Novel Three-Component Stereoselective Synthesis of Spirooxindole Derivatives

Fuchao Yu,[a] Rong Huang,[a] Hangchen Ni,[a] Juan Fan,[a] Shengjiao Yan* [a]

and Jun Lin* [a,b]

[a] *Key Laboratory of Medicinal Chemistry for Natural Resources (Yunnan University), Ministry of Education, School of Chemical Science and Technology, Yunnan University, Kunming, 650091, P. R. China*

[b] *State Key Laboratory of Elemento-organic Chemistry, Nankai University, Tianjin, 300071, P. R. China*

Supporting Information

Table of Contents

General Information 4

General Procedure for the Preparation of Spirooxindole Derivatives **5** and **5'** 4

Spectroscopic Data of Spirooxindole Derivatives **5** and **5'** 5

X-ray Structure and Data of **5r** 23

X-ray Structure and Data of **5r'** 30

Figure 1. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5a** 37

Figure 2. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5a** 38

Figure 3. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5b** 39

Figure 4. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5b** 40

Figure 5. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5c** 41

Figure 6. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5c** 42

Figure 7. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5d** 43

Figure 8. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5d** 44

Figure 9. ^{1}H NMR (500 MHz, DMSO-d_6 + $HClO_4$) spectra of compound **5e** 45

Figure 10. ^{13}C NMR (125 MHz, DMSO-d_6 + $HClO_4$) spectra of compound **5e** 46

Figure 11. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5f** 47

Figure 12. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5f** 48

Figure 13. ^{1}H NMR (500 MHz, $CDCl_3$ + DMSO-d_6) spectra of compound **5g** 49

Figure 14. ^{13}C NMR (125 MHz, $CDCl_3$ + DMSO-d_6) spectra of compound **5g** 50

Figure 15. ^{1}H NMR (500 MHz, $CDCl_3$ + DMSO-d_6) spectra of compound **5h** 51

Figure 16. ^{13}C NMR (125 MHz, $CDCl_3$ + DMSO-d_6) spectra of compound **5h** 52
Figure 17. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5i**.....53
Figure 18. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5i**.....54
Figure 19. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5j** 55
Figure 20. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5j** 56
Figure 21. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5k**.....57
Figure 22. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5k** 58
Figure 23. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5l**.....59
Figure 24. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5l**.....60
Figure 25. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5m** 61
Figure 26. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5m** 62
Figure 27. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5m'** 63
Figure 28. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5m'** 64
Figure 29. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5n**.....65
Figure 30. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5n** 66
Figure 31. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5n'** 67
Figure 32. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5n'** 68
Figure 33. ^{1}H NMR (500 MHz, DMSO-d_6 + $HClO_4$) spectra of compound **5o** 69
Figure 34. ^{13}C NMR (125 MHz, DMSO-d_6 + $HClO_4$) spectra of compound **5o** 70
Figure 35. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5o'**.....71
Figure 36. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5o'**.....72
Figure 37. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5p**.....73
Figure 38. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5p** 74
Figure 39. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5p'** 75
Figure 40. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5p'** 76
Figure 41. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5q**.....77
Figure 42. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5q** 78
Figure 43. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5q'** 79
Figure 44. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5q'** 80
Figure 45. ^{1}H NMR (500 MHz, $CDCl_3$ + DMSO-d_6) spectra of compound **5r** 81
Figure 46. ^{13}C NMR (125 MHz, $CDCl_3$ + DMSO-d_6) spectra of compound **5r** 82
Figure 47. ^{1}H NMR (500 MHz, $CDCl_3$ + DMSO-d_6) spectra of compound **5r'** 83
Figure 48. ^{13}C NMR (125 MHz, $CDCl_3$ + DMSO-d_6) spectra of compound **5r'** 84
Figure 49. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5s** 85
Figure 50. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5s** 86

Figure 51. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5s'** 87
Figure 52. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5s'** 88
Figure 53. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5t** 89
Figure 54. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5t** 90
Figure 55. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5t'** 91
Figure 56. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5t'** 92
Figure 57. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5u**.....93
Figure 58. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5u** 94
Figure 59. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5u'** 95
Figure 60. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5u'** 96
Figure 61. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5v**.....97
Figure 62. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5v**.....98
Figure 63. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5v'**.....99
Figure 64. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5v'**.....100
Figure 65. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5w**.....101
Figure 66. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5w**.....102
Figure 67. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5w'**.....103
Figure 68. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5w'**.....104
Figure 69. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5x**.....105
Figure 71. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5x'**.....107
Figure 72. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5x'**.....108
References and Notes 109

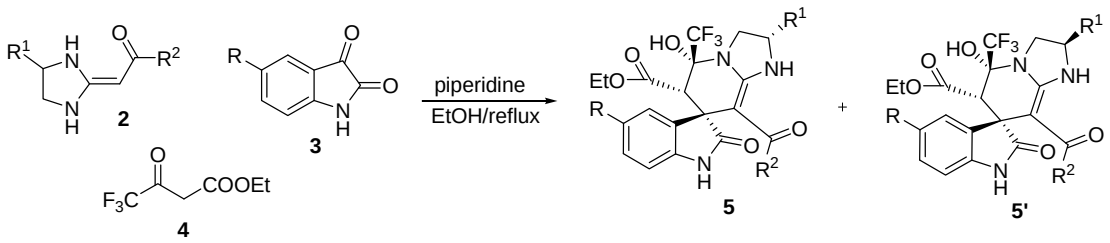
General Information

All compounds were fully characterized by spectroscopic data. The NMR spectra were recorded on a Bruker DRX500 (^{1}H: 500 MHz, ^{13}C: 125 MHz), chemical shifts (δ) are expressed in ppm, and J values are given in Hz, and deuterated $CDCl_3$ and DMSO-d_6 were used as solvent. IR spectra were recorded on a FT-IR Thermo Nicolet Avatar 360 using KBr pellet. The reactions were monitored by thin layer chromatography (TLC) using silica gel GF_{254}. The melting points were determined on XT-4A melting point apparatus and are uncorrected. HRMs were performed on a Agllent LC/Msd TOF instrument.

All chemicals and solvents were used as received without further purification unless otherwise stated. Column chromatography was performed on silica gel (200–300 mesh).

Compounds **2** were prepared according to the literature[1]. The materials **3a–c** were purchased from Aldrich Corporation Limited.

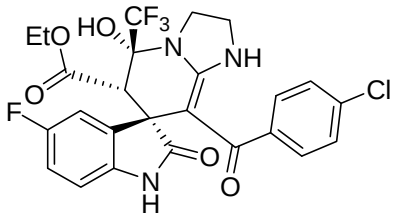
General Procedure for the Preparation of Spirooxindole Derivatives 5 and 5'



HKAs **2** (1 mmol), indoline-2,3-dione **3** (1.1 mmol), ethyl trifluoroacetate **4** (1.1 mmol), ethanol (15 mL) and piperidine (4 drops) were charged into a 25 mL round-bottom flask, and the mixture was refluxed. The resulting solution was stirred for 2 h until the HKAs **2** were completely consumed. The mixture was cooled to room temperature, then EtOAc (50 mL × 2) were added. The organic phase was washed with water (20 mL), dried over Na_2SO_4, concentrated and purified by flash column chromatography to afford spirooxindole derivatives **5** and diastereoisomers **5'** in a 80~93% yield.

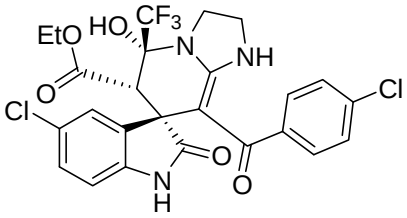
Spectroscopic Data of Spirooxindole Derivatives 5 and 5'

(*3'S,5R,6S*)-Ethyl 8-(4-chlorobenzoyl)-5'-fluoro-5-hydroxy-2'-oxo-5-(trifluoromethyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5a)



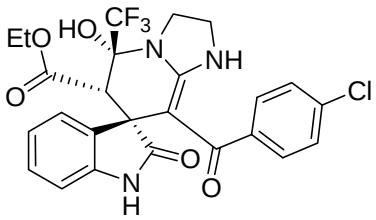
White solid; Mp 235–237 °C; IR (KBr): 3179, 3080, 1743, 1692, 1598, 1499, 1382, 1327, 1170, 1021, 816, 677 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 0.62 (t, J = 6.5 Hz, 3H, CH_3), 3.58–3.79 (m, 7H, NCH_2CH_2N, OCH_2 and CH), 6.21–6.24 (m, 1H, ArH), 6.67–7.37 (m, 7H, ArH), 8.33 (br, 1H, NH), 9.55 (br, 1H, OH), 10.75 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.4, 42.4, 44.2, 51.0, 52.3, 60.8, 83.6–84.1 (q, J = 30.0 Hz), 85.9, 110.8 (d, J = 7.5 Hz), 112.4 (d, J = 25.0 Hz), 115.3 (d, J = 22.5 Hz), 122.8 (q, J = 286.3 Hz), 127.5, 127.7, 132.4, 134.1 (d, J = 8.8 Hz), 137.9, 140.8, 158.2, 160.1 (d, J = 7.5 Hz), 166.5, 182.7, 188.8; HRMS (TOF ES^+): *m/z* calcd for $C_{25}H_{21}ClF_4N_3O_5$ [$(M+H)^+$], 554.1100; found, 554.1097.

(*3'S,5R,6S*)-Ethyl 5'-chloro-8-(4-chlorobenzoyl)-5-hydroxy-2'-oxo-5-(trifluoromethyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5b)



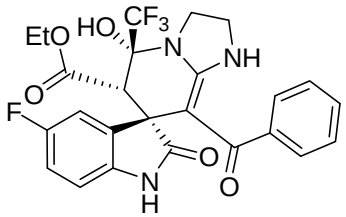
White solid; Mp 203–207 °C; IR (KBr): 3171, 3097, 1744, 1698, 1595, 1502, 1385, 1328, 1178, 1016, 810 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 0.62 (t, J = 7.0 Hz, 3H, CH_3), 3.57–3.82 (m, 7H, NCH_2CH_2N, OCH_2 and CH), 6.27 (d, J = 8.3 Hz, 1H, ArH), 6.68–7.05 (m, 5H, ArH), 7.52 (d, J = 1.7 Hz, 1H, ArH), 8.18 (br, 1H, NH), 9.41 (br, 1H, OH), 10.83 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.9, 42.9, 44.7, 51.4, 52.6, 61.3, 84.2 (q, J = 30.0 Hz), 86.4, 111.9, 123.3 (q, J = 286.3 Hz), 125.3, 127.7, 127.8, 128.4, 129.2, 133.1, 134.8, 141.2, 141.3, 160.5, 170.0, 183.0, 189.2; HRMS (TOF ES^+): *m/z* calcd for $C_{25}H_{21}Cl_2F_3N_3O_5$ [$(M+H)^+$], 570.0805; found, 570.0807.

(*3'S,5R,6S*)-Ethyl 8-(4-chlorobenzoyl)-5-hydroxy-2'-oxo-5-(trifluoro-methyl)-2, 3,5,6-tetra-hydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5c)



White solid; Mp 227–228.5 °C; IR (KBr): 3180, 3072, 1743, 1686, 1601, 1494, 1377, 1180, 1018, 751, 678 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 0.55–0.59 (m, 3H, CH_3), 3.56–3.74 (m, 7H, NCH_2CH_2N, OCH_2 and CH), 6.23 (d, J = 7.5 Hz, 1H, ArH), 6.34 (m, 1H, ArH), 6.63–6.69 (m, 2H, ArH), 6.91–6.97 (m, 5H, ArH), 7.29 (d, J = 7.4 Hz, 1H, ArH), 8.42 (br, 1H, NH), 9.63 (br, 1H, OH), 10.69 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.3, 42.4, 44.2, 51.4, 51.8, 60.8, 83.6 (q, J = 30.0 Hz), 86.1, 110.0, 122.8, 124.3, 127.1, 127.3, 127.5, 127.9, 128.9, 131.3, 140.8, 141.7, 160.2, 166.4, 182.6, 189.2; HRMS (TOF ES^+): *m/z* calcd for $C_{25}H_{22}ClF_3N_3O_5$ $[(M+H)^+]$, 536.1195; found, 536.1198.

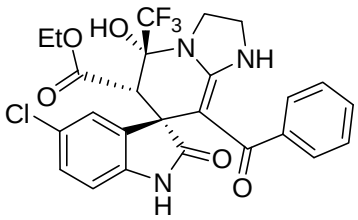
(*3'S,5R,6S*)-Ethyl 8-benzoyl-5'-fluoro-5-hydroxy-2'-oxo-5-(trifluoromethyl)-2,3, 5,6-tetra-hydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5d)



White solid; Mp 183–186 °C; IR (KBr): 3184, 1741, 1688, 1600, 1494, 1378, 1172, 1023, 697 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 0.61 (t, J = 5.6 Hz, 3H, CH_3), 3.56-3.76 (m, 7H, NCH_2CH_2N, OCH_2 and CH), 6.16 (t, J = 4.1 Hz, 1H, ArH), 6.68–7.07 (m, 6H, ArH), 7.33 (d, J = 8.3 Hz, 1H, ArH), 8.37 (br, 1H, NH), 9.51 (br, 1H, OH), 10.71 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.4, 42.3, 44.1, 51.2, 52.4, 60.8, 83.7 (q, J = 11.3 Hz), 85.9, 111.0, 112.2, 115.1, 122.9 (q, J = 287.5 Hz), 125.8, 127.3, 127.6, 134.1, 137.8, 142.2, 158.2, 160.0, 166.5, 182.7, 190.3; HRMS (TOF ES^+): *m/z* calcd for $C_{25}H_{22}F_4N_3O_5$ $[(M+H)^+]$, 520.1490; found, 520.1488.

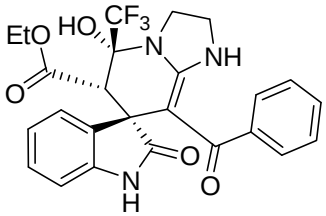
(*3'S,5R,6S*)-Ethyl 8-benzoyl-5'-chloro-5-hydroxy-2'-oxo-5-(trifluoromethyl)-2,3, 5,6-tetra-hydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate

(5e)



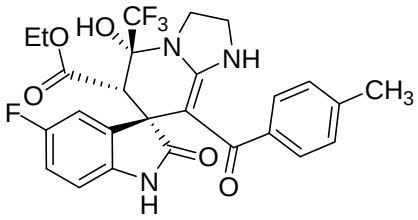
White solid; Mp 228–229 °C; IR (KBr): 3329, 1693, 1600, 1515, 1475, 1379, 1332, 1181, 1015, 633 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6 + $HClO_4$): δ = 0.61 (t, J = 6.1 Hz, 3H, CH_3), 3.59–3.81 (m, 7H, NCH_2CH_2N, OCH_2 and CH), 6.20 (d, J = 3.9 Hz, 1H, ArH), 6.69–7.07 (m, 6H, ArH), 7.50 (s, 1H, ArH), 8.25 (br, 1H, NH), 9.36 (br, 1H, OH), 10.79 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6 + $HClO_4$): δ = 13.4, 42.3, 44.1, 51.0, 52.2, 60.8, 83.6 (q, J = 18.8 Hz), 85.8, 111.4, 122.8 (q, J = 286.3 Hz), 124.6, 125.9, 127.0, 127.4, 127.7, 128.6, 134.3, 140.7, 142.2, 159.9, 166.5, 182.6, 190.2; HRMS (TOF ES^+): *m/z* calcd for $C_{25}H_{22}ClF_3N_3O_5$ $[(M+H)^+]$, 536.1195; found, 536.1194.

(*3'S,5R,6S*)-Ethyl 8-benzoyl-5-hydroxy-2'-oxo-5-(trifluoromethyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5f)



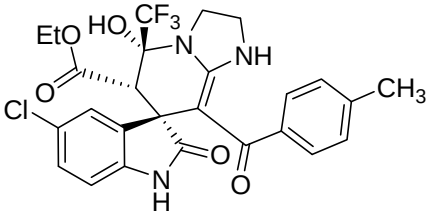
White solid; Mp 220–224 °C; IR (KBr): 3195, 1741, 1678, 1605, 1482, 1177, 1023, 755, 696 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 0.56–0.58 (m, 3H, CH_3), 3.40–3.78 (m, 7H, NCH_2CH_2N, OCH_2 and CH), 6.17 (d, J = 5.0 Hz, 1H, ArH), 6.61–7.05 (m, 7H, ArH), 7.24–7.25 (m, 1H, ArH), 8.46 (br, 1H, NH), 9.51 (br, 1H, OH), 10.63 (m, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.3, 42.3, 44.2, 51.7, 60.7, 83.7 (q, J = 17.5 Hz), 86.1, 110.1, 122.2 (q, J = 17.5 Hz), 121.7, 122.7, 124.1, 125.7, 127.1, 127.4, 128.8, 132.2, 141.7, 142.2, 160.0, 166.4, 182.6, 190.7; HRMS (TOF ES^+): *m/z* calcd for $C_{25}H_{23}F_3N_3O_5$ $[(M+H)^+]$, 502.1584; found, 502.1585.

(*3'S,5R,6S*)-Ethyl 5'-fluoro-5-hydroxy-8-(4-methylbenzoyl)-2'-oxo-5-(trifluoromethyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5g)



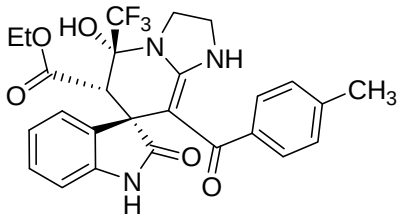
White solid; Mp 224.5–227 °C; IR (KBr): 3218, 1746, 1687, 1606, 1507, 1022, 823 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$ + DMSO-d_6): δ = 0.68 (t, J = 13.7 Hz, 3H, CH_3), 2.12 (s, 3H, $ArCH_3$), 3.17–3.80 (m, 7H, NCH_2CH_2N, OCH_2 and CH), 6.08–6.10 (m, 1H, ArH), 6.52–6.82 (m, 6H, ArH), 8.31 (br, 1H, NH), 9.56 (br, 1H, OH), 10.36 (br, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$ + DMSO-d_6): δ = 13.2, 21.1, 42.0, 44.0, 51.5, 52.2, 60.8, 83.6 (q, J = 81.3 Hz), 86.1, 110.7–111.1 (m), 114.7 (d, J = 23.8 Hz), 122.5 (q, J = 286.3 Hz), 125.5, 127.6, 133.6, 137.1, 137.5, 138.8, 158.2, 160.2, 160.4, 166.1, 182.5, 191.5; HRMS (TOF ES^+): *m/z* calcd for $C_{26}H_{24}F_4N_3O_5$ $[(M+H)^+]$, 534.1647; found, 534.1647.

(*3'S,5R,6S*)-Ethyl 5'-chloro-5-hydroxy-8-(4-methylbenzoyl)-2'-oxo-5-(trifluoromethyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5h)



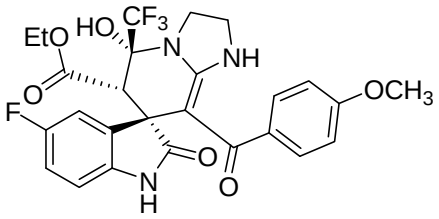
White solid; Mp 223–226 °C; IR (KBr): 3224, 1744, 1689, 1603, 1484, 1377, 1177, 1025, 759 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 0.47 (t, J = 6.8 Hz, 3H, CH_3), 1.92 (s, 3H, $ArCH_3$), 3.22 (s, 1H, CH), 3.36–3.65 (m, 6H, NCH_2CH_2N and OCH_2), 5.88 (d, J = 8.2 Hz, 1H, ArH), 6.41–6.80 (m, 6H, ArH), 7.97 (br, 1H, NH), 9.37 (br, 1H, OH), 10.13 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.5, 21.3, 42.4, 44.3, 51.9, 52.2, 61.2, 83.8 (q, J = 31.3 Hz), 86.4, 111.5, 121.5–128.5 (m), 124.0, 125.9, 127.9, 128.5, 134.0, 137.5, 139.1, 140.4, 160.8, 166.5, 182.5, 192.0; HRMS (TOF ES^+): *m/z* calcd for $C_{26}H_{24}ClF_3N_3O_5$ $[(M+H)^+]$, 550.1351; found, 550.1350.

(*3'S,5R,6S*)-Ethyl 5-hydroxy-8-(4-methylbenzoyl)-2'-oxo-5-(trifluoromethyl)-2,3,5,6-tetra-hydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5i)



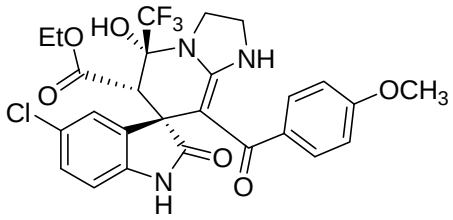
White solid; Mp 164–165.5 °C; IR (KBr): 3228, 1749, 1680, 1599, 1506, 1377, 1167, 1021, 605 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 0.58 (t, J = 6.6 Hz, 3H, CH_3), 2.18 (s, 3H, $ArCH_3$), 3.56–3.72 (m, 7H, NCH_2CH_2N, OCH_2 and CH), 6.25 (d, J = 7.6 Hz, 1H, ArH), 6.60 (d, J = 6.0 Hz, 2H, ArH), 6.59–6.94 (m, 4H, ArH), 7.23 (d, J = 7.4 Hz, 1H, ArH), 8.46 (br, 1H, NH), 9.06 (br, 1H, OH), 10.63 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.4, 21.2, 42.3, 44.2, 51.5, 52.0, 60.7, 83.8 (q, J = 30.0 Hz), 86.3, 110.0, 121.8, 122.6, 124.0, 126.1, 127.8, 128.6, 132.3, 137.0, 139.4, 142.0, 159.6, 166.5, 182.7, 190.8; HRMS (TOF ES^+): *m/z* calcd for $C_{26}H_{25}F_3N_3O_5$ $[(M+H)^+]$, 516.1741; found, 516.1742.

(*3'S,5R,6S*)-Ethyl 5'-fluoro-5-hydroxy-8-(4-methoxybenzoyl)-2'-oxo-5-(trifluoromethyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5j)



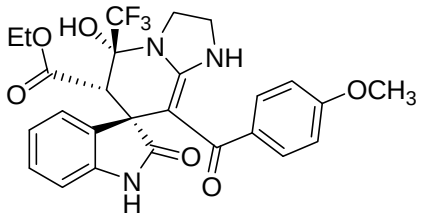
White solid; Mp 225–228.5 °C; IR (KBr): 3223, 1738, 1693, 1597, 1530, 1257, 1169, 1024, 696, 609 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 0.64 (t, J = 6.8 Hz, 3H, CH_3), 3.28–3.81 (m, 10H, NCH_2CH_2N, OCH_2, OCH_3 and CH), 6.34–6.36 (m, 1H, ArH), 6.63–7.00 (m, 5H, ArH), 7.29 (d, J = 8.3 Hz, 1H, ArH), 8.37 (br, 1H, NH), 8.48 (br, 1H, OH), 10.76 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.4, 42.2, 44.2, 50.9, 52.7, 55.4, 60.8, 83.6–84.2 (m), 86.1, 110.7, 111.7 (d, J = 25.0 Hz), 113.1, 114.9 (d, J = 23.8 Hz), 122.9 (q, J = 287.5 Hz), 128.3, 134.6, 138.2, 158.1, 158.9, 159.6, 160.0, 166.6, 182.9, 190.0; HRMS (TOF ES^+): *m/z* calcd for $C_{26}H_{24}F_4N_3O_6$ $[(M+H)^+]$, 550.1596; found, 550.1595.

(*3'S,5R,6S*)-Ethyl 5'-chloro-5-hydroxy-8-(4-methoxybenzoyl)-2'-oxo-5-(trifluoromethyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5k)



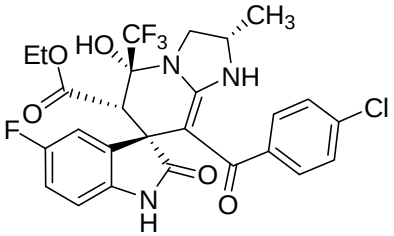
White solid; Mp 178–180 °C; IR (KBr): 3162, 1743, 1692, 1597, 1492, 1382, 1177, 1013, 660 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 0.65 (t, J = 6.9 Hz, 3H, CH_3), 3.48–3.82 (m, 7H, NCH_2CH_2N, OCH_2 and CH), 3.70 (s, 3H, OCH_3), 6.40 (d, J = 8.2 Hz, 1H, ArH), 6.66 (d, J = 7.8 Hz, 2H, ArH), 6.88 (d, J = 7.8 Hz, 2H, ArH), 7.04 (d, J = 8.2 Hz, 1H, ArH), 7.46 (s, 1H, ArH), 8.23 (br, 1H, NH), 8.27 (br, 1H, OH), 10.86 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.4, 42.3, 44.2, 50.9, 52.6, 55.5, 60.8, 83.8 (q, J = 30.0 Hz), 86.1, 111.3, 113.2, 121.8, 124.1, 126.9, 128.4, 128.5, 134.6, 134.6, 141.1, 159.0, 159.7, 166.6, 182.7, 189.8; HRMS (TOF ES^+): *m/z* calcd for $C_{26}H_{24}ClF_3N_3O_6$ [$(M+H)^+$], 566.1300; found, 566.1300.

(*3'S,5R,6S*)-Ethyl 5-hydroxy-8-(4-methoxybenzoyl)-2'-oxo-5-(trifluoromethyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5l)



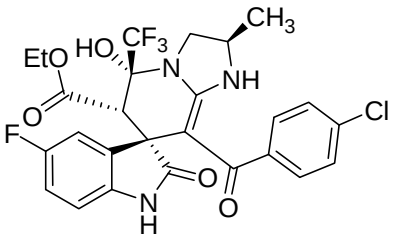
White solid; Mp 227–229.5 °C; IR (KBr): 3153, 1739, 1688, 1595, 1491, 1375, 1251, 1117, 1023, 757 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 0.59 (t, J = 6.3 Hz, 3H, CH_3), 3.39–3.80 (m, 6H, NCH_2CHN, OCH_2 and CH), 3.73–3.76 (m, 3H, OCH_3), 6.34 (d, J = 7.6 Hz, 1H, ArH), 6.58 (d, J = 7.5 Hz, 2H, ArH), 6.76 (d, J = 7.5 Hz, 2H, ArH), 6.86–6.97 (m, 2H, ArH), 7.22 (d, J = 7.4 Hz, 2H, ArH), 8.44 (br, 1H, NH), 8..52 (br, 1H, OH), 10.67 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.4, 42.2, 44.2, 51.5, 52.2, 55.5, 60.7, 83.9 (q, J = 30.0 Hz), 86.4, 110.0, 113.0, 121.8, 122.6, 123.7, 128.1, 128.7, 132.4, 134.7, 142.1, 159.1, 159.4, 166.5, 182.8, 190.3; HRMS (TOF ES^+): *m/z* calcd for $C_{26}H_{25}F_3N_3O_6$ [$(M+H)^+$], 532.1690; found, 532.1689.

(*2S,3'S,5R,6S*)-Ethyl 8-(4-chlorobenzoyl)-5'-fluoro-5-hydroxy-2-methyl-2'-oxo-5-(trifluoromethyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5m)



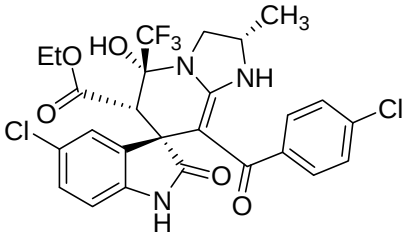
White solid; Mp 217–218 °C; IR (KBr): 3179, 1742, 1691, 1596, 1496, 1382, 1180, 1012, 667 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 0.58–0.62 (m, 3H, CH_3), 1.32 (d, J = 4.9 Hz, 3H, CH_3), 3.24–3.29 (m, 1H, NCH_2), 3.59–4.06 (m, 5H, NCH_2CHN, OCH_2 and CH), 6.18–6.20 (m, 1H, ArH), 6.13–7.00 (m, 5H, ArH), 7.36 (d, J = 7.7 Hz, 1H, ArH), 8.36 (br, 1H, NH), 9.84 (br, 1H, OH), 10.74 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.4, 20.0, 50.6, 50.8, 51.0, 52.2, 60.8, 83.4–83.8 (q, J = 17.5 Hz), 85.6, 110.8, 112.5 (d, J = 26.3 Hz), 115.3 (d, J = 22.5 Hz), 122.8 (q, J = 286.3 Hz) 127.2, 127.5, 132.3, 134.0, 137.7 (d, J = 17.5 Hz), 140.8, 158.3, 159.6–160.1 (m), 166.4, 182.6 (d, J = 16.3 Hz), 189.1; HRMS (TOF ES^+): *m/z* calcd for $C_{26}H_{23}ClF_4N_3O_5$ [$(M+H)^+$], 568.1257; found, 568.1257.

(*2R,3'S,5R,6S*)-Ethyl 8-(4-chlorobenzoyl)-5'-fluoro-5-hydroxy-2-methyl-2'-oxo-5-(trifluoromethyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5m')



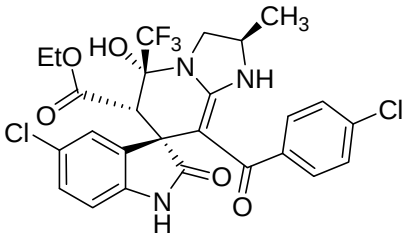
White solid; Mp 221–224.5 °C; IR (KBr): 3324, 3264, 1738, 1691, 1598, 1503, 1381, 1336, 1278, 1179, 1018, 756, 678 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 0.85–0.90 (m, 3H, CH_3), 1.41 (d, J = 6.1 Hz, 3H, CH_3), 3.19–3.21 (m, 1H, NCH_2), 3.69–4.09 (m, 5H, NCH_2CHN, OCH_2 and CH), 6.22–6.24 (m, 1H, ArH), 6.68–6.89 (m, 5H, ArH), 7.34 (d, J = 7.5 Hz, 1H, ArH), 8.22–8.24 (m, 1H, NH), 9.61 (br, 1H, OH), 10.75 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.4, 21.2, 49.7, 50.8, 52.2, 60.9, 79.4, 83.6 (q, J = 30.0 Hz), 85.5, 110.9, 112.4 (d, J = 23.8 Hz), 115.2 (d, J = 22.5 Hz), 122.8 (q, J = 287.5 Hz), 127.2, 127.8, 132.5, 134.0, 137.8 (d, J = 18.8 Hz) 140.7, 158.2, 159.1, 160.1, 166.4, 182.6, 188.7; HRMS (TOF ES^+): *m/z* calcd for $C_{26}H_{23}ClF_4N_3O_5$ [$(M+H)^+$], 568.1257; found, 568.1257.

(*2S,3'S,5R,6S*)-Ethyl 5'-chloro-8-(4-chlorobenzoyl)-5-hydroxy-2-methyl-2'-oxo-5-(trifluoromethyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5n)



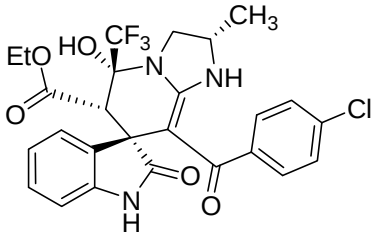
White solid; Mp 228–231 °C; IR (KBr): 3164, 1743, 1693, 1595, 1493, 1383, 1179, 1085, 1010, 663 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 0.60 (q, J = 6.9 Hz, 3H, CH_3), 1.31 (d, J = 5.6 Hz, 3H, CH_3), 3.27 (t, J = 9.9 Hz, 1H, NCH_2), 3.57–4.09 (m, 5H, NCH_2CHN, OCH_2 and CH), 6.22 (d, J = 8.1 Hz, 1H, ArH), 6.61–6.65 (m, 2H, ArH), 6.99–7.02 (m, 3H, ArH), 7.54 (s, 1H, ArH), 8.23 (br, 1H, NH), 9.73 (br, 1H, OH), 10.83 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.4, 20.0, 50.6, 50.7, 51.0, 52.1, 60.8, 83.5, 85.5, 111.4,121.6, 123.9, 122.8, 124.9, 127.2, 127.7, 128.7, 132.4, 134.3, 140.5 (d, J = 20.0 Hz), 140.8, 159.7 (d, J = 18.8 Hz), 166.5, 182.4, 188.9; HRMS (TOF ES^+): *m/z* calcd for $C_{26}H_{23}Cl_2F_3N_3O_5$ $[(M+H)^+]$, 584.0961; found, 584.0964.

(*2R,3'S,5R,6S*)-Ethyl 5'-chloro-8-(4-chlorobenzoyl)-5-hydroxy-2-methyl-2'-oxo-5-(trifluoromethyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5n')



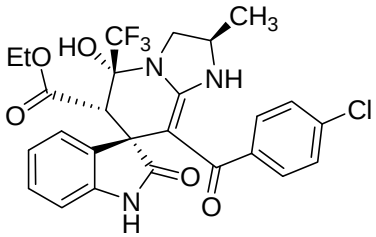
White solid; Mp 176–179.5 °C; IR (KBr): 3353, 1735, 1686, 1601, 1507, 1336, 1181, 1014, 619 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 0.61 (t, J = 6.9 Hz, 3H, CH_3), 1.24 (t, J = 6.1 Hz, 3H, CH_3), 3.18–3.20 (m, 1H, NCH_2), 3.57–4.06 (m, 5H, NCH_2CHN, OCH_2 and CH), 6.26 (t, J = 8.1 Hz, 1H, ArH), 6.68–6.72 (m, 2H, ArH), 7.00–7.04 (m, 3H, ArH), 7.58 (s, 1H, ArH), 8.13 (br, 1H, NH), 9.49 (br, 1H, OH), 10.82 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.4, 21.2, 49.6, 49.8, 50.8, 52.0, 60.8, 83.5, 85.5, 111.3, 122.8 (q, J = 286.3 Hz), 124.9, 127.1, 127.3, 128.0, 128.7, 132.6, 134.3, 140.6, 140.8, 158.8, 166.5, 182.4, 188.5; HRMS (TOF ES^+): *m/z* calcd for $C_{26}H_{23}Cl_2F_3N_3O_5$ $[(M+H)^+]$, 584.0961; found, 584.0963.

(*2S,3'S,5R,6S*)-Ethyl 8-(4-chlorobenzoyl)-5-hydroxy-2-methyl-2'-oxo-5-(trifluoromethyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5o)



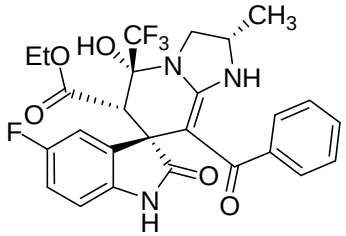
White solid; Mp 199–202 °C; IR (KBr): 3308, 1735, 1690, 1597, 1514, 1336, 1179, 1014, 756, 681 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6 + $HClO_4$): δ = 0.53–0.58 (m, 3H, CH_3), 1.32 (d, J = 5.9 Hz, 3H, CH_3), 3.24–3.29 (m, 1H, NCH_2), 3.38–4.11 (m, 5H, NCH_2CHN, OCH_2 and CH), 6.19 (d, J = 7.6 Hz, 1H, ArH), 6.53–6.56 (m, 2H, ArH), 6.88–6.96 (m, 4H, ArH), 7.27 (d, J = 7.4 Hz, 1H, ArH), 8.45 (br, 1H, NH), 9.88 (br, 1H, OH), 10.68 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6 + $HClO_4$): δ = 13.3, 19.9, 50.4, 50.6, 51.0, 51.7, 60.8, 83.6 (q, J = 30.0 Hz), 85.8, 110.0, 121.7, 122.9, 124.4, 127.0, 127.4, 129.0, 132.0, 132.2, 140.8, 141.5, 159.8, 166.4, 182.6, 189.5; HRMS (TOF ES^+): *m/z* calcd for $C_{26}H_{24}ClF_3N_3O_5$ $[(M+H)^+]$, 550.1351; found, 550.1349.

(*2R,3'S,5R,6S*)-Ethyl 8-(4-chlorobenzoyl)-5-hydroxy-2-methyl-2'-oxo-5-(trifluoromethyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5o')



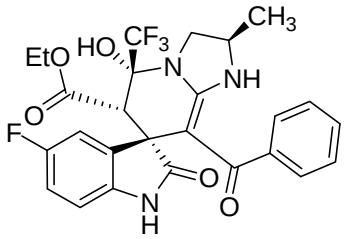
White solid; Mp 195–197 °C; IR (KBr): 3178, 1741, 1680, 1596, 1516, 1470, 1177, 1014, 753, 679 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 0.73 (t, J = 6.9 Hz, 3H, CH_3), 1.32 (d, J = 6.0 Hz, 3H, CH_3), 3.54–4.26 (m, 6H, NCH_2CHN, OCH_2 and CH), 6.19 (d, J = 8.4 Hz, 1H, ArH), 6.77–6.82 (m, 2H, ArH), 7.15–7.21 (m, 4H, ArH), 7.18 (d, J = 7.4 Hz, 1H, ArH), 8.27 (br, 1H, NH), 9.68 (br, 1H, OH), 10.55 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.8, 21.7, 50.1, 50.2, 51.3, 52.1, 61.3, 84.0, 86.3, 110.5, 122.1, 123.3, 124.9, 127.6, 127.6, 128.2, 129.4, 132.7, 141.4, 142.2, 159.6, 166.9, 183.1, 189.7; HRMS (TOF ES^+): *m/z* calcd for $C_{26}H_{24}ClF_3N_3O_5$ $[(M+H)^+]$, 550.1351; found, 550.1349.

(*2S,3'S,5R,6S*)--Ethyl 8-benzoyl-5'-fluoro-5-hydroxy-2-methyl-2'-oxo-5-(trifluoromethyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5p)



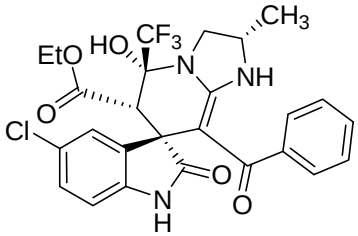
White solid; Mp 226–229 °C; IR (KBr): 3168, 1743, 1691, 1594, 1492, 1329, 1179, 1015, 697 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 0.60 (t, J = 6.5 Hz, 3H, CH_3), 1.30–1.33 (m, 3H, CH_3), 3.23–3.28 (m, 1H, NCH_2), 3.43–3.75 (m, 4H, NCH_2, OCH_2 and CH), 4.02–4.09 (m, 1H, NCH), 6.11–6.13 (m, 1H, ArH), 6.64–6.73 (m, 3H, ArH), 6.96–7.06 (m, 3H, ArH), 7.33 (d, J = 8.5 Hz, 1H, ArH), 8.42 (br, 1H, NH), 9.75 (br, 1H, OH), 10.70 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.4, 19.9, 50.4, 50.5, 51.0, 52.3, 60.8, 83.7 (q, J = 12.5 Hz), 85.6, 110.9, 112.3 (d, J = 25.0 Hz), 115.2 (d, J = 23.8 Hz), 121.7, 125.6, 127.2, 127.4, 134.0, 137.7 (d, J = 18.8 Hz), 142.3, 158.2, 159.8, 166.5, 182.7, 190.6; HRMS (TOF ES^+): *m/z* calcd for $C_{26}H_{24}F_4N_3O_5$ $[(M+H)^+]$, 534.1647; found, 534.1644.

(*2R,3'S,5R,6S*)--Ethyl 8-benzoyl-5'-fluoro-5-hydroxy-2-methyl-2'-oxo-5-(trifluoro-methyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5p')



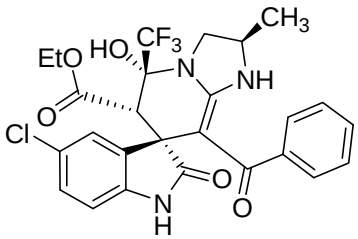
White solid; Mp 225–228 °C; IR (KBr): 3223, 1742, 1687, 1599, 1494, 1279, 1174, 1020, 756, 699 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 0.59–0.64 (m, 3H, CH_3), 1.25 (d, J = 4.8 Hz, 3H, CH_3), 3.17–3.21 (m, 1H, NCH_2), 3.58–4.08 (m, 5H, NCH_2CHN, OCH_2 and CH), 6.17 (s, 1H, ArH), 6.70–6.75 (m, 3H, ArH), 6.98–7.07 (m, 3H, ArH), 7.34 (d, J = 7.5 Hz, 1H, ArH), 8.30 (br, 1H, NH), 9.53 (br, 1H, OH), 10.71 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.4, 21.2, 49.7, 50.7, 51.1, 52.3, 60.8, 83.6 (q, J = 28.8 Hz), 85.5, 110.9, 112.2 (d, J = 25.0 Hz), 115.0 (q, J = 23.8 Hz), 125.9, 127.3, 127.6, 134.1, 137.8, 142.2, 158.2, 159.0, 160.1, 166.5, 182.7, 190.2; HRMS (TOF ES^+): *m/z* calcd for $C_{26}H_{22}F_4N_3O_5$ $[M-H^+]$, 532.1501; found, 532.1510.

(*2S,3'S,5R,6S*)-ethyl 8-benzoyl-5'-chloro-5-hydroxy-2-methyl-2'-oxo-5-(trifluoromethyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5q)



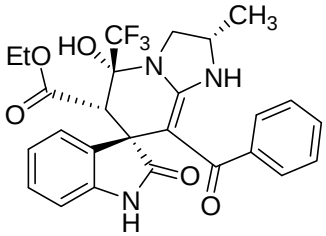
White solid; Mp 206–209.5 °C; IR (KBr): 3169, 1744, 1692, 1598, 1491, 1381, 1180, 1017, 707 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 0.60 (t, J = 6.5 Hz, 3H, CH_3), 1.31 (d, J = 5.5 Hz, 3H, CH_3), 3.25 (t, J = 9.8 Hz, 1H, NCH_2), 3.57–3.79 (m, 3H, NCH_2, OCH_2), 4.03–4.07 (m, 1H, NCH), 6.15 (d, J = 8.1 Hz, 1H, ArH), 6.62–6.66 (m, 2H, ArH), 6.93–7.07 (m, 4H, ArH), 7.50 (s, 1H, ArH), 8.29 (br, 1H, NH), 9.65 (br, 1H, OH), 10.79 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.4, 20.0, 50.4, 50.7, 50.9, 52.1, 60.8, 83.5, 85.5, 111.5, 121.7, 122.8 (q, J = 286.3 Hz), 124.7, 127.0, 127.3, 127.5, 128.6, 134.3, 140.5, 142.2, 159.7, 166.5, 182.6, 190.4; HRMS (TOF ES^+): *m/z* calcd for $C_{26}H_{24}ClF_3N_3O_5$ [$(M+H)^+$], 550.1351; found, 550.1352

(*2R,3'S,5R,6S*)-ethyl 8-benzoyl-5'-chloro-5-hydroxy-2-methyl-2'-oxo-5-(trifluoromethyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5q')



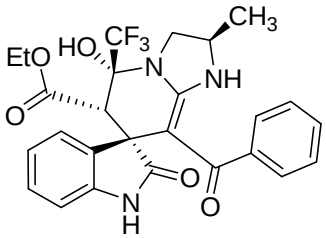
White solid; Mp 206–210 °C; IR (KBr): 3226, 1742, 1688, 1599, 1526, 1334, 1179, 1018, 756, 700 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 0.60 (t, J = 7.0 Hz, 3H, CH_3), 1.24 (d, J = 4.9 Hz, 3H, CH_3), 3.17–3.21 (m, 1H, NCH_2), 3.46–4.07 (m, 5H, NCH_2CHN, OCH_2 and CH), 6.17–6.20 (m, 1H, ArH), 6.67–6.72 (m, 2H, ArH), 6.94–7.08 (m, 4H, ArH), 7.54 (s, 1H, ArH), 8.30 (br, 1H, NH), 9.42 (br, 1H, OH), 10.78 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.4, 21.2, 49.5, 50.8, 51.0, 52.1, 60.8, 83.5 (q, J = 11.3 Hz), 85.4, 111.4, 122.8 (q, J = 286.3 Hz), 124.7, 126.0, 127.0, 127.4, 127.7, 128.6, 134.4, 140.6, 142.2, 158.8, 166.5, 182.6, 190.0; HRMS (TOF ES^+): *m/z* calcd for $C_{26}H_{24}ClF_3N_3O_5$ [$(M+H)^+$], 550.1351; found, 550.1350.

(*2S,3'S,5R,6S*)-ethyl 8-benzoyl-5-hydroxy-2-methyl-2'-oxo-5-(trifluoromethyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5r)



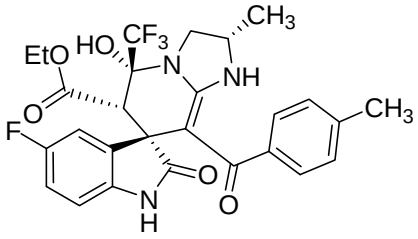
White solid; Mp 209–211.5 °C; IR (KBr): 3223, 1749, 1673, 1602, 1524, 1334, 1181, 1064, 703 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$ + DMSO-d_6): δ = 0.68 (t, J = 6.3 Hz, 3H, CH_3), 1.43 (d, J = 6.0 Hz, 3H, CH_3), 3.43–3.47 (m, 1H, NCH_2), 3.52 (s, 1H, CH), 3.59–3.81 (m, 3H, NCH_2 and OCH_2), 4.18–4.23 (m, 1H, NCH), 6.11 (d, J = 7.6 Hz, 1H, ArH), 6.83–6.97 (m, 7H, ArH), 7.07 (d, J = 7.3 Hz, 1H, ArH), 8.46 (br, 1H, NH), 9.98 (br, 1H, NH), 10.16 (br, 1H, OH); ^{13}C NMR (125 MHz, $CDCl_3$ + DMSO-d_6): δ = 13.5, 20.2, 50.7, 51.5, 52.0, 52.0, 61.2, 83.0 (q, J = 30.0 Hz), 86.4, 110.7, 121.7, 122.9, 123.8, 125.6, 127.2, 127.3, 129.0, 132.1, 141.5, 142.0, 160.8, 166.7, 182.8, 192.6; HRMS (TOF ES^+): *m/z* calcd for $C_{26}H_{25}F_3N_3O_5$ $[(M+H)^+]$, 516.1741; found, 516.1740.

(*2R,3'S,5R,6S*)-ethyl 8-benzoyl-5-hydroxy-2-methyl-2'-oxo-5-(trifluoromethyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5r')



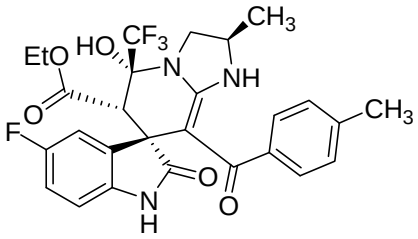
White solid; Mp 169–171 °C; IR (KBr): 3183, 1743, 1681, 1600, 1519, 1333, 1281, 1177, 1017, 754, 695 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$ + DMSO-d_6): δ = 0.60 (t, J = 6.3 Hz, 3H, CH_3), 1.27 (d, J = 6.2 Hz, 3H, CH_3), 3.19–3.22 (m, 1H, NCH_2), 3.32 (s, 1H, CH), 3.47–3.93 (m, 3H, NCH_2, OCH_2), 4.08–4.12 (m, 1H, NCH), 6.13–6.16 (m, 1H, ArH), 6.59–6.63 (m, 2H, ArH), 6.81–7.01 (m, 5H, ArH), 7.17–7.19 (m, 1H, ArH), 8.38 (br, 1H, NH), 9.65 (br, 1H, OH), 10.56 (br, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$ + DMSO-d_6): δ = 13.8, 21.8, 50.1, 51.2, 52.1, 52.2, 61.2, 84.2 (q, J = 28.8 Hz), 86.2, 110.7, 122.1, 123.0, 124.4, 126.2, 127.5, 127.7, 129.1, 132.6, 142.2, 142.6, 159.6, 166.8, 183.1, 191.2; HRMS (TOF ES^+): *m/z* calcd for $C_{26}H_{25}F_3N_3O_5$ $[(M+H)^+]$, 516.1741; found, 516.1740.

(*2S,3'S,5R,6S*)-Ethyl 5'-fluoro-5-hydroxy-2-methyl-8-(4-methylbenzoyl)-2'-oxo-5-(trifluoromethyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5s)



White solid; Mp 218.1–222.7 °C; IR (KBr): 3180, 1744, 1691, 1597, 1495, 1381, 1179, 1014, 706 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 0.60–0.63 (m, 3H, CH_3), 1.28–1.32 (m, Hz, 3H, CH_3), 2.18 (s, 3H, $ArCH_3$), 3.24 (t, J = 9.7 Hz, 1H, NCH_2), 3.57–3.61 (m, 1H, NCH_2), 3.72–3.76 (m, 3H, OCH_2 and CH), 4.00–4.04 (m, 1H, NCH), 6.19 (t, J = 6.2 Hz, 1H, ArH), 6.58–6.62 (m, 2H, ArH), 6.73–6.80 (m, 3H, ArH), 7.29 (d, J = 7.7 Hz, 1H, ArH), 8.42 (br, 1H, NH), 9.43 (br, 1H, OH), 10.72 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.4, 19.9, 21.2, 50.3, 50.9, 51.0, 52.5, 60.8, 83.7 (q, J = 28.8 Hz), 85.8, 110.8, 112.1 (d, J = 26.3 Hz), 115.0 (d, J = 23.8 Hz), 122.8 (d, J = 286.3 Hz), 125.8, 127.8, 134.1, 137.0, 137.9, 139.4, 158.2, 159.5, 160.1, 166.5; HRMS (TOF ES^+): *m/z* calcd for $C_{27}H_{26}F_4N_3O_5$ [$(M+H)^+$], 548.1803; found, 548.1812.

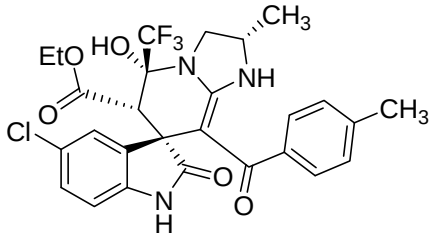
(*2R,3'S,5R,6S*)-Ethyl 5'-fluoro-5-hydroxy-2-methyl-8-(4-methylbenzoyl)-2'-oxo-5-(trifluoromethyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5s')



White solid; Mp 217–219 °C; IR (KBr): 3332, 3240, 1739, 1689, 1599, 1500, 1335, 1278, 1177, 1023, 756 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 0.60–0.64 (m, 3H, CH_3), 1.22 (d, J = 4.7 Hz, 3H, CH_3), 2.10 (s, 3H, $ArCH_3$), 3.16–3.19 (m, 1H, NCH_2), 3.57–3.62 (m, 1H, NCH_2), 3.71–3.87 (m, 3H, OCH_2 and CH), 4.00–4.04 (m, 1H, NCH), 6.22–6.25 (m, 1H, ArH), 6.67–6.82 (m, 5H, ArH), 7.30 (d, J = 7.1 Hz, 1H, ArH), 8.29 (br, 1H, NH), 9.11 (br, 1H, OH), 10.71 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.4, 21.2, 21.2, 49.6, 50.7, 50.8, 52.4, 60.8, 83.7 (q, J = 30.0 Hz), 85.6, 110.7, 112.0 (q, J = 25.0 Hz), 114.9 (q, J = 23.8 Hz), 122.8 (q, J = 286.3 Hz),

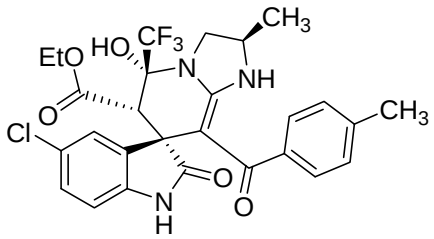
126.2, 127.8, 134.2, 137.4, 138.1, 139.3, 158.2, 158.6, 160.0, 166.5, 182.8, 190.3; HRMS (TOF ES$^+$): *m/z* calcd for $C_{27}H_{26}F_4N_3O_5$ [(M+H)$^+$], 548.1803; found, 548.1813.

(*2S,3'S,5R,6S*)-Ethyl 5'-chloro-5-hydroxy-2-methyl-8-(4-methylbenzoyl)-2'-oxo-5-(trifluoromethyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5t)



White solid; Mp 213–216.5 °C; IR (KBr): 3162, 1743, 1692, 1597, 1493, 1382, 1327, 1177, 1014, 705 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 0.61 (t, J = 6.6 Hz, 3H, CH_3), 1.28 (d, J = 3.6 Hz, 3H, CH_3), 2.17 (s, 3H, $ArCH_3$), 3.24 (t, J = 9.7 Hz, 1H, CH_2), 3.57–3.63 (m, 1H, NCH_2), 3.72–3.76 (m, 2H, OCH_2), 3.78 (s, 1H, CH), 3.99–4.03 (m, 1H, NCH), 6.20–6.23 (m, 1H, ArH), 6.58–6.62 (m, 2H, ArH), 6.78–6.82 (m, 2H, ArH), 6.96 (d, J = 8.1 Hz, 1H, ArH), 7.46 (s, 1H, ArH), 8.28 (br, 1H, NH), 9.30 (br, 1H, OH), 10.79 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.4, 20.0, 21.2, 50.4, 50.8, 51.0, 52.3, 60.8, 83.6 (q, J = 20.0 Hz), 85.7, 111.3, 124.5, 126.0, 126.9, 122.8 (q, J = 287.5 Hz), 128.4, 128.9, 134.4, 137.1, 139.4, 140.6, 159.4, 166.5, 182.5, 190.6; HRMS (TOF ES$^+$): *m/z* calcd for $C_{27}H_{26}ClF_3N_3O_5$ [(M+H)$^+$], 564.1508; found, 564.1514.

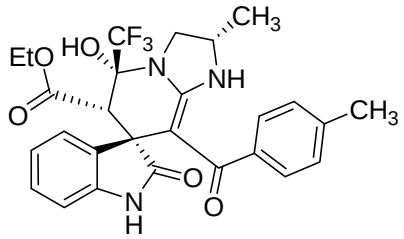
(*2R,3'S,5R,6S*)-Ethyl 5'-chloro-5-hydroxy-2-methyl-8-(4-methylbenzoyl)-2'-oxo-5-(trifluoromethyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5t')



White solid; Mp 182–185 °C; IR (KBr): 3162, 1743, 1692, 1597, 1493, 1382, 1327, 1177, 1014, 705 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 0.61 (t, J = 5.3 Hz, 3H, CH_3), 1.28–1.30 (m, 3H, CH_3), 2.18 (s, 3H, CH_3), 3.21–3.25 (m, 1H, NCH_2), 3.59–3.63 (m, 1H, NCH_2), 3.72–3.78 (m, 2H, OCH_2), 3.78 (s, 1H, CH), 4.00–4.04 (m, 1H, NCH), 6.20–6.23 (m, 1H, ArH), 6.58–6.80 (m, 4H, ArH), 6.97 (d, J = 8.2 Hz, 1H,

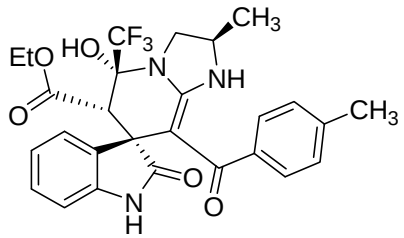
ArH), 7.47(s, 1H, ArH), 8.28 (br, 1H, NH), 9.27 (br, 1H, OH), 10.79 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.4, 20.0, 21.2, 50.4, 50.8, 51.0, 52.3, 60.8, 83.6 (q, J = 30.0 Hz), 85.7, 111.3, 122.8 (q, J = 286.3 Hz), 124.6, 126.0, 126.9, 127.8, 128.4, 134.4, 137.1, 139.4, 140.7, 159.4, 166.6, 182.6, 190.6; HRMS (TOF ES$^+$): *m/z* calcd for $C_{27}H_{26}ClF_3N_3O_5$ [(M+H)$^+$], 564.1508; found, 564.1503.

(*2S,3'S,5R,6S*)-Ethyl 5-hydroxy-2-methyl-8-(4-methylbenzoyl)-2'-oxo-5-(trifluoromethyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5u)



White solid; Mp 213–216.5 °C; IR (KBr): 3312, 3187, 1734, 1690, 1600, 1337, 1178, 1017, 759 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 0.54–0.58 (m, 3H, CH_3), 1.27–1.31 (m, 3H, CH_3), 2.08 (s, 3H, CH_3), 3.22 (d, J = 9.9 Hz, 1H, CH_2), 3.54–3.63 (m, 1H, NCH_2), 3.72–3.75 (m, 2H, OCH_2), 3.78 (s, 1H, CH), 4.00–4.04 (m, 1H, NCH), 6.18–6.22 (m, 1H, ArH), 6.51–6.55 (m, 2H, ArH), 6.72–6.75 (m, 2H, ArH), 6.85–6.93 (m, 2H, ArH), 7.22 (d, J = 8.1 Hz, 1H, ArH), 8.50 (br, 1H, NH), 9.41 (br, 1H, OH), 10.61 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.4, 20.0, 21.2, 50.2, 50.4, 51.4, 51.9, 60.8, 83.7 (q, J = 30.0 Hz), 86.0, 111.0, 121.7, 122.6, 124.0, 125.8, 127.6, 128.7, 128.8, 132.3, 139.5, 141.8, 159.4, 166.5, 182.6, 191.1; HRMS (TOF ES$^+$): *m/z* calcd for $C_{27}H_{27}F_3N_3O_5$ [(M+H)$^+$], 530.1897; found,530.1889.

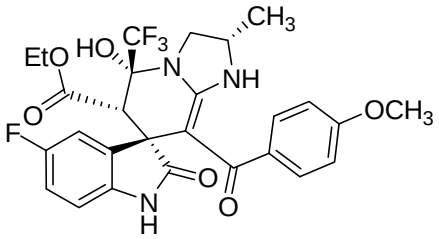
(*2R,3'S,5R,6S*)-Ethyl 5-hydroxy-2-methyl-8-(4-methylbenzoyl)-2'-oxo-5-(trifluoromethyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5u')



White solid; Mp 182–185 °C; IR (KBr): 3203, 1744, 1684, 1600, 1504, 1174, 1018, 755 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 0.66 (t, J = 7.1 Hz, 3H, CH_3), 1.28 (t, J = 4.1 Hz, 3H, CH_3), 2.14 (s, 3H, CH_3), 3.15–3.24 (m, 1H, NCH_2), 3.49–3.83 (m, 4H, NCH_2, OCH_2 and CH), 4.01–4.05 (m, 1H, NCH), 6.14–6.20 (m, 1H, ArH), 6.50–6.55

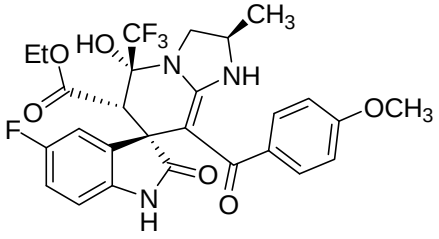
(m, 2H, ArH), 6.80–6.94 (m, 4H, ArH), 7.16 (d, J = 7.4 Hz, 1H, ArH), 8.38 (br, 1H, NH), 9.14 (br, 1H, OH), 10.62 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.8, 21.7, 49.9, 50.0, 51.2, 51.9, 52.4, 61.2, 84.2 (q, J = 28.8 Hz), 86.3, 110.5, 122.2, 123.0, 124.5, 126.7, 128.2, 129.1, 132.8, 137.6, 139.9, 142.3, 159.0, 167.0, 183.2, 191.1; HRMS (TOF ES$^+$): *m/z* calcd for $C_{27}H_{27}F_3N_3O_5$ [(M+H)$^+$], 530.1897; found, 530.1889.

(*2S,3'S,5R,6S*)-Ethyl 5'-fluoro-5-hydroxy-8-(4-methoxybenzoyl)-2-methyl-2'-oxo-5-(trifluoromethyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5v)



White solid; Mp 215–217 °C; IR (KBr): 3189, 1743, 1688, 1595, 1494, 1380, 1247, 1176, 1023, 710 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 0.63 (t, J = 6.7 Hz, 3H, CH_3), 1.20 (t, J = 3.7 Hz, 3H, CH_3), 3.22 (t, J = 9.7 Hz, 1H, NCH_2), 3.53–3.82 (m, 4H, NCH_2, OCH_2 and CH), 3.69 (s, 3H, OCH_3), 3.96–3.99 (m, 1H, NCH), 6.29 (t, J = 4.0 Hz, 1H, ArH), 6.59 (d, J = 4.9 Hz, 2H, ArH), 6.75–6.79 (m, 3H, ArH), 7.29 (d, J = 8.2 Hz, 1H, ArH), 8.40 (br, 1H, NH), 8.95 (br, 1H, OH), 10.73 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.4, 19.9, 50.2, 50.4, 51.0, 52.6, 55.5, 60.8, 83.8, 85.8, 110.8, 111.8 (d, J = 25.0 Hz), 113.0, 115.0 (d, J = 23.8 Hz), 122.8, 127.8, 134.3, 134.7, 138.0 (d, J = 18.8 Hz), 158.9 (d, J = 22.5 Hz), 159.3, 160.1, 166.5, 182.7, 190.4; HRMS (TOF ES$^+$): *m/z* calcd for $C_{27}H_{26}F_4N_3O_6$ [(M+H)$^+$], 564.1752; found, 564.1753.

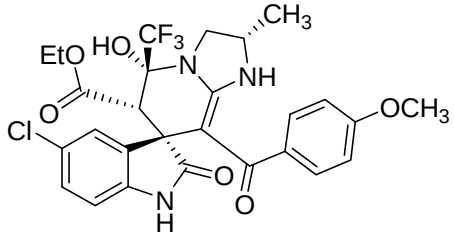
(*2R,3'S,5R,6S*)-Ethyl 5'-fluoro-5-hydroxy-8-(4-methoxybenzoyl)-2-methyl-2'-oxo-5-(trifluoromethyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5v')



White solid; Mp 209–213 °C; IR (KBr): 3248, 1741, 1690, 1600, 1495, 1287, 1174, 1022, 819, 694 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 0.60–0.64 (m, 3H, CH_3),

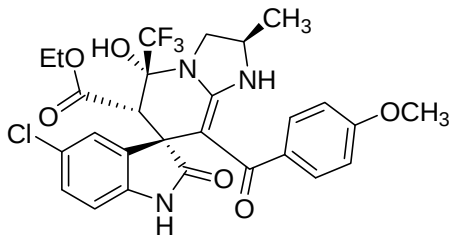
1.17 (d, J = 5.8 Hz, 3H, CH_3), 3.15–3.19 (m, 1H, NCH_2), 3.60–3.88 (m, 5H, NCH_2CHN, OCH_2 and CH), 3.67 (s, 3H, OCH_3), 6.32–6.37 (m, 1H, ArH), 6.75–6.80 (m, 3H, ArH), 7.22 (d, J = 6.5 Hz, 1H, ArH), 8.28 (br, 1H, NH), 10.80 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.3, 21.0, 49.5, 50.7, 51.0, 52.6, 55.4, 60.9, 83.6 (q, J = 30.0 Hz), 85.7, 111.6 (q, J = 25.0 Hz), 112.8, 113.0, 114.9 (q, J = 23.8 Hz), 122.8 (q, J = 286.3 Hz), 123.9, 134.2 (q, J = 8.8 Hz), 134.4, 138.1, 158.2 (q, J = 22.5 Hz), 159.6, 160.0, 166.6, 182.9, 190.0; HRMS (TOF ES$^+$): *m/z* calcd for $C_{27}H_{26}F_4N_3O_6$ [(M+H)$^+$], 564.1752; found, 564.1740.

(*2S,3'S,5R,6S*)-Ethyl 5'-chloro-5-hydroxy-8-(4-methoxybenzoyl)-2-methyl-2'-oxo-5-(trifluoromethyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5w)



White solid; Mp 205–209 °C; IR (KBr): 3162, 1743, 1692, 1597, 1492, 1382, 1283, 1172, 1013, 660 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 0.63 (t, J = 6.7 Hz, 3H, CH_3), 1.26 (d, J = 5.8 Hz, 3H, CH_3), 3.22 (t, J = 9.6 Hz, 2H, NCH_2), 3.60–3.83 (m, 4H, NCH_2, OCH_2 and CH), 3.70 (s, 3H, OCH_3), 3.97–4.02 (m, 1H, NCH), 6.32 (d, J = 8.2 Hz, 1H, ArH), 6.58–6.61 (m, 2H, ArH), 6.74–6.78 (m, 2H, ArH), 6.98–7.00 (m, 1H, ArH), 7.46 (s, 1H, ArH), 8.27 (br, 1H, NH), 8.77 (br, 1H, OH), 10.83 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.4, 20.0, 50.4, 50.8, 51.0, 52.5, 55.5, 60.8, 83.7 (q, J = 28.8 Hz), 85.8, 111.3, 113.1, 124.3, 126.9, 128.0, 128.5, 134.5, 134.7, 140.9, 159.0, 159.4, 166.6, 182.7, 190.2; HRMS (TOF ES$^+$): *m/z* calcd for $C_{27}H_{26}ClF_3N_3O_6$ [(M+H)$^+$], 580.1457; found, 580.1483.

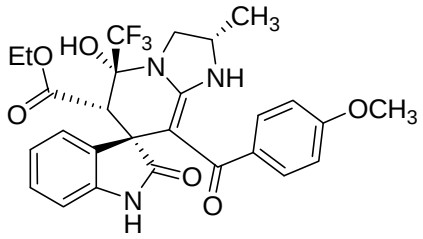
(*2R,3'S,5R,6S*)-Ethyl 5'-chloro-5-hydroxy-8-(4-methoxybenzoyl)-2-methyl-2'-oxo-5-(trifluoromethyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5w')



White solid; Mp 214–216 °C; IR (KBr): 3162, 1743, 1692, 1597, 1491, 1382, 1326,

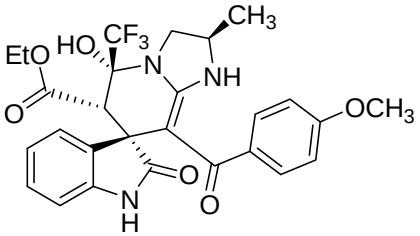
1177, 1013, 660 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 0.65 (t, J = 6.7 Hz, 3H, CH_3), 1.20 (t, J = 5.8 Hz, 3H, CH_3), 3.14–3.17 (m, 1H, NCH_2), 3.60–3.84 (m, 4H, NCH_2, OCH_2 and CH), 3.71 (s, 3H, OCH_3), 3.94–3.98 (m, 1H, NCH), 6.39 (d, J = 8.2 Hz, 1H, ArH), 6.63–6.66 (m, 2H, ArH), 6.87–6.90 (m, 2H, ArH), 7.01 (d, J = 8.2 Hz, 1H, ArH), 7.49 (s, 1H, ArH), 8.18 (br, 1H, NH), 8.38 (br, 1H, OH), 10.84 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.4, 21.1, 49.5, 50.8, 50.9, 52.5, 55.5, 60.7, 83.7 (q, J = 31.3 Hz), 85.6, 111.3, 113.1, 124.0, 124.2, 126.9, 128.4, 128.5, 134.5, 134.6, 141.1, 158.0, 159.8, 166.6, 182.7, 189.6; HRMS (TOF ES^+): m/z calcd for $C_{27}H_{26}ClF_3N_3O_6$ [$(M+H)^+$], 580.1457; found, 580.1457.

(*2S,3'S,5R,6S*)-Ethyl 5-hydroxy-8-(4-methoxybenzoyl)-2-methyl-2'-oxo-5-(tri-fluoromethyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5x)



White solid; Mp 200–203 °C; IR (KBr): 3252, 3183, 1742, 1681, 1601, 1517, 1287, 1174, 1024, 752 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 0.57–0.61 (m, 3H, CH_3), 1.20 (d, J = 5.9 Hz 3H, CH_3), 3.16–3.19 (m, 1H, NCH_2), 3.55–3.67 (m, 2H, NCH_2 and CH), 3.68 (s, 3H, OCH_3), 3.80–3.85 (m, 2H, OCH_2), 3.97–4.01 (m, 1H, NCH), 6.22–6.26 (m, 1H, ArH), 6.33–6.37 (m, 3H, ArH), 6.75–6.78 (m, 2H, ArH), 6.86–6.90 (m, 1H, ArH), 6.94–6.96 (m, 1H, ArH), 7.22 (d, J = 7.2 Hz, 1H, ArH), 8.29 (br, 1H, NH), 8.63 (br, 1H, OH), 10.71 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.4, 21.2, 49.4, 50.7, 51.4, 52.1, 55.4, 60.7, 83.8 (q, J = 30.0 Hz), 85.9, 110.0, 112.9, 122.6, 123.7, 128.1, 128.3, 128.6, 132.3, 134.6, 142.0, 158.2, 159.4, 166.5, 182.8, 190.2; HRMS (TOF ES^+): m/z calcd for $C_{27}H_{27}F_3N_3O_6$ [$(M+H)^+$], 546.1846; found, 546.1855.

(*2R,3'S,5R,6S*)-Ethyl 5-hydroxy-8-(4-methoxybenzoyl)-2-methyl-2'-oxo-5-(tri-fluoromethyl)-2,3,5,6-tetrahydro-1*H*-spiro[imidazo[1,2-*a*]pyridine-7,3'-indoline]-6-carboxylate (5x')



White solid; Mp 205–207 °C; IR (KBr): 3206, 1738, 1685, 1596, 1498, 1248, 1174, 1025, 714 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 0.58–0.65 (m, 3H, CH_3), 1.28 (d, J = 5.8 Hz, 3H, CH_3), 3.17–3.24 (m, 1H, NCH_2), 3.58–3.81 (m, 4H, NCH_2, OCH_2 and CH), 3.68 (s, 3H, OCH_3), 3.99–4.04 (m, 1H, NCH), 6.28 (d, J = 7.5 Hz, 1H, ArH), 6.51–6.55 (m, 3H, ArH), 6.64–6.68 (m, 2H, ArH), 6.86–6.90 (m, 1H, ArH), 6.92–6.96 (m, 1H, ArH), 7.22 (d, J = 7.2 Hz, 1H, ArH), 8.50 (br, 1H, NH), 8.98 (br, 1H, OH), 10.67 (br, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.4, 19.9, 50.3, 51.1, 51.3, 52.1, 55.4, 60.7, 83.8, 86.1, 110.1, 112.9, 122.7, 122.8, 123.8, 127.7, 128.7, 132.3, 134.8, 141.9, 159.1, 159.1, 166.5, 182.8, 190.7; HRMS (TOF ES^+): m/z calcd for $C_{27}H_{27}F_3N_3O_6$ [$(M+H)^+$], 546.1846; found, 546.1856.

X-ray Structure and Data[2] of 5r

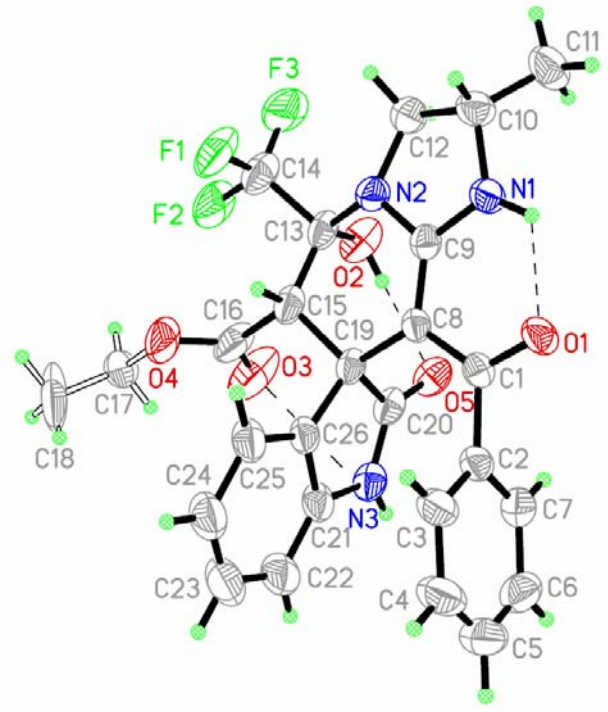


Figure S1 X-Ray crystal structure of **5r**

Table S1 Crystal data and structure refinement for 100903A

Empirical formula	$C_{26}H_{24}F_3N_3O_5$
Formula weight	515.48
Temperature	298(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P2(1)/n
Unit cell dimensions	a = 8.941(2) A alpha = 90 deg.
	b = 22.201(4) A beta = 111.357(10) deg.
	c = 12.975(2) A gamma = 90 deg.
Volume	2398.6(8) A^3
Z, Calculated density	4, 1.427 Mg/m^3
Absorption coefficient	0.115 mm^-1
F(000)	1072
Crystal size	0.23x 0.19 x 0.14 mm
Theta range for data collection	1.83 to 28.26 deg.
Limiting indices	-11<=h<=11, -20<=k<=28, -17<=l<=17
Reflection collected/unique	16431/5607[R(int) = 0.0607]
Completeness to theta = 28.2	94.6%
Absorption correction	Semi-empirical from equivalents
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	5607/ 0/ 358
Goodness-of-fit on F^2	1.041
Final R indices [I>2sigma(I)]	R1 = 0.0702, wR2 = 0.1663
R indices (all data)	R1 = 0.1847, wR2 = 0.2182
Extinction	coefficient
Largest diff. peak and hole	0.339 and -0.353 e.A^-3

Table S2 Bond lengths [A] and angles [deg] for 100903A

C(1)-O(1)	1.252(4)
C(1)-C(8)	1.433(4)
C(1)-C(2)	1.501(4)
C(2)-C(7)	1.383(5)
C(2)-C(3)	1.394(5)
C(3)-C(4)	1.376(5)
C(3)-H(3)	0.9300
C(4)-C(5)	1.367(6)
C(4)-H(4)	0.9300

C(5)-C(6)	1.368(6)
C(5)-H(5)	0.9300
C(6)-C(7)	1.396(5)
C(6)-H(6)	0.9300
C(7)-H(7)	0.9300
C(8)-C(9)	1.392(4)
C(8)-C(19)	1.524(4)
C(9)-N(1)	1.326(4)
C(9)-N(2)	1.380(4)
C(10)-N(1)	1.461(4)
C(10)-C(11)	1.482(5)
C(10)-C(12)	1.524(5)
C(10)-H(10)	0.9800
C(11)-H(11A)	0.9600
C(11)-H(11B)	0.9600
C(11)-H(11C)	0.9600
C(12)-N(2)	1.470(4)
C(12)-H(12A)	0.9700
C(12)-H(12B)	0.9700
C(13)-O(2)	1.401(4)
C(13)-N(2)	1.459(4)
C(13)-C(15)	1.525(5)
C(13)-C(14)	1.527(5)
C(14)-F(3)	1.322(5)
C(14)-F(2)	1.330(4)
C(14)-F(1)	1.338(5)
C(15)-C(16)	1.517(5)
C(15)-C(19)	1.557(5)
C(15)-H(15)	0.9800
C(16)-O(3)	1.189(5)
C(16)-O(4)	1.318(6)
C(17)-C(18)	1.32(3)
C(17)-O(4)	1.542(16)
C(17)-H(17A)	0.9700
C(17)-H(17B)	0.9700
C(18)-H(18A)	0.9600
C(18)-H(18B)	0.9600
C(18)-H(18C)	0.9600
C(19)-C(26)	1.509(5)
C(19)-C(20)	1.561(4)

C(20)-O(5)	1.223(4)
C(20)-N(3)	1.352(4)
C(21)-C(22)	1.378(5)
C(21)-C(26)	1.391(4)
C(21)-N(3)	1.405(4)
C(22)-C(23)	1.386(6)
C(22)-H(22)	0.9300
C(23)-C(24)	1.357(6)
C(23)-H(23)	0.9300
C(24)-C(25)	1.398(6)
C(24)-H(24)	0.9300
C(25)-C(26)	1.375(4)
C(25)-H(25)	0.9300
C(17')-C(18')	1.40(3)
C(17')-O(4)	1.696(14)
C(17')-H(17C)	0.9700
C(17')-H(17D)	0.9700
C(18')-H(18D)	0.9600
C(18')-H(18E)	0.9600
C(18')-H(18F)	0.9600
N(1)-H(1)	0.8600
N(3)-H(3A)	0.8600
O(2)-H(2)	0.8200
O(1)-C(1)-C(8)	123.1(3)
O(1)-C(1)-C(2)	115.3(3)
C(8)-C(1)-C(2)	121.6(3)
C(7)-C(2)-C(3)	119.0(4)
C(7)-C(2)-C(1)	120.1(3)
C(3)-C(2)-C(1)	120.7(3)
C(4)-C(3)-C(2)	120.3(4)
C(4)-C(3)-H(3)	119.9
C(2)-C(3)-H(3)	119.9
C(5)-C(4)-C(3)	120.3(5)
C(5)-C(4)-H(4)	119.8
C(3)-C(4)-H(4)	119.8
C(4)-C(5)-C(6)	120.6(5)
C(4)-C(5)-H(5)	119.7
C(6)-C(5)-H(5)	119.7
C(5)-C(6)-C(7)	119.8(4)
C(5)-C(6)-H(6)	120.1

C(7)-C(6)-H(6)	120.1
C(2)-C(7)-C(6)	120.0(4)
C(2)-C(7)-H(7)	120.0
C(6)-C(7)-H(7)	120.0
C(9)-C(8)-C(1)	118.1(3)
C(9)-C(8)-C(19)	118.4(3)
C(1)-C(8)-C(19)	122.8(3)
N(1)-C(9)-N(2)	108.4(3)
N(1)-C(9)-C(8)	126.8(3)
N(2)-C(9)-C(8)	124.8(3)
N(1)-C(10)-C(11)	113.7(3)
N(1)-C(10)-C(12)	100.6(3)
C(11)-C(10)-C(12)	114.5(3)
N(1)-C(10)-H(10)	109.2
C(11)-C(10)-H(10)	109.2
C(12)-C(10)-H(10)	109.2
C(10)-C(11)-H(11A)	109.5
C(10)-C(11)-H(11B)	109.5
H(11A)-C(11)-H(11B)	109.5
C(10)-C(11)-H(11C)	109.5
H(11A)-C(11)-H(11C)	109.5
H(11B)-C(11)-H(11C)	109.5
N(2)-C(12)-C(10)	103.2(3)
N(2)-C(12)-H(12A)	111.1
C(10)-C(12)-H(12A)	111.1
N(2)-C(12)-H(12B)	111.1
C(10)-C(12)-H(12B)	111.1
H(12A)-C(12)-H(12B)	109.1
O(2)-C(13)-N(2)	112.9(3)
O(2)-C(13)-C(15)	114.9(3)
N(2)-C(13)-C(15)	106.5(3)
O(2)-C(13)-C(14)	103.3(3)
N(2)-C(13)-C(14)	108.5(3)
C(15)-C(13)-C(14)	110.6(3)
F(3)-C(14)-F(2)	105.8(4)
F(3)-C(14)-F(1)	107.3(4)
F(2)-C(14)-F(1)	106.4(4)
F(3)-C(14)-C(13)	114.3(4)
F(2)-C(14)-C(13)	111.5(4)
F(1)-C(14)-C(13)	111.1(4)

C(16)-C(15)-C(13)	112.8(4)
C(16)-C(15)-C(19)	110.1(3)
C(13)-C(15)-C(19)	114.7(3)
C(16)-C(15)-H(15)	106.2
C(13)-C(15)-H(15)	106.2
C(19)-C(15)-H(15)	106.2
O(3)-C(16)-O(4)	124.6(4)
O(3)-C(16)-C(15)	124.2(5)
O(4)-C(16)-C(15)	110.9(4)
C(18)-C(17)-O(4)	109(2)
C(18)-C(17)-H(17A)	109.8
O(4)-C(17)-H(17A)	109.8
C(18)-C(17)-H(17B)	109.8
O(4)-C(17)-H(17B)	109.8
H(17A)-C(17)-H(17B)	108.2
C(17)-C(18)-H(18A)	109.5
C(17)-C(18)-H(18B)	109.5
H(18A)-C(18)-H(18B)	109.5
C(17)-C(18)-H(18C)	109.5
H(18A)-C(18)-H(18C)	109.5
H(18B)-C(18)-H(18C)	109.5
C(26)-C(19)-C(8)	118.6(3)
C(26)-C(19)-C(15)	106.1(3)
C(8)-C(19)-C(15)	110.0(3)
C(26)-C(19)-C(20)	101.2(3)
C(8)-C(19)-C(20)	108.7(3)
C(15)-C(19)-C(20)	112.0(2)
O(5)-C(20)-N(3)	125.6(3)
O(5)-C(20)-C(19)	126.3(4)
N(3)-C(20)-C(19)	107.9(3)
C(22)-C(21)-C(26)	122.8(4)
C(22)-C(21)-N(3)	128.1(3)
C(26)-C(21)-N(3)	109.1(3)
C(21)-C(22)-C(23)	117.2(4)
C(21)-C(22)-H(22)	121.4
C(23)-C(22)-H(22)	121.4
C(24)-C(23)-C(22)	121.3(5)
C(24)-C(23)-H(23)	119.4
C(22)-C(23)-H(23)	119.4
C(23)-C(24)-C(25)	121.1(4)

C(23)-C(24)-H(24)	119.5
C(25)-C(24)-H(24)	119.5
C(26)-C(25)-C(24)	118.9(3)
C(26)-C(25)-H(25)	120.5
C(24)-C(25)-H(25)	120.5
C(25)-C(26)-C(21)	118.8(3)
C(25)-C(26)-C(19)	131.6(3)
C(21)-C(26)-C(19)	109.5(3)
C(18')-C(17')-O(4)	83.7(13)
C(18')-C(17')-H(17C)	114.7
O(4)-C(17')-H(17C)	114.7
C(18')-C(17')-H(17D)	114.7
O(4)-C(17')-H(17D)	114.7
H(17C)-C(17')-H(17D)	111.8
C(9)-N(1)-C(10)	113.5(3)
C(9)-N(1)-H(1)	123.3
C(10)-N(1)-H(1)	123.3
C(9)-N(2)-C(13)	118.9(3)
C(9)-N(2)-C(12)	109.2(3)
C(13)-N(2)-C(12)	121.4(3)
C(20)-N(3)-C(21)	112.1(3)
C(20)-N(3)-H(3A)	123.9
C(21)-N(3)-H(3A)	123.9
C(13)-O(2)-H(2)	109.5
C(16)-O(4)-C(17)	101.8(7)
C(16)-O(4)-C(17')	130.3(4)
C(17)-O(4)-C(17')	53.0(7)

Symmetry transformations used to generate equivalent atoms:

Table S3. Hydrogen bonds for 100903A [A and deg.].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(17)-H(17B)...O(3)	0.97	1.98	2.387(12)	102.7
C(15)-H(15)...F(1)	0.98	2.51	2.872(4)	101.7
O(2)-H(2)...O(5)	0.82	1.94	2.753(3)	169.6
N(1)-H(1)...O(1)	0.86	2.04	2.607(4)	123.1

Symmetry transformations used to generate equivalent atoms:

X-ray Structure and Data[2] of 5r'

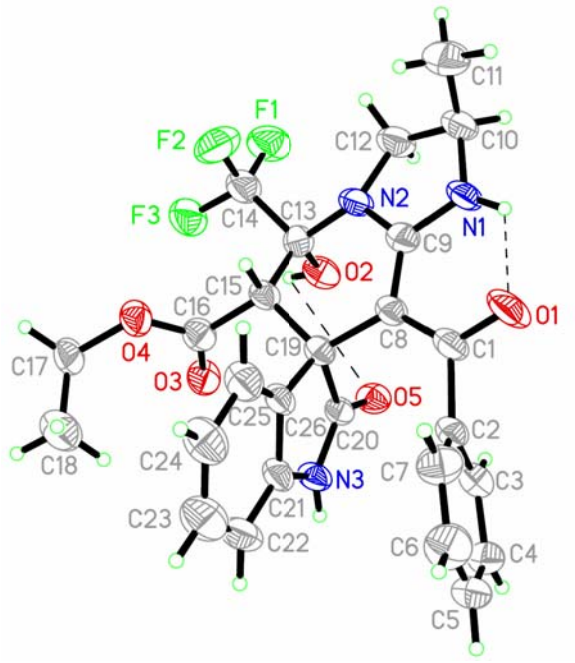


Figure S2 X-Ray crystal structure of **5r'**

Table S4 Crystal data and structure refinement for 100906A

Empirical formula	$C_{27}H_{25}Cl_3F_3N_3O_5$
Formula weight	634.85
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system, space group	Triclinic, P-1
Unit cell dimensions	a = 10.489(5) A alpha = 73.462(5) deg.
	b = 11.635(5) A beta = 80.503(5) deg.
	c = 13.375(5) A gamma = 72.854(5) deg.
Volume	1489.3(11) A^3
Z, Calculated density	2, 1.416 Mg/m^3
Absorption coefficient	0.367 mm^-1
F(000)	652
Crystal size	0.23x 0.19 x 0.14 mm
Theta range for data collection	1.89 to 26.31 deg.
Limiting indices	-12<=h<=13, -15<=k<=15, -17<=l<=17
Reflection collected/unique	10468/6121[R(int) = 0.0656]
Completeness to theta = 28.2	96.6%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9745 and 0.9532
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	6121/ 0/ 374

Goodness-of-fit on F^2	1.028
Final R indices [I>2sigma(I)]	R1 = 0.1239, wR2 = 0.3167
R indices (all data)	R1 = 0.2712, wR2 = 0.4173
Extinction coefficient	0.010(5)
Largest diff. peak and hole	0.689 and -0.735 e.A^-3

Table S5 Bond lengths [A] and angles [deg] for 100906A

C(1)-O(1)	1.244(8)
C(1)-C(8)	1.390(9)
C(1)-C(2)	1.530(10)
C(2)-C(7)	1.371(10)
C(2)-C(3)	1.385(9)
C(3)-C(4)	1.369(10)
C(3)-H(3)	0.9300
C(4)-C(5)	1.352(11)
C(4)-H(4)	0.9300
C(5)-C(6)	1.405(12)
C(5)-H(5)	0.9300
C(6)-C(7)	1.355(12)
C(6)-H(6)	0.9300
C(7)-H(7)	0.9300
C(8)-C(9)	1.403(10)
C(8)-C(19)	1.523(8)
C(9)-N(1)	1.320(8)
C(9)-N(2)	1.359(8)
C(10)-N(1)	1.464(9)
C(10)-C(12)	1.486(10)
C(10)-C(11)	1.503(10)
C(10)-H(10)	0.9800
C(11)-H(11A)	0.9600
C(11)-H(11B)	0.9600
C(11)-H(11C)	0.9600
C(12)-N(2)	1.483(9)
C(12)-H(12A)	0.9700
C(12)-H(12B)	0.9700
C(13)-O(2)	1.396(7)
C(13)-N(2)	1.444(8)
C(13)-C(14)	1.533(10)
C(13)-C(15)	1.534(10)

C(14)-F(3)	1.317(8)
C(14)-F(1)	1.328(10)
C(14)-F(2)	1.341(9)
C(15)-C(16)	1.506(9)
C(15)-C(19)	1.537(9)
C(15)-H(15)	0.9800
C(16)-O(3)	1.210(8)
C(16)-O(4)	1.321(8)
C(17)-C(18)	1.476(12)
C(17)-O(4)	1.477(8)
C(17)-H(17A)	0.9700
C(17)-H(17B)	0.9700
C(18)-H(18A)	0.9600
C(18)-H(18B)	0.9600
C(18)-H(18C)	0.9600
C(19)-C(26)	1.512(9)
C(19)-C(20)	1.577(9)
C(20)-O(5)	1.219(7)
C(20)-N(3)	1.332(8)
C(21)-C(22)	1.389(11)
C(21)-N(3)	1.399(8)
C(21)-C(26)	1.410(9)
C(22)-C(23)	1.385(12)
C(22)-H(22)	0.9300
C(23)-C(24)	1.394(13)
C(23)-H(23)	0.9300
C(24)-C(25)	1.403(11)
C(24)-H(24)	0.9300
C(25)-C(26)	1.346(9)
C(25)-H(25)	0.9300
C(27)-Cl(3)	1.658(17)
C(27)-Cl(2)	1.72(2)
C(27)-Cl(1)	1.85(2)
C(27)-H(27)	0.9800
N(1)-H(1)	0.8600
N(3)-H(3A)	0.8600
O(2)-H(2)	0.8200
O(1)-C(1)-C(8)	124.9(7)
O(1)-C(1)-C(2)	113.1(6)
C(8)-C(1)-C(2)	122.0(6)

C(7)-C(2)-C(3)	118.2(7)
C(7)-C(2)-C(1)	122.1(7)
C(3)-C(2)-C(1)	119.0(7)
C(4)-C(3)-C(2)	121.1(7)
C(4)-C(3)-H(3)	119.4
C(2)-C(3)-H(3)	119.4
C(5)-C(4)-C(3)	119.2(8)
C(5)-C(4)-H(4)	120.4
C(3)-C(4)-H(4)	120.4
C(4)-C(5)-C(6)	121.3(8)
C(4)-C(5)-H(5)	119.3
C(6)-C(5)-H(5)	119.3
C(7)-C(6)-C(5)	117.8(8)
C(7)-C(6)-H(6)	121.1
C(5)-C(6)-H(6)	121.1
C(6)-C(7)-C(2)	122.3(8)
C(6)-C(7)-H(7)	118.9
C(2)-C(7)-H(7)	118.9
C(1)-C(8)-C(9)	118.1(6)
C(1)-C(8)-C(19)	124.3(6)
C(9)-C(8)-C(19)	117.4(6)
N(1)-C(9)-N(2)	108.5(6)
N(1)-C(9)-C(8)	126.0(7)
N(2)-C(9)-C(8)	125.4(6)
N(1)-C(10)-C(12)	101.0(6)
N(1)-C(10)-C(11)	110.1(7)
C(12)-C(10)-C(11)	113.7(7)
N(1)-C(10)-H(10)	110.6
C(12)-C(10)-H(10)	110.6
C(11)-C(10)-H(10)	110.6
C(10)-C(11)-H(11A)	109.5
C(10)-C(11)-H(11B)	109.5
H(11A)-C(11)-H(11B)	109.5
C(10)-C(11)-H(11C)	109.5
H(11A)-C(11)-H(11C)	109.5
H(11B)-C(11)-H(11C)	109.5
N(2)-C(12)-C(10)	103.4(6)
N(2)-C(12)-H(12A)	111.1
C(10)-C(12)-H(12A)	111.1
N(2)-C(12)-H(12B)	111.1

C(10)-C(12)-H(12B)	111.1
H(12A)-C(12)-H(12B)	109.0
O(2)-C(13)-N(2)	112.1(6)
O(2)-C(13)-C(14)	104.2(6)
N(2)-C(13)-C(14)	108.2(6)
O(2)-C(13)-C(15)	114.5(6)
N(2)-C(13)-C(15)	107.3(5)
C(14)-C(13)-C(15)	110.5(6)
F(3)-C(14)-F(1)	106.6(7)
F(3)-C(14)-F(2)	105.4(7)
F(1)-C(14)-F(2)	107.1(7)
F(3)-C(14)-C(13)	112.5(7)
F(1)-C(14)-C(13)	113.5(7)
F(2)-C(14)-C(13)	111.2(7)
C(16)-C(15)-C(13)	114.4(5)
C(16)-C(15)-C(19)	110.4(5)
C(13)-C(15)-C(19)	113.7(5)
C(16)-C(15)-H(15)	105.9
C(13)-C(15)-H(15)	105.9
C(19)-C(15)-H(15)	105.9
O(3)-C(16)-O(4)	123.3(7)
O(3)-C(16)-C(15)	124.1(7)
O(4)-C(16)-C(15)	112.5(6)
C(18)-C(17)-O(4)	110.1(7)
C(18)-C(17)-H(17A)	109.6
O(4)-C(17)-H(17A)	109.6
C(18)-C(17)-H(17B)	109.6
O(4)-C(17)-H(17B)	109.6
H(17A)-C(17)-H(17B)	108.2
C(17)-C(18)-H(18A)	109.5
C(17)-C(18)-H(18B)	109.5
H(18A)-C(18)-H(18B)	109.5
C(17)-C(18)-H(18C)	109.5
H(18A)-C(18)-H(18C)	109.5
H(18B)-C(18)-H(18C)	109.5
C(26)-C(19)-C(8)	115.2(5)
C(26)-C(19)-C(15)	108.1(5)
C(8)-C(19)-C(15)	110.8(5)
C(26)-C(19)-C(20)	100.7(6)
C(8)-C(19)-C(20)	110.2(5)

C(15)-C(19)-C(20)	111.4(5)
O(5)-C(20)-N(3)	126.2(6)
O(5)-C(20)-C(19)	124.6(6)
N(3)-C(20)-C(19)	109.1(6)
C(22)-C(21)-N(3)	129.5(7)
C(22)-C(21)-C(26)	120.2(8)
N(3)-C(21)-C(26)	110.3(6)
C(23)-C(22)-C(21)	118.4(8)
C(23)-C(22)-H(22)	120.8
C(21)-C(22)-H(22)	120.8
C(22)-C(23)-C(24)	121.9(9)
C(22)-C(23)-H(23)	119.0
C(24)-C(23)-H(23)	119.0
C(23)-C(24)-C(25)	117.9(8)
C(23)-C(24)-H(24)	121.0
C(25)-C(24)-H(24)	121.0
C(26)-C(25)-C(24)	121.3(8)
C(26)-C(25)-H(25)	119.3
C(24)-C(25)-H(25)	119.3
C(25)-C(26)-C(21)	120.1(7)
C(25)-C(26)-C(19)	131.5(7)
C(21)-C(26)-C(19)	108.3(6)
Cl(3)-C(27)-Cl(2)	110.5(16)
Cl(3)-C(27)-Cl(1)	111.3(10)
Cl(2)-C(27)-Cl(1)	103.2(7)
Cl(3)-C(27)-H(27)	110.6
Cl(2)-C(27)-H(27)	110.6
Cl(1)-C(27)-H(27)	110.6
C(9)-N(1)-C(10)	113.3(6)
C(9)-N(1)-H(1)	123.4
C(10)-N(1)-H(1)	123.4
C(9)-N(2)-C(13)	120.5(6)
C(9)-N(2)-C(12)	108.7(6)
C(13)-N(2)-C(12)	123.5(6)
C(20)-N(3)-C(21)	111.5(6)
C(20)-N(3)-H(3A)	124.2
C(21)-N(3)-H(3A)	124.2
C(13)-O(2)-H(2)	109.5
C(16)-O(4)-C(17)	117.8(5)

Symmetry transformations used to generate equivalent atoms:

Table S6. Hydrogen bonds for 100903A [A and deg.].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(15)-H(15)...F(2)	0.98	2.54	2.902(8)	101.6
C(12)-H(12A)...F(1)	0.97	2.39	2.795(9)	104.8
C(6)-H(6)...O(2)#1	0.93	2.49	3.400(10)	165.4
N(3)-H(3A)...O(5)#2	0.86	2.05	2.853(7)	155.4
O(2)-H(2)...F(3)	0.82	2.35	2.767(7)	112.6
N(1)-H(1)...O(1)#3	0.86	2.10	2.867(8)	148.4
N(1)-H(1)...O(1)	0.86	2.05	2.623(8)	123.2

Symmetry transformations used to generate equivalent atoms:

#1 x+1,y,z #2 -x,-y+1,-z #3 -x,-y+1,-z+1

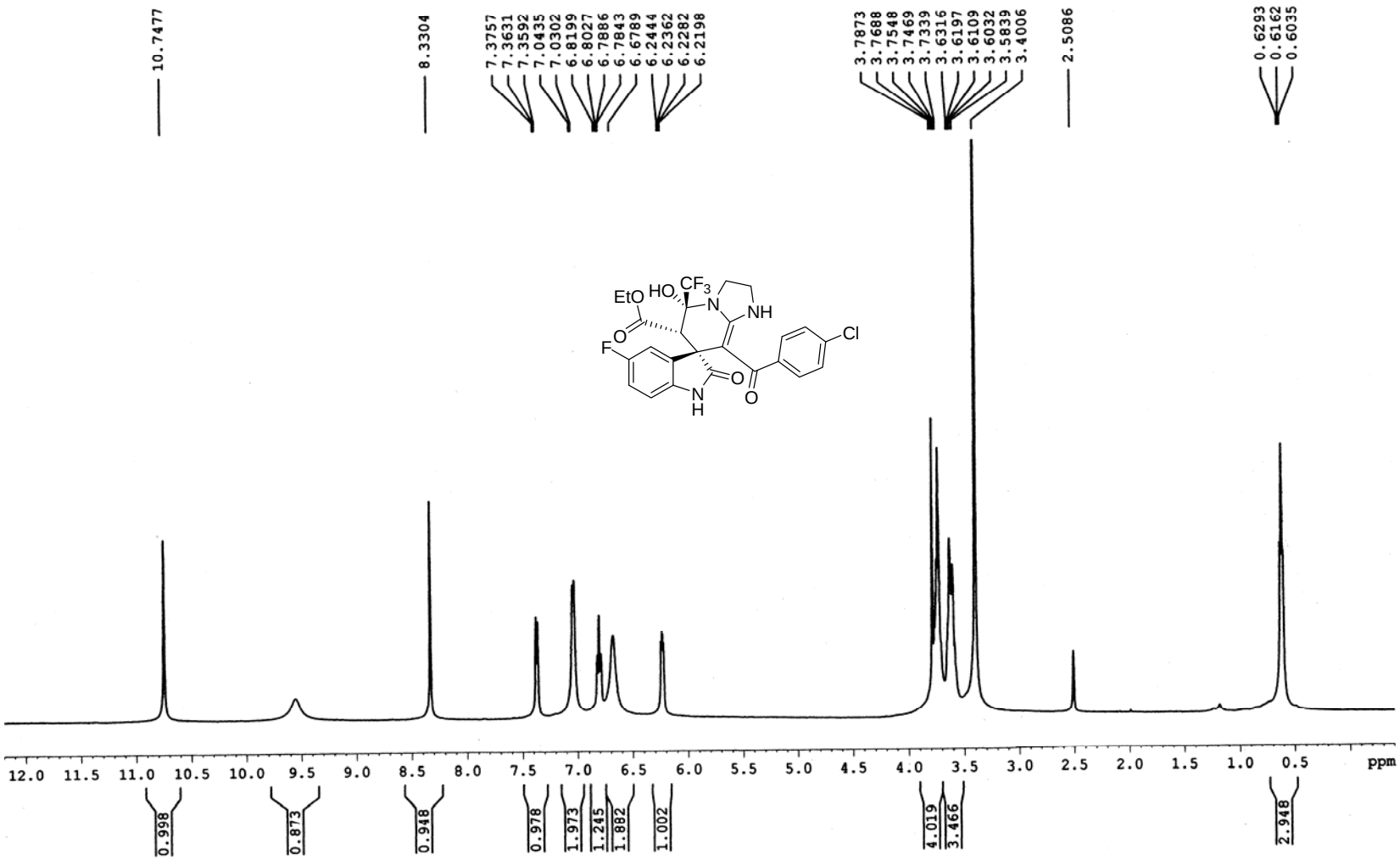


Figure 1. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5a**

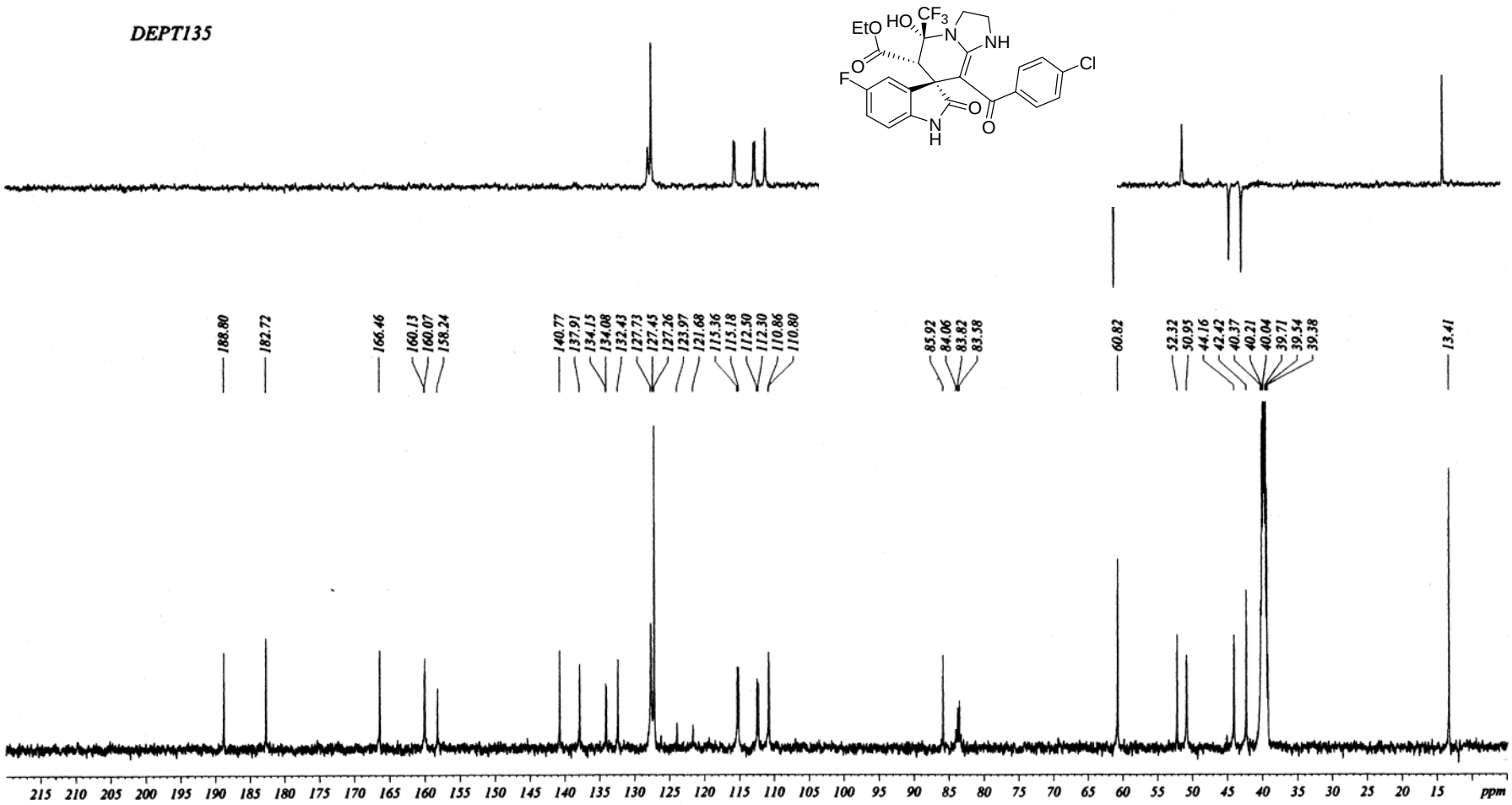


Figure 2. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5a**

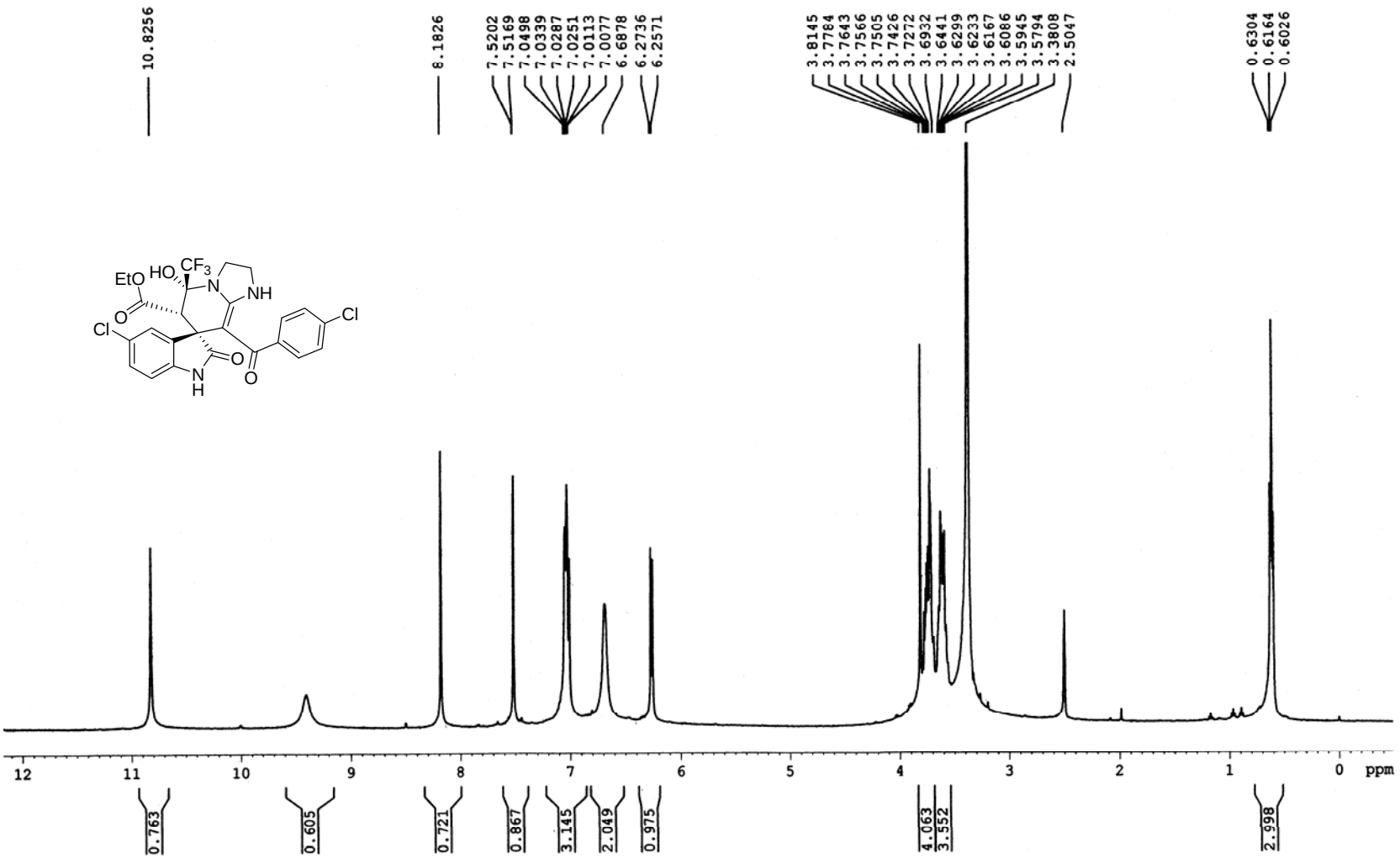


Figure 3. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5b**

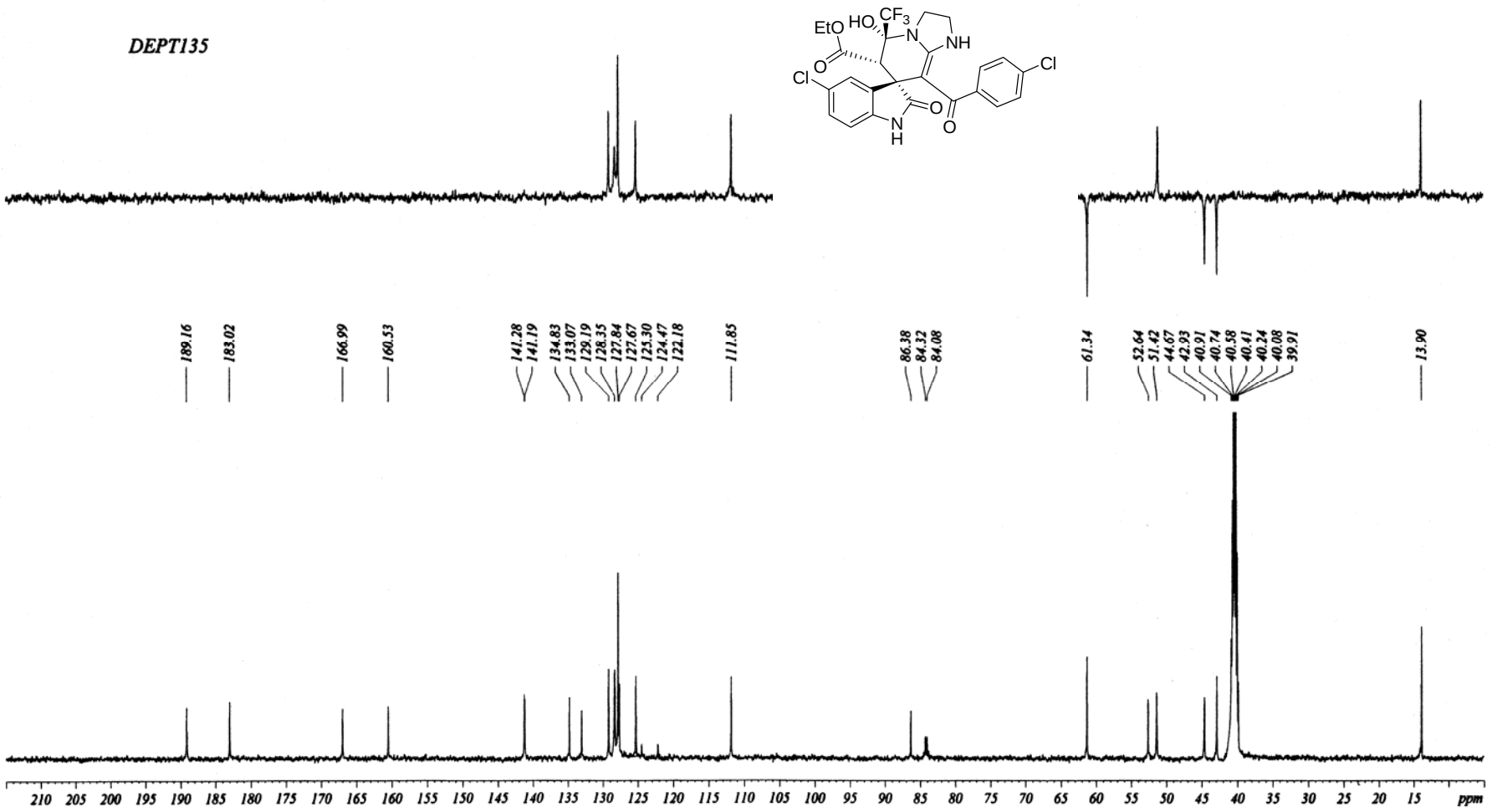


Figure 4. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5b**

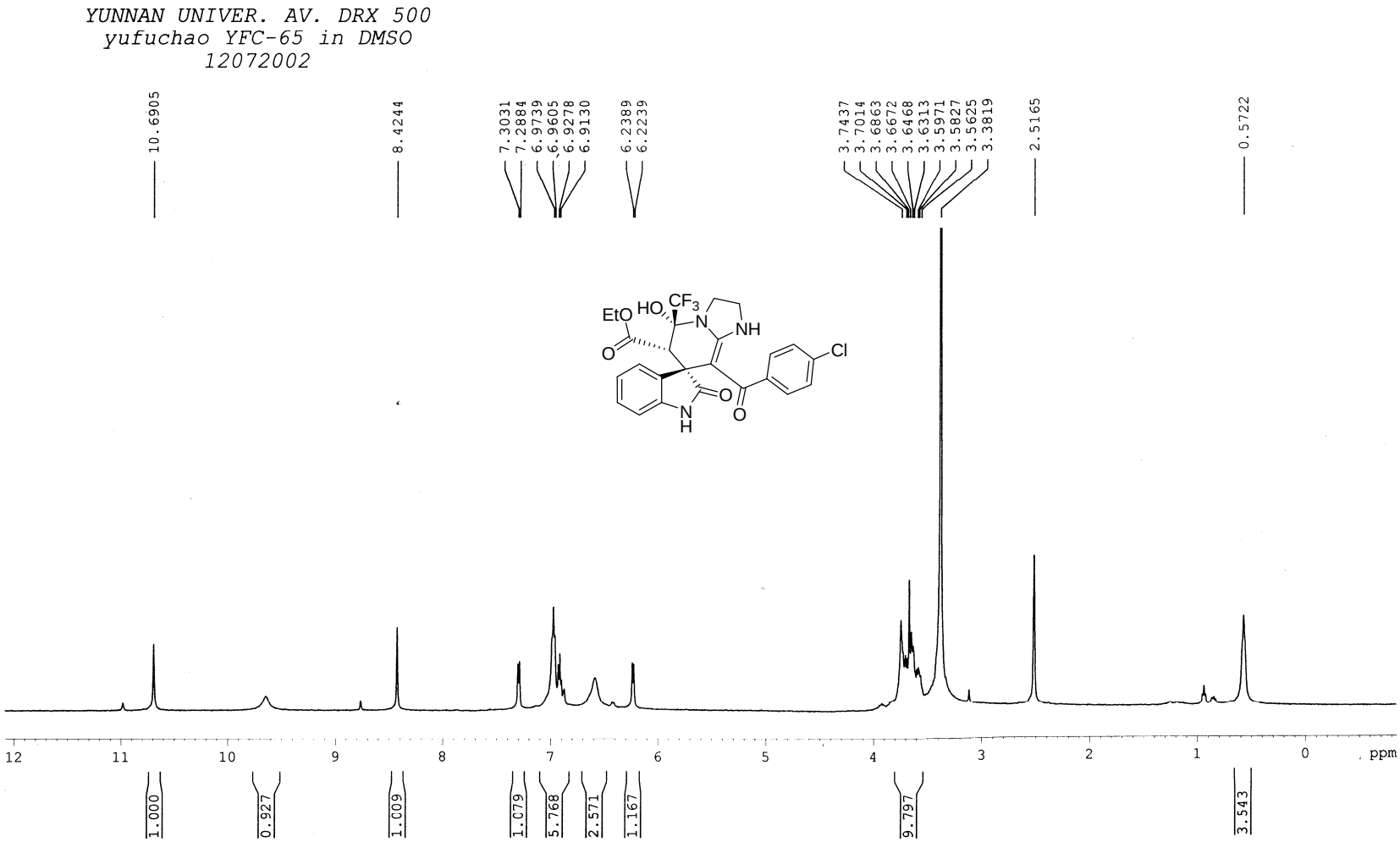


Figure 5. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5c**

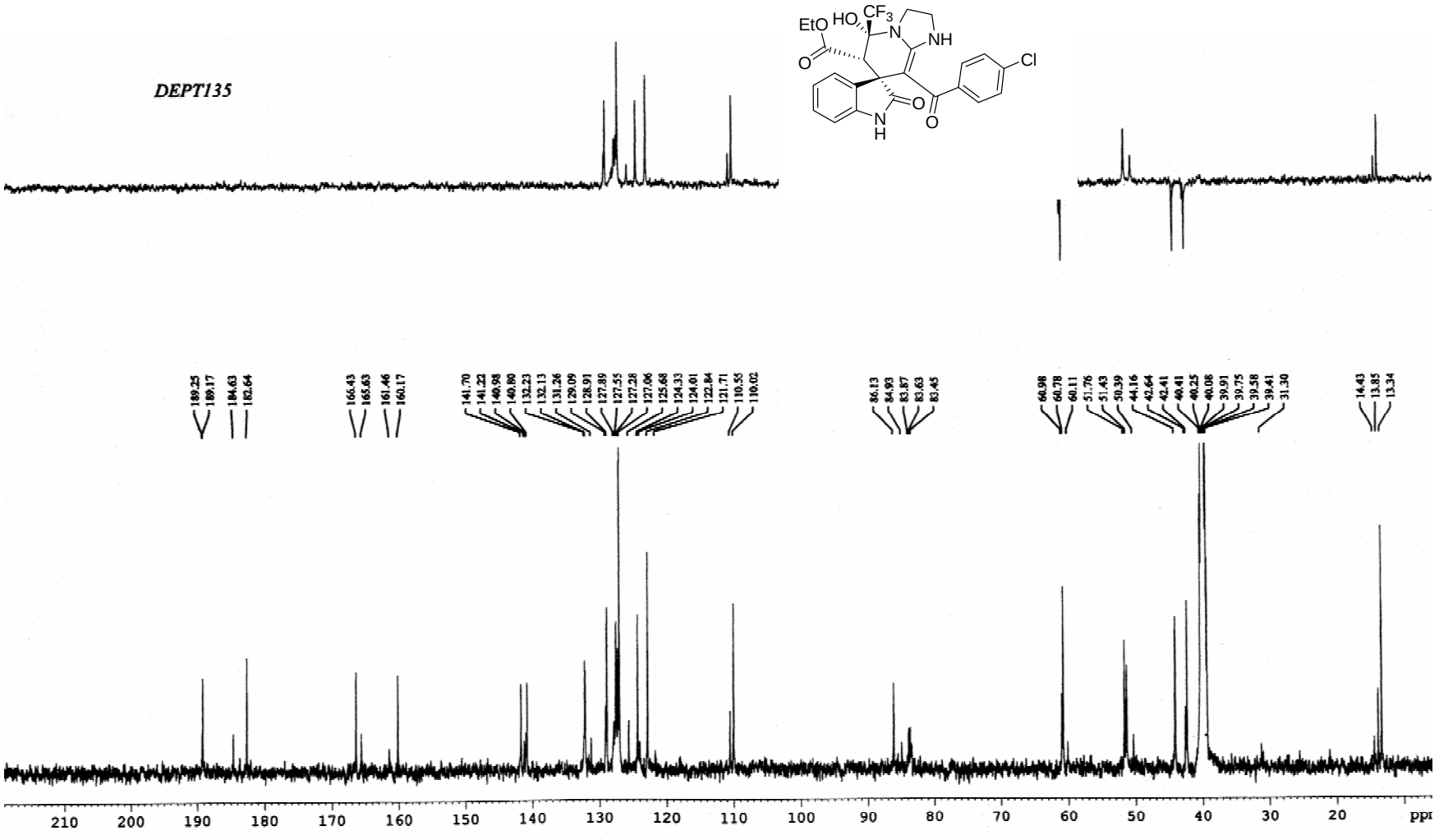


Figure 6. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5c**

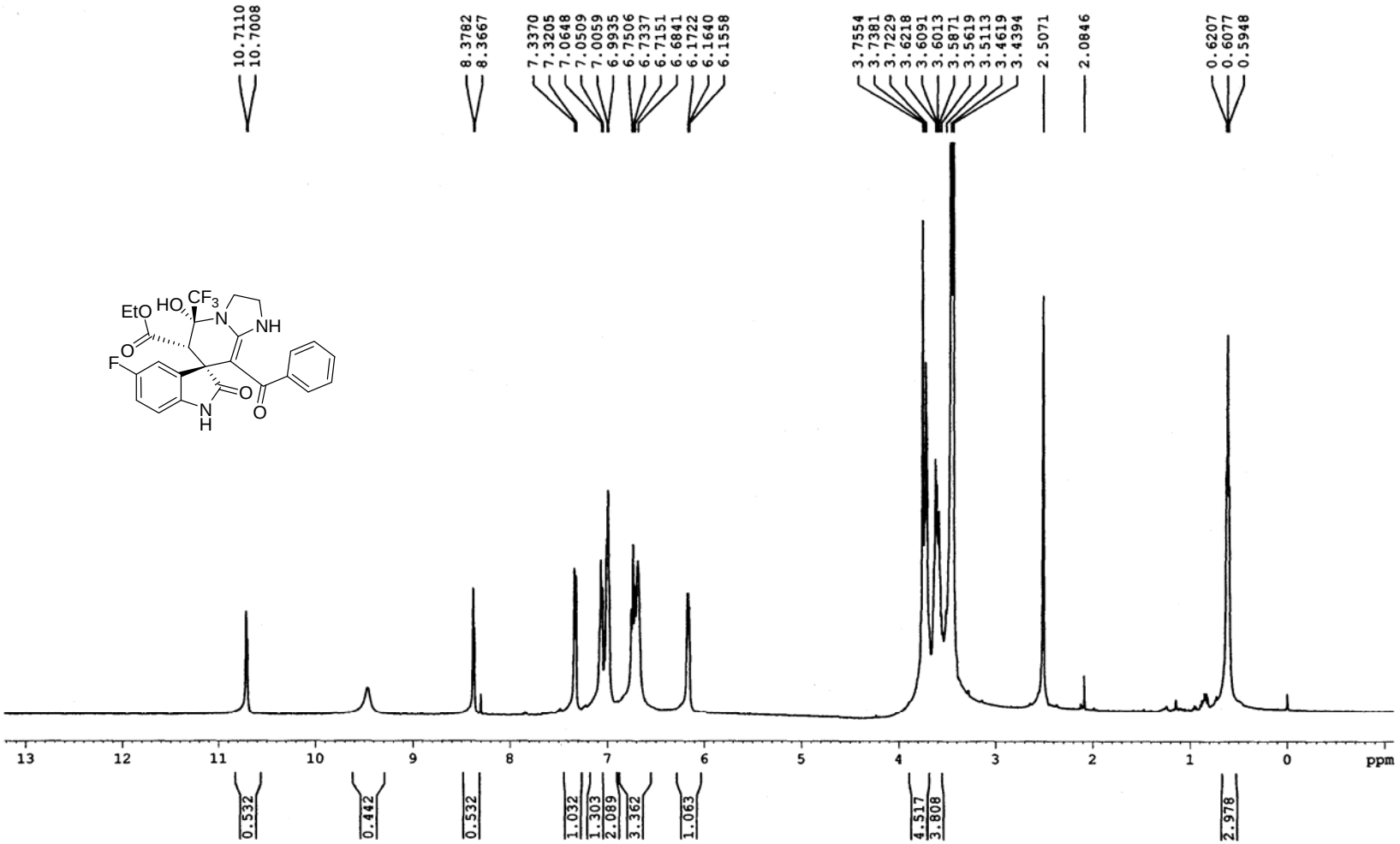


Figure 7. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5d**

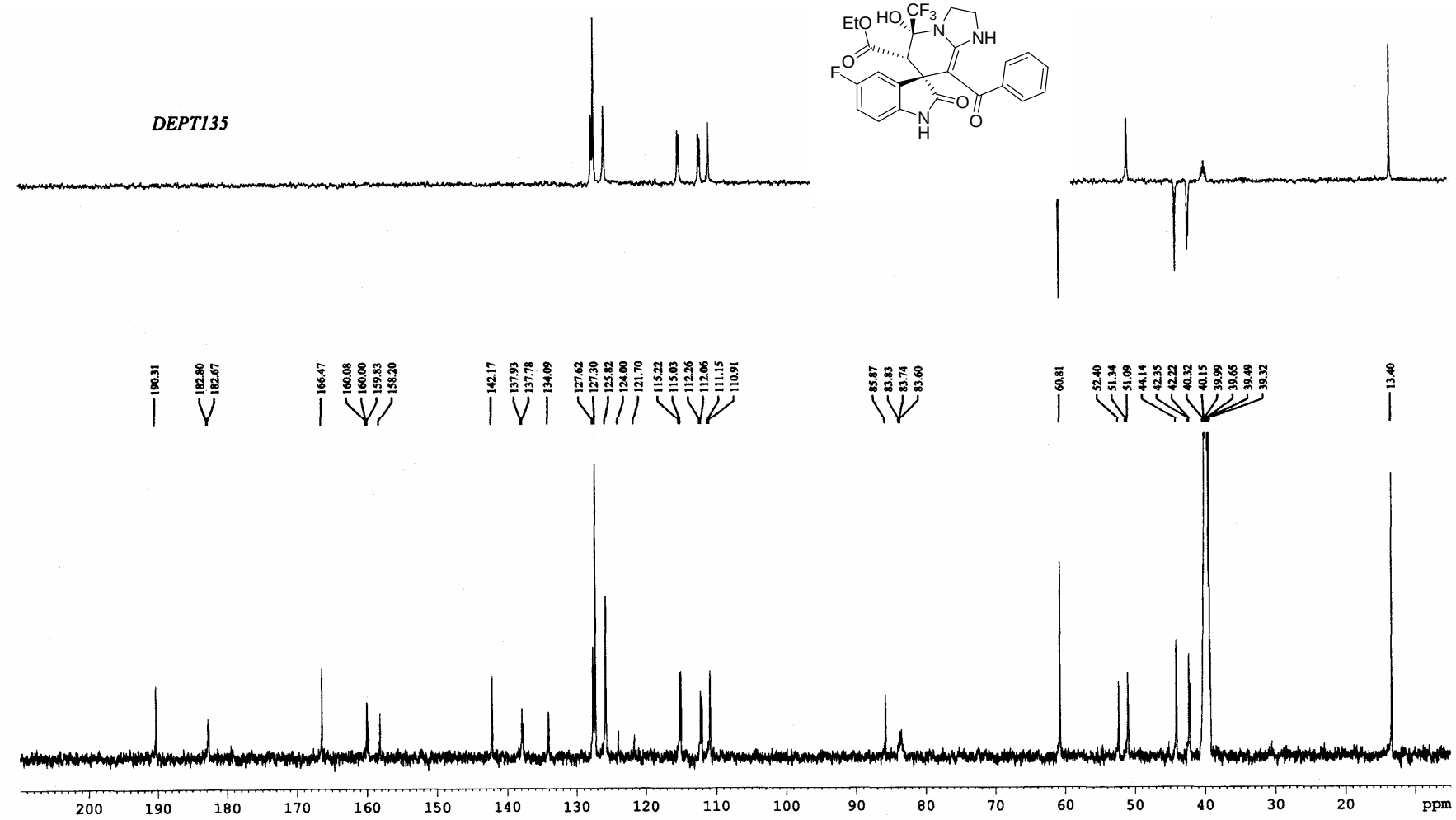


Figure 8. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5d**

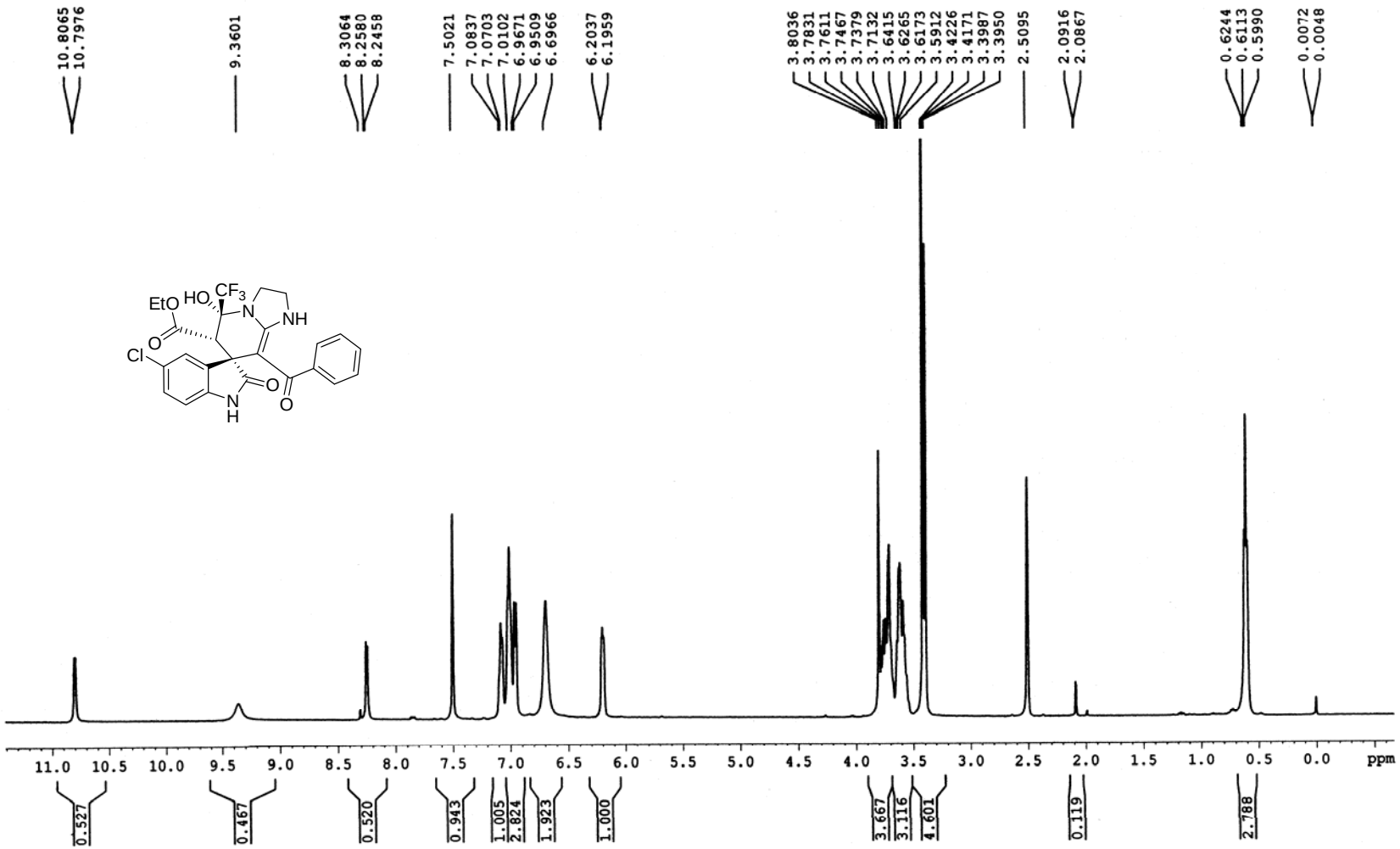


Figure 9. ^{1}H NMR (500 MHz, DMSO-d_6 + $HClO_4$) spectra of compound **5e**

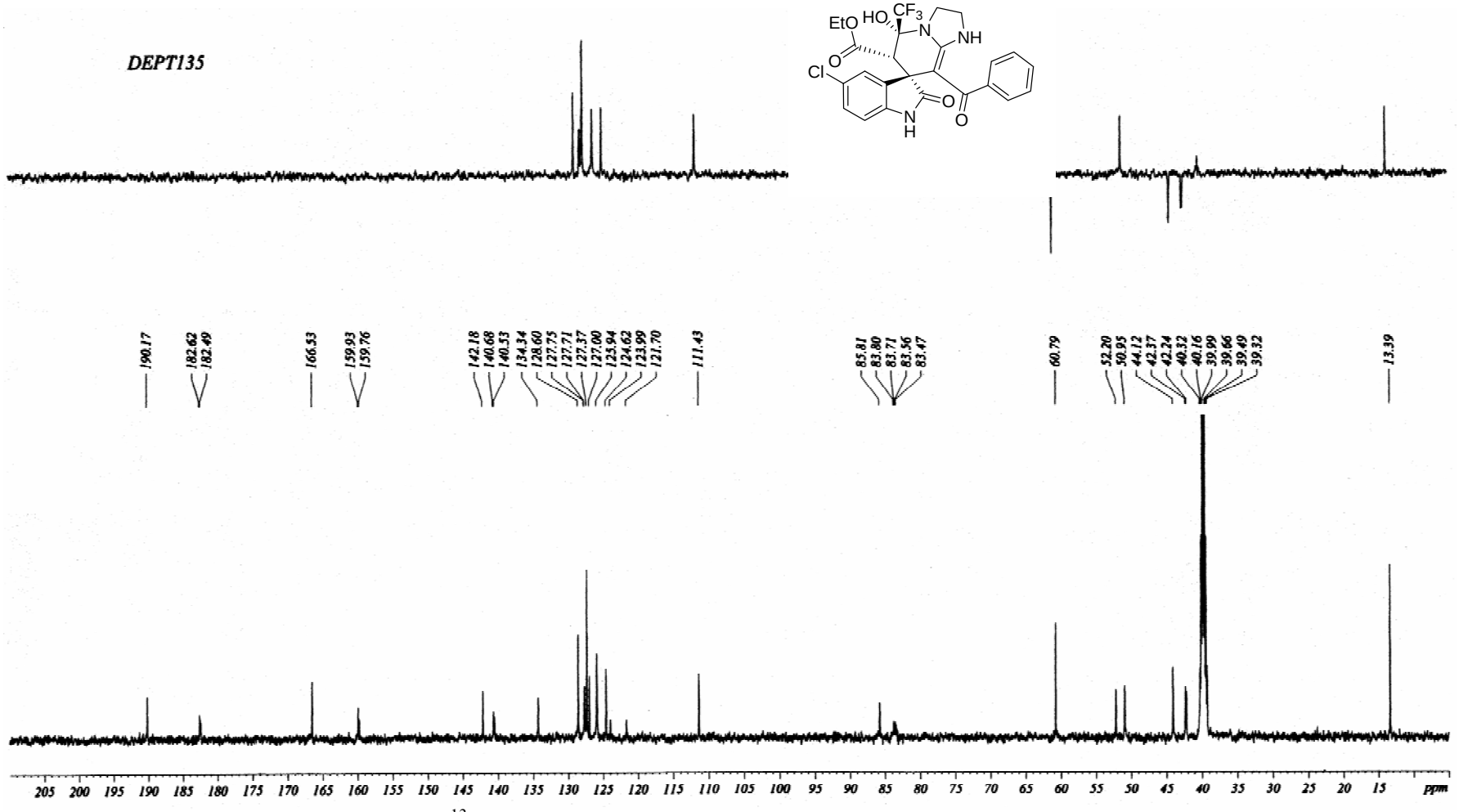


Figure 10. ^{13}C NMR (125 MHz, DMSO-d_6 + $HClO_4$) spectra of compound **5e**

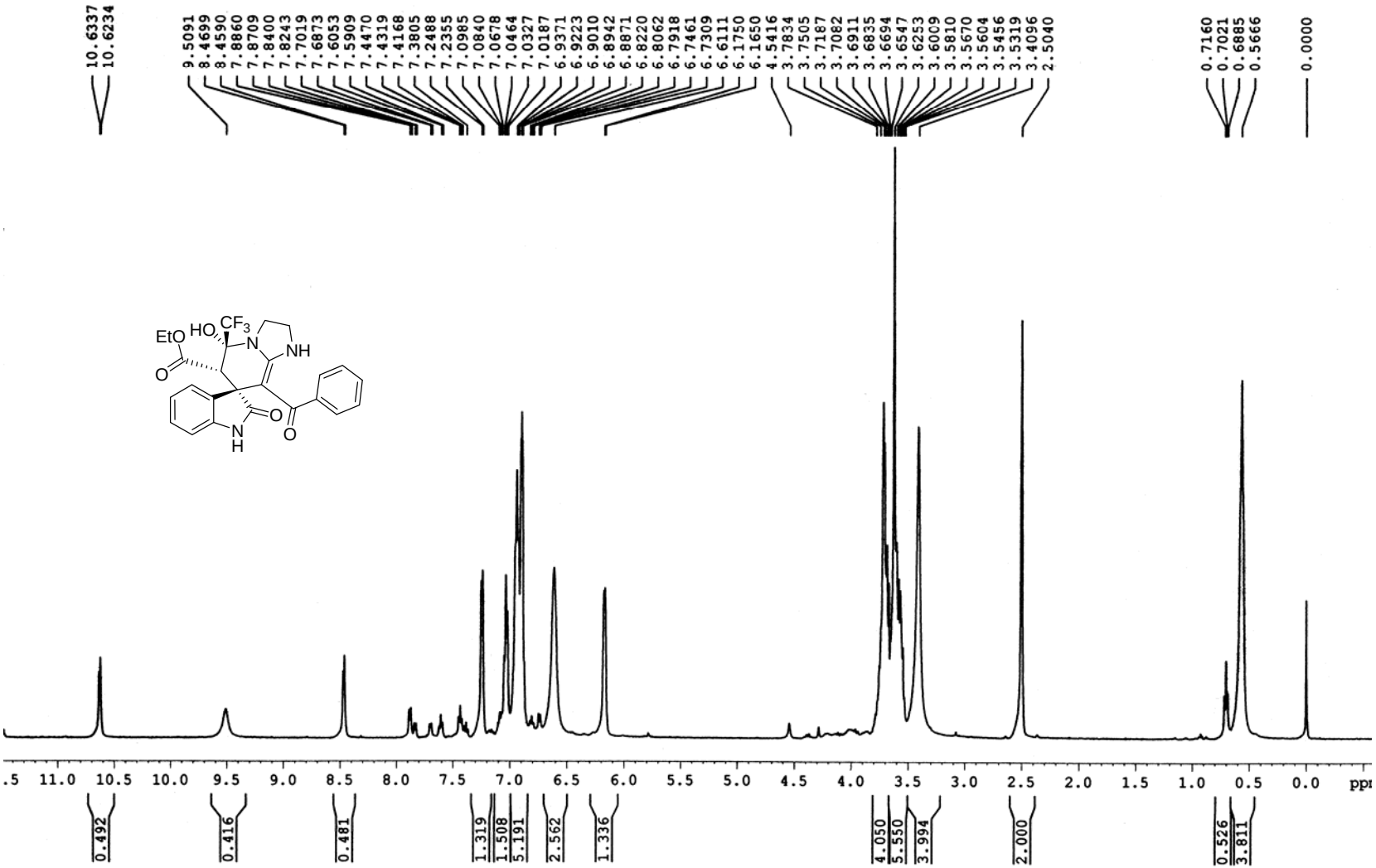


Figure 11. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5f**

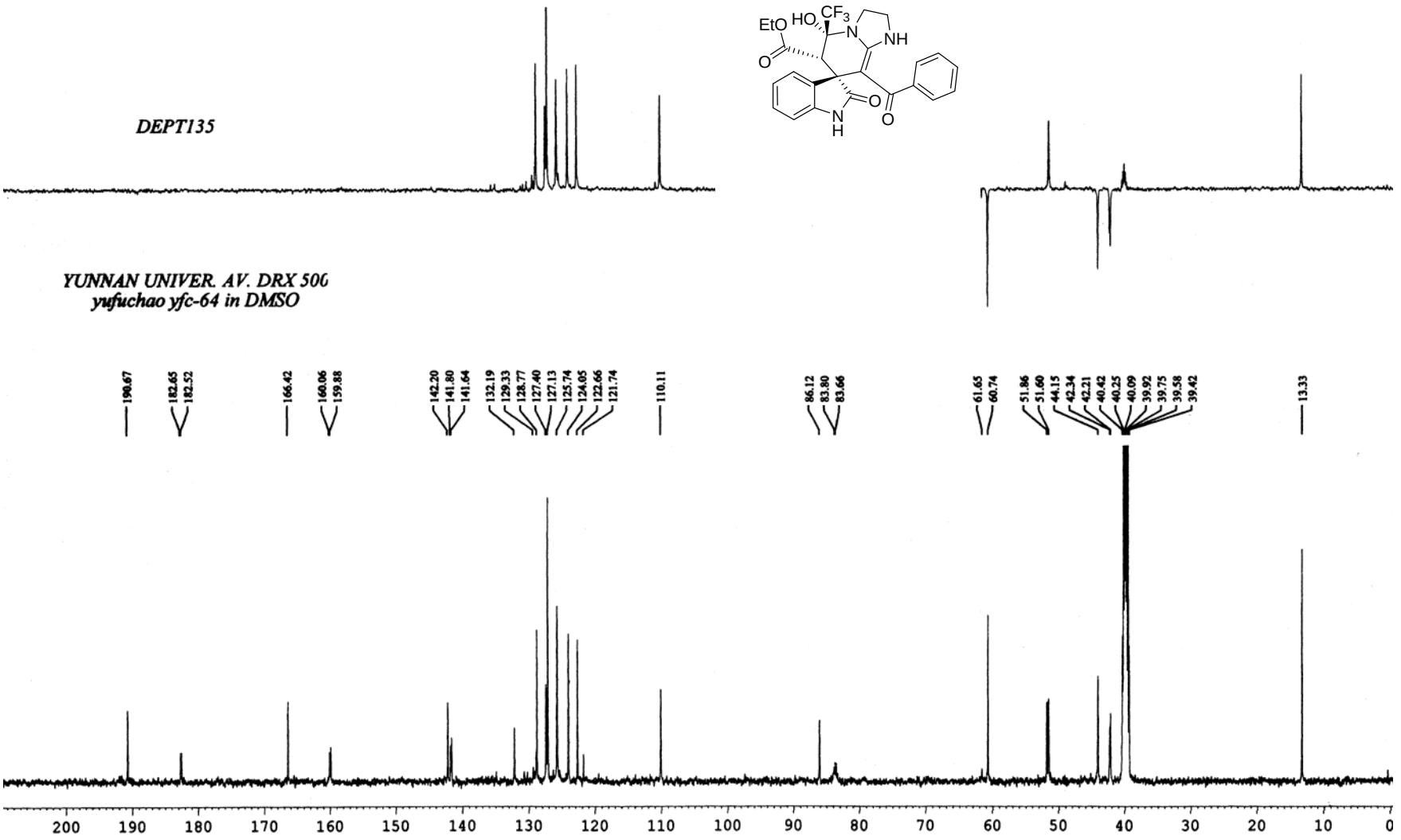


Figure 12. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5f**

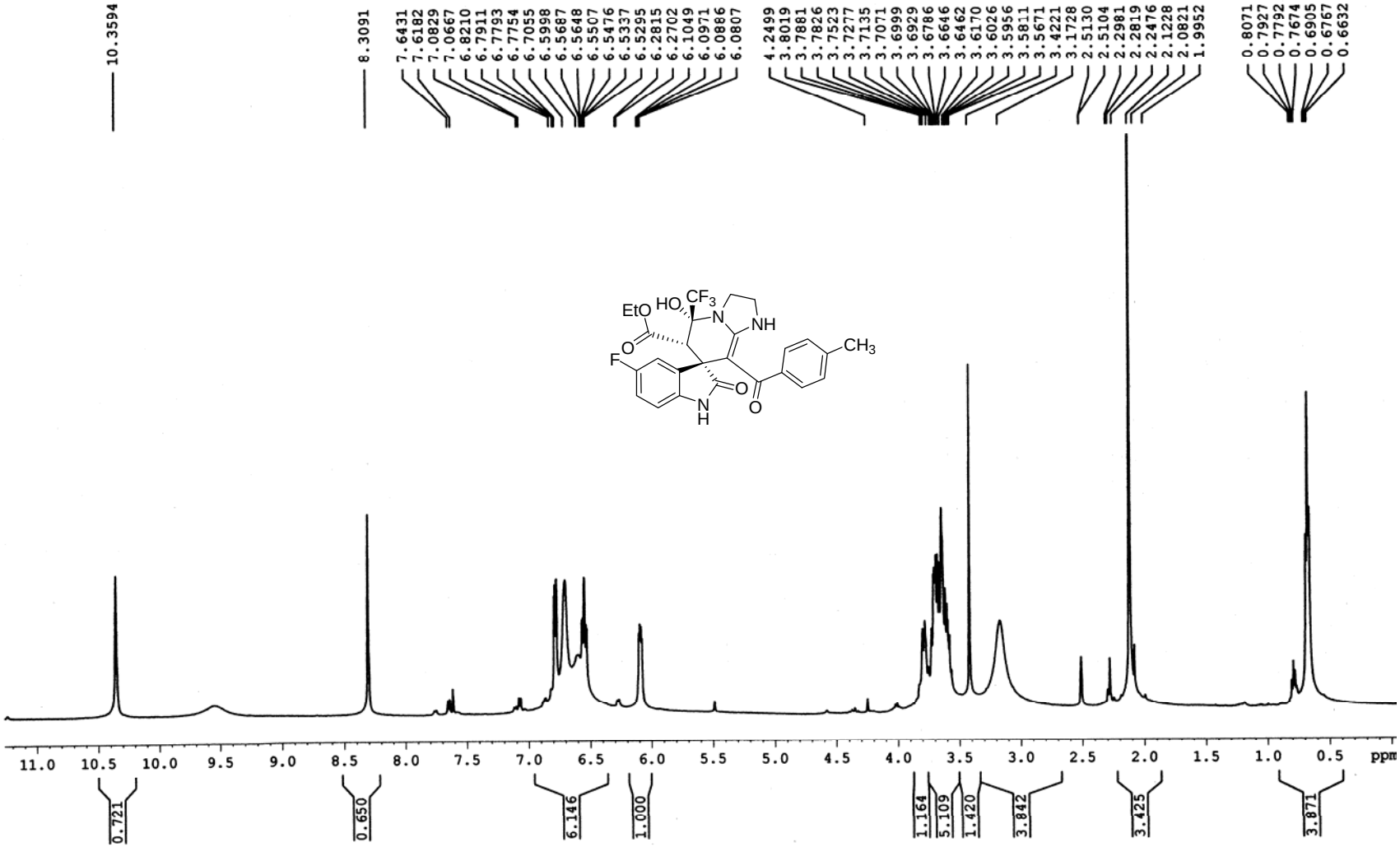


Figure 13. ^{1}H NMR (500 MHz, $CDCl_3$ + DMSO-d_6) spectra of compound **5g**

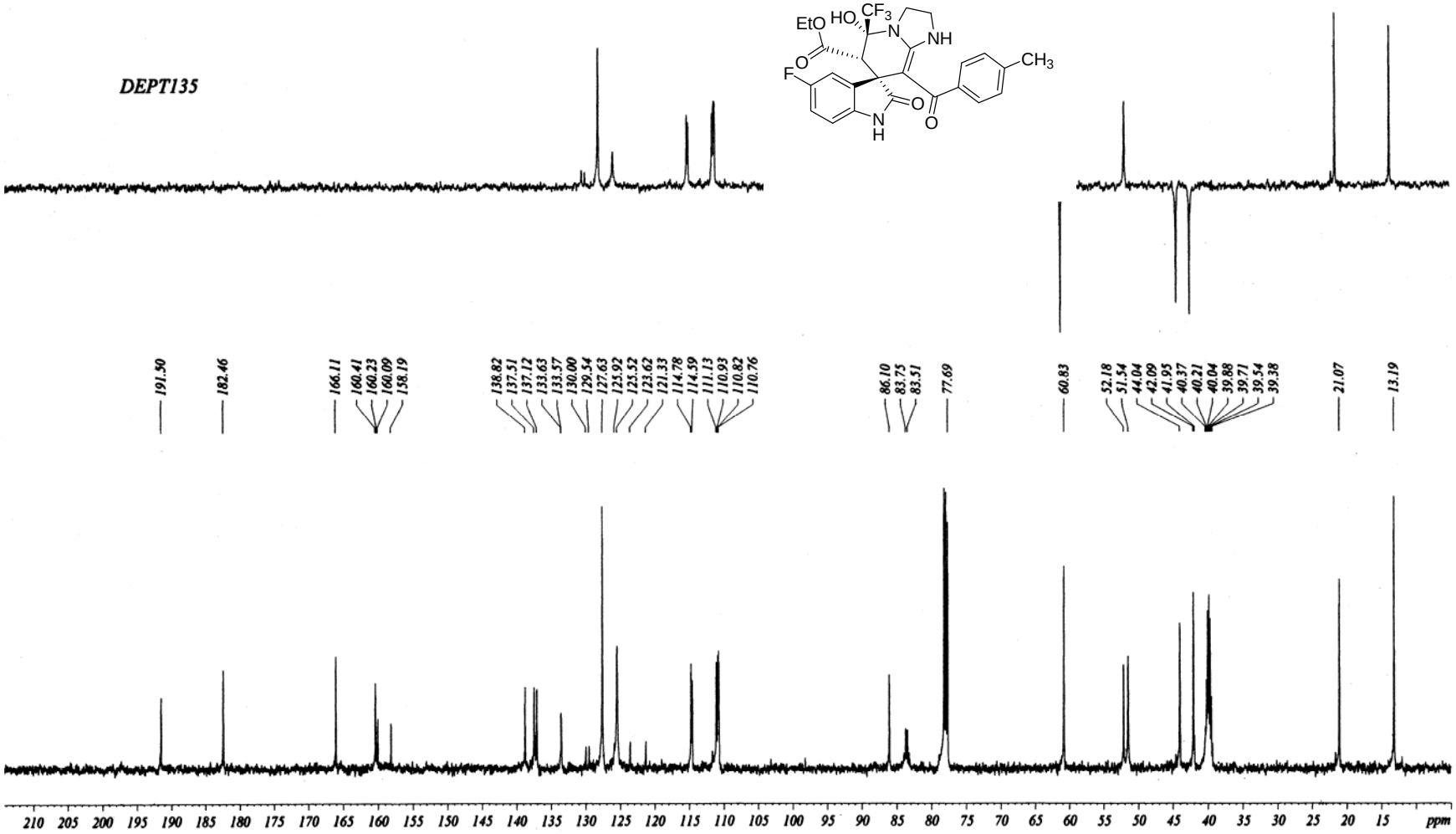


Figure 14. ^{13}C NMR (125 MHz, $CDCl_3$ + DMSO-d_6) spectra of compound **5g**

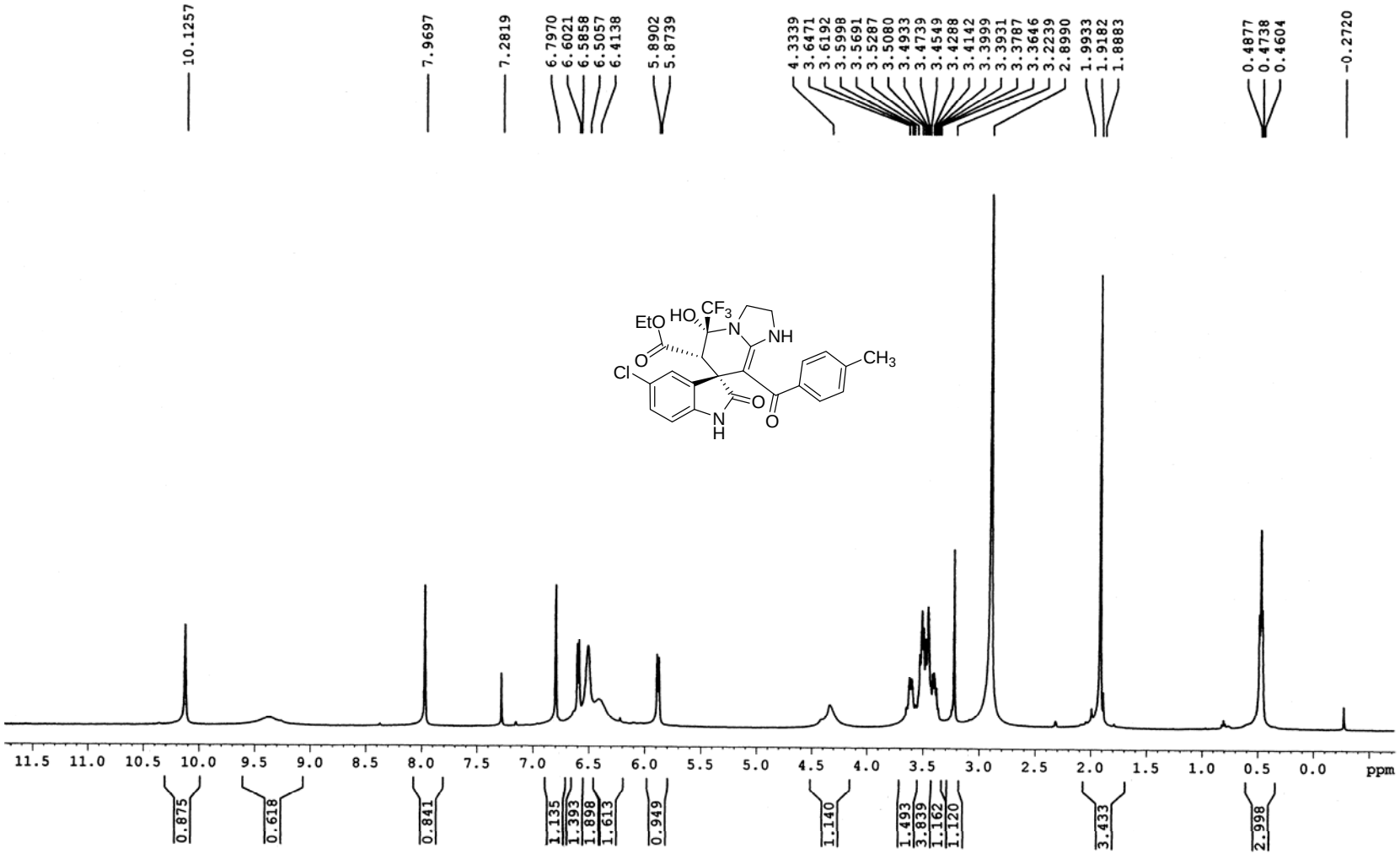


Figure 15. ^{1}H NMR (500 MHz, $CDCl_3$ + DMSO-d_6) spectra of compound **5h**

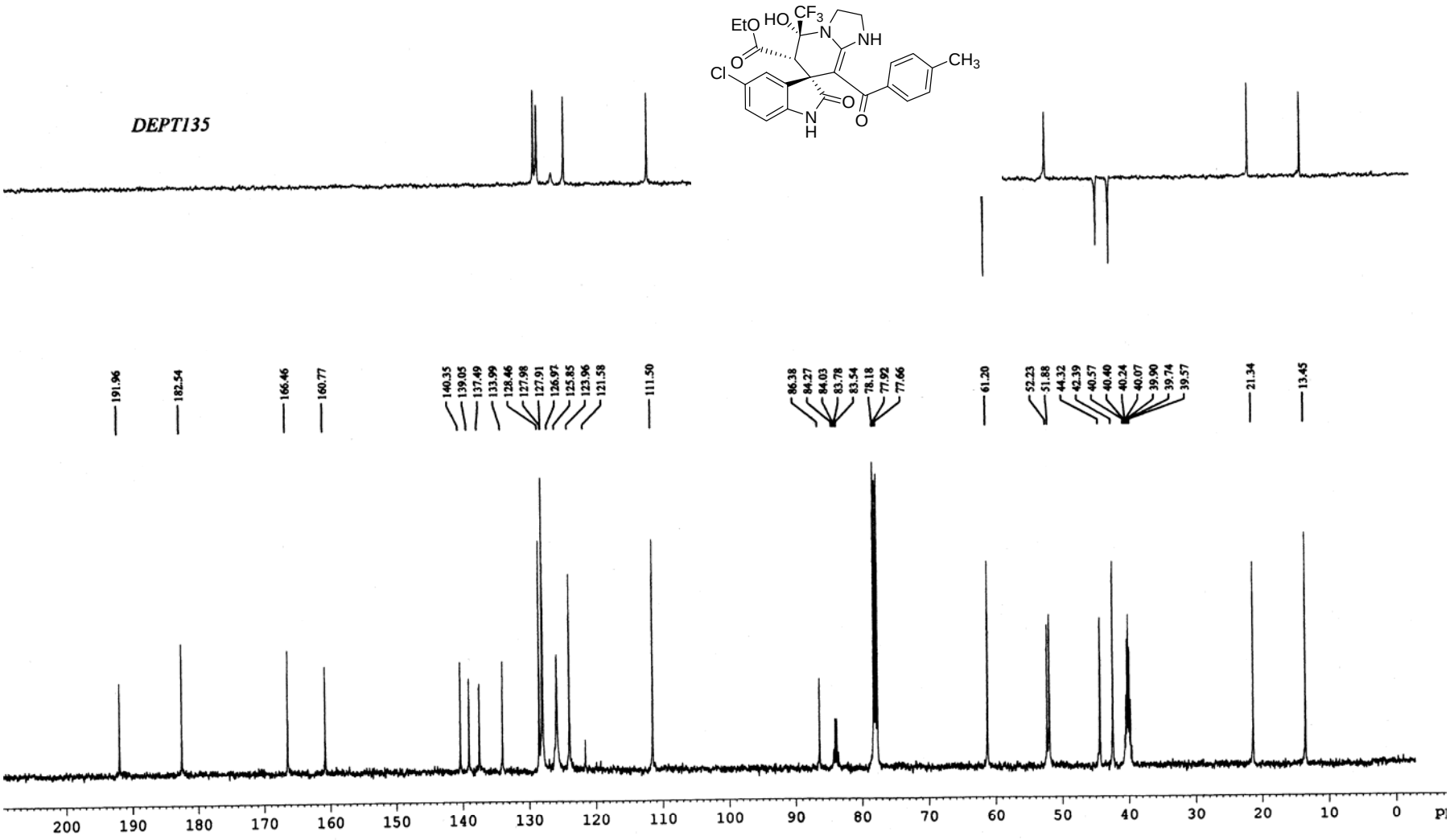


Figure 16. ^{13}C NMR (125 MHz, $CDCl_3$ + DMSO-d_6) spectra of compound **5h**

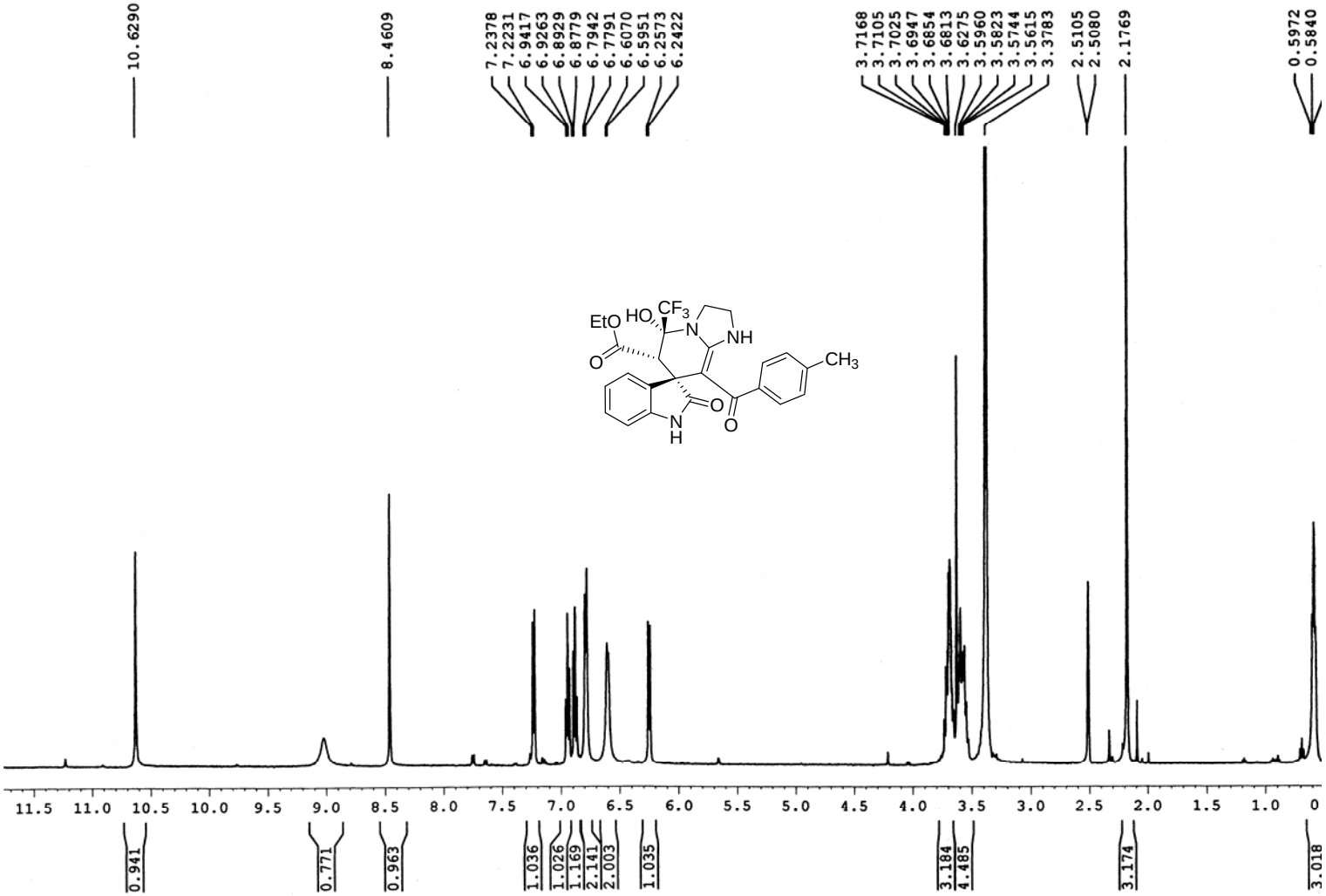


Figure 17. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5i**

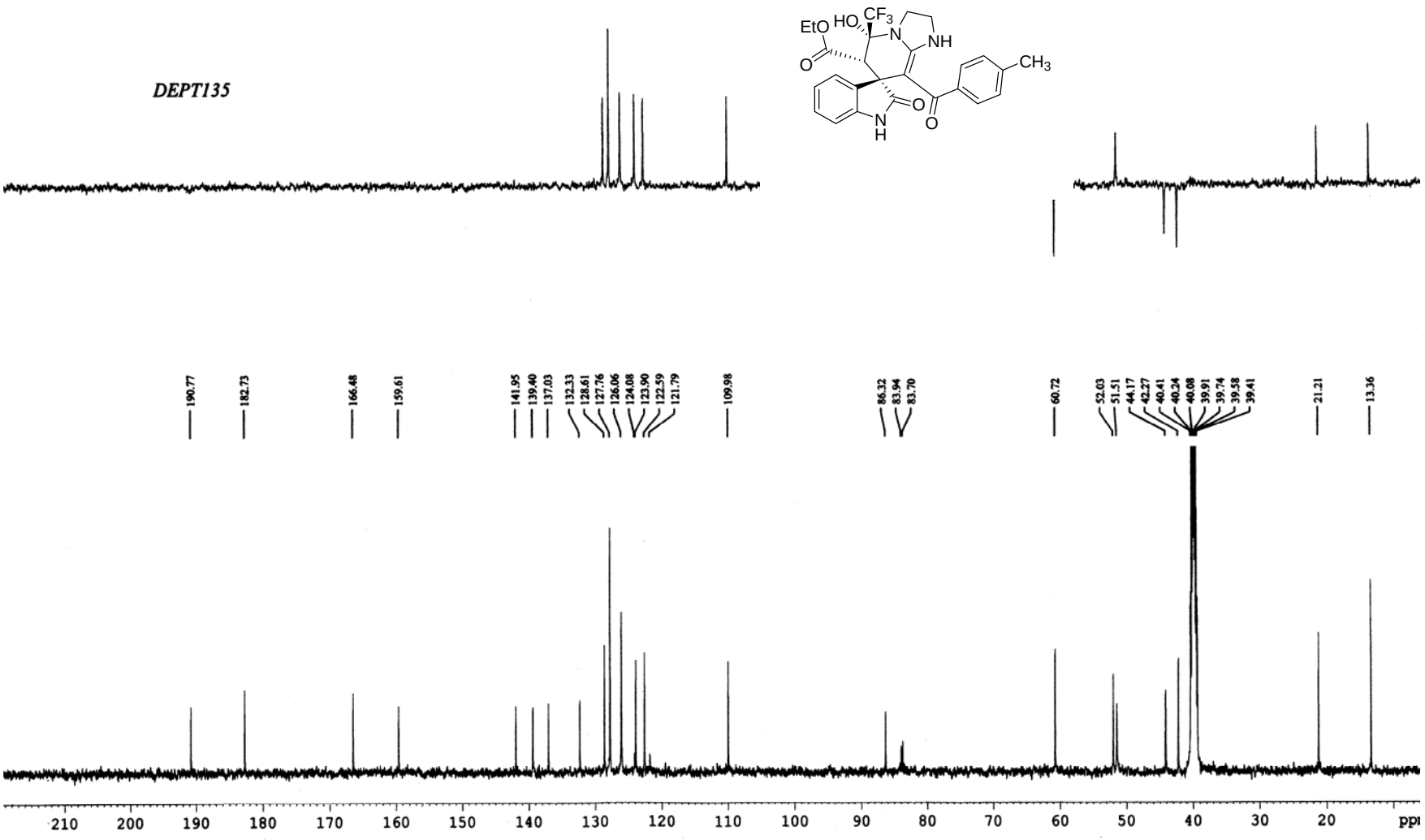


Figure 18. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5i**

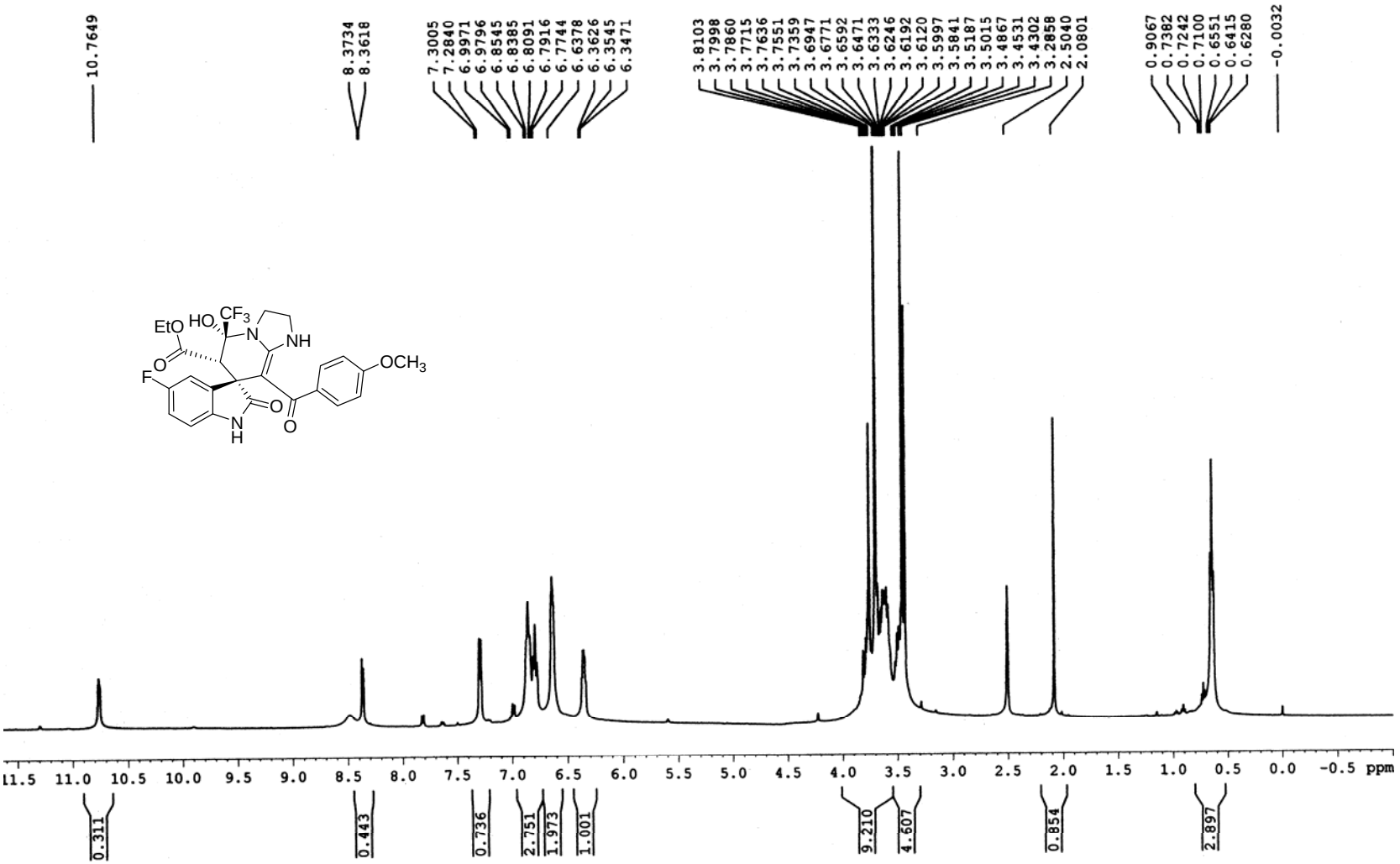


Figure 19. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5j**

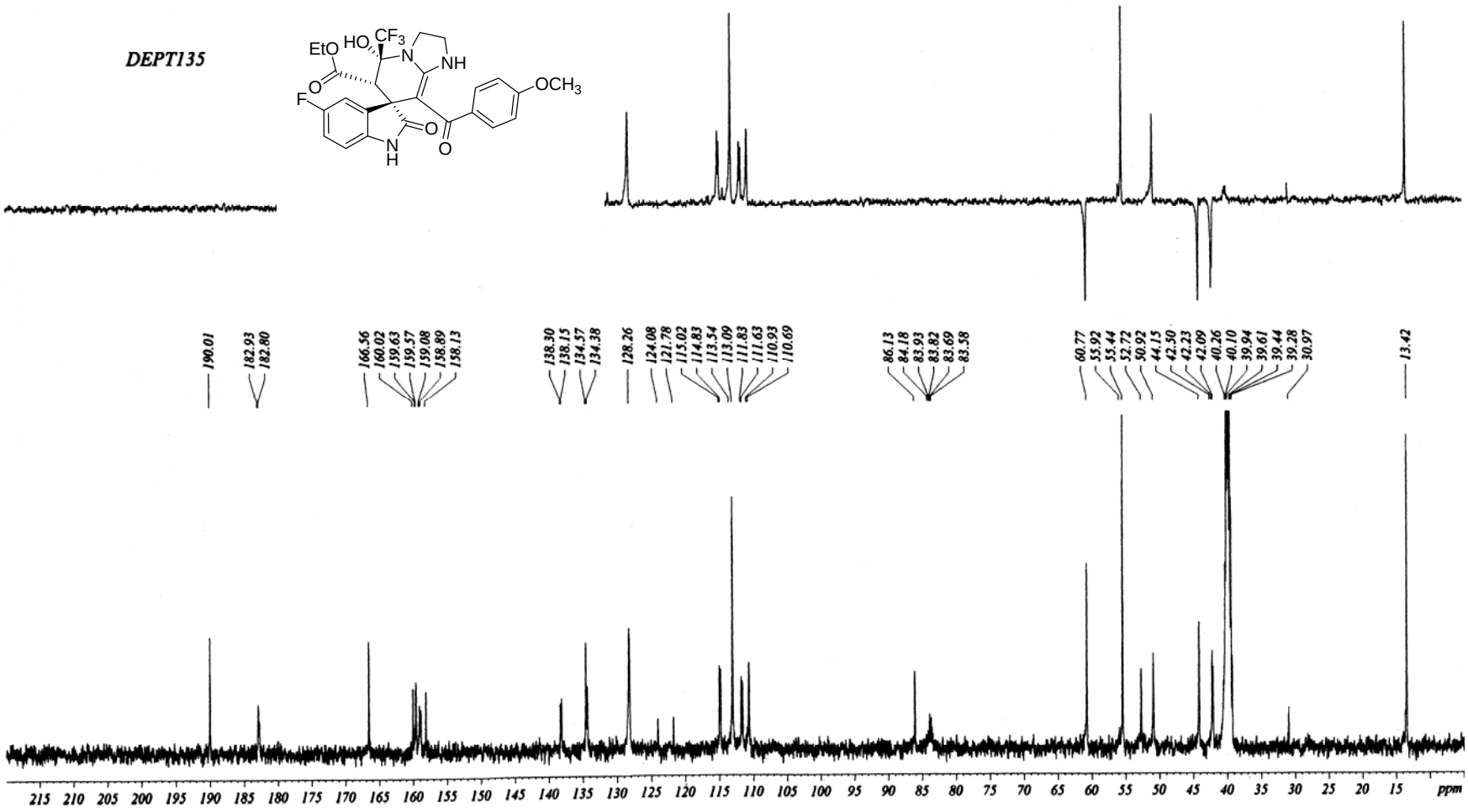


Figure 20. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5j**

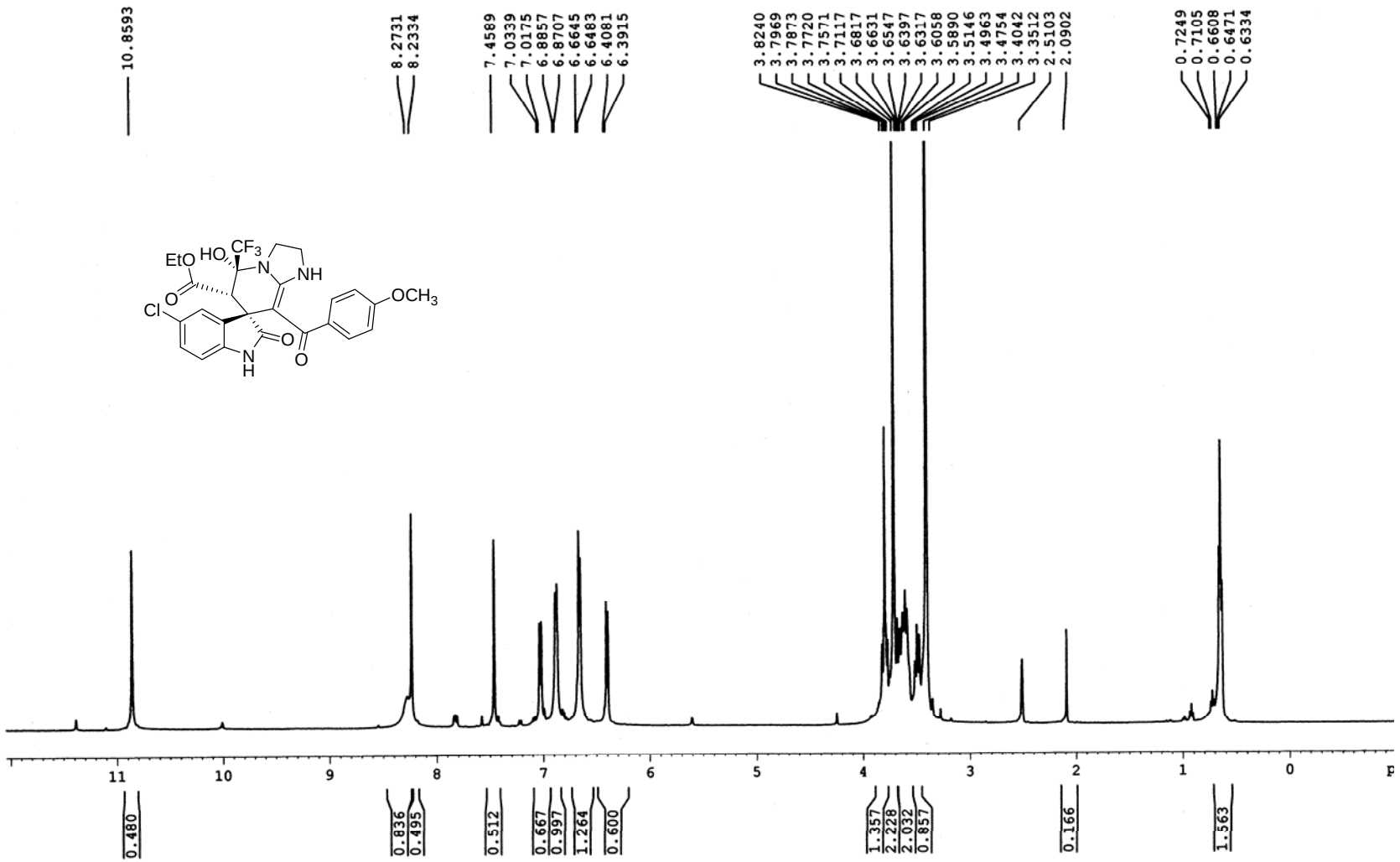


Figure 21. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5k**

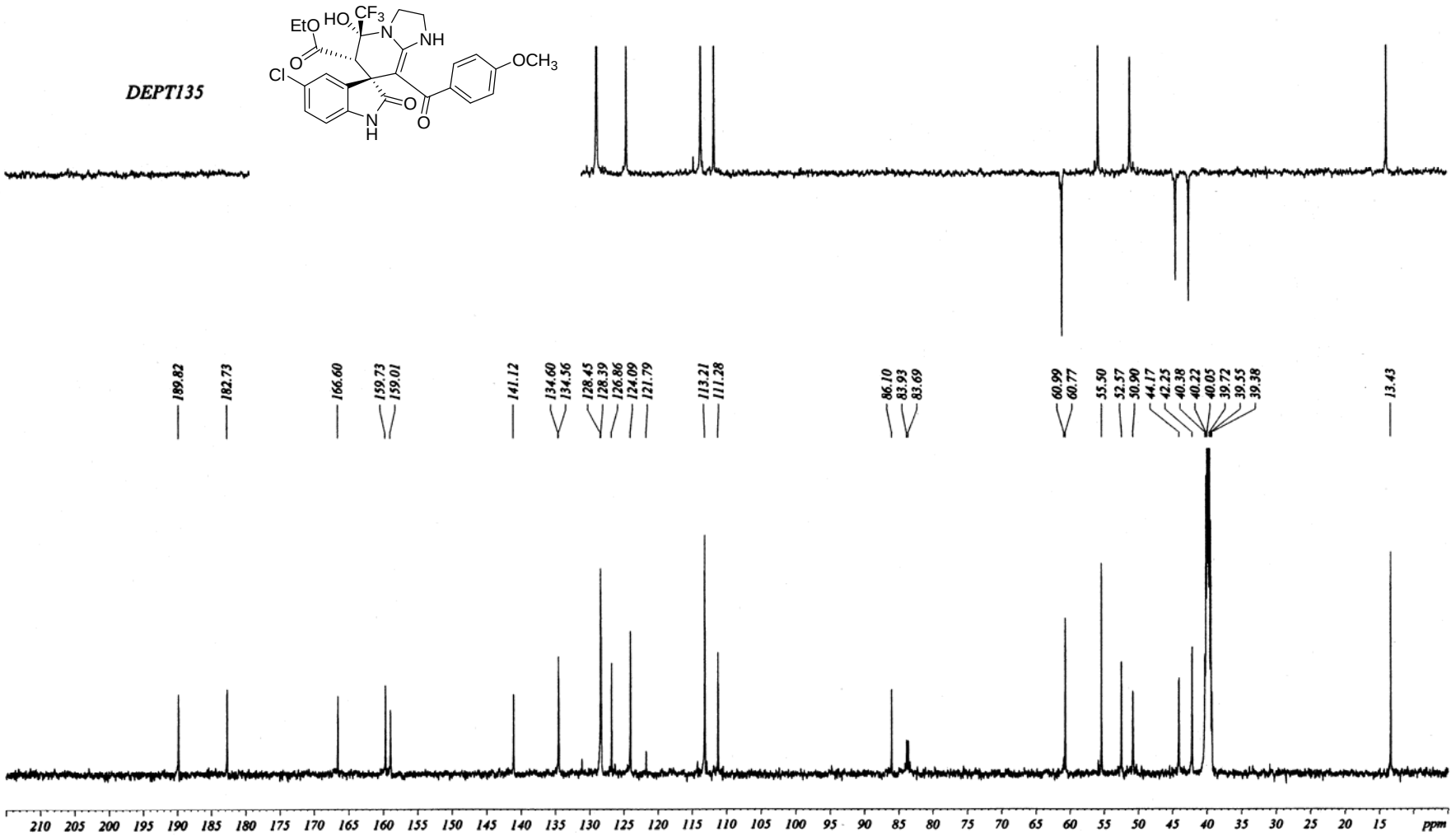


Figure 22. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5k**

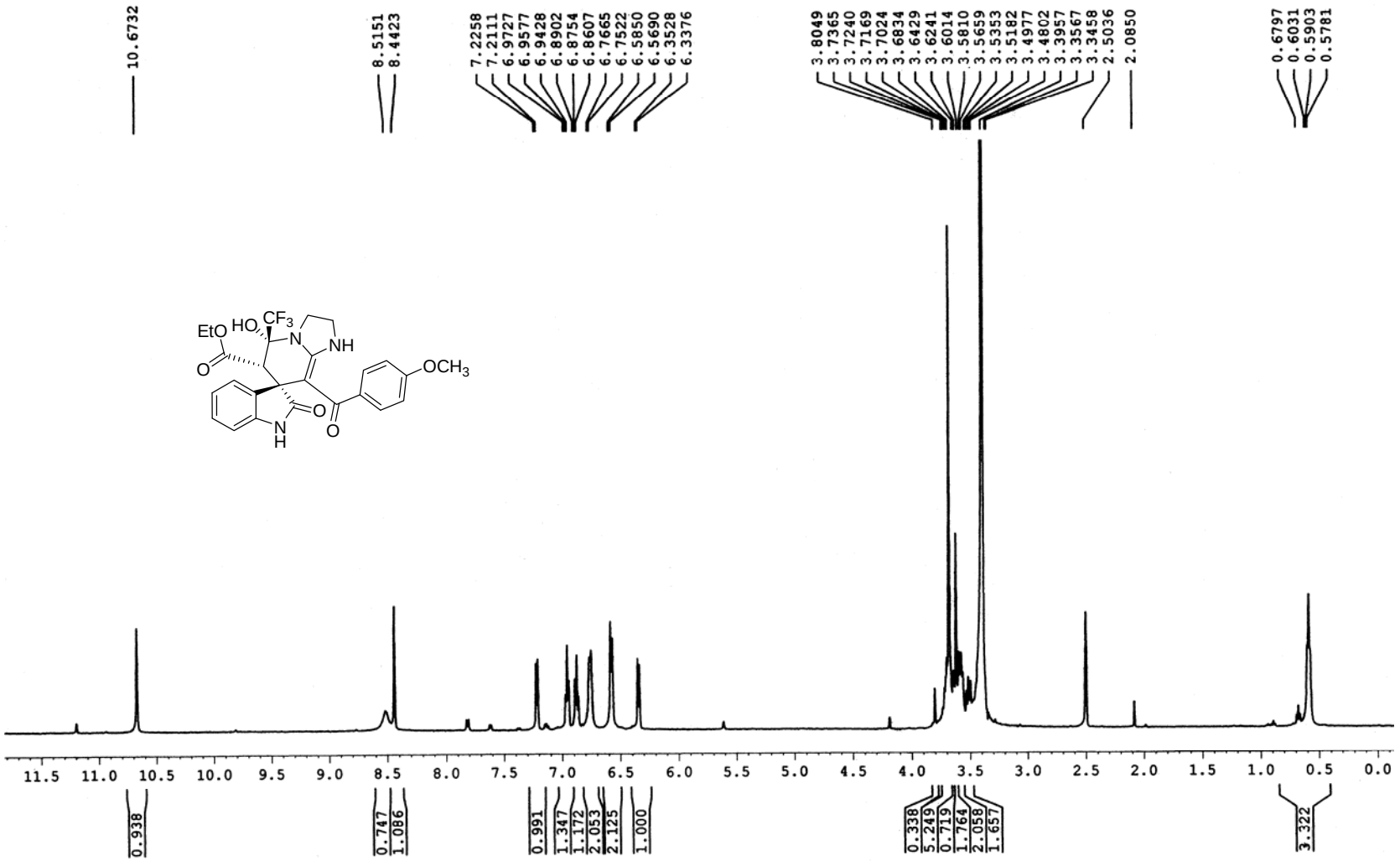


Figure 23. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5l**

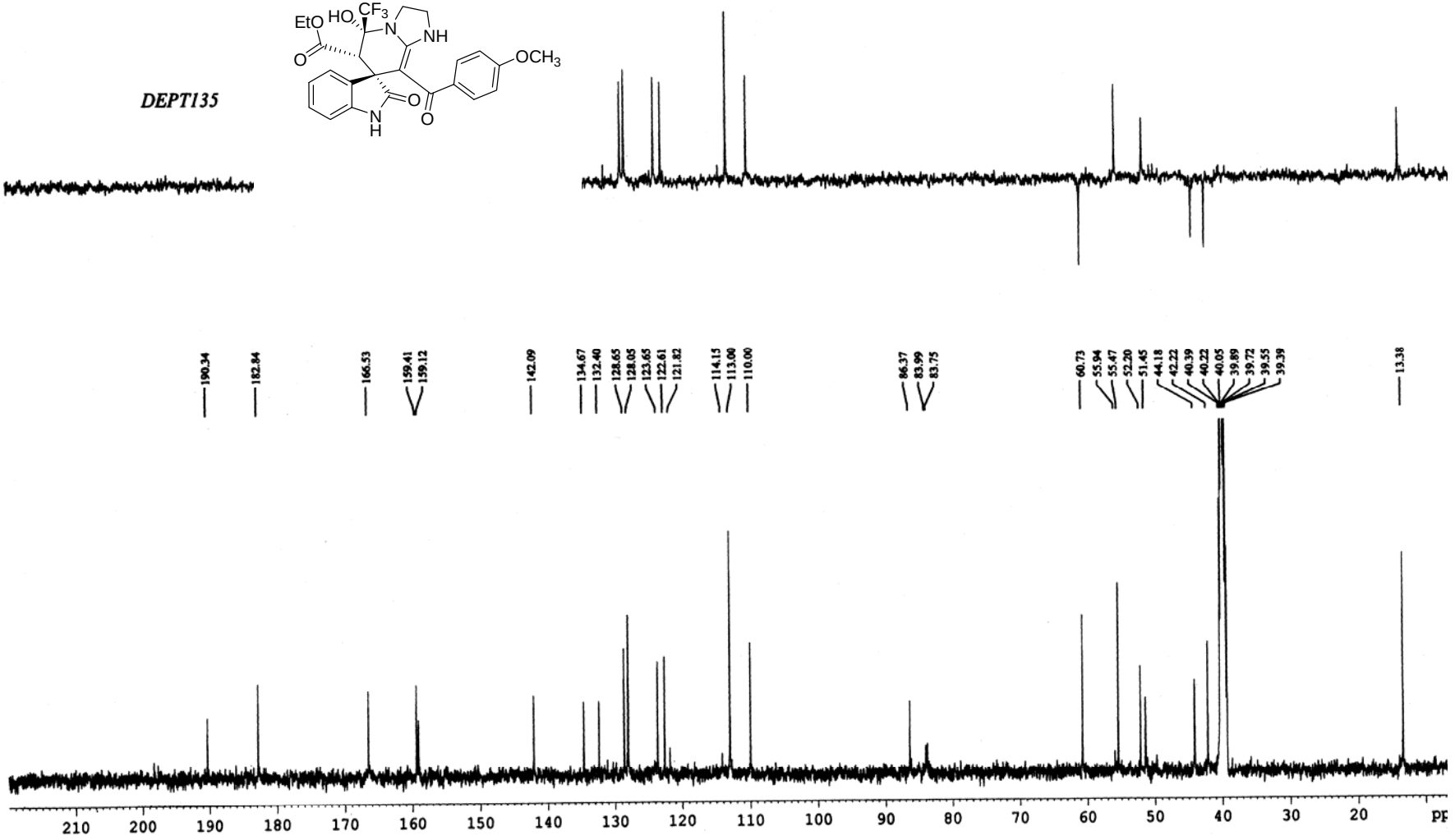


Figure 24. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5l**

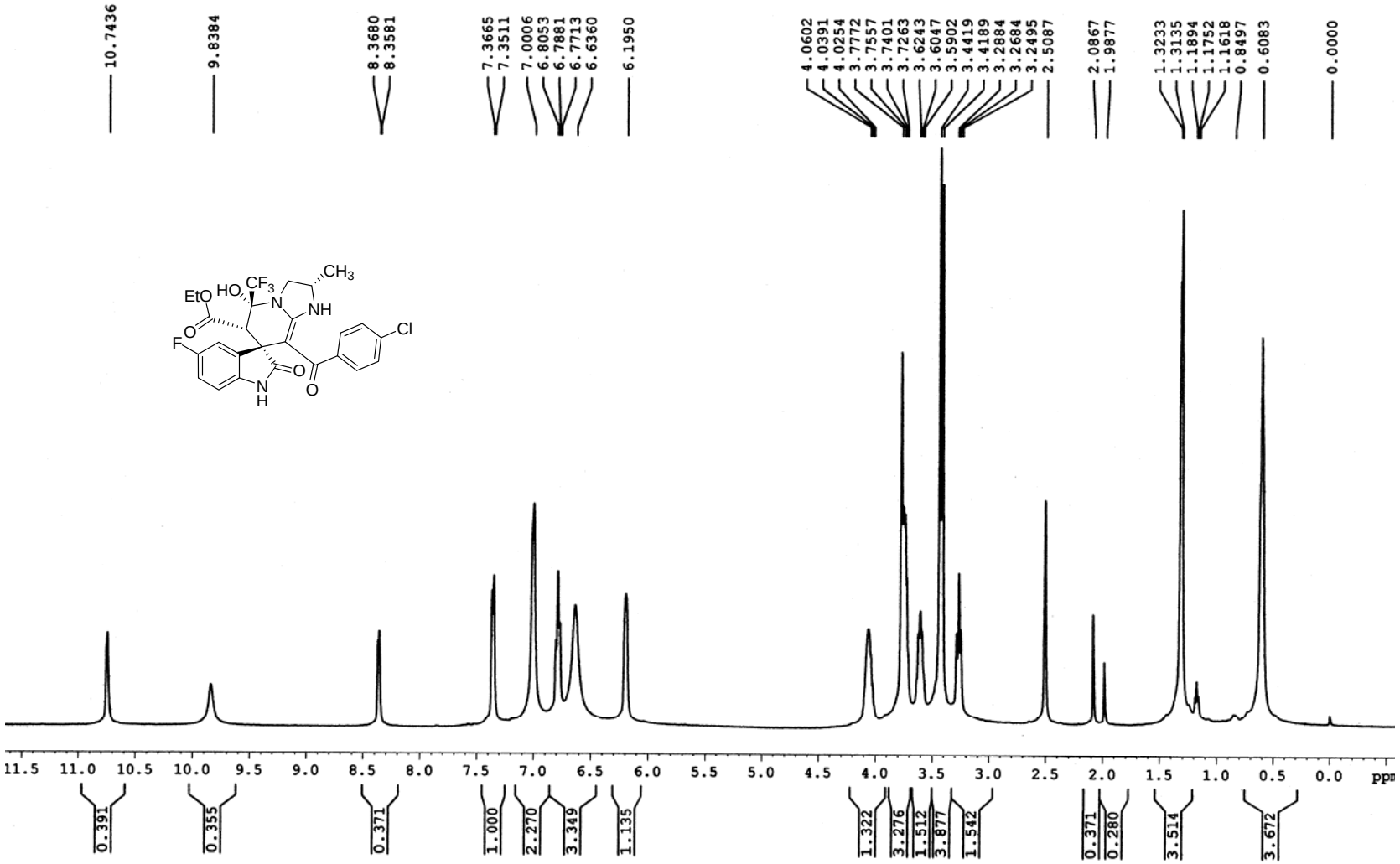


Figure 25. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5m**

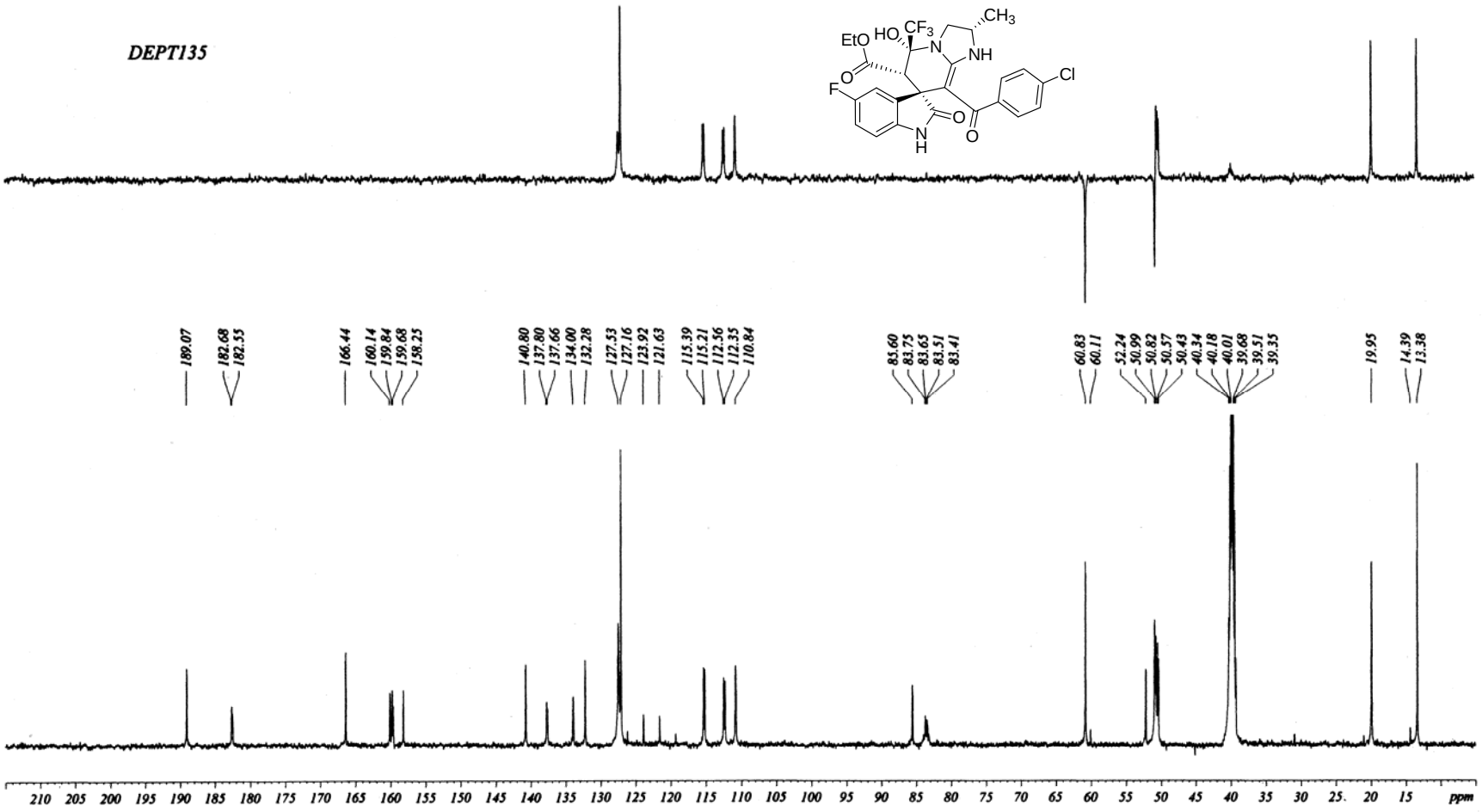


Figure 26. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5m**

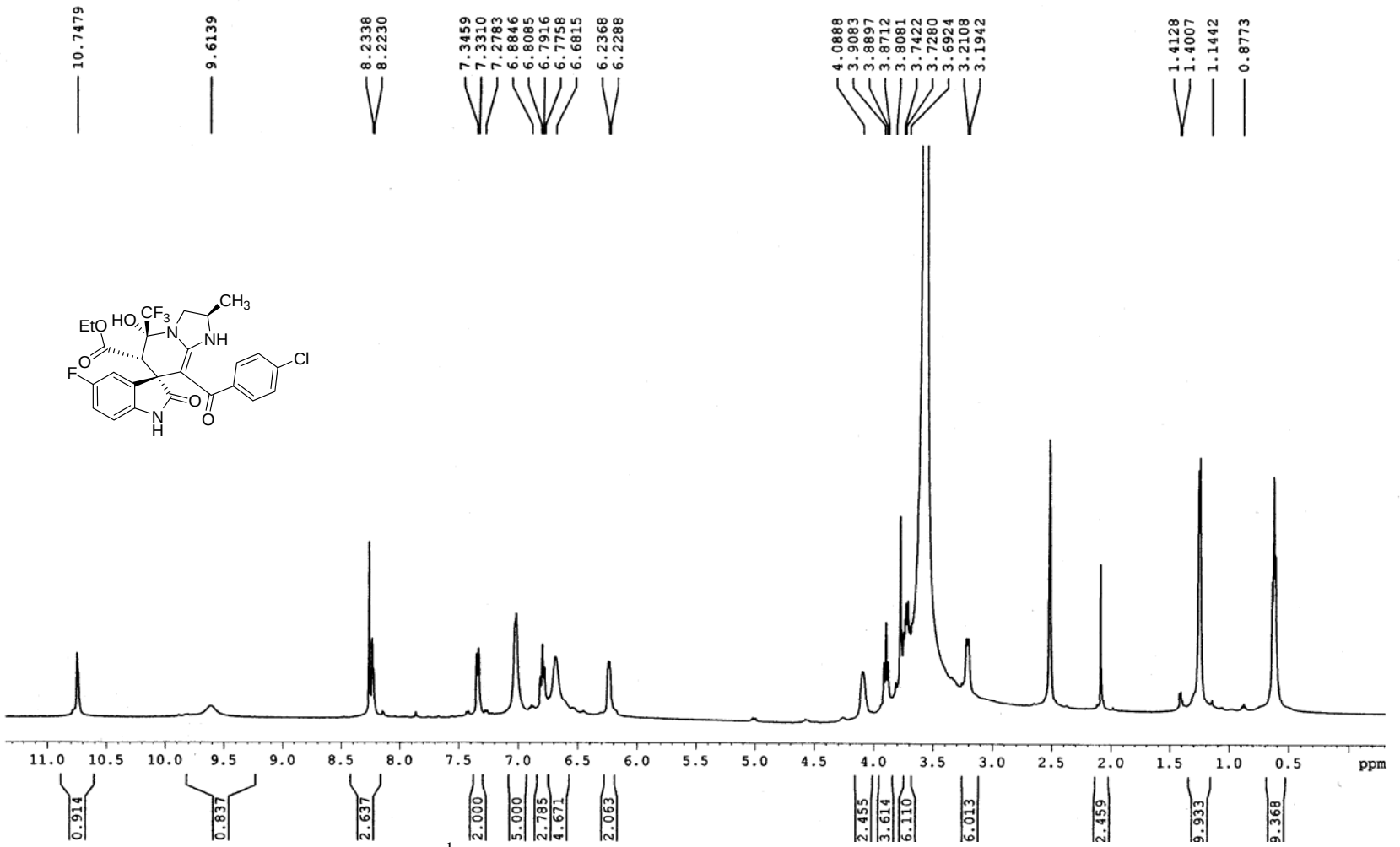


Figure 27. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5m'**

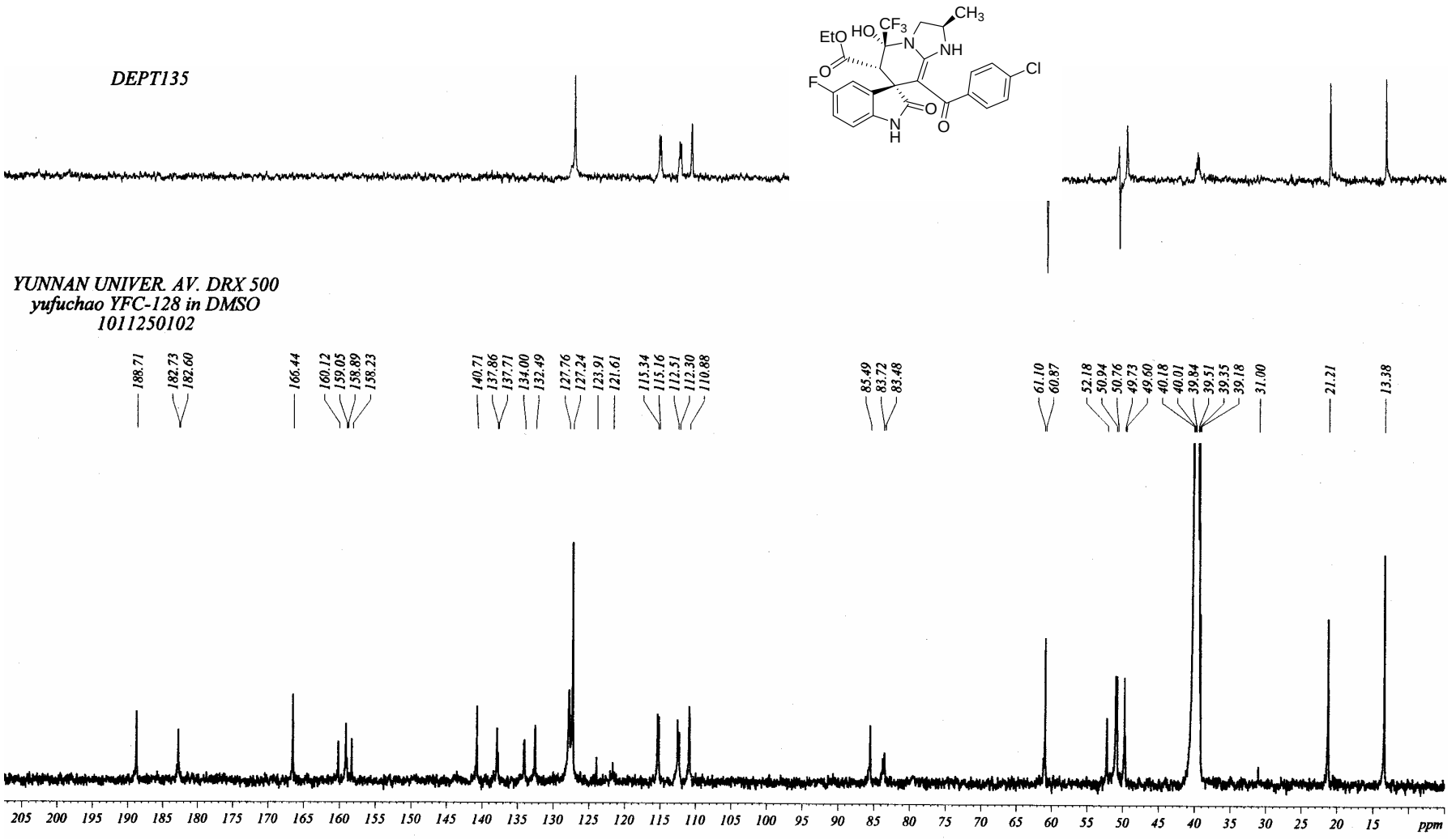


Figure 28. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5m'**

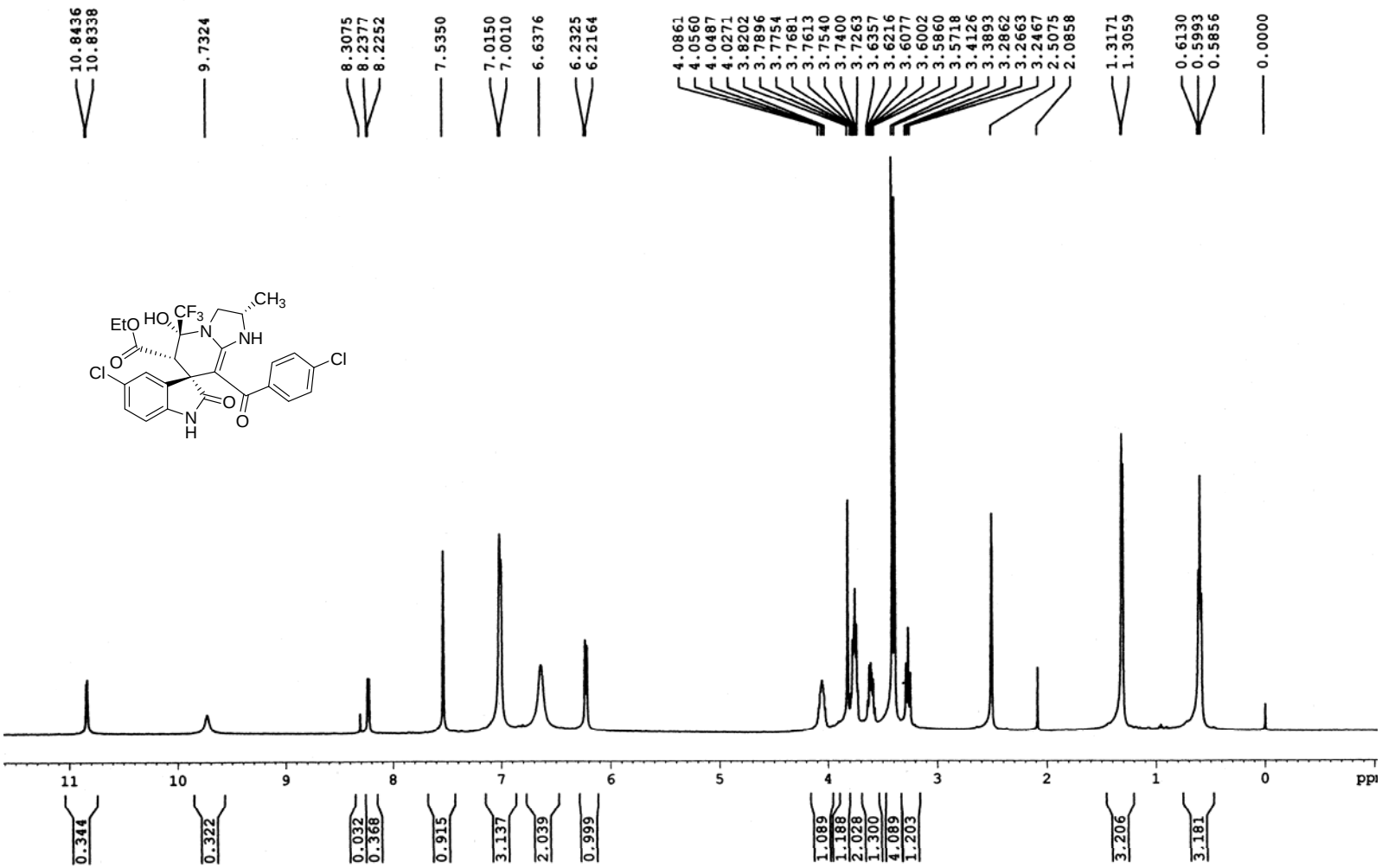


Figure 29. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5n**

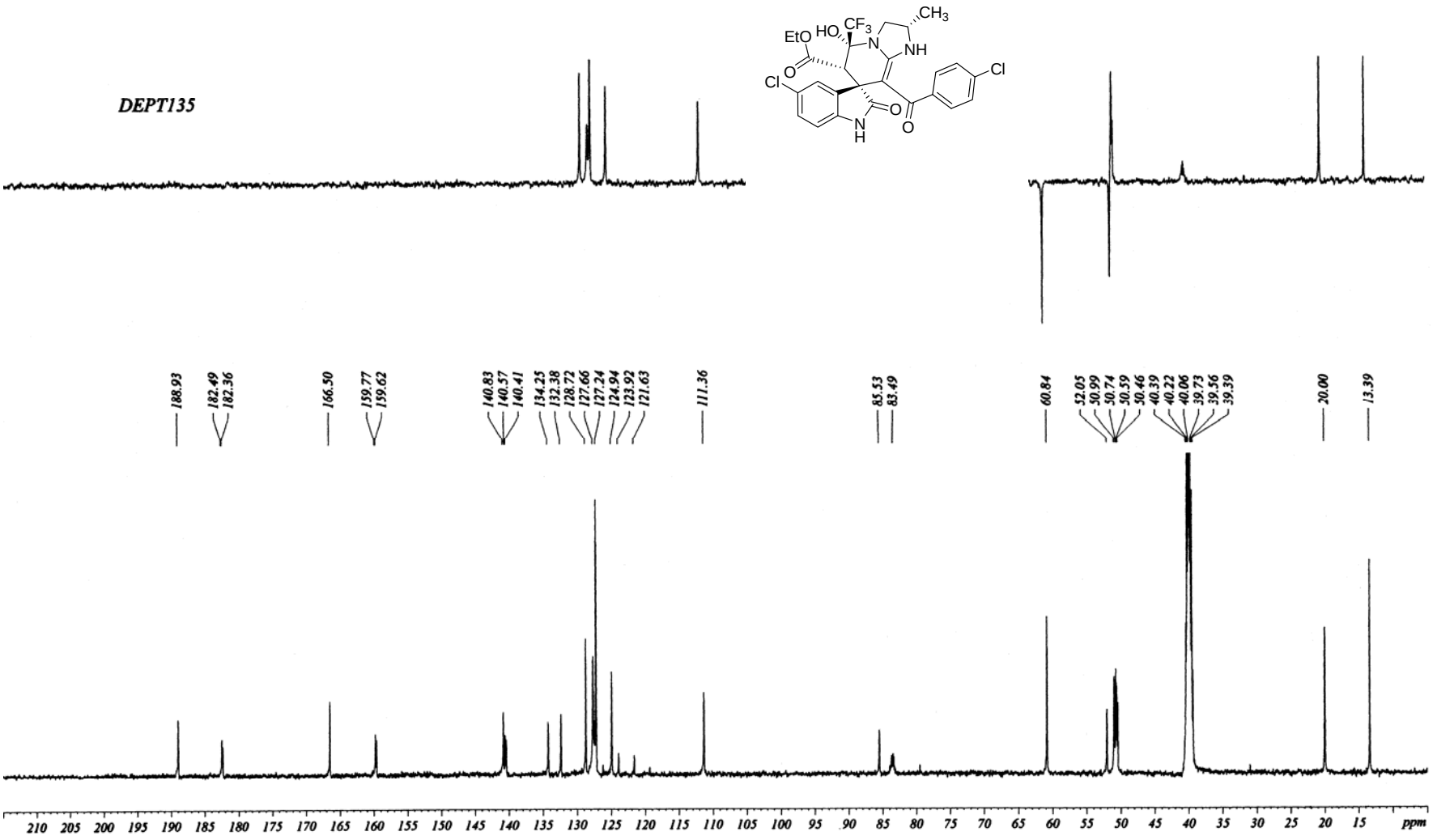


Figure 30. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5n**

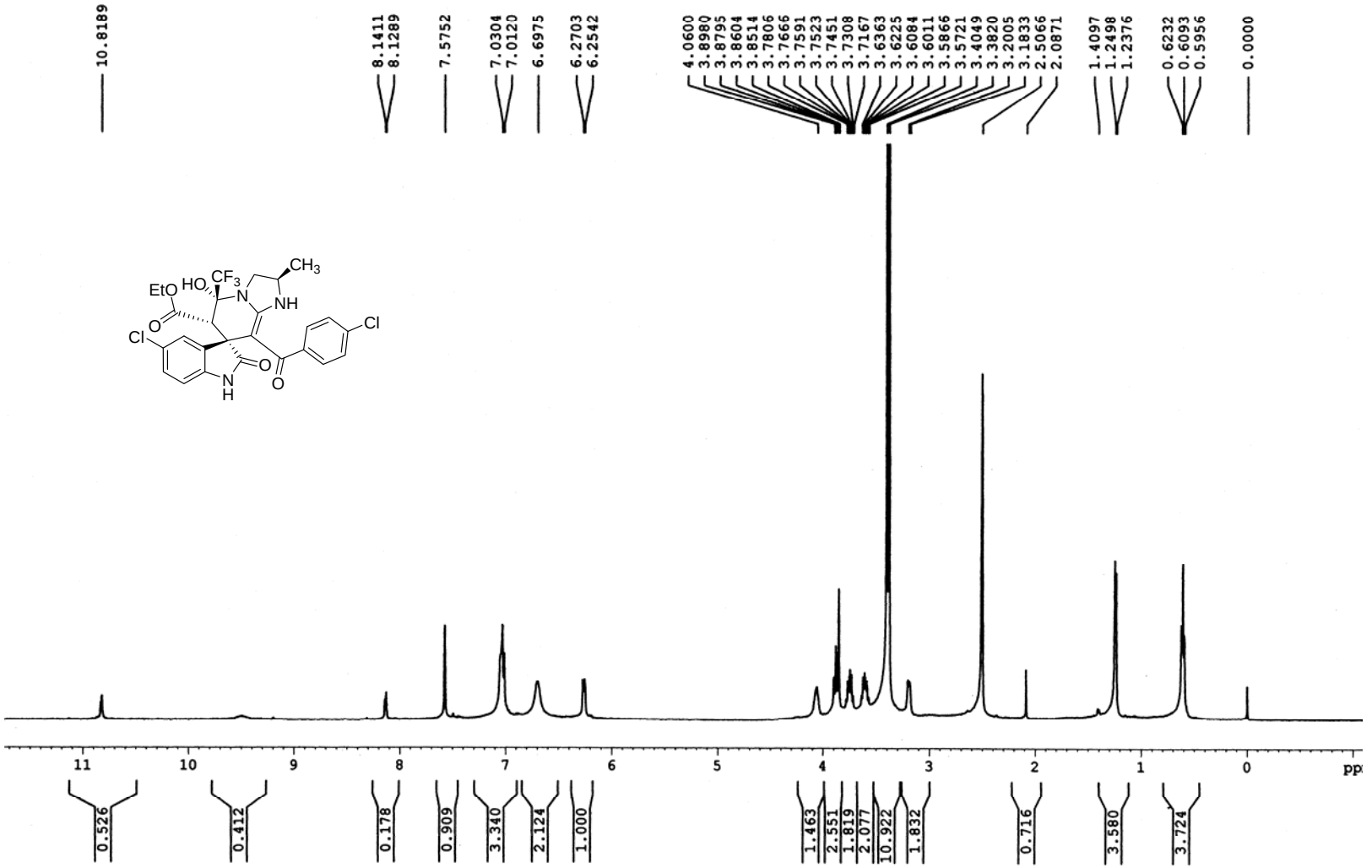


Figure 31. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5n'**

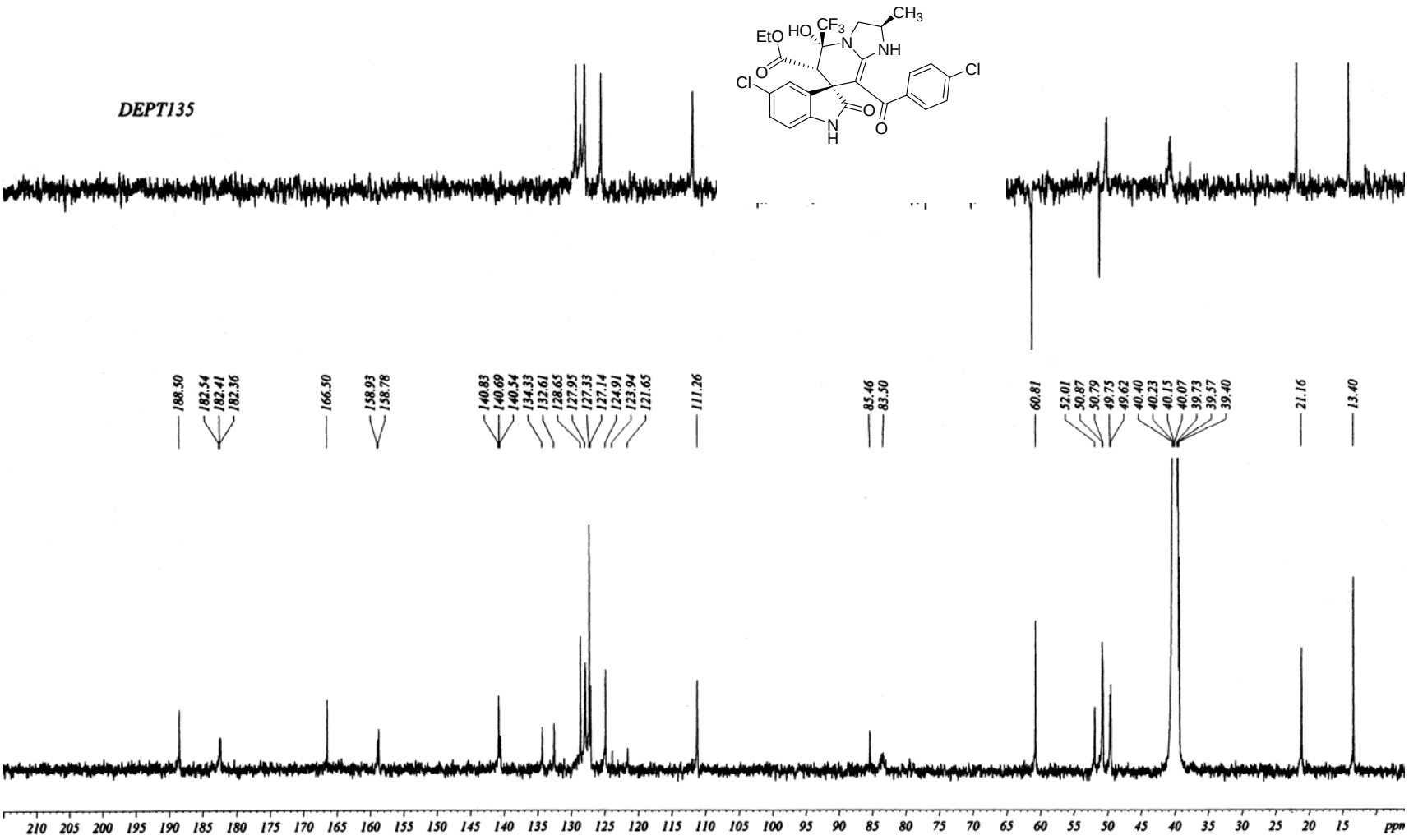


Figure 32. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5n'**

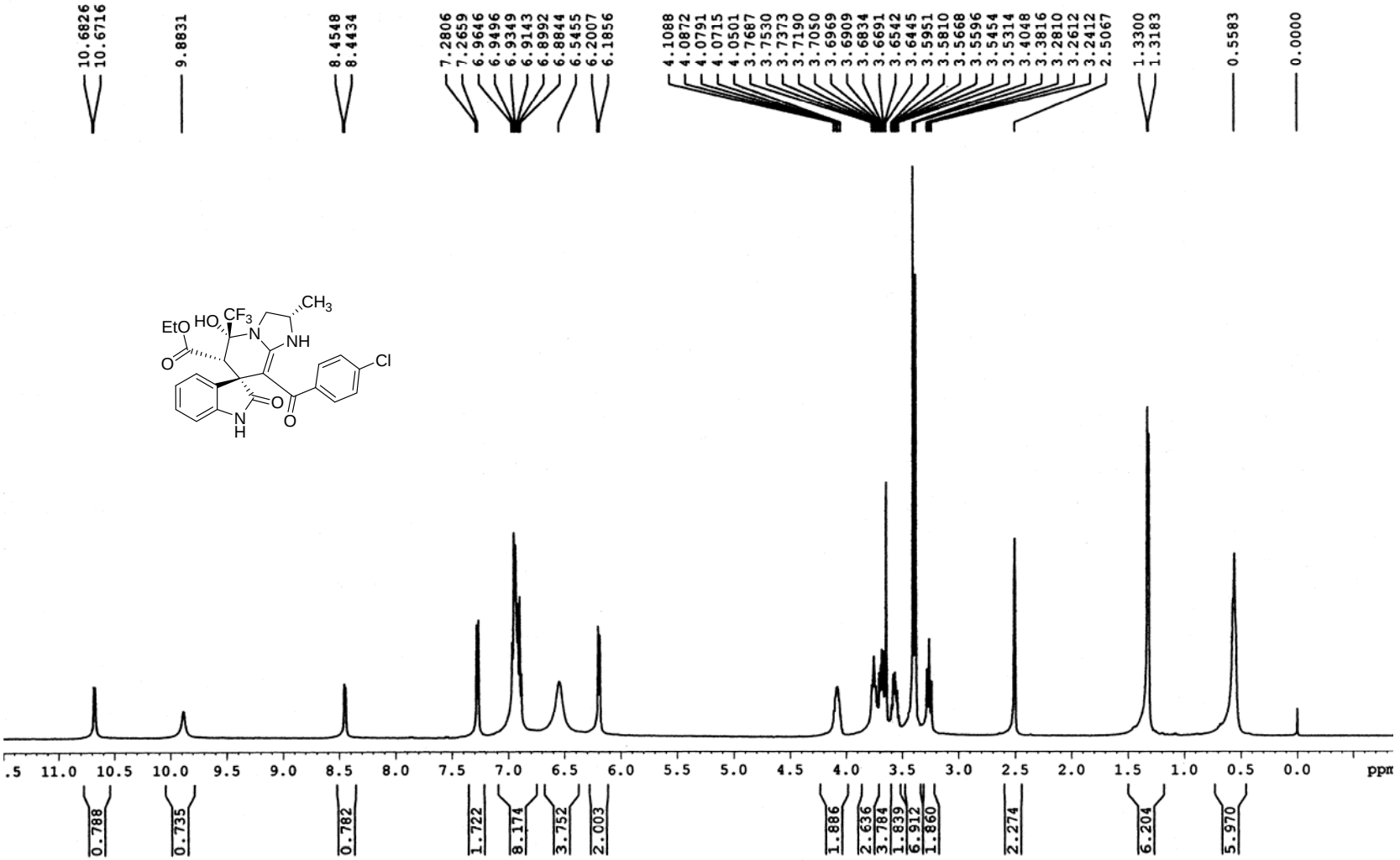


Figure 33. ^{1}H NMR (500 MHz, DMSO-d_6 + $HClO_4$) spectra of compound **5o**

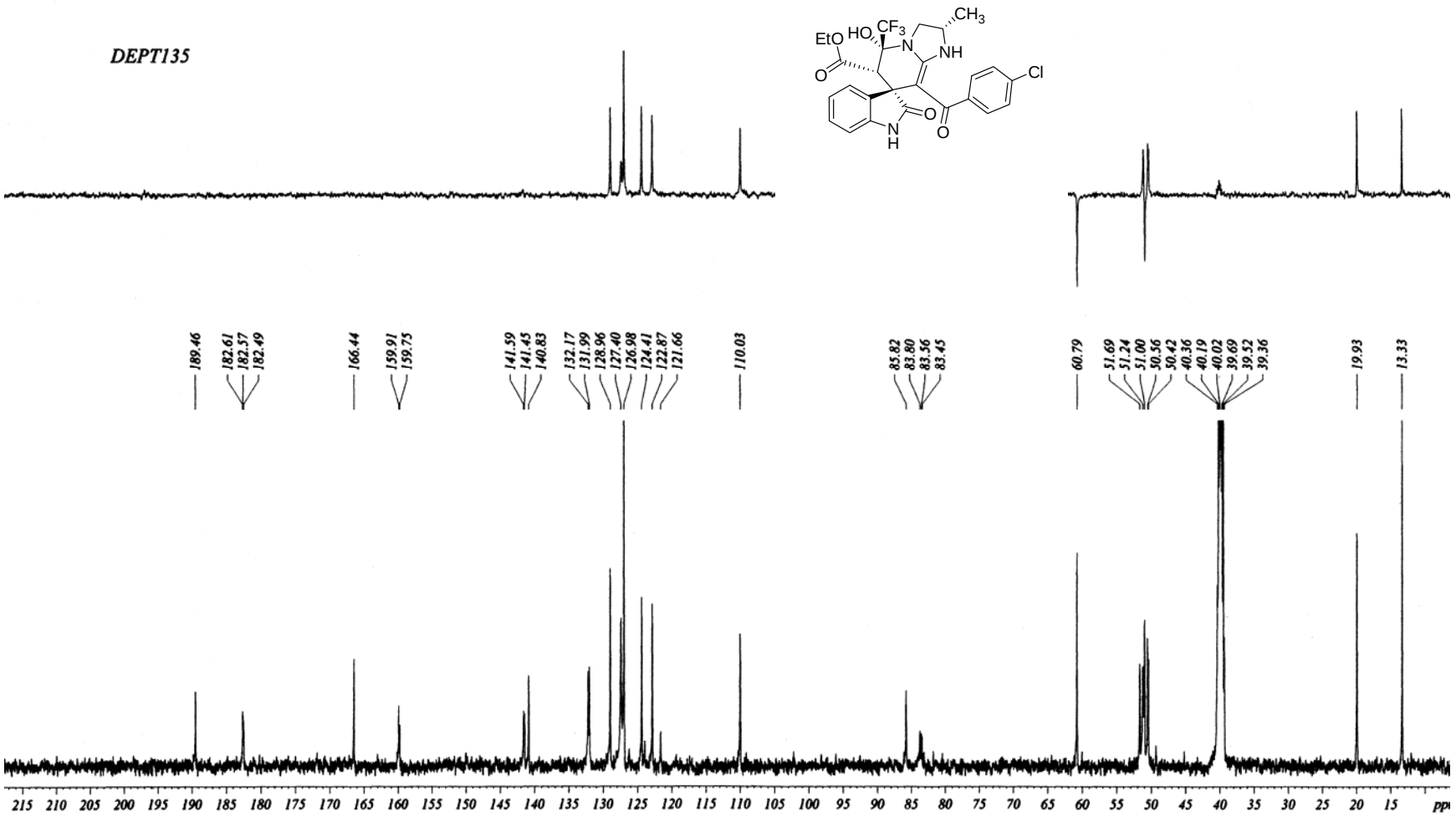


Figure 34. ^{13}C NMR (125 MHz, DMSO-d_6 + $HClO_4$) spectra of compound **5o**

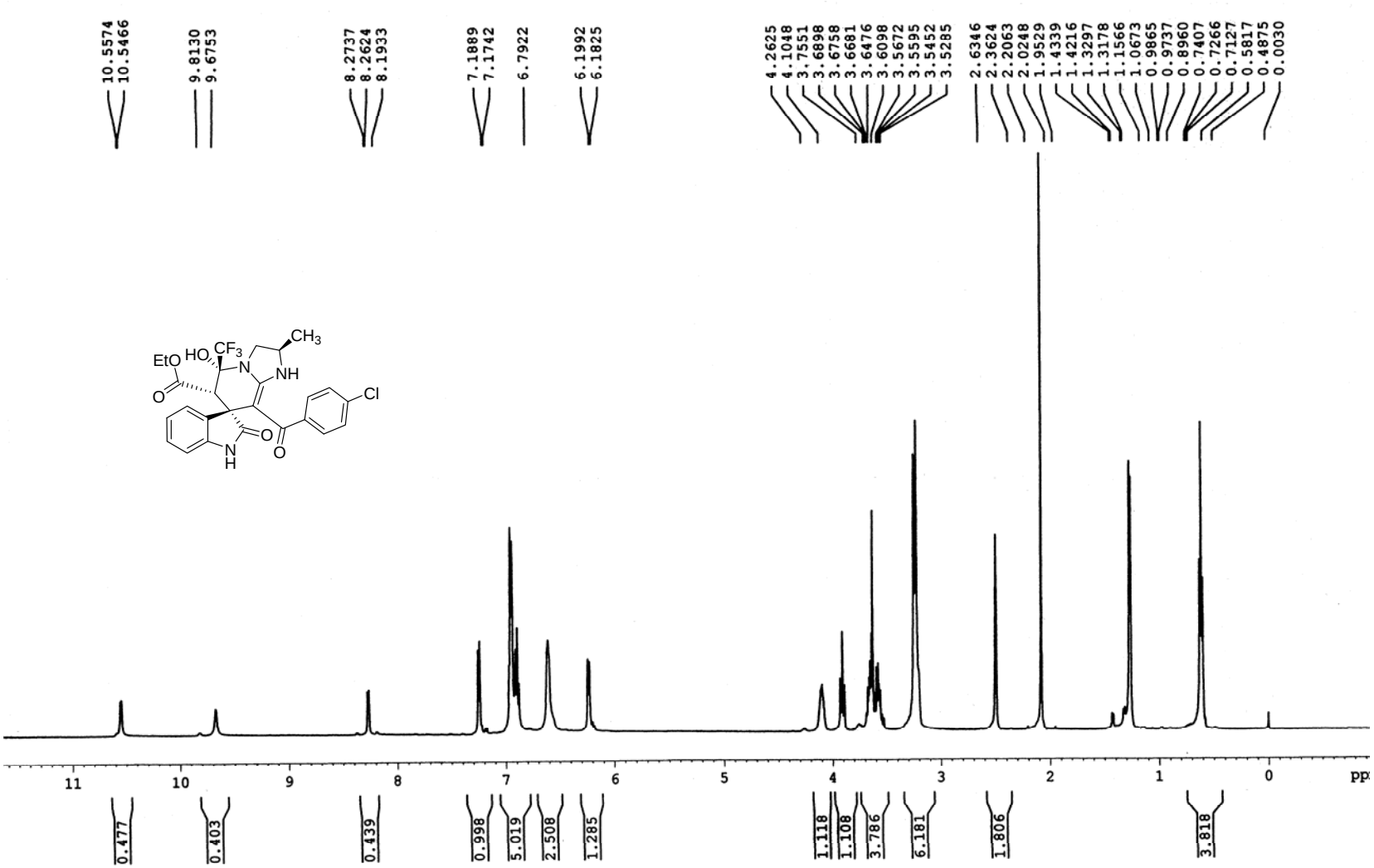


Figure 35. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5o'**

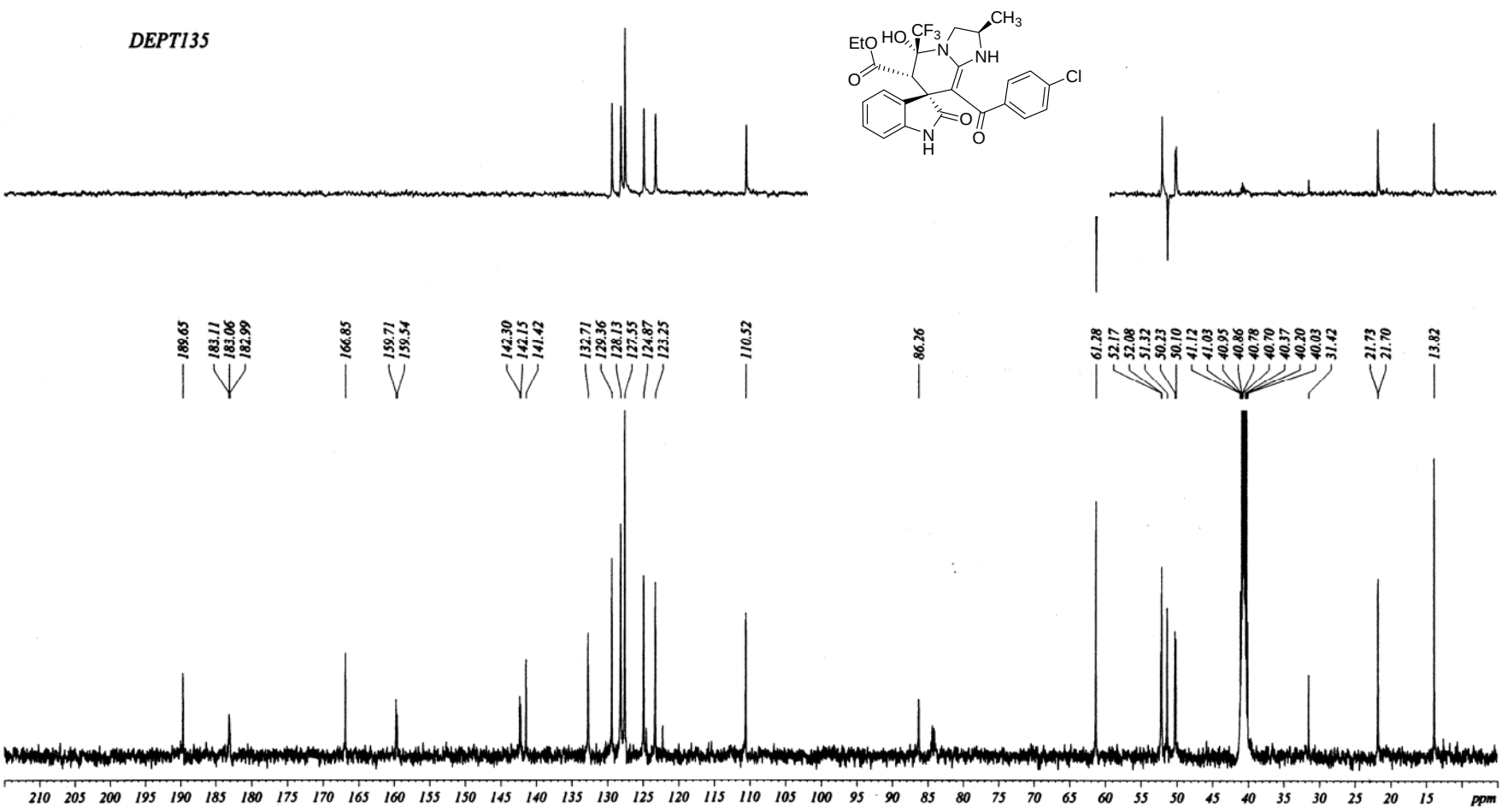


Figure 36. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5o'**

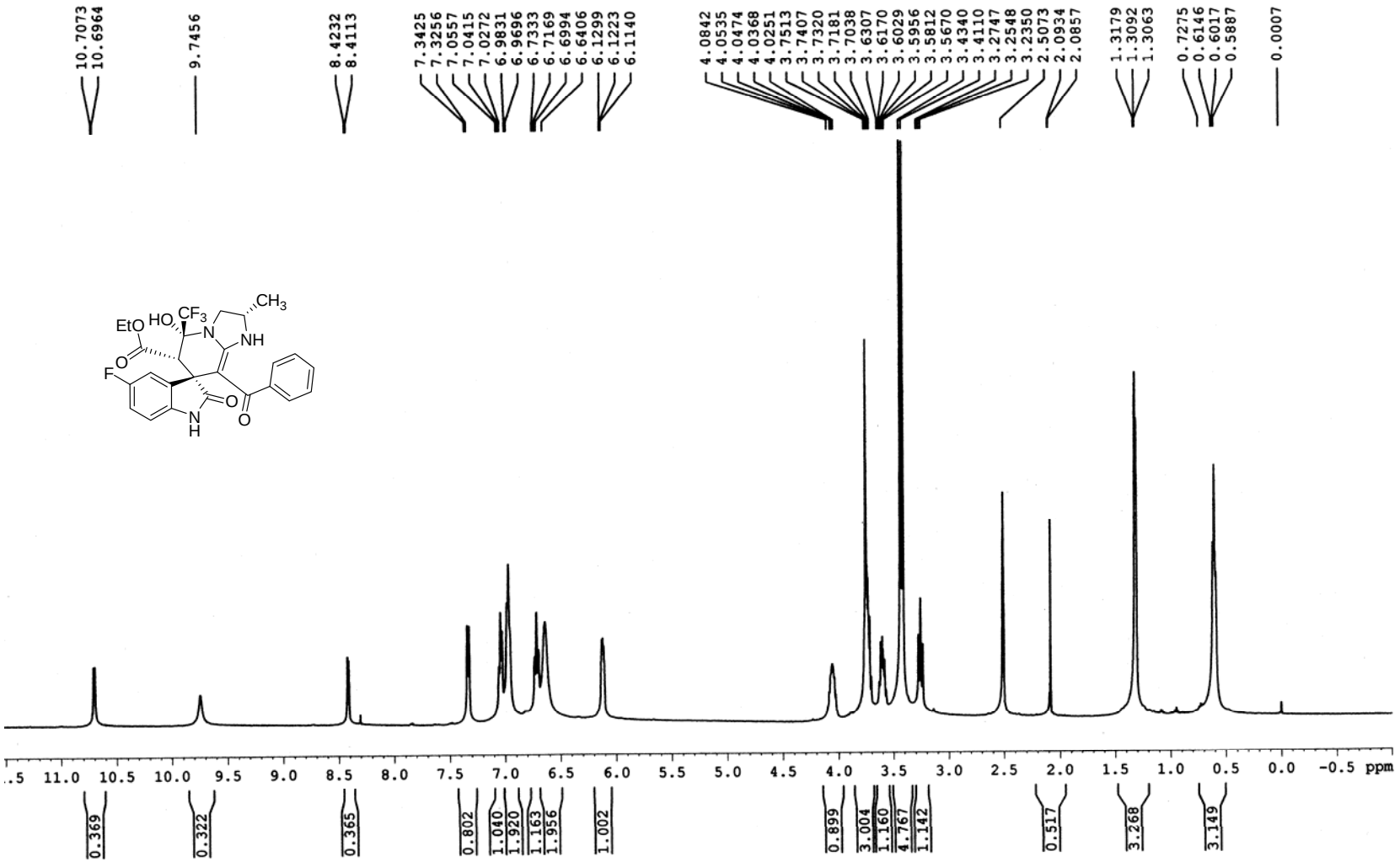


Figure 37. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5p**

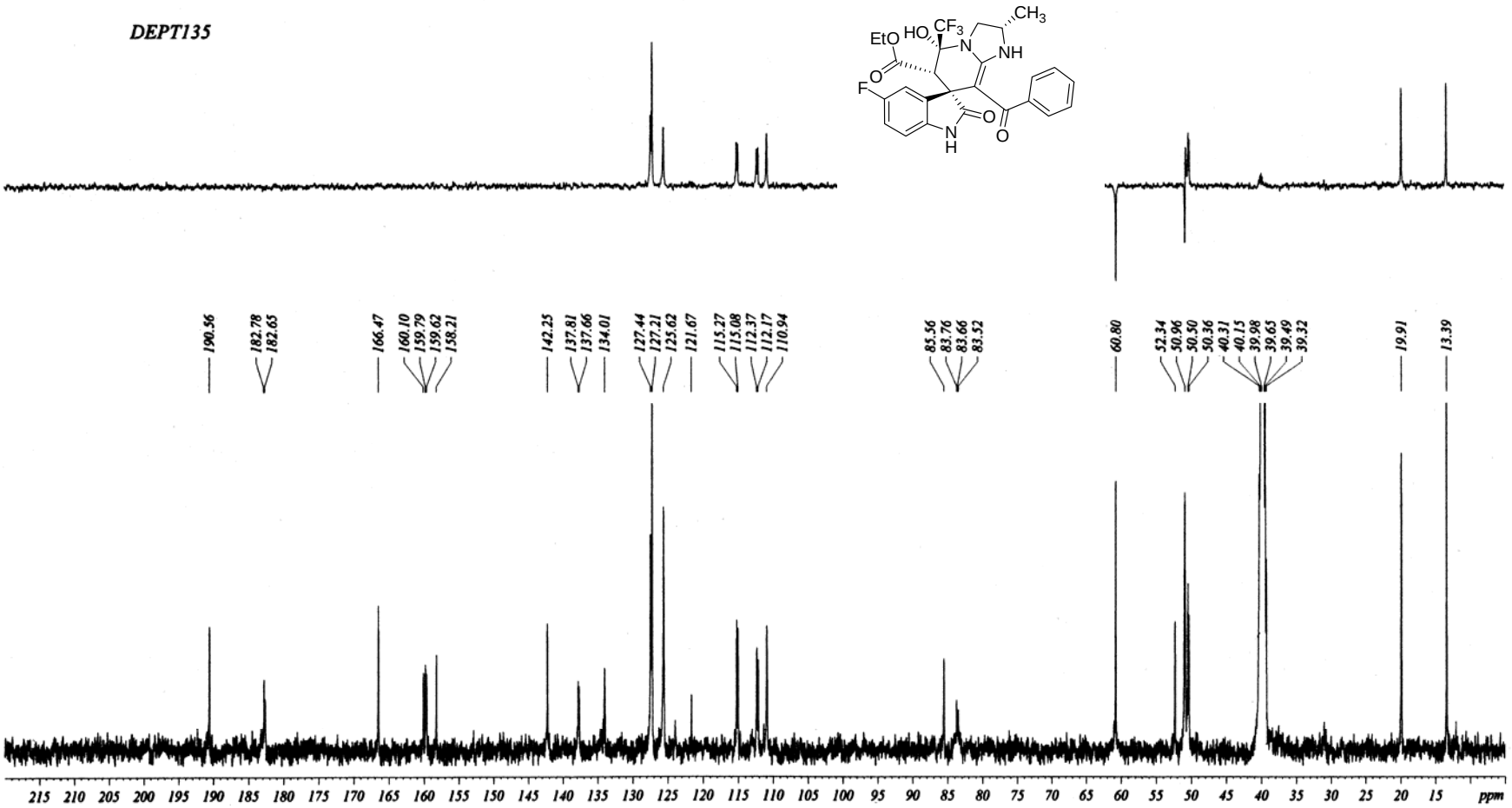


Figure 38. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5p**

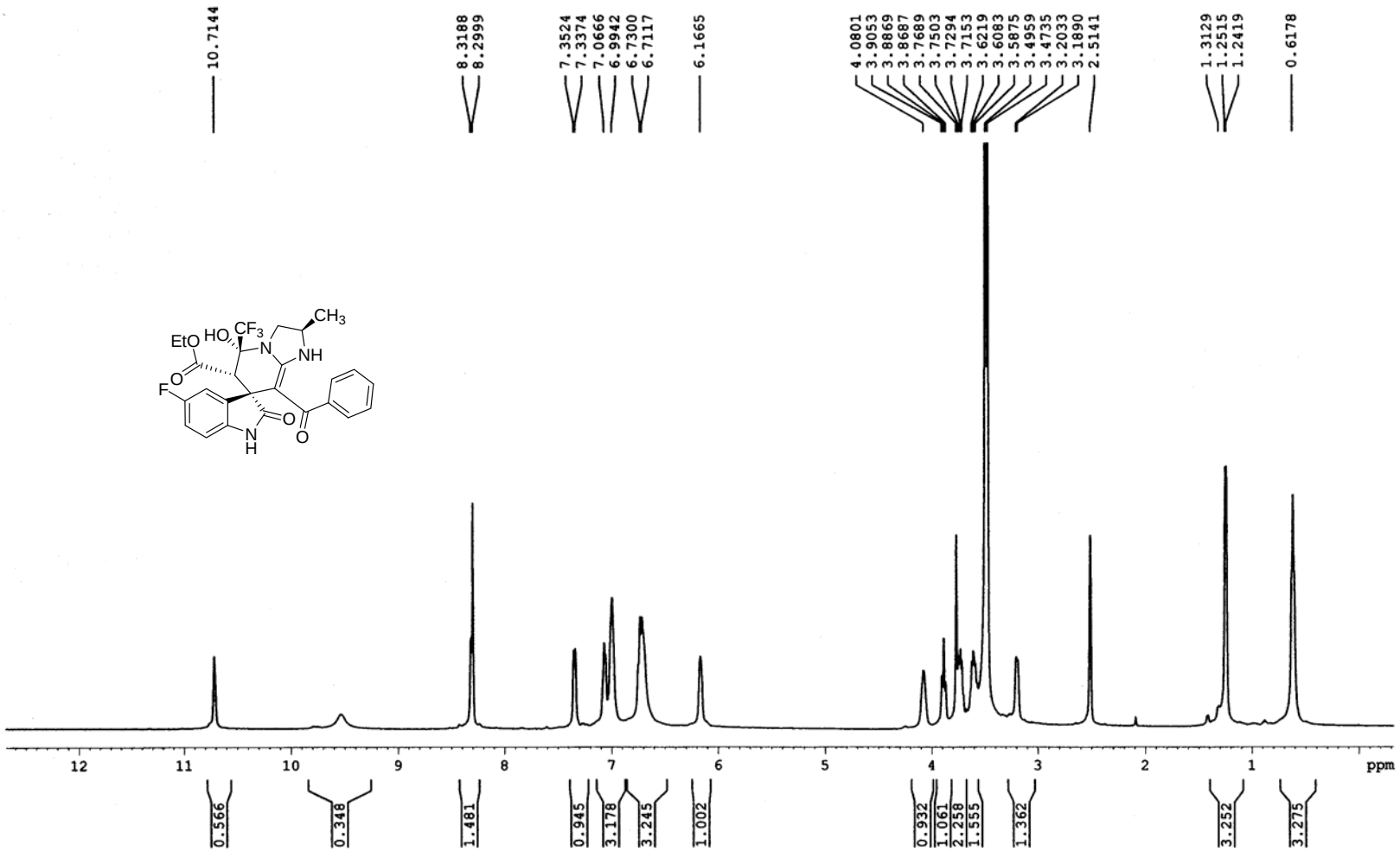


Figure 39. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5p'**

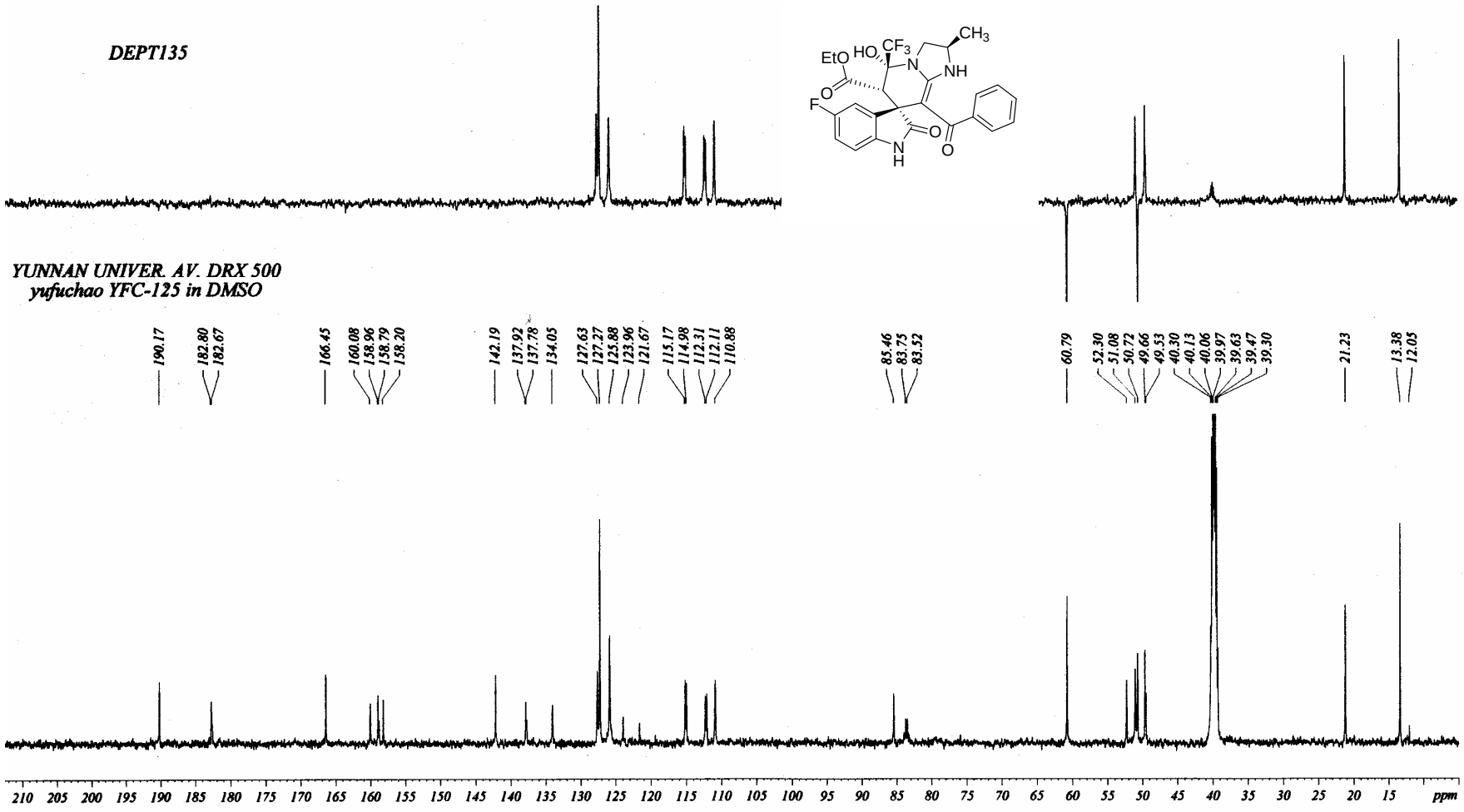


Figure 40. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5p'**

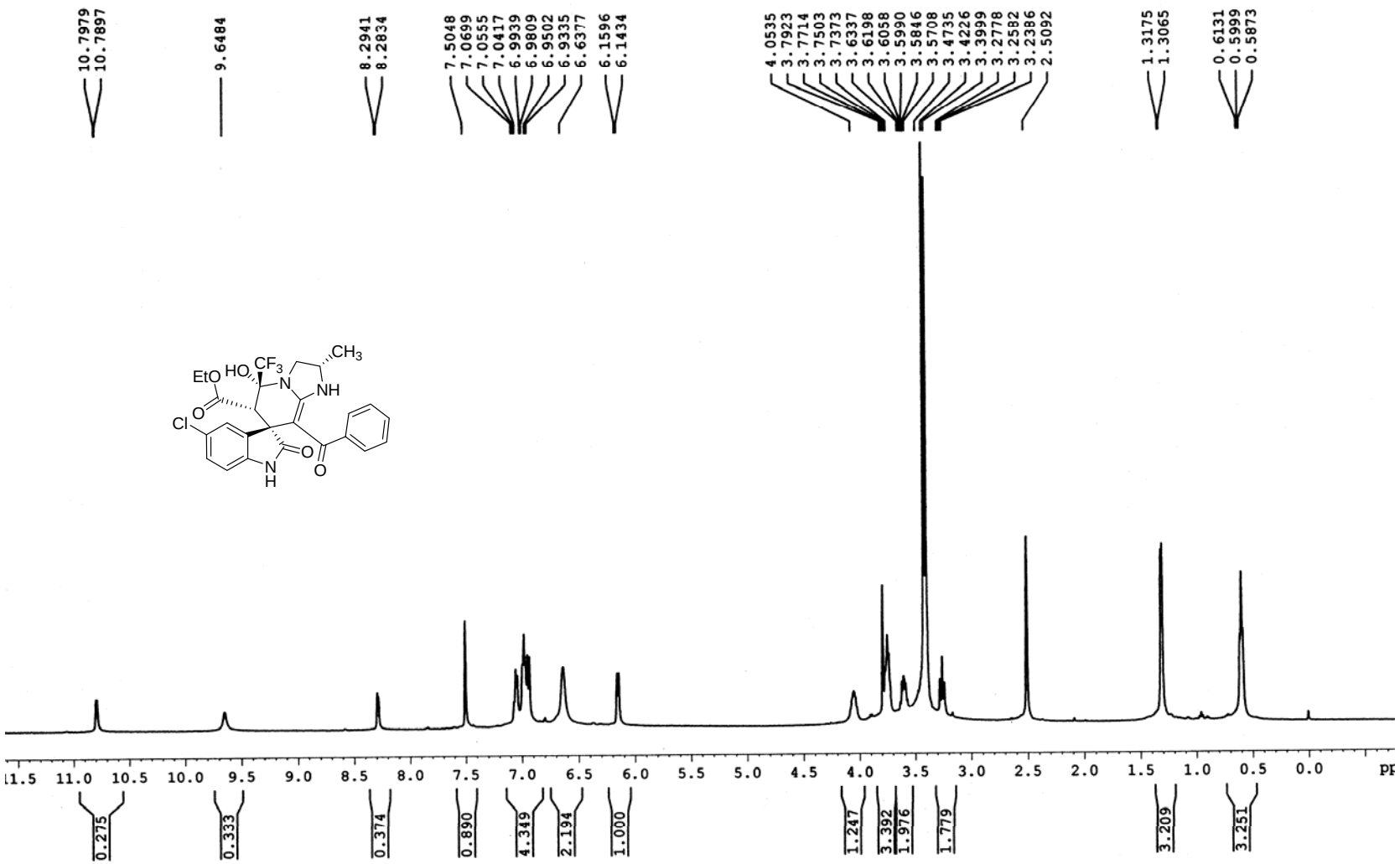


Figure 41. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5q**

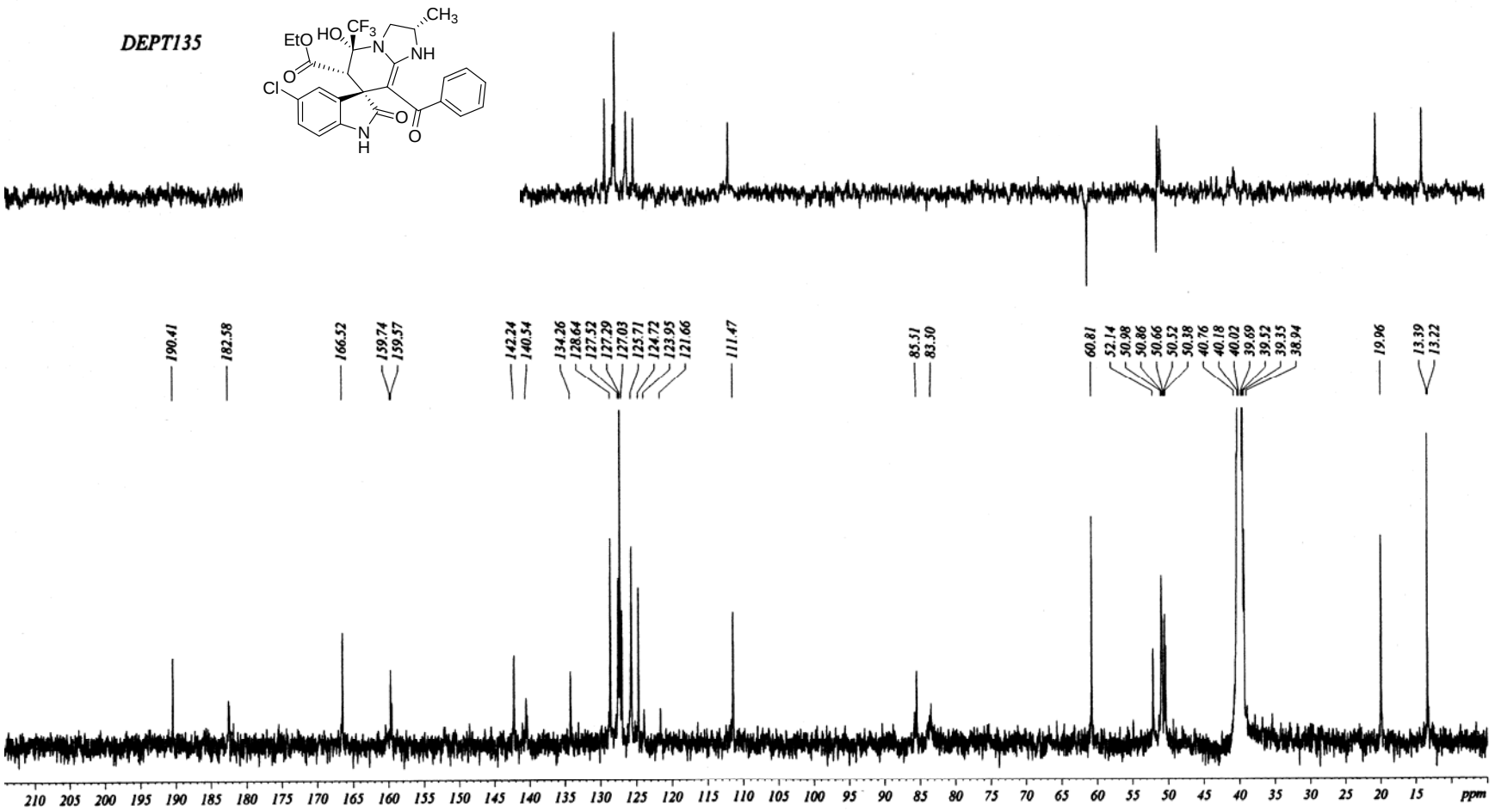


Figure 42. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5q**

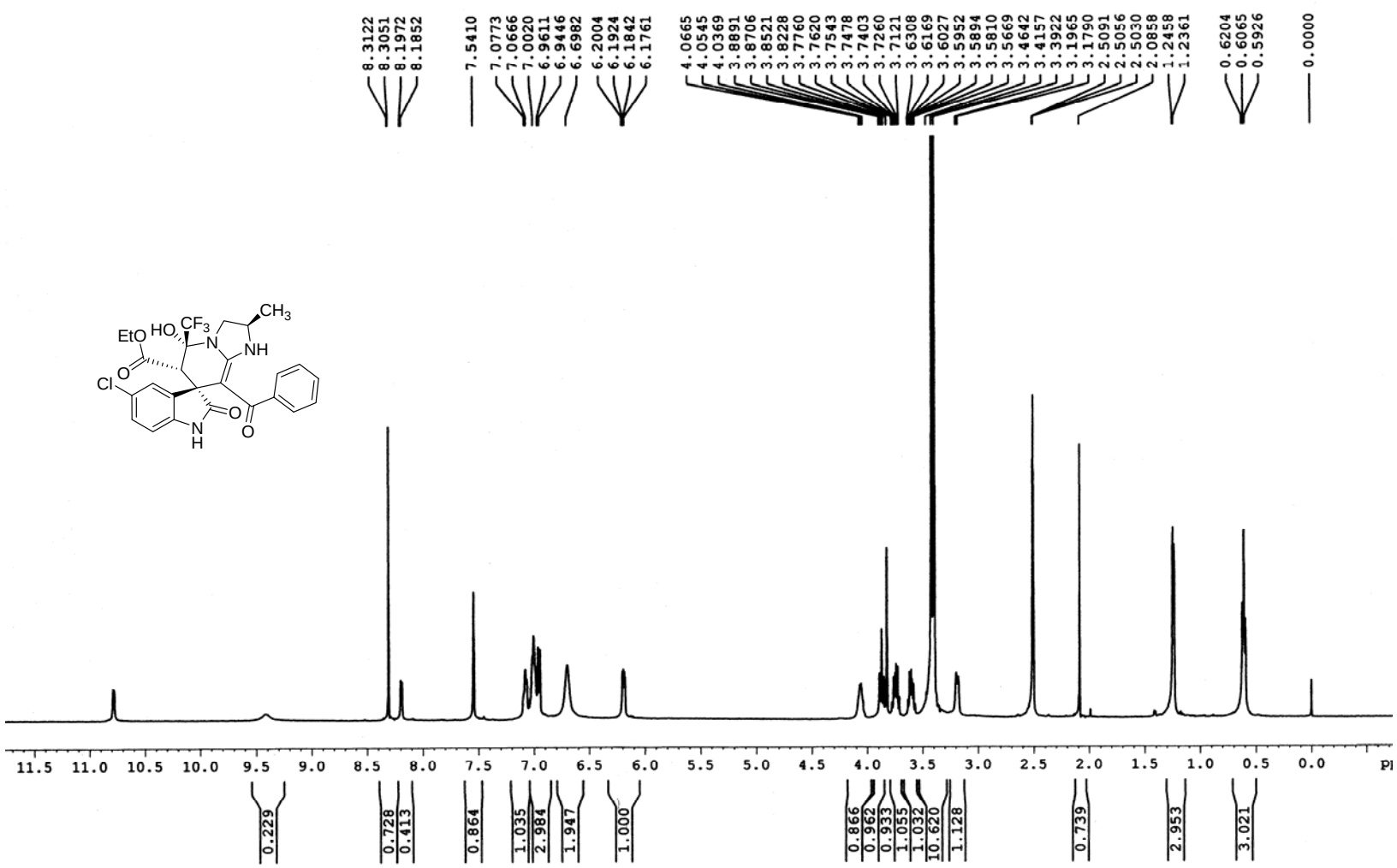


Figure 43. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5q'**

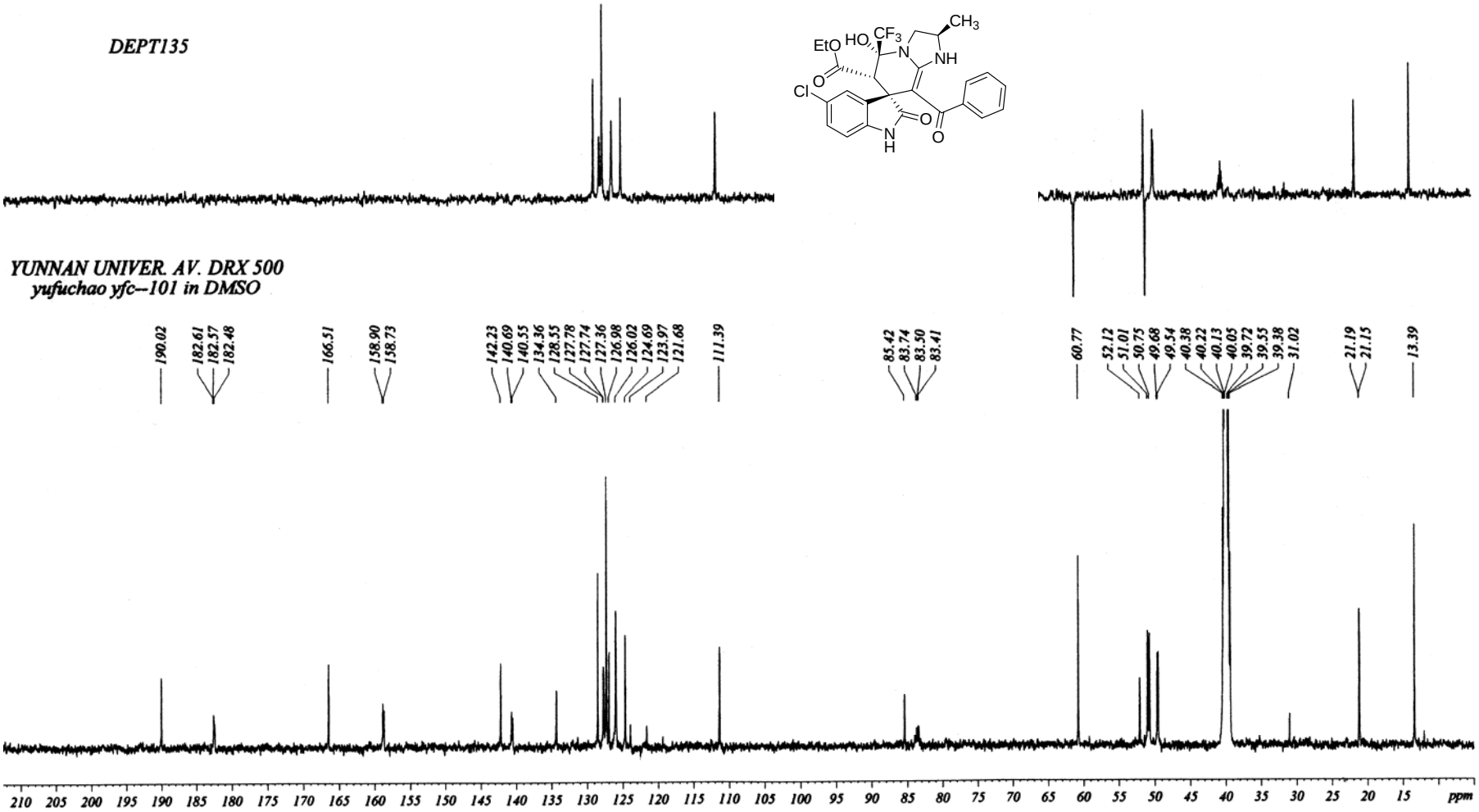


Figure 44. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5q'**

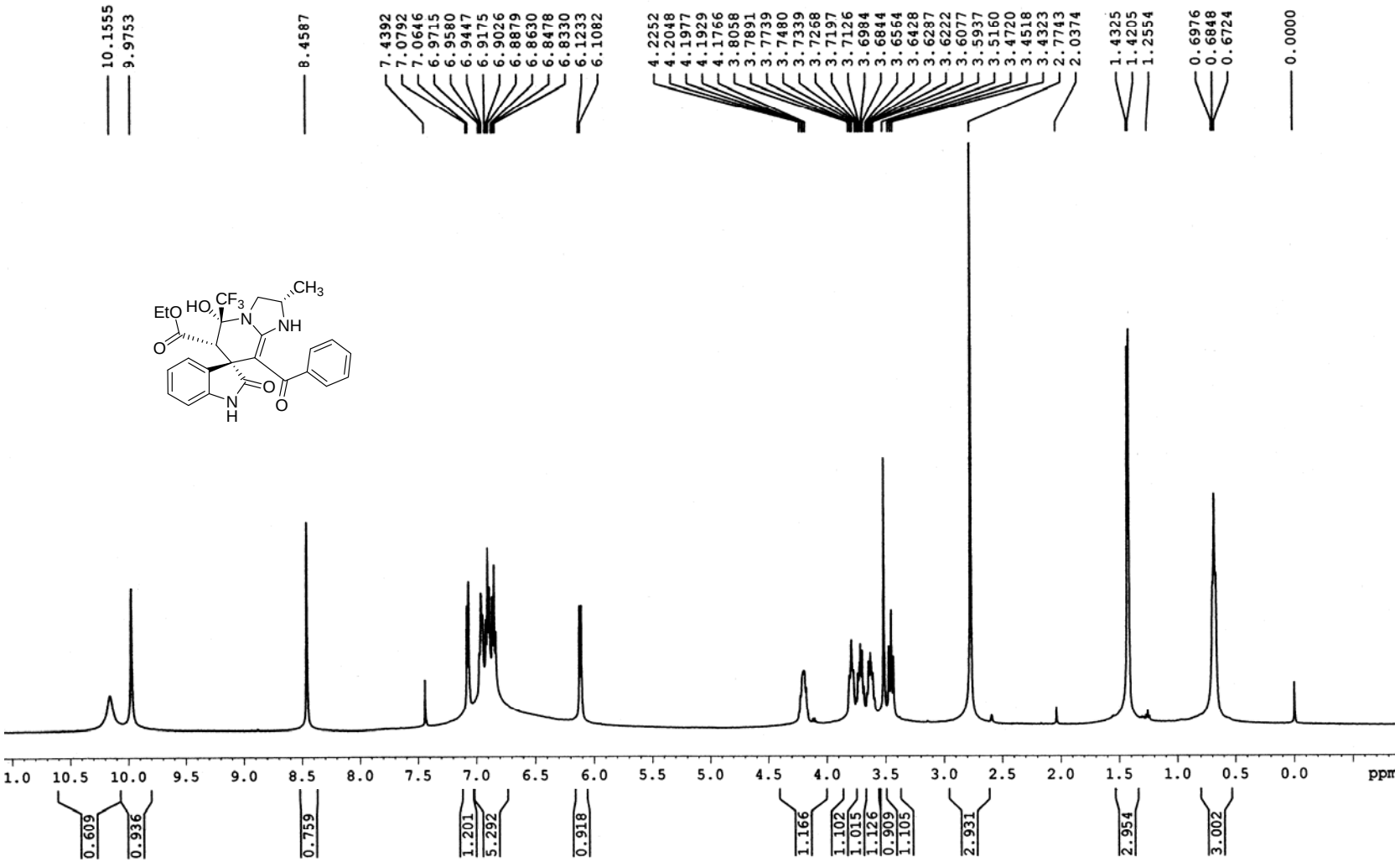


Figure 45. ^{1}H NMR (500 MHz, $CDCl_3$ + DMSO-d_6) spectra of compound **5r**

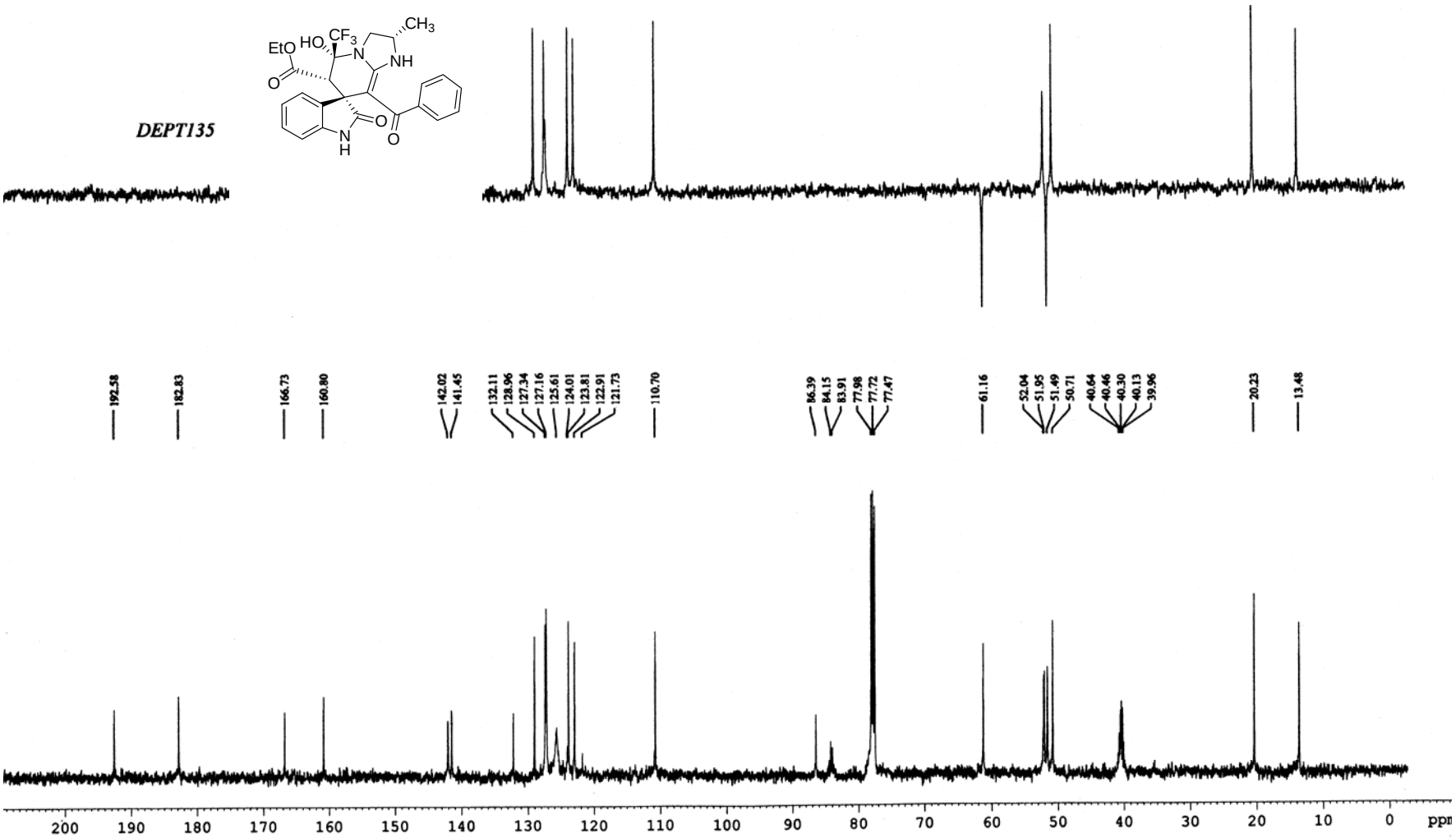


Figure 46. ^{13}C NMR (125 MHz, $CDCl_3$ + DMSO-d_6) spectra of compound **5r**

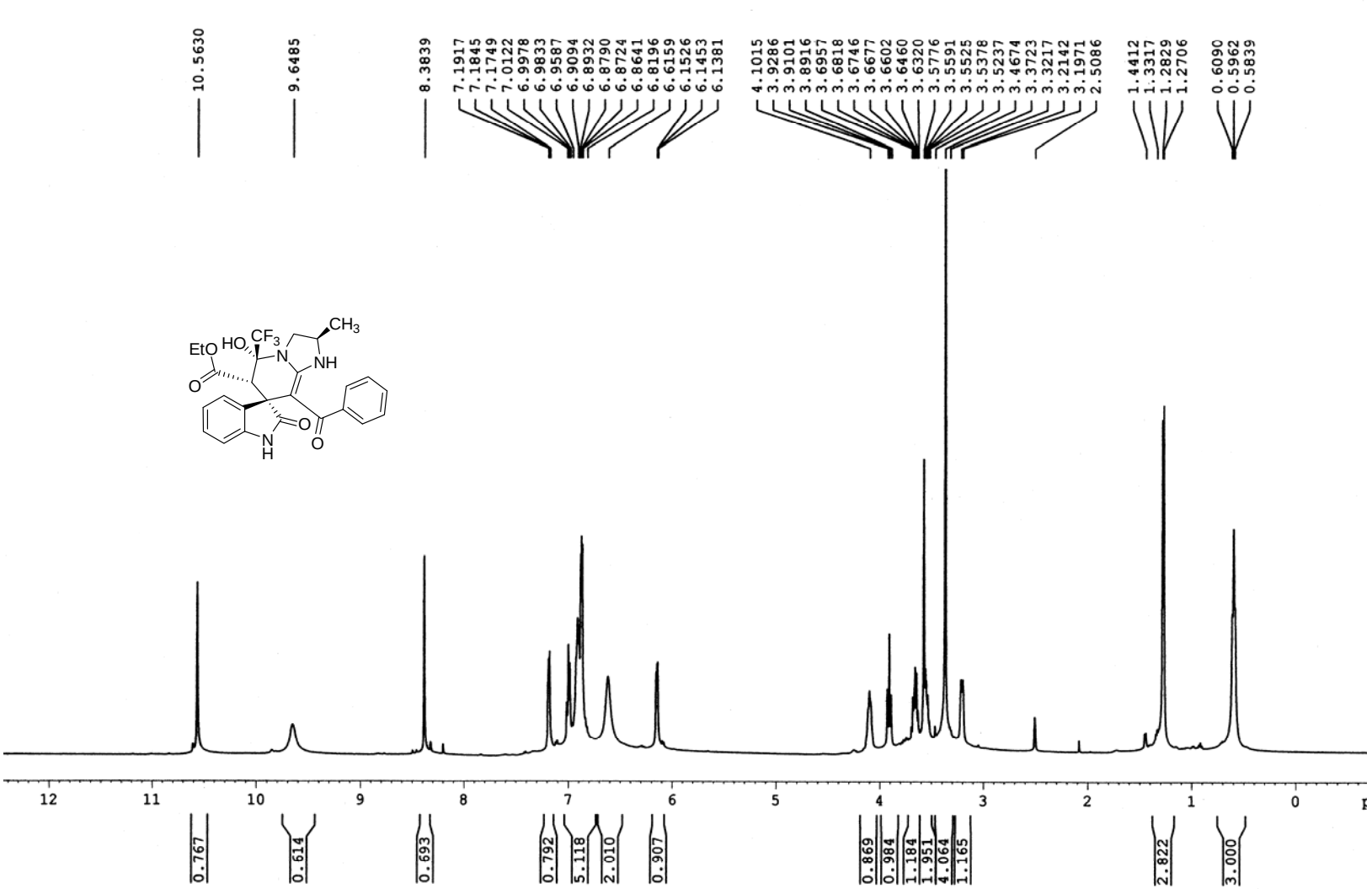


Figure 47. ^{1}H NMR (500 MHz, $CDCl_3$ + DMSO-d_6) spectra of compound **5r'**

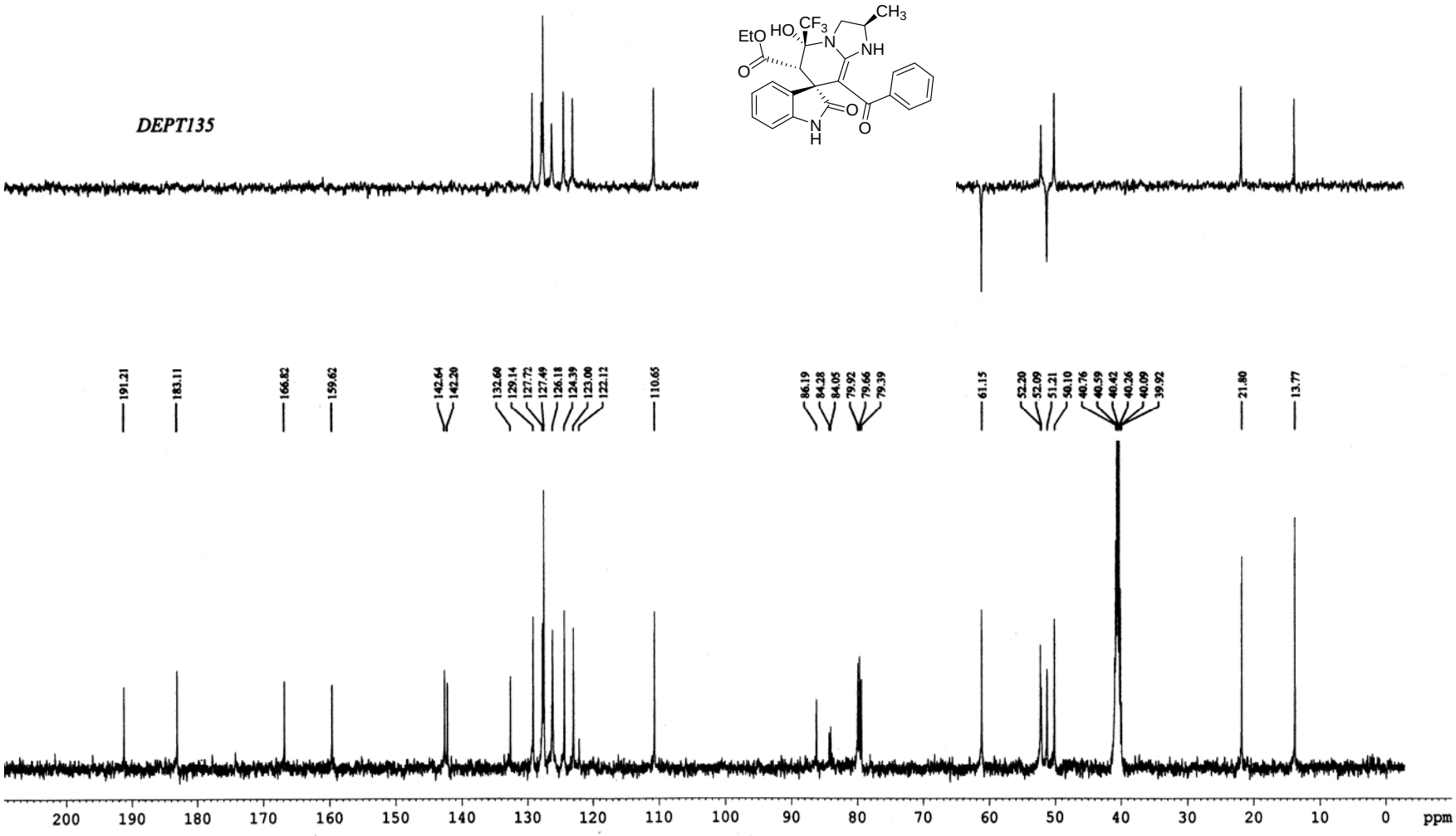


Figure 48. ^{13}C NMR (125 MHz, $CDCl_3$ + DMSO-d_6) spectra of compound **5r'**

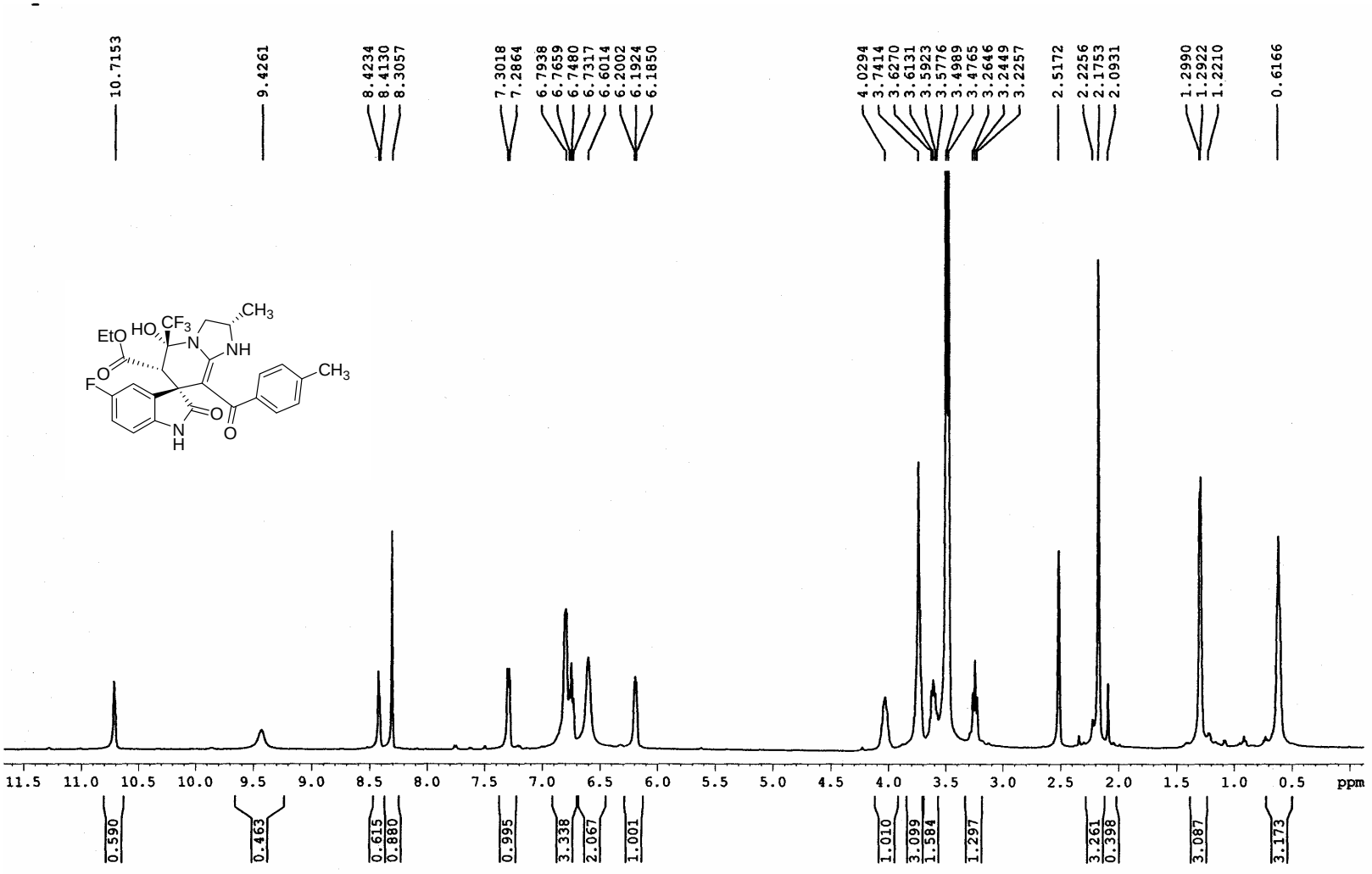


Figure 49. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5s**

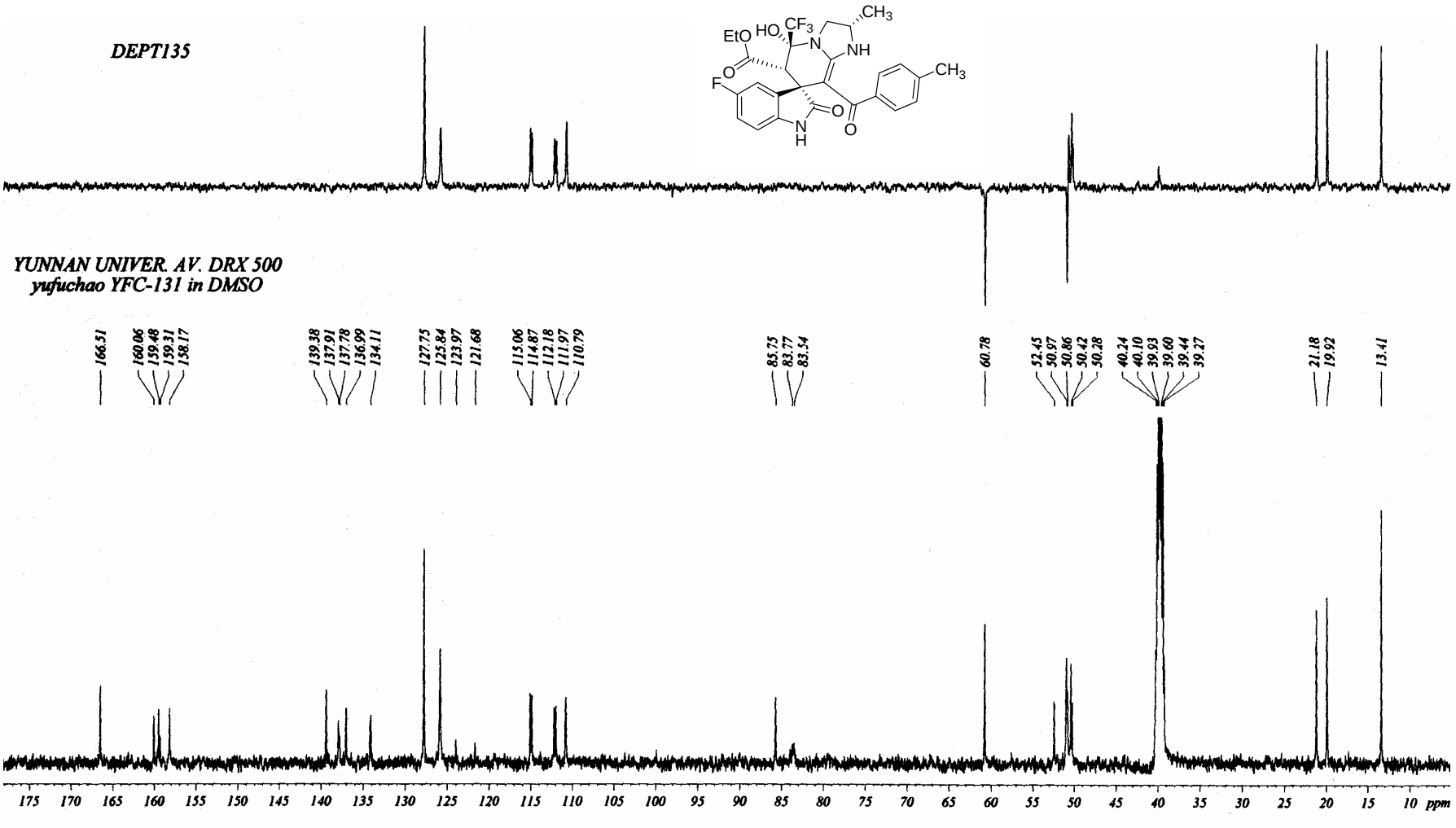


Figure 50. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5s**

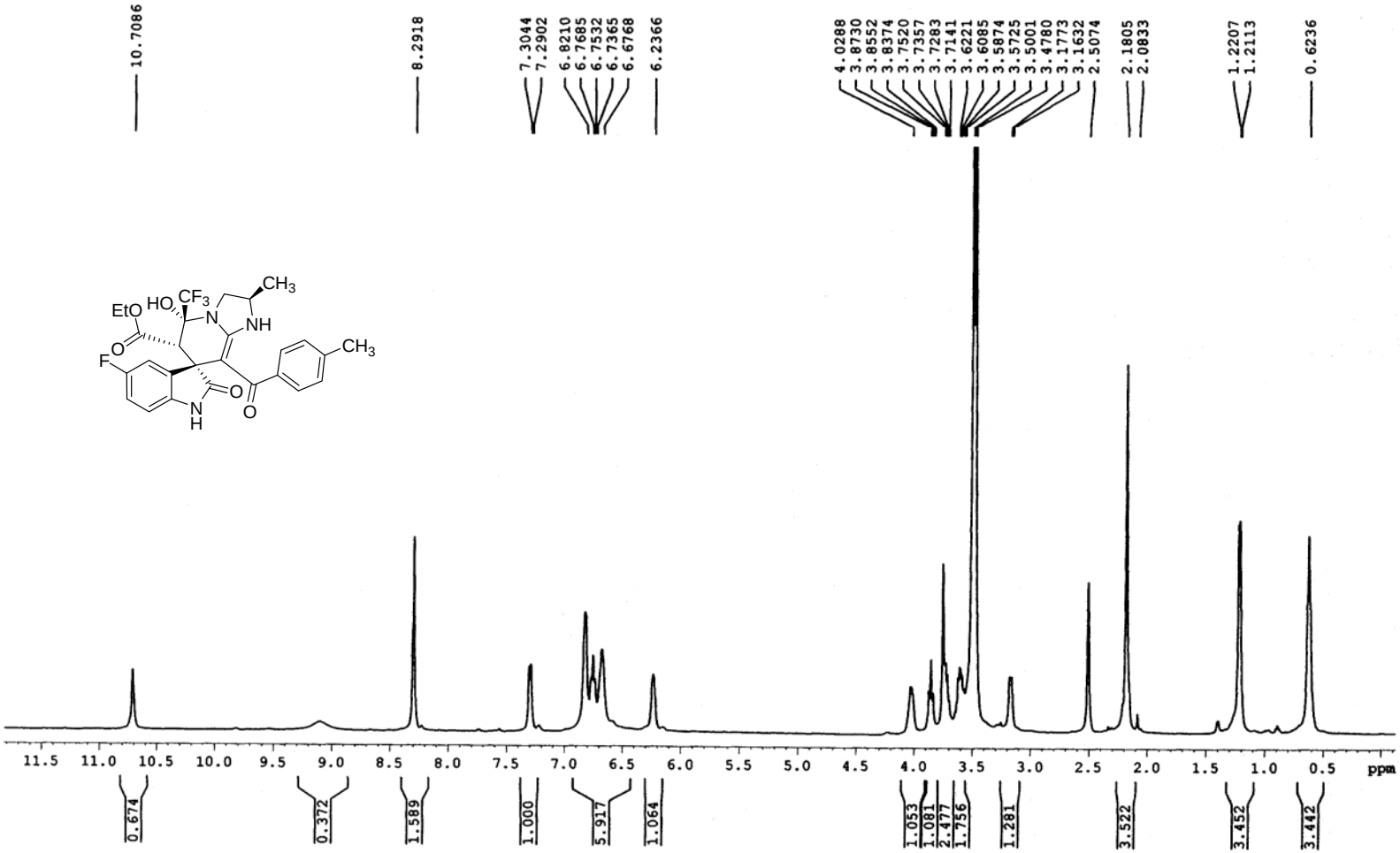


Figure 51. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5s'**

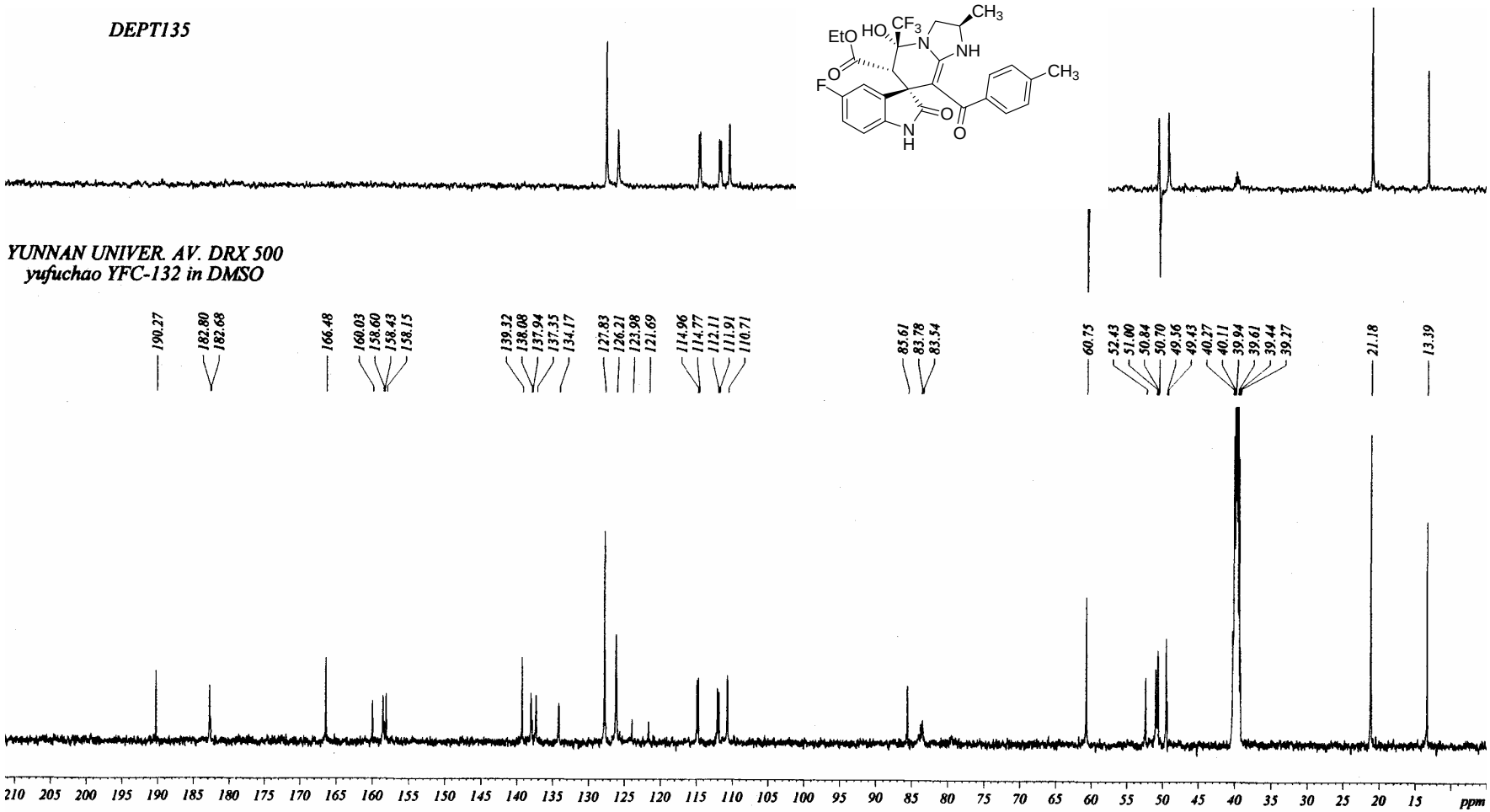


Figure 52. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5s'**

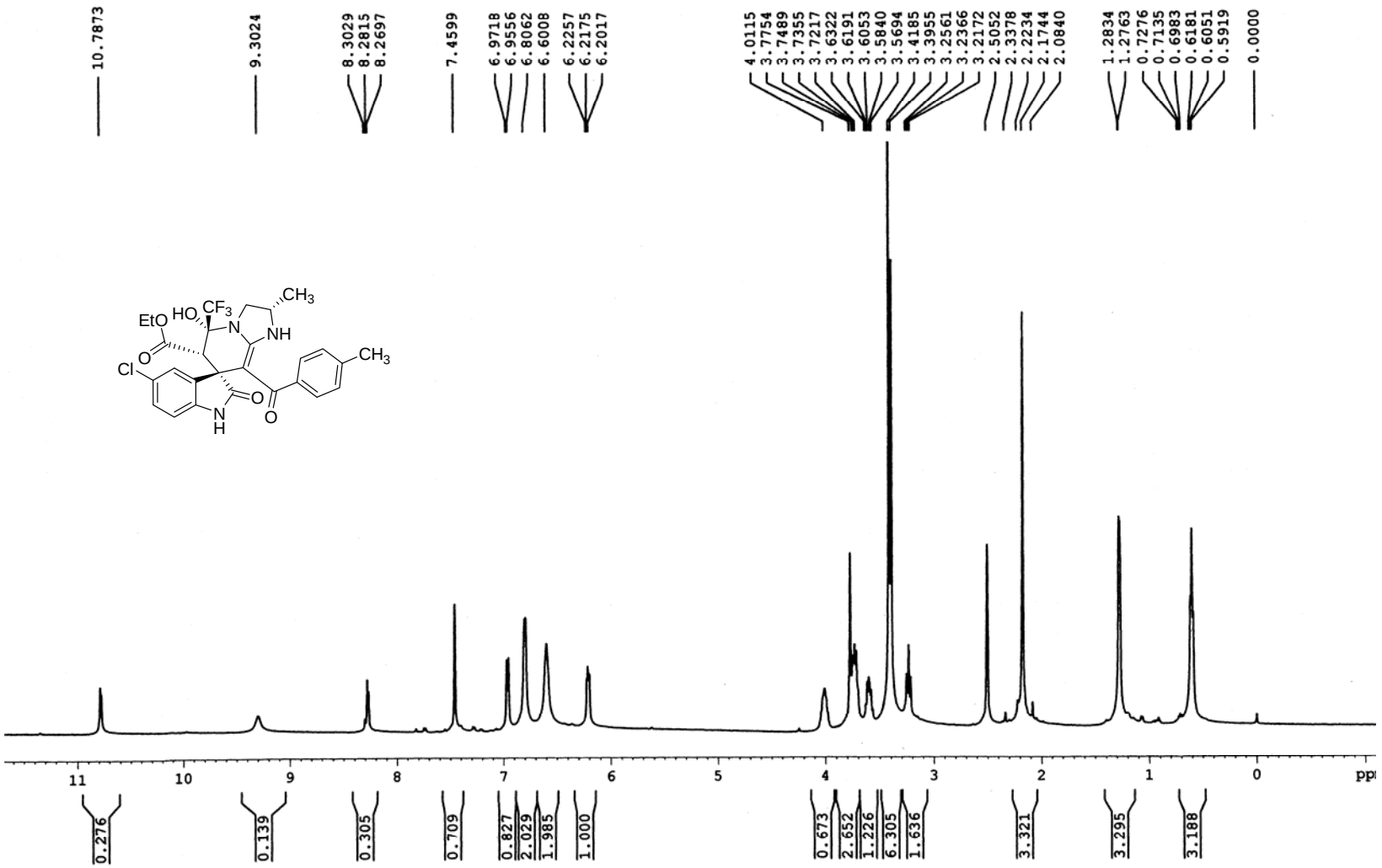


Figure 53. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5t**

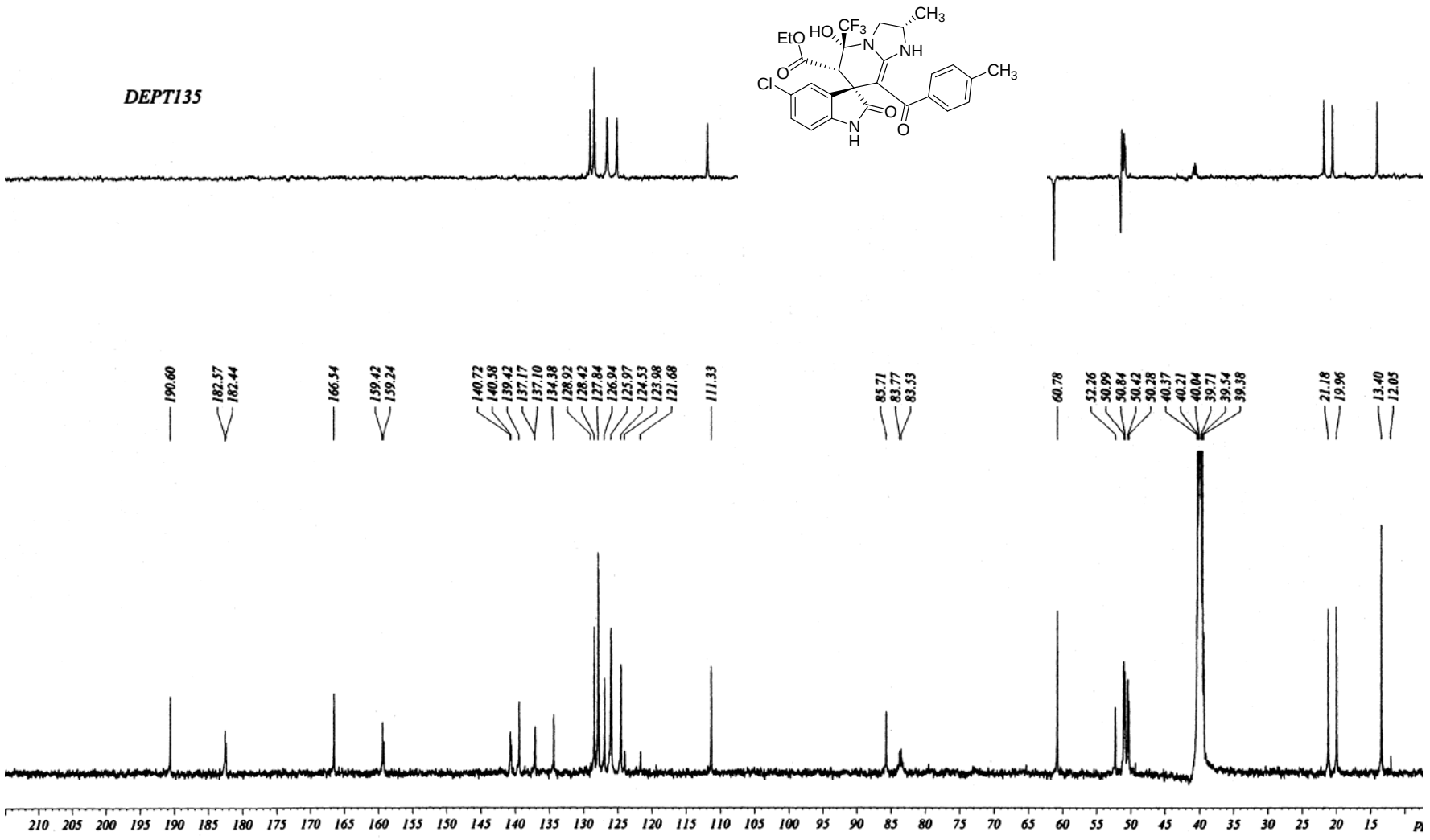


Figure 54. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5t**

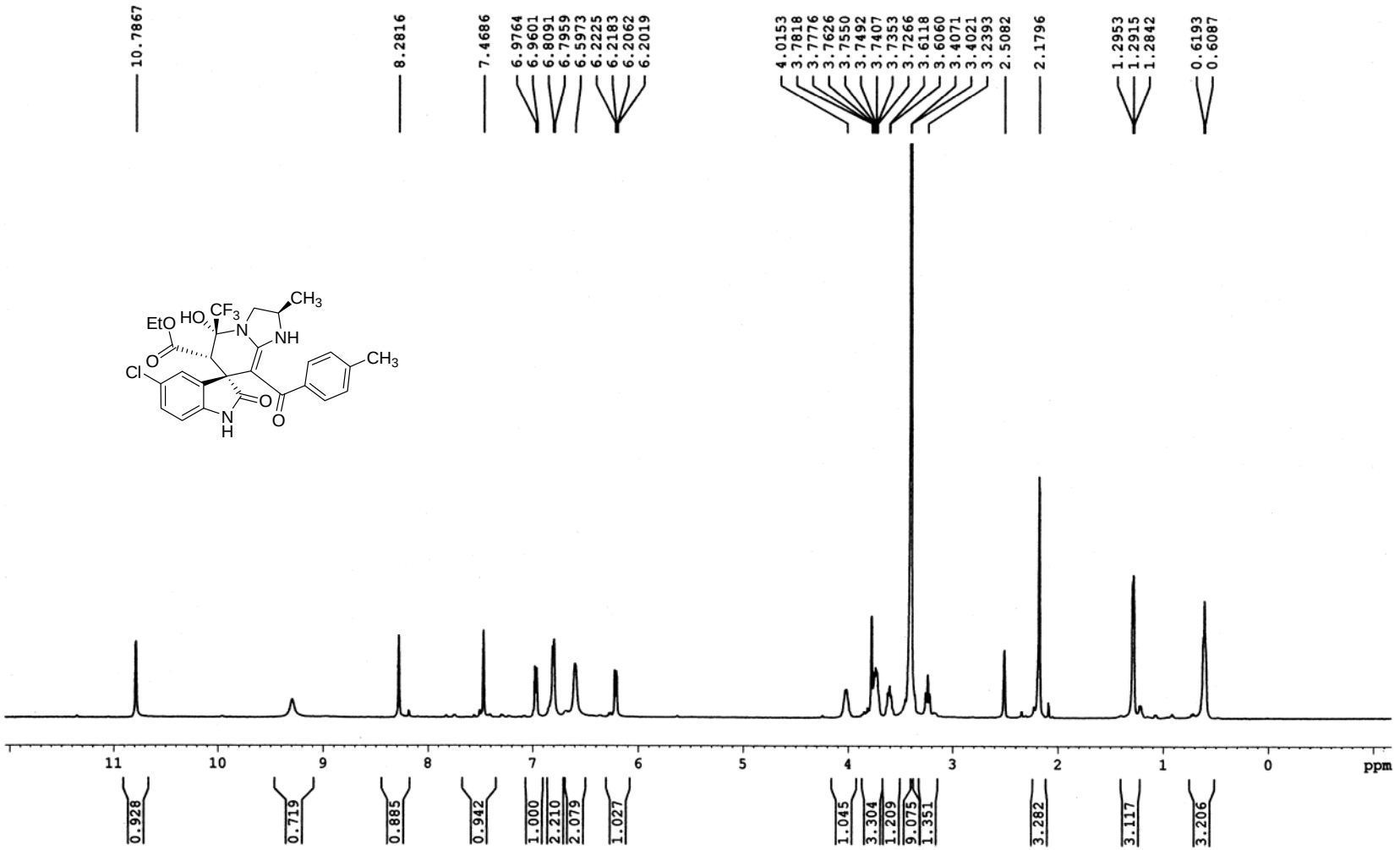


Figure 55. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5t'**

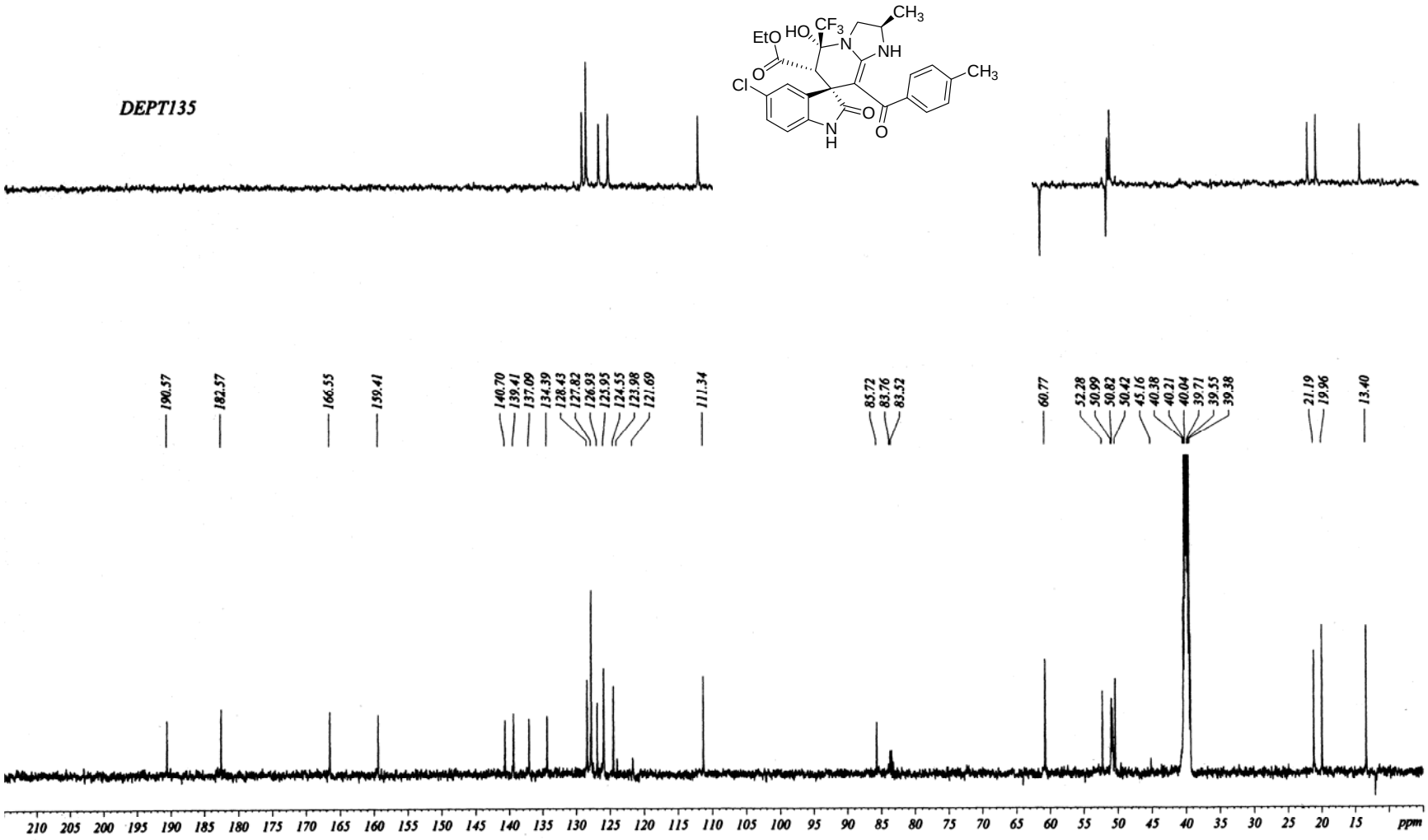


Figure 56. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5t'**

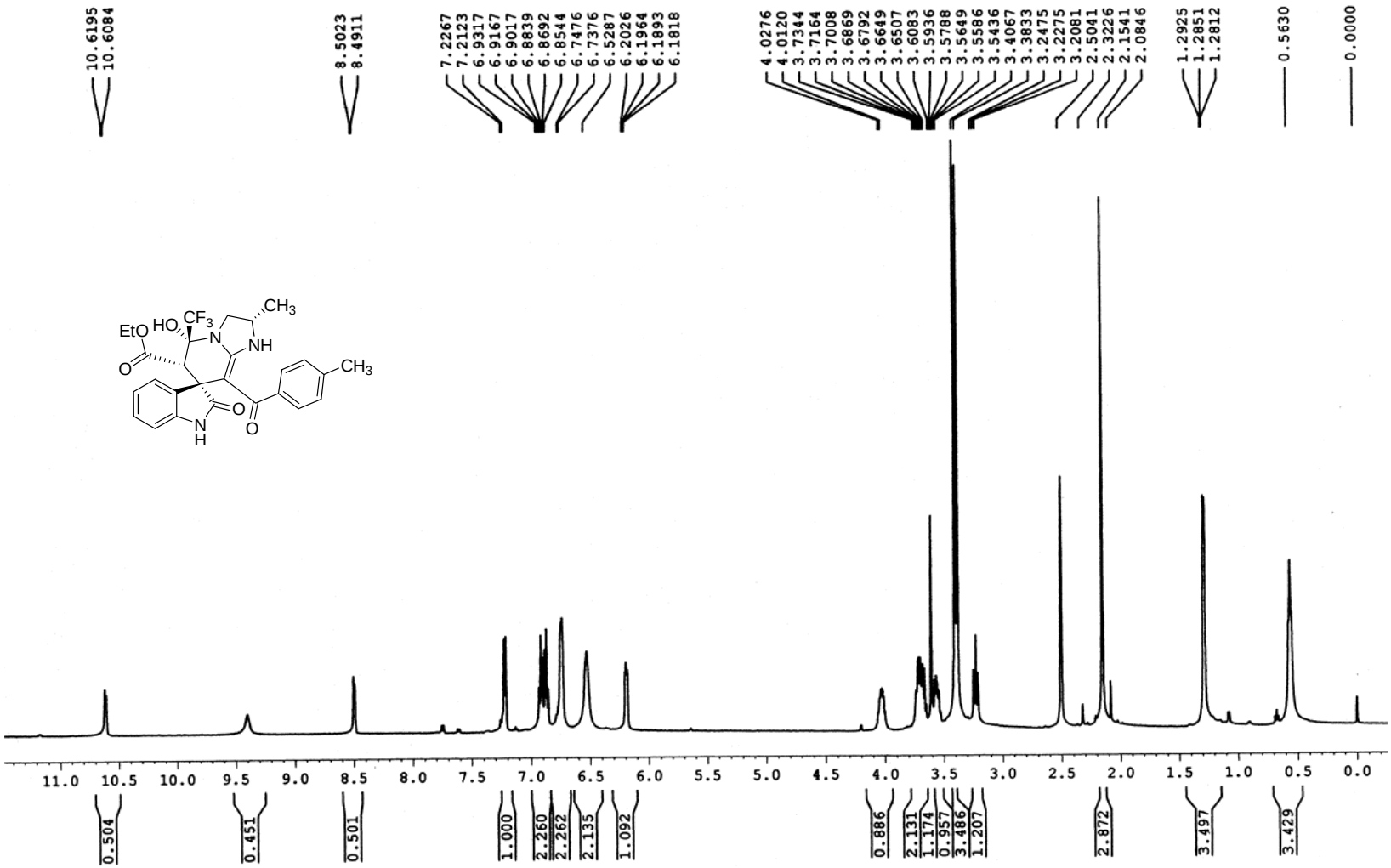


Figure 57. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5u**

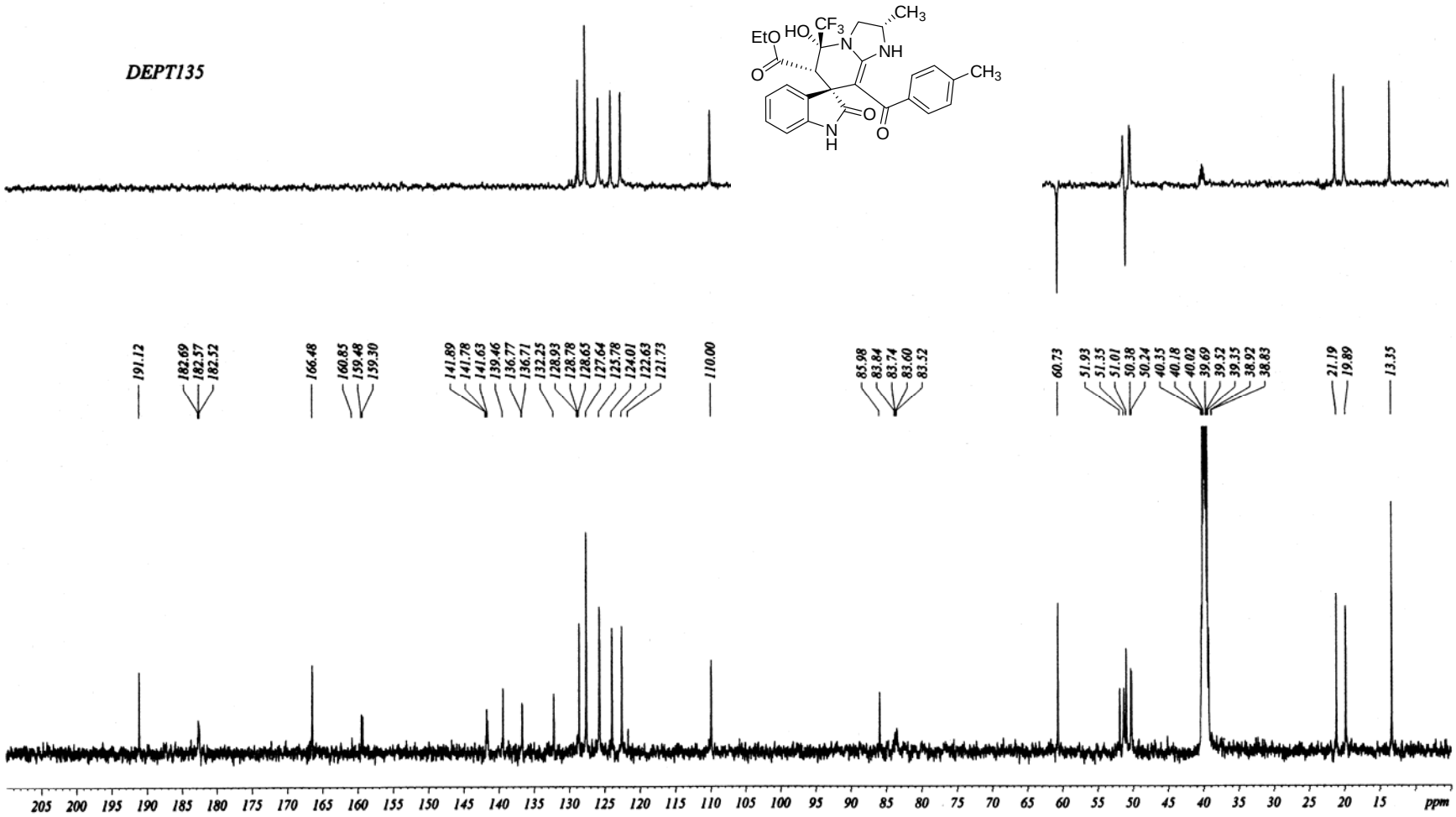


Figure 58. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5u**

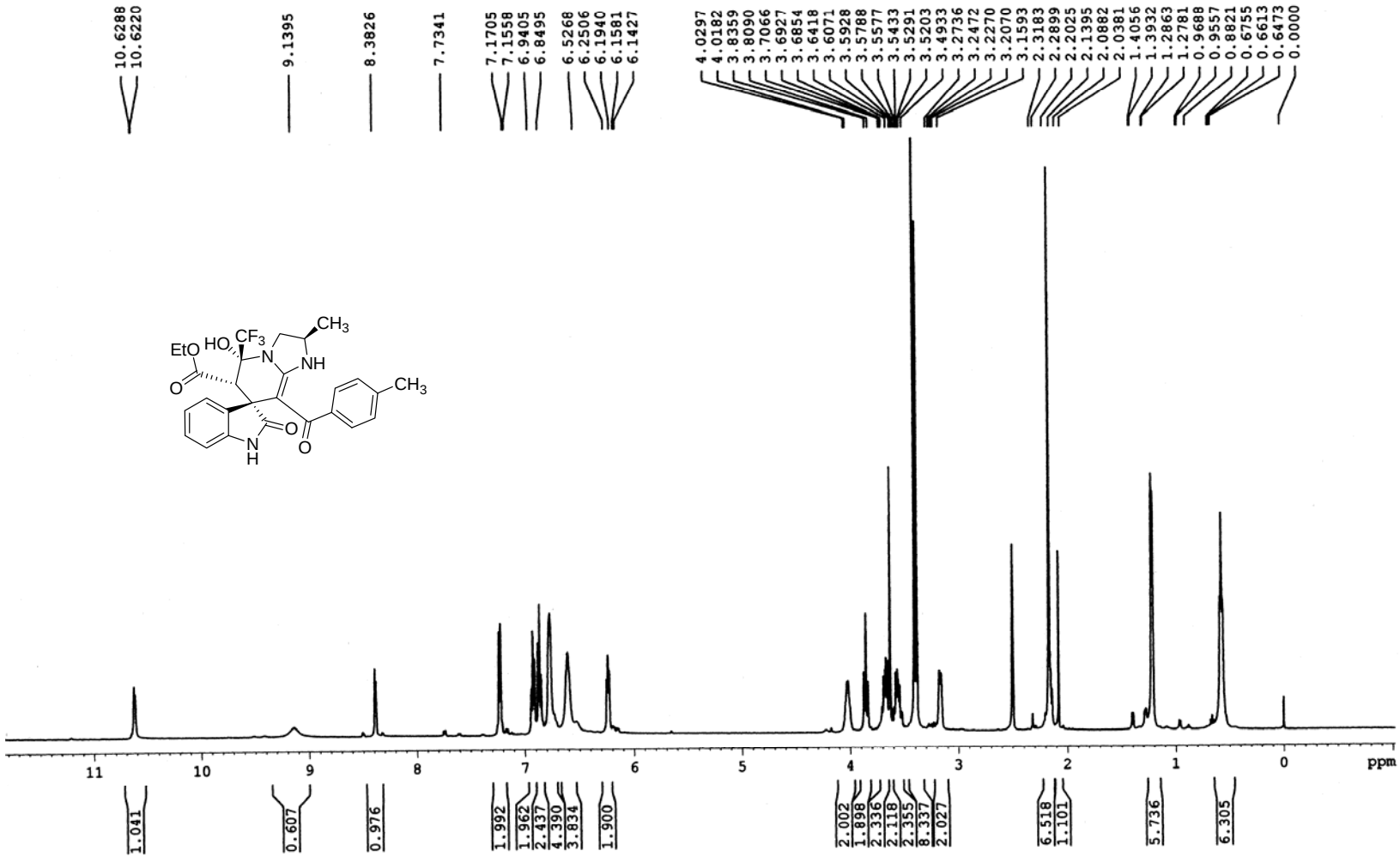


Figure 59. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5u'**

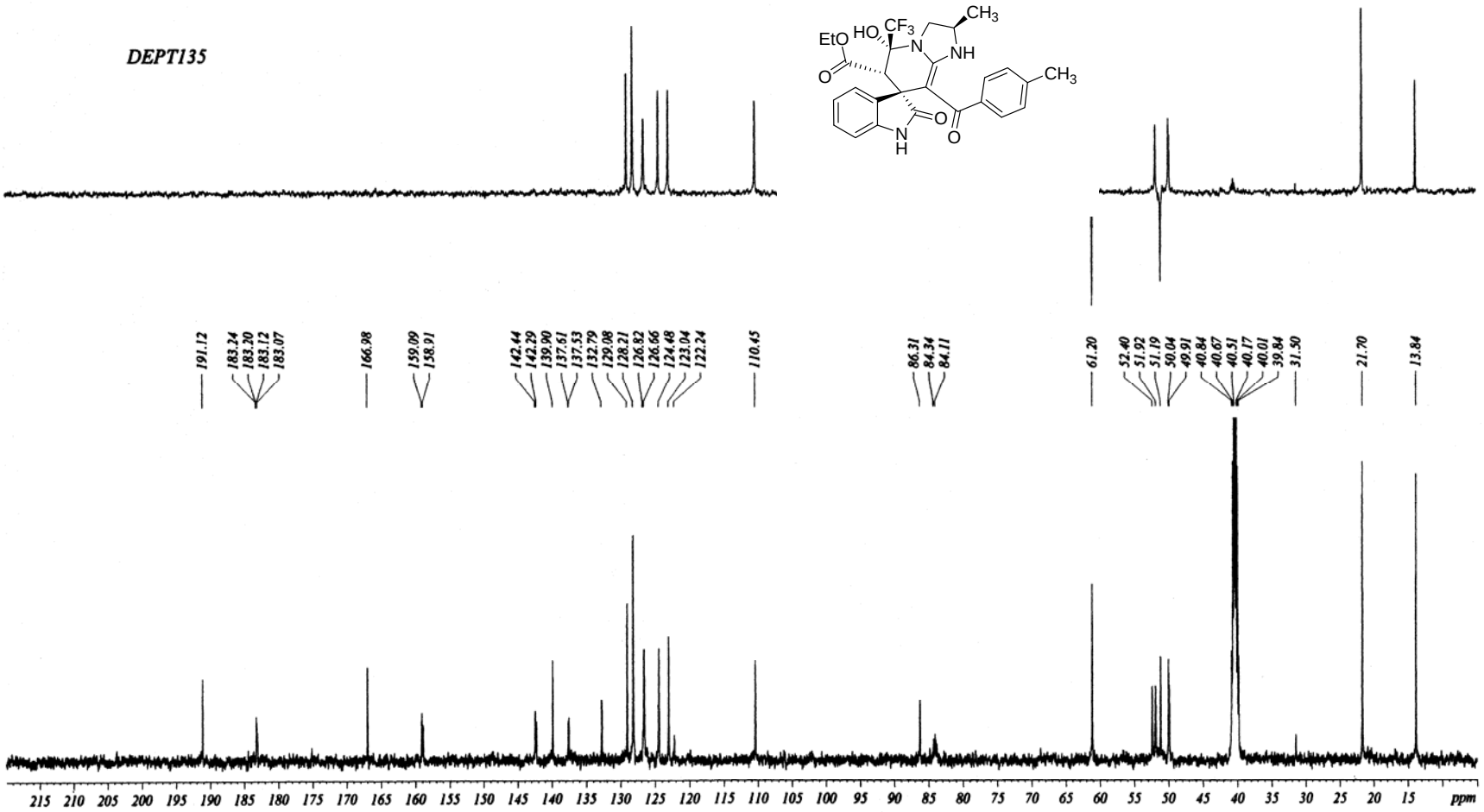


Figure 60. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5u'**

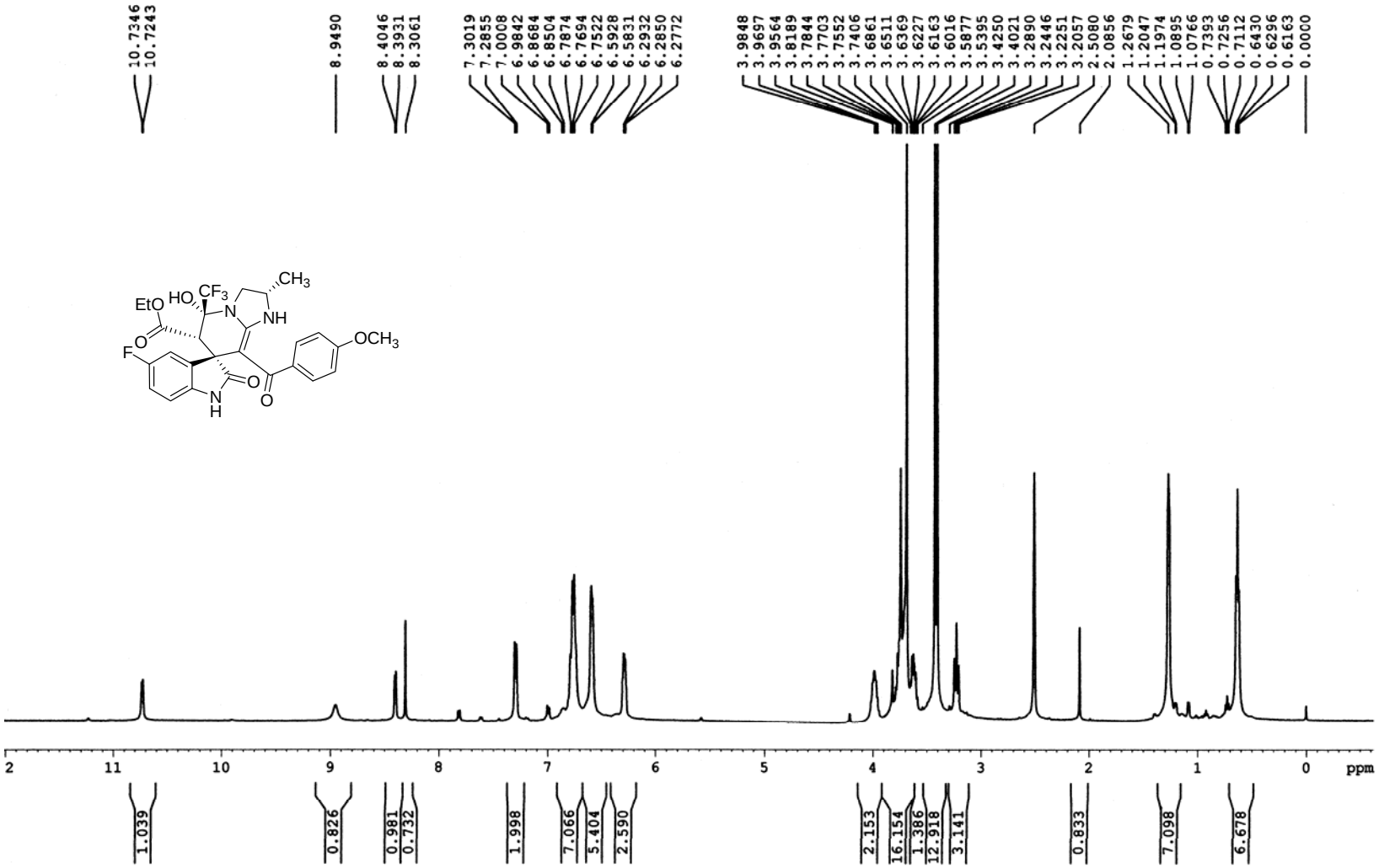


Figure 61. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5v**

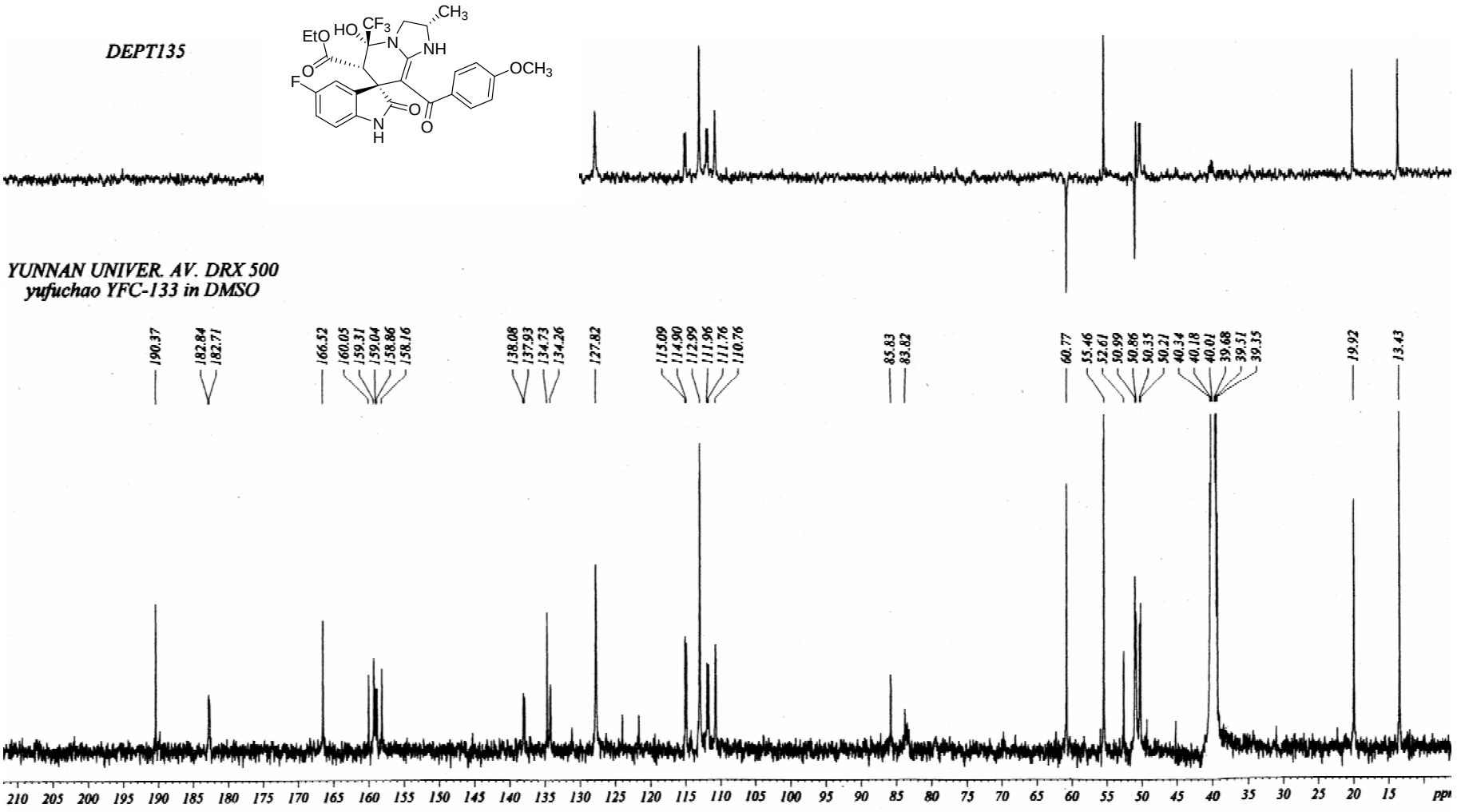


Figure 62. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5v**

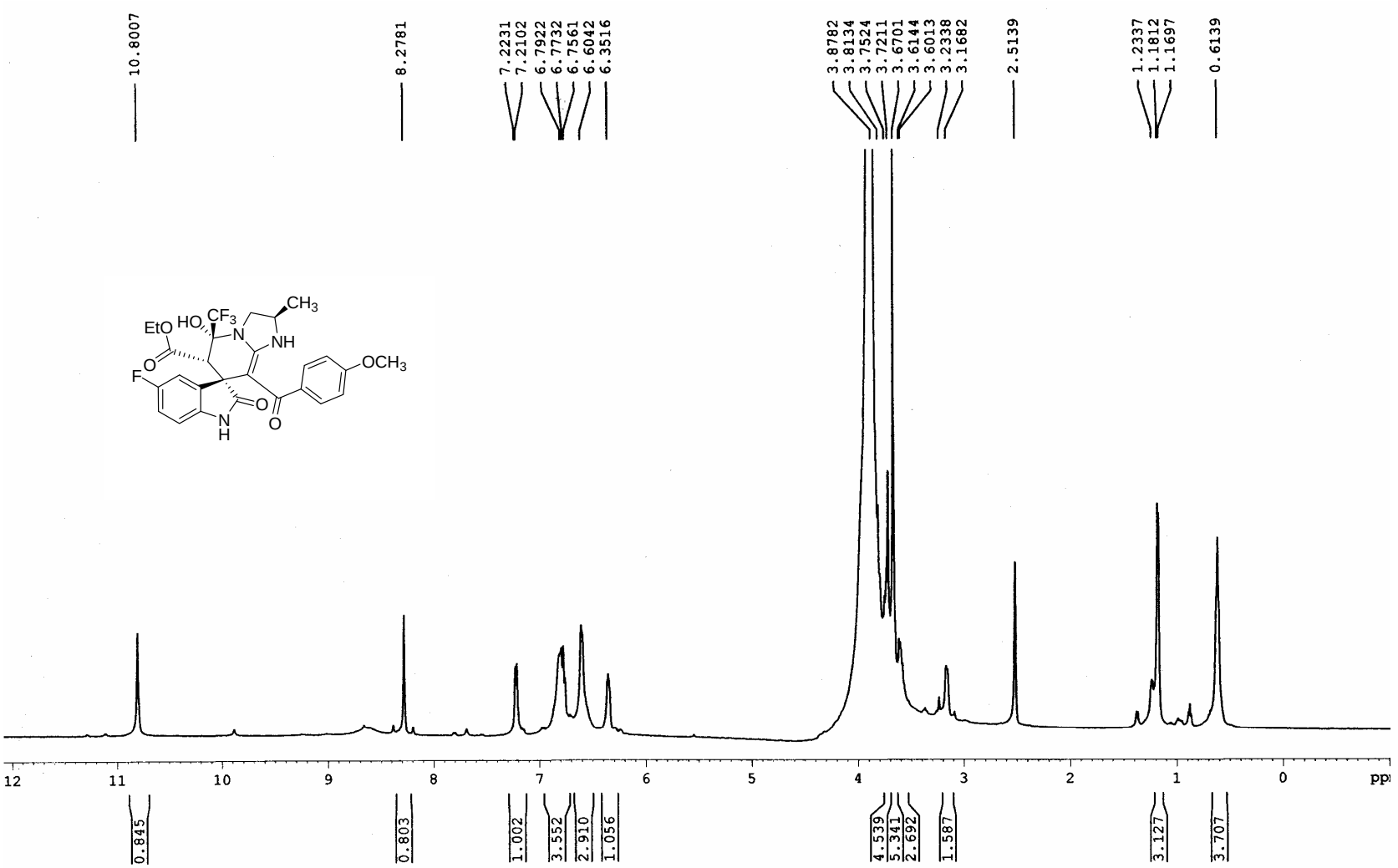


Figure 63. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5v'**

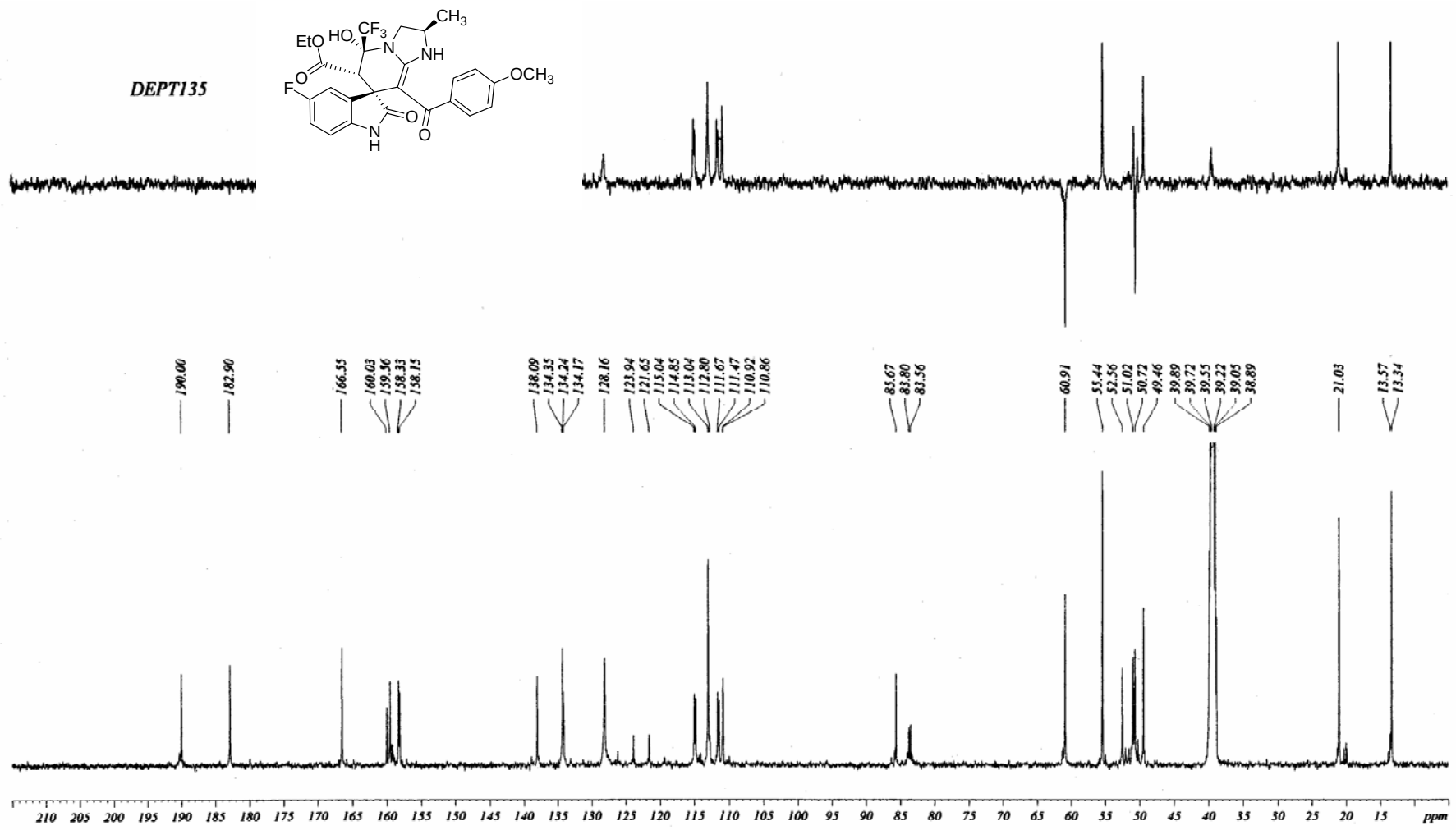


Figure 64. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5v'**

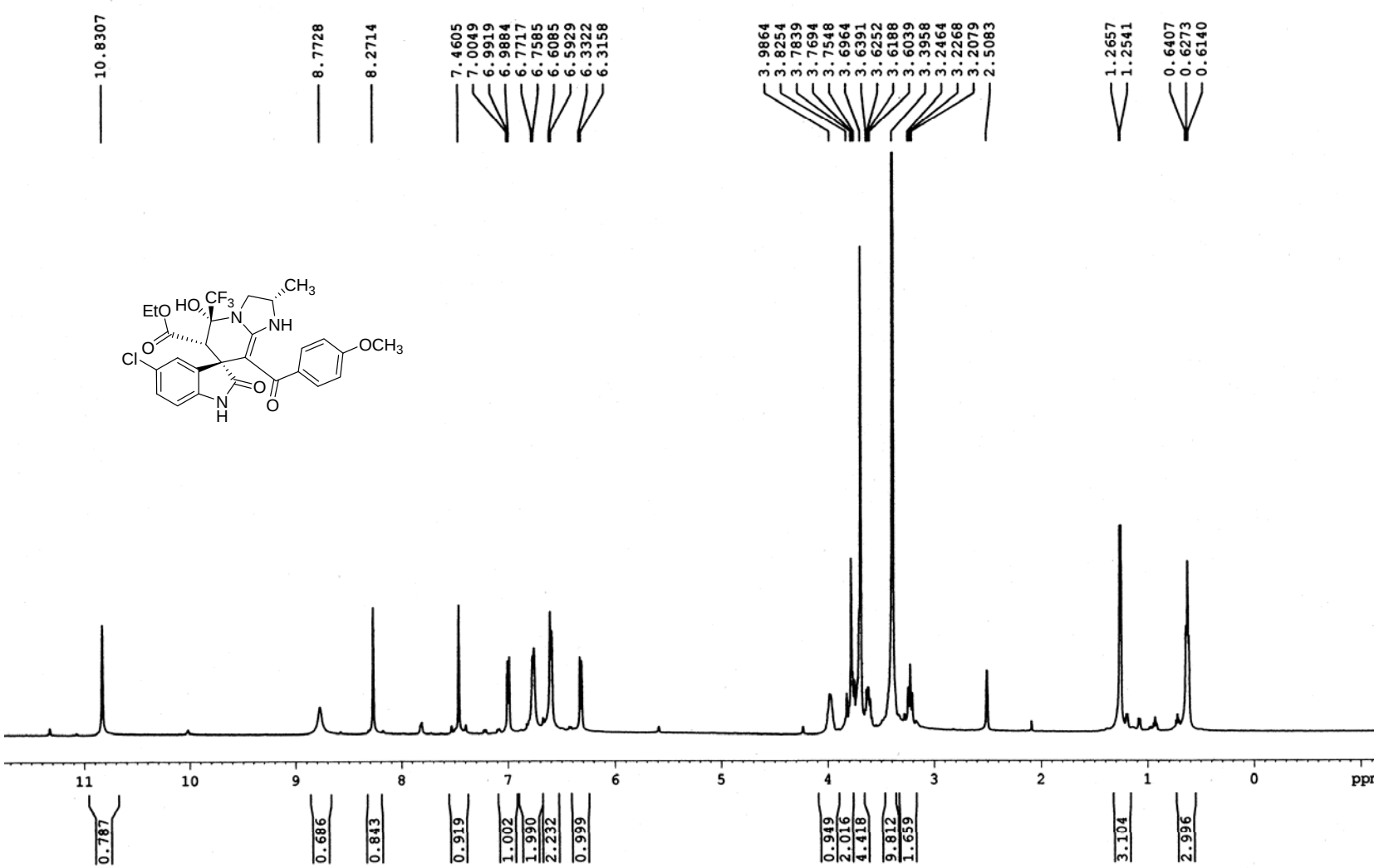


Figure 65. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5w**

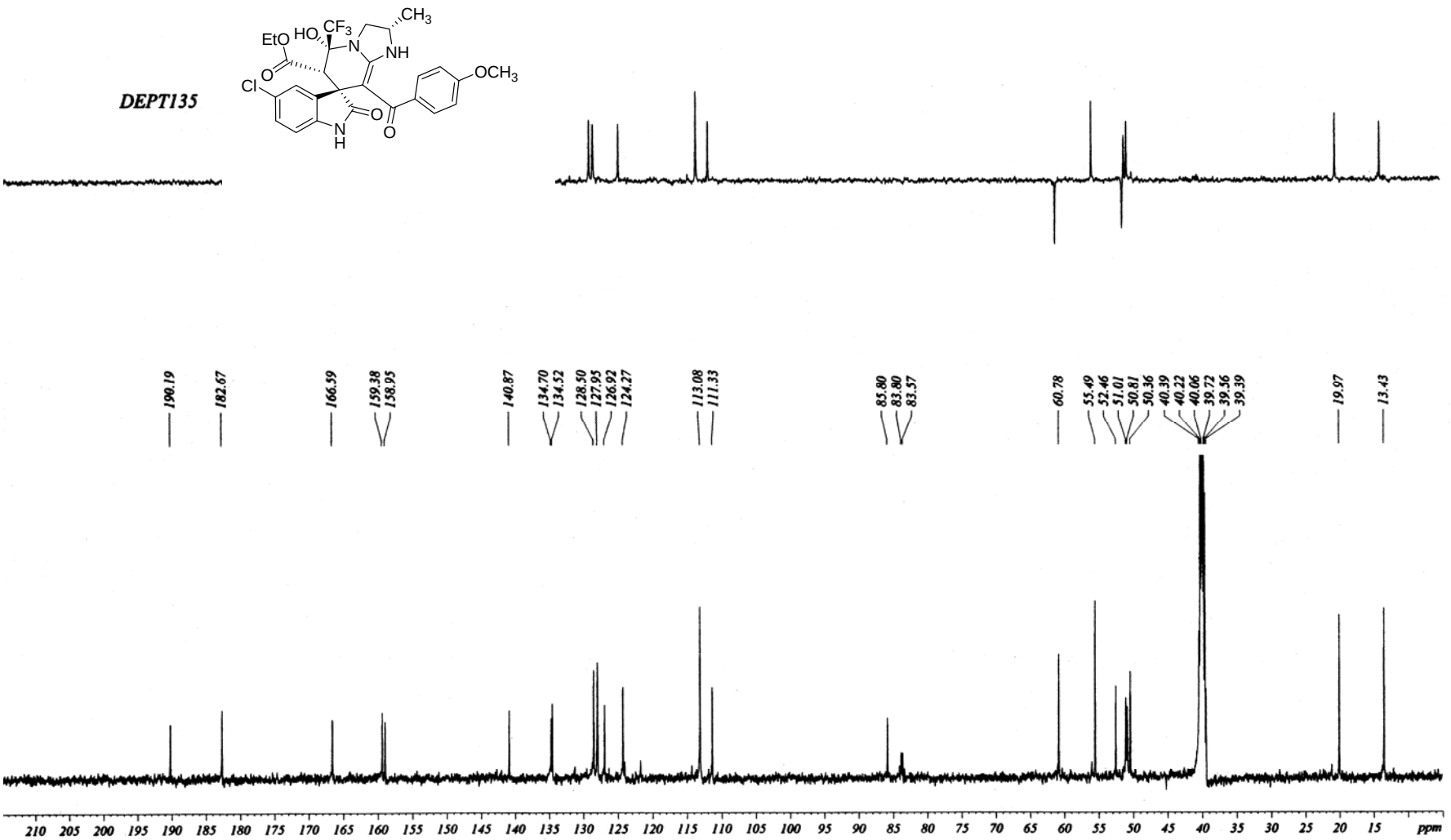


Figure 66. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5w**

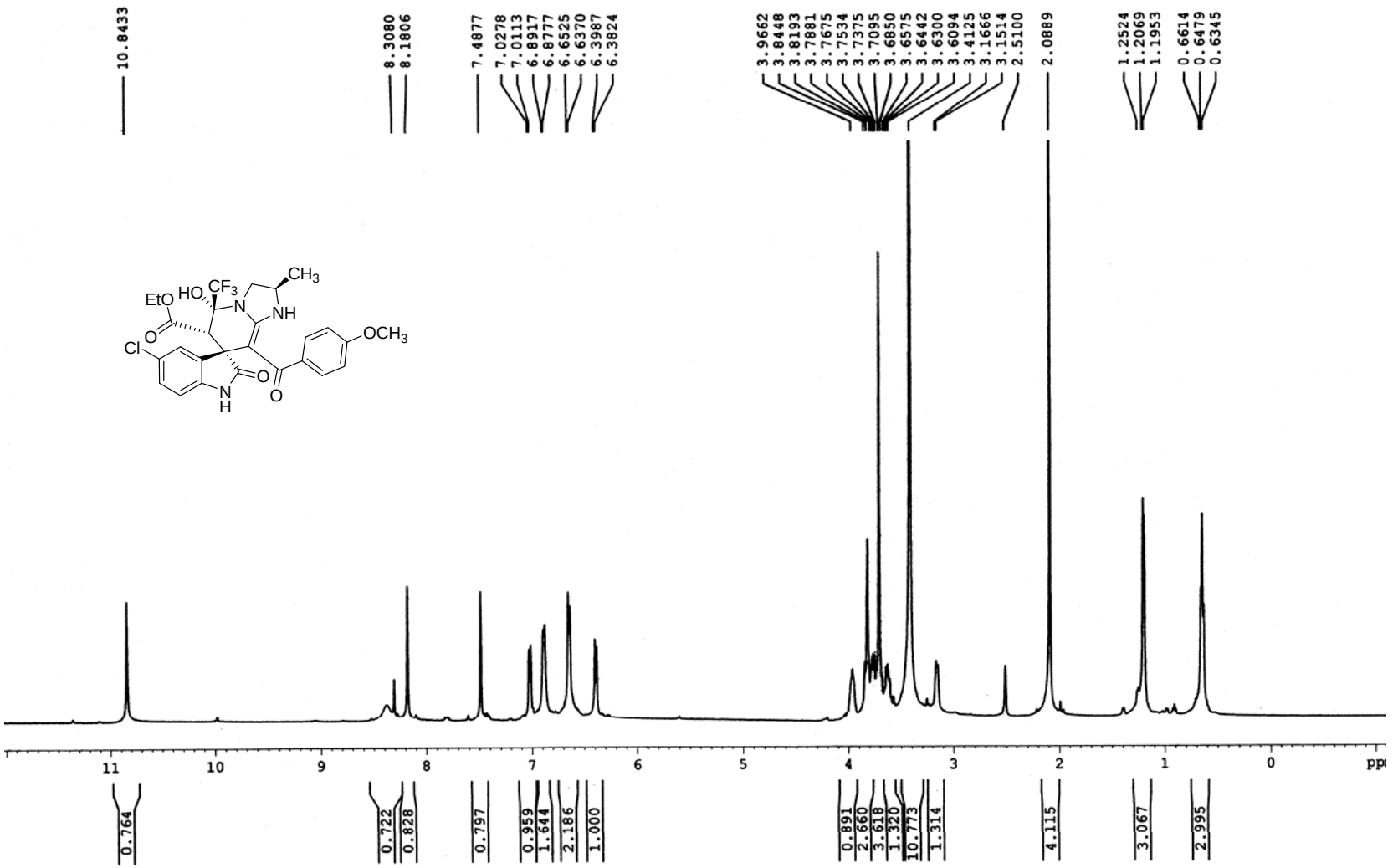


Figure 67. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5w'**

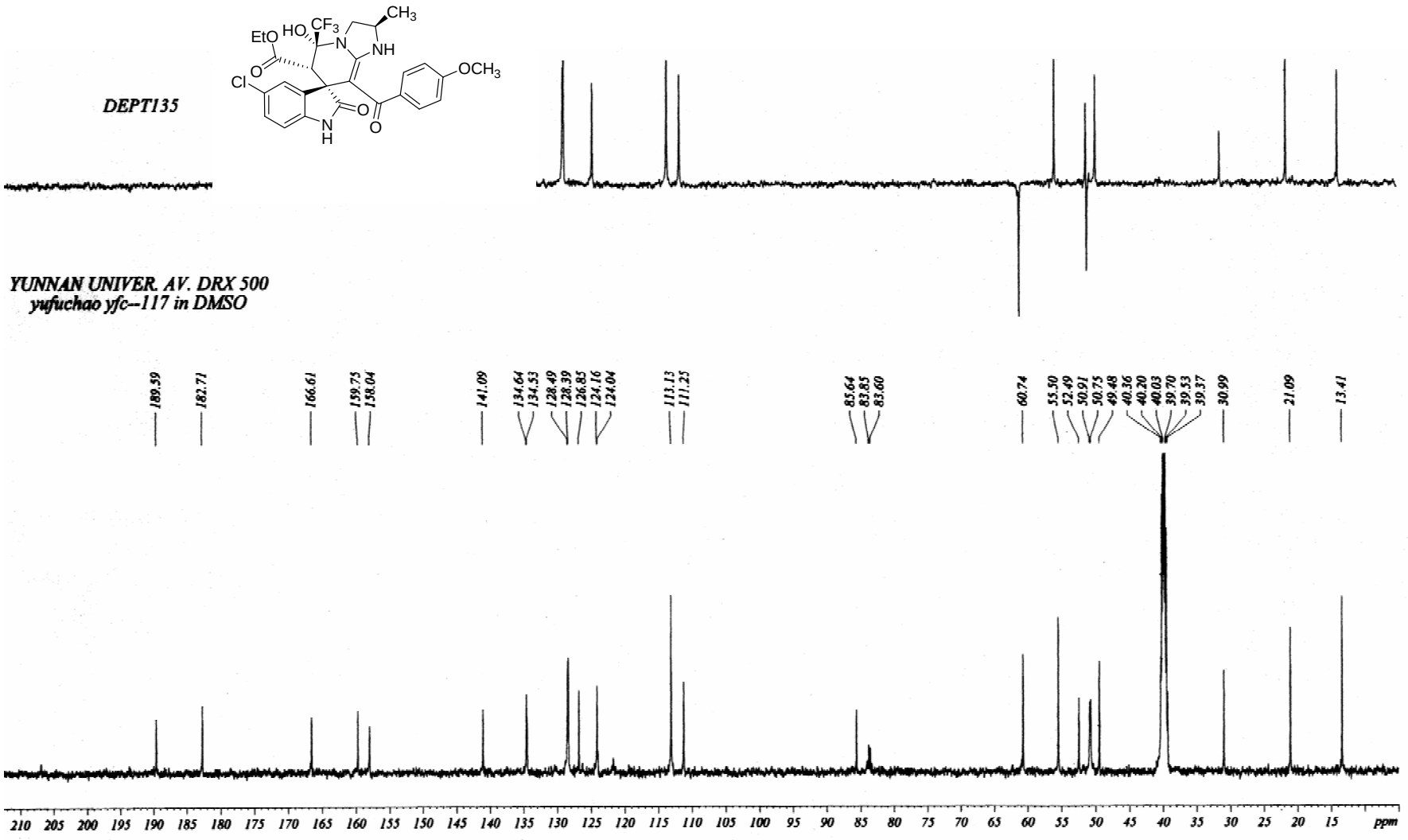


Figure 68. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5w'**

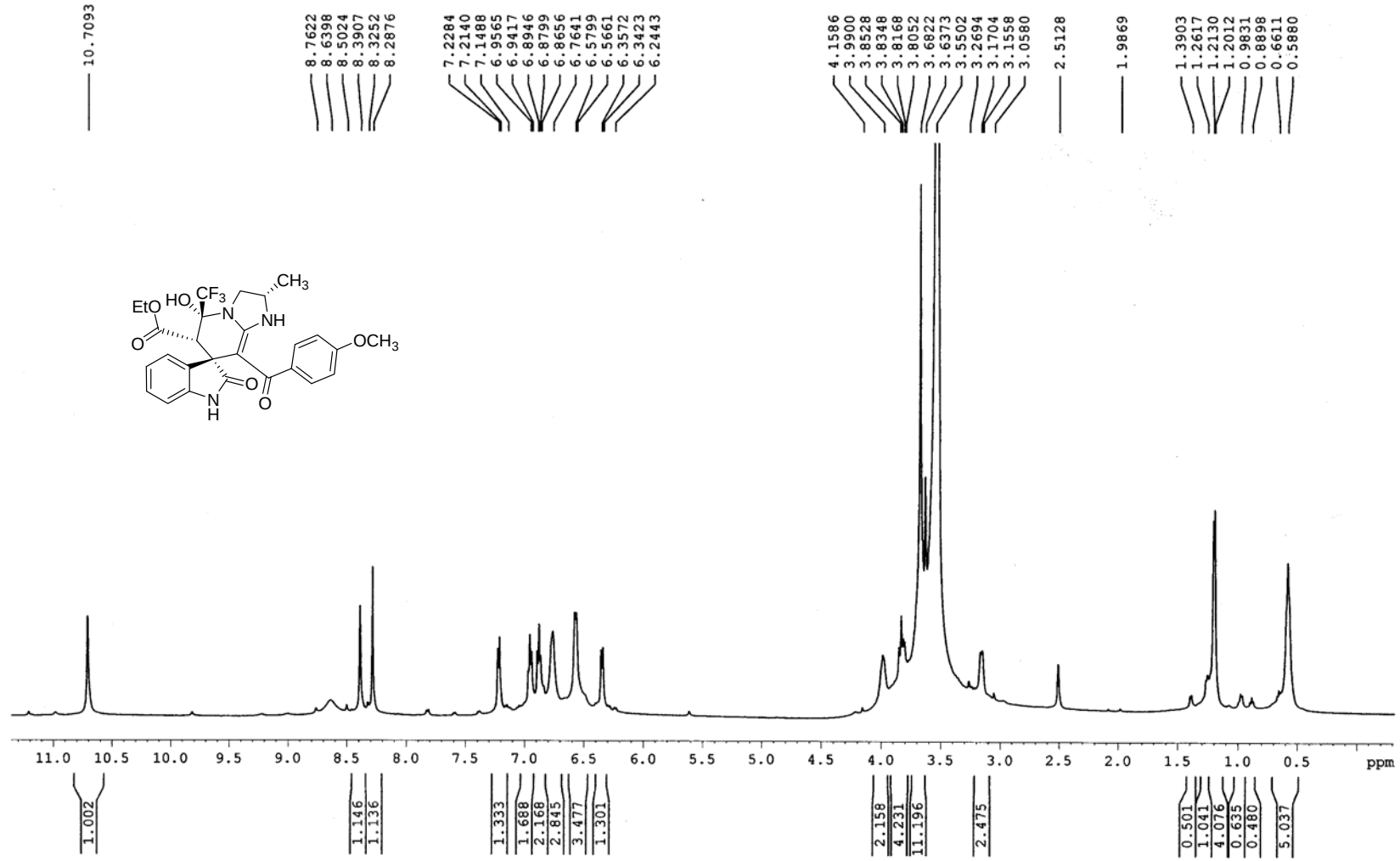


Figure 69. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5x**

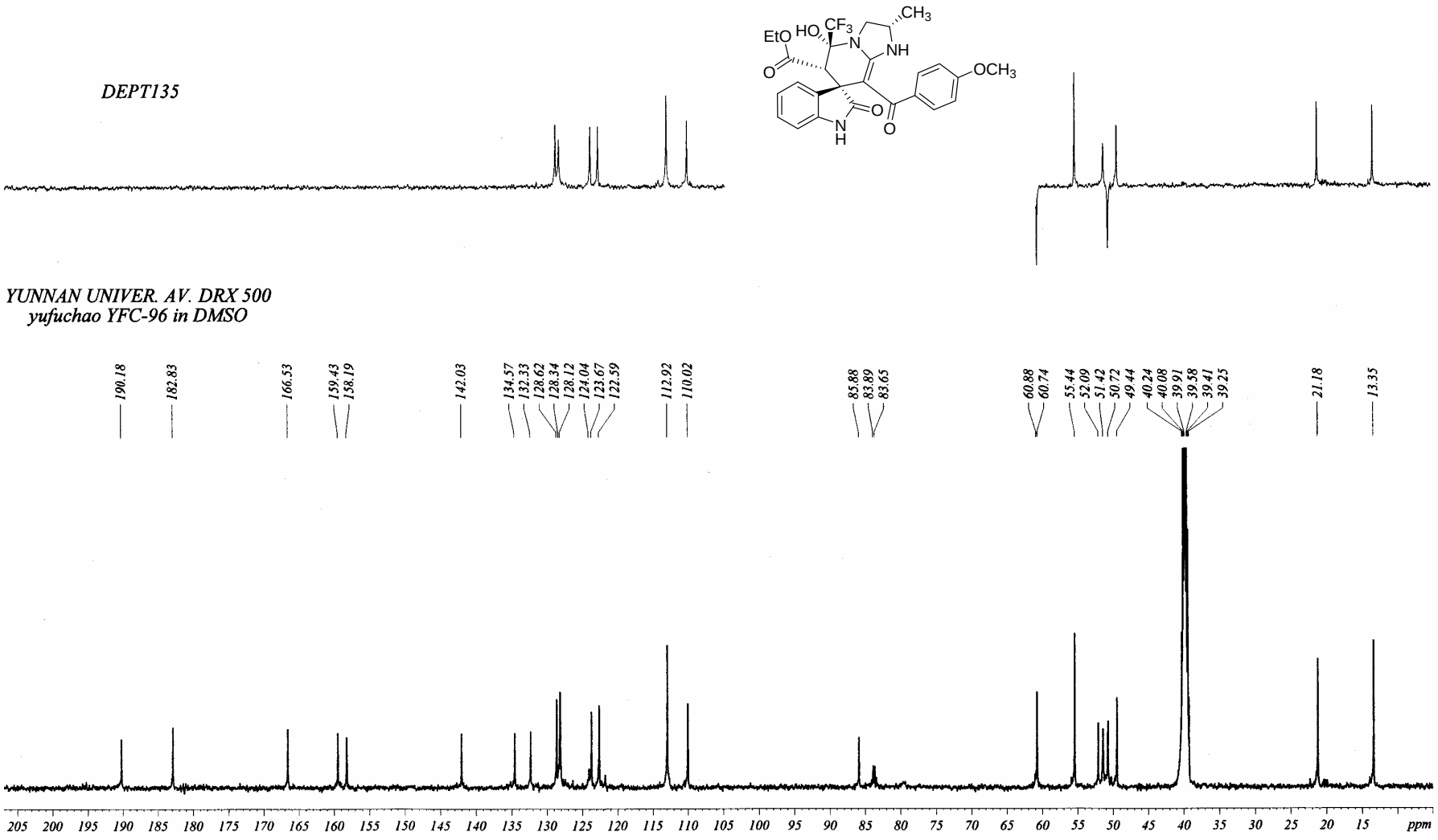


Figure 70. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5x**

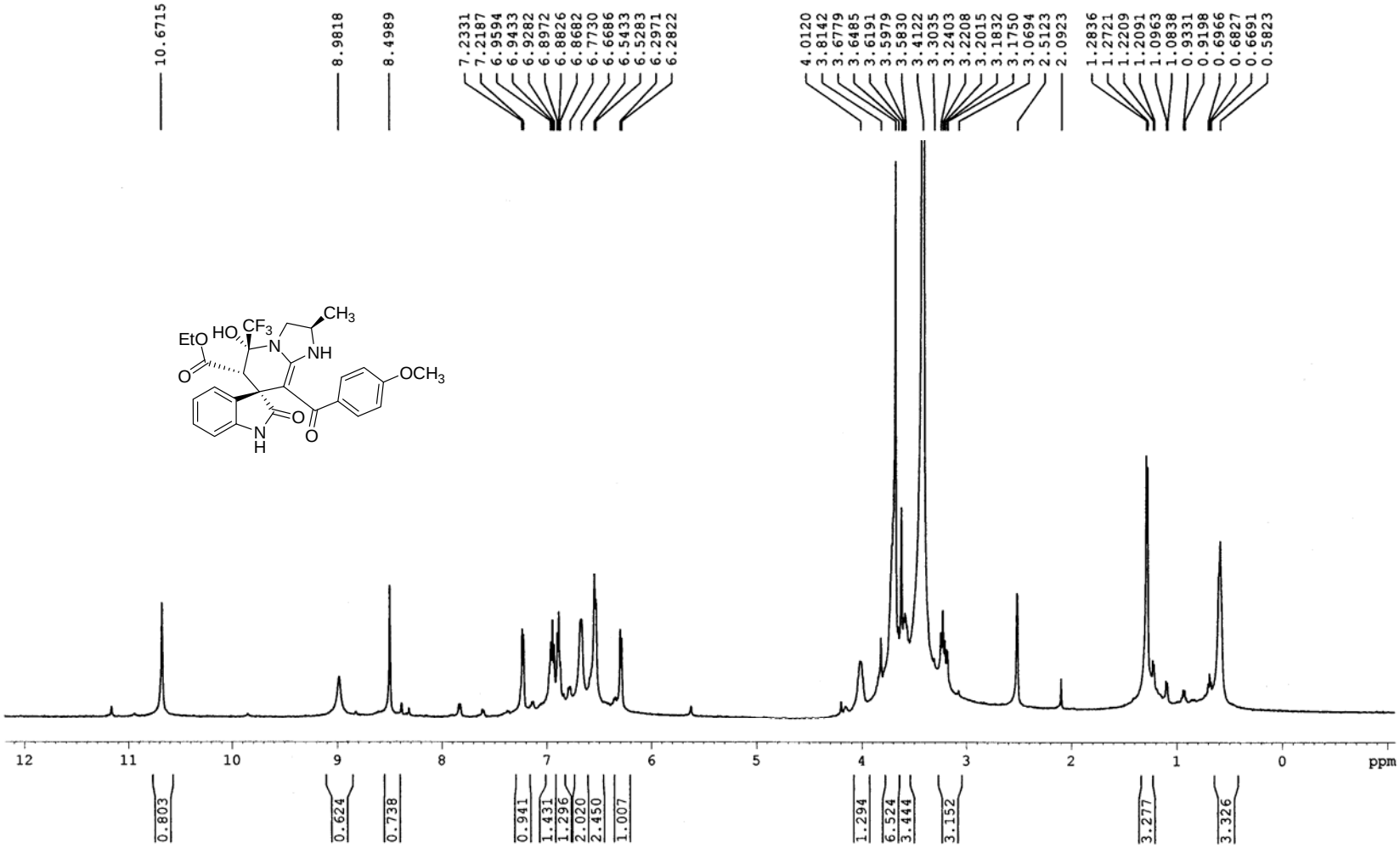


Figure 71. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5x'**

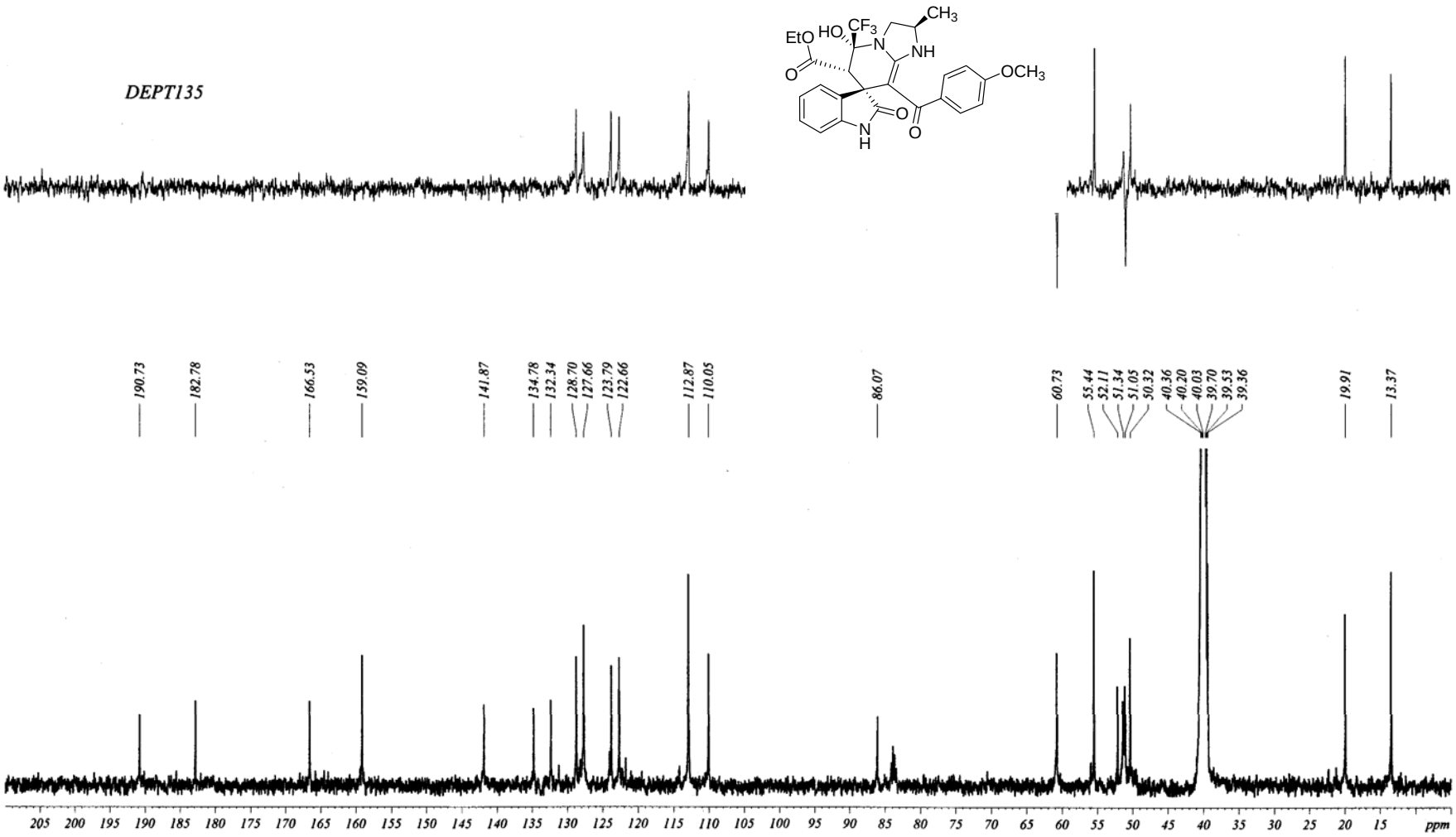


Figure 72. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5x'**

References and Notes

1. (a) Huang, Z.-T.; Wang, M.-X. *Synthesis* **1992**, 12, 1273−1276. (b) Li, Z.-J.; Charles, D. *Synth. Commun.* **2001**, 31, 527−533.
2. CCDC 890741 contain the supplementary crystallographic data for compound **5r**. CCDC 890742 contain the supplementary crystallographic data for compound **5r'**. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.