

Supporting Information

Microwave Assisted Synthesis of Substituted Tetrahydropyrans Catalyzed by ZrCl₄ and Its Application in the Asymmetric Synthesis of *Exo*- and *Endo*-brevicommin

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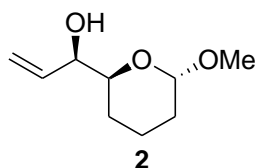
I. General remarks:

Vinyl carbinols, (+)-and (-)-Diisopropyltartrate, $\text{Ti}(\text{O}i\text{-Pr})_4$, 3-butene-2-one, TMSBr , ZrCl_4 , anhydrous methanol, anhydrous acetonitrile, CuI , and Mg turnings were obtained from commercial sources and were used as received. Proton and carbon nuclear magnetic resonance spectra (^1H and ^{13}C NMR, respectively) were recorded on 400 MHz (operating frequencies: ^1H , 400.13 MHz; ^{13}C , 100.61 MHz) 500 MHz (operating frequencies: ^1H , 499.77 MHz; ^{13}C , 125.67 MHz) FT spectrometers at ambient temperature. In the case of ^1H and ^{13}C NMR spectra, the chemical shifts (δ) for all compounds are listed in parts per million downfield from tetramethylsilane using the NMR solvent as an internal reference. The reference values used for deuterated chloroform (CDCl_3) were 7.26 and 77.00 ppm for ^1H and ^{13}C NMR spectra, respectively. High resolution mass spectra were measured on a Micromass instrument. Infrared spectra were recorded on infrared FT spectrometer. Optical rotation values were measured on a polarimeter. GC analysis was done using chiral GC column. Thin layer chromatography was carried out using silica gel plates. Column chromatography separations were performed using silica gel. Solvents were dried immediately before use by distillation from standard drying agents. The diols (**1** and **4–8**)¹ and epoxide **20** were synthesized according to the literature.²

II. General procedure for ZrCl_4 -catalyzed cyclic acetal formation

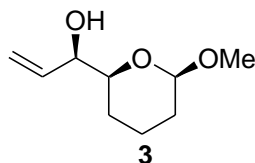
ZrCl_4 (6.8 mg, 5 mol%) and diol (200 mg, 0.606 mmol) were dissolved in methanol (400 μL) and irradiated under MW (150 W) at 50 °C for 3 min. The title compound was purified by flash column chromatography using pentane:EtOAc (8.5/1.5) as the eluent. The % yield of combined epimers is given in the Tables 1 and 2. The epimeric ratio was determined by ^1H NMR spectroscopy by integrating methoxy peaks and by GC also.

III. Spectroscopic data for the cyclic acetals

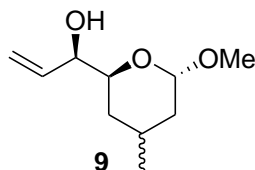


The epimeric ratio of crude reaction mixture was determined by GC using a β -Dex chiral column (column temp. 140 °C isotherms, 1 mL/min column flow, injector temp. 200 °C, and detector temp 220 °C), R_t (major) = 13.21 min and R_t (minor) = 12.91 min.

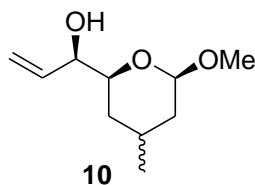
$[\alpha]_D^{20} + 63.5$ ($c = 0.50$, CHCl_3); IR (neat, NaCl): 3456.2, 2944.2, 1442.0, 1372.4, 1199.4, 1125.0, 1030.6 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 5.88 (ddd, $J = 5.9, 10.6, 16.6$ Hz, 1H), 5.33 (d, $J = 17.3$ Hz, 1H), 5.22 (d, $J = 10.6$ Hz, 1H), 4.75 (s, 1H), 4.12 (s, 1H), 3.76 (d, $J = 11.7$ Hz, 1H), 3.36 (s, 3H), 1.89–1.74 (m, 2H), 1.54–1.29 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) $\delta = 136.5, 116.4, 98.8, 74.8, 71.2, 54.5, 29.6, 24.6, 17.5$ ppm.; GC-HRMS (EI): Found 140.0835 $[\text{M}-\text{MeOH}]^+$, $\text{C}_8\text{H}_{12}\text{O}_2$ requires 140.0837.



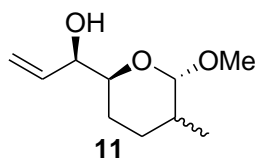
$[\alpha]_D^{20} - 53.3$ ($c = 0.55$, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 5.99 – 5.80 (m, 1H), 5.34 (dt, $J = 1.5, 17.3$ Hz, 1H), 5.21 (dt, $J = 1.4, 10.6$ Hz, 1H), 4.35 (dd, $J = 2.1, 9.5$ Hz, 1H), 4.25 – 4.20 (m, 1H), 3.49 (s, 3H), 3.46 (ddd, $J = 2.1, 4.0, 11.2$ Hz, 1H), 1.93 – 1.85 (m, 1H), 1.80 – 1.75 (m, 1H), 1.56 – 1.31 (m, 4H), ^{13}C NMR (126 MHz, CDCl_3) $\delta = 136.5, 116.4, 103.6, 78.6, 74.6, 56.0, 31.0, 24.3, 21.6$ ppm. The IR and HRMS data are identical to its epimer **2**.



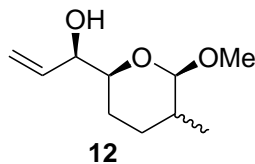
Diastereomeric ratio was 0.70/0.3; $[\alpha]_D^{20} = +127.9$ ($c = 1.45$, CHCl_3); IR (neat, NaCl): 3422.3, 2945.2, 2930.9, 1380.8, 1112.2, 1046.8 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 6.04 – 5.77 (m, 1H), 5.41 – 5.28 (m, 1H), 5.21 (dt, $J = 1.5, 10.6$ Hz, 1H), 4.78 (d, $J = 3.2$ Hz, 0.7H), 4.75 – 4.72 (m, 0.3H), 4.21 – 4.11 (m, 1H), 3.87 (dt, $J = 3.9, 10.7$ Hz, 0.3H), 3.75 (ddd, $J = 2.3, 3.6, 11.8$ Hz, 0.7H), 3.34 (s, 2H), 3.33 (s, 1H), 2.26 (d, $J = 4.6$ Hz, 0.7H), 2.22 (d, $J = 4.5$ Hz, 0.3H), 2.00 – 1.89 (m, 1H), 1.86 – 1.66 (m, 1.7H), 1.59 – 1.52 (m, 0.7H), 1.46 – 1.37 (m, 0.3H), 1.30 – 1.16 (m, 1.2H), 1.12 (d, $J = 7.1$ Hz, 1H), 1.09 – 1.00 (m, 0.7H), 0.89 (d, $J = 6.6$ Hz, 2H). ^{13}C NMR (101 MHz, CDCl_3) $\delta =$ Major diastereomer 136.5, 116.4, 98.9, 74.6, 71.3, 54.6, 38.2, 33.2, 24.0, 22.2 ppm, and minor diastereomer 136.7, 116.5, 99.6, 74.6, 67.4, 54.9, 35.2, 30.6, 23.8, 20.8 ppm. GC-HRMS (EI): Found 155.1078 $[\text{M}-\text{MeO}]^+$, $\text{C}_9\text{H}_{15}\text{O}_2$ requires 155.1067. The diastereomeric ratio was determined by GC using β -Dex chiral column (isothermal 130 $^\circ\text{C}$, 0.99 ml/min column flow, injector temp. 200 $^\circ\text{C}$ and detector temp 220 $^\circ\text{C}$), R_t (major) = 8.86 min and R_t (minor) = 10.18 min.



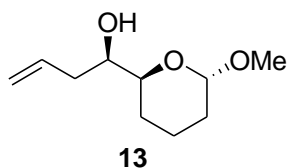
Diastereomeric ratio was 0.67/0.33; $[\alpha]_D^{20} = -41.9$ ($c = 0.35$, CHCl_3); ^1H NMR (400 MHz, CDCl_3) $\delta = 5.90$ (ddd, $J = 6.0, 11.3, 16.6$ Hz, 1H), 5.35 (ddt, $J = 1.6, 3.2, 5.7$ Hz, 1H), 5.22 (dd, $J = 1.5, 10.6$ Hz, 1H), 4.64 (dd, $J = 2.7, 7.4$ Hz, 0.33H), 4.36 (dd, $J = 2.1, 9.6$ Hz, 0.67H), 4.33 – 4.21 (m, 1H), 3.79 – 3.72 (m, 0.33H), 3.49 (2xs, 3H), 3.76 (ddd, $J = 11.5, 3.9, 2.1$ Hz, 0.67 H), 2.87 (d, $J = 3.6$ Hz, 0.33 H), 2.27 (d, $J = 4.4$ Hz, 0.65 H), 1.81–1.44 (m, 4H), 1.20–1.05 (m, 2H), 1.03 (d, $J = 7.1$ Hz, 0.99 H), 0.97 (d, $J = 6.6$ Hz, 2.01 H) ppm; ^{13}C NMR (100 MHz, CDCl_3); major diastereomer, δ 136.4, 116.5, 103.2, 77.7, 74.4, 56.2, 39.6, 32.9, 28.7, 21.8 ppm, and minor diastereomer, δ 136.7, 116.3, 99.5, 75.1, 74.3, 56.1, 37.0, 30.2, 23.9, 20.0 ppm; The IR and HRMS data are identical to its epimer **9**. The diastereomeric ratio was determined by GC using β -Dex chiral column (isothermal 130 °C, 0.99 ml/min column flow, injector temp. 200 °C and detector temp. 220 °C), R_t (major) = 10.13 min and R_t (minor) = 10.85 min.



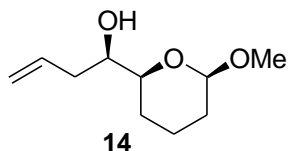
Diastereomeric ratio was 0.64/0.36; $[\alpha]_D^{20} + 159.1$ ($c = 0.6$, CHCl_3); IR (neat, NaCl): 3457.7, 3081.2, 2931.9, 1456.1, 1380.8, 1102.1, 1044.8, 941.1 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 5.99 – 5.81 (m, 1H), 5.34 (ddt, $J = 1.6, 3.2, 17.3$ Hz, 1H), 5.27 – 5.18 (m, 1H), 4.52 (d, $J = 3.2$ Hz, 0.64H), 4.42 (bs, 0.36H), 4.16 – 4.10 (m, 1H), 3.83 – 3.65 (m, 1H), 3.37 (s, 1H), 3.36 (s, 2H), 2.20 (d, $J = 4.6$ Hz, 0.36H), 2.17 (d, $J = 4.7$ Hz, 0.64H), 2.07 – 1.92 (m, 0.36H), 1.86 – 1.63 (m, 1.34H), 1.58 – 1.45 (m, 2.64H), 1.44 – 1.23 (m, 1.0H), 1.04 (d, $J = 7.3$ Hz, 1.08H), 0.88 (d, $J = 6.9$ Hz, 1.92H), ^{13}C NMR (100 MHz, CDCl_3); major diastereomer, $\delta = 136.6, 116.4, 102.1, 74.6, 70.6, 54.8, 34.7, 25.6, 24.9, 16.6$ ppm, minor diastereomer $\delta = 136.4, 116.5, 103.3, 74.8, 71.1, 54.6, 31.2, 23.5, 19.1, 16.1$ ppm. GC-HRMS (EI): Found 186.1256 $[\text{M}]^+$, $\text{C}_{10}\text{H}_{18}\text{O}_3$ requires 186.1256.



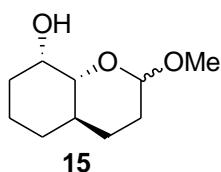
Diastereomeric ratio was 0.70/0.3; $[\alpha]_D^{20}$ -40.3 ($c = 0.3$, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 5.98 – 5.84 (m, 1H), 5.38 – 5.29 (m, 1H), 5.25 – 5.17 (m, 1H), 4.44 – 4.38 (m, 0.3H), 4.22 (m, 0.7H), 4.12 (dd, $J = 14.3, 7.1$ Hz, 0.3H), 3.95 (d, $J = 8.4$ Hz, 0.7H), 3.78 – 3.72 (m, 0.3H), 3.49 (s, 2.1H), 3.47 – 3.42 (m, 0.7H), 2.24 (d, $J = 4.4$ Hz, 0.7H), 2.18 (d, $J = 4.6$ Hz, 0.3H), 1.88 – 1.12 (m, 5H), 1.04 (d, $J = 7.3$ Hz, 0.9H), 0.91 (d, $J = 6.6$ Hz, 2.1H). ^{13}C NMR (126 MHz, CDCl_3); major diastereomer, $\delta = 136.5, 116.4, 108.5, 78.6, 74.5, 56.3, 35.7, 24.9, 16.4$ ppm, minor diastereomer $\delta = 136.4, 116.5, 103.3, 74.5, 71.1, 54.6, 31.2, 22.3, 19.1, 16.1$ ppm. The IR and HRMS data are identical to its epimer **11**.



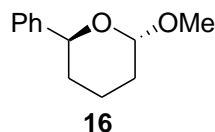
$[\alpha]_D^{20} = +168.7$ ($c = 1.2$, CHCl_3); IR (neat, NaCl): 3446.0, 3072.8, 2943.6, 1443.6, 1385.9, 1149.2, 1074.2, 1032.3 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 5.96 – 5.74 (m, 1H), 5.14 (dd, $J = 12.3, 13.5$ Hz, 2H), 4.74 (bs, 1H), 3.70 – 3.60 (m, 2H), 3.35 (s, 3H), 2.39 – 2.28 (m, 1H), 2.27 – 2.15 (m, 1H), 2.06 (bs, 1H), 1.88 – 1.56 (m, 6H), 1.55 – 1.45 (m, 1H). ^{13}C NMR (101 MHz, CDCl_3) $\delta = 134.9, 117.7, 98.7, 72.8, 70.9, 54.5, 37.0, 29.7, 24.7, 17.5$ ppm. GC-HRMS (EI): Found 186.1264 $[\text{M}]^+$, $\text{C}_{10}\text{H}_{18}\text{O}_3$ requires 186.1256.



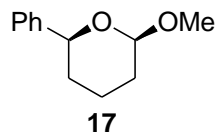
$[\alpha]_D^{20} = -53.0$ ($c = 0.8$, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 5.91 – 5.81 (m, 1H), 5.19 – 5.10 (m, 2H), 4.33 (dd, $J = 2.1, 9.5$ Hz, 1H), 3.87 – 3.63 (m, 1H), 3.50 (s, 3H), 3.44 – 3.26 (m, 1H), 2.45 – 2.32 (m, 1H), 2.32 – 2.19 (m, 1H), 2.11 (d, $J = 3.8$ Hz, 1H), 1.98 – 1.85 (m, 1H), 1.83 – 1.74 (m, 1H), 1.68 – 1.61 (m, 1H), 1.51 (ddt, $J = 3.7, 12.9, 25.9$ Hz, 1H), 1.44 – 1.27 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3) $\delta = 134.7, 117.8, 103.5, 78.2, 72.7, 56.0, 37.2, 31.1, 24.9, 21.6$ ppm. The IR and HRMS data are identical to its epimer **13**.



$[\alpha]_D^{20} = -5.0$ ($c = 0.3$, CHCl_3); IR (neat, NaCl): 3432.4, 2935.4, 1451.4, 1126.0, 1042.0 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 4.69 (d, $J = 3.1$ Hz, 0.8H), 4.31 (dd, $J = 9.6, 2.2$, 0.2H), 3.49 (s, 0.6H), 3.46 – 3.37 (m, 0.8H), 3.36 (s, 2.4H), 3.30 – 3.15 (m, 1H), 3.11 – 3.01 (m, 0.2H), 2.29 – 2.17 (m, 0.2H), 2.02 – 1.10 (m, 10.8H). ^{13}C NMR (101 MHz, CDCl_3), major diastereomer, $\delta = 98.0, 72.9, 69.8, 54.4, 48.5, 35.1, 31.4, 29.8, 20.9, 20.8$ ppm, and minor diastereomer $\delta = 103.0, 77.1, 73.0, 56.1, 48.2, 35.2, 31.1, 25.5, 20.8$ ppm. GC-HRMS (EI): Found 186.1258 $[\text{M}]^+$, $\text{C}_{10}\text{H}_{18}\text{O}_3$ requires 186.1256.



$[\alpha]_D^{20} + 72.0$ ($c = 1.0$, CHCl_3); IR (neat, NaCl): 2939.5, 1602.9, 1448.9, 1377.6, 1124.9, 950.8, 751.0, 698.6 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.41 – 7.31 (m, 4H), 7.31 – 7.23 (m, 1H), 4.87 (bs, 1H), 4.76 (dd, $J = 2.2, 11.5$, 1H), 3.40 (s, 3H), 2.08 – 1.92 (m, 1H), 1.89 – 1.80 (m, 1H), 1.80 – 1.60 (m, 4H), ^{13}C NMR (101 MHz, CDCl_3) $\delta = 143.0, 128.3, 127.4, 126.1, 99.0, 70.8, 54.6, 33.1, 29.5, 18.6$ ppm. GC-HRMS (EI): Found 192.1137 $[\text{M}]^+$, $\text{C}_{12}\text{H}_{16}\text{O}_2$ requires 192.1150.

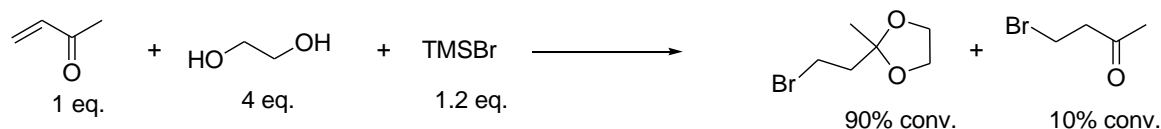


$[\alpha]_D^{20} - 100.0$ ($c = 1.0$, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 7.41 – 7.31 (m, 4H), 7.30 – 7.23 (m, 1H), 4.87 (s, 1H), 4.76 (dd, $J = 2.2, 11.5$, 1H), 3.40 (s, 3H), 2.08 – 1.92 (m, 1H), 1.90 – 1.79 (m, 1H), 1.80 – 1.60 (m, 4H), ^{13}C NMR (101 MHz, CDCl_3) δ 142.4, 128.2, 127.3, 125.8, 103.7, 77.9, 56.1, 33.0, 30.9, 22.6 ppm. The IR and HRMS data are identical to its epimer **16**.

IV. Synthesis of (*S*)-1-((*R*)-oxiran-2-yl)prop-2-en-1-ol (**20**)

Compound **20** was synthesized according to the literature². ^1H NMR (500 MHz, CDCl_3) δ 5.85 (ddd, $J = 17.0, 10.5, 6.2$, 1H), 5.40 (dt, $J = 14.6, 1.3$ Hz, 2H), 5.27 (td, $J = 8.0, 1.3$ Hz, 1H), 4.36–4.32 (m, 1H), 3.10 (dt, $J = 3.8, 3.2$ Hz, 1H), 2.86–2.74 (m, 2H). ^{13}C NMR (125.6 MHz, CDCl_3) δ 135.5, 117.6, 70.2, 53.9, 43.5 ppm. $[\alpha]_D^{20} = +54.3$ ($c = 1.8$, CHCl_3); $[\text{lit}^2][\alpha]_D^{22} = +46.7$ ($c = 1.38$, CHCl_3)

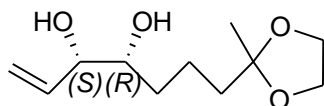
V. Synthesis of 2-(2-bromoethyl)-2-methyl-1,3-dioxolane



The mixture of 3-butene-2-one (4.05 mL, 50 mmol) and ethylene glycol (11.2 mL, 4 equiv) were cooled to 0–5 °C and then TMSBr (7.92 mL, 60 mmol) added slowly under an inert atmosphere. The resulting mixture was stirred for 2 h at room temperature. The conversion of crude mixture was checked by ¹H NMR. The reaction mixture was then poured on to the biphasic pentane (100 mL) over 5% sodium carbonate (50 mL) and the resulting mixture was stirred for 5 min. The organic layer was then washed with 5% sodium thiosulfate (50 mL), washed with water and dried over anhydrous K₂CO₃. After removal of the solvent *in vacuo*, the residue was purified by vacuum distillation (80 °C, 4 mbar vacuum) to afforded 75% yield with 97.5% purity. ¹H NMR (400 MHz, CDCl₃) δ 4.09 – 3.86 (m, 4H), 3.48 – 3.32 (m, 2H), 2.37 – 2.21 (m, 2H), 1.33 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 109.0, 64.8, 42.8, 26.8, 24.0.

VI. Synthesis of (3*S*,4*R*)-7-(2-methyl-1,3-dioxolan-2-yl)hept-1-ene-3,4-diol (**21**)

Compound **21** was synthesized according to the literature¹ with modification (temp -78 °C and 10 mol% of CuI).



21

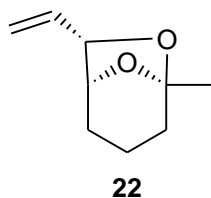
[α]_D²⁰ = +1.2 (c = 1.7, CHCl₃); IR (neat, NaCl): 3422.3, 2945.9, 1643.7, 1378.9, 1220.2, 1061.2 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.92 (ddd, *J* = 17.1, 10.5, 6.4, 1H), 5.36 – 5.25 (m, 2H), 4.10 (dt, *J* = 6.3, 4.2, 1H), 3.97 – 3.89 (m, 4H), 3.69 (dq, *J* = 8.4, 4.3, 1H), 2.11 (dd, *J* = 9.0, 4.9, 2H), 1.71 – 1.58 (m, 4H), 1.51 – 1.38 (m, 2H), 1.31 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 136.2, 117.4, 110.0, 75.9, 74.0, 64.6 (2C), 38.9, 32.0, 23.7, 20.3 ppm. HRMS (ESI) Found 215.1282 [M-H]⁺, C₁₁H₁₉O₄ requires 215.1282.

Synthesis of (3*R*,4*S*)-7-(2-methyl-1,3-dioxolan-2-yl)hept-1-ene-3,4-diol (21**):** All physical data is identical as above mentioned for compound **21**.

[α]_D²⁰ = -1.3 (c = 1.7, CHCl₃);

VII. Synthesis of (1*R*,5*S*,7*S*)-5-methyl-7-vinyl-6,8-dioxabicyclo[3.2.1]octane (**22**)

ZrCl₄ (53 mg, 10 mol%) and diol **21** (500 mg, 2.31 mmol) were dissolved in methanol (1 mL) and irradiated under MW (150 W) at 60 °C for 10 min. The compound was purified by flash column chromatography using pentane:Et₂O (9/1) as the eluent and the compound was volatile, so the solvent was evaporated by rotavapour at 40 °C and then remaining solvent was removed at 40 °C at 150 mbar vacuum. The titled compound **22** was isolated as a colorless oil (306 mg) in 86% yield. Compound **23** was recovered in (51 mg) 12% yield.

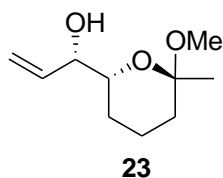


$[\alpha]_D^{20} = + 64.9$ ($c = 1.8$, Et_2O); IR (neat, NaCl): 3084.7, 2942.7, 1435.5, 1382.4, 1172.9, 1016.1, 998.4, 849.5 cm^{-1} . ^1H NMR (500 MHz, CDCl_3) δ 6.03 (ddd, $J = 17.3, 10.5, 6.9$ Hz, 1H), 5.37 (ddt, $J = 64.9, 10.5, 1.5$ Hz, 2H), 4.59 – 4.48 (m, 1H), 4.30 (t, $J = 5.0$ Hz, 1H), 2.00 – 1.86 (m, 1H), 1.84 – 1.71 (m, 1H), 1.68 (dd, $J = 10.7, 4.3$ Hz, 2H), 1.62 – 1.52 (m, 2H), 1.46 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 132.8, 118.9, 107.8, 81.2, 77.7, 34.3, 24.9, 24.2, 17.1 ppm. HRMS (ESI) Found 154.1001 $[\text{M}]^+$, $\text{C}_9\text{H}_{14}\text{O}_2$ requires 154.0994.

Synthesis of (1S,5R,7R)-5-methyl-7-vinyl-6,8-dioxabicyclo[3.2.1]octane (22): All physical data is identical as above mentioned for compound **22**.

$[\alpha]_D^{20} = - 74.6$ ($c = 1.2$, CHCl_3);

(S)-1-((2R,6S)-6-methoxy-6-methyl-tetrahydro-2H-pyran-2-yl)-prop-2-en-1-ol (23)



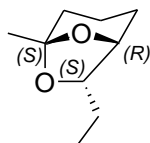
$[\alpha]_D^{20} = - 114.1$ ($c = 1.0$, Et_2O); IR (neat, NaCl): 3455.5, 2944.3, 1329.3, 1224.1, 1056.7, 842.3 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 5.88 (ddd, $J = 17.2, 10.6, 6.0$ Hz, 1H), 5.26 (ddt, $J = 42.4, 10.6, 1.5$ Hz, 2H), 4.16–4.08 (m, 1H), 3.61 (ddd, $J = 11.8, 3.7, 2.5$ Hz, 1H), 3.21 (s, 3H), 2.22 (d, $J = 3.0$ Hz, 1H), 1.89 – 1.67 (m, 2H), 1.59 – 1.30 (m, 4H), 1.30 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 136.6, 116.2, 98.4, 74.8, 72.9, 47.7, 35.4, 23.9, 23.8, 18.4 ppm.; GC-HRMS (EI): Found 154.0990 $[\text{M}-\text{MeOH}]^+$, $\text{C}_9\text{H}_{14}\text{O}_2$ requires 154.0994.

(R)-1-((2S,6R)-6-methoxy-6-methyl-tetrahydro-2H-pyran-2-yl)-prop-2-en-1-ol (23): All physical data is identical as above mentioned for compound **23**.

$[\alpha]_D^{20} = + 108.0$ ($c = 2.0$, CHCl_3).

VIII. The Synthesis of (1*R*, 5*S*, 7*S*)-7-ethyl-5-methyl-6,8-dioxabicyclo[3.2.1]octane (18)

Compound **22** (308 mg, 2 mmol) and 5% Pd/C (5 wt%, 15 mg) was added to in 2 ml of ethyl acetate. The resulting mixture was pressurized in an autoclave at 10 bar pressure of H₂ for 1.5 h. The compound was filtered through a small pad of silica, the solvent was removed carefully at 40 °C and 150 mbar pressure by rotavapour. The compound was purified column chromatography using pentane:Et₂O (9/1) as the eluent. The (+)-*endo*-brevicomine **18** was isolated as a colorless volatile liquid (297 mg) in 95% yield.



18; (+)-endo-brevicommin

$[\alpha]_{\text{D}}^{20} = +77.9$ ($c = 1.2$, Et_2O , 99.3% *ee*) [lit^4 $[\alpha]_{\text{D}}^{20} = +78.8$ ($c = 0.5$, Et_2O), lit^3 $[\alpha]_{\text{D}}^{26} = +74.6$ ($c = 1.06$, Et_2O)], lit^5 $[\alpha]_{\text{D}}^{21} = +79.5$ ($c = 1.18$, Et_2O)]; IR (neat, NaCl): 2943.2, 1458.1, 1381.4, 1237.3, 1179.9, 1026.7, 849.5 cm^{-1} . ^1H NMR (500 MHz, CDCl_3) δ 4.21 (t, $J = 3.8$ Hz, 1H), 3.99 (td, $J = 7.2, 4.5$, 1H), 1.98 – 1.73 (m, 2H), 1.67 – 1.53 (m, 6H), 1.43 (s, 3H), 0.99 (t, $J = 7.5$ Hz, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 106.7, 81.6, 76.5, 34.4, 25.0, 23.6, 21.9, 17.53, 10.9 ppm. HRMS (ESI) Found 156.1150 $[\text{M}]^+$, $\text{C}_9\text{H}_{16}\text{O}_2$ requires 156.1156.

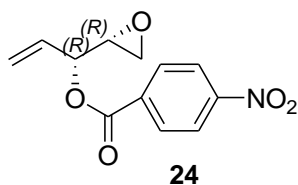
18; (-)-*endo*-brevicommin

All physical data is identical as above mentioned for (+)-*endo*-brevicommin (**18**).

$[\alpha]_{\text{D}}^{20} = -76.6$ ($c = 1.5$, Et_2O , 98.5% ee), $[\text{lit}^4 [\alpha]_{\text{D}}^{20} = -75.9$ ($c = 0.717$, Et_2O), $\text{lit}^6 [\alpha]_{\text{D}}^{20} = -76.7$ ($c = 2.0$, Et_2O), $\text{lit}^5 [\alpha]_{\text{D}}^{22} = -78.9$ ($c = 0.99$, Et_2O)

IX. Synthesis of (*R*)-1-((*R*)-oxiran-2-yl)allyl 4-nitrobenzoate (**24**)

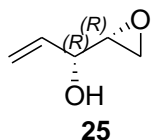
PPh₃ (6.29 g, 24 mmol) and *p*-nitrobenzoic acid (4.01 g, 24mmol) were dissolved in THF (32 mL) and DEAD (3.65 mL, 23.2 mmol) was added dropwise at 0 °C. Then the epoxide **20** (0.8 g, 8 mmol, in 4ml THF) was added slowly and stirred for 5 min at 0 °C and then warmed to 23 °C. The reaction mixture was stirred for 55 min at room temperature and the majority of solvent was removed by rotavapor. The residue was purified by column chromatography using pentane:EtOAc (9/1) as the eluent. Compound **24** was isolated as a pale yellow oil (1.59 g, 80% yield).



$[\alpha]_D^{20} = +31.1$ ($c = 1.5$, CHCl_3); IR (neat, NaCl): 3113.0, 2999.2, 1728.5, 1528.6, 1271.4, 1103.5, 719.7 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 8.42 – 8.18 (m, 4H), 5.98 (ddd, $J = 16.9, 13.8, 8.5$ Hz, 1H), 5.58 – 5.22 (m, 3H), 3.31 (ddd, $J = 6.4, 4.1, 2.6$ Hz, 1H), 2.93 (t, $J = 4.4$ Hz, 1H), 2.77 (dd, $J = 4.8, 2.6$, 1H). ^{13}C NMR (101 MHz, CDCl_3) δ 163.6, 150.7, 135.2, 131.4, 130.9, 123.6, 119.7, 76.8, 52.3, 44.7 ppm; Elemental analysis; calcd. C 57.83; H 4.45; N 5.62, found C 57.72; H 4.49; N 5.54.

X. Synthesis of (*R*)-1-((*R*)-oxiran-2-yl)prop-2-en-1-ol (25)

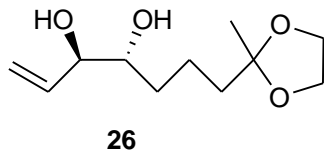
The *p*-nitrobenzoate **24** (1.49 g, 6 mmol) and K_2CO_3 (2 g) were added to methanol (12 mL) at 0 °C and stirred for 2 h. The methanol was removed under reduced pressure and water (5 mL) was added. The resulting mixture was extracted with ethyl acetate (5 X 30 mL) and the organic extracts were dried over anhydrous magnesium sulfate. The solvent was removed by column chromatography using pentane:EtOAc (7:3). (*R*)-1-((*R*)-oxiran-2-yl)prop-2-en-1-ol (**25**) was isolated as a liquid (450 mg, 75% yield).



$[\alpha]_D^{20} = +20.7$ ($c = 1.8$, CHCl_3); IR (neat, NaCl): 3428.4, 2989.1, 2874.3, 1428.9, 1251.7, 1043.8, 933.5, 887.1 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 5.94 (ddd, $J = 17.3, 10.6, 5.5$, 1H), 5.45 – 5.36 (m, 1H), 5.30 – 5.21 (m, 1H), 4.08 – 3.93 (m, 1H), 3.07 (ddd, $J = 4.9, 4.1, 2.8$, 1H), 2.89 – 2.80 (m, 1H), 2.76 (dd, $J = 4.9, 2.7$, 1H), 2.53 – 2.40 (bs, 1H). ^{13}C NMR (101 MHz, CDCl_3) δ 136.2, 116.8, 72.6, 54.7, 44.7 ppm. GC-HRMS (EI) Found 100.0520 $[\text{M}]^+$, $\text{C}_5\text{H}_8\text{O}_2$ requires 100.0524.

XI. Synthesis of (3*R*,4*R*)-7-(2-methyl-1,3-dioxolan-2-yl)hept-1-ene-3,4-diol (26)

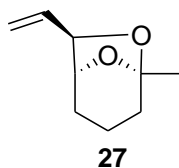
Compound **26** was synthesized similarly to the above mentioned compound **21**.



$[\alpha]_D^{20} = + 3.7$ ($c = 1.8$, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 6.00 – 5.71 (m, 1H), 5.42 – 5.16 (m, 2H), 4.07 – 3.75 (m, 5H), 3.68 – 3.31 (bs, 1H), 1.87 – 1.38 (m, 6H), 1.36 – 1.27 (m, 4H), 1.32 – 1.30 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 137.6, 117.4, 110.0, 76.1, 74.2, 64.6, 38.9, 32.9, 23.8, 23.7, 20.1 ppm. HRMS (ESI) Found 215.1282 $[\text{M}-\text{H}]^+$, $\text{C}_{11}\text{H}_{19}\text{O}_4$ requires 215.1282.

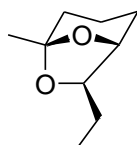
XII. (1*R*,5*S*,7*R*)-5-methyl-7-vinyl-6,8-dioxabicyclo[3.2.1]octane (27)

The entitled compound synthesized similar to compound **22**.



$[\alpha]_D^{20} = + 65.0$ ($c = 1.0$, Et_2O), $[\text{lit}^7 [\alpha]_D^{20} = + 87.2$ ($c = 2.09$, Et_2O)]; ^1H NMR (400 MHz, CDCl_3) δ 5.87 (ddd, $J = 17.0, 10.2, 6.8$ Hz, 1H), 5.34 – 5.01 (m, 2H), 4.43 (d, $J = 6.8$ Hz, 1H), 4.20 (s, 1H), 2.00 – 1.74 (m, 1H), 1.72 – 1.50 (m, 5H), 1.48 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 138.6, 115.6, 108.4, 80.7, 79.7, 34.9, 27.8, 24.9, 17.1 ppm. GC-HRMS (EI) Found 154.1001 $[\text{M}]^+$, $\text{C}_9\text{H}_{14}\text{O}_2$ requires 154.0994.

XIII. Synthesis of (+)-*exo*-brevicomine



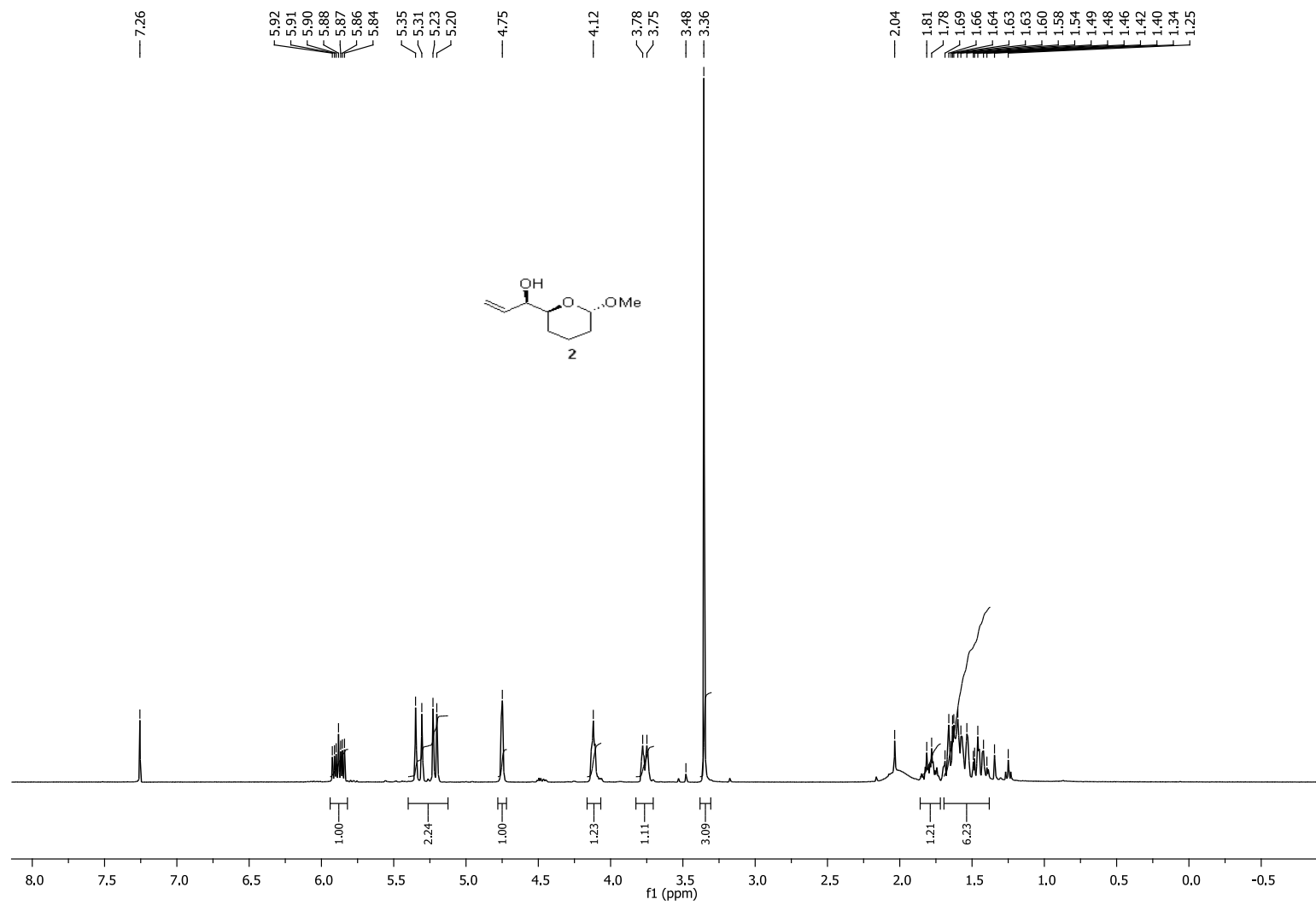
19; (+)-*exo*-brevicomine

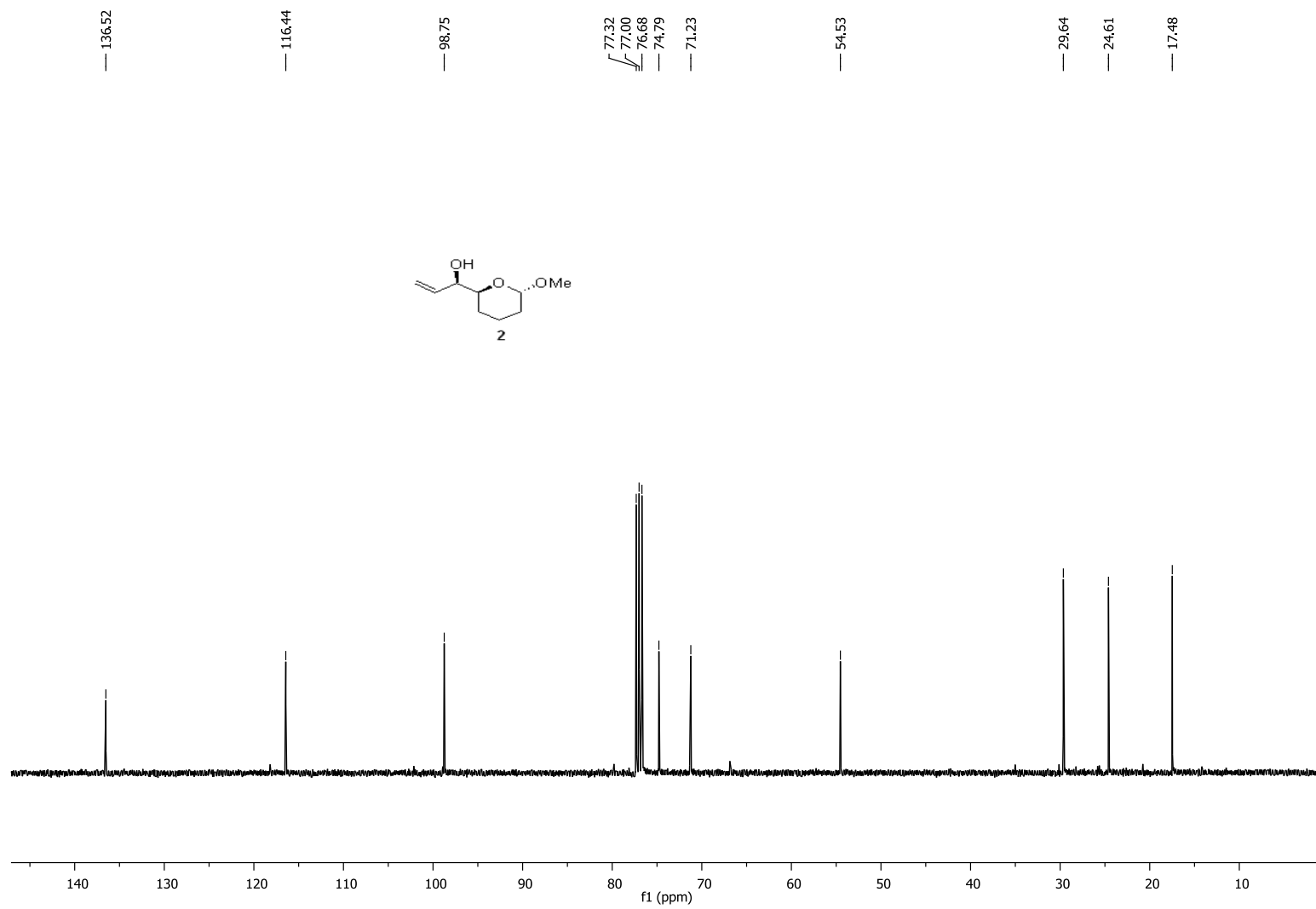
The hydrogenation of compound **27** was carried out according to above stated procedure for the synthesis of (+)-*endo*-brevicomine. $[\alpha]_D^{20} = + 76.3$ ($c = 1.35$, ether, 99.3% ee), $[\text{lit}^8 [\alpha]_D^{20} = + 84.2$ ($c = 2.2$, Et_2O), $\text{lit}^7 [\alpha]_D^{20} = + 67.9$ ($c = 1.41$, Et_2O), $\text{lit}^9 [\alpha]_D^{20} = + 64.8$ ($c = 1.25$, CHCl_3)]; ^1H NMR (400 MHz, CDCl_3) δ 4.12 (s, 1H), 3.92 (t, $J = 6.5$, 1H), 1.96 – 1.72 (m, 1H), 1.68 – 1.43 (m, 6H), 1.41 (s, 3H), 0.90 (t, $J = 7.4$, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 107.7, 81.1, 78.3, 34.9, 28.5, 27.9, 25.0, 17.2, 9.8 ppm. GC-HRMS (EI) Found 156.1150 $[\text{M}]^+$, $\text{C}_9\text{H}_{16}\text{O}_2$ requires 156.1156.

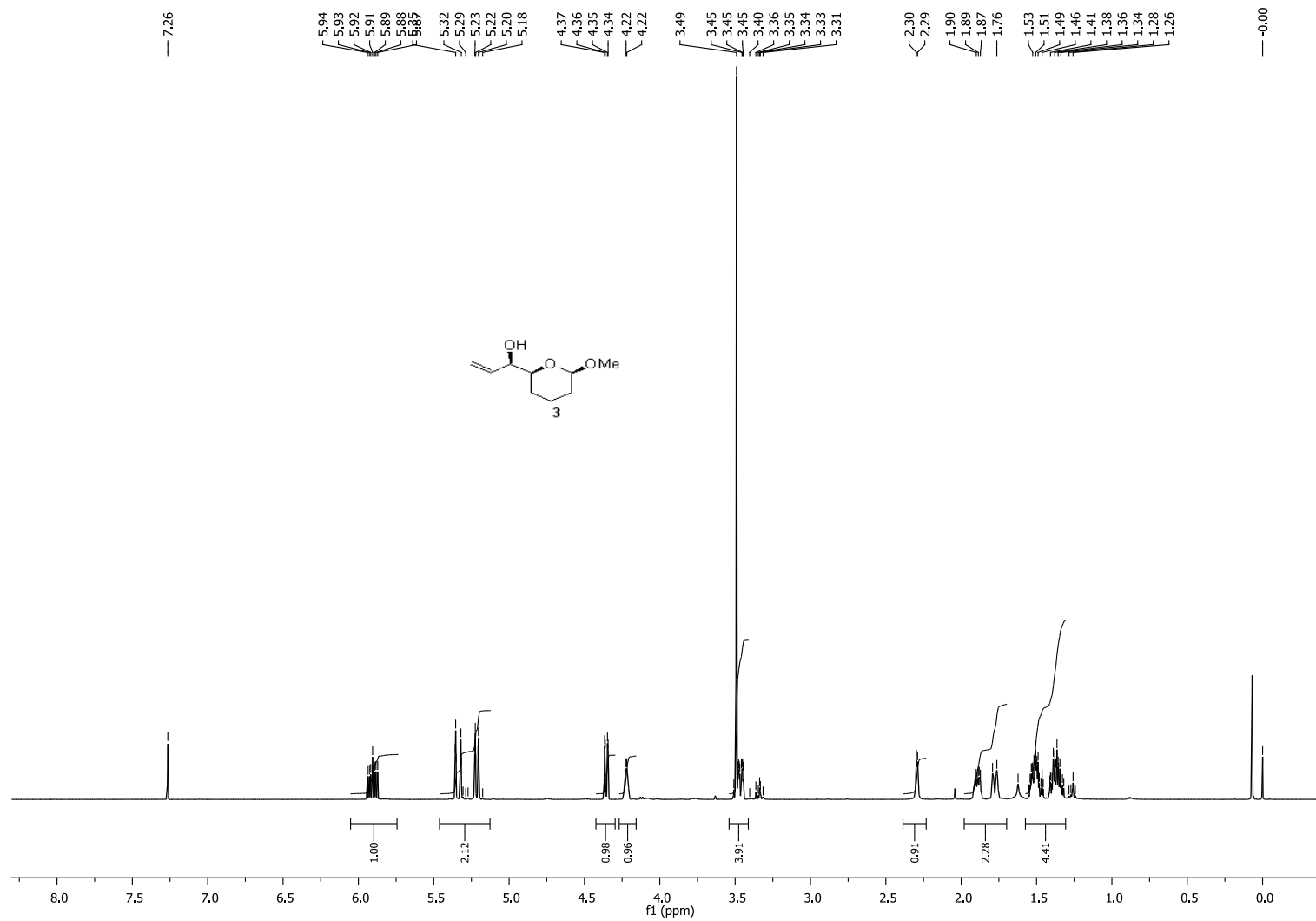
XIV. References

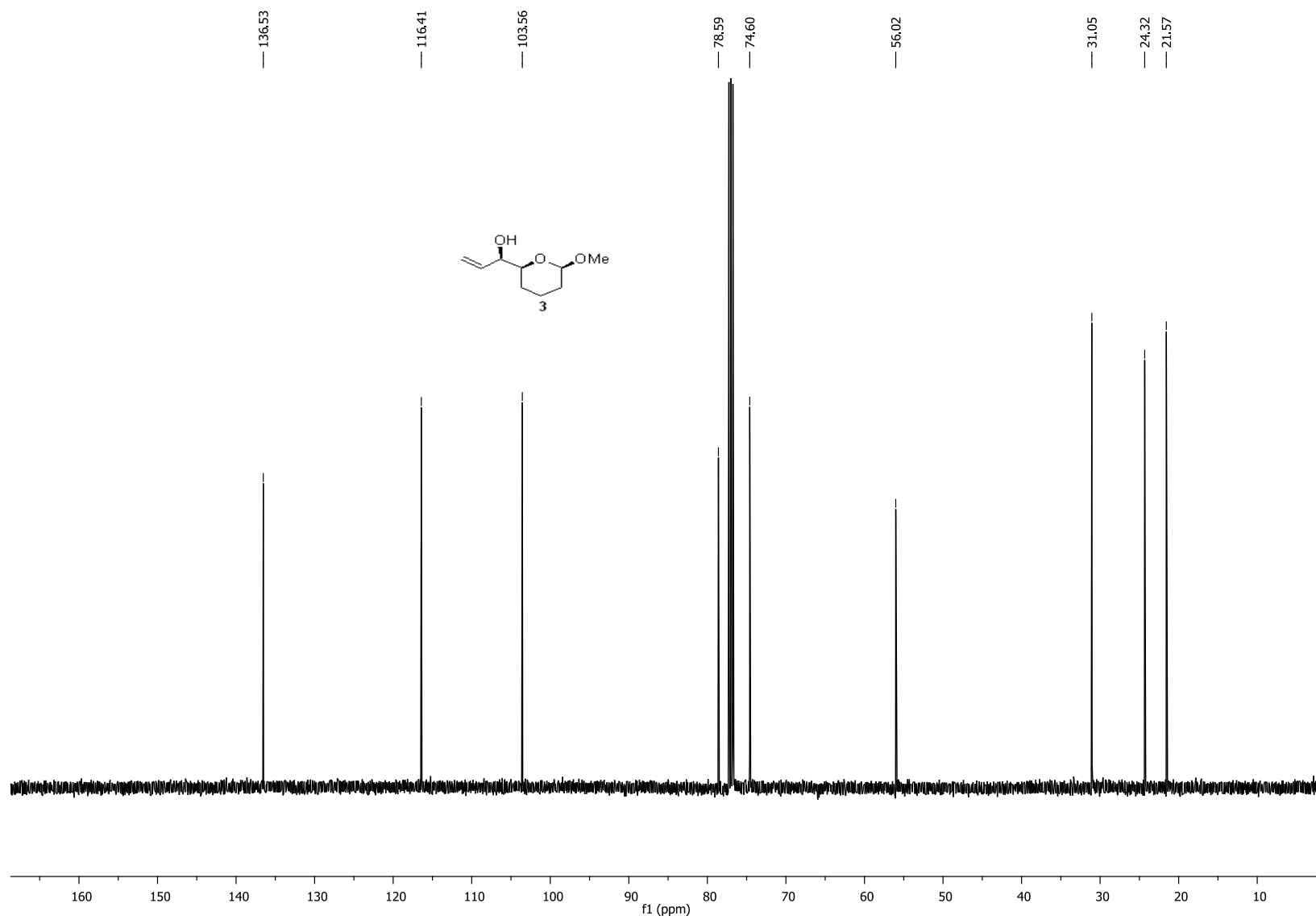
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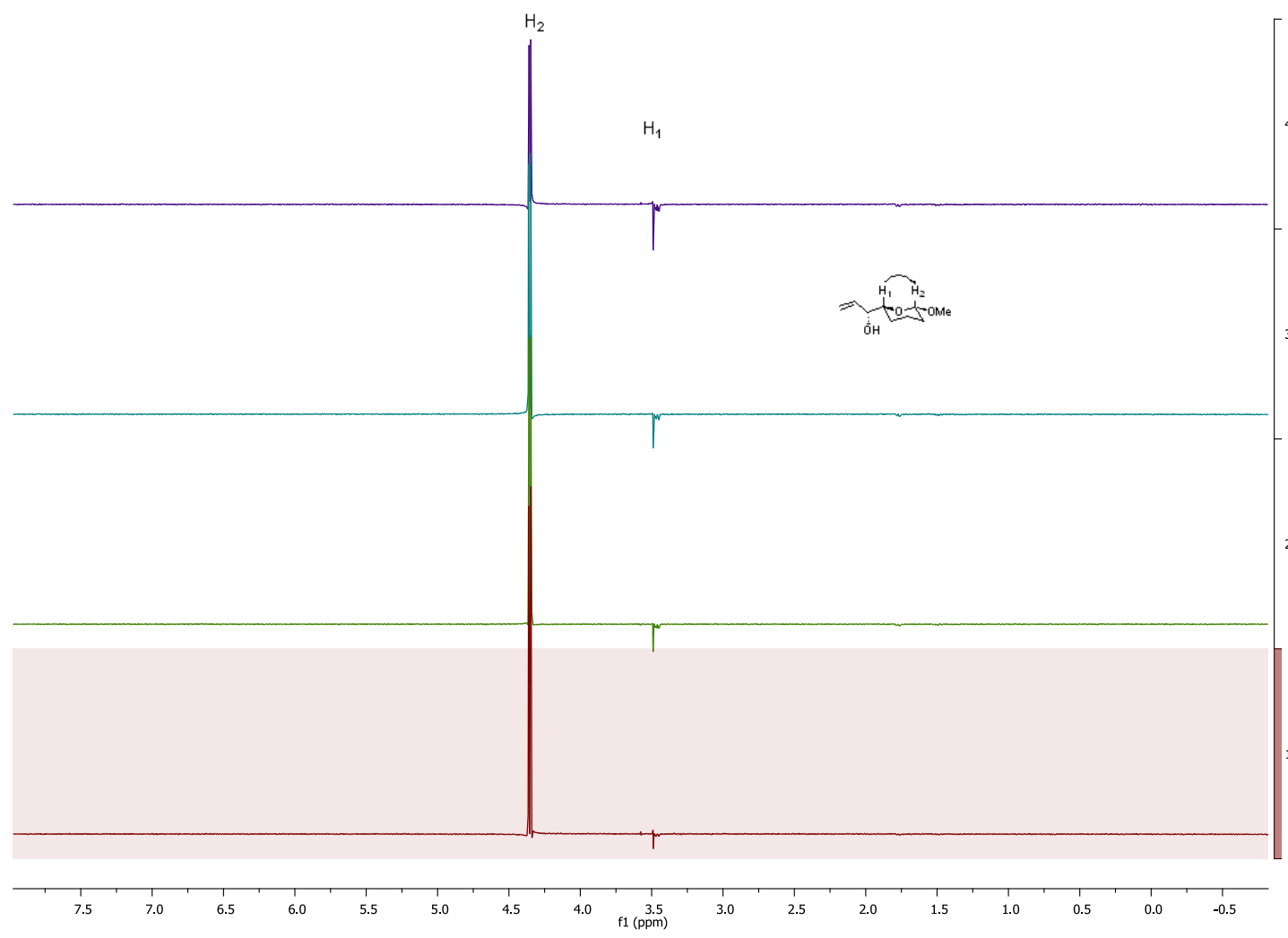


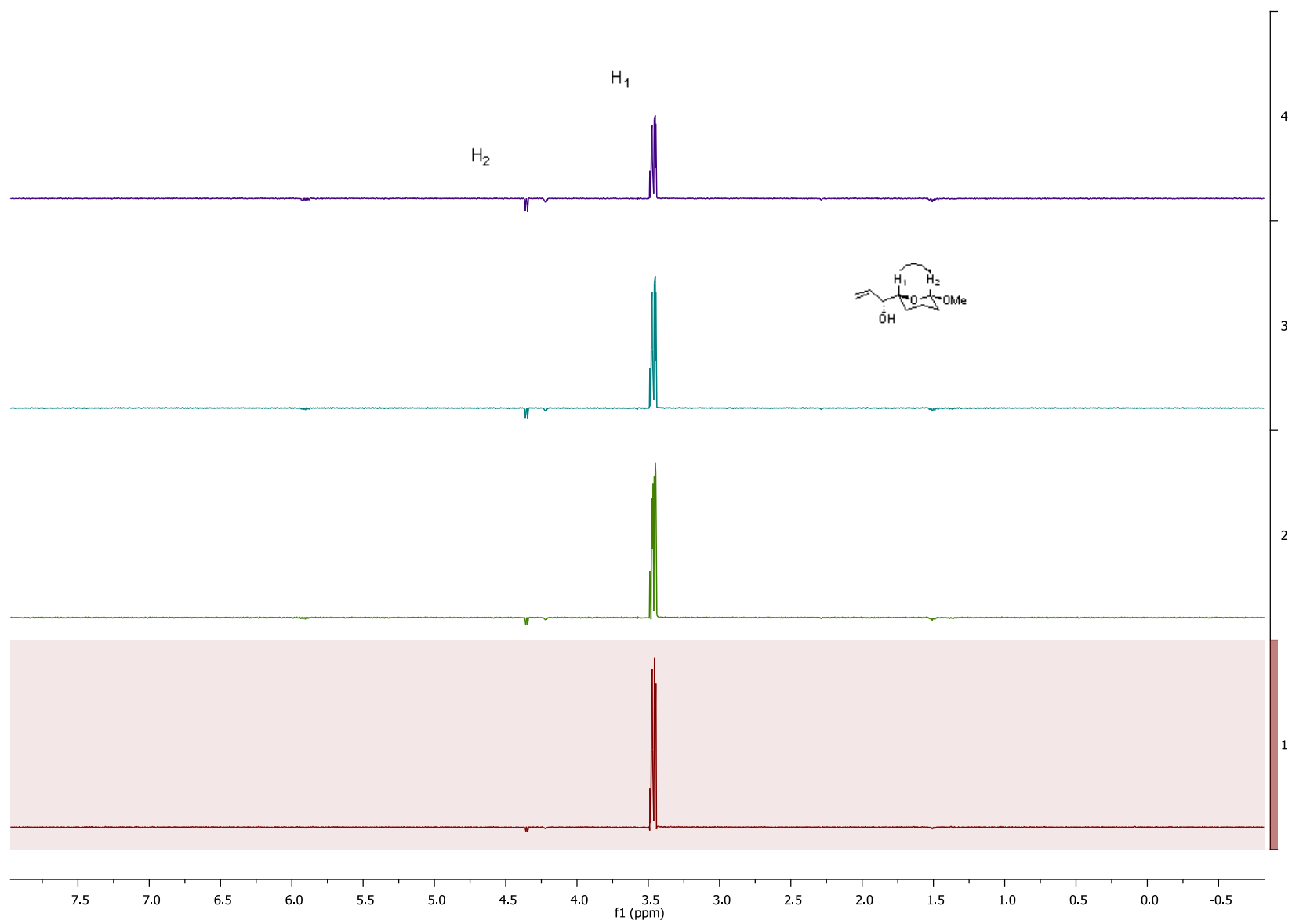


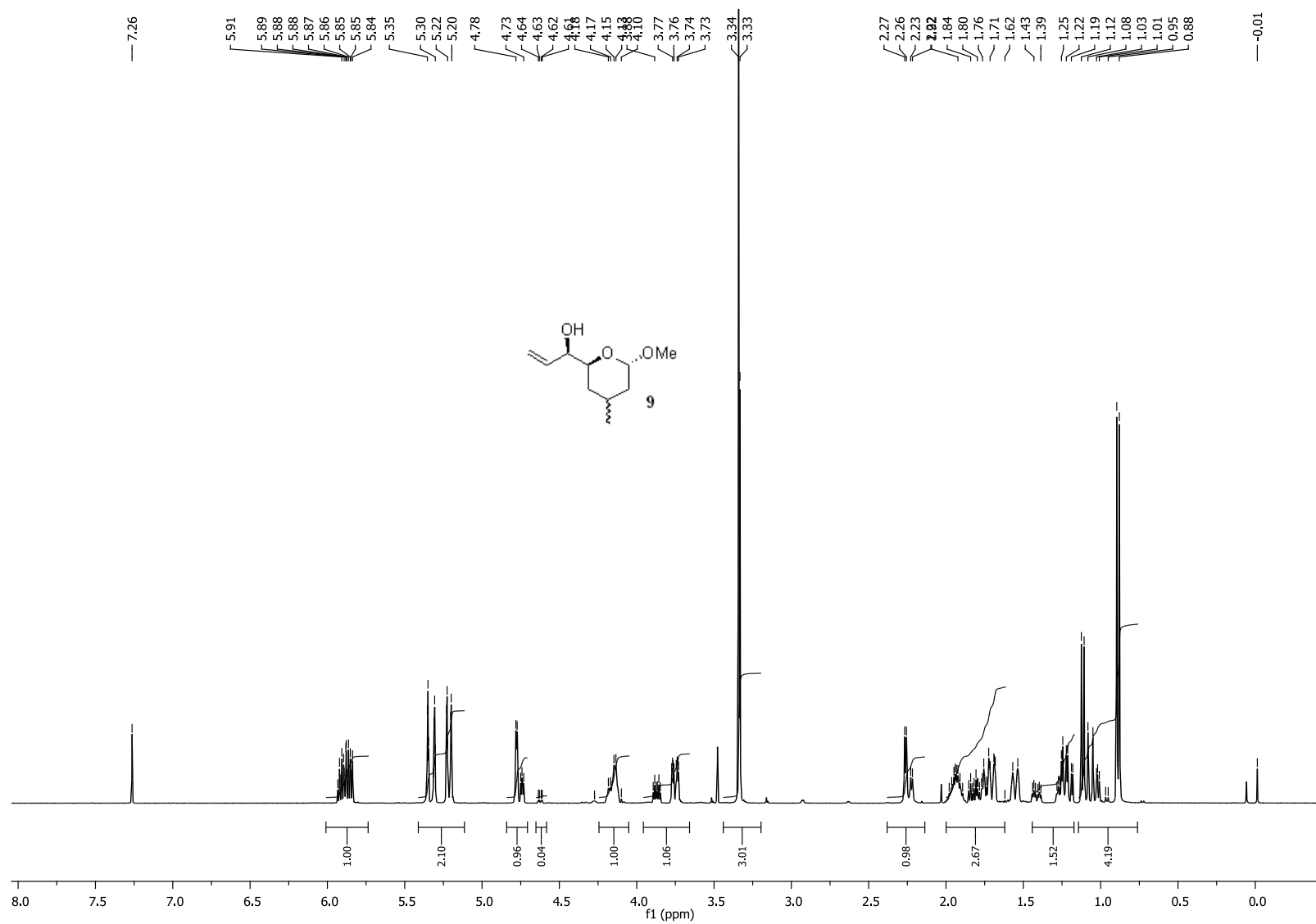


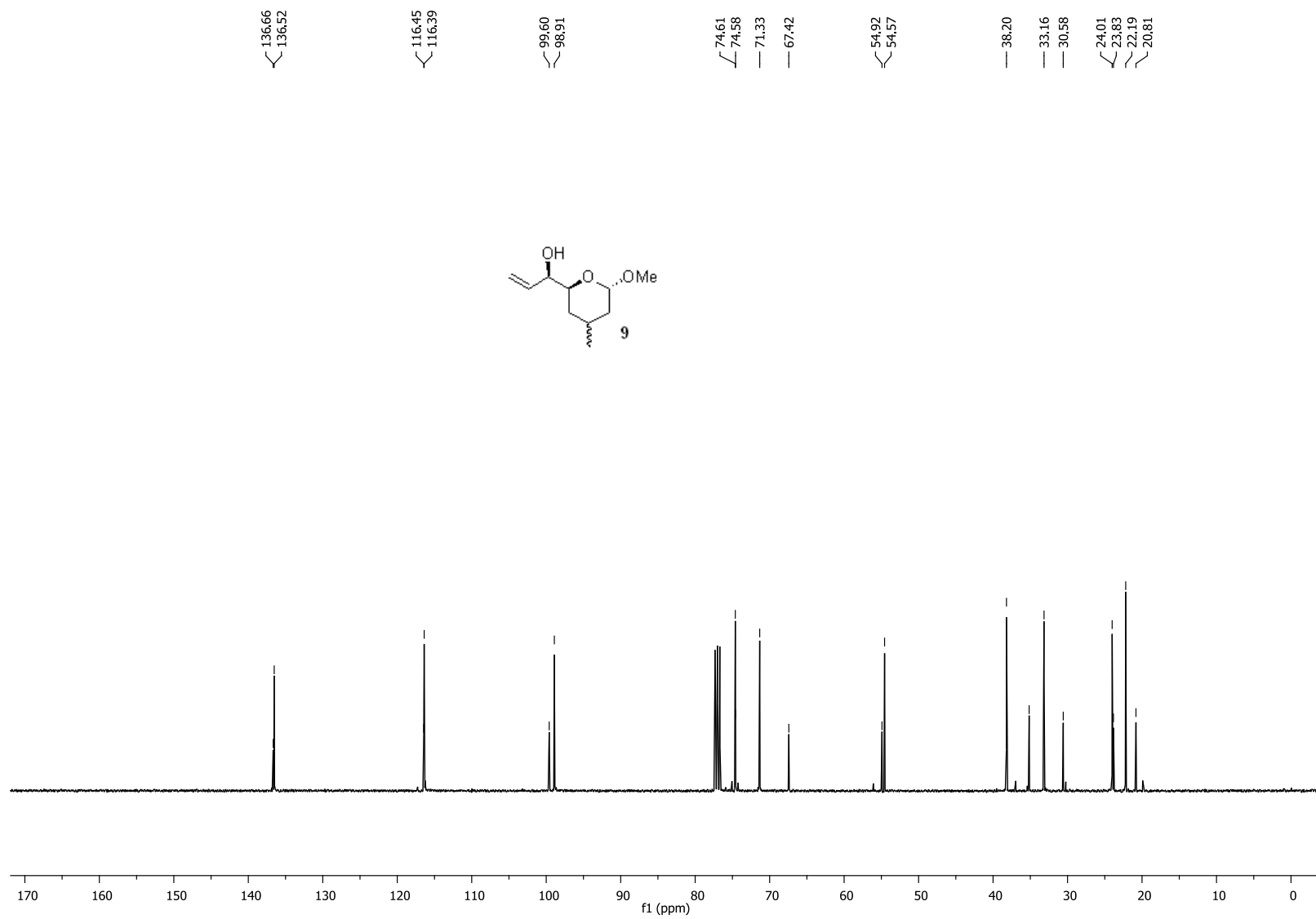


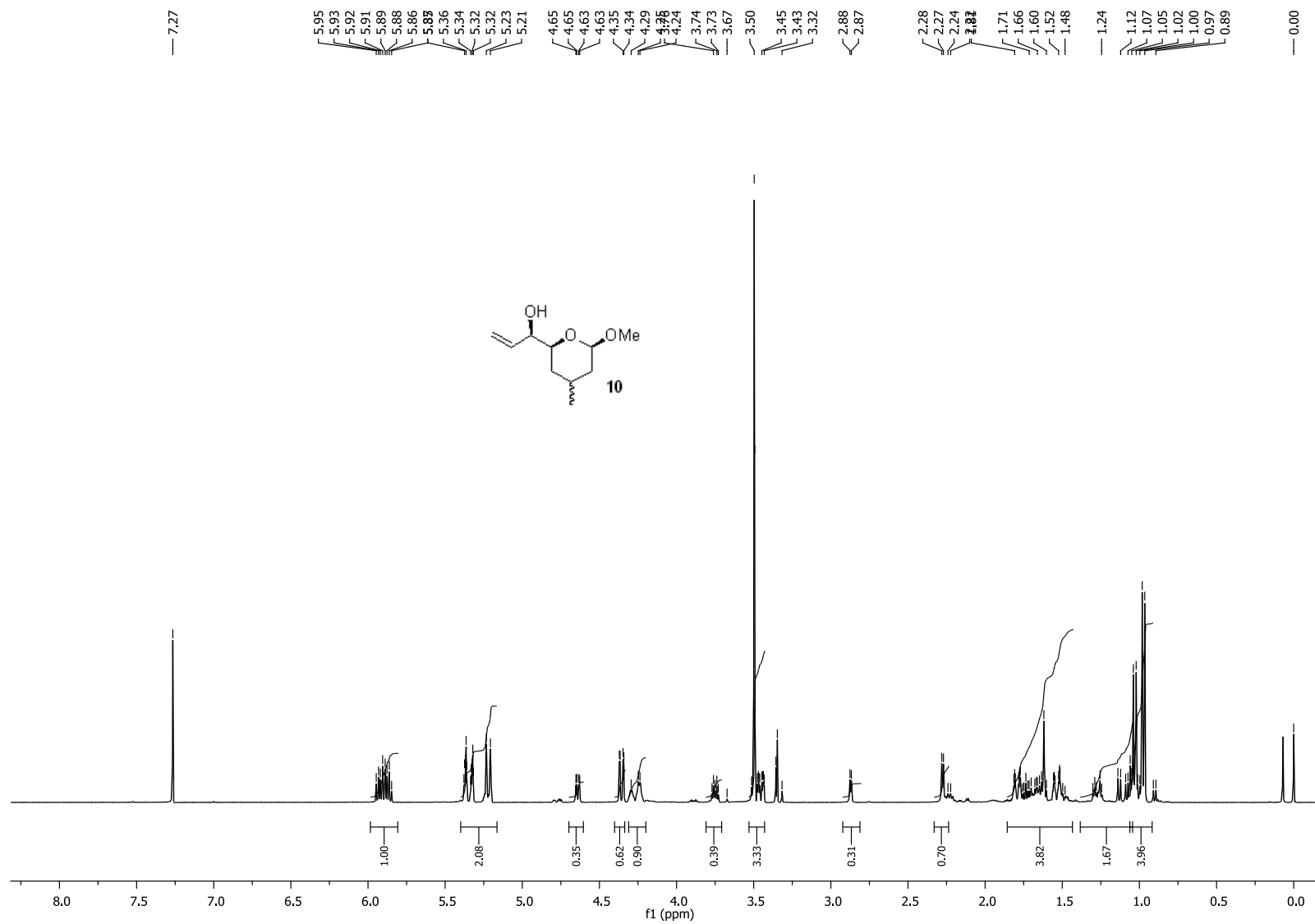
1D NOESY Experiments for the compound **3**

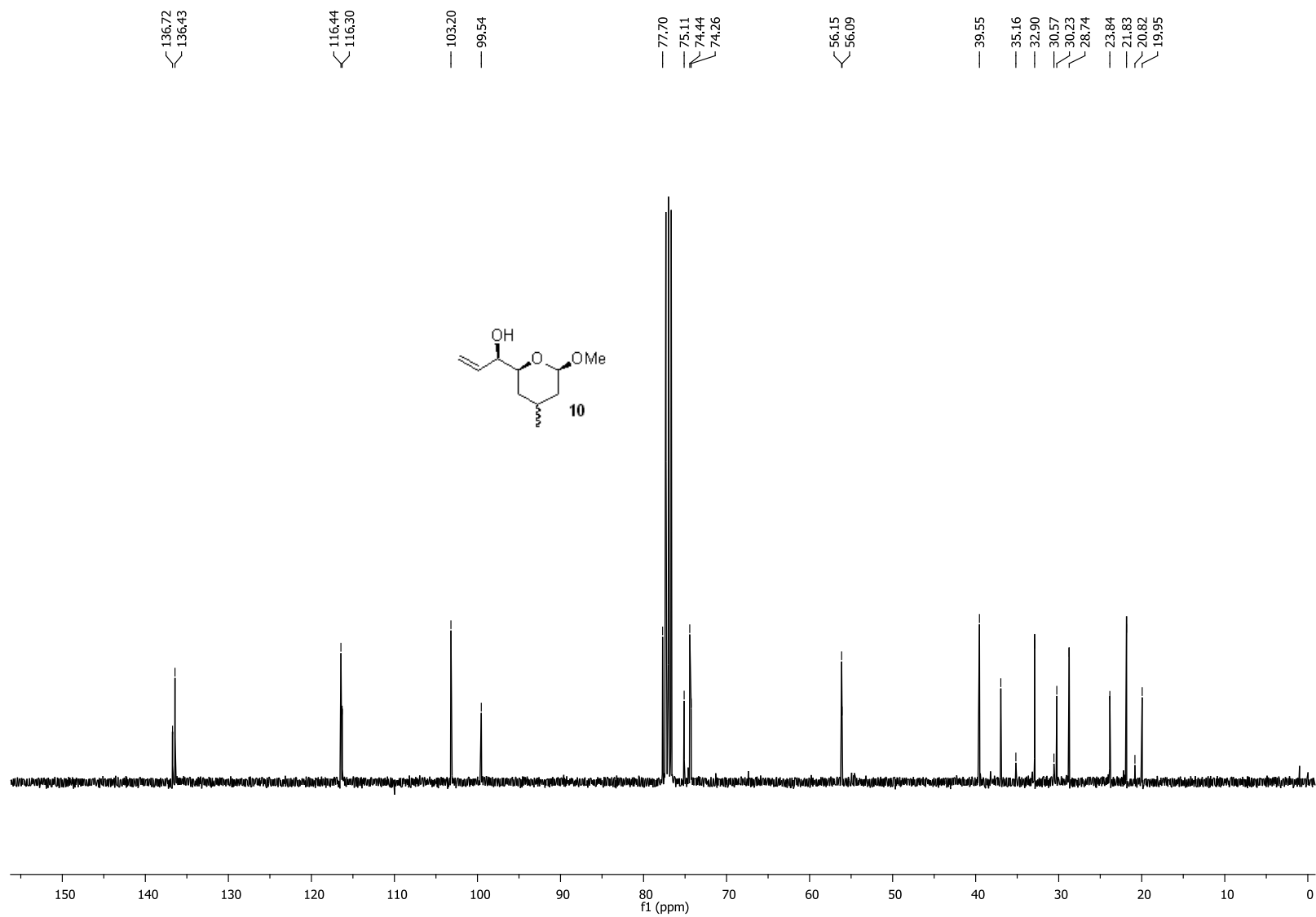


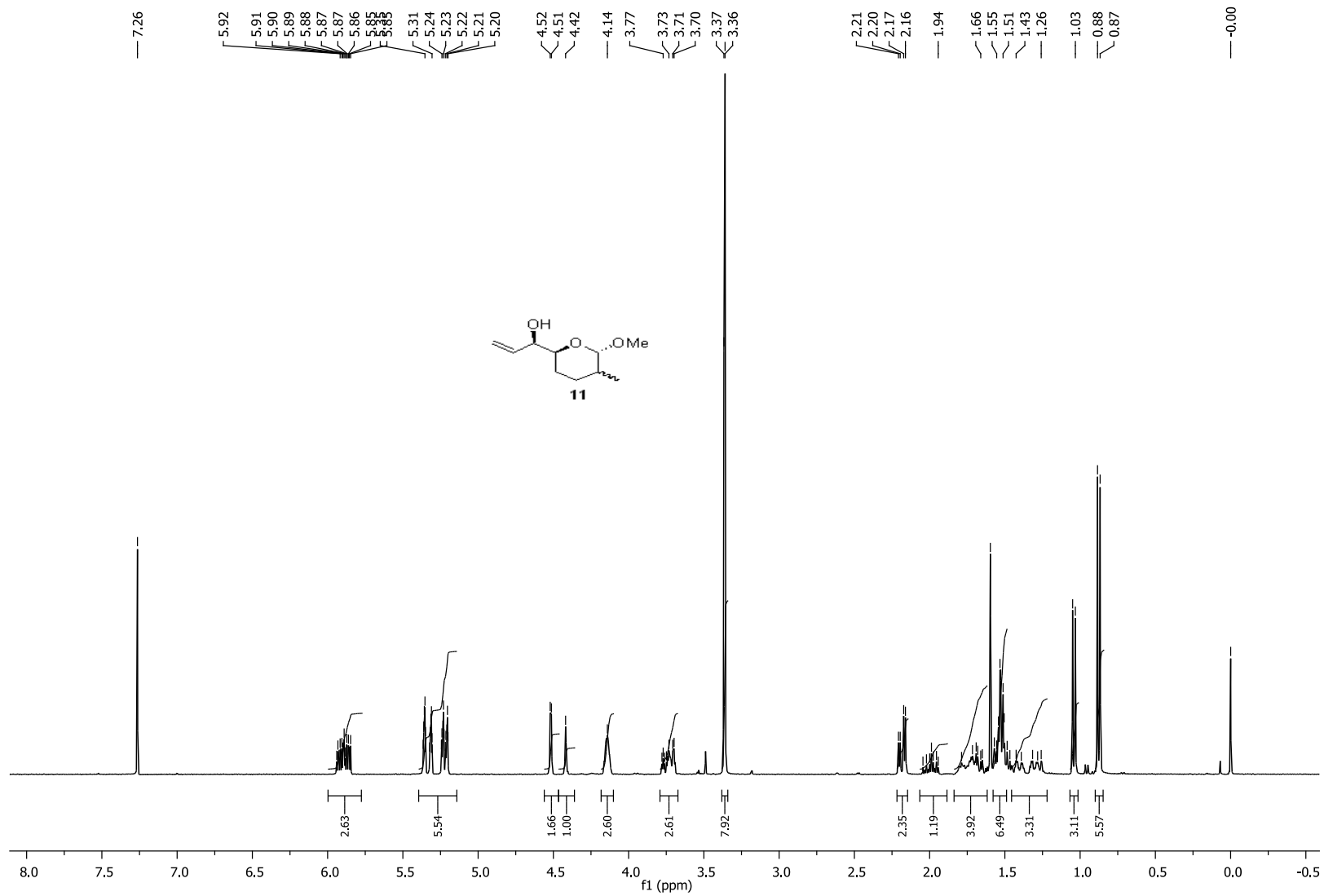


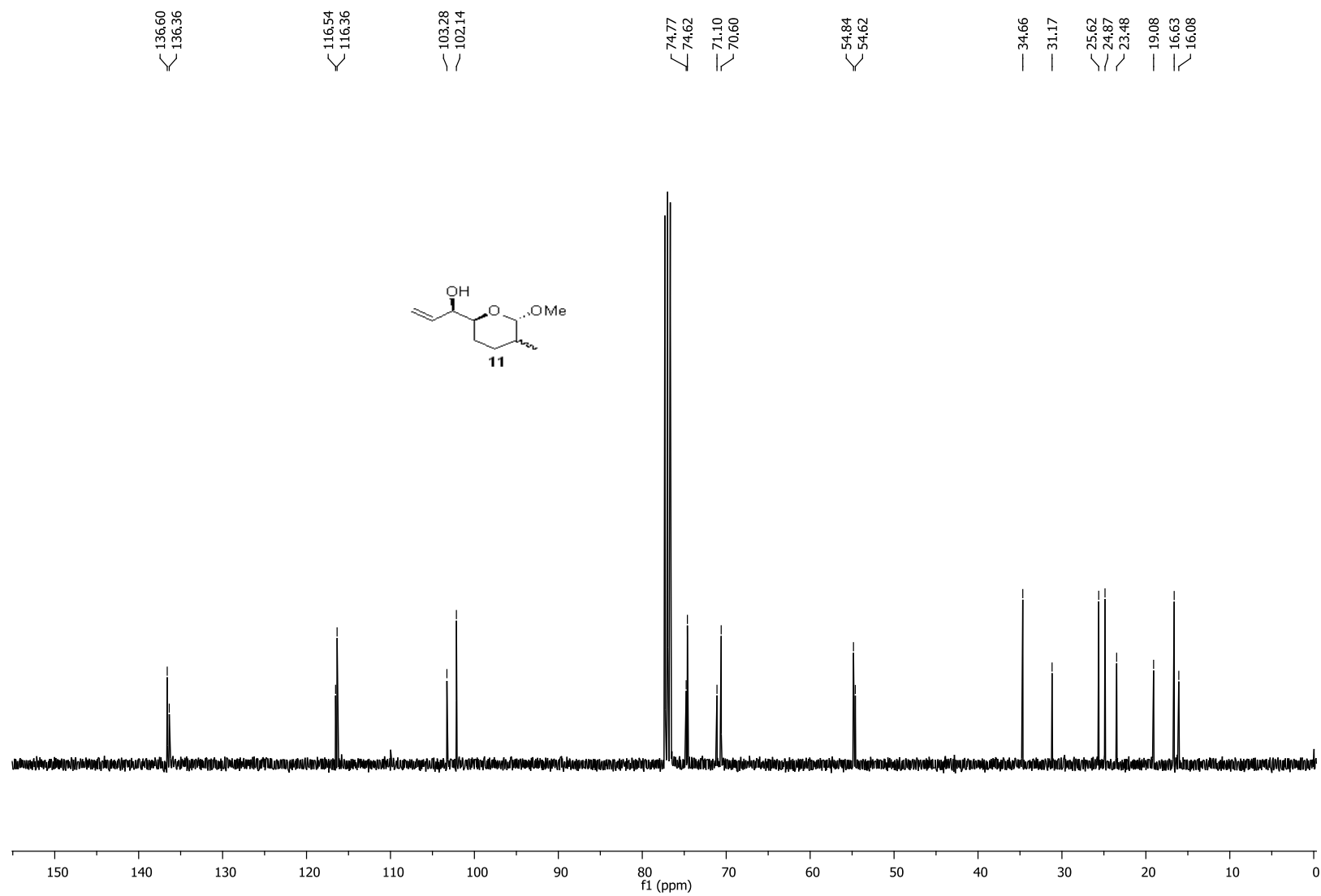


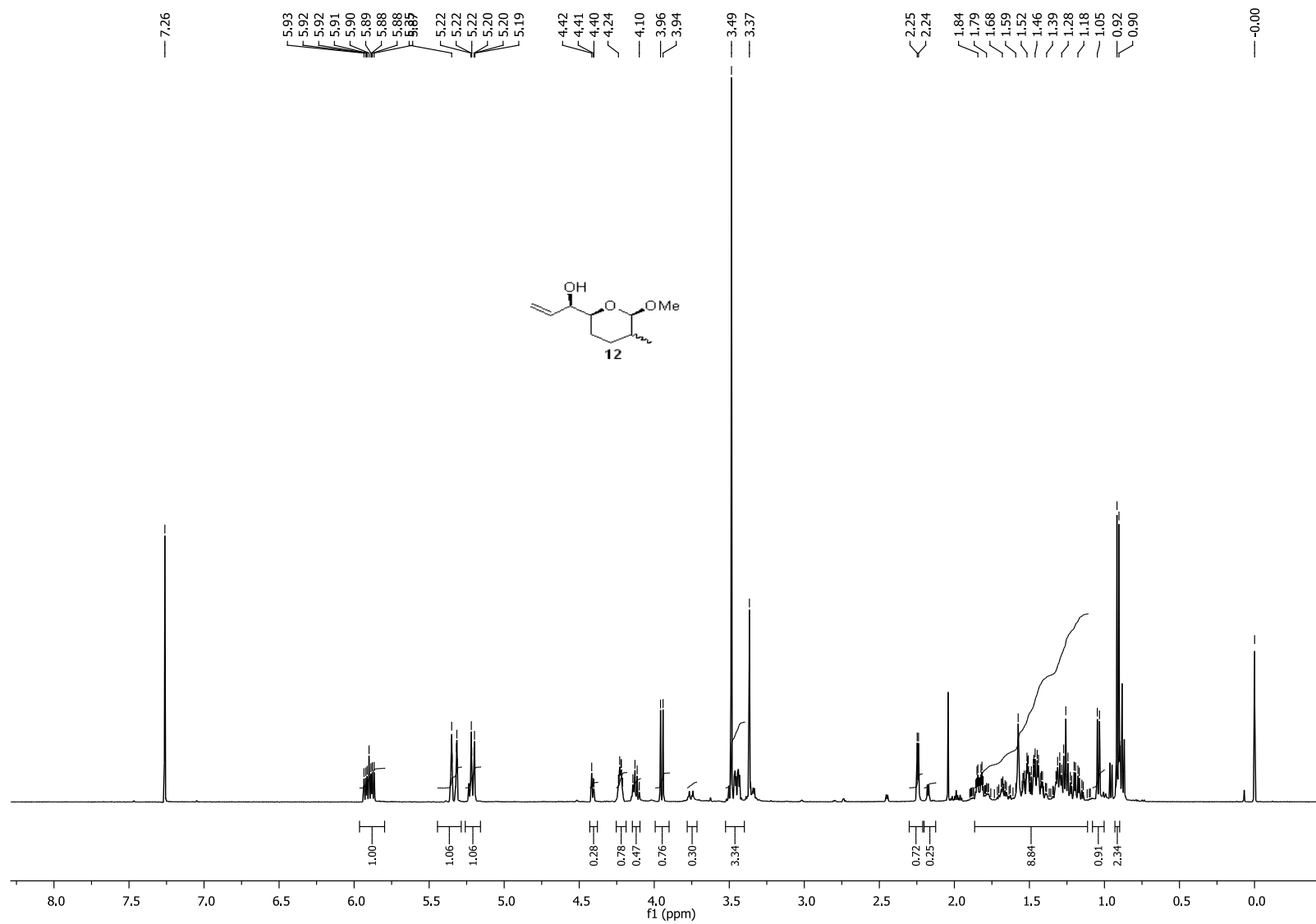


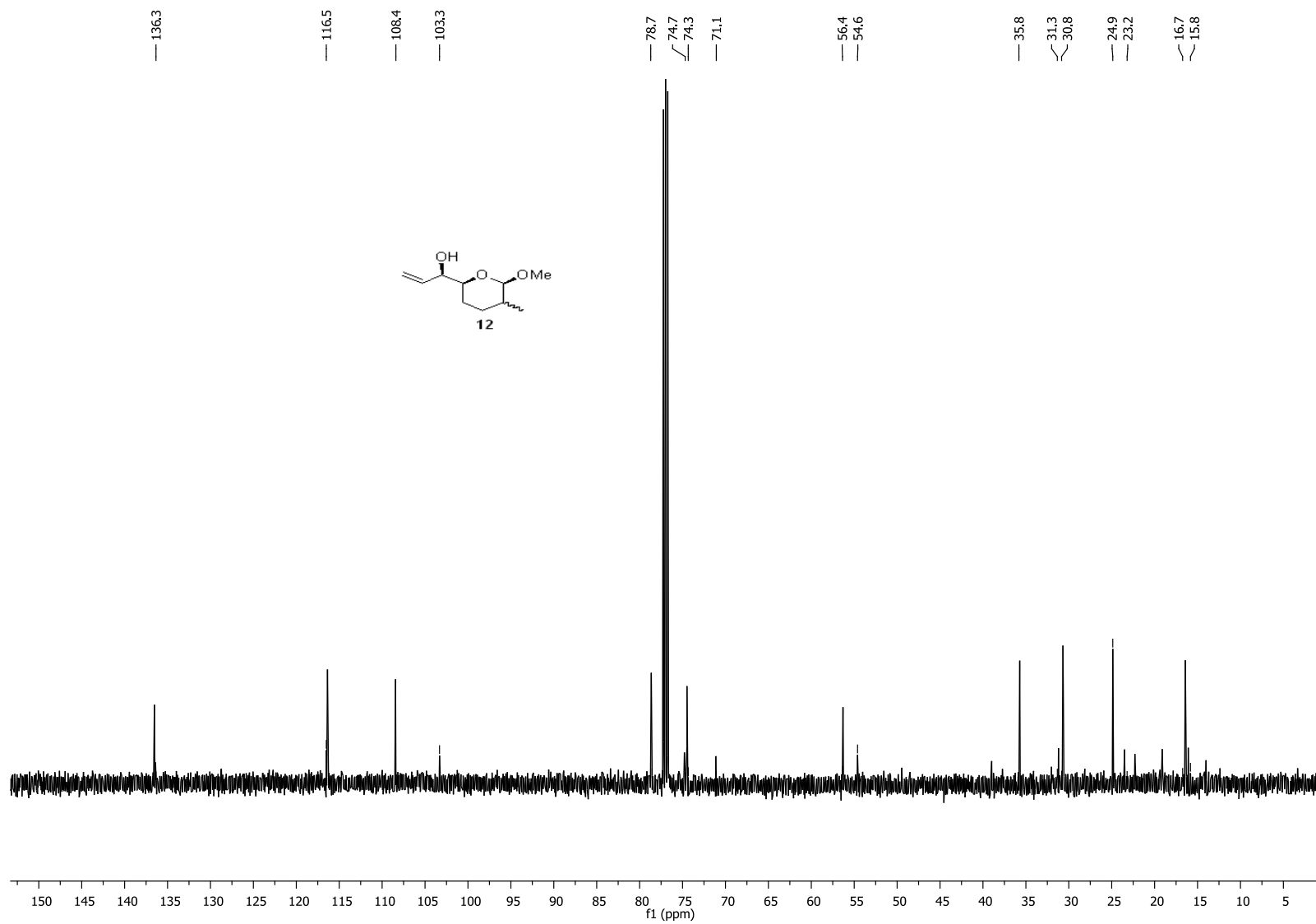


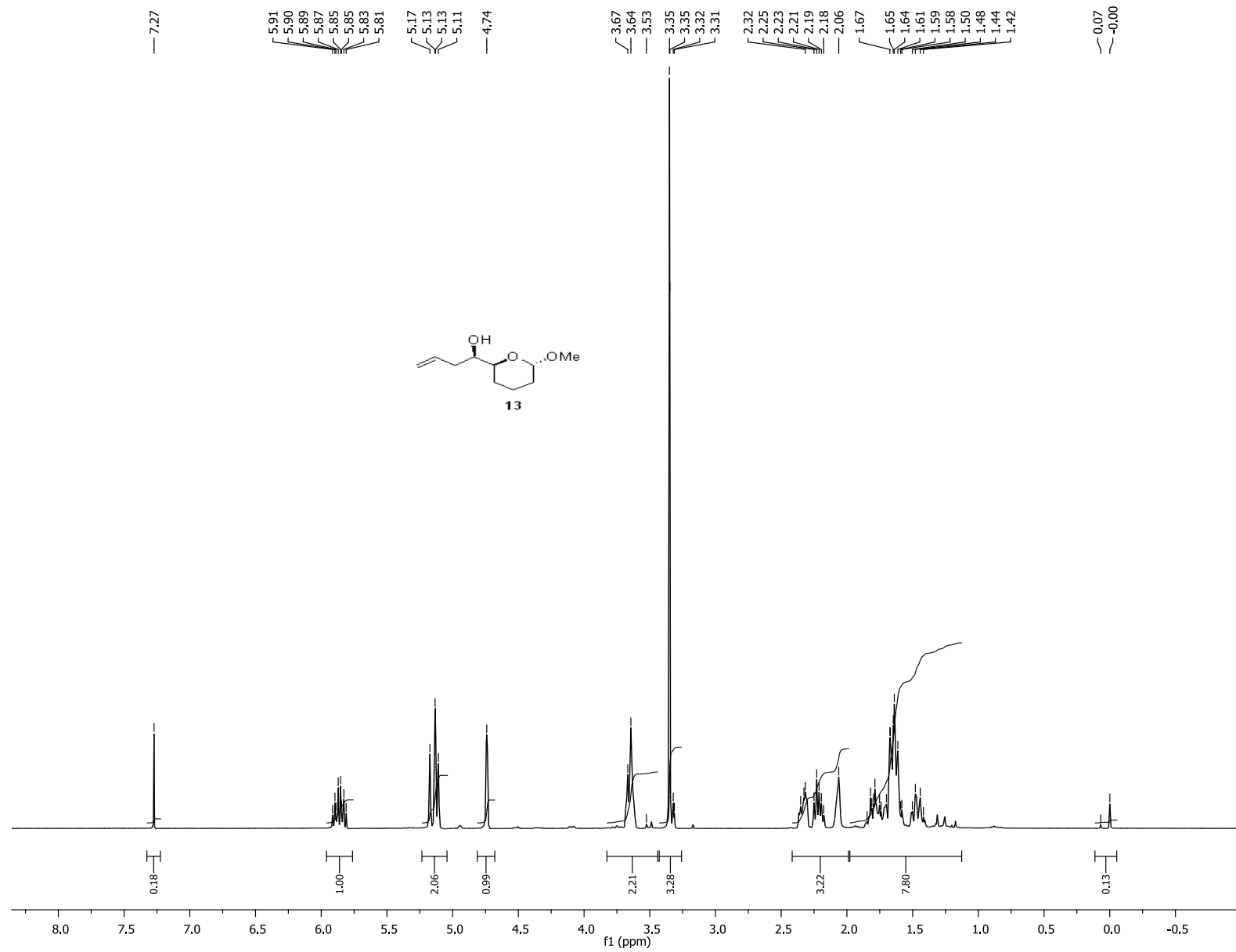


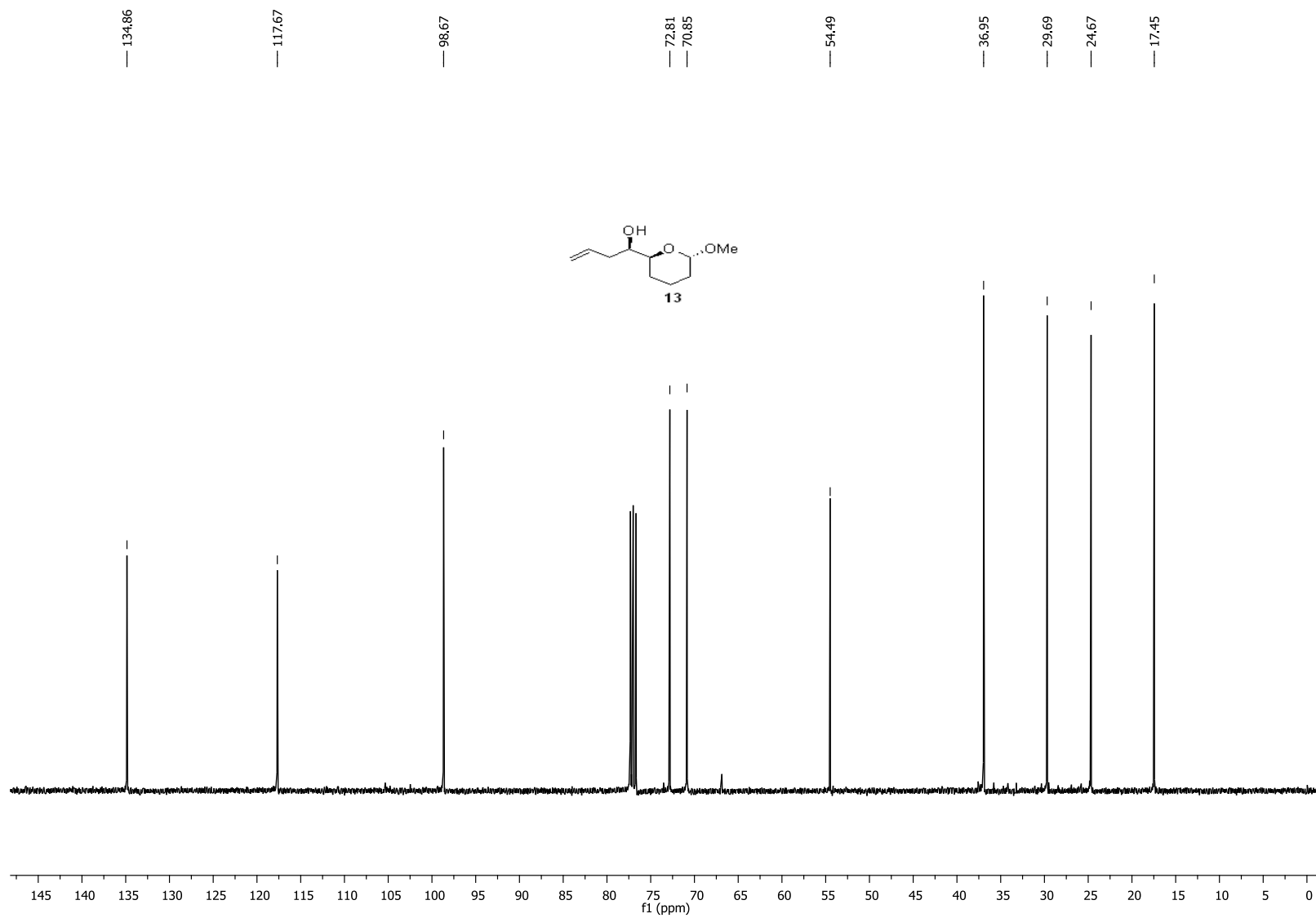


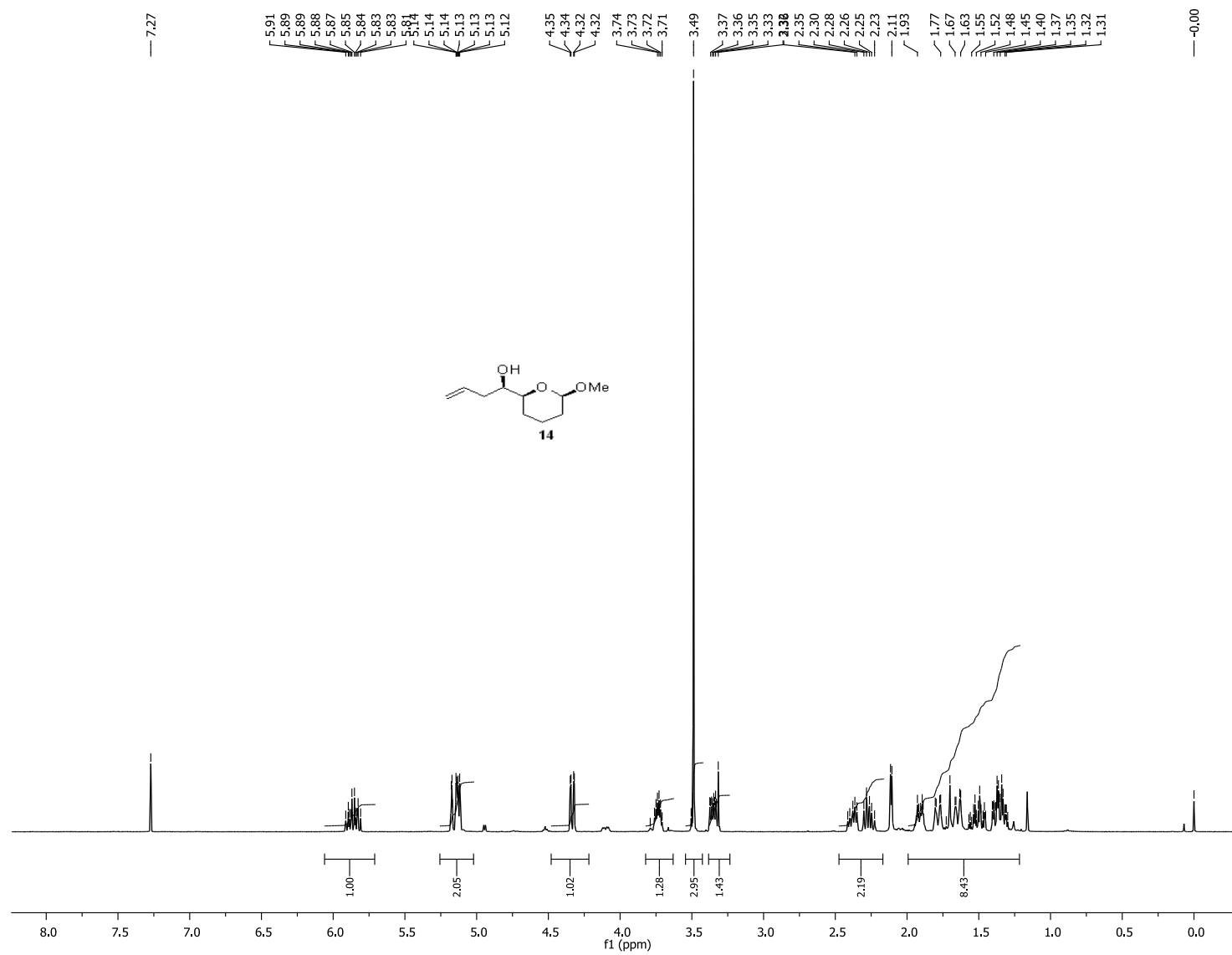


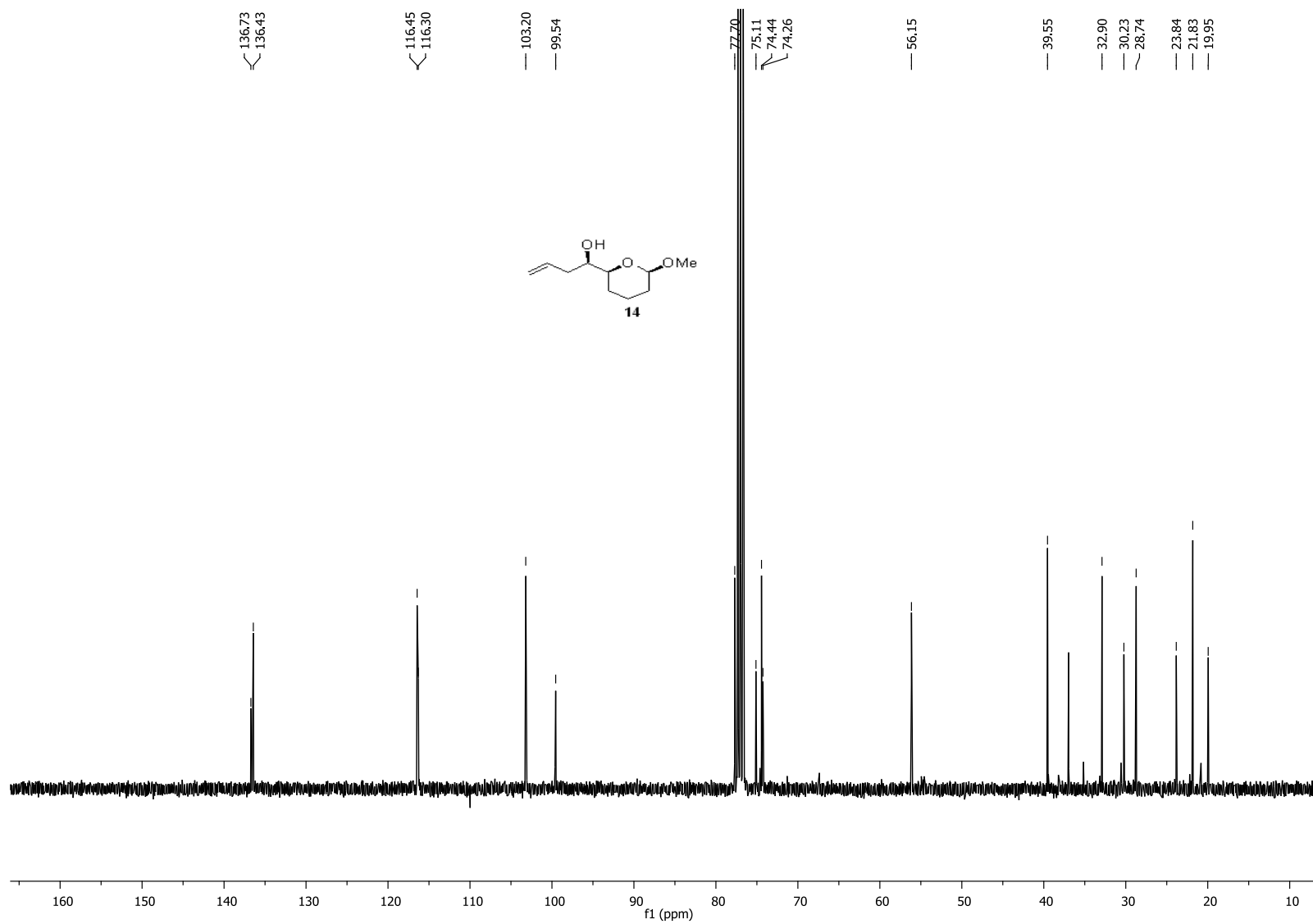


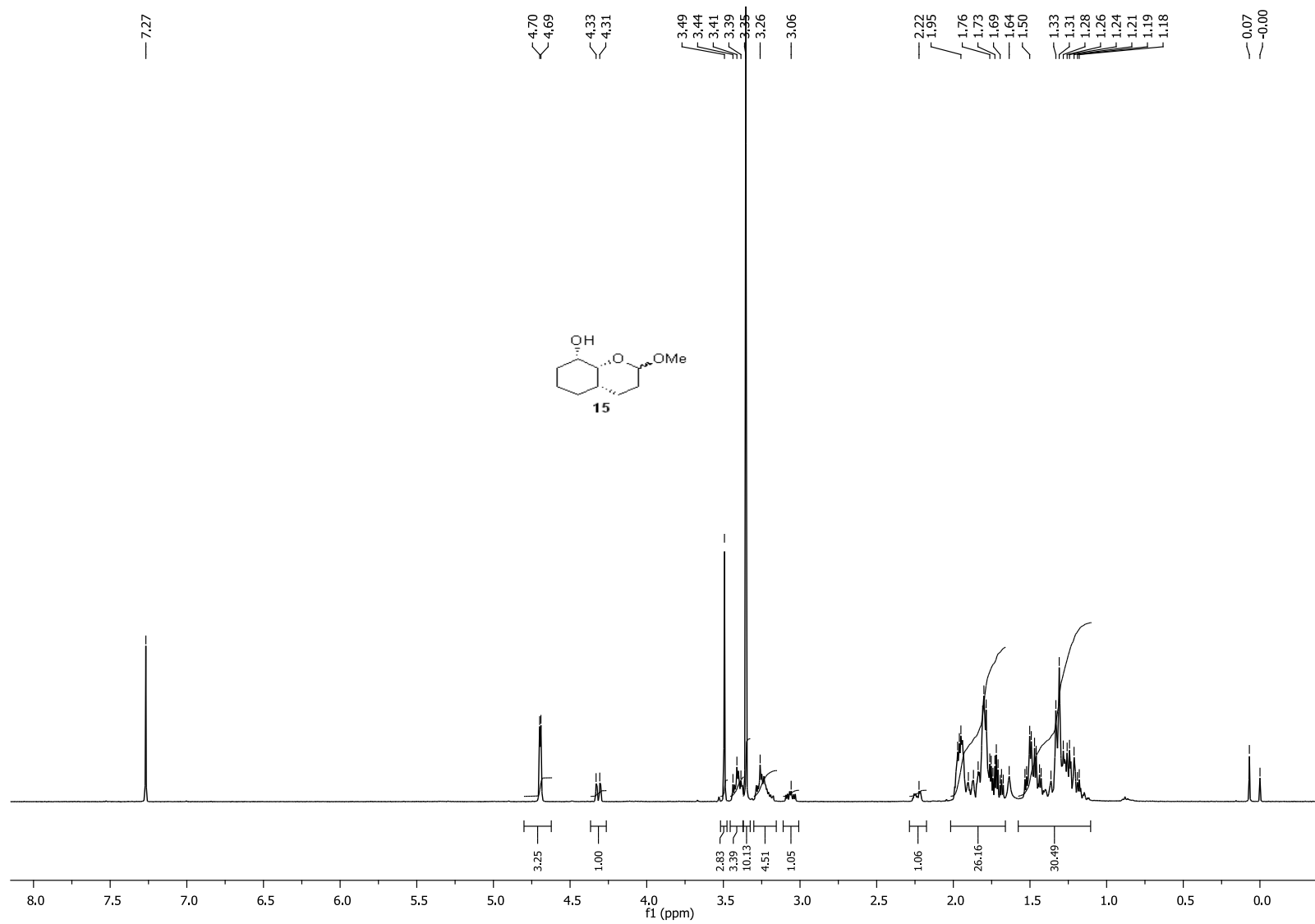


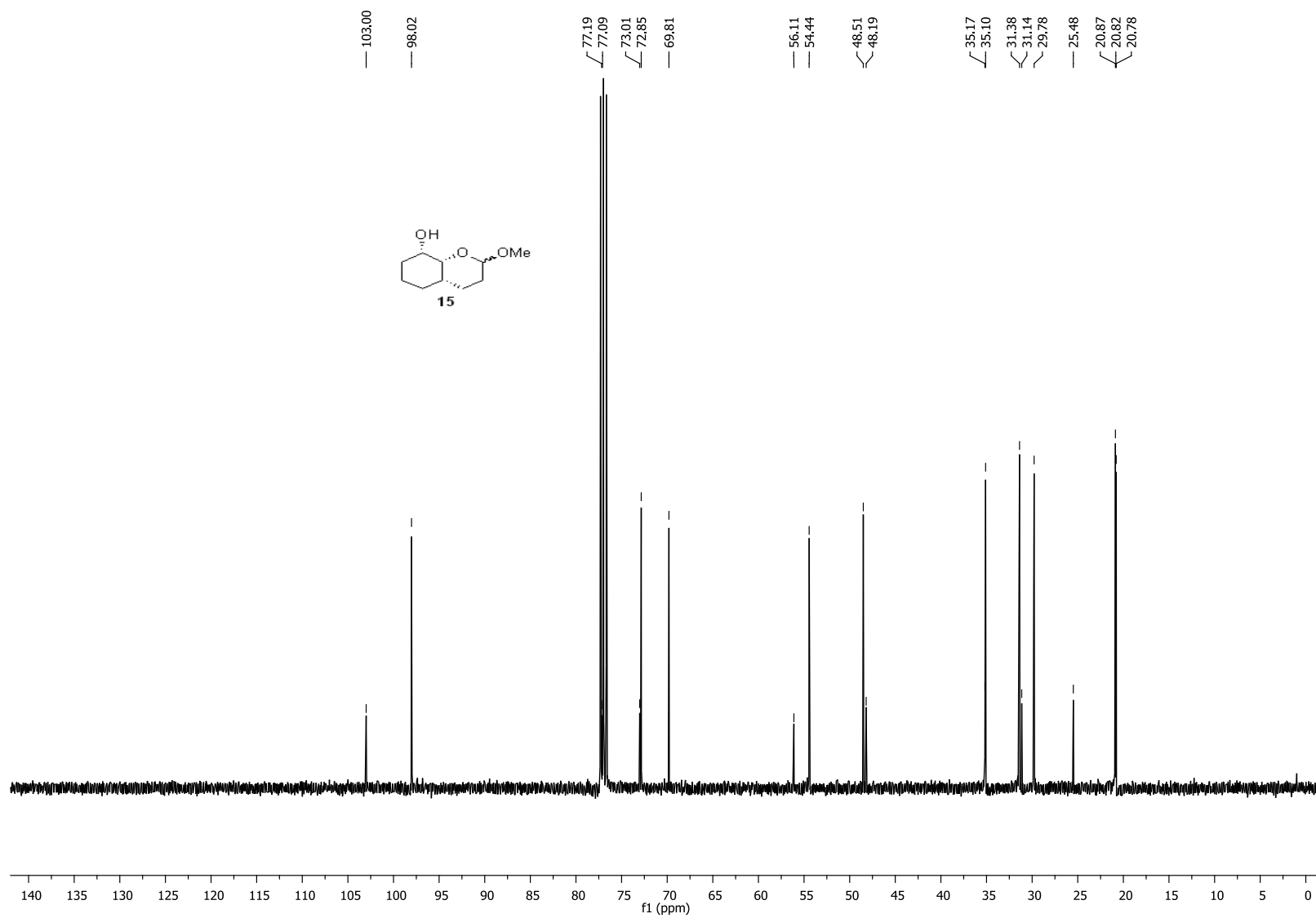


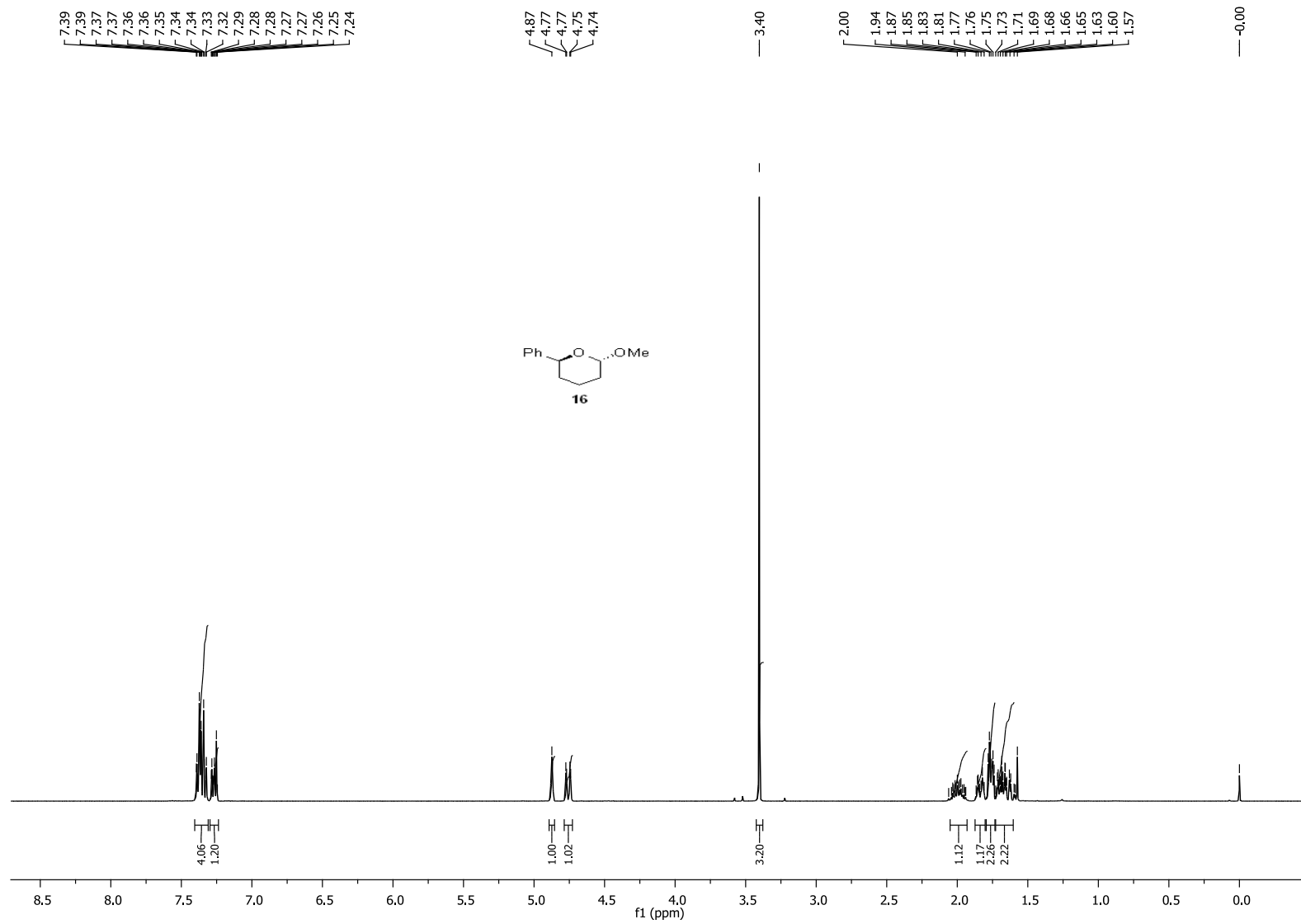


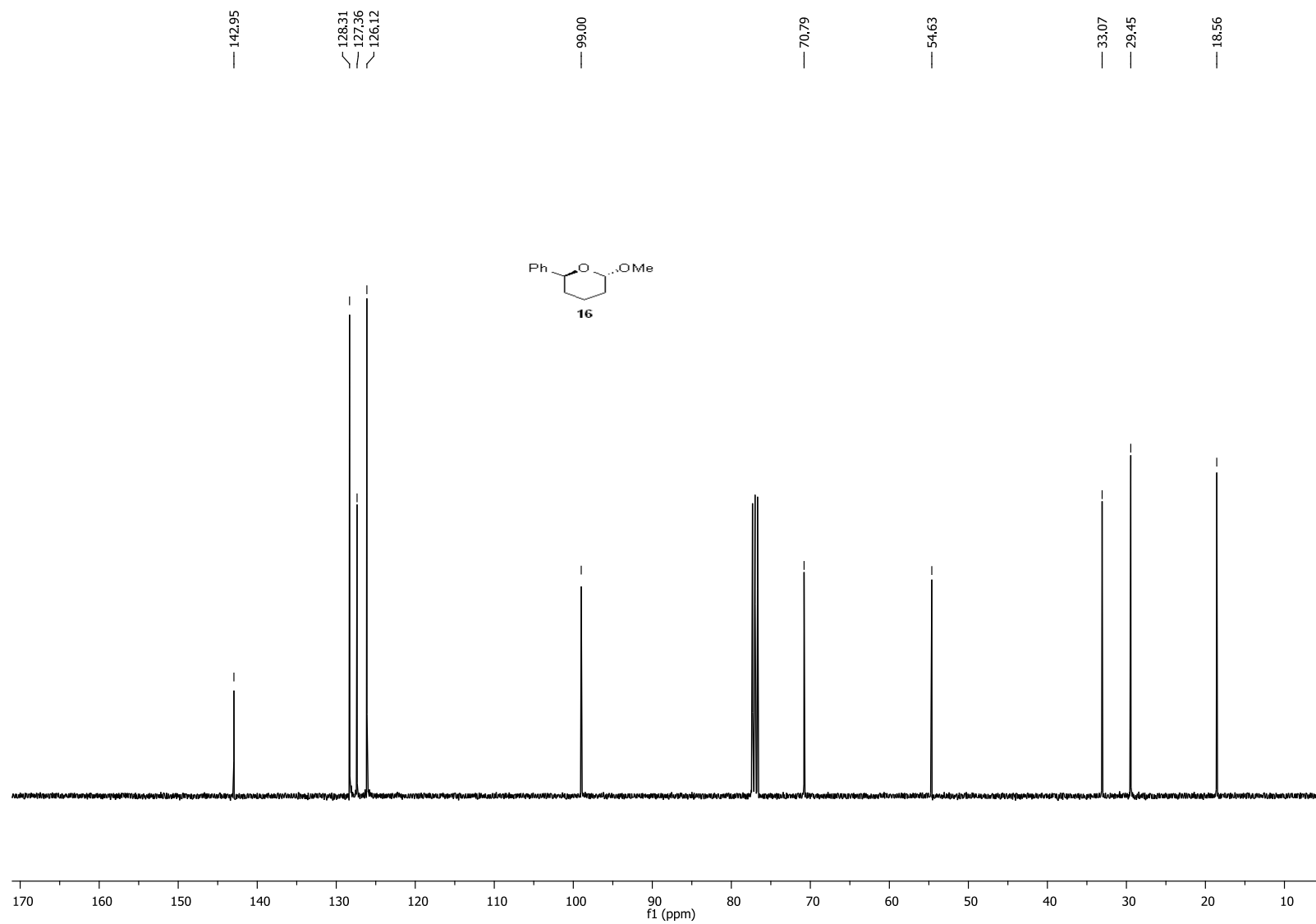


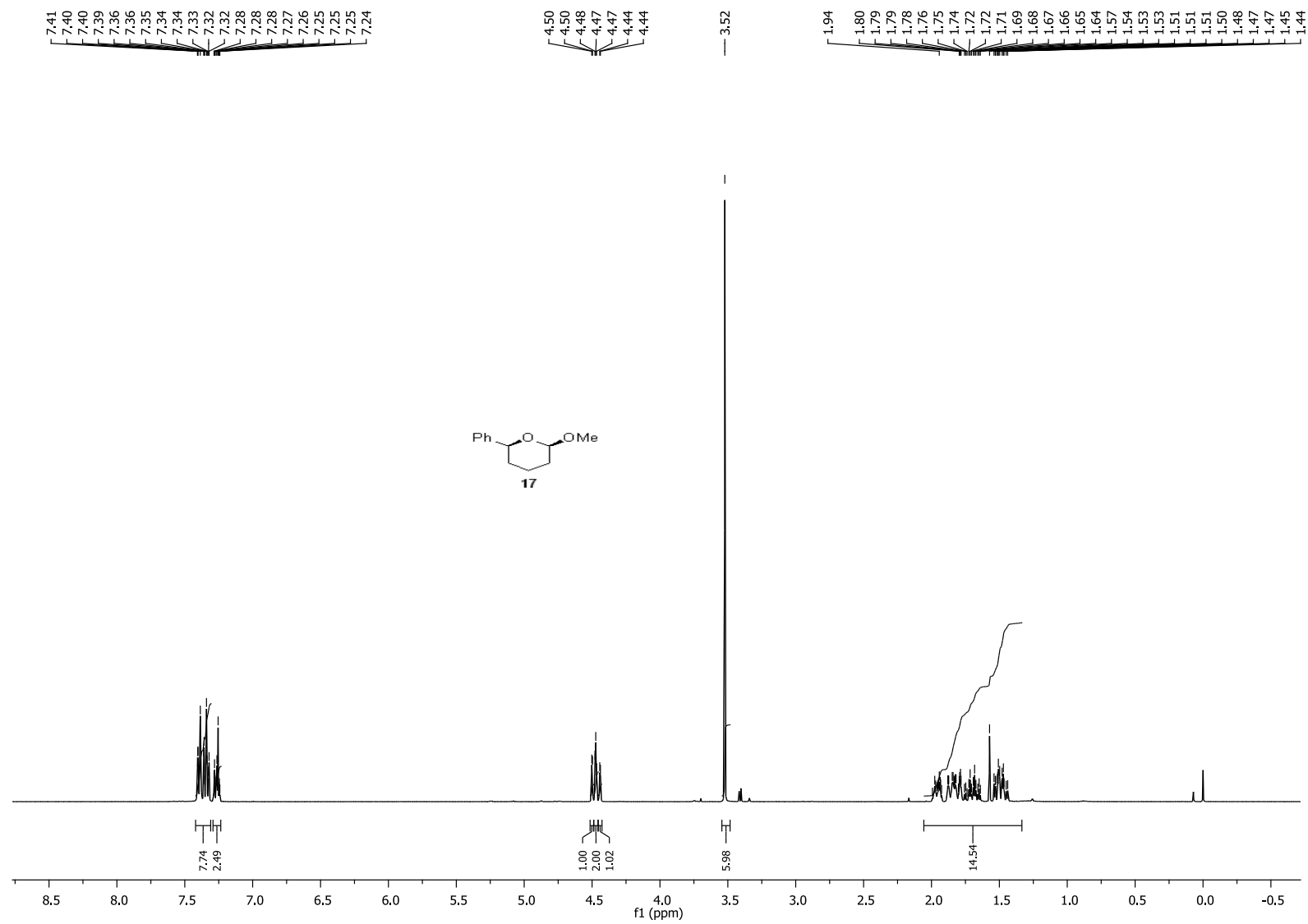


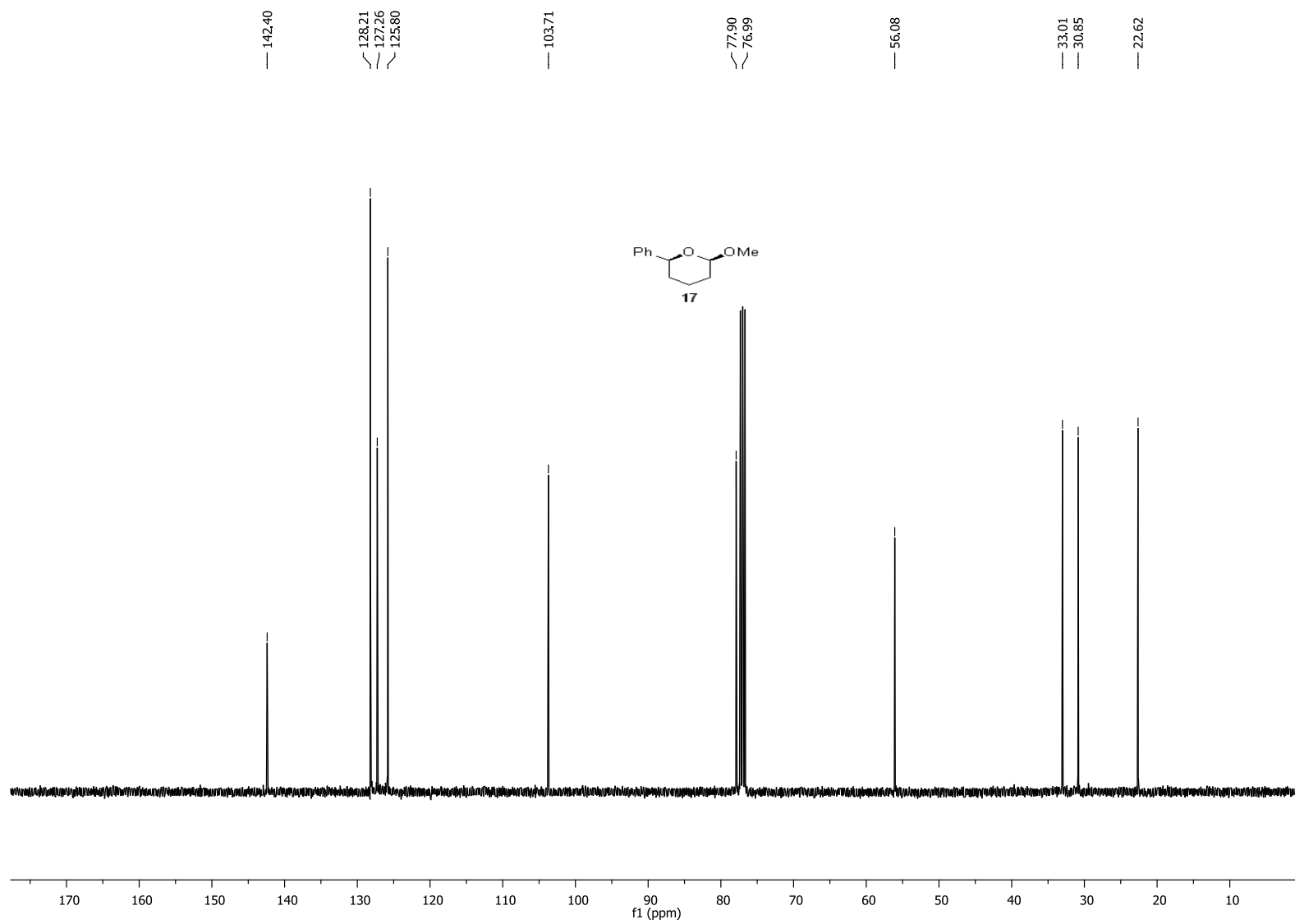


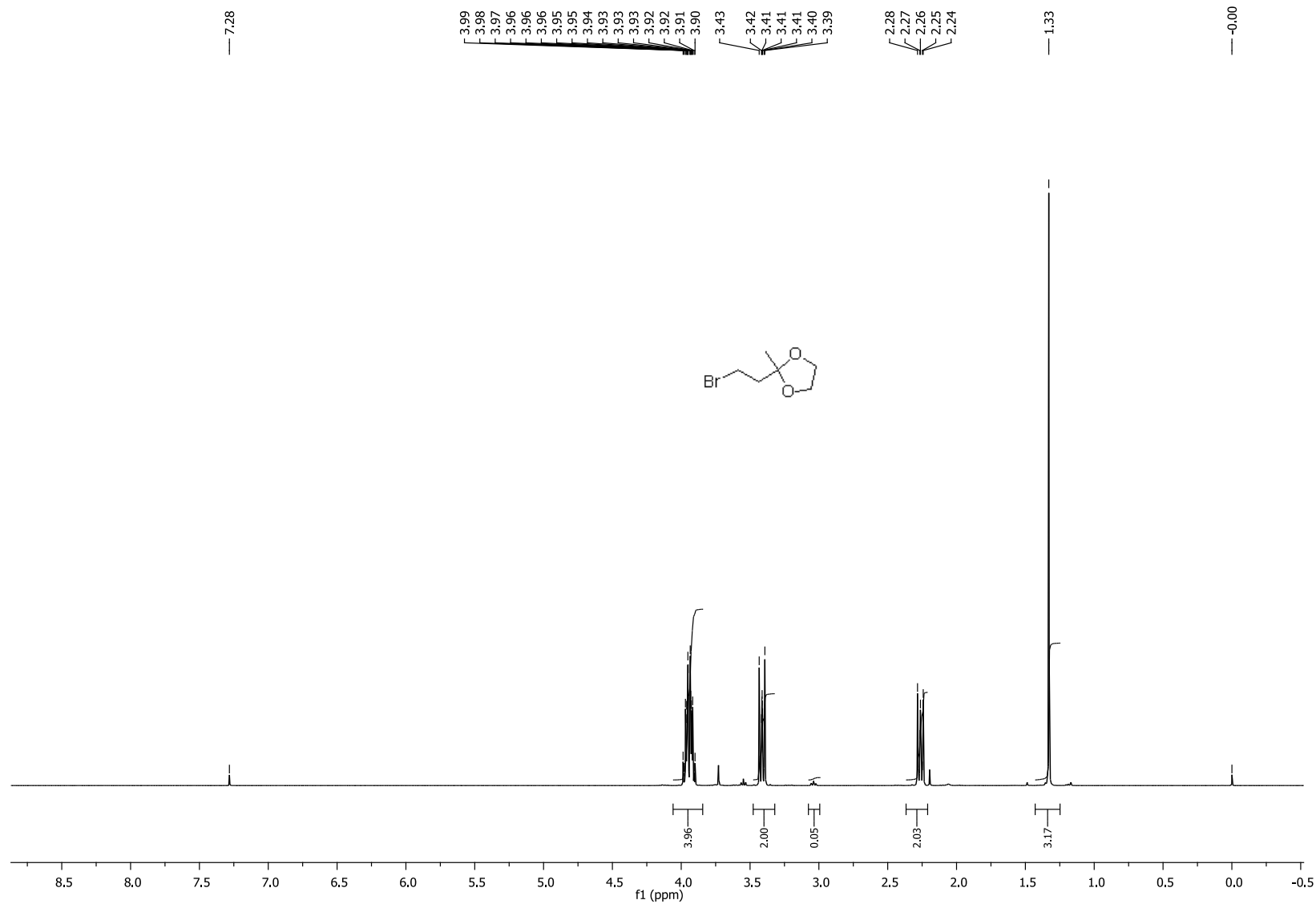


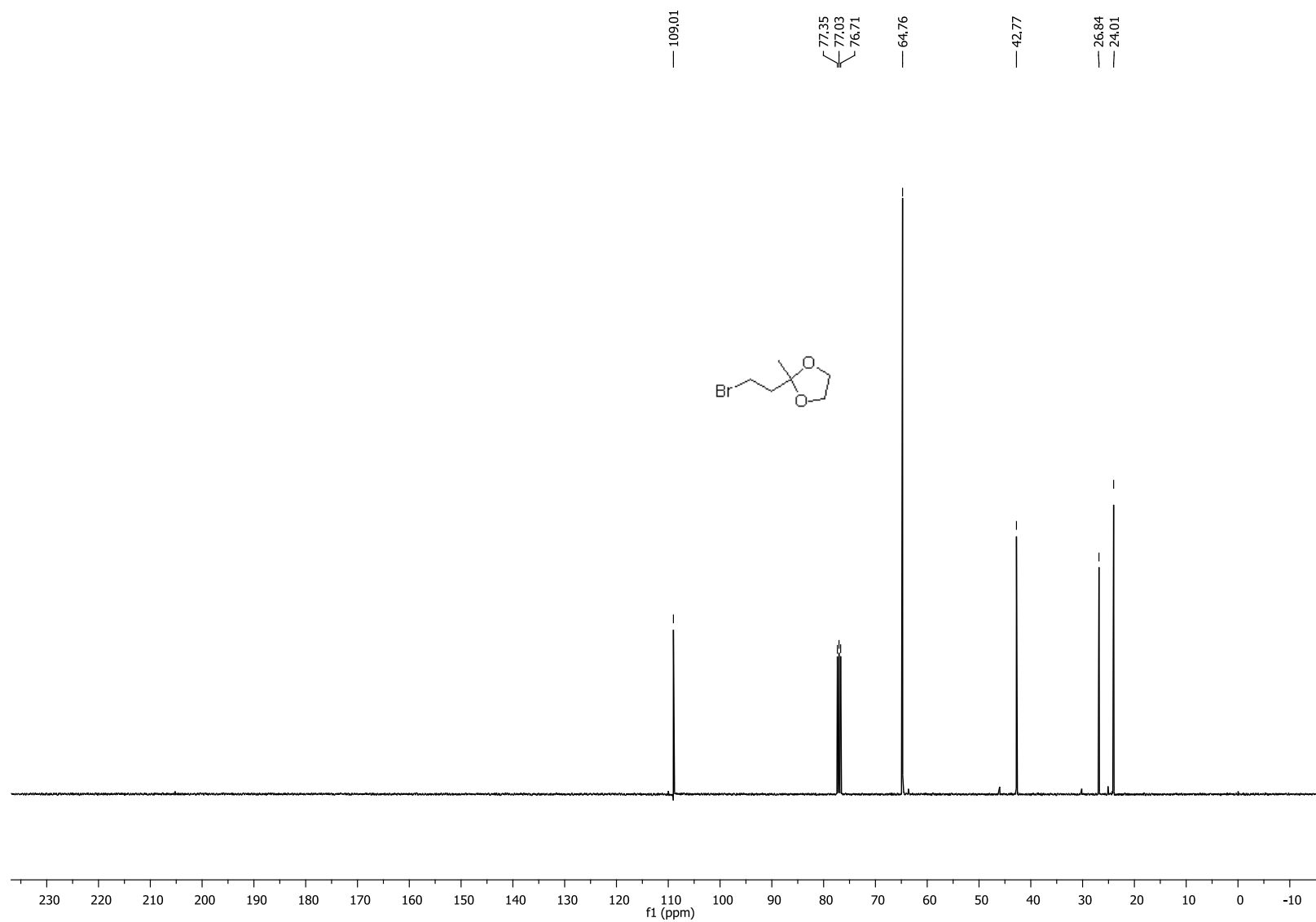


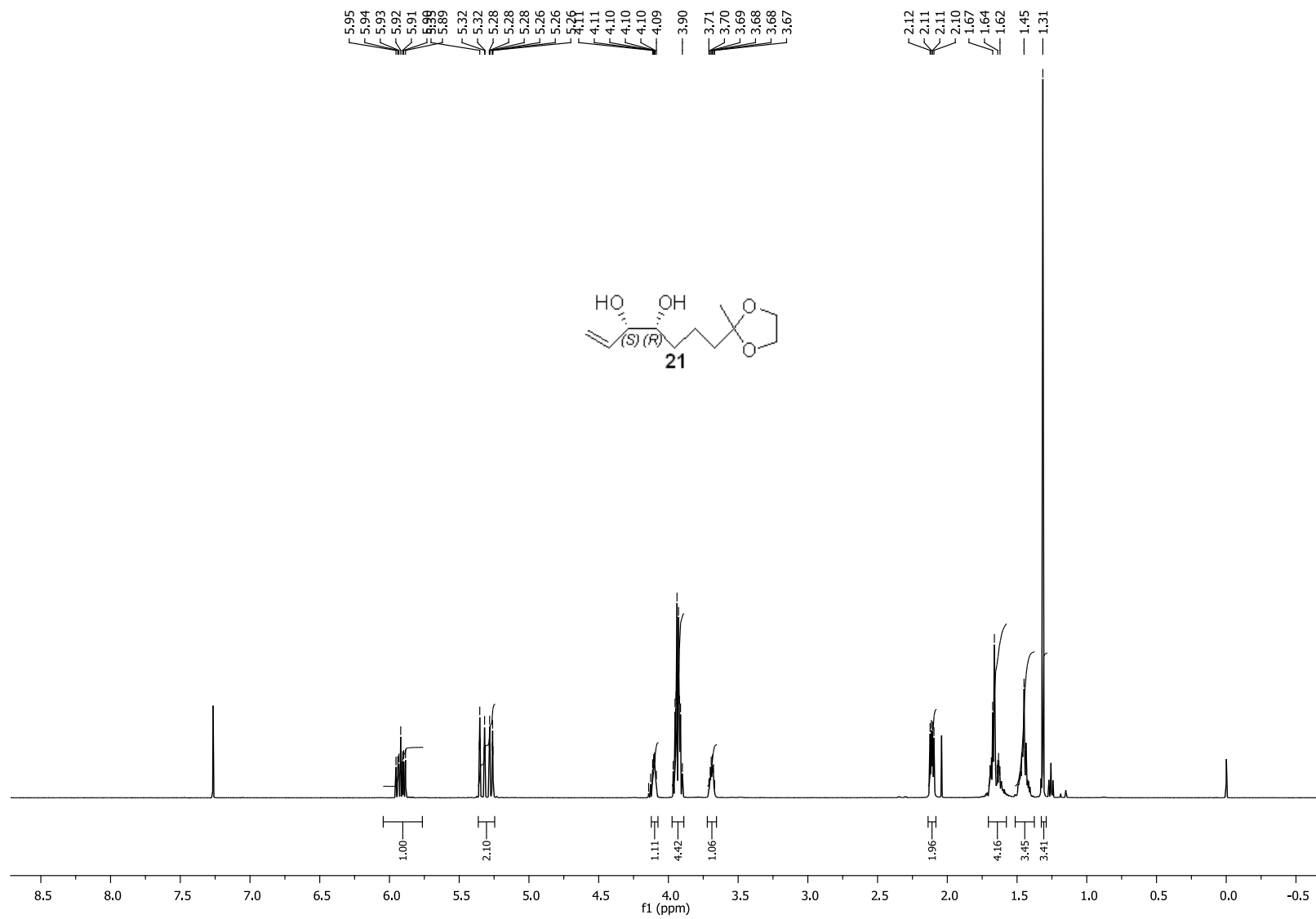


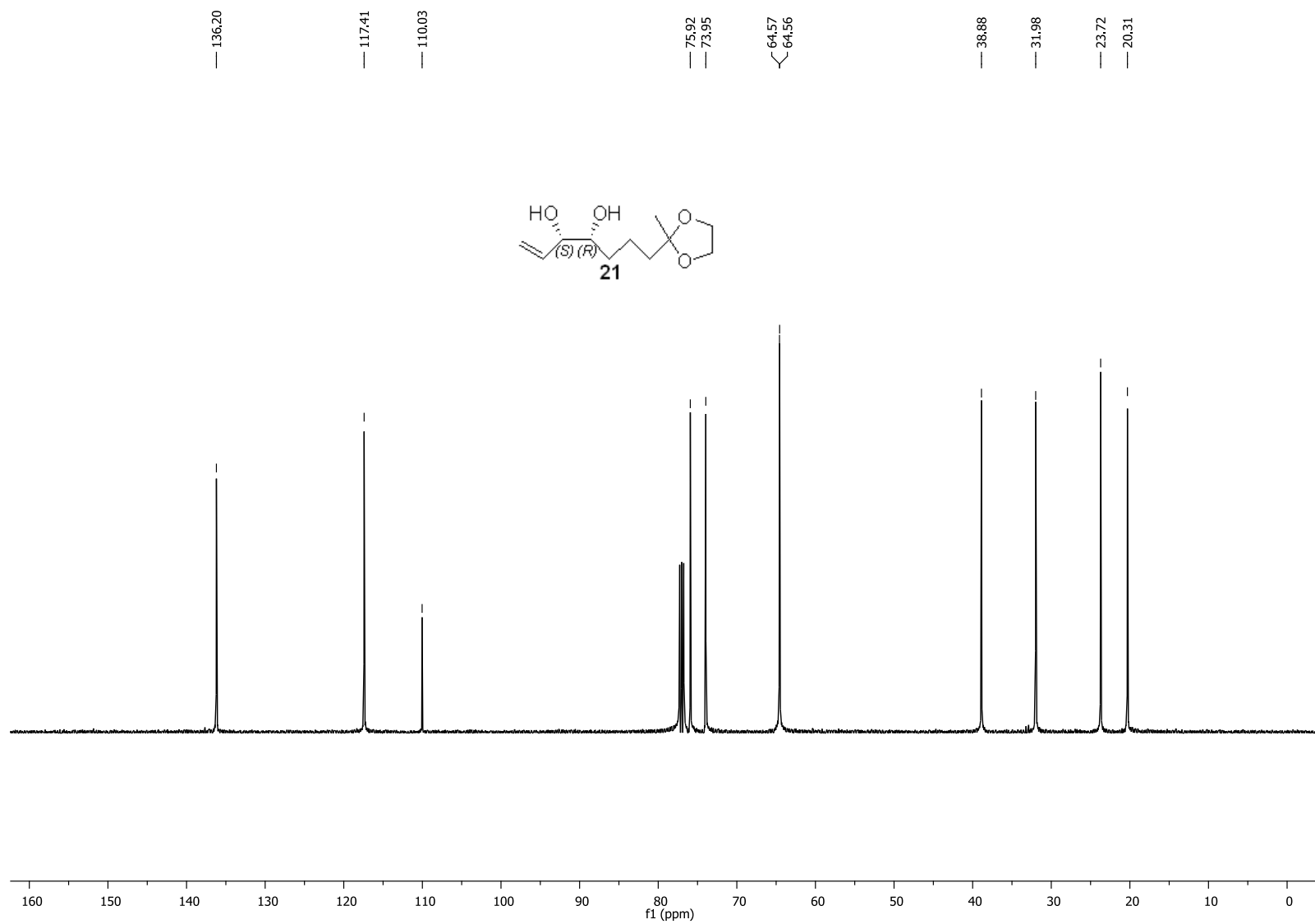


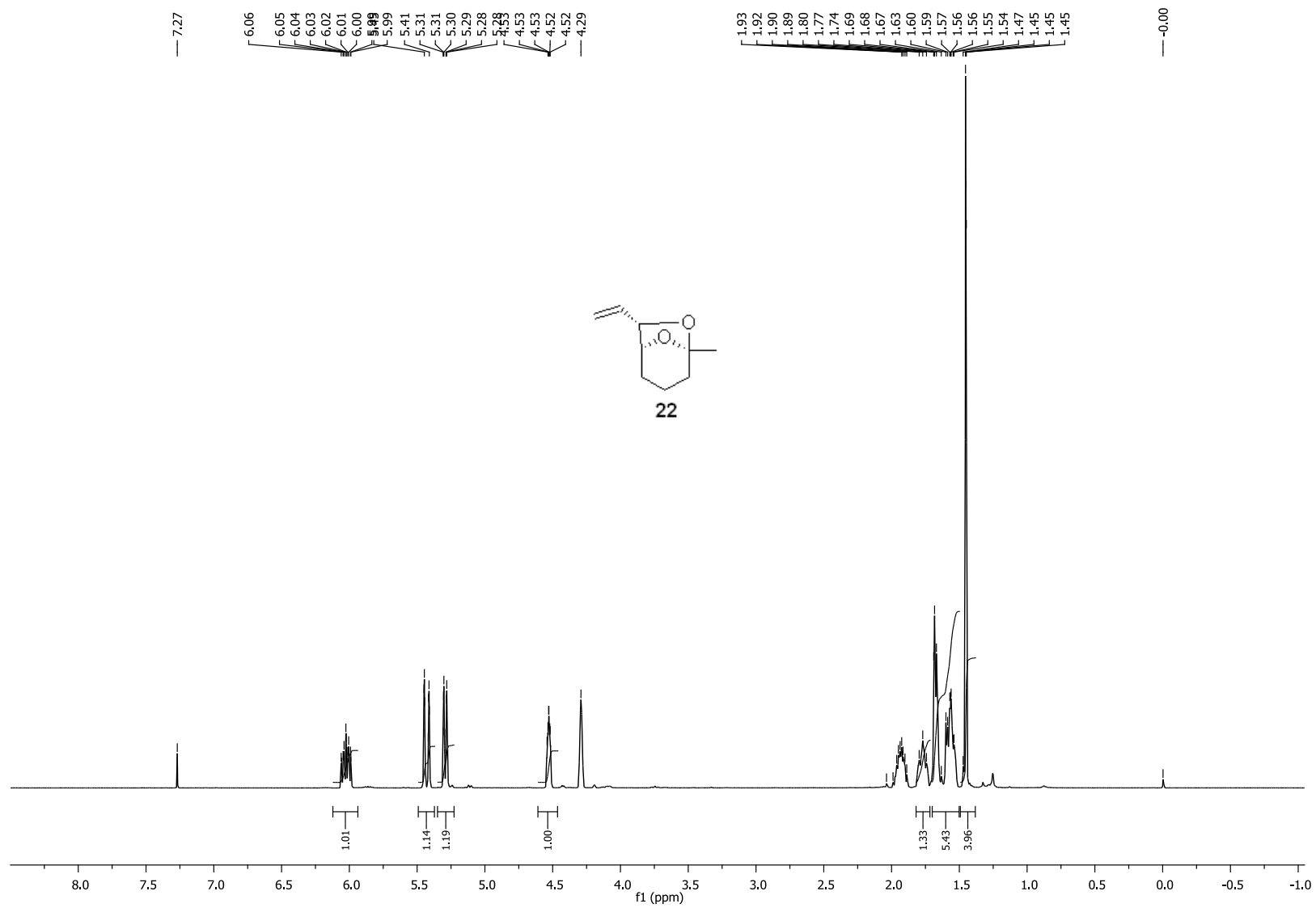


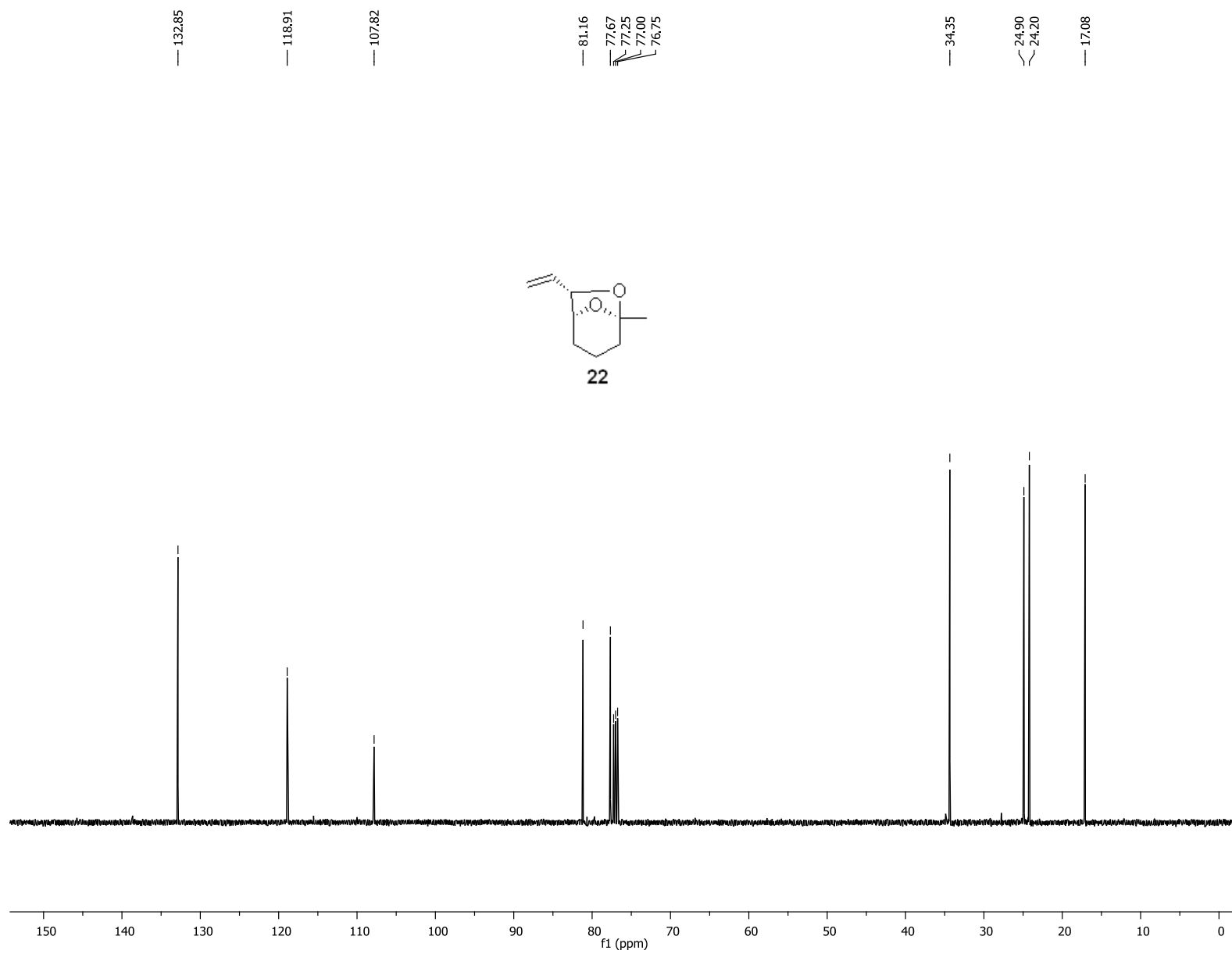


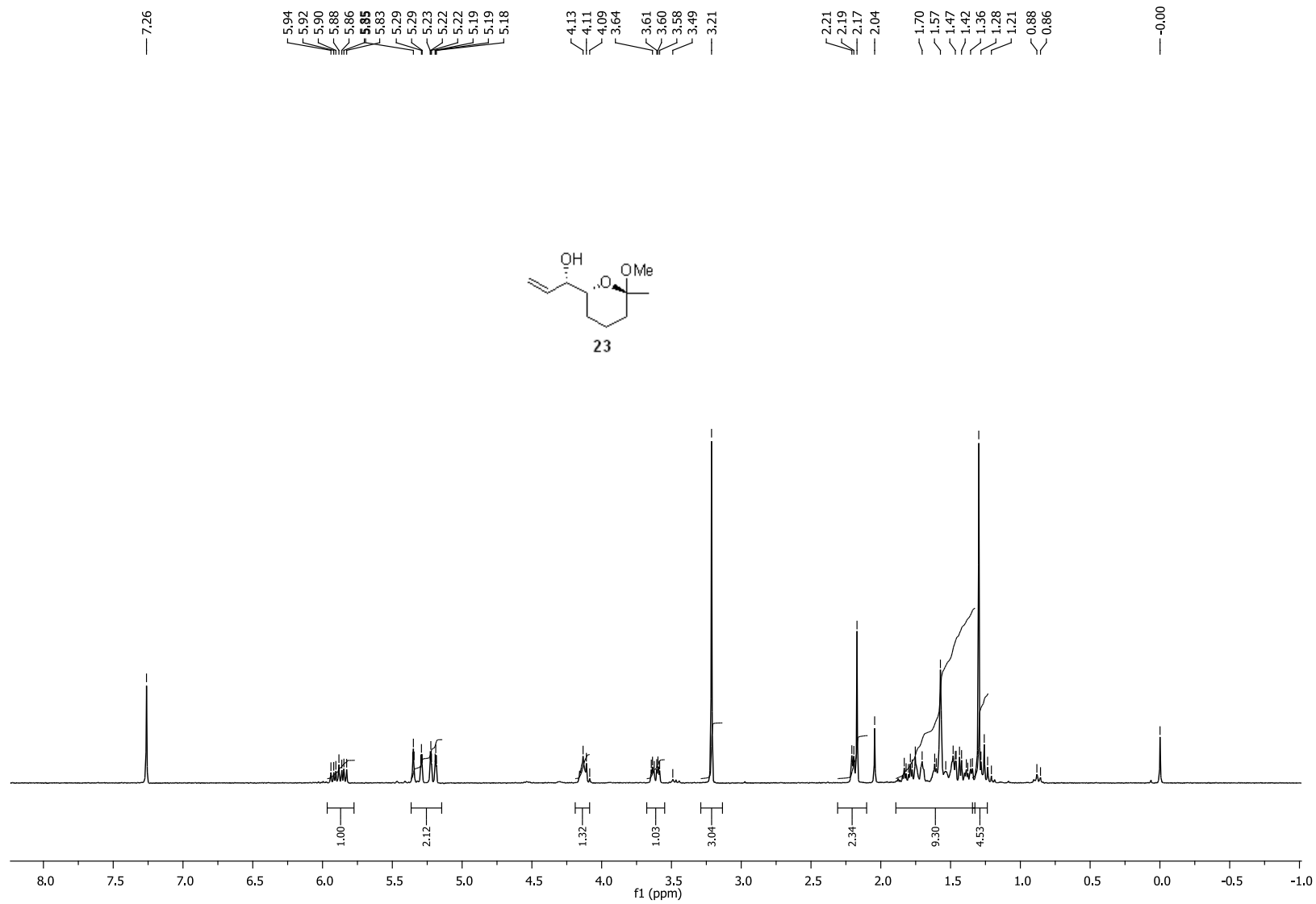


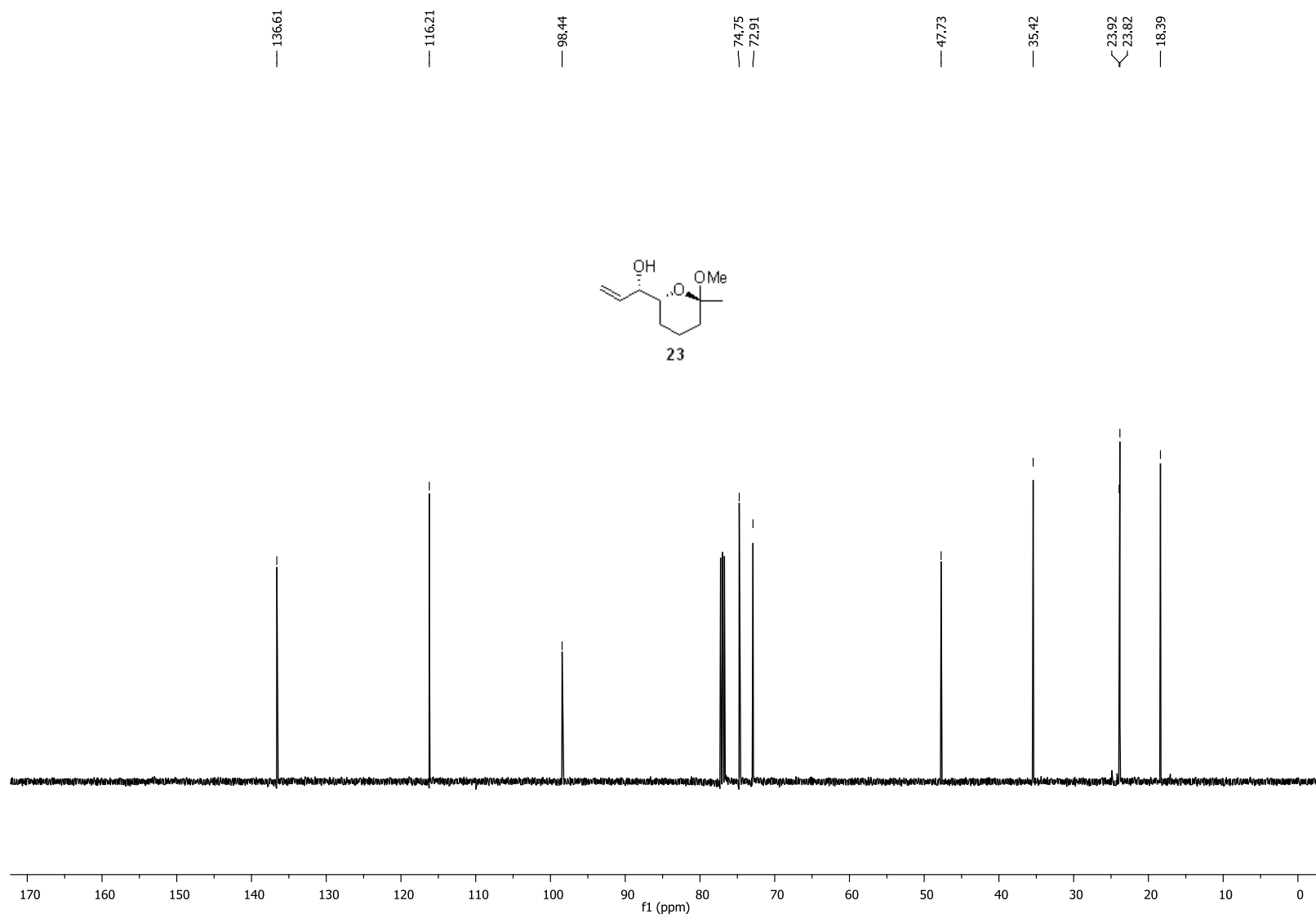


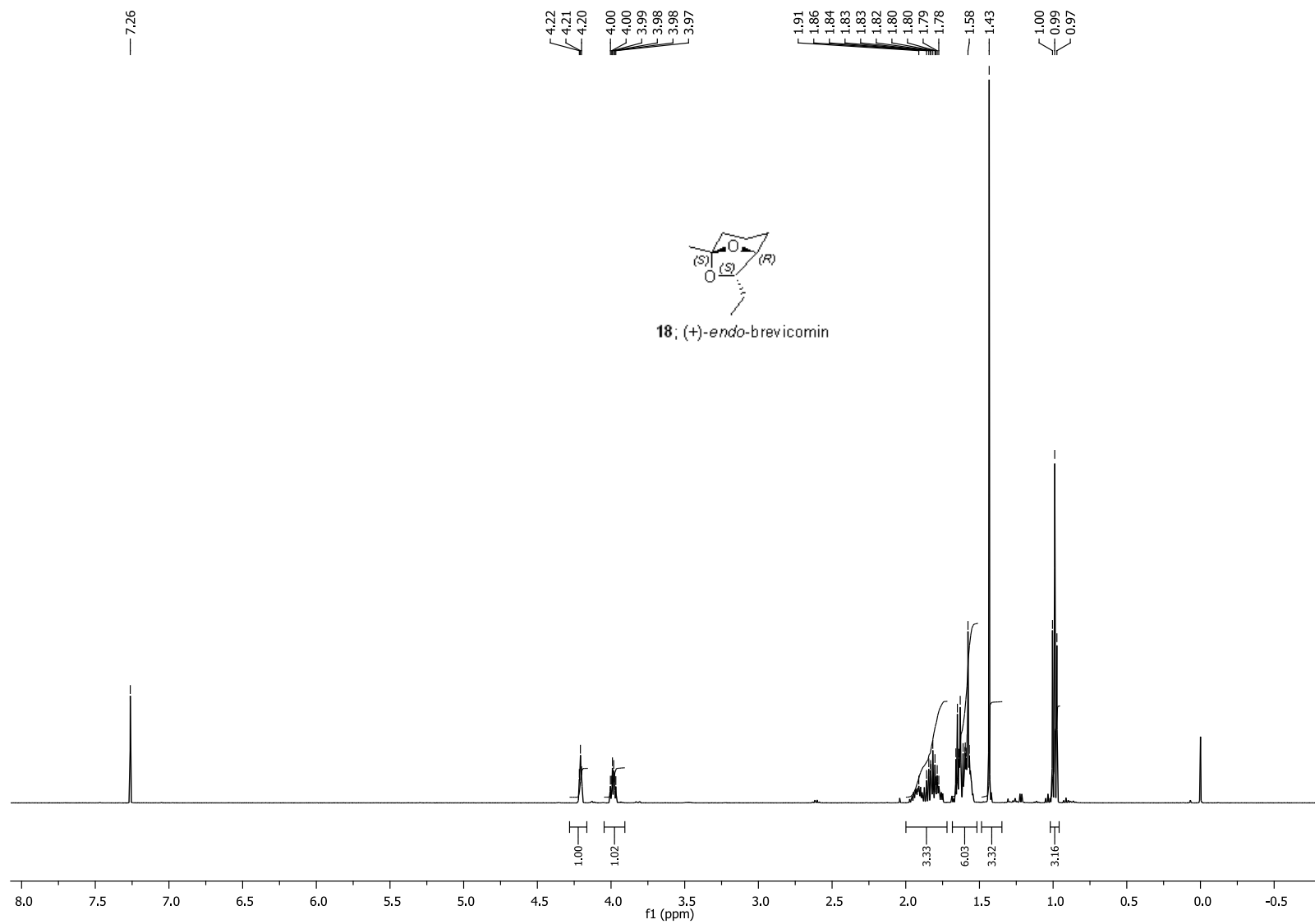


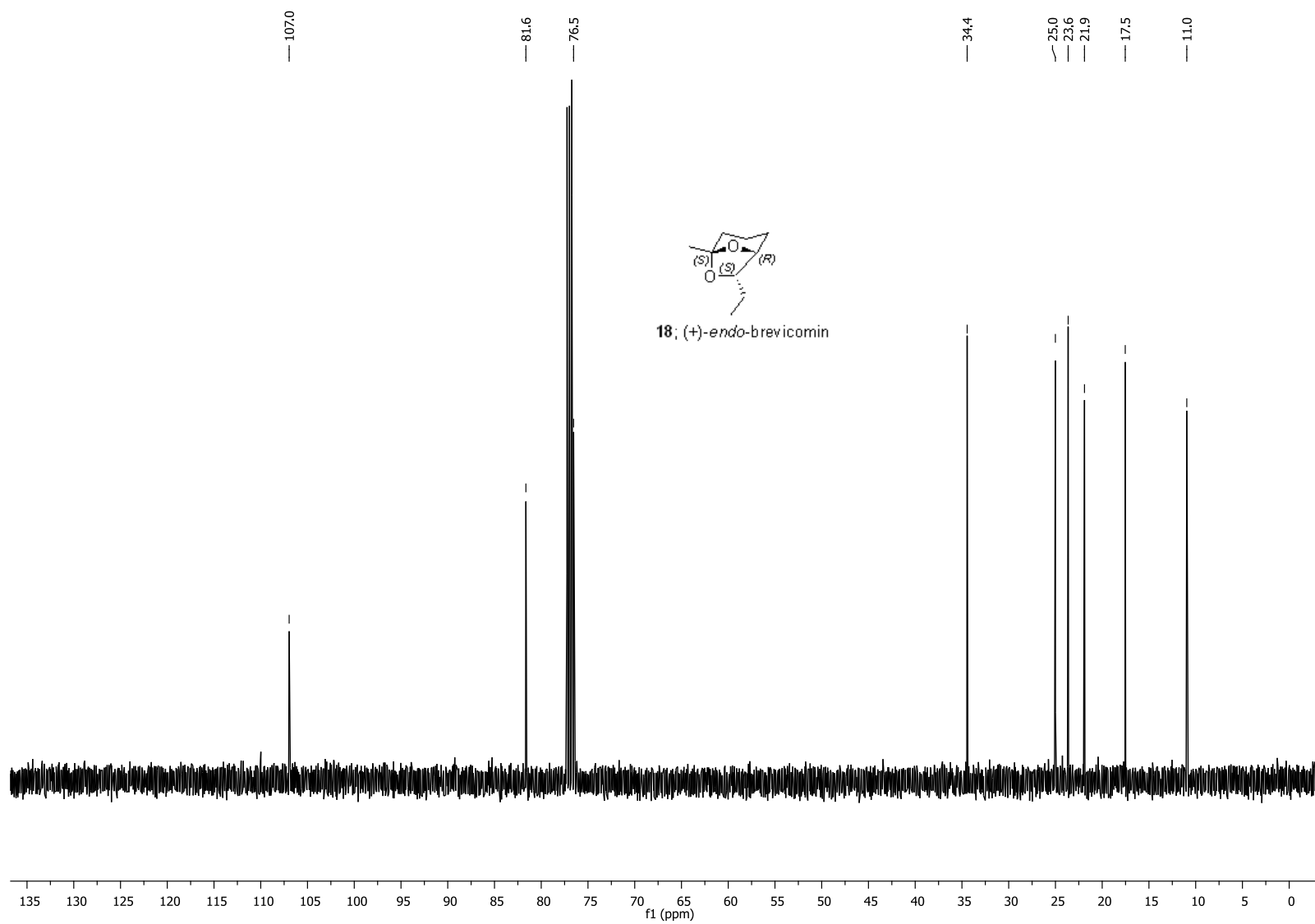


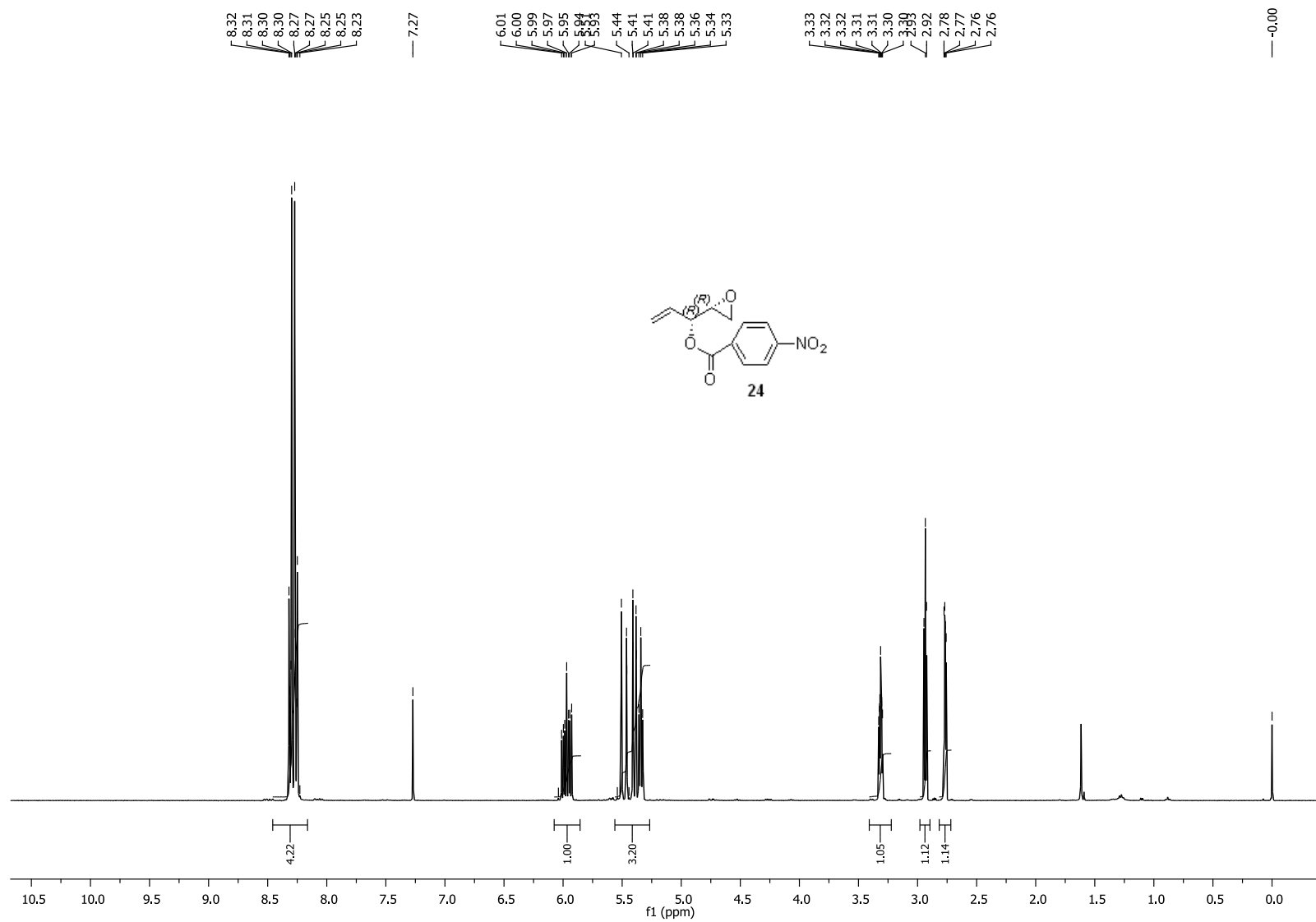


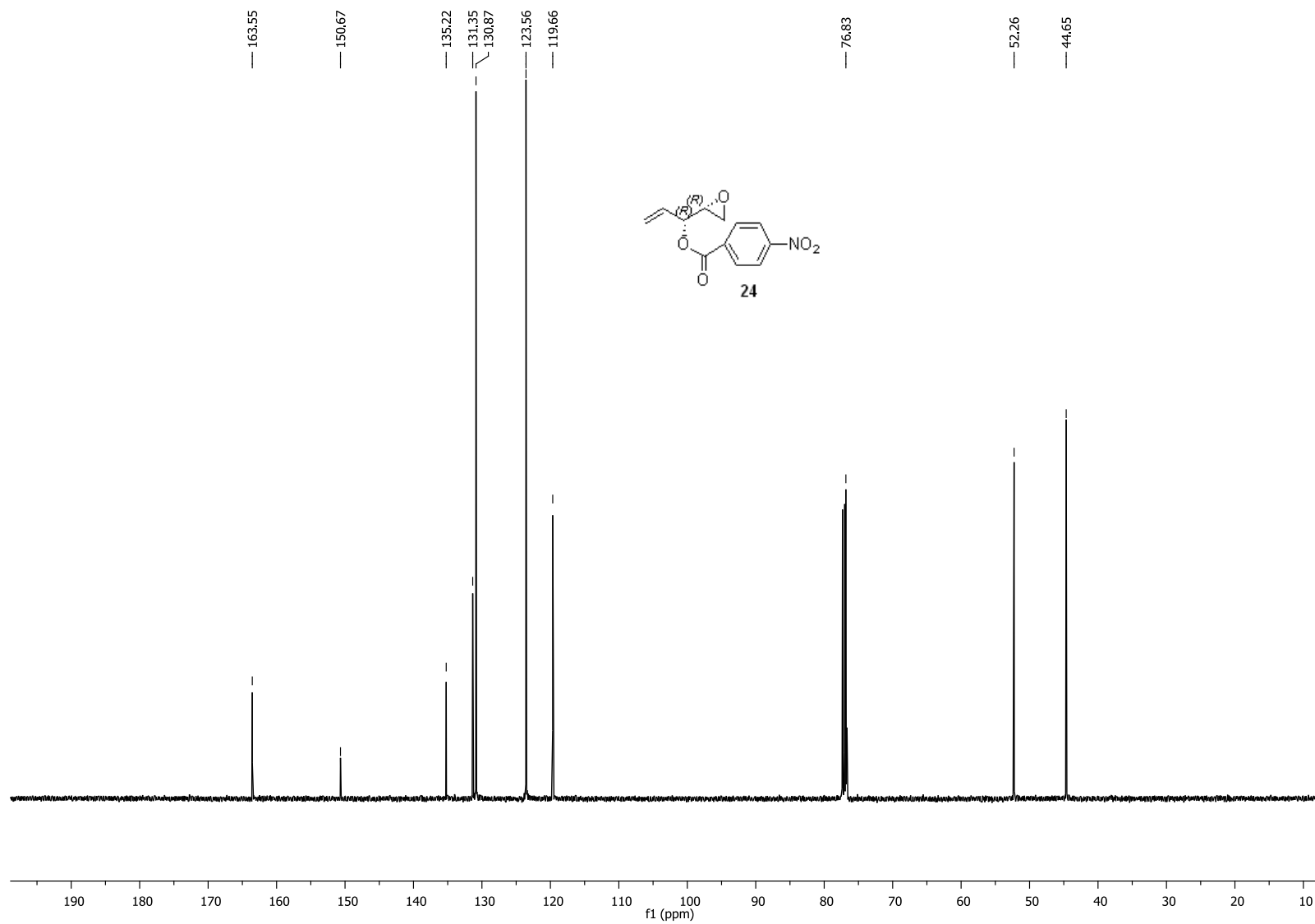


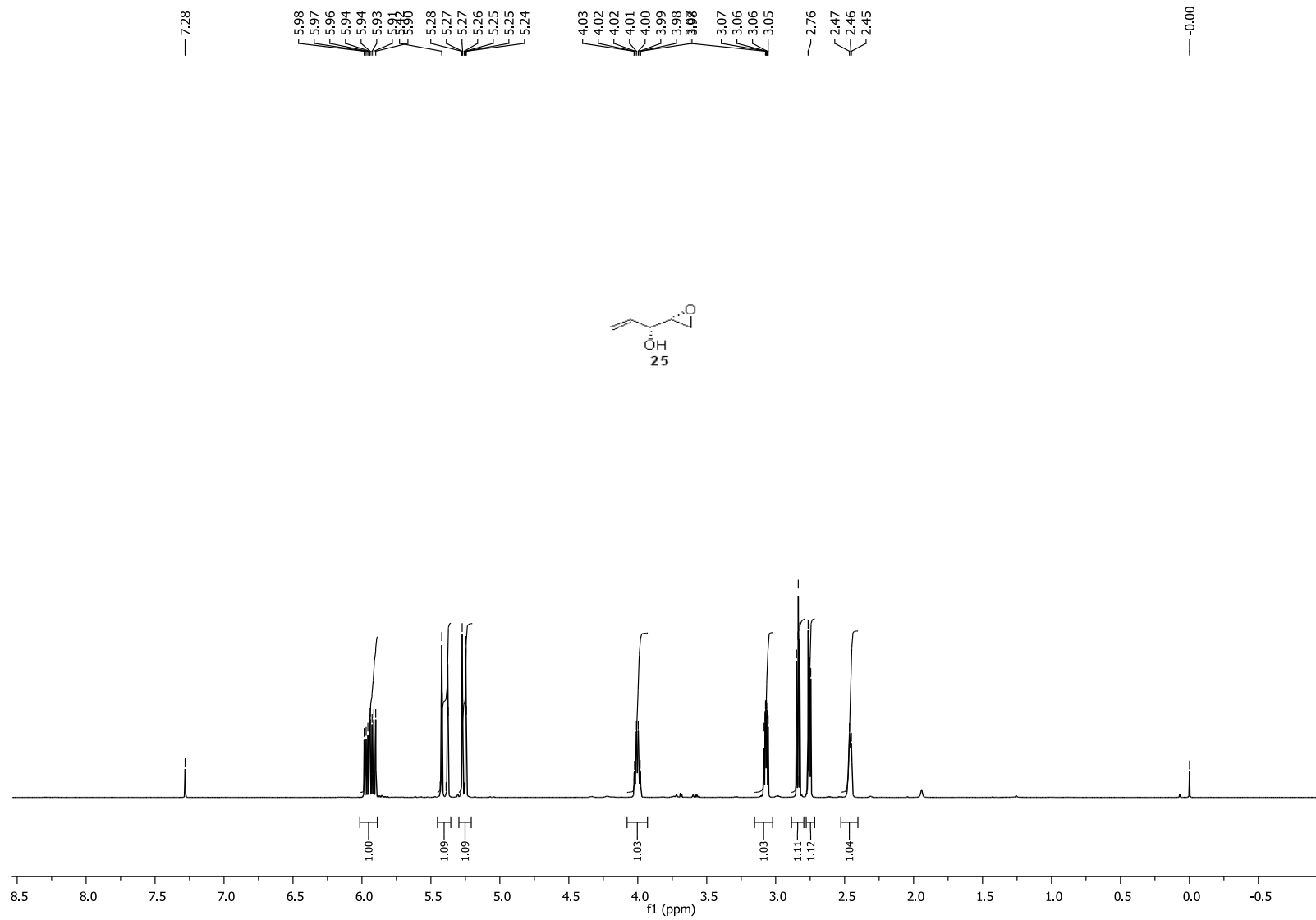


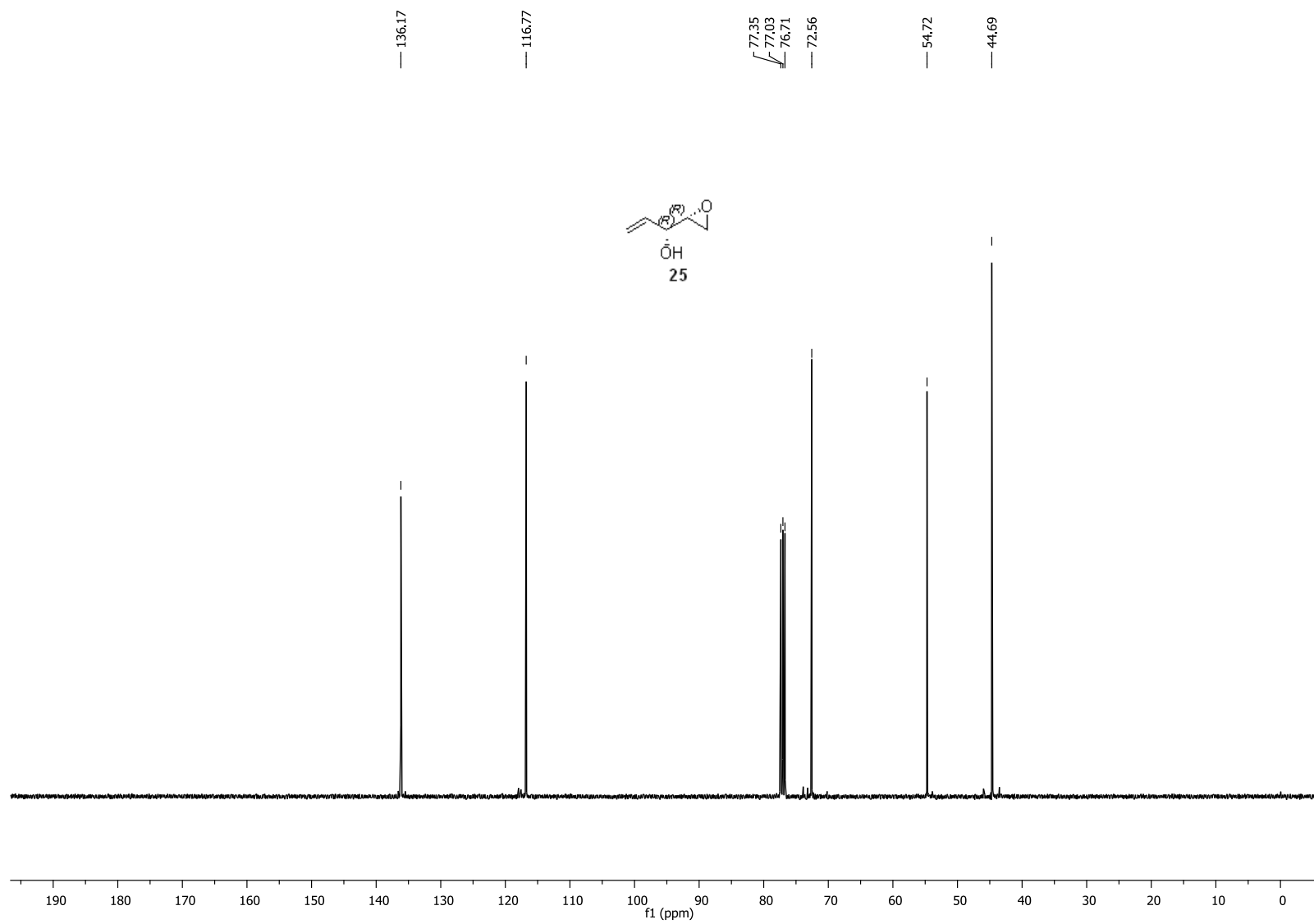


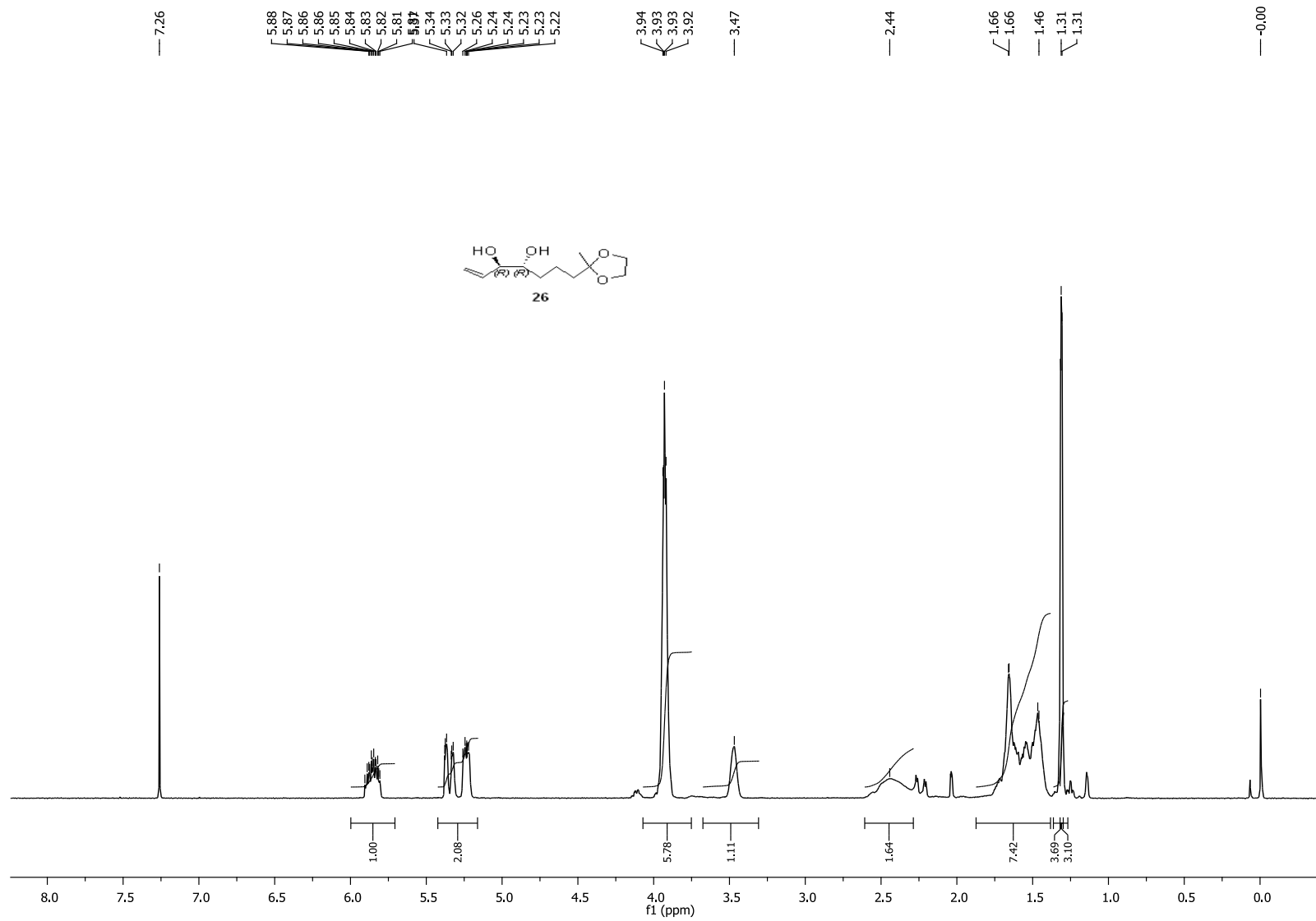


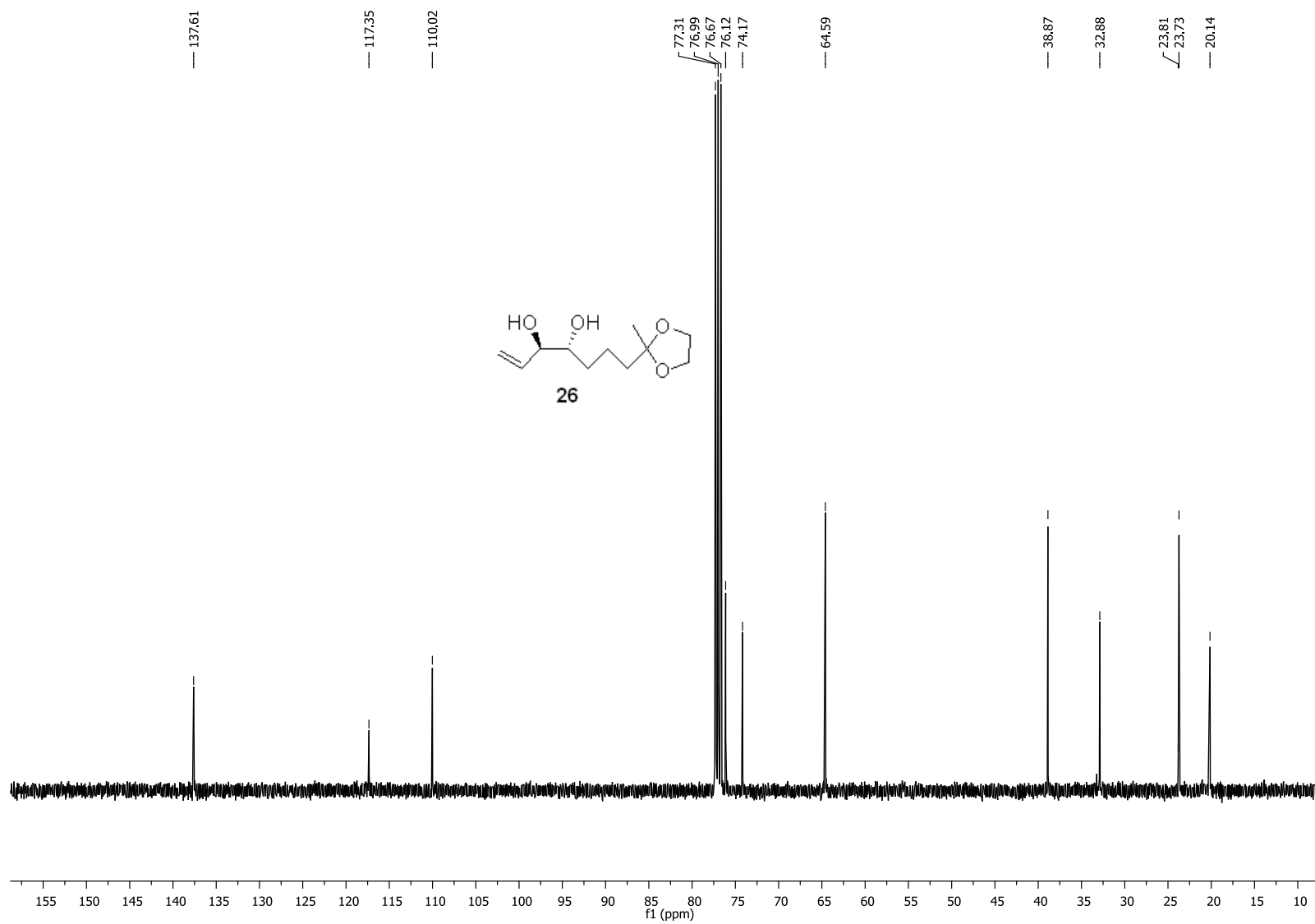


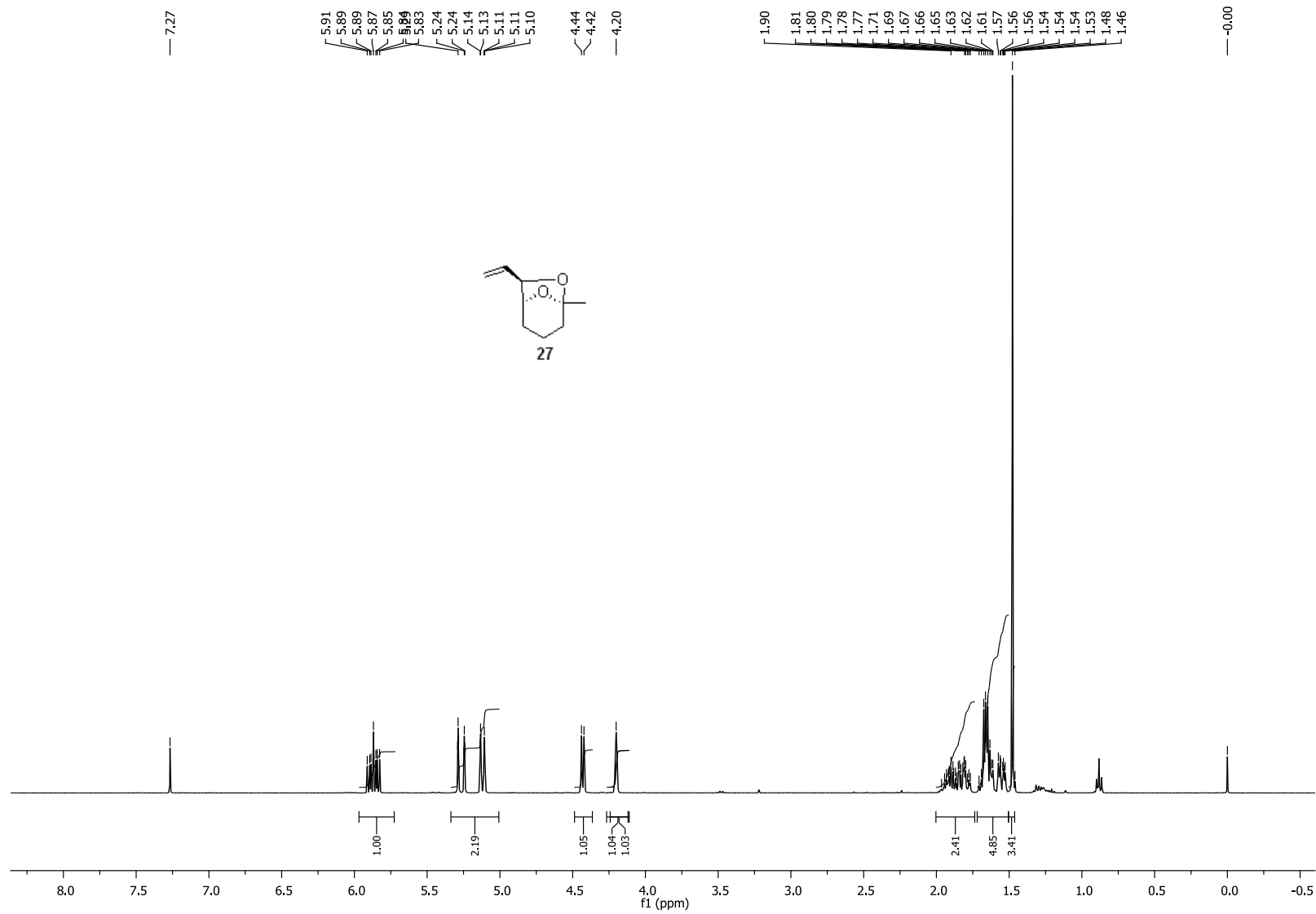


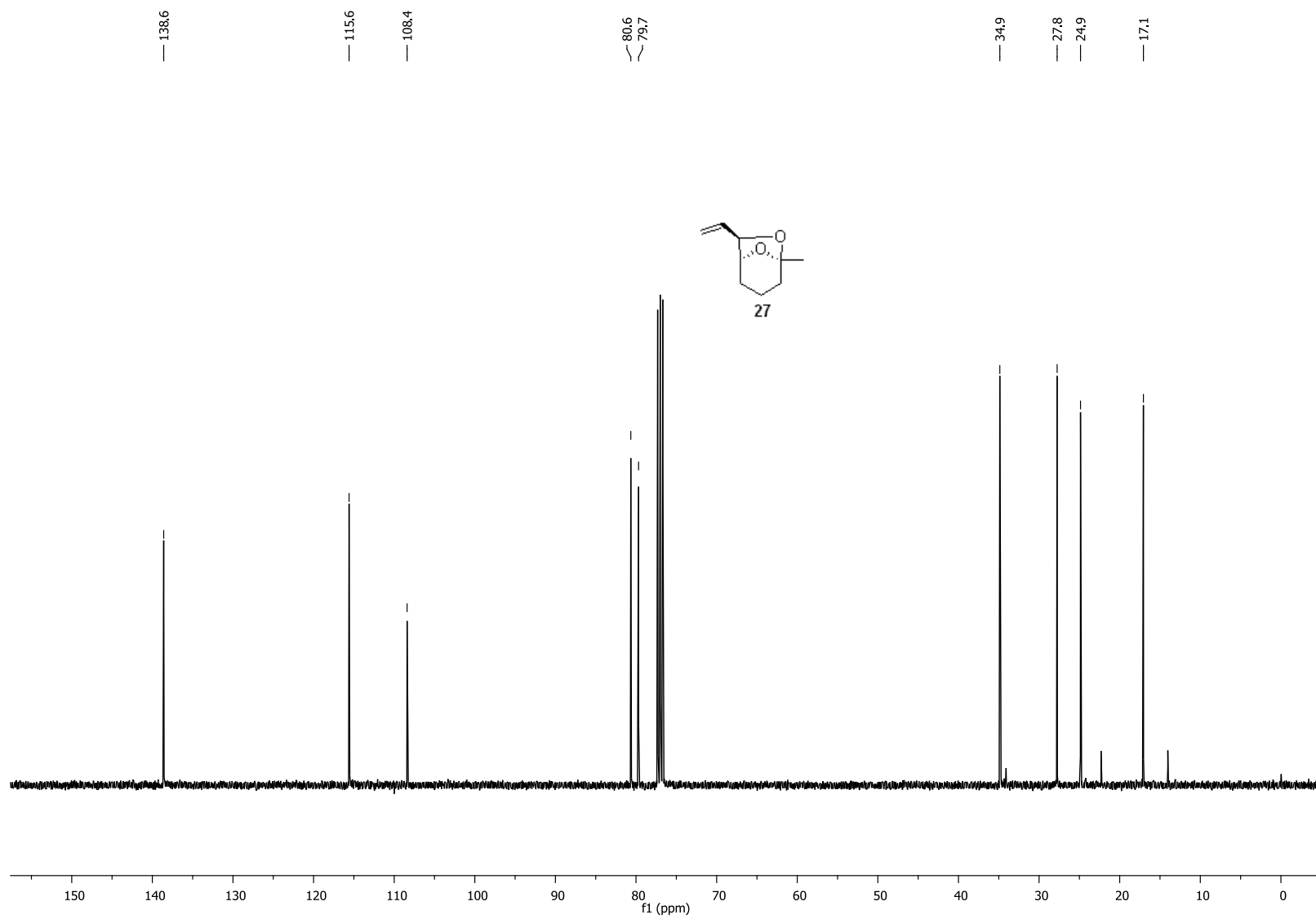


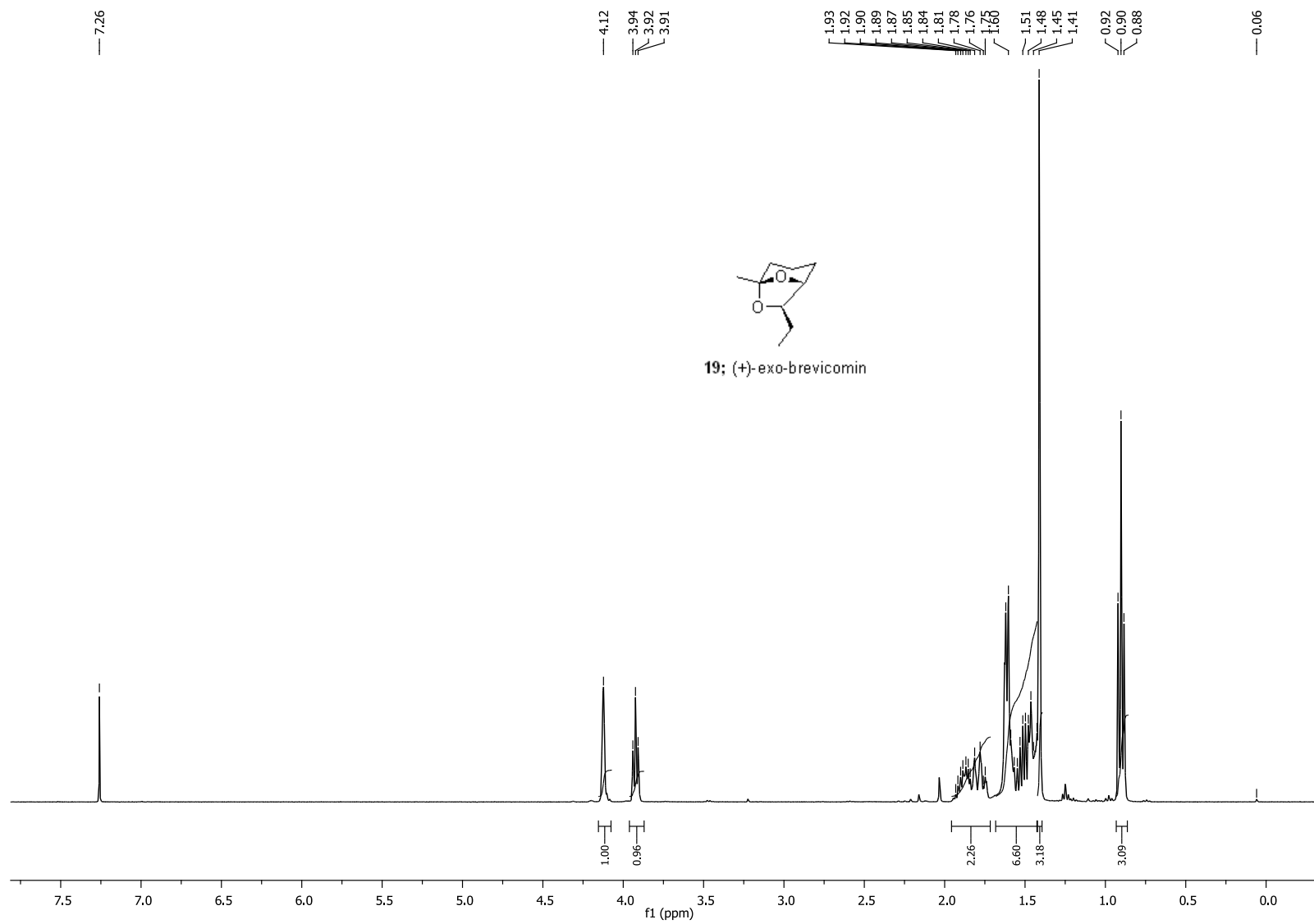


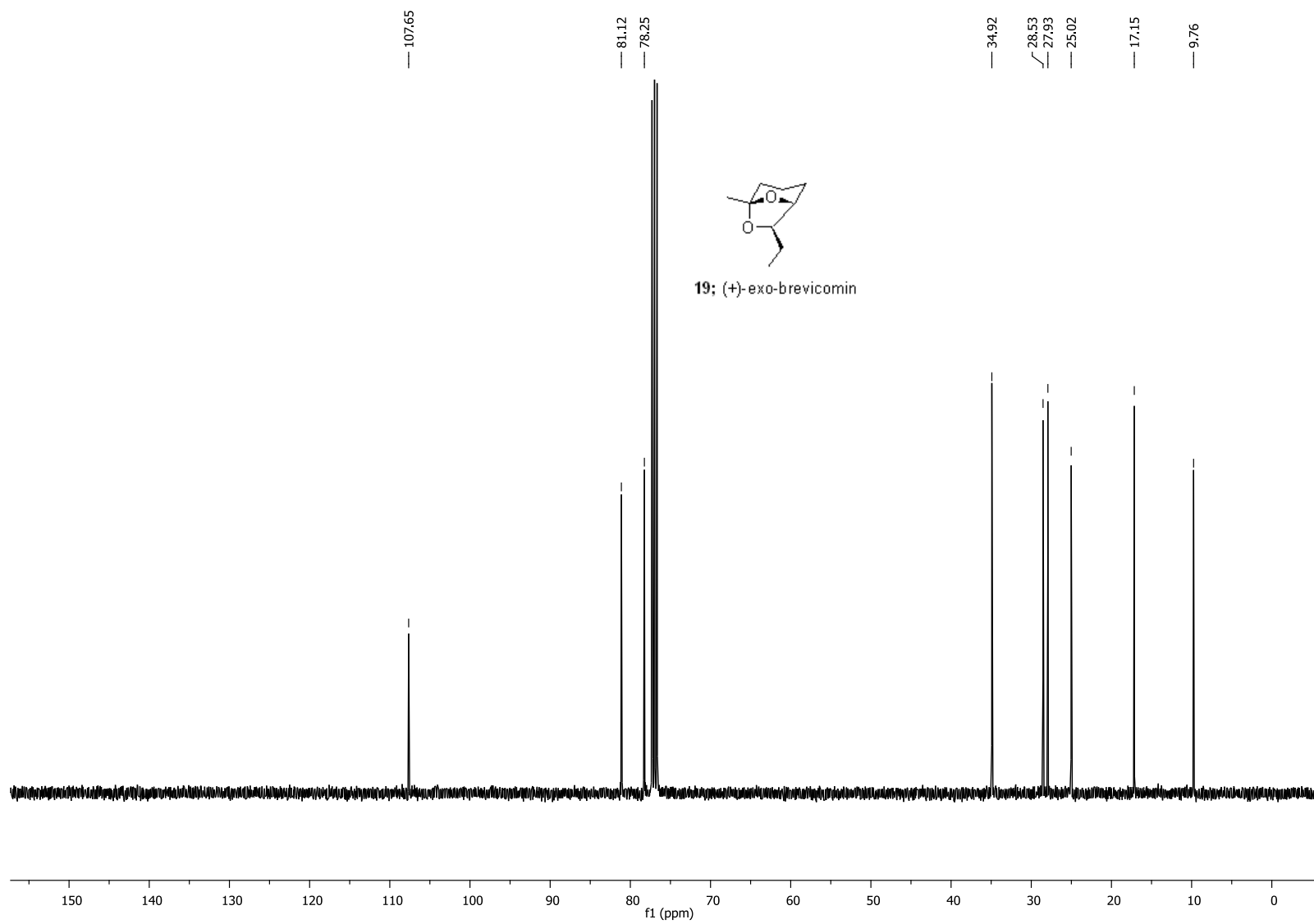








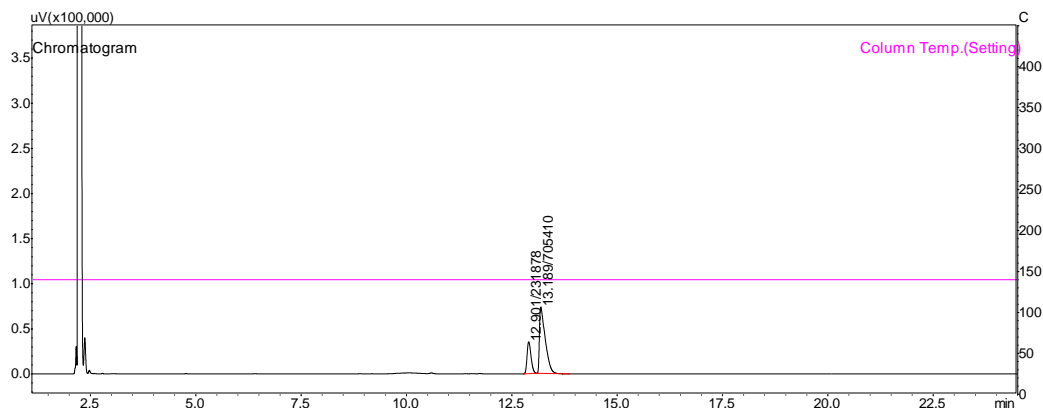




XV. GC Chromatogram

GC chromatogram of Table1, entry 1

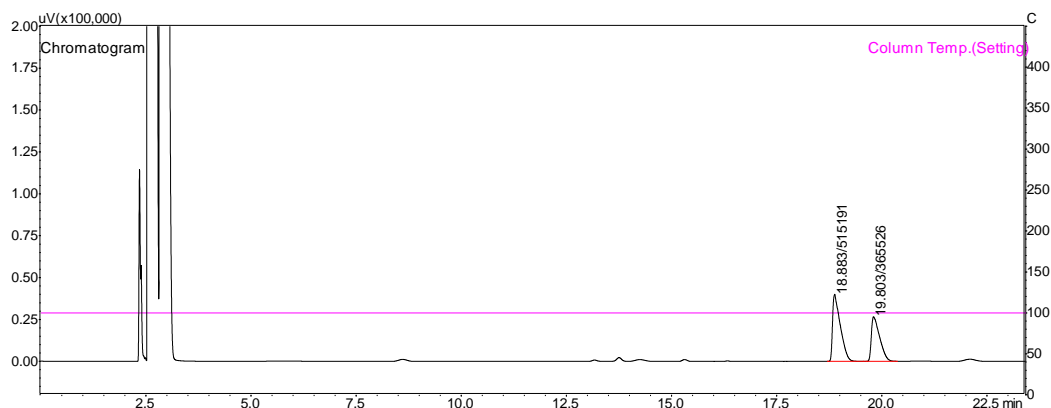
GC conditions for the determination of epimeric ratio of compounds **2** and **3**: 30m β -dex column, 1mL column flow rate, Column temperature 140°C Isotherms, Detector temperature 220 °C and Injector temperature 200 °C.



Peak#	Ret.Time	Area	Area%	Compound Name
1	12.901	231877.7	24.7392	3
2	13.189	705409.6	75.2608	2

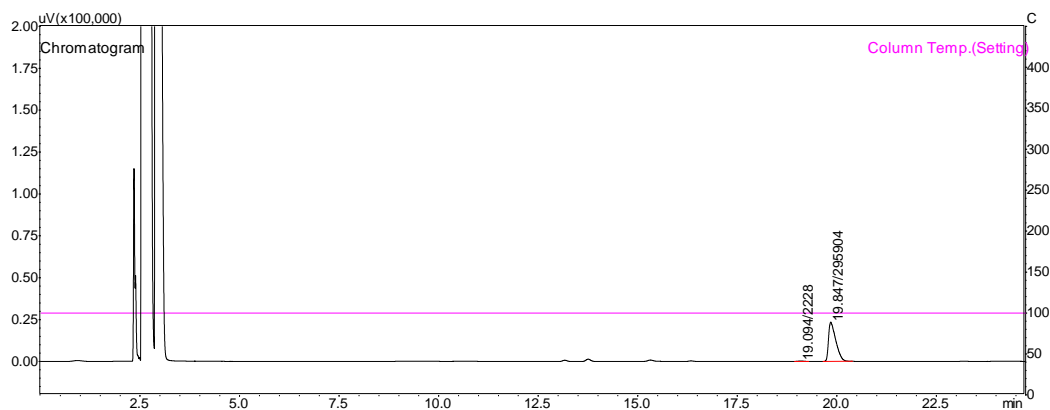
GC Conditions for *ee* determination for *endo* and *exo*-brevicommin

GC conditions for the determination enantiomeric excess of compounds **18**: 30m β -dex column, column flow rate 0.57 mL/min, column temperature 100°C Isotherms, Detector temp. 250 °C and Injector temp 200 °C.



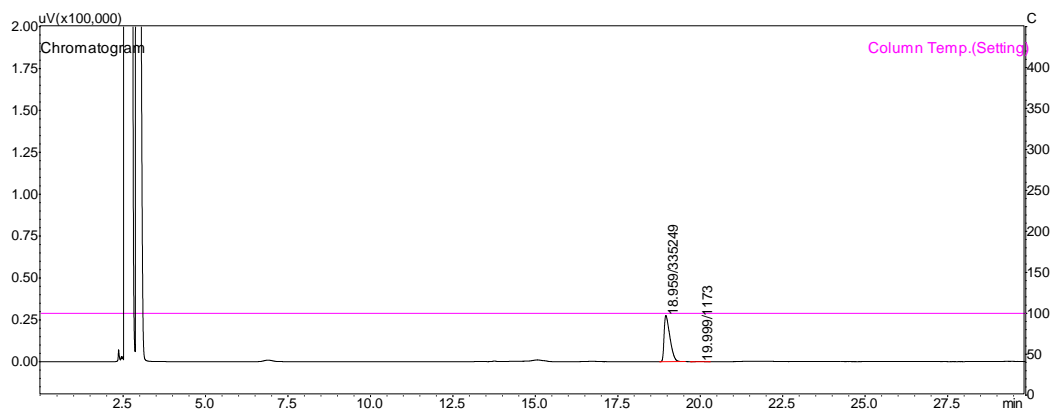
Mixture of *endo*-(+) and *endo*-(-)-brevicommin

Peak#	Ret.Time	Area	Area%	Compound Name
1	18.883	515191.0	58.4968	(-)- <i>endo</i> -brevicommin
2	19.803	365525.5	41.5032	(+)- <i>endo</i> -brevicommin



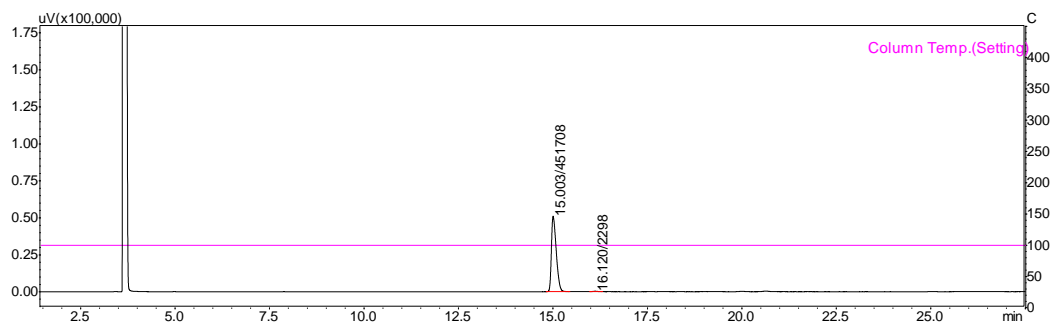
(+)-endo-brevicommin (18)

Peak#	Ret.Time	Area	Area %	Compound Name
19.094	2228.3	241.6	0.7474	(-)-endo-brevicommin
19.847	295904.3	23487.7	99.2526	(+)-endo-brevicommin



(-)-endo-brevicommin (18)

Peak#	Ret.Time	Area	Area%	Compound Name
1	18.959	335248.8	99.6513	(-)-endo-brevicommin
2	19.999	1173.0	0.3487	(+)-endo-brevicommin



(+)-*exo*-Brevicommin (**19**)

Peak#	Ret.Time	Area	Height	Area%	Compound Name
1	15.003	451708.5	51012.3	99.4939	<i>exo</i> -(+)-Brevicommin
2	16.120	2297.5	278.9	0.5061	<i>exo</i> -(-)-Brevicommin