# Anguinomycins C & D and Derivatives: Total Syntheses, Modelling and Biological Evaluation on CRM-1 mediated Nucleocytoplasmic Transport

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**SUPPORTING INFORMATION**

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## 1. General Methods and Materials

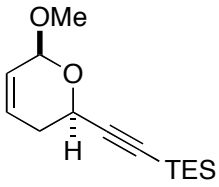
Unless otherwise stated, chemicals were purchased from Sigma-Aldrich, ABCR, Acros or Lancaster and used without further purification. Solvents for work-up and chromatography were distilled from technical quality. Solvents used for chemical transformations were either puriss quality or dried by filtration through activated aluminium oxide under argon or nitrogen ($H_2O$ content < 30 ppm, *Karl-Fisher* titration). All non-aqueous reactions were run in oven-dried or flame-dried glassware under a positive pressure of argon or nitrogen. Concentration under reduced pressure was performed by rotary evaporation at 40 °C (unless otherwise specified). Yields refer to purified, dried and spectroscopically pure compound. Analytical thin layer chromatography (TLC) was performed on Merck silica gel 60 $F_{254}$ plates (0.25 mm thickness) precoated with fluorescent indicator. The developed plates were examined under UV light and stained with ceric ammonium molybdate followed by heating. Flash chromatography was performed using silica gel 60 (230-240 mesh) from Fluka using a forced flow eluant at 0.3-0.5 bar pressure. Kugelrohr distillations were performed with a Büchi Glass Oven B-585. All $^1H$ and $^{13}C$ NMR spectra were recorded using either Varian Gemini 300 MHz ($^1H$) or 75 MHz ($^{13}C$), Varian Mercury 300 MHz ($^1H$) or 75 MHz ($^{13}C$), Bruker DRX 500 MHz ($^1H$) or 125 MHz ($^{13}C$), Bruker DPX 400 MHz ($^1H$) or 100 MHz ($^{13}C$), Bruker DRX 600 MHz ($^1H$) or 150 MHz ($^{13}C$), Bruker Advance 800 MHz ($^1H$) or 200 MHz ($^{13}C$) FT spectrometers at room temperature. Chemical shifts δ are reported in ppm, multiplicity is reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, quint. = quintet, sext. = sextet, sept. = septet, m = multiplet or unresolved and coupling constant *J* in Hz. Analytical gas chromatography (GC) was performed on *Hewelett Packard, HP6810*. *Column*: supelco β dex 120, 30 m x 0.25 mm x 0.25 μm. *Carrier gas*: $H_2$. *Temperature*: 120 °C isothermal. *Flow*: 2 mL/min. *Split ratio*: 40:1. *Detector*: FID. Analytical high-performance liquid chromatography (HPLC) was performed on a *Dionex Chromatography System* (Interface Chromeleon, ASI-100 automated sample injector, UV detector 170U or PDA-100 photodiode array detector, pump P680, TCC thermostated column compartment, degaser, MSQ-ESI mass spectrometric detector). The *flow rate* was 1 mL / min. *Column*: Phenomenex Gemini (5 μm) (C18 (150 x 4.6 mm)), solvent A: $H_2O$, solvent B: MeOH). Semi-preparative reversed-phase high-performance liquid chromatography (SP-HPLC) was performed on a *Dionex Chromatography System* (Interface Chromeleon, UV detector 170U or PDA-100 photodiode array detector, pump P680, TCC thermostated column compartment, degaser). The *flow rate* was 5 mL / min. *Column*: Phenomenex Gemini (5 μm) (C18 110A (150 x 10 mm)), solvent A: $H_2O$, solvent B: MeOH). All separations were performed at ambient temperature. IR spectra were recorded using a *Varian 2000 FT-IR ATR Spectrometer* or *Varian 800 FT-IR ATR Spectrometer*. The absorptions are reported in $cm^{-1}$ and the IR bands were assigned as *s* (strong), *m* (medium) or *w* (weak). Optical rotations $[\alpha]^T_D$ were measured at the sodium D line using a 1 mL cell with a 1 dm path length on a Jasco

DIP 1000 digital polarimeter, Jasco P-1020 digital polarimeter, Jasco P-2000 digital polarimeter and the concentration *c* is given in g/100mL and the used solvent is $CHCl_3$, MeOH or $H_2O$. Elemental analyses were performed by Mikroanalyse Labor of the Laboratorium für Organische Chemie der ETH Zürich or by Dr. *Euro Solari* in the Laboratory of Supramolecular Chemistry at the EPF Lausanne. All masses spectra were recorded by the Mass spectroscopy Service of Laboratorium für Organische Chemie der ETH Zürich on VG-TRIBRID (EI-MS) spectrometer and spectra measured at 70 eV, on TSQ 7000 ESI or by the Mass spectroscopy Service of EPF Lausanne on MICROMASS (ESI) Q-TOF Ultima API. Fragment ions are given in *m*/*z* with relative intensities (%) in parentheses. X-ray analyses were performed by Dr. *B. Schweizer* at the ETH Zürich or Dr. *R. Scopelliti* at the EPF Lausanne. UV spectra were measured on a *Varian Cary 1 Bio* UV-Visible spectrophotometer in a *Starna* quartz cell (10 mm path length). Lyophilisations were performed using a *Christ Freeze Dryer Alpha 1-2 LD plus*. Melting points (M.p.) were determined using a Büchi B-545 apparatus in open capillaries and are uncorrected.

# 2. Total Syntheses of Anguinomycins C & D

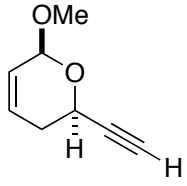
## 2.1. Synthesis of the C(1)-C(7) Fragment

### Triethyl(((2*R*,6*S*)-6-methoxy-3,6-dihydro-2*H*-pyran-2-yl)ethynyl)silane (9)



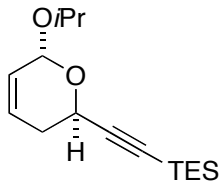

In a 10 mL flask under Ar was added 4 Å molecular sieves (1.26 g), **8** (0.30 g, 0.29 mmol, 0.02 equiv, 2.3 mol%), aldehyde **6** (2.12 g, 12.6 mmol, 1.00 equiv) and 1-methoxy-1,3-butadiene (**7**) (1.28 mL, 12.6 mmol, 1.00 equiv) and the mixture was stirred at RT for 18 hours. The reaction was diluted with pentane, filtered through Celite and concentrated. The residue was purified by chromatography on $SiO_2$ (pentane/$Et_2O$ 100:0 → 98:2) to afford **9** (2.73 g, 10.8 mmol, 86%, *e.e.* = 96.2) as a colorless oil. $R_f$ = 0.37 (pentane/$Et_2O$ 9.5:0.5). Optical rotation $[\alpha]^{27.9}_D$ (*c* 0.92, $CHCl_3$) = +105.8°. $^1$H-NMR (300 MHz, $CDCl_3$) δ 5.96-5.90 (m, 1 H), 5.66 (dq, $J_1$ = 10.3 Hz, $J_2$ = 1.9 Hz, 1 H), 5.01-4.98 (m, 1 H), 4.54 (dd, $J_1$ = 7.3 Hz, $J_2$ = 4.9 Hz, 1 H), 3.46 (s, 3 H), 2.42-2.20 (m, 2 H), 0,96 (t, *J* = 7.9 Hz, 9 H), 0.56 (q, *J* = 7.9 Hz, 6 H). $^{13}$C-NMR (75 MHz, $CDCl_3$) δ 127.5, 126.6, 105.5, 97.2, 86.1, 61.5, 55.2, 31.3, 7.5, 4.3. GC (β-dex chiral column) (T = 120°C): $t_{R1(minor)}$ = 42.08 minutes, $t_{R2\ (major)}$ = 43.00 minutes and *e.e.* = 96.2. Elemental analysis calcd for $C_{14}H_{24}O_2Si$: [C] 66.61 %, [H] 9.58 %, [O] 12.68 %, [Si] 11.13 %; found [C] 66.61 %, [H] 9.67 %. LRMS-ESI 275.3 (100, $[M+Na]^+$). FTIR ν 2956*m*, 2879*m*, 1982*w*, 1735*w*, 1336*w*, 1036*m*, 763*s*, 740*s* $cm^{-1}$.

### (2*R*,6*S*)-2-ethynyl-6-methoxy-3,6-dihydro-2*H*-pyran (10)



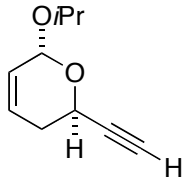

To a solution of **9** (200 mg, 0.79 mmol, 1.00 equiv) in THF (6.30 mL) at 0°C was dropwise added TBAF (1 M in THF) (3.16 mL, 3.16 mmol, 4.00 equiv). The reaction was stirred for 15 min, warmed to RT, stirred for 1 h and quenched with water (20 mL). The mixture was extracted with $Et_2O$ (3 x 30 mL) and the combined organic layers were washed with brine (1 x 30 mL), dried ($MgSO_4$), filtered and carefully concentrated *in vacuo* at 0 °C. The deprotected alkyne **10** was dried over molecular sieves and used directly in the next step without further purification. $R_f$ = 0.27 (pentane/$Et_2O$ 9:1). $^1$H-NMR (300 MHz, $CDCl_3$) δ 6.00 (dtd, $J_1$ = 10.3 Hz, $J_2$ = 4.0 Hz, $J_3$ = 1.5 Hz, 1 H), 5.74 (qd, $J_1$ = 10.3 Hz, $J_2$ = 2.0 Hz, 1 H), 5.01-4.99 (m, 1 H), 4.62 (dt, $J_1$ = 5.7 Hz, $J_2$ = 2.3 Hz, 1 H), 3.50 (s, 3 H), 2.40 (d, *J* = 2.3 Hz, 1 H), 2.37 (ddd, $J_1$ = 7.8 Hz, $J_2$ = 4.1 Hz, $J_3$ = 2.1 Hz, 2 H).

**Triethyl(((2*R*,6*R*)-6-isopropoxy-3,6-dihydro-2*H*-pyran-2-yl)ethynyl)silane (11)**




To a solution of *p*TsOH (76.0 mg, 0.40 mmol, 1.00 equiv) in *i*PrOH (0.4 M) (1.00 mL) was added **10** (100 mg, 0.40 mmol, 1.00 equiv) and the solution was stirred at RT for 2 hours. The reaction was quenched with dilute $NaHCO_3$ and extracted with $Et_2O$ (3 x 20 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated to afford **11** (96.0 mg, 0.34 mmol, 86%) as a colorless oil, which was used without further purification. Optical rotation $[\alpha]^{28.7}_D$ (*c* 0.795, $CHCl_3$) = +33.7°. $^1$H-NMR (400 MHz, $CDCl_3$) δ 5.96 (dd, $J_1$ = 10.0 Hz, $J_2$ = 5.4 Hz, 1 H), 5.71 (dd, $J_1$ = 10.1 Hz, $J_2$ = 1.1 Hz, 1 H), 5.14 (br. s, 1 H), 4.71 (dd, $J_1$ = 11.1 Hz, $J_2$ = 3.7 Hz, 1 H), 4.07 (sept., $J$ = 6.2 Hz, 1 H), 2.41 (dd, $J_1$ = 17.7 Hz, $J_2$ = 11.2 Hz, 1 H), 2.23 (dd, $J_1$ = 17.7 Hz, $J_2$ = 4.1 Hz, 1 H), 1.29 (d, $J$ = 6.2 Hz, 3 H), 1.19 (d, $J$ = 6.1 Hz, 3 H), 1.00 (t, $J$ = 7.8 Hz, 9 H), 0.63 (q, $J$ = 7.8 Hz, 6 H). $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 128.2, 126.3, 106.1, 93.4, 87.0, 70.3, 58.0, 32.1, 24.2, 24.4, 7.8, 4.7. LRMS-ESI 303.2 (100, $[M+Na]^+$). FTIR ν 2957*m*, 2012*m*, 2877*m*, 2186*w*, 1697*w*, 1461*w*, 1380*w*, 1317*w*, 1182*w*, 1098*w*, 1059*w*, 1024*s*, 1000*s*, 799*w*, 726*s* $cm^{-1}$.

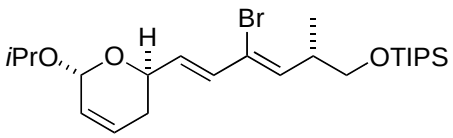
**(2*R*,6*R*)-2-ethynyl-6-isopropoxy-3,6-dihydro-2*H*-pyran (12)**




To a cooled (0 °C) solution of **11** (2.97 g, 10.6 mmol, 1.00 equiv) in THF (26.0 mL) was added TBAF (1 M in THF) (10.6 mL, 10.6 mmol, 1.0 equiv). The reaction was stirred for 15 minutes, warmed to RT, stirred for 1 hour and quenched with water (50 mL). The mixture was extracted with $Et_2O$ (3 x 40 mL) and the combined organic layers were washed with brine (1 x 60 mL), dried ($MgSO_4$), filtered and carefully concentrated *in vacuo* at 0 °C. The residue was purified by chromatography on $SiO_2$ (pentane/$Et_2O$ 100:0 → 95:5) to give the deprotected alkyne **12** (1.68 g, 10.1 mmol, 95%) as a colorless volatile oil. $R_f$ = 0.45 (cyclohexane/AcOEt 9:1). Optical rotation $[\alpha]^{26.9}_D$ (*c* 0.58, $CHCl_3$) = +80.6°. $^1$H-NMR (300 MHz, $CDCl_3$) δ 5.93 (dd, $J_1$ = 10.1 Hz, $J_2$ = 5.7 Hz, 1 H), 5.68 (ddd, $J_1$ = 10.2 Hz, $J_2$ = 2.9 Hz, $J_3$ = 1.3 Hz, 1H), 5.10 (br. s, 1 H), 4.67 (dddd, $J_1$ = 11.2 Hz, $J_2$ = 3.7 Hz, $J_3$ = 2.2 Hz, $J_4$ = 0.6 Hz, 1 H), 4.03 (sept., $J$ = 6.3 Hz, 1 H), 2.44 (d, $J$ = 2.2 Hz, 1 H), 2.37 (dddd, $J_1$ = 11.2 Hz, $J_2$ = 4.3 Hz, $J_3$ = 2.1 Hz, $J_4$ = 0.6 Hz, 1H), 2.19 (dddd, $J_1$ = 17.8 Hz, $J_2$ = 5.2 Hz, $J_3$ = 3.8 Hz, $J_4$ = 1.3 Hz, 1 H), 1.25 (d, $J$ = 6.2 Hz, 3 H), 1.16 (d, $J$ = 6.2 Hz, 3 H). $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 128.0, 126.4, 93.3, 83.2, 73.1, 70.3, 57.3, 32.4, 24.2, 22.4. FTIR ν 3306*m*, 2971*m*, 2928*m*, 2053*w*, 1736*w*, 1380*w*, 1184*w*, 1023*m*, 1002*w*, 784*s* $cm^{-1}$.

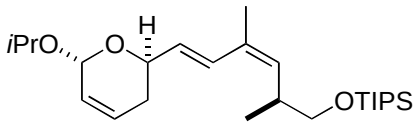
## 2.2. Synthesis of the Alkyl Iodides Fragments

### ((*S*,3*Z*,5*E*)-4-bromo-6-((2*R*,6*R*)-6-isopropoxy-3,6-dihydro-2*H*-pyran-2-yl)-2-methylhexa-3,5-dienyloxy)triisopropylsilane (16)




To a cooled (0 °C) solution of alkyne **12** (312 mg, 1.87 mmol, 1.00 equiv) in THF (9.40 mL, 0.2 M *vs* **12**) was added $Cp_2ZrHCl$ (374 mg, 1.44 mmol, 1.20 equiv). The flask was covered with an aluminium foil, stirred for 5 min at 0 °C and 1 hour at RT. In a separate flask $ZnCl_2$ (357 mg, 2.62 mmol, 1.40 equiv) was fused and dissolved in THF (11.2 mL). The solution was added to the solution of alkenylzirconocene at RT and the reaction stirred at RT for 30 minutes. In a separate flask, to a mixture of $Pd(PPh_3)_4$ (109 mg, 0.09 mmol, 0.05 equiv, 5 mol %) in THF (9.40 mL, 0.2 M *vs* **15**) was added DIBAL-H (10% in hexane) (187 μL, 0.19 mmol, 0.10 equiv, 10 %) and the mixture was stirred 20 minutes at RT and then dibromo olefin **15** (750 mg , 1.87 mmol, 1.00 equiv) was added. The dibromoolefin solution was stirred for 5 minutes at RT and then was added to the organozinc solution. The mixture was stirred 5 minutes at RT and then 13 hours at 40 °C. The reaction was quenched with water (30 mL) and extracted with $Et_2O$ (3 x 40 mL). The combined organic layers were dried ($MgSO_4$), filtered and concentrated. The residue was purified by chromatography on $SiO_2$ ($CH_2Cl_2$/cyclohexane 7:3) to give the coupled product **16** (756 mg, 1.55 mmol, 83%) as a pale yellow oil. $R_f$ = 0.39 ($CH_2Cl_2$/cyclohexane 7:3). Optical rotation $[\alpha]^{25.0}_D$ (*c* 0.97, $CHCl_3$) = +50.0°. $^1$H-NMR (300 MHz, $CDCl_3$) δ 6.28 (dd, $J_1$ = 14.8 Hz, $J_2$ = 1.2 Hz, 1 H), 6.07 (dd, $J_1$ = 14.8 Hz, $J_2$ = 5.3 Hz, 1 H), 6.02-5.97 (m, 1 H), 5.88 (d, $J$ = 8.9 Hz, 1 H), 5.72 (ddd, $J_1$ = 10.0 Hz, $J_2$ = 4.3 Hz, $J_3$ = 2.6 Hz, 1 H), 5.12 (d, $J$ = 2.8 Hz, 1 H), 4.58-4.51 (m, 1 H), 4.00 (sept., $J$ = 6.2 Hz, 1 H), 3.61 (ddd, $J_1$ = 15.8 Hz, $J_2$ = 9.4 Hz, $J_3$ = 5.8 Hz, 2 H), 2.99-2.86 (m, 1 H), 2.10-2.05 (m, 2 H), 1.22 (d, $J$ = 6.2 Hz, 3 H), 1.17 (d, $J$ = 6.1 Hz, 3 H), 1.05 (s, 24 H). $^{13}$C-NMR (75 MHz, $CDCl_3$) δ 137.3, 133.4, 129.3, 128.2, 126.0, 124.0, 93.1, 69.6, 66.8, 65.7, 39.5, 30.9, 24.0, 22.1, 18.1, 16.2, 12.1. HRMS-EI calcd for $C_{44}H_{43}BrO_3Si$: $[M–C_3H_7]^+$ 443.1612; found 443.1610. FTIR ν 2942*m*, 2893*m*, 2866*m*, 1463*w*, 1383*w*, 1180*w*, 1102*m*, 1028*s*, 1000*m*, 952*w*, 883*w*, 787*m*, 684*m* $cm^{-1}$.

**((*S*,*3Z*,*5E*)-6-((2*R*,6*R*)-6-isopropoxy-3,6-dihydro-2*H*-pyran-2-yl)-2,4-dimethylhexa-3,5-dienyloxy)–triisopropylsilane (17)**

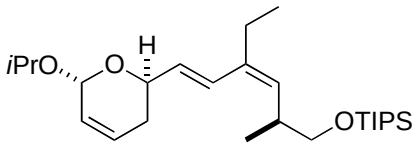



To a solution of **16** (100 mg , 0.23 mmol, 1.00 equiv) in THF (1.00 mL, 0.23 M *vs* **16**) was added $Pd(PPh_3)_4$ (24.0 mg, 0.02 mmol, 0.10 equiv). The solution was stirred for 10 minutes at RT, treated with $Me_2Zn$ (2.0 M in toluene) (0.21 mL, 0.42 mmol, 2.00 equiv) and the reaction was stirred at 45 °C for 24 hours. An additional portion of $Me_2Zn$ (0.10 mL, 0.21 mmol, 1.00 equiv) was added and the solution was stirred at 45 °C for 14 hours. The reaction was quenched with dilute $NH_4Cl$ and extracted with $Et_2O$ (3 x 15 mL). The combined organic layers were dried ($MgSO_4$), filtered and concentrated. The residue was purified by chromatography on $SiO_2$ ($CH_2Cl_2$/cyclohexane 7:3) to afford product **17** (66.3 mg, 0.16 mmol, 68%, *d.r.* > 97:3) as a colorless oil. $R_f$ = 0.21 ($CH_2Cl_2$/cyclohexane 7:3). Optical rotation $[\alpha]^{28.2}_D$ (*c* 0.62, $CHCl_3$) = +37.9°. $^1$H-NMR (300 MHz, $CDCl_3$) δ 6.69 (d, *J* = 15.7 Hz, 1 H), 6.01 (dddd, $J_1$ = 7.7 Hz, $J_2$ = 5.3 Hz, $J_3$ = 1.9 Hz, $J_4$ = 0.9 Hz, 1 H), 5.77-5.67 (m, 2 H), 5.19 (d, *J* = 9.6 Hz, 1 H), 5.13-5.12 (m, 1 H), 4.54-5.47 (m, 1 H), 4.02 (sept., *J* = 6.2 Hz, 1 H), 3.50 (ddd, $J_1$ = 16.9 Hz, $J_2$ = 9.4 Hz, $J_3$ = 6.5 Hz, 2 H), 2.87-2.74 (m, 1 H), 2.20-2.00 (m, 2 H), 1.82 (d, *J* = 1.2 Hz, 3 H), 1.24 (d, *J* = 6.2 Hz, 3 H), 1.18 (d, *J* = 6.1 Hz, 3 H), 1.05-1.04 (m, 24 H). $^{13}$C-NMR (75 MHz, $CDCl_3$) δ 134.2, 131.3, 129.3, 128.4, 128.1, 126.0, 93.0, 69.4, 68.0, 66.9, 34.9, 30.7, 23.8, 21.9, 20.4, 17.9, 17.5, 11.9. Elemental analysis calcd for $C_{25}H_{46}O_3Si$: [C] 71.03, [H] 10.97, [O] 11.35, [Si] 6.64; found [C] 71.11, [H] 10.99. HRMS-EI calcd for $C_{25}H_{46}O_3Si$: $[M]^+$ 422,3211; found 422.3219. FTIR ν 2942*m*, 2867*m*, 1462*w*, 1382*w*, 1182*w*, 1122*w*, 1101*w*, 1029*m*, 1000*w*, 780*s*, 683*m* $cm^{-1}$.

**Preparation of $Cl_2Pd$(DPEphos)**

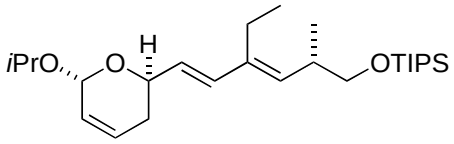
A mixture of $PdCl_2$ (200 mg, 1.12 mmol, 1.00 equiv) and LiCl (94.0 mg, 2.24 mmol, 2.00 equiv) in MeOH (2 mL) was heated to 50 °C for 10 minutes. DPE(phos) (638 mg, 1.18 mmol, 1.05 equiv) was added and the resulting mixture stirred at 50 °C for 8.5 hours, then cooled to RT, filtered, washed with MeOH and dried under high vacuum overnight affording $Cl_2Pd$(DPEphos) (755 mg, 1.05 mmol, 94%) as a yellow powder.

**((*S*,3*Z*,5*E*)-4-ethyl-6-((2*R*,6*R*)-6-isopropoxy-3,6-dihydro-2*H*-pyran-2-yl)-2-methylhexa-3,5-dienyloxy)triisopropylsilane (18)**




In a 5 mL flask containing $Cl_2Pd$(DPEphos) (2.20 mg, 0.003 mmol, 0.05 equiv) was added a solution of **16** (30.0 mg , 0.06 mmol, 1.00 equiv) in degassed[1] THF (0.75 mL). To the yellow mixture was slowly added $Et_2Zn$ (1.5 M in toluene) (80 μL, 0.12 mmol, 2.00 equiv) and a pale yellow solution was obtained. The tube was sealed and stirred at 50 °C for 14 hours. The red-brown colored solution was quenched by slow addition of saturated $NH_4Cl$ solution and extracted with $Et_2O$ (3x). The combined organic layers were dried ($MgSO_4$), filtered and concentrated. The residue was purified by chromatography on $SiO_2$ (hexane/acetone 99:1) to give product **18** (22.8 mg, 0.05 mmol, 84%, *d.r.* > 97:3) as a colorless oil. $R_f$ = 0.65 (hexane/acetone 99.5:0.5). Optical rotation $[\alpha]^{26.4}_D$ (*c* 0.28, $CHCl_3$) = +38.5°. $^1$H-NMR (300 MHz, $CDCl_3$) δ 6.61 (d, *J* = 15.9 Hz, 1 H), 6.04-5.99 (m, 1 H), 5.74 (dd, $J_1$ = 15.8 Hz, $J_2$ = 6.1 Hz, 1 H), 5.75-5.69 (m, 2 H), 5.19 (d, *J* = 9.5 Hz, 1 H), 5.13-5.12 (m, 1 H), 4.54-4.47 (m, 1 H), 4.02 (sept., *J* = 6.2 Hz, 1 H), 3.51 (ddd, $J_1$ = 16.6 Hz, $J_2$ = 9.4 Hz, $J_3$ = 6.5 Hz, 2 H), 2.79 (dq, $J_1$ = 9.3 Hz, $J_2$ = 6.6 Hz, 1 H), 2.20 (qd, $J_1$ = 7.4 Hz, $J_2$ = 0.9 Hz, 2 H), 2.14-2.00 (m, 2 H), 1.24 (d, *J* = 6.3 Hz, 3 H), 1.18 (d, *J* = 6.2 Hz, 3 H), 1.05-1.04 (m, 27 H). $^{13}$C-NMR (75 MHz, $CDCl_3$) δ 136.9, 132.1, 128.6, 128.4, 127.2, 126.0, 93.1, 69.5, 68.2, 67.1, 34.9, 30.9, 26.4, 23.9, 22.2, 18.1, 17.8, 17.7, 17.6, 13.3, 12.1, 12.0. Elemental analysis calcd for $C_{25}H_{46}O_3Si$: [C] 71.50, [H] 11.08, [O] 10.99, [Si] 6.43; found [C] 71.73, [H] 10.93. HRMS-EI calcd for $C_{22}H_{39}O_3Si$: $[M–C_3H_7]^+$ 393.2820; found 393.2830. FTIR ν 2961*m*, 2867*m*, 1463*w*, 1381*w*, 1181*w*, 1100*m*, 1029*m*, 1002*m*, 882*w*, 785*s*, 683*m* $cm^{-1}$.

**((*S*,3*E*,5*E*)-4-ethyl-6-((2*R*,6*R*)-6-isopropoxy-3,6-dihydro-2*H*-pyran-2-yl)-2-methylhexa-3,5-dienyloxy)triisopropylsilane (19)**

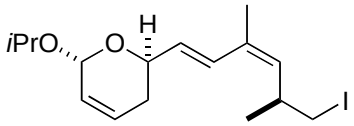



In a 5 mL flask containing $Pd(^tBu_3P)_2$ (0.60 mg, 0.001 mmol, 0.10 equiv) was added a solution of **16** (5.00 mg , 0.01 mmol, 1.00 equiv) in degassed THF (0.2 mL). To the mixture was slowly added $Et_2Zn$ (1.5 M in toluene) (13 μL, 0.02 mmol, 2.00 equiv) and a pale yellow solution was obtained. The tube was sealed and stirred at 50 °C for 3.5 hours. The dark brown solution was quenched by addition of saturated $NH_4Cl$ solution and extracted with $Et_2O$ (3x). The combined organic layers were

[1] The solvent was degassed using three freeze/pump/thaw cycles.

dried ($MgSO_4$), filtered and concentrated. The residue was purified by chromatography on $SiO_2$ (hexane/acetone 99:1 → 99:5) to give product **19** (3.25 mg, 0.008 mmol, 75%, *d.r.* > 97:3) as a colorless oil. $R_f$ = 0.65 (hexane/acetone 99.5:0.5). Optical rotation $[\alpha]^{22.4}_D$ (*c* 0.47, $CHCl_3$) = +21.0°. $^1$H-NMR (500 MHz, $CDCl_3$) δ 6.17 (d, *J* = 15.9 Hz, 1 H), 6.05-6.02 (m, 1 H), 5.77-5.74 (m, 1 H), 5.67 (dd, $J_1$ = 15.9 Hz, $J_2$ = 6.4 Hz, 1 H), 5.27 (d, *J* = 9.5 Hz, 1 H), 5.15-5.14 (m, 1 H), 4.52-4.48 (m, 1 H), 4.06 (sept., *J* = 6.0 Hz, 1 H), 3.61 (dd, $J_1$ = 9.5 Hz, $J_2$ = 5.6 Hz, 1 H), 3.48 (dd, $J_1$ = 9.5 Hz, $J_2$ = 7.5 Hz, 1 H), 2.73-2.67 (m, 1 H), 2.34-2.25 (m, 2 H), 2.19-2.03 (m, 2 H), 1.28 (d, *J* = 6.4 Hz, 3 H), 1.21 (d, *J* = 6.0 Hz, 3 H), 1.10-1.07 (m, 24 H), 1.05 (d, *J* = 6.8 Hz, 3 H). $^{13}$C-NMR (75 MHz, $CDCl_3$) δ 139.3, 135.6, 134.4, 128.6, 126.4, 126.1, 93.1, 69.4, 68.2, 67.0, 35.9, 31.0, 23.9, 22.1, 20.2, 18.1, 17.5, 14.2, 12.0. HRMS-ESI calcd for $C_{26}H_{48}O_3SiNa$: $[M+Na]^+$ 459.3271; found 459.3282. FTIR ν 2963*m*, 2943*m*, 2916*m*, 2866*m*, 1462*w*, 1381*w*, 1180*w*, 1099*w*, 1030*s*, 999*m*, 883*w*, 779*s*, 683*m* $cm^{-1}$.

**(2*R*,6*R*)-2-((*S*,1*E*,3*Z*)-6-iodo-3,5-dimethylhexa-1,3-dienyl)-6-isopropoxy-3,6-dihydro-2*H*-pyran (20)**

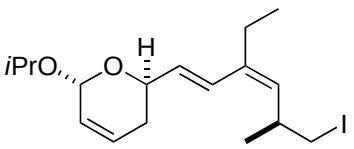



To a cooled (0 °C) solution of **17** (13.8 mg, 0.03 mmol, 1.00 equiv) in THF (160 µL) was added TBAF (1 M in THF) (64 µL, 0.06 mmol, 2.00 equiv). The reaction was stirred 1 hour at 0 °C and then 1 hour at RT. The reaction was quenched with water and extracted with $Et_2O$ (3x). The combined organic layers were dried ($MgSO_4$), filtered and concentrated. The residue was purified by chromatography on $SiO_2$ (hexane/AcOEt 8:2) to give the corresponding alcohol (8.4 mg, 0.03 mmol, 99%) as a colorless oil. $R_f$ = 0.19 ($CH_2Cl_2$/AcOEt 9:1). Optical rotation $[\alpha]^{28.9}_D$ (*c* 0.49, $CHCl_3$) = +29.2°. $^1$H-NMR (300 MHz, $CDCl_3$) δ 6.69 (d, *J* = 15.7 Hz, 1 H), 6.01 (ddd, $J_1$ = 10.0 Hz, $J_2$ = 4.7 Hz, $J_3$ = 2.1 Hz, 1 H), 5.77 (dd, $J_1$ = 15.8 Hz, $J_2$ = 6.0 Hz, 1 H), 5.76-5.70 (m, 1 H), 5.17-5.12 (m, 2 H), 4.52 (dt, $J_1$ = 10.3 Hz, $J_2$ = 5.3 Hz, 1 H), 4.01 (sept., *J* = 6.2 Hz, 1 H), 3.54-3.35 (m, 2 H), 2.94-2.79 (m, 1 H), 2.19-2.00 (m, 2 H), 1.86 (s, 3 H), 1.24 (d, *J* = 6.2 Hz, 3 H), 1.18 (d, *J* = 6.2 Hz, 3 H), 0.97 (d, *J* = 6.7 Hz, 3 H). $^{13}$C-NMR (75 MHz, $CDCl_3$) δ 133.6, 130.5, 128.5, 127.9, 127.8, 126.3, 93.3, 69.8, 67.9, 66.9, 34.9, 30.9, 24.0, 22.2, 20.8, 17.3. HRMS-EI calcd for $C_{16}H_{26}O_3$: $[M]^+$ 266.1877; found 266.1869. FTIR ν 3416*m*, 2970*m*, 2925*m*, 1455*w*, 1379*w*, 1317*w*, 1126*w*, 1100*m*, 1027*s*, 999*s*, 774*m*, 670*m* $cm^{-1}$.

To a cooled (0 °C) solution of the previously prepared alcohol (4.00 mg, 0.015 mmol, 1.00 equiv) in a mixture toluene/$Et_2O$ (375 µL/100µL) were added imidazole (14.4 mg, 0.21 mmol, 14.1 equiv) and $PPh_3$ (21.2 mg, 0.08 mmol, 5.4 equiv) and the resulting mixture stirred at 0 °C for 15 minutes. A solution of $I_2$ (19.8 mg, 0.078 mmol, 5.2 equiv) in $Et_2O$ (375 µL) was added dropwise and the resulting mixture covered by an aluminium foil, stirred for 10 minutes at 0 °C and then 2 hours at RT. The

mixture was directly filtered over cotton and concentrated. The residue was diluted in pentane, the precipitate filtered and the filtrated concentrated. Purification by chromatography on $SiO_2$ (hexane/EtOAc 100:0 → 99:1) afforded alkyl iodide **30** (4.2 mg, 0.011 mmol, 75%) as a colorless oil. $R_f$ = 0.48 (hexane/AcOEt 8.5:1.5). Optical rotation $[\alpha]^{25.0}_D$ (*c* 0.11, $CHCl_3$) = +6.4°. $^1$H-NMR (400 MHz, $CDCl_3$) δ 6.64 (d, *J* = 15.7 Hz, 1 H), 6.05-6.02 (m, 1 H), 5.80 (dd, $J_1$ = 15.7 Hz, $J_2$ = 5.8 Hz, 1 H), 5.77-5.75 (m, 1 H), 5.17 (d, *J* = 9.5 Hz, 1 H), 5.16 (s, 1 H), 4.58-4.53 (m, 1 H), 4.05 (sept., *J* = 6.2 Hz, 1 H), 3.17 (dd, $J_1$ = 9.4 Hz, $J_2$ = 5.7 Hz, 1 H), 3.09 (dd, $J_1$ = 9.4 Hz, $J_2$ = 7.3 Hz, 1 H), 2.92-2.82 (m, 1 H), 2.20-2.03 (m, 2 H), 1.87 (s, 3 H), 1.29 (d, *J* = 6.1 Hz, 3 H), 1.22 (d, *J* = 6.1 Hz, 3 H), 1.13 (d, *J* = 6.6 Hz, 3 H). $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 134.3, 132.7, 131.1, 128.6, 128.0, 126.7, 93.7, 70.1, 67.2, 34.4, 31.2, 24.3, 22.5, 21.9, 20.7, 15.2. HRMS-EI calcd for $C_{16}H_{25}O_2NaI$: $[M + Na]^+$ 399.0797; found 399.0801. FTIR ν 3322*w*, 2968*w*, 2924*w*, 1659*w*, 1377*w*, 1454*w*, 1377*w*, 1180*w*, 1099*w*, 1028*m*, 1000*m*, 785*s* $cm^{-1}$.

**(2*R*,6*R*)-2-((*S*,1*E*,3*Z*)-3-ethyl-6-iodo-5-methylhexa-1,3-dienyl)-6-isopropoxy-3,6-dihydro-2*H*-pyran (21)**

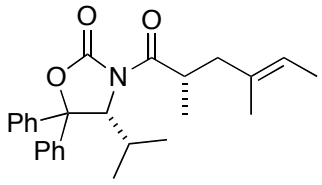



To a cooled (0 °C) solution of **18** (200 mg , 0.46 mmol, 1.00 equiv) in THF (3.0 mL) was added TBAF (1 M in THF) (970 µL, 0.97 mmol, 2.10 equiv). The reaction was stirred 5 minutes at 0 °C and then 1.5 hour at RT. The reaction was cooled to 0°C, quenched with water and extracted with $Et_2O$ (3x). The combined organic layers were dried ($MgSO_4$), filtered and concentrated. The residue was purified by chromatography on $SiO_2$ (hexane/AcOEt 8:2 → 7:3) to give the corresponding alcohol (126 mg, 0.45 mmol, 98%) as a colorless oil. $R_f$ = 0.25 (hexane/AcOEt 8:2). Optical rotation $[\alpha]^{22.7}_D$ (*c* 0.19, $CHCl_3$) = +21.2°. $^1$H-NMR (300 MHz, $CDCl_3$) δ 6.62 (d, *J* = 16.0 Hz, 1 H), 6.03-5.99 (m, 1 H), 5.80 (dd, $J_1$ = 16.0 Hz, $J_2$ = 6.1 Hz, 1 H), 5.75-5.71 (m, 1 H), 5.14-5.12 (m, 2 H), 4.52 (m, 1 H), 4.02 (sept., *J* = 6.1 Hz, 1 H), 3.53-3.47 (m, 1 H), 3.41-3.36 (m, 1 H), 2.91-2.80 (m, 1 H), 2.25 (q, *J* = 7.4 Hz, 2 H), 2.17-2.02 (m, 2 H), 1.35 (dd, $J_1$ = 8.0, $J_2$ = 4.2 Hz, 1 H), 1.25 (d, *J* = 6.1 Hz, 3 H), 1.18 (d, *J* = 6.1 Hz, 3 H), 1.08 (t, *J* = 7.4 Hz, 3 H), 0.98 (d, *J* = 6.4 Hz, 3 H). $^{13}$C-NMR (75 MHz, $CDCl_3$) δ 139.7, 131.7, 130.2, 128.9, 127.2, 126.6, 93.7, 70.1, 68.4, 67.4, 35.1, 31.2, 26.9, 24.3, 22.6, 17.7, 13.8. HRMS-ESI calcd for $C_{17}H_{27}O_3Na$: $[M + Na]^+$ 303.1931; found 303.1934. FTIR ν 3426*m*, 2967*m*, 2924*m*, 2874*m*, 1462*w*, 1381*w*, 1315*w*, 1261*w*, 1180*w*, 1099*m*, 1030*s*, 1003*m*, 799*w*, 718*w* $cm^{-1}$.

To a cooled (0 °C) solution of the previously prepared alcohol (125 mg, 0.45 mmol, 1.00 equiv) in a mixture toluene/$Et_2O$ (2:1) (20 mL), imidazole (425 mg, 6.24 mmol, 14. equiv) and $PPh_3$ (643 mg, 2.45 mmol, 5.5 equiv) were added and the resulting mixture was stirred at 0 °C for 10 minutes. A solution of $I_2$ (599 mg, 2.36 mmol, 5.3 equiv) in $Et_2O$ (6 mL) was added dropwise over a period of 15 minutes. The resulting mixture was covered by an aluminium foil and stirred 0 °C for 45 minutes. The mixture was filtered and the precipitate washed with $Et_2O$. The precipitate was triturated in EtOAc and filtered. The combined organic phase was concentrated and the residue diluted in a mixture hexane/EtOAc 7:3 and filtered over a pad of silica and concentrated. Purification by chromatography on $SiO_2$ (hexane/EtOAc 99.5:0.5 → 98:2) afforded alkyl iodide **21** (156 mg, 0.40 mmol, 89%) as a colorless oil. $R_f$ = 0.52 (hexane/AcOEt 9.5:0.5). Optical rotation $[\alpha]^{22.7}_D$ (*c* 1.00, $CHCl_3$) = –2.8°. $^1$H-NMR (400 MHz, $CDCl_3$) δ 6.53 (d, *J* = 16.0 Hz, 1 H), 6.03-6.00 (m, 1 H), 5.80 (dd, $J_1$ = 15.7 Hz, $J_2$ = 6.1 Hz, 1 H), 5.75-5.72 (m, 1 H), 5.14-5.12 (m, 2 H), 4.54-4.49 (m, 1 H), 4.03 (sept., *J* = 6.4 Hz, 1 H), 3.14 (dd, $J_1$ = 9.3 Hz, $J_2$ = 5.4 Hz, 1 H), 3.07 (dd, $J_1$ = 9.3 Hz, $J_2$ = 7.4 Hz, 1 H), 2.88-2.79 (m, 1 H), 2.22 (q, *J* = 7.4 Hz, 2 H), 2.14-2.02 (m, 2 H), 1.27 (d, *J* = 6.4 Hz, 3 H), 1.19 (d, *J* = 6.1 Hz, 3 H), 1.11 (d, *J* = 6.7 Hz, 3 H), 1.07 (t, *J* = 7.4 Hz, 3 H). $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 138.5, 132.5, 130.3, 128.9, 127.2, 126.6, 93.7, 70.2, 67.4, 34.4, 31.2, 26.7, 24.4, 22.6, 22.0, 15.7, 13.7. HRMS-ESI calcd for $C_{17}H_{27}O_2NaI$: $[M + Na]^+$ 413.0953; found 413.0941. FTIR ν 2967*m*, 2928*m*, 2878*w*, 1454*w*, 1377*w*, 1315*w*, 1180*w*, 1126*w*, 1099*w*, 1030*s*, 1003*m*, 964*w*, 718*w* $cm^{-1}$.

### 2.3. Synthesis of the Polyketidic Chain

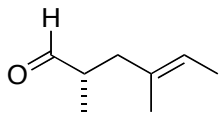
**(*R*)-3-((*S*,*E*)-2,4-dimethylhex-4-enoyl)-4-isopropyl-5,5-diphenyloxazolidin-2-one (24)**




In a 1L double-necked round bottom flask, a solution of DIPA (11.7 mL, 89.0 mmol, 1.25 equiv) in THF (200 mL) was cooled to 0 °C and *n*BuLi (1.6 M in hexane) (55.7 mL, 89.0 mmol, 1.25 equiv) was slowly added. The resulting solution was stirred at 0 °C for 30 minutes and then cooled to –78 °C. A precooled solution of **22** (24.0 g, 71.0 mmol, 1.00 equiv) in THF (130 mL) was slowly added and the resulting mixture stirred at –78 °C for 30 minutes followed by the slow addition of a precooled solution of (*E*)-1-bromo-2-methylbut-2-ene (**23**) (22.2 g, 149 mmol, 2.10 equiv) in THF (60 mL). The reaction was stirred at –78 °C for 5 minutes and then allowed to warm up to –10 °C while stirring was continued for 26 hours. The reaction was quenched by addition of saturated $NH_4Cl$ solution and extracted with $Et_2O$ (3x). The combined organic layers were dried ($MgSO_4$) and concentrated. The crude

pale yellow solid was washed with a small amount of ice-cold pentane to afford product **24** (26.4 g, 65.0 mmol, 92%, *d.r.* > 97:3) as a white crystalline solid. $R_f$ = 0.50 (cyclohexane/EtOAc 9:1). M.p. = 101-103 °C. Optical rotation $[\alpha]^{28.3}_D$ (*c* 1.00, $CHCl_3$) = +177.0°. $^1$H-NMR (300 MHz, $CDCl_3$) δ 7.48-7.44 (m, 2 H), 7.42-7.26 (m, 8 H), 5.40 (d, *J* = 3.2 Hz, 1H), 5.30-5.22 (m, 1 H), 3.90 (sext., *J* = 7.2 Hz, 1 H), 2.54 (dd, $J_1$ = 13.4 Hz, $J_1$ = 7.2 Hz, 1 H), 2.01-1.89 (m, 2 H), 1.65-1.64 (m, 3 H), 1.55 (dd, $J_1$ = 6.7 Hz, $J_2$ = 1.0 Hz, 3 H), 0.85 (d, *J* = 7.0 Hz, 3 H), 0.79 (d, *J* = 6.8 Hz, 3 H), 0.74 (d, *J* = 6.7 Hz, 3 H). $^{13}$C-NMR (75 MHz, $CDCl_3$) δ 176.7, 152.7, 142.2, 138.0, 132.8, 128.6, 128.4, 128.2, 127.7, 125.7, 125.5, 120.9, 89.0, 64.2, 43.6, 35.3, 29.6, 21.5, 16.1, 16.0, 15.3, 13.2. Elemental analysis calcd for $C_{26}H_{31}NO_3$: [C] 77.01 %, [H] 7.70 %, [N] 3.45 %; found [C] 76.79 %, [H] 7.67 %, [N] 3.52 %. HRMS-EI calcd for $C_{26}H_{31}NO_3$: $[M]^+$ 405.2299; found 405.2301. FTIR ν 2968*w*, 2934*w*, 2888*w*, 1776*s*, 1698*s*, 1495*w*, 1450*m*, 1385*m*, 1371*m*, 1348*m*, 1312*m*, 1246*m*, 1207*s*, 1174*s*, 1149*m*, 1123*m*, 1094*m*, 1056*m*, 1035*w*, 986*s*, 949*m*, 764*s*, 750*s*, 703*s*, 694*s*, 668*s*, 636*m* $cm^{-1}$.

**(*S*,*E*)-2,4-dimethylhex-4-enal (25)**

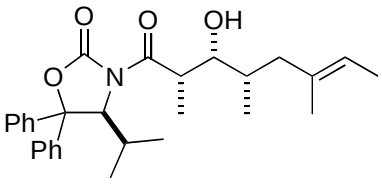


To a cooled (0 °C) suspension of $LiAlH_4$ (1.56 g, 41.2 mmol, 8.00 equiv) in $Et_2O$ (20 mL) was slowly added a solution of **24** ( 2.09 g, 5.15 mmol, 1.00 equiv) in $Et_2O$ (48 mL). The resulting solution was stirred for 30 minutes at 0 °C and then 3 hours at RT. The reaction was cooled to 0 °C and quenched by addition of $H_2O$ (3 mL), NaOH (15 %) (3 mL) and $H_2O$ (9 mL). The white granular aluminium salts were filtered over Celite and washed with $Et_2O$ (3x). The combined organic layers were dried ($MgSO_4$) and concentrated to afford the corresponding alcohol (0.66 g, 5.15 mmol, 100%) as a colorless oil. $R_f$ = 0.19 (cyclohexane/EtOAc 8.5:1.5). Optical rotation $[\alpha]^{24.6}_D$ (*c* 0.55, $CHCl_3$) = –4.7°. $^1$H-NMR (300 MHz, $CDCl_3$) δ 5.24 (qd, $J_1$ = 6.6 Hz, $J_2$ = 1.2 Hz, 1 H), 3.52-3.39 (m, 2 H), 2.11-2.02 (m, 1 H), 1.89-1.77 (m, 2 H), 1.61-1.57 (m, 6 H), 0.86 (d, *J* = 6.5 Hz, 3 H). $^{13}$C-NMR (75 MHz, $CDCl_3$) δ 134.3, 120.1, 68.5, 44.3, 33.7, 16.8, 15.7, 13.5. FTIR ν 3320*m*, 2917*m*, 1456*w*, 1037*m*, 786*s*, 668*w* $cm^{-1}$.

To a cooled (–78 °C) solution of oxalyl chloride (867 µL, 9.94 mmol, 2.00 equiv) in $CH_2Cl_2$ (10.5 mL) was added dropwise a solution of DMSO (1.41 mL, 20.0 mmol, 4.00 equiv) in $CH_2Cl_2$ (10.5 mL). After 5 minutes a solution of the previously prepared alcohol (637 mg, 4.97 mmol, 1.00 equiv) in $CH_2Cl_2$ (10.0 mL) was slowly added. Stirring at –78 °C was continued for 15 minutes, followed by addition of a solution of $NEt_3$ (4.16 mL, 29.8 mmol, 6 equiv) in $CH_2Cl_2$ (10.5 mL). The resulting solution was stirred at –78 °C for 20 minutes and then at 0 °C for 30 minutes. The reaction was quenched by addition of buffer phosphate (pH = 7) (32 mL) and the solution stirred at RT for 15 minutes. The organic phase was

separated and the aqueous phase extracted with $CH_2Cl_2$ (3x). The combined organic layers were washed with water (2x) and brine (1x), dried ($MgSO_4$) and concentrated. Purification by chromatography on $SiO_2$ ($CH_2Cl_2$/cyclohexane 7:3) afforded aldehyde **25** (619 mg, 4.91 mmol, 99%) as a colorless oil. $R_f$ = 0.42 (pentane/$Et_2O$ 9.5:0.5). Optical rotation $[\alpha]^{22.0}_D$ (*c* 0.93, $CHCl_3$) = +9.9°. $^1$H-NMR (300 MHz, $CDCl_3$) δ 9.61 (d, *J* = 2.1 Hz, 1 H), 5.29-5.23 (m, 1 H), 2.57-2.45 (m, 1 H), 2.41 (dd, $J_1$ = 13.4 Hz, $J_2$ = 6.6, Hz, 1 H), 1.98 (dd, $J_1$ = 13.7 Hz, $J_2$ = 7.7 Hz, 1 H), 1.59 (s, 3 H), 1.58 (d, *J* = 7.0 Hz, 3 H), 1.03 (d, *J* = 6.8 Hz, 3 H). $^{13}$C-NMR (75 MHz, $CDCl_3$) δ 205.5, 132.2, 121.6, 44.5, 40.9, 15.7, 13.5, 13.3. FTIR ν 2922*m*, 1708*w*, 1442*w*, 1378*w*, 777*s* cm$^{-1}$.

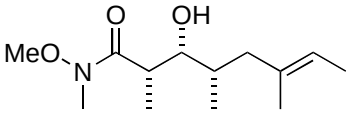
**(*S*)-3-((2*S*,3*R*,4*S*,*E*)-3-hydroxy-2,4,6-trimethyloct-6-enoyl)-4-isopropyl-5,5-diphenyloxazolidin-2-one (26)**




To a cooled (–5°C) solution of *ent*-**22** (84.4 mg, 0.25 mmol, 1.00 equiv) in $CH_2Cl_2$ (0.30 mL), $Bu_2BOTf$ (1 M in $CH_2Cl_2$) (263 μL, 0.26 mmol, 1.05 equiv) was slowly added and the solution turns from colorless to pale green. $NEt_3$ (42 μL, 0.30 mmol, 1.20 equiv) was slowly added over a period of 5 minutes and the solution turned to pale yellow. Stirring at 0 °C was continued for 1 hour. The resulting solution was cooled to –78 °C and aldehyde **25** (63 mg, 0.50 mmol, 2.00 equiv) in $CH_2Cl_2$ (0.20 mL) was slowly added and the mixture stirred for 1 hour at –78 °C and finally for 1 hour at 0 °C. The reaction was quenched at 0 °C by sequentially addition of buffer phosphate (pH = 7) (0.3 mL), MeOH (0.9 mL) and MeOH/$H_2O_2$ (2:1) (0.9 mL). The mixture was stirred for 1.5 hours at RT before dilution with $Et_2O$, washed with HCl (0.5 M) (1x), saturated $NaHCO_3$ solution (1x) and brine (1x), dried ($MgSO_4$) and concentrated. The residue was purified by chromatography on $SiO_2$ ($Et_2O$/pentane 8:2) to afford product **26** (89.2 mg, 0.19 mmol, 77%, *d.r.* > 87:13) as a white crystalline solid. $R_f$ = 0.33 (pentane/$Et_2O$ 7:3). M.p. = 98-99 °C. Optical rotation $[\alpha]^{24.5}_D$ (*c* 1.00, $CHCl_3$) = –103.6°. $^1$H-NMR (300 MHz, $CDCl_3$) δ 7.53-7.50 (m, 2 H), 7.43-7.28 (m, 8 H), 5.37 (d, *J* = 3.6 Hz, 1 H), 5.18-5.11 (m, 1 H), 3.83-3.74 (m, 1 H), 3.43 (td, $J_1$ = 6.7 Hz, $J_2$ = 4.9 Hz, 1 H), 2.06-1.90 (m, 2 H), 1.86 (d, *J* = 5.1 Hz, 1 H), 1.66-1.57 (m, 2 H), 1.56 (d, *J* = 6.6 Hz, 3 H), 1.51 (s, 3 H), 1.31 (d, *J* = 6.9 Hz, 3 H), 0.86 (d, *J* = 6.9 Hz, 3 H), 0.78 (d, *J* = 6.8 Hz, 3 H), 0.41 (d, *J* = 6.7 Hz, 3 H). $^{13}$C-NMR (75 MHz, $CDCl_3$) δ 176.1, 152.4, 142.2, 137.6, 133.6, 128.7, 128.4, 128.3, 127.8, 125.6, 125.2, 120.3, 89.4, 64.6, 44.0, 40.4, 33.0, 29.8, 21.7, 16.5, 15.4, 13.9, 13.5, 13.4. Elemental analysis calcd for $C_{29}H_{37}NO_4$: [C] 74.57 %, [H] 8.19 %, [N] 2.91 %; found [C] 74.68 %, [H] 8.03 %, [N] 2.91 %. HRMS-EI calcd for $C_{29}H_{35}NO_3$: $[M–H_2O]^+$

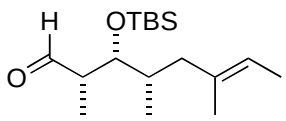
445.2611; found 445.2611. FTIR ν 3475*m*, 2965*m*, 2931*m*, 1781*s*, 1697*m*, 1494*w*, 1450*m*, 1374*m*, 1316*w*, 1254*w*, 1208*s*, 1176*s*, 1050*m*, 987*m*, 954*w*, 760*m*, 704*m*, 668*m* $cm^{-1}$.

**(2*S*,3*R*,4*S*,*E*)-3-hydroxy-*N*-methoxy-*N*,2,4,6-tetramethyloct-6-enamide (27)**




To a cooled (0 °C) suspension of MeONHMe•HCl (503 mg, 5.16 mmol, 6.00 equiv) in $CH_2Cl_2$ (5.2 mL) was added $AlMe_3$ (2 M in toluene) (2.10 mL, 5.16 mmol, 6.00 equiv). The resulting solution was stirred at 0 °C for 5 minutes, then at RT for 1 hour. The clear solution was cooled to 0 °C and **26** (400 mg, 0.86 mmol, 1.00 equiv) in $CH_2Cl_2$ (1.0 mL) was added by canula. Stirring at 0 °C was continued for 5 minutes, then at RT for 15 hours. The reaction mixture was slowly transferred in a diluted HCl solution (0.5 M) (27.0 mL), diluted with more $CH_2Cl_2$ and stirred at RT for 1hour. The aqueous layer was separated and extracted with $CH_2Cl_2$ (3x). The combined organic phases were washed with saturated $NaHCO_3$ (1x) and brine (1x), dried ($MgSO_4$) and concentrated. The residue was diluted in ice-cold $Et_2O$, the precipitated cleaved auxiliary was filtered and the filtrate was concentrated. Purification by chromatography on $SiO_2$ (pentane/$Et_2O$ 4:6) afforded product **27** (179 mg, 0.74 mmol, 86%) as white crystalline solid. An analytical sample was recrystallized (hexane) for X-ray analysis (crystallographic data are given at the end of the experimental part). $R_f$ = 0.21 (pentane/$Et_2O$ 4:6). M.p. = 54-55 °C. Optical rotation $[\alpha]^{22.4}_D$ (*c* 0.50, $CHCl_3$) = +6.7°. $^1$H-NMR (300 MHz, $CDCl_3$) δ 5.23 (q, *J* = 6.2 Hz, 1 H), 3.70 (s, 3 H), 3.57-3.53 (m, 1 H), 3.33 (d, *J* = 2.5 Hz, 1 H), 3.19 (s, 3 H), 3.12 (br. s, 1 H), 2.08 (d, *J* = 8.5 Hz, 1 H), 1.82-1.68 (m, 2 H), 1.60-1.58 (m, 6 H), 1.19 (d, *J* = 7.0 Hz, 3 H), 0.90 (d, *J* = 6.3 Hz, 3 H). $^{13}$C-NMR (75 MHz, $CDCl_3$) δ 178.0, 133.8, 120.4, 75.3, 61.4, 43.7, 36.3, 33.0, 31.9, 15.2, 14.7, 13.2, 11.2. Elemental analysis calcd for $C_{13}H_{25}NO_3$: [C] 64.17 %, [H] 10.35 %, [N] 5.76 %, [O] 19.72 %; found: [C] 64.23 %, [H] 10.46 %, [N] 5.67 %. LRMS-ESI 266.2 (100, $[M + Na]^+$). FTIR ν 3452*m*, 2965*s*, 2934*s*, 1640*s*, 1513*w*, 1457*s*, 1382*s*, 1300*m*, 1249*m*, 1176*m*, 1122*m*, 993*s*, 826*w* $cm^{-1}$.

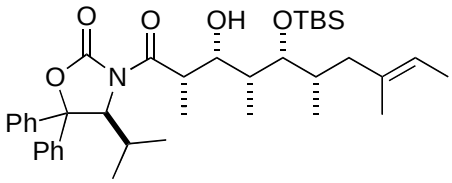
**(2*S*,3*R*,4*S*,*E*)-3-(*tert*-butyldimethylsilyloxy)-2,4,6-trimethyloct-6-enal (28)**




To a cooled (–20 °C) solution of **27** (467 mg, 1.92 mmol, 1.00 equiv) in $CH_2Cl_2$ (4.0 mL) were sequentially added 2,6-lutidine (257 $\mu$L, 2.21 mmol, 1.15 equiv) and TBSOTf (354 $\mu$L, 2.02 mmol, 1.05 equiv). The resulting solution was stirred for 15 min at –20 °C; then at 0 °C for 45 min. The reaction mixture was diluted in more $CH_2Cl_2$ and washed with diluted citric acid (pH = 4) (1x), saturated $NaHCO_3$ (1x), brine (1x), dried ($MgSO_4$) and concentrated. Purification by chromatography on $SiO_2$ (pentane/$Et_2O$ 9:1) afforded the corresponding TBS-protected product (680 mg, 1.90 mmol, 99%) as a clear oil. $R_f$ = 0.38 (hexane/EtOAc 9:1). Optical rotation $[\alpha]^{24.3}_D$ (*c* 1.00 , $CHCl_3$) = +6.8°. $^1$H-NMR (300 MHz, $CDCl_3$) δ 5.17 (q, *J* = 6.6 Hz, 1 H), 3.85 (dd, $J_1$ = 8.5 Hz, $J_2$ = 2.3 Hz, 1 H), 3.69 (s, 3 H), 3.16 (s, 3 H), 3.06 (br. s, 1 H), 2.14 (d, *J* = 12.4 Hz, 1 H), 1.86-1.78 (m, 1 H), 1.71-1.61 (m, 1 H), 1.56 (d, *J* = 6.6 Hz, 3 H), 1.52 (s, 3 H), 1.14 (d, *J* = 7.0 Hz, 3 H), 0.92 (s, 9 H), 0.73 (d, *J* = 6.8 Hz, 3 H), 0.08 (s, 6 H). $^{13}$C-NMR (75 MHz, $CDCl_3$) δ 176.9, 134.3, 119.7, 77.3, 61.4, 44.2, 39.0, 35.9, 32.4, 26.3, 18.6, 15.9, 15.4, 13.4, 13.3, –3.4, –3.5. Elemental analysis calcd for $C_{19}H_{39}NO_3Si$: [C] 63.82 %, [H] 10.99 %, [N] 3.92 %, [O] 13.42 %, [Si] 7.85 %; found [C] 63.79 %, [H] 11.00 %, [N] 4.10 %. LRMS-ESI 380.2 (100, $[M + Na]^+$). FTIR ν 3369*s*, 2959*m*, 2931*m*, 2857*m*, 1662*s*, 1461*m*, 1382*m*, 1252*m*, 1176*w*, 1108*m*, 1049*s*, 997*s*, 869*m*, 833*s*, 773*s* $cm^{-1}$.

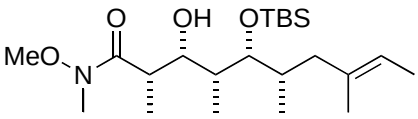
To a cooled (–78 °C) solution of the previously prepared TBS-protected product (663 mg, 1.85 mmol, 1.00 equiv) in THF (13.2 mL) was added DIBAL-H (1 M in hexane) (3.60 mL, 3.60 mmol, 2.00 equiv). The resulting solution was stirred at –78 °C for 1 hour; then quenched by addition of saturated Rochelle's salt, diluted in $Et_2O$ and vigorously stirred at RT for 1 hour. The aqueous layer was extracted with $Et_2O$ (3x) and the combined organic phase dried ($MgSO_4$) and concentrated (bath T < 20 °C). Purification by chromatography on $SiO_2$ (hexane/EtOAc 9.5:0.5) afforded aldehyde **28** (551 mg, 1.85 mmol, 100%) as a colorless oil. $R_f$ = 0.70 (cyclohexane/EtOAc 9:1). Optical rotation $[\alpha]^{25.0}_D$ (*c* 0.20, $CHCl_3$) = +53.5°. $^1$H-NMR (400 MHz, $CDCl_3$) δ 9.85 (s, 1 H), 5.22 (q, *J* = 6.5 Hz, 1 H), 4.00-3.98 (m, 1 H), 2.59-2.53 (m, 1 H), 2.16-2.09 (m, 1 H), 1.85-1.78 (m, 2 H), 1.60 (d, *J* = 6.7 Hz, 3 H), 1.57 (s, 3 H), 1.10 (d, *J* = 7.0 Hz, 3 H), 0.92 (s, 9 H), 0.78 (d, *J* = 6.1 Hz, 3 H), 0.11 (s, 3 H), 0.06 (s, 3 H). $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 205.7, 134.2, 120.9, 75.9, 51.4, 44.7, 35.1, 26.3, 18.7, 15.8, 14.7, 13.7, 9.7, –3.5, –3.7. HRMS-ESI calcd for $C_{17}H_{35}O_2Si$: $[M + H]^+$ 299.2406, found 299.2419.

**(*S*)-3-((2*S*,3*R*,4*R*,5*R*,6*S*,*E*)-5-(*tert*-butyldimethylsilyloxy)-3-hydroxy-2,4,6,8-tetramethyldec-8-enoyl)-4-isopropyl-5,5-diphenyloxazolidin-2-one (29)**



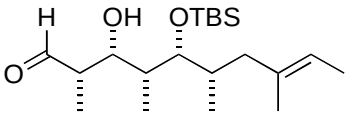

To a cooled (–5°C) solution of *ent*-**22** (81.0 mg, 0.24 mmol, 1.20 equiv) in $CH_2Cl_2$ (0.48 mL) were sequentially added $Bu_2BOTf$ (1 M in $CH_2Cl_2$) (240 μL, 0.24 mmol, 1.20 equiv) and $NEt_3$ (39 μL, 0.28 mmol, 1.40 equiv). Stirring at 0 °C was continued for 45 minutes; then the resulting solution was cooled to –78 °C and aldehyde **28** (59 mg, 0.20 mmol, 1.00 equiv) in $CH_2Cl_2$ (0.45 mL) was slowly added by canula. The reaction was stirred for 45 minutes at –78 °C, then allowed to return to 0 °C over 3 hours. The reaction was quenched at 0 °C by sequentially addition of buffer phosphate (pH = 7) (0.24 mL), MeOH (0.72 mL) and MeOH/$H_2O_2$ (2:1) (0.72 mL). The mixture was stirred at RT for 30 minutes before dilution with $Et_2O$, washed with HCl (0.5 M) (1x), saturated $NaHCO_3$ (1x) and brine (1x), dried ($MgSO_4$) and concentrated. The residue was purified by chromatography on $SiO_2$ (hexane/EtOAc 9.5:0.5) to afford **29** (77.0 mg, 0.12 mmol, 61%, *d.r.* > 97:3) as a white crystalline solid. $R_f$ = 0.60 (pentane/$Et_2O$ 7:3). M.p. = 105-107 °C. Optical rotation $[\alpha]^{25.0}_D$ (*c* 0.29, $CHCl_3$) = –118.6°. $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.52-7.51 (m, 2 H), 7.43-7.41 (m, 2 H), 7.37-7.26 (m, 6 H), 5.44 (d, *J* = 3.5 Hz, 1 H), 5.24 (q, *J* = 6.3 Hz, 1 H), 3.79-3.78 (m, 2 H), 3.50 (t, *J* = 3.8 Hz, 1 H), 2.49 (br. s, 1 H), 2.12 (d, *J* = 12.3 Hz, 1 H), 2.05-1.98 (m, 1 H), 1.82-1.76 (m, 1 H), 1.73-1.68 (m, 1 H), 1.62 (d, *J* = 6.6 Hz, 3 H), 1.58 (s, 3 H), 1.53-1.49 (m, 1 H), 1.36 (d, *J* = 6.4 Hz, 3 H), 0.89 (d, *J* = 7.1 Hz, 3 H), 0.87 (s, 9 H), 0.80 (d, *J* = 6.8 Hz, 3 H), 0.76 (d, *J* = 6.6 Hz, 3 H), 0.67 (d, *J* = 6.9 Hz, 3 H), 0.01 (s, 3 H), –0.24 (s, 3 H). $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 177.3, 152.7, 142.6, 138.3, 134.8, 129.3, 129.0, 128.8, 128.4, 126.2, 125.8, 120.4, 89.7, 77.1, 74.0, 64.3, 44.2, 40.9, 38.4, 35.9, 30.3, 26.5, 22.1, 18.8, 16.7, 15.9, 15.3, 13.9, 13.8, 9.4, –3.0, –3.9. HRMS-ESI calcd for $C_{38}H_{57}NO_5NaSi$: $[M + Na]^+$ 658.3904, found 658.3911. FTIR ν 3360*w*, 2928*m*, 2857*m*, 1786*m*, 1693*w*, 1458*w*, 1374*w*, 1253*w*, 1210*w*, 1044*w*, 892*w*, 766*w*, 689*w* $cm^{-1}$.

**(2*S*,3*R*,4*R*,5*R*,6*S*,*E*)-5-(*tert*-butyldimethylsilyloxy)-3-hydroxy-*N*-methoxy-*N*,2,4,6,8--pentamethyldec-8-enamide (30)**




To a cooled (0 °C) suspension of MeONHMe·HCl (28.0 mg, 0.28 mmol, 6.00 equiv) in $CH_2Cl_2$ (140 μL) was added $AlMe_3$ (2 M in toluene) (142 μL, 0.28 mmol, 6.00 equiv). The resulting solution was stirred at 0 °C for 5 minutes, then at RT for 45 minutes. The clear solution was cooled to 0 °C and **29** (30.0 mg, 0.05 mmol, 1.00 equiv) in $CH_2Cl_2$ (100 μL) was added. Stirring at 0 °C was continued for 5 minutes, then at RT for 68 hours. The reaction was quenched by slow addition of diluted HCl solution (0.5 M) and stirred at RT for 1hour. The aqueous layer was separated and extracted with $CH_2Cl_2$ (3x). The combined organic phases were washed with saturated $NaHCO_3$ (1x) and brine (1x), dried ($MgSO_4$) and concentrated. Purification by chromatography on $SiO_2$ (pentane/$Et_2O$ 6:4) afforded product **30** (8.1 mg, 0.02 mmol, 41%). $R_f$ = 0.19 (pentane/$Et_2O$ 1:1). Optical rotation $[\alpha]^{25.0}_D$ (*c* 0.12, $CHCl_3$) = –7.5°. $^1$H-NMR (400 MHz, $CDCl_3$) δ 5.19 (q, *J* = 6.21 Hz, 1 H), 3.83-3.79 (m, 1 H), 3.71 (s, 3 H), 3.54 (t, *J* = 3.5 Hz, 1 H), 3.21 (br s, 1 H), 3.19 (s, 3 H), 3.14 (br s, 1 H), 2.15 (d, *J* = 12.5 Hz, 1 H), 1.85-1.70 (m, 3 H), 1.57 (d, *J* = 7.3 Hz, 3 H), 1.55 (s, 3 H), 1.19 (d, *J* = 7.0 Hz, 3 H), 0.97 (d, *J* = 7.0 Hz, 3 H), 0.91 (s, 9 H), 0.78 (d, *J* = 6.6 Hz, 3 H), 0.07 (s, 3 H), 0.06 (s, 3 H). $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 178.4, 134.8, 120.5, 78.6, 74.5, 62.0, 44.6, 39.2, 38.1, 35.9, 26.6, 18.9, 15.9, 15.6, 13.8, 12.6, 10.7, –3.1, –3.5. HRMS-ESI calcd for $C_{22}H_{45}NO_4SiNa$: $[M + Na]^+$ 438.3016, found 338.3010. FTIR ν 3456*w*, 2959*m*, 2931*m*, 2858*w*, 1642*w*, 1462*w*, 1384*w*, 1254*w*, 1095*w*, 1041*m*, 1001*m*, 834*m*, 776*s*, 677*m*, 630*m* $cm^{-1}$.

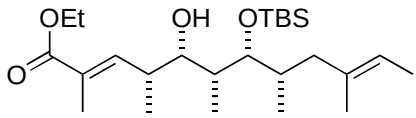
**(2*S*,3*R*,4*R*,5*R*,6*S*,*E*)-5-(*tert*-butyldimethylsilyloxy)-3-hydroxy-2,4,6,8-tetramethyldec-8-enal (31)**




To a cooled (–17 °C) solution of **29** (320 mg, 0.50 mmol, 1.00 equiv) in toluene (10 mL) was slowly added a solution of $LiAlH_4$ (1 M in $Et_2O$) (1.00 mL, 1.00 mmol, 2.00 equiv). The resulting solution was stirred for 20 minutes, then quenched at –17 °C by dropwise addition of saturated Rochelle's salt and diluted in $Et_2O$. The mixture was vigorously stirred at RT for 2 hours, then extracted with $Et_2O$ (3x) and the combined organic phase dried ($MgSO_4$) and concentrated (bath T < 20 °C). The residue was diluted in $Et_2O$ and the precipitated cleaved auxiliary recovered. The filtered was concentrated and the residue purified by chromatography on $SiO_2$ (pentane/$Et_2O$ 9:1) to afford aldehyde **31** (149 mg, 0.42 mmol, 83%) as a colorless oil. $R_f$ = 0.28 (pentane/$Et_2O$ 7:3). Optical rotation $[\alpha]^{25.0}_D$ (*c* 0.08, $CHCl_3$) = –23.8°. $^1$H-NMR (400 MHz, $CDCl_3$) δ 9.73 (d, *J* = 1.2 Hz, 1 H), 5.21 (q, *J* = 6.4 Hz, 1 H), 4.03 (q, *J* = 5.2 Hz,

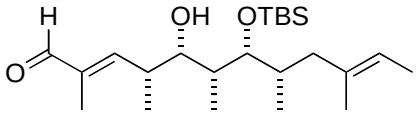
1 H), 3.58 (dd, $J_1$ = 4.2 Hz, $J_2$ = 2.9 Hz, 1 H), 2.68-2.62 (m, 1 H), 2.20 (d, $J$ = 12.3 Hz, 1 H), 1.97 (d, $J$ = 4.4 Hz, 1 H), 1.89-1.77 (m, 2 H), 1.76-1.67 (m, 1 H), 1.60 (d, $J$ = 6.8 Hz, 3 H), 1.57 (s, 3 H), 1.17 (d, $J$ = 7.1 Hz, 3 H), 1.00 (d, $J$ = 6.9 Hz, 3 H), 0.94 (s, 9 H), 0.81 (d, $J$ = 6.7 Hz, 3 H), 0.11 (s, 3 H), 0.09 (s, 3 H). $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 204.8, 134.5, 120.7, 78.2, 73.2, 50.1, 44.3, 39.3, 36.1, 26.5, 18.8, 15.8, 13.7, 10.0, 8.8, –2.8, –3.5. HRMS-ESI calcd for $C_{20}H_{40}O_3SiNa$: $[M + Na]^+$ 379.2644, found 379.2639. FTIR ν 2957*m*, 2931*m*, 2859*m*, 1727*w*, 1462*w*, 1384*w*, 1255*w*, 1096*w*, 1032*w*, 837*w*, 775*w* $cm^{-1}$.

**(2*E*,4*R*,5*S*,6*R*,7*R*,8*S*,10*E*)-ethyl 7-(*tert*-butyldimethylsilyloxy)-5-hydroxy-2,4,6,8,10-pentamethyl-dodeca-2,10-dienoate (32)**




To a solution of aldehyde **31** (61.1 mg, 0.17 mmol, 1.00 equiv) in toluene (1.7 mL) was added 1-carbethoxyethylidentriphenylphosphorane (123.2 mg, 0.34 mmol, 2.00 equiv) and the mixture was stirred at 35 °C for 5 hours. The reaction was diluted in pentane, filtered over cotton and concentrated. The residue was purified by chromatography on $SiO_2$ (pentane/$Et_2O$ 9:1) to afford **32** (73.8 mg, 0.17 mmol, 99%, *d.r.* > 97:3). $R_f$ = 0.39 (pentane/$Et_2O$ 8:2). Optical rotation $[\alpha]^{25.0}_D$ (*c* 0.09, $CHCl_3$) = +24.7°. $^1$H-NMR (400 MHz, $CDCl_3$) δ 6.53 (dd, $J_1$ = 10.5 Hz, $J_2$ = 1.2 Hz, 1 H), 5.21 (q, $J$ = 6.2 Hz, 1 H), 4.27-4.15 (m, 2 H), 3.65 (t, $J$ = 3.9 Hz, 1 H), 3.53-3.49 (m, 1 H), 2.70-2.60 (m, 1 H), 2.17 (d, $J$ = 12.6 Hz, 1 H), 1.93 (d, $J$ = 4.3 Hz, 1 H), 1.89 (d, $J$ = 1.1 Hz, 3 H), 1.87-1.82 (m, 1 H), 1.80-1.74 (m, 1 H), 1.72-1.66 (m, 1 H), 1.59 (d, $J$ = 6.6 Hz, 3 H), 1.57 (s, 3 H), 1.31 (t, $J$ = 7.1 Hz, 3 H), 1.10 (d, $J$ = 6.6 Hz, 3 H), 0.94 (s, 9 H), 0.87 (d, $J$ = 7.0 Hz, 3 H), 0.77 (d, $J$ = 6.7 Hz, 3 H), 0.12 (s, 3 H), 0.11 (s, 3 H). $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 168.5, 144.0, 134.7, 127.7, 120.5, 79.9, 78.6, 60.9, 44.1, 39.0, 38.0, 35.7, 26.5, 18.7, 16.9, 15.9, 15.0, 14.6, 13.7, 13.0, 8.8, –2.8, –3.7. HRMS-ESI calcd for $C_{25}H_{49}O_4Si$: $[M + H]^+$ 441.3400, found 441.3404. FTIR ν 3519*w*, 2959*m*, 2923*m*, 2858*m*, 1712*m*, 1650*w*, 1462*w*, 1369*w*, 1252*m*, 1094*m*, 1038*m*, 835*m*, 773*m*, 675*m* $cm^{-1}$.

**(2*E*,4*R*,5*S*,6*R*,7*R*,8*S*,10*E*)-7-(*tert*-butyldimethylsilyloxy)-5-hydroxy-2,4,6,8,10-pentamethyldodeca-2,10-dienal (33)**

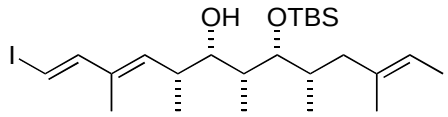



To a cooled (–78 °C) solution of **32** (67.0 mg, 0.15 mmol, 1.00 equiv) in THF (1.6 mL) was slowly added DIBAL-H (1M in hexane) (800 $\mu$L, 0.80 mmol, 5.30 equiv). The resulting solution was allowed to return to–15 °C and stirred from –15 °C to –5 °C over 1.5 hours. The reaction was quenched by addition of MeOH, diluted in saturated Rochelle's salt and $Et_2O$ and vigorously stirred at RT for 1 hour. The aqueous layer was extracted with $Et_2O$ (3x) and the combined organic phase dried ($MgSO_4$) and concentrated (bath T < 25 °C). Purification by chromatography on $SiO_2$ (pentane/$Et_2O$ 9:1 → 7:3) afforded the corresponding diol (56.3 mg, 0.14 mmol, 93%) as a colorless oil. $R_f$ = 0.15 (pentane/$Et_2O$ 7:3). Optical rotation $[\alpha]^{22.5}_D$ (*c* 0.41, $CHCl_3$) = –1.0°. $^1$H-NMR (400 MHz, $CDCl_3$) δ 5.23-5.17 (m, 2 H), 4.01 (s, 2 H), 3.63-3.60 (m, 1 H), 3.39 (d, *J* = 8.8 Hz, 1 H), 2.59-2.49 (m, 1 H), 2.16 (d, *J* = 12.2 Hz, 1 H), 1.91-1.75 (m, 4 H), 1.71 (d, *J* = 0.5 Hz, 3 H), 1.59 (d, *J* = 7.0 Hz, 3 H), 1.57 (s, 3 H), 1.04 (d, *J* = 6.6 Hz, 3 H), 0.93 (s, 9 H), 0.88 (d, *J* = 7.0 Hz, 3 H), 0.76 (d, *J* = 6.6 Hz, 3 H), 0.11 (s, 3 H), 0.10 (s, 3 H). $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 135.0, 134.8, 129.1, 120.4, 79.9, 78.9, 69.2, 44.3, 38.5, 36.8, 35.6, 26.5, 18.8, 17.8, 15.9, 14.9, 14.3, 13.8, 9.0, –2.8, –3.6. HRMS-ESI calcd for $C_{23}H_{46}O_3NaSi$: $[M + Na]^+$ 421.3114, found 421.3116. FTIR ν 3349*m*, 2956*m*, 2930*m*, 2860*m*, 1459*w*, 1383*w*, 1253*m*, 1070*m*, 1035*m*, 1011*m*, 836*m*, 775*m*, 676*m* $cm^{-1}$.

To a solution of the previously prepared diol (121 mg, 0.30 mmol, 1.00 equiv) in $CH_2Cl_2$ (3.0 mL), $MnO_2$ (396 mg, 4.50 mmol, 15.0 equiv) was added. The mixture was stirred at RT for 2.5 hours, then filtered over Celite, rinsed with $CH_2Cl_2$ and concentrated (bath T < 25 °C). The $\alpha,\beta$-unsaturated aldehyde **33** (103 mg, 0.26 mmol, 86%) crystallized under high vacuum. An analytical sample was recrystallized (hexane) for X-ray analysis and the rest directly used in the next step without further purification (crystallographic data are given at the end of the experimental part). $R_f$ = 0.37 (pentane/$Et_2O$ 7:3). M.p. = 75-77 °C. Optical rotation $[\alpha]^{22.5}_D$ (*c* 0.82, $CHCl_3$) = –10.9°. $^1$H-NMR (400 MHz, $CDCl_3$) δ 9.42 (s, 1 H), 6.27 (dd, $J_1$ = 10.3 Hz, $J_2$ = 1.0 Hz, 1 H), 5.21 (q, *J* = 6.3 Hz, 1 H), 3.65 (t, *J* = 3.8 Hz, 1 H), 3.59-3.56 (m, 1 H), 2.92-2.82 (m, 1 H), 2.18 (d, *J* = 12.8 Hz, 1 H), 2.00 (d, *J* = 4.2 Hz, 1 H), 1.92-1.83 (m, 1 H), 1.81 (d, *J* = 0.9 Hz, 3 H), 1.79-1.73 (m, 1 H), 1.66-1.63 (m, 1 H), 1.60 (d, *J* = 7.1 Hz, 3 H), 1.57 (s, 3 H), 1.16 (d, *J* = 6.6 Hz, 3 H), 0.94 (s, 9 H), 0.90 (d, *J* = 7.0 Hz, 3 H), 0.77 (d, *J* = 6.8 Hz, 3 H), 0.13 (s, 3 H), 0.11 (s, 3 H). $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 195.6, 156.4, 139.1, 134.5, 120.6, 79.8, 78.1, 44.1, 39.3, 38.3, 35.7, 26.5, 18.7, 16.7, 15.9, 15.2, 13.8, 9.9, 8.9, –2.8, –3.7. HRMS-ESI calcd for

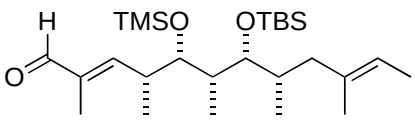
$C_{23}H_{44}O_3SiNa$: $[M + Na]^+$ 419.2957, found 419.2960. FTIR ν 3520*w*, 2961*m*, 2928*m*, 2889*m*, 2885*m*, 1667*m*, 1635*w*, 1459*w*, 1378*w*, 1251*w*, 1096*w*, 1073*w*, 1040*w*, 1011*m*, 974*w*, 883*m*, 772*m*, 681*m* $cm^{-1}$.

**(1*E*,3*E*,5*R*,6*S*,7*R*,8*R*,9*S*,11*E*)-8-(*tert*-butyldimethylsilyloxy)-1-iodo-3,5,7,9,11-pentamethyltrideca-1,3,11-trien-6-ol (34)**




To a cooled (–5 °C) suspension of $CrCl_2$ (446 mg, 3.63 mmol, 24.00 equiv) in dry THF (4.4 mL) was slowly added a solution of $\alpha,\beta$-unsaturated aldehyde **33** (60.0 mg, 0.15 mmol, 1.00 equiv) and $CHI_3$ (358 mg, 0.91 mmol, 6.00 equiv) in THF (4.4 mL). The dark brown mixture was covered with an aluminium foil and stirred between –5 and 0 °C for 2.5 hours. The mixture was quenched by addition of water and extracted with $Et_2O$ (3x). The combined organic layers were washed with saturated sodium thiosulfate (1x), water (1x), dried ($MgSO_4$) and concentrated (bath T < 20 °C). Purification by chromatography on $SiO_2$ (pentane/$Et_2O$ 9:1) afforded vinyl iodide **34** (78.4 mg, 0.15 mmol, quant., *d.r.* > 97:3) as a colorless oil. $R_f$ = 0.68 (pentane/$Et_2O$ 7:3). Optical rotation $[\alpha]^{22.4}_D$ (*c* 0.60, $CHCl_3$) = +25.4°. $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.04 (d, *J* = 14.6 Hz, 1 H), 6.20 (d, *J* = 14.6 Hz, 1 H), 5.24-5.19 (m, 2 H), 3.63 (t, *J* = 3.9 Hz, 1 H), 3.43-3.40 (m, 1 H), 2.65-2.56 (m, 1 H), 2.17 (d, *J* = 12.3 Hz, 1 H), 1.87 (d, *J* = 4.3 Hz, 1 H), 1.86-1.82 (m, 1 H), 1.77 (d, *J* = 0.7 Hz, 3 H), 1.76-1.70 (m, 2 H), 1.60 (d, *J* = 6.9 Hz, 3 H), 1.58 (s, 3 H), 1.06 (d, *J* = 6.6 Hz, 3 H), 0.94 (s, 9 H), 0.86 (d, *J* = 7.0 Hz, 3 H), 0.77 (d, *J* = 6.6 Hz, 3 H), 0.12 (s, 3 H), 0.11 (s, 3 H). $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 150.0, 137.0, 134.7, 134.3, 120.5, 80.0, 78.8, 74.1, 44.2, 38.8, 37.4, 35.7, 26.5, 18.8, 17.6, 15.9, 15.0, 13.8, 12.6, 8.8, –2.7, –3.6. HRMS-ESI calcd for $C_{24}H_{45}O_2SiINa$: $[M + Na]^+$ 543.2131, found 543.2133. FTIR ν 3482*w*, 2958*m*, 2929*m*, 2858*m*, 1461*w*, 1387*w*, 1254*w*, 1091*w*, 1039*w*, 980*w*, 950*w*, 836*w*, 774*w*, 678*w* $cm^{-1}$.

**(2*E*,4*R*,5*S*,6*S*,7*R*,8*S*,10*E*)-7-(*tert*-butyldimethylsilyloxy)-2,4,6,8,10-pentamethyl-5-(trimethylsilyloxy)dodeca-2,10-dienal (35)**




To a cooled (–5 °C) solution of **32** (7.6 mg, 0.017 mmol, 1.00 equiv) in $CH_2Cl_2$ (170 $\mu$L) were sequentially added DMAP (2.0 mg, 0.017 mmol, 1.00 equiv), $NEt_3$ (14 $\mu$L, 0.102 mmol, 6.00 equiv) and TMSCl (6.6 $\mu$L, 0.052 mmol, 3.00 equiv). The resulting solution was stirred at 0 °C for 1 hour; then quenched by addition of saturated $NH_4Cl$ and extracted with $CH_2Cl_2$ (3x). The combined organic layers were dried

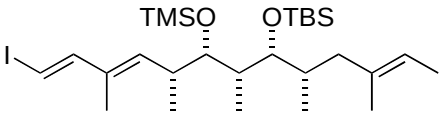
($MgSO_4$) and concentrated. Purification by chromatography on $SiO_2$ (pentane/$Et_2O$ 9.75:0.25) afforded the protected $\alpha,\beta$-unsaturated ester (6.7 mg, 0.13 mmol, 77%). $R_f$ = 0.76 (pentane/$Et_2O$ 9:1). Optical rotation $[\alpha]^{25.0}_D$ (*c* 0.285, $CHCl_3$) = +14.4°. $^1$H-NMR (400 MHz, $CDCl_3$) δ 6.59 (dd, $J_1$ = 10.4 Hz, $J_2$ = 1.0 Hz, 1 H), 5.20-5.17 (m, 1 H), 4.26-4.10 (m, 2 H), 3.49 (dd, $J_1$ = 6.0 Hz, $J_2$ = 4.3 Hz, 1 H), 3.42 (dd, $J_1$ = 7.0 Hz, $J_2$ = 2.1 Hz, 1 H), 2.73-2.64 (m, 1 H), 2.03 (d, *J* = 12.7 Hz, 1 H), 1.91 (d, *J* = 10.9 Hz, 1 H), 1.85 (d, *J* = 1.0 Hz, 3 H), 1.82-1.76 (s, 1 H), 1.72-1.64 (s, 1 H), 1.59-1.56 (m, 6 H), 1.28 (t, *J* = 7.1 Hz, 3 H), 0.97 (d, *J* = 6.7 Hz, 3 H), 0.91 (s, 9 H), 0.85 (d, *J* = 6.9 Hz, 3 H), 0.70 (d, *J* = 6.5 Hz, 3 H), 0.15 (s, 9 H), 0.05 (s, 3 H), 0.02 (s, 3 H). $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 168.6, 145.2, 134.6, 127.0, 120.6, 77.5, 77.4, 60.8, 45.8, 40.6, 37.8, 35.0, 26.7, 19.0, 16.0, 15.9, 14.6, 13.8, 13.0, 12.6, 12.0, 1.3, –2.6, –2.9. HRMS-ESI calcd for $C_{28}H_{56}O_4Si_2Na$: $[M + Na]^+$ 535.3615, found 535.3610. FTIR ν 2958*m*, 2932*m*, 2859*w*, 1714*m*, 1460*w*, 1384*w*, 1252*m*, 1096*m*, 1032*m*, 836*m*, 772*w*, 750*w*, 676*w*, 631*s* $cm^{-1}$.

To a cooled (–78 °C) solution of the previously prepared compund (5.5 mg, 0.01 mmol, 1.00 equiv) in $CH_2Cl_2$ (100 μL) was slowly added DIBAL-H (1 M in hexane) (20 μL, 0.02 mmol, 2.00 equiv). The resulting solution was stirred at –78 °C for 1 hour, then quenched by addition of MeOH (0.1 mL), saturated Rochelle's salt (2 mL), diluted in more $CH_2Cl_2$ (2 mL) and vigorously stirred at RT for 1 hour. The aqueous layer was extracted with $CH_2Cl_2$ (3x) and the combined organic layers dried ($MgSO_4$) and concentrated (bath T < 20 °C). Purification by chromatography on $SiO_2$ (pentane/$Et_2O$ 9:1) afforded the corresponding primary alcohol (4.7 mg, 0.01 mmol, 100%) as a colorless oil. $R_f$ = 0.19 (cyclohexane/EtOAc 9:1). Optical rotation $[\alpha]^{25.0}_D$ (*c* 0.29, $CHCl_3$) = +1.7°. $^1$H-NMR (400 MHz, $CDCl_3$) δ 5.23-5.21 (m, 2 H), 4.02 (d, *J* = 5.7 Hz, 2 H), 3.45-3.41 (m, 2 H), 2.64-2.54 (s, 1 H), 2.03 (d, *J* = 12.0 Hz, 1 H), 1.94 (t, *J* = 11.8 Hz, 1 H), 1.86-1.78 (m, 1 H), 1.78-1.72 (m, 1 H), 1.70 (s, 3 H),1.61-1.59 (m, 6 H), 0.95 (d, *J* = 7.0 Hz, 3 H), 0.93 (s, 9 H), 0.87 (d, *J* = 6.9 Hz, 3 H), 0.71 (d, *J* = 6.6 Hz, 3 H), 0.16 (s, 9 H), 0.08 (s, 3 H), 0.06 (s, 3 H). $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 134.7, 134.3, 130.1, 120.6, 78.1, 77.8, 69.3, 46.0, 40.2, 36.8, 34.7, 26.7, 19.0, 17.5, 16.0, 14.4, 13.8, 12.3, 11.9, 1.4, –2.5, –2.9. FTIR ν 3314*w*, 2958*m*, 2929*m*, 2858*w*, 1462*w*, 1381*w*, 1251*m*, 1127*w*, 1105*w*, 1061*w*, 1032*m*, 866*w*, 836*m*, 772*w* $cm^{-1}$.

To a solution of the previously prepared primary alcohol (5.2 mg, 0.011 mmol, 1.00 equiv) in $CH_2Cl_2$ (110 μL) was added $MnO_2$ (14.7 mg, 0.165 mmol, 15.0 equiv). The mixture was stirred at RT for 3.5 hours, then filtered over Celite, rinsed with $CH_2Cl_2$ and concentrated (bath T < 20 °C). The $\alpha,\beta$-unsaturated aldehyde **35** was obtained in quantitative yield and directly used in the next step without further purification. $R_f$ = 0.60 (pentane/$Et_2O$ 9:1). Optical rotation $[\alpha]^{25.0}_D$ (*c* 0.27, $CHCl_3$) = –1.9°. $^1$H-NMR (400 MHz, $CDCl_3$) δ 9.41 (s, 1 H), 6.32 (d, *J* = 10.3 Hz, 1 H), 5.23-5.22 (m, 1 H), 3.58 (dd, $J_1$ = 6.5 Hz, $J_2$ = 4.0 Hz, 1 H), 3.45 (dd, $J_1$ = 7.1 Hz, $J_2$ = 2.1 Hz, , 1 H), 2.97-2.89 (m, 1 H), 2.05 (d, *J* =

12.5 Hz, 1 H), 1.93 (d, *J* = 11.0 Hz, 1 H), 1.84-1.82 (m, 1 H), 1.80 (d, *J* = 0.7 Hz, 3 H), 1.70-1.65 (m, 1 H), 1.62-1.60 (m, 6 H), 1.06 (d, *J* = 6.7 Hz, 3 H), 0.93 (s, 9 H), 0.89 (d, *J* = 6.9 Hz, 3 H), 0.72 (d, *J* = 6.6 Hz, 3 H), 0.18 (s, 9 H), 0.09 (s, 3 H), 0.08 (s, 3 H). $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 195.7, 157.5, 138.5, 134.5, 120.8, 77.5, 77.0, 45.8, 40.9, 38.3, 34.9, 26.7, 19.0, 16.1, 16.0, 13.8, 12.7, 12.0, 9.9, 1.4, –2.6, –2.9. HRMS-ESI calcd for $C_{26}H_{53}O_3Si_2$: $[M]^+$ 469.3533, found 469.3534. FTIR ν 2959*m*, 2930*m*, 2858*w*, 1694*m*, 1471*w*, 1462*w*, 1381*w*, 1252*m*, 1123*w*, 1107*w*, 1031*m*, 837*m*, 772*w*, 631*s* $cm^{-1}$.

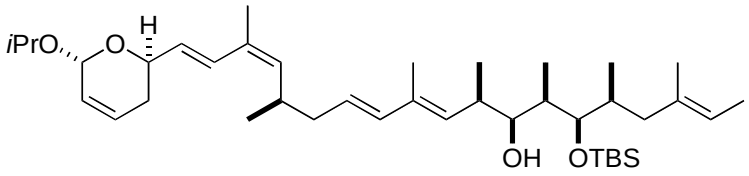
**(4*S*,5*S*,6*R*)-4-((*R*,3*E*,5*E*)-6-iodo-4-methylhexa-3,5-dien-2-yl)-2,2,5,8,8,9,9-heptamethyl-6-((*S*,*E*)-4-methylhex-4-en-2-yl)-3,7-dioxa-2,8-disiladecane (36)**




To a cooled (–5 °C) suspension of $CrCl_2$ (11.0 mg, 0.088 mmol, 8.00 equiv) in dry THF (300 μL) was added a solution of α,β-unsaturated aldehyde **35** (5.1 mg, 0.011 mmol, 1.00 equiv) and $CHI_3$ (9.0 mg, 0.022 mmol, 2.00 equiv) in THF (200 μL). The dark brown mixture was covered with an aluminium foil and stirred at 0 °C for 2.5 hours. The mixture was diluted with $Et_2O$ (2 mL) and water (1.5 mL) and the aqueous phase extracted with $Et_2O$ (3x). The combined organic layers were washed with water (2x), saturated sodium thiosulfate solution (1x), dried ($MgSO_4$) and concentrated (bath T < 20 °C). Purification by chromatography on $SiO_2$ (pentane 100%) afforded vinyl iodide **36** (5.7 mg, 0.010 mmol, 88%, *d.r.* > 95:5) as a colorless oil. $R_f$ = 0.16 (pentane 100%). Optical rotation $[\alpha]^{25.0}_D$ (*c* 0.105, $CHCl_3$) = +24.8°. $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.02 (d, *J* = 14.6 Hz, 1 H), 6.19 (d, *J* = 14.6 Hz, 1 H), 5.26 (d, *J* = 10.2 Hz, 1 H), 5.23 (dd, $J_1$ = 12.8 Hz, $J_2$ = 6.7 Hz, 1 H), 3.46-3.43 (m, 2 H), 2.70-2.61 (m, 1 H), 2.03 (d, *J* = 11.9 Hz, 1 H), 1.94 (t, *J* = 11.8 Hz, 1 H), 1.83-1.78 (m, 1 H), 1.76 (s, 3 H), 1.73-1.69 (m, 1 H), 1.62-1.61 (m, 6 H), 0.96 (d, *J* = 6.7 Hz, 3 H), 0.93 (s, 9 H), 0.85 (d, *J* = 6.8 Hz, 3 H), 0.71 (d, *J* = 6.6 Hz, 3 H), 0.16 (s, 9 H), 0.07 (s, 3 H), 0.04 (s, 3 H). $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 150.0, 138.1, 134.6, 133.8, 120.7, 77.8, 73.9, 46.0, 40.5, 37.4, 34.7, 30.1, 26.7, 19.0, 17.3, 16.0, 13.8, 12.6, 12.4, 11.9, 1.4, –2.6, –2.8. HRMS-ESI calcd for $C_{27}H_{53}O_2ISi_2Na$: $[M + Na]^+$ 615.2527, found 615.2536. FTIR ν 2958*m*, 2928*m*, 2857*w*, 1461*w*, 1381*w*, 1253*w*, 1105*w*, 1032*w*, 890*w*, 836*w*, 772*w*, 631*s* $cm^{-1}$.

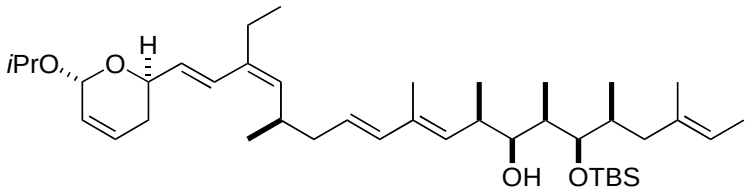
**2.4. The Suzuki sp$^3$-sp$^2$ Cross Coupling and Synthesis Completion**

**(2*E*,5*S*,6*R*,7*R*,8*S*,9*R*,10*E*,12*E*,15*R*,16*Z*,18*E*)-6-(*tert*-butyldimethylsilyloxy)-19-((2*R*,6*R*)-6-iso-propoxy-3,6-dihydro-2*H*-pyran-2-yl)-3,5,7,9,11,15,17-heptamethylnonadeca-2,10,12,16,18-pentaen-8-ol (39)**



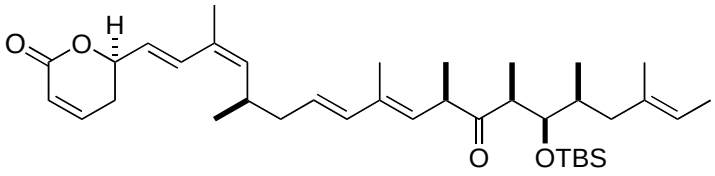

To a solution of alkyl iodide **20** (29.0 mg, 0.077 mmol, 1.30 equiv) in $Et_2O$ (850 $\mu$L) was added 9-MeO-9-BBN (1 M in hexane) (202 $\mu$L, 0.202 mmol, 3.42 equiv). The resulting solution was cooled to –78 °C and treated with *t*BuLi (1.5 M in pentane) (118 $\mu$L, 0.177 mmol, 3.00 equiv). After 5 minutes THF (850 $\mu$L) was added and the solution allowed to return to RT; stirring was continued for 1 hour. Separately in another flask vinyl iodide **34** (30.7 mg, 0.059 mmol, 1.00 equiv) was taken up in DMF (850 $\mu$L) to which $Pd(dppf)Cl_2 \bullet CH_2Cl_2$ (2.2 mg, 0.003 mmol, 0.05 equiv), $AsPh_3$ (2.8 mg, 0.009, 0.15 equiv), $Cs_2CO_3$ (77.0 mg, 0.236 mmol, 4.0 equiv) and $H_2O$ (26 $\mu$L, 1.416 mmol, 24 equiv) were sequentially added. The alkyl boronate solution was transferred in the DMF solution and the resulting red-brown mixture stirred at RT overnight. The reaction was diluted with water and extracted with $Et_2O$ (3x). The combined organic layers were washed with water (1x) and brine (1x), dried ($MgSO_4$) and concentrated. Purification by chromatography on $SiO_2$ (pentane/$Et_2O$ 92.5:7.5) afforded **39** (30.2 mg, 0.047 mmol, 80%) as a pale yellow oil. $R_f$ = 0.13 (pentane/$Et_2O$ 9:1). Optical rotation $[\alpha]^{22.0}_D$ (*c* 0.34, $CHCl_3$) = +52.1°. $^1$H-NMR (400 MHz, $CDCl_3$) δ 6.70 (d, *J* = 15.7 Hz, 1 H), 6.06-6.02 (m, 1 H), 6.02 (d, *J* = 15.5 Hz, 1 H), 5.77-5.70 (m, 2 H), 5.53 (dt, $J_1$ = 15.5 Hz, $J_2$ = 7.2 Hz, 1 H), 5.24-5.18 (m, 2 H), 5.15 (s, 1 H), 5.09 (d, *J* = 9.9 Hz, 1 H), 4.57-4.51 (m, 1 H), 4.05 (sept., *J* = 6.2 Hz, 1 H), 3.63-3.61 (m, 1 H), 3.39 (dd, $J_1$ = 8.86 Hz, $J_2$ = 2.57 Hz, 1 H), 2.75-2.68 (m, 1 H), 2.65-2.55 (m, 1 H), 2.20-2.02 (m, 5 H), 1.90-1.86 (m, 1 H), 1.84 (s, 3 H), 1.81-1.78 (m, 3 H), 1.75 (s, 3 H), 1.59 (d, *J* = 5.5 Hz, 3 H), 1.57 (s, 3 H), 1.27 (d, *J* = 6.2 Hz, 3 H), 1.21 (d, *J* = 6.1 Hz, 3 H), 1.05 (d, *J* = 6.5 Hz, 3 H), 0.99 (d, *J* = 6.6 Hz, 3 H), 0.94 (s, 9 H), 0.86 (d, *J* = 7.0 Hz, 3 H), 0.76 (d, *J* = 6.6 Hz, 3 H), 0.11 (s, 3 H), 0.10 (s, 3 H). $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 137.9, 136.5, 134.8, 133.5, 133.4, 130.4, 129.6, 128.9, 128.6, 126.5, 126.3, 120.3, 93.7, 79.9, 79.1, 70.0, 67.4, 44.3, 41.2, 38.6, 37.3, 35.6, 32.5, 31.2, 26.6, 24.3, 22.5, 20.9, 20.8, 18.8, 18.0, 15.9, 14.9, 13.8, 13.2, 8.9, –2.8, –3.6. HRMS-ESI calcd for $C_{40}H_{70}O_4SiNa$: $[M + Na]^+$ 665.4941, found 665.4946. FTIR ν 3503*w*, 2962*m*, 2928*m*, 2859*m*, 1459*w*, 1381*w*, 1317*w*, 1253*w*, 1181*w*, 1099*m*, 1029*m*, 1001*m*, 964*m*, 836*w*, 774*w*, 718*w*, 678*w* $cm^{-1}$.

**(2*E*,5*S*,6*R*,7*R*,8*S*,9*R*,10*E*,12*E*,15*R*,16*Z*,18*E*)-6-(*tert*-butyldimethylsilyloxy)-17-ethyl-19-((2*R*,6*R*)-6-isopropoxy-3,6-dihydro-2*H*-pyran-2-yl)-3,5,7,9,11,15-hexamethylnonadeca-2,10,12,16,18-pentaen-8-ol (41)**




To a solution of alkyl iodide **21** (49.0 mg, 0.12 mmol, 1.30 equiv) in $Et_2O$ (1.3 mL) was added 9-MeO-9-BBN (1M in hexane) (330 $\mu$L, 0.33 mmol, 3.42 equiv). The resulting solution was cooled to –78 °C and treated with *t*BuLi (1.5 M in pentane) (192 $\mu$L, 0.29 mmol, 3.00 equiv). After 5 minutes THF (1.3 mL) was added and the solution allowed to return to RT; stirring was continued for 1 hour. Separately in another flask vinyl iodide **34** (50.0 mg, 0.096 mmol, 1.00 equiv) was taken up in DMF (1.3 mL) to which $Pd(dppf)Cl_2 \bullet CH_2Cl_2$ (4.0 mg, 0.005 mmol, 0.05 equiv), $AsPh_3$ (4.4 mg, 0.014, 0.15 equiv), $Cs_2CO_3$ (125 mg, 0.384 mmol, 4.00 equiv) and $H_2O$ (41 $\mu$L, 2.30 mmol, 24 equiv) were sequentially added. The alkyl boronate solution was transferred in the DMF solution and the resulting red-brown mixture stirred at RT for 20 hours. The reaction was diluted with water and extracted with $Et_2O$ (3x). The combined organic layers were washed with water (1x) and brine (1x), dried ($MgSO_4$) and concentrated. Purification by chromatography on $SiO_2$ (pentane/$Et_2O$ 98:2) afforded **41** (30.0 mg, 0.046 mmol, 48%) as a pale yellow oil and a second fraction (41.4 mg) containing a mixture of product and a side compound that was directly used in the next step without further purifications. $R_f$ = 0.71 (hexane/EtOAc 8:2). Optical rotation $[\alpha]^{22.2}_D$ (*c* 0.30, $CHCl_3$) = +50.5°. $^1$H-NMR (400 MHz, $CDCl_3$) δ 6.59 (d, *J* = 15.7 Hz, 1 H), 6.03-6.00 (m, 1 H), 5.99 (d, *J* = 15.7 Hz, 1 H), 5.76-5.70 (m, 2 H), 5.53-5.46 (m, 1 H), 5.19-5.16 (m, 2 H), 5.13 (s, 1 H), 5.06 (d, *J* = 9.9 Hz, 1 H), 4.53-4.48 (m, 1 H), 4.02 (sept., *J* = 6.1 Hz, 1 H), 3.61-3.59 (m, 1 H), 3.37-3.33 (m, 1 H), 2.71-2.63 (m, 1 H), 2.61-2.53 (m, 1 H), 2.22-2.01 (m, 7 H), 1.89-1.76 (m, 4 H), 1.72 (s, 3 H), 1.59-1.55 (m, 6 H), 1.25 (d, *J* = 6.1 Hz, 3 H), 1.19 (d, *J* = 6.1 Hz, 3 H), 1.04 (m, 6 H), 0.97 (d, *J* = 6.4 Hz, 3 H), 0.91 (m, 9 H), 0.84 (d, *J* = 7.0 Hz, 3 H), 0.74 (d, *J* = 6.7 Hz, 3 H), 0.09 (s, 6 H). $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 136.6, 136.2, 135.9, 134.9, 133.6, 133.4, 129.0, 128.9, 127.7, 126.6, 126.4, 120.4, 93.7, 80.0, 79.2, 70.1, 67.6, 44.4, 41.4, 38.7, 37.4, 35.7, 32.4, 31.3, 26.8, 26.6, 24.3, 22.6, 21.0, 18.8, 18.1, 16.0, 14.9, 13.9, 13.8, 13.3, 9.00, –2.9, –3.6. HRMS-ESI calcd for $C_{41}H_{72}O_4SiNa$: $[M + Na]^+$ 679.5098, found 679.5063. FTIR ν 3503*w*, 2963*m*, 2928*m*, 2858*w*, 1458*w*, 1381*w*, 1323*w*, 1254*w*, 1099*w*, 1030*m*, 1003*m*, 964*w*, 833*w*, 775*s* $cm^{-1}$.

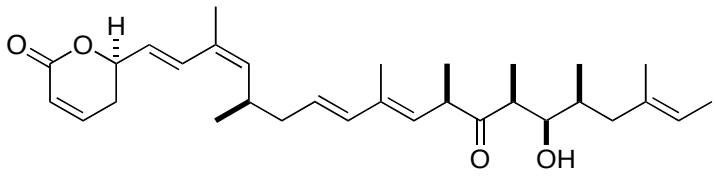
**(*R*)-6-((1*E*,3*Z*,5*R*,7*E*,9*E*,11*R*,13*S*,14*R*,15*S*,17*E*)-14-(*tert*-butyldimethylsilyloxy)-3,5,9,11,13,15,17-heptamethyl-12-oxononadeca-1,3,7,9,17-pentaenyl)-5,6-dihydro-2*H*-pyran-2-one (42)**




To a solution of **39** (6.8 mg, 0.011 mmol, 1.00 equiv) in a mixture acetone/water (3/1) (220 $\mu$L), PPTS (1.3 mg, 0.005 mmol, 0.5 equiv) was added and the resulting solution stirred at RT for 22 hours. The reaction was diluted with water, extracted with $Et_2O$ (3x) and the combined organic layer dried ($MgSO_4$) and concentrated. Purification by chromatography on $SiO_2$ (pentane/$Et_2O$ 9:1 → 7:3) afforded the corresponding lactol (6.3 mg, 0.010 mmol, 95%) as a pale yellow oil. $R_f$ = 0.20 (pentane/$Et_2O$ 7:3). Optical rotation $[\alpha]^{22.8}_D$ (*c* 0.10, $CHCl_3$) = +53.1°. $^1$H-NMR (300 MHz, $CDCl_3$) δ 6.73 (d, *J* = 15.7 Hz, 1 H), 6.11-6.07 (m, 1 H), 6.02 (d, *J* = 15.5 Hz, 1 H), 5.85 (dd, $J_1$ = 10.1 Hz, $J_2$ = 0.8 Hz, 1 H), 5.73 (dd, $J_1$ = 15.7 Hz, $J_2$ = 6.5 Hz, 1 H), 5.53 (dt, $J_1$ = 15.5 Hz, $J_2$ = 7.3 Hz, 1 H), 5.48 (br. s, 1 H), 5.24 (d, *J* = 9.7 Hz, 1 H), 5.23-5.18 (m, 1 H), 5.10 (d, *J* = 9.9 Hz, 1 H), 4.61-4.56 (m, 1 H), 3.63-3.61 (m, 1 H), 3.42-3.39 (m, 1 H), 2.79-2.69 (m, 2 H), 2.66-2.56 (m, 1 H), 2.21-2.01 (m, 5 H), 1.91-1.86 (m, 1 H), 1.84 (s, 3 H), 1.82-1.78 (m, 3 H), 1.75 (s, 3 H), 1.59-1.57 (m, 6 H), 1.05 (d, *J* = 6.5 Hz, 3 H), 0.98 (d, *J* = 6.6 Hz, 3 H), 0.94 (s, 9 H), 0.87 (d, *J* = 7.0 Hz, 3 H), 0.76 (d, *J* = 6.6 Hz, 3 H), 0.11 (s, 3 H), 0.10 (s, 3 H). $^{13}$C-NMR (75 MHz, $CDCl_3$) δ 138.2, 136.5, 134.9, 133.6, 133.4, 130.2, 129.2, 129.1, 126.4, 126.3, 120.3, 89.7, 79.9, 79.1, 67.8, 44.3, 41.2, 38.6, 37.3, 35.6, 32.5, 31.2, 26.6, 21.0, 20.8, 18.8, 17.9, 15.9, 14.9, 13.8, 13.3, 9.0, –2.8, –3.6. HRMS-ESI calcd for $C_{37}H_{64}O_4SiNa$: $[M + Na]^+$ 623.4472, found 623.4475. FTIR ν 3396*w*, 2959*m*, 2928*m*, 2859*w*, 1684*w*, 1457*w*, 1382*w*, 1253*w*, 1094*w*, 1033*w*, 964*w*, 835*w*, 772*w*, 680*m* $cm^{-1}$.

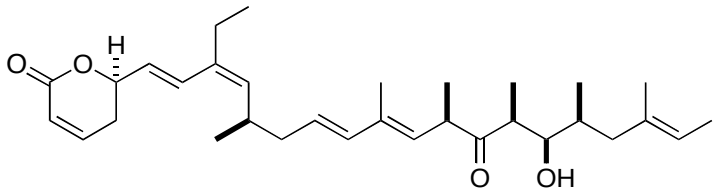
To a solution of the previously obtained lactol (3.2 mg, 0.005 mmol, 1.00 equiv) in $CH_2Cl_2$ (100 $\mu$L) was added DMP (5.6 mg, 0.013 mmol, 1.00 equiv) and the resulting mixture stirred at RT for 4 hours. The mixture was directly loaded over a pipette column of silica and eluted with pentane/$Et_2O$ 9.5/0.5 → 7/3. The mixture of lactol-ketone and lactone-ketone was concentrated and directly treated with $MnO_2$ (7.0 mg, 0.080 mmol, 15.0 equiv) in $CH_2Cl_2$ (300 $\mu$L) at RT for 14 hours. The mixture was filtered over Celite, washed with $CH_2Cl_2$ and concentrated to afford $\alpha,\beta$-unsaturated lactone **42** (1.5 mg, 0.003 mmol, 47%) as a pale yellow oil, which was directly used in the next step without further purification. $R_f$ = 0.19 (pentane/$Et_2O$ 7:3).

**(*R*)-6-((1*E*,3*Z*,5*R*,7*E*,9*E*,11*R*,13*S*,14*R*,15*S*,17*E*)-14-hydroxy-3,5,9,11,13,15,17-heptamethyl-12-oxononadeca-1,3,7,9,17-pentaenyl)-5,6-dihydro-2*H*-pyran-2-one (anguinomycin C) (1)**



In a 10 ml plastic vial under Ar, a solution of $\alpha,\beta$-unsaturated lactone **42** (1.4 mg, 0.002 mmol, 1.00 equiv) in THF (300 $\mu$L) was cooled to 0 °C and treated dropwise with a solution of HF·pyridine (120 $\mu$L) and pyridine (60 $\mu$L) in THF (200 $\mu$L). After addition the resulting pale yellow solution was allowed to return to RT and stirred for 4.5 days. The reaction mixture was diluted in $Et_2O$ and transferred by canula in a saturated $NaHCO_3$ solution and extracted with $Et_2O$ (3x). The combined organic layers were washed with saturated $NH_4Cl$ (1x), dried ($MgSO_4$) and concentrated. The crude mixture was directly purified by HPLC to afford anguinomycin C (**1**) (0.9 mg, 0.0019 mmol, 82%) as a colorless oil. Optical rotation $[\alpha]^{23.1}_D$ (*c* 0.012, $CHCl_3$) = –116.7°. Optical rotation $[\alpha]^{22.5}_D$ (*c* 0.0064, MeOH) = –101.2°. $^1$H-NMR (600 MHz, $CDCl_3$) $\delta$ 6.93 (dt, $J_1$ = 9.8 Hz, $J_2$ = 4.3 Hz, 1 H), 6.76 (d, $J$ = 15.6 Hz, 1 H), 6.09 (td, $J_1$ = 9.7 Hz, $J_2$ = 1.8 Hz, 1 H), 6.04 (d, $J$ = 15.6 Hz, 1 H), 5.75 (dd, $J_1$ = 15.6 Hz, $J_2$ = 6.9 Hz, 1 H), 5.61 (dt, $J_1$ = 15.5 Hz, $J_2$ = 7.4 Hz, 1 H), 5.30 (d, $J$ = 9.8 Hz, 1 H), 5.22 (qd, $J_1$ = 6.6 Hz, $J_2$ = 1.1 Hz, 1 H), 5.15 (d, $J$ = 10.1 Hz, 1 H), 5.01 (dt, $J_1$ = 7.3 Hz, $J_2$ = 7.1 Hz, 1 H), 3.69 (dq, $J_1$ = 10.1 Hz, $J_2$ = 6.7 Hz, 1 H), 3.59 (ddd, $J_1$ = 5.5 Hz, $J_2$ = 5.5 Hz, $J_3$ = 4.0 Hz, 1 H), 2.88 (qd, $J_1$ = 7.1 Hz, $J_2$ = 5.7 Hz, 1 H), 2.74-2.67 (m, 1 H), 2.51-2.49 (m, 2 H), 2.40 (d, $J$ = 4.0 Hz, 1 H), 2.15-2.06 (m, 2 H), 2.02 (dd, $J_1$ = 13.0 Hz, $J_2$ = 6.1 Hz, 1 H), 1.85 (d, $J$ = 1.1 Hz, 3 H), 1.84 (d, $J$ = 1.1 Hz, 3 H), 1.74 (dd, $J_1$ = 13.0 Hz, $J_2$ = 8.8 Hz, 1 H), 1.69-1.64 (m, 1 H), 1.60 (dd, $J_1$ = 6.8 Hz, $J_2$ = 0.5 Hz, 3 H), 1.58 (s, 3 H), 1.17 (d, $J$ = 7.1 Hz, 3 H), 1.16 (d, $J$ = 6.6 Hz, 3 H), 0.99 (d, $J$ = 6.7 Hz, 3 H), 0.80 (d, $J$ = 6.6 Hz, 3 H). $^{13}$C-NMR (150 MHz, $CDCl_3$) $\delta$ 215.4, 163.7, 144.3, 138.7, 135.8, 135.1, 133.6, 130.4, 129.1, 128.1, 127.3, 125.0, 121.3, 120.1, 78.3, 74.0, 46.1, 45.3, 43.7, 40.4, 32.8, 31.9, 29.7, 20.3, 20.0, 15.8, 14.9, 13.8, 13.0, 12.7, 11.8. HRMS-ESI calcd for $C_{31}H_{46}O_4Na$: $[M + Na]^+$ 505.3294, found 505.3281. FTIR $\nu$ 3440*m*, 2963*m*, 2927*m*, 2856*w*, 1709*m*, 1454*w*, 1381*w*, 1248*w*, 891*m* $cm^{-1}$. UV spectrum $\lambda_{max}$ = 241 nm in MeOH. Analytical HPLC $R_t$ = 32.35 minutes ($C_{18}$, 60%-100% MeOH in 50 minutes). Semi-preparative HPLC $R_t$ = 38.82 minutes ($C_{18}$, 60%-80% MeOH in 50 minutes).

**(*R*)-6-((1*E*,3*Z*,5*R*,7*E*,9*E*,11*R*,13*S*,14*R*,15*S*,17*E*)-3-ethyl-14-hydroxy-5,9,11,13,15,17- hexamethyl-12-oxononadeca-1,3,7,9,17-pentaenyl)-5,6-dihydro-2*H*-pyran-2-one (anguinomycin D) (2)**



To a solution of **41** (27.0 mg, 0.041 mmol, 1.00 equiv) in a mixture acetone/water (5/1) (830 $\mu$L) was added PPTS (6.0 mg, 0.024 mmol, 0.4 equiv) and the resulting solution stirred at RT for 43 hours. The reaction was transferred in a saturated $NaHCO_3$ solution, extracted with $Et_2O$ (3x) and the combined organic layer washed with brine (1x), dried ($MgSO_4$) and concentrated. Purification by chromatography on $SiO_2$ (pentane/$Et_2O$ 9:1 → 1:1) afforded the lactol (23.0 mg, 0.037 mmol, 91%).

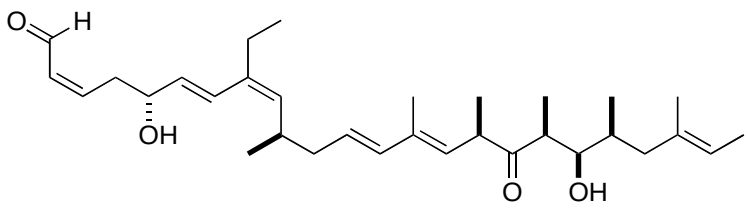
To a solution of lactol (1.30 mg, 0.002 mmol, 1.00 equiv) in $CH_2Cl_2$ (0.5 mL), 4Å MS (50 mg), PCC (3.00 mg, 0.013 mmol, 6.00 equiv) and glacial acetic acid (12 $\mu$L, 0.21 mmol, 100 equiv) were sequentially added and the resulting mixture stirred at RT for 1.5 hours. The mixture was directly loaded over a column of silicagel and eluted with hexane/AcOEt 8.5/1.5 → 1/1 to afford the ketolactone intermediate which was directly used in the last step.

In a 10 ml plastic tube a solution of the previous obtained ketolactone in THF (0.5 mL) was cooled to 0 °C. Pyridine (100 $\mu$L) and HF·pyridine (100 $\mu$L) were sequentially added and the tube sealed. After 5 minutes the solution was allowed to return to RT and stirred for 4.5 days. The solution was cooled to 0 °C and silicagel (100 mg) was added. After 5 minutes, the mixture was loaded on a pipette column of silicagel and eluted with hexane/EtOAc 8:2 → 1:1 affording anguinomycin D (**2**) (0.62 mg, 0.0013 mmol, 60%) as a colorless oil. An analytical sample of anguinomycin D was purified by HPLC. $R_f$ = 0.17 (hexane/EtOAc 6:4). Optical rotation $[\alpha]^{22.7}_D$ (*c* 0.014, MeOH) = –112.0°. $^1$H-NMR (800 MHz, $CDCl_3$) δ 6.90 (dddd, $J_1$ = 9.7 Hz, $J_2$ = 4.9 Hz, $J_3$ = 3.6 Hz, $J_4$ = 0.8 Hz, 1 H), 6.63 (d, $J$ = 15.8 Hz, 1 H), 6.06 (dt, $J_1$ = 9.8 Hz, $J_2$ = 1.8 Hz, 1 H), 6.01 (d, $J$ = 15.6 Hz, 1 H), 5.76 (dd, $J_1$ = 15.7 Hz, $J_2$ = 6.9 Hz, 1 H), 5.58 (dt, $J_1$ = 15.5 Hz, $J_2$ = 7.3 Hz, 1 H), 5.25 (d, $J$ = 9.8 Hz, 1 H), 5.19 (qd, $J_1$ = 6.8 Hz, $J_2$ = 1.2 Hz, 1 H), 5.11 (d, $J$ = 10.1 Hz, 1 H), 4.99-4.96 (m, 1 H) or 4.98 (dtd, $J_1$ = 6.9 Hz, $J_2$ = 7.6 Hz, $J_3$ = 0.8 Hz, 1 H), 3.66 (dq, $J_1$ = 10.1 Hz, $J_2$ = 6.7 Hz, 1 H), 3.55 (t, $J$ = 5.6 Hz, 1 H), 2.87 (dt, $J_1$ = 5.7 Hz, $J_2$ = 7.1 Hz, 1 H), 2.68-2.64 (m, 1 H), 2.48-2.46 (m, 2 H), 2.22-2.15 (m, 2 H), 2.08 (t, $J$ = 7.0 Hz, 2 H), 1.98 (dd, $J_1$ = 13.1 Hz, $J_2$ = 6.2 Hz, 1 H), 1.82 (d, $J$ = 1.2 Hz, 3 H), 1.70 (dd, $J_1$ = 13.1 Hz, $J_2$ = 8.6 Hz, 1 H), 1.65-1.61 (m, 1 H), 1.57 (dd, $J_1$ = 6.7 Hz, $J_2$ = 0.8 Hz, 3 H), 1.55 (s, 3 H), 1.14 (d, $J$ = 7.3 Hz, 3 H), 1.13 (d, $J$ = 7.1 Hz, 3 H), 1.04 (t, $J$ = 7.5 Hz, 3 H), 0.96 (d, $J$ = 6.6 Hz, 3 H), 0.77 (d, $J$ = 6.6 Hz, 3 H). $^{13}$C-NMR (150 MHz, $CDCl_3$) δ 215.8, 164.1, 144.7, 137.3, 136.2, 135.4, 135.3, 134.0, 130.0, 128.4, 127.7, 124.8,

121.7, 120.5, 79.9, 74.4, 46.5, 45.6, 44.1, 40.8, 33.2, 32.2, 30.1, 26.4, 20.8, 16.3, 15.3, 14.2, 13.5, 13.4, 13.1, 12.2. HRMS-ESI calcd for $C_{32}H_{48}O_4Na$: $[M + Na]^+$ 519.3450; found 519.3429. UV spectrum $\lambda_{max}$ = 242 nm in MeOH. Analytical HPLC $R_t$ = 32.87 minutes ($C_{18}$, 60% → 100% MeOH in 50 minutes).

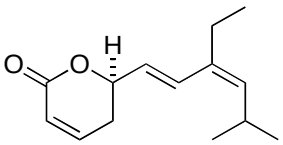
The same three last steps procedure (i. PPTS, acetone/water; ii. PCC, 4 Å MS, AcOH, $CH_2Cl_2$; iii. HF•pyridine, pyridine) was applied using the mixed fraction obtained from the $sp^3$-$sp^2$ Suzuki Cross-Coupling for the synthesis of product **41**. In addition to anguinomycin D (**2**), the following compounds were isolated:

**2*Z*,5*R*,6*E*,8*Z*,10*R*,12*E*,14*E*,16*R*,18*S*,19*R*,20*S*,22*E*)-8-ethyl-5,19-dihydroxy-10,14,16,18,20,22-hexamethyl-17-oxotetracosa-2,6,8,12,14,22-hexaenal (44)**




$R_f$ = 0.11 (hexane/EtOAc 7:3). $^1$H-NMR (400 MHz, $CDCl_3$) δ 9.56 (d, *J* = 7.5 Hz, 1 H), 6.91 (dt, $J_1$ = 15.8 Hz, $J_2$ = 7.5 Hz, 1 H), 6.56 (d, *J* = 15.8 Hz, 1 H), 6.23 (ddt, $J_1$ = 15.8 Hz, $J_2$ = 7.9 Hz, $J_3$ = 1.3 Hz, 1 H), 6.04 (d, *J* = 15.3 Hz, 1 H), 5.73 (dd, $J_1$ = 15.3 Hz, $J_2$ = 6.6 Hz, 1 H), 5.64-5.59 (m, 1 H), 5.24-5.20 (m, 2 H), 5.16 (d, *J* = 10.1 Hz, 1 H), 4.41 (q, *J* = 6.1 Hz, 1 H), 3.70-3.65 (m, 1 H), 3.60 (t, *J* = 5.3 Hz, 1 H), 2.91-2.86 (m, 1 H), 2.70-2.66 (m, 1 H), 2.65-2.63 (m, 1 H), 2.22-2.18 (m, 1 H), 2.11 (t, *J* = 6.6 Hz, 1 H), 2.01 (dd, $J_1$ = 13.2 Hz, $J_2$ = 6.1 Hz, 1 H), 1.84 (d, *J* = 1.3 Hz, 3 H), 1.76-1.73 (m, 1 H), 1.68-1.64 (m, 1 H), 1.61 (d, *J* = 6.6 Hz, 3 H), 1.58-1.57 (m, 3 H), 1.17 (d, *J* = 7.0 Hz, 3 H), 1.16 (d, *J* = 6.6 Hz, 3 H), 1.07 (t, *J* = 7.5 Hz, 3 H), 1.00 (d, *J* = 7.0 Hz, 3 H), 0.91 (t, *J* = 7.0 Hz, 3 H), 0.80 (d, *J* = 6.6 Hz, 3 H). HRMS-ESI calcd for $C_{32}H_{50}O_4Na$: $[M + Na]^+$ 521.3607; found 521.3607. Analytical HPLC $R_t$ = 32.37 minutes ($C_{18}$, 60% → 100% MeOH in 50 minutes). $\lambda_{max}$ = 239 nm.

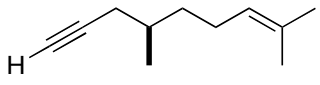
**(*R*)-6-((1*E*,3*Z*)-3-ethyl-5-methylhexa-1,3-dienyl)-5,6-dihydro-2*H*-pyran-2-one (4)**



$R_f$ = 0.44 (hexane/EtOAc 7:3). $^1$H-NMR (400 MHz, $CDCl_3$) δ 6.93 (dt, $J_1$ = 9.6 Hz, $J_2$ = 4.1 Hz, 1 H), 6.70 (d, $J$ = 15.8 Hz, 1 H), 6.09 (dt, $J_1$ = 9.8 Hz, $J_2$ = 1.9 Hz, 1 H), 5.78 (dd, $J_1$ = 15.8 Hz, $J_2$ = 6.9 Hz, 1 H), 5.29 (d, $J$ = 9.6 Hz, 1 H), 5.05-4.99 (m, 1 H), 2.81-2.72 (m, 1 H), 2.52-2.48 (m, 2 H), 2.19 (q, $J$ = 7.4 Hz, 2 H), 1.07 (t, $J$ = 7.4 Hz, 3 H), 1.00 (d, $J$ = 1.5 Hz, 3 H), 0.98 (d, $J$ = 1.4 Hz, 3 H). HRMS-ESI calcd for $C_{14}H_{20}O_2$: $[M]^+$ 221.1542; found 221.1548. Analytical HPLC $R_t$ = 38.55 minutes ($C_{18}$, 30% → 80% MeOH in 50 minutes), $\lambda_{max}$ = 239 nm.

## 3. Synthesis of Anguinomycin/Terpene Hybrid

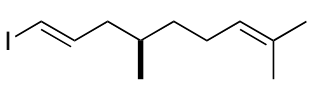
**(*E*)-4,8-dimethylnona-3,7-dien-1-yne (46)**



To a cooled (0 °C) solution of $CBr_4$ (292 mg, 0.88 mmol, 2.20 equiv) in $CH_2Cl_2$ (500 μL), $PPh_3$ (462 mg, 1.76 mmol, 4.40 equiv) was added in portion over 2 minutes. After 5 minutes stirring at 0 °C a solution of citronelal (62 mg, 0.40 mmol, 1.00 equiv) and 2,6-lutidine (61 μL, 0.88 mmol, 2.20 equiv) in $CH_2Cl_2$ (500 μL) was added via syringe over 10 minutes. The resulting brown mixture was stirred at 0 °C for 2 hours. The mixture was precipitated with pentane and the supernatant was filtered over Celite. The precipitate was dissolved in the minimum of $CH_2Cl_2$ and precipitated with pentane. The supernatant was filtered over Celite. This process was repeated 5 times. The combined supernatants were concentrated and purified by flash chromatography on $SiO_2$ (hexane/EtOAc 95:5) to afford the title compound (116 mg, 0.37 mmol, 92%) as a colorless oil. $R_f$ = 0.86 (hexane/EtOAc 9:1). $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.11 (d, $J$ = 10.5 Hz, 1 H), 5.87-5.83 (m, 1 H), 5.10-5.05 (m, 1 H), 2.17-2.06 (m, 4 H), 1.75 (d, $J$ = 1.4 Hz, 3 H), 1.69 (d, $J$ = 1.0 Hz, 3 H), 1.61 (s, 3 H). $^{13}$C-NMR (75 MHz, $CDCl_3$) δ 144.9, 133.6, 132.2, 123.4, 121.8, 88.9, 40.0, 29.7, 26.3, 25.6, 17.78. FTIR ν 2967*m*, 2924*s*, 2855*m*, 1636*w*, 1443*m*, 1381*m* $cm^{-1}$.

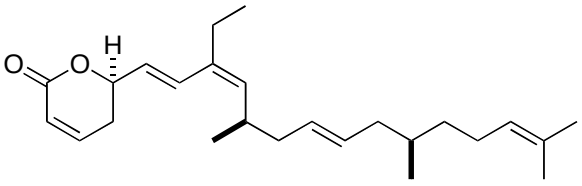
To a cooled (–78 °C) solution of (*E*)-1,1-dibromo-4,8-dimethylnona-1,3,7-triene (112 mg, 0.37 mmol, 1.00 equiv) in THF (600 μL) under Ar was added *n*BuLi (1.6 M in hexanes) (552 μL, 0.88 mmol, 2.40 equiv). The reaction was stirred during 10 minutes at –78 °C and allowed to reach RT over 1 hour. The solution was further stirred at RT for 1 hour. A saturated solution of $NH_4Cl$ (500 μL) was added and the mixture stirred at RT for 15 minutes. The mixture was diluted with $H_2O$ (2 mL) and extracted with $Et_2O$ (3x). The combined organic phase was washed with brine (1x), dried ($Na_2SO_4$) and concentrated to afford alkyne (**46**), which was directly used in the next step without further purification.

**(1*E*,3*E*)-1-iodo-4,8-dimethylnona-1,3,7-triene (47)**



To a cooled (–20 °C) solution of the previously obtained terminal alkyne in THF (1.5 mL) under Ar was added $Cp_2ZrHCl$ (105 mg, 0.41 mmol, 1.10 equiv) in one portion. The reaction flask was covered with an aluminium foil and the suspension stirred at –20 °C for 30 minutes. The resulting clear solution was cooled to –78 °C followed by addition of $I_2$ (36 mg, 0.28 mmol, 1.30 equiv) in THF (1.0 mL). The mixture was stirred at –78 °C for 30 minutes and then allowed to return to RT over 1 hour. The reaction was quenched by addition of HCl (1 M) and extracted with $Et_2O$ (3x). The combined organic phase was washed with saturated $Na_2S_2O_3$ (1x), saturated $NaHCO_3$ (1x), brine (1x), dried ($Na_2SO_3$) and concentrated. The residue was purified by flash chromatography on $SiO_2$ (pentane/$Et_2O$ 100:0 → 98:2) to give the iodoolefin **47** (88 mg, 0.32 mmol, 87% over 2 steps) as a colorless oil. $R_f$ = 0.46 (pentane/$Et_2O$ 9:1). $^1$H-NMR (400 MHz, $CDCl_3$) δ 6.48 (dt, $J_1$ = 14.4 Hz, $J_2$ = 7.7 Hz, 1 H), 5.96 (dt, $J_1$ = 14.4 Hz, $J_2$ = 1.1 Hz, 1 H), 5.11-5.05 (m, 1 H), 2.10-1.86 (m, 4 H), 1.68 (d, $J$ = 1.2 Hz, 3 H), 1.60 (s, 3 H), 1.57-1.49 (m, 1 H), 1.28 (m, 1 H), 1.19-1.10 (m, 1 H), 0.88 (d, $J$ = 6.7 Hz, 3 H). $^{13}$C-NMR (75 MHz, $CDCl_3$) δ 145.5, 124.5, 75.0, 43.4, 36.4, 32.1, 25.5, 25.7, 19.3, 17.7. FTIR ν 2963*m*, 2913*s*, 2870*m*, 2851*m*, 1605*w*, 1454*m*, 1377*m*, 1188*w*, 949*s* cm$^{-1}$.

**(*R*)-6-((*R*,1*E*,3*Z*,7*E*,9*E*)-3-ethyl-5,10,14-trimethylpentadeca-1,3,7,9,13-pentaenyl)-5,6-dihydro-2*H*-pyran-2-one (3)**

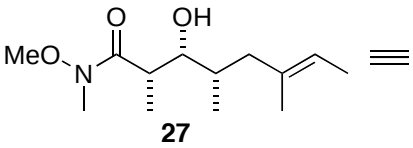


To a solution of alkyl iodine (**21**) (5.00 mg, 0.013 mmol, 1.00 equiv) in $Et_2O$ (150 μL) under Ar, 9-MeO-9-BBN (1 M in hexane) (44 μL, 0.044 mmol, 3.40 equiv) was added. The resulting solution was cooled to –78 °C and treated with *t*BuLi (1.5 M in pentane) (26 μL, 0.038 mmol, 3.00 equiv). After 5 minutes THF (150 μL) was added and the solution allowed to return to RT. Stirring was continued for 1 hour. Separately in another flask the iodoolefin **47** (7.00 mg, 0.026 mmol, 2.00 equiv) was taken up in DMF (150 μL) to which $Pd(dppf)Cl_2•CH_2Cl_2$ (1.10 mg, 0.001 mmol, 0.10 equiv), $AsPh_3$ (1.00 mg, 0.003, 0.25 equiv), $Cs_2CO_3$ (17.0 mg, 0.051 mmol, 4.00 equiv) and $H_2O$ (6 μL, 0.307 mmol, 24 equiv) were sequentially added. The alkyl boronate solution was transferred in the DMF solution and the resulting red-brown mixture stirred at RT overnight. The reaction was diluted with water and extracted with $Et_2O$ (3x). The combined organic layers were washed with water (1x) and brine (1x), dried ($Na_2SO_4$) and concentrated. Purification by chromatography on $SiO_2$ (pentane/$Et_2O$ 100:0 → 98:2) afforded the coupled product (4.20 mg, 0.011 mmol, 74%) as a pale yellow oil.

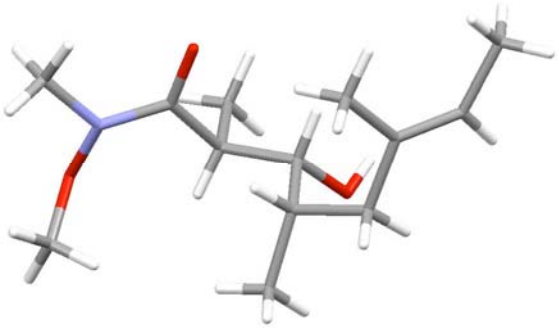
To a solution of the previously obtained coupled product (3.90 mg , 0.01 mmol, 1.00 equiv) in a mixture of acetone/water (3/1) (200 $\mu$L) was added PPTS (2.4 mg, 0.01 mmol, 1.00 equiv). The reaction was stirred at RT for 4 hours, then quenched with water and extracted with $Et_2O$ (3x). The combined organic layers were dried ($MgSO_4$) and concentrated to afford the crude lactol. The residue was dissolved in $CH_2Cl_2$ (1/0.025) (200 $\mu$L) with 4 Å molecular sieves (50 mg), treated with PCC (6.1 mg, 0.028 mmol, 3.00 equiv) and the suspension was stirred for 3 hours. The mixture was diluted with $CH_2Cl_2$ and filtered through Celite, washed with water (1x) and extracted with $CH_2Cl_2$. The organic layer was dried ($Na_2SO_4$) and concentrated. The residue was purified by chromatography on $SiO_2$ (pentane/$Et_2O$ 96:4) to give the α,β-unsaturated lactone (**3**) (1.84 mg, 0.005 mmol, 46%) as a colorless oil. $R_f$ = 0.38 (pentane/$Et_2O$ 9:1). $^1$H-NMR (800 MHz, $CDCl_3$) δ 6.90 (ddd, $J_1$ = 10.5 Hz, $J_2$ = 4.4 Hz, $J_3$ = 3.9 Hz, 1 H), 6.64 (d, $J$ = 15.7 Hz, 1 H), 6.07 (ddd, $J_1$ = 9.9 Hz, $J_2$ = 2.1 Hz, $J_3$ = 1.6 Hz, 1 H), 5.76 (dd, $J_1$ = 15.9 Hz, $J_2$ = 6.8 Hz, 1 H), 5.38-5.34 (m, 1H), 5.32-5.28 (m, 1 H), 5.25 (d, $J$ = 9.9 Hz, 1 H), 5.10-5.07 (m, 1 H), 5.01-4.98 (m, 1 H), 2.64-2.59 (m, 1 H), 2.48-2.46 (m, 2 H), 2.21-2.14 (m, 2 H), 2.01-1.97 (m, 4 H), 1.95-1.91 (m, 1 H), 1.81-1.79 (m, 1 H), 1.68 (s, 3 H), 1.60 (s, 3 H), 1.47-1.41 (m, 1 H), 1.29-1.34 (m, 1 H), 1.08-1.13 (m, 1 H), 1.04 (t, $J$ = 7.3 Hz, 3 H), 0.95 (d, $J$ = 6.8 Hz, 3 H), 0.84 (d, $J$ = 6.8 Hz, 3 H). $^{13}$C-NMR (200 MHz, $CDCl_3$) δ 164.2, 144.8, 137.7, 134.8, 131.1, 130.7, 130.0, 129.2, 125.0, 124.6, 121.7, 79.0, 40.7, 40.1, 36.7, 32.8, 32.1, 30.1, 26.3, 25.8, 25.7, 20.8, 19.4, 17.7, 13.4. FTIR ν 2963*m*, 2916*m*, 2870*m*, 2361*m*, 2338*w*, 1732*s*, 1454*w*, 1381*m*, 1242*s*, 1053*w*, 1022*w*, 964*m*, 814*w* cm$^{-1}$. HRMS-ESI-TOF calcd for $C_{25}H_{38}O_2$: $[M + H]^+$ 371.2945; found 371.2950.

## 4. X-ray Cristallography

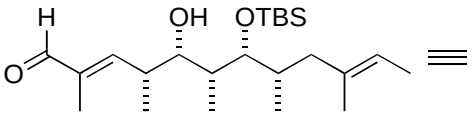
**(2*S*,3*R*,4*S*,*E*)-3-hydroxy-*N*-methoxy-*N*,2,4,6-tetramethyloct-6-enamide (27) (CCDC674800)**



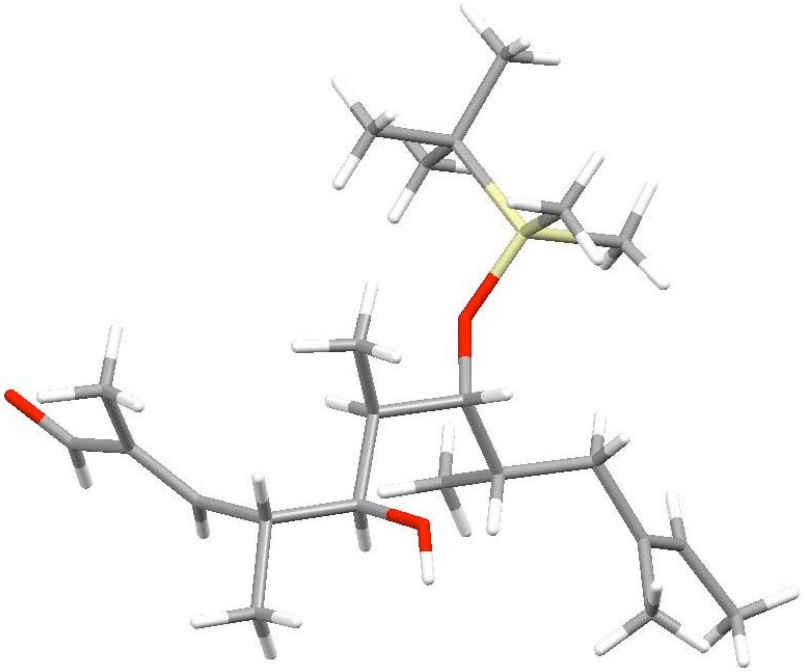

**27**



**(2*E*,4*R*,5*S*,6*R*,7*R*,8*S*,10*E*)-7-(*tert*-butyldimethylsilyloxy)-5-hydroxy-2,4,6,8,10-pentamethyldodeca-2,10-dienal (33) (CCDC674799)**




**33**



## 5. Biological Evaluation: Cell Culture Techniques, Antibodies and Indirect Immunofluorescence

HeLa cells were cultured at 37 °C in Dulbecco's modified eagle's medium (DMEM), supplemented with 10% fetal calf serum, 100 units/ml penicillin and 100 µg/ml streptomycin. For studying the inhibition of CRM1-mediated nuclear export, HeLa cells were grown on coverslips for 24 h to about 75% confluency. Cells were then incubated with different concentrations of LMB (LC laboratories, USA) or anguinomycins C or D for 90 min at 37 °C. For detection of Rio2, cells were fixed in 4% paraformaldehyde for 20 min and permeabilized for 5 minutes in 1 x detergent (0.1% Triton-X, 0.02% SDS in 1xPBS). Incubation with α-Rio2 antibody (polyclonal antibody, raised against recombinant full-length human Rio2 in rabbit, affinity-purified) and fluorescently labeled secondary antibody (a-rabbit, Alexa 488-labeled, Invitrogen). Pictures were acquired using a Leica TCS NT1 laser-scanning confocal microscope.

## 6. Modeling

LMB was modeled covalently bound to cysteine 528 of the CRM1-SNUPN structure from Dong *et al*. (PDB code 3GB8).[2] The structure of the protein, including the coordinates of the covalently modified cysteine 528, was kept rigid. Only the inhibitor and the sulfur atom of modified cysteine 528 were allowed to move. The program Coot[3] was used in the modeling. The program Sketcher from the CCP4 suite[4] was used to generate coordinates and bond restraints for the covalently modified cysteine 528. Initial inhibitor conformations were minimized using Phenix[5] to remove clashes with the protein. Then the coordinates were subjected to an energy minimization using PLOP[6] to generate the final LMB

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[2] Dong, X.; Biswas, A.; Suel, K. E.; Jackson, L. K.; Martinez, R.; Gu, H.; Chook, Y. M. *Nature* **2009**, *458*, 1136-1141.
[3] Emsley, P.; Cowtan, K. *Acta Crystallogr D Biol Crystallogr* **2004**, *60*, 2126-2132.
[4] Collaborative Computational Project, N. *Acta Crystallogr D Biol Crystallogr* **1994**, *50*, 760-763.
[5] Adams, P. D.; Grosse-Kunstleve, R.W.; Hung, L.W.; Ioerger, T.R.; McCoy, A.J.; Moriarty, N.W.; Read, R.J.; Sacchettini, J.C.; Sauter, N.K.; Terwilliger, T.C. *Acta Crystallogr D Biol Crystallogr* **2002**, *58*, 1948-1954.
[6] Kalyanaraman, C.; Bernacki, K.; Jacobson, M.P. *Biochemistry* **2005**, *44*, 2059-2071.

model. For the derivatives, we used the LMB conformation as a starting point and subjected to them also to an energy minimization. PyMOL[7] was used to make the molecular pictures.

**Supplementary figure**

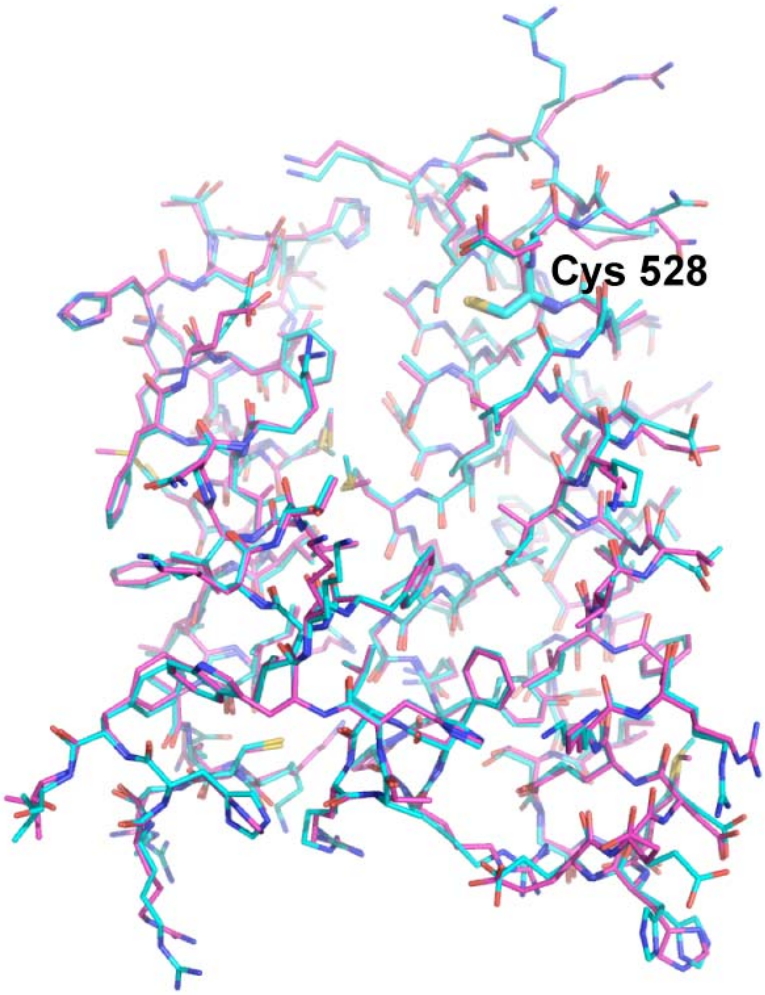


Figure S1: Superposition of two CRM1 structures,[2,8] focusing on the nuclear export signal (NES) binding sites. The structures are almost identical in this region with a RMSD of 0.31 Å for residues 490-600.

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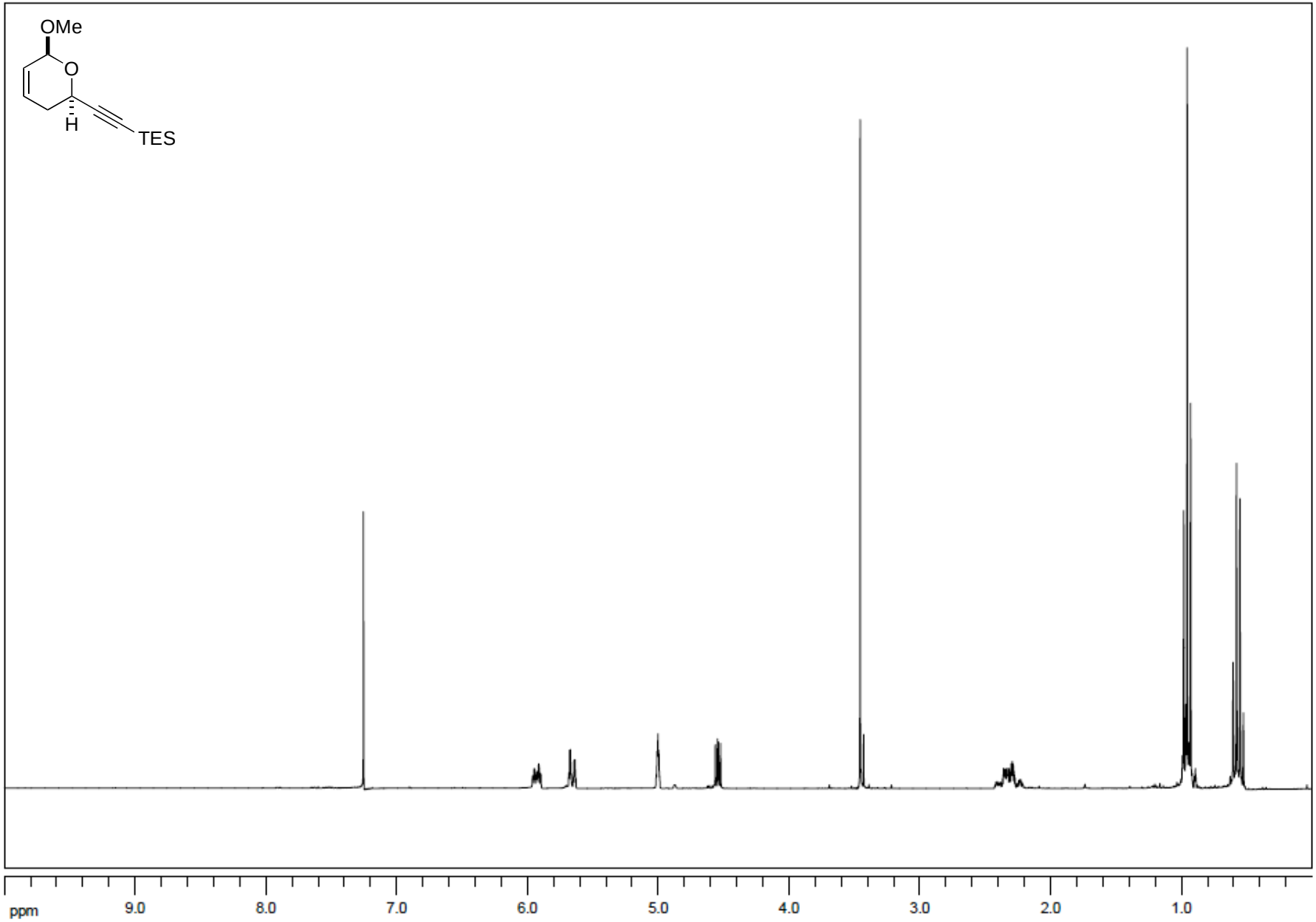
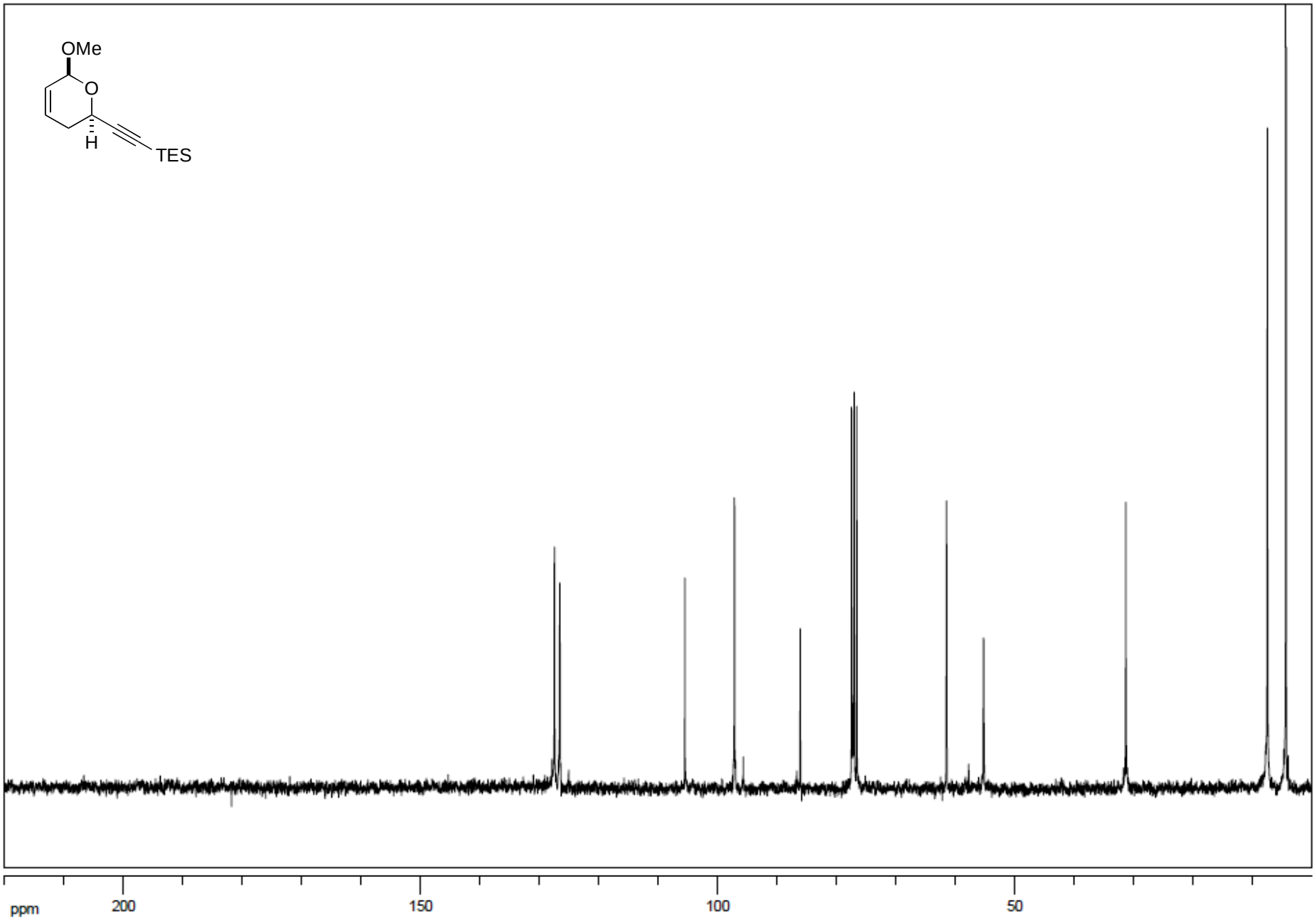
[7] DeLano, W.L.; *The PyMOL Molecular Graphics System*, DeLano Scientific, Palo Alto, CA, USA, **2002**.

[8] Monecke, T.; Guttler, T.; Neumann, P.; Dickmanns, A.; Gorlich, D.; Ficner, R. *Science* **2009**, *324*, 1087-1091.

**7. Spectra**

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H
TES
ppm
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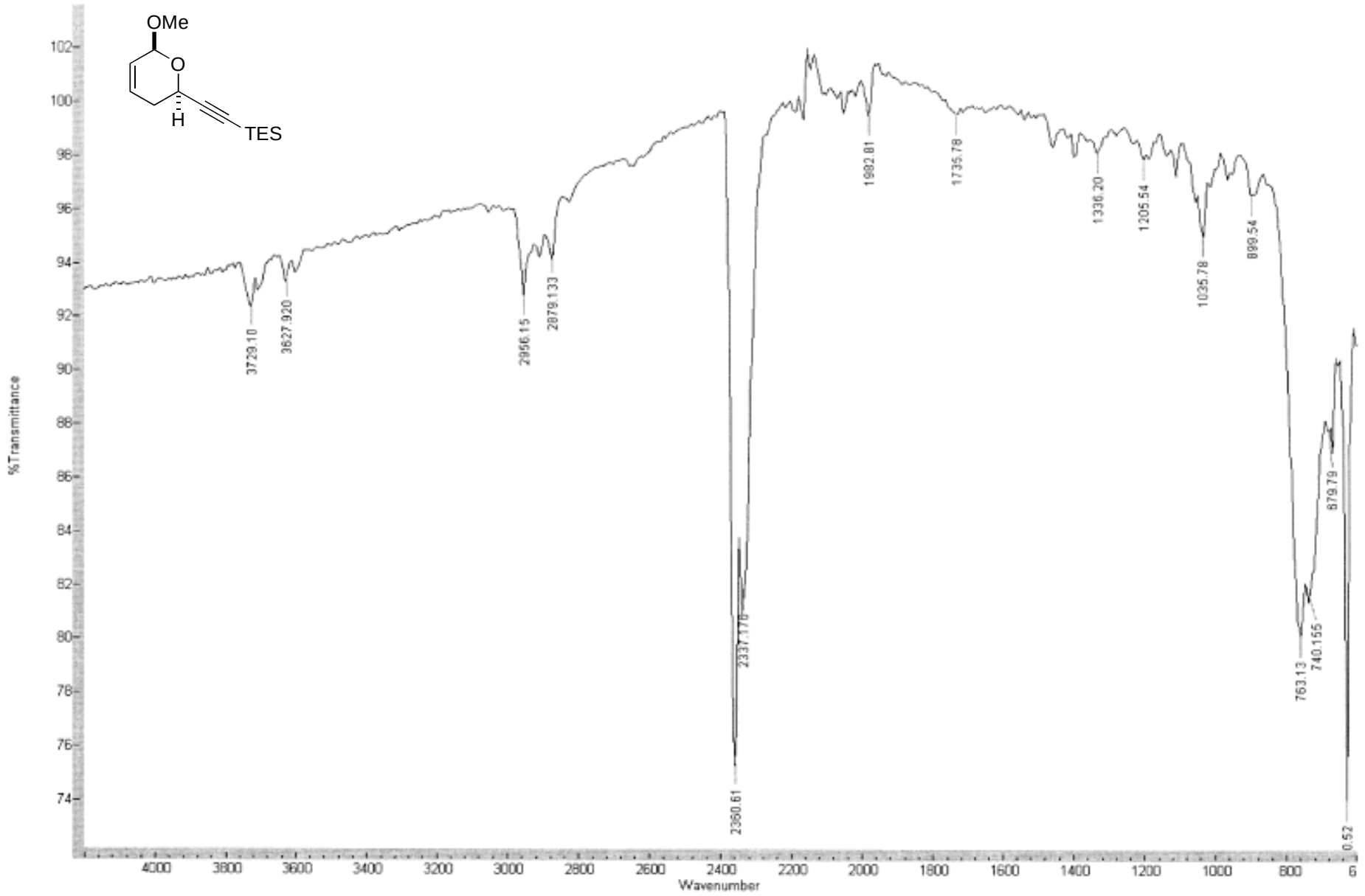
150
100
50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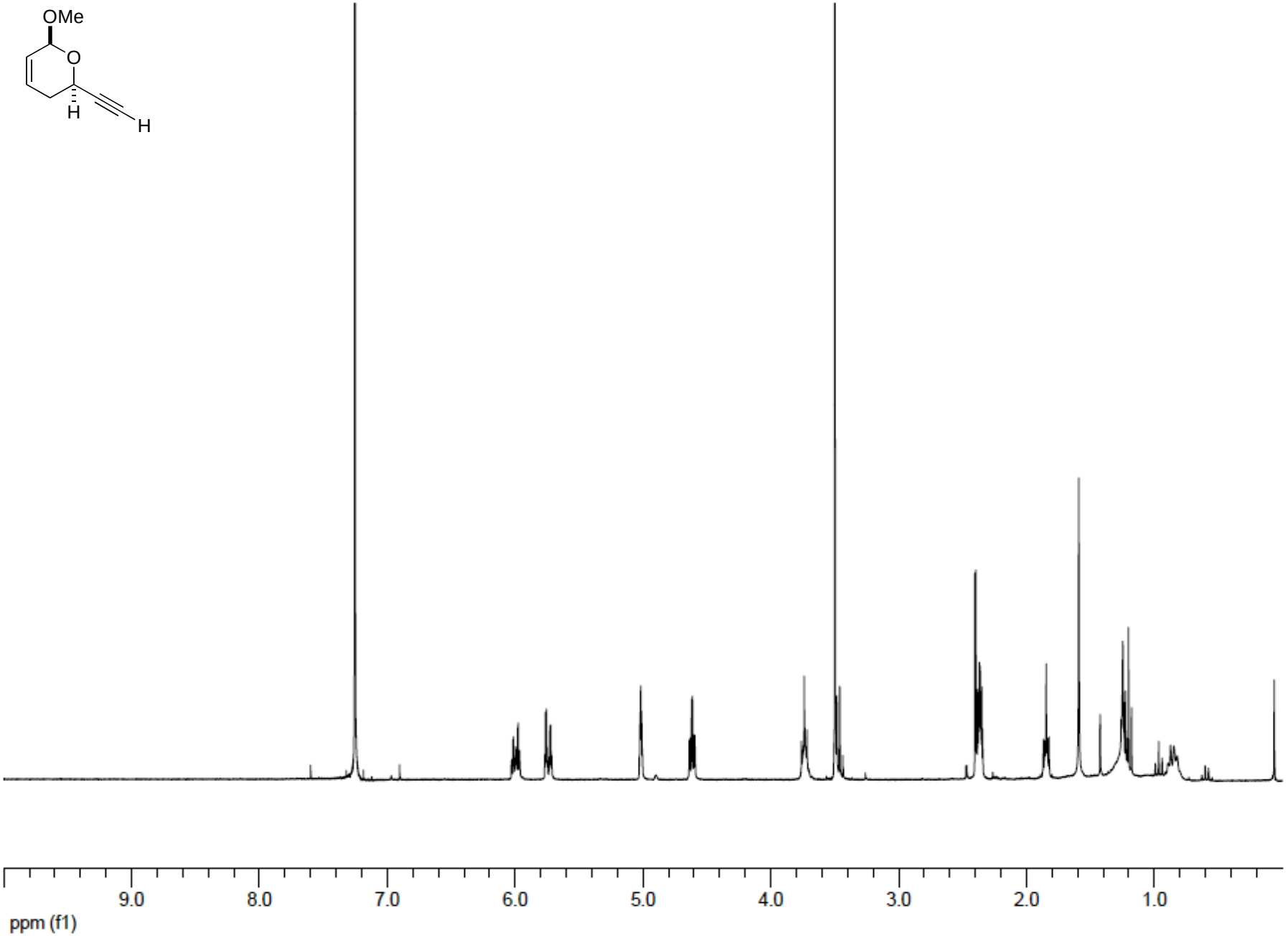
740.155
0.52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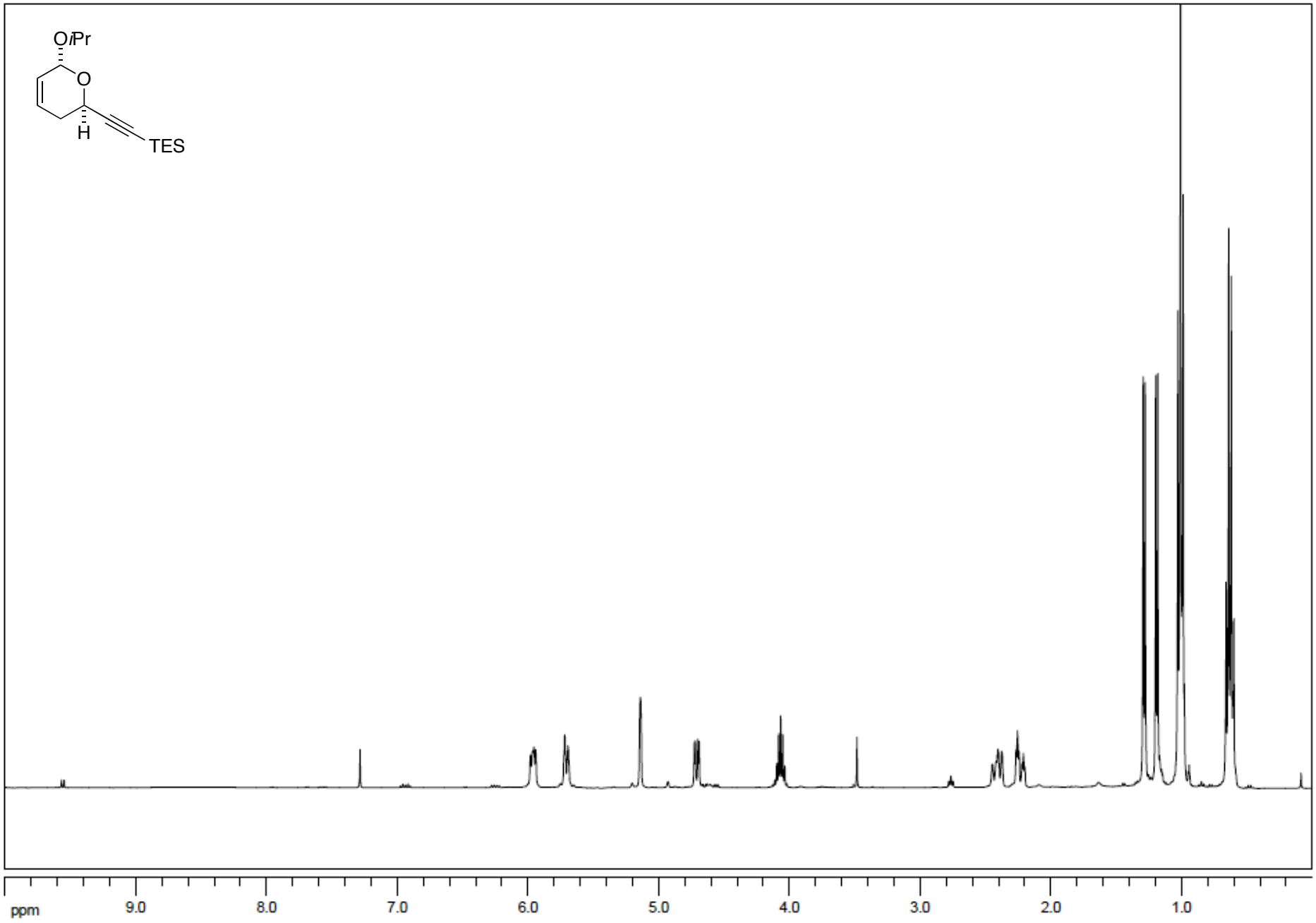
ppm (f1)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ppm
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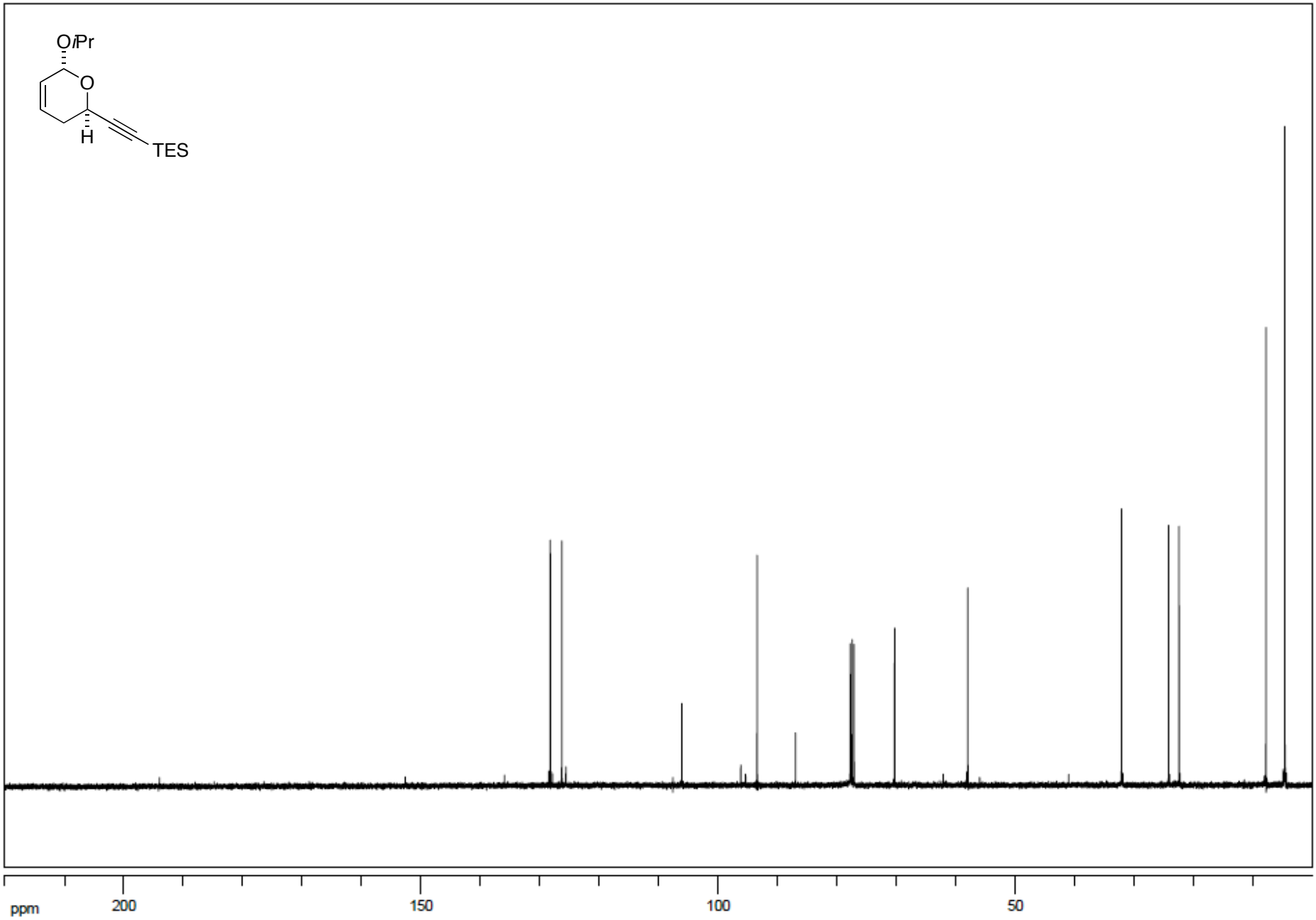
2.0
1.0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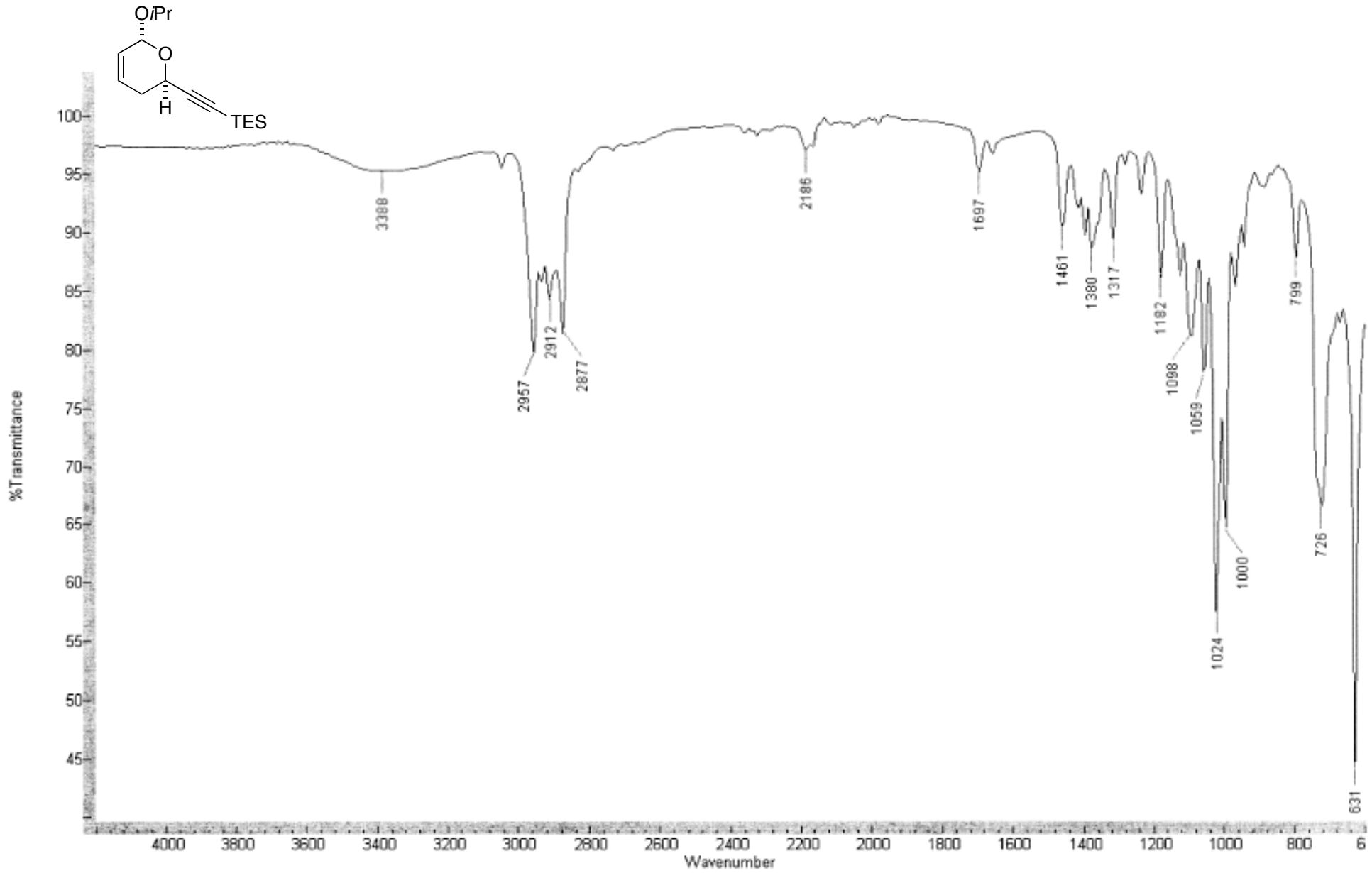
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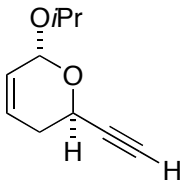
726
631


OiPr
O
H
H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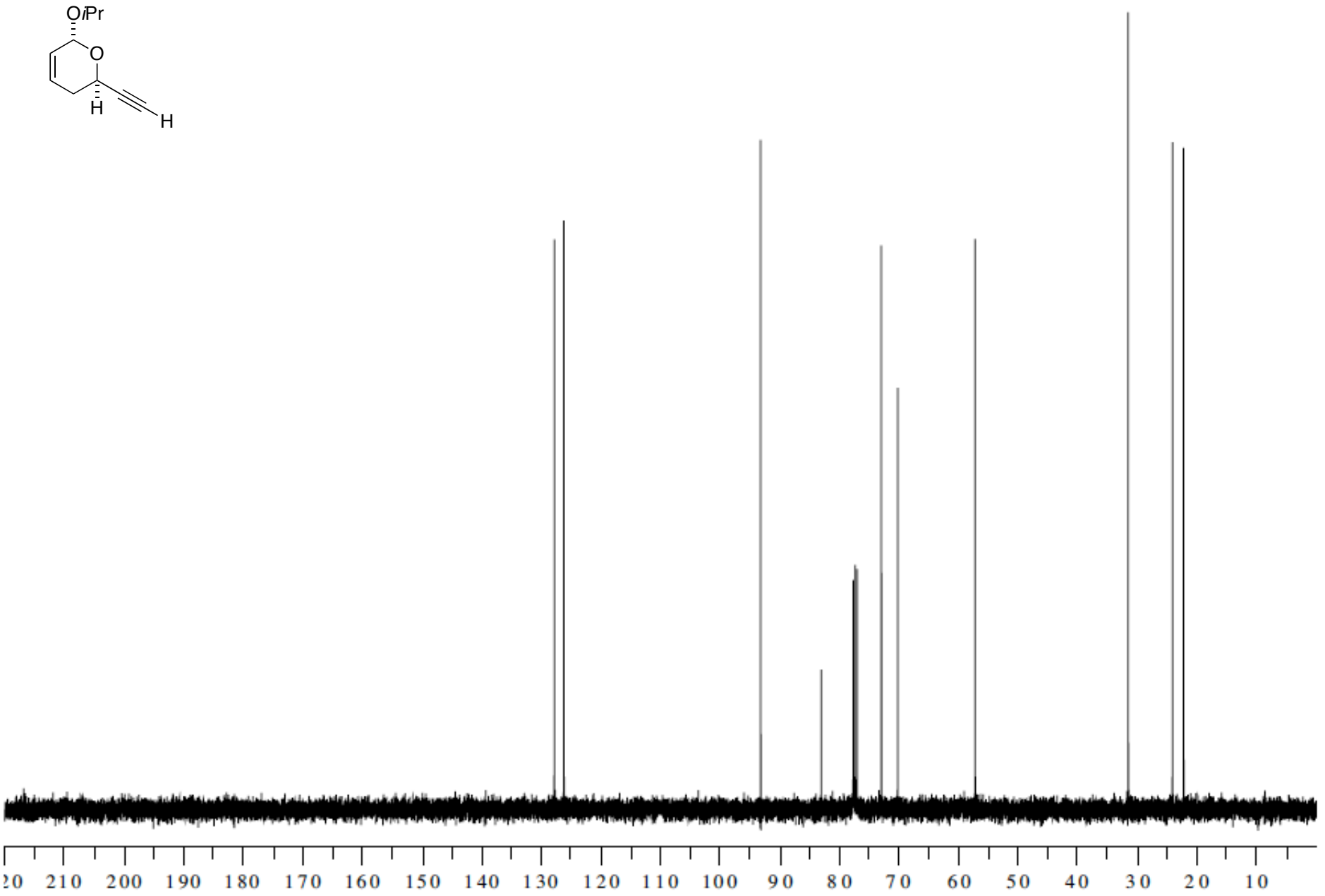
2
1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H
H
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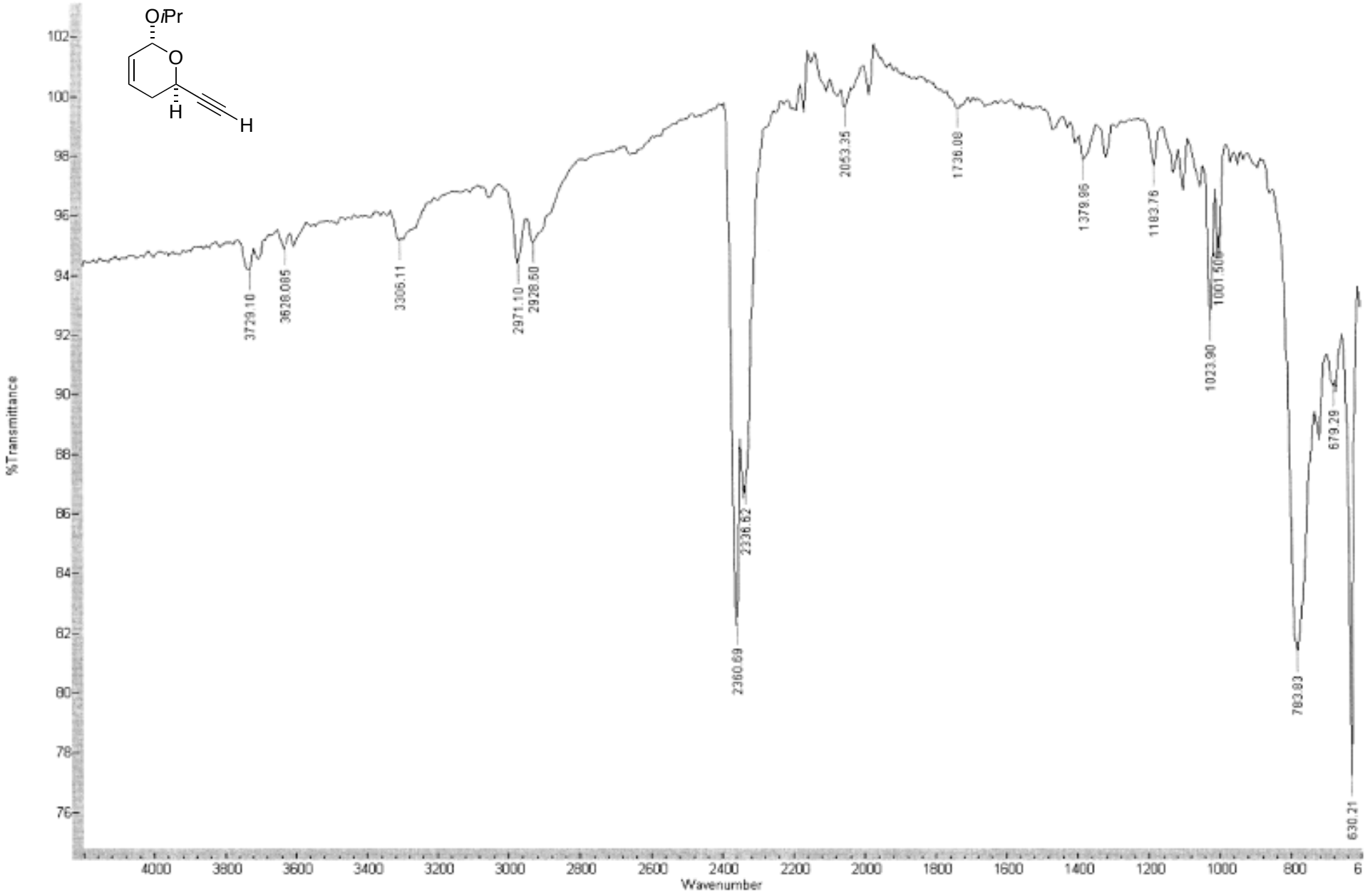
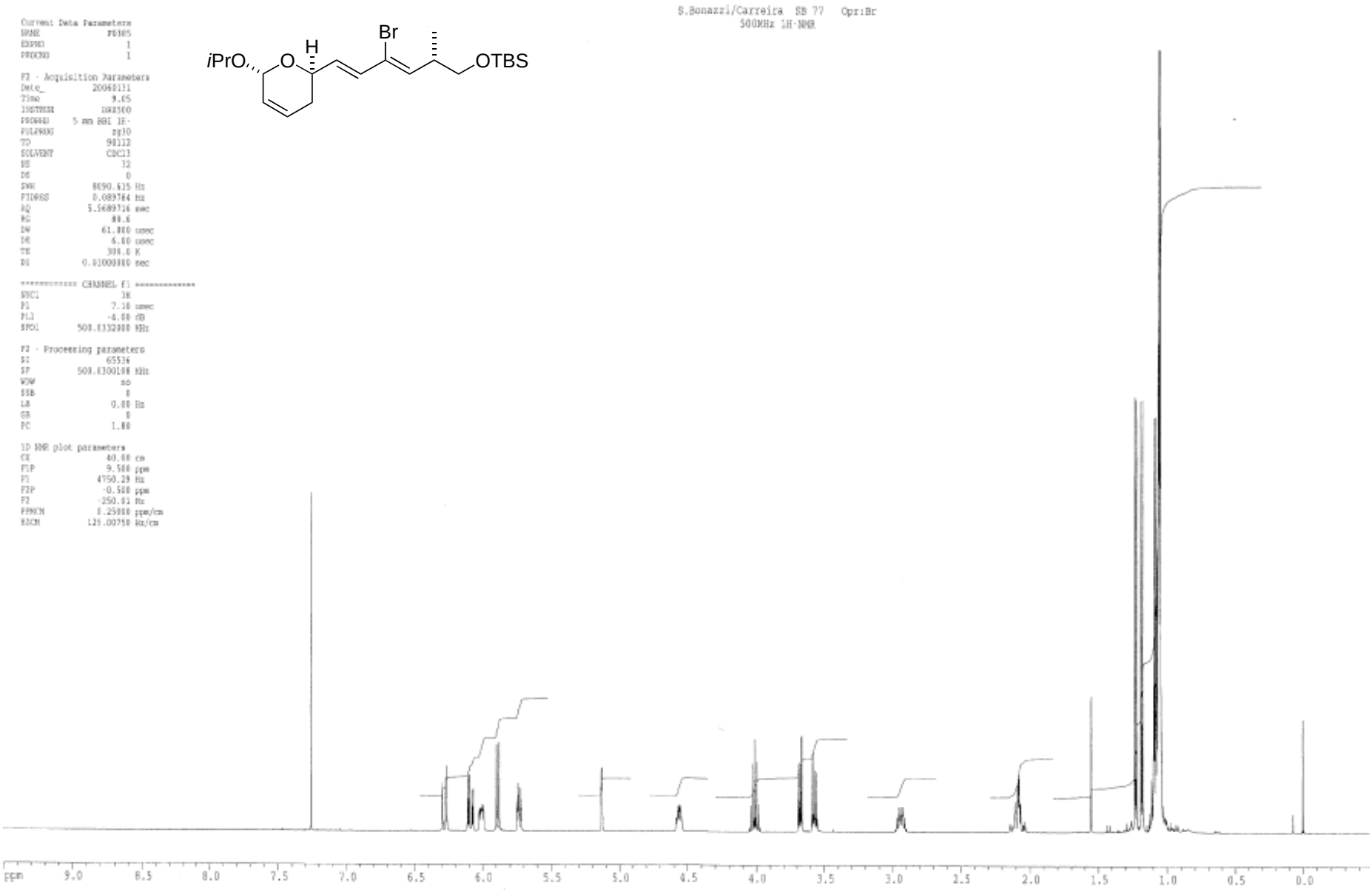
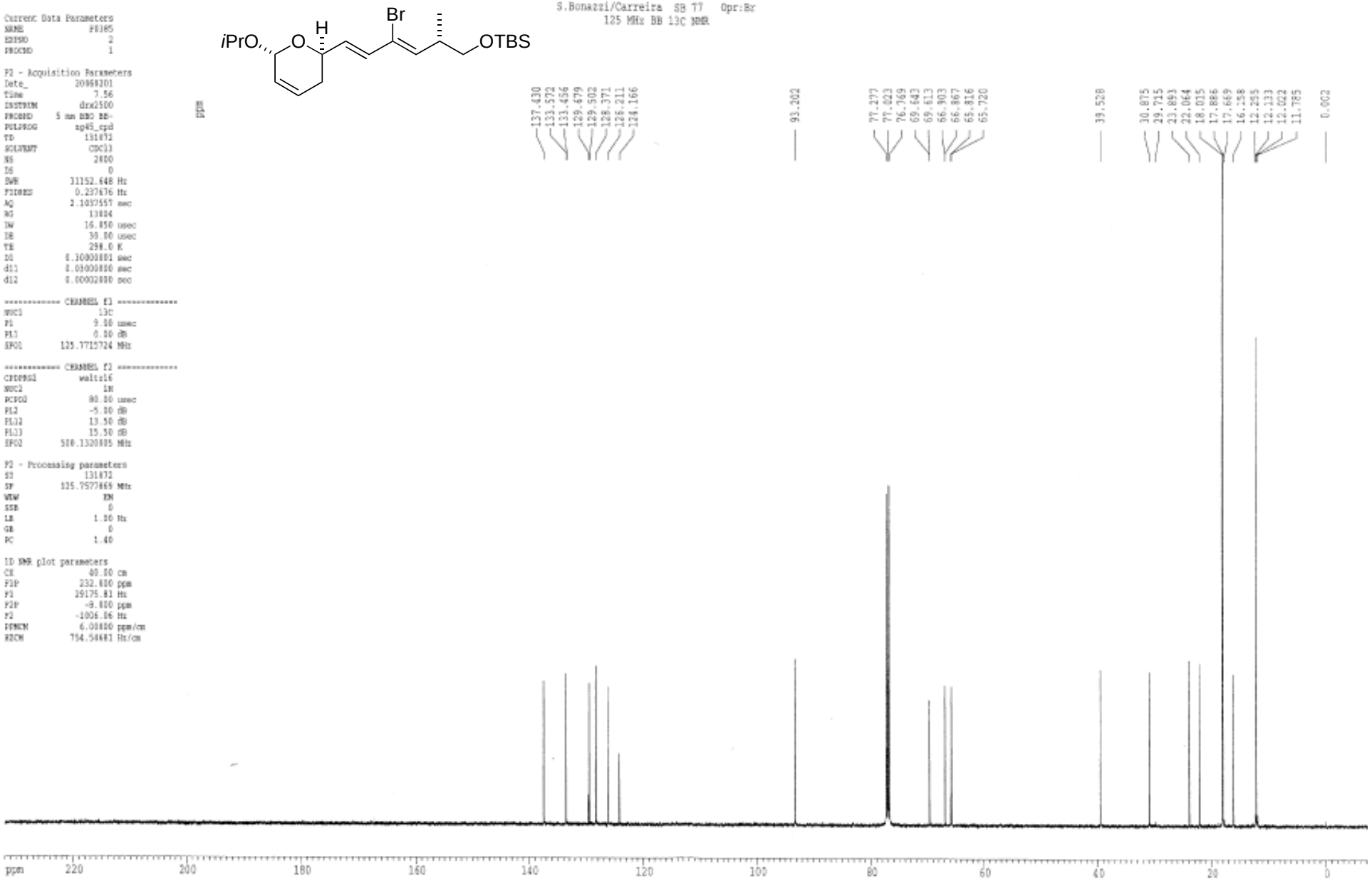

OiPr
O
H
H
%Transmittance
Wavenumber
3729.10
3628.085
3305.11
2971.10
2928.60
2360.69
2336.62
2053.35
1736.08
1378.95
1183.76
1023.90
1001.50
783.93
679.29
630.21


S.Bonazzi/Carreira SB 77 Opr:Br
500MHz 1H-NMR
Current Data Parameters
NAME PB105
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20060131
Time 9.05
INSTRUM DRX500
PROBHD 5 mm BBI 1H-
PULPROG zg30
TD 98112
SOLVENT CDCl3
NS 12
DS 0
SWH 8090.615 Hz
FIDRES 0.083784 Hz
AQ 5.5689716 sec
RG 80.6
DW 61.800 usec
DE 6.00 usec
TE 308.0 K
D1 0.01000000 sec
CHANNEL f1
SFO1 500.0332000 MHz
F2 - Processing parameters
SI 65536
SF 500.0300108 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 40.00 cm
F1P 9.500 ppm
F1 4750.29 Hz
F2P -0.500 ppm
F2 -250.81 Hz
PPMCM 0.25000 ppm/cm
HZCM 125.00750 Hz/cm
iPrO
O
H
Br
OTBS
ppm
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0




Current Data Parameters
NAME PB185
EXPNO 2
PROCNO 1

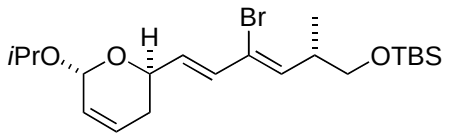
F2 - Acquisition Parameters
Date_ 20060201
Time 7.56
INSTRUM drx2500
PROBHD 5 mm BBO BB-
PULPROG zg45_cpd
TD 131072
SOLVENT CDCl3
NS 2400
DS 0
SWH 31152.648 Hz
FIDRES 0.237676 Hz
AQ 2.1037557 sec
RG 13884
DW 16.050 usec
DE 30.00 usec
TE 298.0 K
D1 0.30000001 sec
d11 0.03000000 sec
d12 0.00002000 sec

======== CHANNEL f1 ========
NUC1 13c
P1 9.00 usec
PL1 0.00 dB
SFO1 125.7715724 MHz

======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -5.00 dB
PL12 13.50 dB
PL13 15.50 dB
SFO2 500.1320005 MHz

F2 - Processing parameters
SI 131072
SF 125.7577869 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

1D NMR plot parameters
CX 40.00 cm
F1P 232.600 ppm
F1 29175.81 Hz
F2P -8.800 ppm
F2 -1006.86 Hz
PPMCM 6.00800 ppm/cm
HZCM 754.54681 Hz/cm

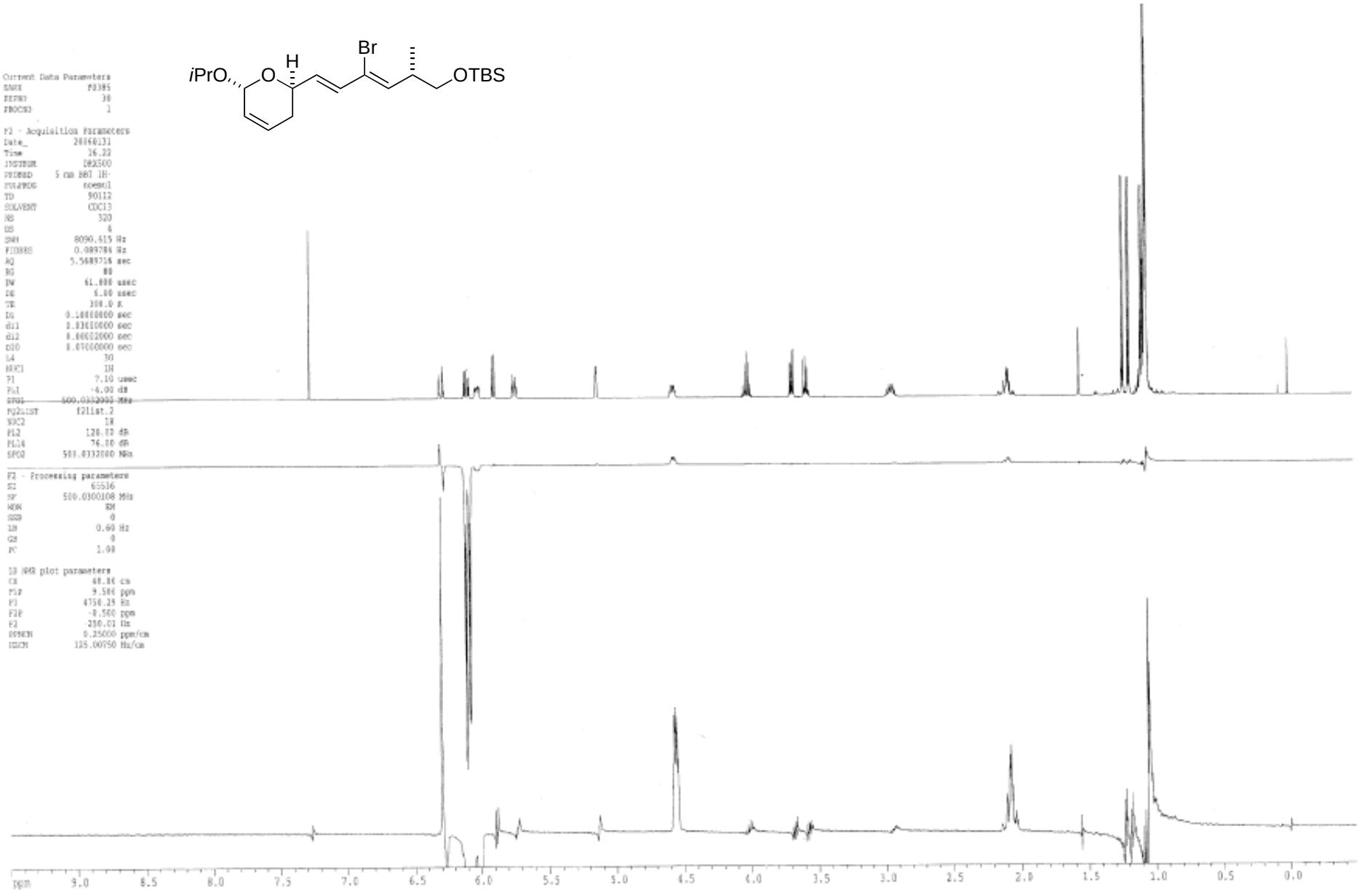


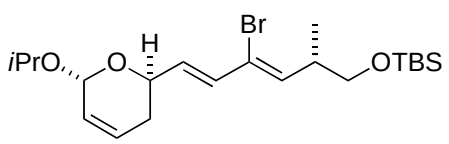

S.Bonazzi/Carreira SB 77 Opr:Br
125 MHz 13C DEPT 90+135 NMR

```
Current Data Parameters
NAME              F0385
EXPNO                 3
PROCNO                1

F2 - Acquisition Parameters
Date_          20060201
Time               9.43
INSTRUM         drx2500
PROBHD     5 mm BBO BB-
PULPROG         deptleth
TD                131072
SOLVENT             CDCl3
NS                    400
DS                      0
SWH           31152.648 Hz
FIDRES         0.237676 Hz
AQ             2.1037557 sec
RG                  13004
DW                16.050 usec
DE                30.00 usec
TE                298.0 K
CNST2       145.0000000
D1             2.00000000 sec
d2             0.00344828 sec
d12            0.00002000 sec
DELTA          0.00001146 sec

============ CHANNEL f1 =============
NUC1                 13C
P1                  9.00 usec
p2                 18.00 usec
PL1                0.00 dB
SFO1        125.7715724 MHz

============ CHANNEL f2 =============
CPDPRG2          waltz16
NUC2                  1H
PCPD2              80.00 usec
PL2                -3.00 dB
PL12               13.58 dB
SFO2        500.1320005 MHz

F2 - Processing parameters
SI                 65536
SF          125.7577869 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.40

1D NMR plot parameters
CX                 40.00 cm
F1P               232.000 ppm
F1              29175.80 Hz
F2P                -8.000 ppm
F2              -1006.06 Hz
PPMCM              6.00000 ppm/cm
HZCM            754.54675 Hz/cm
```


S.Bomazzi/Carreira SB 77 Opr:Br
500 MHz 1H NOE difference spectrum
iPrO
O
H
Br
OTBS
Current Data Parameters
NAME FO385
EXPNO 32
PROCNO 1
F1 - Acquisition Parameters
Date_ 20060331
Time 16.27
INSTRUM DRX500
PROBHD 5 mm BBI 1H-
PULPROG noesy1
TD 90112
SOLVENT CDCl3
NS 320
DS 4
SWH 8090.615 Hz
FIDRES 0.089784 Hz
AQ 5.5689716 sec
RG 80
DW 61.800 usec
DE 6.00 usec
TE 300.0 K
D1 0.10000000 sec
d11 0.03000000 sec
d12 0.00002000 sec
D20 0.07000000 sec
D4 30
NUC1 1H
P1 7.10 usec
PL1 -4.00 dB
SFO1 500.0332000 MHz
F2 - Processing parameters
SI 65536
SF 500.0300108 MHz
WDW EM
SSB 0
LB 0.60 Hz
GB 0
PC 1.00
2D NMR plot parameters
CX 40.00 cm
F1P 9.500 ppm
F1 4758.29 Hz
F2P -0.500 ppm
F2 -251.01 Hz
PPMCM 0.25000 ppm/cm
HZCM 125.01750 Hz/cm
ppm
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


S.Bonazzi/Carreira SD 77 Opr:Br
500 MHz 1H NOE difference spectrum
Br
H
iPrO
O
OTBS
Current Data Parameters
NAME PRJ85
EXPNO 31
PROCNO 1
F2 - Acquisition Parameters
Date_ 20160131
Time 16.25
INSTRUM DRX500
PROBHD 5 mm BBI 1H-
PULPROG noesy
TD 98512
SOLVENT CDCl3
NS 320
DS 4
SWH 8093.615 Hz
FIDRES 0.082784 Hz
AQ 5.5689716 sec
RG 80
DW 61.800 usec
DE 6.00 usec
TE 300.0 K
D1 0.10000000 sec
d11 0.03000000 sec
d12 0.00002000 sec
D20 0.07000000 sec
14 30
NUC1 1H
P1 7.10 usec
PL1 -4.00 dB
SFO1 500.0332680 MHz
FQ2LIST f2list.3
NUC2 1H
PL2 120.00 dB
PL10 76.00 dB
SFO2 500.0332680 MHz
F2 - Processing parameters
SI 65536
SF 500.0300108 MHz
WDW EM
SSB 0
LB 0.60 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 40.00 cm
F1P 9.500 ppm
F1 4750.29 Hz
F2P -0.500 ppm
F2 -250.01 Hz
PPMCM 0.25000 ppm/cm
HZCM 125.00750 Hz/cm
ppm 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

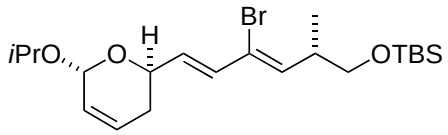

iPrO
O
H
Br
OTBS
Current Data Parameters
NAME F0305
EXPNO 30
PROCNO 1
F2 - Acquisition Parameters
Date_ 20060131
Time 16.22
INSTRUM DRX500
PROBHD 5 mm BBT 1H-
PULPROG noesytp1
TD 90112
SOLVENT CDCl3
NS 320
DS 4
SWH 8090.615 Hz
FIDRES 0.089786 Hz
AQ 5.5689716 sec
RG 80
DW 61.800 usec
DE 6.00 usec
TE 300.0 K
D1 0.10000000 sec
d11 0.03000000 sec
d12 0.00002000 sec
D10 0.07000000 sec
L4 30
NUC1 1H
P1 7.10 usec
PL1 -4.00 dB
SFO1 500.0332000 MHz
F2 - Processing parameters
SI 65536
SF 500.0300108 MHz
WDW EM
SSB 0
LB 0.60 Hz
GB 0
PC 1.00
1H NMR plot parameters
CX 48.86 cm
F1P 9.586 ppm
F1 4750.25 Hz
F2P -0.500 ppm
F2 -250.01 Hz
PPMCM 0.25000 ppm/cm
HZCM 125.00750 Hz/cm
ppm
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0







```
                    Current Data Parameters
NAME                  PF305
EXPNO                    10
PROCNO                    1

                    F2 - Acquisition Parameters
Date_              20060131
Time                  5.31
INSTRUM             DRX500
PROBHD     5 mm BBI 1H-
PULPROG          cosydfqgpp
TD                     2048
SOLVENT               CDCl3
NS                        4
DS                       16
SWH                696.403 Hz
FIDRES             2.199509 Hz
AQ                 0.2277876 sec
RG                      4096
DW                 111.200 usec
DE                   6.00 usec
TE                   308.0 K
D0                 0.00003390 sec
D1                 2.00000000 sec
D11                0.03000000 sec
D12                0.00002000 sec
D13                0.00000300 sec
D16                0.00015000 sec
ZGO                0.06235392 sec
IN0                0.00011220 sec

======== CHANNEL f1 ========
NUC1                      1H
P1                     7.10 usec
P2                    14.20 usec
PL1                   -4.00 dB
PL12                   8.00 dB
SFO1            500.8319318 MHz

======== GRADIENT CHANNEL ========
GPNAM1               sine.100
GPNAM2               sine.100
GPZ1                  0.00 %
GPZ2                  0.00 %
GPZ11                 0.00 %
GPZ12                 0.00 %
GPZ13                15.00 %
GPZ22                10.00 %
TD6                2000.00 usec

                    F1 - Acquisition parameters
NDO                       2
TD1                     512
SFO1            500.0315 MHz
FIDRES             8.782837 Hz
SW                 8.932 ppm

                    F2 - Processing parameters
SI                     1024
SF              500.0300108 MHz
WDW                    QSINE
SSB                       3
LB                    0.00 Hz
GB                        0
PC                     1.00

                    F1 - Processing parameters
SI                     1024
MC2                    TPPI
SF              500.0300108 MHz
WDW                    QSINE
SSB                       2
LB                    0.00 Hz
GB                        0

                    2D NMR plot parameters
CX1                   20.00 cm
CY1                   20.00 cm
F2PPM                 6.406 ppm
F2LO               3203.18 Hz
F2PPM                 0.900 ppm
F2HI                450.01 Hz
F1PPM                 6.406 ppm
F1LO               3203.18 Hz
F1PPM                 0.900 ppm
F1HI                450.01 Hz
F2PPCM             0.27538 ppm/cm
F2HZCM             137.65843 Hz/cm
F1PPCM             0.27533 ppm/cm
```








Current Data Parameters
NAME PGUEC
EXPNO 11
PROCNO 1

F2 - Acquisition Parameters
Date_ 20060131
Time 10.31
INSTRUM DRX500
PROBHD 5 mm BBI 1H-
PULPROG invigpo
TD 2048
SOLVENT CDCl3
NS 4
DS 16
SWH 4896.081 Hz
FIDRES 2.395589 Hz
AQ 0.2217876 sec
RG 8192
DW 102.200 usec
DE 6.00 usec
TE 303.0 K
CNST2 145.0000000
d0 0.00000300 sec
d1 2.00000000 sec
d4 0.00171914 sec
d11 0.03000000 sec
d13 0.00000300 sec
d16 0.00010000 sec
d20 0.00030000 sec
d21 0.00061714 sec
IN0 0.00001830 sec

---------- CHANNEL f1 ----------
NUC1 1H
P1 7.30 usec
p2 14.30 usec
PL1 -4.00 dB
SFO1 500.0333316 MHz

---------- CHANNEL f2 ----------
CPDPRG2 garp
NUC2 13C
P3 12.50 usec
p4 25.00 usec
PCPD2 96.00 usec
PL2 -3.00 dB
PL12 13.00 dB
SFO2 125.7611995 MHz

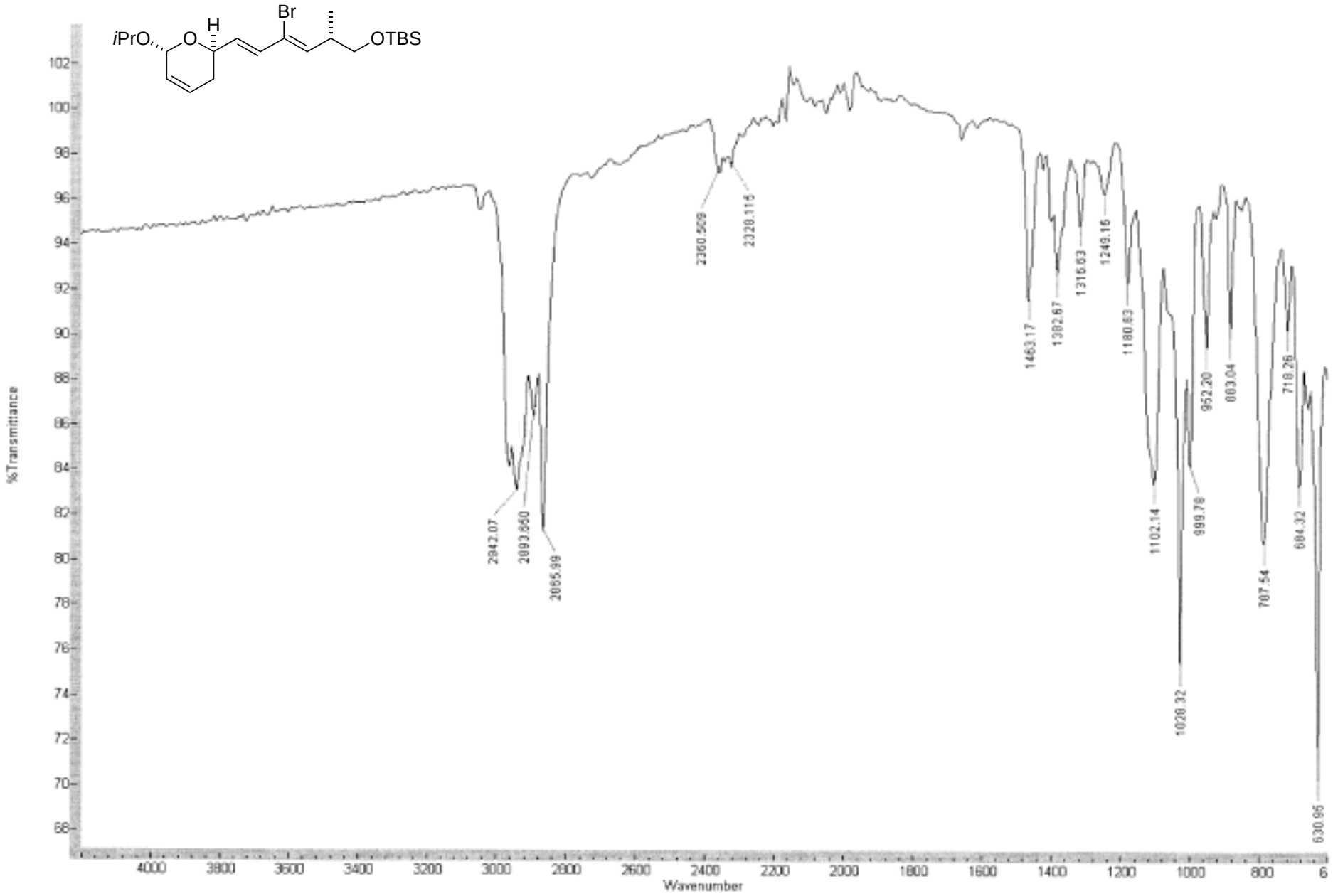
---------- GRADIENT CHANNEL ----------
GPNAM1 sine.100
GPNAM2 sine.100
GPNAM3 sine.100
GPZ1 0.00 %
GPZ2 0.00 %
GPZ3 0.00 %
GPZ4 0.00 %
GPZ5 0.00 %
GPZ7 0.00 %
GPZ8 40.00 %
GPZ9 10.00 %
GPZ13 30.00 %
P16 1000.00 usec

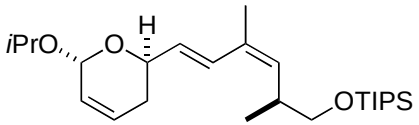
F2 - Acquisition parameters
EXSI 0
TD 512
SFO1 125.7432 MHz
FIDRES 47.405815 Hz
SW 191.017 ppm

F2 - Processing parameters
SI 1024
SF 500.0330330 MHz
WDW QSINE
SSB 2
LB 0.00 Hz
GB 0
PC 1.00

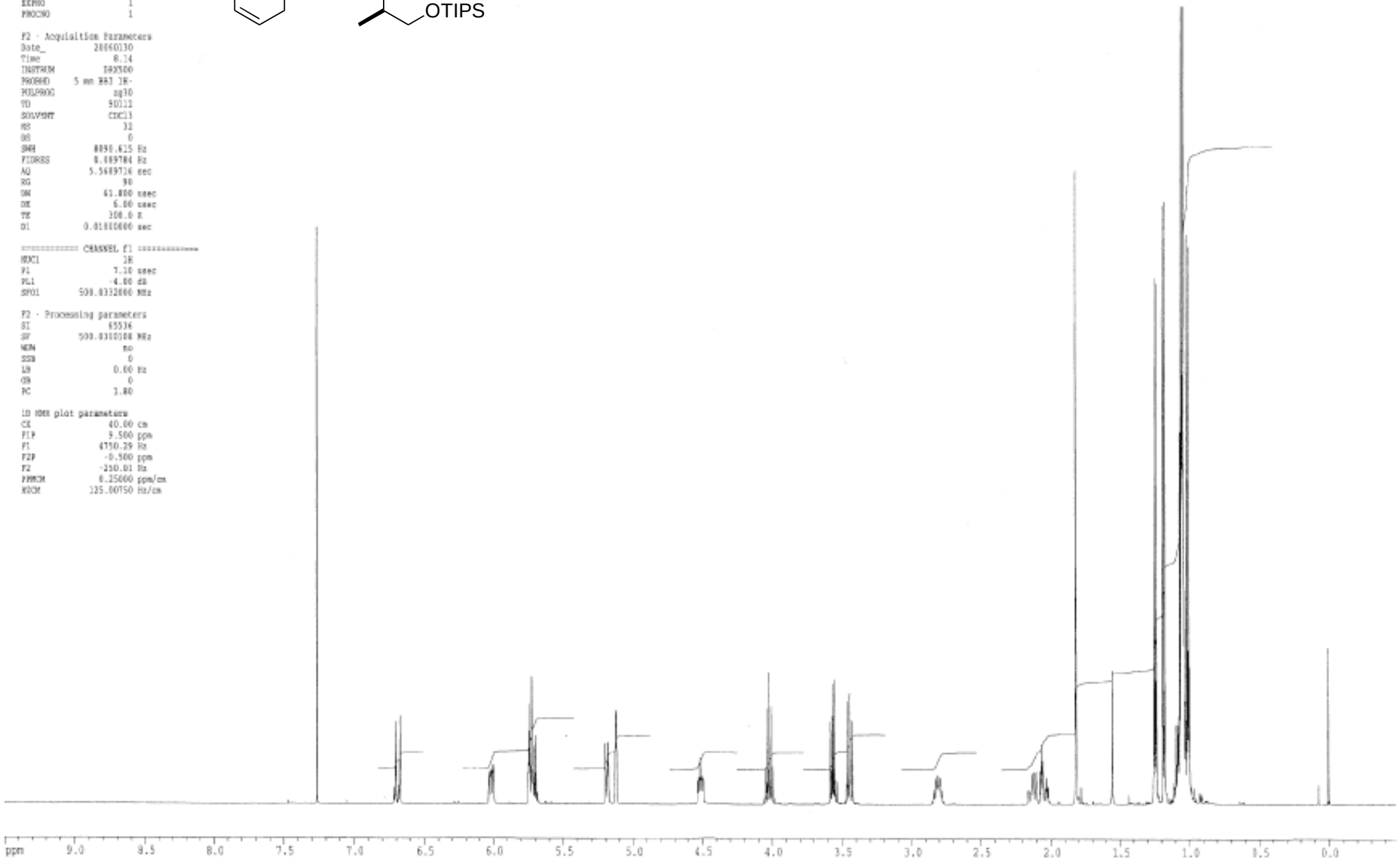
F1 - Processing parameters
SI 1024
MC2 TPPI
SF 125.7728524 MHz
WDW SINE
SSB 2
LB 0.00 Hz
GB 0

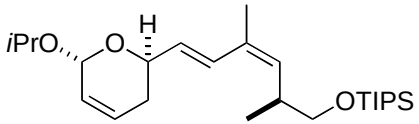
2D NMR plot parameters
CS1 20.50 cm
CS2 20.50 cm
F1PH1 5.500 ppm
F1LO 1256.20 Hz
F2PH1 8.000 ppm
F2LO 450.03 Hz
F1PH2 143.000 ppm
F1HI 37728.30 Hz
F1PPL 9.000 ppm
F1LO 1131.59 Hz
F2PPMCM 0.28000 ppm/cm
F1HZCM 140.03879 Hz/cm
F1PPMCM 5.00800 ppm/cm


iPrO
O
H
Br
OTBS
%Transmittance
Wavenumber
2942.07
2893.650
2865.99
2360.509
2328.115
1463.17
1382.67
1316.63
1249.16
1180.63
1102.14
1028.32
999.78
952.20
883.04
787.54
718.26
684.32
630.95

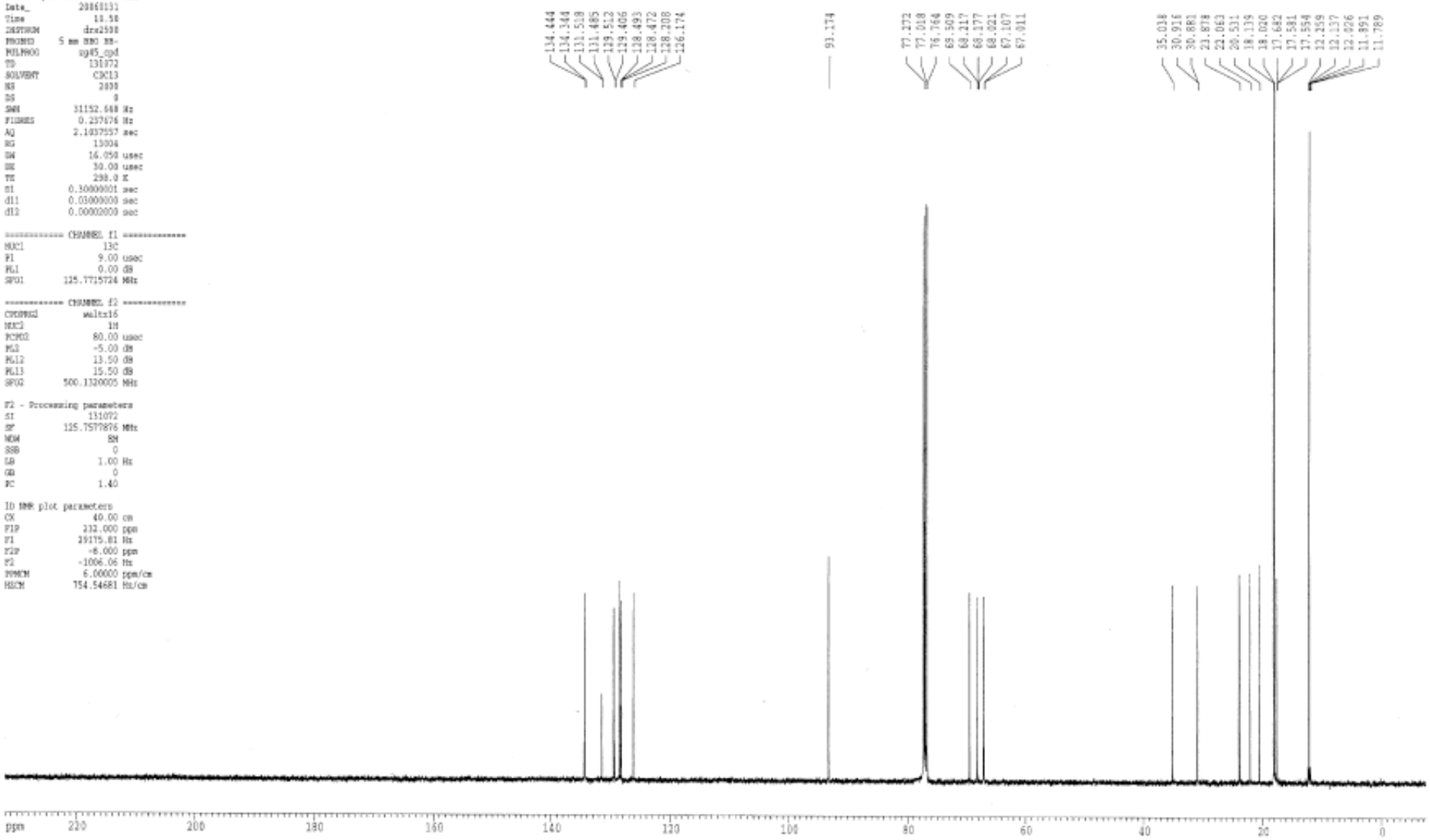


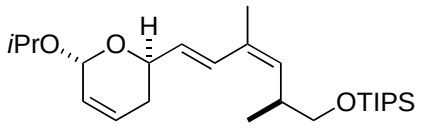

```
Current Data Parameters
NAME                  FD384
EXPNO                     1
PROCNO                    1

F2 - Acquisition Parameters
Date_           20060130
Time                 8.14
INSTRUM           DRX500
PROBHD     5 mm BBI 1H-
PULPROG             zg30
TD                 90112
SOLVENT            CDCl3
NS                    32
DS                     0
SWH             8890.625 Hz
FIDRES          0.089784 Hz
AQ              5.5689716 sec
RG                    90
DW                61.800 usec
DE                 6.00 usec
TE                 308.0 K
D1           0.01000000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                 7.10 usec
PL1                4.00 dB
SFO1         500.0332860 MHz

F2 - Processing parameters
SI                 65536
SF           500.0310108 MHz
WDW                   no
SSB                    0
LB                  0.00 Hz
GB                     0
PC                  1.40

1D NMR plot parameters
CX                 40.00 cm
F1P                9.500 ppm
F1                4750.29 Hz
F2P               -0.500 ppm
F2                -250.01 Hz
PPMCM             0.25000 ppm/cm
HZCM            125.00750 Hz/cm
```



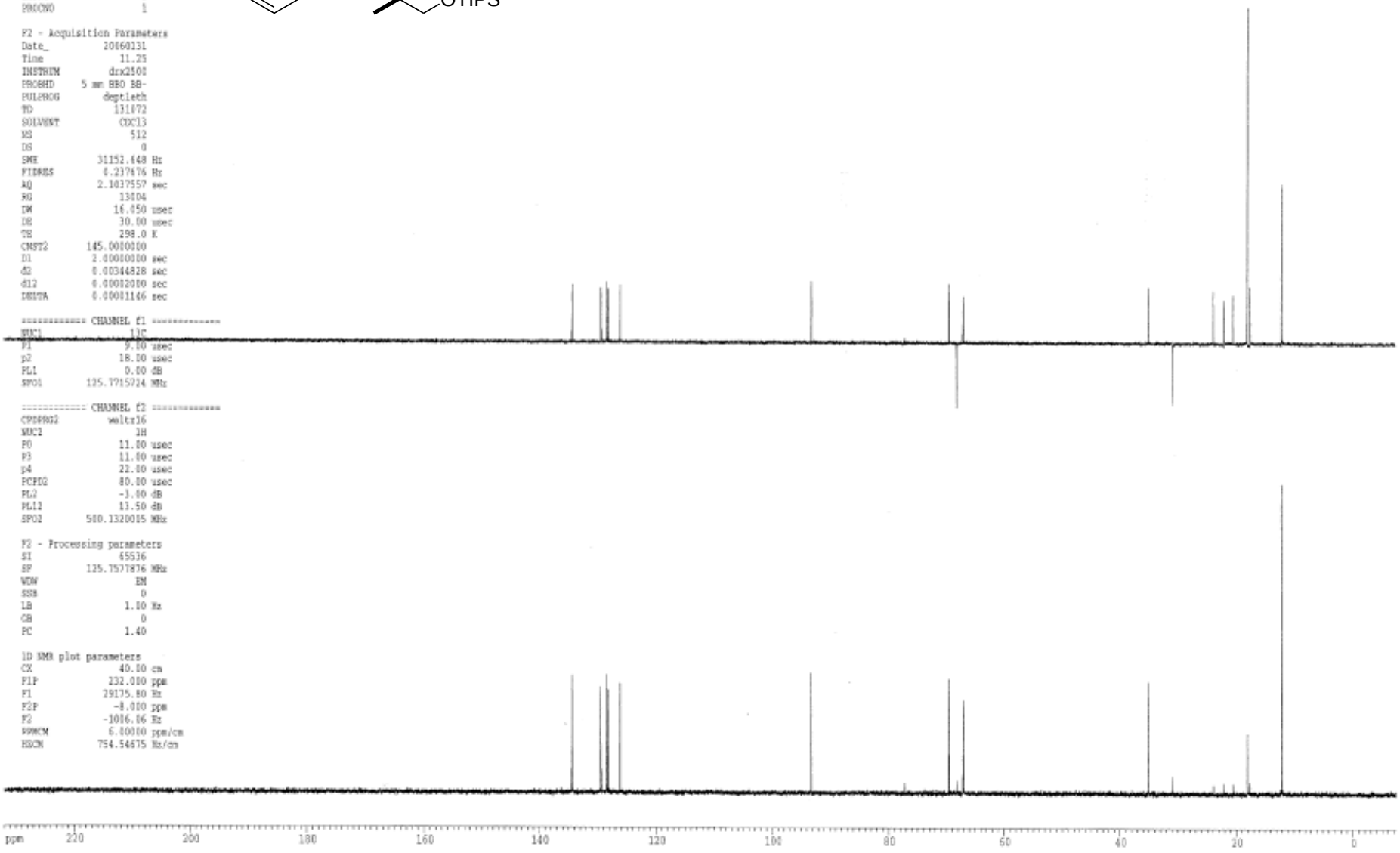


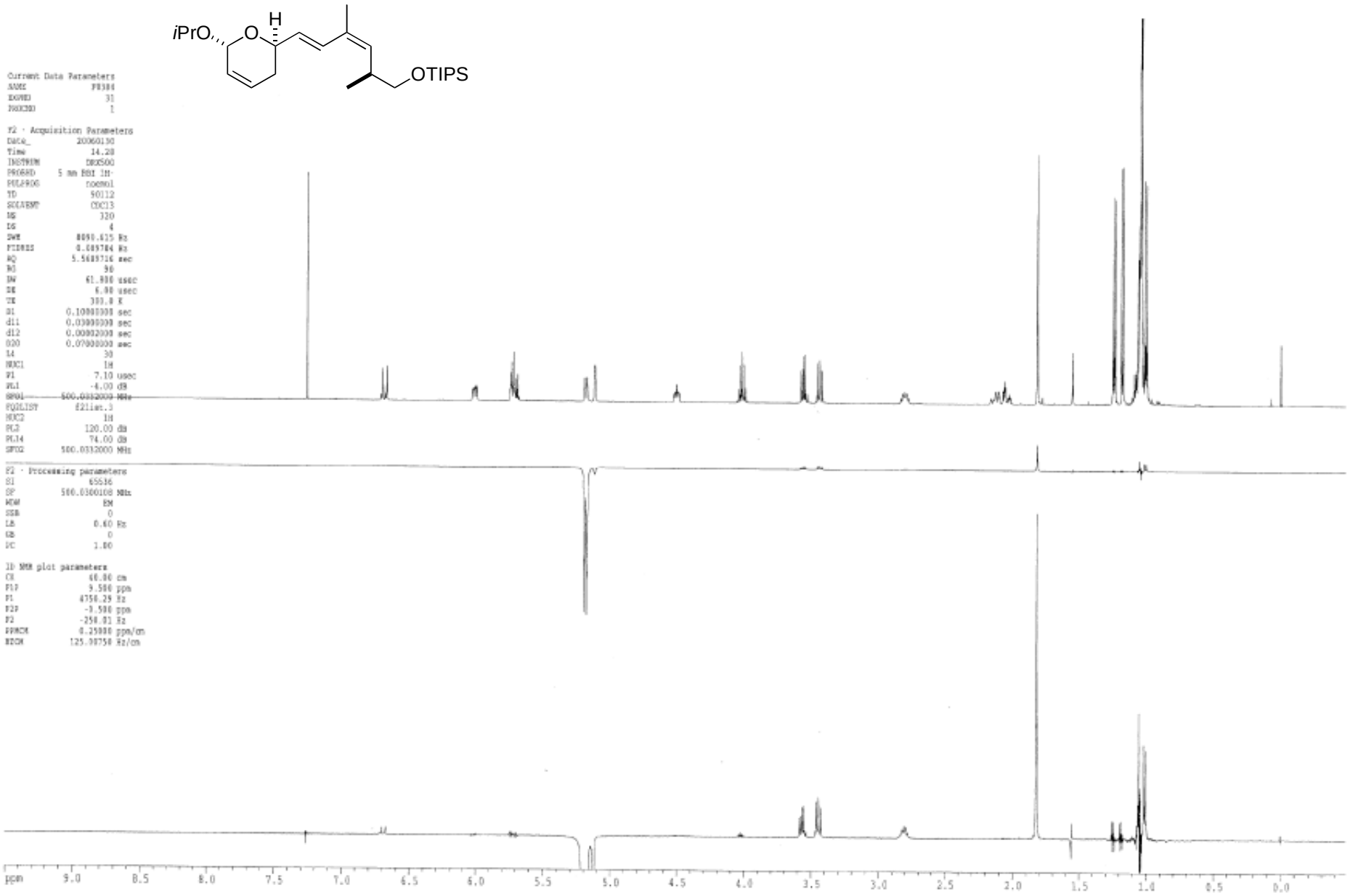

```
Current Data Parameters
NAME                  FU384
EXPNO                     2
PROCNO                    1

F2 - Acquisition Parameters
Date_              20161131
Time                  11.58
INSTRUM              drx2500
PROBHD     5 mm BBO BB-
PULPROG              zg45_cpd
TD                     131072
SOLVENT                CDCl3
NS                       2000
DS                          0
SWH                31152.668 Hz
FIDRES             0.237676 Hz
AQ                 2.1037557 sec
RG                      13004
DW                   16.050 usec
DE                   30.00 usec
TE                     298.0 K
D1                0.30000001 sec
d11               0.03000000 sec
d12               0.00002000 sec

========== CHANNEL f1 ============
NUC1                     13C
P1                      9.00 usec
PL1                     0.00 dB
SFO1              125.7715724 MHz

========== CHANNEL f2 ============
CPDPRG2              waltz16
NUC2                      1H
PCPD2                  80.00 usec
PL2                    -5.00 dB
PL12                   13.50 dB
PL13                   15.50 dB
SFO2              500.1320005 MHz

F2 - Processing parameters
SI                       131072
SF                125.7577876 MHz
WDW                         EM
SSB                          0
LB                        1.00 Hz
GB                           0
PC                        1.40

1D NMR plot parameters
CX                       40.00 cm
F1P                     232.000 ppm
F1                    29175.81 Hz
F2P                    -6.000 ppm
F2                    -1006.06 Hz
PPMCM                 6.00000 ppm/cm
HZCM                754.54681 Hz/cm
```

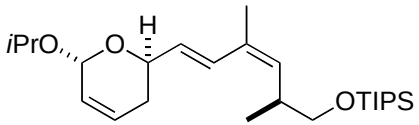


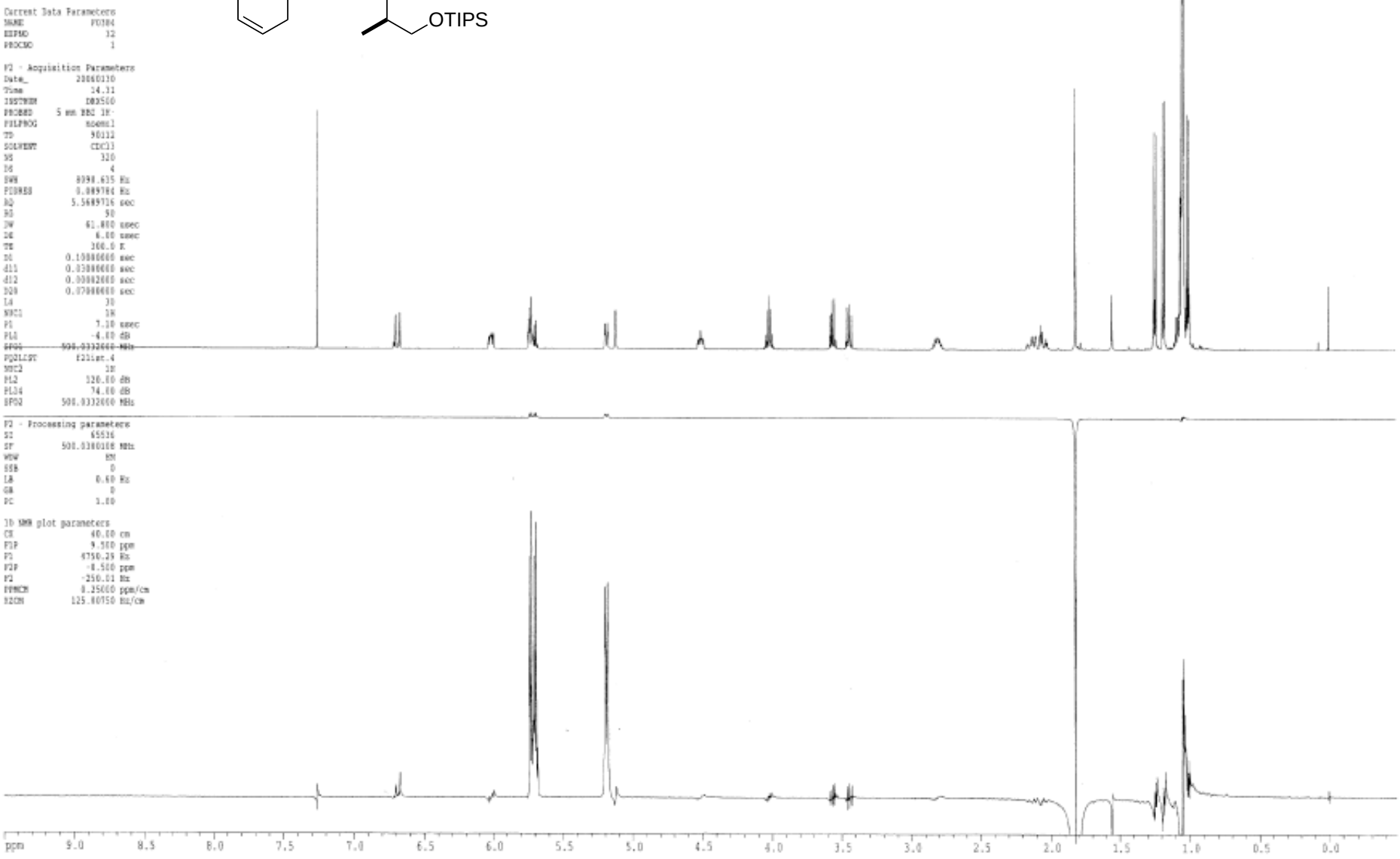


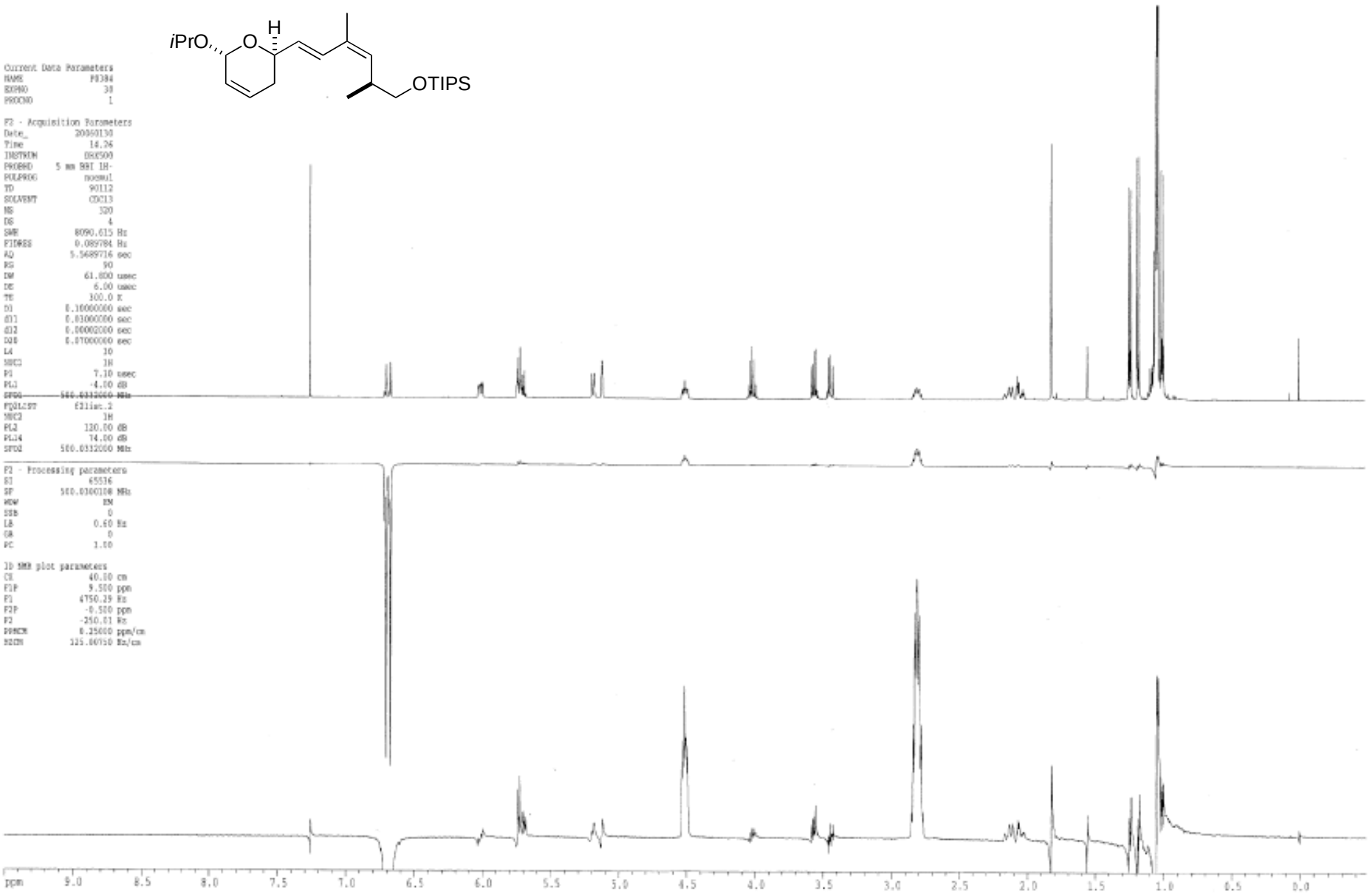

```
Current Data Parameters
NAME                 P0184
EXPNO                    3
PROCNO                   1

F2 - Acquisition Parameters
Date_             20060131
Time                 11.25
INSTRUM              drx250
PROBHD     5 mm BBO BB-
PULPROG           deptletb
TD                   131072
SOLVENT                CDCl3
NS                       512
DS                         0
SWH               31152.648 Hz
FIDRES             0.237676 Hz
AQ                 2.1037557 sec
RG                      13804
DW                    16.050 usec
DE                    30.00 usec
TE                    298.0 K
CNST2            145.0000000
D1                 2.00000000 sec
d2                 0.00344828 sec
d12                0.00002000 sec
DELTA              0.00011166 sec

============ CHANNEL f1 =============
NUC1                     13C
P1                      9.80 usec
p2                     18.00 usec
PL1                     0.00 dB
SFO1             125.7715724 MHz

============ CHANNEL f2 =============
CPDPRG2               waltz16
NUC2                      1H
P0                     11.00 usec
P3                     11.00 usec
p4                     22.00 usec
PCPD2                  80.00 usec
PL2                    -1.00 dB
PL12                   13.50 dB
SFO2             500.1320015 MHz

F2 - Processing parameters
SI                       65536
SF               125.7577876 MHz
WDW                        EM
SSB                         0
LB                      1.00 Hz
GB                          0
PC                      1.40

1D NMR plot parameters
CX                     40.00 cm
F1P                   232.000 ppm
F1                  29175.80 Hz
F2P                    -8.000 ppm
F2                  -1006.06 Hz
PPMCM                 6.00000 ppm/cm
HZCM                754.54675 Hz/cm
```

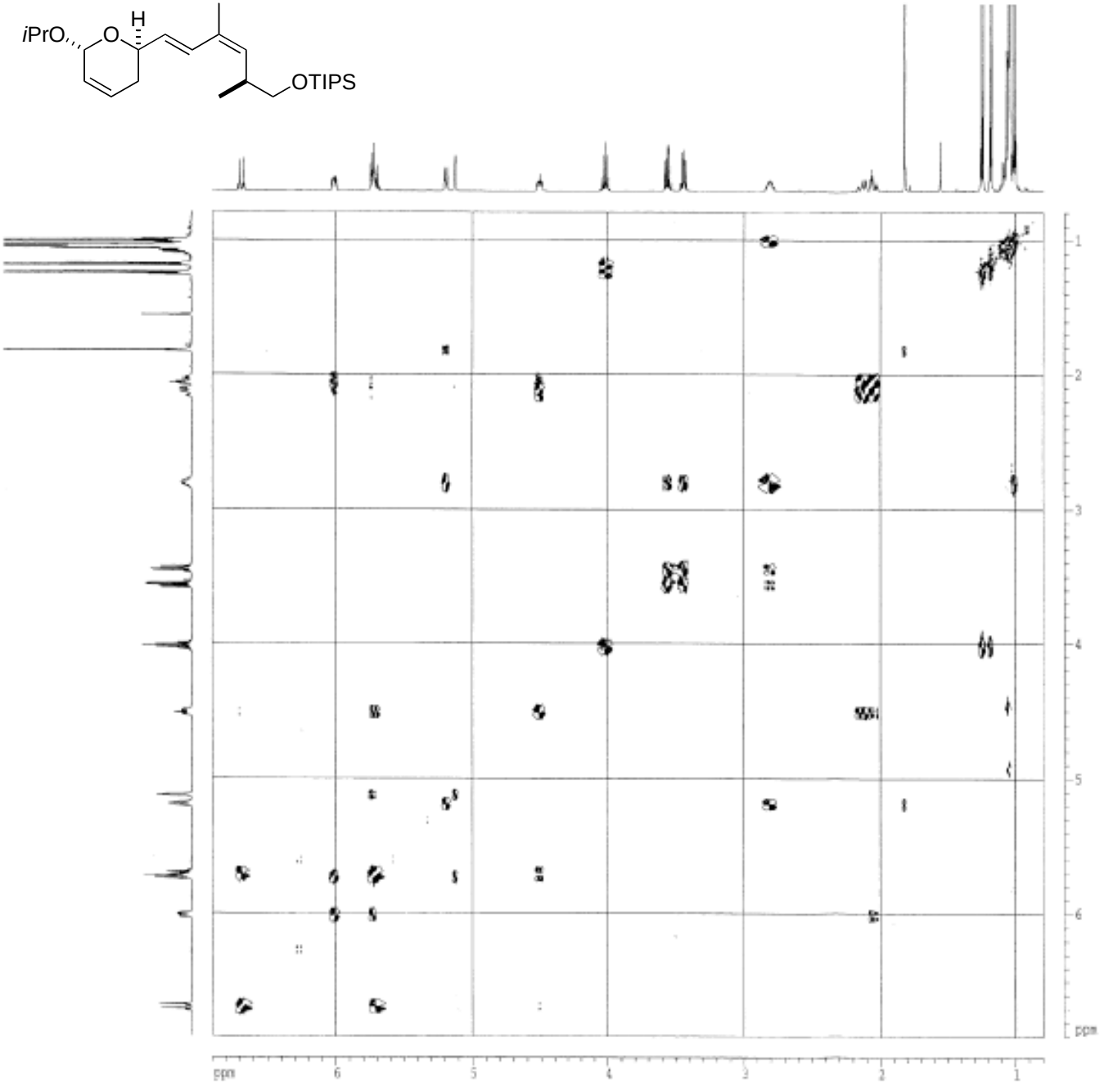



iPrO
O
H
OTIPS
Current Data Parameters
NAME FR384
EXPNO 31
PROCNO 1
F2 - Acquisition Parameters
Date_ 20060130
Time 14.28
INSTRUM DRX500
PROBHD 5 mm BBI 1H-
PULPROG roesyal
TD 90112
SOLVENT CDCl3
NS 320
DS 4
SWH 8993.615 Hz
FIDRES 0.099784 Hz
AQ 5.5689716 sec
RG 90
DW 61.800 usec
DE 6.00 usec
TE 300.0 K
D1 0.10000000 sec
d11 0.03000000 sec
d12 0.00002000 sec
d20 0.07000000 sec
l4 30
NUC1 1H
P1 7.10 usec
PL1 -4.00 dB
SFO1 500.0332000 MHz
FQ1LIST f21las.3
NUC2 1H
PL2 120.00 dB
PL14 74.00 dB
SFO2 500.0332000 MHz
F2 - Processing parameters
SI 65536
SF 500.0300108 MHz
WDW EM
SSB 0
LB 0.60 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 60.00 cm
F1P 9.500 ppm
F1 4756.25 Hz
F2P -9.500 ppm
F2 -250.81 Hz
PPMCM 0.25000 ppm/cm
HZCM 125.09750 Hz/cm
ppm
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


iPrO
O
H
OTIPS


Current Data Parameters
NAME PD384
EXPNO 32
PROCNO 1
F2 - Acquisition Parameters
Date_ 20060110
Time 14.31
INSTRUM DRX500
PROBHD 5 mm BBI 1H-
PULPROG noesy1
TD 98112
SOLVENT CDCl3
NS 320
DS 4
SWH 8098.635 Hz
FIDRES 0.089784 Hz
AQ 5.5689716 sec
RG 90
DW 61.800 usec
DE 6.00 usec
TE 300.0 K
D1 0.10000000 sec
d11 0.03000000 sec
d12 0.00002000 sec
D20 0.07000000 sec
L4 30
NUC1 1H
P1 7.10 usec
PL1 -4.00 dB
SFO1 500.0332000 MHz
FQ1LIST f231nr.4
NUC2 1H
PL2 120.00 dB
PL34 74.00 dB
SFO2 500.0332000 MHz
F2 - Processing parameters
SI 65536
SF 500.0300108 MHz
WDW EM
SSB 0
LB 0.60 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 40.00 cm
F1P 9.500 ppm
F1 4750.25 Hz
F2P -0.500 ppm
F2 -250.01 Hz
PPMCM 0.25000 ppm/cm
HZCM 125.00750 Hz/cm
ppm
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


iPrO
O
H
OTIPS
Current Data Parameters
NAME P0384
EXPNO 38
PROCNO 1
F2 - Acquisition Parameters
Date_ 20060130
Time 18.26
INSTRUM DRX500
PROBHD 5 mm BBI 1H-
PULPROG noesyml
TD 90112
SOLVENT CDCl3
NS 320
DS 4
SWH 8090.615 Hz
FIDRES 0.089784 Hz
AQ 5.5689716 sec
RG 90
DW 61.800 usec
DE 6.00 usec
TE 300.0 K
D1 0.10000000 sec
D11 0.03000000 sec
D12 0.00002000 sec
D16 0.07000000 sec
L4 10
SBC1 1H
P1 7.10 usec
PL1 -4.00 dB
SFO1 500.0332000 MHz
FQ1LIST f21iac.2
SBC2 1H
PL2 120.00 dB
PL14 74.00 dB
SFO2 500.0332000 MHz
F2 - Processing parameters
SI 65536
SF 500.0300108 MHz
WDW EM
SSB 0
LB 0.60 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 40.00 cm
F1P 9.500 ppm
F1 4750.29 Hz
F2P -0.500 ppm
F2 -250.01 Hz
PPMCM 0.25000 ppm/cm
HZCM 125.00750 Hz/cm
ppm
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

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                    Current Data Parameters
NAME                  PE584
EXPNO                    10
PROCNO                    3

                F2 - Acquisition Parameters
Date_              20060110
Time                  8.35
INSTRUM             DRX500
PROBHD     5 mm BBI 1H-
PULPROG          cosydfgptp
TD                     2048
SOLVENT                CDCl3
NS                        4
DS                       16
SWH                4496.401 Hz
FIDRES             2.195605 Hz
AQ                 0.2277876 sec
RG                      4096
DW                  111.188 usec
DE                    6.00 usec
TE                   300.0 K
D0                 0.00003161 sec
D1                 2.00000000 sec
D11                0.03000000 sec
D12                0.00002000 sec
D13                0.00000100 sec
D16                0.00075000 sec
D20                0.00235100 sec
IN0                0.00031133 sec

======== CHANNEL f1 ========
NUC1                      1H
P1                    7.10 usec
P2                   14.20 usec
PL1                  -4.00 dB
PL12                  8.00 dB
SFO1            500.0329510 MHz

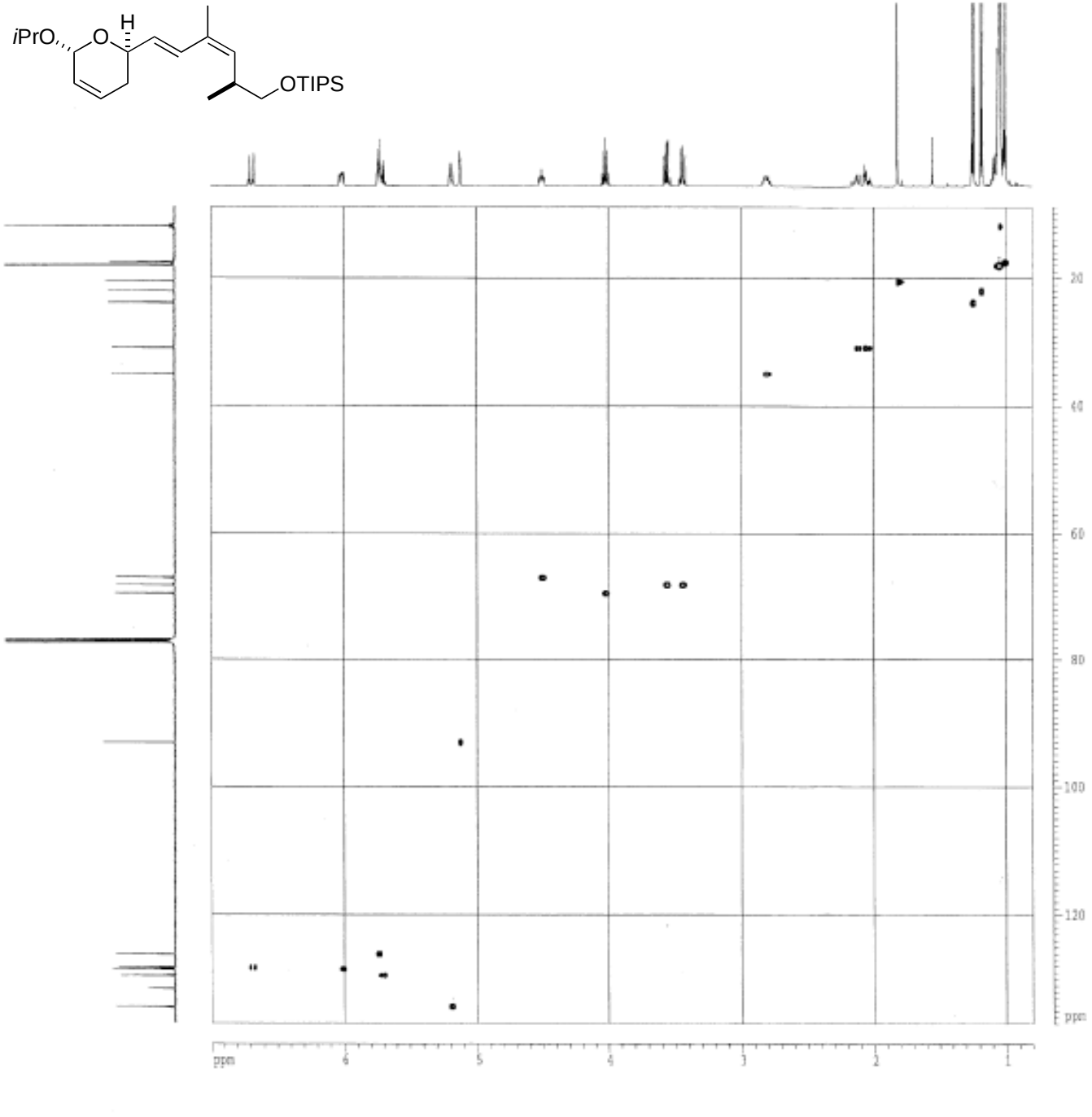
======== GRADIENT CHANNEL ========
GPNAM1              sine.100
GPNAM2              sine.100
GPZ1                  0.00 %
GPZ2                  0.00 %
GPY1                  0.00 %
GPY2                  0.00 %
GPX1                 15.00 %
GPX2                 30.00 %
P16                2000.00 usec

                F1 - Acquisition parameters
NDO                       2
TD                      512
SFO1            500.0519 MHz
FIDRES             8.782037 Hz
SW                 8.992 ppm

                F2 - Processing parameters
SI                      1024
SF              500.0300108 MHz
WDW                     QSINE
SSB                       3
LB                    0.00 Hz
GB                        0
PC                    1.00

                F1 - Processing parameters
SI                      1024
MC2                     TPPI
SF              500.0300108 MHz
WDW                     QSINE
SSB                       2
LB                    0.00 Hz
GB                        0

              2D NMR plot parameters
CX2                   20.00 cm
CY1                   20.00 cm
F2PLO                 6.907 ppm
F2LO               3453.47 Hz
F2PHI                 0.795 ppm
F2HI                397.32 Hz
F1PLO                 6.907 ppm
F1LO               3453.47 Hz
F1PHI                 0.795 ppm
F1HI                397.32 Hz
F2PPMCM           0.30560 ppm/cm
F2HZCM          152.80763 Hz/cm
F1PPMCM           0.30560 ppm/cm
```

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Current Data Parameters
NAME                 FR186
EXPNO                   11
PROCNO                   1

F2 - Acquisition Parameters
Date_           20164158
Time                 9.44
INSTRUM           smp500
PROBHD     5 mm BBI 30
PULPROG         invigptp
TD                   2048
SOLVENT              CDCl3
NS                      4
DS                     16
SWH              6494.455 Hz
FIDRES           2.395539 Hz
AQ               0.2277876 sec
RG                   8192
DW                 111.308 usec
DE                   6.00 usec
TE                 300.0 K
CNST2            145.0030010
CD0              0.00003320 sec
D1               3.00000000 sec
D0               0.00172414 sec
CD13             0.03600000 sec
CD1              0.00030100 sec
CD6              0.00010000 sec
CD8              0.00110400 sec
CD21             0.00063716 sec
IN0              0.00030250 sec

======== CHANNEL F1 ========
NUC1                    1H
PL1                  7.18 usec
PL1                 14.20 usec
PL1                  -4.00 dB
SFO1            500.6133118 MHz

======== CHANNEL F2 ========
CPDPRG2              garp
NUC2                    13C
PCPD2                90.00 usec
PL2                  -1.00 dB
PL12                 13.00 dB
SFO2            125.7437995 MHz

======== GRADIENT CHANNEL ========
GPNAM1               sine.100
GPNAM2               sine.100
GPNAM3               sine.100
GPZ1                 50.00 %
GPZ2                  0.00 %
GPZ3                  0.00 %
GPZ4                  0.00 %
GPZ5                  0.00 %
GPZ6                  0.00 %
GPZ7                 80.00 %
GPZ8                 30.00 %
GPZ9                 20.00 %
P16                1000.00 usec

F1 - Acquisition parameters
NS                       4
TD                     400
SFO1            125.7432 MHz
FIDRES           62.453431 Hz
SW                 197.827 ppm

F2 - Processing parameters
SI                    1024
SF              500.2300308 MHz
WDW                  QSINE
SSB                      2
LB                    0.60 Hz
GB                       0
PC                    1.00

F1 - Processing parameters
SI                    1024
MC2                   TPPI
SF              125.7328423 MHz
WDW                   SINE
SSB                      2
LB                    0.00 Hz
GB                       0

2D CHN plot parameters
CS2                  20.00 cm
CS1                  20.00 cm
F2PLO                7.000 ppm
F2LO              3500.21 Hz
F2PHI                0.600 ppm
F2HI               496.82 Hz
F1PLO              157.000 ppm
F1LO             17225.37 Hz
F1PHI                9.000 ppm
F1HI              1131.55 Hz
F2PPMCM              0.31080 ppm/cm
F2HZCM             156.80629 Hz/cm
F1PPMCM              0.01080 ppm/cm
```
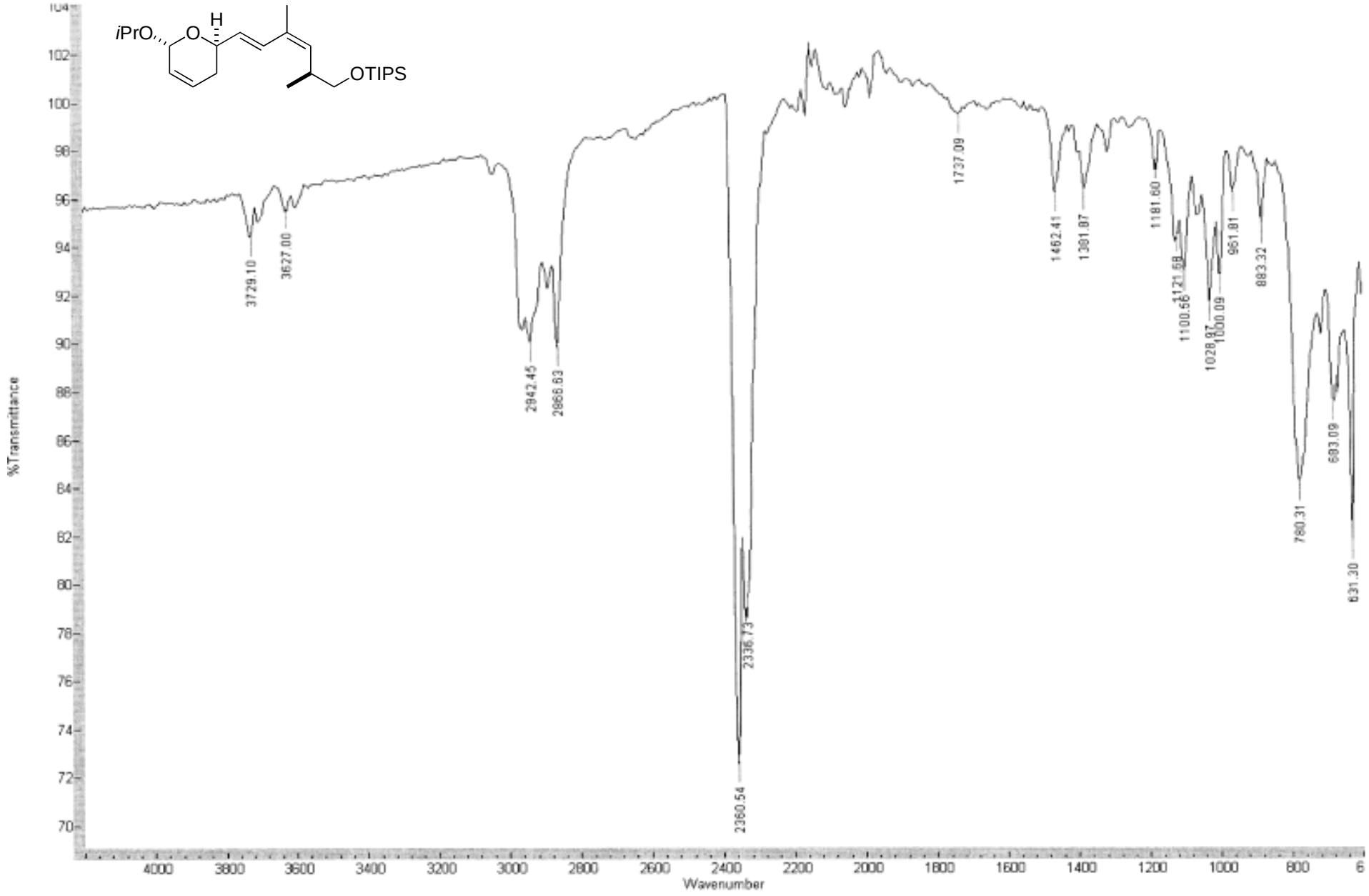
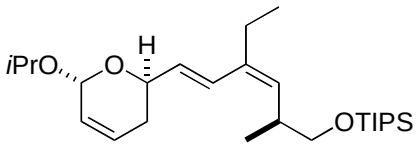
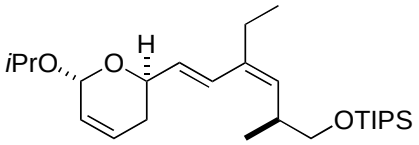
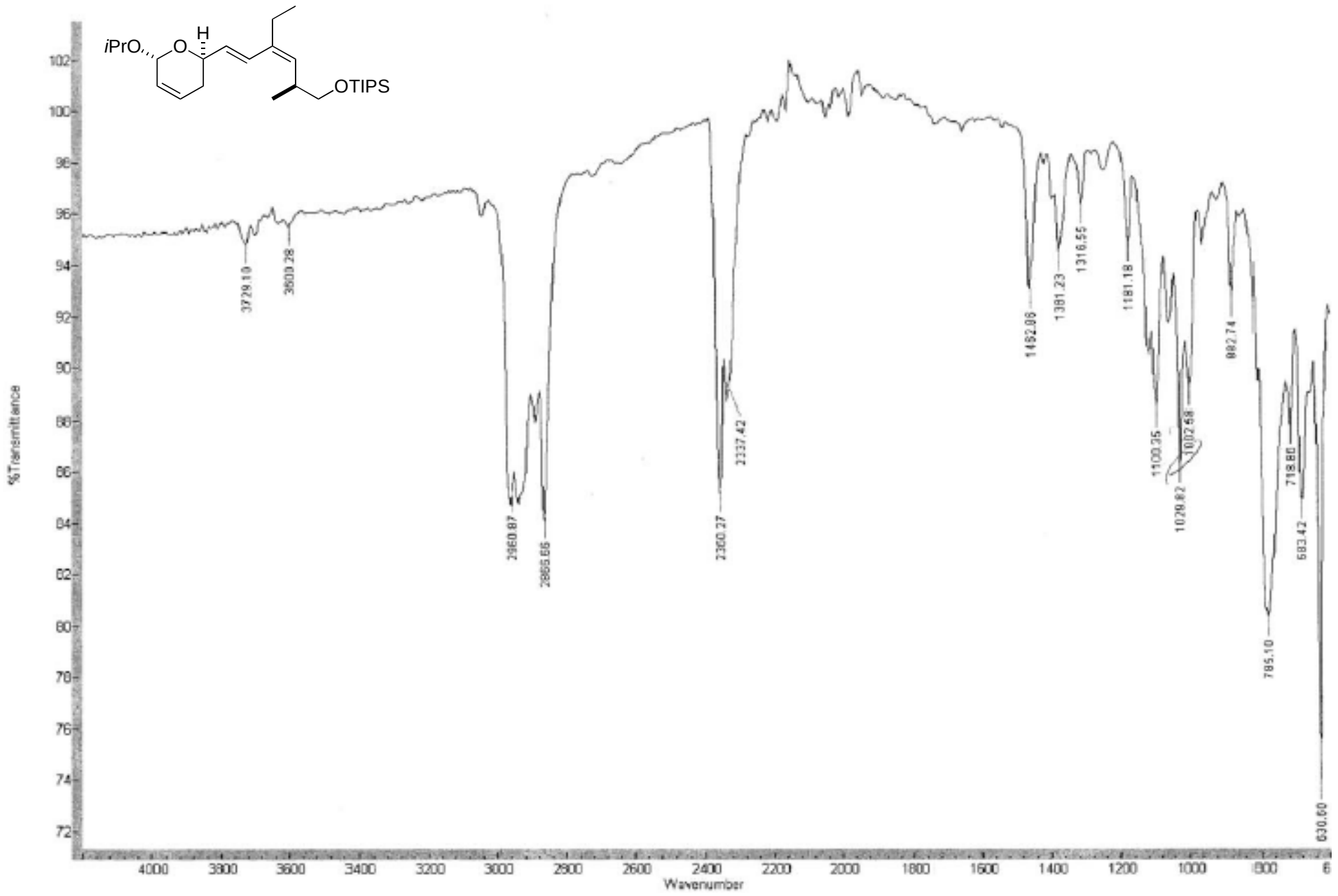


iPrO
O
H
OTIPS
%Transmittance
Wavenumber
3729.10
3627.00
2942.45
2866.63
2360.54
2336.73
1737.09
1462.41
1381.87
1181.60
1121.58
1100.56
1028.87
1000.09
961.81
883.32
780.31
683.09
631.30

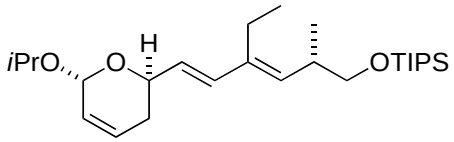

iPrO
O
H
OTIPS


9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (f1)

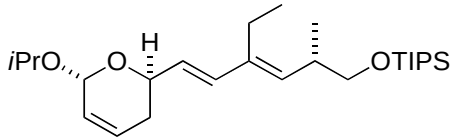

iPrO
O
H
OTIPS


210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (f1)


iPrO
O
H
OTIPS
%Transmittance
Wavenumber
3729.10
3609.28
2960.87
2865.66
2360.27
2337.42
1462.08
1381.23
1316.55
1181.18
1100.35
1029.82
1002.68
882.74
785.10
718.80
683.42
630.60


iPrO
O
H
OTIPS


0
9
8
7
6
5
4
3
2
1


iPrO
O
H
OTIPS


210
200
190
180
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160
150
140
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120
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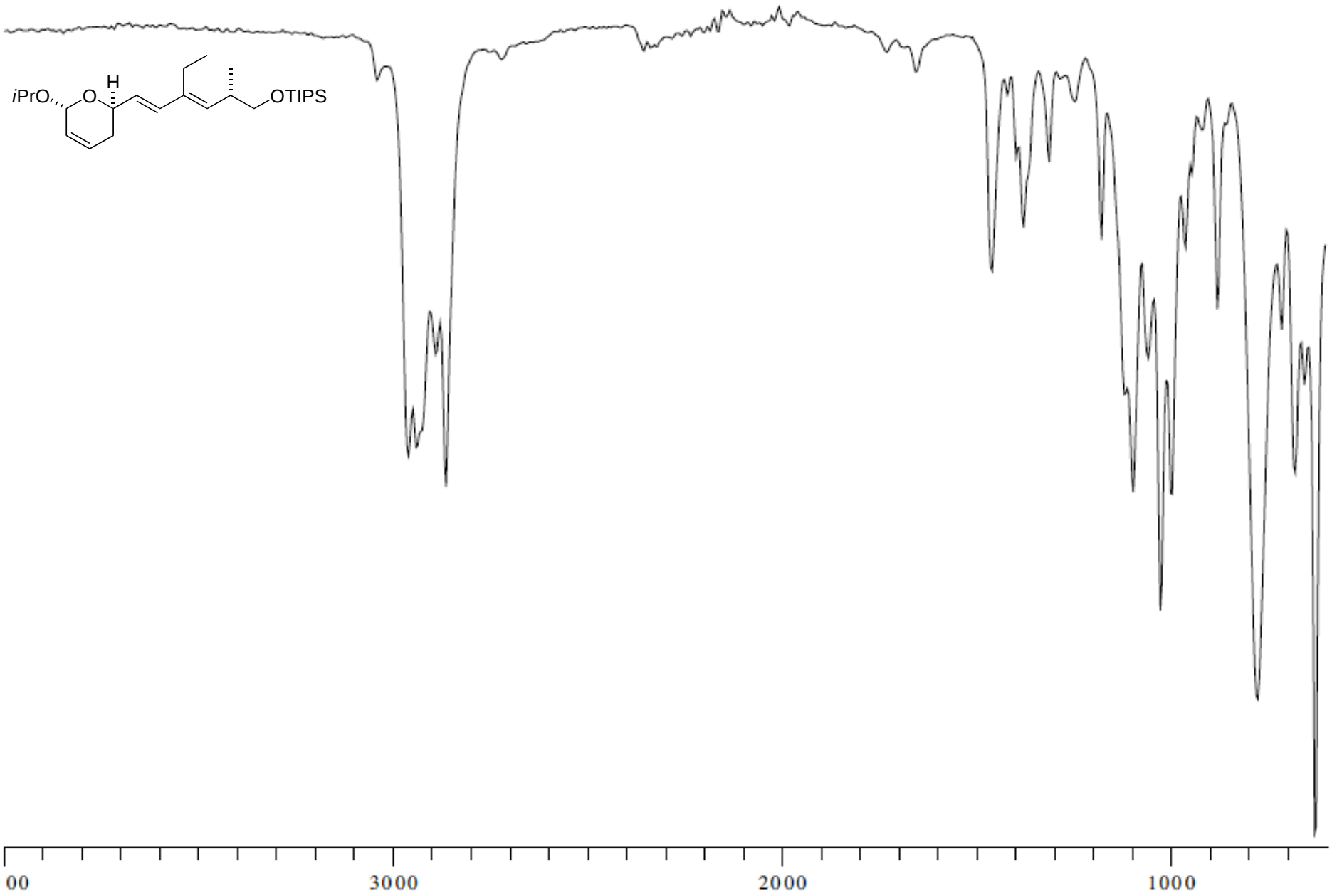
40
30
20
10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O
H
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2000
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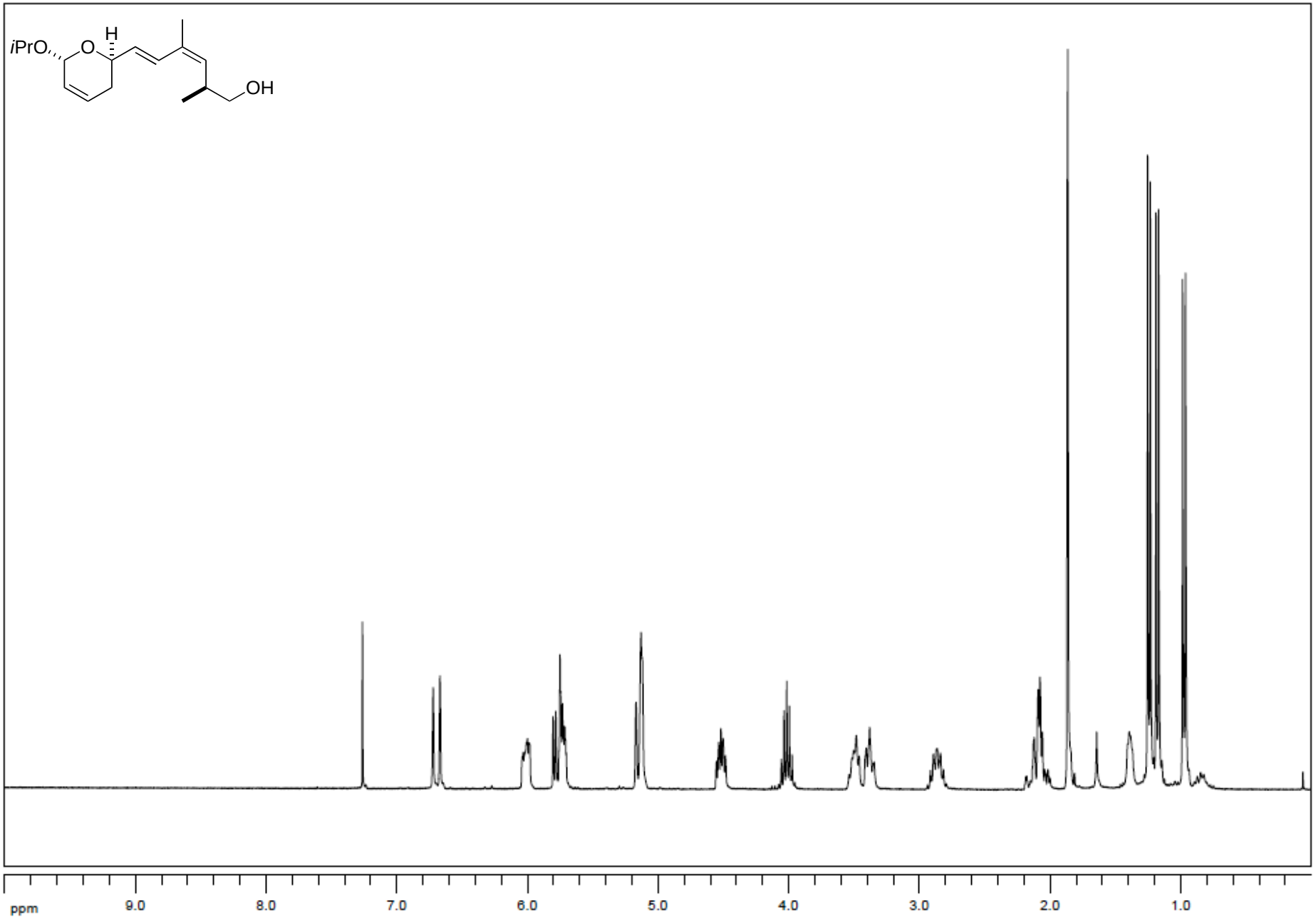
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H
OH
ppm
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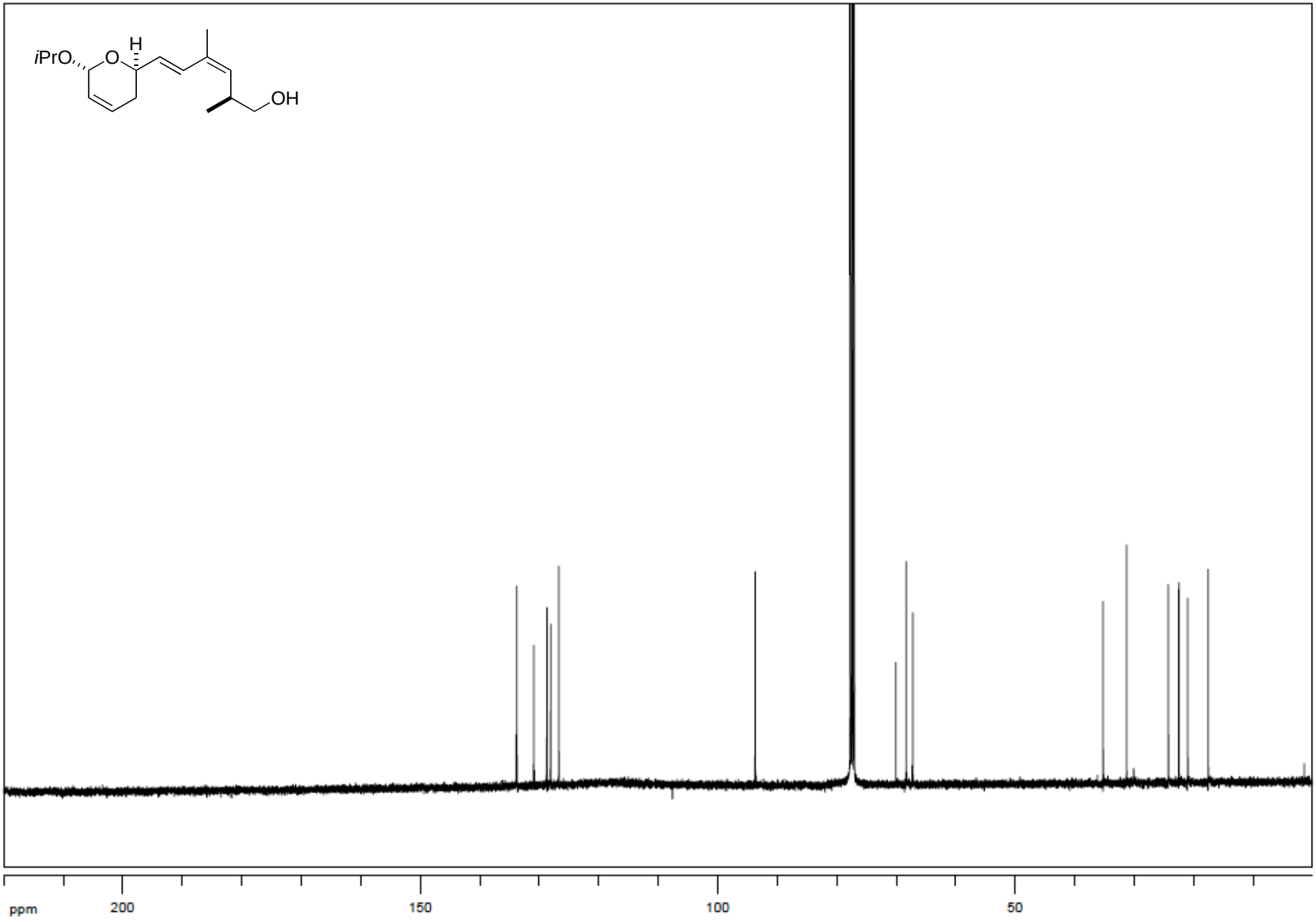
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0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O
H
OH
ppm
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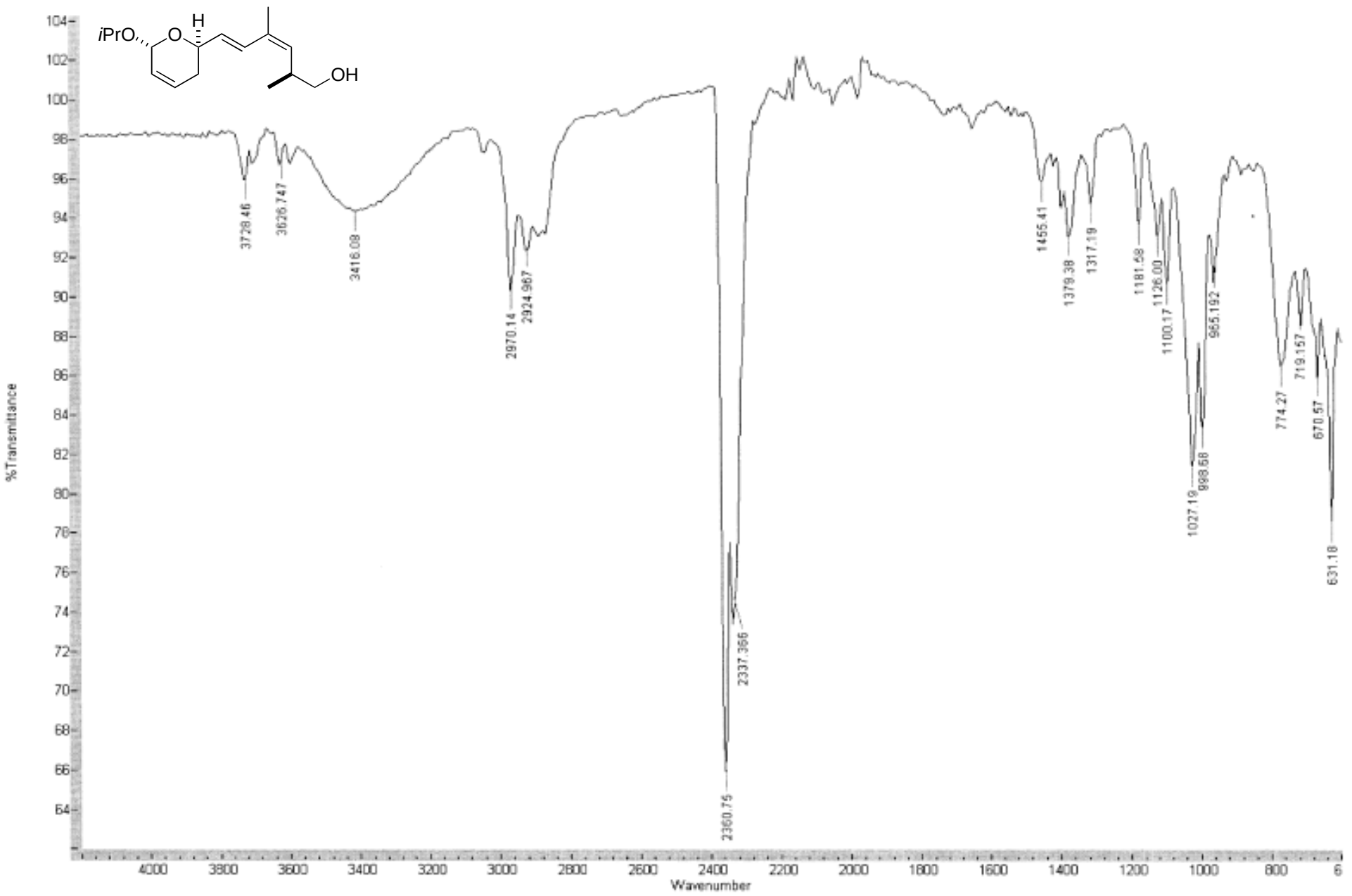
150
100
50


iPrO
O
H
OH
%Transmittance
Wavenumber
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3416.08
2970.14
2924.987
2360.75
2337.366
1455.41
1379.38
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1100.17
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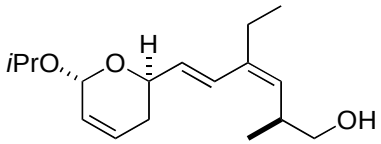
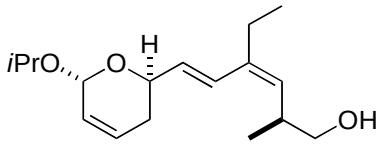
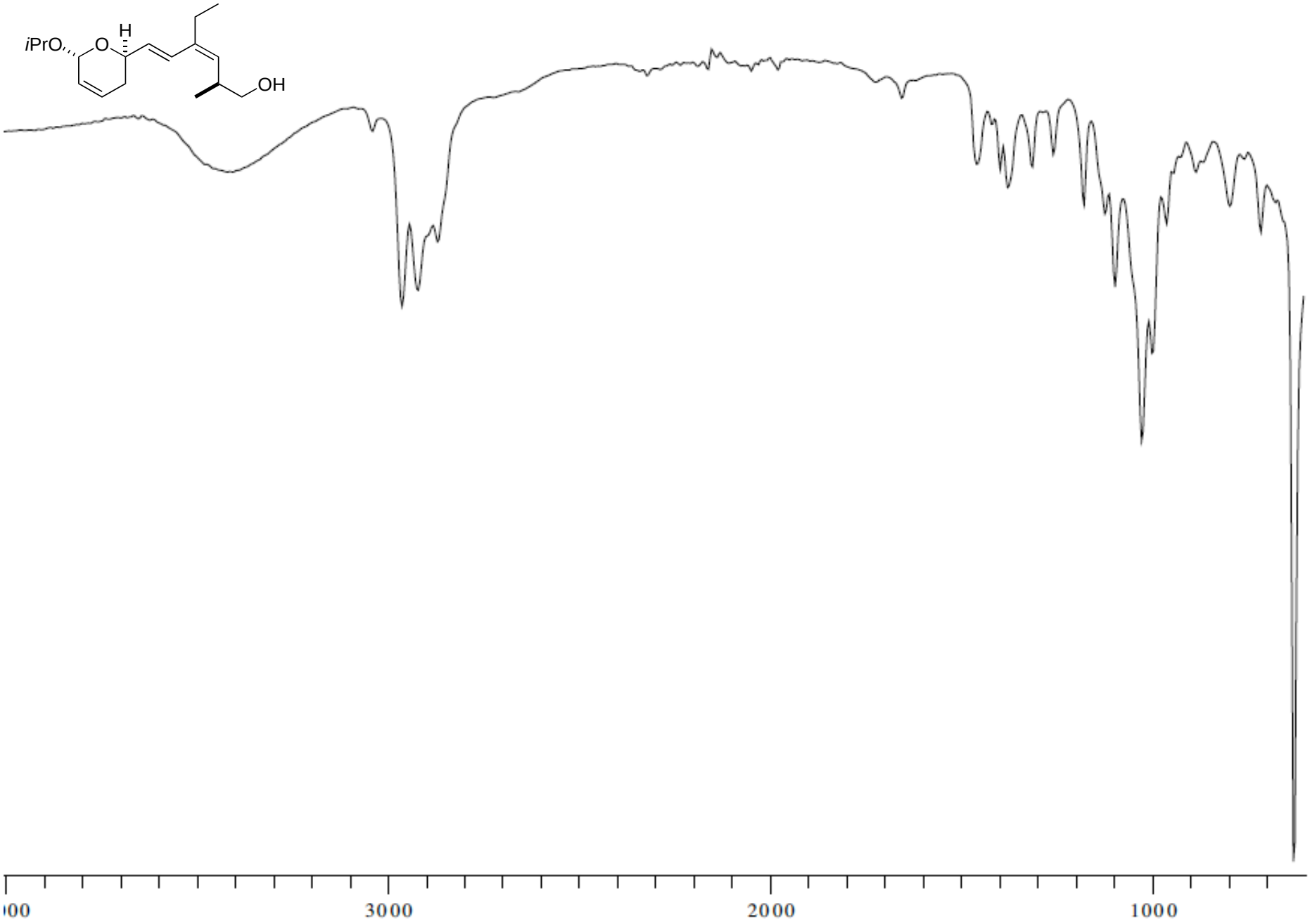
774.27
719.157
670.57
631.18

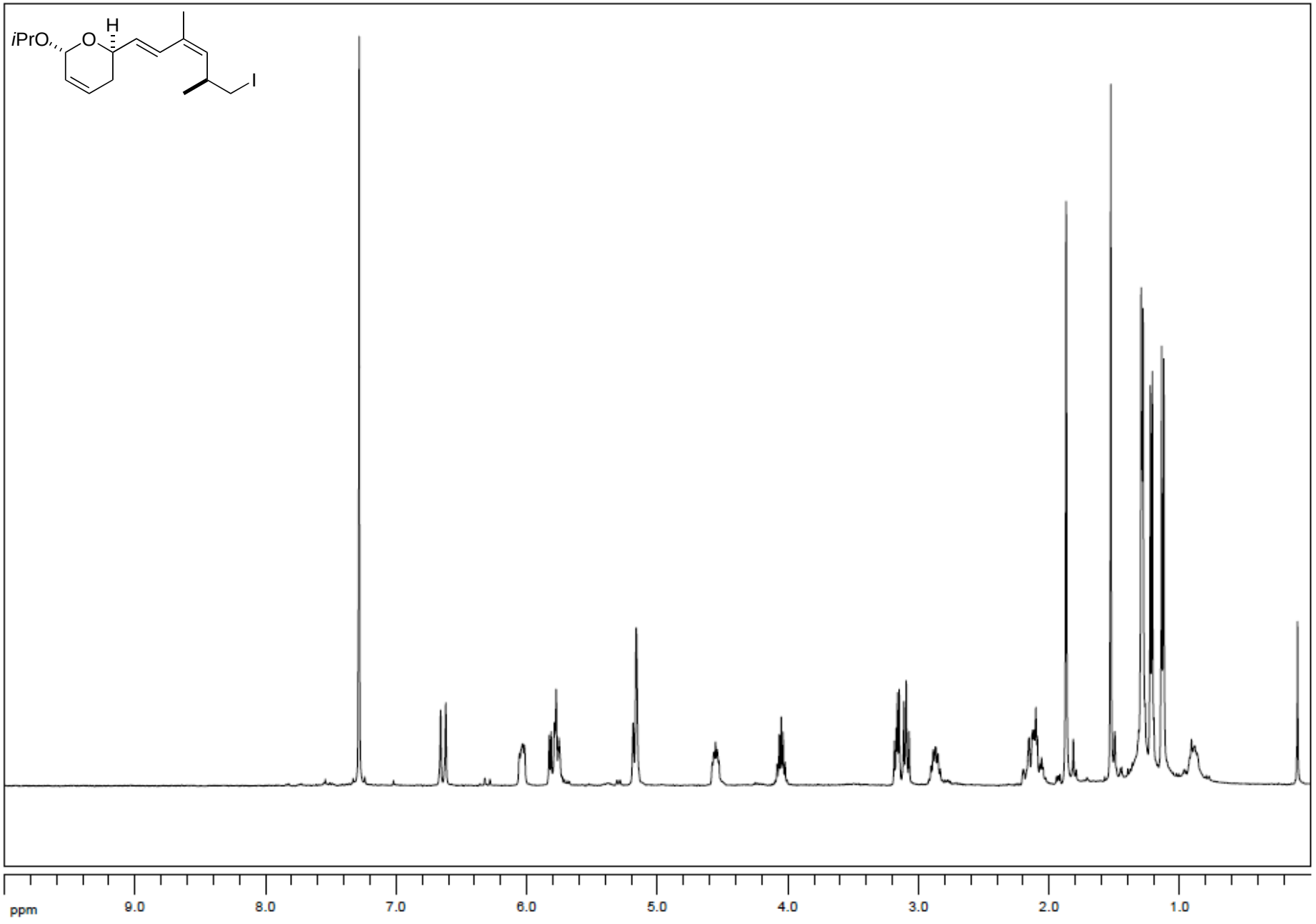

iPrO
O
H
OH


0
9
8
7
6
5
4
3
2
1


iPrO
O
H
OH


220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10


iPrO
O
H
OH
3000
2000
1000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O
H
I
ppm
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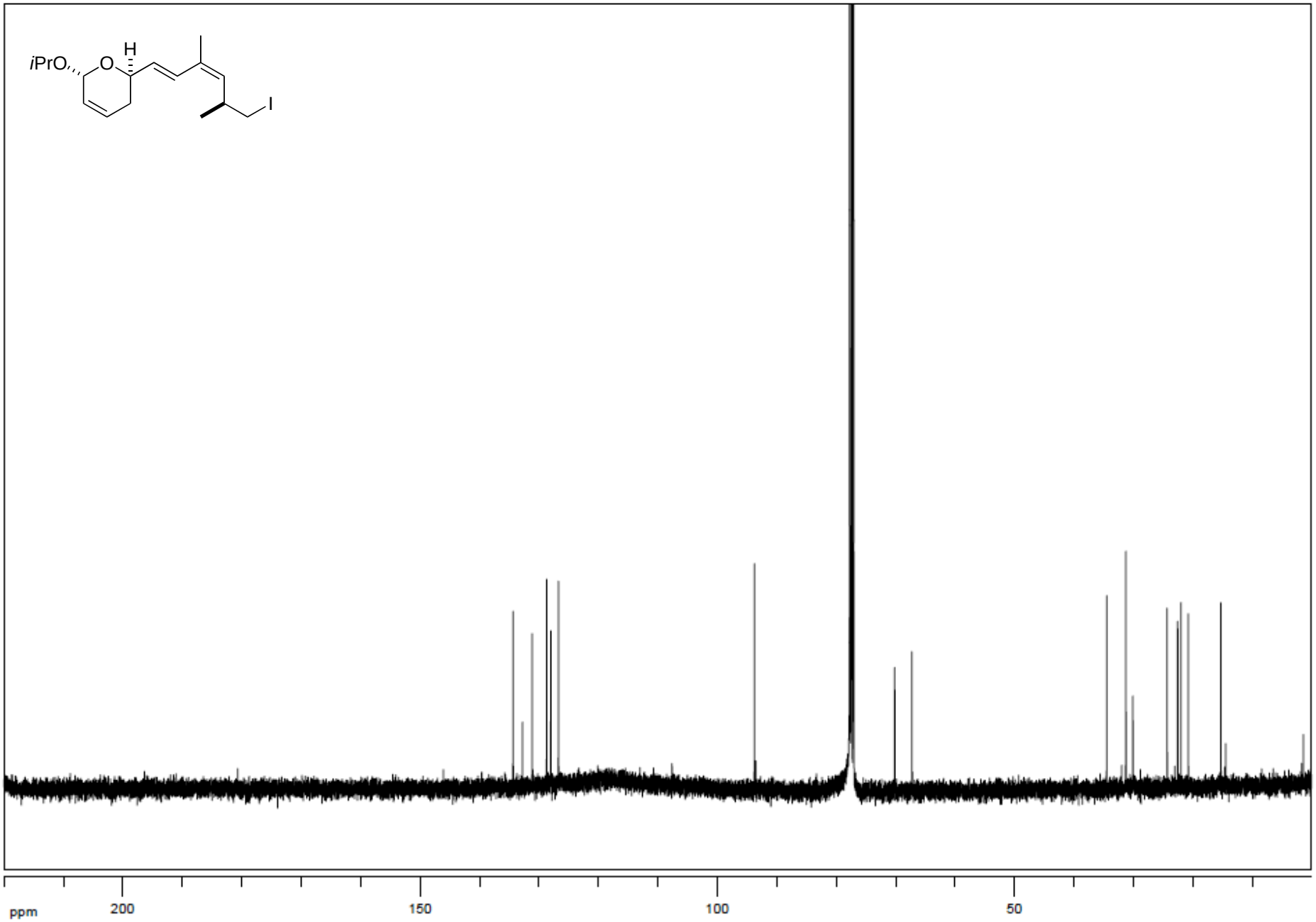
6.0
5.0
4.0
3.0
2.0
1.0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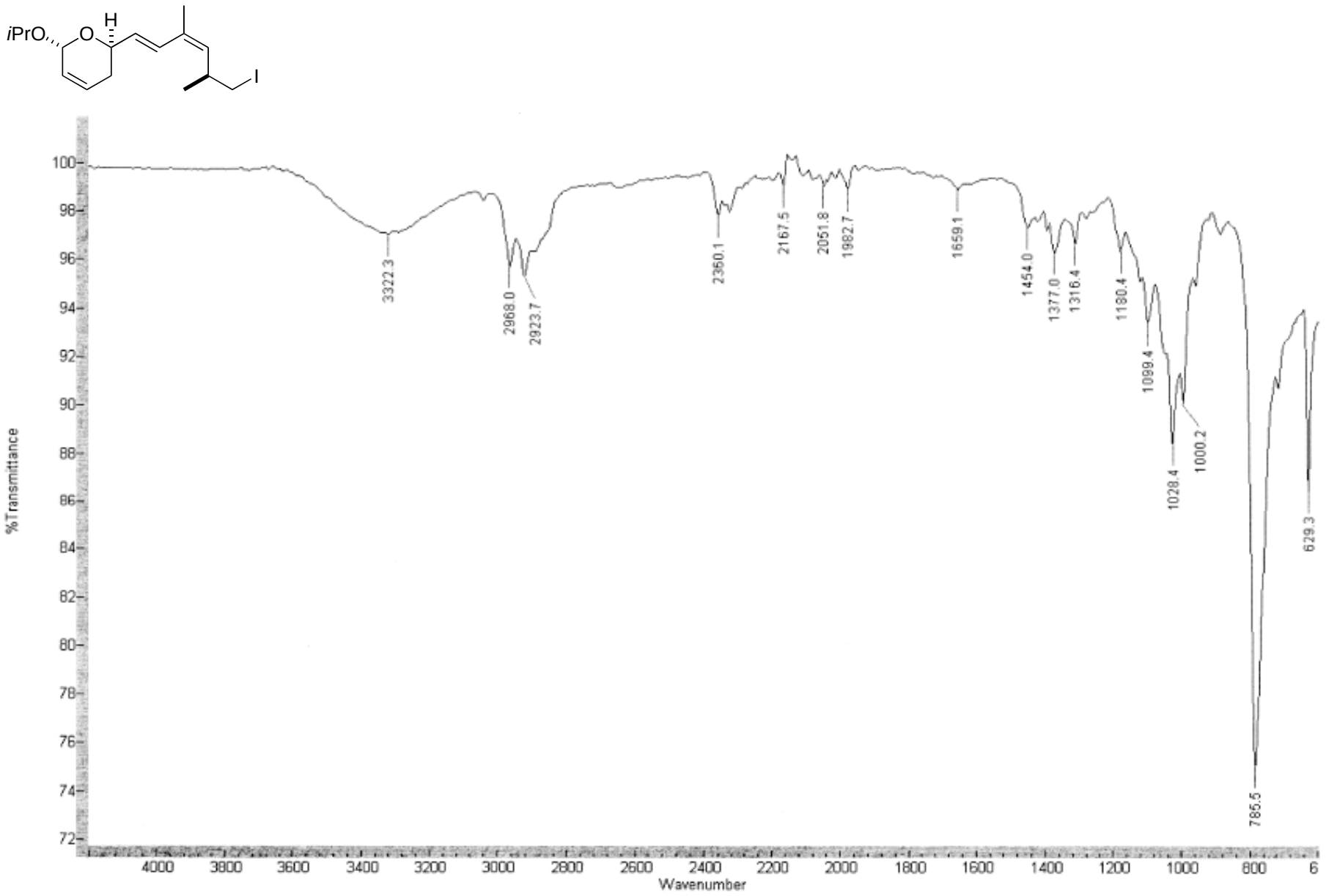
H
I
ppm
200
150
100
50


iPrO
O
H
I
%Transmittance
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98
96
94
92
90
88
86
84
82
80
78
76
74
72
3322.3
2968.0
2923.7
2360.1
2167.5
2051.8
1982.7
1659.1
1454.0
1377.0
1316.4
1180.4
1099.4
1028.4
1000.2
785.5
629.3
4000
3800
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2800
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1600
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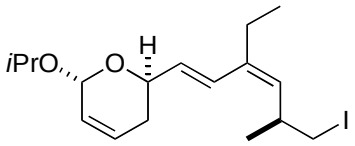
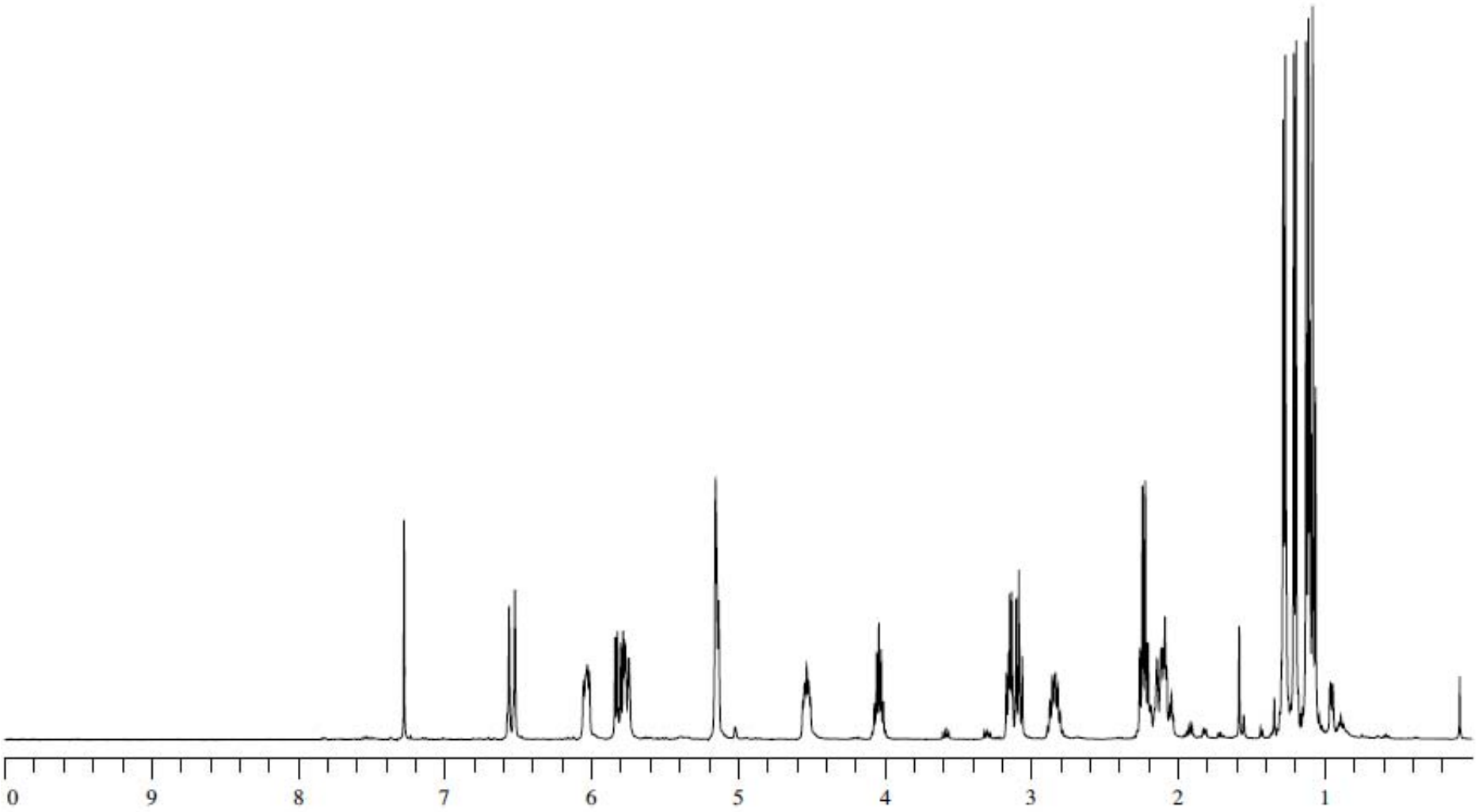
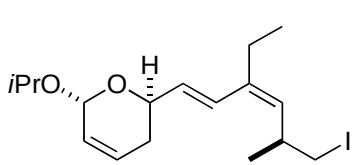
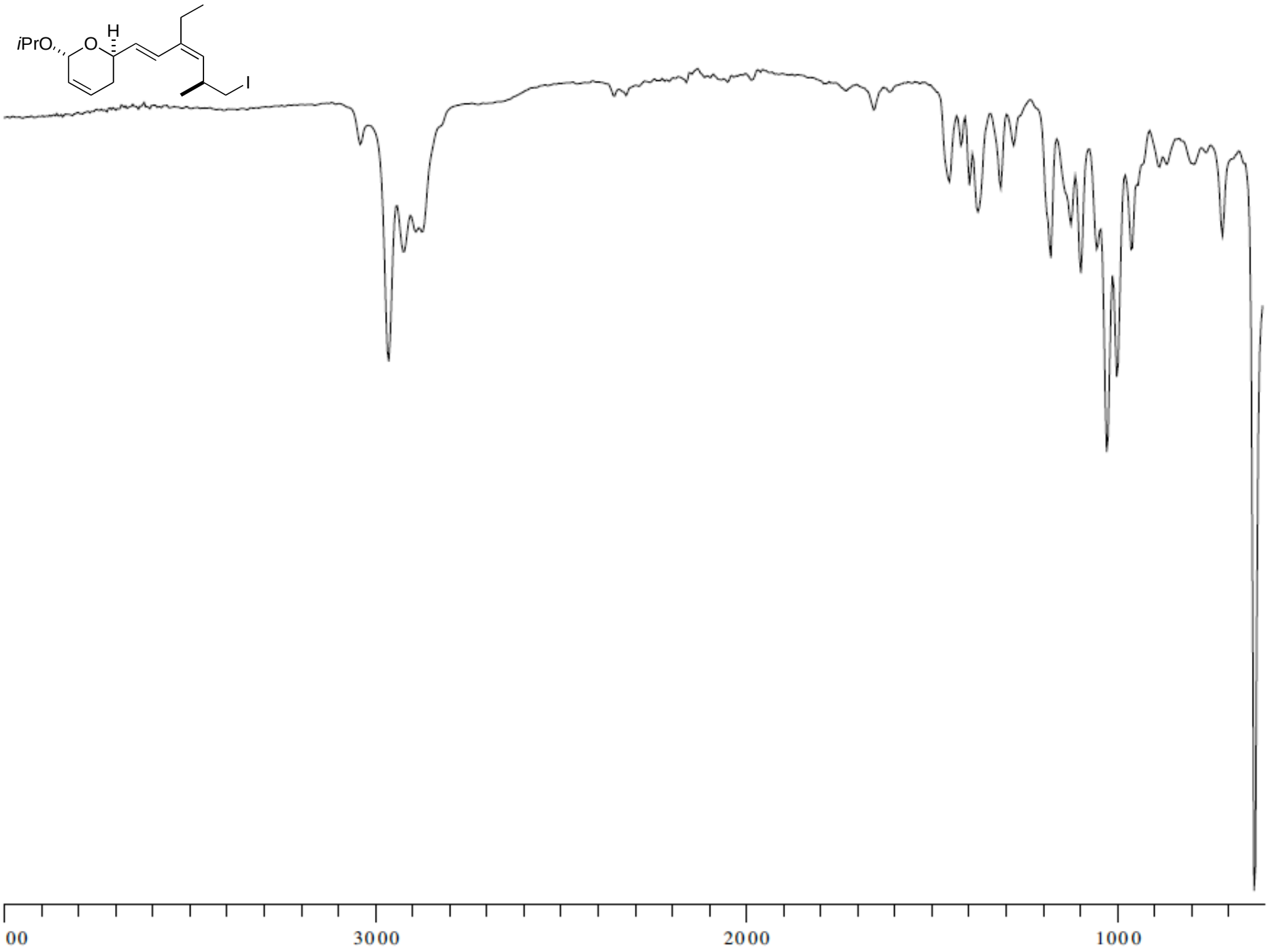
800
6
Wavenumber

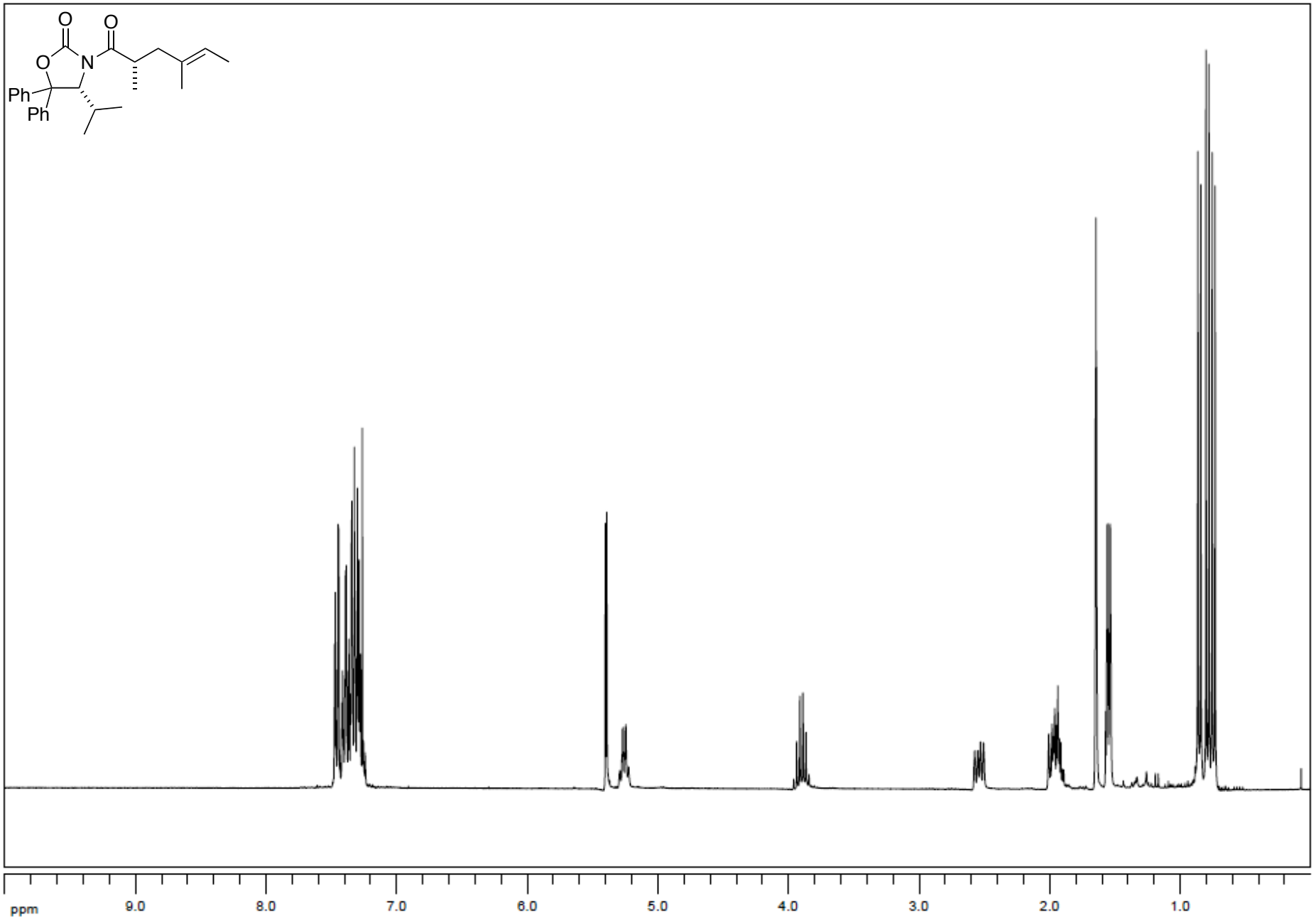

iPrO
O
H
I


0
9
8
7
6
5
4
3
2
1


iPrO
O
H
I


20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10


iPrO
O
H
I
00
3000
2000
1000


O
O
O
N
Ph
Ph
ppm
9.0
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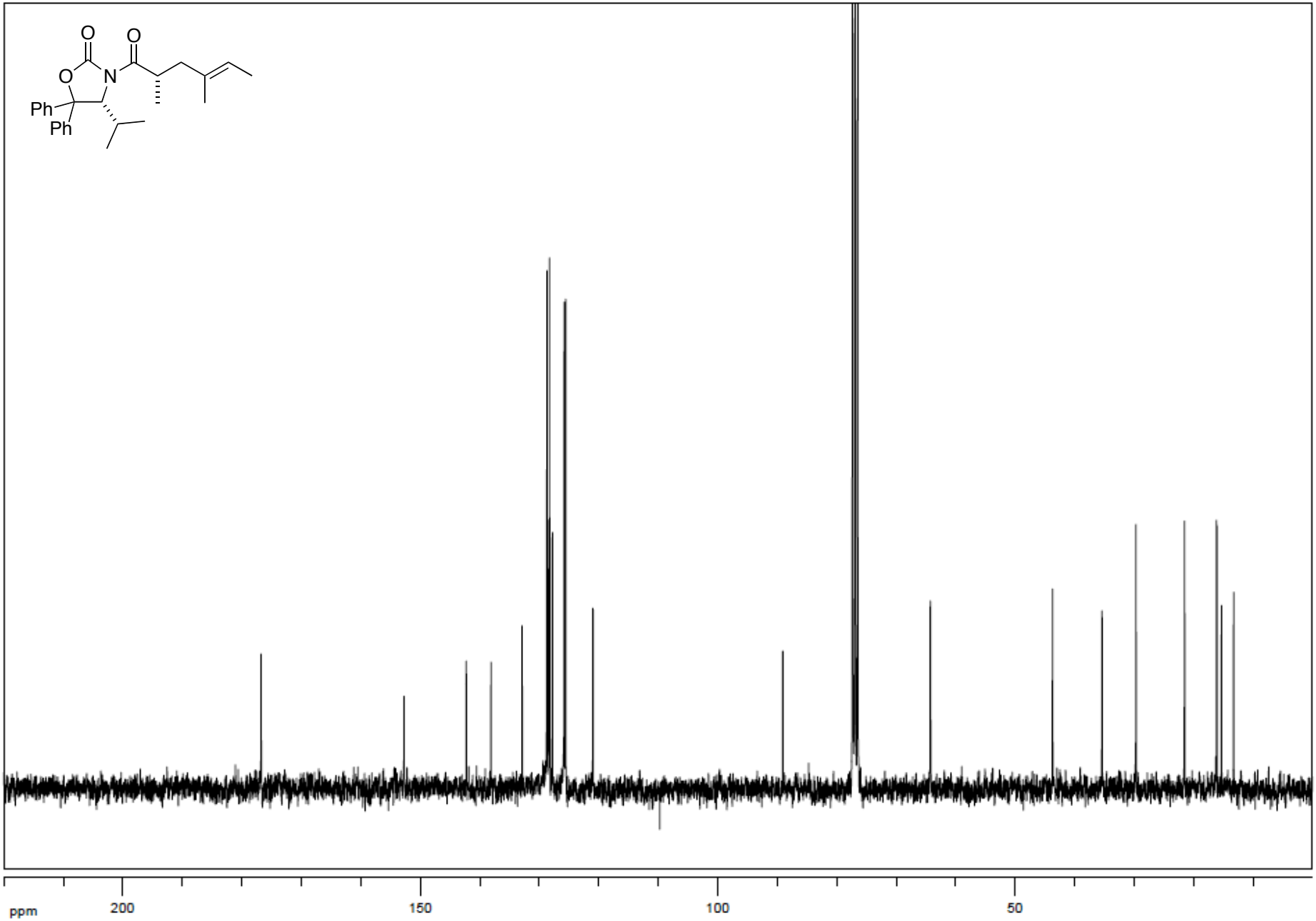
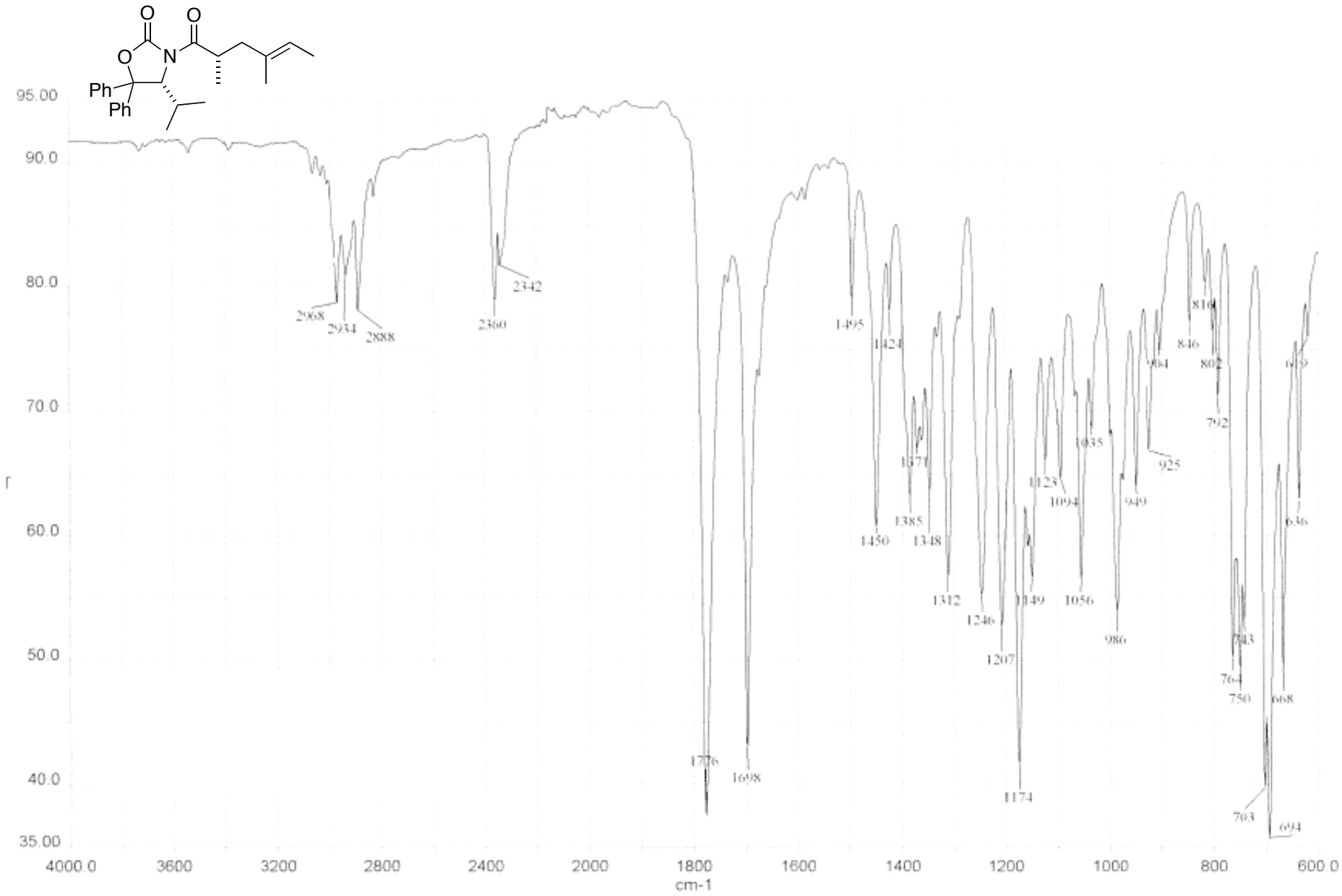
7.0
6.0
5.0
4.0
3.0
2.0
1.0


O
O
O
N
Ph
Ph
ppm
200
150
100
50


O
O
O
N
Ph
Ph
95.00
90.0
80.0
70.0
60.0
50.0
40.0
35.00
T
2968
2934
2888
2360
2342
1776
1698
1495
1424
1450
1385
1371
1348
1312
1246
1207
1174
1149
1123
1094
1056
1035
986
949
925
904
846
816
802
792
764
750
743
703
694
668
636
619
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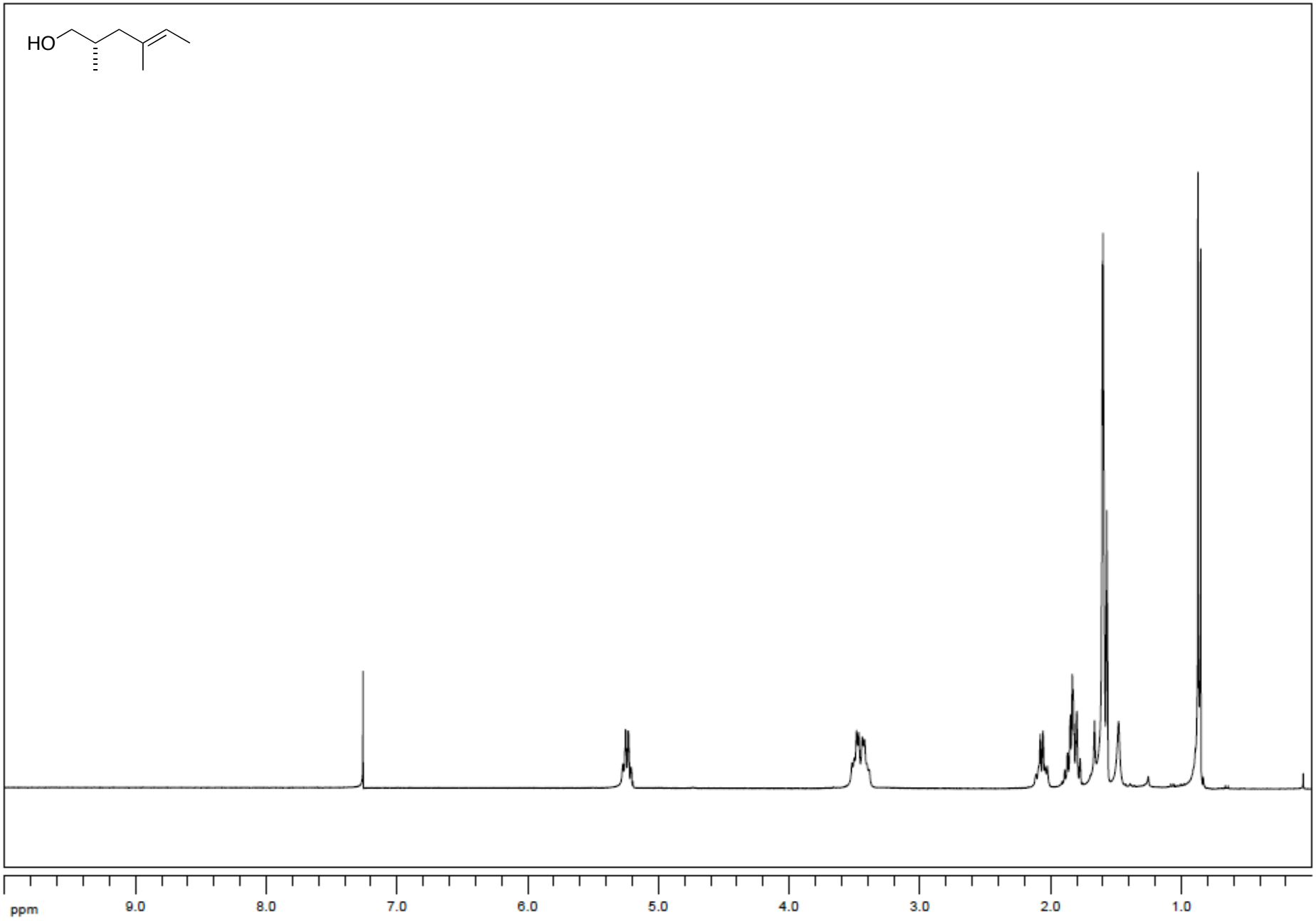
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600.0
cm-1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ppm
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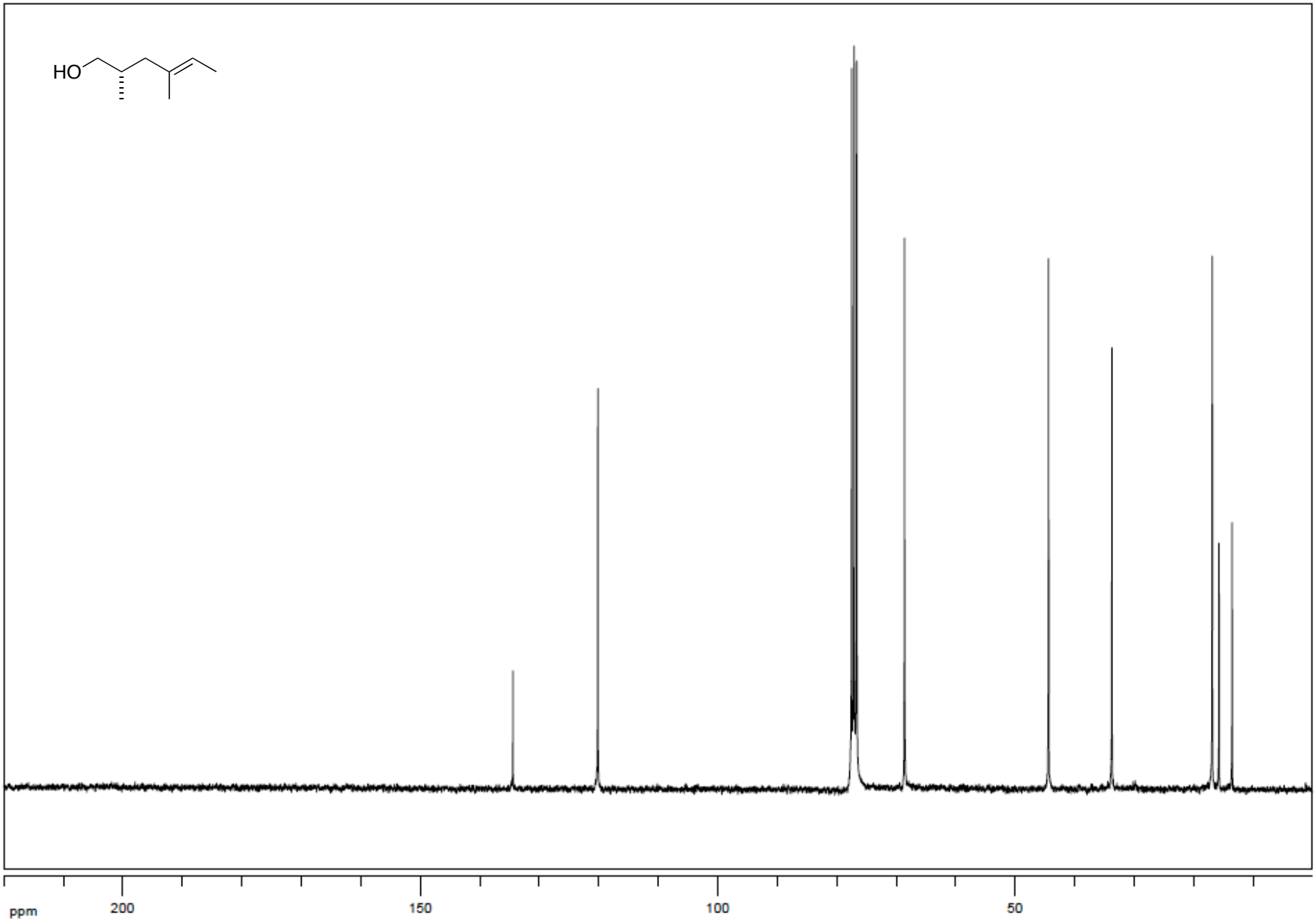
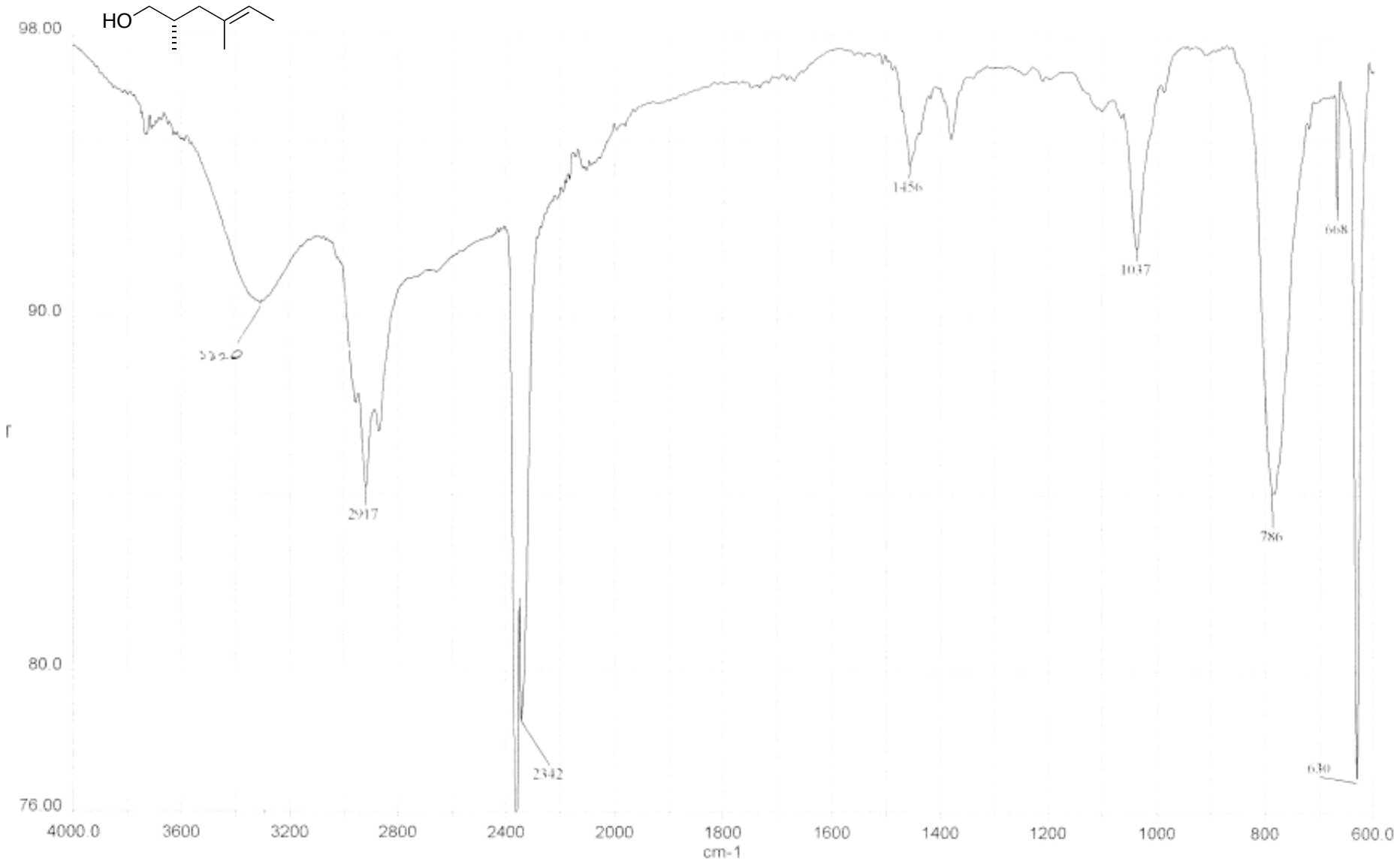
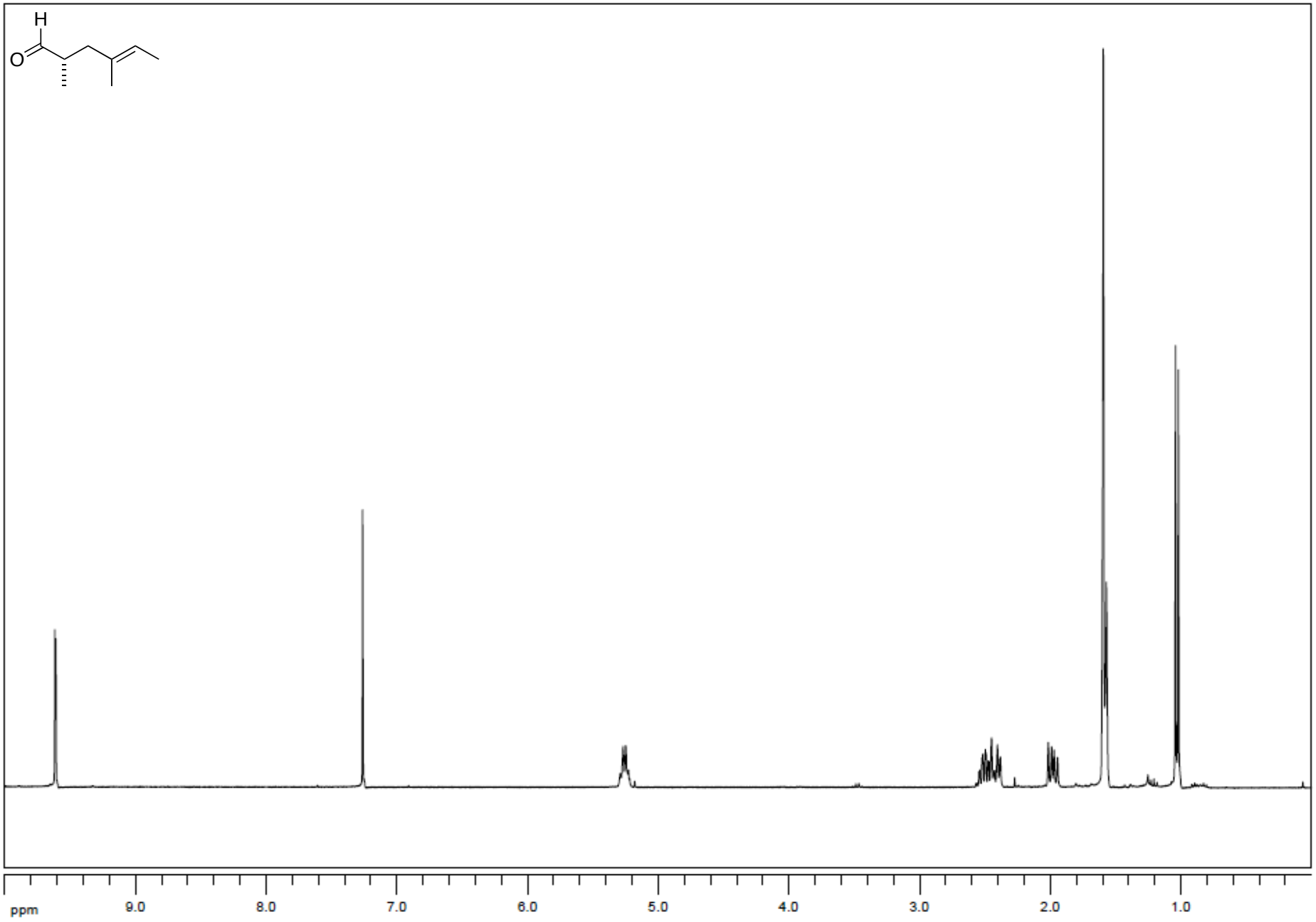
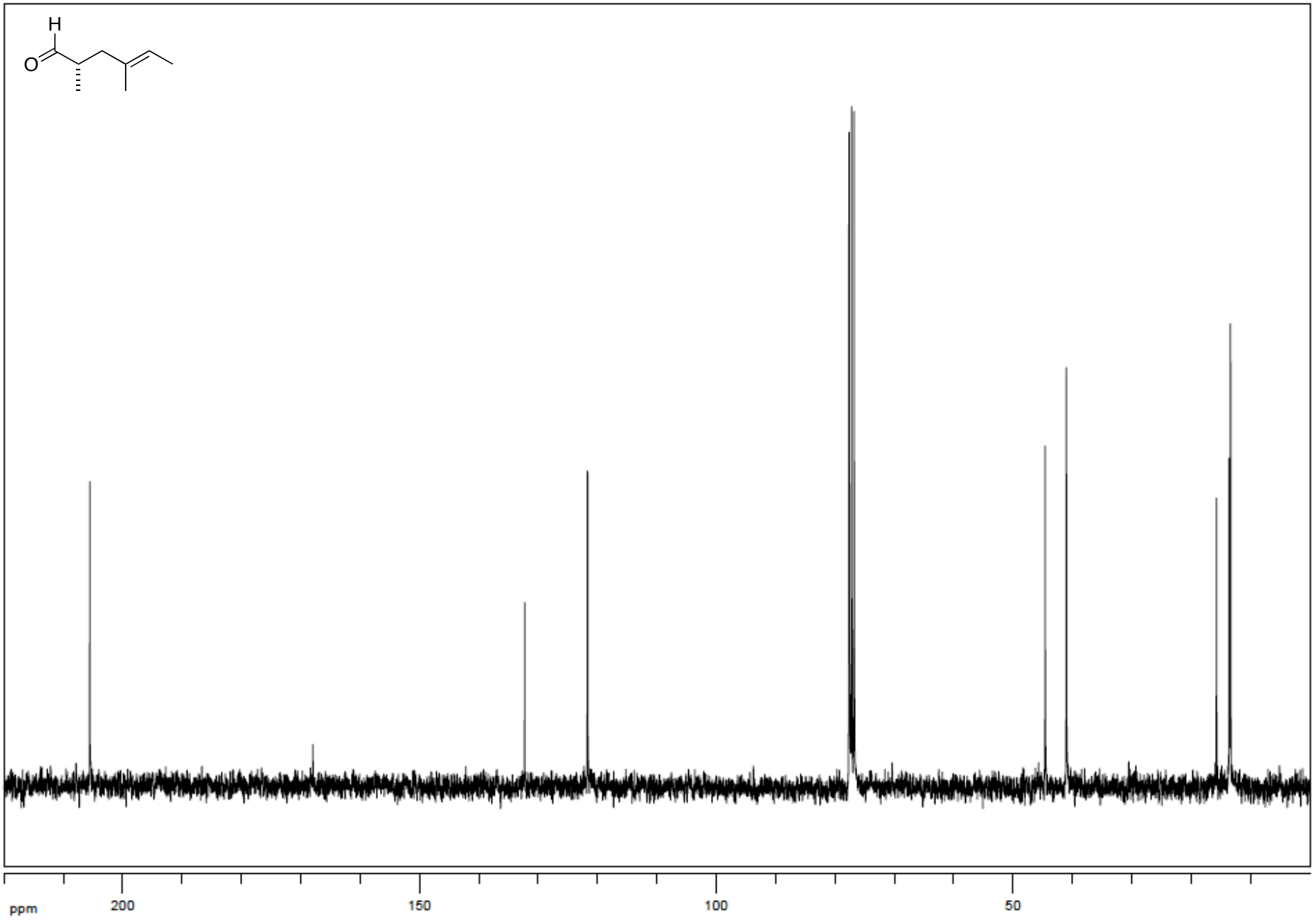
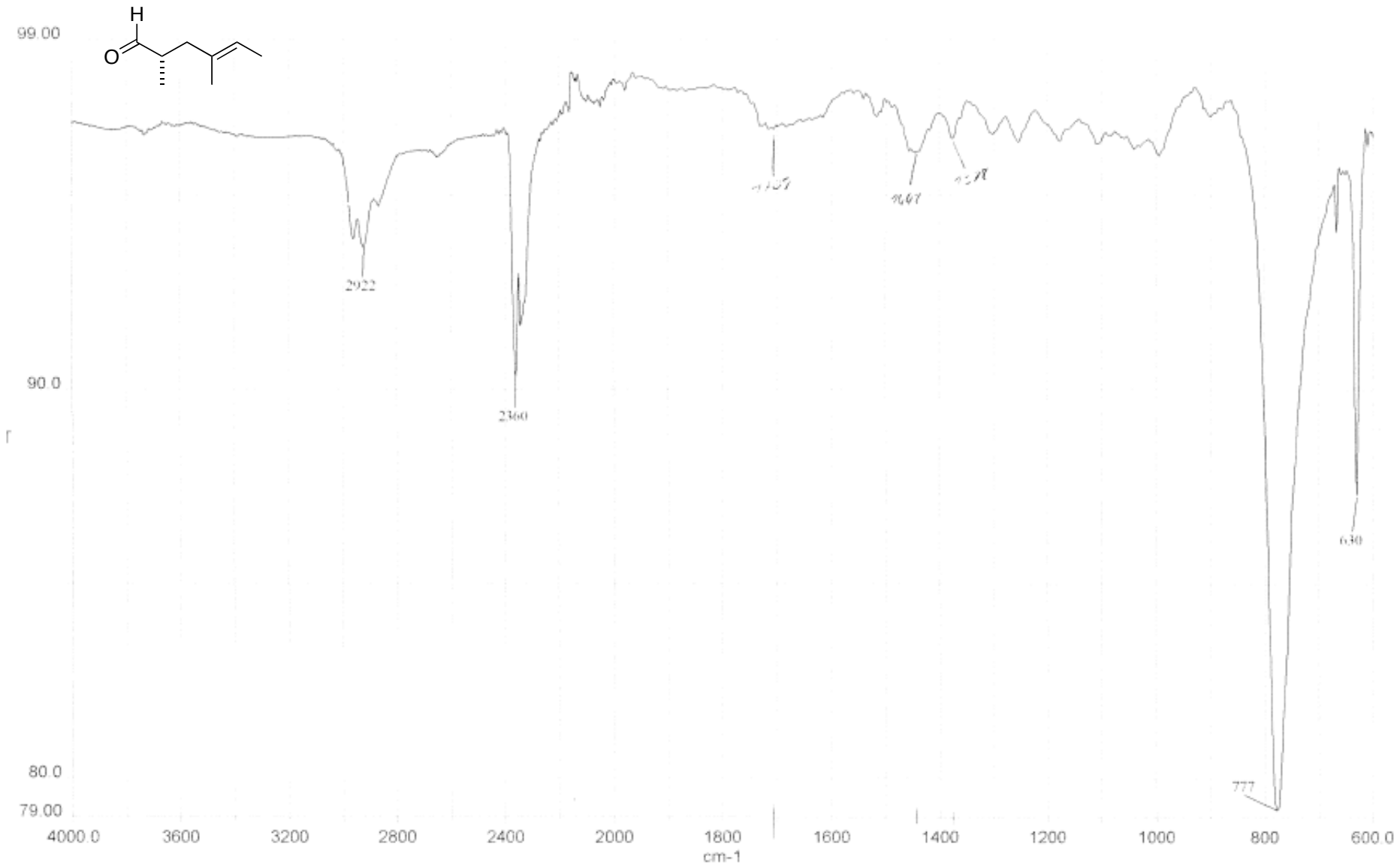
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0

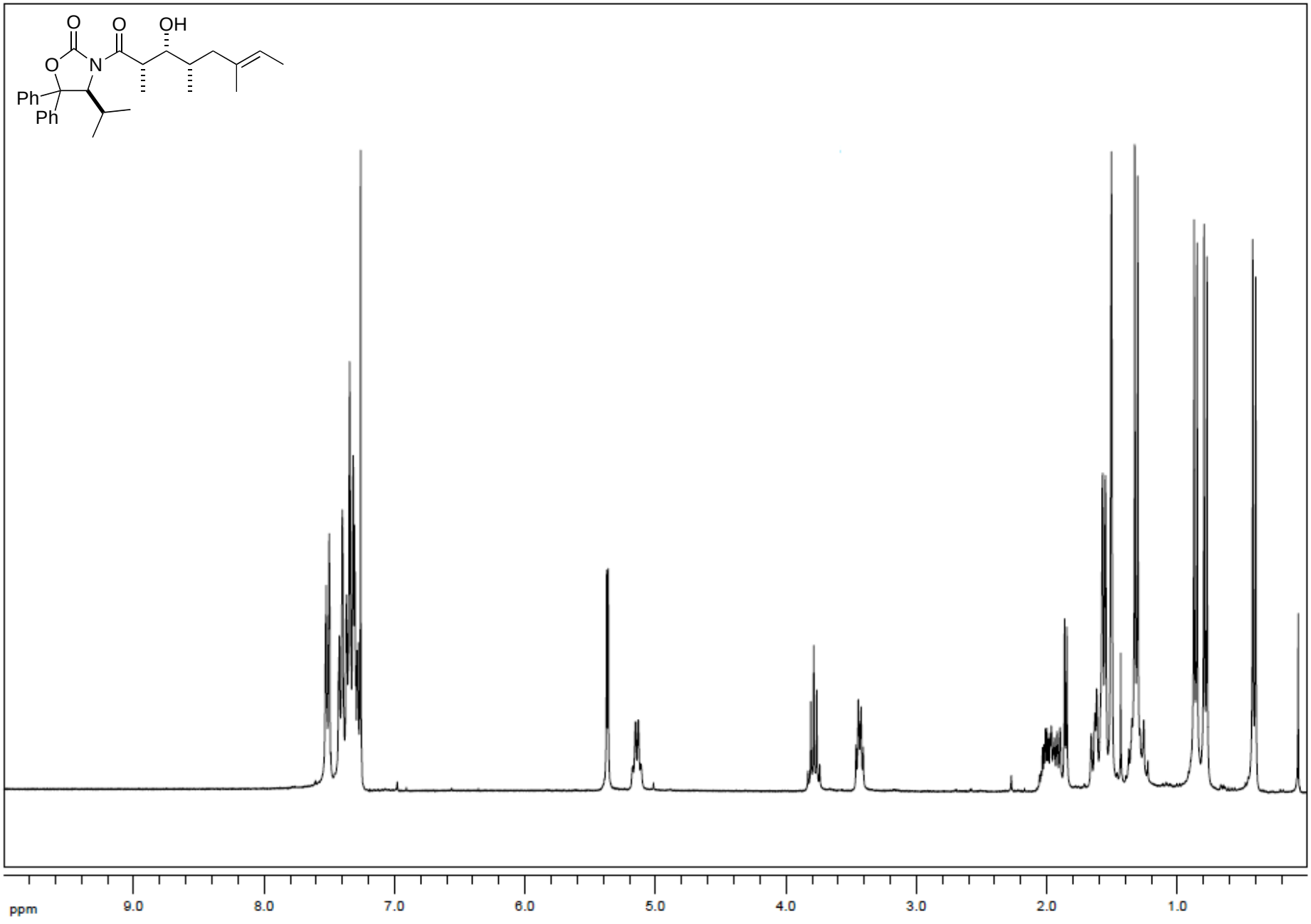

HO
ppm
200
150
100
50

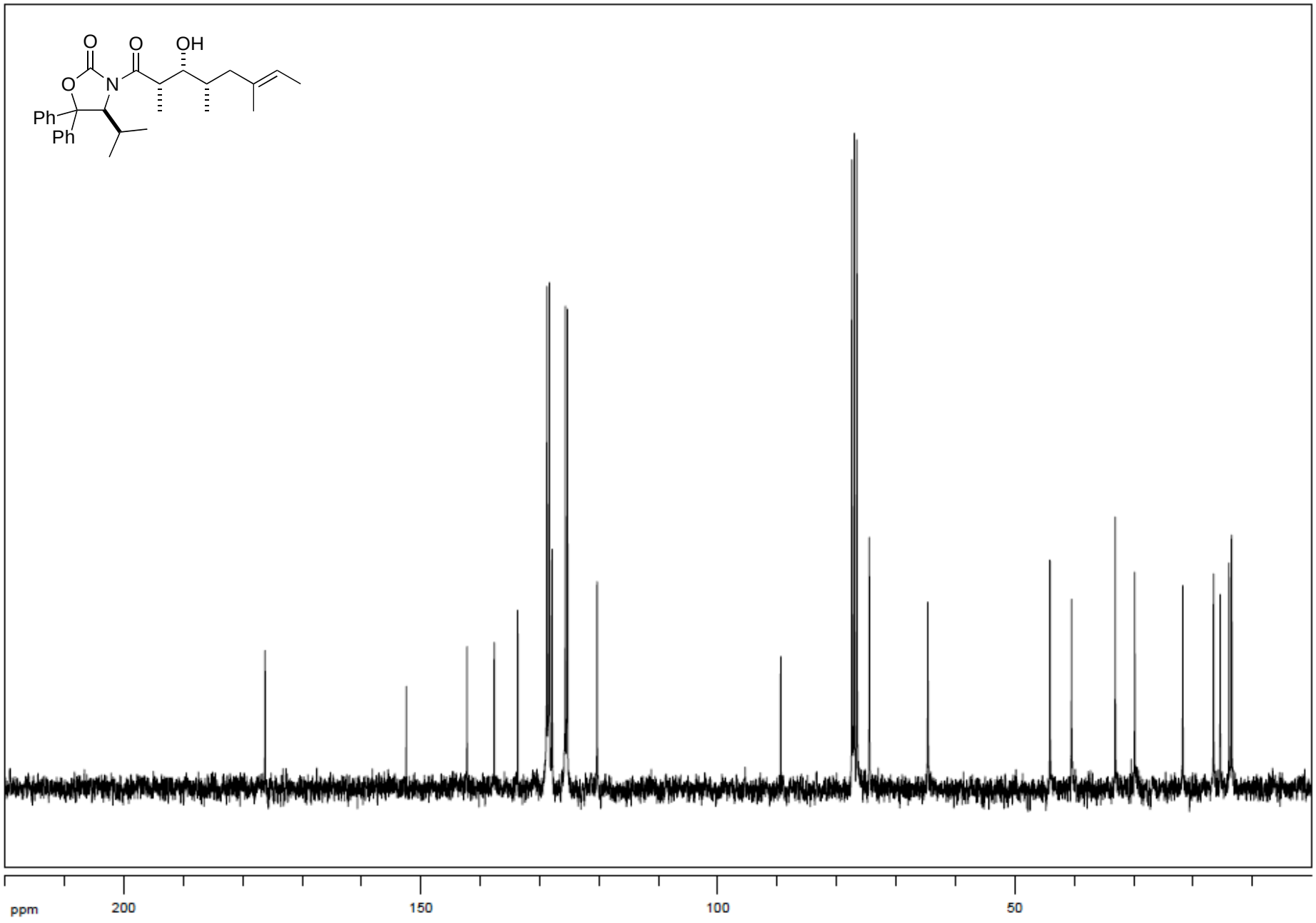

HO
98.00
90.0
80.0
76.00
T
3320
2917
2342
1456
1037
786
668
630
4000.0
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600.0
cm-1

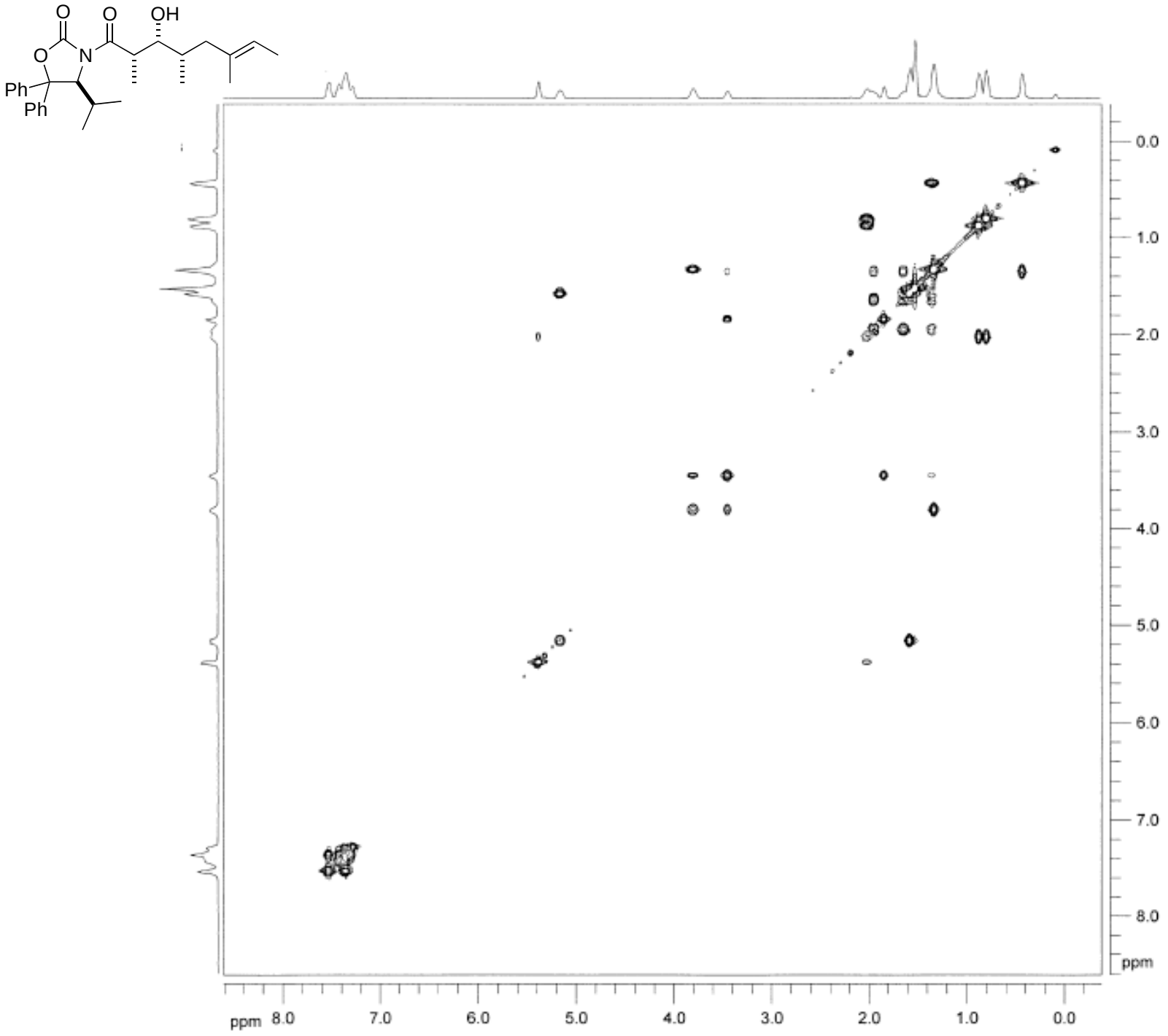

H
O
ppm
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0

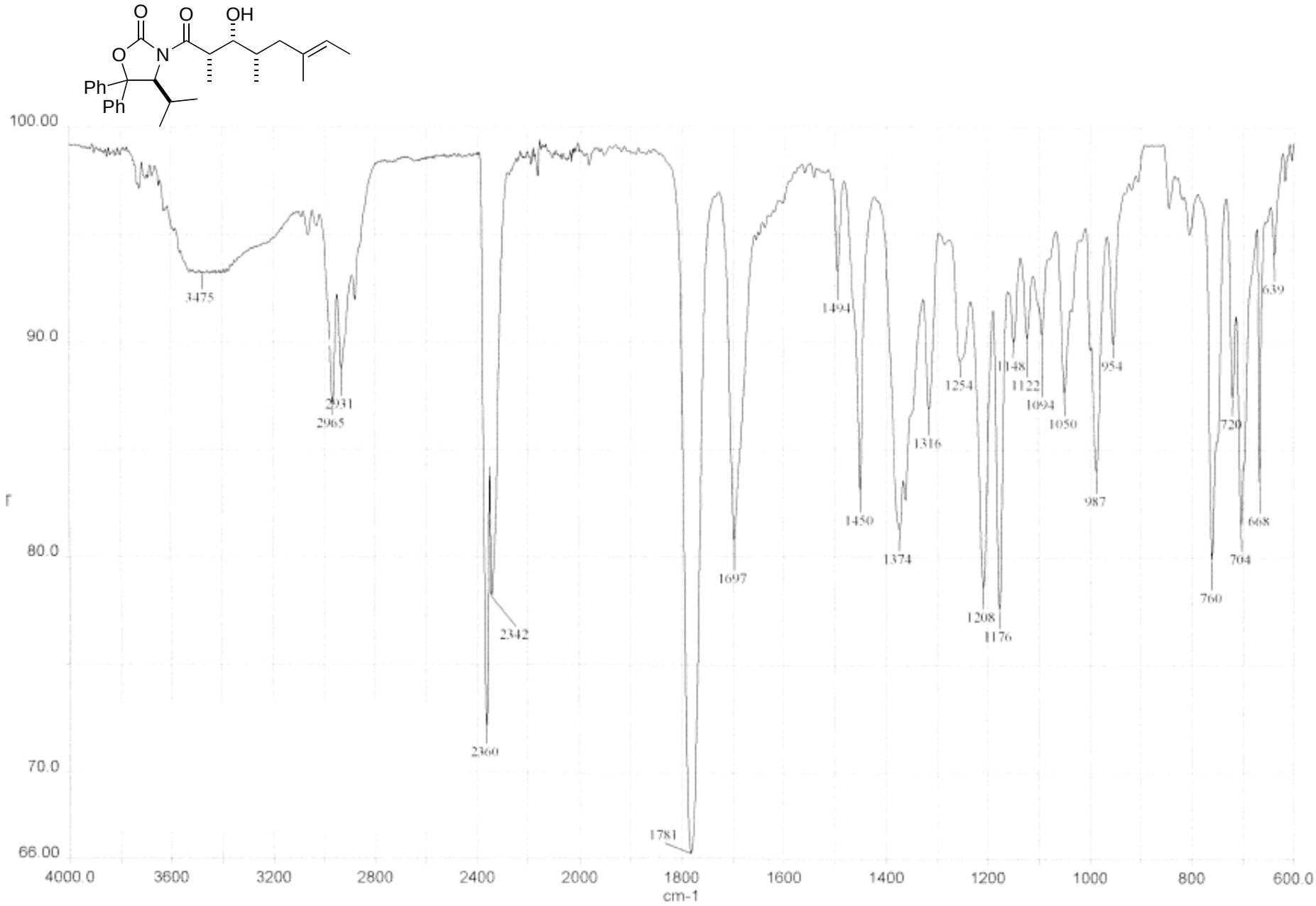

H
O
ppm
200
150
100
50

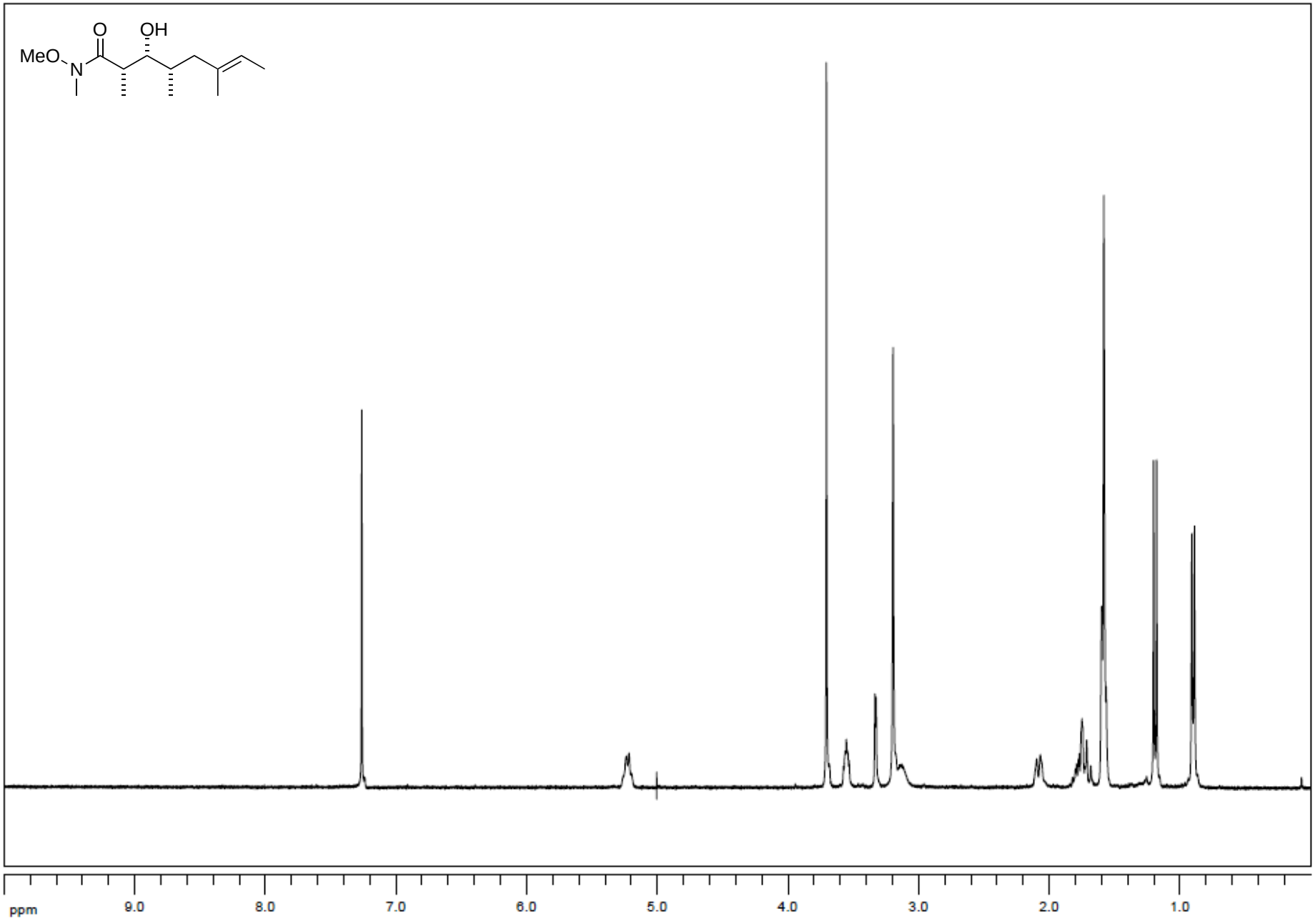

H
O
99.00
90.0
80.0
79.00
2922
2360
777
630
4000.0
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600.0
cm-1

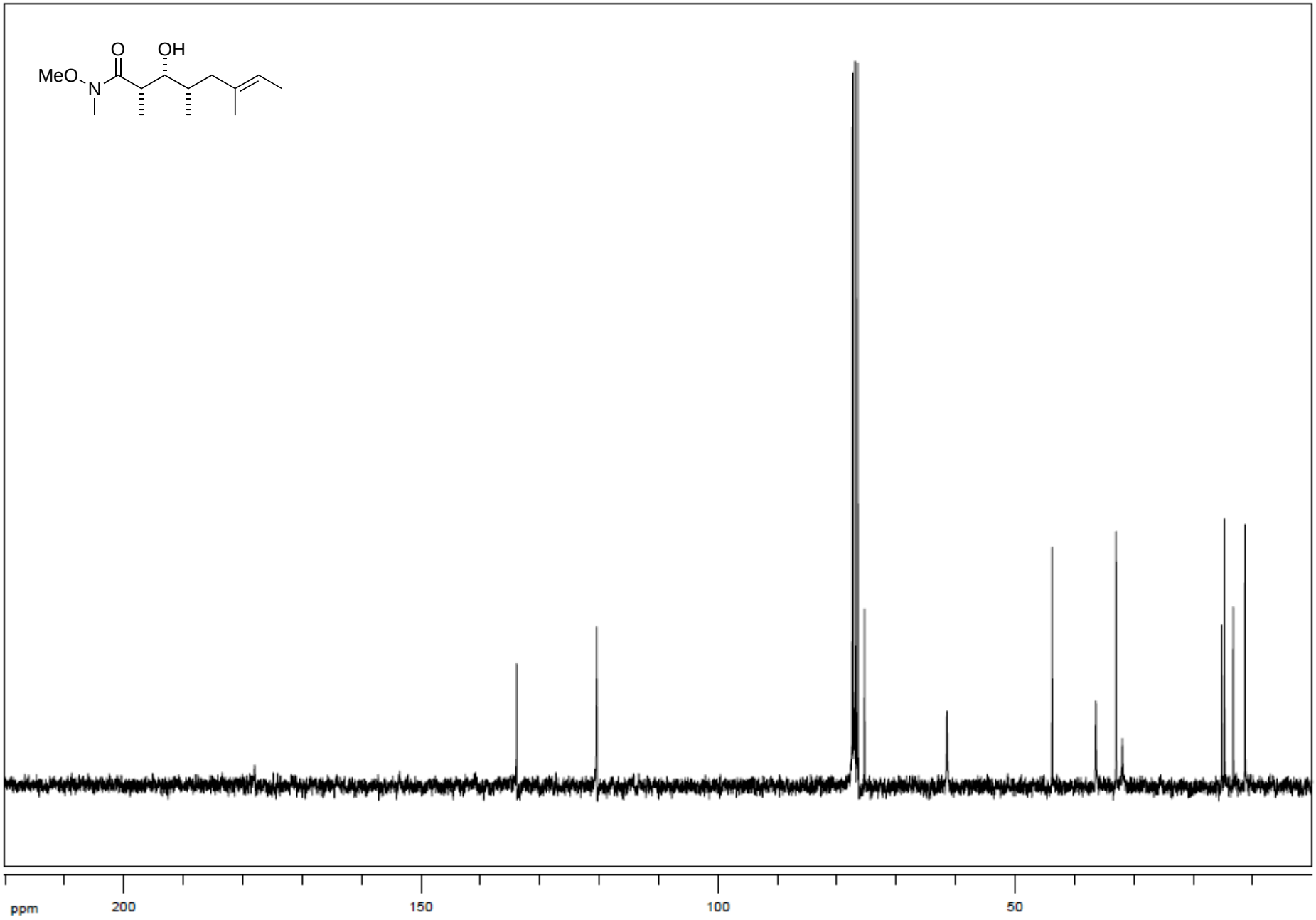

O
O
OH
O
N
Ph
Ph
ppm
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0

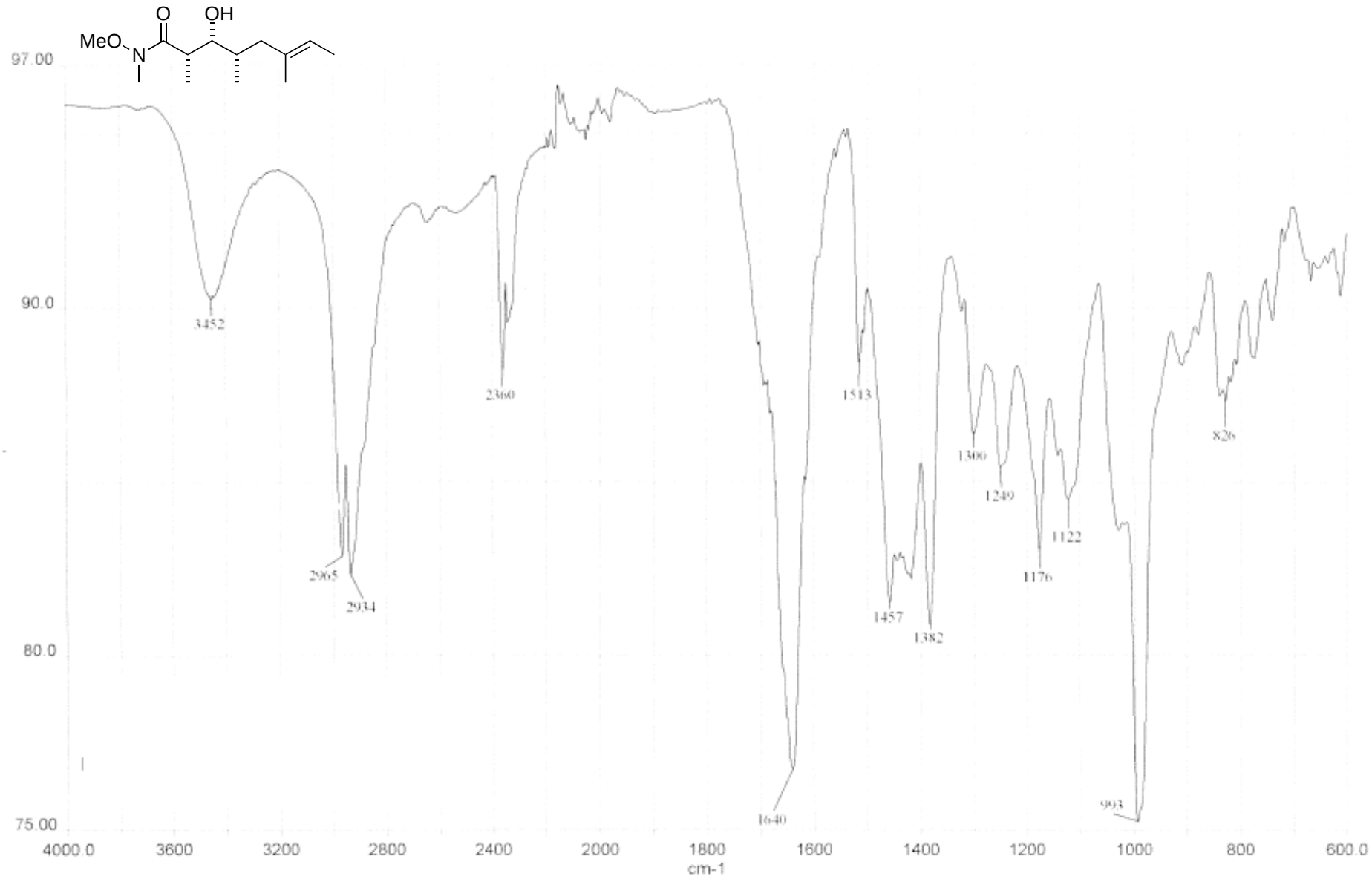

O
O
OH
O
N
Ph
Ph
ppm
200
150
100
50

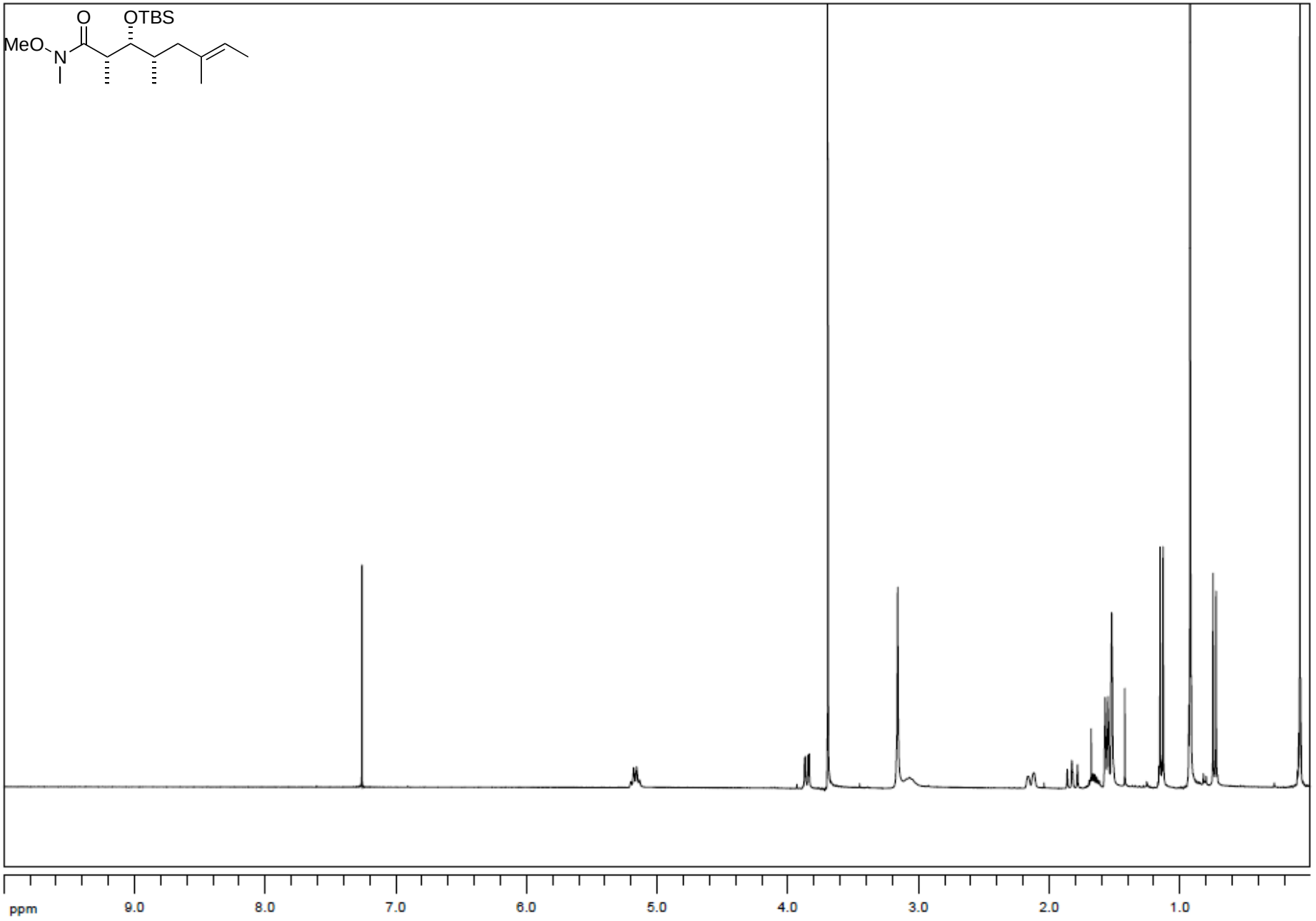

O
O
OH
O
N
Ph
Ph
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
ppm
ppm 8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

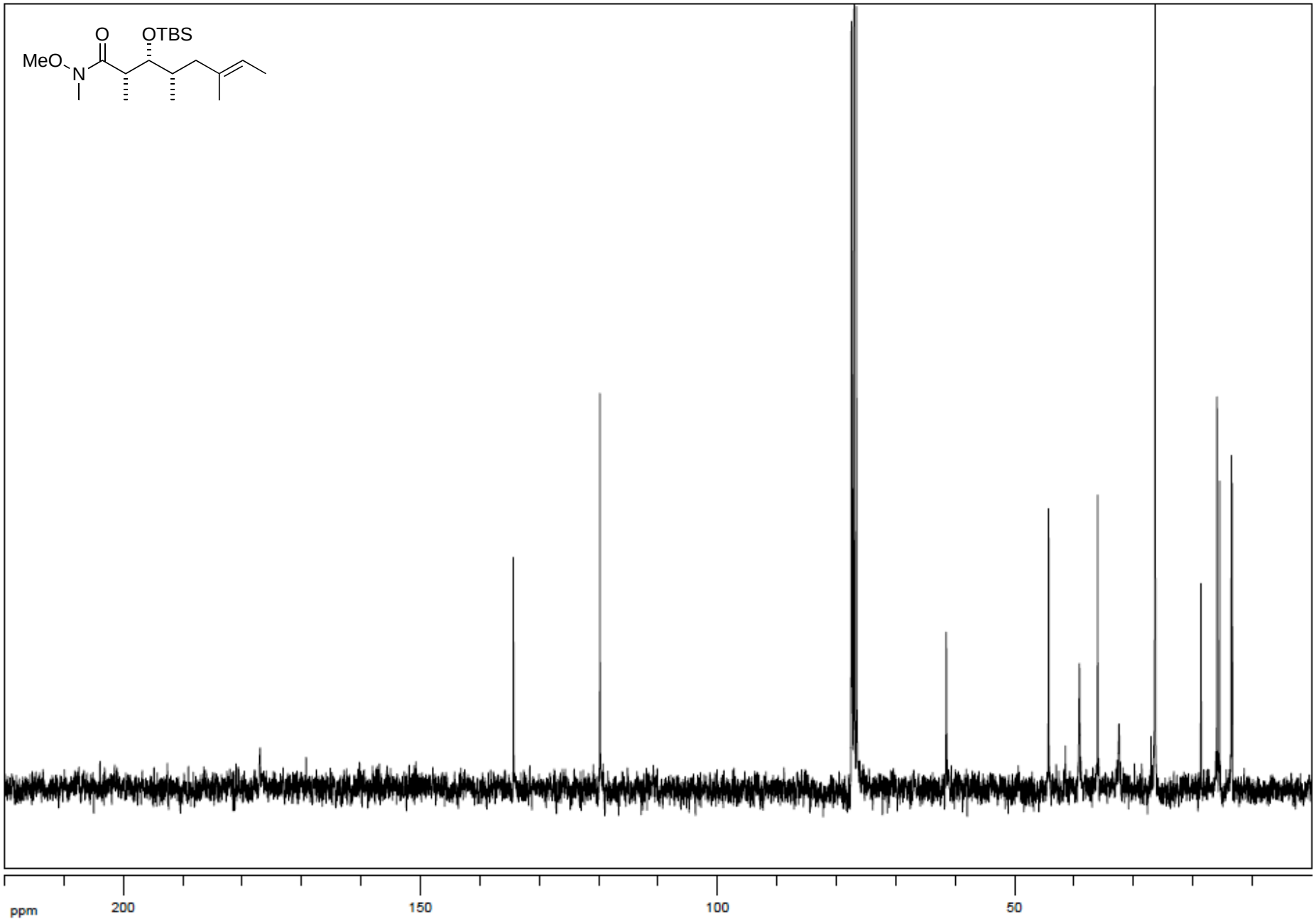

O
O
OH
O
N
Ph
Ph
100.00
90.0
80.0
70.0
66.00
T
3475
2931
2965
2360
2342
1781
1697
1494
1450
1374
1316
1254
1208
1176
1148
1122
1094
1050
987
954
760
720
704
668
639
4000.0
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600.0
cm-1

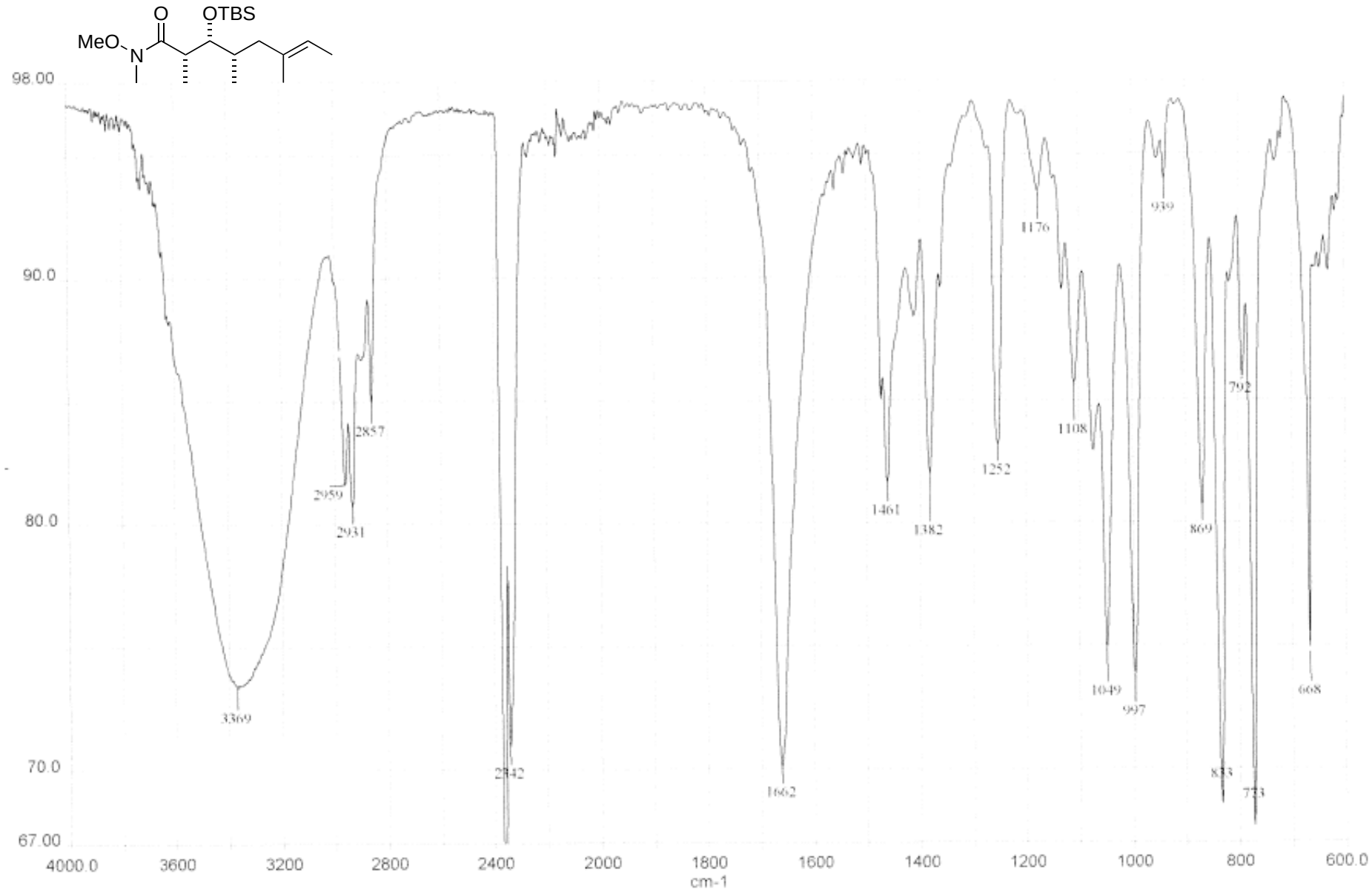

O
OH
MeO
N
ppm
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0

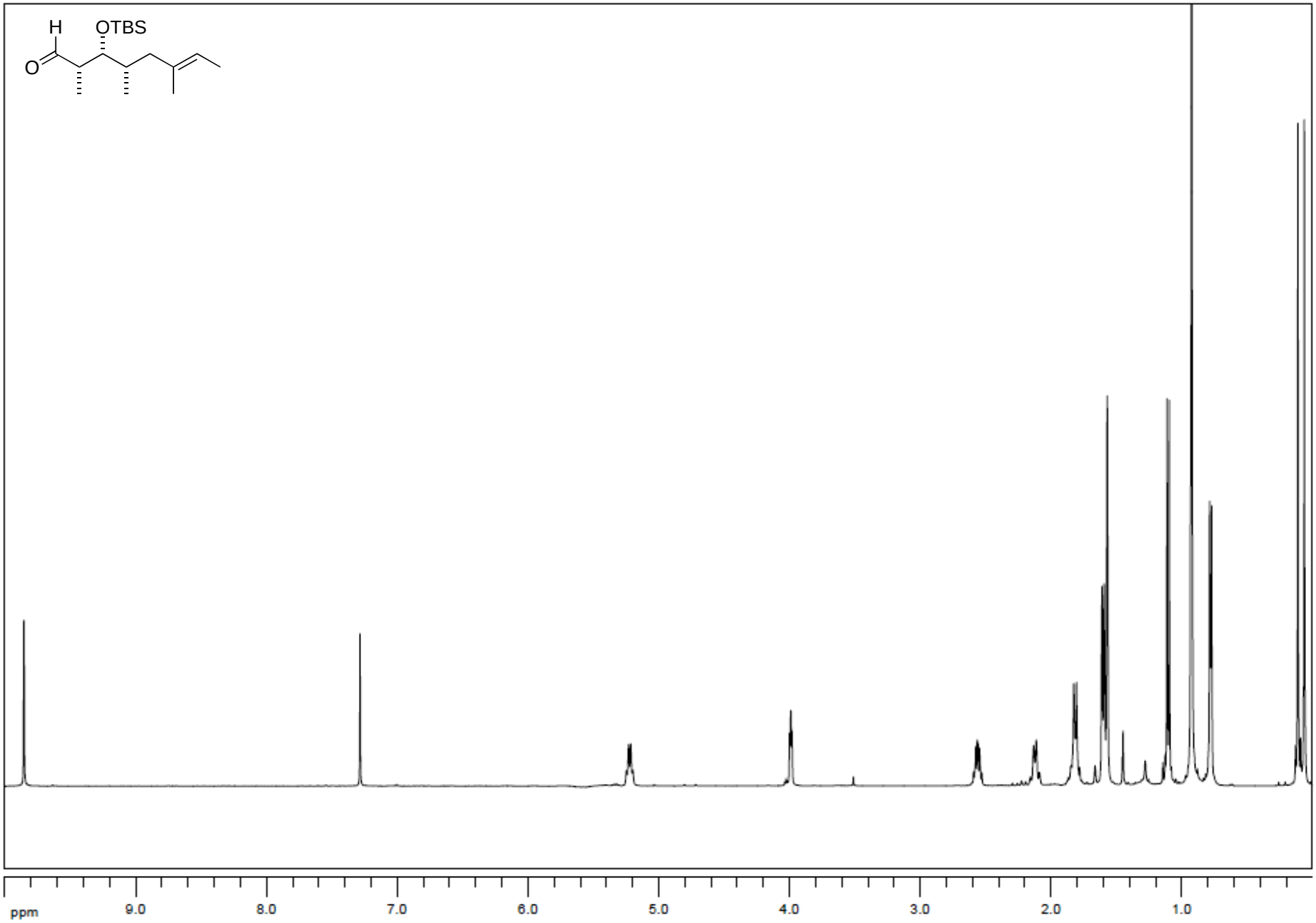

O
OH
MeO
N
ppm
200
150
100
50

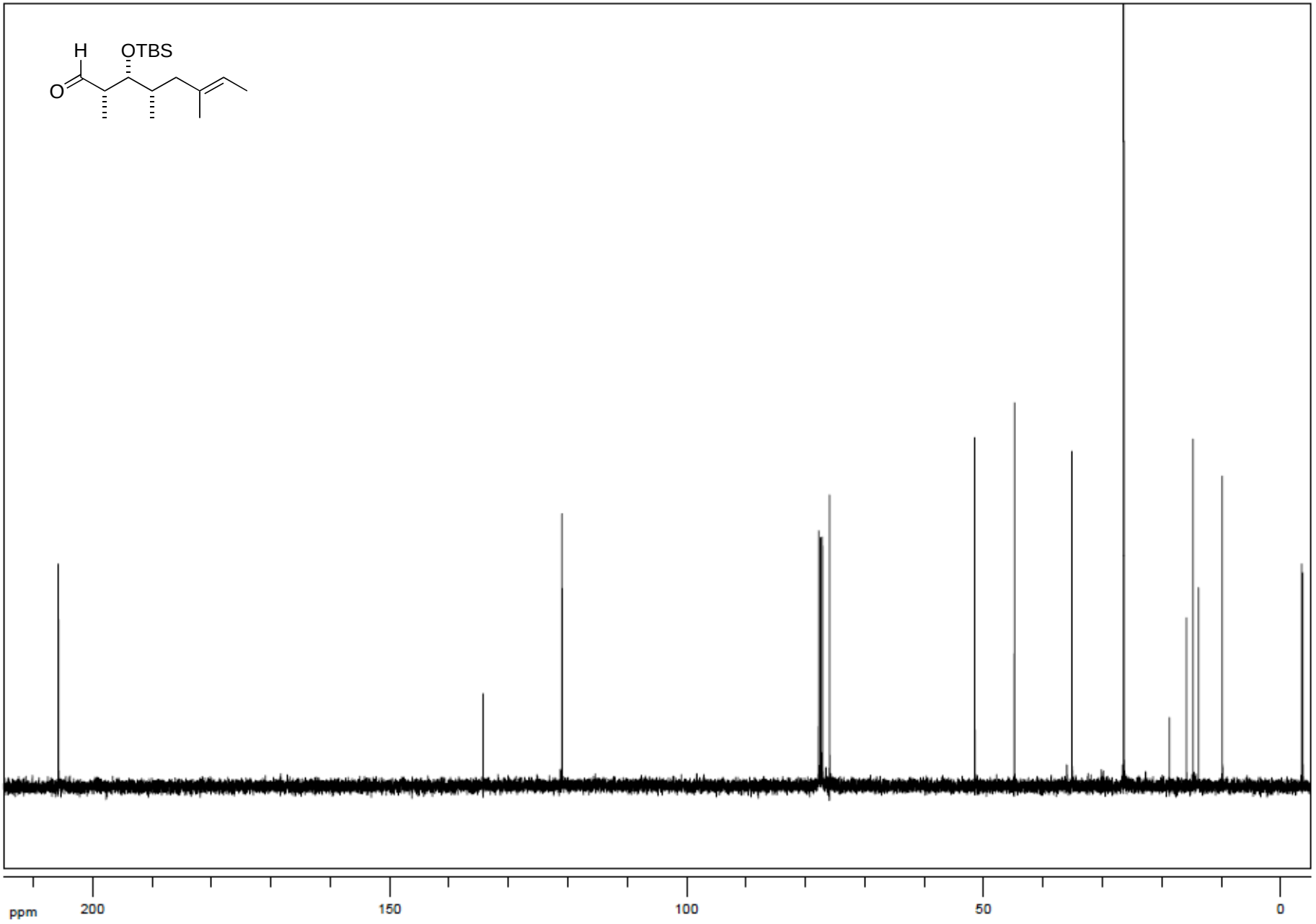

MeO
N
O
OH
97.00
90.0
80.0
75.00
3452
2965
2934
2360
1640
1513
1457
1382
1380
1249
1176
1122
993
826
4000.0
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600.0
cm-1

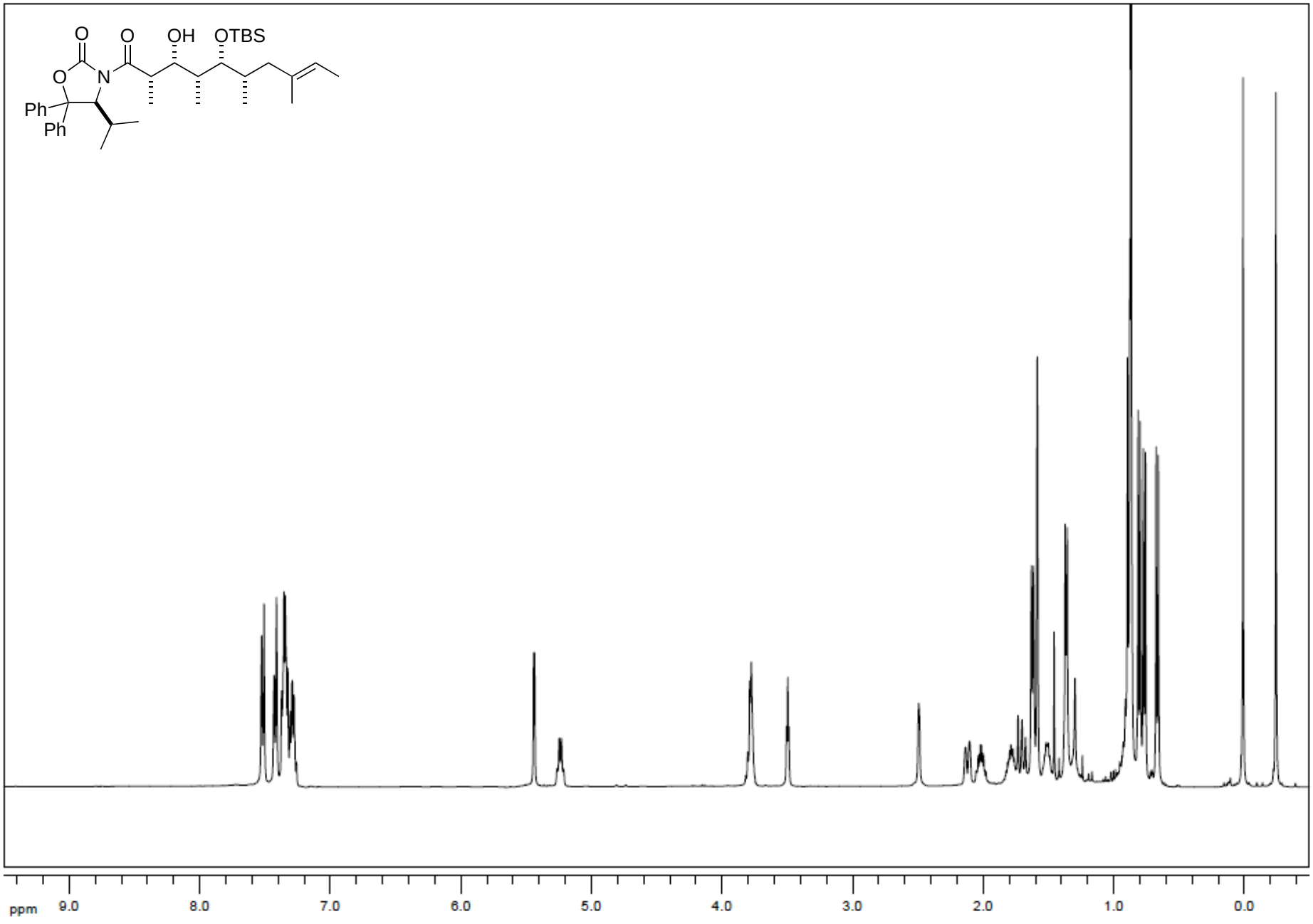

O
OTBS
MeO
N
ppm
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0

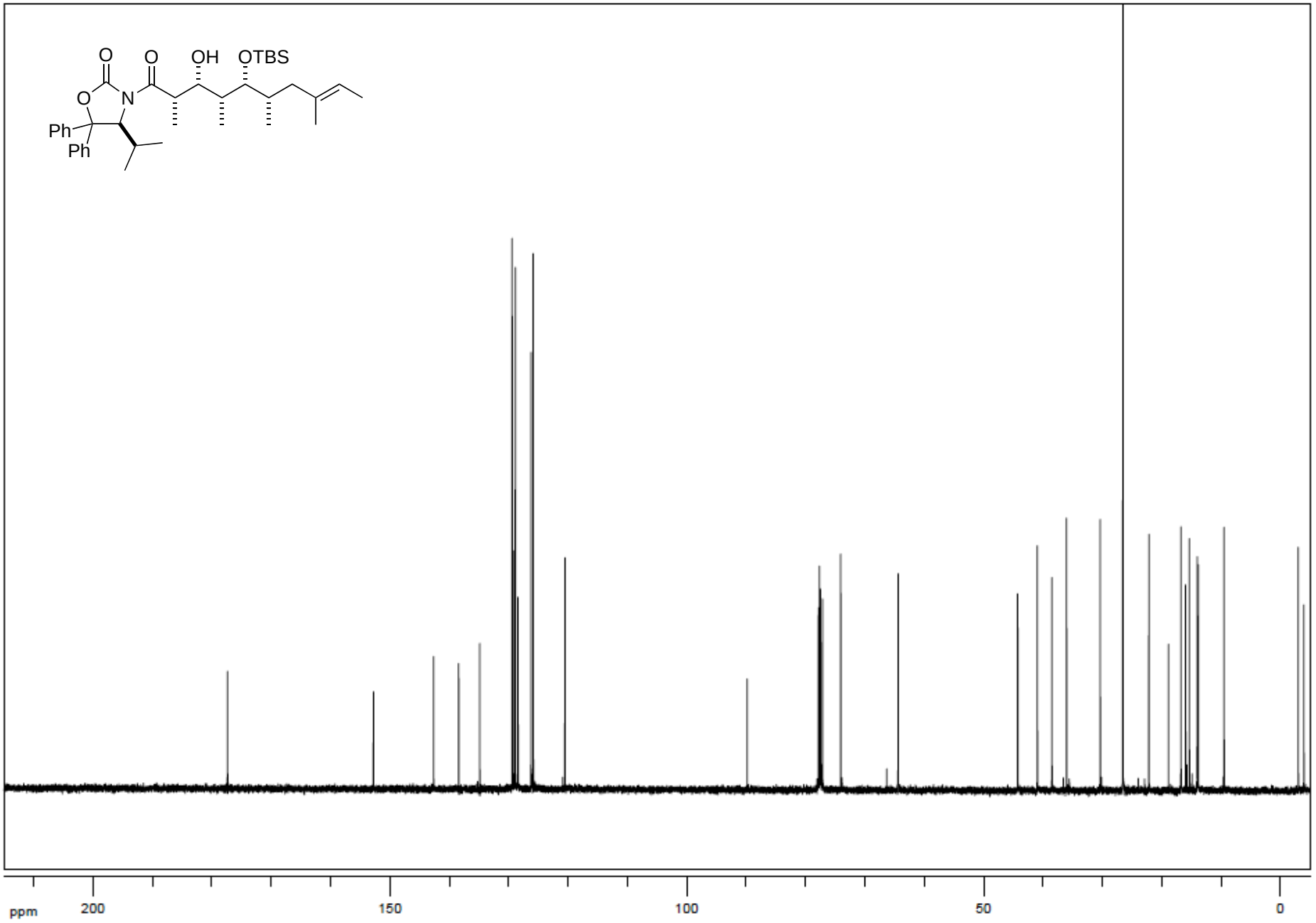

O
OTBS
MeO
N
ppm
200
150
100
50

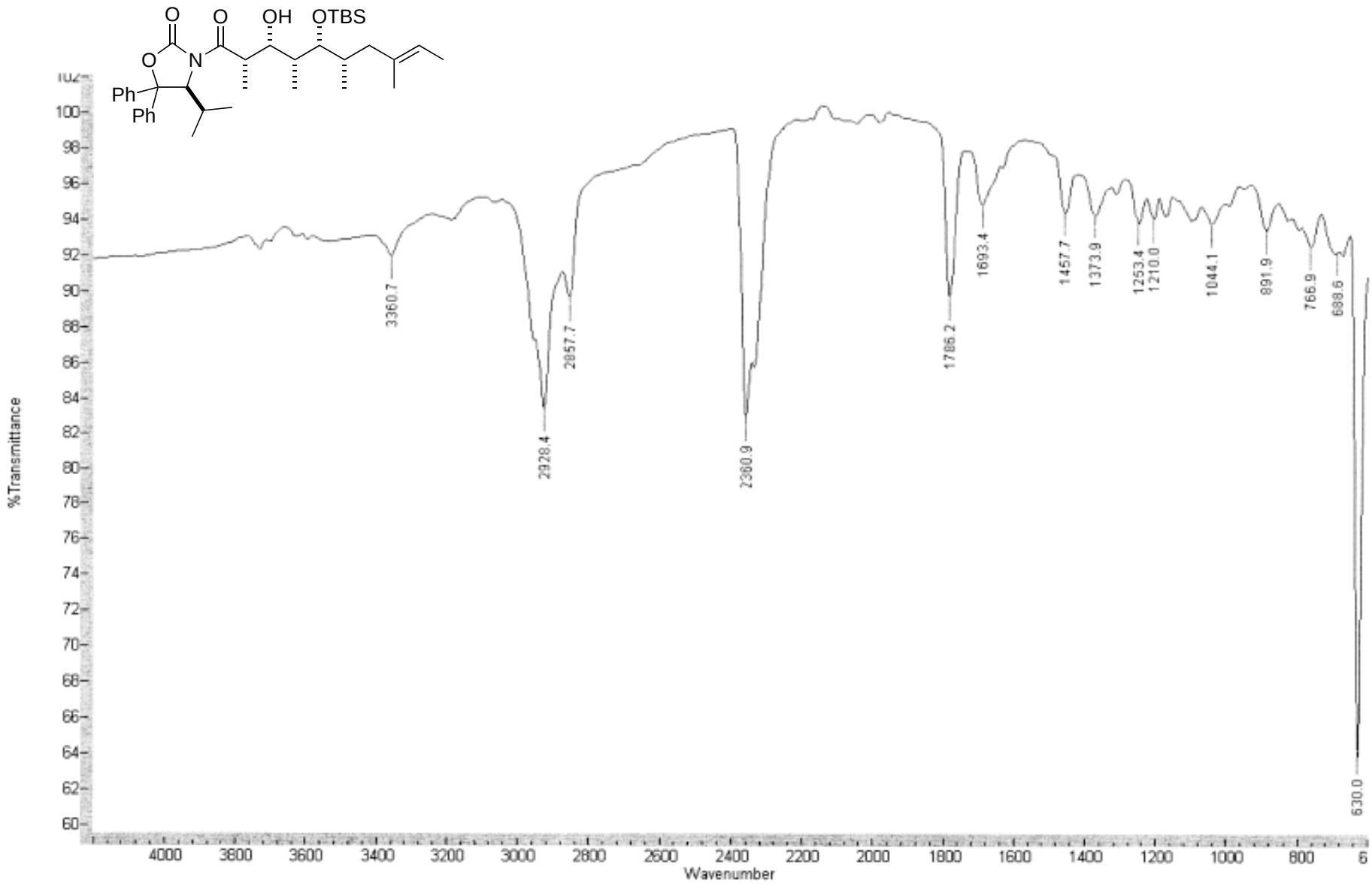

O
OTBS
MeO
N
98.00
90.0
80.0
70.0
67.00
4000.0
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600.0
cm-1
3369
2959
2931
2857
2842
1662
1461
1382
1252
1176
1108
1049
997
939
869
833
792
733
668

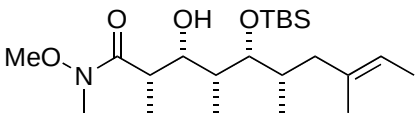

H
OTBS
O
ppm
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0


H
OTBS
O
ppm
200
150
100
50
0

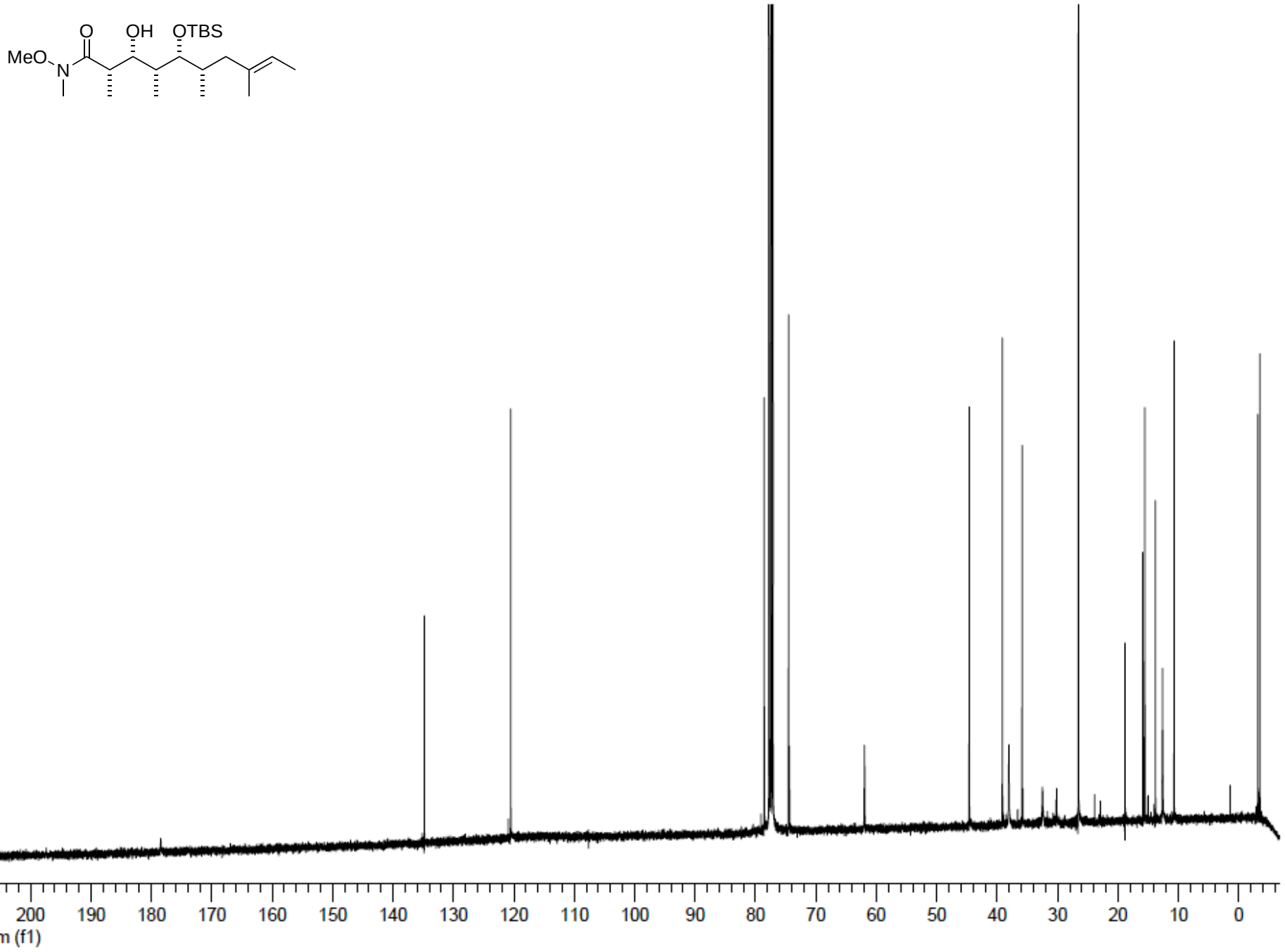

O
O
OH
OTBS
O
N
Ph
Ph
ppm
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

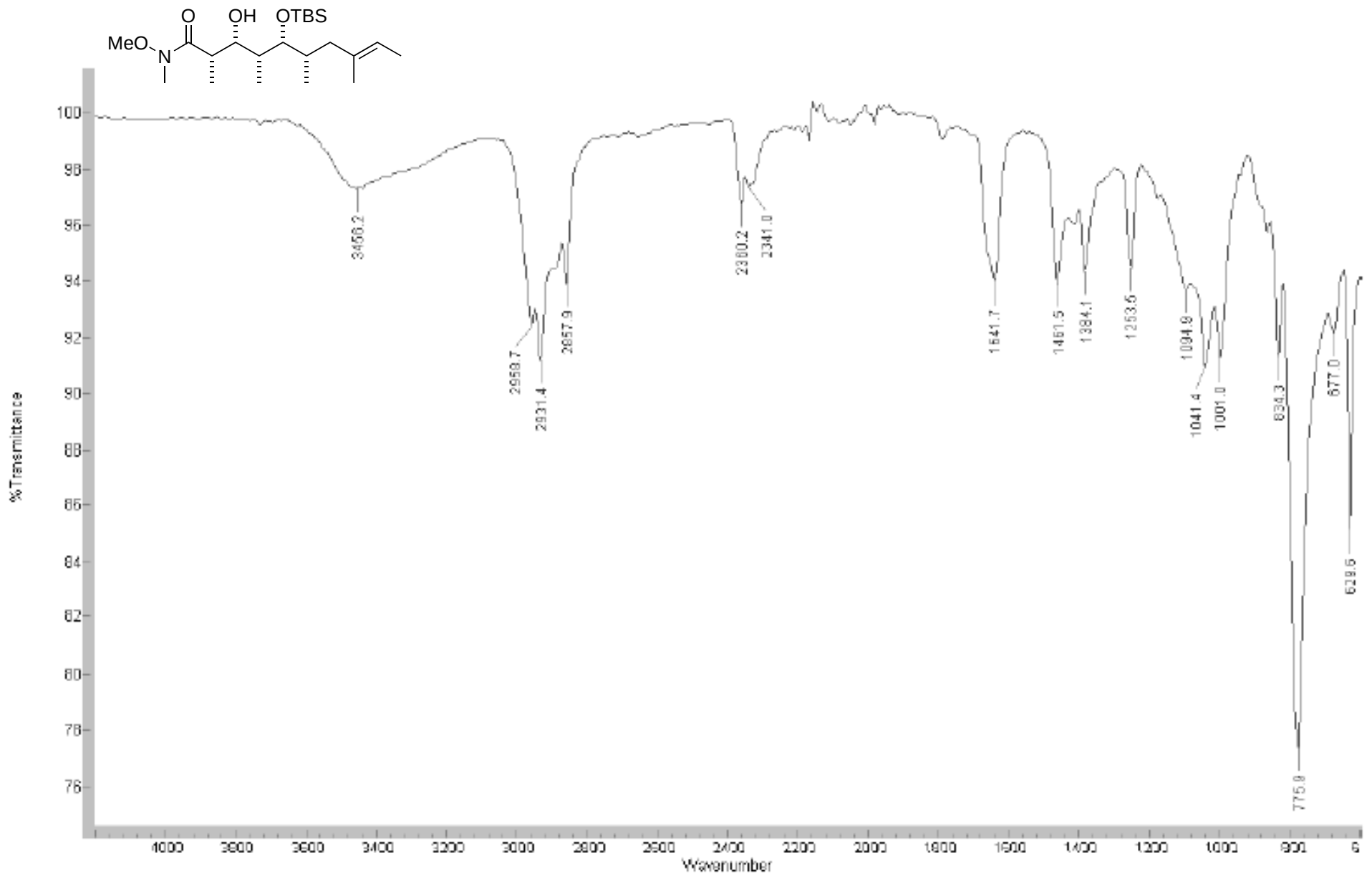

O
O
OH
OTBS
O
N
Ph
Ph
ppm
200
150
100
50
0

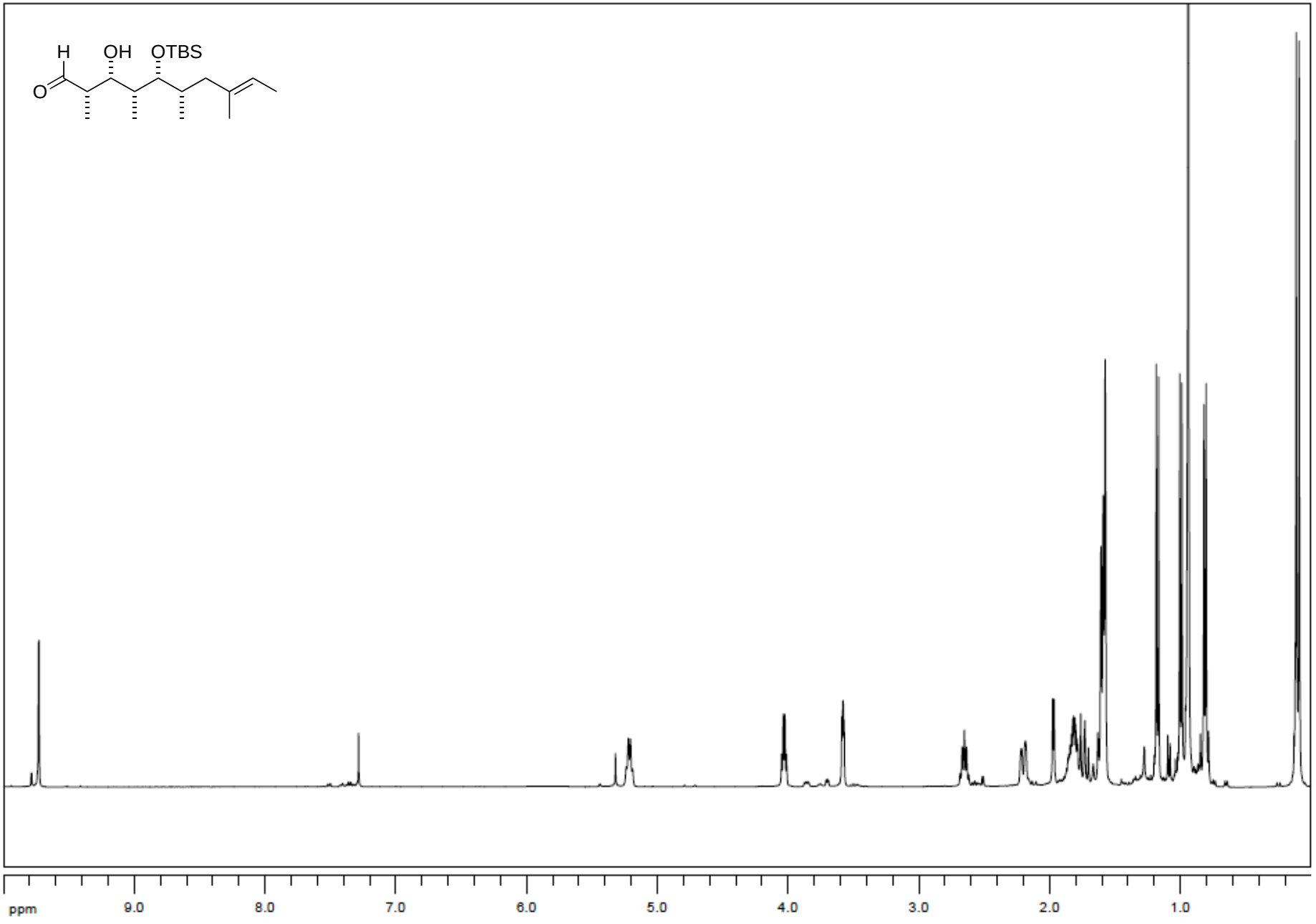

O
O
OH
OTBS
O
N
Ph
Ph
%Transmittance
100
98
96
94
92
90
88
86
84
82
80
78
76
74
72
70
68
66
64
62
60
3360.7
2928.4
2857.7
2360.9
1786.2
1693.4
1457.7
1373.9
1253.4
1210.0
1044.1
891.9
766.9
688.6
630.0
4000
3800
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
6
Wavenumber

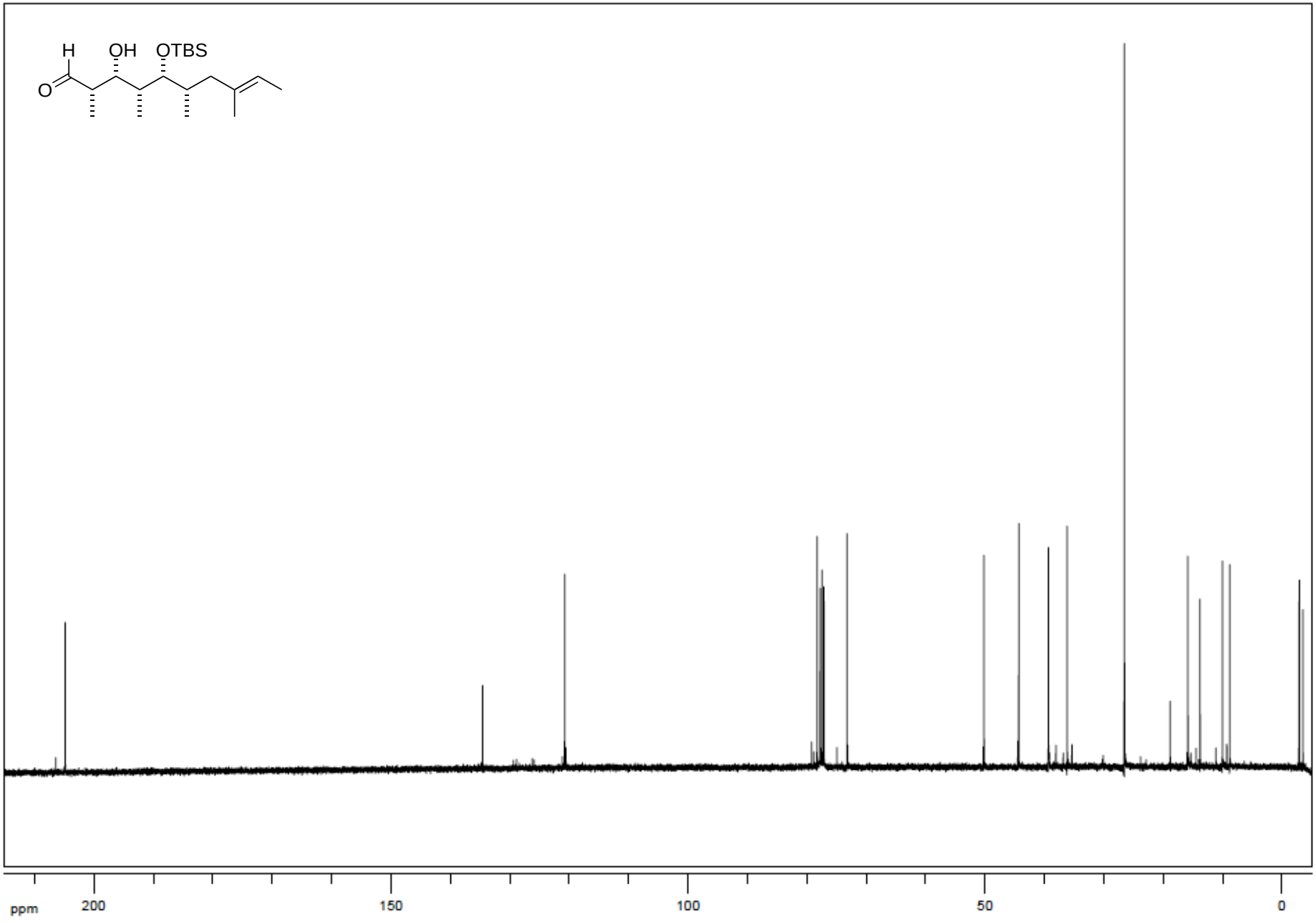

O
OH
OTBS
MeO
N

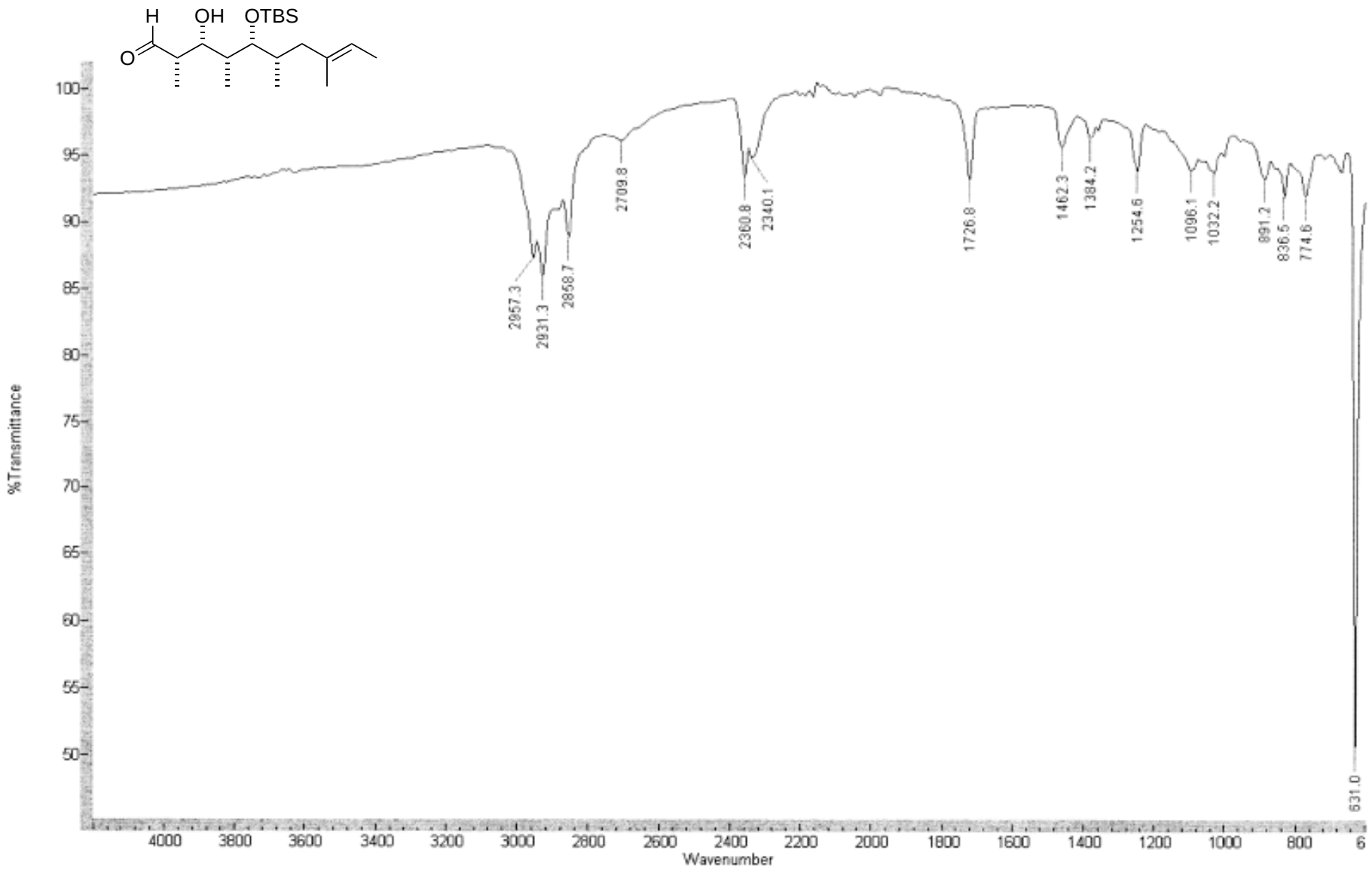

9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)

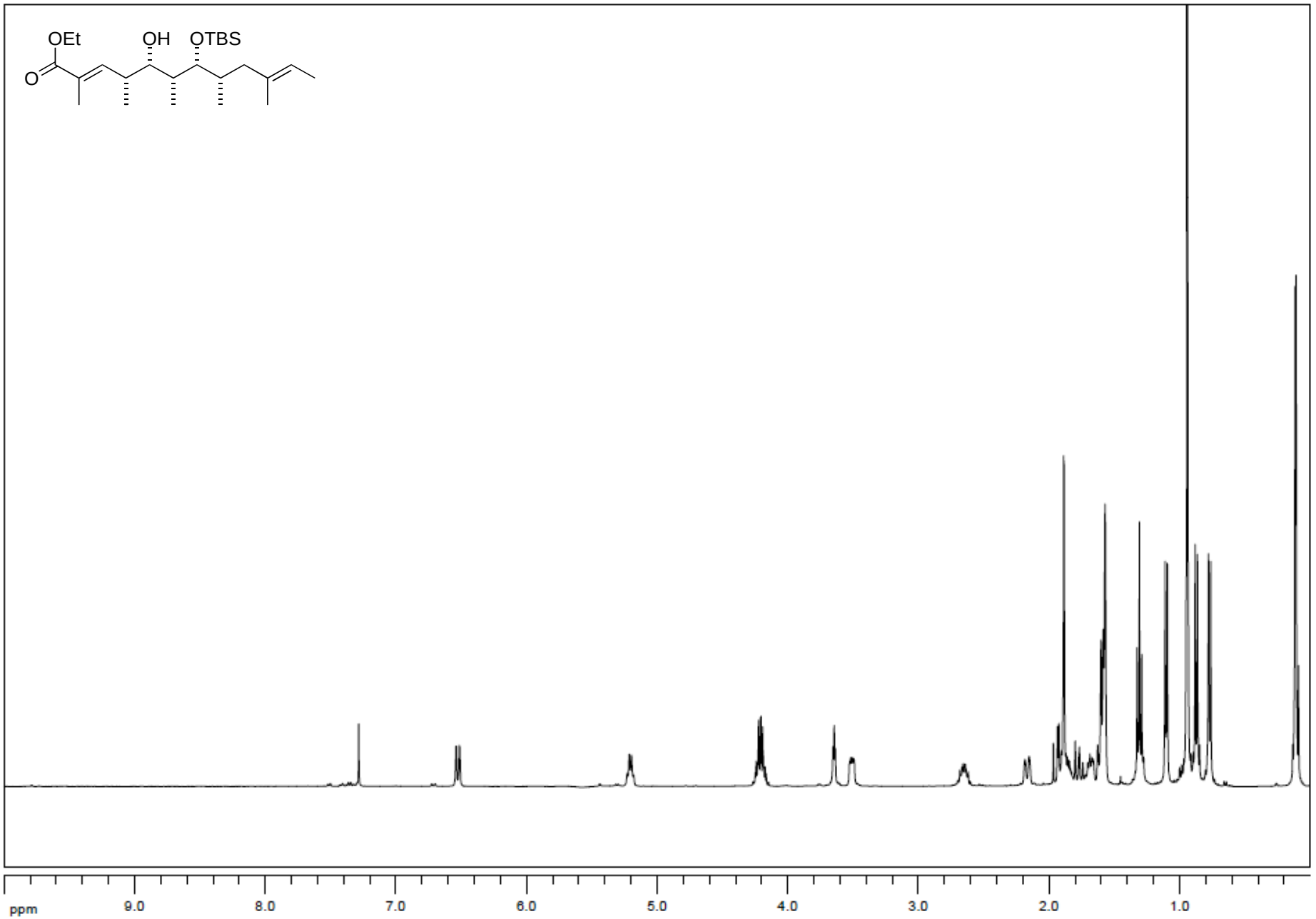

O
OH
OTBS
MeO
N
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm (f1)

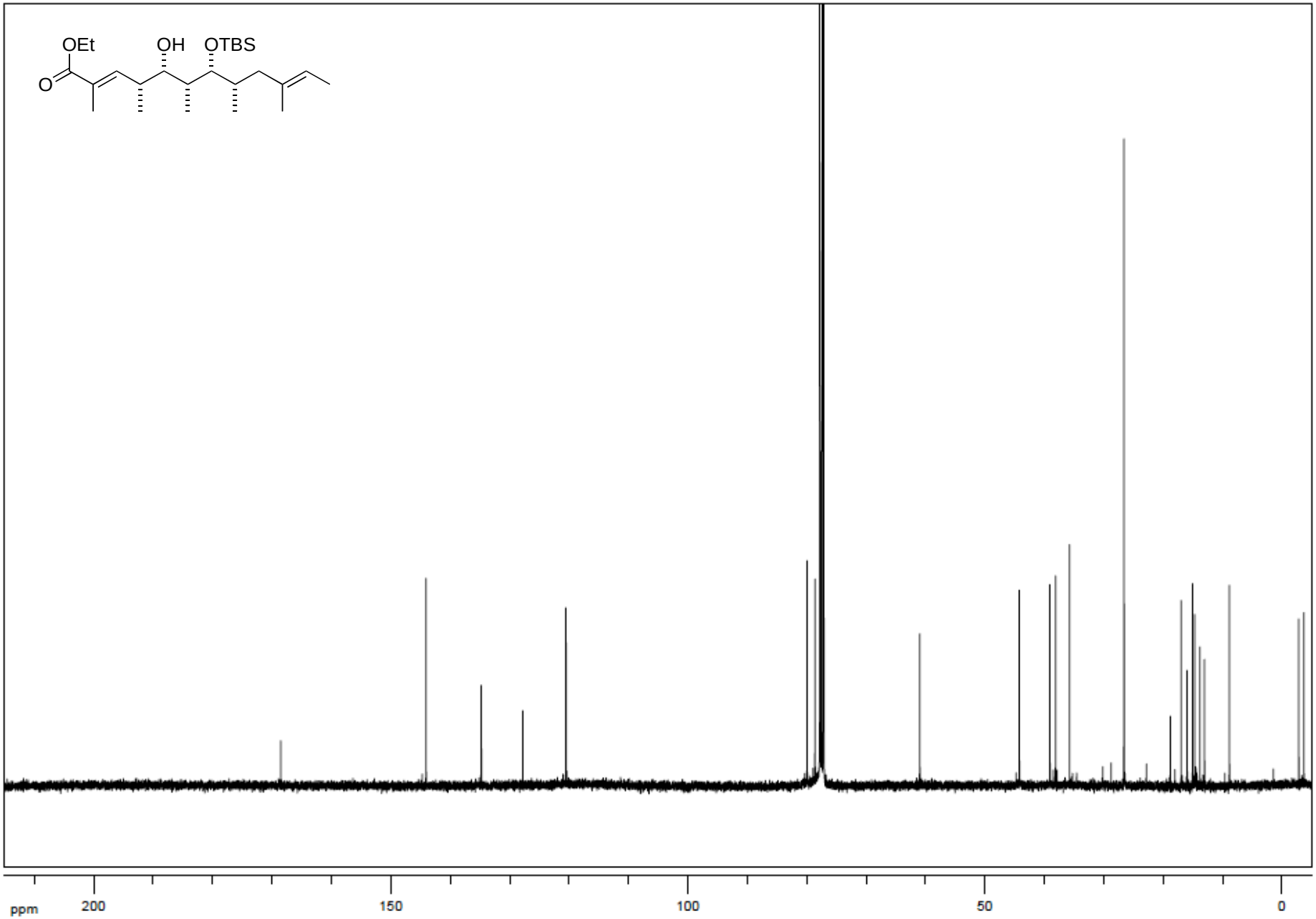

O
OH
OTBS
MeO
N
%Transmittance
Wavenumber
3456.2
2958.7
2931.4
2857.9
2360.2
2341.0
1641.7
1461.5
1384.1
1253.6
1094.8
1041.4
1001.0
834.3
775.8
677.0
629.6

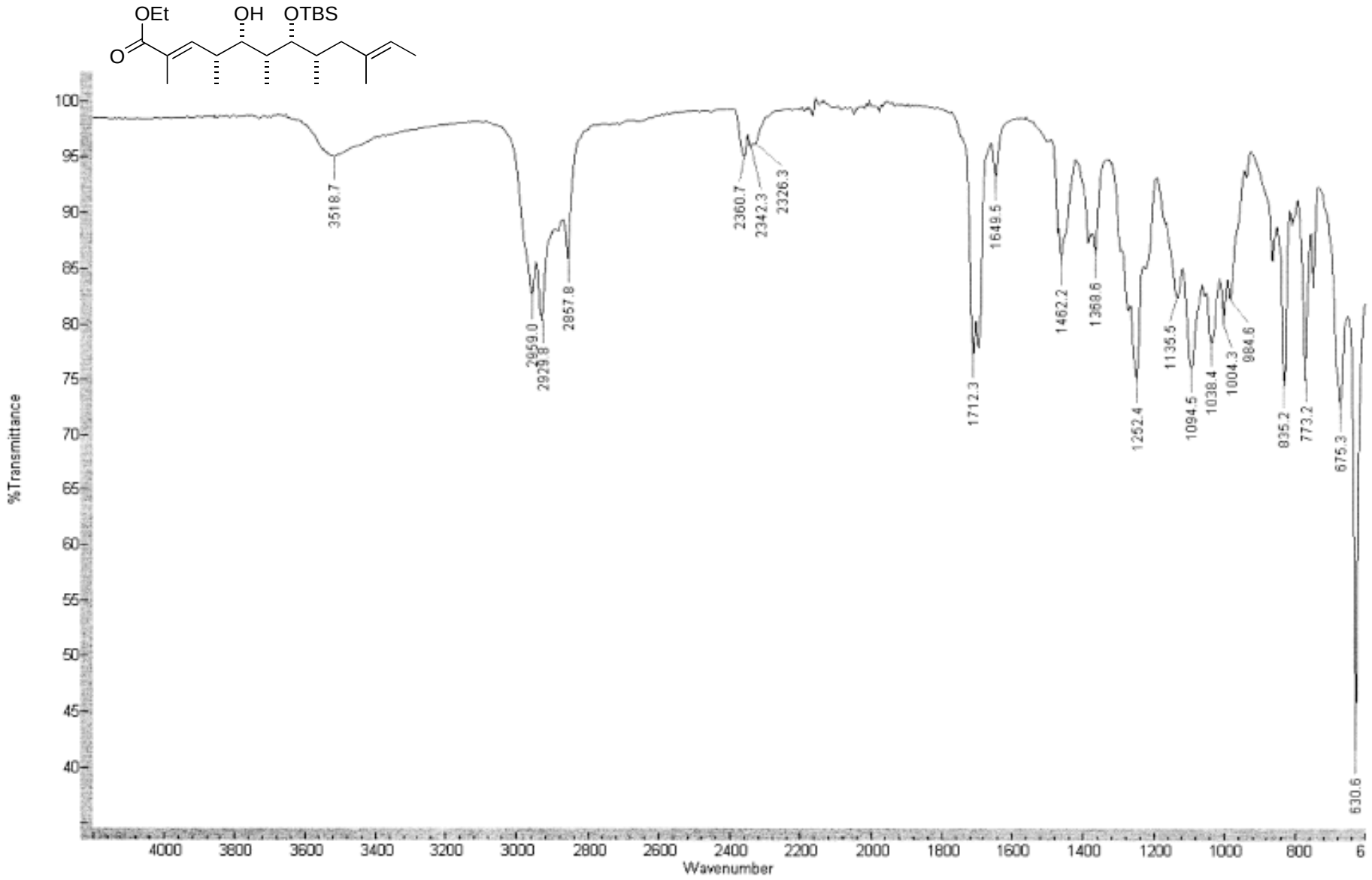

H
OH
OTBS
O
ppm
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0

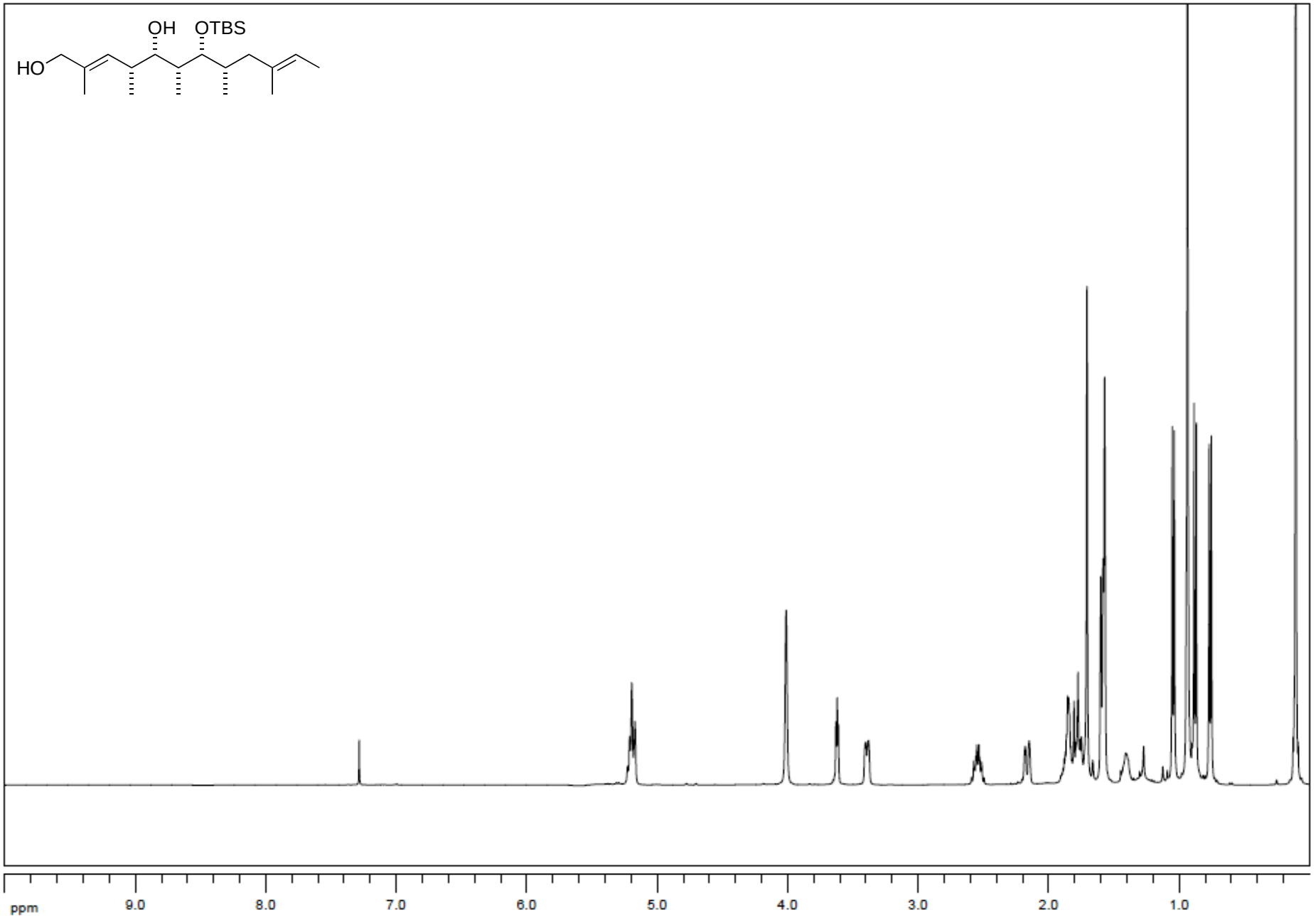

H
OH
OTBS
O
ppm
200
150
100
50
0

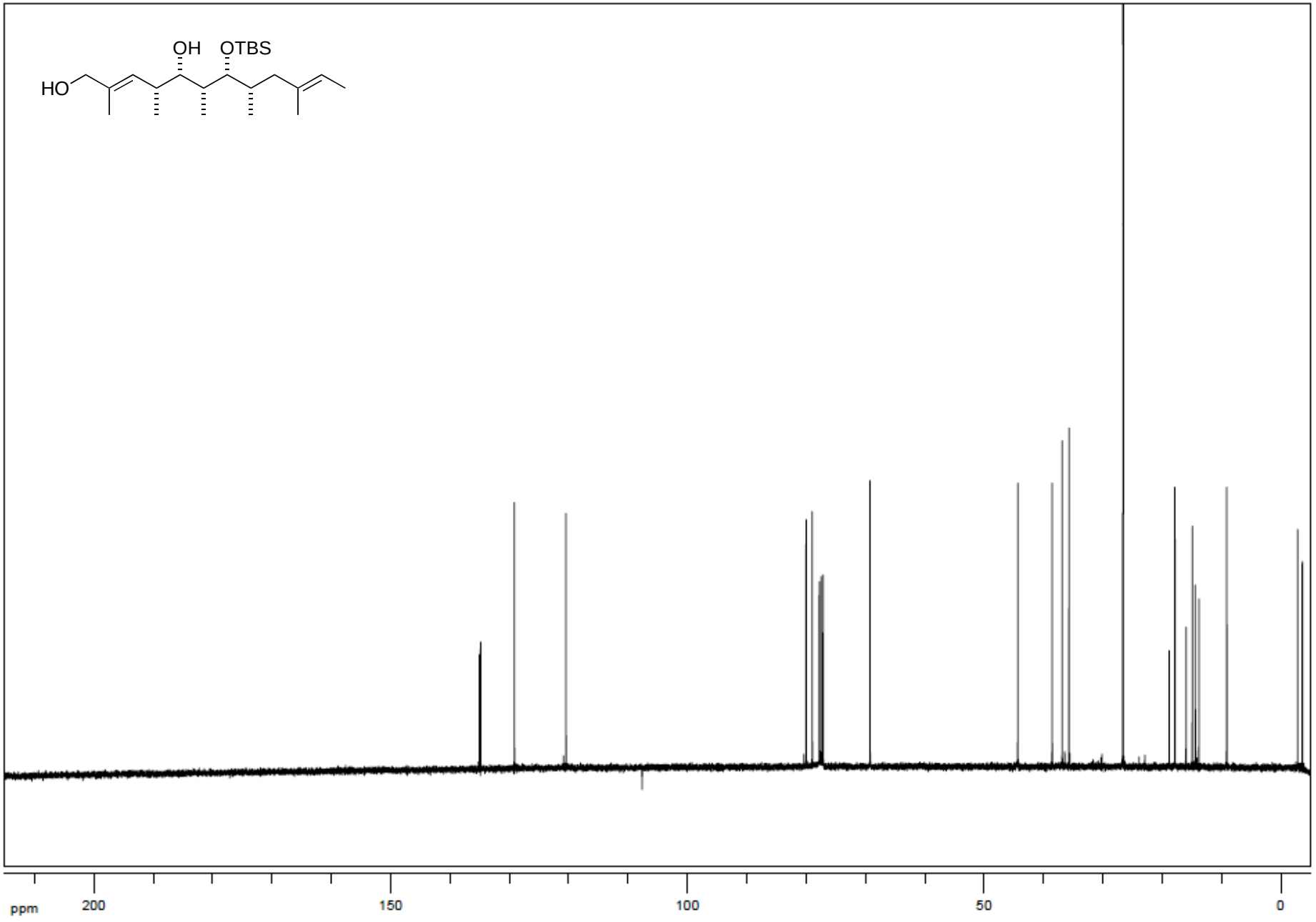

H
OH
OTBS
O
%Transmittance
100
95
90
85
80
75
70
65
60
55
50
2957.3
2931.3
2858.7
2709.8
2360.8
2340.1
1726.8
1462.3
1384.2
1254.6
1096.1
1032.2
891.2
836.5
774.6
631.0
4000
3800
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
6
Wavenumber

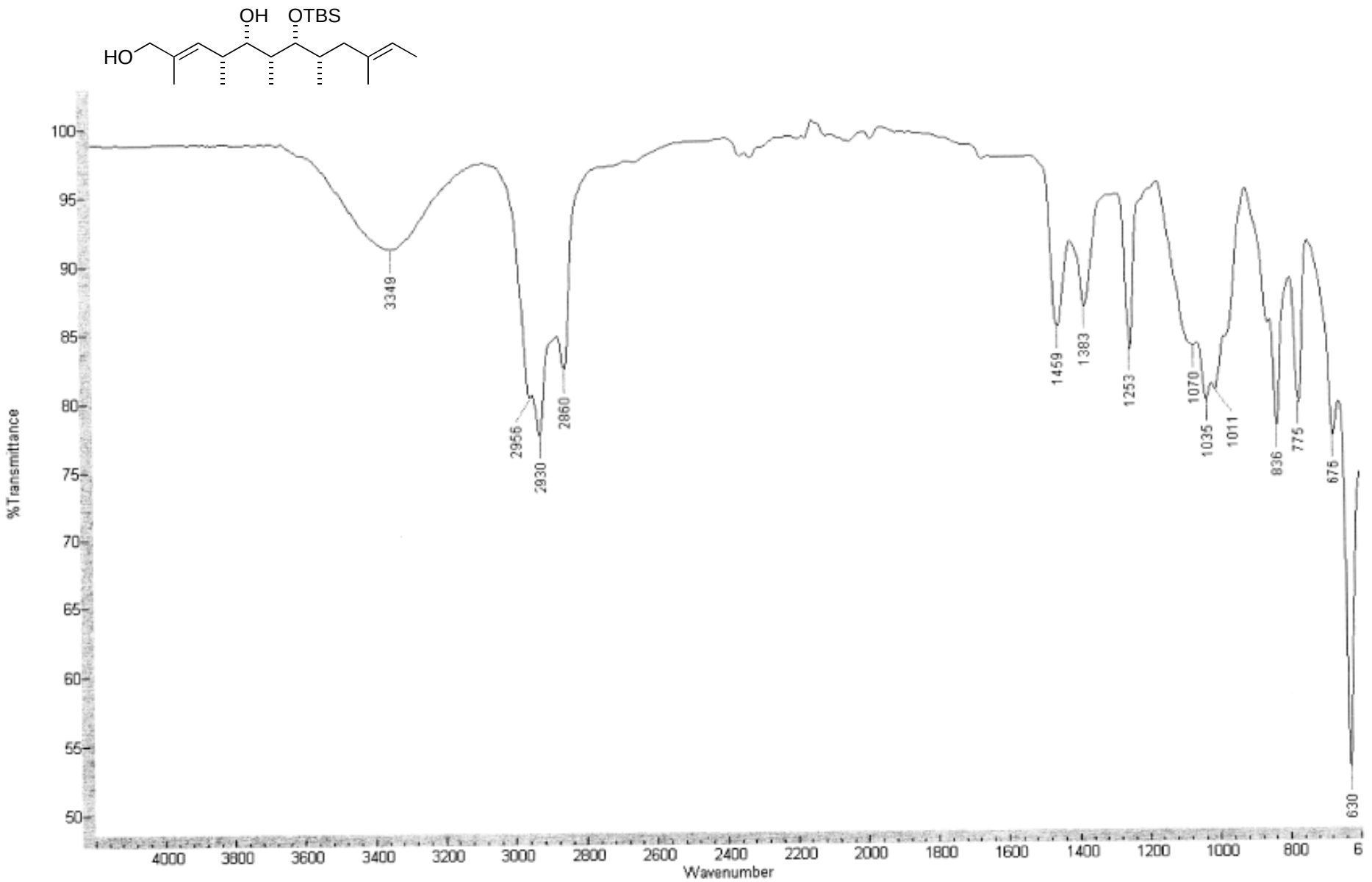

OEt
OH
OTBS
O
ppm
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0

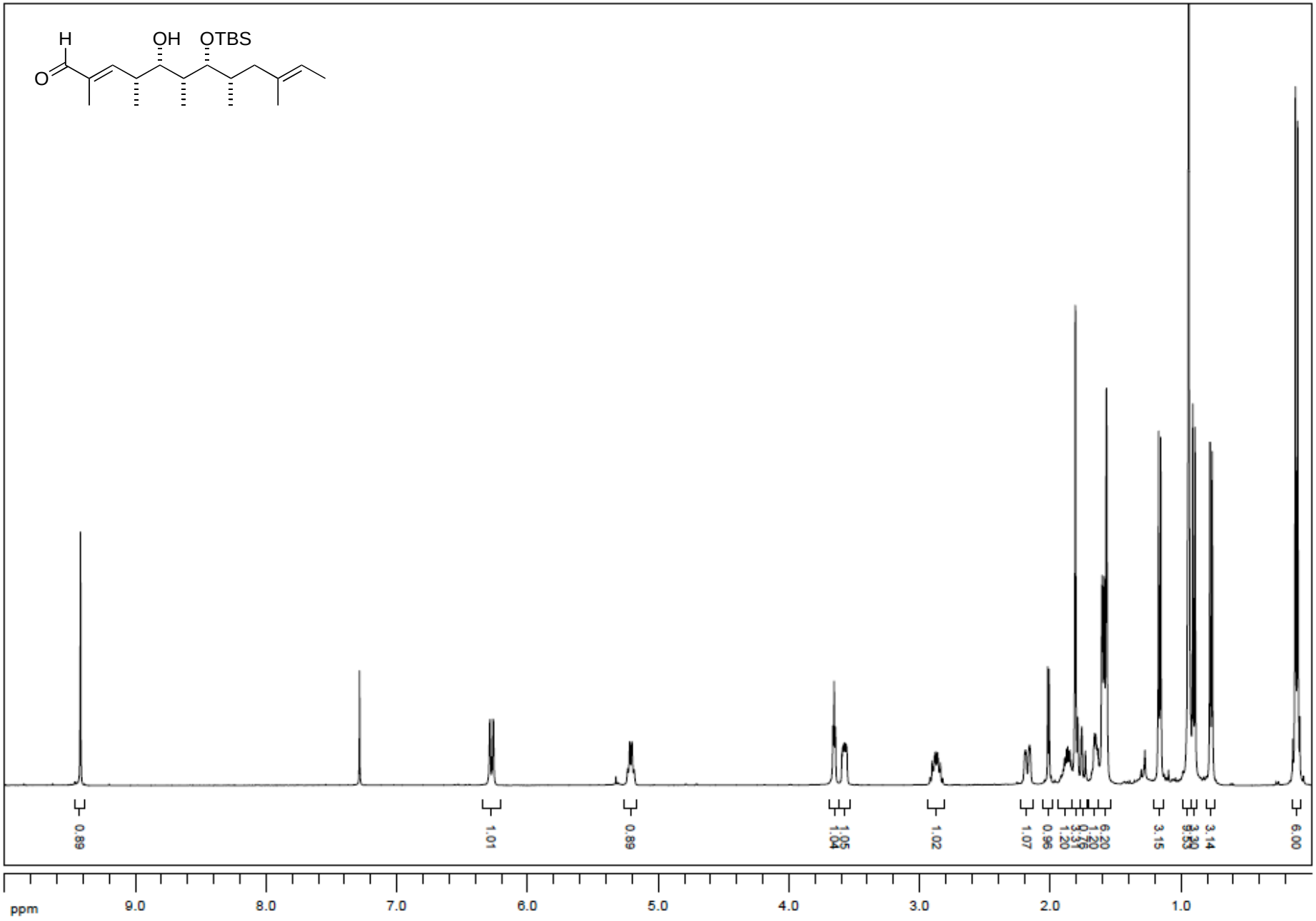

OEt
OH
OTBS
O
ppm
200
150
100
50
0

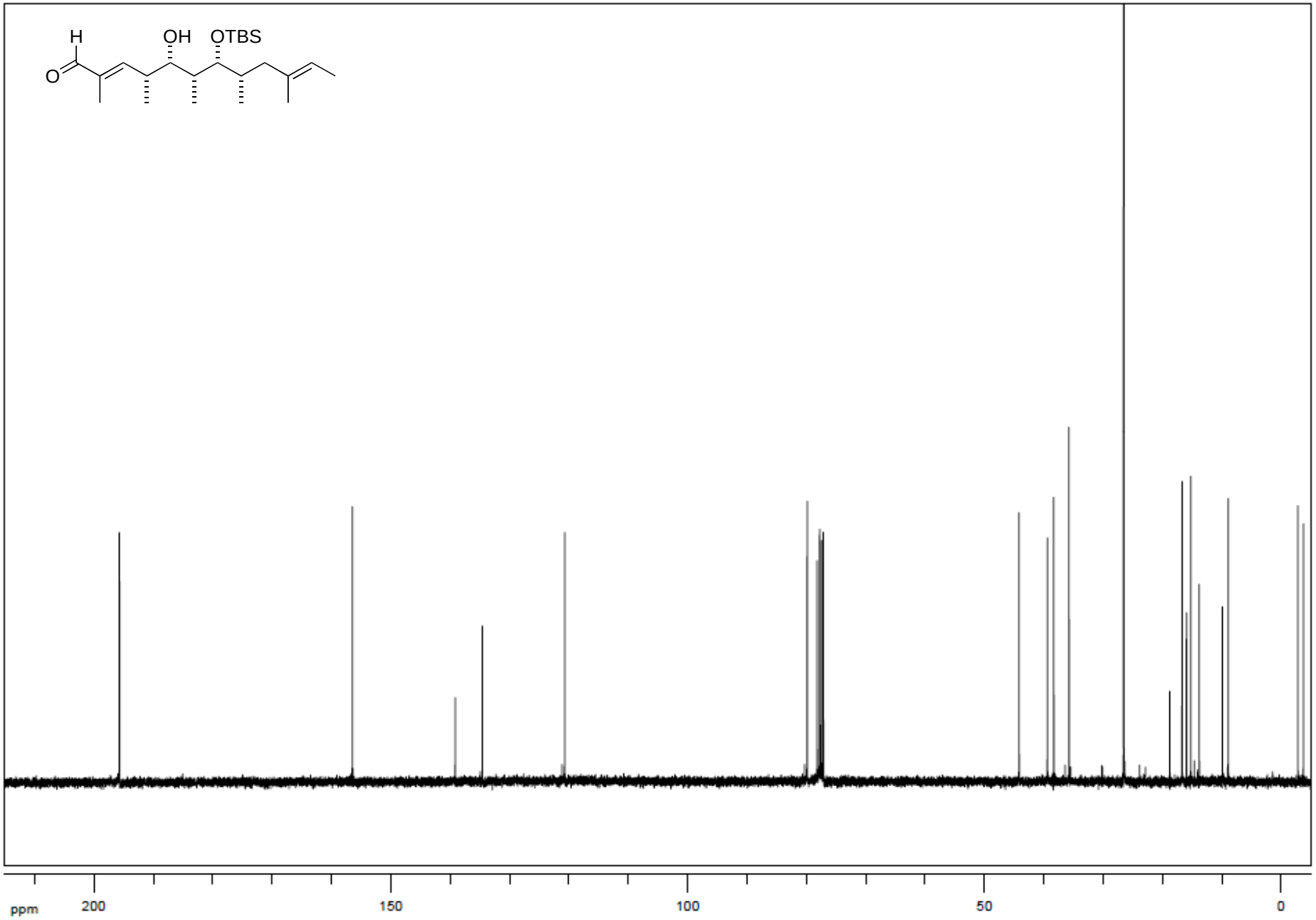

OEt
OH
OTBS
O
%Transmittance
Wavenumber
3518.7
2959.0
2929.8
2857.8
2360.7
2342.3
2326.3
1712.3
1649.5
1462.2
1368.6
1252.4
1135.5
1094.5
1038.4
1004.3
984.6
835.2
773.2
675.3
630.6

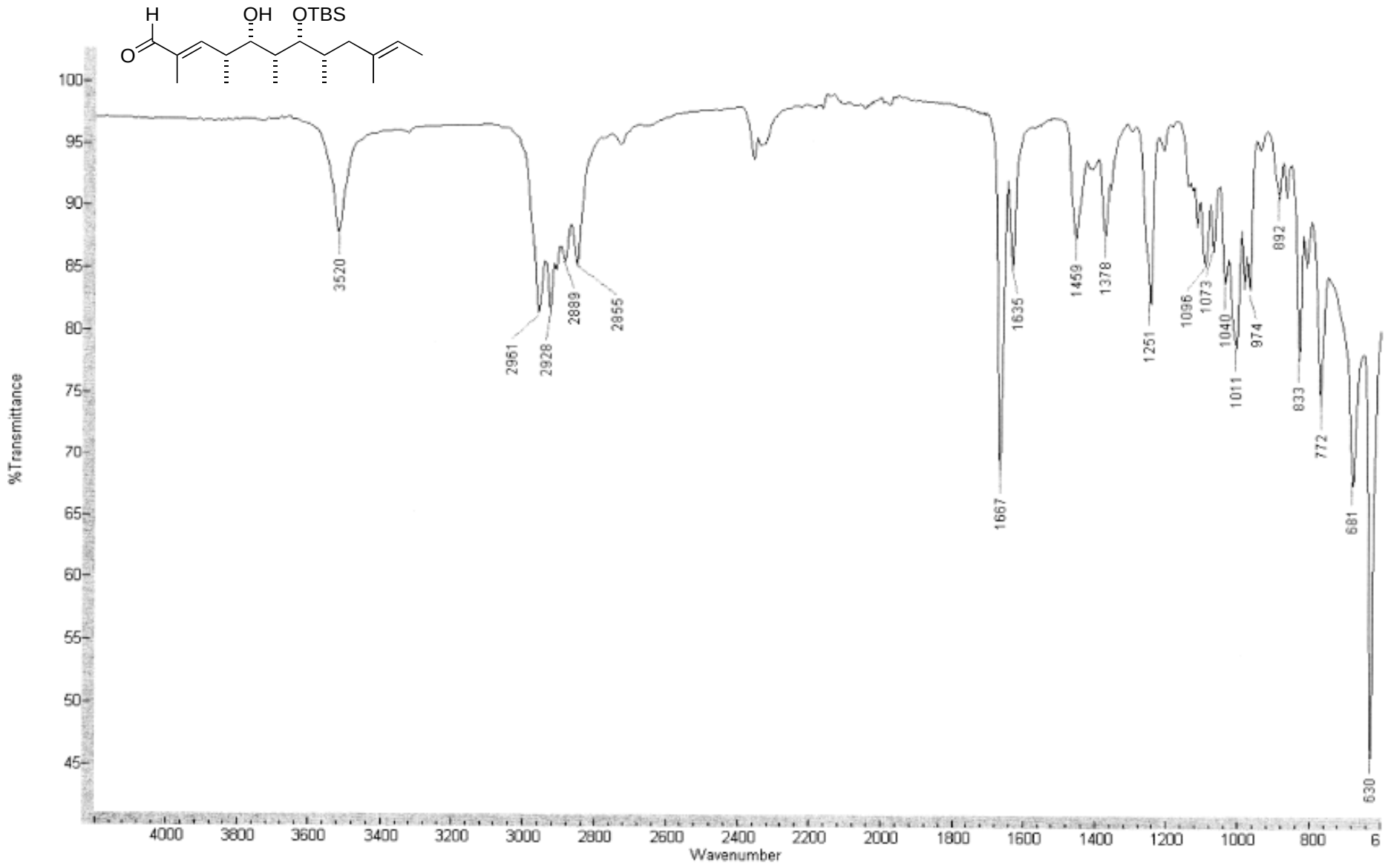

OH
OTBS
HO
ppm
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0

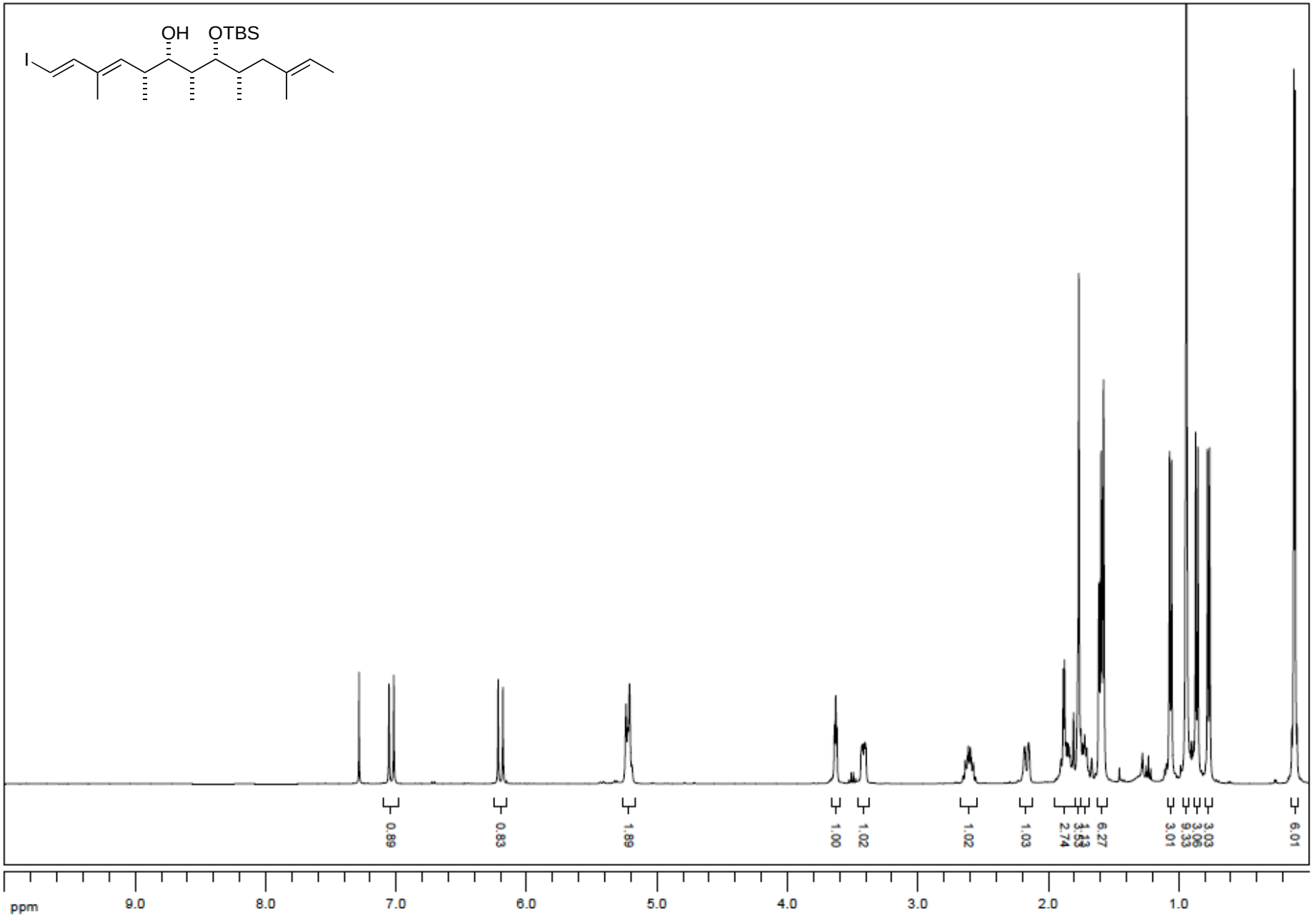

OH
OTBS
HO
ppm
200
150
100
50
0

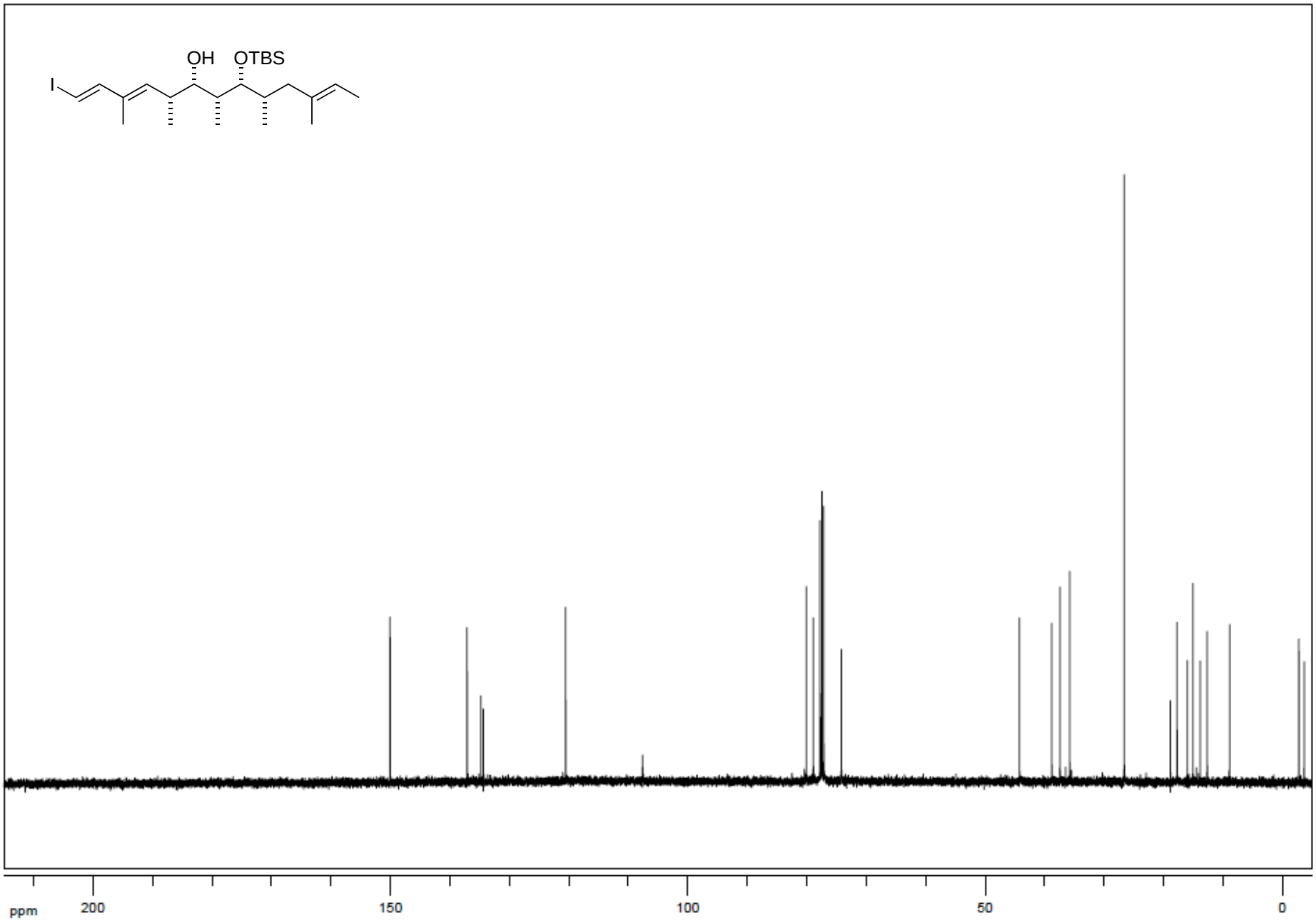

OH
OTBS
HO
%Transmittance
Wavenumber
3349
2956
2930
2860
1459
1383
1253
1070
1035
1011
836
775
676
630

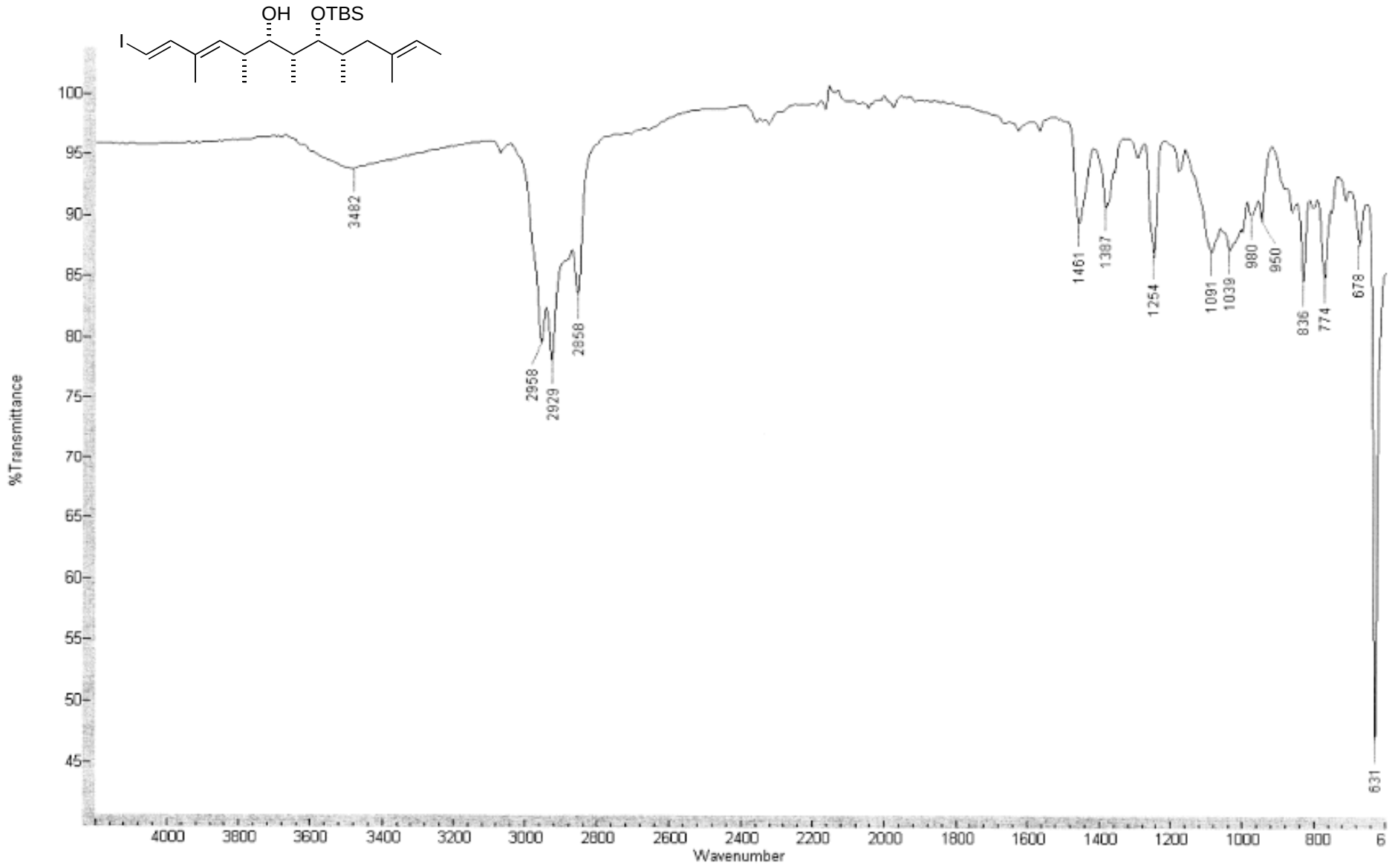

H
O
OH
OTBS
0.89
1.01
0.89
1.05
1.04
1.02
1.07
0.96
1.20
6.20
3.15
3.14
6.00
ppm
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0

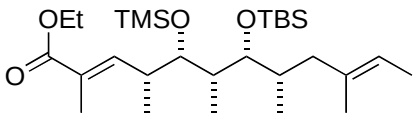

H
O
OH
OTBS
ppm
200
150
100
50
0


H
O
OH
OTBS
%Transmittance
100
95
90
85
80
75
70
65
60
55
50
45
3520
2961
2928
2889
2855
1667
1635
1459
1378
1251
1096
1073
1040
1011
974
892
833
772
681
630
4000
3800
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
6
Wavenumber

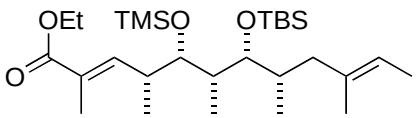

OH
OTBS
I
0.89
0.83
1.89
1.00
1.02
1.02
1.03
2.74
3.53
3.13
6.27
3.01
9.33
3.06
3.03
6.01
ppm
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0


OH
OTBS
I
ppm
200
150
100
50
0

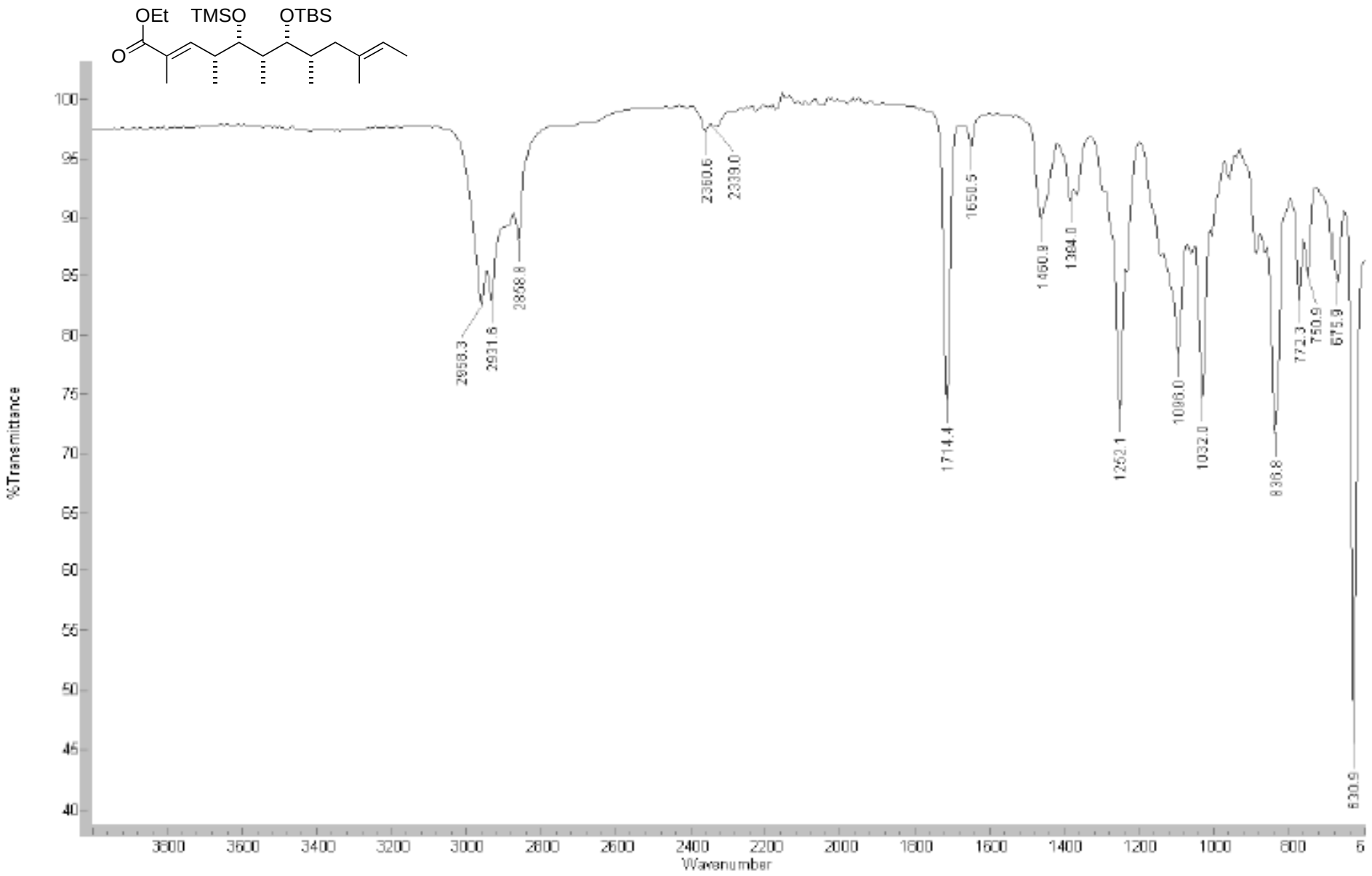

OH
OTBS
I
%Transmittance
Wavenumber
3482
2958
2929
2858
1461
1387
1254
1091
1039
980
950
836
774
678
631

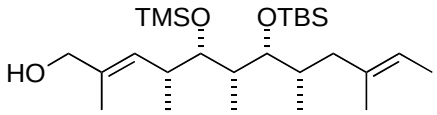

OEt
TMSO
OTBS
O


9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

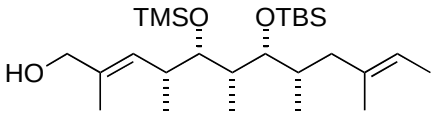

OEt
TMSO
OTBS
O


200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm (t1)

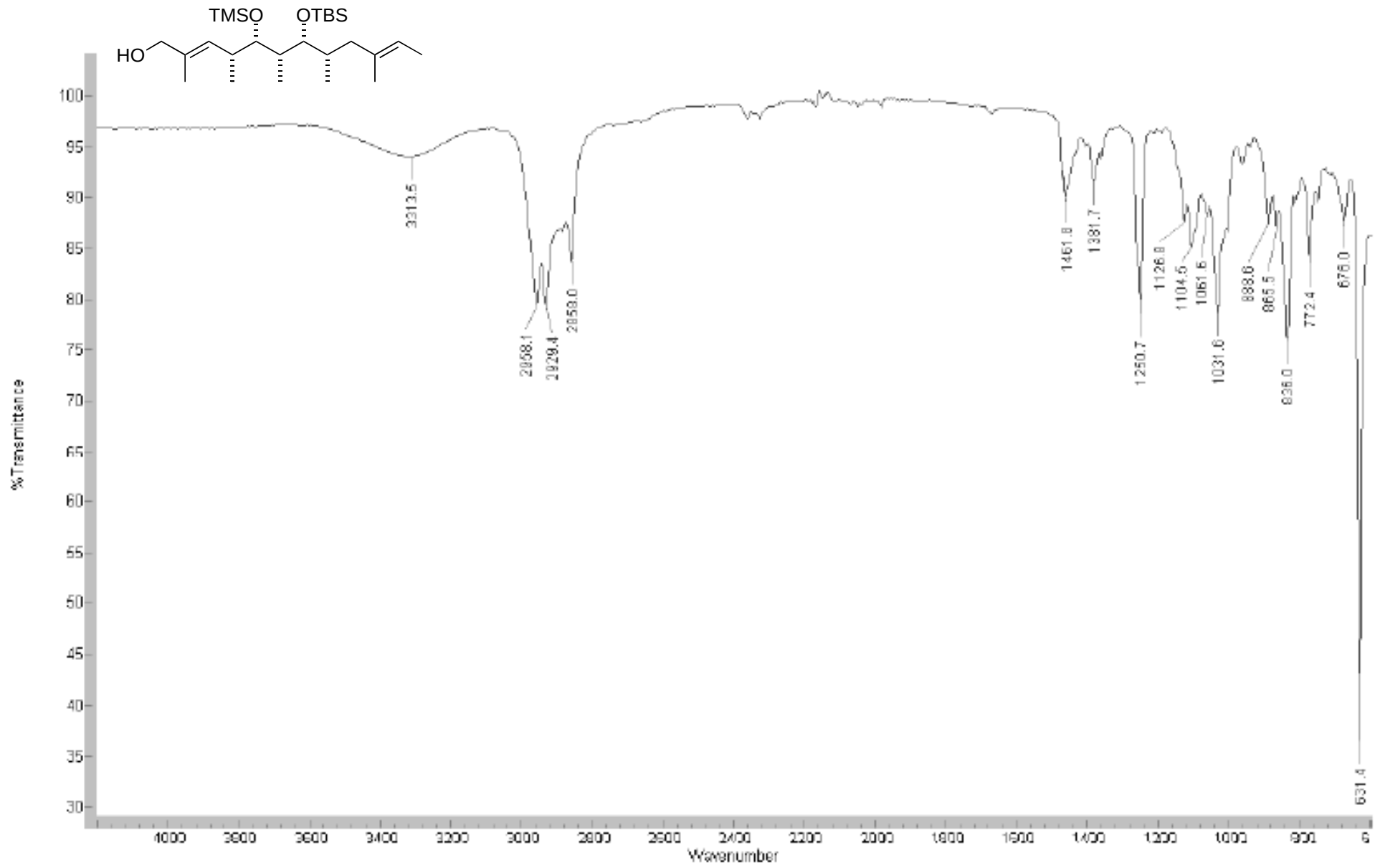

OEt
TMSO
OTBS
O
%Transmittance
Wavenumber
2958.3
2931.6
2858.8
2360.6
2339.0
1714.4
1650.5
1460.9
1384.0
1252.1
1098.0
1032.0
836.8
772.3
750.9
675.9
630.9

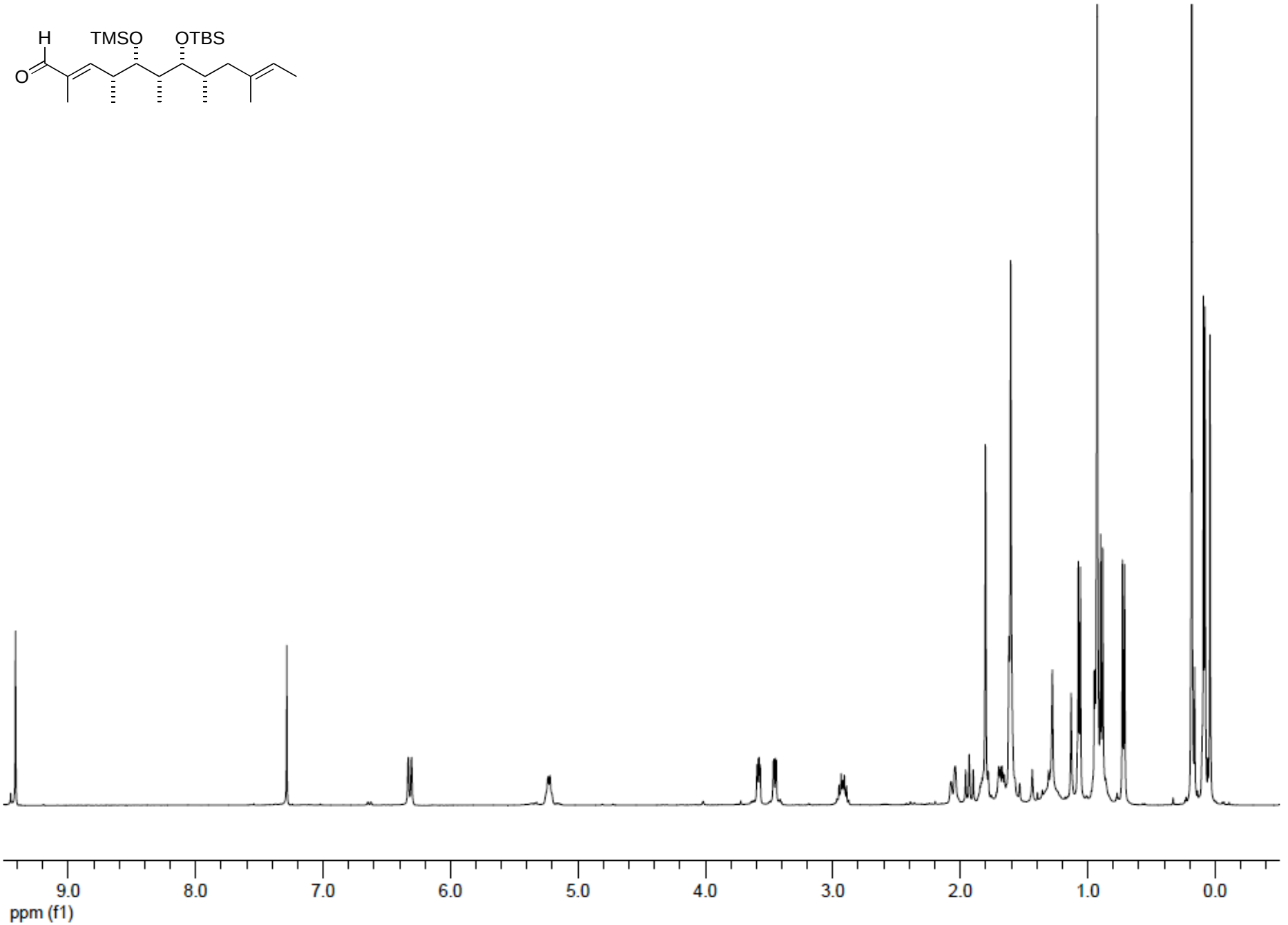

TMSO
OTBS
HO

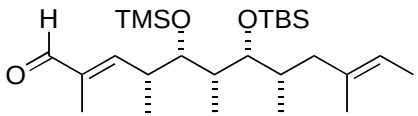

9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)


TMSO
OTBS
HO

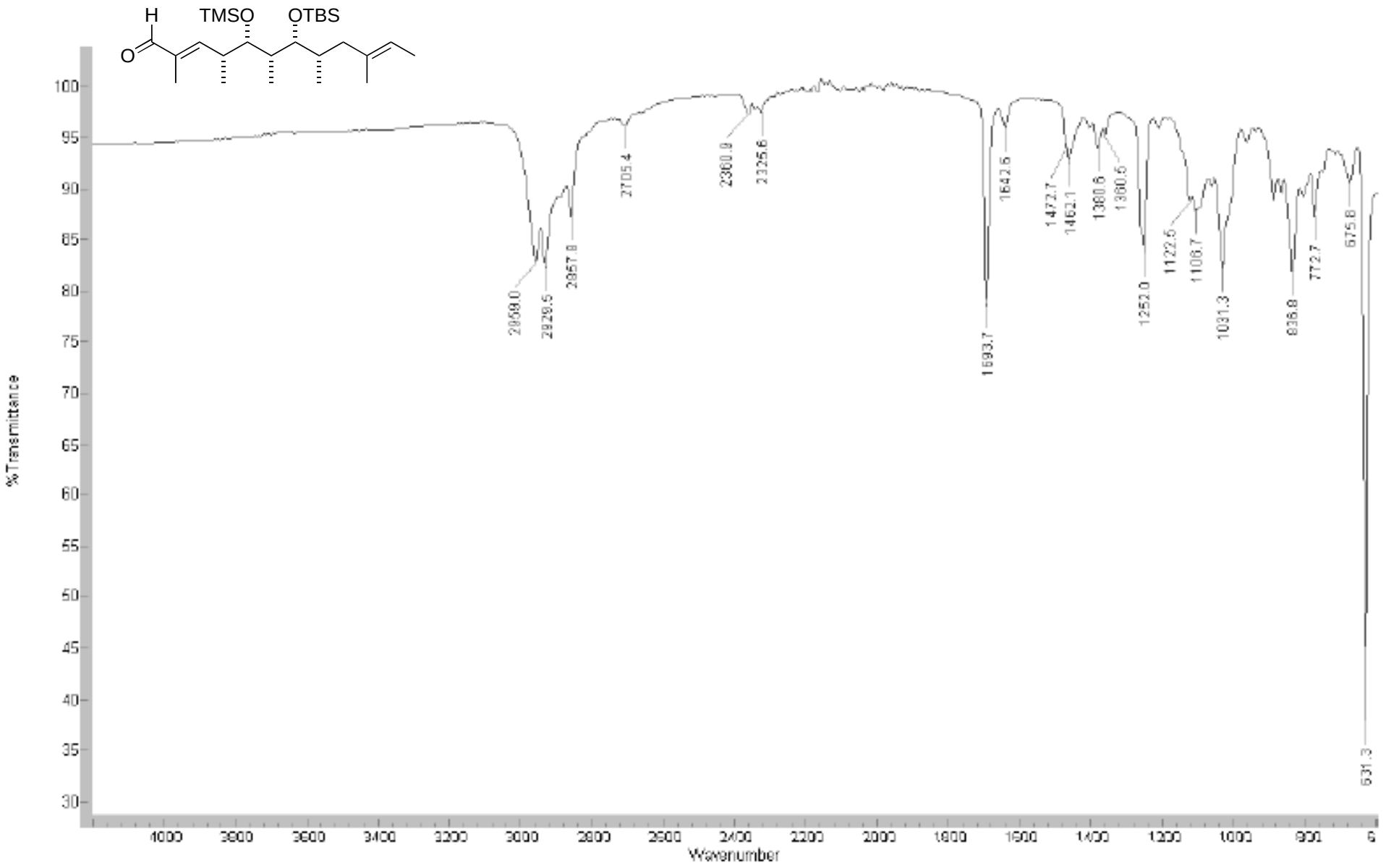

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm (f1)

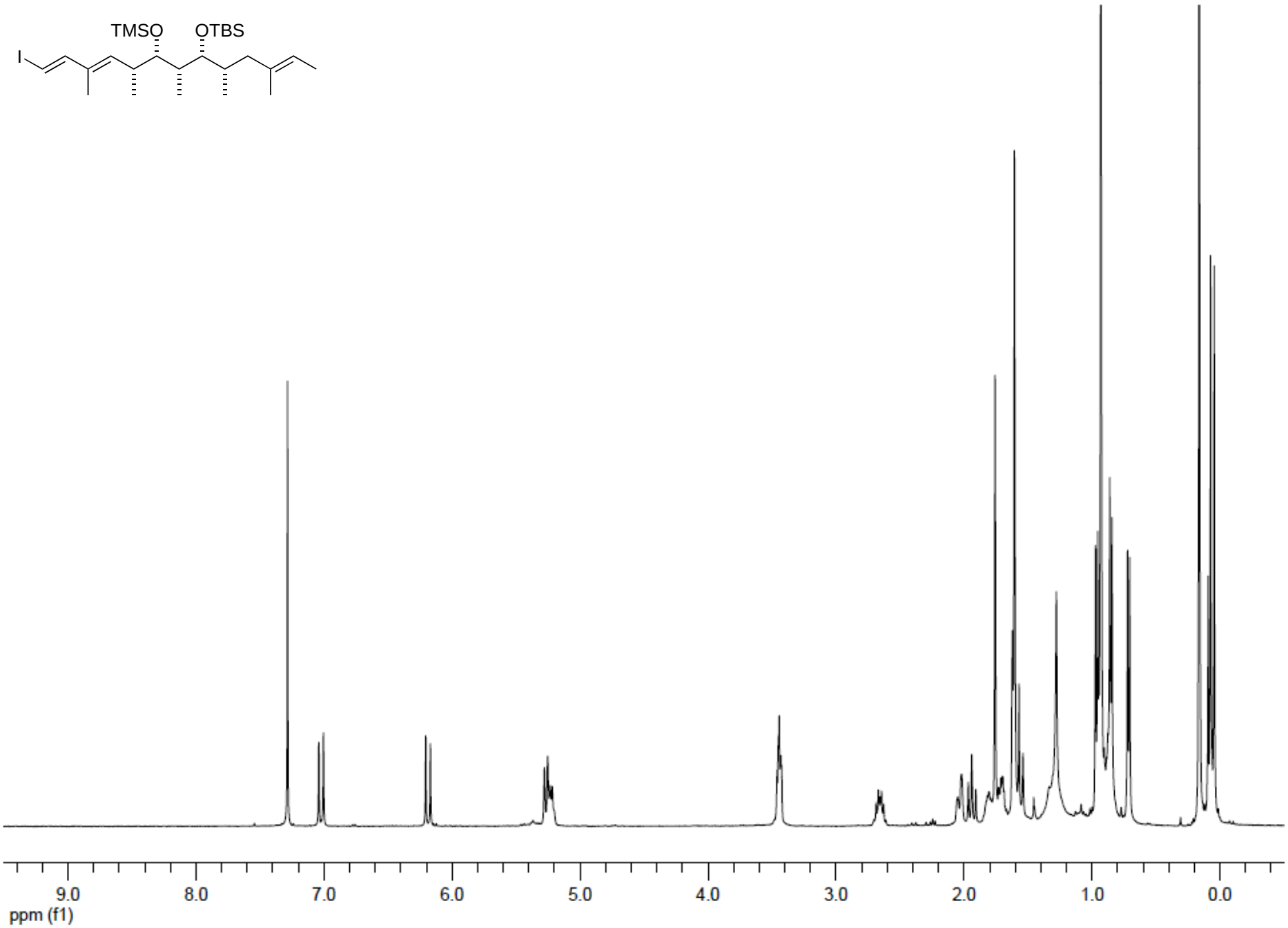

TMSO
OTBS
HO
%Transmittance
Wavenumber
3313.5
2958.1
2929.4
2859.0
1461.8
1381.7
1250.7
1126.8
1104.5
1061.6
1031.6
888.6
865.5
836.0
772.4
676.0
631.4

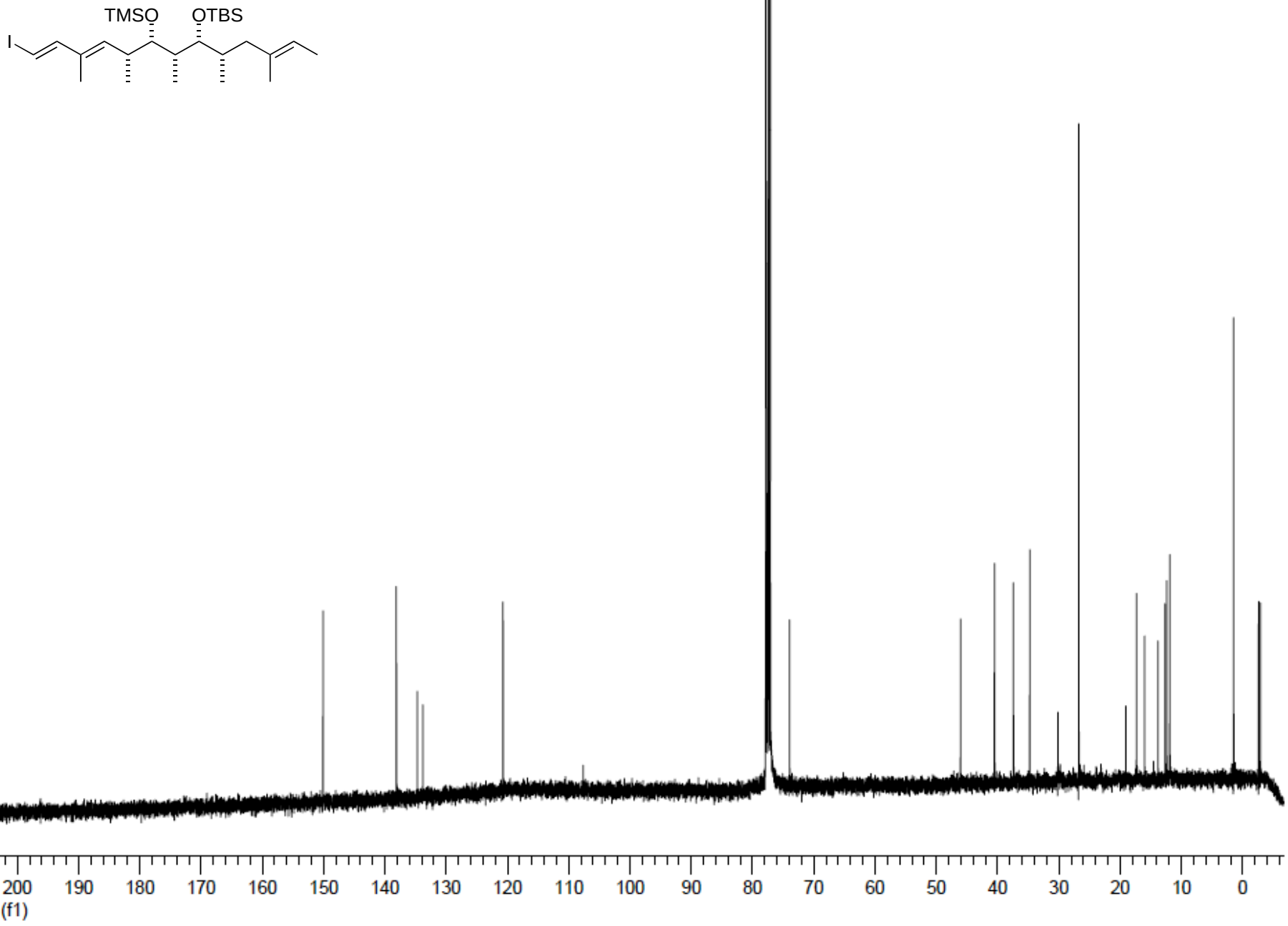

H
TMSO
OTBS
O
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)

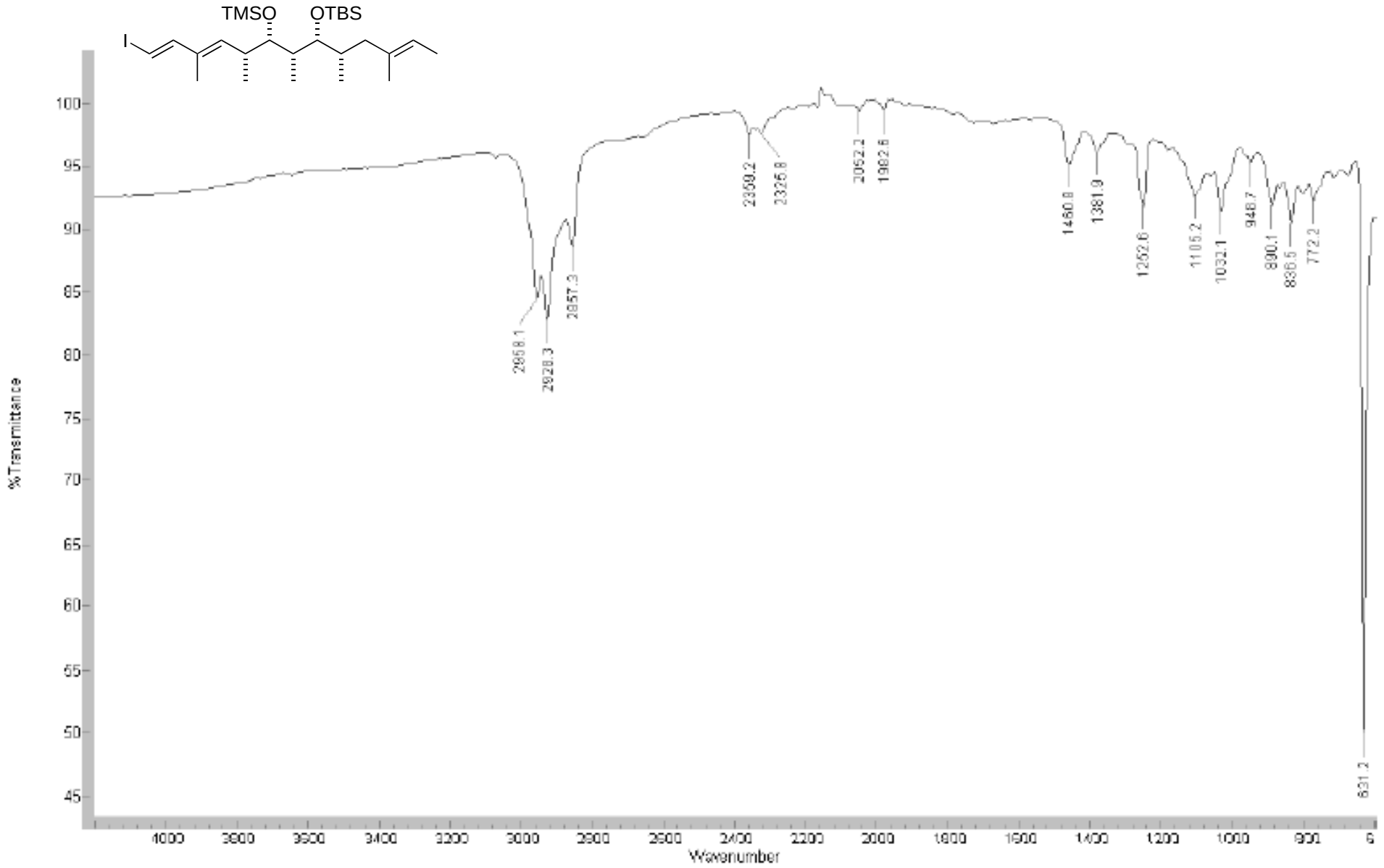

H
TMSO
OTBS
O

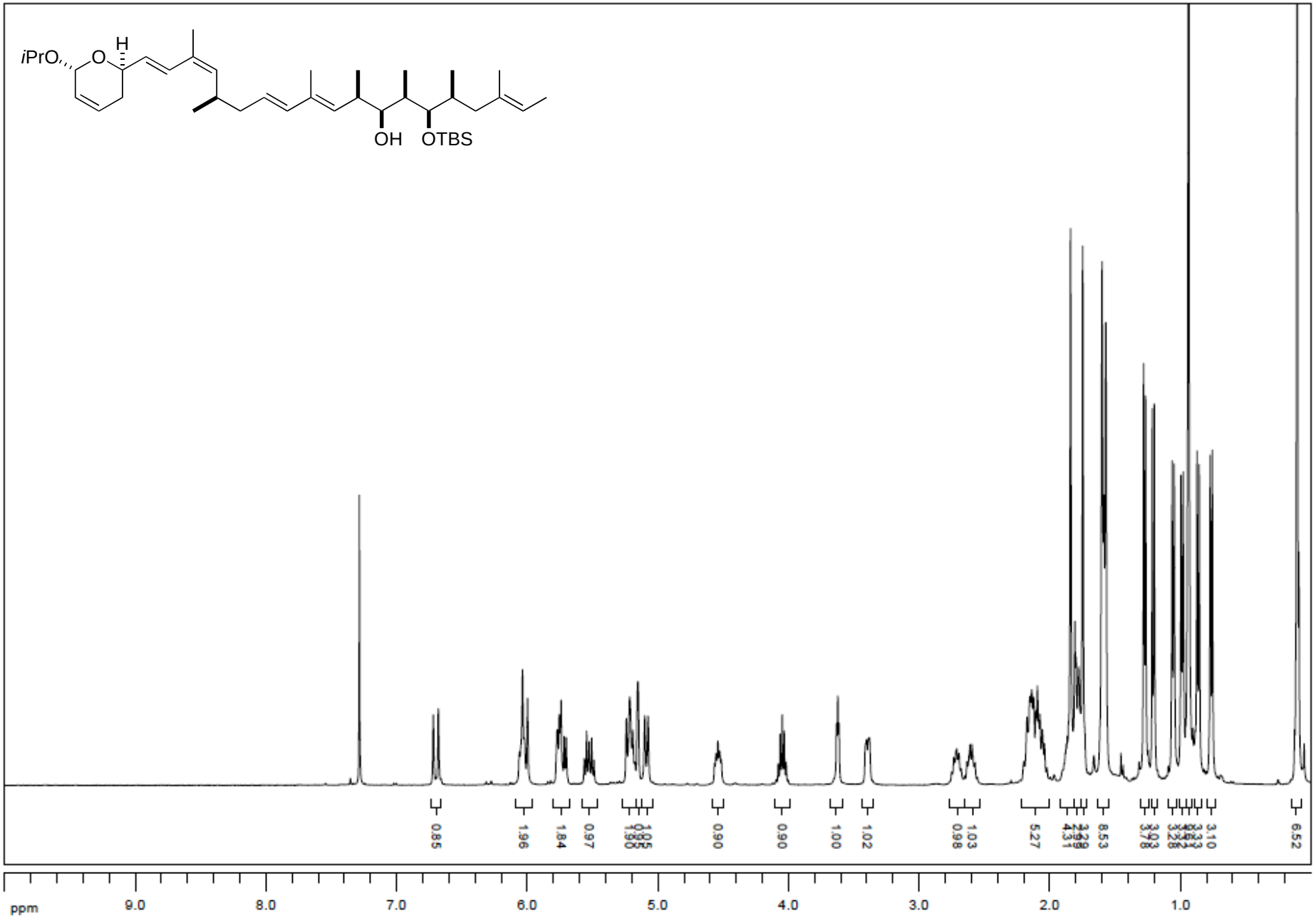

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm (f1)


H
TMSO
OTBS
O
%Transmittance
Wavenumber
2859.0
2929.5
2957.8
2705.4
2360.9
2335.6
1693.7
1642.6
1472.7
1462.1
1380.6
1360.6
1252.0
1122.5
1106.7
1031.3
836.8
772.7
675.8
631.3


TMSO
OTBS
I
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)


TMSO
OTBS
I
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm (f1)


TMSO
OTBS
I
100
95
90
85
80
75
70
65
60
55
50
45
%Transmittance
2958.1
2928.3
2857.3
2359.2
2325.8
2052.2
1982.6
1460.8
1381.9
1252.6
1105.2
1032.1
948.7
890.1
836.5
772.2
631.2
4000
3800
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
Wavenumber


iPrO
O
H
OH
OTBS
0.85
1.96
1.84
0.97
1.90
0.90
0.90
1.00
1.02
0.98
1.03
5.27
4.31
8.53
3.78
3.10
6.52
ppm
9.0
8.0
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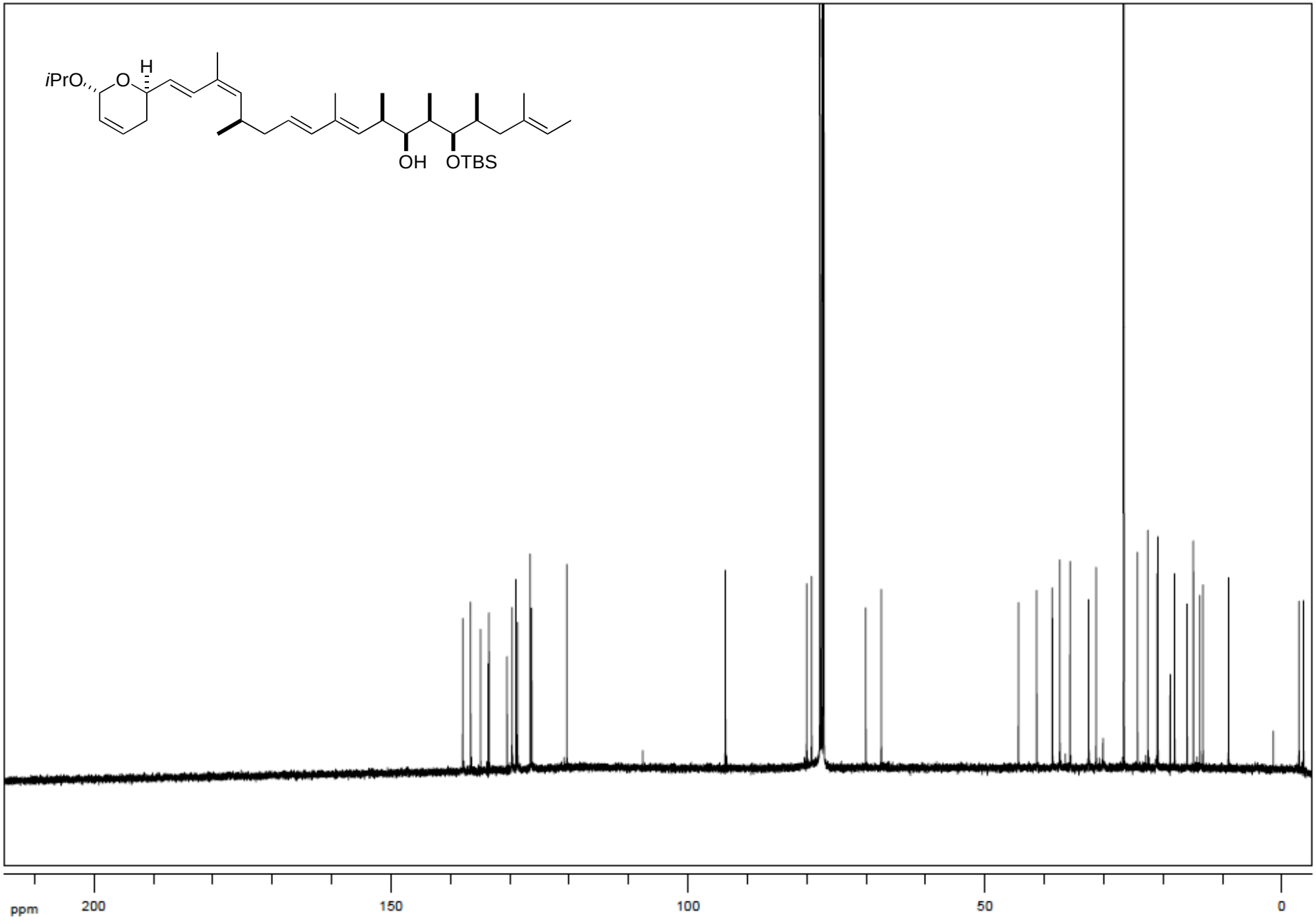
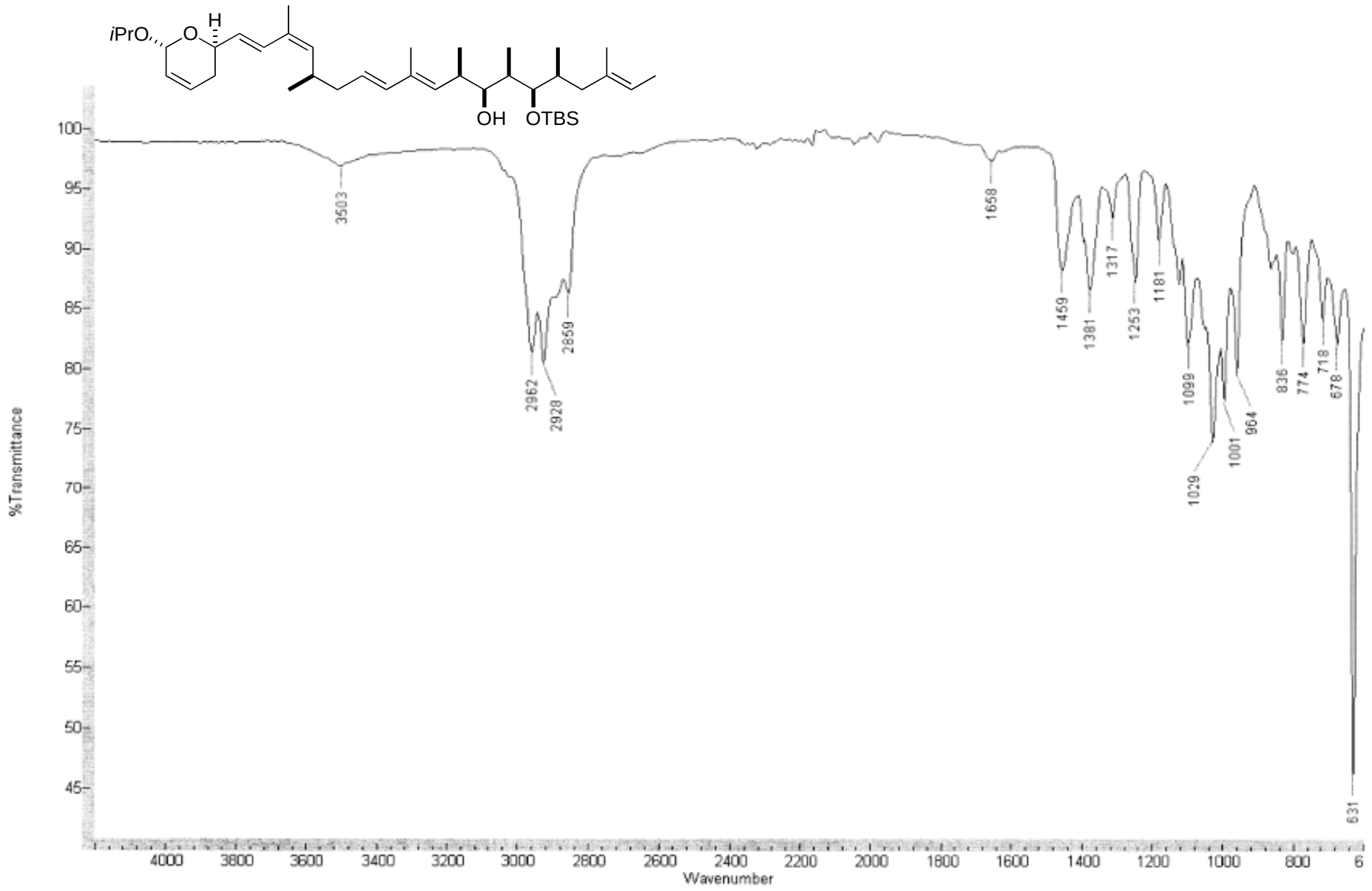
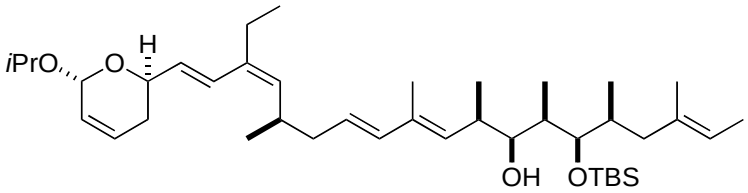
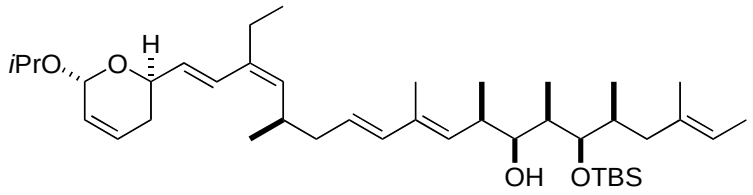
6.0
5.0
4.0
3.0
2.0
1.0


iPrO
O
H
OH
OTBS
ppm
200
150
100
50
0

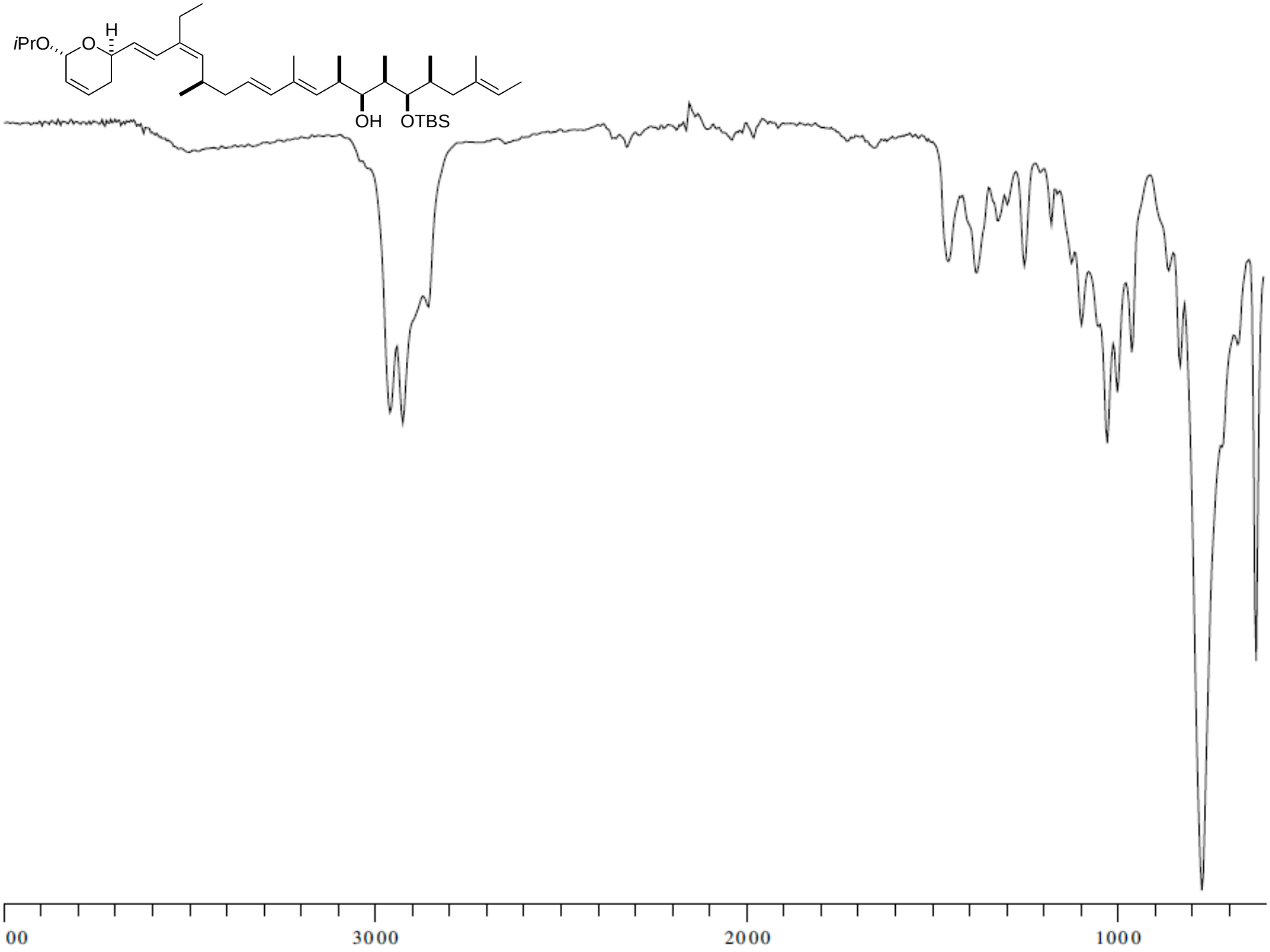

iPrO
O
H
OH
OTBS
%Transmittance
100
95
90
85
80
75
70
65
60
55
50
45
3503
2962
2928
2859
1658
1459
1381
1317
1253
1181
1099
1029
1001
964
836
774
718
678
631
4000
3800
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
6
Wavenumber

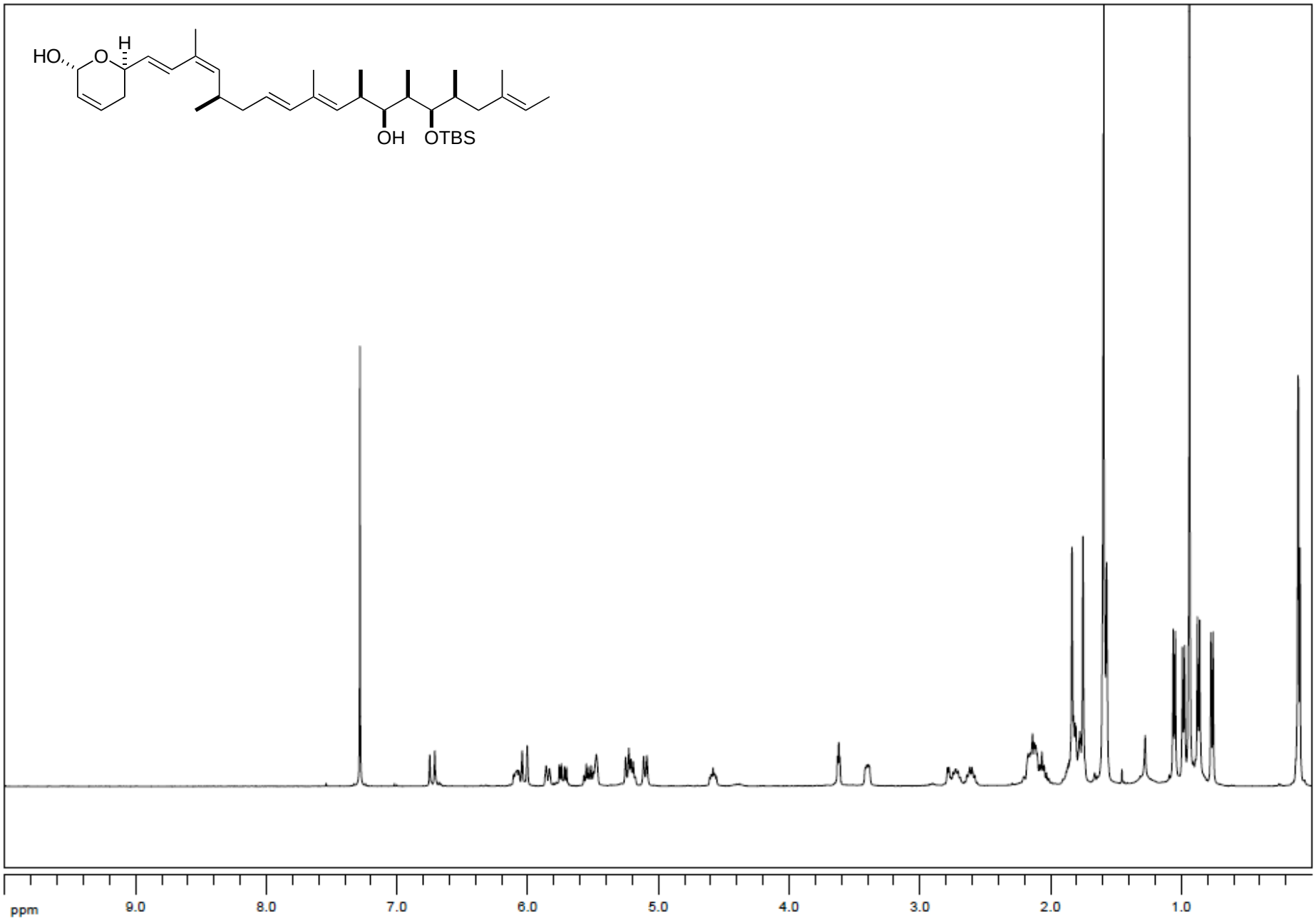

iPrO
O
H
OH
OTBS

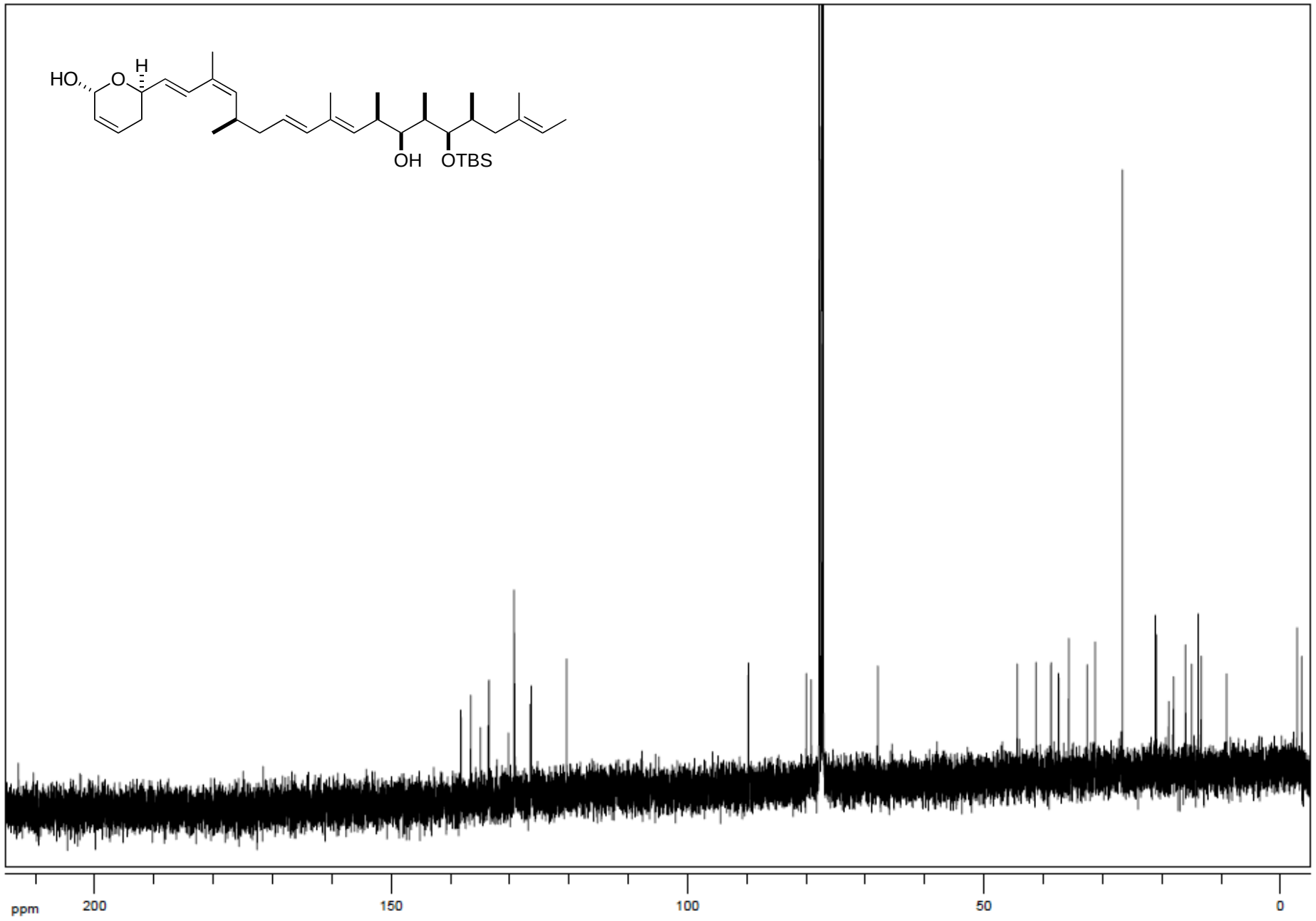

0
9
8
7
6
5
4
3
2
1

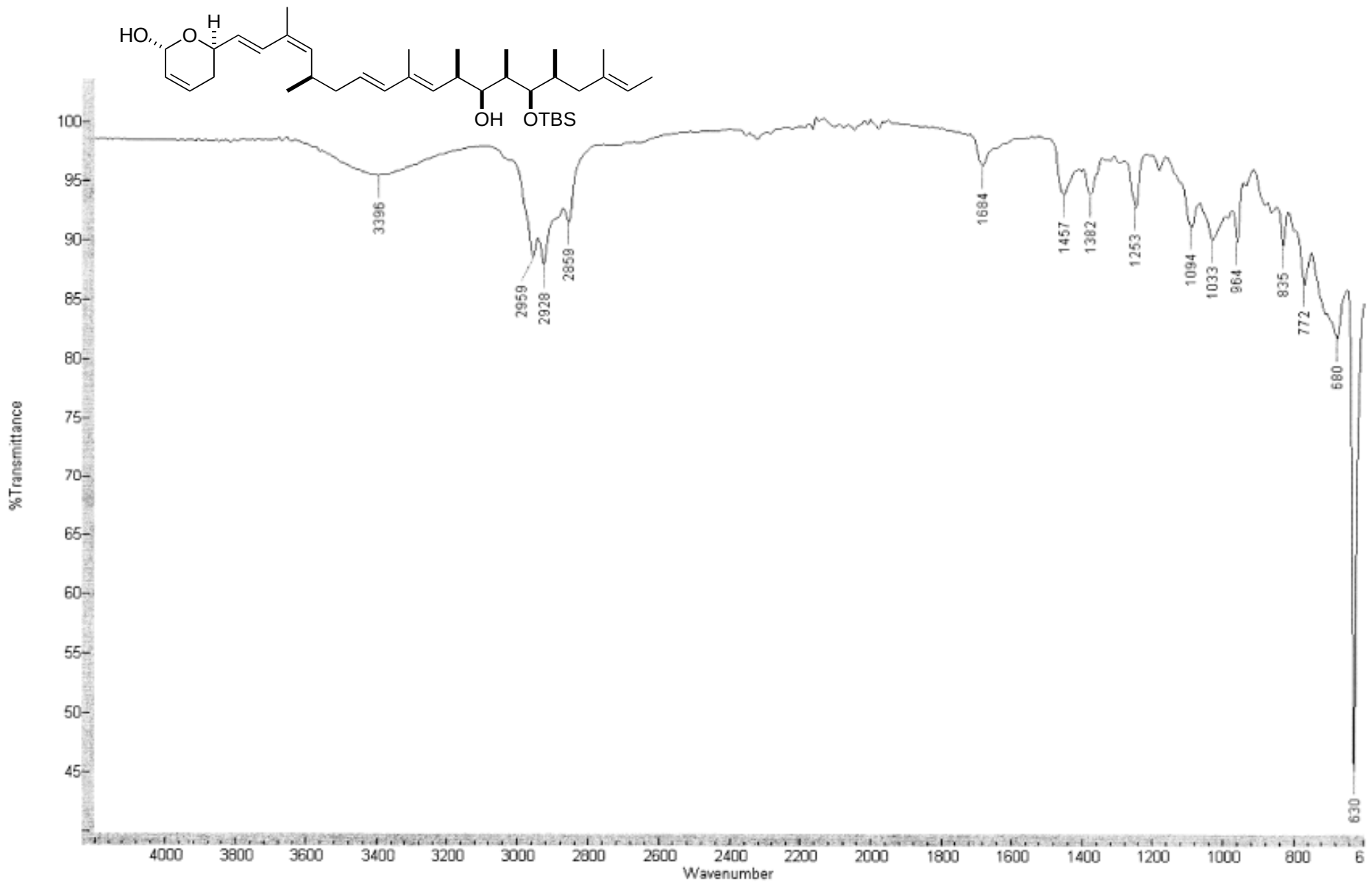

iPrO
O
H
OH
OTBS

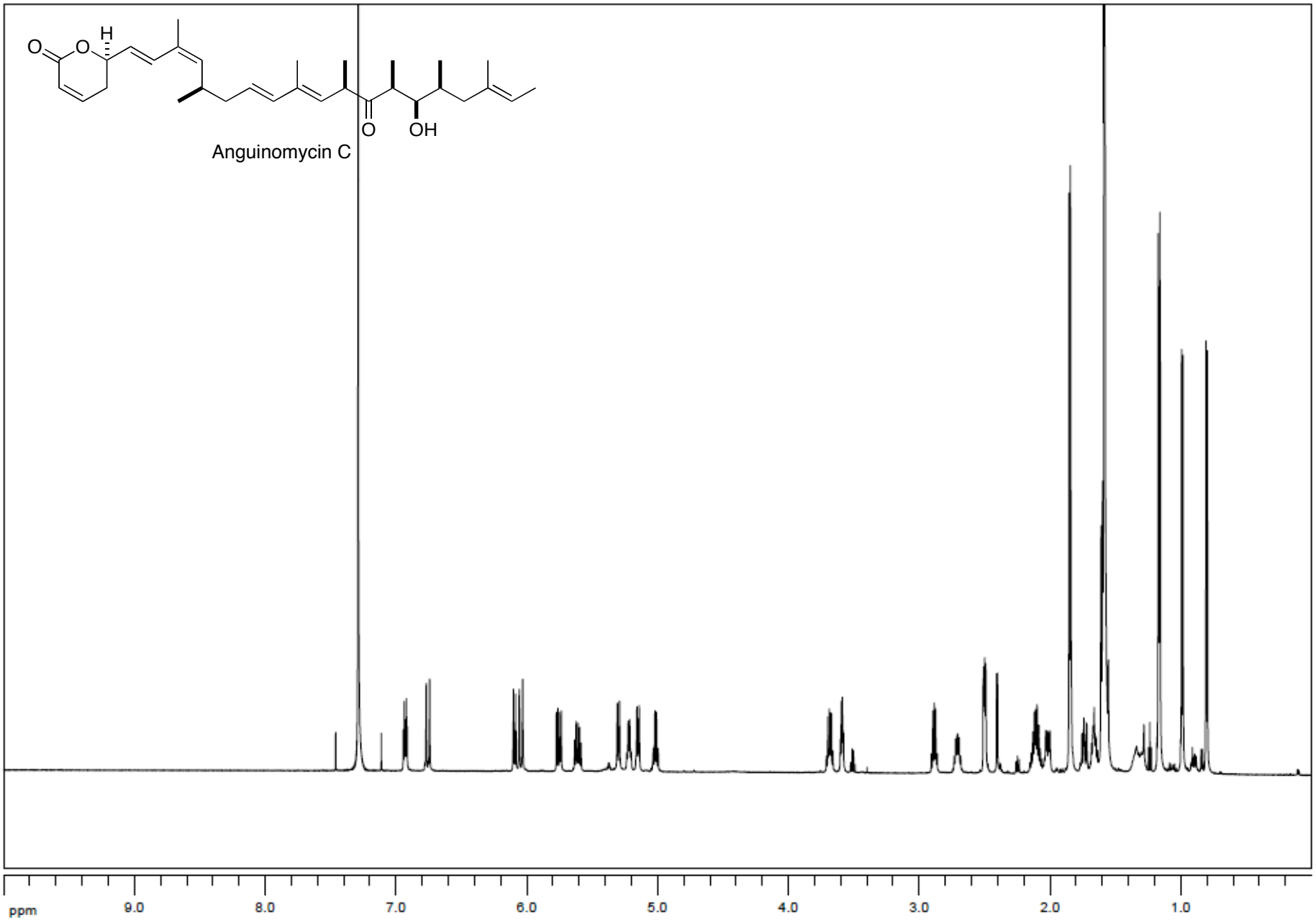

10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

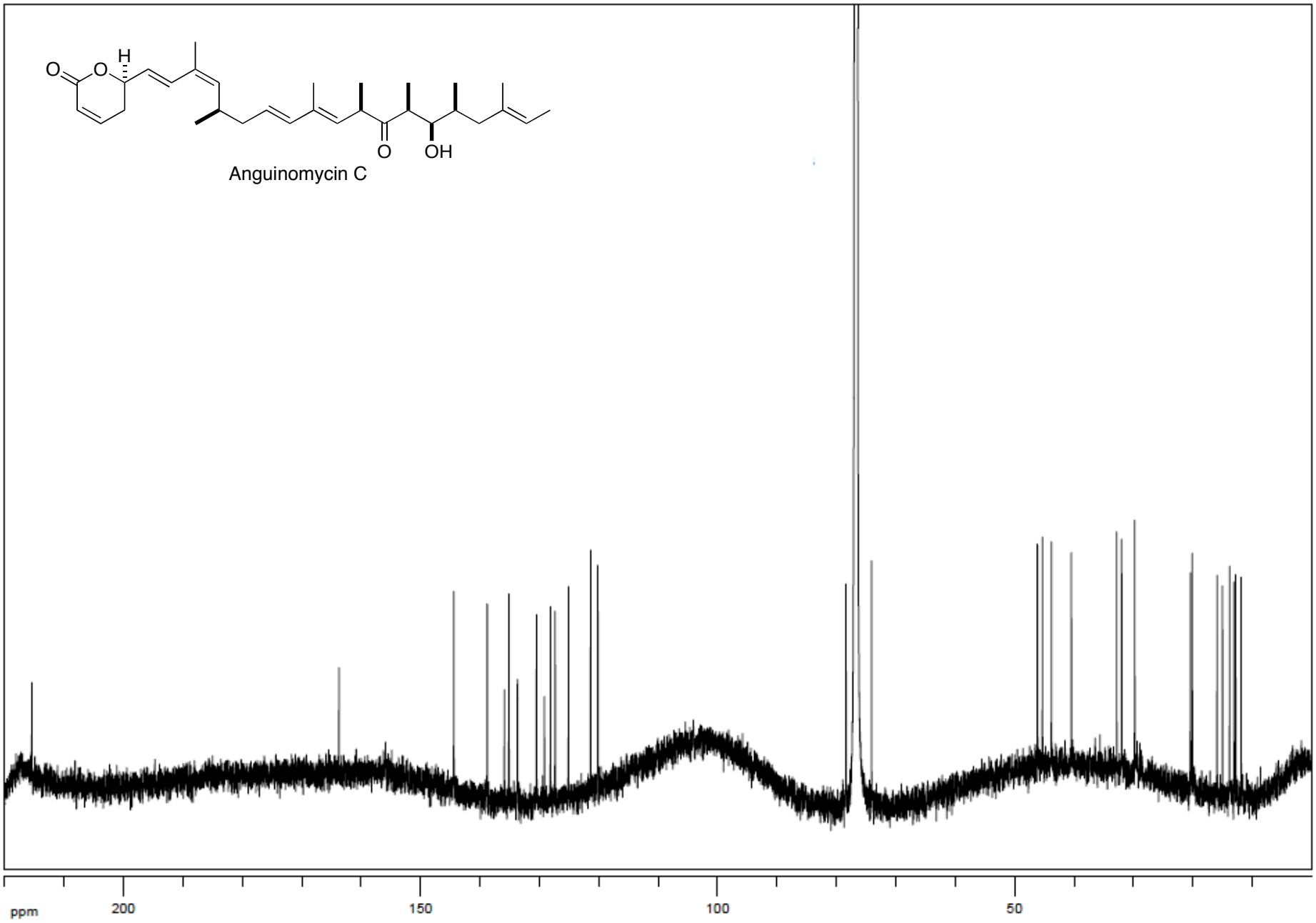

iPrO
O
H
OH
OTBS
00
3000
2000
1000


HO
O
H
OH
OTBS
ppm
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0

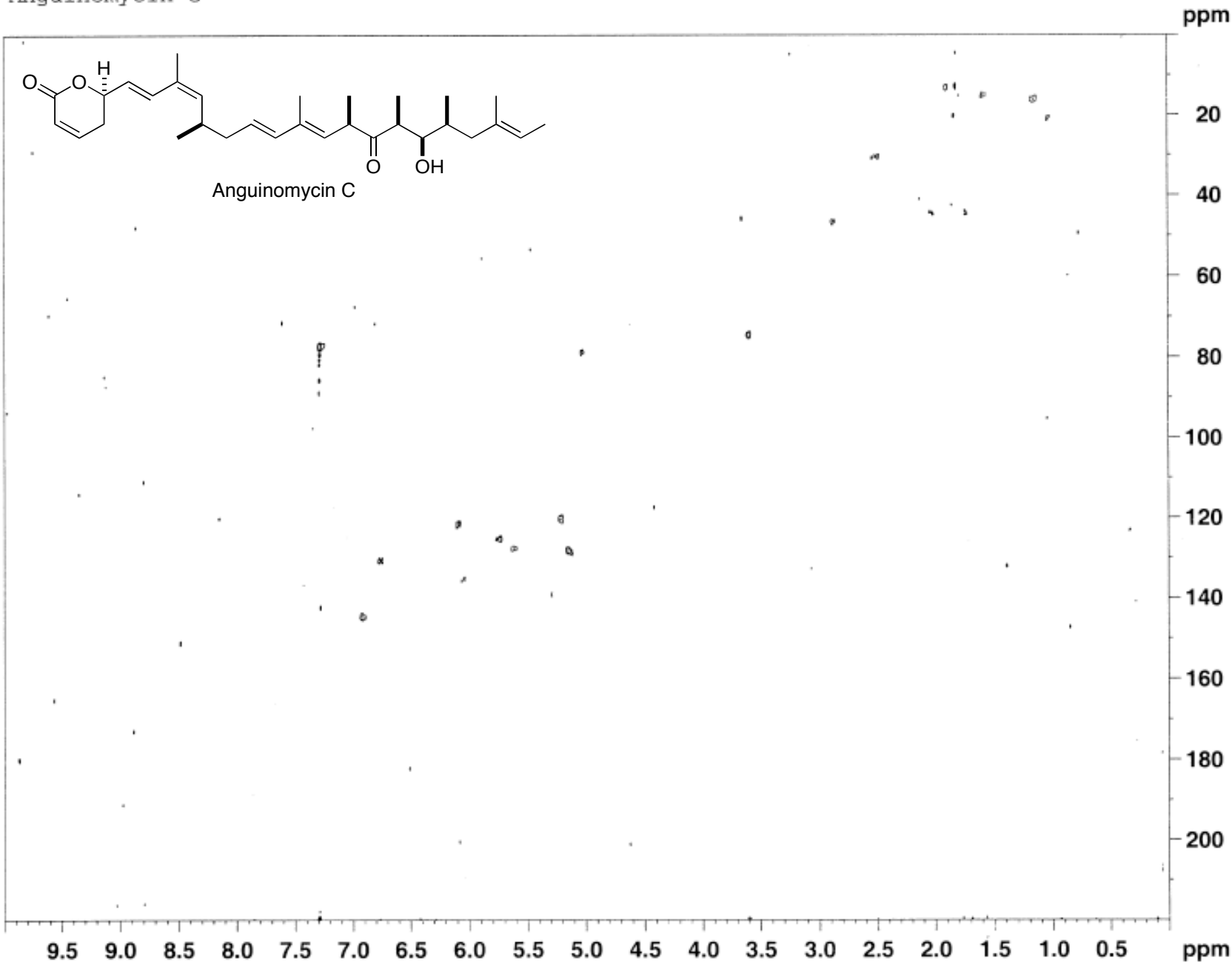

HO
O
H
OH
OTBS
ppm
200
150
100
50
0


HO
O
H
OH
OTBS
%Transmittance
100
95
90
85
80
75
70
65
60
55
50
45
3396
2959
2928
2859
1684
1457
1382
1253
1094
1033
964
835
772
680
630
4000
3800
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
6
Wavenumber


O
O
H
O
OH
Anguinomycin C
ppm
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0


O
O
H
O
OH
Anguinomycin C
ppm
200
150
100
50

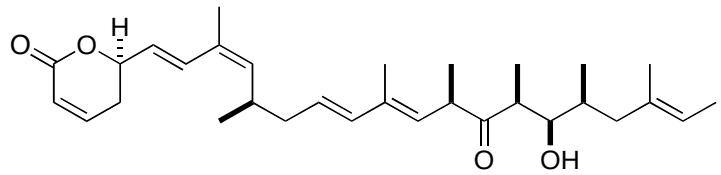
Anguinomycin C



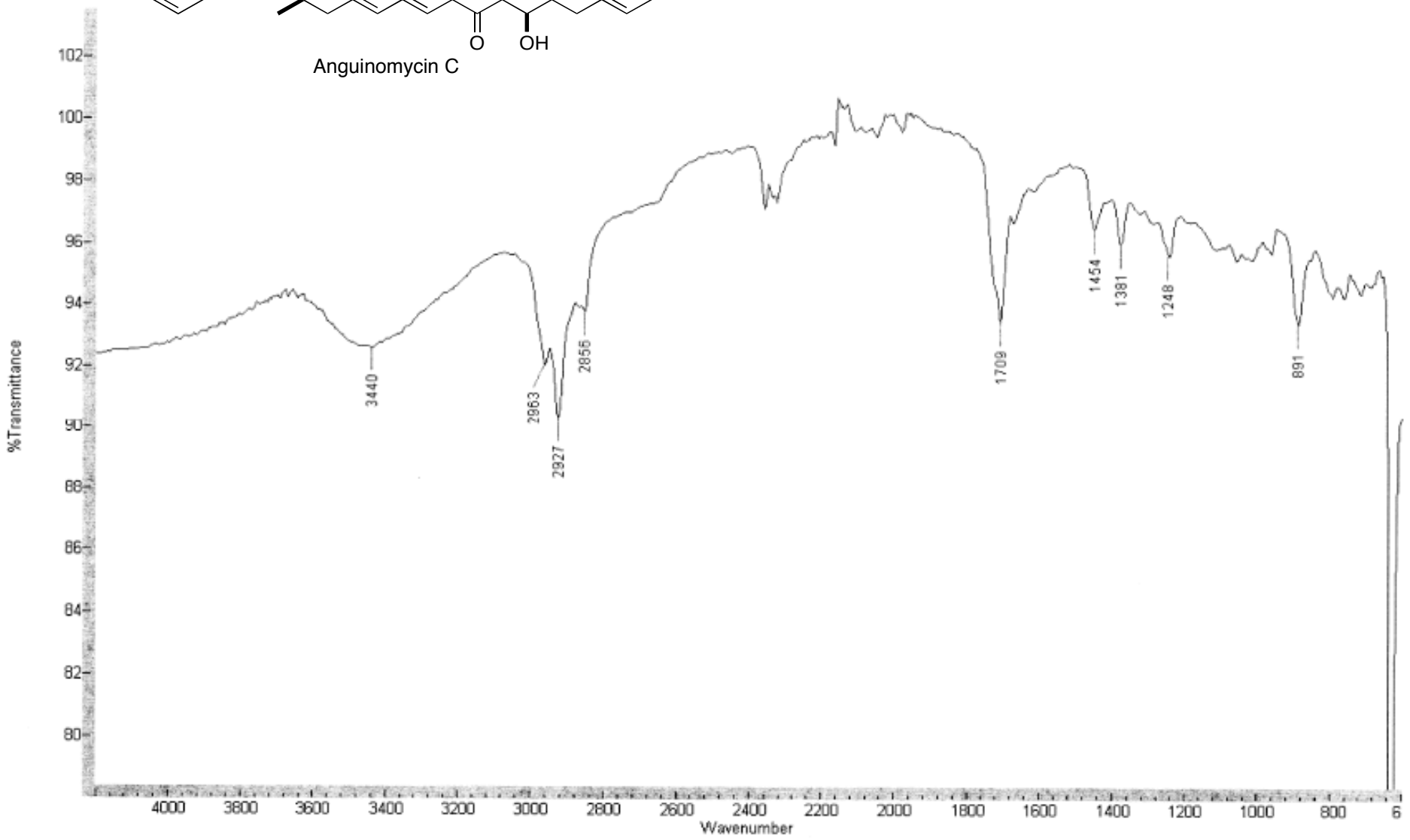




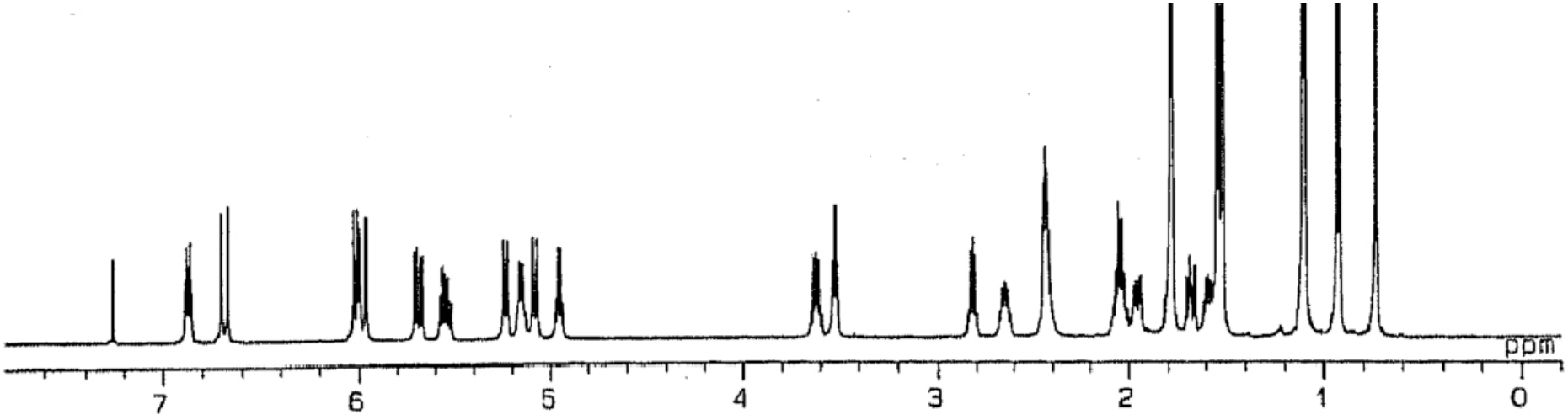
Anguinomycin C



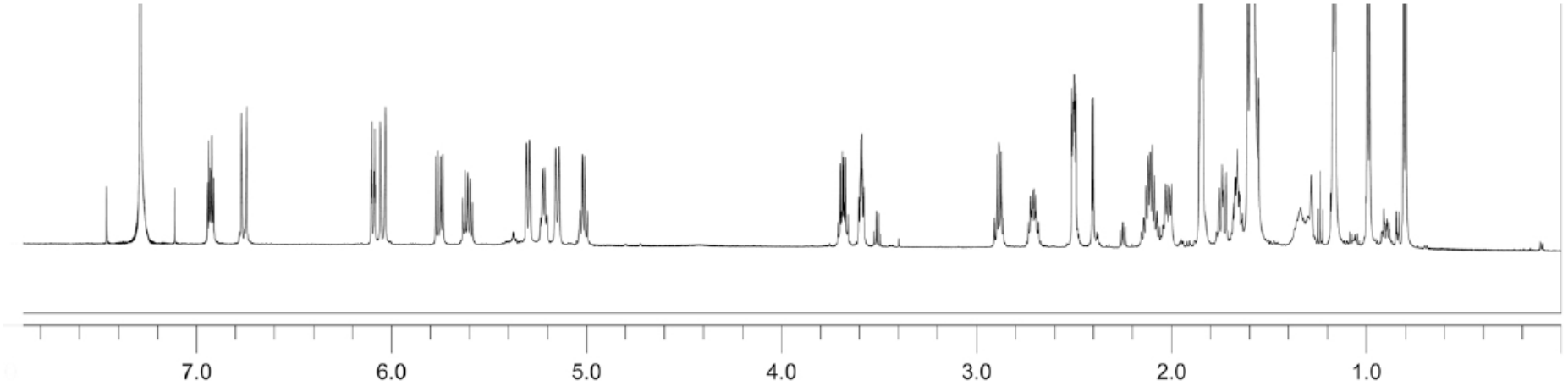

Anguinomycin C

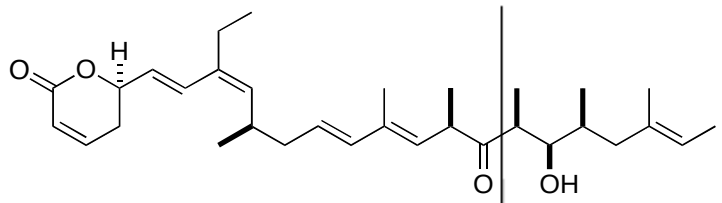


**Natural Anguinomycin C**

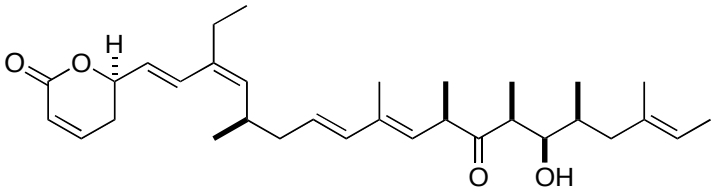



**Synthetic Anguinomycin C**



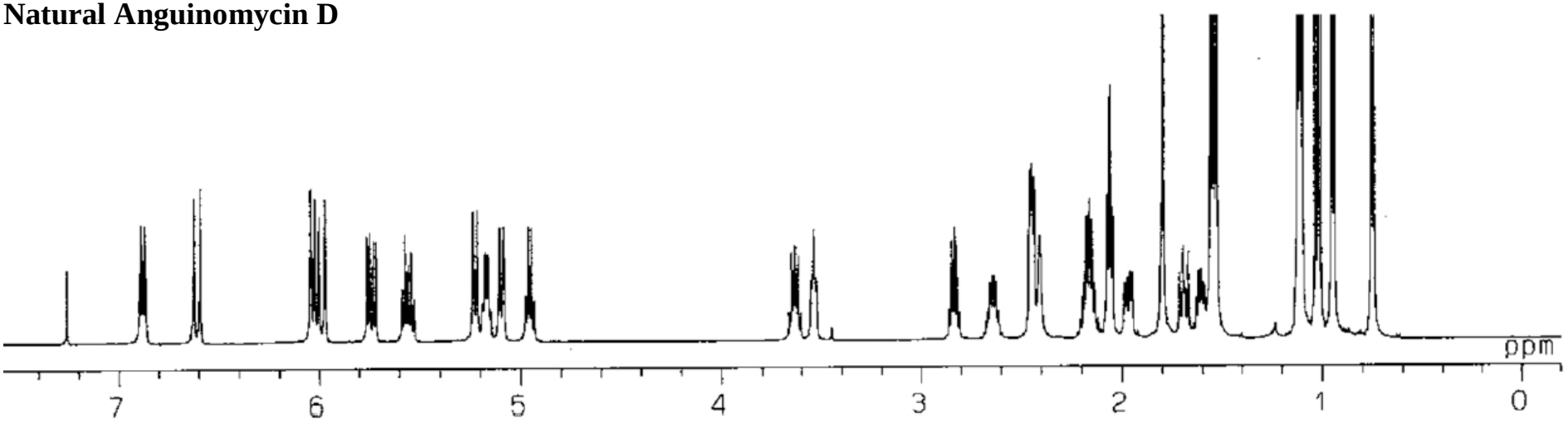



Anguinomycin D

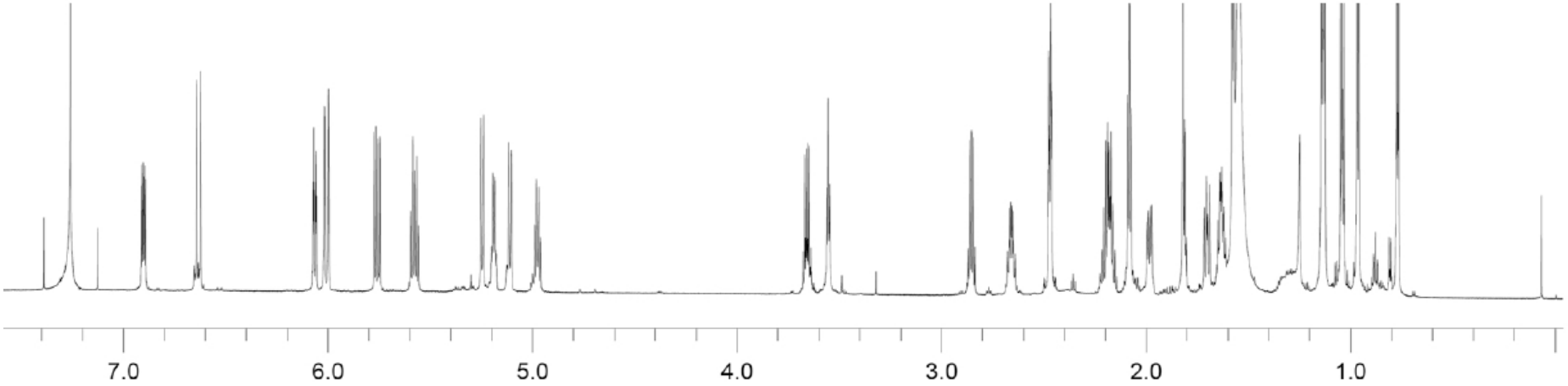


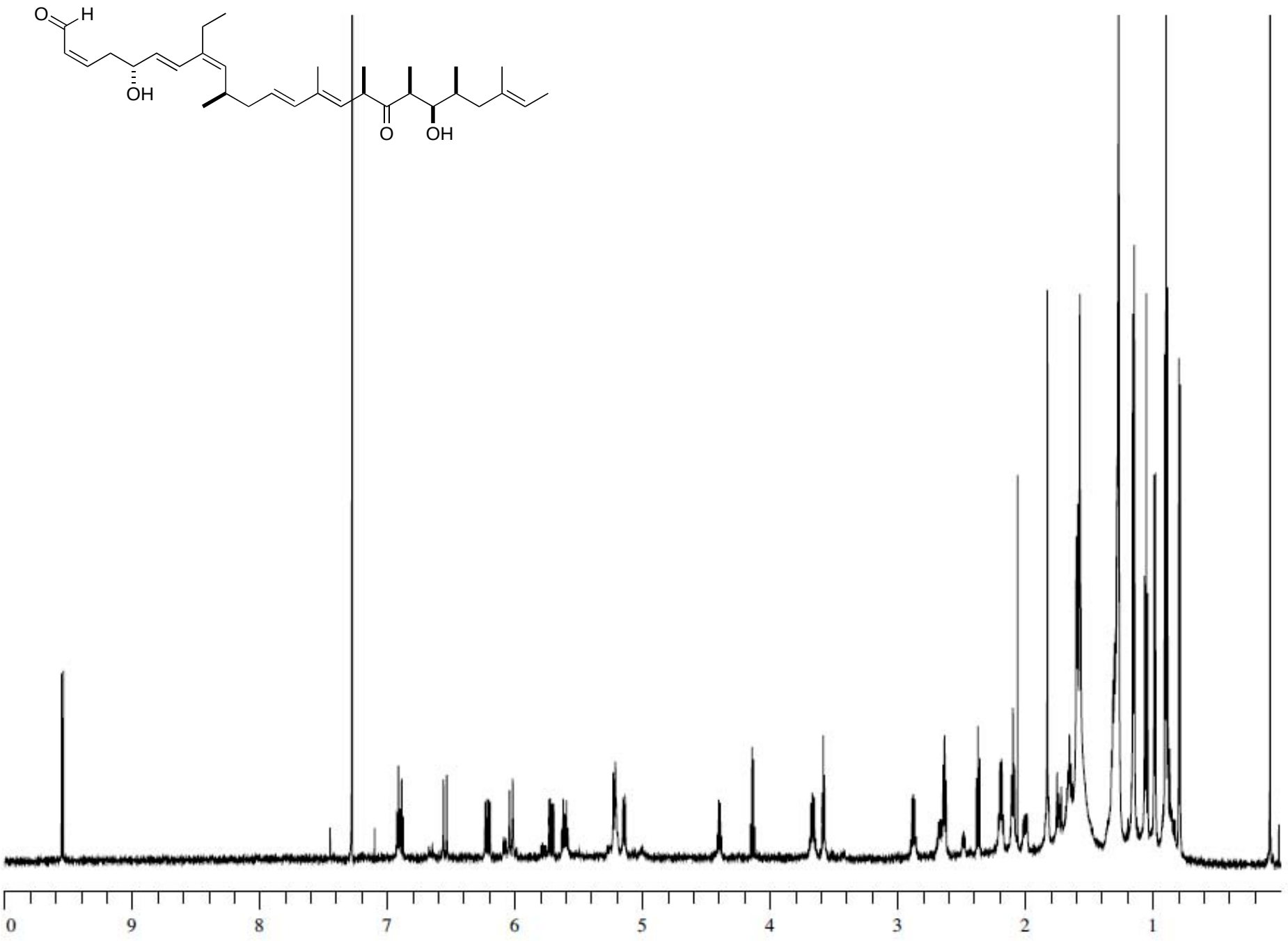

Anguinomycin D

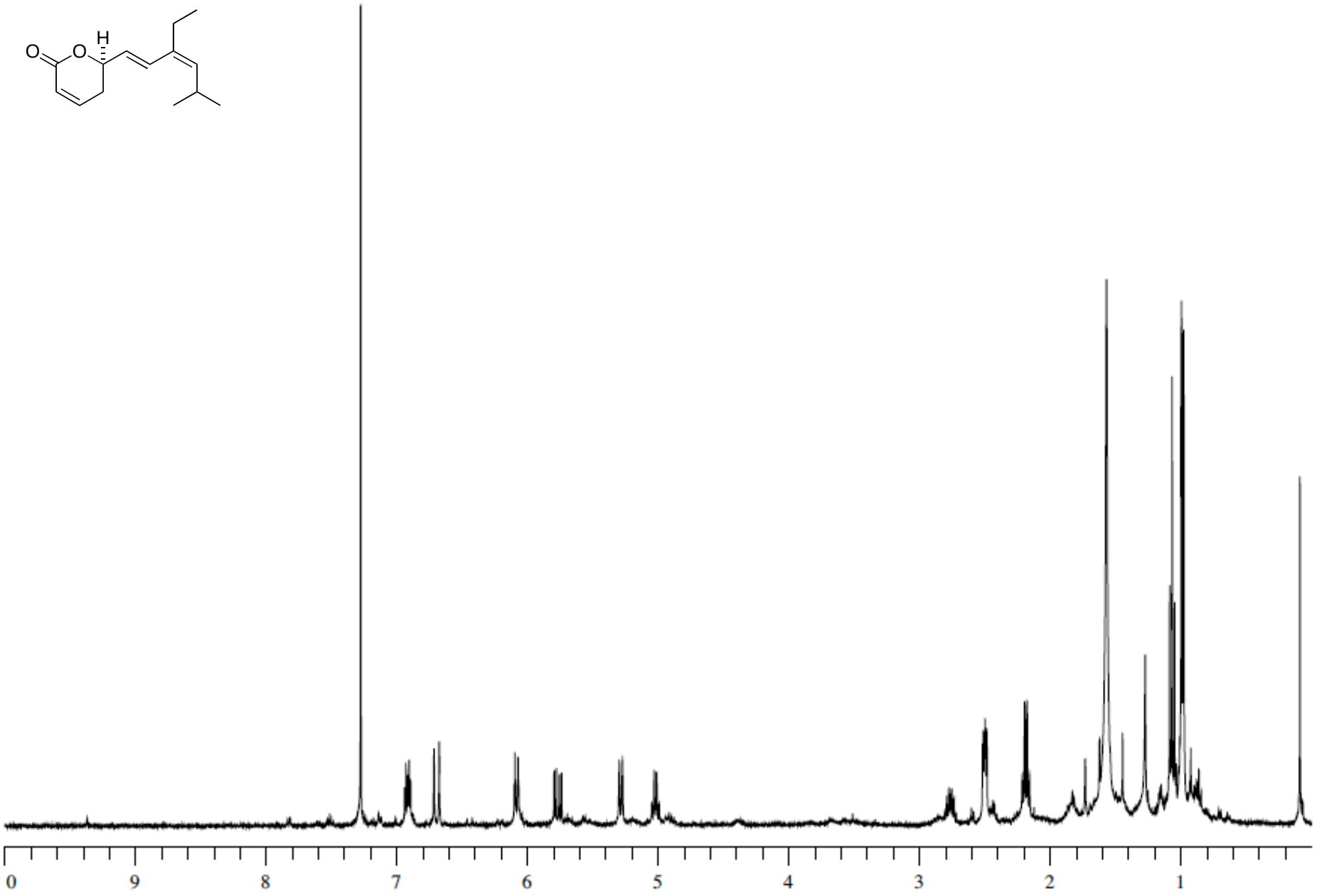
**Natural Anguinomycin D**

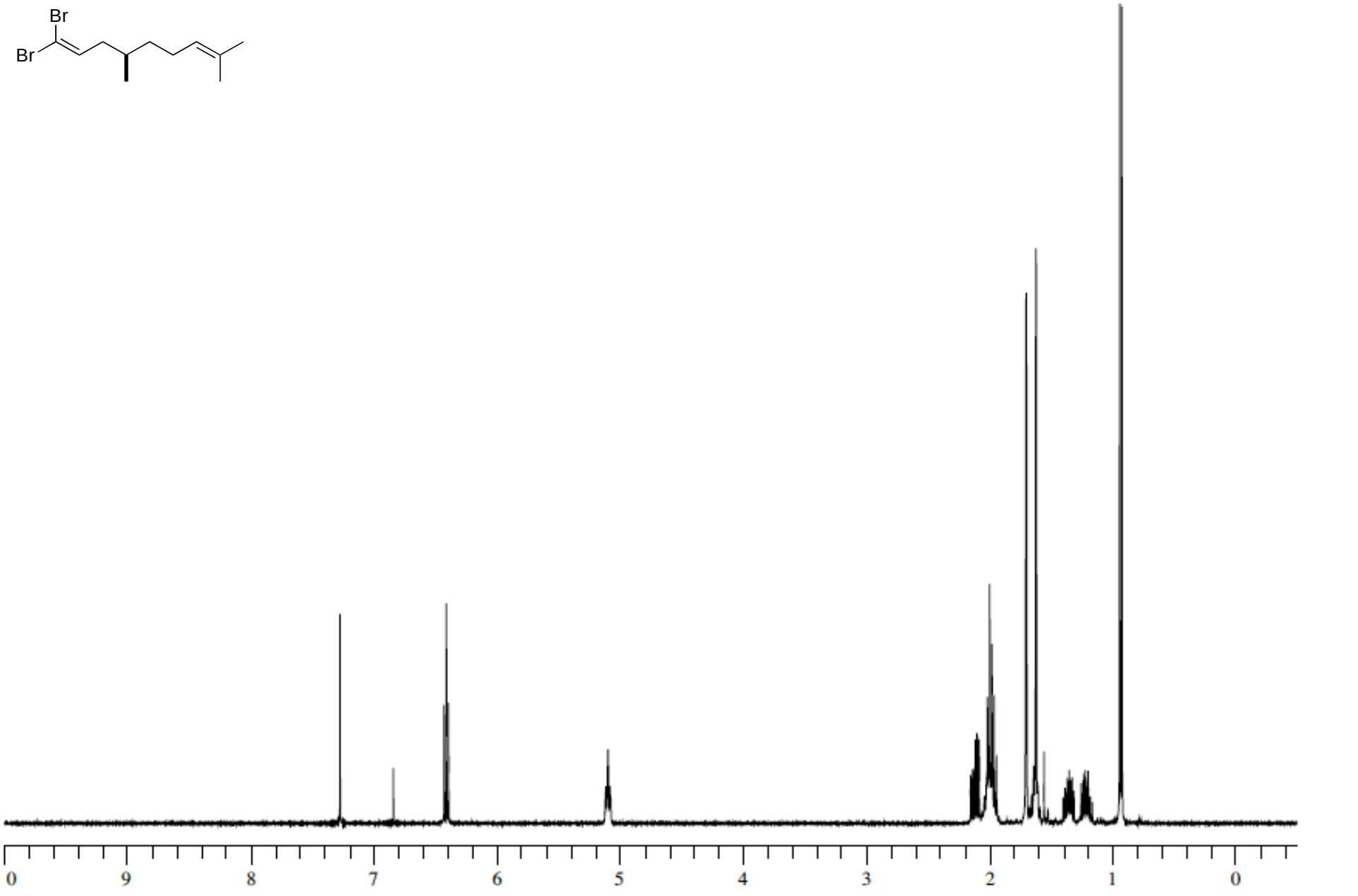


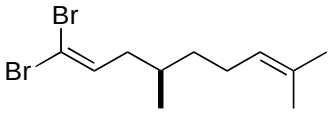

**Synthetic Anguinomycin D**



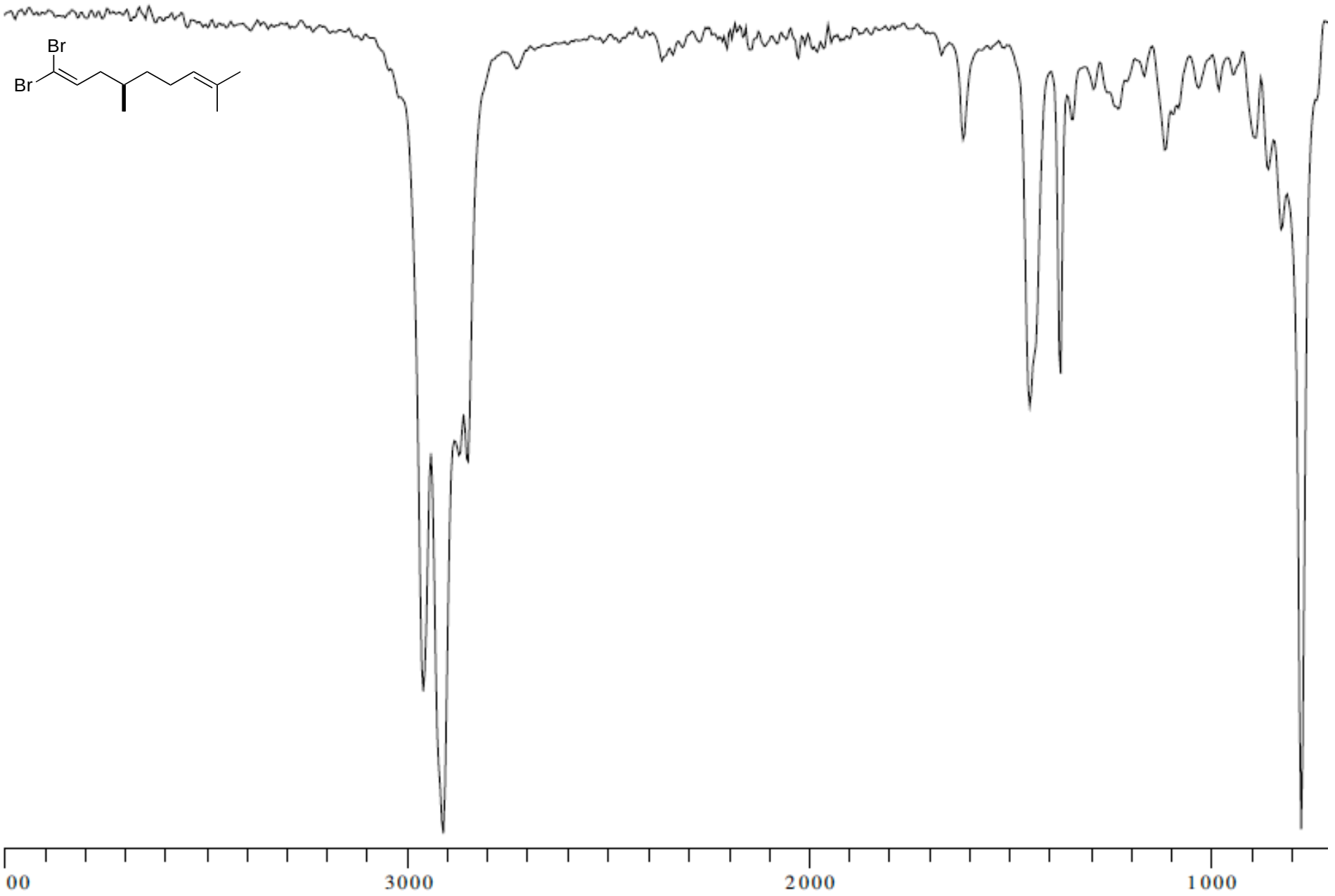

O
H
OH
O
OH
0
9
8
7
6
5
4
3
2
1

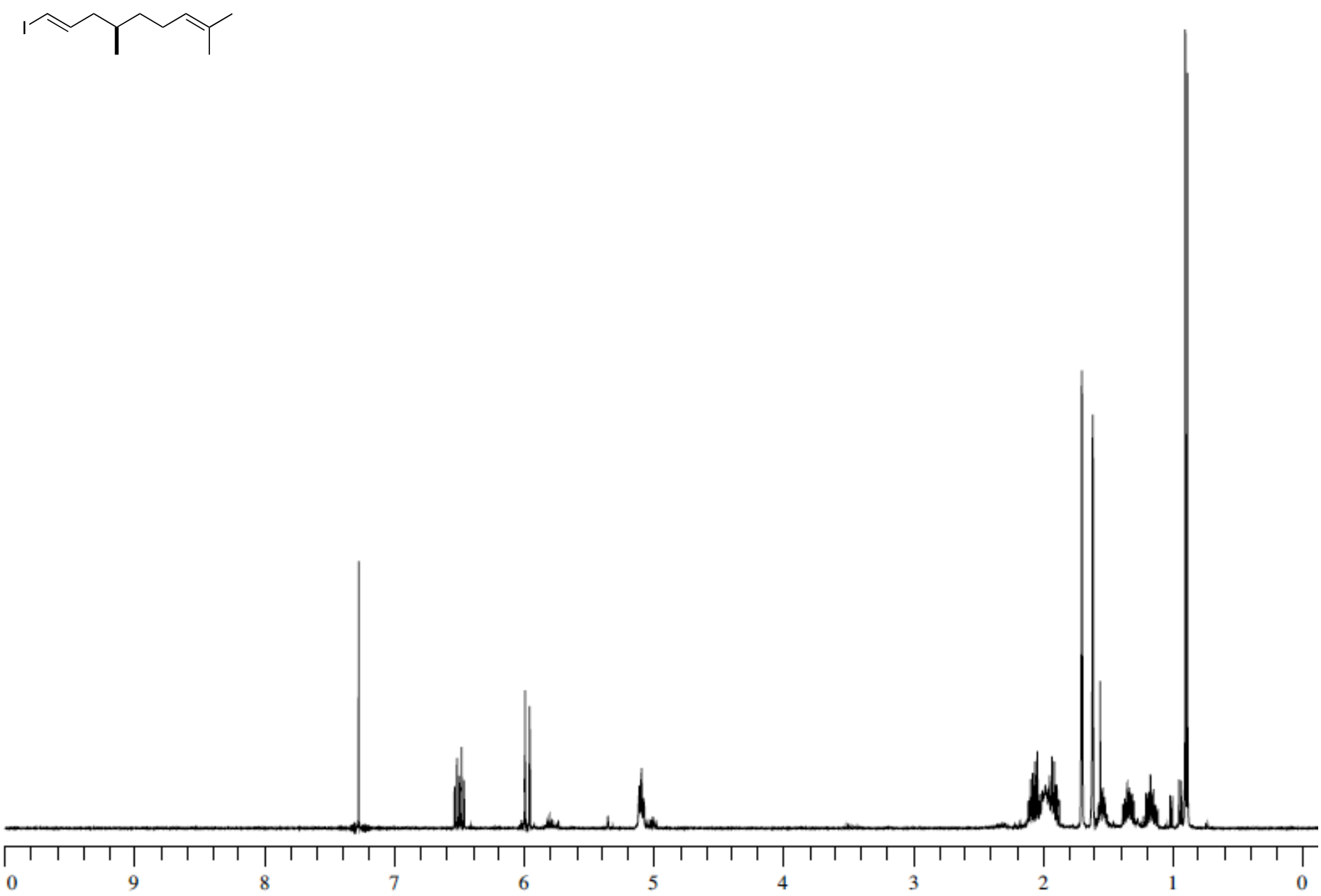

O
O
H
0
9
8
7
6
5
4
3
2
1

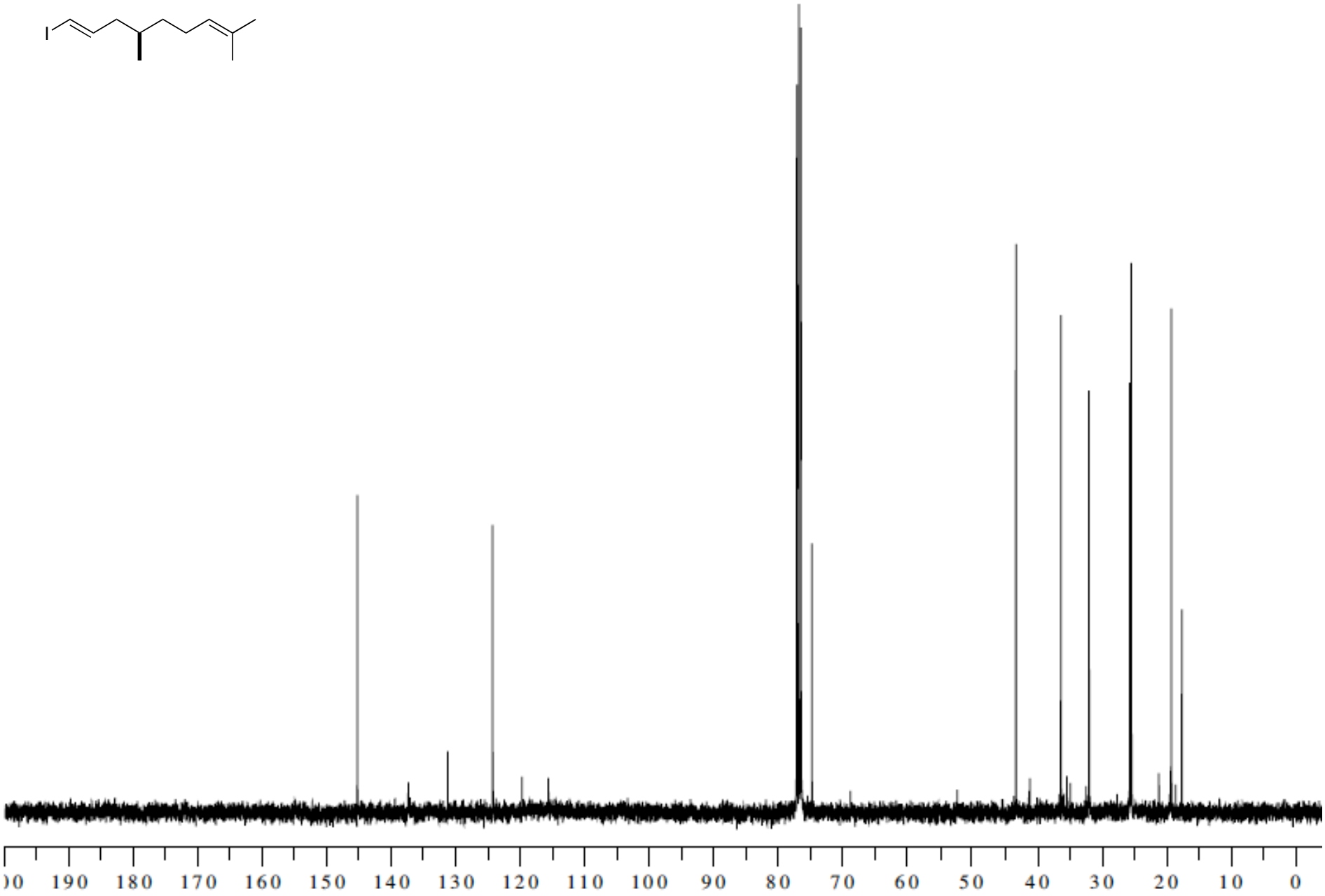

Br
Br
0
9
8
7
6
5
4
3
2
1
0


Br
Br


190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


Br
Br
00
3000
2000
1000


I
0
9
8
7
6
5
4
3
2
1
0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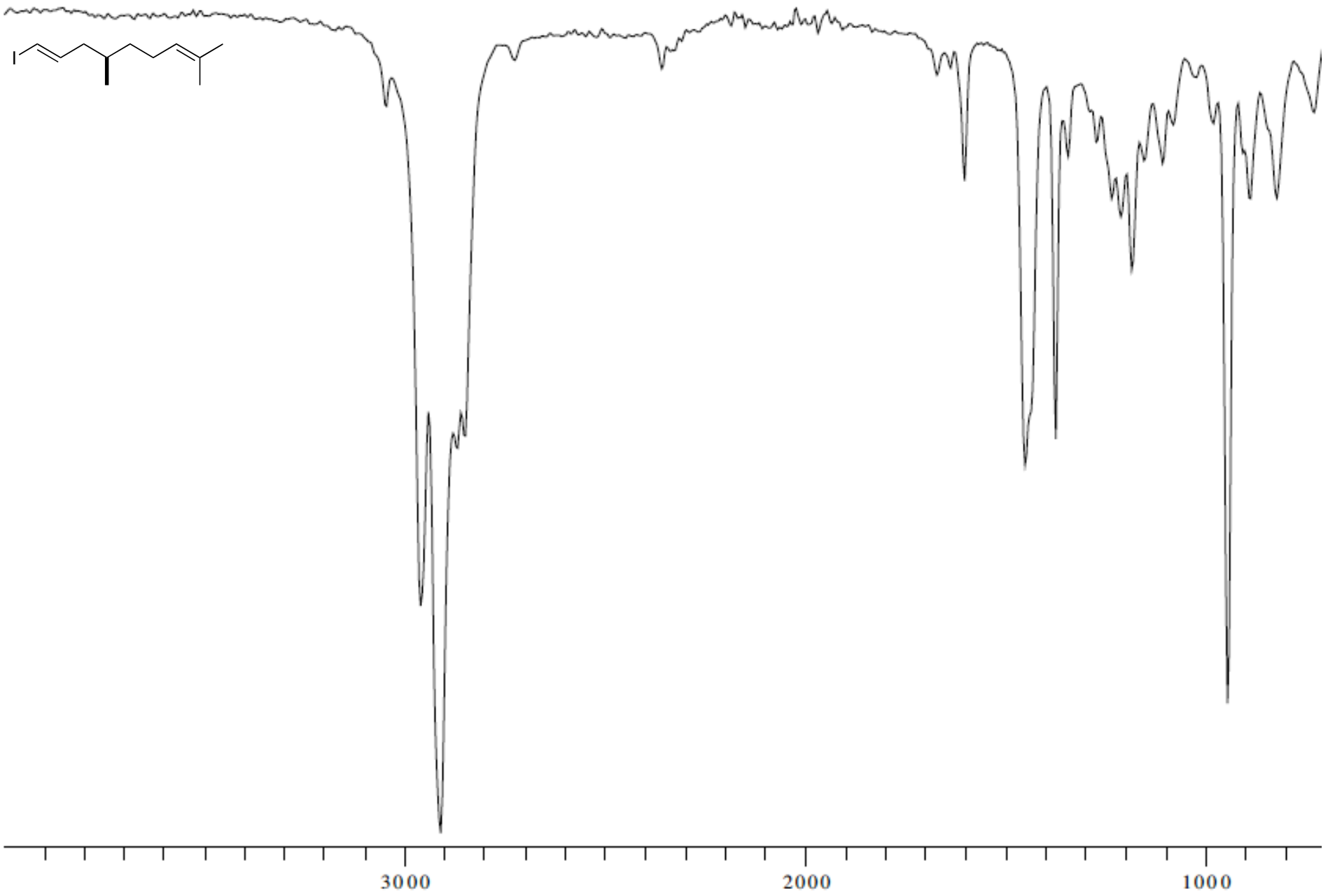
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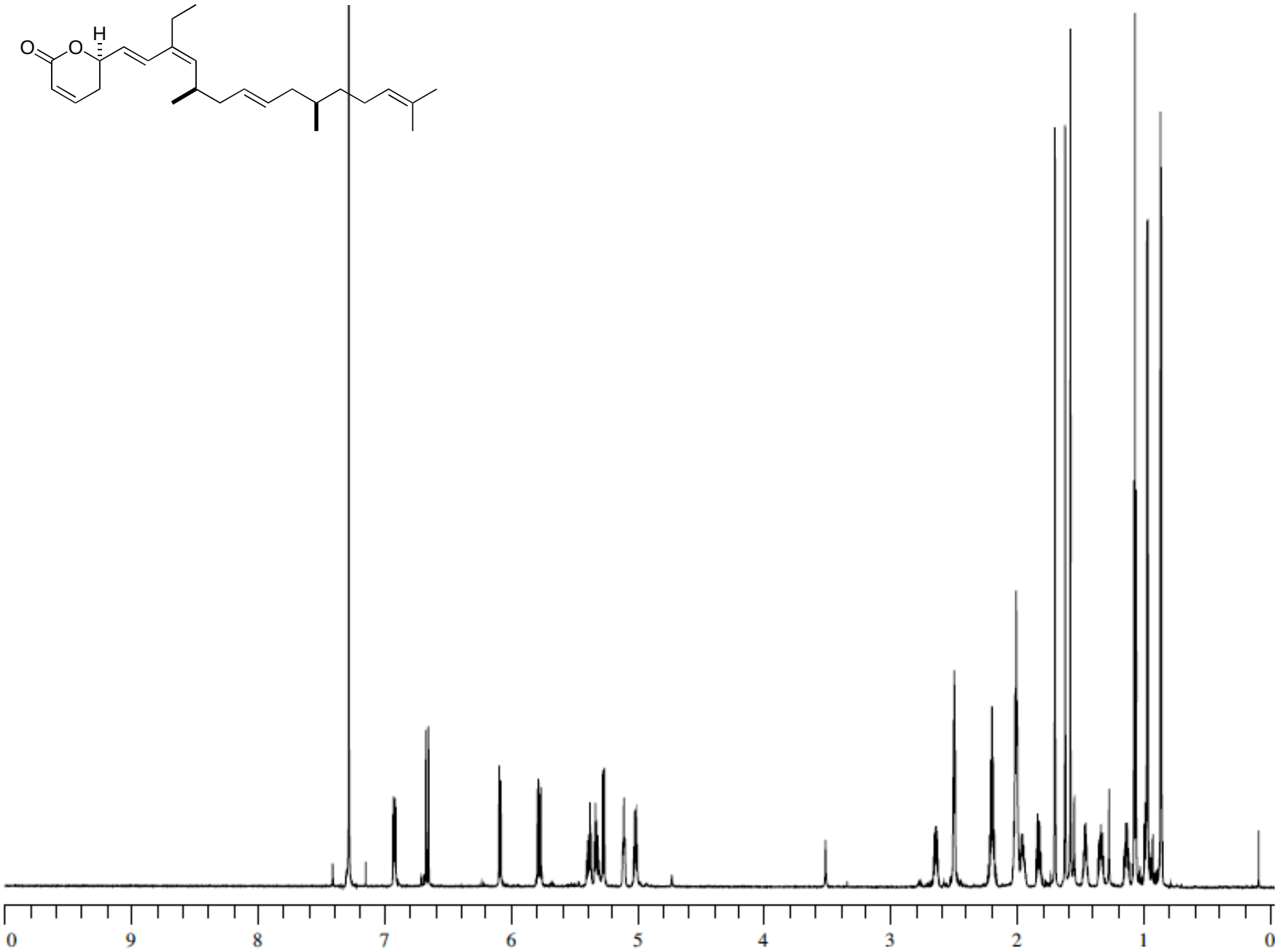
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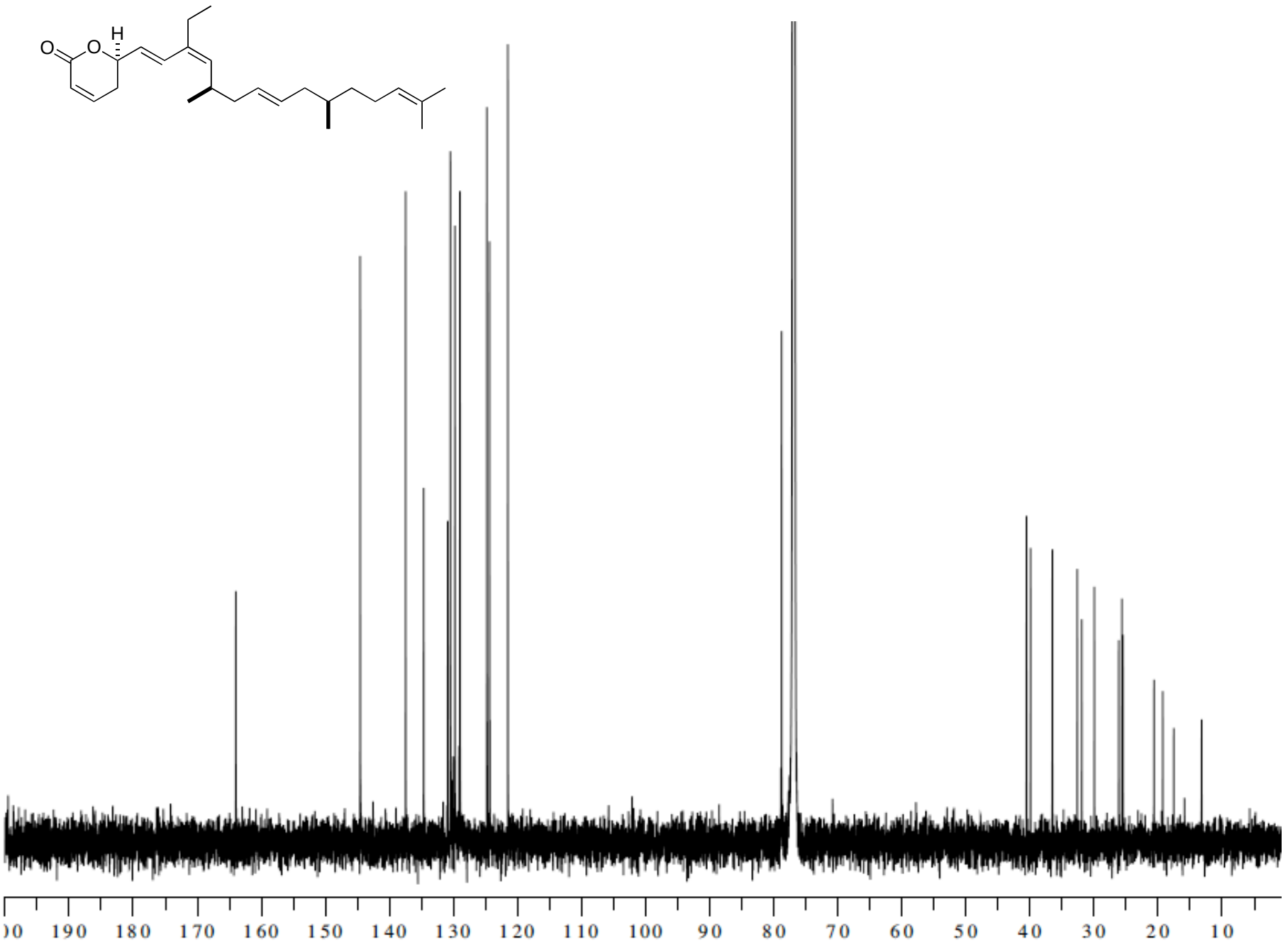
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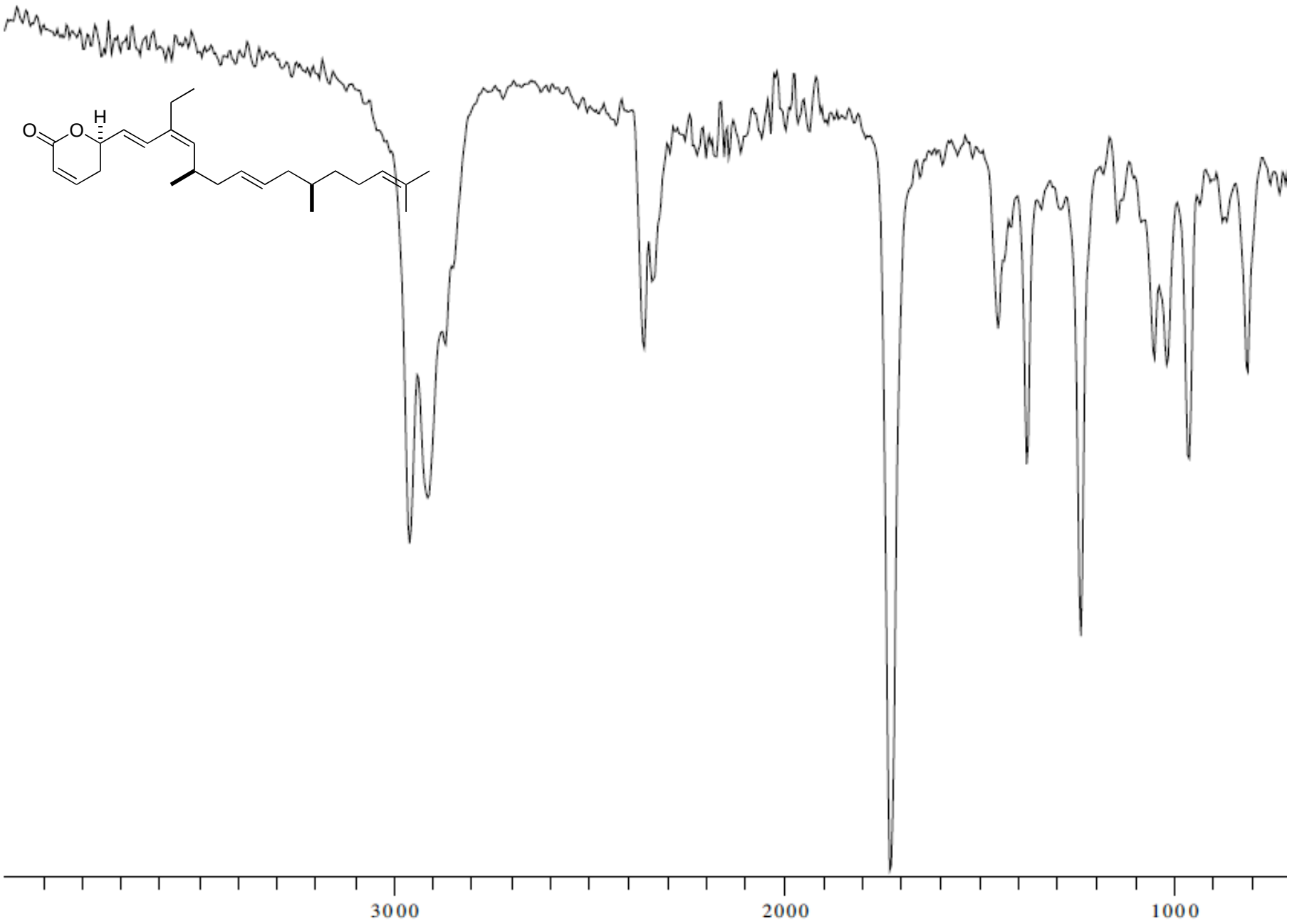
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