Design, synthesis, *in-silico* and *in-vitro* evaluation of Novel Complex Naphthalimide-Ciprofloxacin Hybrids as next-generation antimicrobial agents

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Table –

NMR Data

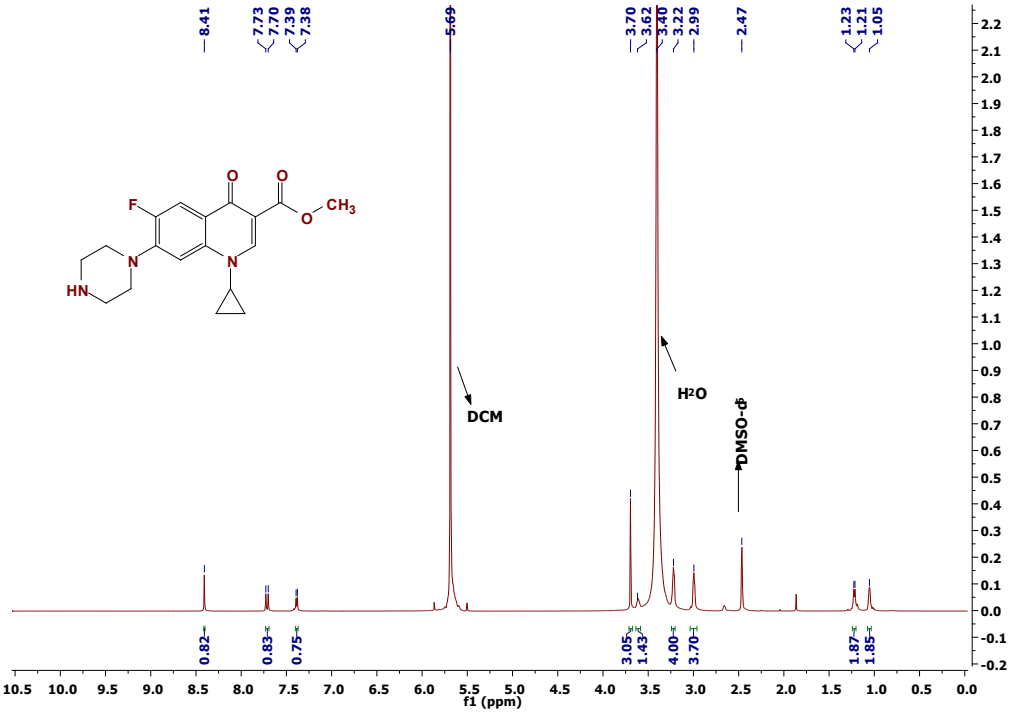

Figure S1. ^{1}H NMR (500MHz in DMSO-d_6) of compound (2)

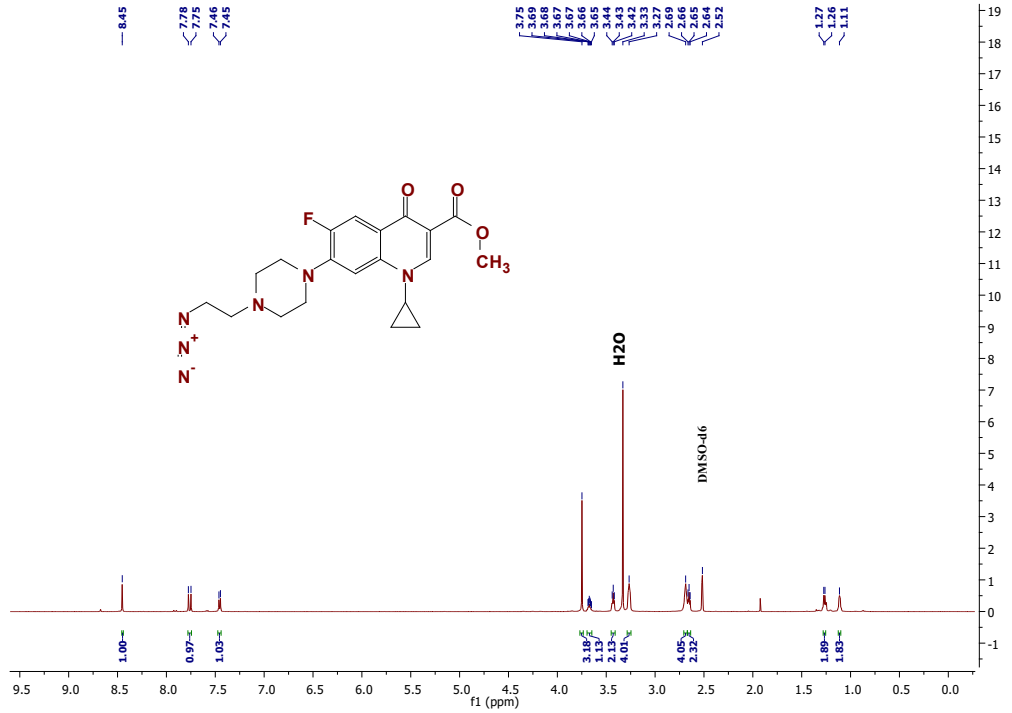

Figure S2. ^{1}H NMR (500MHz in DMSO-d_6) of compound (3)

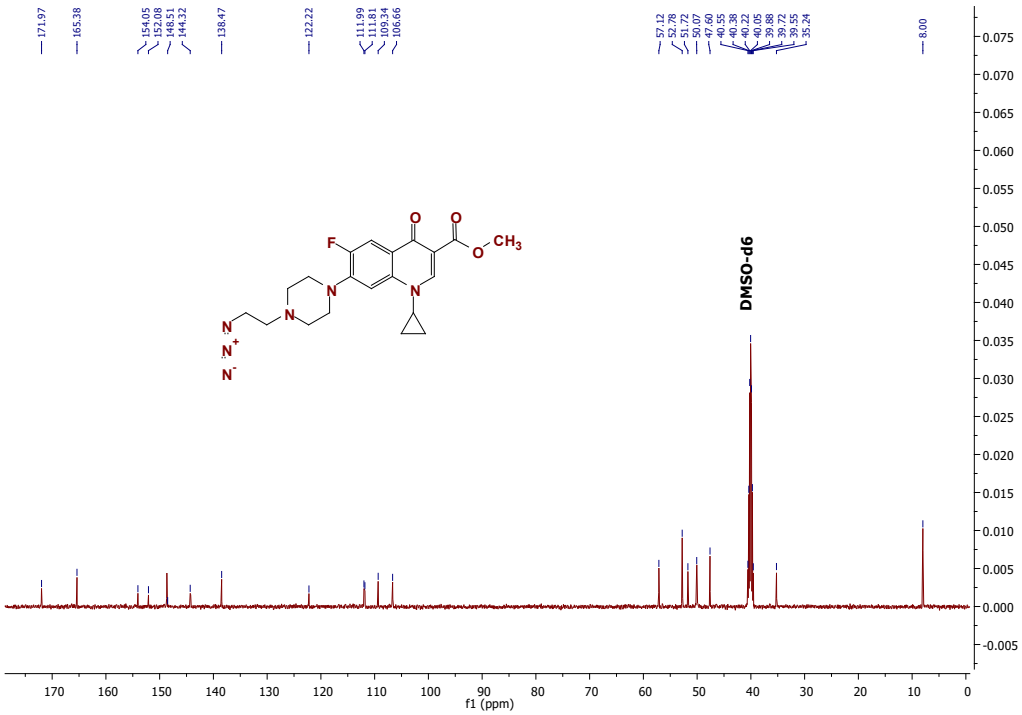

Figure S3.^{13}C NMR (126 MHz in DMSO-d_6) of compound (3)

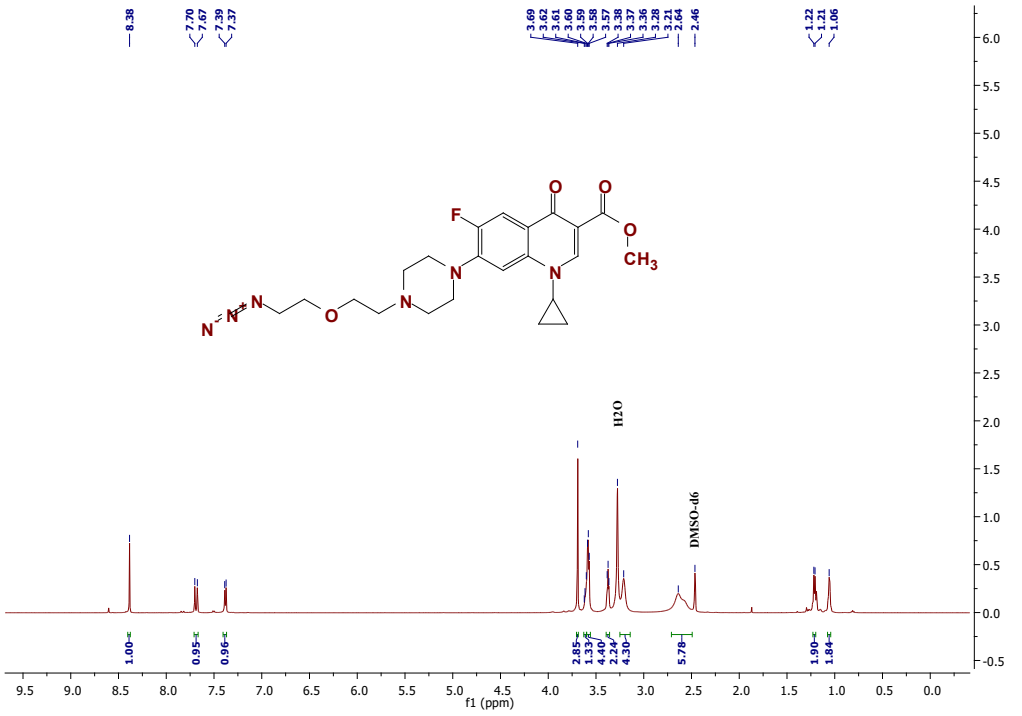

Figure S4. ^{1}H NMR (500MHz in DMSO-d_6) of compound (4)

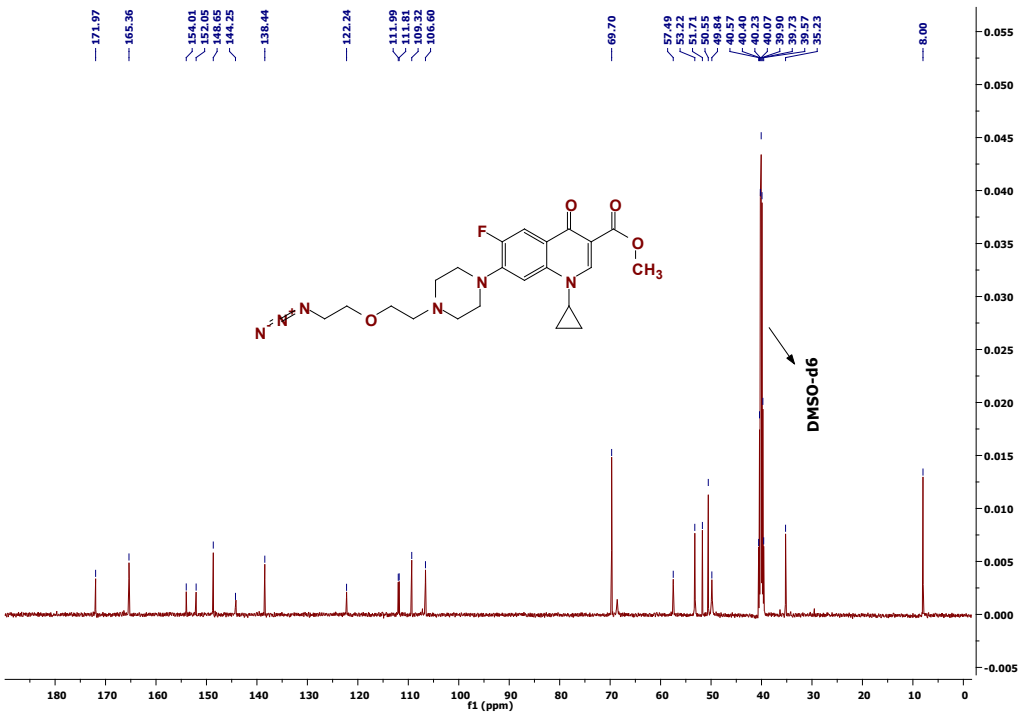

Figure S5.^{13}C NMR (126 MHz in DMSO-d_6) of compound (4)

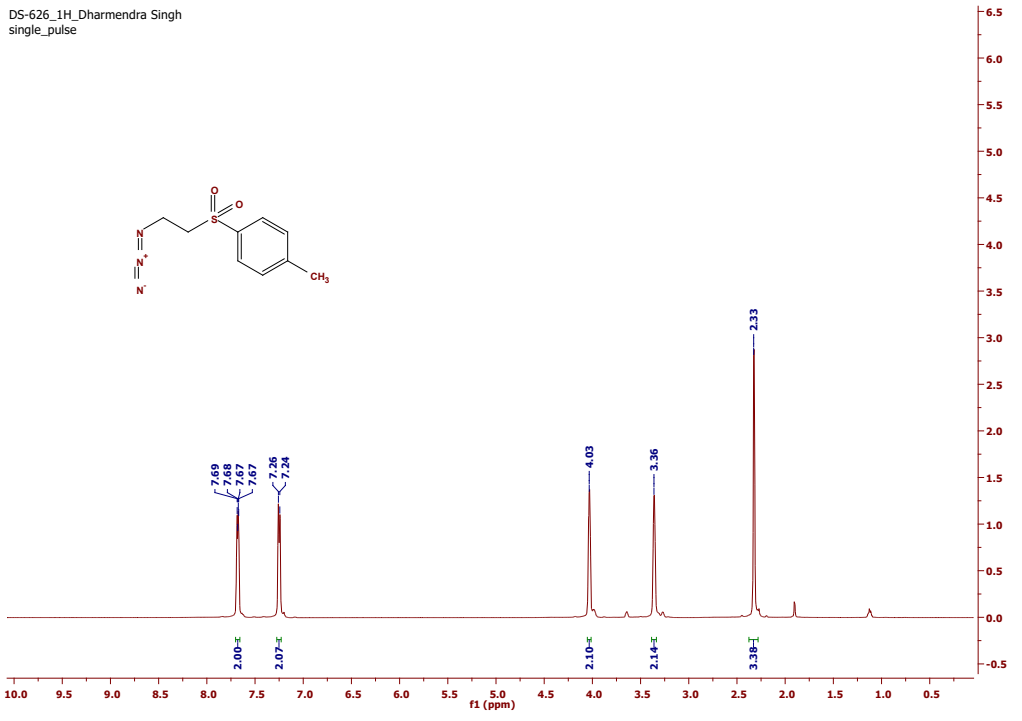

Figure S6. ^{1}H NMR (500MHz in $CDCl_3$) of compound (9)

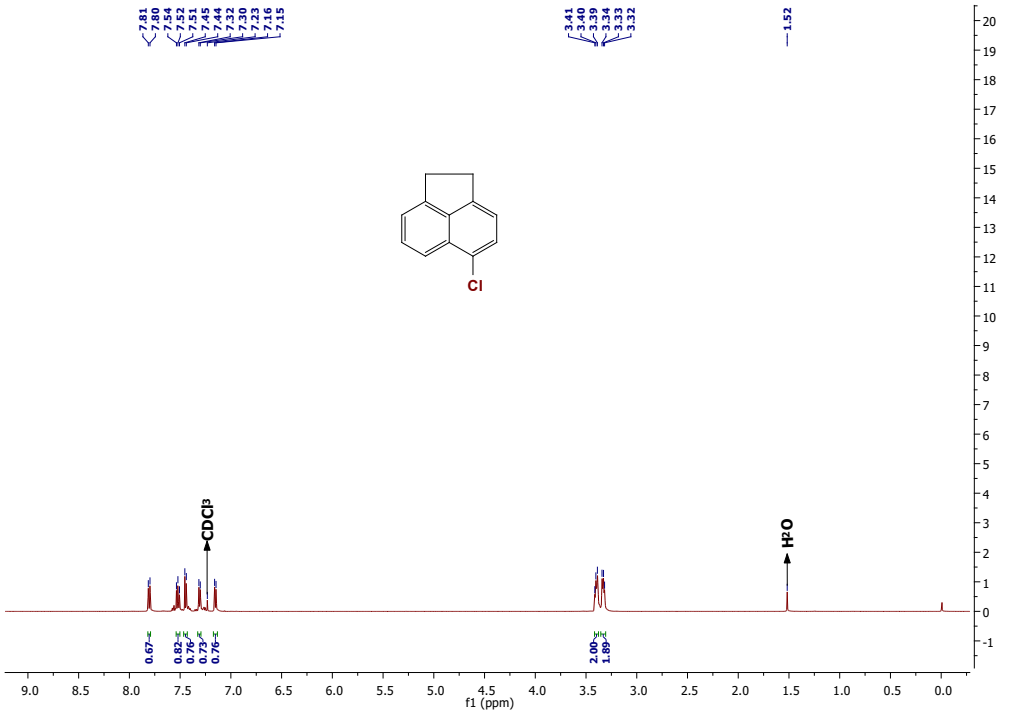

Figure S7. ^{1}H NMR (500MHz in $CDCl_3$) of compound (11a)

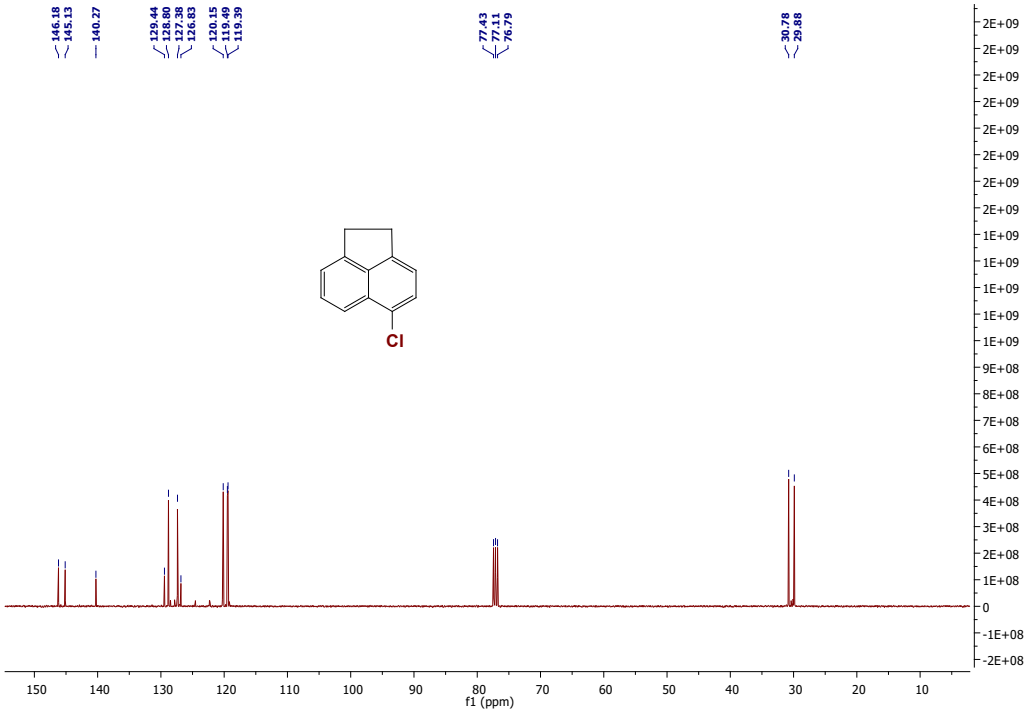

Figure S8 .^{13}C NMR (126 MHz in $CDCl_3$) of compound (11a)

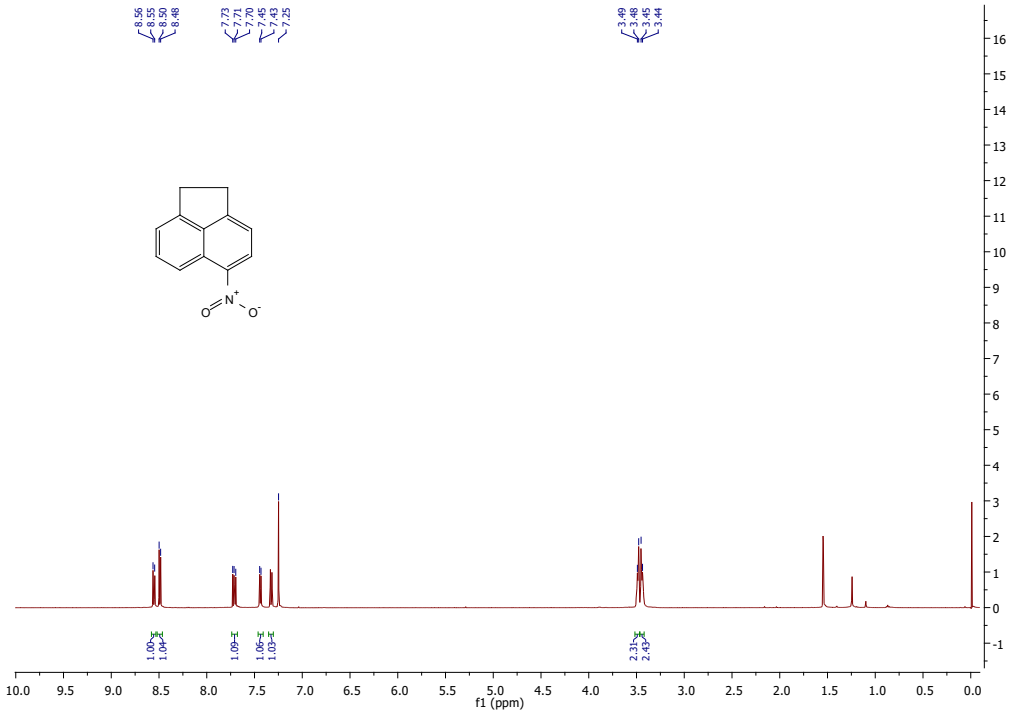

Figure S9. ^{1}H NMR (500MHz in $CDCl_3$) of compound (11b)

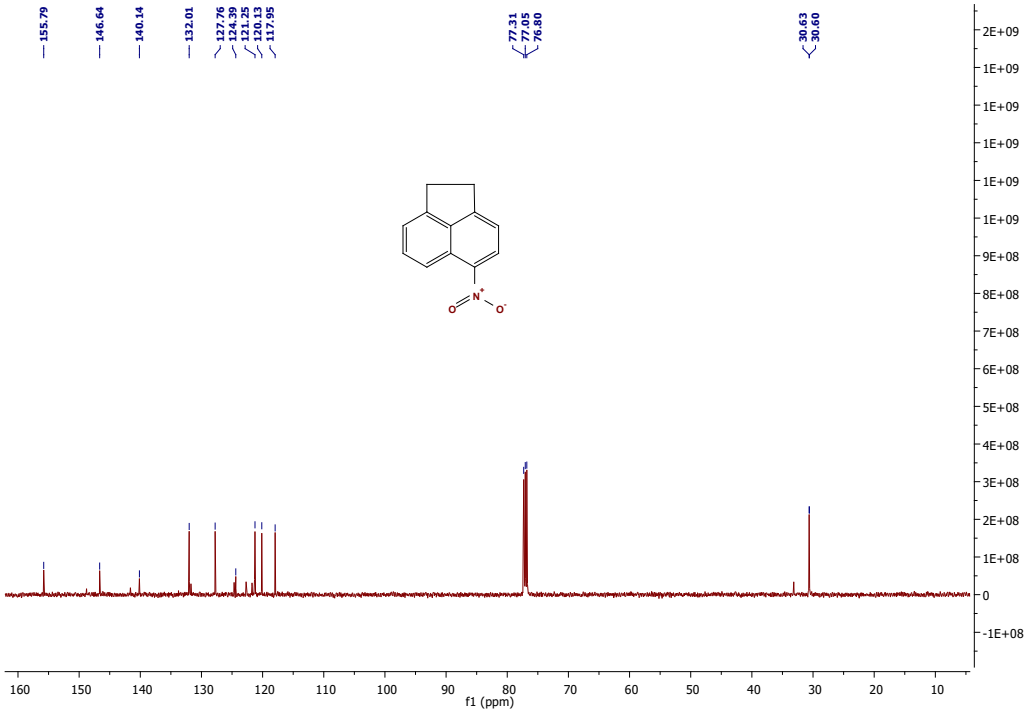

Figure S10 .^{13}C NMR (126 MHz in $CDCl_3$) of compound (11b)

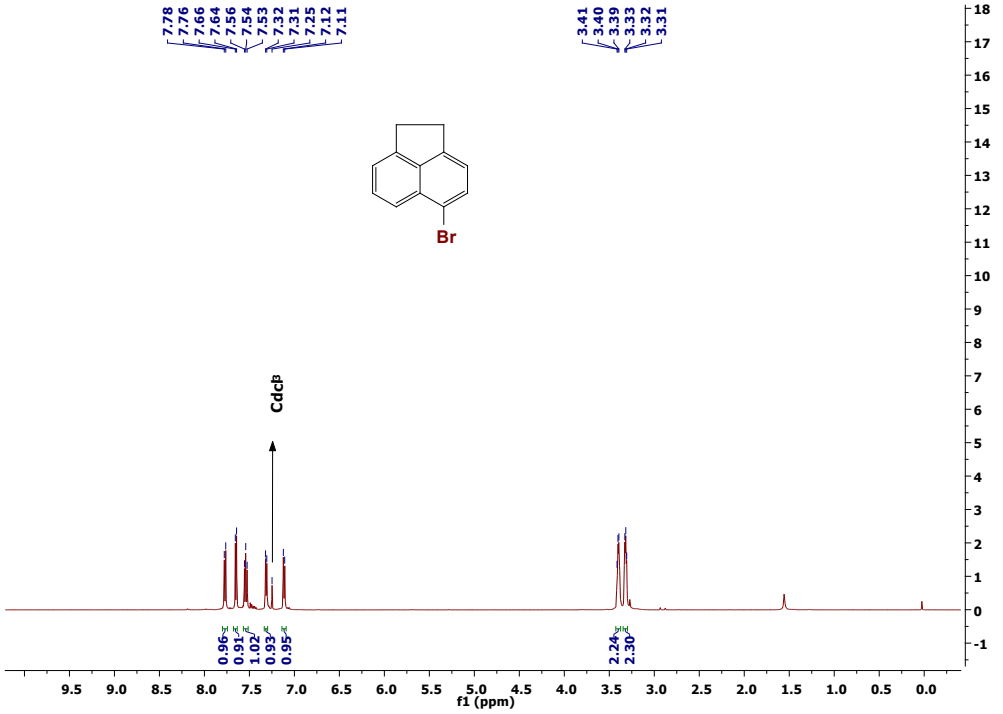

Figure S11. ^{1}H NMR (500MHz in $CDCl_3$) of compound (11c)

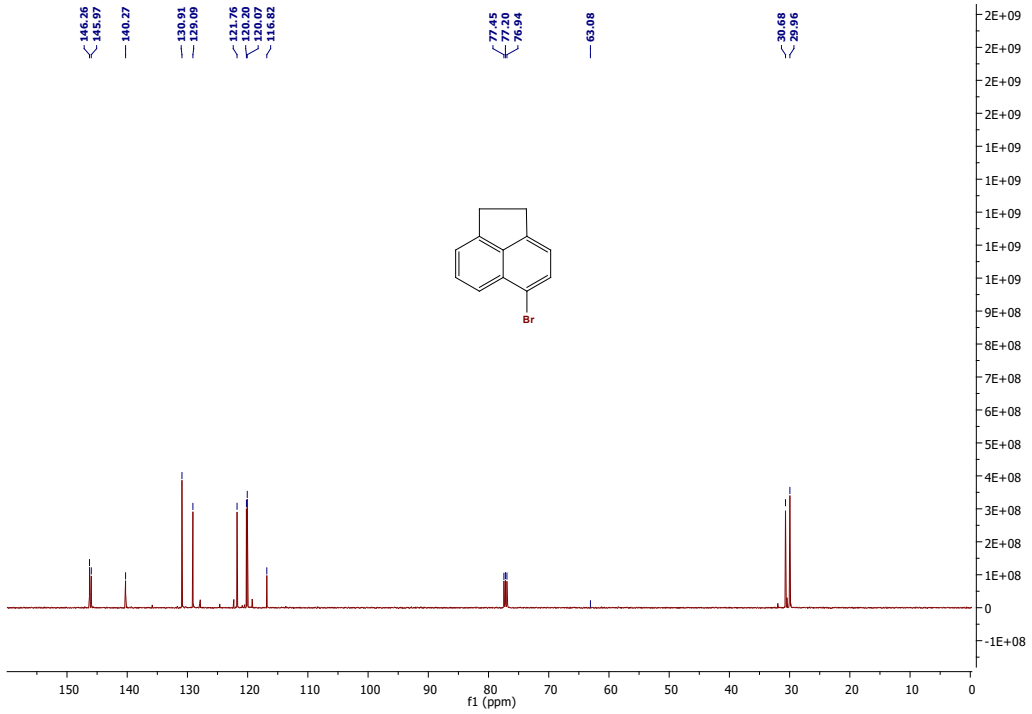

Figure S12. ^{13}C NMR (126 MHz in $CDCl_3$) of compound (11c)

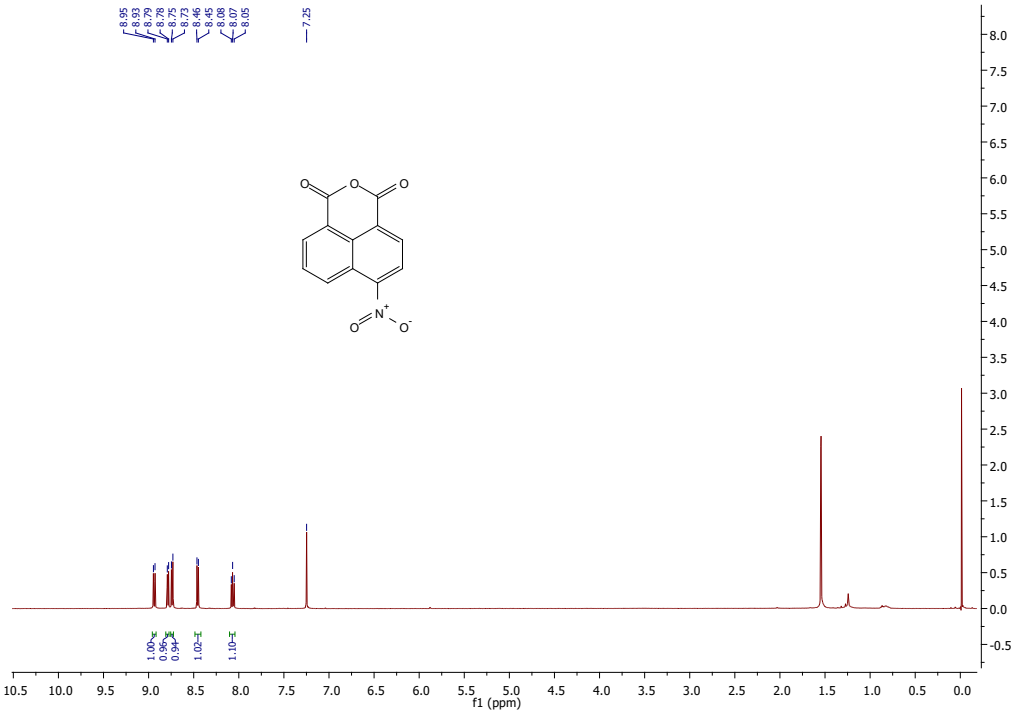

Figure S13. ^{1}H NMR (500MHz in $CDCl_3$) of compound (12a)

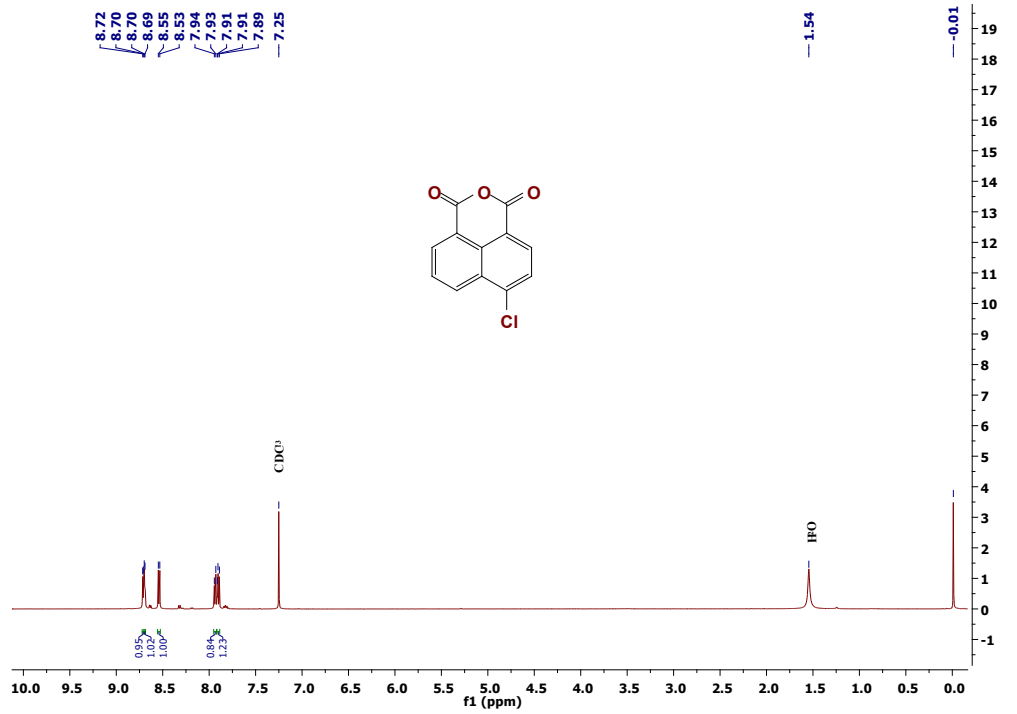

Figure S14. ^{1}H NMR (500MHz in $CDCl_3$) of compound (12b)

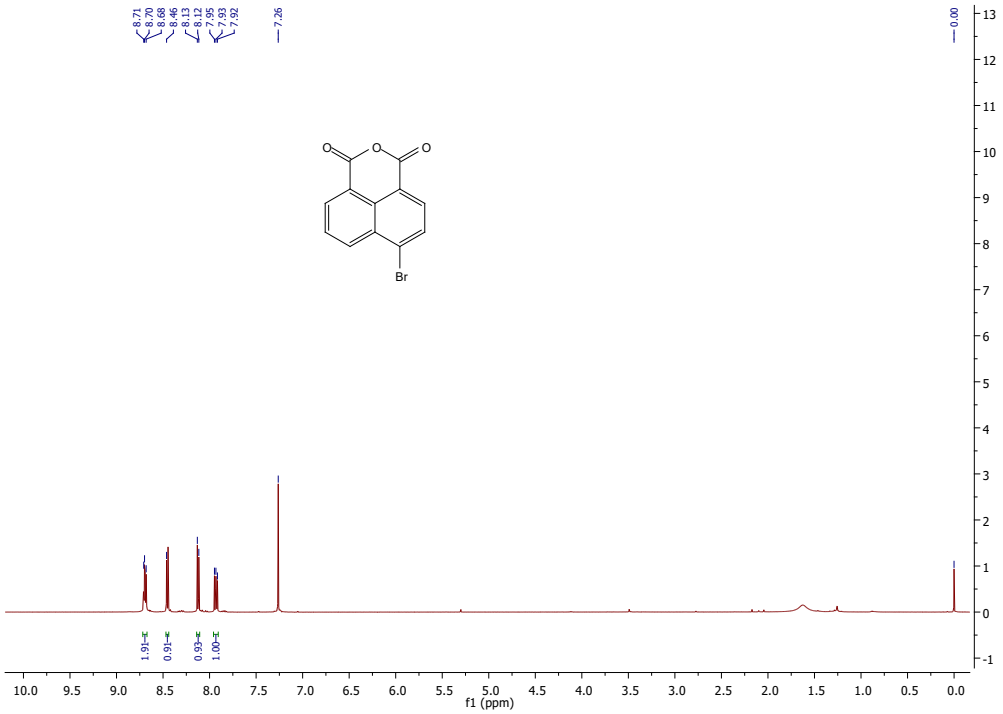

Figure S15. ^{1}H NMR (500MHz in $CDCl_3$) of compound (12c)

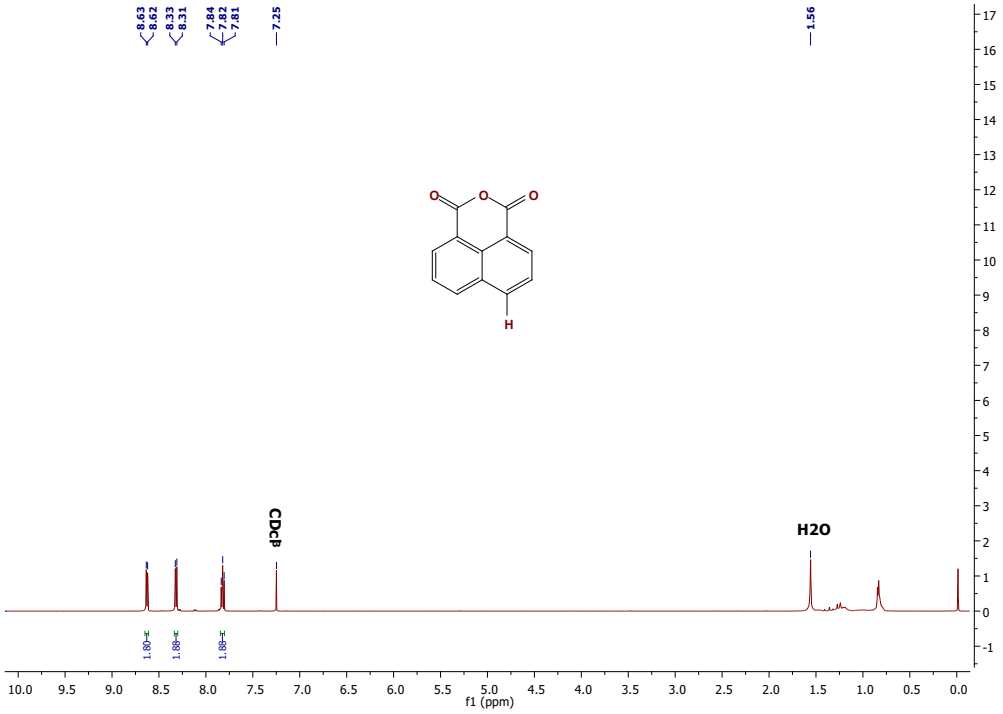

Figure S16. ^{1}H NMR (500MHz in $CDCl_3$) of compound (12d)

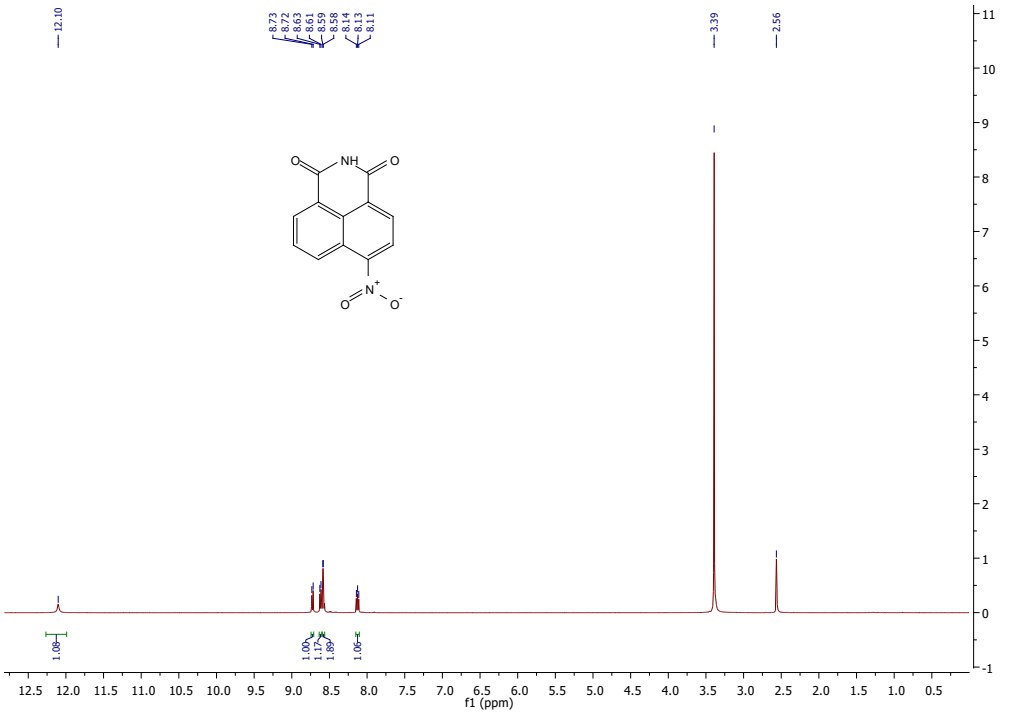

Figure S17. ^{1}H NMR (500MHz in DMSO-d_6) of compound (13a)

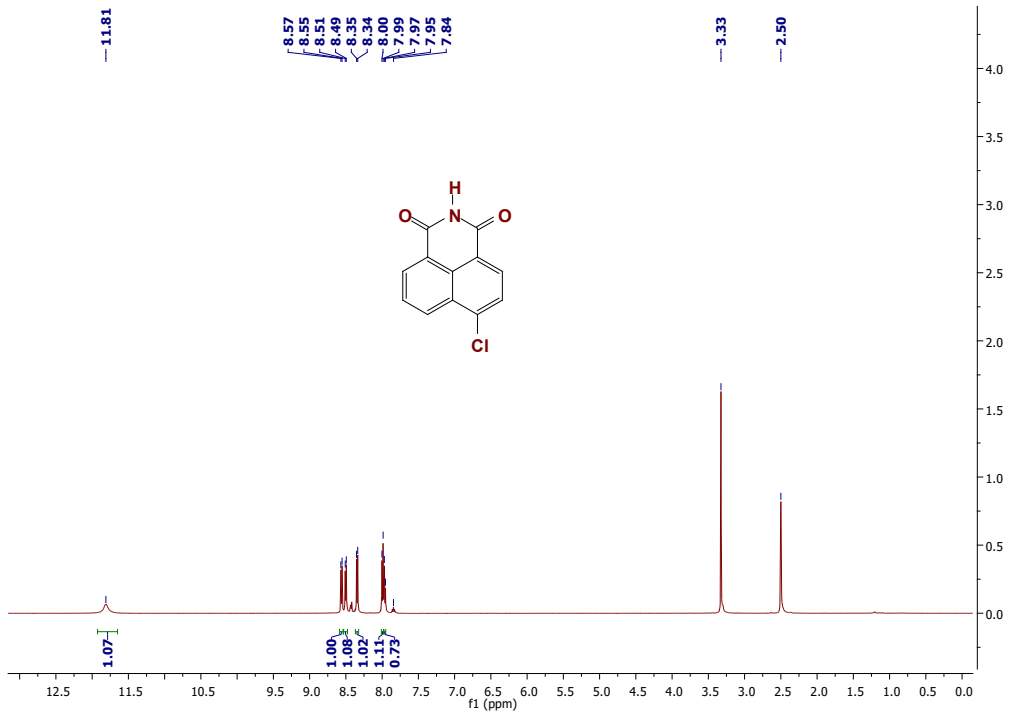

Figure S18. ^{1}H NMR (500MHz in DMSO-d_6) of compound (13b)

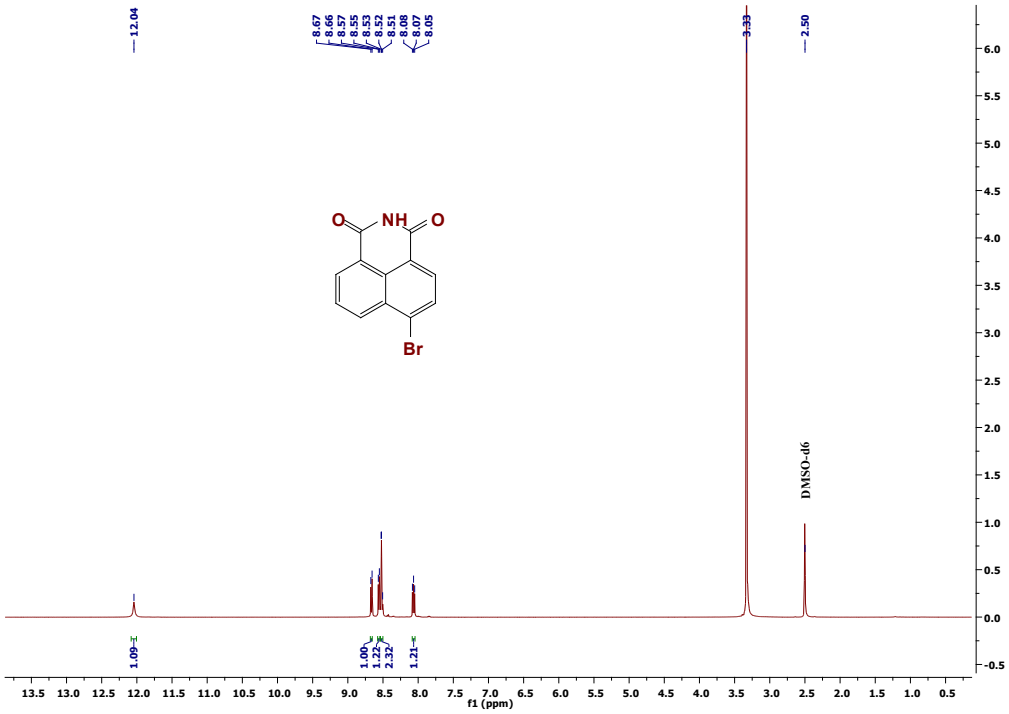

Figure S19. ^{1}H NMR (500MHz DMSO-d_6) of compound (13c)

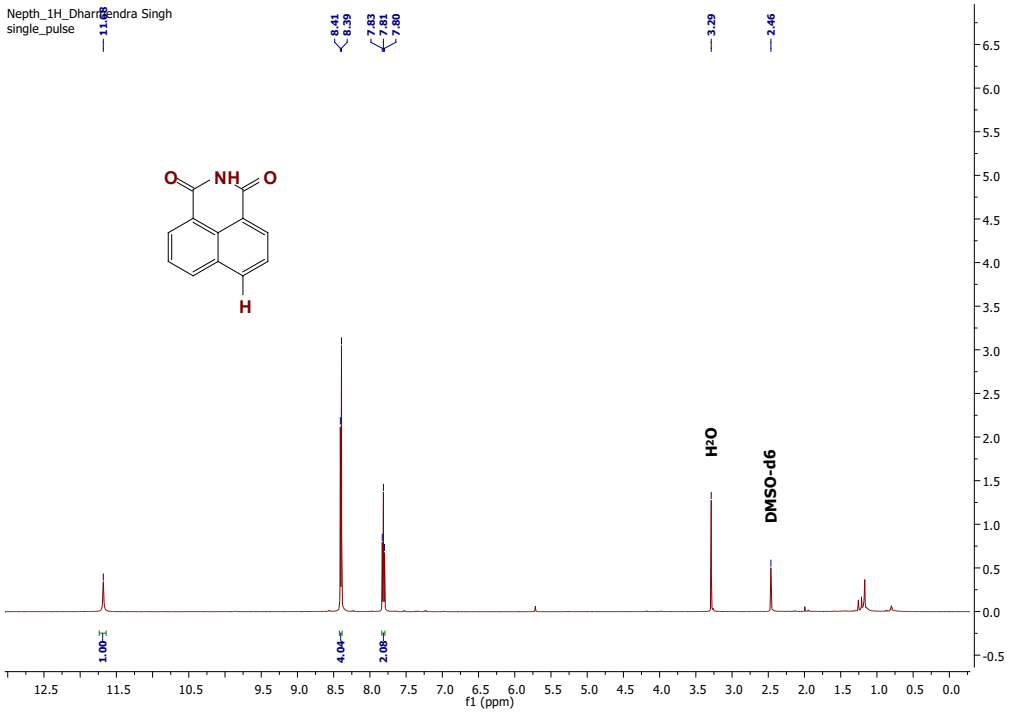

Figure S20. ^{1}H NMR (500MHz in DMSO-d_6) of compound (13d)

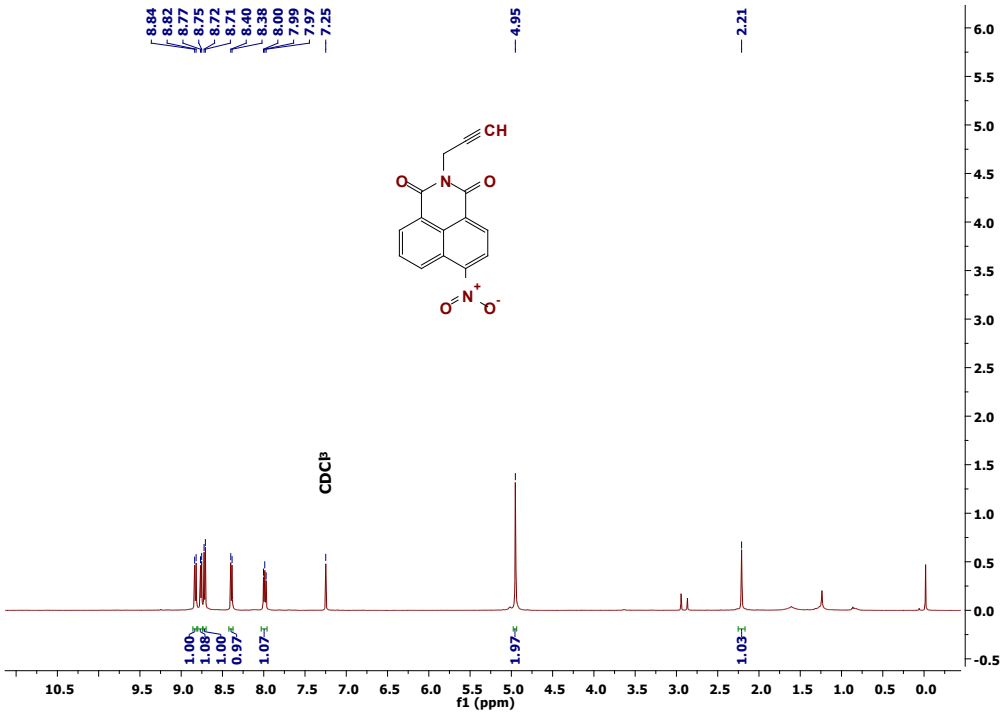

Figure S21. ^{1}H NMR (500MHz in $CDCl_3$) of compound (14a)

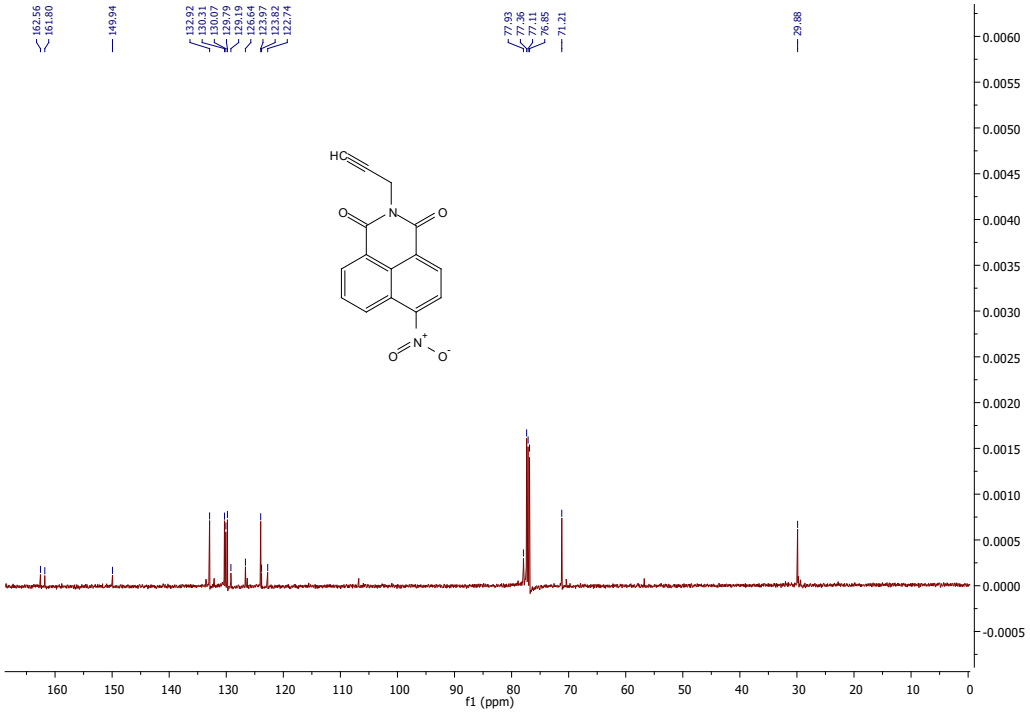

Figure S22.^{13}C NMR (126 MHz in $CDCl_3$) of compound (14a)

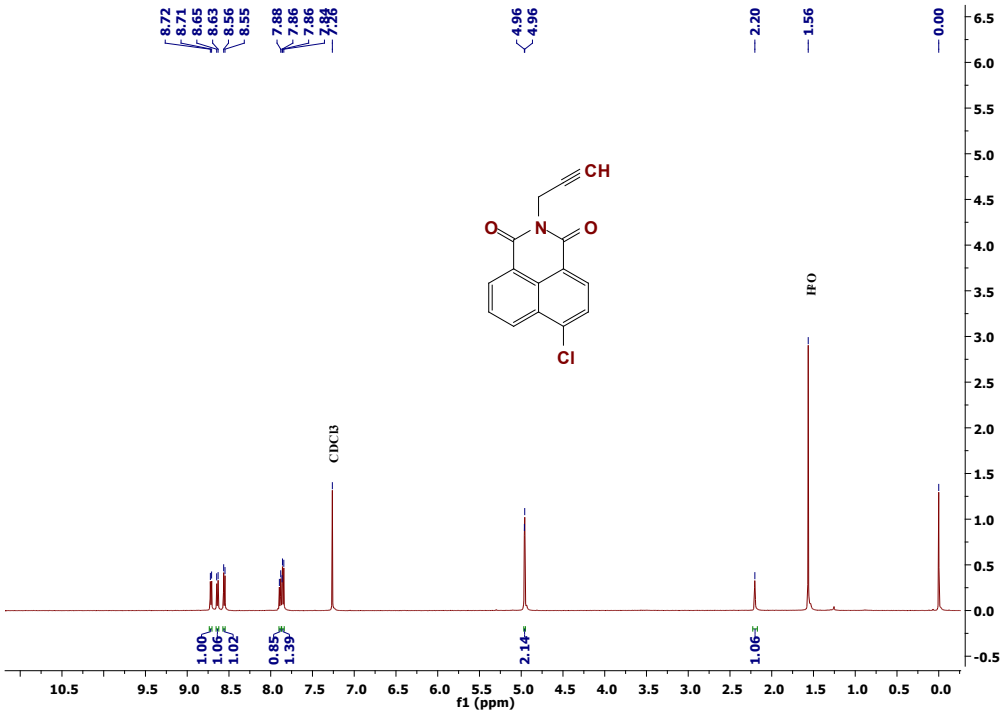

Figure S23. ^{1}H NMR (500MHz in $CDCl_3$) of compound (14b)

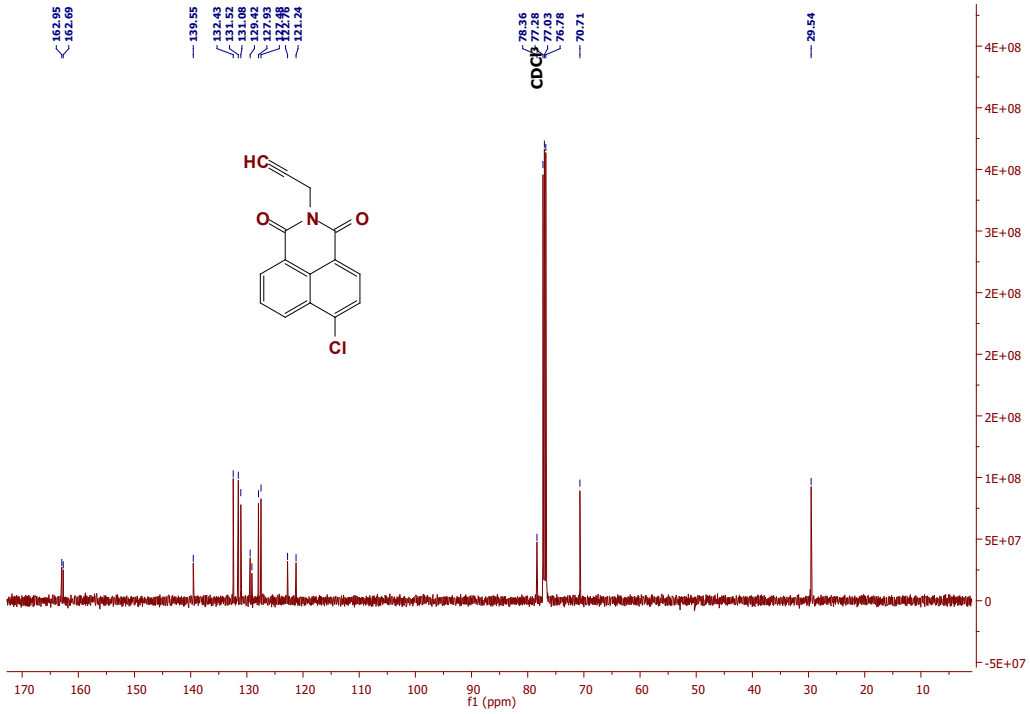

Figure S24.^{13}C NMR (126 MHz in $CDCl_3$) of compound (14b)

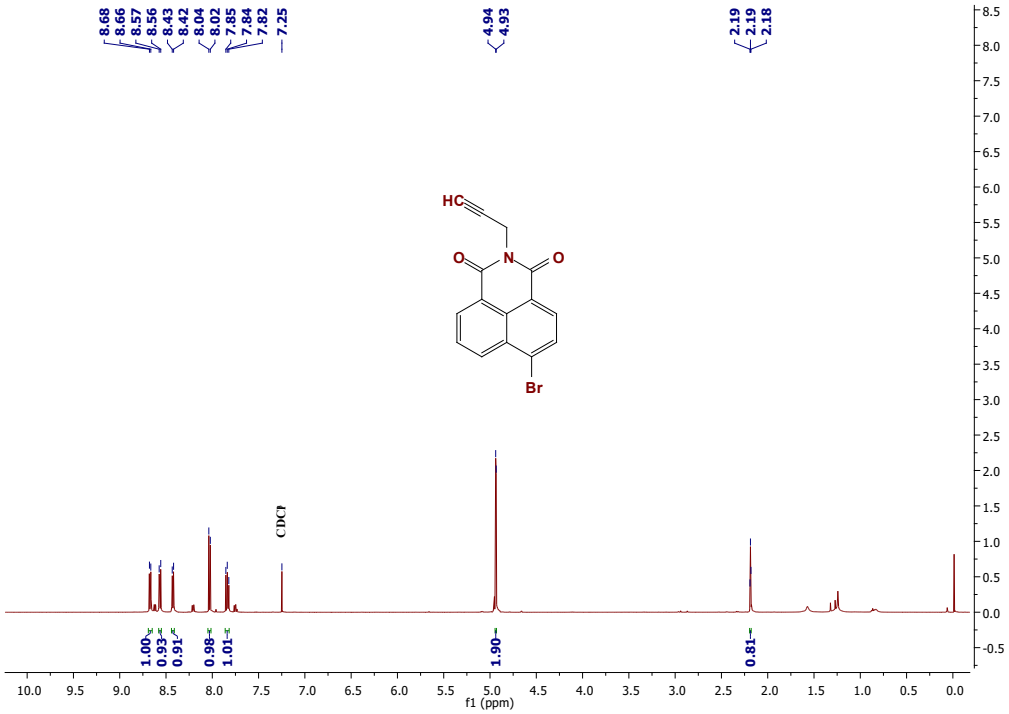

Figure S25. ^{1}H NMR (500MHz in $CDCl_3$) of compound (14c)

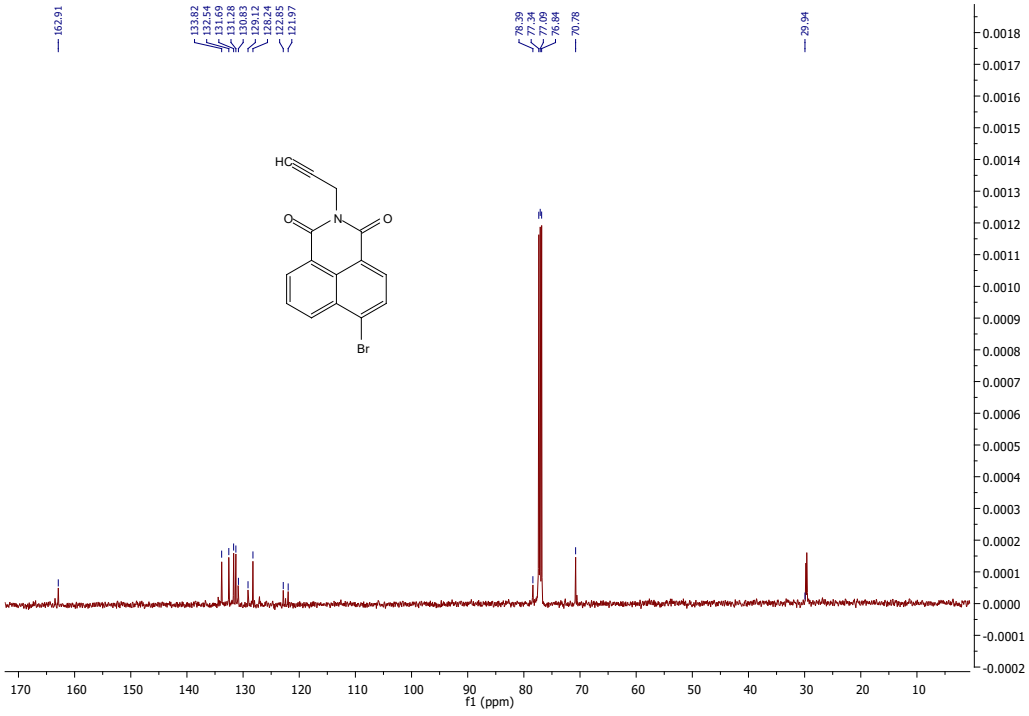

Figure S26.^{13}C NMR (126 MHz in $CDCl_3$) of compound (14c)

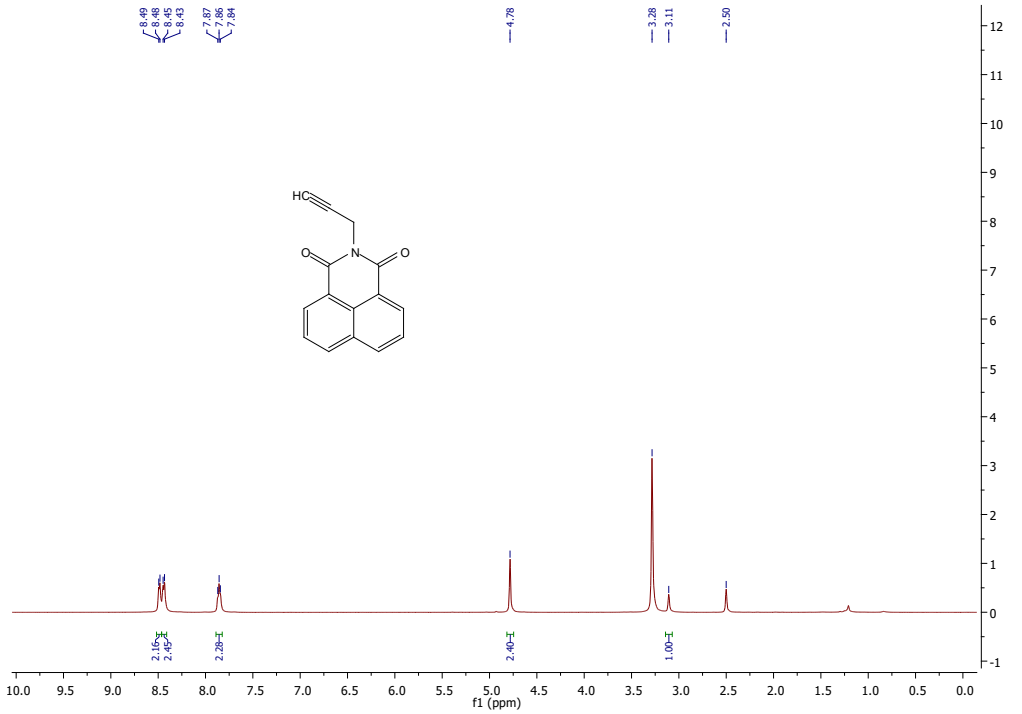

Figure S27. ^{1}H NMR (500MHz in DMSO-d_6) of compound (14d)

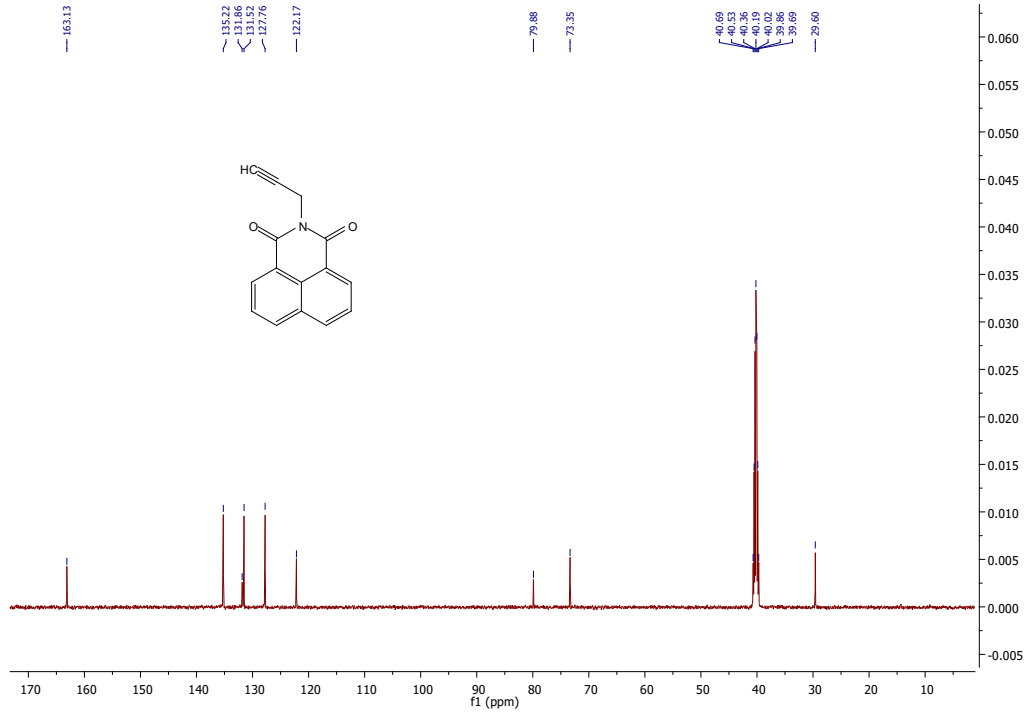

Figure S28.^{13}C NMR (126 MHz in DMSO-d_6) of compound (14d)

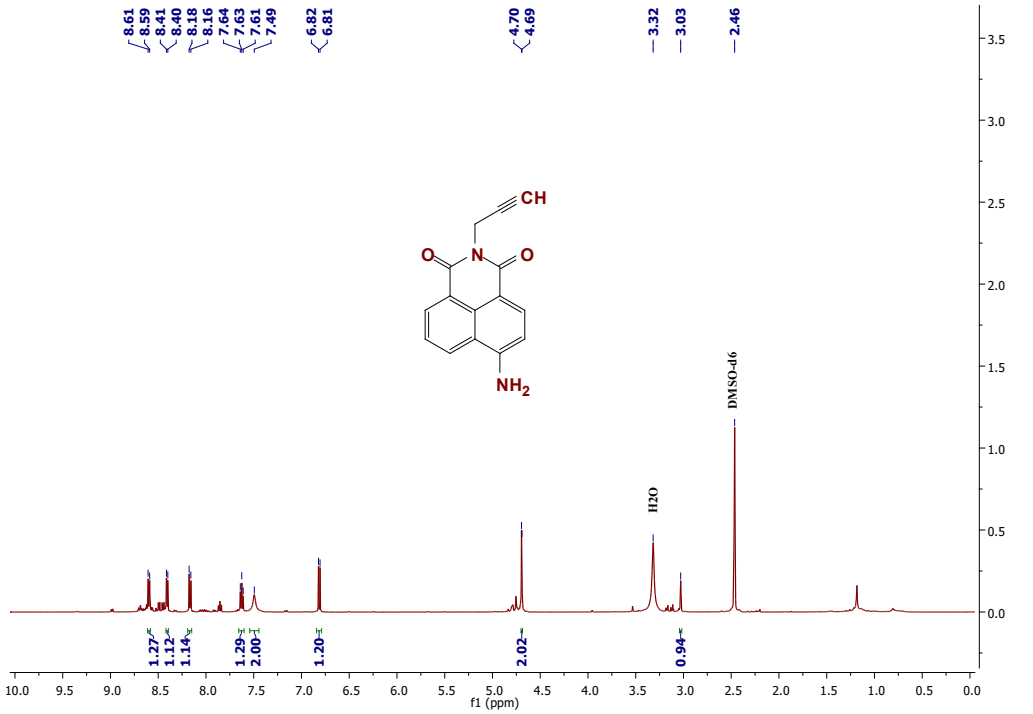

Figure S29. ^{1}H NMR (500MHz in DMSO-d_6) of compound (15a)

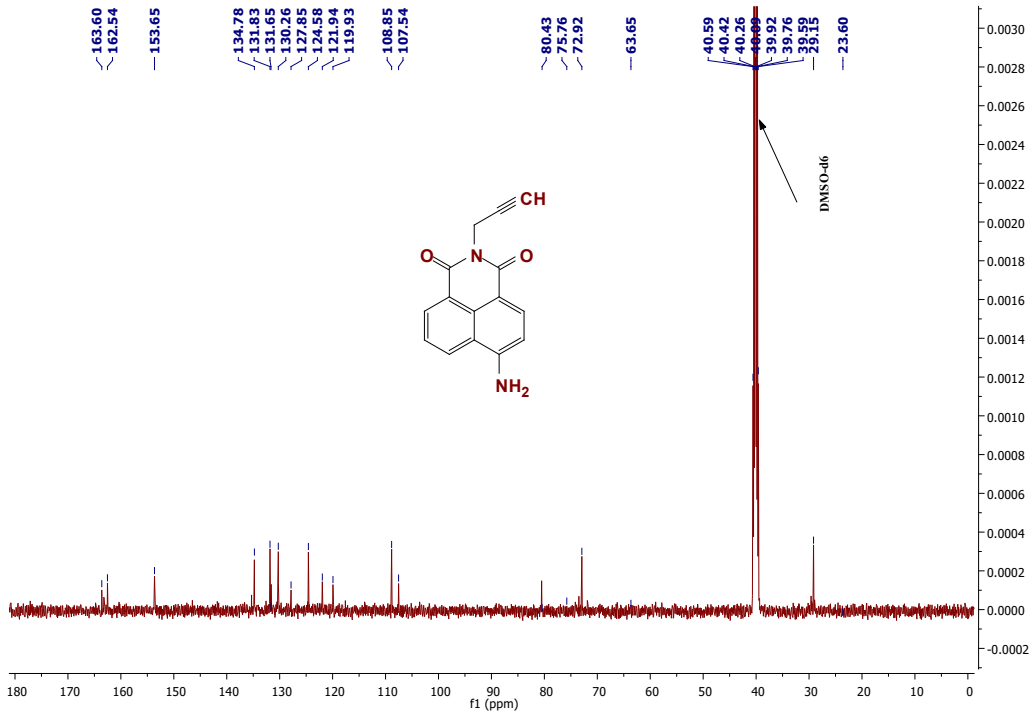

Figure S30.^{13}C NMR (126 MHz in DMSO-d_6) of compound (15a)

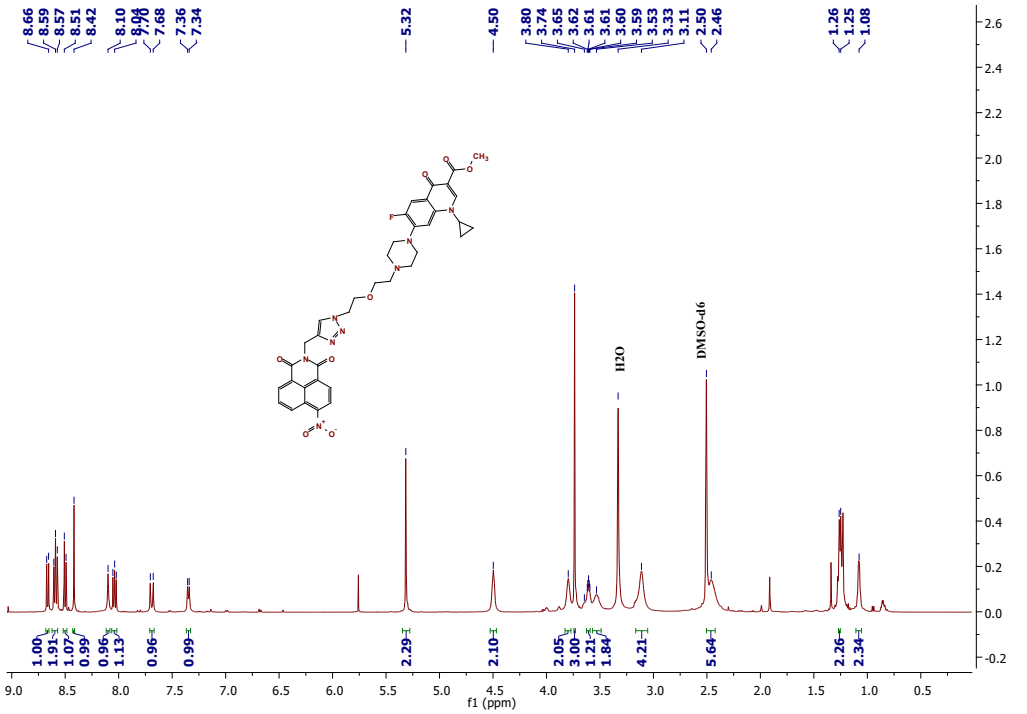

Figure S31. ^{1}H NMR (500MHz in DMSO-d_6) of compound (17a)

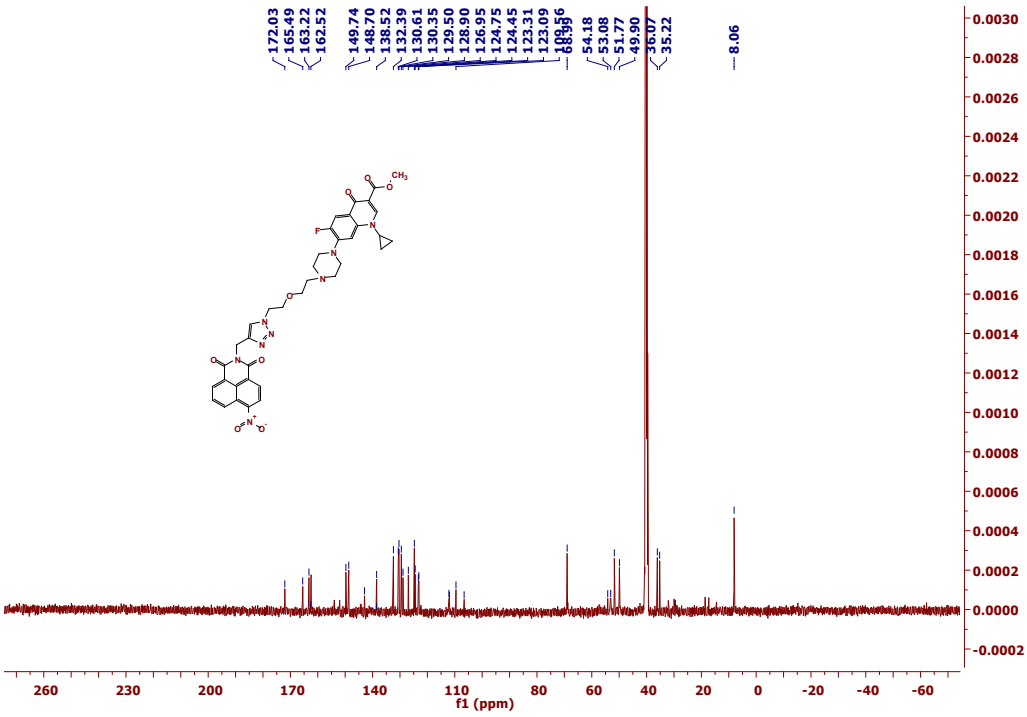

Figure S32.^{13}C NMR (126 MHz in DMSO-d_6) of compound (17a)

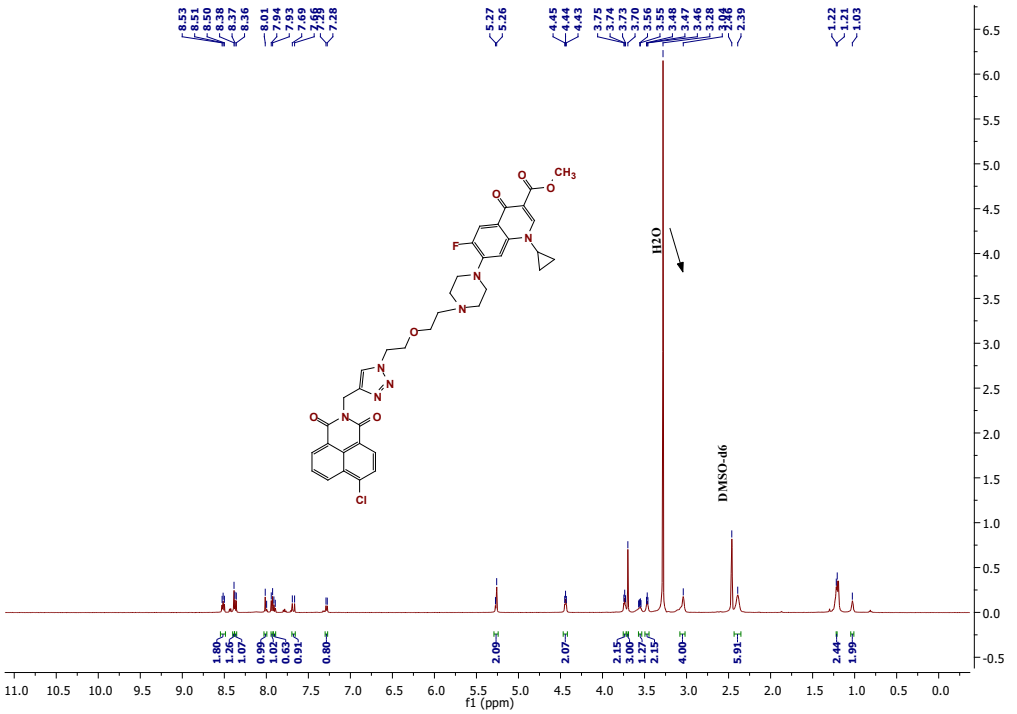

Figure S33. ^{1}H NMR (500MHz in DMSO-d_6) of compound (17b)

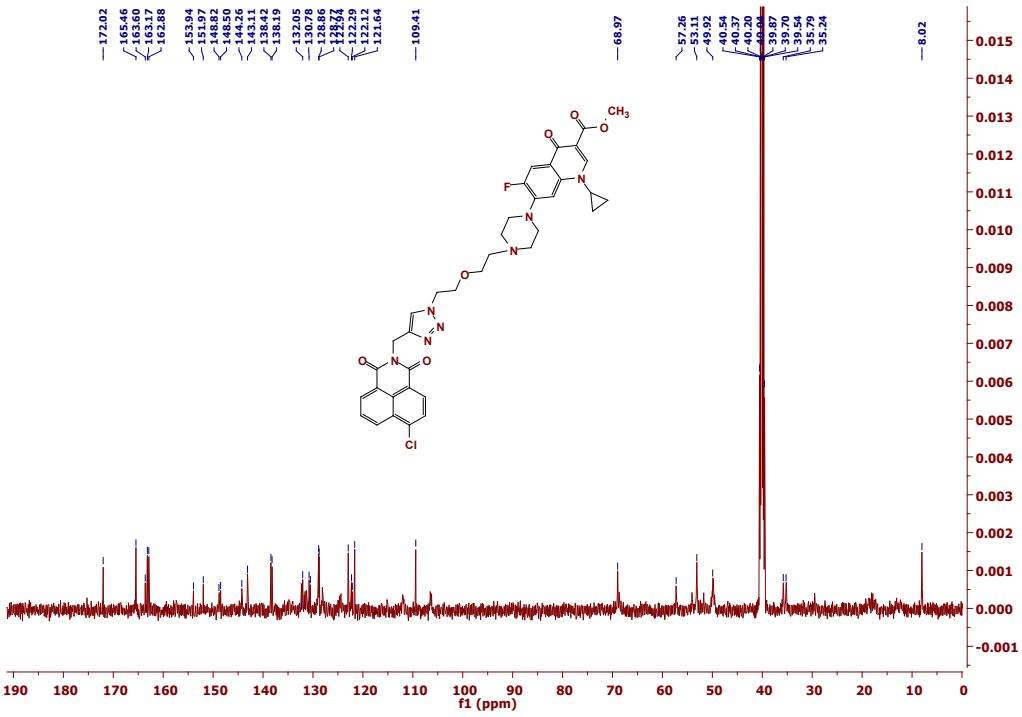

Figure S34.^{13}C NMR (126 MHz in DMSO-d_6) of compound (17b)

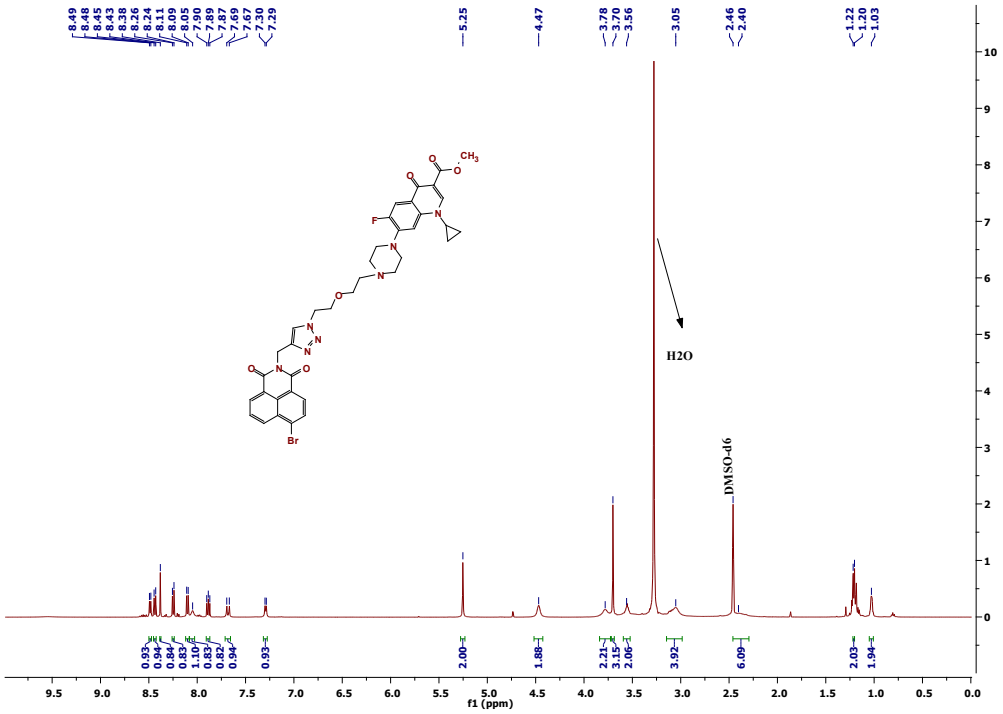

Figure S35. ^{1}H NMR (500MHz in DMSO-d_6) of compound (17c)

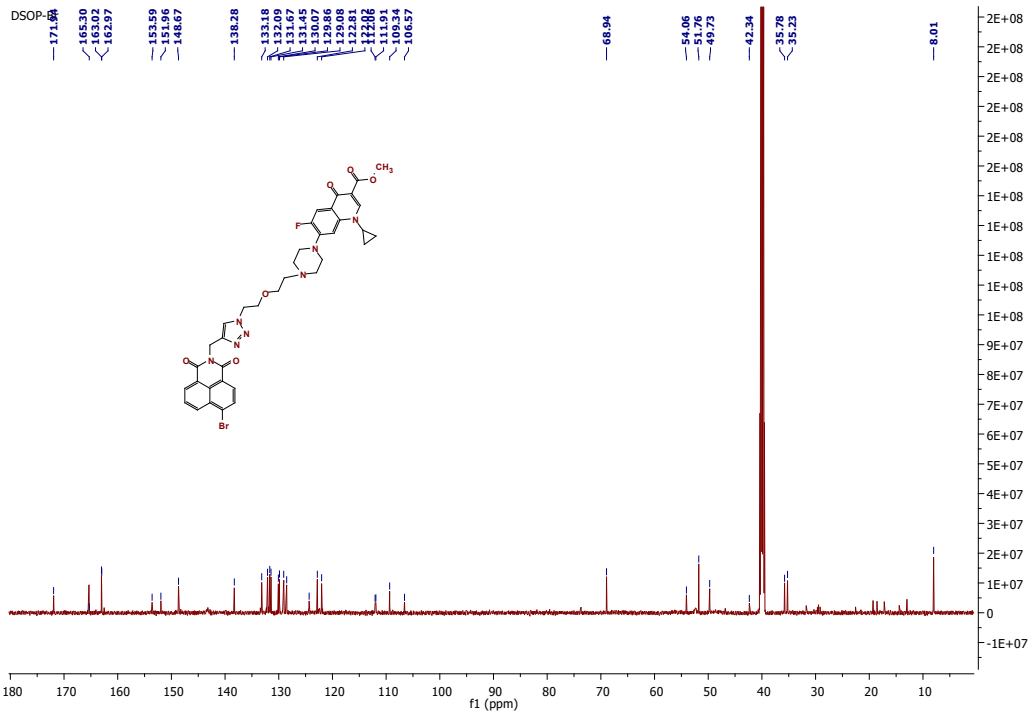

Figure S36.^{13}C NMR (126 MHz in DMSO-d_6) of compound (17c)

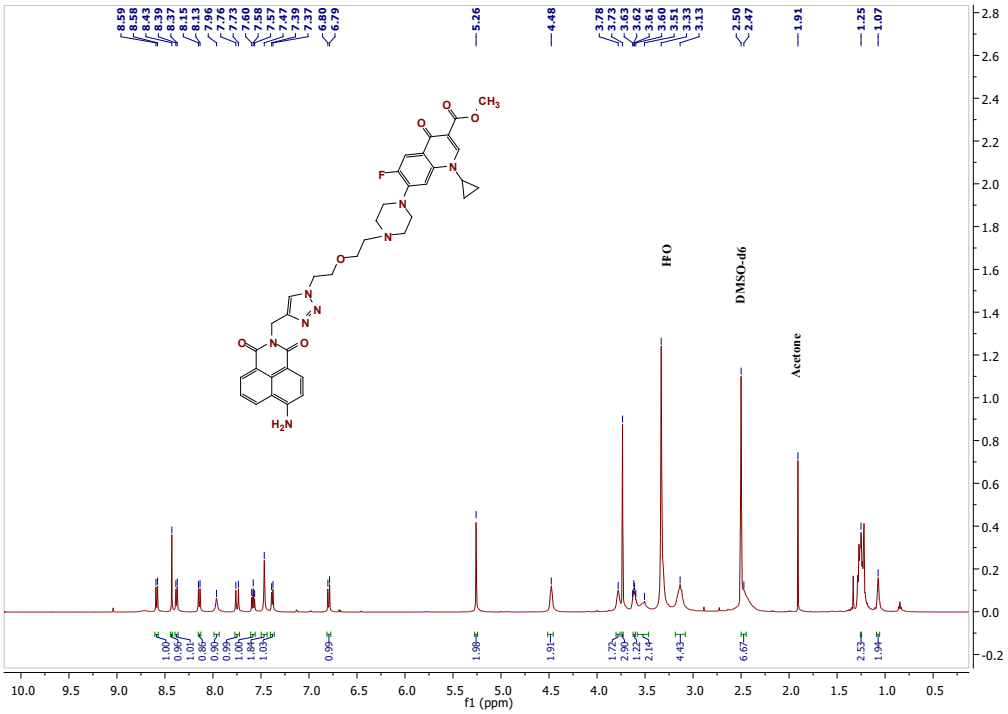

Figure S37. ^{1}H NMR (500MHz in DMSO-d_6) of compound (17d)

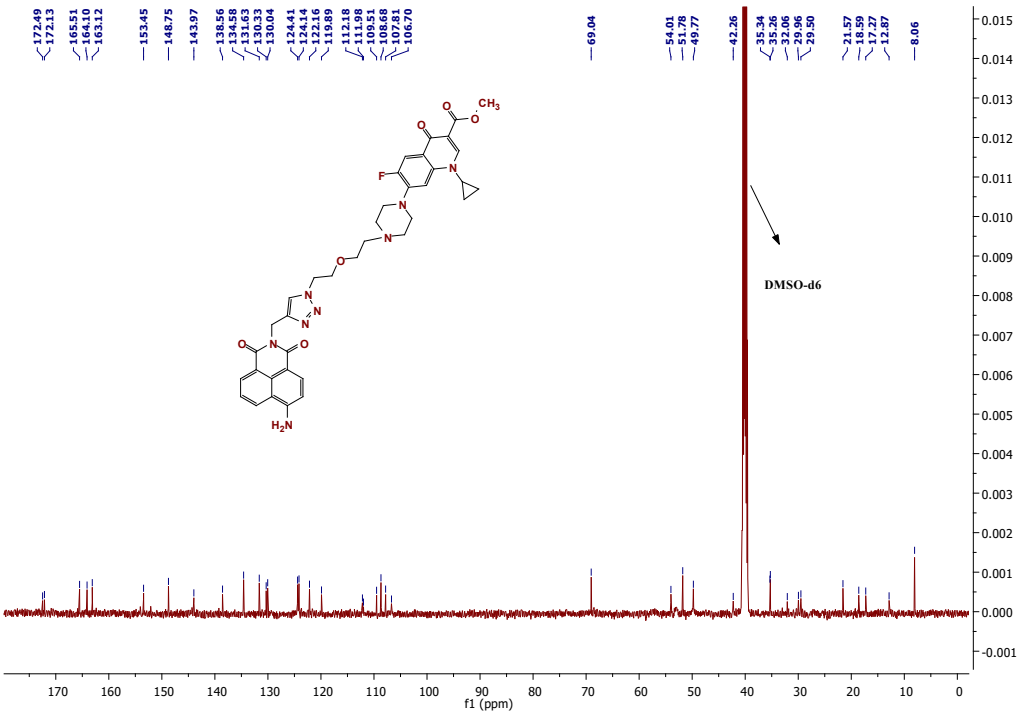

Figure S38.^{13}C NMR (126 MHz in DMSO-d_6) of Compound (17d)

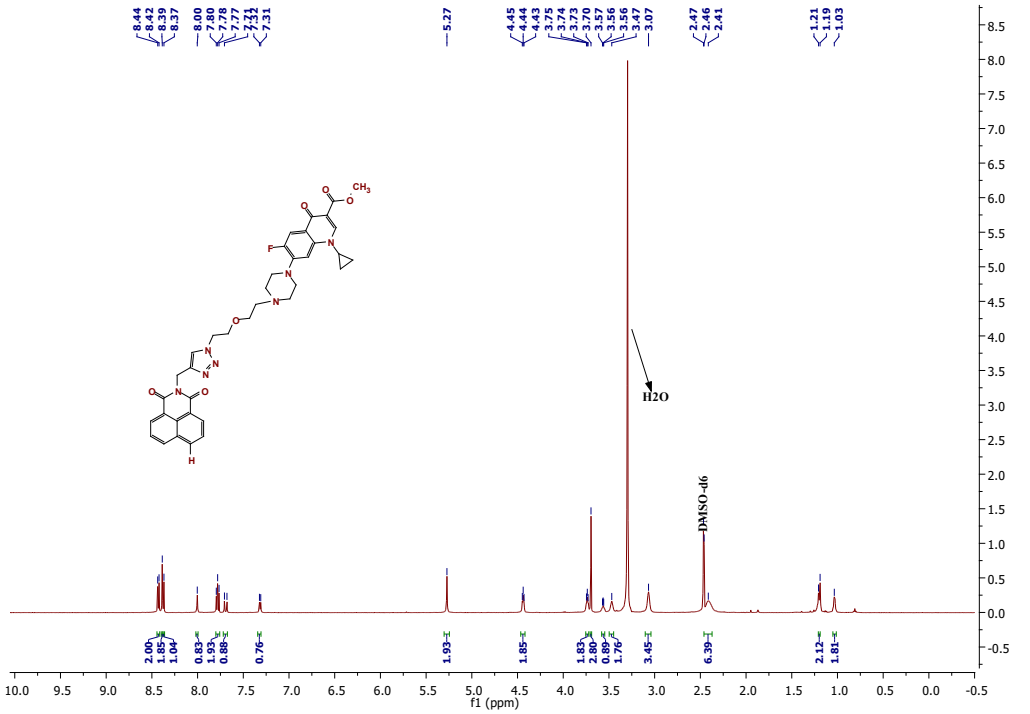

Figure S39. ^{1}H NMR (500MHz in DMSO-d_6) of compound (17e)

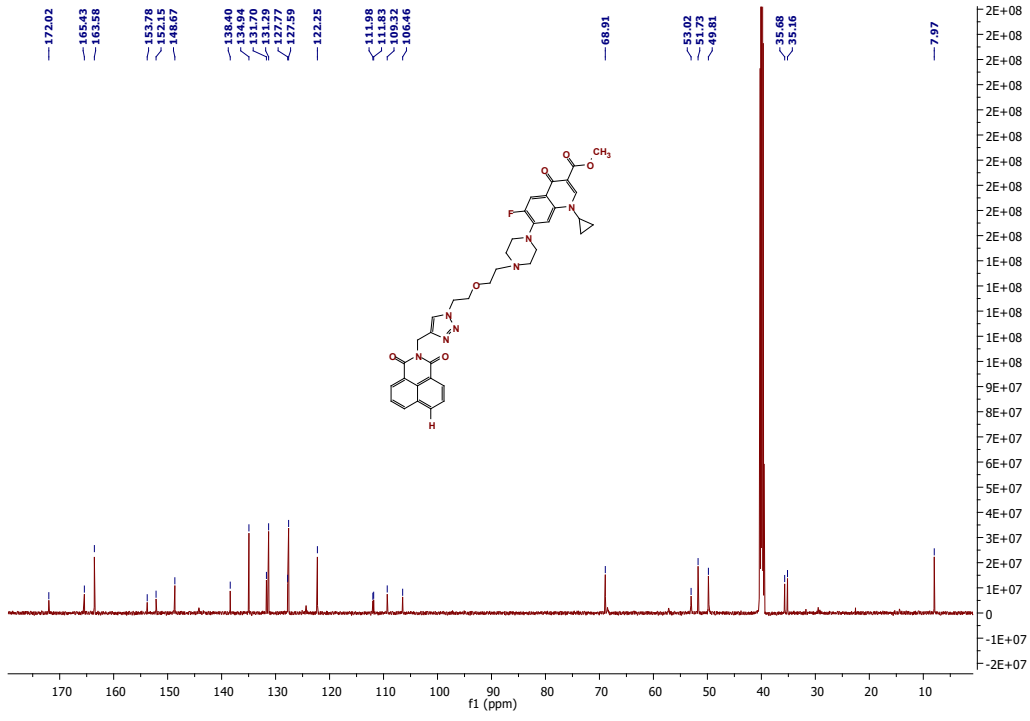

Figure S40.^{13}C NMR (126 MHz in DMSO-d_6) of compound (17e)

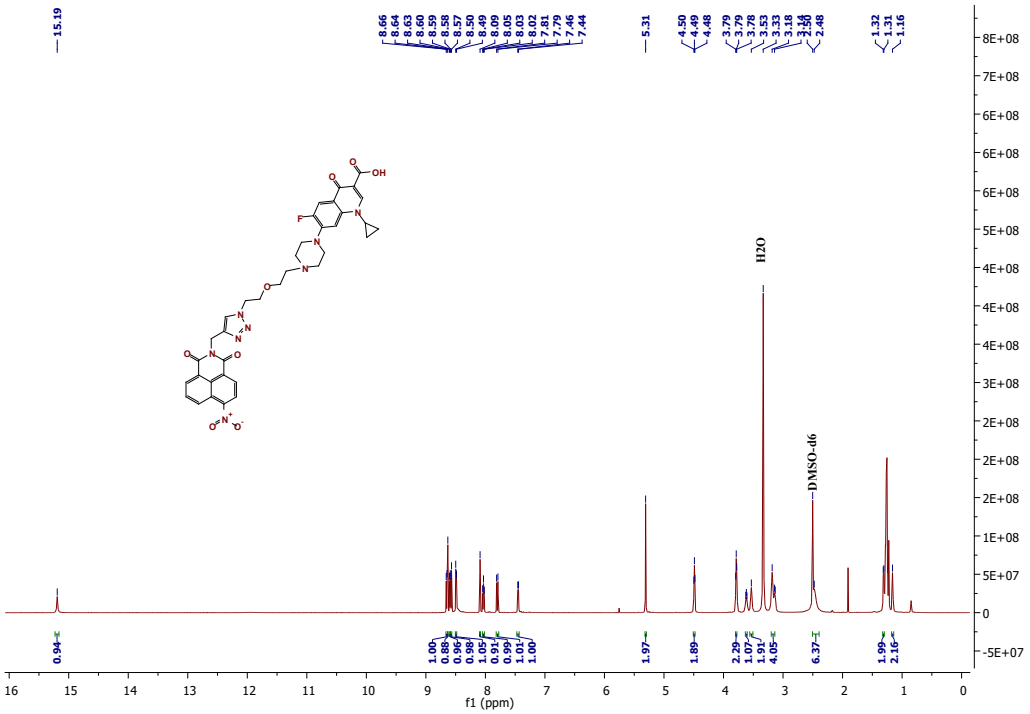

Figure S41. ^{1}H NMR (500MHz in DMSO-d_6) of compound (18a)

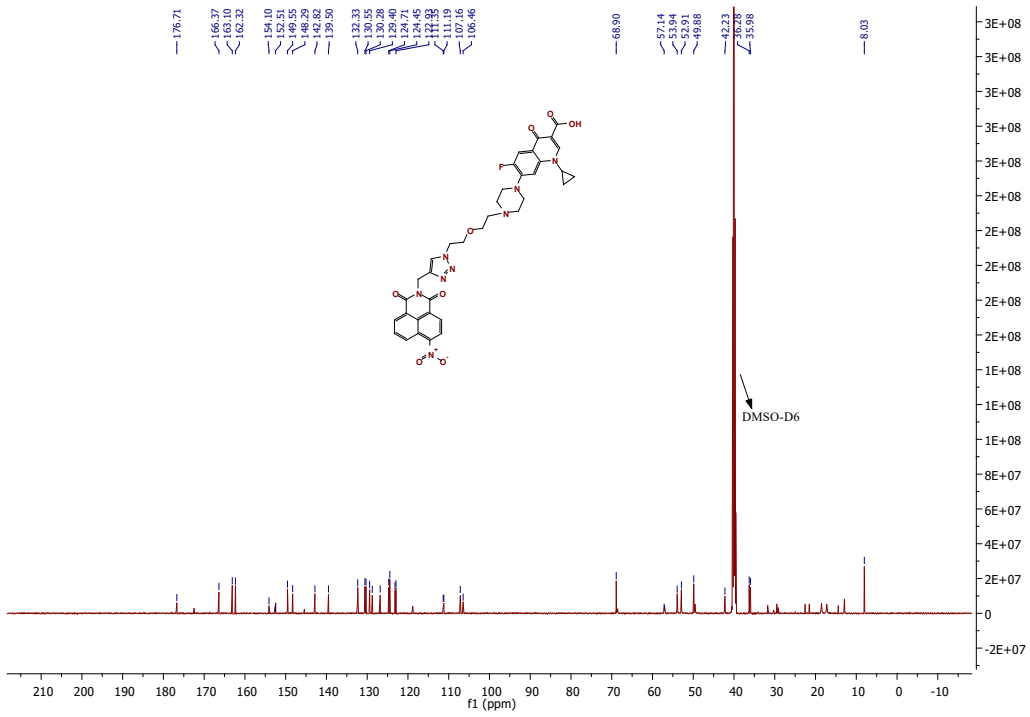

Figure S42.^{13}C NMR (126 MHz in DMSO-d_6) of compound (18a)

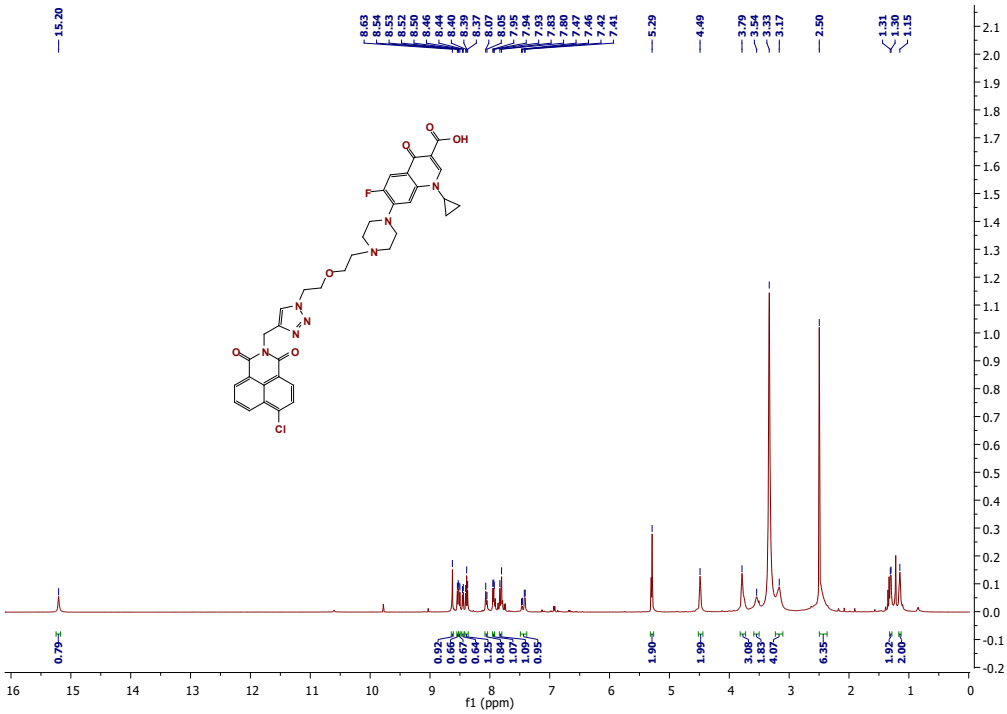

Figure S43. ^{1}H NMR (500MHz in DMSO-d_6) of compound (18b)

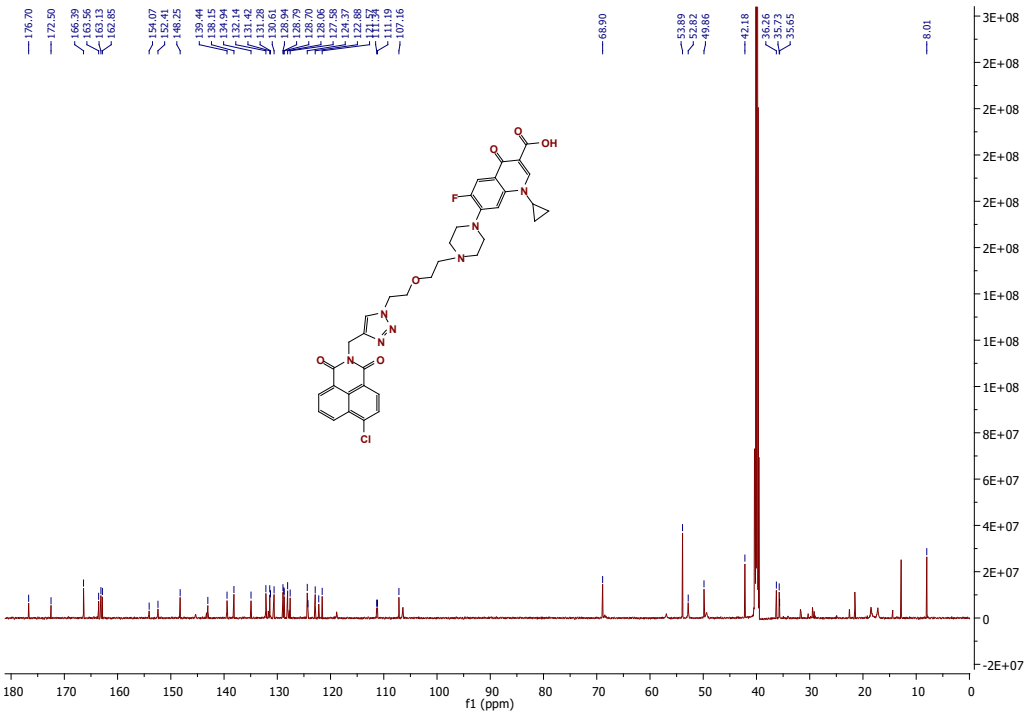

Figure S44.^{13}C NMR (151 MHz in DMSO-d_6) of compound (18b)

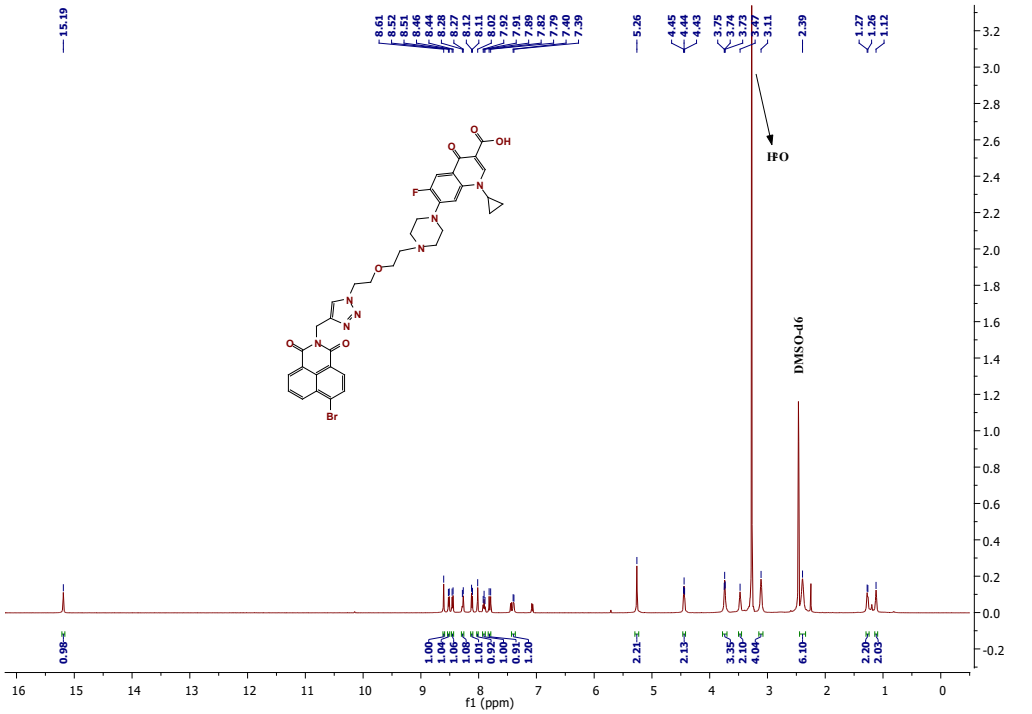

Figure S45. ^{1}H NMR (500MHz in DMSO-$d_6$of compound (18c)

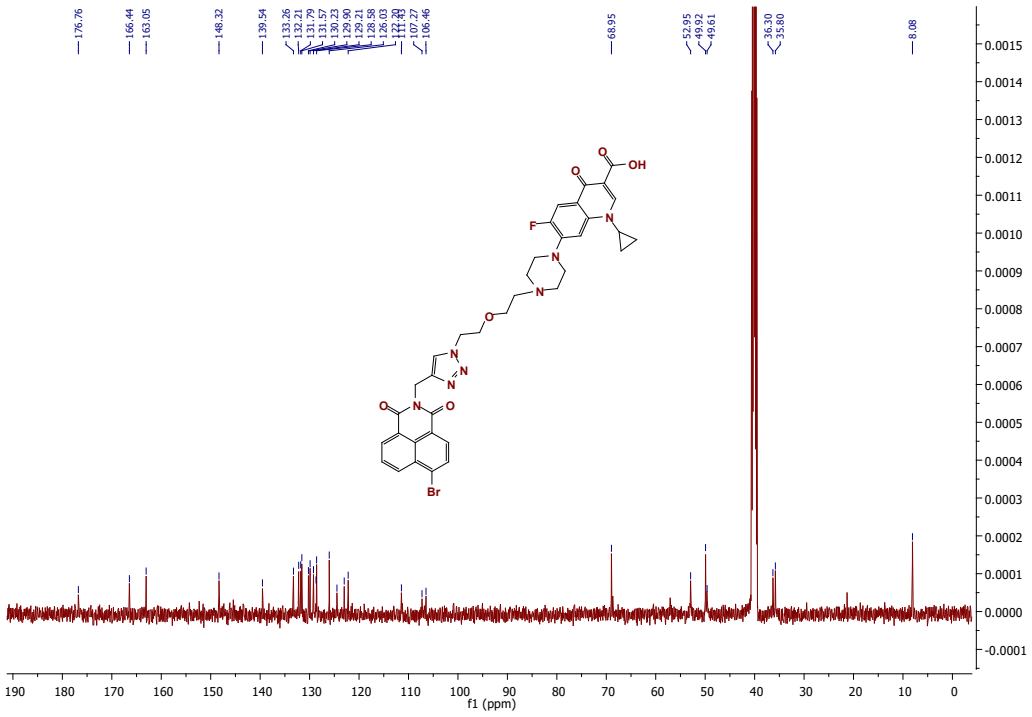

Figure S46.^{13}C NMR (126 MHz in DMSO-d_6) of compound (18c)

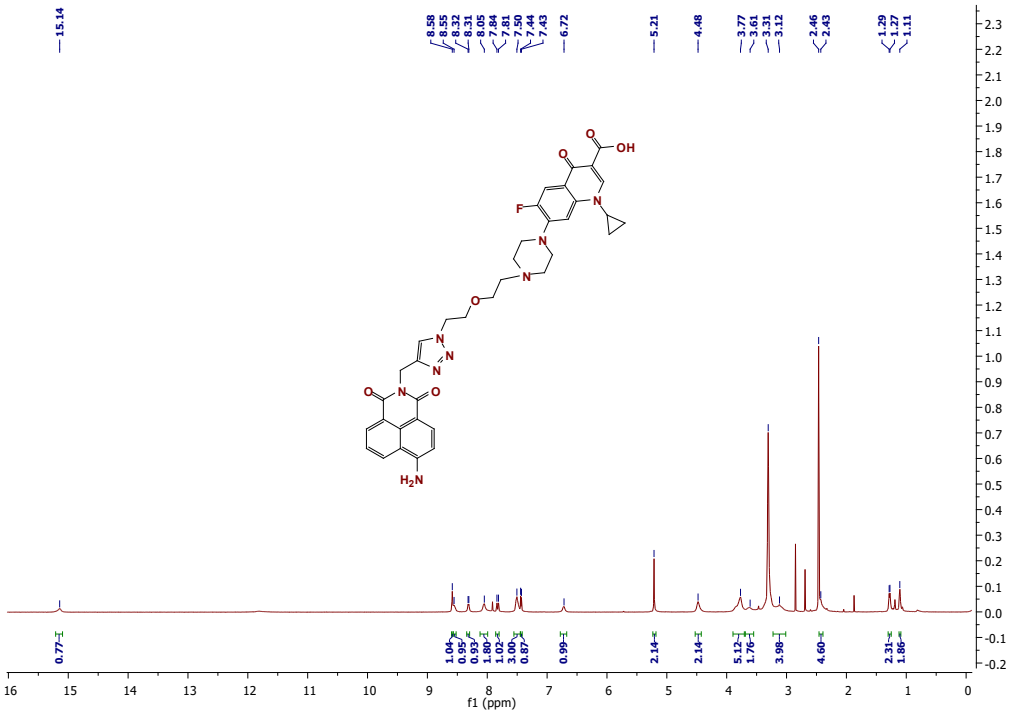

Figure S47. ^{1}H NMR (500MHz in DMSO-d_6) of compound (18d)

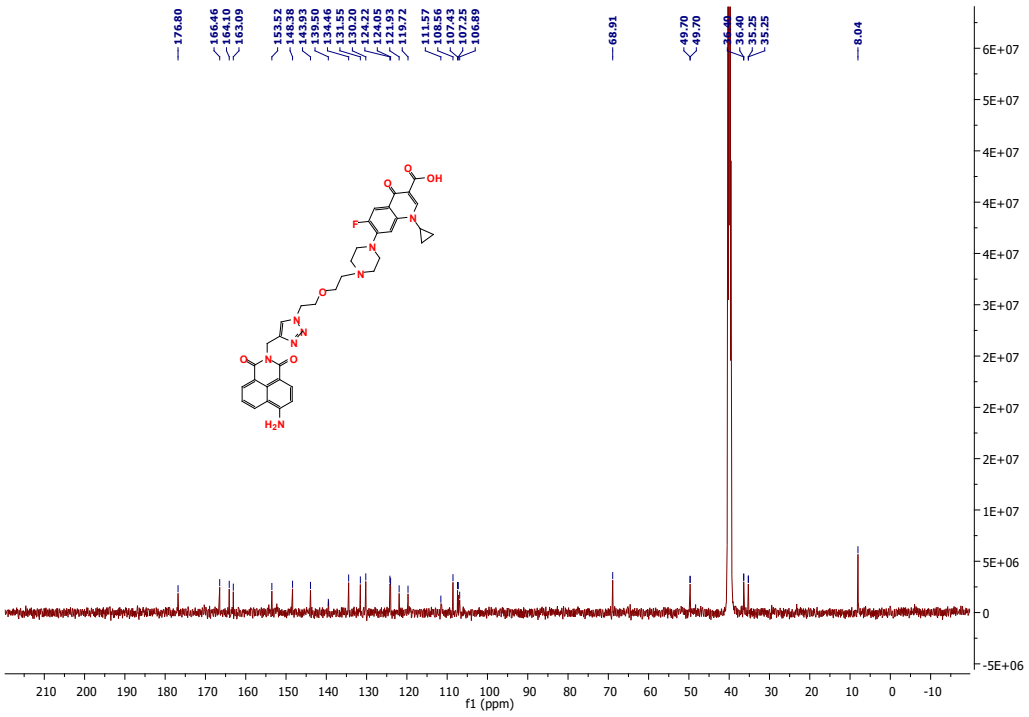

Figure S48.^{13}C NMR (126 MHz in DMSO-d_6) of compound (18d)

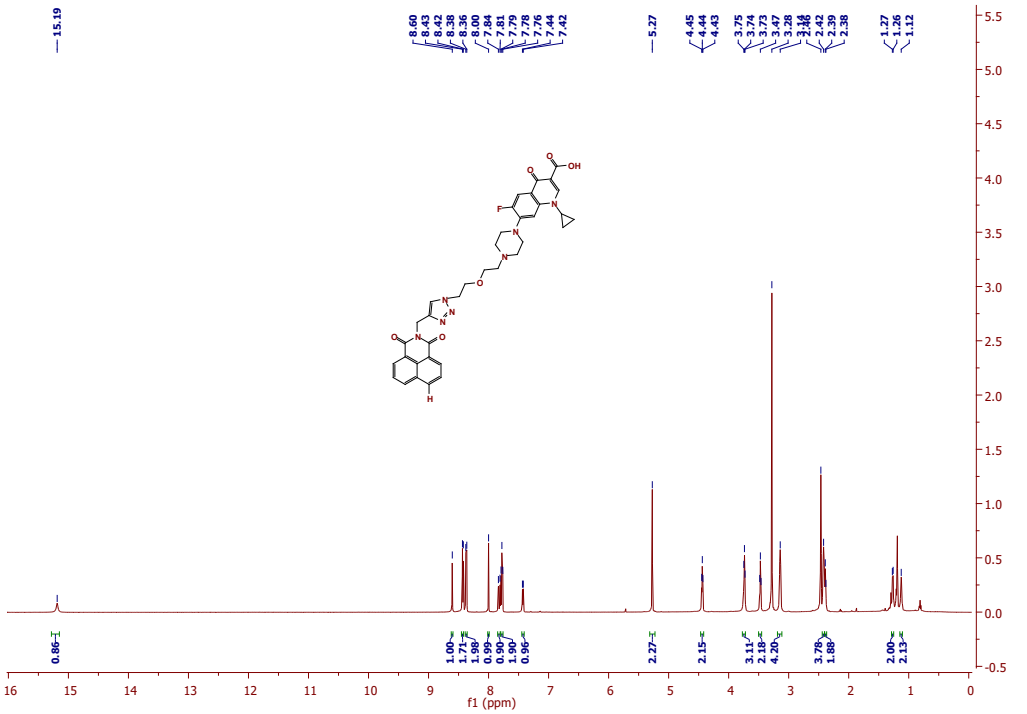

Figure S49. ^{1}H NMR (500MHz in DMSO-d_6) of compound (18e)

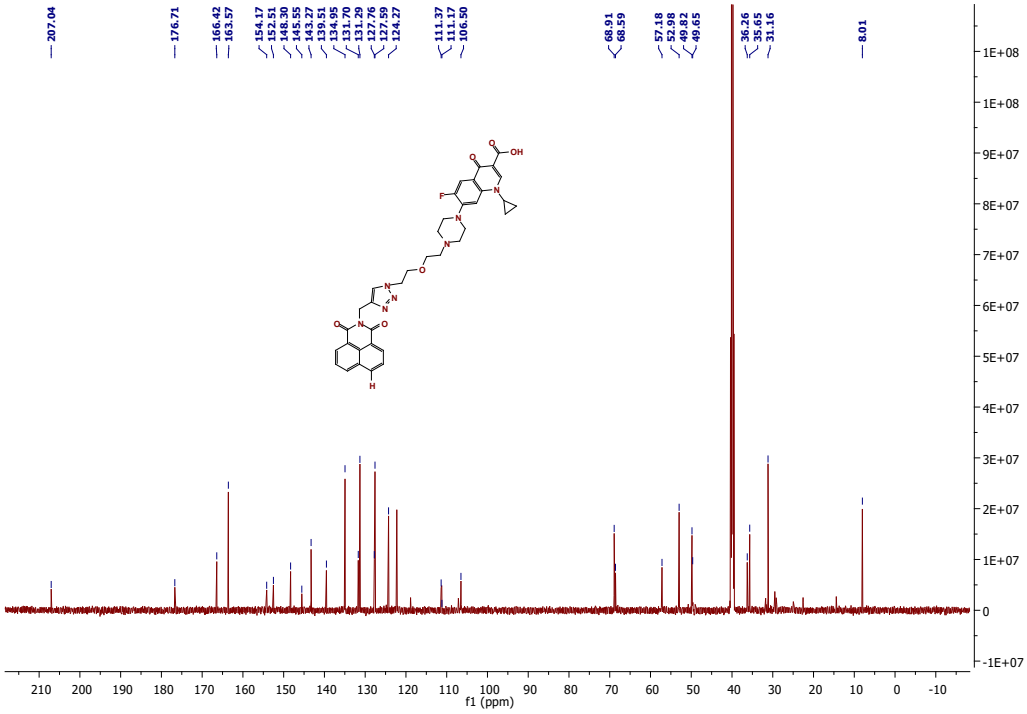

Figure S50.^{13}C NMR (151 MHz in DMSO-d_6) of compound (18e)

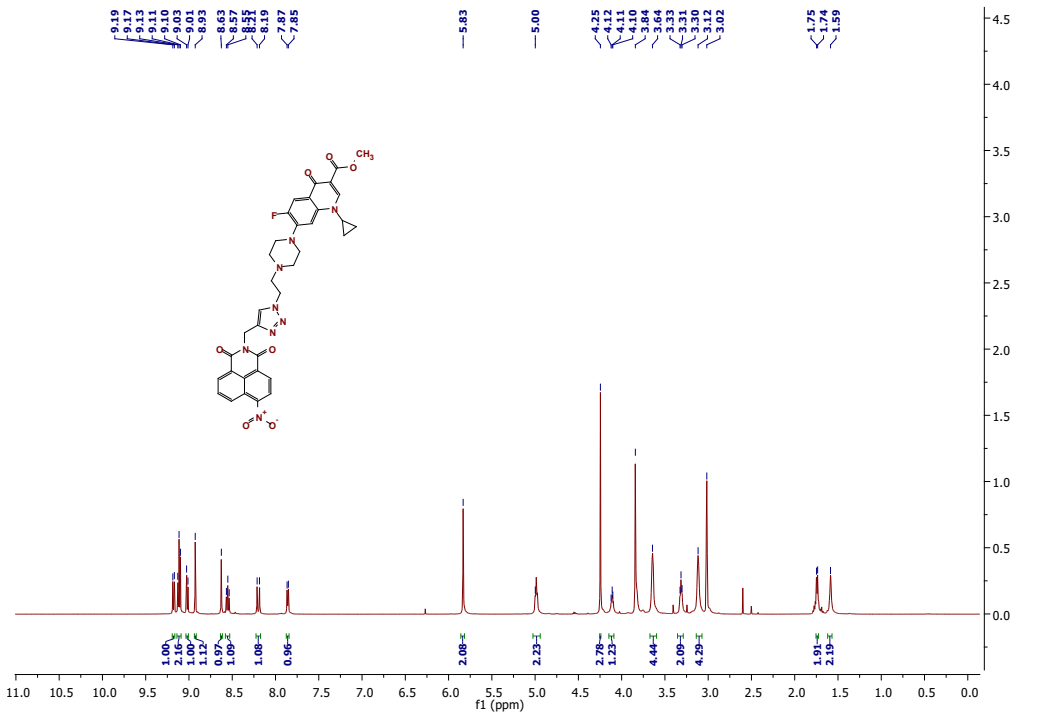

Figure S51. ^{1}H NMR (500MHz in DMSO-d_6) of compound (19a)

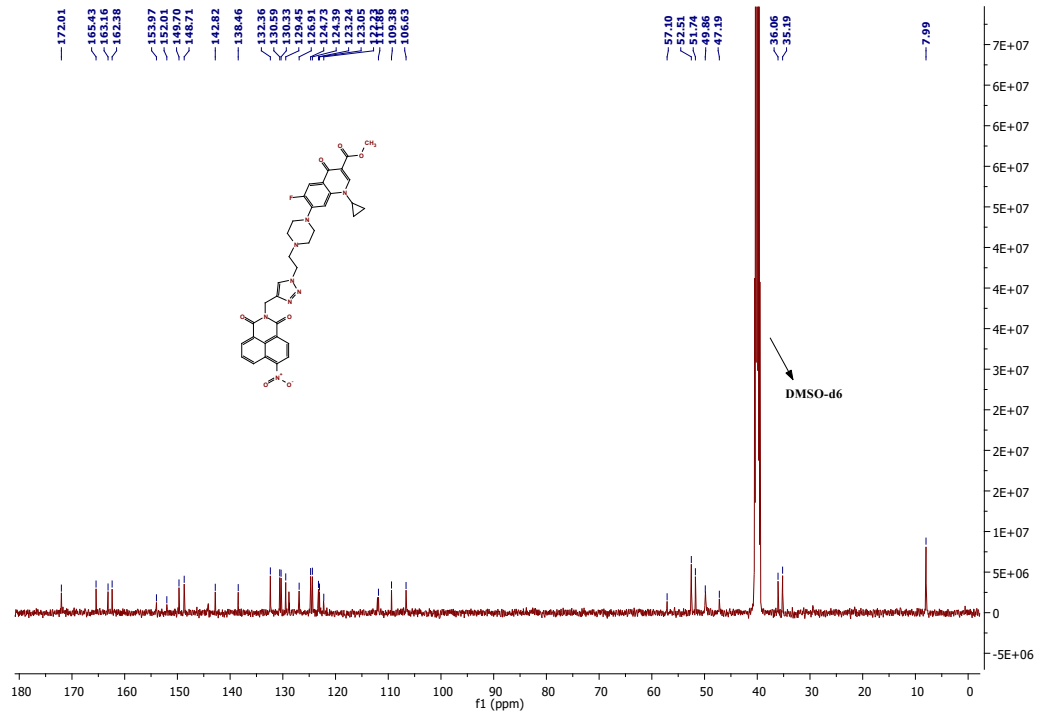

Figure S52.^{13}C NMR (126 MHz in DMSO-d_6) of compound (19a)

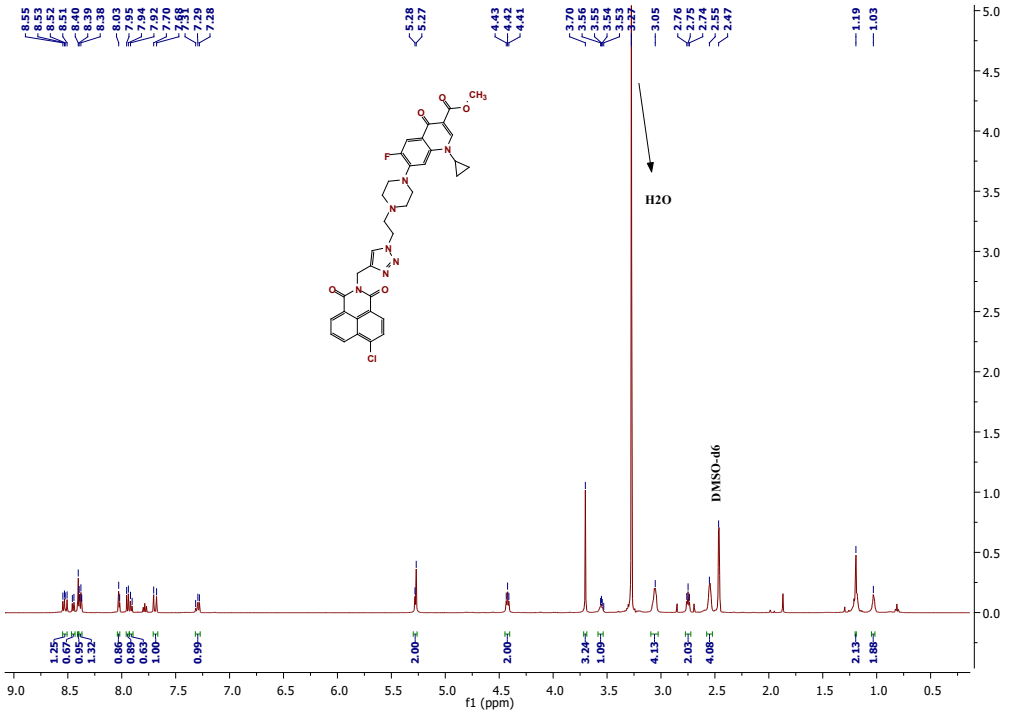

Figure S53. ^{1}H NMR (500MHz in DMSO-d_6) of compound (19b)

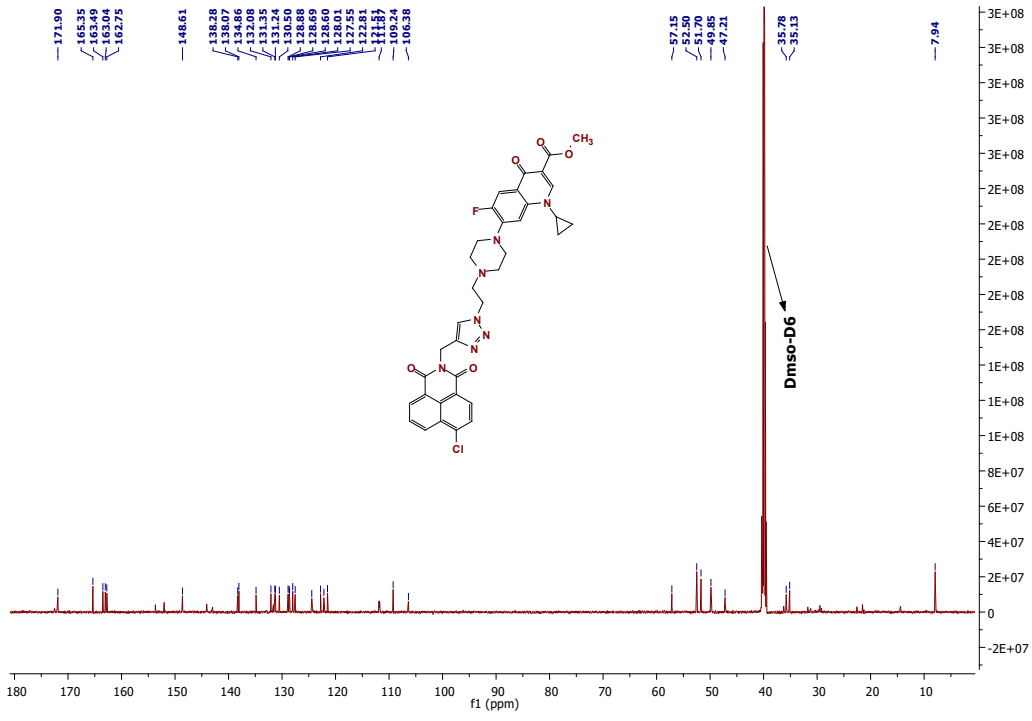

Figure S54.^{13}C NMR (151 MHz in DMSO-d_6) of compound (19b)

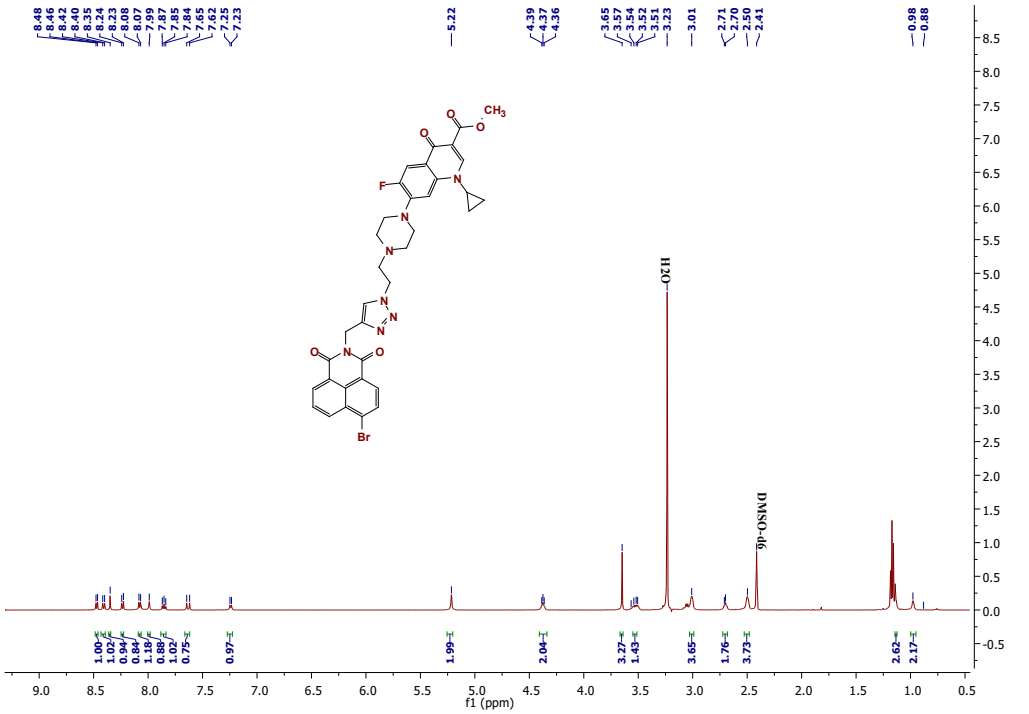

Figure S55. ^{1}H NMR (500MHz in DMSO-d_6) of compound (19c)

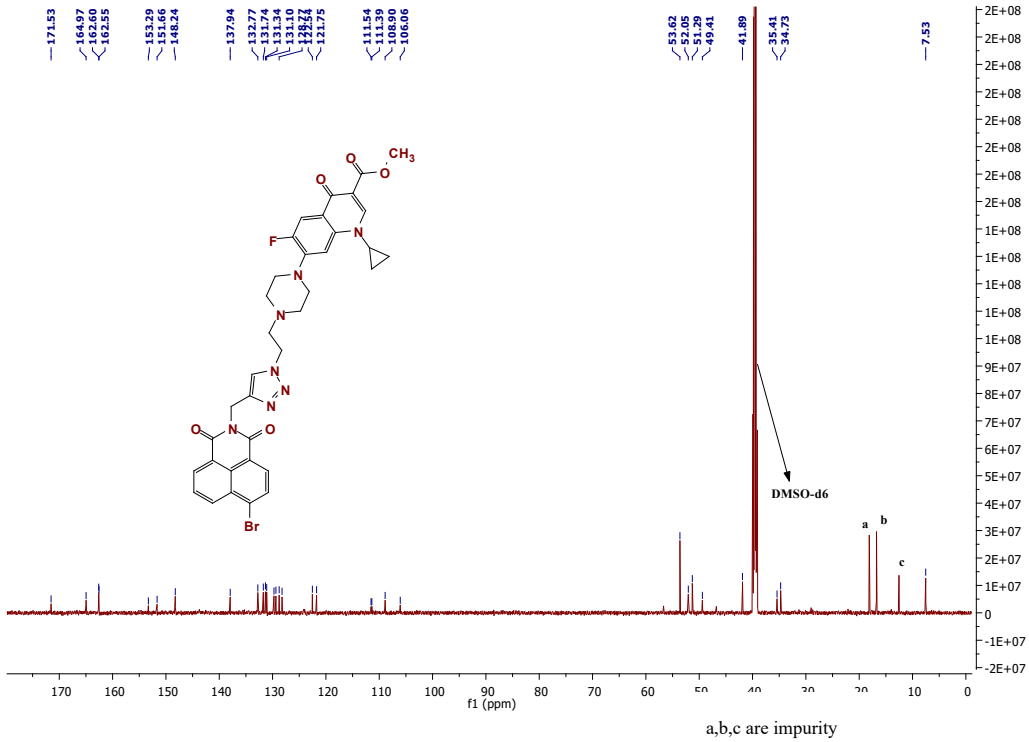

Figure S56.^{13}C NMR (151 MHz in DMSO-d_6) of compound (19c)

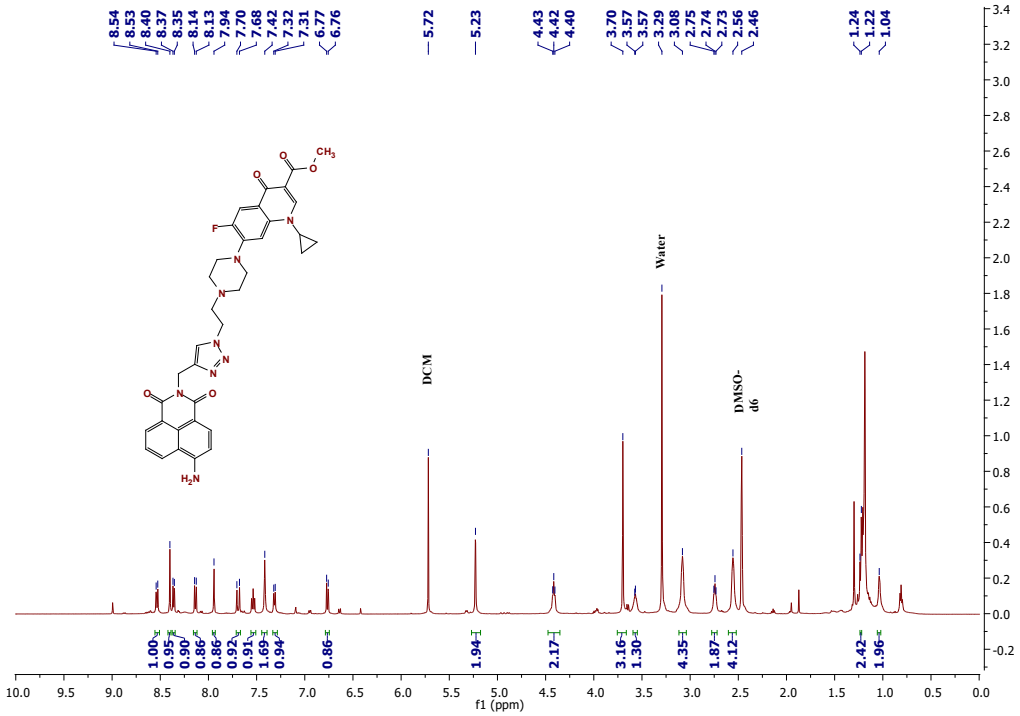

Figure S57. ^{1}H NMR (500MHz in DMSO-d_6) of compound (19d)

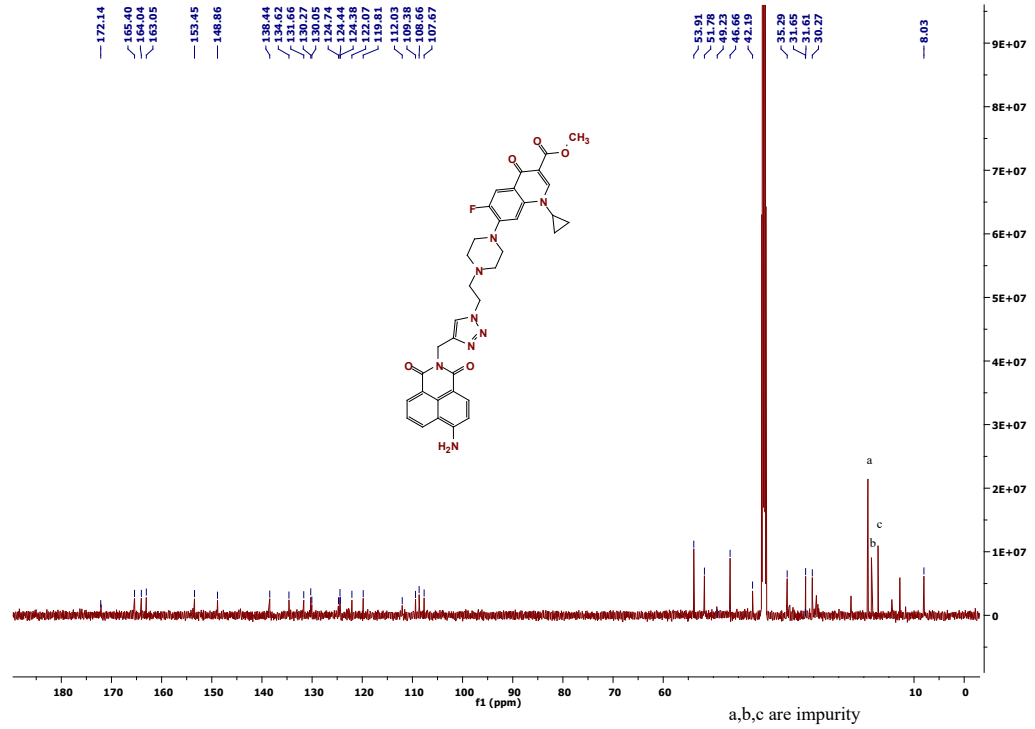

Figure S58.^{13}C NMR (151 MHz in DMSO-d_6) of compound (19d)

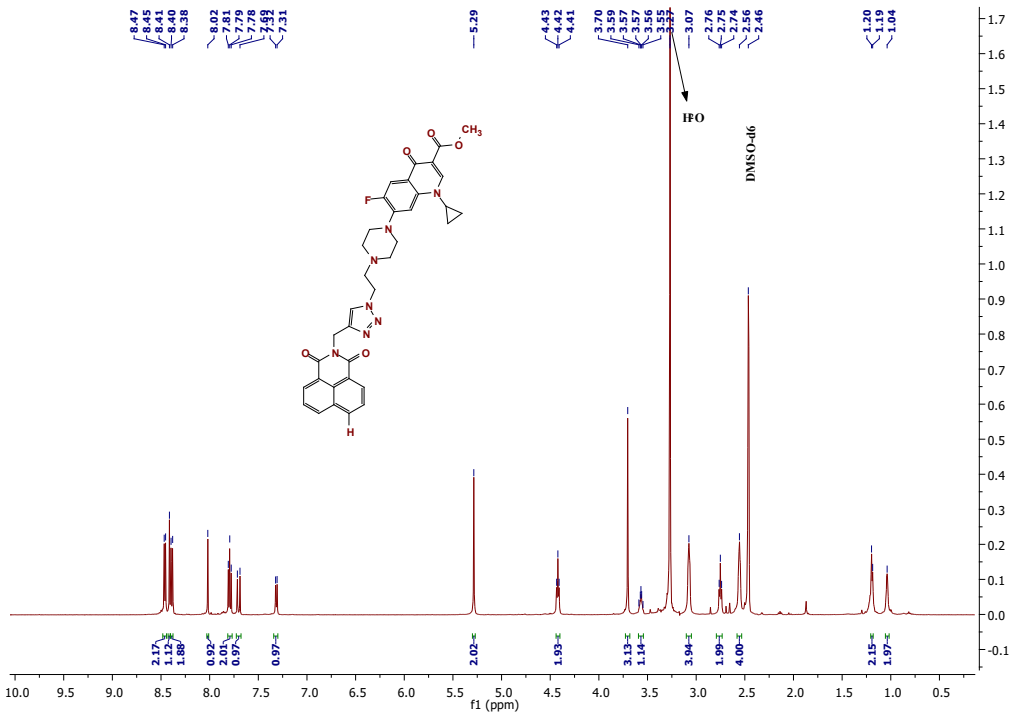

Figure S59. ^{1}H NMR (500MHz in DMSO-d_6) of compound (19e)

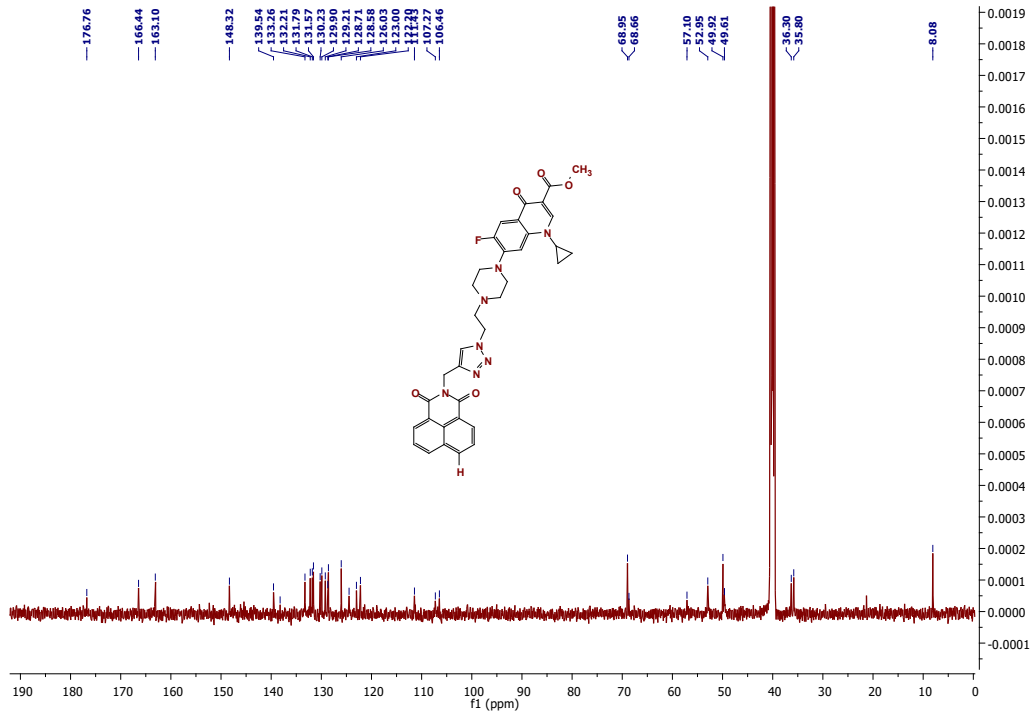

Figure S60.^{13}C NMR (126 MHz in DMSO-d_6) of compound (19e)

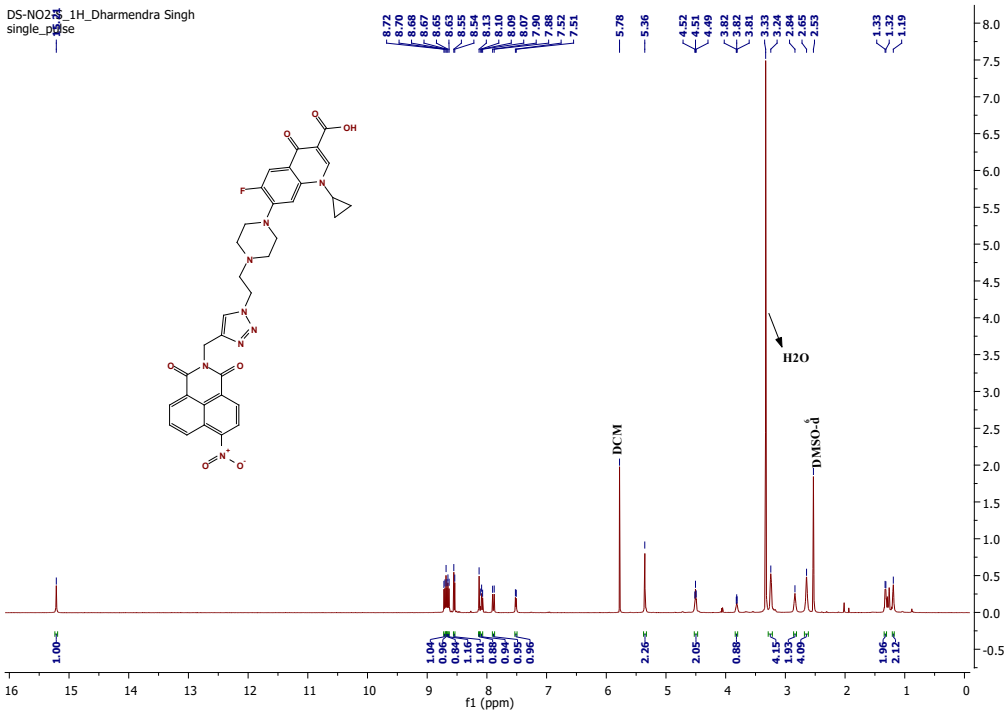

Figure S61. ^{1}H NMR (500MHz in DMSO-d_6) of compound (20a)

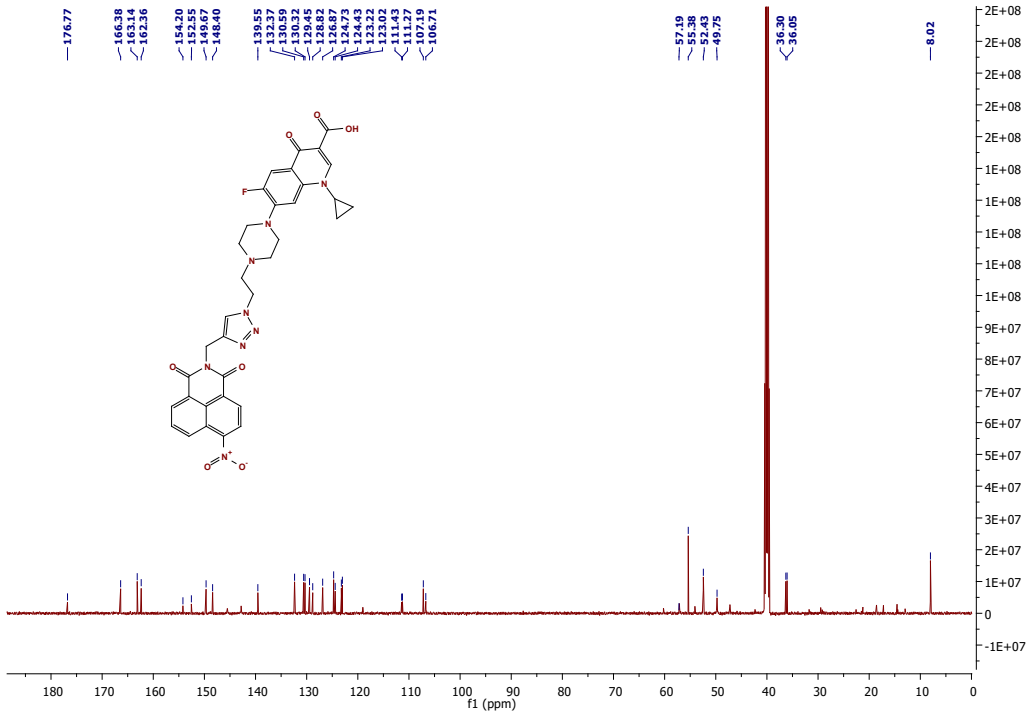

Figure S62.^{13}C NMR (151 MHz in DMSO-d_6) of compound (20a)

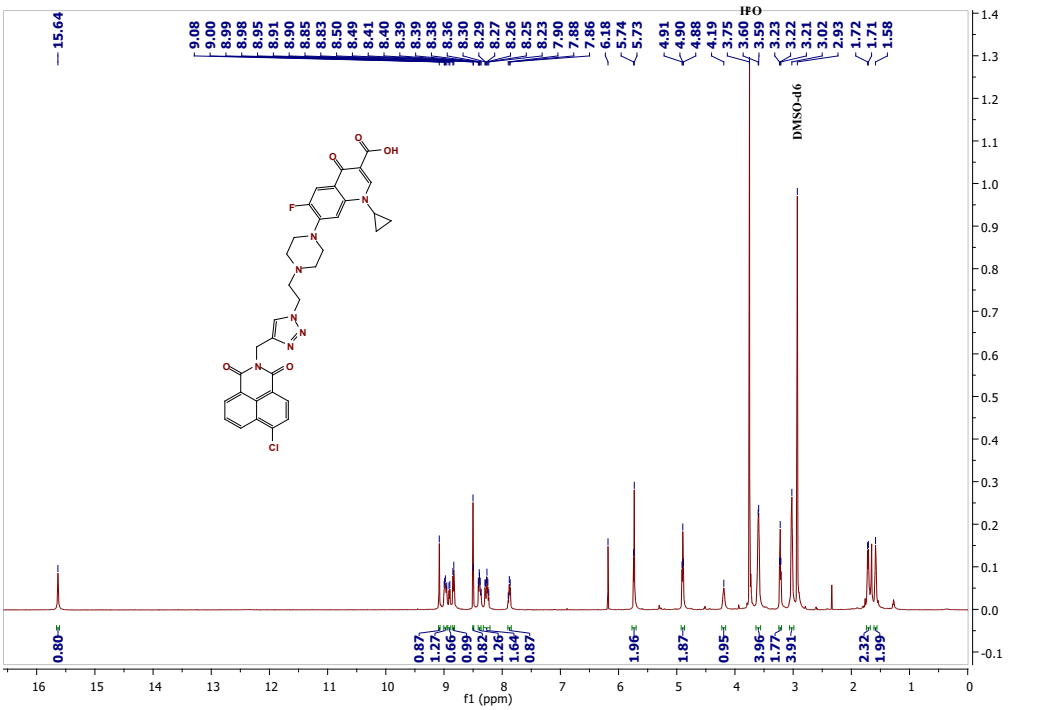

Figure S63. ^{1}H NMR (500MHz in DMSO-d_6) of compound (20b)

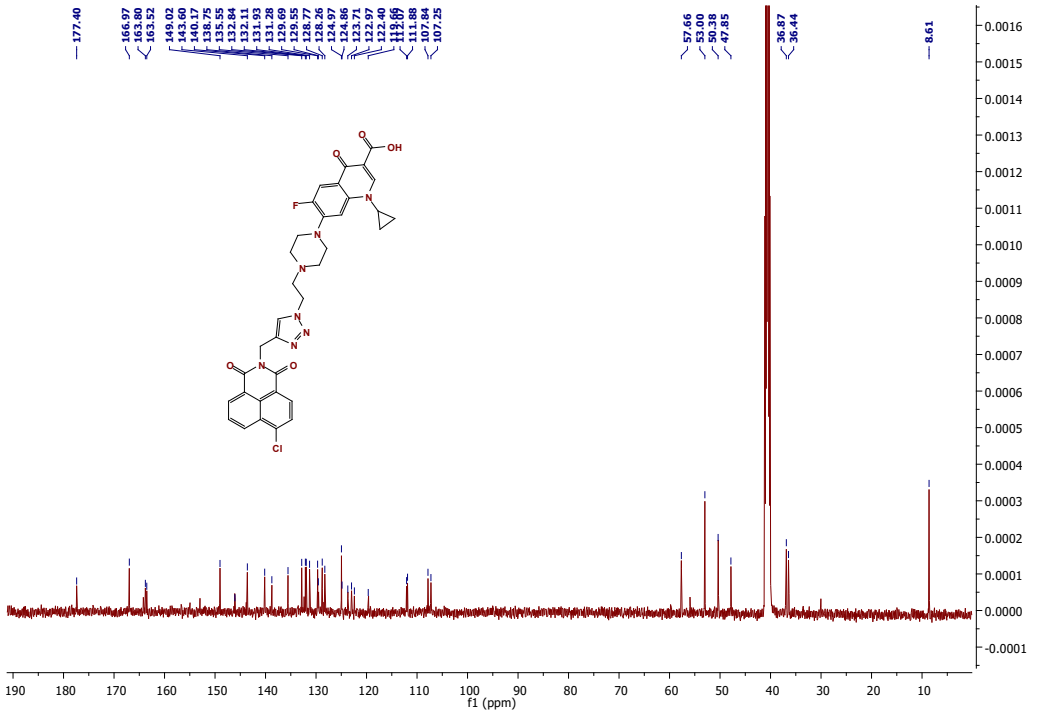

Figure S64.^{13}C NMR (126 MHz in DMSO-d_6) of compound (20b)

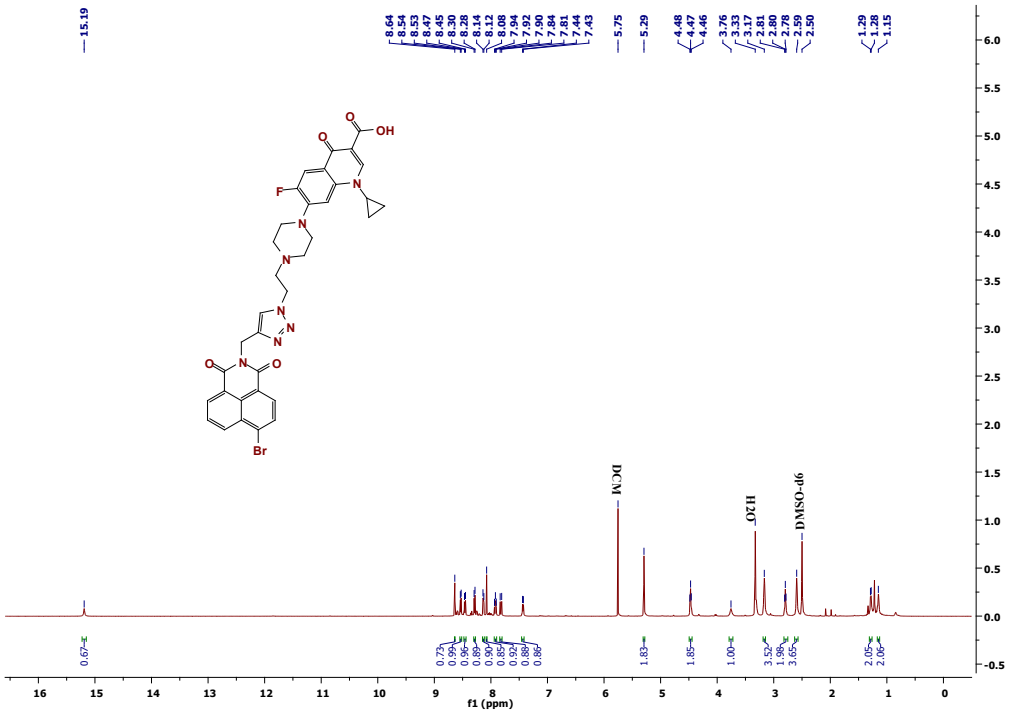

Figure S65. ^{1}H NMR (500MHz in DMSO-d_6) of compound (20c)

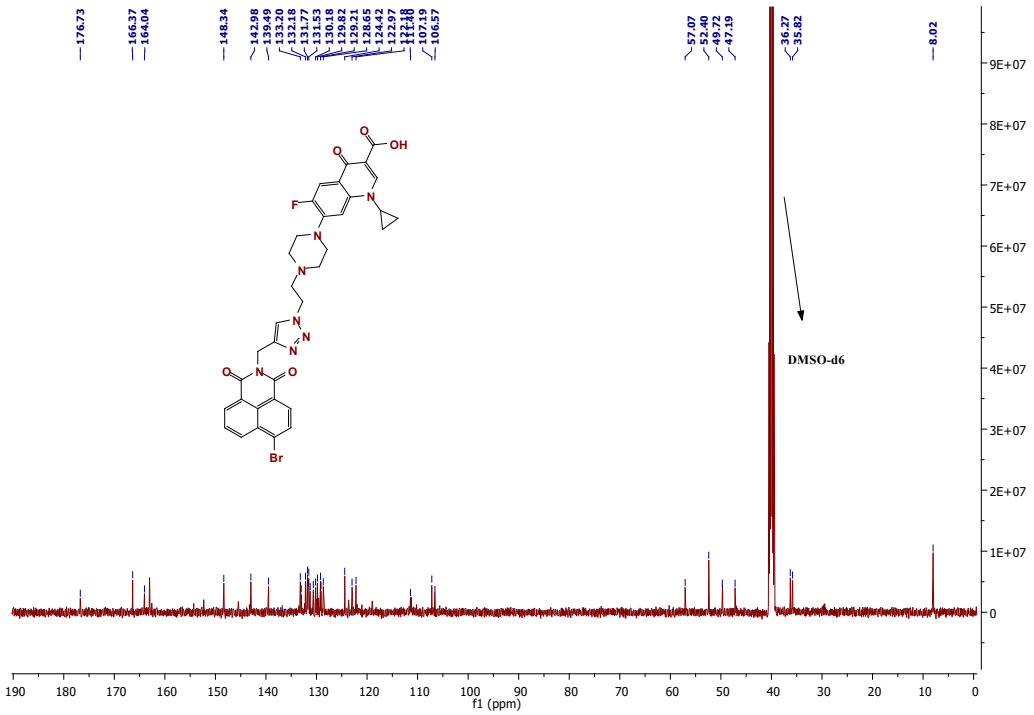

Figure S66.^{13}C NMR (126 MHz in DMSO-d_6) of compound (20c)

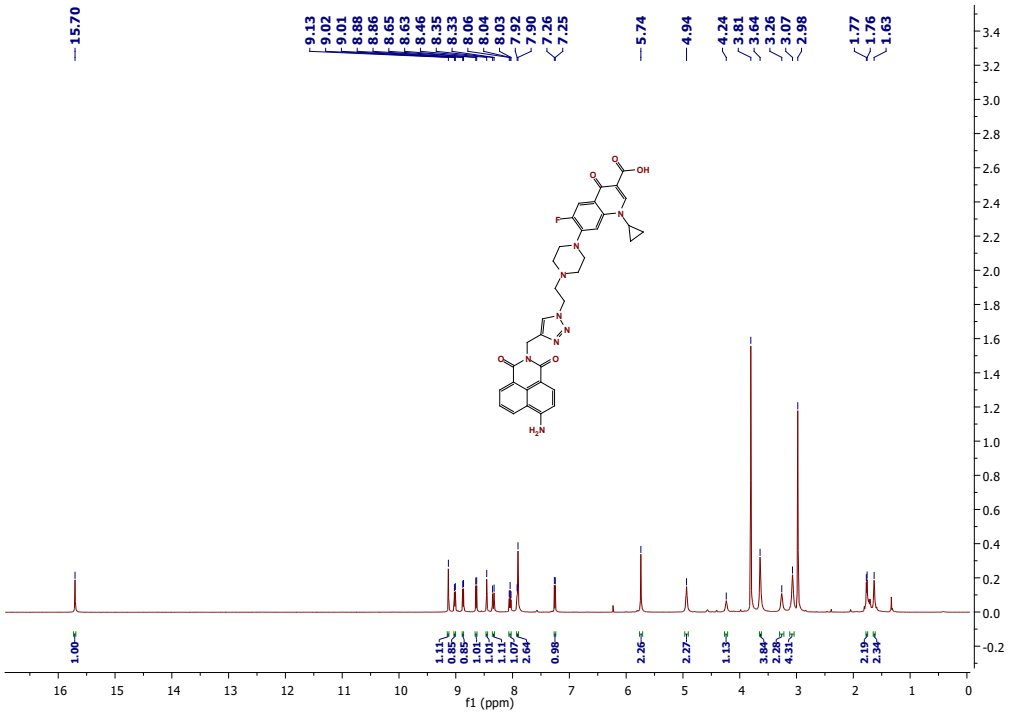

Figure S67. ^{1}H NMR (500MHz in DMSO-d_6) of compound (20d)

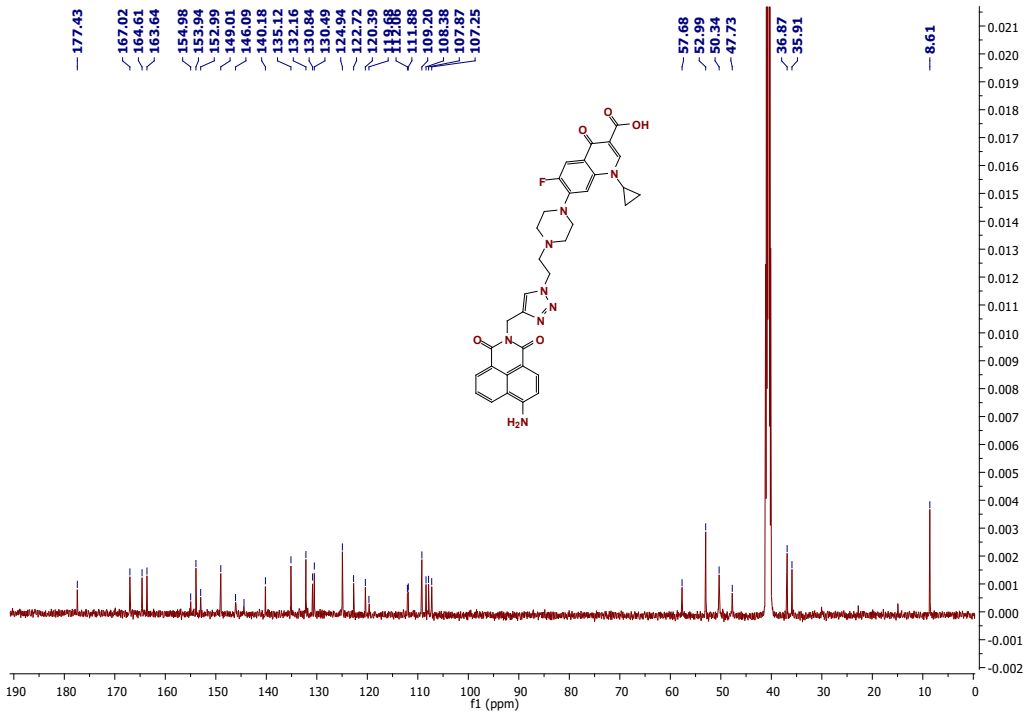

Figure S68.^{13}C NMR (126 MHz in DMSO-d_6) of compound (20d)

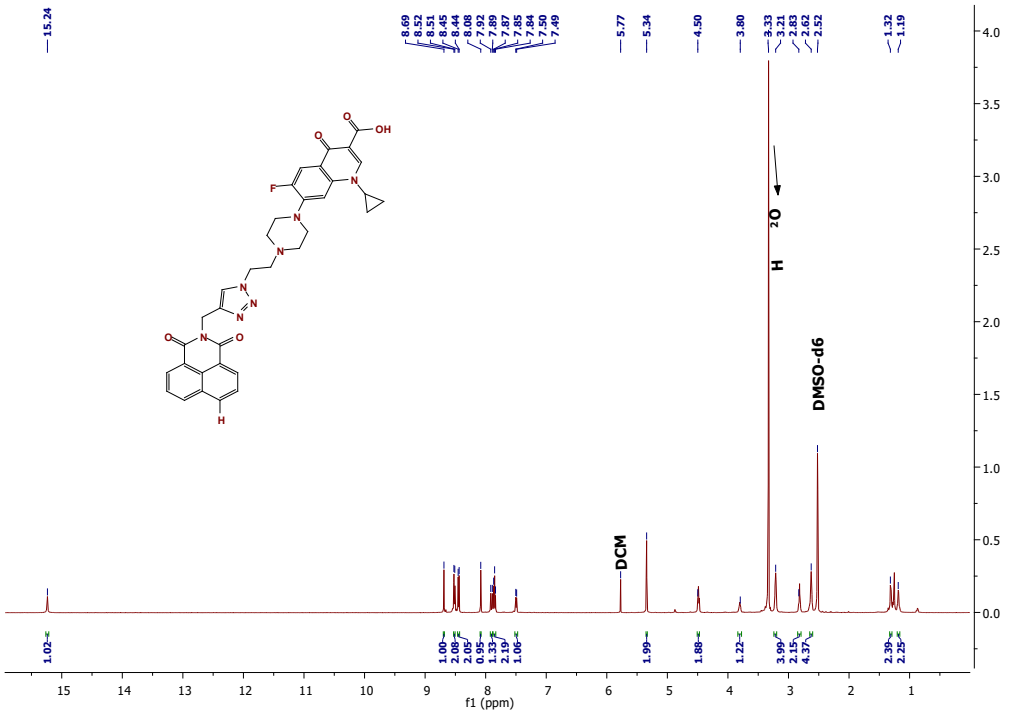

Figure S69 . ^{1}H NMR (500MHz in DMSO-d_6) of compound (20e)

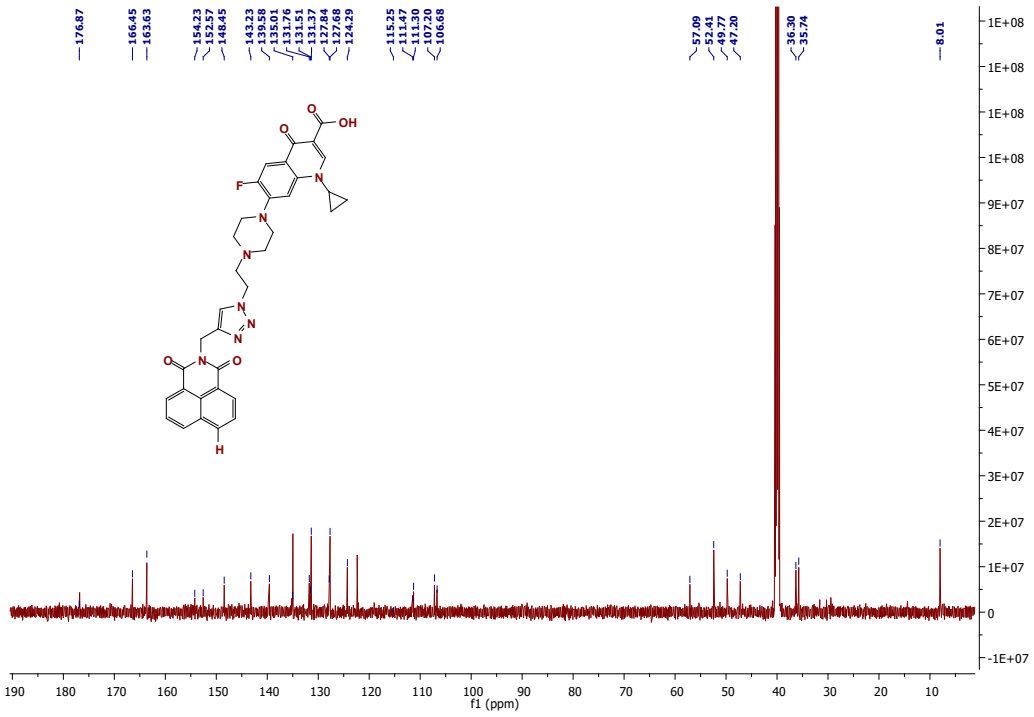

Figure S70.^{13}C NMR (151 MHz in DMSO-d_6) of compound (20e)

HRMS data

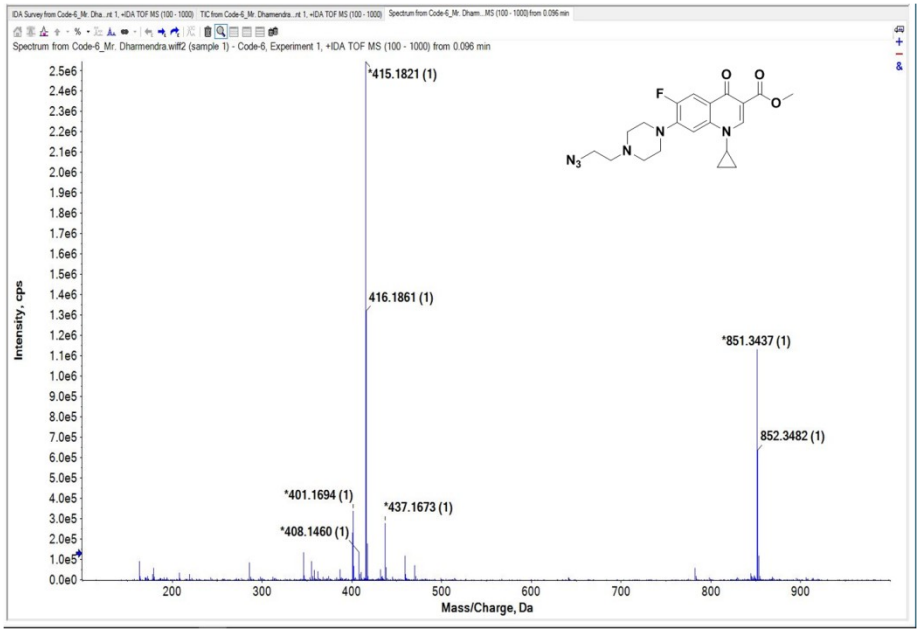

Figure S71. HMRS of compound (3) $C_{22}H_{27}FN_6O_4$ $[M+H]^+$=459.2078 found 459.2086

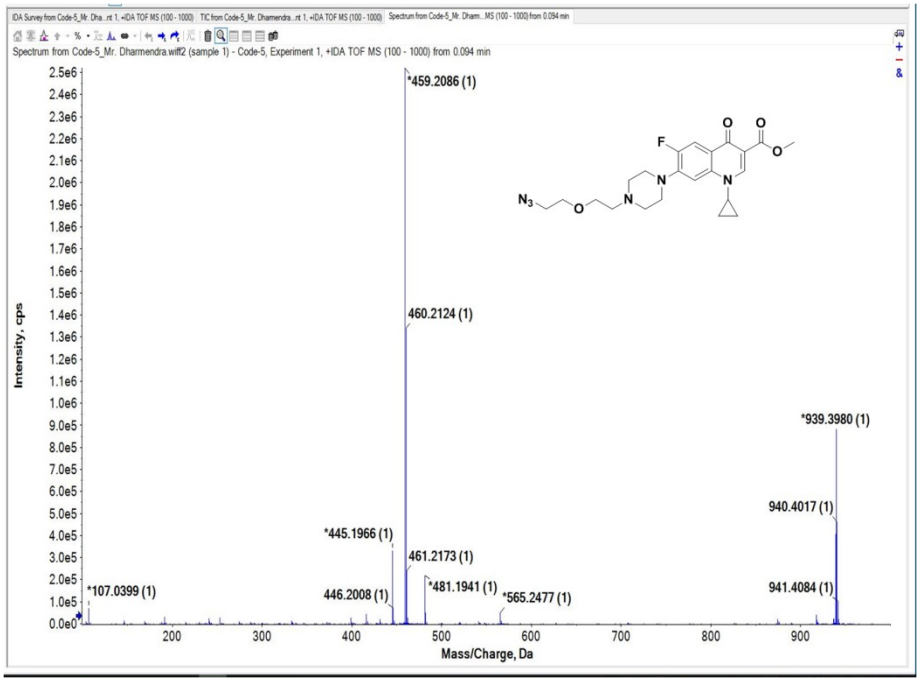

Figure S72. HMRS of compound (4) $C_{22}H_{27}FN_6O_4$ $[M+H]^+$=459.2078 found 459.2086

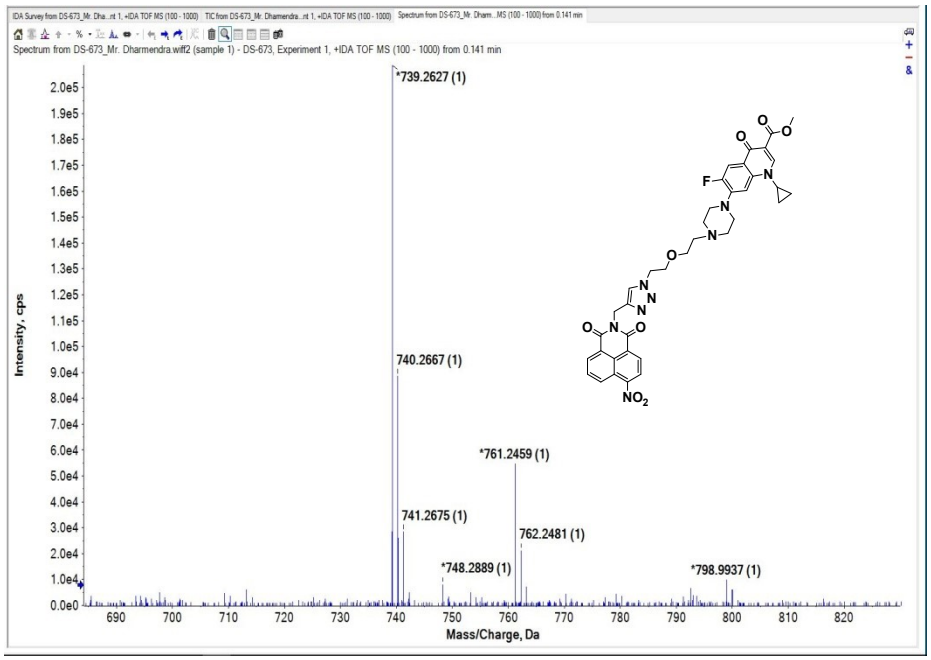

Figure S73. **HMRS of compound (17a) $C_{37}H_{35}FN_8O_8$ [M+H]$^+$=739.256 found 739.2646**

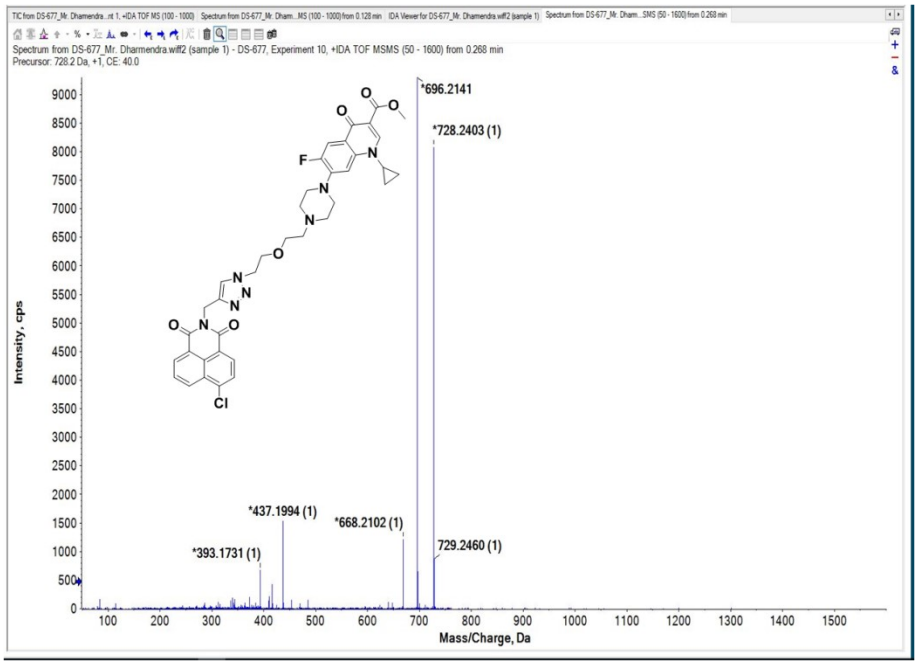

Figure S74. HMRS of compound (17b) $C_{37}H_{35}ClFN_7O_6$ [M+H]$^+$= 728.2321 found 728.2402

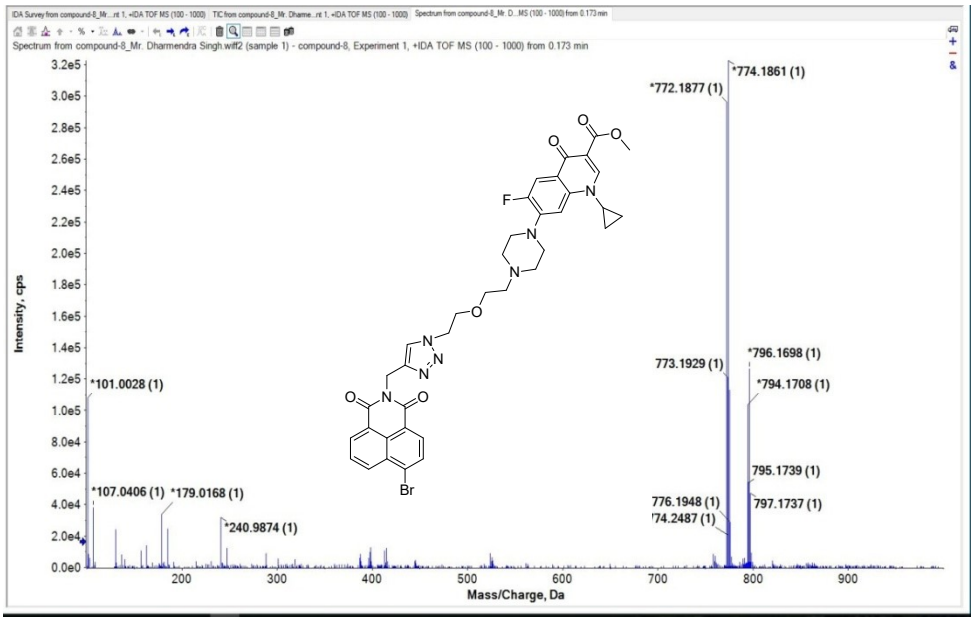

Figure S75. HMRS of compound (17c) $C_{36}H_{33}BrFN_7O_6$ $[M+H]^+$=772.1816 found 772.18

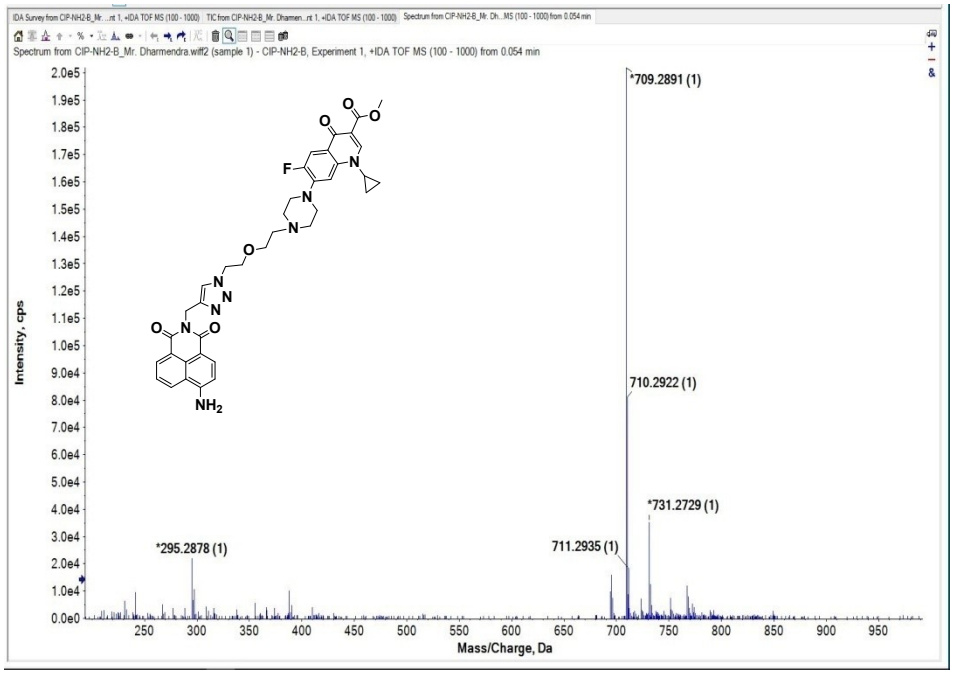

Figure S76. HMRS of compound (17d) $C_{37}H_{37}FN_8O_6$ $[M+H]^+$= 709.2820 found 709.2891

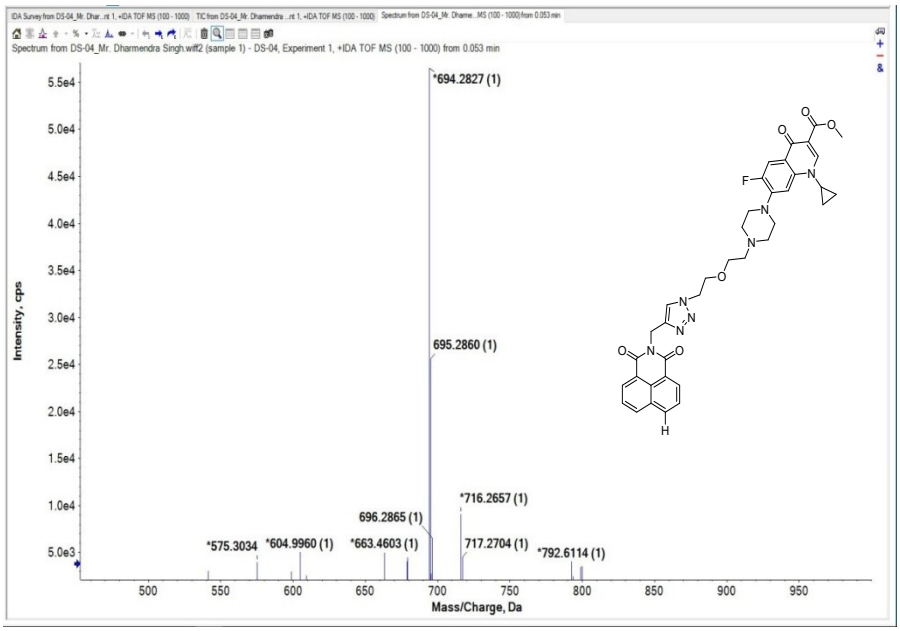

Figure S77. HMRS of compound (17e) $C_{37}H_{36}FN_7O_6$ [M+H]$^+$= 694.2711 found 694.2813

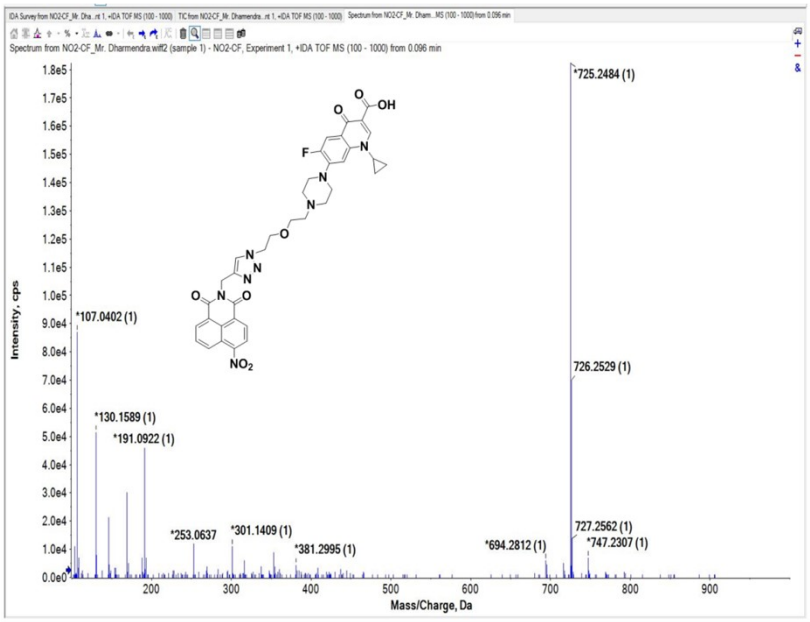

Figure S78. HMRS of compound (18a) $C_{36}H_{33}FN_8O_8$ [M+H]$^+$=725.2405 found 725.2484

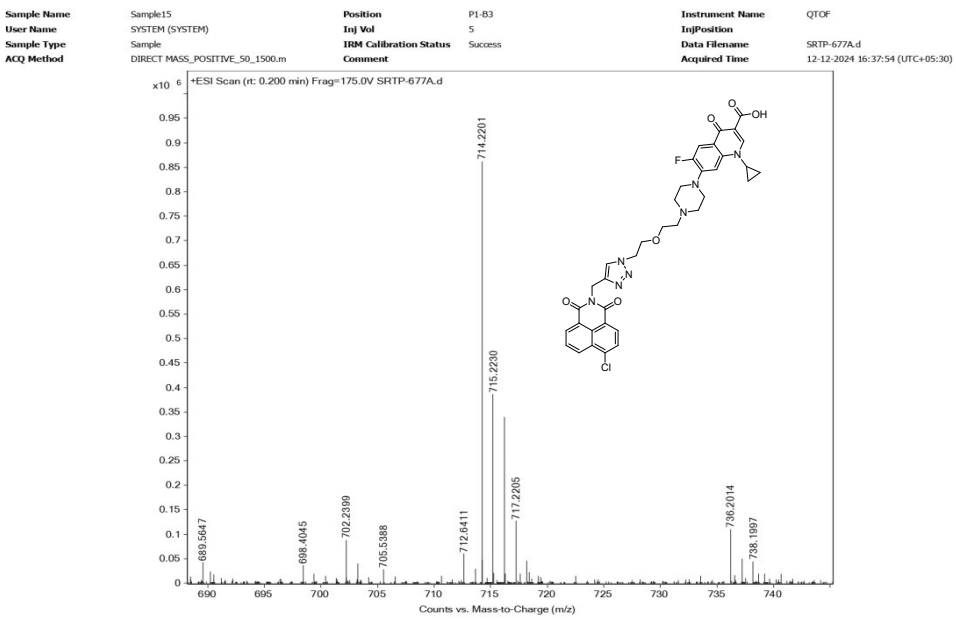

Figure S79. HMRS of compound(18b) $C_{36}H_{33}ClFN_7O_6$ $[M+H]^+$= 714.2165 found 714.2201

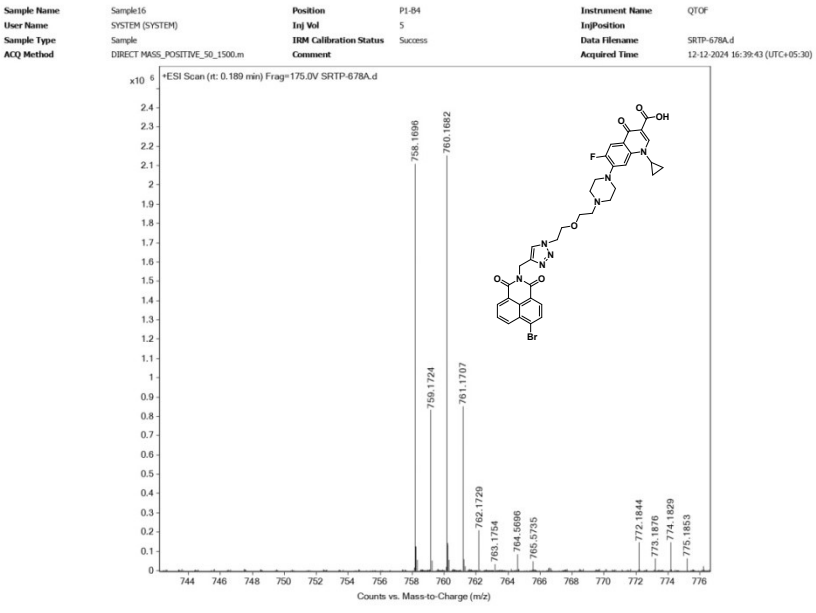

Figure S80. HMRS of compound(18c) $C_{36}H_{33}BrFN_7O_6$ $[M+H]^+$ = 758.166 found 758.1696

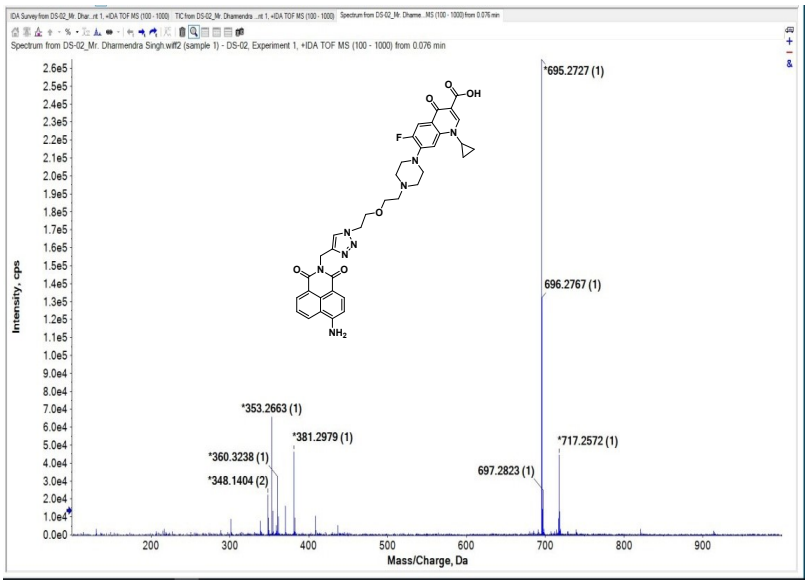

Figure S81. HMRS of compound(18d) $C_{36}H_{35}FN_8O_6$ [M+H] $^+$ = 695.2664 found 695.262

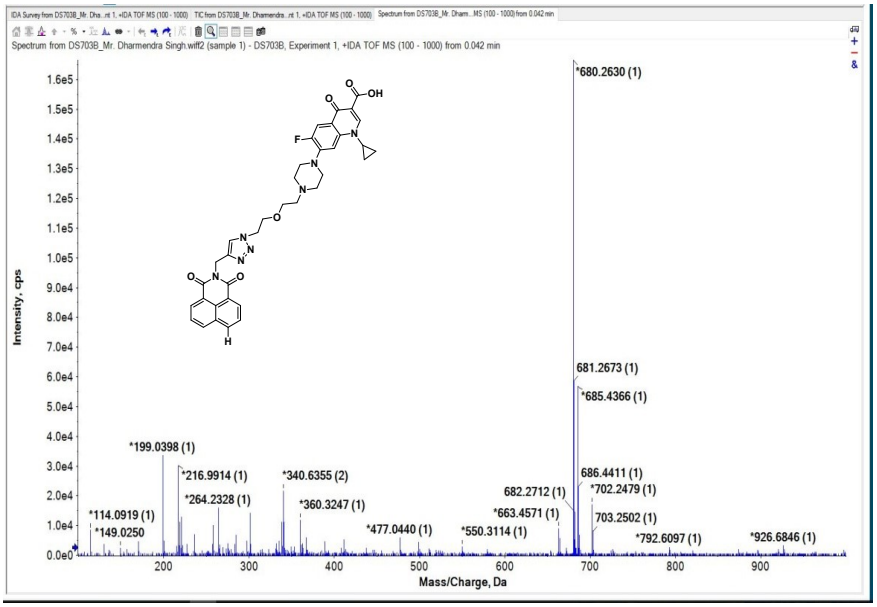

Figure S82. HMRS of compound (18e) $C_{36}H_{34}FN_7O_6$ [M+H] $^+$ = 680.2555 found 680.2630

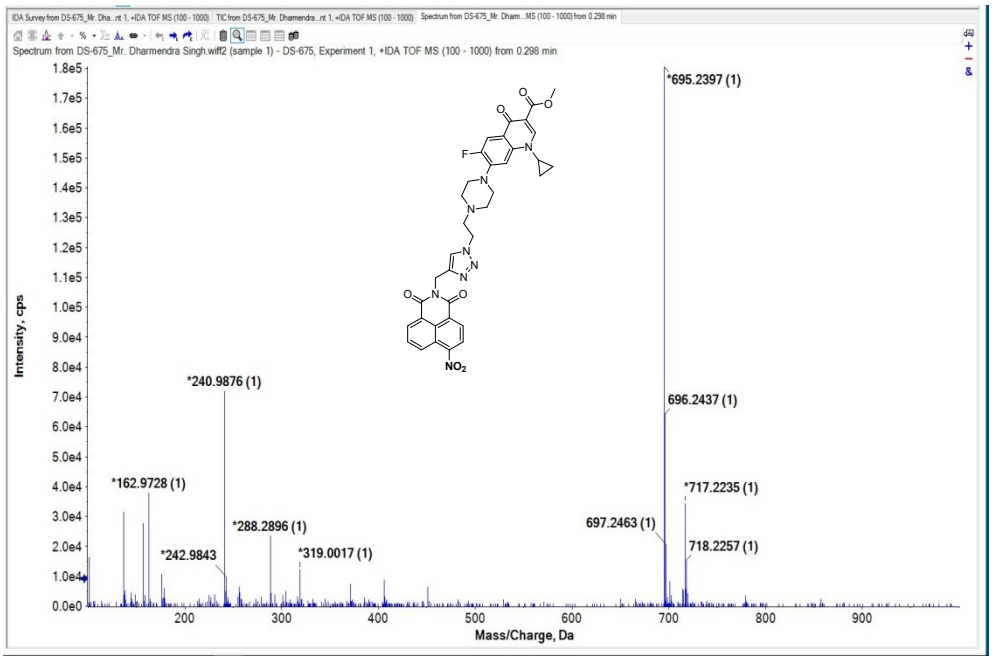

Figure S83. HMRS of compound (19a) $C_{35}H_{31}FN_8O_7$ [M+H] $^+$ = 695.2300 found 695.2331

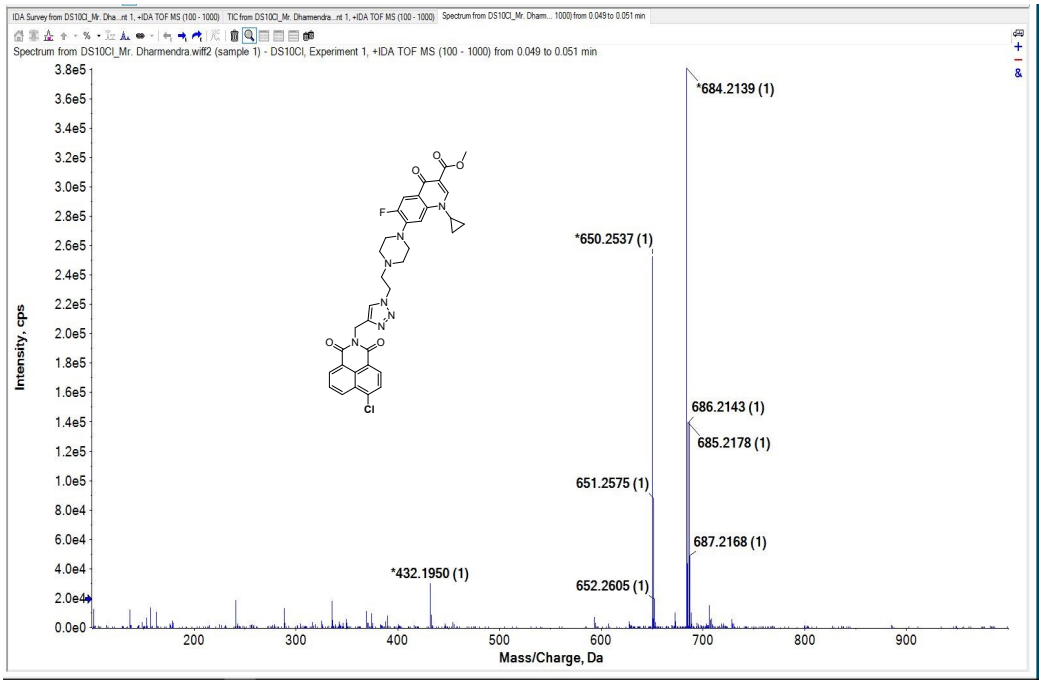

Figure S84. HMRS of compound (19b) $C_{35}H_{31}ClFN_7O_5$ [M+H] $^+$ = 684.2059 found 684.2053

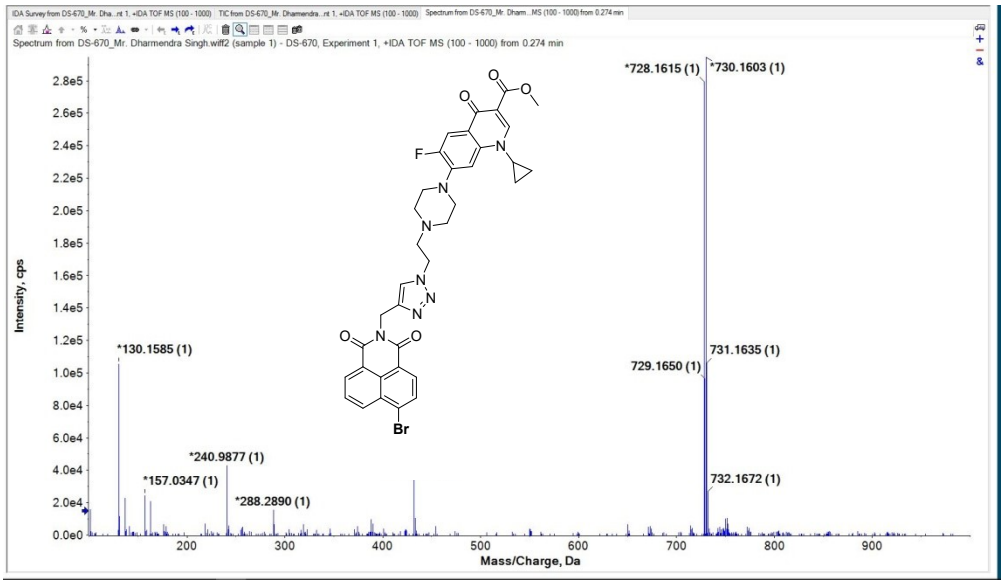

Figure S85. HMRS of compound (19c) $C_{35}H_{31}BrFN_7O_5$ $[M+H]^+$ = 728.1554 found 728.1584

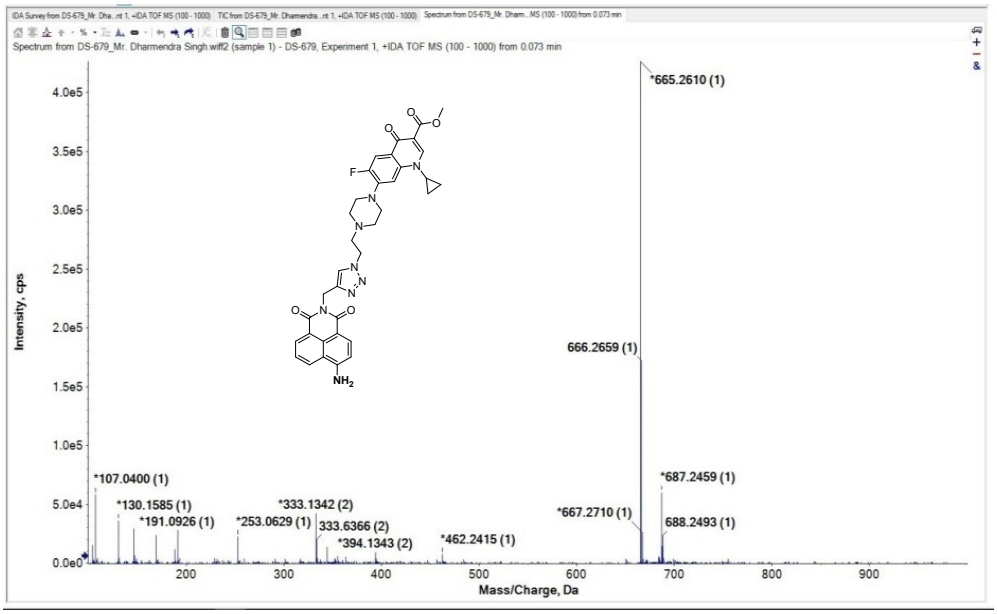

Figure S86. HMRS of compound (19d) $C_{35}H_{33}FN_8O_5$ $[M+H]^+$ = 665.2558 found 665.2610

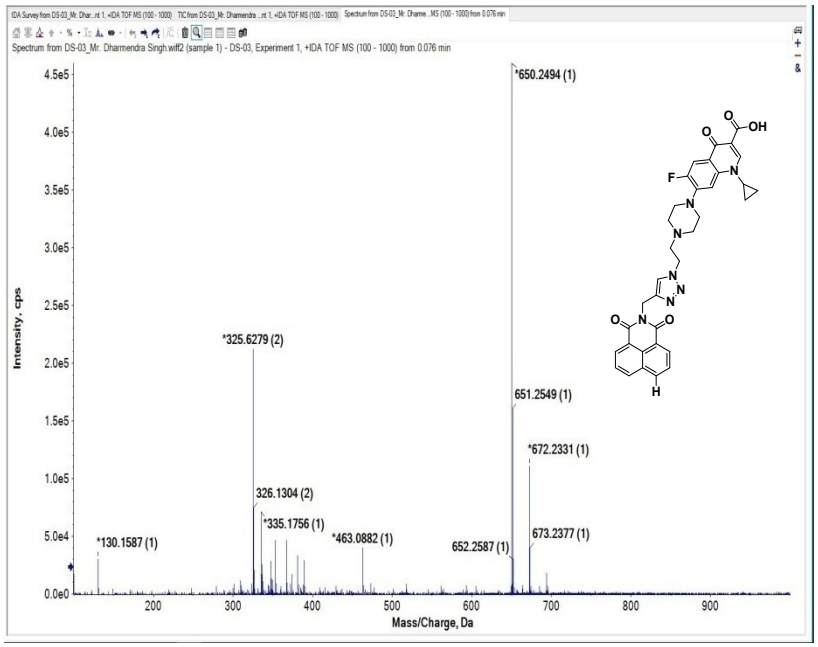

Figure S87. HMRS of compound (19e) $C_{35}H_{32}FN_7O_5$ [M+H] $^+$ = 650.2449 found 650.2494

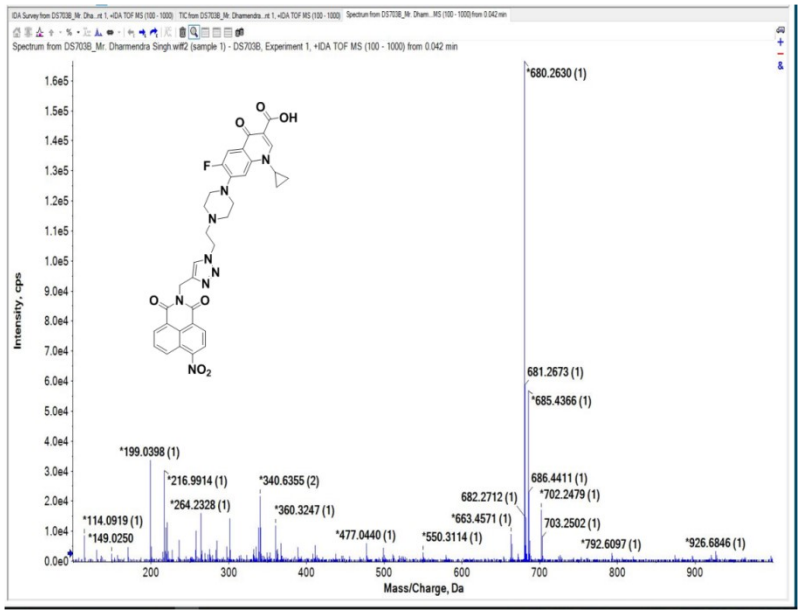

Figure S88. HMRS of compound (20a) $C_{34}H_{29}FN_8O_7$ [M+H] $^+$ =681.2143 found 681.2202

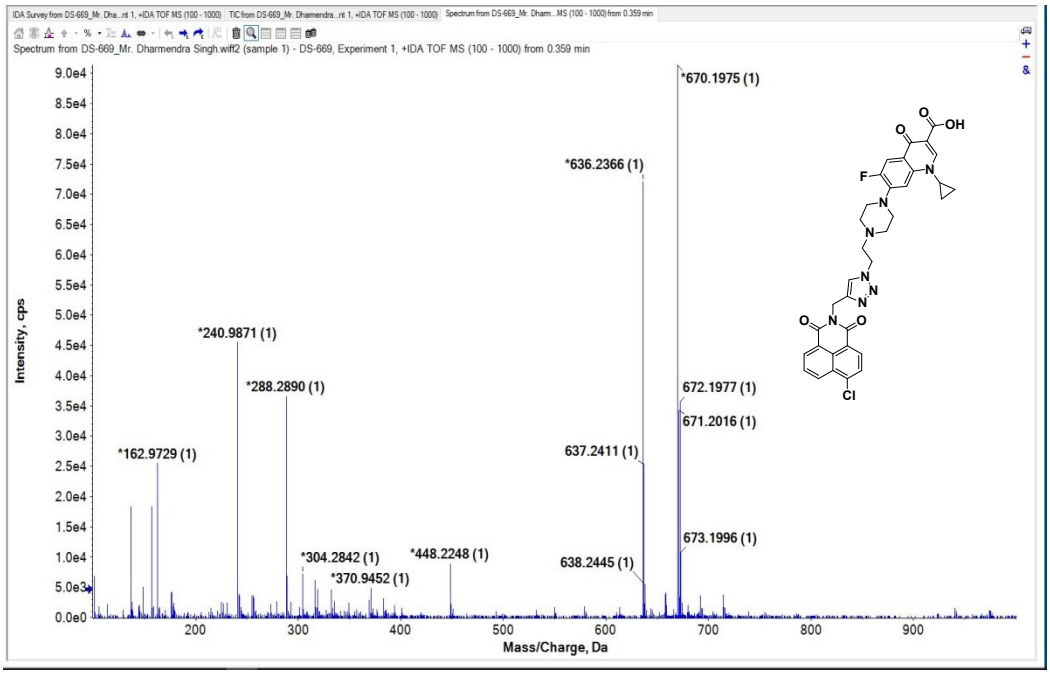

Figure S89. HMRS of compound (20b) $C_{35}H_{32}FN_7O_5$ [M+H] $^+$=670.1940 found 670.1968

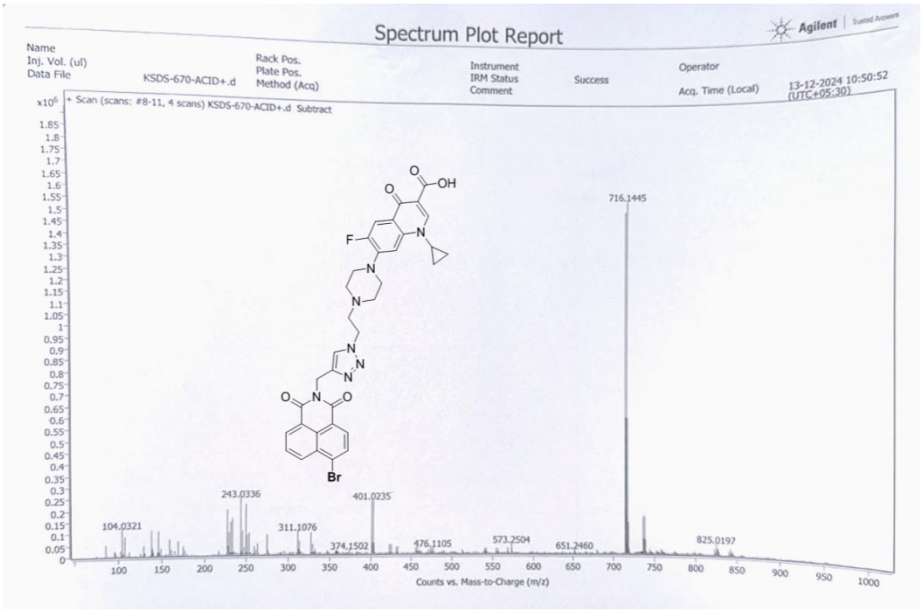

Figure S90. HMRS of compound (20c) $C_{34}H_{29}BrFN_7O_5$ [M+H] $^+$ = 714.1398 found 714.1445

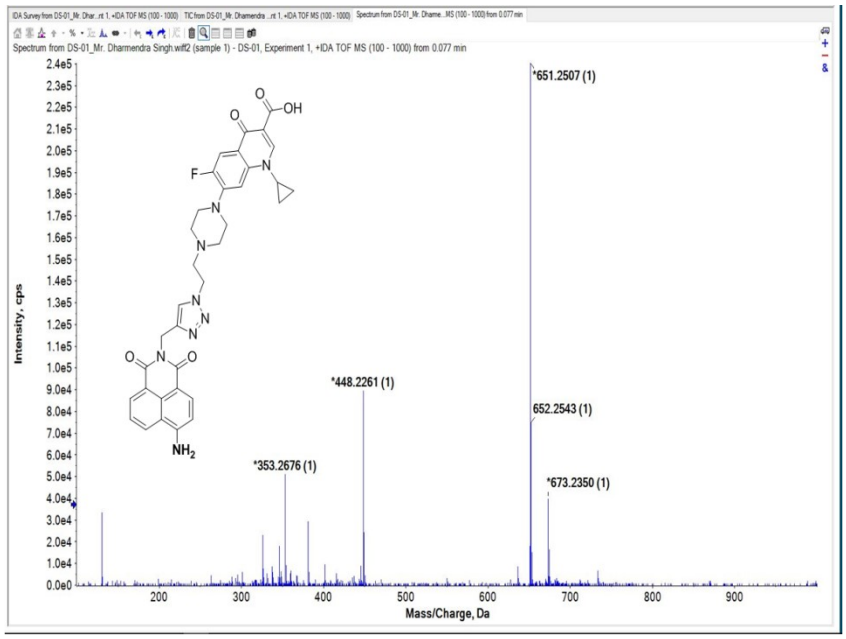

Figure S91. HMRS of compound (20d) $C_{34}H_{31}FN_8O_5$ [M+H] $^+$ = 651.2410 found 651.2507

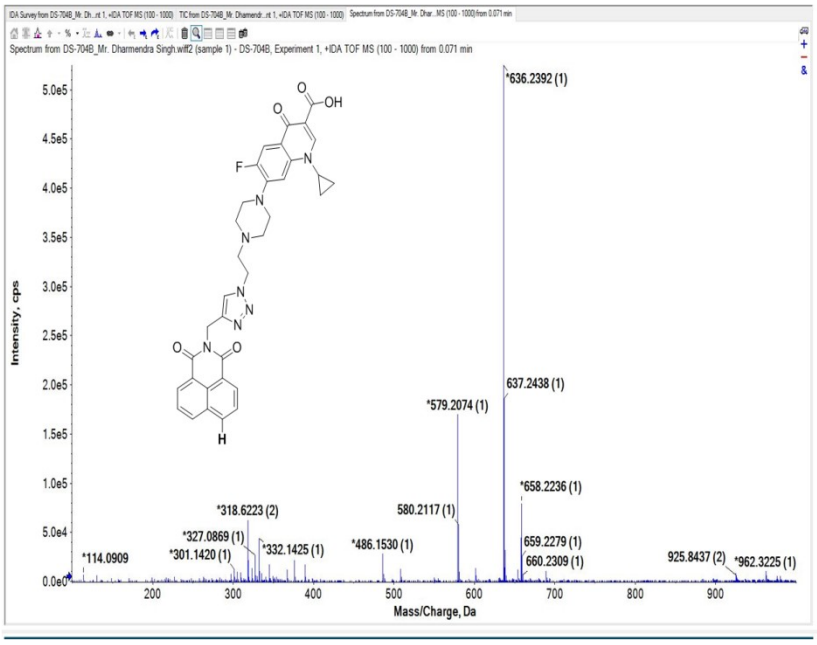

Figure S92. HMRS of compound (20e) $C_{34}H_{30}FN_7O_5$ [M+H] $^+$ =636.2292 found 636.2392

The first derivative curve of Thermal Denaturation study

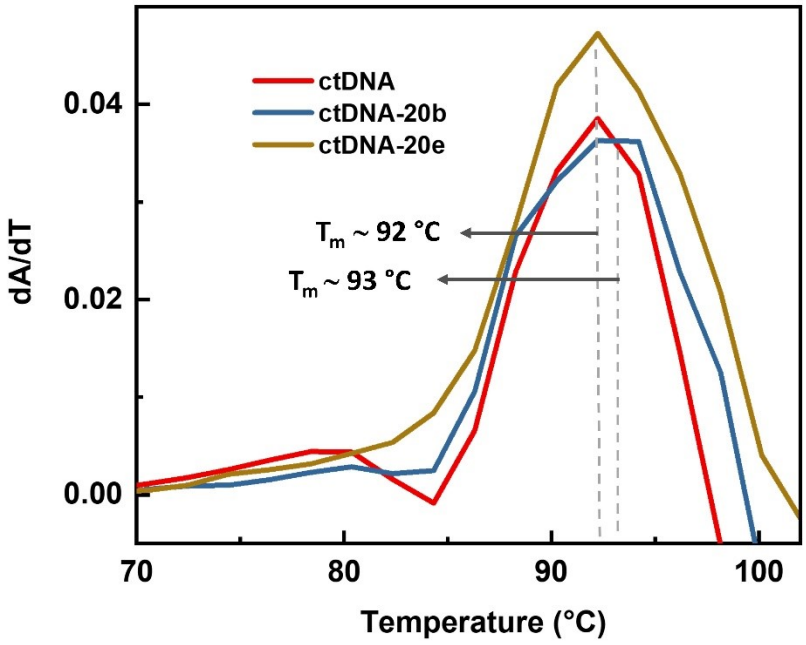

Figure S93. First derivative plot of ctDNA, ctDNA-20b (1:1), and ctDNA-20e (1:1) systems in Trizma hydrochloride buffer solution (pH 7.4) with their melting temperature.

Molecular dynamic analysis

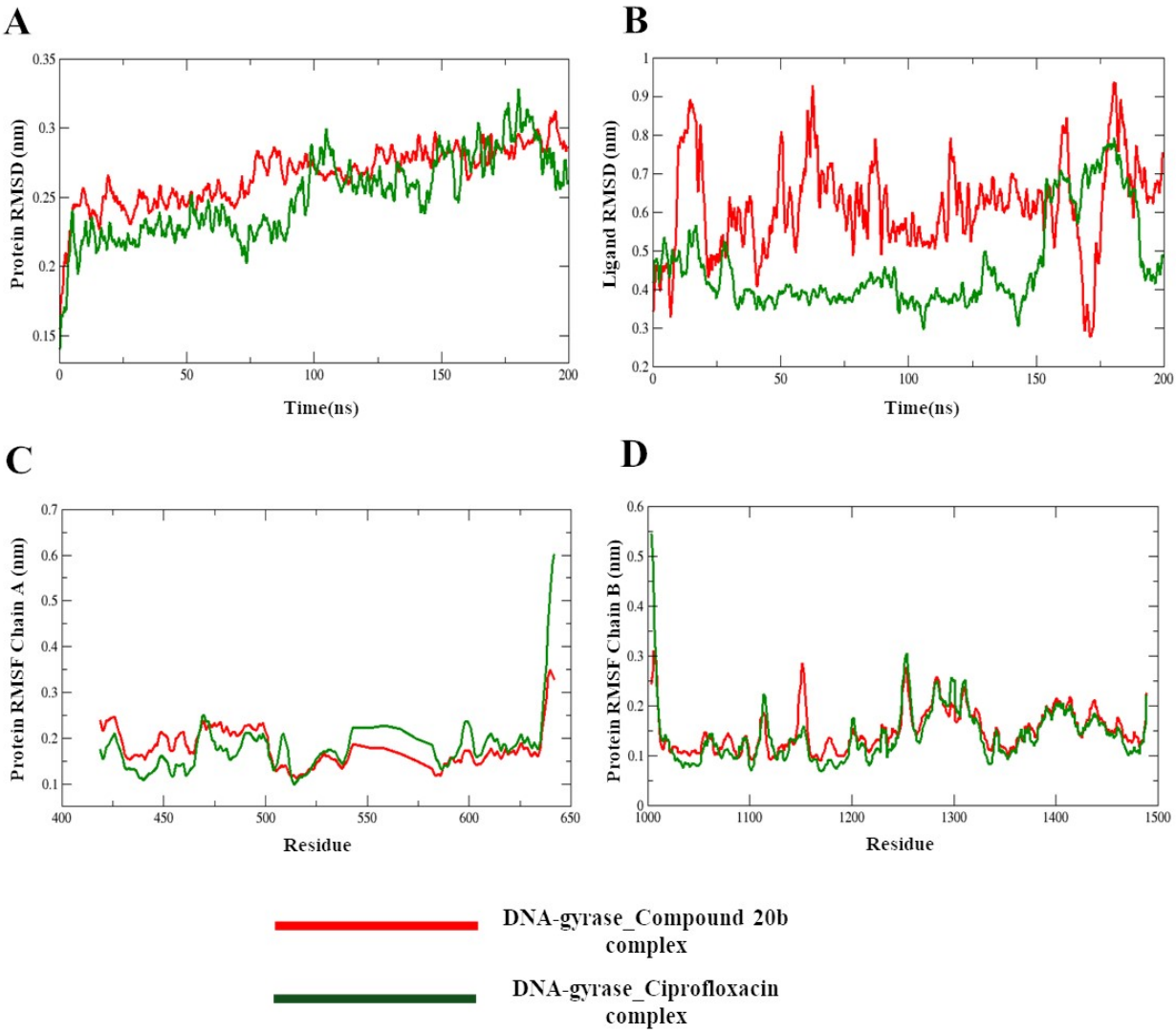

Figure S94. Molecular dynamic analysis of DNA gyrase-compound 20b complex and DNA gyrase-Ciprofloxacin complex (A) Protein RMSD, (B) Ligand RMSD, (C) Protein RMSF Chain A (D) Protein RMSF Chain B.

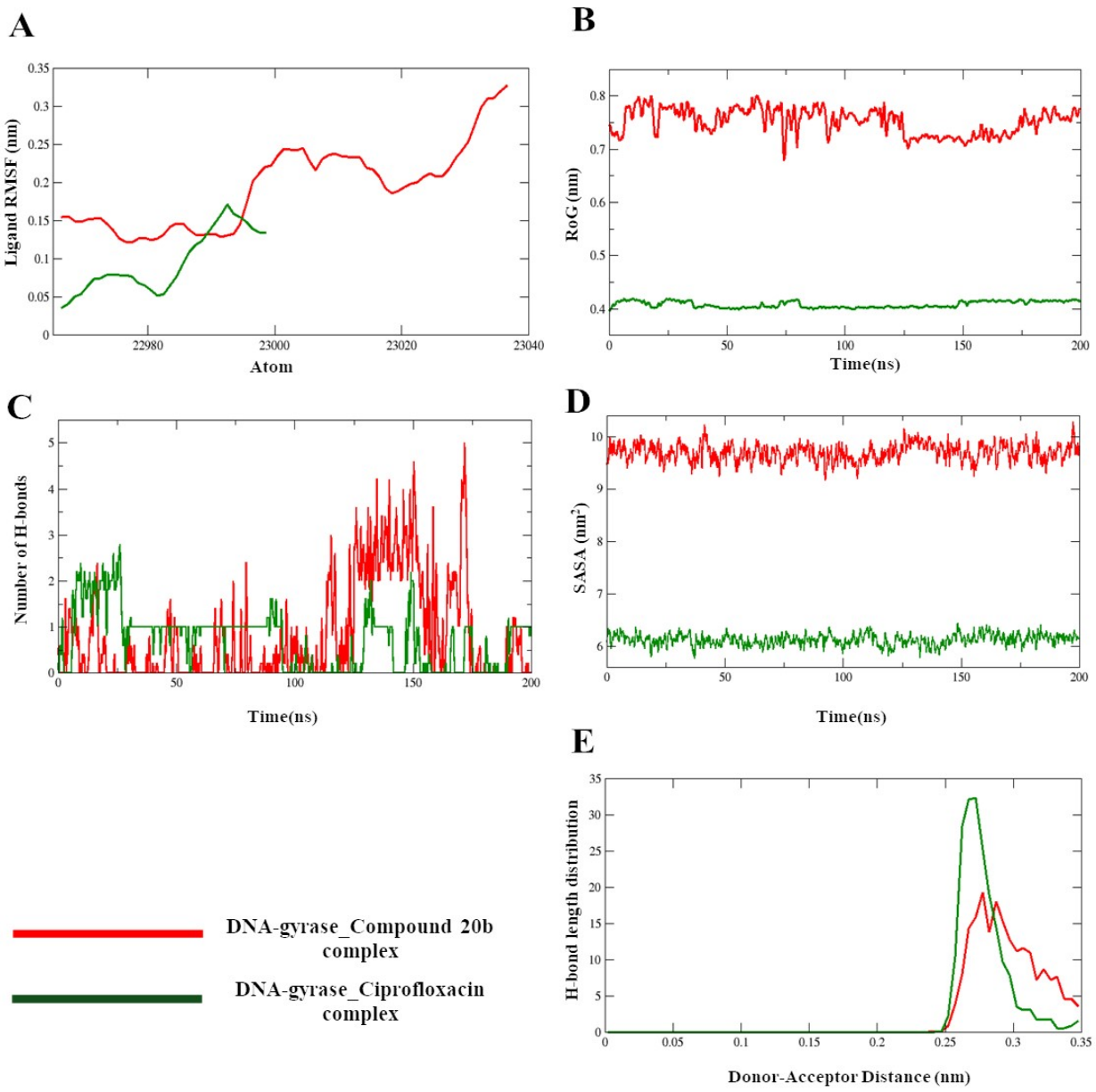

Figure S95. Molecular dynamic analysis of DNA gyrase compound 20b complex and DNA gyrase Ciprofloxacin complex, (A) Ligand RMSF, (B) RoG, (C) Number of H-bonds, (D) SASA, (E) H-bond length distribution.