Supplementary data

Synthesis and evaluation of azalamellarin N and its A-ring-modified analogues as non-covalent inhibitors of the EGFR T790M/L858R mutant

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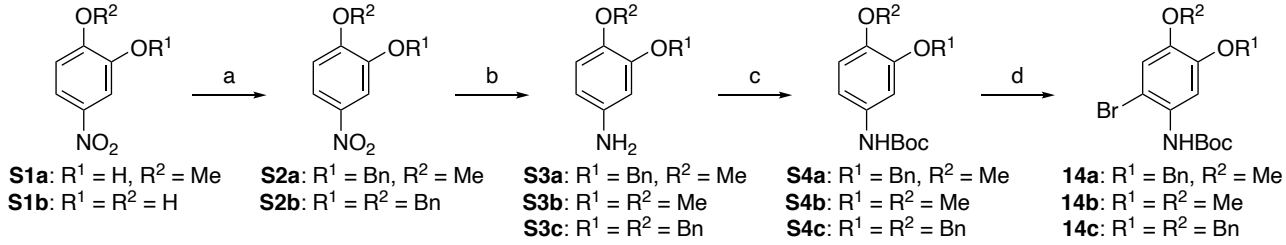
Synthesis of *tert*-butyl *N*-(2-bromophenyl)carbamates 14a–c.



S1a: R^1 = H, R^2 = Me
S1b: R^1 = R^2 = H

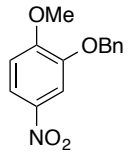
S2a: R^1 = Bn, R^2 = Me
S2b: R^1 = R^2 = Bn

S3a: R^1 = Bn, R^2 = Me
S3b: R^1 = R^2 = Me
S3c: R^1 = R^2 = Bn

S4a: R^1 = Bn, R^2 = Me
S4b: R^1 = R^2 = Me
S4c: R^1 = R^2 = Bn

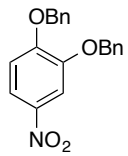
14a: R^1 = Bn, R^2 = Me
14b: R^1 = R^2 = Me
14c: R^1 = R^2 = Bn

Scheme S1. Synthesis of *tert*-butyl *N*-(2-bromophenyl)carbamates **14a**–**c**. *Reagents and conditions:* (a) BnBr (1.0–2.0 equiv), K_2CO_3 (1.5–3.0 equiv), acetone, reflux (**S2a**: 82%, **S2b**: 88%); (b) Zn powder (8.0 equiv), AcOH, DCM, 0 °C, 10 min then rt (**S3a**: 89%, **S3c**: 73%); (c) Boc_2O (1.05 equiv), THF, reflux (**S4a**: 66%, **S4b**: 93%, **S4c**: 89%); (d) NBS (1.1 equiv), THF, –78 °C to 0 °C (**14a**: 92%, **14b**: 91%, **14c**: 93%).



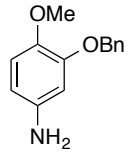
S2a

2-(Benzyloxy)-1-methoxy-4-nitrobenzene (S2a). Under an argon atmosphere, a neat liquid of benzyl bromide (14.0 mL, 118 mmol) was added to a suspension of 5-nitroguaiacol (**S1a**) (20.0 g, 118 mmol) and K_2CO_3 (24.5 g, 177 mmol) in acetone (500 mL) at room temperature and the mixture was refluxed for 7 h. The reaction mixture was cooled to room temperature and evaporated. To the residue was added water and the product was extracted with DCM. The extract was washed with water and brine, dried over Na_2SO_4, and evaporated. The residue was recrystallized from methanol to give **S2a** as a pale yellow powder (25.0 g, 82%). Mp 92.5–93.5 °C (lit.[1] 97–98 °C). IR (KBr): 1514, 1340, 1262, 1226, 1091, 994 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 3.98 (s, 3H), 5.20 (s, 2H), 6.92 (d, J = 8.9 Hz, 1H), 7.32–7.36 (m, 1H), 7.37–7.42 (m, 2H), 7.45–7.48 (m, 2H), 7.80 (d, J = 2.6 Hz, 1H), 7.92 (dd, J = 2.6 and 8.9 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 56.4, 71.2, 108.6, 110.2, 118.1, 127.6, 128.4, 128.8, 135.7, 141.3, 147.9, 155.1. HRFABMS *m*/*z*. Calcd for $C_{14}H_{14}NO_4$ $[(M+H)^+]$: 260.0923. Found: 260.0923. These physical and spectroscopic data are in good agreement with those previously reported.[2]



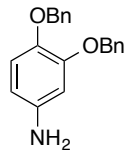
S2b

1,2-Bis(benzyloxy)-4-nitrobenzene (S2b). According to the procedure described for the preparation of **S2a**, 4-nitrocatechol (**S1b**) (5.00 g, 32.2 mmol), benzyl bromide (7.70 mL, 64.8 mmol), K_2CO_3 (13.4 g, 96.7 mmol), and acetone (320 mL) were reacted for 18 h. After recrystallization from methanol, **S2b** was obtained as a pale yellow powder (9.54 g, 88%). Mp 95.0–96.0 °C (lit.[3] 98.8–99.5 °C). IR (KBr): 1510, 1353, 1287, 1243, 1092, 1022 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.21 (s, 2H), 5.25 (s, 2H), 6.93 (d, J = 8.7 Hz, 1H), 7.30–7.46 (m, 10H), 7.81 (d, J = 2.6 Hz, 1H), 7.84 (dd, J = 2.6 and 8.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 71.1, 71.3, 109.3, 112.4, 118.0, 127.1, 127.4, 128.2, 128.3, 128.7, 128.7, 135.8, 135.9, 141.5, 148.3, 154.3. HRDARTMS *m*/*z*. Calcd for $C_{20}H_{18}NO_4$ $[(M+H)^+]$: 336.1236. Found: 336.1246. These physical and spectroscopic data are in good agreement with those previously reported.[2]



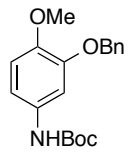
S3a

3-(Benzyloxy)-4-methoxyaniline (S3a). Reduction was carried out using modified procedure reported by Zhou et al.[4] Under an argon atmosphere, activated zinc powder[5] (20.2 g, 309 mmol) was added portionwise to a solution of **S2a** (10.0 g, 38.6 mmol) in DCM (390 mL) at room temperature. After cooling to 0 °C, AcOH (57.9 mL) was added dropwise to the suspension. After stirring for 10 min at 0 °C, the suspension was allowed to warm to room temperature and then passed through a pad of Celite. The filtrate was evaporated and the residue was diluted with DCM. The mixture was washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography over silica gel 60N (DCM–ethyl acetate = 100:1) to give **S3a** as a dark purple solid (7.86 g, 89%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.33 (br s, 2H), 3.81 (s, 3H), 5.11 (s, 2H), 6.24 (dd, J = 2.6 and 8.4 Hz, 1H), 6.32 (d, J = 2.6 Hz, 1H), 6.74 (d, J = 8.4 Hz, 1H), 7.27–7.32 (m, 1H), 7.34–7.38 (m, 2H), 7.41–7.45 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 57.0, 70.9, 103.3, 107.2, 114.1, 127.2, 127.8, 128.5, 137.3, 140.6, 142.8, 149.2. HRFABMS *m/z* calcd for $C_{14}H_{16}NO_2$ [$(M+H)^+$]: 230.1181, found 230.1181. These physical and spectroscopic data are in good agreement with those previously reported.[2]



S3c

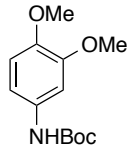
3,4-Bis(benzyloxy)aniline (S3c). According to the procedure described for the preparation of **S3a**, **S2b** (3.68 g, 11.0 mmol) and Zn powder (5.75 g, 87.9 mmol) were reacted. After chromatographic purification over silica gel 60N (DCM–ethyl acetate = 100:1), **S3c** was obtained as a dark-purple solid (2.45 g, 73%). Recrystallization from DCM–hexane gave a pale purple powder. Mp 96.5–97.5 °C (lit.[6] 113 °C). IR (KBr): 3456, 3368, 1622, 1508, 1224, 1132, 1012 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.43 (br s, 2H), 5.04 (s, 2H), 5.10 (s, 2H), 6.19 (dd, J = 2.6 and 8.4 Hz, 1H), 6.34 (d, J = 2.6 Hz, 1H), 6.77 (d, J = 8.4 Hz, 1H), 7.25–7.39 (m, 6H), 7.39–7.45 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 71.1, 73.0, 103.5, 107.5, 118.5, 127.3, 127.6, 127.8, 128.3, 128.5, 137.3, 137.9, 141.7, 141.7, 150.4. HRDARTMS *m/z*. Calcd for $C_{20}H_{20}NO_2$ [$(M+H)^+$]: 306.1494. Found: 306.1486. These physical and spectroscopic data are in good agreement with those previously reported.[2]



S4a

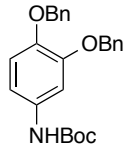
***tert*-Butyl *N*-[3-(benzyloxy)-4-methoxyphenyl]carbamate (S4a).** Under an argon atmosphere, di-*tert*-butyl dicarbonate (7.85 g, 36.0 mmol) was added as a neat liquid to a solution of **S3a** (7.86 g, 34.3 mmol) in THF (150 mL) at room temperature and the solution was refluxed for 1.5 h. The reaction mixture was then cooled to room temperature and evaporated. After successive purification by column chromatography over Chromatorex NH-DM1020 (hexane−ethyl acetate = 3:1) and column chromatography over silica gel 60N (hexane − ethyl acetate = 3:1), **S4a** was obtained as a colorless solid (7.49 g, 66%). Recrystallization from Et_2O−hexane gave a colorless powder. Mp 100–101 °C. IR (KBr): 3362, 1697, 1517, 1407, 1267, 1238, 1169, 1134 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.50 (s, 9H), 3.83 (s, 3H),

5.12 (s, 2H), 6.37 (br s, 1H), 6.81 (s, 2H), 7.12 (br s, 1H), 7.27–7.32 (m, 1H), 7.33–7.39 (m, 2H), 7.42–7.47 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.3, 56.4, 70.9, 80.2, 106.1, 111.2, 112.4, 127.4, 127.8, 128.5, 131.9, 136.9, 145.6, 148.4, 152.9. HRDARTMS *m/z* calcd for $C_{19}H_{23}NO_4$ (M^+): 329.1627, found 329.1639.



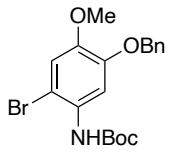
S4b

***tert*-Butyl *N*-(3,4-dimethoxyphenyl)carbamate (S4b).** According to the procedure described for the preparation of **S4a**, 3,4-dimethoxyaniline (4.34 g, 28.3 mmol) was reacted. After recrystallization from Et_2O–hexane, **S4b** was obtained as a pale brown powder (6.68 g, 93%). Mp 96–97 °C (lit.[7] 87–89 °C). IR (KBr): 3355, 1697, 1518, 1238, 1170, 1026 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.51 (s, 9H), 3.84 (s, 3H), 3.87 (s, 3H), 6.47 (br s, 1H), 6.72 (dd, J = 2.2 and 8.6 Hz, 1H), 6.78 (d, J = 8.6 Hz, 1H), 7.18 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.4, 55.9, 56.2, 80.3, 103.8, 110.4, 111.6, 132.1, 145.0, 149.2, 153.0. HRDARTMS *m/z* calcd for $C_{13}H_{20}NO_4$ [$(M+H)^+$]: 254.1392, found 254.1399. These physical and spectroscopic data are in good agreement with those previously reported.[8]



S4c

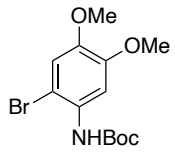
***tert*-Butyl *N*-[3,4-bis(benzyloxy)phenyl]carbamate (S4c).** According to the procedure described for the preparation of **S4a**, **S3c** (3.02 g, 9.89 mmol) was reacted. After chromatographic purification over silica gel 60N (hexane–ethyl acetate = 5:1), **S4c** was obtained as a colorless solid (3.56 g, 89%). Recrystallization from Et_2O–hexane gave a colorless powder. Mp 73.0–74.0 °C. IR (KBr): 3326, 1688, 1603, 1526, 1430, 1228, 1164 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.50 (s, 9H), 5.08 (s, 2H), 5.12 (s, 2H), 6.39 (br s, 1H), 6.72 (dd, J = 2.4 and 8.6 Hz, 1H), 6.84 (d, J = 8.6 Hz, 1H), 7.20 (br s, 1H), 7.25–7.38 (m, 6H), 7.38–7.42 (m, 2H), 7.43–7.47 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.4, 71.1, 72.1, 80.3, 106.5, 111.3, 116.5, 127.5, 127.7, 127.8, 128.4, 128.4, 132.9, 137.1, 137.5, 144.6, 149.6, 152.9. HRDARTMS *m*/*z*. Calcd for $C_{25}H_{27}NO_4$ (M^+): 405.1940. Found: 405.1918.



14a

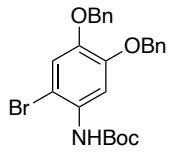
***tert*-Butyl *N*-[5-(benzyloxy)-2-bromo-4-methoxyphenyl]carbamate (14a).** Under an argon atmosphere, NBS (4.45 g, 25.0 mmol) was added portionwise to a solution of **S4a** (7.49 g, 22.7 mmol) in THF (140 mL) at −78 °C. After stirring for 1 h at −78 °C, the mixture was allowed to warm to 0 °C and stirred for an additional 17 h at the same temperature. The reaction mixture was quenched with water at the same temperature and allowed to warm to room temperature. The product was extracted with DCM and the extract was washed with water and brine, dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography over silica gel 60N (hexane–ethyl acetate = 10:1) to give **14a** as a colorless solid (8.50 g, 92%). Recrystallization from Et_2O–hexane gave a colorless powder. Mp 94–95 °C. IR (KBr): 3418, 1721, 1529, 1325, 1238, 1156 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.53 (s, 9H), 3.82 (s, 3H),

5.13 (s, 2H), 6.75 (br s, 1H), 6.99 (s, 1H), 7.28–7.33 (m, 1H), 7.34–7.39 (m, 2H), 7.45–7.50 (m, 2H), 7.90 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.3, 56.5, 71.0, 80.8, 106.4, 115.4, 127.8, 128.0, 128.5, 129.9, 136.5, 145.6, 148.0, 152.6. HRDARTMS *m*/*z*. Calcd for $C_{19}H_{22}BrNO_4$ (M^+): 407.0732. Found: 407.0743.



14b

***tert*-Butyl *N*-(2-bromo-4,5-dimethoxyphenyl)carbamate (14b).** According to the procedure described for the preparation of **14a**, **S4b** (6.18 g, 24.4 mmol) and NBS (4.76 g, 26.7 mmol) were reacted. After chromatographic purification over silica gel 60N (hexane–ethyl acetate = 7:1), **14b** was obtained as a colorless solid (7.38 g, 91%). Recrystallization from Et_2O–hexane gave a colorless powder. Mp 89.0–89.5 °C. IR (KBr): 3415, 1720, 1526, 1486, 1400, 1325, 1159 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.53 (s, 9H), 3.84 (s, 3H), 3.91 (s, 3H), 6.80 (br s, 1H), 6.96 (s, 1H), 7.82 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.3, 56.1, 56.3, 80.9, 101.7, 104.2, 114.7, 130.0, 145.0, 148.7, 152.6. HRDARTMS *m/z* calcd for $C_{13}H_{18}BrNO_4$ (M^+): 331.0419, found 331.0425.



14c

***tert*-Butyl *N*-[4,5-bis(benzyloxy)-2-bromophenyl]carbamate (14c).** According to the procedure described for the preparation of **14a**, **S4c** (1.00 g, 2.47 mmol) and NBS (483 mg, 2.71 mmol) were reacted. After chromatographic purification over silica gel 60N (hexane–ethyl acetate = 7:1), **14c** was obtained as a colorless solid (1.11 g, 93%). Recrystallization from Et_2O–hexane gave a colorless powder. Mp 89.5–90.5 °C. IR (KBr): 3416, 1717, 1525, 1237, 1170 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.53 (s, 9H), 5.06 (s, 2H), 5.15 (s, 2H), 6.78 (br s, 1H), 7.06 (s, 1H), 7.28–7.41 (m, 8H), 7.46–7.49 (m, 2H), 7.94 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 28.3, 71.1, 72.3, 80.9, 102.4, 106.9, 119.5, 127.5, 127.7, 127.9, 127.9, 128.4, 128.5, 130.9, 136.7, 136.9, 144.6, 149.2, 152.6. HRDARTMS *m*/*z*. Calcd for $C_{25}H_{26}BrNO_4$ (M^+): 483.1045. Found: 483.1071.

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and ether and drying using a vacuum line (Shriner, R. L.; Neumann, F. W. *Org. Synth.* **1946**, *26*, 7). https://doi.org/10.15227/orgsyn.026.0007.

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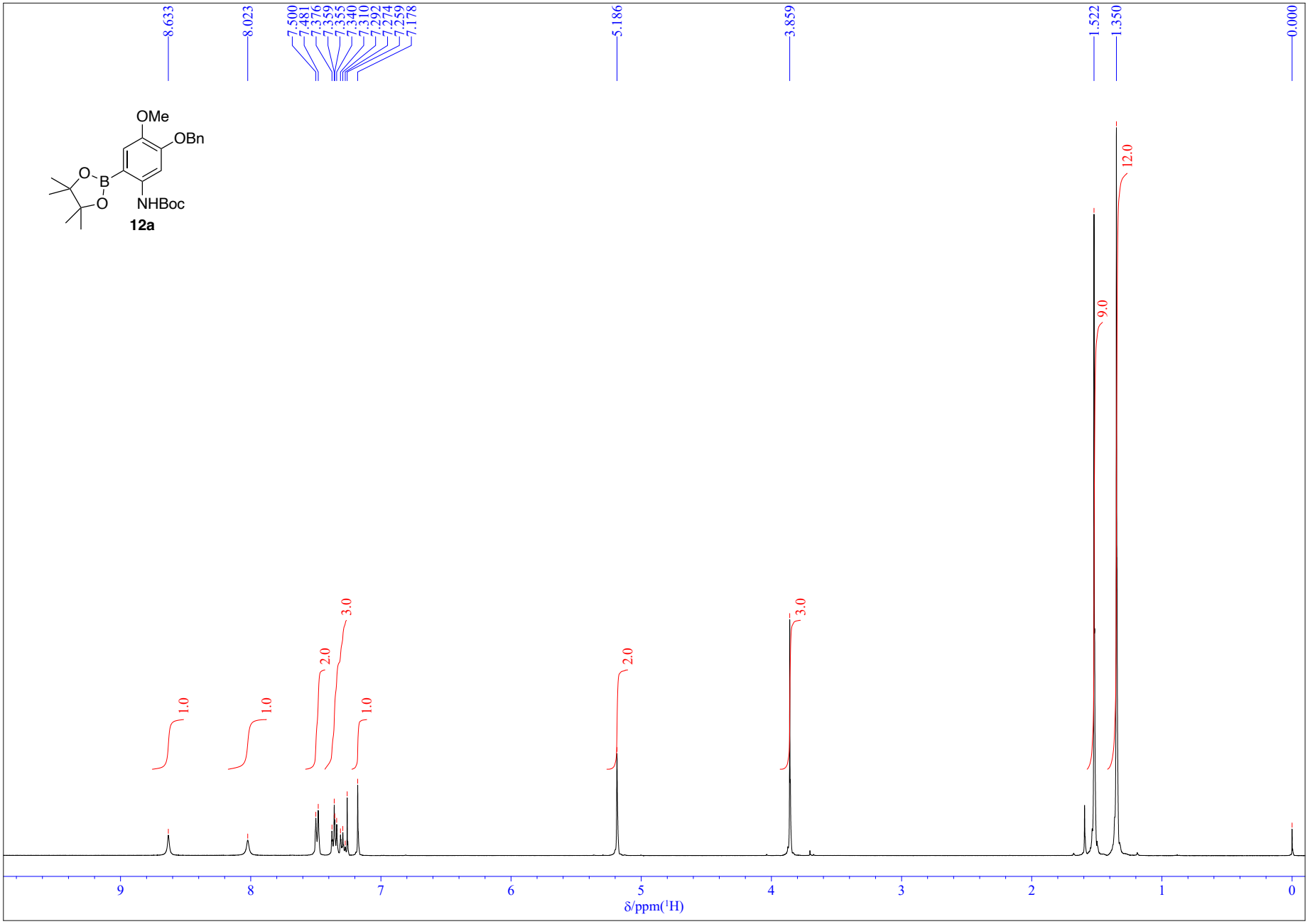

Figure S1. ^{1}H NMR spectrum of compound **12a** (400 MHz, $CDCl_3$).

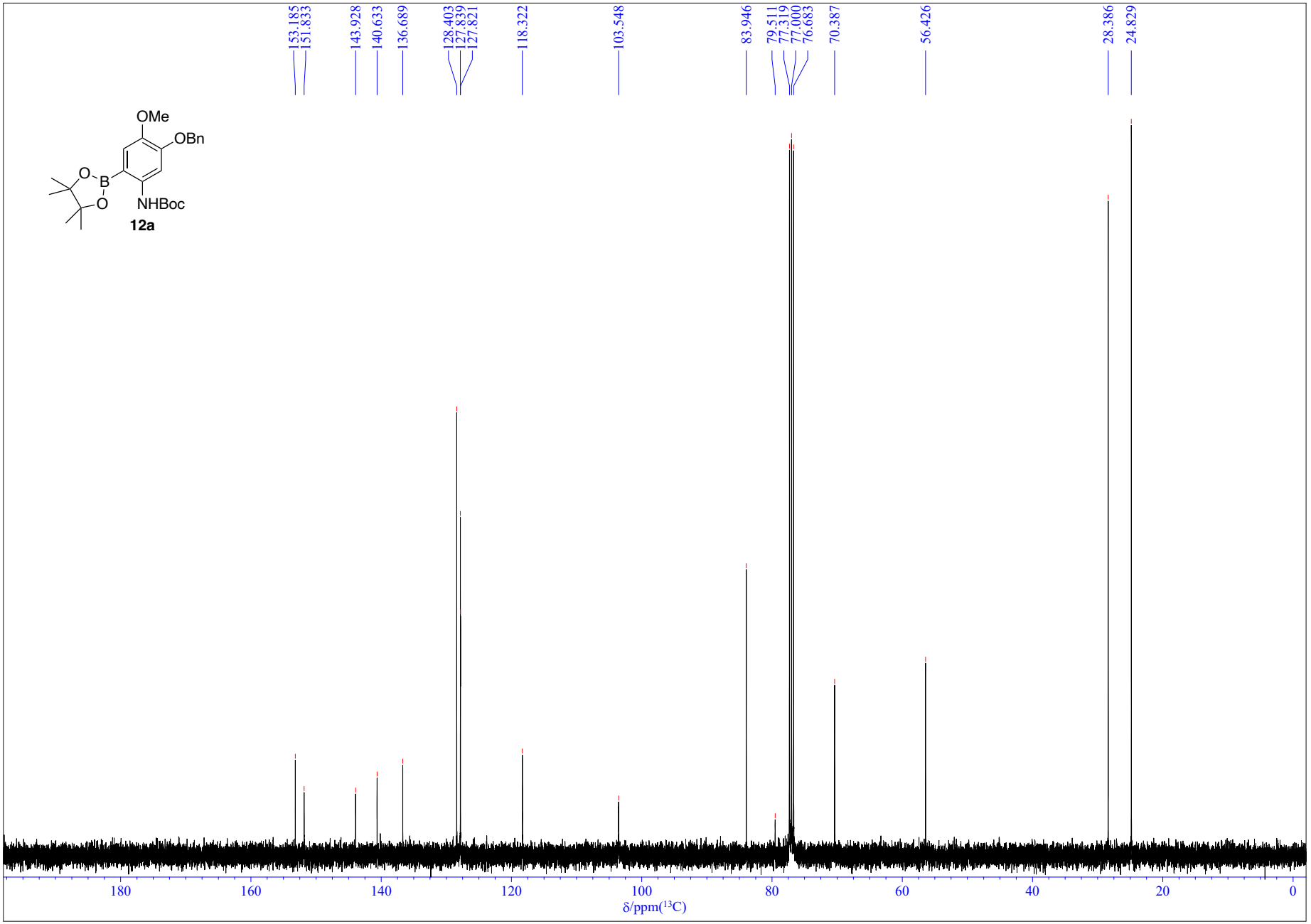

Figure S2. ^{13}C NMR spectrum of compound **12a** (100 MHz, $CDCl_3$).

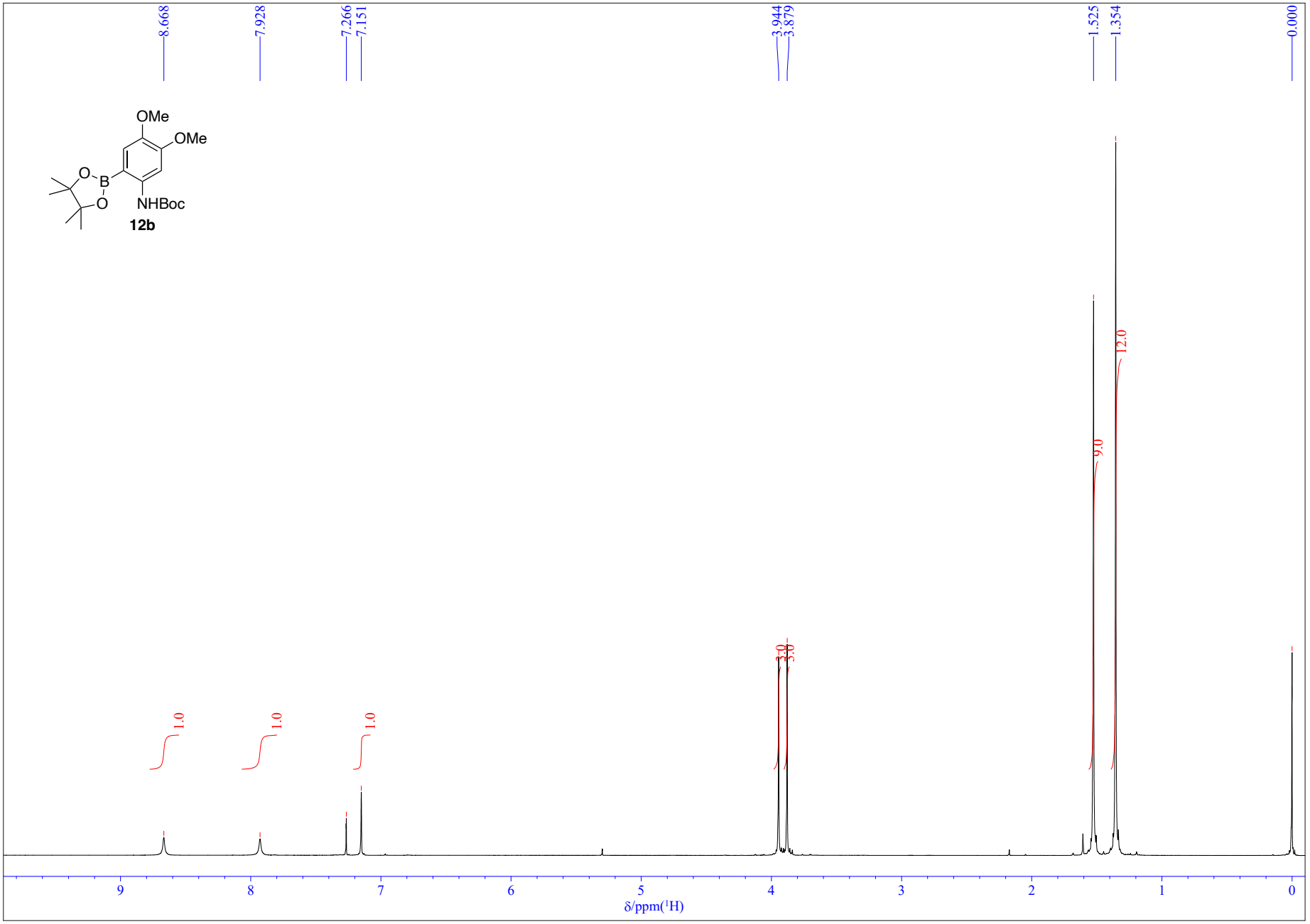

Figure S3. ^{1}H NMR spectrum of compound **12b** (400 MHz, $CDCl_3$).

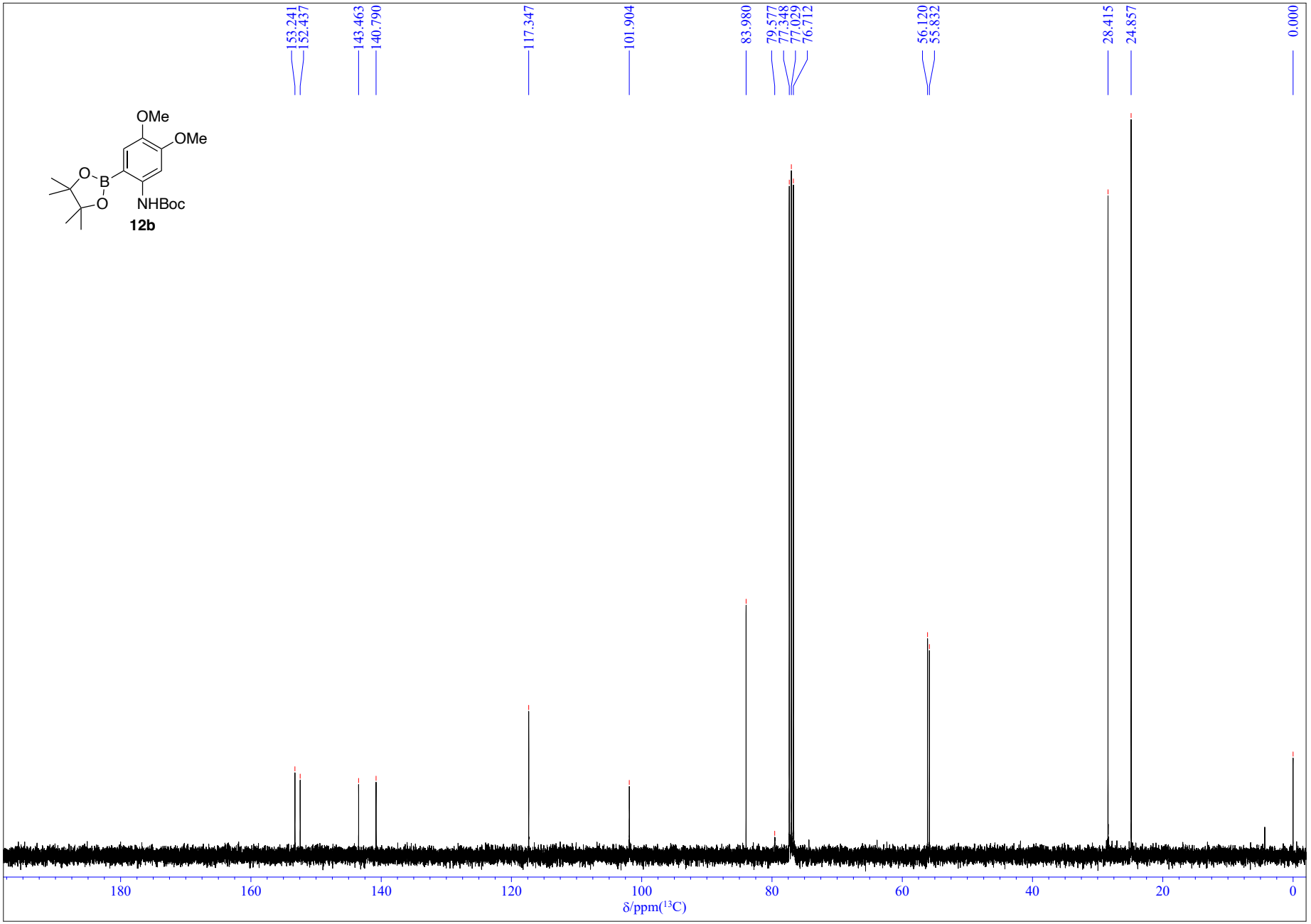

Figure S4. ^{13}C NMR spectrum of compound **12b** (100 MHz, $CDCl_3$).

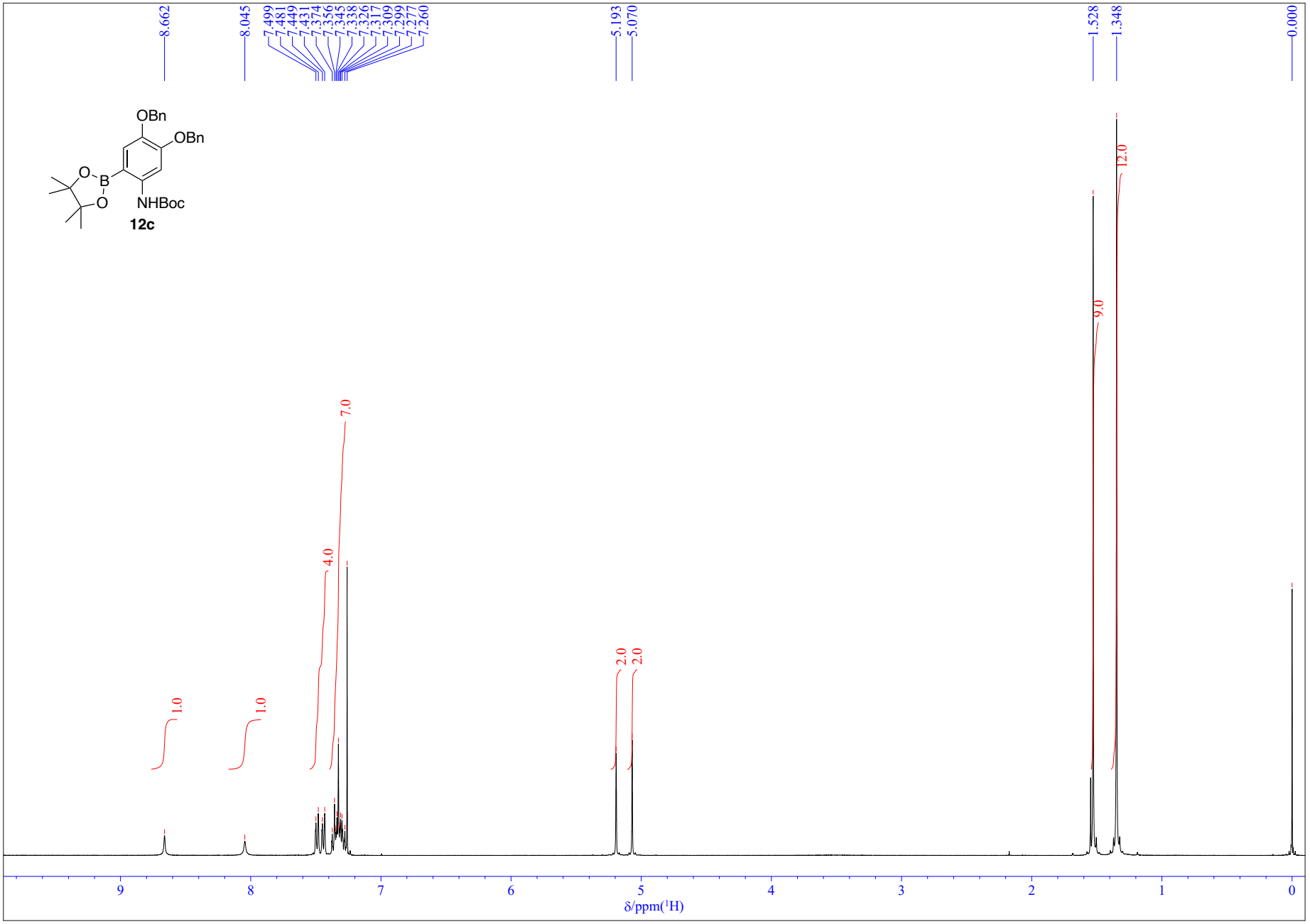

Figure S5. ^{1}H NMR spectrum of compound **12c** (400 MHz, $CDCl_3$).

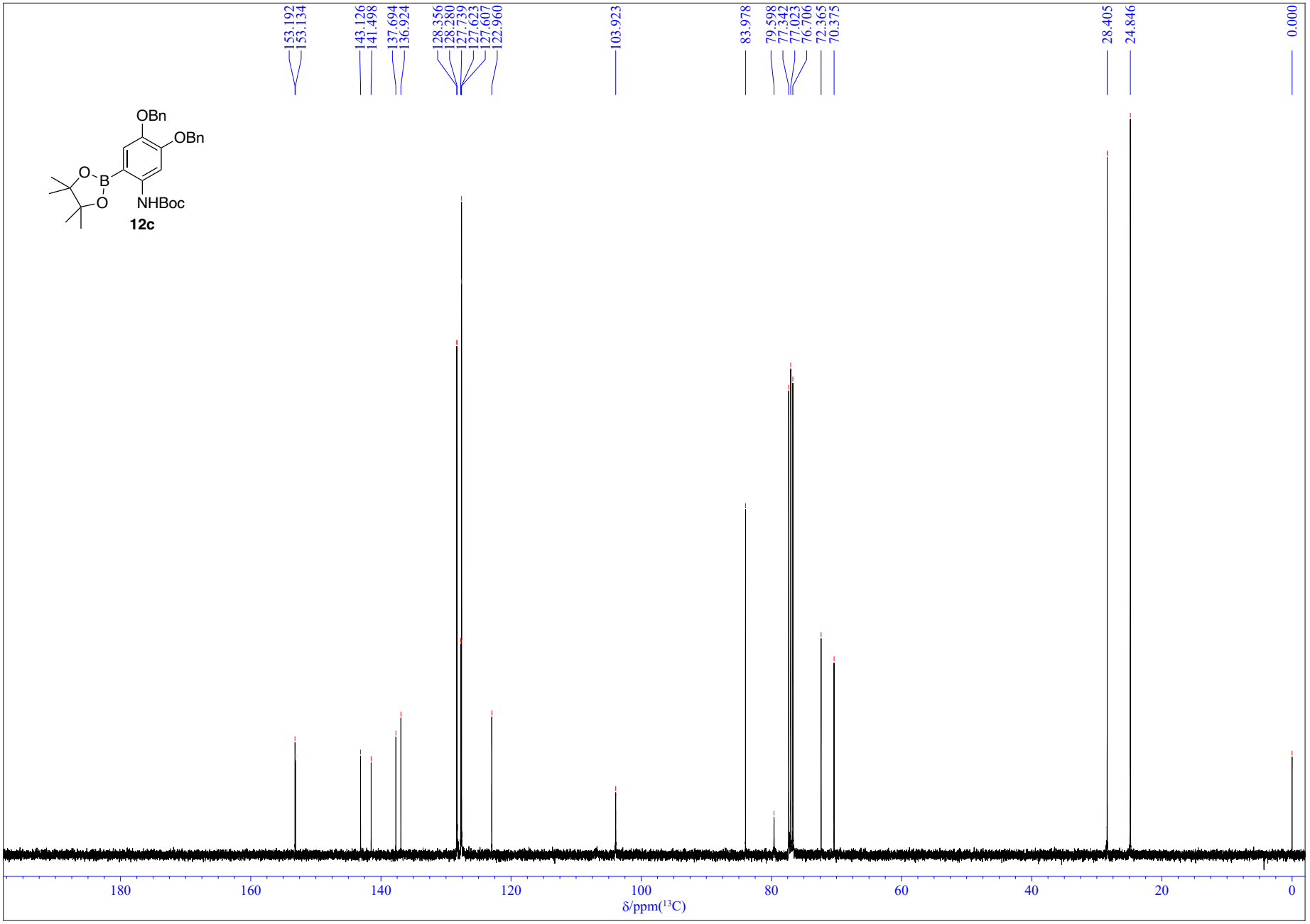

Figure S6. ^{13}C NMR spectrum of compound **12c** (100 MHz, $CDCl_3$).

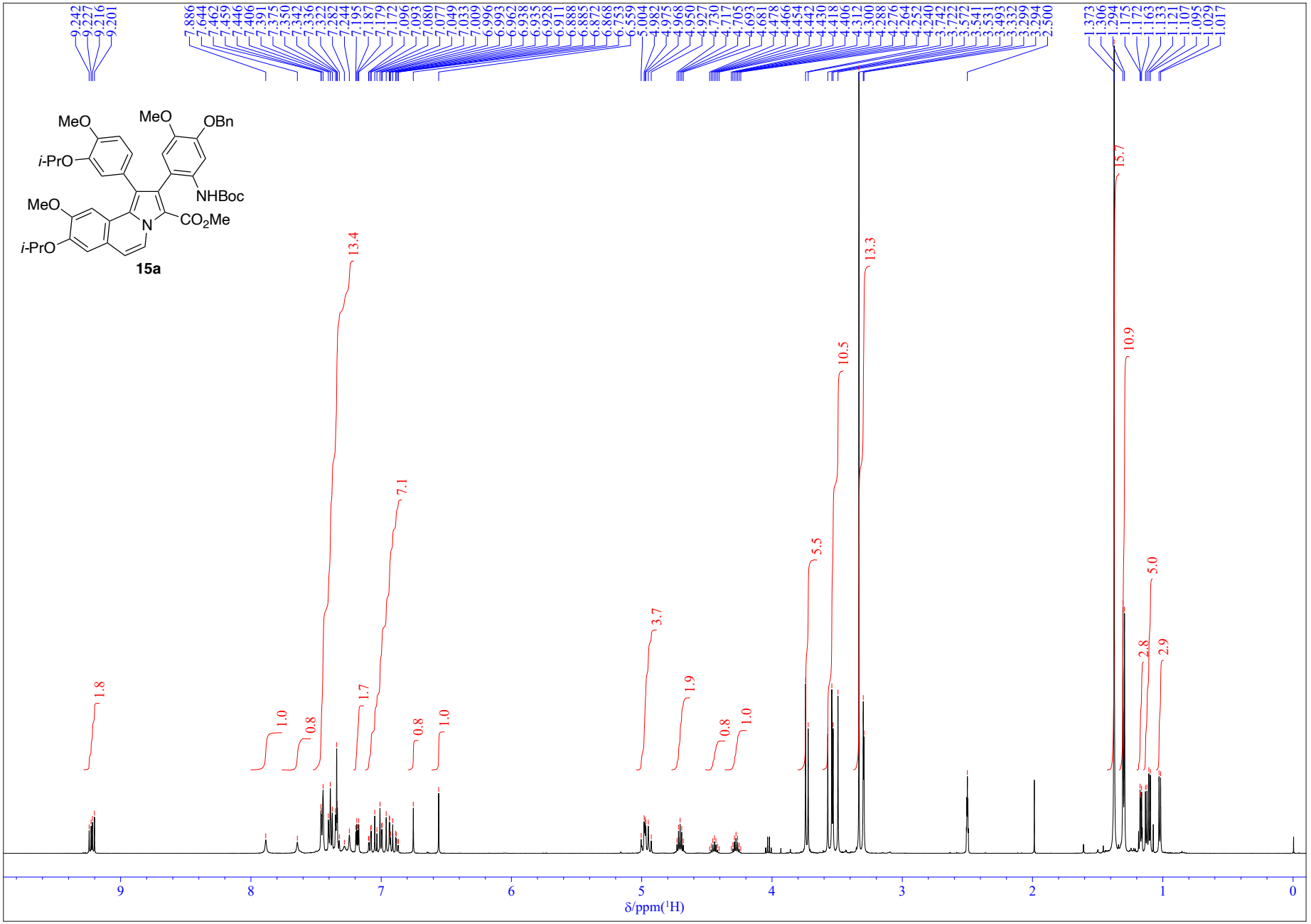

Figure S7. ^{1}H NMR spectrum of compound **15a** (500 MHz, DMSO-d_6).

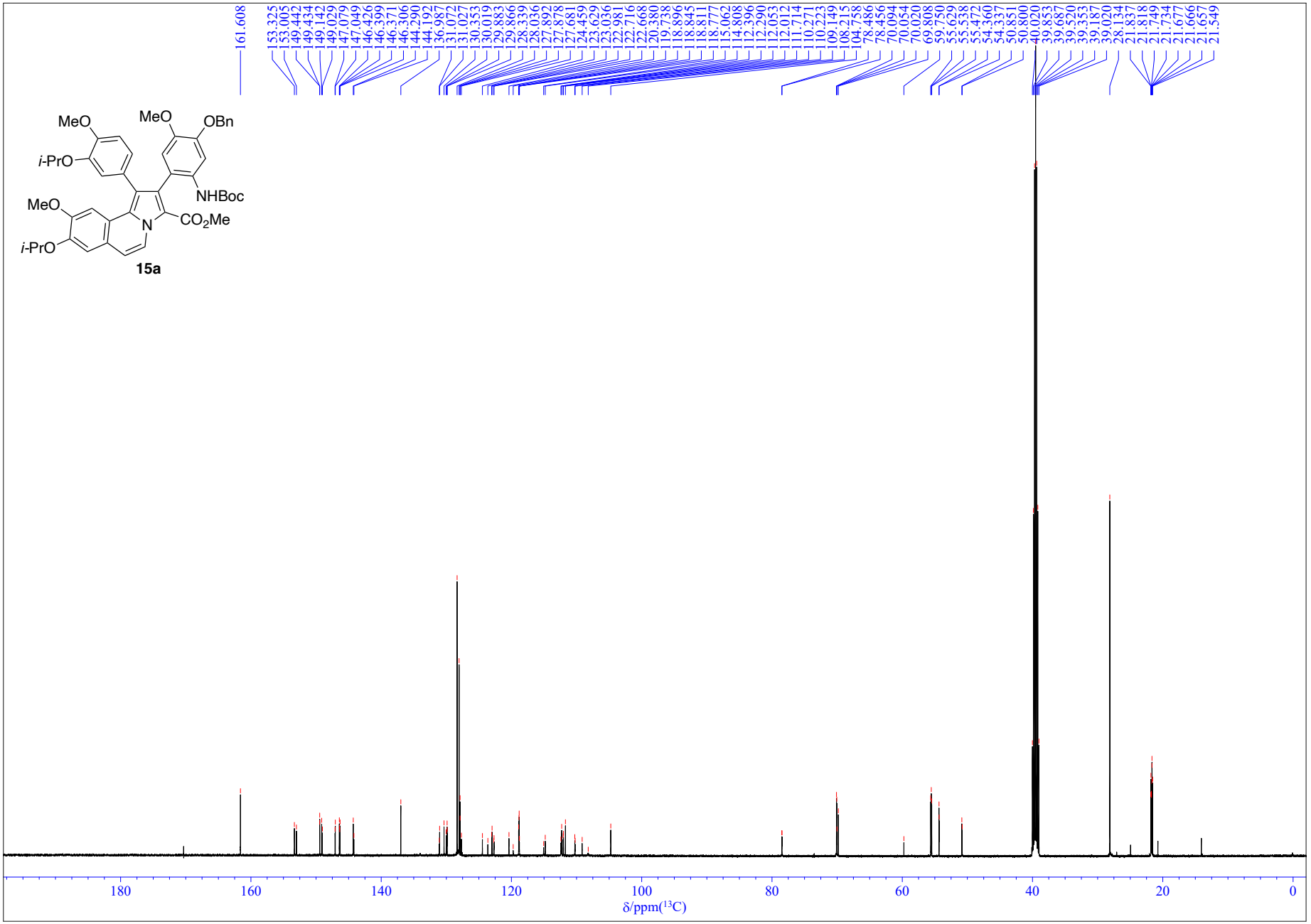

Figure S8. ^{13}C NMR spectrum of compound **15a** (126 MHz, DMSO-d_6).

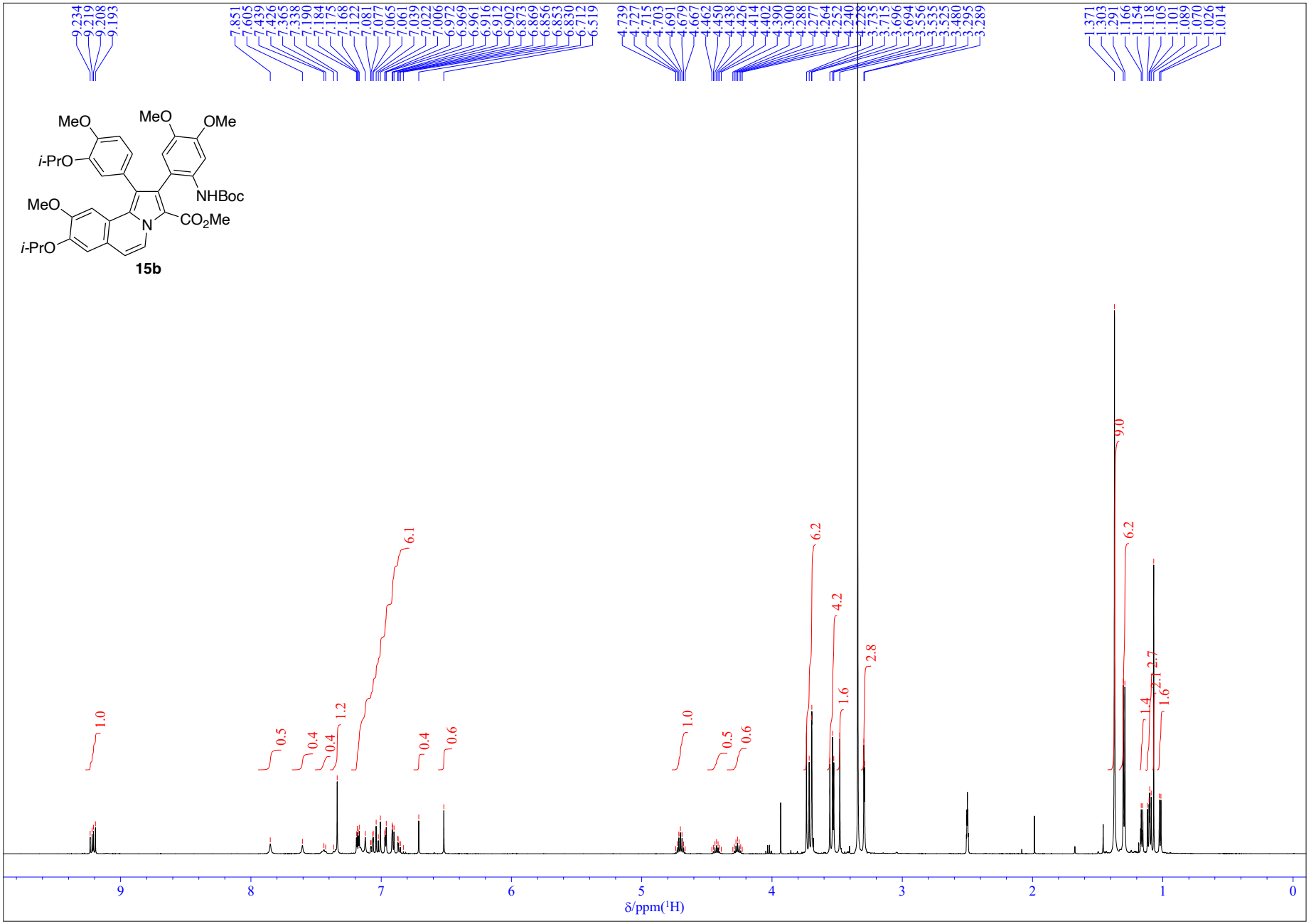

Figure S9. ^{1}H NMR spectrum of compound **15b** (500 MHz, DMSO-d_6).

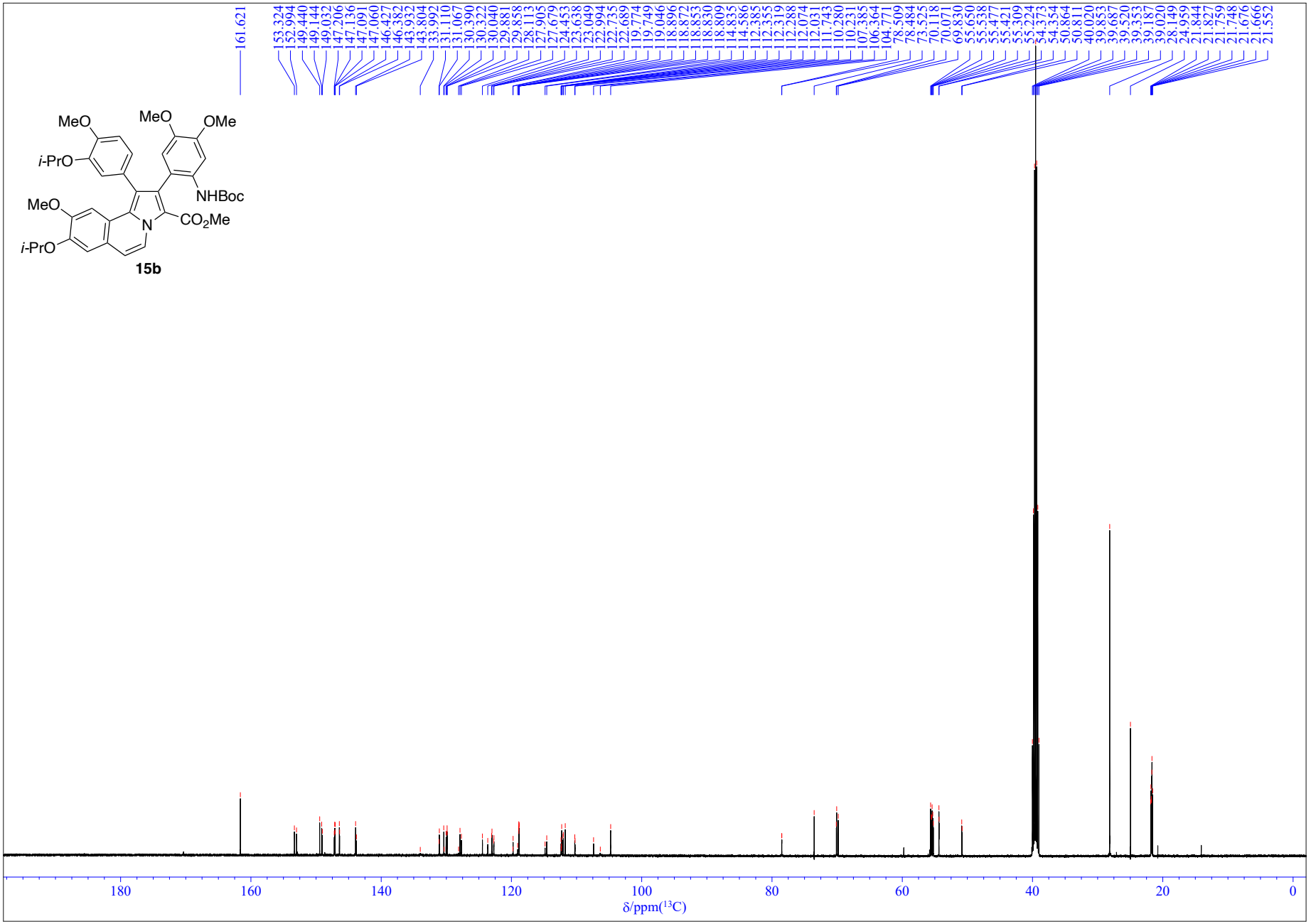

Figure S10. ^{13}C NMR spectrum of compound **15b** (126 MHz, DMSO-d_6).

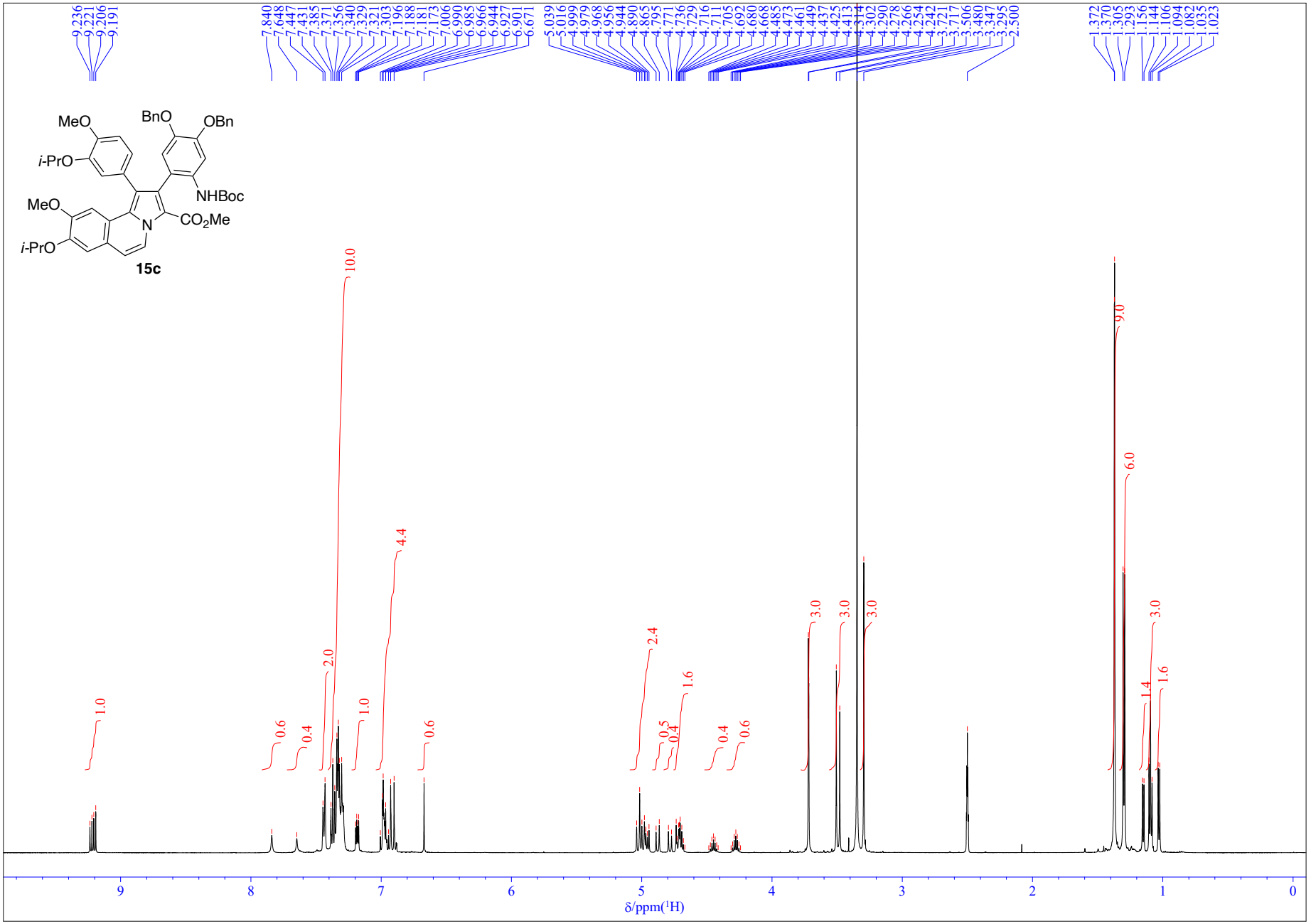

Figure S11. ^{1}H NMR spectrum of compound **15c** (500 MHz, DMSO-d_6).

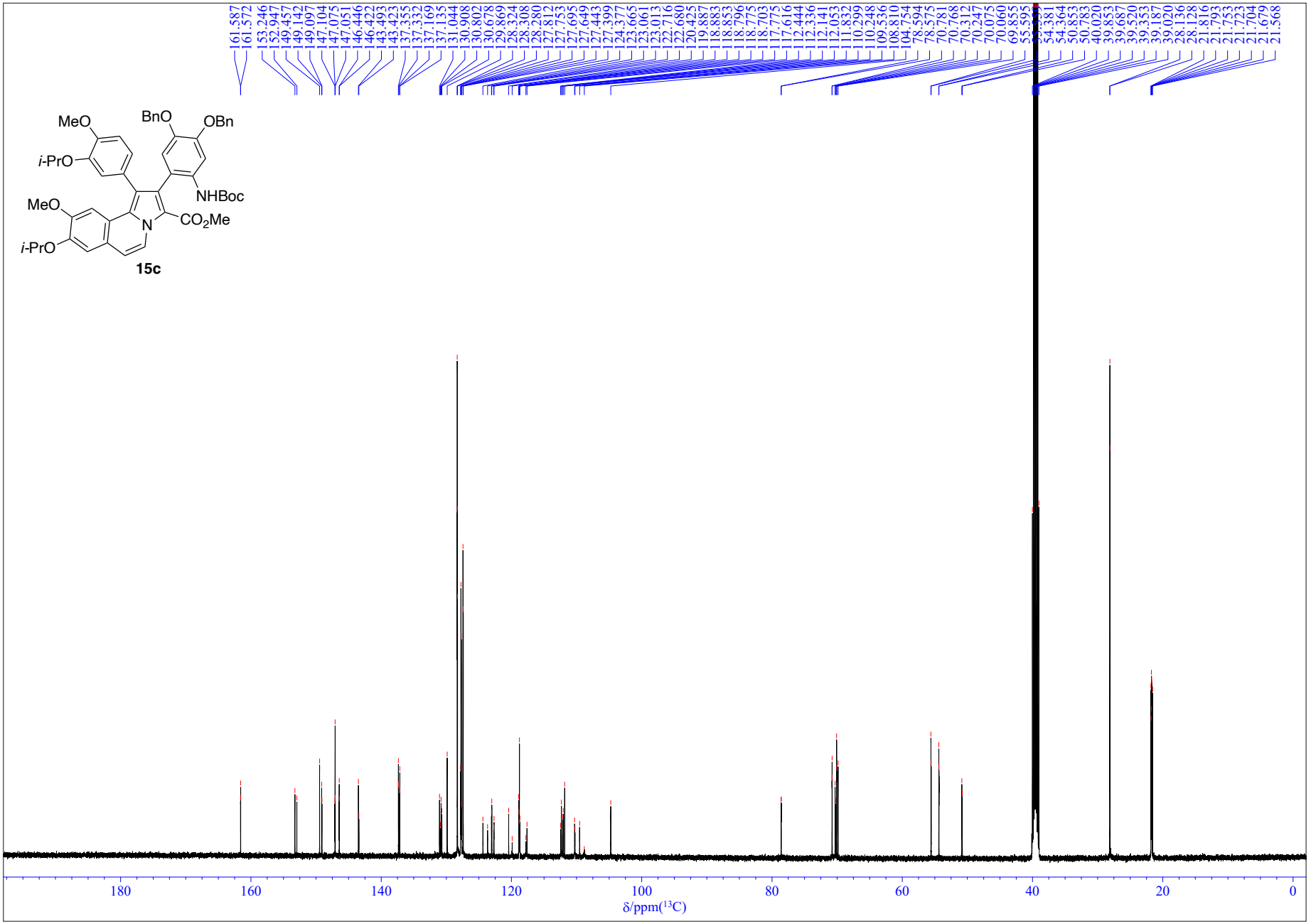

Figure S12. ^{13}C NMR spectrum of compound **15c** (126 MHz, DMSO-d_6)

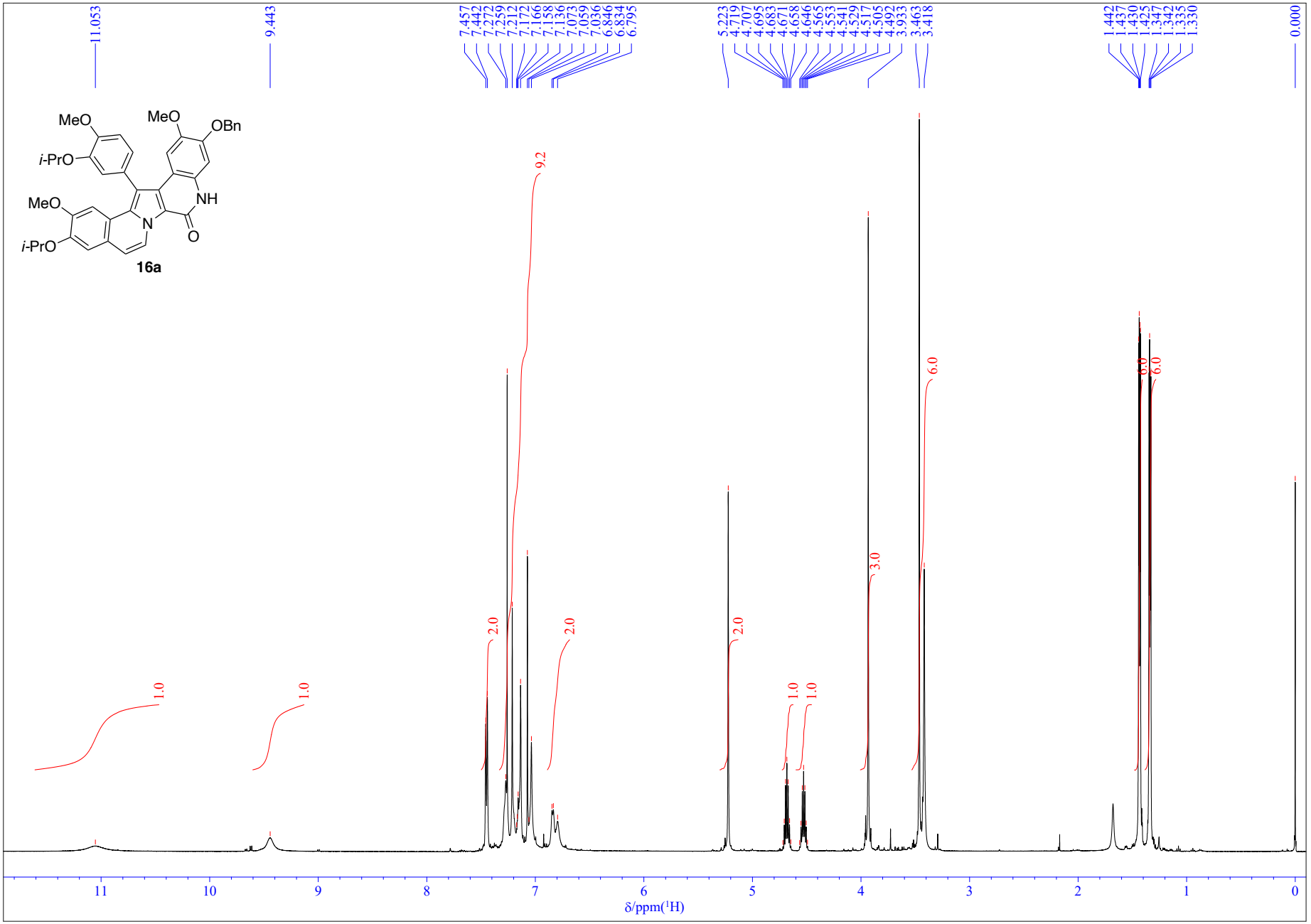

Figure S13. ^{1}H NMR spectrum of compound **16a** (500 MHz, $CDCl_3$).

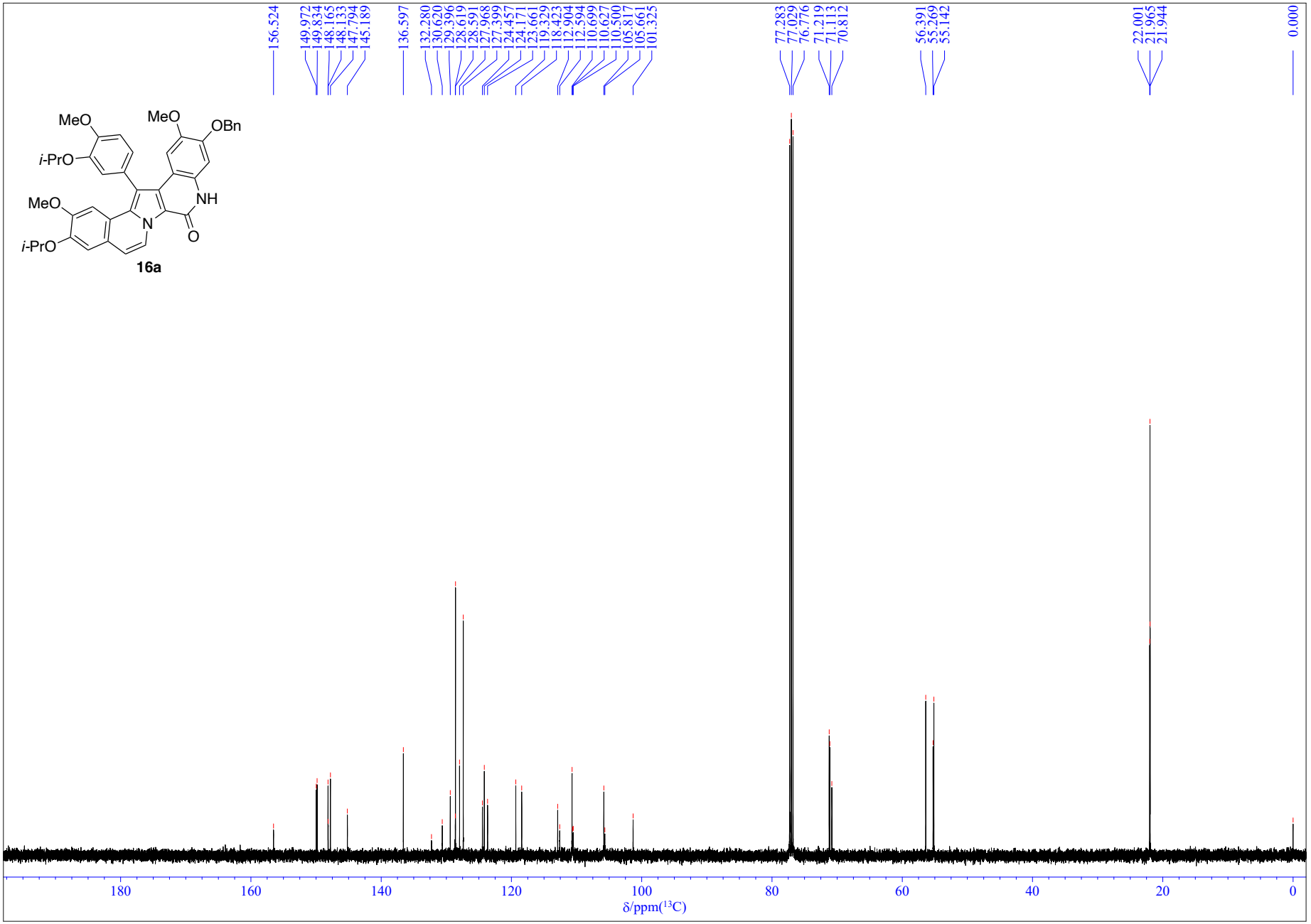

Figure S14. ^{13}C NMR spectrum of compound **16a** (126 MHz, $CDCl_3$).

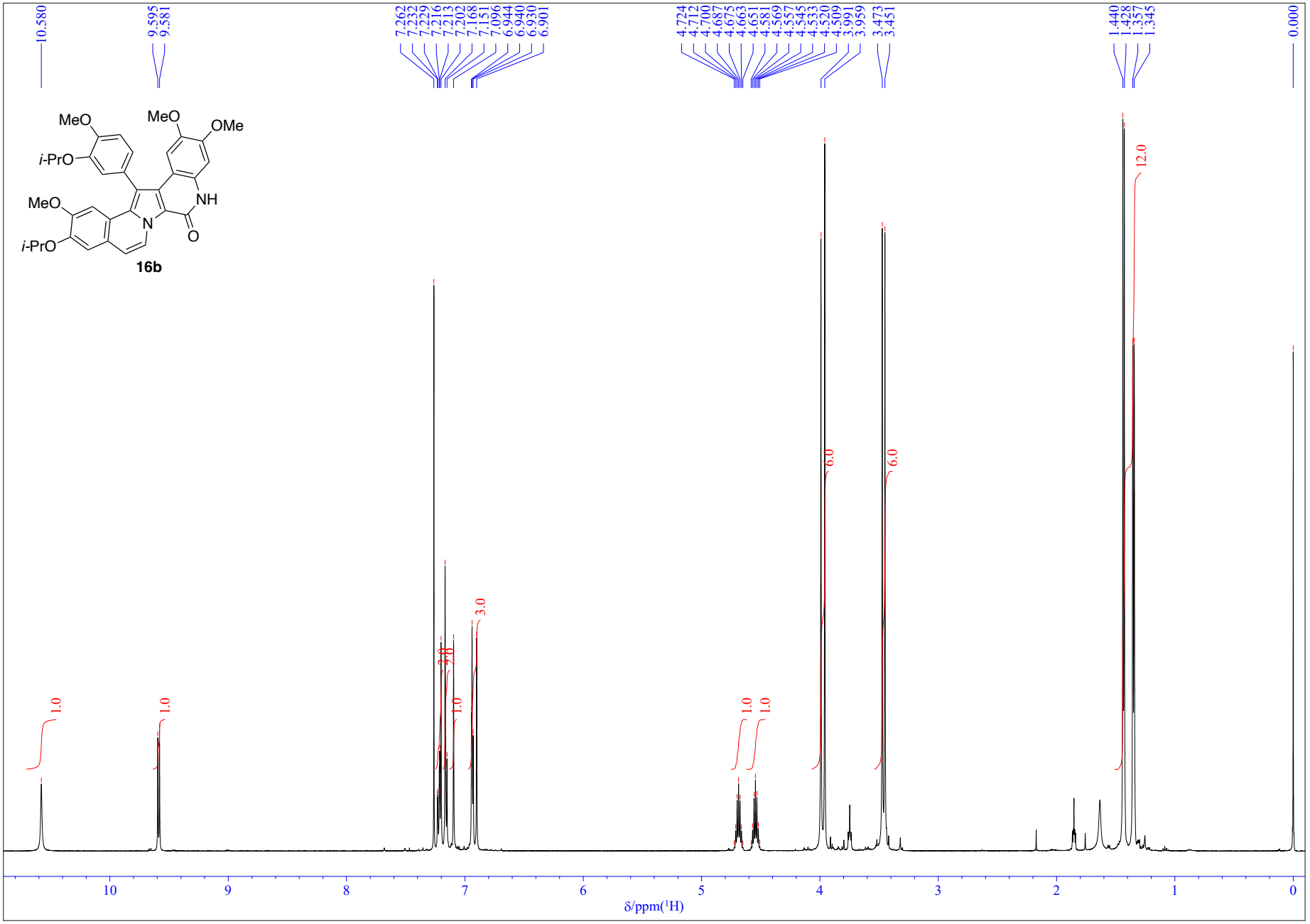

Figure S15. ^{1}H NMR spectrum of compound **16b** (500 MHz, $CDCl_3$).

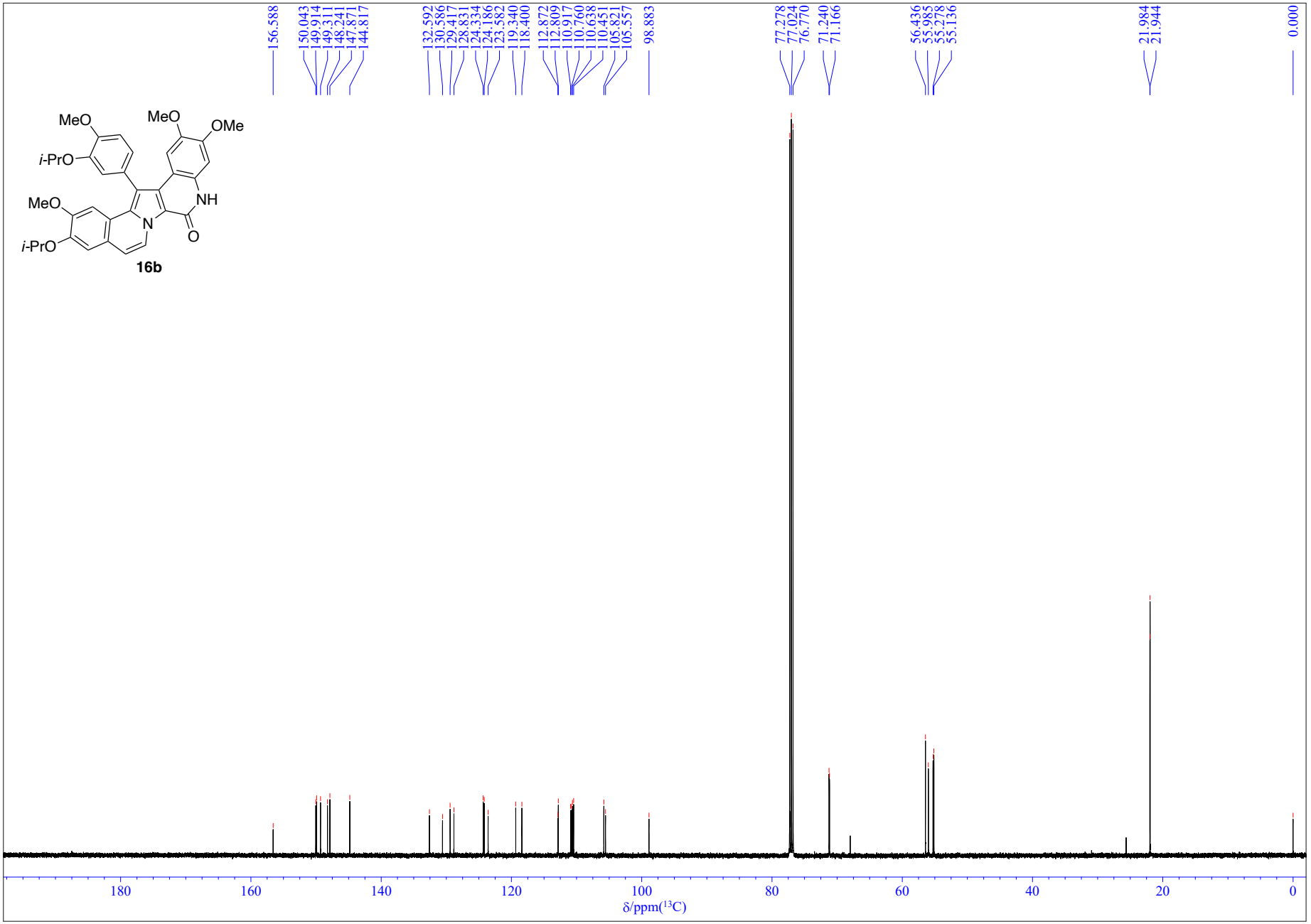

Figure S16. ^{13}C NMR spectrum of compound **16b** (126 MHz, $CDCl_3$).

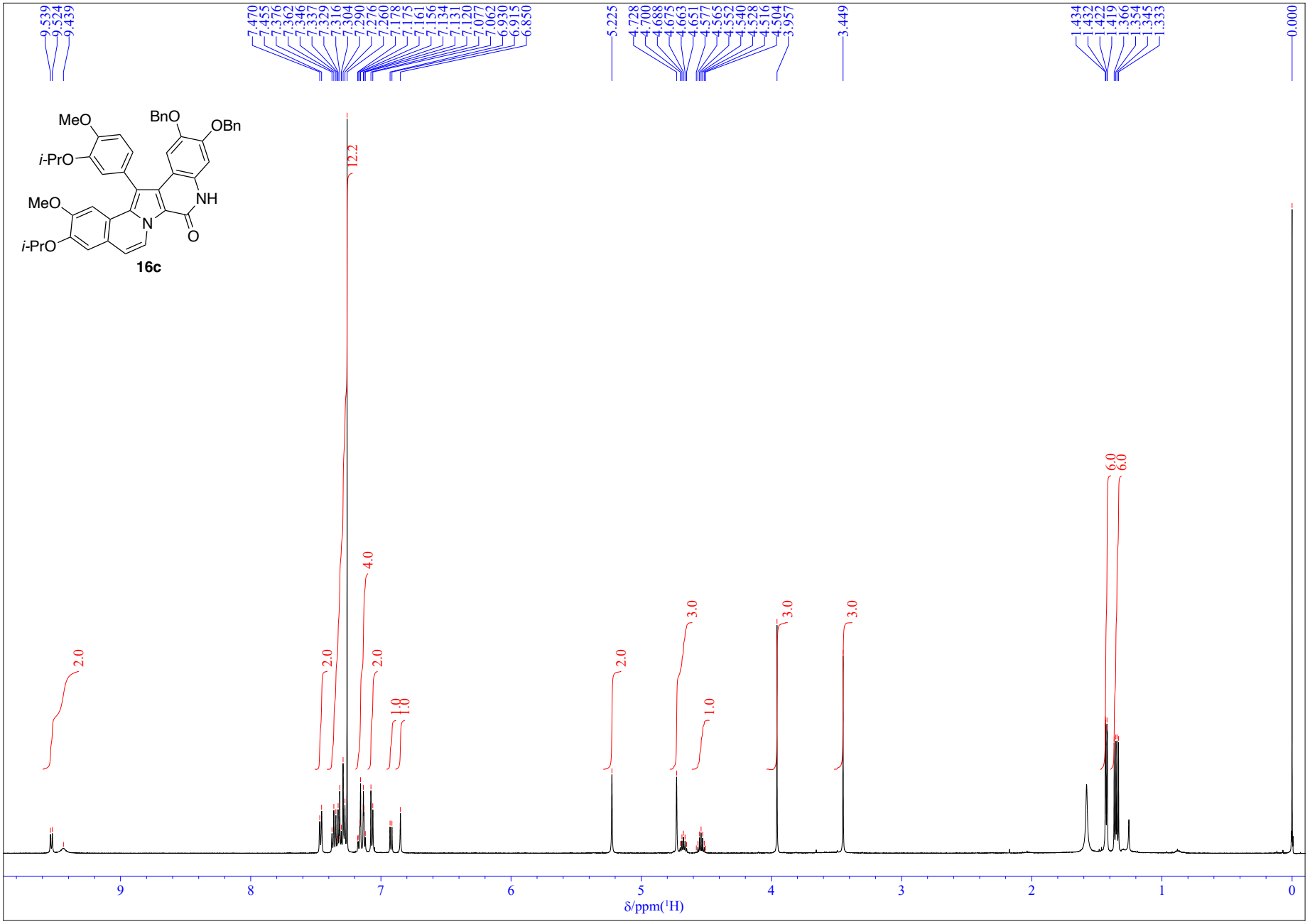

Figure S17. ^{1}H NMR spectrum of compound **16c** (500 MHz, $CDCl_3$).

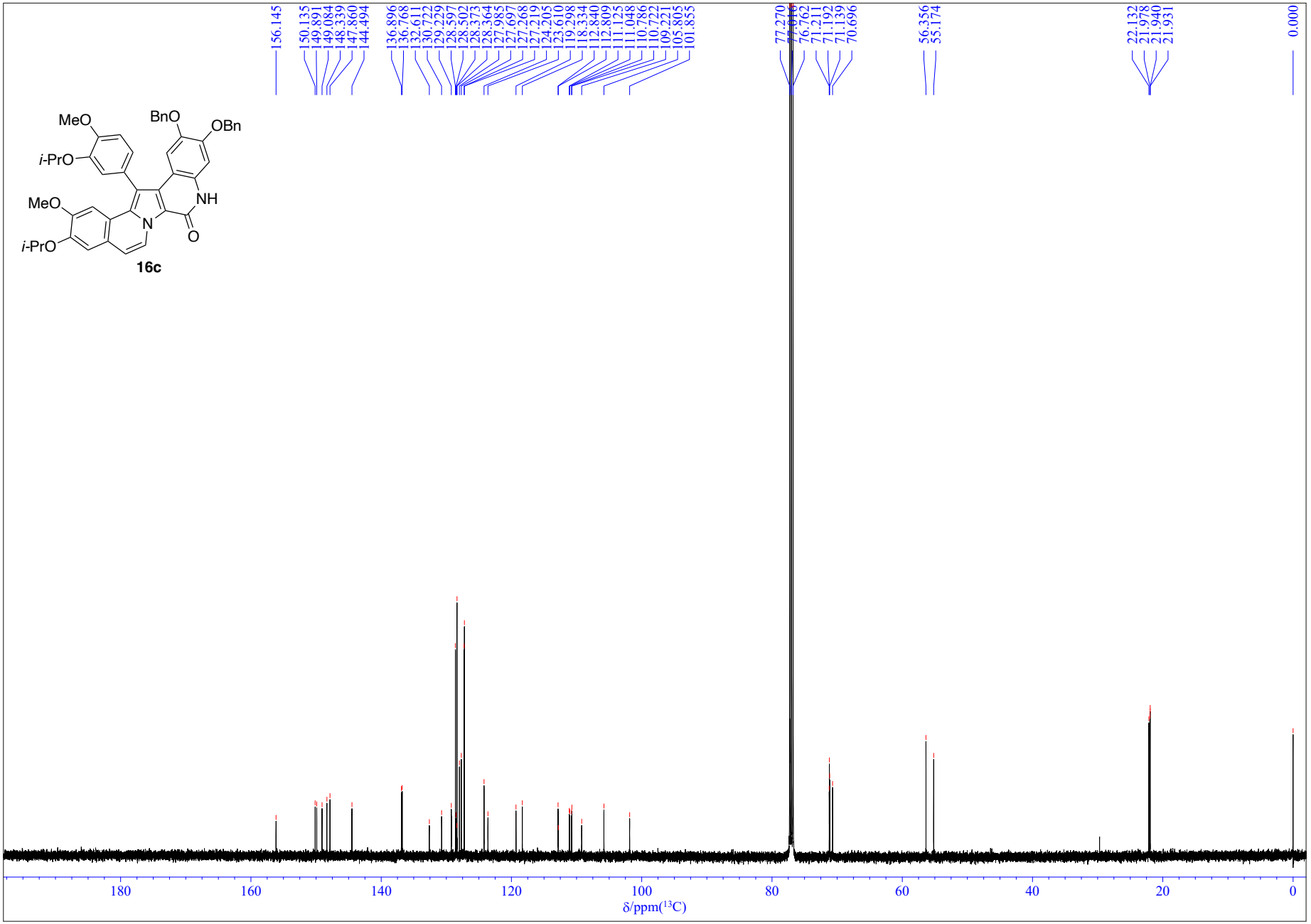

Figure S18. ^{13}C NMR spectrum of compound **16c** (126 MHz, $CDCl_3$)

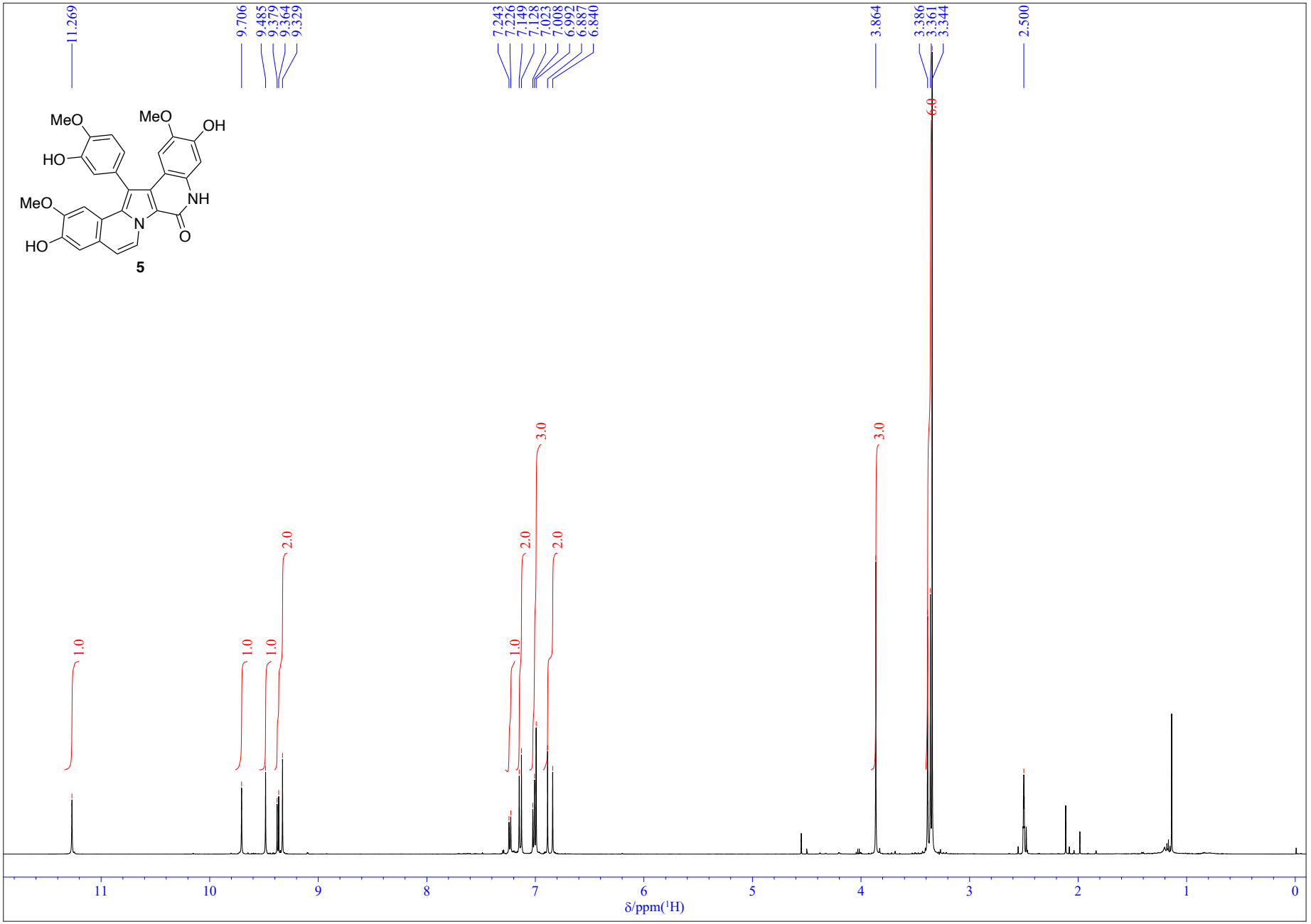

Figure S19. ^{1}H NMR spectrum of compound **5** (500 MHz, DMSO-d_6).

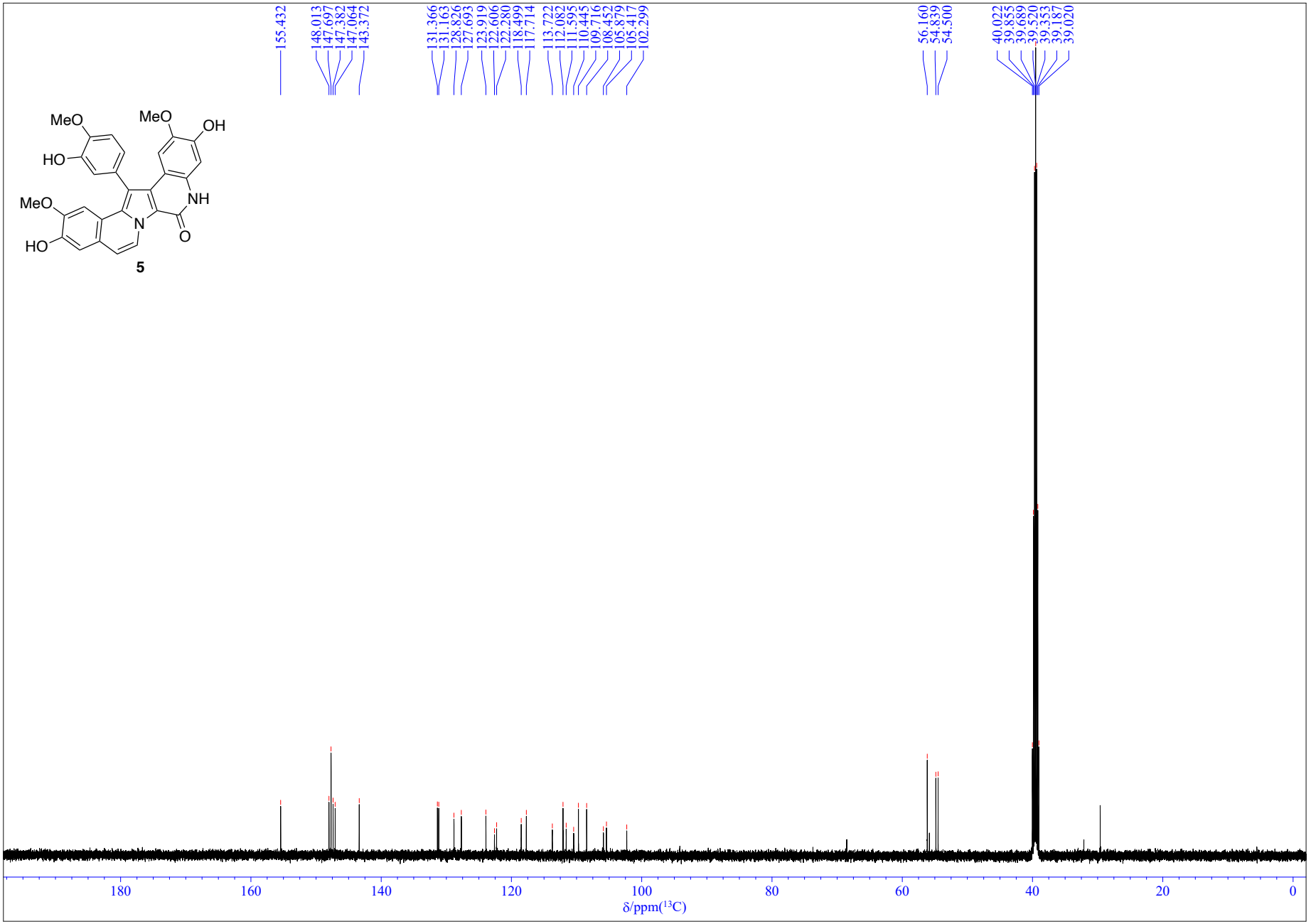

Figure S20. ^{13}C NMR spectrum of compound **5** (126 MHz, DMSO-d_6).

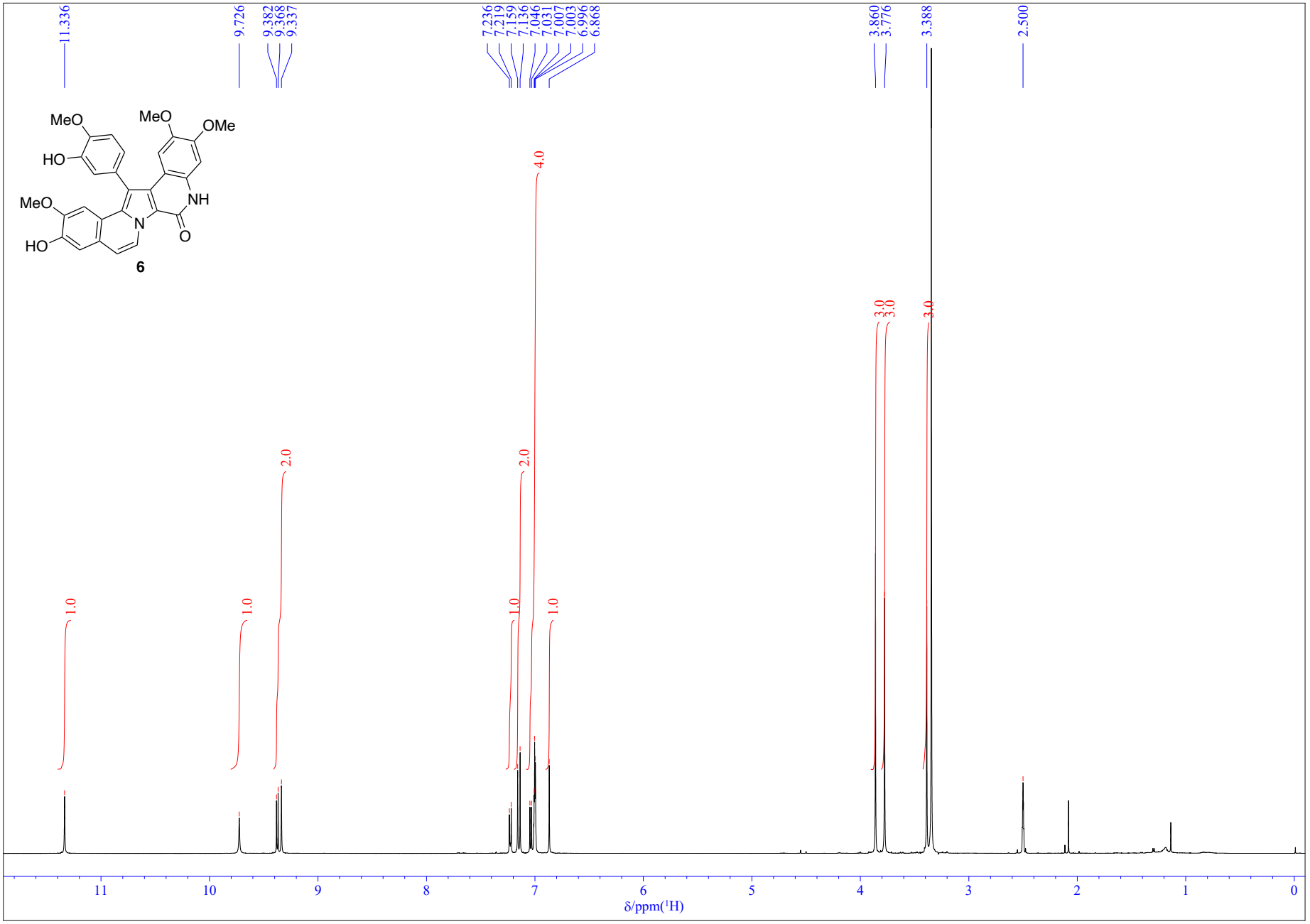

Figure S21. ^{1}H NMR spectrum of compound **6** (500 MHz, DMSO-d_6).

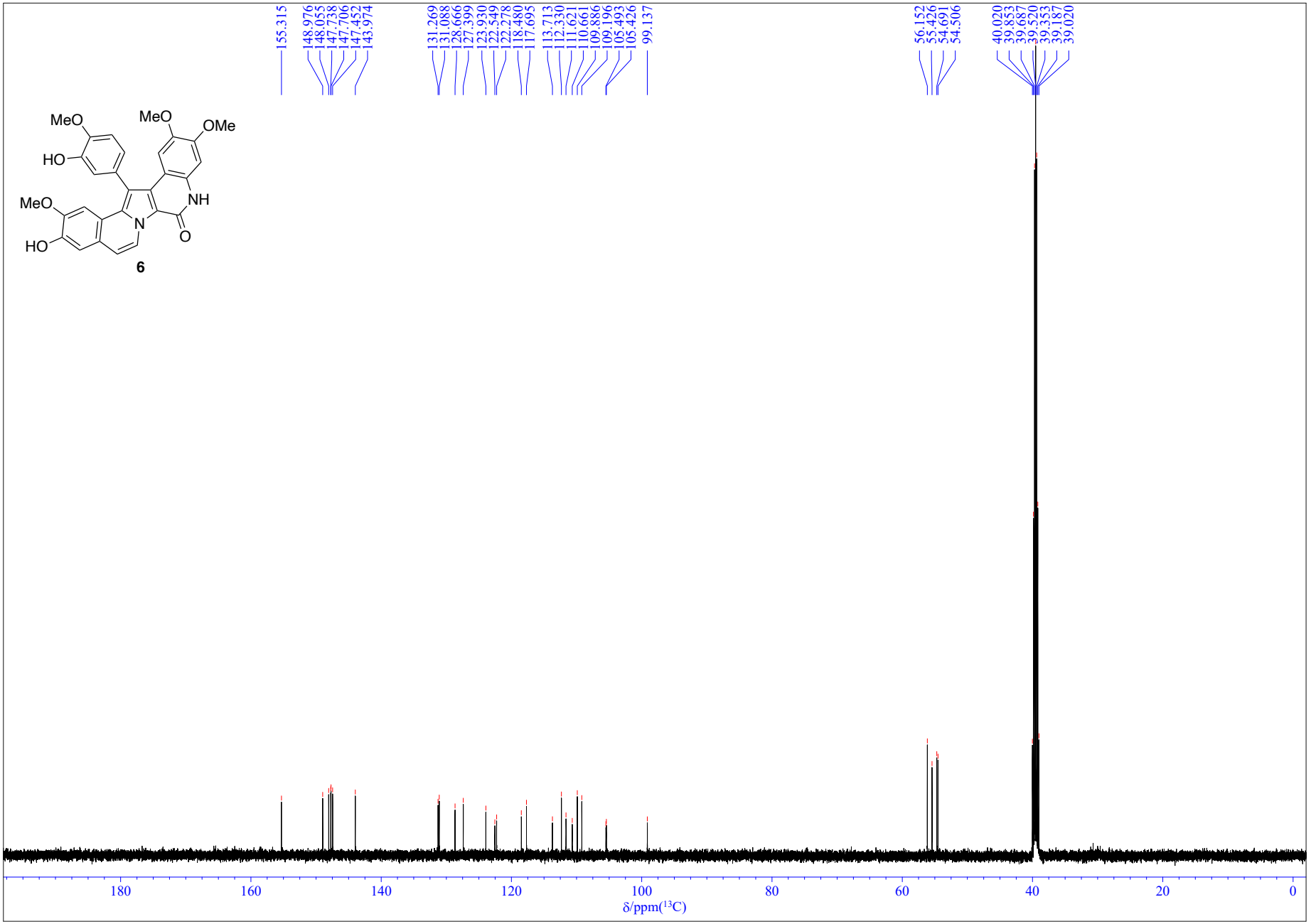

Figure S22. ^{13}C NMR spectrum of compound **6** (126 MHz, DMSO-d_6).

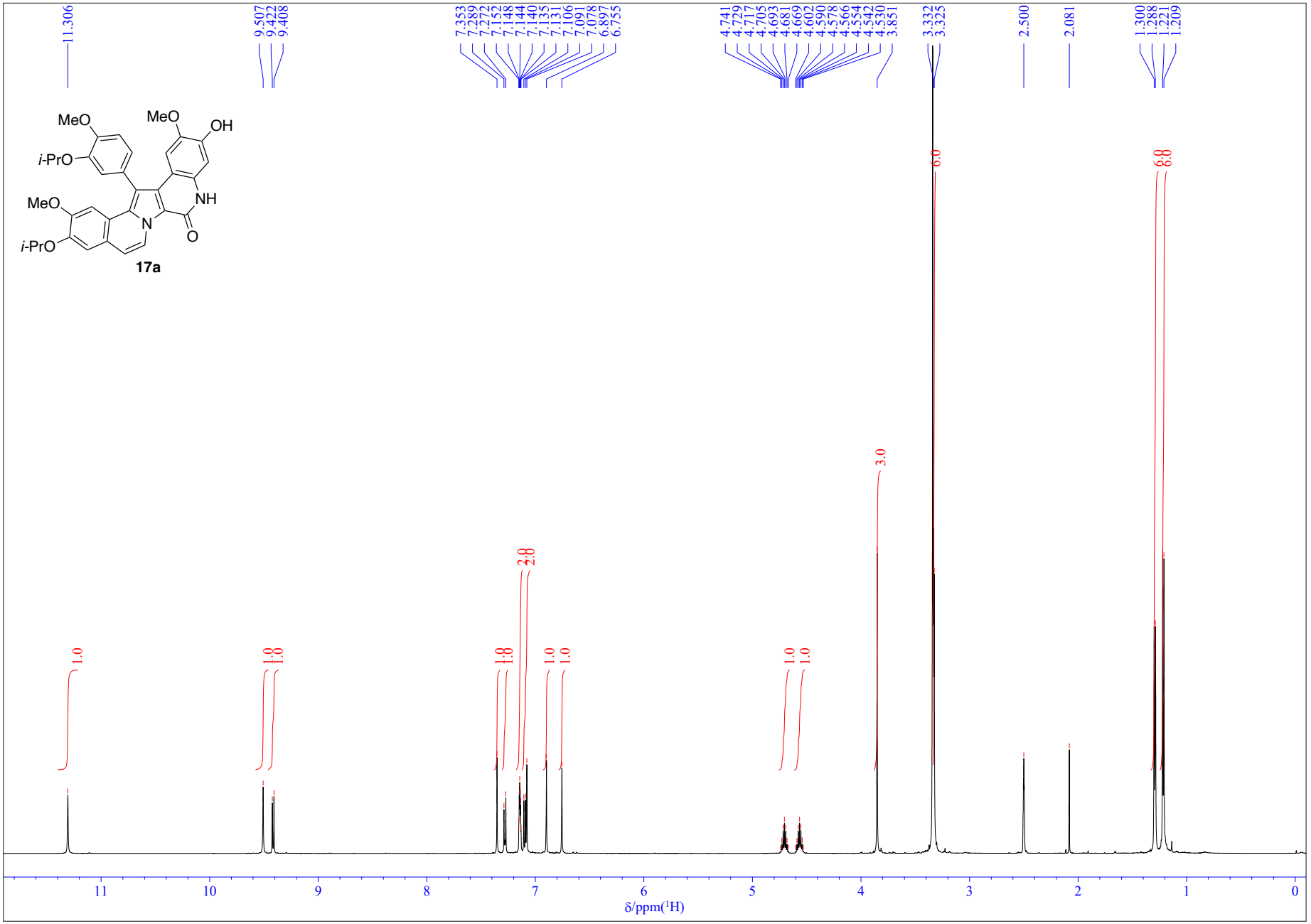

Figure S23. ^{1}H NMR spectrum of compound **17a** (500 MHz, DMSO-d_6).

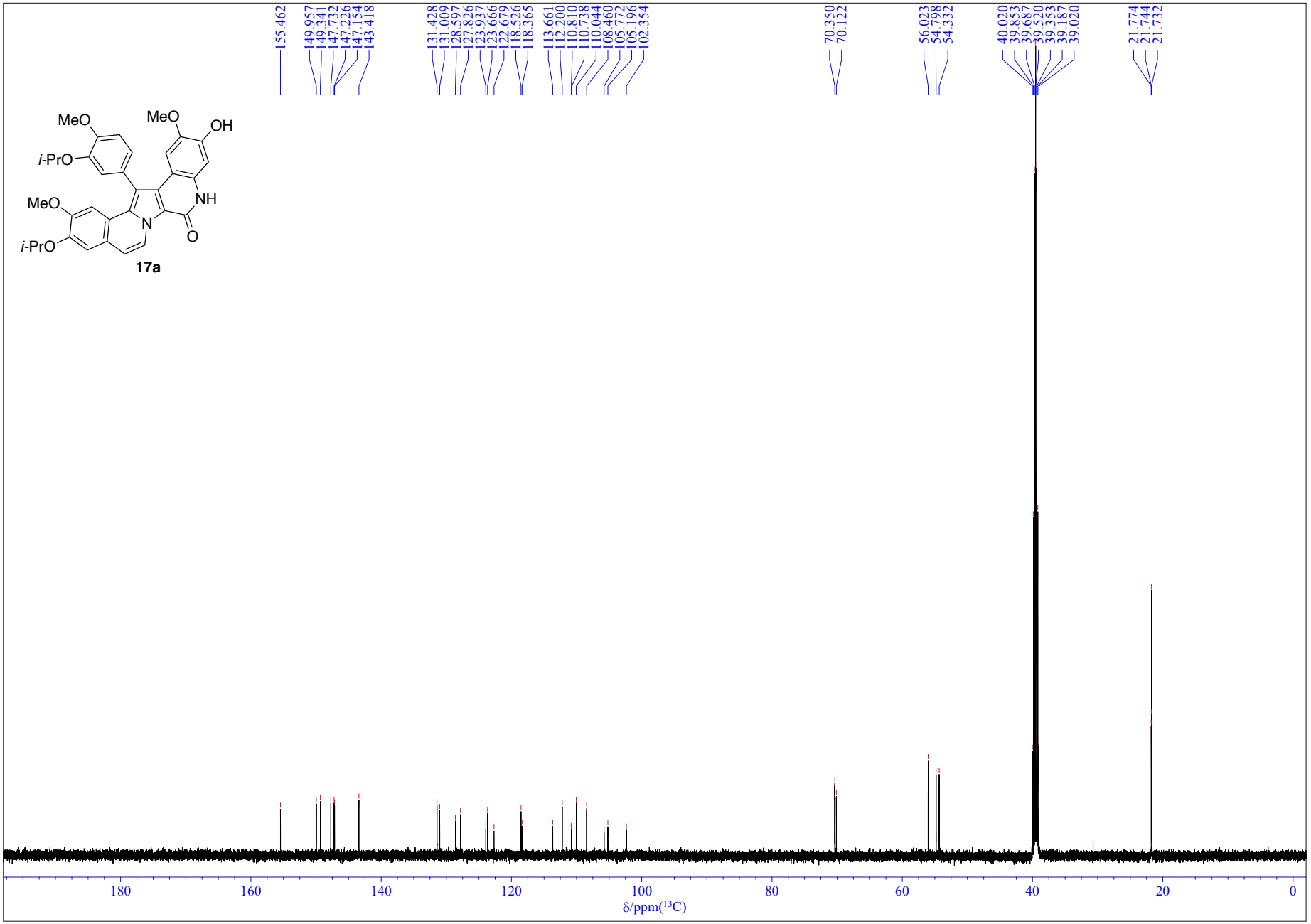

Figure S24. ^{13}C NMR spectrum of compound **17a** (126 MHz, DMSO-d_6).

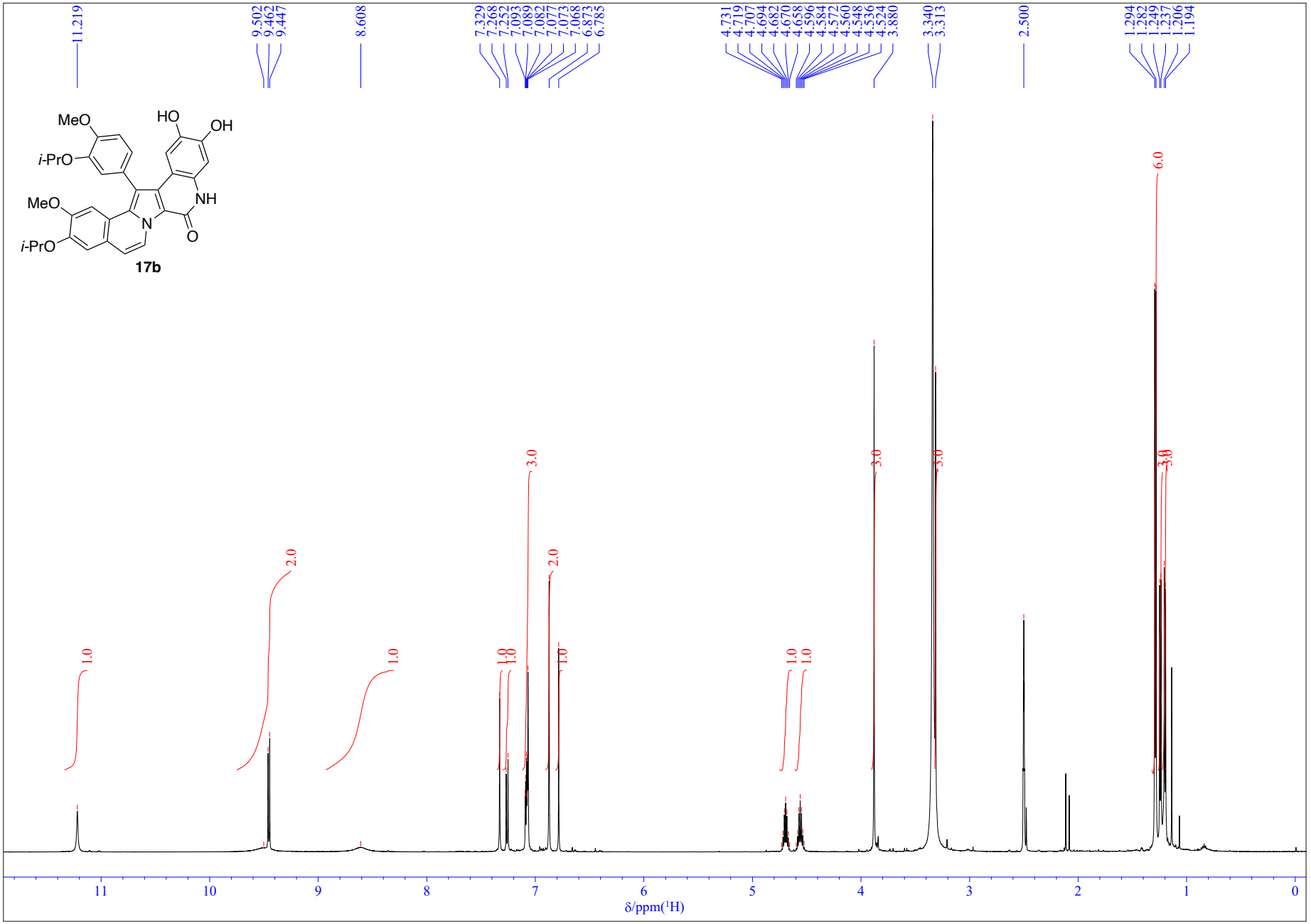

Figure S25. ^{1}H NMR spectrum of compound **17b** (500 MHz, DMSO-d_6).

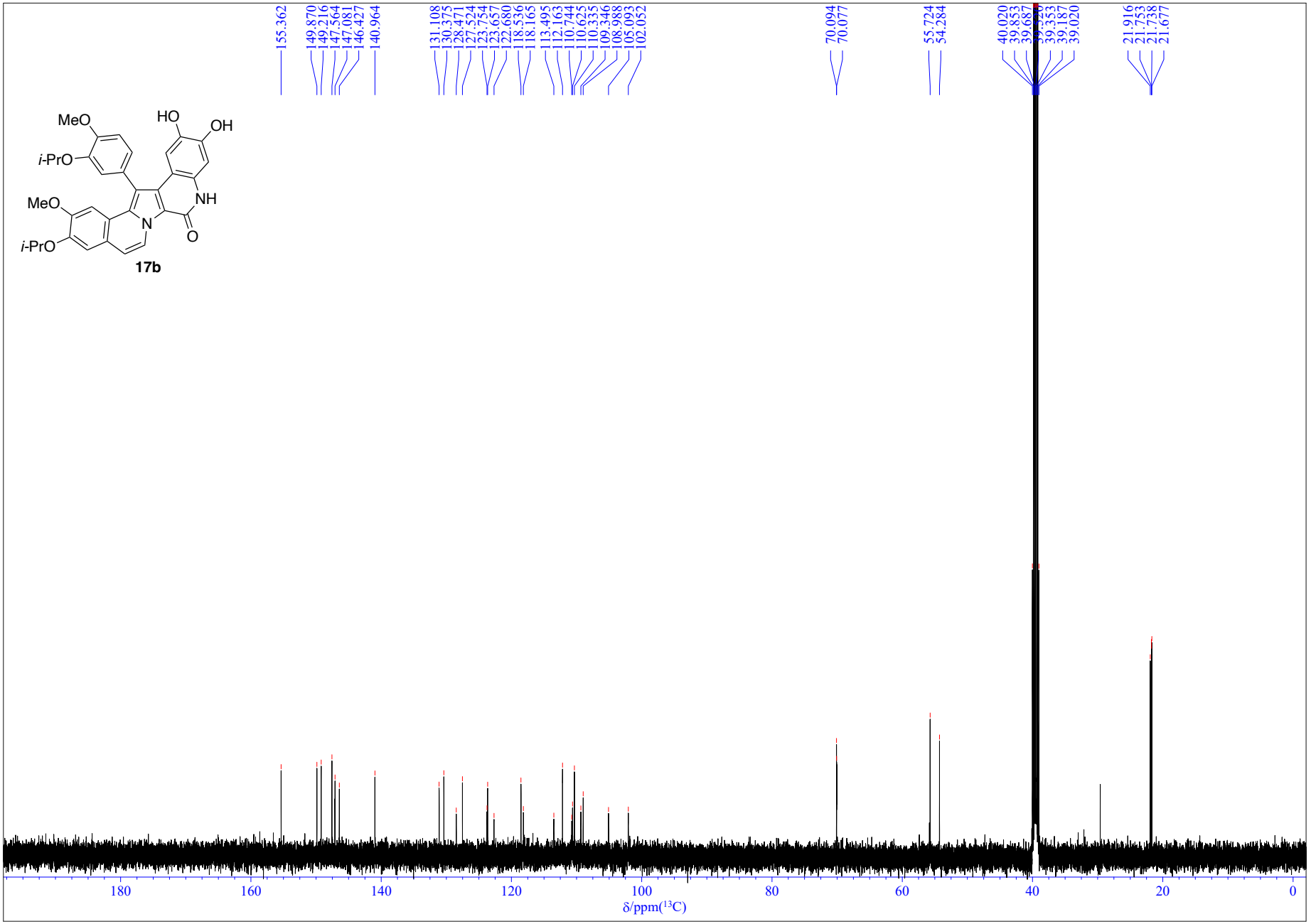

Figure S26. ^{13}C NMR spectrum of compound **17b** (126 MHz, DMSO-d_6).

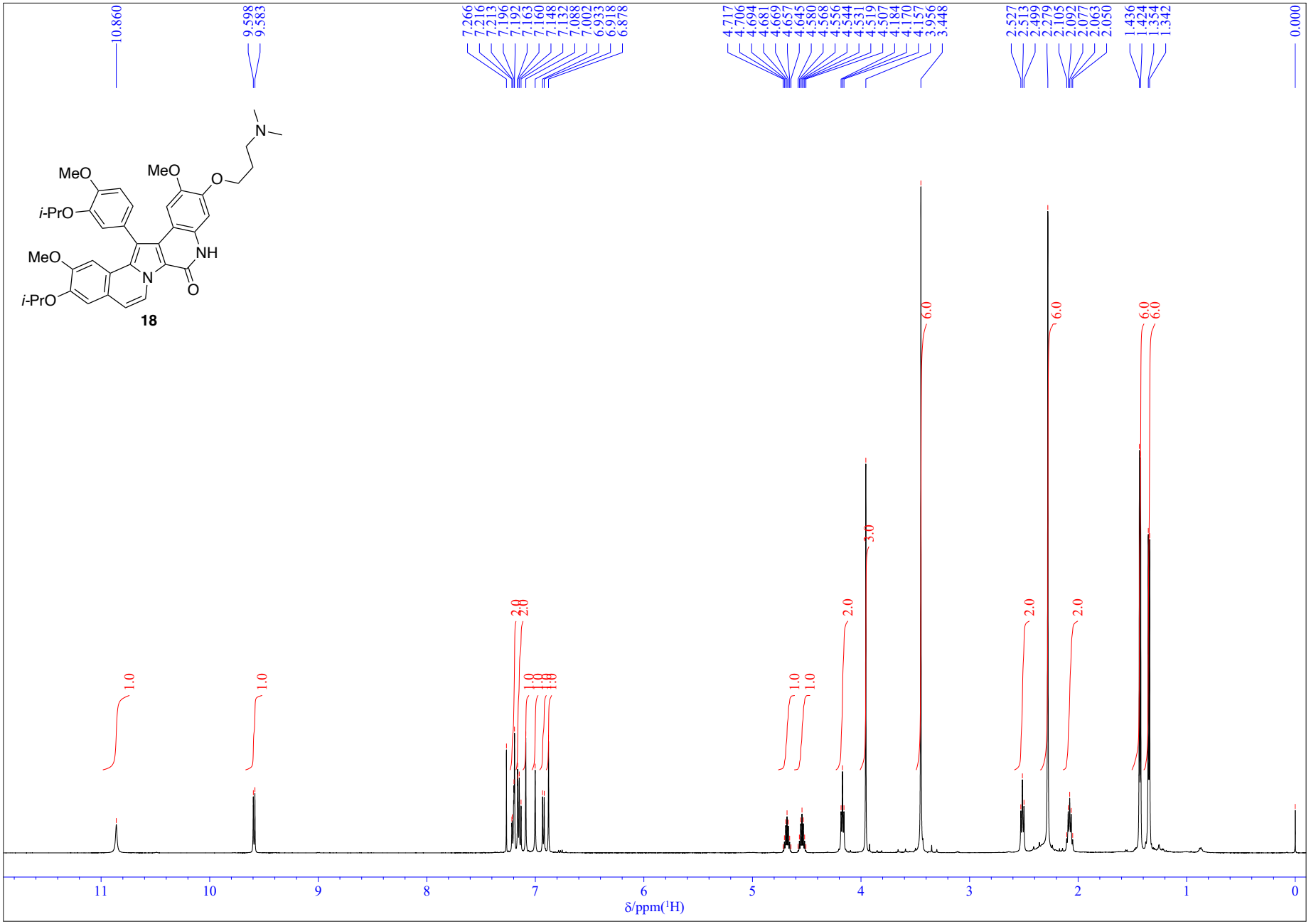

Figure S27. ^{1}H NMR spectrum of compound **18** (500 MHz, $CDCl_3$).

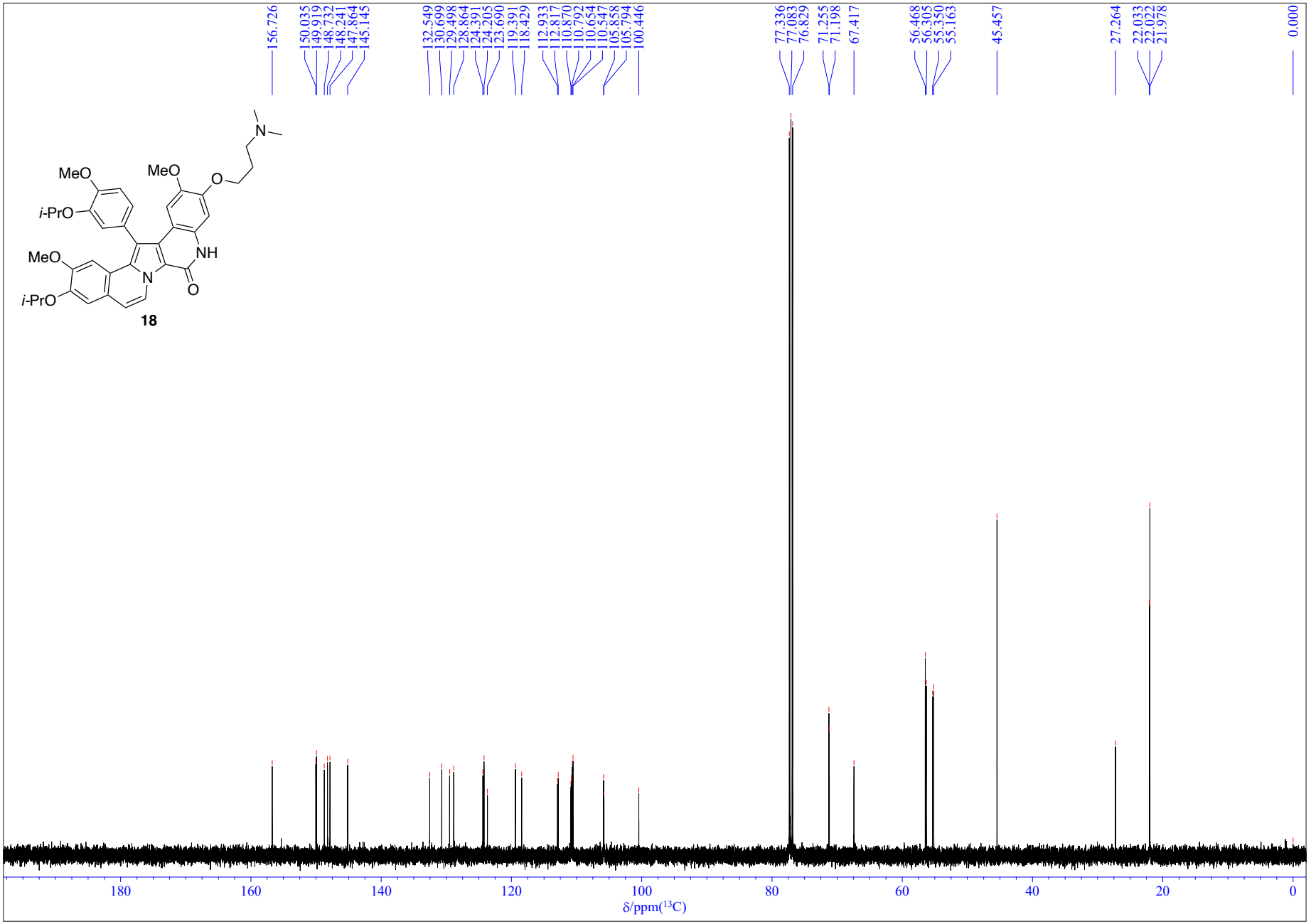

Figure S28. ^{13}C NMR spectrum of compound **18** (126 MHz, $CDCl_3$).

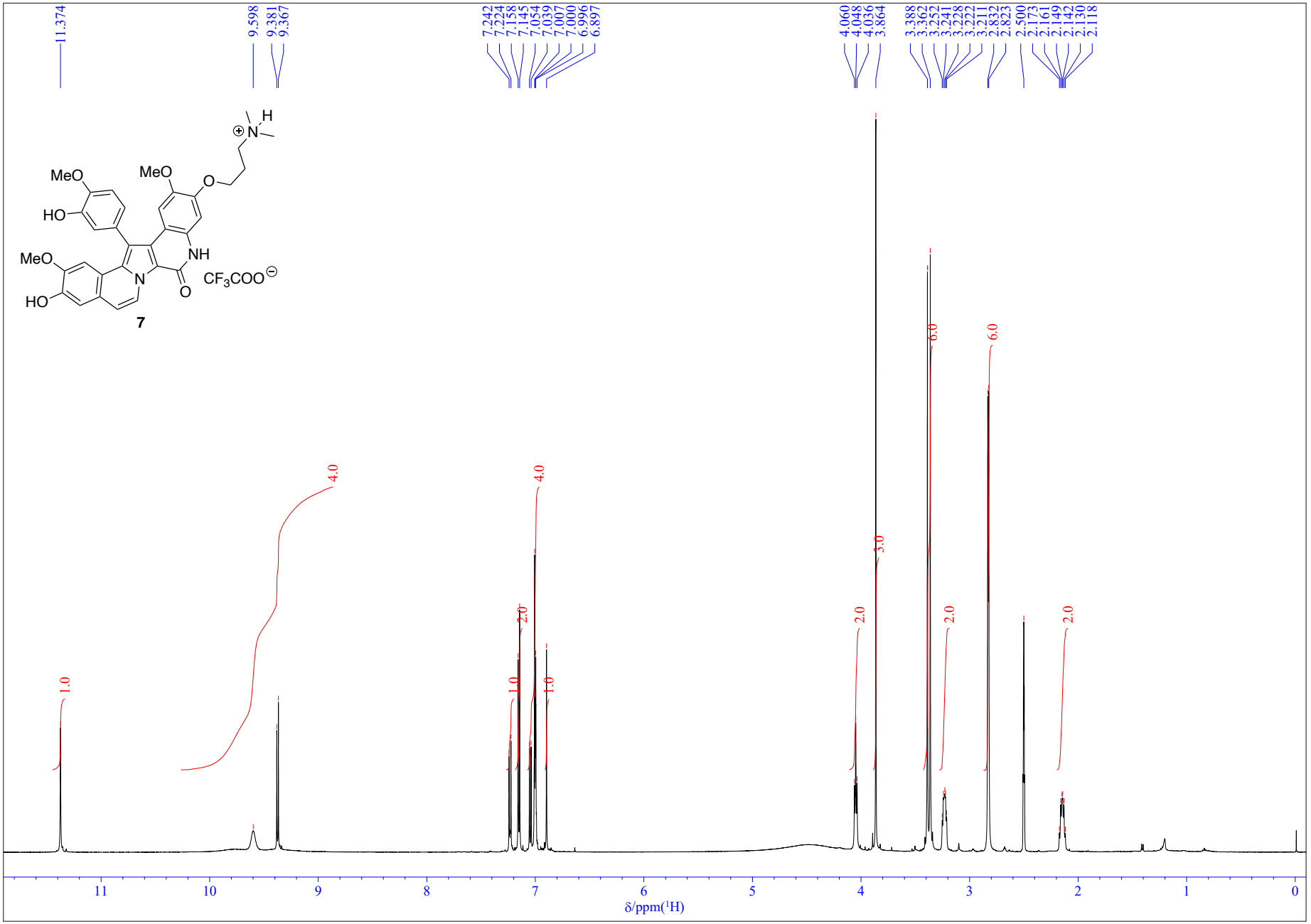

Figure S29. ^{1}H NMR spectrum of compound **7** (500 MHz, DMSO-d_6).

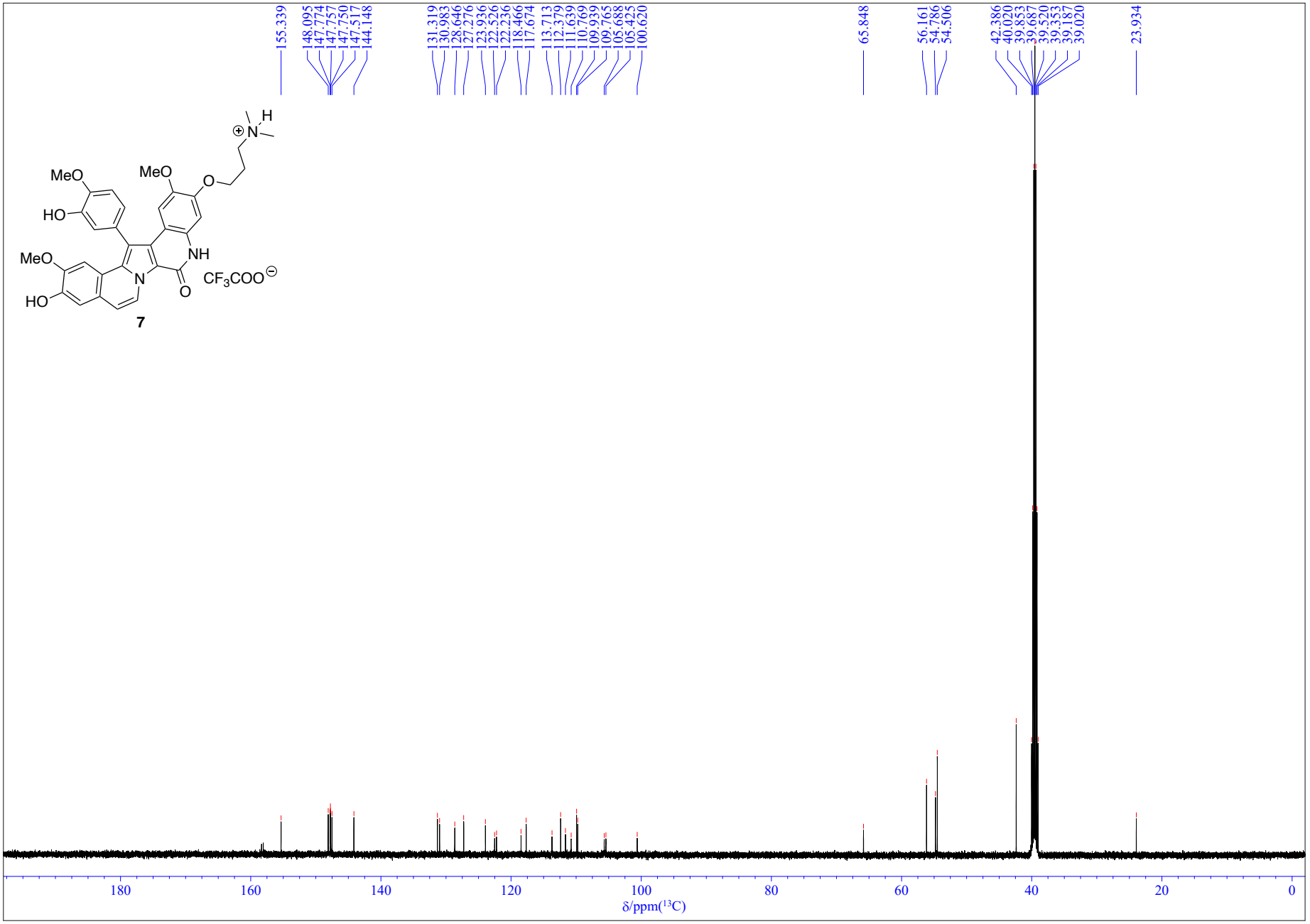

Figure S30. ^{13}C NMR spectrum of compound **7** (126 MHz, DMSO-d_6).

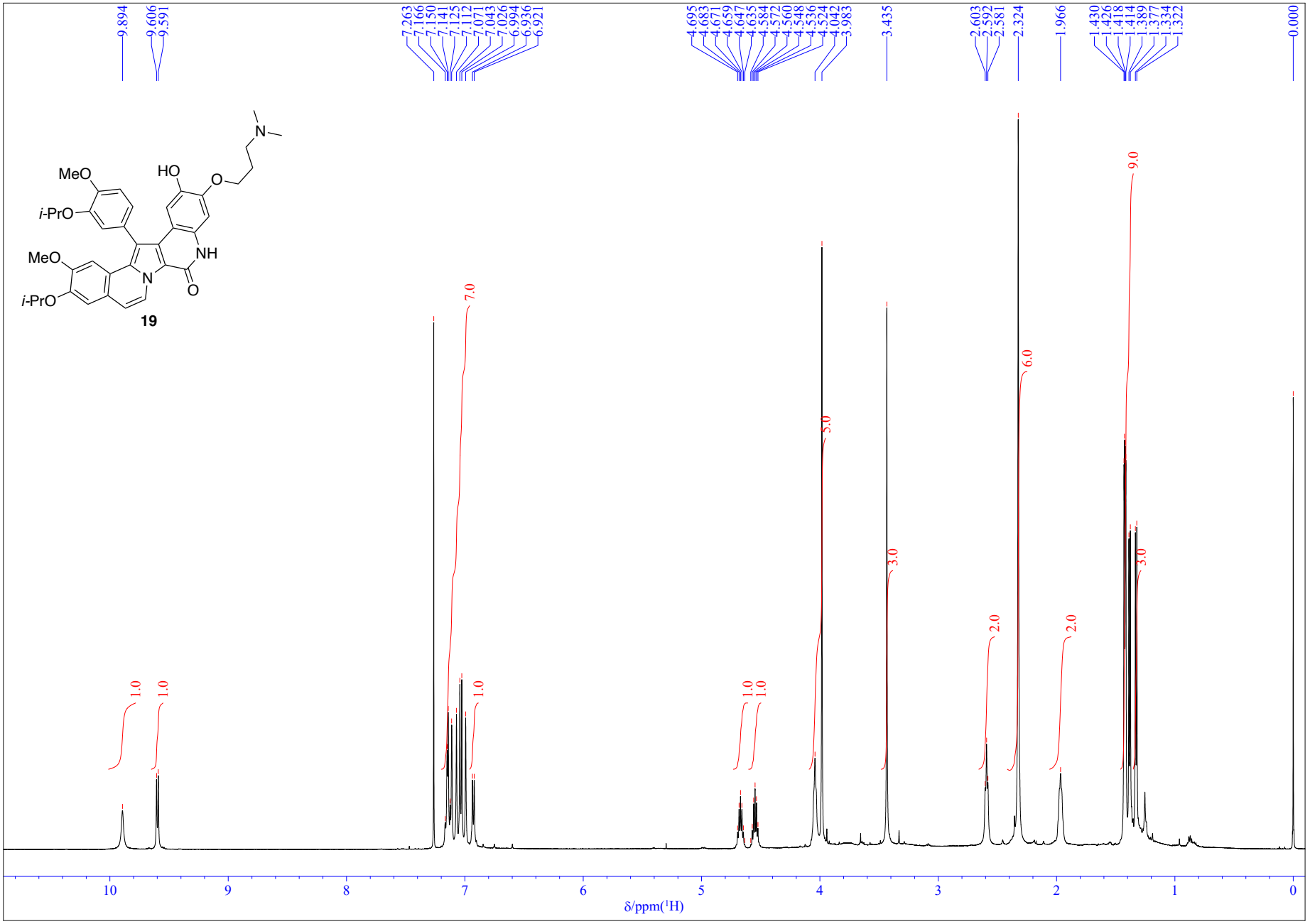

Figure S31. ^{1}H NMR spectrum of compound **19** (500 MHz, $CDCl_3$).

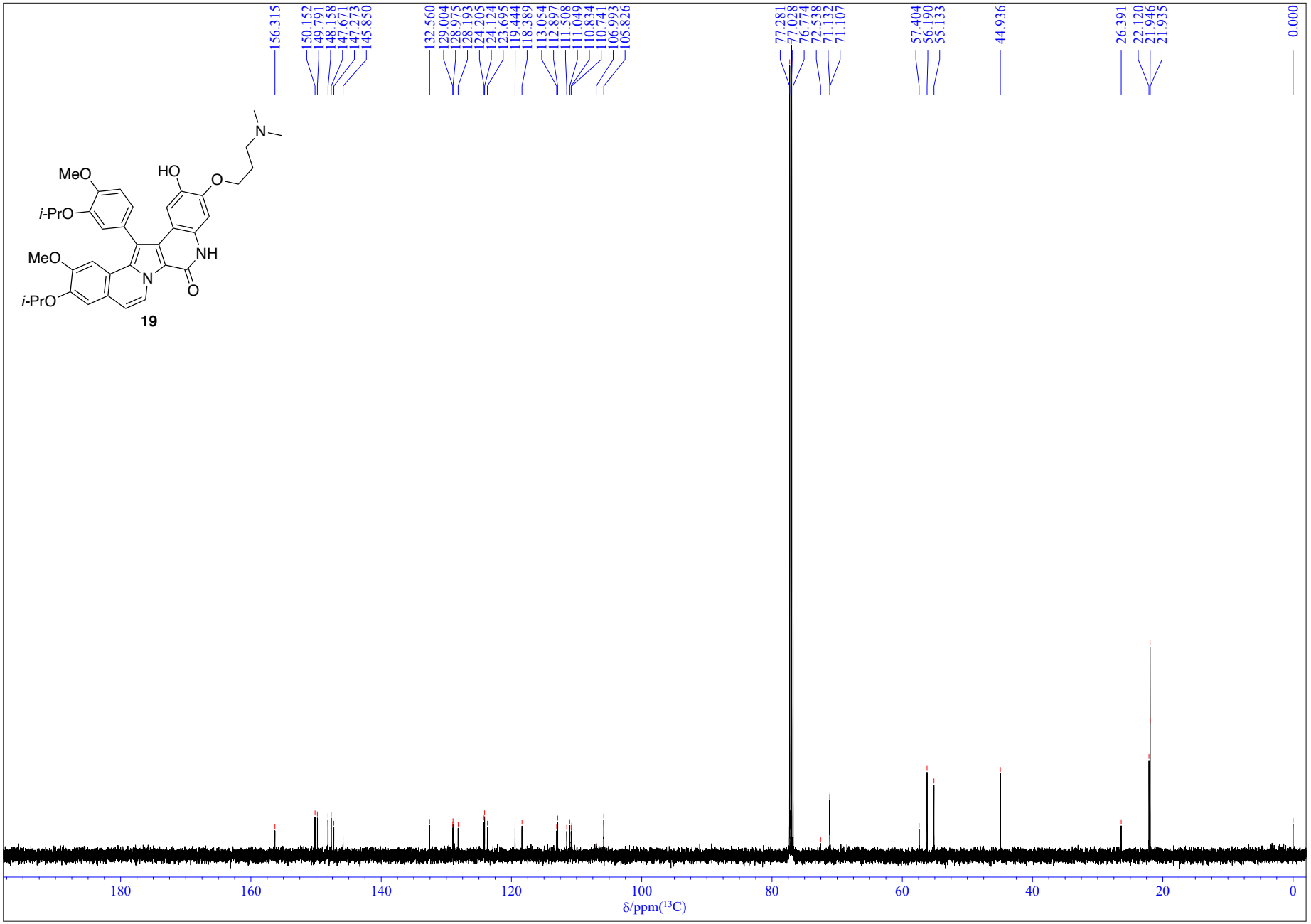

Figure S32. ^{13}C NMR spectrum of compound **19** (126 MHz, $CDCl_3$).

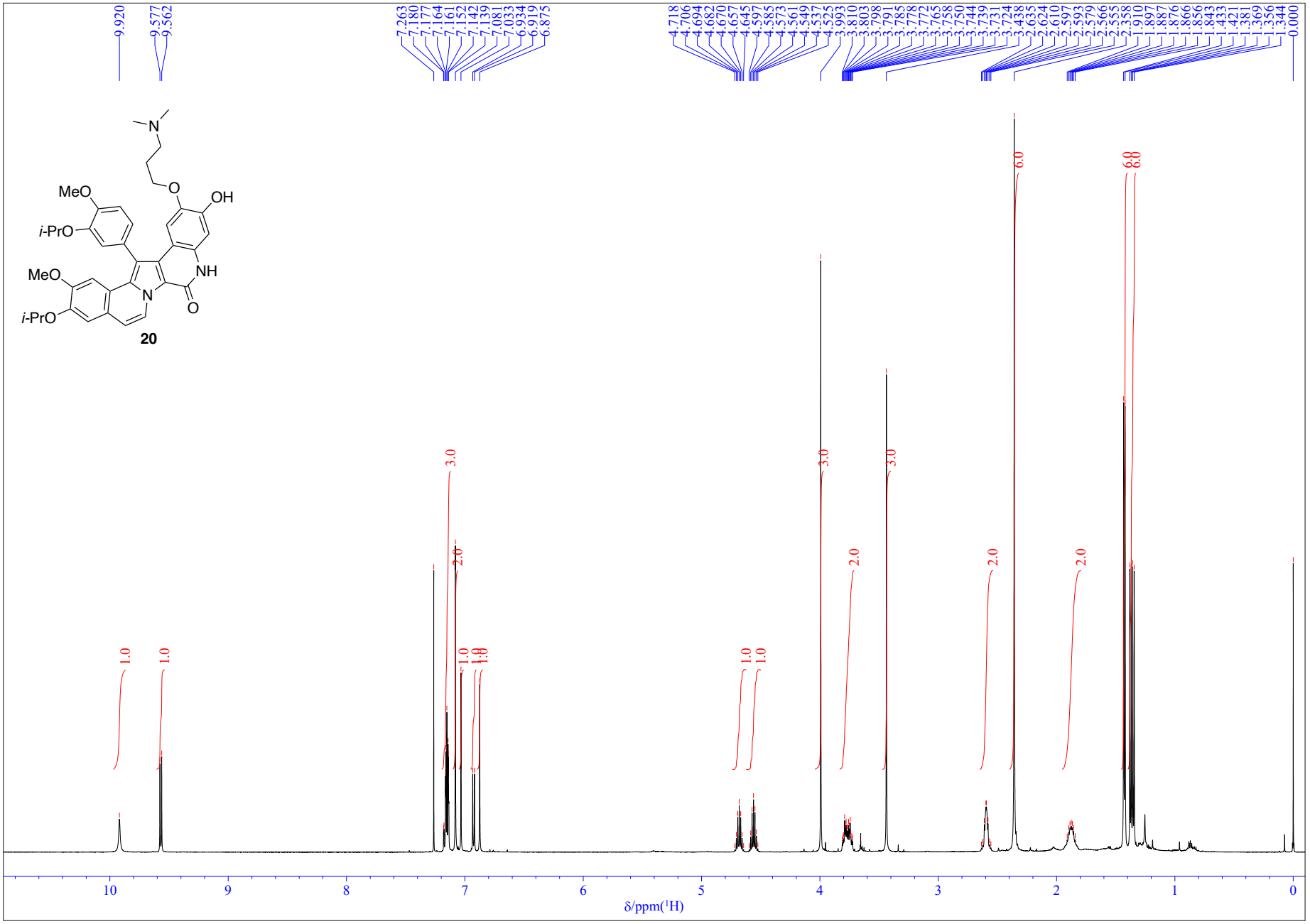

Figure S33. ^{1}H NMR spectrum of compound **20** (500 MHz, $CDCl_3$).

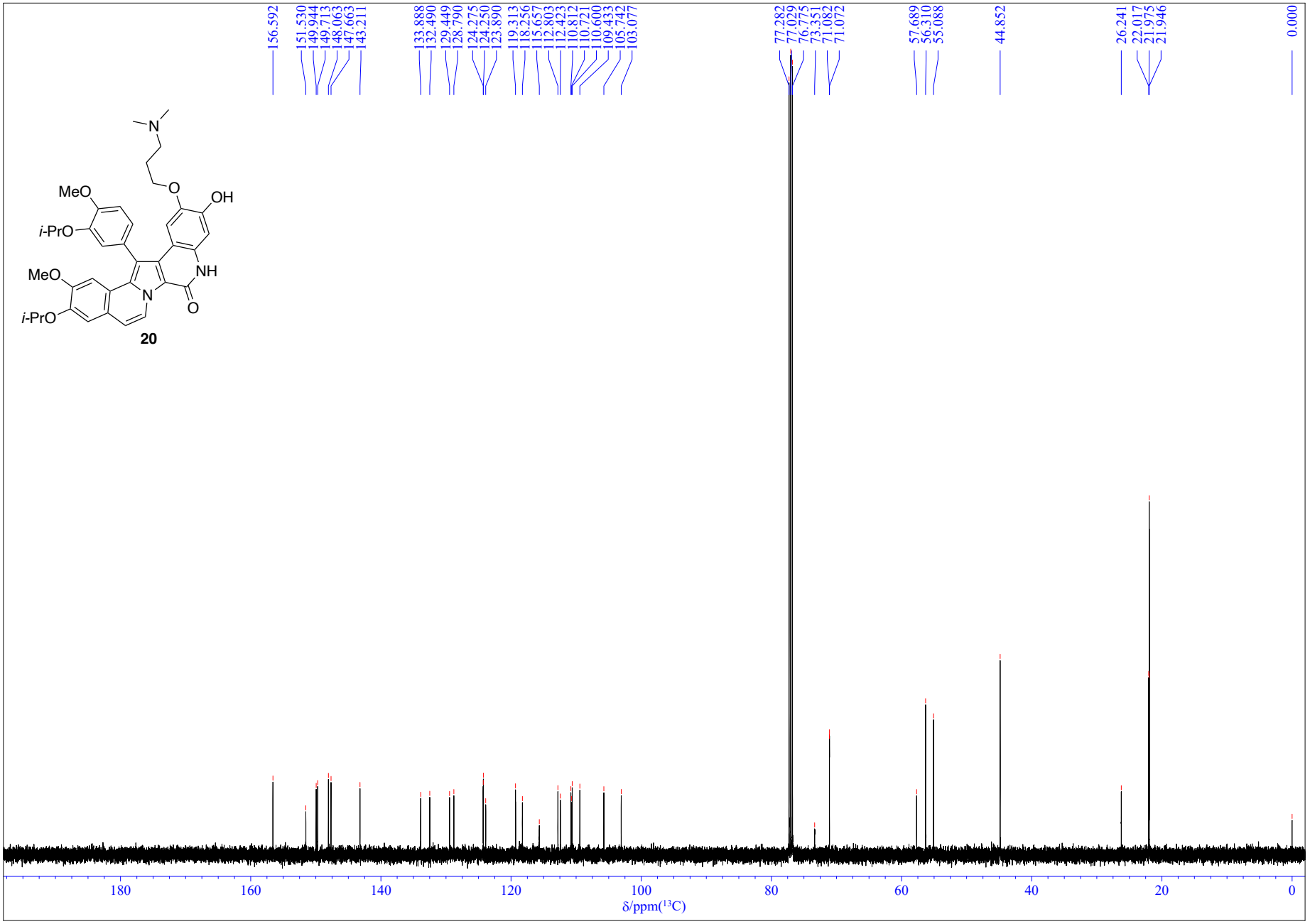

Figure S34. ^{13}C NMR spectrum of compound **20** (126 MHz, $CDCl_3$).

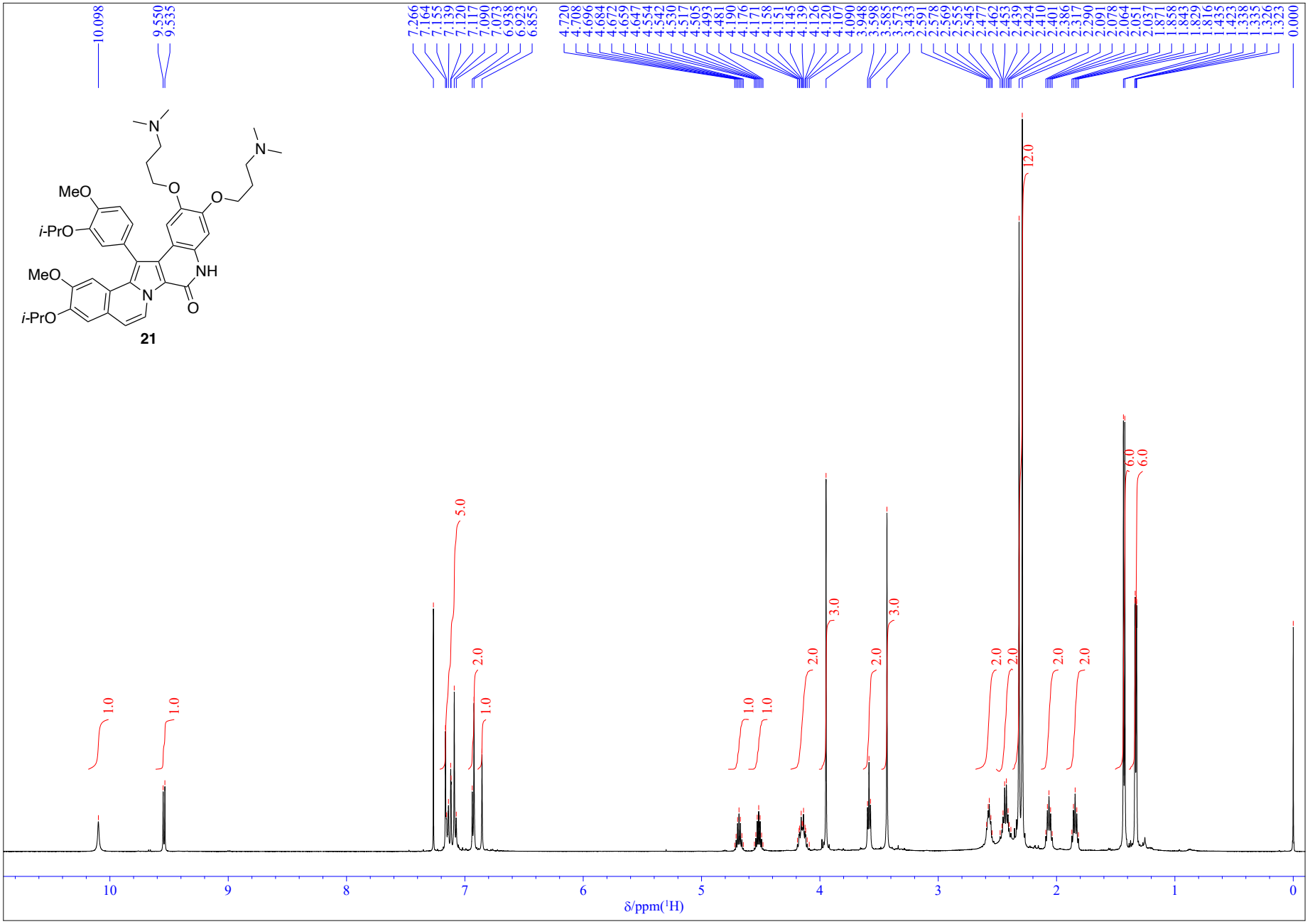

Figure S35. ^{1}H NMR spectrum of compound **21** (500 MHz, $CDCl_3$).

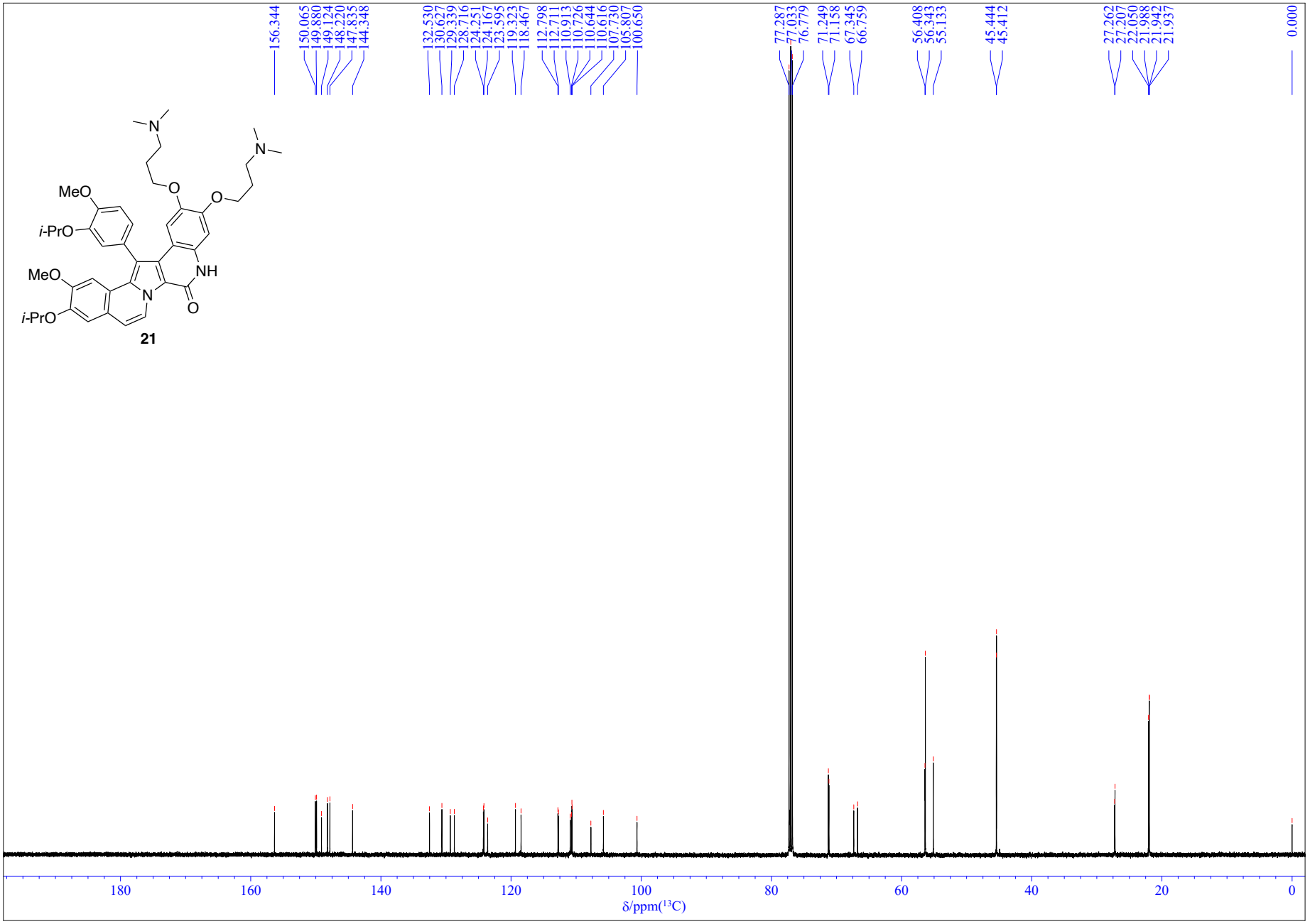

Figure S36. ^{13}C NMR spectrum of compound **21** (126 MHz, $CDCl_3$).

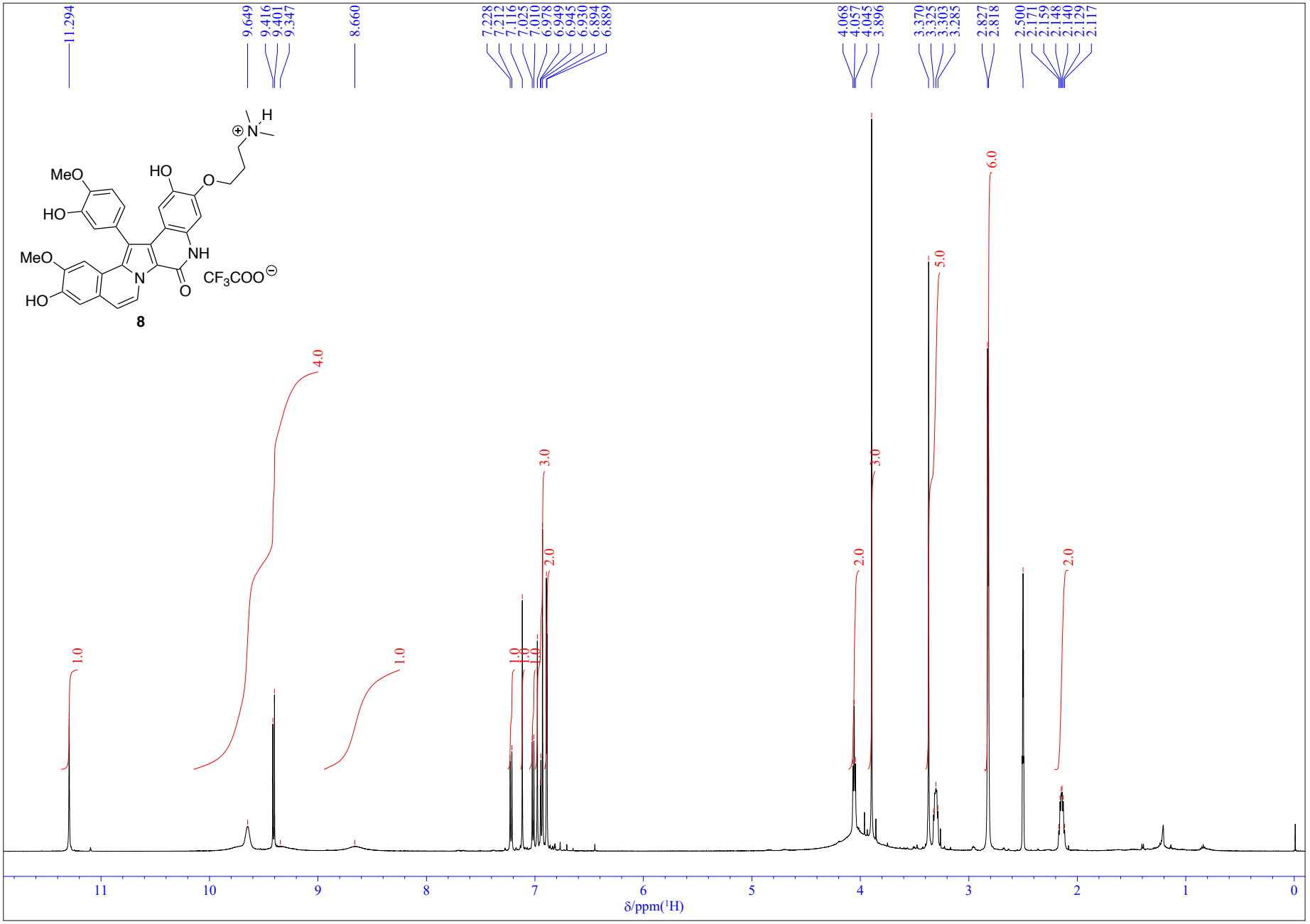

Figure S37. ^{1}H NMR spectrum of compound **8** (500 MHz, DMSO-d_6).

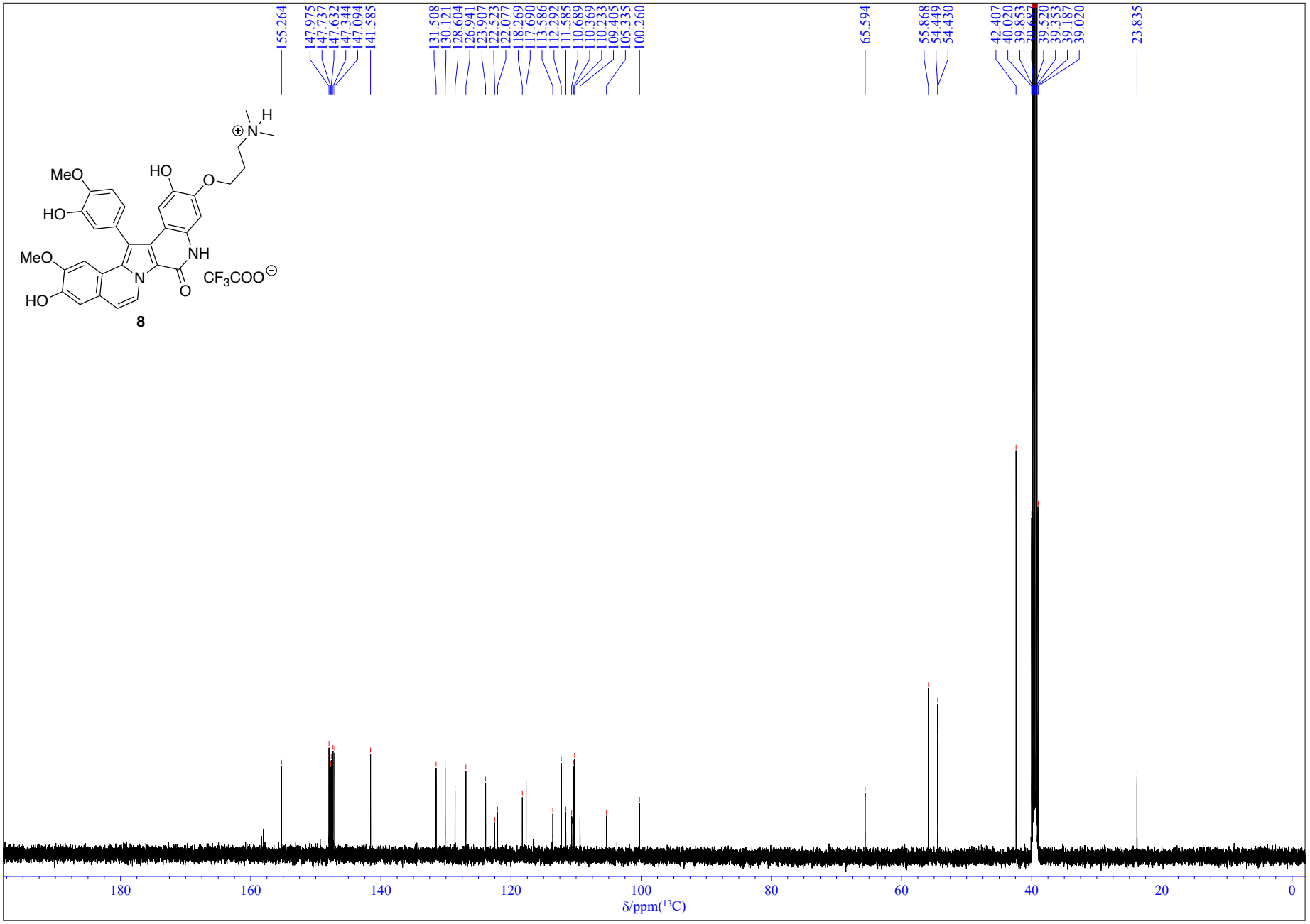

Figure S38. ^{13}C NMR spectrum of compound **8** (126 MHz, DMSO-d_6).

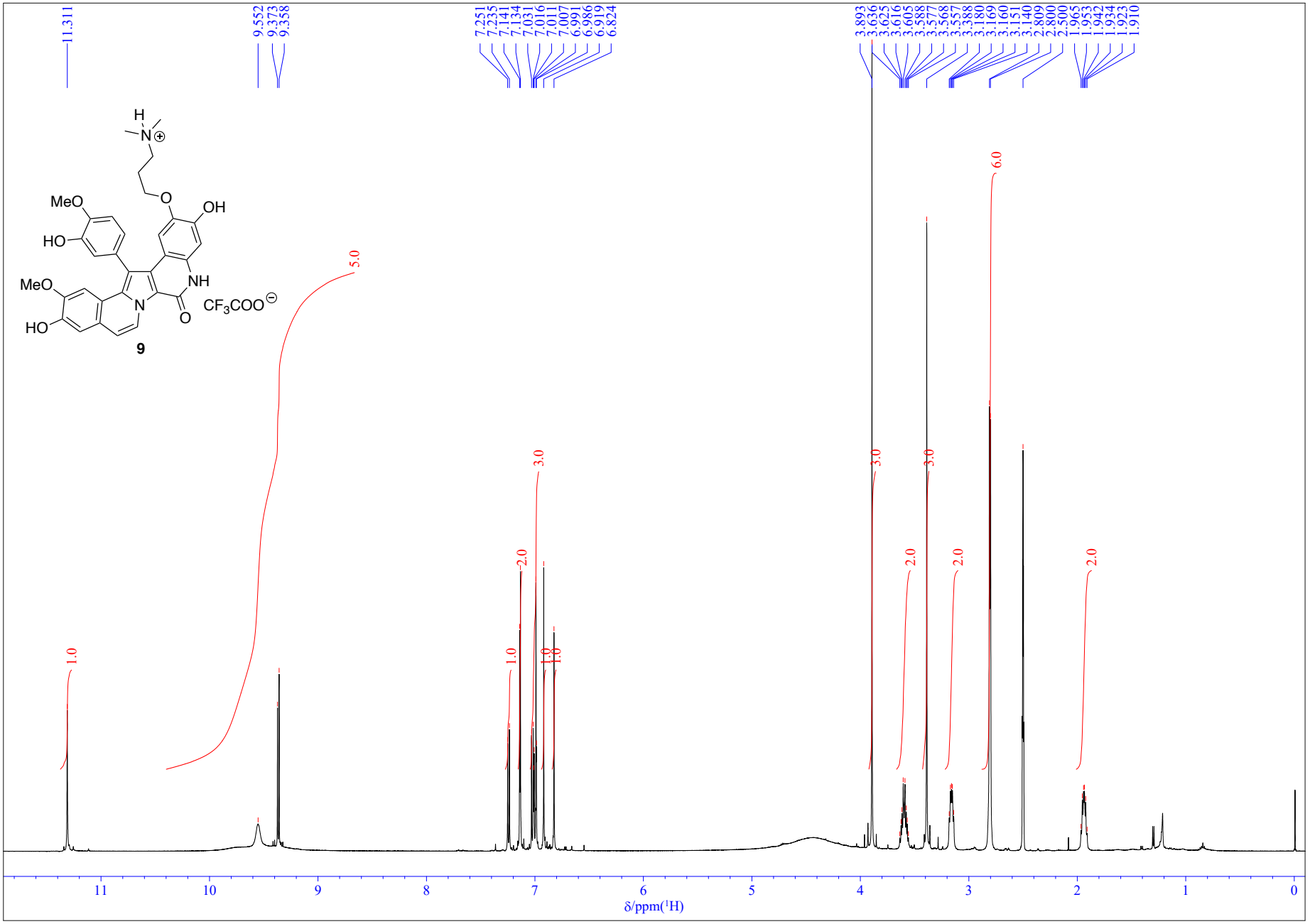

Figure S39. ^{1}H NMR spectrum of compound **9** (500 MHz, DMSO-d_6).

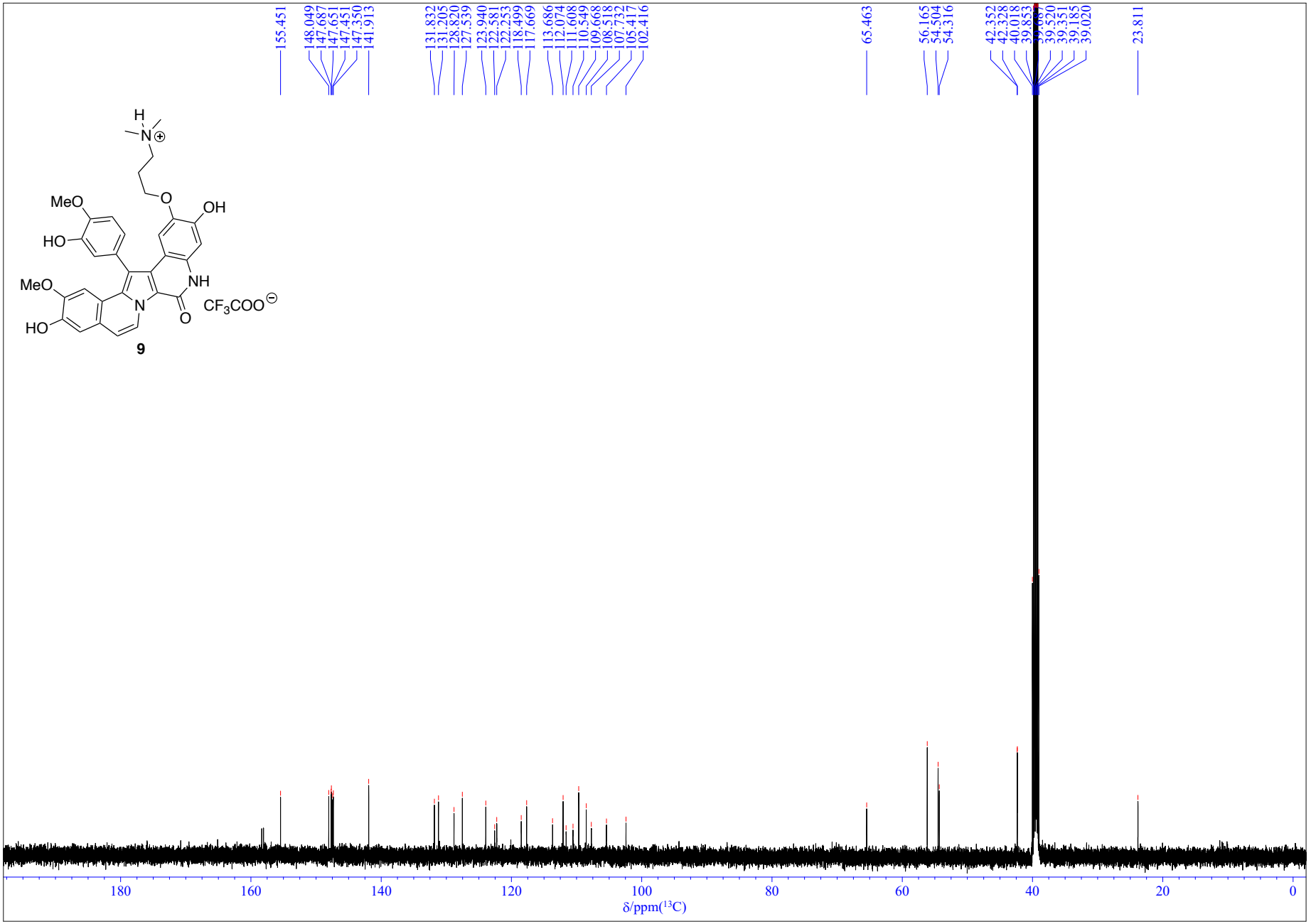

Figure S40. ^{13}C NMR spectrum of compound **9** (126 MHz, DMSO-d_6).

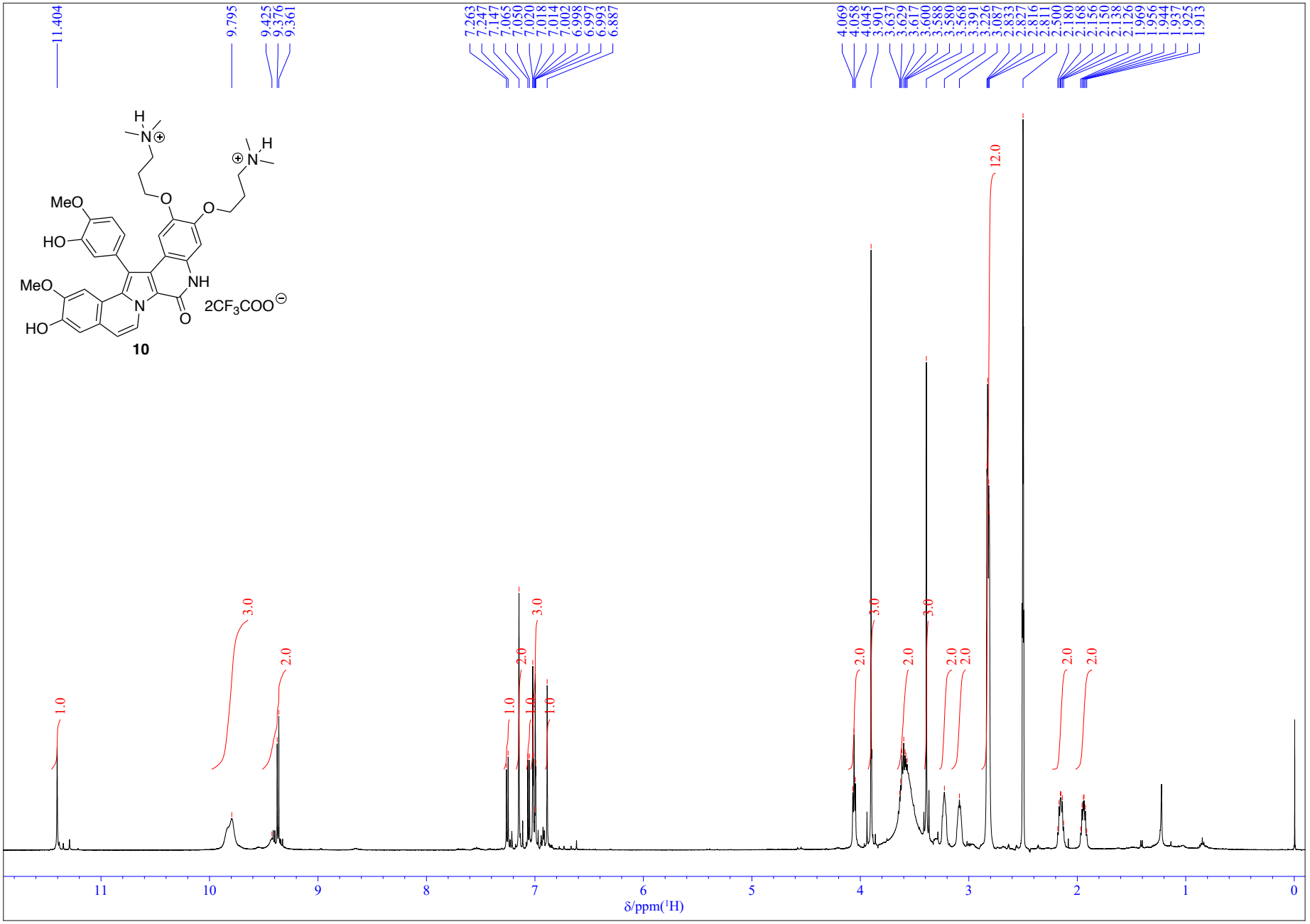

Figure S41. ^{1}H NMR spectrum of compound **10** (500 MHz, DMSO-d_6).

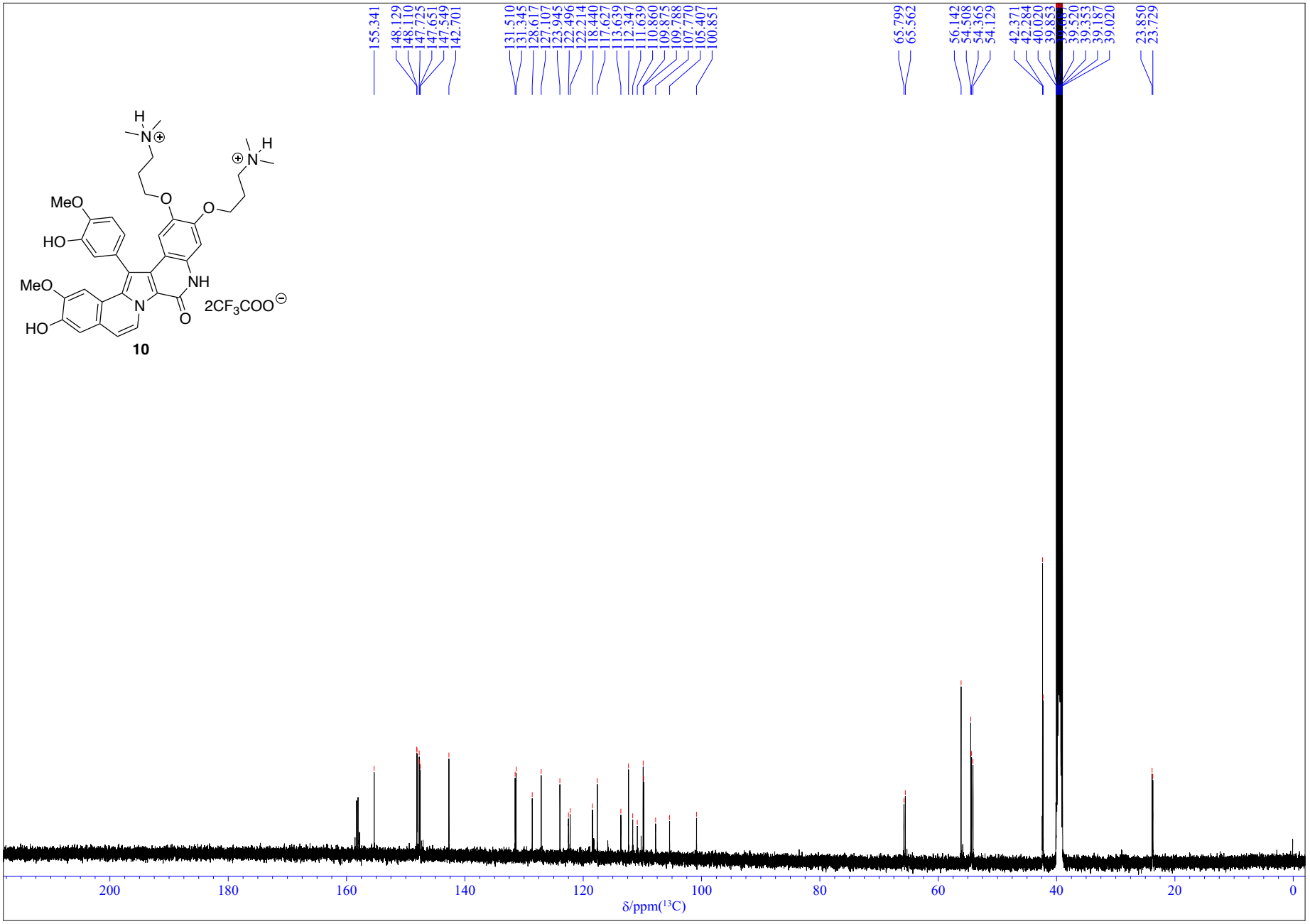

Figure S42. ^{13}C NMR spectrum of compound **10** (126 MHz, DMSO-d_6).

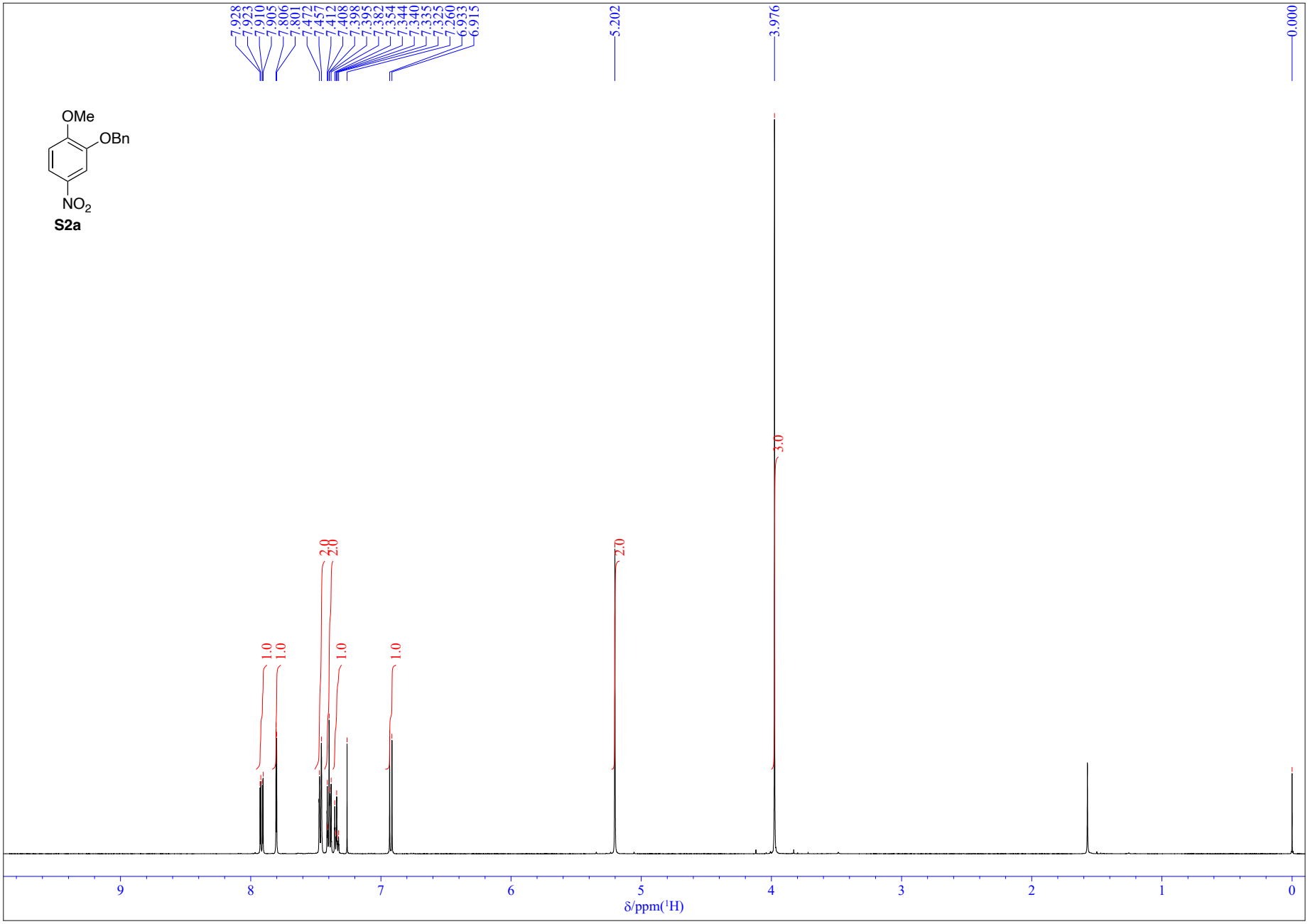

Figure S43. ^{1}H NMR spectrum of compound **S2a** (500 MHz, $CDCl_3$).

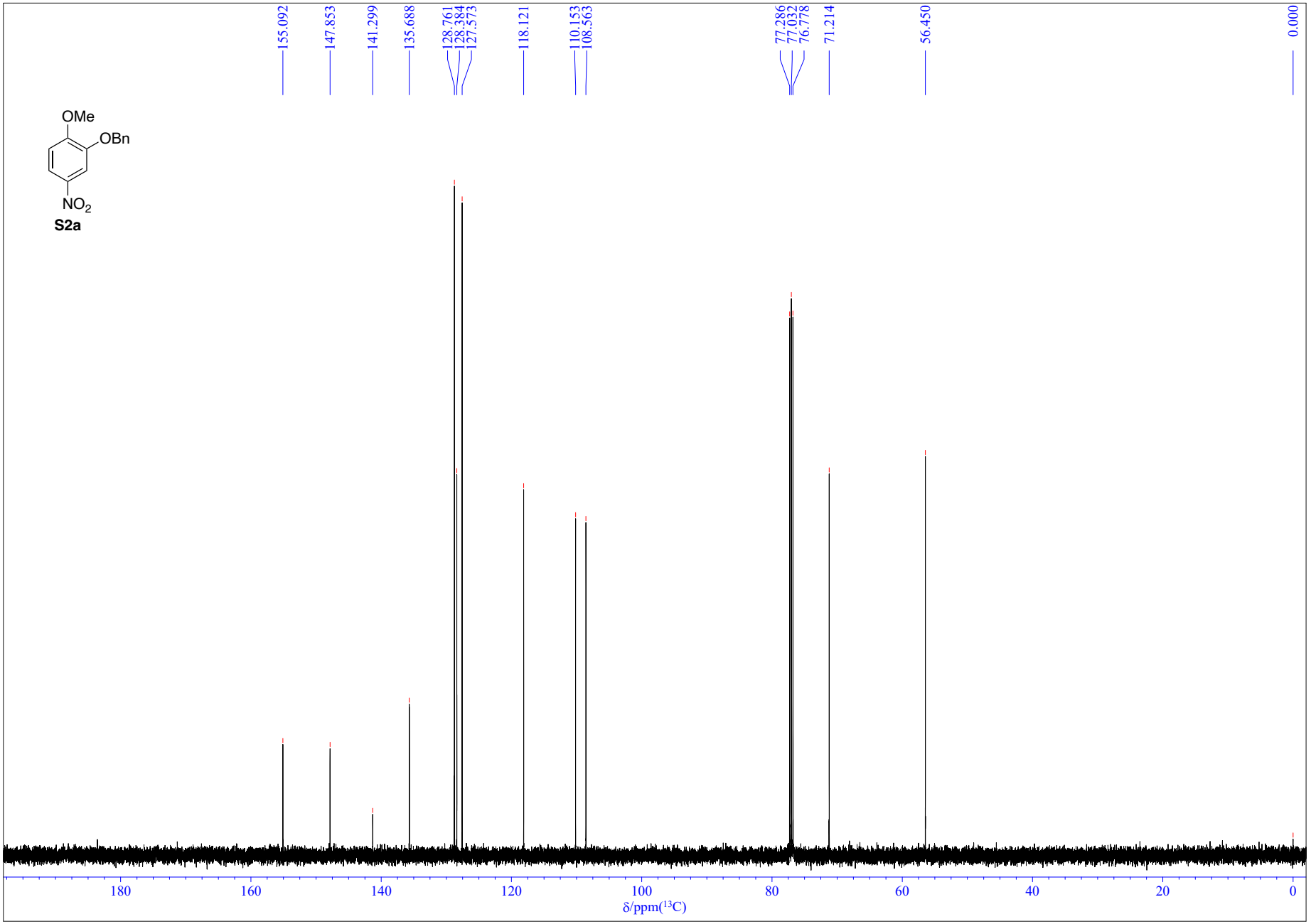

Figure S44. ^{13}C NMR spectrum of compound **S2a** (126 MHz, $CDCl_3$).

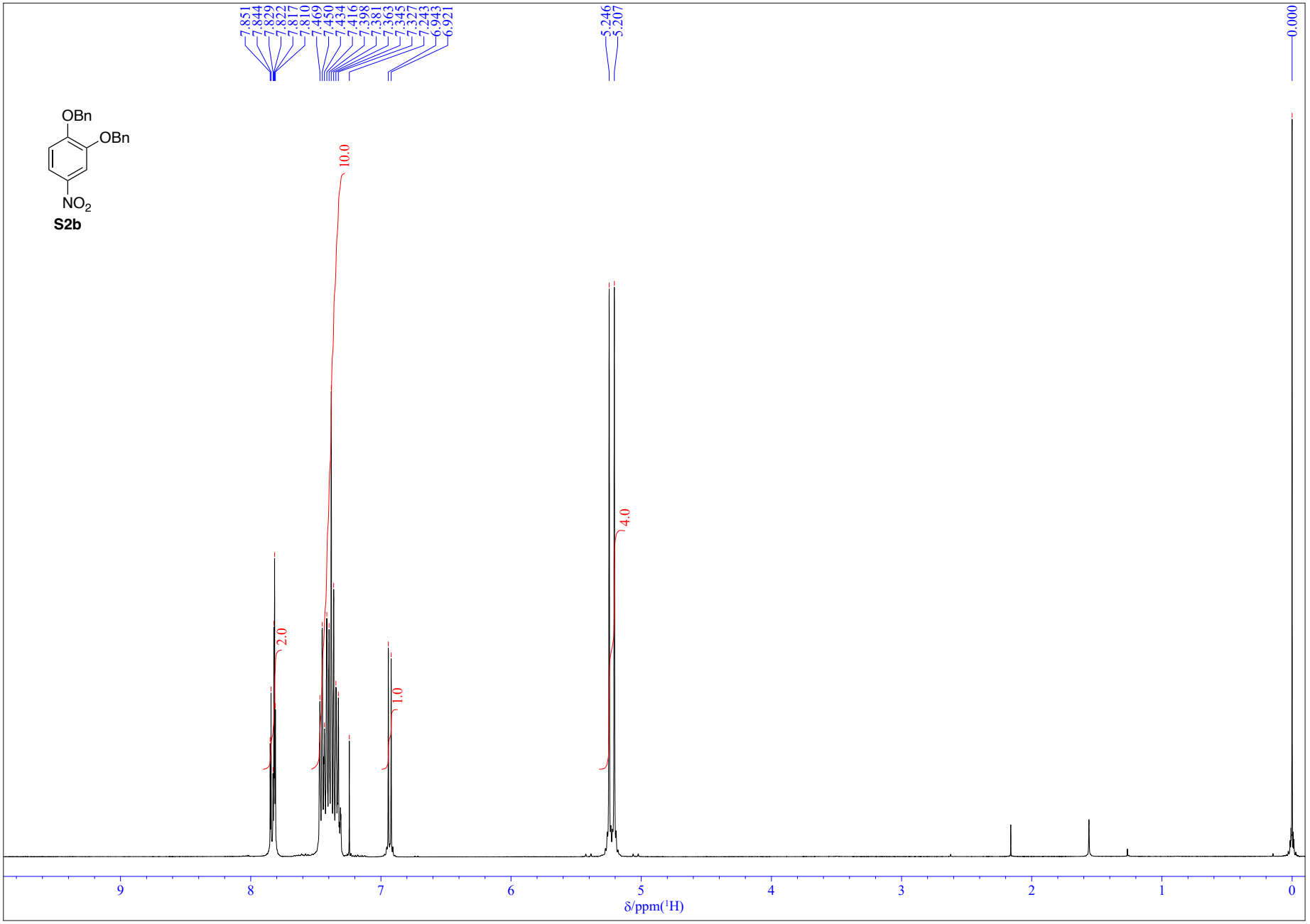

Figure S45. ^{1}H NMR spectrum of compound **S2b** (400 MHz, $CDCl_3$).

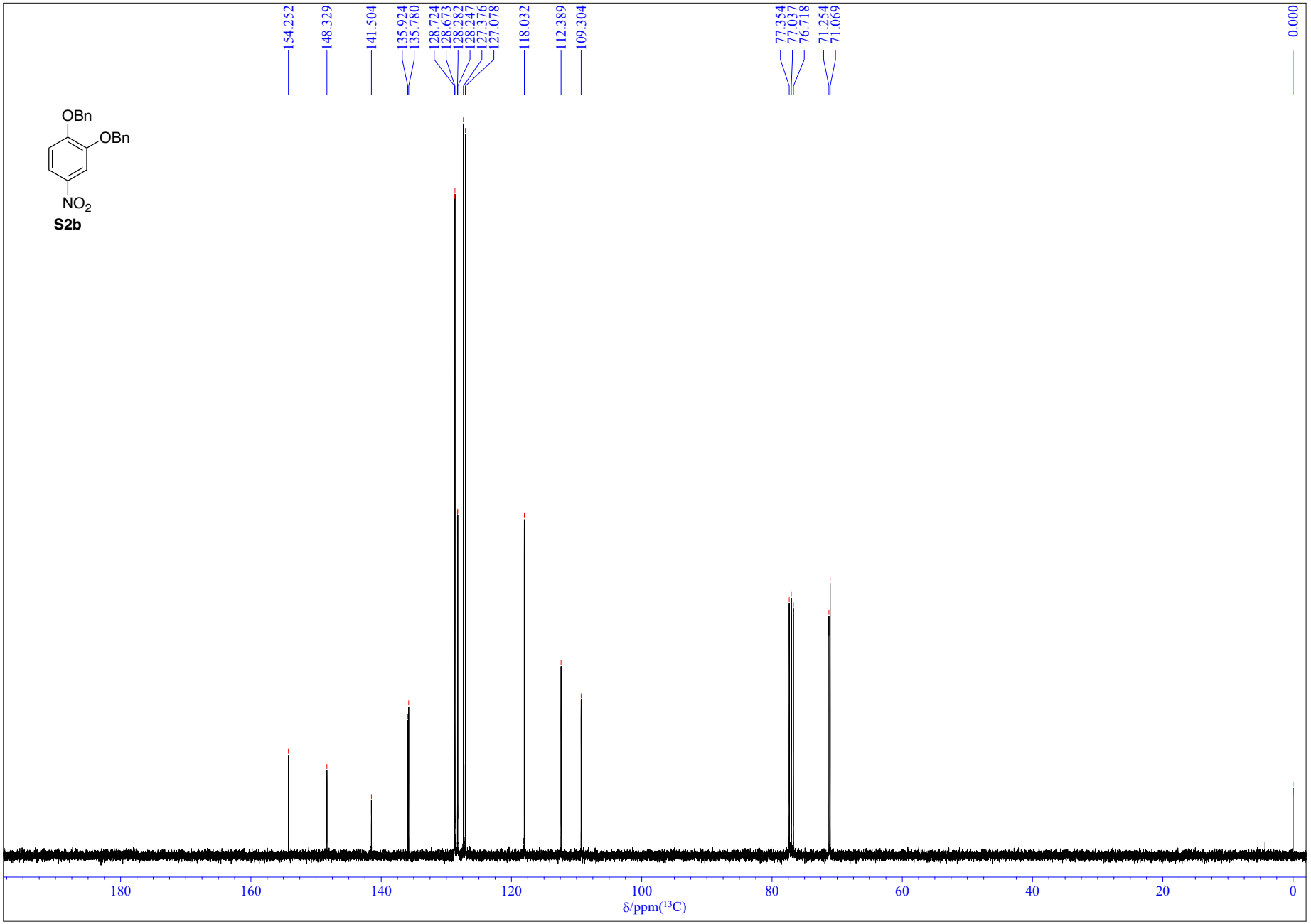

Figure S46. ^{13}C NMR spectrum of compound **S2b** (100 MHz, $CDCl_3$).

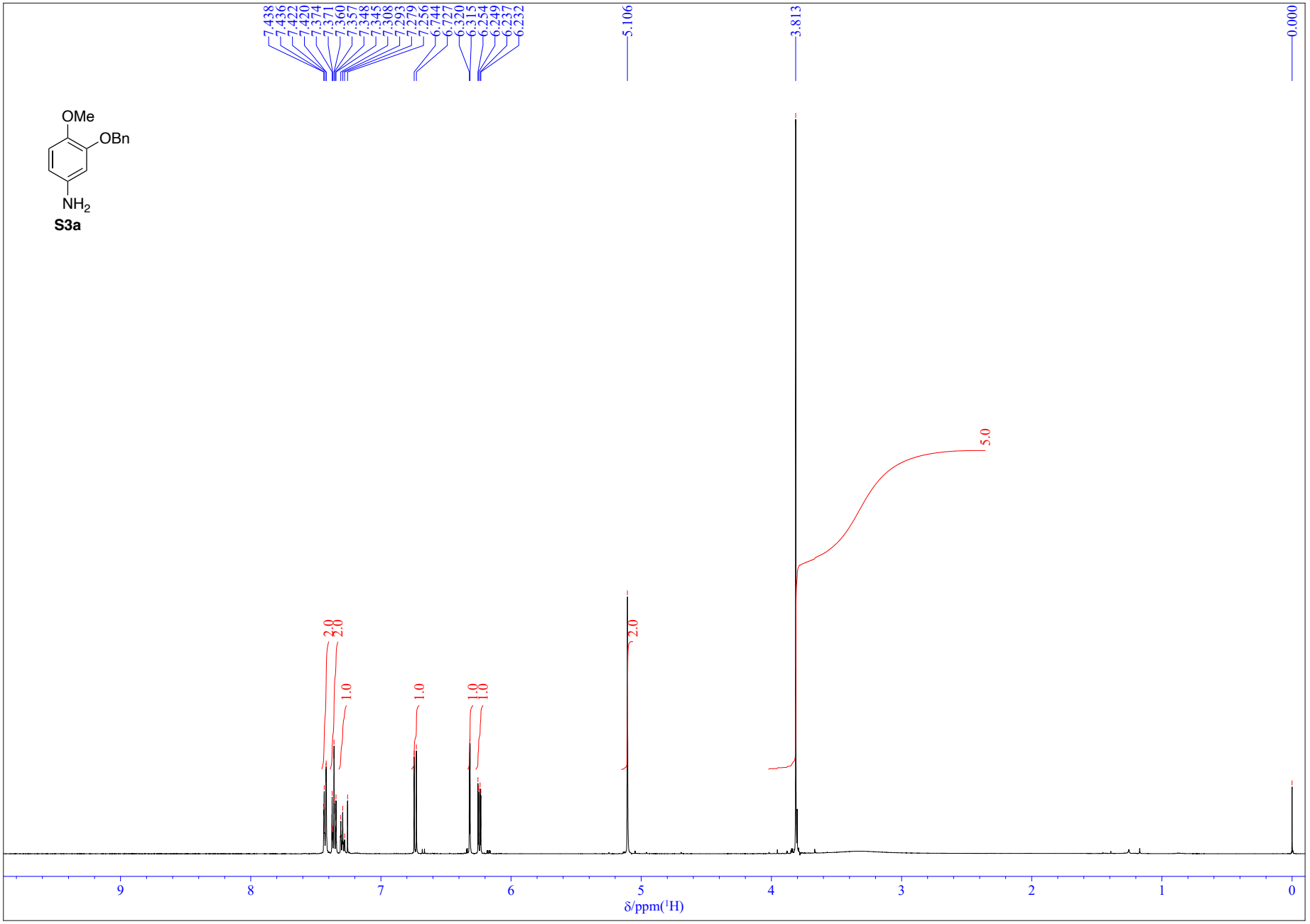

Figure S47. ^{1}H NMR spectrum of compound **S3a** (500 MHz, $CDCl_3$).

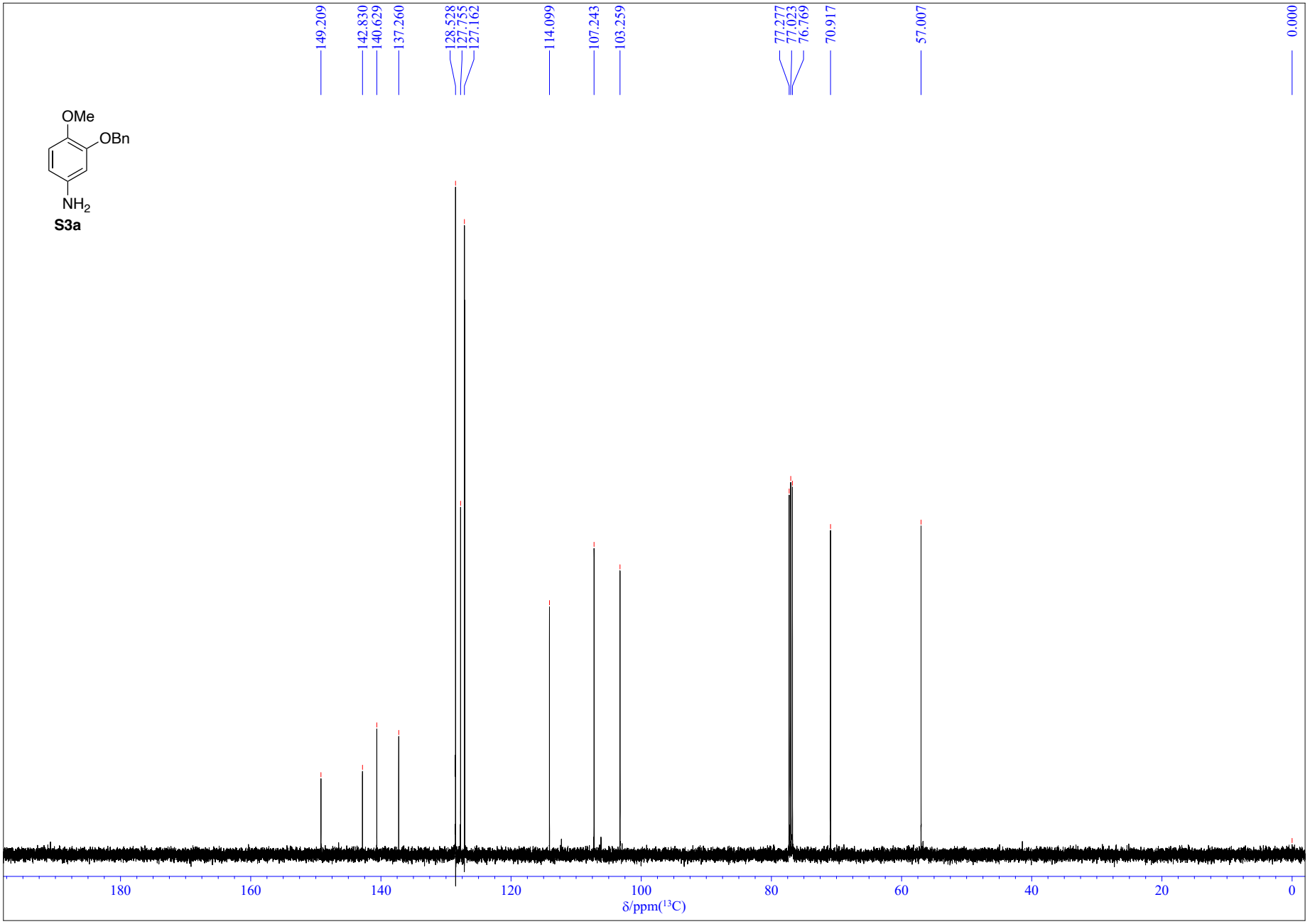

Figure S48. ^{13}C NMR spectrum of compound **S3a** (126 MHz, $CDCl_3$).

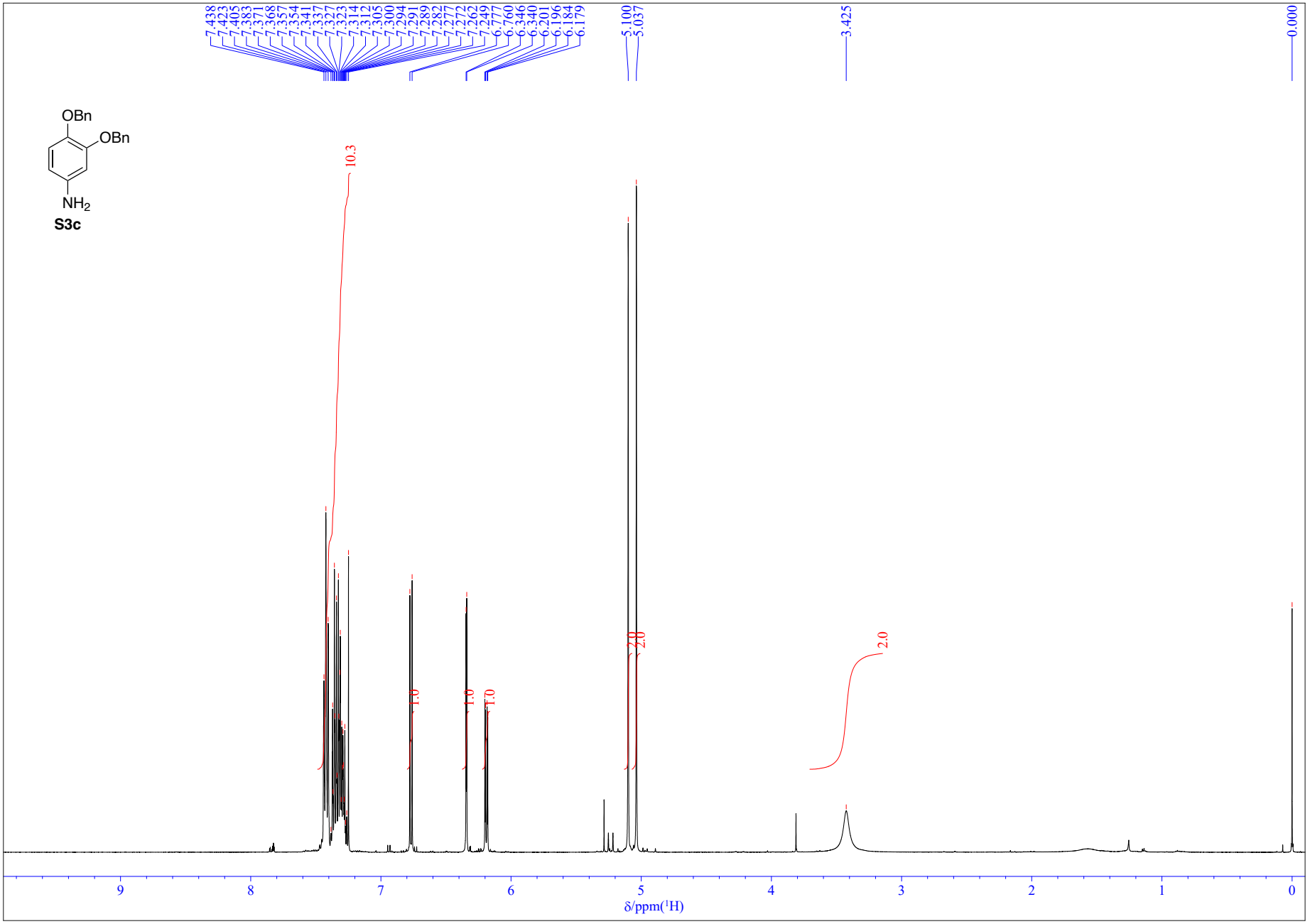

Figure S49. ^{1}H NMR spectrum of compound **S3c** (500 MHz, $CDCl_3$).

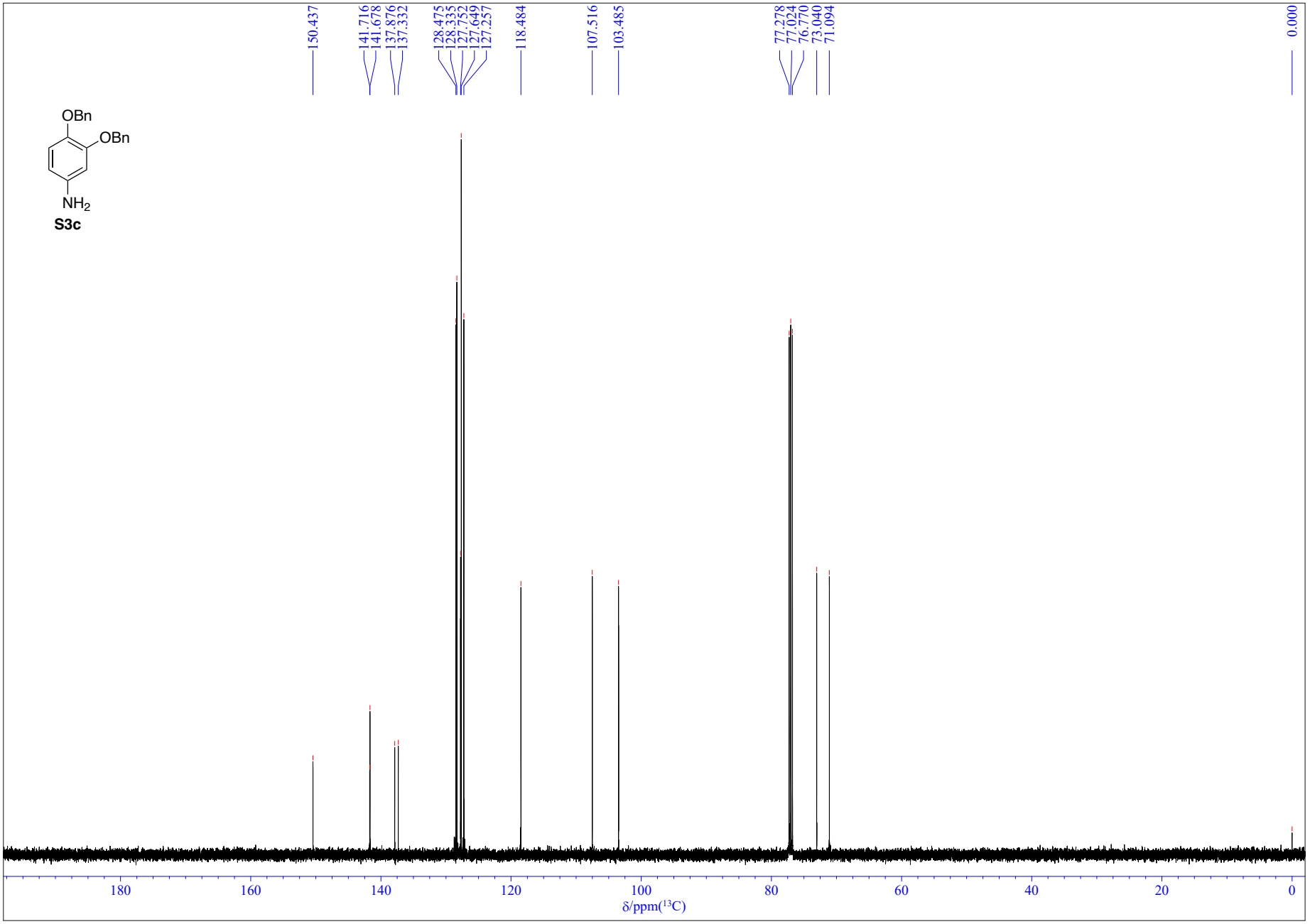

Figure S50. ^{13}C NMR spectrum of compound **S3c** (126 MHz, $CDCl_3$).

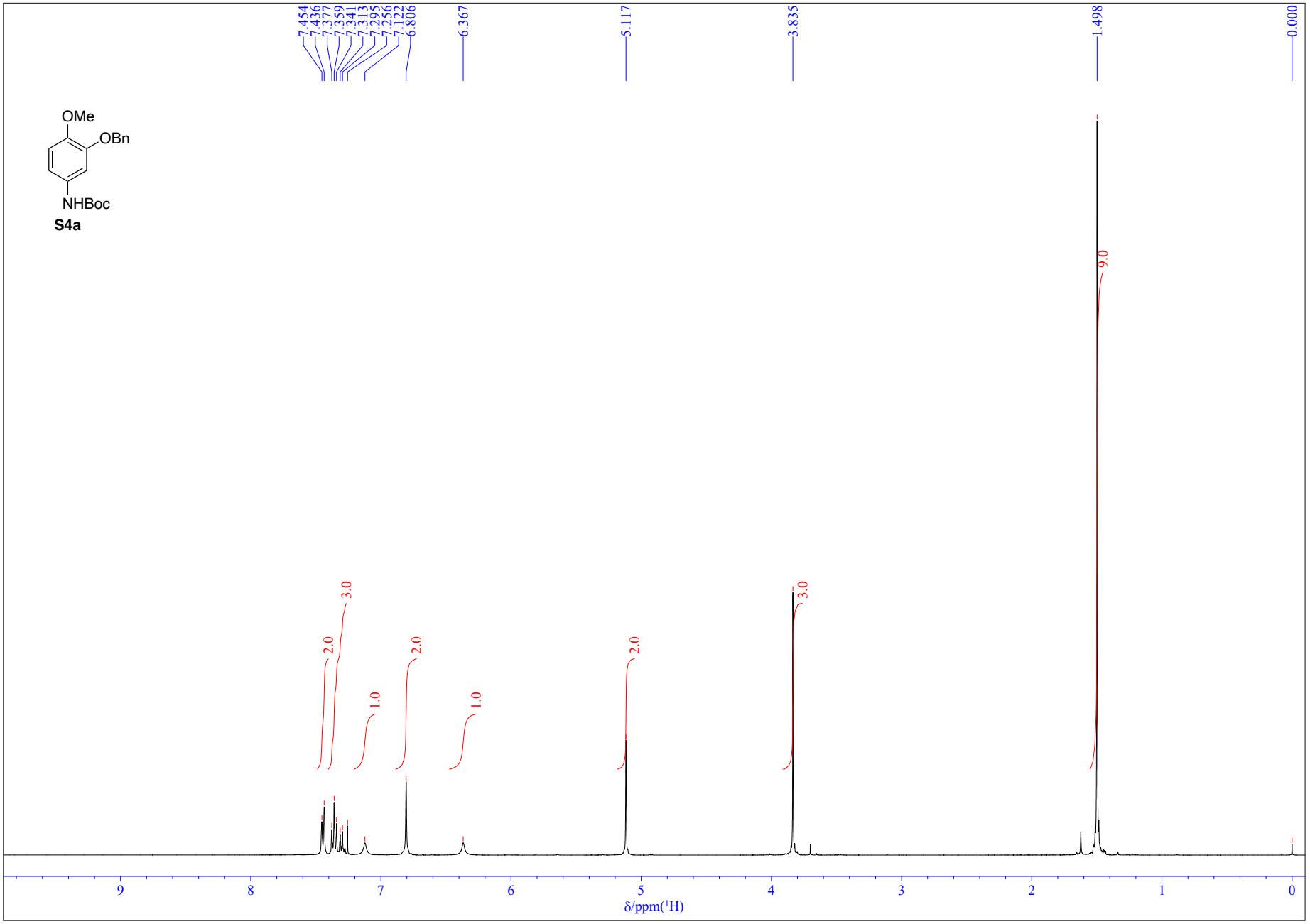

Figure S51. ^{1}H NMR spectrum of compound **S4a** (400 MHz, $CDCl_3$).

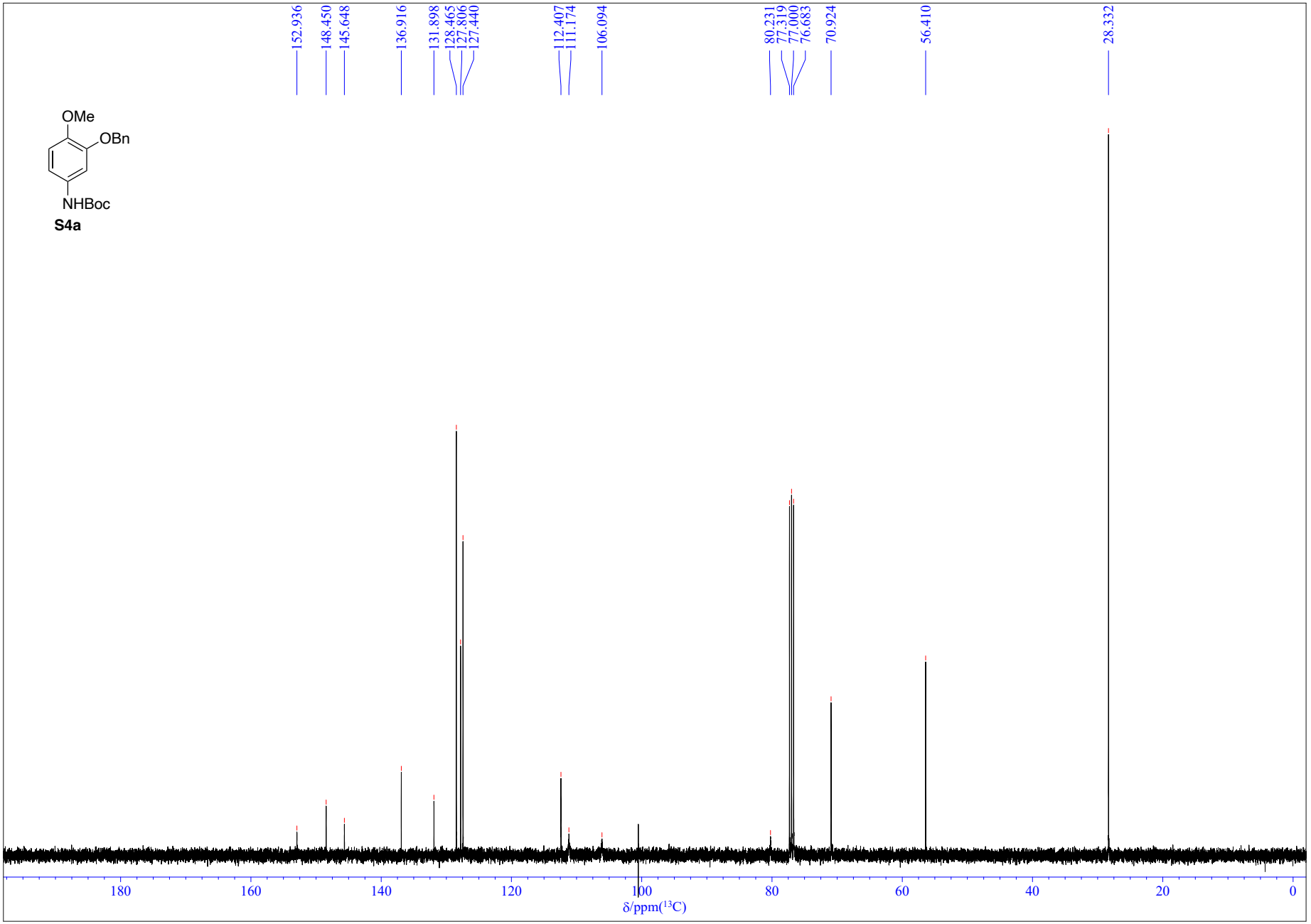

Figure S52. ^{13}C NMR spectrum of compound **S4a** (100 MHz, $CDCl_3$).

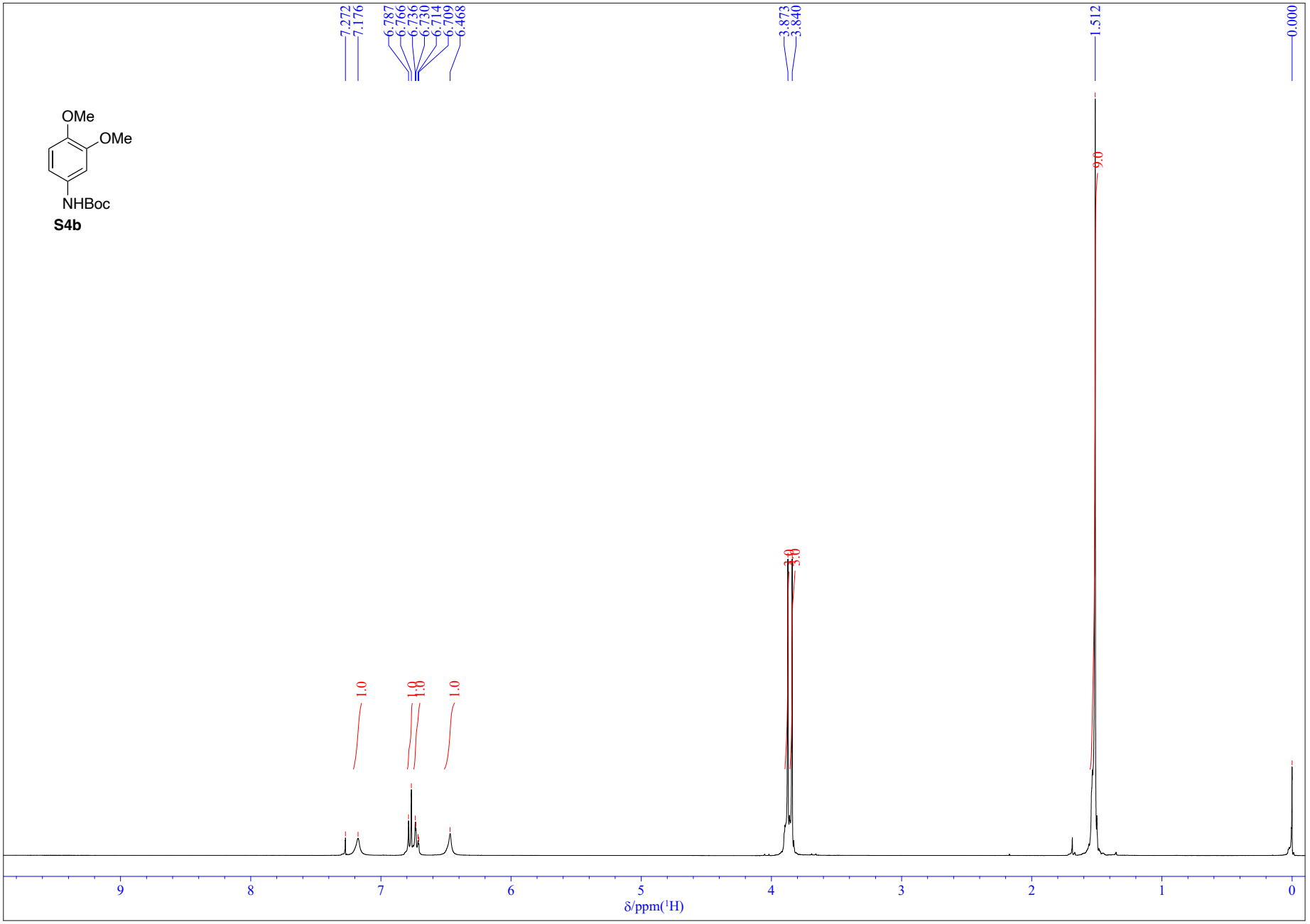

Figure S53. ^{1}H NMR spectrum of compound **S4b** (400 MHz, $CDCl_3$).

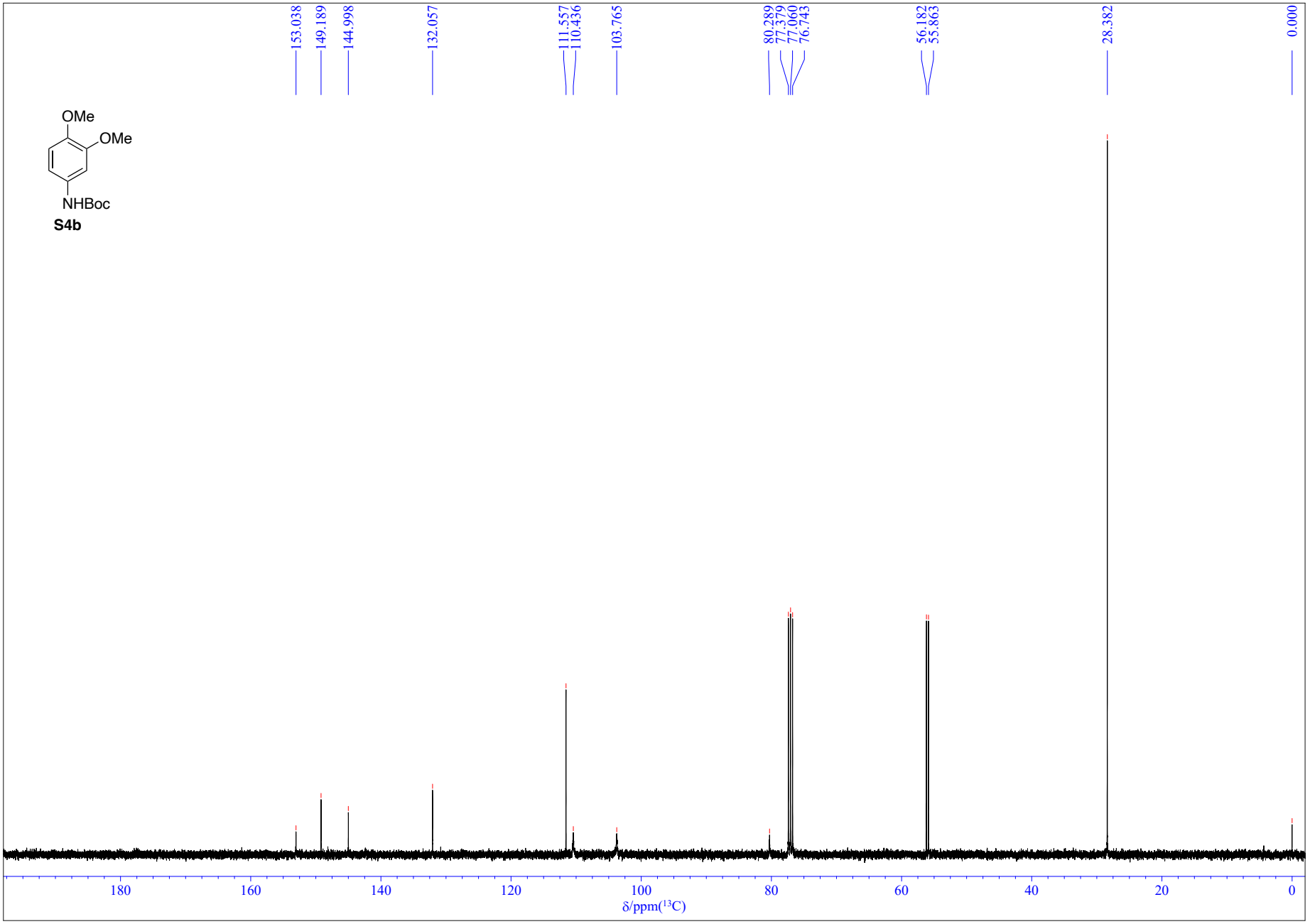

Figure S54. ^{13}C NMR spectrum of compound **S4b** (100 MHz, $CDCl_3$)

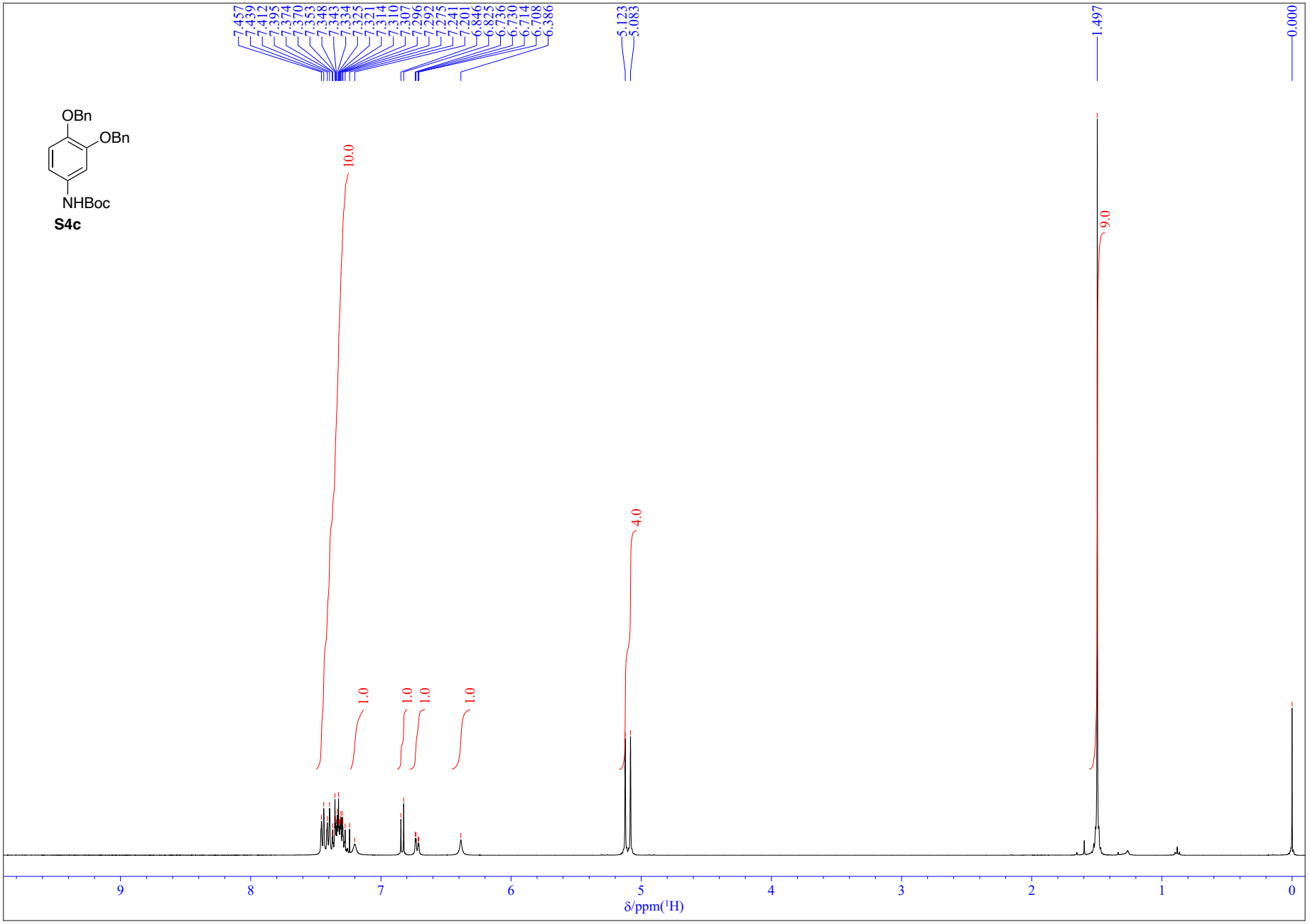

Figure S55. ^{1}H NMR spectrum of compound **S4c** (400 MHz, $CDCl_3$).

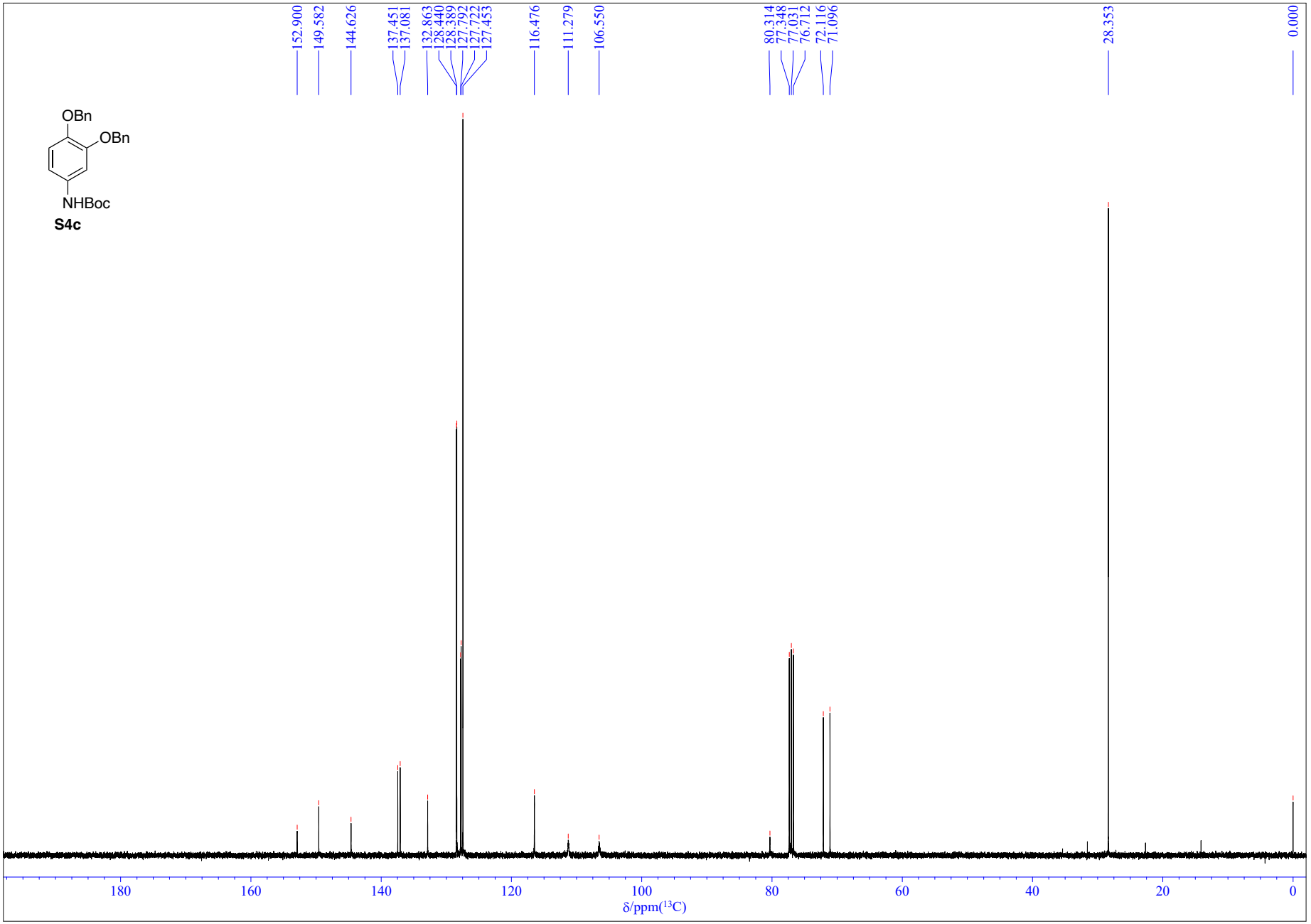

Figure S56. ^{13}C NMR spectrum of compound **S4c** (100 MHz, $CDCl_3$).

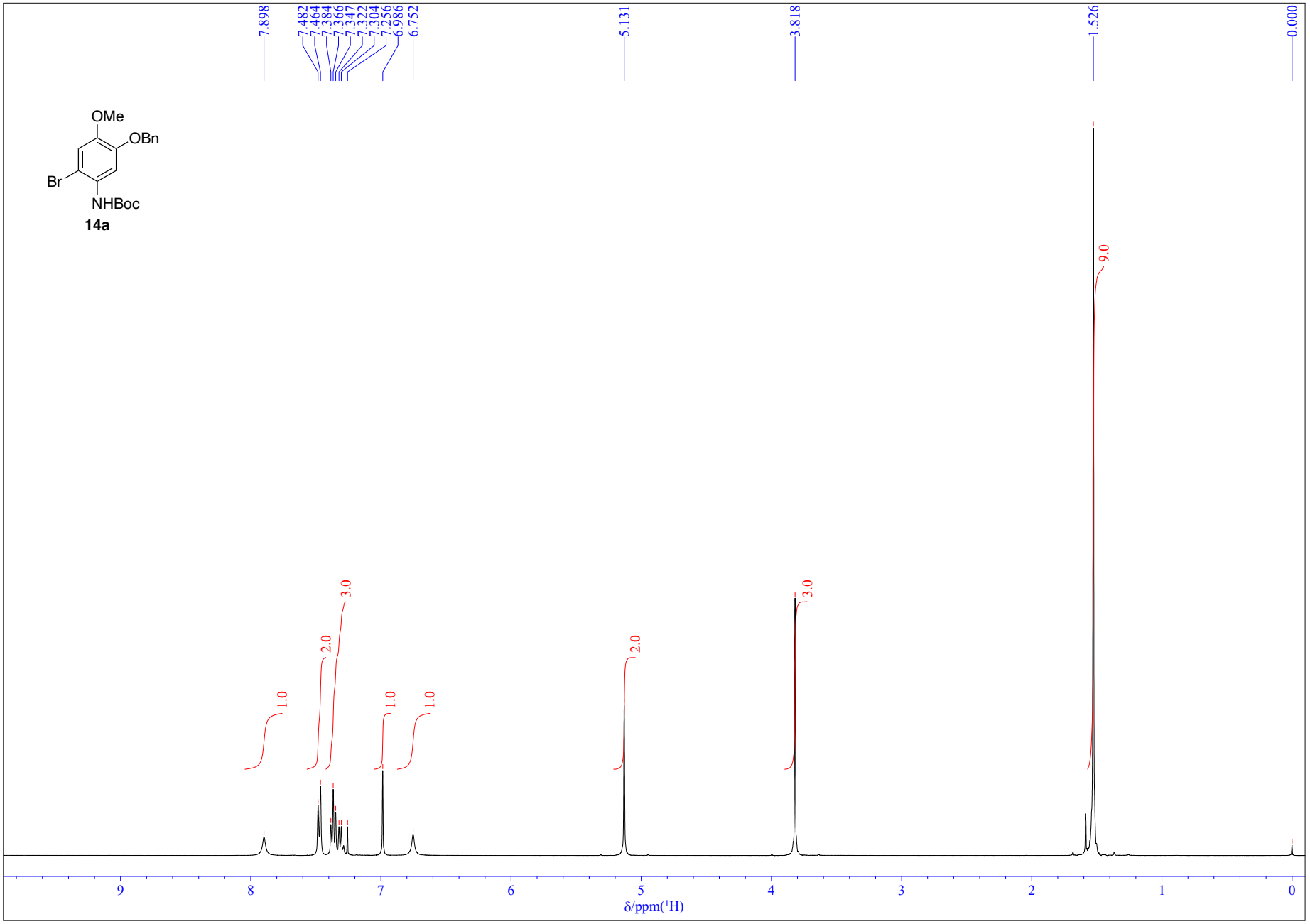

Figure S57. ^{1}H NMR spectrum of compound **14a** (400 MHz, $CDCl_3$).

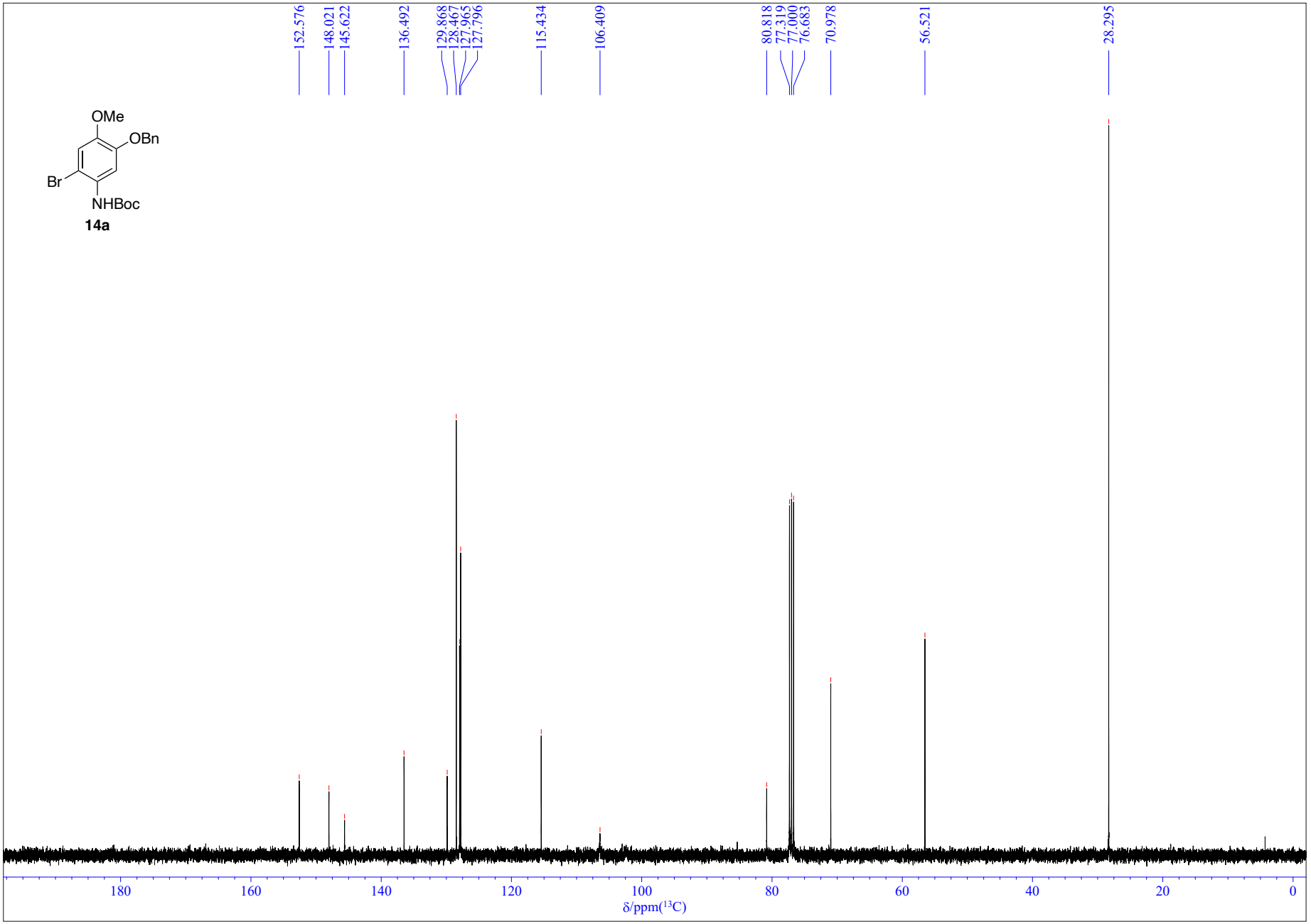

Figure S58. ^{13}C NMR spectrum of compound **14a** (100 MHz, $CDCl_3$).

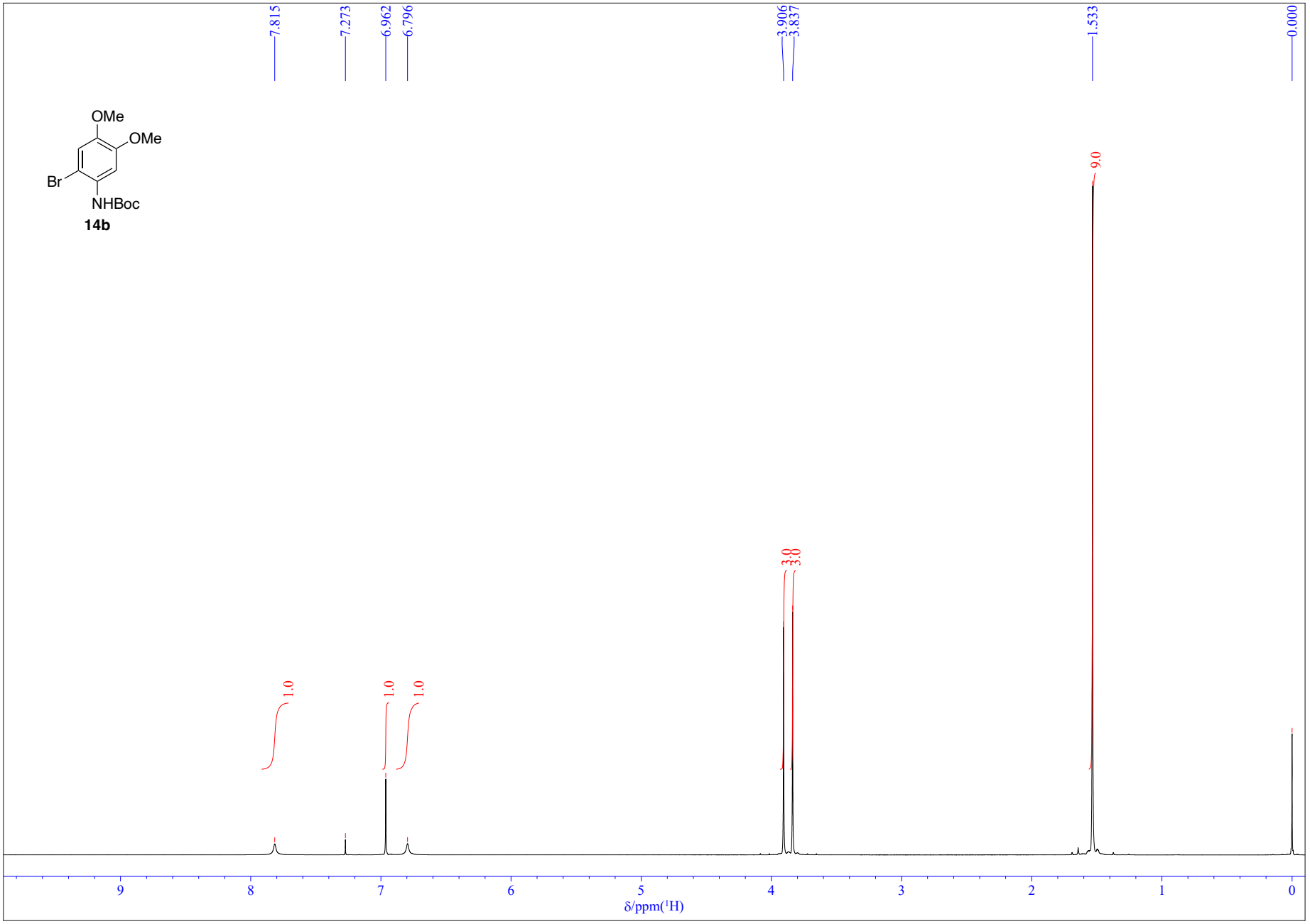

Figure S59. ^{1}H NMR spectrum of compound **14b** (400 MHz, $CDCl_3$).

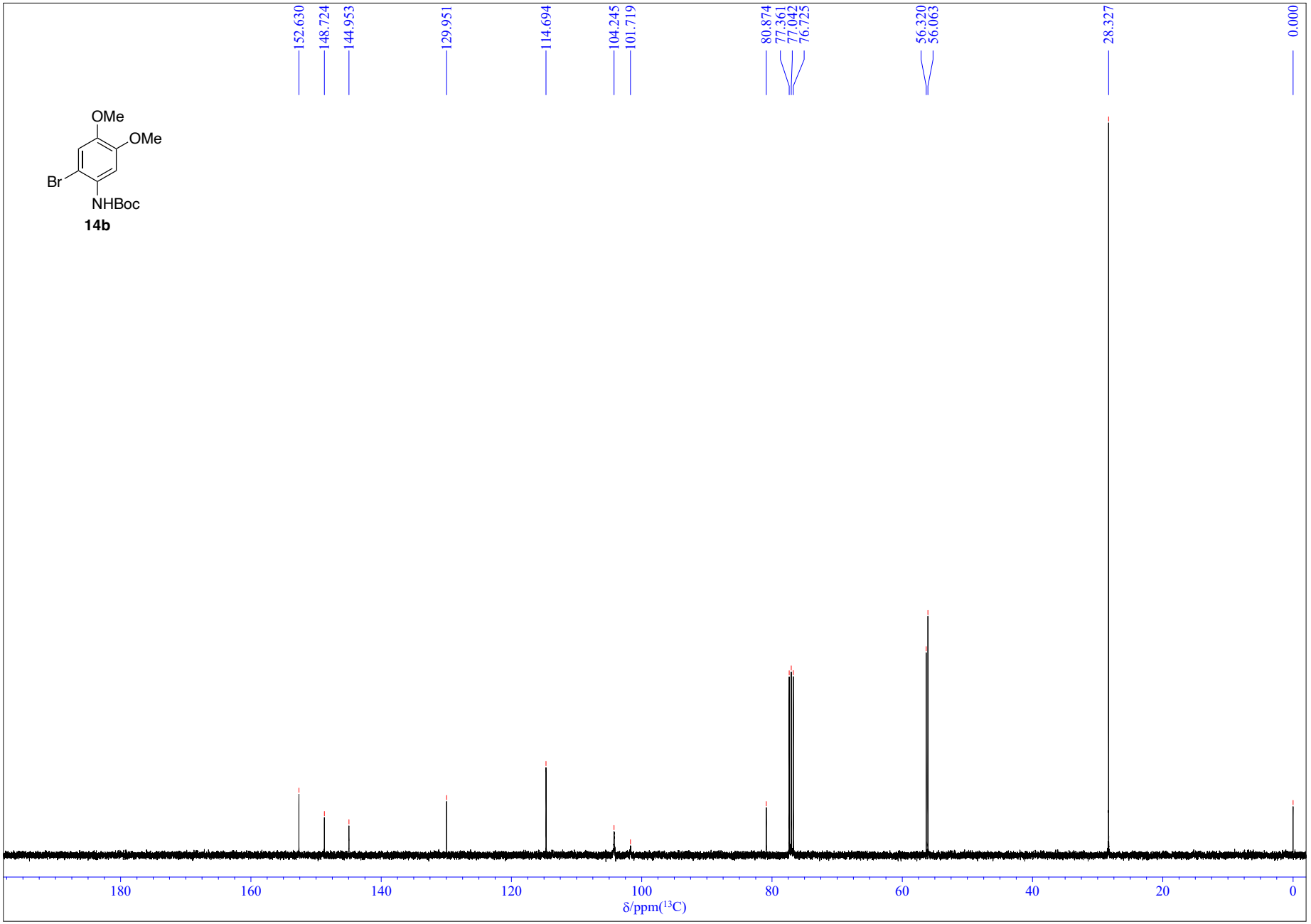

Figure S60. ^{13}C NMR spectrum of compound **14b** (100 MHz, $CDCl_3$).

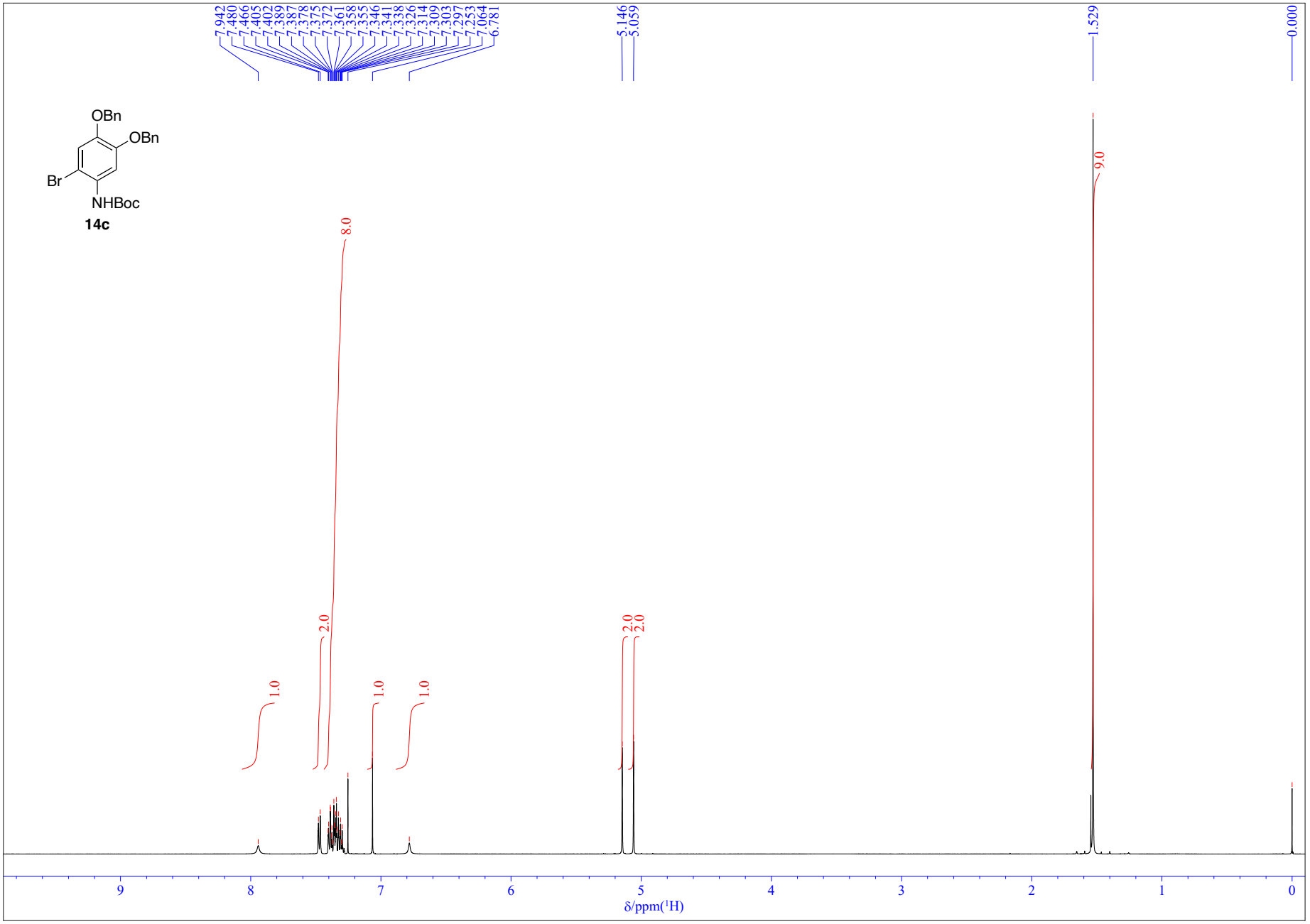

Figure S61. ^{1}H NMR spectrum of compound **14c** (500 MHz, $CDCl_3$).

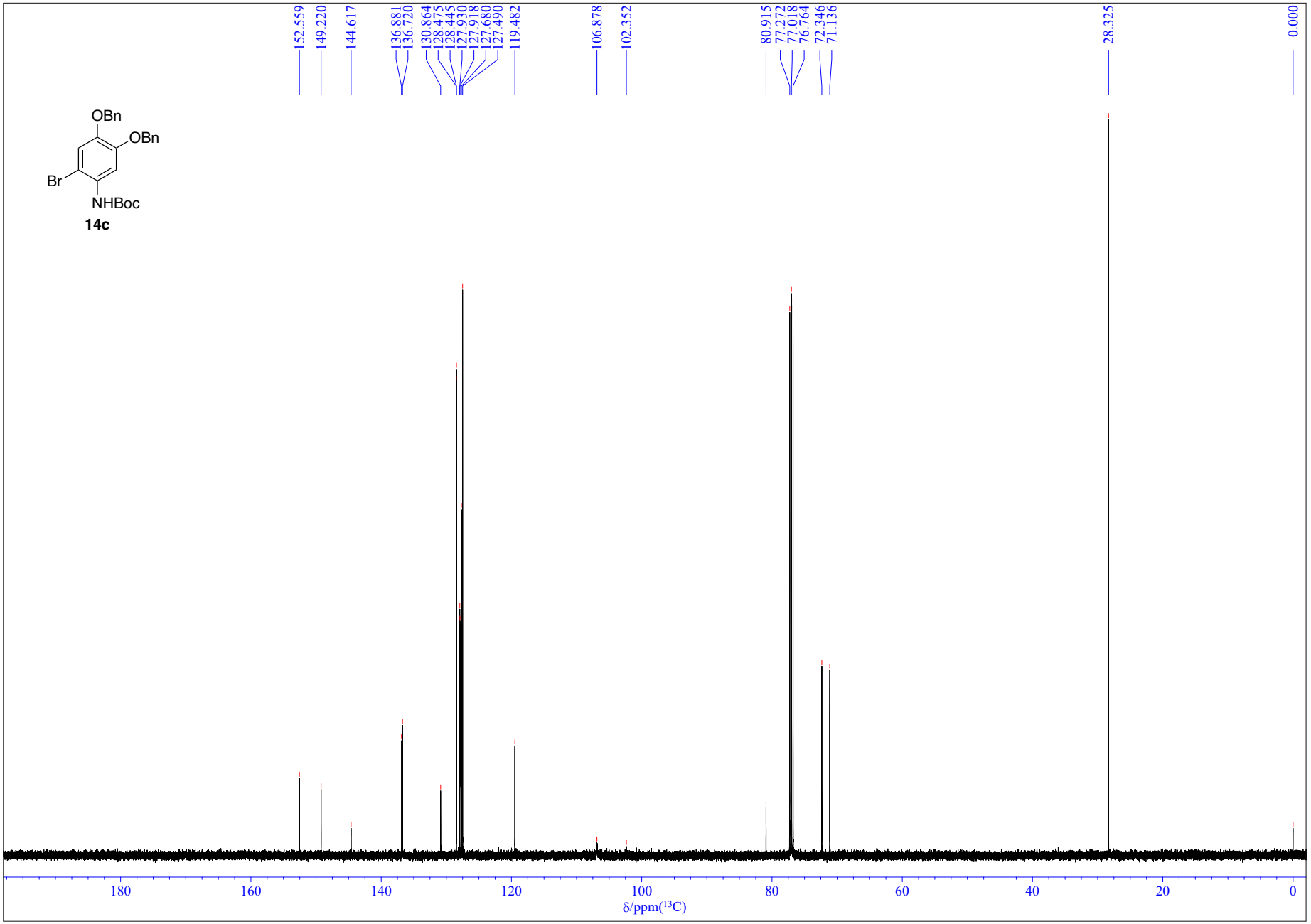

Figure S62. ^{13}C NMR spectrum of compound **14c** (126 MHz, $CDCl_3$).