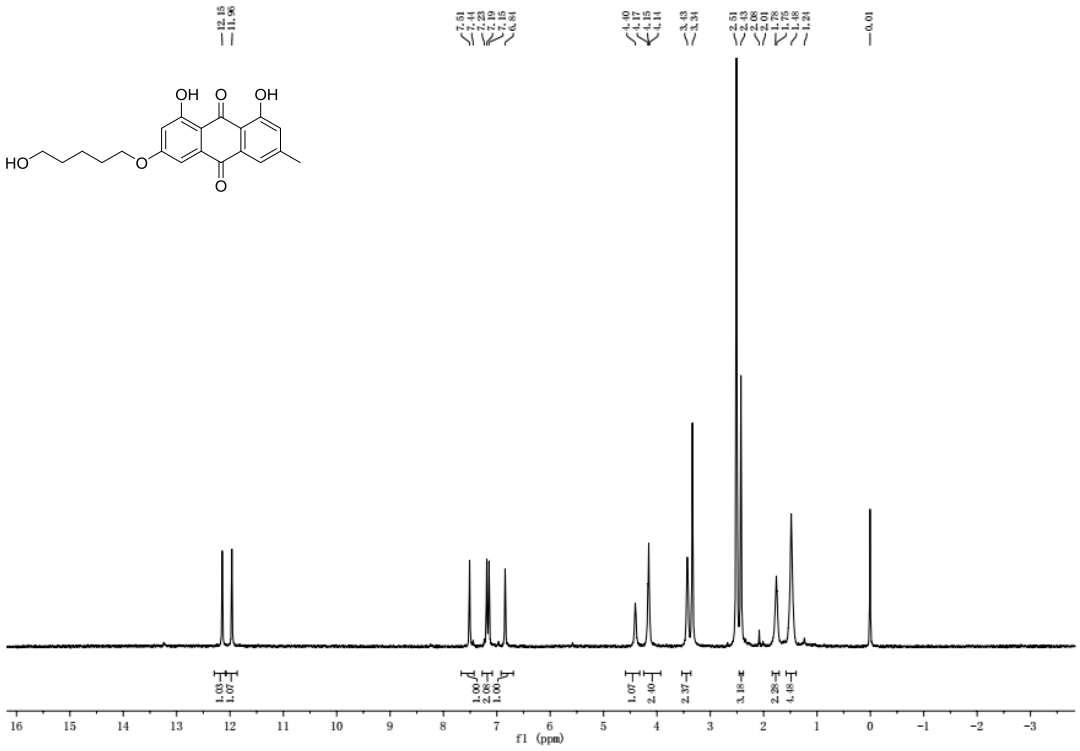

Figure S97. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **6c**.

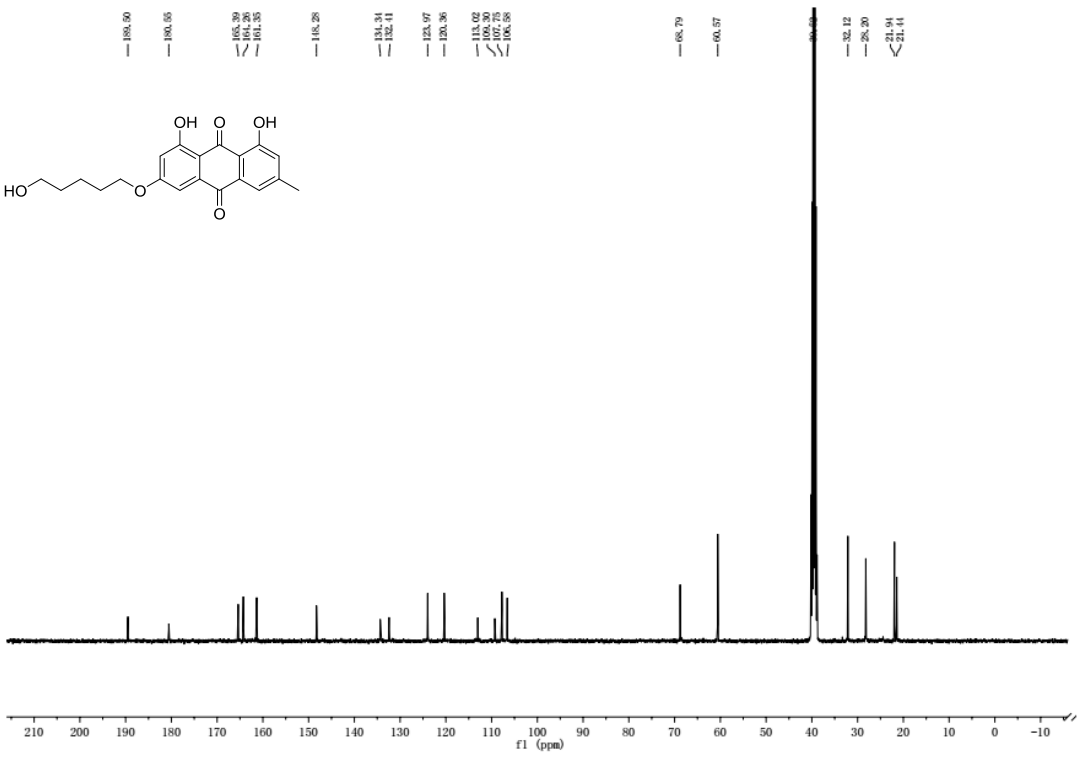

Figure S98. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **6c**

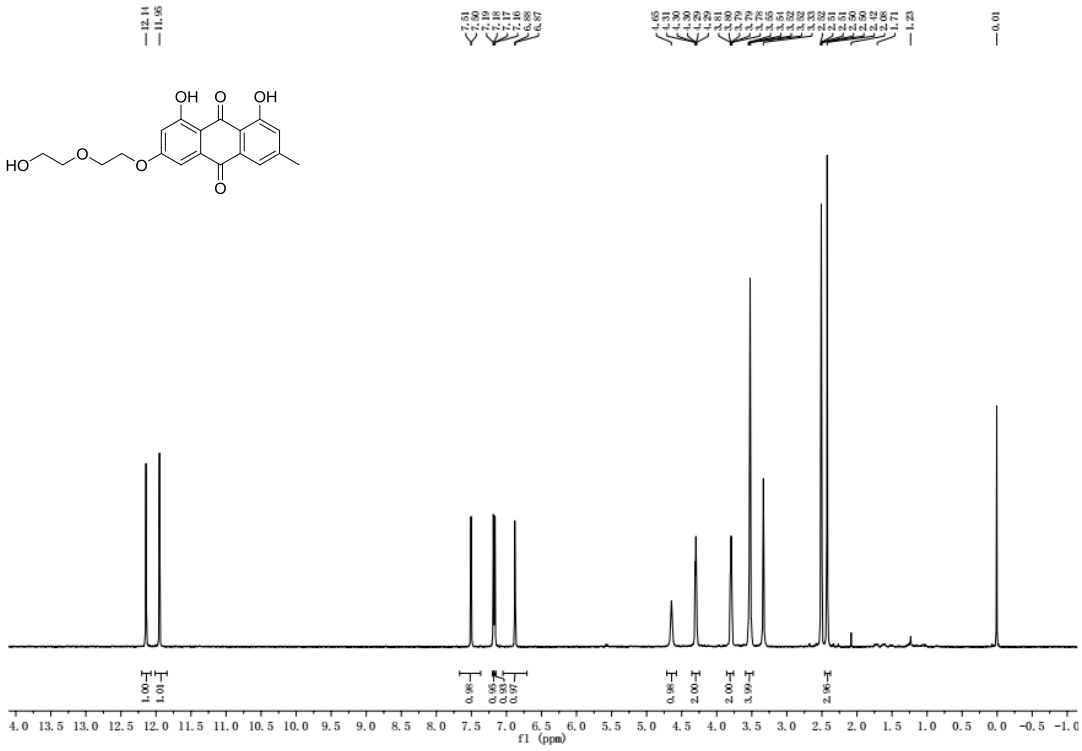

Figure S99. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **6d**.

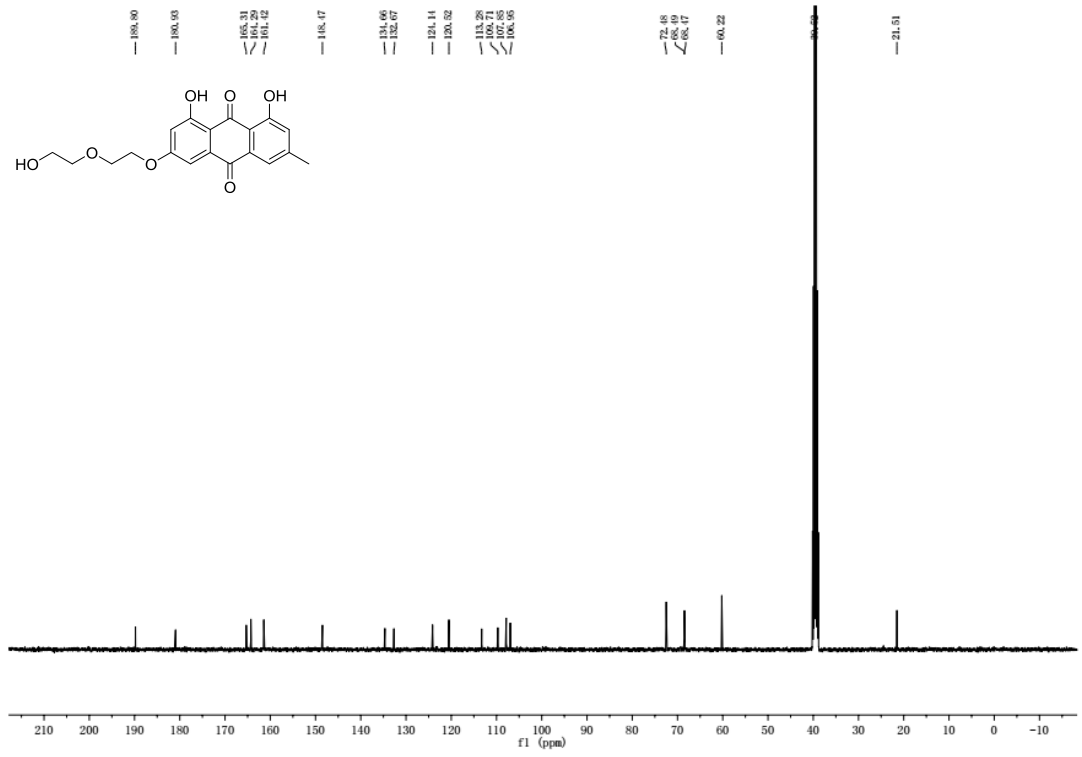

Figure S100. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **6d**.

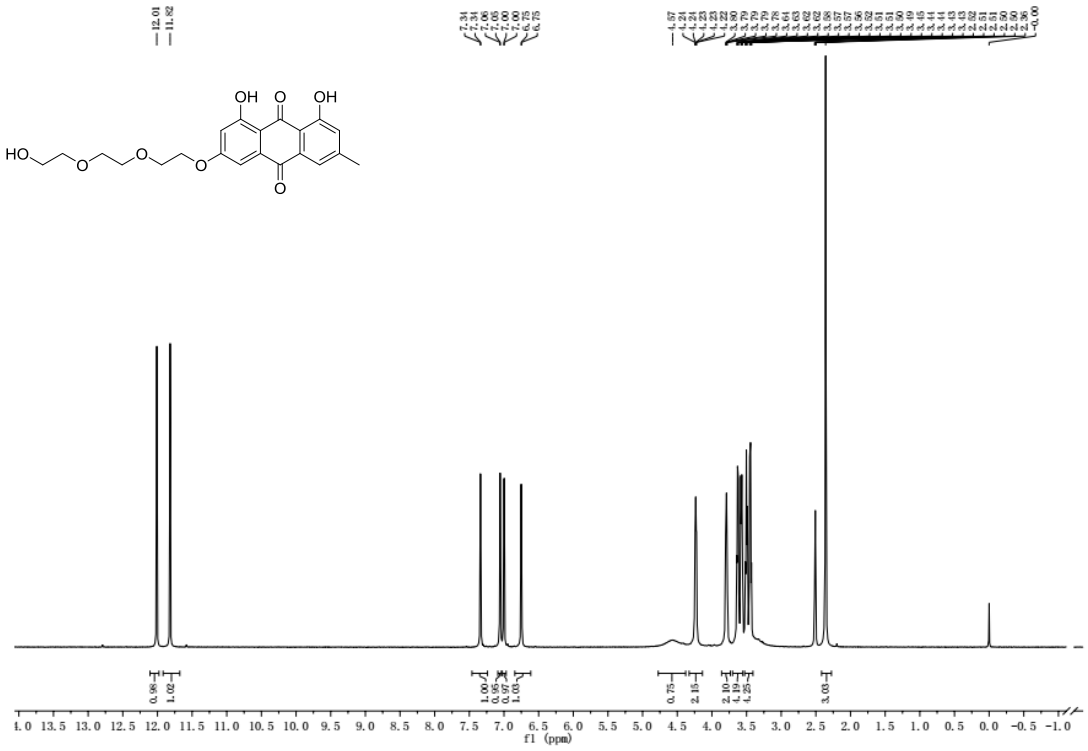

Figure S101. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **6e**.

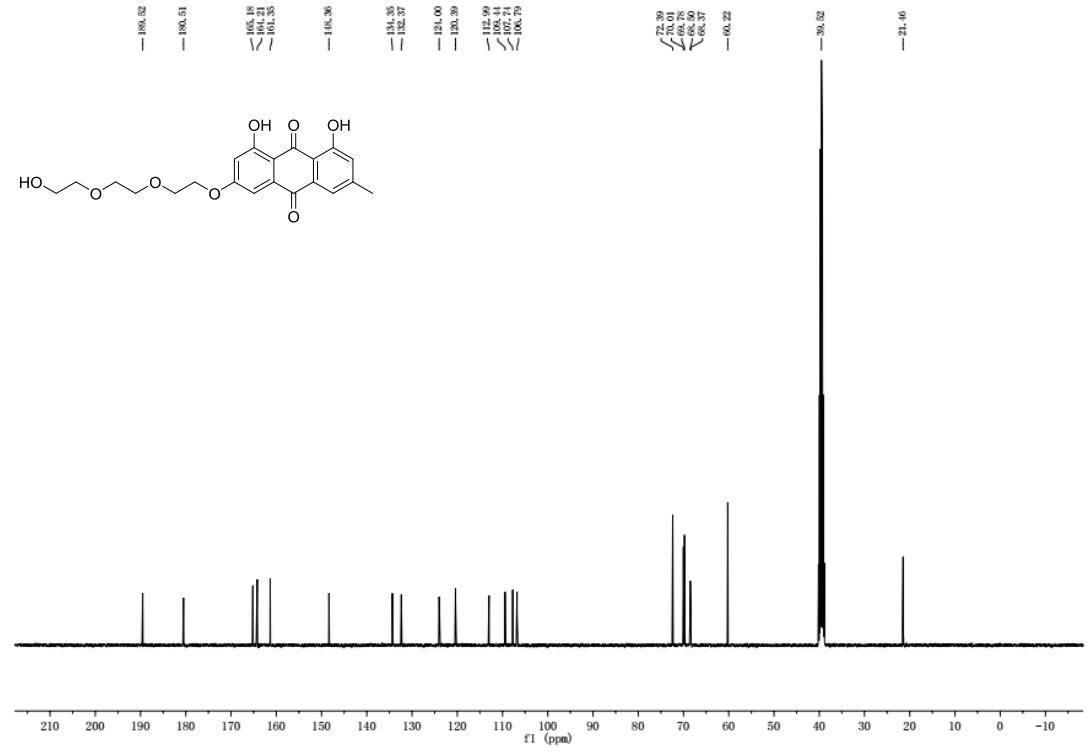

Figure S102. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **6e**.

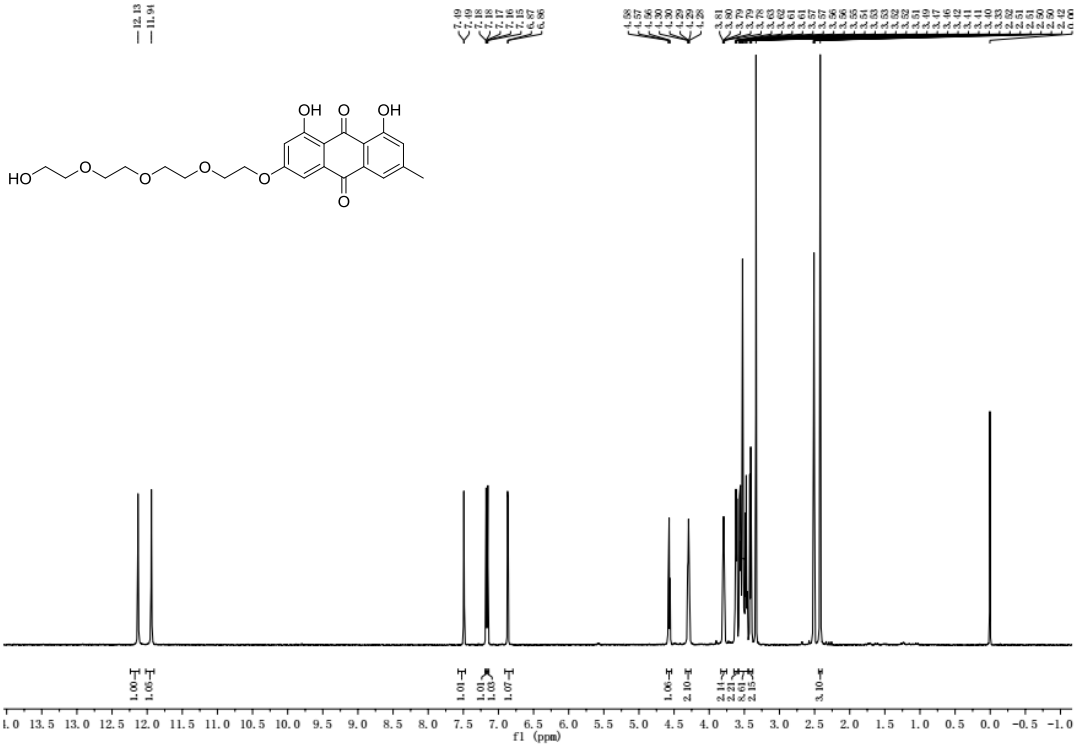

Figure S103. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **6f**.

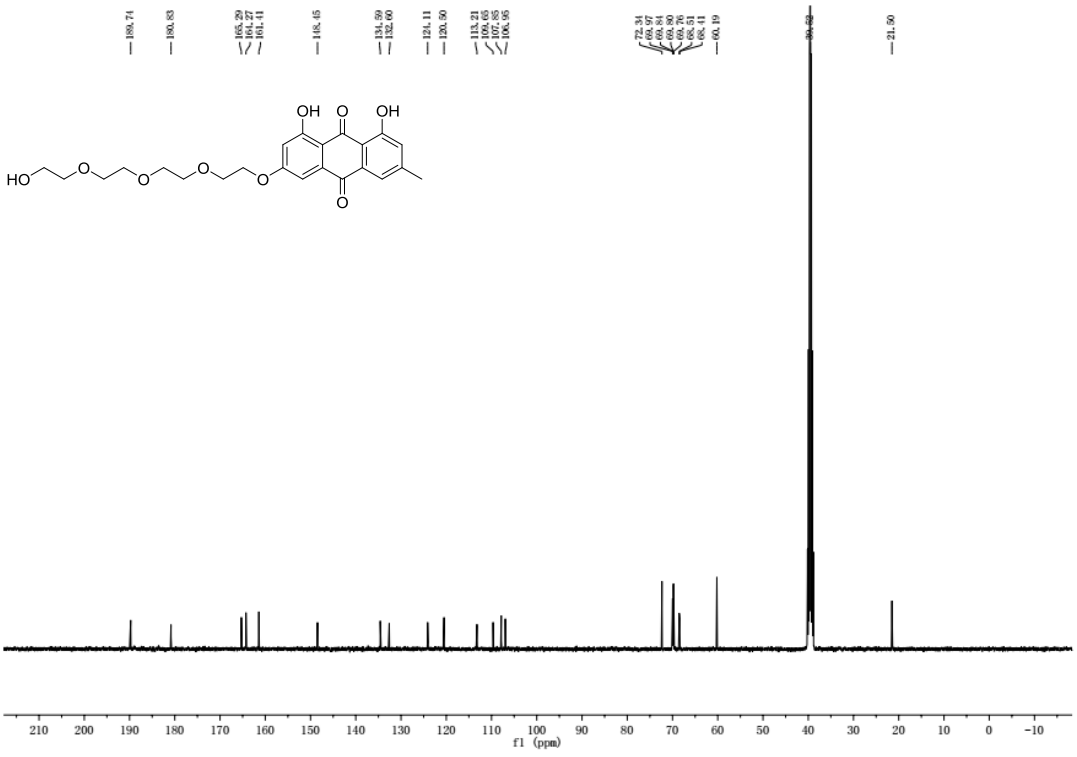

Figure S104. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **6f**.

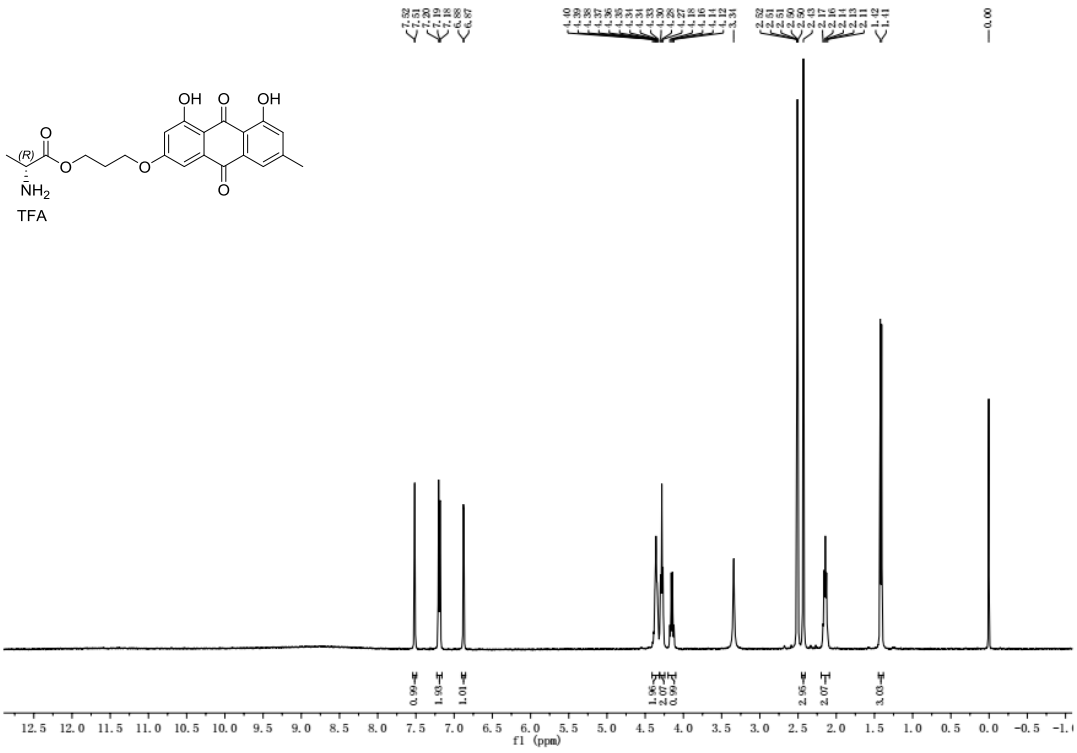

Figure S105. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **7a**.

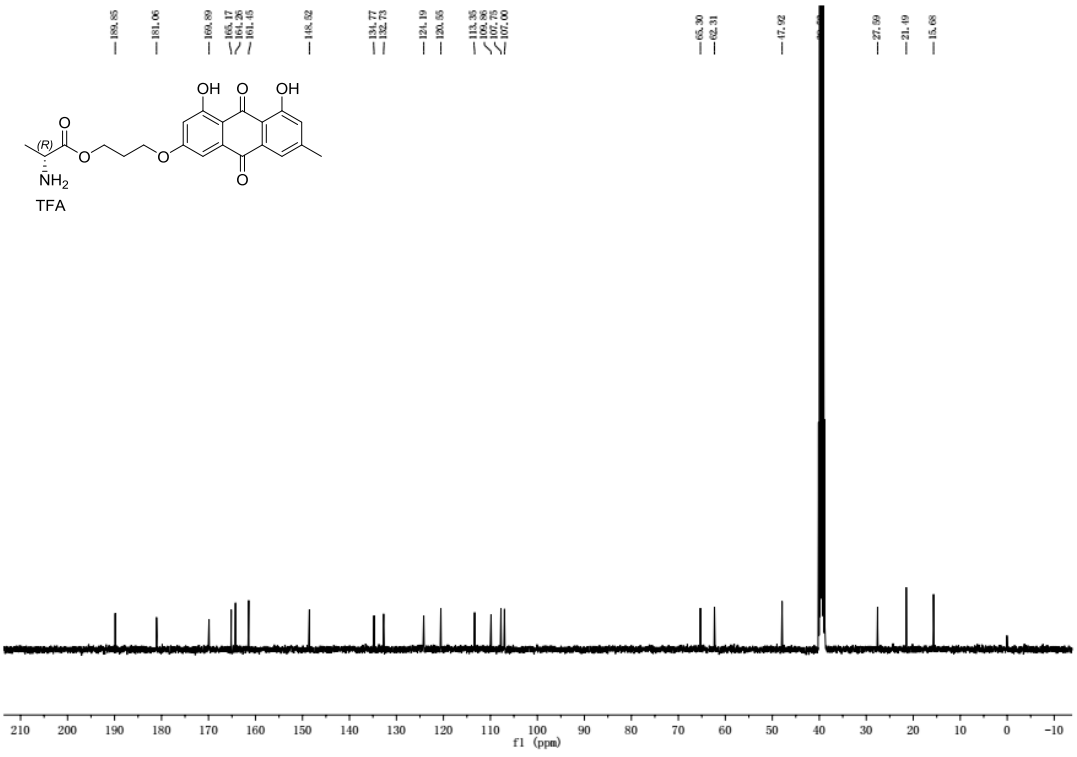

Figure S106. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **7a**.

Figure S107. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **7a**.

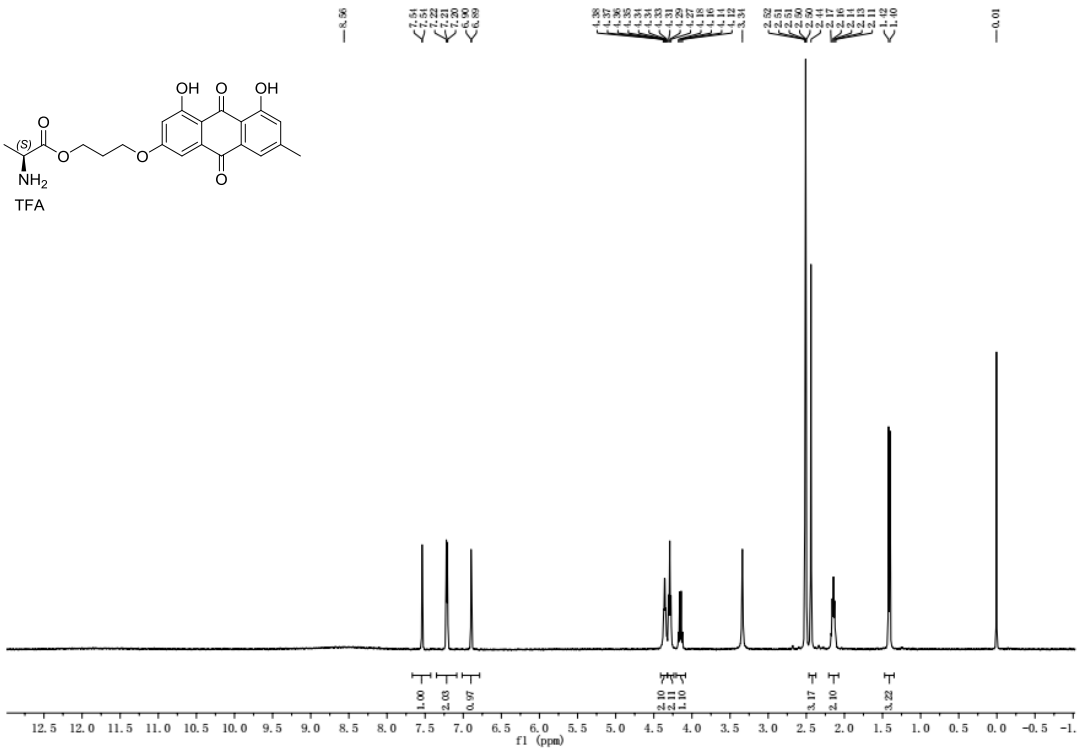

Figure S108. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **7b**.

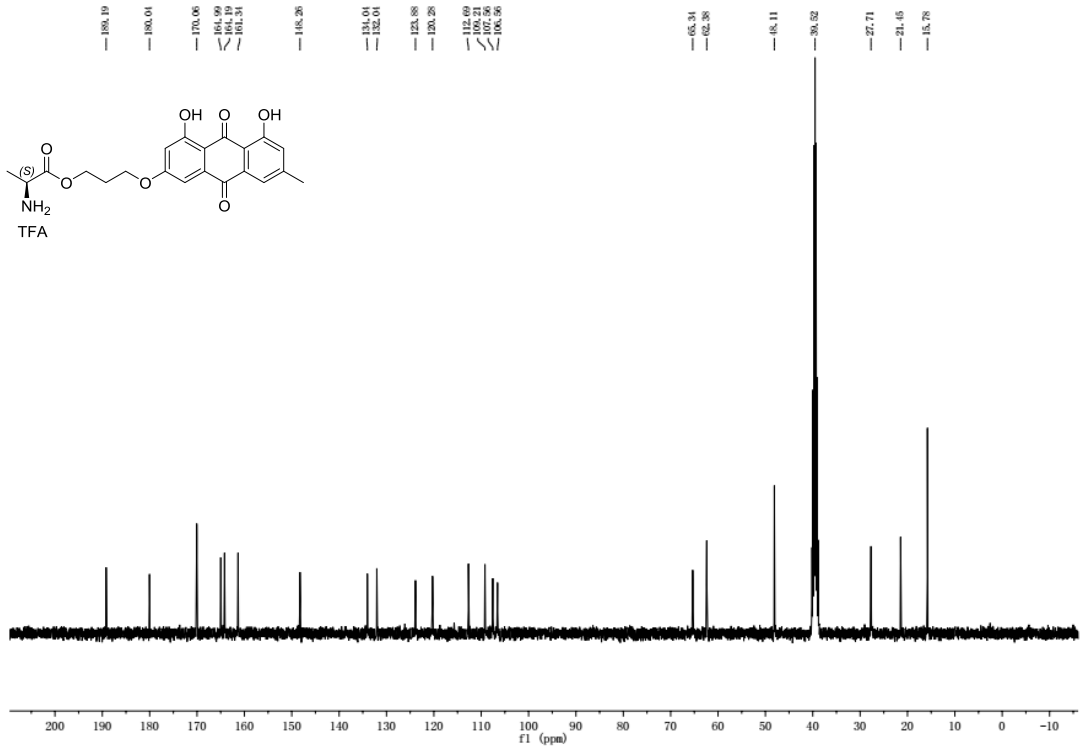

Figure S109. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **7b**.

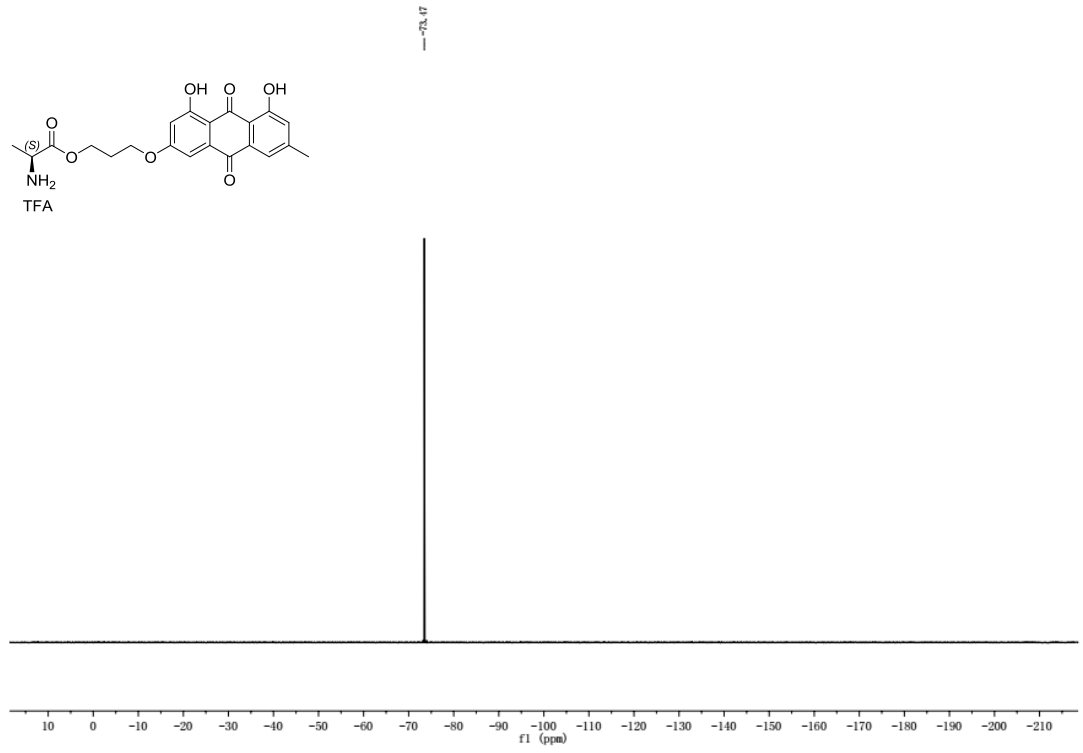

Figure S110. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **7b**.

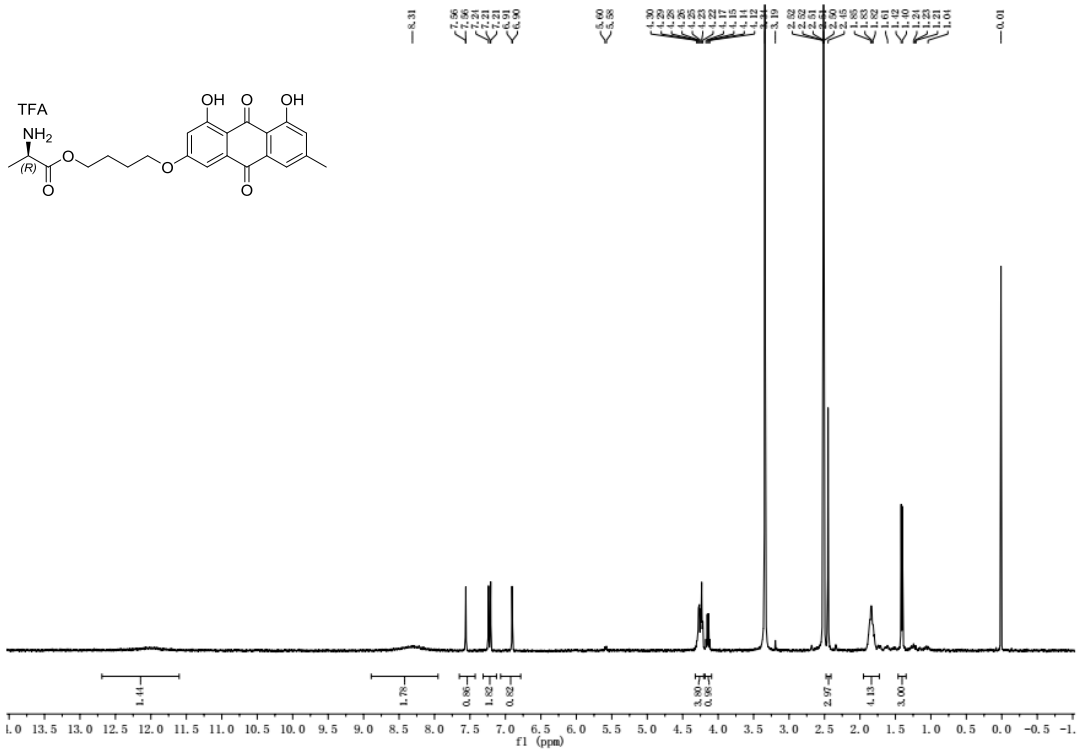

Figure S111. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **7c**.

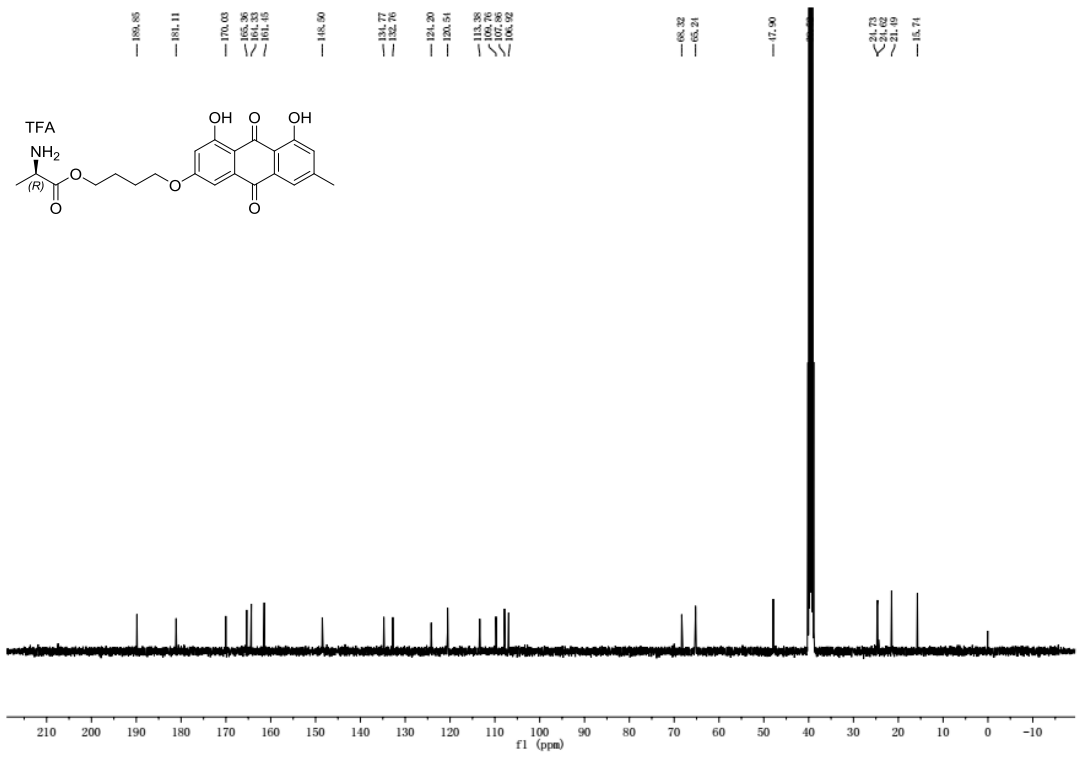

Figure S112. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **7c**.

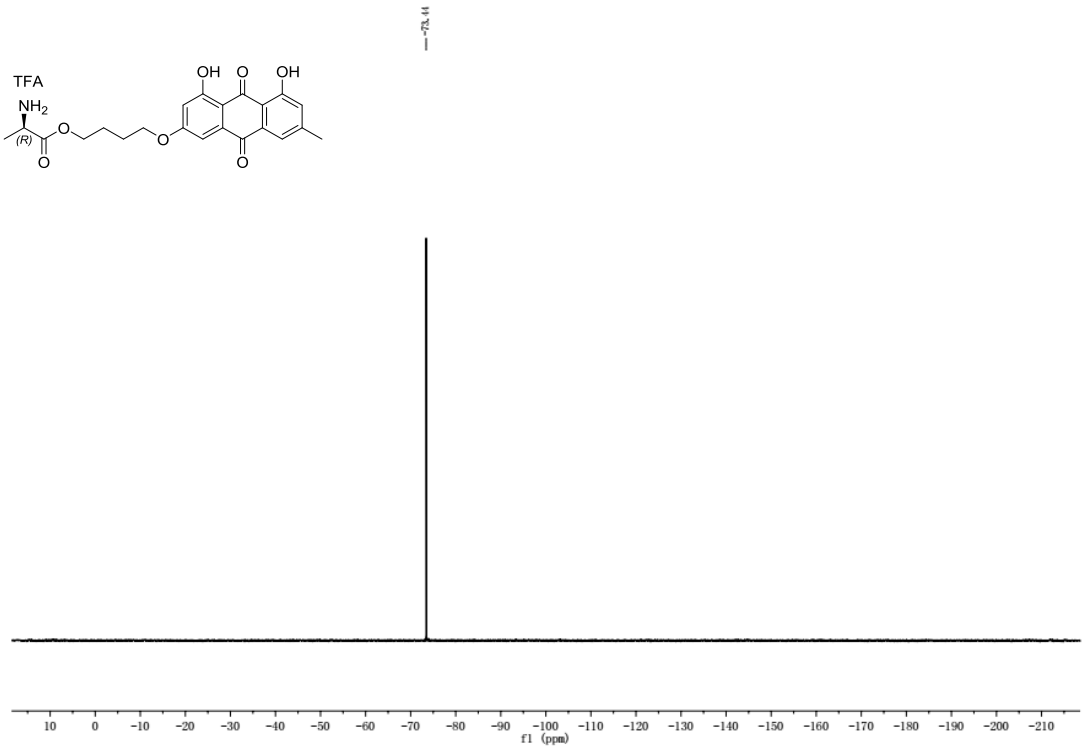

Figure S113. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **7c**.

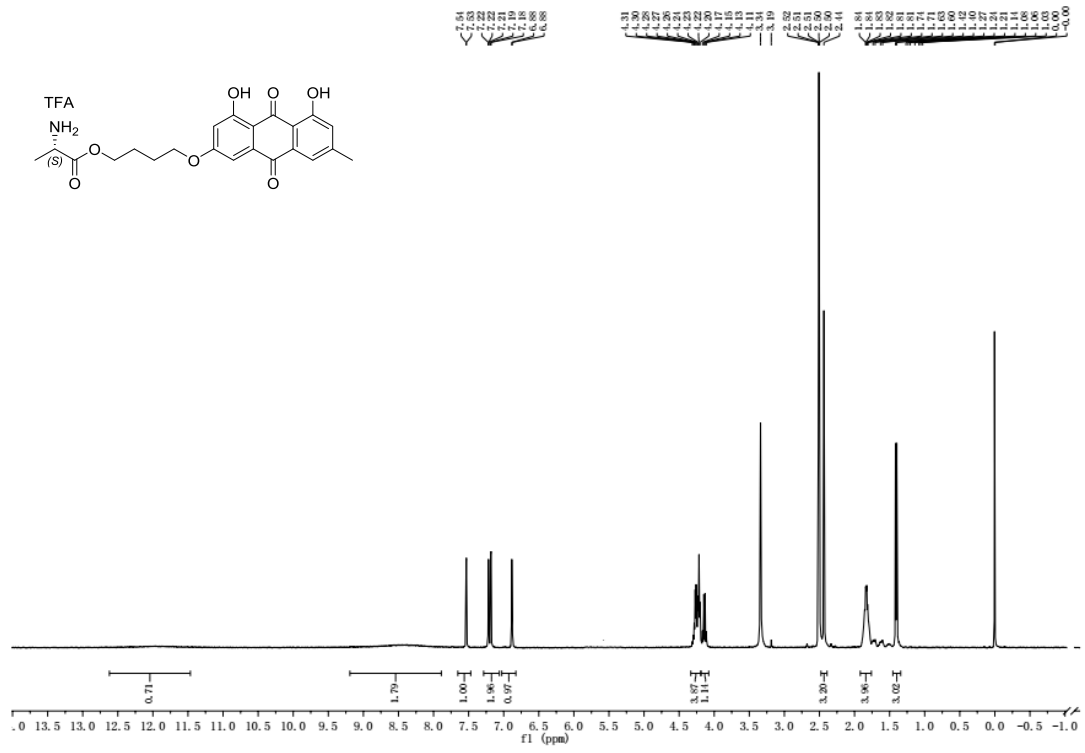

Figure S114. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **7d**.

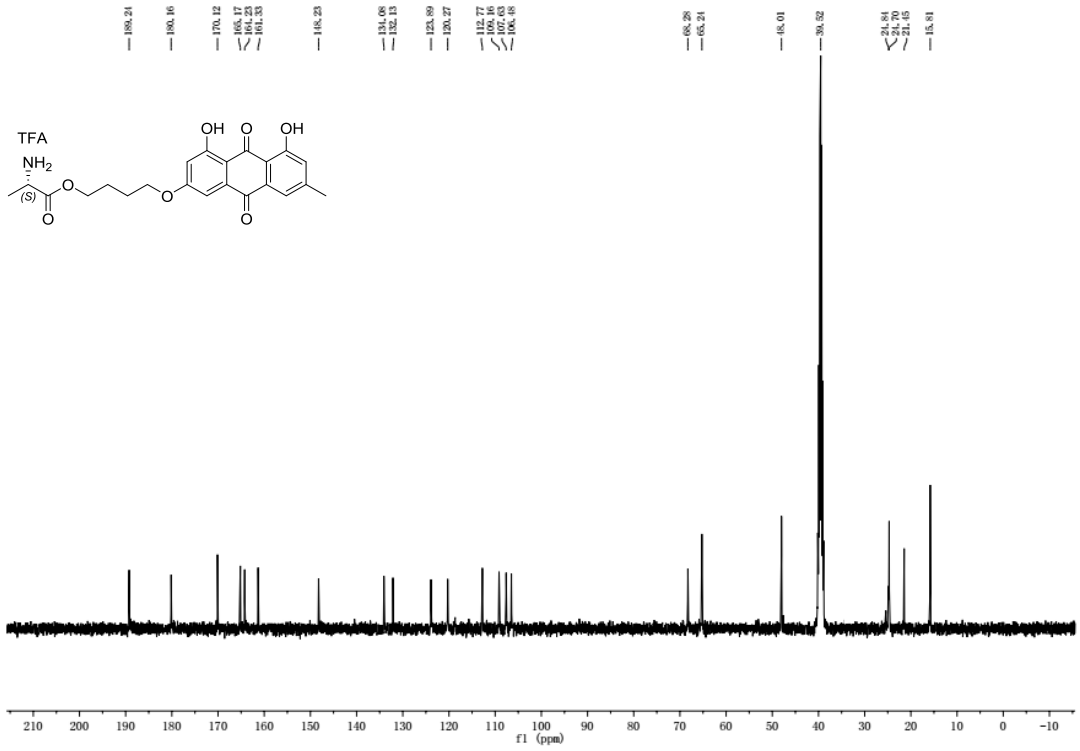

Figure S115. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **7d**.

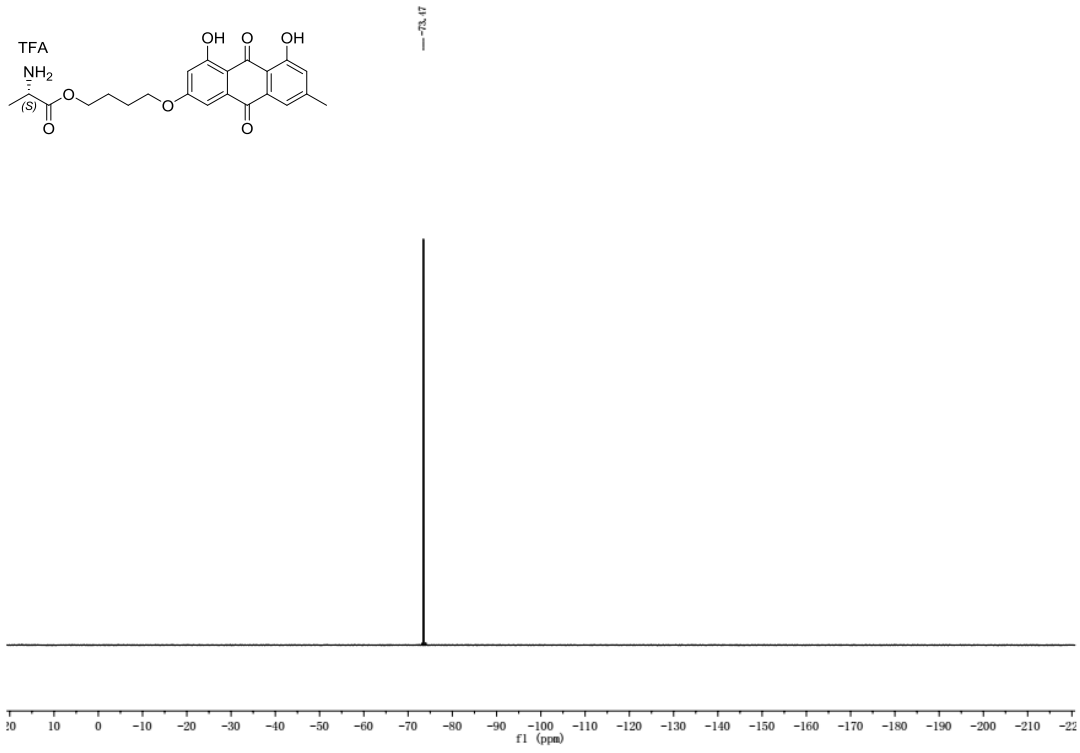

Figure S116. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **7d**.

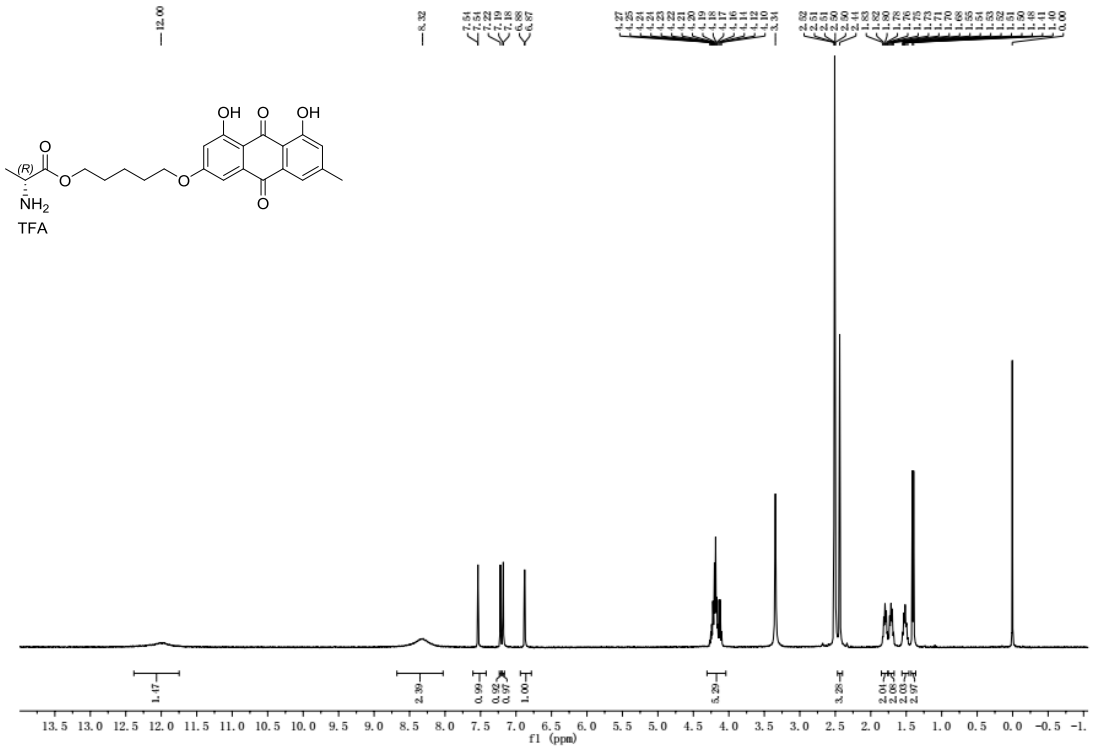

Figure S117. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **7e**.

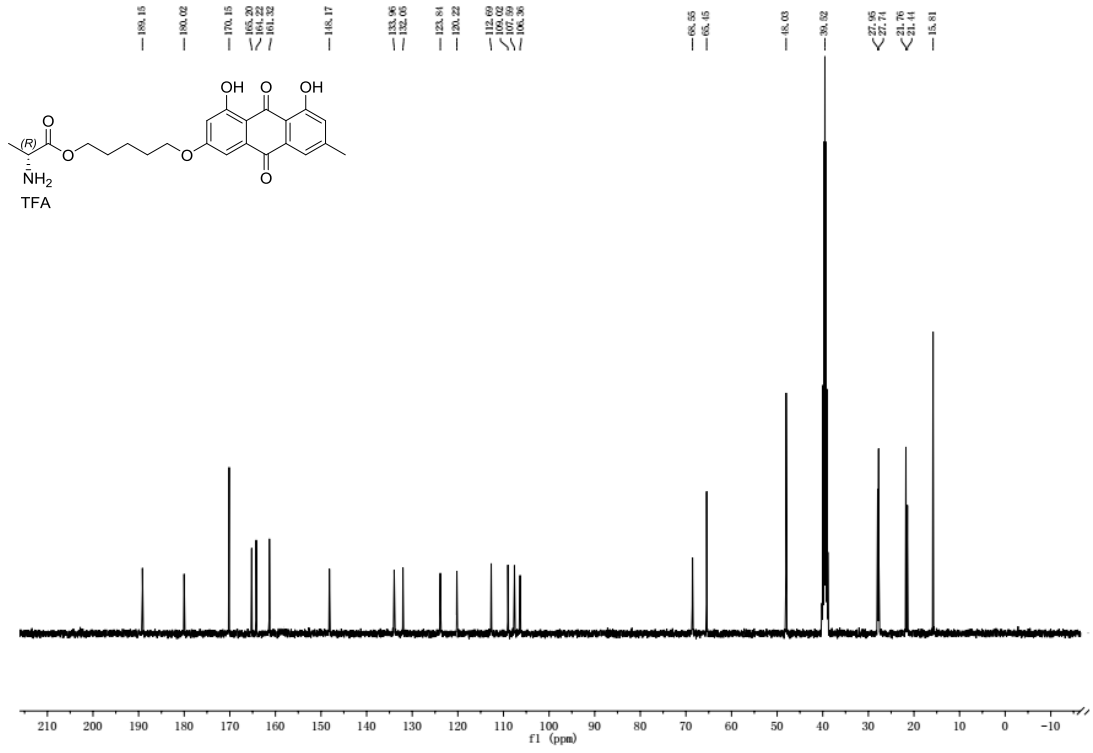

Figure S118. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **7e**.

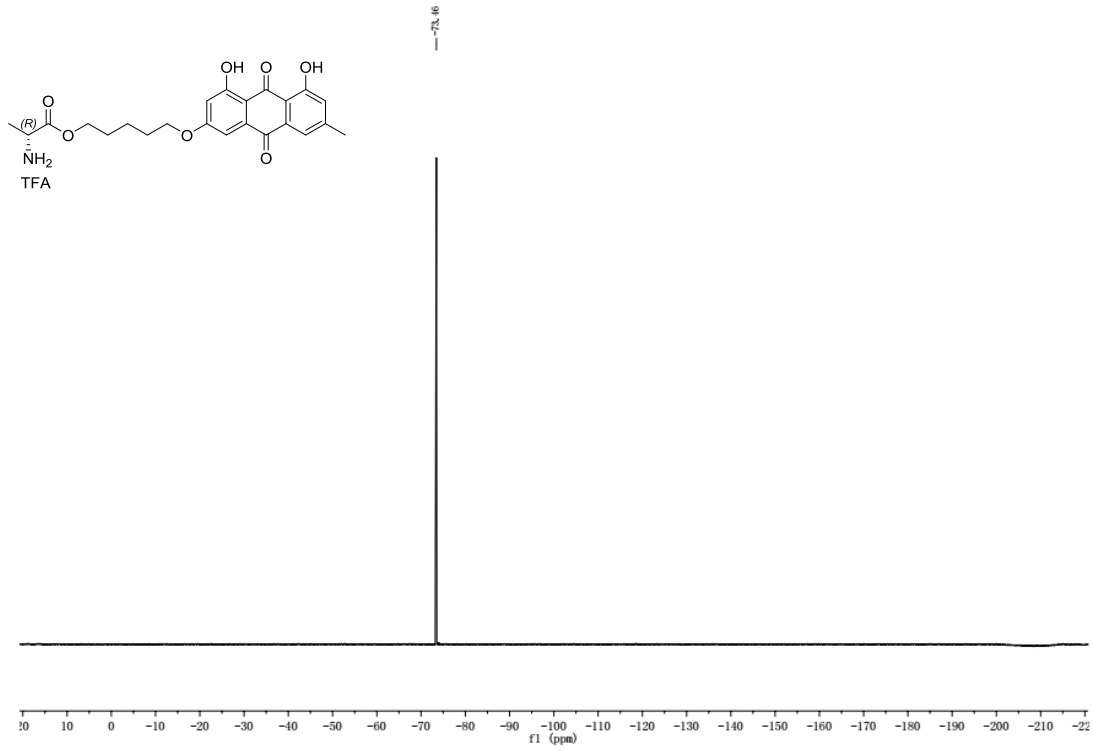

Figure S119. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **7e**.

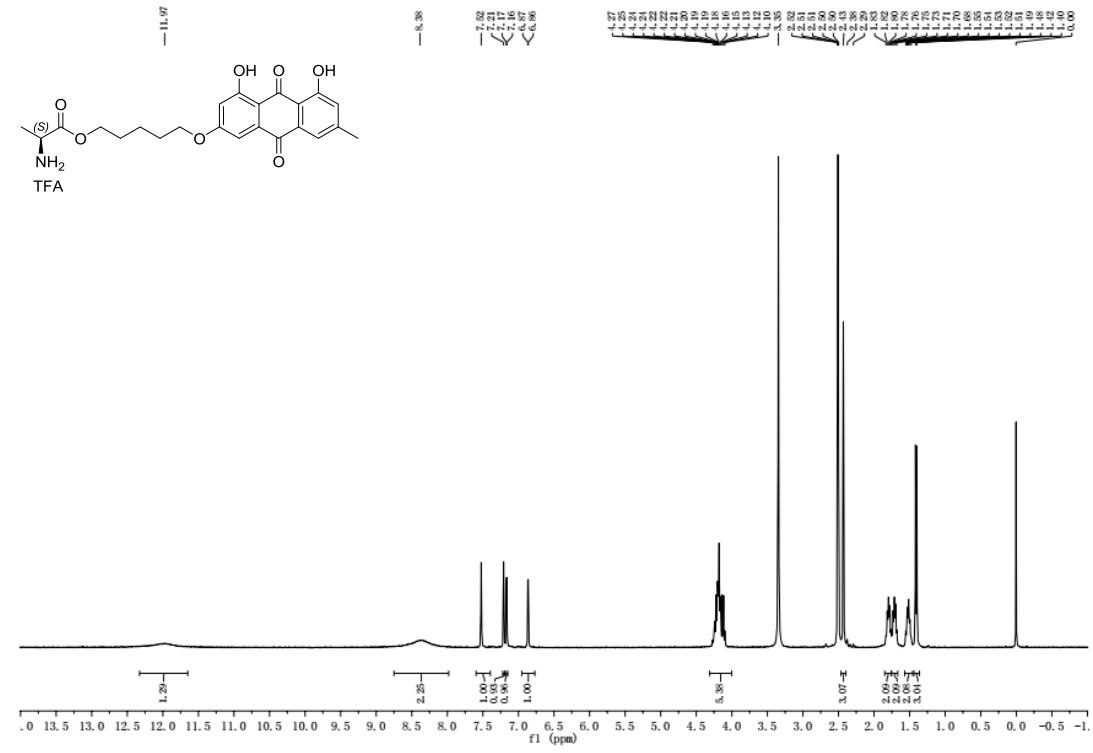

Figure S120. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **7f**.

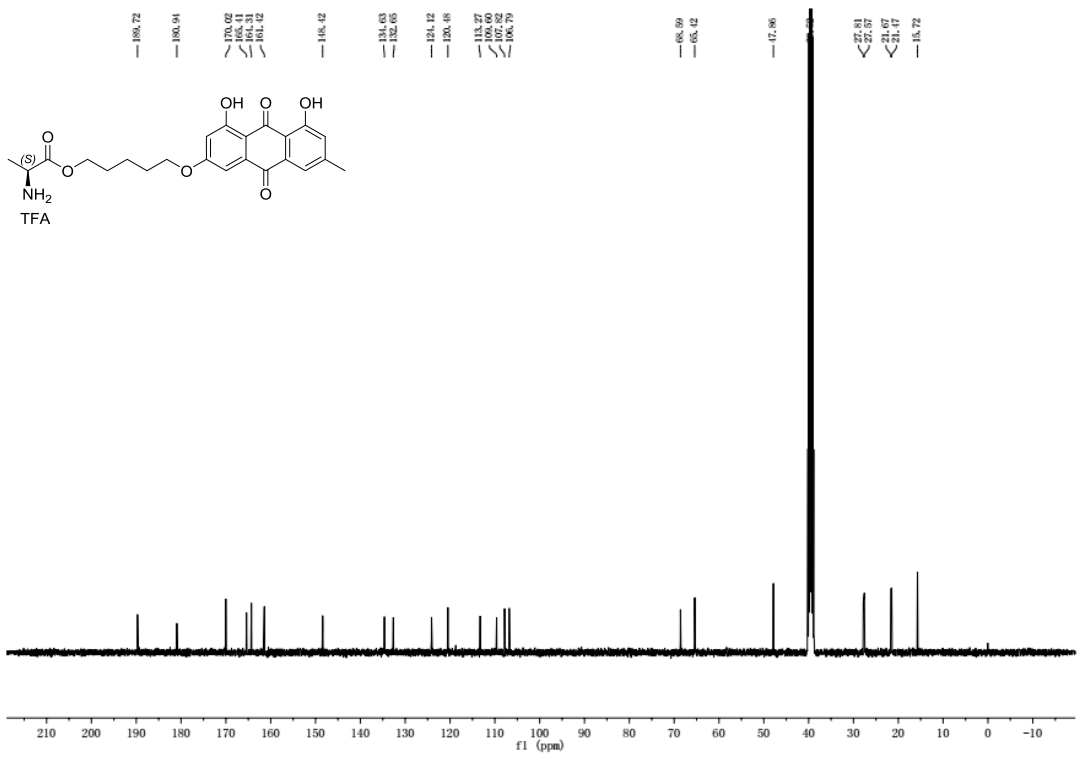

Figure S121. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **7f**.

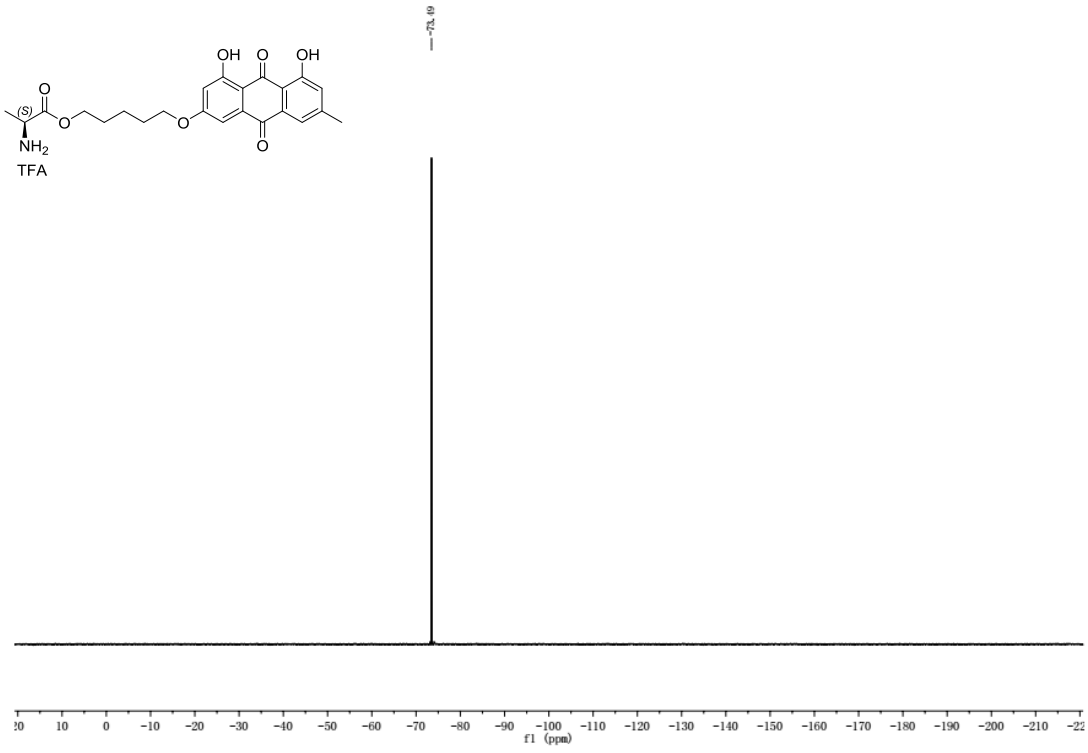

Figure S122. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **7f**.

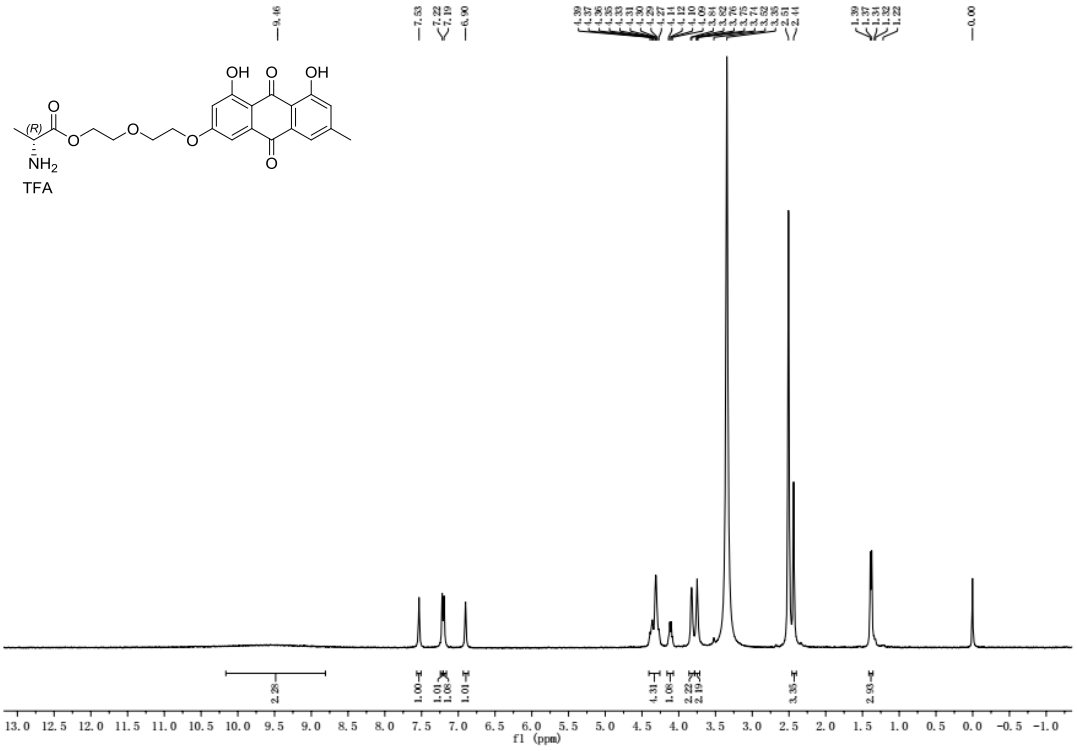

Figure S123. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **7g**.

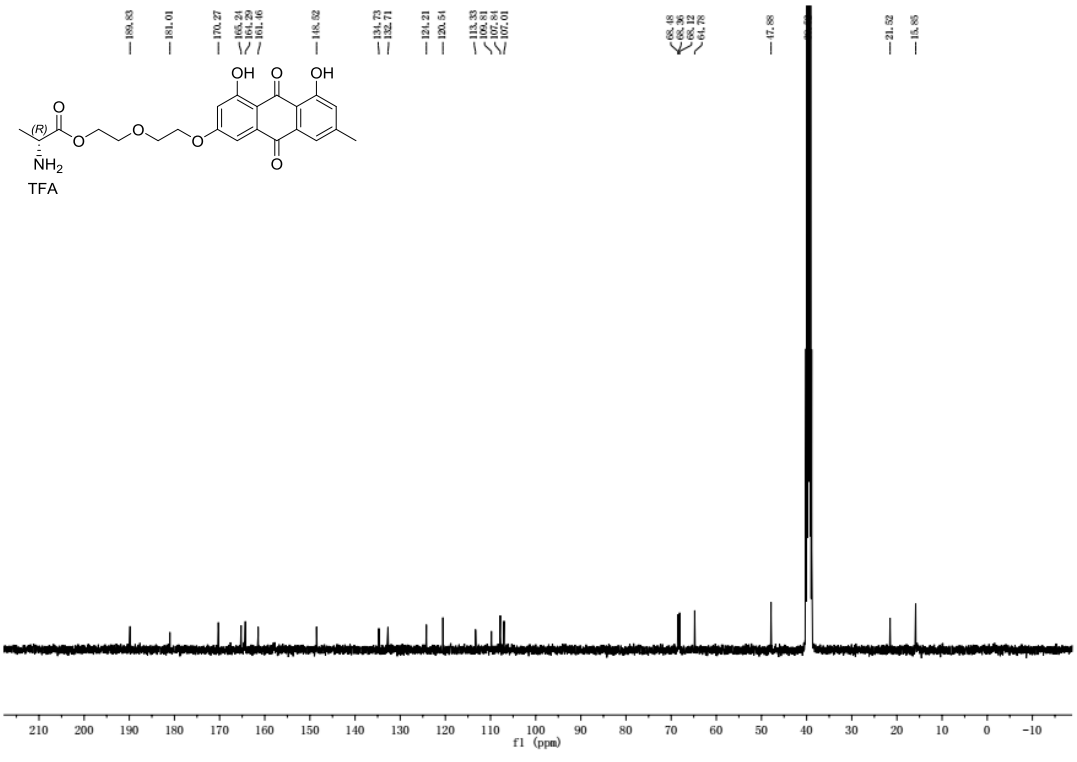

Figure S124. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **7g**.

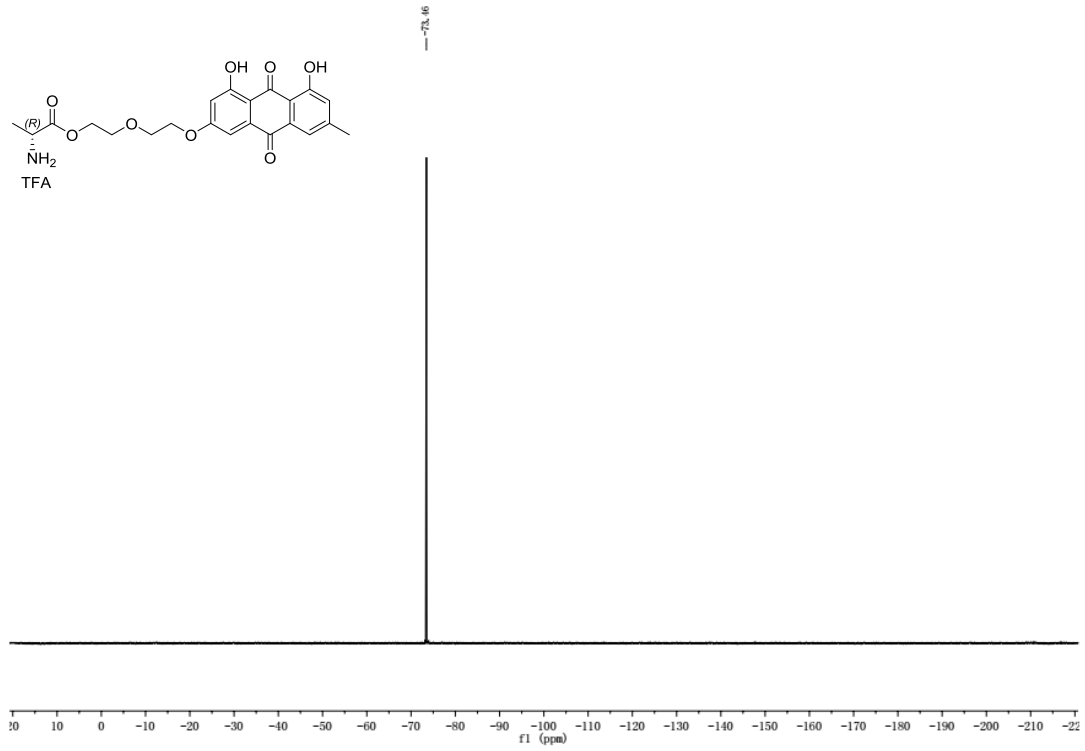

Figure S125. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **7g**.

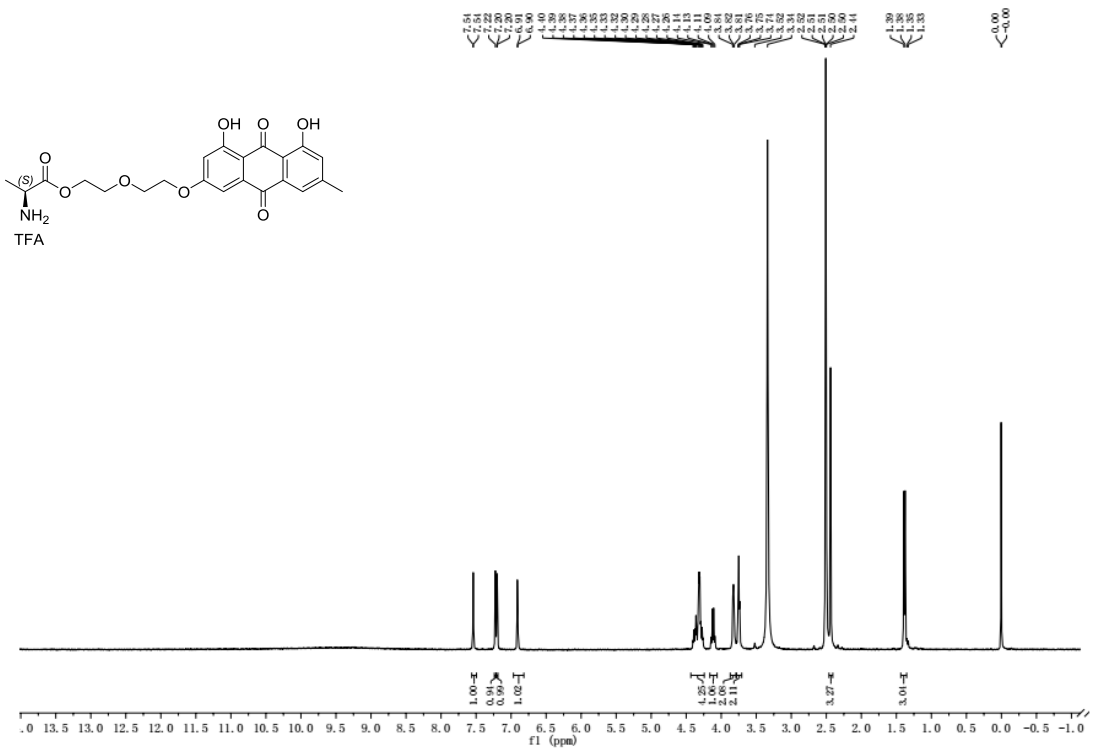

Figure S126. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **7h**.

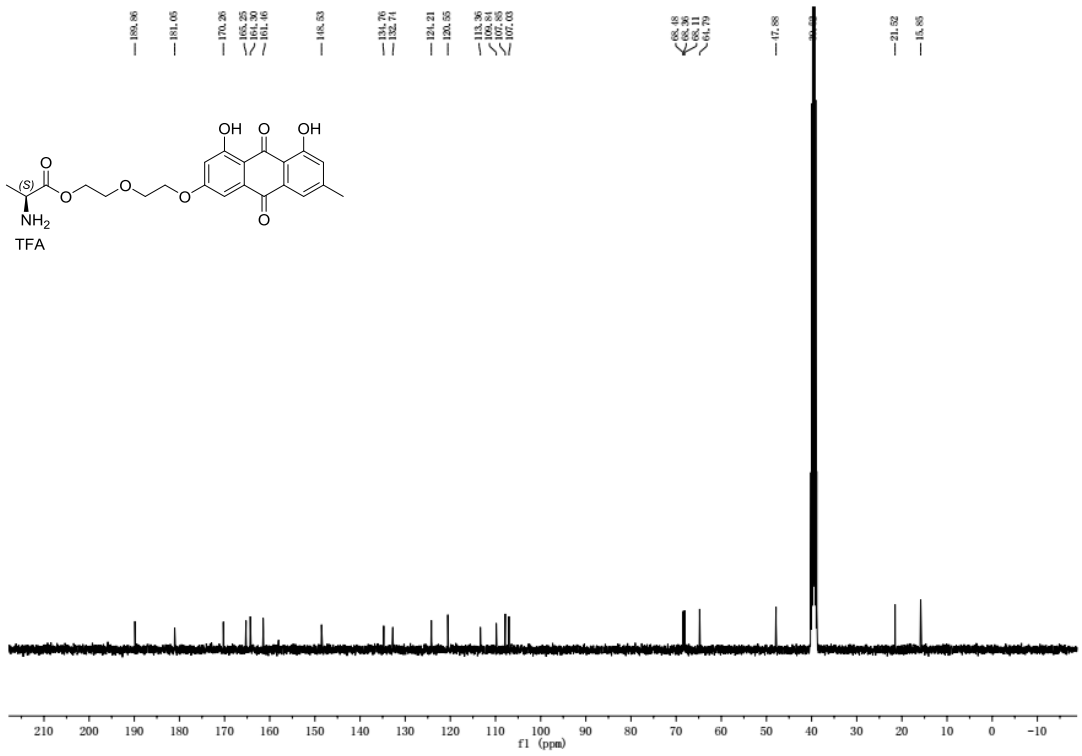

Figure S127. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **7h**.

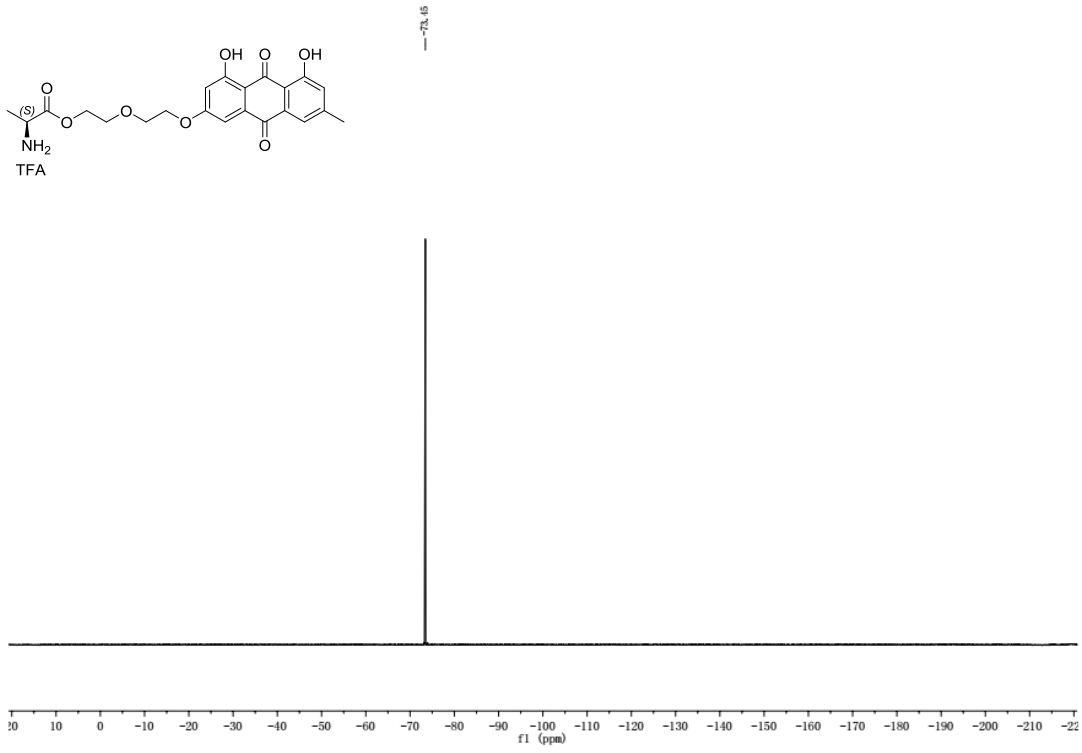

Figure S128. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **7h**.

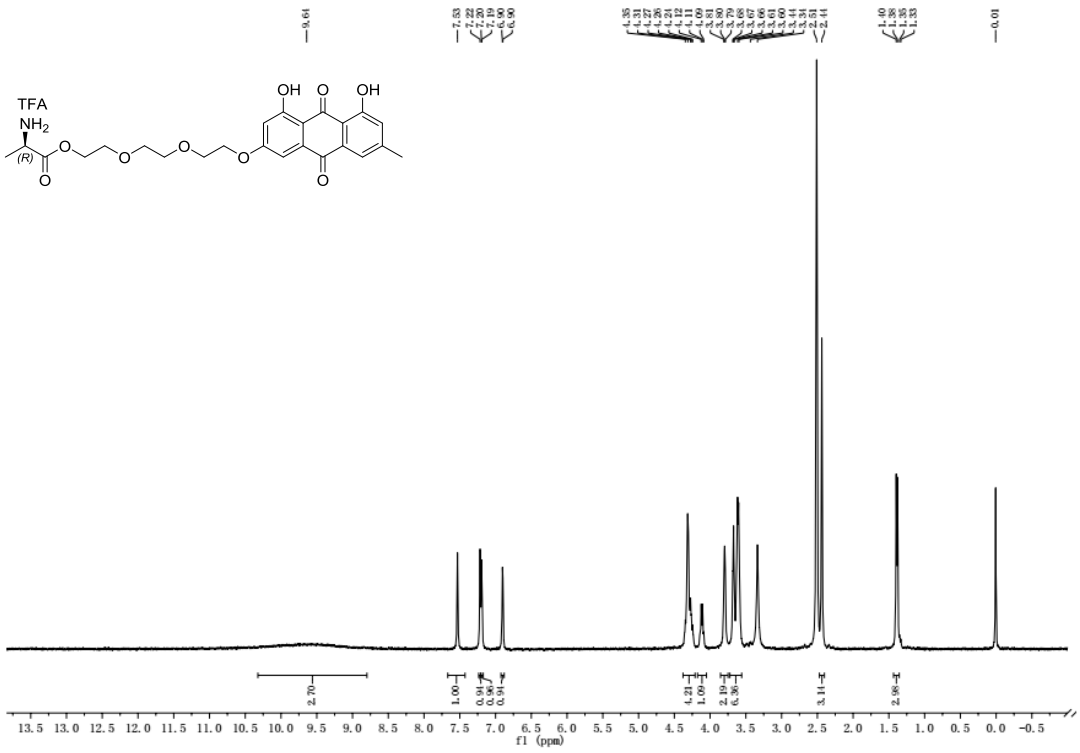

Figure S129. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **7i**.

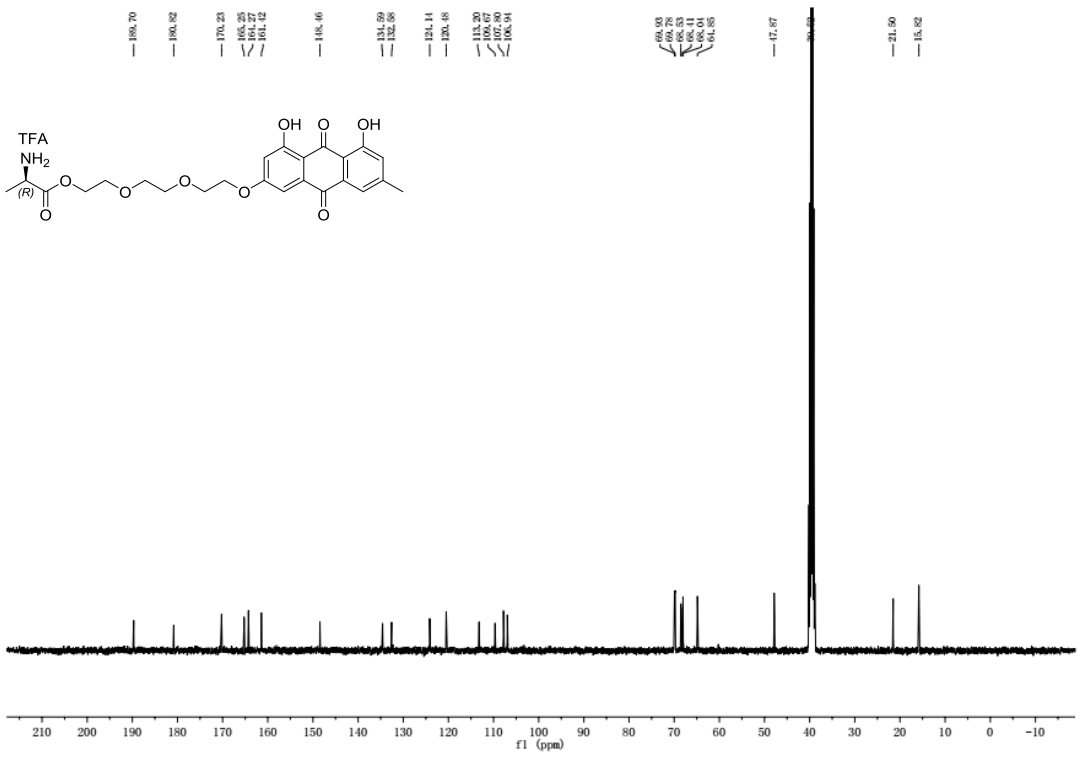

Figure S130. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **7i**.

Figure S131. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **7i**.

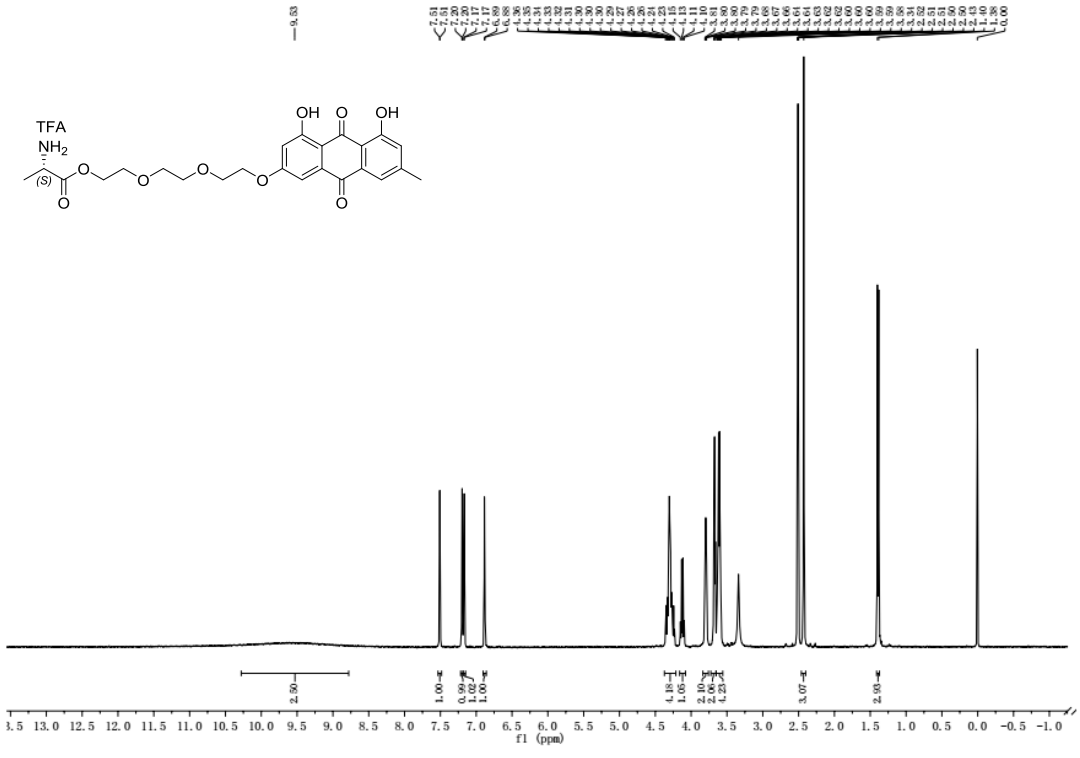

Figure S132. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **7j**.

Figure S133. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **7j**.

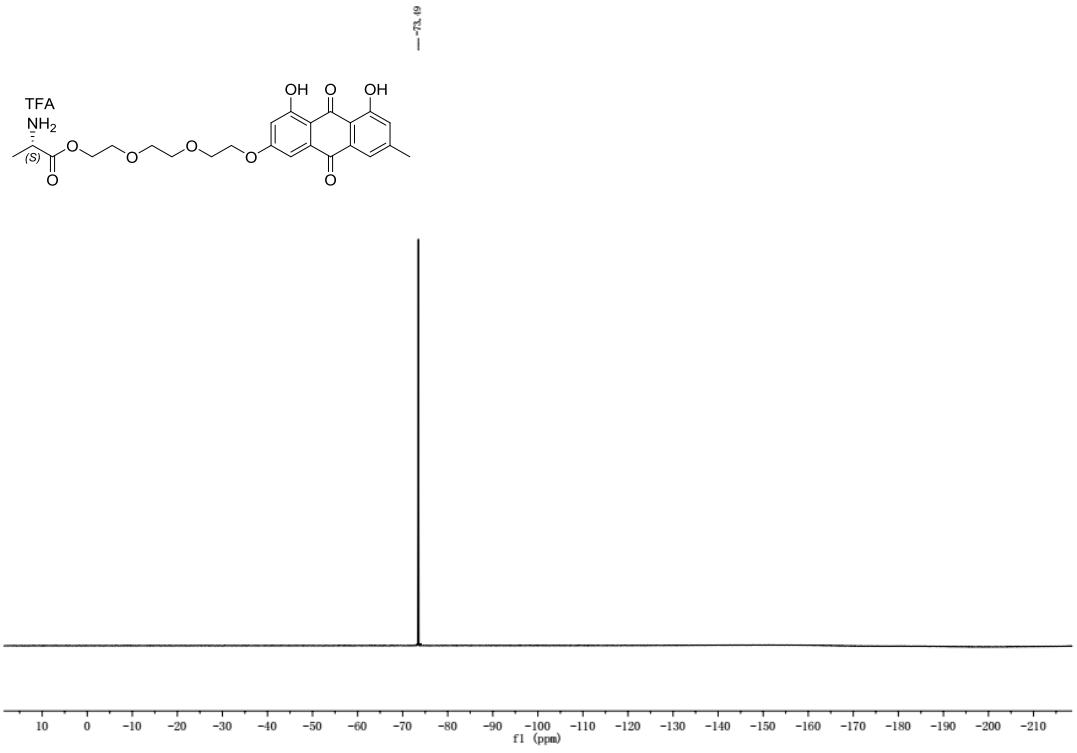

Figure S134. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **7j**.

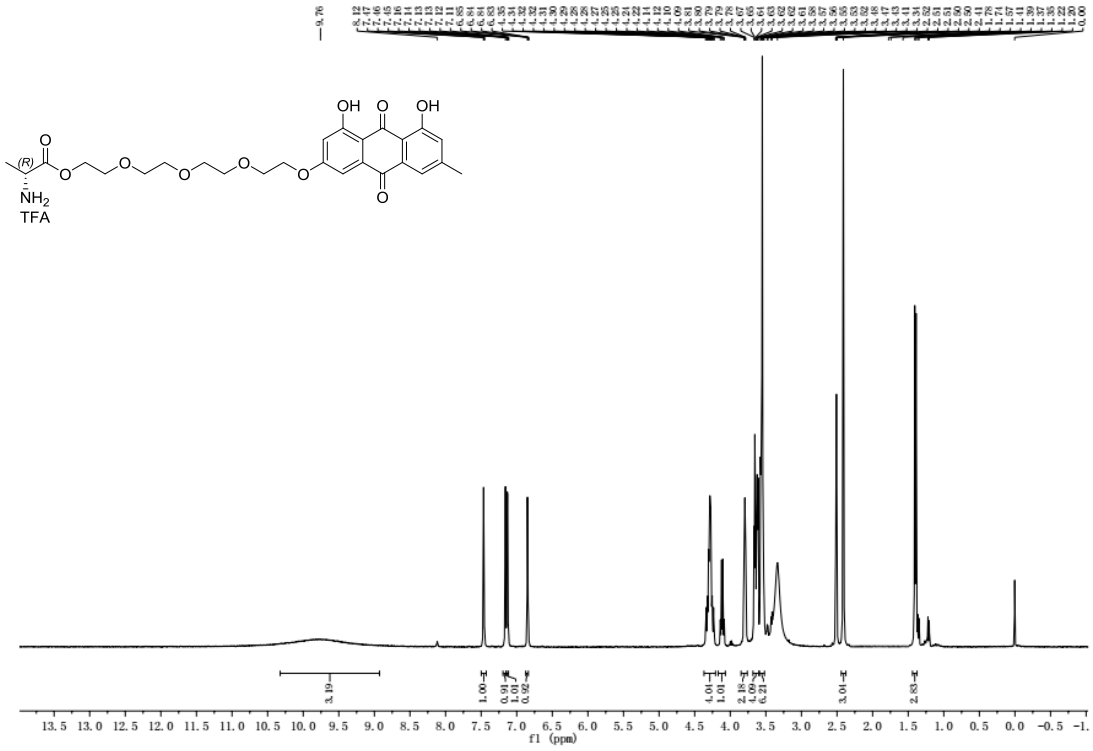

Figure S135. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **7k**.

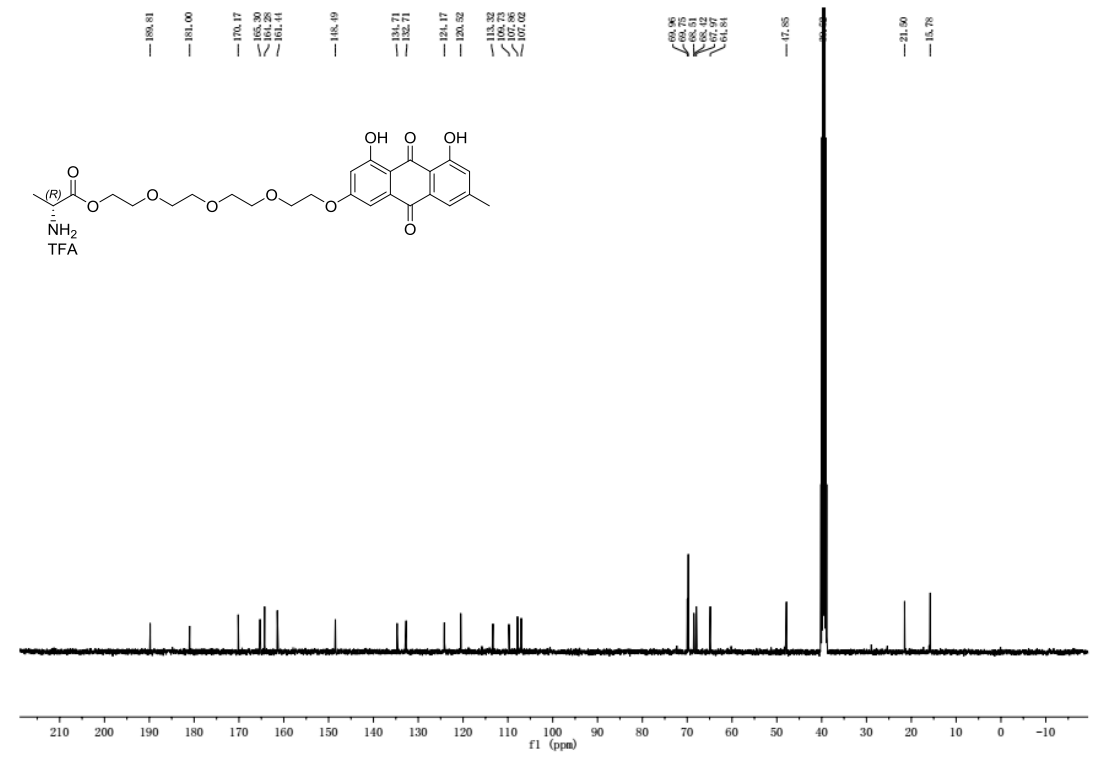

Figure S136. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **7k**.

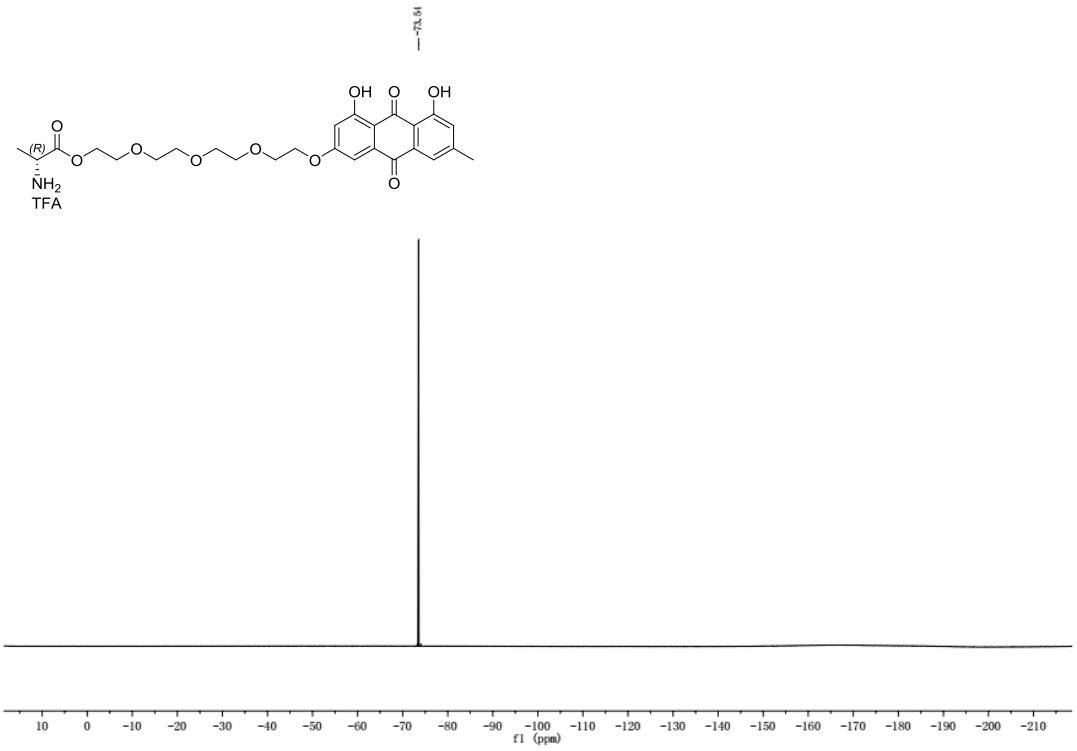

Figure S137. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **7k**.

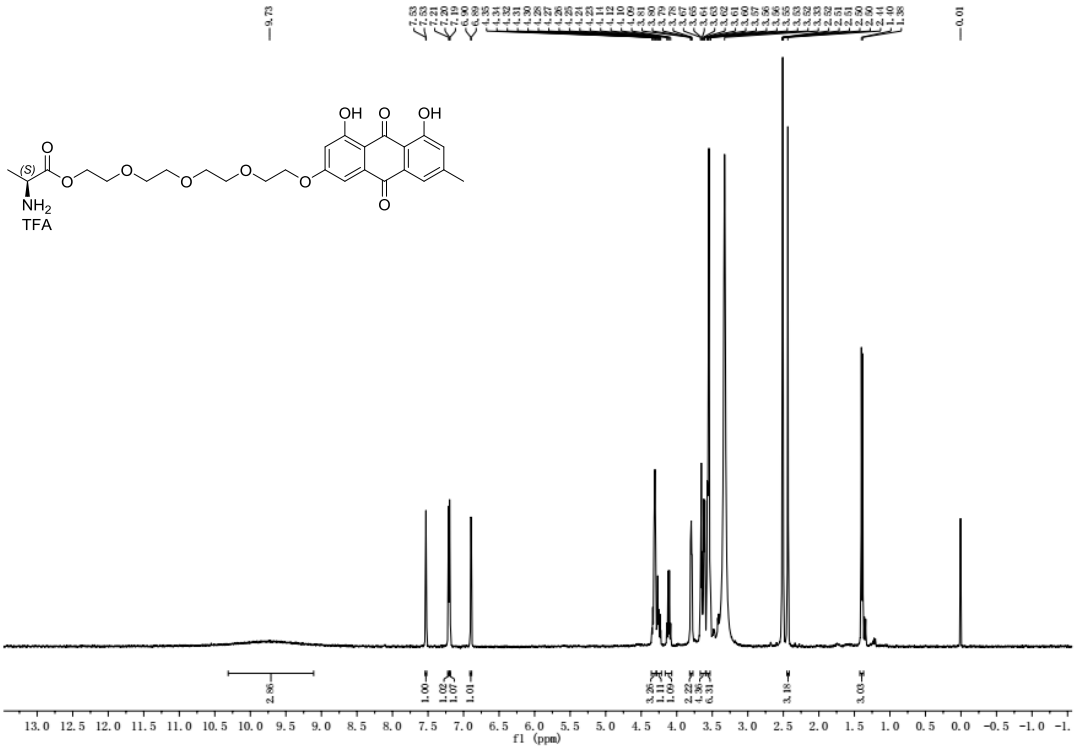

Figure S138. ^{1}H NMR (400 MHz, DMSO–d_6) spectrum of compound **7l**.

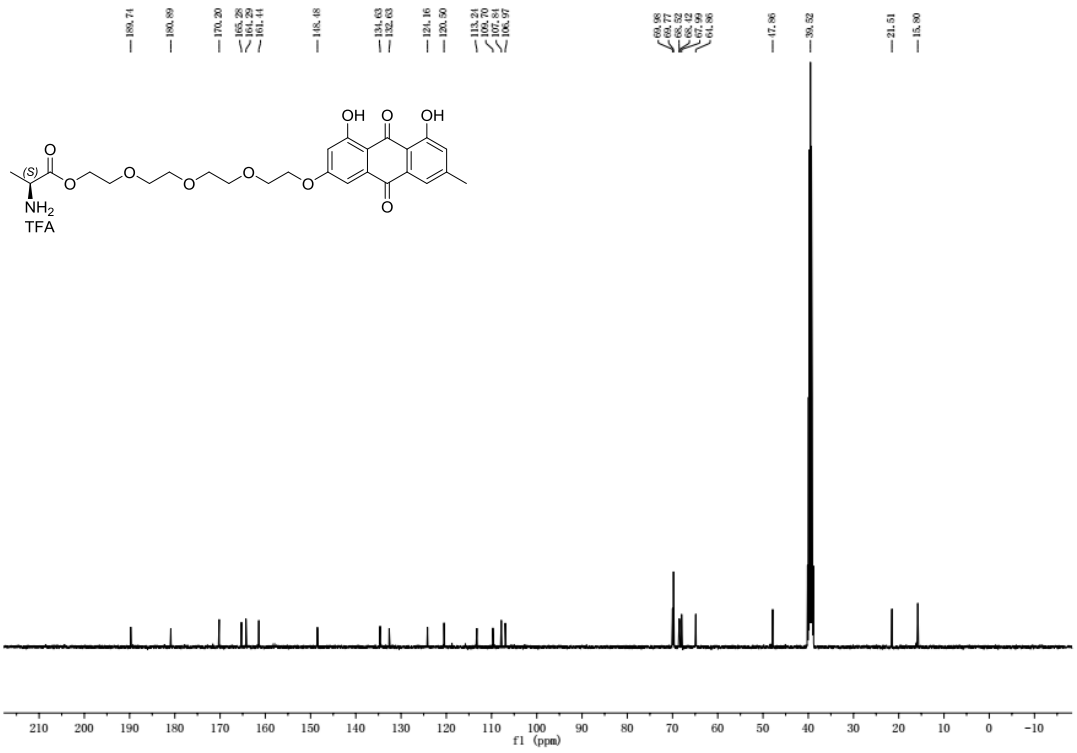

Figure S139. ^{13}C NMR (101 MHz, DMSO–d_6) spectrum of compound **7l**.

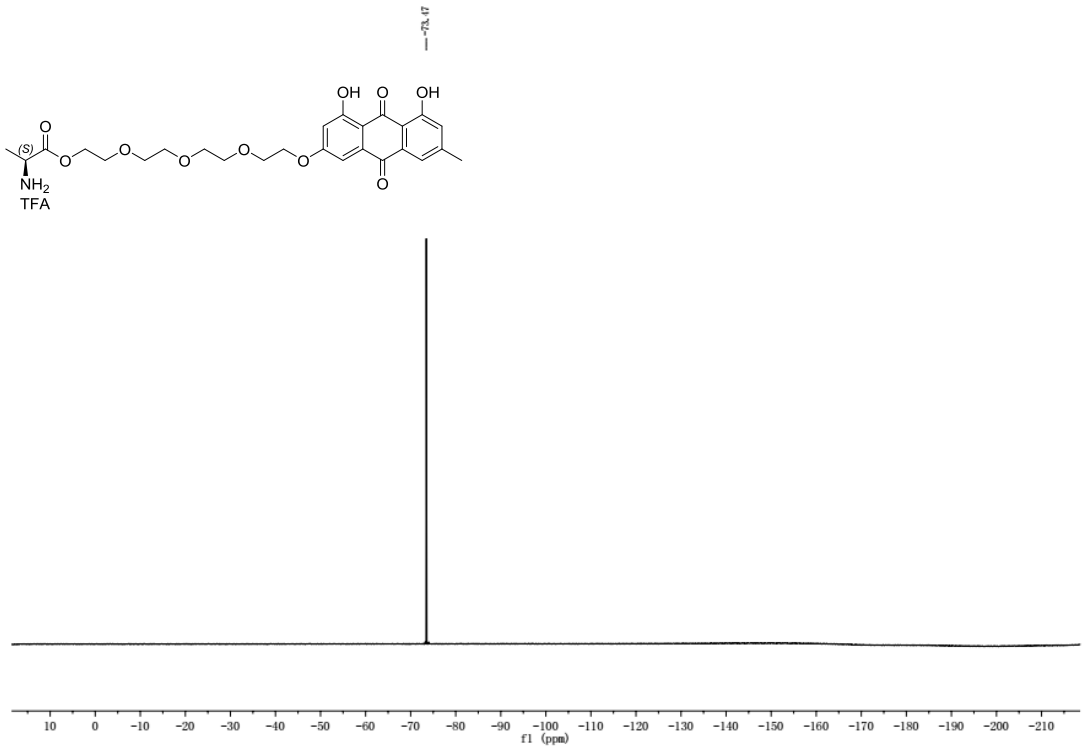

Figure S140. ^{19}F NMR (376 MHz, DMSO–d_6) spectrum of compound **7l**.