Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

A concise gram-scale synthesis of ht-13-A via a rhodium-catalyzed intramolecular C-H activation reaction

Pengyu Tao, Zhuang Chen, Yanxing Jia*

State Key Laboratory of Natural and Biomimetic Drugs, School of Pharmaceutical Sciences, Peking University, 38 Xueyuan Road, Beijing 100191, China, and

State Key Laboratory of Bioorganic and Natural Products Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, China

General information

All reagents were obtained from commercial suppliers unless otherwise stated. Toluene was distilled over sodium and tetrahydrofuran (THF) was distilled from potassium sodium alloys; Dichloromethane was distilled from calcium hydride. Flasks were flame-dried under vacuum and cooled under a stream of nitrogen or argon.

Visualization was achieved under a UV lamp (254 nm and 365 nm), and by developing the plates with phosphomolybdic acid or p-methoxybezaldehyde in ethanol. Flash column chromatography was performed using silica gel (200-300 mesh) with solvents distilled prior to use.

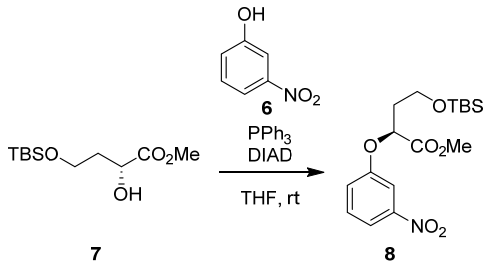
^{1}H NMR were recorded 400 MHz NMR spectrometer, ^{13}C NMR at 100 MHz NMR spectrometer unless otherwise stated. The following abbreviations are used for the multiplicities: s: singlet, d: doublet, t: triplet, q: quartet, quint: quintet, m: multiplet, br s: broad singlet for proton spectra and carbon spectra. Coupling constants (*J*) are reported in Hertz (Hz). Infrared spectra were recorded with a thin layer of the product on a KBr disk.

High resolution mass spectral (HRMS) data were obtained with an ionization mode of ESI.

The following abbreviations are used: **EtOAc**; ethyl acetate; **THF**: Tetrahydrofuran; **MeCN**: methyl cyanide; **PE**: petroleum ether; **DCM**: dichloromethane; **PPh_3**: triphenylphosphine; **DIAD**: diisopropyl azodicarboxylate; **DIBAL-H**: diisobutyl aluminium hydride; **TMSCl**: trimethyl chlorosilane; **TBSOTf**: tertbutyldimethylsilyl trifluoromethanesulfonate; **DMAP**: 4-dimethylaminopyridine; **Ac_2O**: acetic anhydride; **Et_3N**: triethylamine. **MsCl**: methanesulfonyl chloride

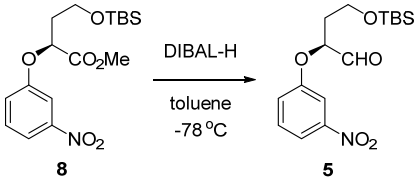
Experimental procedure and physical data

Methyl (*S*)-4-((*tert*-butyldimethylsilyl)oxy)-2-(3-nitrophenoxy)butanoate (8).



To a stirred solution of **7** (3.11 g, 12.5 mmol) and 3-nitrophenol **6** (2.09 g, 15.0 mmol) in dry THF (24 mL) was added PPh_3 (3.95 g, 15.1 mmol). The mixture was cooled down to 0 °C and DIAD (3.15 mL, 15.1 mmol) was added dropwisely. The solution was warmed to room temperature and kept stirring for 12 h. Then water was added and the mixture was extracted with EtOAc, dried over Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the resulting residue was purified by silica gel column chromatography (PE/EtOAc = 20:1) to afford **8** (3.98 g, 86%) as a yellow oil. $[\alpha]_D^{25}$ -36.5 (*c* 2.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.0 Hz, 1H), 7.73 (s, 1H), 7.43 (t, *J* = 8.4 Hz, 1H), 7.23 (dd, *J* = 8.0, 1.6 Hz, 1H), 4.97 (dd, *J* = 8.8, 4.0 Hz, 1H), 3.83-3.80 (m, 2H), 3.77 (s, 3H), 2.25-2.09 (m, 2H), 0.84 (s, 9H), 0.02 (s, 3H), -0.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 158.6, 149.1, 130.1, 121.8, 116.6, 110.1, 73.5, 58.0, 52.4, 35.5, 25.8, 18.2, -5.5, -5.6; IR(KBr): 2955, 2930, 2859, 1758, 1532, 1480, 1099, 838, 738 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{17}H_{28}NO_6Si$ $(M + H)^+$ 370.1686, found 370.1689.

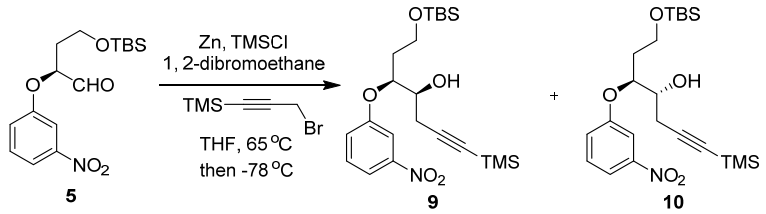
(*S*)-4-((*tert*-Butyldimethylsilyl)oxy)-2-(3-nitrophenoxy)butanal (5).



To a stirred solution of **8** (3.80 g, 10.3 mmol) in dry toluene (41 mL) was added DIBAL-H (1 M, 12.4 mL, 12.4 mmol) dropwisely at -78 °C. The resulting mixture was stirred at -78 °C for 10 min. Then the reaction was quenched with MeOH, warmed to room temperature, and poured into saturated aqueous potassium sodium tartrate solution. The mixture was vigorously stirred until the phase separation occurred and extracted with EtOAc. The combined organic extracts were washed with brine, dried over Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the resulting residue was purified by

silica gel column chromatography (PE/EtOAc = 8:1) to afford **5** (3.28 g, 94%) as a yellow oil. $[\alpha]_D^{25}$ -34.7 (*c* 2.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 9.73 (d, *J* = 0.8 Hz, 1H), 7.84 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.73 (t, *J* = 2.0 Hz, 1H), 7.44 (t, *J* = 8.0 Hz, 1H), 7.24 (dd, *J* = 8.4, 2.0 Hz, 1H), 4.88 (t, *J* = 5.6 Hz, 1H), 3.90-3.85 (m, 1H), 3.80-3.75 (m, 1H), 2.22-2.10 (m, 2H), 0.85 (s, 9H), 0.03 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.9, 158.2, 149.2, 130.3, 121.7, 116.6, 110.2, 79.4, 57.5, 33.5, 25.8, 18.2, -5.55, -5.64; IR(KBr): 2955, 2930, 1531, 1351, 1246, 1096, 836, 778, 738 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{16}H_{26}NO_5Si$ $(M + H)^+$ 340.1580, found 340.1576.

(4S,5S)-7-((*tert*-Butyldimethylsilyl)oxy)-5-(3-nitrophenoxy)-1-(trimethylsilyl)hept-1-yn-4-ol (9) and (4R,5S)-7-((*tert*-butyldimethylsilyl)oxy)-5-(3-nitrophenoxy)-1-(trimethylsilyl)hept-1-yn-4-ol (10)[1]



To a flame-dried Schlenk flask backfilled with argon was added powdered Zn metal (1.95 g, 30 mmol). After brief vacuum purging and backfilling the flask with argon, the metal was suspended in THF (30 mL). To this suspension was cannula transferred a prepared solution of 1, 2-dibromoethane (0.41 mL, 4.8 mmol) and trimethylsilyl chloride (0.17 mL, 1.3 mmol) in THF (14 mL). The reaction vessel was sealed, then heated to 65 °C for 15 min. Then the reaction mixture was cooled to room temperature, and 3-(trimethylsilyl)propargyl bromide (1.70 mL, 10.4 mmol) was added dropwisely into the suspension of activated Zn metal. The reaction mixture was heated to 65 °C for 2 h. Then the reaction mixture was cooled to room temperature.

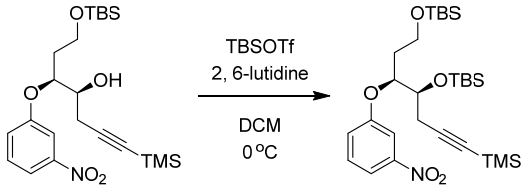
To a stirred solution of compound **5** (2.95 g, 8.7 mmol) in THF (12 mL) was added the prepared propargyl zinc solution dropwisely at -78 °C. The resulting mixture was stirred at -78 °C for 0.5 h. Then the reaction was quenched with saturated aqueous NH_4Cl solution and extracted with EtOAc. The combined organic extracts were washed with brine, dried over Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the resulting residue was purified by silica gel column chromatography (PE/EtOAc = 10:1) to afford **9** (1.31 g, 30%) and **10** (1.76 g, 40%) as yellow oil.

Compound **9**: $[\alpha]_D^{25}$ +16.3 (*c* 2.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.81 (dd, *J* = 6.8, 2.0 Hz, 1H), 7.41-7.36 (m, 2H), 4.86-4.82 (m, 1H), 3.95-3.94 (m, 1H), 3.81-3.76 (m, 1H), 3.71-3.66 (m,

1H), 2.87 (d, *J* = 6.0 Hz, 1H), 2.64-2.53 (m, 2H), 2.07-1.94 (m, 2H), 0.88 (s, 9H), 0.11 (s, 9H), 0.04 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 149.2, 130.0, 122.5, 116.1, 110.6, 102.3, 87.7, 76.6, 71.3, 58.5, 33.5, 25.8, 25.1, 18.2, -0.1, -5.5, -5.6; IR(KBr): 2956, 2929, 1532, 1350, 1249, 1093, 841, 777, 738 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{38}NO_5Si_2$ $(M + H)^+$ 452.2289; found 452.2290.

Compound **10**: $[\alpha]_D^{25}$ +17.9 (*c* 2.0 $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82-7.80 (m, 2H), 7.41 (t, *J* = 8.0 Hz, 1H), 7.04-6.93 (dd, *J* = 8.0, 0.8 Hz, 1H), 4.73 (q, *J* = 5.6 Hz, 1H), 4.03-3.97 (m, 1H), 3.87-3.82 (m, 1H), 3.73-3.68 (m, 1H), 3.01 (d, *J* = 4.8 Hz, 1H), 2.65-2.54 (m, 2H), 1.99 (q, *J* = 5.2 Hz, 2H), 0.88 (s, 9H), 0.13 (s, 9H), 0.05 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 149.3, 130.0, 122.4, 116.0, 110.8, 102.1, 88.0, 77.5, 70.7, 58.5, 32.6, 25.8, 24.6, 18.2, 0.0, -5.5, -5.6; IR(KBr): 2956, 2930, 1532, 1351, 1249, 1091, 842, 777, 738 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{38}NO_5Si_2$ $(M + H)^+$ 452.2289, found 452.2286.

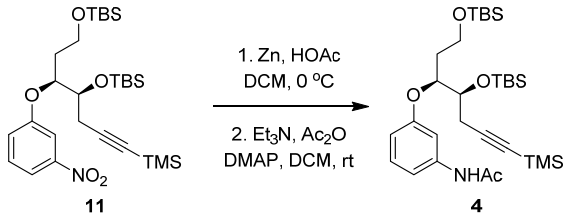
(5S,6S)-2,2,3,3,10,10,11,11-Octamethyl-6-(3-nitrophenoxy)-5-(3-(trimethylsilyl)prop-2-yn-1-yl)-4,9-dioxa-3,10-disiladodecane (11).



To a stirred solution of **9** (1.21 g, 2.69 mmol) in dry CH_2Cl_2 was added TBSOTf (1.24 mL, 5.38 mmol) and 2, 6-lutidine (0.62 mL, 5.38 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 0.5 h. Then the reaction was quenched with H_2O and extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried over Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the resulting residue was purified by silica gel column chromatography (PE/EtOAc = 50:1) to afford **11** (1.13 g, 74%) as a yellow oil. $[\alpha]_D^{25}$ -2.9 (*c* 2.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (t, *J* = 2.4 Hz, 1H), 7.79 (ddd, *J* = 8.0, 2.0, 1.2 Hz, 1H), 7.38 (t, *J* = 8.0 Hz, 1H), 7.33 (ddd, *J* = 8.4, 2.4, 1.2 Hz, 1H), 4.79-4.75 (m, 1H), 4.01-3.97 (m, 1H), 3.76-3.71 (m, 1H), 3.65 (dt, *J* = 9.6, 4.0 Hz, 1H), 2.59 (dd, *J* = 16.8, 5.2 Hz, 1H), 2.42 (dd, *J* = 16.8, 6.4 Hz, 1H), 2.02-1.93 (m, 1H), 1.81-1.73 (m, 1H), 0.88 (s, 9H), 0.84 (s, 9H), 0.12 (s, 3H), 0.12 (s, 9H), 0.05 (s, 3H), -0.01 (s, 3H), -0.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0, 149.1, 129.8, 122.4, 115.6, 110.5, 103.6, 86.8, 71.7, 58.5, 32.7, 25.8, 25.7, 24.6, 18.2, 18.0, -0.1, -4.4, -4.7, -5.5, -5.7 (one signal was overlapped with $CDCl_3$ solvent peaks); IR(KBr): 2956, 2930, 1533, 1250, 1106, 840,

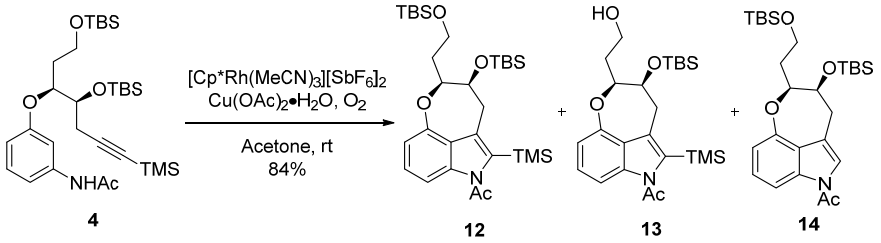
777, 737 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{28}H_{51}NO_5NaSi_3$ $(M + Na)^+$ 588.2973, found 588.2973.

***N*-(3-(((5S,6S)-2,2,3,3,10,10,11,11-Octamethyl-5-(3-(trimethylsilyl)prop-2-yn-1-yl)-4,9-dioxa-3,10-disiladodecan-6-yl)oxy)phenyl)acetamide (4).**



To a stirred solution of **11** (1.06 g, 1.88 mmol) in dry CH_2Cl_2 (20 mL) was added activated zinc dust (8.67 g, 133 mmol). The solution was cooled down to 0 °C and HOAc (3.8 mL) was added dropwisely. After stirred for 10 min at 0 °C, the mixture was filtered through a pad of Celite and the Celite was washed with CH_2Cl_2. The filtrate was neutralized with saturated aqueous $NaHCO_3$ solution, dried over Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the resulting residue was used in the next step without further purification. To a stirred solution of the above crude product in CH_2Cl_2 was added Et_3N (0.37 mL, 2.67 mmol), Ac_2O (0.34 mL, 3.56 mmol) and DMAP (43 mg, 0.36 mmol). The reaction mixture was stirred at room temperature for 0.5 h. Then the reaction was quenched with H_2O and extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried over Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the resulting residue was purified by silica gel column chromatography (PE/EtOAc = 4:1) to afford **4** (948 mg, 87% for 2 steps) as a white amorphous. $[\alpha]_D^{25}$ -4.6 (*c* 2.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.40 (br s, 1H), 7.18-7.14 (m, 2H), 7.09 (d, J = 7.6 Hz, 1H), 6.74 (d, J = 8.0 Hz, 1H), 4.58-4.56 (m, 1H), 4.03-3.99 (m, 1H), 3.74-3.62 (m, 2H), 2.60 (dd, J = 16.8, 4.0 Hz, 1H), 2.37 (dd, J = 16.8, 7.6 Hz, 1H), 2.14 (s, 3H), 2.01-1.93 (m, 1H), 1.74-1.66 (m, 1H), 0.90 (s, 9H), 0.86 (s, 9H), 0.13 (s, 3H), 0.12 (s, 9H), 0.08 (s, 3H), -0.01 (s, 3H), -0.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 159.4, 139.1, 129.6, 112.3, 110.8, 108.1, 104.9, 85.9, 75.8, 71.4, 59.0, 32.1, 25.9, 25.8, 24.6, 23.9, 18.2, 18.1, 0.0, -4.3, -4.6, -5.5, -5.6; IR(KBr): 2955, 2929, 1698, 1598, 1551, 1252, 1100, 838, 776 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{30}H_{56}NO_4Si_3$ $(M + H)^+$ 578.3517, found 578.3517.

1-((2S,3S)-3-((*tert*-Butyldimethylsilyl)oxy)-2-(2-((tert-butyldimethylsilyl)oxy)ethyl)-5-(trimethylsilyl)-3,4-dihydrooxepino[4,3,2-*cd*]indol-6(2H)-yl)ethan-1-one (12).[2]



To a stirred solution of **4** (900 mg, 1.56 mmol) in acetone (22 mL) was added $[Cp^*Rh(MeCN)_3][SbF6]_2$ (65 mg, 0.08 mmol) and $Cu(OAc)_2 \cdot H_2O$ (62 mg, 0.31 mmol). Molecular oxygen was briefly purged through the solution (~ 1.5 min) via a balloon of oxygen. The reaction mixture was stirred at room temperature for 72 h. Then the reaction was extracted with EtOAc. The combined organic extracts were washed with brine, dried over Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the resulting residue was purified by silica gel column chromatography (PE/EtOAc = 40:1) to afford **12** (475 mg, 53%) as a white amorphous, **13** (188 mg, 26%) as a white amorphous and **14** (41 mg, 5%) as a white amorphous.

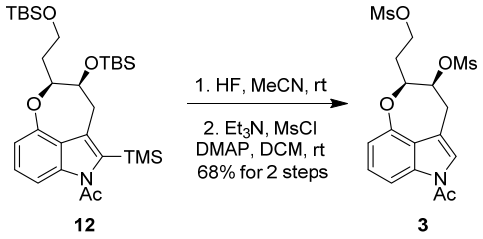
Compound **12**: $[\alpha]_D^{25}$ -10.5 (*c* 2.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, J = 8.0 Hz, 1H), 7.16 (t, J = 7.2 Hz, 1H), 6.77 (d, J = 7.6 Hz, 1H), 4.41 (d, J = 10.4 Hz, 1H), 4.30-4.27 (m, 1H), 3.85-3.74 (m, 2H), 3.31 (dd, J = 16.4, 4.8 Hz, 1H), 3.07 (dd, J = 16.0, 9.6 Hz, 1H), 2.76 (s, 3H), 2.07-2.00 (m, 1H), 1.90-1.83 (m, 1H), 0.89 (s, 9H), 0.86 (s, 9H), 0.37 (s, 9H), 0.12 (s, 6H), 0.034 (s, 3H), 0.028 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 152.1, 138.7, 135.8, 127.6, 125.6, 123.4, 112.0, 106.9, 81.6, 72.5, 59.5, 34.5, 32.4, 26.6, 25.9, 25.7, 18.3, 18.1, 3.0, -4.5, -4.8, -5.3, -5.4; IR(KBr): 2954, 2929, 1698, 1580, 1472, 1247, 1097, 837, 775 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{30}H_{54}NO_4Si_3$ $(M + H)^+$ 576.3361, found 576.3354.

Compound **13**: $[\alpha]_D^{25}$ -3.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, J = 8.4 Hz, 1H), 7.16 (t, J = 8.4 Hz, 1H), 6.76 (d, J = 7.6 Hz, 1H), 4.40 (ddd, J = 9.2, 4.0, 2.0 Hz, 1H), 4.29 (ddd, J = 9.2, 4.8, 2.0 Hz, 1H), 3.84 (t, J = 5.6 Hz, 2H), 3.34 (dd, J = 16.0, 5.2 Hz, 1H), 3.13 (dd, J = 16.4, 10.0 Hz, 1H), 2.76 (s, 3H), 2.15-2.07 (m, 2H), 1.96-1.87 (m, 1H), 0.89 (s, 9H), 0.36 (s, 9H), 0.13 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 152.1, 138.7, 136.1, 127.2, 125.7, 123.5, 111.7, 107.3, 83.9, 72.7, 60.2, 34.3, 32.8, 26.5, 25.7, 18.0, 3.0, -4.5, -4.9; IR(KBr): 2954, 2931, 1699, 1582, 1474, 1249, 1099, 837, 775 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{40}NO_4Si_2$ $(M + H)^+$ 462.2496, found 462.2492.

Compound **14**: $[\alpha]_D^{25}$ -19.2 (*c* 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.03 (d, J = 4.4 Hz, 1H), 7.21 (t, J = 5.2 Hz, 1H), 7.14 (br s, 1H), 6.79 (d, J = 5.2 Hz, 1H), 4.49-4.47 (m, 1H), 4.38 (ddd, J = 6.8, 3.2, 1.2 Hz, 1H), 3.79 (dt, J = 6.8, 3.6 Hz, 1H), 3.74-3.70 (m, 1H), 3.07 (dd, J = 11.2, 3.2 Hz, 1H), 2.99 (ddd, J = 10.8, 6.4, 1.2 Hz, 1H), 2.59 (s, 3H), 1.99-1.88 (m, 2H), 0.88 (s, 9H), 0.87 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H),

0.04 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.2, 150.1, 137.4, 126.3, 120.8, 120.7, 116.1, 112.5, 109.5, 80.7, 72.1, 59.3, 31.9, 31.0, 26.0, 25.7, 24.1, 18.3, 18.0, -4.7, -4.8, -5.37, -5.43; IR(KBr): 2952, 2927, 1710, 1571, 1471, 1246, 1084, 834, 774 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{27}H_{46}NO_4Si_2$ $(M + H)^+$ 504.2965, found 504.2974.

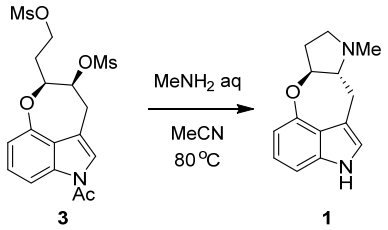
(2S,3S)-6-Acetyl-2-(2-((methylsulfonyl)oxy)ethyl)-2,3,4,6-tetrahydrooxepino[4,3,2-*cd*]indol-3-yl methanesulfonate (3).



To a stirred solution of **12** (132 mg, 0.23 mmol) in MeCN (2 mL) was added HF (0.25 mL). The reaction mixture was stirred at room temperature for 12 h. Then the reaction was extracted with EtOAc. The combined organic extracts were washed with brine, dried over Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the resulting residue was used in the next step without purification. To a stirred solution of the above crude product in CH_2Cl_2 was added Et_3N (0.2 mL, 1.37 mmol), MsCl (0.1 mL, 1.37 mmol), and DMAP (5 mg, 0.04 mmol). The reaction mixture was stirred at room temperature for 1 h. Then the reaction was quenched with H_2O and extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried over Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the resulting residue was purified by silica gel column chromatography (CH_2Cl_2/EtOAc = 16:1) to afford **3** (67 mg, 68% for 2 steps) as a white solid. $[\alpha]_D^{25}$ -46.8 (*c* 0.5, $CHCl_3$); m.p. 135-136 ^oC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.0 Hz, 1H), 7.28-7.24 (m, 2H), 6.87 (d, *J* = 8.0 Hz, 1H), 5.20 (t, *J* = 4.8 Hz, 1H), 4.56 (dt, *J* = 10.0, 4.0 Hz, 1H), 4.50-4.45 (m, 2H), 3.54 (dd, *J* = 17.2, 5.2 Hz, 1H), 3.26 (ddd, *J* = 17.2, 3.6, 1.6 Hz, 1H), 3.05 (s, 3H), 2.98 (s, 3H), 2.60 (s, 3H), 2.49-2.41 (m, 1H), 2.25-2.17 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 150.7, 137.5, 126.4, 122.1, 119.8, 114.0, 111.9, 110.8, 78.1, 77.5, 66.1, 38.8, 37.3, 32.9, 31.6, 24.0; IR(KBr): 2930, 2853, 1708, 1340, 1254, 1173, 979, 909, 742, 529 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{17}H_{22}NO_8S_2$ $(M + H)^+$ 432.0787, found 432.0790.

Compound **13** and **14** could be converted to **3** following the same procedure.

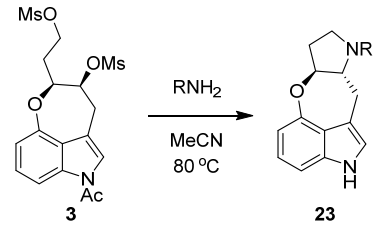
(6aS,9aR)-9-Methyl-6a,7,8,9,9a,10-hexahydro-2H-pyrrolo[2',3':6,7]oxepino[4,3,2-*cd*]indole (1).[3]



3 1

To a stirred solution of **3** (268 mg, 0.62 mmol) in MeCN (16 mL) was added aqueous methylamine (40%, 0.4 mL). The reaction mixture was stirred at 80 °C for 12 h. Then the reaction was extracted with EtOAc. The combined organic extracts were washed with brine, dried over Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the resulting residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH = 20:1) to afford **1** (136 mg, 96%) as a light yellow solid. $[\alpha]_D^{25}$ -194 (*c* 1.0, MeOH); m.p. 234-235 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (br s, 1H), 7.07 (t, *J* = 8.0 Hz, 1H), 7.00 (s, 1H), 6.98 (d, *J* = 8.4 Hz, 1H), 6.63 (d, J = 7.6 Hz, 1H), 4.49-4.45 (m, 1H), 3.42 (dd, *J* = 14.4, 2.8Hz, 1H), 3.11 (t, *J* = 8.0 Hz, 1H), 2.69-2.47 (m, 4H), 2.43 (s, 3H), 2.11-2.06 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.8, 138.7, 122.8, 120.1, 117.1, 111.0, 106.1, 104.0, 86.6, 72.9, 55.6, 40.5, 30.8, 29.2; IR(KBr): 3146, 3099, 3062, 3034, 1621, 1514, 1458, 1344, 1294, 1243, 1066, 777, 741 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{14}H_{17}N_2O$ $(M + H)^+$ 229.1341, found 229.1348.

Preparation of analogues of ht-13-A



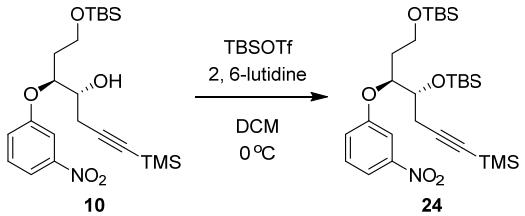
3 23

Compound **23a** (R = *n*-Pr): Compound **3** was treated with the procedure described for **1** to afford compound **23a** as a light yellow solid in 88% yield. Purification by silica gel column chromatography (CH_2Cl_2/MeOH = 20:1). $[\alpha]_D^{25}$ -176.4 (*c* 1.0, $CDCl_3$); m.p. 150-151 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (br s, 1H), 7.07 (t, *J* = 8.0 Hz, 1H), 6.98-6.96 (m, 2H), 6.64 (d, *J* = 7.6 Hz, 1H), 4.47-4.46 (m, 1H), 3.48-3.40 (m, 1H), 3.24-3.22 (m, 1H), 2.88-2.81 (m, 1H), 2.70-2.62 (m, 2H), 2.52-2.42 (m, 2H), 2.20-2.10 (m, 2H), 1.64-1.50 (m, 2H), 0.96 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.8, 138.7, 122.7, 120.1, 117.1, 111.1, 106.0, 104.0, 86.4, 71.8, 56.2, 52.1, 30.7, 29.4, 21.2, 12.1; IR(KBr): 3151, 3104, 2927, 1621, 1505, 1445, 1349, 1288, 1247, 1066, 773, 747 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{16}H_{21}N_2O$ $(M + H)^+$ 257.1654, found 257.1654.

Compound **23b** (R = *n*-Bu): Compound **3** was treated with the procedure described for **1** to afford compound **23b** as a light yellow amorphous in 92% yield. Purification by silica gel column chromatography (CH_2Cl_2/MeOH = 20:1). $[\alpha]_D^{25}$ -138.4 (*c* 1.0, $CDCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.23 (br s, 1H), 7.07 (t, *J* = 8.0 Hz, 1H), 6.98-6.96 (m, 2H), 6.64 (d, *J* = 7.6 Hz, 1H), 4.49-4.45 (m, 1H), 3.48-3.40 (m, 1H), 3.26-3.22 (m, 1H), 2.91 (dt, *J* = 11.2, 6.4 Hz, 1H), 2.70-2.62 (m, 2H), 2.54-2.42 (m, 2H), 2.22-2.10 (m, 2H), 1.61-1.47 (m, 2H), 1.43-1.33 (m, 2H), 0.96 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.8, 138.7, 122.7, 120.1, 117.1, 111.1, 106.0, 104.0, 86.4, 71.8, 53.9, 52.1, 30.7, 30.1, 29.4, 20.9, 14.0; IR(KBr): 3159, 3112, 3057, 1621, 1501, 1442, 1349, 1286, 1247, 1069, 777, 744 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{17}H_{23}N_2O$ $(M + H)^+$ 271.1810, found 271.1813.

Compound **23c** (R = Bn): Compound **3** was treated with the procedure described for **1** to afford compound **23c** as a light yellow solid in 90% yield. Purification by silica gel column chromatography (CH_2Cl_2/MeOH = 20:1). $[\alpha]_D^{25}$ -110.8 (*c* 1.0, $CDCl_3$); m.p. 151-152 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 8.13 (br s, 1H), 7.35-7.28 (m, 5H), 7.09 (t, *J* = 8.0 Hz, 1H), 7.00-6.98 (m, 2H), 6.65 (d, *J* = 7.6 Hz, 1H), 4.52-4.51 (m, 1H), 4.13 (d, *J* = 12.8 Hz, 1H), 3.54 (d, *J* = 12.8 Hz, 1H), 3.33 (d, *J* = 12.8 Hz, 1H), 2.97 (t, *J* = 8.0 Hz, 1H), 2.85-2.73 (m, 2H), 2.54-2.38 (m, 2H), 2.08-2.04 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.8, 138.7, 138.4, 129.1, 128.3, 127.1, 122.8, 120.1, 117.1, 111.0, 106.0, 104.0, 86.5, 71.1, 58.2, 52.2, 30.5, 29.5; IR(KBr): 3152, 3105, 3055, 3027, 1620, 1508, 1453, 1344, 1291, 1240, 1068, 777, 747 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{20}H_{21}N_2O$ $(M + H)^+$ 305.1654, found 305.1651.

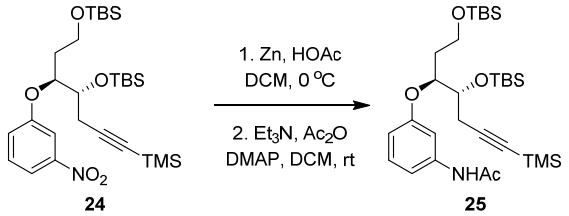
(5R,6S)-2,2,3,3,10,10,11,11-Octamethyl-6-(3-nitrophenoxy)-5-(3-(trimethylsilyl)prop-2-yn-1-yl)-4,9-dioxa-3,10-disiladodecane (24).



Compound **10** was treated with the procedure described for **11** to afford compound **24** as a yellow oil in 90% yield. Purification by silica gel column chromatography (PE/EtOAc = 50:1). $[\alpha]_D^{25}$ -5.9 (*c* 2.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.79 (d, *J* = 7.2 Hz, 1H), 7.41-7.35 (m, 2H), 4.85-4.82 (m, 1H), 4.06 (dt, *J* = 7.2, 2.4 Hz, 1H), 3.79-3.74 (m, 1H), 3.71-3.65 (m, 1H), 2.52-2.41 (m, 2H), 1.90-1.89 (m, 2H), 0.85 (s, 9H), 0.84 (s, 9H), 0.16 (s, 9H), 0.02 (s, 3H), 0.01 (s, 3H), 0.00 (s, 3H), -0.07 (s, 3H); ^{13}C NMR

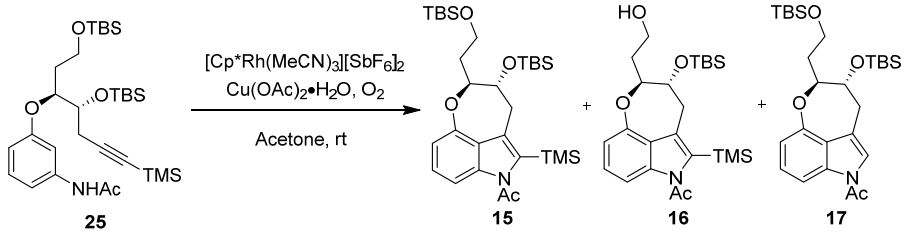
(100 MHz, $CDCl_3$) δ 159.5, 149.3, 129.9, 121.9, 115.5, 110.9, 102.9, 87.2, 77.3, 72.0, 28.7, 32.3, 25.9, 25.7, 25.3, 18.2, 18.0, -0.1, -4.65, -4.74, -5.4, -5.5; IR(KBr): 2955, 2929, 1533, 1250, 1097, 839, 777, 737 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{28}H_{51}NO_5NaSi_3$ $(M + Na)^+$ 588.2973, found 588.2969.

_N_-(3-(((5R,6S)-2,2,3,3,10,10,11,11-Octamethyl-5-(3-(trimethylsilyl)prop-2-yn-1-yl)-4,9-dioxa-3,10-disiladodecan-6-yl)oxy)phenyl)acetamide (25).



Compound **24** was treated with the procedure described for **4** to afford compound **25** as a white amorphous in 88% yield. Purification by silica gel column chromatography (PE/EtOAc = 4:1). $[\alpha]_D^{25}$ -8.9 (*c* 2.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.35 (br s, 1H), 7.18-7.15 (m, 2H), 7.05 (s, 1H), 6.79 (d, *J* = 6.4 Hz, 1H), 4.67-4.65 (m, 1H), 4.08 (dt, *J* = 6.8, 2.4 Hz, 1H), 3.77-3.66 (m, 2H), 2.44-2.41 (m, 2H), 2.14 (s, 3H), 1.89-1.83 (m, 2H), 0.87 (s, 9H), 0.86 (s, 9H), 0.16 (s, 9H), 0.03 (s, 3H), 0.01 (s. 3H), 0.00 (s, 3H), -0.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 159.2, 139.0, 129.6, 112.2, 110.5, 108.1, 103.6, 86.7, 76.1, 71.9, 59.1, 32.2, 25.9, 25.8, 25.5, 24.6, 18.2, 18.1, 0.0, -4.6, -4.8, -5.4, -5.5; IR(KBr): 2956, 2930, 1667, 1609, 1553, 1252, 1097, 840, 777 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{30}H_{56}NO_4Si_3$ $(M + H)^+$ 578.3517, found 578.3516.

1-((2S,3R)-3-((*tert*-Butyldimethylsilyl)oxy)-2-(2-((tert-butyldimethylsilyl)oxy)ethyl)-5-(trimethylsilyl)-3,4-dihydrooxepino[4,3,2-*cd*]indol-6(2H)-yl)ethan-1-one (15).[2]



Compound **25** was treated with the procedure described above to afford compound **15** as a white amorphous in 44% yield, compound **16** as a white amorphous in 26% yield and compound **17** as a white amorphous in 7% yield. Purification by silica gel column chromatography (PE/EtOAc = 40:1 to 10:1 to 4:1).

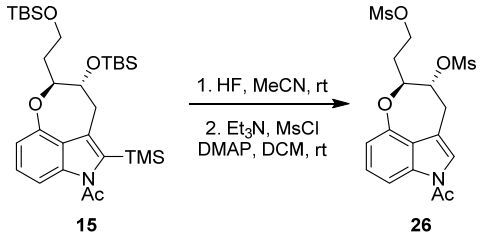
Compound **15**: $[\alpha]_D^{25}$ -45.5 (*c* 2.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.0 Hz, 1H), 7.17

(t, *J* = 8.0 Hz, 1H), 6.76 (d, *J* = 7.6 Hz, 1H), 4.20-4.16 (m, 1H), 4.01-3.96 (m, 1H), 3.90-3.87 (m, 2H), 3.33 (dd, *J* = 16.0, 3.2 Hz, 1H), 3.12 (dd, *J* = 16.0, 8.4 Hz, 1H), 2.77 (s, 3H), 2.16-2.09 (m, 1H), 1.87-1.79 (m, 1H), 0.91 (s, 9H), 0.87 (s, 9H), 0.36 (s, 9H), 0.14 (s, 3H), 0.11 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 152.5, 138.8, 136.0, 128.0, 125.5, 123.3, 111.8, 107.4, 84.1, 74.5, 59.7, 36.3, 35.9, 26.5, 25.9, 25.8, 18.3, 18.0, 2.93, -4.4, -4.7, -5.25, -5.28; IR(KBr): 2954, 2929, 1698, 1582, 1472, 1251, 1097, 837, 775 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{30}H_{54}NO_4Si_3$ $(M + H)^+$ 576.3361, found 576.3365.

Compound **16**: $[\alpha]_D^{25}$ -71.9 (*c* 2.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, *J* = 8.0 Hz, 1H), 7.18 (t, *J* = 8.0 Hz, 1H), 6.77 (d, *J* = 8.0 Hz, 1H), 4.22 (ddd, *J* = 10.0, 7.2, 2.8 Hz, 1H), 4.01 (ddd, *J* = 10.8, 7.2, 4.0 Hz, 1H), 3.92 (t, *J* = 5.6 Hz, 2H), 3.36 (dd, *J* = 16.0, 4.0 Hz, 1H), 3.08 (dd, *J* = 16.0, 8.8 Hz, 1H), 2.77 (s, 3H), 2.23-2.15 (m, 1H), 2.07 (br s, 1H), 2.00-1.91 (m, 1H), 0.91 (s, 9H), 0.36 (s, 9H), 0.14 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 152.2, 138.9, 136.4, 127.2, 125.6, 122.7, 111.3, 107.6, 86.2, 74.3, 60.6, 36.7, 35.2, 26.6, 25.8, 18.0, 2.9, -4.4, -4.7; IR(KBr): 2952, 2930, 1697, 1582, 1473, 1255, 1094, 838, 774 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{40}NO_4Si_2$ $(M + H)^+$ 462.2496, found 462.2484.

Compound **17**: $[\alpha]_D^{25}$ -65.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 6.8 Hz, 1H), 7.21 (t, *J* = 8.0 Hz, 1H), 7.16 (br s, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 4.22-4.17 (m, 1H), 4.06-4.01 (m, 1H), 3.90-3.87 (m, 2H), 3.20 (dd, *J* = 16.4, 3.6 Hz, 1H), 2.91 (ddd, *J* = 16.0, 9.2, 1.2 Hz, 1H), 2.60 (s, 3H), 2.22-2.14 (m, 1H), 1.89-1.81 (m, 1H), 0.91 (s, 9H), 0.84 (s, 9H), 0.12 (s, 6H), 0.03 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 151.9, 137.4, 126.1, 120.8, 120.2, 116.3, 111.7, 109.8, 83.9, 74.0, 59.6, 35.4, 34.7, 25.9, 25.8, 24.1, 18.3, 18.0, -4.5, -4.8, -5.28, -5.30; IR(KBr): 2955, 2930, 1706, 1592, 1473, 1257, 1081, 840, 776 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{27}H_{46}NO_4Si_2$ $(M + H)^+$ 504.2965, found 504.2960.

(2S,3R)-6-Acetyl-2-(2-((methylsulfonyl)oxy)ethyl)-2,3,4,6-tetrahydrooxepino[4,3,2-*cd*]indol-3-yl methanesulfonate (26).

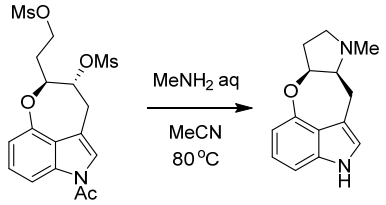


15 **26**

Compound **15** was treated with the procedure described for **3** to afford compound **26** as a white solid in 73% yield. Purification by silica gel column chromatography (CH_2Cl_2/EtOAc = 16:1). $[\alpha]_D^{25}$ -58.3 (*c* 2.0,

$CHCl_3$); m.p. 160-161 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 8.4 Hz, 1H), 7.24-7.22 (m, 2H), 6.86 (d, J = 7.6 Hz, 1H), 5.09 (dt, J = 6.8, 4.4 Hz, 1H), 4.57-4.41 (m, 3H), 3.50 (dd, J = 16.4, 3.2 Hz, 1H), 3.30 (dd, J = 16.4, 7.2 Hz, 1H), 3.10 (s, 3H), 2.97 (s, 3H), 2.60 (s, 3H), 2.38-2.30 (m, 1H), 2.27-2.19 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 150.8, 137.2, 126.5, 121.8, 120.6, 113.7, 112.1, 111.3, 79.9, 79.8, 65.7, 38.8, 37.3, 31.6, 31.0, 24.0; IR(KBr): 2937, 1733, 1707, 1432, 1357, 1249, 1174, 743, 528 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{17}H_{22}NO_8S_2$ $(M + H)^+$ 432.0787, found 432.0781.

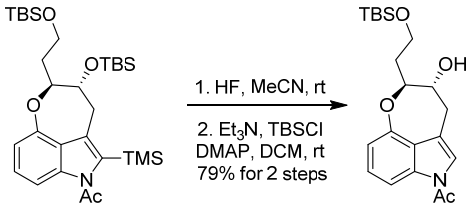
(6aS,9aS)-9-Methyl-6a,7,8,9,9a,10-hexahydro-2H-pyrrolo[2',3':6,7]oxepino[4,3,2-*cd*]indole (19).[3]



26 **19**

Compound **26** was treated with the procedure described for **1** to afford compound **19** as a light yellow solid in 96% yield. Purification by silica gel column chromatography (CH_2Cl_2/MeOH = 20:1). $[\alpha]_D^{25}$ -47.6 (*c* 1.0, MeOH); m.p. 229-230 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (br s, 1H), 7.02-7.01 (m, 2H), 6.87 (br s, 1H), 6.62 (dd, J = 4.4, 3.6 Hz, 1H), 4.74 (m, 1H), 3.25-3.15 (m, 2H), 3.10 (dd, J = 14.0, 5.6 Hz, 1H), 2.53-2.47 (m, 1H), 2.41 (s, 3H), 2.39-2.34 (m, 1H), 2.25-2.15 (m, 1H), 2.11-2.04 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.9, 137.7, 123.1, 122.3, 119.0, 112.4, 108.2, 106.4, 87.1, 71.7, 54.6, 40.7, 31.6, 26.7; IR(KBr): 3144, 2927, 2842, 2780, 1622, 1502, 1437, 1348, 1290, 1235, 1050, 789, 745 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{14}H_{17}N_2O$ $(M + H)^+$ 229.1341, found 229.1339.

1-((2S,3R)-2-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-3-hydroxy-3,4-dihydrooxepino[4,3,2-*cd*]indol-6(2H)-yl)ethan-1-one (20).

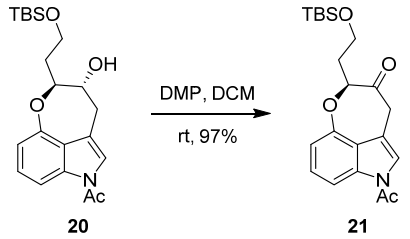


15 **20**

To a stirred solution of **15** (93 mg, 0.16 mmol) in MeCN (1.5 mL) was added HF (0.18 mL). The reaction mixture was stirred at room temperature for 12 h. Then the reaction was extracted with EtOAc. The combined organic extracts were washed with brine, dried over Na_2SO_4 and filtered. The filtrate was

concentrated under reduced pressure and the resulting residue was used in the next step without purification. To a stirred solution of the above crude product in CH_2Cl_2 was added Et_3N (0.026 mL, 0.19 mmol), TBSCl (29 mg, 0.19 mmol), and DMAP (4 mg, 0.03 mmol). The reaction mixture was stirred at room temperature for 24 h. Then the reaction was quenched with H_2O and extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried over Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the resulting residue was purified by silica gel column chromatography (PE/EtOAc = 5:2) to afford **20** (49 mg, 79% for 2 steps) as a white solid. $[\alpha]_D^{25}$ -23.4 (*c* 1.0, $CHCl_3$); m.p. 117-118 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.0 Hz, 1H), 7.22 (t, *J* = 8.0 Hz, 1H), 7.20 (s, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 4.43 (d, *J* = 3.6 Hz. 1H), 4.28-4.24 (m, 1H), 4.17 (dt, *J* = 10.0, 1.6 Hz, 1H), 4.12-4.07 (m, 1H), 3.83-3.79 (m, 1H), 3.33 (dd, *J* = 16.4, 3.6 Hz, 1H), 2.90 (ddd, *J* = 16.0, 10.4, 1.6 Hz, 1H), 2.60 (s, 3H), 2.40-2.32 (m, 1H), 2.09-2.05 (m, 1H), 0.92 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 151.4, 137.6, 126.1, 121.2, 119.5, 116.0, 111.7, 109.8, 84.1, 71.9, 58.3, 33.9, 33.1, 25.8, 24.1, 18.2, -5.6, -5.7; IR(KBr): 2953, 2929, 1698, 1573, 1472, 1258, 1081, 835, 778 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{32}NO_4Si$ $(M + H)^+$ 390.2101, found 390.2091.

(S)-6-Acetyl-2-(2-((tert-butyldimethylsilyl)oxy)ethyl)-4,6-dihydrooxepino[4,3,2-*cd*]indol-3(2H)-one (21)

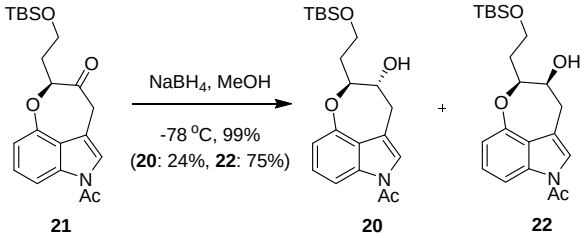


20 **21**

To a stirred solution of **19** (67 mg, 0.17 mmol) in DCM (4 mL) was added DMP (146 mg, 0.34 mmol). The reaction mixture was stirred at room temperature for 0.5 h. Then the reaction was extracted with EtOAc. The combined organic extracts were washed with saturated aqueous $NaHCO_3$ solution, dried over Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the resulting residue was purified by silica gel column chromatography (PE/EtOAc = 5:1) to afford **21** (64 mg, 97%) as yellow oil. $[\alpha]_D^{25}$ -51.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.0 Hz, 1H), 7.27 (t, *J* = 8.0 Hz, 1H), 7.16 (br s, 1H), 6.92 (d, *J* = 8.0 Hz, 1H), 4.64 (dd, *J* = 7.6, 4.4 Hz. 1H), 4.34 (dd, *J* = 14.0, 2.0 Hz, 1H), 3.97-3.86 (m, 2H), 3.77 (d, *J* = 14.0 Hz, 1H), 2.60 (s, 3H), 2.24-2.17 (m, 1H), 2.14-2.06 (m, 1H), 0.87 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.7, 168.2, 151.9, 136.8, 126.8, 123.3, 120.1, 113.7,

112.8, 112.6, 87.0, 58.4, 40.7, 35.8, 25.9, 23.9, 18.3, -5.40, -5.42; IR(KBr): 2954, 2929, 1715, 1573, 1490, 1254, 1096, 836, 778 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{30}NO_4Si$ $(M + H)^+$ 388.1944, found 388.1937.

1-((2S,3S)-2-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-3-hydroxy-3,4-dihydrooxepino[4,3,2-*cd*]indol-6(2H)-yl)ethan-1-one (22)



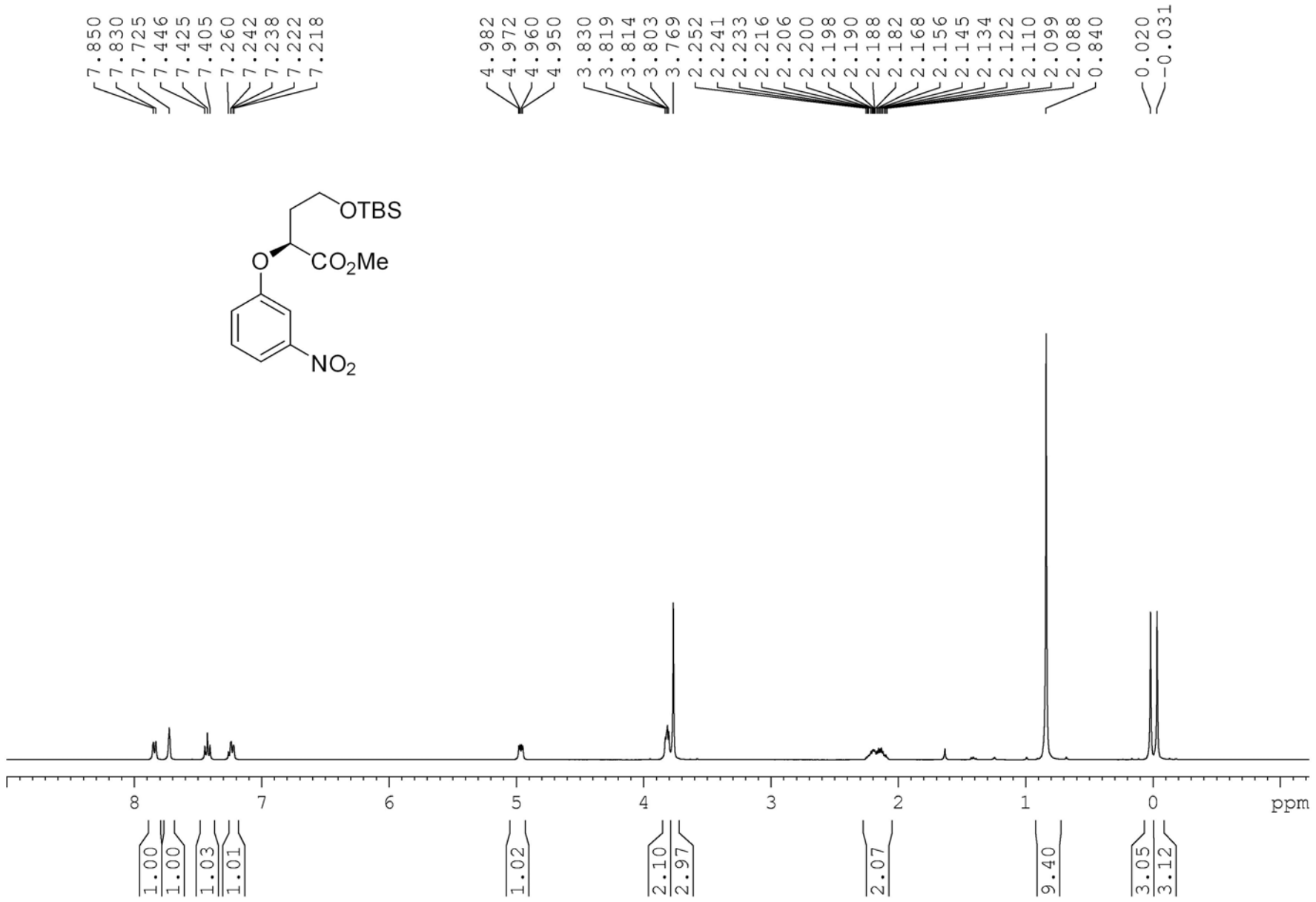
21 **20** **22**

To a stirred solution of **21** (64 mg, 0.16 mmol) in MeOH was added $NaBH_4$ (13 mg, 0.34 mmol). The reaction mixture was stirred at -78 °C for 0.5 h. Then the reaction was quenched with H_2O and extracted with EtOAc. The combined organic extracts were washed with brine, dried over Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the resulting residue was purified by silica gel column chromatography (PE/EtOAc = 5:2) to afford **20** (15 mg, 24%) and **22** (48 mg, 75%) as white solid. $[\alpha]_D^{25}$ -33.2 (*c* 1.0, $CHCl_3$); m.p. 107-108 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, J = 8.0 Hz, 1H), 7.23 (t, J = 8.0 Hz, 1H), 7.19 (s, 1H), 6.86 (d, J = 8.0 Hz, 1H), 4.37 (dd, J = 7.2, 5.2 Hz. 1H), 4.22 (br s, 1H), 3.99-3.87 (m, 2H), 3.31 (dd, J = 16.8, 4.4 Hz, 1H), 3.07 (br s, 1H), 2.97 (d, J = 16.8 Hz, 1H), 2.58 (s, 3H), 2.18-2.10 (m, 1H), 2.07-1.99 (m, 1H), 0.87 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 151.4, 137.7, 126.0, 121.9, 119.9, 116.5, 112.0, 110.2, 80.2, 71.1, 59.2, 37.3, 33.4, 25.9, 24.0, 18.3, -5.4; IR(KBr): 2955, 2928, 1694, 1574, 1485, 1255, 1084, 835, 777 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{32}NO_4Si$ $(M + H)^+$ 390.2101, found 390.2103.

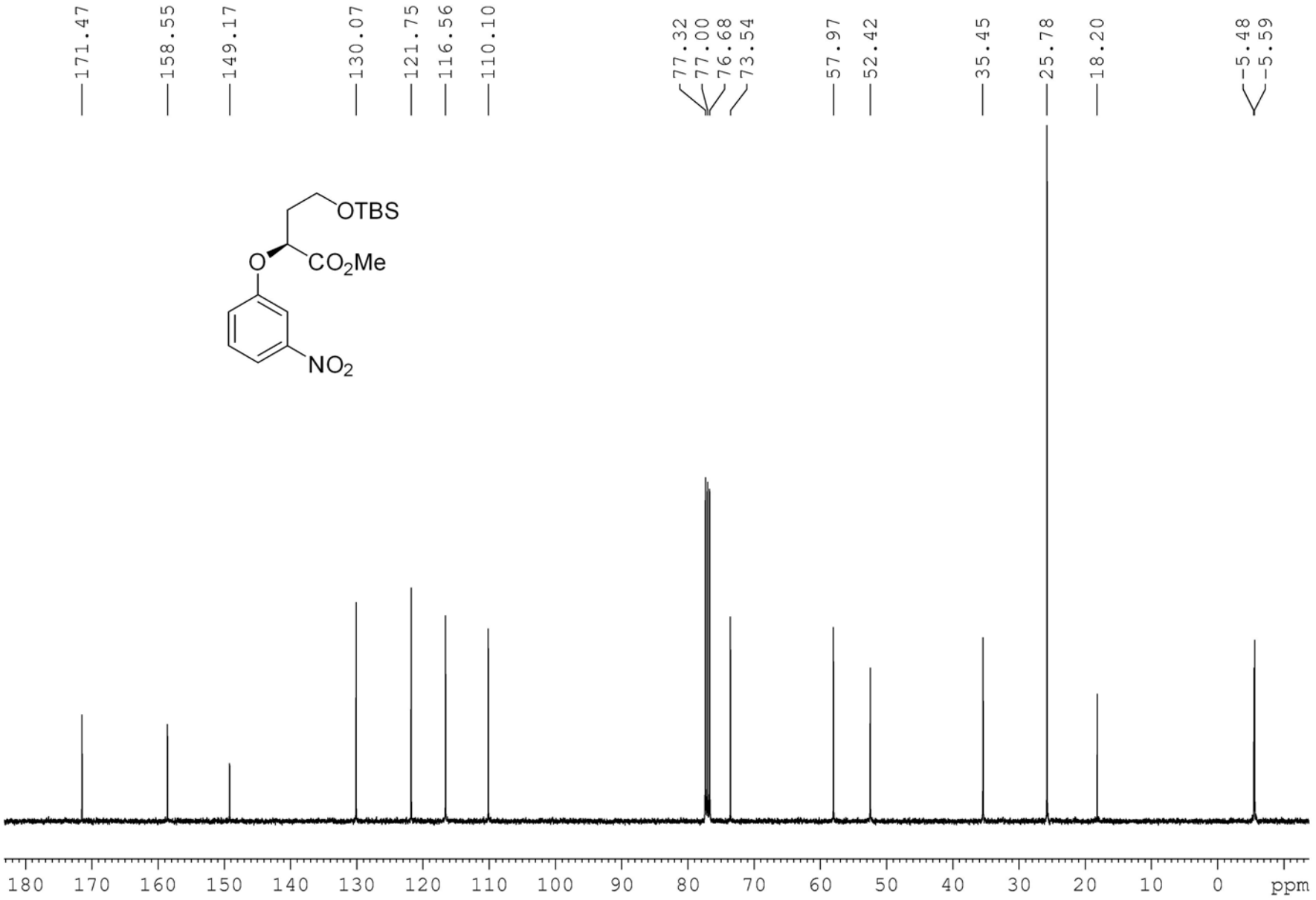
Reference:

1. Enquist, J. A.; Stoltz, B. M. *Nature*. **2008**, *453*, 1225-1231.
2. Tao, P.; Jia, Y. *Chem. Commum*. **2014**, *50(55)*, 7367-7370
3. Zhu, J.; Keltjens, R.; Firet, J. J. PCT Int Appl. (2008), WO 2008081010.

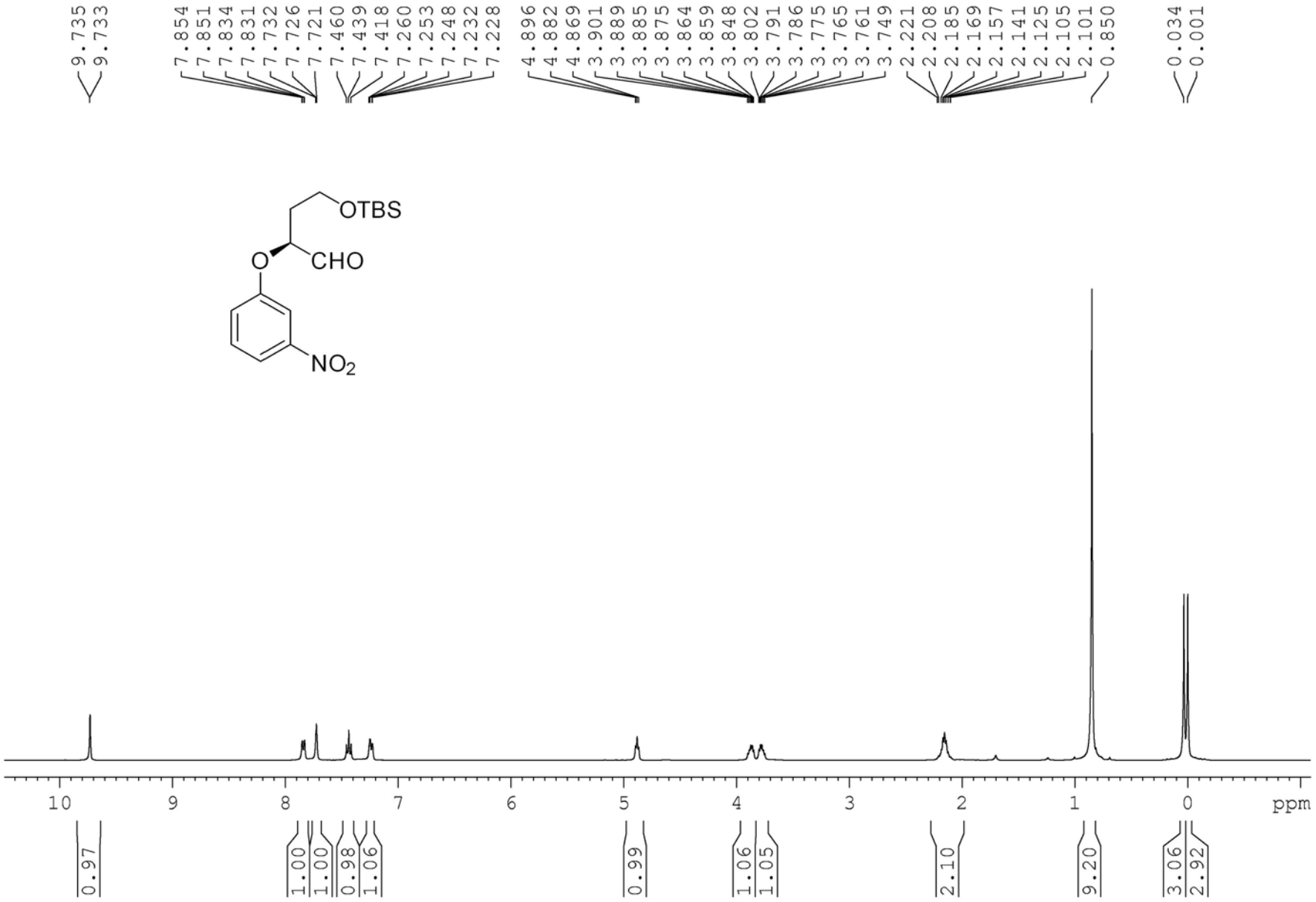
^{1}H NMR of compound 8 ($CDCl_3$; 400 MHz)



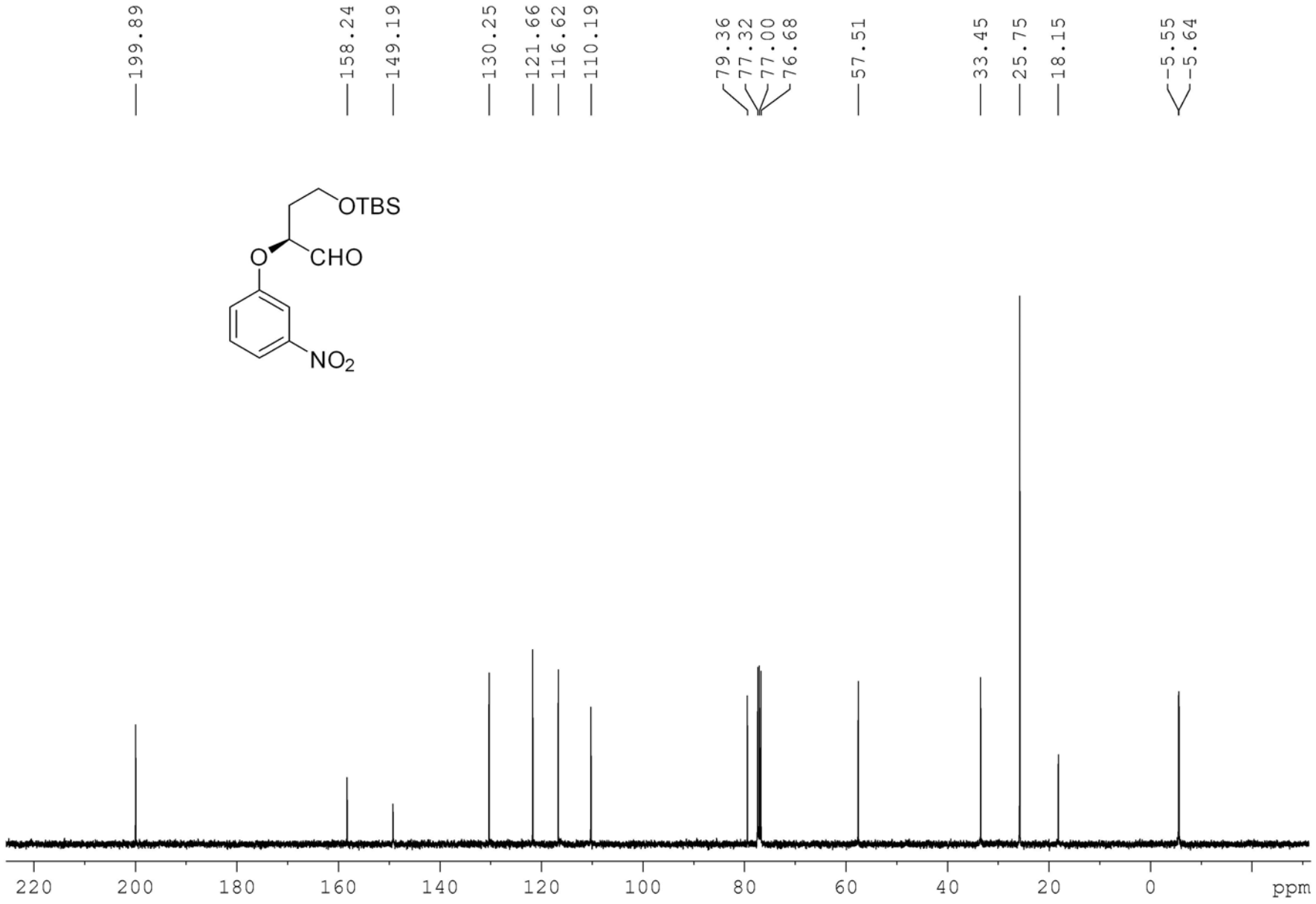
^{13}C NMR of compound 8 ($CDCl_3$; 100 MHz)



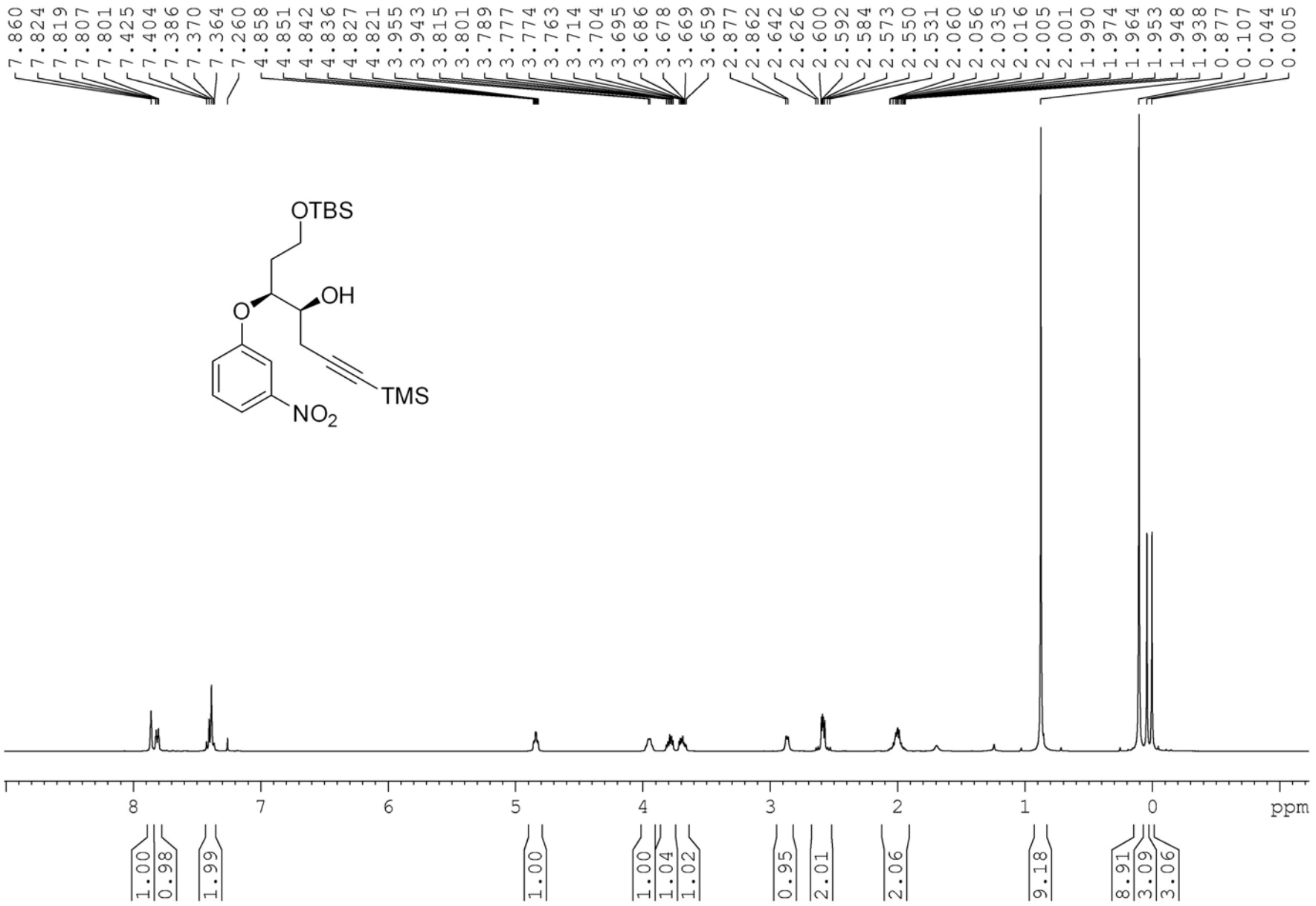
^{1}H NMR of compound 5 ($CDCl_3$; 400 MHz)



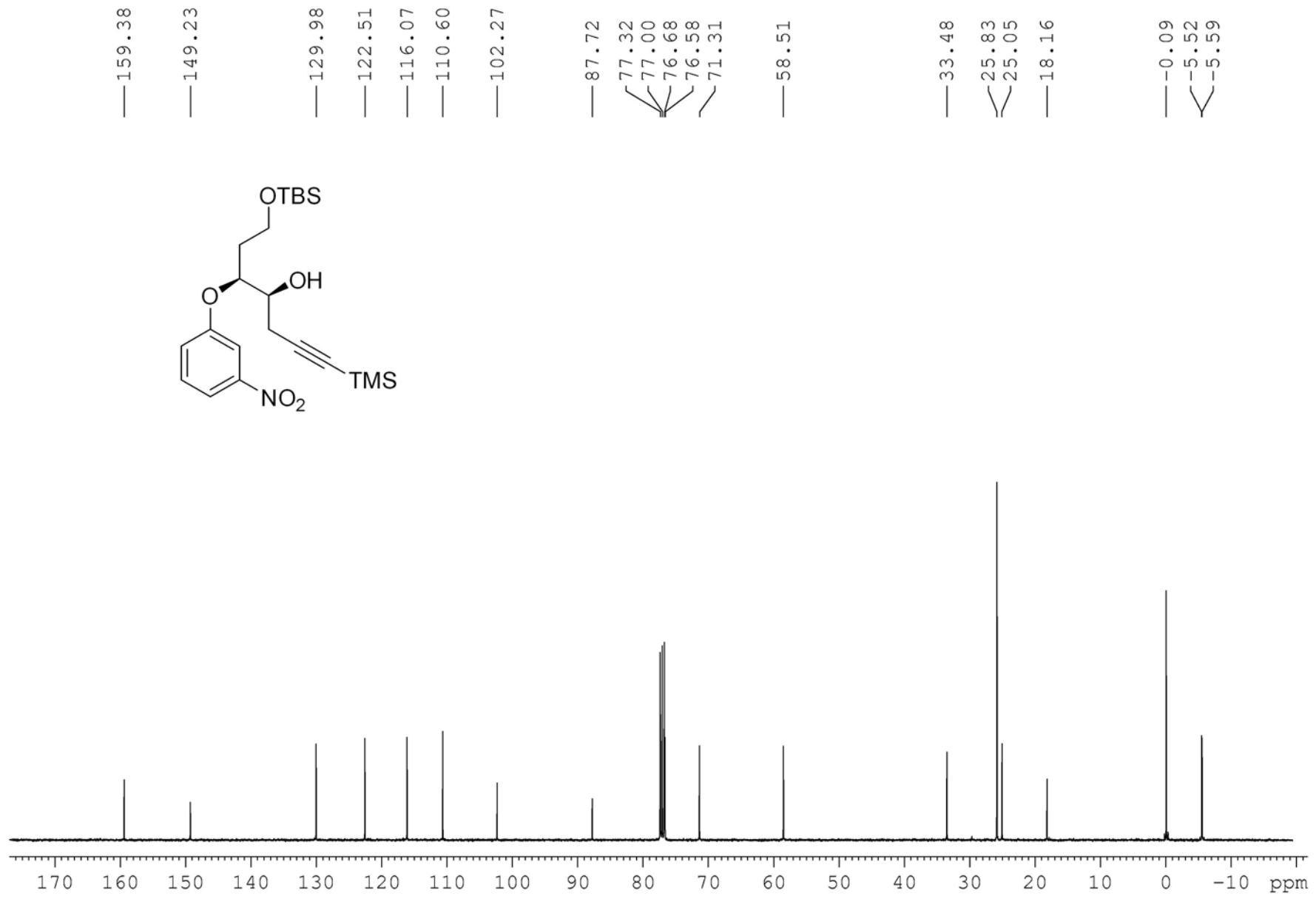
^{13}C NMR of compound 5 ($CDCl_3$; 100 MHz)



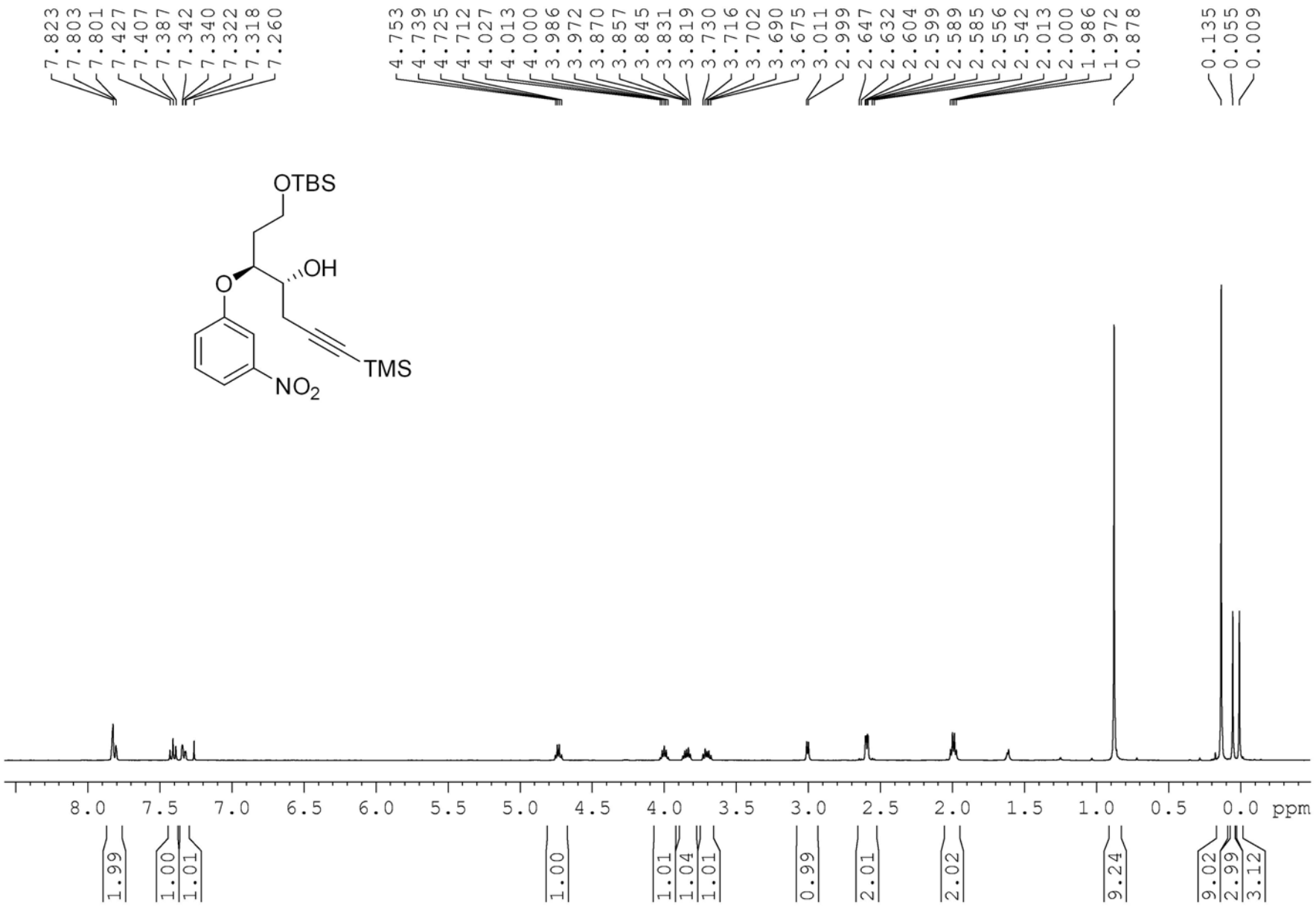
^{1}H NMR of compound 9 ($CDCl_3$; 400 MHz)



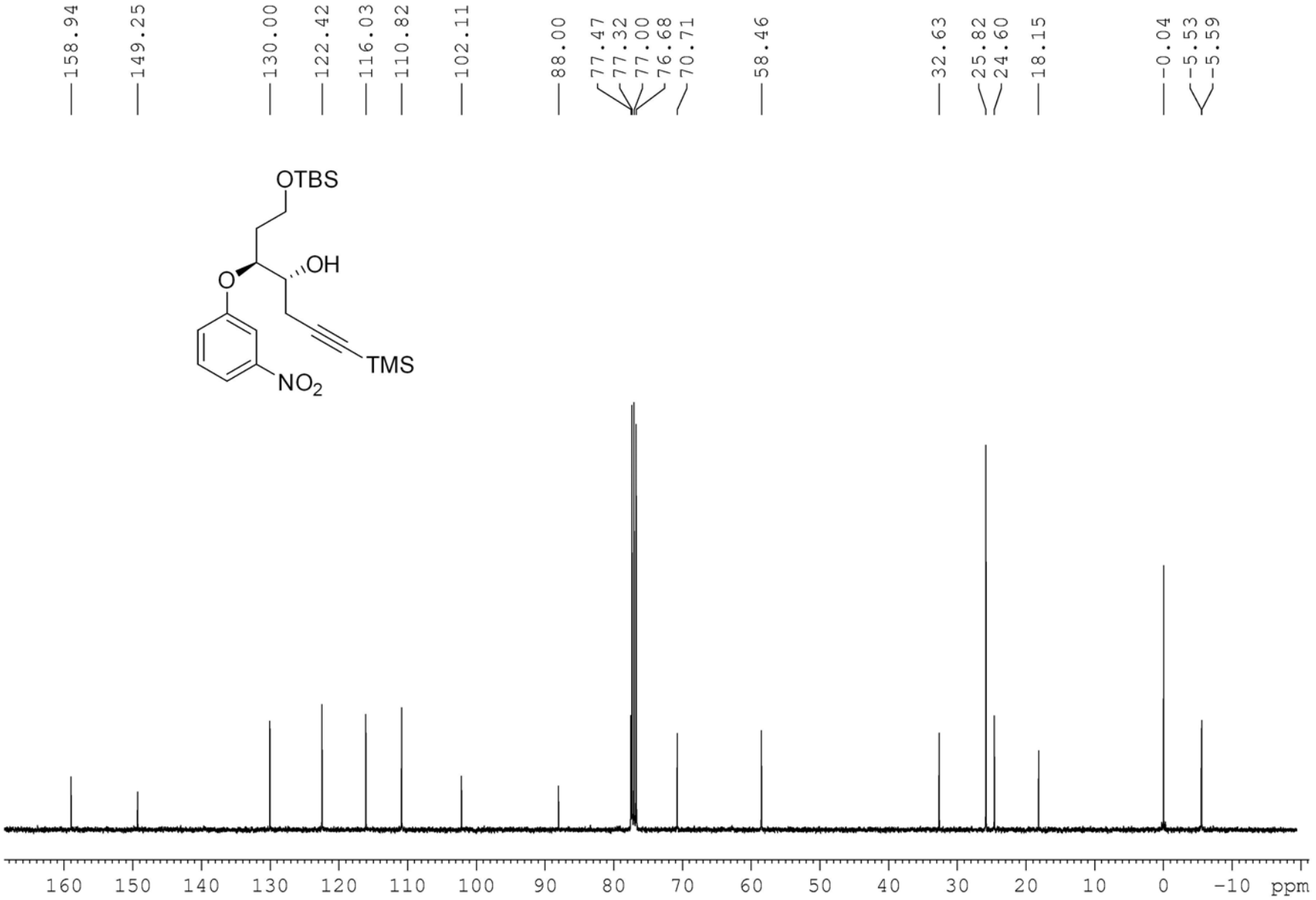
^{13}C NMR of compound 9 ($CDCl_3$; 100 MHz)



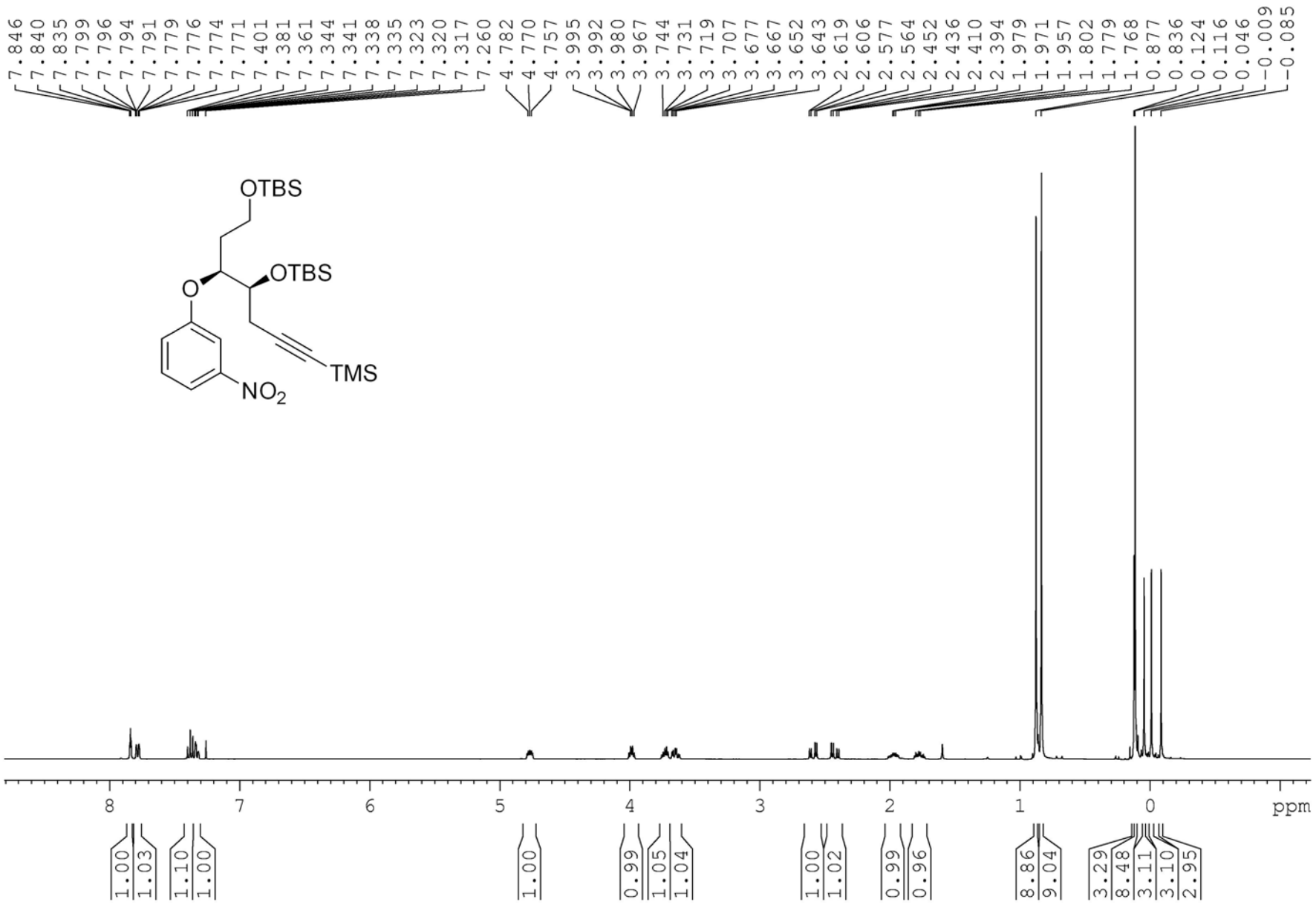
^{1}H NMR of compound 10 ($CDCl_3$; 400 MHz)



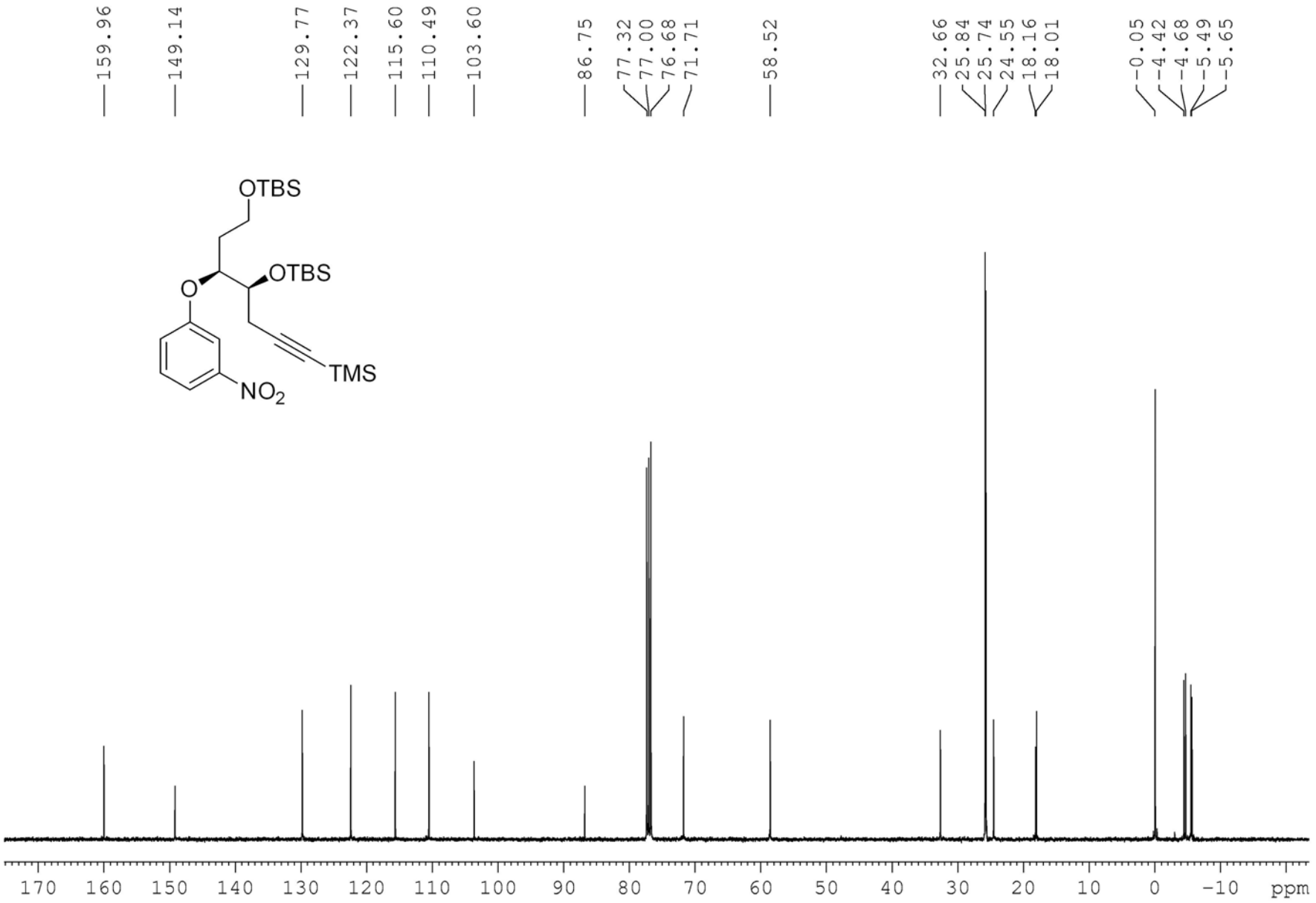
^{13}C NMR of compound 10 ($CDCl_3$; 100 MHz)



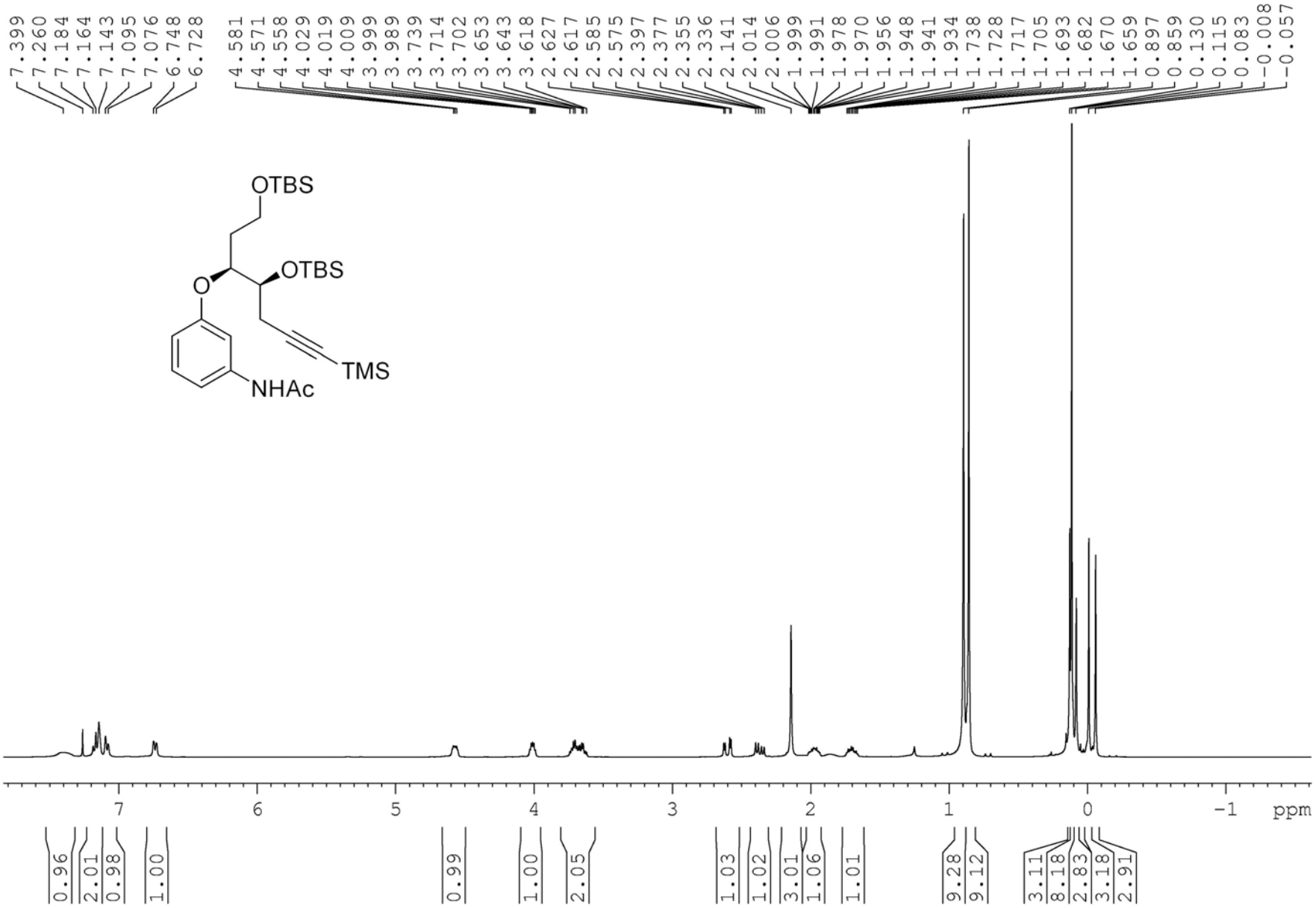
^{1}H NMR of compound 11 ($CDCl_3$; 400 MHz)



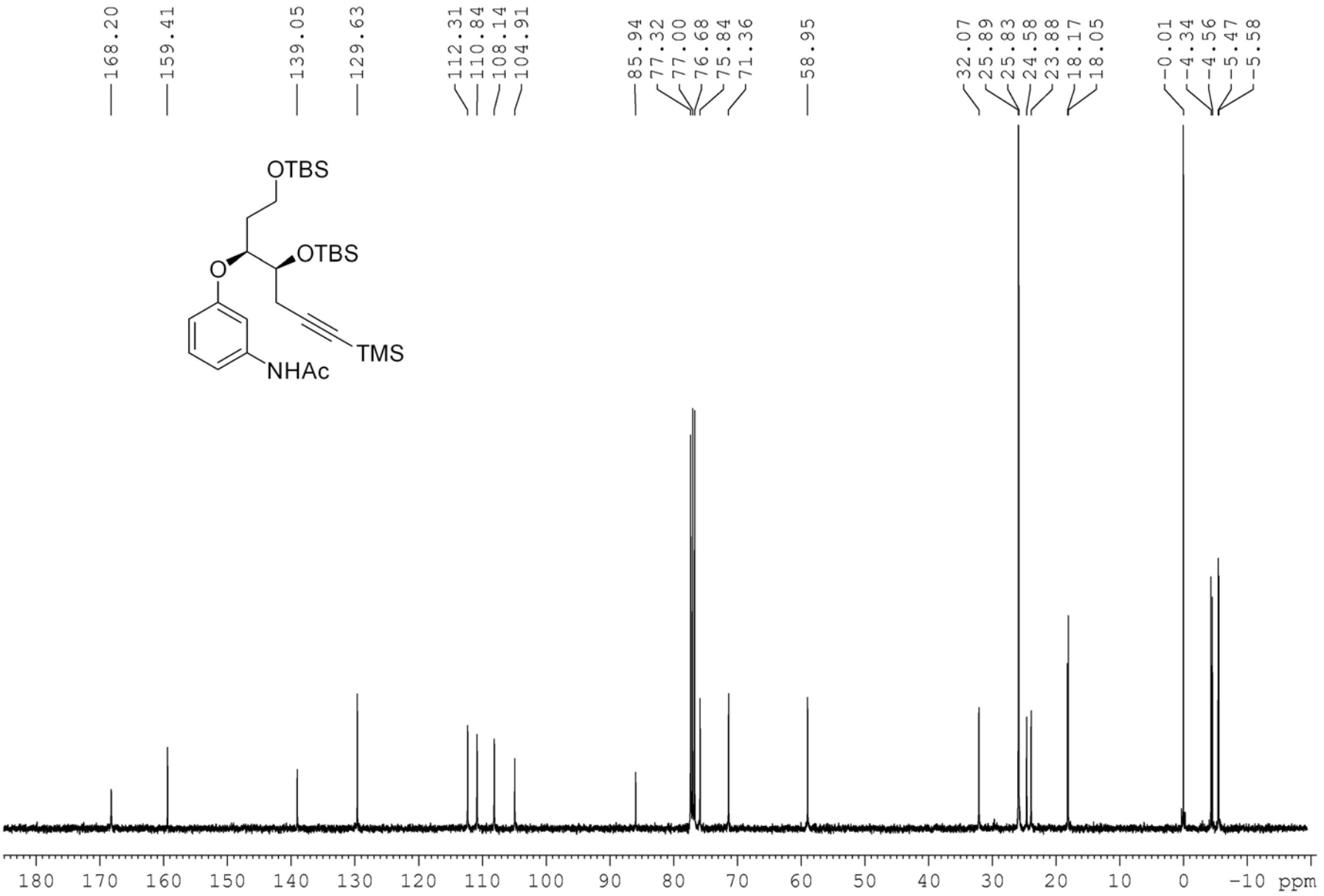
^{13}C NMR of compound 11 ($CDCl_2$; 100 MHz)



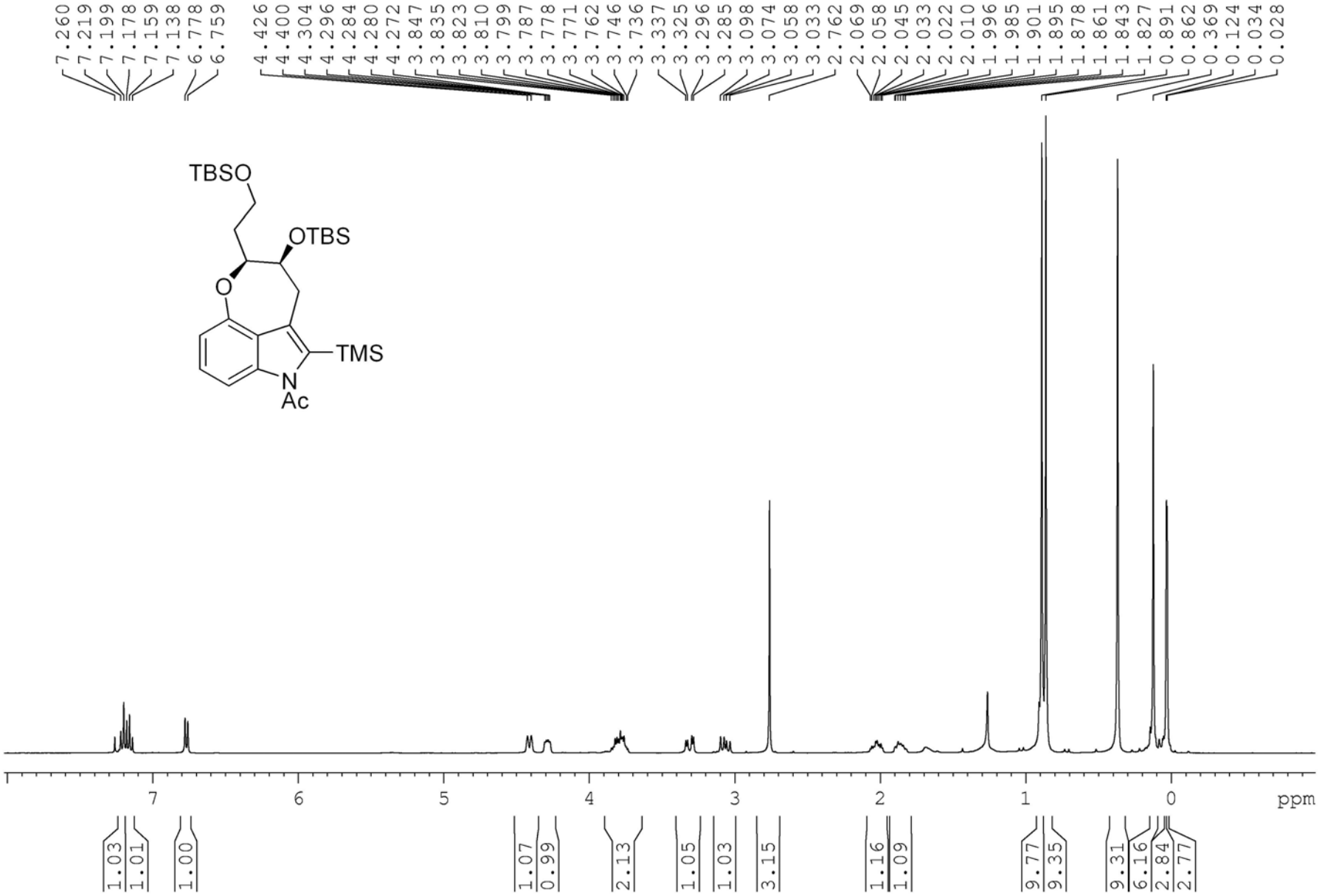
^{1}H NMR of compound 4 ($CDCl_3$; 400 MHz)



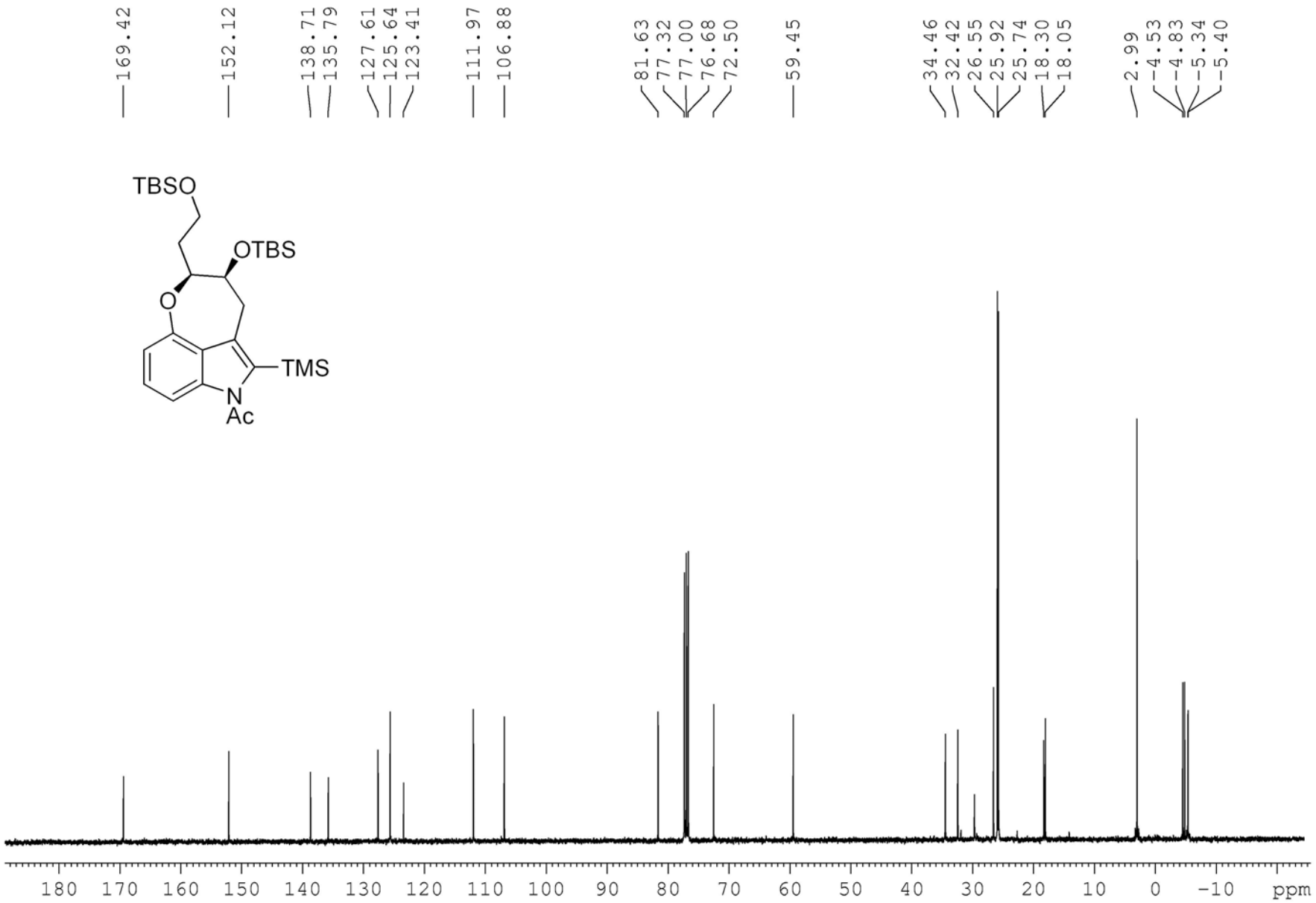
^{13}C NMR of compound 4 ($CDCl_3$; 100 MHz)



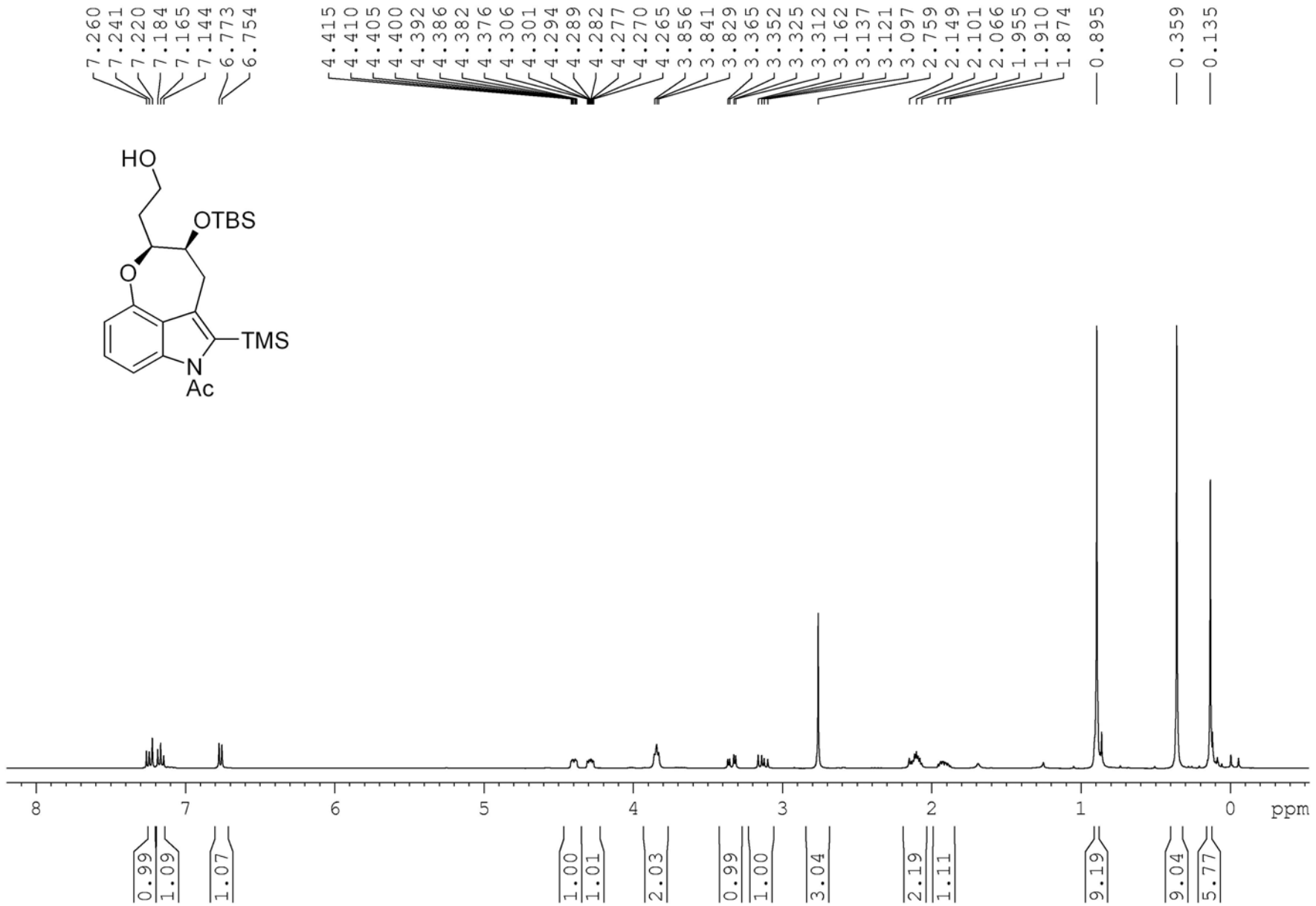
^{1}H NMR of compound 12 ($CDCl_3$; 400 MHz)



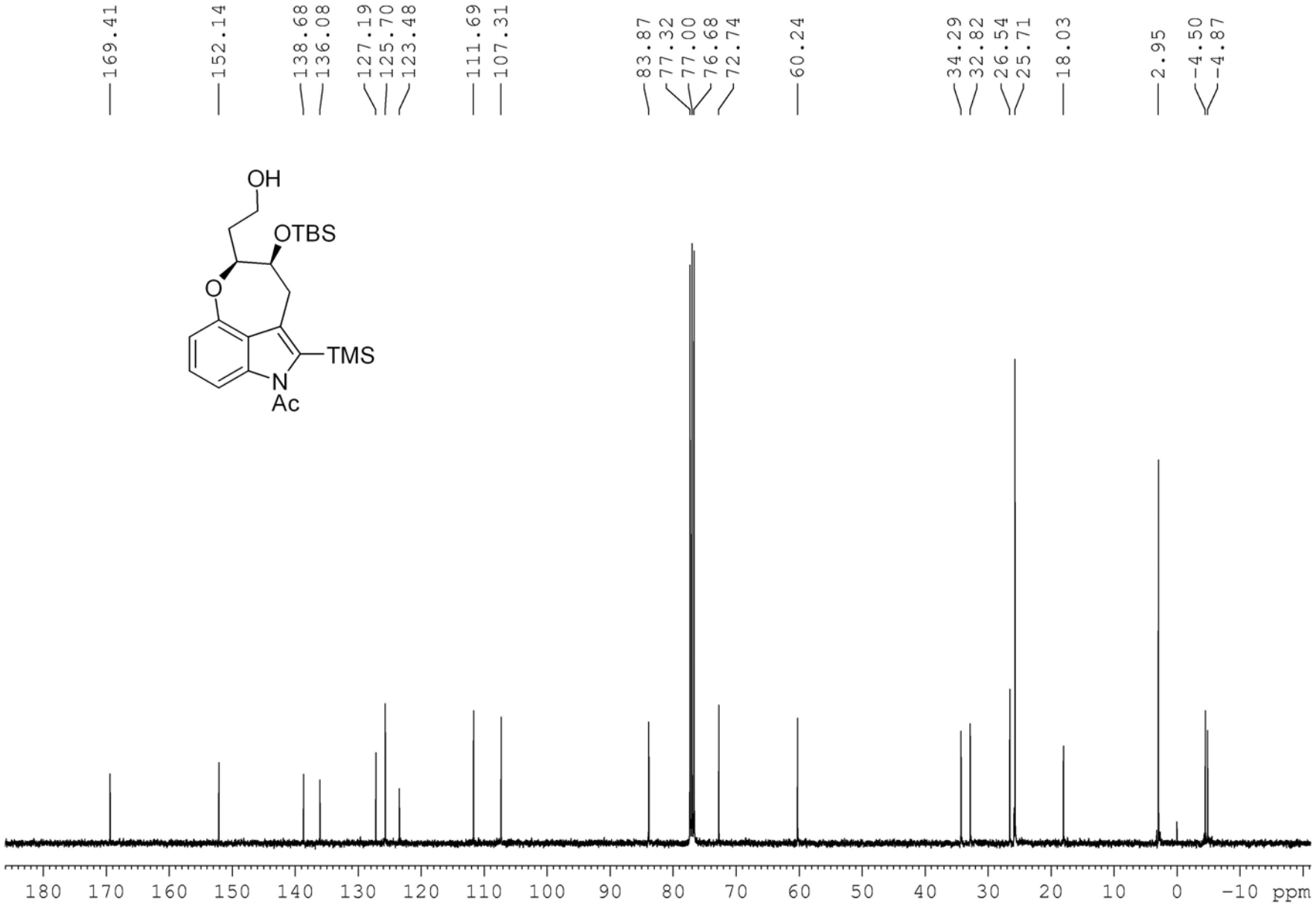
^{13}C NMR of compound 12 ($CDCl_3$; 100 MHz)



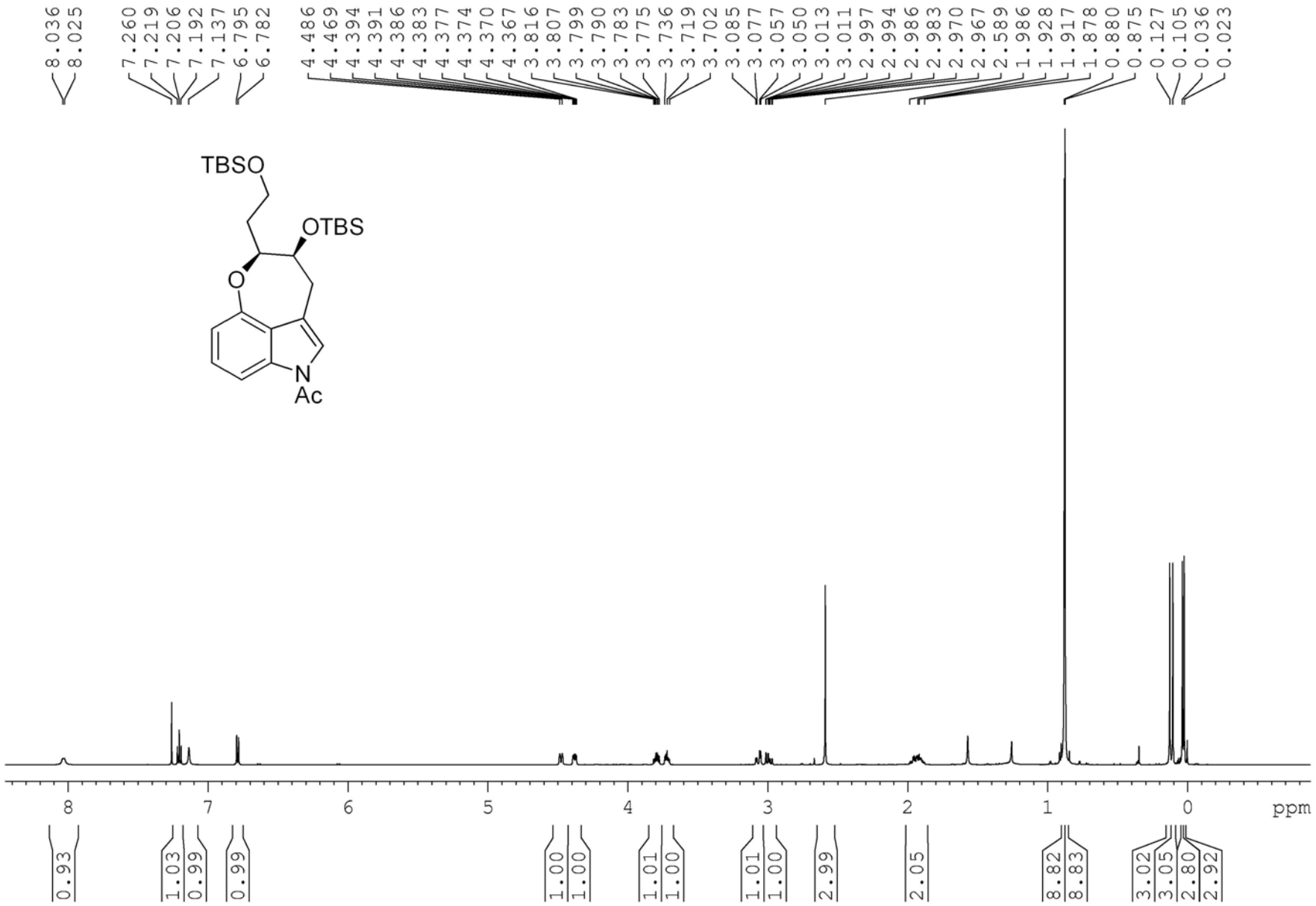
^{1}H NMR of compound 13 ($CDCl_3$; 400 MHz)



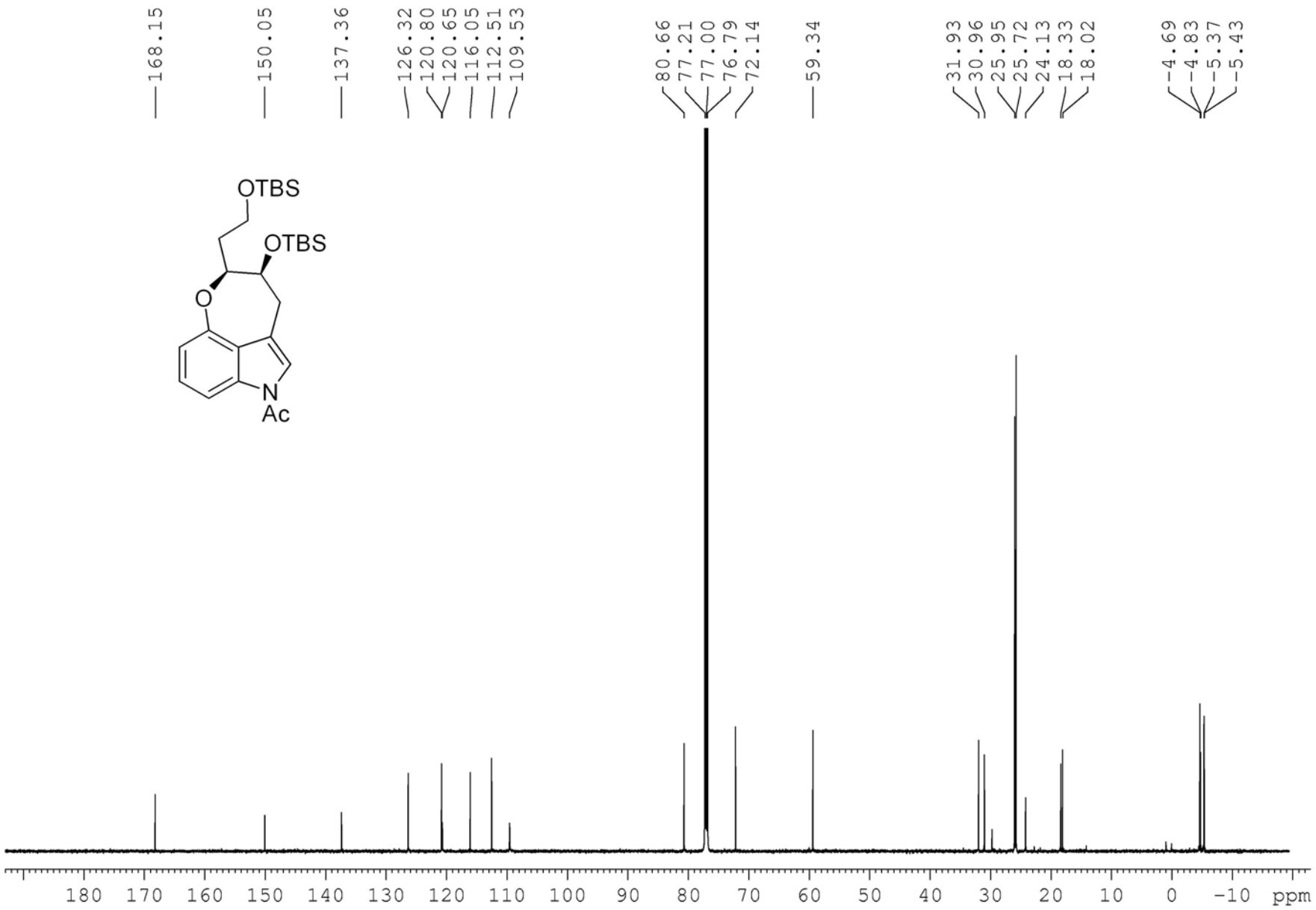
^{13}C NMR of compound 13 ($CDCl_3$; 100 MHz)



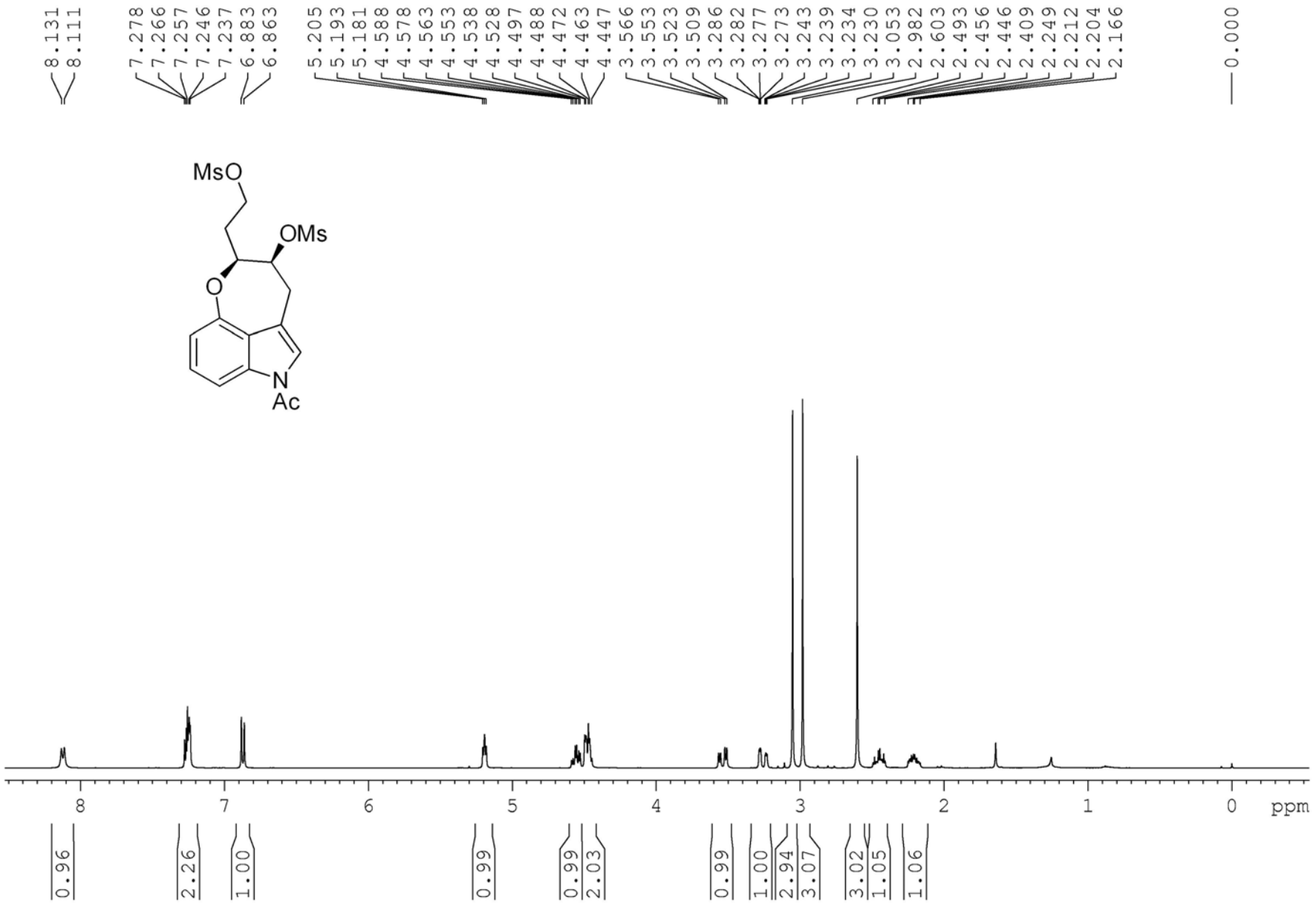
^{1}H NMR of compound 14 ($CDCl_3$; 600 MHz)



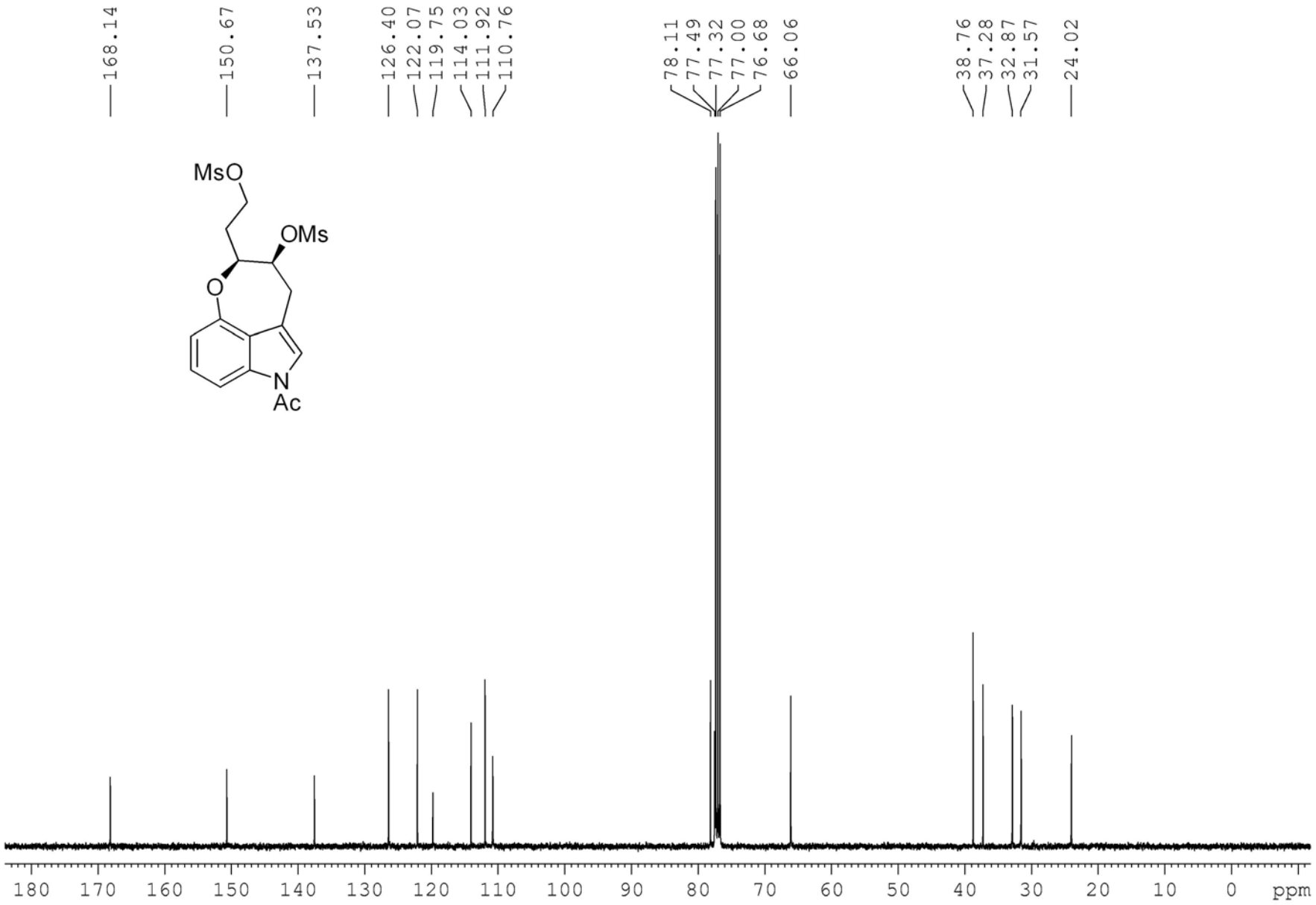
^{13}C NMR of compound 14 ($CDCl_3$; 150 MHz)



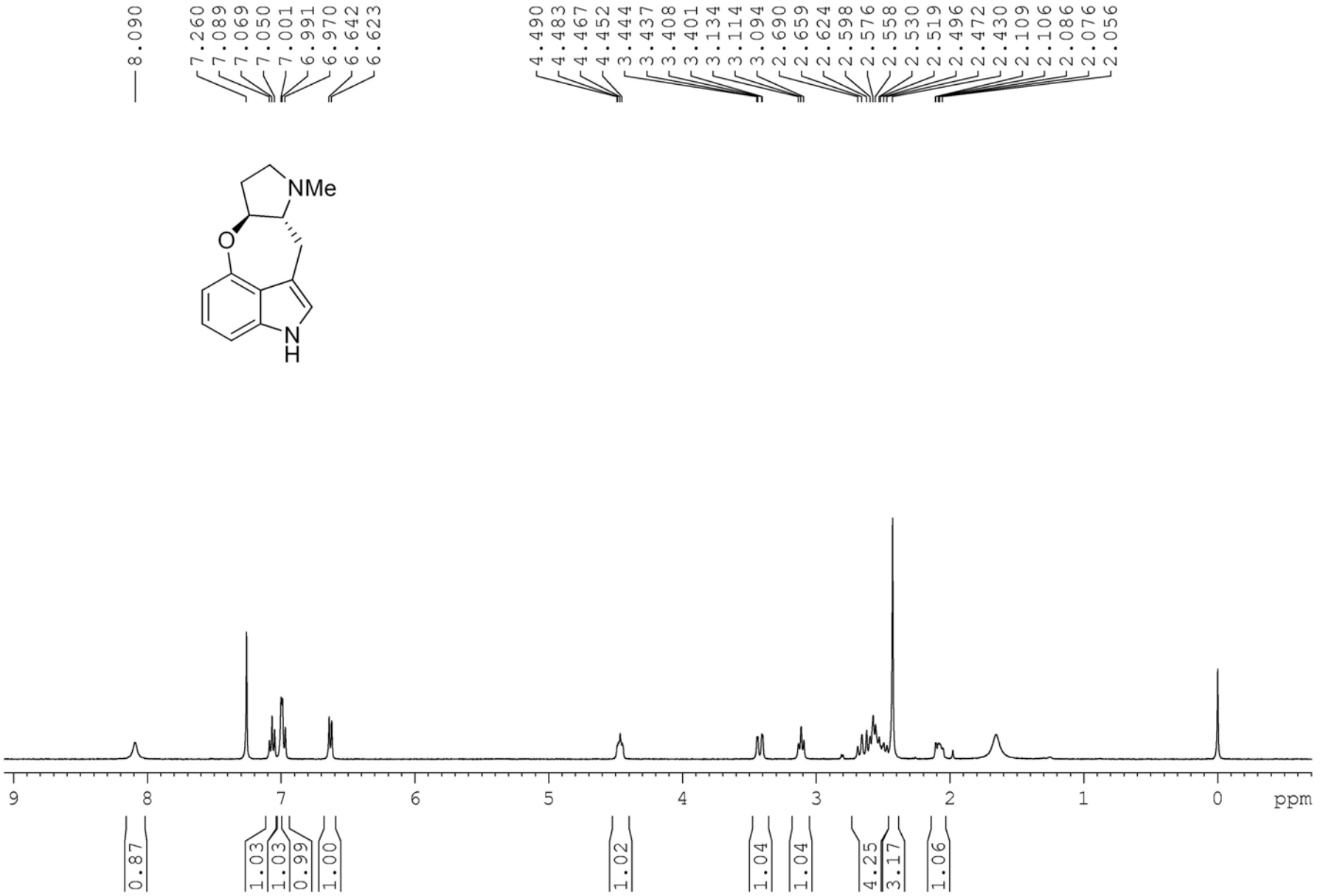
^{1}H NMR of compound 3 ($CDCl_3$; 400 MHz)



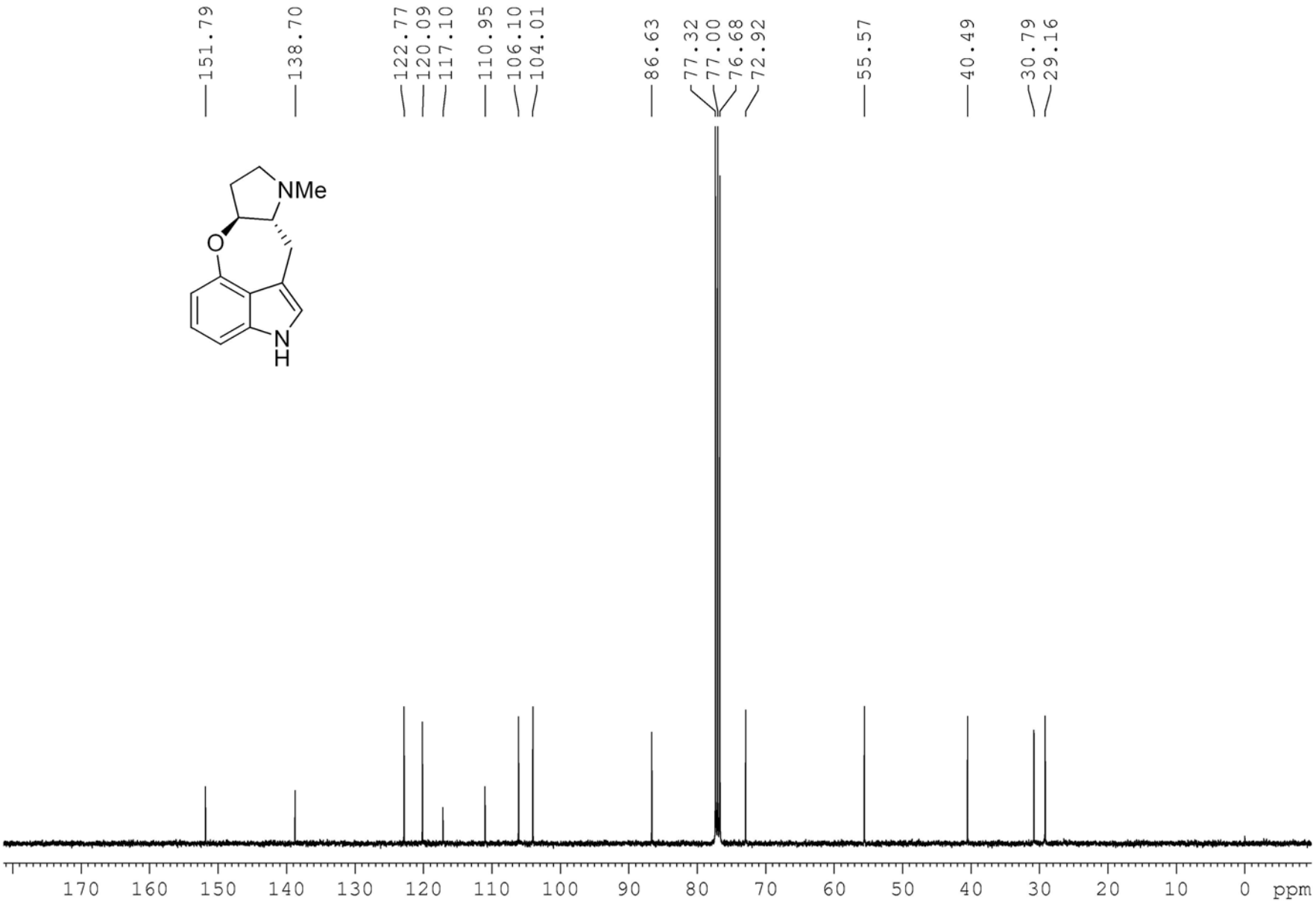
^{13}C NMR of compound 3 ($CDCl_3$; 100 MHz)



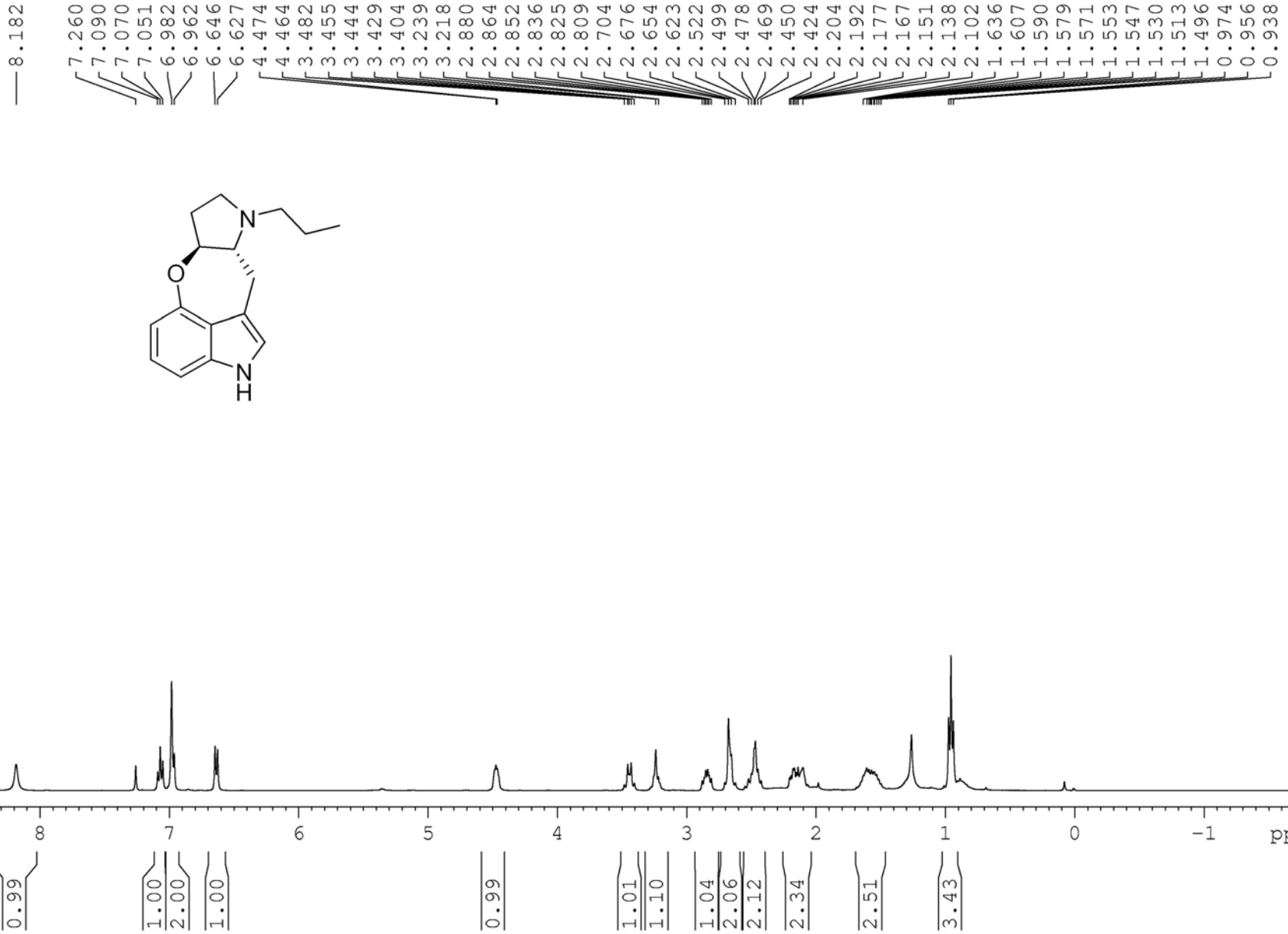
^{1}H NMR of compound 1 ($CDCl_3$; 400 MHz)



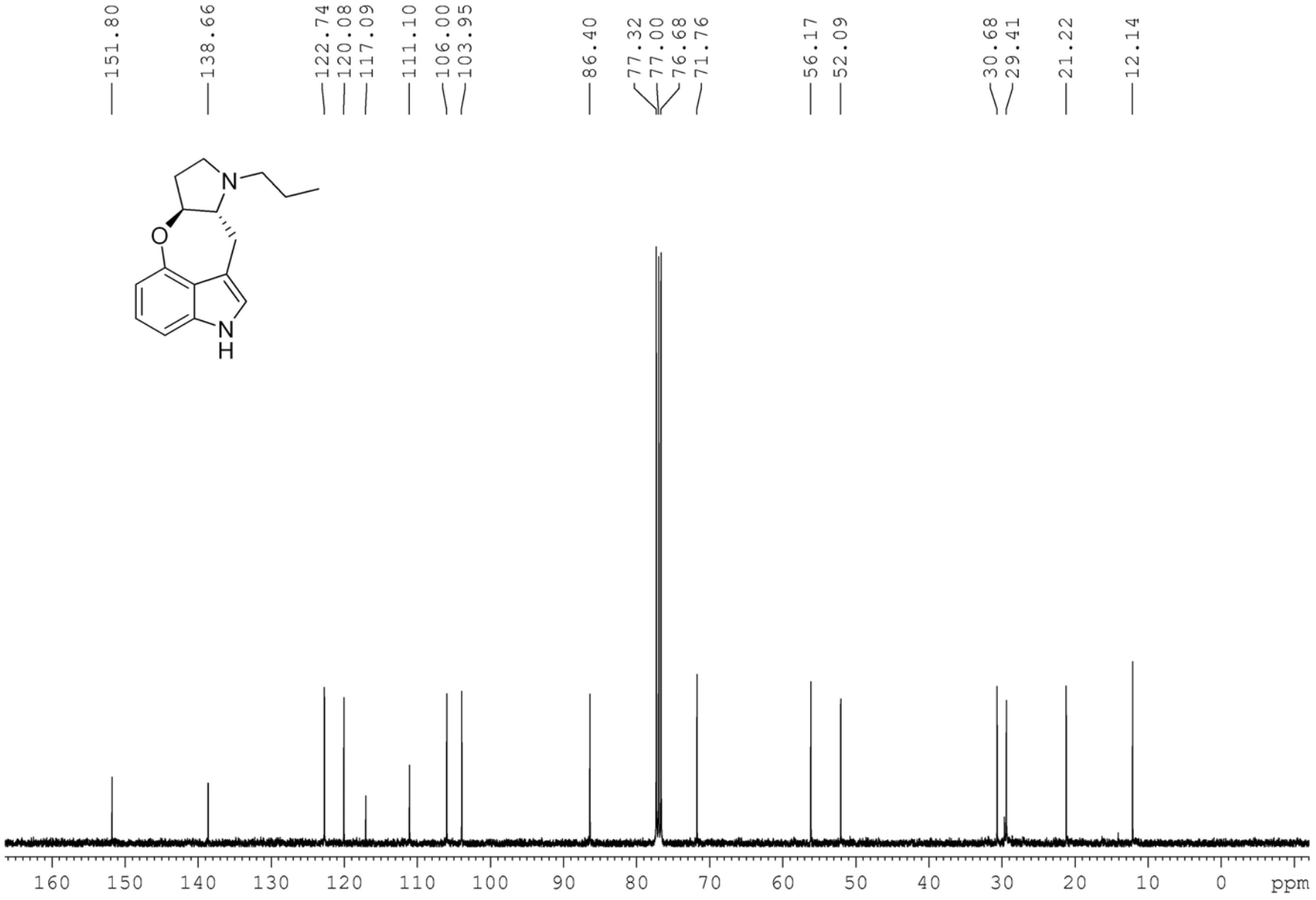
^{13}C NMR of compound 1 ($CDCl_3$; 100 MHz)



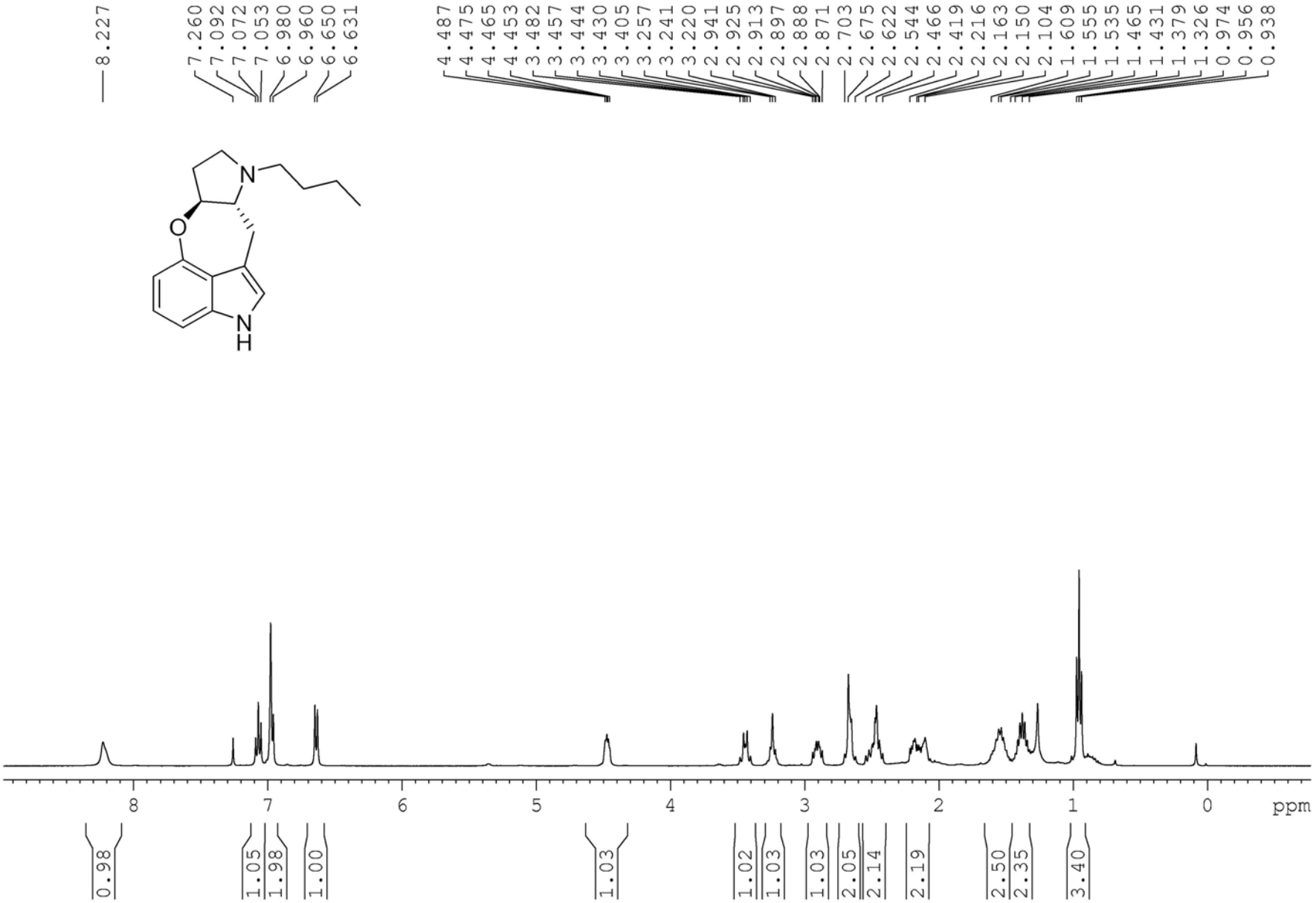
^{1}H NMR of compound 23a ($CDCl_3$; 400 MHz)



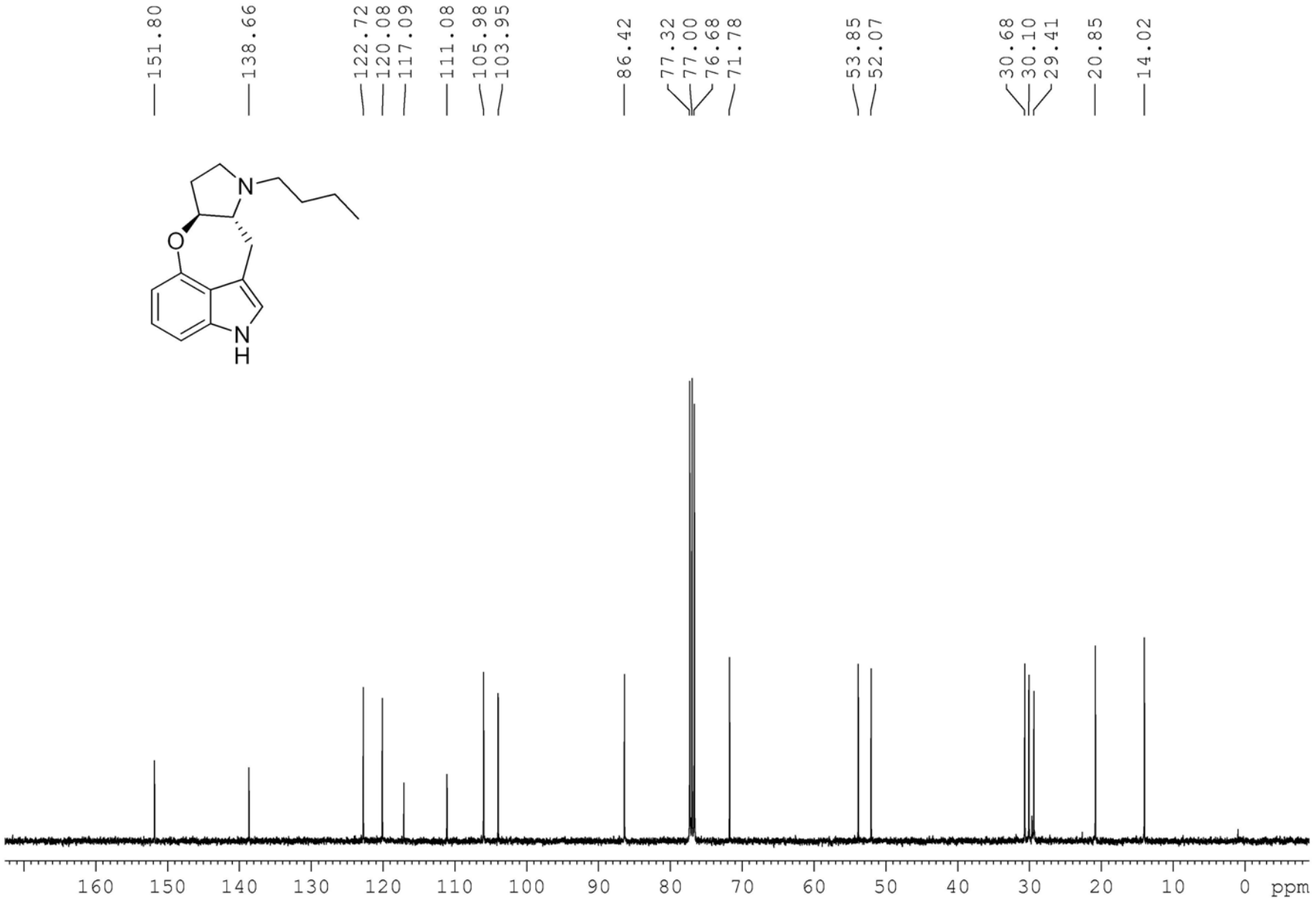
^{13}C NMR of compound 23a ($CDCl_3$; 100 MHz)



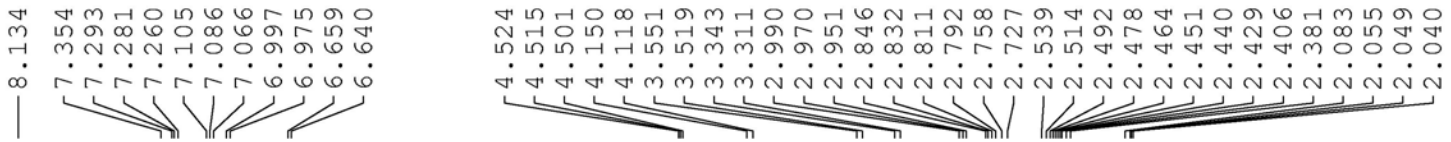
^{1}H NMR of compound 23b ($CDCl_3$; 400 MHz)

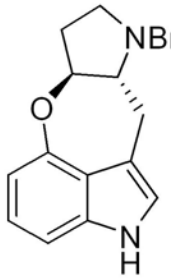


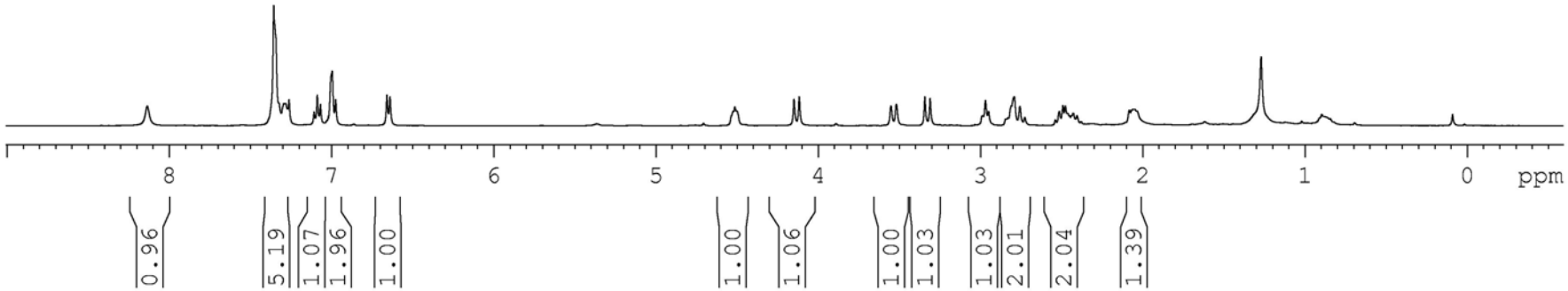
^{13}C NMR of compound 23b ($CDCl_3$; 100 MHz)



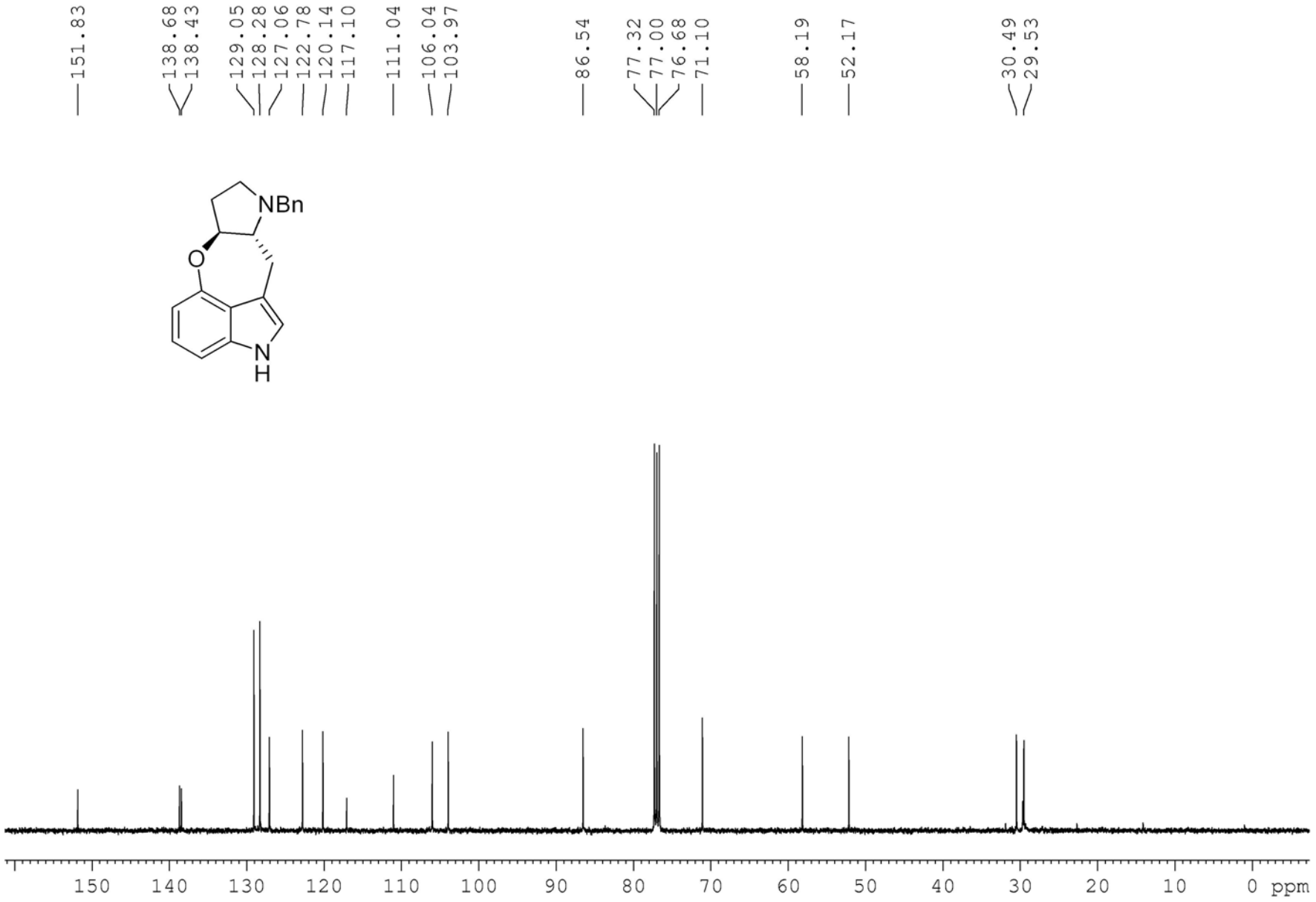
^{1}H NMR of compound 23c ($CDCl_3$; 400 MHz)



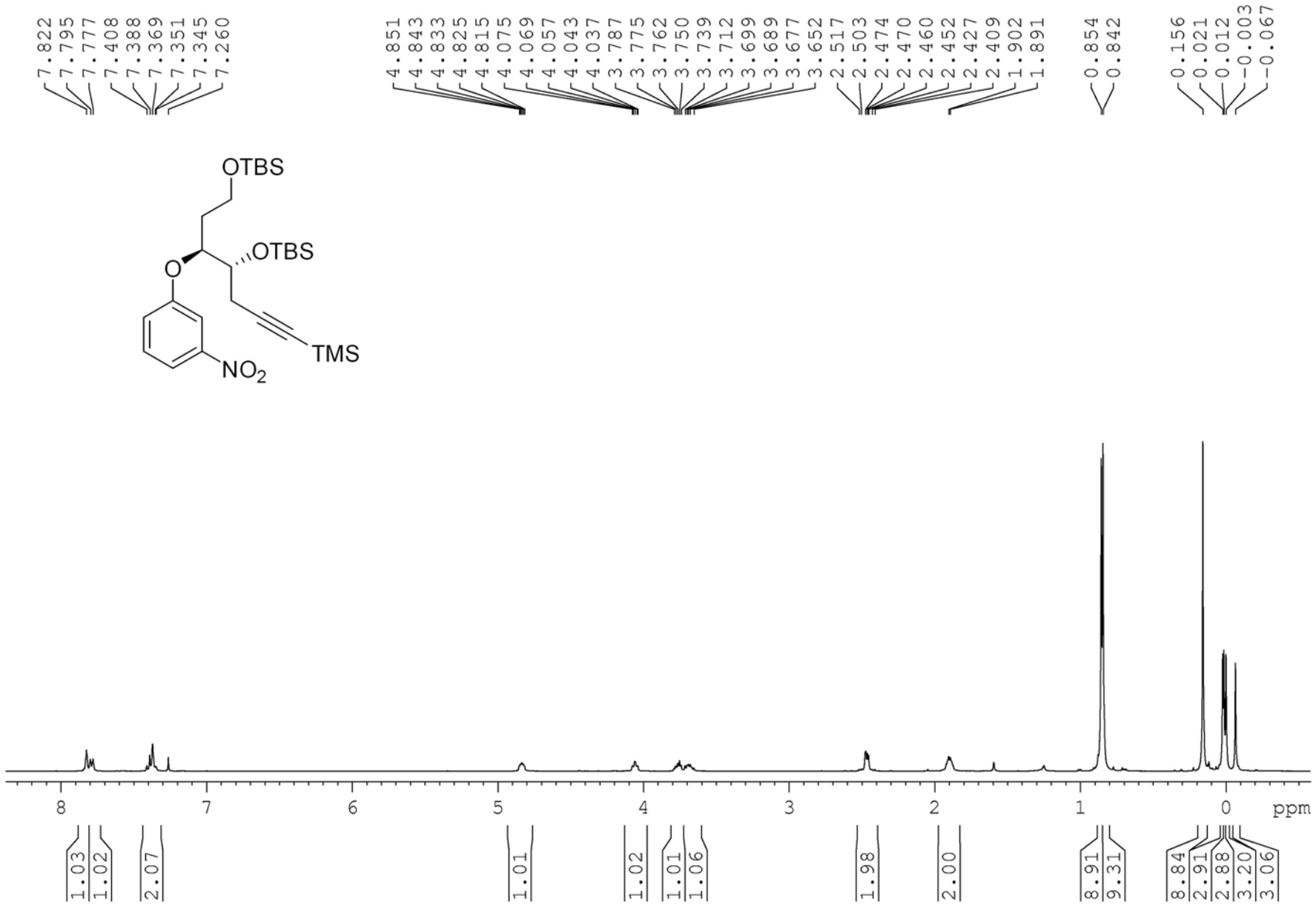




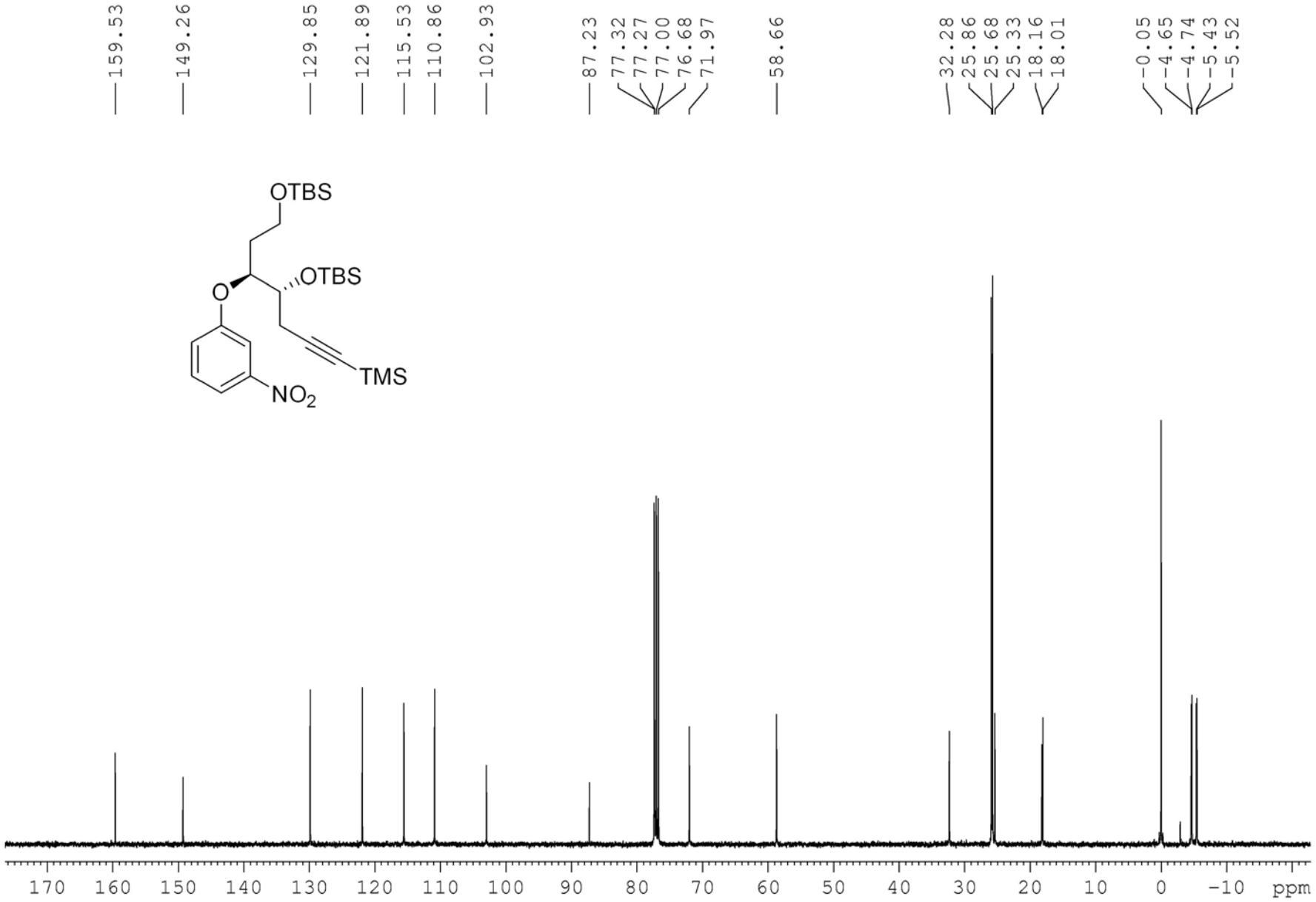
^{13}C NMR of compound 23c ($CDCl_3$; 100 MHz)



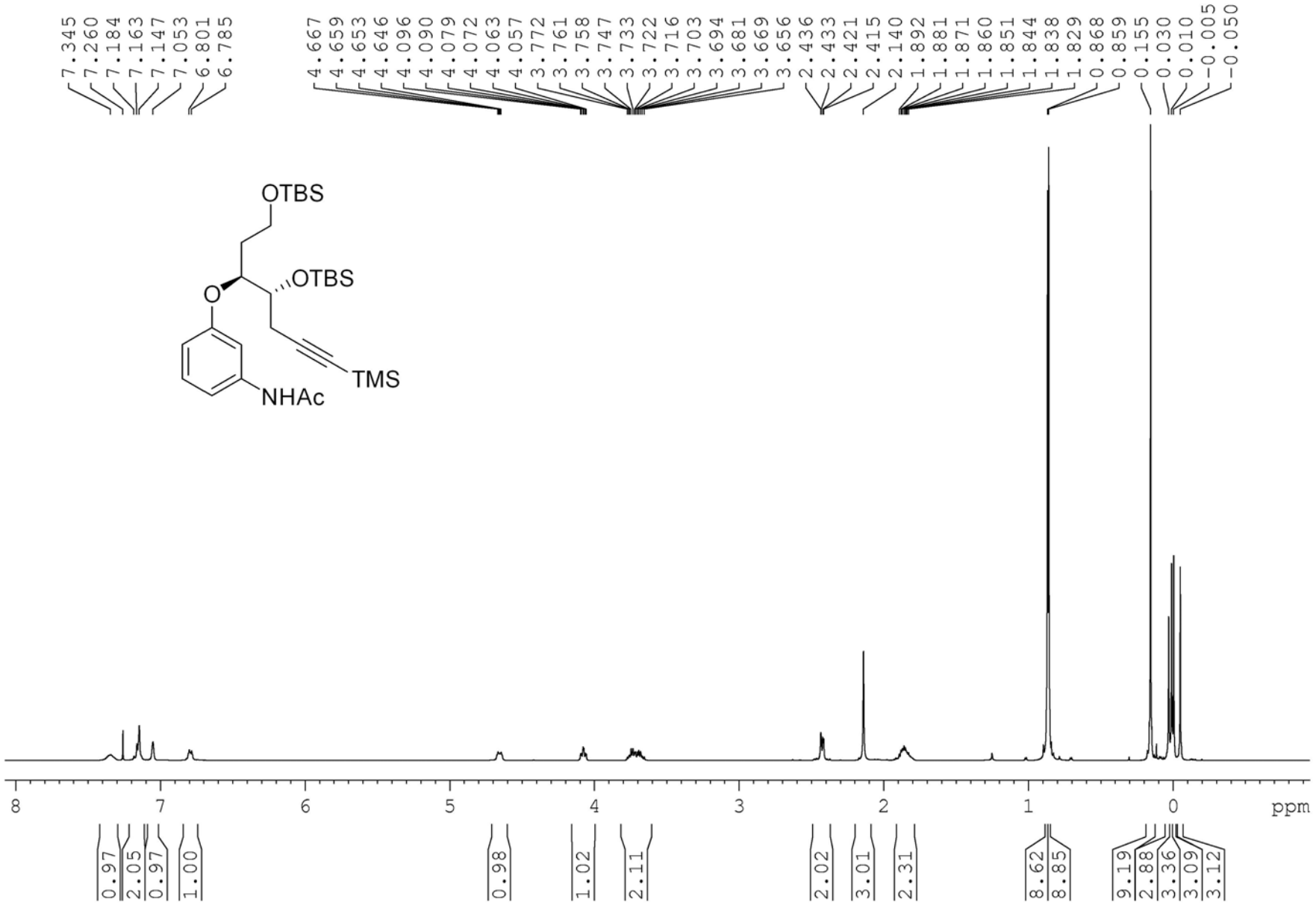
^{1}H NMR of compound 24 ($CDCl_3$; 400 MHz)



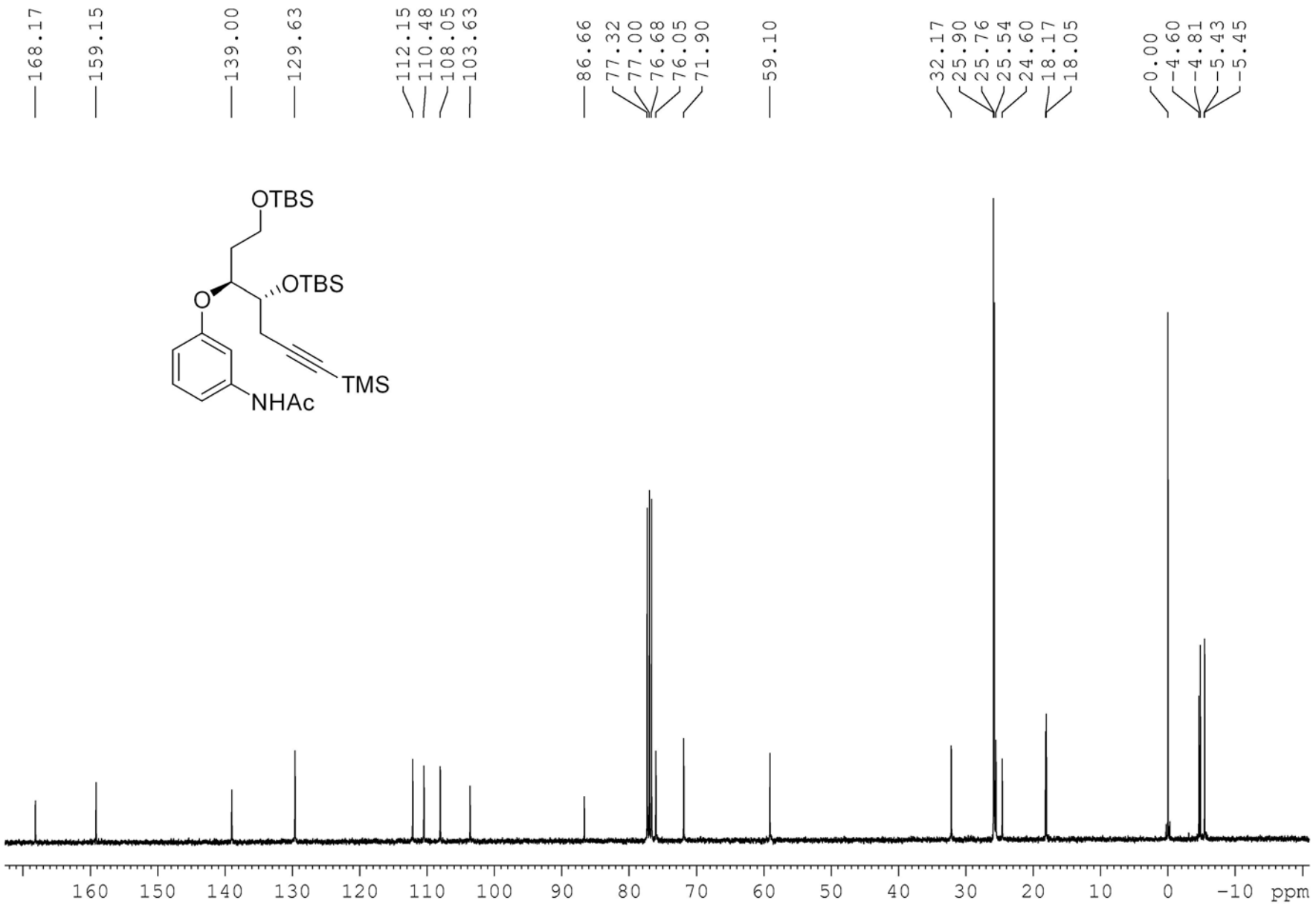
^{13}C NMR of compound 24 ($CDCl_3$; 100 MHz)



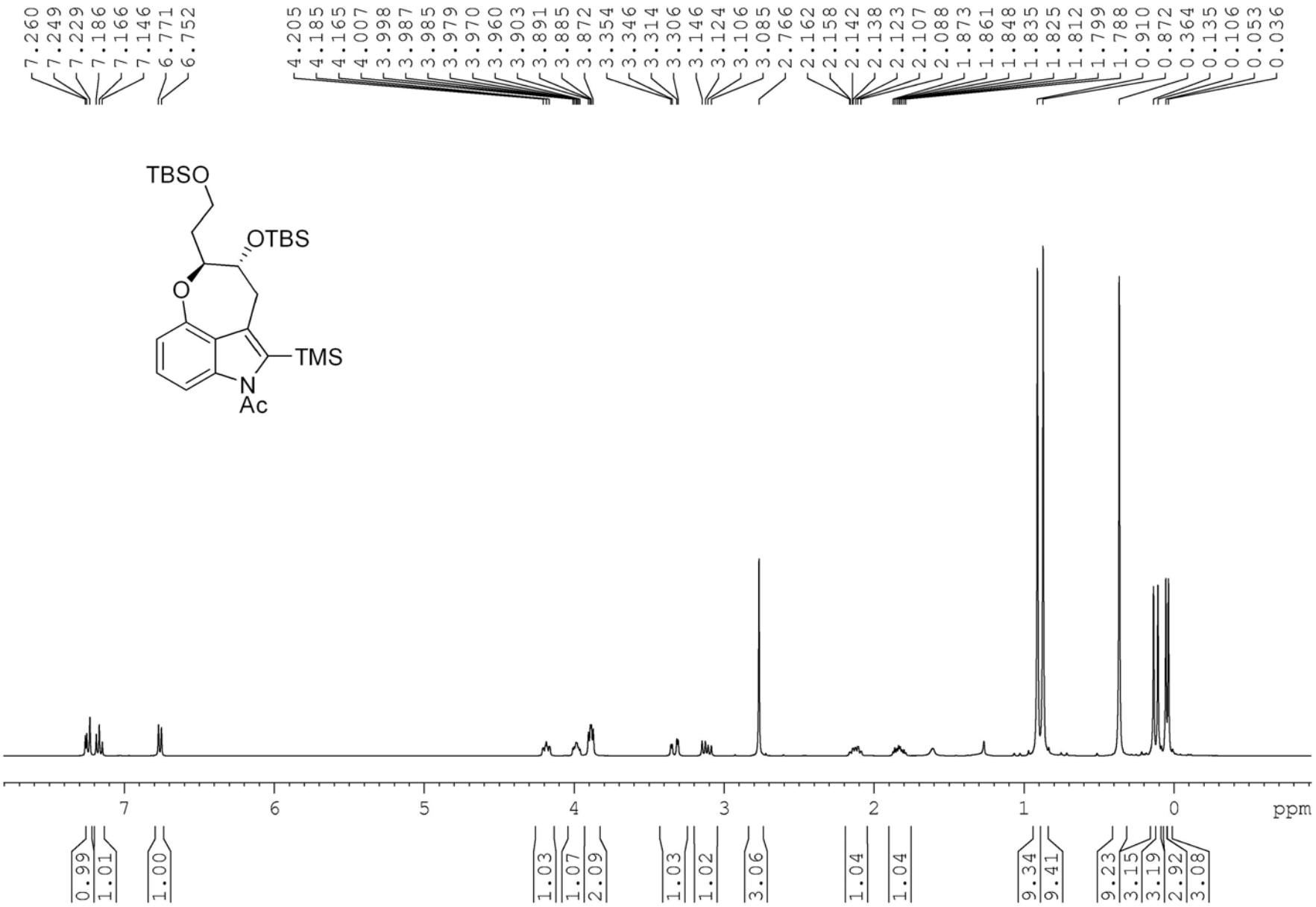
^{1}H NMR of compound 25 ($CDCl_3$; 400 MHz)



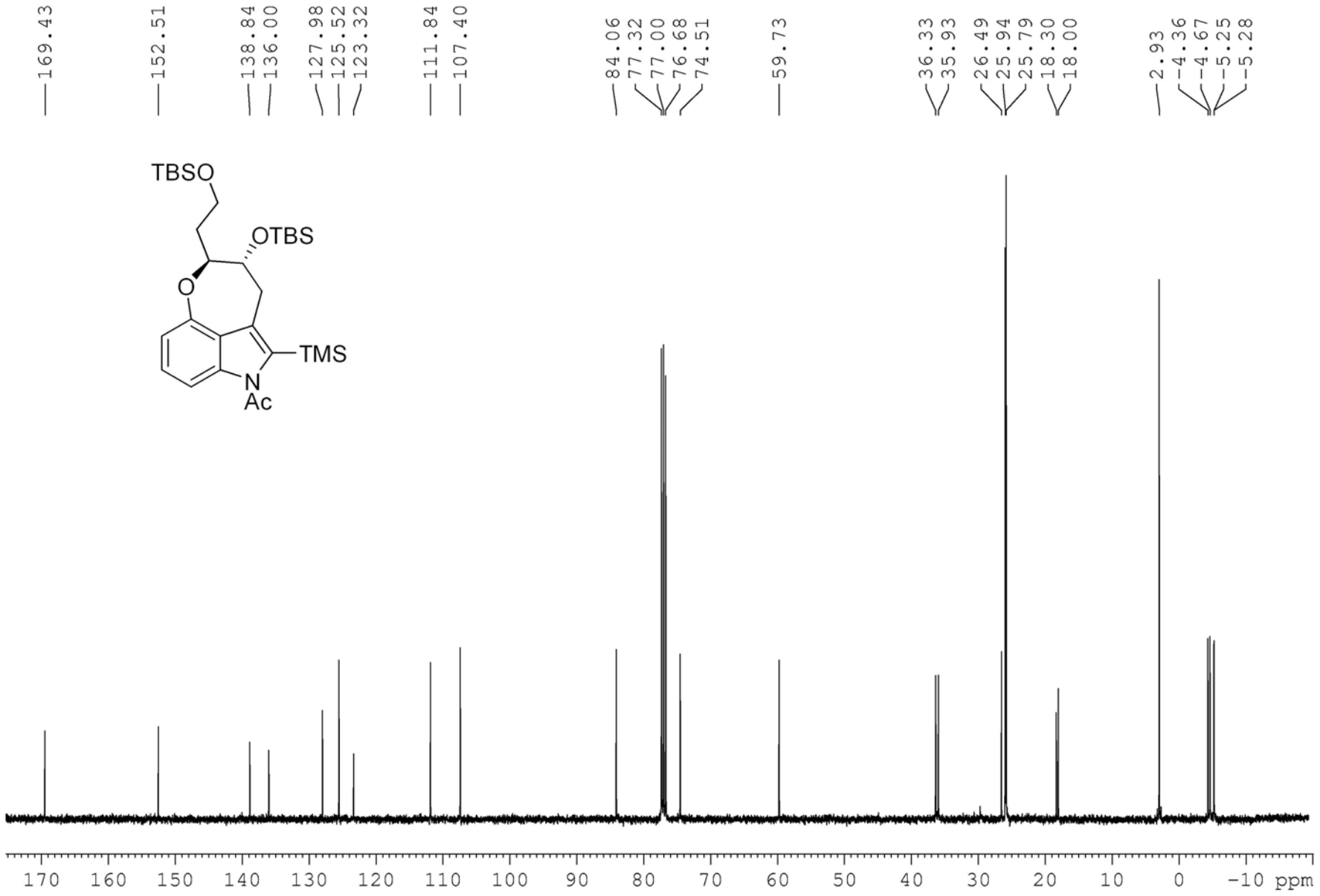
^{13}C NMR of compound 25 ($CDCl_3$; 100 MHz)



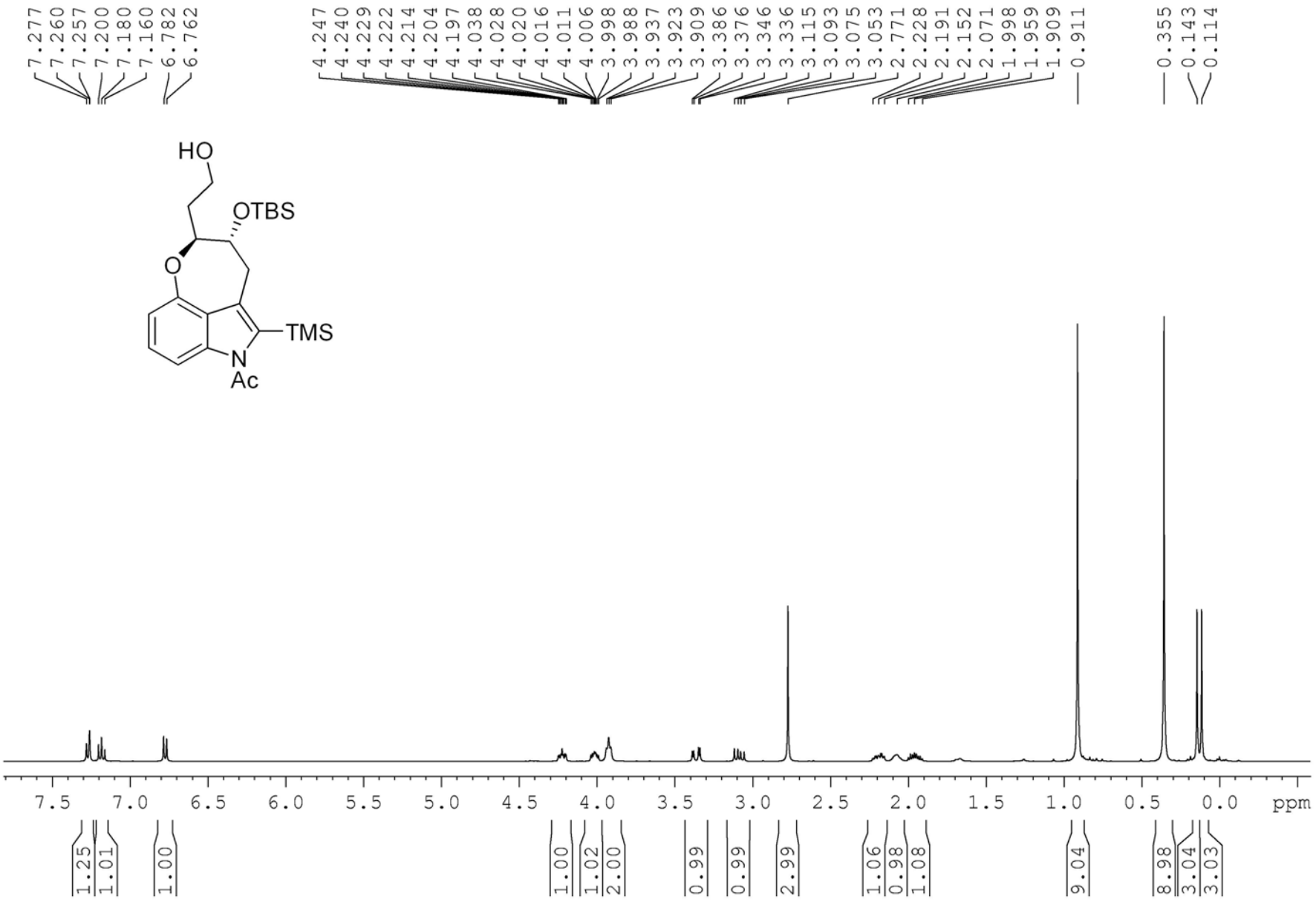
^{1}H NMR of compound 15 ($CDCl_3$; 400 MHz)



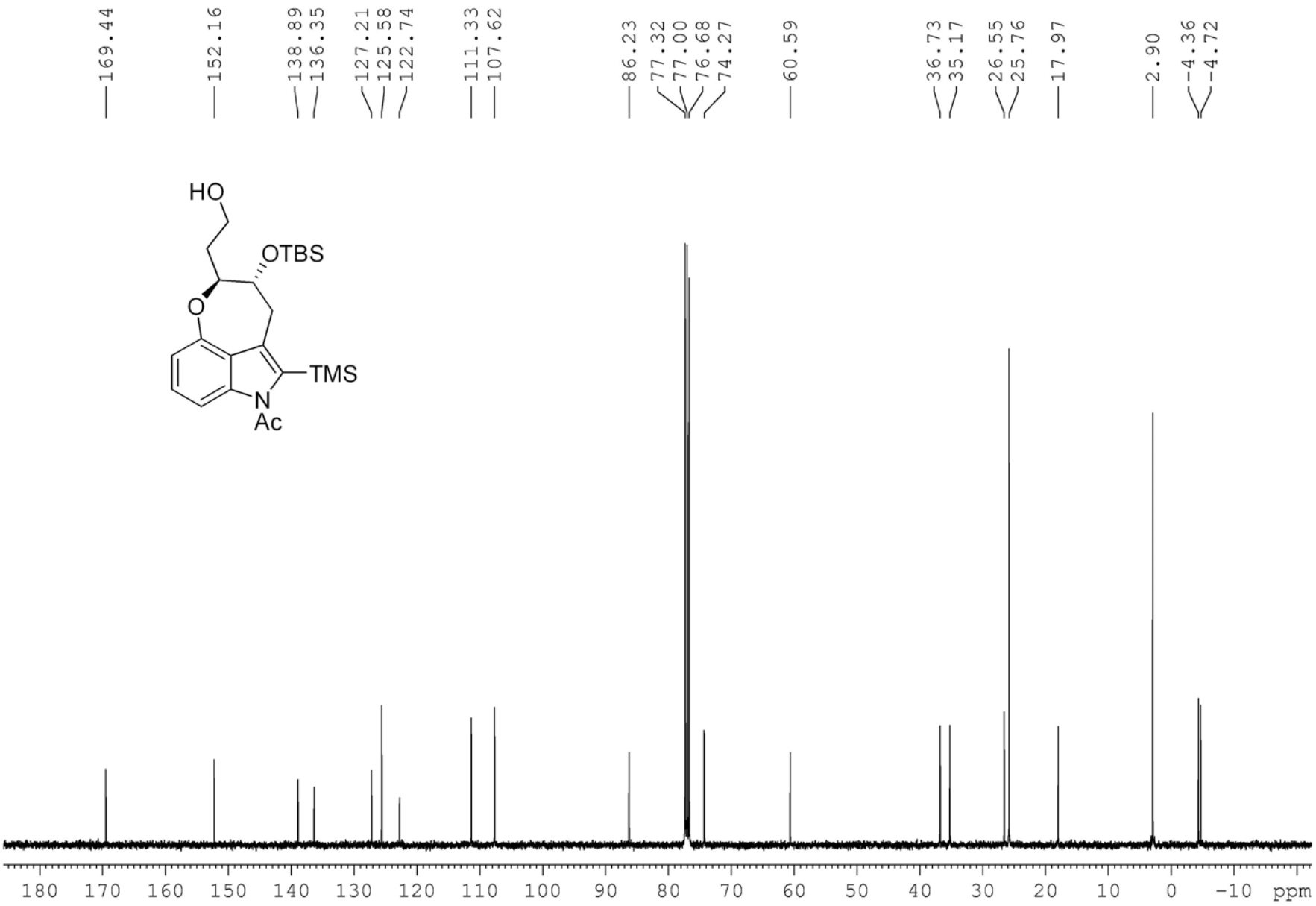
^{13}C NMR of compound 15 ($CDCl_3$; 100 MHz)



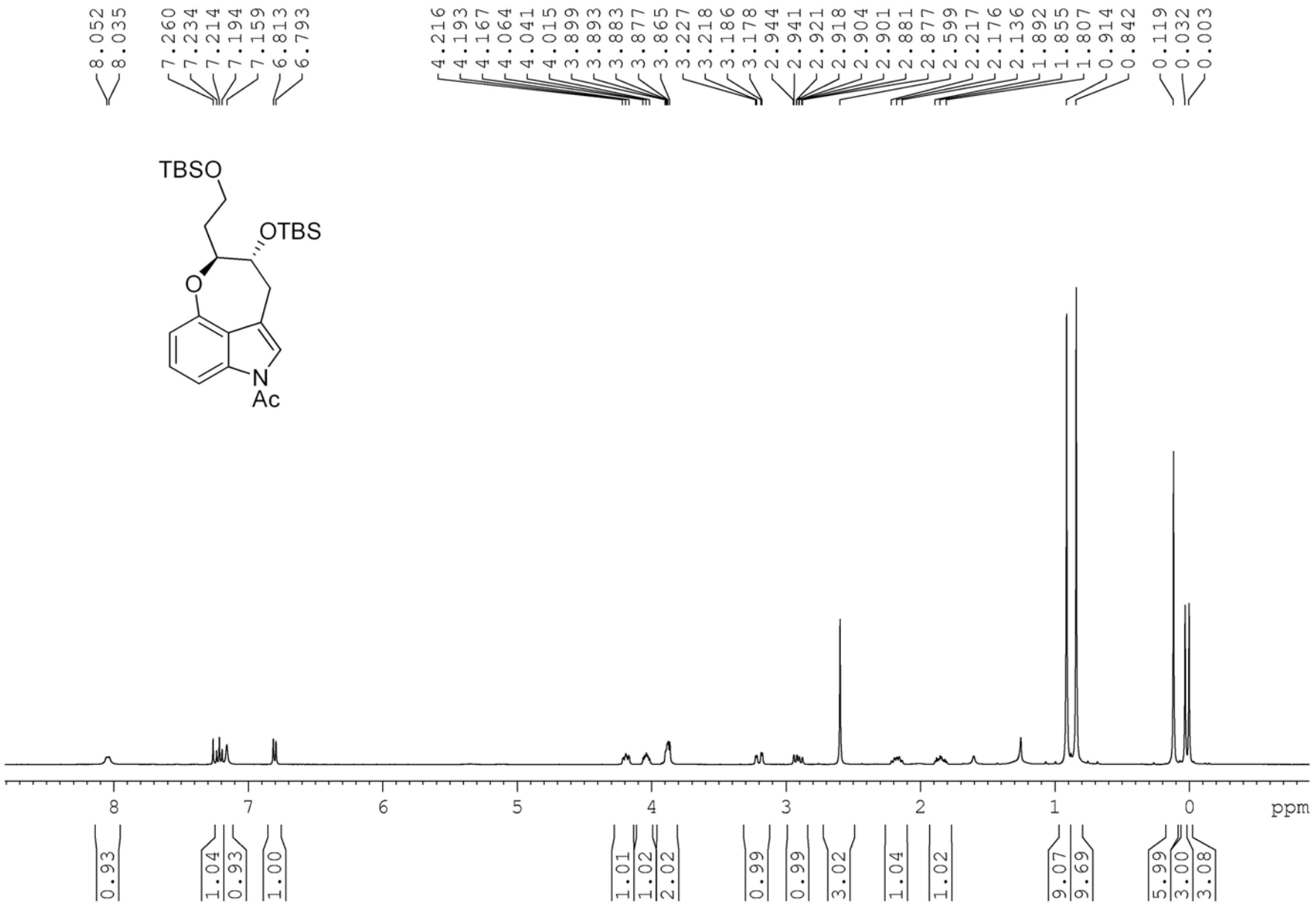
^{1}H NMR of compound 16 ($CDCl_3$; 400 MHz)



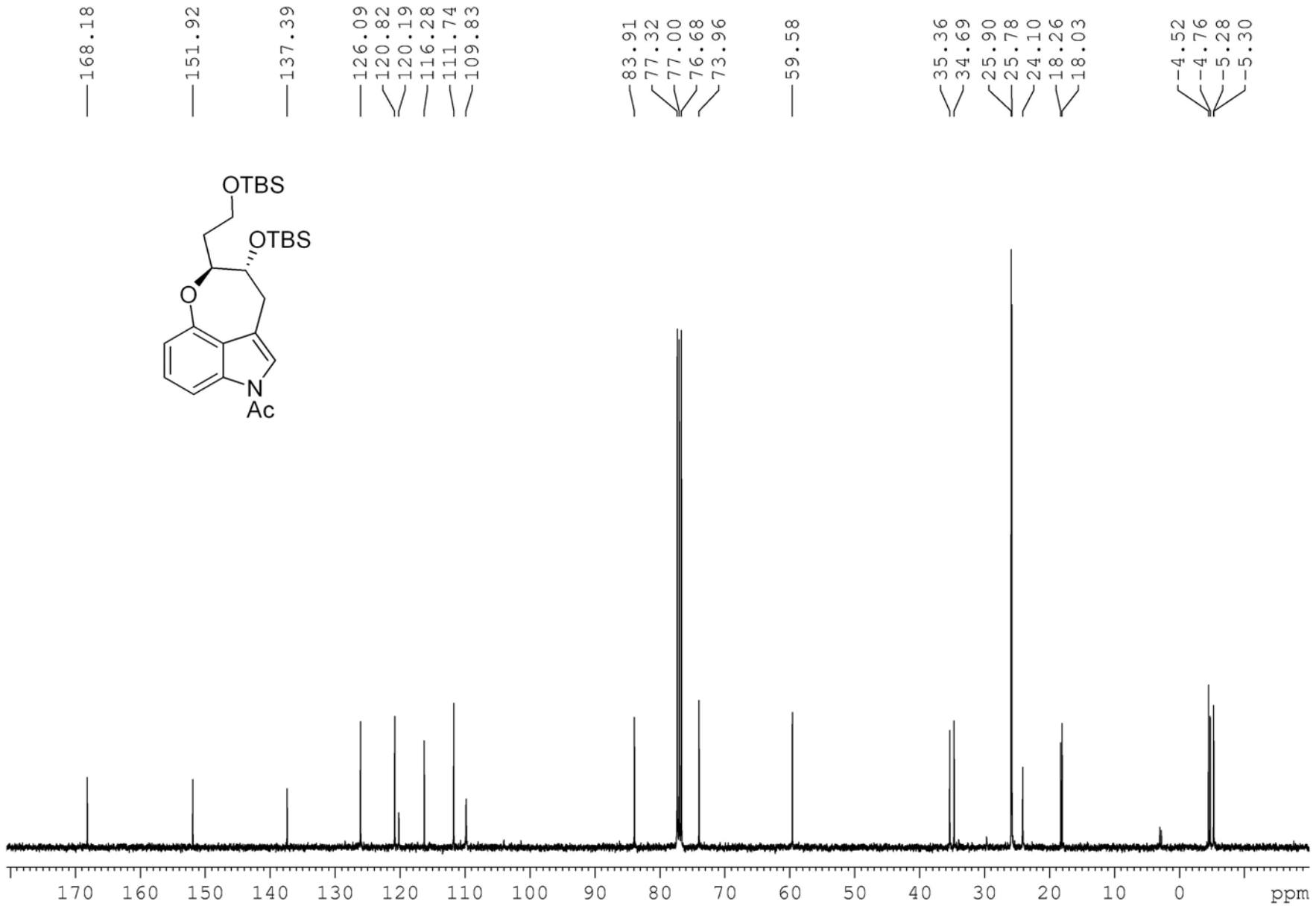
^{13}C NMR of compound 16 ($CDCl_3$; 100 MHz)



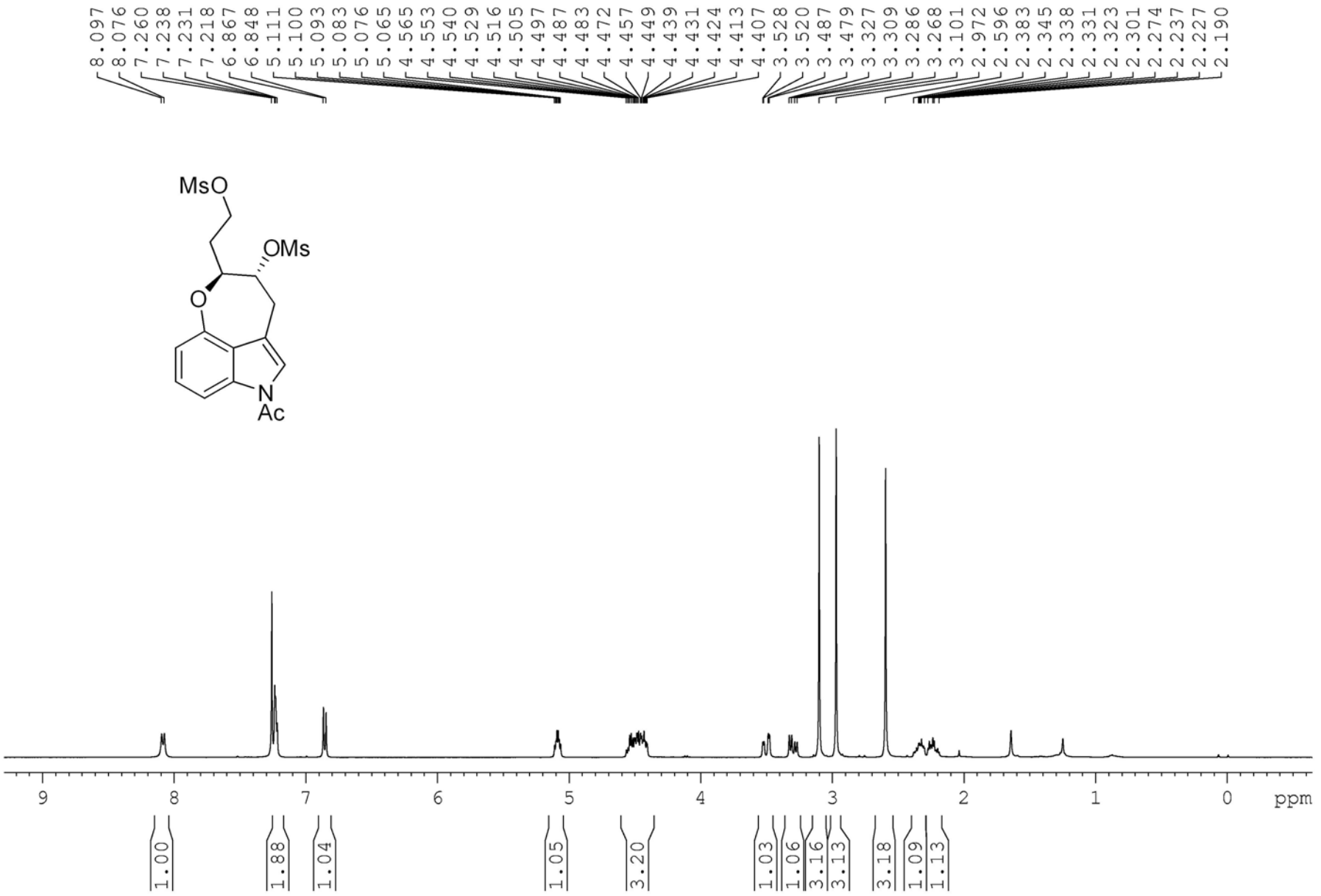
^{1}H NMR of compound 17 ($CDCl_3$; 400 MHz)



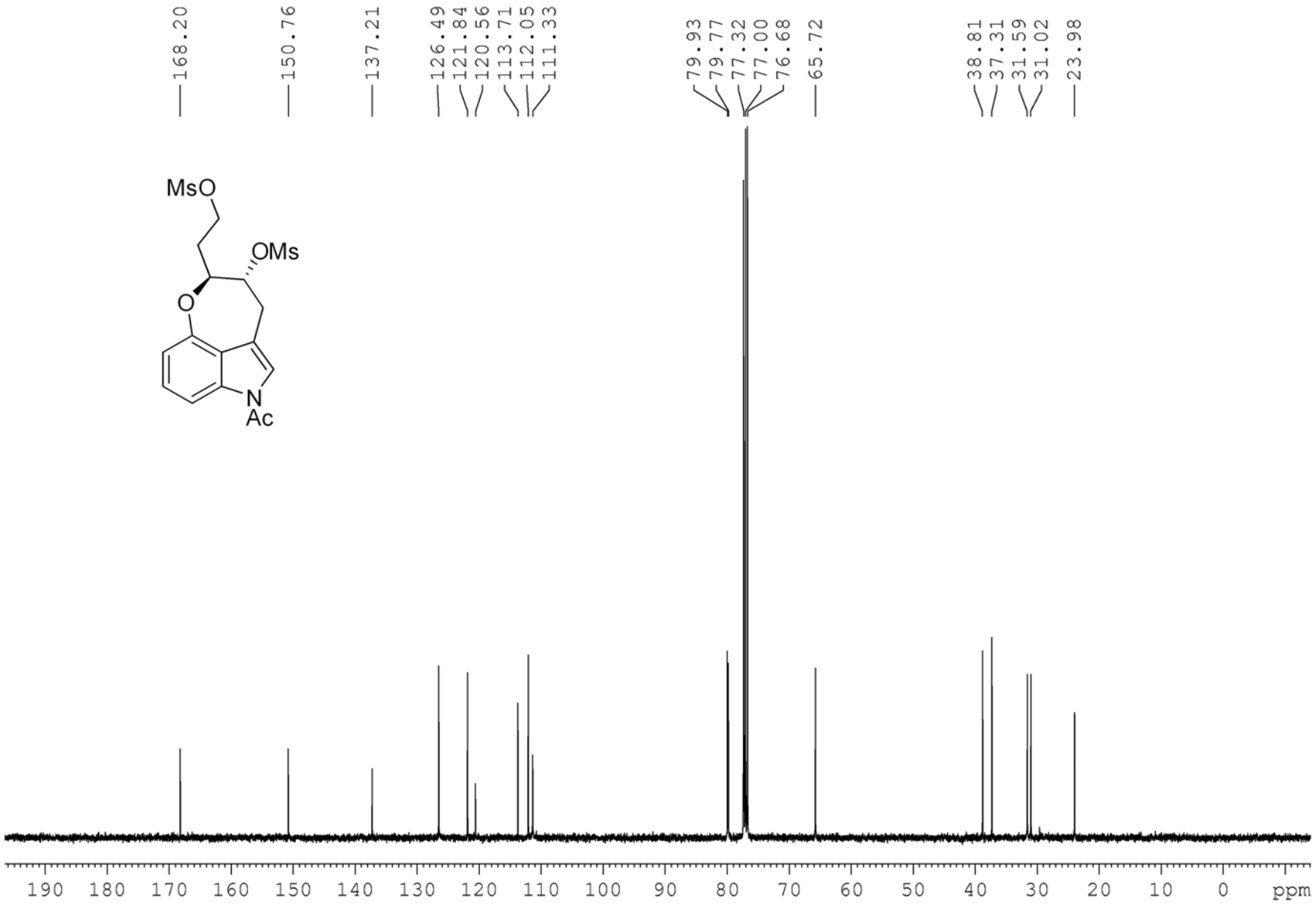
^{13}C NMR of compound 17 ($CDCl_3$; 100 MHz)



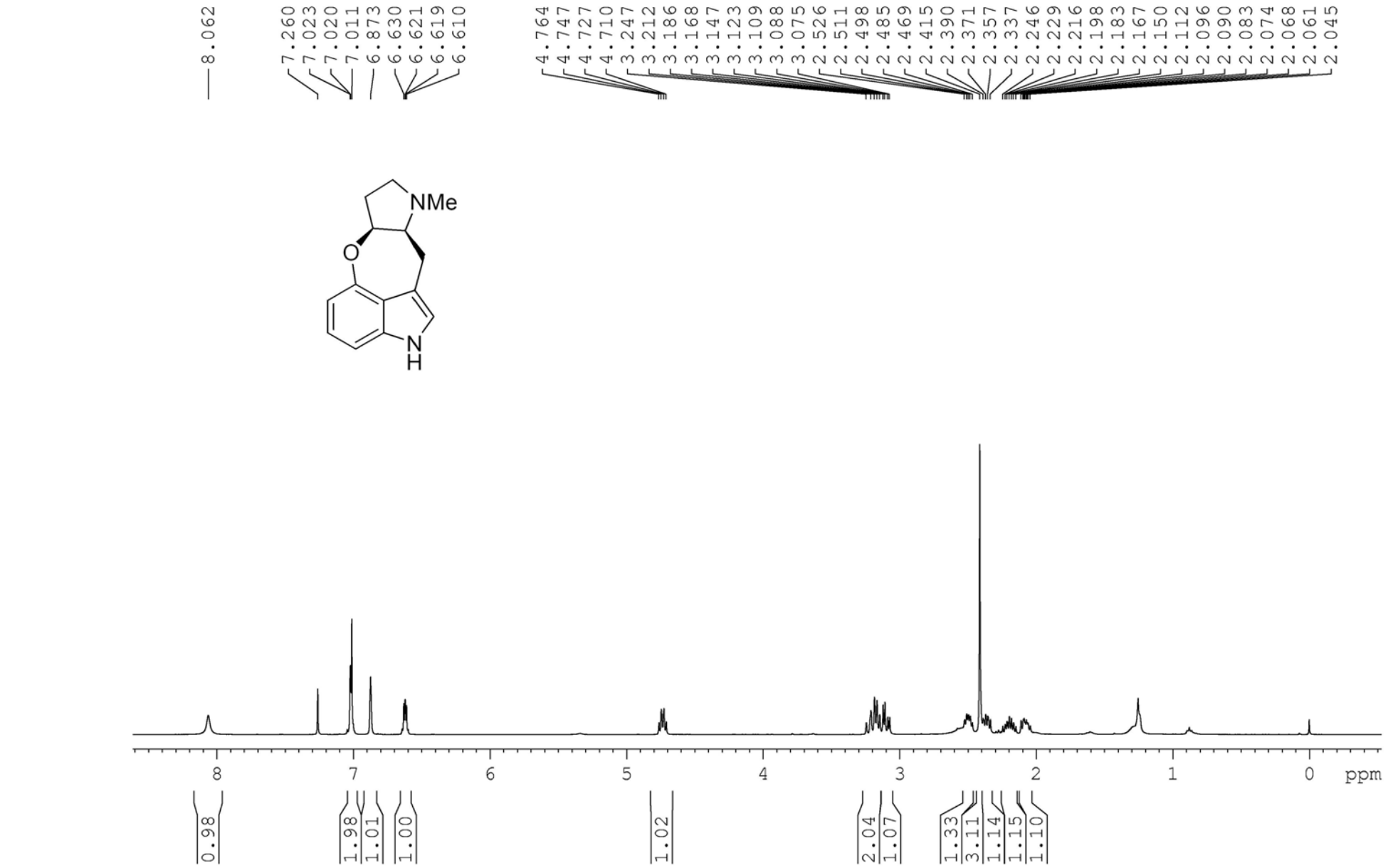
^{1}H NMR of compound 26 ($CDCl_3$; 400 MHz)



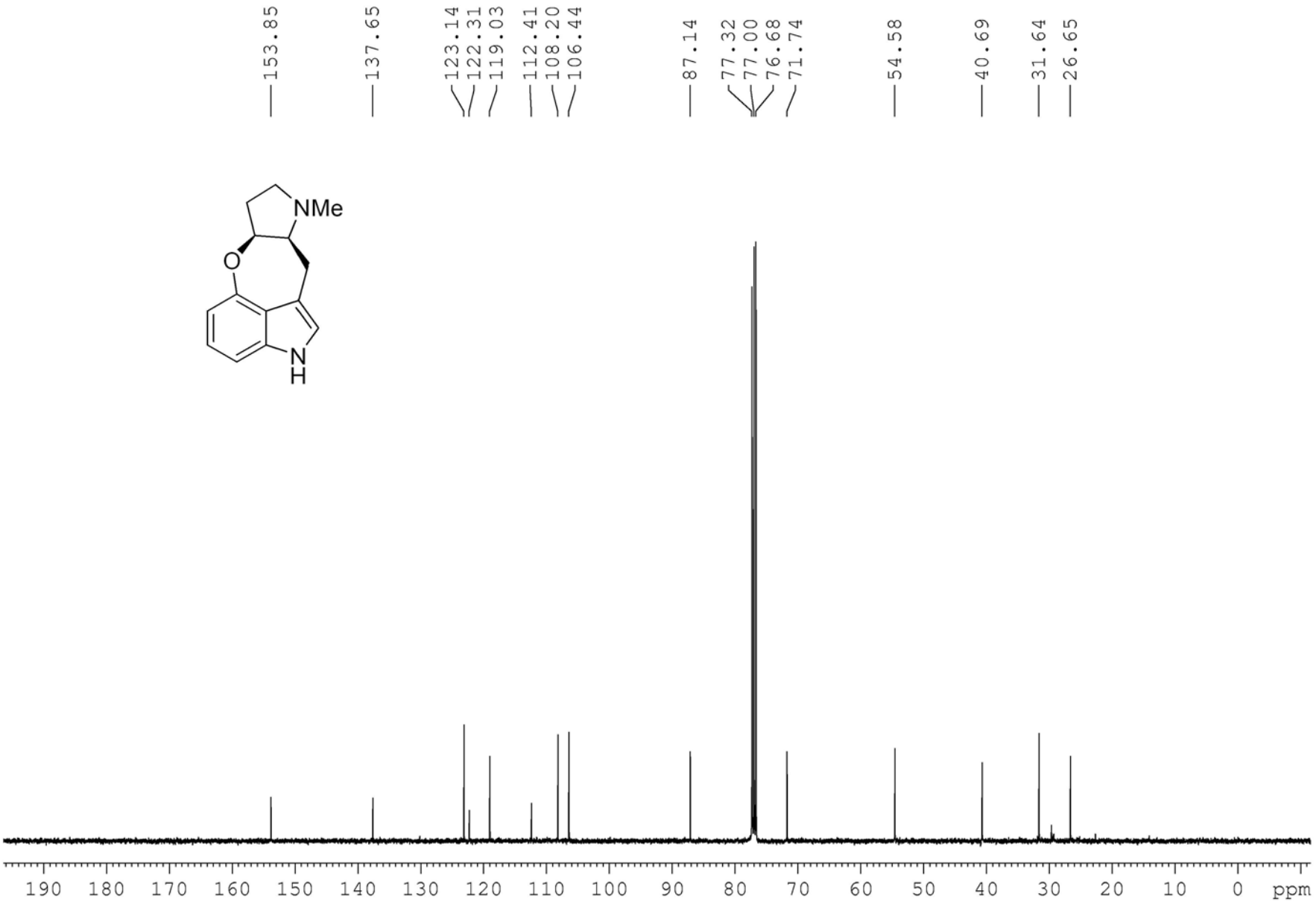
^{13}C NMR of compound 26 ($CDCl_3$; 100 MHz)



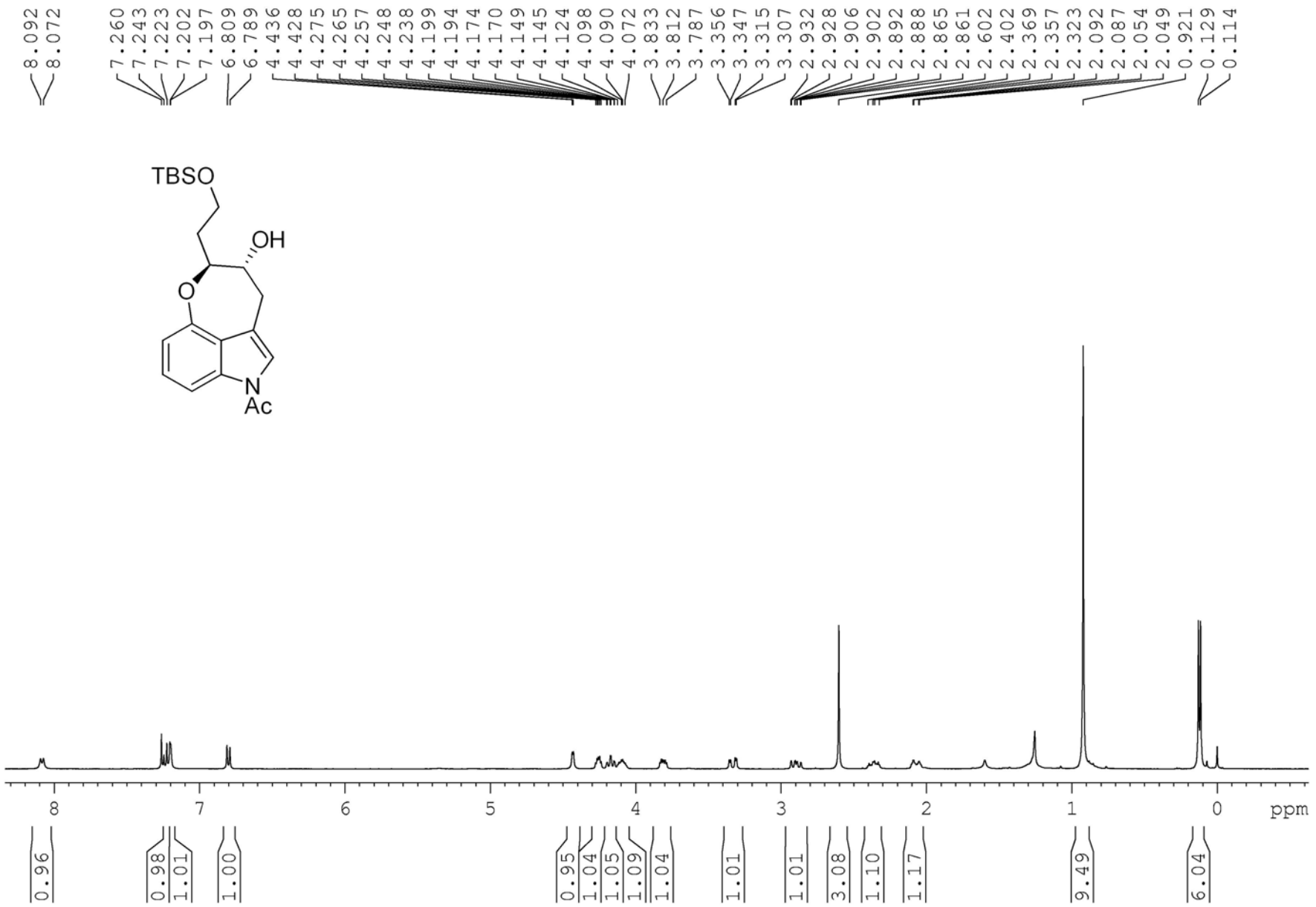
^{1}H NMR of compound 19 ($CDCl_3$; 400 MHz)



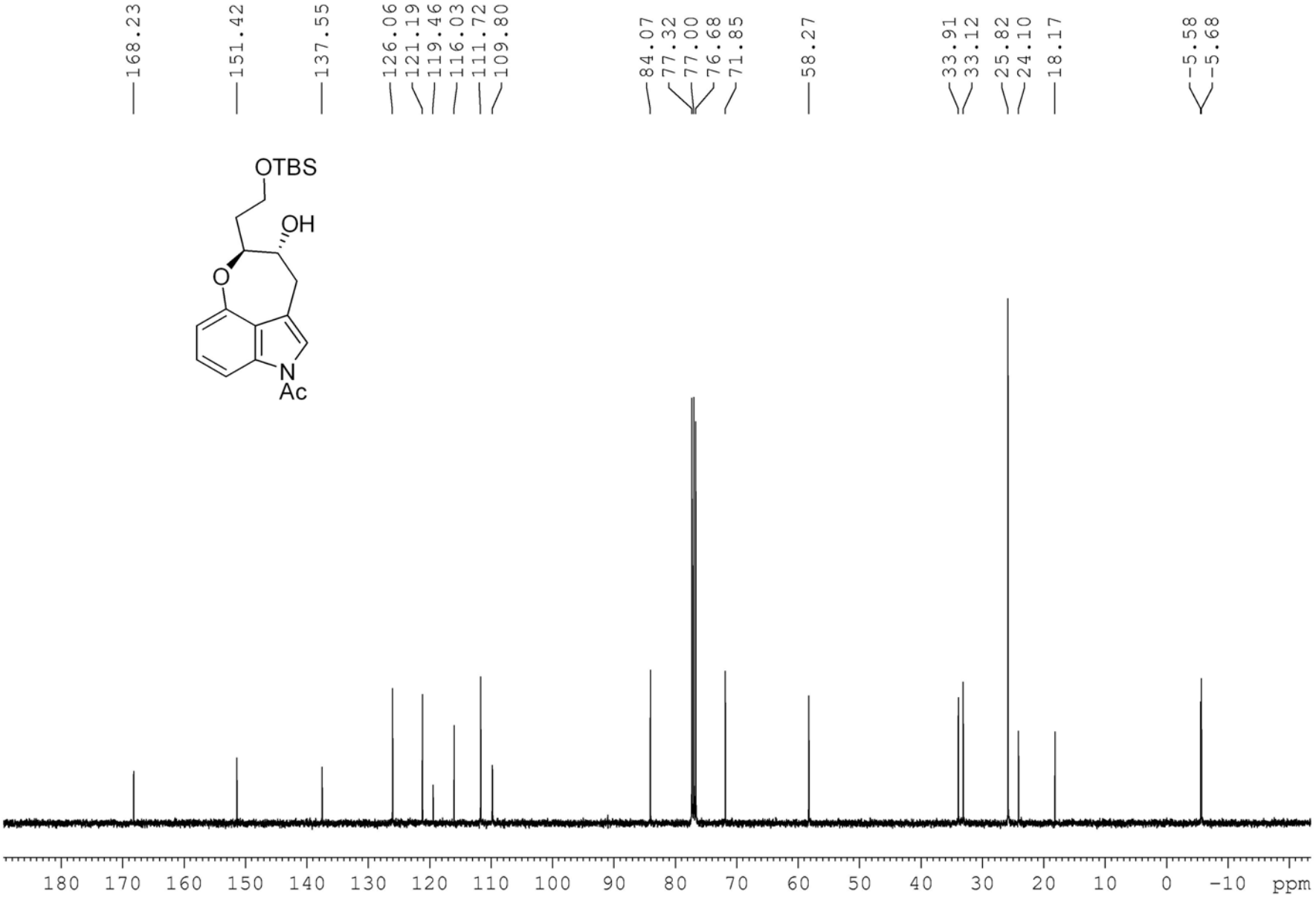
^{13}C NMR of compound 19 ($CDCl_3$; 100 MHz)



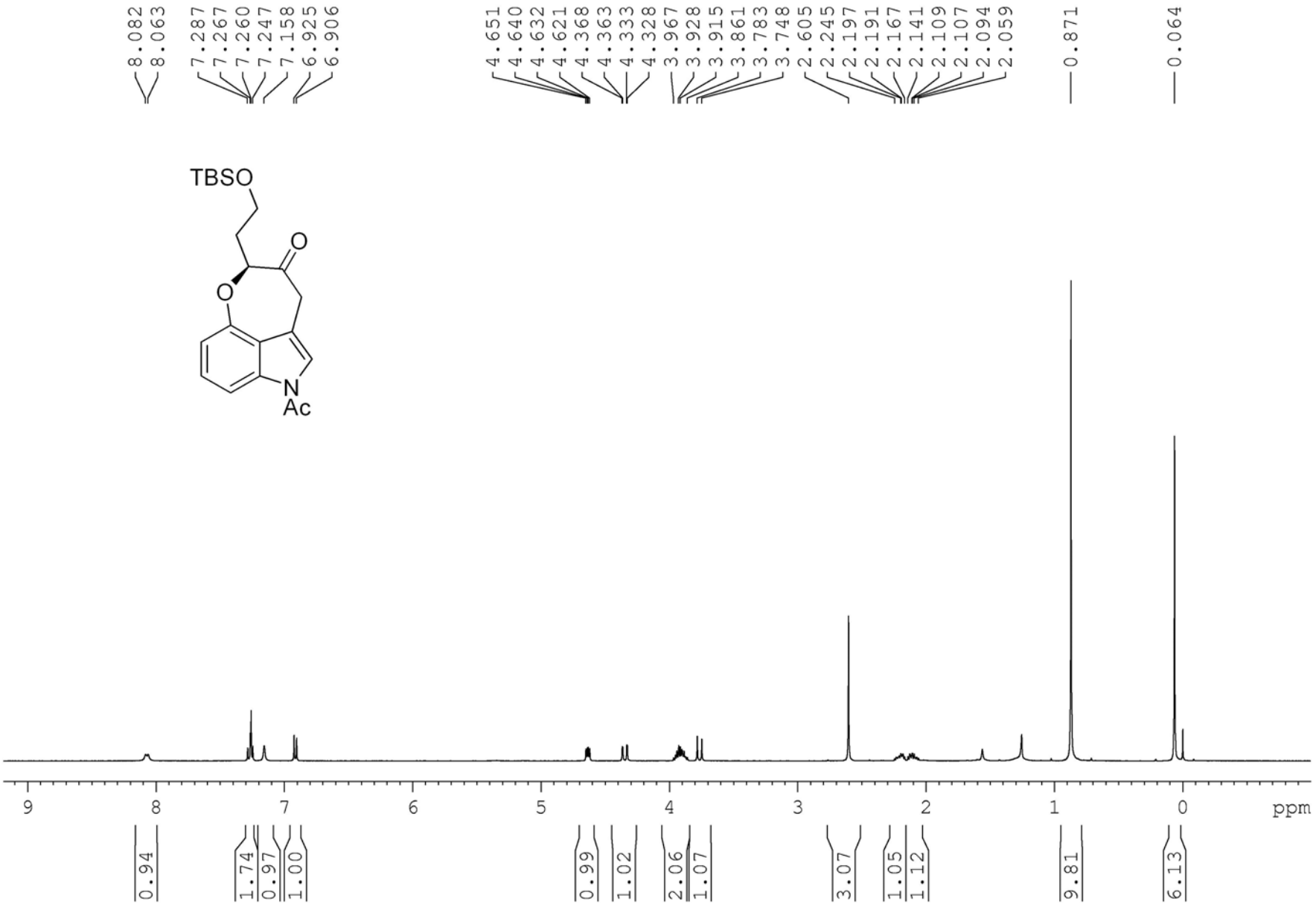
^{1}H NMR of compound 20 ($CDCl_3$; 400 MHz)



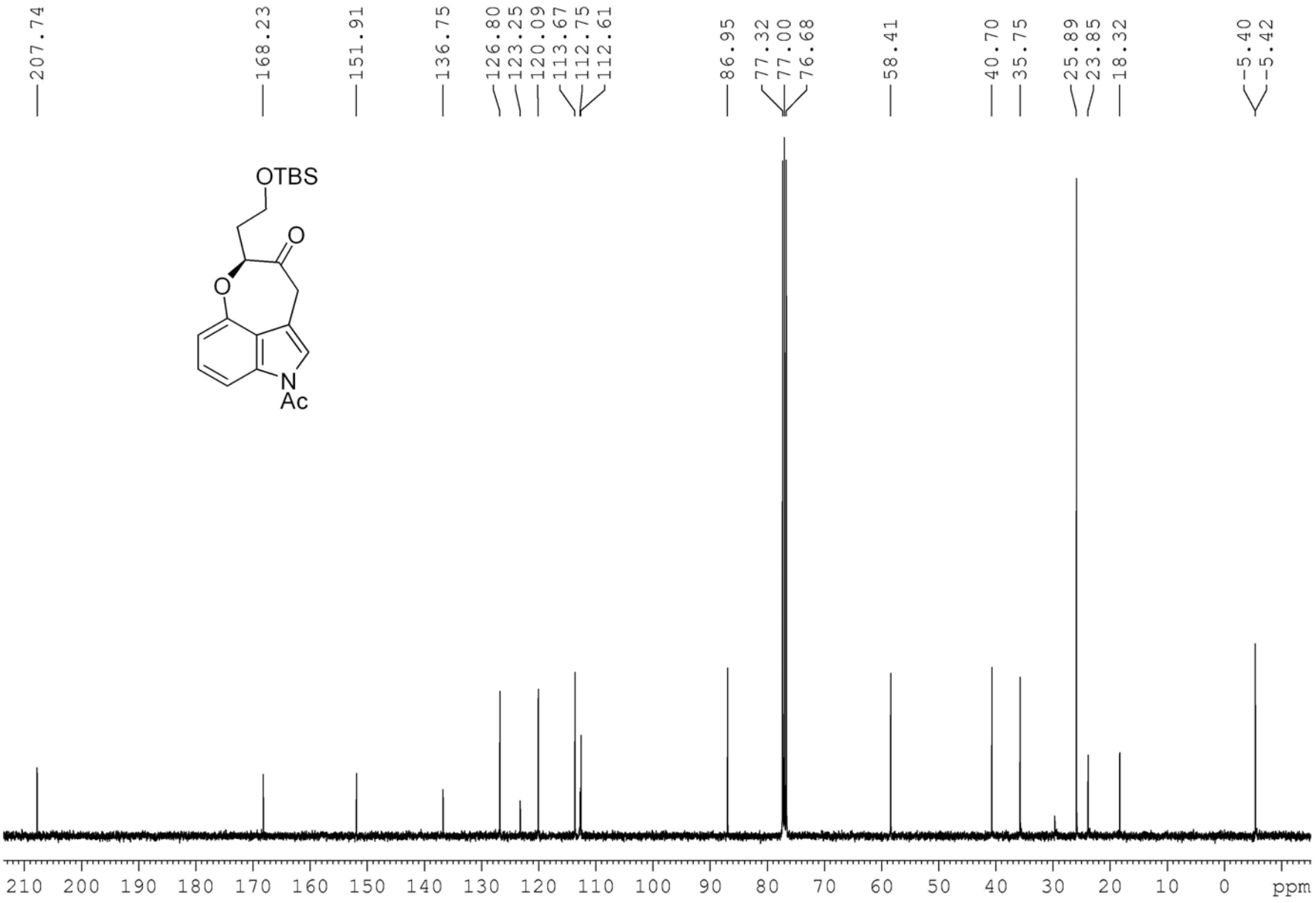
^{13}C NMR of compound 20 ($CDCl_3$; 100 MHz)



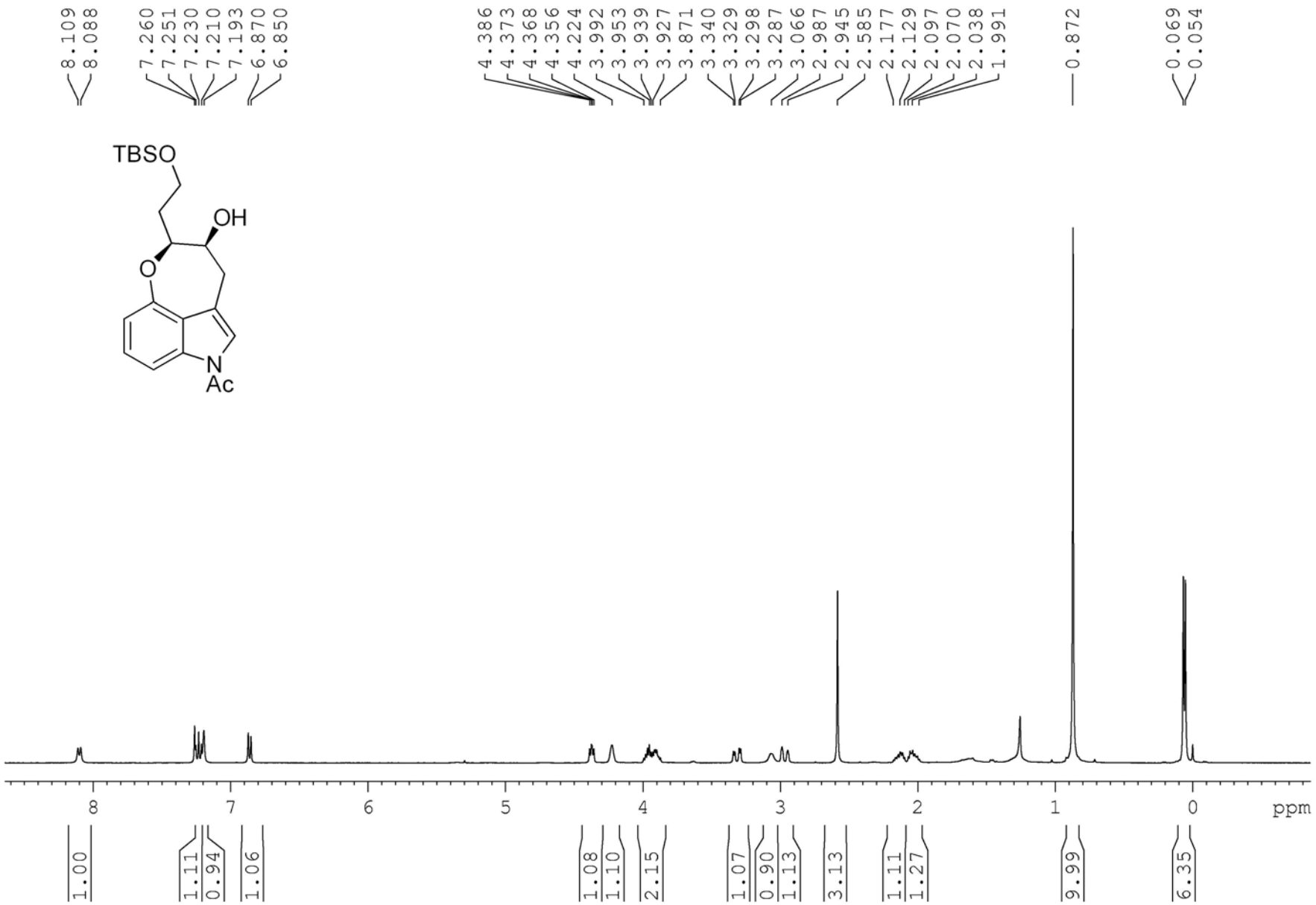
^{1}H NMR of compound 21 ($CDCl_3$; 400 MHz)



^{13}C NMR of compound 21 ($CDCl_3$; 100 MHz)



^{1}H NMR of compound 22 ($CDCl_3$; 400 MHz)



^{13}C NMR of compound 22 ($CDCl_3$; 100 MHz)