Supporting Information

Total Syntheses of (±)-penicibilaenes A and B via intramolecular aldol condensation

Rintaro Matsuo, Ayumu Watanabe, Shogo Kamo, Akinobu Matsuzawa, and Kazuyuki Sugita*

Department of Synthetic Medicinal Chemistry, Faculty of Pharmaceutical Sciences, Hoshi University, 2-4-41 Ebara, Shinagawa-ku, Tokyo 142-8501, Japan

Index

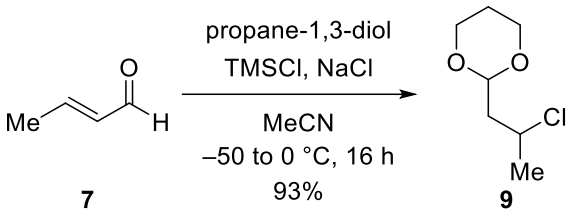
1. General 2
3. Experimental Procedures 2
2. Supplementary Tables and Scheme 13
4. Single-crystal X-ray analysis of 3 15
5. 1H and 13C NMR spectroscopic data 16
6. References 55

1. General

All reactions were carried out in a round-bottom flask or a test tube fitted with a 3-way glass stopcock under Ar atmosphere unless otherwise stated. Reagents were purchased from commercial suppliers and used as received unless otherwise noted. All work-up and purification procedures were carried out with reagent-grade solvents under ambient atmosphere. Analytical thin layer chromatography (TLC) was performed on Merck precoated TLC plates (silica gel 60 F_{254}, 0.25 mm). Flash chromatography was performed using silica gel 60N (neutral, 40-50 μm; Kanto Chemical Co., Inc.). Melting point (Mp) data were determined using a Yanaco MP apparatus and were uncorrected. IR spectra were recorded on a JASCO FT/IR 4100 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on JEOL ECA-600 spectrometers, using $CDCl_3$ or acetone-d_6 as solvent. Chemical shift values are reported in δ (ppm) relative to residual solvent signals ($CDCl_3$: 7.26 ppm for ^{1}H and 77.00 ppm for ^{13}C, acetone-d_6: 2.04 ppm for ^{1}H and 29.80 ppm or 206.26 ppm for ^{13}C). NMR data are reported as follows: chemical shifts, multiplicity (s: singlet, d: doublet, t: triplet, q: quartet, quin: quintet, m: multiplet, br: broad signal), coupling constant, and integration. High-resolution mass spectra (ESI-TOF or EI) were measured on JEOL JMS-T100LP or JMS-700. Single-crystal X-ray analyses were performed on Rigaku XtaLaB Synergy-DW instruments.

2. Experimental Procedures

2-(2-chloropropyl)-1,3-dioxane (9)

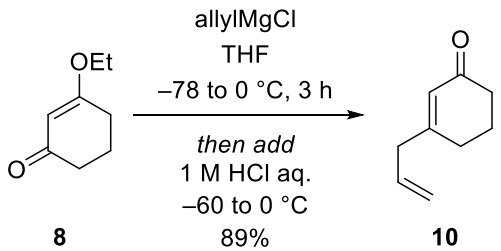


7 **9**

To a suspension of NaCl (25.01 g, 428.0 mmol), 1,3-propanediol (12.3 mL, 171.2 mmol), and TMSCl (21.7 mL, 171.2 mmol) in MeCN (143 mL) was added **7** (11.7 mL, 142.7 mmol) dropwise via syringe at −50 °C. After complete addition, the solution was allowed to warm to 0 °C and stirred for 16 h. The reaction mixture was quenched by the addition of sat. $NaHCO_3$ aq. and diluted with hexane. After the layers were separated, the aqueous layer was extracted with hexane. The combined organic solution was washed with brine, dried over Na_2SO_4, filtered, and concentrated to give **9** (21.73 g, 132.0 mmol, 93%) as a yellow oil.

IR (neat) ν_{max} = 2971, 2928, 2856, 1380. 1142, 1104, 1032, 1000 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.74 (dd, *J* = 7.2, 3.6 Hz, 1H), 4.21-4.15 (m, 1H), 4.12-4.07 (m, 2H), 3.79 (tdd, *J* = 12.0, 4.2, 3.0 Hz, 2H), 2.11-2.03 (m, 1H), 2.01-1.92 (m, 2H), 1.52 (d, *J* = 6.0 Hz, 3H), 1.37-1.34 (m, 1H); ^{13}C NMR (150 MHz, acetone-d_6) δ 100.3, 67.3, 67.2, 54.9, 46.3, 26.5, 25.8; HRMS (ESI) *m*/*z* calcd. for $C_7H_{13}ClO_2Na$ ([M+Na]$^+$) 187.0496, found 187.0499.

3-allylcyclohex-2-en-1-one (10)

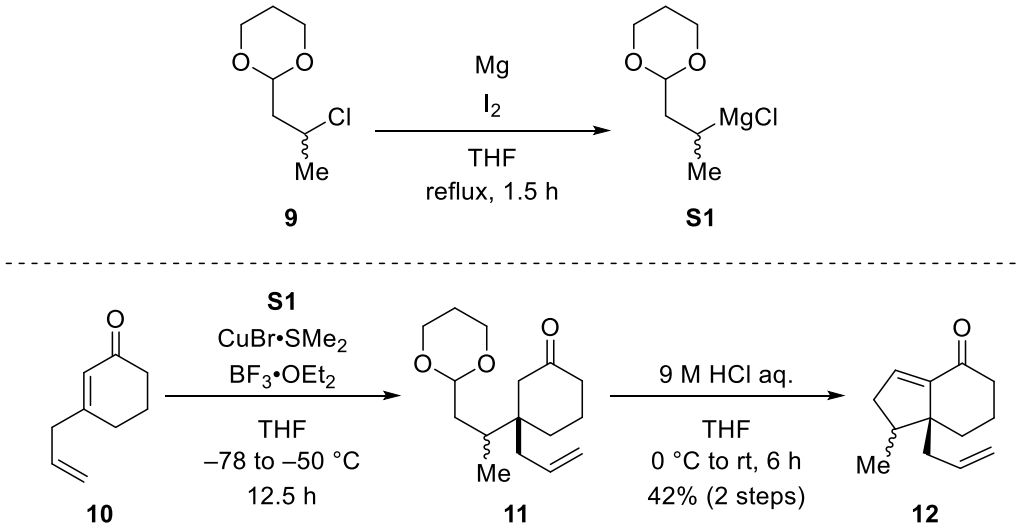


8 **10**

To a solution of **8** (11.3 g, 80.6 mmol) in THF (150 mL) was added allylMgCl (2.0 M in THF, 44.0 mL, 88.7 mmol) dropwise via syringe at −78 °C. After complete addition, the solution was allowed to warm to 0 °C and stirred for 3 h. The reaction mixture was cooled to −60 °C, 1 M HCl aq. was added, and the resulting mixture was allowed to warm to 0 °C. After the mixture was diluted with EtOAc, the biphasic solution was separated and the aqueous layer was extracted with EtOAc. The combined organic solution was washed with sat. $NaHCO_3$ aq. and brine, dried over Na_2SO_4, filtered, and concentrated to give a residue. The residue was purified by distillation at 88 °C (4 mmHg) **10** (9.82 g, 72.1 mmol, 89%) as a colorless oil.

IR (neat) ν_{max} = 2940, 2887, 1671, 1628, 1427, 1372, 1348, 1325, 1251, 1191, 1139, 997, 969, 921, 885 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.88 (d, *J* = 1.8 Hz, 1H), 5.81-5.75 (m, 1H), 5.14 (d, *J* = 9.6 Hz, 1H), 5.12 (dd, *J* = 16.8, 1.2 Hz, 1H), 2.94 (d, *J* = 7.2 Hz, 2H), 2.35 (dd, *J* = 7.2, 6.0 Hz, 2H), 2.29 (t, *J* = 6.0 Hz, 2H), 1.98 (quin, *J* = 6.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 199.8, 164.1, 133.2, 126.3, 118.3, 42.2, 37.3, 29.5, 22.6; HRMS (ESI) *m/z* calcd. for C_9H_2ONa ($[M+Na]^+$) 159.0780, found 159.0782.

7a-allyl-1-methyl-1,2,5,6,7,7a-hexahydro-4*H*-inden-4-one (12)



To a suspension of Mg (1.3 g, 53 mmol) and I_2 (4.5 mg, 35 μmol) in THF (19 mL) was added a solution of **9** (5.81 g, 35.3 mmol) in THF (4 mL) at rt. The mixture was refluxed for 25 min and was then diluted with THF (21 mL). After the resulting mixture was refluxed for further 60 min., the reaction mixture was cooled to rt to give Grignard reagent **S1** (~0.8 M).

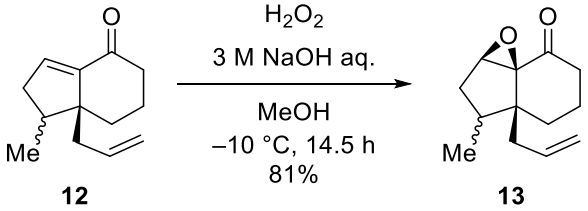
To a suspension of $CuBr{\cdot}SMe_2$ (1.37 g, 6.64 mmol) in THF (65 mL) was added the Grignard reagent **S1** (~0.8 M in THF, 28.0 mL, 22.4 mmol) dropwise via syringe at −78 °C. The mixture was allowed to warm to −60 °C and stirred for 40 min. After cooling to −78 °C, $BF_3{\cdot}OEt_2$ (2.2 mL, 18 mmol) was added to the mixture and stirred for 10 min. To this mixture was added a solution of **10** (754 mg, 5.54 mmol) in THF (4 mL) dropwise via syringe at −78 °C. After complete addition, the solution was allowed to warm to −50 °C and the additional Grignard reagent **S1** (~0.8 M in THF, 6.0 mL, 4.8 mmol) was then added. The mixture was stirred for 12.5 h at −50 °C. The reaction mixture was quenched by addition of 1 M HCl aq. and diluted with EtOAc. After the layers were separated, the aqueous layer was extracted with EtOAc. The combined organic solution was washed with sat. $NaHCO_3$ aq. and brine, dried over Na_2SO_4, filtered, and concentrated to give a residue. The residue was purified by flash column chromatography (Hexane/EtOAc = 100/0 to 1/3) to give **11** (1:1 diastereomer mixture) with a small amount of

inseparable byproduct. This mixture was used next reaction without further purification.

To a solution of **11** in THF (55 mL) was added 9 M HCl aq. (15.3 mL) at 0 °C. After being stirred for 6 h at rt, the reaction mixture was quenched by the addition of sat. $NaHCO_3$ aq. and diluted with Et_2O. After the layers were separated, the aqueous layer was extracted with Et_2O. The combined organic solution was washed with brine, dried over Na_2SO_4, filtered, and concentrated to give a residue. The residue was purified by flash column chromatography (Pentane/Et_2O = 19/1 to 17/3) to give **12** (446.2 mg, 2.34 mmol, 42% over 2 steps from **10**, 1.4:1 diastereomer mixture) as a yellow oil.

IR (neat) ν_{max} = 3073, 2931, 2876, 1685, 1616, 1442, 1248, 1161, 916 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.56 (dd, *J* = 4.2, 2.4 Hz, 1H), 6.49 (t, *J* = 2.4 Hz, 0.7 H), 5.78-5.67 (m, 1.7H), 5.08 (d, *J* = 8.4 Hz, 1H), 5.06 (dd, *J* = 16.8, 2.4 Hz, 1H), 5.23-5.01 (m, 1.4 H), 2.75 (ddd, *J* = 18.6, 7.2, 2.4 Hz, 0.7H), 2.49-2.45 (m, 0.7H), 2.43-2.34 (m, 2.7H), 2.28-2.16 (m, 3H), 2.15-2.10 (m, 3.4H), 2.04 (dd, *J* = 13.8, 6.0 Hz, 0.7H), 1.96-1.83 (m, 4.1H), 1.77-1.71 (m, 1.7H), 1.64 (dt, *J* = 13.2, 4.2 Hz, 0.7H), 1.50-1.44 (m, 1H), 1.10 (d, *J* = 6.6 Hz, 3H), 0.89 (d, *J* = 7.2 Hz, 2.1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 200.8 (2C), 149.1, 146.7, 137.4, 135.1, 134.5, 117.9, 117.8, 52.5, 50.7, 48.9, 41.3, 40.2, 40.0, 39.8, 39.3, 38.2, 37.9, 34.2, 27.4, 20.4, 19.9, 17.5, 13.2; HRMS (ESI) *m*/*z* calcd. for $C_{13}H_{18}ONa$ ($[M+Na]^+$) 213.1250, found 213.1251.

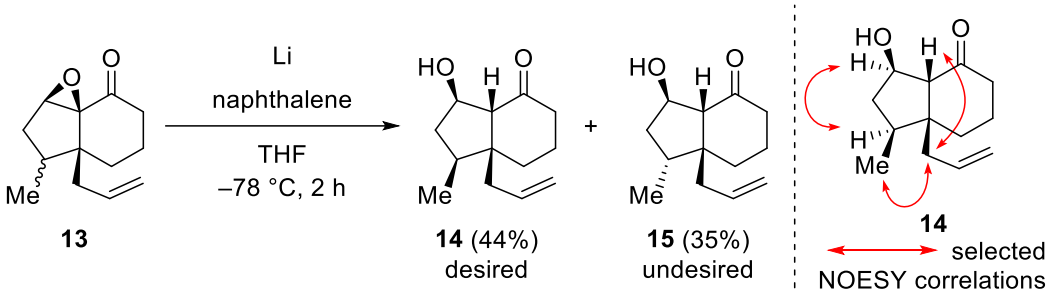
3a-allyl-3-methylhexahydroindeno[1,7a-*b*]oxiren-7(1a*H*)-one (13)



To a solution of **12** (318.6 mg, 1.67 mmol, 1:0.7 diastereomer mixture) in MeOH (17 mL) was added a mixture of 30% H_2O_2 aq. (437 μL, 5.0 mmol) and 3 M NaOH aq. (1.1 mL, 3.4 mmol) at −10 °C. The solution was stirred for 14.5 h at same temperature. The reaction mixture was quenched by the addition of sat. $Na_2S_2O_3$ aq. and neutralized with sat. NH_4Cl aq. The volatiles were removed under reduced pressure, and the residue was dissolved with EtOAc and H_2O. After the layers were separated, the aqueous layer was extracted with EtOAc. The combined organic solution was washed with brine, dried over Na_2SO_4, filtered, and concentrated to give a residue. The residue was purified by flash column chromatography (Hexane/EtOAc = 100/0 to 3/1) to give **13** (280.4 mg, 1.36 mmol, 81%, 1.4:1 diastereomer mixture) as an orange oil.

IR (neat) ν_{max} = 3074, 2939, 2882, 1717, 1638, 1446, 1414, 1314, 1142, 993, 917, 841 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.88-5.81 (m, 0.7H), 5.72-5.65 (m, 1H), 5.12 (d, 17.4 Hz, 1H), 5.10 (d, *J* = 10.2 Hz, 1H), 5.06 (d, *J* = 15.0 Hz, 0.7H), 5.05 (d, *J* = 10.2 Hz, 0.7H), 3.48 (s, 1H), 3.41 (s, 0.7H), 2.63-2.55 (m, 1.7H), 2.45 (ddd, *J* = 15.0, 7.2, 1.2 Hz, 1H), 2.39-2.22 (m, 6.1H), 2.12-1.88 (m, 6.2H), 1.79 (dd, *J* = 15.0, 1.8 Hz, 1H), 1.77-1.74 (m, 0.7H), 1.63-1.51 (m, 2H), 1.03 (d, *J* = 7.8 Hz, 3H), 0.90 (d, *J* = 7.8 Hz, 2.1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 205.3, 205.1, 134.3, 134.1, 118.0, 117.7, 74.7, 72.9, 65.1, 63.8, 50.2, 49.5, 41.1, 40.9, 39.4, 37.8, 36.1, 35.4, 35.1, 33.0, 32.5, 27.5, 20.4, 20.0, 19.9, 13.5 ; HRMS (ESI) *m*/*z* calcd. for $C_{13}H_{19}O_2$ ($[M+H]^+$) 207.1380, found 207.1376.

(1*S,3*R**,3a*R**,7a*S**)-7a-allyl-3-hydroxy-1-methyloctahydro-4*H*-inden-4-one (14) and (1*R**,3*R**,3a*R**,7a*S**)-7a-allyl-3-hydroxy-1-methyloctahydro-4*H*-inden-4-one (15)**

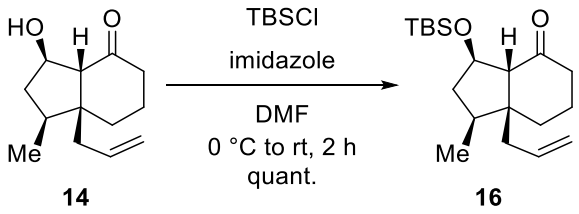


To a solution of naphthalene (392 mg, 3.06 mmol) in THF (5 mL) was added Li (66.9 mg, 9.70 mmol) at rt. The solution was stirred for 1 h at same temperature, and THF (12 mL) was then added. After cooling to −78 °C, a solution of **13** (211.2 mg, 1.02 mmol, 1:0.7 diastereomer mixture) in THF (4 mL) was added. After being stirred for 2 h, the reaction mixture was quenched by the addition of sat. NH_4Cl aq. and diluted with EtOAc. After the layers were separated, the aqueous layer was extracted with EtOAc. The combined organic solution was washed with brine, dried over Na_2SO_4, filtered, and concentrated to give a residue. The residue was purified by flash column chromatography (Hexane/EtOAc = 100/0 to 3/2) to give **14** (94.1 mg, 452 μmol, 44%) as a white solid and **15** (73.9 mg, 355 μmol, 35%) as a pale yellow oil. The stereochemistry of **14** was determined by NOESY correlations.

14: Mp = 35–36 °C; IR (neat) ν_{max} = 3411, 3074, 2955, 1689, 1442, 1092, 996, 922 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.86-5.79 (m, 1H), 5.16 (d, *J* = 10.2 Hz, 1H), 5.12 (brd, *J* = 16.8 Hz, 1H), 4.52-4.48 (m, 1H), 2.46 (d, *J* = 4.8 Hz, 1H), 2.38 (dt, *J* = 16.8, 4.8 Hz, 1H), 2.28-2.15 (m, 3H), 2.06 (dd, *J* = 13.8, 6.6 Hz, 1H), 1.99 (brt, *J* = 4.2 Hz, 1H), 1.86-1.80 (m, 2H), 1.75-1.67 (m, 2H), 1.49-1.40 (m, 2H), 0.96 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 213.7, 134.6, 119.1, 73.6, 64.6, 48.4, 40.5, 39.7, 39.3, 39.1, 30.1, 20.3, 13.6; HRMS (ESI) *m/z* calcd. for $C_{13}H_{21}O_2$ ($[M+H]^+$) 209.1536, found 209.1539.

15: IR (KBr) ν_{max} = 3415, 3075, 2949, 2876, 1697, 1640, 1454, 1345, 1245, 1072, 1000, 914 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.83-5.76 (m, 1H), 5.11 (dd, *J* = 10.2, 1.2 Hz, 1H), 5.04 (d, *J* = 16.2 Hz, 1H), 4.45 (brs, 1H), 2.44-2.38 (m, 2H), 2.32 (brd, *J* = 15.6 Hz, 1H), 2.22-2.15 (m, 2H), 2.10 (dd, *J* = 15.0, 7.2 Hz, 1H), 1.99-1.93 (m, 2H), 1.90-1.83 (m, 3H), 1.49-1.42 (m, 2H), 0.90 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 213.7, 133.5, 118.7, 74.8, 68.7, 51.6, 41.4, 40.0, 39.3, 38.0, 26.4, 21.6, 13.3; HRMS (ESI) *m/z* calcd. for $C_{13}H_{21}O_2$ ($[M+H]^+$) 209.1536, found 209.1543.

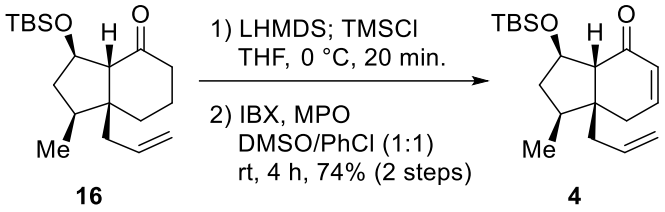
7a-allyl-3-((*tert*-butyldimethylsilyl)oxy)-1-methyloctahydro-4*H*-inden-4-one (16)



To a solution of **14** (1.77 g, 8.50 mmol) in DMF (21 mL) was added imidazole (1.74 g, 25.5 mmol) and TBSCl (1.93 g, 12.8 mmol) at 0 °C. The solution was stirred for 2 h at rt. The reaction mixture was quenched by the addition of H_2O and diluted with a mixture of EtOAc/hexane (3/7). After the layers were separated, the aqueous layer was extracted with a mixture of EtOAc/hexane (3/7). The combined organic solution was washed with brine, dried over Na_2SO_4, filtered, and concentrated to give a residue. The residue was purified by flash column chromatography (Hexane/EtOAc = 100/0 to 9/1) to give **16** (2.73 g, 8.46 mmol, quant.) as a colorless oil.

IR (neat) ν_{max} = 3076, 2953, 2884, 1706, 1638, 1464, 1383, 1254, 1042, 915, 837, 777 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.92-5.85 (m, 1H), 5.15 (dd, *J* = 10.2, 2.4 Hz, 1H), 5.11 (dd, *J* = 16.8, 2.4 Hz, 1H), 4.78-4.76 (m, 1H), 2.54 (d, *J* = 1.8 Hz, 1H), 2.37 (dd, *J* = 13.8, 6.6 Hz, 1H), 2.32-2.25 (m, 2H), 2.21-2.16 (m, 1H), 1.95 (dd, *J* = 13.8, 7.2 Hz, 1H), 1.86-1.79 (m, 2H), 1.73-1.65 (m, 2H), 1.46-1.42 (m, 1H), 1.39-1.34 (m, 1H), 0.88 (d, *J* = 6.6 Hz, 3H), 0.86 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 212.3, 135.3, 118.7, 71.8, 64.9, 50.3, 42.2, 40.4, 38.6, 37.4, 29.0, 25.8 (3C), 21.5, 17.9, 13.5, −4.8, −4.9; HRMS (ESI) *m*/*z* calcd. for $C_{19}H_{34}O_2SiNa$ ($[M+Na]^+$) 345.2220, found 345.2236.

7a-allyl-3-((*tert*-butyldimethylsilyl)oxy)-1-methyl-1,2,3,3a,7,7a-hexahydro-4*H*-inden-4-one (4)



16 **4**

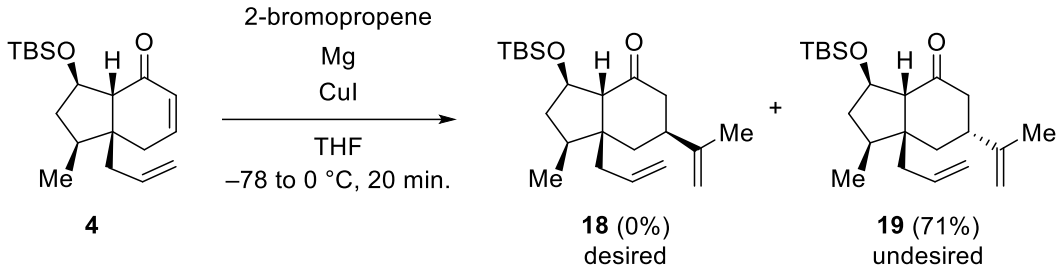
To a solution of **16** (87.9 mg, 273 μmol) in THF (5.5 mL) was added LHMDS (1 M in THF, 0.8 mL, 0.8 mmol) at 0 °C. The solution was stirred for 40 min at same temperature. To this solution was added TMSCl (69.0 μL, 545 μmol) and the resulting mixture was stirred for 20 min at 0 °C. The reaction mixture was quenched by the addition of sat. $NaHCO_3$ aq. and diluted with hexane. After the layers were separated, the aqueous layer was extracted with hexane. The combined organic solution was washed with brine, dried over Na_2SO_4, filtered, and concentrated to give crude silyl enol ether, which was used next reaction without further purification.

To a solution of crude silyl enol ether in a mixture of DMSO (0.9 mL) and PhCl (0.9 mL) was added IBX (229.0 mg, 818 μmol) and MPO (102.3 mg, 818 μmol) at rt. The solution was stirred for 4 h at same temperature. The reaction mixture was quenched by the addition of sat. $NaHCO_3$ aq. and diluted with EtOAc. After the layers were separated, the aqueous layer was extracted with EtOAc. The combined organic solution was washed with brine, dried over Na_2SO_4, filtered, and concentrated to give a residue. The residue was purified by flash column chromatography (Hexane/EtOAc = 100/0 to 1/20) to give **4** (64.9 mg, 202 μmol, 74%) as yellow oil.

IR (neat) ν_{max} = 3076, 3034, 2954, 2890, 2858, 1669, 1465, 1389, 1253, 1072, 1057, 1032, 928, 839, 778 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.75-6.72 (m, 1H), 5.96-5.94 (dt, *J* = 10.2, 1.8 Hz, 1H), 5.82-5.75 (m, 1H), 5.12 (dd, *J* = 10.2, 1.8 Hz, 1H), 5.07 (dd, *J* = 16.2, 1.8 Hz, 1H), 4.65 (dt, *J* = 8.4, 3.6 Hz, 1H), 2.63 (d, *J* = 2.4 Hz, 1H), 2.49 (dt, *J* = 19.8, 3.0 Hz, 1H), 2.43 (dd, *J* = 13.8, 7.2 Hz, 1H), 2.33 (dt, *J* = 14.4, 8.4 Hz, 1H), 2.11 (ddd, *J* = 19.8, 4.8, 1.8 Hz, 1H), 1.97 (dd, *J* = 13.8, 7.2 Hz, 1H), 1.93-1.86 (m, 1H), 1.38 (ddd, *J* = 14.4, 9.6, 4.8 Hz, 1H), 0.96 (d, *J* = 7.2 Hz, 3H), 0.87 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 199.5, 147.8, 135.5, 128.0, 118.6, 75.3, 61.7, 47.0, 42.9, 39.6, 37.3, 30.5, 25.8 (3C), 17.9, 14.7, −4.8, −5.0; HRMS (ESI) *m*/*z* calcd. for $C_{19}H_{32}O_2SiNa$ ($[M+Na]^+$) 343.2064, found 343.2054.

Installation of the isopropenyl group.

Cu mediated 1,4-addition reaction. (1*S,3*R**,3a*R**,6*R**,7a*R**)-7a-allyl-3-((*tert*-butyldimethylsilyl)oxy)-1-methyl-6-(prop-1-en-2-yl)octahydro-4*H*-inden-4-one (19)**

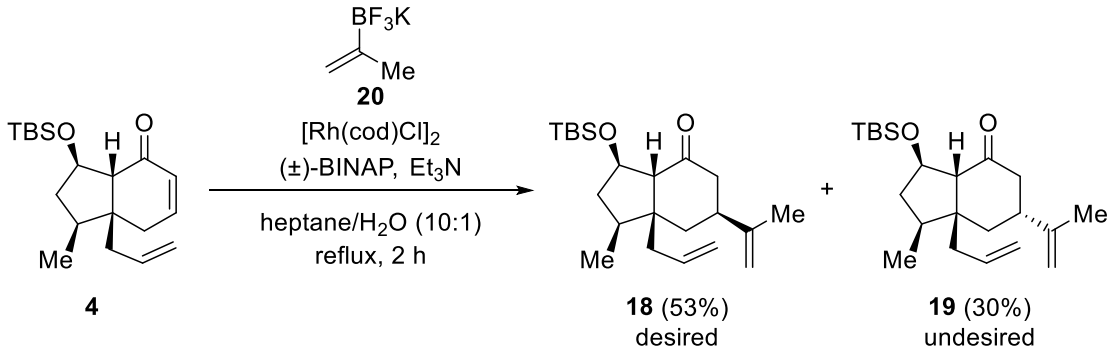


To a suspension of magnesium powder (20.9 mg, 0.86 mmol) in THF (0.8 mL) was added 2-bromopropene (69 μL, 0.79 mmol) at rt. The mixture was stirred at 60 °C until Mg disappeared and then cooled to rt to give Grignard reagent **17**. The resulting Grignard reagent **17** was added to a suspension of CuI (74.7 mg, 393 μmol) in THF (3.9 mL) at −78 °C. The solution was stirred for 20 min. To this mixture was added a solution of **4** (62.9 mg, 196 μmol) in THF (0.4 mL) dropwise via syringe at same temperature. The reaction mixture was allowed to warm to 0 °C over 20 min. The mixture was quenched by the addition of sat. $NaHCO_3$ aq. and diluted with EtOAc. After the layers were separated, the aqueous layer was extracted with a mixture of EtOAc. The combined organic solution was washed with brine, dried over Na_2SO_4, filtered, and concentrated to give a residue. The residue was purified by flash column chromatography (Hexane/EtOAc = 100/0 to 40/1) to give **19** (50.2 mg, 138 μmol, 71%) as a colorless oil.

19: IR (neat) ν_{max} = 3077, 2953, 2934, 2894, 2858, 1707, 1643, 1462, 1380, 1255, 1051, 919, 838, 778 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.87-5.80 (m, 1H), 5.16-5.08 (m, 2H), 4.75 (s, 1H), 4.69 (s, 1H), 4.68-4.65 (m, 1H), 2.58 (d, *J* = 4.8 Hz, 1H), 2.55 (dt, *J* = 13.8, 3.0 Hz, 1H), 2.44-2.35 (m, 2H), 2.28-2.17 (m, 3H), 1.85 (dt, *J* = 13.8, 2.4 Hz, 1H), 1.71 (s, 3H), 1.66-1.62 (m, 1H), 1.61 (d, *J* = 1.2 Hz, 1H), 1.39-1.34 (m, 1H), 1.19 (t, *J* = 7.2 Hz, 1H), 0.99 (d, *J* = 6.6 Hz, 3H), 0.86 (s, 9H), 0.01 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 212.5, 147.5, 134.7, 118.2, 109.5, 73.4, 65.7, 49.3, 43.4, 43.0, 43.1, 40.1, 37.9, 37.8, 25.8 (3C), 20.7, 17.9, 15.7, −4.8 (2C); HRMS (ESI) *m*/*z* calcd. for $C_{22}H_{39}O_2Si$ ($[M+H]^+$) 363.2714, found 363.2702.

Rh mediated 1,4-addition reaction.

(1*S,3*R**,3a*R**,6*S**,7a*R**)-7a-allyl-3-((*tert*-butyldimethylsilyl)oxy)-1-methyl-6-(prop-1-en-2-yl)octahydro-4*H*-inden-4-one (18) and (1*S**,3*R**,3a*R**,6*R**,7a*R**)-7a-allyl-3-((*tert*-butyldimethylsilyl)oxy)-1-methyl-6-(prop-1-en-2-yl)octahydro-4*H*-inden-4-one (19)**

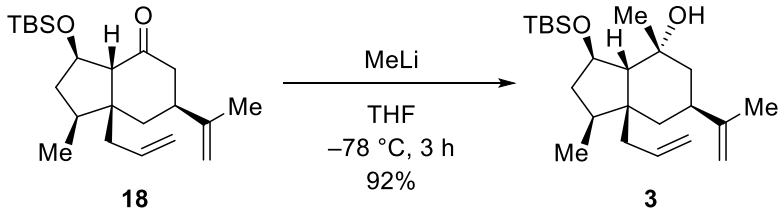


To a solution of **4** (497.7 mg, 1.55 mmol), (±)-BINAP (442.0 mg, 710 μmol), potassium isopropenyltrifluoroborate (**20**, 2.10 g, 14.2 mmol), and $[Rh(cod)Cl]_2$ (353.9 mg, 718 μmol) in heptane (142 mL) and H_2O (14 mL) was added Et_3N (2.0 mL, 14.3 mmol) at rt. The solution was refluxed for 2 h. The reaction mixture was cooled to rt and passed through a pad of Celite, and the filtrate was diluted with hexane and brine. After the layers were separated, the aqueous layer was extracted with hexane. The combined organic solution was washed

with brine, dried over Na_2SO_4, filtered, and concentrated to give a residue. The residue was purified by flash column chromatography (Hexane/toluene = 100/0 to 11/9) to give **18** (300.5 mg, 829 μmol, 53%) as a white solid and **19** (171.5 mg, 473 μmol, 30%) as a colorless oil.

18: Mp = 34–35 °C; IR (KBr) ν_{max} = 3078, 2955, 2931, 2858, 1704, 1642, 1460, 1381, 1255, 1084, 1040, 912, 837, 775 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.94 (m, 1H), 5.18 (dd, *J* = 10.2, 2.4 Hz, 1H), 5.13 (dd, *J* = 17.4, 1.8 Hz, 1H), 4.83 (ddd, *J* = 7.8, 4.8, 1.2 Hz, 1H), 4.76 (d, *J* = 1.8 Hz, 1H), 4.71 (s, 1H), 2.55 (s, 1H), 2.46 (dd, *J* = 13.2, 6.6 Hz, 1H), 2.36-2.29 (m, 2H), 2.24 (td, *J* = 13.2, 8.4 Hz, 1H), 2.14 (t, *J* = 7.8 Hz, 1H), 1.89 (dd, *J* = 13.8, 7.8 Hz, 1H), 1.76-1.65 (m, 2H), 1.73 (s, 3H), 1.59 (td, *J* = 14.4, 3.0 Hz, 1H), 1.38 (ddd, *J* = 13.2, 12.0, 4.8 Hz, 1H), 0.88-0.86 (overlap, 3H), 0.86 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 211.5, 147.6, 135.2, 119.2, 109.7, 71.0, 63.8, 49.7, 46.1, 41.9, 39.9, 38.1, 37.2, 33.9, 38.1, 37.2, 33.9, 25.9 (3C), 20.6, 17.9, 12.7, −4.8, −4.9; HRMS (ESI) *m*/*z* calcd. for $C_{22}H_{39}O_2Si$ ($[M+H]^+$) 363.2714, found 363.2700.

(1*S,3*R**,3a*R**,4*R**,6*S**,7a*R**)-7a-allyl-3-((*tert*-butyldimethylsilyl)oxy)-1,4-dimethyl-6-(prop-1-en-2-yl)octahydro-1*H*-inden-4-ol (3)**

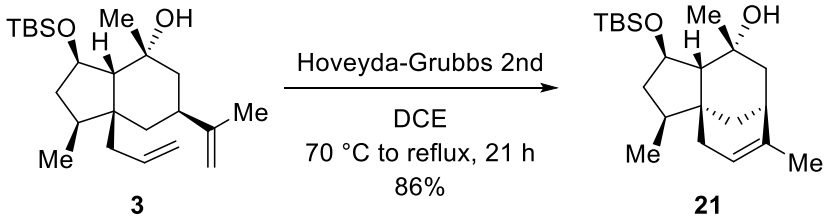


18 **3**

To a solution of **18** (105.0 mg, 290 μmol) in THF (2.8 mL) was added MeLi (3.1 M in dimethoxymethane, 470 μL, 1.46 mmol) dropwise via syringe at −78 °C. The solution was stirred for 3 h. The reaction mixture was quenched by the addition of sat NH_4Cl aq. and diluted with EtOAc. After the layers were separated, the aqueous layer was extracted with EtOAc. The combined organic solution was washed with brine, dried over Na_2SO_4, filtered, and concentrated to give a residue. The residue was purified by flash column chromatography (Hexane/Et_2O = 100/0 to 19/1) to give **3** (100.6 mg, 266 μmol, 92%) as a white solid.

Mp = 40–41 °C; IR (KBr) ν_{max} = 3519, 3075, 2952, 2929, 2856, 1643, 1463, 1373, 1254, 1044, 911, 881, 835, 773 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.87-5.80 (m 1H), 5.07 (dd, *J* = 10.2, 3.0 Hz, 1H), 5.02 (d, *J* = 17.4 Hz, 1H), 4.71 (s, 1H), 4.69 (s, 1H), 4.36 (dd, *J* = 7.2, 3.0 Hz, 1H), 2.44 (dd, *J* = 13.8, 6.0 Hz, 1H), 2.36-2.29 (m, 3H), 1.77 (dd, *J* = 13.8, 7.8 Hz, 1H), 1.72 (s, 3H), 1.68 (s, 1H), 1.55 (td, *J* = 13.8, 2.4 Hz, 1H), 1.44 (td, *J* = 13.8, 2.4 Hz, 1H), 1.37-1.28 (m, 2H), 1.28 (s, 3H), 1.20 (t, *J* = 7.2 Hz, 1H), 0.87 (s, 9H), 0.84 (d, *J* = 7.2 Hz, 3H), 0.78 (s, 1H), 0.061 (s, 3H), 0.058 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 150.3, 136.6, 117.8, 108.4, 74.0, 72.0, 57.7, 46.2, 45.3, 44.5, 38.6, 38.3, 34.6, 34.0, 31.6, 25.8 (3C), 21.1, 17.8, 13.4, −4.4, −4.7; HRMS (ESI) *m*/*z* calcd. for $C_{23}H_{42}O_2SiNa$ ($[M+Na]^+$) 401.2846, found 401.2859.

(1*R,3*S**,3a*R**,7*S**,9*R**,9a*R**)-1-((*tert*-butyldimethylsilyl)oxy)-3,6,9-trimethyl-1,2,3,4,7,8,9,9a-octahydro-3a,7-methanocyclopenta[8]annulen-9-ol (21)**

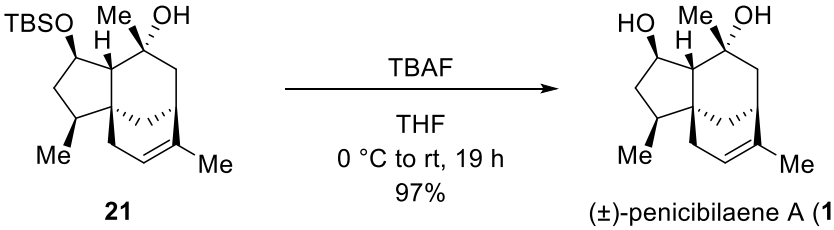


3 **21**

To a solution of **3** (73.5 mg, 194 μmol) in DCE (3.8 mL) was degassed with sonication under an argon atmosphere. To this solution was added Hoveyda-Grubbs 2nd catalyst (62.5 mg, 99.7 μmol) at rt. The solution was stirred for 16.5 h at 70 °C. The reaction mixture was then refluxed for further 4.5 h. The reaction mixture was cooled to rt and passed through a pad of Celite, and the filtrate was concentrated to give a residue. The residue was purified by flash column chromatography (Hexane/CH_2Cl_2 = 100/0 to 3/2) to give **21** (58.3 mg, 166 μmol, 86%) as a colorless oil.

IR (neat) ν_{max} = 3491, 2955, 2930, 2888, 2860, 1459, 1372, 1254, 1117, 1072, 836, 774 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.26-5.25 (brm, 1H), 4.42-4.38 (m, 1H), 2.18 (brd, *J* = 7.8 Hz, 1H), 2.08-2.02 (m, 2H), 1.80 (dd, *J* = 15.0, 9.0 Hz, 1H), 1.73 (dd, *J* = 16.8, 4.8 Hz, 1H), 1.67-1.61 (m, 2H), 1.65 (s, 3H), 1.57-1.55 (m, 1H), 1.49 (s, 1H), 1.42-1.36 (m, 2H), 1.24 (s, 3H), 0.91 (d, *J* = 6.6 Hz, 3H), 0.88 (t, *J* = 7.2 Hz, 1H), 0.86 (s, 9H), 0.063 (s, 3H), 0.060 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 139.8, 119.9, 73.8, 71.6, 60.5, 40.0, 41.9, 41.6, 41.0, 34.60, 34.56, 32.7, 31.3, 25.8 (3C), 21.9, 17.8, 14.5, −3.6, −4.9; HRMS (ESI) *m*/*z* calcd. for $C_{21}H_{38}O_2SiNa$ ($[M+Na]^+$) 373.2533, found 373.2525.

(±)-Penicibilaene A (1)

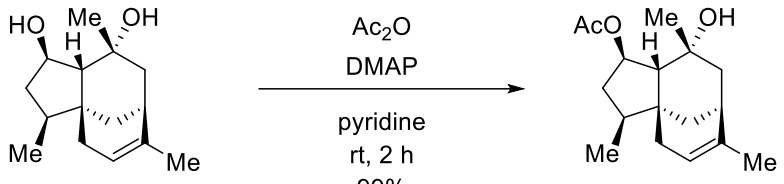


21 (±)-penicibilaene A (**1**)

To a solution of **21** (50.1 mg, 143 μmol) in THF (950 μL) was added TBAF (1.0 M in THF, 500 μL, 500 μmol) at 0 °C. The solution was stirred for 19 h at rt. The reaction mixture was quenched by the addition sat NH_4Cl aq. and diluted with EtOAc. After the layers were separated, the aqueous layer was extracted with EtOAc. The combined organic solution was washed with brine, dried over Na_2SO_4, filtered, and concentrated to give a residue. The residue was purified by flash column chromatography (Hexane/EtOAc = 100/0 to 3/2) to give (±)-penicibilaene A (**1**) (32.6 mg, 138 μmol, 97%) as a white solid.

IR (KBr) ν_{max} = 3361, 3306, 2962, 2942, 2912, 2887, 1442, 1415, 1145, 1114, 1037, 807 cm^{-1}; ^1H NMR (600 MHz, acetone-d_6) δ 5.22 (dd, *J* = 3.0, 1.8 Hz, 1H), 4.46-4.42 (m, 1H), 3.41 (d, *J* = 5.4 Hz, 1H), 3.21 (s, 1H), 2.14 (brd, *J* = 9.0 Hz, 1H), 2.06-2.02 (m, 1H), 2.02-1.99 (m, 1H), 1.88 (dd, *J* = 14.4, 9.0 Hz, 1H), 1.86 (td, *J* = 11.4, 3.0 Hz, 1H), 1.75-1.71 (m, 1H), 1.70-1.66 (m, 1H), 1.62 (d, *J* = 1.8 Hz, 3H), 1.49 (d, *J* = 13.8 Hz, 1H), 1.45 (d, *J* = 6.6 Hz, 1H), 1.38 (td, *J* = 11.4, 9.0 Hz, 1H), 1.29 (ddd, *J* = 11.4, 4.2, 1.2 Hz, 1H), 1.25 (s, 3H), 0.87 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 140.9, 120.7, 73.4, 71.3, 61.4, 42.6, 42.5 (2C), 42.4, 36.0, 35.3, 33.2, 31.4, 22.2, 15.0; HRMS (ESI) *m*/*z* calcd. for $C_{15}H_{24}O_2Na$ ($[M+Na]^+$) 259.1699, found 259.1707.

(±)-Penicibilaene B (2)

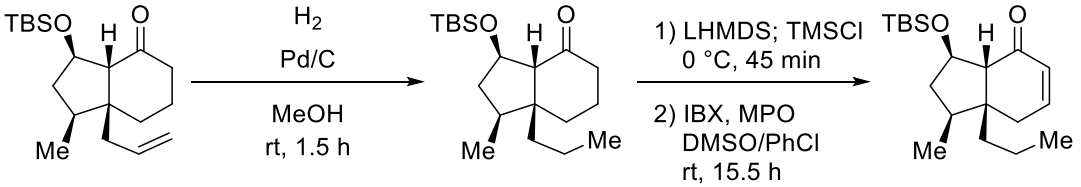


(±)-penicibilaene A (**1**) (±)-penicibilaene B (**2**)

To a solution of (±)-penicibilaene A (**1**) (5.03 mg, 21.3 μmol) and DMAP (1.1 mg, 9.0 μmol) in pyridine (450 μL) was added Ac_2O (10.0 μL, 106 μmol) at rt. The solution was stirred for 2 h at rt. The reaction mixture was quenched by the addition sat NH_4Cl aq. and diluted with EtOAc. After the layers were separated, the aqueous layer was extracted with EtOAc. The combined organic solution was washed with brine, dried over Na_2SO_4, filtered, and concentrated to give a residue. The residue was purified by flash column chromatography (Hexane/EtOAc = 100/0 to 7/3) to give (±)-penicibilaene B (**2**) (5.87 mg, 21.1 μmol, 99%) as a white solid.

IR (KBr) ν_{max} = 3493, 2955, 2926, 2888, 2842, 1716, 1456, 1372, 1276, 1147, 1111, 1022, 929, 818 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.36 (ddd, *J* = 13.8, 7.8, 6.0 Hz, 1H), 5.26 (d, *J* = 4.8 Hz, 1H), 2.31 (ddd, *J* = 12.6, 7.8, 6.0 Hz, 1H), 2.21 (d, *J* = 9.0 Hz, 1H), 2.05 (d, *J* = 16.8 Hz, 1H), 2.00 (s, 3H), 1.83 (dd, *J* = 15.0, 9.6 Hz, 1H), 1.79-1.70 (m, 4H), 1.65 (brs, 3H), 1.53 (d, *J* = 15.0 Hz, 1H), 1.44 (dd, *J* = 11.4, 2.4 Hz, 1H), 1.37 (dt, *J* = 12.6, 9.0 Hz, 1H), 1.15 (s, 3H), 1,15 (overlap, 1H), 0.91 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.9, 140.3, 119.4, 71.1, 56.8, 41.8, 41.7, 41.2, 38.3, 34.4, 34.2, 31.9, 30.3, 21.8, 21.4, 13.9; HRMS (ESI) *m/z* calcd. for $C_{17}H_{26}O_3Na$ ($[M+Na]^+$) 301.1774, found 301.1782.

(1*S,3*R**,3a*R**,7a*R**)-3-((*tert*-butyldimethylsilyl)oxy)-1-methyl-7a-propyl-1,2,3,3a,7,7a-hexahydro-4*H*-inden-4-one (S3)**



16 **S2** **S3**

A suspension of **16** (202.9 mg, 629 μmol) and 10% Pd/C (67.2 mg, 63.2 μmol) in MeOH (6.3 mL) was stirred under hydrogen atmosphere at rt for 1.5 h. The mixture was filtered through a pad of Celite and washed with MeOH. The filtrate was concentrated to give crude **S2**, which was used next reaction without further purification.

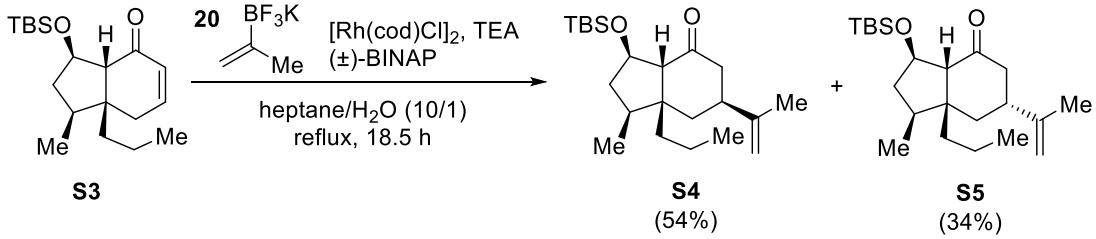
To a solution of crude **S2** in THF (12.5 mL) was added LHMDS (1 M in THF, 1.9 mL, 1.9 mmol) at 0 °C. The solution was stirred for 55 min at same temperature. To this solution was added TMSCl (360 μL, 2.84 mmol) and the resulting mixture was stirred for 45 min at 0 °C. The reaction mixture was quenched by the addition of sat. $NaHCO_3$ aq. and diluted with hexane. After the layers were separated, the aqueous layer was extracted with hexane. The combined organic solution was washed with H_2O and brine, dried over Na_2SO_4, filtered, and concentrated to give crude silyl enol ether, which was used next reaction without further purification.

To a solution of crude silyl enol ether in a mixture of a mixture of PhCl (2.1 mL) and DMSO (2.1 mL) was added IBX (529.7 mg, 1.89 mmol) and MPO (237.3 mg, 1.90 mmol) at rt. The solution was stirred for 15.5 h at the same temperature. The reaction mixture was quenched by the addition of sat. $NaHCO_3$ aq. and diluted with a mixture of hexane/EtOAc (7:3). After the layers were separated, the aqueous layer was extracted with a mixture of

hexane/EtOAc (7:3). The combined organic solution was washed with brine, dried over Na_2SO_4, filtered, and concentrated to give a residue. The residue was purified by flash column chromatography (Hexane/Et_2O = 100/0 to 24/1) to give **S3** (105.2 mg, 326 μmol, 52%) as pale yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.76-6.73 (m, 1H), 5.96 (ddd, *J* = 10.2, 3.0, 1.8 Hz, 1H), 4.61 (quin, 1H), 2.58 (d, *J* = 3.0 Hz, 1H), 2.40 (dt, *J* = 19.8, 3.0 Hz, 1H), 2.30 (dt, *J* = 13.8, 8.4 Hz, 1H), 2.13 (ddd, *J* = 19.8, 4.8, 1.8 Hz, 1H), 1.87-1.81 (m, 1H), 1.61 (td, *J* = 12.0, 4.8 Hz, 1H), 1.37-1.28 (m, 2H), 1.26-1.17 (m, 1H), 1.11 (td, *J* = 12.0, 3.6 Hz, 1H), 0.92 (d, *J* = 6.6 Hz, 3H), 0.90 (t, *J* = 6.6 Hz, 3H), 0.87 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 200.0, 147.9, 128.1, 75.3, 61.8, 47.1, 42.8, 40.0, 35.4, 31.3, 25.8 (3C), 18.2, 17.9, 14.8, 14.7, −4.9, −5.0; HRMS (ESI) *m*/*z* calcd. for $C_{19}H_{35}O_2Si$ ([M+H]$^+$) 323.2401, found 323.2401.

(1*S,3*R**,3a*R**,6*S**,7a*R**)-3-((*tert*-butyldimethylsilyl)oxy)-1-methyl-6-(prop-1-en-2-yl)-7a-propyloctahydro-4*H*-inden-4-one (S4) and (1*S**,3*R**,3a*R**,6*R**,7a*R**)-3-((*tert*-butyldimethylsilyl)oxy)-1-methyl-6-(prop-1-en-2-yl)-7a-propyloctahydro-4*H*-inden-4-one (S5)**

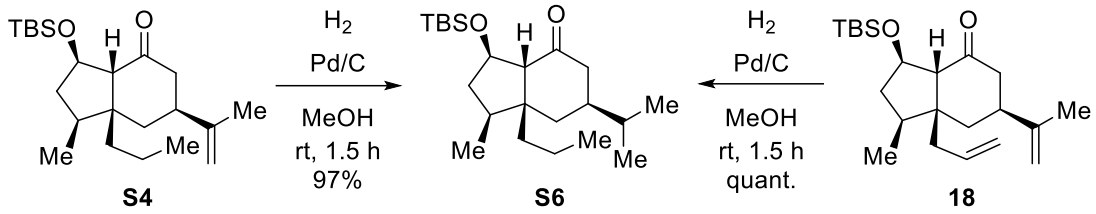


To a solution of **S3** (30.0 mg, 93.0 μmol), (±)-BINAP (29.0 mg, 46.6 μmol), **20** (138.3 mg, 935 μmol), and $[Rh(cod)Cl]_2$ (28.2 mg, 57.2 μmol) in heptane (9.3 mL) and H_2O (930 μL) was added Et_3N (130 μL, 933 mmol) at rt. The solution was refluxed for 18.5 h. The reaction mixture was cooled to rt and passed through a pad of Celite, and the filtrate was diluted with hexane and brine. After the layers were separated, the aqueous layer was extracted with hexane. The combined organic solution was dried over Na_2SO_4, filtered, and concentrated to give a residue. The residue was purified by flash column chromatography (Hexane/toluene = 100/0 to 3/1) to give **S4** (18.2 mg, 49.9 μmol, 54%) as a white solid and **S5** (11.4 mg, 31.3 μmol, 34%) as colorless oil.

S4: ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.77-4.75 (m, 2H), 4.71 (brs, 1H), 2.50 (brs, 1H), 2.38-2.33 (m, 2H), 2.21-2.15 (m, 2H), 1.73 (s, 3H), 1.71-1.55 (m, 4H), 1.40-1.33 (m 3H), 1.10-1.05 (m, 1H), 0.93 (t, *J* = 7.2 Hz, 3H), 0.85 (s, 9H) 0.84 (d, *J* = 8.4 Hz, 3H), 0.03 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 211.9, 147.7, 109.6, 71.0, 64.0, 49.5, 45.9, 41.8, 40.0, 38.3, 35.4, 34.5, 25.7 (3C), 20.6, 17.8, 17.5, 14.7, 12.6, −4.8, −5.0; HRMS (ESI) *m*/*z* calcd. for $C_{22}H_{40}O_2SiNa$ ([M+Na]$^+$) 387.2690, found 387.2680.

S5: ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.77 (brt, *J* = 1.2 Hz, 1H), 4.72 (brs, 1H), 4.57-4.54 (m, 1H), 2.52-2.47 (m, 3H), 2.39-2.36 (m, 1H), 2.28 (dd, *J* = 15.0, 13.2 Hz, 1H), 1.76 (brd, 13.8 Hz, 1H), 1.74 (s, 3H), 1.74-1.70 (m, 1H), 1.48-1.42 (m, 1H), 1.35-1.20 (m, 5H), 0.95 (d, *J* = 7.2 Hz, 3H), 0.90 (t, *J* = 7.2 Hz, 3H), 0.85 (s, 9H), −0.010 (s, 3H), −0.012 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 212.8, 147.6, 109.6, 74.6, 66.9, 50.2, 43.4, 43.2, 42.2, 40.7, 35.4, 25.7 (3C), 20.7, 17.9, 17.4, 16.7, 14.7, −4.83, −4.85; HRMS (ESI) *m*/*z* calcd. for $C_{22}H_{40}O_2SiNa$ ([M+Na]$^+$) 387.2690, found 387.2687.

(1*S,3*R**,3a*R**,6*S**,7a*R**)-3-((*tert*-butyldimethylsilyl)oxy)-6-isopropyl-1-methyl-7a-propyloctahydro-4H-inden-4-one (S6)**



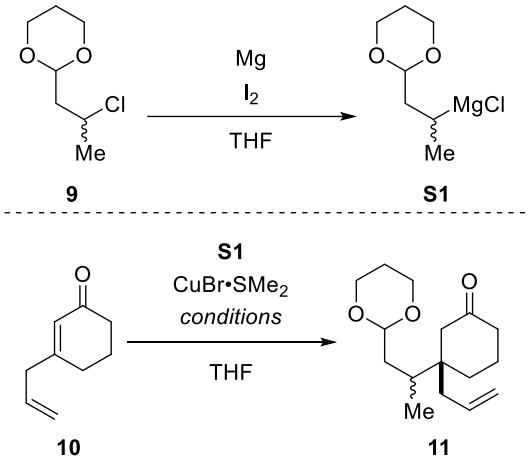
From S4: A suspension of **S4** (5.3 mg, 14.5 μmol) and 10% Pd/C (2.3 mg, 2.2 μmol) in MeOH (730 μL) was stirred under hydrogen atmosphere at rt for 1.5 h. The mixture was filtered through a pad of Celite and washed with MeOH. The filtrate was concentrated to give a residue. The residue was purified by flash column chromatography (Hexane/Et_2O = 100/0 to 19/1) to give **S6** (5.2 mg, 14.2 μmol, 97%) as a colorless oil.

From 18: A suspension of **18** (14.6 mg, 40.3 μmol) and 10% Pd/C (4.6 mg, 4.3 μmol) in MeOH (800 μL) was stirred under hydrogen atmosphere at rt for 1.5 h. The mixture was filtered through a pad of Celite and washed with MeOH. The filtrate was concentrated to give a residue. The residue was purified by flash column chromatography (Hexane/Et_2O = 100/0 to 19/1) to give **S6** (16.1 mg, 43.9 μmol, quant.) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 474-4.71 (m, 1H), 2.47 (brs, 1H), 2.31 (ddd, *J* = 13.2, 3.0, 1.8 Hz, 1H), 2.18-2.13 (m, 1H), 1.92 (t, *J* = 12.0 Hz, 1H), 1.65-1.43 (m, overlap with H_2O, 6H), 1.39-1.31 (m, 3H), 1.08-1.03 (m, 1H), 0.93 (t, *J* = 6.6 Hz, 3H), 0.89 (d, *J* = 6.6 Hz, 3H), 0.88 (d, *J* = 6.6 Hz, 3H), 0.85 (s, 9H), 0.82 (d, *J* = 6.6 Hz, 3H), 0.02 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 212.9, 71.1, 64.1, 49.4, 44.5, 41.8, 39.3, 38.3, 35.6, 32.74, 32.66, 25.8 (3C), 19.7, 19.3, 17.8, 17.5, 14.8, 12.5, −4.8, −5.0; HRMS (ESI) *m*/*z* calcd. for $C_{22}H_{43}O_2Si$ ($[M+H]^+$) 367.3027, found 367.3017.

3. Supplementary Tables and Scheme

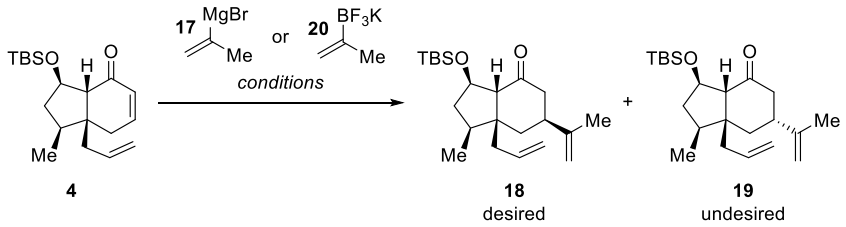
Table S1. Optimization of 1,4-addition of the Grignard reagent prepared from chloride 9.



entry	**S1** (eq.)	CuBr•SMe_2 (eq.)	additive (eq.)	temp. (°C)	time (h)	results[a, b]
1	3.0	1.0	TMSCl (7.0), TMEDA (7.0)	−78 to −25	1.5	**11** (72%), dr = 1:1.7
2	10.0	1.3	-	−78 to −35	16.5	**11** (52%), dr = 1:1
3	3.0	1.0	TMSCl (7.0)	−78 to −50	16.5	**11** (65%), dr = 1:1.7
4	4.0	1.0	$BF_3{\cdot}Et_2O$ (3.0)	−78 to −50	14	**11** (97%), dr = 1:1
5	3.0	1.0	$BF_3{\cdot}Et_2O$ (1.7)	−78 to −50	14	**11** (83%), dr = 1:1.2
6	5.0	1.0	$BF_3{\cdot}Et_2O$ (1.7)	−78	14.5	**11** (46%), dr = 1:1

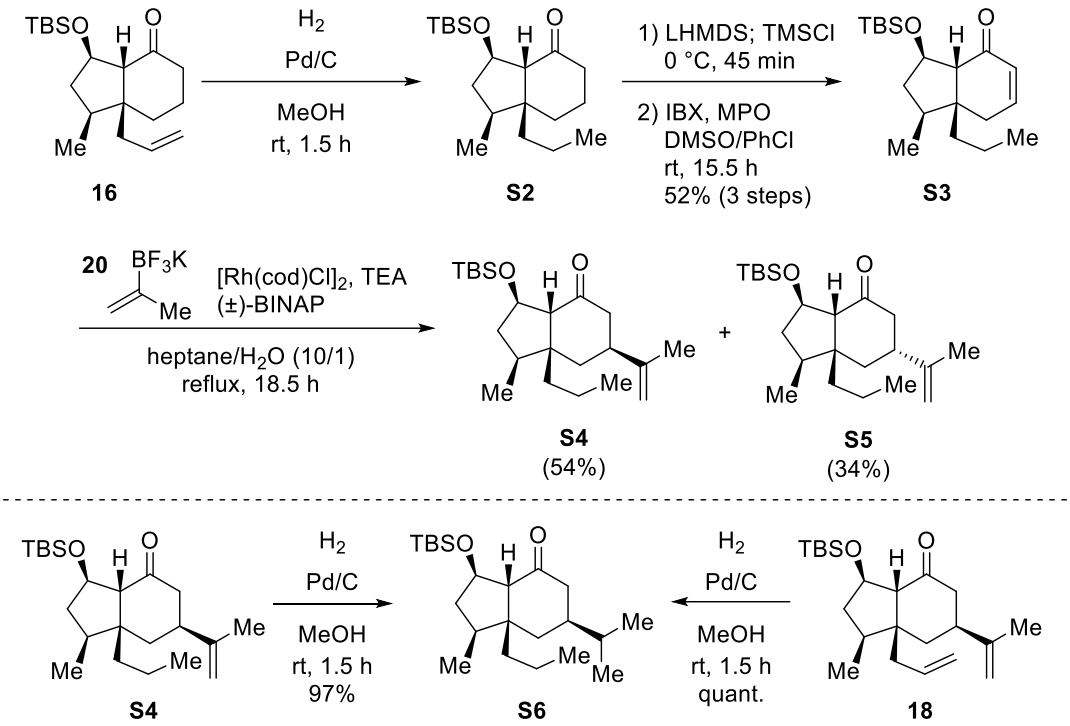
[a]NMR yield. [b]dr = desired : undesired

Table S2. Optimization of the stereoselective incorporation of the isopropenyl group.



entry	reagent (eq.)	solvents	temp. (°C)	time	results[a]
1	CuI (2.0), **17** (4.0)	THF	–78 to 0	20 min	**19** (71%)[b]
2	CuI (2.0), **17** (6.0), TMEDA (10.0)	THF	–78 to 0	1 h	**18** (trace), **19** (84%)
3	CuI (2.0), **17** (12.0), $BF_3{\cdot}EtO_2$ (5.0)	THF	–78 to 0	1 h	**18** (trace), **19** (58%)
4	$[Rh(cod)Cl]_2$ (0.5), **20** (10), KF (10), TTBP·HBF_4[c] (1.0)	heptane/H_2O (10/1)	50 to 60	18.5 h	**18** (35%), **19** (18%)
5	$[Rh(cod)Cl]_2$ (0.5), **20** (10), KF (10), TTBP·HBF_4[c] (1.0)	heptane/H_2O (10/1)	30	7 days	**4** (56%), **18** (22%), **19** (8%)
6	$[Rh(cod)Cl]_2$ (0.5), **20** (10), TEA (10), TTBP·HBF_4[c] (1.0)	heptane/H_2O (10/1)	60	22 h	**18** (59%), **19** (32%)
7	$[Rh(cod)Cl]_2$ (0.5), **20** (10), TEA (10), BINAP (0.5)	heptane/H_2O (10/1)	reflux	2 h	**18** (53%)[b], **19** (30%)[b]
8	$[Rh(cod)Cl]_2$ (0.5), **20** (10), TEA (10), BINAP (0.5)	heptane/H_2O (10/1)	30	24 h	**18** (41%), **19** (18%)

[a]NMR yield (DMF was used as an internal standard). [b]Isolated yield. [c]Tri-*tert*-butylphosphin tetrafluoroborate



Scheme S1. Reduction of double bond of allyl group and Rh-mediated 1,4-addition of 20.

4. Single-crystal X-ray analysis of 3.

Single crystals of **3** suitable for X-ray crystallographic analysis was obtained by slow evaporation of a solution of **3** in Hexane at 23 °C. All measurements were made on a Rigaku XtaLaB Synergy-DW diffractometer using graphite monochromated Cu-Kα radiation. The structure was solved by direct methods and expanded using Fourier techniques. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined using the riding model. Refined crystallographic parameters are summarized in **Table S3**. The ORTEP representation of **3** is depicted in **Figure S1**.

Table S3. Summary of crystallographic data of 3.

	3
Empirical formula	$C_{46}H_{84}O_4Si_2$
Formula Weight	757.31
Temperature/K	90(2)
Crystal system	monoclinic
Space group	$P2_1$
a (Å)	15.8123(9)
b (Å)	10.6777(6)
c (Å)	14.1023(7)
α	90°
β	95.002(5)°
γ	90°
Volume ($Å^3$)	2371.9(2)
Z	2
D_{calc} (g/cm^3)	1.060
F_{000}	840.0
Goodness of Fit Indicator	1.074

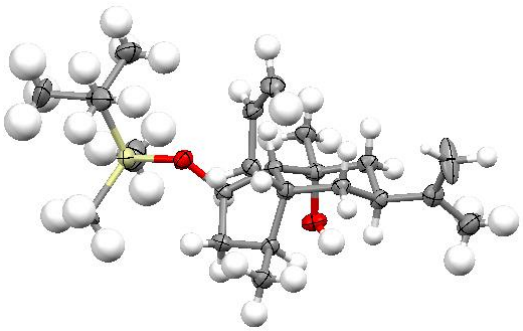
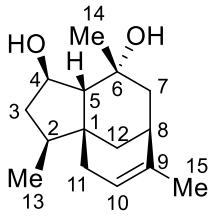


Figure S1. ORTEP diagram of 3 at the 50% probability level.

5. ^{1}H and ^{13}C NMR spectroscopic data

Table S2. NMR spectroscopic data (acetone-d_6) for natural and synthetic (±)-penicibilaene A (1).[S1,S2]

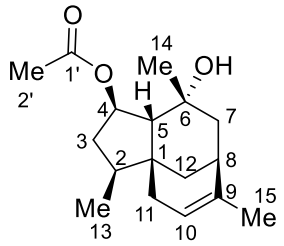


penicibilaene A (**1**)

	Natural **1**[a, S1]		Dong's synthetic **1**[a, S2]		Our synthetic **1**[b]	
No.	δ_C	δ_H (mult, *J* in Hz)	δ_C	δ_H (mult, *J* in Hz)	δ_C	δ_H (mult, *J* in Hz)
1	42.58		42.54		42.52	
2	42.62	1.69 (m)	42.60	1.69 (m)	42.57	1.68 (m)
3α	42.5	2.07 (m)	42.5	2.07 (m)	42.52	2.06 (m)
3β		1.38 (dt, 11.7, 8.6)		1.38 (dt, 11.8, 8.6)		1.38 (dt, 11.4, 9.0)
4	73.4	4.45 (m)	73.4	4.45 (p, 6.9)	73.4	4.44 (m)
5	61.5	1.46 (d, 6.2)	61.5	1.46 (d, 6.2)	61.4	1.45 (d, 6.6)
6	71.3		71.3		71.3	
7α	33.3	1.86 (dd, 12.0, 4.8)	33.3	1.86 (m)	33.2	1.86 (td, 11.4, 3.0)
7β		1.30 (dd, 12.0, 3.9)		1.30 (ddd, 11.6, 4.0, 1.4)		1.29 (ddd, 11.4, 4.2, 1.2)
8	36.1	2.15 (dd, 4.8, 3.9)	36.0	2.15 (d, 8.5)	36.0	2.14 (brd, 9.0)
9	140.9		140.9		140.9	
10	120.7	5.23 (dd, 3.1, 1.5)	120.7	5.23 (d, 4.9)	120.7	5.22 (dd, 3.0, 1.8)
11α	35.4	2.01 (d, 16.3)	35.4	2.00 (m)	35.3	2.01 (brd, 15.6)
11β		1.74 (m)		1.74 (m)		1.73 (m)
12α	42.4	1.90 (dd, 14.2, 5.6)	42.4	1.89 (m)	42.4	1.88 (dd, 14.4, 9.0)
12β		1.50 (d, 14.2)		1.50 (d, 14.2)		1.49 (d, 13.8)
13	15.0	0.89 (d, 7.1)	15.0	0.88 (d, 7.0)	15.0	0.87 (d, 7.2)
14	31.4	1.26 (s)	31.4	1.26 (s)	31.2	1.25 (s)
15	22.2	1.63 (brs)	22.2	1.63 (d, 2.0)	22.2	1.62 (d, 1.8)
4-OH		3.40 (d, 5.2)		3.41 (d, 5.3)		3.41 (d, 5.4)
6-OH		3.20 (s)		3.21 (s)		3.21 (s)

[a]Measured at 500 MHz for ^{1}H and 125 MHz for ^{13}C. [b]Measured at 600 MHz for ^{1}H and 150 MHz for ^{13}C.

Table S3. NMR spectroscopic data ($CDCl_3$) for natural and synthetic (±)-penicibilaene B (2). [S1,S2]



penicibilaene B (**2**)

	Natural **2**[a, S1]		Dong's synthetic **2**[a, S2]		Our synthetic **2**[b]	
No.	δ_C	δ_H (mult, *J* in Hz)	δ_C	δ_H (mult, *J* in Hz)	δ_C	δ_H (mult, *J* in Hz)
1	41.5		41.2		41.2	
2	42.1	1.80 (m)	41.8	1.83 (dd, 14.7, 9.1)	41.8	1.83 (dd, 15.0, 9.6)
3α	38.6	2.28 (ddd, 12.5, 7.1, 6.6)	38.3	2.31 (ddd, 12.8, 7.5, 5.8)	38.3	2.31 (ddd, 12.6, 7.8, 6.0)
3β		1.34 (dt, 12.5, 8.7)		1.37 (dt, 12.4, 8.7)		1.37 (dt, 12.6, 9.0)
4	75.8	5.33 (ddd, 8.7, 6.6, 6.0)	75.5	5.36 (ddd, 8.7, 7.6, 6.0)	75.5	5.36 (ddd, 13.8, 7.8, 6.0)
5	57.1	1.70 (d, 6.0)	56.8	1.72 (d, 6.1)	56.8	1.72 (d, 6.0)
6	71.3		71.1		71.1	
7α	32.2	1.78 (dd, 11.9, 6.2)	31.9	1.77 (m)	31.9	1.77 (m)
7β		1.41 (dd, 11.9, 2.5)		1.44 (ddd, 11.8, 3.9, 1.5)		1.44 (dd, 11.4, 2.4)
8	34.7	2.18 (dd, 6.2, 2.5)	34.4	2.22 (d, 9.2)	34.4	2.21 (d, 9.0)
9	140.5		140.3		140.3	
10	119.7	5.24 (d, 4.2)	119.4	5.26 (d, 4.9)	119.4	5.26 (d, 4.8)
11α	34.4	2.02 (d, 16.0)	34.2	2.05 (d, 17.0)	34.2	2.05 (d, 16.8)
11β		1.70 (m)		1.70 (m)		1.70 (m)
12α	41.9	1.75 (dd, 14.5, 6.3)	41.7	1.75 (m)	41.7	1.74 (m)
12β		1.50 (d, 14.5)		1.53 (dt, 14.6, 1.3)		1.53 (d, 15.0)
13	14.1	0.88 (d, 6.9)	13.9	0.91 (d, 6.9)	13.9	0.91 (d, 6.6)
14	30.5	1.13 (s)	30.3	1.15 (s)	30.3	1.15 (s)
15	22.1	1.63 (m)	21.8	1.65 (dt, 2.7, 1.5)	21.8	1.65 (brs)
1′	171.1		170.9		170.9	
2′	21.6	1.97 (s)	21.4	2.00 (s)	21.4	2.00 (s)
6-OH				1.13 (s)		1.15 (s)

[a]Measured at 500 MHz for ^1H and 125 MHz for ^{13}C. [b]Measured at 600 MHz for ^1H and 150 MHz for ^{13}C.

Figure S2. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound 9.

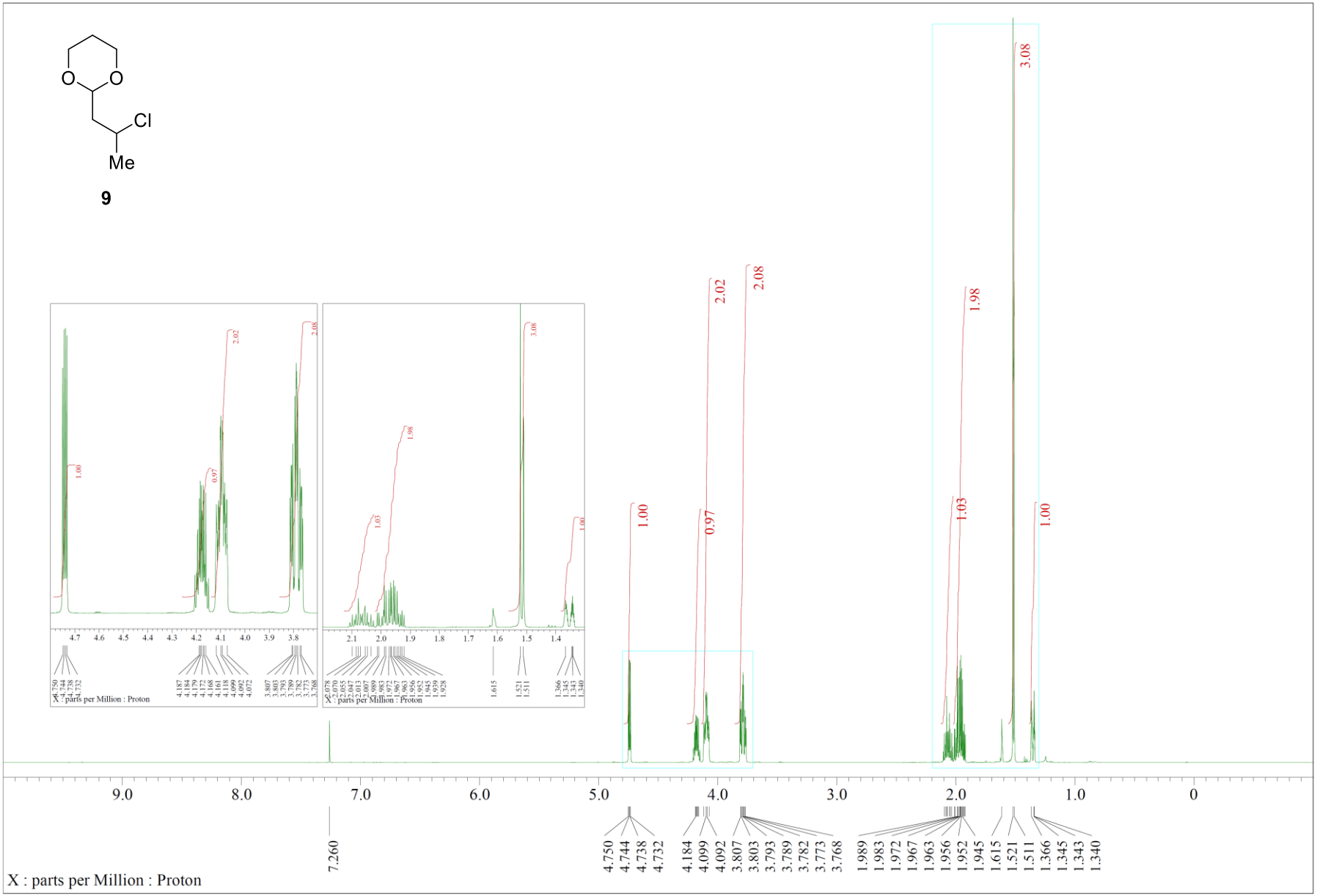


Figure S3. ^{13}C NMR spectrum (150 MHz, acetone-d_6) of compound 9.

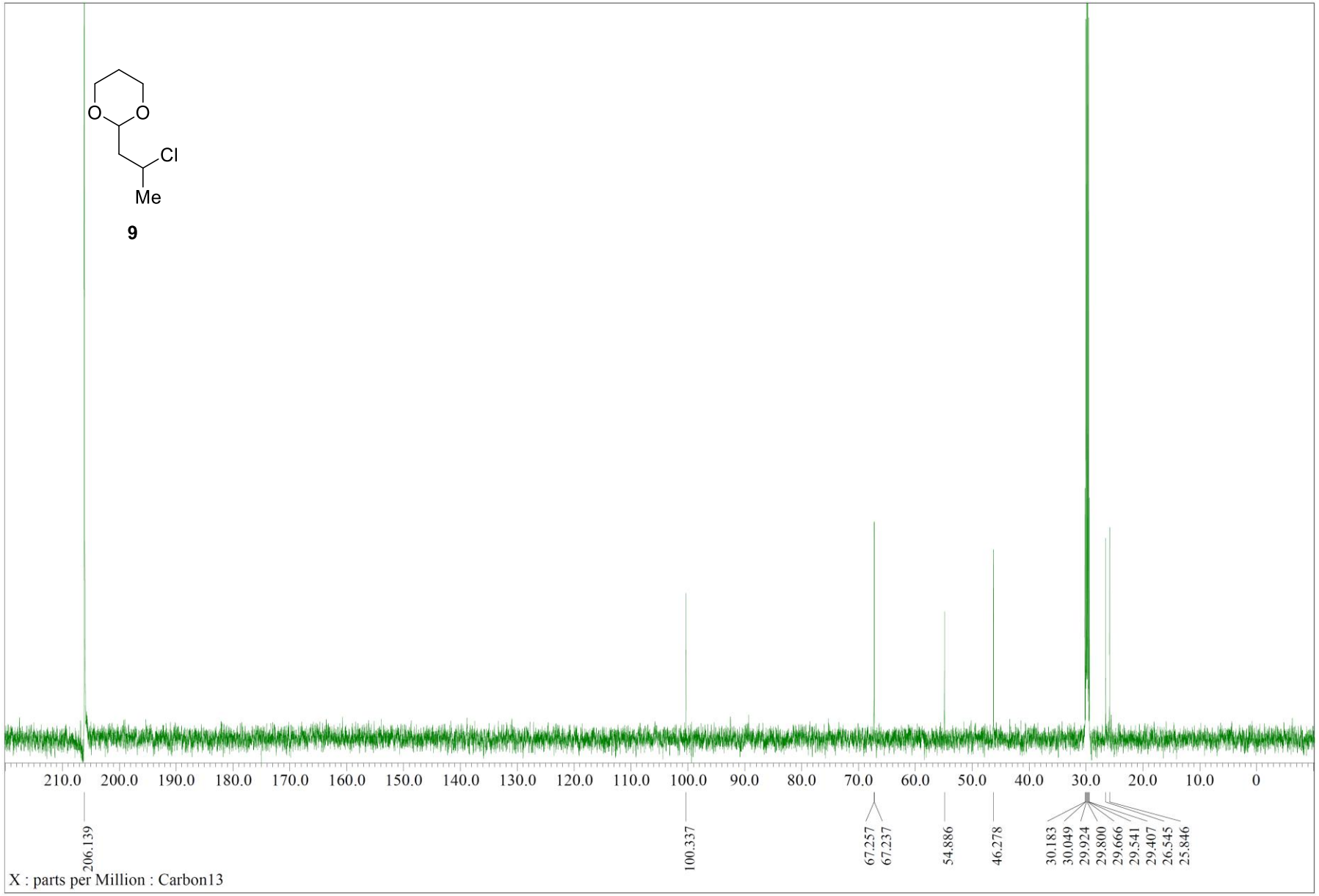


Figure S4. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound 10.

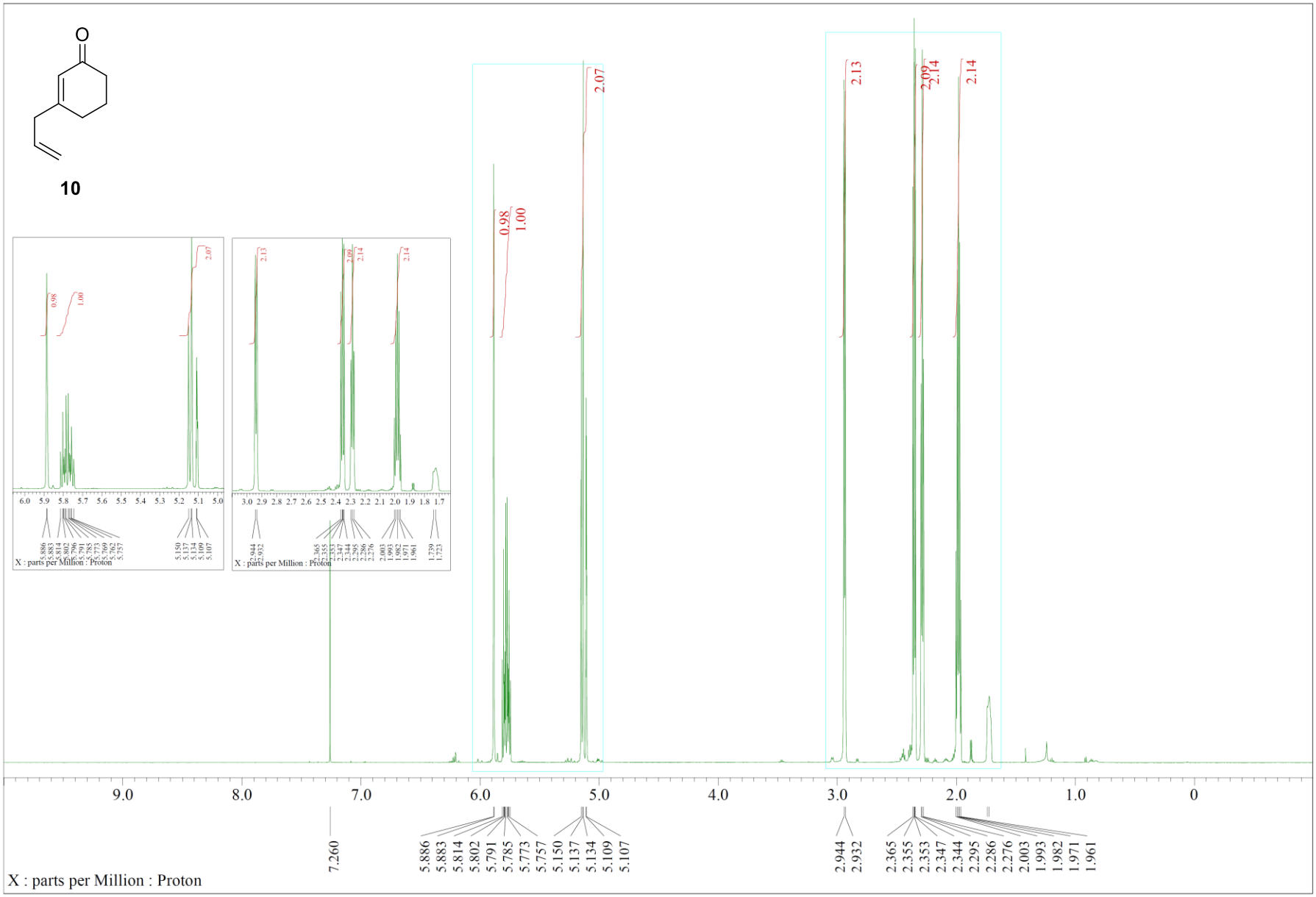


Figure S5. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of compound 10.

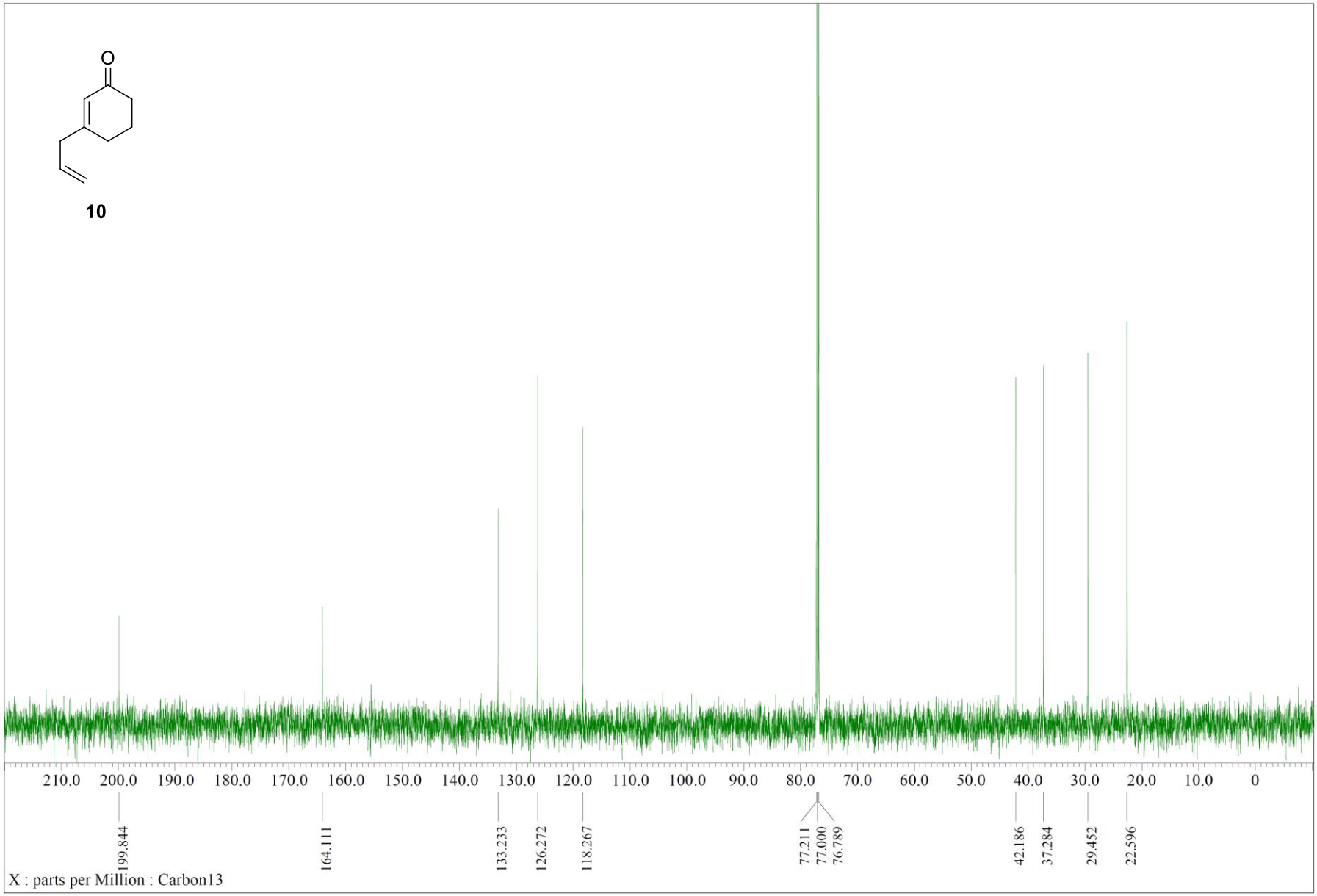


Figure S6. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound 12.

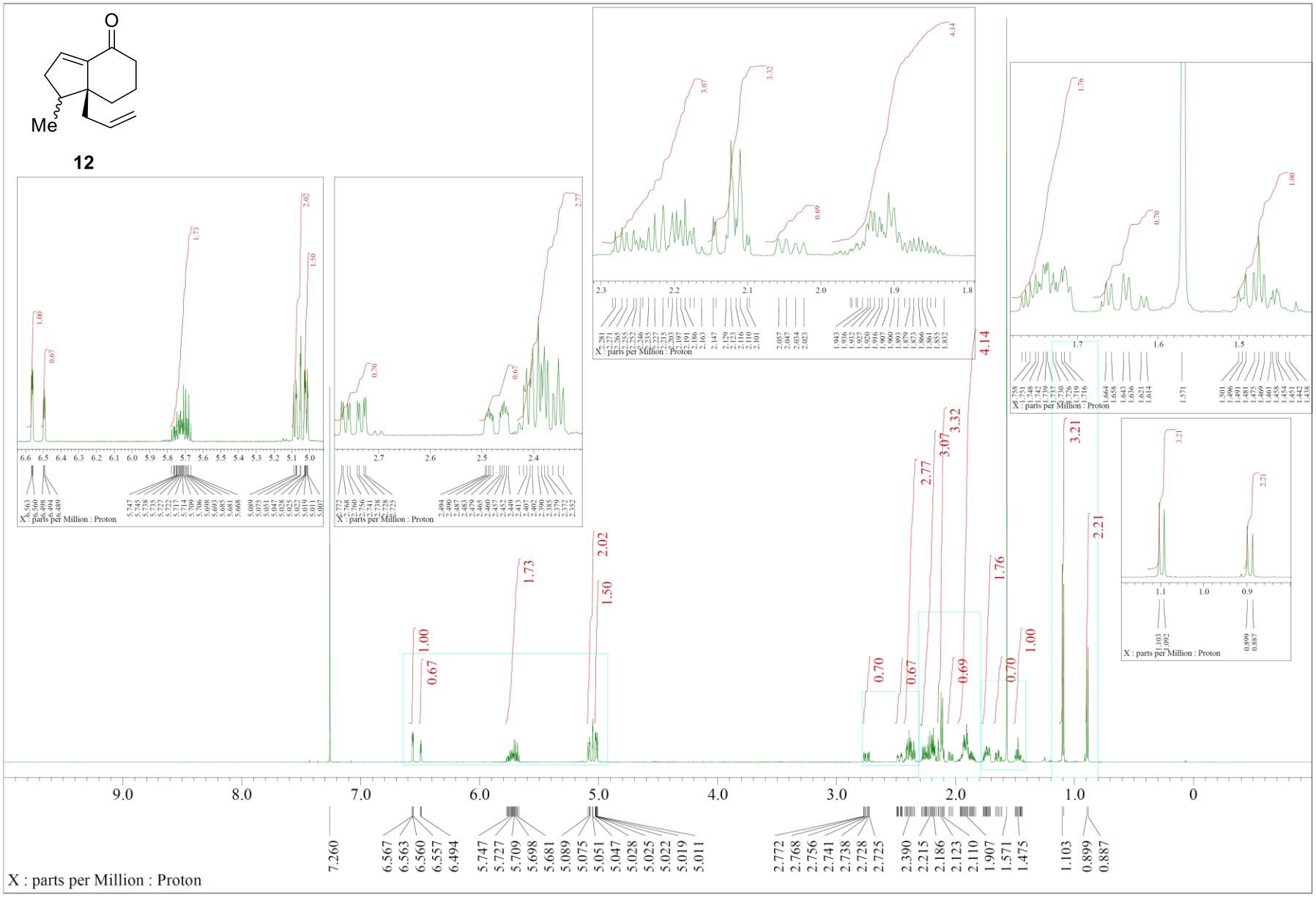


Figure S7. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of compound 12.

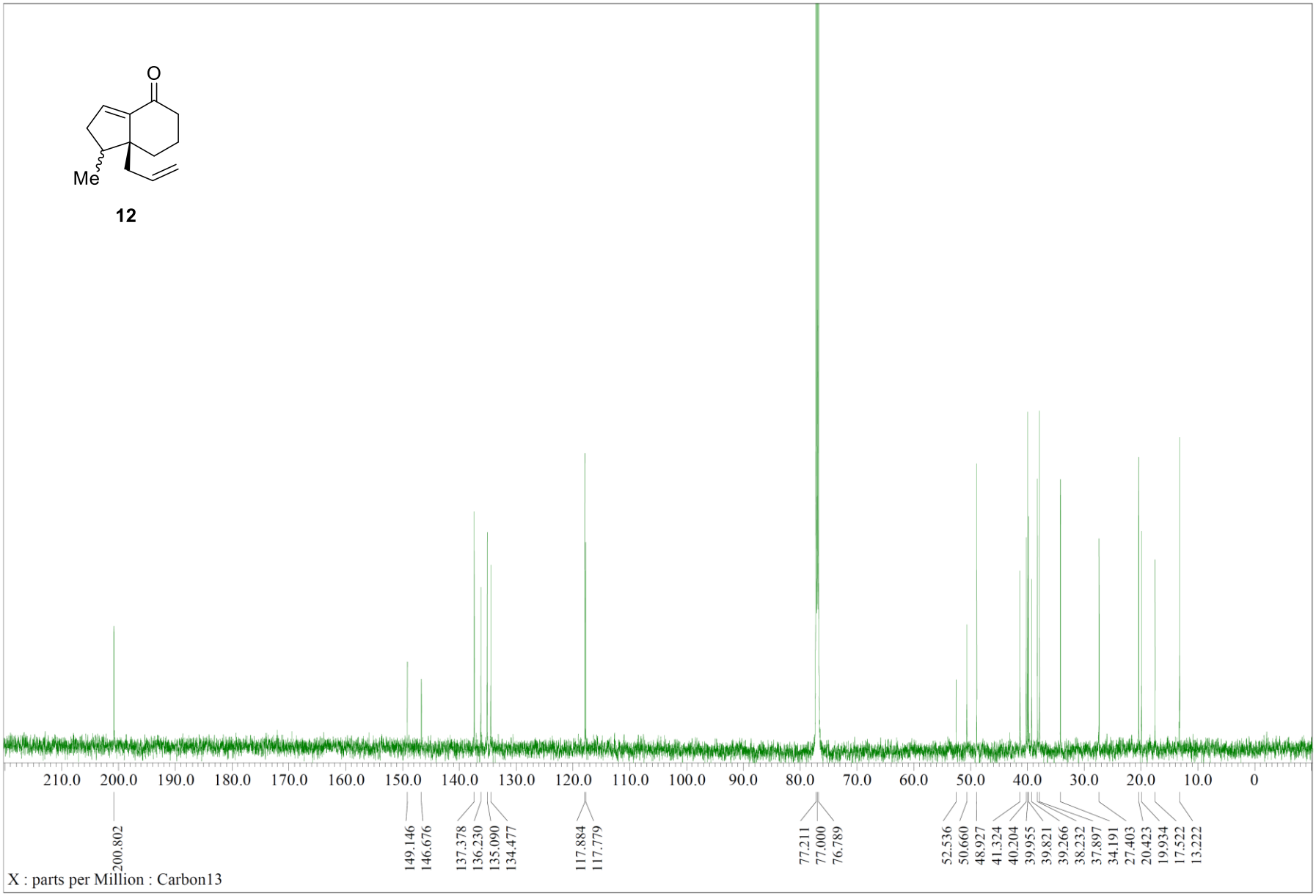


Figure S8. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound 13.

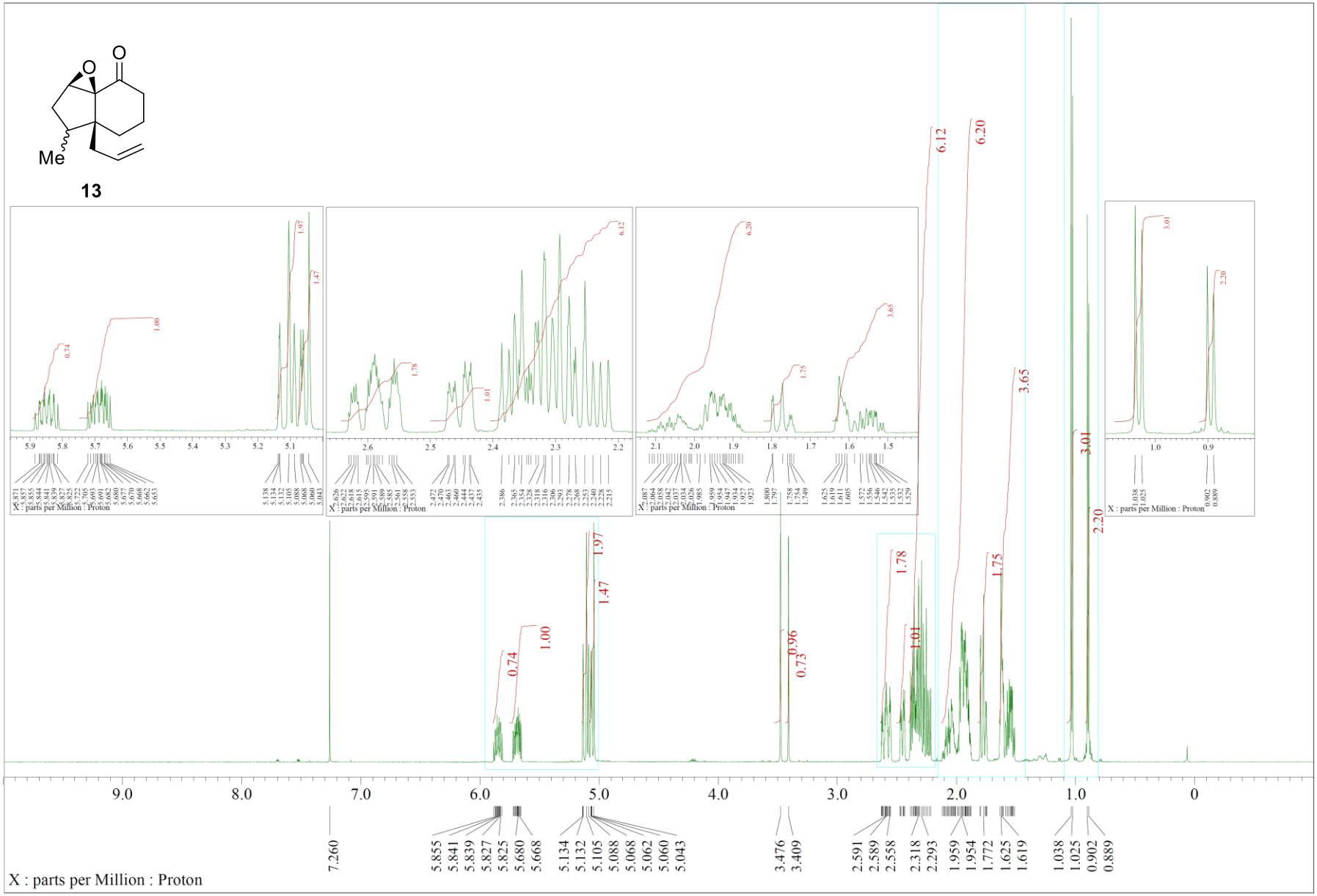


Figure S9. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of compound 13.

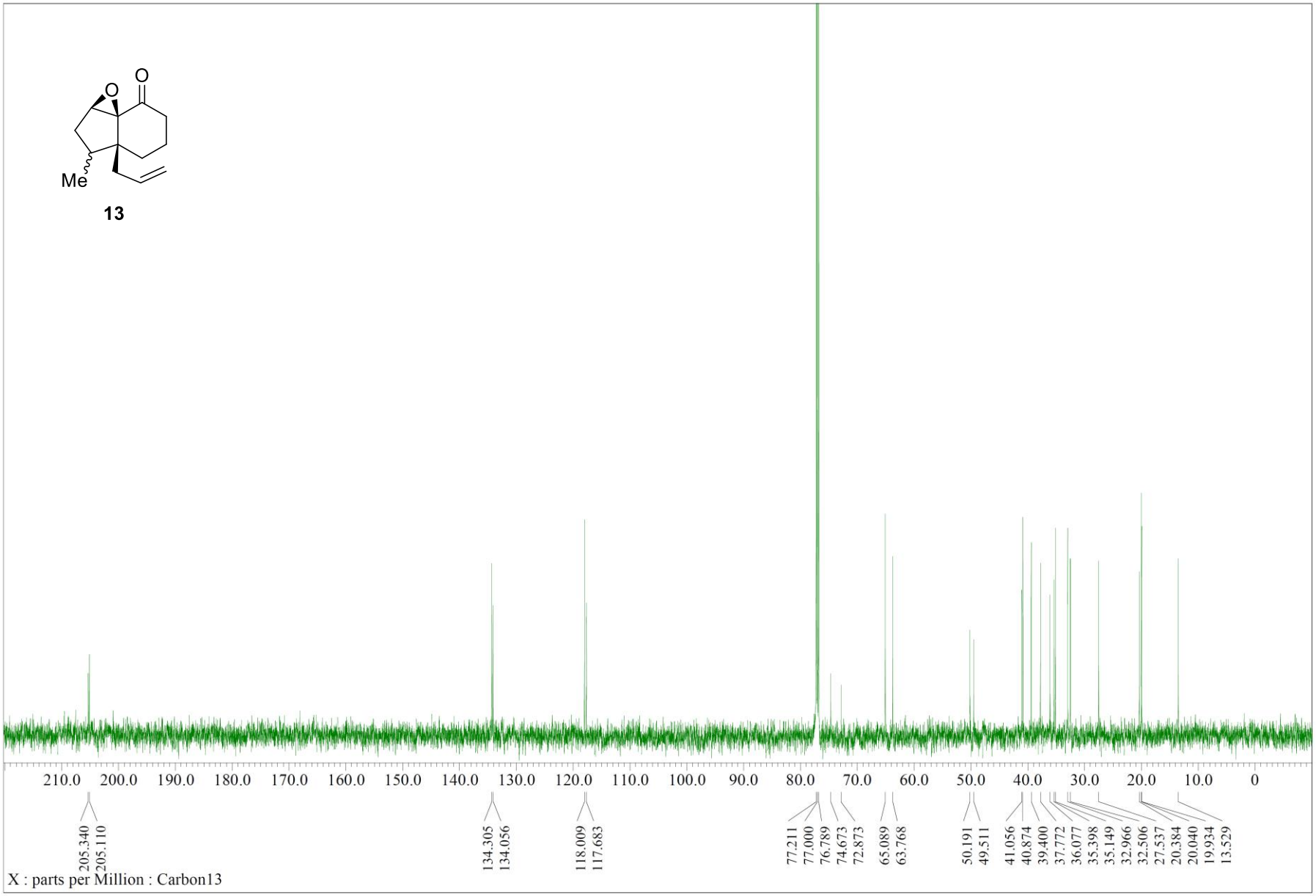


Figure S10. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound 14.

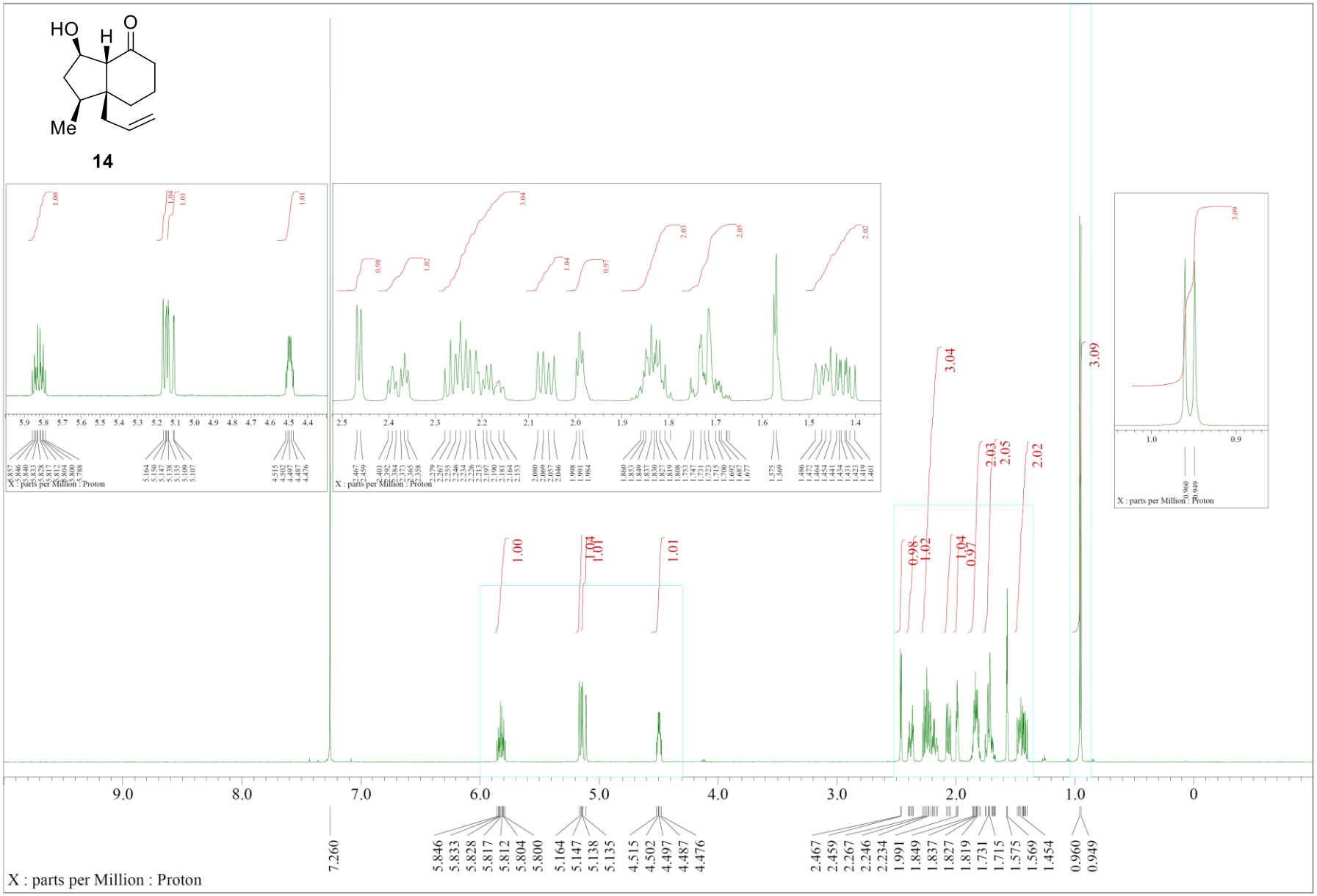


Figure S11. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of compound 14.

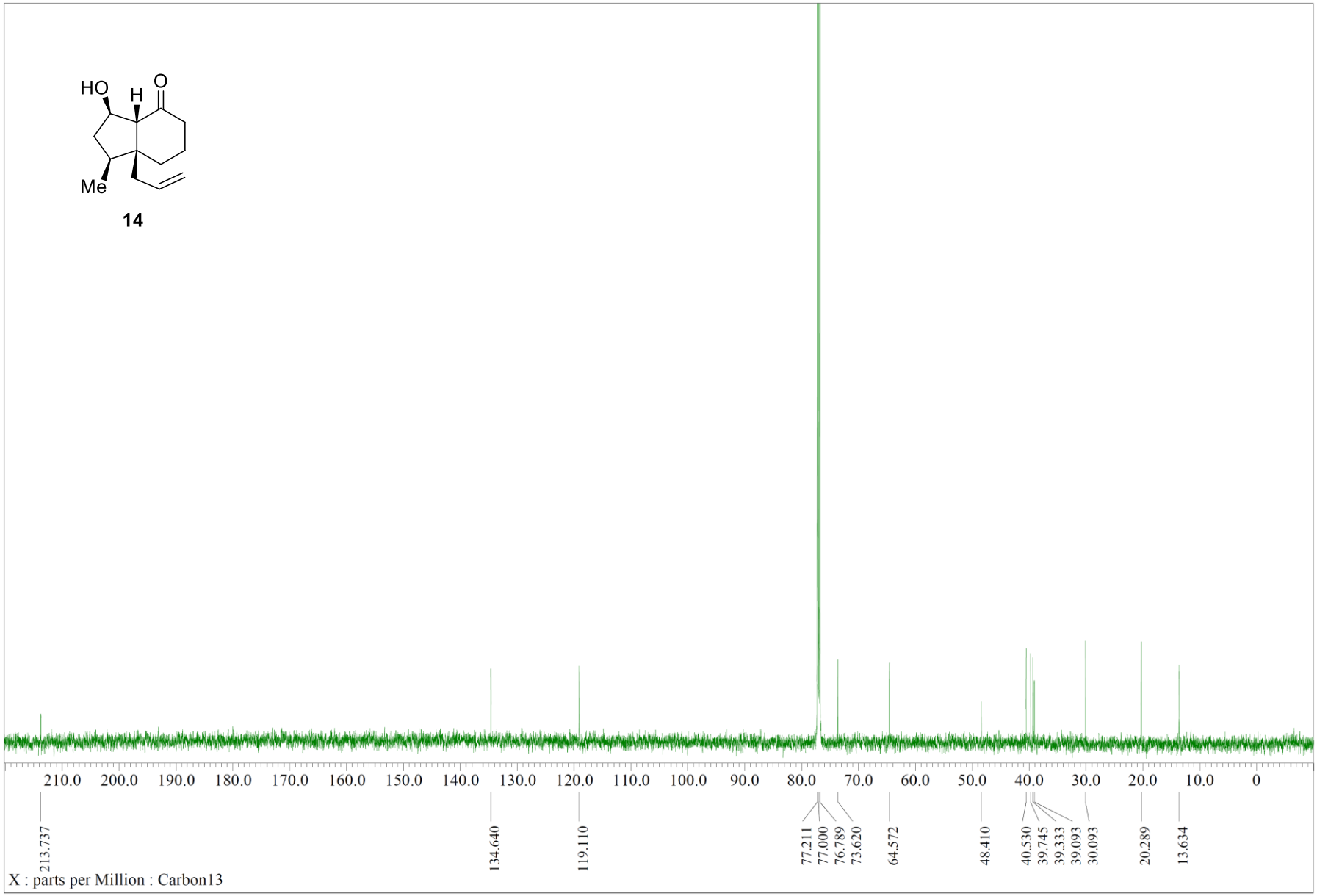


Figure S12. NOESY spectrum (600 MHz, $CDCl_3$) of compound 14.

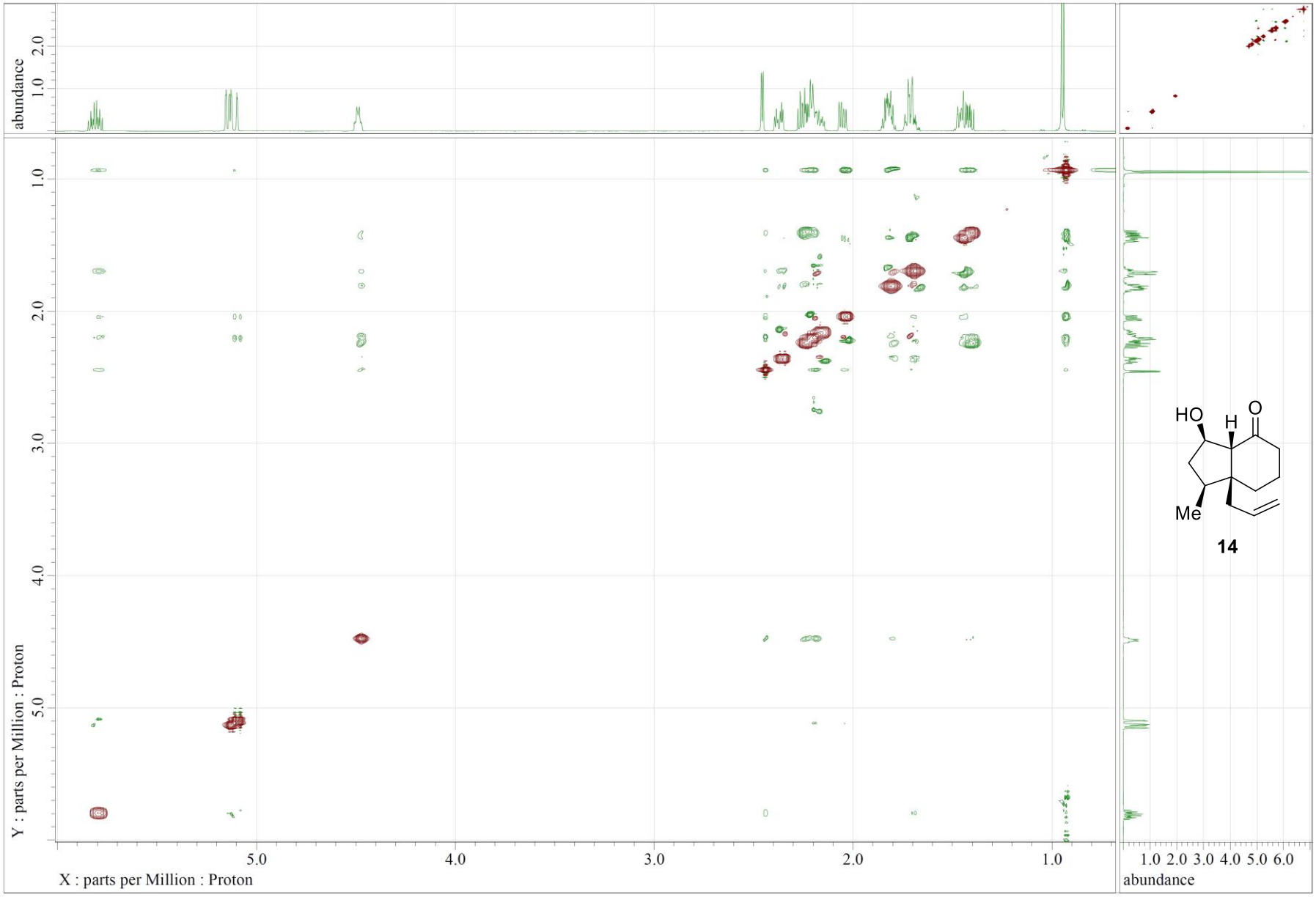


Figure S13. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound 15.

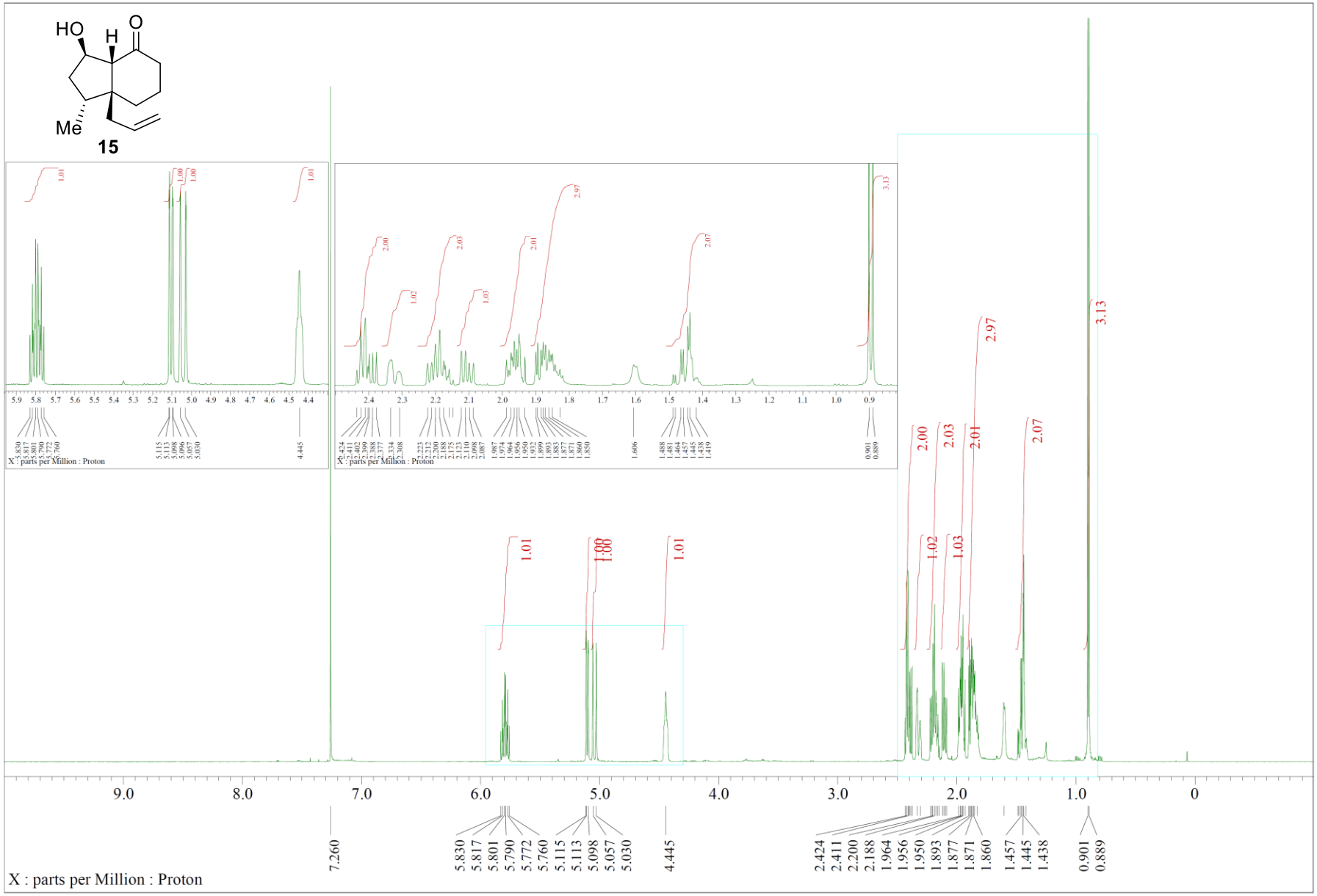


Figure S14. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of compound 15.

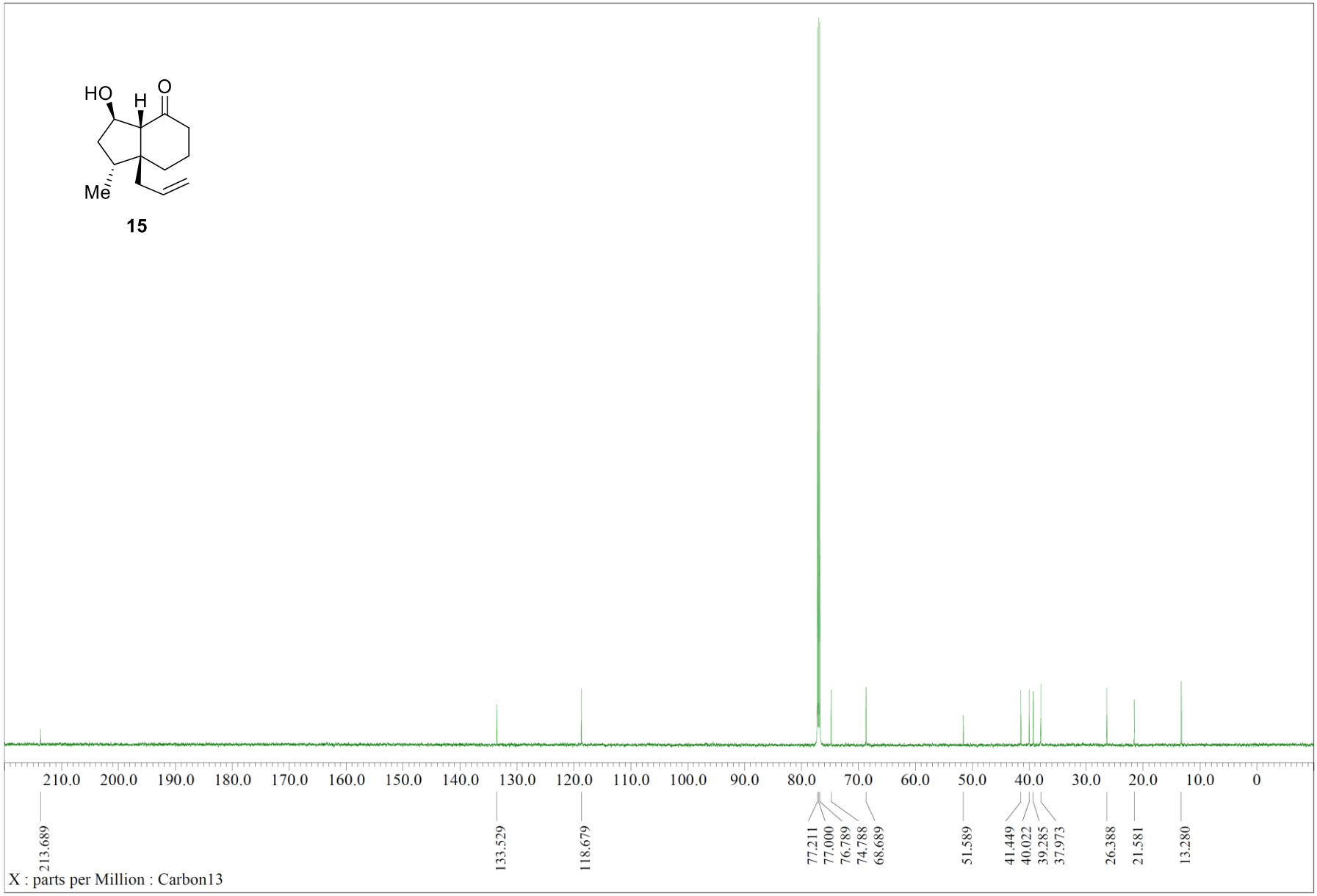


Figure S15. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound 16.

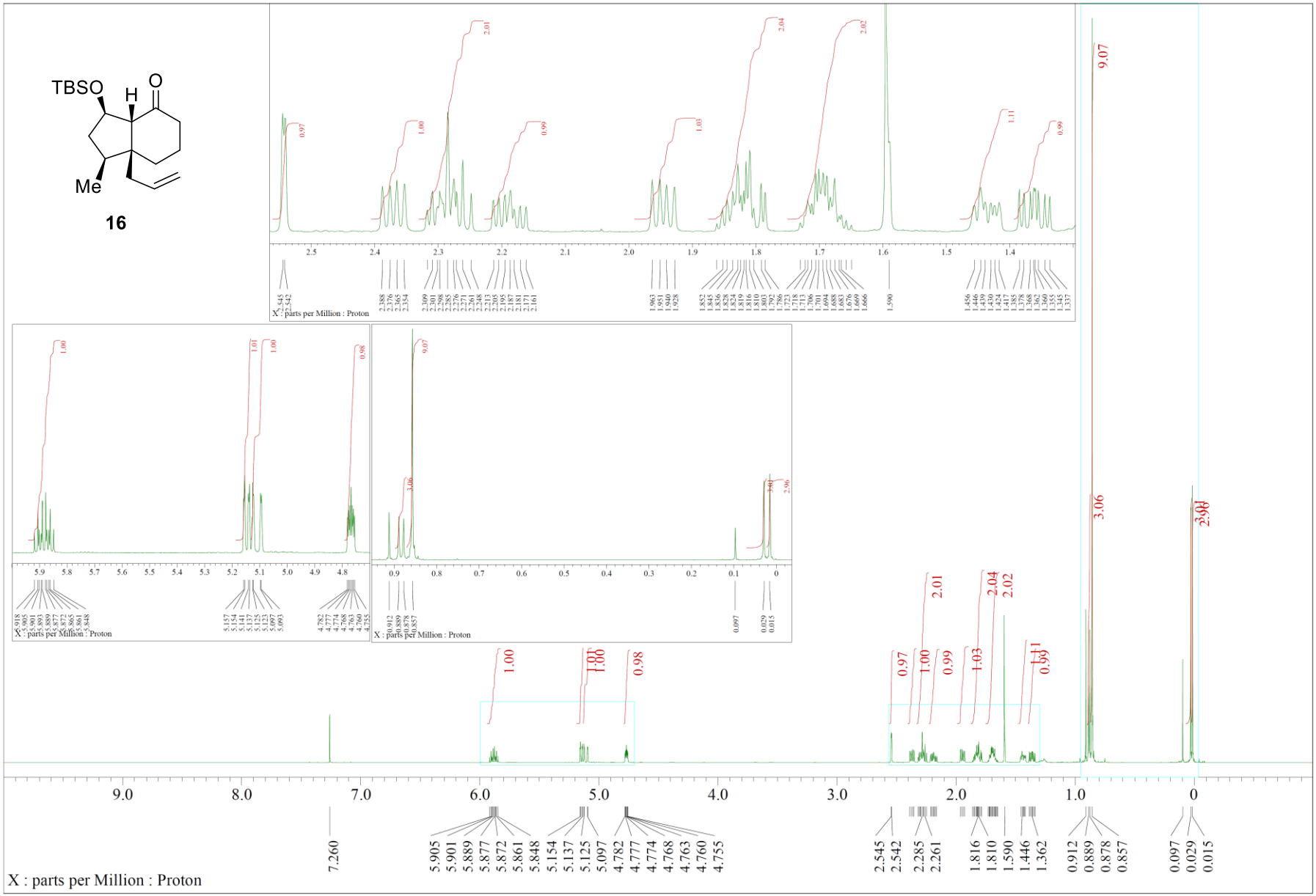


Figure S16. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of compound 16.

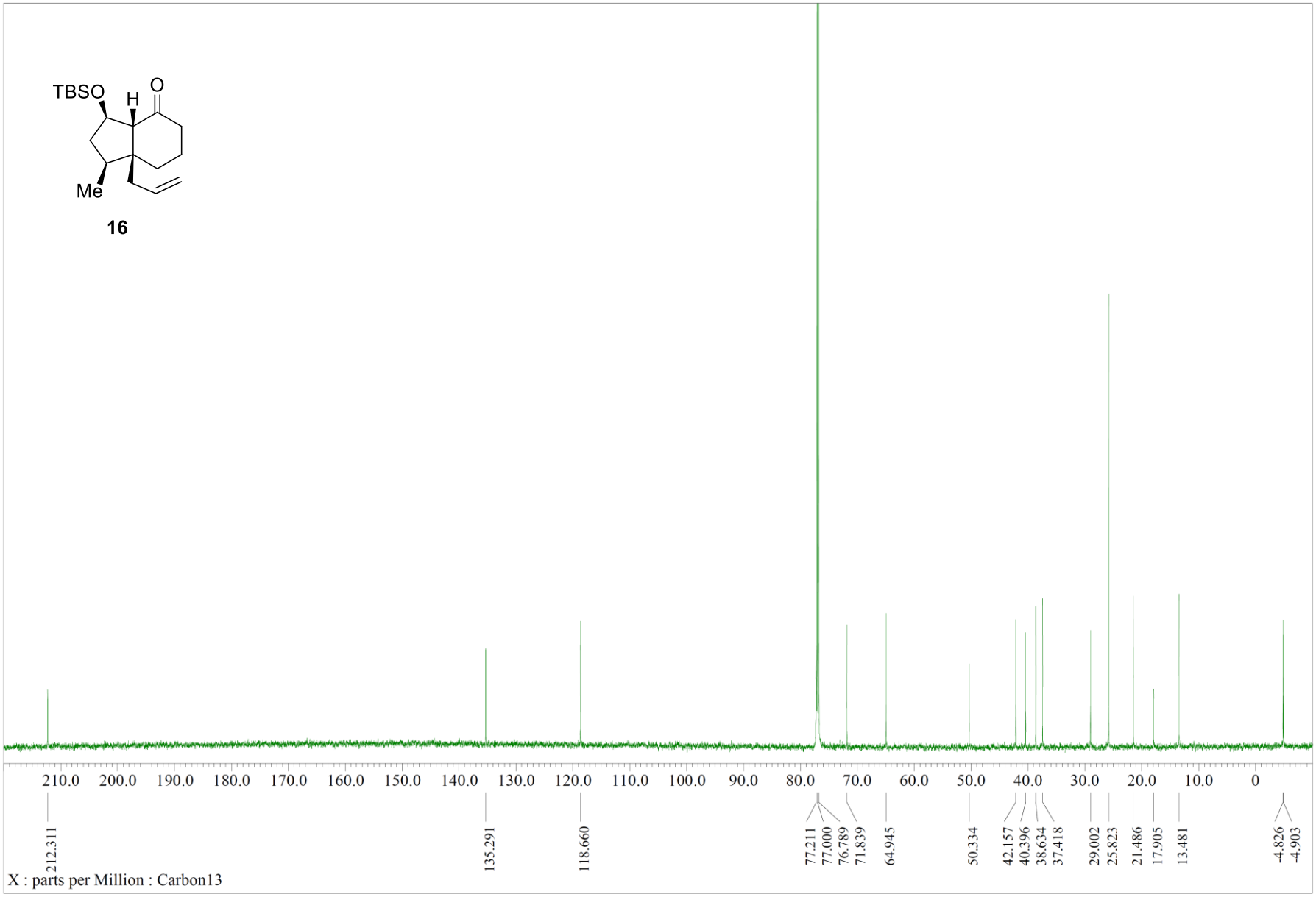


Figure S17. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound 4.

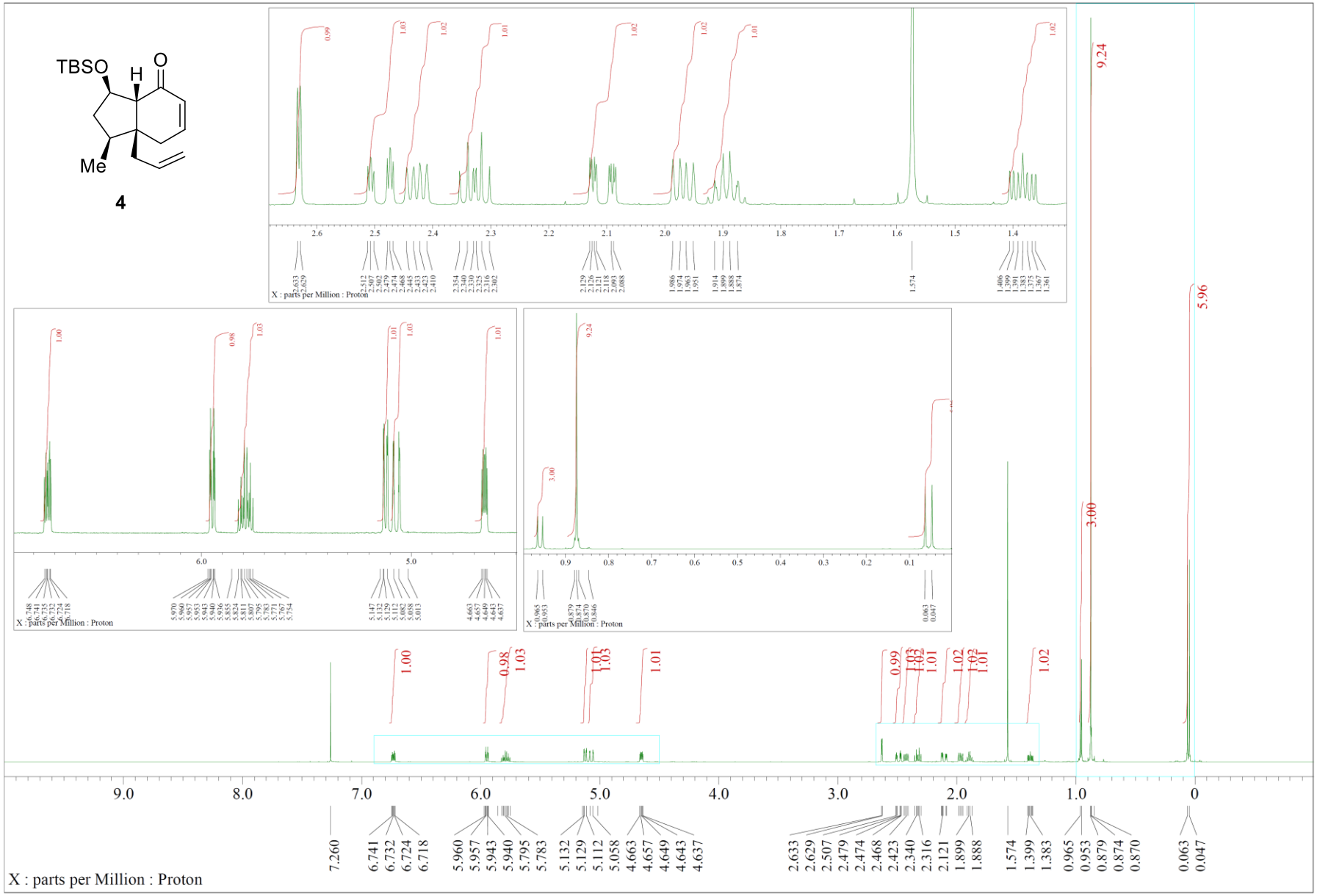


Figure S18. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of compound 4.

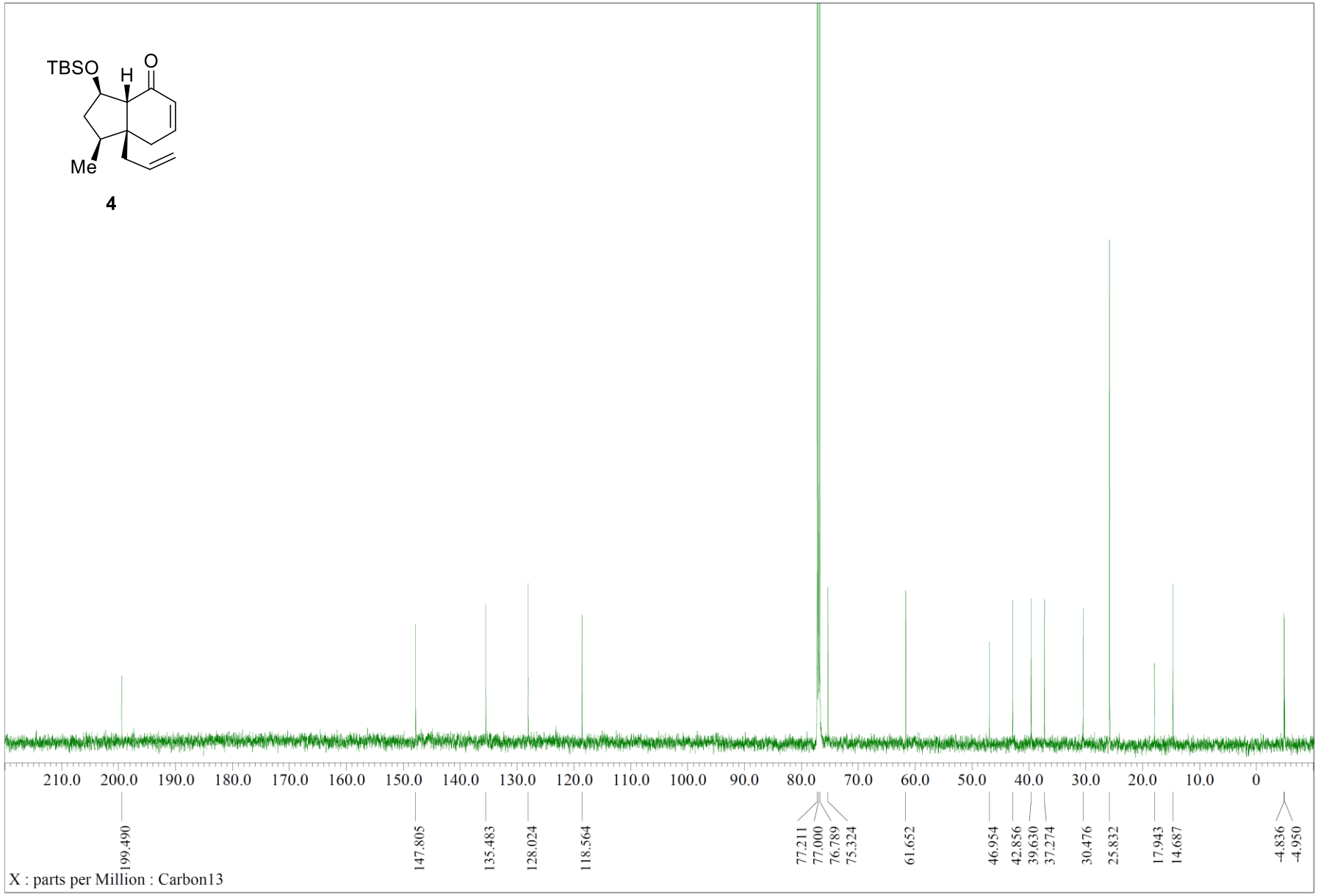


Figure S19. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound 18.

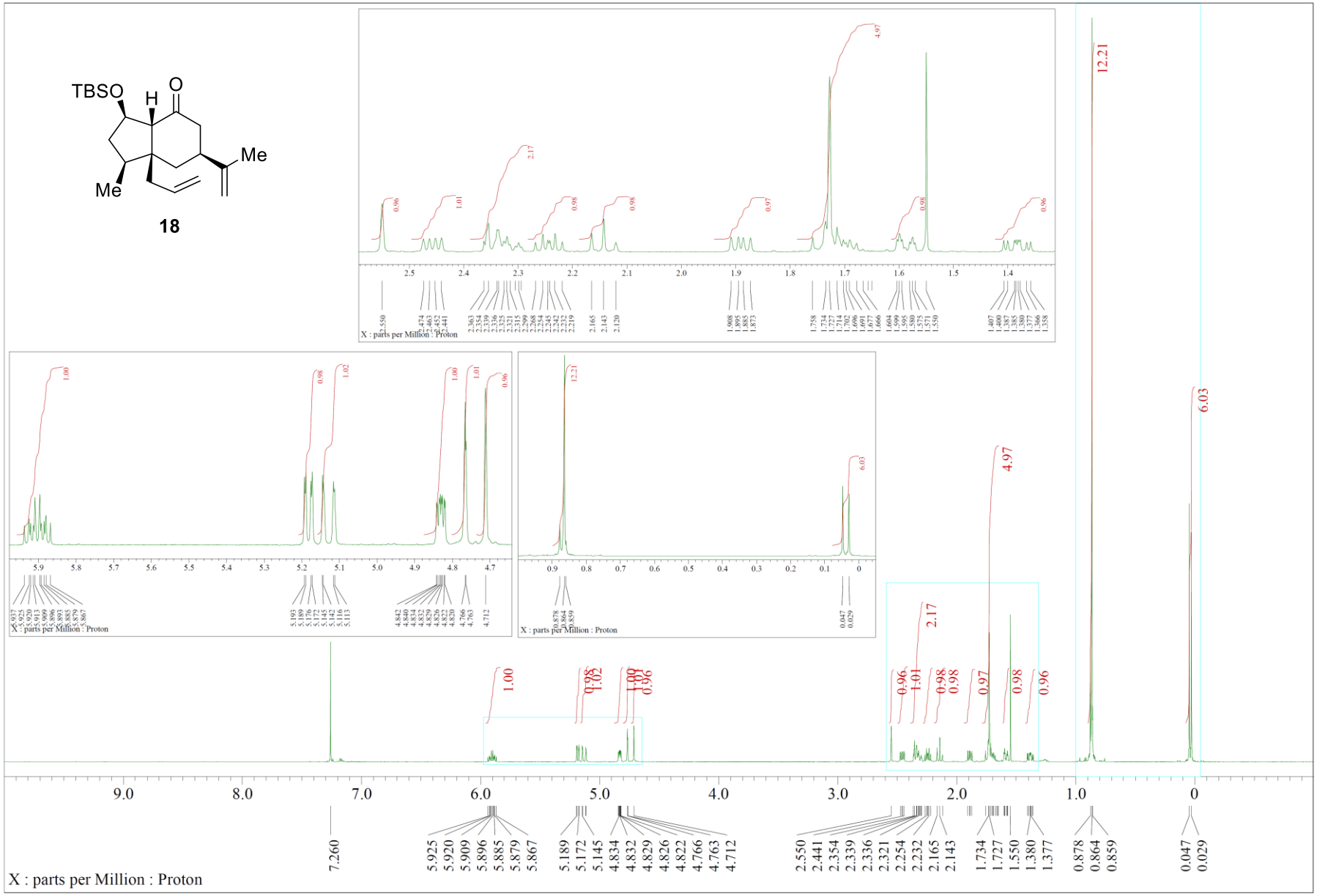


Figure S20. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of compound 18.

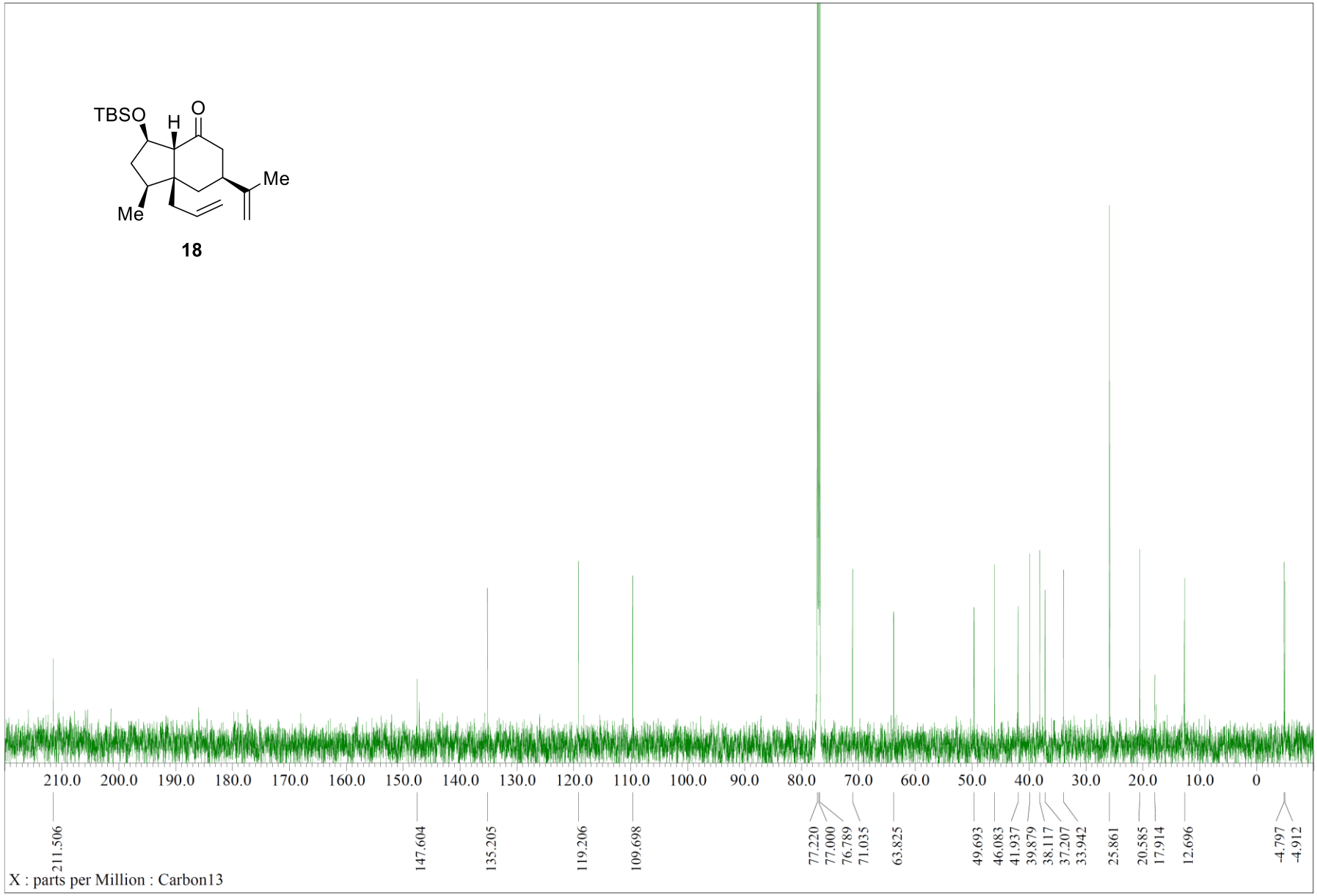


Figure S21. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound 19.

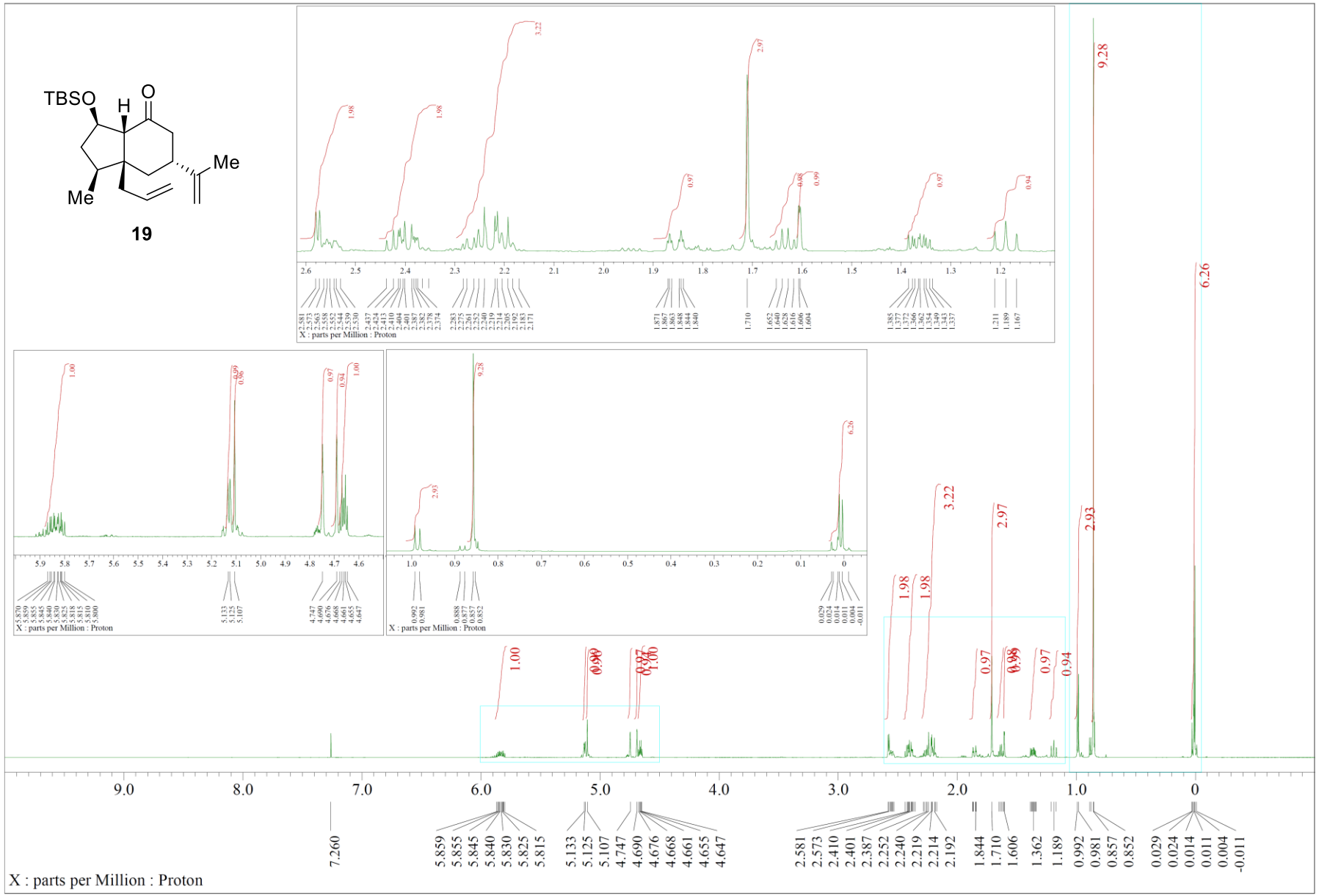


Figure S22. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of compound 19.

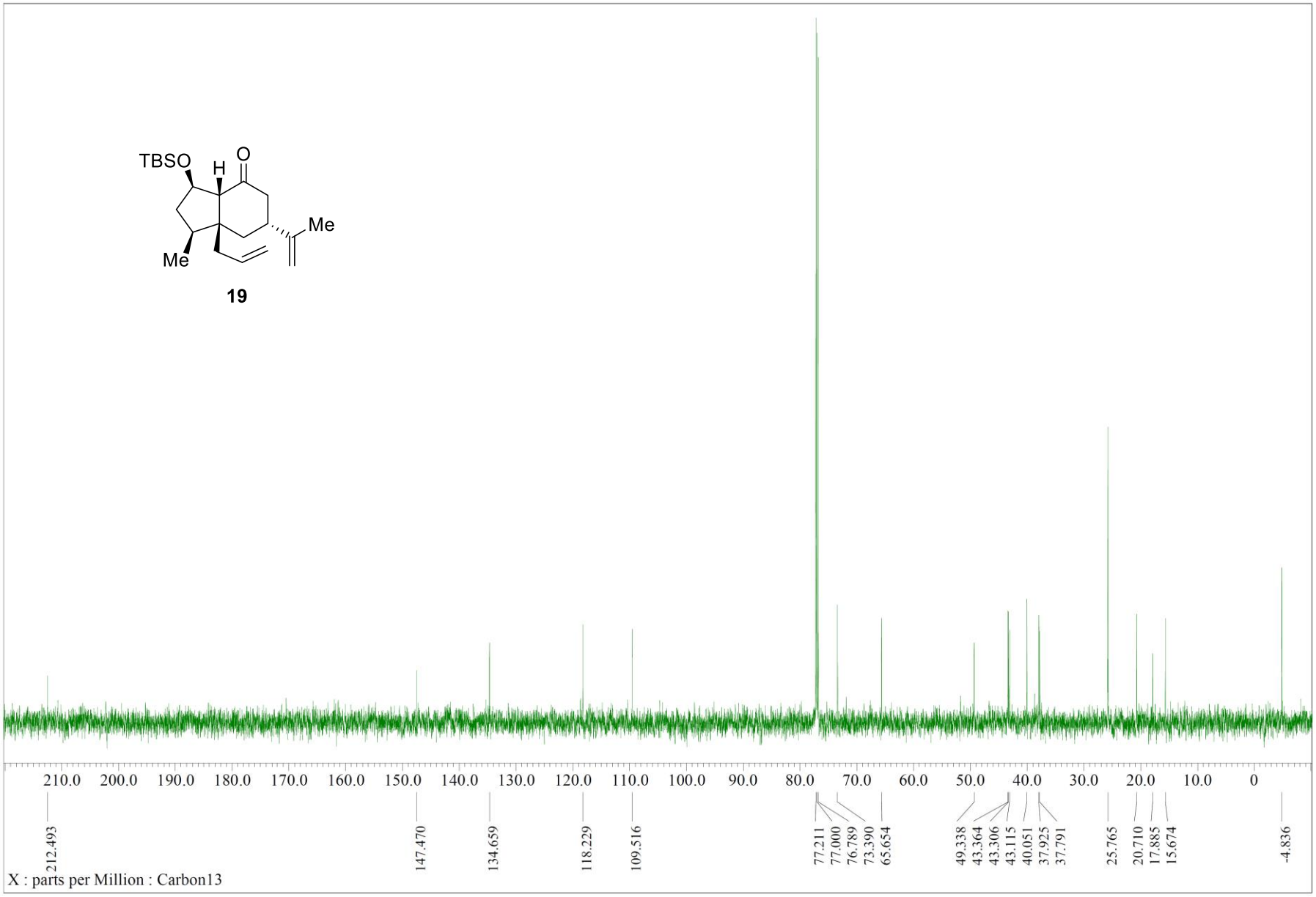


Figure S23. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound 3.

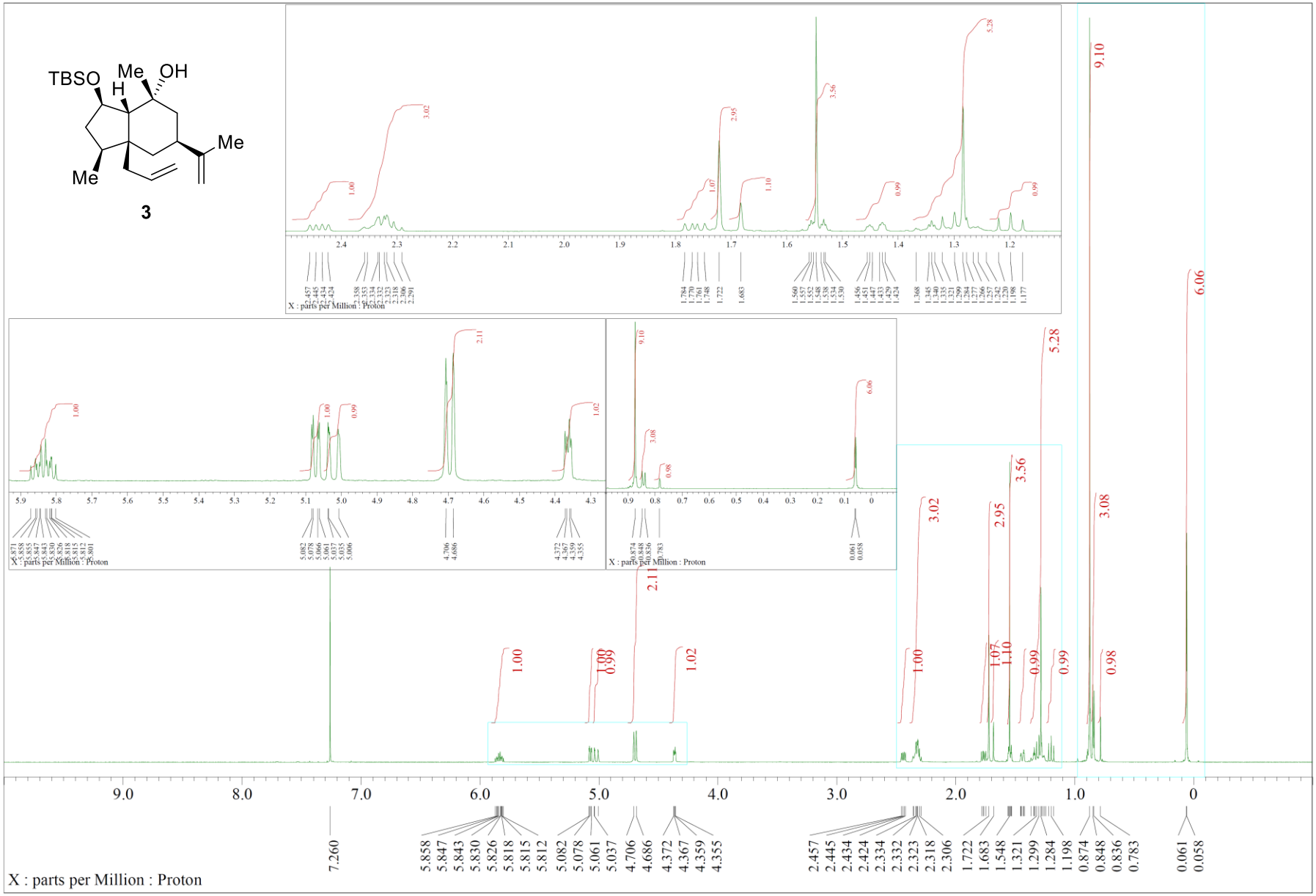


Figure S24. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of compound 3.

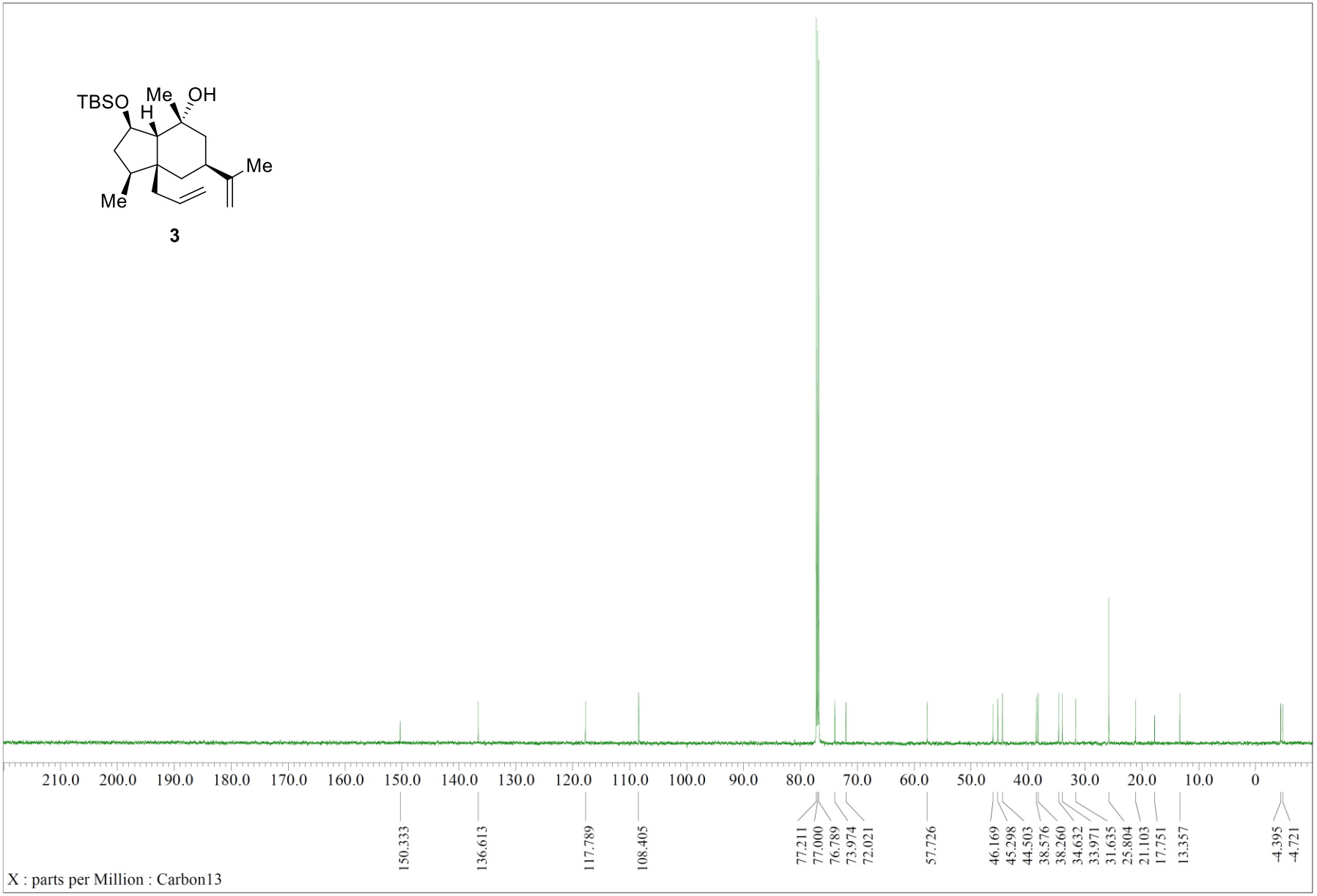


Figure S25. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound 21.

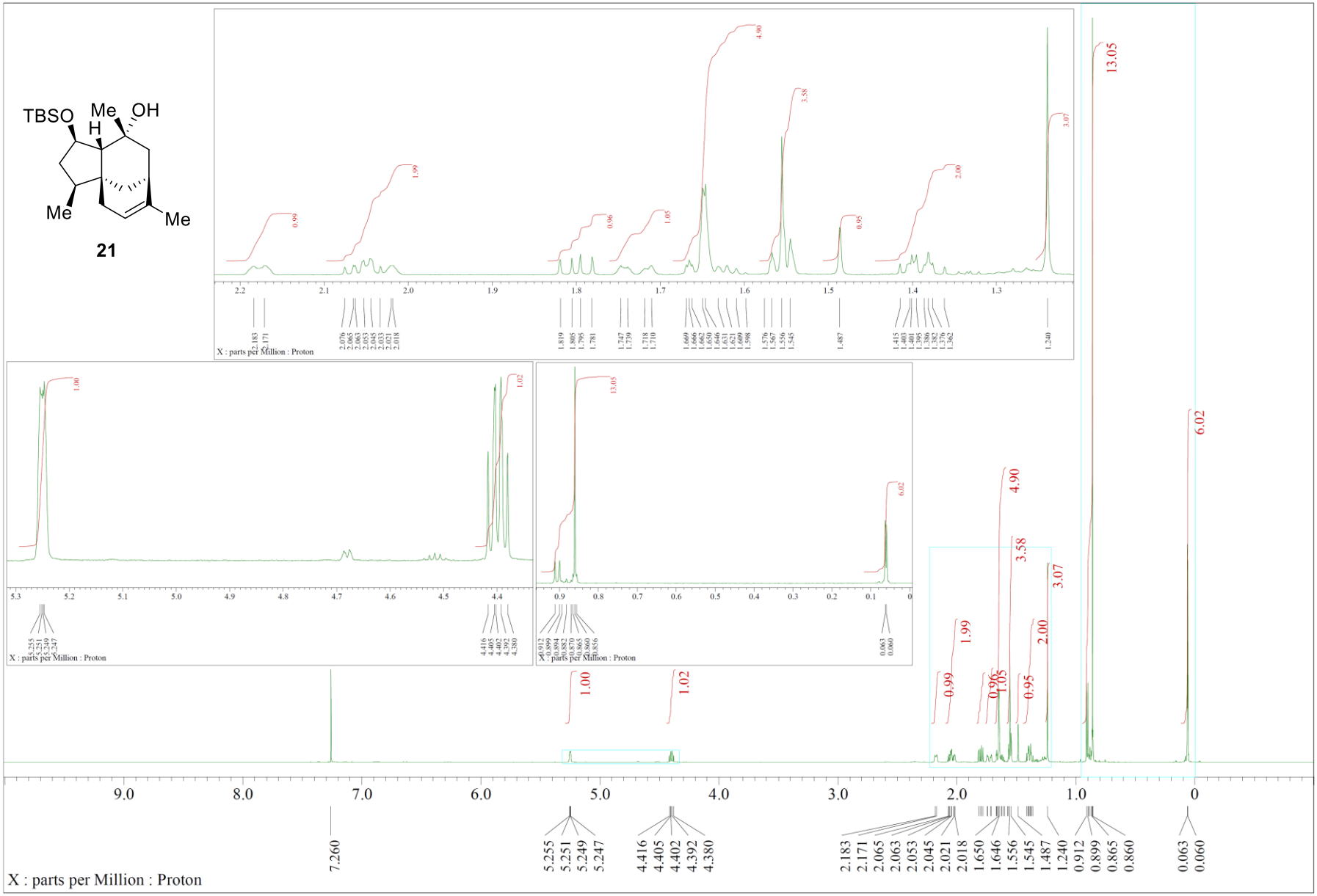


Figure S26. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of compound 21.

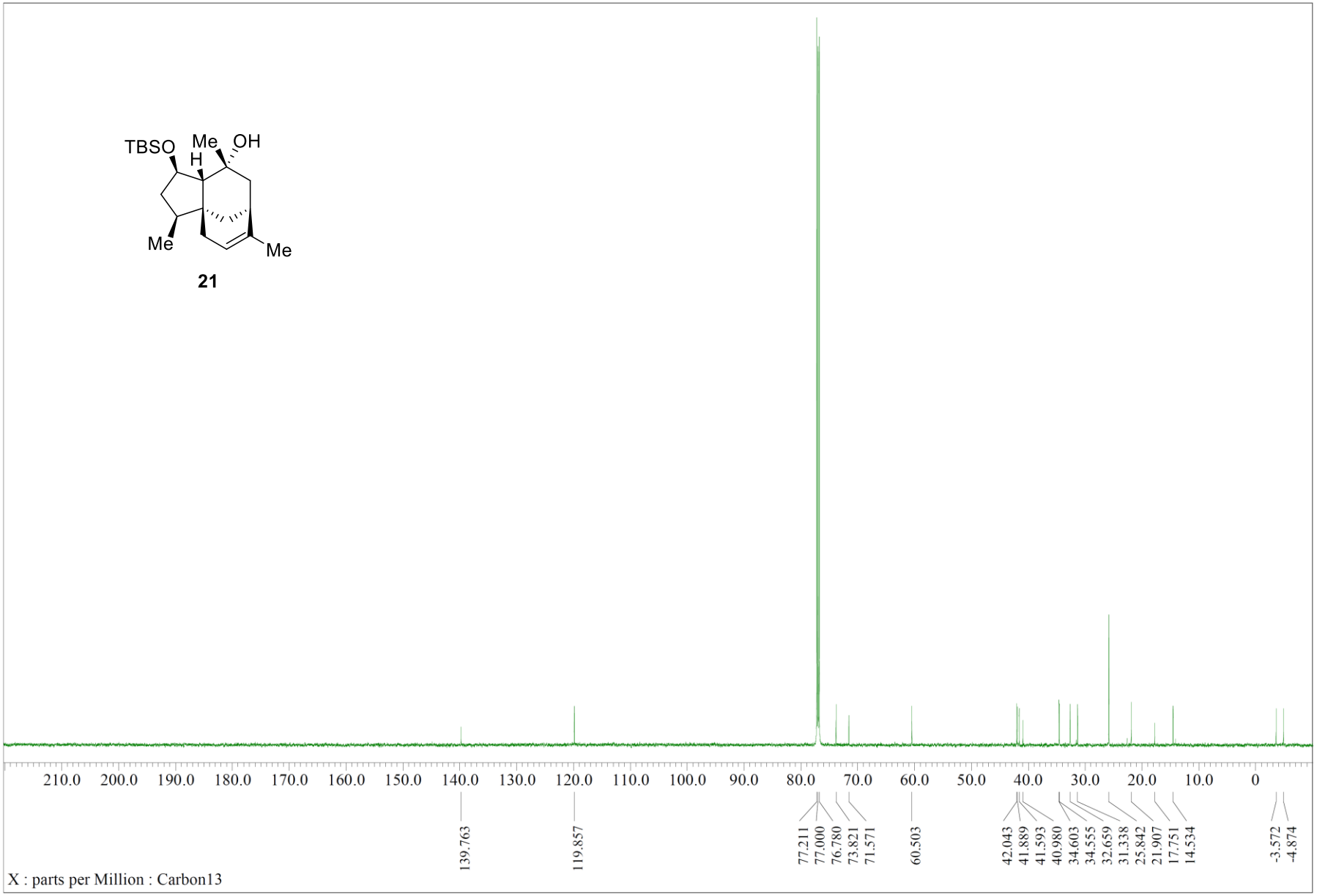


Figure S27. ^{1}H NMR spectrum (600 MHz, acetone-d_6) of penicibilaene A (1).

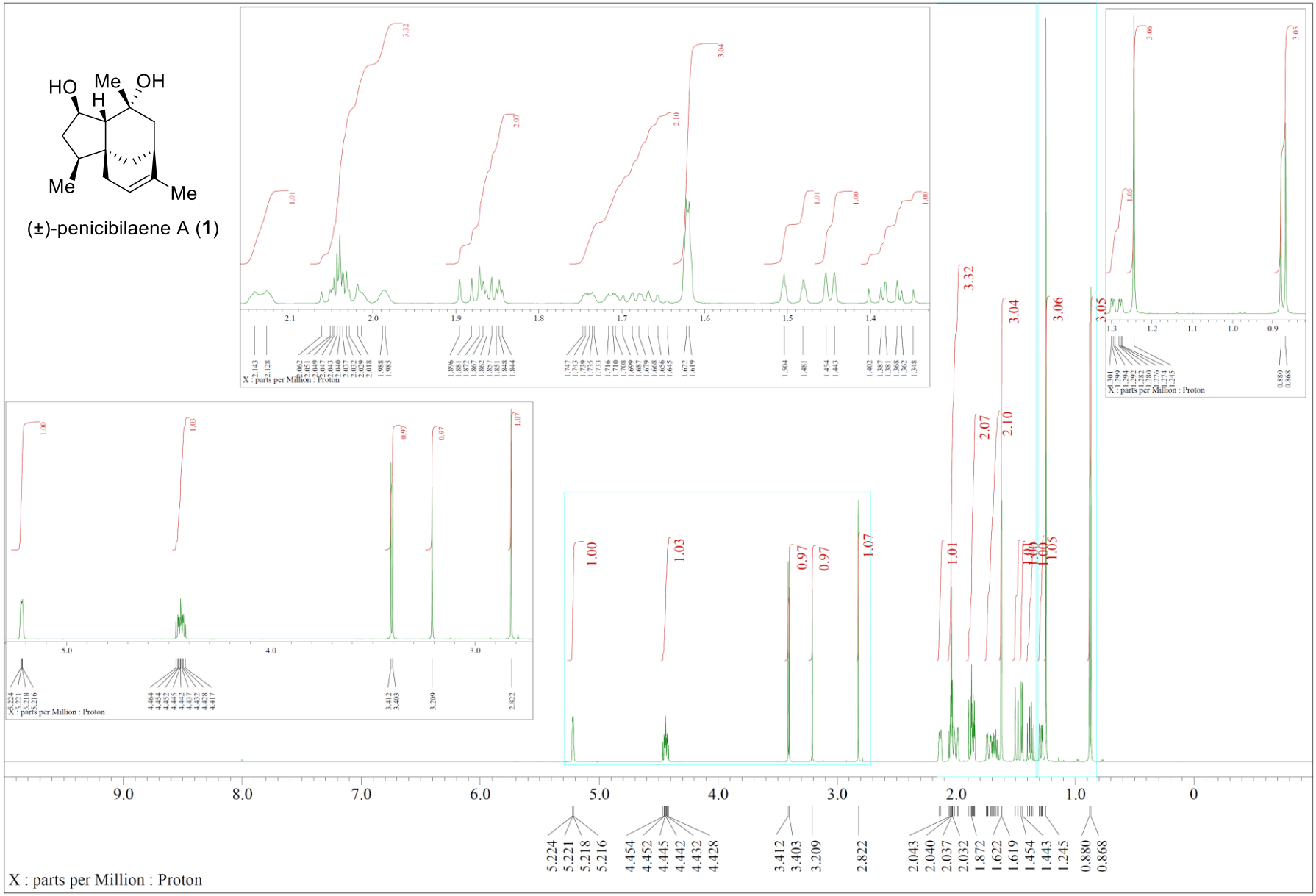


Figure S28. ^{13}C NMR spectrum (150 MHz, acetone-d_6) of penicibilaene A (1).

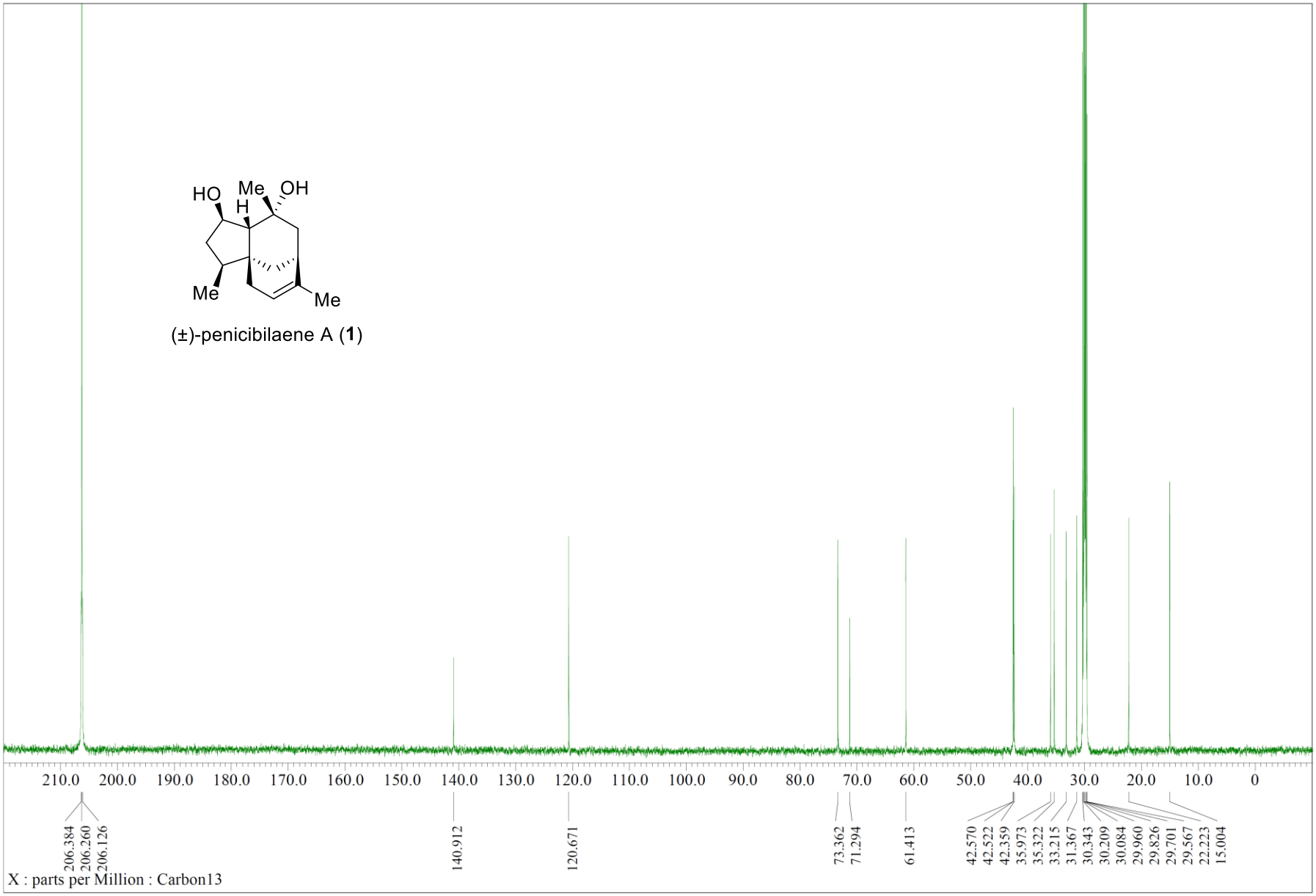


Figure S29. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of penicibilaene B (2).

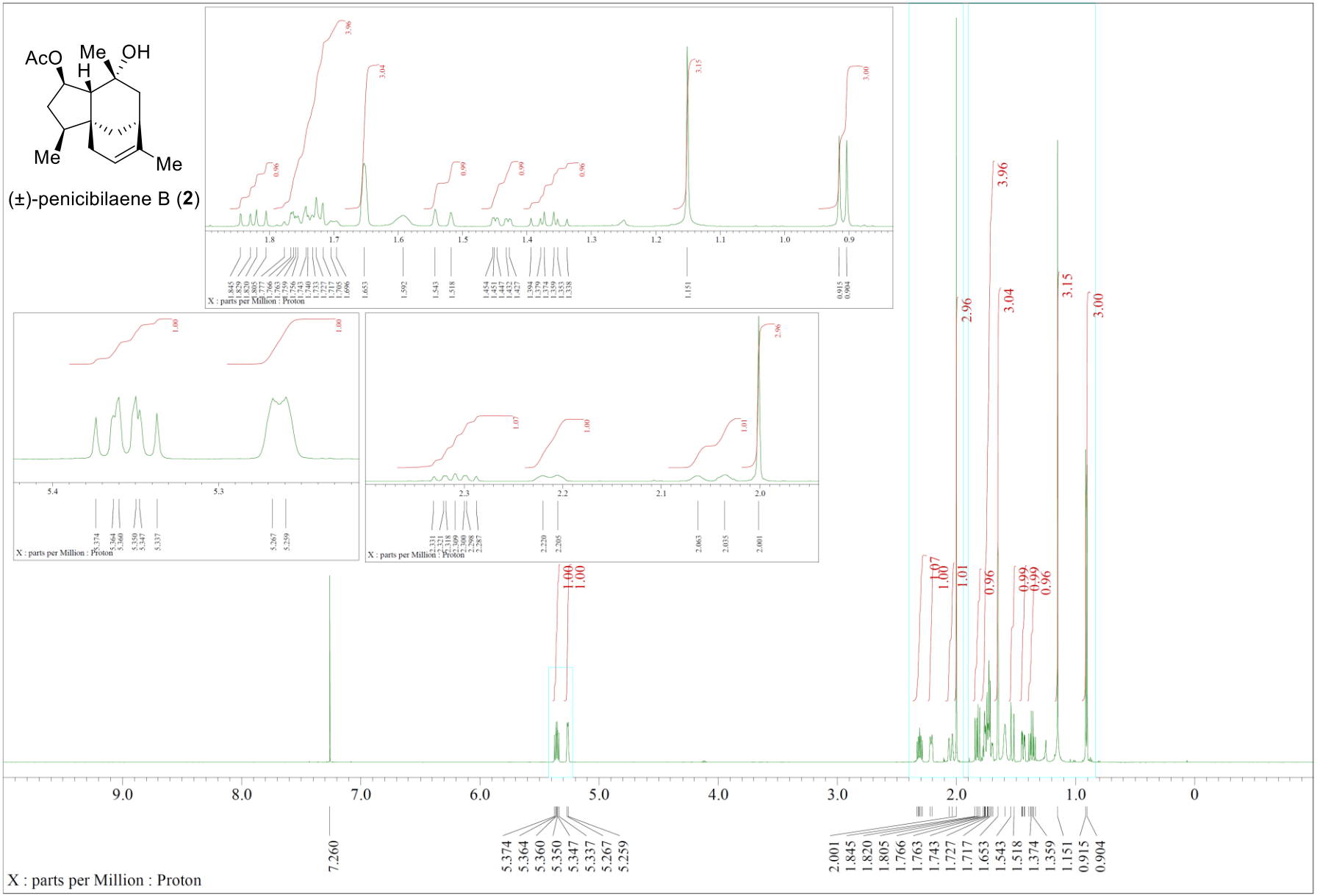


Figure S30. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of penicibilaene B (2).

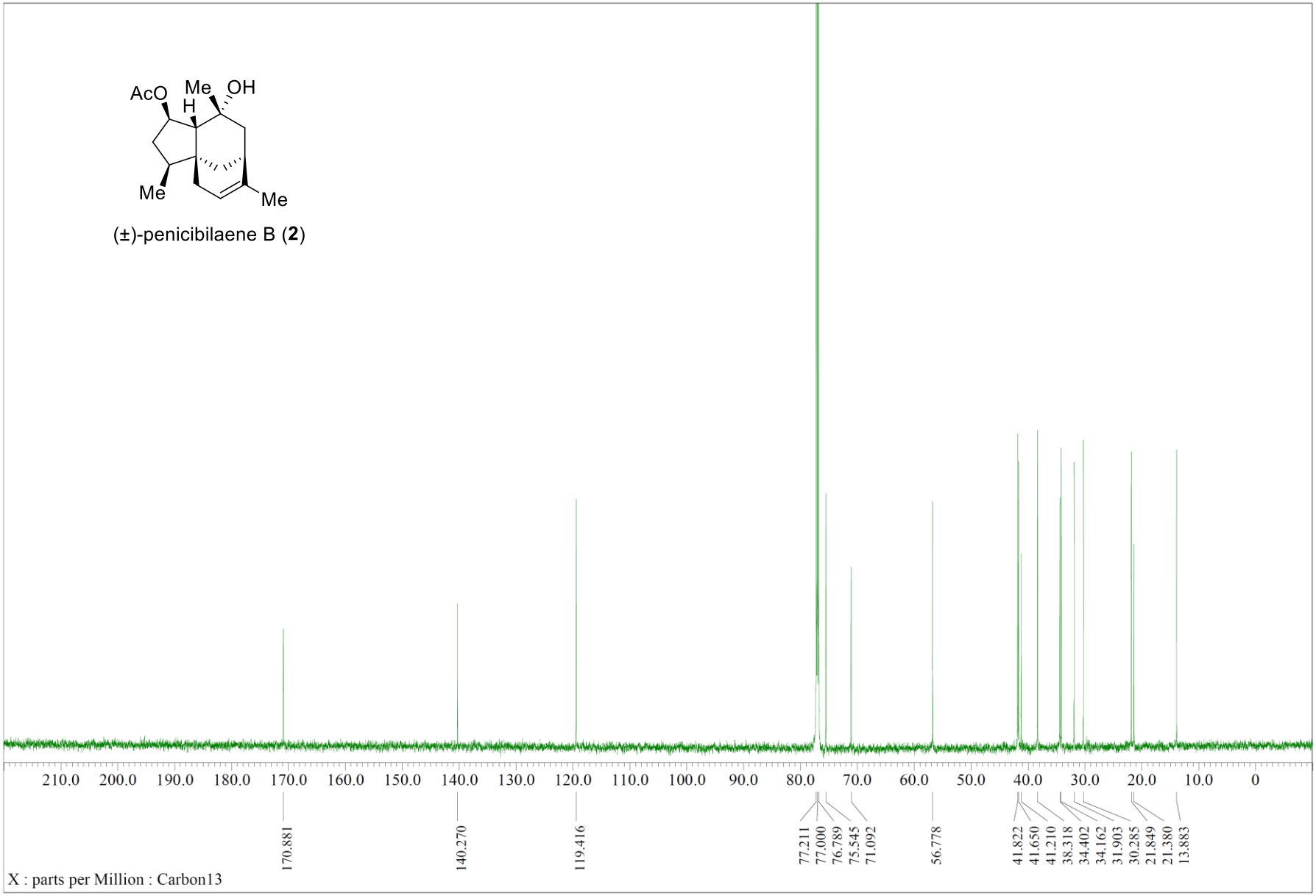


Figure S31. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound S3.

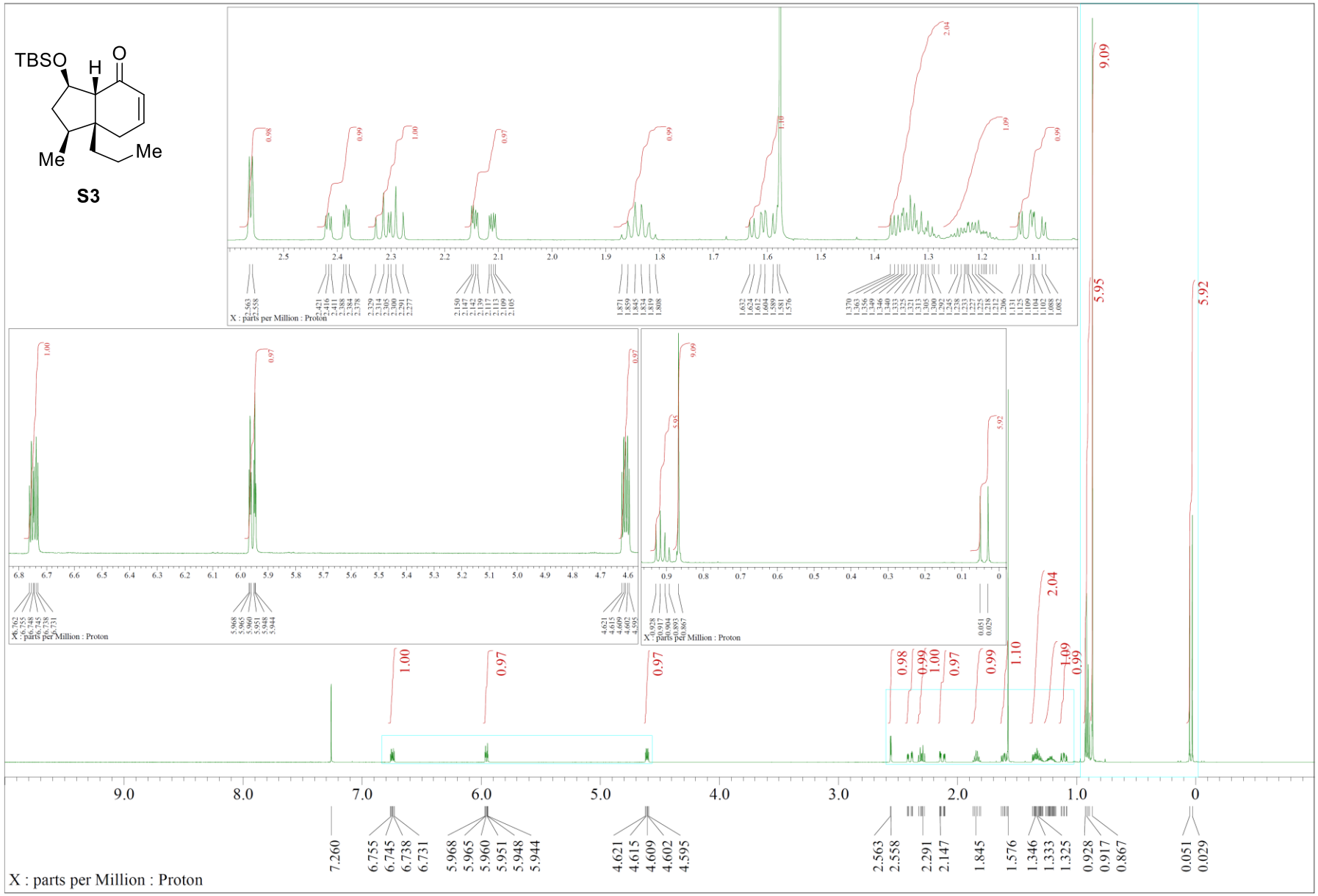


Figure S32. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of compound S3.

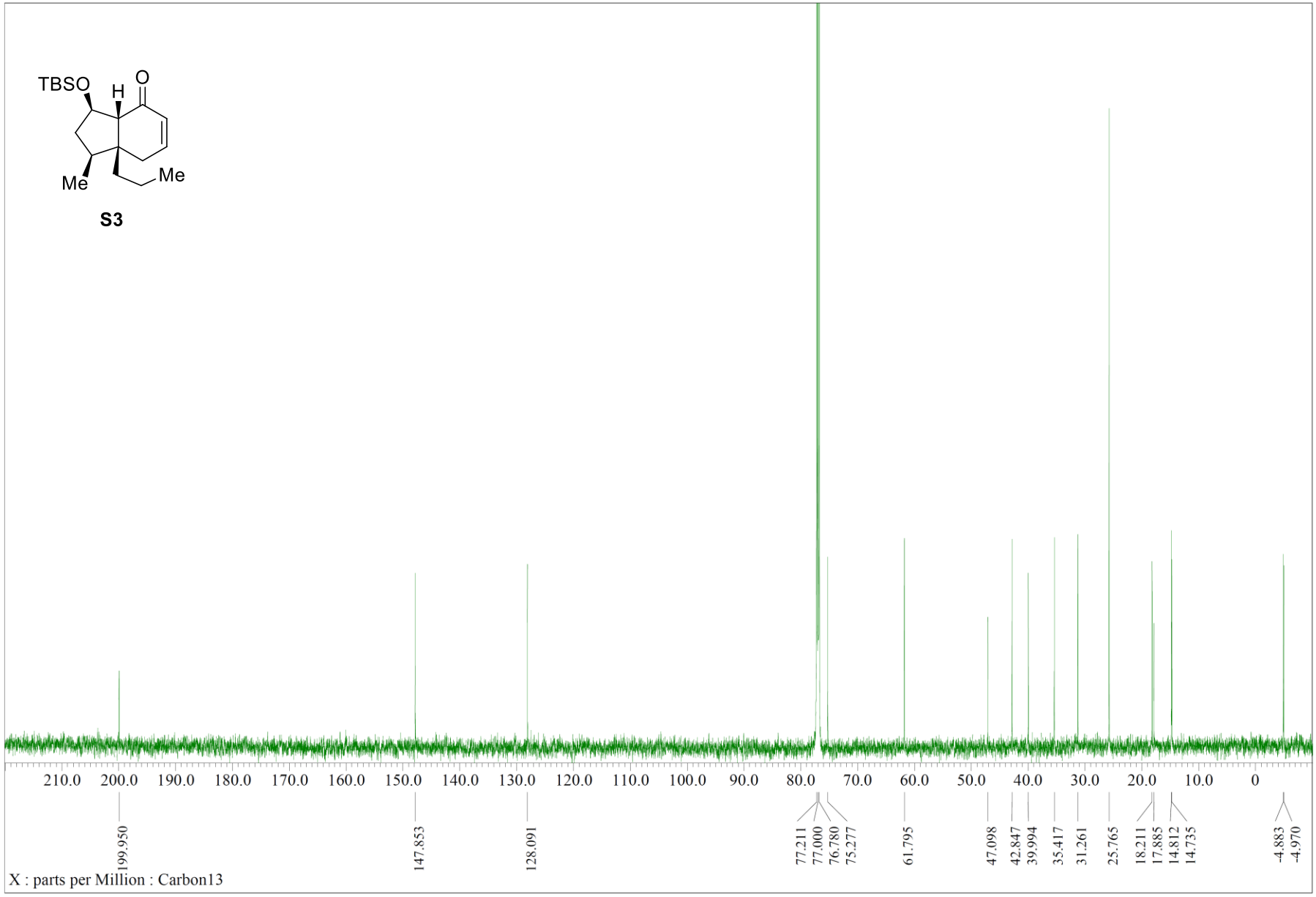


Figure S33. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound S4.

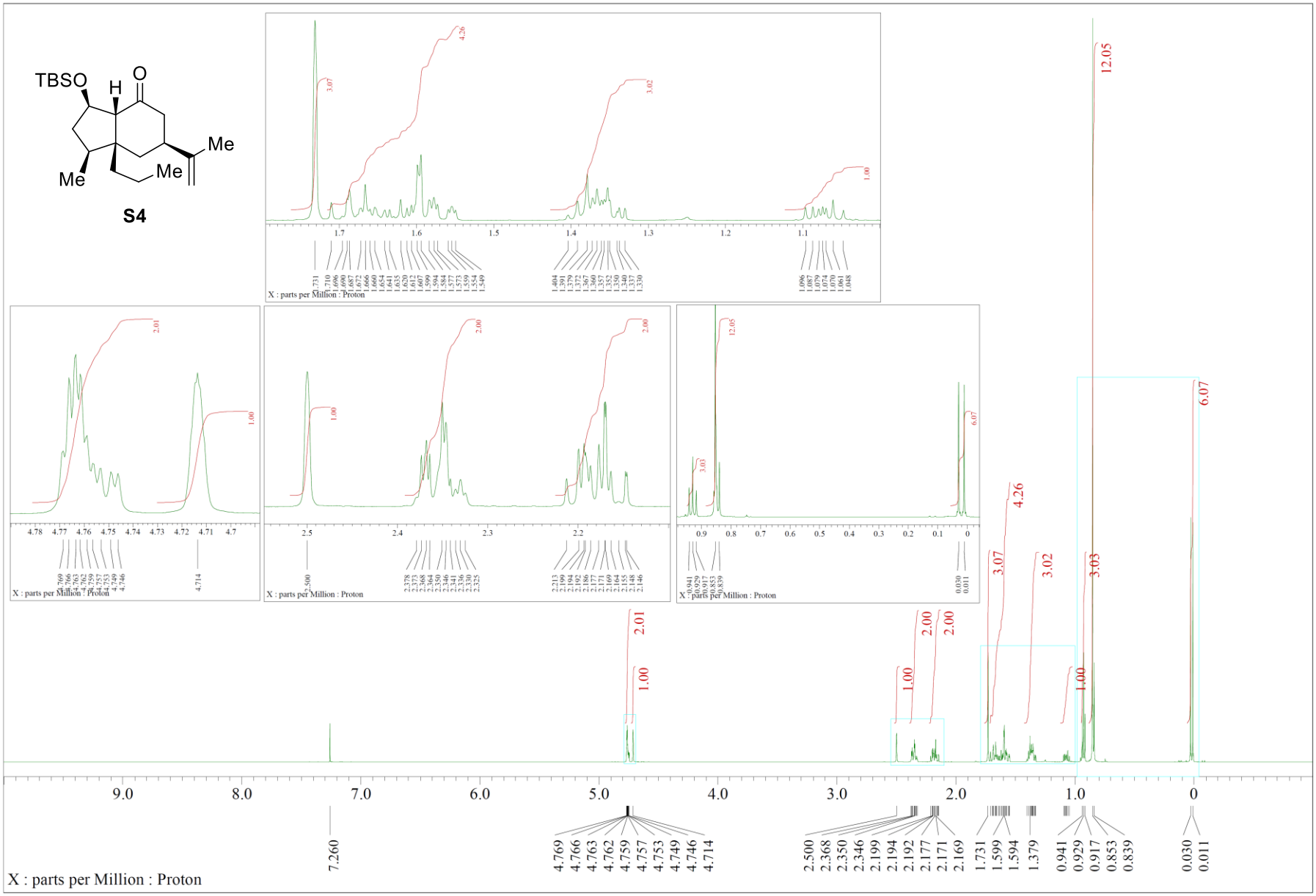


Figure S34. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of compound S4.

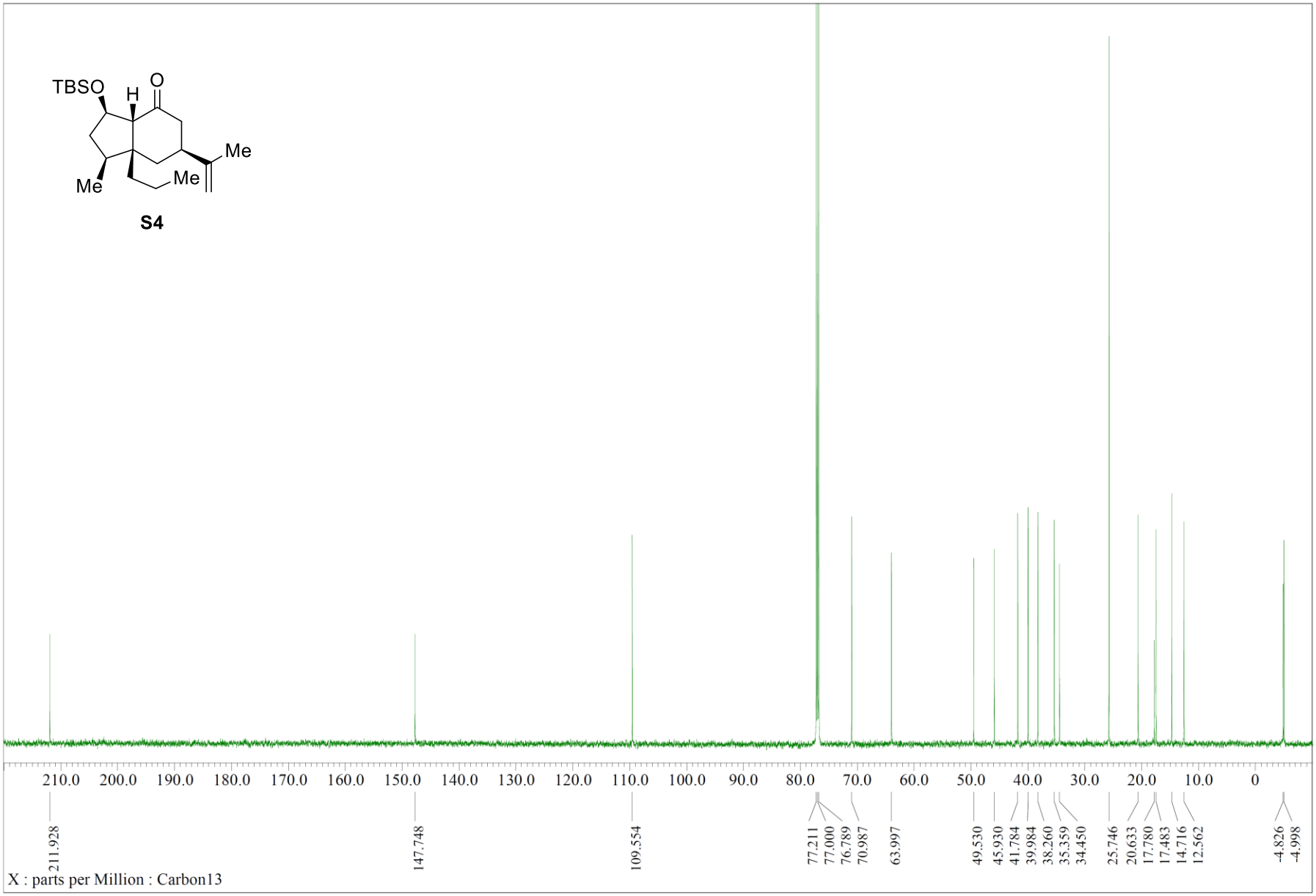


Figure S35. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound S5.

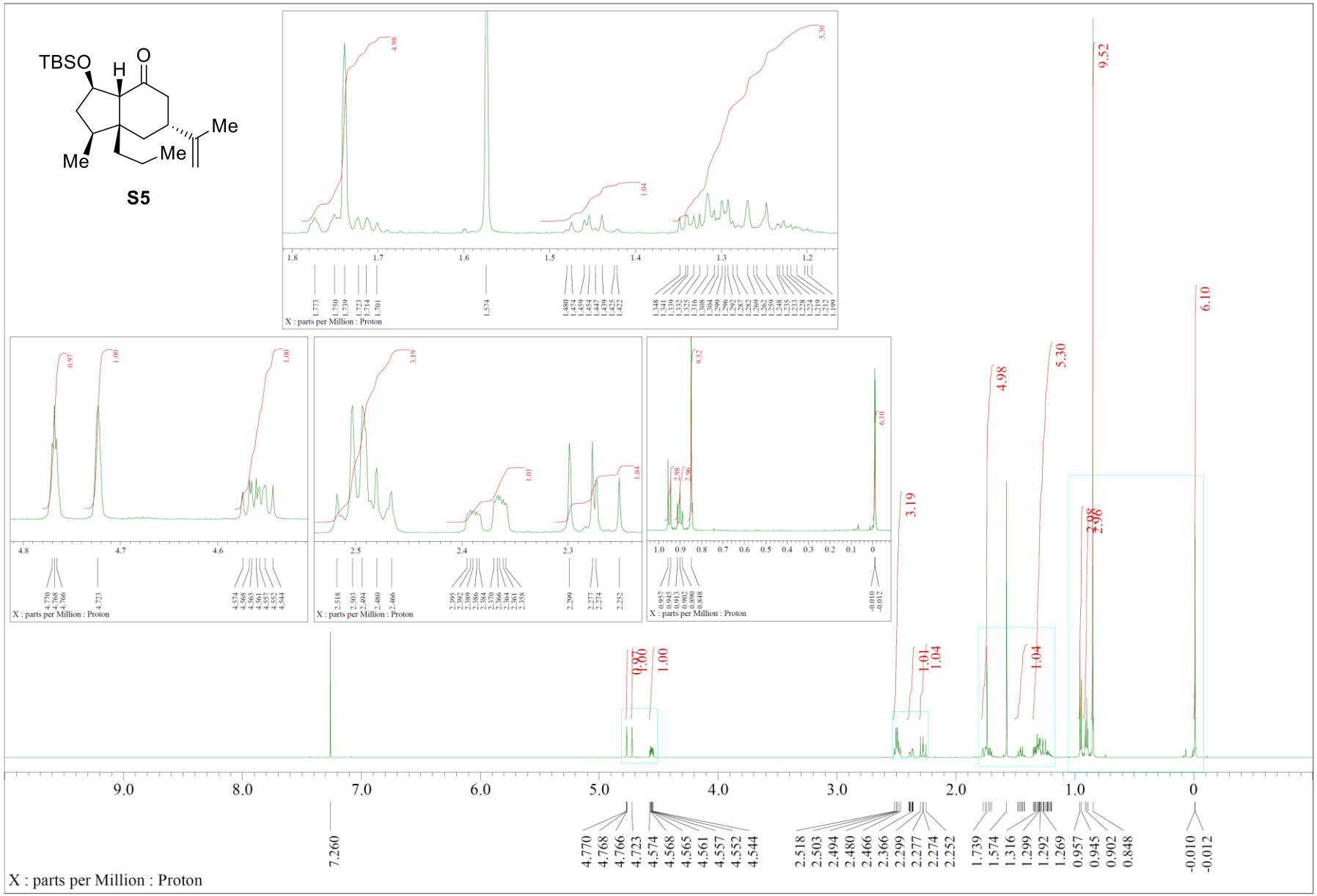


Figure S36. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of compound S5.

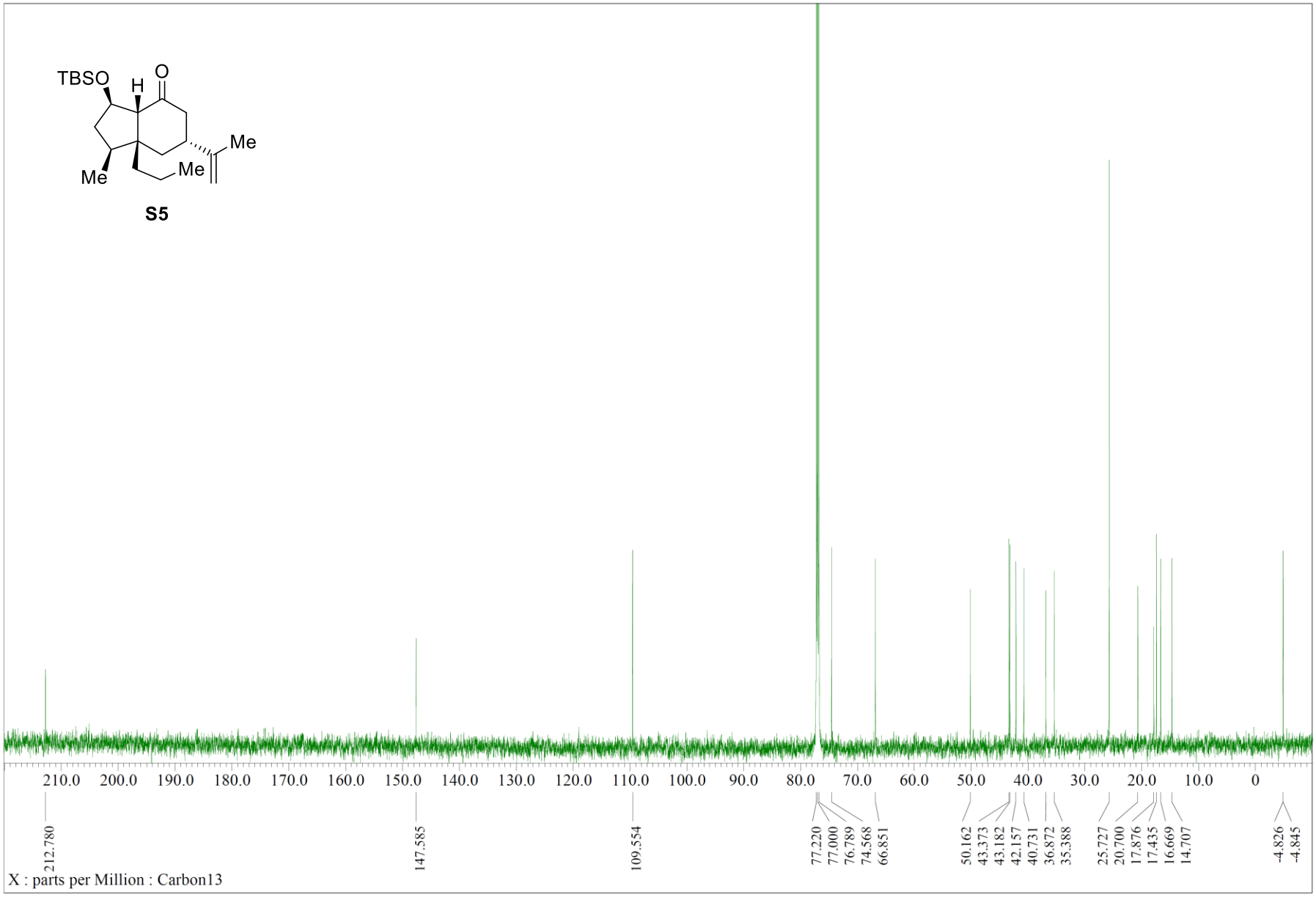


Figure S37. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound S6.

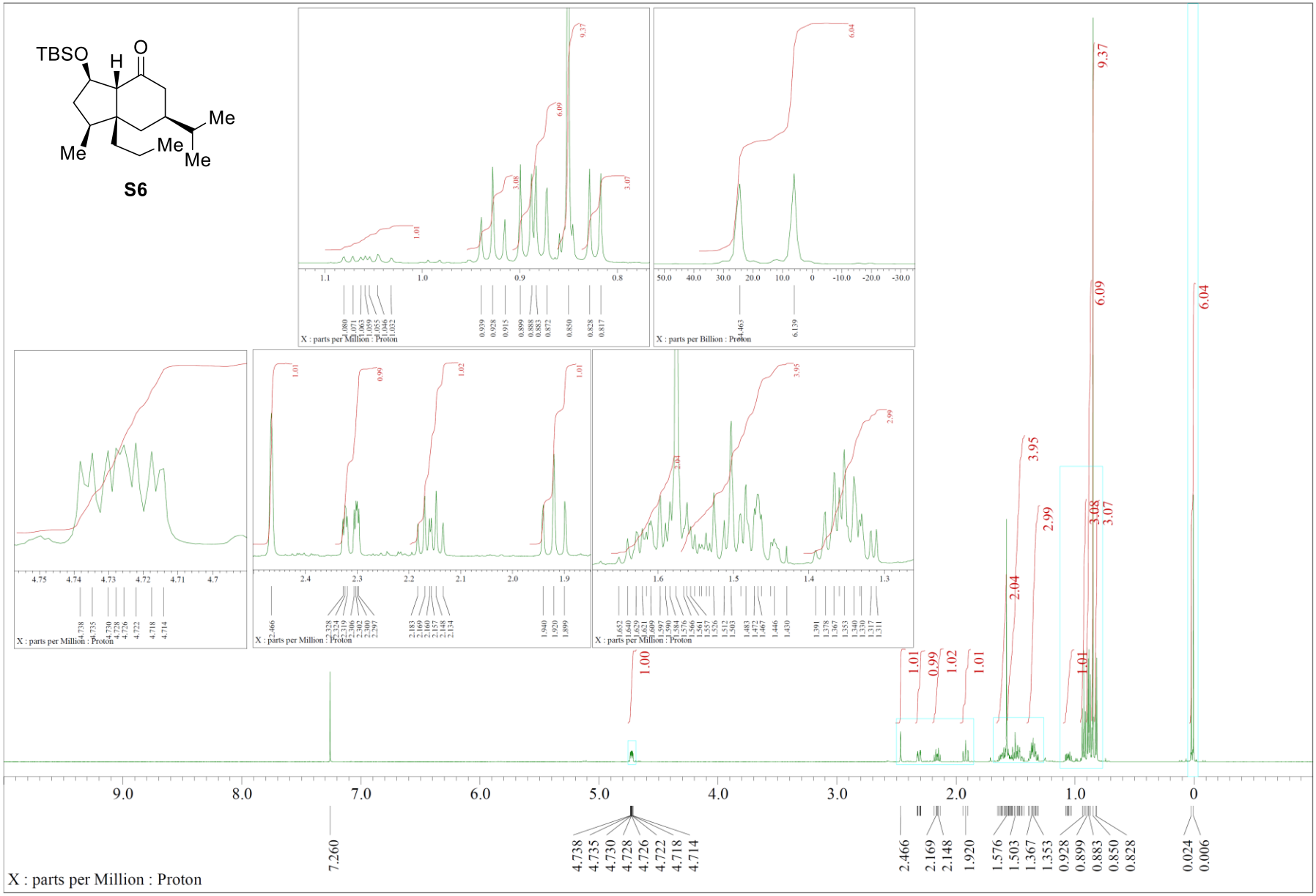
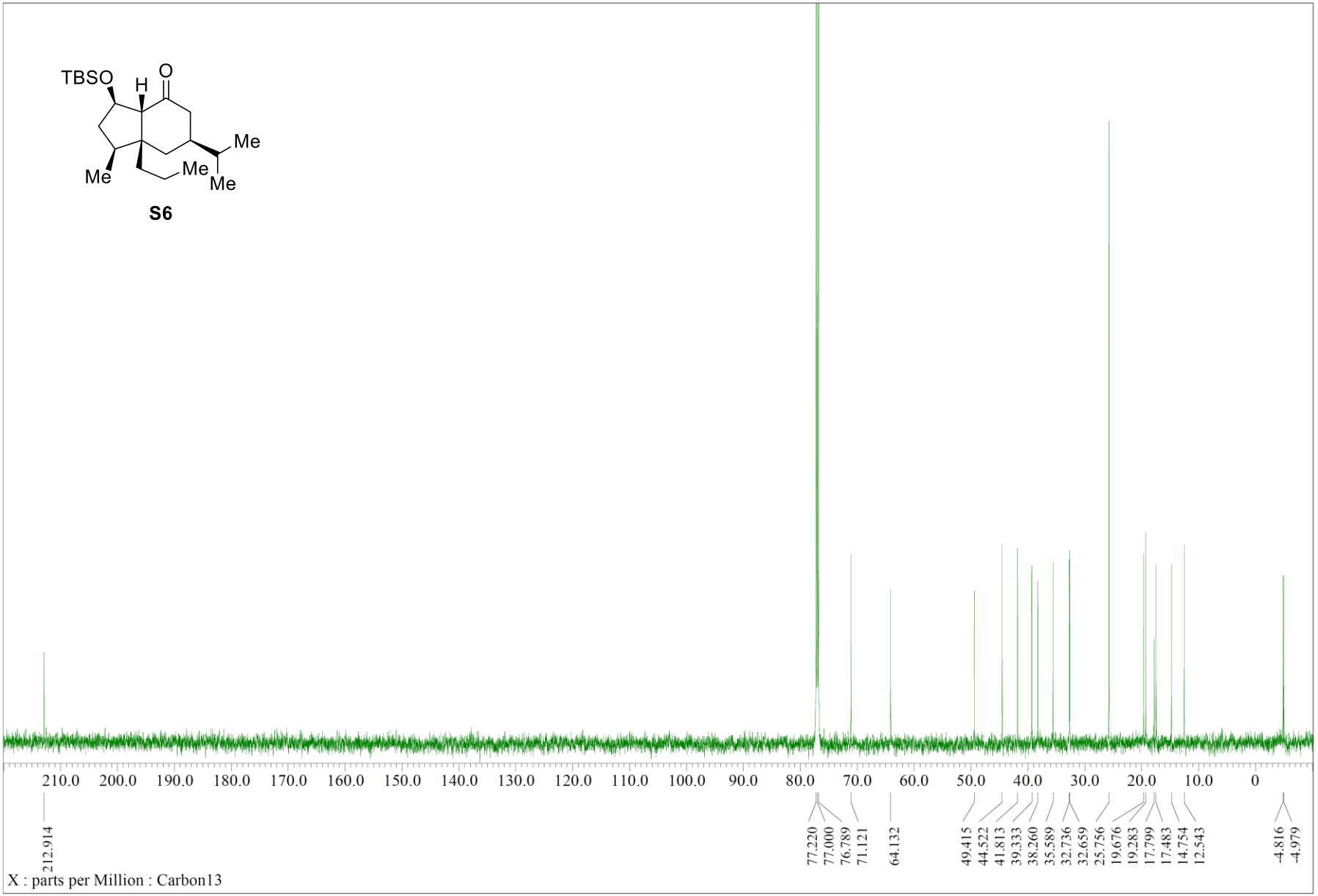


Figure S38. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of compound S6.



6. References

(S1) Meng, L. H.; Li, X. M.; Liu, Y.; Wang, B. G. *Org. Lett.* **2014**, *16*, 6052–6055.

(S2) Xue, Y.; Dong, G. *J. Am. Chem. Soc.* **2021**, *143*, 8272–8277.