Supporting Information

Tandem Rh(I)-Catalyzed [(5 + 2) + 1] Cycloaddition/Aldol Reaction for the Construction of Linear Triquinane Skeleton: Total Syntheses of (±)-Hirsutene and (±)-1-Desoxyhypnophilin

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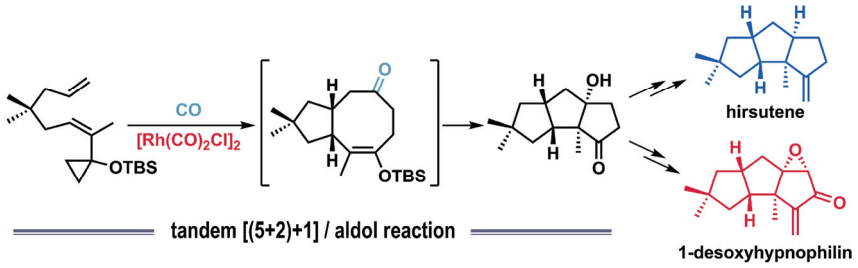


Contents

1. General

Air and moisture sensitive reactions were carried out in oven-dried glassware sealed with rubber septa under a positive pressure of dry argon. Similarly sensitive liquids and solutions were transferred via syringe. Reactions were stirred using Teflon-coated magnetic stir bars. Elevated temperatures were maintained using Thermostat-controlled silicone oil baths. Organic solutions were concentrated using a Büchi rotary evaporator with a desktop vacuum pump. Tetrahydrofuran, diethyl ether, and toluene were distilled from sodium and benzophenone prior to use. Dichloromethane was distilled from CaH_2 prior to use. Dioxane (extra dry, water < 50 ppm) was commercially available and used as received. Synthetic reagents were purchased from Acros, Aldrich, and Alfa Aesar and used without further purification, unless otherwise indicated. Analytical TLC was performed with 0.25 mm silica gel G plates with a 254 nm fluorescent indicator. The TLC plates were visualized by ultraviolet light and treatment with phosphomolybdic acid stain followed by gentle heating. Purification of products was accomplished by flash chromatography on silica gel and the purified compounds show a single spot by analytical TLC.

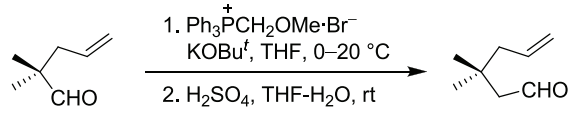
NMR spectra were measured on a Varian Mercury 300 (^{1}H at 300 MHz, ^{13}C at 75 MHz) nuclear magnetic resonance spectrometer. Data for ^{1}H-NMR spectra are reported as follows: chemical shift (ppm, referenced to TMS; s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, td = triplet of doublets, ddd = doublet of doublet of doublets, tdd = triplet of doublet of doublets, m = multiplet), coupling constant (Hz), and integration. Data for ^{13}C-NMR are reported in terms of chemical shift (ppm) relative to residual solvent peak ($CDCl_3$: 77.0 ppm; C_6D_6: 128.0 ppm). Infrared spectra were recorded on an AVATAR 330 Fourier transform spectrometer (FT-IR) with an OMNI sampler and are reported in wavenumbers (cm^{-1}). Mass spectra (MS) and high-resolution mass spectra (HRMS) were recorded on a VG-ZAB-HS mass spectrometer (EI, 70 eV).

Abbreviations:
DCC = dicyclohexylcarbodiimide
DMAP = 4-(*N*,*N*-dimethylamino)pyridine
THF = tetrahedrofuran
TMEDA = *N*,*N*,*N*',*N*'-tetramethylethylenediamine
VCP = vinylcyclopropane

2. Experimental Procedures and Characterization Data

2.1 Initial Attempt of the Tandem [(5+2)+1]/Aldol Reaction

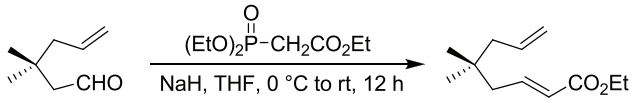
3,3-Dimethylhex-5-enal (3)



S1 **3**

To a stirred suspension of (methoxymethyl)triphenylphosphonium chloride (76.34 g, 223 mmol) in 350 mL of anhydrous THF was slowly added a solution of $KOBu^t$ (26.09 g, 233 mmol) in THF (300 mL) at 0 °C via cannula under argon. The resulting cherry-red solution was stirred at 0 °C for another 1 h. A solution of 2,2-dimethylpent-4-enal[1] (**S1**, 14.01 g, 125 mmol) in THF (100 mL) was added dropwise within 20 min, and the resulting mixture was stirred at 20 °C for 2 h. The reaction was quenched by addition of water (10 mL) and the reaction mixture turned from light cherry-red to yellow. The reaction mixture was evaporated under reduced pressure in a water bath (35 °C) to a volume of ca. 300 mL, then aqueous 30% H_2SO_4 (60 mL) was added at room temperature under stirring. When GC indicated the disappearance of the enol ether, saturated $NaHCO_3$ (200 mL) was added. The reaction mixture was extracted with ether and the combined organic extract was washed with water, dried over $MgSO_4$, and concentrated to give a light yellow oil. Flash column chromatography on silica gel (eluted with pentane/ether 30:1) gave aldehyde **3** (10.66 g, 68%) as a colorless oil. Spectroscopic data was identical to that reported.[2]

(*E*)-Ethyl 5,5-dimethylocta-2,7-dienoate (4)



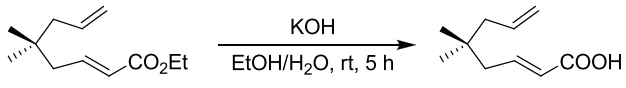
3 **4**

To a suspension of NaH (294 mg, 12.3 mmol) in dry THF (30 mL) was added ethyl 2-(diethoxyphosphoryl)acetate (3.03 g, 13.5 mmol) dropwise at 0 °C within 15 min. Hydrogen gas was generated during the course of addition and a semi-clear solution formed. After stirred for 30 min at 25 °C, the solution was cooled to 0 °C again and 3,3-dimethylhex-5-enal (1.22 g, 8.98 mmol) was added dropwise over 10 min. The reaction mixture was allowed to warm up to room temperature and stirred overnight. Brine was added to quench the reaction, and the resulting mixture was extracted with ether. The extract was dried over Na_2SO_4 and evaporated to give the crude product, which was purified by flash column chromatography (silica gel 50g, petroleum ether/ethyl acetate 50:1) to afford the ester **4** as a clear, colorless oil (1.15 g, 86%).

4: ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.91 (s, 6H), 1.30 (t, J = 7.2 Hz, 3H), 1.98 (dt, J = 7.2 and 0.9 Hz, 2H), 2.09 (dd, J = 8.1 and 1.2 Hz, 2H), 4.19 (q, 7.2 Hz, 2H), 4.99-5.08 (m, 2H), 5.74-5.85 (m, 2H), 6.99 (dt, J = 15.6 and 8.1 Hz, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 14.2, 26.9, 34.1, 44.5, 46.4, 60.2, 117.5, 123.5, 134.9, 146.4, 166.5. MS (EI, 70 eV): m/z 196 (M^+, 1.1), 181 (1.2), 155 (10), 114 (75), 88 (100). IR (neat): ν 1721, 1654, 1468 cm^{-1}. Calcd for $C_{12}H_{20}O_2$: 196.1463. Found: 196.1469.

(1) This aldehyde was prepared according to Salomon, R. G.; Ghosh, S. *Org. Synth.* **1984**, *62*, 125. It is also commercially available.
(2) Pattenden, G.; Teague, S. J. *Tetrahedron* **1987**, *43*, 5637.

(*E*)-5,5-Dimethylocta-2,7-dienoic acid (5)

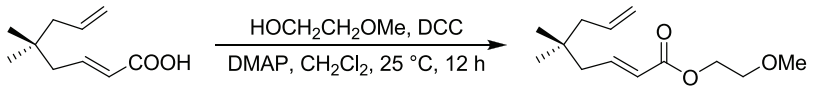


4 **5**

To a solution of unsaturated ester **4** (1.22 g, 9.00 mmol) in ethanol (35 mL) was added water (10 mL) and KOH (1.01 g, 18.0 mmol). The resulting mixture was stirred at room temperature for 14 hours. The solution was extracted by CH_2Cl_2 twice to remove organic impurities and the water phase was acidified with concentrated HCl to pH ~ 1. The water phase was extracted by ether and the combined ether layer was dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography (40 g of silica gel, eluted with petroleum ether/ethyl acetate 2:1) to afford 1.016 g (75%) of unsaturated acid **5** as a colorless oil.

5: ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.92 (s, 6H), 1.99 (d, J = 7.5 Hz, 2H), 2.13 (dd, J = 7.8 and 1.4 Hz, 2H), 5.00-5.08 (m, 2H), 5.74-5.86 (m, 2H), 7.11 (dt, J = 15.4 and 7.8 Hz, 1H), 11.82 (s, br, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 26.9, 34.2, 44.5, 46.5, 117.6, 122.8, 134.7, 149.6, 171.9. IR (neat): ν 1695, 1650 cm^{-1}.

(*E*)-2-Methoxyethyl 5,5-dimethylocta-2,7-dienoate (6)

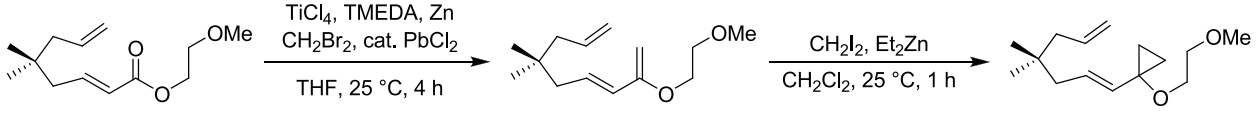


5 **6**

To a stirred solution of unsaturated acid **5** (997 mg, 5.93 mmol), glycol mono methyl ether (489 mg, 6.43 mmol), and DMAP (149 mg, 1.22 mmol) in dry CH_2Cl_2 (15 mL) was slowly added a solution of DCC (1.46 g, 7.08 mmol) in CH_2Cl_2 (8 mL) under argon at room temperature. After the addition, white participate was generated and the reaction mixture was stirred overnight. The suspension was filtered and the filter cake was washed with CH_2Cl_2. The combined filtrate was evaporated and the residue was purified by flash column chromatography (50 g of silica gel, eluted with petroleum ether/ethyl acetate 20:1 to 10:1) to afford 1.149 g (86%) of unsaturated ester **6** as a colorless oil.

6 : ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.91 (s, 6H), 1.98 (d, J = 7.2 Hz, 2H), 2.10 (dd, J = 7.8 and 1.2 Hz, 2H), 3.41 (s, 3H), 3.63 (t, J = 4.5 Hz, 2H), 4.29 (t, J = 4.5 Hz, 2H), 5.04 (m, 2H), 5.73-5.90 (m, 2H), 7.02 (dt, J = 15.3 and 7.8 Hz, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 26.8, 34.1, 44.5, 46.4, 59.0, 63.3, 70.5, 117.5, 123.0, 134.8, 147.0, 166.4. IR (neat): ν 1721, 1654 cm^{-1}.

(*E*)-1-(4,4-Dimethylhepta-1,6-dienyl)-1-(2-methoxyethoxy)cyclopropane (7)



6 **S2** **7**

The synthesis of enol ether **S2** from ester **6** follows the procedure of Takai *et al.*[3] In a flame-dried flask a solution of $TiCl_4$ (17.5 mL, 17.5 mmol, 1 M in CH_2Cl_2) was added dropwise to freshly distilled THF (20 mL) at

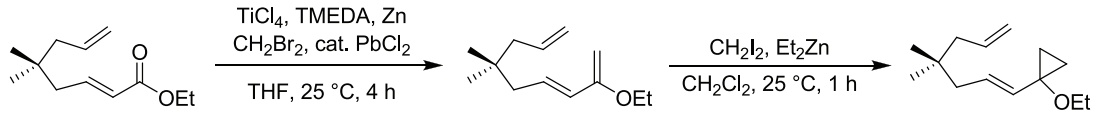
(3) Takai, K.; Kataoka, Y.; Miyai, J.; Okazoe, T.; Oshima, K.; Utimoto, K. Org. Synth. **1998**, *Coll. Vol. 9*, 404.

0 ºC under argon. The flask was warmed to 25 ºC and TMEDA (5.0 mL, 33.3 mmol) was added. After stirred for 10 min, activated Zn dust (2.28 g, 35.0 mmol) and $PbCl_2$ (27.5 mg, 0.10 mmol) was added and the reaction mixture turned dark-blue immediately. After stirred for 30 min, a solution of CH_2Br_2 (1.53 g, 8.8 mmol) and unsaturated ester **6** (214 mg, 0.95 mmol) in THF (10 mL) was added dropwise over 10 min. The reaction mixture gradually became brown and the reaction completed within 2 h as indicated by GC. Triethylamine (7 mL) and saturated aqueous K_2CO_3 (10 mL) was added to quench the reaction. The mixture was filtered through a thin pad of basic Al_2O_3 (deactivated with 5% water) to remove the Ti / Zn complex and the combined filtrate was evaporated. The residue was quickly passed through a silica gel column (20 g of silica gel, eluted with petroleum ether/ethyl acetate 20:1 to 10:1, containing 1% Et_3N) to afford 94.8 mg (45%) of crude enol ether **S2** as a light-yellow oil, which was used in the cyclopropanation reaction without further purification.

Diethyl zinc solution (0.50 mL, 0.88 M in hexane, 0.44 mmol) and CH_2I_2 (144 mg, 0.54 mmol) was sequentially added to a solution of crude enol ether **S2** (94 mg, 0.42 mmol) in anhydrous CH_2Cl_2 (5 mL) at 25 °C. The reaction mixture gradually became a white suspension while stirred at 25 °C. The reaction was monitored by GC. Upon completion (1-2 h), saturated NH_4Cl was added to quench the reaction. The resulting mixture was extracted with CH_2Cl_2 and the combined organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography (5 g of silica gel, eluted with petroleum ether/ethyl acetate 20:1 containing 1% Et_3N) to afford 65.0 mg (65%) of the ene-VCP product **7** as a light-yellow oil.

7: ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.65 (dd, J = 5.1 and 7.0 Hz, 2H), 0.86 (s, 6H), 0.99 (dd, J = 5.1 and 7.0 Hz, 2H), 1.93-1.96 (m, 4H), 3.37 (s, 3H), 3.49-3.52 (m, 2H), 3.59-3.63 (m, 2H), 4.97-5.04 (m, 2H), 5.32 (d, J = 15.6 Hz, 1H), 5.66 (dt, J = 15.4 and 7.7 Hz, 1H), 5.75-5.88 (m, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 14.0, 26.8, 33.7, 44.6, 46.3, 59.0, 61.3, 66.7, 72.0, 116.8, 125.9, 132.5, 135.6. MS (EI, 70 eV): m/z 308 (M^+, 0.4), 238 (2.0), 223 (10), 195 (78), 167 (22), 141 (100). IR (neat): ν 2957, 2909, 1468, 1366, 1132 cm^{-1}. HRMS calcd for $C_{15}H_{26}O_2$: 238.1933. Found: 238.1936.

(*E*)-1-(4,4-Dimethylhepta-1,6-dienyl)-1-ethoxycyclopropane (8)

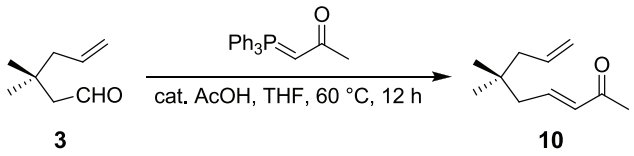


4 **S3** **8**

Ethyloxy ene-VCP **8** was prepared following the procedures to synthesize ene-VCP **7**. The synthesis started from 520 mg (2.65 mmol) of unsaturated ester **4** and the final ethyloxy ene-VCP product **8** was obtained as a colorless oil (178 mg, 33% for two steps).

8: ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.64 (dd, J = 7.0 and 4.7 Hz, 2H), 0.86 (s, 6H), 0.95 (dd, J = 7.0 and 4.7 Hz, 2H), 1.17 (t, J = 7.1 Hz, 3H), 1.94 (d, J = 7.6 Hz, 4H), 3.50 (q, J = 7.1 Hz, 2H), 4.97-5.04 (m, 2H), 5.30 (d, J = 15.3 Hz, 1H), 5.60 (dt, J = 15.3 and 7.6 Hz, 1H), 5.82 (m, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 14.0, 15.5, 26.8, 33.7, 44.5, 46.3, 60.9, 62.7, 116.8, 125.3, 133.0, 135.6. MS (EI, 70 eV): m/z 208 (M^+, 0.6), 193 (6.0), 165 (41), 111 (100).

(*E*)-6,6-Dimethylnona-3,8-dien-2-one (10)

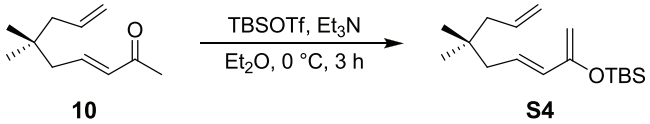


3 **10**

Two drops of glacial AcOH was added to a solution of 3,3-dimethylhex-5-enal (1.95 g, crude, ca. 10.0 mmol) and triphenyl(2-oxopropyl)phosphorine (4.89 g, 15.4 mmol) in dry THF (90 mL), and the resulting mixture was stirred at 60 °C for 12 h. The reaction mixture was filtered through a pad of silica gel, and the filtrate was evaporated using a rotatory evaporator in a water bath (20 °C). The crude product was purified by flash column chromatography (silica gel, eluted with petroleum ether/ethyl acetate 20:1) to afford unsaturated ketone **10** as a pale-yellow oil (0.57 g, 34%).

10: ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.92 (s, 6H), 1.99 (d, J = 7.5 Hz, 2H), 2.12 (dd, J = 7.8 and 0.9 Hz, 2H), 2.26 (s, 3H), 5.00-5.09 (m, 2H), 5.74-5.88 (m, 1H), 6.08 (dt, J = 16.2 and 1.5 Hz, 1H), 6.83 (dt, J = 15.9 and 8.0 Hz, 1H). ^{13}C NMR (75.5 Hz): δ 26.9, 27.0, 34.2, 44.7, 46.5, 117.5, 133.4, 134.7, 145.3, 198.3. MS (EI, 70 eV): m/z 166 (M^+, 6.0), 151 (7.0), 125 (17), 109 (12), 84 (61), 43 (100). IR (neat): ν 1675, 1628 cm^{-1}.

(*E*)-2-*tert*-Butyldimethylsiloxy-6,6-trimethylnona-1,3,8-triene (S4)

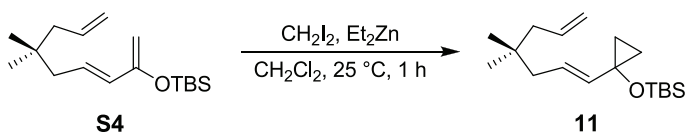


10 **S4**

Triethyl amine (1.00 g, 9.55 mmol) and TBSOTf (1.60 g, 3.79 mmol) was sequentially added to a solution of enone **10** (543 mg, 3.26 mmol) in anhydrous ether (14 mL) at 0 °C in argon. After stirred for 2 h at 0 °C, brine was added and the resulting mixture was extracted by ether. The combined extract was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by flash column chromatography on silica gel (30 g, eluted with petroleum ether/acetate 20:1 containing 1% Et_3N) to afford the crude silylenol ether **S4** (916 mg, quantitative yield) as a colorless oil.

S4: ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.18 (s, 6H), 0.87 (s, 6H), 0.97 (s, 9H), 1.95 (d, J = 7.2 Hz, 2H), 1.99 (d, J = 8.0 Hz, 2H), 4.22 (s, 1H), 4.23 (s, 1H), 4.97-5.05 (m, 2H), 5.75-5.89 (m, 2H), 6.04 (dt, J = 15.2 and 7.6 Hz, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ –4.6, 18.3, 25.8, 26.9, 34.0, 44.4, 46.4, 94.1, 116.9, 128.4, 130.0, 135.5, 155.1. MS (EI, 70 eV): m/z 280 (M^+, 3.0), 265 (4.0), 223 (40), 141 (39), 127 (38), 86 (97), 75 (100). IR (neat): ν 1595, 1472 cm^{-1}. Calcd for $C_{17}H_{32}OSi$: 280.2222. Found: 280.2218.

(*E*)-1-*tert*-Butyldimethylsiloxy-1-(4,4-dimethylhepta-1,6-dienyl)cyclopropane (11)



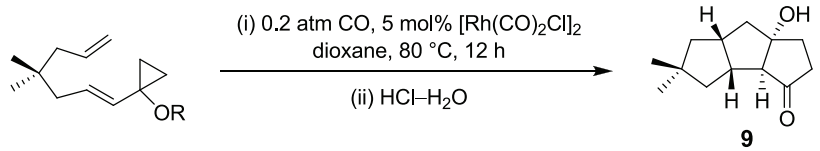
S4 **11**

Diethyl zinc solution (4.8 mL, 0.88 M in hexane, 3.10 mmol) and CH_2I_2 (0.955 g, 3.70 mmol) was sequentially added to a solution of silylenol ether **S4** (868 mg, 3.10 mmol) in anhydrous CH_2Cl_2 (30 mL) at 25

°C. The reaction mixture gradually became a white suspension. Upon completion (1-2 h), saturated NH_4Cl was added to quench the reaction. The resulting mixture was extracted with CH_2Cl_2 and the combined organic extract was dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography (25 g of silica gel, eluted with petroleum ether/ethyl acetate 20:1) to afford 887 mg (98%) of the ene-VCP product **11** as a light yellow oil.

11: ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.12 (s, 6H), 0.68 (dd, J = 7.2 and 5.1 Hz, 2H), 0.86 (s, 6H), 0.88 (s, 9H), 0.96 (dd, J = 7.2 and 5.1 Hz, 2H), 1.92 (d, J = 7.2 Hz, 2H), 1.95 (d, J = 7.5 Hz, 2H), 4.97-5.04 (m, 2H), 5.27 (d, J = 15.3 Hz, 1H), 5.62 (dt, J = 15.3 and 7.5 Hz, 1H), 5.81 (m, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ –3.4, 15.4, 18.0, 25.9, 26.8, 33.8, 44.6, 46.3, 56.6, 116.8, 123.4, 135.6, 136.6. MS (EI, 70 eV): m/z 294 (M^+, 2.5), 279 (4.0), 251 (26), 197 (82), 73 (100). IR (neat): ν 1473, 1386 cm^{-1}. Calcd for $C_{18}H_{34}OSi$: 294.2379. Found: 294.2379.

Cis-anti-*cis*-8-Hydroxy-4,4-dimethyltricyclo[6.3.0.0^{2,6}]undecan-11-one (9)

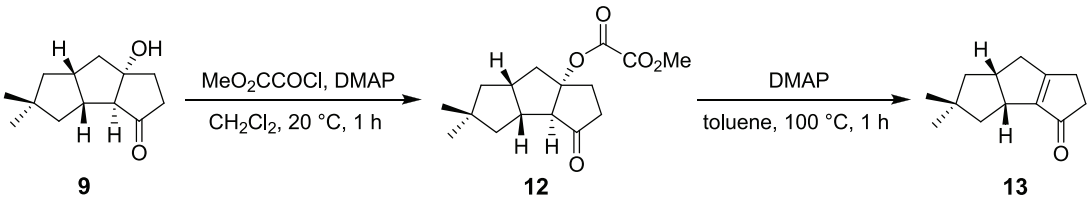


7 R = CH_2CH_2OMe — **9** 16%
8 R = Et — 0%
11 R = TBS — 19%

General procedure for the tandem [(5+2)+1]/aldol reaction employing ene-VCPs 7, 8, and 11 as substrates. A solution of ene-VCP (0.2 mmol) in anhydrous dioxane (8 mL) was degassed by bubbling CO/N_2 (1:4 V/V) for 5 min. The catalyst $[Rh(CO)_2Cl]_2$ (4.0 mg, 10 μmol, 5 mol% to ene-VCP) was added in one potion and a light yellow solution formed, which was further bubbled by the above mixture gas for 5 min. The solution was heated to 80 °C in an oil bath with stirring under a positive pressure of the mixture gas. After 12 h, TLC indicated the absence of the starting material and the resulting brown solution was cooled to room temperature. The reaction mixture was hydrolyzed by adding 1% HCl in EtOH (0.3 mL) and water (0.1 mL) and stirred at rt for 20 min. Solvent was evaporated and the residue was purified by flash column chromatography on silica gel (5 g, eluted with petroleum ether/ethyl acetate 5:1 to 3:1) to afford cycloadduct **9** as a light-yellow oil, which solidified on standing.

9: ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.89 (s, 3H), 1.07 (s, 3H), 1.36 (m, 2H), 1.68-1.86 (m, 4H), 1.96-2.17 (m, 3H), 2.26-2.38 (m, 2H), 2.52-2.72 (m, 3H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 26.9, 29.0, 34.1, 37.5, 42.4, 43.2, 45.5, 46.1, 48.5, 48.8, 66.4, 90.0, 219.8. MS (EI, 70 eV): m/z 208 (M^+, 37), 193 (12), 179 (19), 152 (42), 95 (100). IR (neat): ν 3406, 1736, 1722 cm^{-1}. Calcd for $C_{13}H_{20}O_2$: 208.1463. Found: 208.1460.

5,5-Dimethyl-3b,4,5,6,6a,7-hexahydro-1*H*-cyclopenta[a]pentalen-3(2*H*)-one (13)



9 **12** **13**

Methyl oxalyl chloride (24.0 mg, 0.19 mmol) was added to a solution of tricyclic ketone **9** (18.2 mg, 0.087 mmol) and DMAP (22.4 mg, 0.18 mmol) in dry CH_2Cl_2 (1.5 mL) at room temperature under argon. After 2 h,

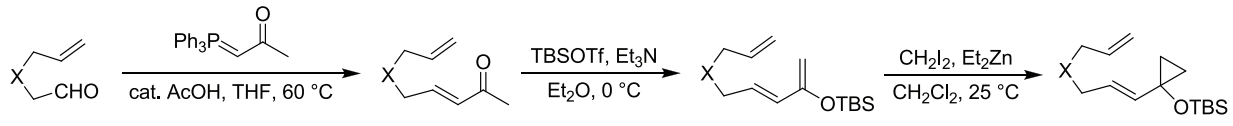
saturated $NaHCO_3$ was added and the organic layer was saperated. The water phase was extracted with CH_2Cl_2 and the combined organic phase was dried over Na_2SO_4 and concentrated. The residue (compound **12**) was dissolved in freshly distilled toluene (2 mL) and was added DMAP (14.0 mg, 0.11 mmol). The resulting solution was heated to 100 ºC in an oil bath and stirred under argon for 3 h. The reaction mixture was evaporated and the residue was purified by flash column chromatography (5 g of silica gel, eluted with petroleum ether/ethyl acetate 6:1) to afford 14.3 mg (86%) of product **13** as a colorless oil.

13: ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.93 (s, 3H), 1.02 (s, 3H), 1.18 (m, 2H), 1.79 (ddd, J = 1.8, 7.8, and 12.3 Hz, 1H), 1.87 (ddd, J = 1.8, 8.4, and 12.6 Hz, 1H), 2.21 (d, J = 19.2 Hz, 1H), 2.48 (m, 2H), 2.70-2.78 (m, 3H), 3.28 (m, 2H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 25.6, 26.9, 28.6, 38.5, 41.0, 41.4, 42.7, 44.8, 47.2, 49.2, 151.6, 184.6, 204.2. MS (EI, 70 eV): m/z 190 (M^+, 100), 175 (78), 147 (38), 133 (92), 105 (39), 91 (44). IR (neat): ν 2952, 1696, 1637 cm^{-1}. Calcd for $C_{13}H_{18}O$: 190.1358. Found: 190.1361.

2.2 Experiments for Model Reaction Study

General route for siloxy-ene-VCP synthesis

For (*E*)-ene-VCPs **14a** and **14b**:



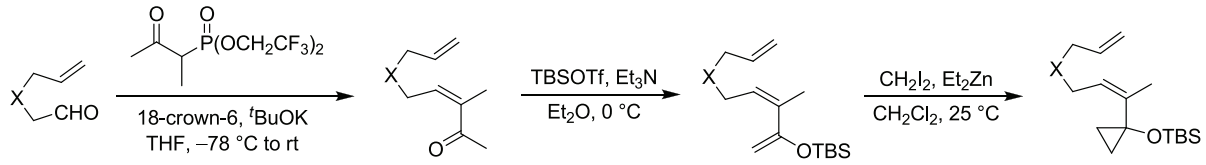
S5a: X = TsN
S5b: X = $(EtO_2C)_2C$

S6a
S6b

S7a
S7b

14a
14b

For (*Z*)-ene-VCPs **14c**-**e**:



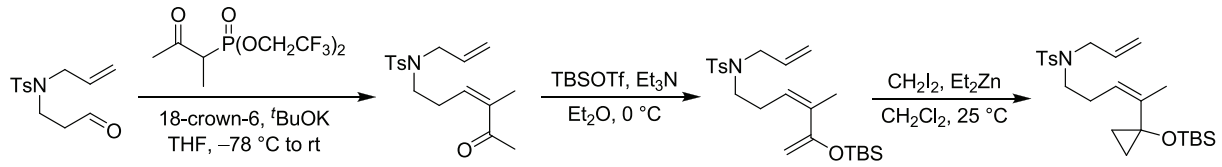
S5c: X = CH_2
S5a: X = TsN
S5b: X = $(EtO_2C)_2C$

S6c
S6d
S6e

S7c
S7d
S7e

14c
14d
14e

For (*Z*)-ene-VCP **14f**:



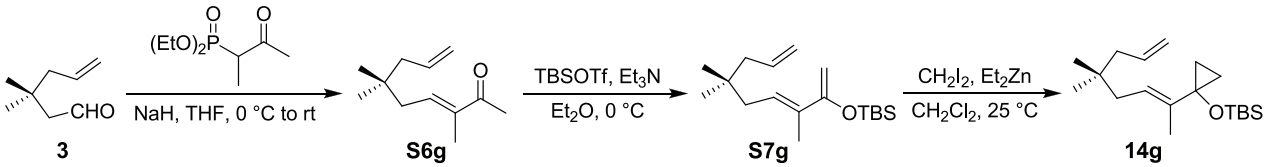
S5d

S6f

S7f

14f

For (*E*)-ene-VCP **14g**:



3

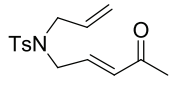
S6g

S7g

14g

Synthetic procedures and spectroscopic data for substrates 14a-g

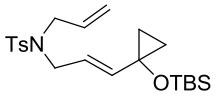
(*E*)-*N*-Tosyl-5-(allylamino)pent-3-en-2-one (S6a)



This compound was prepared from aldehyde **S5a** (380 mg, 1.50 mmol) following the procedure for the synthesis of compound **10**. Yield: 340 mg (77%). **S6a**: ^{1}H NMR (300 MHz, $CDCl_3$): 2.21 (s, 3H), 2.44 (s, 3H), 3.80 (d, *J* = 6.4 Hz, 2H), 3.93 (dd, *J* = 1.5 and 6.0 Hz, 2H), 5.11-5.18 (m, 2H), 5.60 (ddt, *J* = 10.4, 17.0, and 6.4 Hz, 1H), 6.10 (dt, *J* = 16.2 and 1.5 Hz, 1H), 6.56 (dt, *J* = 15.9 and 5.9 Hz, 1H), 7.33 (d, *J* = 8.3 Hz, 2H), 7.71 (d, *J* = 7.8 Hz). ^{13}C NMR (75.7 MHz, $CDCl_3$): 21.5, 27.1, 47.7, 50.6, 119.7, 127.1, 129.8, 132.2, 132.6, 136.6,

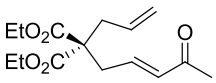
141.4, 143.7, 197.7.

(*E*)-1-*tert*-Butyldimethylsiloxy-1-(*N*-tosyl-4-azahepta-1,6-dienyl)cyclopropane (14a)



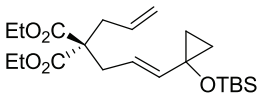
First, enone **S6a** (318 mg, 1.08 mmol) was converted to silylenol ether **S7a** (424 mg, crude, 96%) following the procedure for the synthesis of compound **S4**. The crude silylenol ether **S7a** (393 mg) was elaborated to ene-VCP **14a** following the procedure for the synthesis of compound **11**. Yield: 370 mg (90%). **14a**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.04 (s, 6H), 0.64 (dd, J = 5.4 and 7.4 Hz, 2H), 0.84 (s, 9H), 0.98 (dd, J = 5.4 and 7.4 Hz, 2H), 2.42 (s, 3H), 3.81(m, 4H), 5.14 (m, 2H), 5.34 (m, 2H), 5.63 (m, 1H), 7.29 (d, J = 8.0 Hz, 2H), 7.70 (d, J = 8.0 Hz, 2H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ -3.5, 15.8, 17.9, 21.4, 25.8, 48.0, 48.9, 56.2, 118.7, 120.2, 127.1, 129.6, 132.9, 137.6, 140.0, 143.1. IR (neat): ν 2955, 1472 cm^{-1}.

Diethyl (*E*)-2-allyl-2-(4-oxopent-2-enyl)malonate (S6b)



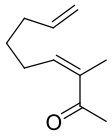
This compound was prepared from aldehyde **S5b** (2.35 g, 9.70 mmol) following the procedure for the synthesis of compound **10**. Yield: 1.45 g (53%). **S6b**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.26 (t, J = 7.3 Hz, 6H), 2.24 (s, 3H), 2.66 (d, J = 7.4 Hz, 2H), 2.77 (dd, J = 1.4 and 7.6 Hz, 2H), 4.21 (q, J = 7.3 Hz, 4H), 5.11-5.17 (m, 2H), 5.58-5.72 (m, 1H), 6.10 (d, J = 15.9 Hz, 1H), 6.67 (dt, J = 15.9 and 7.6 Hz, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 14.1, 26.8, 35.6, 37.5, 57.0, 61.6, 119.8, 131.6, 134.5, 141.8, 170.2, 198.0.

(*E*)-1-*tert*-Butyldimethylsiloxy-1-(4,4-diethoxycarbonylhepta-1,6-dienyl)cyclopropane (14b)



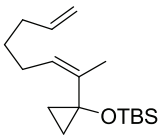
First, enone **S6b** (553 mg, 1.96 mmol) was converted to silylenol ether **S7b** (738 mg, crude, 95%) following the procedure for the synthesis of compound **S4**. The crude silylenol ether **S7b** (716 mg) was elaborated to ene-VCP **14b** following the procedure for the synthesis of compound **11**. Yield: 728 mg (98%). **14b**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.10 (s, 6H), 0.65 (dd, J = 5.2 and 7.2 Hz, 2H), 0.87 (s, 9H), 0.98 (dd, J = 5.0 and 7.2 Hz, 2H), 1.24 (t, J = 7.2 Hz, 6H), 2.64 (d, J = 7.5 Hz, 4H), 4.18 (q, J = 7.2 Hz, 4H), 5.07-5.12 (m, 2H), 5.31 (d, J = 15.3 Hz, 1H), 5.43 (dt, J = 7.2 and 15.0 Hz, 1H), 5.59-5.70 (m, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ -3.5, 14.1, 15.6, 17.9, 25.8, 35.0, 36.6, 56.4, 57.4, 61.2, 119.0, 119.8, 132.5, 139.2, 170.7. MS (EI, 70 eV): m/z 410 (M^+, 0.5), 381 (6.0), 365 (6.0), 337 (5.0), 257 (8.0), 210 (100), 197 (32), 153 (13). IR (neat): ν 2956, 1734 cm^{-1}. Calcd for $C_{22}H_{38}O_5Si$: 410.2489. Found: 410.2485.

(Z)-3-Methylnona-3,8-dien-2-one (S6c)



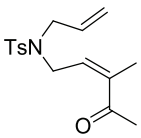
To a solution of bis(2,2,2-trifluoroethyl) 3-oxobutan-2-ylphosphonate (1.08 g, 80% purity, 2.26 mmol) and 18-crown-6 (1.01 mg, 3.82 mmol) in 20 mL anhydrous THF at −78 °C was added a solution of $KOBu^t$ (282 mg, 2.52 mmol) in 7 mL THF dropwise under argon. After stirring for 20 min at −78 °C, a solution of aldehyde **S5c** (200 mg, 2.04 mmol) in 5 mL THF was added at −78 °C dropwise and the resulting mixture was stirred for another 1 h at −78 °C. The reaction was gradually warmed to room temperature in 4 h. Saturated NH_4Cl (20 mL) was added and the reaction mixture was extracted with ether. The combined organic extract was washed with brine, dried over Na_2SO_4, and concentrated. The crude product was purified by flash column chromatography on silica gel (36 g, eluted with pentane/ether 30:1) to afford (*Z*)-enone **S6c** (139 mg, 45%) as a colorless oil. **S6c:** ^{1}H NMR (300 MHz, C_6D_6): δ 1.35 (quantet, J = 7.5 Hz, 2H), 1.60 (t, J = 2.7 Hz, 3H), 1.85 (s, 3H), 1.92 (q, J = 7.2 Hz, 2H), 2.29 (q, J = 7.5 Hz, 2H), 4.92-5.02 (m, 2H), 5.38 (tt, J = 1.5 and 7.5 Hz, 1H), 5.71 (ddt, J = 10.5, 17.1, and 6.6 Hz, 1H). ^{13}C NMR (75.5 MHz, C_6D_6): δ 21.0, 29.2, 29.3, 29.7, 33.6, 114.8, 135.8, 138.4, 138.6, 200.7.

(*Z*)-1-*tert*-Butyldimethylsiloxy-1-(1-methylhepta-1,6-dienyl)cyclopropane (14c)



First, enone **S6c** (120 mg, 0.79 mmol) was converted to silylenol ether **S7c** (185 mg, crude, 88%) following the procedure for the synthesis of compound **S4**. The crude silylenol ether **S7c** (183 mg) was elaborated to ene-VCP **14c** following the procedure for the synthesis of compound **11**. Yield: 131 mg (68%). **14c**: ^{1}H NMR (300 MHz, C_6D_6): δ 0.12 (s, 6H), 0.59 (dd, J = 5.0 and 7.2 Hz, 2H), 0.89 (dd, J = 5.0 and 7.2 Hz, 2H), 0.94 (s, 9H), 1.41 (quantet, J = 7.6 Hz, 2H), 1.79 (m, 3H), 2.02 (q, J = 7.2 Hz, 2H), 2.31 (q, J = 7.5 Hz, 2H), 4.97-5.07 (m, 2H), 5.16 (tq, J = 7.3 and 1.4 Hz, 1H), 5.79 (ddt, J = 10.3, 17.3, and 6.7 Hz, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ -3.7, 14.7, 18.0, 22.4, 25.8, 28.6, 29,3, 34.0, 56.3, 114.7, 130.4, 135.6, 138.9. MS (EI, 70 eV): *m*/*z* 280 (M^+, 8.0), 239 (50), 211 (32). IR (neat): ν 2958, 2857, 1472, 1251 cm^{-1}. HRMS calcd for $C_{17}H_{32}OSi$: 280.2222. Found: 280.2217.

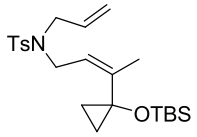
(Z)-*N*-Tosyl-5-(allylamino)-3-methylpent-3-en-2-one (S6d)



This compound was prepared from aldehyde **S5a** (485 mg, 1.91 mmol) following the procedure for the synthesis of compound **S6c**. Yield: 425 mg (72%). **S6d**: ^{1}H NMR (300 MHz, C_6D_6): δ 1.46 (q, J = 1.7 Hz, 3H), 1.74 (s, 3H), 1.89 (s, 3H), 3.64 (d, J = 6.5 Hz, 2H), 4.22 (dq, J = 5.9 and 1.7 Hz, 2H), 4.78-4.86 (m, 2H), 5.52

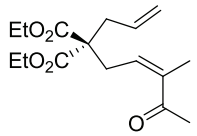
(ddt, J = 10.3, 17.4, and 6.1 Hz, 1H), 5.74 (tq, J = 5.5 and 1.7 Hz, 1H), 6.77 (d, J = 8.1 Hz, 2H), 7.68 (d, J = 8.1 Hz, 2H). ^{13}C NMR (75.5 MHz, C_6D_6): δ 20.4, 21.1, 28.8, 47.6, 51.8, 118.6, 127.6, 129.7, 133.5, 135.8, 137.7, 137.9, 142.9, 200.5.

(*Z*)-1-*tert*-Butyldimethylsiloxy-1-(*N*-tosyl-4-aza-1-methylhepta-1,6-dienyl)cyclopropane (14d)



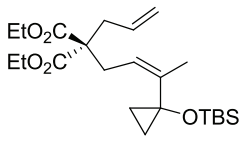
First, enone **S6d** (405 mg, 1.32 mmol) was converted to silylenol ether **S7d** (490 mg, crude, 88%) following the procedure for the synthesis of compound **S4**. The crude silylenol ether **S7d** (468 mg) was elaborated to ene-VCP **14d** following the procedure for the synthesis of compound **11**. Yield: 410 mg (85%). **14d**: ^{1}H NMR (300 MHz, C_6D_6): δ 0.03 (s, 6H), 0.51 (dd, J = 5.3 and 7.3 Hz, 2H), 0.79 (dd, J =5.3 and 7.3, 2H), 0.87 (s, 9H), 1.54 (d, J = 1.5 Hz, 3H), 1.89 (s, 3H), 3.79 (d, J = 6.1 Hz, 2H), 4.29 (d, J = 5.0 Hz, 2H), 4.89 (dd, J = 1.3 and 10.4 Hz, 1H), 4.98 (dd, J = 1.3 and 17.2 Hz, 1H), 5.33 (t, J = 6.1 Hz, 1H), 5.60-5.76 (m, 1H), 6.81 (d, J = 8.0 Hz, 2H), 7.79 (d, J = 8.1 Hz, 2H). ^{13}C NMR (75.5 MHz, C_6D_6): δ -3.7, 14.2, 17.9, 21.1, 21.8, 25.8, 46.3, 50.7, 56.0, 117.9, 127.4, 128.3, 129.6, 134.0, 138.6, 13.8, 142.7. MS (EI, 70 eV): m/z 435 (M^+, 1.0), 378 (10.0), 280 (49), 211 (66), 73 (100). IR (neat): ν 2955, 1472 cm^{-1}. Calcd for $C_{23}H_{37}NO_3SSi$: 435.2263. Found: 435.2260.

Diethyl (*Z*)-2-allyl-2-(3-methyl-4-oxopent-2-enyl)malonate (S6e)



This compound was prepared from aldehyde **S5b** (512 mg, 2.11 mmol) following the procedure for the synthesis of compound **S6c**. Yield: 570 mg (92%). **S6e**: ^{1}H NMR (300 MHz, C_6D_6): δ 0.91 (t, J = 7.3 Hz, 6H), 1.56 (s, 3H), 1.84 (s, 3H), 2.80-2.84 (m, 2H), 3.22-3.25 (m, 2H), 3.96 (q, 7.3 Hz, 4H), 4.94-5.05 (m, 2H), 5.65 (t, J = 7.8 Hz, 1H), 5.71-5.87 (m, 1H). ^{13}C NMR (75.5 MHz, C_6D_6): δ 14.0, 21.0, 29.4, 32.9, 38.1, 57.6, 61.2, 119.1, 131.2, 132.9, 138.6, 170.6, 201.0.

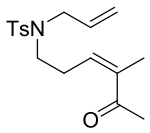
(*Z*)-1-*tert*-Butyldimethylsiloxy-1-(4,4-diethoxycarbonyl-1-methylhepta-1,6-dienyl)cyclopropane (14e)



First, enone **S6e** (570 mg, 1.92 mmol) was converted to silylenol ether **S7e** (712 mg, crude, 90%) following the procedure for the synthesis of compound **S4**. The crude silylenol ether **S7e** (697 mg) was elaborated to ene-VCP **14e** following the procedure for the synthesis of compound **11**. Yield: 416 mg (58%). **14e**: ^{1}H NMR (300 MHz, C_6D_6): δ 0.11 (s, 6H), 0.64 (dd, J = 5.3, 7.2 Hz, 2H), 0.92 (t, J = 7.2 Hz, 6H), 0.93 (s, 9H), 0.94 (m, 2H), 1.70 (dd, J = 1.4 and 3.1 Hz, 3H), 2.95 (dt, J = 7.5 and 1.1 Hz, 2H), 3.30 (dq, J = 7.0 and 1.4 Hz, 2H), 3.98

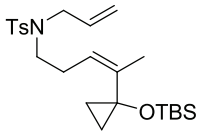
(m, 4H), 5.03-5.13 (m, 2H), 5.45 (tq, J = 6.8 and 1.4 Hz, 1H), 5.98 (m, 1H). ^{13}C NMR (75.5 MHz, C_6D_6): δ -3.6, 14.1, 14.5, 18.0, 22.6, 25.8, 32.5, 38.3, 56.3, 57.7, 61.0, 118.8, 124.7, 133.5, 138.9, 171.0. MS (EI, 70 eV): m/z 424 (M^+, 6.0), 379 (8.0), 337 (28), 211 (44), 73 (100). IR (neat): ν 2958, 1733, 1445 cm^{-1}. Calcd for $C_{23}H_{40}O_5Si$: 424.2645. Found: 424.2625.

(*Z*)-*N*-Tosyl-6-(allylamino)-3-methylhex-3-en-2-one (S6f)



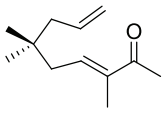
This compound was prepared from aldehyde **S5d** (446 mg, 1.59 mmol) following the procedure for the synthesis of compound **S6c**. Yield: 422 mg (83%). **S6f**: ^{1}H NMR (300 MHz, C_6D_6): δ 1.54 (s, 3H), 1.81 (s, 3H), 1.92 (s, 3H), 2.53-2.60 (q, J = 7.5 Hz, 2H), 3.15 (t, J = 7.2 Hz, 2H), 3.72 (d, J = 6.3 Hz, 2H), 4.87 (d, J = 10.2 Hz, 1H), 5.00 (d, J = 17.4 Hz, 1H), 5.46 (dt, J = 1.5 and 7.5 Hz, 1H), 5.55 (ddt, J = 10.2, 17.1, and 6.6 Hz, 1H), 6.82 (d, J = 7.8 Hz, 2H), 7.70 (d, J = 7.8 Hz, 2H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 21.0, 21.1, 28.7, 29.4, 47.0, 50.6, 118.6, 127.5, 129.7, 133.7, 135.0, 137.1, 138.3, 142.7, 200.8.

(*Z*)-1-*tert*-Butyldimethylsiloxy-1-(*N*-tosyl-5-aza-1-methylocta-1,7-dienyl)cyclopropane (14f)



First, enone **S6f** (400 mg, 1.24 mmol) was converted to silylenol ether **S7f** (513 mg, crude, 95%) following the procedure for the synthesis of compound **S4**. The crude silylenol ether **S7f** (485 mg) was elaborated to ene-VCP **14f** following the procedure for the synthesis of compound **11**. Yield: 445 mg (89%). **14f**: ^{1}H NMR (300 MHz, C_6D_6): δ 0.06 (s, 6H), 0.53 (dd, J = 5.1 and 7.2 Hz, 2H), 0.82 (dd, J = 5.1 and 7.2 Hz, 2H), 0.88 (s, 9H), 1.69 (s, 3H), 1.96 (s, 3H), 2.54 (q, J = 7.5 Hz, 2H), 3.09 (t, J = 7.8 Hz, 2H), 3.73 (d, J = 6.3 Hz, 2H), 4.88-5.04 (m, 3H), 5.59 (ddt, J = 10.2, 17.1, and 6.3 Hz, 1H), 6.85 (d, J = 8.1 Hz, 2H), 7.71 (d, J = 8.1 Hz, 2H). ^{13}C NMR (75.5 MHz, C_6D_6): δ -3.6, 14.5, 17.9, 21.1, 22.3, 25.8, 28.3, 47.1, 50.9, 56.1, 118.3, 126.4, 127.5, 129.7, 134.1, 137.8, 138.4, 142.7. MS (EI, 70 eV): m/z 449 (M^+, 0.5), 420 (2.0), 392 (31), 294 (16), 225 (42), 155 (39), 91 (64) . IR (neat): ν 2928, 1472, 1345, 1159 cm^{-1}. HRMS calcd for $C_{24}H_{39}NO_3SSi$: 449.2420. Found: 449.2412.

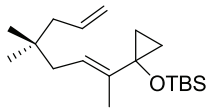
(*E*)-3,6,6-Trimethylnona-3,8-dien-2-one (S6g)



To a stirred suspension of NaH (382 mg, 15.9 mmol, washed with pentane prior to use) in 30 mL of anhydrous THF was slowly added diethyl 3-oxobutan-2-ylphosphonate (3.31 g, 15.9 mmol) at 0 °C via syringe under argon. The resulting solution was stirred at 0 °C for another 1 h. A solution of aldehyde **3** (1.004 g, 7.92 mmol) in THF

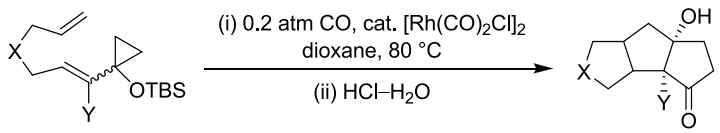
(5 mL) was added dropwise during 10 min, and the resulting mixture was stirred at room temperature for 4 h. The reaction was quenched by addition of saturated NH_4Cl (20 mL) and the mixture was extracted with ether. The combined organic extract was washed with brine, dried over Na_2SO_4, and concentrated to give a light yellow oil as the crude product. Flash column chromatography on silica gel (40 g, eluted with pentane/ether 30:1 to 20:1) afforded enone **S6g** (1.193 g, *E*/*Z* = 13:1, 83%) as a colorless oil. **S6g**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.94 (s, 6H), 1.77 (s, 3H), 2.01 (d, *J* = 7.2 Hz, 2H), 2.15 (d, *J* = 7.5 Hz, 2H), 2.33 (s, 3H), 4.99-5.09 (m, 2H), 5.76-5.89 (m, 1H), 6.73 (dt, *J* = 1.5 and 7.8 Hz, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 11.4, 25.5, 26.9, 34.6, 40.9, 46.6, 117.4, 134.9, 138.9, 140.5, 199.8. MS (EI, 70 eV): *m*/*z* 180 (M^+, 18), 165 (20), 139 (22), 123 (12), 109 (10), 98 (73), 83 (60), 67 (12). IR (neat): *v* 1670, 1639, 1468 cm^{-1}. HRMS calcd. for $C_{12}H_{20}O$: 180.1514. Found: 180.1514.

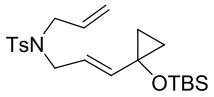
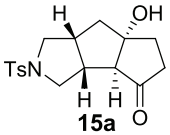
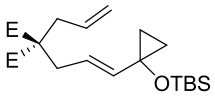
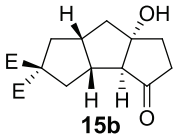
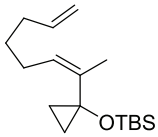
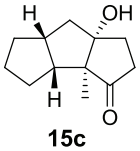
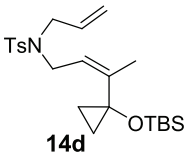
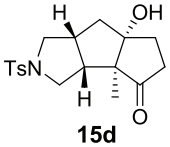
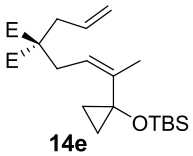
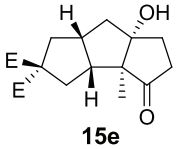
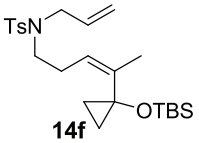
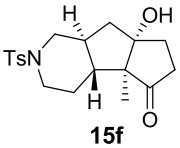
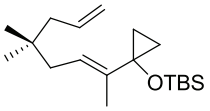
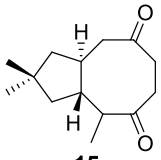
(*E*)-1-*tert*-Butyldimethylsilyloxy-1-(5,5-dimethylocta-2,7-dien-2-yl)cyclopropane (14g)



First, enone **S6g** (803 mg, 4.45 mmol) was converted to silylenol ether **S7g** (1.419 g, crude, 100%) following the procedure for the synthesis of compound **S4**. The crude silylenol ether **S7g** (1.381 g) was elaborated to ene-VCP **14g** following the procedure for the synthesis of compound **11**. Yield: 1.014 g (74%). **14g**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.04 (s, 6H), 0.68 (dd, *J* = 4.2 and 7.8 Hz, 2H), 0.76 (dd, *J* = 4.2 and 7.8 Hz, 2H), 0.82 (s, 9H), 0.83 (s, 6H), 1.67 (s, 3H), 1.88 (d, *J* = 7.5 Hz, 2H),1.92 (d, *J* = 7.5 Hz, 2H), 4.94-5.01 (m, 2H), 5.45 (dt, *J* = 1.2 and 8.7 Hz, 1H), 5.72-5.86 (m, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ -3.7, 13.3, 14.1, 17.9, 25.8, 26.8, 34.5, 39.6, 46.5, 61.3, 116.8, 121.3, 135.7, 137.6. MS (EI, 70 eV): *m*/*z* 308 (M^+, 12), 293 (5.0), 265 (38), 237 (11), 211 (100), 153 (7.0). IR (neat): *v* 2957, 2929, 1472, 1250, 1236, 1205 cm^{-1}. HRMS calcd for $C_{19}H_{36}OSi$: 308.2535. Found: 308.2530.

Table S1. Model Tandem [(5+2)+1]/Aldol Reactions[a]

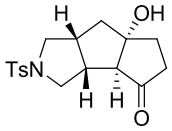


entry	substrate	mol % $[Rh(CO)_2Cl]_2$	time (h)	product	yield[b]
1	 **14a**	6	18	 **15a**	22%
2	 **14b**	5	20	 **15b**	28%
3	 **14c**	10	36	 **15c**	26%[c]
4	 **14d**	8	48	 **15d**	50%[d]
5	 **14e**	11	48	 **15e**	67%
6	 **14f**	9	36	 **15f**	52%[e]
7	 **14g**	6	24	 **15g**	50%[f]

[a] E = COOEt. [b] Isolated yields. [c] A *trans*-fused cyclooctanedione **15c'** was also isolated in 26% yield. [d] Based on recovered starting material. [e] A degredation product, enone **15f'**, was also isolated in 24% yield. Relative stereochemistry of **15f** was determined by X-ray crystallographic analysis. [f] Single diastereomer.

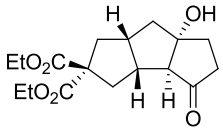
The model reactions were conducted following the general procedure for cycloaddition reactions of substrate **7**, **8**, and **11** (on page S7), except at different catalyst loading and reaction time as indicated in the above table.

***Cis-anti-cis-N*-Tosyl-4-aza-8-hydroxytricyclo[6.3.0.0^{2,6}]undecan-11-one (15a)**



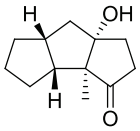
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.90 (m, 2H), 2.15 (m, 2H), 2.26-2.35 (m, 2H), 2.39 (s, 1H), 2.45 (s, 3H), 2.56-2.71 (m, 2H), 2.81-2.93 (m, 3H), 3.31-3.37 (m, 2H), 7.36 (d, J = 8.1 Hz, 2H), 7.70 (d, J = 8.1 Hz, 2H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 21.6, 31.6, 37.3, 42.5, 44.5, 45.2, 55.2, 67.4, 86.8, 128.4, 129.7, 130.8, 144.4, 217.2. MS (ESI): m/z 336 ([M+H]$^+$). IR (neat): ν 2922, 2851, 1736 cm^{-1}.

***Cis-anti-cis*-4,4-Diethoxycarbonyl-8-hydroxytricyclo[6.3.0.0^{2,6}]undecan-11-one (15b)**



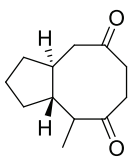
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.24 (t, J = 7.1 Hz, 3H), 1.25 (t, J = 7.1 Hz, 3H), 1.79-1.81 (m, 2H), 1.98 (m, 1H), 2.08-2.15 (m, 3H), 2.20 (m, 1H), 2.25-2.38 (m, 1H), 2.38 (s, 1H), 2.56-2.71 (m, 5H), 4.17 (q, J = 7.1 Hz, 2H), 4.18 (dq, J = 1.3 and 7.1 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0, 34.2, 37.5, 40.7, 40.8, 43.1, 44.8, 45.5, 61.4, 62.7, 65.8, 89.5, 171.6, 171.7, 218.2. MS (EI, 70 eV): m/z 324 (M$^+$, 46), 306 (16), 279 (14), 250 (28), 204 (34), 173 (78), 152 (51). IR (neat): ν 2980, 1727, 1260 cm^{-1}. Calcd for $C_{17}H_{24}O$: 324.1573. Found: 324.1572.

***Cis-anti-cis*-8-Hydroxytricyclo[6.3.0.0^{2,6}]undecan-11-one (15c)**



^{1}H NMR (300 MHz, $CDCl_3$): δ 0.97 (s, 3H), 1.32-1.40 (m, 1H), 1.43-1.51 (m, 1H), 1.54-1.64 (m, 4H), 1.65-1.76 (m, 1H), 1.78-1.86 (m, 1H), 1.88-1.96 (m, 1H), 2.03 (dd, J = 9.0 and 14.4 Hz, 1H), 2.11-2.17 (m, 1H), 2.28-2.40 (m, 2H), 2.46-2.58 (m, 2H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 12.2, 27.3, 28.1, 32.4, 34.0, 35.5, 41.0, 45.1, 49.4, 60.2, 89.0, 222.0. MS (EI, 70 eV): m/z 194 (M$^+$, 52), 165 (23), 135 (35), 113 (100), 109 (59). IR (neat): ν 3458, 2948, 2866, 1725, 1450, 1038 cm^{-1}. HRMS calcd for $C_{12}H_{18}O_2$: 194.1307. Found: 194.1312.

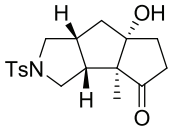
***Trans*-2-Methylbicyclo[6.3.0]undecan-3,6-dione (15c')**



^{1}H NMR (300 MHz, $CDCl_3$): δ 1.04 (d, J = 6.9 Hz, 3H), 1.43-1.45 (m, 1H), 1.55-1.61 (m, 3H), 1.78-1.84 (m,

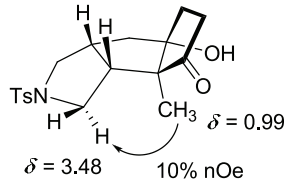
4H), 2.23 (dd, J = 7.8 and 14.1 Hz, 1H), 2.45 (d, J = 7.2 Hz, 2H), 2.60-2.66 (m, 1H), 2.74-2.80 (m, 1H), 2.87 (d, J = 7.2 Hz, 2H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 12.1, 20.9, 27.6, 32.3, 38.8, 39.5, 40.6, 45.5, 47.1, 47.4, 213.0, 214.9. MS (EI, 70 eV): m/z 194 (M^+, 52), 137 (12), 122 (15), 109 (24), 96 (100). IR (neat): ν 2959, 2876, 1452, 1126 cm^{-1}. HRMS calcd for $C_{12}H_{18}O_2$: 194.1307. Found: 194.1314.

***Cis-anti-cis*-*N*-Tosyl-4-aza-8-hydroxy-1-methyltricyclo[6.3.0.0^{2,6}]undecan-11-one (15d)**

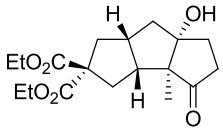


^{1}H NMR (300 MHz, $CDCl_3$): δ 0.99 (s, 3H), 1.80-1.87 (m, 2H), 1.92-2.03 (m, 1H), 2.10 (dd, J = 2.8 and 9.3 Hz, 1H), 2.13-2.23 (m, 1H), 2.29 (t, J = 9.3 Hz, 1H), 2.45 (s, 3H), 2.56 (dd, J = 2.2 and 10.3 Hz, 1H), 2.58 (m, 1H), 2.61 (dd, J = 7.5 and 10.0 Hz, 1H), 2.73 (dd, J = 8.4 and 9.4 Hz, 1H), 2.83 (dt, J = 2.9 and 8.1 Hz, 1H), 3.25 (d, J = 9.5 Hz, 1H), 3.48 (dd, J = 1.1 and 10.3 Hz, 1H), 7.37 (d, J = 8.0 Hz, 2H), 7.70 (d, J = 8.0 Hz, 2H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 12.5, 21.6, 29.2, 34.8, 39.9, 45.0, 47.1, 50.1, 55.3, 61.7, 86.1, 128.4, 129.7, 130.5, 144.4, 219.8. MS (EI, 70 eV): m/z 349 (M^+, 1.0), 331 (1.1), 222 (11), 194 (100), 176 (14), 155 (12), 91 (38). IR (neat): ν 2957, 1735, 1340, 1160 cm^{-1}. Calcd for $C_{18}H_{23}NO_4S$: 349.1348. Found: 349.1346.

The relative configuration of this cycloadduct was determined by nOe experiments, as shown below:

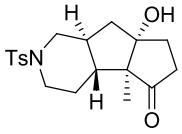


***Cis-anti-cis*-4,4-Diethoxycarbonyl-8-hydroxy-1-methyltricyclo[6.3.0.0^{2,6}]undecan-11-one (15e)**



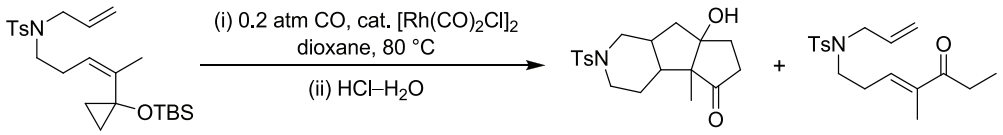
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.00 (s, 3H), 1.25 (m, 6H), 1.73 (dd, J = 4.7 and 17.4 Hz, 1H), 1.94 (m, 3H), 2.08-2.37 (m, 5H), 2.45-2.64 (m, 3H), 2.76 (q, J = 9.4Hz, 1H), 4.17 (q, J = 7.2 Hz, 2H), 4.19(m, 2H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 12.6, 14.0, 32.2, 35.1, 35.4, 40.0, 41.2, 44.4, 48.3, 60.3, 61.3, 61.4, 62.2, 88.8, 171.5, 171.8, 220.7. MS (EI, 70 eV): m/z 338 (M^+, 55), 173 (90), 113 (44), 99 (35). IR (neat): ν 3519, 2979, 1727 cm^{-1}. Calcd for $C_{18}H_{26}O_6$: 338.1729. Found: 338.1734.

***N*-Tosyl-5-aza-9-hydroxy-1-methyltricyclo[7.3.0.0^{2,7}]dodecan-12-one (15f)**



^{1}H NMR (300 MHz, $CDCl_3$): δ 0.96 (s, 3H), 0.98-1.05 (m, 1H), 1.47-1.63 (m, 2H), 1.72 (dq, J = 13.2 and 2.7 Hz, 1H), 1.77 (s, 1H), 1.94-2.19 (m, 6H), 2.36-2.42 (m, 2H), 2.43 (s, 3H), 3.90 (d, J = 11.7 Hz, 1H), 4.01 (d, J = 8.7 Hz, 1H), 7.32 (d, J = 8.1 Hz, 2H), 7.62 (d, J = 8.1 Hz, 2H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 10.6, 21.5, 25.5, 35.3, 36.1, 41.0, 44.1, 46.2, 50.4, 51.3, 59.1, 87.5, 127.4, 129.6, 133.1, 143.5, 219.7. MS (EI, 70 eV): *m*/*z* 363 (M^+, 24), 306 (19), 236 (6.0), 208 (94), 162 (29), 152 (65), 119 (18), 91 (100) . IR (neat): *v* 3497, 2933, 1726, 1597, 1463, 1382, 1017 cm^{-1}. HRMS calcd for $C_{19}H_{25}NO_4S$: 363.1504. Found: 363.1501.

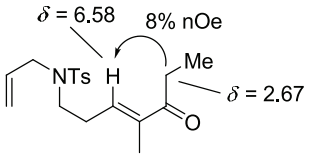
In the reaction of ene-VCP **14f**, small amount of degredation product **15f'** was also observed:



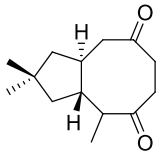
14f **15f** (52%) **15f'** (24%)

15f': ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.09 (t, J = 7.3 Hz, 3H), 1.76 (s, 3H), 2.43 (s, 3H), 2.49 (q, J = 7.3 Hz, 2H), 2.67 (q, J = 7.3 Hz, 2H), 3.23 (t, J = 7.2 Hz, 2H), 3.82 (d, J = 6.3 Hz, 2H), 5.15-5.23 (m, 2H), 5.65 (ddt, J = 10.1, 17.0, and 6.3 Hz, 1H), 6.58 (dt, J = 1.2 and 7.0 Hz, 1H), 7.32 (d, J = 8.1 Hz, 2H), 7.70 (d, J = 8.1 Hz, 2H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 8.6, 11.6, 21.5, 28.3, 30.4, 45.9, 51.1, 119.1, 127.1, 129.7, 133.1, 136.6, 137.1, 138.6, 143.4, 202.2.

The C=C configuration of enone **15f'** was determined by nOe experiments, as shown below:



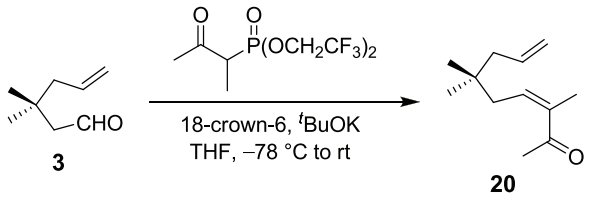
***Trans*-2,10,10-Trimethylbicyclo[6.3.0]undecan-3,6-dione (15g)**



^{1}H NMR (300 MHz, $CDCl_3$): δ 0.92 (d, J = 4.5 Hz, 3H), 0.94 (s, 6H), 1.24 (dd, J = 11.1 and 12.3 Hz, 1H), 1.37-1.51 (m, 2H), 1.55 (dd, J = 6.6 and 12.6 Hz, 1H), 1.82-1.96 (m, 2H), 2.10 (dd, J = 8.7 and 13.8 Hz, 1H), 2.36-2.41 (m, 2H), 2.48 (dd, J = 3.6 and 13.8 Hz, 1H), 2.62-2.67 (m, 1H), 2.76-2.81 (m, 2H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 12.4, 31.5, 31.7, 34.4, 38.7, 39.3, 41.0, 43.2, 45.0, 47.1, 47.1, 48.0, 213.0, 214.8. MS (EI, 70 eV): *m*/*z* 222 (M^+, 19), 207 (12), 179 (6.0), 150 (22), 137 (19), 124 (100), 109 (51), 95 (82). IR (neat): *v* 2947, 2866, 1704, 1451, 1129 cm^{-1}. HRMS calcd for $C_{14}H_{22}O_2$: 222.1620. Found: 222.1619.

2.3 Experimental Procedures for Total Syntheses

(*Z*)-3,6,6-Trimethylnona-3,8-dien-2-one (20)

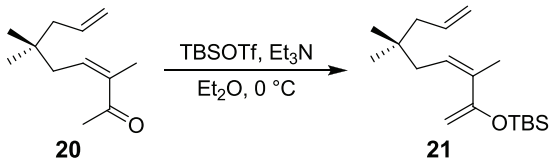


3 **20**

To a solution of bis(2,2,2-trifluoroethyl) 3-oxobutan-2-ylphosphonate (3.44 g, 80% purity, 10.9 mmol) and 18-crown-6 (2.81 g, 10.6 mmol) in 45 mL anhydrous THF at −78 °C was added a solution of $KOBu^t$ (955 mg, 8.51 mmol) in 10 mL THF dropwise under argon. After stirring for 20 min at −78 °C, a solution of aldehyde **3** (959 mg, 7.60 mmol) in 10 mL THF was added at −78 °C dropwise and the resulting mixture was stirred for another 1 h at −78 °C. The reaction was gradually warmed to room temperature in 4 h. Saturated NH_4Cl (30 mL) was added and the reaction mixture was extracted with ether. The combined organic extract was washed with brine, dried over Na_2SO_4, and concentrated. The crude product was purified by flash column chromatography on silica gel (100 g, eluted with pentane/ether 50:1 to 30:1) to afford 1.191 g (87%) of enone product **20** as a 7:1 ratio *Z*/*E* isomers.

20: ^{1}H NMR (300 MHz, C_6D_6): δ 0.82 (s, 6H), 1.63 (d, J = 1.2 Hz, 3H), 1.87 (s, 3H), 1.89 (d, J = 7.5 Hz, 2H), 2.30 (dd, J = 7.8 and 1.2 Hz, 2H), 4.93-5.02 (m, 2H), 5.54 (dt, J = 1.2 and 7.5 Hz, 1H), 5.68-5.82 (m, 1H). ^{13}C NMR (75.5 MHz, C_6D_6): δ 21.2, 26.8, 29.7, 34.0, 41.1, 46.7, 117.2, 134.1, 135.6, 137.4, 201.2. MS (EI, 70 eV): *m*/*z* 180 (M^+, 6.0), 165 (7.0), 139 (70), 123 (9.0), 98 (60), 83 (52). IR (neat): ν 1693, 1638, 1466 cm^{-1}. HRMS calcd. for $C_{12}H_{20}O$: 180.1514. Found: 180.1510. This compound tends to isomerize to its *E*-isomer in $CDCl_3$.

(*Z*)-2-*tert*-Butyldimethylsilyloxy-3,6,6-trimethylnona-1,3,8-triene (21)

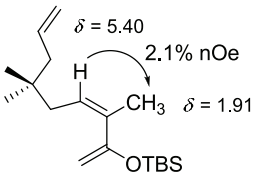


20 **21**

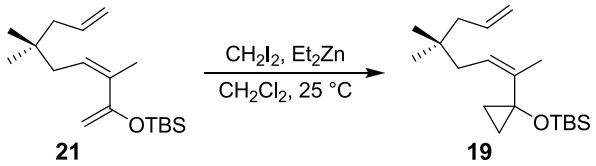
Triethyl amine (1.26 g, 12.5 mmol) and TBSOTf (1.96 g, 7.4 mmol) was sequentially added to a solution of enone **20** (735 mg, 4.08 mmol) in anhydrous ether (30 mL) at 0 °C. After stirring for 3 h at 0 °C, brine was added and the resulting mixture was extracted by ether three times. The combined ether extract was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by flash column chromatography on silica gel (60 g, eluted with petroleum ether containing 1% Et_3N) to afford silylenol ether **21** as a colorless oil (1.2003 g, quantitative yield).

21: ^{1}H NMR (300 MHz, C_6D_6): δ 0.17 (s, 6H), 0.89 (s, 6H), 0.97 (s, 9H), 1.91 (d, J = 1.5 Hz, 3H), 1.97 (d, J = 7.2 Hz, 2H), 2.28 (dd, J = 1.2 and 7.2 Hz, 2H), 4.30 (s, 1H), 4.44 (s, 1H), 4.98-5.07 (m, 2H), 5.40 (dt, J = 1.2 and 7.2 Hz, 1H), 5.76-5.90 (m, 1H). ^{13}C NMR (75.5 MHz, C_6D_6): δ −4.5, 18.3, 22.9, 25.9, 27.0, 34.0, 41.4, 46.8, 93.9, 117.0, 126.0, 135.4, 135.9, 157.0. MS (EI, 70 eV): *m*/*z* 294 (M^+, 11), 253 (50), 237 (22), 181 (7.0), 161 (56), 75 (100). IR (neat): ν 2957, 2929, 1617, 1471, 1252, 1043, 1015, 1004 cm^{-1}. HRMS calcd for $C_{18}H_{34}OSi$: 294.2379. Found: 294.2388. This compound tends to isomerize to its *E*-isomer in $CDCl_3$.

The C=C configuration of **21** was determined by nOe experiment, as shown below:



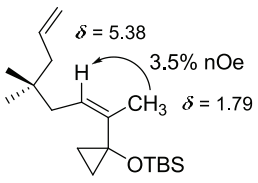
(*Z*)-1-*tert*-Butyldimethylsilyloxy-1-(5,5-dimethylocta-2,7-dien-2-yl)cyclopropane (19)



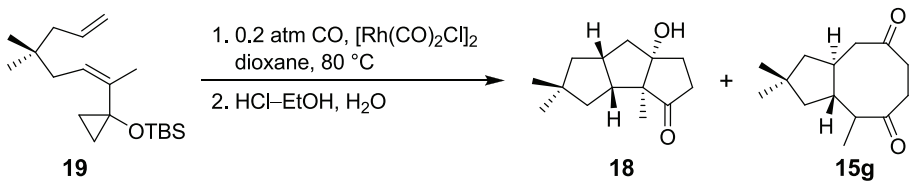
Diethyl zinc solution (5.2 mL, 0.88 M in hexane, 4.56 mmol) and CH_2I_2 (1.339 g, 5.00 mmol) was sequentially added to a solution of silylenol ether **21** (1.168 g, 3.97 mmol) in anhydrous methylene chloride (50 mL) at 25 °C. The reaction mixture gradually became a white suspension while stirred at 20 °C. The reaction was monitored by GC and upon completion (1-2 h), it was quenched with saturated NH_4Cl (40 mL). The resulting mixture was extracted with ether and the combined organic extract was dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography (60 g of silica gel, eluted with petroleum ether containing 1% triethyl amine) to afford 1.049 g (86%) of the ene-VCP product **19** as a colorless oil.

19: ^{1}H NMR (300 MHz, C_6D_6): δ 0.13 (s, 6H), 0.62 (m, 2H), 0.91 (s, 6H), 0.95 (s, 9H), 0.96 (m, 2H), 1.79 (s, 3H), 2.00 (d, J = 7.5 Hz, 2H), 2.35 (d, J = 7.2 Hz, 2H), 5.01-5.07 (m, 2H), 5.38 (t, J = 7.2 Hz, 1H), 5.79-5.93 (m, 1H). ^{13}C NMR (75.5 MHz, C_6D_6): δ –3.6, 14.7, 18.0, 22.7, 25.8, 26.9, 33.8, 40.8, 47.1, 56.3, 117.1, 127.4, 135.9, 136.7. MS (EI, 70 eV): *m*/*z* 308 (M^+, 0.4), 293 (4.0), 267 (98), 211 (60), 135 (10), 73 (100). IR (neat): ν 2957, 2929, 1472, 1255, 1229, 1033 cm^{-1}. HRMS calcd for $C_{19}H_{36}OSi$: 308.2535. Found: 308.2528.

The C=C configuration of **19** was determined by nOe experiment, as shown below:



***Cis-anti-cis*-8-Hydroxy-1,4,4-trimethyltricyclo[6.3.0.0^{2,6}]undecan-11-one (18)**

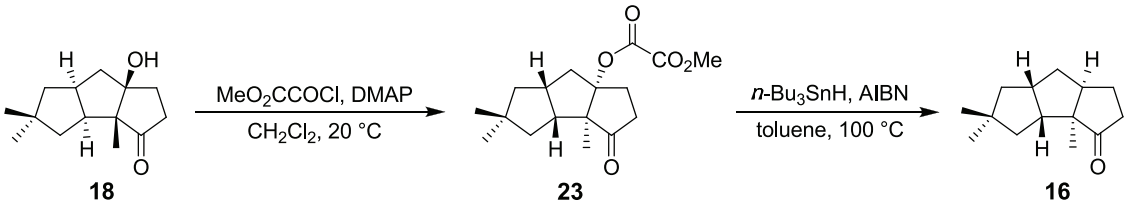


A solution of ene-VCP **19** (62.7 mg, 0.203 mmol) in anhydrous dioxane (8 mL) was degassed by bubbling CO/N_2 (1:4 V/V) for 5 min. The catalyst $[Rh(CO)_2Cl]_2$ (6.0 mg, 15 μmol) was added in one potion and a light yellow solution formed, which was further bubbled the above gas for 5 min. The solution was heated to 80 °C in

an oil bath with stirring under a positive pressure of the mixture gas. After 48 h, TLC indicated the absence of the starting material and the resulting brown solution was cooled to room temperature. The reaction mixture was hydrolyzed by adding 1% HCl in EtOH (0.3 mL) and water (0.1 mL) and stirred at rt for 20 min. Solvent was evaporated and the residue was purified by flash column chromatography on silica gel (5 g, eluted with petroleum ether/ethyl acetate 5:1 to 3:1) to afford tricyclic compound **18** (28.2 mg, 62%) as a pale yellow oil, and dione **15g** (4.4 mg, 10%) as a yellow oil.

18: ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.90 (s, 3H), 0.96 (s, 3H), 1.07 (s, 3H), 1.22 (dd, J = 9.6 and 11.7 Hz, 1H), 1.37-1.56 (m, 2H), 1.60-1.74 (m, 3H), 1.85-1.97 (m, 2H), 2.07-2.16 (m, 1H), 2.25-2.37 (m, 1H), 2.47-2.58 (m, 2H), 2.77 (dd, J = 9.9 and 19.2 Hz, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 12.6, 26.5, 29.0, 32.1, 35.2, 40.3, 41.6, 42.1, 44.6, 48.6, 49.2, 60.0, 89.5, 221.8. MS (EI, 70 eV): m/z 222 (M^+, 26), 207 (5.0), 189 (7.0), 165 (42), 149 (14), 113 (100), 95 (20). IR (neat): ν 2950, 2863, 1728, 1463, 1365, 1261, 1216 cm^{-1}. HRMS calcd for $C_{14}H_{22}O_2$: 222.1620. Found: 222.1621.

***Cis-anti-cis*-1,4,4-Trimethyltricyclo[6.3.0.0^{2,6}]undecan-11-one (16)**



To a stirred solution of tricyclic ketone **18** (55.0 mg, 0.247 mmol) and DMAP (46.5 mg, 0.381 mmol) in 4 mL of dry CH_2Cl_2 was added methyl chlorooxalate (63.8 mg, 0.521 mmol) dropwise. After stirred at room temperature for 1 h, the resulting solution was washed with water, dried over Na_2SO_4, and concentrated. The residue was purified by flash column chromatography on silica gel (5 g, eluted with petroleum/acetate 6:1) to give oxalate **23** (70.3 mg, 92%) as a colorless oil.

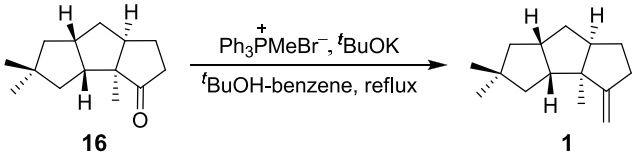
23: ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.91 (s, 3H), 1.06 (s, 3H), 1.07 (s, 3H), 1.44 (ddd, J = 2.0, 8.1, and 12.3 Hz, 1H), 1.58 (t, J = 11.5 Hz, 1H), 1.68 (m, 1H), 2.04 (dd, J = 9.5 and 15.6 Hz, 1H), 2.12-2.20 (m, 3H), 2.33 (dt, J = 19.8 and 8.8 Hz, 1H), 2.52-2.66 (m, 2H), 2.77 (ddd, J = 3.3, 9.0, and 13.4 Hz, 1H), 2.90 (app. q, J = 10.0 Hz, 1H), 3.91 (s, 3H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 13.3, 26.4, 28.1, 28.9, 34.6, 40.4, 40.6, 41.4, 42.0, 47.9, 48.8, 53.4, 61.7, 99.0, 156.6, 158.2, 218.0. MS (EI, 70 eV): m/z 308 (M^+, 8.0), 280 (4.0), 252 (12), 221 (12), 204 (29), 176 (100), 163 (22), 147 (19). IR (neat): ν 2956, 1774, 1746, 1463, 1329, 1204, 1166 cm^{-1}. HRMS calcd. for $C_{17}H_{24}O_5$: 308.1624. Found: 308.1628.

A solution of oxalate **23** (20.9 mg, 0.0678 mmol) in 1.4 mL of degassed toluene was heated to reflux in an oil bath under argon. A solution of *n*-Bu_3SnH (84 mg, 0.289 mmol) and AIBN (4.6 mg) in degassed toluene (1.0 mL) was added in one potion. The reaction mixture was stirred for another 45 min under reflux. The resulting mixture was cooled to room temperature and evaporated. The crude product was purified by flash column chromatography on silica gel (2 g, eluted with petroleum ether/ethyl acetate 20:1) to afford hirsutene norketone **16** (9.2 mg, 66%) as a colorless oil, which solidifies on standing.

16: ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.90 (s, 3H), 0.94 (s, 3H), 0.98-1.02 (m, 1H), 1.04 (s, 3H), 1.18 (dd, J = 11.6 Hz, 1H), 1.32-1.48 (m, 2H), 1.56-1.76 (m, 3H), 2.00 (dddd, J = 6.2, 8.4, 9.8, and 13.1 Hz, 1H), 2.19-2.45 (m, 3H), 2.52 (dquintet, J = 3.4 and 9.0 Hz, 1H), 2.80 (dt, J = 10.6 and 8.7 Hz, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 17.2, 22.3, 26.5, 29.2, 29.7, 34.2, 37.5, 41.1, 41.8, 43.3, 46.6, 48.8, 59.3, 224.8. The spectroscopic data was

identical to that reported.[4]

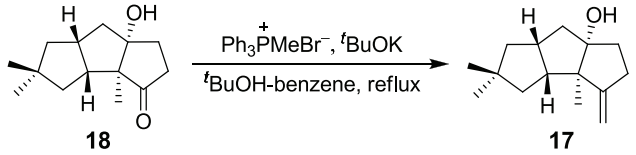
(±)-Hirsutene (1)[5]



To a solution of KOBu^t (37.9 mg, 0.338 mmol) in ^{t}BuOH (0.5 mL) and benzene (2.2 mL) was added at room temperature under argon methyltriphenylphosphonium bromide (134 mg, 0.375 mmol) in one portion and the resulting yellow solution was stirred at room temperature for 30 min. A solution of hirsutene norketone **16** (13.4 mg, 0.065 mmol) in dry benzene (1 mL) was added and the reaction mixture was brought to reflux for 1 h in a 100 °C oil bath. The resulting mixture was cooled, poured into water, and extracted with petroleum ether. The combined extract was dried over $MgSO_4$ and evaporated. Flash column chromatography on neutral alumina provided crude hirsutene as a colorless oil (containing unidentified non-polar impurities). Another column chromatography on $AgNO_3$ impregnated silica gel (eluting with petroleum ether and then petroleum ether/acetone 50:1 to 25:1) afforded pure (±)-hirsutene (8.3 mg, 63%) as a colorless oil.

1: ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.92 (s, 3H), 0.95 (s, 3H), 0.99-1.04 (m, 1H), 1.05 (s, 3H), 1.21 (t, J = 11.7 Hz, 1H), 1.40-1.48 (m, 4H), 1.64 (ddd, J = 2.0, 8.4, and 10.6 Hz, 1H), 1.69-1.78 (m, 1H), 2.11-2.19 (m, 1H), 2.43-2.49 (m, 2H), 2.50-2.65 (m, 2H), 4.77 (s, 1H), 4.82 (s, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 23.2, 26.8, 27.2, 29.7, 30.9, 38.6, 40.9, 41.9, 44.3, 49.0, 49.9, 53.4, 56.0, 103.5, 162.9. The spectroscopic data was identical to that reported.[4,5]

***Cis-anti-cis*-8-Hydroxy-11-methylene-1,4,4-trimethyltricyclo[6.3.0.0^{2,6}]undecane (17)**



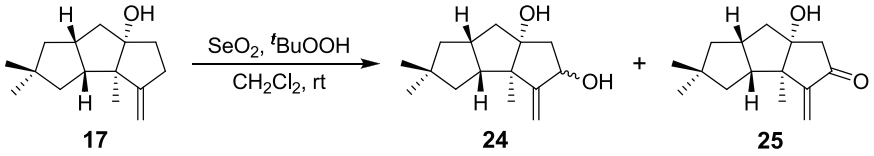
To a solution of KOBu^t (92.8 mg, 0.828 mmol) in ^{t}BuOH (1 mL) and benzene (4.5 mL) was added at room temperature under argon methyltriphenylphosphonium bromide (247 mg, 0.692 mmol) in one portion and the resulting yellow solution was stirred at room temperature for 30 min. A solution of hydroxy ketone **18** (28.0 mg, 0.126 mmol) in dry benzene (0.5 mL) was added and the reaction mixture was brought to reflux for 2 h in a 100 °C oil bath. The resulting mixture was cooled, poured into water, and extracted with petroleum ether. The combined extract was dried over $MgSO_4$ and evaporated. Flash column chromatography on silica gel (6 g, eluent with petroleum ether/ethyl acetate 10:1) provided hydroxy alkene **17** (23.4 mg, 85%) as a colorless oil.

17: ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.91 (s, 3H), 0.96 (s, 3H), 1.07 (s, 3H), 1.22 (dd, J = 8.4 and 12.3 Hz, 1H), 1.25 (s, 1H), 1.39 (ddd, J = 2.0, 7.8, and 12.0 Hz, 1H), 1.50 (dd, J = 5.3 and 8.4 Hz, 1H), 1.54-1.61 (m, 1H), 1.63-1.71 (m, 2H), 1.89 (ddd, J = 5.2, 8.8, and 12.8 Hz, 1H), 1.99 (dd, J = 9.2 and 13.7 Hz, 1H), 2.30-2.65 (m, 4H), 4.81 (m, 2H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 18.0, 27.2, 29.0, 29.5, 35.9, 40.0, 41.4, 42.7, 45.0, 49.1, 53.4, 55.5, 92.3, 105.2, 161.1. MS (EI, 70 eV): m/z 220 (M^+, 18), 205 (11), 187 (6.0), 177 (12), 151 (12), 124 (10),

(4) Banwell, M. G.; Edwards, A. J.; Harfoot, G. J.; Jolliffe, K. A. *Tetrahedron* **2004**, *60*, 535.
(5) Sternbach, D. D.; Ensinger, C. L. *J. Org. Chem*. **1990**, *55*, 2725.

111 (100). IR (neat): *v* 2950, 2864, 1650, 1463, 1365, 1069 cm^{-1}. HRMS calcd. for $C_{15}H_{24}O$: 220.1827. Found: 220.1827.

Cis-anti-cis-8,10-Dihydroxy-11-methylene-1,4,4-trimethyltricyclo[6.3.0.0^{2,6}]undecane (24)



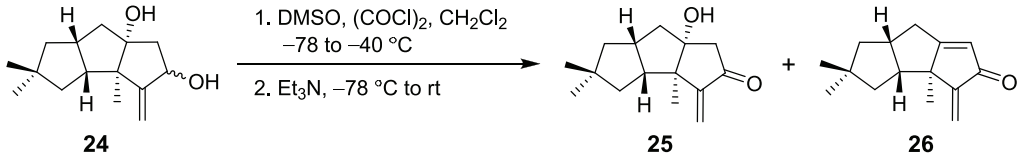
17 **24** **25**

To a stirred solution of hydroxy alkene **17** (38.3 mg, 0.174 mmol) in CH_2Cl_2 (3 mL) was sequentially added SeO_2 (13.0 mg, 0.117 mmol) and ^{t}BuOOH (65% aqueous solution, 70 mg, 0.50 mmol). The resulting solution was stirred at room temperature for 2 h and TLC indicated the reaction was complete. The reaction mixture was poured into water, extracted with CH_2Cl_2, dried over $MgSO_4$, and concentrated. Flash column chromatography on silica gel (5 g, eluted with petroleum ether/ethyl acetate 6:1 to 3:1) afforded diol **24** (34.2 mg, 83%) as a colorless oil and hydroxy enone **25** (6.3 mg, 16%) as a white solid.

24: ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88 (s, 3H), 1.07 (s, 3H), 1.09 (s, 3H), 1.11-1.16 (m, 1H), 1.26 (s, 2H), 1.36-1.51 (m, 3H), 1.62-1.70 (m, 1H), 1.86 (dd, J = 2.5 and 14.0 Hz, 1H), 2.02-2.09 (m, 1H), 2.11 (dd, J = 5.4 and 14.0 Hz, 1H), 2.32-2.44 (m, 2H), 4.55 (br s, 1H), 4.98 (d, J = 1.0 Hz, 1H), 5.18 (d, J = 1.0 Hz, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 19.3, 27.5, 29.6, 29.7, 39.2, 41.7, 41.9, 43.6, 45.0, 48.5, 54.7, 75.7, 92.2, 108.9, 165.8. MS (EI, 70 eV): *m*/*z* 236 (M^+, 4.0), 218 (10), 203 (11), 179 (22), 166 (28), 126 (74), 122 (53), 109 (66), 95 (42). IR (neat): *v* 3383, 2950, 2935, 2864, 1465, 1284, 1115, 1070 cm^{-1}. HRMS calcd. for $C_{15}H_{24}O_2$: 236.1776. Found: 236.1784.

25: ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.92 (s, 3H), 1.09 (s, 3H), 1.14 (s, 3H), 1.23-1.29 (m, 3H), 1.45-1.52 (m, 1H), 1.58-1.77 (m, 3H), 1.98 (dd, J = 8.9 and 14.0 Hz, 1H), 2.46 (d, J = 18.1 Hz, 1H), 2.52-2.65 (m, 1H), 2.61 (d, J = 18.1 Hz, 1H), 5.22 (s, 1H), 6.03 (s, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 17.6, 26.5, 29.1, 39.9, 41.9, 42.8, 44.9, 49.1, 49.3, 52.8, 54.6, 87.0, 116.9, 155.4, 204.5. MS (EI, 70 eV): *m*/*z* 234 (M^+, 14), 216 (6.0), 201 (6.0), 192 (7.0), 177 (6.0), 149 (5.0), 124 (100). IR (neat): *v* 2952, 2935, 2866, 1726, 1635, 1465, 1384, 1267, 1116 cm^{-1}. HRMS calcd. for $C_{15}H_{22}O_2$: 234.1620. Found: 234.1620.

11-Methylene-1,4,4-trimethyltricyclo[6.3.0.0^{2,6}]undec-8-en-10-one (26)



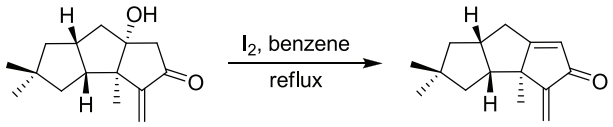
24 **25** **26**

To a stirred solution of oxalyl chloride (132 mg, 1.04 mmol) in dry CH_2Cl_2 (3 mL) at −78 °C was added a solution of DMSO (152 mg, 1.95 mmol) in CH_2Cl_2 (1 mL) dropwise. The solution was stirred at −78 °C for 30 min and a solution of diol **24** (21.2 mg, 90 mmol) in CH_2Cl_2 (1 mL) was added. After stirred at −78 °C for 30 min, the reaction mixture was allowed to warm to −30 °C and further stirred for 1.5 h. The reaction was recooled to −78 °C and neat Et_3N (253 mg, 2.50 mmol) was added. The solution was stirred for 2 h and allowed to warm to room temperature. The reaction mixture was washed with aqueous HCl (2 M) and saturated $NaHCO_3$ and dried over $MgSO_4$. Evaporation of the solvent gave the crude product as a brown oil. Flash column chromatography on silica gel (5 g, eluted with petroleum ether/ethyl acetate 20:1 to 3:1) afforded dienone **26**

(10.1 mg, 52%) as a pale-yellow oil and hydroxy enone **25** (5.4 mg, 26%) as a white solid.

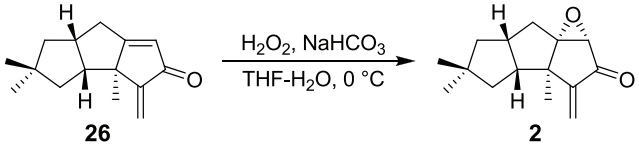
26: ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.95 (s, 3H), 1.13 (s, 3H), 1.16 (s, 3H), 1.22-1.29 (m, 1H), 1.57 (d, J = 9.0 Hz, 2H), 1.81 (dd, J = 6.5 and 12.3 Hz, 1H), 2.24-2.34 (m, 1H), 2.36-2.46 (m, 1H), 2.71-2.84 (m, 2H), 5.15 (s, 1H), 5.88 (s, 1H), 5.89 (d, J = 1.4 Hz, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 23.5, 27.4, 29.0, 32.6, 40.2, 44.1, 44.9, 48.1, 49.6, 51.7, 112.9, 123.1, 154.2, 189.9, 197.8. The spectroscopic data is identical to that reported.[6]

11-Methylene-1,4,4-trimethyltricyclo[6.3.0.0^{2,6}]undec-8-en-10-one (26)



To a solution of hydroxy enone **25** (4.3 mg, 0.018 mmol) in benzene (2 mL) was added a small piece of iodine (2.9 mg, 0.012 mmol). The resulting solution was heated to reflux under stirring for 4 h and allowed to cool to room temperature. The reaction mixture was washed with aqueous $Na_2S_2O_3$ solution to remove iodine. The organic phase was dried over $MgSO_4$ and evaporated to give the crude product as a brown oil. Flash column chromatography on silica gel (2 g, eluted with petroleum ether / ethyl acetate 20:1 to 10:1) afforded dienone **26** (3.3 mg, 83%) as a colorless oil. This material was identical to compound **26** obtained from Swern oxidation of diol **25**.

(±)-1-Desoxyhypnophilin (2)[6]



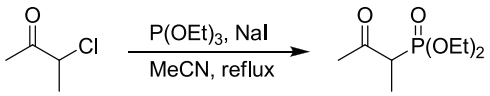
To a stirred solution of dienone **26** (10.5 mg, 0.0486 mmol) in THF (1.4 mL) and water (1.4 mL) at 0 °C was sequentially added $NaHCO_3$ (69 mg, 0.82 mmol) and H_2O_2 (30% aqueous solution, 0.14 mL, 1.2 mmol) and the reaction mixture was stirred at 0 °C for 5 h. The reaction mixture was extracted with ether and the combined extract was dried over $MgSO_4$. Evaporation of the solvent gave the crude product as a colorless oil. Flash column chromatography on silica gel (5 g, eluted with petroleum ether/ethyl acetate 20:1 to 10:1) afforded (±)-1-desoxyhypnophilin (8.2 mg, 73%) as a colorless oil and recovered dienone **26** (2.4 mg, 23%) as a colorless oil.

2: ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.92 (s, 3H), 1.12 (s, 3H), 1.16 (s, 3H), 1.17-1.26 (m, 1H), 1.48-1.56 (m, 2H), 1.80 (ddd, J = 1.4, 7.6, and 12.3 Hz, 1H), 1.99 (d, J = 8.7 Hz, 2H), 2.39 (dt, J = 11.5 and 9.2 Hz, 1H), 2.73 (tq, J = 8.6 and 11.1 Hz, 1H), 3.44 (s, 1H), 5.27 (s, 1H), 6.05 (s, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 17.5, 27.2, 28.9, 30.0, 39.1, 40.0, 42.5, 46.5, 49.5, 49.8, 61.0, 120.0, 153.2, 198.1. The spectroscopic data is identical to that reported.[6]

(6) Harrowven, D. C.; Lucas, M. C.; Howes, P. D. *Tetrahedron* **2001**, *57*, 9157.

2.4 Preparation of the HWE Reagents Used in the Synthesis

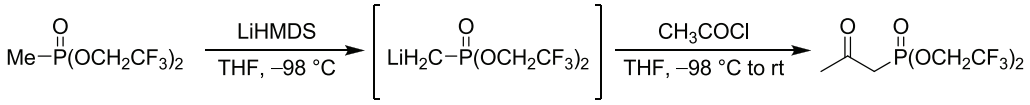
Diethyl 3-oxobutan-2-ylphosphonate (reagent for Horner-Wadsworth-Emmons reaction)



To a stirred suspension of anhydrous NaI (7.51 g, 50.0 mmol) in anhydrous MeCN (40 mL) was added 3-chloro-2-butanone (5.70 g, 53.5 mmol) dropwise at room temperature. The reaction mixture was brought to reflux under argon, and triethyl phosphite (9.47 g, 57.0 mmol) was added dropwise. After 8 h, the reaction mixture was cooled to toom temperature, filtered through a thin pad of silica gel, and concentrated to give a brown oil. Distillation under reduced pressure produced crude diethyl 3-oxobutan-2-ylphosphonate (6.44 g, 58%) as a light yellow oil, b.p. 118–132 °C/0.5 kPa. Redistillation under reduced pressure afforded a colorless oil (3.80 g), b.p. 128-134 °C/0.5 kPa, which was used in the HWE reaction to synthesize **S6g**.

Bis(2,2,2-trifluoroethyl) 3-oxobutan-2-ylphosphonate (Still-Jin reagent for *Z*-selective HWE reaction)[7]

I. Bis(2,2,2-trifluoroethyl) 2-oxopropylphosphonate

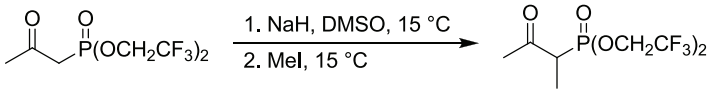


An oven-dried, 500 mL round-bottom flask was charged with 86 mL of *n*-butyllithium solution (1.6 M in hexane, 138 mmol, 2.5 equiv.) and cooled to –20 °C. A solution of 1,1,1,3,3,3-hexamethyldisilazane (26.70 g, 165 mmol, 3.0 equiv.) in THF (50 mL) was added dropwise over 10 min and the resulting mixture was stirred at –20 °C for 20 min. The solution was cooled to –98 °C in a liquid-nitrogen/methanol bath and a fine white suspension formed. A solution of bis(2,2,2-trifluoroethyl) methylphosphonate (14.32 g, 55.1 mmol, 1 equiv.) in THF (60 mL) was added dropwise over 30 min and the reaction mixture was stirred at –98 °C for an additional 15 min. Subsequently, a solution of acetyl chloride (5.24 g, 66.8 mmol, 1.2 equiv.) in THF (50 mL) was added dropwise over 20 min, during which time the reaction mixture became clear. The resulting yellow solution was stirred at low temperature for 1 h with the bath temperature changed from –98 °C to –78 °C. The reaction mixture was slowly acidified with hydrochloride acid (80 mL, 2 M) at low temperature. The cold bath was removed and the reaction mixture was allowed to warm to ambient temperature. The organic phase was separated and the water layer was extracted with methylene chloride (3 × 50 mL). The combined organic phase was dried over sodium sulfate and concentrated to give the crude product as a yellow oil. Flash column chromatography (150 g of silica gel, eluted with petroleum ether/ethyl acetate 3:1) afforded 8.91 g (54%) of bis(2,2,2-trifluoroethyl) 2-oxopropylphosphonate as a pale yellow oil.

Spectroscopic data: ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.33 (d, J = 0.9 Hz, 3H), 3.31 (d, J = 21.6 Hz, 2H), 4.45 (dq, J = 8.1 and 8.1 Hz, 4H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 31.5 (d, J = 4.8 Hz), 42.1 (d, J = 62.2 Hz), 62.3 (dq, J = 5.7 and 38.3 Hz), 122.4 (dq, J = 8.4 and 277 Hz), 198.6 (d, J = 6.6 Hz).

(7) The initially reported synthesis refers to Yu, W.; Jin, Z. *Tetrahedron Lett.* **1999**, *40*, 6725. We thank Prof. Jin for sharing their original synthetic procedure.

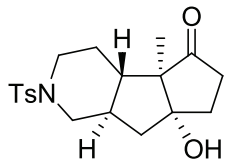
II. Bis(2,2,2-trifluoroethyl) 3-oxobutan-2-ylphosphonate



To a stirred solution of bis(2,2,2-trifluoroethyl) 2-oxopropylphosphonate (6.60 g, 21.9 mmol) in anhydrous DMSO (35 mL) was slowly added NaH (586 mg, 24.4 mmol, washed with pentane prior to use) at 15 °C. After 15 min, methyl iodide (3.41 g, 24.0 mmol) was added dropwise and the resulting mixture was stirred overnight. The reaction mixture was poured into water and extracted with methylene chloride. The combined organic extract was washed with water and brine, dried over Na_2SO_4, and concentrated to give a yellow oil. Flash column chromatography on silica gel (150 g, eluted with petroleum/ethyl acetate 3:1 to 1:1) afforded bis(2,2,2-trifluoroethyl) 3-oxobutan-2-ylphosphonate (3.44 g, 50%, ca. 80% purity by GC) as a light yellow oil, together with the recovered bis(2,2,2-trifluoroethyl) 2-oxopropylphosphonate (0.94 g, 14%) as a light yellow oil. The dimethylation product is the major impurity in the final product and this product is used in *Z*-selective HWE reaction without further purification.

Spectroscopic data: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.45 (dd, J = 7.2 and 19.5 Hz, 3H), 2.34 (s, 3H), 3.38 (dq, J = 6.9 and 23.7 Hz, 1H), 4.43 (dq, J = 8.1 and 8.1 Hz, 4H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 10.9 (d, J = 6.6 Hz), 30.1 (d, J = 2.4 Hz), 46.8 (d, J = 134 Hz), 62.3 (dq, J = 6.0 and 38.4 Hz), 62.5 (dq, J = 6.0 and 37.7 Hz), 122.4 (dq, J = 8.4 and 278 Hz), 202.5 (d, J = 4.8 Hz).

3. X-Ray Structure of Tricyclic Cycloadduct 15f



CCDC 674958

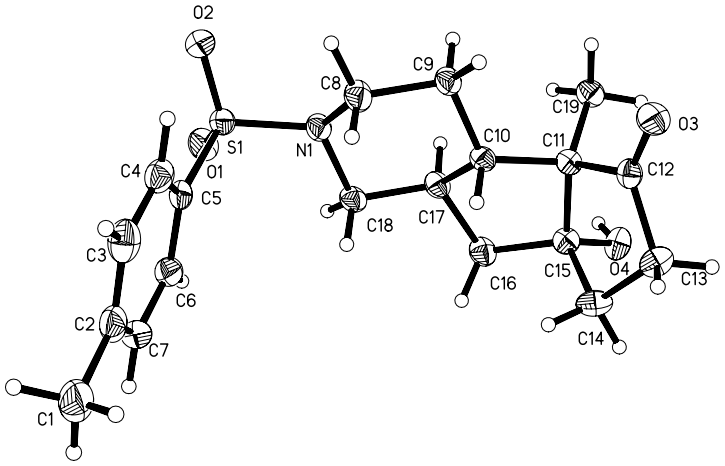
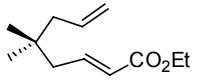


Table S2. Crystal Data and Structure Refinement for **15f**[a]

Identification code	2296
Empirical formula	$C_{19}H_{25}NO_4S$
Formula weight	363.46
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system, space group	triclinic, P-1
Unit cell dimensions	a = 6.3978(13) Å α = 83.29(3) deg
	b = 8.4177(17) Å β = 84.99(3) deg
	c = 17.485(4) Å γ = 70.12(3) deg
Volume	878.3(3) $Å^3$
Z, Calculated density	2, 1.374×10^6 g/m^3
Absorption coefficient	0.209 mm^{-1}
F(000)	388
Crystal size	0.27 × 0.18 × 0.08 mm
Theta range for data collection	1.17 to 25.00 deg.
Limiting indices	$-7 \le h \le 7$, $-9 \le k \le 9$, $-20 \le l \le 20$
Reflections collected / unique	5583 / 3098 [R(int) = 0.0230]
Completeness to theta = 25.00	99.8 %
Max. and min. transmission	0.9835 and 0.9459
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3098 / 0 / 226
Goodness-of-fit on F^2	1.124
Final R indices [I>2sigma(I)]	R1 = 0.0505, wR2 = 0.1164
R indices (all data)	R1 = 0.0633, wR2 = 0.1221
Largest diff. peak and hole	0.387 and –0.315 e.$Å^{-3}$

[a] CCDC 674958 contains the supplementary crystallographic data for this structure. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

4. ^{1}H and ^{13}C-NMR Spectra for Synthetic Intermediates



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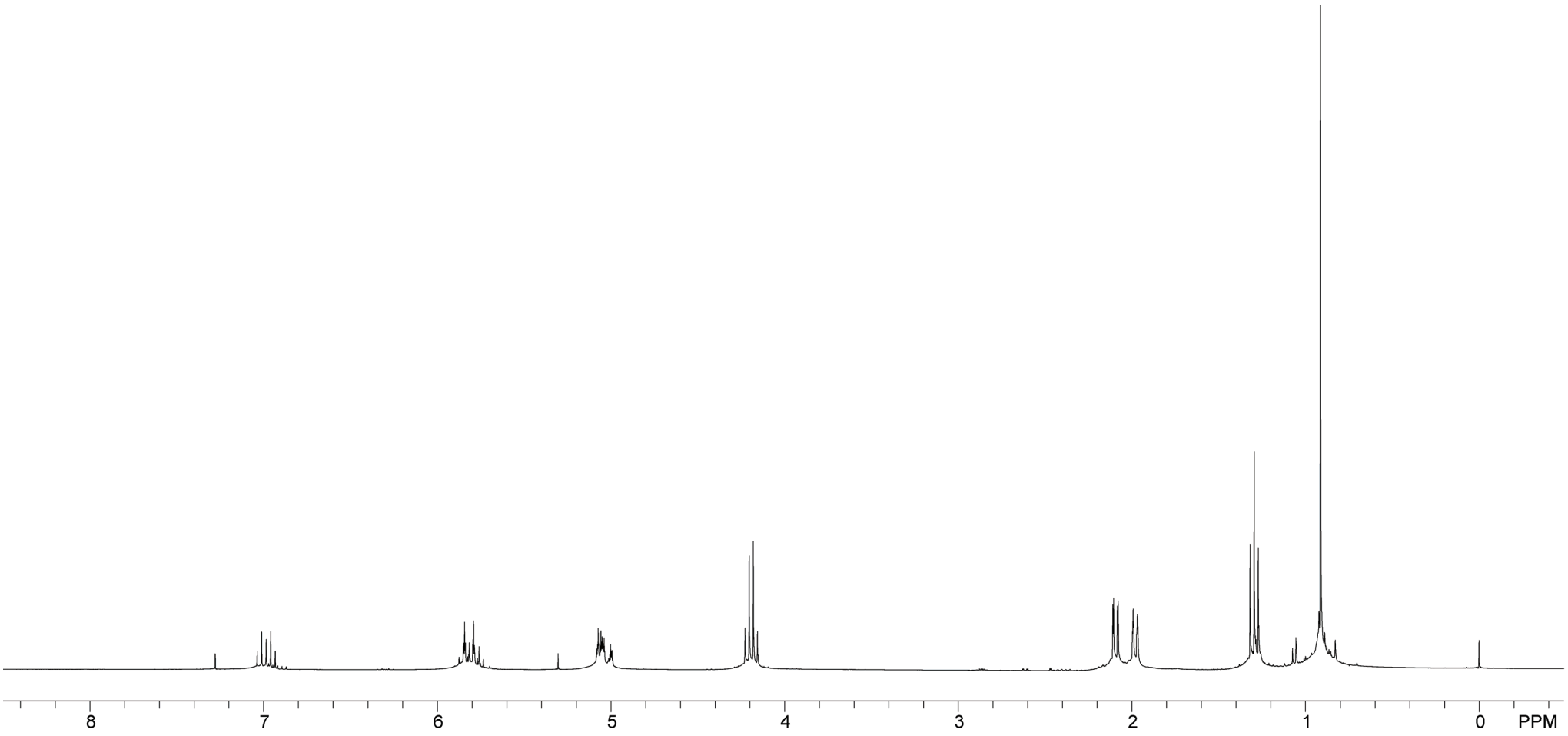

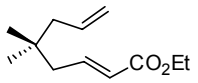

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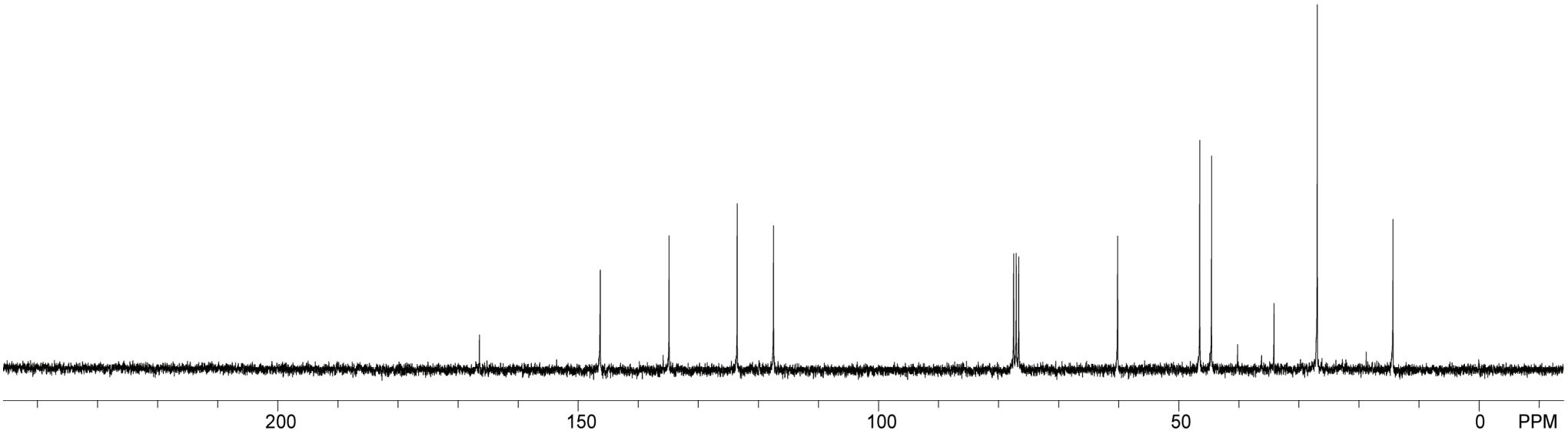

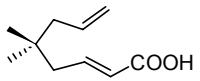

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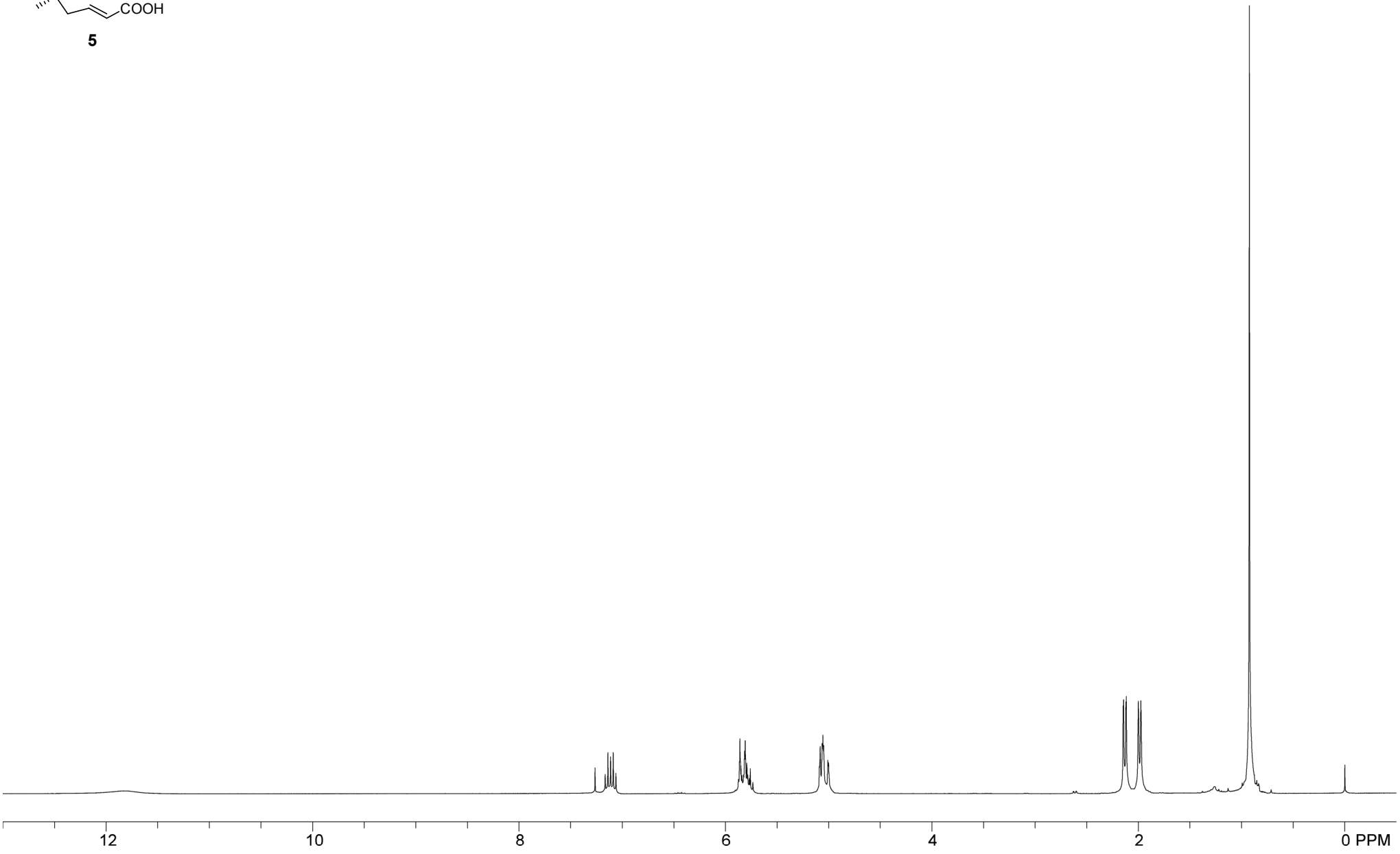

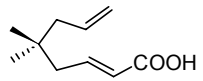

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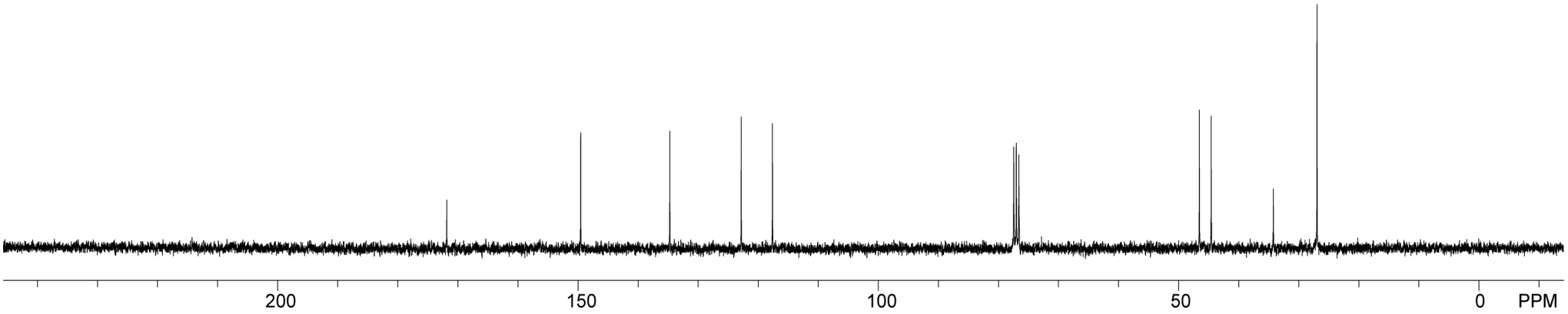

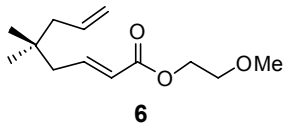

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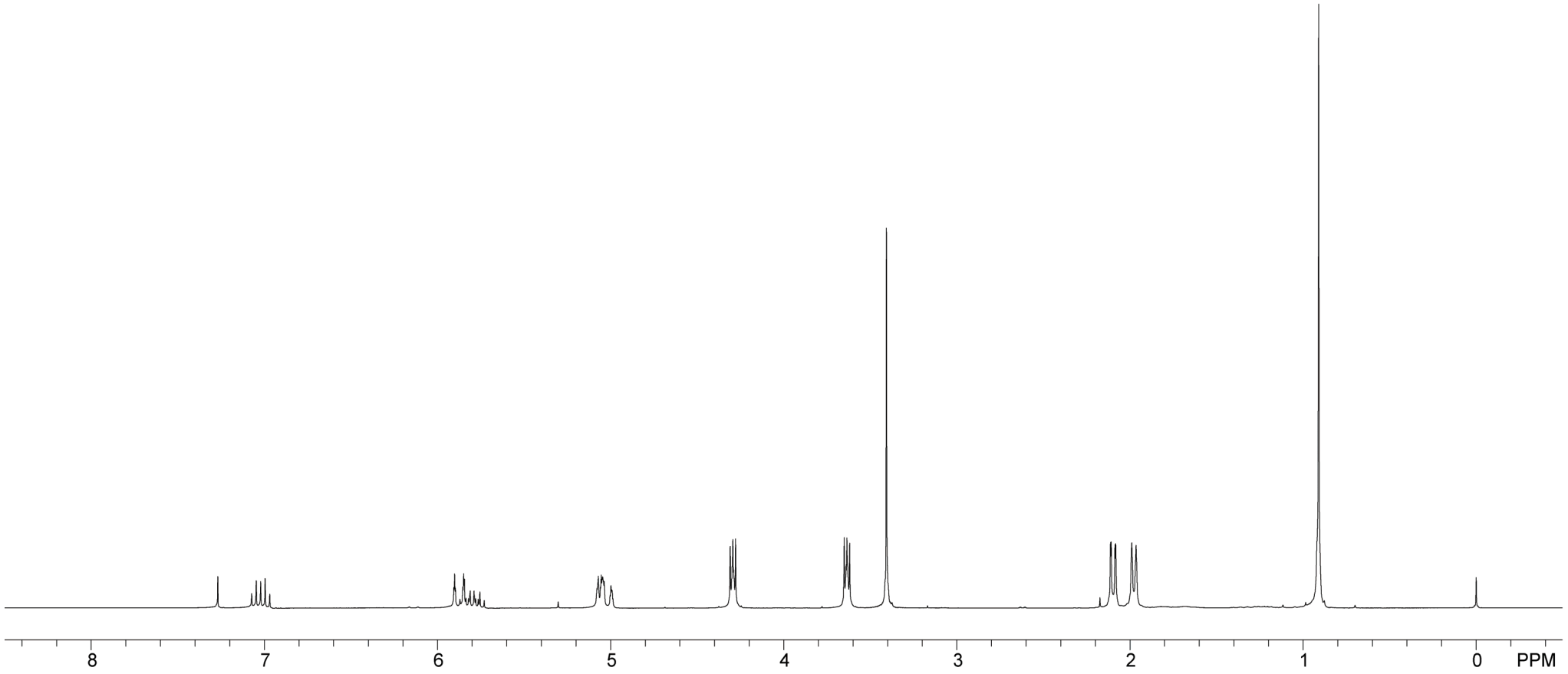

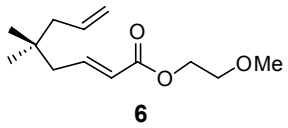

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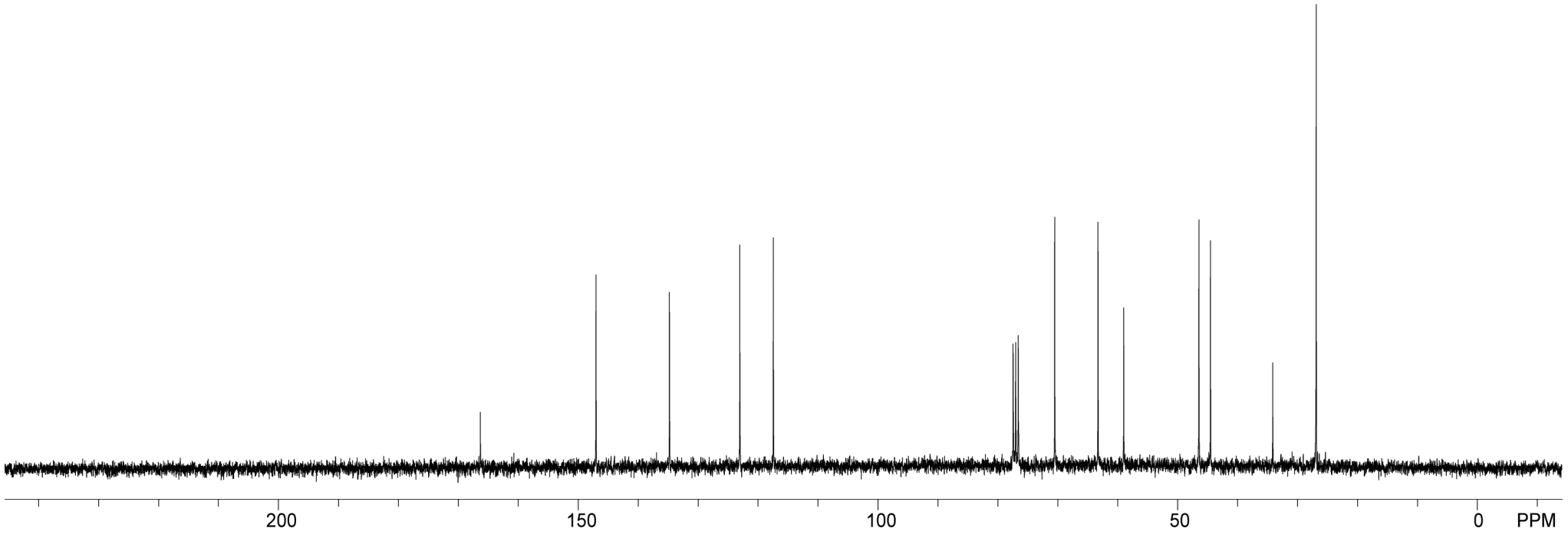

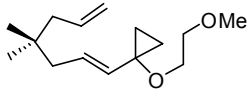

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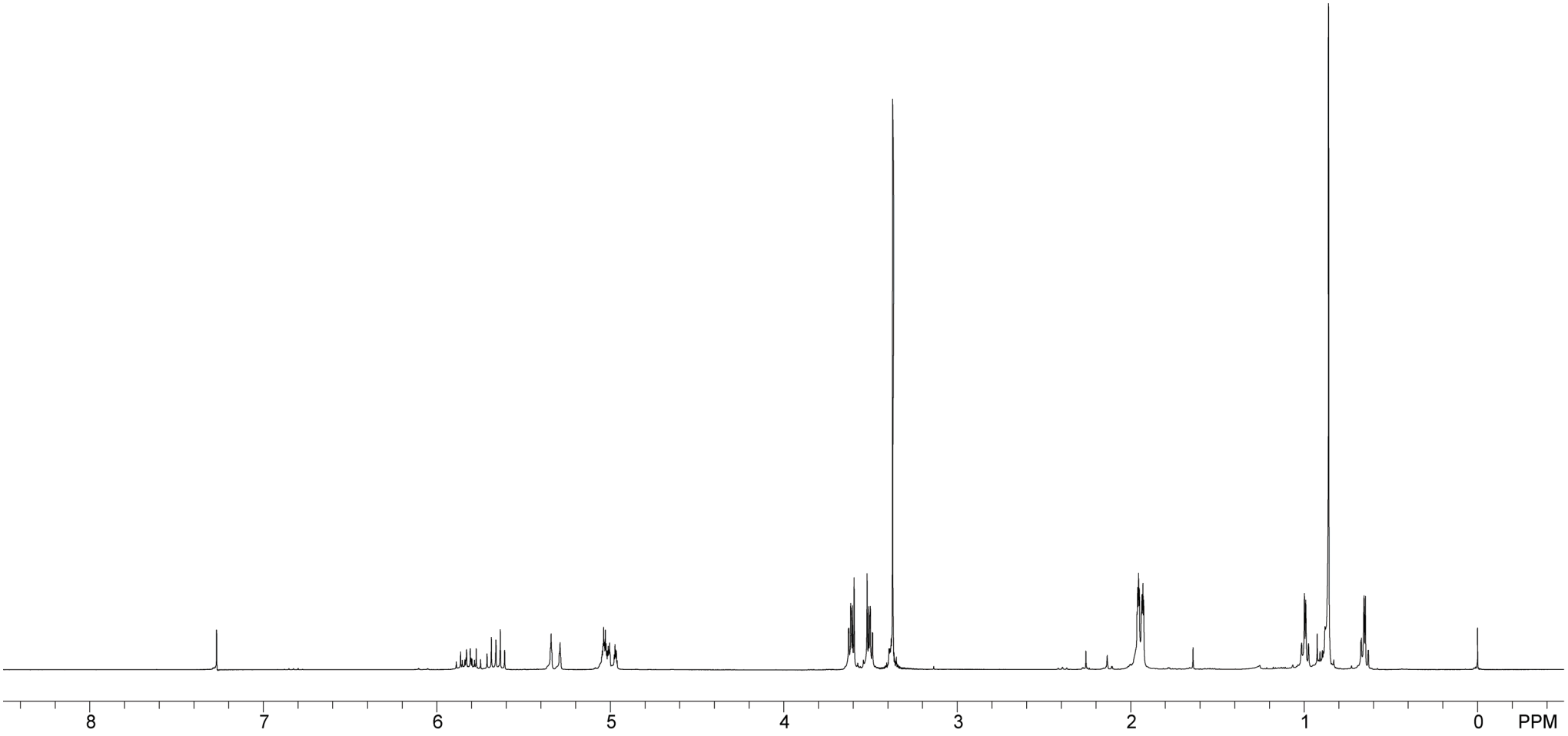

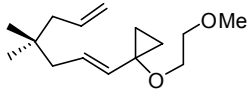

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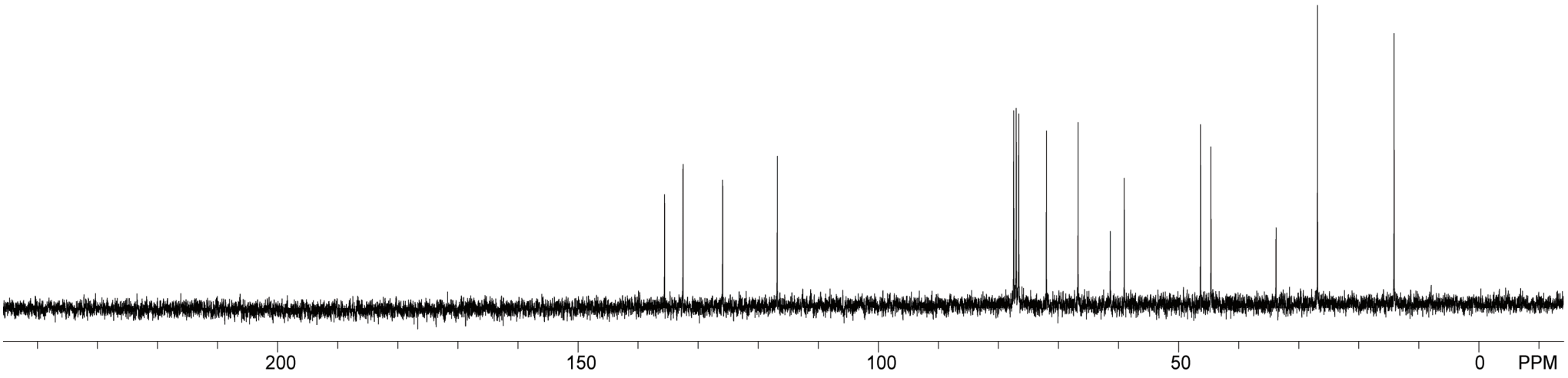

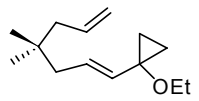

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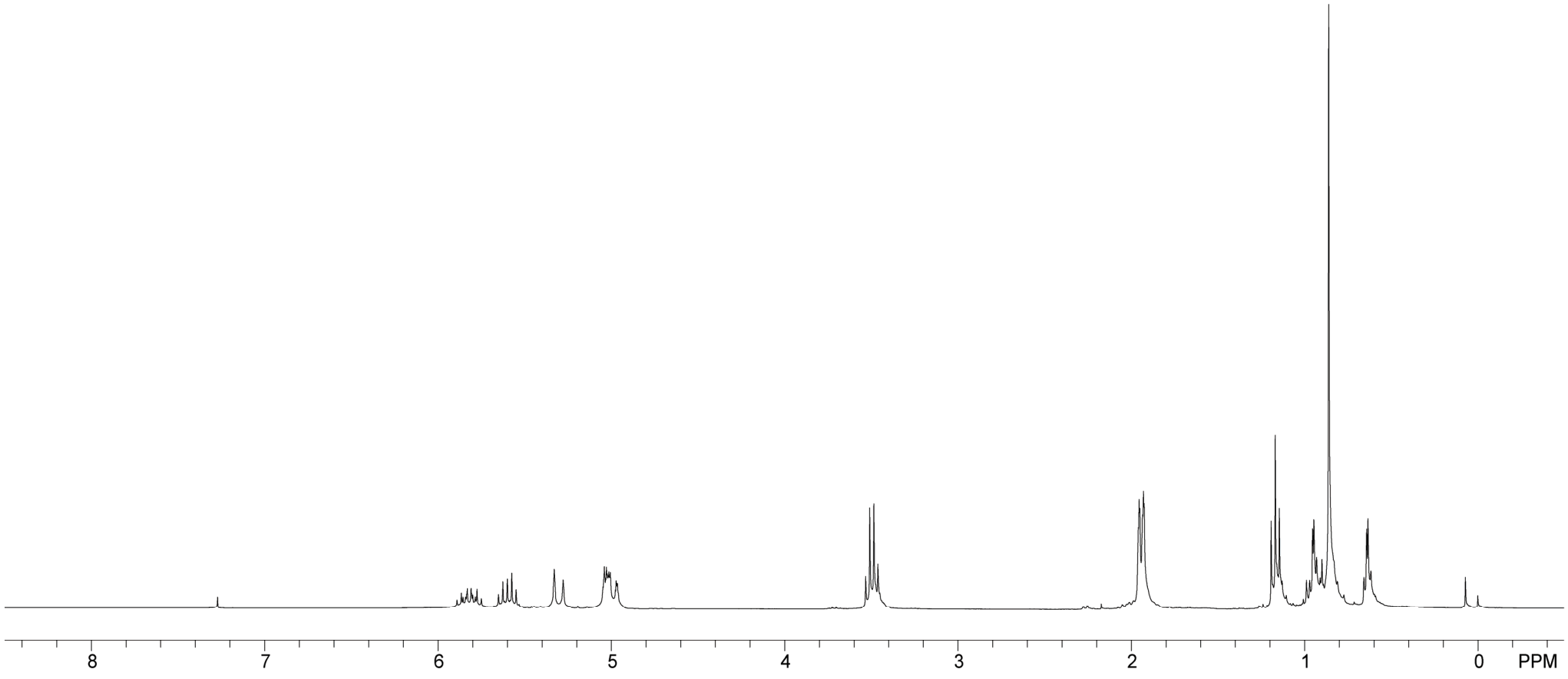

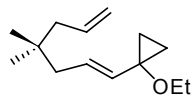

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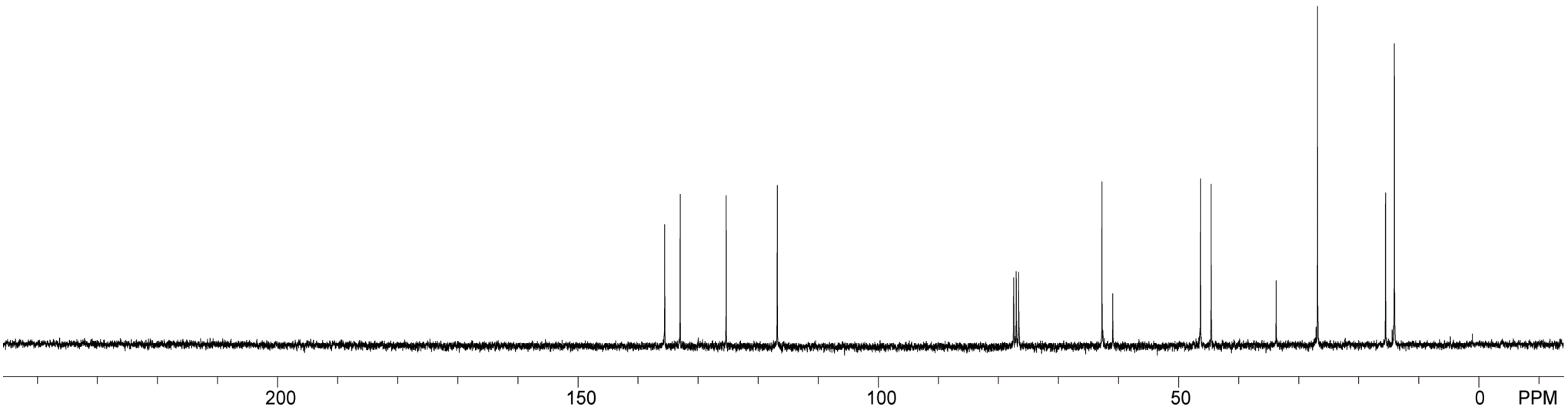

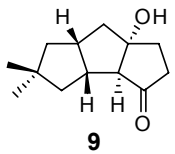

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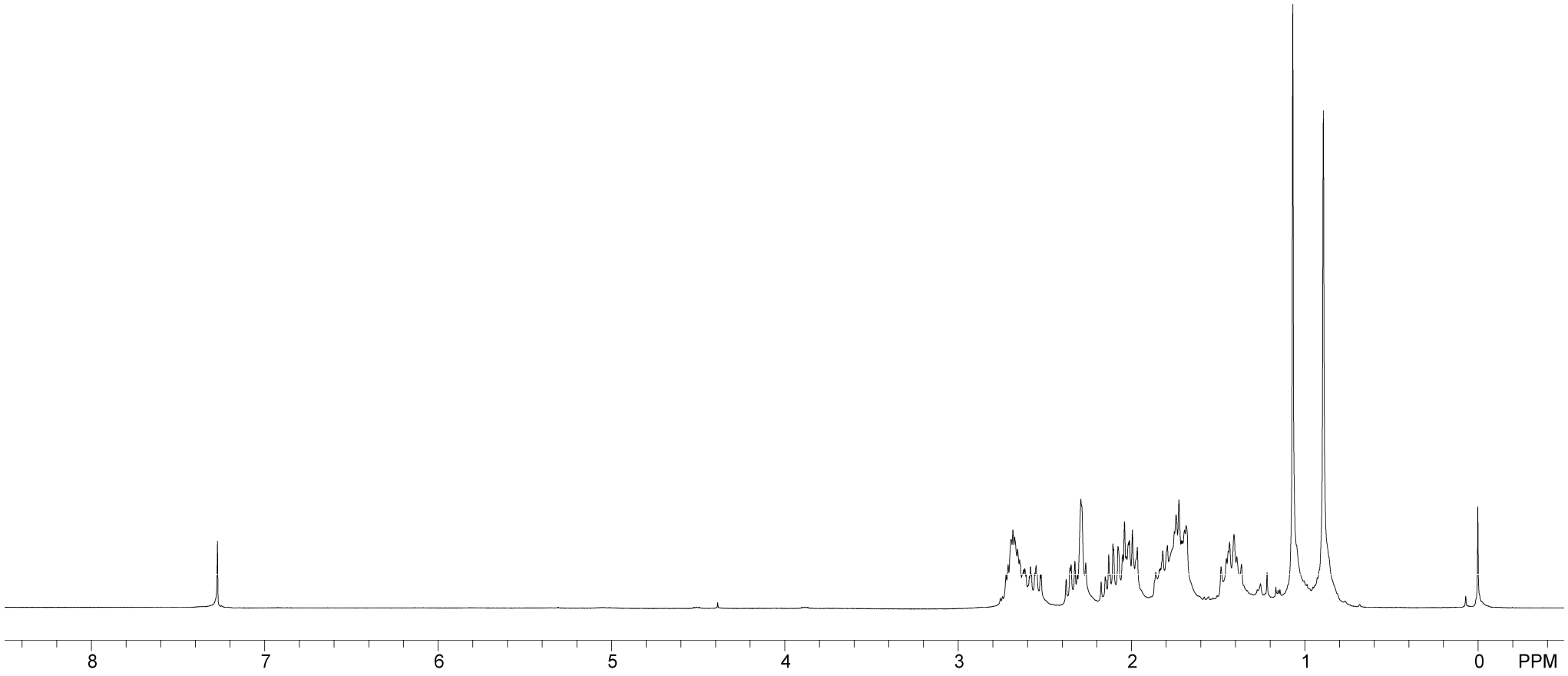

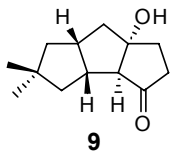

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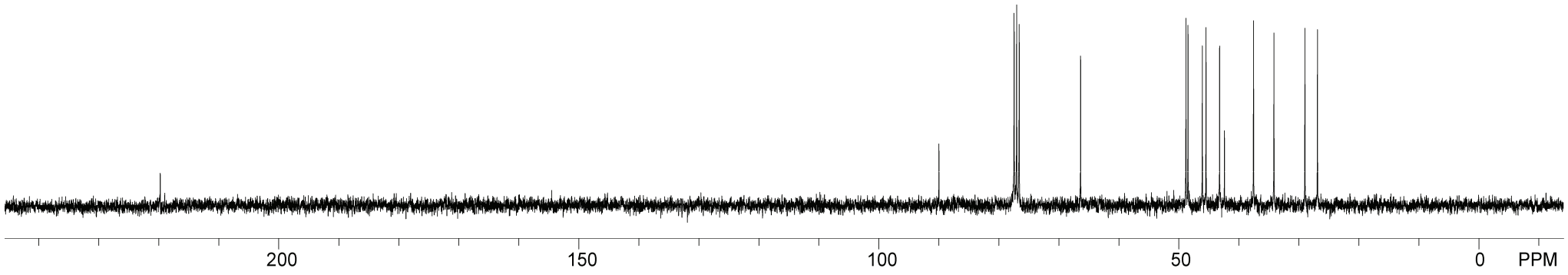

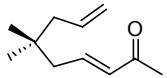

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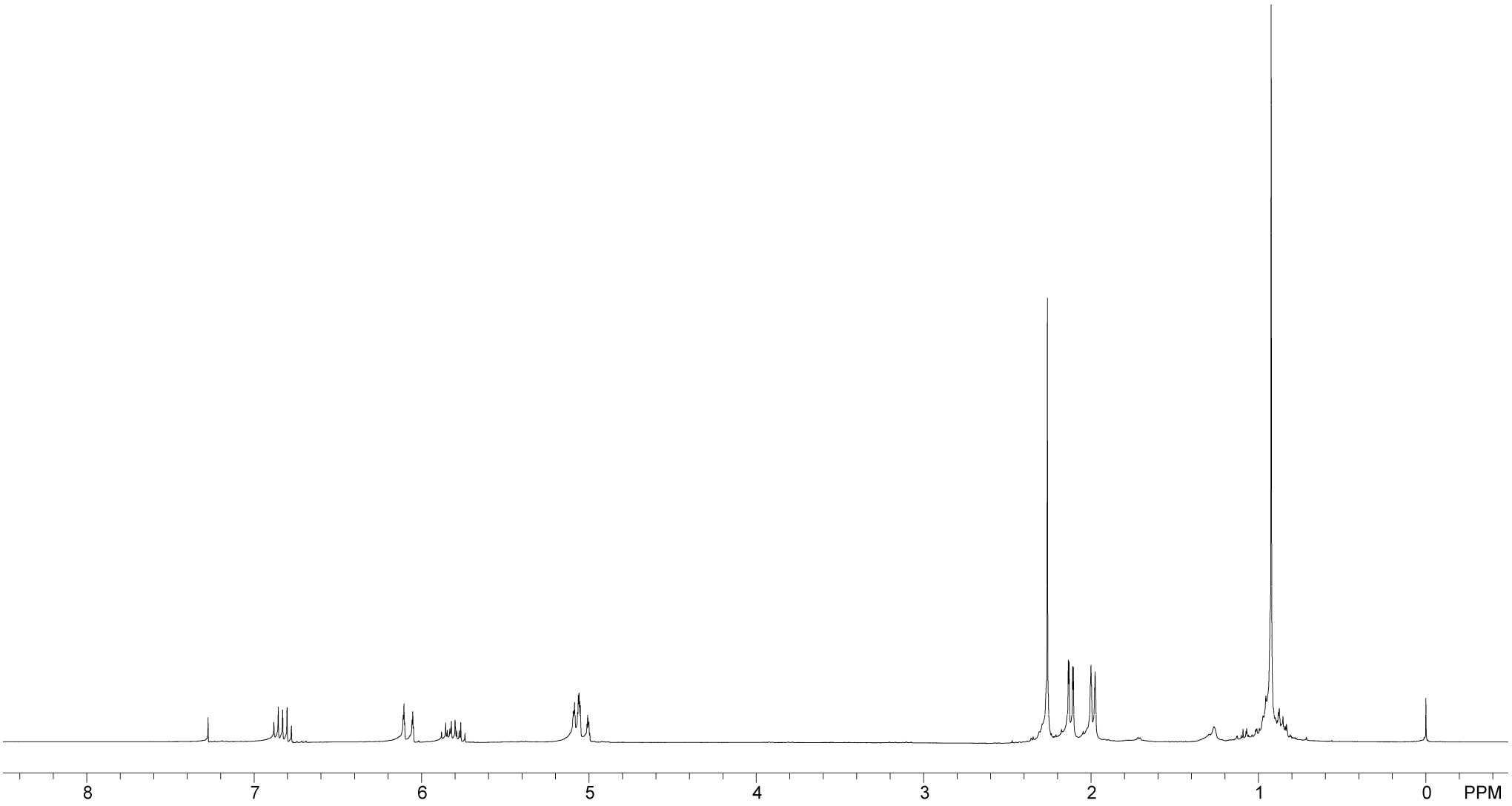

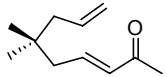

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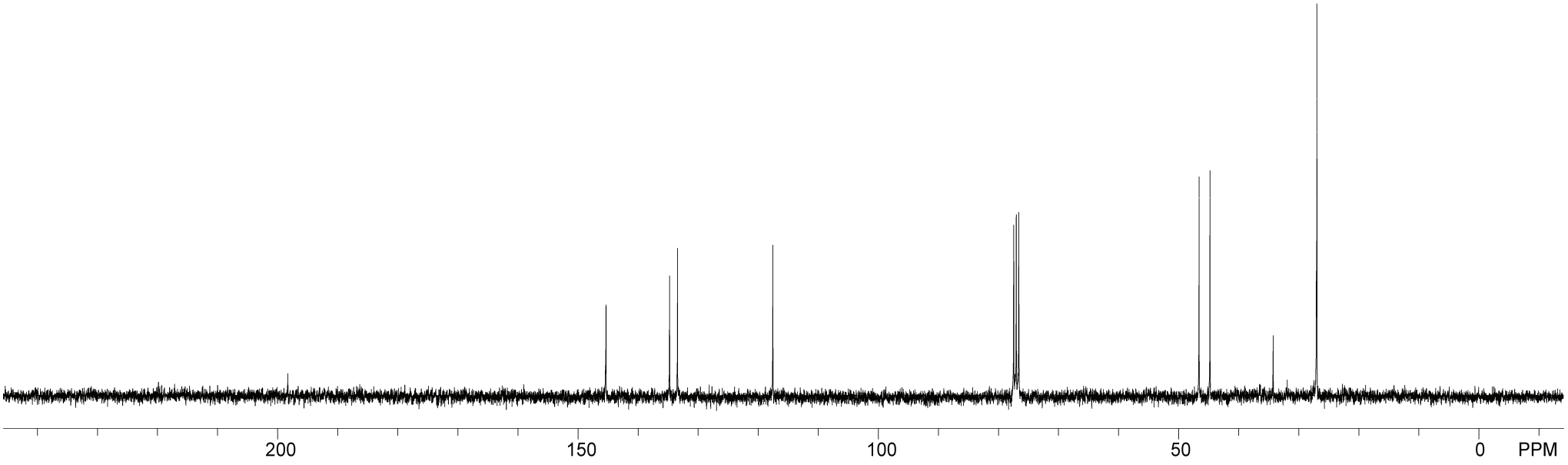

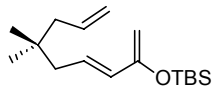

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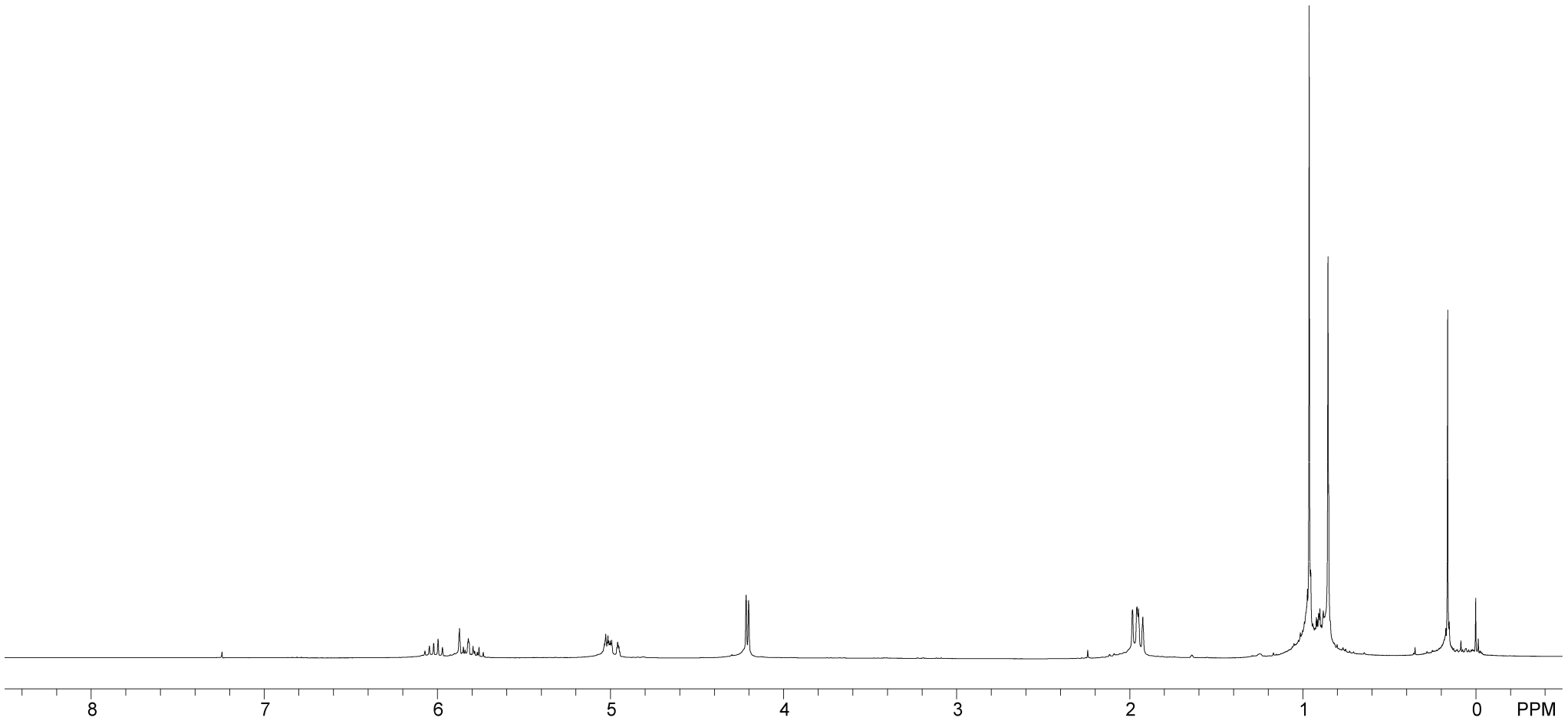

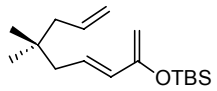

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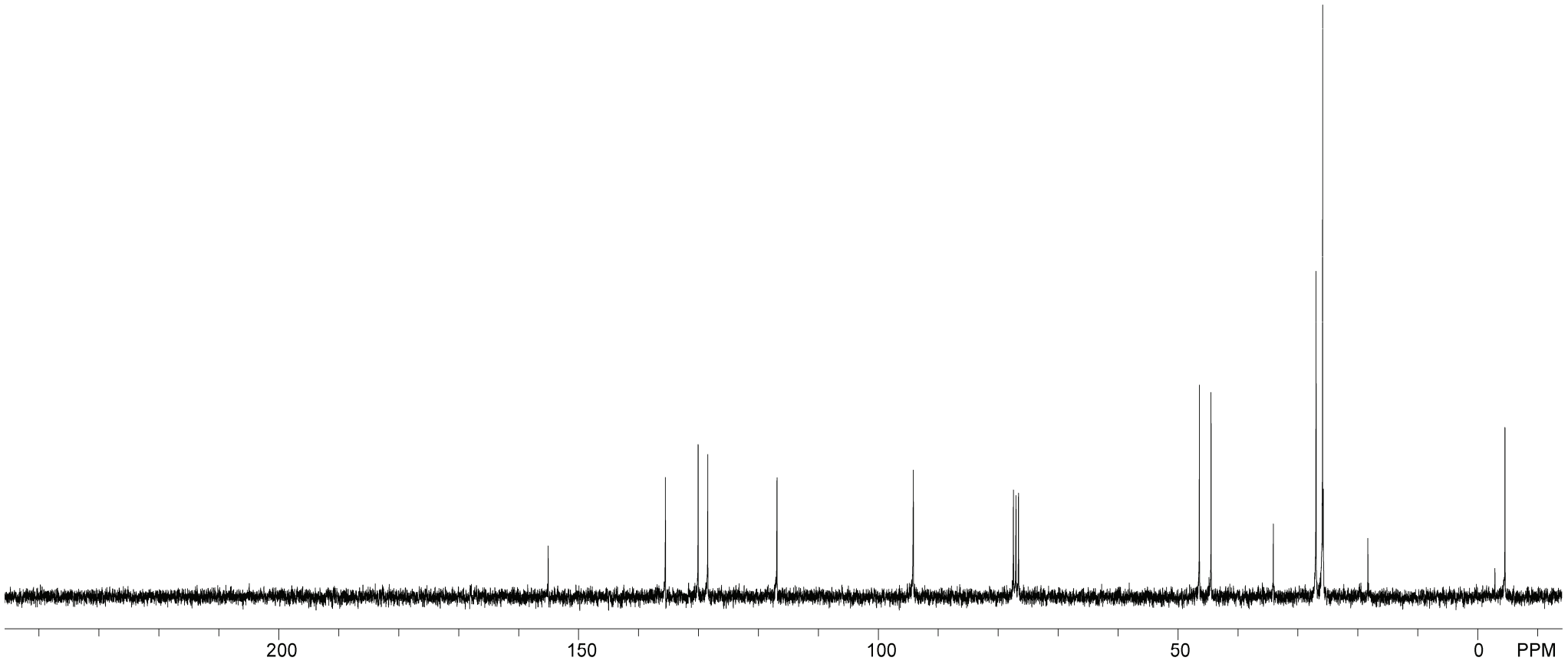

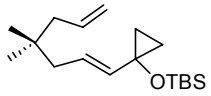

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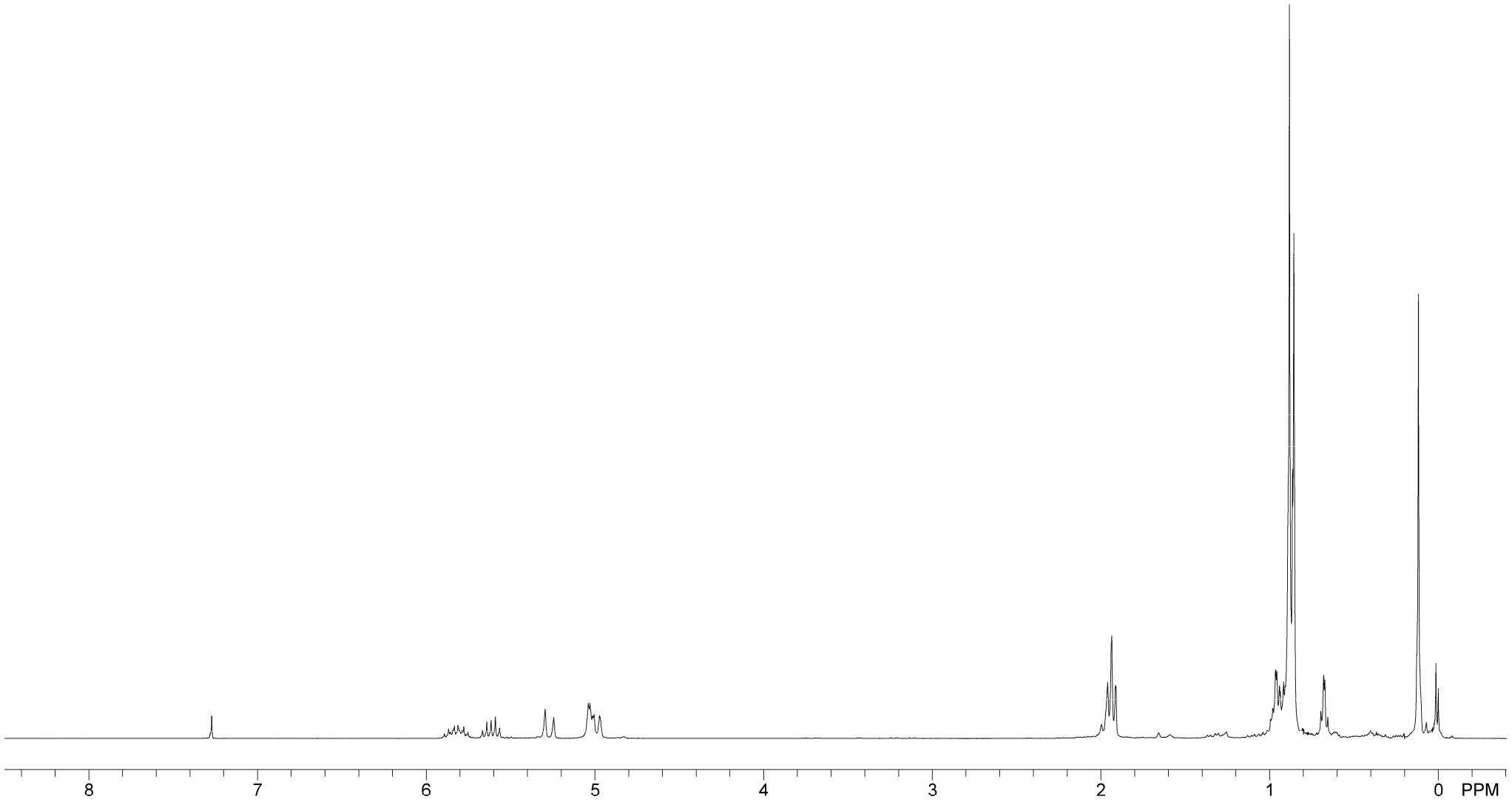

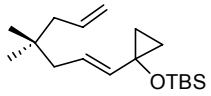

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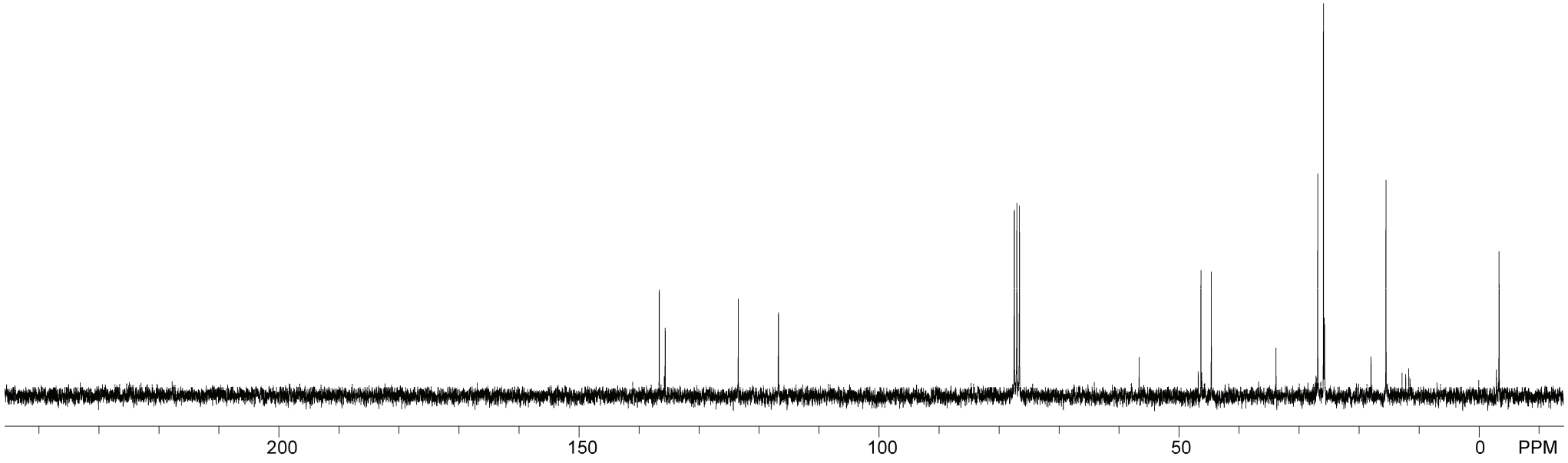

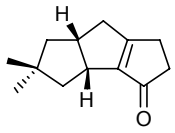

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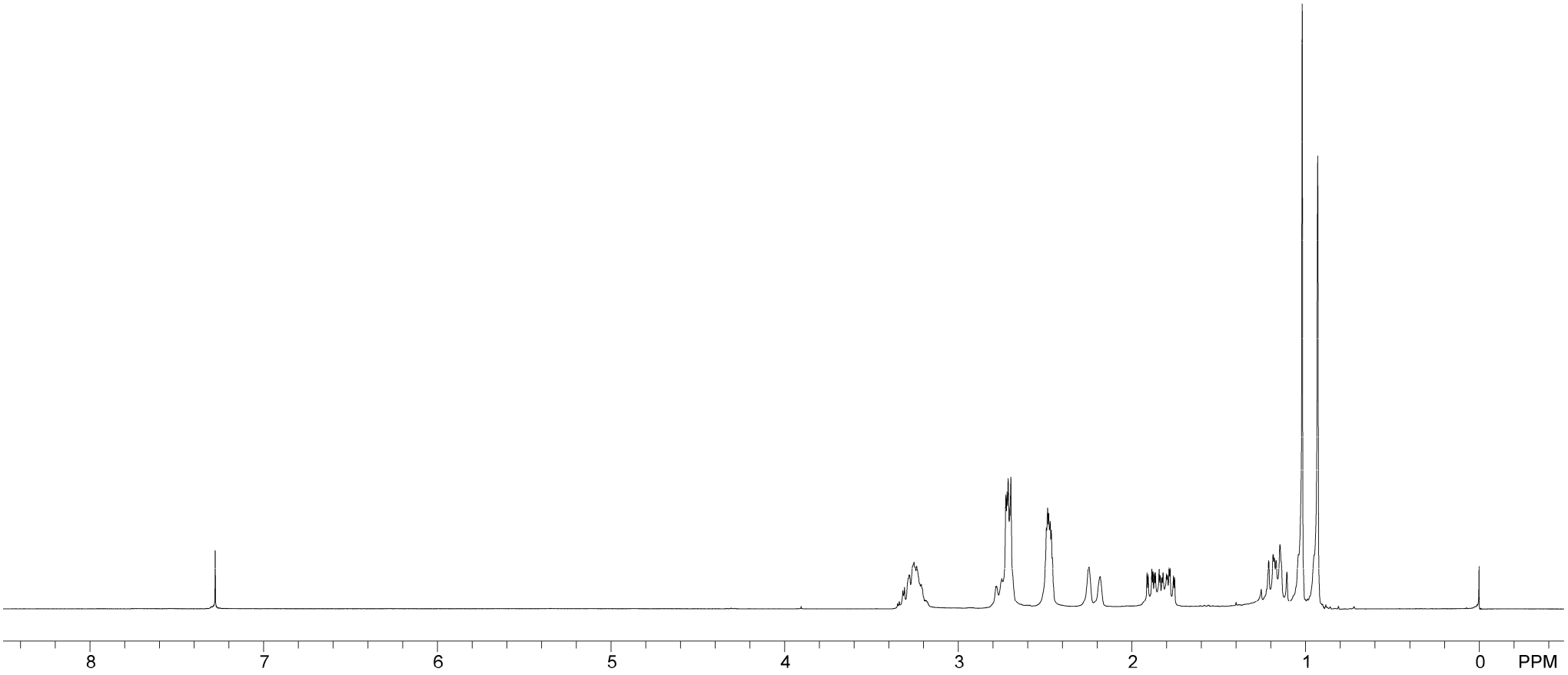

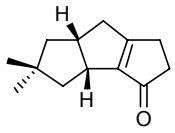

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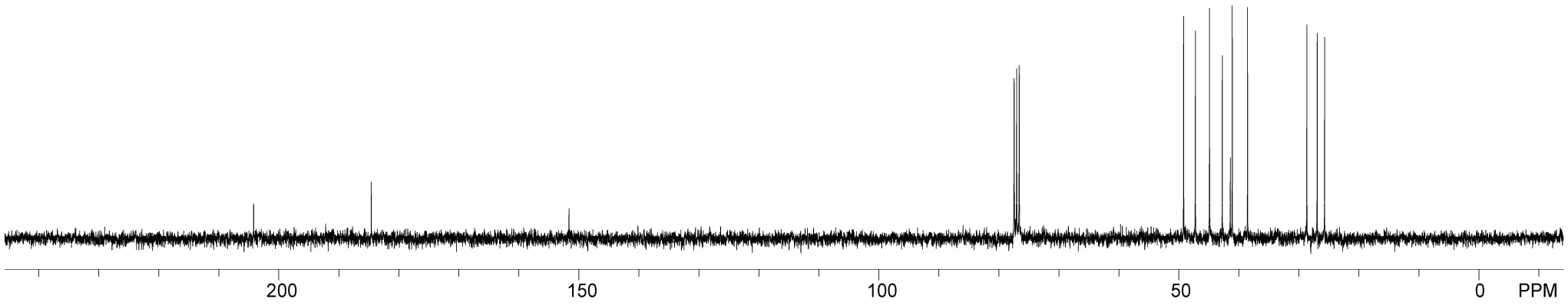

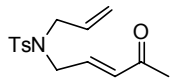

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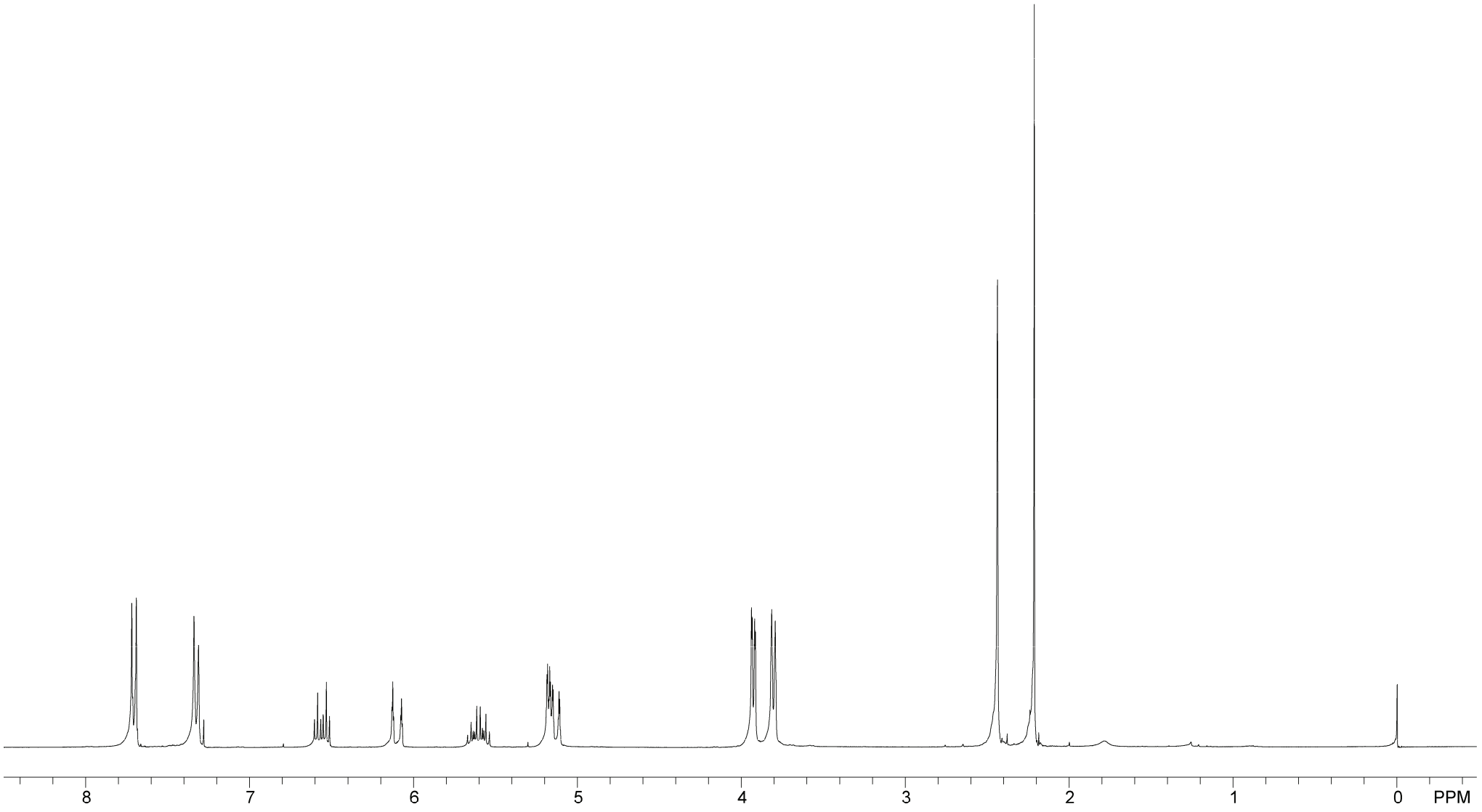

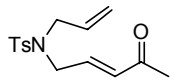

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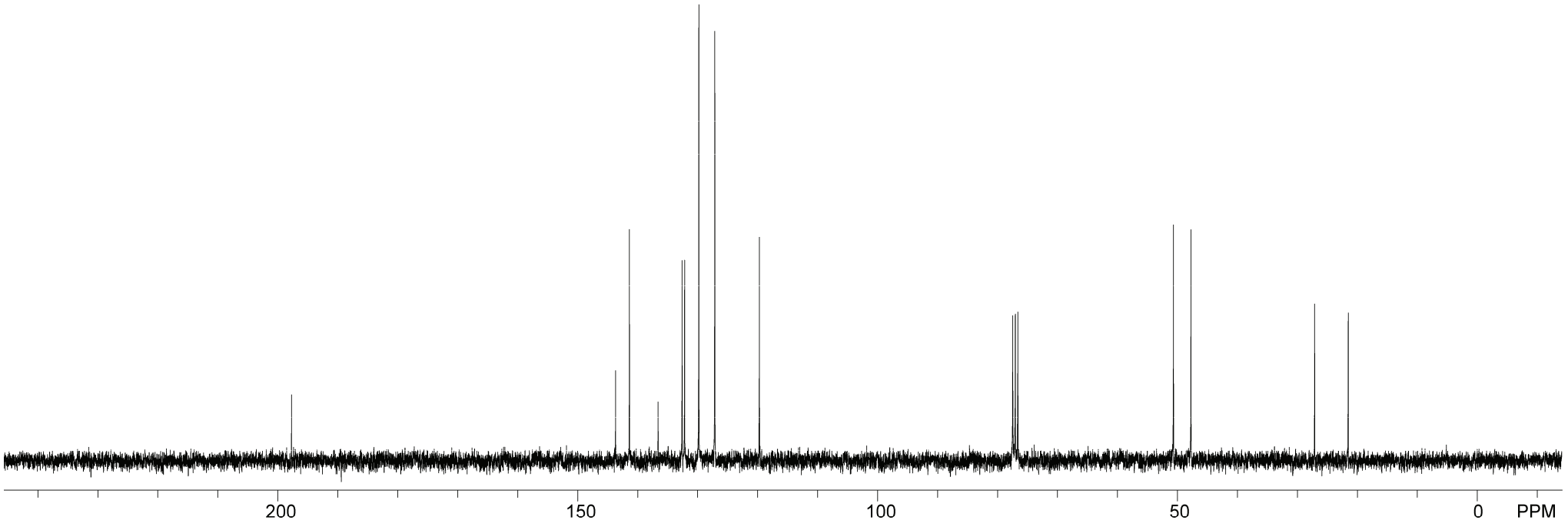

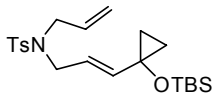

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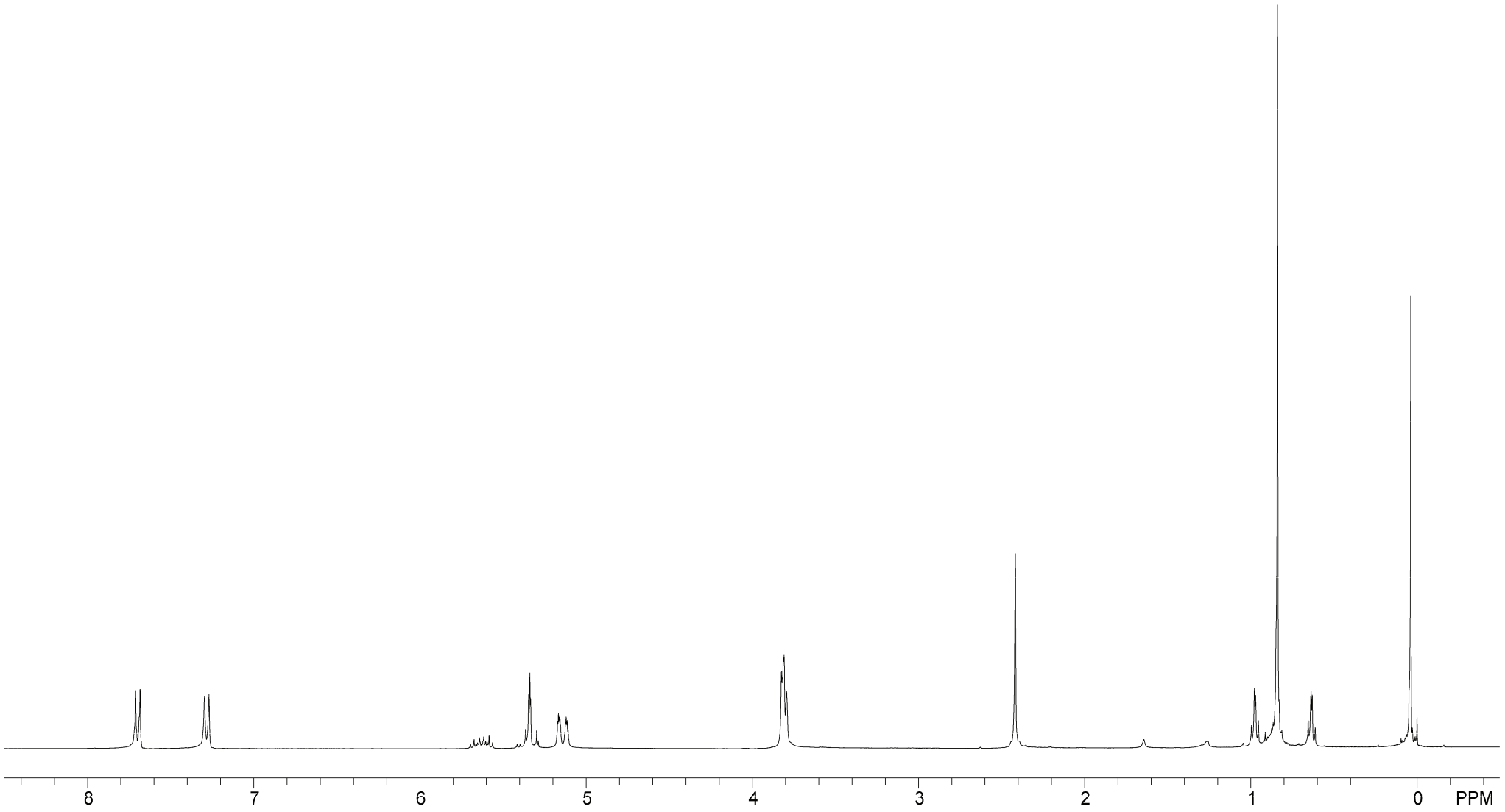

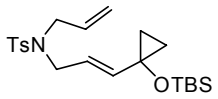

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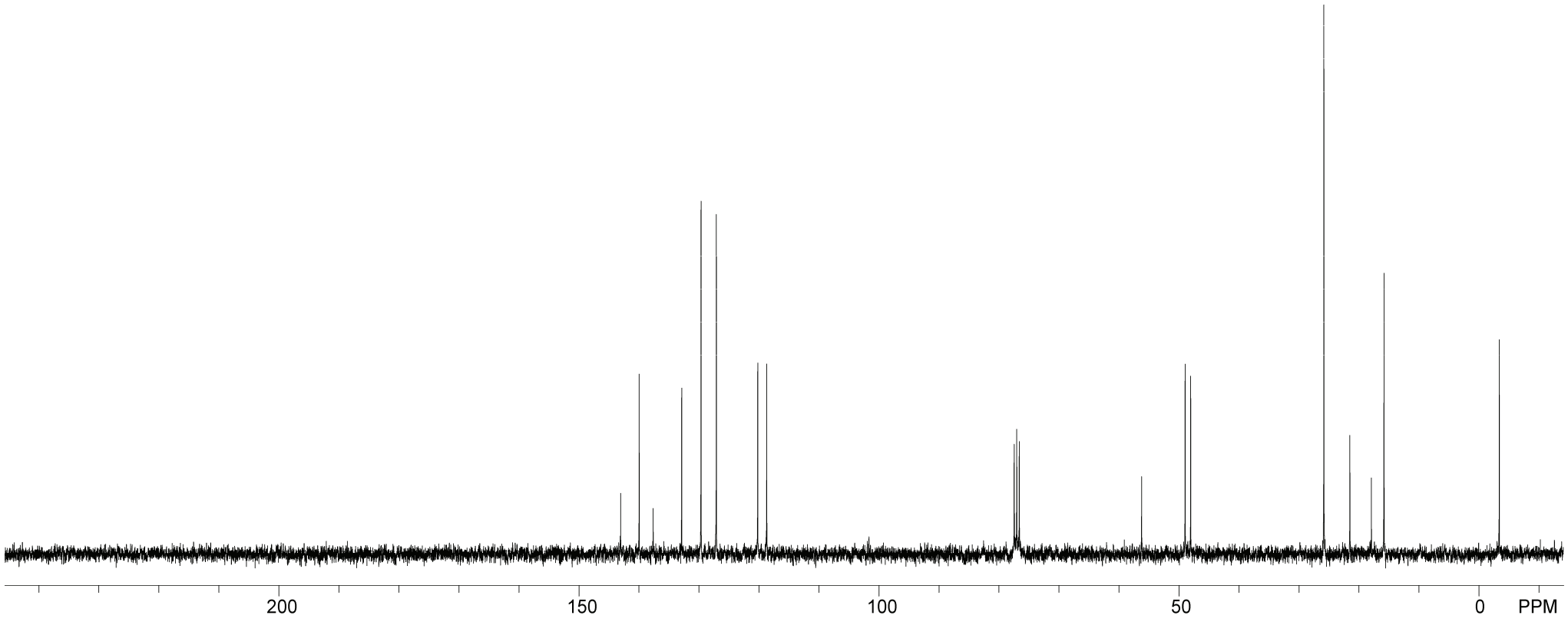

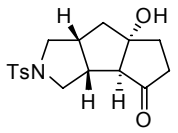

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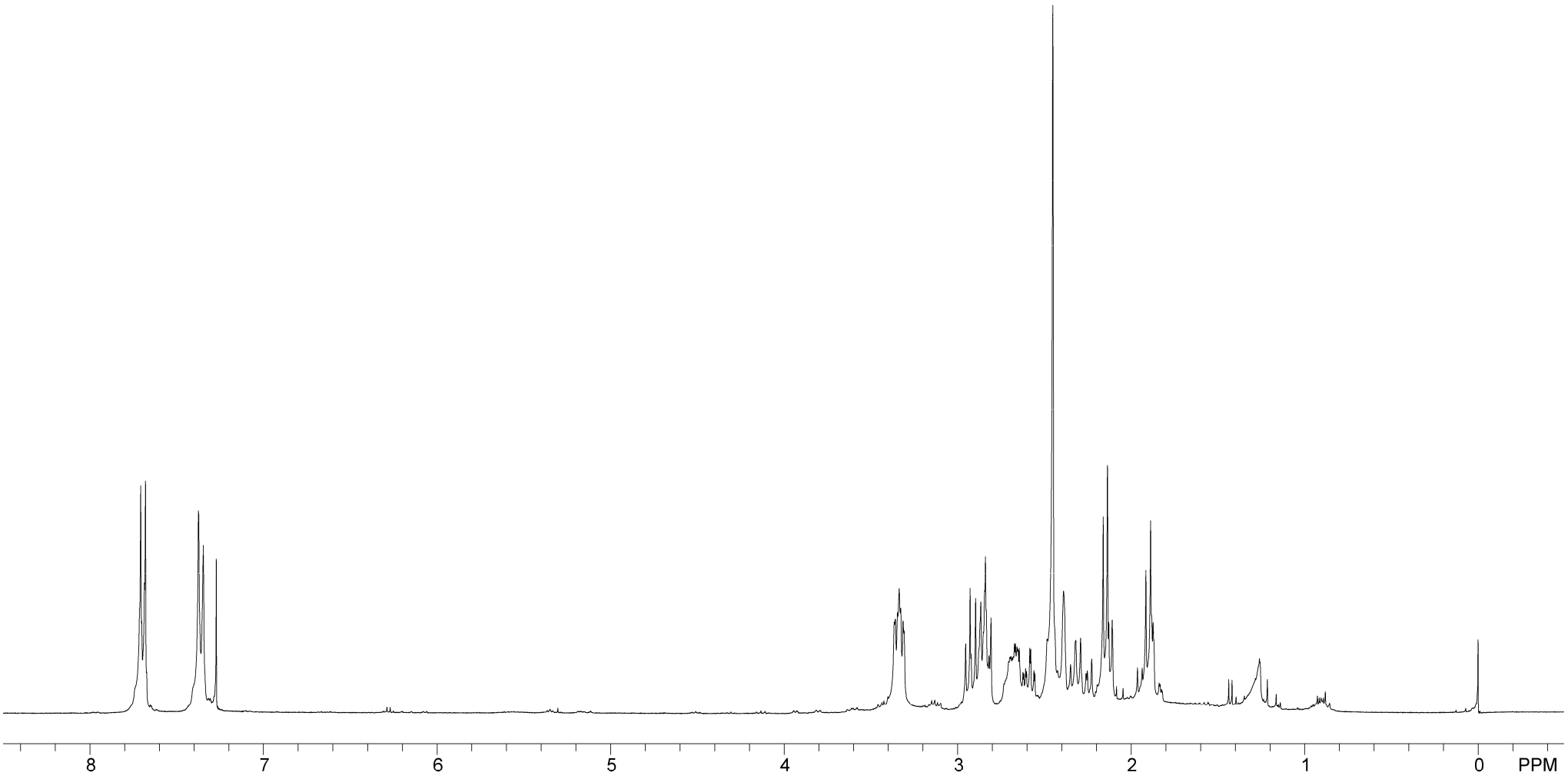

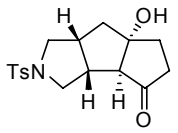

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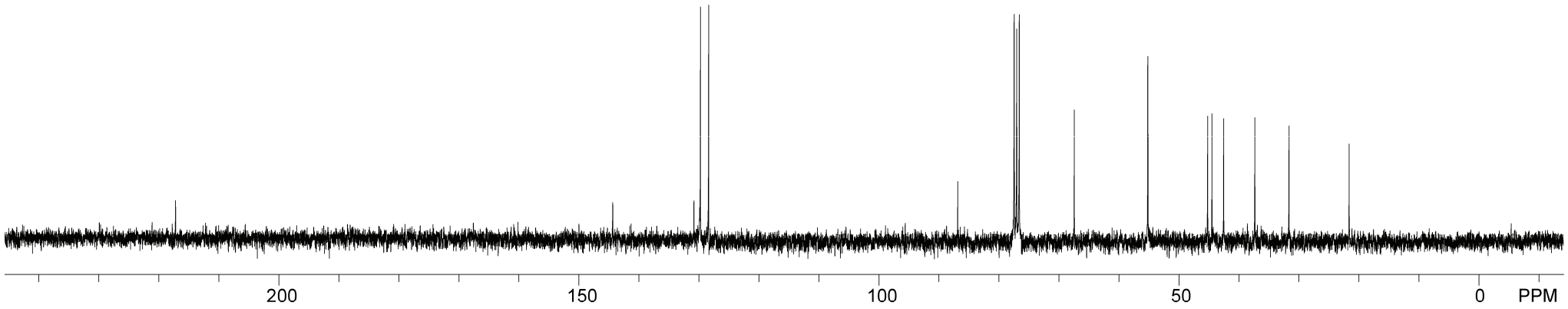

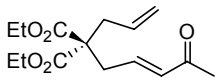

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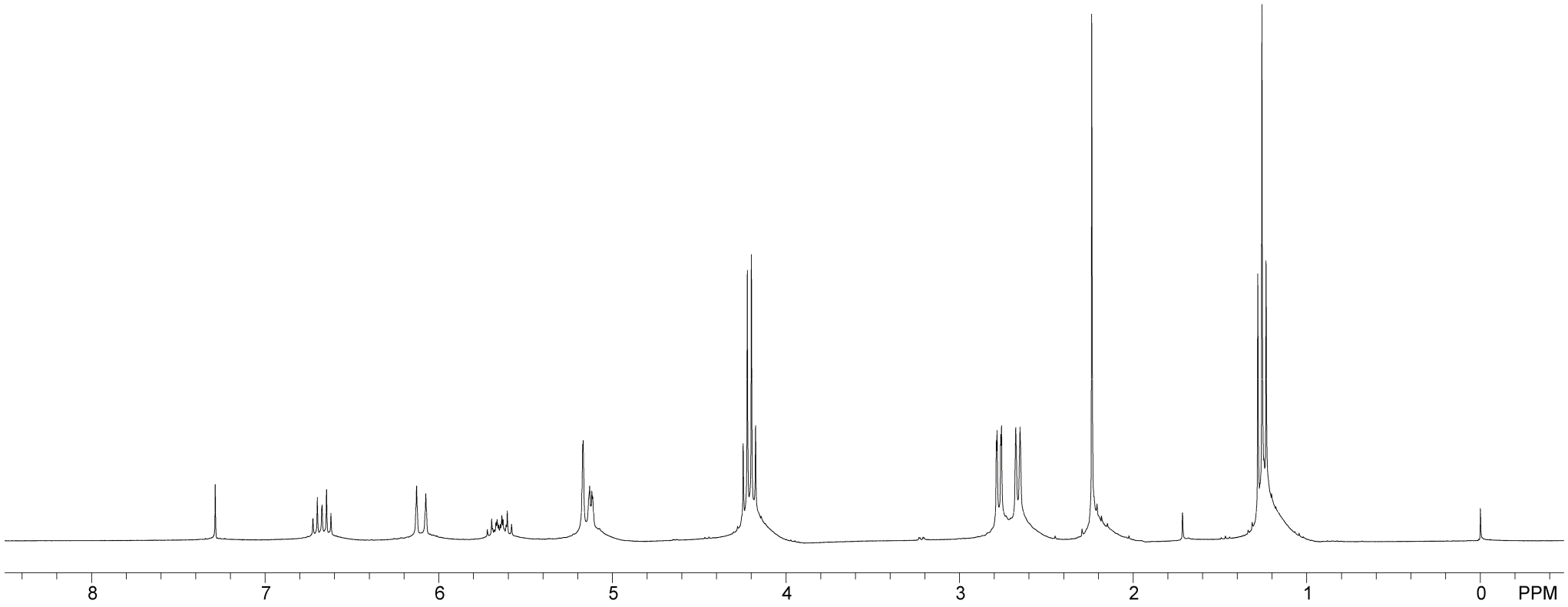

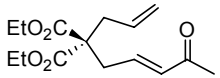

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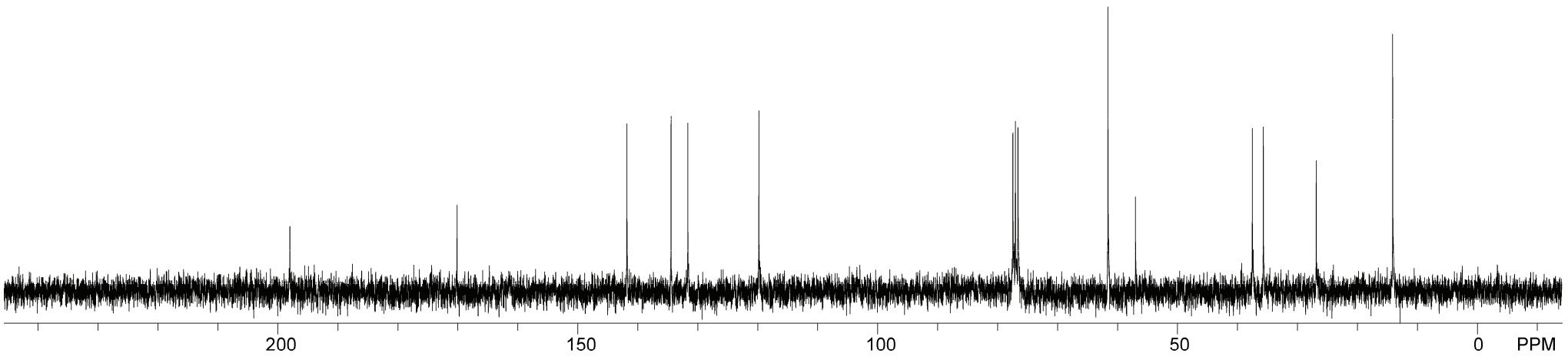

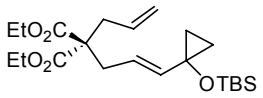

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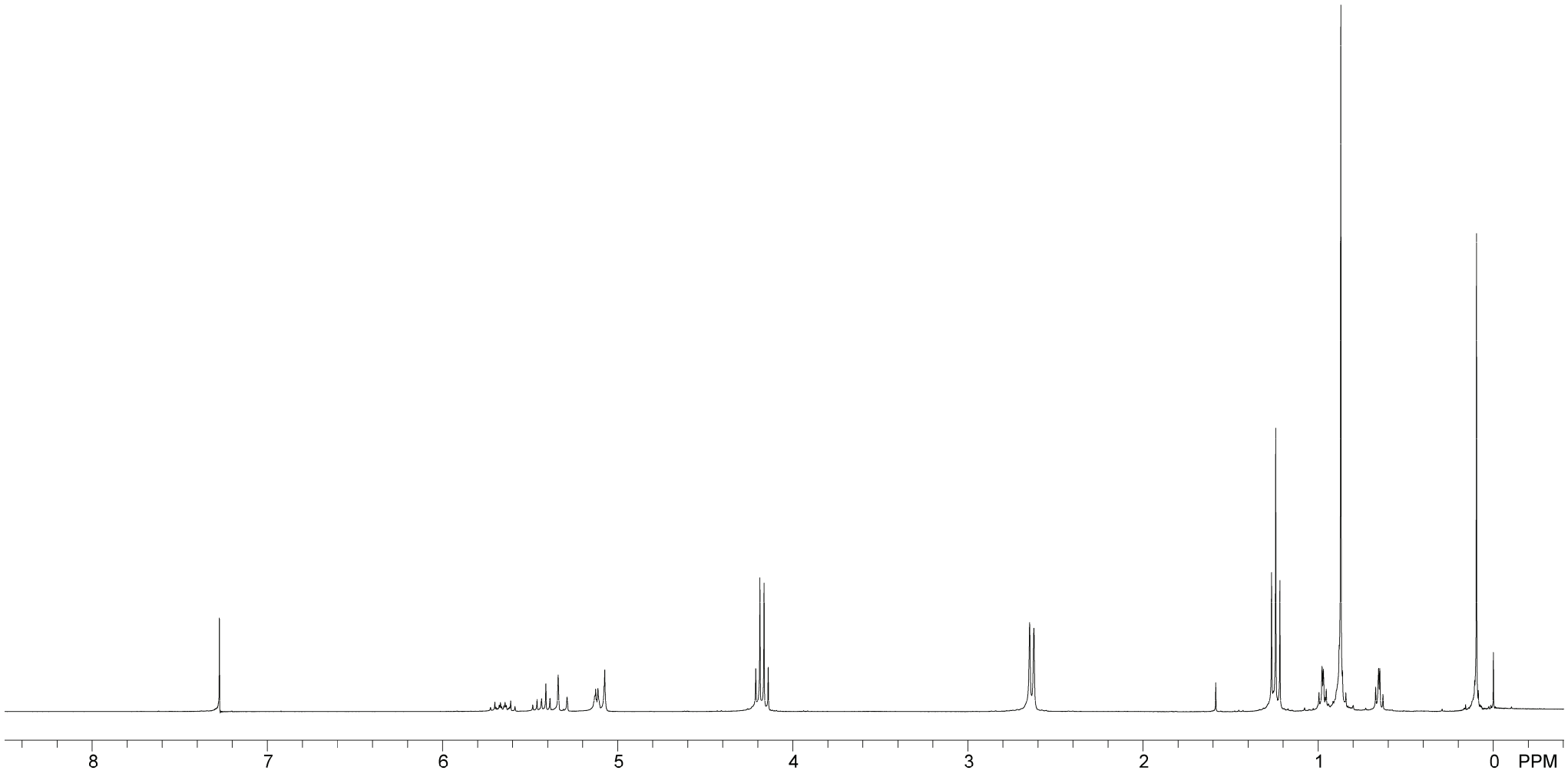

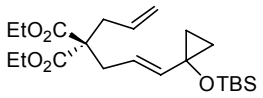

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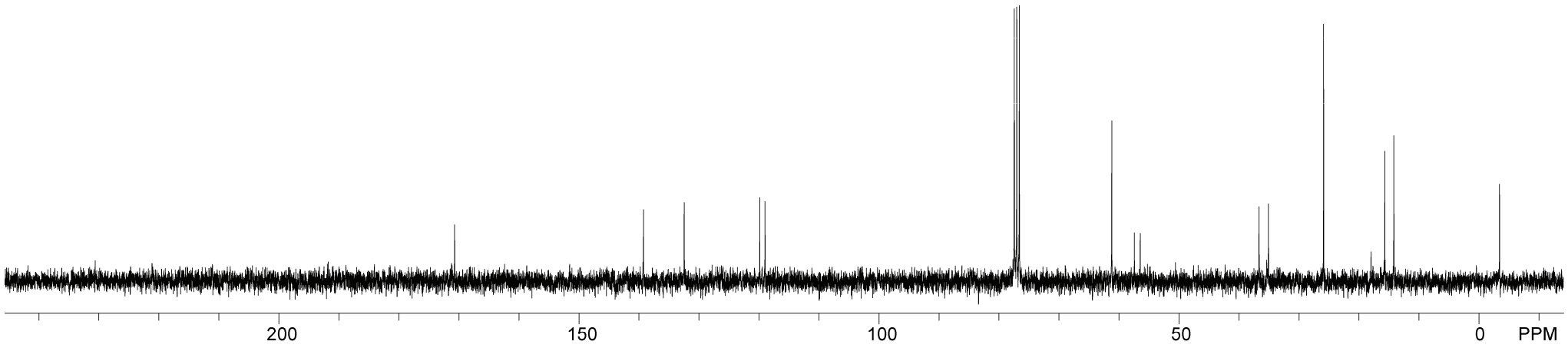

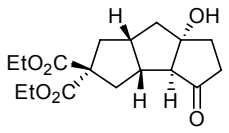

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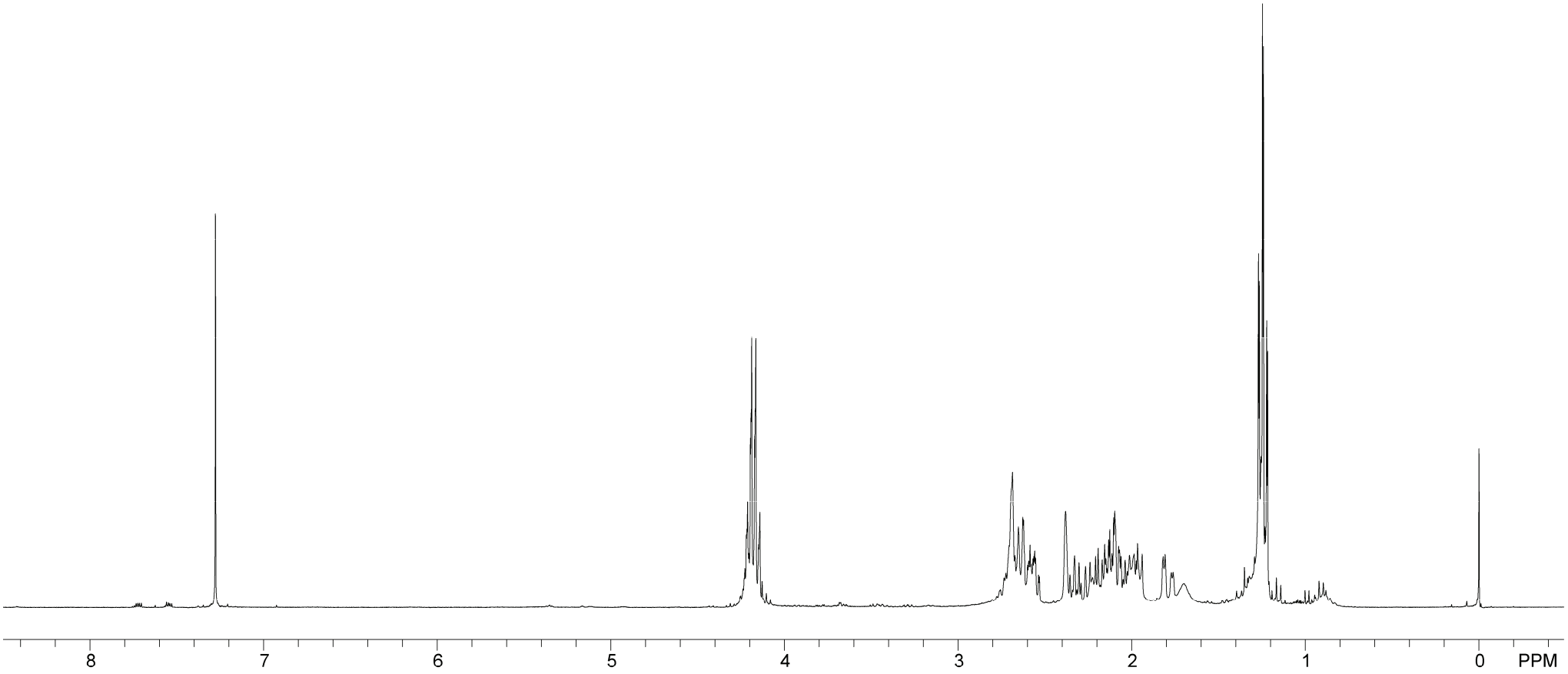

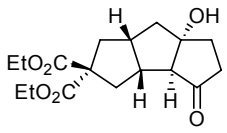

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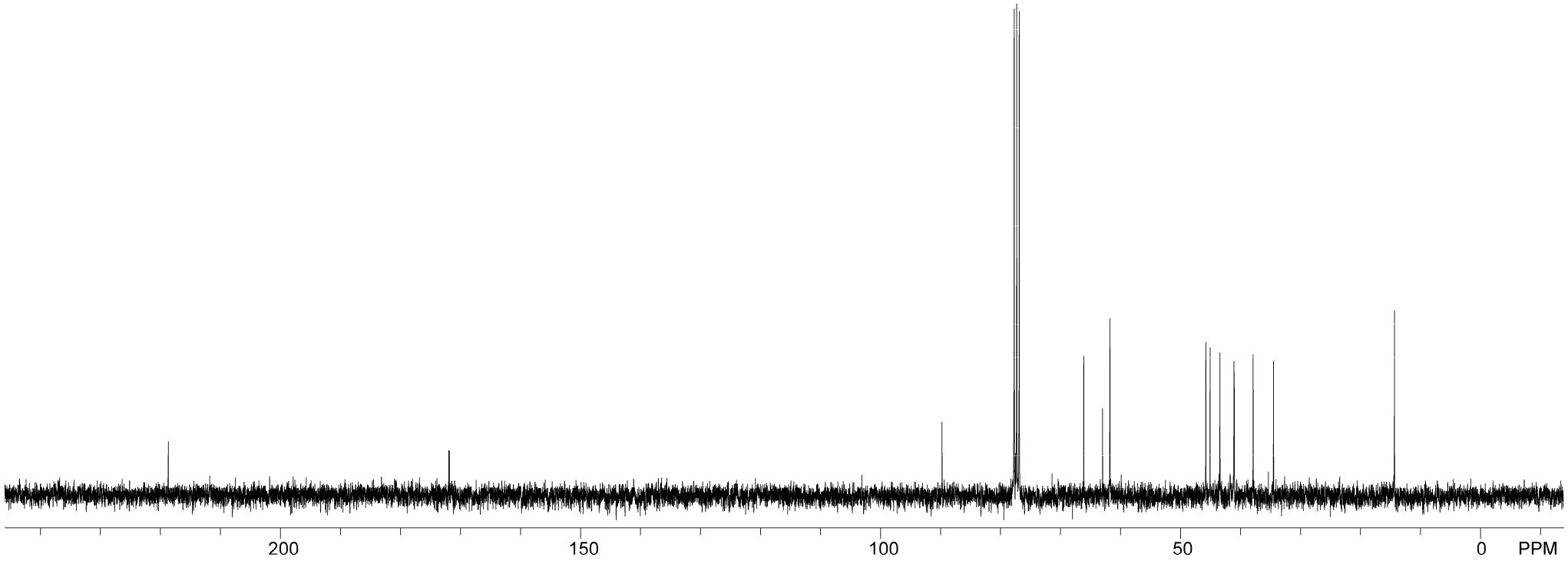

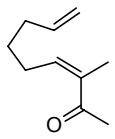

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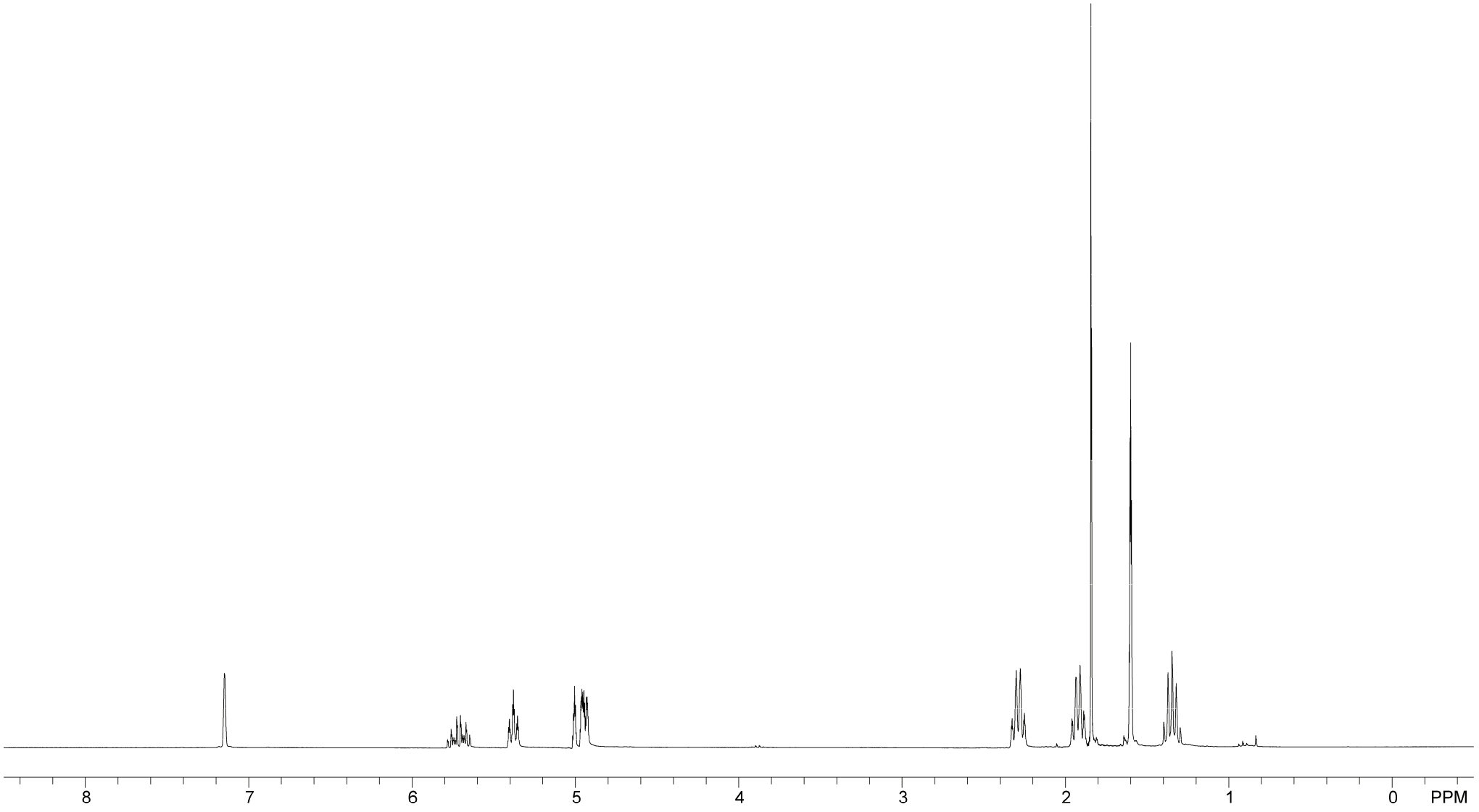

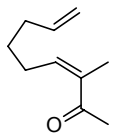

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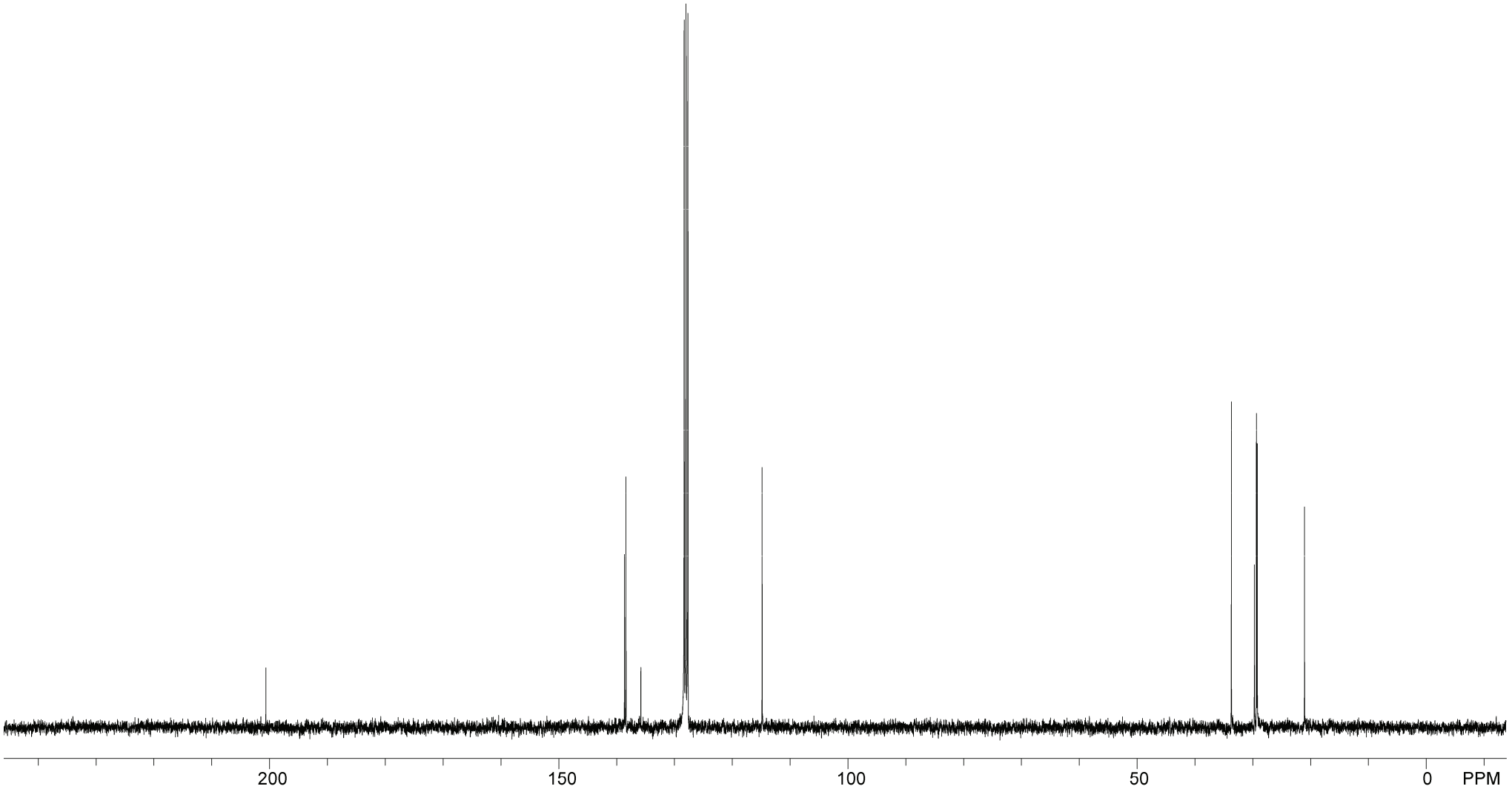

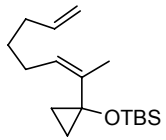

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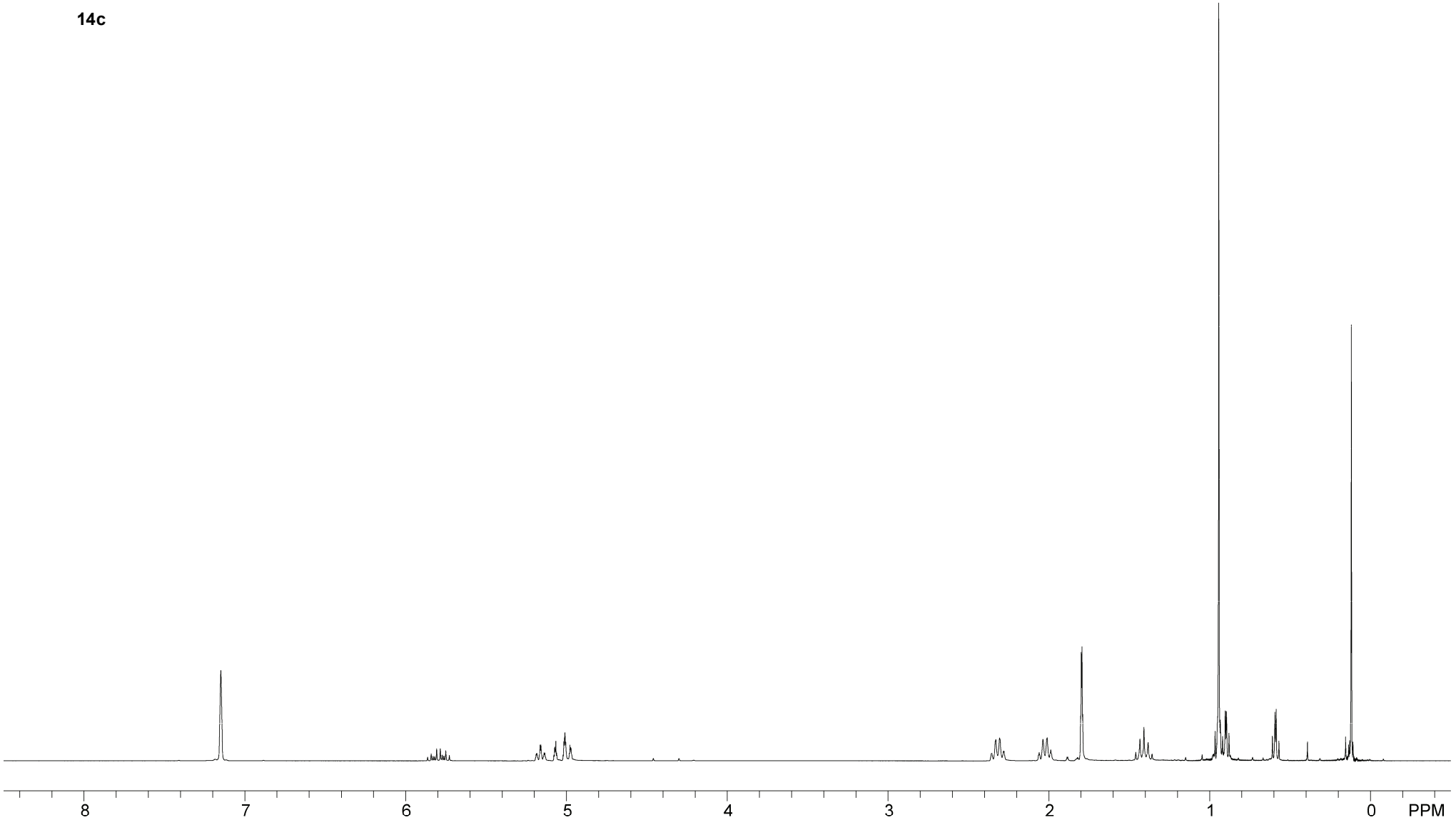

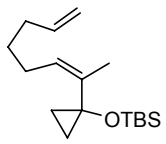

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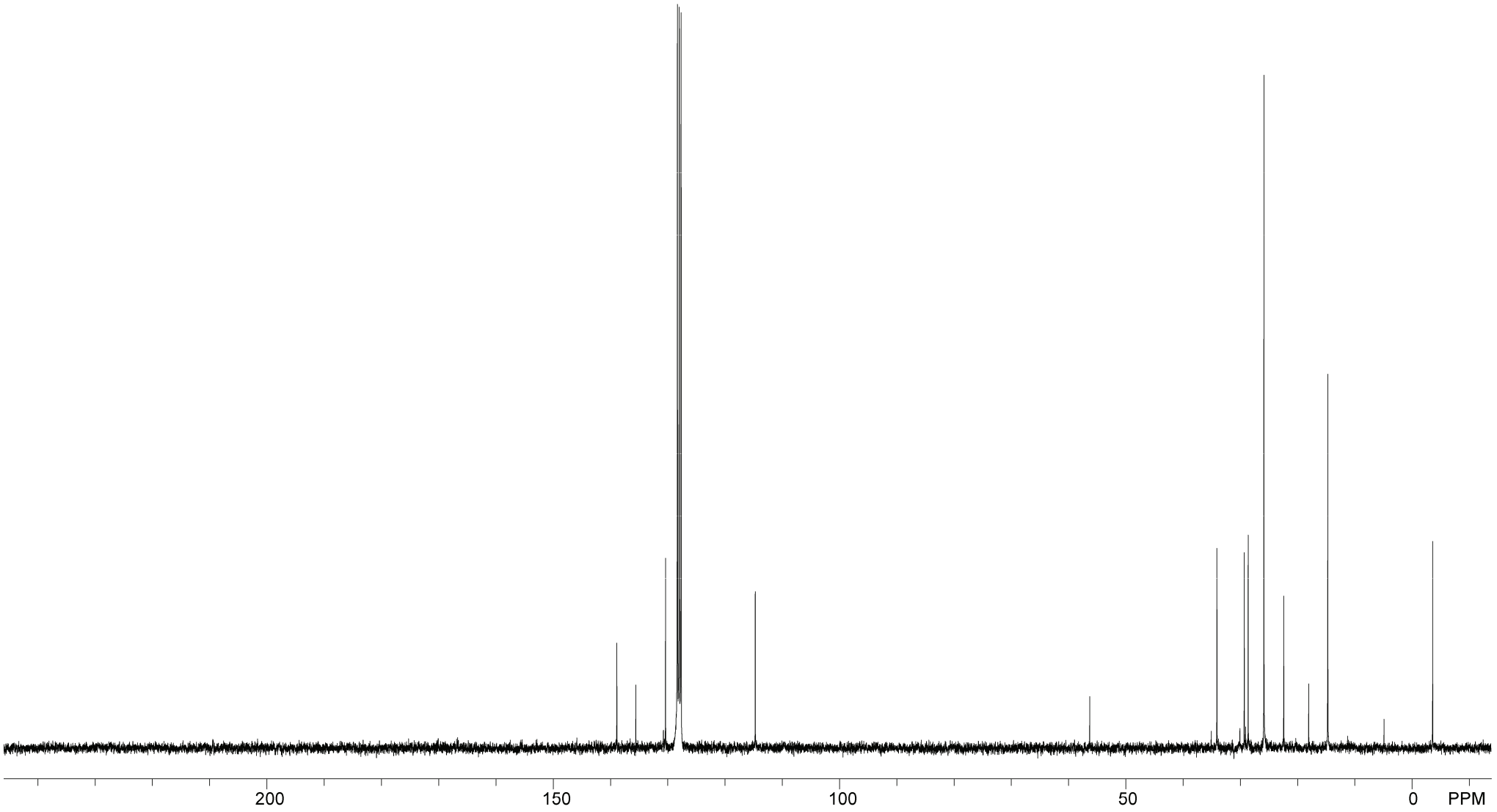

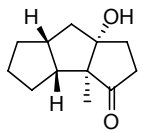

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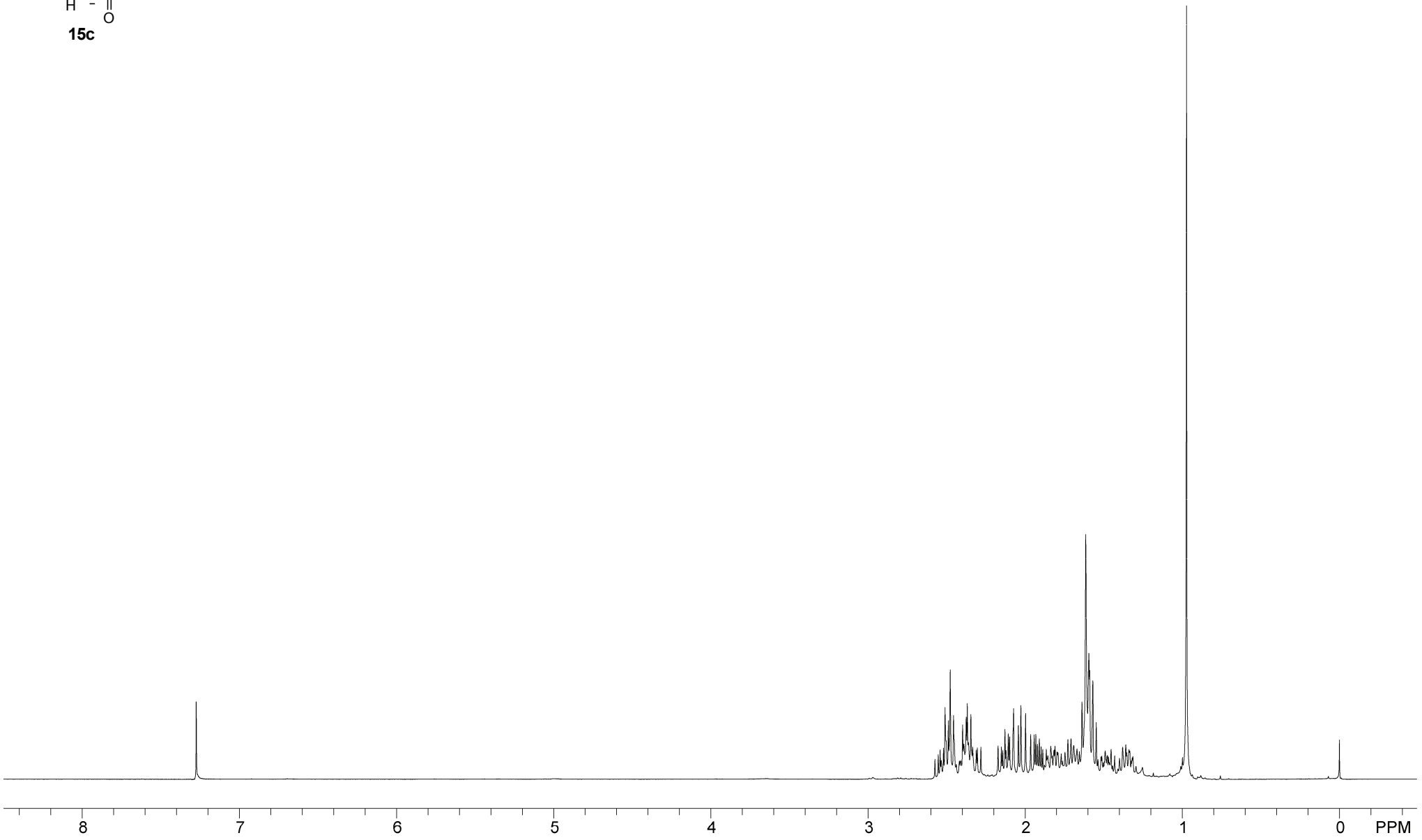

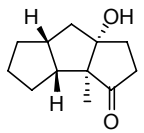

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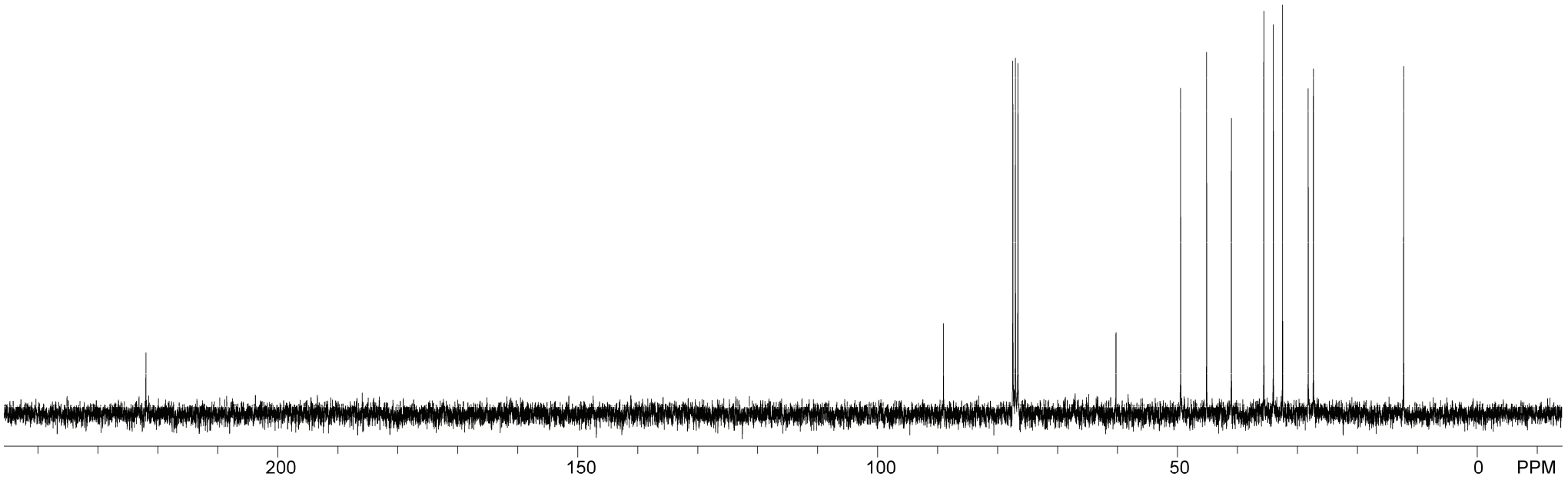

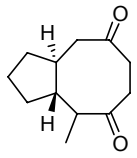

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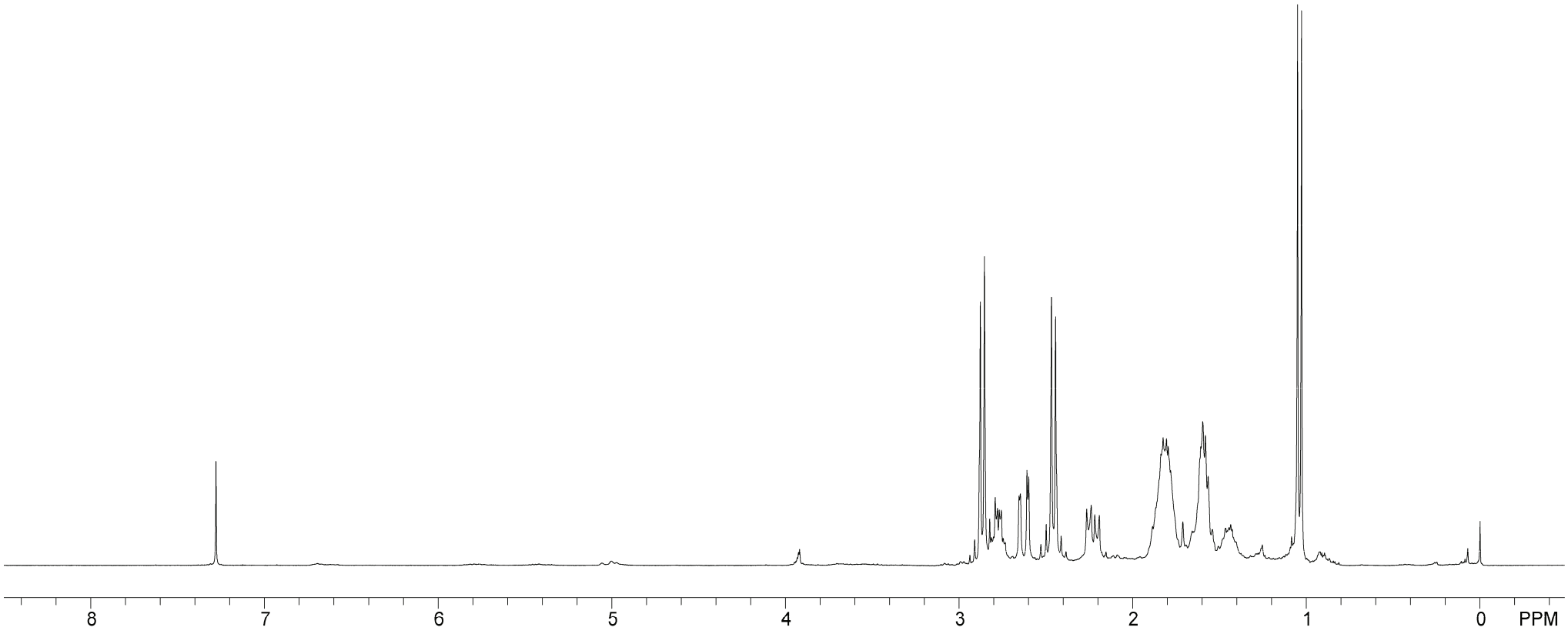

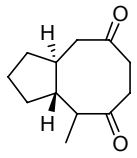

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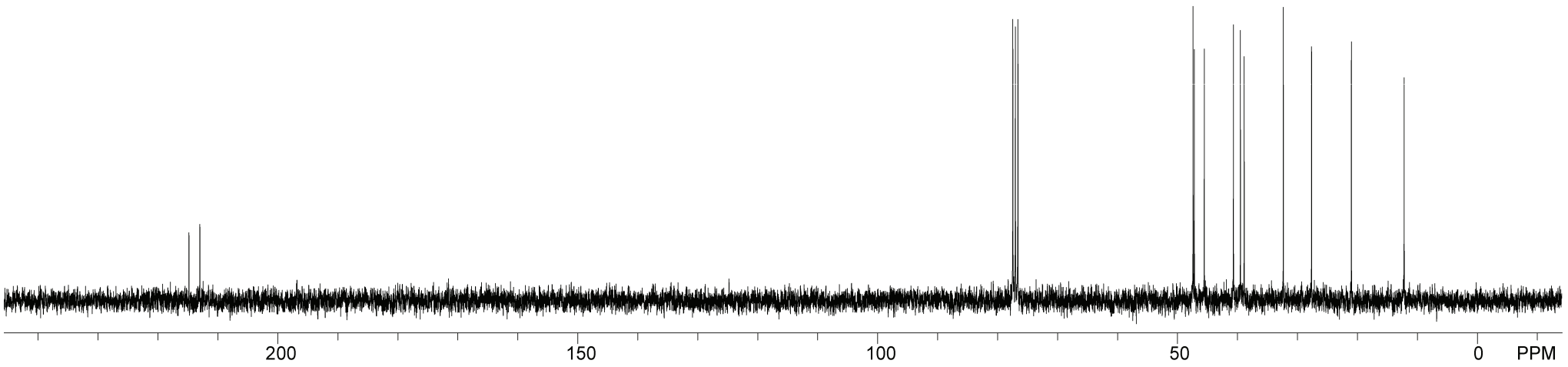

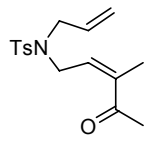

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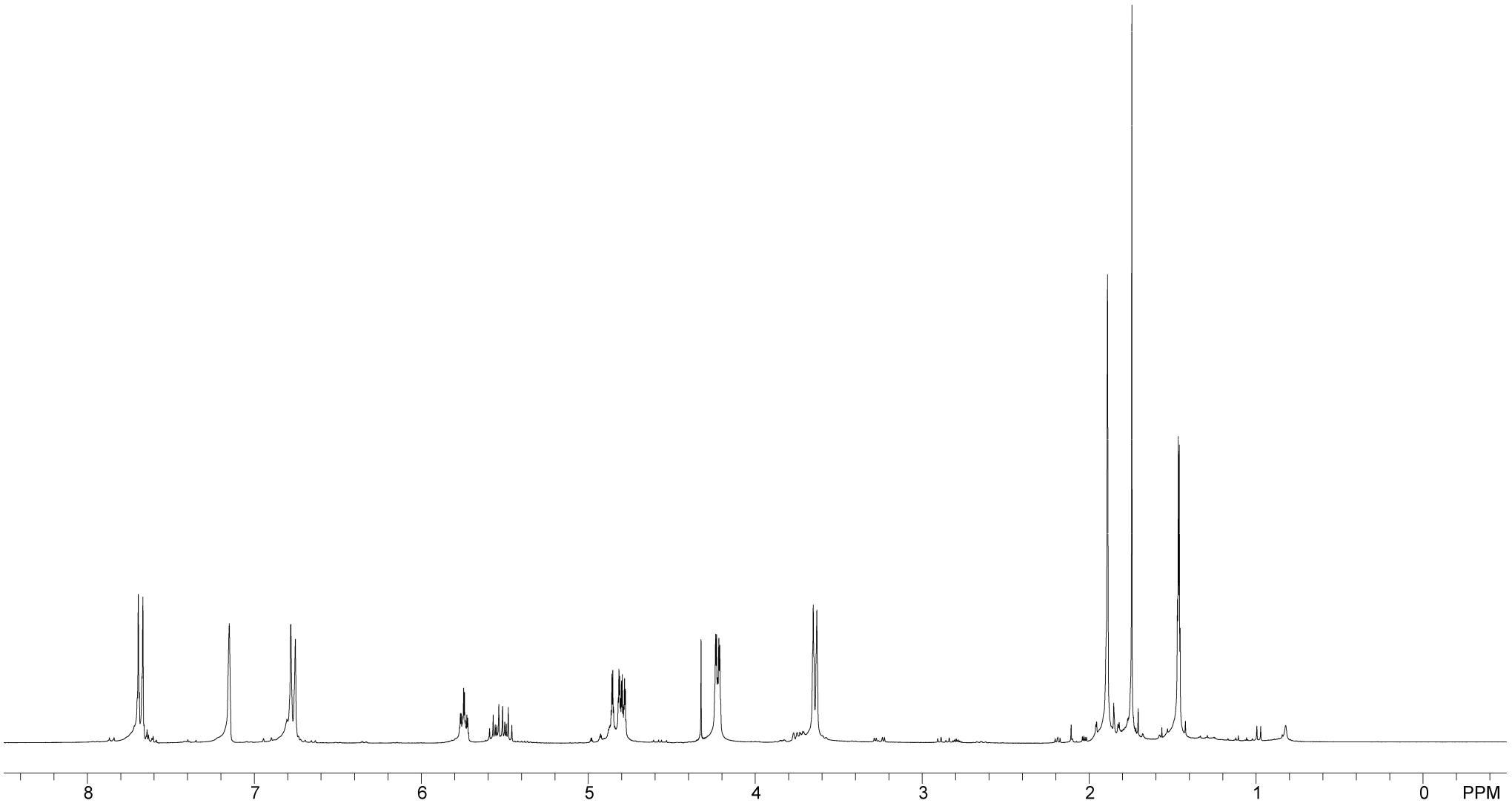

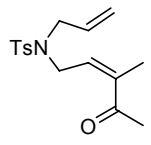

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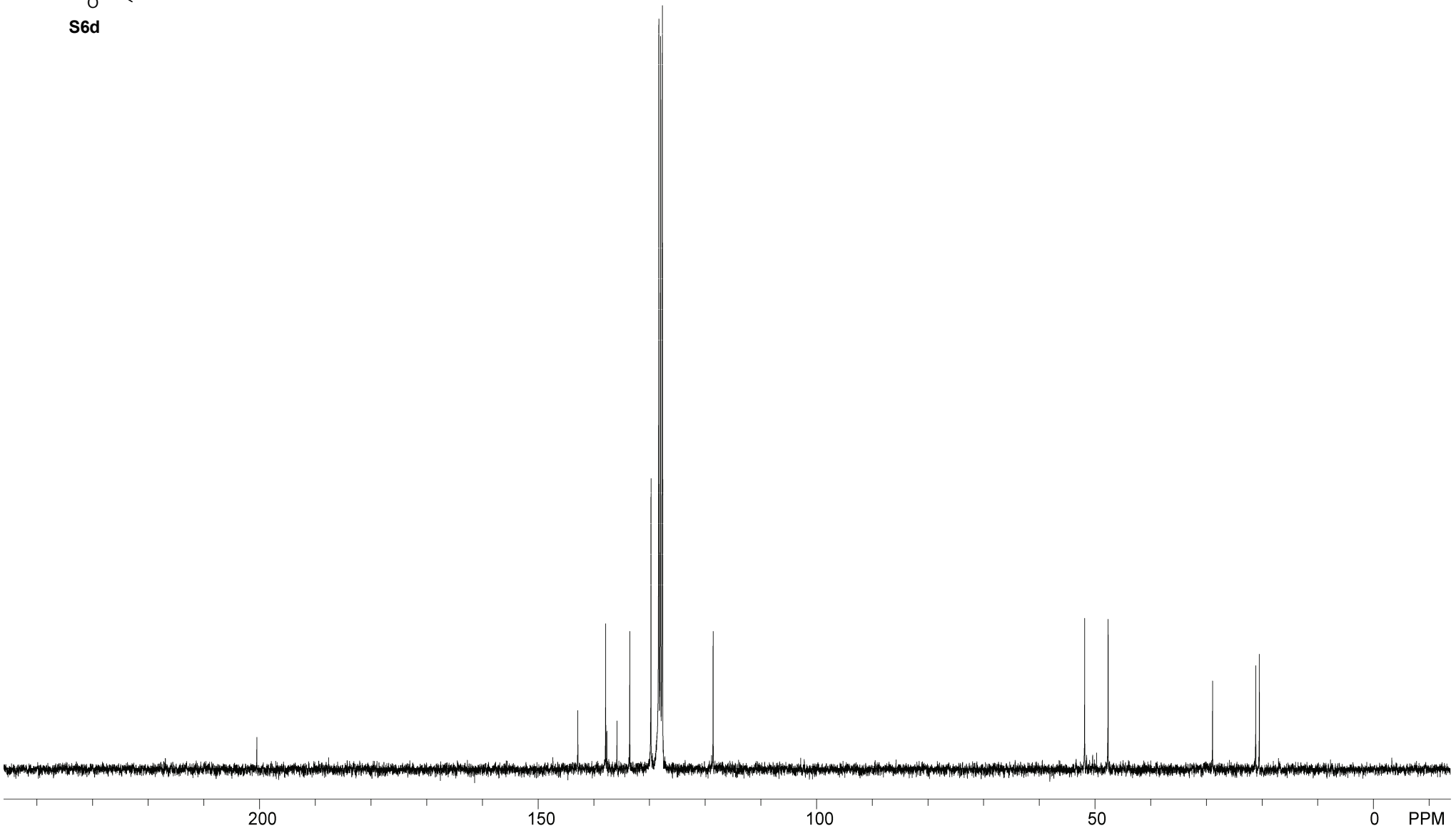

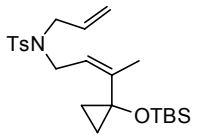

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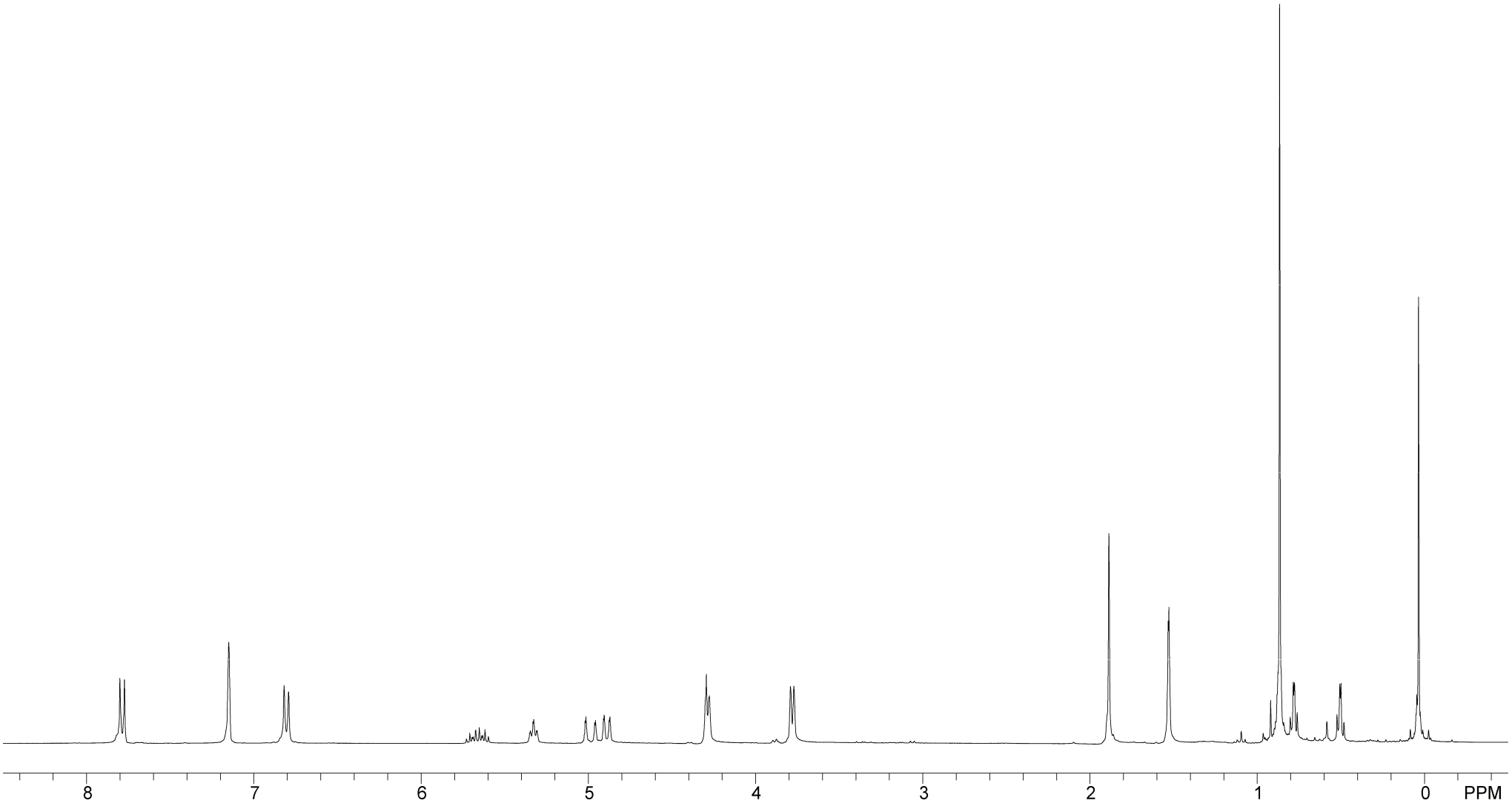

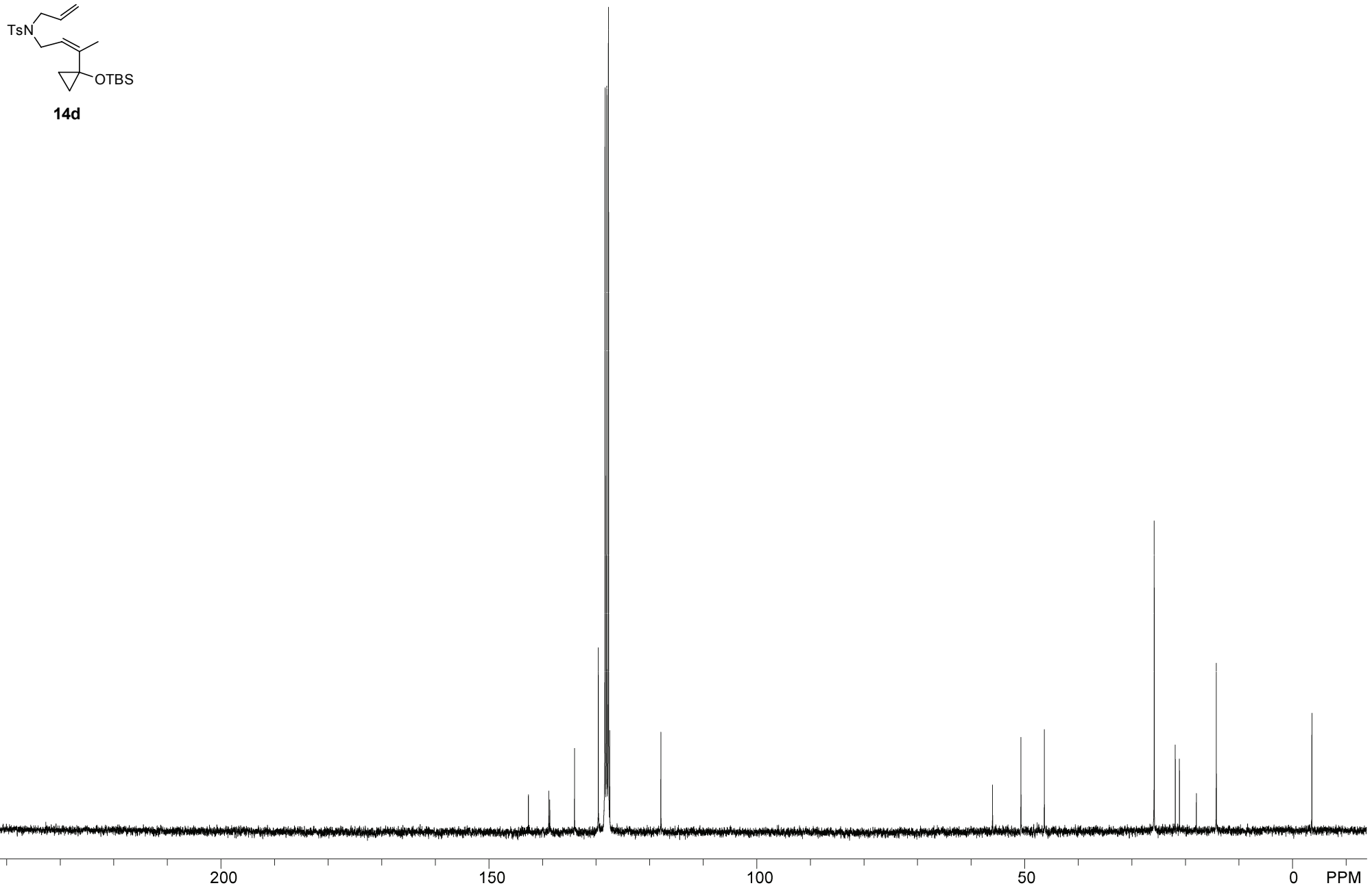
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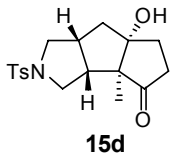

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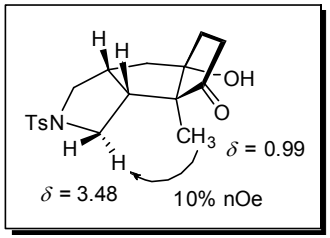

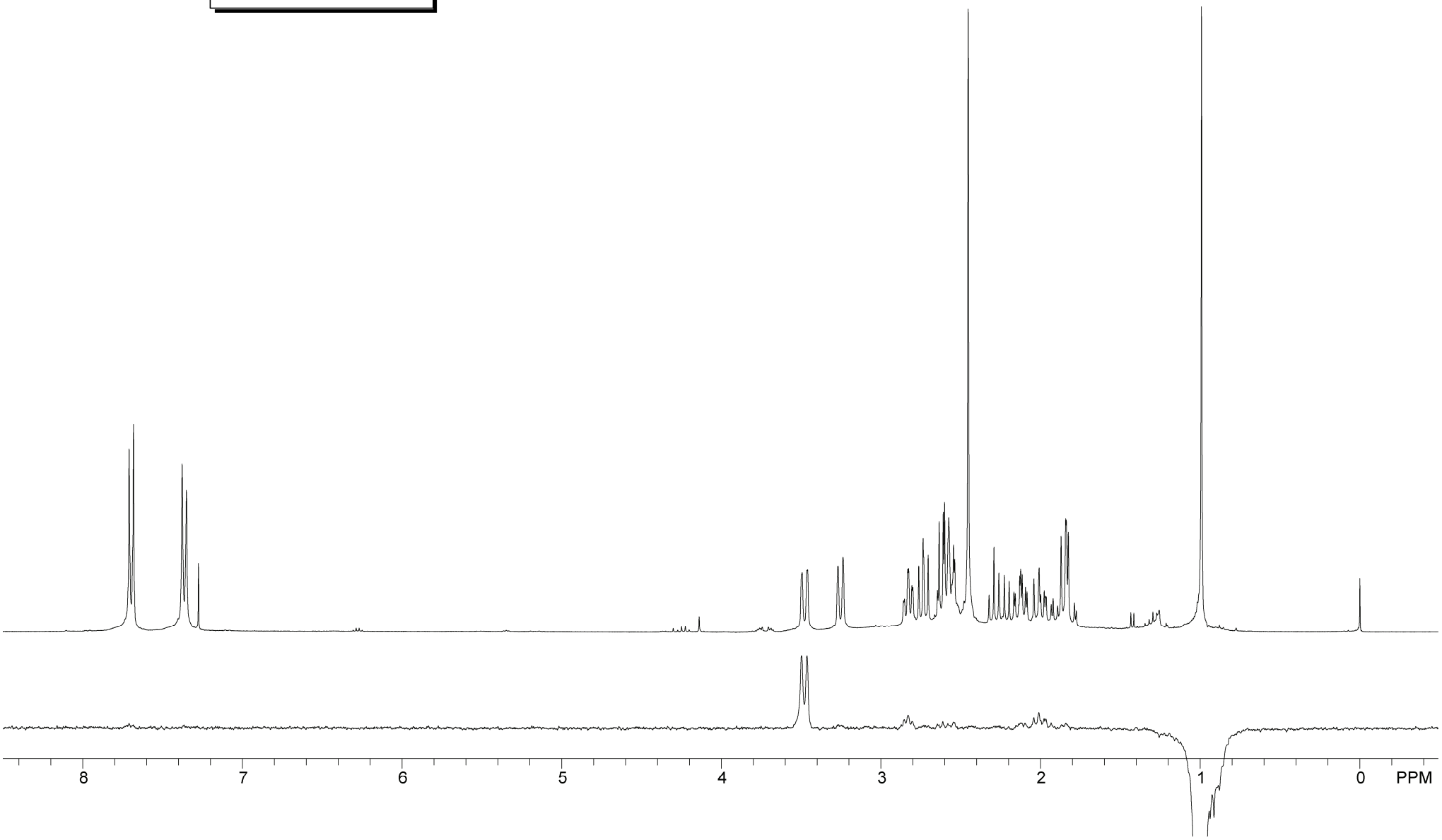

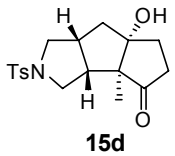

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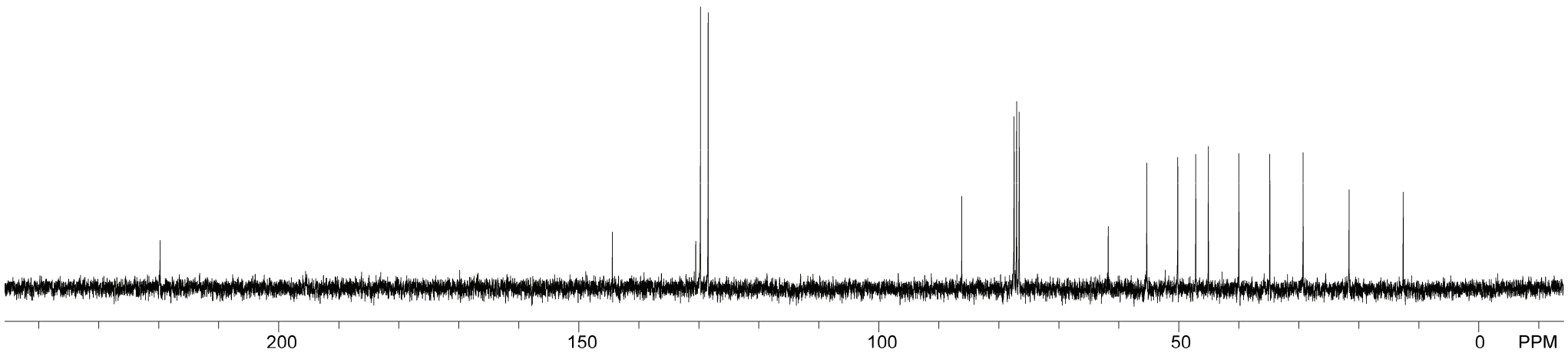

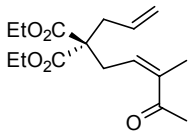

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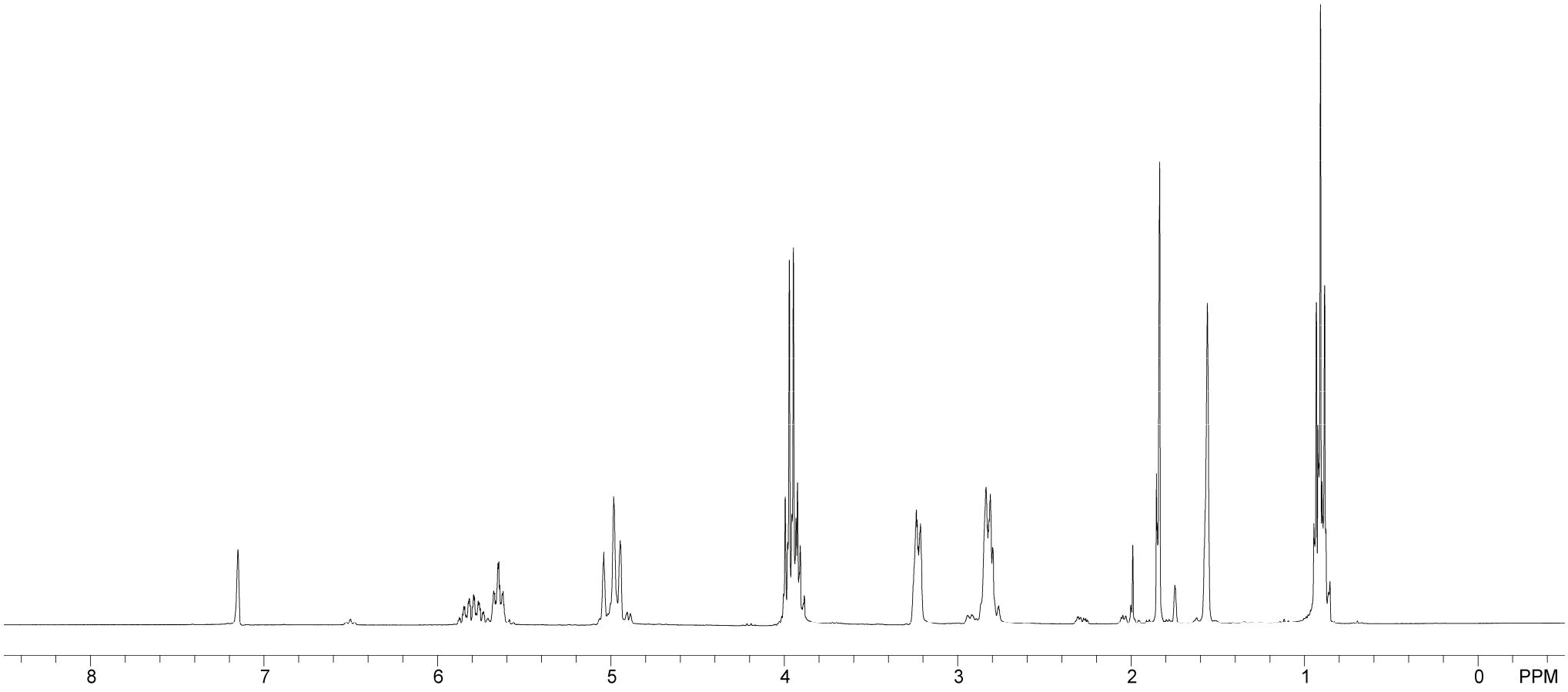

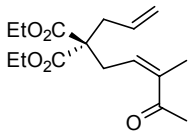

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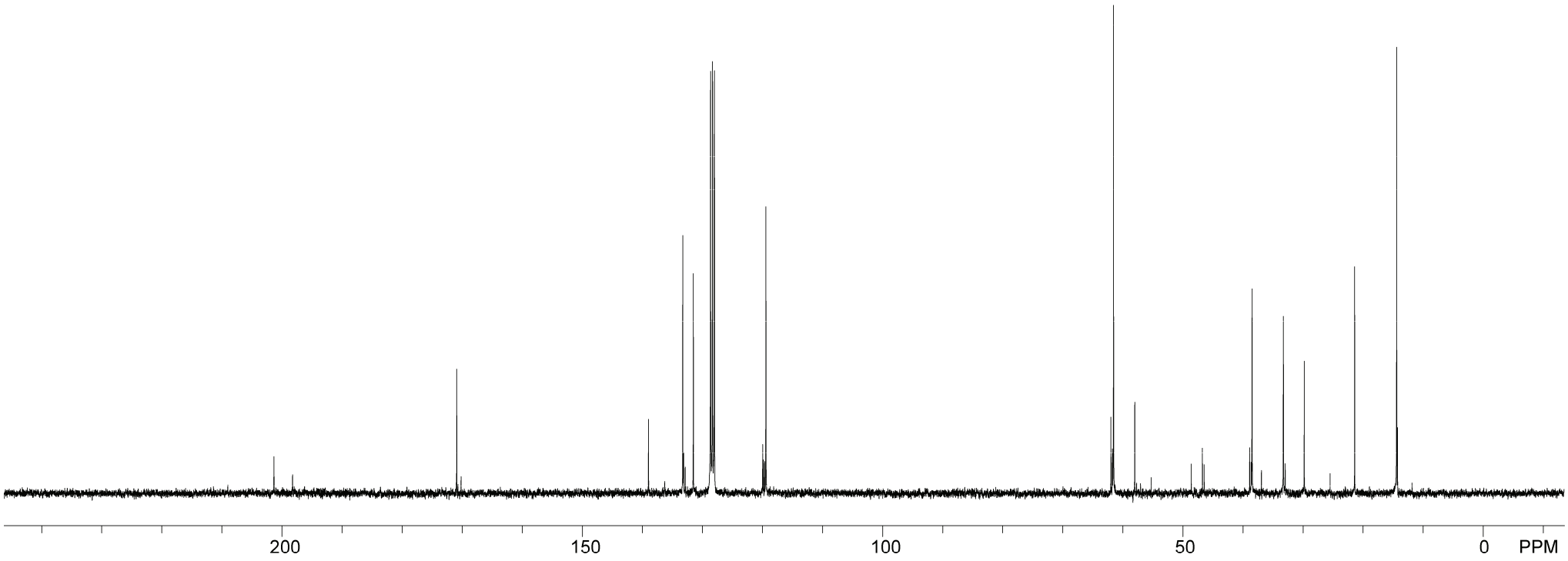

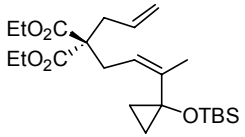

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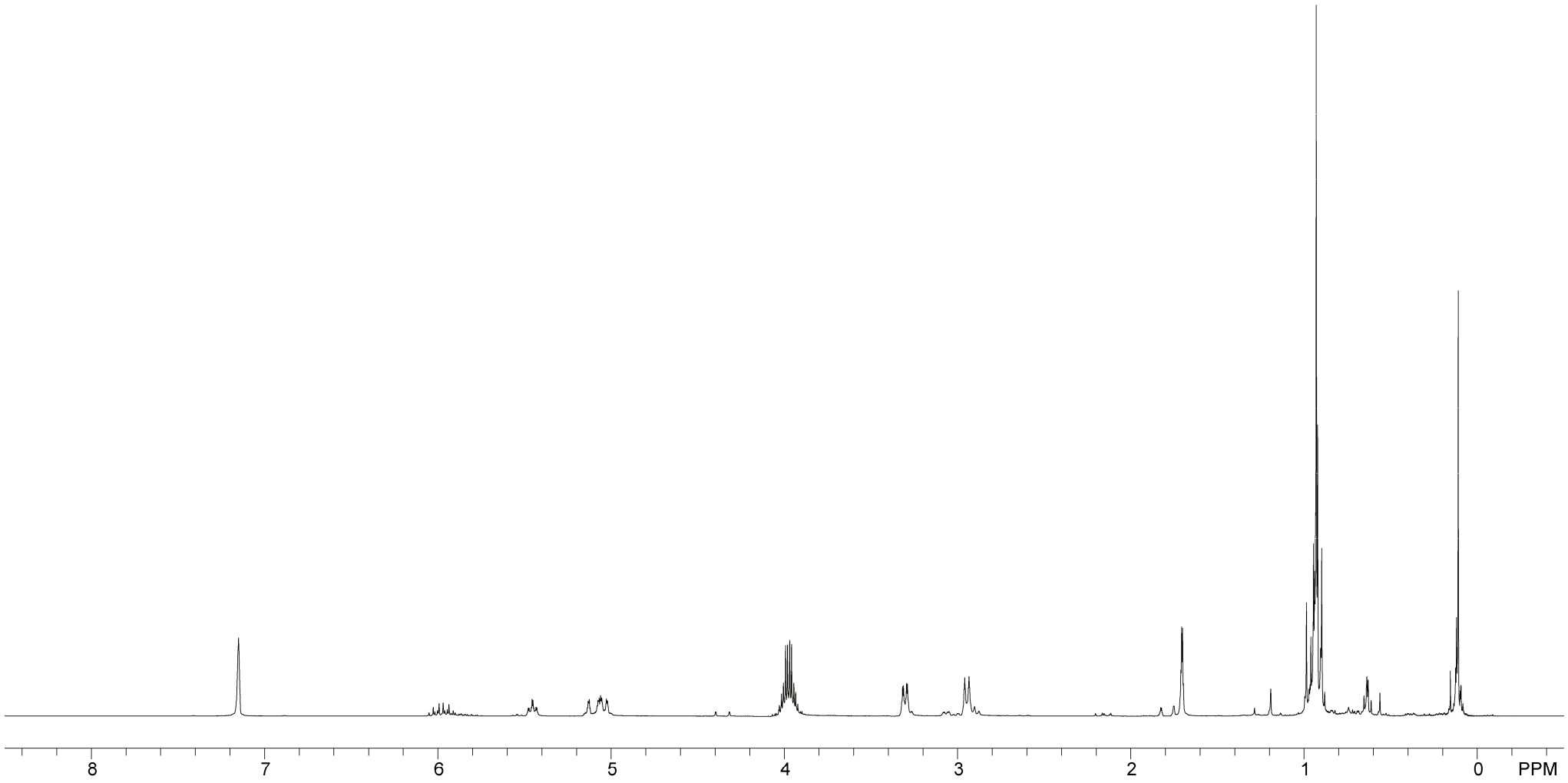

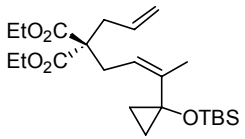

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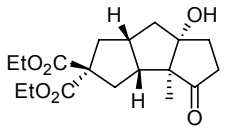

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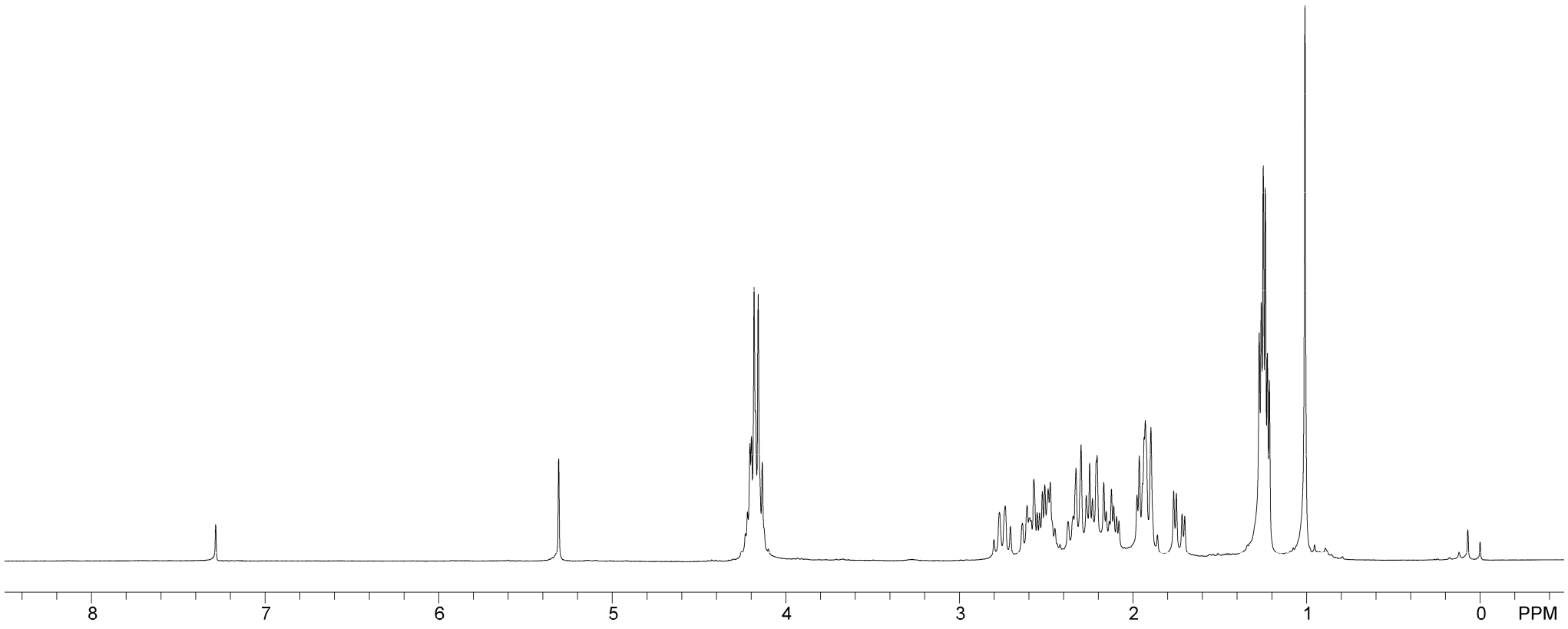

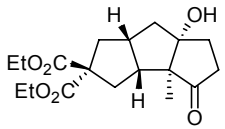

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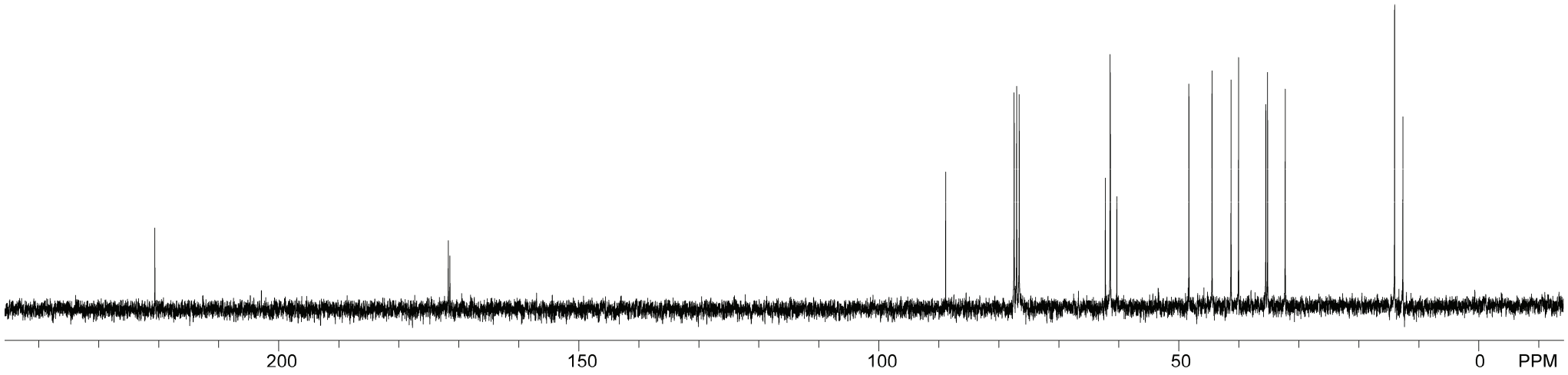

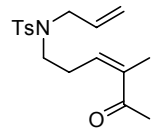

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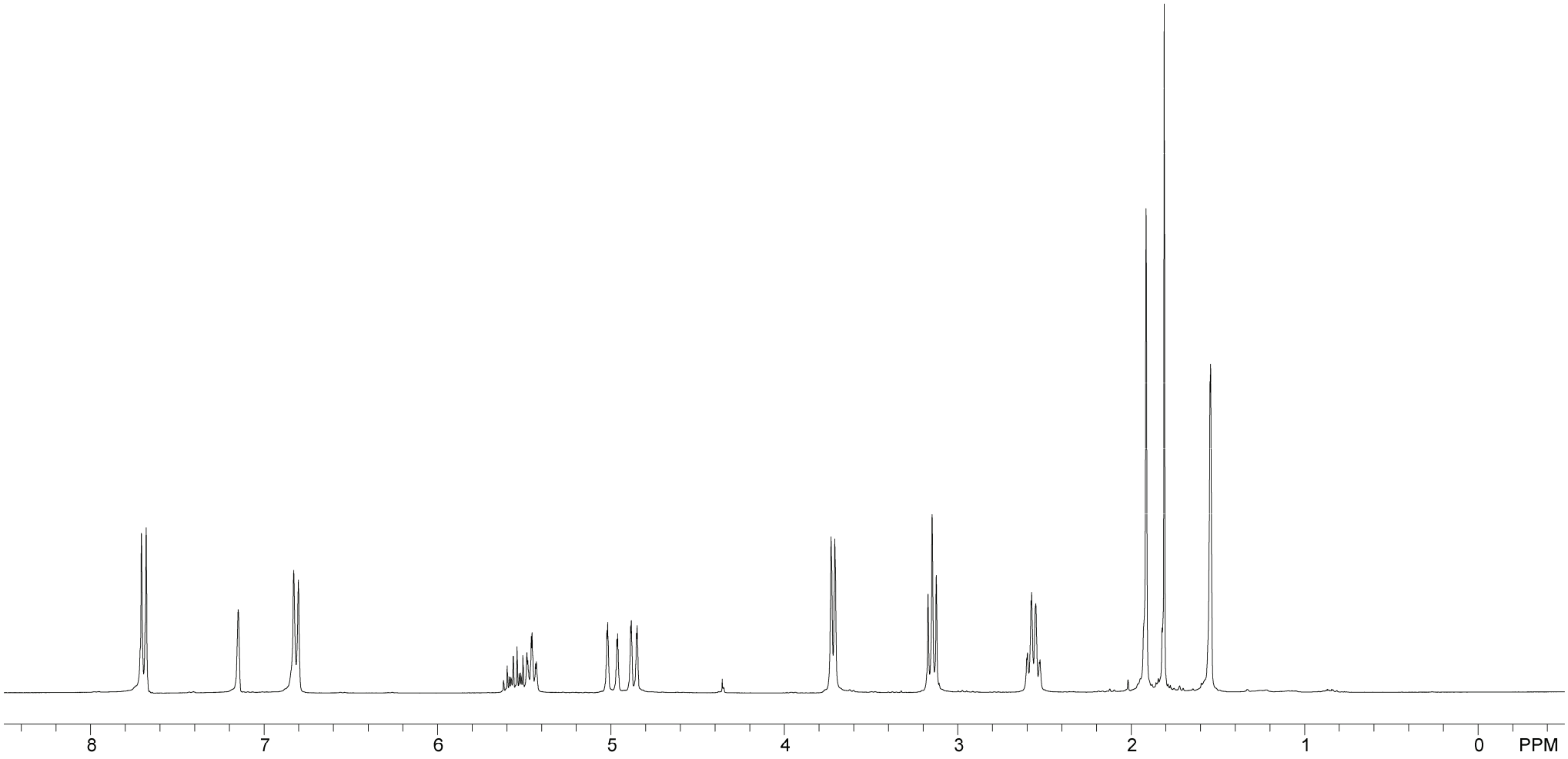

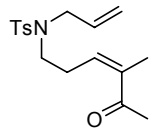

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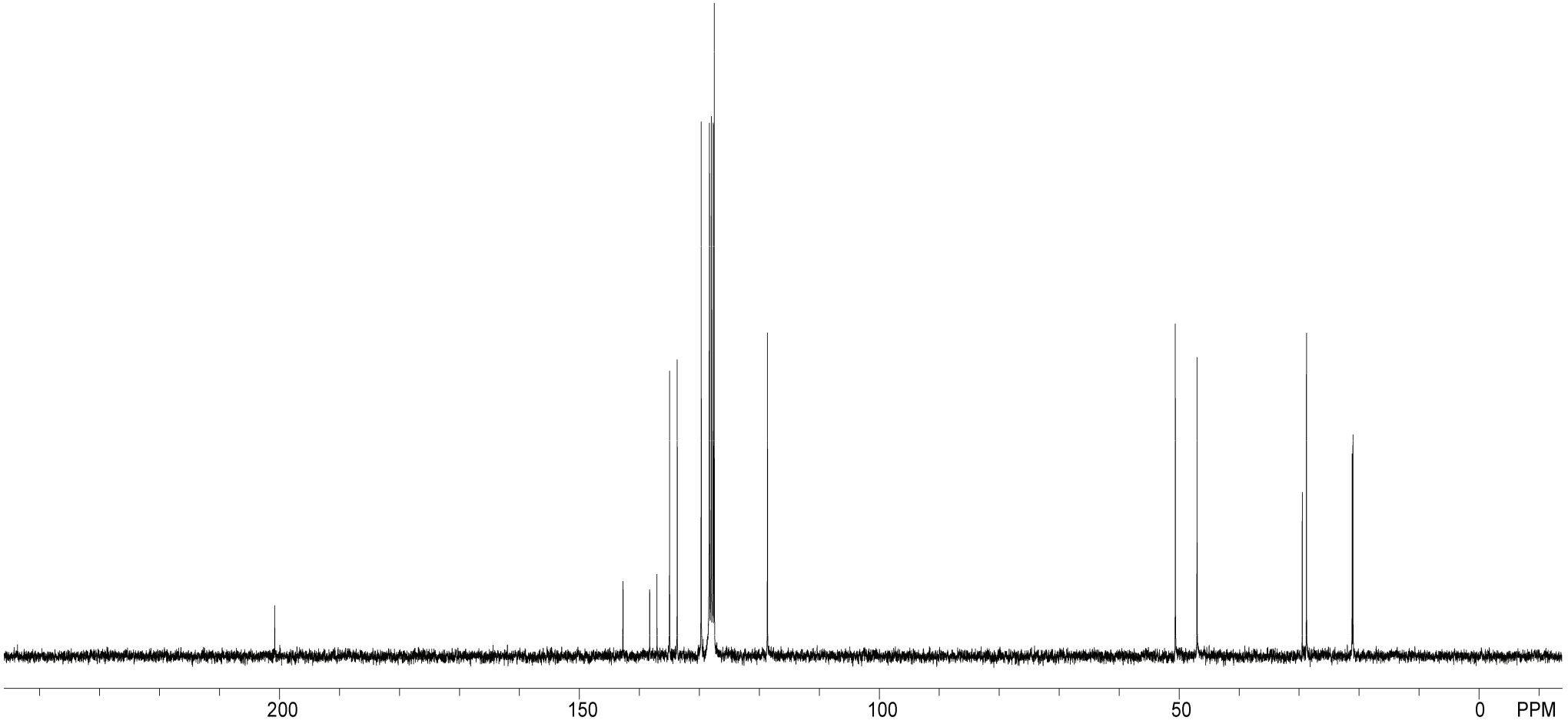

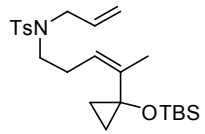

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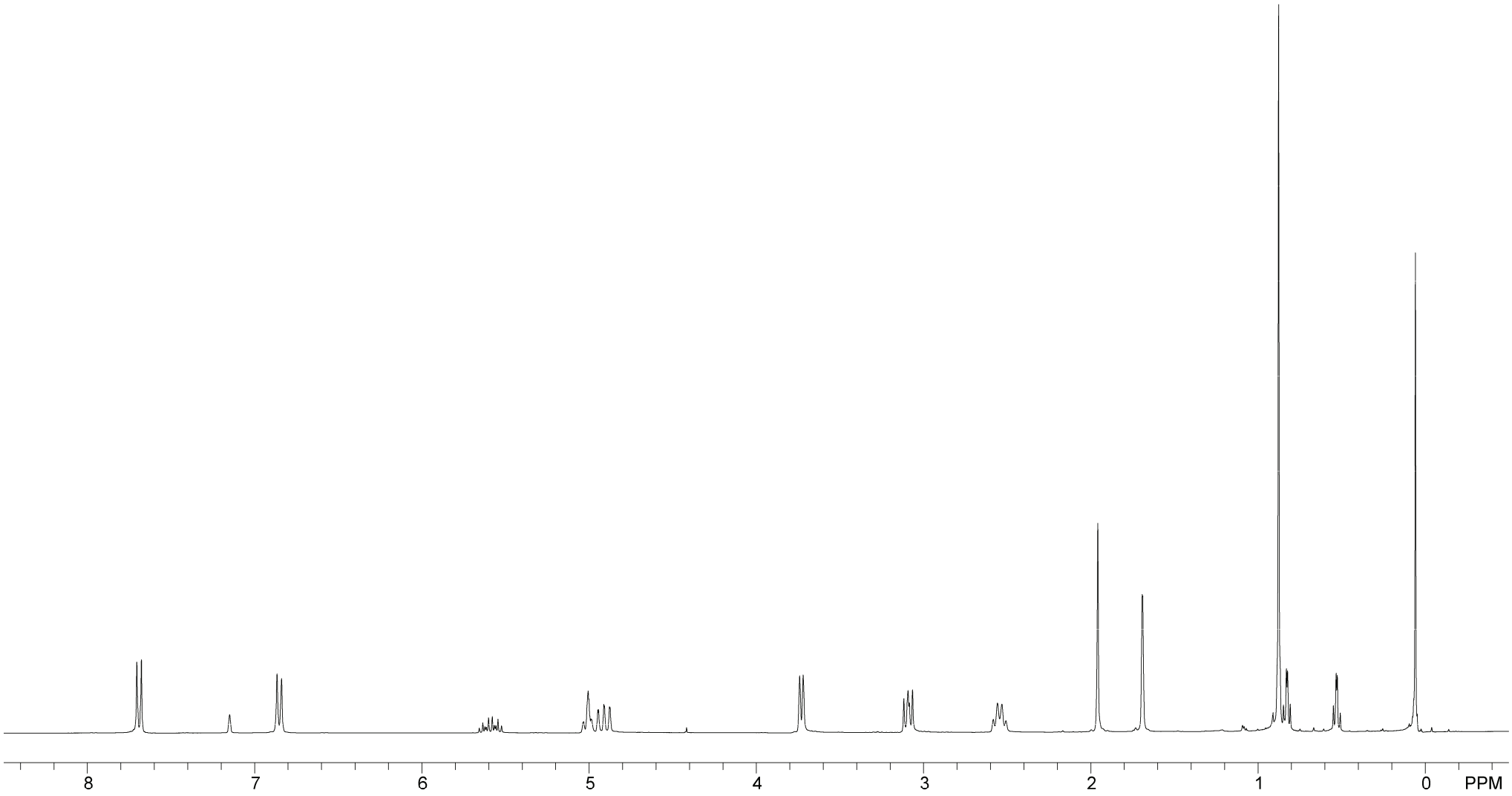

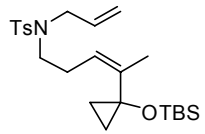

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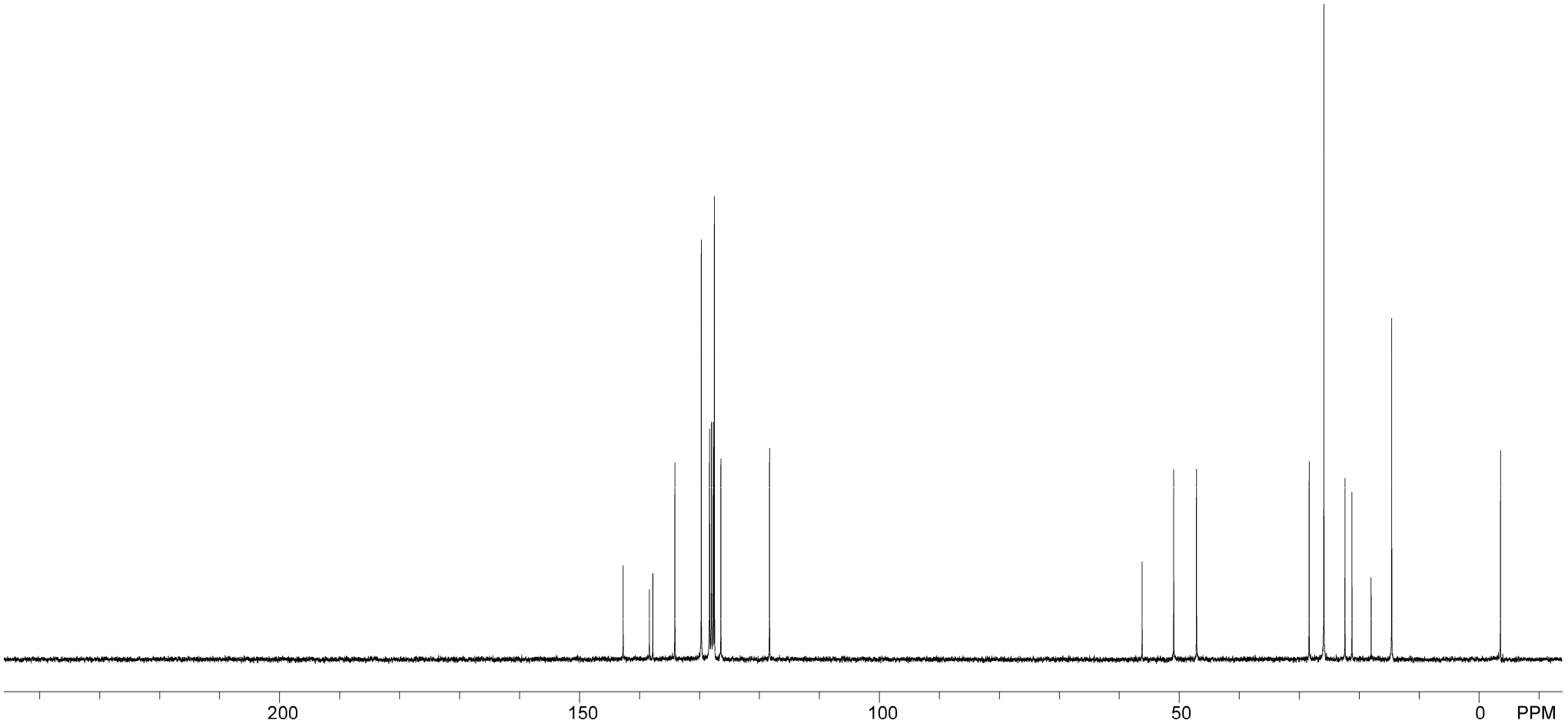

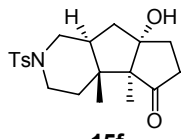

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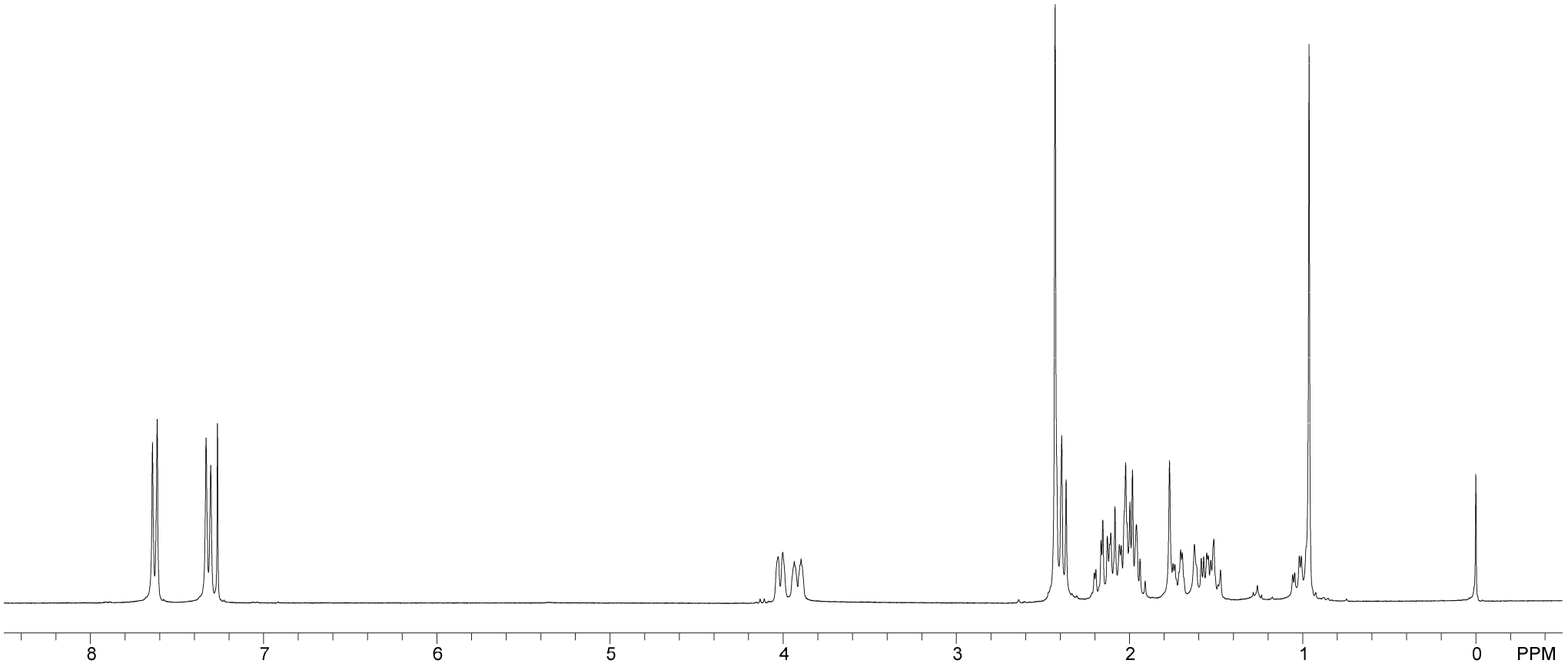

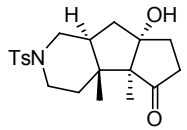

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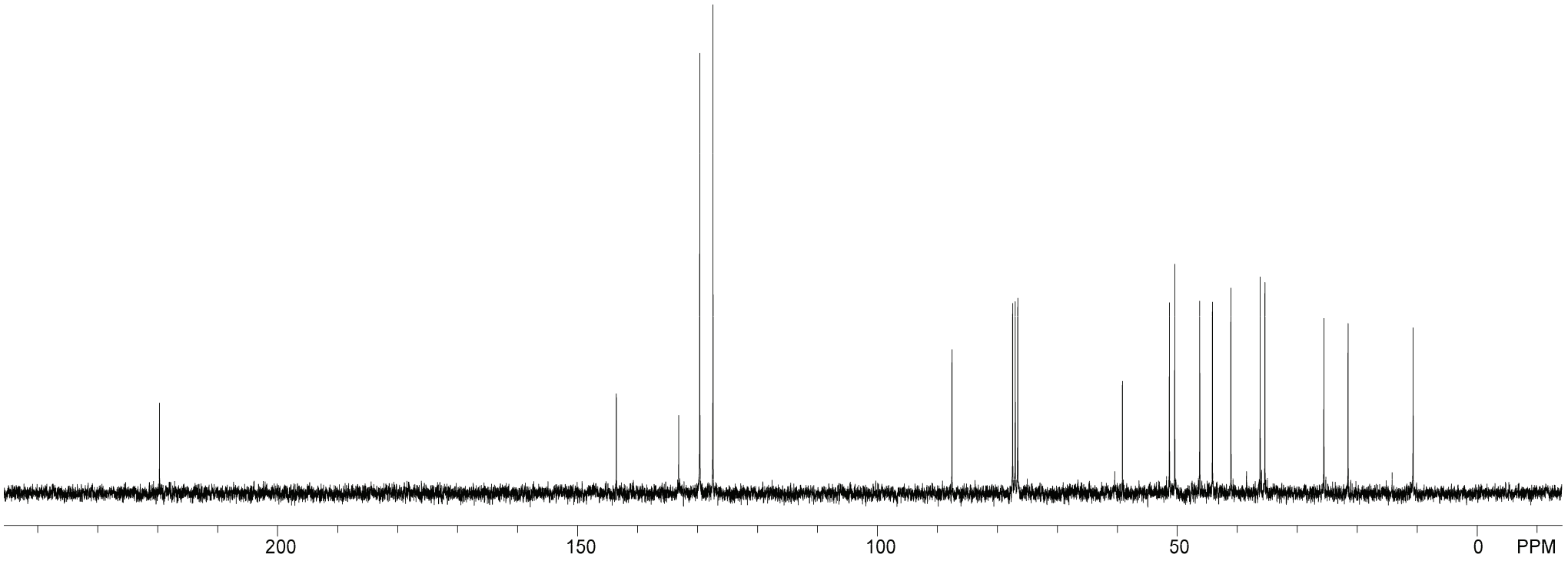

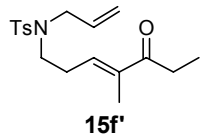

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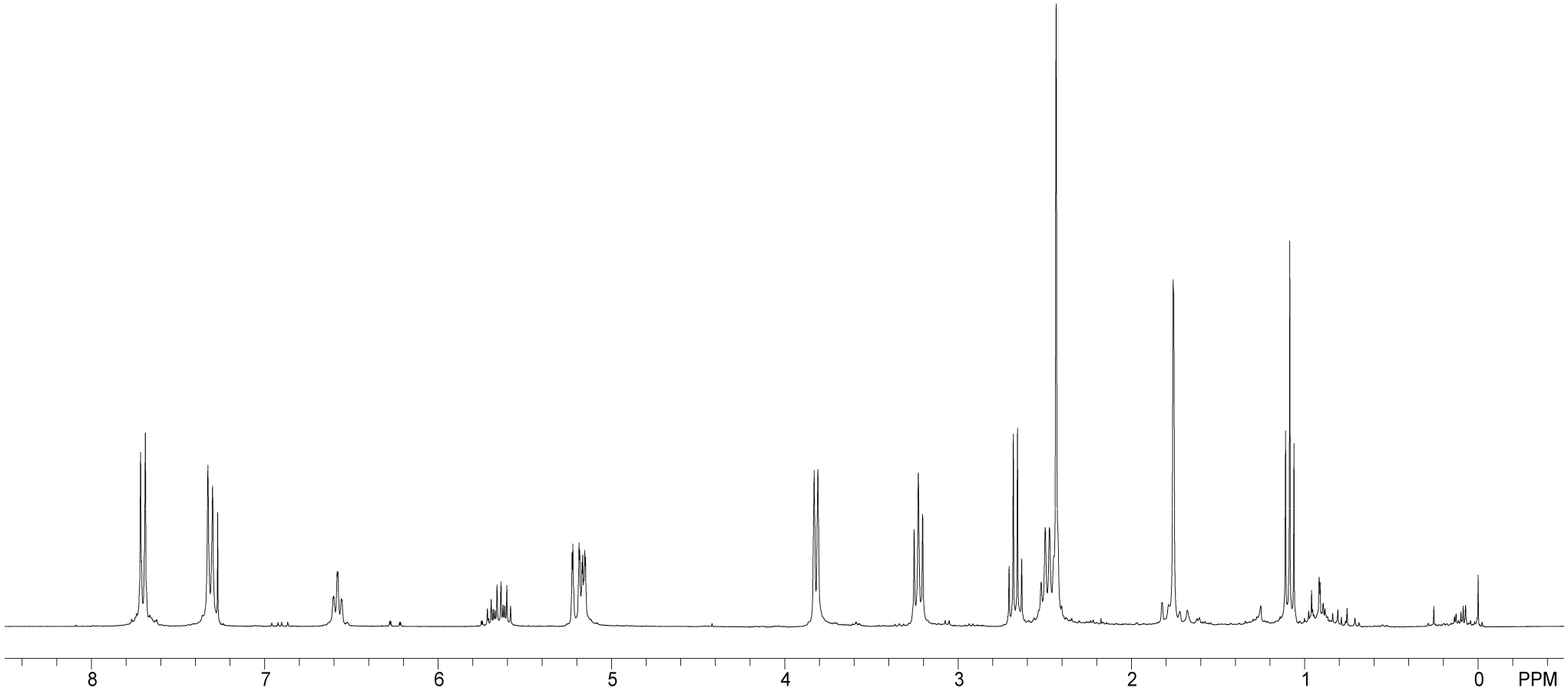

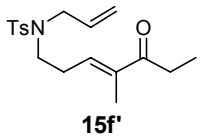

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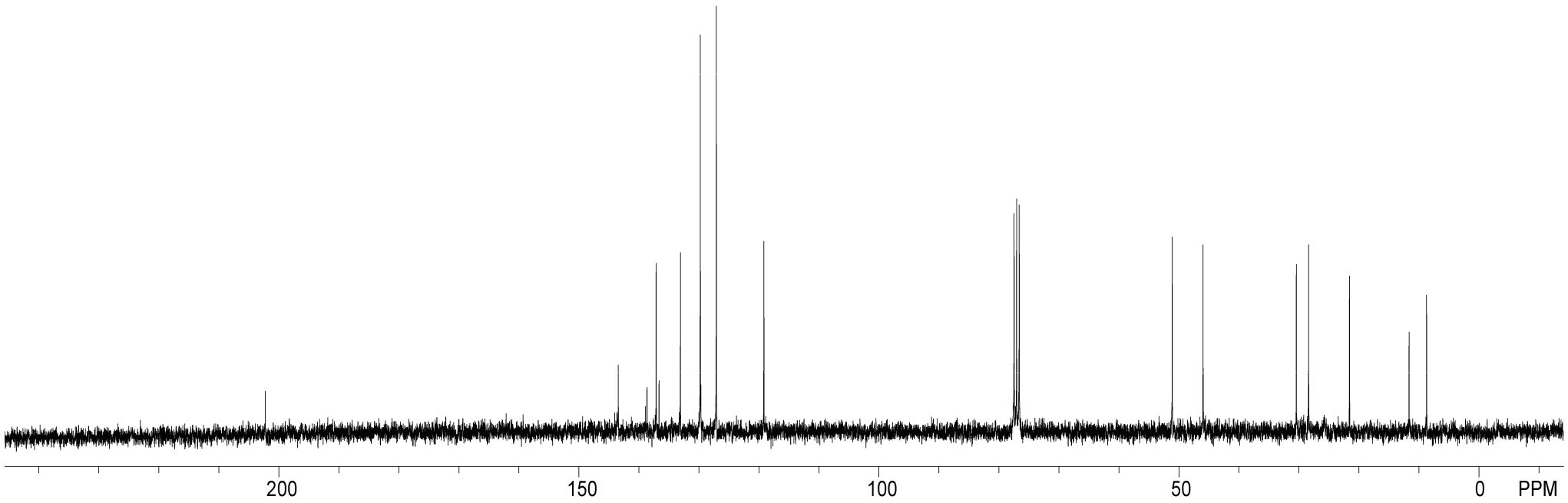

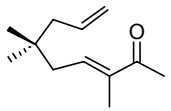

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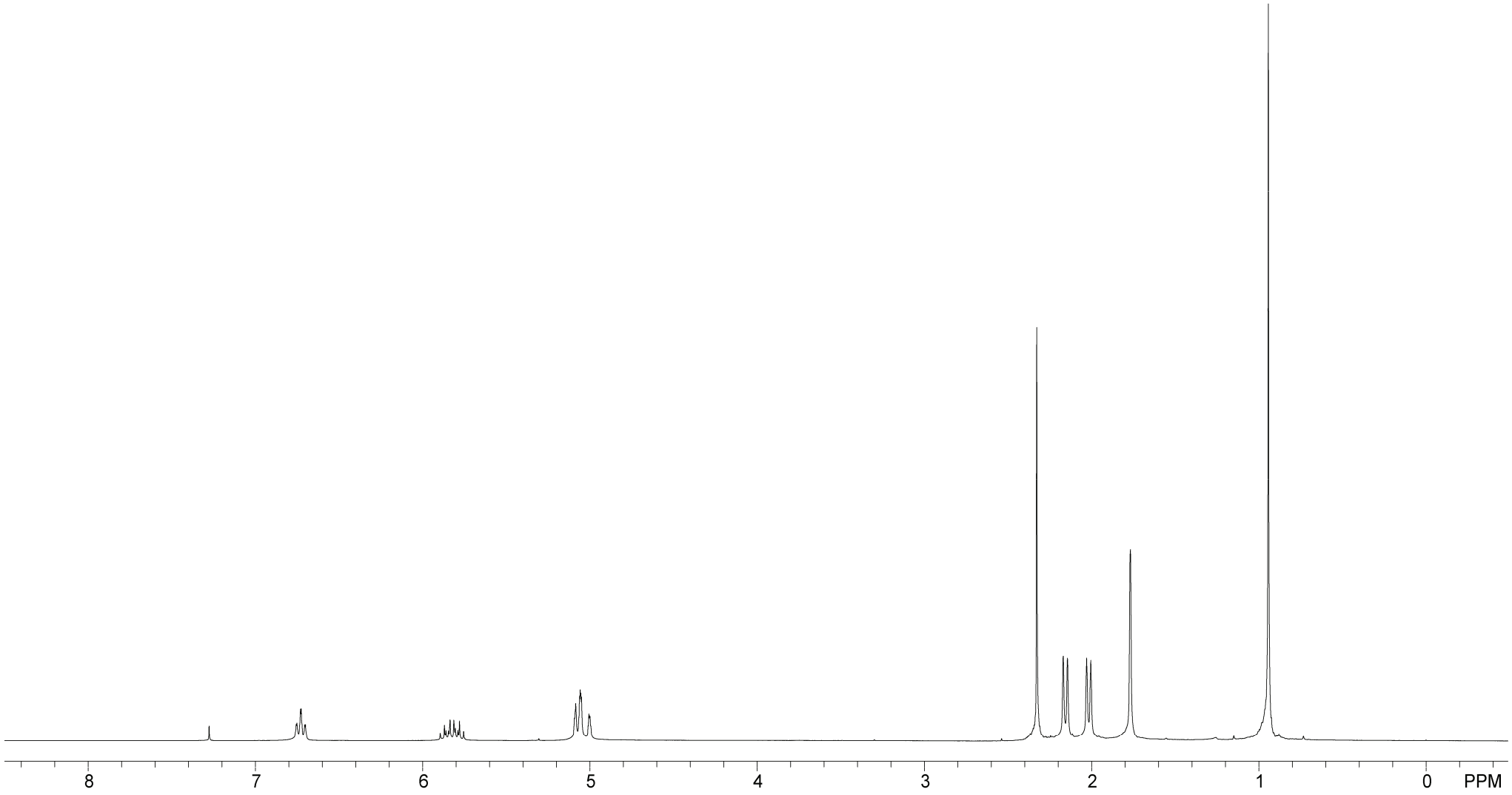

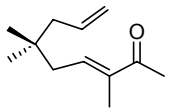

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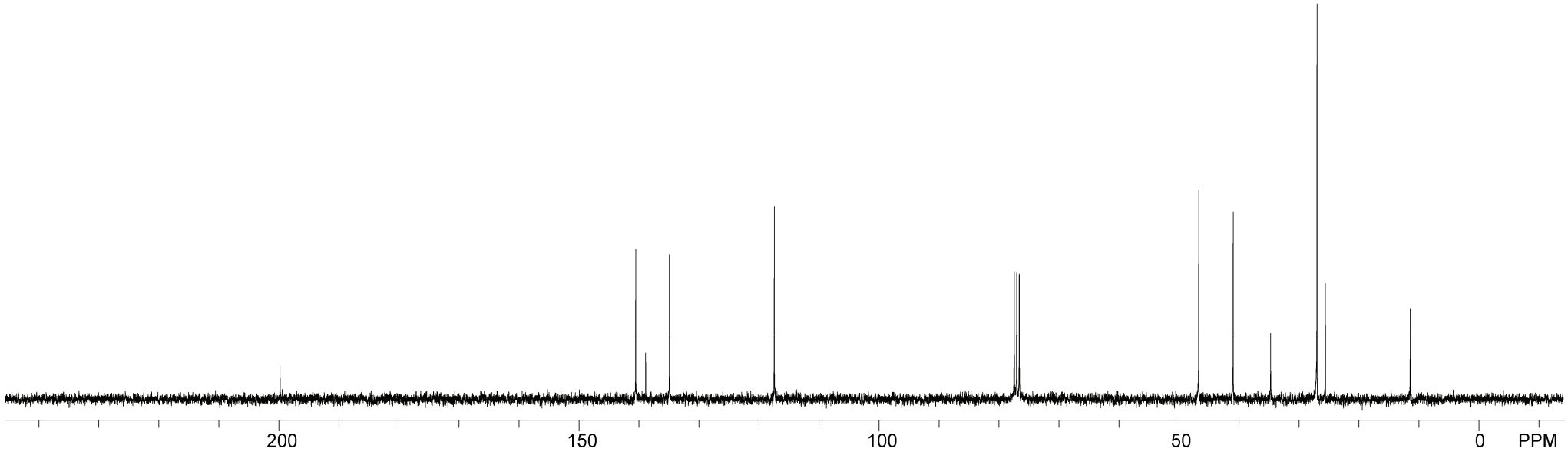

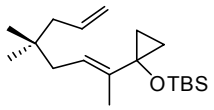

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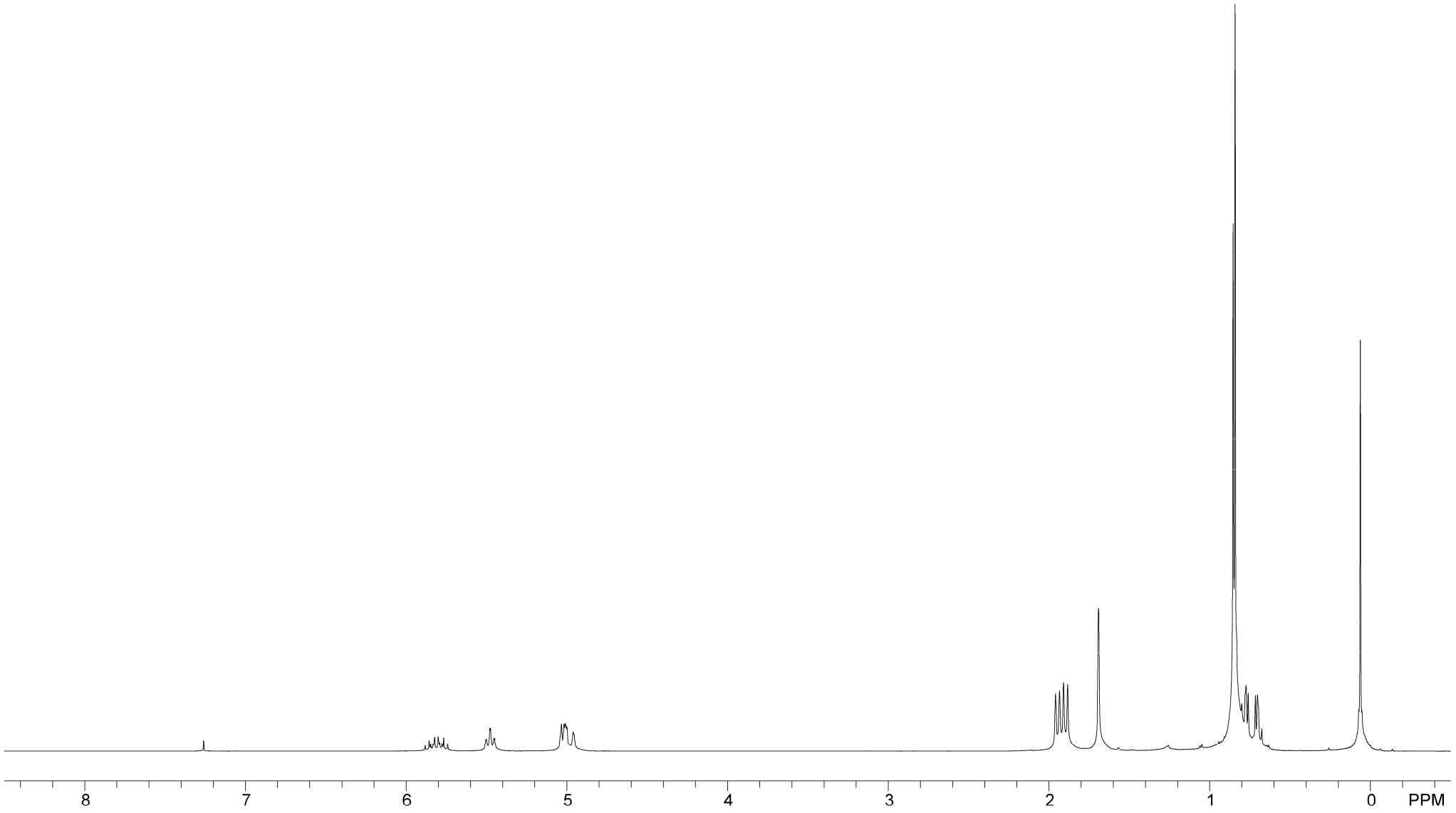

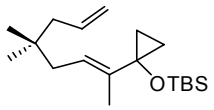

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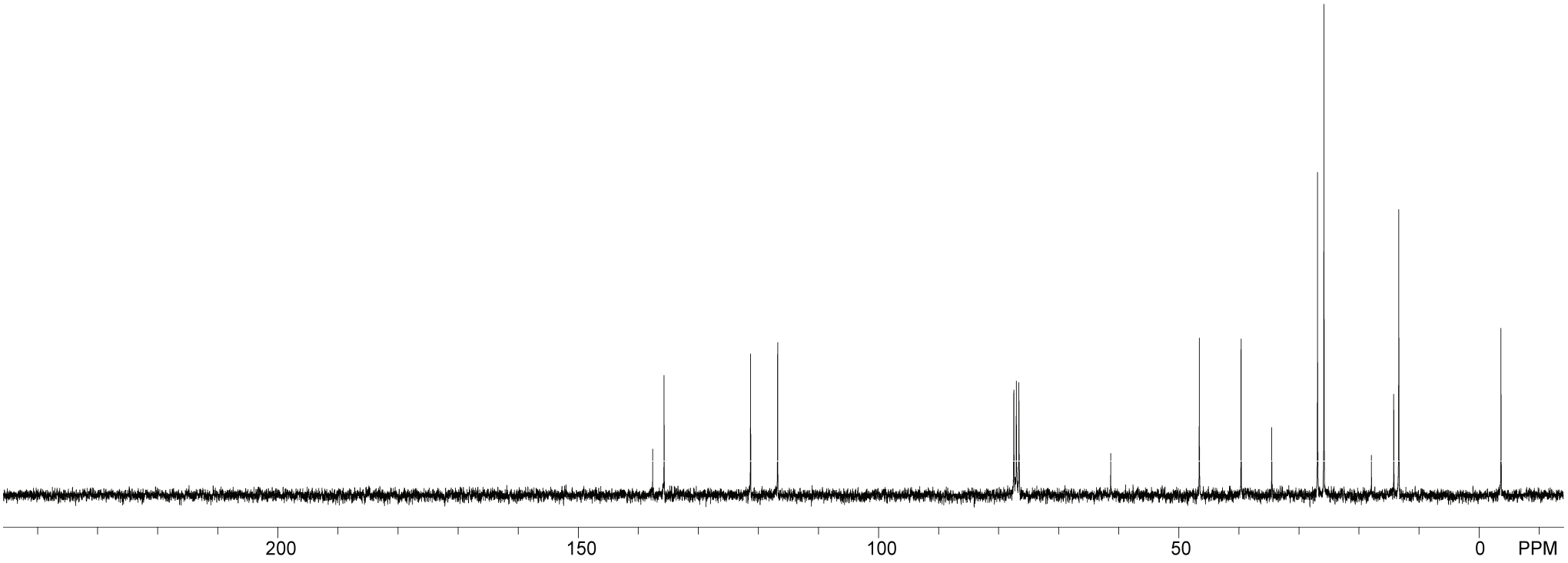

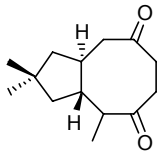

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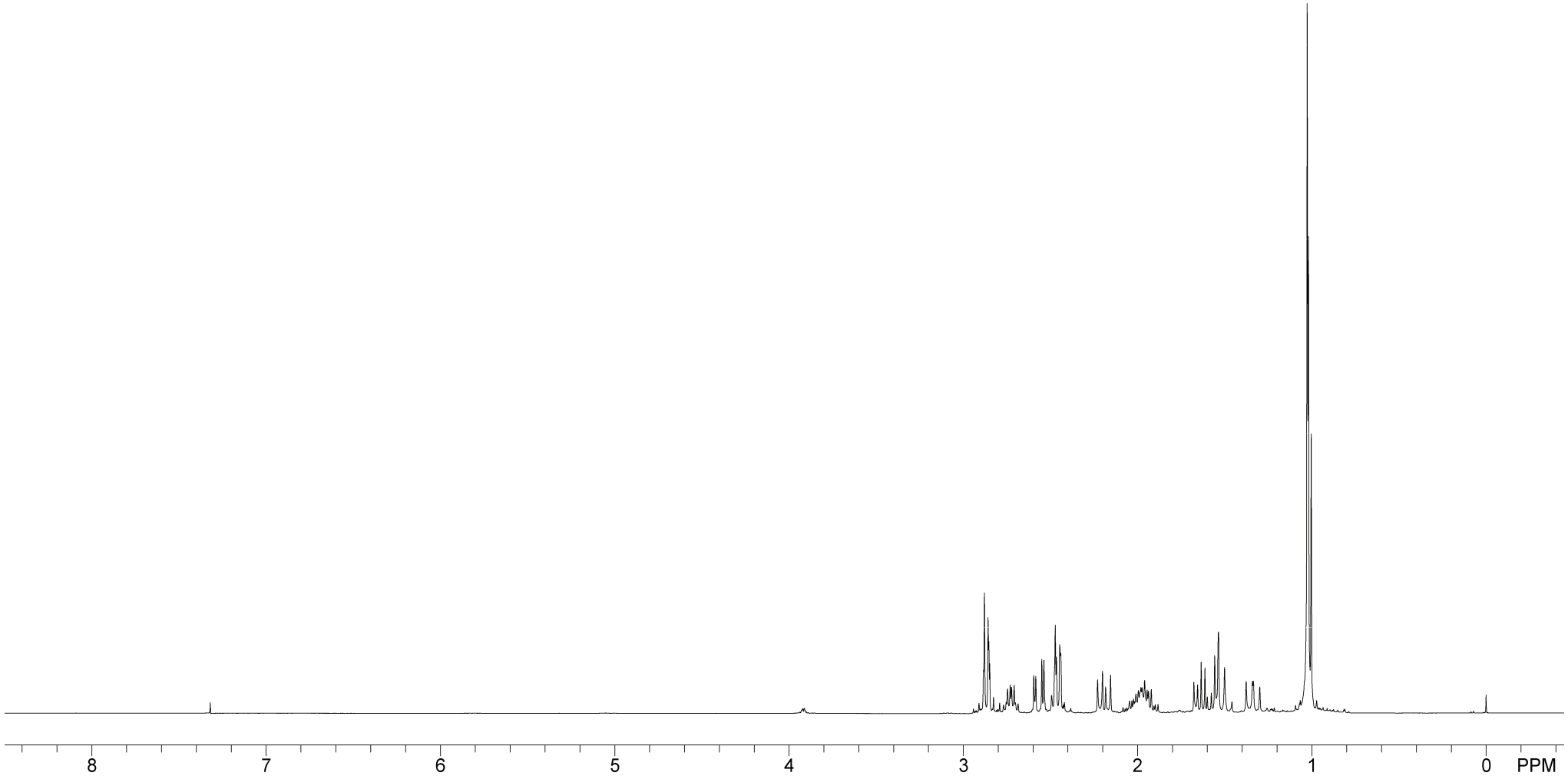

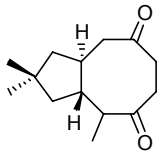

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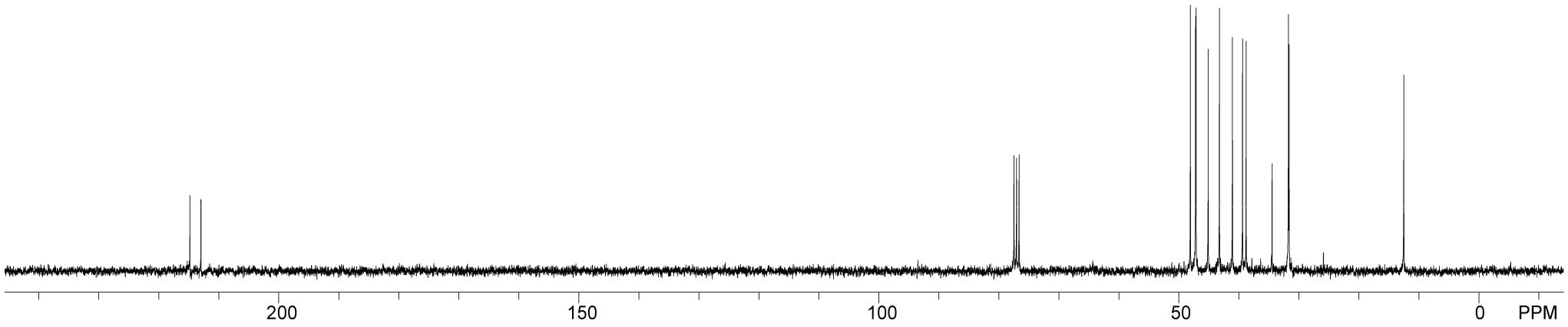

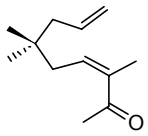

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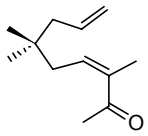

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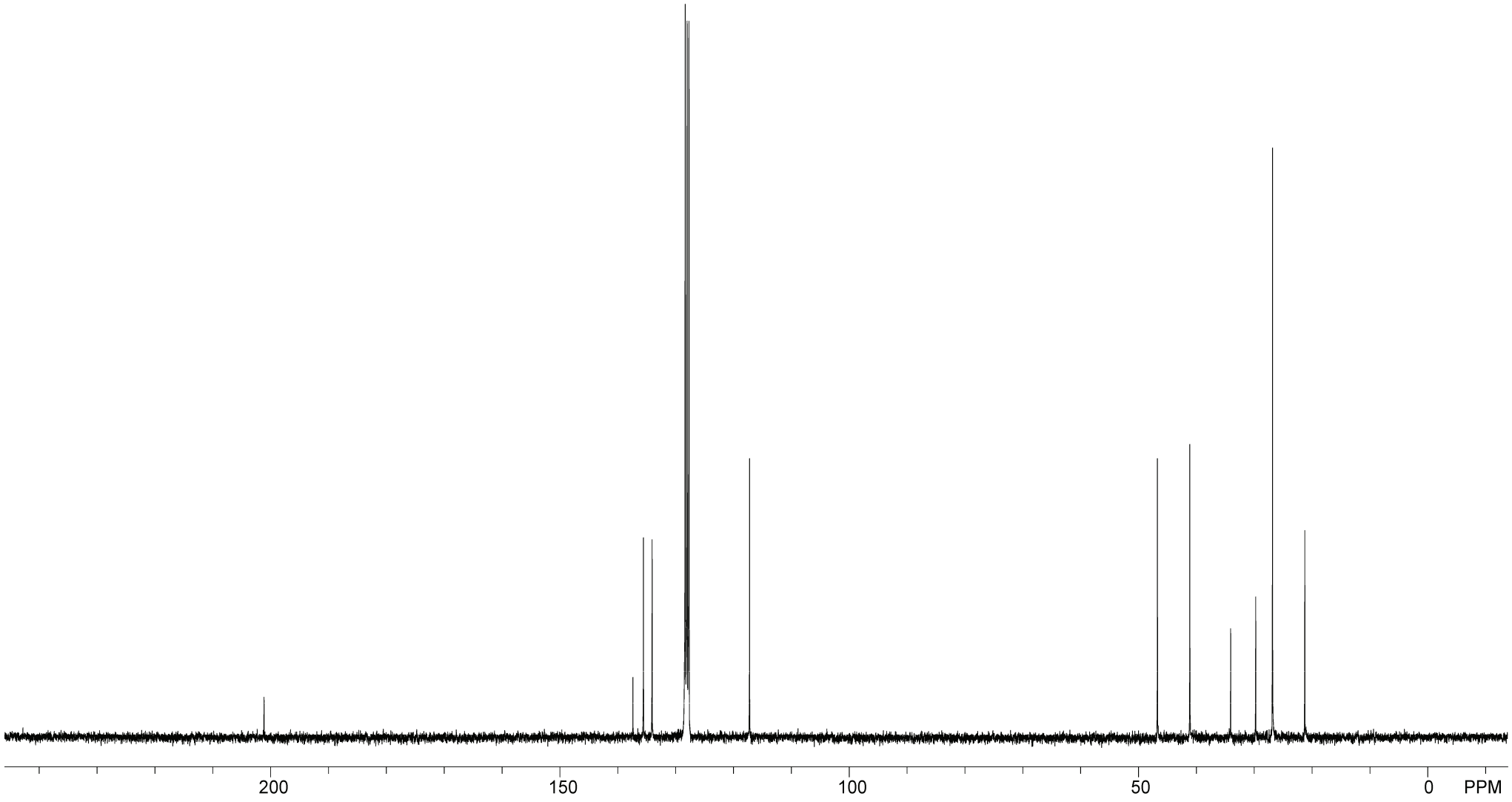

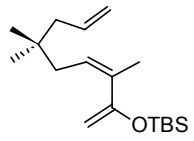

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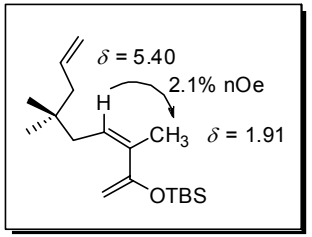

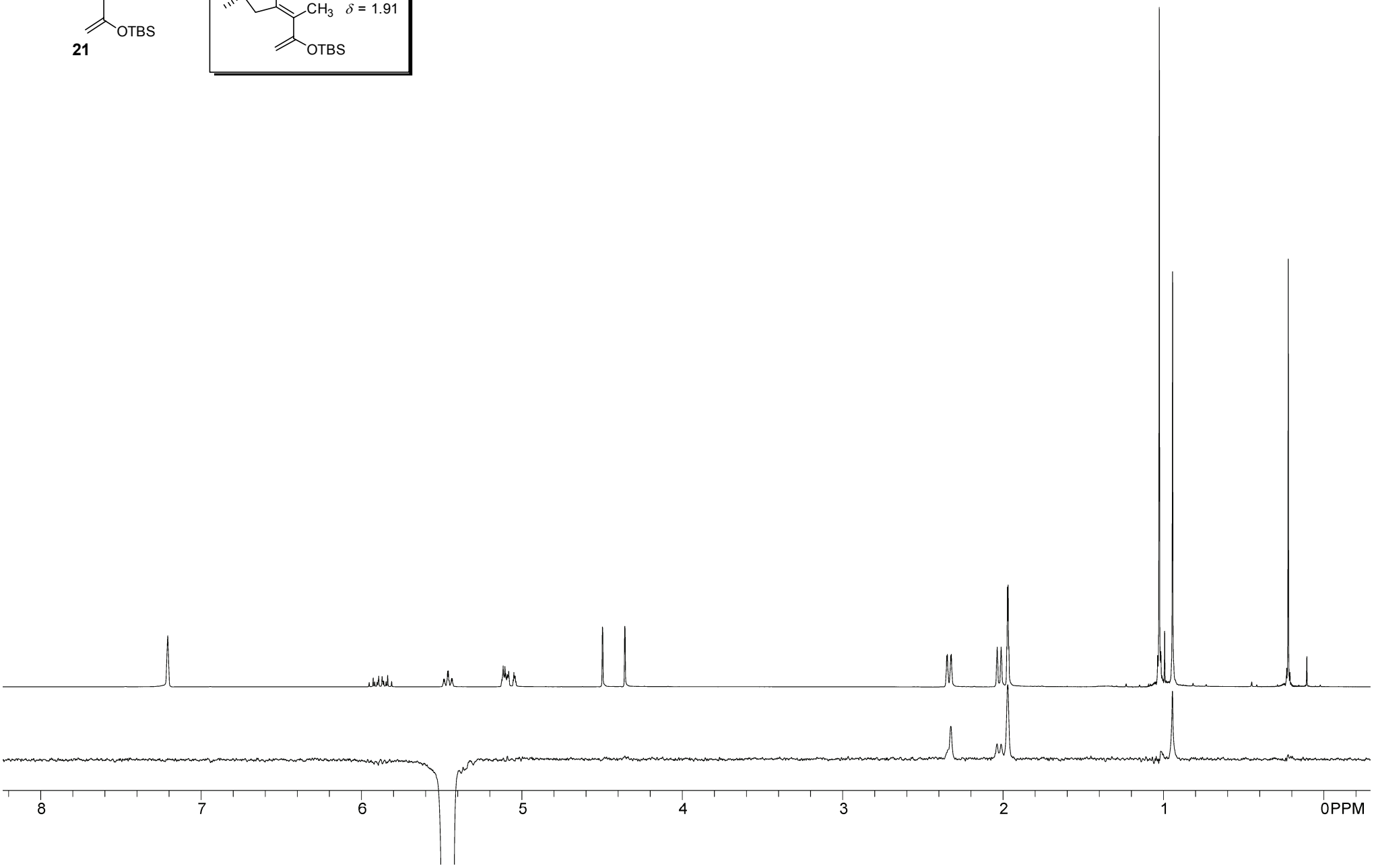

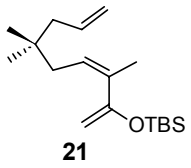

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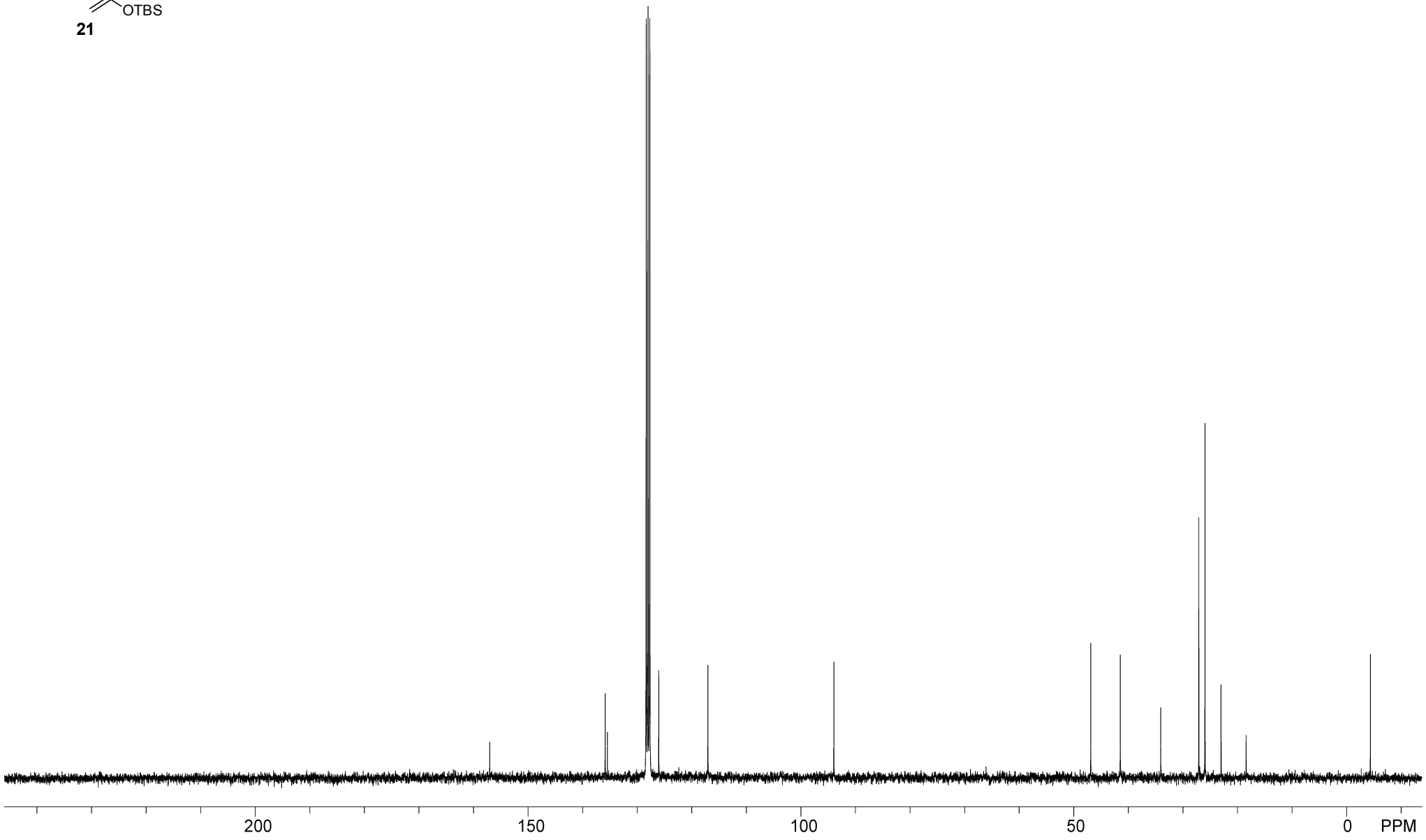

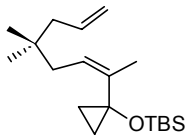

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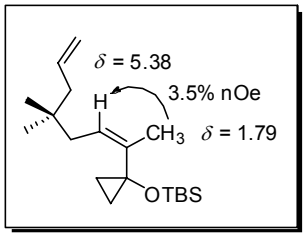

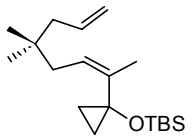

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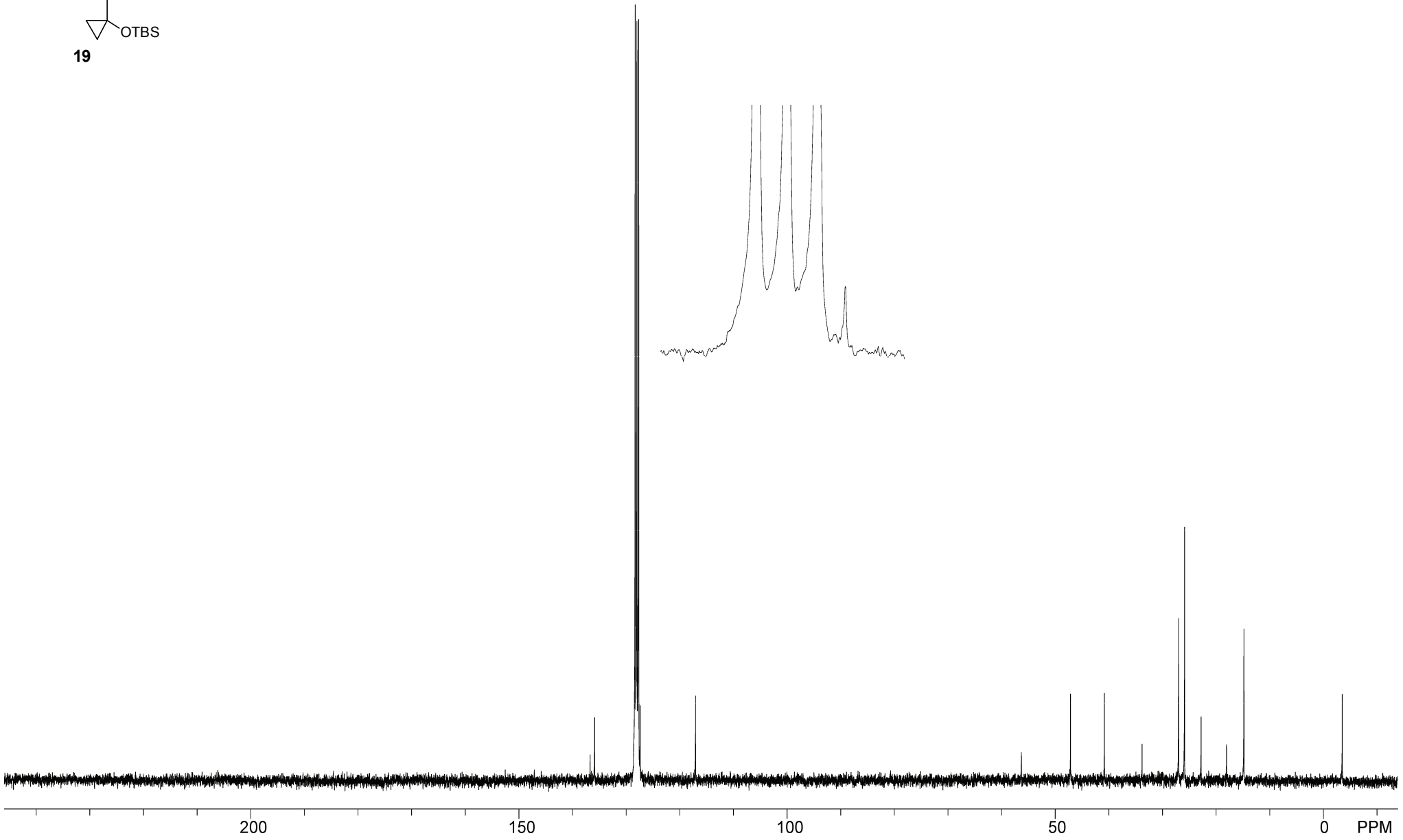

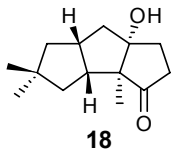

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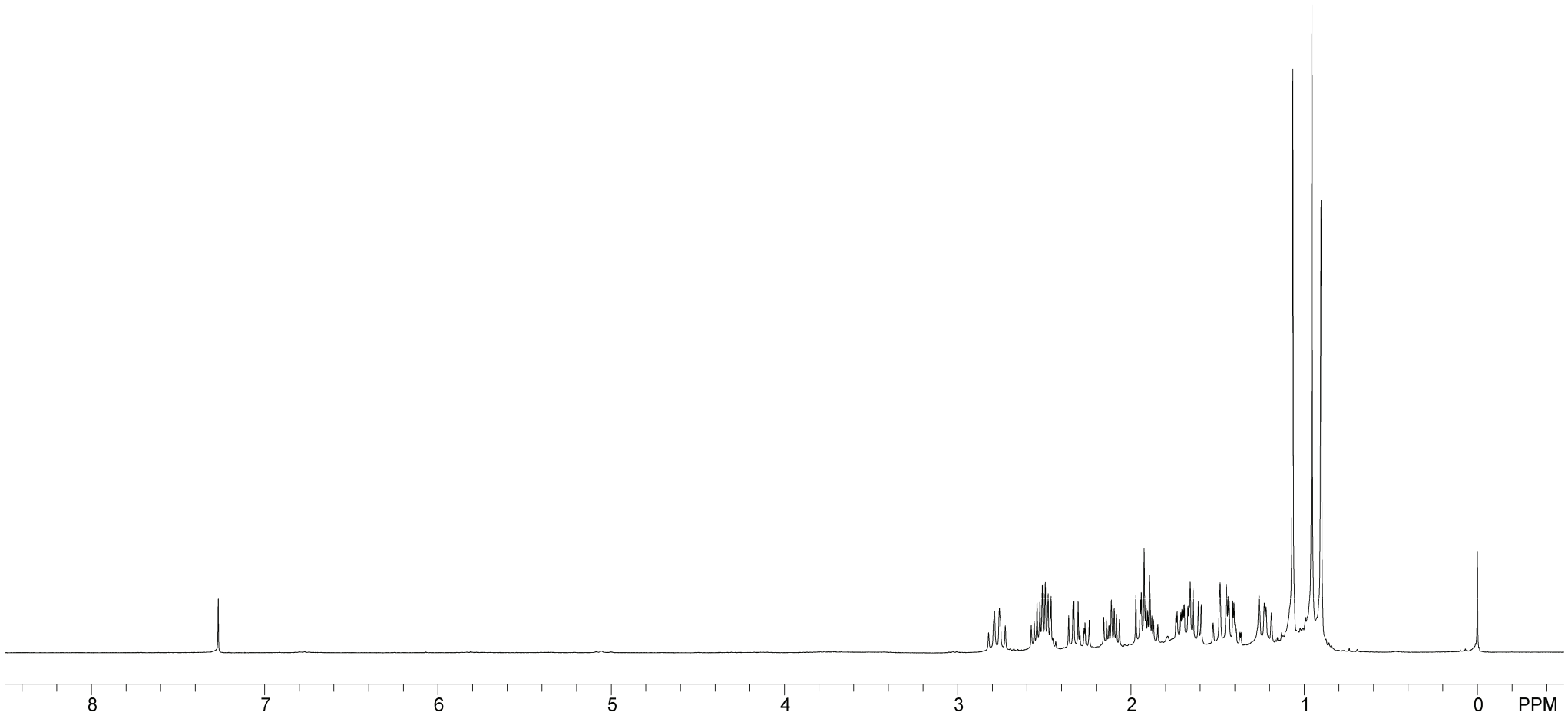

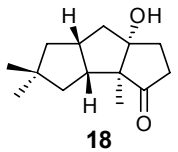

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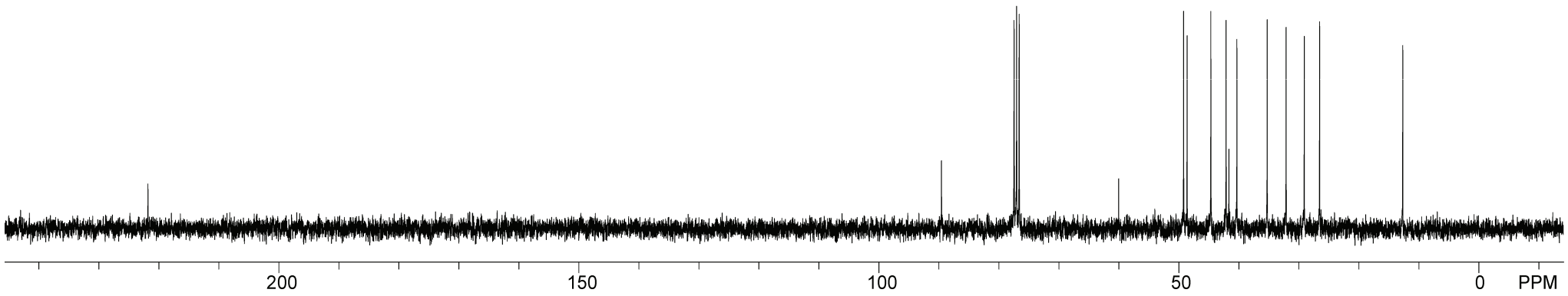

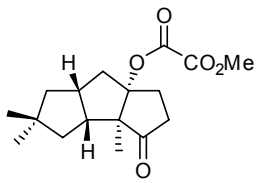

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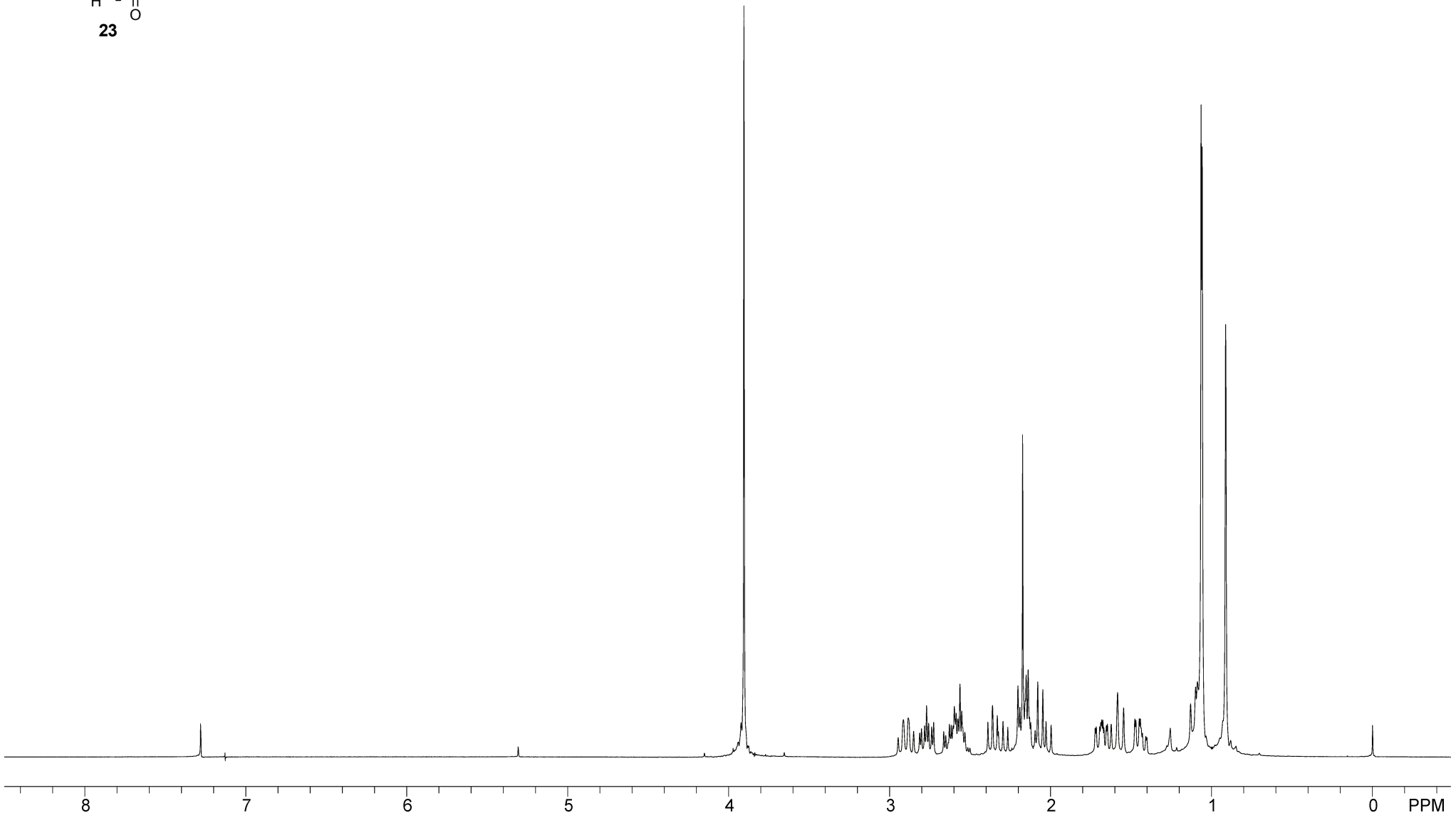

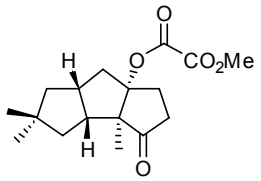

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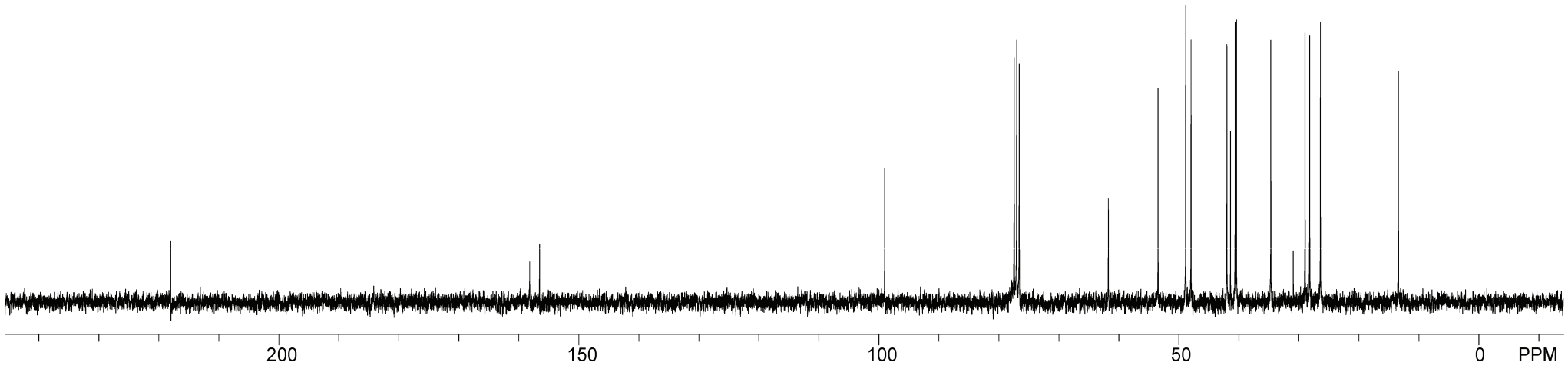

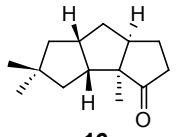

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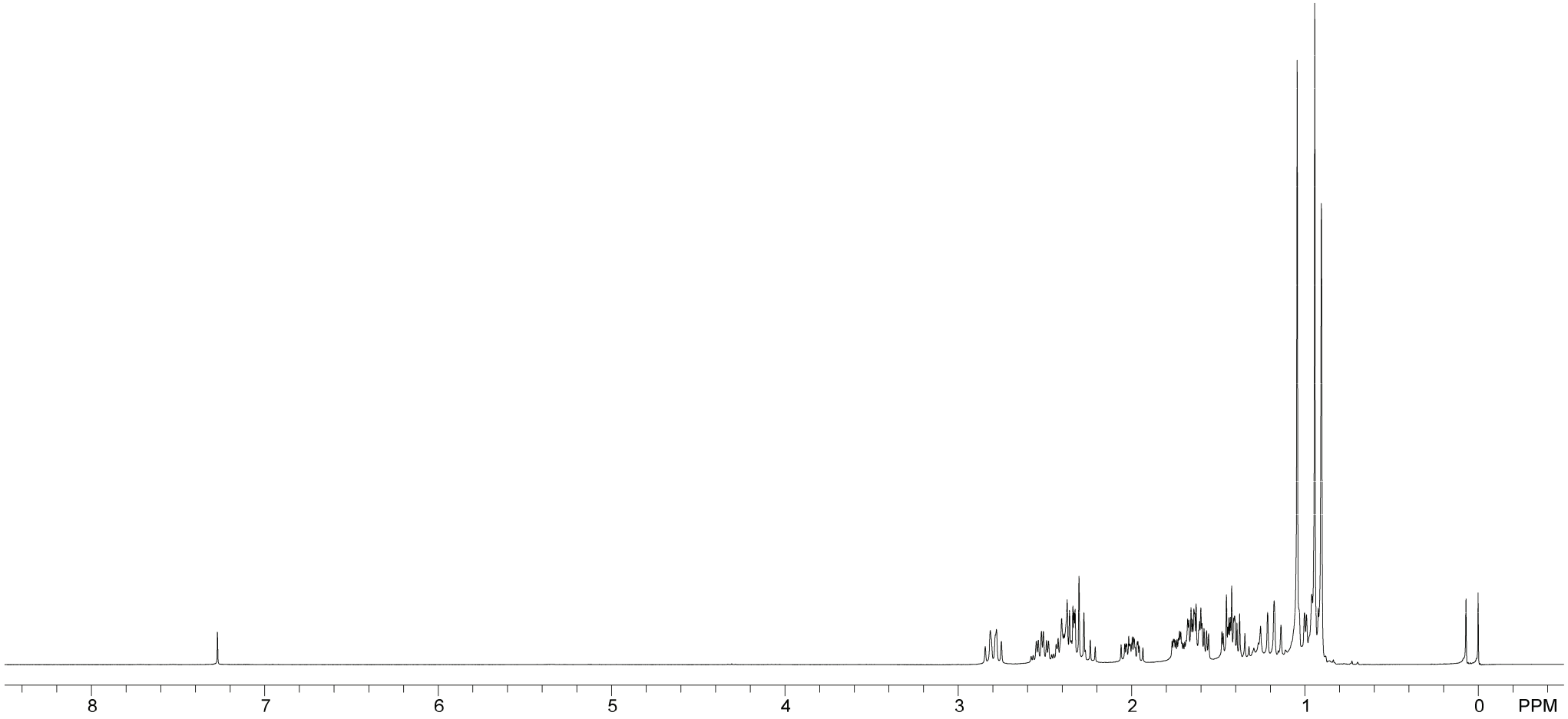

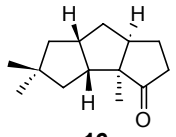

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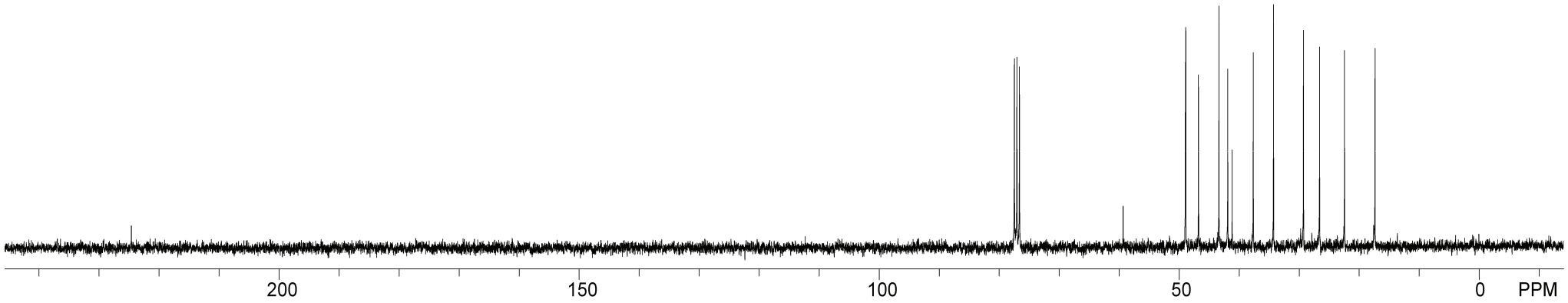

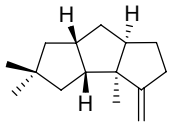

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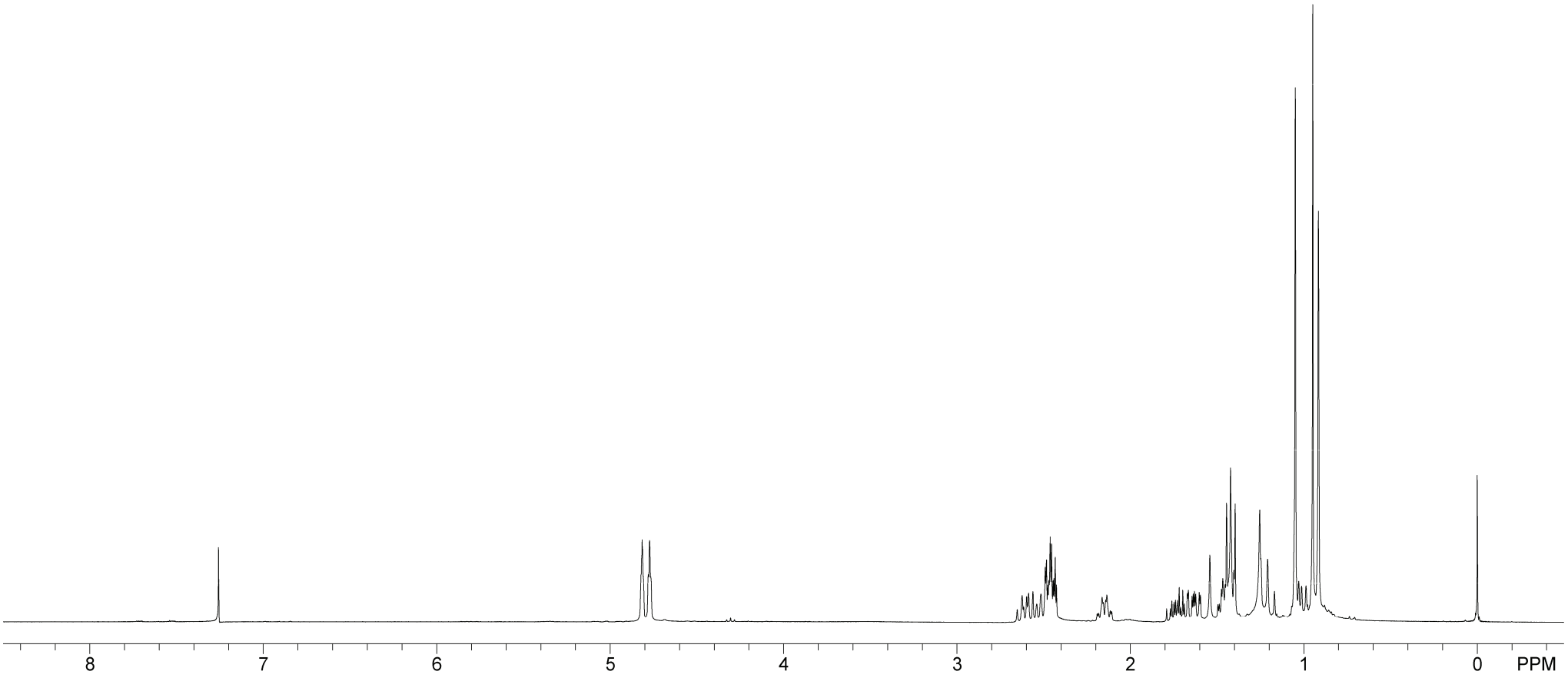

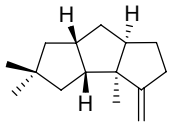

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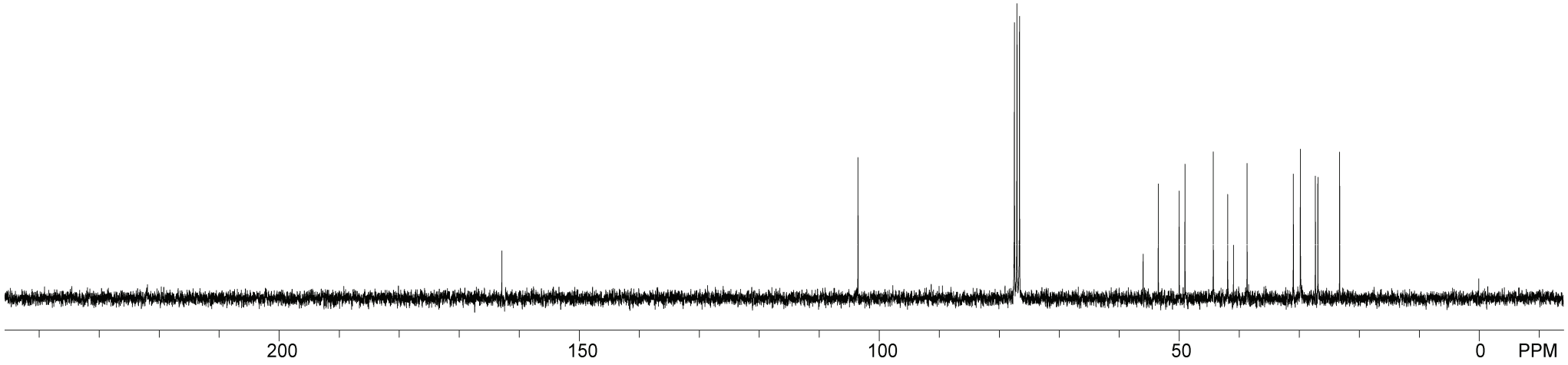

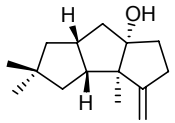

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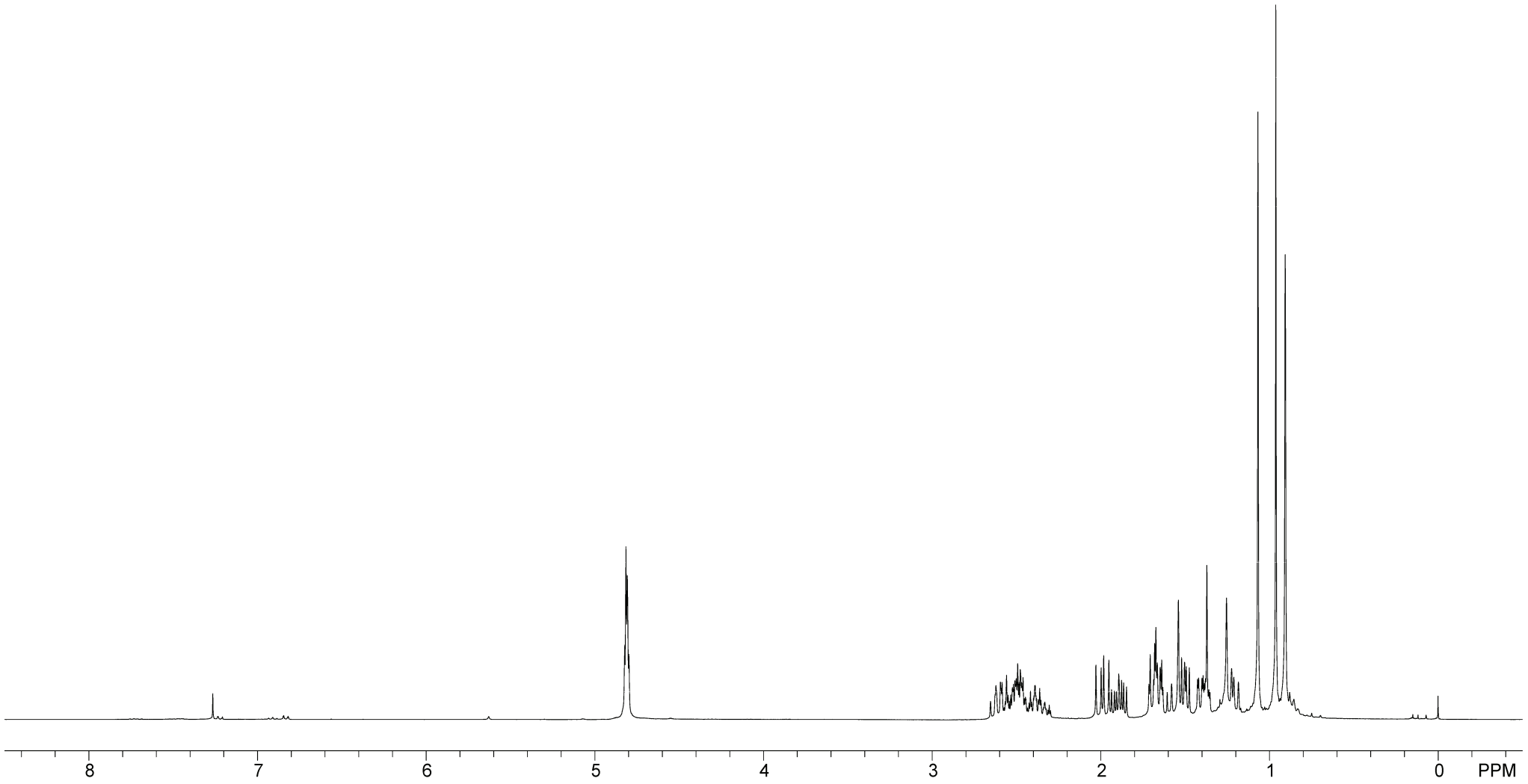

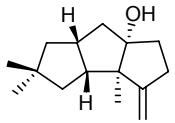

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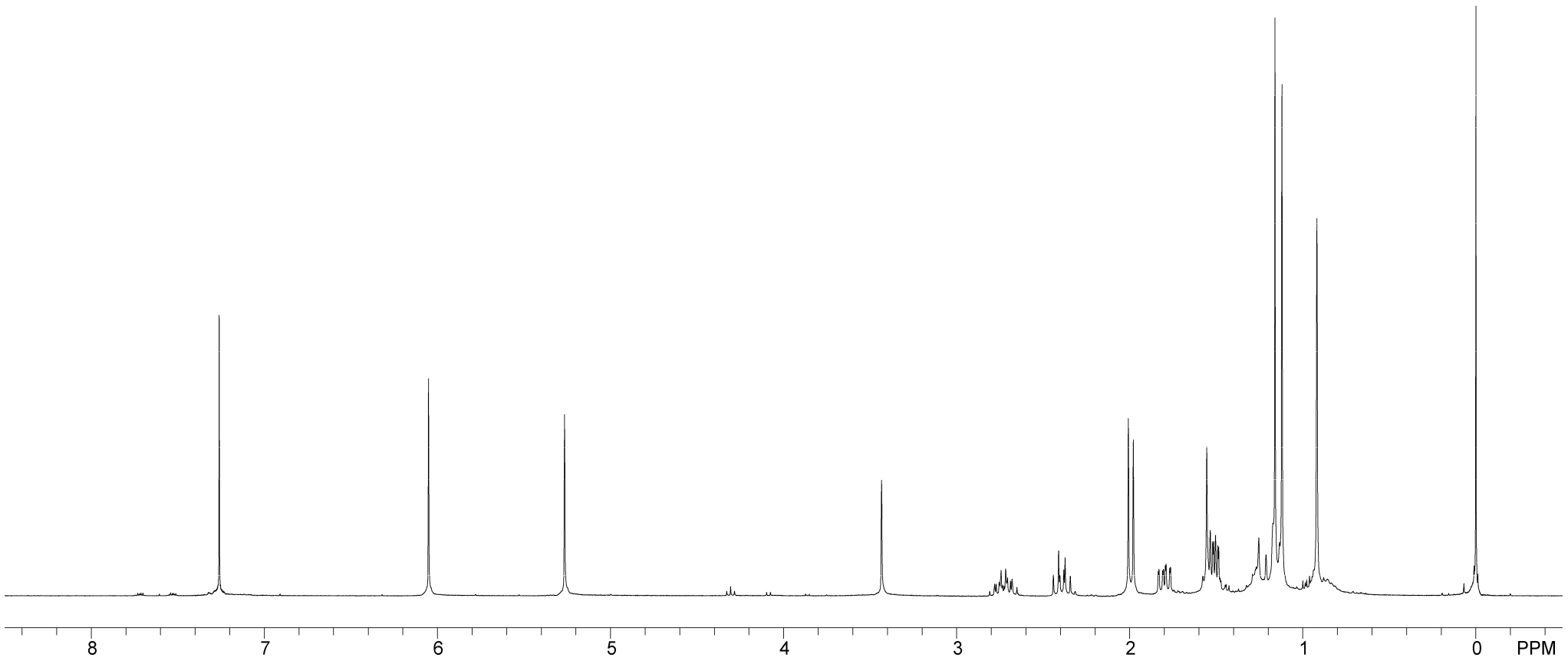

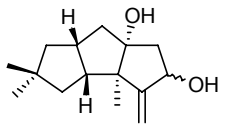

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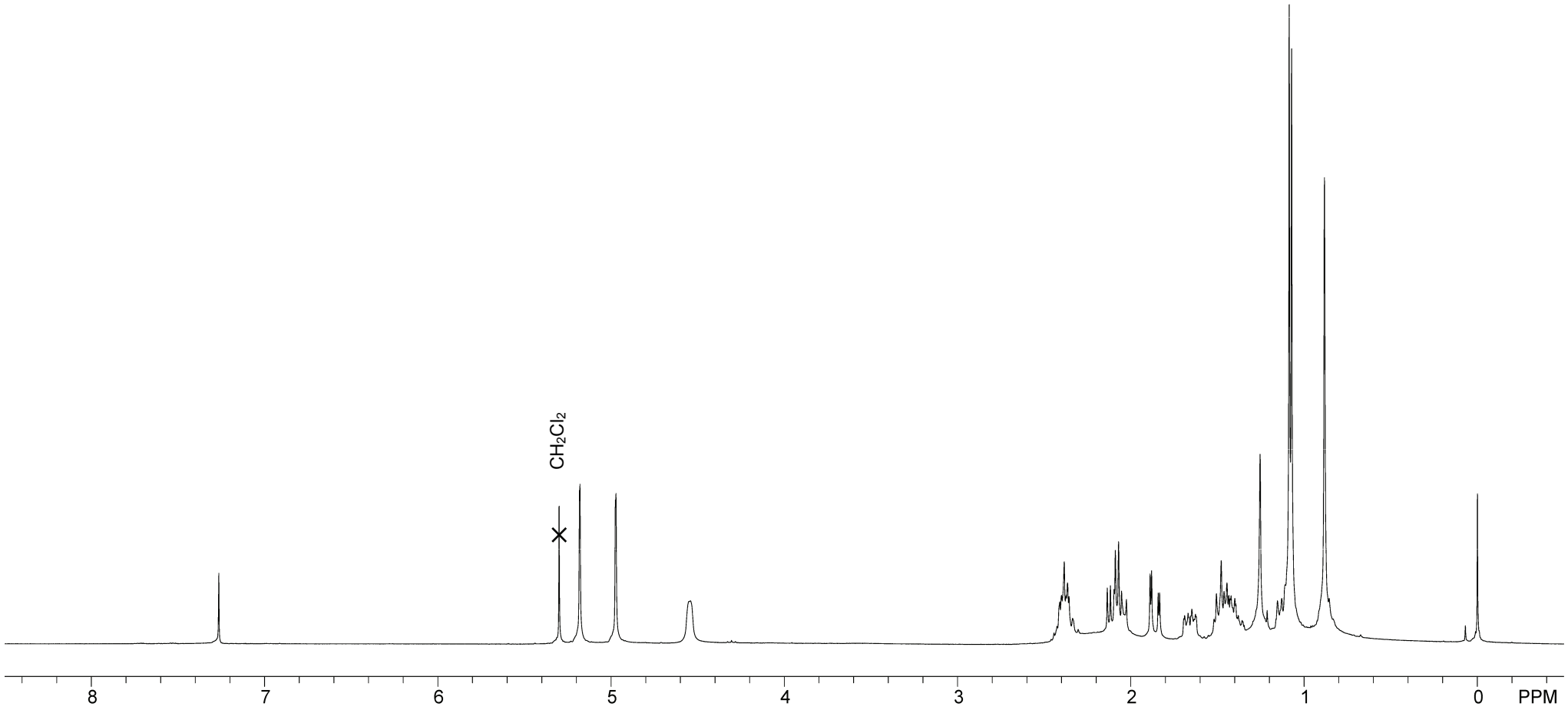

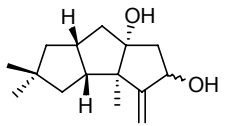

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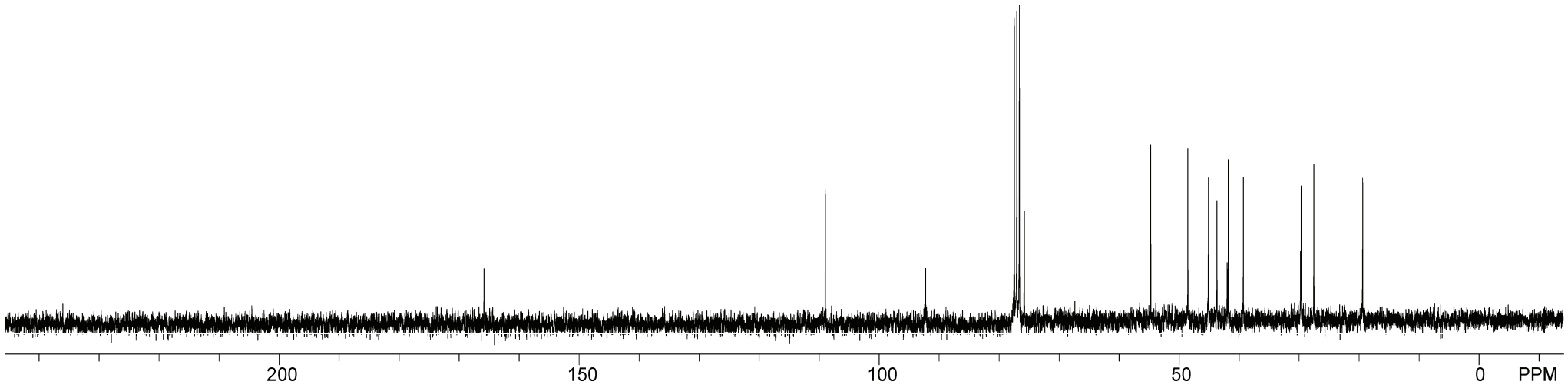

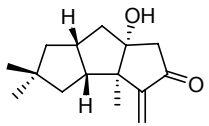

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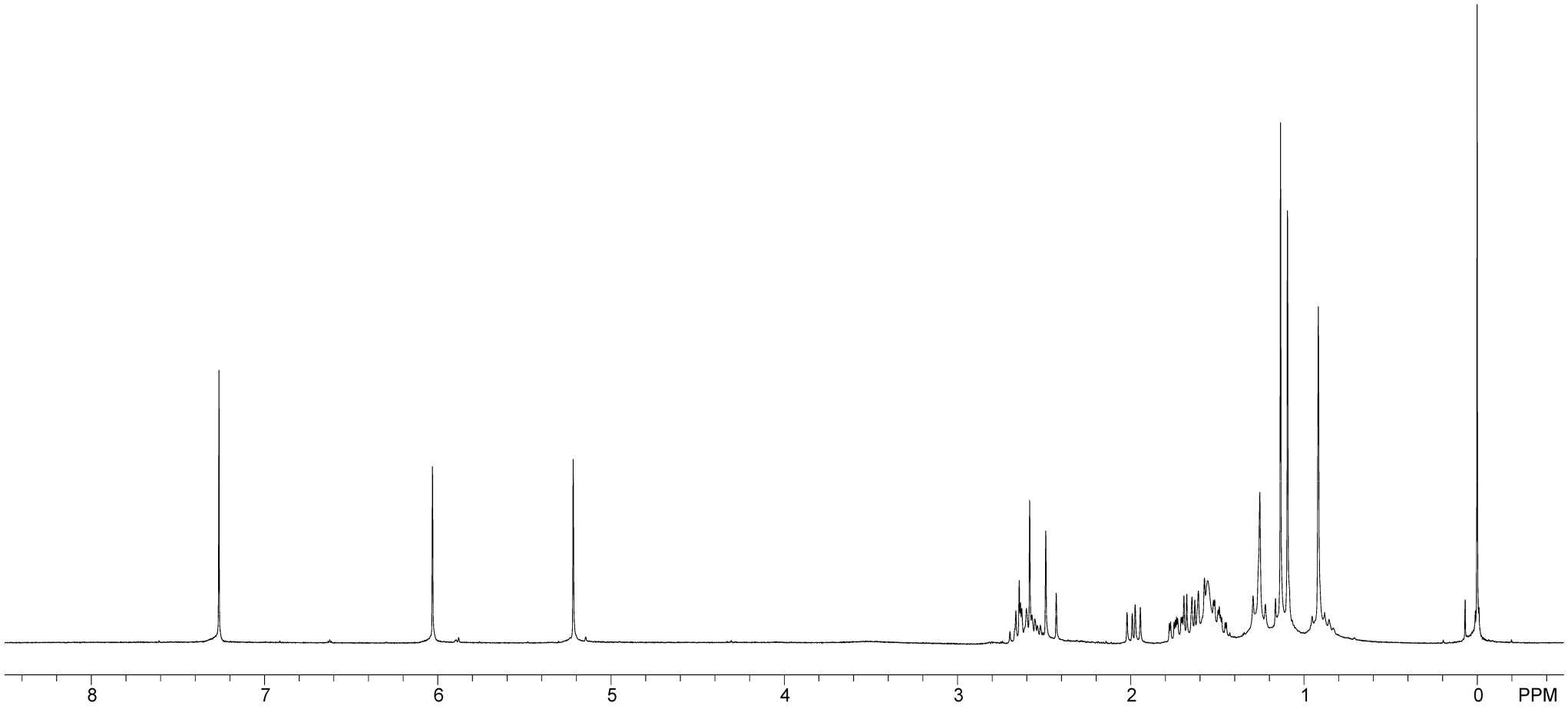

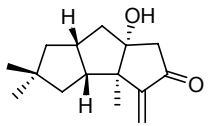

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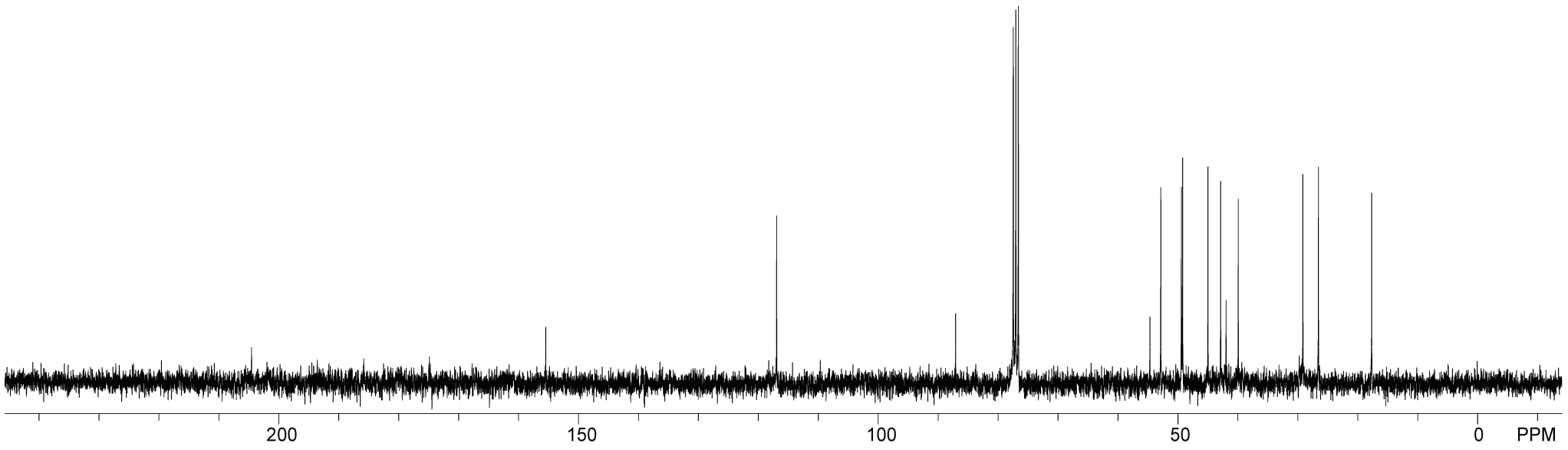

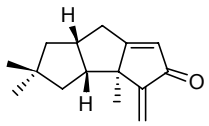

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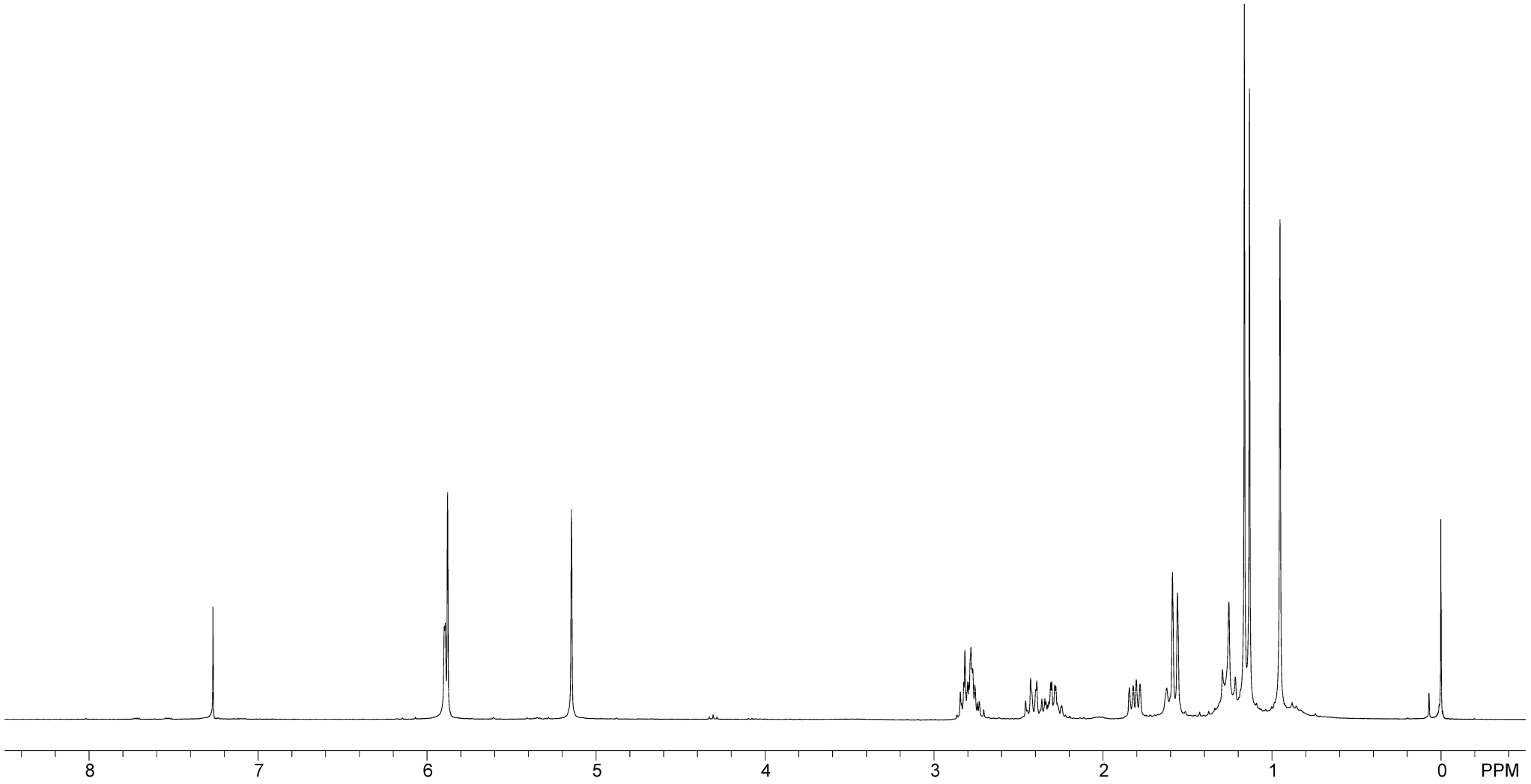

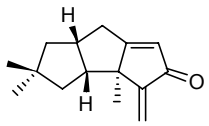

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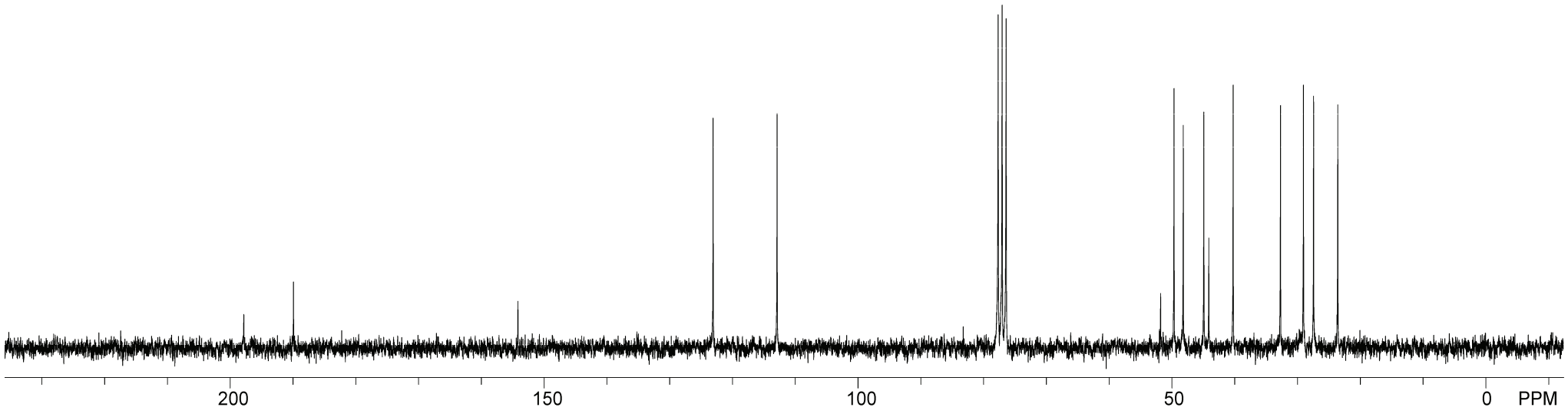

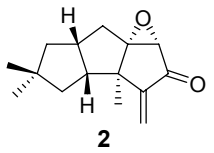

2

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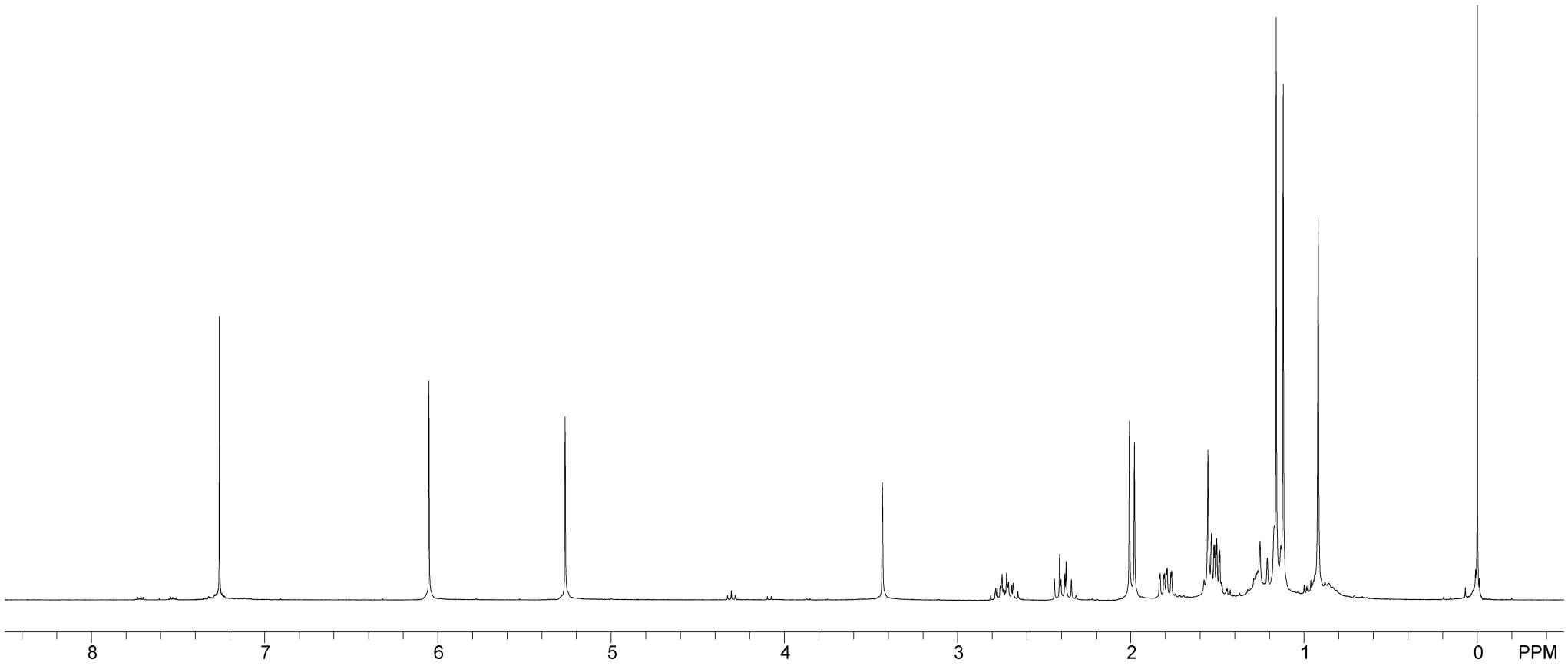

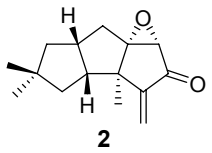

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1-desoxyhypnophilin