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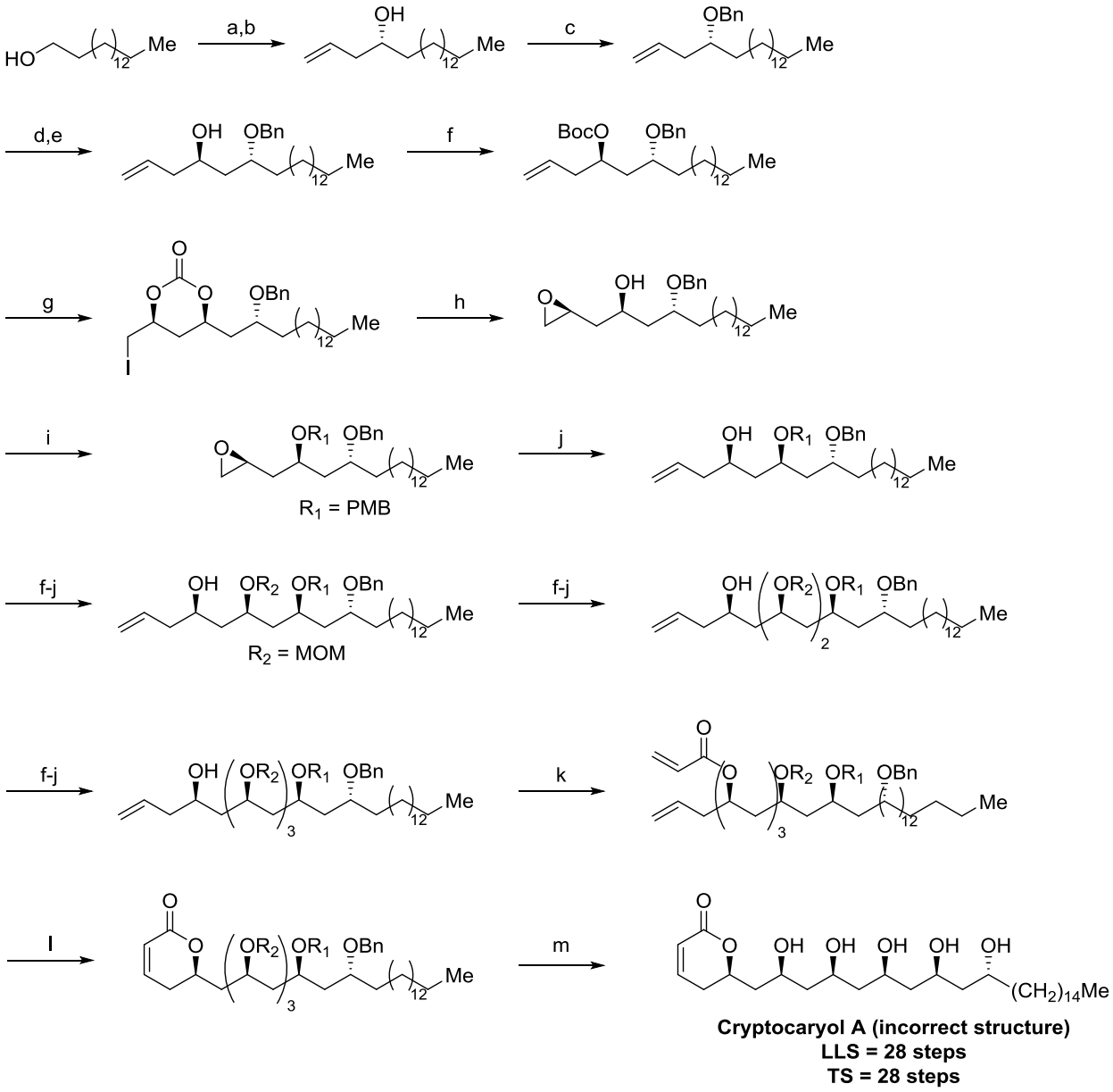
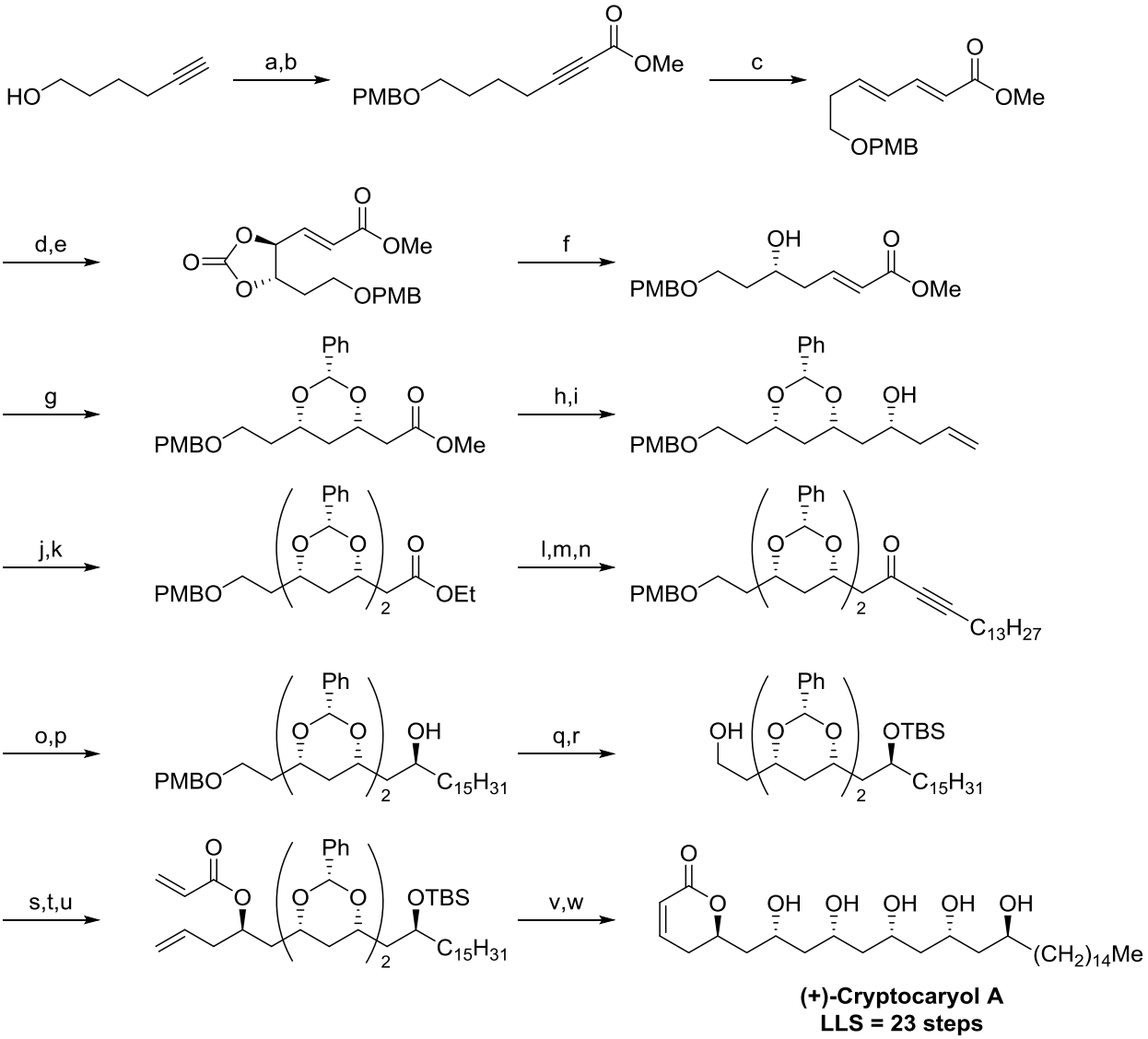
A. Mohapatra and coworkers, *Eur. J. Org. Chem.* 2013, 1051.



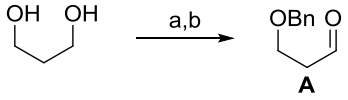
(a) PCC, CH_2Cl_2, rt; (b) $TiCl_4$, Ti(O*i*Pr)$_4$, (*S*)-BINOL, Ag_2O, allyltributylstannane, -20 °C; (c) NaH, BnBr, THF, 0 °C; (d) OsO_4, $NaIO_4$, 2,6-lutidine, dioxane, rt; (e) allylTMS, $TiCl_4$, -78 °C; (f) Boc_2O, Et_3N, CH_2Cl_2, rt; (g) NIS, CH_3CN, -40 to 0 °C; (h) K_2CO_3, MeOH, rt; (i) first iteration: NaH, PMBCl, THF, DMF, 0 °C (subsequent iterations: NaH, MOMCl, THF, DMF, 0 °C); (j)vinylmagnesium bromide, CuI, THF, -20 °C; (k) acryloyl chloride, DIPEA, CH_2Cl_2, 0°C; (l) Grubbs I, CH_2Cl_2, reflux; (m) $TiCl_4$, CH_2Cl_2, rt.

B. O'Doherty and coworkers, *J. Am. Chem. Soc.* **2013**, *135*, 9334.

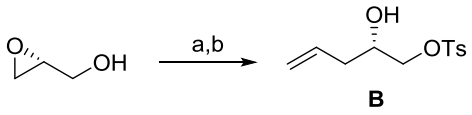


(a) PMBCl, NaH, TFAB, 0 °C; (b) $ClCO_2Me$, *n*-BuLi, THF, -78 to 0 °C; (c) PPh_3, PhOH, benzene, 50 °C; (d) AD-mix-α, *t*-BuOH/H_2O, 0 °C; (e) triphosgene, pyridine, DMAP, CH_2Cl_2, -78 °C; (f) $PdPPh_3$, Et_3N, HCO_2H, THF, reflux; (g)PhCHO, KO*t*Bu, THF, 0 °C; (h) DIBALH, CH_2Cl_2, -78 °C; (i) (*R,R*)-Leighton, $Sc(OTf)_3$, CH_2Cl_2, -10 °C, (j) ethyl acetate, Grubbs II, CH_2Cl_2; (k) PhCHO, KO*t*Bu, THF, 0 °C; (l) DIBALH, CH_2Cl_2, -78 °C; (m) 1-pentadecyne, *n*-BuLi, THF, -78 °C; (n) DMP, CH_2Cl_2, 0 °C; (o) (*R,R*)-Noyori, Et_3N, HCO_2H; (p) NBSH, Et_3N, CH_2Cl_2; (q) TBSCl, imidazole, DMF; (r) DDQ, CH_2Cl_2, H_2O, 0 °C; (s) DMP, CH_2Cl_2, 0 °C; (t) (*S,S*)-Leighton, $Sc(OTf)_3$, CH_2Cl_2, -10 °C; (u) acrylic acid, DCC, DMAP, CH_2Cl_2; (v) Grubbs I, CH_2Cl_2, reflux; (w) AcOH/H_2O = 4:1, 80 °C.

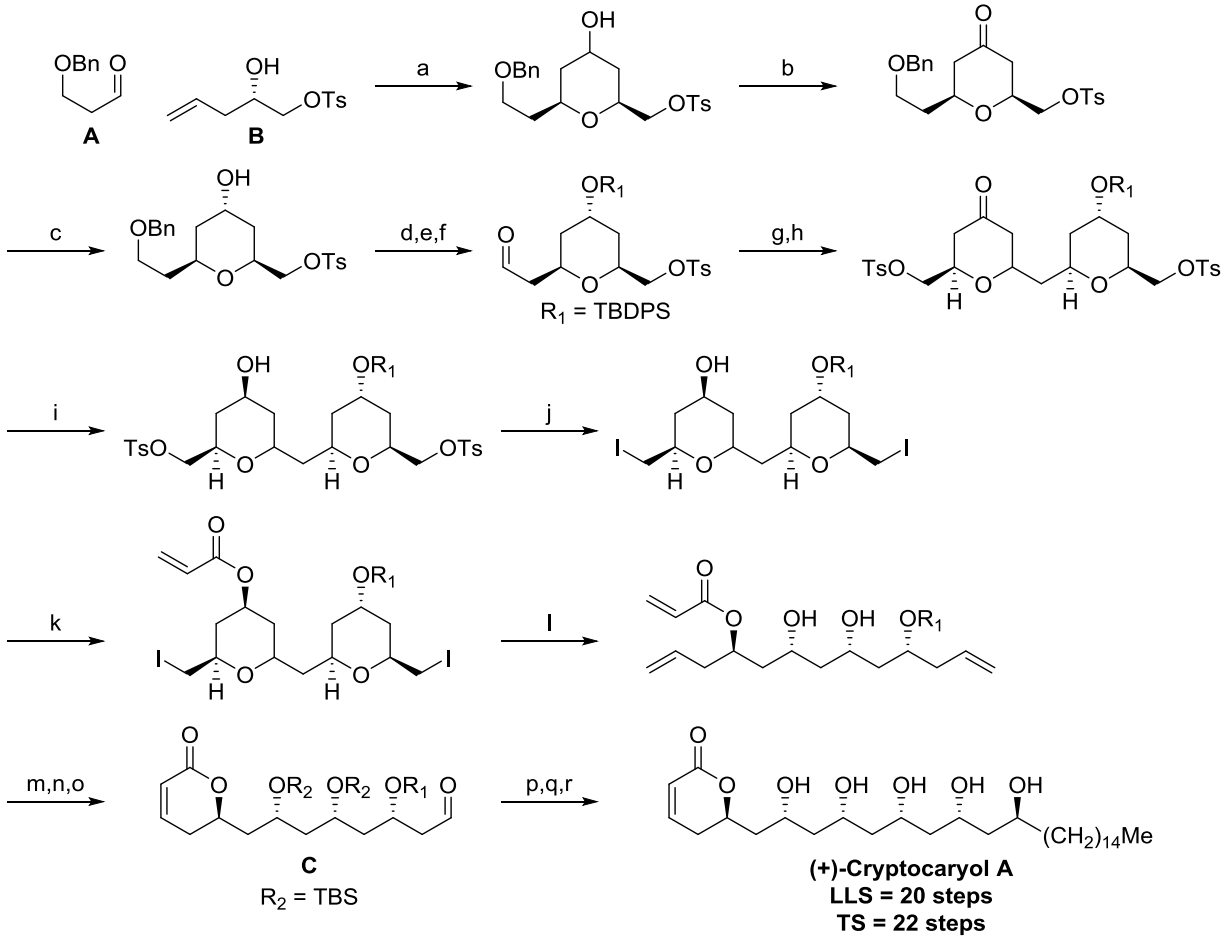
C. Cossy and coworkers, *J. Org. Chem.* **2015**, *80*, 8668.



(a) NaH, BnBr, *n*-Bu_4NI, THF, rt, 7h; (b) PCC, NaOAc, 4 Å MS, CH_2Cl_2, rt, 3h.

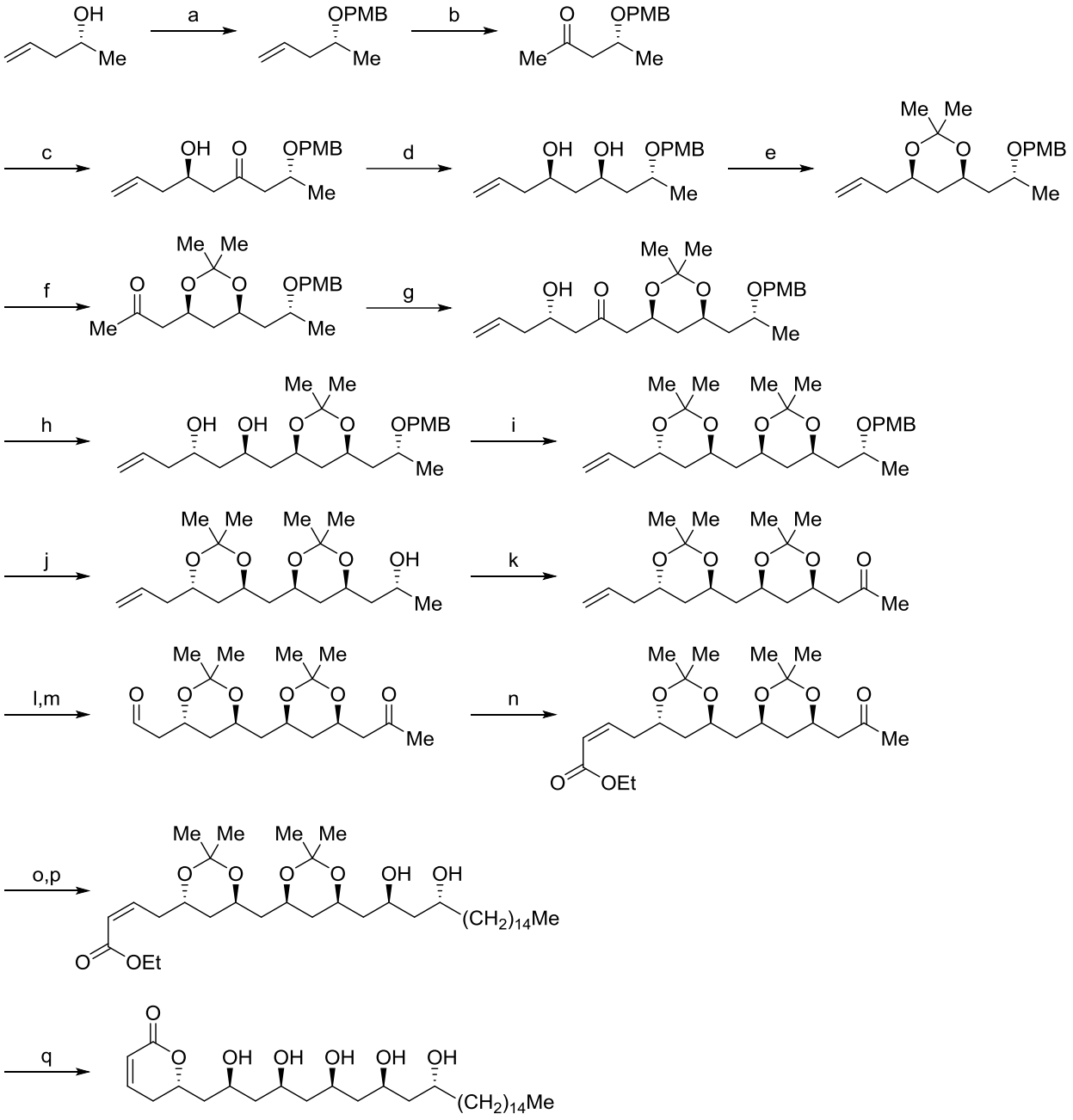


(a) TsCl, Et_3N, DMAP, CH_2Cl_2, 0 °C to rt, 3 h; (b) Li_2CuCl_4, vinylmagnesium bromide, THF, -40 °C, 3h.



(a) TFA, CH_2Cl_2, rt, 3 then $NaHCO_3$, Et_3N; (b) DMP, CH_2Cl_2, rt 2.5 h; (c) L-Selectride, THF, -78 °C, 1 h; (d) TBDPSCl, imidazole, CH_2Cl_2, rt, 14 h; (e) H_2, Pd/C, MeOH, EtOAc, rt, 16 h; (f) TPAP, NMO, CH_2Cl_2, rt, 2 h; (g) **B**, TFA, CH_2Cl_2, rt, 3 h then Et_3N, $NaHCO_3$ (aq); (h) DMP, CH_2Cl_2, rt, 2h; (i) $NaBH_4$, MeOH, -40 °C, 1 h; (j) NaI, acetone, ∝w, 120 °C, 2 h; (k) acryloyl chloride, *i*Pr_2NEt, CH_2Cl_2, 0 °C to rt, 3.5 h; (l) Zn, THF/H_2O = 5:1, 70 °C, 1 h; (m) TBSOTf, 2,6-lutidine, CH_2Cl_2, -78 °C, 1 h; (n) Grubbs **I** (10 mol%), CH_2Cl_2, 45 °C, 2.5 h; (o) O_3, CH_2Cl_2, -78 °C then PPh_3; (p) (1) heptadecan-2-one, Cy_2BCl, Et_3N, pentane, 0 °C, 2 h (2) **C**, pentane, -78 °C to 40 °C, 4 h (3) MeOH/pH7 buffer/H_2O_2, -40 °C to rt, 16 h; (q) $Me_4NBH(OAc)_3$, CH_3CN/MeOH = 1:1, -20 °C, 7 h; (r) HF•CH_3CN, rt, 2.5 h.

D. Dias and coworkers, *Org. Biomol. Chem.* **2015**, *13*, 3575.



(-)-Cryptocaryol A
LLS = 17 steps
TS = 17 steps

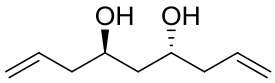
(a) PMB trichloroacetimidate, CSA, CH_2Cl_2, rt; (b) $PdCl_2$, CuCl, O_2, DMF, H_2O, rt; (c) (1) Cy_2BCl, Et_3N, Et_2O, -30 °C (2) 3-butenal, -78 °C; (d) $LiBH_4$, Et_2BOMe, THF, MeOH, -78 °C; (e) 2,2-DMP, CSA, rt; (f)$PdCl_2$, CuCl, O_2, DMF, H_2O, rt; (g) (1) Cy_2BCl, Et_3N, Et_2O, -30 °C (2) 3-butenal, -78 °C; (h) $Me_4NHB(OAc)_3$, MeCN, AcOH, -30 to -20 °C; (i) 2,2-DMP, PPTS, rt; (j) DDQ, CH_2Cl, buffer, 0 °C; (k) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, -78 °C; (l) OsO_4, NMO, *t*-BuOH, THF, H_2O, rt; (m) $NaIO_4$, THF, H_2O; (n) ethyl 2-(bis(*o*-tolyloxy)phosphoryl)acetate, NaH, THF, -78 °C; (o) (1) Cy_2BCl, Et_3N, Et_2O, -30 °C (2) palmitaldehyde, CH_2Cl_2, -78 °C; (p) $Me_4NHB(OAc)_3$, MeCN, AcOH, -30 to -20 °C; (q) CSA, MeOH.

II. General Methods

All reactions were run under an atmosphere of argon under anhydrous conditions unless otherwise indicated. Dichloroethane (DCE), triethylamine (Et_3N), Hünig's Base (iPr$_2$EtN) and dichloromethane (CH_2Cl_2) were distilled over CaH_2. Diethyl ether (Et_2O), tetrahydrofuran (THF), and toluene (PhMe) were distilled over sodium. Pressure tubes (25x150 mm, PYREXPLUS, and 350 mL flask, purchased from Chem Glass) were dried in an oven overnight and cooled under a stream of nitrogen prior to use. Commercially available allyl acetate (Aldrich) was purified by distillation prior to use. Acrolein was purified by distillation prior to use. All other commercial reagents were used directly without further purification unless specified. All analytical thin-layer chromatography (TLC) was carried out using 0.2 mm commercial silica gel plates (DC-Fertigplatten Kieselgel 60 F_{254}). Plates were visualized by treatment with UV, acidic *p*-anisaldehyde stain, ceric ammonium molybdate stain, or $KMnO_4$ stain with gentle heating. Infrared spectra were recorded on a Nicolet 380 FTIR. High-resolution mass spectra (HRMS) were obtained on a Karatos MS9 and are reported as m/z (relative intensity). Accurate masses are reported for the molecular ion ($[M+H]^+$, $[M-H]^+$, or $[M+Na]^+$). Nuclear magnetic resonance spectra (^{1}H NMR and ^{13}C NMR) were recorded with a Varian Gemini (400 MHz or 600 MHz) spectrometer for $CDCl_3$ and $(CD_3)_2O$ solutions and chemical shifts are reported as parts per million (ppm) relative to residual $CHCl_3$ δ_H (7.26 ppm), $CDCl_3$ δ_C (77.0 ppm), CD_3OD δ_H (4.87 ppm), CD_3OD δ_C (49.0 ppm) respectively, as internal standards. Coupling constants are reported in hertz (Hz). Optical rotations were measured on an ATAGO AP-300 automatic polarimeter at a path length of 100 mm.

III. Procedure, Characterization Data, and Spectra for Compounds

(4*R*,6*R*)-nona-1,8-diene-4,6-diol (1)



To an oven-dried sealed tube under one atmosphere of argon gas charged with $[Ir(cod)Cl]_2$ (0.672 g, 1.00 mmol, 5 mol%), (*R*)-BINAP (1.25 g, 2.00 mmol, 10 mol%), Cs_2CO_3 (2.61 g, 8.00 mmol, 40 mol%) and 4-chloro-3-nitrobenzoic acid (0.806 g, 4.00 mmol, 20 mol%) was added THF (50 mL) followed by allyl acetate (20.0 g, 200 mmol, 1000 mol%). The reaction mixture was stirred at 90 ºC for 0.5 h before cooling to ambient temperature. 1,3-propanediol (1.52 g, 20.0 mmol, 100 mol%) in THF (50 mL, 0.2 M overall) was added and the reaction mixture was stirred at 100 ºC for 5 days. The reaction mixture was cooled to ambient temperature, filtered through Celite, and excess solvent was removed under reduced pressure. The crude material was dissolved in EtOAc (50 mL) and vigorously stirred. Et_2O (100 mL) was added slowly followed by hexanes (100 mL). The precipitate was filtered through Celite and the solution was concentrated onto silca gel. Column chromatography (SiO_2, EtOAc:hexanes, 1:6 to 1:4 with 0.1% TEA) furnished the title compound (1.68 g, 10.8 mmol, dr = 20:1, ee > 99%) in 54% yield as a pale yellow oil.

TLC (SiO_2): R_f = 0.25 (EtOAc:hexanes, 1:4).

^{1}H NMR: (400 MHz, $CDCl_3$): δ 5.87-5.77 (m, 2H), 5.17-5.15 (m, 2H), 5.13-5.12 (m, 2H), 4.04-3.97 (m, 2H), 2.39 (d, *J* = 3.5 Hz, 2H), 2.30-2.24 (m, 4H), 1.66-1.63 (m, 2H).

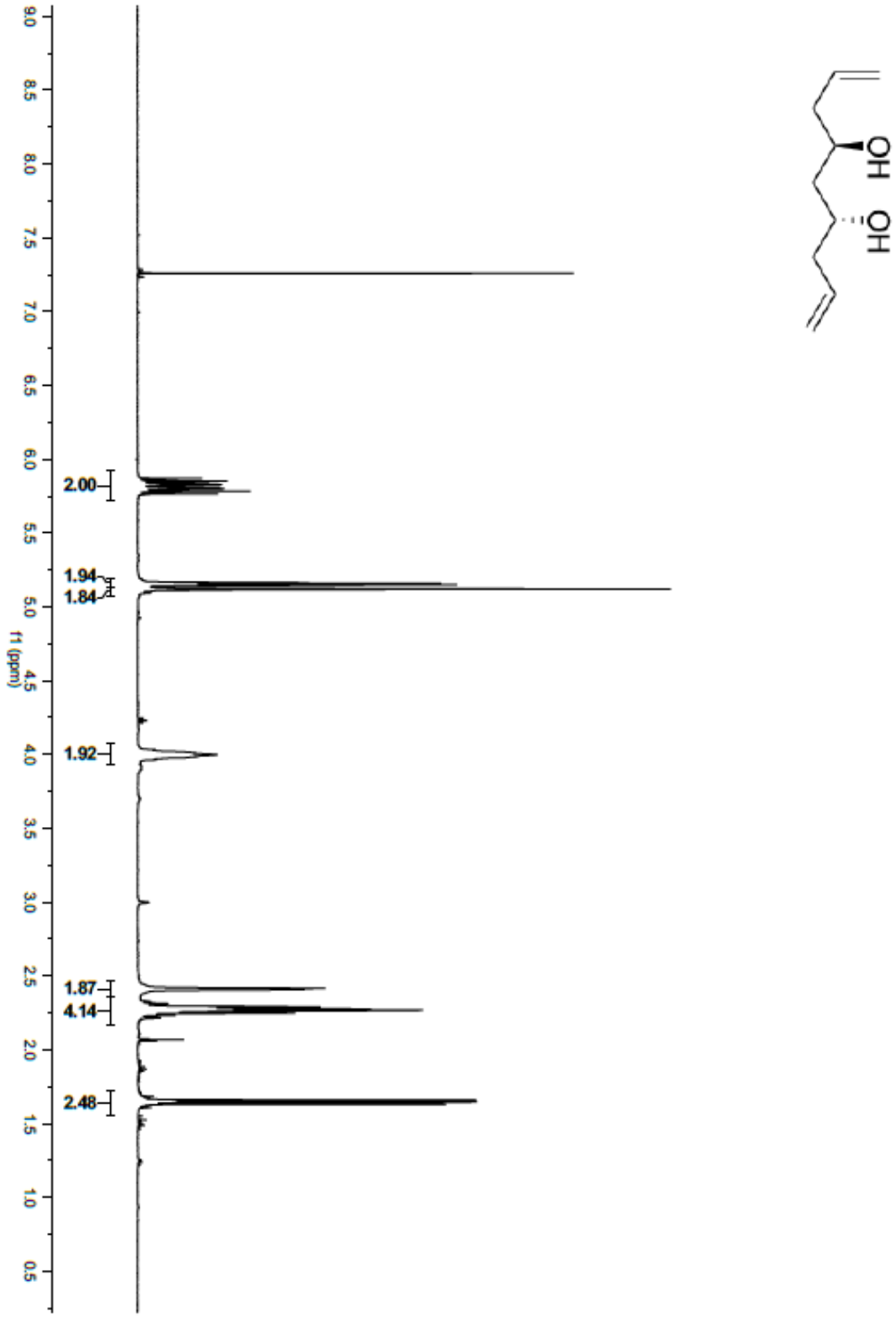
^{13}C NMR: (100 MHz, $CDCl_3$): δ 134.8, 118.4, 68.23, 42.17, 41.63.

FTIR (neat): ν 3333, 2936, 2359, 2342, 1214, 1434, 1325, 1133, 1047.cm^{-1}.

HRMS: (ESI) Calcd. for $C_9H_{16}O_2Na$ $(M+Na)^+$: 179.1048, Found: 179.1042.

HPLC: The enantiomeric excess was determined by chiral HPLC as described by Krische and coworkers.[1]

[1] Lu, Y.; Kim, I. S.; Hassan, A.; Del Valle, D. J.; Krische, M. J. *Angew. Chem. Int. Ed.* **2009**, *48*, 5018.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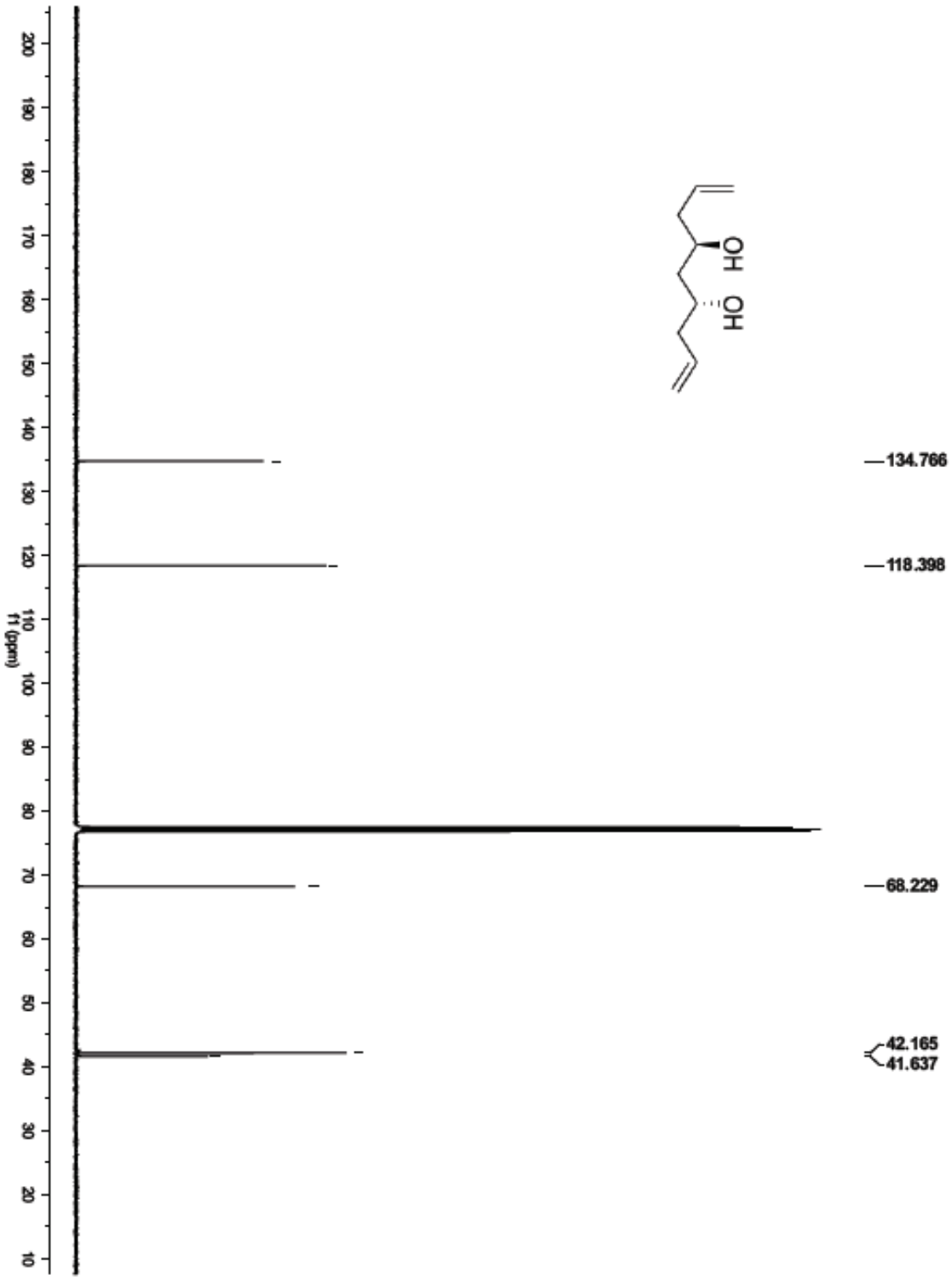
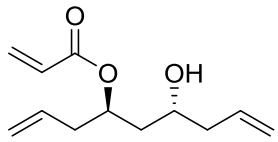
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)
2.00
1.94
1.84
1.92
1.87
4.14
2.48
HO
OH


134.766
118.398
68.229
42.165
41.637
f1 (ppm)

(4*R*,6*R*)-6-hydroxynona-1,8-dien-4-yl acrylate (2)



To a stirred solution of diol **1** (104.1 mg, 0.666 mmol, 100 mol%) in dry MeCN (3.30 mL, 0.2 M) was added $^{i}Pr_2NEt$ (230 μL, 1.33 mmol, 200 mol%) followed by 2-aminoethyl diphenylborinate (14.9 mg, 0.07 mmol, 10 mol%). Acryloyl chloride (90.5 mg, 1.00 mmol, 150 mol%) was added dropwise and the solution was stirred at ambient temperature for 3 h. The reaction mixture was poured into H_2O and EtOAc and extracted with EtOAc (3 x 10 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered through Celite and concentrated by rotary evaporation. The crude material was subjected to flash column chromatography (SiO_2, EtOAc:hexanes 1:9) to afford the title compound (136.4 mg, 0.646 mmol) as a colorless oil in 97% yield.

TLC (SiO_2): R_f = 0.21 (1:9 EtOAc:hexanes)

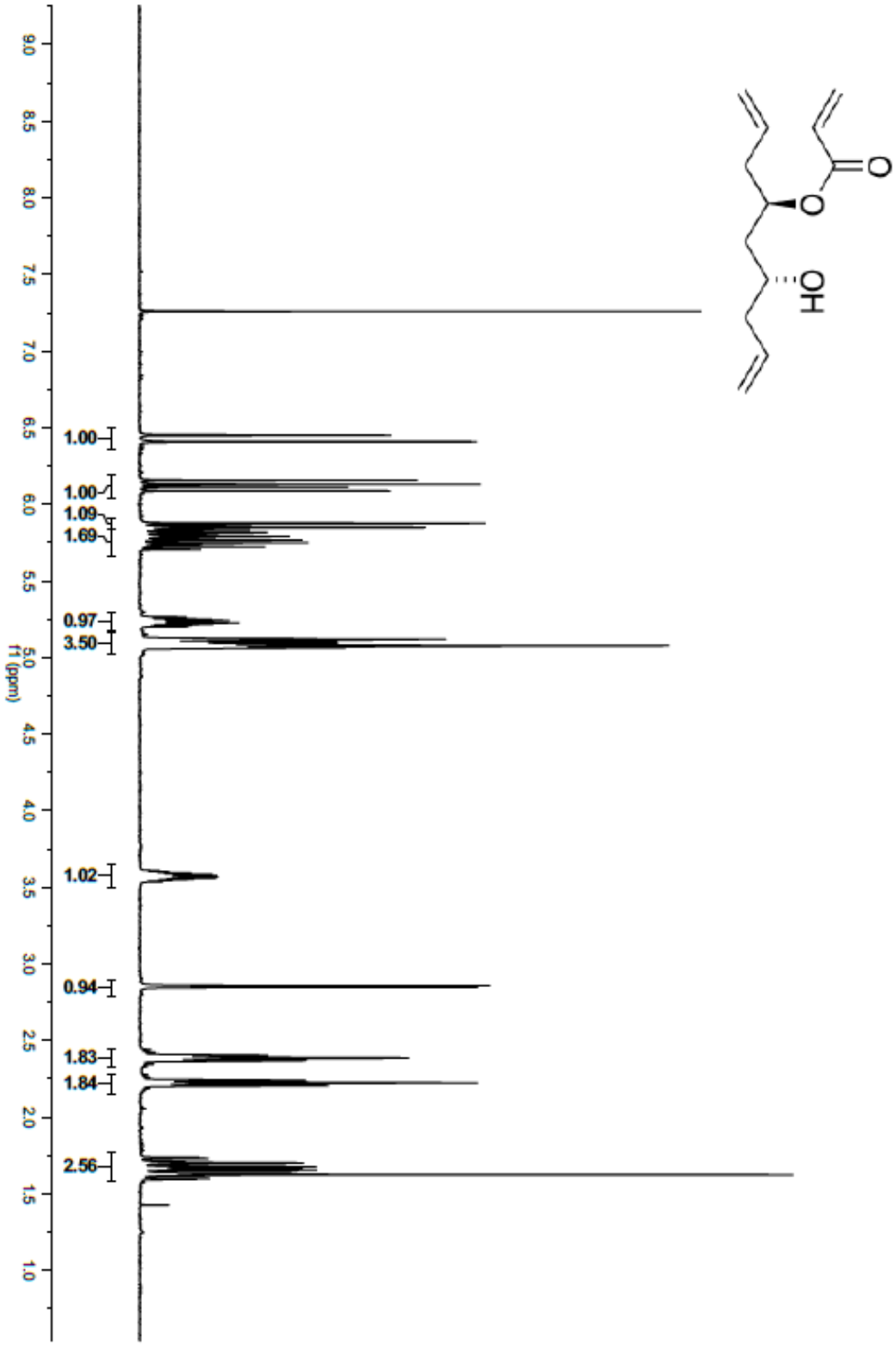
^{1}H NMR: (400 MHz, $CDCl_3$): δ = 6.43 (dd, *J* = 17.3, 1.4 Hz, 1H), 6.13 (dd, *J* = 17.3, 10.4 Hz, 1H), 5.87 (dd, *J* = 10.4, 1.4 Hz, 1H), 5.84-5.71 (m, 2H), 5.27-5.21 (m, 1H), 5.13-5.06 (m, 4H), 3.61-3.54 (m, 1H), 2.83 (d, *J* = 3.8 Hz, 1H), 2.41-2.37 (m, 2H), 2.25-2.21 (m, 2H), 1.74-1.60 (m, 2H).

^{13}C NMR: (100 MHz, $CDCl_3$): δ = 166.9, 134.7, 133.3, 131.4, 128.2, 118.0, 117.6, 70.94, 66.52, 41.59, 41.57, 39.24.

FTIR (neat): ν 3464, 3016, 2970, 1739, 1407, 1366, 1297, 1228, 1217, 1206, 1049 cm^{-1}.

HRMS: (ESI) Calcd. for $C_{12}H_{18}O_3Na$ $(M+Na)^+$: 233.1154, Found: 233.1147

$[\alpha]^{23}_D$: - 28.94° (c = 0.36, $CHCl_3$).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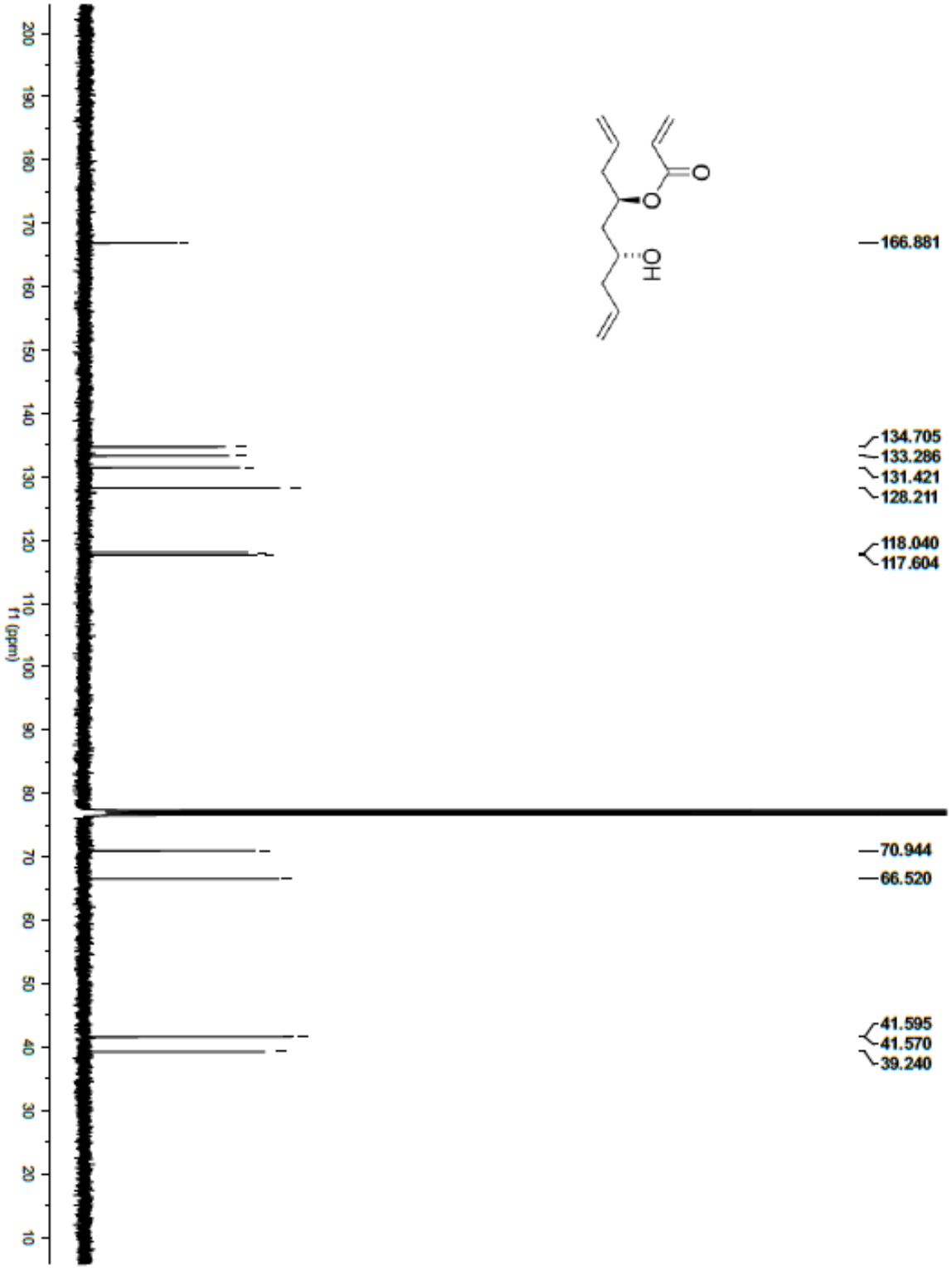
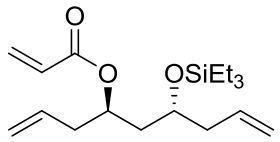
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)
1.00
1.00
1.09
1.69
0.97
3.50
1.02
0.94
1.83
1.84
2.56
O
O
OH


166.881
134.705
133.286
131.421
128.211
118.040
117.604
70.944
66.520
41.595
41.570
39.240
f1 (ppm)

(4*R*,6*R*)-6-((triethylsilyl)oxy)nona-1,8-dien-4-yl acrylate (3)



To a stirred solution of acrylate **2** (136.4 mg, 0.65 mmol, 100 mol%) in dry CH_2Cl_2 (13.0 mL, 0.05 M) was added 2,6-lutidine (150 μL, 1.30 mmol, 200 mol%). The reaction cooled to -78 °C. TESOTf (220 μL, 0.97 mmol, 150 mol%) was added dropwise and the solution was stirred at -78 °C for 1.5 h. The reaction was quenched with saturated NH_4Cl and warmed to ambient temperature. The reaction mixture was poured into separatory funnel containing water and was extracted with CH_2Cl_2 (3 x 15 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered through Celite and concentrated by rotary evaporation. The crude material was subjected to flash column chromatography (SiO_2, EtOAc:hexanes 1:32) to furnish the title compound (198.4 mg, 0.61 mmol) as a colorless oil in 94% yield.

TLC (SiO_2): R_f = 0.42 (1:19 ethyl acetate:hexanes)

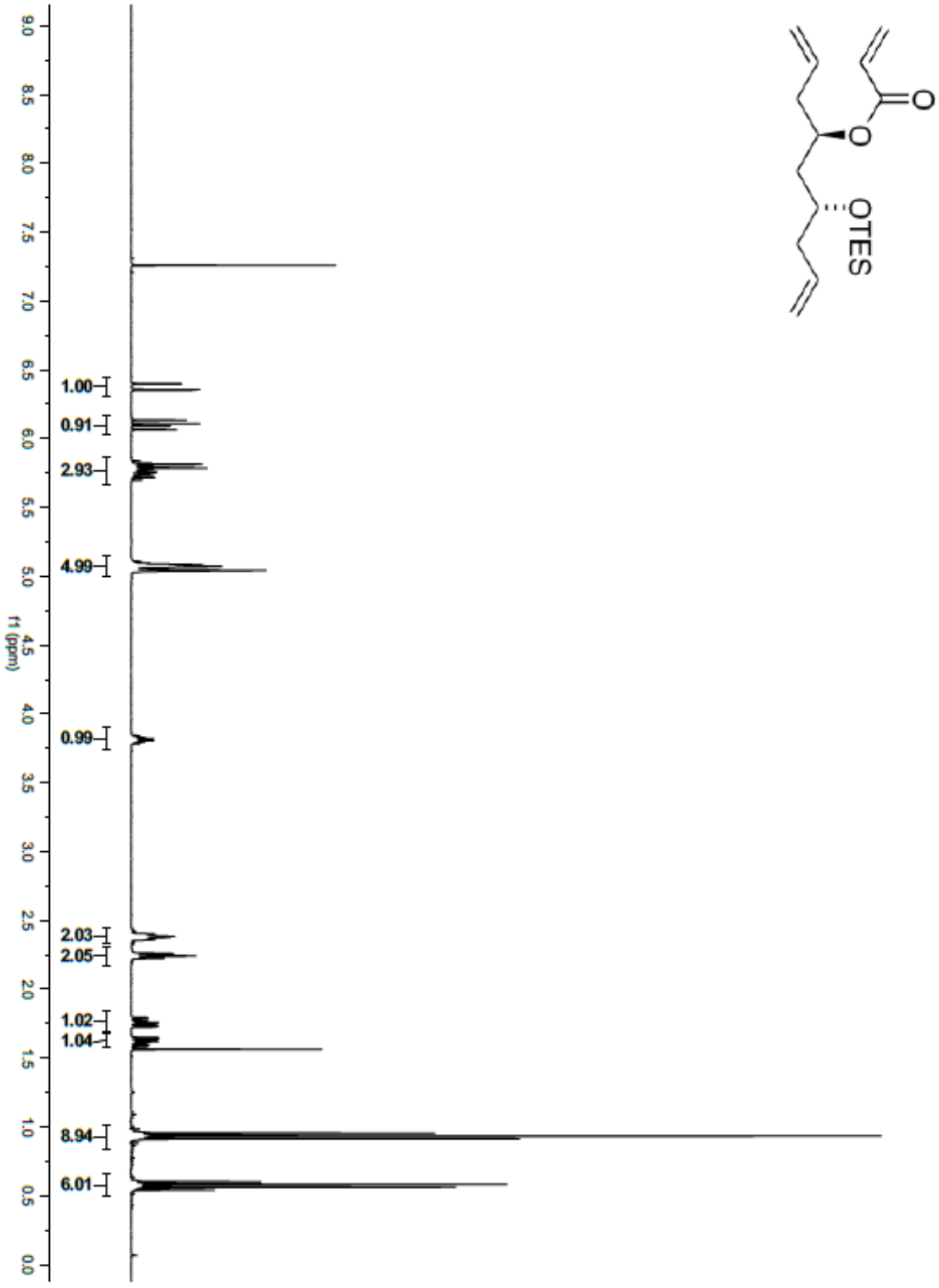
^{1}H NMR: (400 MHz, $CDCl_3$): δ = 6.38 (dd, *J* = 17.3, 1.5 Hz, 1H), 6.10 (dd, *J* = 17.3, 10.4 Hz, 1H), 5.84-5.70 (m 2H), 5.80 (dd, *J* = 10.4, 1.5 Hz, 1H), 5.09-5.03 (m, 5H), 3.84-3.78 (m, 1H), 2.40-2.36 (m, 2H), 2.26-2.22 (m, 2H), 1.76 (ddd, *J* = 14.5, 9.5, 3.2 Hz, 1H), 1.62 (ddd, *J* = 14.5, 9.0, 3.2 Hz, 1H), 0.94 (t, *J* = 7.9 Hz, 9H), 0.57 (q, *J* = 8.0 Hz, 6H).

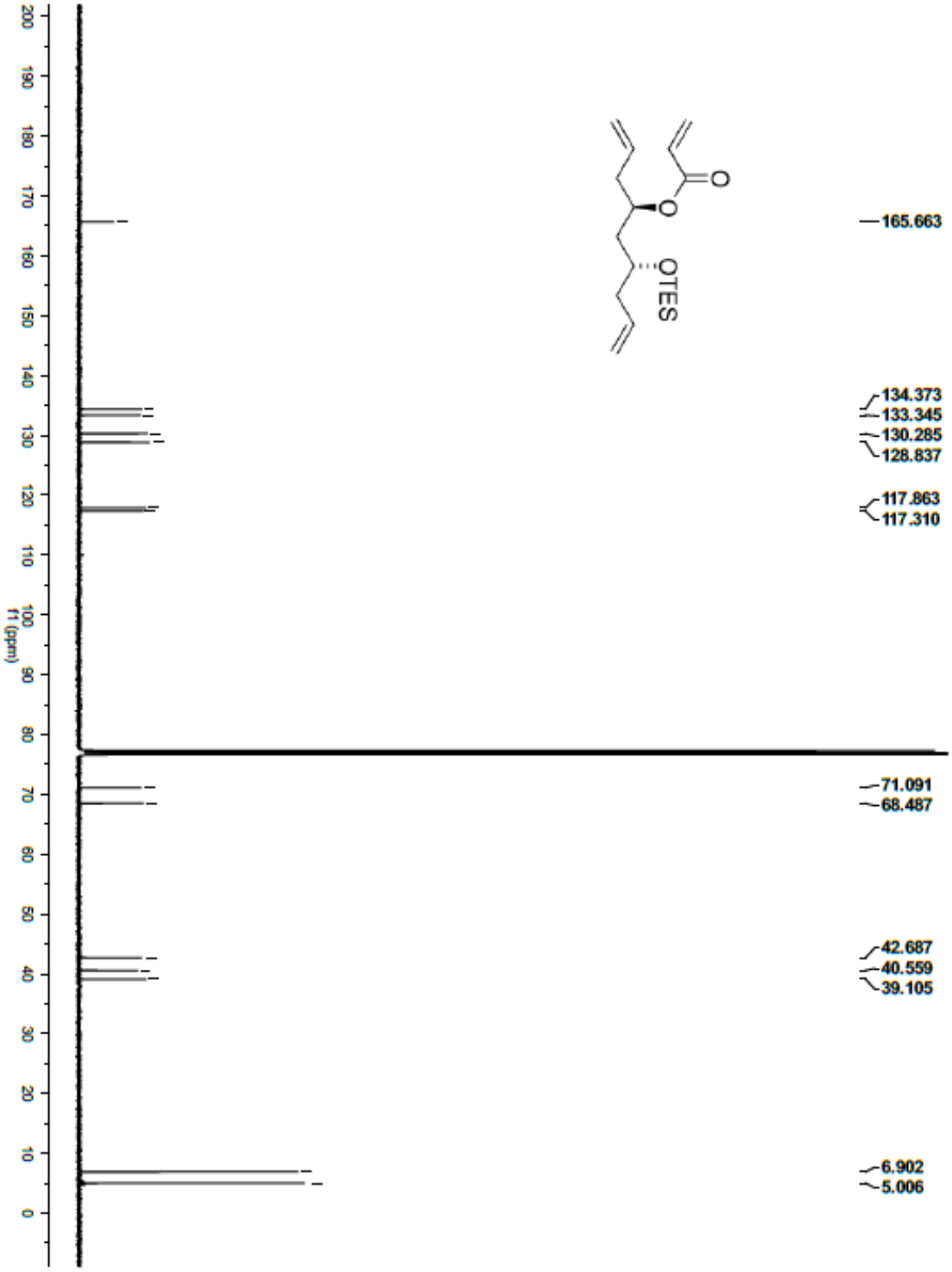
^{13}C NMR: (100 MHz, $CDCl_3$): δ = 165.8, 134.6, 133.5, 130.5, 129.0, 118.0, 117.5, 71.3, 68.7, 42.9, 40.7, 39.3, 7.1, 5.2.

FTIR (neat): ν 3016, 2970, 1739, 1405, 1366, 1229, 1217, 1205, 1092 cm^{-1}.

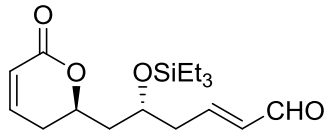
HRMS: (ESI) Calcd. for $C_{18}H_{32}O_3SiNa$ $(M+Na)^+$: 347.2018, Found: 347.2015

$[\alpha]^{23}_D$: -30.87 ° (c = 0.65, $CHCl_3$).


OTES
O
O
1.00
0.91
2.93
4.99
0.99
2.03
2.05
1.02
1.04
8.94
6.01
f1 (ppm)


165.663
134.373
133.345
130.285
128.837
117.863
117.310
71.091
68.487
42.687
40.559
39.105
6.902
5.006
OTES
O
O
f1 (ppm)

(R,E)-6-((R)-6-oxo-3,6-dihydro-2H-pyran-2-yl)-5-((triethylsilyl)oxy)hex-2-enal (4)



A 100 mL round bottom flask equipped with a with a reflux condenser was charged with the Hoveyda-Grubbs II catalyst (62.7 mg, 0.10 mmol, 10 mol%). The flask was purged with argon, sealed with a septum and octafluorotoluene (10 mL) was injected *via* syringe. The solvent was sparged with argon. A solution of **3** (325.5 mg, 1.0 mmol, 100 mol%) and freshly distilled acrolein (100 mg, 1.8 mmol, 180 mol%) in octafluorotoluene (10 mL, 0.05 M overall) was delivered via syringe. The reaction mixture was sparged with argon for an additional 5 minutes. The solution was stirred at room temperature for 10 minutes and gradually heated to 120 °C over 30 minutes. Stirring at 120 °C was continued for 2 h and the mixture was cooled to room temperature. The mixture was concentrated *in vacuo* and the dark oil was subjected to flash column chromatography (SiO_2, EtOAc:hexanes 1:4 to 3:7) to furnish the title compound as an orange oil (269.1 mg, 0.82 mmol) in 82% yield.

TLC (SiO_2): 0.29 (3:7 EtOAc:hexanes).

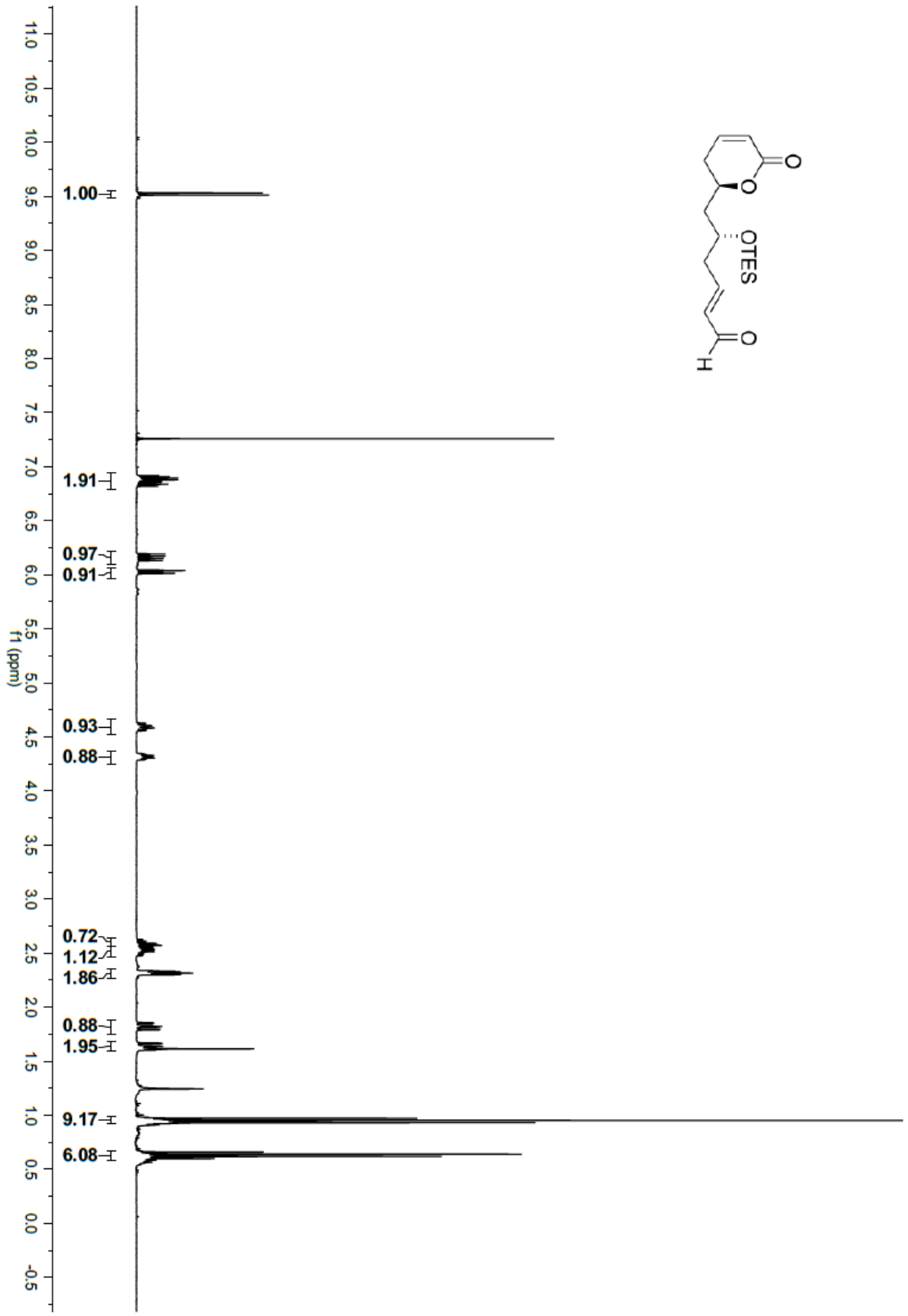
^{1}H NMR: (400 MHz, $CDCl_3$): δ = 9.52 (d, *J*=7.9, 1H), 6.94 – 6.79 (m, 2H), 6.16 (ddt, *J*=15.7, 7.9, 1.3, 1H), 6.03 (dt, *J*=9.8, 1.8, 1H), 4.66 – 4.52 (m, 1H), 4.37 – 4.25 (m, 1H), 2.60 (ddd, *J*=14.4, 6.7, 1.4, 1H), 2.56 – 2.46 (m, 1H), 2.35 – 2.27 (m, 2H), 1.82 (ddd, *J*=14.3, 10.3, 2.4, 1H), 1.63 (ddd, *J*=14.3, 10.1, 2.2, 1H), 0.95 (t, *J*=7.9, 9H), 0.63 (q, *J*=7.8, 6H).

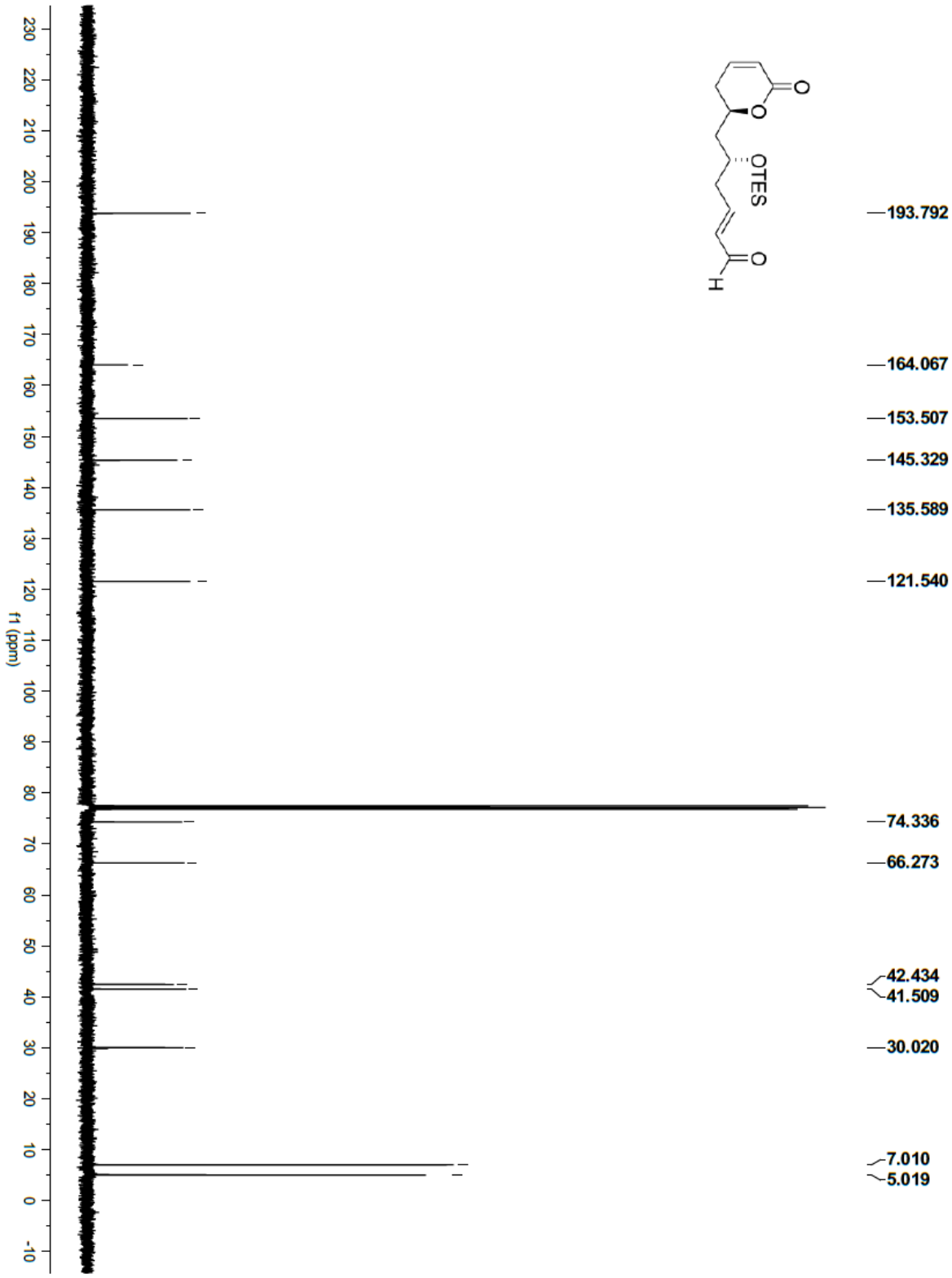
^{13}C NMR: (100 MHz, $CDCl_3$): δ = 193.8, 164.1, 153.5, 145.3, 135.6, 121.5, 74.3, 66.3, 42.4, 41.5, 30.0, 7.0, 5.0.

FTIR (neat): 2954, 2876, 1720, 1689, 1381, 1246 cm^{-1}

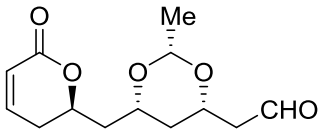
HRMS: (ESI) Calcd. for $C_{17}H_{28}O_4SiNa$ $(M+Na)^+$: 347.16490, Found: 347.16530.

$[\alpha]^{22}_D$: -11.42 ° (c = 1.08, $CHCl_3$).


1.00
1.91
0.97
0.91
0.93
0.88
0.72
1.12
1.86
0.88
1.95
9.17
6.08
f1 (ppm)
OTES
O
H


OTES
O
O
O
H
193.792
164.067
153.507
145.329
135.589
121.540
74.336
66.273
42.434
41.509
30.020
7.010
5.019
f1 (ppm)

2-((4S,6R)-2-methyl-6-(((R)-6-oxo-3,6-dihydro-2H-pyran-2-yl)methyl)-1,3-dioxan-4-yl)acetaldehyde (Fragment A)



A 10 mL screw cap tube was charged with $Bi(NO_3)_3 \cdot 5H_2O$ (14.9 mg, 0.031 mmol, 10 mol%). A solution of **4** (100 mg, 0.308 mmol, 100 mol%) and acetaldehyde (271.3 mg, 6.16 mmol, 2000 mol%) in dichloromethane (3.1 mL, 0.1 M) was added *via* syringe. The mixture was stirred for three days at room temperature. The cloudy mixture was filtered through Celite with the aid of chloroform (10 mL). The filtrate was washed with saturated $NaHCO_3$ (3 x 5 mL), water (5 x 5 mL), brine (1 x 5 mL) and dried (Na_2SO_4). The organic extract was filtered and concentrated *in vacuo*. The yellow oil was dissolved in acetonitrile (5 mL) and washed with pentane (4 x 5 mL) to remove residual triethylsilanol. The acetonitrile layer was concentrated to a viscous yellow oil, providing the aldehyde (71.5 mg, 91% yield) in good purity. Alternatively, the aldehyde could be subjected to flash chromatography (florisil, EtOAc:$CHCl_3$, 1:19 to 2:3) to provide the title compound as a clear viscous oil (45.4 mg, 0.18 mmol) in 58% yield.

TLC (SiO_2): 0.26 (1:4 EtOAc:$CHCl_3$).

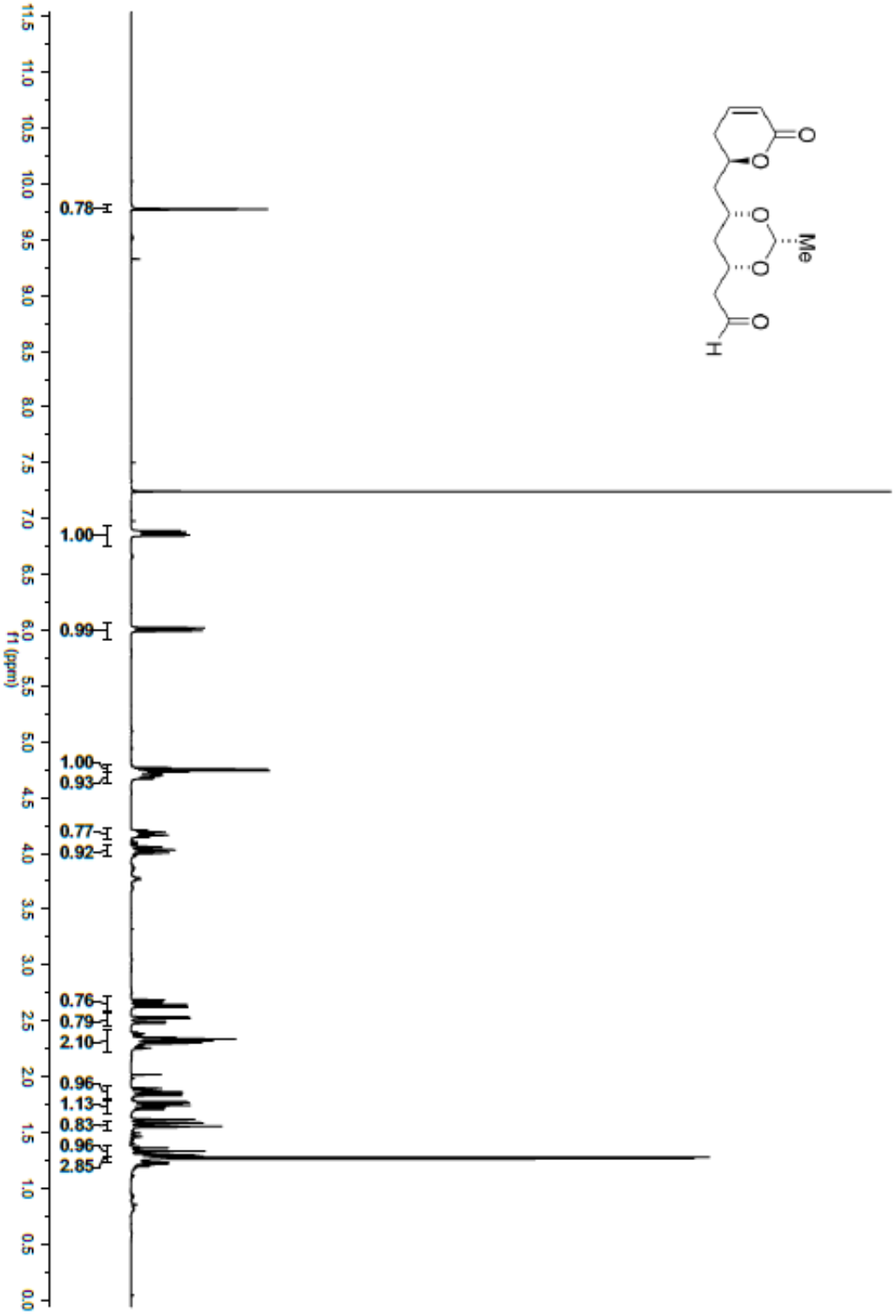
^{1}H NMR: (400 MHz, $CDCl_3$): δ = 9.81 – 9.74 (m, 1H), 6.87 (ddd, *J*=9.7, 5.6, 2.9, 1H), 6.01 (ddd, *J*=9.7, 2.4, 1.2, 1H), 4.75 (q, *J*=5.1, 1H), 4.72 – 4.63 (m, 1H), 4.18 (dddd, *J*=11.2, 7.5, 4.9, 2.5, 1H), 4.07 – 3.97 (m, 1H), 2.66 (ddd, *J*=16.7, 7.5, 2.4, 1H), 2.51 (ddd, *J*=16.7, 4.9, 1.6, 1H), 2.41 – 2.23 (m, 2H), 1.86 (ddd, *J*=14.6, 9.8, 2.4, 1H), 1.74 (ddd, *J*=14.6, 10.1, 2.7, 1H), 1.57 (dt, *J*=12.9, 2.5, 1H), 1.29-1.38 (m, 1H), 1.27 (d, *J*=5.1, 3H).

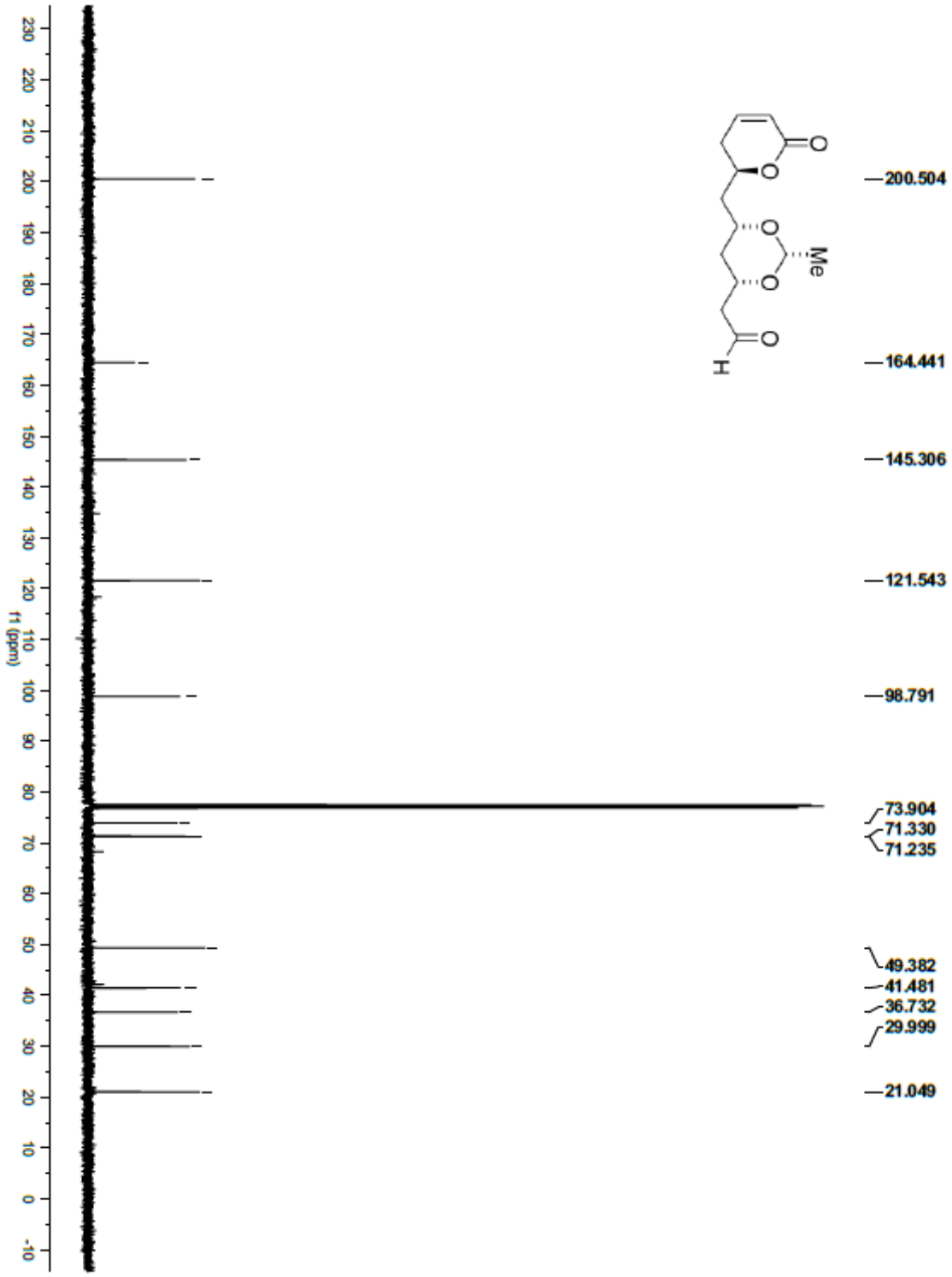
^{13}C NMR: (100 MHz, $CDCl_3$): δ 200.5, 164.4, 145.3, 121.5, 98.8, 73.9, 71.3, 71.2, 49.4, 41.5, 36.7, 30.0, 21.1.

FTIR (neat): 2918, 1716, 1380, 1342, 1248, 1133, 1096 cm^{-1}

HRMS: (ESI) Calcd. for $C_{13}H_{18}O_5Na$ $(M+Na)^+$: 277.10460, Found: 277.10440.

$[\alpha]^{22}_D$: +16.49 ° (c = 0.93, $CHCl_3$).


0.78
1.00
0.99
1.00
0.93
0.77
0.92
0.76
0.79
2.10
0.96
1.13
0.83
0.96
2.85
f1 (ppm)
Me


f1 (ppm)
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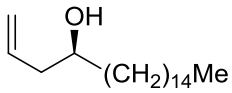
164.441
145.306
121.543
98.791
73.904
71.330
71.235
49.382
41.481
36.732
29.999
21.049
Me
H

(*S*)-nonadec-1-en-4-ol (5)



Cetyl alcohol (4.849 g, 20.0 mmol, 100 mol%), $[Ir(cod)Cl]_2$ (336.0 mg, 0.50 mmol, 2.5 mol%), (*R*)-BINAP (622.7 mg, 1.00 mmol, 5 mol%), 4-chloro-3-nitrobenzoic acid (403.1 mg, 2.00 mmol, 10 mol%), and Cs_2CO_3 (1.303 g, 4.00 mmol, 20 mol%) were added to a flame-dried pressure tube. The solution was sparged with Ar for 5 minutes. Dry THF (100 mL, 0.2 M) was added followed by freshly distilled allyl acetate (4.4 mL, 40.0 mmol, 200 mol%) and the vessel was sealed. The reaction mixture was heated to 100 °C for 24 h. The reaction mixture was allowed to cool to room temperature, at which point the reaction mixture was filtered through a plug of Celite with the aid of THF. The volatiles were removed by *in vacuo* and the crude material was subjected to column chromatography (SiO_2, Et_2O:hexanes 1:19) to furnish the title compound (4.091 g, 14.4 mmol) as a waxy white solid in 72% yield.

TLC (SiO_2): R_f = 0.20 (1:19 ethyl acetate:hexanes)

^{1}H NMR: (400 MHz, $CDCl_3$): δ 5.85-5.78 (m, 1H), 5.16-5.14 (m, 1H), 5.13-5.11 (m, 1H), 3.65-3.63 (m, 1H), 2.30-2.27 (m, 1H), 2.17-2.12 (m, 1H), 1.56-1.54 (m, 1H), 1.47-1.43 (m, 3H), 1.34-1.23 (m, 25H), 0.89-0.86 (m, 3H).

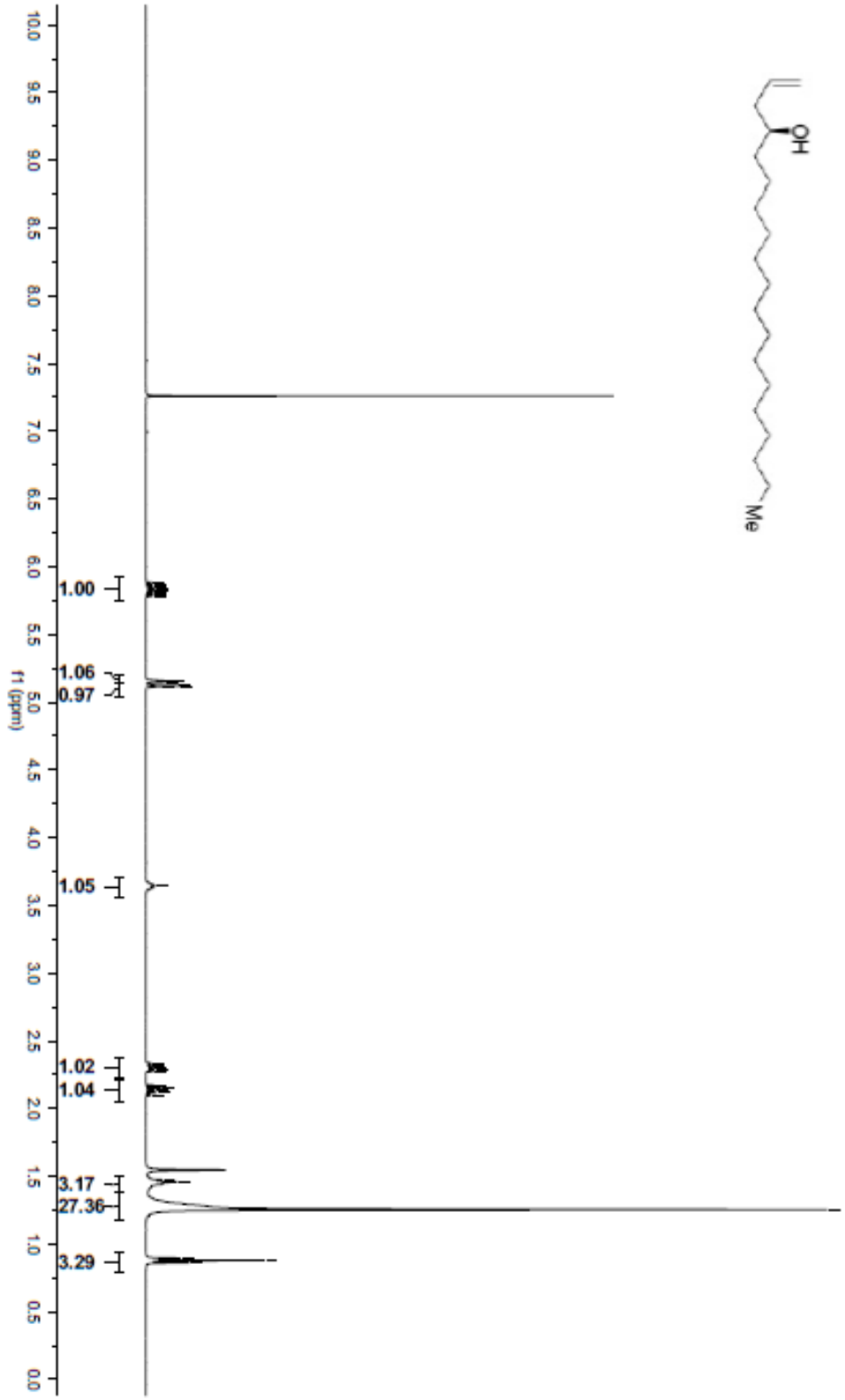
^{13}C NMR: (100 MHz, $CDCl_3$): δ 135.1, 118.2, 70.8, 42.1, 37.0, 32.1, 29.8, 29.8, 29.5, 25.8, 22.9, 14.3.

FTIR (neat): ν 3319, 2915, 2849, 2360, 1636, 1470 cm^{-1}.

HRMS: (CI) Calcd. for $C_{19}H_{39}O$ $(M+H)^+$: 283.3001, Found: 283.3000

MP: 47 - 48 °C

$[\alpha]^{23}_D$: -18.33 ° (c = 0.36, $CHCl_3$).


10.0
9.5
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
f1 (ppm)
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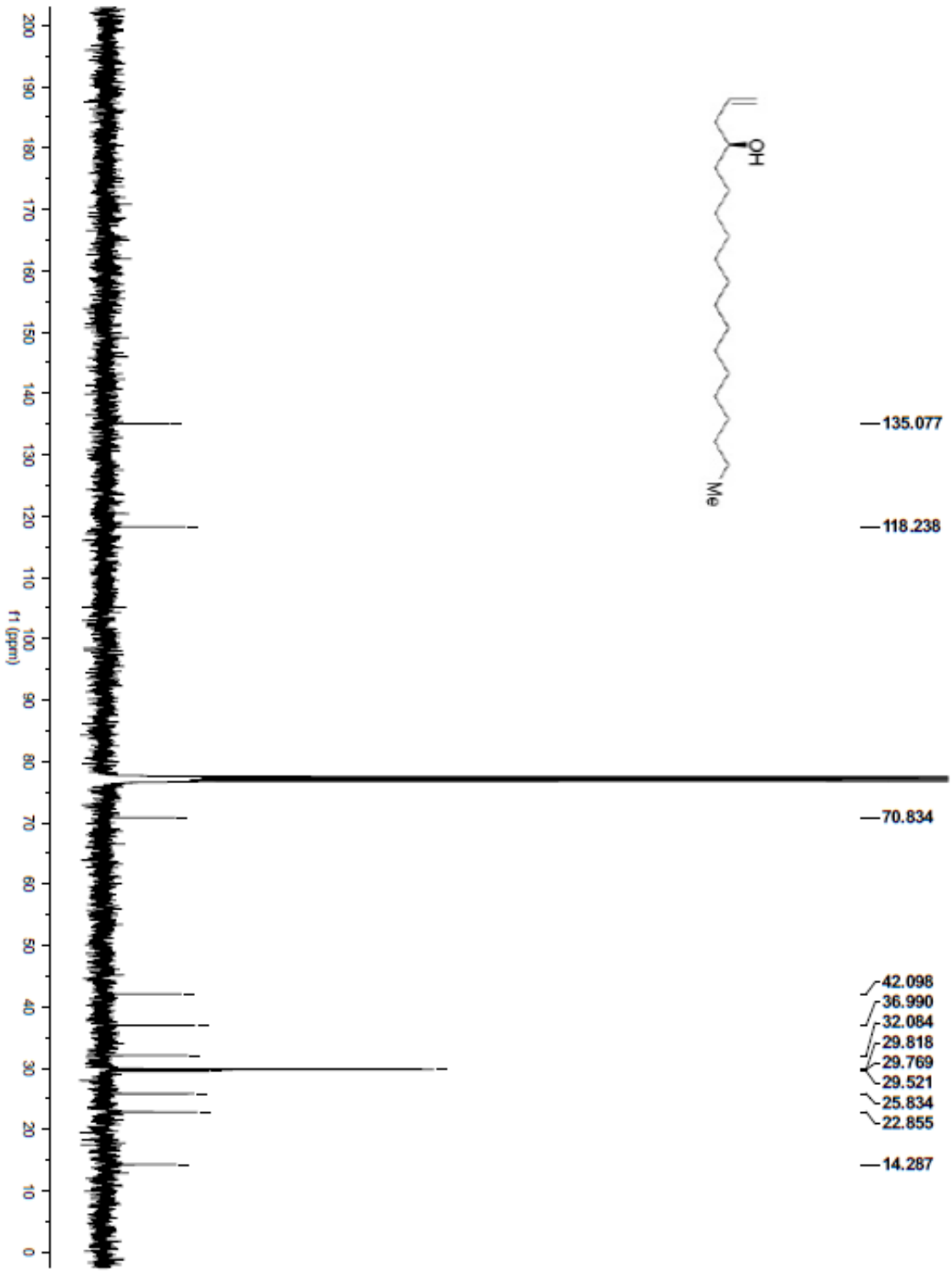
1.06
0.97
1.05
1.02
1.04
3.17
27.36
3.29
OH
Me


f1 (ppm)
OH
Me
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118.238
70.834
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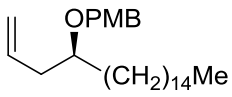
36.990
32.084
29.818
29.769
29.521
25.834
22.855
14.287

(*S*)-1-methoxy-4-((nonadec-1-en-4-yloxy)methyl)benzene (6)



To a solution of alcohol **5** (1.009 g, 3.57 mmol, 100 mol%) in dry toluene (24 mL, 0.15 M) was added 4-methoxybenzyl-2,2,2-trichloroacetimidate (1.514 g, 5.36 mmol, 150 mol%) followed by $La(OTf)_3$ (0.1046 g, 0.179 mmol, 5 mol%). The solution was stirred at ambient temperature overnight. The reaction mixture was transferred to a separatory funnel containing H_2O and hexanes. The aqueous phase was extracted with hexanes (5 x 35 mL) and the combined organic extracts were dried (Na_2SO_4), filtered and concentrated *in vacuo* onto silica gel. The residue was subjected to column chromatography (SiO_2, Et_2O:hexanes 1:19) to furnish the title compound (1.333 g, 3.32 mmol) as a colorless oil in 93% yield.

TLC (SiO_2): R_f = 0.36 (1:19 Et_2O:hexanes)

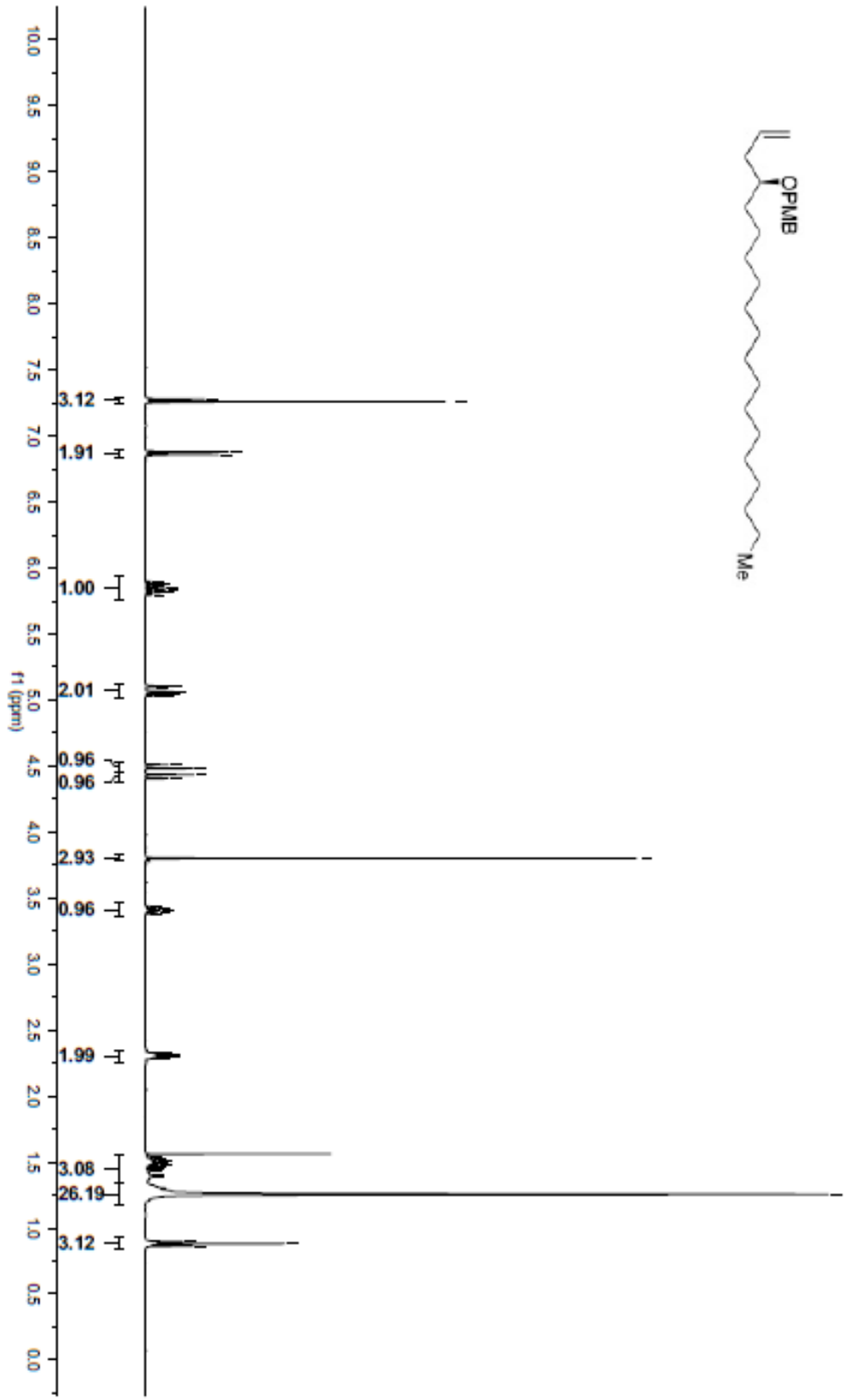
^{1}H NMR: (400 MHz, $CDCl_3$): δ 7.29-7.25 (m, 2H), 6.89-6.85 (m, 2H), 5.85 (ddt, *J* = 17.2, 10.1, 7.1 Hz, 1H), 5.11-5.03 (m, 2H), 4.46 (q, *J* = 15.2 Hz, 2H), 3.80 (s, 3H), 3.41 (qd, *J* = 6.0, 5.5 Hz, 1H), 2.34-2.28 (m, 2H), 1.54-1.46 (m, 2H), 1.34-1.21 (m, 26H), 0.88 (t, *J* = 6.9 Hz, 3H).

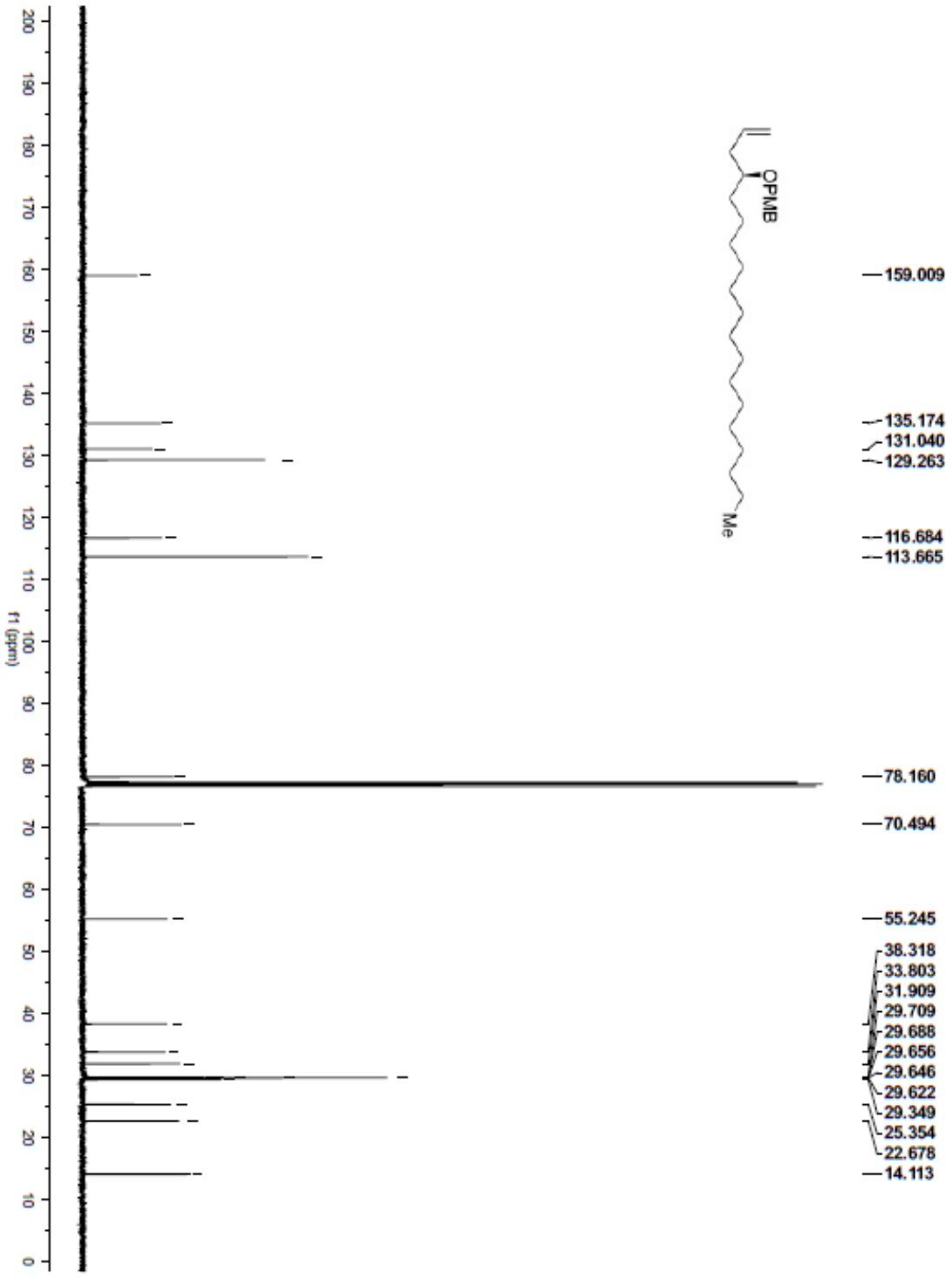
^{13}C NMR: (100 MHz, $CDCl_3$): δ 159.0, 135.2, 131.0, 129.3, 116.7, 113.7, 78.2, 70.5, 55.3, 38.3, 33.8, 31.9, 29.7, 29.7, 29.7, 29.7, 29.6, 29.4, 25.4, 22.7, 14.1.

FTIR (neat): ν 2924, 2853, 1513, 1247, 1215, 1037 cm^{-1}.

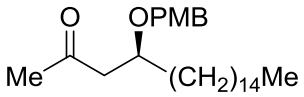
HRMS: (ESI) Calcd. for $C_{27}H_{46}O_2Na$ $(M+Na)^+$: 425.3396, Found: 425.3372

$[\alpha]^{24}_D$: -3.62 ° (c = 0.57, $CHCl_3$).


OPMB
Me
3.12
1.91
1.00
2.01
0.96
0.96
2.93
0.96
1.99
3.08
26.19
3.12
f1 (ppm)


OPMB
Me
159.009
135.174
131.040
129.263
116.684
113.665
78.160
70.494
55.245
38.318
33.803
31.909
29.709
29.688
29.656
29.646
29.622
29.349
25.354
22.678
14.113
f1 (ppm)

(S)-4-((4-methoxybenzyl)oxy)nonadecan-2-one (Fragment B)



The following procedure was performed in the dark. To a sealed tube was added Pd(Quinox)Cl_2 (7.1 mg, 0.0159 mmol, 5 mol%) and $AgSbF_6$ (16.2 mg, 0.0472 mmol, 12.5 mol%) followed by CH_2Cl_2 (2.8 mL). The solution was stirred at ambient temperature for 10 minutes, at which point ^{t}BuOOH (70% w/w, 0.64 mL, 4.54 mmol, 1200 mol%) was added and the reaction vessel was transferred to an ice water bath. After 10 minutes, PMB ether **6** (152.2 mg, 0.378 mmol, 100 mol%) in CH_2Cl_2 (1.0 mL, 0.1 M overall) was added dropwise. The reaction was warmed to ambient temperature and was allowed to stir for 16 h. The reaction mixture was diluted with hexanes and was washed with saturated $Na_2S_2O_3$ (2 x 10 mL). The aqueous portion was then extracted with hexanes (2 x 15 mL) and the combined organic extracts were dried (Na_2SO_4), filtered and concentrated *in vacuo*. The residue was subjected to column chromatography (SiO_2, Et_2O:$CHCl_3$ 1:99) to furnish the title compound (112.3 mg, 0.27 mmol) as a colorless oil in 71% yield.

TLC (SiO_2): R_f = 0.45 (1:4 EtOAc:hexanes)

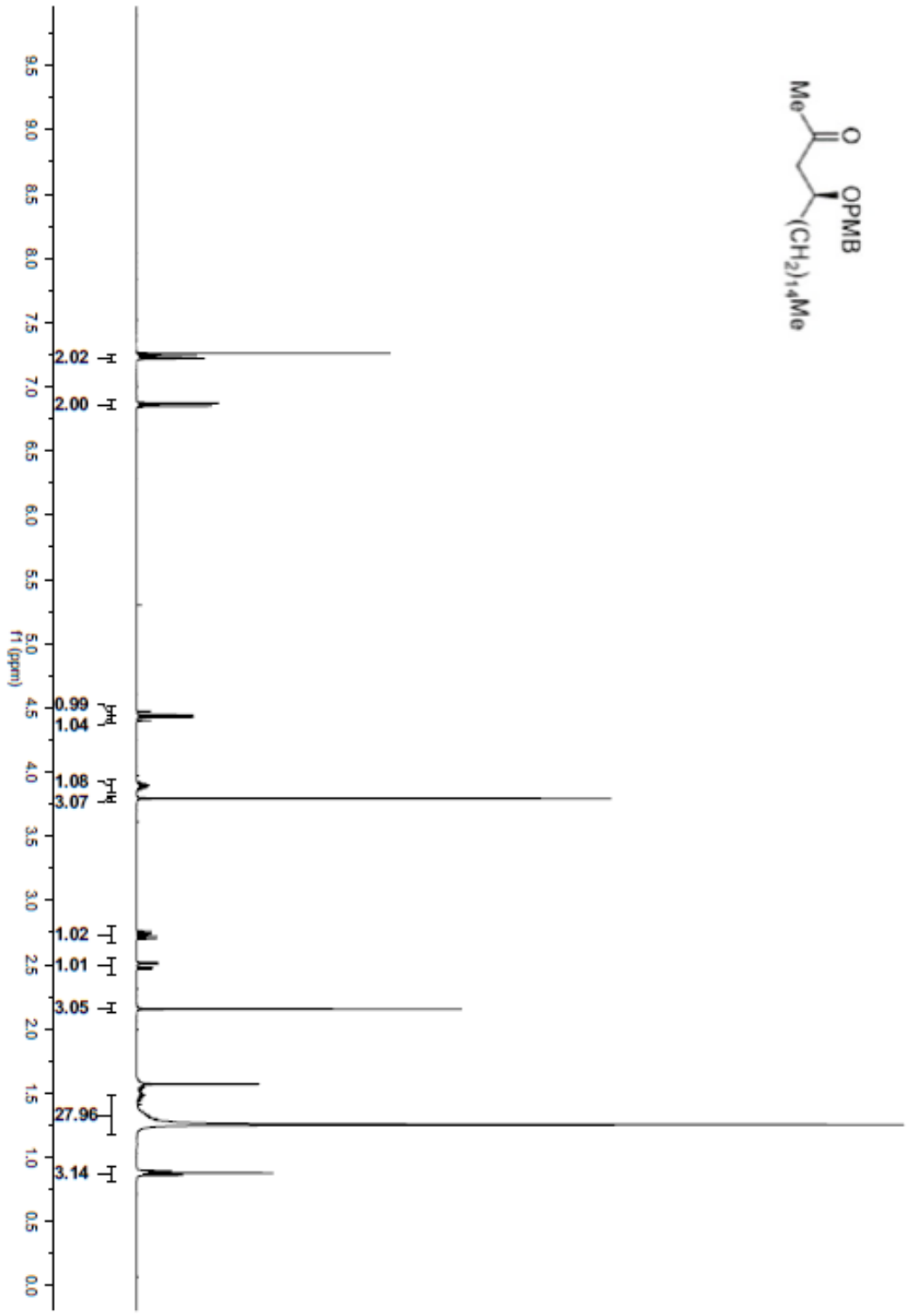
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.23 (d, *J*=8.7, 2H), 6.86 (d, *J*=8.7, 2H), 4.46 (d, *J*=10.9, 1H), 4.41 (d, *J*=10.9, 1H), 3.94 – 3.84 (m, 1H), 3.79 (s, 3H), 2.73 (dd, *J*=15.7, 7.6, 1H), 2.49 (dd, *J*=15.8, 4.8, 1H), 2.15 (s, 3H), 1.25 (s, 28H), 0.88 (t, *J*=6.9, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 207.9, 159.1, 130.6, 129.4, 113.7, 75.3, 71.1, 55.3, 55.2, 48.6, 34.3, 31.9, 31.2, 31.2, 29.7, 29.6, 29.4, 25.2, 22.7, 14.1.

FTIR (neat): 2922, 2852, 1717, 1613, 1513, 1465, 1356, 1249 cm^{-1}

HRMS: (ESI) Calcd. for $C_{27}H_{46}O_2Na$ $(M+Na)^+$: 425.3396, Found: 425.3372

$[\alpha]^{24}_D$: +6.03 ° (c = 0.94, $CHCl_3$).


Me
O
OPMB
(CH2)14Me
f1 (ppm)
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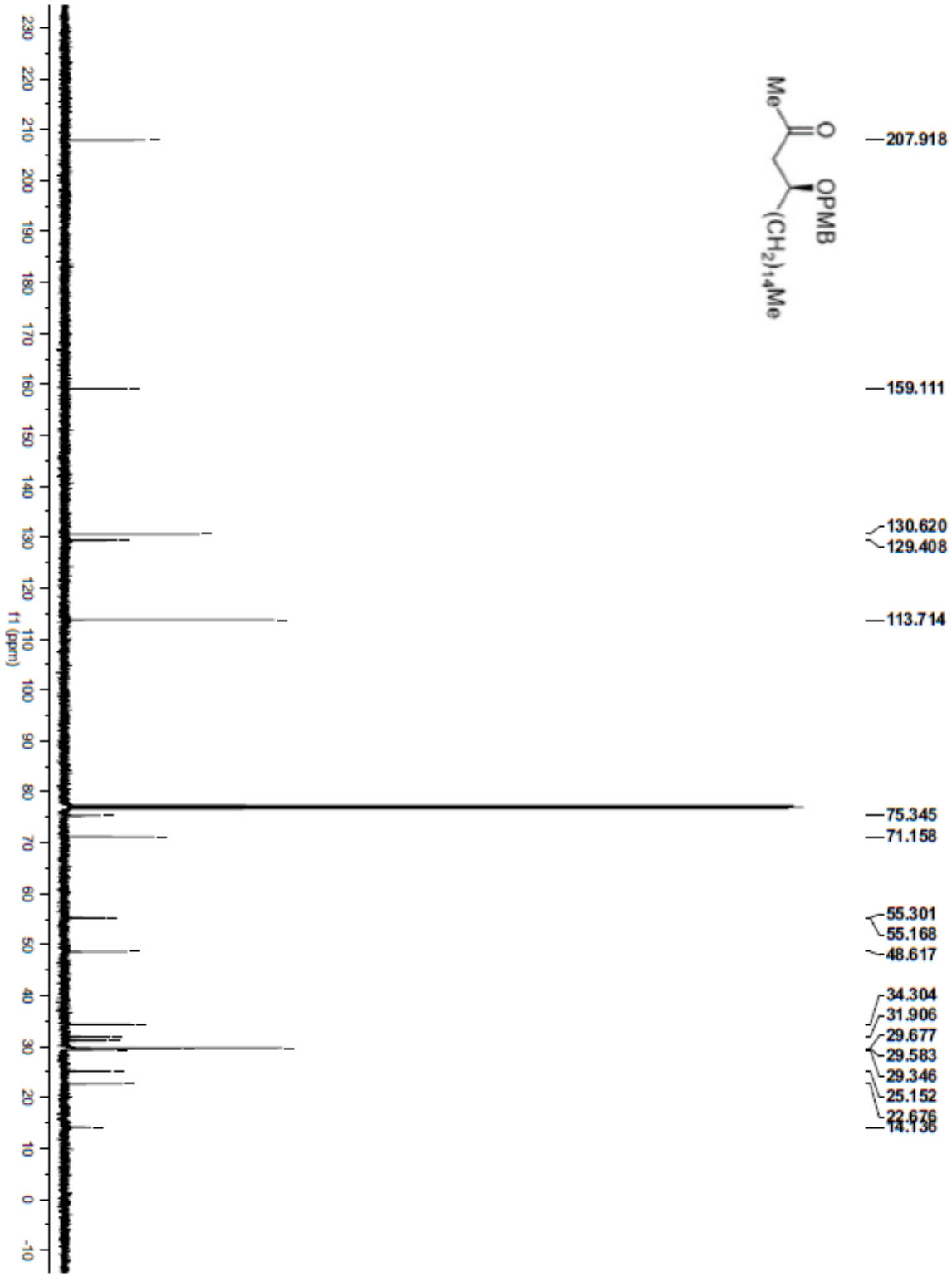
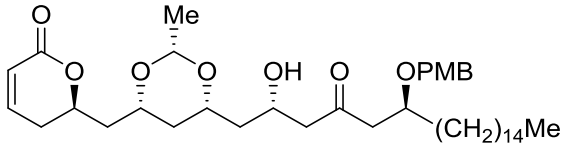
2.00
0.99
1.04
1.08
3.07
1.02
1.01
3.05
27.96
3.14


f1 (ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Me
O
OPMB
(CH2)14Me
207.918
159.111
130.620
129.408
113.714
75.345
71.158
55.301
55.168
48.617
34.304
31.906
29.677
29.583
29.346
25.152
22.676
14.136

(6R)-6-(((4R,6R)-6-((2S,6S)-2-hydroxy-6-((4-methoxybenzyl)oxy)-4-oxohenicosyl)-2-methyl-1,3-dioxan-4-yl)methyl)-5,6-dihydro-2H-pyran-2-one(7)



To a 50 mL round bottom flask was charged with ketone **Fragment B** (205.7 mg, 0.491 mmol, 125 mol%) was added diethyl ether (9.0 mL, 0.05 M). The solution was sparged with argon and cooled to -30 °C. Dicyclohexylchloroborane (208.9, 0.983 mmol, 250 mol%) was injected neat via syringe and the mixture was stirred vigorously for 15 minutes. Triethylamine (107.9 mg, 1.06 mmol, 270 mol%) was injected via syringe and the cloudy mixture was allowed to stir for 30 minutes. The mixture was cooled to -78 °C and a solution of aldehyde **Fragment A** (100 mg, 0.393 mmol, 100 mol%) in diethyl ether (800 μL) was added dropwise with stirring. The mixture was allowed to stir for 1.5 h, then warmed to 0 °C. A solution of methanol, pH 7 buffer and 30% hydrogen peroxide (1:1:1, 6 mL) was added. The biphasic mixture was allowed to stir overnight, washed with saturated $NaHCO_3$ (3 x 10 mL), brine (1 x 10 mL) and dried (Na_2SO_4). The organic extract was filtered and concentrated *in vacuo*. The clear residual oil was subjected to flash column chromatography (SiO_2, acetone:hexanes 1:9 to 1:4) to furnish the title compound as a clear, colorless oil (168.5 mg, 0.25 mmol) in 64% yield.

TLC (SiO_2): R_f = 0.31 (1:2 acetone:hexanes)

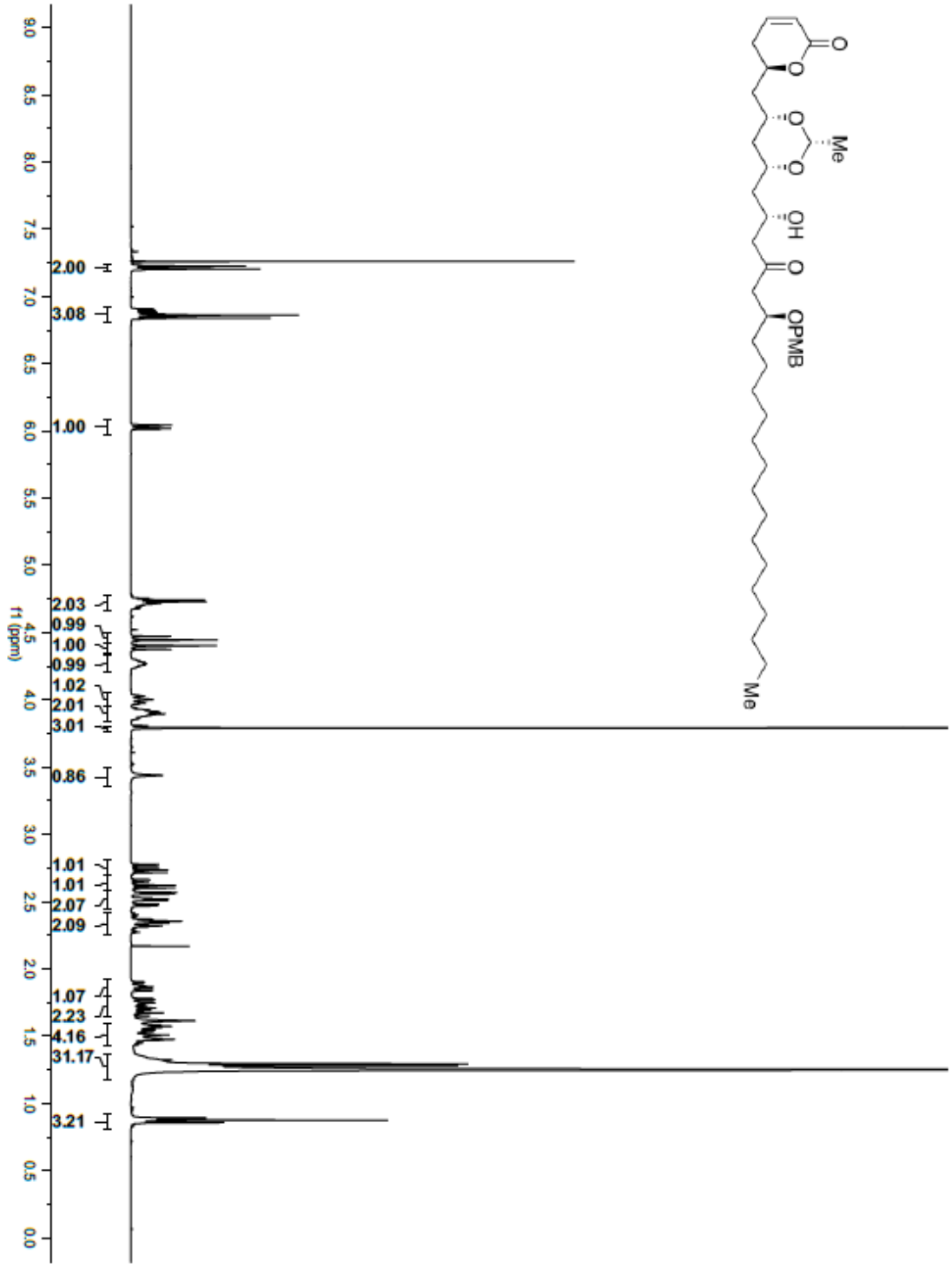
^{1}H NMR: (400 MHz, $CDCl_3$): δ = 7.24 – 7.18 (m, 2H), 6.92 – 6.81 (m, 3H), 6.03 (ddd, *J*=9.7, 2.4, 1.1, 1H), 4.78 – 4.66 (m, 2H), 4.46 (d, *J*=10.9, 1H), 4.39 (d, *J*=10.9, 1H), 4.27 (dq, *J*=12.0, 3.9, 1H), 4.00 (ddd, *J*=13.5, 3.9, 1.6, 1H), 3.95 – 3.84 (m, 2H), 3.79 (s, 3H), 3.44 (s, 1H), 2.75 (dd, *J*=15.8, 7.9, 1H), 2.63 (dd, *J*=16.9, 7.8, 1H), 2.52 (ddd, *J*=18.4, 16.4, 4.5, 2H), 2.42 – 2.25 (m, 2H), 1.87 (ddd, *J*=14.6, 9.7, 2.3, 1H), 1.80 – 1.65 (m, 2H), 1.60 – 1.42 (m, 3H), 1.36 – 1.18 (m, 31H), 0.87 (t, *J*=6.9, 3H).

^{13}C NMR: (100 MHz, $CDCl_3$): δ 209.8, 164.5, 159.3, 145.3, 130.7, 129.5, 121.6, 113.9, 98.5, 75.6, 75.5, 74.0, 71.5, 71.4, 66.5, 55.4, 50.9, 48.8, 41.5, 37.0, 34.4, 32.1, 30.0, 29.9, 29.8, 29.8, 29.5, 25.3, 22.8, 21.2, 14.3.

FTIR (neat): 3529, 3432, 2923, 2853, 1810, 1713, 1613, 1587, 1514, 1487, 1465, 1380, 1342, 1248, 1171, 1138, 1094, 1058, 1035 cm^{-1}.

HRMS: (ESI) Calcd. for $C_{40}H_{64}O_8Na$ $(M+Na)^+$: 695.4499, Found: 695.4495.

$[\alpha]^{22}_D$: -11.81° (c = 0.57, $CHCl_3$).


f1 (ppm)
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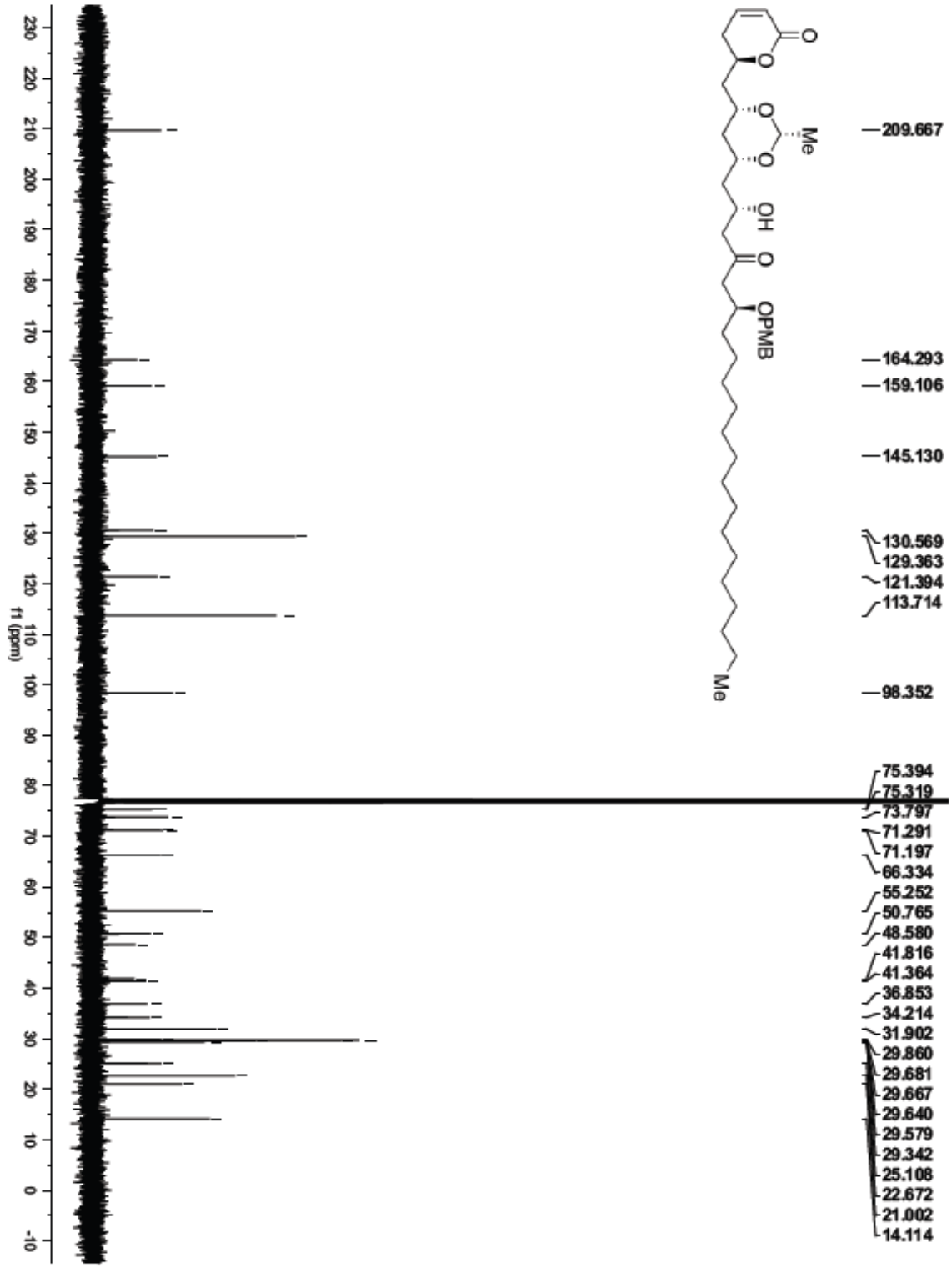
1.00
2.03
0.99
1.00
0.99
1.02
2.01
3.01
0.86
1.01
1.01
2.07
2.09
1.07
2.23
4.16
31.17
3.21
Me
OH
O
OPMB
Me


209.667
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159.106
145.130
130.569
129.363
121.394
113.714
98.352
75.394
75.319
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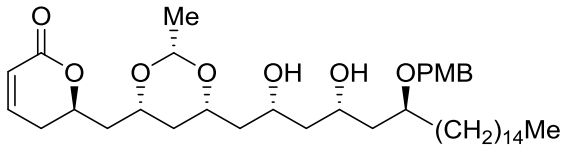
71.197
66.334
55.252
50.765
48.580
41.816
41.364
36.853
34.214
31.902
29.860
29.681
29.667
29.640
29.579
29.342
25.108
22.672
21.002
14.114
f1 (ppm)
OPMB
OH
Me
Me

(6R)-6-(((4R,6R)-6-((2R,4S,6S)-2,4-dihydroxy-6-((4-methoxybenzyl)oxy)henicosyl)-2-methyl-1,3-dioxan-4-yl)methyl)-5,6-dihydro-2H-pyran-2-one (8)



To a solution of ketone **7** (67.2 mg, 0.100 mmol, 100 mol%) in THF:MeOH (4:1, 0.1 M, 1 mL) at -78 °C under an atmosphere of argon was added diethylmethoxy borane (200 uL, 1.0 M in THF, 0.2 mmol, 200 mol%). The mixture was allowed to stir for 30 minutes, at which point $NaBH_4$ (220 uL, 0.5 M in diglyme, 0.110 mmol, 110 mol%) was added. After stirring for 3 hours at -78 °C, the mixture was warmed to 0 °C and diluted with diethyl ether (10 mL) and stirred vigorously with a mixture of methanol, pH 7 buffer and 30% hydrogen peroxide (1.5 mL, 1:1:1) as the solution warmed to room temperature. After 1 h at room temperature, the organic phase was washed with saturated $NaHCO_3$ (3 x 5 mL), brine (1 x 5 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo* to provide the title compound as a yellow oil (63.2 mg, 0.094 mmol) in 94% yield.

TLC (SiO_2): R_f = 0.24 (3:7 acetone:hexanes)

^{1}H NMR: (400 MHz, $CDCl_3$): δ = 7.29 – 7.23 (m, 2H), 6.94 – 6.80 (m, 3H), 6.03 (ddd, *J*=9.7, 2.4, 1.1, 1H), 4.76 (q, *J*=5.2, 1H), 4.74 – 4.66 (m, 1H), 4.51 (d, *J*=11.0, 1H), 4.46 (d, *J*=11.0, 1H), 4.19 – 3.96 (m, 3H), 3.90 (ddd, *J*=21.3, 8.6, 6.4, 3H), 3.80 (s, 3H), 3.74 – 3.63 (m, 1H), 2.43 – 2.25 (m, 2H), 1.88 (ddd, *J*=14.6, 9.7, 2.4, 1H), 1.80 – 1.71 (m, 2H), 1.71 – 1.37 (m, 8H), 1.36 – 1.20 (m, 30H), 0.88 (t, *J*=6.9, 3H).

^{13}C NMR: (100 MHz, $CDCl_3$): δ 164.4, 159.4, 145.3, 130.8, 129.7, 121.6, 114.0, 98.5, 76.6, 76.0, 74.0, 71.6, 71.2, 69.2, 55.4, 44.0, 43.2, 41.6, 41.3, 37.2, 34.0, 32.1, 30.1, 29.0, 30.85, 29.8 (3C), 29.5, 25.5, 22.8, 21.2, 14.3.

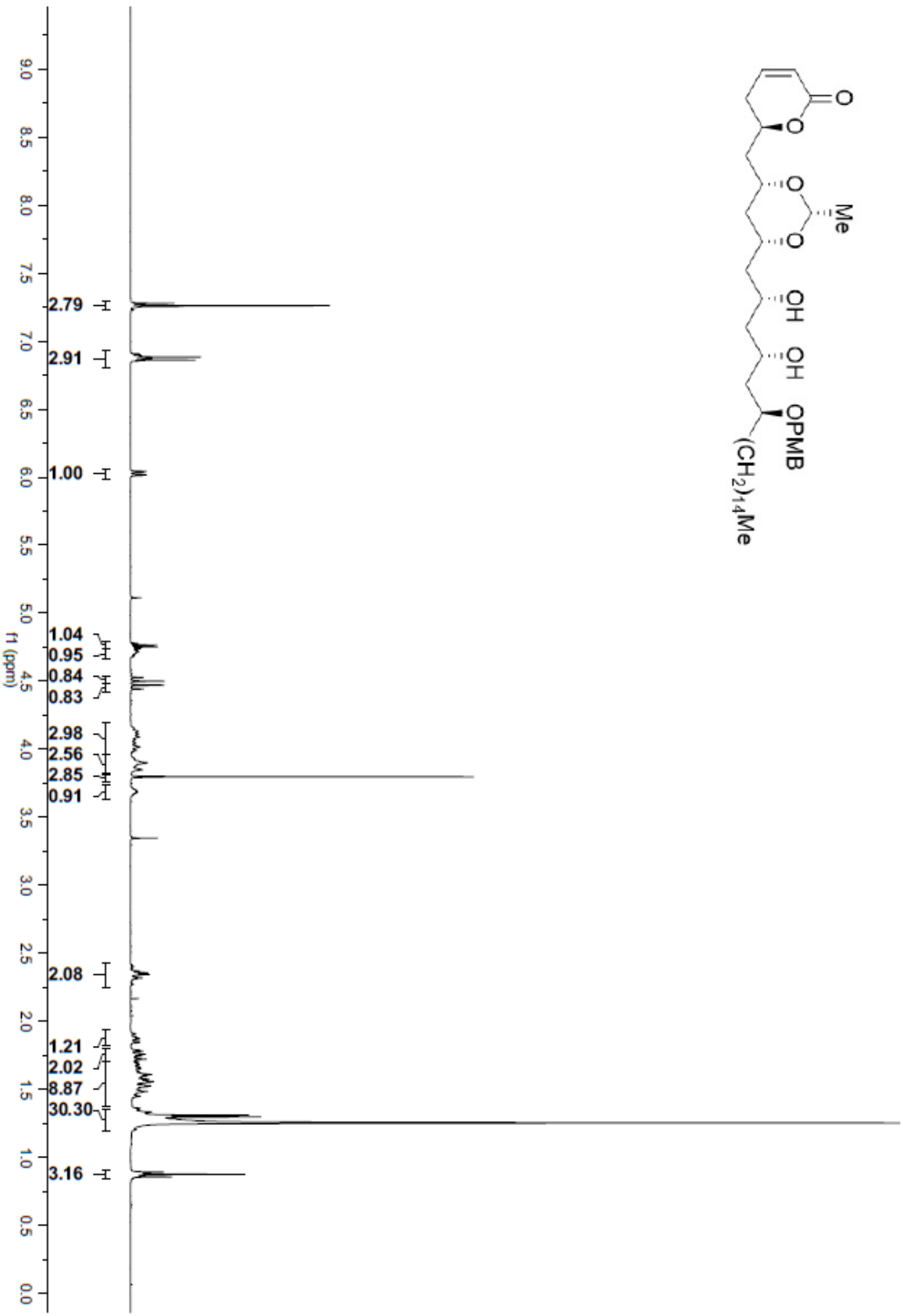
FTIR (neat): 3488, 2924, 2853, 1716, 1248 cm^{-1}.

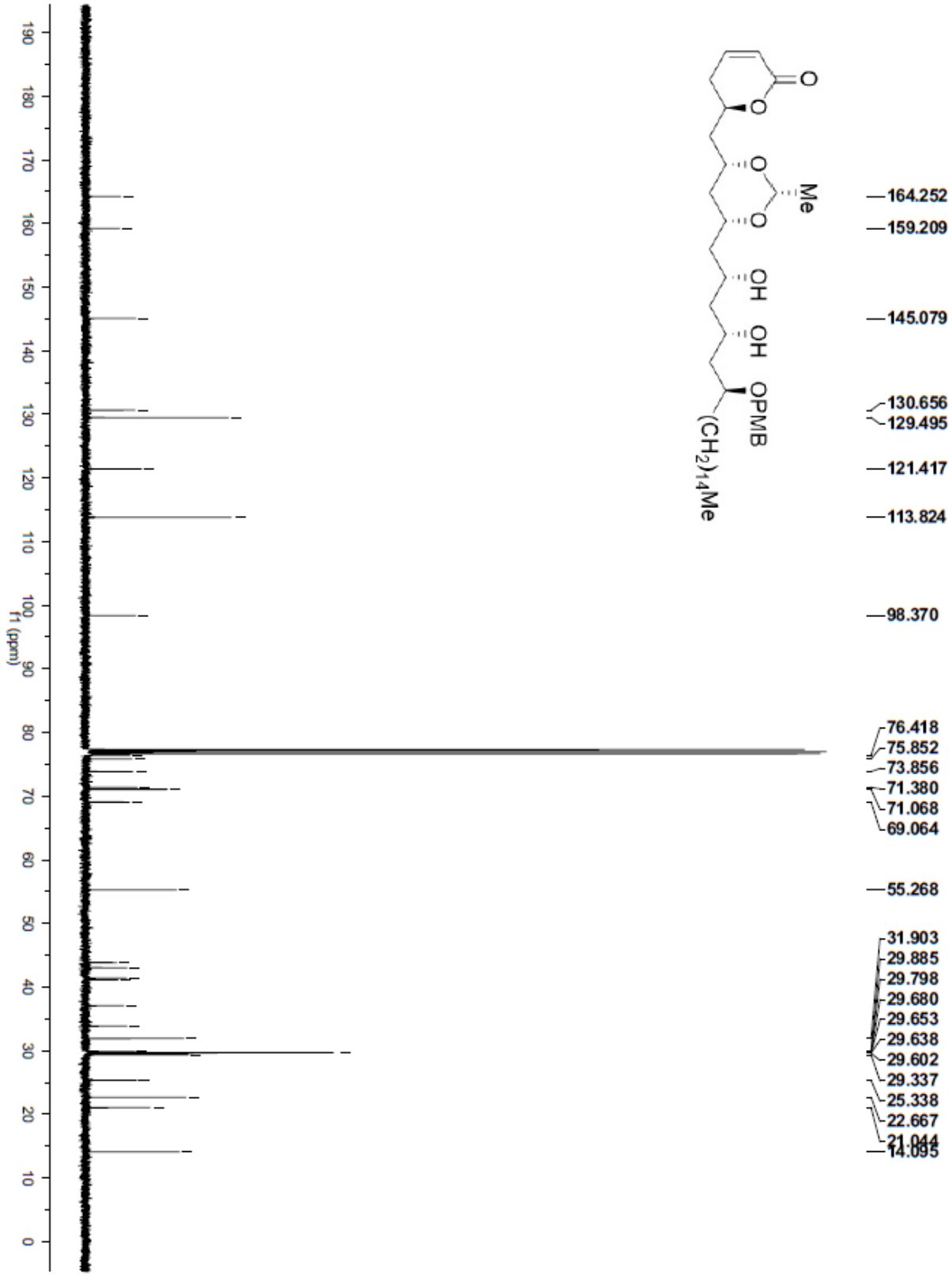
HRMS: (ESI) Calcd. for $C_{40}H_{66}O_8Na$ $(M+Na)^+$: 697.46500, Found:.697.46500

$[\alpha]^{22}_D$: +19.87 ° (c = 0.52, $CHCl_3$).

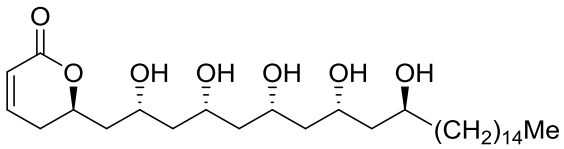
Synthesis of 8 starting from crude Fragment A: Due to the instability of **Fragment A** during storage and the instability of the aldol product **7** during chromatography, procedures were developed to carry out the aldol and reduction with crude reaction products. A 10 mL screw cap vial was charged with stir bar and solution of ketone **Fragment B** (41.9 mg, 0.1 mmol, 100 mol%) in diethyl ether (1 mL). The vial was sealed and the solution sparged with argon, then cooled to -30 °C. Chlorodicyclohexylborane (31.9 mg, 1.5 mmol, 150 mol%) was injected neat, resulting in a yellow solution. After 5 min, triethylamine (20.3 mg, 0.200 mmol, 200 mol%) was injected and a cloudy mixture formed immediately. The mixture was allowed to stir for 30 minutes, then cooled to -78 °C. Crude aldehyde **Fragment A** (31.8mg, 0.125 mmol, 125 mol%) in diethyl ether (1 mL) was added dropwise. After 4 hours, the mixture was warmed 0 °C and a solution of methanol, pH 7 buffer and 30% hydrogen peroxide (1:1:1, 6 mL) was added. The biphasic mixture was allowed to stir overnight at room temperature, extracted with diethyl ether (3 x 5 mL), washed with saturated $NaHCO_3$ (3 x 10 mL), brine (1 x 10 mL) and dried (Na_2SO_4). The organic extract was filtered and concentrated *in vacuo* to furnish a clear oil. The oil was dissolved in acetonitrile (5 mL), washed with pentane (4 x 5 mL) to remove methyl ketone **Fragment B**, then concentrated *in vacuo* to a clear oil, providing crude aldol (64.8 mg) in good purity. The methyl ketone **Fragment B** could be recovered from the pentane extract (6.2 mg, 15%).

A 10 mL screw cap vial was charged with crude aldol **7** (64.8 mg, 0.0964 mmol) and dissolved in THF/MeOH (4:1, 1 mL). The solution was cooled to -78 °C and diethylmethoxyborane (1.0 M in THF, 0.2 mL, 200 mol%) was added dropwise. The cloudy solution was stirred for 30 minutes then $NaBH_4$ (0.5 M in diglyme, 0.22 mL, 110 mol%) was added dropwise. The mixture was allowed to stir for 3 h, then warmed to 0 °C, diluted with diethyl ether (10 mL), and stirred vigorously with a mixture of methanol, pH 7 buffer, and 30% hydrogen peroxide (1.5 mL, 1:1:1) allowing the solution to warm to room temperature. After 1 h at room temperature, the organic phase was washed with saturated $NaHCO_3$ (3 x 5 mL), brine (1 x 5 mL), dried (Na_2SO_4), filtered and concentrated. The yellow oil was subjected to flash column chromatography (SiO_2, 1:4 to 3:7 acetone:hexanes) to furnish the diol as a colorless oil (49.3 mg, 73% over two steps).


O
O
Me
O
O
OH
OH
OPMB
(CH2)14Me
2.79
2.91
1.00
1.04
0.95
0.84
0.83
2.98
2.56
2.85
0.91
2.08
1.21
2.02
8.87
30.30
3.16
f1 (ppm)


f1 (ppm)
Me
OH
OH
OPMB
(CH2)14Me
164.252
159.209
145.079
130.656
129.495
121.417
113.824
98.370
76.418
75.852
73.856
71.380
71.068
69.064
55.268
31.903
29.885
29.798
29.680
29.653
29.638
29.602
29.337
25.338
22.667
14.095

(+)-Cryptocaryol A



A 10 mL screw cap vial was charged with diol **8** (32.4 mg, 0.0480 mmol, 100 mol%), 1,3-dimethoxybenzene (59.7 mg, 0.200 mmol, 900 mol%) and dichloromethane (2.4 mL, 0.02 M). Triflic acid (21.6 mg, 0.144 mmol, 300 mol%) was added and a dark red solution developed immediately. The solution was stirred at ambient temperature for 30 min, at which point saturated $NaHCO_3$ (5 mL) was added with vigorous stirring. The cloudy mixture was extracted with chloroform (5 x 5 mL), dried (Na_2SO_4) and concentrated *in vacuo*. The white semi-solid was absorbed onto silica gel and subjected to flash column chromatography (SiO_2, MeOH:$CHCl_3$ 1:99 to 1:19) to provide **(+)-cryptocaryol A** as a white solid (19.1 mg, 0.036 mmol) in 75% yield.

TLC (SiO_2): 0.32 (1:9 MeOH:$CHCl_3$)

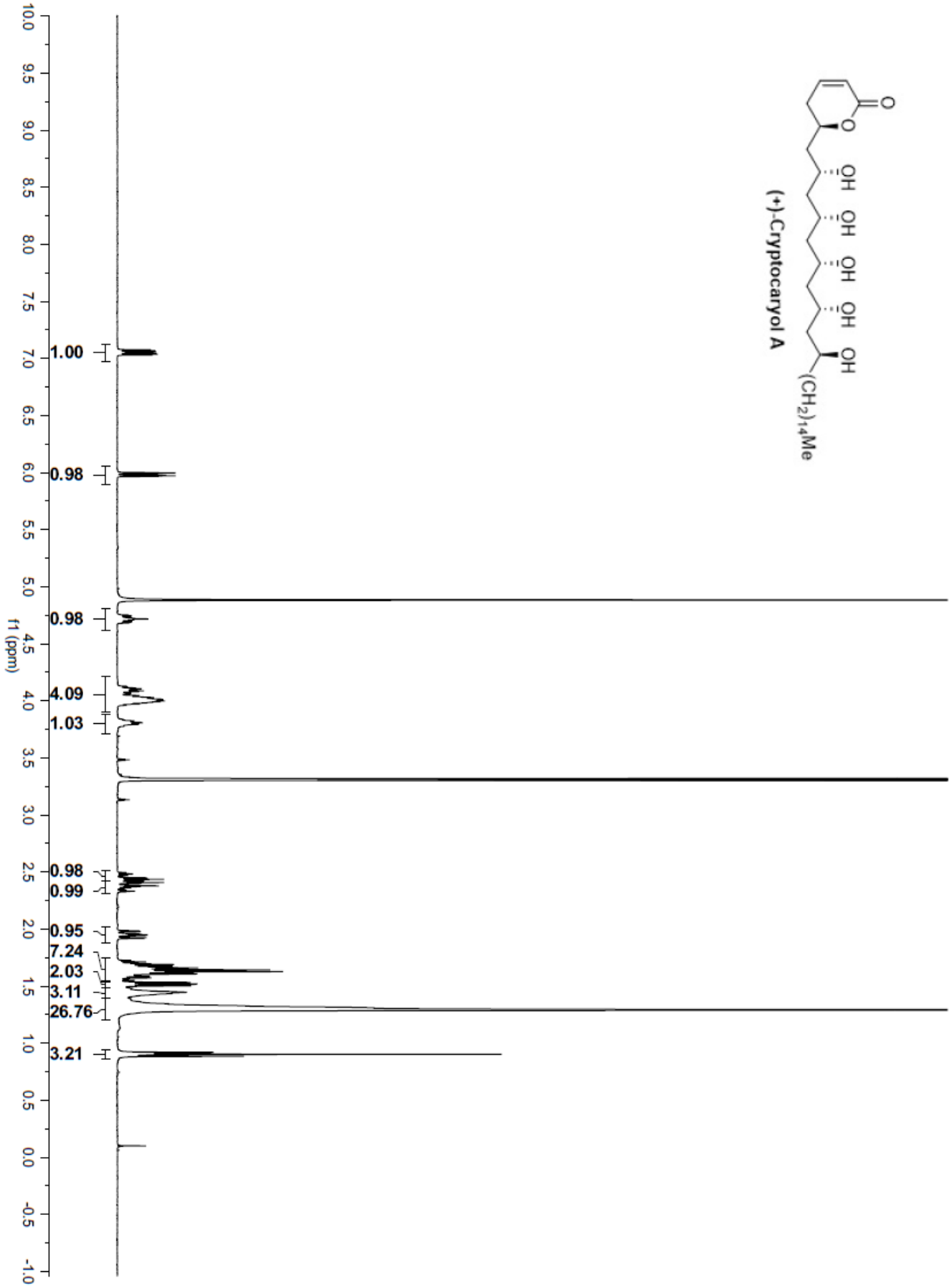
^{1}H NMR: (400 MHz, CD_3OD): δ = 7.05 (ddd, *J*=9.7, 5.9, 2.6, 1H), 5.98 (ddd, *J*=9.7, 2.6, 1.1, 1H), 4.82 – 4.61 (m, 1H), 4.22 – 3.92 (m, 4H), 3.90 – 3.69 (m, 1H), 2.46 (dddd, *J*=18.6, 5.8, 4.4, 1.1 Hz, 1H), 2.37 (ddt, *J*=18.7, 11.4, 2.6, 1H), 1.95 (ddd, *J*=14.5, 9.8, 2.6, 1H), 1.74 – 1.54 (m, 7H), 1.52 (dd, *J*=6.7, 5.5 Hz, 2H), 1.48 – 1.40 (m, 3H), 1.38 – 1.21 (m, 27H), 0.90 (t, *J*=6.9, 3H).

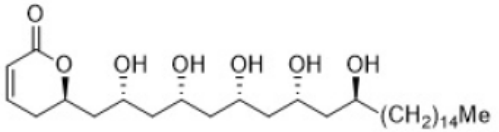
^{13}C NMR: (126 MHz, CD_3OD) δ = 166.9, 148.5, 121.4, 76.6, 70.1, 69.9, 69.1, 68.2, 66.6, 46.0, 45.9, 45.7, 45.2, 43.9, 39.2, 33.1, 30.9, 30.84-30.76 (9C), 30.5, 26.8, 23.7, 14.4.

FTIR (neat): 3365, 2916, 2849, 1718, 1470, 1389, 1268, 1139 cm^{-1}.

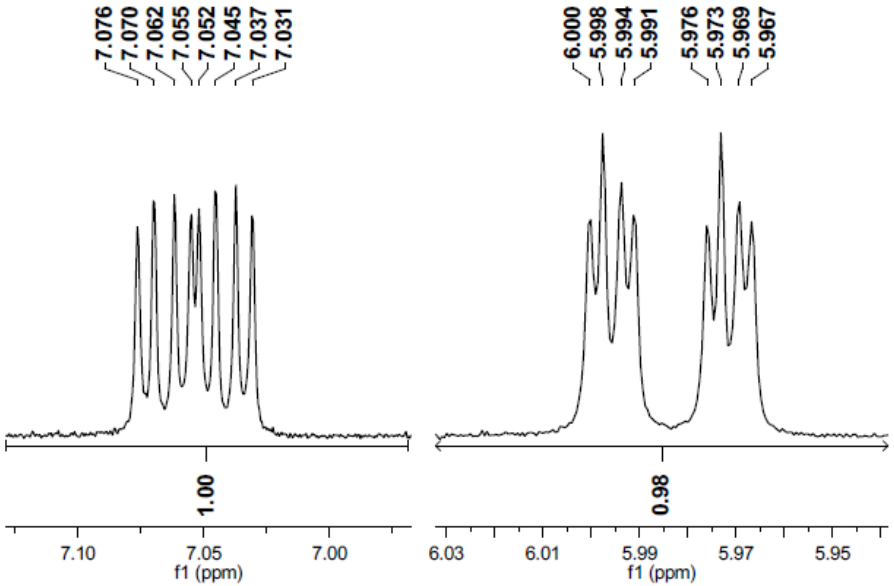
HRMS: (ESI) Calcd. for $C_{30}H_{56}O_7$ $(M+Na)^+$: 551.39180, Found: 551.39200.

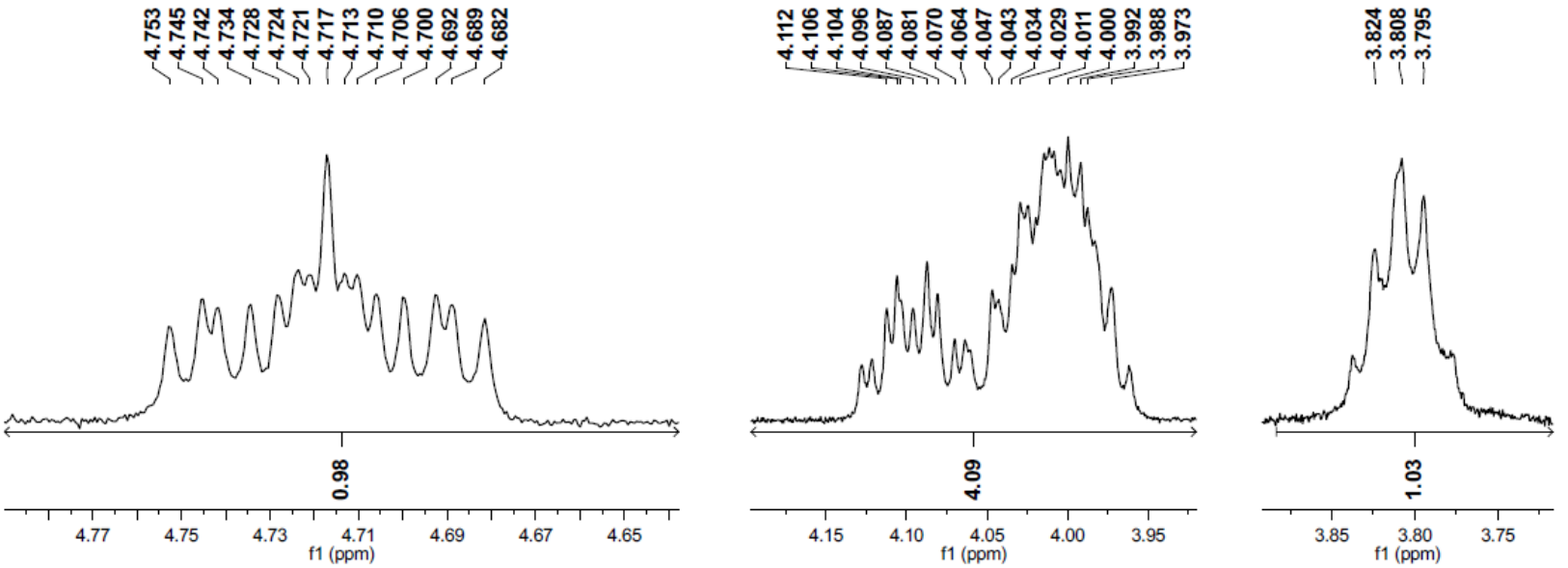
$[\alpha]^{22}_D$: +27.45 ° (c = 0.51, MeOH).

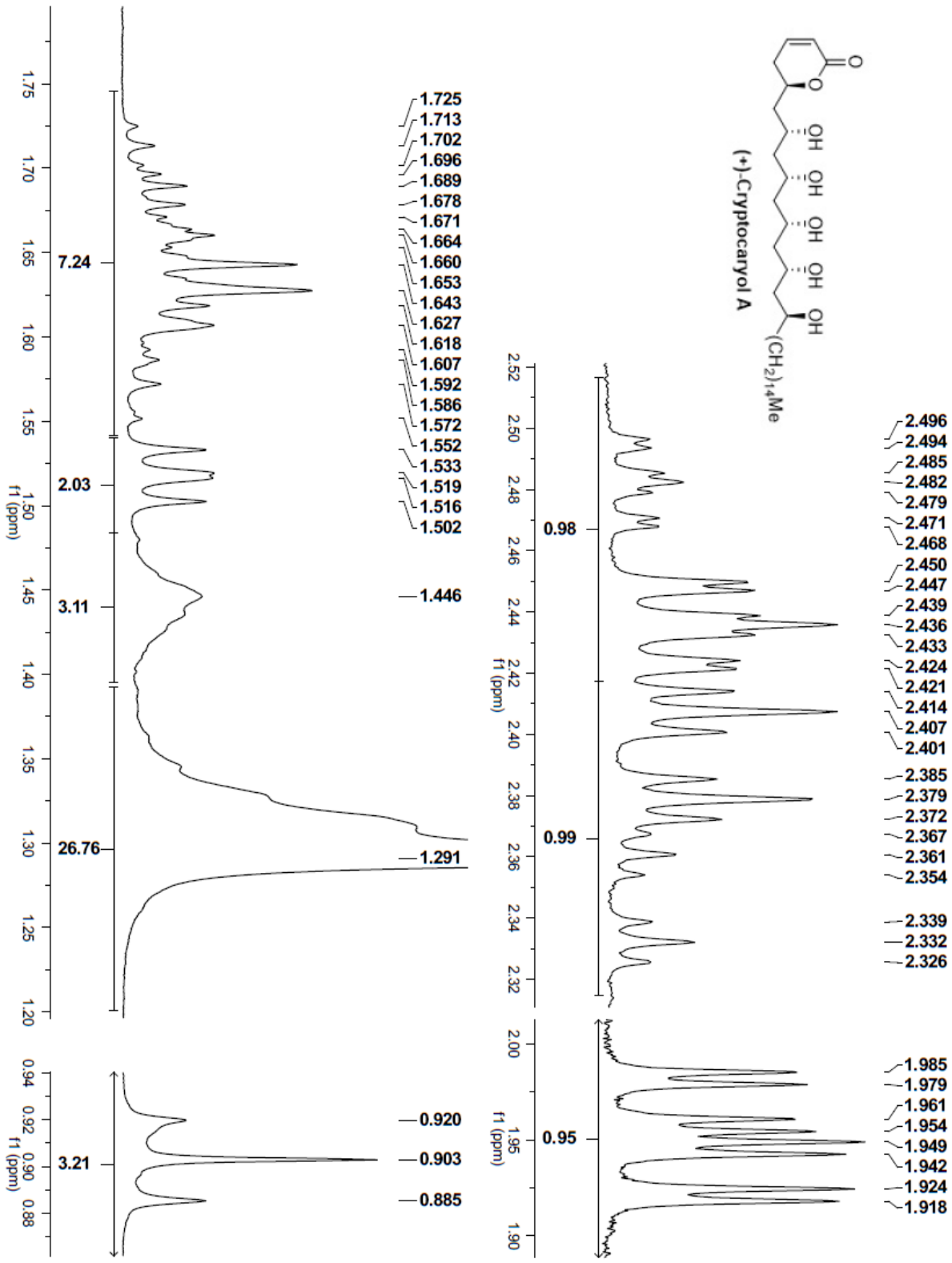

(+)-Cryptocaryol A
OH OH OH OH OH
(CH2)14Me
f1 (ppm)
1.00
0.98
0.98
4.09
1.03
0.98
0.99
0.95
7.24
2.03
3.11
26.76
3.21

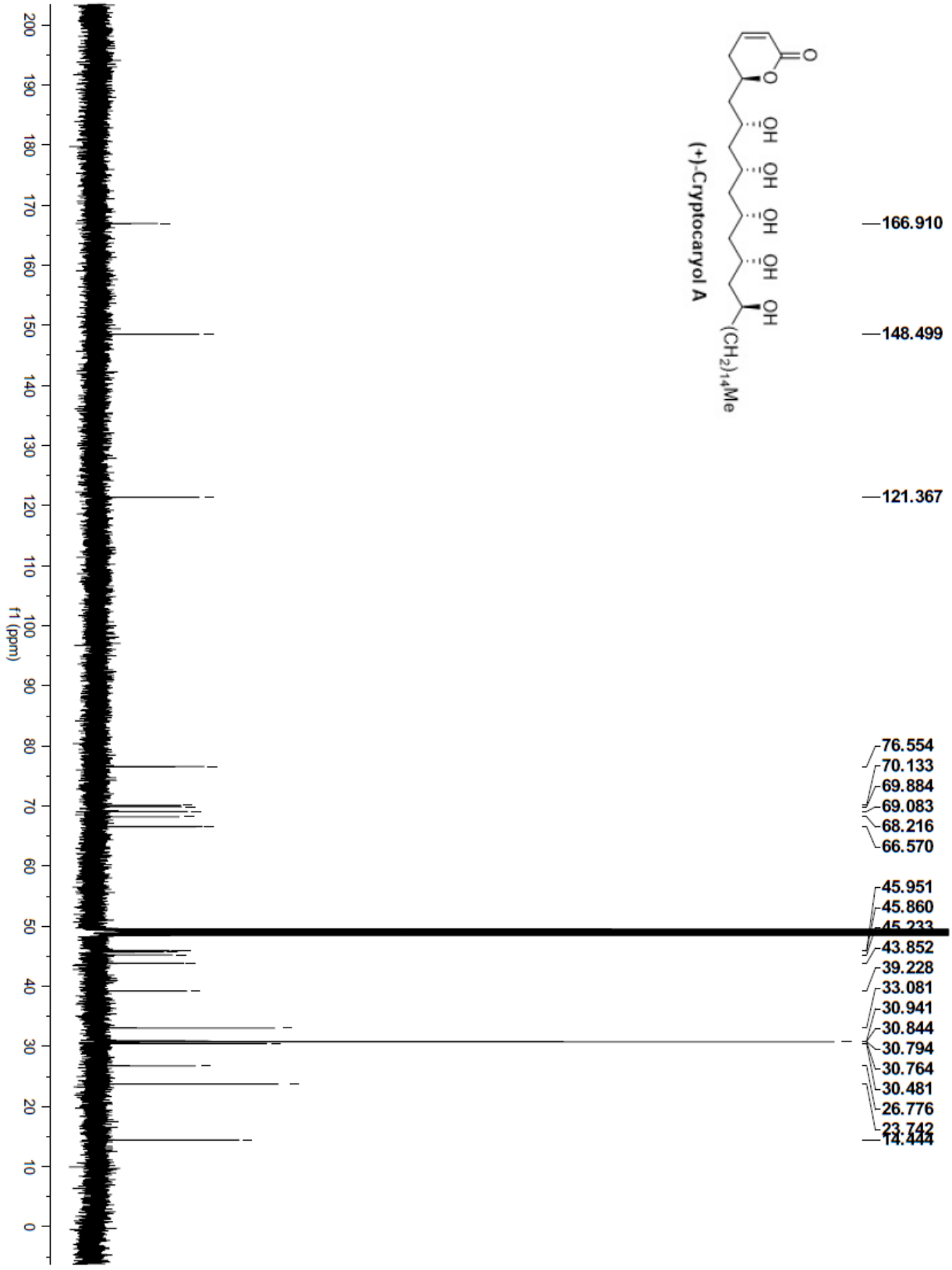


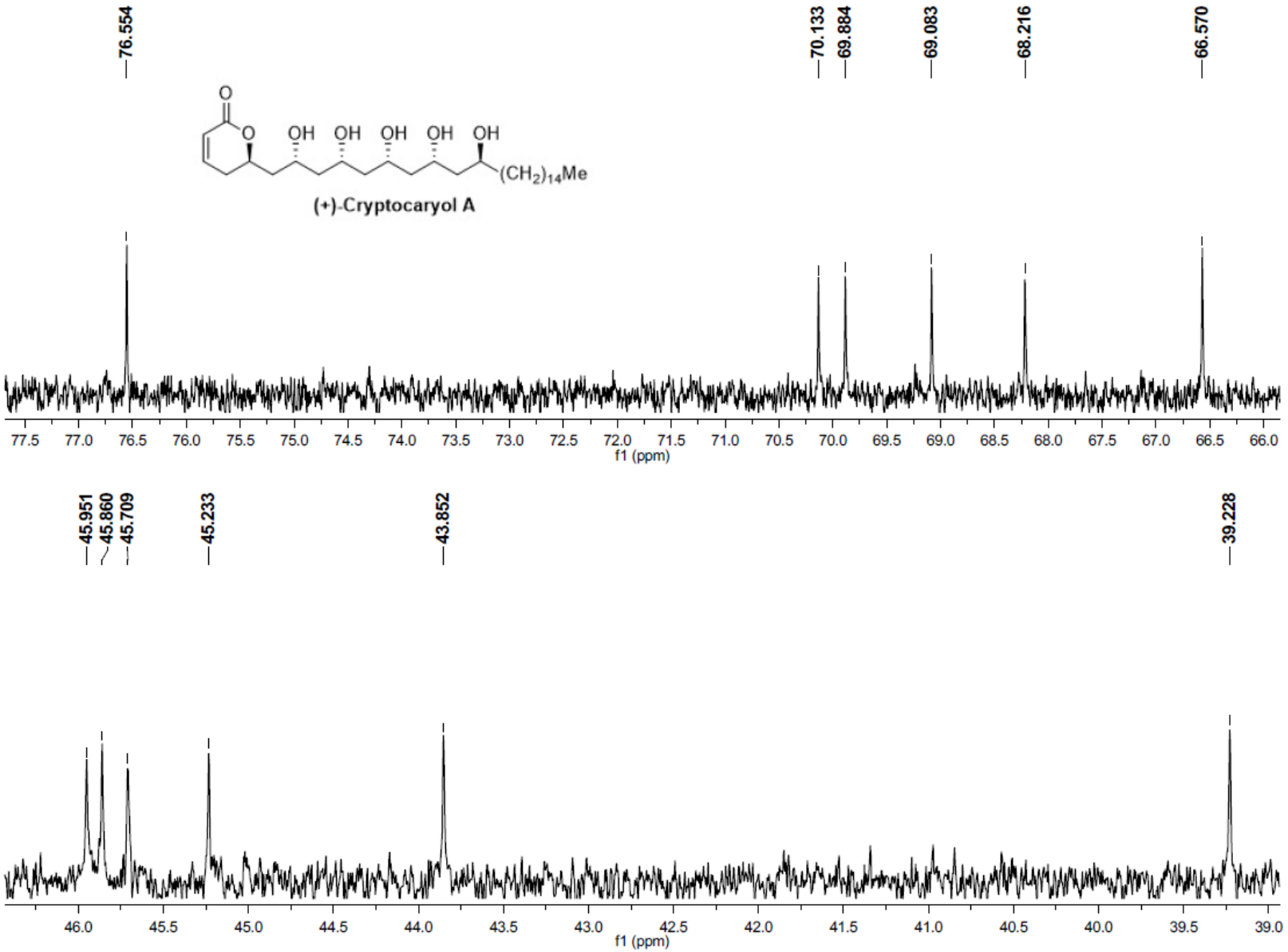
(+)-Cryptocaryol A

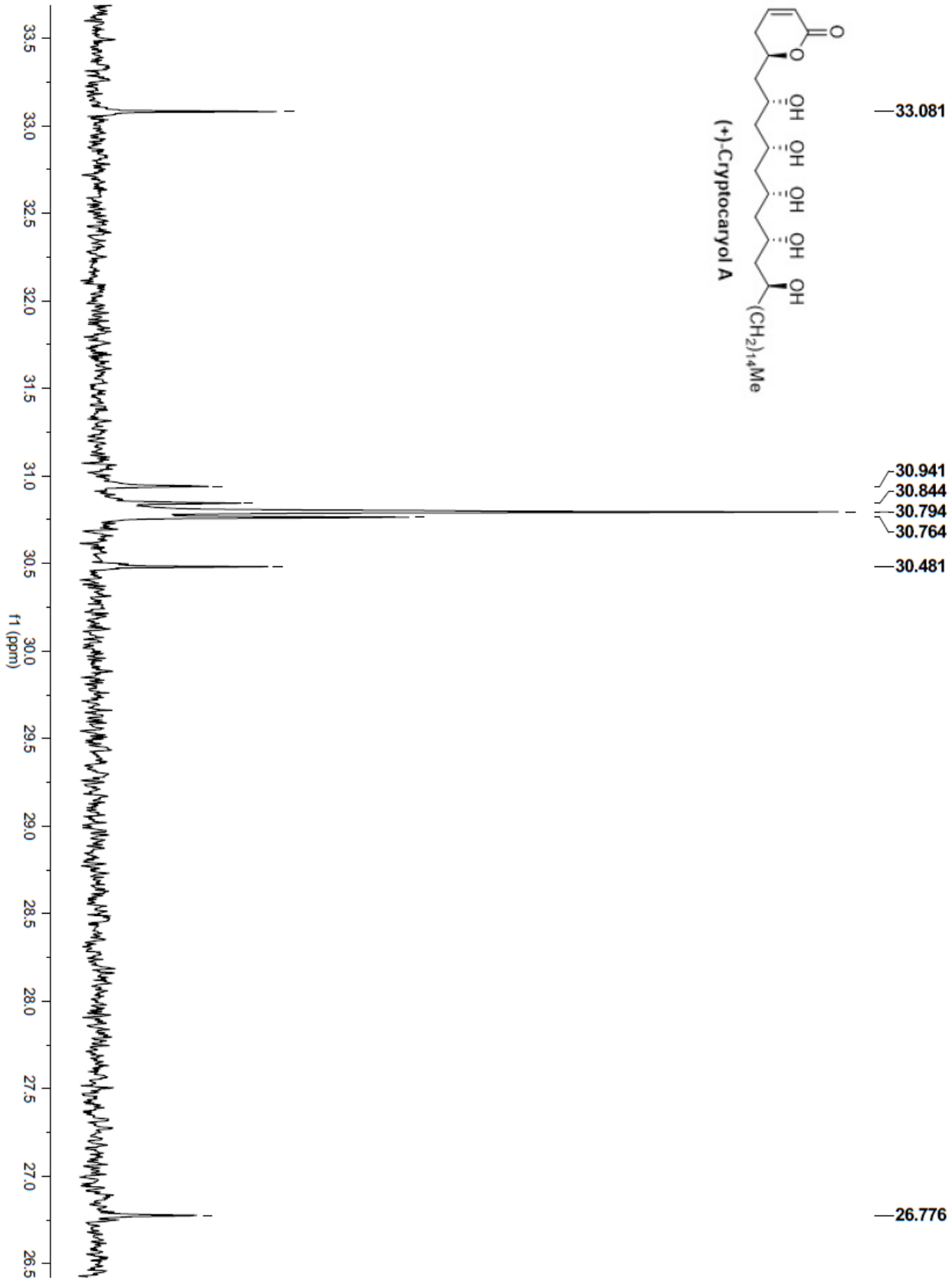





(+)-Cryptocaryol A
OH OH OH OH OH
(CH2)14Me
1.725
1.713
1.702
1.696
1.689
1.678
1.671
1.664
1.660
1.653
1.643
1.627
1.618
1.607
1.592
1.586
1.572
1.552
1.533
1.519
1.516
1.502
1.446
1.291
0.920
0.903
0.885
7.24
2.03
3.11
26.76
3.21
2.496
2.494
2.485
2.482
2.479
2.471
2.468
2.450
2.447
2.439
2.436
2.433
2.424
2.421
2.414
2.407
2.401
2.385
2.379
2.372
2.367
2.361
2.354
2.339
2.332
2.326
1.985
1.979
1.961
1.954
1.949
1.942
1.924
1.918
0.98
0.99
0.95
f1 (ppm)


(+)-Cryptocaryol A
166.910
148.499
121.367
76.554
70.133
69.884
69.083
68.216
66.570
45.951
45.860
43.852
39.228
33.081
30.941
30.844
30.794
30.764
30.481
26.776
14.444
f1 (ppm)


76.554
70.133
69.884
69.083
68.216
66.570
O
O
OH OH OH OH OH
(CH2)14Me
(+)-Cryptocaryol A
77.5 77.0 76.5 76.0 75.5 75.0 74.5 74.0 73.5 73.0 72.5 72.0 71.5 71.0 70.5 70.0 69.5 69.0 68.5 68.0 67.5 67.0 66.5 66.0
f1 (ppm)
45.951
45.860
45.709
45.233
43.852
39.228
46.0 45.5 45.0 44.5 44.0 43.5 43.0 42.5 42.0 41.5 41.0 40.5 40.0 39.5 39.0
f1 (ppm)


(+)-Cryptocaryol A
33.081
30.941
30.844
30.794
30.764
30.481
26.776
f1 (ppm)