Au-Catalyzed Cyclization of Monoallylic Diols

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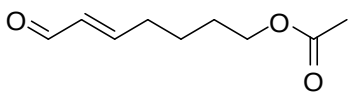
Supporting Information

General:

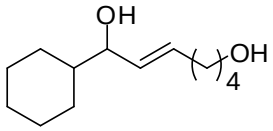
All reactions were carried out under an atmosphere of nitrogen unless otherwise specified. Anhydrous solvents were transferred via syringe to flame-dried glassware, which had been cooled under a stream of dry nitrogen. Anhydrous tetrahydrofuran (THF), acetonitrile, ether, dichloromethane, pentane were dried using a mBraun solvent purification system.

Analytical thin layer chromatography (TLC) was performed using 250 μm Silica Gel 60 F_{254} pre-coated plates (EMD Chemicals Inc.). Flash column chromatography was performed using 230-400 Mesh 60A Silica Gel (Whatman Inc.). The eluents employed are reported as volume:volume percentages. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded using Varian Unity Inova 500 MHz and Varian Mercury 300 MHz spectrometers. Chemical shift (δ) is reported in parts per million (ppm) downfield relative to tetramethylsilane (TMS, 0.0 ppm) or $CDCl_3$ (7.26 ppm). Coupling constants (*J*) are reported in Hz. Multiplicities are reported using the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad; Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were recorded using a Varian Unity Mercury 300 spectrometer at 75 MHz. Chemical shift is reported in ppm relative to the carbon resonance of $CDCl_3$ (77.00 ppm). Infrared spectra were obtained on a Bruker Vector 22 IR spectrometer at 4.0 cm^{-1} resolution and are reported in wavenumbers. High resolution mass spectra (HRMS) were obtained by Mass Spectrometry Core Laboratory of University of Florida, and are reported as m/e (relative ratio). Accurate masses are reported for the molecular ion (M+) or a suitable fragment ion.

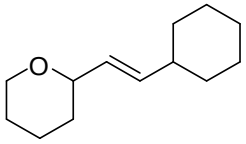


(*E*)-7-oxohept-5-enyl acetate (4a). A solution of hex-5-enyl acetate (170.1 mg, 1 mmol) and crotonaldehyde (350.1 mg, 5 mmol) in dry CH_2Cl_2 (2 mL) was added to a solution of Grubbs 2nd generation catalyst (25.5 mg, 0.03 mmol, 3 mol%) in dry CH_2Cl_2 (3 mL). The mixture was stirred at reflux for 2 hours and then cooled to rt. Silica gel (200 mg) was

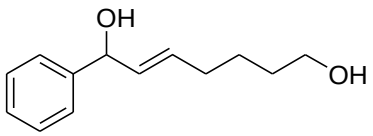
added and the reaction mixture was stirred open to air for 30 min. The solvent was removed and the crude product was purified by flash chromatography (50% EtOAc/Hexanes) to give the product as a yellow oil (116.8 mg, 92%) that satisfactorily matched all previously reported data.[1]



(*E*)-1-cyclohexylhept-2-ene-1,7-diol (4). A solution of cyclohexylmagnesium bromide (2 M in Et_2O, 1.120 mL, 3.3 eq.) was added dropwise to a solution of **4a** (100 mg, 0.78 mmol) in dry THF (6 mL) at -78°C. The mixture was stirred 2 h and then quenched with NH_4Cl (6 mL of a saturated aqueous solution), diluted with water (30 mL) and extracted with CH_2Cl_2 (3x20 mL). The combined organic layers were dried over $MgSO_4$, concentrated, and purified by flash chromatography (30% EtOAc/Hexanes) to give the product as a colorless oil (146.9 mg, 71%). R_f = 0.12 (20% EtOAc/hexanes); IR (neat) 3356, 2924, 2852, 1449, 1003, 433 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.59 (dt, *J* = 6.3, 15.3 Hz, 1H), 5.45 (dd, *J* = 6.9, 15.3 Hz, 1H), 3.75 (t, *J* = 7.2 Hz, 1H), 3.63 (t, *J* = 6 Hz, 2H), 2.06 (q, *J* = 6.9 Hz, 2H), 1.86-0.88 (m, 18H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 132.7, 132.1, 77.84, 62.93, 43.88, 32.40, 32.18, 29.0, 28.9, 26.7, 26.3, 26.2, 25.6; HRMS (ESI) Calcd for $C_{13}H_{23}O_2$ $(M-H)^+$ 211.1693, found 211.1704.

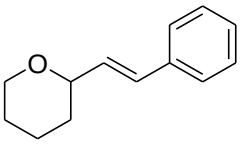


(*E*)-2-(2-cyclohexylvinyl)-tetrahydropyran (5). Dry CH_2Cl_2 (0.7 mL) was added to an aluminum foil covered test tube containing PPh_3AuCl (1.3 mg, 0.003 mmol), AgOTf (0.7 mg, 0.003 mmol) and activated MS-4Å (25 mg). After stirring for 10 minutes, a solution of diol **4** (56.1 mg, 0.26 mmol) in dry CH_2Cl_2 (0.7 mL) was added. After TLC analysis showed the reaction to be complete (40 min), it was diluted with CH_2Cl_2 and filtered through a short plug of silica. The solution of crude product was concentrated, and then purified by flash chromatography (5% EtOAc/hexanes) to give the product as a colorless oil (48.6 mg, 96%). R_f = 0.81 (5% EtOAc/hexanes); IR (neat) 2925, 2851, 1448, 1085, 968, 412 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.59 (dd, *J* = 6.3, 15.3 Hz, 1H), 5.39 (dd, 6.3, 15.3 Hz, 1H), 3.98 (dt, *J* = 2.7, 10.8 Hz, 1H), 3.70 (dd, *J* = 6.0, 10.5 Hz, 1H), 3.45 (dt, *J* = 2.4, 11.7 Hz, 1H), 1.95-0.97 (m, 17H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.8, 128.9, 78.7, 68.6, 40.5, 32.9, 33.0, 32.5, 26.4, 26.3, 26.1, 23.7; HRMS (ESI) Calcd for $C_{13}H_{23}O$ $(M+H)^+$ 195.1754, found 195.1749.

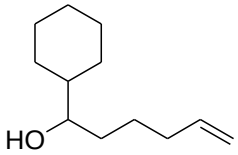


(*E*)-1-phenylhept-2-ene-1,7-diol (6). To a solution of Grubb's catalyst 2nd generation (3 mol%, 25.5 mg) in dry CH_2Cl_2 (3 mL) in a flamed dried flask was added solution of 1-phenylprop-2-en-1-ol (134.0 mg, 1 mmol) and hex-5-enyl acetate (284.0 mg, 2 mmol) in dry CH_2Cl_2 (2 mL). The mixture was stirred at reflux for 6 hours, cooled to r.t, and then filtered through a short plug of silica. The solvent was removed and the crude product was purified by flash chromatography (15% EtOAc/Hexanes) to give (E)-7-hydroxy-7-phenylhept-5-enyl acetate as a colorless oil(109 mg, 44%).

The oil was dissolved in 3 mL MeOH, and then mixed with 1 mL aqueous K_2CO_3 (91 mg, 0.66 mmol). The mixture stirred at room temperature for 9 h, diluted with 10 mL water, extracted with CH_2Cl_2 (3x10 mL), The organic layer was dried over Na_2SO_4, concentrated and then purified by flash chromatography (30% EtOAc/Hexanes) to give a colorless oil (57 mg, 63%). IR (neat) 3356, 3029, 2933, 1453, 970 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.34-7.24 (m, 5H), 5.76-5.59 (m, 2H), 5.11 (d, *J* = 5.1 Hz, 1H), 3.55 (t, *J* = 5.7 Hz, 2H), 2.05 (q, *J* =6.3 Hz, 2H), 1.74 (br s, 1H), 1.55-1.39 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.3, 132.6, 132.0, 128.4, 127.4, 126.1, 75.0, 62.6, 32.1, 31.8, 25.1. HRMS (ESI) Calcd for $C_{13}H_{18}NaO_2$ $(M+Na)^+$ 229.1199, found 229.1213.

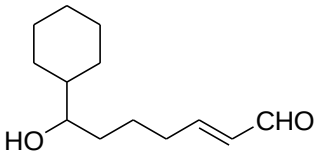


(*E*)-2-styryl-tetrahydro-2*H*-pyran (7). Dry CH_2Cl_2 (0.5 mL) was added to an aluminum foil covered test tube containing PPh_3AuCl (1.0 mg, 0.002 mmol), AgOTf (0.5 mg, 0.002 mmol) and activated MS-4Å (17 mg). After stirring for 10 minutes, a solution of the (*E*)-1-phenylhept-2-ene-1,7-diol **6** (43.0 mg, 0.2 mmol) in dry CH_2Cl_2 (0.5 mL) was added. The reaction mixture was stirred at r.t. under nitrogen for 30 minutes. After TLC analysis showed the reaction to be complete it was diluted with CH_2Cl_2 and filtered through a short plug of silica. The solution was concentrated, and the crude product purified by flash chromatography (2% EtOAc/hexanes) to give the product as a colorless oil (35.0 mg, 89 %) that satisfactorily matched all previously reported data.[2]

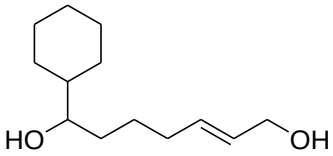


1-cyclohexylhex-5-en-1-ol (8a). To a solution of cyclohexane carbaldehyde (1.12 g, 10 mmol) in dry THF (20 mL) at -78℃ was added dropwise a solution of pent-4-enylmagnesium bromide (prepared from 5-bromopent-1-ene (1.49 g, 10.mmol),

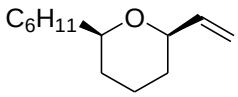
Mg (252 mg, 10.5 mmol), THF (20 mL)). The mixture was stirred at -78°C for 60 min and then quenched with a saturated aqueous solution of NH_4Cl (20 mL). After separation, the aqueous layer was extracted with CH_2Cl_2 (3x20 mL). The organic layer was dried over $MgSO_4$ and then purified by flash chromatography (10% EtOAc/Hexanes) to give the product as a colorless oil (1.0 g, 55%) that satisfactorily matched all previously reported data.[3a]



(*E*)-7-cyclohexyl-7-hydroxyhept-2-enal (8b). To a solution of Grubb's catalyst 2nd generation (3 mol%, 25.5 mg) in dry CH_2Cl_2 (3 mL) in a flamed dried flask was added solution of 1-cyclohexylhex-5-en-1-ol **8a** (182.2 mg, 1 mmol) and crotonaldehyde (350.5 mg, 5 mmol) in dry CH_2Cl_2 (2 mL). The mixture was stirred at reflux for 11 hours, cooled to r.t. and then filtered through a short plug of silica. The solvent was removed and the crude product was purified by flash chromatography (10% EtOAc/Hexanes) to give the product as a colorless oil (166 mg, 79%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.50 (d, *J* = 8.1 Hz, 1H), 6.85 (dt, *J* = 15.6, 6.6 Hz, 1H), 6.12 (ddt, *J* = 15.6, 8.1, 1.5 Hz, 1H), 3.39-3.33 (m, 1H), 2.40-2.32 (m, 2H), 1.80-0.91 (m, 16H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.0, 158.8, 132.8, 75.5, 43.6, 33.2, 32.6, 29.0, 27.7, 26.3, 26.1, 26.0, 24.1.

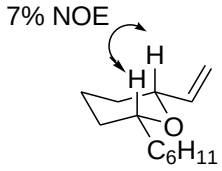


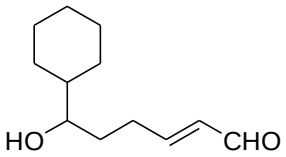
(*E*)-7-cyclohexylhept-2-ene-1,7-diol (8). To a solution of (*E*)-7-cyclohexyl-7-hydroxyhept-2-enal **8b** (166 mg, 0.79 mmol) in MeOH (4 mL) at 0℃ was added $NaBH_4$ (36 mg, 0.95 mmol) over 1 minute. After stirring at 0℃ for 30 minutes, a saturated aqueous solution of NH_4Cl (2 mL) was added, and then 10 mL water. The aqueous layer was extracted with CH_2Cl_2 (3x10 mL). The combined organic extract was dried over $MgSO_4$ and then purified by flash chromatography (30% EtOAc/Hexanes) to give the product as a colorless oil (145 mg, 86%). IR (neat) 3383, 2924, 1670, 1449, 969. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.74-5.58 (m, 2H), 4.07 (d, *J* = 4.5 Hz, 2H), 3.36-3.32 ((m, 1H), 2.10-2.03 (m, 2H), 1.80-0.95 (m, 17H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 132.5, 129.2, 75.8, 63.2, 43.5, 33.3, 32.1, 29.1, 27.7, 26.4, 26.2, 26.1, 25.3. HRMS (ESI) Calcd for $C_{13}H_{24}NaO_2$ $(M+Na)^+$ 235.1669, found 235.1649.



***Cis*-2-cyclohexyl-6-vinyl-tetrahydro-2*H*-pyran (9).** [3b] Dry CH_2Cl_2 (0.5 mL) was added to an aluminum foil covered test tube containing PPh_3AuCl (1.0 mg, 0.002 mmol), AgOTf (0.5 mg, 0.002 mmol) and activated MS-4Å (17 mg). After stirring for 10 minutes, the mixture was cooled to -50℃ and a solution of diol **8** (42.4 mg, 0.2 mmol) in dry CH_2Cl_2 (0.5 mL) was added. After TLC analysis showed the reaction to be complete (8h), it was diluted with CH_2Cl_2 and filtered through a short plug of silica. The solution of crude product was concentrated, and then purified by flash chromatography (1% EtOAc/hexanes) to give the product as a colorless oil (30.8 mg, 80 %). Data for major product (*Cis*): IR (neat) 2926, 2853, 1645, 1450, 1076, 918. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.86 (ddd, *J* = 17.4, 10.8, 5.1 Hz, 1H), 5.23 (dt, *J* = 17.4, 1.8 Hz, 1H), 5.05 (dt, *J* = 10.8, 1.8 Hz, 1H), 3.80-3.73 (m, 1H), 3.09-3.02 (m, 1H), 1.98-1.71 (m, 2H), 1.63-0.96 (m, 15H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.9, 113.9, 82.1, 78.2, 43.2, 31.7, 29.3, 28.7, 27.9, 26.7, 26.3, 26.2, 23.7. HRMS (ESI) Calcd for $C_{13}H_{22}NaO$ $(M+Na)^+$ 217.1563, found 217.1571.

The relative configuration of the major diastereomer was determined by NOE DIFF experiments as follows:

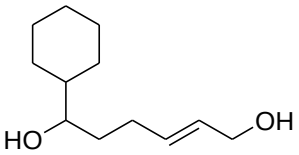




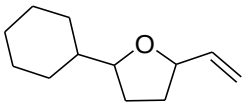
(*E*)-6-cyclohexyl-6-hydroxyhex-2-enal (10a). To a solution of cyclohexane carbaldehyde (1.68 g, 15 mmol) in dry THF (30 mL) at -78°C was added dropwise a solution of but-3-enylmagnesium bromide (prepared from 4-bromobut-1-ene (2.03 g, 15 mmol), Mg (380 mg, 15.8 mmol), THF (20 mL)). The mixture was stirred at -78°C for 30 min and then quenched with a saturated aqueous solution of NH_4Cl (30 mL). After separation, the aqueous layer was extracted with CH_2Cl_2 (3x20 mL). The combined organic extract was dried over $MgSO_4$ and then purified by flash chromatography (10% EtOAc/Hexanes) to give 1-cyclohexylpent-4-en-1-ol as a colorless oil (1.40 g, 55%).

To a solution of Grubb's catalyst 2nd generation (3 mol%, 51.0 mg) in dry CH_2Cl_2 (6 mL) in a flamed dried flask was added solution of 1-cyclohexylpent-4-en-1-ol (336 mg, 2 mmol) and crotonaldehyde (700.9 mg, 10 mmol) in dry CH_2Cl_2 (4 mL). The mixture was stirred at reflux for 11 hours, cooled to r.t. and then filtered through a short plug of silica.

The solvent was removed and the crude was purified by flash chromatography (10% EtOAc/Hexanes) to give the product as a colorless oil (242 mg, 62%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.47 (d, *J* = 7.8 Hz, 1H), 6.88 (dt, *J* = 15.6, 6.6 Hz, 1H), 6.11 (ddt, *J* = 15.6, 7.8, 1.2 Hz, 1H), 3.38-3.32 (m, 1H), 2.60-2.31 (m, 2H), 1.80-0.92 (m, 13H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.0, 158.8, 132.9, 75.3, 43.8, 32.1, 29.3, 29.1, 27.8, 26.4, 26.2, 26.0.



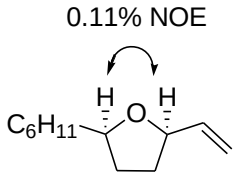
(*E*)-6-cyclohexylhex-2-ene-1,6-diol (10). To a solution of (*E*)-6-cyclohexyl-6-hydroxyhex-2-enal **10a** (242 mg, 1.23 mmol) in MeOH (6 mL) at 0℃ was added $NaBH_4$ (57 mg, 1.5 mmol) over 1 minute. After stirring at 0℃ for 30 minutes, a saturated aqueous solution of NH_4Cl (3 mL) was added, and then 15 mL water. The aqueous layer was extracted with CH_2Cl_2 (3x15 mL). The combined organic extract was dried over $MgSO_4$ and then purified by flash chromatography (30% EtOAc/Hexanes) to give the product as a colorless oil (213 mg, 88%). IR (neat) 3332, 2924, 1670, 1449, 969. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.74-5.58 (m, 2H), 4.04 (d, *J* = 4.5 Hz, 2H), 3.36-3.30 (m, 1H), 2.26-2.04 (m, 2H), 1.75-0.94 (m, 13H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 132.7, 129.3, 75.5, 63.4, 43.7, 33.4, 29.1, 28.7, 27.8, 26.5, 26.3, 26.1. HRMS (ESI) Calcd for $C_{12}H_{22}NaO_2$ $(M+Na)^+$ 221.1512, found 221.1519.

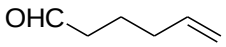


2-cyclohexyl-5-vinyl-tetrahydrofuran (11). Dry CH_2Cl_2 (0.5 mL) was added to an aluminum foil covered test tube containing PPh_3AuCl (1.0 mg, 0.002 mmol), AgOTf (0.5 mg, 0.002 mmol) and activated MS-4Å (17 mg). After stirred for 10 minutes, cooled to -50℃, a solution of diol **10** (39.6 mg, 0.2 mmol) in dry CH_2Cl_2 (0.5 mL) was added. After TLC analysis showed the reaction to be complete (10 h), it was diluted with CH_2Cl_2 and filtered through a short plug of silica. The solution of crude product was concentrated, and then purified by flash chromatography (2% EtOAc/hexanes) to give the product as a colorless oil (28.4 mg, 79 %). Data for major product (*Cis*): IR (neat) 3080, 2924, 2853, 1449, 1055, 950. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.83 (ddd, *J* = 17.4, 10.5, 6.6 Hz, 1H), 5.20 (dt, *J* = 17.4, 1.5 Hz, 1H), 5.05 (dt, *J* = 10.5, 1.5 Hz, 1H), 4.32 (q, *J* = 7.0 Hz, 1H), 3.68 (q, *J* = 7.2 Hz, 1H), 2.09-0.90 (m, 15H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.7, 114.7, 83.8, 79.6, 43.2, 32.7, 29.9, 29.6, 28.8, 26.6, 26.1, 26.0. HRMS (ESI) Calcd for $C_{12}H_{19}$ $(M+H-H_2O)^+$ 163.1481, found 163.1494.

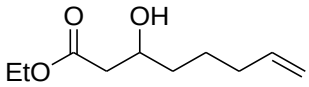
The relative configuration of the major diastereomer was determined by NOE DIFF

experiments as follows:

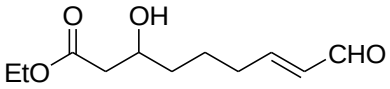




Hex-5-enal (12a). [4] To a solution of 5-hexen-1-ol (0.9 mL, 7.49 mmol) in CH_2Cl_2 (12 mL) was added pyridinium chlorochromate (2.45 g, 11.4 mmol). The resulting dark red solution was stirred for 14 h at room temperature, diluted with pentane (12 mL), filtered through a plug of silica with 1:1 CH_2Cl_2/pentane (7 × 25 mL). The filtrate was concentrated to give 5-hexen-1-al as a clear, colorless oil. The unpurified aldehyde was carried immediately into the next step without further purification.

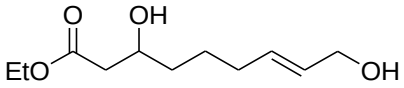


Ethyl 3-hydroxyoct-7-enoate (12b). To a solution of *i*-Pr_2NH (2.2 mL, 15.8 mmol) in dry THF (20 mL) was added *n*-BuLi (6 mL, 2.5 M in hexane) at -78℃. The mixture was kept at this temperature for 1 h, then a mixture of ethyl acetate (15 mmol) and dry THF (10 mL) was added at low temperature. After stirring for 1 h at -78℃, a mixture of Hex-5-enal **12a** (7.5 mmol) and dry THF (10 mL) was added. After the mixture was stirred for an additional 1 h, saturated NH_4Cl solution was added and the aqueous layer was extracted with ethyl acetate (3x30 mL), the combined extracts were dried and evaporated in vacuum. The residue was subjected to flash chromatography to furnish the product as a colorless oil (761 mg, 55% for two steps) that satisfactorily matched all previously reported data.[5]

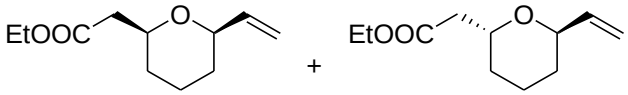


(*E*)-ethyl 3-hydroxy-9-oxonon-7-enoate (12c). To a solution of Grubb's catalyst 2nd generation (3 mol%, 51.0 mg) in dry CH_2Cl_2 (6 mL) in a flamed dried flask was added solution of ethyl 3-hydroxyoct-7-enoate **12b** (372 mg, 2 mmol) and crotonaldehyde (700.9 mg, 10 mmol) in dry CH_2Cl_2 (4 mL). The mixture was stirred at reflux for 11 hours, cooled to r.t. and then filtered through a short plug of silica. The solvent was removed and the crude was purified by flash chromatography (30% EtOAc/Hexanes) to give the product as a colorless oil (411 mg, 96%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.37 (d, *J* = 7.8 Hz, 1H), 6.76 (dt, *J* = 15.6, 6.9 Hz, 1H), 6.00 (ddt, *J* = 15.6, 7.8, 1.5 Hz, 1H), 4.04

(q, *J* = 6.9 Hz, 2H), 3.95-3.87 (m, 1H), 3.34 (br s, 1H), 2.36-2.23 (m, 4H), 1.63-1.35 (m, 4H), 1.15 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.8, 172.4, 158.2, 132.8, 67.2, 60.4, 41.3, 35.6, 32.1, 23.5, 13.9.



(*E*)-ethyl 3,9-dihydroxynon-7-enote (12). To a solution of (*E*)-ethyl 3-hydroxy-9-oxonon-7-enoate **12c** (411 mg, 1.92 mmol) in MeOH (8 mL) at 0℃ was added $NaBH_4$ (87 mg, 2.3 mmol) over 1 minute, After stirred at 0℃ for 30 minutes, a saturated aqueous solution of NH_4Cl (4 mL) was added, and then 15 mL water. The aqueous layer was extracted with CH_2Cl_2 (3x15 mL). The combined organic extract was dried over $MgSO_4$ and then purified by flash chromatography (30% EtOAc/Hexanes) to give the product as a colorless oil (355 mg, 86%). IR (neat) 3387, 2934, 2861, 1731, 1300, 972. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.70-5.55 (m, 2H), 4.14 (q, *J* = 7.2 Hz, 2H), 4.04, (d, *J* = 3.6 Hz, 2H), 3.99-3.91 (m, 1H), 3.14 (br s, 1H), 2.46 (dd, *J* = 16.2, 3.6 Hz, 1H), 2.37 (dd, *J* = 16.2, 8.4 Hz, 1H), 2.08-2.01 (m, 2H), 1.95 (br s, 1H), 1.55-1.38 (m, 4H), 1.24 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.9, 132.4, 129.4, 67.8, 63.5, 60.6, 41.3, 35.8, 31.8, 24.8, 14.1. HRMS (ESI) Calcd for $C_{11}H_{26}NaO_4$ $(M+Na)^+$ 239.1254, found 239.1262.

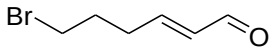


13a **13b**

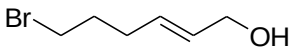
Dry CH_2Cl_2 (0.5 mL) was added to an aluminum foil covered test tube containing PPh_3AuCl (1.0 mg, 0.002 mmol), AgOTf (0.5 mg, 0.002 mmol) and activated MS-4Å (17 mg). After stirring for 10 minutes, cooled to -10℃, a solution of diol **12** (43.2 mg, 0.2 mmol) in dry CH_2Cl_2 (0.5 mL) was added. After TLC analysis showed the reaction to be complete (9 h), it was diluted with CH_2Cl_2 and filtered through a short plug of silica. The solution of crude product was concentrated, and then purified by flash chromatography (50% CH_2Cl_2/hexanes) to give the *trans* and *cis* products as colorless oil.

***Cis*-Ethyl 2-(6-vinyl-tetrahydro-2*H*-pyran-2-yl) acetate (13a).** (36.2 mg, 91 %). IR (neat) 2982, 2936, 2860, 1737, 1647, 1192. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.82 (ddd, *J* = 17.4, 10.5, 4.8 Hz, 1H), 5.19 (dt, *J* = 17.4, 1.5 Hz, 1H), 5.05 (dt, *J* = 10.5, 1.5 Hz, 1H), 4.13 (q, *J* = 7.2 Hz, 2H), 3.87-3.77 (m, 2H), 2.58 (dd, *J* = 15.0, 6.9 Hz, 1H), 2.39 (dd, *J* = 15.0, 6.3 Hz, 1H), 1.87-1.81 (m, 1H), 1.70-1.55 (m, 3H), 1.30-1.21 (m, 2H), 1.24 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.3, 139.2, 114.4, 78.2, 74.3, 60.3, 41.7, 31.0, 30.9, 23.2, 14.2. HRMS (ESI) Calcd for $C_{11}H_{19}O_3$ $(M+H)^+$ 199.1329, found 199.1328.

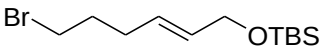
***Trans*-Ethyl 2-(6-vinyl-tetrahydro-2*H*-pyran-2-yl) acetate (13b).** (3.1 mg, 8 %). IR (neat) 2931, 2855, 1738, 1038. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.88 (ddd, *J* = 17.7, 11.1, 4.2 Hz, 1H), 5.25 (dt, *J* = 17.7, 1.8 Hz, 1H), 5.20 (dt, *J* = 11.1, 1.8 Hz, 1H), 4.41-4.36 (m, 1H), 4.25-4.17 (m, 1H), 4.14 (q, *J* = 7.2 Hz, 2H), 2.58 (dd, *J* = 14.7, 8.4 Hz, 1H), 2.39 (dd, *J* = 14.7, 5.4 Hz, 1H), 1.79-1.61 (m, 4H), 1.41-1.23 (m, 2H), 1.26 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.4, 138.3, 116.1, 72.5, 68.0, 60.4, 40.4, 30.4, 28.6, 18.6, 14.2. HRMS (ESI) Calcd for $C_{11}H_{19}O_3$ $(M+H)^+$ 199.1329, found 199.1339.



(*E*)-6-bromohex-2-enal (14a). To a solution of Grubb's catalyst 2nd generation (1 mol%, 84.9 mg) in dry CH_2Cl_2 (40 mL) in a flamed dried flask was added solution of 5-bromopent-1-ene (1.49 g, 10 mmol) and crotonaldehyde (3.5 g, 50 mmol) in dry CH_2Cl_2 (10 mL). The mixture was stirred at reflux for 20 hours, cooled to r.t. and then filtered through a short plug of silica. The solvent was removed and the crude was purified by flash chromatography (20% Ether/Hexanes) to give the product as a colorless oil (1.69 g, 96%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.51 (d, *J* = 7.2 Hz, 1H), 6.82 (dt, *J* = 15.6, 7.2 Hz, 1H), 6.15 (ddt, *J* = 15.6, 8.1, 1.8 Hz, 1H), 3.43 (t, *J* = 6.6 Hz, 2H), 2.51 (dq, *J* = 6.9, 1.5 Hz, 2H), 2.06 (dt, *J* = 14.4, 7.2 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.7, 156.0, 133.7, 32.3, 30.9, 30.5.

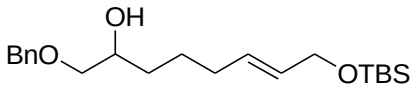


(*E*)-6-bromohex-2-en-1-ol (14b). To a solution of (*E*)-6-bromohex-2-enal **14a** (266 mg, 1.5 mmol) in THF (6 mL) at -78℃ was added DIBAL-H (1.6 mL, 1.0 M in hexane) over 2 min. After stirring at -78℃ for 30 min, a saturated aqueous solution of NH_4Cl (3 mL) was added, followed by 5 mL water and 1 mL 6 N HCl. The aqueous layer was extracted with ether (3x8 mL). The combined extract was dried over $MgSO_4$ and then purified by flash chromatography (50% Ether/Hexanes) to give the product as a colorless oil (253 mg, 95%) that satisfactorily matched all previously reported data.[6]

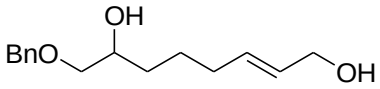


(*E*)-(6-bromohex-2-enyloxy)(*tert*-butyl)dimethylsilane (14c). To a solution of (*E*)-6-bromohex-2-en-1-ol **14b** (859 mg, 4.8 mmol) and imidazole (544 mg, 8.0 mmol) in dry CH_2Cl_2 (15 mL) at 0℃ was added portion-wise TBDMSCl (600 mg, 4.0 mmol). The reaction was stirred at r.t. for 1.5 h, 10 mL water was added, and then 1 M HCl (4 mL). The aqueous layer was extracted with CH_2Cl_2 (3x10 mL). The combined extracts were dried over $MgSO_4$ and then purified by flash chromatography (20% Ether/Hexanes) to give the product as a colorless oil (905 mg, 77%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.63-5.59 (m, 2H), 4.13-4.11 (m, 2H), 3.41 (t, *J* = 6.6 Hz, 2H), 2.23-2.16 (m, 2H),

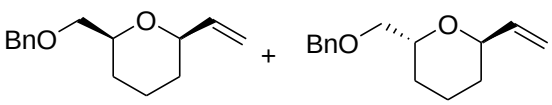
1.98-1.89 (m, 2H), 0.91 (s, 9H), 0.07 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 130.8, 128.7, 63.7, 33.2, 32.1, 30.5, 25.9, 18.4, -5.1.



(*E*)-1-(benzyloxy)-8-(*tert*-butyldimethylsilyloxy)oct-6-en-2-ol (14d). To a solution of *t*-BuLi (1.2 mL, 1.7 M in pentane) in ether (0.5 mL) at -78℃ was added a solution of (*E*)-(6-bromohex-2-enyloxy)(*tert*-butyl)dimethylsilane **14c** in 0.5 mL ether. After stirring for 0.5 h at -78℃, a mixture of 2-(benzyloxy)acetaldehyde (150 mg, 1.0 mmol) and dry ether (1.0 mL) was added. After the mixture was stirred for 45 minutes, saturated NH_4Cl solution (2 mL) and water (3 mL) was added and the aqueous layer was extracted with ether (3x10 mL), the combined extracts were dried over $MgSO_4$, and evaporated in vacuum. The residue was subjected to flash chromatography to furnish the product as a colorless oil (117 mg, 32%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39-7.26 (m, 5H), 5.68-5.48 (m, 2H), 4.55 (s, 2H), 4.11 (dd, *J* = 5.1, 1.2 Hz, 2H), 3.83-3.78 (m, 1H), 3.50 (dd, *J* = 9.3, 3.0 Hz, 1H), 3.32 (dd, *J* = 9.3, 7.8 Hz, 1H), 2.37 (br s, 1H), 2.09-2.02 (m, 2H), 1.56-1.41 (m, 4H), 0.91 (s, 9H), 0.07 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.9, 130.8, 129.6, 128.4, 127.8, 127.7, 74.6, 73.3, 70.2, 64.0, 32.6, 32.1, 26.0, 25.0, 18.4, -5.1.



(*E*)-8-(benzyloxy)oct-2-ene-1,7-diol (14). *p*- Toluenesulfonic acid hydrate (13.9 mg, 0.073 mmol) was added to a solution of (*E*)-1-(benzyloxy)-8-(*tert*-butyldimethylsilyloxy) oct-6-en-2-ol **14d** (267 mg, 0.73 mmol) in dry methanol (7.3 mL). After 20 min, analysis of the reaction by TLC indicated that the starting material had been consumed. The reaction mixture was then diluted with ether (30 mL) and washed sequentially with saturated aqueous $NaHCO_3$ (10 mL) and brine (2x10 mL). The organic layer was dried over $MgSO_4$ and the solvent removed in *vacuo*. Flash chromatography (40% Ethyl acetate/Hexane) afforded the product as a colorless oil (150 mg, 82%). IR (neat) 3384, 2929, 2860, 1496, 1090, 735. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39-7.26 (m, 5H), 5.73-5.58 (m, 2H), 4.55 (s, 2H), 4.07 (d, *J* = 3.6 Hz, 2H), 3.82-3.78 (m, 1H), 3.50 (dd, *J* = 9.3, 3.3 Hz, 1H), 3.32 (dd, *J* = 9.3, 8.1 Hz, 1H), 2.37 (br s, 1H), 2.10-2.04 (m, 2H), 1.63-1.25 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.9, 132.7, 129.3, 128.4, 127.8, 127.7, 74.6, 73.3, 70.2, 63.7, 32.5, 32.1, 25.0. HRMS (ESI) Calcd for $C_{15}H_{21}O_2$ $(M+H-H_2O)^+$ 233.1536, found 233.1537.

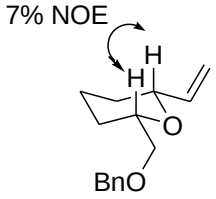


15a **15b**

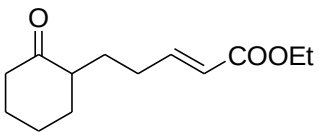
Dry CH_2Cl_2 (0.5 mL) was added to an aluminum foil covered test tube containing PPh_3AuCl (1.0 mg, 0.002 mmol), AgOTf (0.5 mg, 0.002 mmol) and activated MS-4Å (17 mg). After stirring for 10 minutes, cooled to -50℃, a solution of diol **14** (50.0 mg, 0.2 mmol) in dry CH_2Cl_2 (0.5 mL) was added. After TLC analysis showed the reaction to be complete (24 h), it was diluted with CH_2Cl_2 and filtered through a short plug of silica. The solution of crude product was concentrated, and then purified by flash chromatography (50% CH_2Cl_2/hexanes) to give the *trans* and *cis* products as colorless oil.

***Cis*-2-(benzyloxymethyl)-6-vinyl-tetrahydro-2*H*-pyran (15a).** (39.8 mg, 86%) IR (neat) 2934, 2857, 1496, 1089, 735, 698. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.25 (m, 5H), 5.89 (ddd, *J* = 17.4, 10.5, 5.7 Hz, 1H), 5.23 (dt, *J* = 17.4, 1.5 Hz, 1H), 5.09 (dt, *J* = 10.5, 1.5 Hz, 1H), 4.58 (dd, *J* = 16.8, 12.6 Hz, 2H), 3.90-3.84 (m, 1H), 3.67-3.59 (m, 1H), 3.54 (dd, *J* = 9.9, 5.7 Hz, 1H), 3.43 (dd, *J* = 9.9, 4.5 Hz, 1H), 1.93-1.84 (m, 1H), 1.67-1.50 (m, 3H), 1.40-1.25 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.4, 138.4, 128.3, 127.7, 127.5, 114.6, 78.3, 76.8, 73.6, 73.4, 31.3, 28.0, 23.1. HRMS (ESI) Calcd for $C_{15}H_{19}O_2$ $(M-H)^+$ 231.1385, found 231.1374.

The relative configuration of the major diastereomer was determined by NOE DIFF experiments as follows:



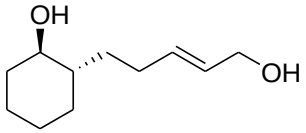
***Trans*-2-(benzyloxymethyl)-6-vinyl-tetrahydro-2*H*-pyran (15b).** (5.2 mg, 11%) IR (neat) 2933, 2858, 1454, 1102, 735, 698. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.26 (m, 5H), 5.95 (ddd, *J* = 17.7, 11.1, 4.5 Hz, 1H), 5.24 (dt, *J* = 17.7, 1.8 Hz, 1H), 5.21 (dt, *J* = 11.1, 1.8 Hz, 1H), 4.57 (dd, *J* = 15.3, 12.3 Hz, 2H), 4.42-4.40 (m, 1H), 3.99-3.90 (m, 1H), 3.54 (dd, *J* = 10.2, 6.0 Hz, 1H), 3.44 (dd, *J* = 10.2, 5.1 Hz, 1H), 1.82-1.37 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.43, 138.42, 128.3, 127.6, 127.5, 116.1, 73.3, 72.8, 72.6, 70.1, 28.7, 27.6, 18.5. HRMS (ESI) Calcd for $C_{15}H_{19}O_2$ $(M-H)^+$ 231.1385, found 231.1381.



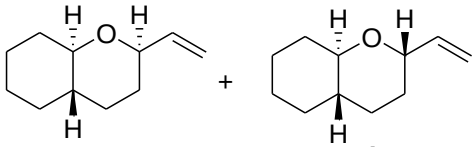
Ethyl 5-(2-oxocyclohexyl) pent-2-enoate (16a). A solution of 1-N-pyrrolidylcyclohexene (4.8 mL, 30 mmol) in anhydrous ether (23 mL) was cooled to -7℃. With efficient stirring and cooling in an ice-salt bath, acrolein (1.71 g, 30.5 mmol)

in 2 mL of ether was added over 100 min. The temperature was kept between -7 and -2℃ during the addition, and then was kept at 0℃ for another hour, when 1.0 mL of water was added. After the solution was stirred for 20 min., 4.9 mL of 6 ***N*** hydrochloric acid was added to bring the pH to 5-6. The ether layer was separated, washed with a saturated sodium bicarbonate solution, dried over $MgSO_4$ and concentrated. The crude 3-(2-oxocyclohexyl)propanal was used in next step directly.

To a solution of the above crude aldehyde in 15 mL of MeCN at 0℃ was added Ethyl (triphenylphosphoranyliden)acetate (3.98 g, 11.4 mmol), the mixture was stirred at r.t for 5 h. The solvent was removed in vacuo and the solid was repeatedly washed with ether. The etheral layer was concentrated in vacuo, and then purified by flash chromatography (10% Ethyl acetate/hexanes) to give the *E* and *Z* mixture (*E*/*Z* = 10/1) as colorless oil (1.31 g, 20% for two steps) that satisfactorily matched all previously reported data.[7]



***Trans*-(*E*)-2-(5-hydroxypent-3-enyl) cyclohexanol (16).** To a solution of Ethyl 5-(2-oxocyclohexyl) pent-2-enoate **16a** (1.31 g, 5.8 mmol) in THF (10 mL) at -78℃ was added DIBAL-H (18.4 mL, 1.0 M in hexane) over 5 minutes. After stirring at -78℃ for 2 h, the reaction mixture was poured into 6 N HCl (10 mL) and the aqueous layer was extracted with ether (4x10 mL). The combined extract was dried over $MgSO_4$ and then purified by flash chromatography (25% Ether/Hexanes) to give the products as colorless oil. The diols are partially separable, and 298 mg of *Trans*-(*E*)-2-(5-hydroxypent-3-enyl) cyclohexanol **16** was obtained. IR (neat) 3331, 2926, 2855, 1670, 1448, 969. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.68-5.52 (m, 2H), 3.99 (d, *J* = 4.2 Hz, 2H), 3.17-3.11 (m, 1H), 2.80 (br s, 2H), 2.16-1.55 (m, 7H), 1.23-0.78 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 133.0, 128.9, 74.3, 63.2, 44.1, 35.6, 31.5, 30.0, 29.0, 25.3, 24.8. HRMS (ESI) Calcd for $C_{11}H_{19}O$ $(M+H-H_2O)^+$ 167.1430, found 167.1427.



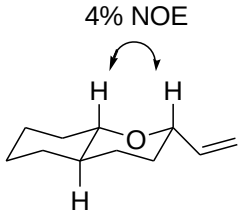
17a **17b**

Dry CH_2Cl_2 (0.5 mL) was added to an aluminum foil covered test tube containing PPh_3AuCl (5.0 mg, 0.01 mmol), AgOTf (2.5 mg, 0.01 mmol) and activated MS-4Å (17

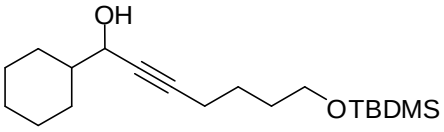
mg). After stirring for 10 minutes, cooled to -78℃, a solution of diol **16** (36.8 mg, 0.2 mmol) in dry CH_2Cl_2 (0.5 mL) was added. After TLC analysis showed the reaction to be complete (10 h), it was diluted with CH_2Cl_2 and filtered through a short plug of silica. The solution of crude product was concentrated, and then purified by flash chromatography (20% CH_2Cl_2/hexanes) to give the *trans* and *cis* products as colorless oil.

(2*R,4a*S**,8a*R**)-2-vinyl-octahydro-2*H*-chromene (17a).** (23.7 mg, 71.4 %) IR (neat) 2925, 2854, 1462, 1377, 1080. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.87 (ddd, *J* = 17.4, 10.5, 5.7 Hz, 1H), 5.23 (dt, *J* = 17.4, 1.5 Hz, 1H), 5.08 (dt, *J* = 10.5, 1.5 Hz, 1H), 3.87-3.81 (m, 1H), 3.02-2.94 (m, 1H), 1.94-1.01 (m, 13H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.5, 114.7, 81.8, 78.5, 41.5, 32.6, 32.2, 31.7, 30.7, 25.8, 25.1. HRMS (ESI) Calcd for $C_{11}H_{17}O$ $(M-H)^+$ 165.1274, found 165.1271.

The relative configuration of the major diastereomer was determined by NOE DIFF experiments as follows:

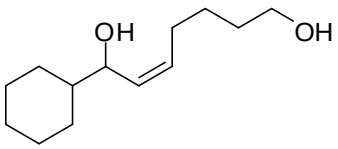


(2*S,4a*S**,8a*R**)-2-vinyl-octahydro-2*H*-chromene (17b).** (2.6 mg, 7.8 %) IR (neat) 2930, 2856, 1727, 1448, 1286. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.01 (ddd, *J* = 17.4, 11.4, 4.2 Hz, 1H), 5.24 (dt, *J* = 11.4, 1.8 Hz, 1H), 5.21 (dt, *J* = 17.4, 1.8 Hz, 1H), 4.50-4.45 (m, 1H), 3.23 (dt, *J* = 9.9, 3.9 Hz, 1H), 1.99-1.14 (m, 13H). HRMS (ESI) Calcd for $C_{11}H_{17}O$ $(M-H)^+$ 165.1274, found 165.1264.



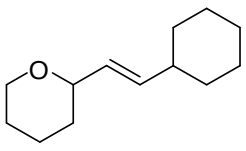
7-(*tert*-butyldimethylsilyloxy)-1-cyclohexylhept-2-yn-1-ol (18a). A solution of *n*-BuLi in hexane 2.5M (1.04 mL, 2.6 mmol) was added dropwise over 10 minutes at -78°C to a solution of *tert*-butyl(hex-5-ynyloxy)dimethylsilane[8] (500.8 mg, 2.36 mmol) in dry THF (35 mL). The reaction was then stirred at the same temperature for 45 minutes and a solution of cyclohexane carboxaldehyde (344.2 mg, 3.07 mmol) in dry THF (3 mL) was added. The mixture was allowed to warm to -30°C and stirred for 30 minutes, quenched with NH_4Cl (20 mL of a saturated aqueous solution), diluted with water (20 mL) and extracted with CH_2Cl_2 (2x30 mL). The organic layers were dried over $MgSO_4$ and then purified by flash chromatography (20% EtOAc/Hexanes) to give the product as a colorless oil (697.2 mg, 91%). R_f = 0.42 (10% EtOAc/hexanes); IR (neat) 3333, 3011,

2852, 1446 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 4.01 (d, *J* = 7.2 Hz, 1H), 3.61 (t, *J* = 7.2 Hz, 2H), 2.21 (q, *J* = 7.1 Hz, 2H), 1.99-0.95 (m, 15H), 0.86 (s, 9H), 2.20-0.91 (m, 19H), 0.86 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 86.2, 80.5, 67.6, 62.9, 44.5, 32.1, 28.8, 28.3, 26.6, 26.1, 25.4, 19.7, 18.7, 18.5, -5.1; HRMS (ESI) Calcd for $C_{19}H_{35}O_2Si$ $(M-H)^+$ 323.2401, found 323.2398.



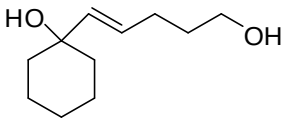
(*Z*)-1-cyclohexylhept-2-ene-1,7-diol (18). Lindlar catalyst (5% palladium on calcium carbonate, poisoned with lead, 30 mg) was added to a solution of **18a** (150.2 mg, 0.46 mmol) in a mixture of EtOAc/pyridine/1-hexene (10:1:1, 250 μL). The reaction mixture was stirred 16h under H_2 (1 atm). After filtration over celite and removal of the solvent, crude product was recovered as a colorless oil which was used for the next step without further purification.

A solution of HF pyridine (550 μL) was added dropwise at 0°C to a solution of the silane obtained above (116.1 mg, 0.35 mmol) in dry THF (4 mL). The reaction was stirred for 2 hours at the same temperature and $NaHCO_3$ saturated (30 mL of a saturated aqueous solution) was added dropwise. After dilution in water (20 mL), the crude product was extracted with CH_2Cl_2 (2 x 30 mL), the combined organic layers were dried over $MgSO_4$ and the solvent removed by vacuum. Flash chromatography (30% EtOAc/Hexanes) afforded the product as a colorless oil (58.4 mg, 78%). R_f = 0.12 (20% EtOAc/hexanes); IR (neat) 3330, 2924, 2852, 1449 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.42 (dt, *J* = 7.2, 11.1 Hz, 1H), 5.36 (dd, *J* = 9, 10.5 Hz, 1H), 4.09 (t, *J* = 7.2 Hz, 1H), 3.61 (t, *J* = 6.3 Hz, 2H), 2.06 (q, *J* = 6.9 Hz, 2H), 2.20-0.81 (m, 19H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 132.7, 131.6, 72.1, 62.9, 44.2, 32.4, 29.0, 28.8, 27.7, 26.7, 26.3, 26.2, 26.1; HRMS (ESI) Calcd for $C_{13}H_{23}O_2$ $(M-H)^+$ 211.1693, found 211.1704.

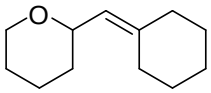


(*E*)-2-(2-cyclohexylvinyl)tetrahydro-2H-pyran (5). Dry CH_2Cl_2 (0.3 mL) was added to an aluminum foil covered test tube containing PPh_3AuCl (0.7 mg, 0.001 mmol), AgOTf (0.4 mg, 0.001 mmol) and activated MS-4Å (25 mg). After stirring for 10 minutes, a solution of diol **18** (21.1 mg, 0.10 mmol) in dry CH_2Cl_2 (0.3 mL) was added. After TLC analysis showed the reaction to be complete (40 min), it was diluted with CH_2Cl_2 and filtered through a short plug of silica. The solution of crude product was concentrated, and then purified by flash chromatography (5% EtOAc/hexanes) to give the product as a

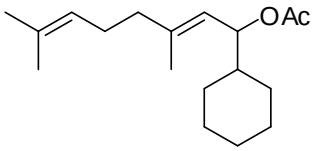
colorless oil (17.9 mg, 92%) that satisfactorily matched all reported data above.



(*E*)-1-(6-hydroxyhex-1-enyl)-cyclohexanol (19): A solution of hex-5-en-1-ol (100.2 mg, 1 mmol) and 1-vinylcyclohexanol (252.4 mg, 2 mmol) in dry CH_2Cl_2 (2 mL) was added to a solution of Grubb's 2nd generation catalyst (42.5 mg, 0.05 mmol, 5 mol%) in dry CH_2Cl_2 (3 mL). The mixture was stirred at reflux for 1 hour and then cooled to rt. Silica gel (200 mg) was added and the reaction mixture was stirred open to air for 1 hour. The solvent was removed and the crude product was purified by flash chromatography (20% EtOAc/Hexanes) to give the product as a yellow oil (116.8 mg, 93%). R_f = 0.18 (20% EtOAc/hexanes); IR (neat) 3417, 2976, 2932, 2860, 1382, 1120, 423 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.63 (m, 2H), 3.63 (t, J = 6.6 Hz, 2H), 2.06 (q, J = 6.9 Hz, 1H), 1.74-1.26 (m, 16H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.2, 127.8, 89.1, 81.9, 71.5, 62.9, 38.3, 32.3, 32.2, 25.7, 25.6, 22.4, 22.3; HRMS (ESI) Calcd for $C_{12}H_{19}O_2$ $(M-2H_2O+H)^+$ 163.1487, found 163.1491.

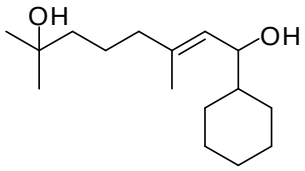


2-(cyclohexylidenemethyl)tetrahydropyran (20). Dry CH_2Cl_2 (0.7 mL) was added to an aluminum foil covered test tube containing PPh_3AuCl (1.3 mg, 0.003 mmol), AgOTf (0.7 mg, 0.003 mmol) and activated MS-4Å (25 mg). After stirring for 10 minutes, a solution of diol **19** (51.5 mg, 0.26 mmol) in dry CH_2Cl_2 (0.7 mL) was added. After TLC analysis showed the reaction to be complete (2.5 h), it was diluted with CH_2Cl_2 and filtered through a short plug of silica. The solution of crude product was concentrated, and then purified by flash chromatography (5% EtOAc/hexanes) to give the product as a colorless oil (42.1 mg, 91%). R_f = 0.85 (5% EtOAc/hexanes); IR (neat) 2929, 2852, 1086, 1033 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.08 (dd, J = 8.1, 0.9 Hz, 1H), 4.04-3.92 (m, 2H), 3.44 (dt, J = 11.7, 2.7 Hz, 1H), 2.14-2.03 (m, 4H), 1.82-1.22 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 142.9, 123.4, 74.4, 68.4, 37.1, 32.8, 29.7, 28.6, 28.0, 26.9, 26.0, 23.7; HRMS (ESI) Calcd for $C_{12}H_{19}O$ $(M-H)^+$ 179.1427, found 179.1436.



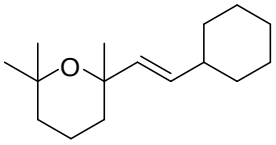
(*E*)-1-cyclohexyl-3,7-dimethylocta-2,6-dienyl acetate (21a). A solution of cyclohexylmagnesium bromide (2 M in Et_2O, 1.083 mL, 1.1 eq.) was added dropwise at 0°C to a solution of geranial[9] (300 mg, 1.97 mmol) in dry THF (10 mL). The mixture was

stirred 20 minutes and then acetylchloride (309 μL, 3.94 mmol) was added dropwise. The reaction mixture was warmed to rt and stirred for 2h, then quenched with water (20 mL) and extracted with Et_2O (3x20 mL). The organic layers were dried over $MgSO_4$, concentrated, and the crude product was purified by flash chromatography (10% EtOAc/Hexanes) to give the product as a colorless oil (477.2 mg, 87%). R_f = 0.57 (20% EtOAc/hexanes); IR (neat) 2928, 2854, 1727, 1264, 1247, 740 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.24 (dd, J = 7.5, 9.6 Hz, 1H), 5.00 (m, 2H), 2.07-1.98 (m, 7H), 1.75-0.85 (m, 20H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.7, 140.8, 131.8, 124.2, 122.6, 75.5, 42.4, 39.9, 29.0, 28.5, 26.6, 26.4, 26.2, 26.0, 25.9, 21.5, 17.9, 17.0; HRMS (ESI) Calcd for $C_{18}H_{29}O_2$ $(M-H)^+$ 277.2185, found 277.2168.



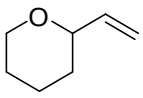
(*E*)-1-cyclohexyl-3,7-dimethyloct-2-ene-1,7-diol (21). A solution of *meta*-chloroperoxybenzoic acid (77% max., 244.7 mg, 1.09 mmol) in CH_2Cl_2 (2 mL) was added dropwise at 0°C to a solution of **21a** (276.4 mg, 0.99 mmol) in CH_2Cl_2 (8 mL). After for 3 hours, the reaction mixture was quenched with NaOH (10 mL of a 1M aqueous solution), diluted with water (20 mL) and extracted with CH_2Cl_2 (2x40 mL). The combined organic layers were dried over $MgSO_4$ and the solvent removed to give the product as a crude colorless oil which was used for the next step without further purification.

A solution of the epoxide obtained above (292 mg, 0.99 mmol) in Et_2O (5 mL) was added dropwise over 10 min at 0°C to a vigorously stirred suspension of lithium aluminum hydride 95% (119 mg, 2.98 mmol) in dry Et_2O (10 mL). The reaction mixture was allowed to warm to rt and was then stirred at reflux for 45 minutes. The reaction was cooled to 0°C and was added successively water (120 μL), NaOH (120 μL of a 15% aqueous solution) and then water (360 μL). After filtration, the solution was dried over $MgSO_4$ and purified by flash chromatography (15% to 30% EtOAc/Hexanes) to give the product as a colorless oil (110.2 mg, 40% over 2 steps). IR (neat) 3373, 2923, 2851, 1001, 423 cm-1; ^1H NMR (300 MHz, $CDCl_3$): δ 5.15 (d, *J* = 9.0 Hz, 1H), 4.04 (t, *J* = 8.7 Hz, 1H), 1.99 (t, *J* = 6.6 Hz, 2H) 1.91-0.86 (m, 24H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.05, 126.84, 73.08, 71.11, 44.52, 44.39, 43.67, 40.27, 29.49, 29.17, 28.79, 26.79, 26.35, 26.23, 22.63, 16.89. HRMS (ESI) Calcd for $C_{16}H_{29}O_2$ $(M-H)^+$ 253.2162, found 253.2175.

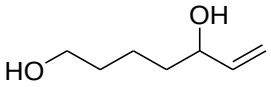


(*E*)-2-(2-cyclohexylvinyl)-2,6,6-trimethyltetrahydropyran (22). Dry CH_2Cl_2 (0.5

mL) was added to an aluminum foil covered test tube containing PPh_3AuCl (0.9 mg, 0.002 mmol), AgOTf (0.5 mg, 0.002 mmol) and activated MS-4Å (25 mg). After stirring for 10 minutes, a solution of diol **21** (45.0 mg, 0.18 mmol) in dry CH_2Cl_2 (0.4 mL) was added. After TLC analysis showed the reaction to be complete (6h), it was diluted with CH_2Cl_2 and filtered through a short plug of silica. The solution of crude product was concentrated, and then purified by flash chromatography (5% EtOAc/hexanes) to give the product as a colorless oil (37.2 mg, 89%). R_f = 0.81 (5% EtOAc/hexanes); IR (neat) 2970, 2925, 2852, 1093, 430, 409 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.45 (d, J = 16.2 Hz, 1H), 5.27 (dd, J = 15.9, 6.3 Hz, 1H), 1.92-0.81 (m, 26H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.1, 132.0, 73.3, 72.3, 40.7, 37.0, 33.9, 33.1, 32.9, 32.8, 32.5, 27.7, 26.5, 26.3, 17.2; HRMS (ESI) Calcd for $C_{16}H_{27}O$ $(M-H)^+$ 235.2049, found 235.2062.



2-vinyltetrahydro-2H-pyran (23a). Dry CH_2Cl_2 (1.0 mL) was added to an aluminum foil covered test tube containing PPh_3AuCl (12.0 mg, 0.025 mmol), AgOTf (6.1 mg, 0.025 mmol) and activated MS-4Å (25 mg). After stirring for 10 minutes, a solution of (*E*)-hex-1-ene-1,6-diol **23**[10] (75.2 mg, 0.50 mmol) in dry CH_2Cl_2 (1.0 mL) was added. After TLC analysis showed the reaction to be complete (15min), it was diluted with CH_2Cl_2 and filtered through a short plug of silica. The solution of crude product was concentrated, and then purified by flash chromatography (5% EtOAc/hexanes) to give the product as a colorless oil that satisfactorily matched previously reported data.[11]



Hept-6-ene-1,5-diol (24). DIBAL-H (22 mL, 1 M in hexane) was added dropwise to a stirred and cooled (-78 °C) solution of δ-valerolactone (2.0 g, 20 mmol) in a mixture of pentane-ether (34 mL, 1:1). After 2 h at -78 °C vinylmagnesium chloride (22.0 mL, 1 M in THF) was added. The solution was warmed to rt and stirred overnight. Ammonium chloride solution was added (35 mL), and after separation, the aqueous phase was extracted with CH_2Cl_2 (4x30 mL). The combined organic extract was dried (Na_2SO_4) and concentrated. Chromatography of the residue over silica gel (ether) gave 0.87 g of diol (33%) that satisfactorily matched all previously reported data.[12]

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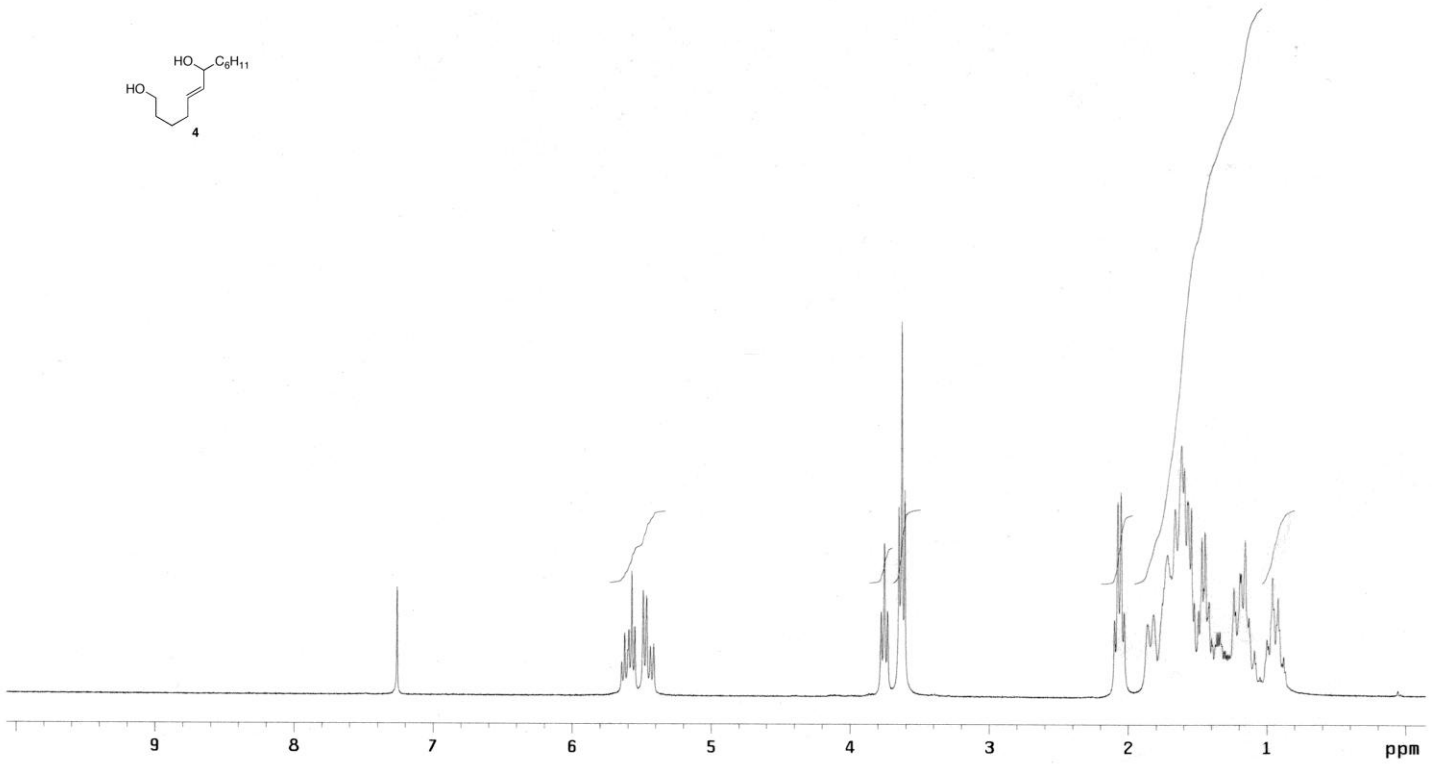
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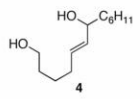
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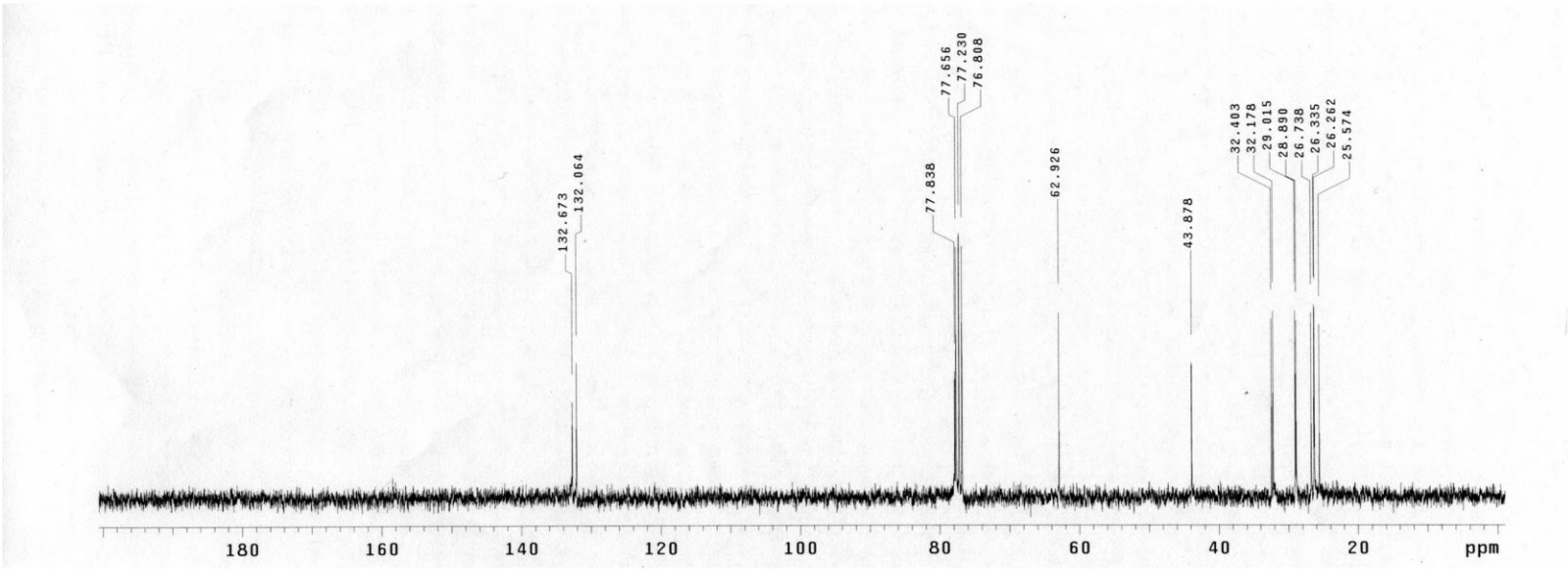
HO

4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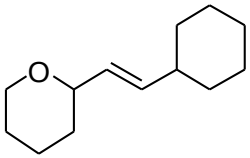

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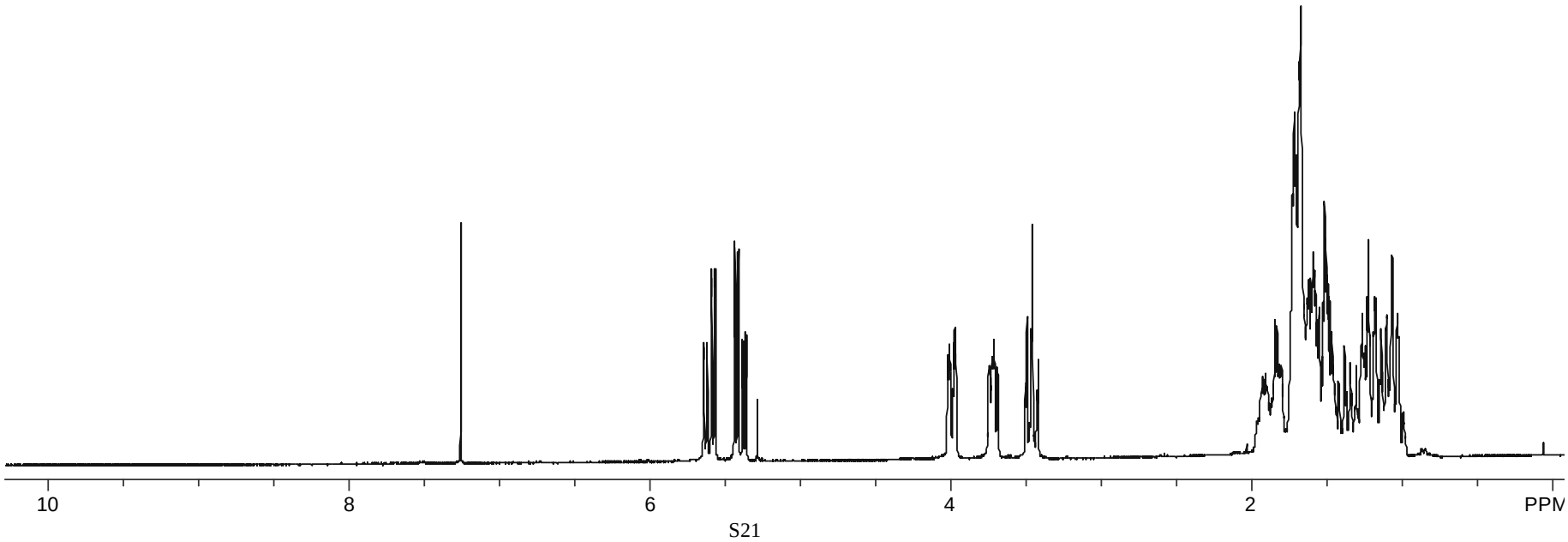

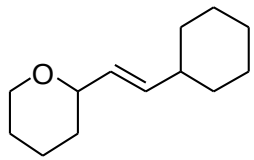

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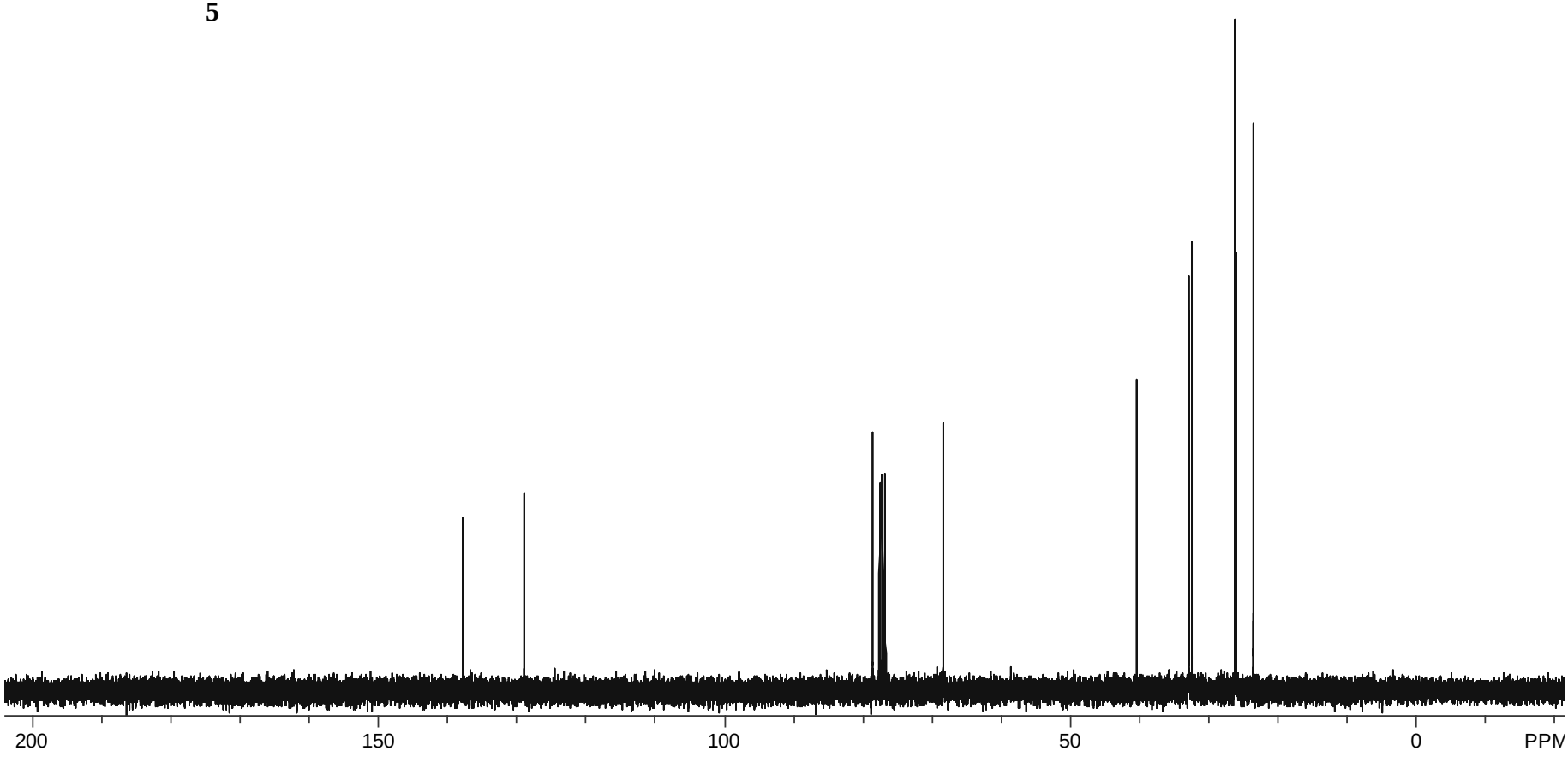

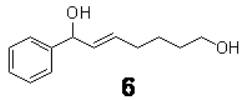

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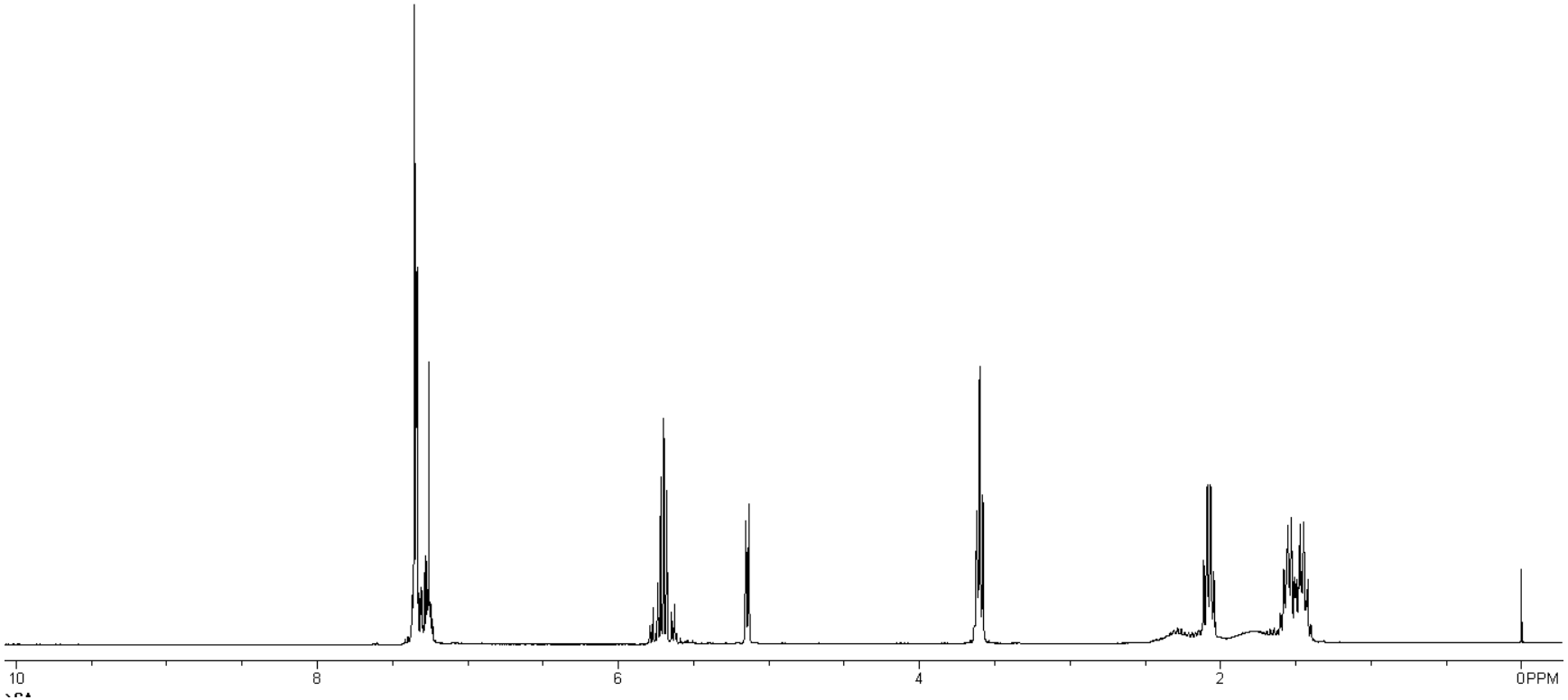

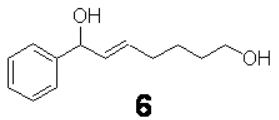

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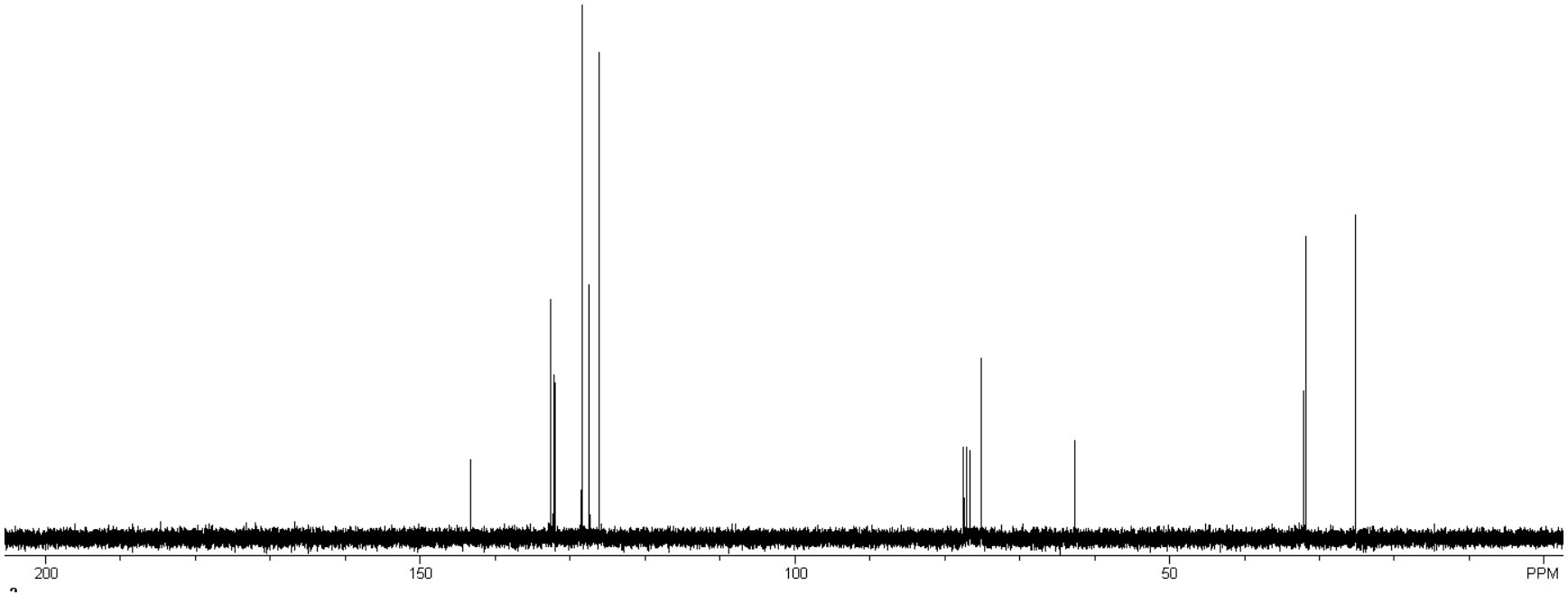

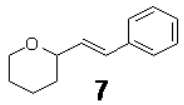

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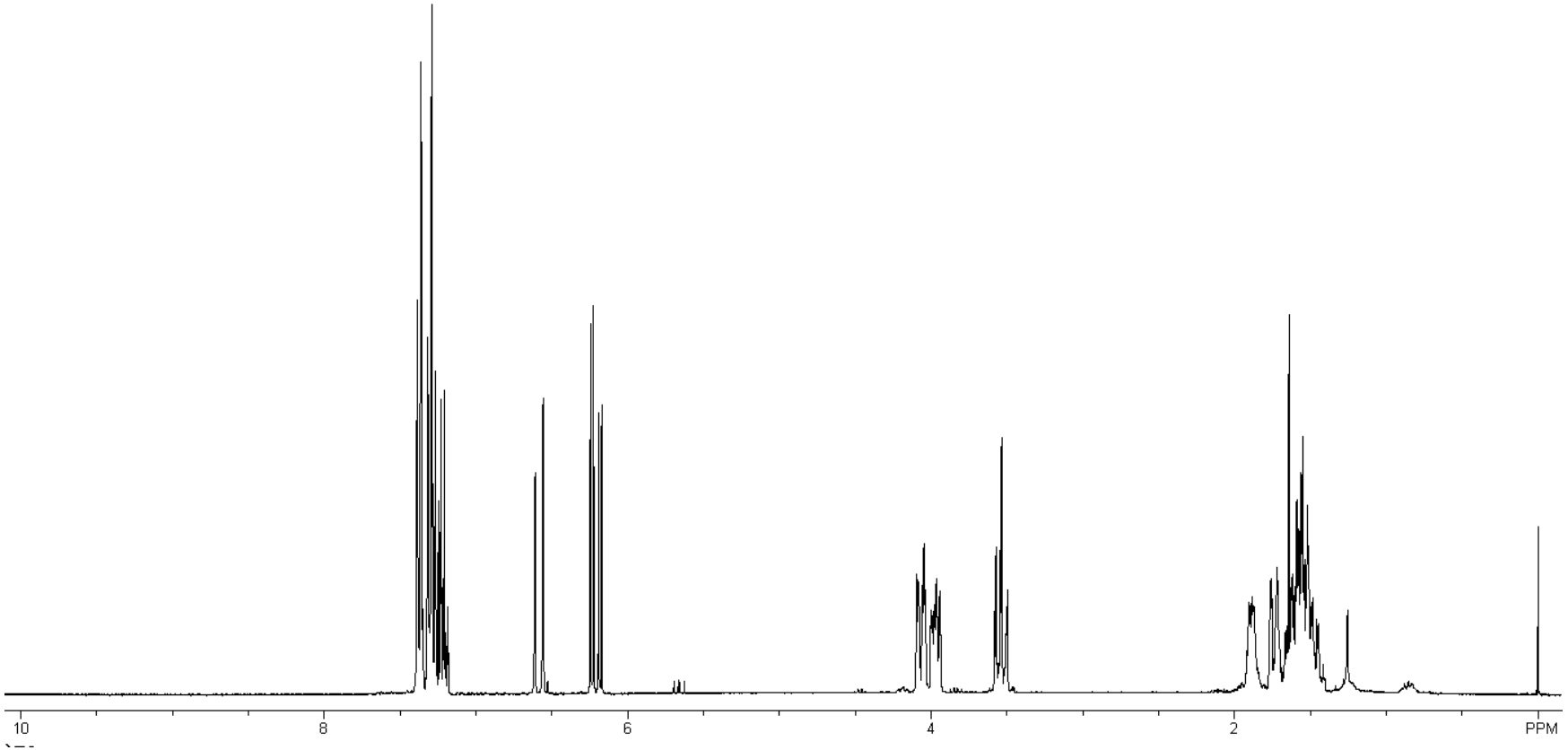

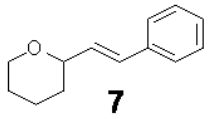

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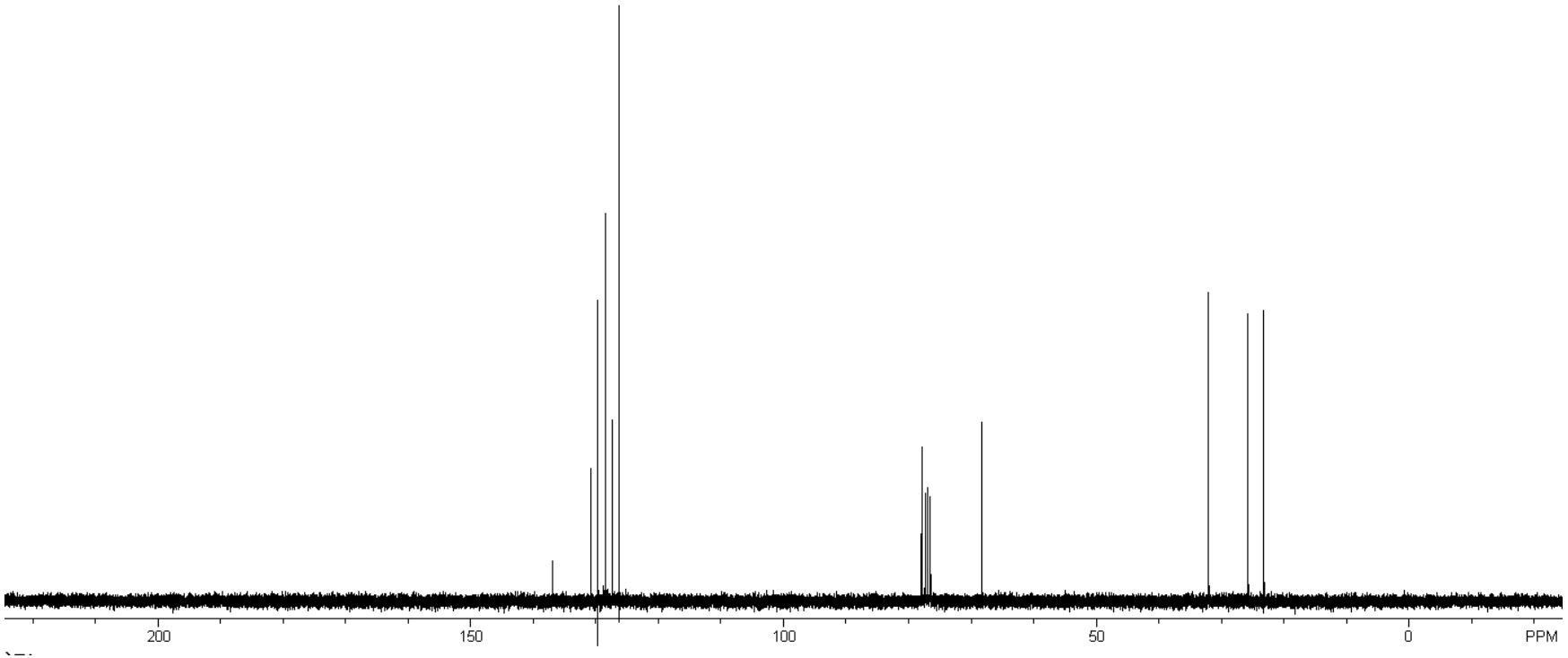

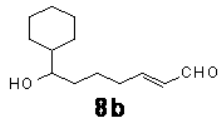

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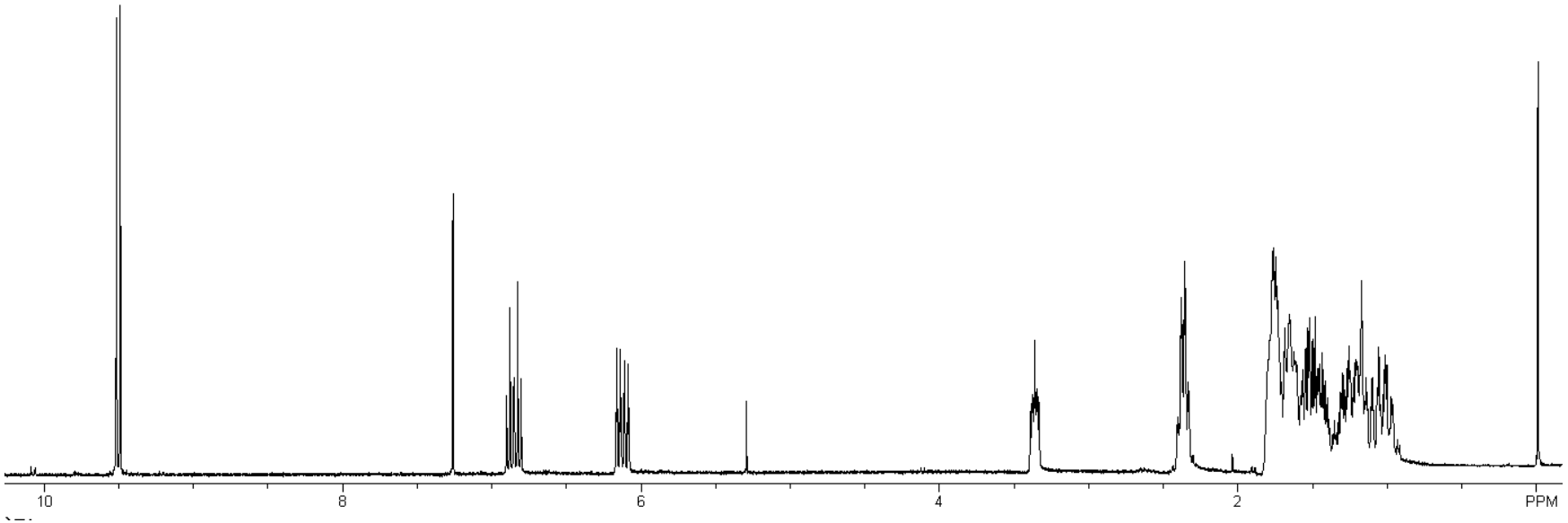

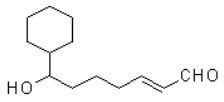

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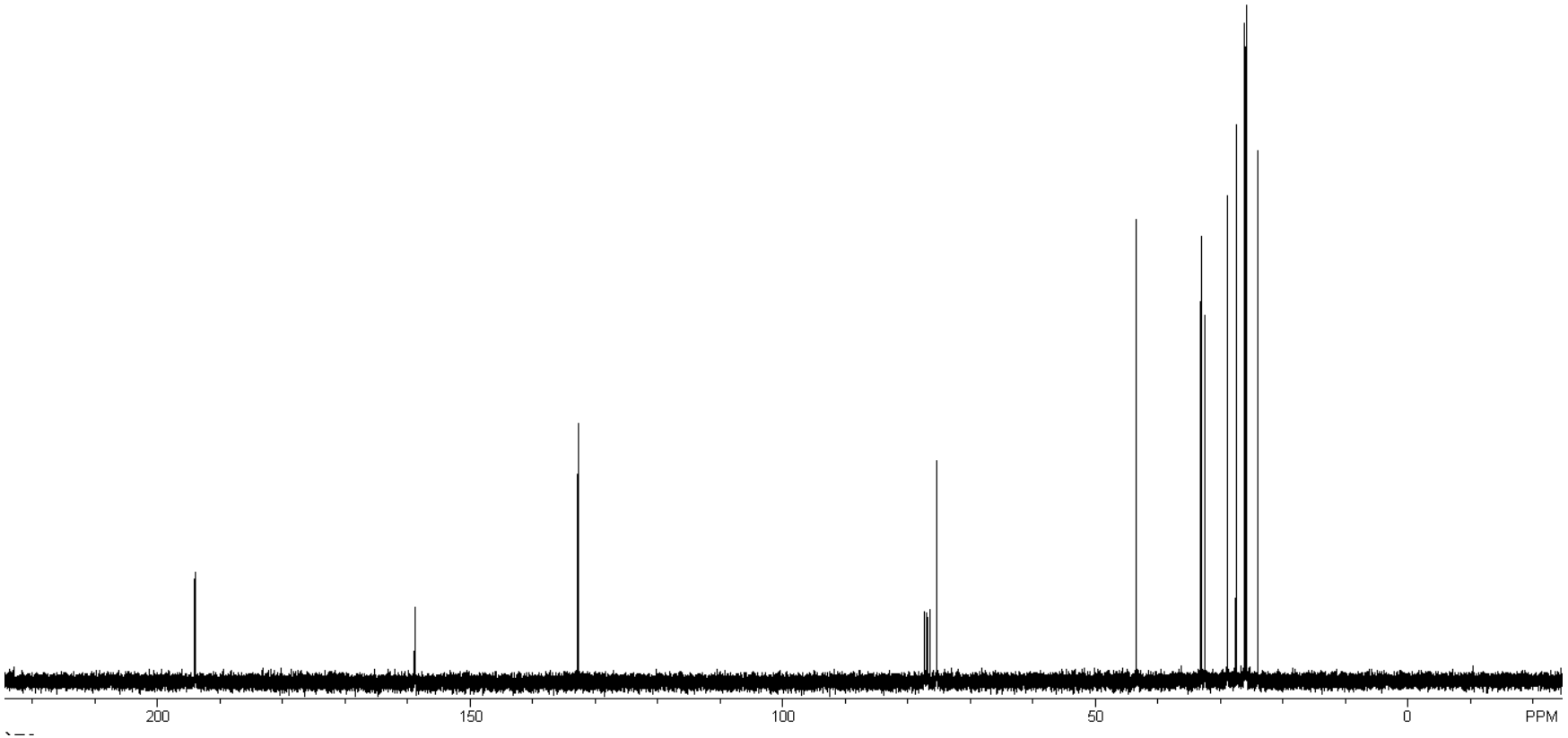

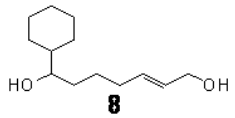

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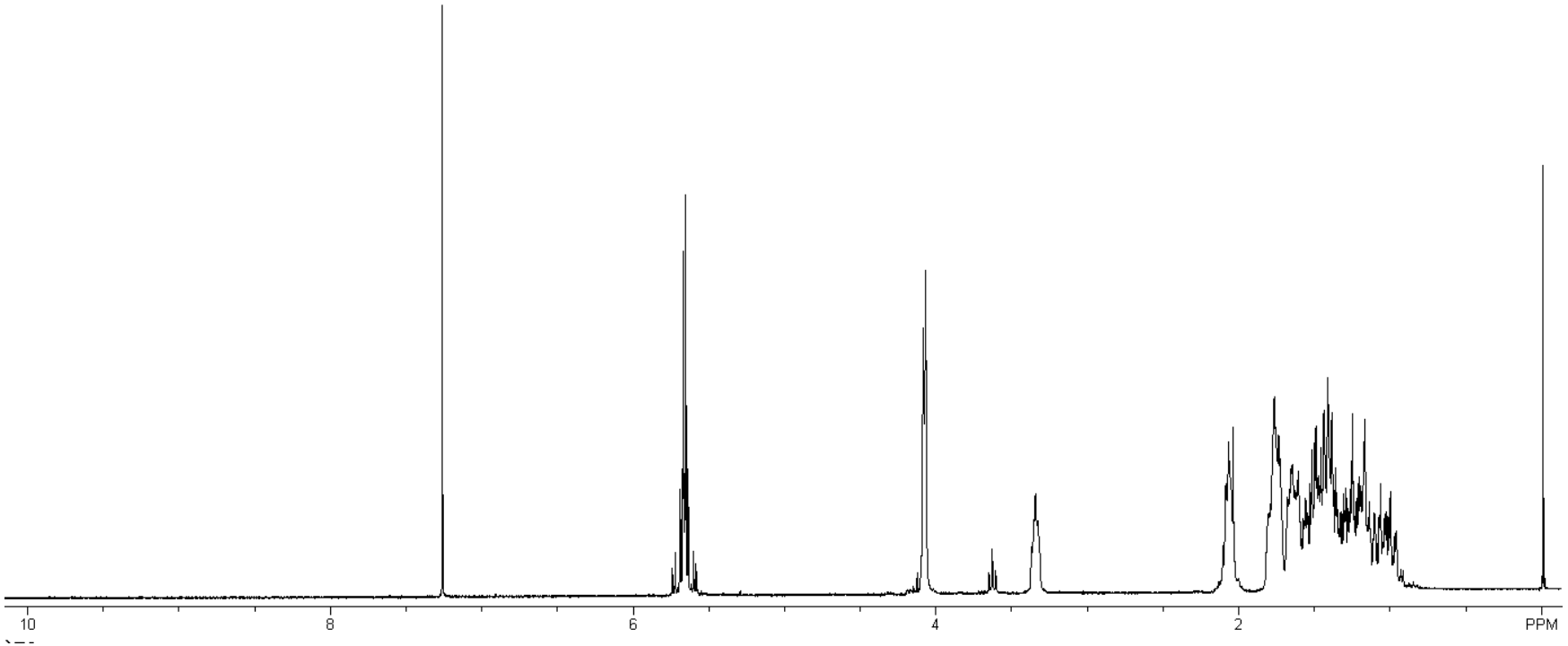

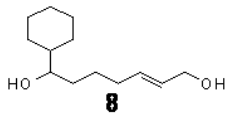

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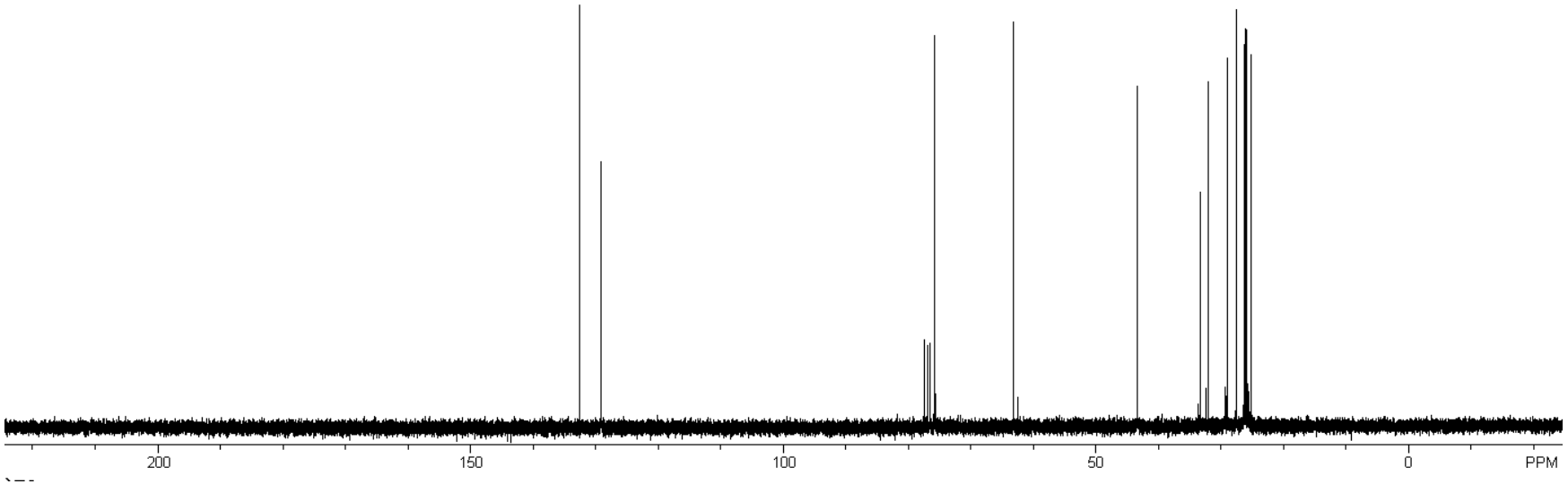

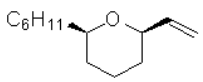

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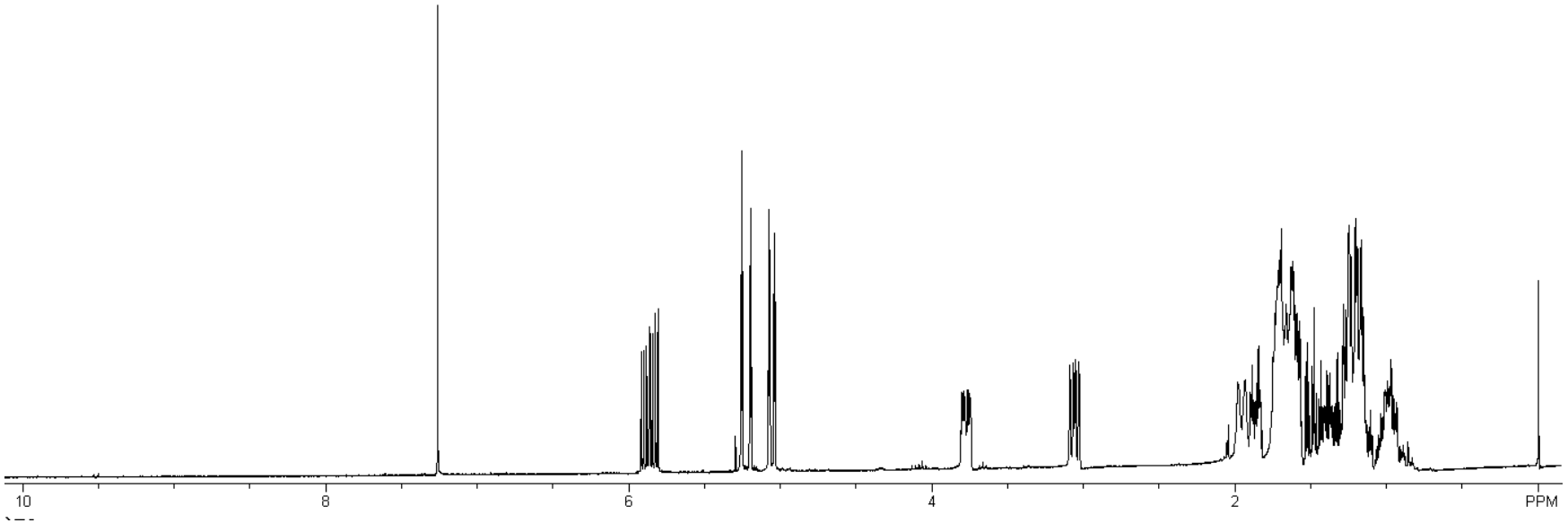

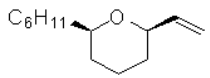

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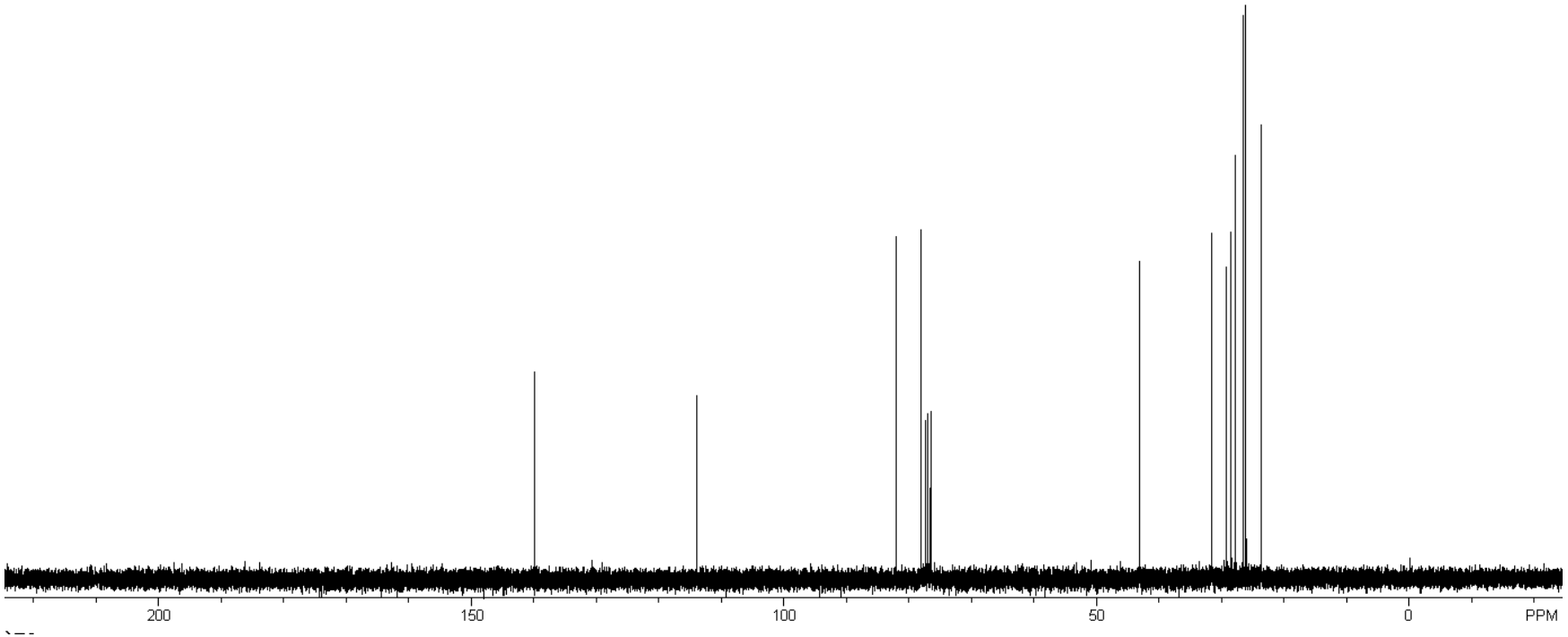

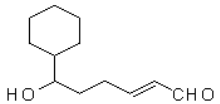

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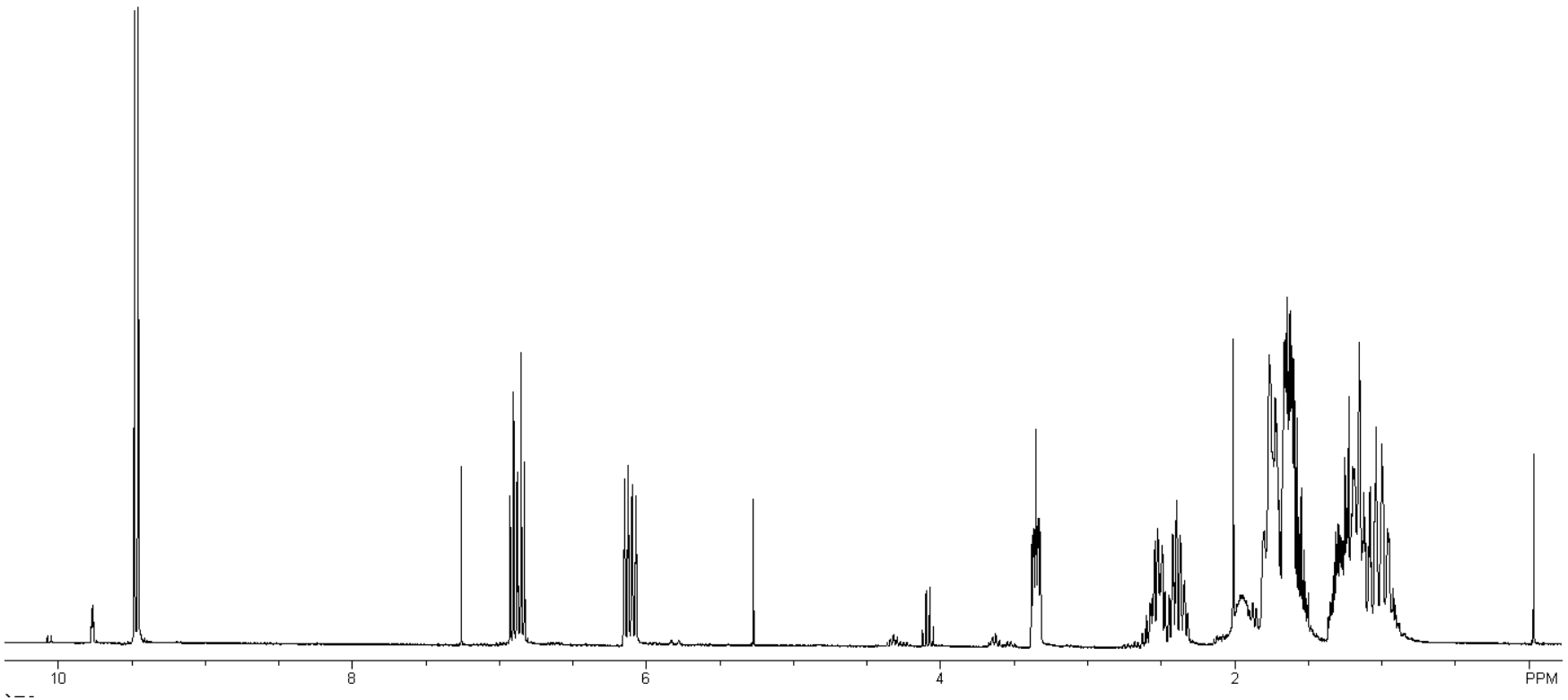

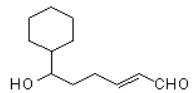

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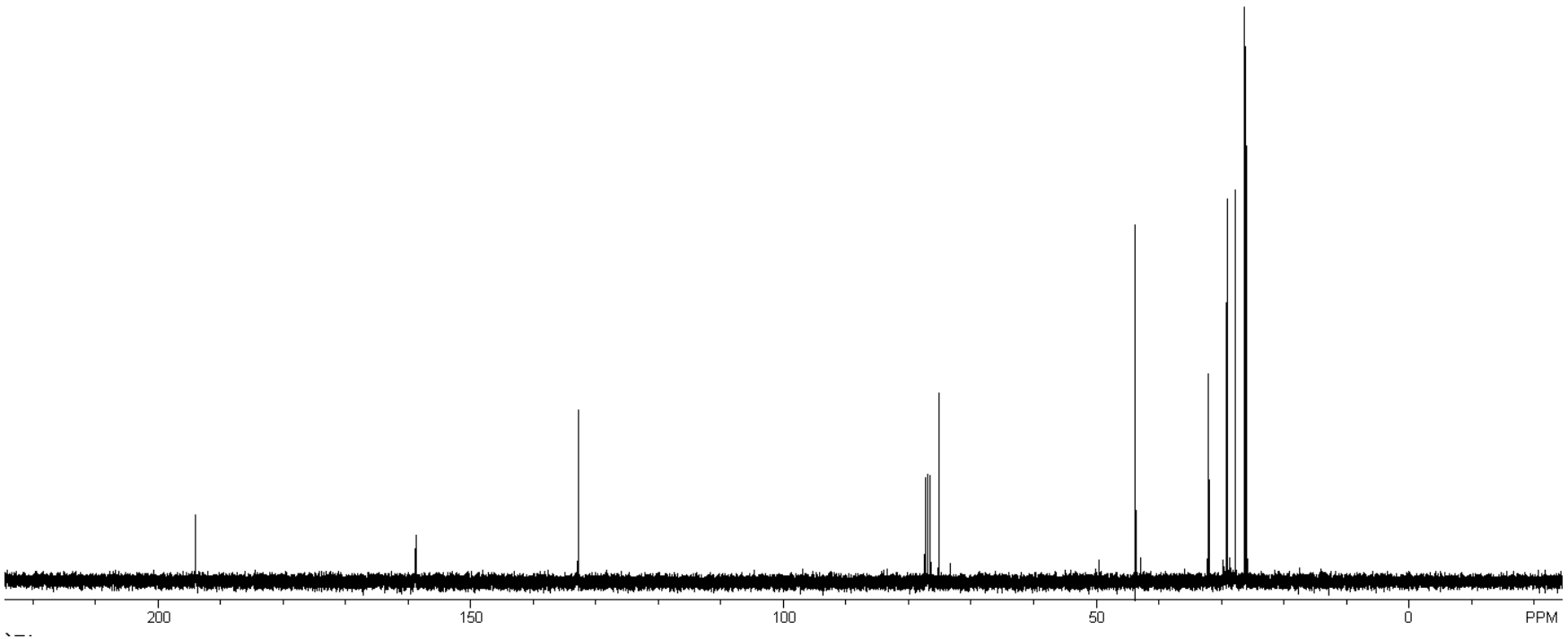

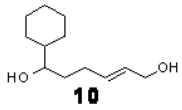

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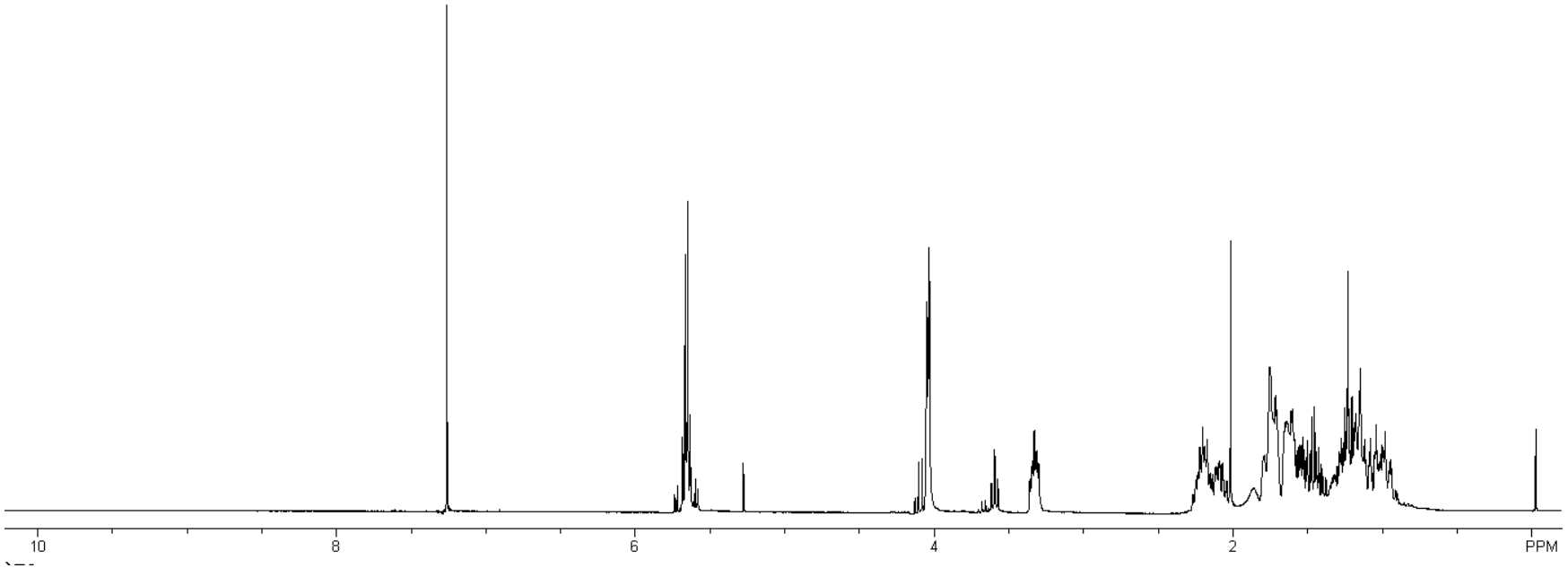

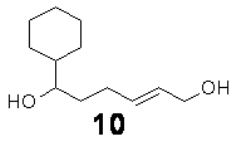

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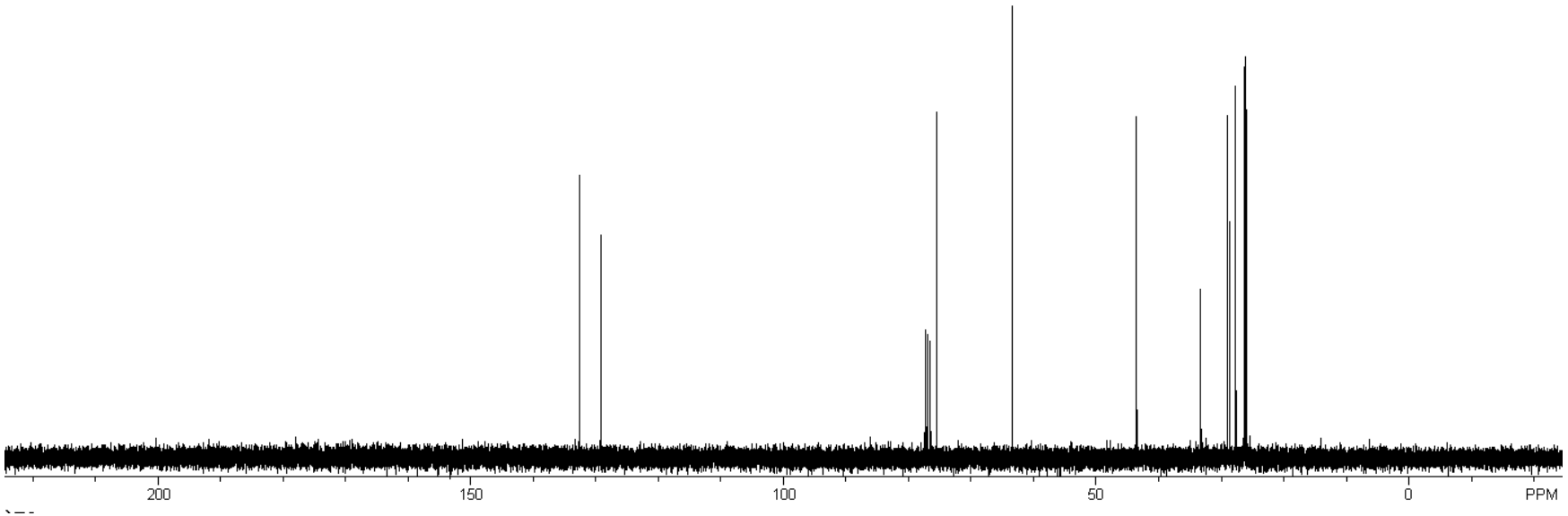

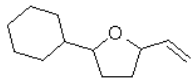

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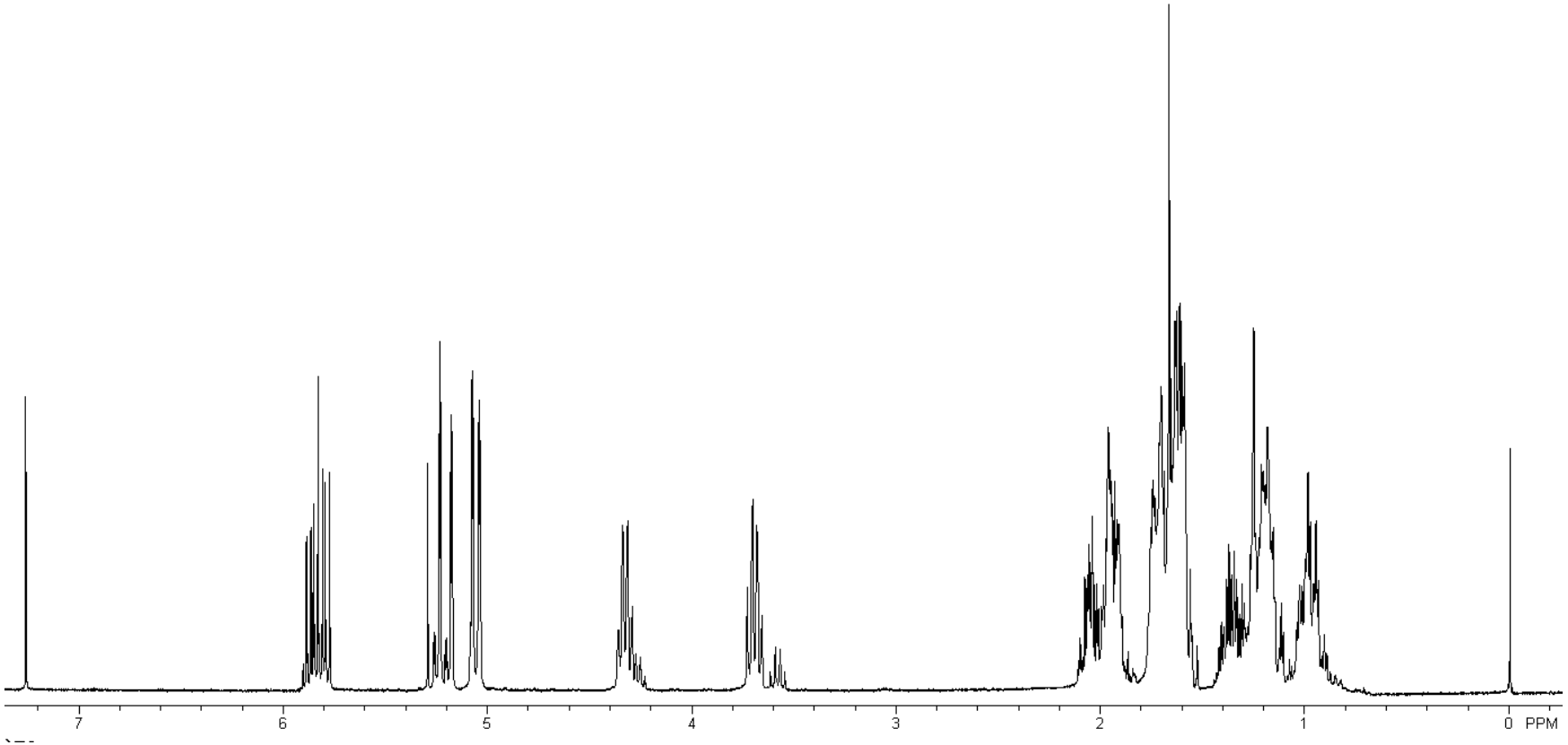

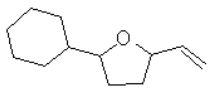

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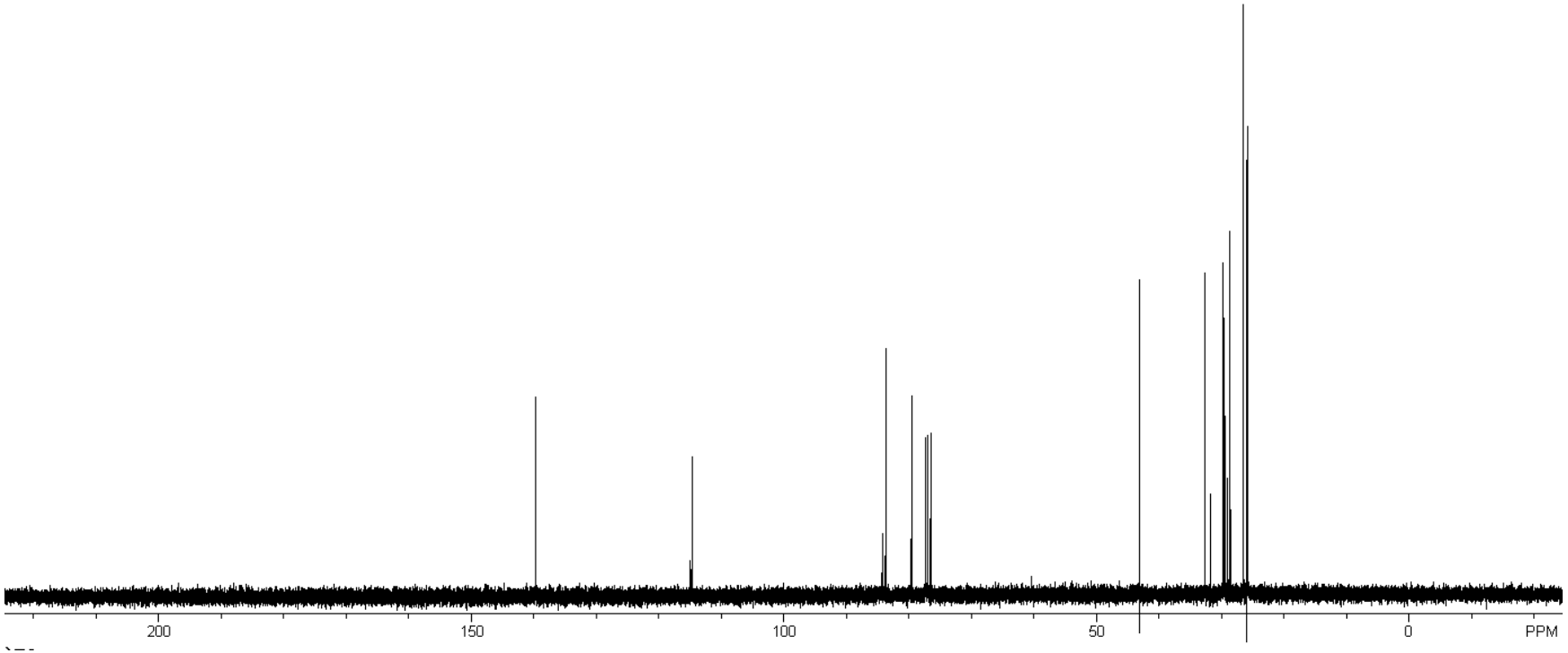

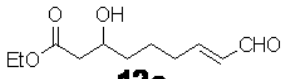

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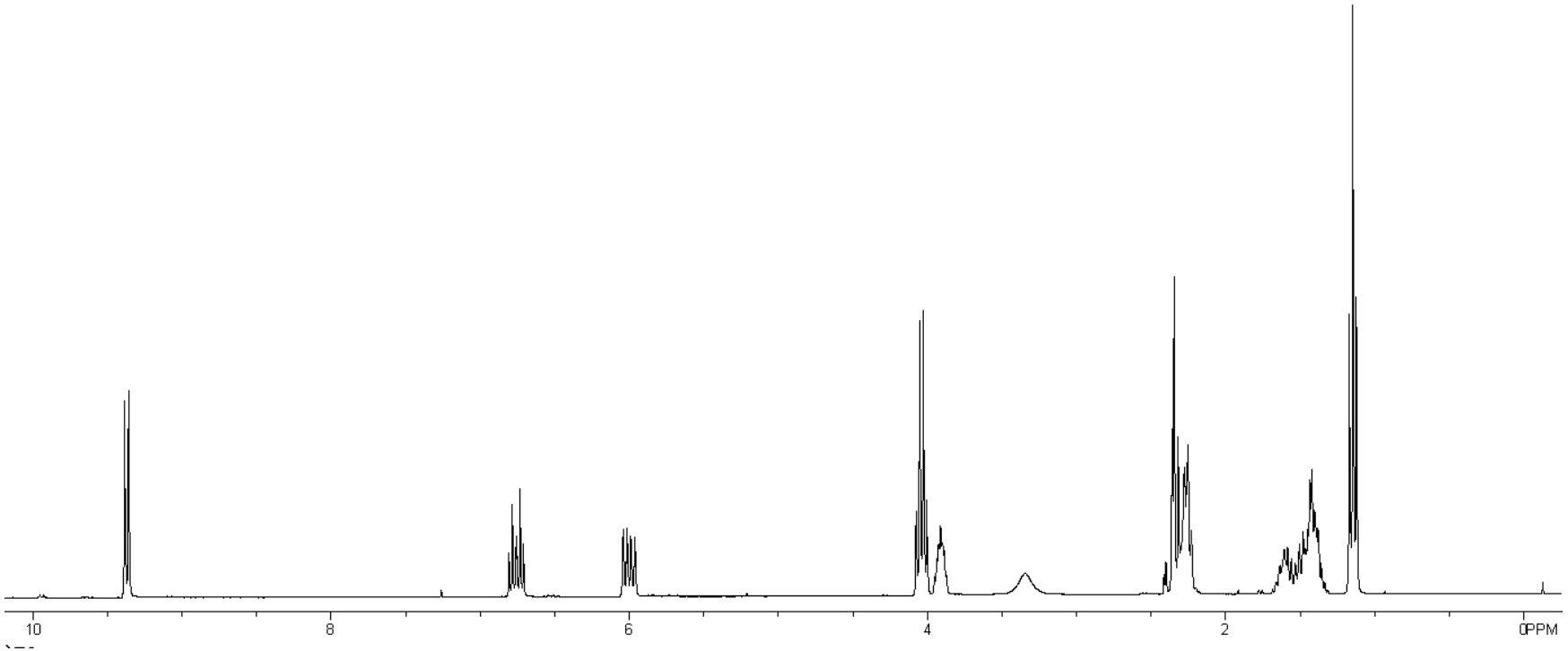

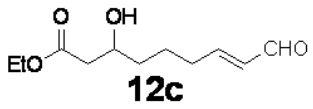

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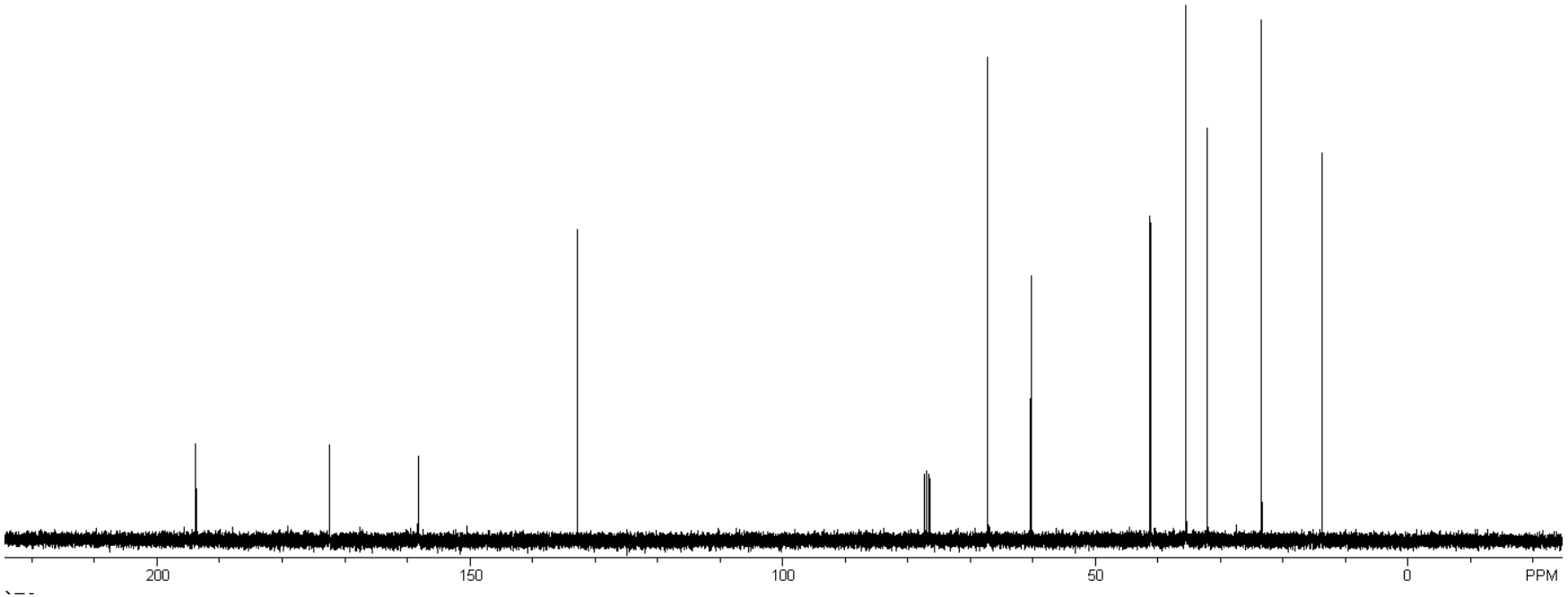

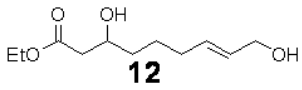

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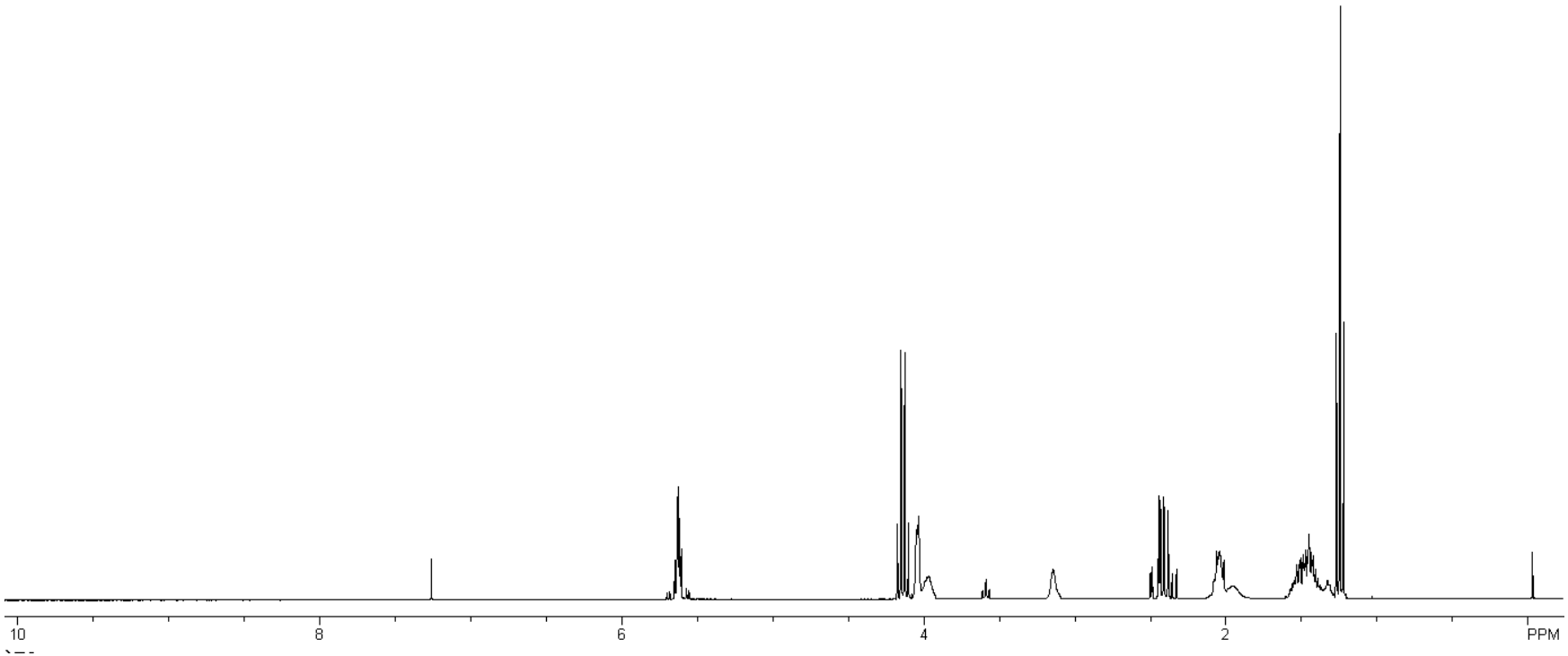

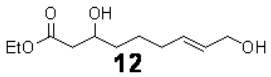

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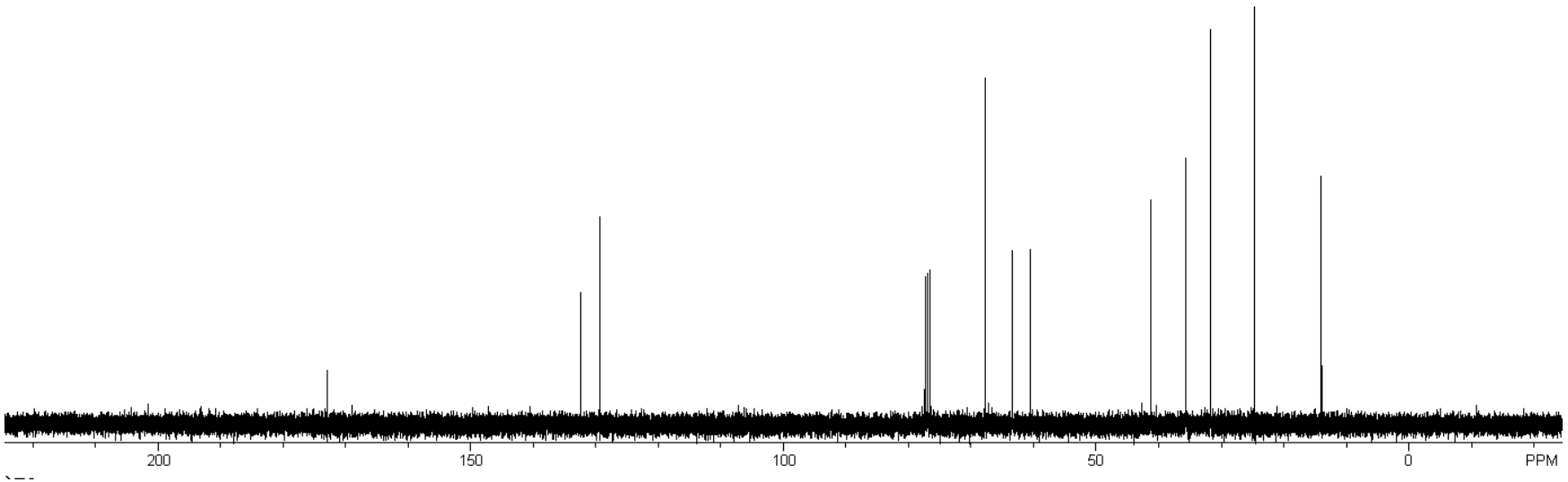

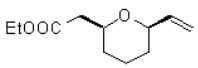

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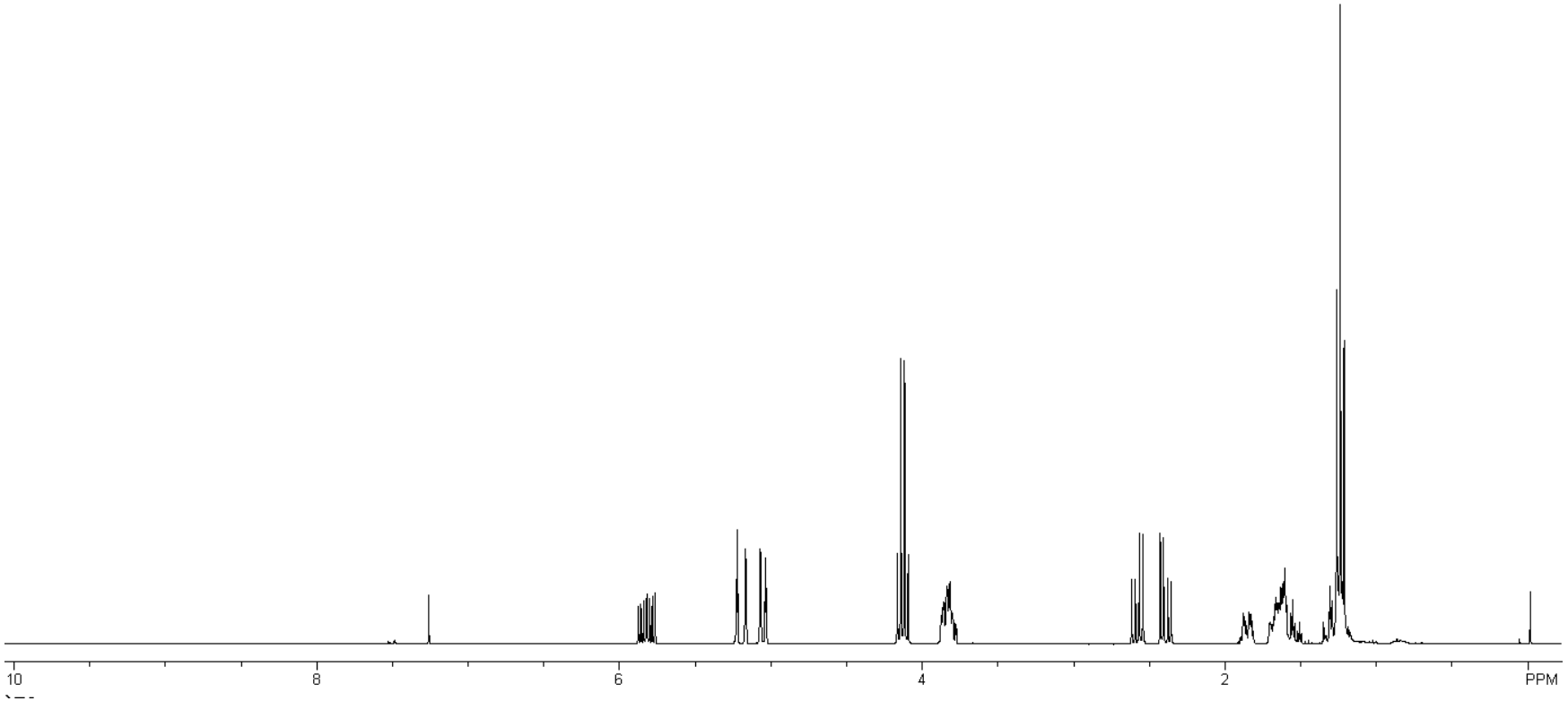

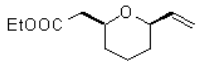

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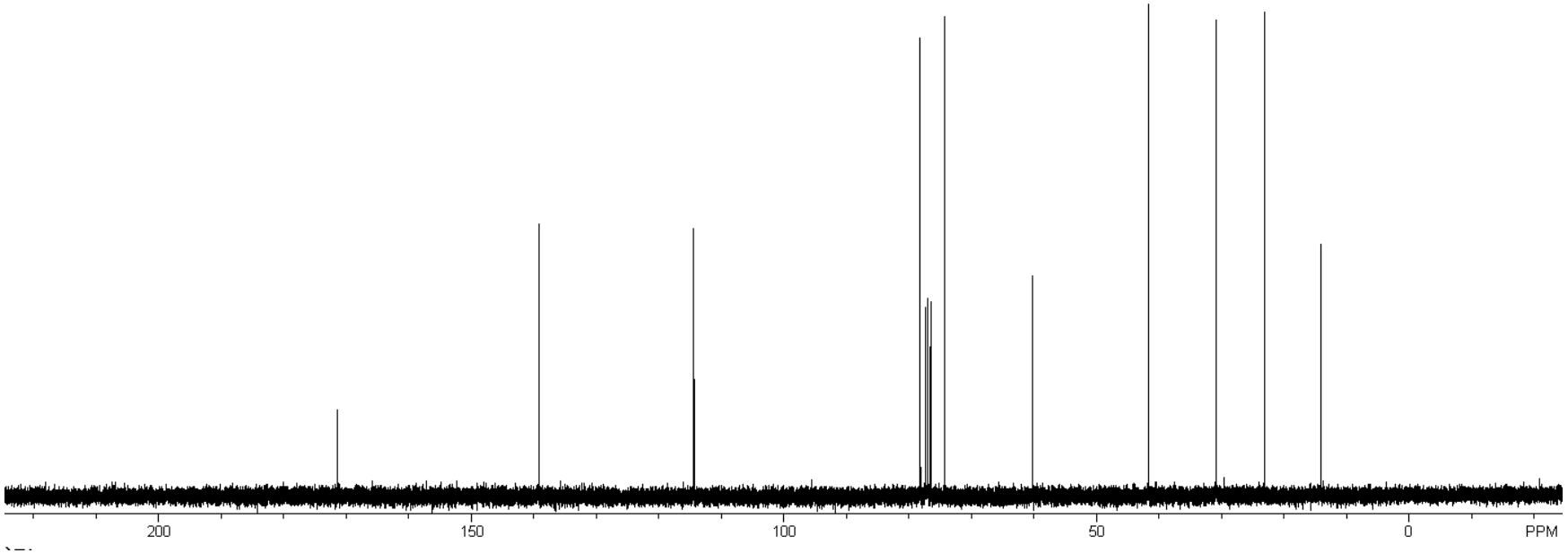

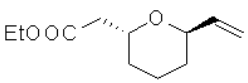

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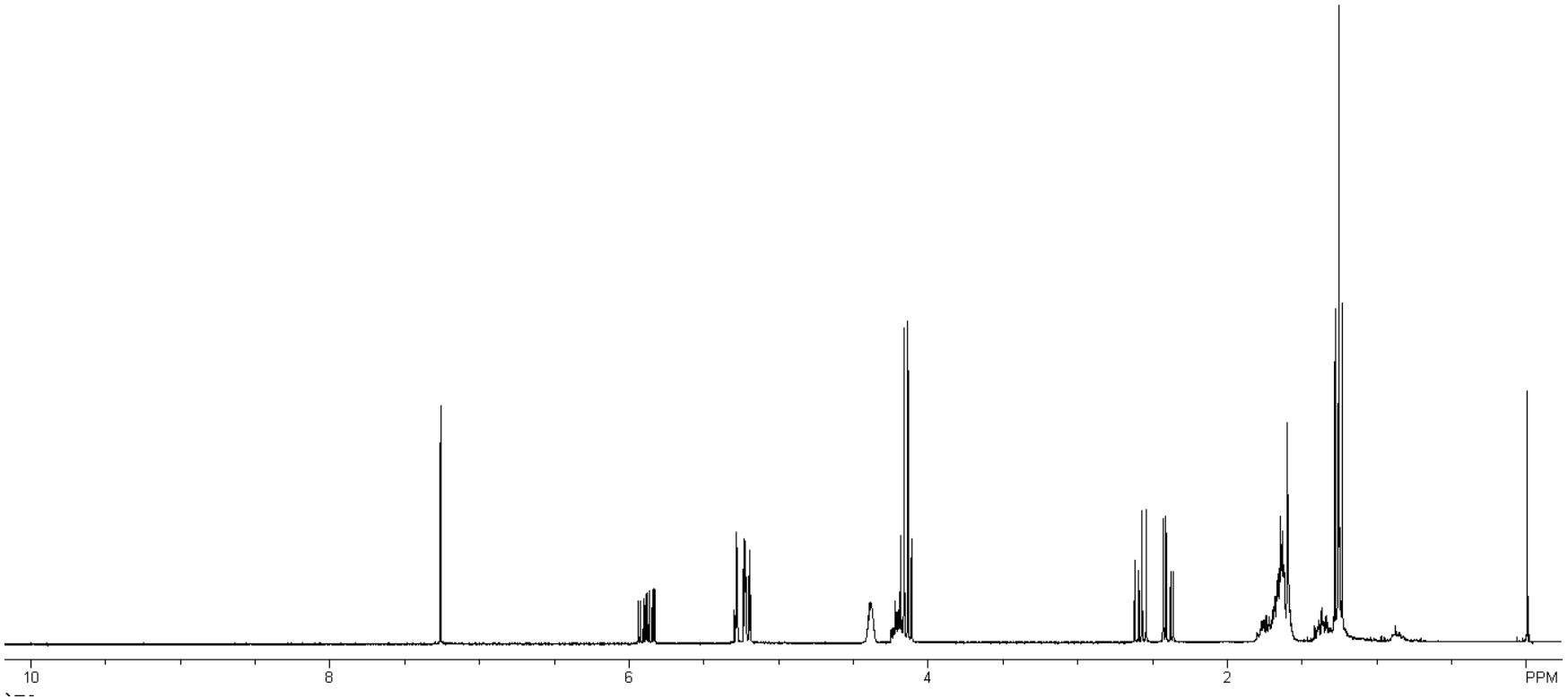

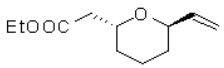

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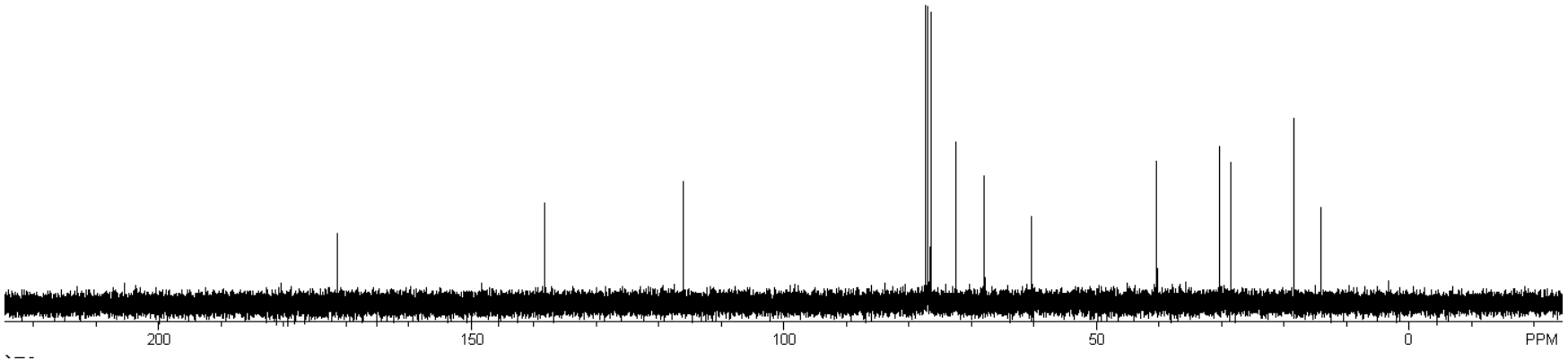

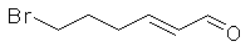

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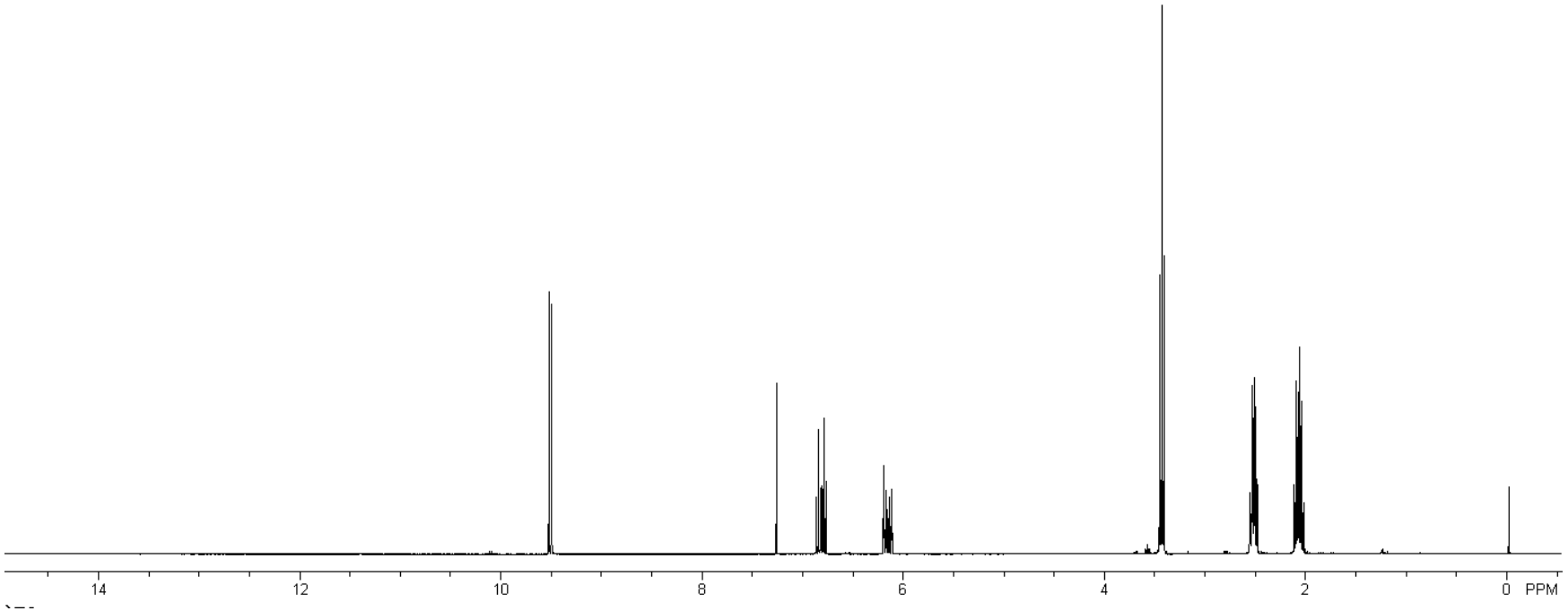

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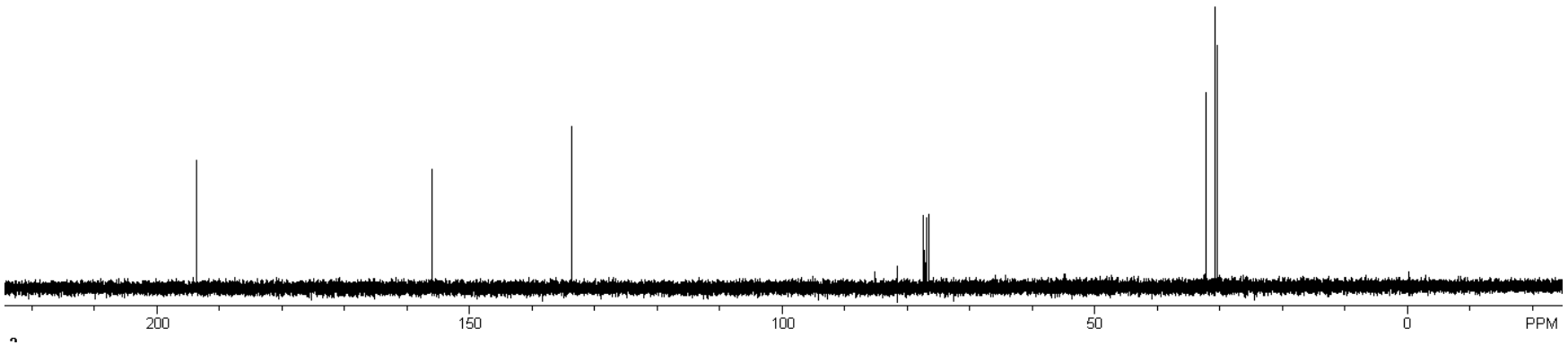

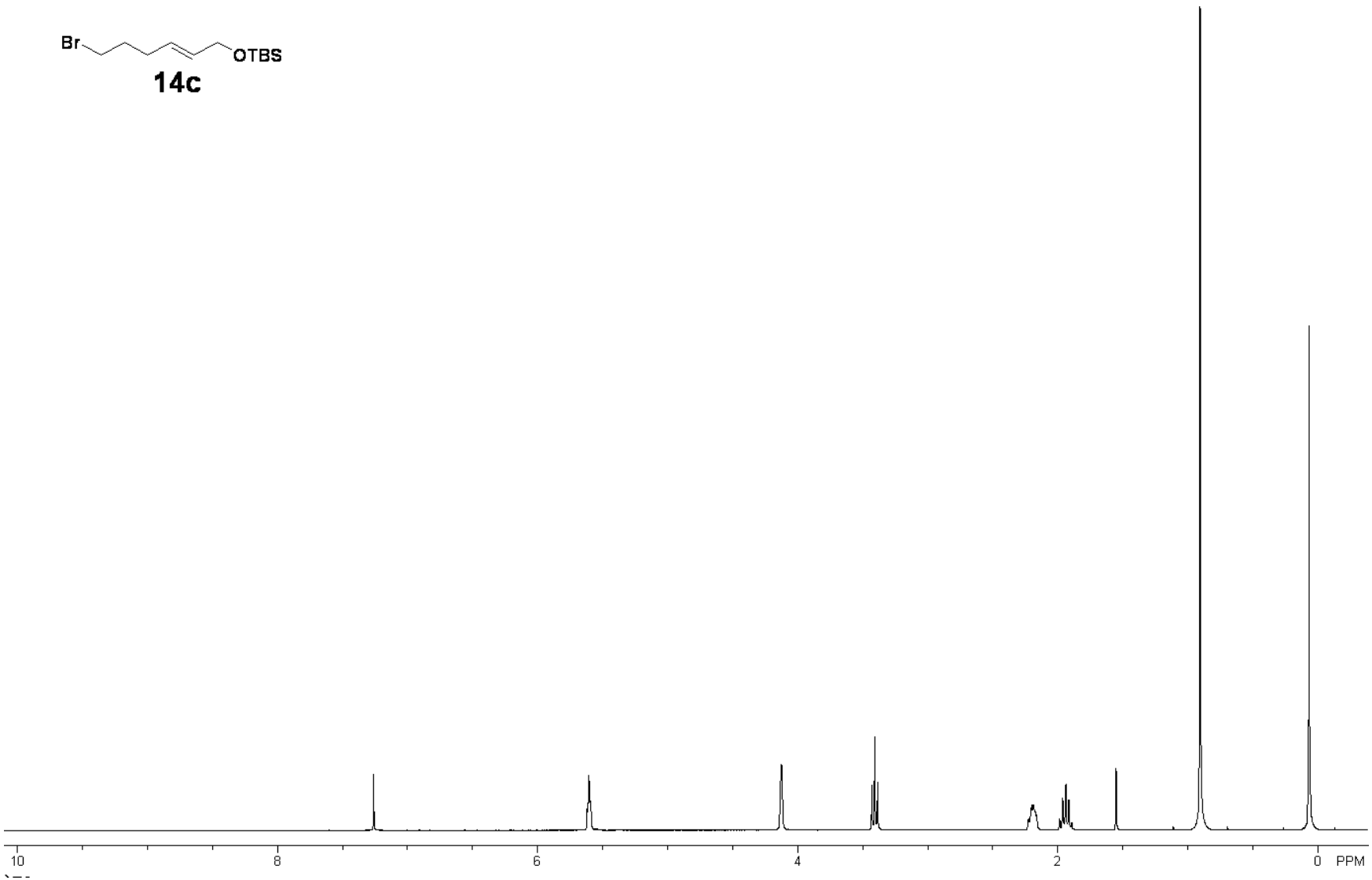
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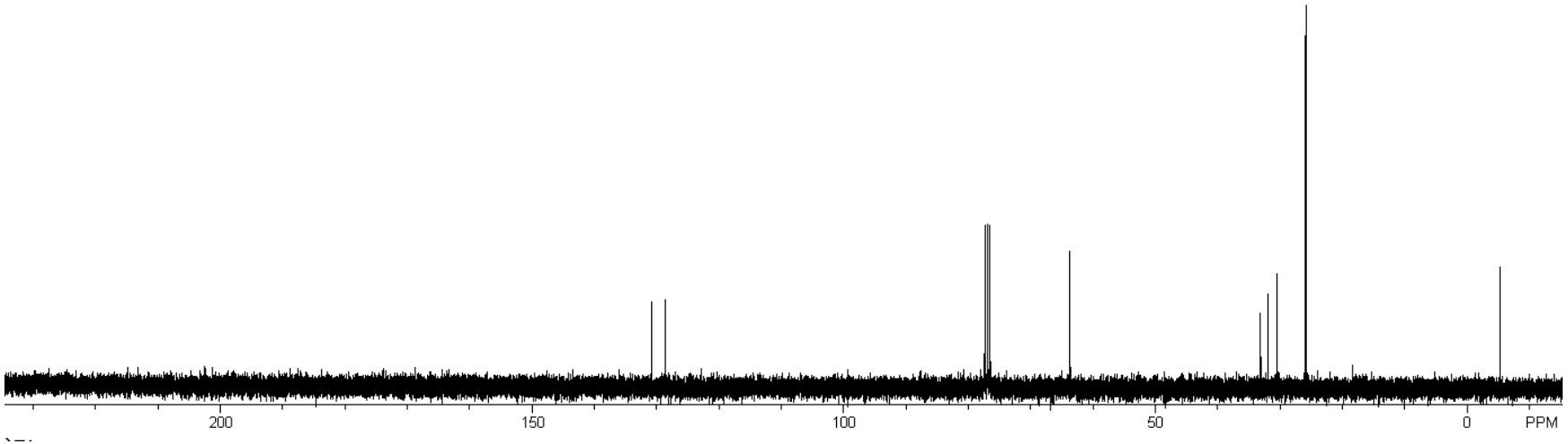
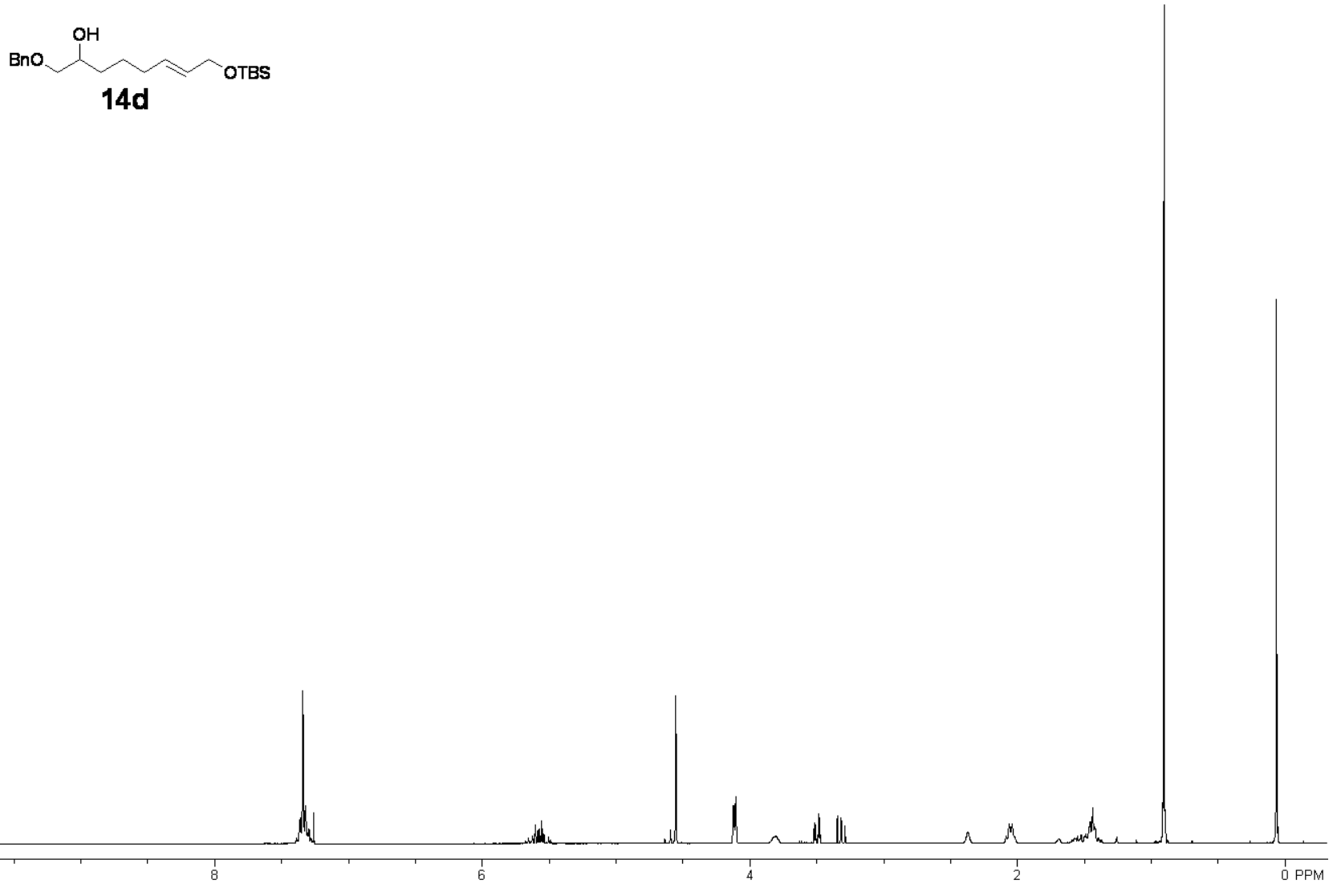
PPM

14c

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BnO
OTBS
14d
10
8
6
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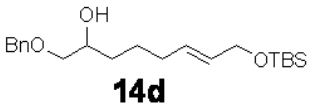
0 PPM



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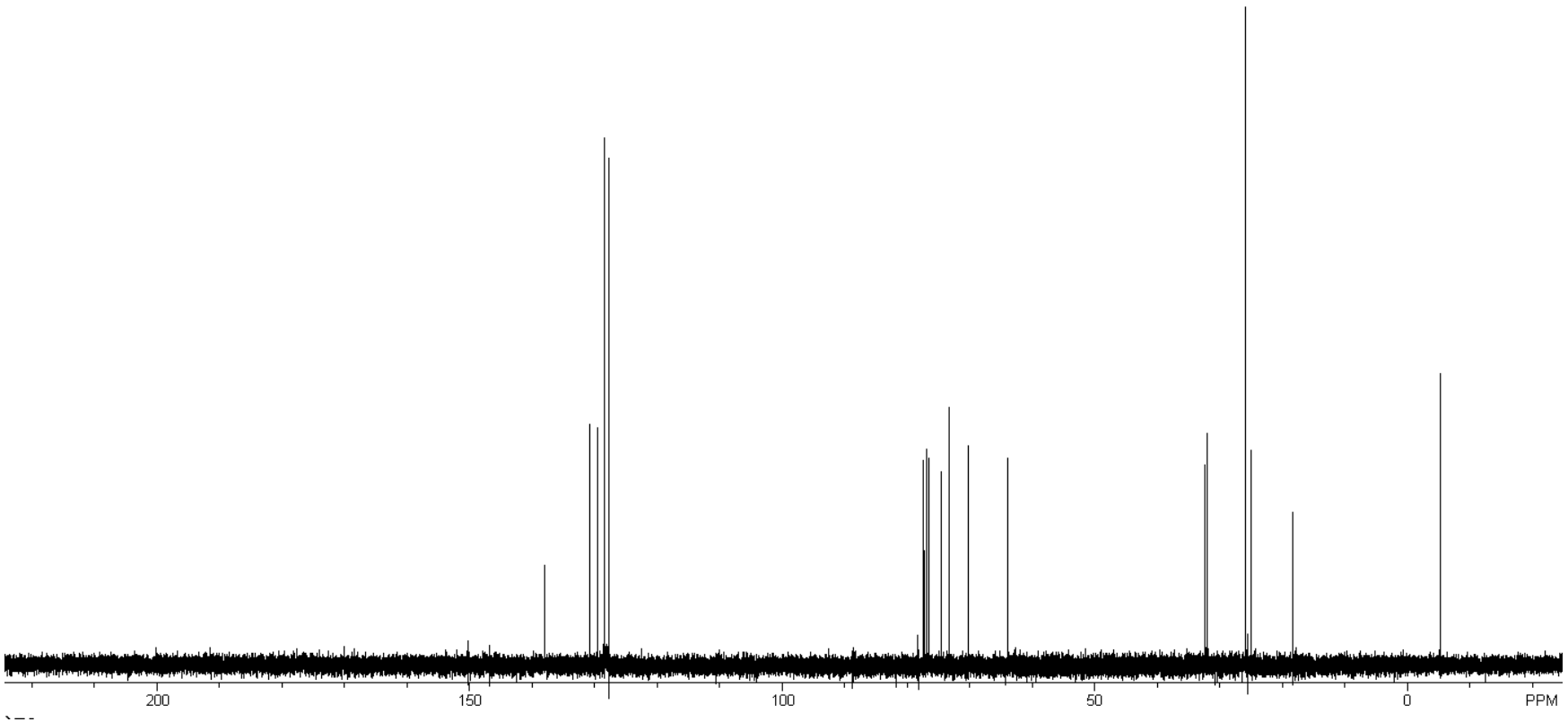

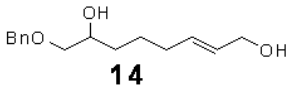

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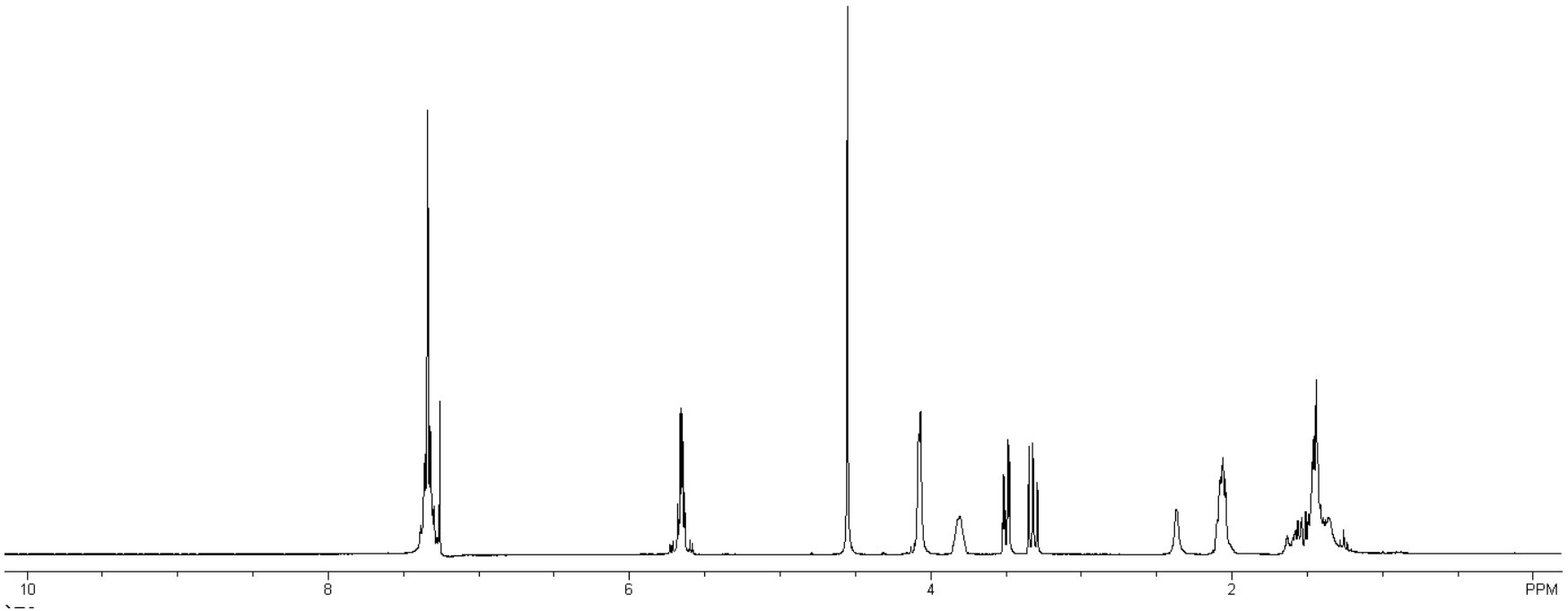

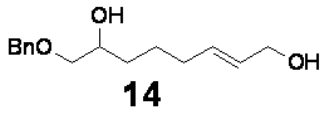

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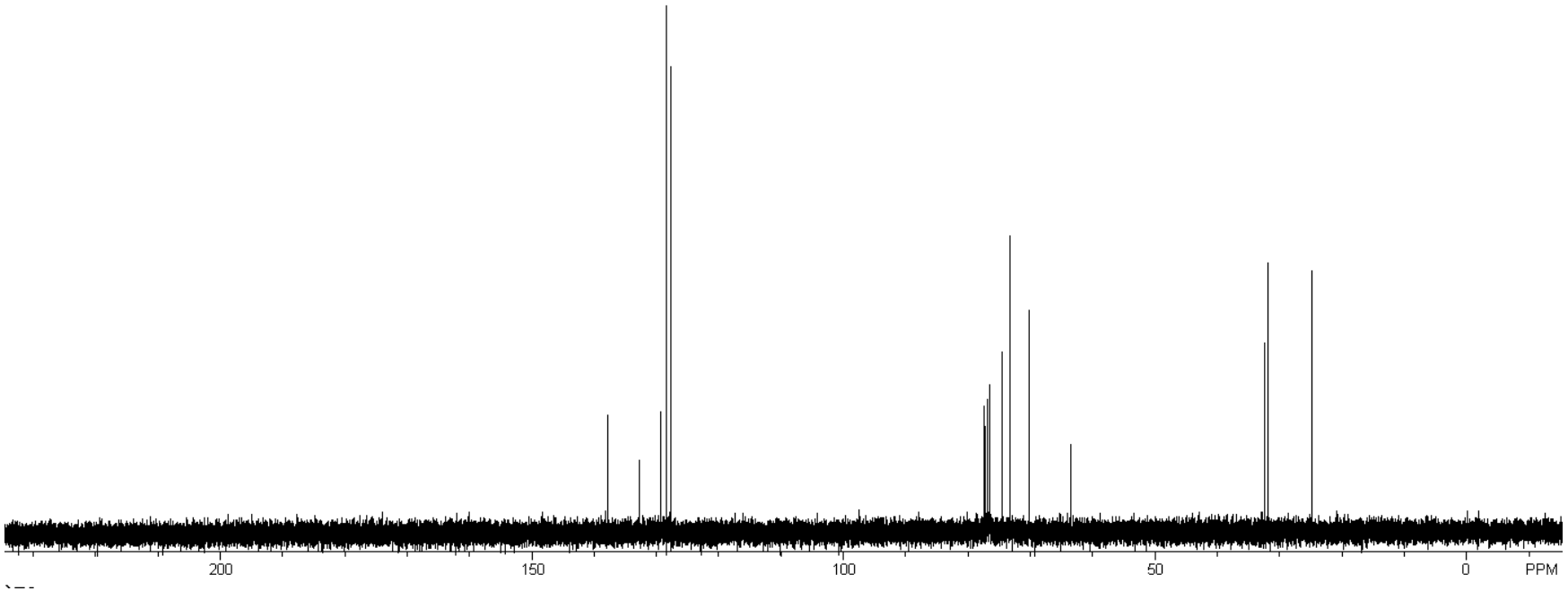

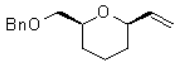

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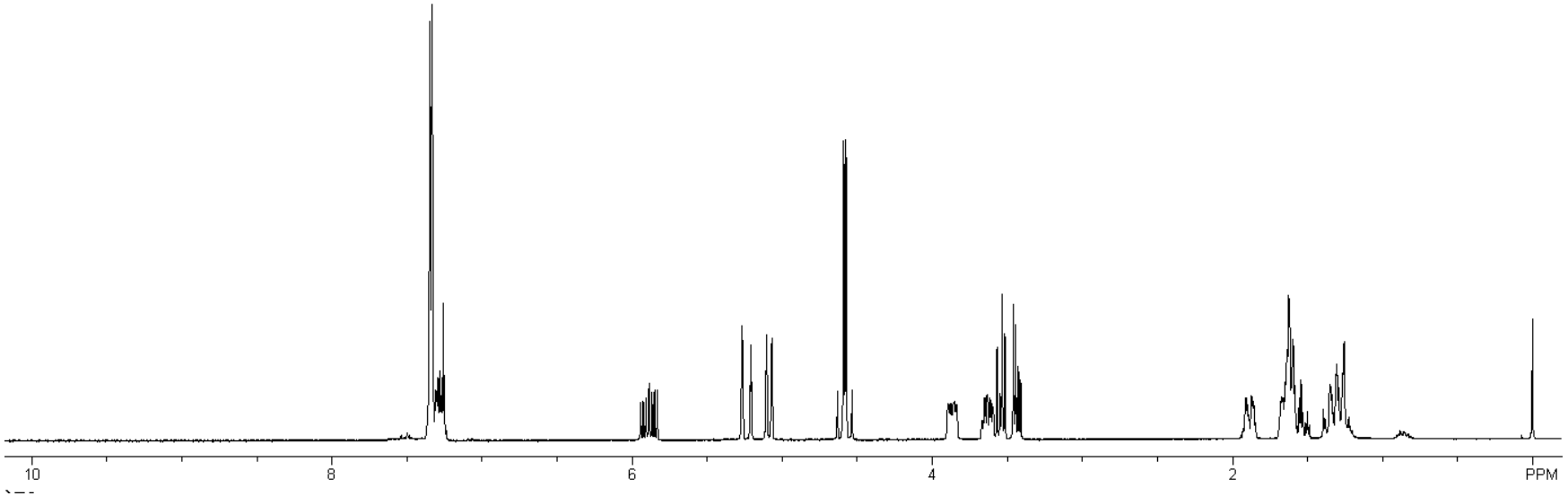

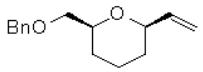

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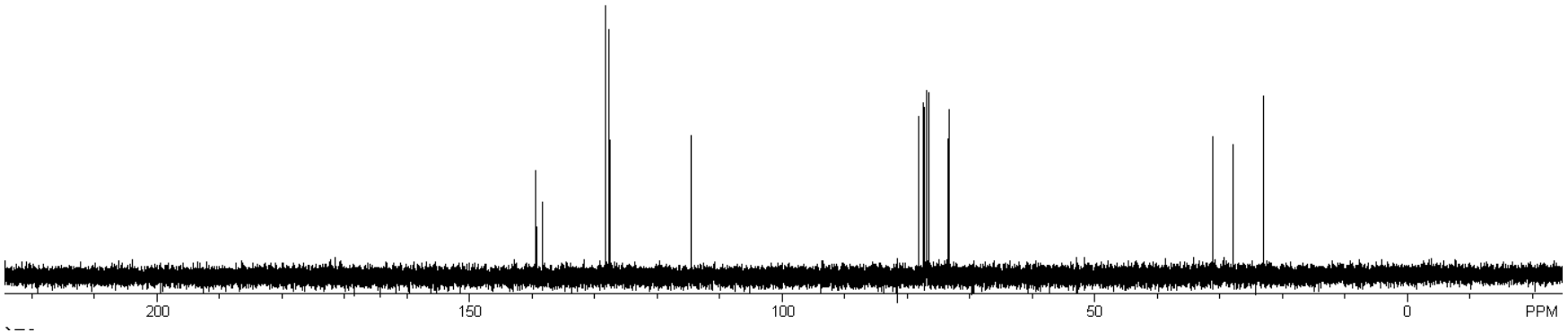

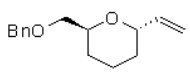

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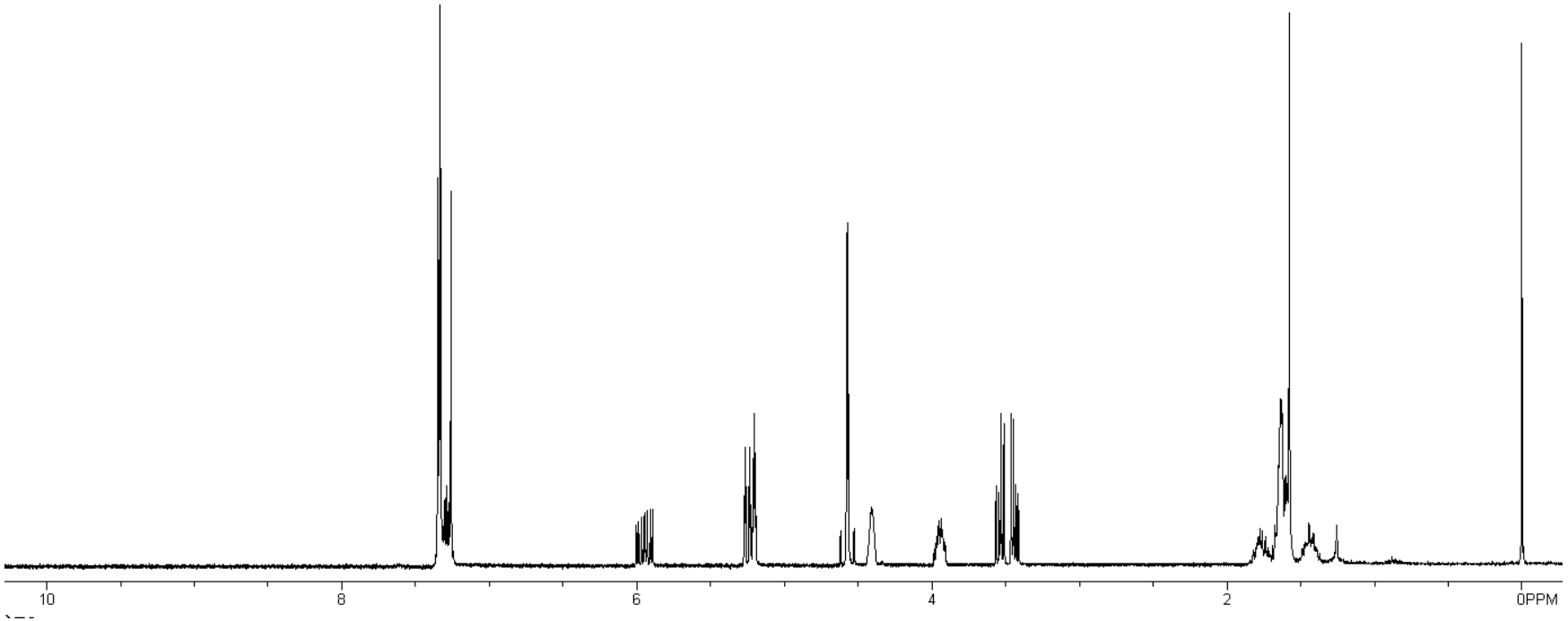

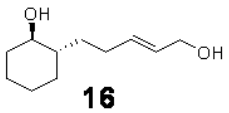

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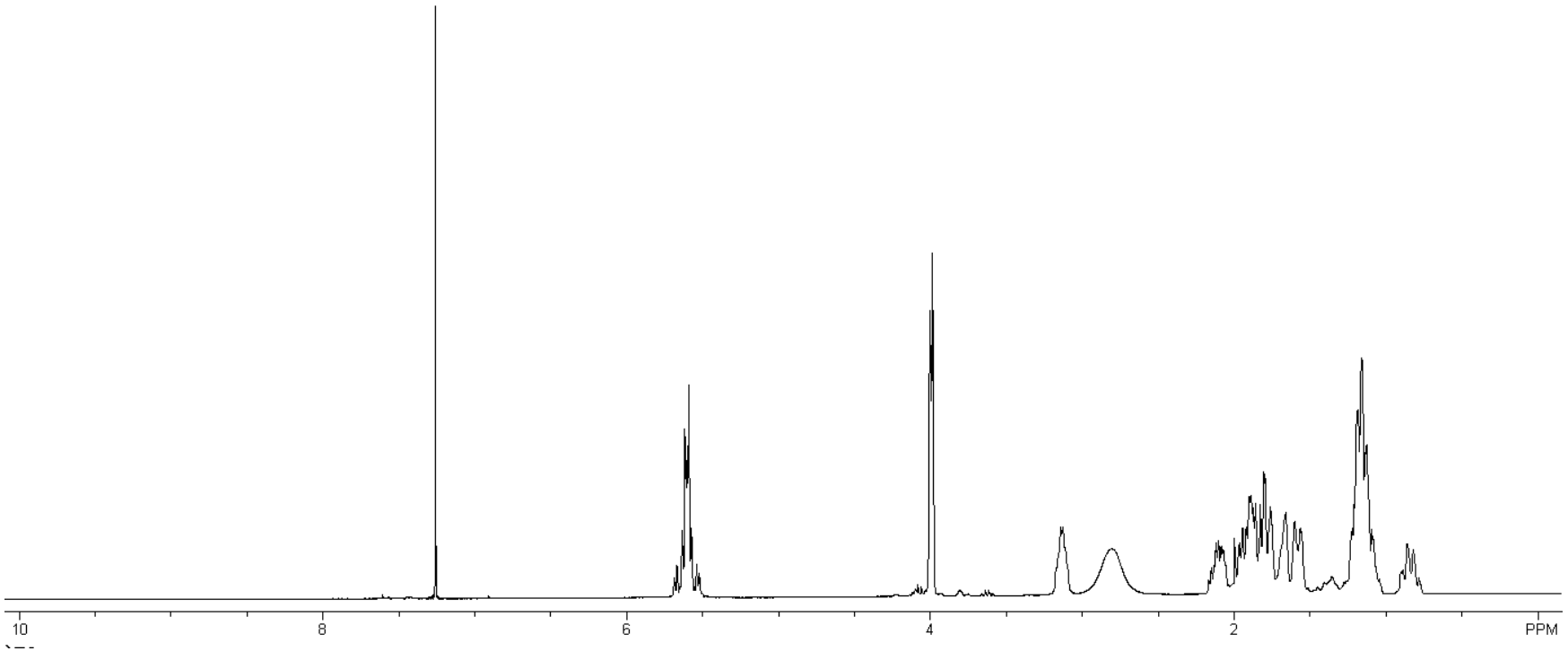

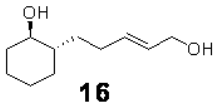

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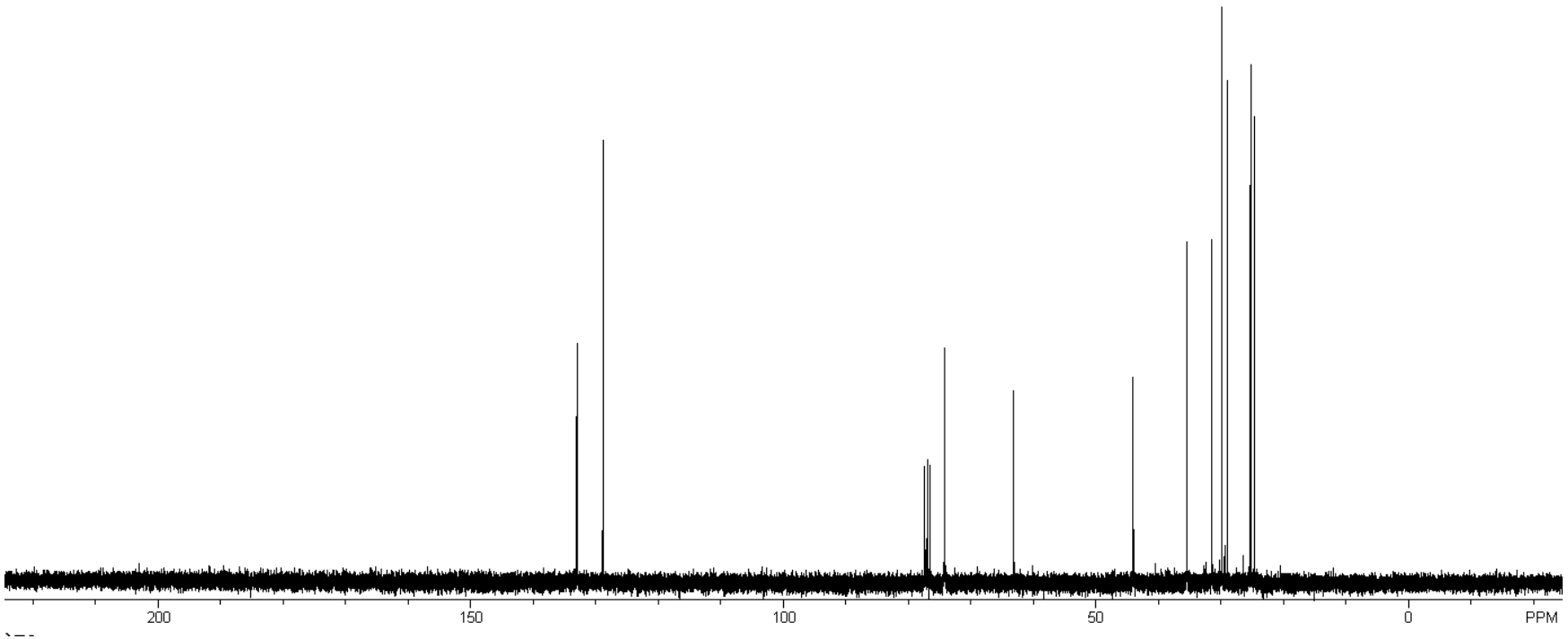

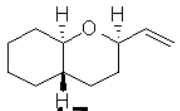

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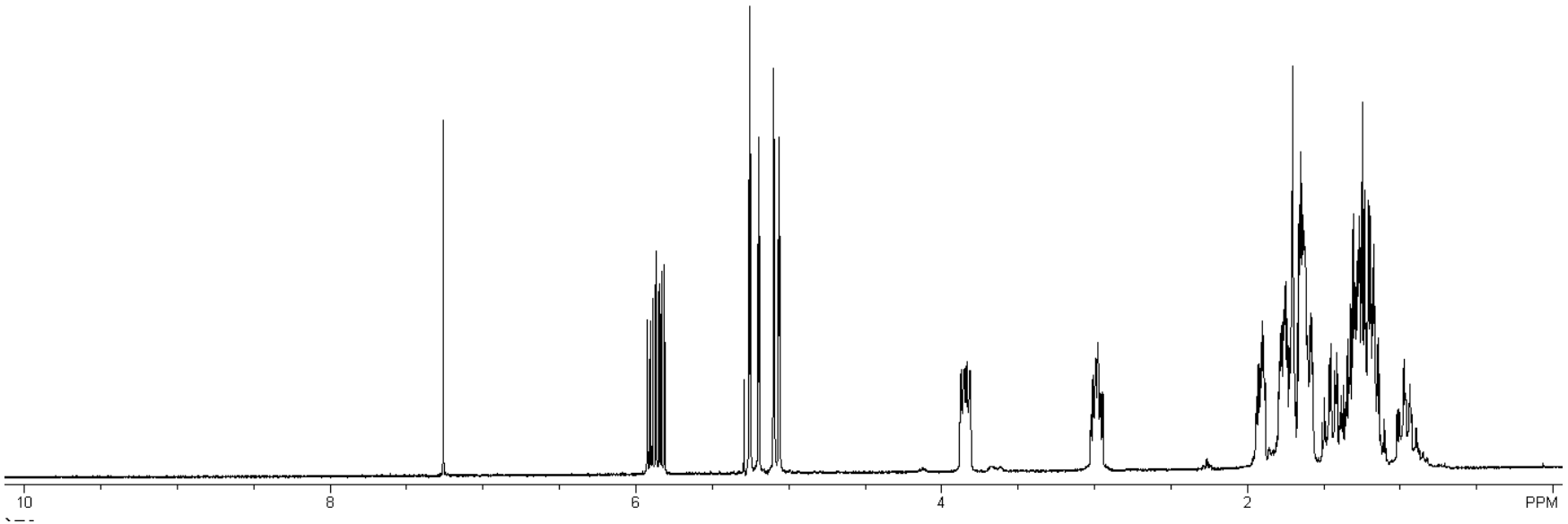

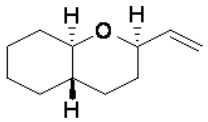

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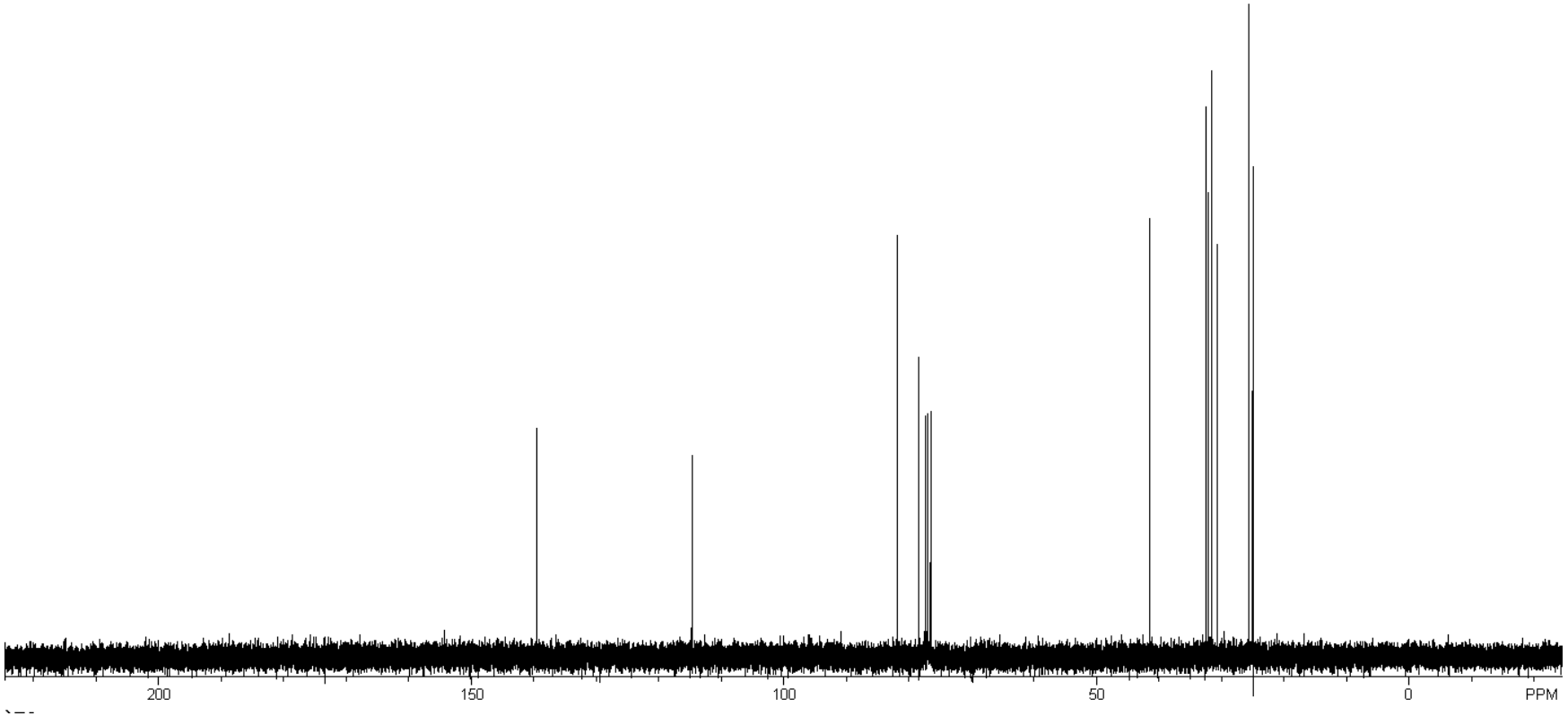

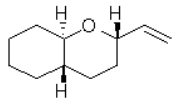

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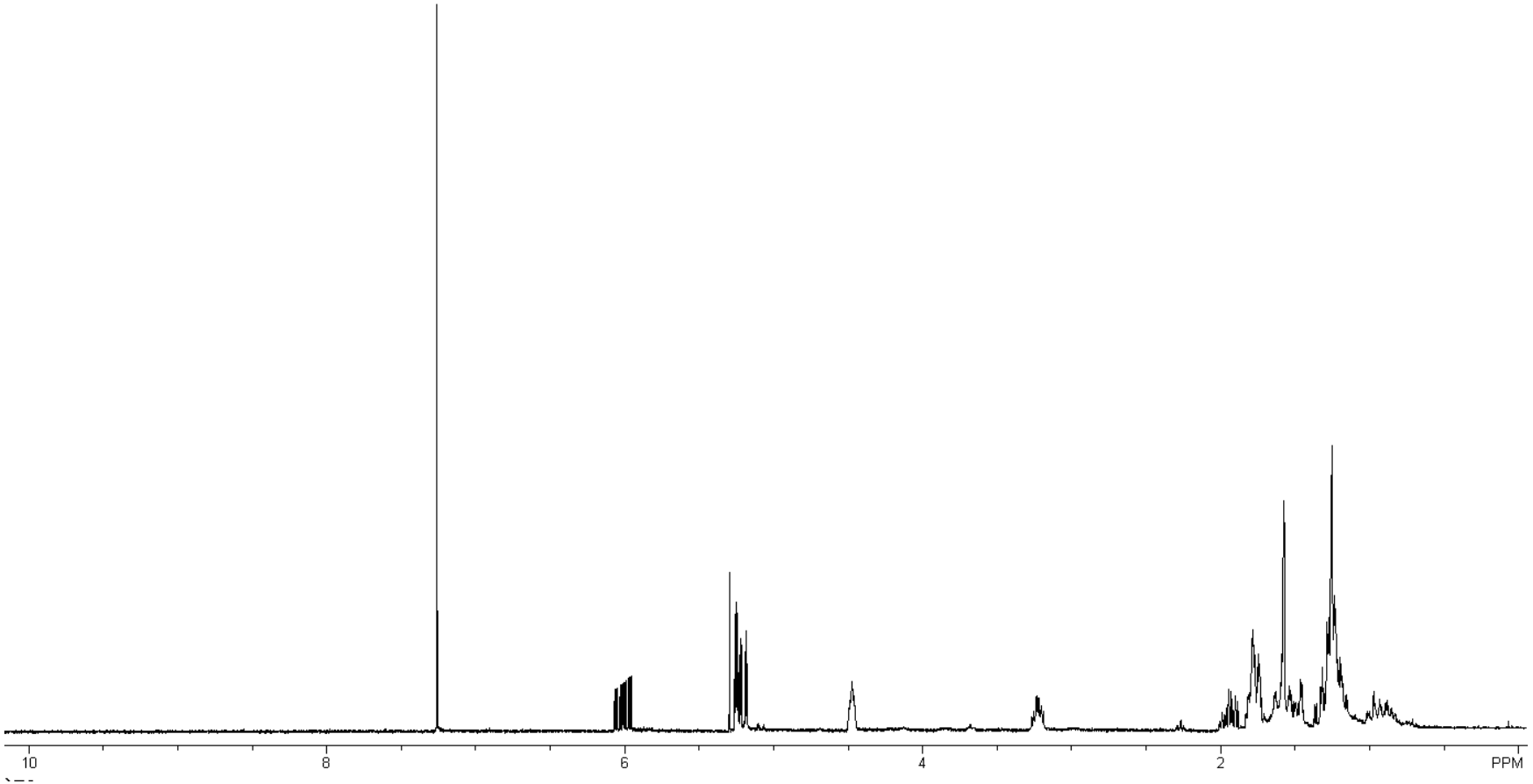

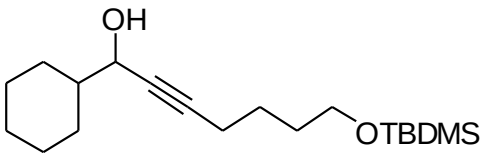

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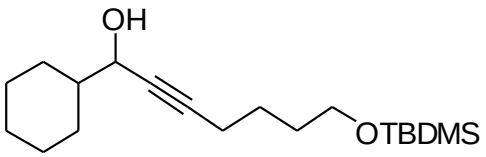

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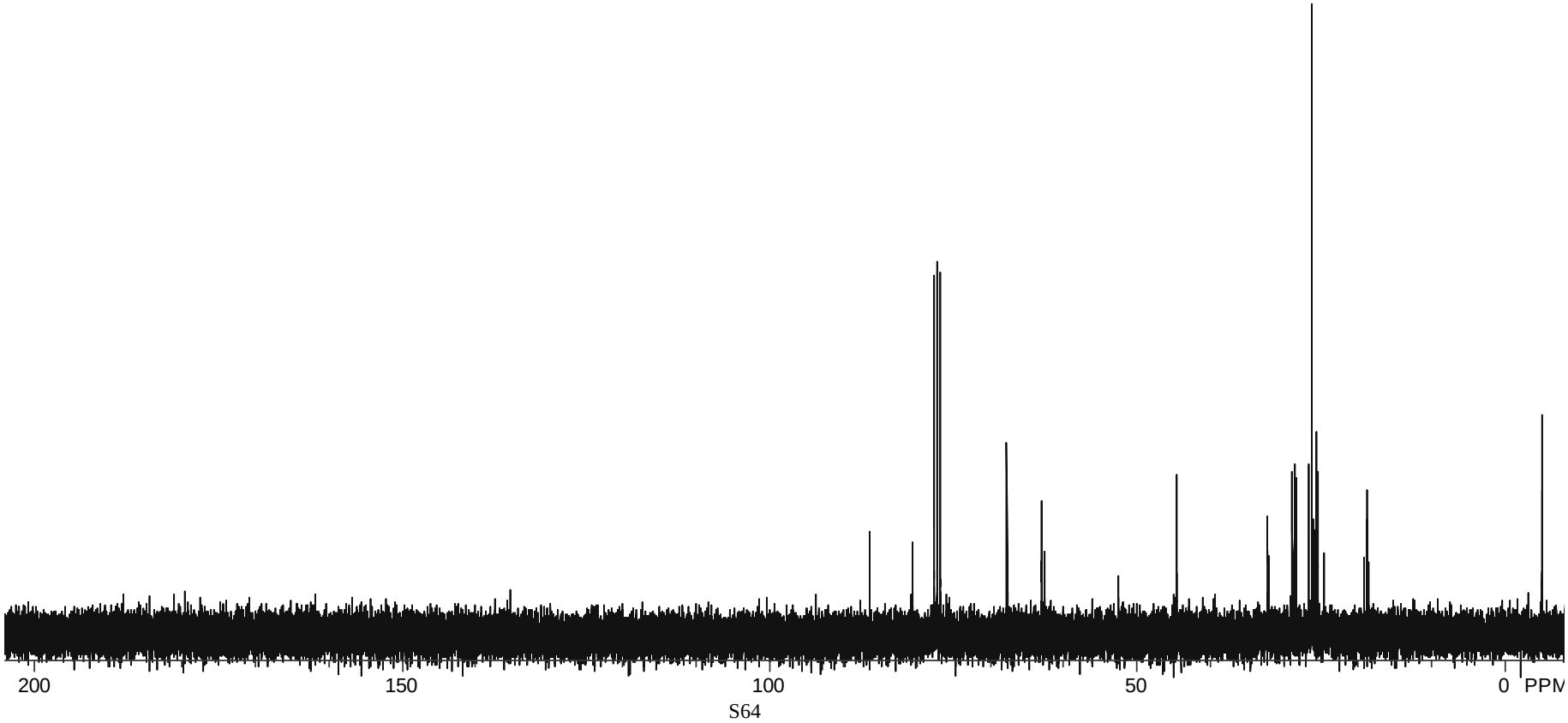

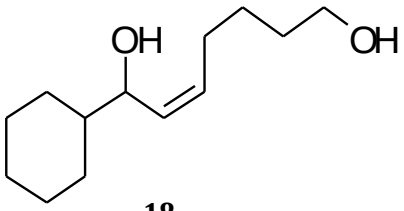

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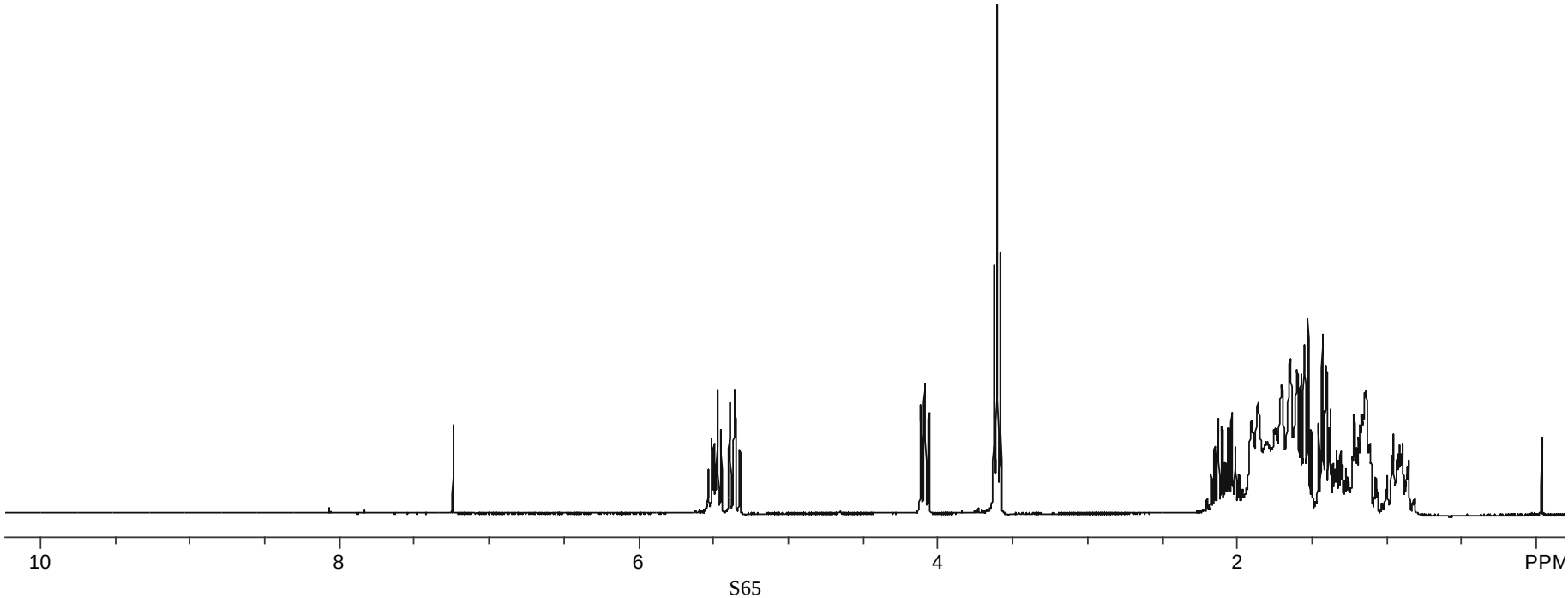

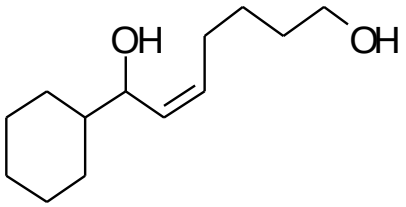

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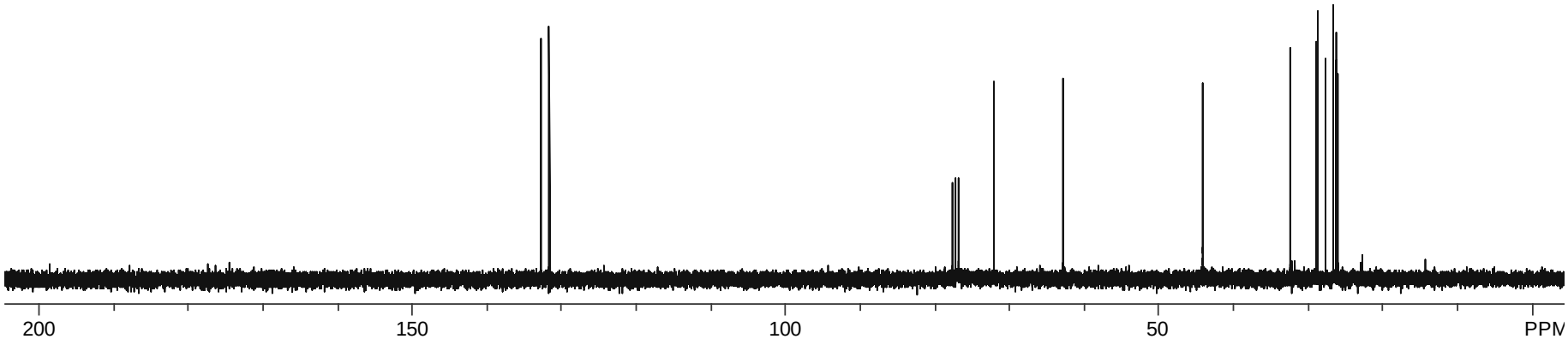

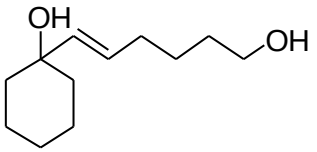

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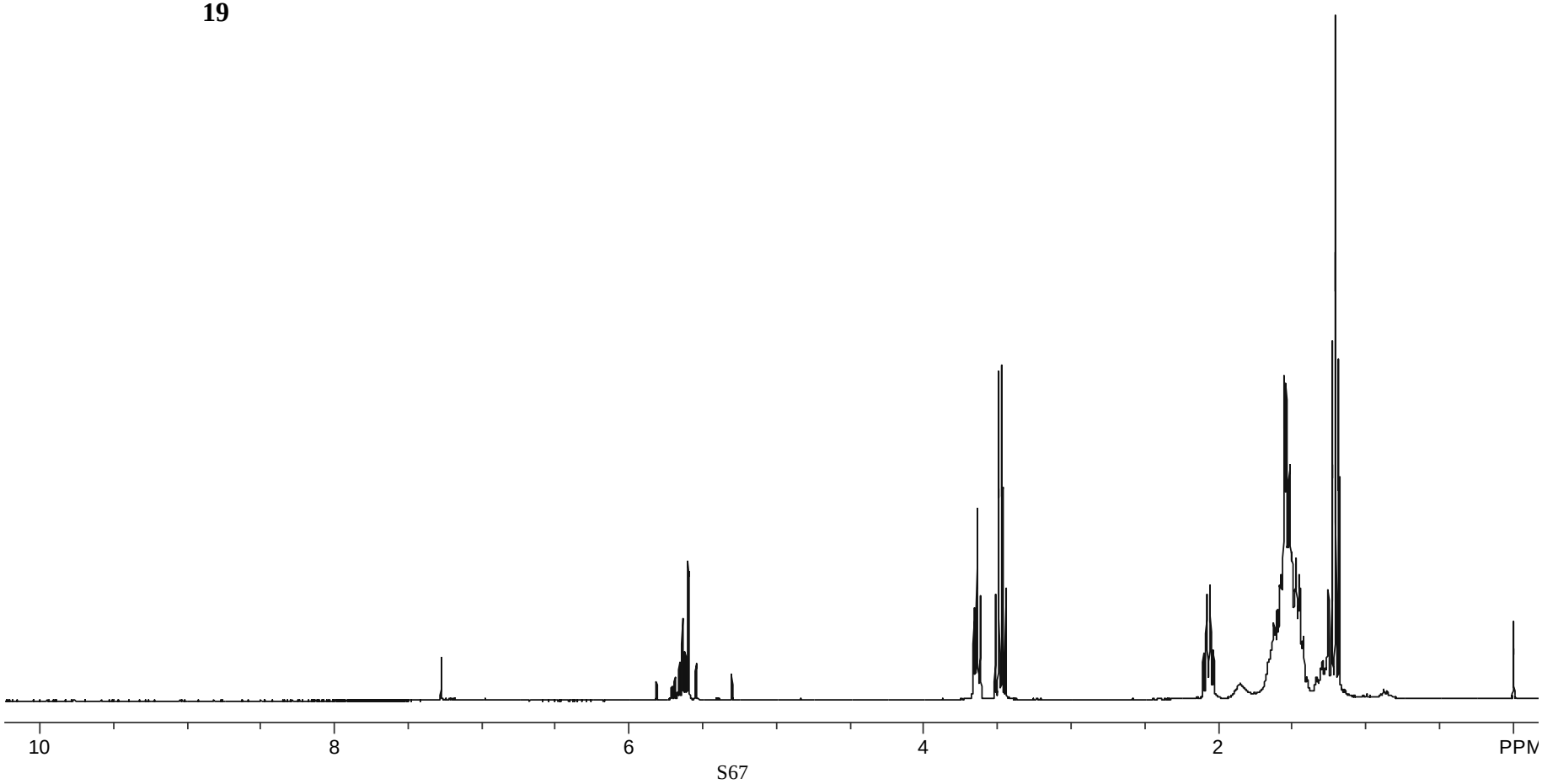

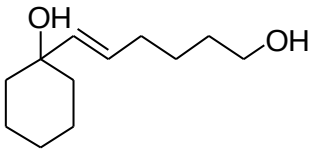

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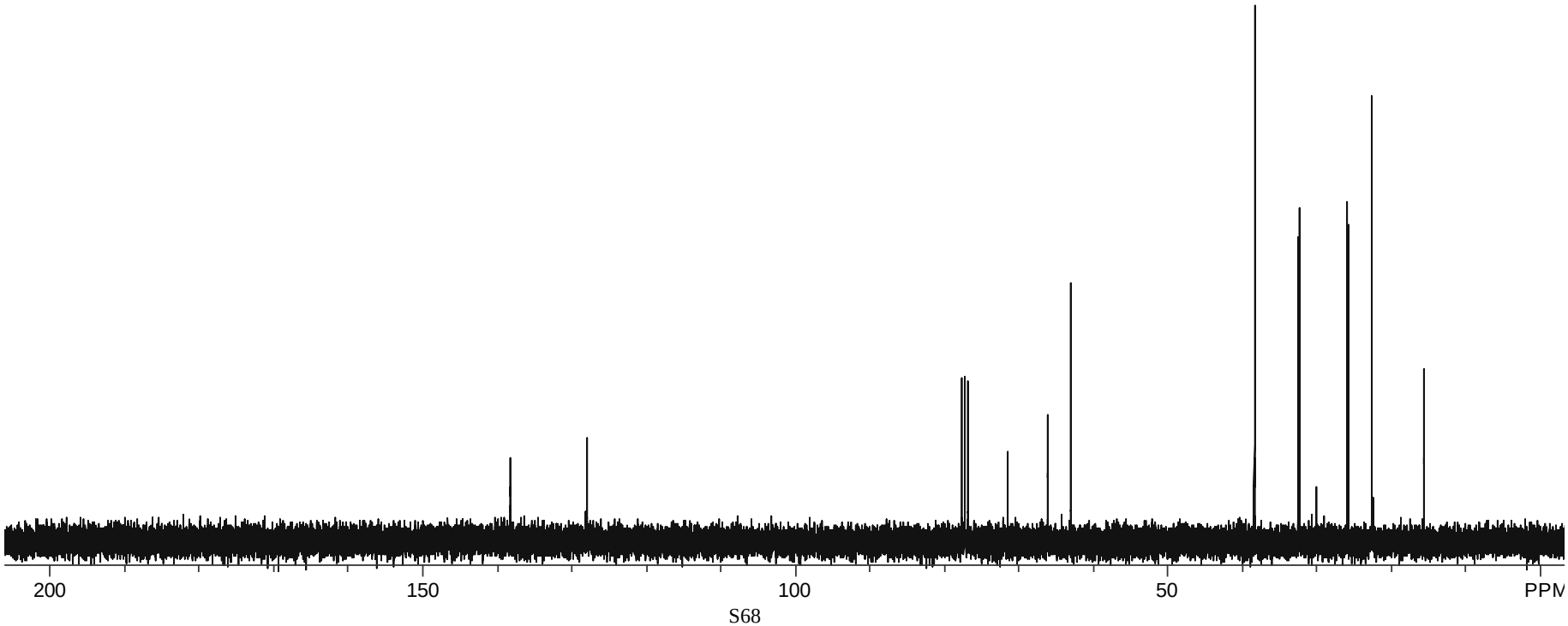

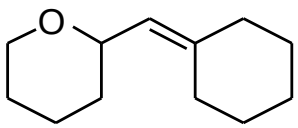

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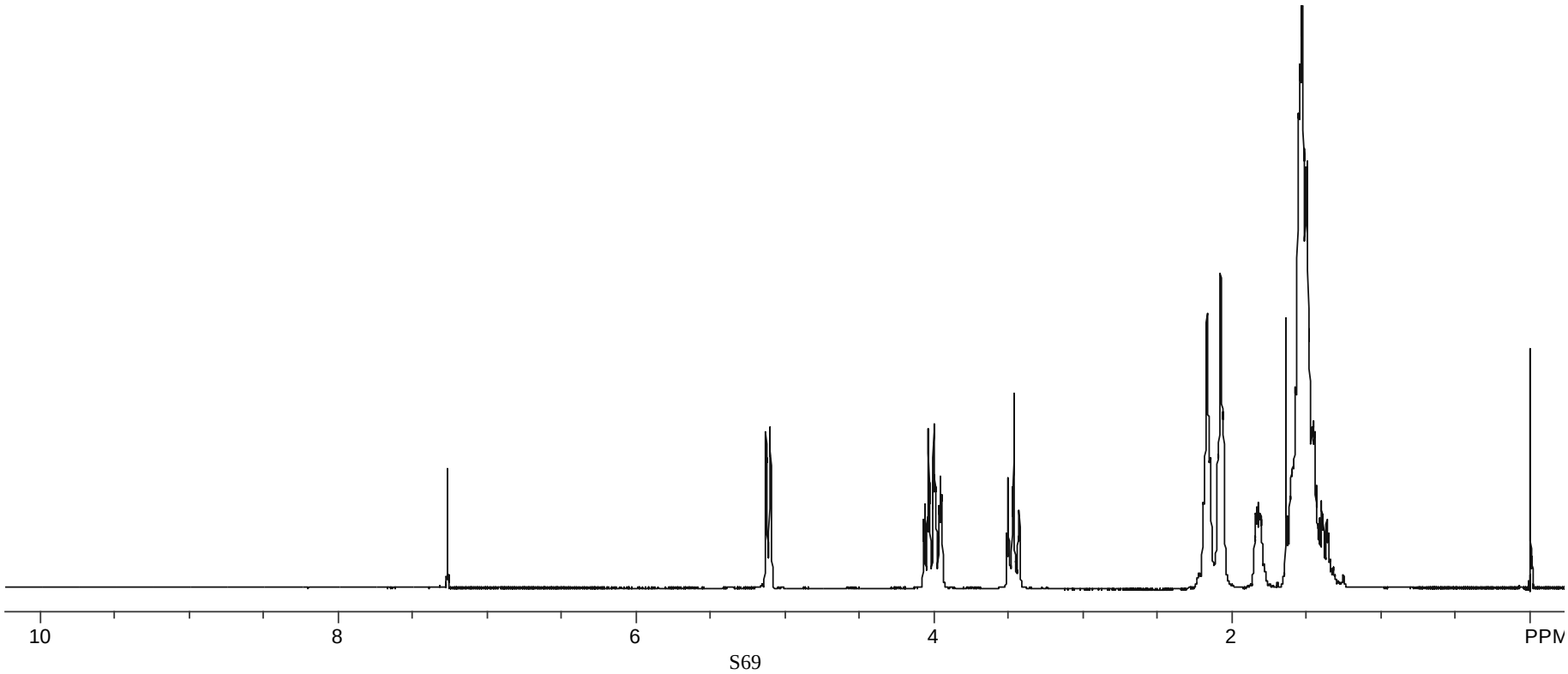

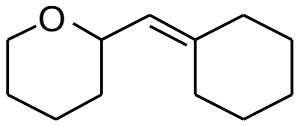

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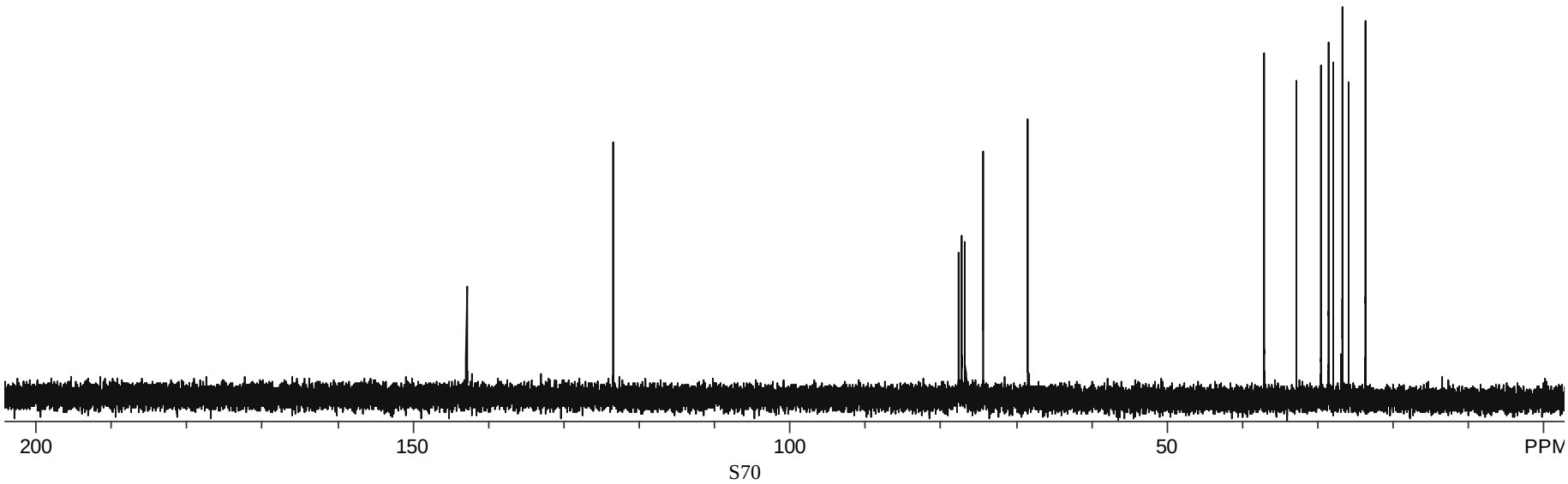

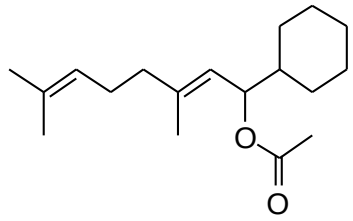

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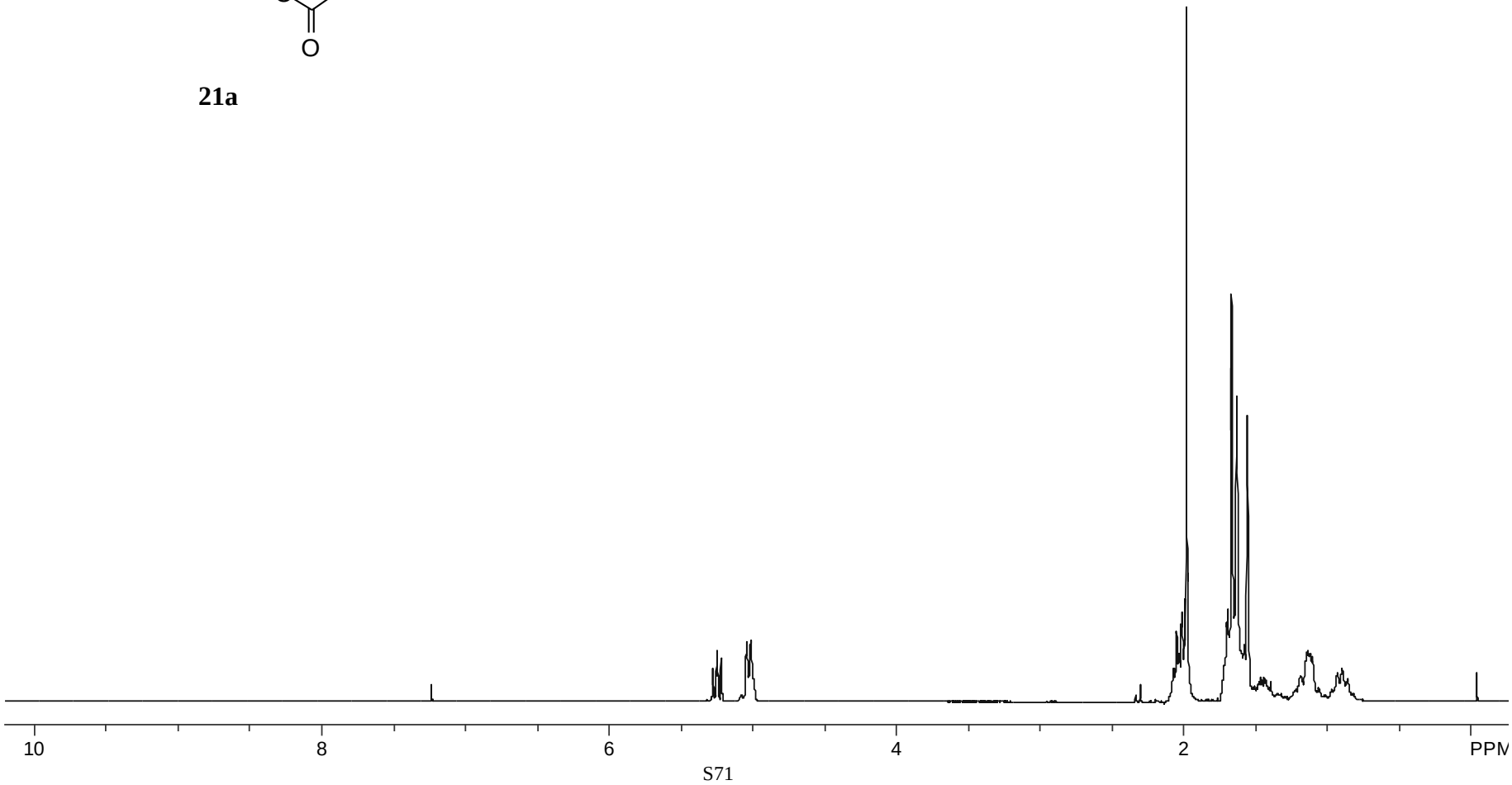

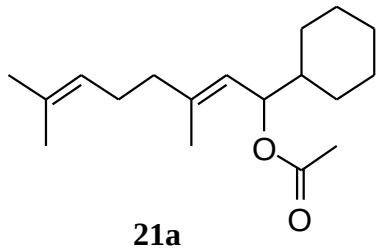

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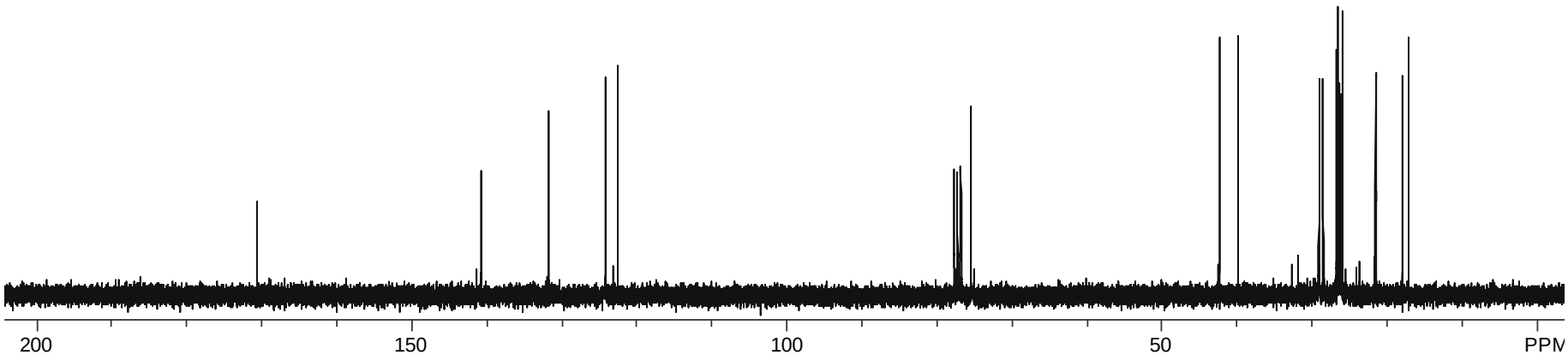

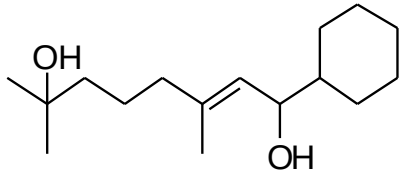

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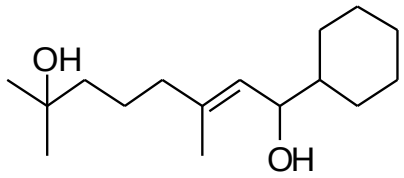

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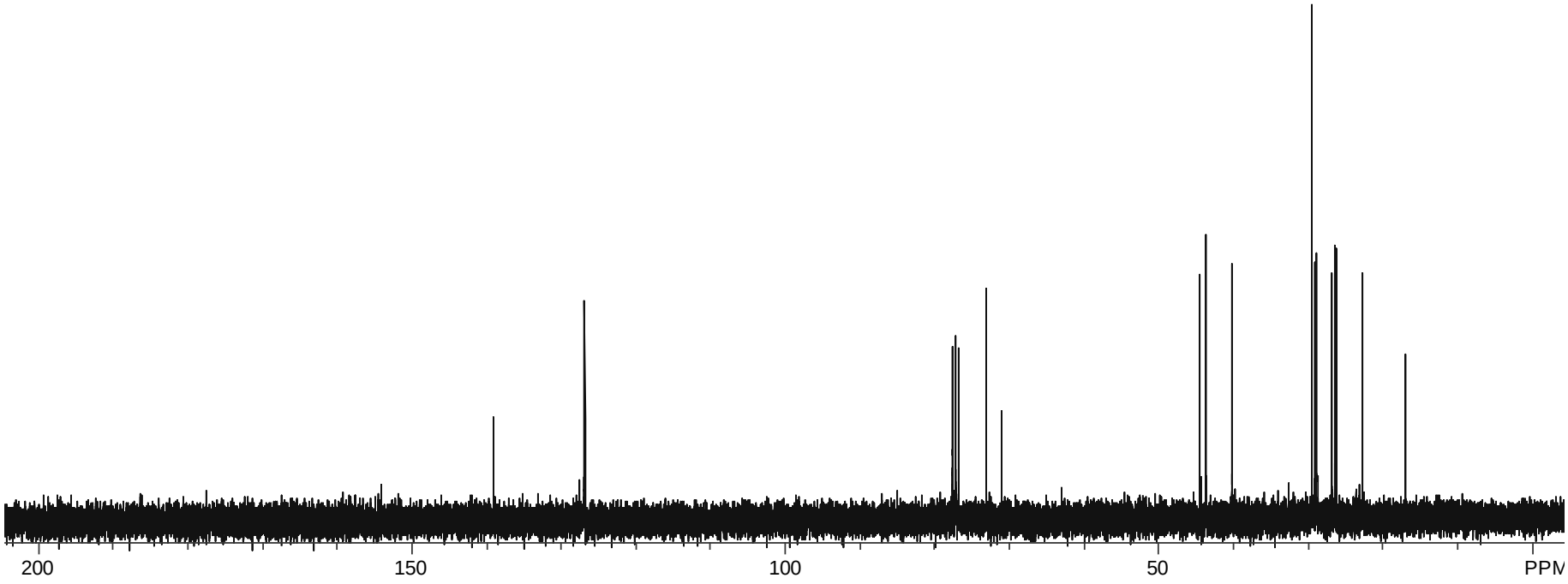

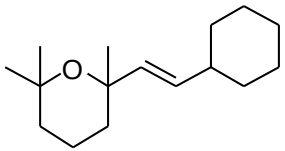

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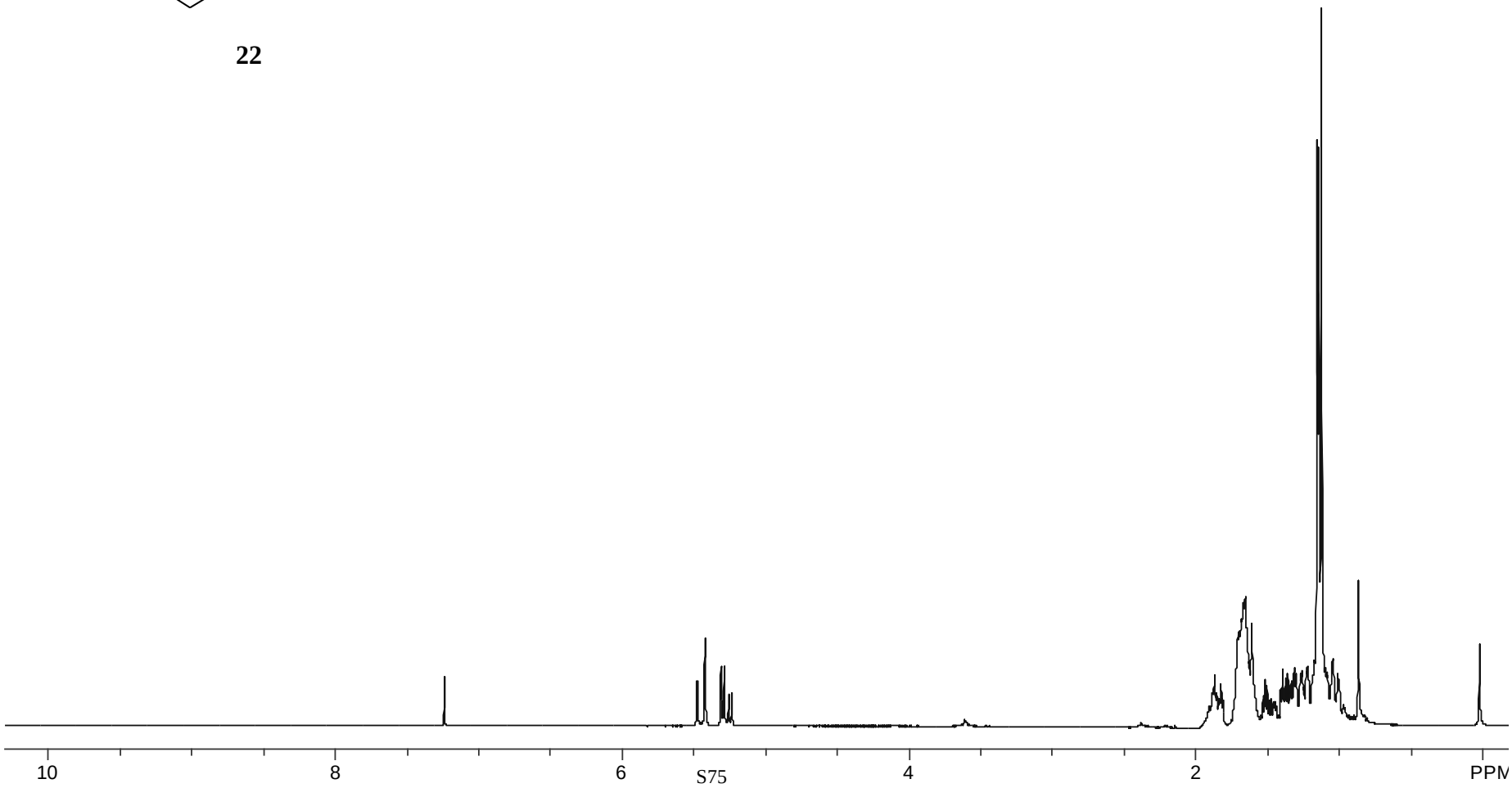

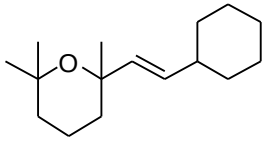

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