Supporting Information

Total Synthesis Study of Rauvomines A and B: Construction of the Pentacyclic Core Structure

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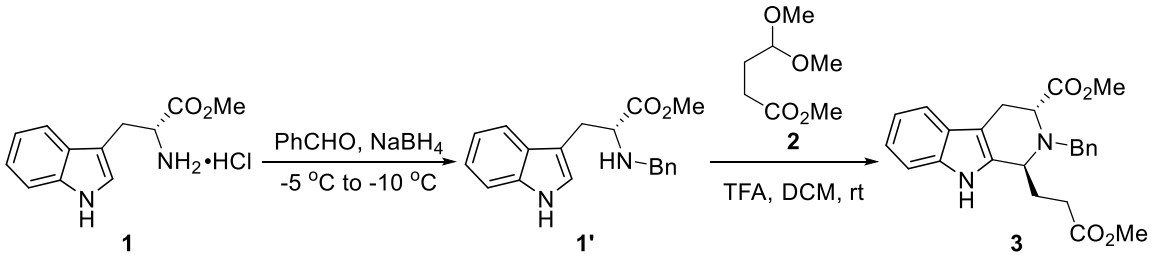
Contents

1. General Information

Reagents were purchased from commercial suppliers such as Aladdin and Macklin, which was used directly without further purification unless stated otherwise. All reactions were run under the protection of nitrogen atmosphere, with oven-dried glassware. Anhydrous solvents were obtained using standard drying techniques. The reaction progress was monitored by thin-layer chromatography. Flash chromatography was performed on 200-300 mesh silica gel with the indicated solvent systems. ^{1}H NMR were recorded on a Bruker Avance III HD (400, 500, 600 MHz) spectrometer and chemical shifts are reported in ppm down field from TMS, using residual $CDCl_3$ (7.26 ppm) as an internal standard. Data are reported as: (s = singlet, br = broad, d= doublet, t = triplet, q = quartet, m = multiplet; *J*= coupling constant in Hz, integration.). ^{13}C NMR spectra were recorded on a Bruker Avance III HD (126, 151 MHz) spectrometer with proton decoupled. Chemical shifts are reported in ppm down field from TMS, using the central resonance of $CDCl_3$ (77.00 ppm) as the internal standard. HRMS were recorded by using Agilent accurate-mass Q-TOF HRMS spectrometers. Optical rotations were measured on a Yimai IP-DIGI 300 spectrometer with a sodium lamp (average of five measurements for each sample). Infrared (IR) data were recorded on a Nexus FT-IR spectrometer using KBr plates.

2. Experimental Procedures and Characterization of Compounds

Methyl(1*S*,3*R*)-2-benzyl-1-(3-methoxy-3-oxopropyl)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole-3-carboxylate (3) [1]



To a solution of methyl D-tryptophanate hydrochloride **1** (80.0 g, 0.31 mol, 1.00 equiv) was added benzaldehyde (40.8 g, 0.38 mol, 1.23 equiv) in MeOH (240 mL) in several portions at room temperature. Afterwards, the mixture was stirred for 4 h at room temperature before sodium borohydride (6.6 g, 0.17 mol, 0.55 equiv) was added portionwise over a period of 1 h. The internal temperature was kept between -10 and -5 °C, which was tracked by TLC until the reaction finished. Then, ice water (40 mL) was added to the mixture and stirred for 10 min, which was then concentrated under reduced pressure removing MeOH. The mixture was dissolved in CH_2Cl_2 (300 mL) and H_2O (300 mL), the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (100 mL). The combined organic layers were washed with saturated NaCl solution, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was recrystallized by ethanol to provide the intermediate **1'** (72.3 g, 0.23 mol, 75%) as a white solid.

Then, to a solution of the comound **1'** (30.0 g, 0.097 mol, 1.0 equiv) in CH_2Cl_2 (300 mL) was added first methyl 4,4-dimethoxybutanoate **2** (17.36 g, 0.107 mol, 1.1 equiv) and then a solution of TFA (26.57 g, 0.233 mol, 2.4 equiv) dropwise in several portions at 0 °C, The reaction mixture was tracked by TLC until the completion of the reaction before cooled in low temperature brought to pH = 8 with an aqueous solution of $NaHCO_3$ (10%). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (100 mL). The combined organic layers were washed with saturated NaCl solution, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was beaten in mixture solution (*n*-Hexane/EtOAc, 3:1) to provide compound **3** (25.5 g, 0.063 mol, 64%) as a white solid.

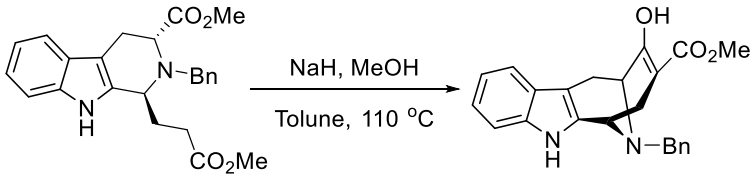
Characterization for Compound 1':

R_f = 0.70 (*n*-Hexane/EtOAc, 4:1); **mp** 106 – 107 °C; **$[\alpha]_D^{25}$** + 9.4 (*c* 1.0, CH_3OH); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.65 – 7.58 (m, 1H), 7.38 – 7.34 (m, 1H), 7.32 – 7.19 (m, 5H), 7.14 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H), 7.03 (d, *J* = 2.4 Hz, 1H), 3.87 (d, *J* = 13.3 Hz, 1H), 3.71 (q, *J* = 6.8 Hz, 2H), 3.67 (s, 3H), 3.24 (ddd, *J* = 14.4, 6.1, 0.8 Hz, 1H), 3.19 (dd, *J* = 14.4, 6.9 Hz, 1H), 2.00 (s, 1H); **MS** (ESI): calcd. for $C_{19}H_{21}N_2O_2^+$ $[M+H]^+$: 309.1, found 309.1. This is in agreement with the literature.[1]

Characterization for Compound 3:

R_f = 0.50 (*n*-Hexane/EtOAc, 4:1); **mp** 146 – 147 °C; **$[\alpha]_D^{25}$** -37.1 (*c* 1.0, CH_3OH); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.54 (d, *J* = 7.7 Hz, 1H), 7.37 – 7.28 (m, 6H), 7.17 (dd, *J* = 11.1, 4.0 Hz, 1H), 7.12 (dd, *J* = 10.9, 3.9 Hz, 1H), 4.01 (dd, *J* = 9.1, 5.0 Hz, 1H), 3.94 (dd, *J* = 8.3, 4.0 Hz, 1H), 3.86 (d, *J* = 13.5 Hz, 1H), 3.77 (s, 3H), 3.60 (d, *J* = 13.5 Hz, 1H), 3.51 (s, 3H), 3.14 (dd, *J* = 15.7, 9.1 Hz, 1H), 3.03 (dd, *J* = 15.8, 5.0 Hz, 1H), 2.43 (dt, *J* = 16.6, 7.4 Hz, 1H), 2.31 (dt, *J* = 16.8, 6.4 Hz, 1H), 2.13 – 2.04 (m, 1H), 1.97 (td, *J* = 14.7, 6.6 Hz, 1H); **MS** (ESI): calcd. for $C_{24}H_{27}N_2O_4^+$ $[M+H]^+$: 407.2, found 407.1. This is in agreement with the literature.[1]

Methyl (6*S*,10*S*)-12-benzyl-9-hydroxy-6,7,10,11-tetrahydro-5H-6,10-epiminocycloocta[b]indole -8-carboxylate (4) [1].



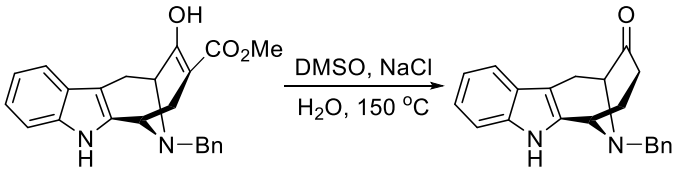
3 **4**

To a solution of compound **3** (12.0 g, 0.03 mol, 1.0 equiv) in dry toluene (160 mL) was added first sodium hydride (3.0 g, 0.075 mol, 2.5 equiv) and then a solution of ultra-dry CH_3OH (6 mL, 0.15 mol, 5.0 equiv) dropwise over 1.5 h under an atmosphere of nitrogen in several portions at 0 °C. The mixture was held at reflux for an additional 36 h at 110 °C. The reaction mixture was analyzed by TLC indicated the completion of the reaction. The solution was treated with EtOAc (150 mL) and H_2O (150 mL), the layers were separated and the aqueous layer was extracted with EtOAc (2 × 100 mL). The combined organic layers were washed with saturated NaCl solution, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (*n*-Hexane/EtOAc, 6:1) to provide compound **4** (9.99 g, 0.0267 mol, 89%) as a white solid.

Characterization for compound 4:

R_f = 0.50 (*n*-Hexane/EtOAc, 4:1); **mp** 106 – 108 °C (lit. 149 – 150 °C); **$[\alpha]_D^{25}$** -105.0 (*c* 1.0, CH_3OH); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 11.98 (s, 1H), 7.67 (s, 1H), 7.51 (d, *J* = 7.6 Hz, 1H), 7.39 – 7.30 (m, 6H), 7.16 (t, *J* = 7.5 Hz, 1H), 7.12 (t, *J* = 7.4 Hz, 1H), 4.02 (d, *J* = 5.3 Hz, 1H), 3.83 (d, *J* = 13.4 Hz, 1H), 3.79 (d, *J* = 5.5 Hz, 1H), 3.73 (d, *J* = 13.5 Hz, 1H), 3.67 (s, 3H), 3.18 (dd, *J* = 16.0, 5.9 Hz, 1H), 2.92 (d, *J* = 16.0 Hz, 1H), 2.83 (dd, *J* = 15.6, 5.6 Hz, 1H), 2.33 (d, *J* = 15.6 Hz, 1H); **MS** (ESI): calcd. for $C_{23}H_{23}N_2O_3^+$ $[M+H]^+$: 375.2, found 375.1. This is in agreement with the literature.[1]

(6*S*,10*S*)-12-benzyl-5,6,7,8,10,11-hexahydro-9H-6,10-epiminocycloocta[b]indol-9-one (5). [1]



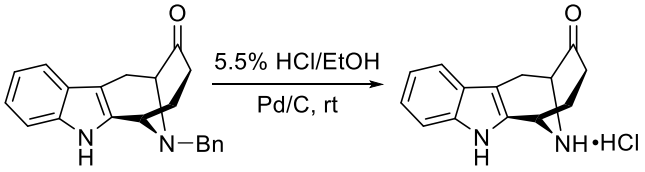
4 **5**

To a solution of compound **4** (16.7 g, 44.6 mmol, 1.0 equiv) in H_2O (16.7 g, 927.7 mmol, 20.8 equiv) was added sdium chloride (16.7 g, 285.5 mmol, 6.4 equiv) and dimethyl sulfoxide (150 mL, 2.11 mol, 47.3 equiv), and then was held at reflux under an atmosphere of nitrogen for 5 h in several portions at 150 °C. The solvent was removed under reduced pressure, and the residue was treated with EtOAc (150 mL) and H_2O (150 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 × 100 mL). The combined organic layers were washed with saturated NaCl solution, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (*n*-Hexane/EtOAc, 4:1) to provide compound **5** (13.8 g, 43.6 mmol, 97%) as a white solid.

Characterization for compound 5:

R_f = 0.4 (*n*-Hexane/EtOAc, 4:1); **mp** 175 – 176 °C; **$[\alpha]_D^{25}$** -220.5 (*c* 1.0, CH_3OH); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.52 (d, *J* = 7.7 Hz, 1H), 7.33 (q, *J* = 8.3 Hz, 5H), 7.30 – 7.27 (m, 1H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.15 (t, *J* = 7.4 Hz, 1H), 4.00 (s, 1H), 3.77 (s, 3H), 3.25 (dd, *J* = 16.8, 6.7 Hz, 1H), 2.69 (d, *J* = 16.8 Hz, 1H), 2.51 – 2.39 (m, 2H), 2.17 – 2.06 (m, 1H), 2.06 – 1.96 (m, 1H); **MS** (ESI): calcd. for $C_{21}H_{21}N_2O^+$ $[M+H]^+$: 317.2, found 317.1. This is in agreement with the literature. [1]

(6*S*,10*S*)-5,6,7,8,10,11-hexahydro-9H-6,10-epiminocycloocta[b]indol-9-one hydrochloride(6).[1]



5 **6**

To a solution of compound **5** (1.54 g, 4.87 mmol, 1.0 equiv) in EtOH (30 mL) was added 5.5% HCl/EtOH (6.46 g, 9.74 mmol, 2.0 equiv), the solvent was removed under reduced pressure. The mixture was dissolved with EtOH (15 mL) and then was removed under reduced pressure, this process was recycled four times. The mixture was dissolved with EtOH (15 mL) and added Pd/C (10%, 3.0 g) under an atmosphere of hydrogen for 12 h. The mixture that resulted was allowed to stir at room temperature under an atmosphere of hydrogen for 5 h. The reaction mixture was analyzed by TLC indicated the completion of the reaction. The Pd/C was removed by filtration and was washed with EtOH (4 ×15 mL), then the solvent was removed under reduced pressure to provide compound **6** (1.39 g, 109%) as solid.

Subsequent, the residue was treated with EtOAc (30 mL) and NaOH (aq). The layers were separated and the aqueous layer was extracted with EtOAc (2 × 30 mL). The combined organic layers were washed with saturated NaCl solution, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (CH_2Cl_2/MeOH, 30:1 → 10:1) to provide pure compound **6'** (660.70 mg, 2.922 mmol, 60%) as solid.

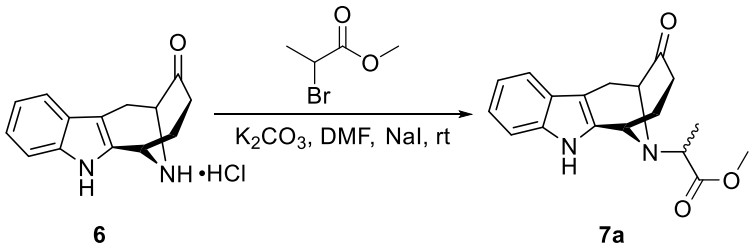
Characterization for compound 6:

R_f = 0.60 (CH_2Cl_2/MeOH, 10:1); **mp** 71 – 73 °C; **$[\alpha]_D^{25}$** -87.2 (*c* 1.0, CH_3OH); **IR (KBr)** 3403, 2930.54, 1702.65, 1630.11, 1550.81, 1451.02, 1388.06, 1300.60, 1141.39, 746.78 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.47 (d, *J* = 7.8 Hz, 1H), 7.34 (d, *J* = 8.1 Hz, 1H), 7.19 (t, *J* = 7.6 Hz, 1H), 7.12 (t, *J* = 7.5 Hz, 1H), 4.35 (d, *J* = 4.6 Hz, 1H), 3.96 (d, *J* = 6.7 Hz, 1H), 3.13 (dd, *J* = 16.5, 6.8 Hz, 1H), 2.84 (d, *J* = 16.5 Hz, 1H), 2.53 – 2.44 (m, 2H), 2.20 – 2.12 (m, 2H), 1.67 (s, 1H).

Characterization for compound 6':

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.47 (d, *J* = 7.8 Hz, 1H), 7.32 (d, *J* = 8.1 Hz, 1H), 7.19 (t, *J* = 7.6 Hz, 1H), 7.12 (t, *J* = 7.4 Hz, 1H), 4.31 (d, *J* = 4.4 Hz, 1H), 3.95 (d, *J* = 6.7 Hz, 1H), 3.12 (dd, *J* = 16.4, 6.8 Hz, 1H), 2.82 (d, *J* = 16.4 Hz, 1H), 2.52 – 2.36 (m, 3H), 2.20 – 2.09 (m, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 210.92, 135.70, 133.97, 126.89, 122.11, 119.75, 118.14, 110.91, 107.57, 59.77, 46.09, 35.03, 32.00, 25.82; **HRMS** (ESI): calcd. for $C_{14}H_{15}N_2O^+$ $[M+H]^+$: 227.1179, found 227.1174. This is in agreement with the literature. [1]

Methyl 2-((6*S*,10*S*)-9-oxo-6,7,8,9,10,11-hexahydro-5H-6,10-epiminocycloocta[*b*]indol-12-yl) propanoate (7a).



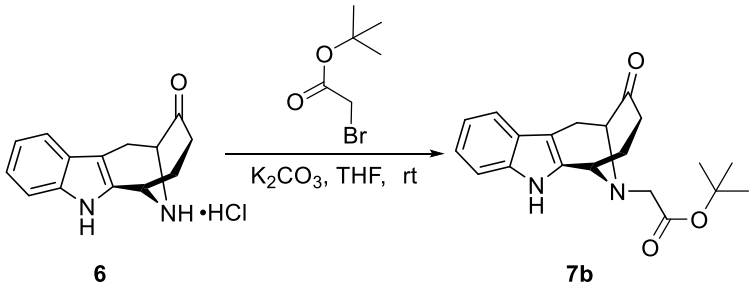
6 **7a**

To a solution of **6** (80.0 mg, 0.30 mmol, 1.0 equiv) in DMF(3 mL) and potassium carbonate (124.4 mg, 0.90 mmol, 3.0 equiv) was added first sodium iodide (67.5 mg, 0.45 mmol, 1.5 equiv) and then 2-bromo-1,1-diethoxyethane (50 μL, 0.45 mmol, 1.5 equiv) at room temperature. Afterwards, the mixture was allowed to stir at 120 °C under an atmosphere of nitrogen for 3 h. The reaction mixture was analyzed by TLC indicated the completion of the reaction. The solvent was removed under reduced pressure, and the residue was treated with EtOAc (10 mL) and H_2O (10 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with saturated NaCl solution, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (*n*-Hexane/EtOAc, 2:1 → 1:1) to provide compound **7a** (65 mg, 0.198 mmol, 66%) as a yellow sticky substance.

Characterization for compound 7a:

R_f = 0.50 (*n*-Hexane/EtOAc, 4:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.09 (d, *J* = 18.1 Hz, 1H), 7.45 (dd, *J* = 8.0, 3.3 Hz, 1H), 7.31 (dd, *J* = 12.7, 8.1 Hz, 1H), 7.17 (td, *J* = 7.5, 3.7 Hz, 1H), 7.11 (td, *J* = 7.4, 2.8 Hz, 1H), 4.42 – 4.15 (m, 1H), 3.92 (dd, *J* = 70.2, 6.5 Hz, 1H), 3.61 – 3.49 (m, 4H), 3.19 (ddd, *J* = 40.9, 16.8, 6.7 Hz, 1H), 2.67 (t, *J* = 16.1 Hz, 1H), 2.48 (ddt, *J* = 18.7, 11.9, 4.8 Hz, 2H), 2.18 – 1.95 (m, 2H), 1.36 (dd, *J* = 49.3, 6.9 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 209.56, 209.41, 174.63, 174.15, 135.80, 135.76, 132.40, 132.03, 126.75, 126.67, 122.04, 119.66, 118.14, 118.06, 110.94, 110.89, 107.14, 107.07, 63.79, 62.76, 58.72, 58.59, 51.96, 51.93, 49.91, 47.93, 34.44, 34.35, 30.49, 30.12, 21.38, 21.34, 16.80, 16.45; **HRMS** (ESI): calcd. for $C_{18}H_{21}N_2O_3^+$ $[M+H]^+$: 313.1547, found 313.1545.

Methyl 2-((6*S*,10*S*)-9-oxo-6,7,8,9,10,11-hexahydro-5H-6,10-epiminocycloocta[*b*]indol-12-yl)acetate (7b).



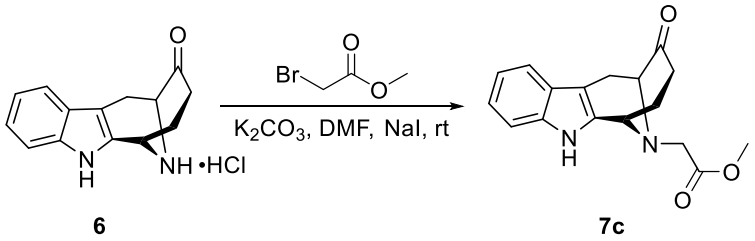
6 **7b**

To a solution of **6** (0.80 g, 3.05 mmol, 1.0 equiv) in dry THF (16 mL) was added potassium carbonate (2.11 g, 15.25 mmol, 5.0 equiv) and tert-butyl 2-bromoacetate (0.89 mL, 6.10 mmol, 2.0 equiv) in several portions at room temperature. Afterwards, the light yellow turbid mixture was allowed to stir at room temperature under an atmosphere of nitrogen for 24 h. The reaction mixture was analyzed by TLC indicated the completion of the reaction. The solution was treated with CH_2Cl_2 (10 mL) and H_2O (10 mL), the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were washed with saturated NaCl solution, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (*n*-Hexane/EtOAc, 6:1 → 3:2) to provide compound **7b** (467.8 mg, 1.31 mmol, 43%) as solid.

Characterization for compound 7b:

R_f = 0.50 (*n*-Hexane/EtOAc, 4:1); **mp** 73 – 75 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.46 (dd, J = 7.8, 1.1 Hz, 1H), 7.33 (dd, J = 8.0, 1.0 Hz, 1H), 7.18 (ddd, J = 8.2, 7.0, 1.2 Hz, 1H), 7.12 (ddd, J = 8.0, 7.1, 1.0 Hz, 1H), 4.32 – 4.26 (m, 1H), 3.77 (d, J = 6.5 Hz, 1H), 3.39 (d, J = 17.2 Hz, 1H), 3.27 (d, J = 17.3 Hz, 1H), 3.14 (dd, J = 16.8, 6.6 Hz, 1H), 2.70 (dd, J = 16.9, 1.0 Hz, 1H), 2.63 – 2.54 (m, 1H), 2.52 – 2.45 (m, 1H), 2.10 – 2.01 (m, 2H), 1.45 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 209.67, 170.00, 135.90, 131.42, 126.62, 122.11, 119.72, 118.17, 110.91, 106.55, 81.44, 65.52, 53.90, 51.08, 34.06, 29.87, 28.04, 20.79; **HRMS** (ESI): calcd. for $C_{20}H_{25}N_2O_3^+$ $[M+H]^+$: 341.1860, found 341.1857.

methyl 2-((6S,10S)-9-oxo-6,7,8,9,10,11-hexahydro-5H-6,10-epiminocycloocta[b]indol-12-yl)acetate (7c).



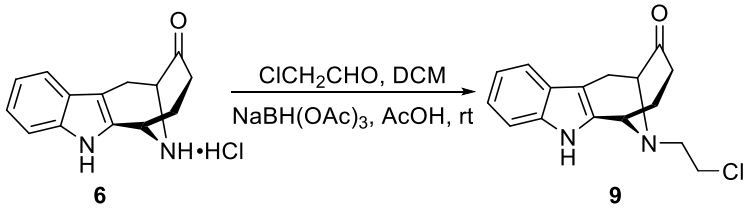
6 **7c**

To a solution of **6** (80.0 mg, 0.30 mmol, 1.0 equiv) in DMF(3 mL) and potassium carbonate (124.4 mg, 0.90 mmol, 3.0 equiv) was added first sodium iodide (67.5 mg, 0.45 mmol, 1.5 equiv) and then methyl 2-bromoacetate (45 μL, 0.45 mmol, 1.5 equiv) at room temperature. Afterwards, the mixture was allowed to stir at 120 °C under an atmosphere of nitrogen for 3 h. The reaction mixture was analyzed by TLC indicated the completion of the reaction. The solvent was removed under reduced pressure, and the residue was treated with EtOAc (10 mL) and H_2O (10 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with saturated NaCl solution, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (*n*-Hexane/EtOAc, 2:1 → 1:1) to provide compound **7c** (72 mg, 0.241 mmol, 80%) as a yellow sticky substance.

Characterization for compound 7c:

R_f = 0.40 (*n*-Hexane/EtOAc, 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.47 (d, *J* = 7.8 Hz, 1H), 7.34 (d, *J* = 8.1 Hz, 1H), 7.19 (dd, *J* = 11.1, 4.0 Hz, 1H), 7.12 (t, *J* = 7.1 Hz, 1H), 4.29 (d, *J* = 4.7 Hz, 1H), 3.79 (d, *J* = 6.5 Hz, 1H), 3.72 (s, 3H), 3.49 (d, *J* = 16.9 Hz, 1H), 3.38 (d, *J* = 16.9 Hz, 1H), 3.16 (dd, *J* = 16.9, 6.6 Hz, 1H), 2.72 (d, *J* = 16.9 Hz, 1H), 2.61 (ddd, *J* = 12.2, 11.0, 8.4 Hz, 1H), 2.50 (dd, *J* = 14.9, 6.6 Hz, 1H), 2.13 – 2.03 (m, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 209.33, 171.14, 135.93, 131.20, 126.59, 122.17, 119.76, 118.19, 110.93, 106.53, 65.41, 53.29, 51.91, 51.34, 33.98, 29.85, 20.63; **HRMS** (ESI): calcd. for $C_{17}H_{19}N_2O_3^+$ $[M+H]^+$: 299.1390, found 299.1391.

(6*S*,10*S*)-12-(2-chloroethyl)-5,6,7,8,10,11-hexahydro-9H-6,10-epiminocycloocta[*b*]indol-9-one (9).



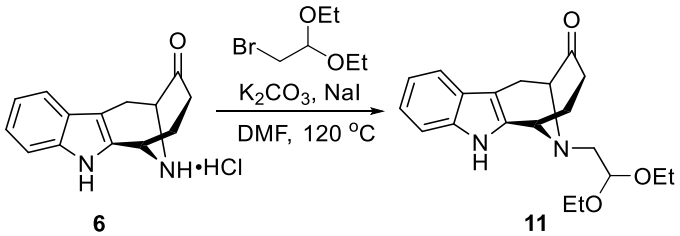
To a solution of **6** (160.0 mg, 0.61 mmol, 1.0 equiv) in CH_2Cl_2 (5 mL) was added first glacial acetic acid (80 μL, 1.34 mmol, 2.2 equiv) and 2-chloroacetaldehyde (40% in water, 150 μL, 0.91 mmol, 1.5 equiv), and then sodium triacetoxyborohydride (284.4 mg, 1.34 mmol, 2.2 equiv) at room temperature. Afterwards, the mixture was allowed to stir at room temperature under an atmosphere of nitrogen for 2 h. The reaction mixture was analyzed by TLC indicated the completion of the reaction. The solution was treated with a solution of NaOH (1 M, 2 mL), the layers were separated and the aqueous layer was extracted with EtOAc (2 × 15 mL). The combined organic layers were washed with saturated NaCl solution, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (*n*-Hexane/EtOAc, 3:1 → 1:1) to provide compound **9** (129 mg, 0.44 mmol, 73%) as a white solid.

Characterization for compound 9:

R_f = 0.50 (*n*-Hexane/EtOAc, 4:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.51 – 7.45 (m, 1H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.20 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.16 – 7.11 (m, 1H), 4.13 (q, *J* = 2.4 Hz, 1H), 3.75 (d, *J* = 6.6 Hz, 1H), 3.61 (td, *J* = 6.7, 2.3 Hz, 2H), 3.20 (dd, *J* = 16.9, 6.7 Hz, 1H), 3.01 – 2.87 (m, 2H), 2.68 (d, *J* = 16.8 Hz, 1H), 2.55 – 2.39 (m, 2H), 2.16 – 2.01 (m, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 209.87, 135.83, 131.79, 126.69, 122.19, 119.80, 110.95, 106.92, 65.17, 53.94, 51.78, 42.21, 34.23, 30.21, 20.52; **HRMS** (ESI): calcd. for $C_{16}H_{18}ClN_2O^+$ $[M+H]^+$: 289.1102, found 289.1101.

.

(6*S*,10*S*)-12-(2,2-diethoxyethyl)-5,6,7,8,10,11-hexahydro-9H-6,10-epiminocycloocta[b]indol-9-one (11).

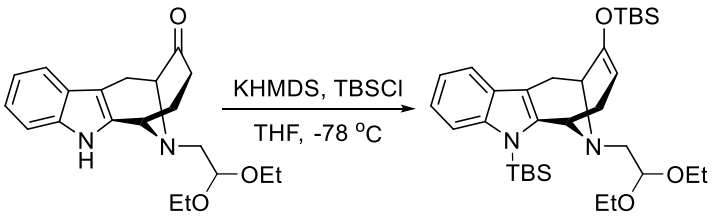


To a solution of **6** (3.10 g, 11.8 mmol, 1.0 equiv) in dry DMF(50 mL) and potassium carbonate (4.9 g, 35.4 mmol, 3.0 equiv) was added first sodium iodide (2.65 g, 17.7 mmol, 1.5 equiv) and then 2-bromo-1,1-diethoxyethane (3.48 g, 17.7 mmol, 1.5 equiv) at room temperature. Afterwards, the mixture was allowed to stir at 120 °C under an atmosphere of nitrogen for 6 h. The reaction mixture was analyzed by TLC indicated the completion of the reaction. The solvent was removed under reduced pressure, and the residue was treated with CH_2Cl_2 (50 mL) and H_2O (50 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were washed with saturated NaCl solution, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (*n*-Hexane/EtOAc, 2:1 → 1:1) to provide compound **11** (3.37 g, 9.85 mmol, 83%) as a white solid.

Characterization for compound 11:

R_f = 0.7 (CH_2Cl_2/MeOH, 10:1); **mp** 123 – 124 °C; **$[\alpha]_D^{25}$** -136.3 (*c* 1.0, CH_3OH); **IR (KBr)** 3351.27, 2973.09, 2944.21, 2880.87, 2849.48, 1708.08, 1450.79, 1438.93, 1401.17, 1383.96, 1374.48, 1346.95, 1323.70, 1301.93, 1288.39, 1274.96, 1247.96, 1229.22, 1141.39, 1121.82, 1108.15, 1107.25, 998.48, 980.16, 850.82, 741.32, 666.57, 548.39 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.46 (d, *J* = 7.7 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.19 – 7.14 (m, 1H), 7.13 – 7.08 (m, 1H), 4.64 (t, *J* = 5.3 Hz, 1H), 4.27 (d, *J* = 2.5 Hz, 1H), 3.76 (d, *J* = 6.6 Hz, 1H), 3.68 (ddq, *J* = 20.9, 9.3, 7.1 Hz, 2H), 3.54 (ddq, *J* = 14.0, 9.3, 7.1 Hz, 2H), 3.19 (dd, *J* = 16.8, 6.7 Hz, 1H), 2.77 (dd, *J* = 13.7, 5.7 Hz, 1H), 2.68 (dd, *J* = 13.8, 4.8 Hz, 1H), 2.62 (d, *J* = 16.8 Hz, 1H), 2.51 – 2.35 (m, 2H), 2.09 – 1.98 (m, 2H), 1.21 (dt, *J* = 11.6, 7.1 Hz, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 210.64, 136.02, 132.52, 127.00, 122.00, 119.71, 118.25, 111.03, 107.10, 103.03, 66.05, 62.87, 62.26, 55.22, 52.17, 34.41, 30.37, 20.69, 15.55, 15.50; **HRMS** (ESI): calcd. for $C_{20}H_{27}N_2O_3^+$ $[M+H]^+$: 343.2016, found 343.2009.

(6*S*,10*S*)-5-(tert-butyldimethylsilyl)-9-((tert-butyldimethylsilyl)oxy)-12-(2,2-diethoxyethyl)-6,7,10,11-tetra-hydro-5H-6,10-epiminocycloocta[b]indole (12).



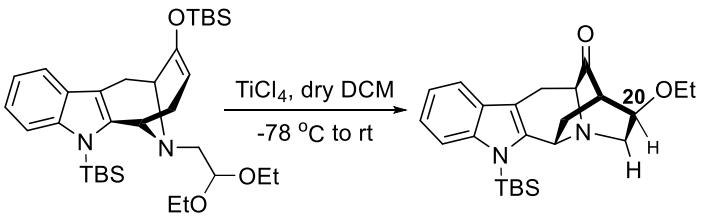
11 **12**

To a solution of **11** (1.00 g, 2.92 mmol, 1.0 equiv) in dry THF (15 mL) was added KHMDS solution (1.0 M in THF, 11.70 mL, 11.70 mol, 4.0 equiv) at -78 °C. The mixture was stirred at this temperature for 0.5 h before it was added TBSCl (2.20 g, 14.60 mmol, 5.0 equiv). Afterwards, the mixture was allowed to stir at room temperature under an atmosphere of nitrogen for 5 h. The reaction mixture was analyzed by TLC indicated the completion of the reaction. The solution was treated with *n*-Hexane (40 mL) and H_2O (40 mL), the layers were separated and the aqueous layer was extracted with n-Hexane (2 × 40 mL). The combined organic layers were washed with saturated NaCl solution, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (*n*-Hexane/EtOAc, 20:1 → 8:1) to provide compound **12** (1.58 g, 2.77 mmol, 95%) as solid.

Characterization for compound 12:

R_f = 0.50 (*n*-Hexane/EtOAc, 8:1); **mp** 126 °C; **$[\alpha]_D^{25}$** -39.1 (*c* 0.2, CH_3OH); **IR (KBr)** 3442.27, 3046.65, 2955.74, 2930.56, 2890.34, 2856.67, 1681.67, 1460.22, 1450.72, 1390.74, 1361.44, 1307.58, 1255.70, 1193.63, 1136.14, 1103.09, 1061.07, 1038.17, 1014.00, 990.85, 963.91, 943.01, 877.21, 819.19, 779.36, 742.78, 686.85, 575.87 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.55 (dd, *J* = 5.8, 3.2 Hz, 1H), 7.43 (dd, *J* = 5.7, 3.1 Hz, 1H), 7.08 (dd, *J* = 5.8, 2.9 Hz, 2H), 4.70 (s, 1H), 4.62 (d, *J* = 3.8 Hz, 1H), 4.33 (d, *J* = 4.1 Hz, 1H), 3.72 (dq, *J* = 14.4, 7.2 Hz, 1H), 3.69 – 3.61 (m, 1H), 3.61 – 3.52 (m, 2H), 3.45 (d, *J* = 3.8 Hz, 1H), 3.01 (dd, *J* = 15.8, 5.6 Hz, 1H), 2.75 (d, *J* = 14.9 Hz, 4H), 2.11 (dd, *J* = 16.3, 5.1 Hz, 1H), 1.22 (dt, *J* = 13.8, 7.0 Hz, 6H), 0.93 (s, 9H), 0.89 (s, 9H), 0.76 (s, 3H), 0.62 (s, 3H), 0.14 (s, 3H), 0.03 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 150.85, 142.02,140.95, 131.00, 120.74, 119.47, 117.66, 114.62, 110.61, 103.36, 98.20, 62.76, 61.60, 56.30, 55.72, 52.20, 31.16, 27.45, 25.80, 22.30, 20.96, 18.08, 15.60, 15.58, -0.40, -0.50, -4.04, -4.46; **HRMS** (ESI): calcd. for $C_{32}H_{55}N_2O_3Si_2^+$ $[M+H]^+$: 571.3746, found 571.3739.

(6*S*,10*S*,11a*S*)-5-(tert-butyldimethylsilyl)-9-ethoxy-5,6,9,10,11a,12-hexahydro-6,10-methanoindolo[3,2-*b*] quinolizin-11(8H)-one (13).



12 **13**

To a solution of **12** (1.50 g, 2.63 mmol, 1.0 equiv) in dry CH_2Cl_2 (30.0 mL) was added titanium tetrachloride (575.0 μL, 5.25 mmol, 2.0 equiv) at -78 °C. Afterwards, the mixture was allowed to stir at room temperature under an atmosphere of nitrogen for 4 h. The reaction mixture was analyzed by TLC indicated the completion of the reaction. The mixture was added NaOH solution (6.0 M, 5.0 mL) and EDTA-2Na (0.50 g) at -50 °C and then the solvent was removed under reduced pressure. The solution was treated with with Et_2O and H_2O, the layers were separated and the aqueous layer was extracted with Et_2O. The combined organic layers were washed with saturated NaCl solution, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (*n*-Hexane/EtOAc, 2:1 → 1:1) to provide compound **13** (758.1 mg, 1.85 mmol, 70%) as solid.

NOE experiment was conducted to determine the stereochemistry of C20-ethoxy.

Characterization for compound 13:

R_f = 0.20 (*n*-Hexane/EtOAc, 4:1); **mp** 84 – 86 °C; **$[\alpha]_D^{25}$** -76.6 (*c* 0.04, CH_3OH); **IR (KBr)** 3342.94, 2930.16, 2857.63, 1611.07, 1452.12, 1408.21, 1369.25, 1285.81, 1230.65, 1173.54, 1103.41, 1083.26, 964.10, 844.11, 815.68, 741.93, 686.67 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.56 – 7.49 (m, 1H), 7.48 – 7.40 (m, 1H), 7.14 – 7.05 (m, 2H), 4.25 (dd, *J* = 9.5, 2.4 Hz, 1H), 4.01 (ddd, *J* = 7.0, 4.2, 1.4 Hz, 1H), 3.71 – 3.65 (m, 1H), 3.65 – 3.57 (m, 1H), 3.47 (dd, *J* = 14.9, 7.4 Hz, 1H), 3.39 (td, *J* = 14.1, 7.0 Hz, 1H), 3.28 (d, *J* = 15.7 Hz, 1H), 3.22 (d, *J* = 14.6 Hz, 1H), 2.96 (dd, *J* = 15.7, 7.0 Hz, 1H), 2.82 (t, *J* = 3.4 Hz, 1H), 2.23 (ddd, *J* = 13.1, 9.6, 1.5 Hz, 1H), 2.02 (ddd, *J* = 7.3, 4.8, 3.2 Hz, 1H), 1.16 (t, *J* = 7.0 Hz, 3H), 0.86 (s, 9H), 0.75 (s, 3H), 0.57 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 142.31, 141.71, 130.11, 121.55, 119.90, 118.24, 114.51, 109.52, 76.84, 63.83, 62.87, 56.93, 51.70, 44.14, 34.85, 27.02, 22.50, 20.74, 15.42, -0.37, -0.46; **HRMS** (ESI): calcd. for $C_{24}H_{35}N_2O_2Si^+$ $[M+H]^+$: 411.2462, found 411.2457.

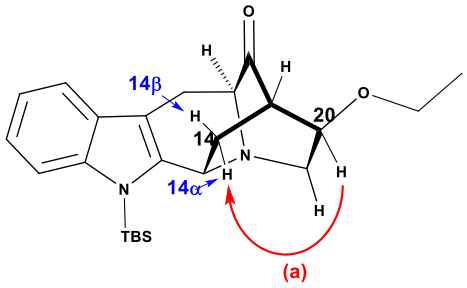


Figure S1 NOE relationship of compound 13

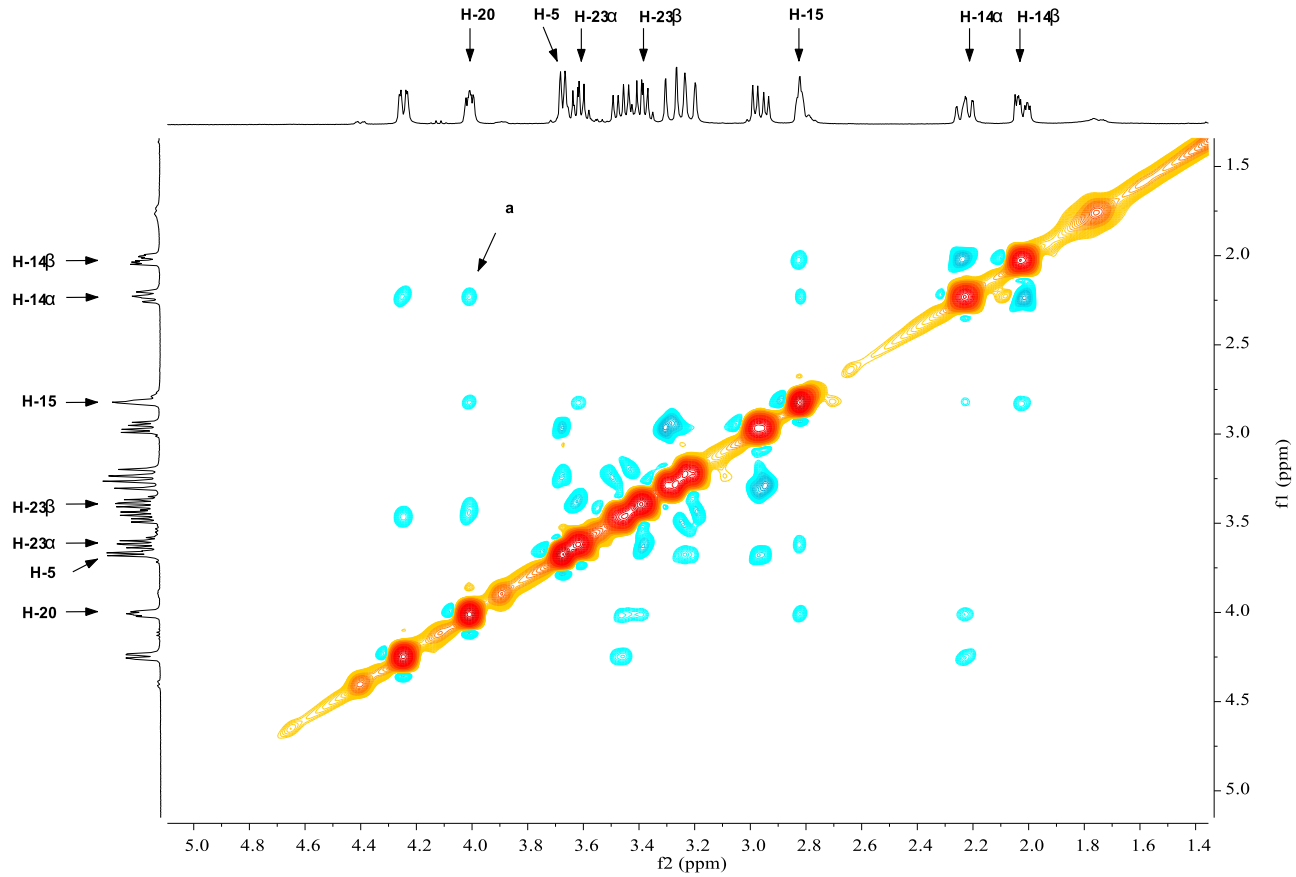
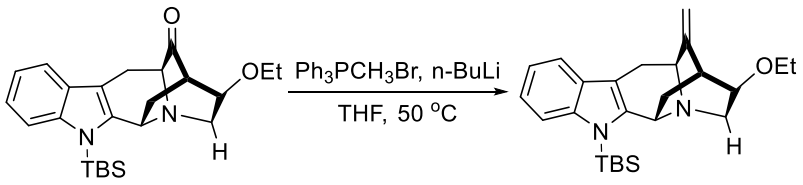


Figure S2 The partial NOE spectrum of compound 13 (For full range NOE spectrum see page S43.)

The irradiation of the proton at H-20 resulted in enhancement of the signal at H-14α (strong) indicating the proton at H-20 were located at the same surface with H-14α, means the α position.

(6*S*,11a*S*)-5-(tert-butyldimethylsilyl)-9-ethoxy-11-methylene-5,6,8,9,10,11,11a,12-octahydro-6,10-methano-indolo[3,2-b]quinolizine (15).



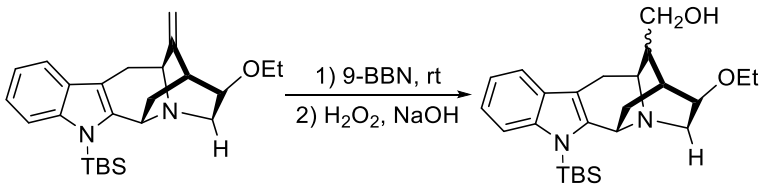
13 **15**

To a stirred solution of methyltriphenylphosphonium bromide (6.1 g, 17.3 mmol, 3.0 equiv) in anhydrous THF (84 mL) was added n-butyllithium (2.5 M in n-hexane, 7.2 mL, 17.9 mmol, 3.1 equiv) dropwise under an atmosphere of nitrogen. The solution was warmed at 50 °C and stirred for 2 h, obtaining orange-red reaction solution. At this time, the solution was added **13** (2.37 g, 5.78 mmol, 1.0 equiv) dropwise in anhydrous THF (15 mL). The mixture was allowed to stir under reflux for 2.5 h and analyzed by TLC indicated the completion of the reaction, and then cooled at room temperature, the solvent was removed under reduced pressure. The solution was treated with with EtOAc (50 mL) and H_2O (50 mL), the layers were separated and the aqueous layer was extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with saturated NaCl solution, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (*n*-Hexane/EtOAc, 4:1 → 2:1) to provide pure compound **15** (2.20 g, 5.38 mmol, 93%) as solid.

Characterization for compound 15:

R_f = 0.50 (CH_2Cl_2/MeOH, 30:1); **mp** 106 – 107 °C; **$[\alpha]_D^{25}$** -4.3 (*c* 0.08, CH_3OH); **IR (KBr)** 3448.62, 3064.87, 2856.74, 1737.67, 1650.71, 1612.03, 1452.37, 1408.52, 1368.63, 1321.25, 1281.56, 1260.16, 1234.76, 1204.15, 1176.76, 1111.19, 1082.44, 1061.14, 1026.56, 1003.56, 965.26, 940.73, 914.23, 881.95, 841.02, 814.37,740.32, 686.95, 581.02, 535.23 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.59 – 7.56 (m, 1H), 7.50 – 7.46 (m, 1H), 7.14 – 7.09 (m, 2H), 5.05 (d, *J* = 2.1 Hz, 1H), 4.88 (d, *J* = 2.7 Hz, 1H), 4.11 (dd, *J* = 9.9, 2.8 Hz, 1H), 3.98 – 3.94 (m, 1H), 3.70 – 3.61 (m, 2H), 3.45 – 3.35 (m, 2H), 3.17 (dd, *J* = 15.4, 5.9 Hz, 1H), 3.06 (dd, *J* = 14.7, 1.7 Hz, 1H), 3.00 (dd, *J* = 15.5, 1.1 Hz, 1H), 2.72 (t, *J* = 3.5 Hz, 1H), 1.93 (ddd, *J* = 11.8, 10.0, 1.5 Hz, 1H), 1.78 (ddd, *J* = 12.8, 4.7, 3.1 Hz, 1H), 1.23 (t, *J* = 7.0 Hz, 3H), 0.89 (s, 9H), 0.78 (s, 3H), 0.60 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 149.57, 143.22, 142.28, 130.88, 121.00, 119.63, 117.85, 114.53, 109.05, 108.26, 75.38, 63.23, 57.82, 55.22, 51.63, 36.73, 35.59, 27.12, 26.90, 20.75, 15.55, -0.45, -0.46; **HRMS** (ESI): calcd. for $C_{25}H_{37}N_2OSi^+$ $[M+H]^+$: 409.2670, found 409.2661.

((6*S*,11a*S*)-5-(tert-butyldimethylsilyl)-9-ethoxy-5,6,8,9,10,11,11a,12-octahydro-6,10-methanoindolo[3,2-*b*] quinolizin-11-yl)methanol (16).



To a solution of compound **15** (1.49 g, 3.65 mmol, 1.0 equiv) in THF (30 mL) at 0 °C was added 9-BBN (0.5 M in THF, 22 mL, 10.95 mmol, 3.0 equiv). After the resulting mixture was allowed to stir at room temperature under an atmosphere of nitrogen for 4 h, NaOH (3.0 M, 3.65 mL, 10.95 mmol, 3.0 equiv) and H_2O_2 (30% in water, 2.43 mL, 21.9 mmol, 6.0 equiv) were added. After stirring for 1 h at room temperature, the solvent was removed under reduced pressure. The solution was treated with with EtOAc (45 mL) and H_2O (45 mL), the layers were separated and the aqueous layer was extracted with EtOAc (3 × 45 mL). The combined organic layers were washed with saturated NaCl solution, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (CH_2Cl_2/MeOH, 50:1) to provide compound **16A** (802.6 mg, 1.88 mmol, 51.5%), **16B** (165.6 mg, 0.38 mmol, 10.1%) as solid.

Characterization for compound 16A:

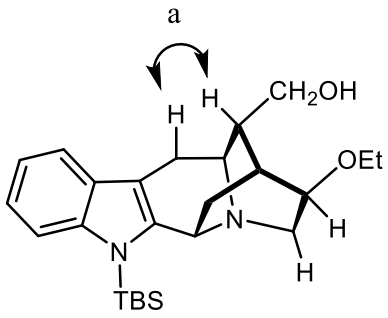
R_f = 0.40 (CH_2Cl_2/MeOH, 20:1); **mp** 91 – 93 °C; **$[\alpha]_D^{25}$** +23 (*c* 0.02, CH_3OH); **IR (KBr)** 3421.77, 2929.72, 2858.16, 1636.70, 1551.80, 1452.13, 1379.68, 1329.81, 1261.02, 1182.21, 1155.72, 1019.19, 959.67, 841.26, 815.40, 788.97, 741.93, 688.33, 581.50 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.57 – 7.53 (m, 1H), 7.45 – 7.41 (m, 1H), 7.11 – 7.07 (m, 2H), 4.02 (dd, *J* = 9.9, 3.0 Hz, 1H), 3.71 (s, 1H), 3.66 – 3.55 (m, 4H), 3.48 – 3.42 (m, 1H), 3.34 (dd, *J* = 14.7, 8.6 Hz, 1H), 3.06 (dd, *J* = 15.6, 5.7 Hz, 1H), 3.01 (dd, *J* = 14.7, 3.0 Hz, 1H), 2.60 (d, *J* = 15.5 Hz, 1H), 2.04 (s, 1H), 1.82 (ddd, *J* = 12.1, 10.1, 1.7 Hz, 1H), 1.65 – 1.59 (m, 1H), 1.56 (s, 1H), 1.27 (t, *J* = 7.0 Hz, 3H), 0.87 (s, 9H), 0.76 (s, 3H), 0.58 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.88, 142.25, 131.04, 121.04, 119.67, 117.78, 114.53, 108.59, 74.56, 64.72, 63.83, 57.49, 51.09, 50.60, 40.98, 36.88, 32.03, 27.11, 20.71, 15.34, -0.45, -0.46; **HRMS** (ESI): calcd. for $C_{25}H_{39}N_2O_2Si^+$ $[M+H]^+$: 427.2775, found 427.2767.

Characterization for compound 16B:

R_f = 0.40 (CH_2Cl_2/MeOH, 20:1); **mp** 93 – 95 °C; **$[\alpha]_D^{25}$** +15 (*c* 0.02, CH_3OH); **IR (KBr)** 3422.40, 2929.51, 2857.62, 1737.05, 1612.92, 1452.32, 1409.86, 1370.16, 1326.05, 1282.87, 1260.49, 1236.45, 1206.48, 1182.15, 1109.94, 1025.04, 950.13, 842.42, 814.82, 740.93, 684.25, 579.66 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.57 – 7.53 (m, 1H), 7.42 – 7.39 (m, 1H), 7.11 – 7.06 (m, 2H), 3.97 (dd, *J* = 10.3, 3.4 Hz, 1H), 3.63 – 3.51 (m, 4H), 3.41 (dq, *J* = 9.1, 7.0 Hz, 1H), 3.26 – 3.19 (m, 2H), 2.95 (dd, *J* = 14.7, 2.4 Hz, 1H), 2.89 (qd, *J* = 16.2, 3.6 Hz, 2H), 2.46 – 2.38 (m, 1H), 2.16 (s, 1H), 1.66 (dt, *J* = 13.7, 4.0 Hz, 1H), 1.55 (dd, *J* = 12.7, 11.3 Hz, 1H), 1.23 (t, *J* = 7.0 Hz, 3H), 0.85 (s, 9H), 0.76 (s, 3H), 0.57 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 142.28, 129.80, 121.00, 119.54, 117.78, 114.40, 110.12, 75.40, 63.74, 61.78, 57.91, 50.80, 50.58, 33.30, 28.31, 27.01, 26.55, 22.72, 20.59, 15.52, -0.59, -0.69; **HRMS** (ESI): calcd. for $C_{25}H_{39}N_2O_2Si^+$ $[M+H]^+$: 427.2775, found 427.2769.

The stereocenter assignment at C16:

The assignment of configuration was depended on the nuclear Overhauser analysis, where the 16A possessed the signal of H-H relationship between C6 and C16 (Figure S3), which didn't appear in the NOE spectra of 16B (Figure S4 and S5).



16A

Figure S3 NOE relationship of compound 16A

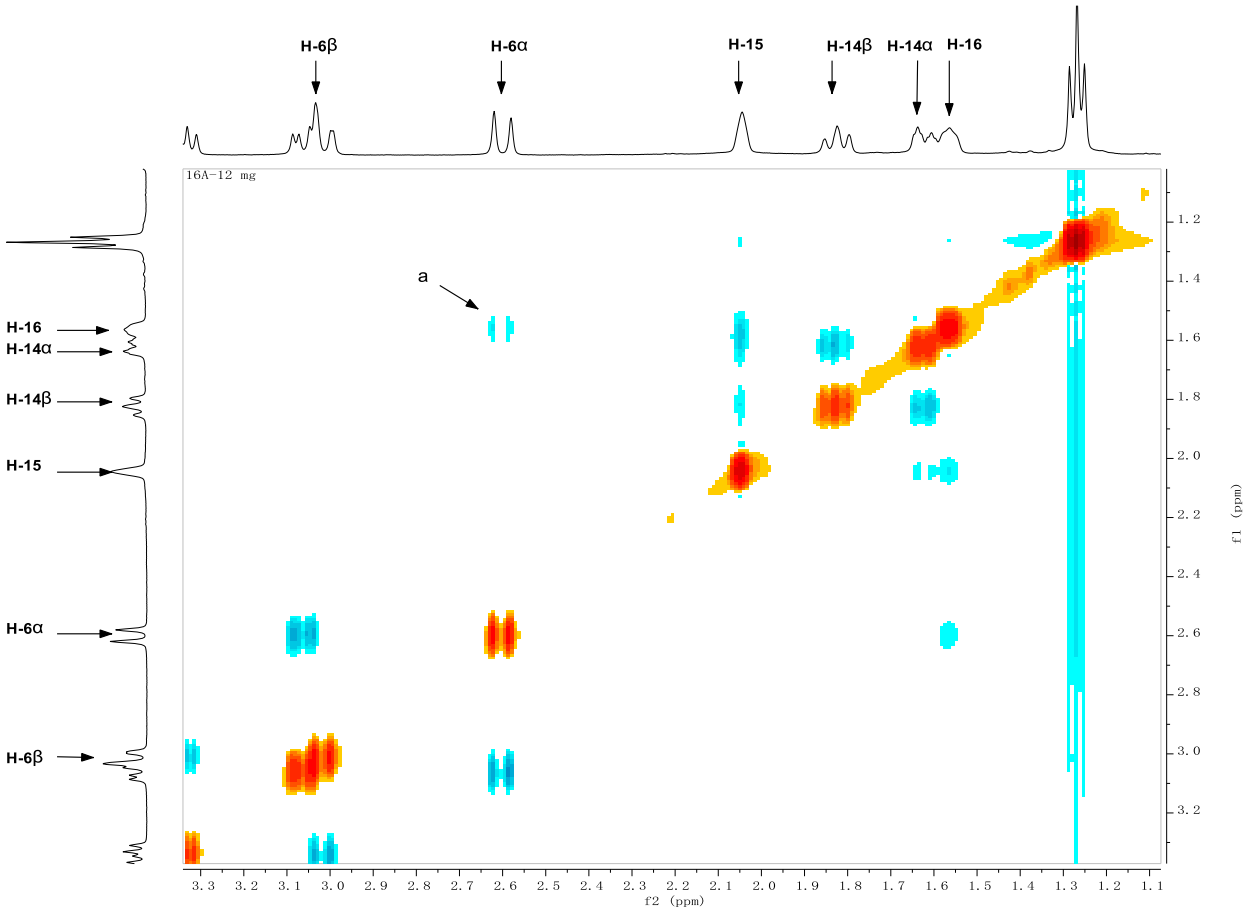


Figure S4 The partial NOE spectrum of compound 16A (For full range NOE spectrum see page S48)

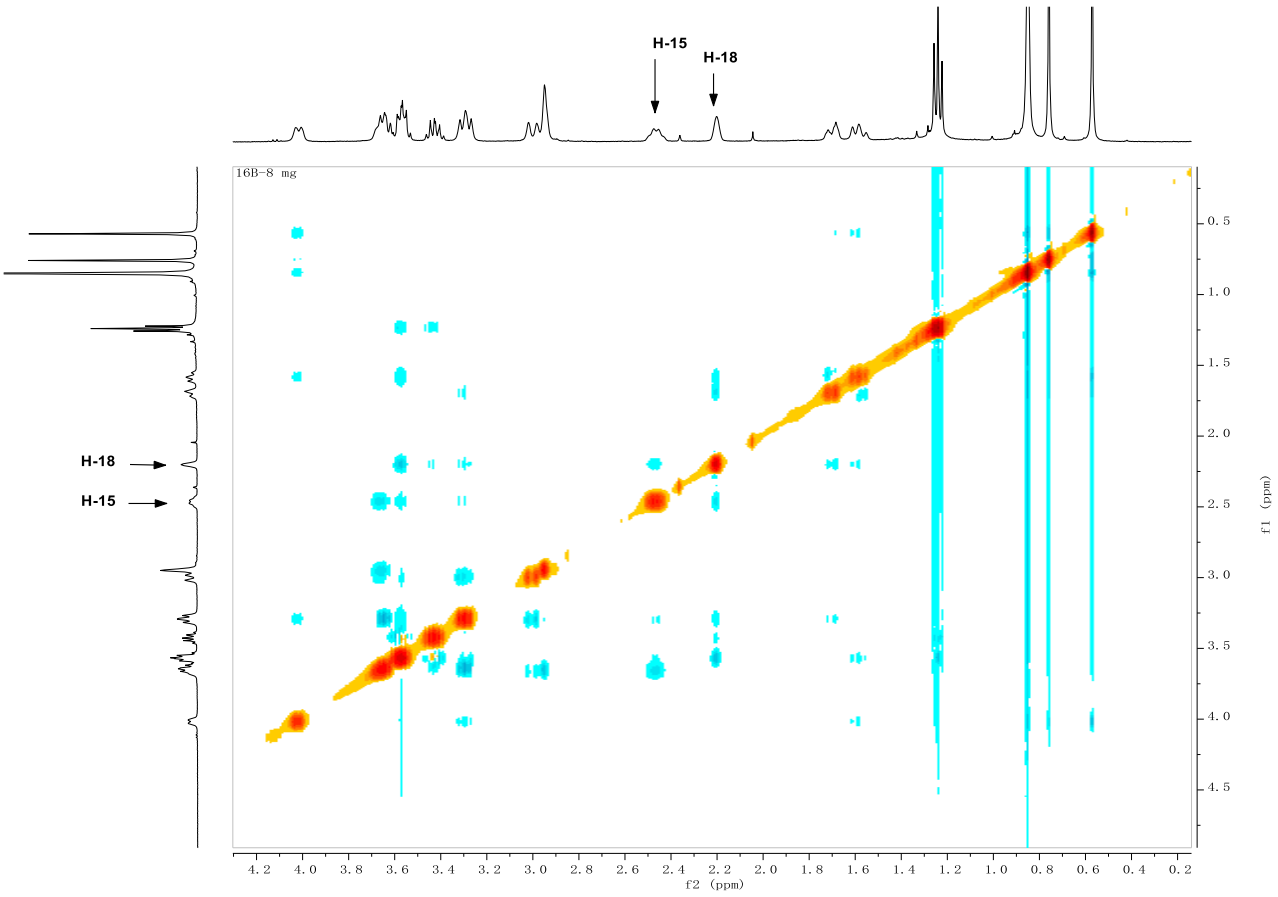
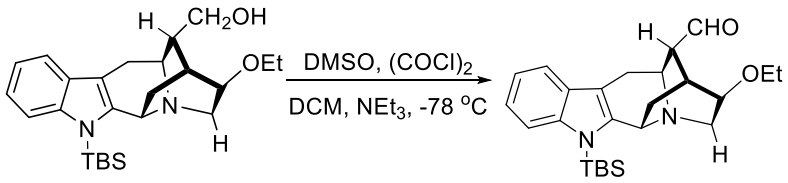


Figure S5 The partial NOE spectrum of compound 16B (For full range NOE spectrum see page S51.)

(6S,10S,11R,11aS)-5-(tert-butyldimethylsilyl)-9-ethoxy-5,6,8,9,10,11,11a,12-octahydro-6,10-methanoindolo[3,2-b]quinolizine-11-carbaldehyde (17A)



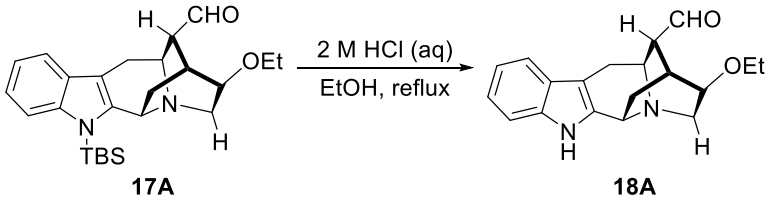
16A **17A**

A solution of oxalyl chloride (70.0 μL, 0.82 mmol, 2.0 equiv) in dry CH_2Cl_2 (2.0 mL) was cooled to -78 ºC under an atmosphere of nitrogen. A solution of dry DMSO (116.0 μL, 1.64 mmol, 4.0 equiv) in dry CH_2Cl_2 (2.0 mL) was added slowly such that the reaction temperature remained -78 °C. After stirring for 15 min, a solution of compound **16A** (175.10 mg, 0.411 mmol, 1.0 equiv) in dry CH_2Cl_2 (3.0 mL) was added slowly, and the resulting mixture was stirred for 15 min. Next, NEt_3 (571.0 μL, 4.11 mmol, 10.0 equiv) was added slowly. After stirring the reaction for additional 10 min at -78 °C, the cooling bath was removed and the reaction was allowed to warm to room temperature for 3 h. The solution was treated with with CH_2Cl_2 (15 mL) and H_2O (15 mL), the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (15 mL). The combined organic layers were washed with saturated NaCl solution, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (*n*-Hexane/EtOAc, 4:1 → 2:1) to provide pure compound **17A** (100.0 mg, 0.236 mmol, 57%) as solid.

Characterization for compound 17A:

R_f = 0.60 (CH_2Cl_2/MeOH, 20:1); **mp** 87 – 88 °C; **$[\alpha]_D^{25}$** +24.0 (*c* 0.05, CH_3OH); **IR (KBr)** 3754.09, 3449.08, 3049.78, 2929.97, 2857.90, 2711.46, 1716.00, 1637.55, 1452.26, 1407.76, 1370.72, 1329.76, 1258.07, 1236.30, 1208.33, 1177.40, 1153.47, 1086.90, 1023.61, 987.98, 961.36, 919.75, 842.92, 815.01, 742.99, 688.63, 603.65, 579.43, 525.49 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.67 (s, 1H), 7.58 – 7.54 (m, 1H), 7.43 – 7.40 (m, 1H), 7.12 – 7.07 (m, 2H), 4.08 (dd, *J* = 9.8, 2.3 Hz, 1H), 3.79 – 3.74 (m, 1H), 3.46 – 3.39 (m, 2H), 3.22 – 3.14 (m, 2H), 3.04 (d, *J* = 14.9 Hz, 1H), 2.66 (s, 1H), 2.63 (d, *J* = 15.6 Hz, 1H), 2.02 (dd, *J* = 7.4, 1.3 Hz, 1H), 1.85 – 1.80 (m, 1H), 1.67 (ddd, *J* = 13.2, 4.5, 2.8 Hz, 1H), 1.14 (t, *J* = 7.0 Hz, 3H), 0.86 (s, 9H), 0.77 (s, 3H), 0.59 (s, 3H); **^{13}C NMR** (151 MHz, CDCl3) δ 203.35, 143.27, 142.38, 130.76, 121.22 , 119.75, 117.82, 114.52, 108.34, 73.03, 64.12, 57.05, 51.57, 50.23, 49.60, 32.75, 29.36, 28.14, 27.04, 20.69, 15.21, -0.49, -0.52; **HRMS** (ESI): calcd. for $C_{25}H_{37}N_2O_2Si^+$ $[M+H]^+$: 425.2619, found 425.2617.

(6S,10S,11R,11aS)-9-ethoxy-5,6,8,9,10,11,11a,12-octahydro-6,10-methanoindolo[3,2-b]quinolizine-11-carbaldehyde (18A).



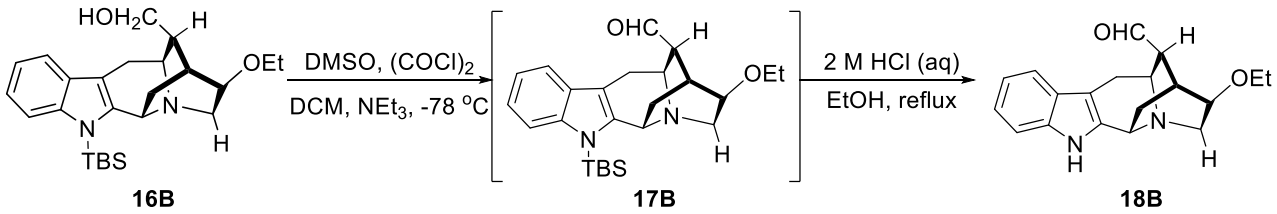
17A **18A**

To a solution of compound **17A** (96.8 mg, 0.228 mmol, 1.0 equiv) in EtOH (6.0 mL) at room temperature was added HCl (2.0 M in water, 7 mL), and then the mixture was allowed to stir under reflux for 6 h. The crude product was treated with CH_2Cl_2 (15 mL). The solution was then diluted with EtOAc (15 mL) and the aqueous phase was adjusted to pH = 8 by dropwise addition of NaOH solution (4 M in water). The solvent was removed under reduced pressure. The solution was treated with EtOAc (15 mL) and H_2O (15 mL), the layers were separated and the aqueous layer was extracted with EtOAc (15 mL). The combined organic layers were washed with saturated NaCl solution, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (CH_2Cl_2/MeOH, 30:1) to provide pure compound **18A** (58 mg, 0.187 mmol, 82%) as solid.

Characterization for compound 18A:

R_f = 0.30 (CH_2Cl_2/MeOH, 20:1); **mp** 110 °C; **$[\alpha]_D^{25}$** +66.6 (*c* 0.1, CH_3OH); **IR (KBr)** 3444.87, 3141.34, 3101.75, 3059.85, 2926.89, 2875.19, 2728.55, 1713.89, 1625.54, 1447.47, 1376.46, 1350.77, 1327.53, 1298.99, 1232.77, 1209.77 1176.87, 1150.56, 1121.18, 1086.86, 1022.43, 983.76, 846.31, 797.19, 741.91, 663.78, 580.17 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.62 (s, 1H), 8.31 (s, 1H), 7.44 (d, *J* = 7.8 Hz, 1H), 7.28 (d, *J* = 8.2 Hz, 1H), 7.13 (t, *J* = 7.6 Hz, 1H), 7.08 (t, *J* = 7.5 Hz, 1H), 3.96 (d, *J* = 9.5 Hz, 1H), 3.77 (t, *J* = 6.4 Hz, 1H), 3.38 (dt, *J* = 10.1, 6.9 Hz, 2H), 3.31 (t, *J* = 6.0 Hz, 1H), 3.15 (dd, *J* = 15.7, 5.1 Hz, 1H), 3.07 (dd, *J* = 14.8, 7.6 Hz, 1H), 2.94 (d, *J* = 14.6 Hz, 1H), 2.64 (d, *J* = 15.3 Hz, 2H), 2.09 (d, *J* = 7.5 Hz, 1H), 1.80 – 1.62 (m, 2H), 1.10 (t, *J* = 6.9 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 202.86, 137.08, 136.48, 127.51, 121.75, 119.59, 118.25, 111.03, 104.45, 72.89, 64.15, 56.11, 51.33, 49.81, 49.01, 30.50, 29.20, 27.73, 15.16; **HRMS** (ESI): calcd. for $C_{19}H_{23}N_2O_2^+$ $[M+H]^+$: 311.1754, found 311.1744.

(6S,10S,11S,11aS)-9-ethoxy-5,6,8,9,10,11,11a,12-octahydro-6,10-methanoindolo[3,2-b]quinolizine-11-carbaldehyde (18B)



16B **17B** **18B**

The compound **18B** was prepared under same condition as **18A**, where the compound **16B** (200.0 mg, 0.47 mmol, 1.0 equiv) were used to afford the crude product **17B** (268 mg). Subsequent, the crude product was subjected with HCl (aq.) affording **18B** (124 mg, 0.399 mmol, 85%, 2-steps from **16B**) as solid. The characterization of 17B was conducted with small sample purified by flash column chromatography on silica gel (CH_2Cl_2/MeOH, 20:1).

Characterization for compound 17B:

R_f = 0.60 (CH_2Cl_2/MeOH, 20:1); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.67 (s, 1H), 7.57 – 7.55 (m, 1H), 7.42 (dd, *J* = 6.1, 3.0 Hz, 1H), 7.11 – 7.08 (m, 2H), 4.08 (dd, *J* = 9.8, 2.1 Hz, 1H), 3.80 – 3.74 (m, 1H), 3.45 – 3.40 (m, 3H), 3.18 (dt, *J* = 13.0, 6.3 Hz, 2H), 3.05 (d, *J* = 14.7 Hz, 1H), 2.66 (s, 1H), 2.63 (d, *J* = 15.5 Hz, 1H), 2.03 (dd, *J* = 7.4, 1.2 Hz, 1H), 1.86 – 1.79 (m, 1H), 1.67 (ddd, *J* = 13.2, 4.5, 2.8 Hz, 1H), 1.14 (t, *J* = 7.0 Hz, 3H), 0.86 (s, 9H), 0.77 (s, 3H), 0.58 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 203.32, 143.23, 142.38, 130.76, 121.22, 119.76, 117.83, 114.52, 108.34, 73.02, 64.12, 57.04, 51.56, 50.23, 49.59, 32.73, 29.36, 28.13, 27.04, 20.69, 15.20, -0.49, -0.53. **HRMS** (ESI): calcd. for $C_{25}H_{37}N_2O_2Si^+$ $[M+H]^+$: 425.2619, found 425.2606.

Characterization for compound 18B:

R_f = 0.50 (CH_2Cl_2/MeOH, 10:1); **mp** 115 °C; **$[\alpha]_D^{25}$** +59.8 (*c* 0.1, CH_3OH); **IR (KBr)** 3420, 3200.21, 2973.37, 2927.25, 2714.92, 2501.48, 1721.55, 1625.99, 1452.81, 1379.70, 1350.58, 1302.13, 1239.81, 1106.91, 1060.89, 1022.79, 746.64, 686.06, 633.47 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 11.50 (s, 1H), 9.41 (s, 1H), 7.47 (d, *J* = 8.2 Hz, 1H), 7.40 (d, *J* = 7.9 Hz, 1H), 7.17 (t, *J* = 7.5 Hz, 1H), 7.08 (t, *J* = 7.5 Hz, 1H), 4.81 (s, 1H), 4.18 (dd, *J* = 8.0, 4.8 Hz, 1H), 3.53 (dd, *J* = 16.6, 5.0 Hz, 1H), 3.32 – 3.19 (m, 2H), 3.07 (d, *J* = 6.1 Hz, 1H), 2.97 (d, *J* = 13.7 Hz, 1H), 2.83 (d, *J* = 16.5 Hz, 1H), 2.73 (d, *J* = 4.7 Hz, 1H), 2.58 (s, 1H), 2.36 (d, *J* = 7.5 Hz, 1H), 2.09 (d, *J* = 10.5 Hz, 1H), 1.96 (dd, *J* = 14.3, 4.8 Hz, 1H), 1.04 (t, *J* = 6.9 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 197.67, 136.91, 131.72, 125.94, 122.81, 119.91, 118.15, 112.39, 101.82, 69.80, 65.02, 54.15, 53.15, 51.15, 48.04, 28.00, 27.98, 25.59, 14.83; **HRMS** (ESI): calcd. for $C_{19}H_{23}N_2O_2^+$ $[M+H]^+$: 311.1754, found 311.1748.

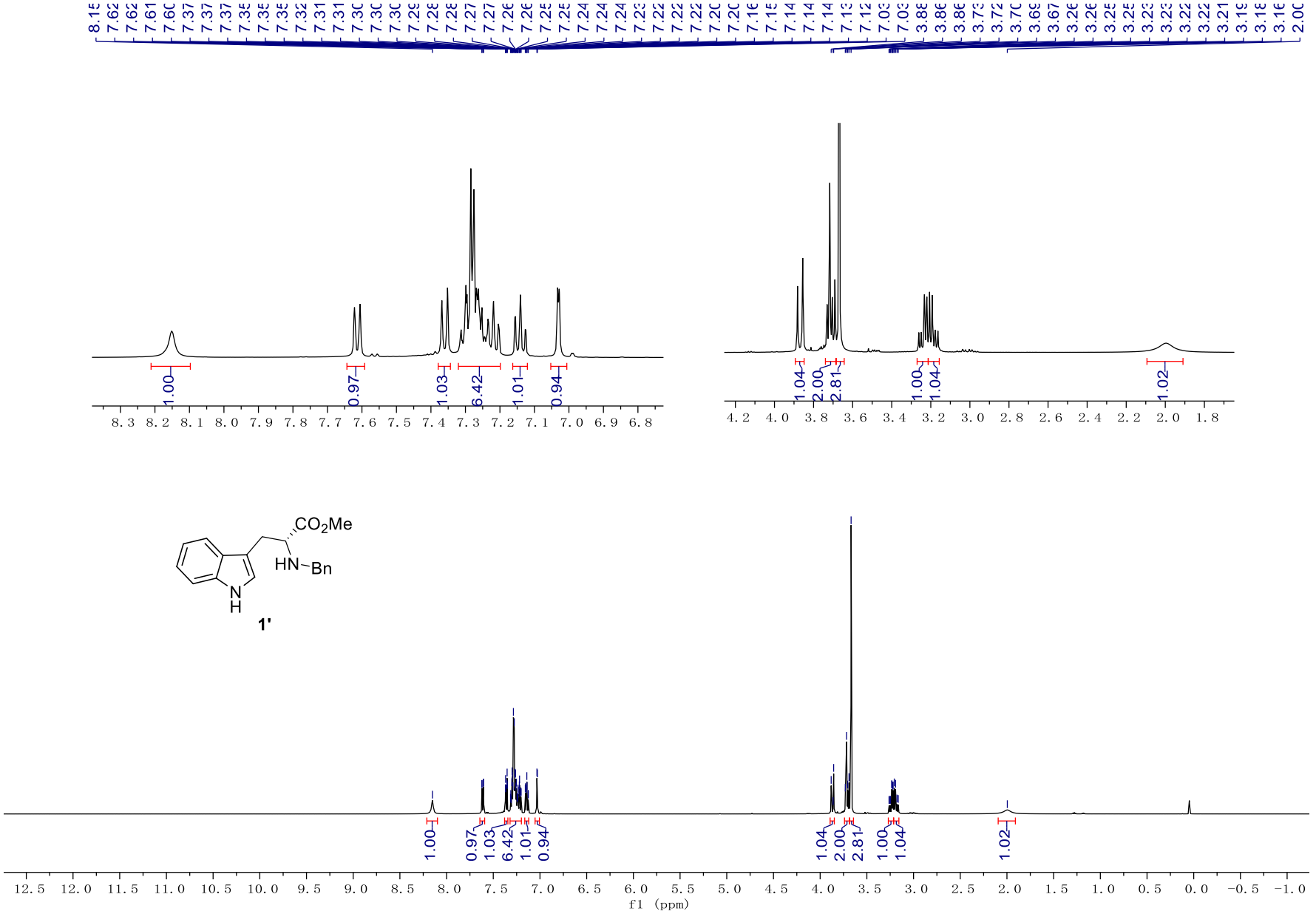
Reference:

1. P. Yu, T. Wang, J. Li and J. M. Cook, *J. Org. Chem.*, 2000, 65, 3173-3191.

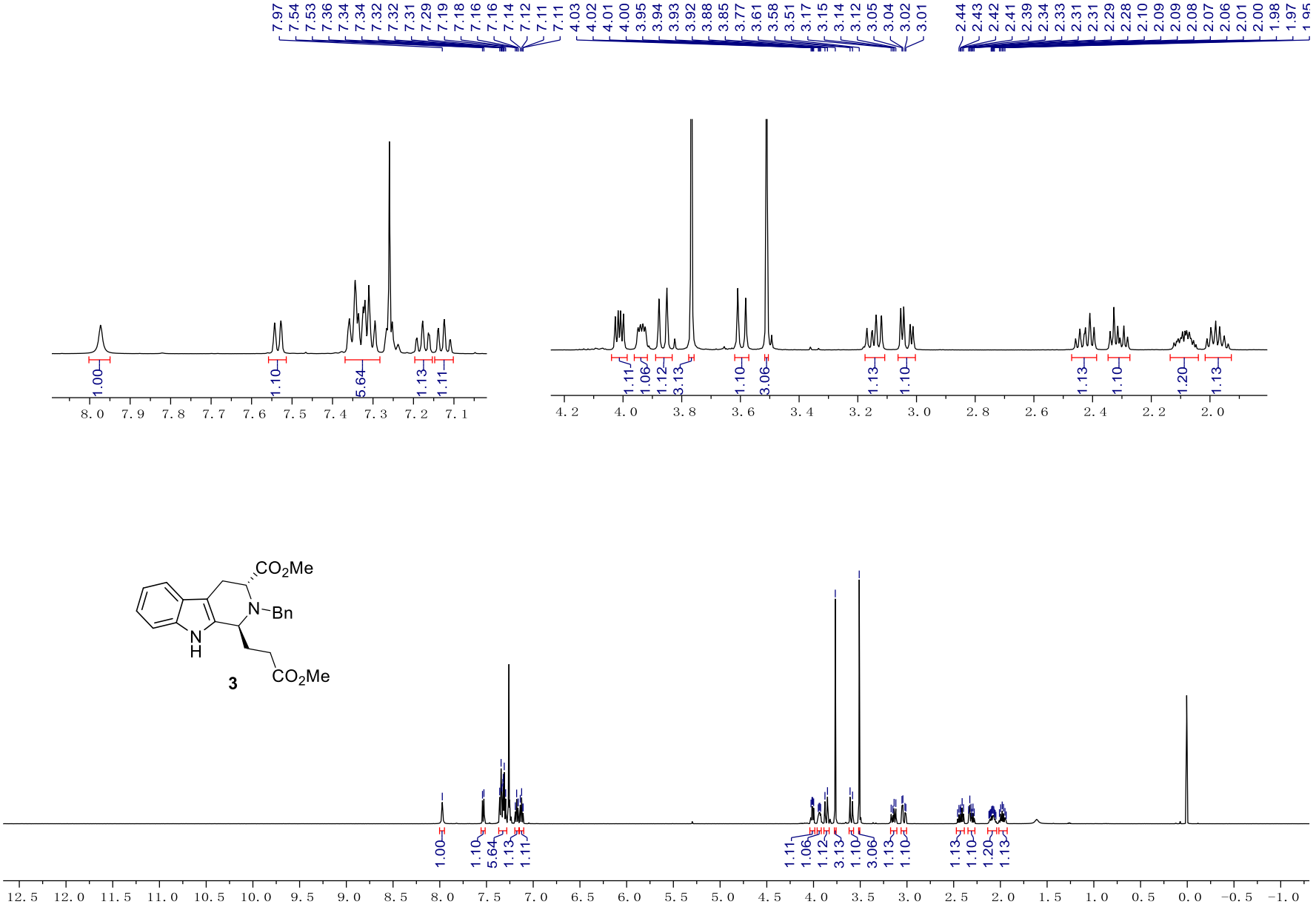
3. Copies of 1H, 13C NMR spectra

(See next page)

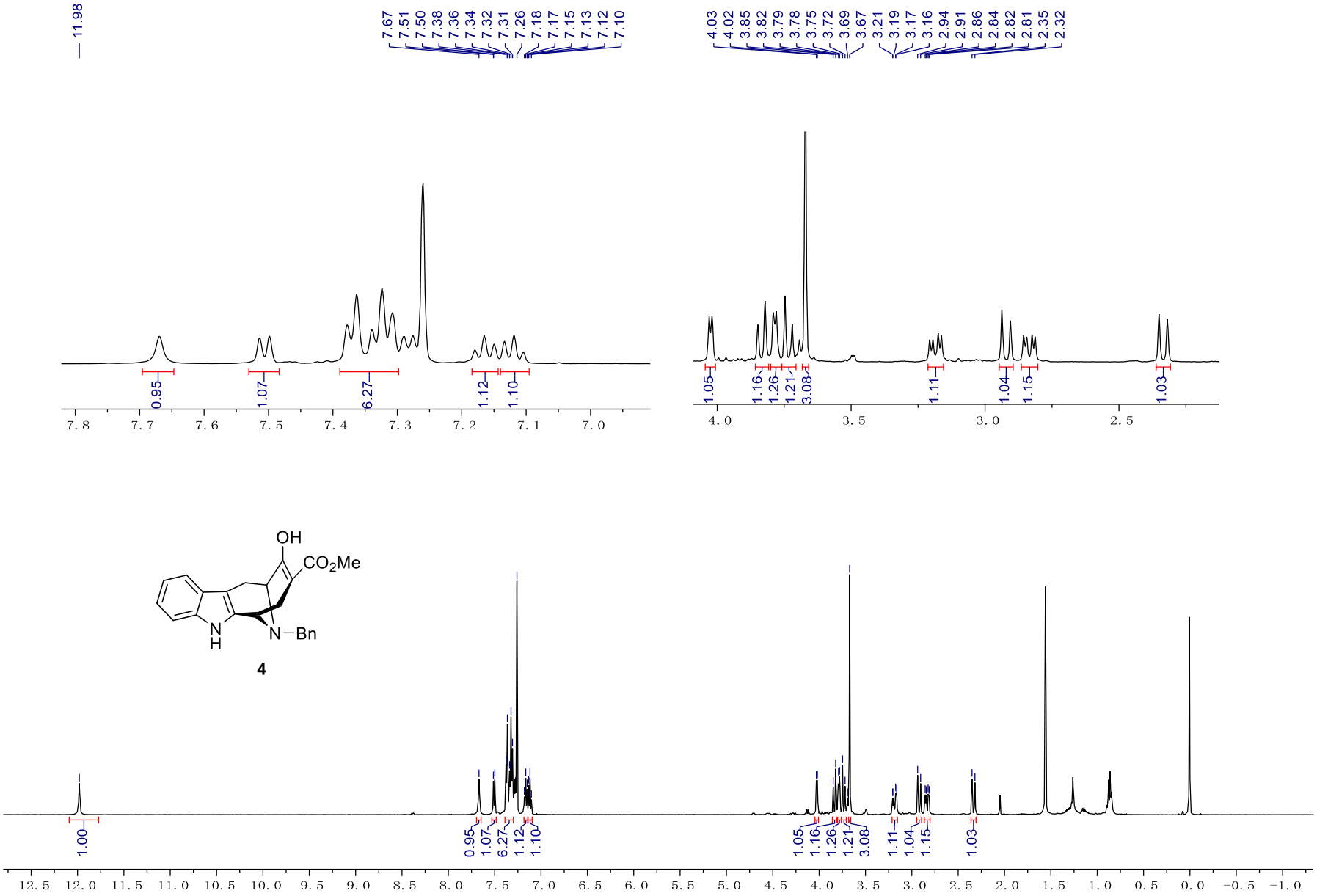
^{1}H NMR (500 MHz, $CDCl_3$) Spectra for 1'



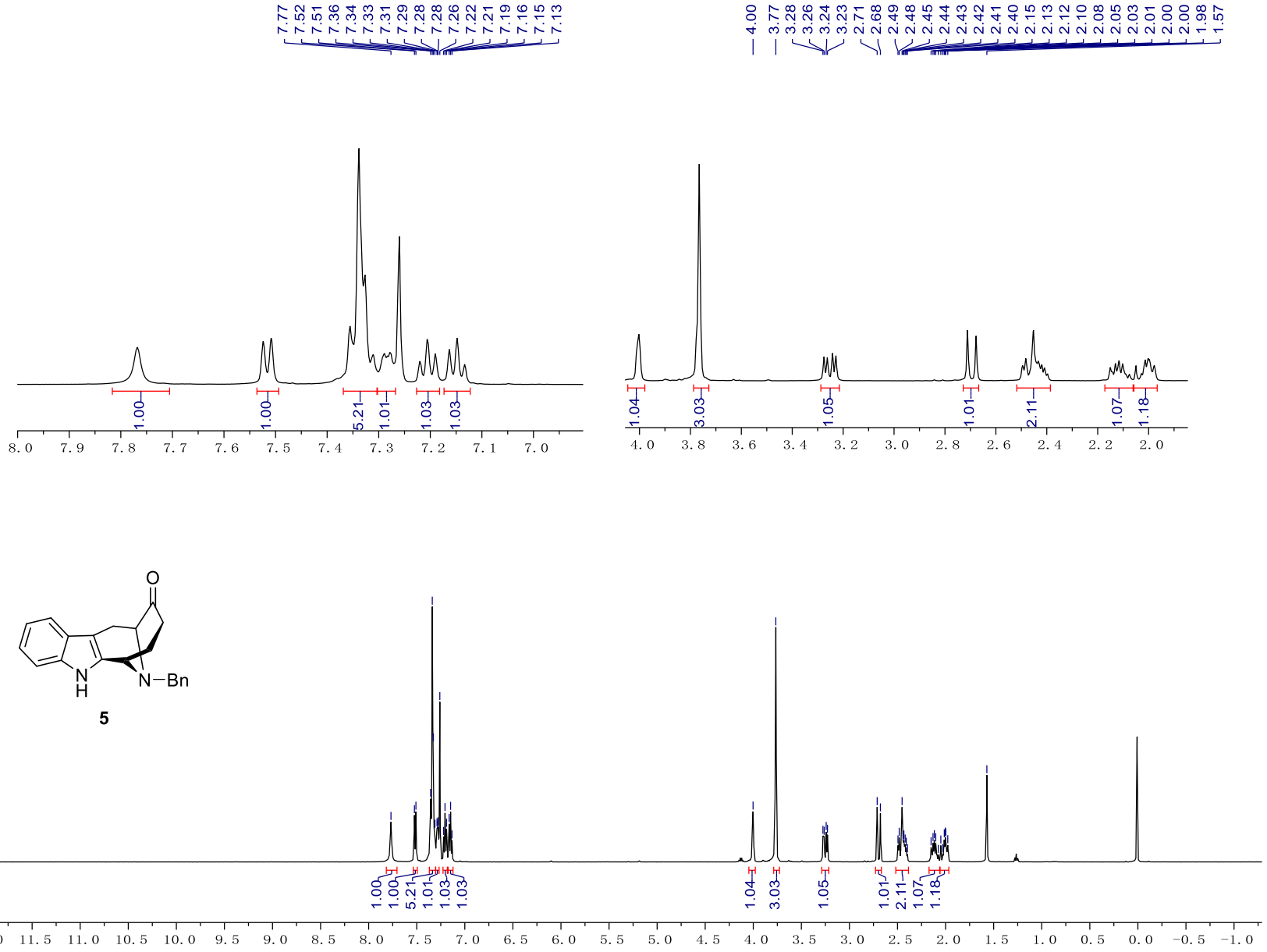
^{1}H NMR (500 MHz, $CDCl_3$) Spectra for 3



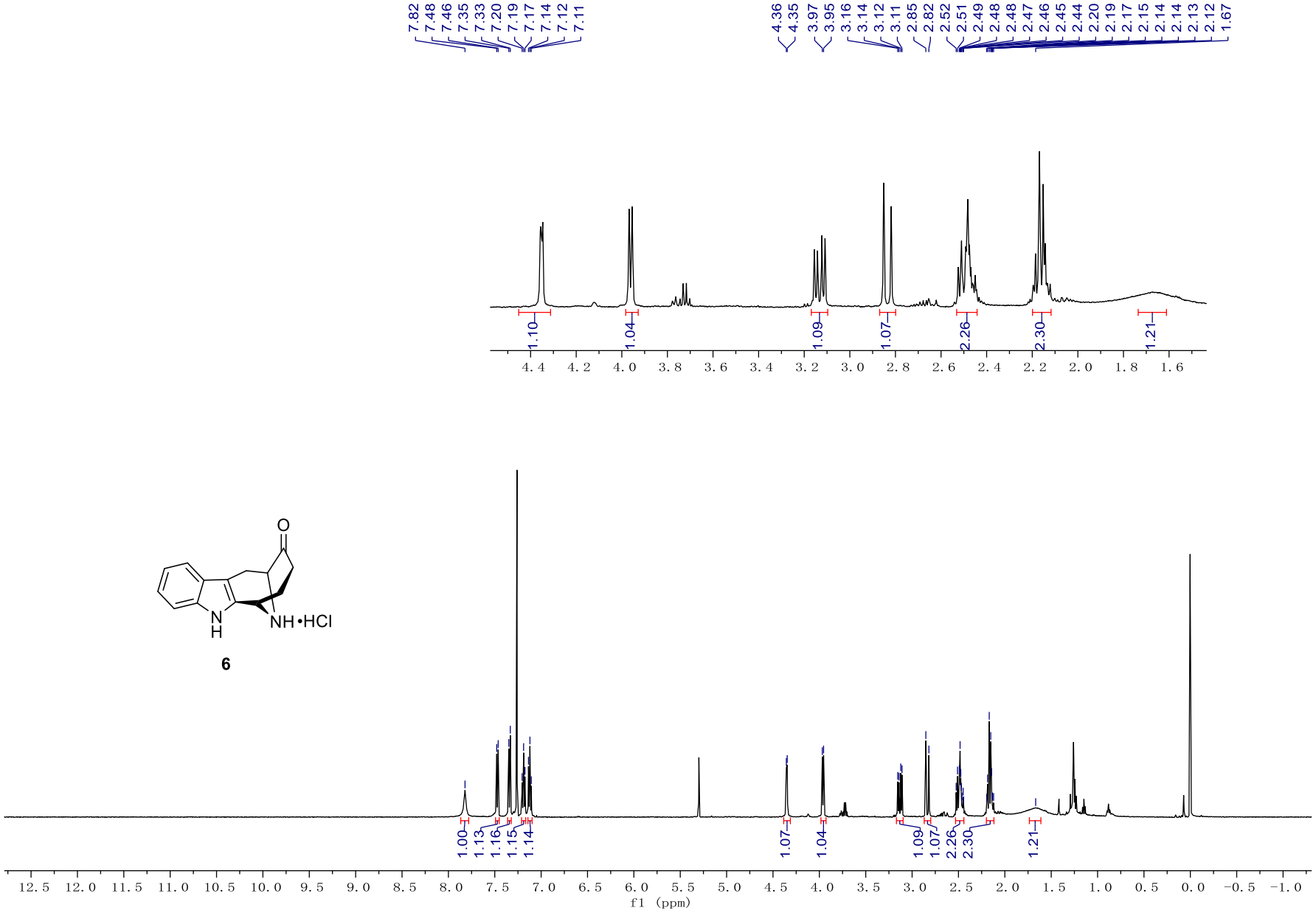
^{1}H NMR (500 MHz, $CDCl_3$) Spectra for 4



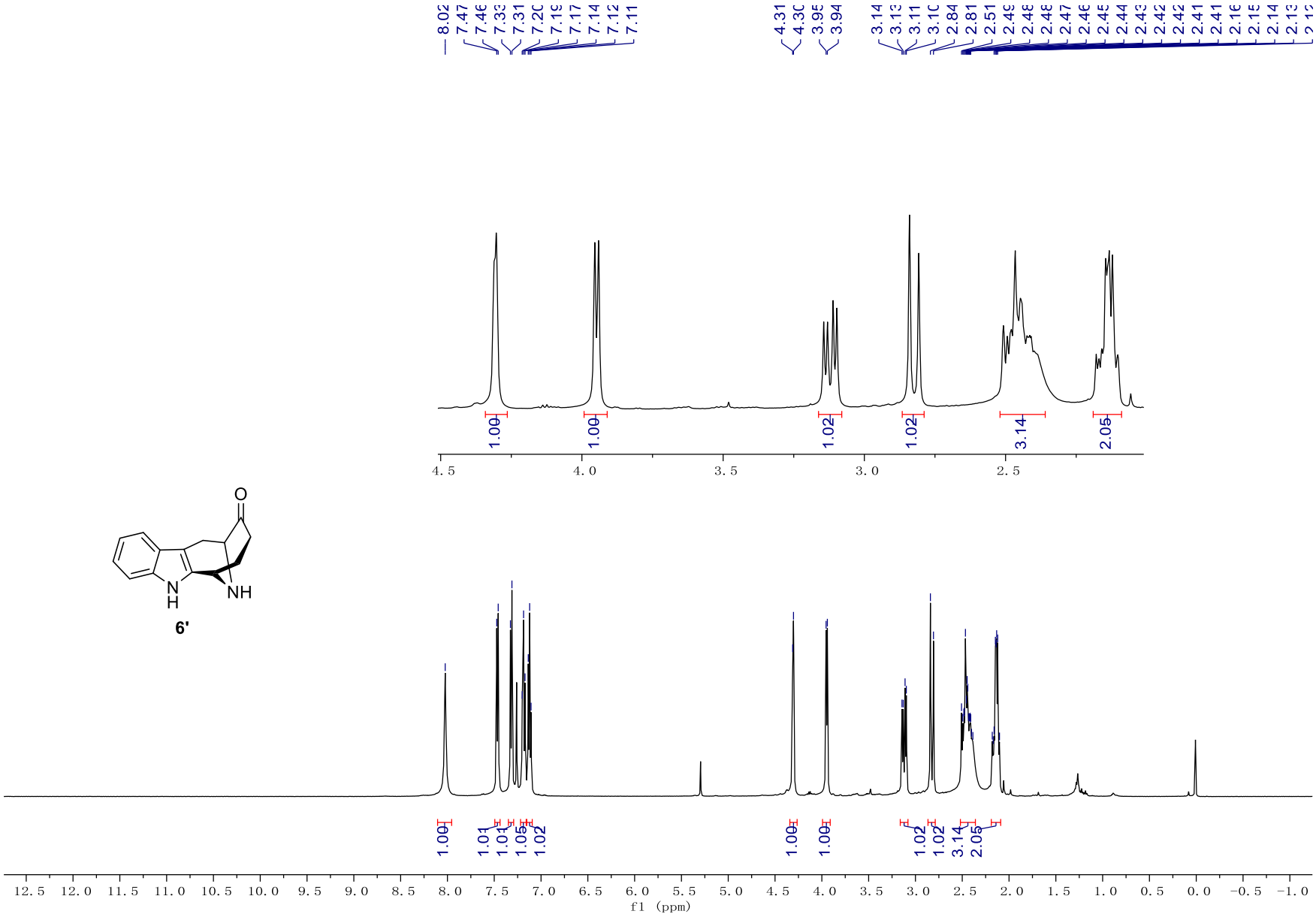
^{1}H NMR (500 MHz, $CDCl_3$) Spectra for 5



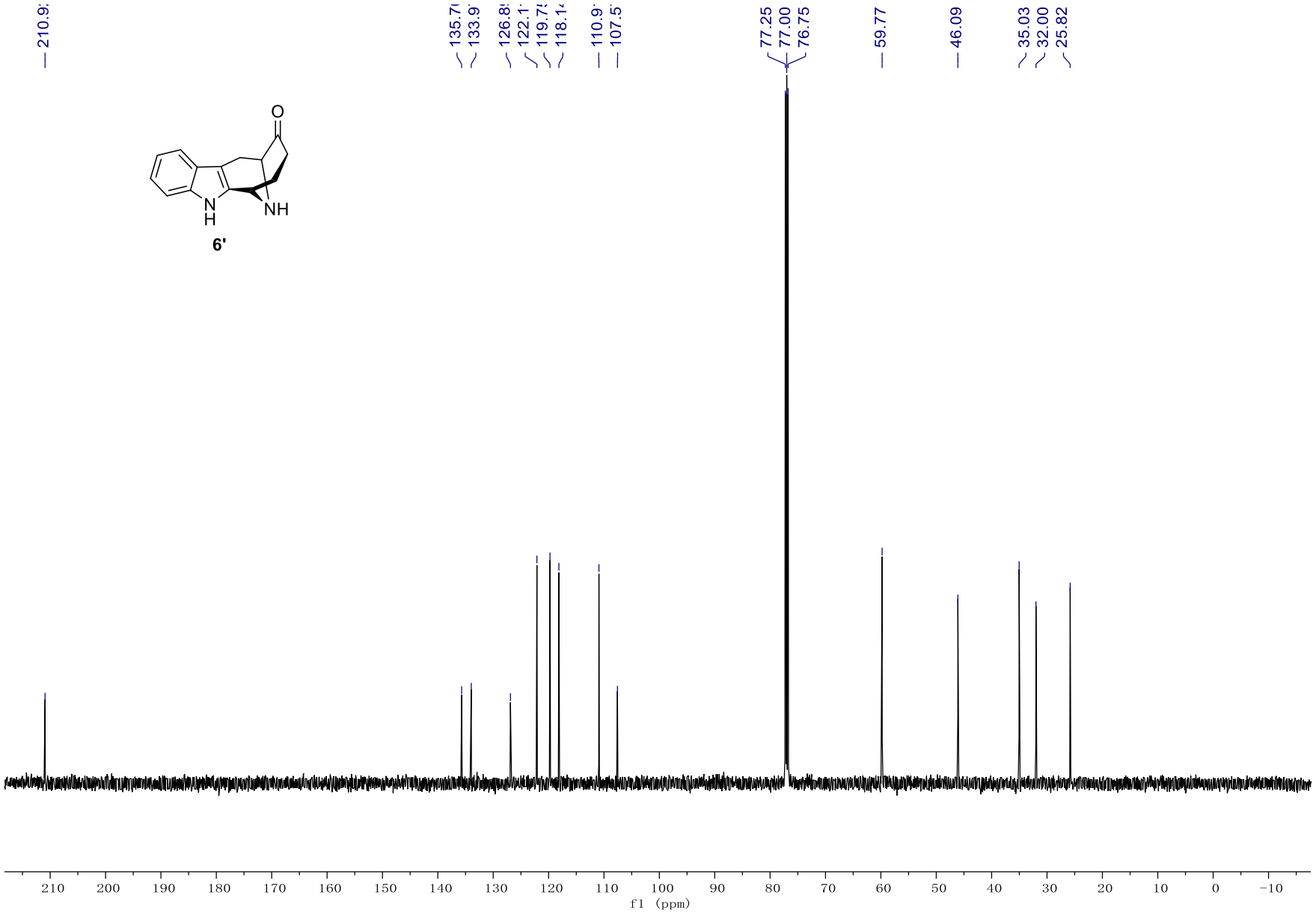
^{1}H NMR (500 MHz, $CDCl_3$) Spectra for 6



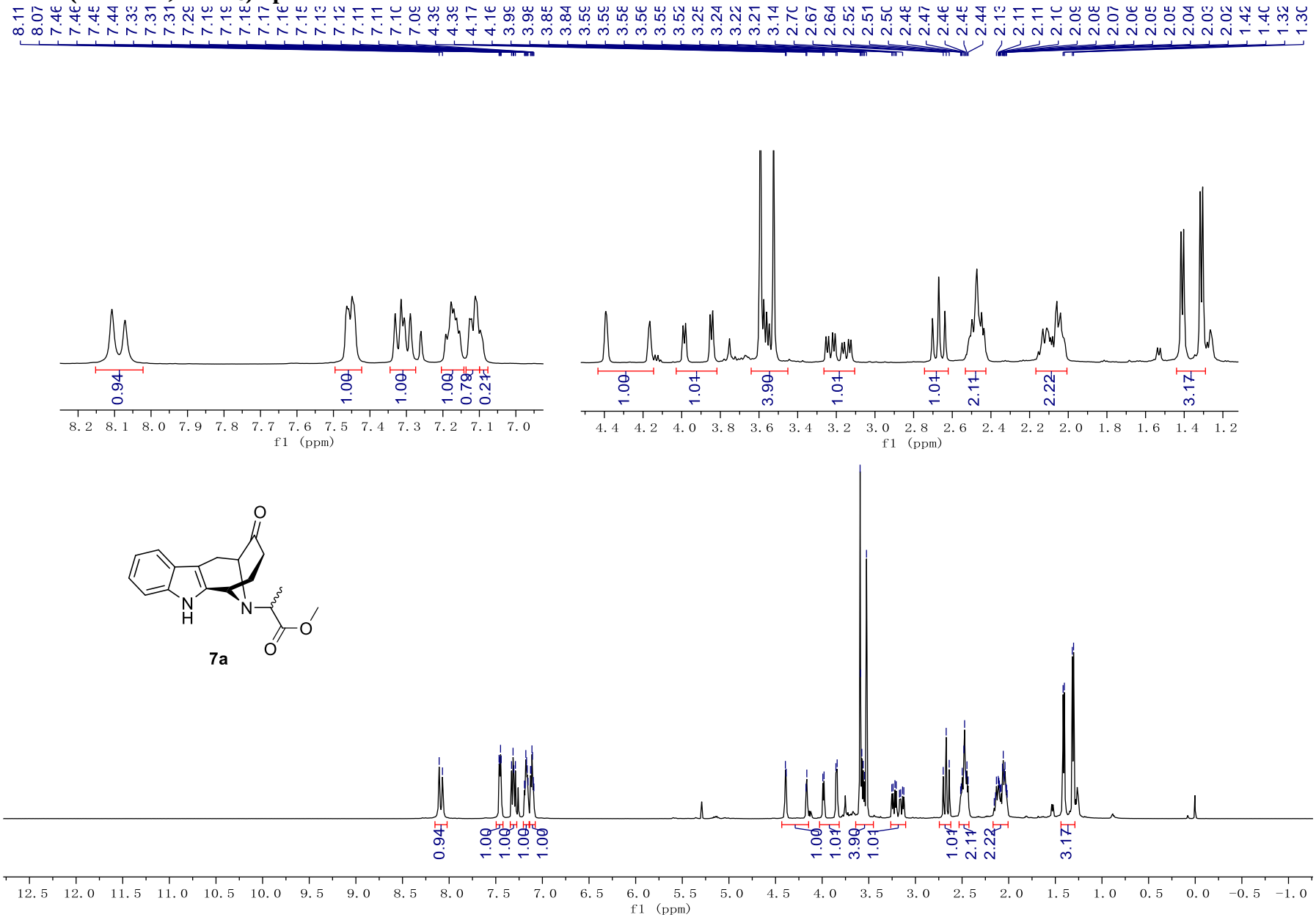
^{1}H NMR (500 MHz, $CDCl_3$) Spectra for 6'



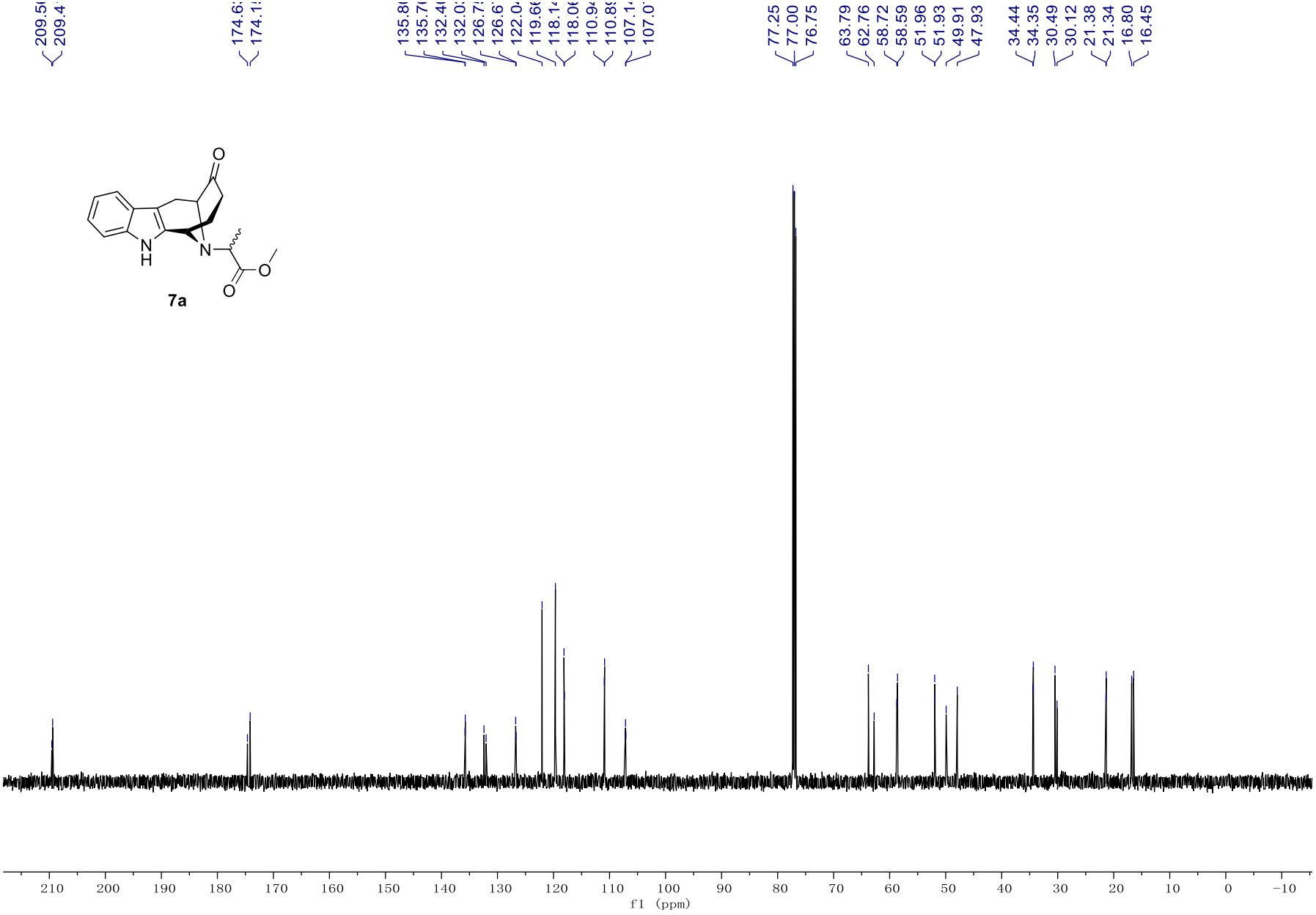
^{13}C NMR (126 MHz, $CDCl_3$) Spectra for 6'



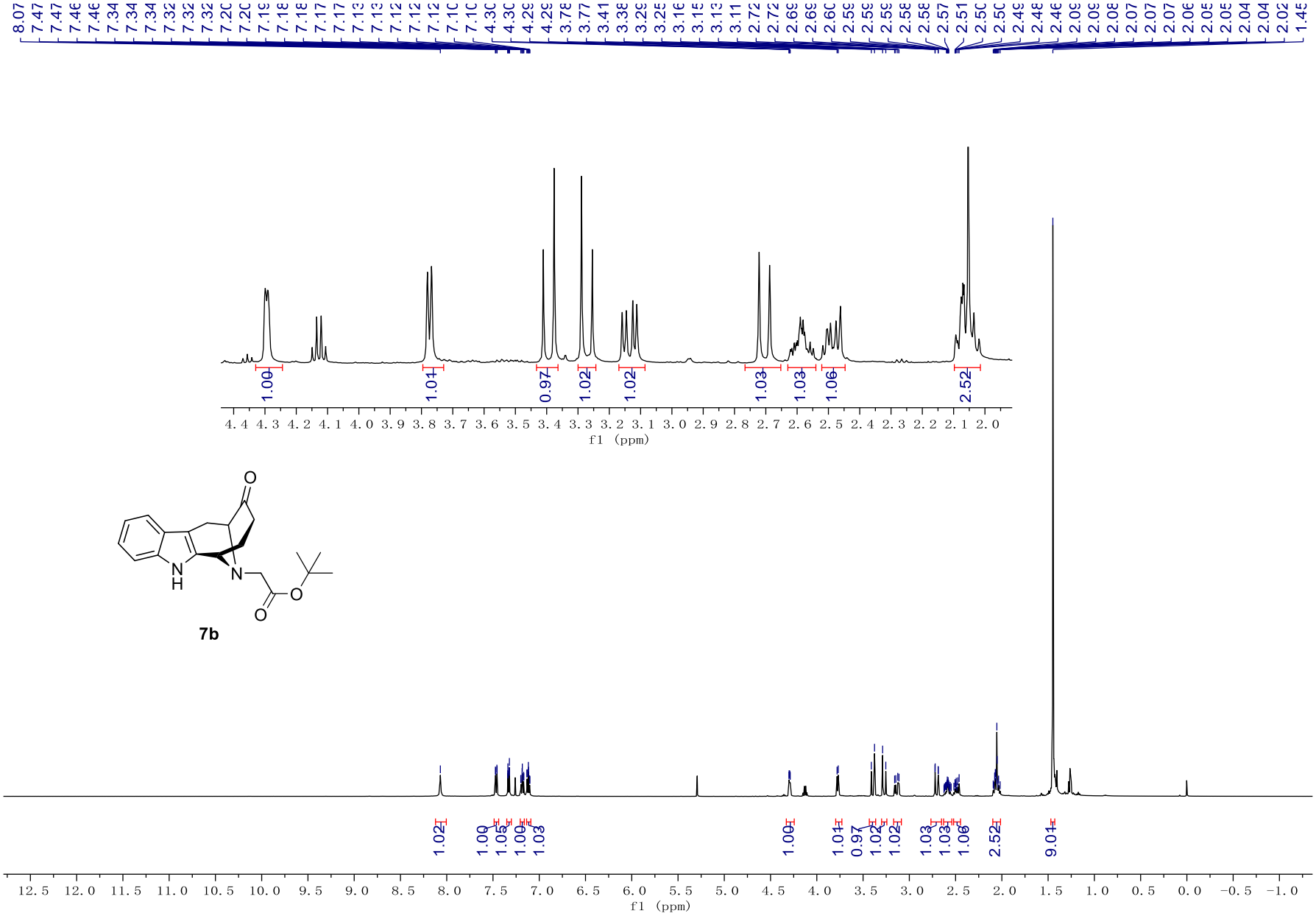
^{1}H NMR (500 MHz, $CDCl_3$) Spectra for 7a



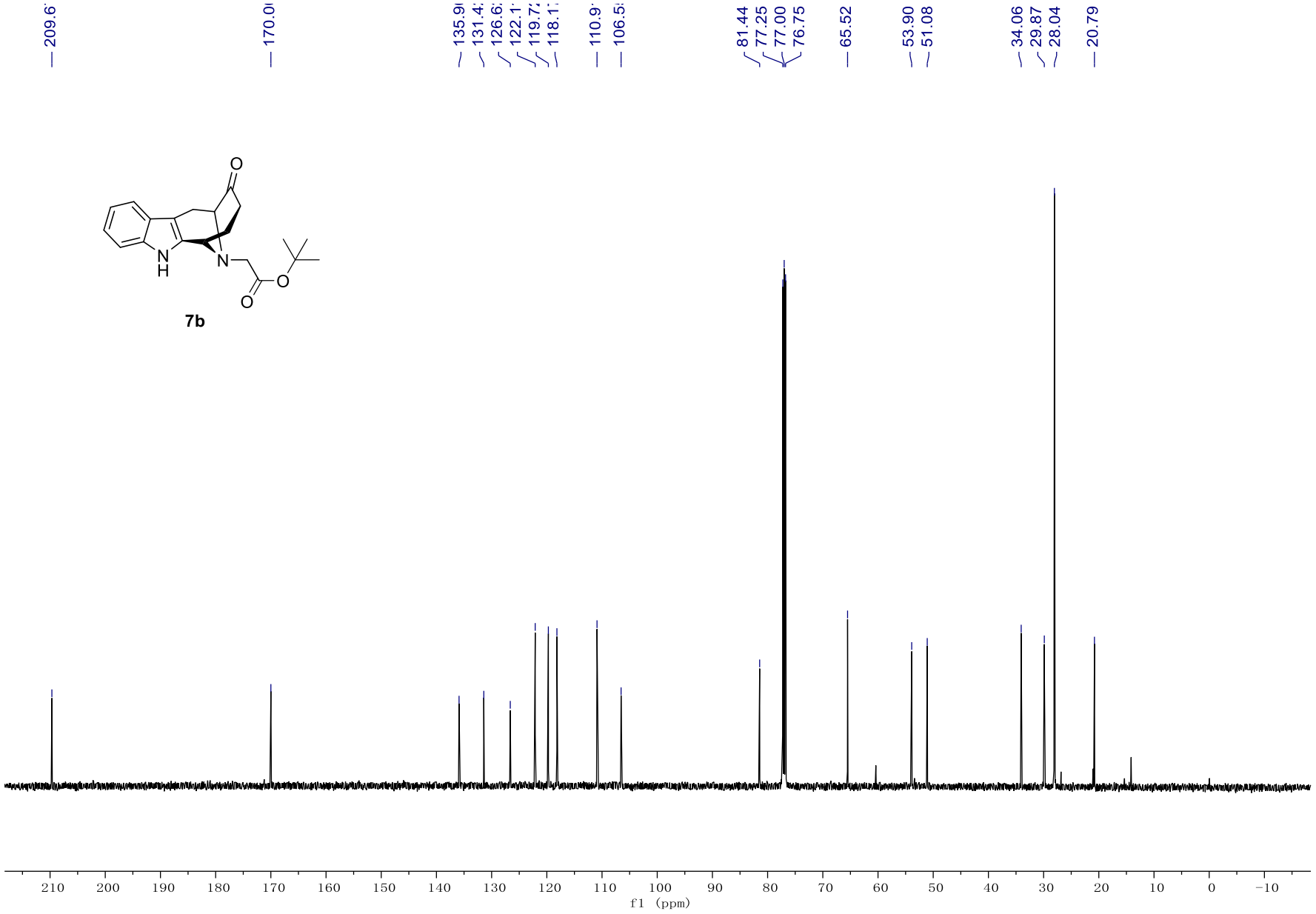
^{13}C NMR (126 MHz, $CDCl_3$) Spectra for 7a



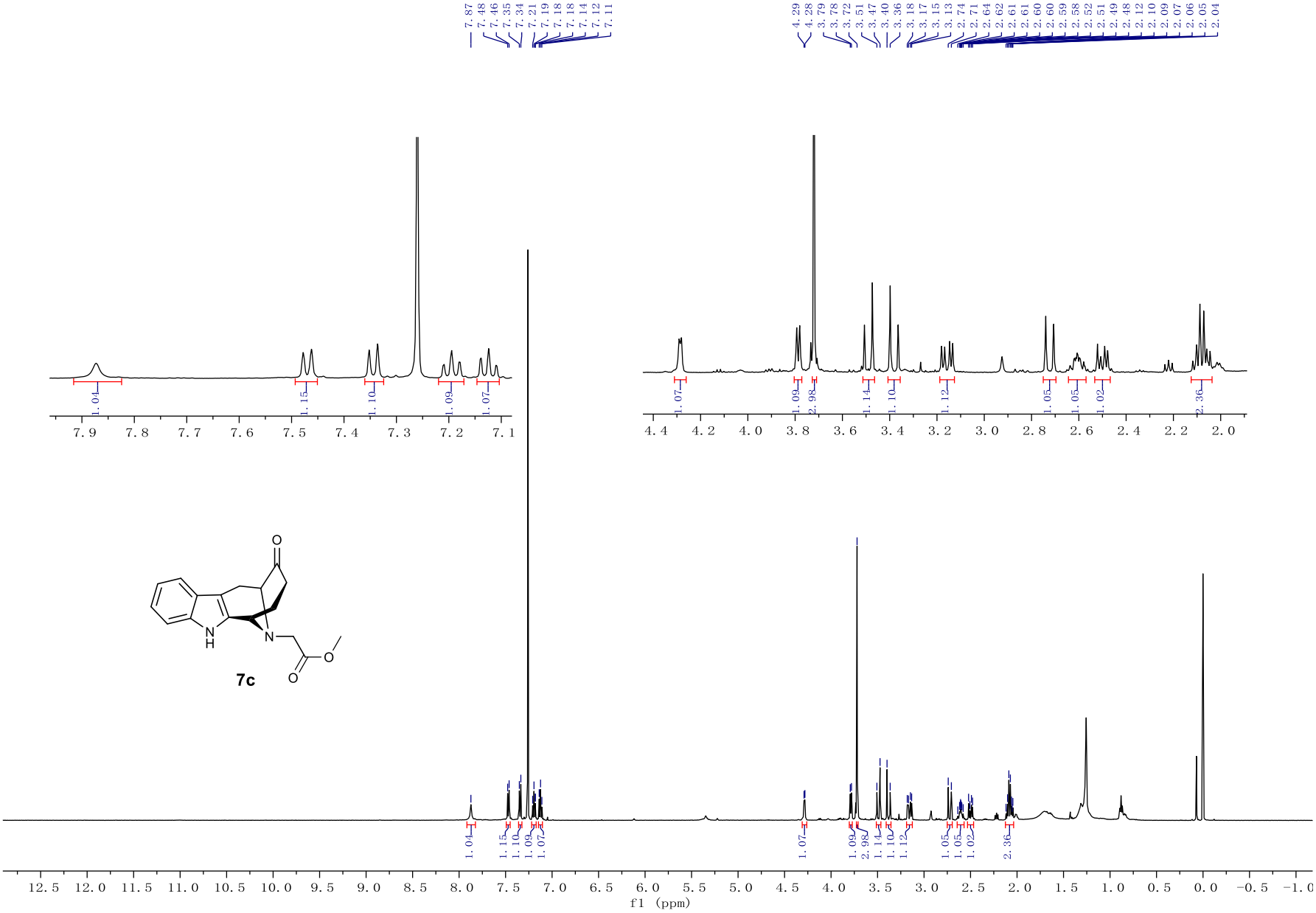
^{1}H NMR (500 MHz, $CDCl_3$) Spectra for 7b



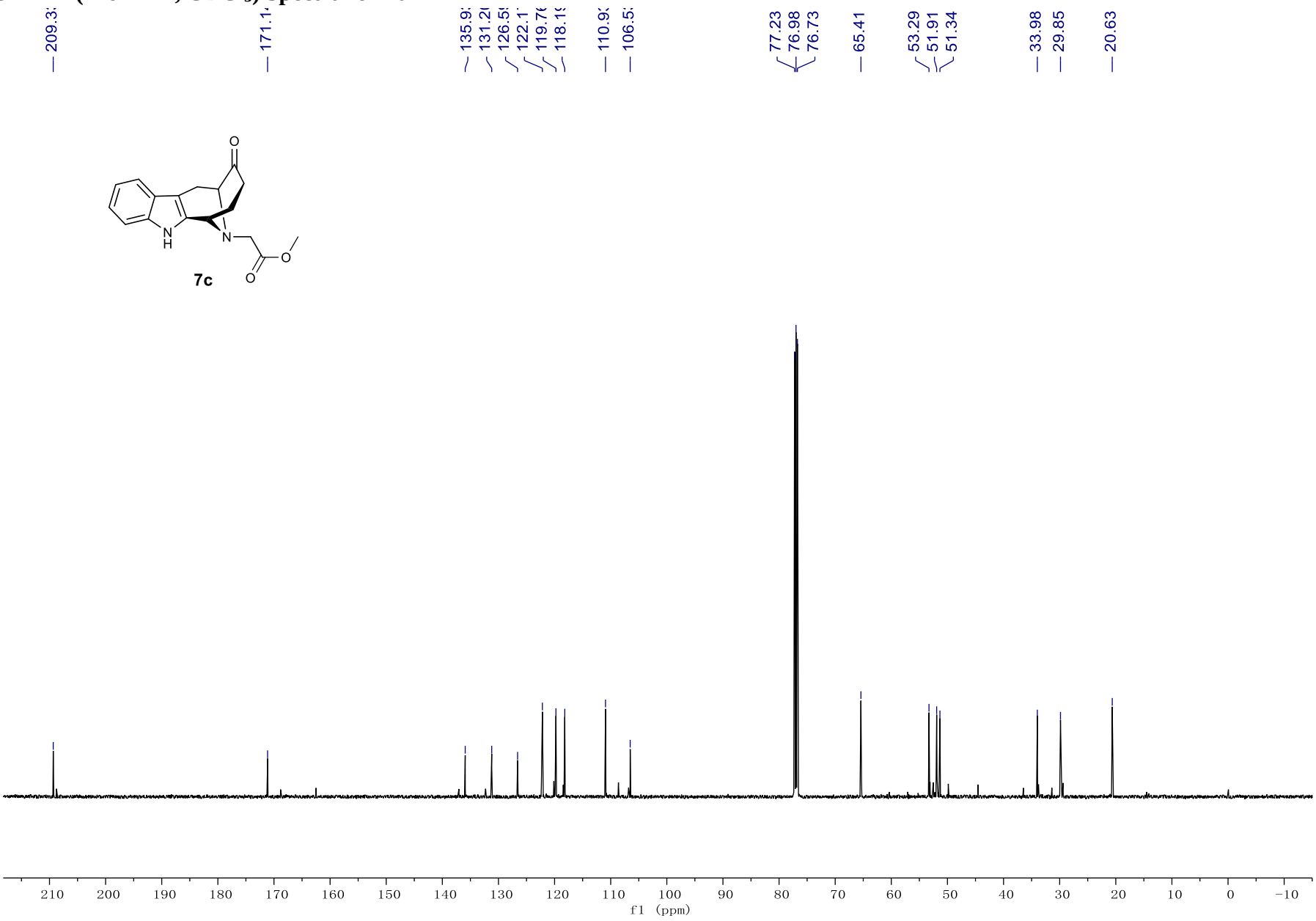
^{13}C NMR (126 MHz, $CDCl_3$) Spectra for 7b



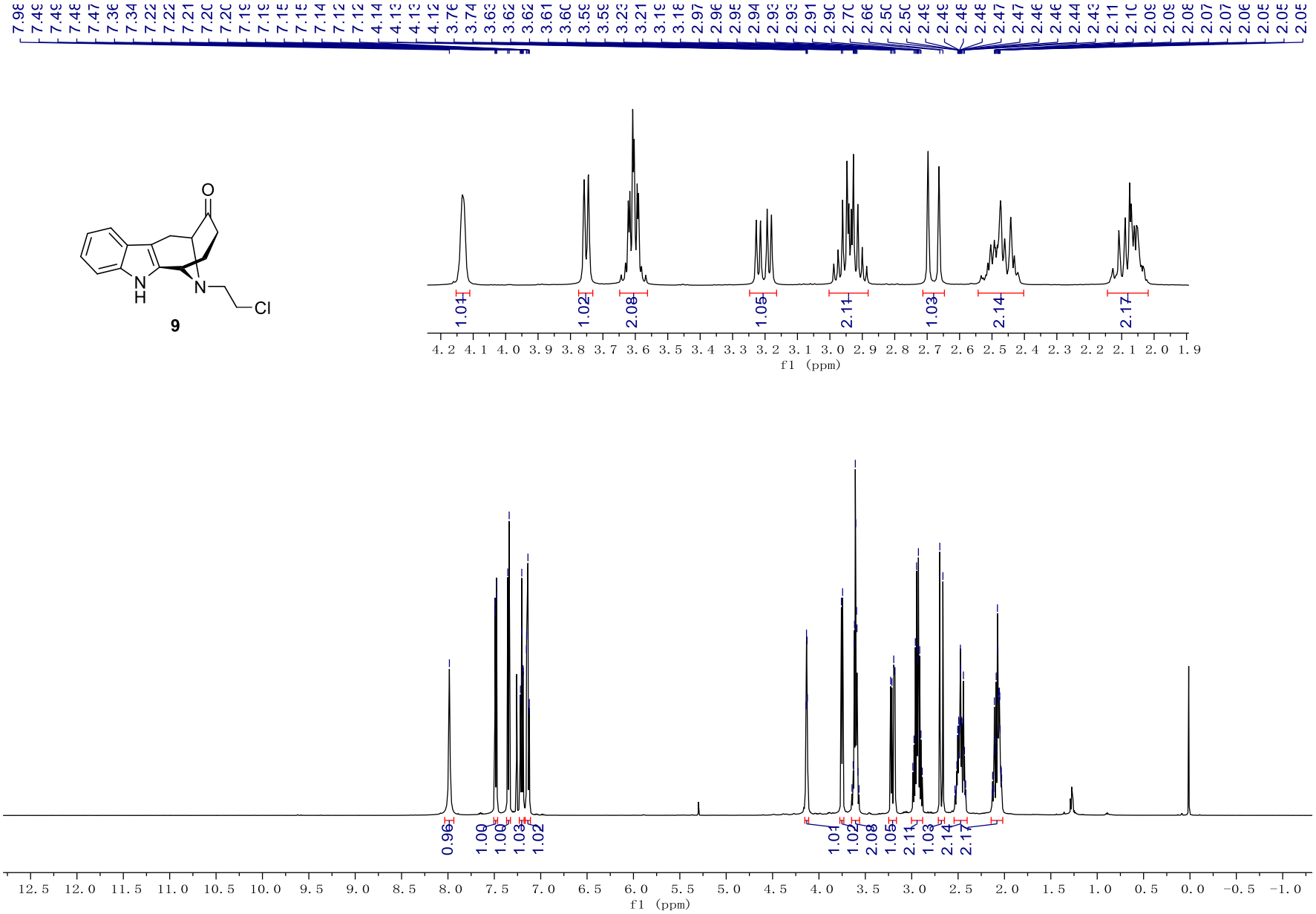
^{1}H NMR (500 MHz, $CDCl_3$) Spectra for 7c



^{13}C NMR (126 MHz, $CDCl_3$) Spectra for 7c



^{1}H NMR (500 MHz, $CDCl_3$) Spectra for 9



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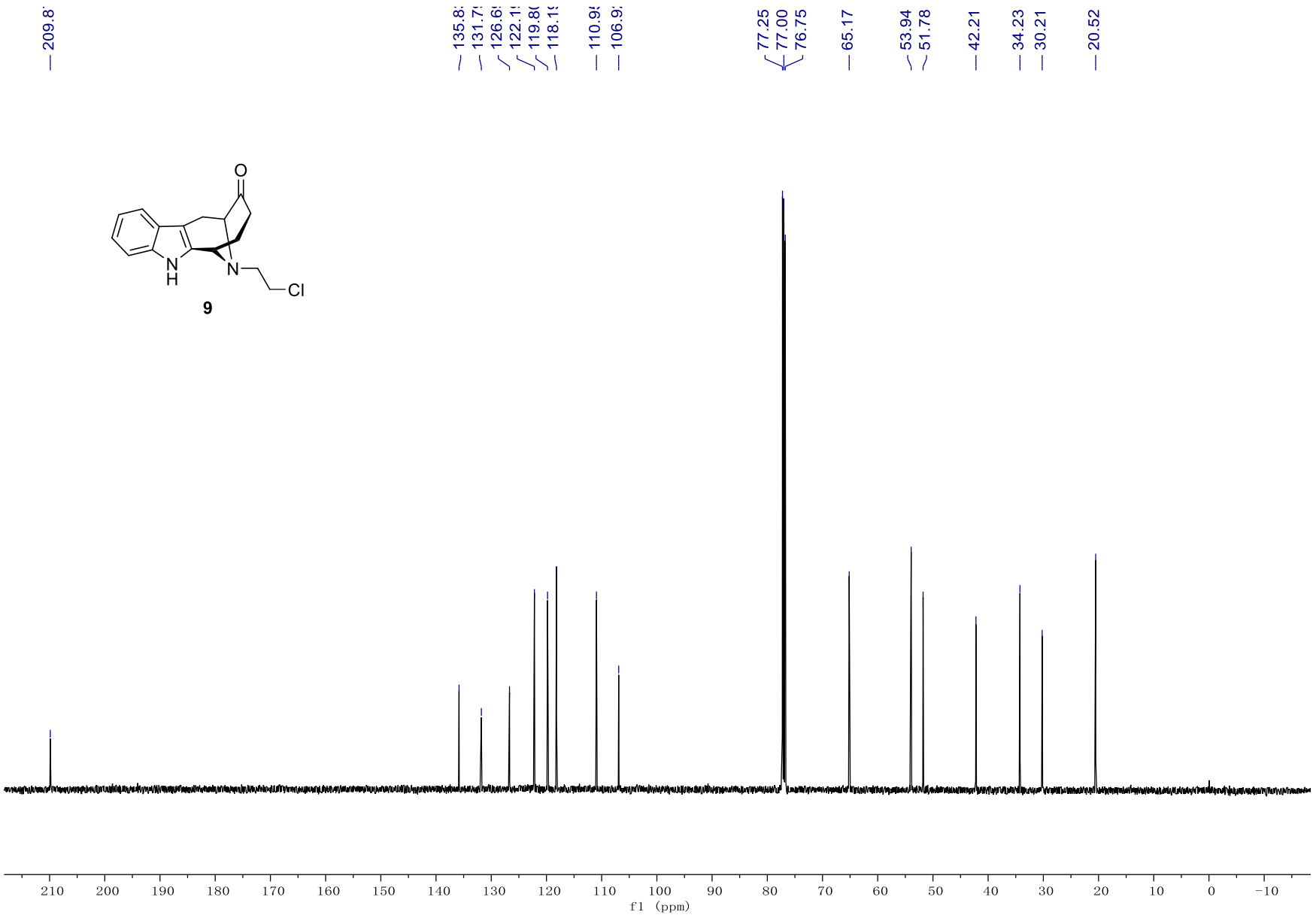
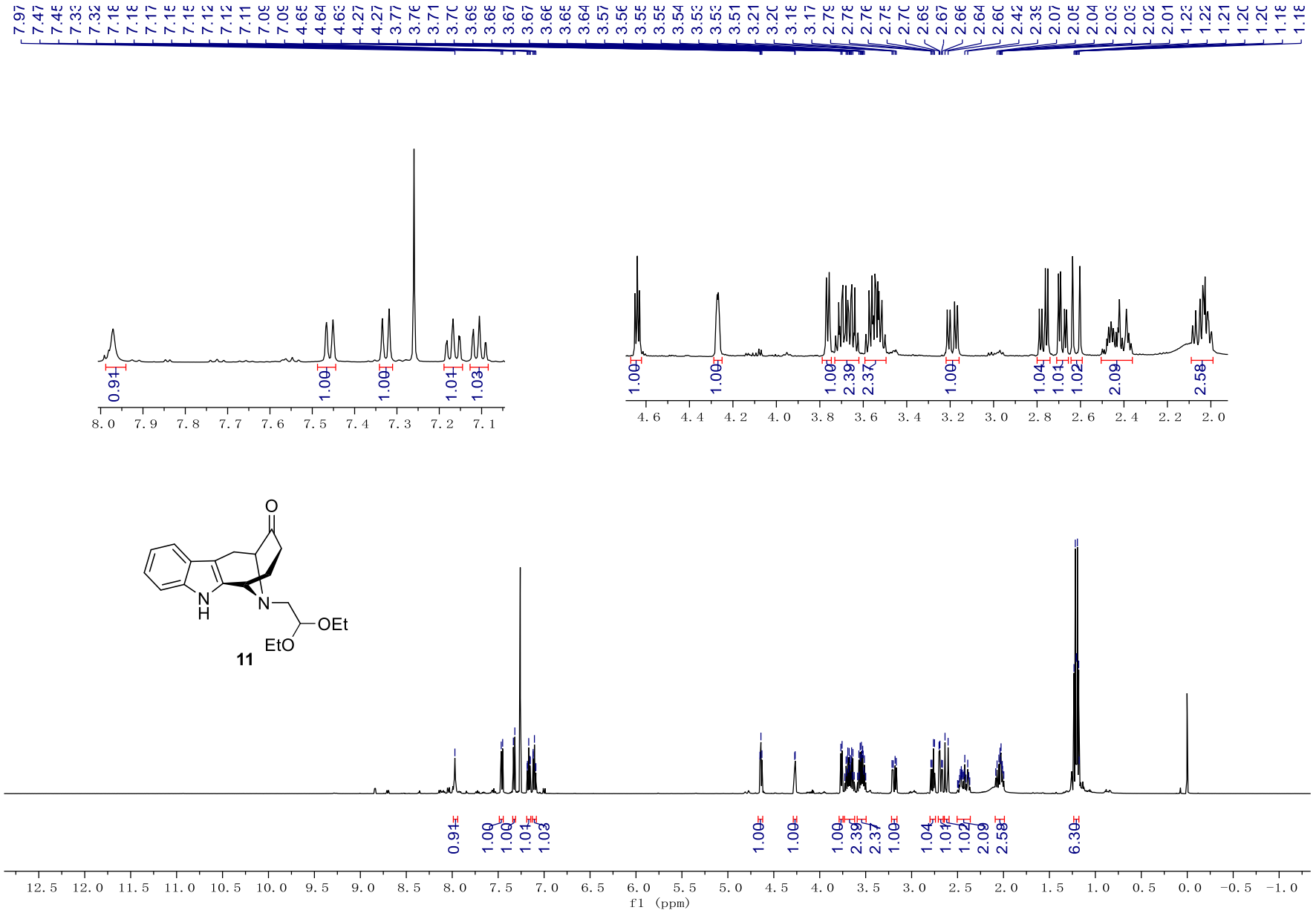
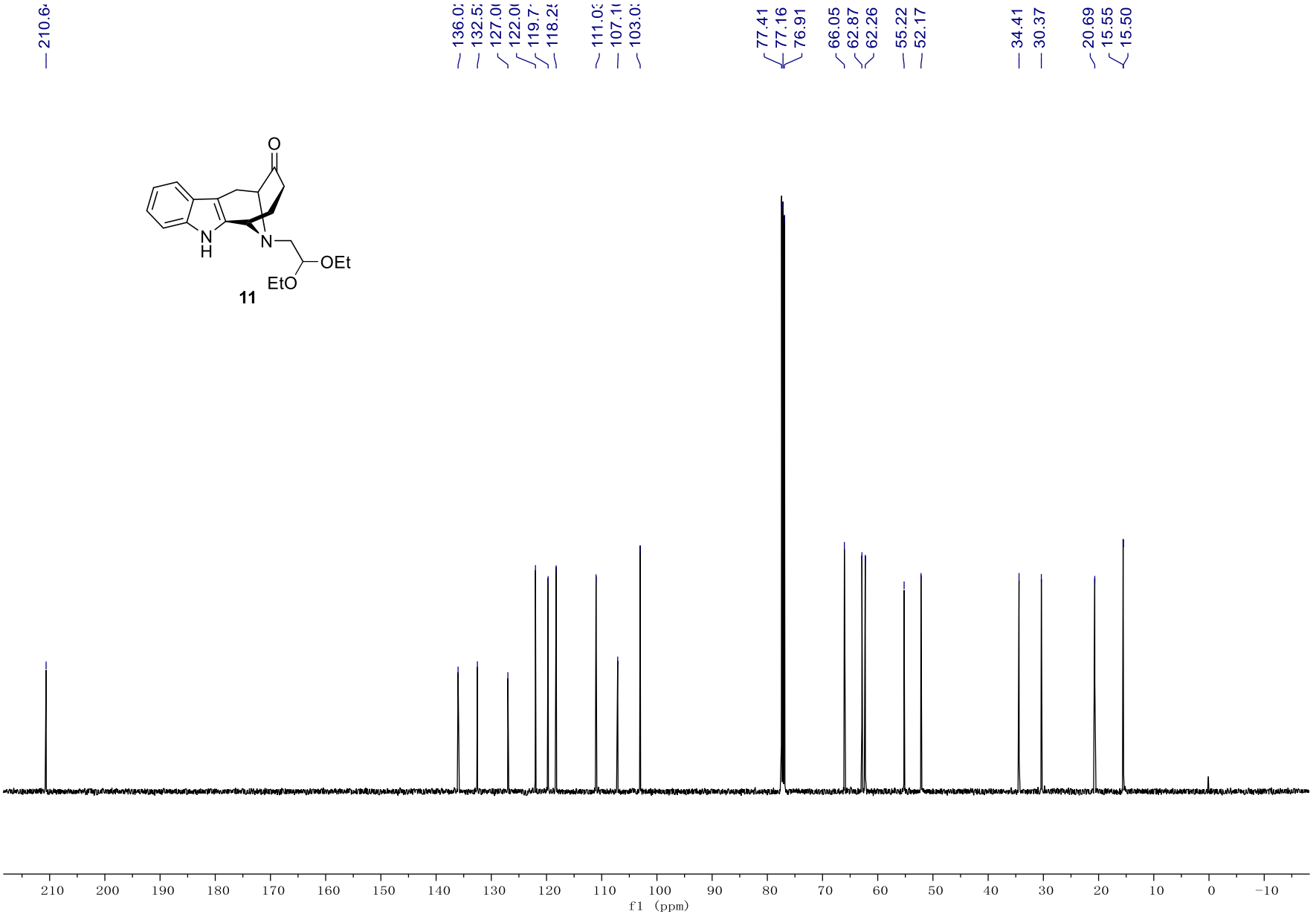


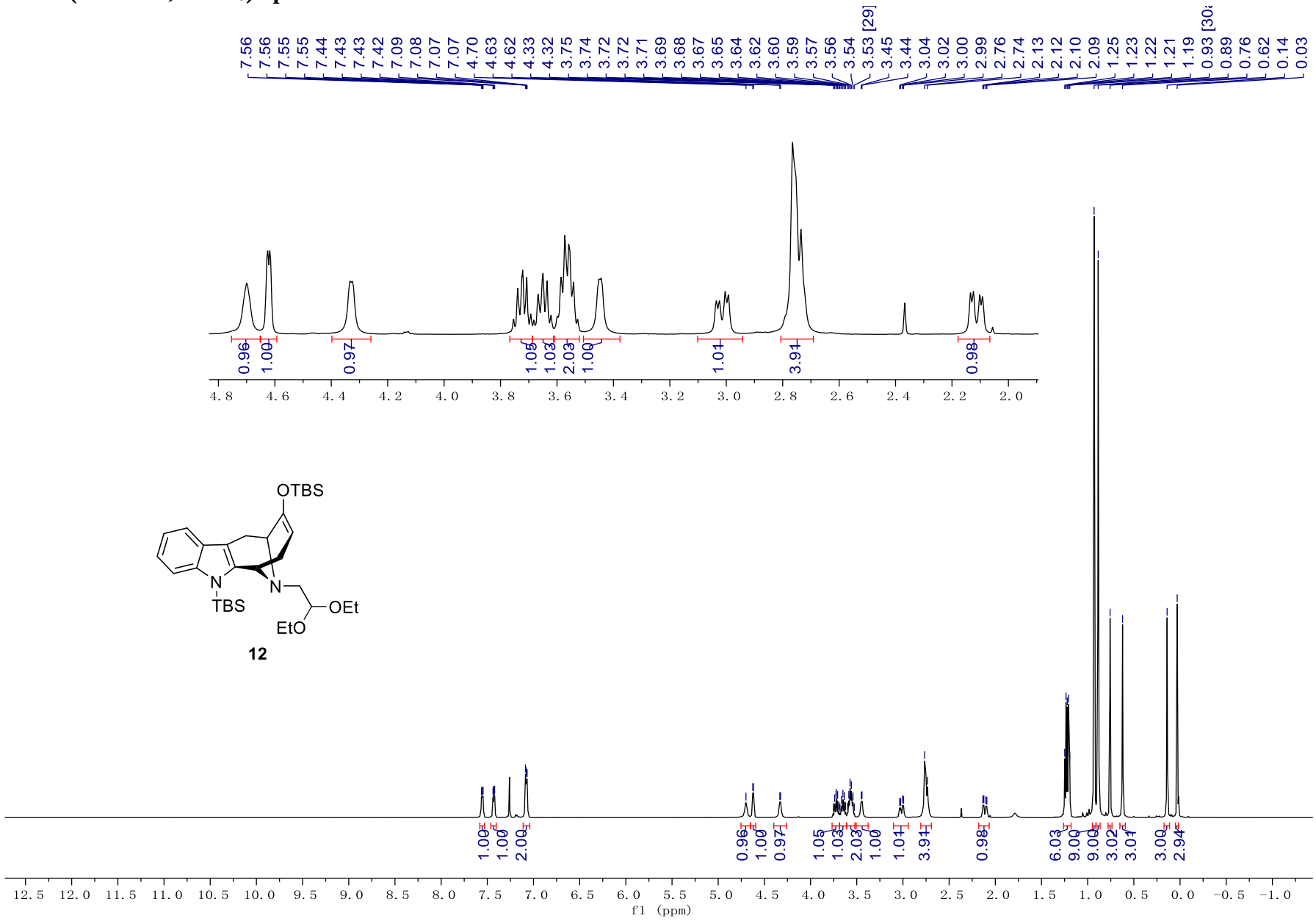
^{1}H NMR (500 MHz, $CDCl_3$) Spectra for 11



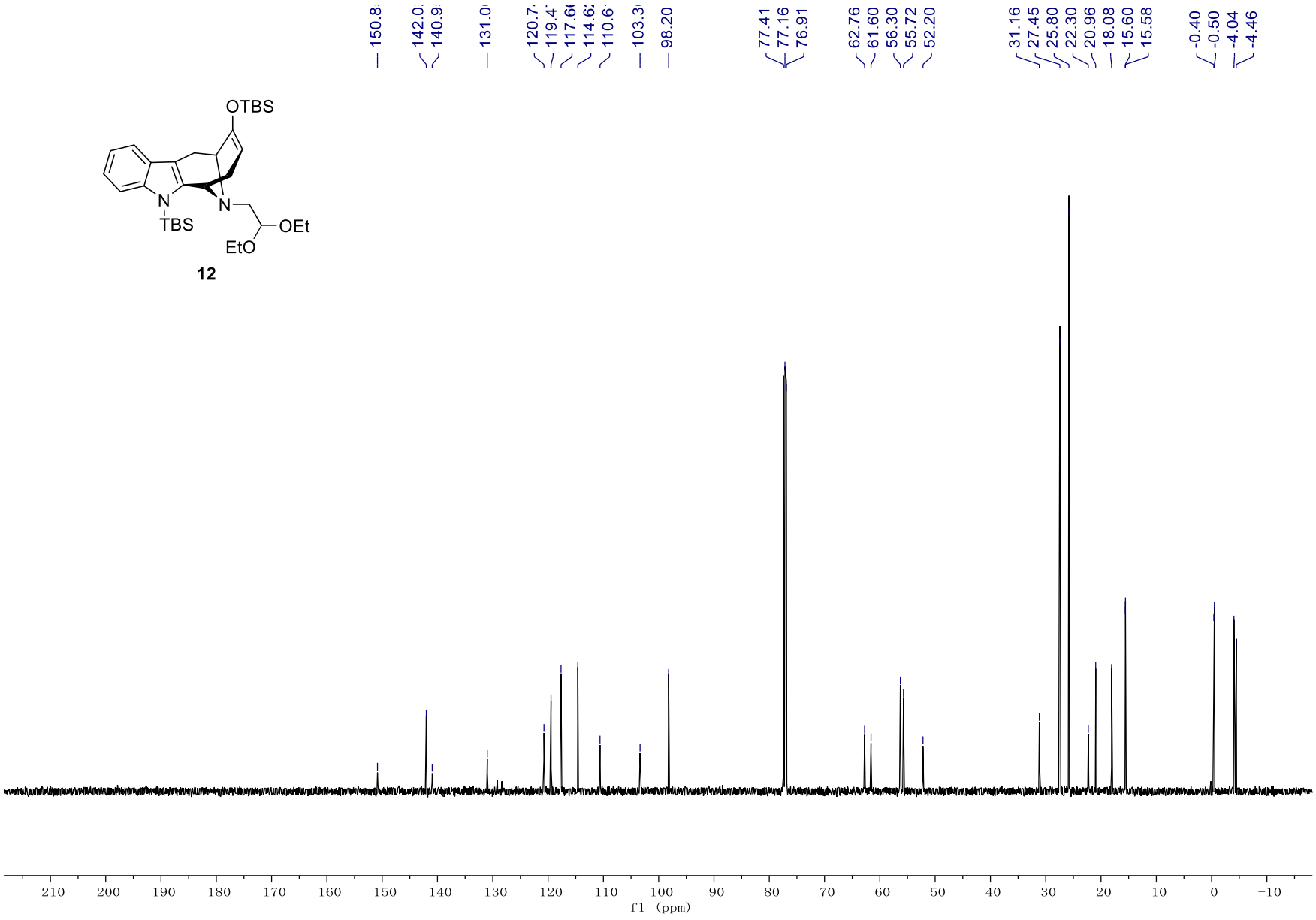
^{13}C NMR (126 MHz, $CDCl_3$) Spectra for 11



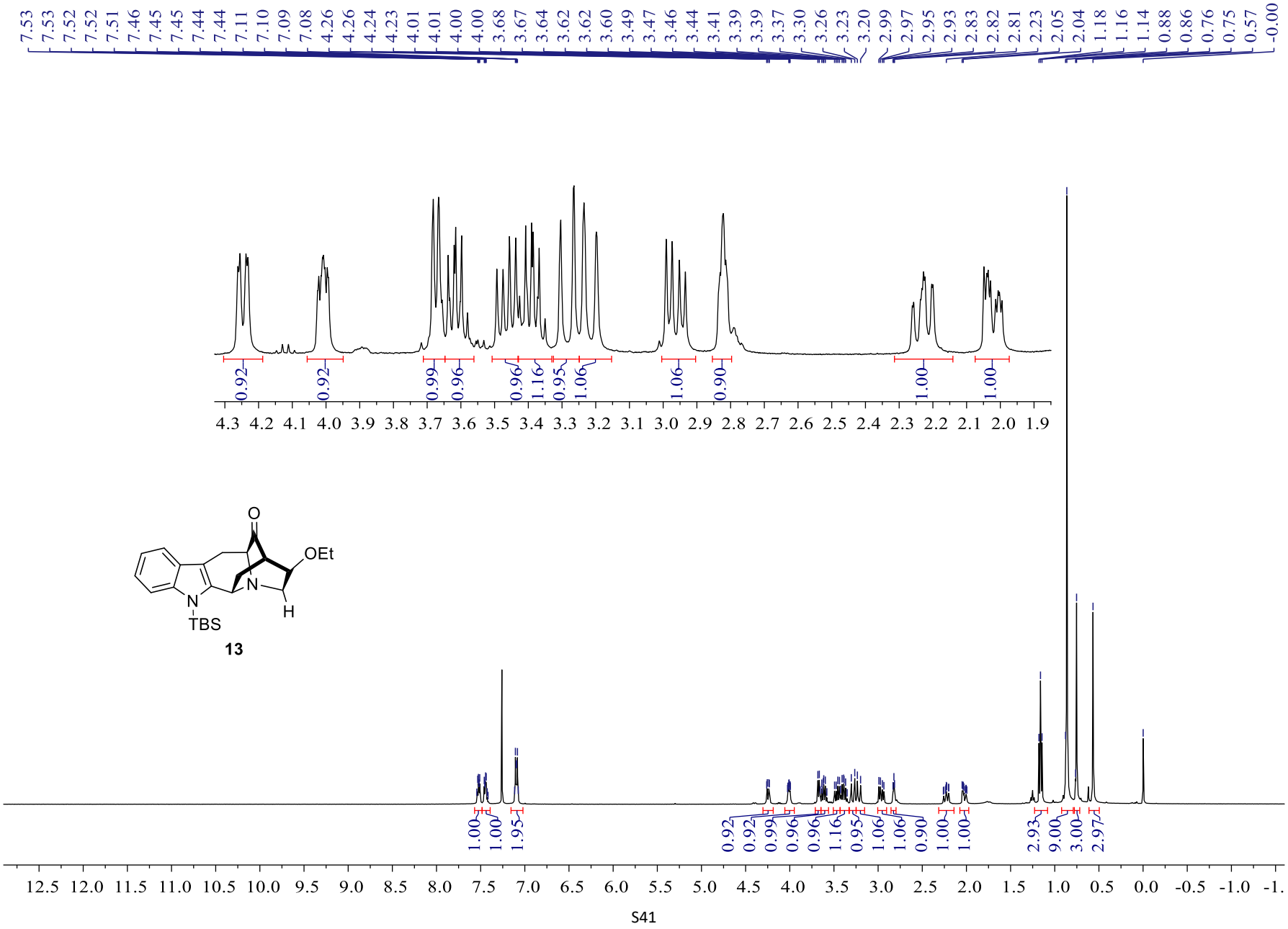
^{1}H NMR (500 MHz, $CDCl_3$) Spectra for 12



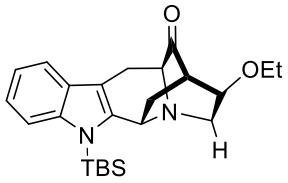
^{13}C NMR (126 MHz, $CDCl_3$) Spectra for 12



^{1}H NMR (400 MHz, $CDCl_3$) Spectra for 13

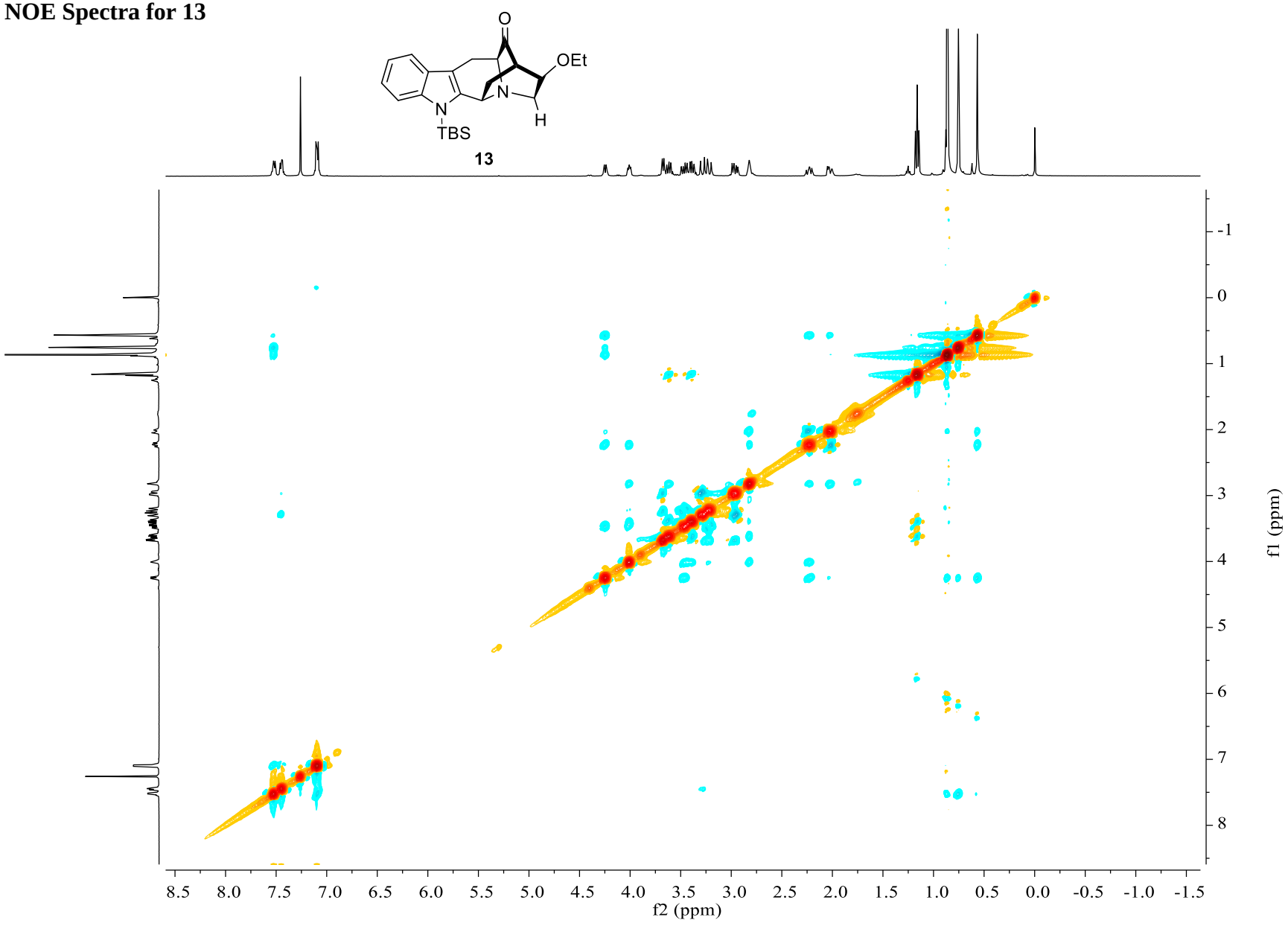


^{13}C NMR (126 MHz, $CDCl_3$) Spectra for 13

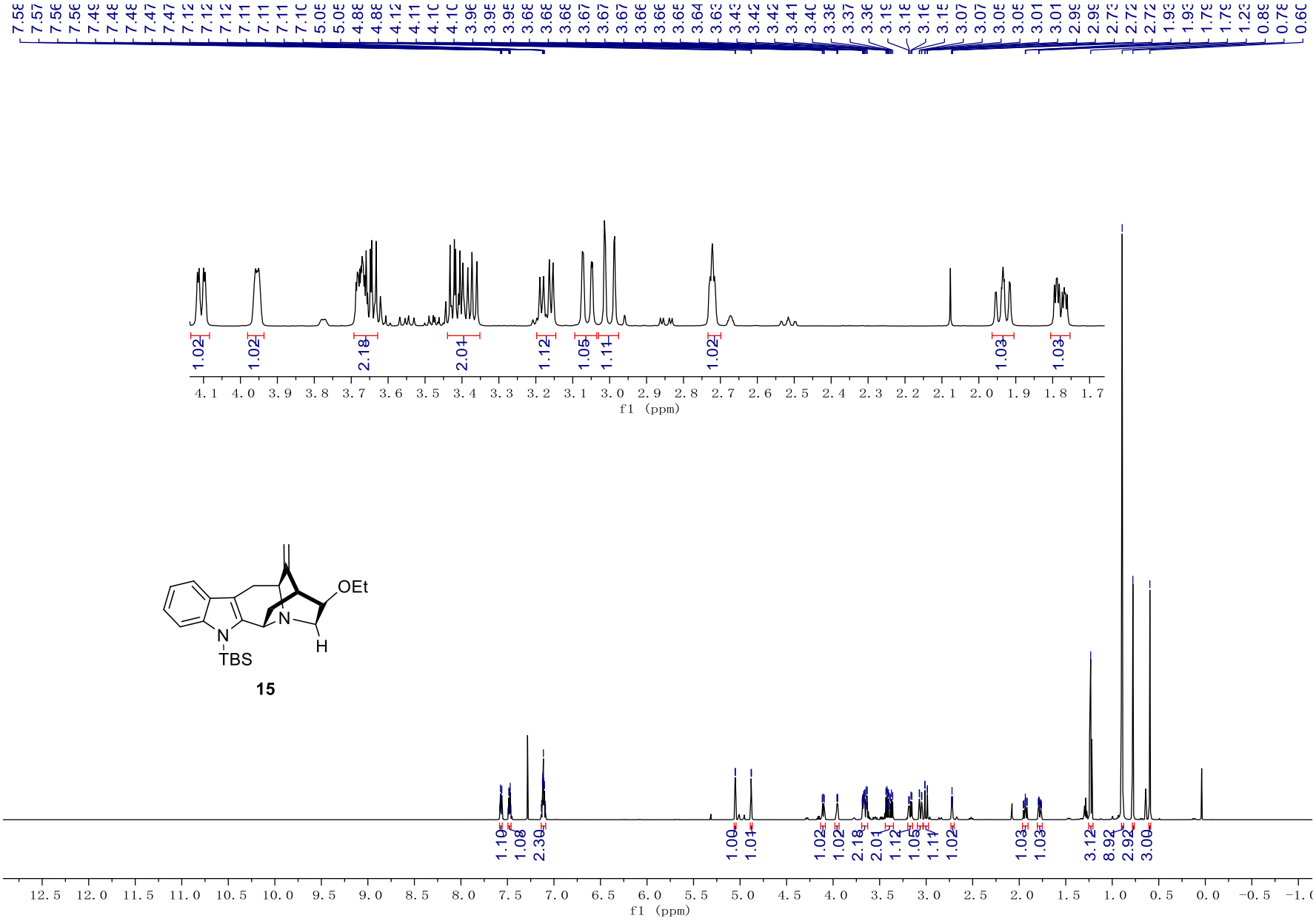


13

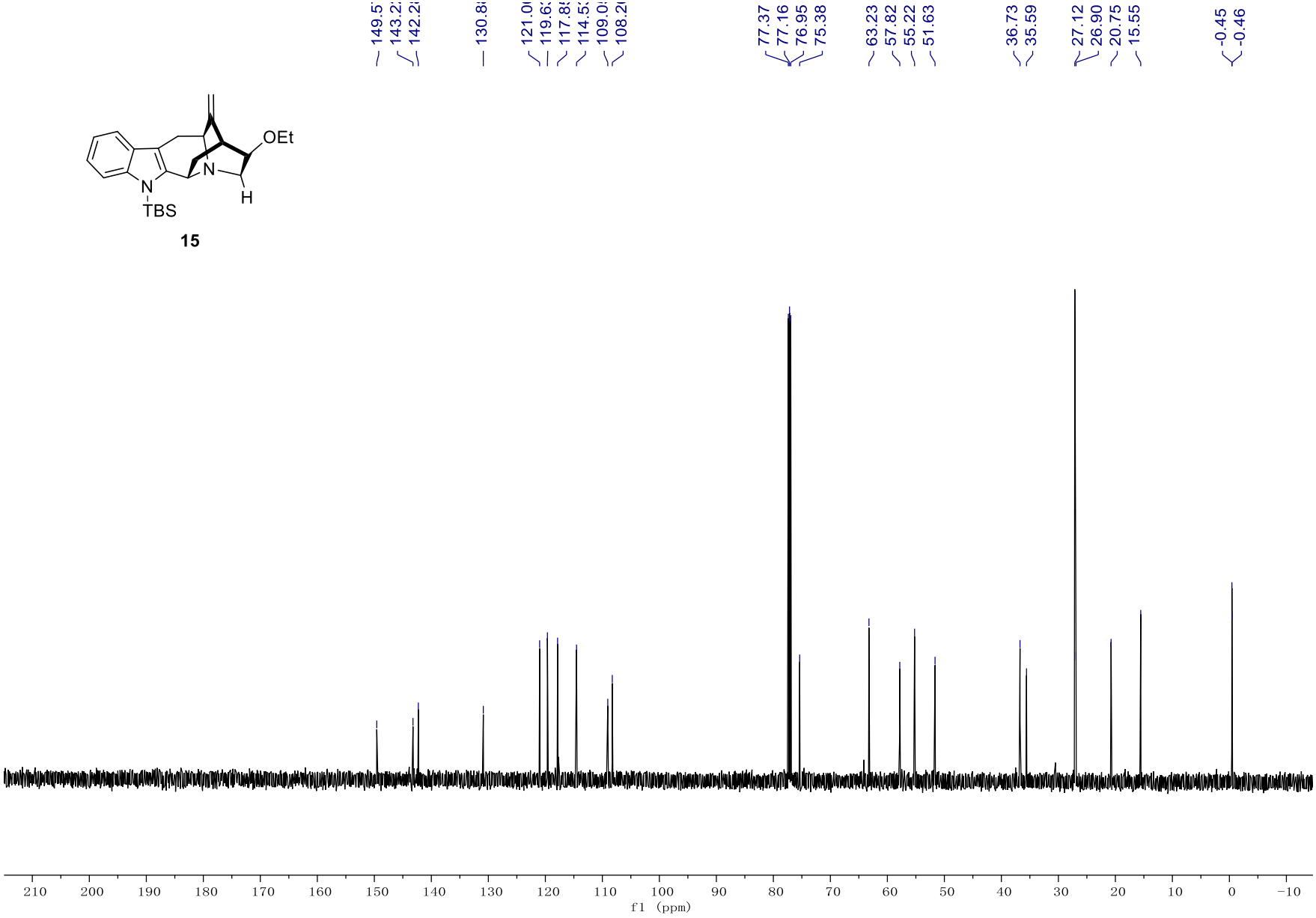
NOE Spectra for 13



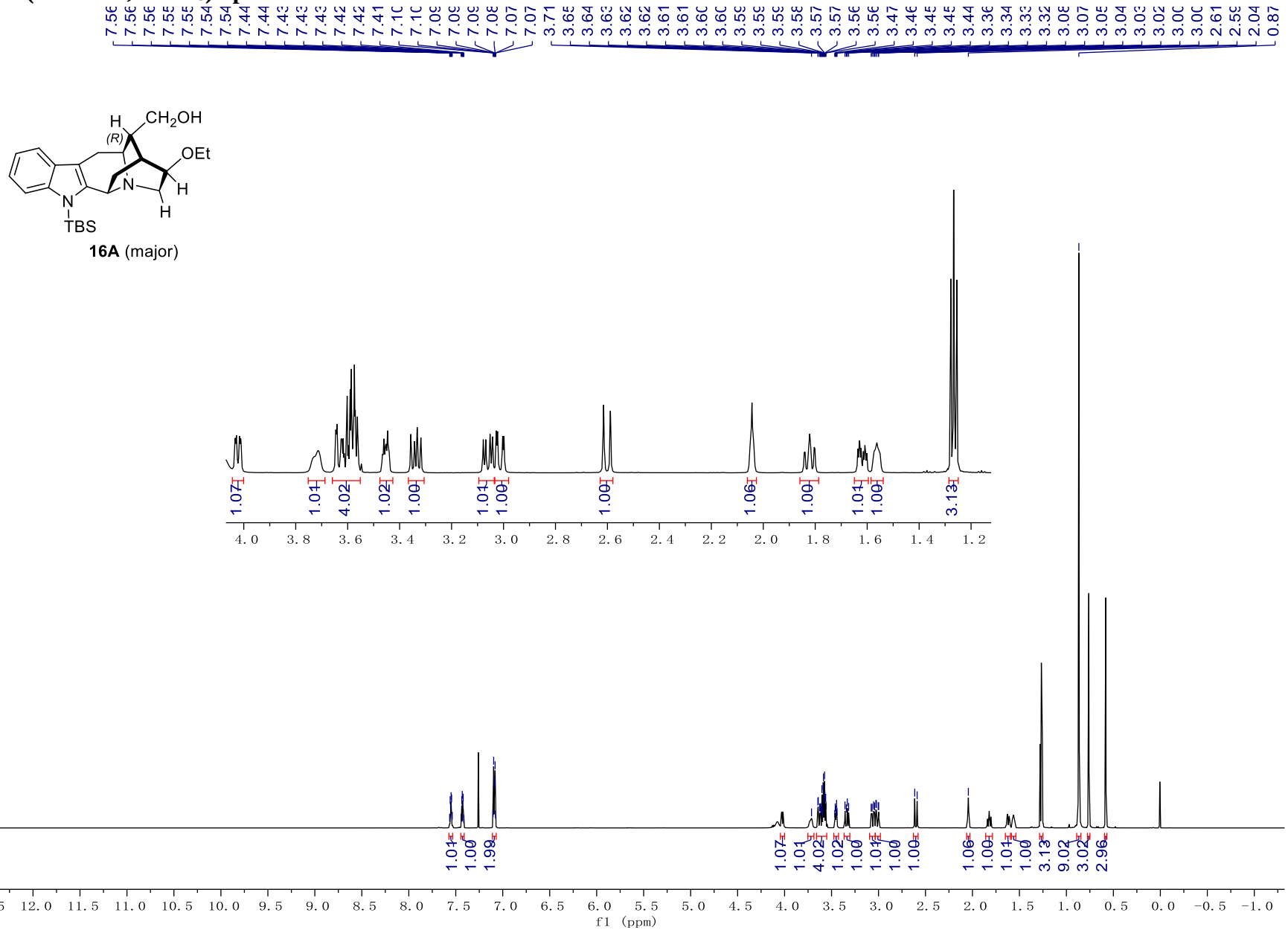
^{1}H NMR (600 MHz, $CDCl_3$) Spectra for 15



^{13}C NMR (151 MHz, $CDCl_3$) Spectra for 15

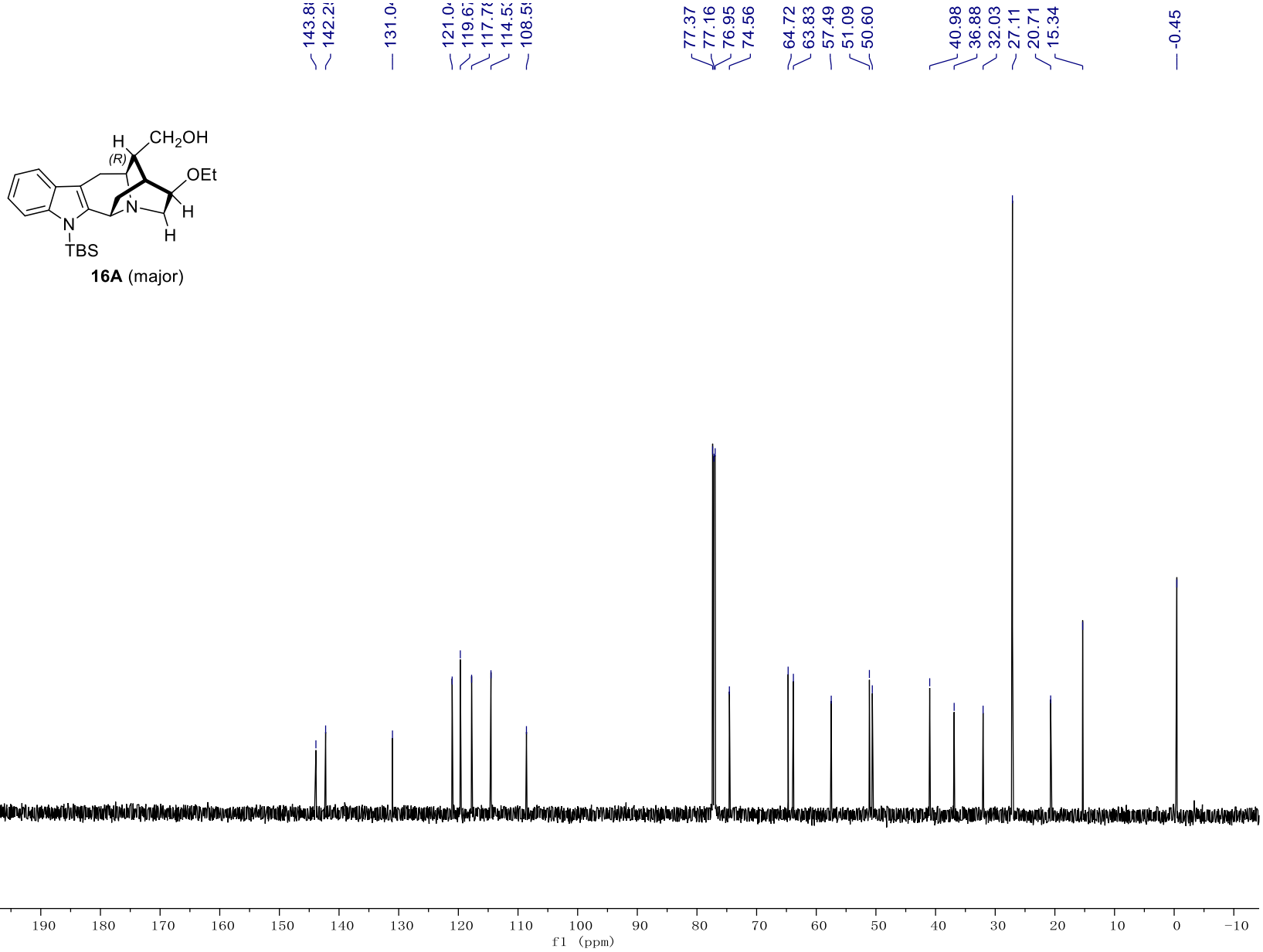


^{1}H NMR (600 MHz, $CDCl_3$) Spectra for 16A

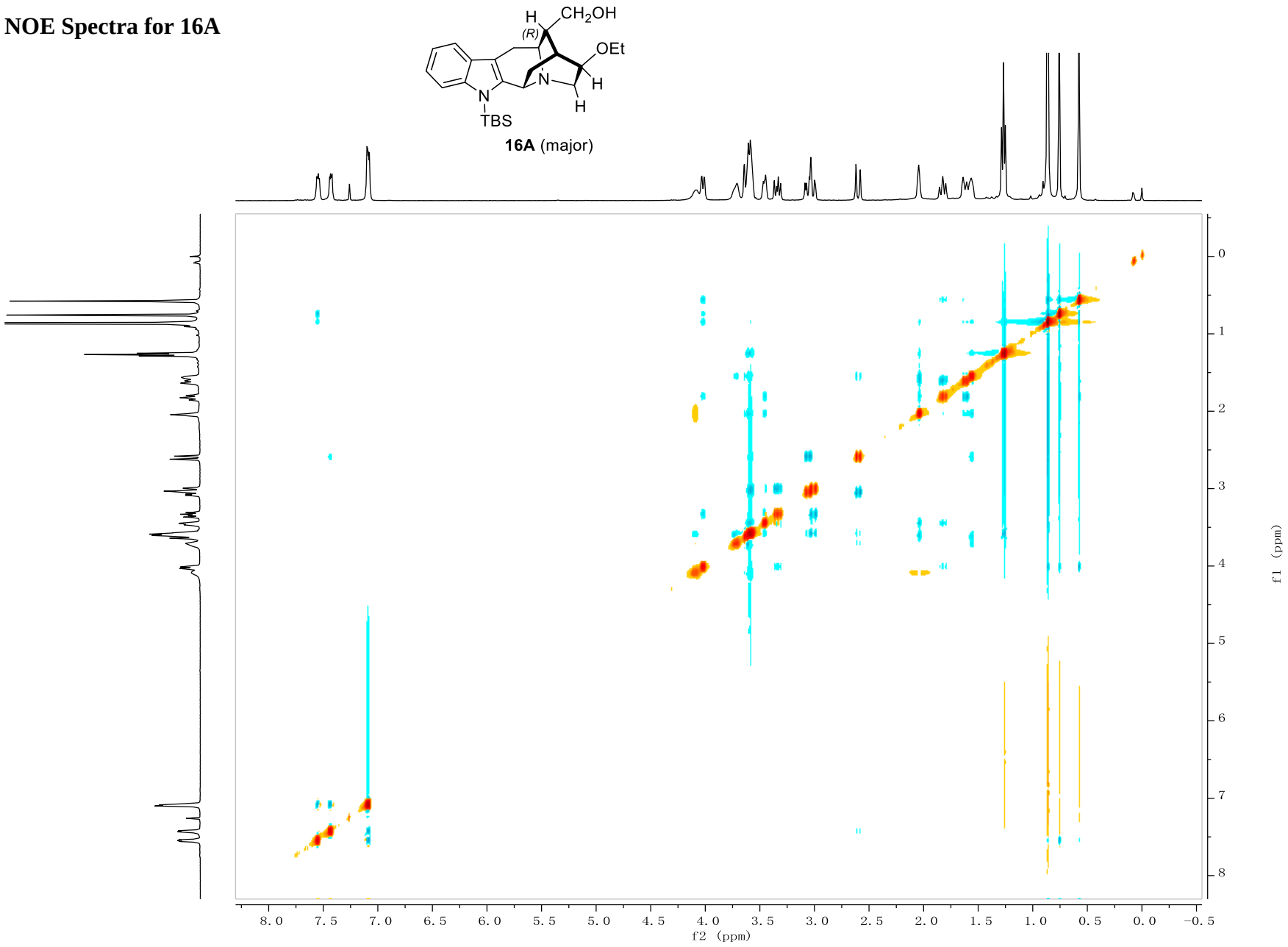


16A (major)

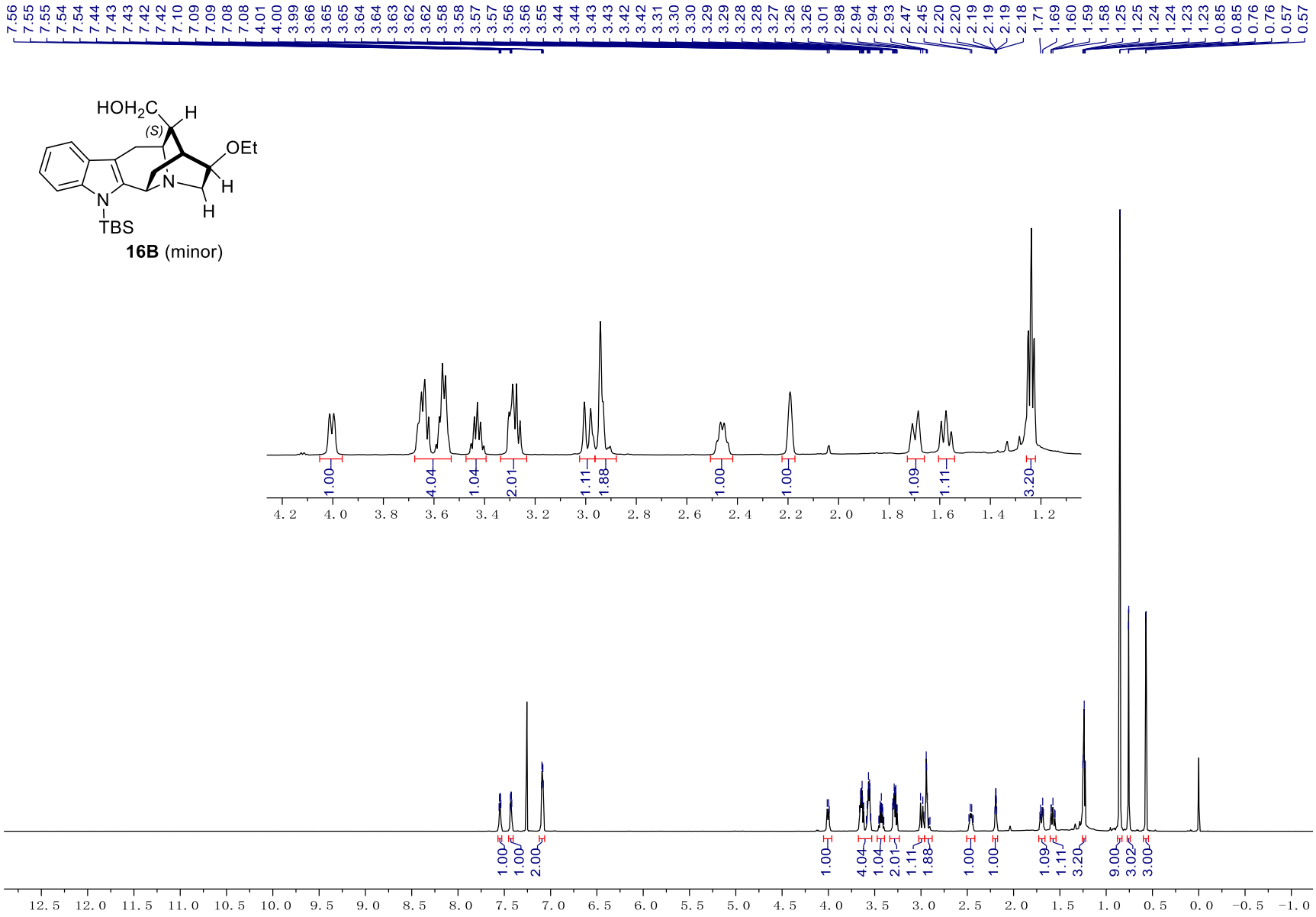
^{13}C NMR (151 MHz, $CDCl_3$) Spectra for 16A



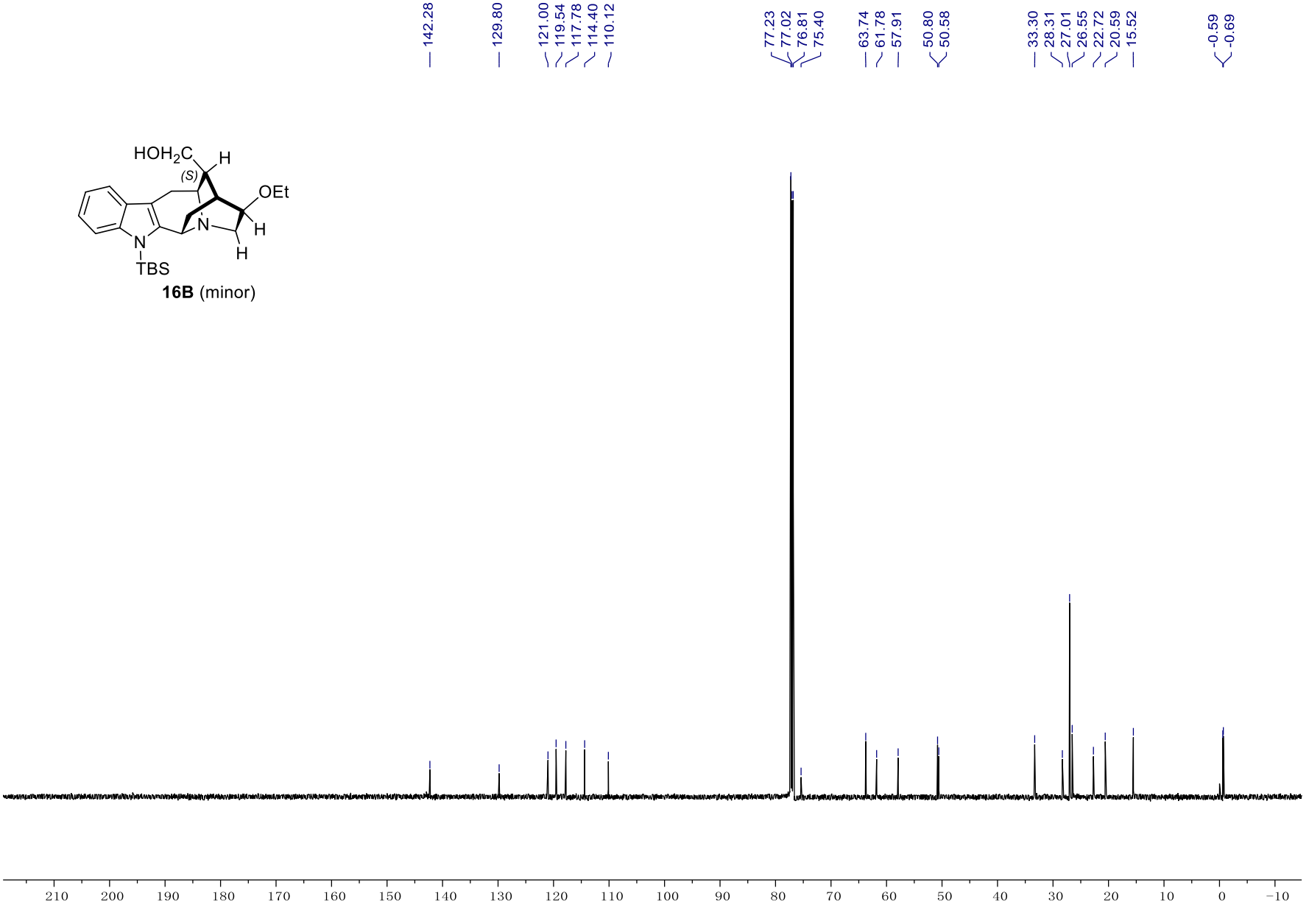
NOE Spectra for 16A



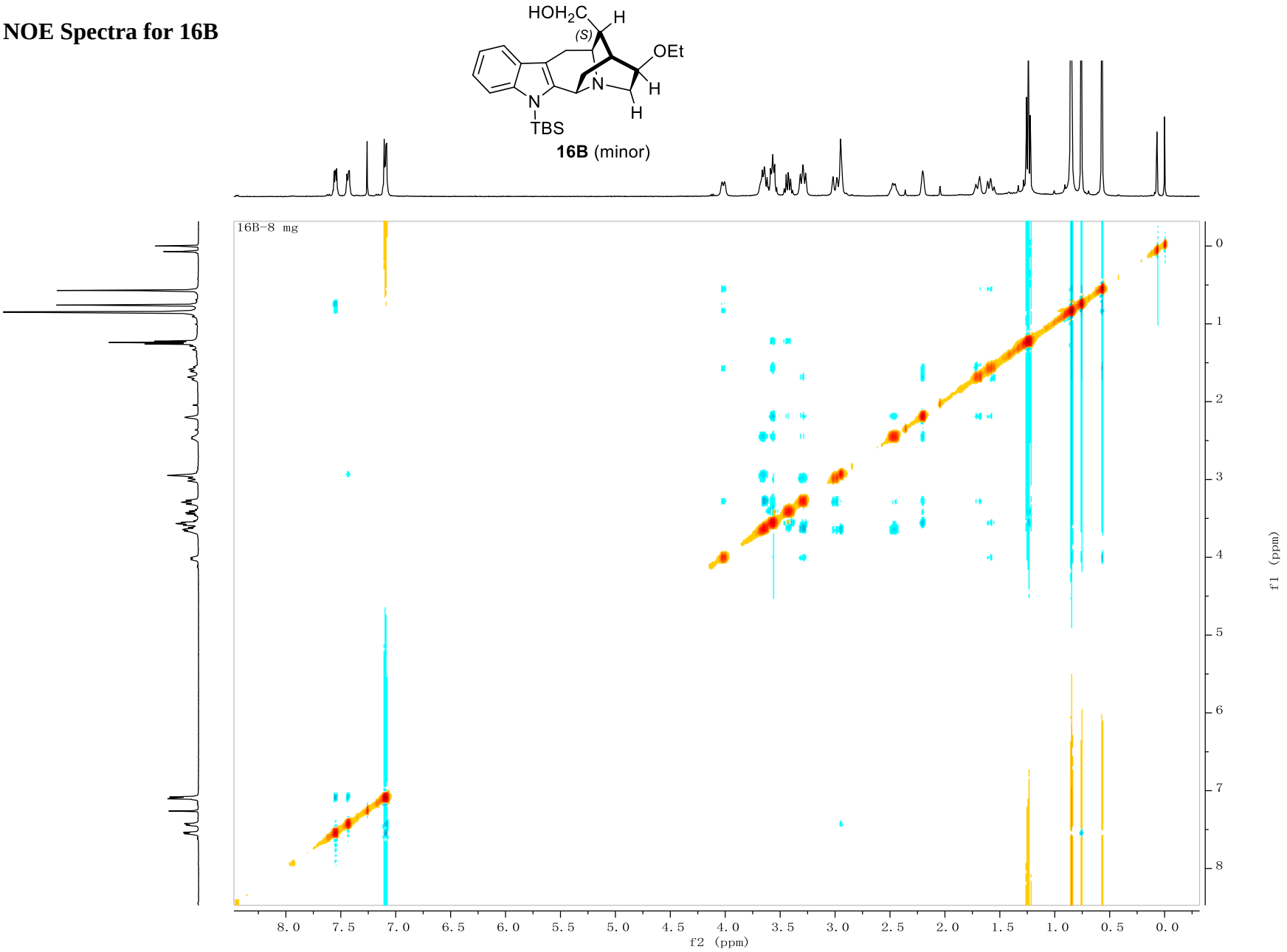
^{1}H NMR (600 MHz, $CDCl_3$) Spectra for 16B



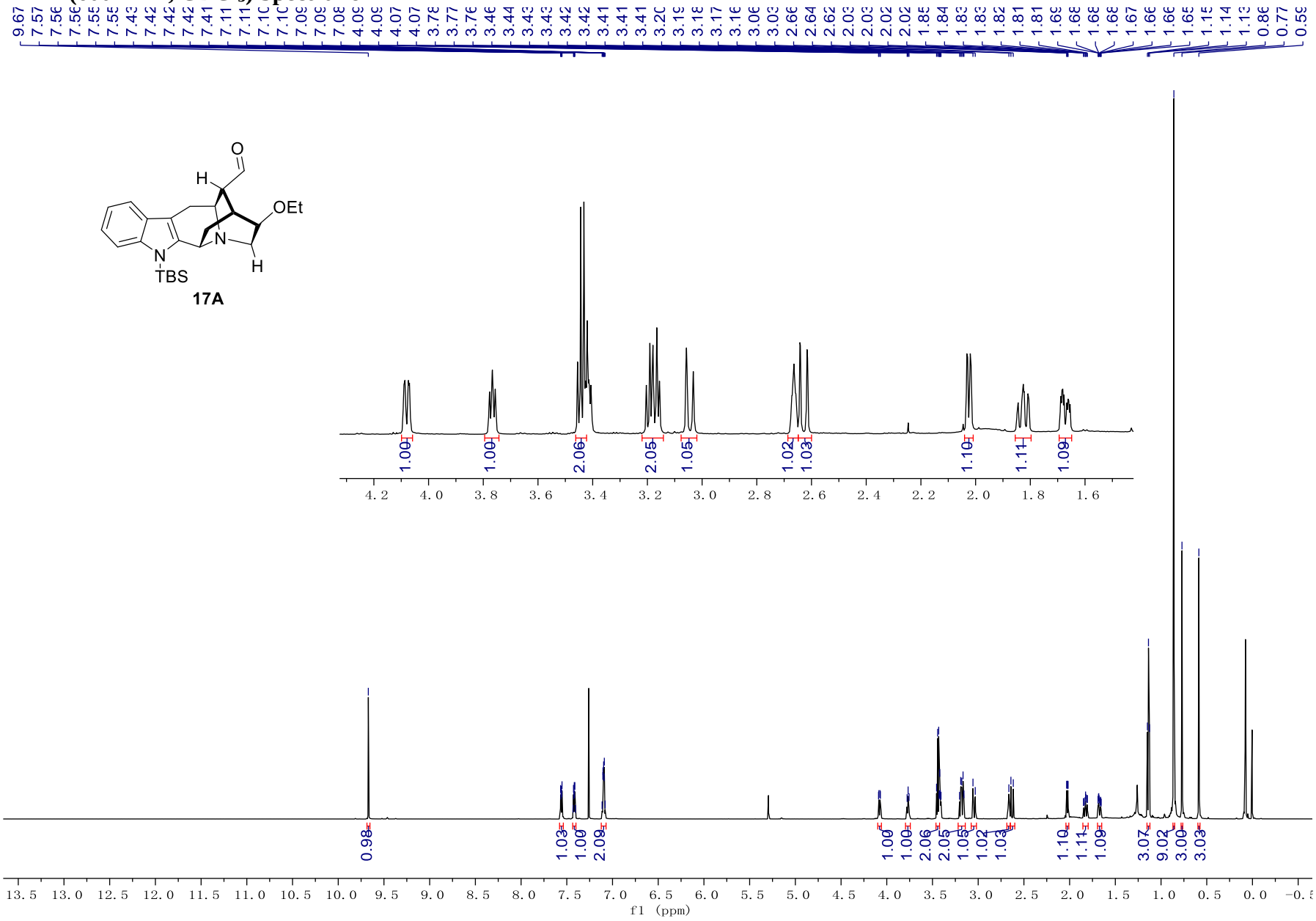
^{13}C NMR (151 MHz, $CDCl_3$) Spectra for 16B



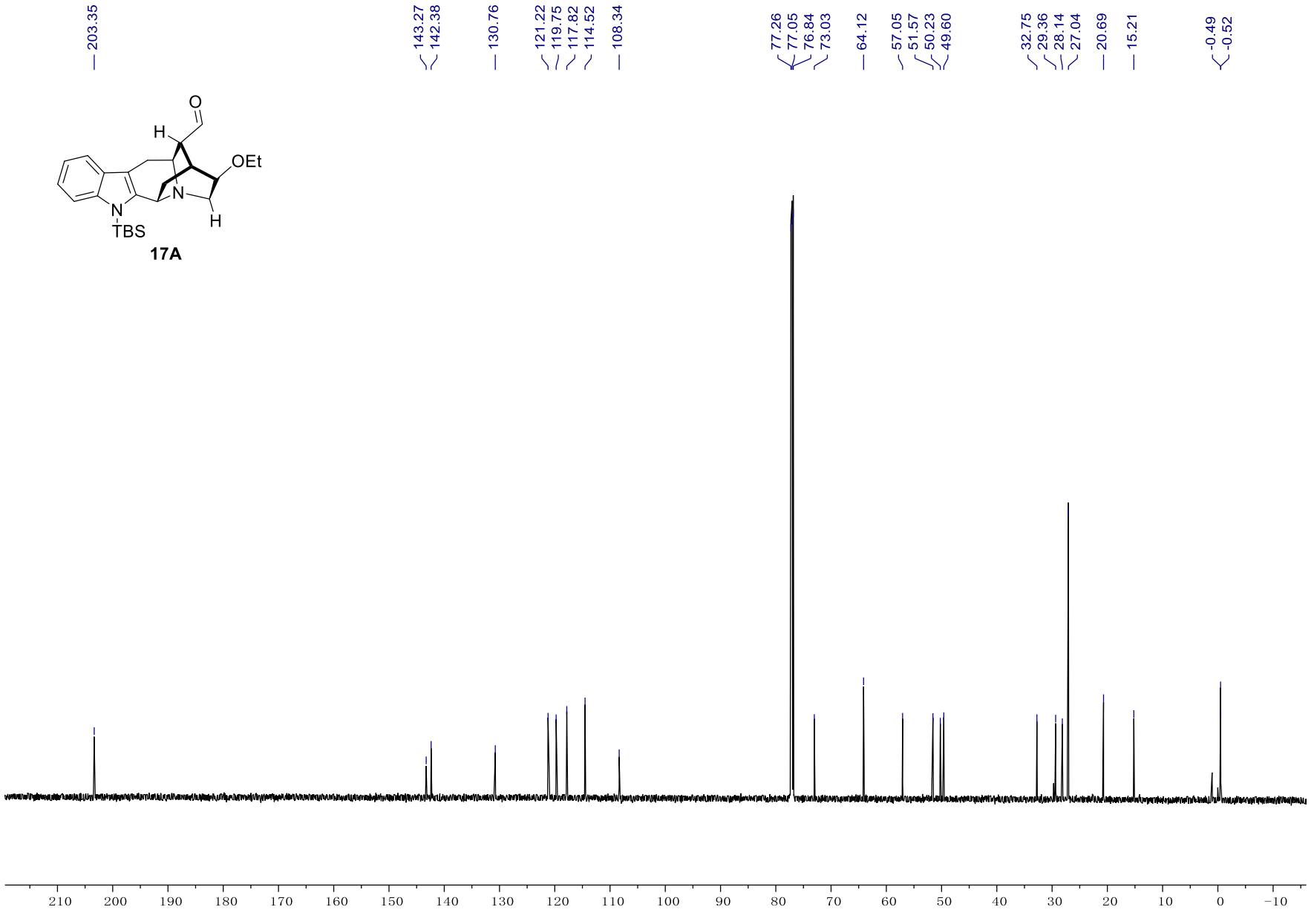
NOE Spectra for 16B



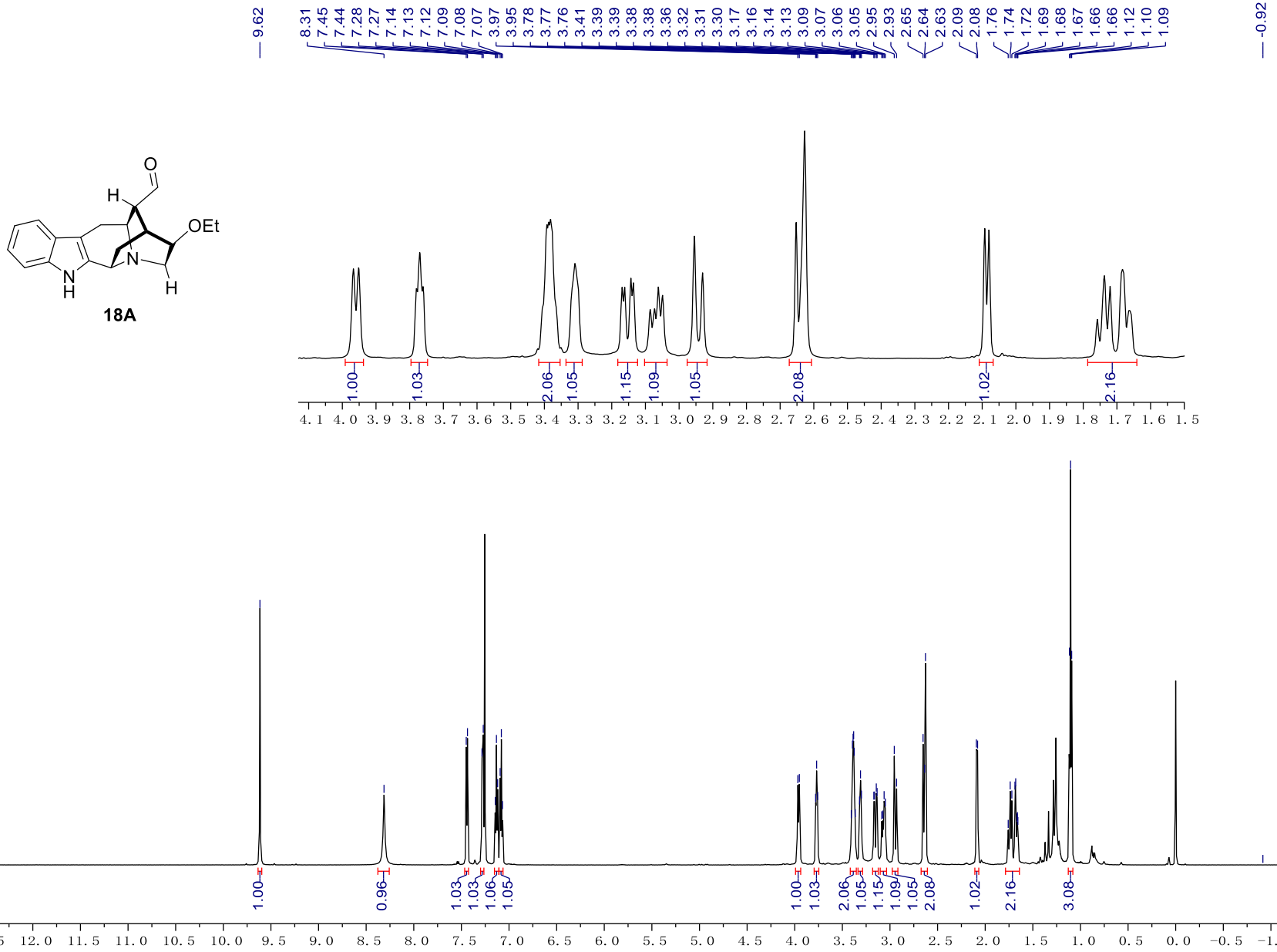
^{1}H NMR (600 MHz, $CDCl_3$) Spectra for 17A



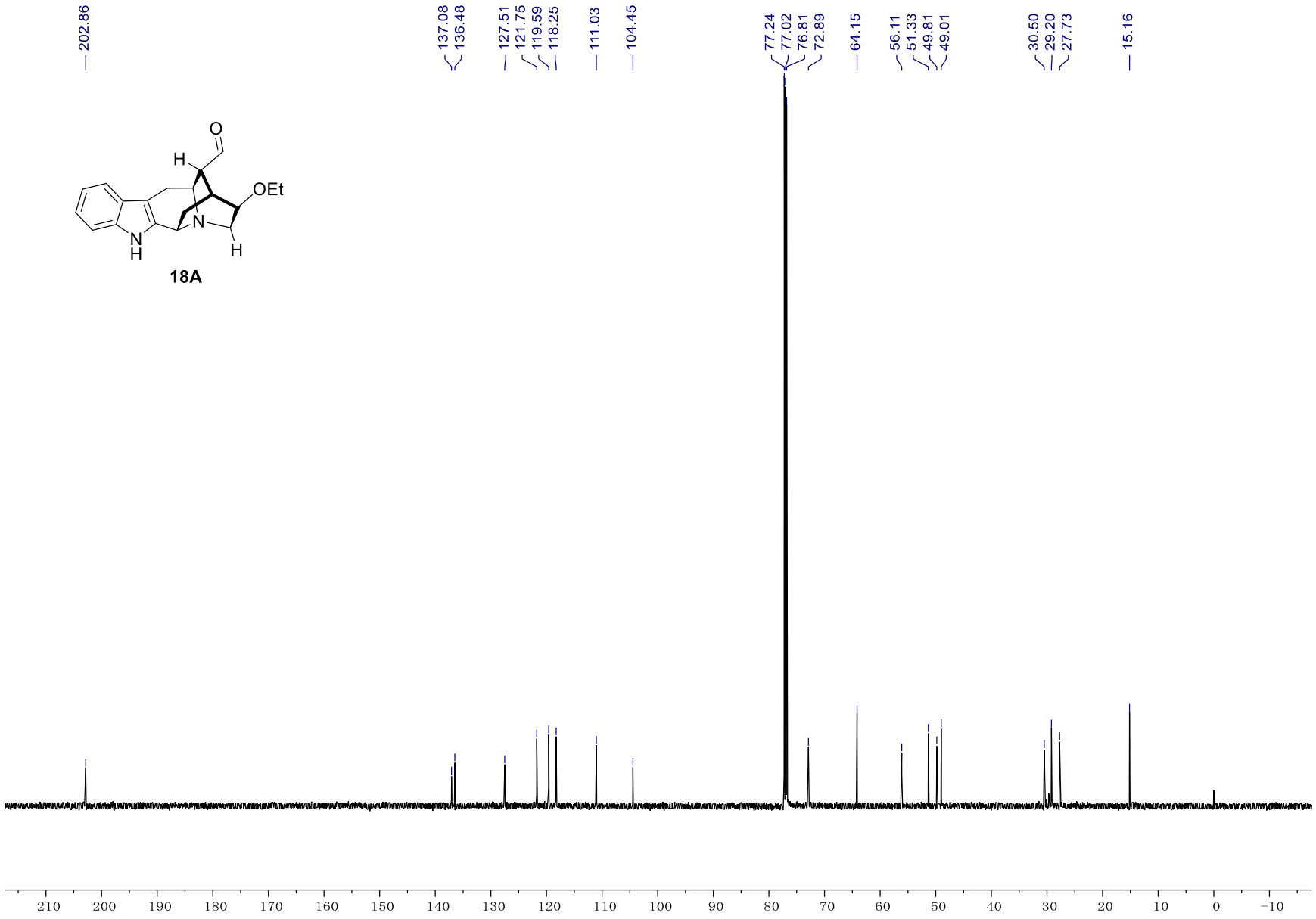
^{13}C NMR (151 MHz, $CDCl_3$) Spectra for 17A



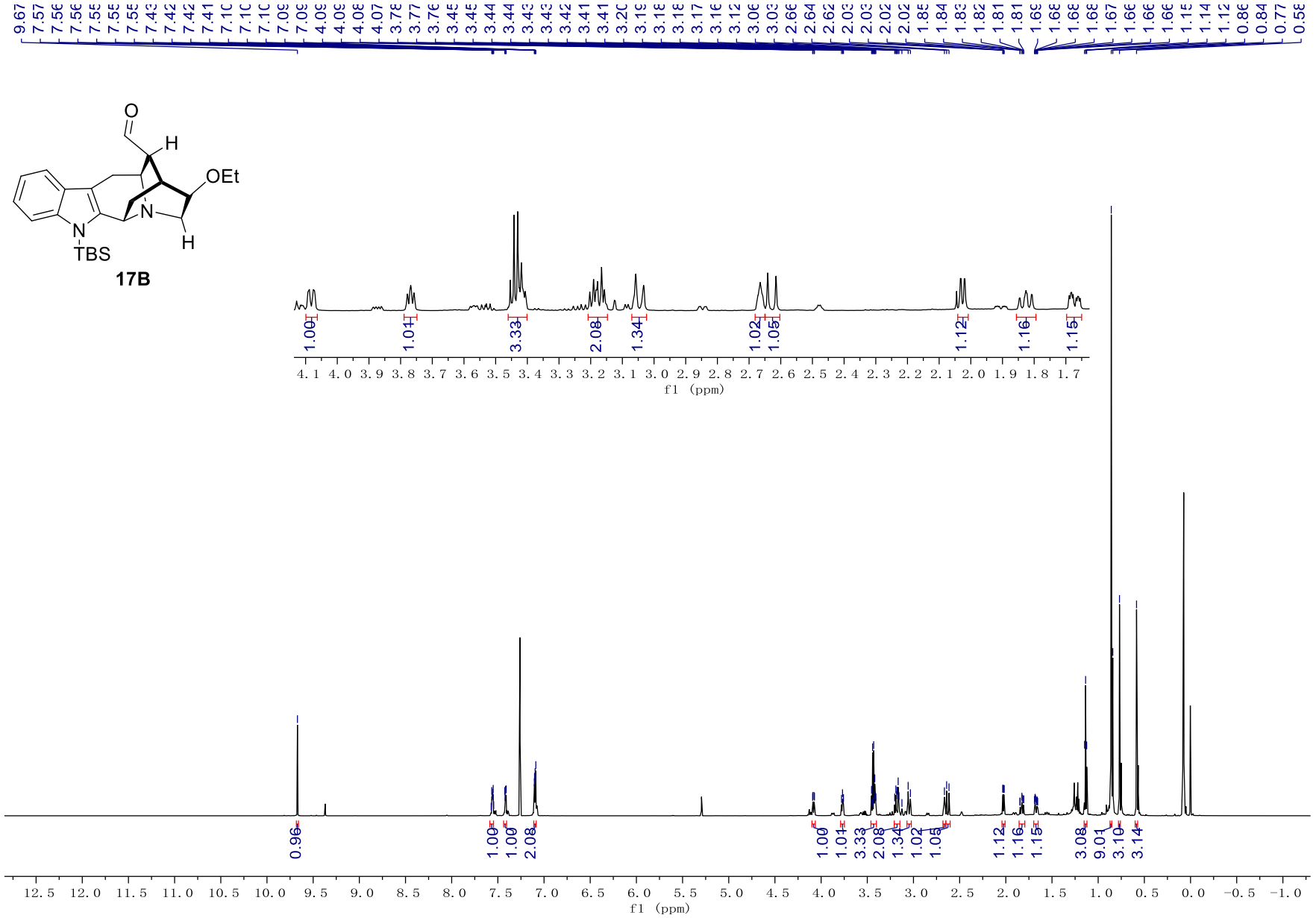
^{1}H NMR (600 MHz, $CDCl_3$) Spectra for 18A



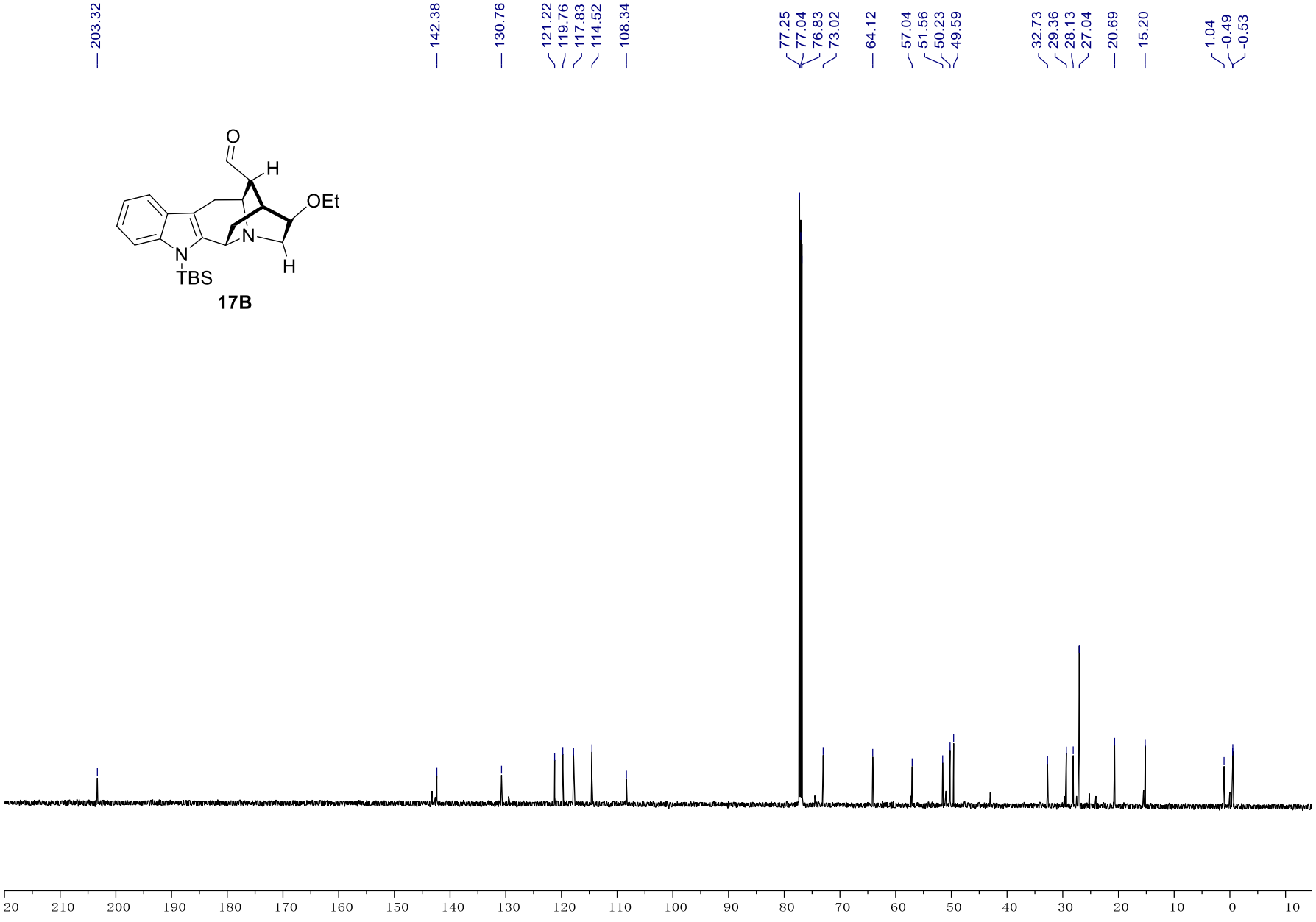
^{13}C NMR (151 MHz, $CDCl_3$) Spectra for 18A



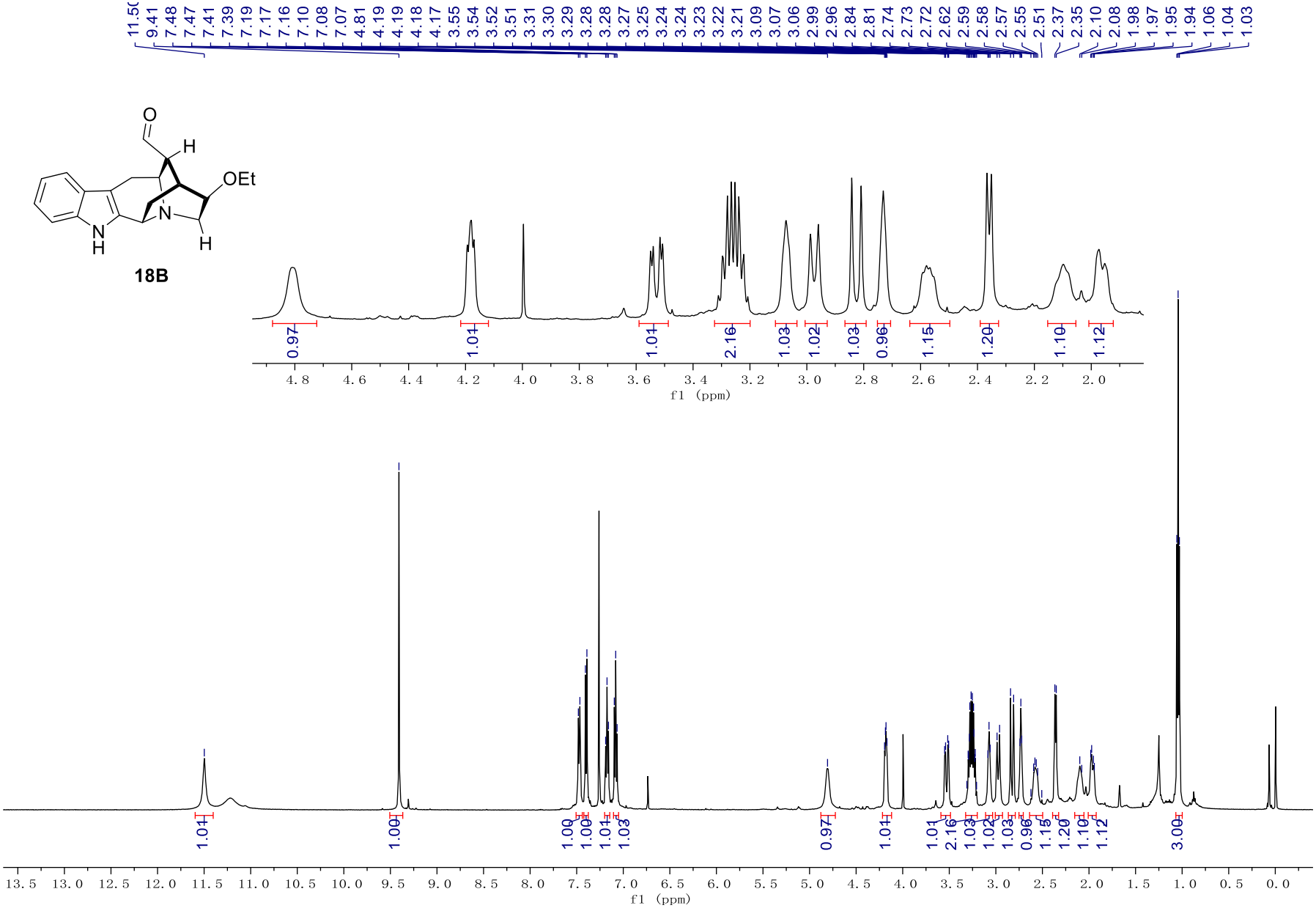
^{1}H NMR (600 MHz, $CDCl_3$) Spectra for 17B



^{13}C NMR (151 MHz, $CDCl_3$) Spectra for 17B



^{1}H NMR (500 MHz, $CDCl_3$) Spectra for 18B



^{13}C NMR (126 MHz, $CDCl_3$) Spectra for 18B