

Application of Stereoselective Ether Transfer to the Synthesis of Isotactic Polyethers

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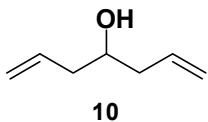
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Supporting Information

Experimental procedures and characterization data for compounds;

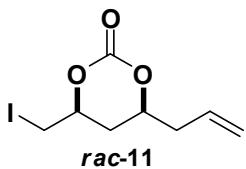
10, 11, rac-5, (S)-5.....Pages 2-6.

Proton and ¹³C NMR data for all compounds.....Pages 7-37.



Hepta-1,6-dien-4-ol (10).¹ A two-necked 500 mL flask was charged with Mg turnings (12.7 g, 520 mmol, briefly crushed) and THF (20 mL) under a N₂ atmosphere. A few drops of allyl bromide were added to the suspension and the exothermic formation of allylmagnesium bromide began. Once the reaction had started, a mixture of allyl bromide (44 mL, 51 mmol) and ethyl formate (20.0 mL, 248 mol) in THF (20 mL) was added via an addition funnel at a rate fast enough to maintain a controllable auto-reflux of the reaction mixture. The addition took about 30 minutes. The mixture was then heated to reflux for 2 hours. The reaction was cooled in an ice bath and HCl (1 M) was carefully added with vigorous stirring until the aqueous phase was acidic to litmus paper. The layers were separated and the aqueous layer was extracted with ether (2 x 100 mL). The organic layers were combined and washed with water (50 mL), sat. NaHCO₃ (50 mL), and brine (50 mL), then dried with MgSO₄ and filtered through Celite®. Removal of solvents gave a yellow oil that was purified by distillation at atmospheric pressure (bp 150–151 °C) to yield **10** as a colorless oil (21.1 g, 188 mmol, 76%). **10**: R_f = 0.48 (silica gel, 10% EtOAc/hexanes); ¹H NMR (500 MHz, CDCl₃) δ_H 1.77 (1H, bs), 2.15–2.36 (4H, m), 3.67–3.77 (1H, m), 5.10–5.20 (2H, m), 5.77–5.92 (1H, m); ¹³C NMR (125 MHz, CDCl₃) δ_C 41.4, 69.9, 118.3, 134.9.

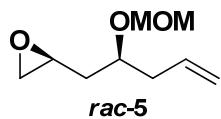
¹ Parks, B. W.; Gilbertson, R. D.; Domaille, D. W.; Hutchison, J. E. *J. Org. Chem.* **2006**, *71*(26), 9622–9627.



(±)-(4S,6S)-4-Allyl-6-(iodomethyl)-1,3-dioxan-2-one (*rac-11*).² To a stirred solution of **10** (22.4 g, 200 mmol) in THF (200 mL) at 0 °C was added *n*-BuLi (2.5 M in hexanes, 85 mL, 210 mmol) dropwise, and the solution was stirred for an additional 10 minutes. CO₂ gas (generated from a 250 mL round-bottomed flask, and passed through a drying tube) was bubbled into the solution via a Pasteur pipette for 30 minutes, then the light yellow solution stirred for an additional 30 minutes under a balloon of CO₂ at 0 °C. A THF solution (200 mL) of iodine (101.4 g, 400 mmol) was added dropwise to the reaction mixture over 60 minutes at 0 °C. The reaction was allowed to warm to room temperature overnight, diluted with 200 mL EtOAc, and the excess iodine destroyed by addition of saturated Na₂S₂O₃ solution until the red color disappeared. The organic layer was separated and washed with saturated NaHCO₃ and brine, then dried with MgSO₄ and filtered. Removal of the solvent at reduced pressure gave **rac-11** as a yellow oil. Crude **rac-11** could be used in the next step without purification for a 70% yield over two steps, or purified (flash chromatography eluting with 20% EtOAc/hexanes) for an isolated yield of 84% (d.r. >15:1). **Rac-11:** $R_f = 0.23$ (silica gel, 20% EtOAc/hexanes); ¹H NMR (500 MHz, CDCl₃) δ_{H} 1.71 (1H, m), 2.40 (1H, m), 2.42–2.49 (1H, m), 2.52–2.58 (1H, m), 3.27 (1H, dd, $J=10.58, 7.41$ Hz), 3.41 (1H, dd, $J=10.58, 4.29$ Hz), 4.45 (1H, ddt, $J=7.46, 4.16,$

² a) Butler, D. E.; Deering, C. F.; Millar, A.; Nanninga, T. N.; Roth, B. D. (Warner-Lambert Co.) US Patent 5,245,047. b) Kim, Y.-J.; Tae, J. *Synlett* **2006**, 61–64. c) Rádl, S.; Stach, J.; Hajicek, J. *Tet. Lett.* **2002**, 43, 2087–2090.

3.35 Hz), 4.52 (1H, dtd, $J=8.88, 6.15, 2.77$ Hz), 5.19–5.25 (2H, m), 5.76–5.85 (1H, m); ^{13}C NMR (125 MHz, CDCl_3) δ_{C} 5.5, 32.7, 39.4, 77.2, 77.34, 77.8, 120.2, 131.1.

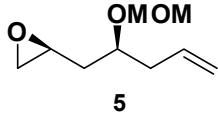


(\pm)-(S)-2-((S)-2-(Methoxymethoxy)pent-4-enyl)oxirane (*rac*-5). To a stirred solution of **rac-11** (12.6 g, 44.6 mmol) in MeOH (200 mL) at room temperature was added K_2CO_3 (18.5 g, 134 mmol). After 2 hours, the mixture was filtered, diluted with H_2O (100 mL) and extracted with EtOAc (2 x 200 mL). The organic layer was washed with sat. NaHCO_3 (100 mL) and brine (100 mL), dried with MgSO_4 filtered and concentrated at reduced pressure. Flash chromatography (40% EtOAc/hexanes) afforded (\pm)-(S)-1-((S)-oxiran-2-yl)pent-4-en-2-ol as a colorless liquid (4.33 g, 33.8 mmol, 76%). Physical data were in agreement with previously reported values:^{2,3} $R_f = 0.42$ (silica gel, 50% EtOAc/hexanes); ^1H NMR (500 MHz, CDCl_3) δ_{H} 1.54–1.61 (1H, m), 1.88 (1H, td, $J=14.40, 4.07$ Hz), 2.15 (1H, d, $J=3.09$ Hz), 2.24–2.30 (1H, m), 2.31–2.37 (1H, m), 2.53 (1H, dd, $J=4.95, 2.74$ Hz), 2.80 (1H, dd, $J=4.79, 4.14$ Hz), 3.11 (1H, dtd, $J=7.09, 4.18, 2.75$ Hz), 3.91–3.98 (1H, m), 5.14–5.19 (2H, m), 5.79–5.88 (1H, m); ^{13}C NMR (125 MHz, CDCl_3) δ_{C} 39.2, 42.1, 46.8, 50.6, 69.4, 118.7, 134.4.

The alcohol (10.0 g, 78 mmol) resulting from the above methanolysis step was dissolved in dry DCM (100 mL) and cooled to 0 °C under inert atmosphere. DIPEA (68 mL, 390 mmol) was added by syringe followed by MOMCl (45 mL of a 3.5 M solution

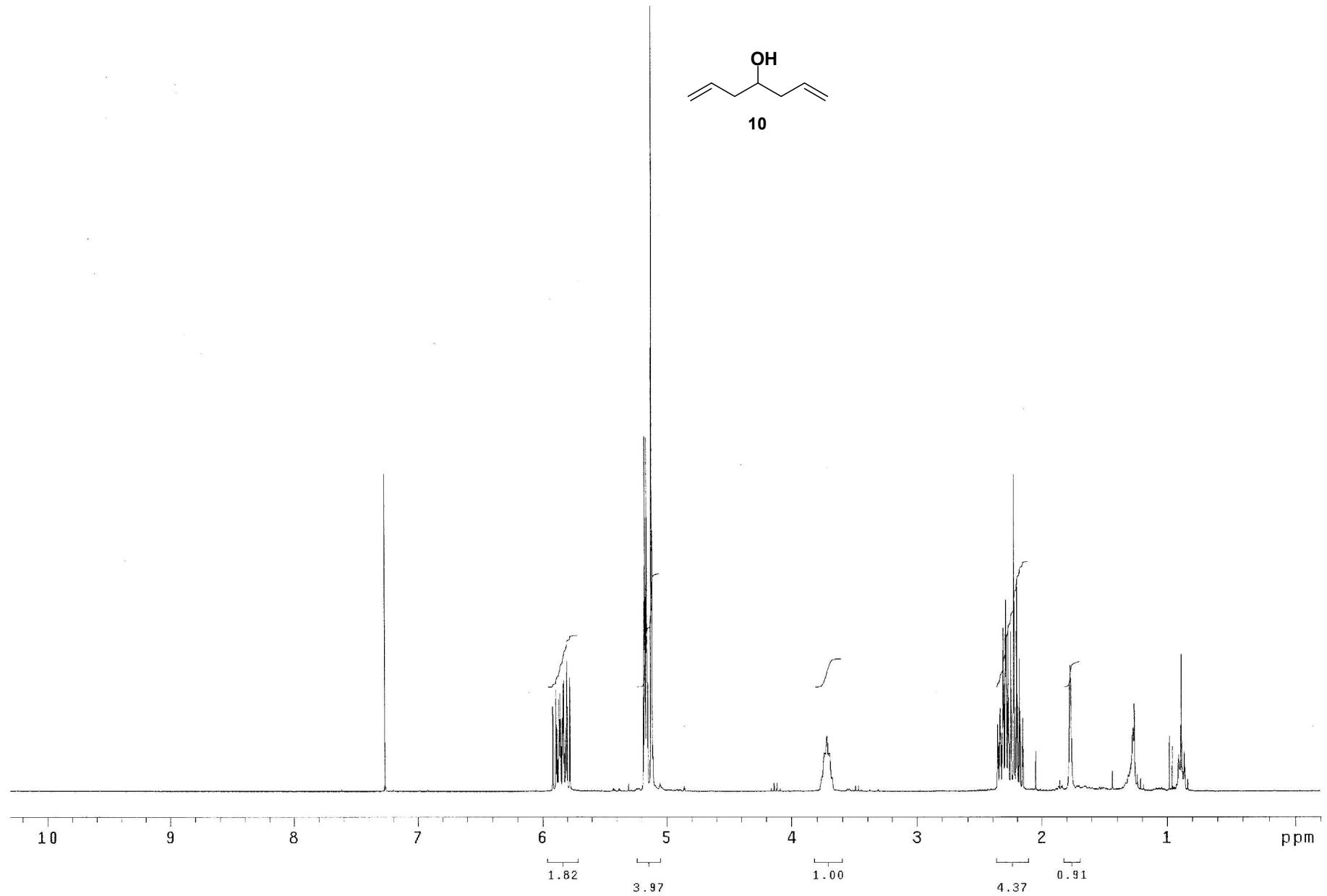
³ Palombi, L.; Bonadies, F.; Scettri, A. *Tetrahedron* **1997**, 53(33), 11369–11376.

in toluene, 156 mmol). The mixture was warmed to room temperature and allowed to stir for 24 hours. The reaction was quenched with sat. NH₄Cl (50 mL), allowed to stir for 10 min, then the organic layer was separated. The aqueous layer was extracted with DCM (2 x 50 mL) and the combined organic layers washed with water (50 mL) and brine (50 mL). The residue obtained after drying with MgSO₄, filtering, and evaporating *in vacuo* was purified by flash chromatography (10→20% EtOAc/hexanes), and **rac-5** was isolated as a colorless liquid (13.0 g, 75.6 mmol, 97%). **Rac-5:** R_f = 0.27 (silica gel, 10% EtOAc/hexanes); ¹H NMR (500 MHz, CDCl₃) δ _H 1.76 (1H, ap. t, J = 5.67 Hz), 2.38 (1H, ap. t, J = 6.60 Hz), 2.47 (1H, dd, J = 5.04, 2.71 Hz), 2.76 (1H, ap. t, J = 4.47 Hz), 3.01–3.07 (1H, m), 3.38 (3H, s), 3.77–3.87 (1H, m), 4.67 (1H, d, J = 7.01 Hz), 4.70 (1H, d, J = 7.01 Hz), 5.05–5.15 (2H, m), 5.75–5.89 (1H, m); ¹³C NMR (125 MHz, CDCl₃) δ _C 37.3, 39.1, 46.8, 49.7, 55.8, 75.0, 95.5, 117.8, 134.5; HRMS calcd for C₉H₁₆NaO₃ [M + Na]⁺ 195.0992, found: 195.0984.

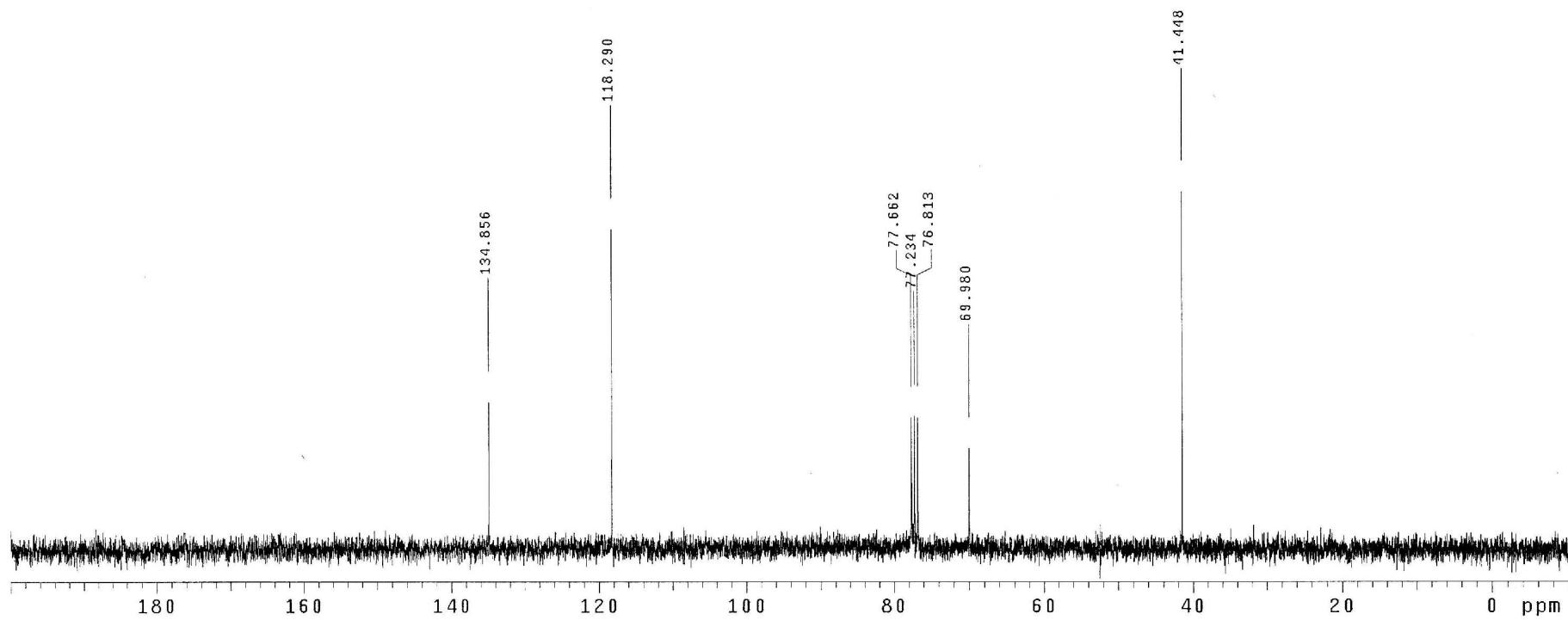
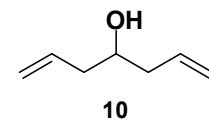


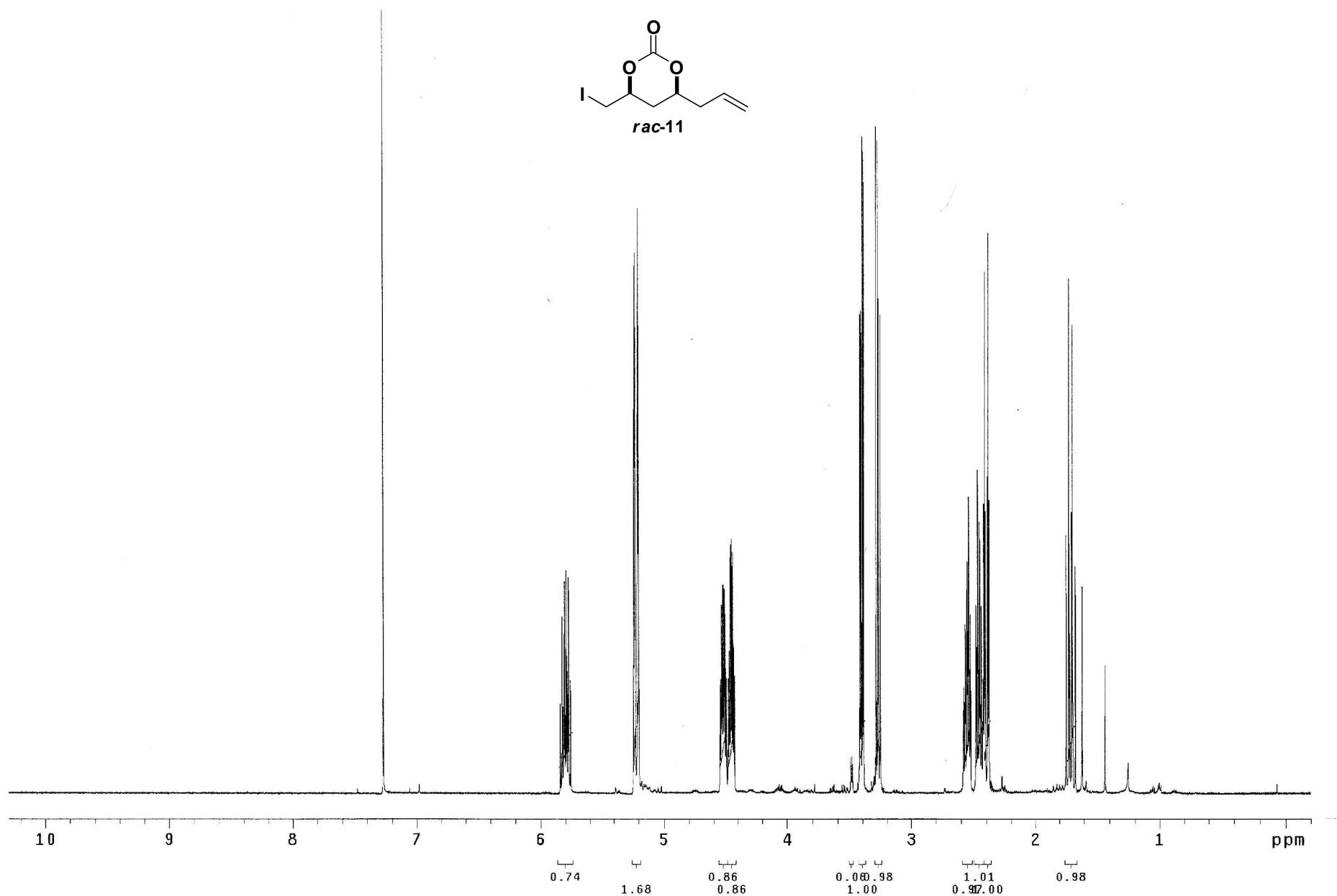
(S)-2-((S)-2-(Methoxymethoxy)pent-4-enyl)oxirane (5). To a stirred solution of toluene (1 mL) and acetic acid (0.06 mL, 0.98 mmol) was added (*S,S*)-(+)−N,N'-Bis(3,5-di-*tert*-butylalicylidene)-1,2-cyclohexanediaminocobalt(II) (147 mg, 0.24 mmol), and the solution was allowed to stir open to air for 30 minutes before concentration under vacuum. To the resulting black solid was added THF (5 mL) and **rac-5** (8.4 g, 49 mmol). The solution was then cooled to 0 °C, and H₂O (0.48 mL, 26.8 mmol) was added dropwise. The reaction was allowed to warm to room temperature and stir for an

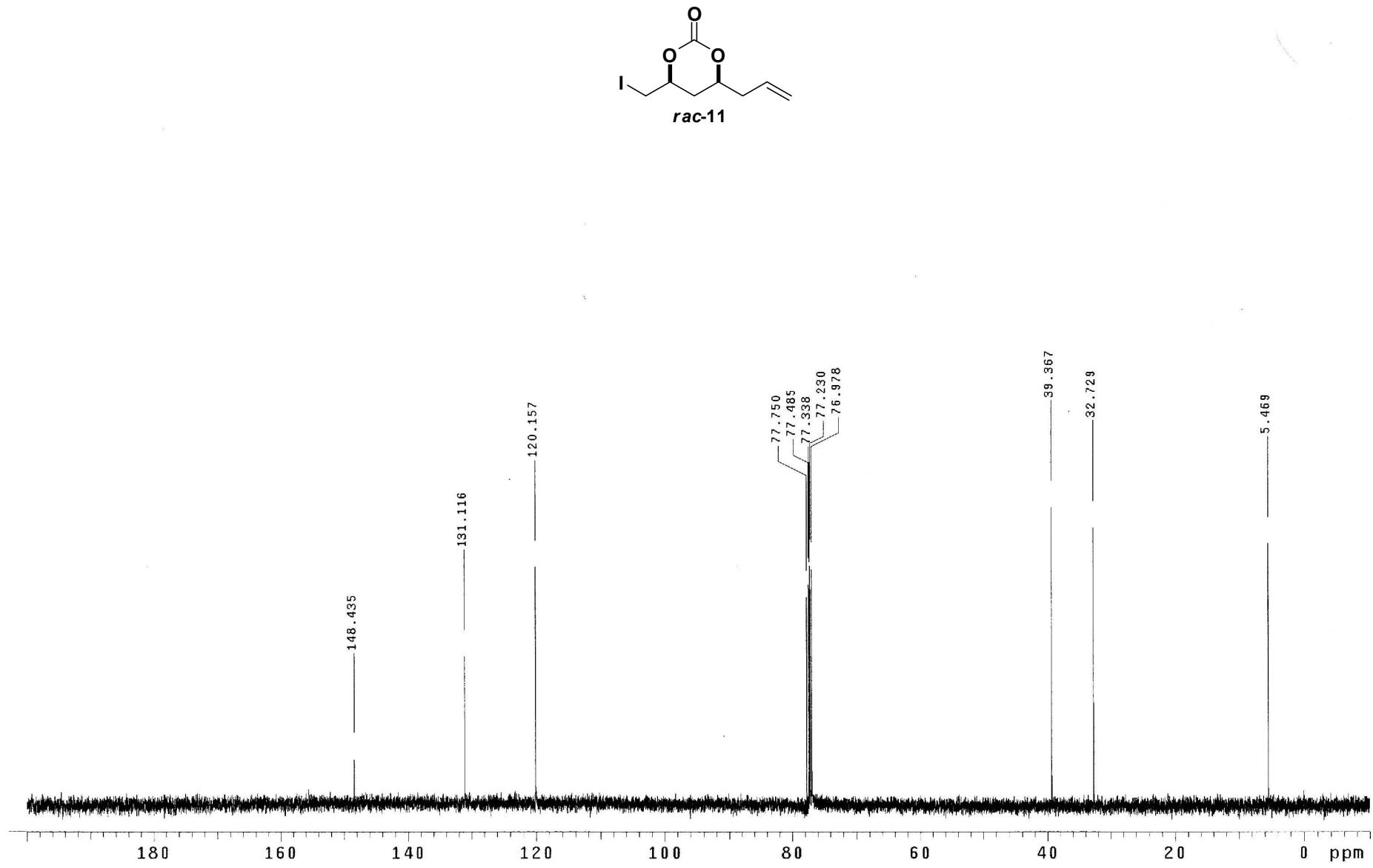
additional 16 hours. Diethyl ether (30 mL) was added to dilute the reaction and the solution was filtered through a pad of Celite® and the solvent was removed under reduced pressure. Flash chromatography (0→15% EtOAc/hexanes) afforded **5** as a colorless oil (4.1 g, 24 mmol, 49%). $[\alpha]^{20}_D = +20.46^\circ$ (*c.* 1.3, CHCl₃); NMR: see *rac*-**5**.

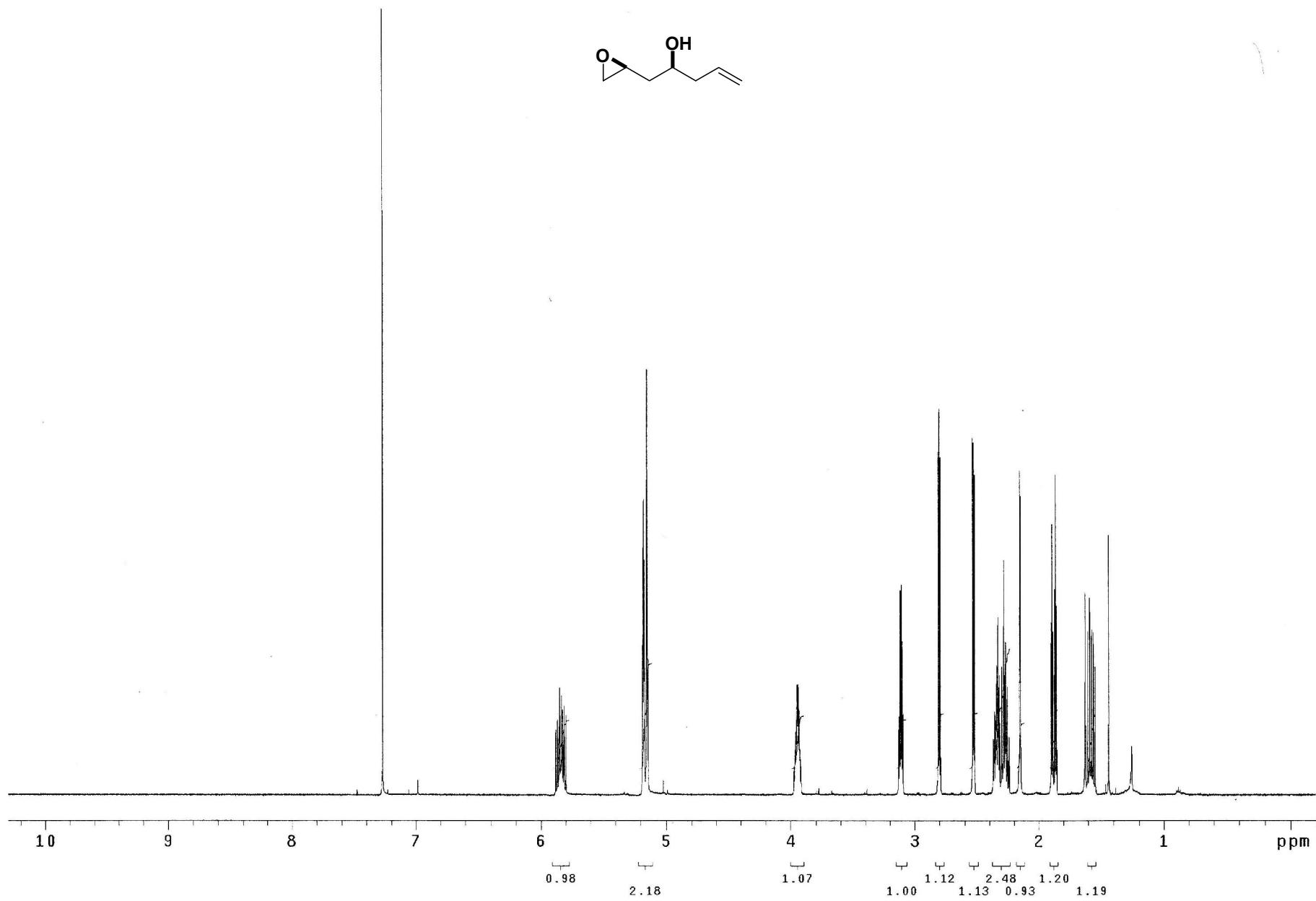


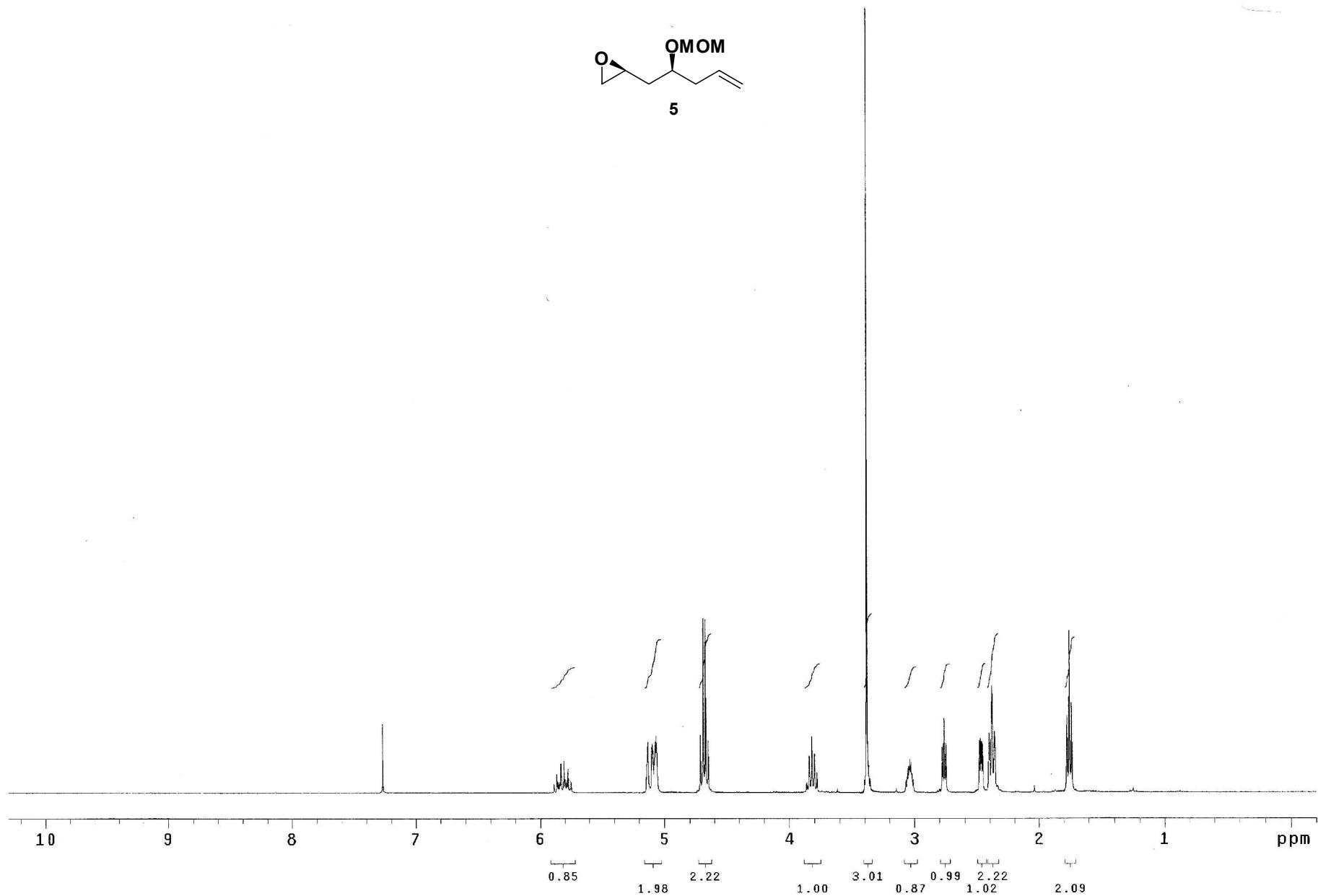
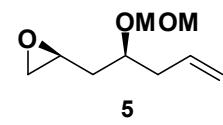
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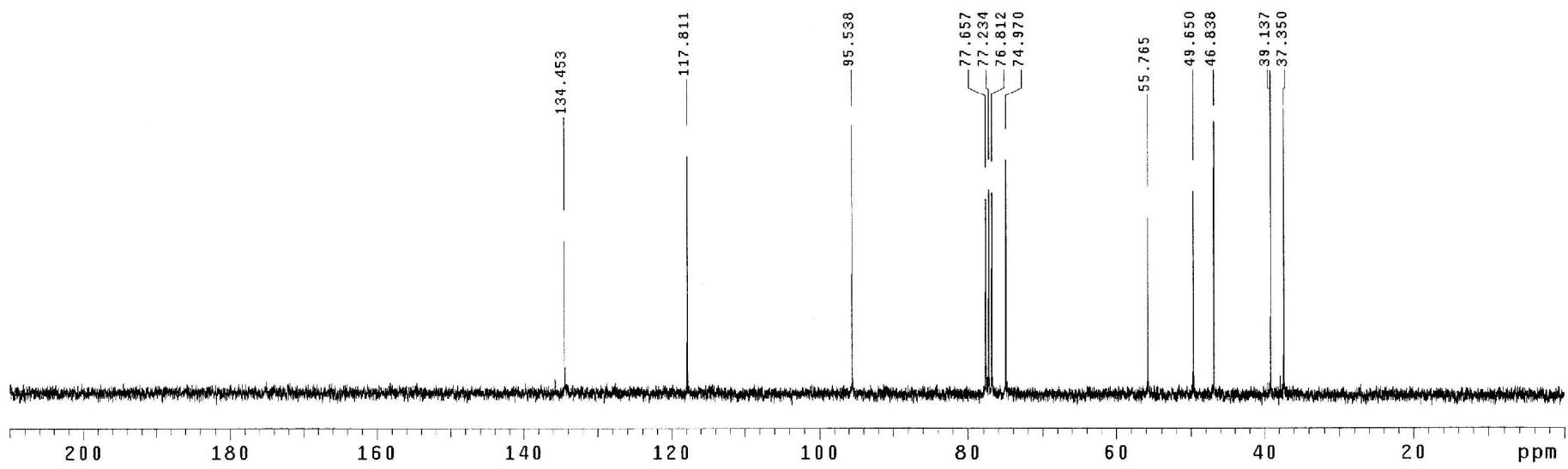
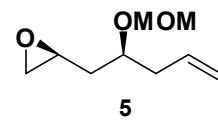


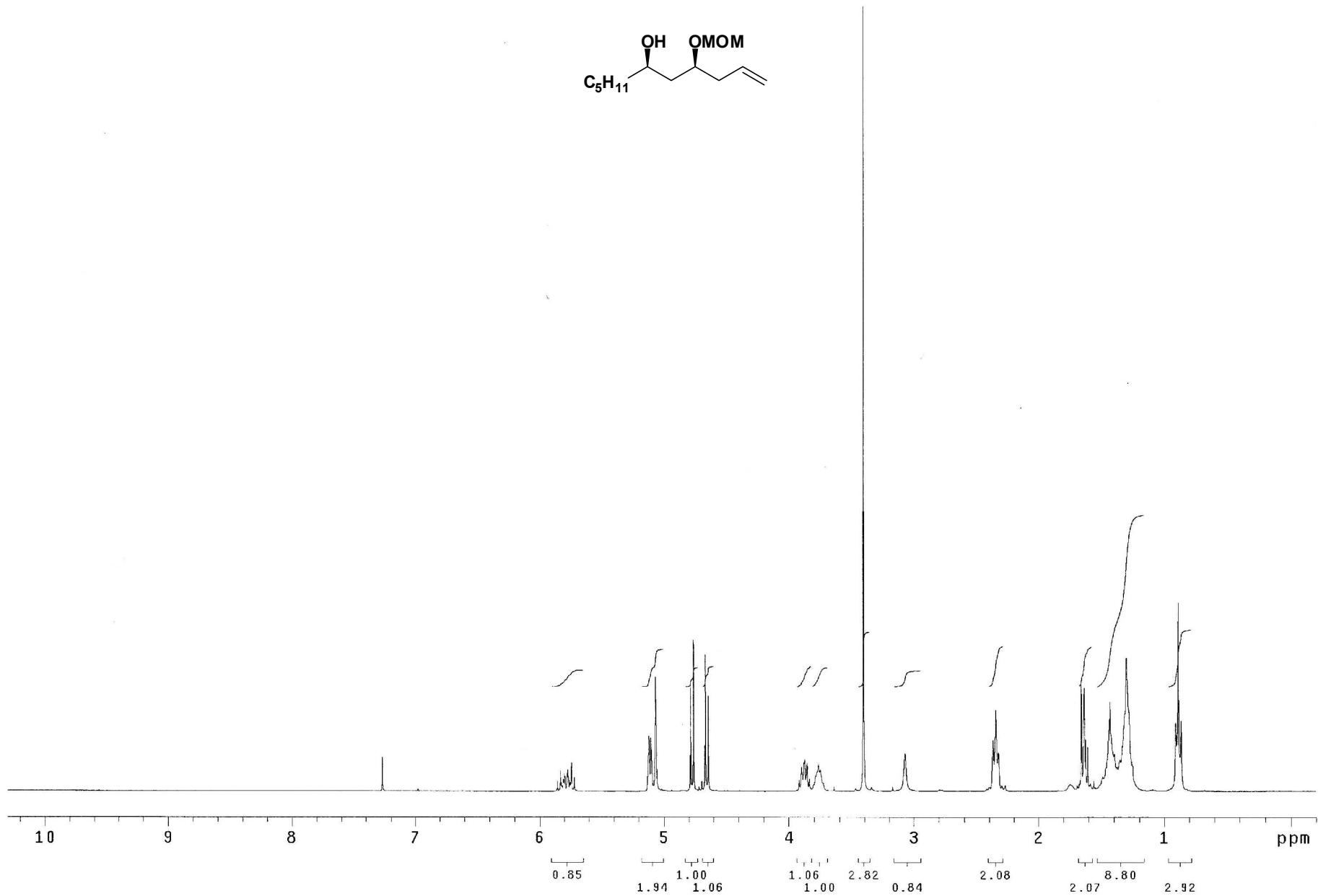
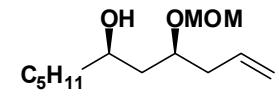


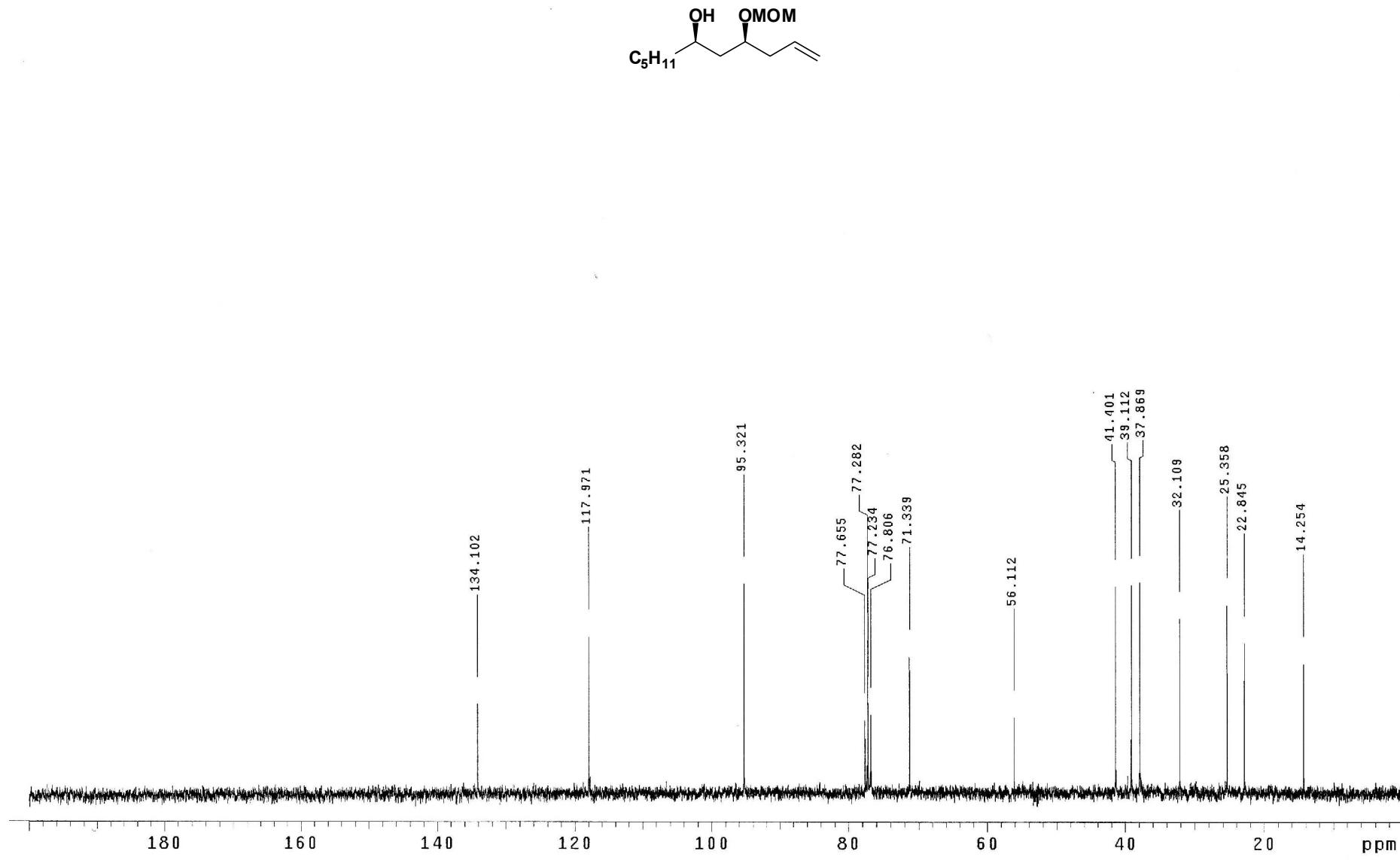


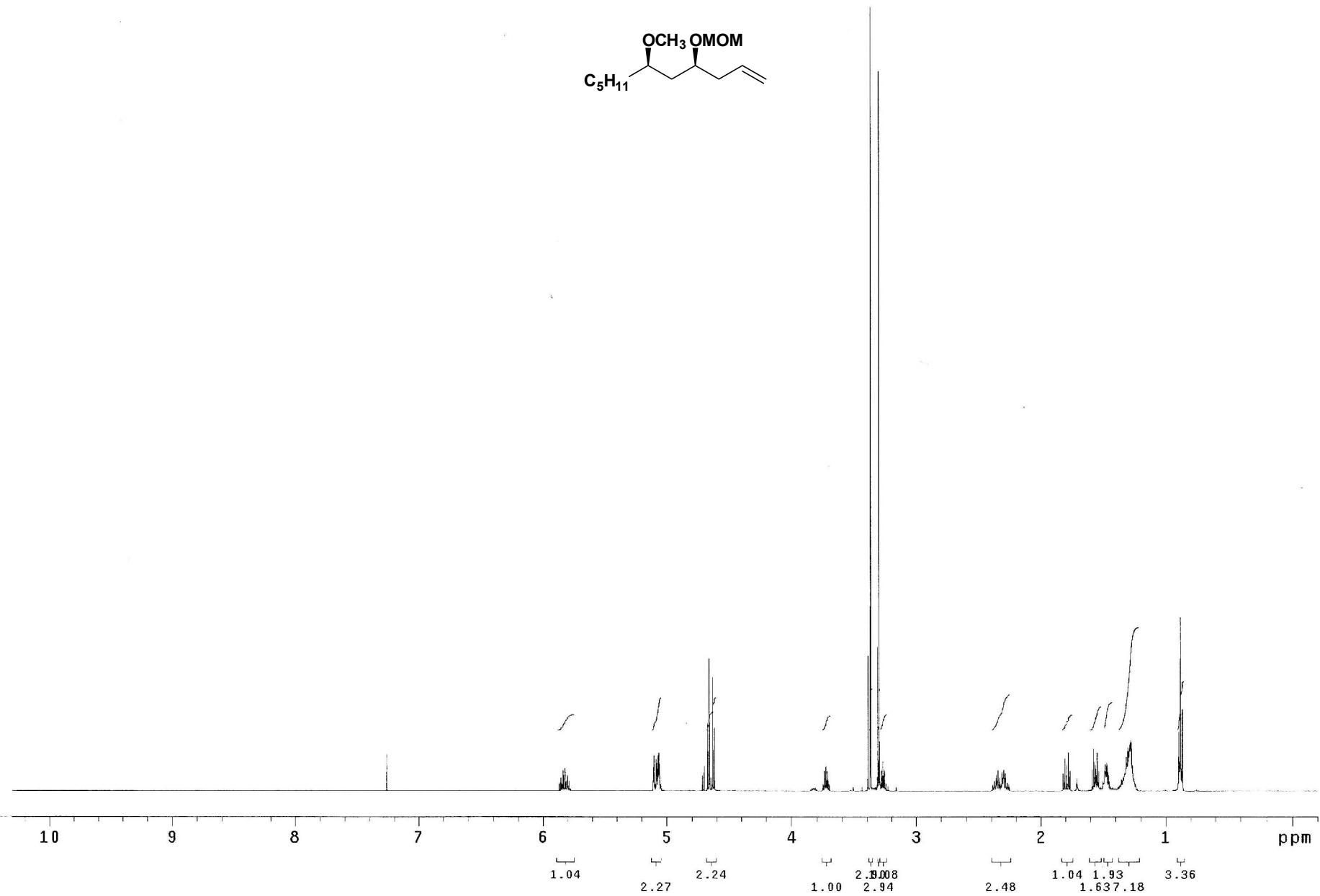


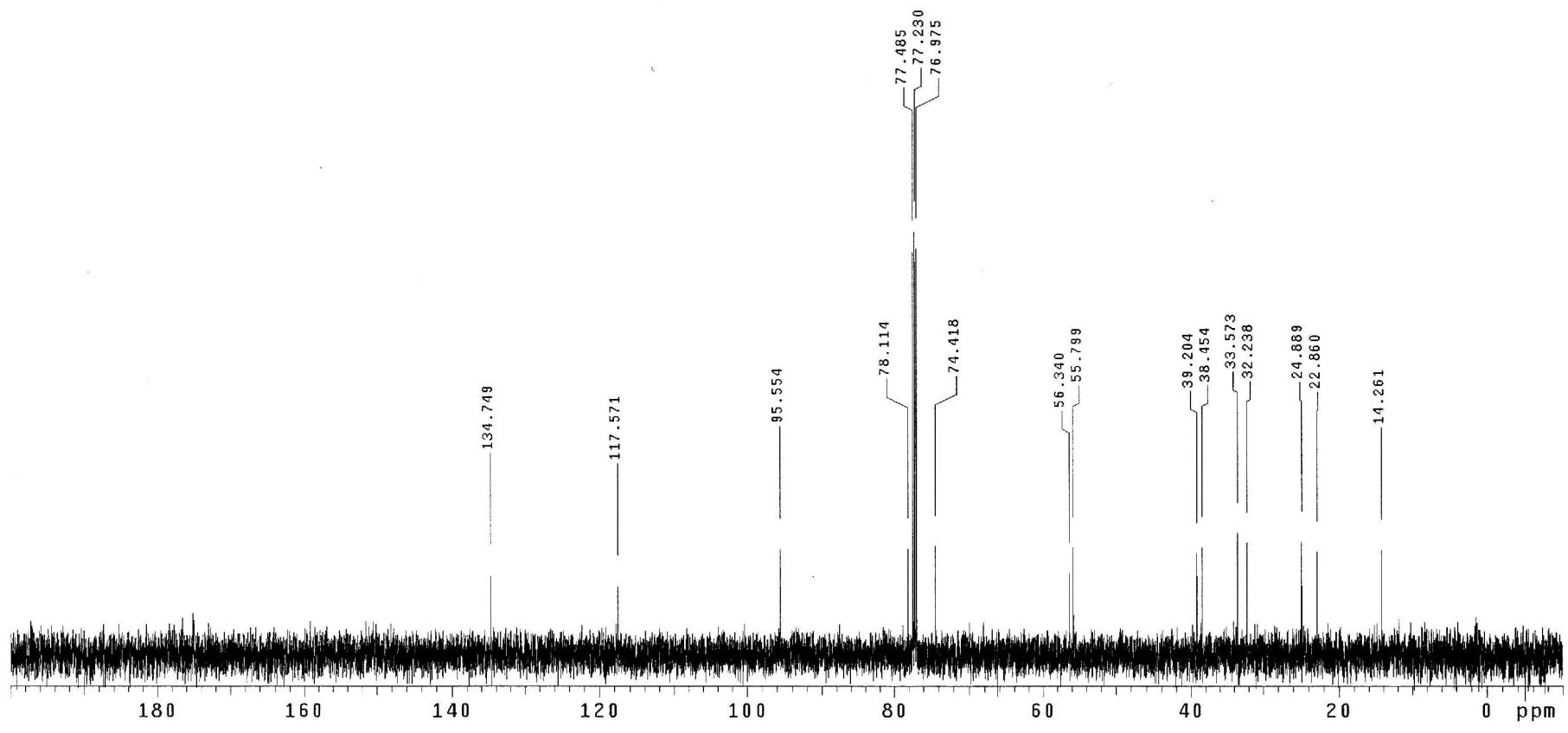


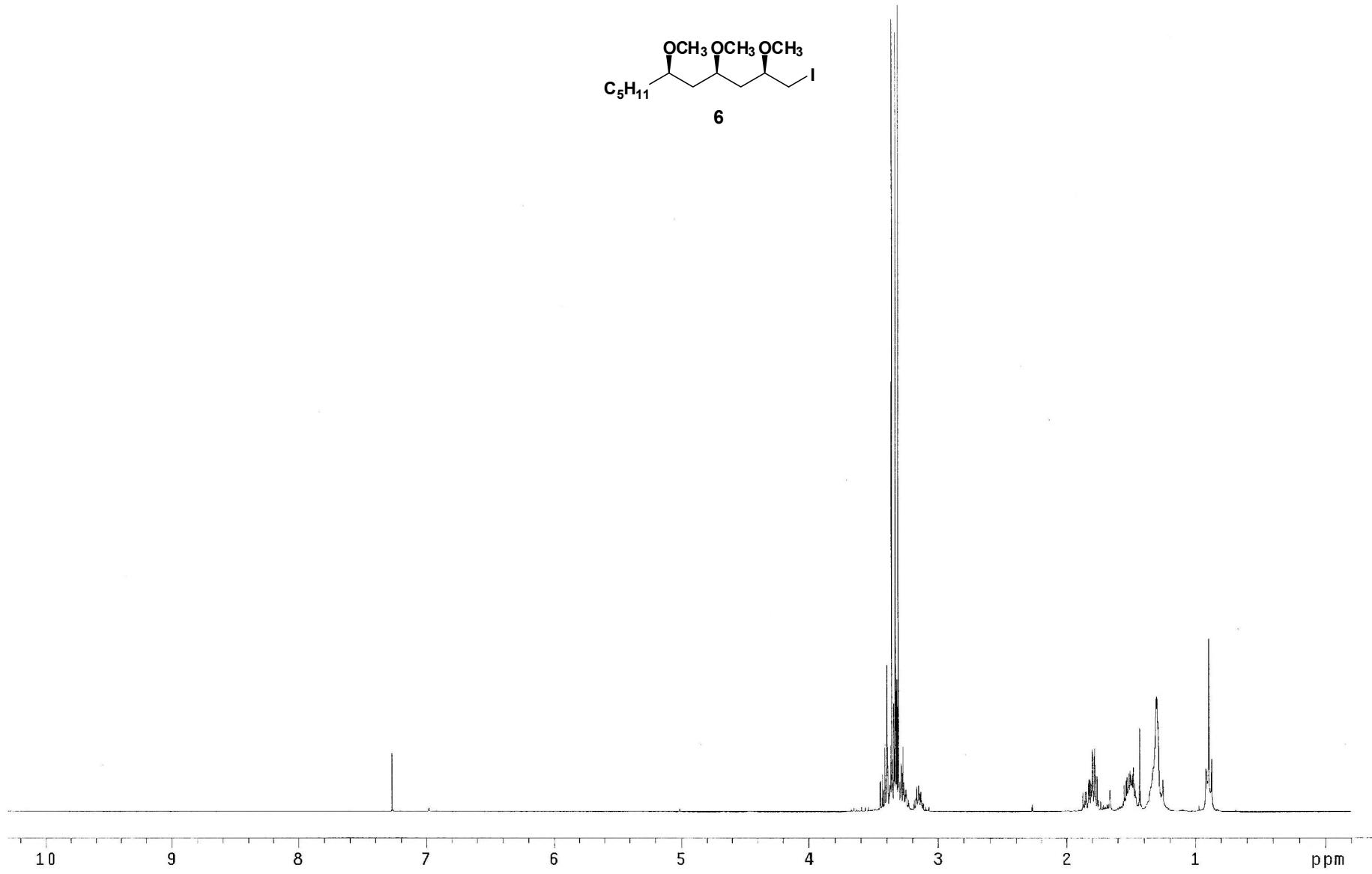
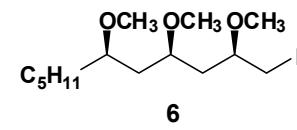




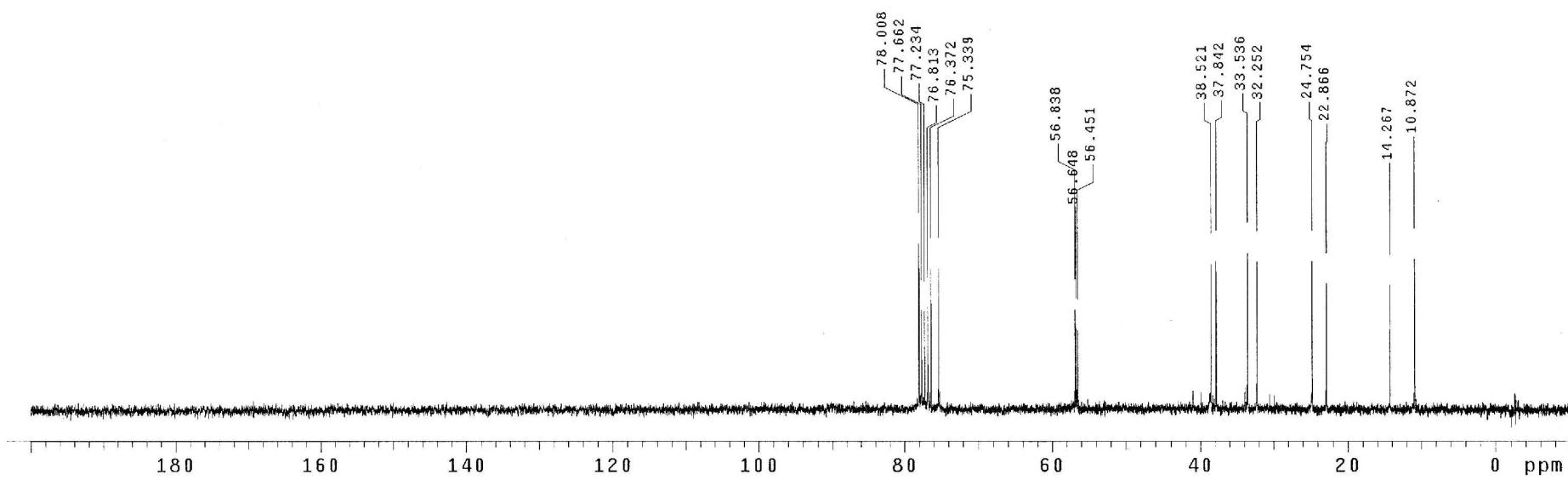
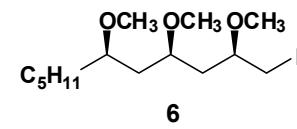


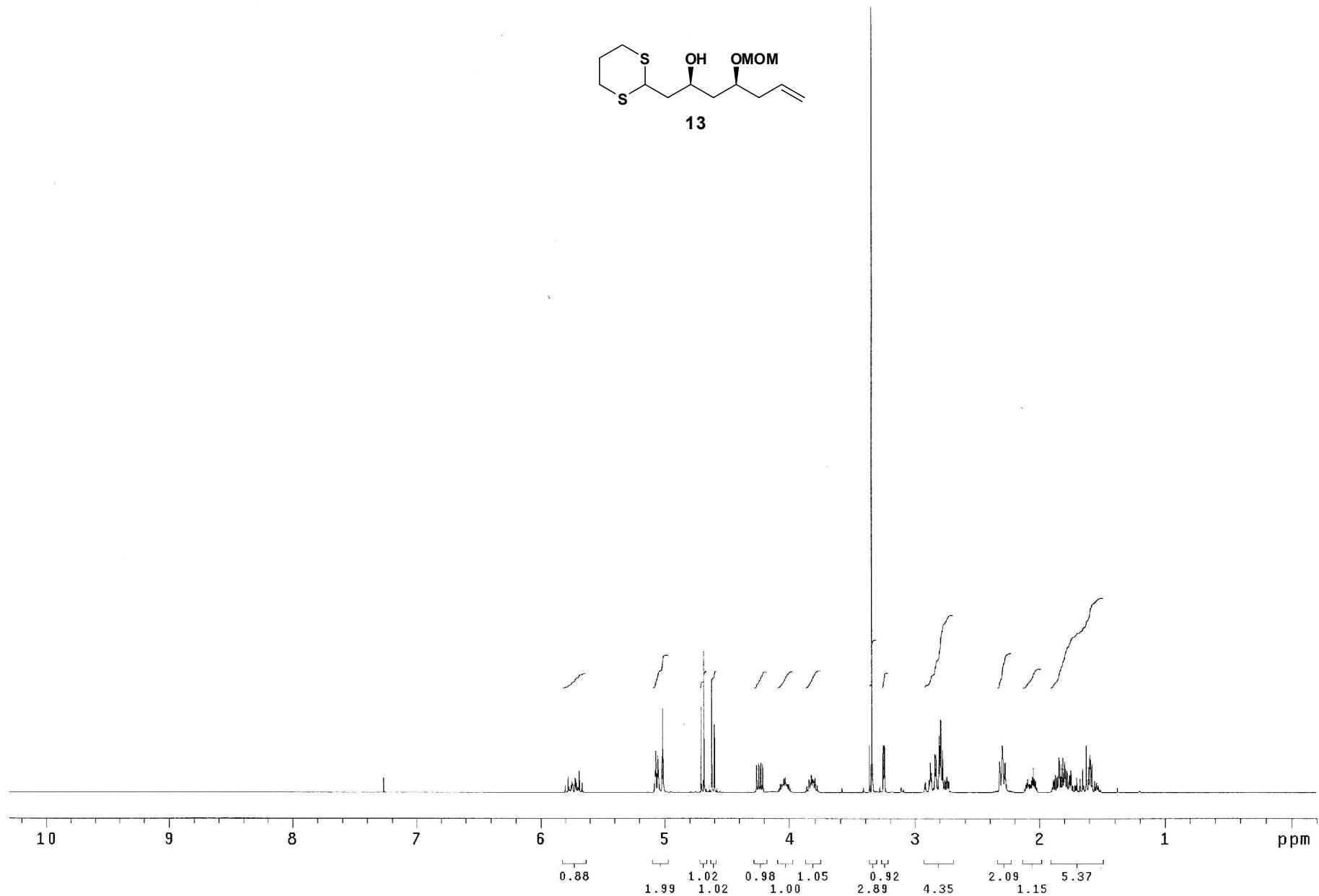
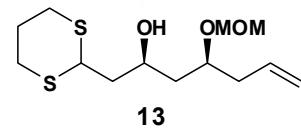


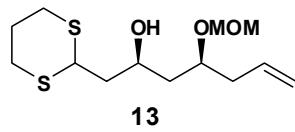
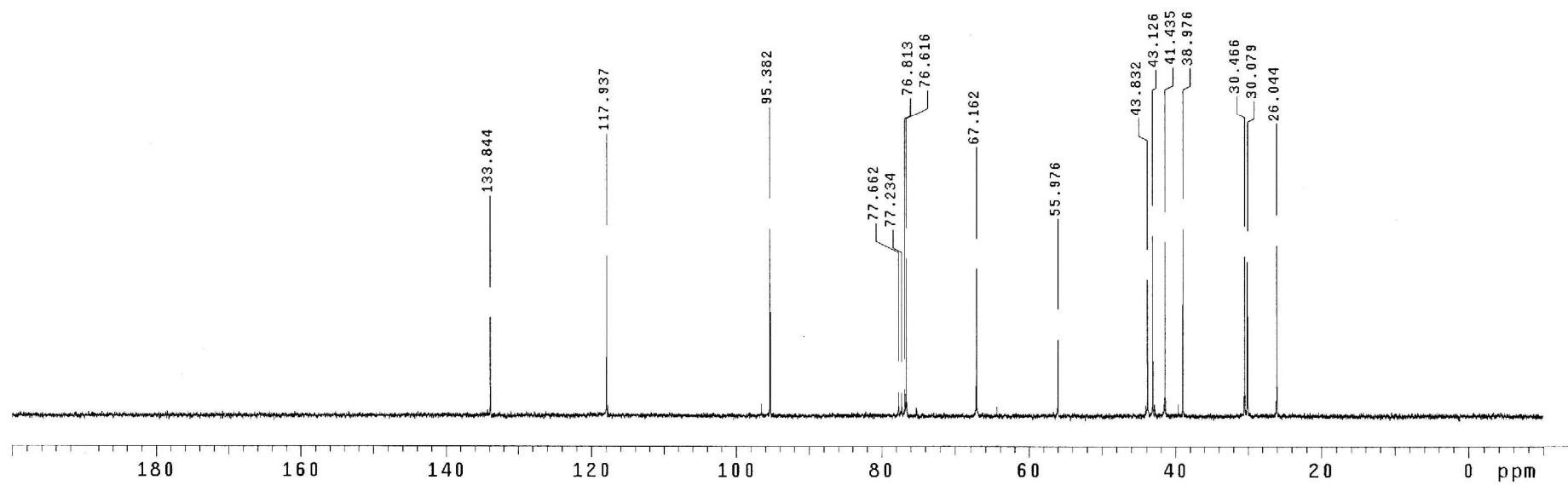


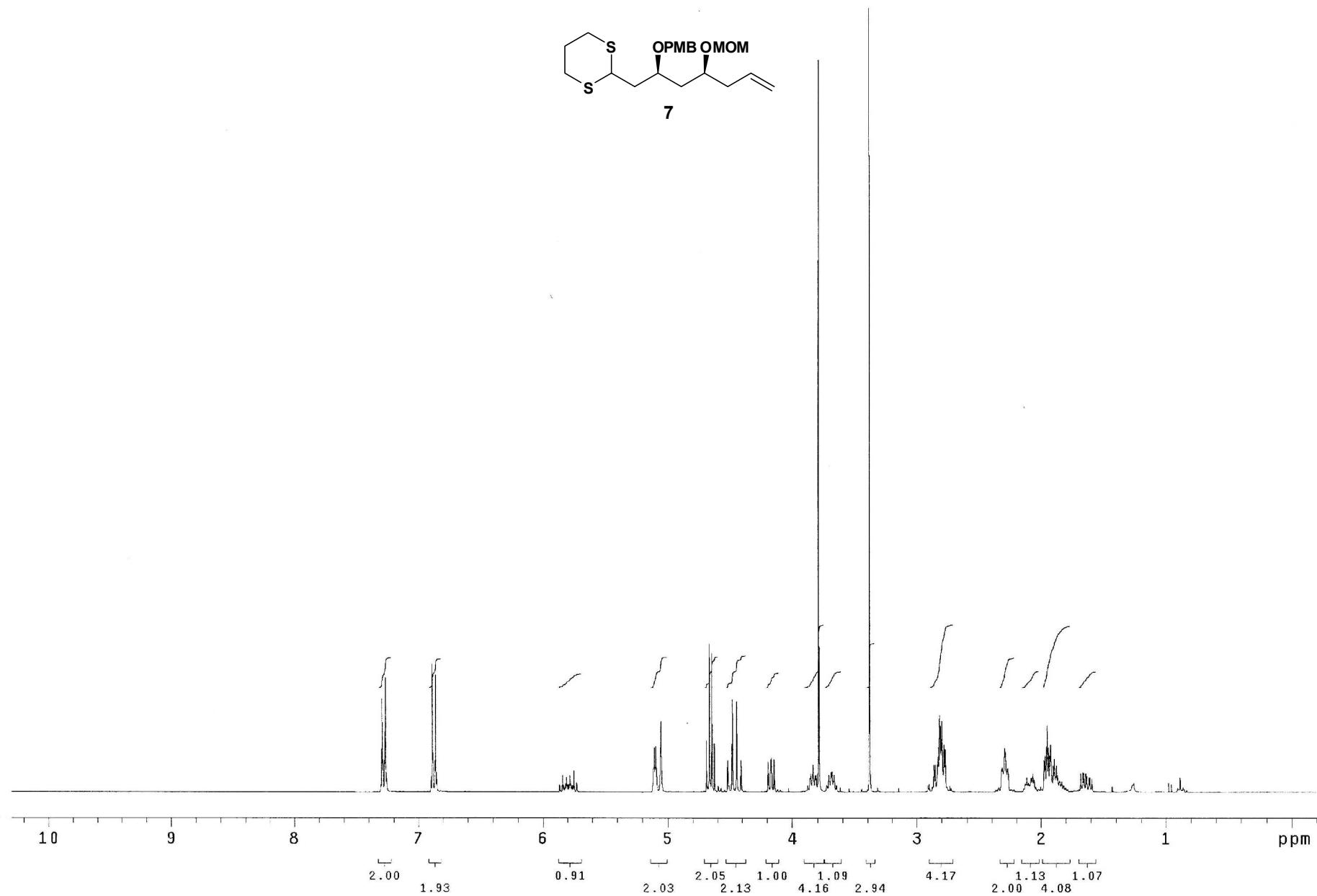


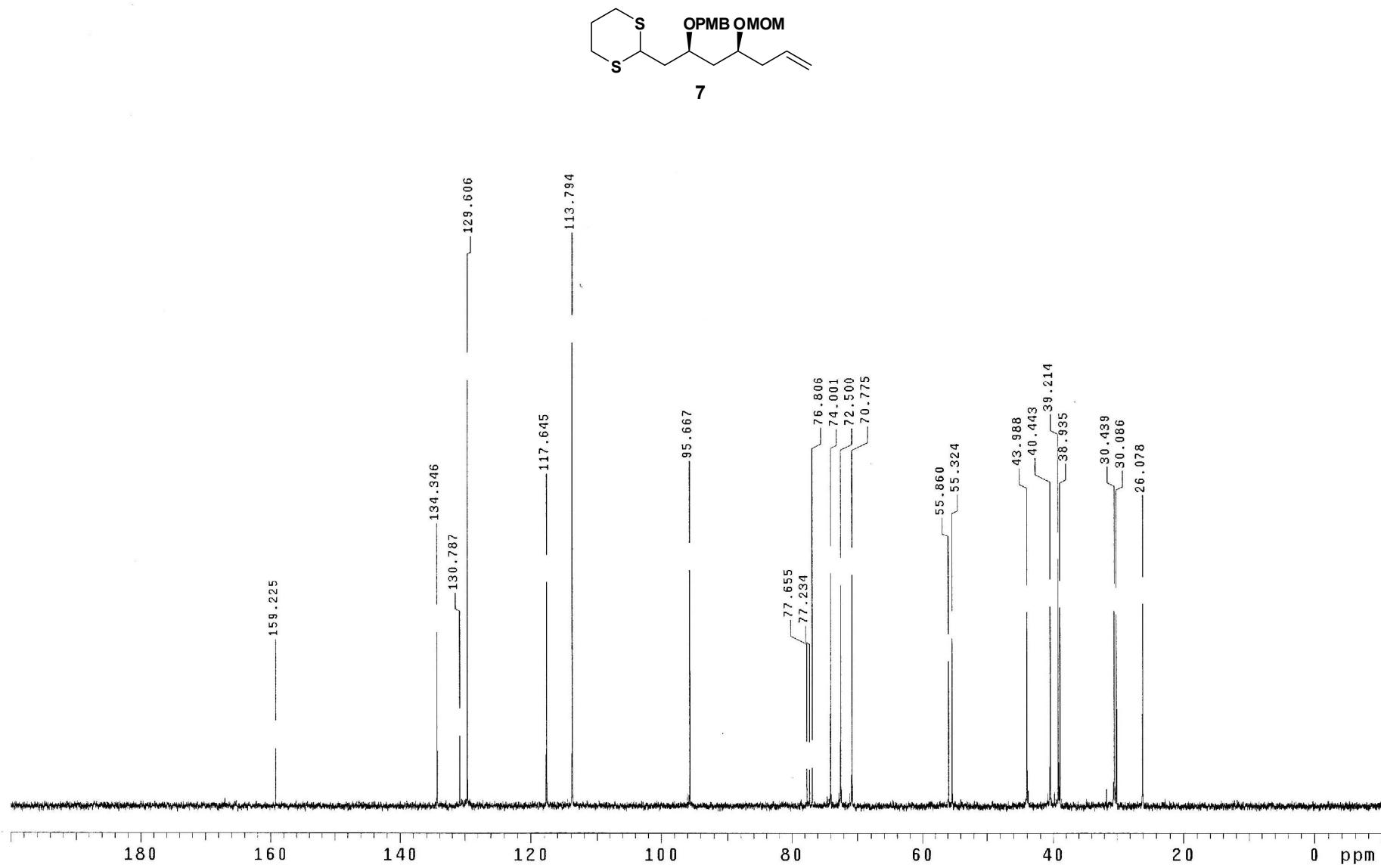
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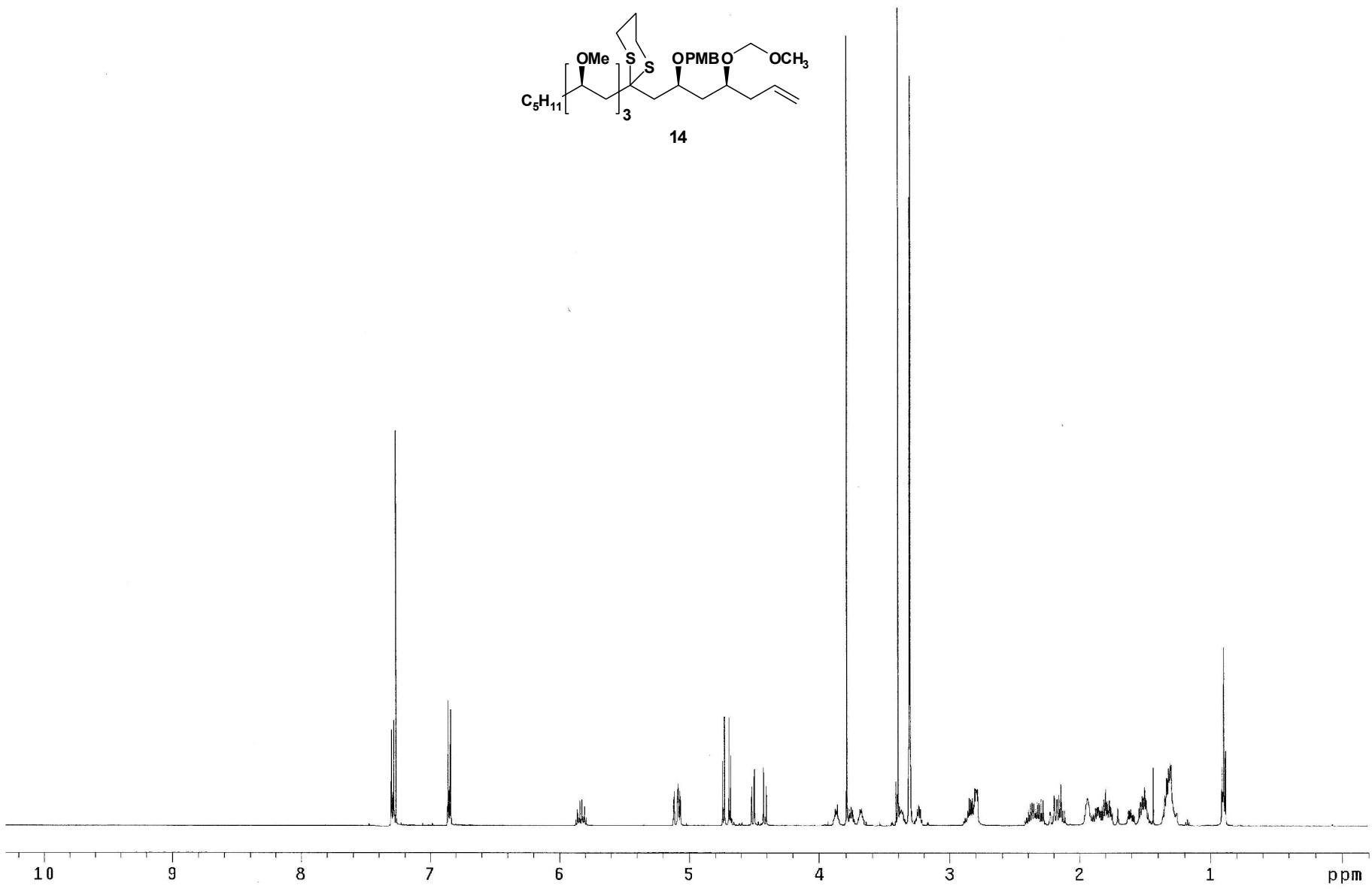
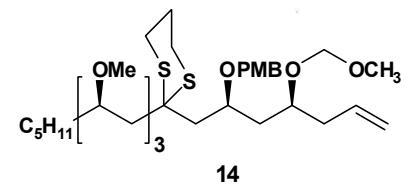


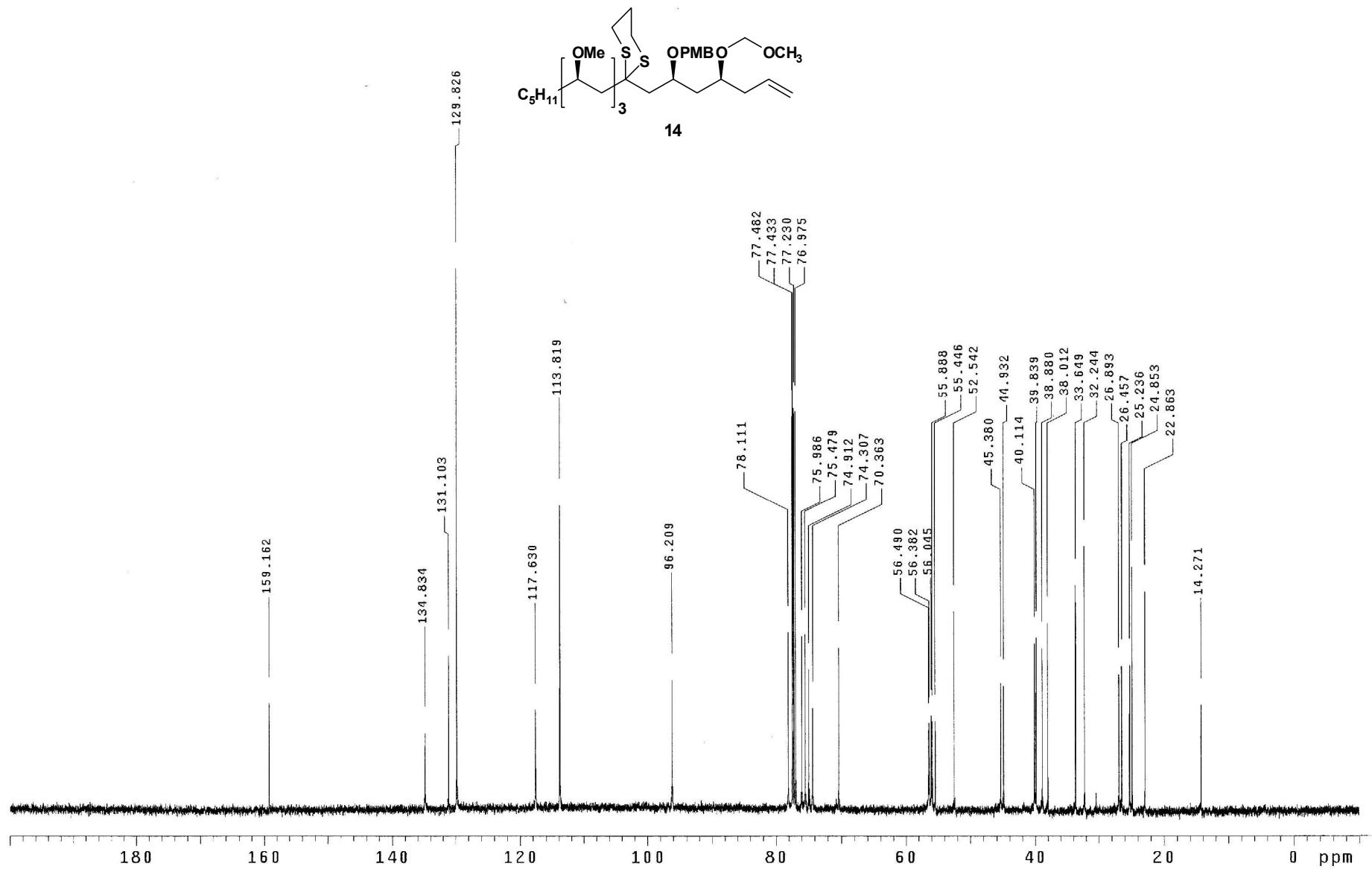


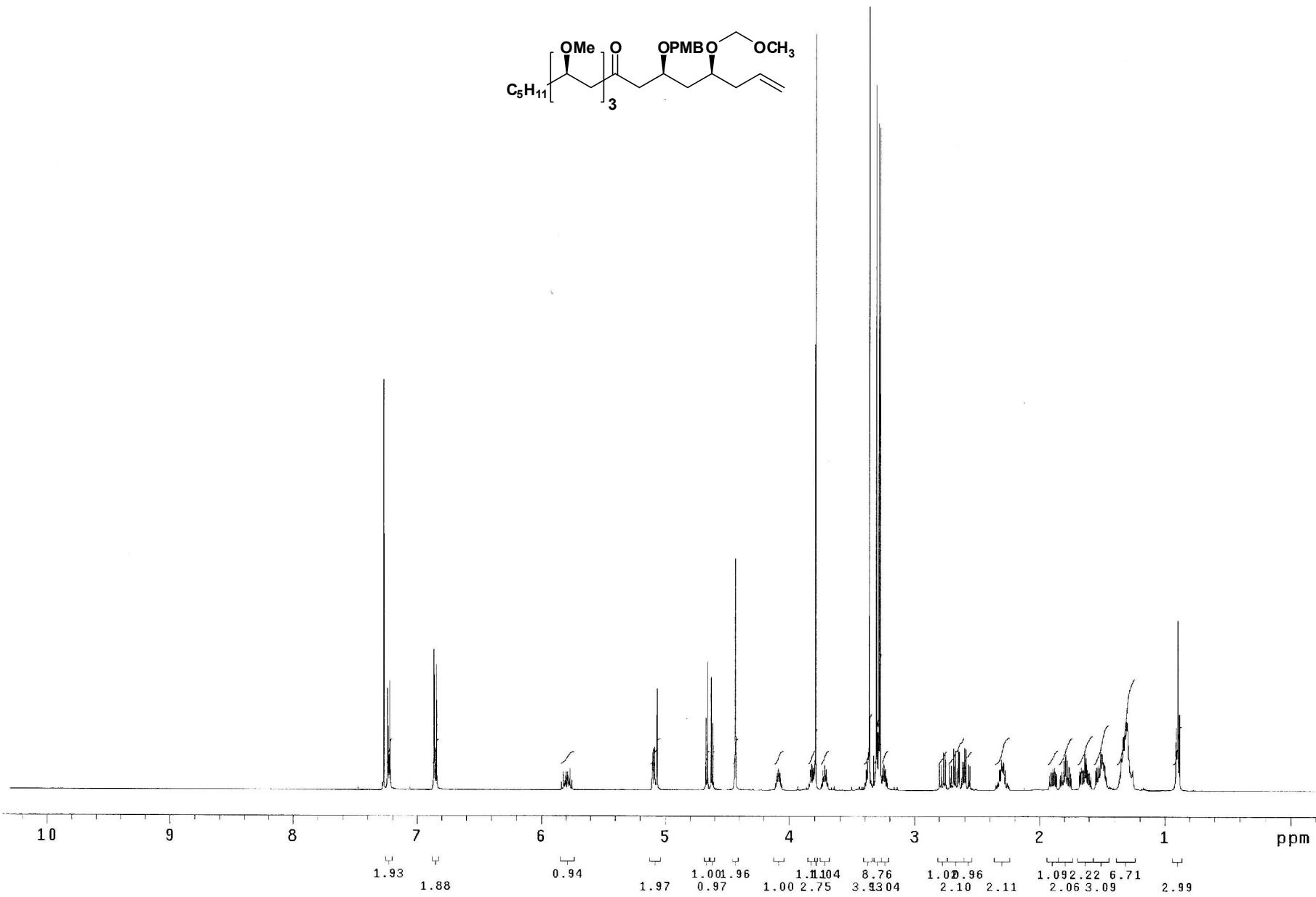


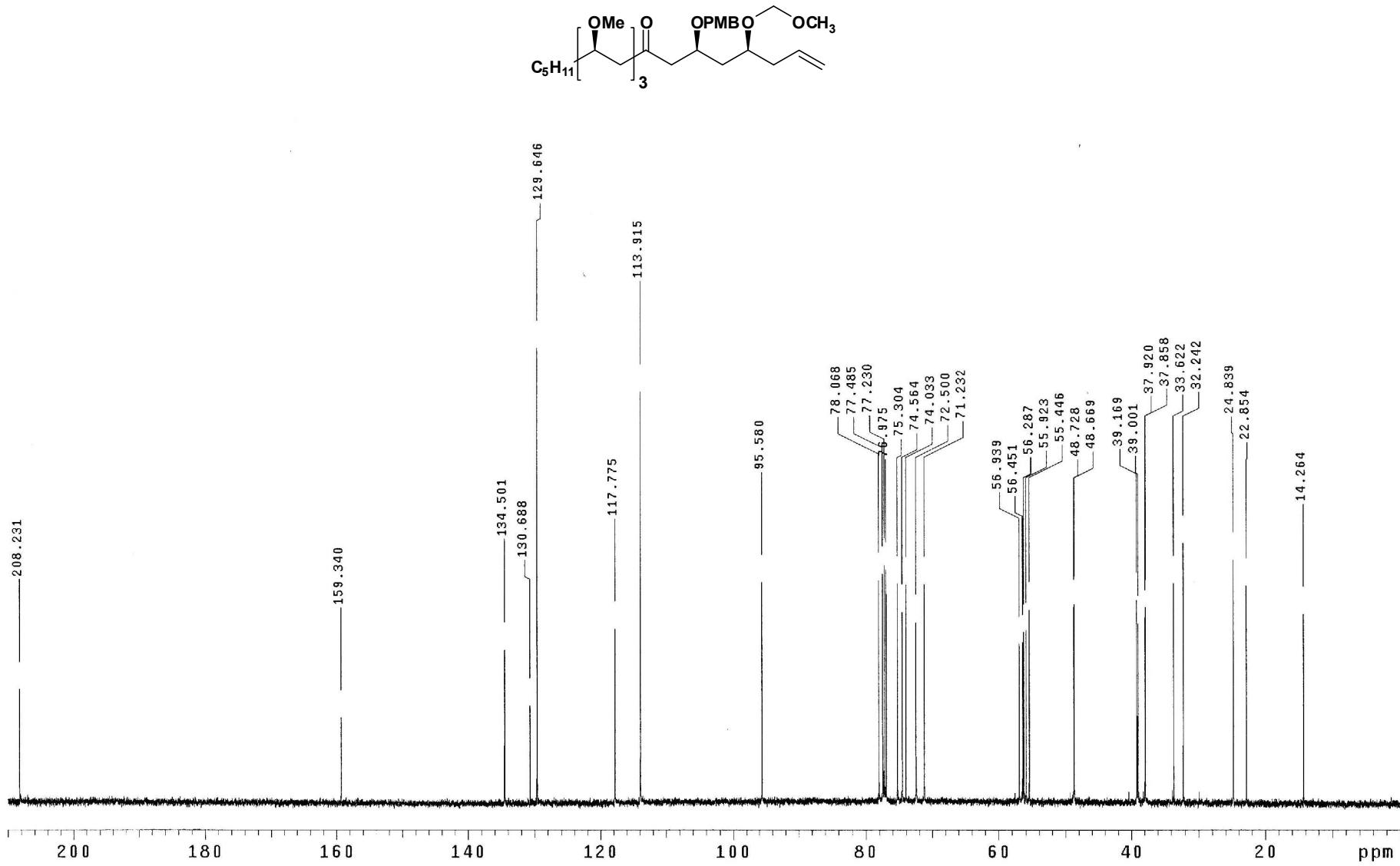


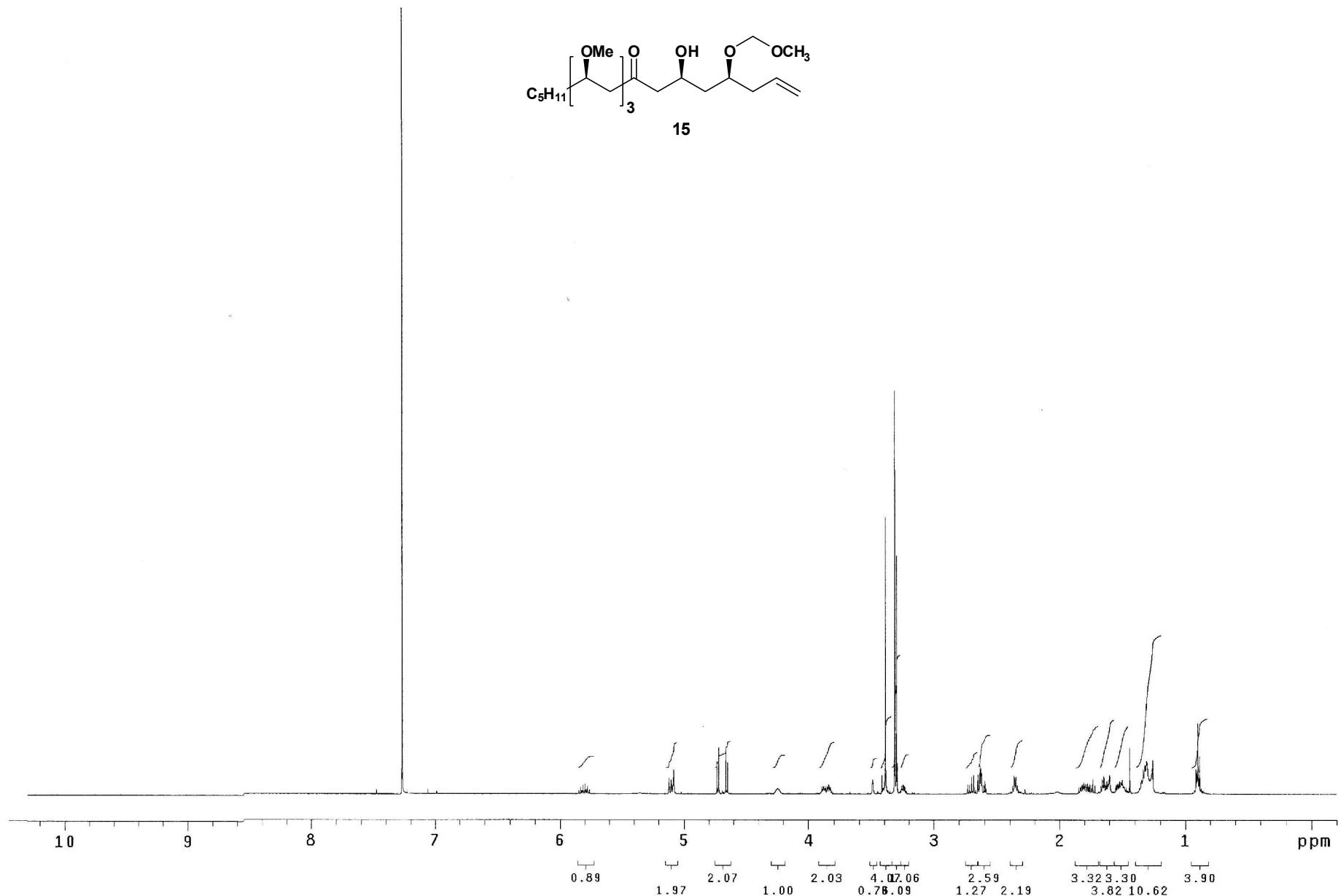


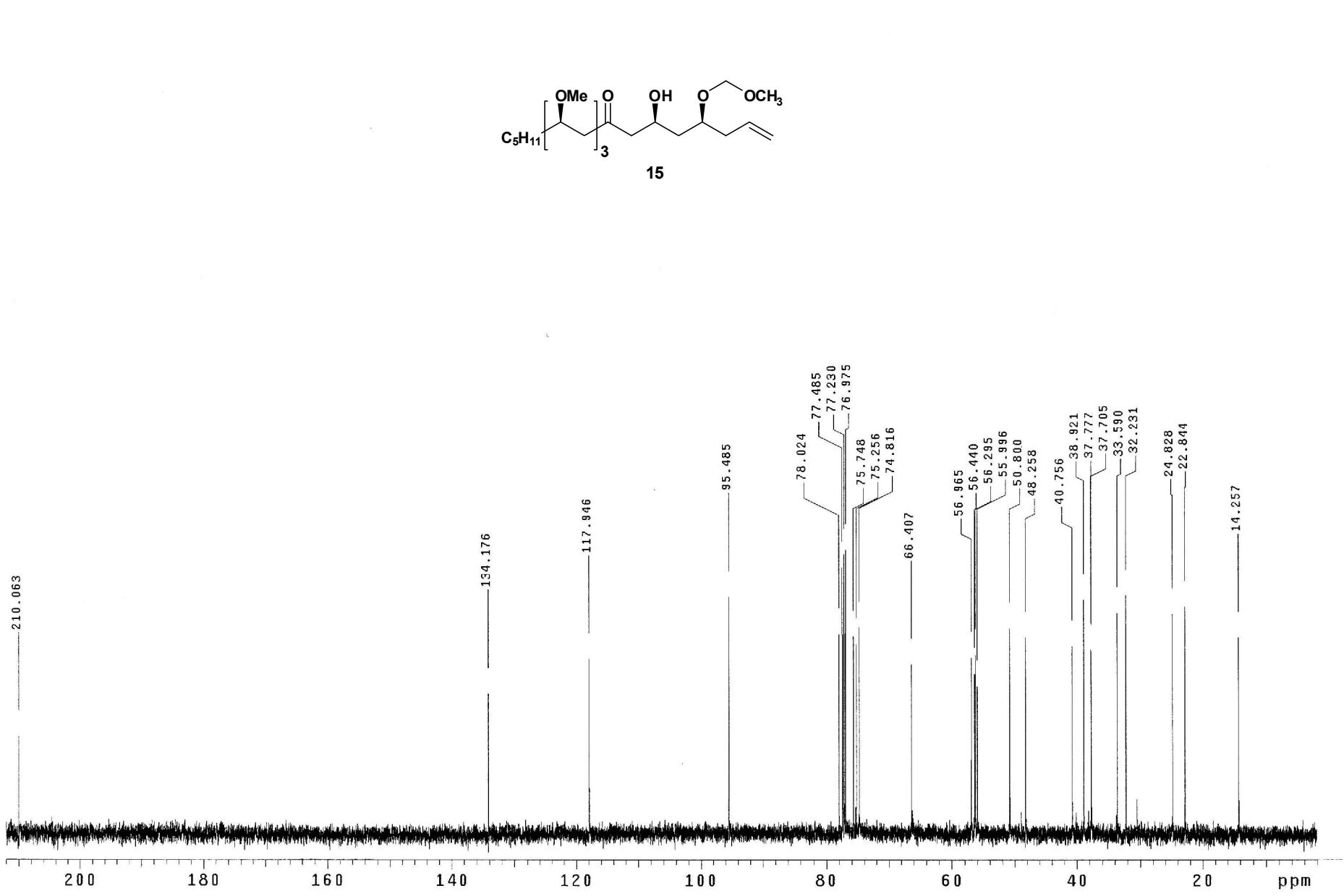


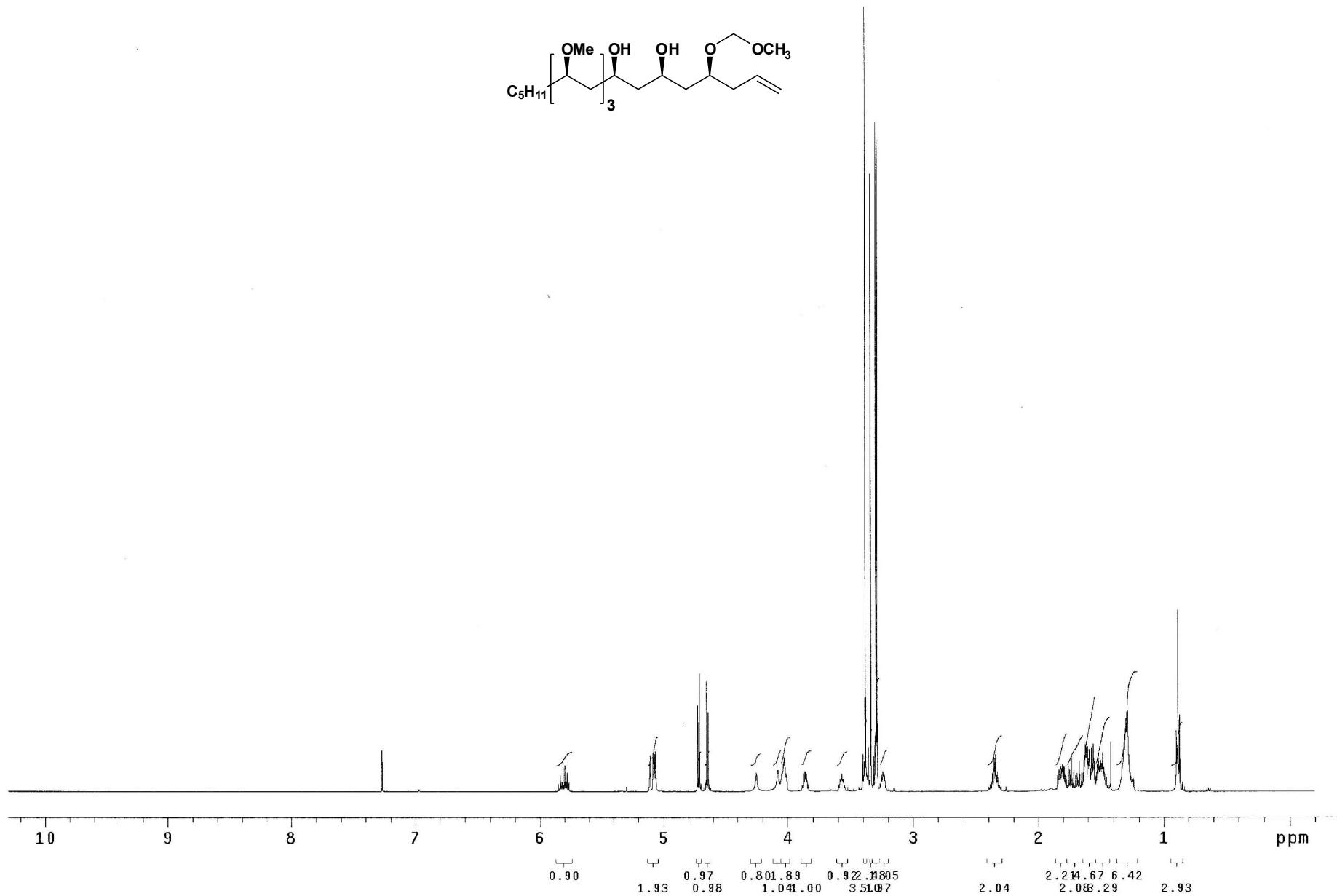


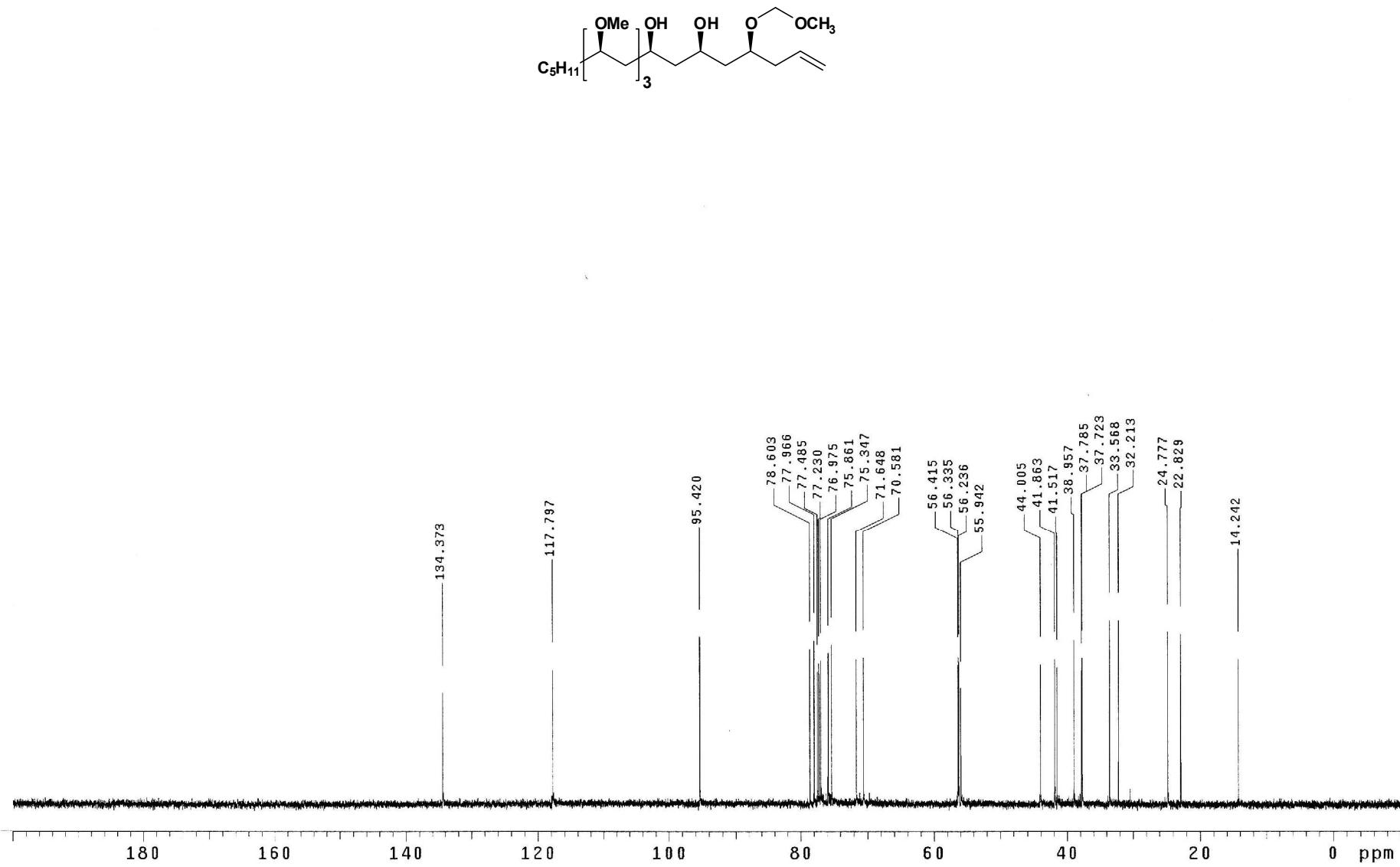


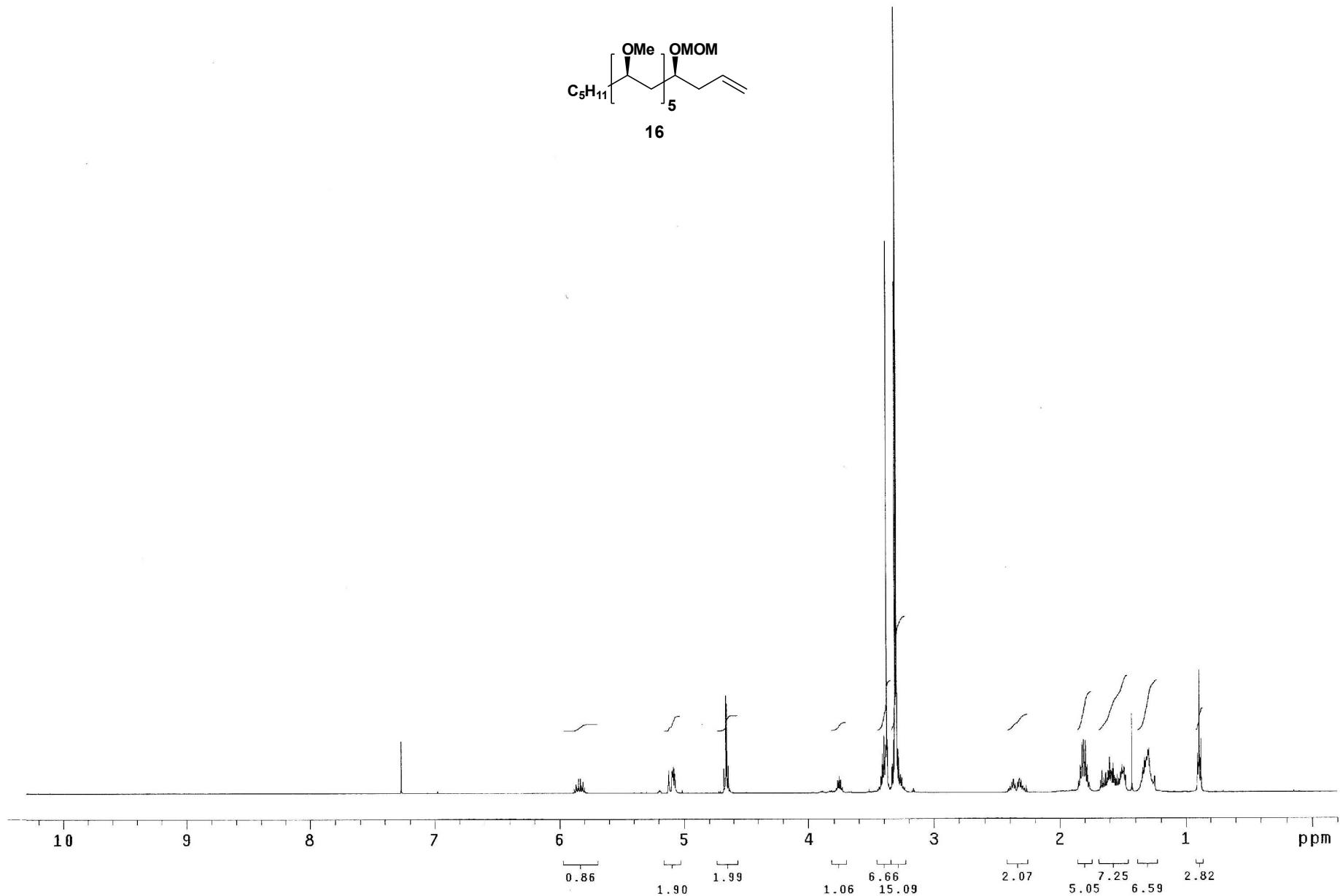
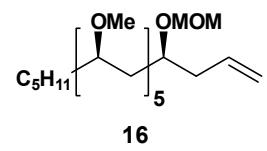


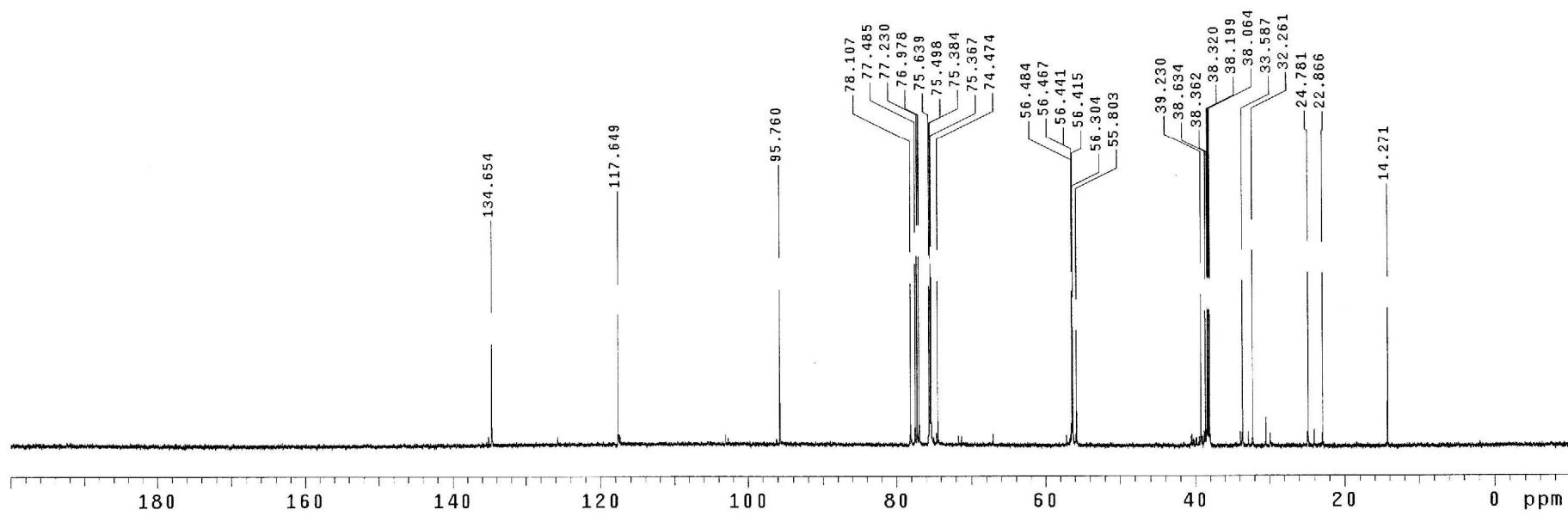
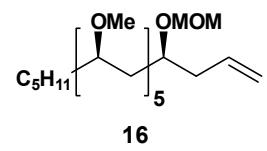




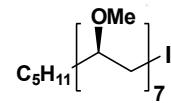




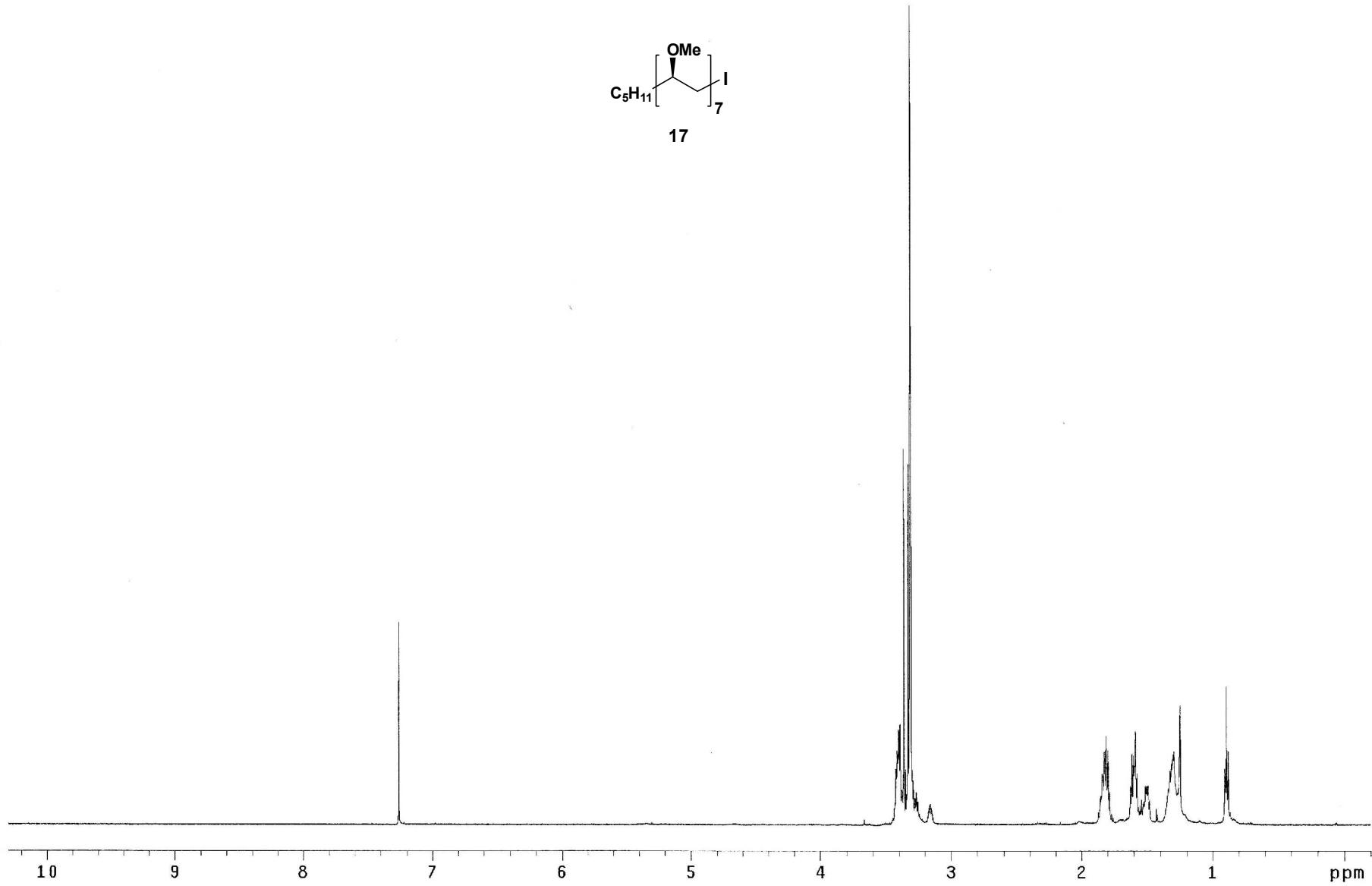


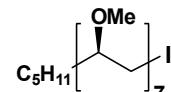


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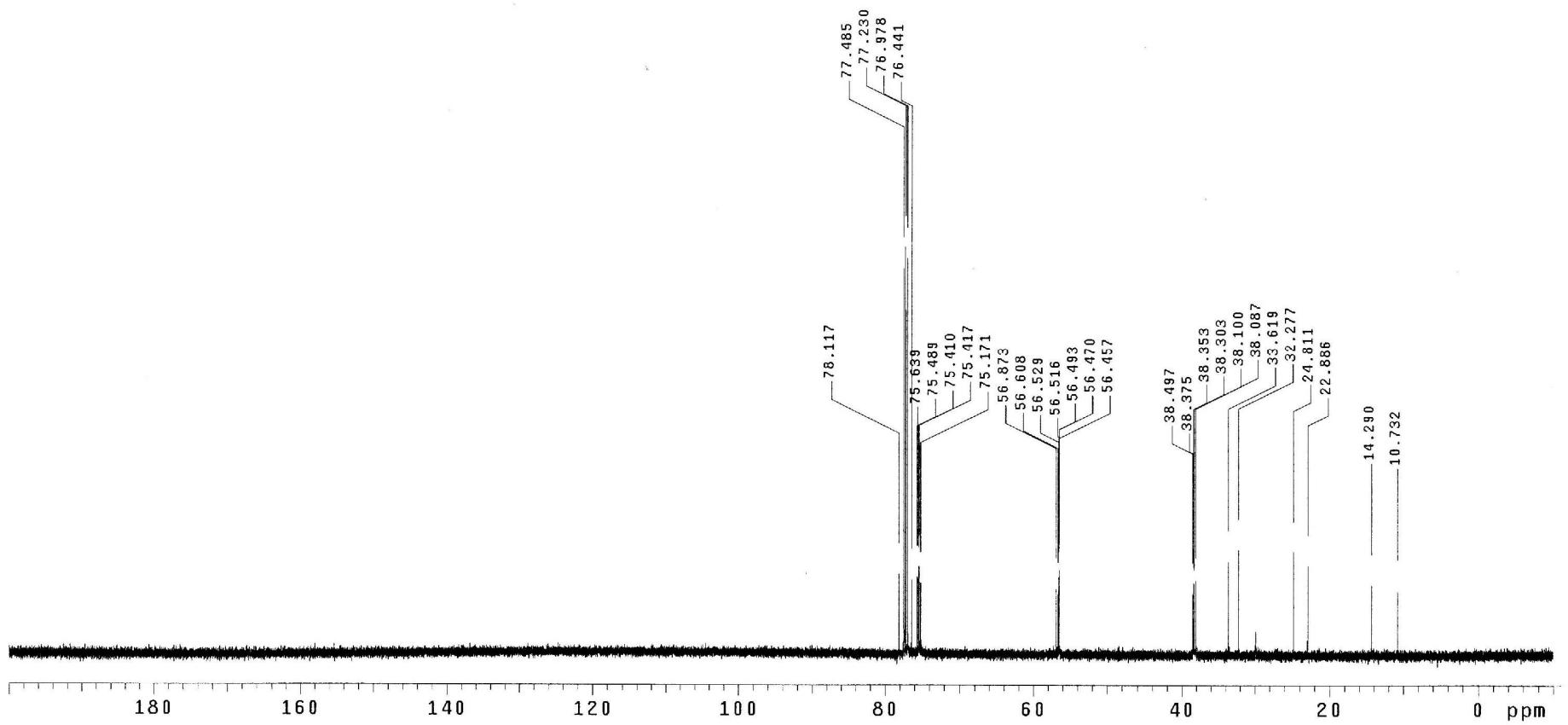


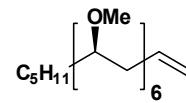
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Tolypothrix Hexaether

