Supporting Information

Direct Generation of Triketide Stereopolyads *via* Merged Redox-Construction Events: Total Synthesis of (+)-Zincophorin Methyl Ester

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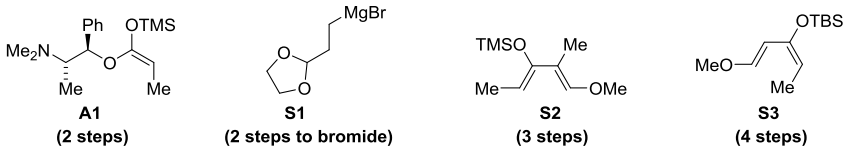
Table of Contents pg

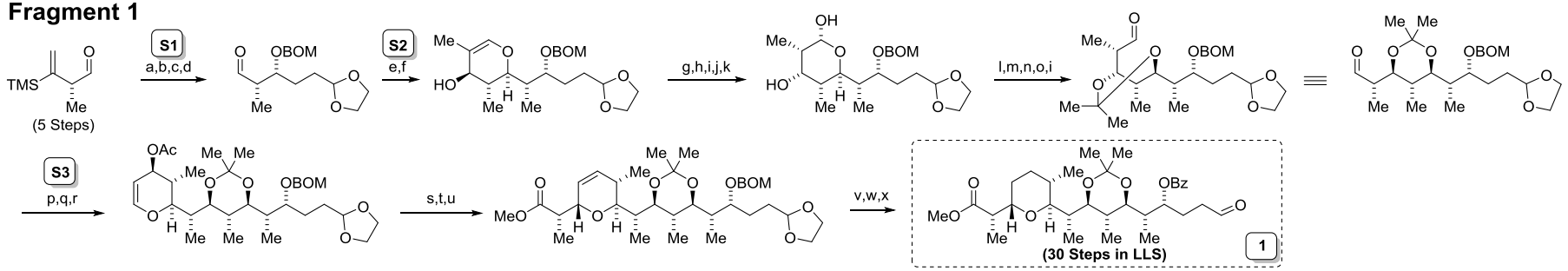
1. Summaries of Previous Syntheses

Zincophorin Methyl Ester (Danishefsky, *J. Am. Chem. Soc.* **1987**, *109*, 1572; *J. Am. Chem. Soc.* **1988**, *110*, 4368.)

Reagents

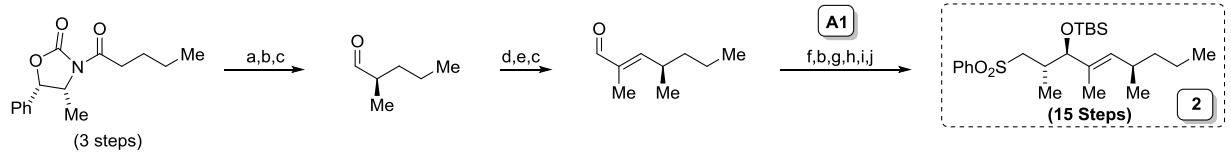


Fragment 1



Key: (a) **S1**; (b) NaH, HMPA, then H_2O; (c) BOMCl, *i*-Pr_2EtN; (d) Ozonolysis; (e) **S2**, $MgBr_2$; (f) $NaBH_4$, $CeCl_3$; (g) 3,4-$(OMe)_2PhCH_2Cl$, *p*-TsOH; (h) BH_3-THF, then H_2O_2, NaOH; (i) $(COCl)_2$, DMSO, then Et_3N; (j) L-Selectride; (k) DDQ; (l) $LiBH_4$; (m) TBDPSCl; (n) $Me_2C(OMe)_2$, PPTS; (o) TBAF; (p) **S3**; (q) $NaBH_4$, $CeCl_3$; (r) Ac_2O, DMAP ; (s) (*E*)-crotylsilane, BF_3-OEt_2; (t) OsO_4, $NaIO_4$; (u) CrO_3; (v) H_2, Pd-C; (w) BzCl, pyridine; (x)*p*-TsOH

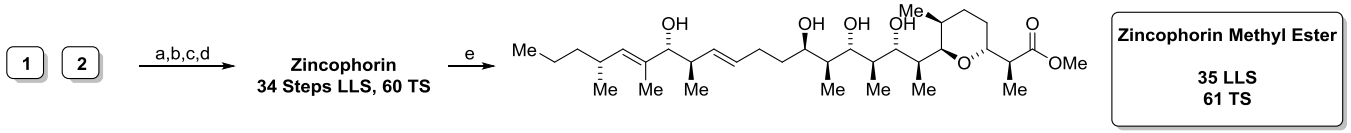
Fragment 2



Key: (a) LDA, then MeI; (b) LAH; (c) $(COCl)_2$, DMSO, then Et_3N; (d) $Ph_3PC(Me)CO_2Et$; (e) DIBAL-H; (f) **A1**, $TiCl_4$; (g) *p*-TsCl, pyridine, DMAP; (h) TBSOTf, Et_3N; (i) KSPh; (j) PhSeSePh, H_2O_2.

Zincophorin (Danishefsky, *J. Am. Chem. Soc.* **1987**, *109*, 1572; *J. Am. Chem. Soc.* **1988**, *110*, 4368.) (*continued*)

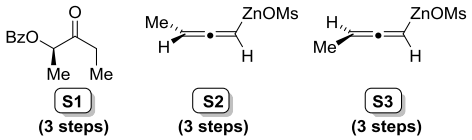
Fragment Union and End Game



Key: (a) *n*-BuLi, $MgBr_2$; (b) Na/Hg; (c) 1M HCl/MeOH/THF; (d) 2.0 M LiOH in MeOH/THF, then 1N HCl; (e) CH_2N_2

Zincophorin Methyl Ester (Cossy, *Org. Lett.* **2003**, *5*, 4037; *J. Org. Chem.* **2004**, *69*, 4626.)

Reagents



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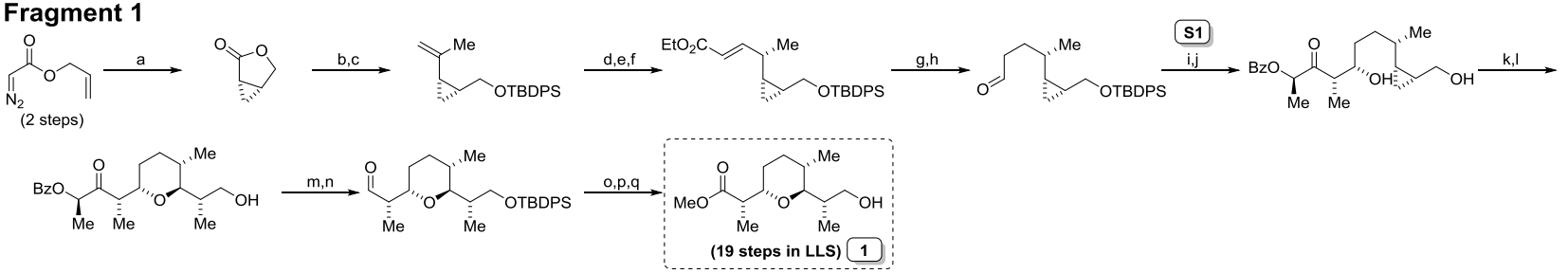
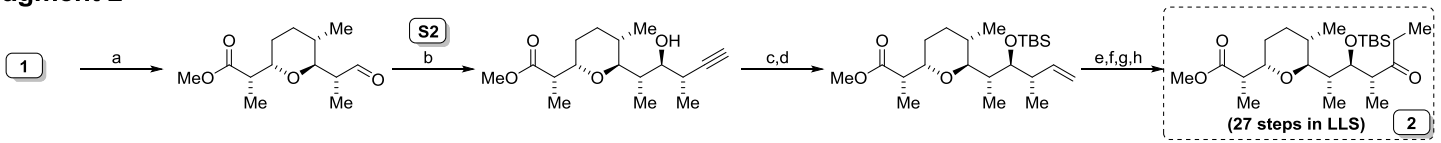


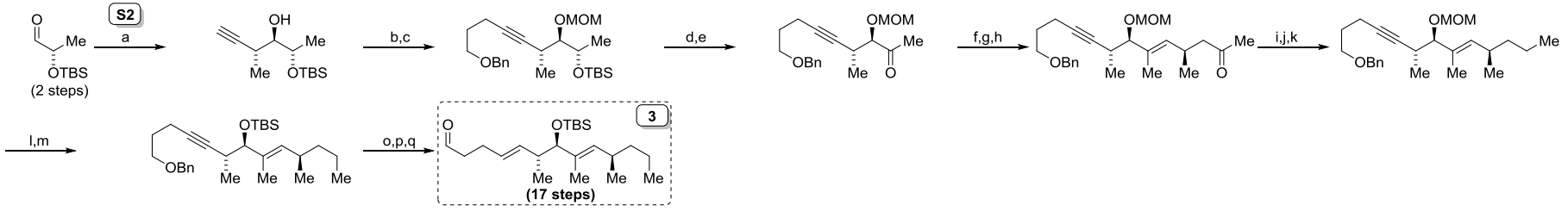
Key: (a) Rh_2(R-MEPY)$_4$; (b) MeLi, then TBDPSCl; (c) MsCl, NEt_3, DMAP; (d) BH_3-THF, H_2O_2; (e) PCC, 4A MS; (f) $(EtO)_2P(O)CH_2COOEt$; (g) H_2, PtO_2; (h) DIBAL-H; (i) Cy_2BCl, Et_2NMe; (j) HF-Py; (k) $Hg(TFA)_2$, KBr; (l) Bu_3SnH; (m) TBDPSCl, IM; (n) $LiBH_4$, then $NaIO_4$; (o) $NaClO_2$; (p) $TMSCHN_2$; (q) HF-Py

Fragment 2



Key: (a) DMP; (b) $Pd(OAc)_2$, PPh_3, $ZnEt_2$; (c) H_2, Pd/$BaSO_4$; (d) TBSOTf, 2,6-lutidine; (e) OsO_4, NMO; (f) $NaIO_4$; (g) Et_2CuLi; (h) DMP

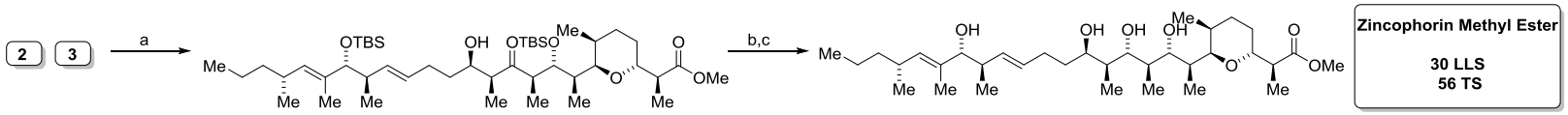
Fragment 3



Key: (a) $Pd(OAc)_2$, PPh_3, $ZnEt_2$; (b) MOMCl; (c) BuLi, RBr, HMPA; (d) TBAF; (e) DMP, Py; (f) (*Z*)-propenyl MgBr, $MgBr_2$-OEt_2; (g) diketene, DMAP; (h) Al_2O_3; (i) DIBAL-H; (j) MsCl, NEt_3; (k) LAH; (l) TsOH; (m) TBSOTf; (n) Li, NH_3; (o) DMP, Py.

Zincophorin (Cossy, *Org. Lett.* **2003**, *5*, 4037; *J. Org. Chem.* **2004**, *69*, 4626.) (*continued*)

Fragment Union and End Game



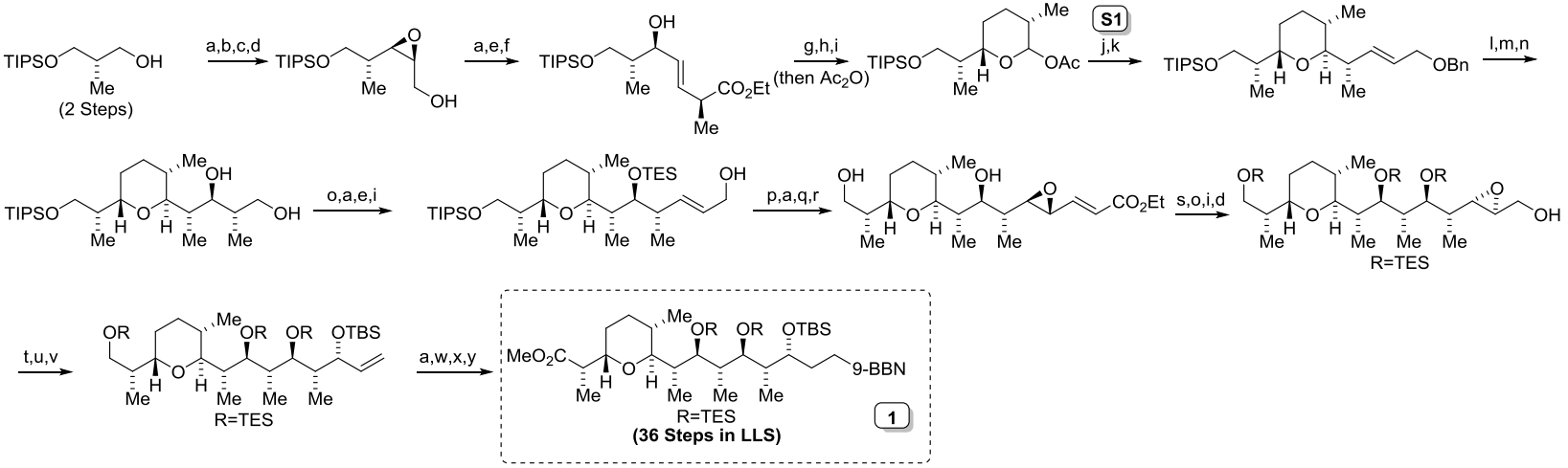
Key: (a) $TiCl_4$; (b) $NaBH_4$; (c) HF-Py

Zincophorin (Miyashita, *Angew. Chem. Int. Ed.* **2004**, *43*, 4341.)

Reagents

Key: (a) ($SiClPh_2SiMe_2Ph$, Et_3N; (b) $Cp_2Zr(H)Cl$, then Me_2Zn, 4Å sieves, BOMCl; (c) $Pd(acac)_2$, *t*-$BuCH_2C(Me)_2NC$; (d) *n*-BuLi. (Fukuda, K.; Miyashita, M.; Tanino, K. *Tetrahedron Lett.* **2010**, *51*, 4523.)

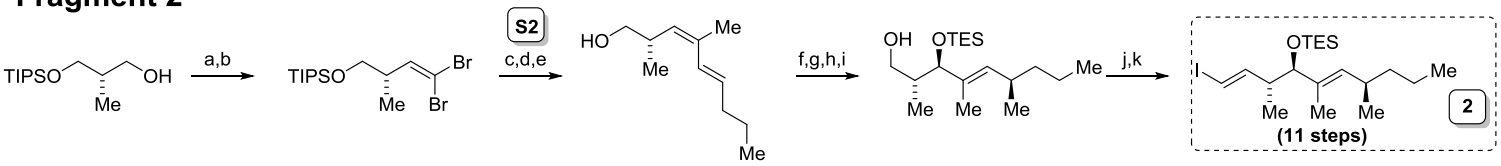
Fragment 1



Key: (a) $(COCl)_2$, DMSO, then Et_3N; (b) (*o*-Me-PhO)$_2$P(O)CH_2CO_2Et, NaH; (c) DIBAL-H; (d) MCPBA; (e) (*i*-PrO)$_2$P(O)CH_2CO_2Et, *t*-BuOK; (f) Me_2Zn-CuCN; (g) H_2, PtO_2; (h) Ti(O*i*-Pr)$_4$; (i) DIBAL-H; (j) **S1**, TiCl(O*i*-Pr)$_4$; (k) TIPSOTf, 2,6-lutidine; (l) Ca, NH_3; (m) Ti(O*i*-Pr)$_4$, D-(−)-DIPT, *t*-BuOOH, 4Å sieves; (n) Me_2CuLi; (o) TESOTf, 2,6-lutidine; (p) Ti(O*i*-Pr)$_4$, D-(−)-DET, *t*-BuOOH, 4Å sieves; (q) (EtO)$_2$P(O)CH_2CO_2Et, NaH; (r) TBAF; (s) Me_3Al-D_2O; (t) PPh_3, I_2, imidazole; (u) BuLi; (v) TBSCl, DMAP; (w) $NaClO_2$, NaH_2PO_4, 2-methyl-2-butene; (x) $TMSCHN_2$ (y) 9-BBN.

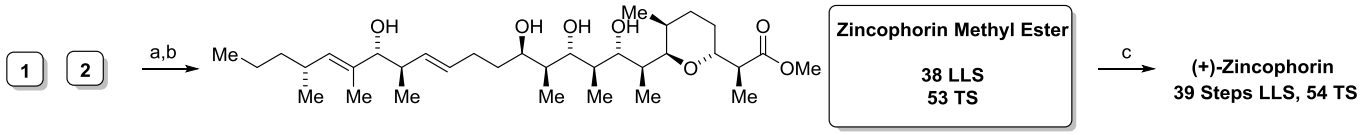
Zincophorin (Miyashita, *Angew. Chem. Int. Ed.* **2004**, *43*, 4341.) (*continued*)

Fragment 2



Key: (a) $(COCl)_2$, DMSO, then Et_3N; (b) CBr_4, PPh_3, pyridine; (c) Me_2CuLi, then I_2; (d) **S2**, $ZnBr_2$, $[PdCl_2(PPh_3)]$, DIBAL-H; (e) HF; (f) MCPBA; (g) Me_2CuLi; (h) TESOTf, 2,6-lutidine; (i) HF-pyridine; (j) DMP; (k) $CrCl_2$, CHI_3.

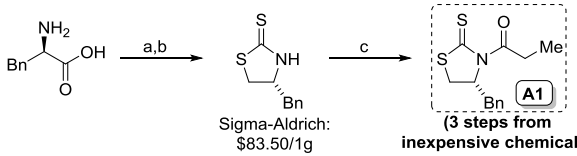
Fragment Union and End Game



Key: (a) aq. Cs_2CO_3, $AsPh_3$, $[PdCl_2(dppf)]$; (b) TEAF; (c) LiOH, H_2O/MeOH/THF.

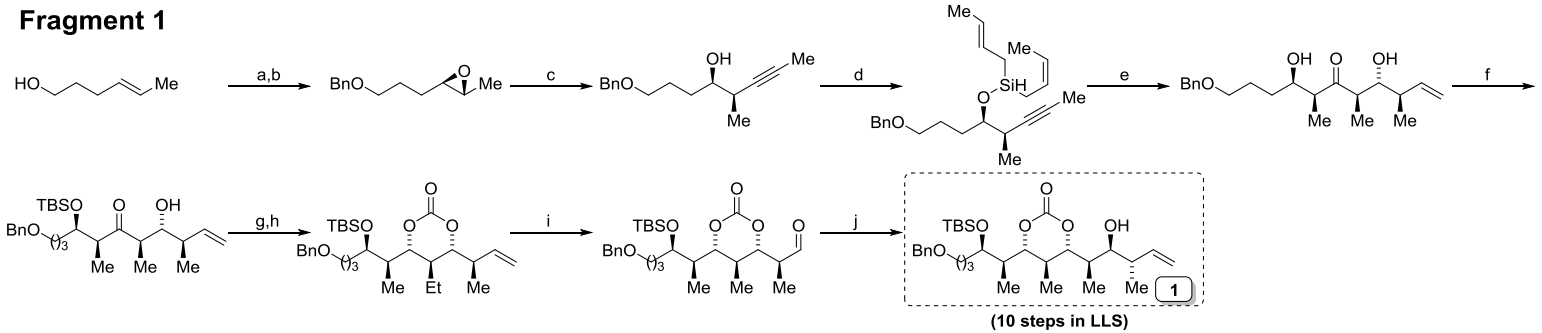
Zincophorin (Leighton, *J. Am. Chem. Soc.* **2011**, *133*, 7308.)

Chiral Auxiliary Synthesis



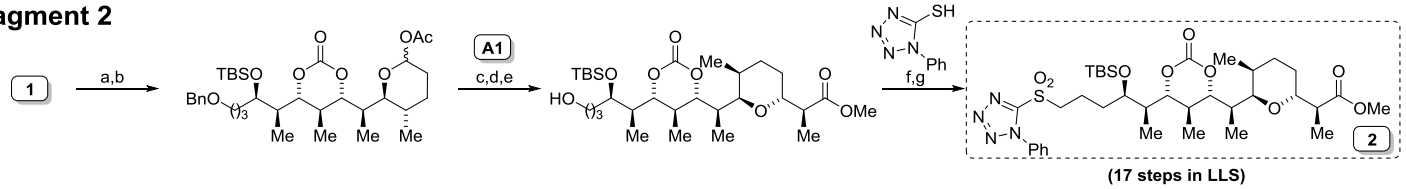
Key: (a) $NaBH_4$, I_2; (b) KOH, CS_2, H_2O, reflux; (c) propionyl chloride, DMAP, TEA.

Fragment 1



Key: (a) NaH, BnBr; (b) Shi epoxidation, oxone, Na_2EDTA; (c) Propyne, BuLi, $AlMe_3$; (d) dicrotylsilane, NaH; (e)$Rh(acac)(CO)_2$, then H_2O_2, KF; (f) TBSOTf, 2,6-lutidine; (g) DIBAL-H; (h) CDI; (i) OsO_4, NMO, then $NaIO_4$; (j) K-trifluorocrotylborate, TBAI.

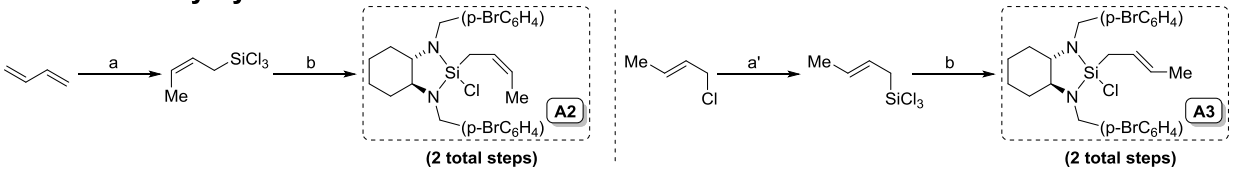
Fragment 2



Key: (a) $Rh(acac)(CO)_2$, PPh_3, CO/H_2; (b) Ac_2O, Py, DMAP; (c) $TiCl_4$, $SnCl_4$, iPr_2NEt; (d) DMAP, MeOH; (e) Pd/C; (f) DIAD, PPh_3; (g) $(NH_4)_6Mo_7O_{24}{}^{\cdot 4}H_2O$, H_2O_2.

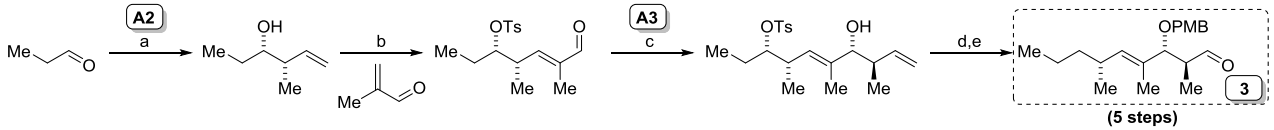
Zincophorin (Leighton, *J. Am. Chem. Soc.* **2011**, *133*, 7308.) (*continued*)

Chiral Auxiliary Synthesis



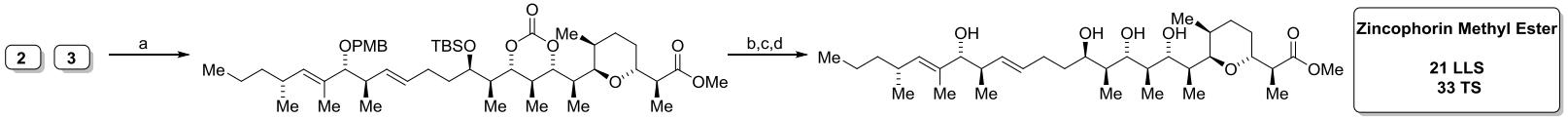
Key: (a) $HSiCl_3$, Pd; (b) diamine, DBU
(a') $HSiCl_3$, NEt_3, CuCl

Fragment 3



Key: (a) $Sc(OTf)_3$; (b) Hoveyda-Grubbs-II, then TsCl, Et_3N; (c) $Sc(OTf)_3$; (d) KHMDS, PMBBr, then $LiBEt_3H$; (e) OsO_4, $NaIO_4$, 2,6-lutidine.

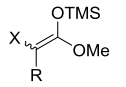
Fragment Union and End Game



Key: (a) KHMDS; (b) DDQ, pH = 7 buffer; (c) NaOMe; (d) HF, H_2O.

Zincophorin (Guindon, *Tetrahedron* **2015**, *71*, 709.)

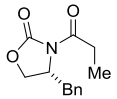
Reagents and Chiral Auxiliary Synthesis



S1 X=Br, R=Me
S2 X=SePh, R=H

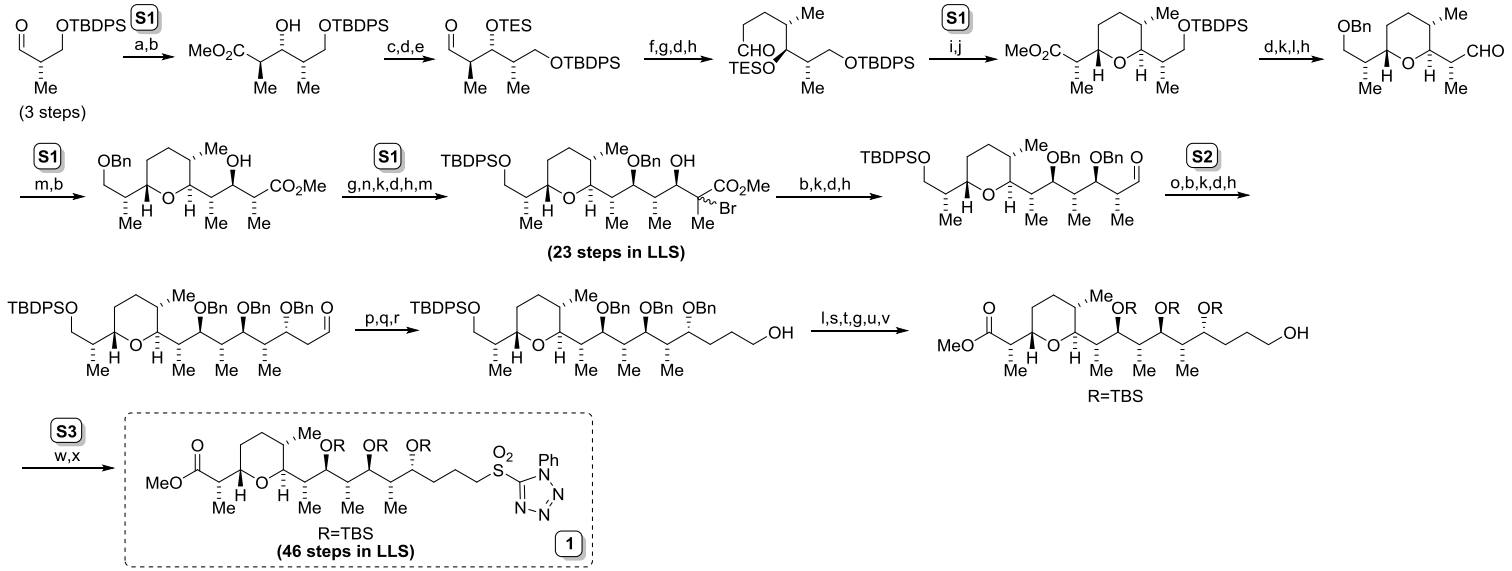
S1: (1 Step)
S2: (2 Steps)

S3



A1
(3 Steps)

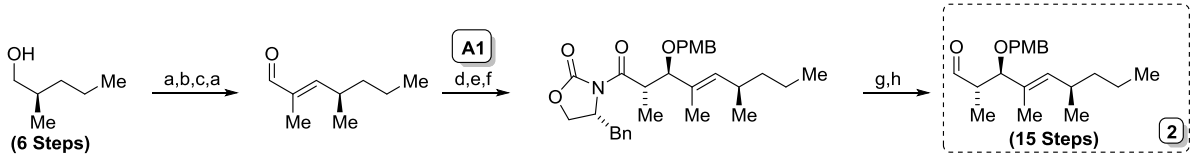
Fragment 1



Key: (a) BF_3OEt_2, **S1**; (b)Bu_2BOTf, DIEA, then Bu_3SnH, BEt_3, air; (c) TESOTf, 2,6- lutidine; (d) DIBAL-H; (e) $(COCl)_2$, DMSO, then Et_3N; (f) $Ph_3PC(H)=CO_2Me$; (g) H_2, Pd–C; (h) DMP, $NaHCO_3$; (i) $BiBr_3$, **S1**; (j) Ph_3SnH, BEt_3, air; (k) BnO=CNHCl$_3$, TfOH; (l) TBAF; (m) $TiCl_4$, **S1**; (n) TBDPSCl, Et_3N, DMAP; (o) BF_3OEt_2, **S2**; (p)$MePPh_3Br$, *n*-BuLi; (q) 9-BBN, then $NaOH/H_2O_2$; (r) PivCl, pyridine; (s) $NaClO_2$, NaH_2PO_4, 2-methyl-2-butene; (t) $TMSCHN_2$; (u) TBSOTf, 2,6-lutidine; (v) K_2CO_3; (w) DIAD, PPh_3, **S3**; (x) $(NH_4)_6Mo_7O_{24}$-$4H_2O$, H_2O_2.

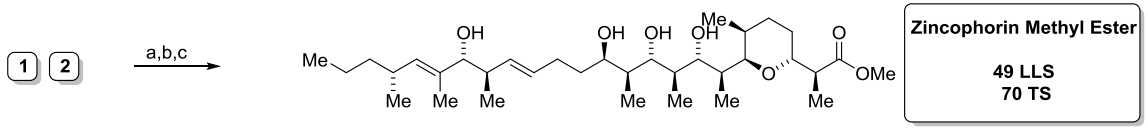
Zincophorin (Guindon, *Tetrahedron* **2015**, *71*, 709.) (*continued*)

Fragment 2



Key: (a) $(COCl)_2$, DMSO, then Et_3N; (b) $Ph_3P{=}C(Me)CO_2Et$; (c) DIBAL-H; (d) $MgCl_2$, Et_3N, TMSCl, **A1**; (e) TFA; (f) $PMPOC(NH)CCl_3$ (g) $LiBH_4$; (h) DMP, $NaHCO_3$.

Fragment Union and End Game



Key: (a) KHMDS; (b) DDQ, pH 7 buffer; (c) TBAF.

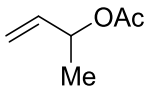
Synthesis	Construction Steps	Strategic Redox	Non-strategic Redox	Protecting Group Manipulations	Functional Group Interconversions	**Total Steps (LLS)**
Danishefsky (1987)	12	4	15	14	16	**61 (35)**
Cossy (2003)	13	3	18	10	12	**56 (30)**
Miyashita (2004)	21	1	13	12	5	**53 (38)**
Leighton (2011)	10	1	3	8	11	**33 (21)**
Guindon (2015)	12	2	21	18	17	**70 (49)**
Krische (2015)	10	0	3	3	9	**25 (13)**

2. General Information

All reactions were carried out in oven- or flame-dried flasks, under an inert atmosphere of argon or nitrogen if anhydrous conditions were required. Anhydrous solvents were transferred by oven-dried syringes and needles. All reactions were carried out at room temperature unless otherwise stated. Reagents obtained from Acros, Sigma-Aldrich, Alfa Aesar, Fisher Scientific, Takasago, Oakwood, or Strem Fine Chemicals suppliers were used directly as supplied or following purification according to procedures described by Amarego and Chai.[1] Tetrahydrofuran, dichloromethane, diethyl ether, and toluene were distilled prior to use. Thin layer chromatography (TLC) was performed on Dynamic Adsorbents F_{254} 0.25 mm precoated silica gel plates. Compounds were visualised under UV light and by staining with potassium permanganate, phosphomolybdic acid or *para*-anisaldehyde solution. Flash column chromatography was performed using silica gel (40–63 μm, Silicycle) and using head pressure by means of a positive pressure from an air line, according to Still.[2] Infra-red spectra were recorded on a Thermo Nicolet 380 spectrometer. Melting points were obtained using a Thomas-Hoover apparatus and are uncorrected. High-resolution mass spectra were recorded on an Agilent Technologies 6530 Accurate Mass Q-Tof LC/MS instrument for electrospray ionisation (ESI) or a Micromass Autospec Ultima instrument for chemical ionization (CI) and are reported as a ratio of mass to charge (*m*/*z*) in Daltons. Specific optical rotations were recorded on an Atago AP-300 automatic polarimeter at the sodium line (589.3 nm) in $CHCl_3$ or CH_2Cl_2. Solution concentrations are given in the units of 10^{-2} g mL^{-1}. ^{1}H NMR spectra were recorded on an Agilent MR (400 MHz), Varian DirectDrive (400, 600 MHz), or Varian INOVA (500 MHz) spectrometer in $CDCl_3$ or C_6D_6 at ambient temperature. Chemical shifts are quoted to two decimal places in parts per million (ppm) with splittings recorded as singlet (s), doublet (d), triplet (t), quartet (q), quintet (quin) and multiplet (m). Coupling constants, *J*, are quoted to one decimal place in Hz. ^{13}C NMR spectra were recorded on an Agilent MR (100 MHz), Varian DirectDrive (100, 150 MHz), or Varian INOVA (125 MHz) spectrometer in $CDCl_3$ or C_6D_6 with broadband decoupling. All NMR chemical shifts were referenced to residual solvent peaks ($CDCl_3$, δ_H 7.26 ppm, δ_C 77.0 ppm; C_6D_6 δ_H 7.16 ppm, δ_C 128.06 ppm).

3. Preparation of Starting Materials and Reagents

(*rac*)-But-3-en-2-yl acetate (S1)

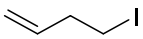


To a stirred solution of (*rac*)-3-butene-2-ol (13.0 mL, 150.0 mmol), 4-dimethylaminopyridine (1.00 g, 8.1 mmol, 5.4 mol%), Et_3N (45 ml, 323.0 mmol, 215 mol%), and CH_2Cl_2 (150 mL) in a round bottom flask was added Ac_2O dropwise (23.0 mL, 242.3 mmol, 160 mol%) at 0 °C. The reaction was allowed to warm to room temperature over 4 h. The reaction mixture was transferred into a separatory funnel with 70 mL 2M HCl. The layers were separated. The organic layer was washed once with 50 mL saturated $NaHCO_3$ and 50 mL of a 1:1 mixture of saturated brine and saturated $CuSO_4$. The organic layer was dried with Na_2SO_4, filtered, and the volatiles were removed *via* rotary evaporation (250 mbar, 35 °C). The residue was subjected to distillation over K_2CO_3 (bp = 120-125 °C) to afford but-3-en-2-yl acetate (**S1**) (14.21 g, 124.5 mmol, 83 % yield) as a colorless oil. The spectral data were identical to those reported.[3]

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.84 (ddd, *J* = 17.2, 10.8, 6.0 Hz, 1H), 5.34 (quin.t, *J* = 6.4, 1.2, 1H), 5.24 (dt, *J* = 17.2, 1.2 Hz, 1H), 5.13 (dt, *J* = 10.8, 1.2 Hz, 1H), 2.05 (s, 3H), 1.31 (d, *J* = 6.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 137.7 115.6, 70.9, 21.2, 19.8.

4-Iodo-1-butene (S2)

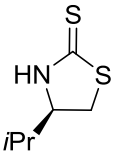


To a stirred solution of NaI (9.97 g, 66.52 mmol, 200 mol%) in acetone (27 mL) in a round bottomed flask was added 4-bromo-1-butene (4.49 g, 33.26 mmol, 100 mol%). The flask was equipped with a reflux condenser, and the reaction was heated at reflux for 45 min. The reaction was cooled to room temperature, and water (10 mL) was added. The reaction mixture was extracted with Et_2O (3 × 10 mL) and the combined extracts were dried with Na_2SO_4, and filtered. The volatiles were removed *via* rotary evaporation (400 mbar, water bath temperature 35 °C), and the remaining residue was distilled over K_2CO_3 and Cu wire (bp = 128-130 °C) to yield 4-iodo-1-butene (**S2**) (3.60g, 19.78 mmol), 59% yield). The spectral data were consistent with those reported. [4]

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.81-5.70 (m, 1H), 5.14-5.09 (m, 2H), 3.18 (t, *J* = 7.2 Hz, 2H), 2.62 (qt, *J* = 7.2, 1.2 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 136.8, 117.0, 37.6, 4.7.

(*R*)-4-Isopropylthiazolidine-2-thione (S3)



To a solution of D-valine (4.00 g, 34.1 mmol) in THF (100 mL) at 0 °C was added $NaBH_4$ (3.10 g, 81.8 mmol, 240 mol%) in one portion. The resulting mixture was stirred for 5 min before a solution of iodine (8.65 g, 34.1 mmol, 100 mol%) in THF (10.0 mL) was added dropwise over 20 min (vigorous gas evolution). The reaction mixture was warmed to room temperature and stirred until no more effervescence was observed and then heated to reflux. After 24 hrs the reaction was cooled to room temperature and MeOH was added dropwise until the mixture became clear. The volatiles were removed *via* rotary evaporation and the resultant white paste was dissolved in an aqueous solution of KOH (20% w/v, 25 mL). The solution was stirred for 4 hrs before being extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and the volatiles were removed *via* rotary evaporation to afford crude D-valinol (3.0 g) as a white semisolid, which was used in the next step without further purification.

To a solution of crude D-valinol (1.10 g, 10.6 mmol) in EtOH (3.0 mL) was added carbon disulfide (1.66 mL, 27.6 mmol, 260 mol%). A solution of KOH (1.61 g, 28.7 mmol, 270 mol%) in a 1:1 mixture of EtOH (6.0 mL) and H_2O (6.0 mL) was added slowly over 20 min using a pressure-equalising addition funnel. The addition funnel was replaced with a reflux condenser and the resulting mixture was heated at reflux for 72 hrs, at which the reaction was cooled to room temperature and the volatiles were removed *via* rotary evaporation. The resulting suspension was acidified with an aqueous solution of HCl (0.5 M, 60 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were dried over $MgSO_4$, filtered and the volatiles were removed *via* rotary evaporation to give (*R*)-4-isopropylthiazolidine-2-thione (**S3**) (1.47 g, 9.12 mmol, 86%) as a dark yellow solid, which was used in the next step without further purification. The spectral data were identical to those reported[5]

TLC (SiO_2): R_f = 0.15 (hexanes/CH_2Cl_2 50:50)

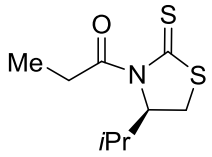
$[\alpha]_D^{20}$: +31.2 (*c* 1.0, $CHCl_3$).[5]

mp 64–66 °C, (lit.5 68–69 °C)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.74 (s, 1H), 4.02 (td, *J* = 8.2, 6.2 Hz, 1H), 3.43 (dd, *J* = 11.2, 8.4 Hz, 1H), 3.22 (dd, *J* = 11.2, 8.0 Hz, 1H), 1.90 (dq, *J* = 13.4, 6.7 Hz, 1H), 0.92 (d, *J* = 6.8 Hz, 3H), 0.89 (d, *J* = 6.8 Hz, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): δ 200.2, 69.7, 35.3, 31.5, 18.3, 17.7

(*R*)-1-(4-Isopropyl-2-thioxothiazolidin-3-yl)propan-1-one (S4)



To a stirred solution of (*R*)-4-isopropylthiazolidine-2-thione (**S3**) (730 mg, 4.53 mmol) in THF (3.0 mL) was added *n*-BuLi (2.5 M in hexanes, 2.0 mL, 4.98 mmol, 110 mol%) dropwise at −78 °C and the resultant solution was stirred for 10 min. Freshly distilled propionyl chloride (0.515 mL, 5.89 mmol, 130 mol%) was added dropwise and the resulting mixture was stirred for 15 min before being warmed to room temperature and stirred for a total period of 2 h. The reaction was then cooled to 0 °C and quenched with a saturated aqueous solution of NH_4Cl (5.0 mL) and H_2O (5.0 mL). The mixture was extracted with CH_2Cl_2 (3 × 15 mL) and the combined organics were dried over $MgSO_4$, filtered and the volatiles were removed *via* rotary evaporation. The residue was subjected to flash column chromatography (SiO_2, hexanes/CH_2Cl_2 80:20) to afford (*R*)-1-(4-isopropyl-2-thioxothiazolidin-3-yl)propan-1-one (**S4**) (748 mg, 3.44 mmol, 76%) as a yellow oil. The spectral data were identical to those reported.[5]

TLC (SiO_2): R_f = 0.75 (hexanes/CH_2Cl_2 50:50)

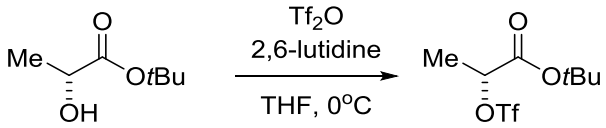
$[\alpha]_D^{20}$: –417.1 (*c* 1.0, $CHCl_3$).[5]

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.20–5.13 (m, 1H), 3.50 (dd, *J* = 11.5, 8.0 Hz, 1H), 3.36 (qd, *J* = 18.0, 7.3 Hz, 1H), 3.15 (qd, *J* = 18.1, 7.1 Hz, 1H), 3.01 (dd, *J* = 11.5, 1.0 Hz, 1H), 2.36 (qd, *J* = 13.4, 6.8 Hz, 1H), 1.16 (t, *J* = 7.0 Hz, 3H), 1.05 (d, *J* = 7.0 Hz, 3H), 0.97 (d, *J* = 7.0 Hz, 3H)

^{13}C NMR (100 MHz, $CDCl_3$): δ 202.6, 174, 7, 71.5, 32.0, 30.7, 30.3, 19.0, 17.6, 8.9

4. Experimental Procedures and Characterization of Materials

(*R*)-*tert*-Butyl-2-(((trifluoromethyl)sulfonyl)oxy)propanoate (S5)



To a stirred solution of (*R*)-*t*-butyl 2-hydroxypropanoate (**3**)[6] (4.0 g, 27.4 mmol) and 2,6-lutidine (4.80 mL, 41.1 mmol, 150 mol%) in CH_2Cl_2 (110 mL) was added trifluoromethanesulfonic anhydride (6.44 mL, 38.3 mmol, 140 mol%) dropwise using a syringe pump (4 mL/h) at 0 °C. The resulting solution was stirred for 1 hr before being slowly diluted with petroleum ether (550 mL, 20 mL/mmol) and washed with a 3:1 mixture of brine and 1 M HCl (3 × 250 mL). The organic layer was dried over $MgSO_4$ and filtered. The volatiles were removed *via* rotary evaporation (300 mbar, water bath temperature 25 °C) and the residue was subjected to flash column chromatography (SiO_2, petroleum ether/CH_2Cl_2 50:50) to afford triflate **S5** (6.71 g, 24.1 mmol, 88%) as a colorless oil. The spectral data were identical to those reported.[7]

TLC (SiO_2): R_f = 0.70 (petroleum ether/CH_2Cl_2 70:30).

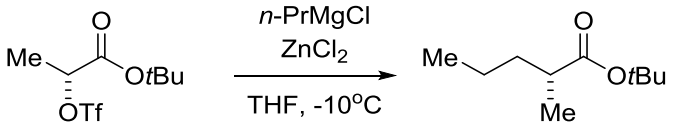
$[\alpha]_D^{20}$: −42.2 (*c* 2.50, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.10 (q, *J* = 6.9 Hz, 1H), 1.66 (d, *J* = 6.7 Hz, 3H), 1.51 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 166.4, 118.5 (q, *J* = 319.3 Hz), 84.3, 80.6, 27.8, 18.0.

^{19}F NMR (376 MHz, $CDCl_3$): δ -75.3.

(*R*)-*tert*-Butyl-2-methylpentanoate (S6)



To a solution of anhydrous $ZnCl_2$ (308 mg, 2.26 mmol, 10 mol%) in THF (75 mL) was added triflate **S5** (6.30 g, 22.6 mmol) and the resultant solution was cooled to −10 °C. *n*-Propylmagnesium chloride (2.0 M in Et_2O, 14.1 mL, 28.2 mmol, 125 mol%) was added dropwise over 15 min and the reaction mixture was stirred −10 °C for 5 hrs before being diluted with pentane (75 mL) and quenched with a saturated aqueous solution of NH_4Cl (50 mL). The layers were separated and the aqueous layer was extracted with pentane (3 × 50 mL). The combined organic extracts were dried over $MgSO_4$ and filtered. The volatiles were removed *via* rotary evaporation (250 mbar, water bath temperature 35 °C) and the residue was subjected to flash column chromatography (SiO_2, pentane/Et_2O 95:5) to afford ester **S6** (3.34 g, 19.4 mmol, 86%) as a colorless oil.

TLC (SiO_2): R_f = 0.75 (hexanes/Et_2O 98:2).

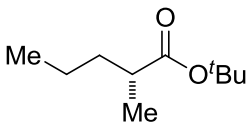
$[\alpha]_D^{20}$: −12.5 (*c* 0.80, $CHCl_3$).

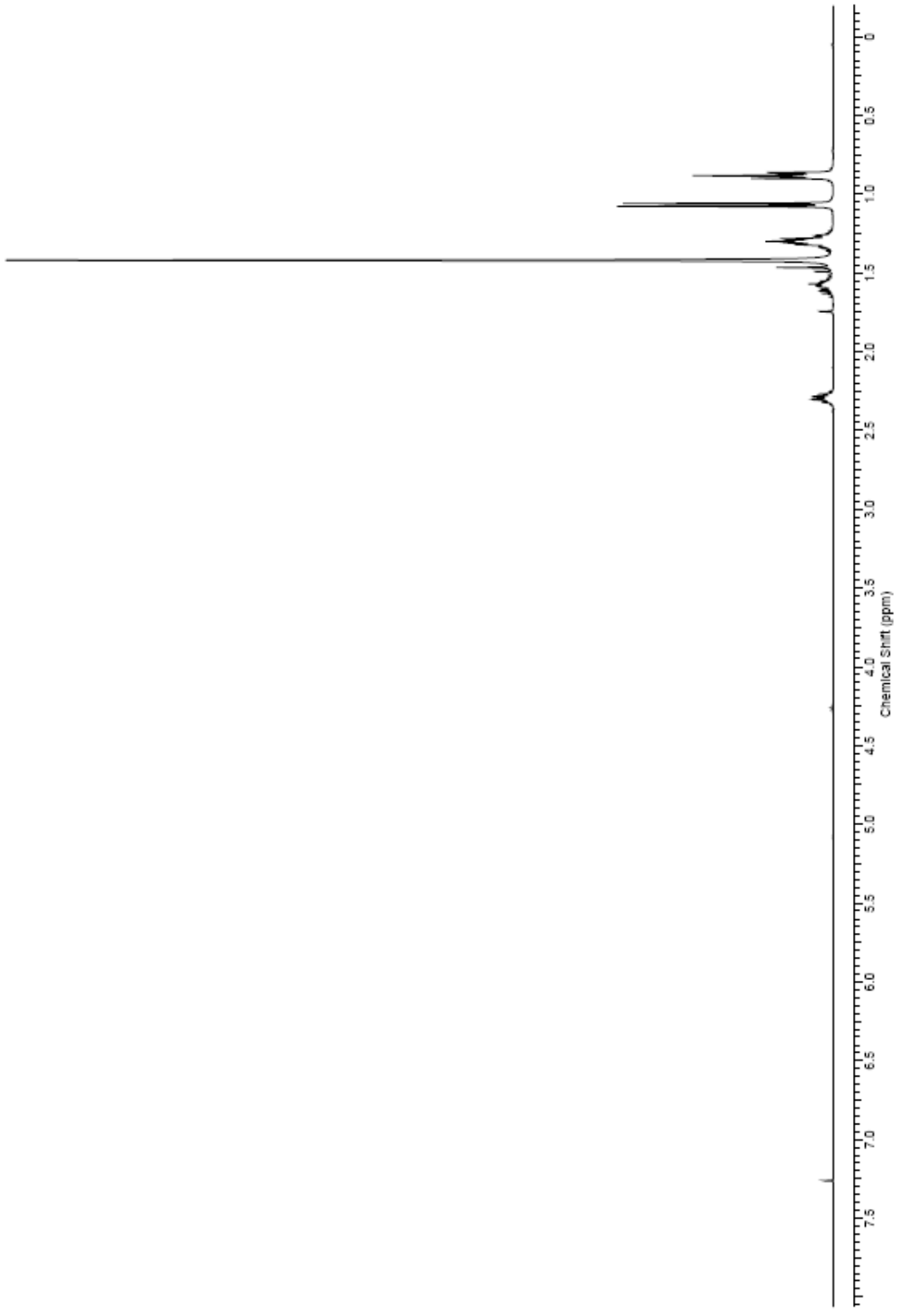
^{1}H NMR (400 MHz, $CDCl_3$): δ 2.37–2.25 (m, 1H), 1.65–1.56 (m, 1H), 1.43 (s, 9H), 1.38–1.23 (m, 3H), 1.08 (d, *J* = 7.0 Hz, 3H), 0.90 (t, *J* = 7.2 Hz, 3H).

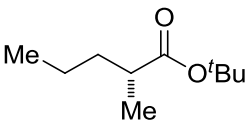
^{13}C NMR (100 MHz, $CDCl_3$): δ 176.4, 79.7, 40.2, 36.1, 28.1, 20.4, 17.1, 14.0.

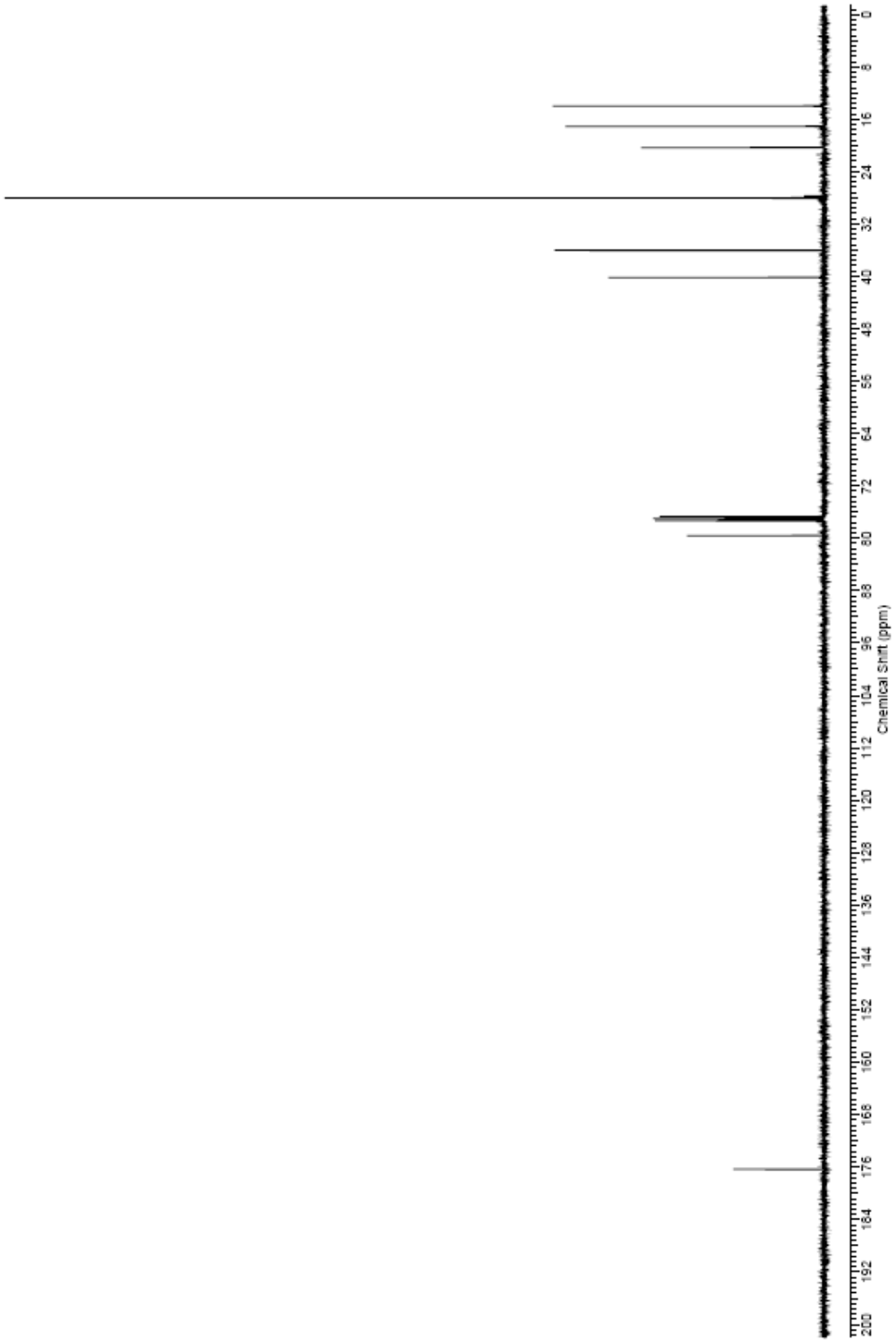
FTIR (neat): 2972, 1757, 1416, 1371, 1244, 1202 cm^{-1}.

HRMS: (ESI, *m/z*) for $C_{10}H_{20}NaO_2$ calculated 195.1356, found 195.1354.

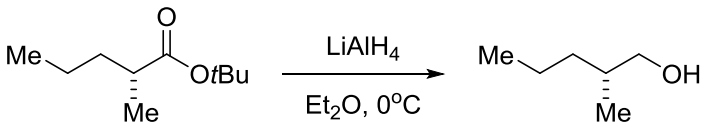

O
Me
O^{t}Bu
Me


Chemical Shift (ppm)


O
Me
O^{t}Bu
Me


0
8
16
24
32
40
48
56
64
72
80
88
96
104
112
120
128
136
144
152
160
168
176
184
192
200
Chemical Shift (ppm)

(*R*)-2-Methylpentan-1-ol (4)



To a stirred solution of ester **S6** (7.00 g, 40.7 mmol) in Et_2O (200 mL) at 0 °C was added $LiAlH_4$ (1.73 g, 45.6 mmol, 120 mol%) portionwise over 10 min. The resulting mixture was allowed to warm to room temperature and stirred for 2 h. The reaction was carefully quenched by the sequential addition of H_2O (7.0 mL), an aqueous solution of NaOH (15% w/v, 7.0 mL) and H_2O (21 mL). The mixture was diluted with Et_2O and stirred for 30 min. The layers were portioned, and the aqueous layer was extracted with Et_2O (3 × 15 mL). The combined organics were dried over Na_2SO_4 and filtered through a plug of celite before being concentrated *via* rotary evaporation (400 mbar, water bath temperature 35 °C) to give alcohol **4** (4.00 g, 39.1 mmol, 96%) as a colorless oil, which was used in the next step without further purification. The spectral data were identical to those reported.[8]

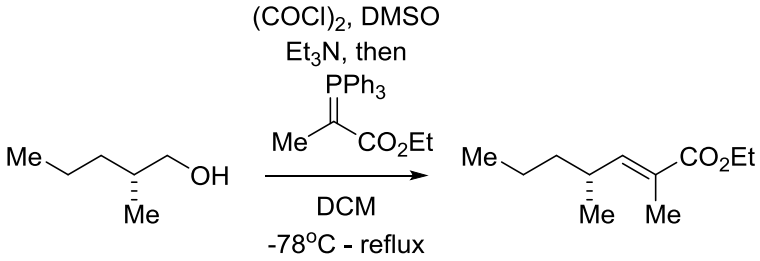
TLC (SiO_2): R_f = 0.35 (hexanes/Et_2O 70:30).

$[\alpha]_D^{20}$: +11.0 (*c* 1.0, $CHCl_3$).[9]

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.50 (dd, *J* = 10.6, 5.9 Hz, 1H), 3.40 (dd, *J* = 10.6, 6.7 Hz, 1H), 1.68–1.55 (m, 1H), 1.41–1.31 (m, 3H), 1.16–1.01 (m, 1H), 0.94–0.86 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 68.4, 35.5, 35.4, 20.0, 16.5, 14.3.

(*R*,*E*)-Ethyl-2,4-dimethylhept-2-enoate (S7)



To a solution of oxalyl chloride (3.05 mL, 36.0 mmol, 200 mol%) in CH_2Cl_2 (120 mL) at −78 °C was added DMSO (5.10 mL, 72.0 mmol, 400 mol%) dropwise over 5 min. The resulting solution was stirred for 30 min before a solution of alcohol **4** (1.84 g, 18.0 mmol) in CH_2Cl_2 (10 mL) was added dropwise over 10 min. The reaction mixture was stirred for 45 min at −78 °C before triethylamine (10.0 mL, 72.0 mmol, 400 mol%) was added slowly over 10 min. The resultant white suspension was stirred for 30 min and slowly warmed to room temperature. A solution of (carbethoxymethylene)triphenylphosphorane (7.83 g, 21.6 mmol, 120 mmol%) in CH_2Cl_2 (20 mL) was slowly added and the resulting mixture was heated at reflux for 48 h. The mixture was cooled to room temperature and the volatiles removed *via* rotary evaporation. The residue was triturated with hexanes (100 mL) and filtered through a plug of celite. The volatiles of the filtrate were removed *via* rotary evaporation, and the residue was subjected to flash column chromatography (SiO_2, hexanes/CH_2Cl_2 50:50) to afford ester **S7** (2.38 g, 13.0 mmol, 72%) as a colorless oil. The spectral data were identical to those reported.[8]

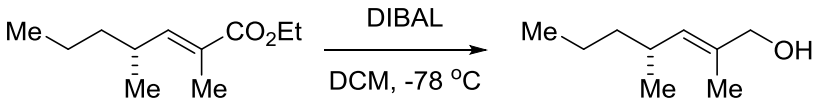
TLC (SiO_2): R_f = 0.75 (hexanes/CH_2Cl_2 50:50).

$[\alpha]_D^{20}$: −4.3 (*c* 1.0, $CHCl_3$).[10]

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.52 (dd, *J* = 10.2 and 1.2 Hz, 1H), 4.17 (q, *J* = 7.2 Hz, 2H), 2.55–2.45 (m, 1H), 1.82 (d, *J* = 1.2 Hz, 3H), 1.36–1.20 (m, 7H), 0.98 (d, *J* = 6.7 Hz, 3H), 0.87 (t, *J* = 6.7 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.5, 148.1, 126.2, 60.4, 39.1, 33.0, 20.6, 20.0, 14.3, 14.1, 12.5.

(*R*,*E*)-2,4-Dimethylhept-2-en-1-ol (5)



To a stirred solution of ester **S7** (1.80 g, 9.83 mmol) in CH_2Cl_2 (100 mL) was added diisobutylaluminium hydride (1.0 M solution in hexanes, 29.4 mL, 29.4 mmol, 300 mol%) dropwise at −78 °C. The resulting solution was stirred for 1 hr before being slowly quenched with MeOH (10 mL) and a saturated aqueous solution of Rochelle's salt (100 mL). The resultant mixture was warmed to room temperature and was stirred vigorously for 2 h. The layers were separated and the aqueous layer was extracted with Et_2O (3 × 50 mL). The combined organic extracts were washed with brine (50 mL), dried over $MgSO_4$ and filtered. The volatiles were removed *via* rotary evaporation, and the residue was subjected to flash column chromatography (SiO_2, hexanes/Et_2O 70:30) afforded alcohol **5** (1.23 g, 8.65 mmol, 88%) as a colorless oil. The spectral data were identical to those reported.[8]

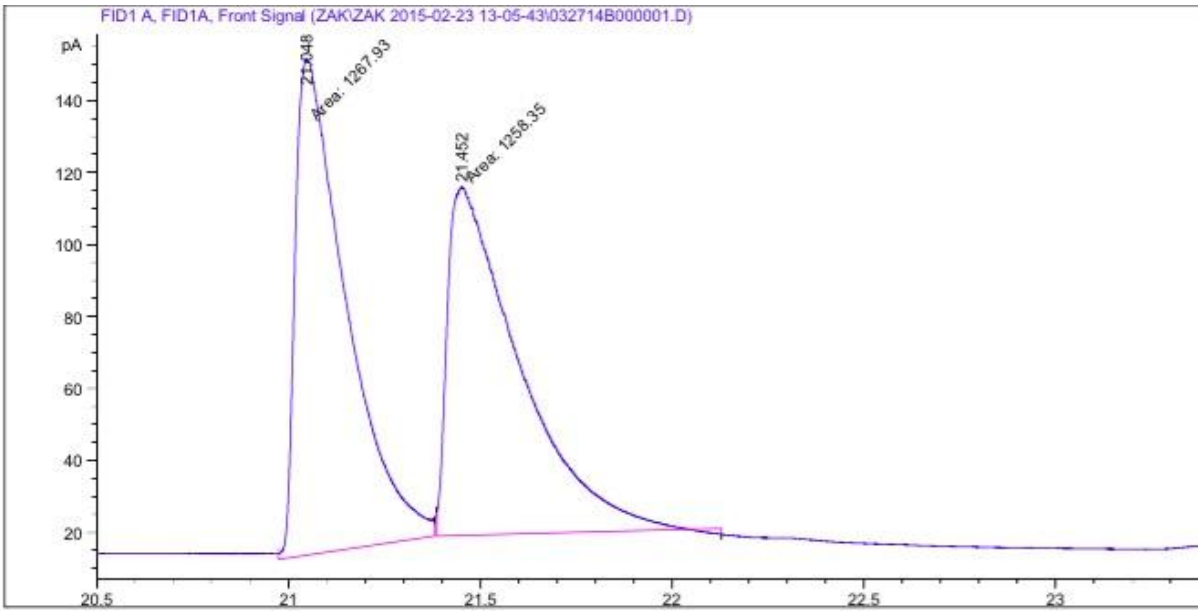
TLC (SiO_2): R_f = 0.40 (hexanes/Et_2O 70:30).

$[\alpha]_D^{20}$: −14.4 (*c* 1.1, $CHCl_3$).[11]

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.14 (dd, *J* = 9.6, 1.0 Hz, 1H), 3.95 (s, 2H), 2.43–2.28 (m, 1H), 1.63 (d, *J* = 1.2 Hz, 3H), 1.33–1.09 (m, 5H), 0.90 (d, *J* = 6.7 Hz, 3H), 0.88–0.80 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 133.1, 132.9, 68.9, 39.8, 31.7, 20.9, 20.5, 14.2, 13.7.

GC Cyclosil-B: initial temperature 50 °C; final temperature 80 °C; rate = 1.5 °C/min; 5 min hold; flow rate = 2 mL/min; T_{minor} = 21.25 min, T_{major} = 21.55 min; *ee* = 92%.



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
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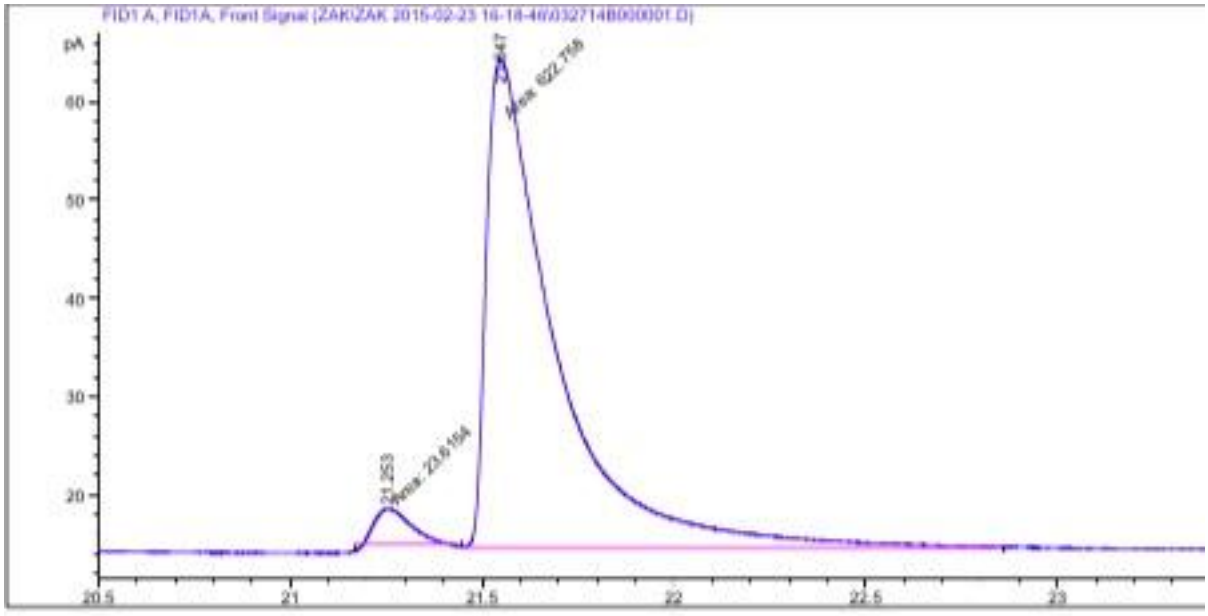
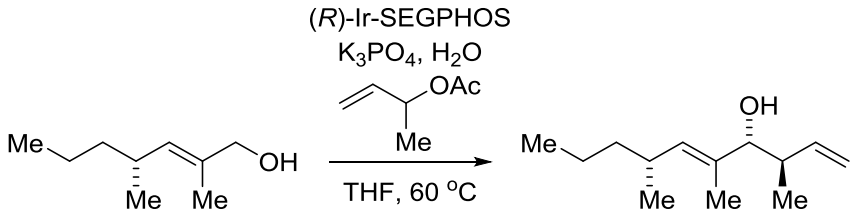
2	21.452	MM	0.2163	1258.34558	96.98020	49.81030



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	21.253	MM	0.1087	23.61542	3.62064	3.65353
2	21.547	MM	0.2084	622.75787	49.81336	96.34647

(3*R*,4*R*,7*R*,*E*)-3,5,7-Trimethyldeca-1,5-dien-4-ol (6)



A resealable pressure tube equipped with a magnetic stir bar was charged with (*R*)-Ir-SEGPHOS (210 mg, 0.203 mmol, 5 mol%) and anhydrous K_3PO_4 (431 mg, 2.03 mmol, 50 mol%), then the tube was sealed with a rubber septum and purged with argon for 2 min. Alcohol **5** (577 mg, 4.06 mmol) and THF (2.03 mL) were added and the resulting suspension was sparged with argon for 2 min. But-3-en-2-yl acetate (**S1**) (926 mg, 8.12 mmol, 200 mol%) and H_2O (0.365 mL, 20.3 mmol, 500 mol%) were added and the rubber septum was quickly replaced with a screw cap. The reaction mixture stirred for 15 min at room temperature before being heated to 60 °C for 48 h. The mixture was then allowed to cool to room temperature and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, hexanes/Et_2O 90:10) afforded alcohol **6** (572 mg, 2.92 mmol, 72%) as a colorless oil in a 5.5:1 dr. The diastereomers were carried forward as a mixture. The major diastereomer is characterized below.

TLC (SiO_2): R_f = 0.65 (hexanes/Et_2O 70:30).

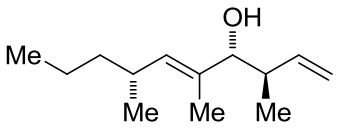
$[\alpha]_D^{20}$: −13.0 (*c* 1.0, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.73 (ddd, *J* = 17.2, 10.0, 8.4 Hz, 1H), 5.20–5.08 (m, 3H), 3.60 (d, *J* = 9.0 Hz, 1H), 2.47–2.34 (m, 1H), 2.34–2.22 (m, 1H), 1.79 (br. s., 1H), 1.60 (d, *J* = 1.2 Hz, 3H), 1.32–1.11 (m, 5H), 0.93 (d, *J* = 6.7 Hz, 3H), 0.87 (d, *J* = 7.0 Hz, 5H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 141.4, 136.0, 133.0, 116.3, 81.7, 42.1, 39.8, 31.8, 20.9, 20.6, 16.8, 14.1, 10.8.

FTIR (neat): 2957, 2927, 2871, 1691, 1638, 1455, 1377, 1005, 909 cm^{-1}.

HRMS: (ESI, *m/z*) for $C_{13}H_{24}NaO$ calculated 219.1719, found 219.1721.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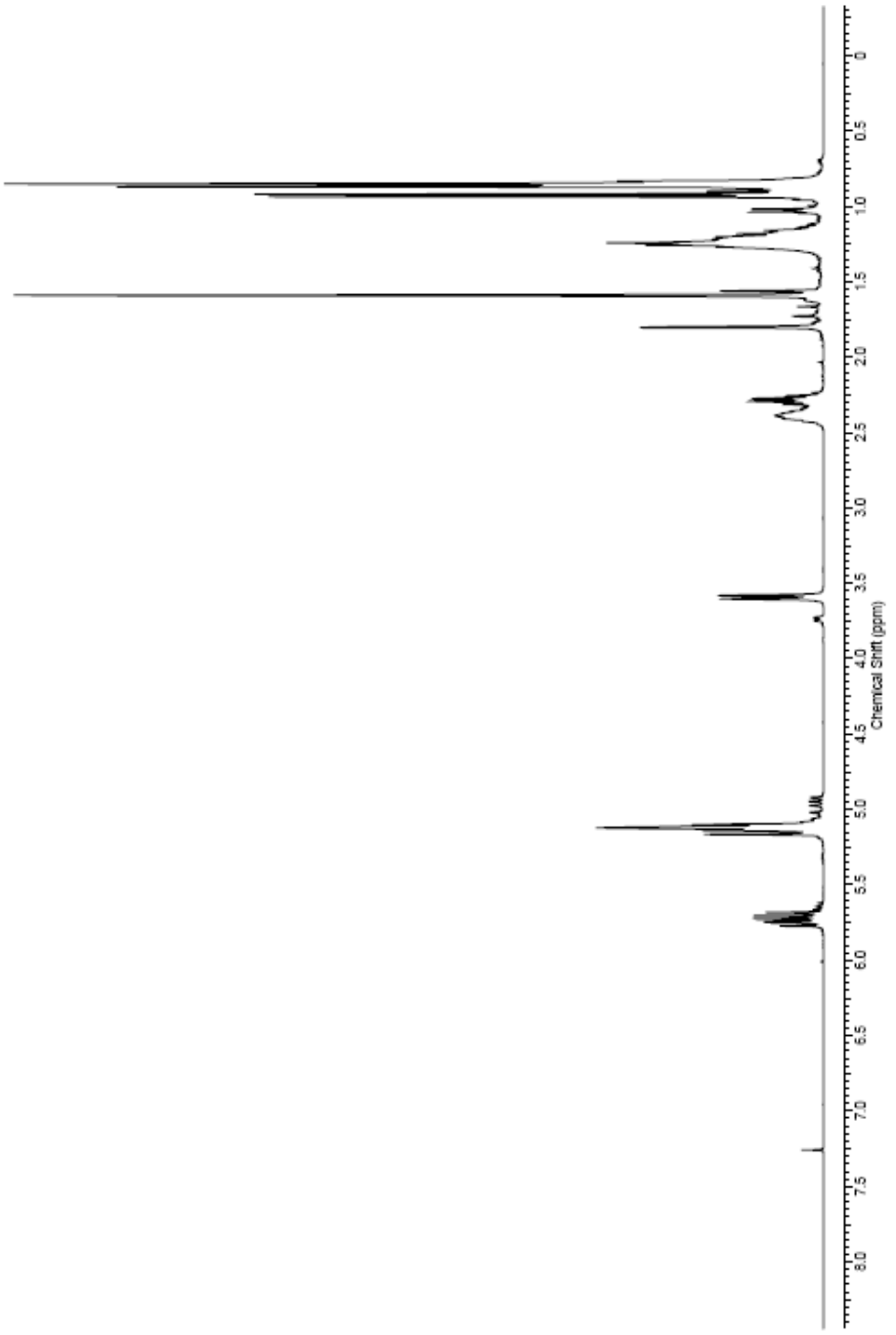
Me
Me
Me
Me


Chemical Shift (ppm)
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1.5
2.0
2.5
3.0
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6.0
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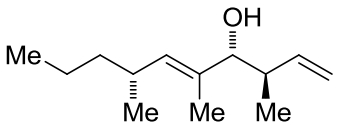
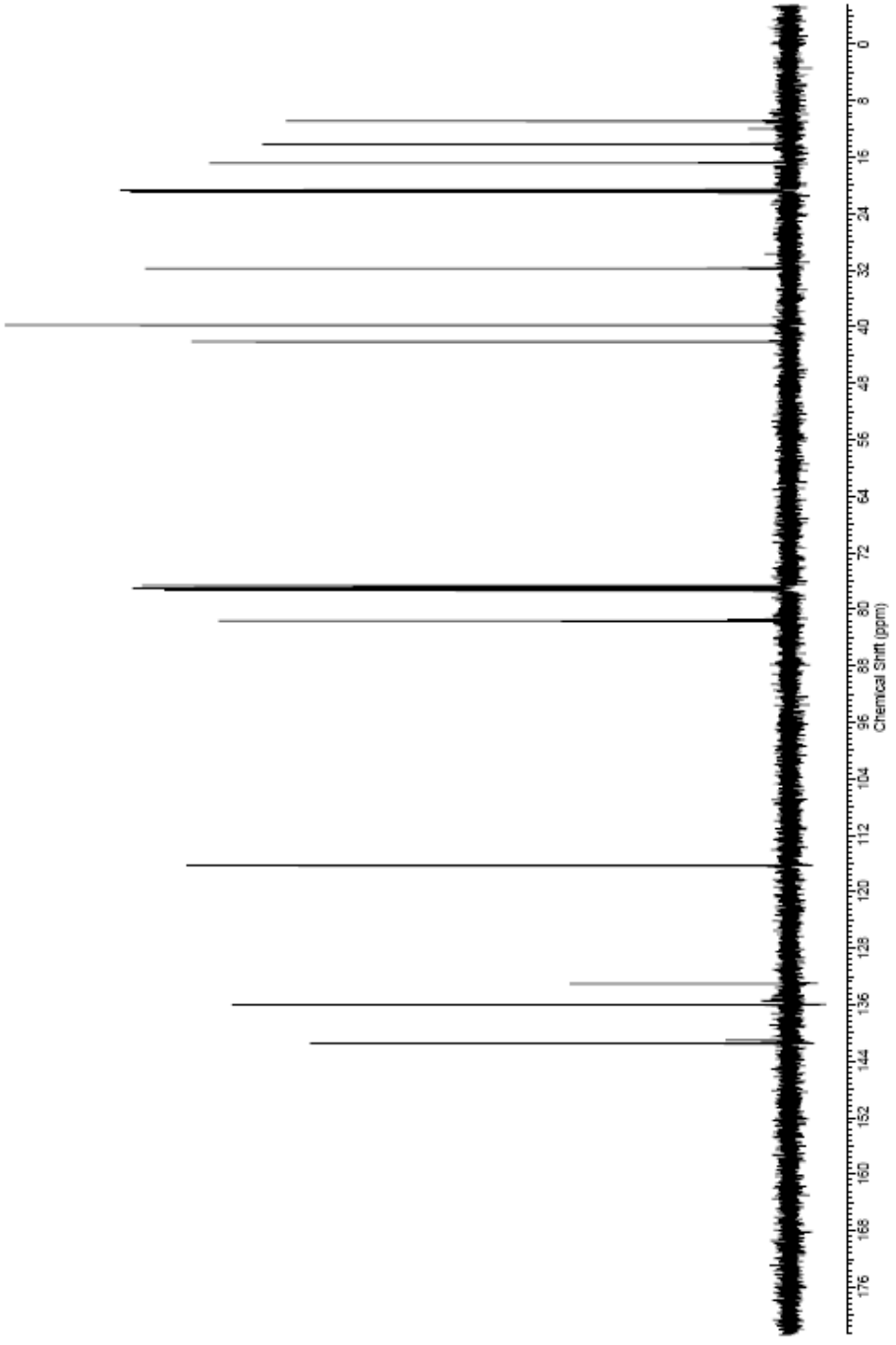
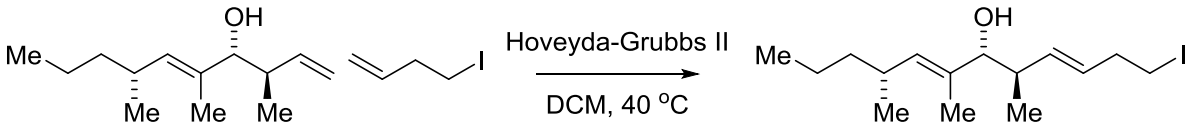
7.0
7.5
8.0


OH
Me
Me
Me
Me


0
8
16
24
32
40
48
56
64
72
80
88
96
104
112
120
128
136
144
152
160
168
176
Chemical Shift (ppm)

(3*E*,5*R*,6*R*,7*E*,9*R*)-1-Iodo-5,7,9-trimethyldodeca-3,7-dien-6-ol (S8)



A flame-dried round bottom flask was charged with Hoveyda–Grubbs 2nd Generation catalyst (89.3 mg, 0.143 mmol, 15 mol%) and purged with argon for 5 min. A solution of alkene **6** (187 mg, 0.950 mmol) in sparged CH_2Cl_2 (3.8 mL) was added slowly, followed by 4-iodo-1-butene (**S2**) (1.383g mL, 7.60 mmol, 800 mol%), and the resulting mixture was heated to 40 °C and stirred for 24 hrs. The reaction was allowed to cool to room temperature and the volatiles were removed *via* rotary evaporation. The residue was subjected to flash column chromatography (SiO_2, hexanes/Et_2O 90:10) to afford iodide **S8** (221mg, 0.675 mmol, 71%) as a colorless oil.

TLC (SiO_2): R_f = 0.25 (hexanes/Et_2O 70:30)

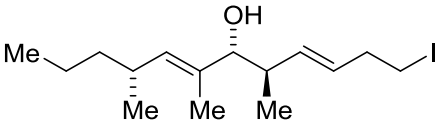
$[\alpha]_D^{20}$: +1.5 (*c* 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.53-5.36 (m, 2H), 5.15 (d, *J* = 9.6 Hz, 1H), 3.60 (d, *J* = 9.2 Hz, 1H), 3.27-3.11 (m, 2H), 2.65-2.51 (m, 2H), 2.44-2.24 (m, 2H), 1.96 (s, 1H), 1.60 (d, *J* = 1.2 Hz, 3H), 1.30-1.14 (m, 4H), 0.94 (d, *J* = 6.8 Hz, 3H), 0.88-0.84 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 136.3, 136.1, 132.9, 130.7, 81.8, 41.2, 39.8, 36.3, 31.8, 21.0, 20.7, 17.1, 14.2, 10.9, 6.8.

FTIR (neat): 3356, 2956, 2925, 1636, 1454, 1376, 1243, 1168, 1003, 970, 668 cm^{-1}.

HRMS: (CI+, *m/z*) for $C_{15}H_{28}IO^+$ calculated 351.1179, found 351.1185.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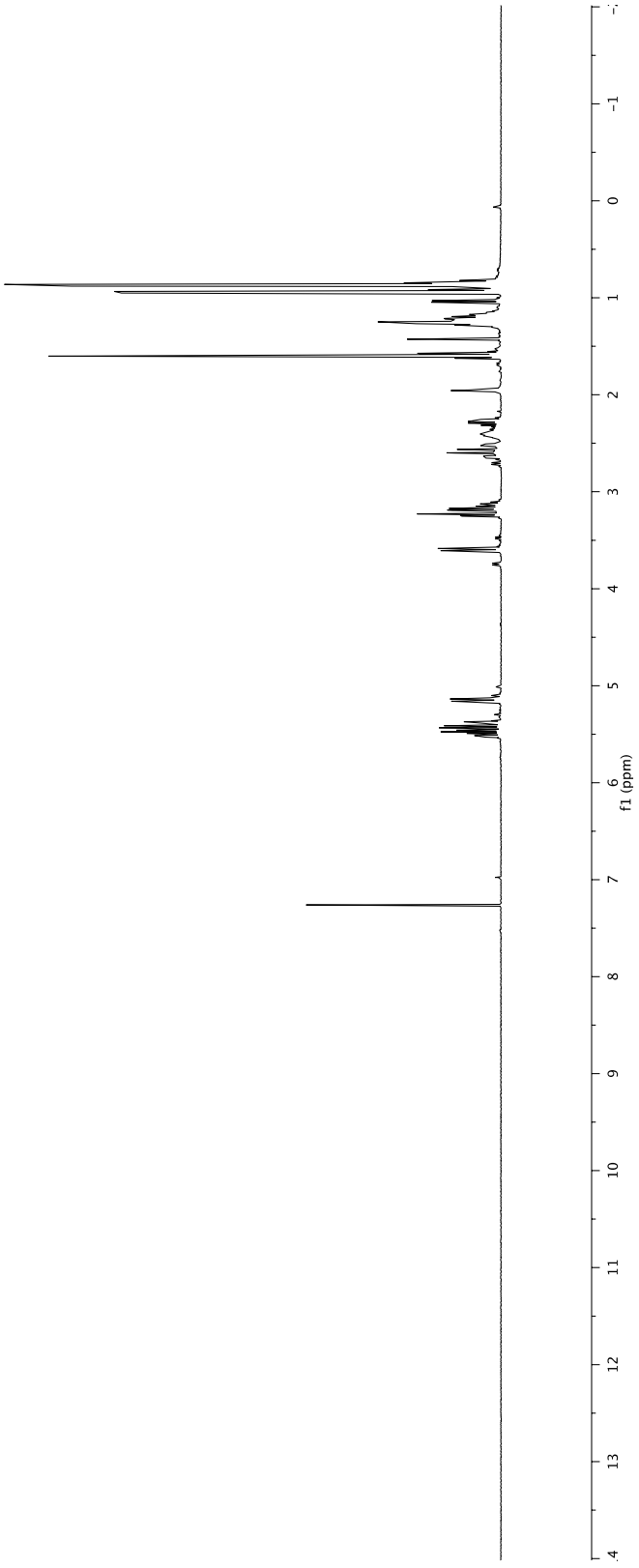
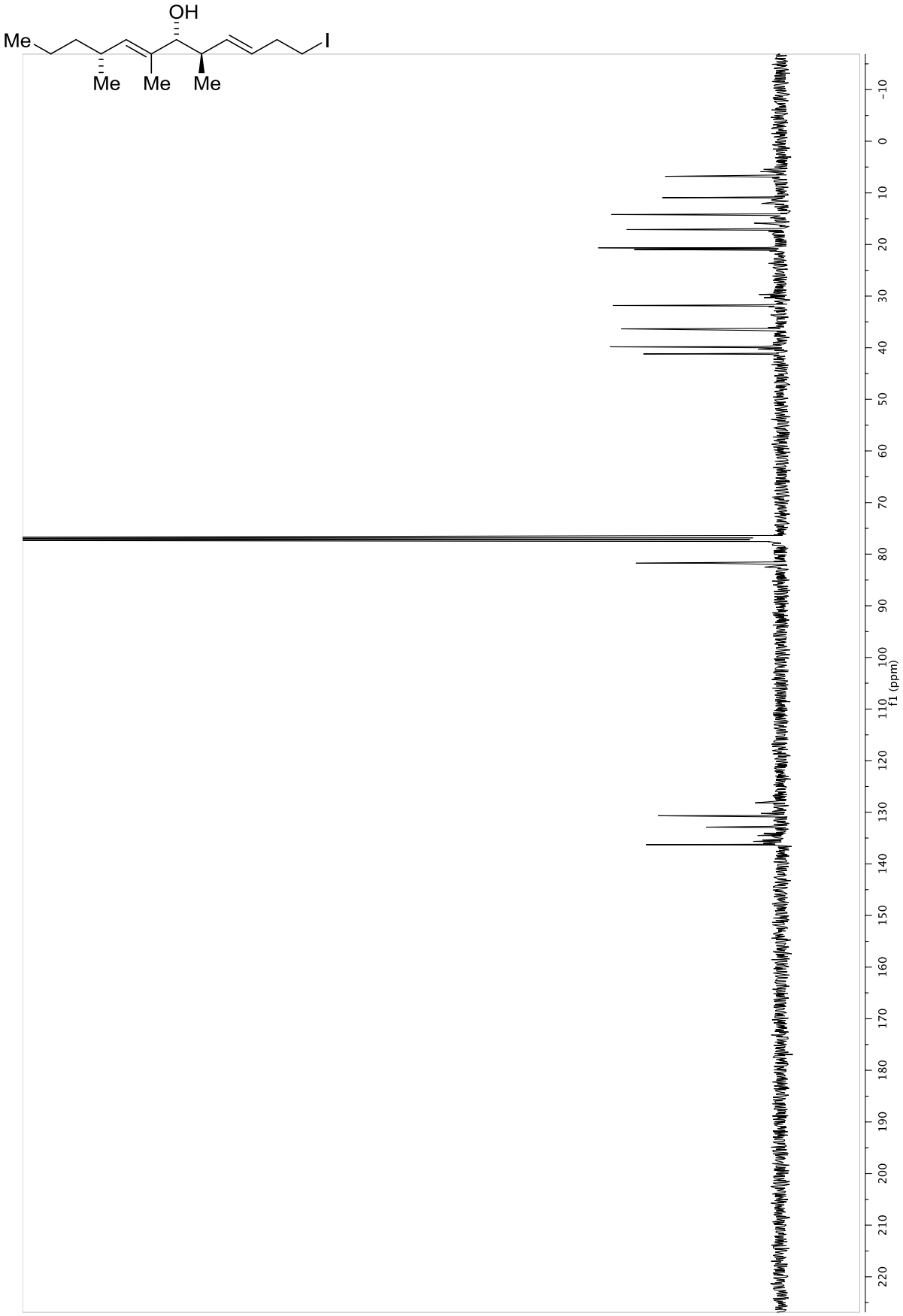
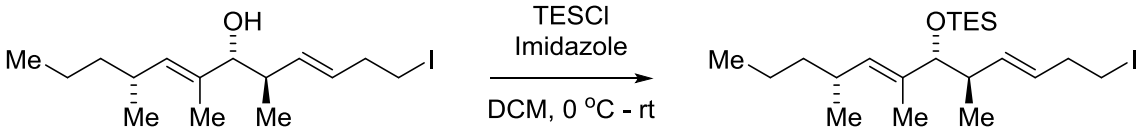
Me
I
Me
Me
Me


f1 (ppm)


OH
Me
I
Me
Me
Me
f1 (ppm)

Triethyl(((3*E*,5*R*,6*R*,7*E*,9*R*)-1-iodo-5,7,9-trimethyldodeca-3,7-dien-6-yl)oxy)silane (Fragment A)



To a stirred solution of iodide **S8** (134.0 mg, 0.383 mmol) in CH_2Cl_2 (3.8 mL) at 0 °C was added imidazole (104.2 mg, 1.530 mmol, 400 mol%), followed by the dropwise addition of chlorotriethylsilane (96 μL, 0.574 mmol, 150 mol%). The resulting mixture was allowed to warm to room temperature and stirred for 2 hrs before being quenched with a saturated aqueous solution of $NaHCO_3$ (3 mL). The layers were separated and the aqueous layer was extracted with Et_2O (3 × 3 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4, and filtered. The volatiles were removed *via* rotary evaporation and the residue was subjected to flash column chromatography (SiO_2, hexanes/Et_2O 97:3) afforded ether (**Fragment A)** (174.6 mg, 0.376 mmol, 98%) as a colorless oil.

TLC (SiO_2): R_f = 0.73 (hexanes/Et_2O 95:5)

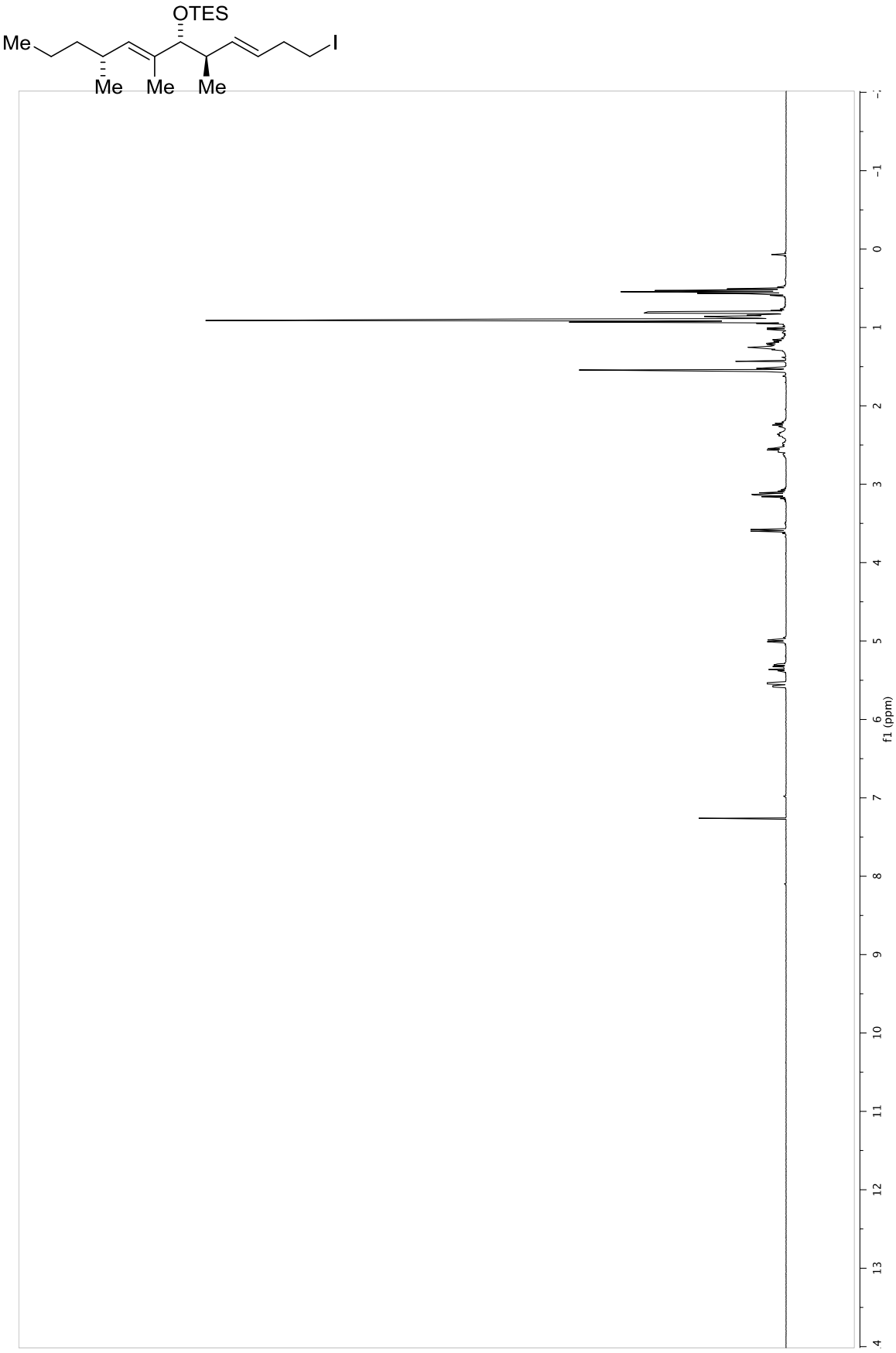
$[\alpha]_D^{20}$: −14.3 (*c* 1.0, $CHCl_3$)

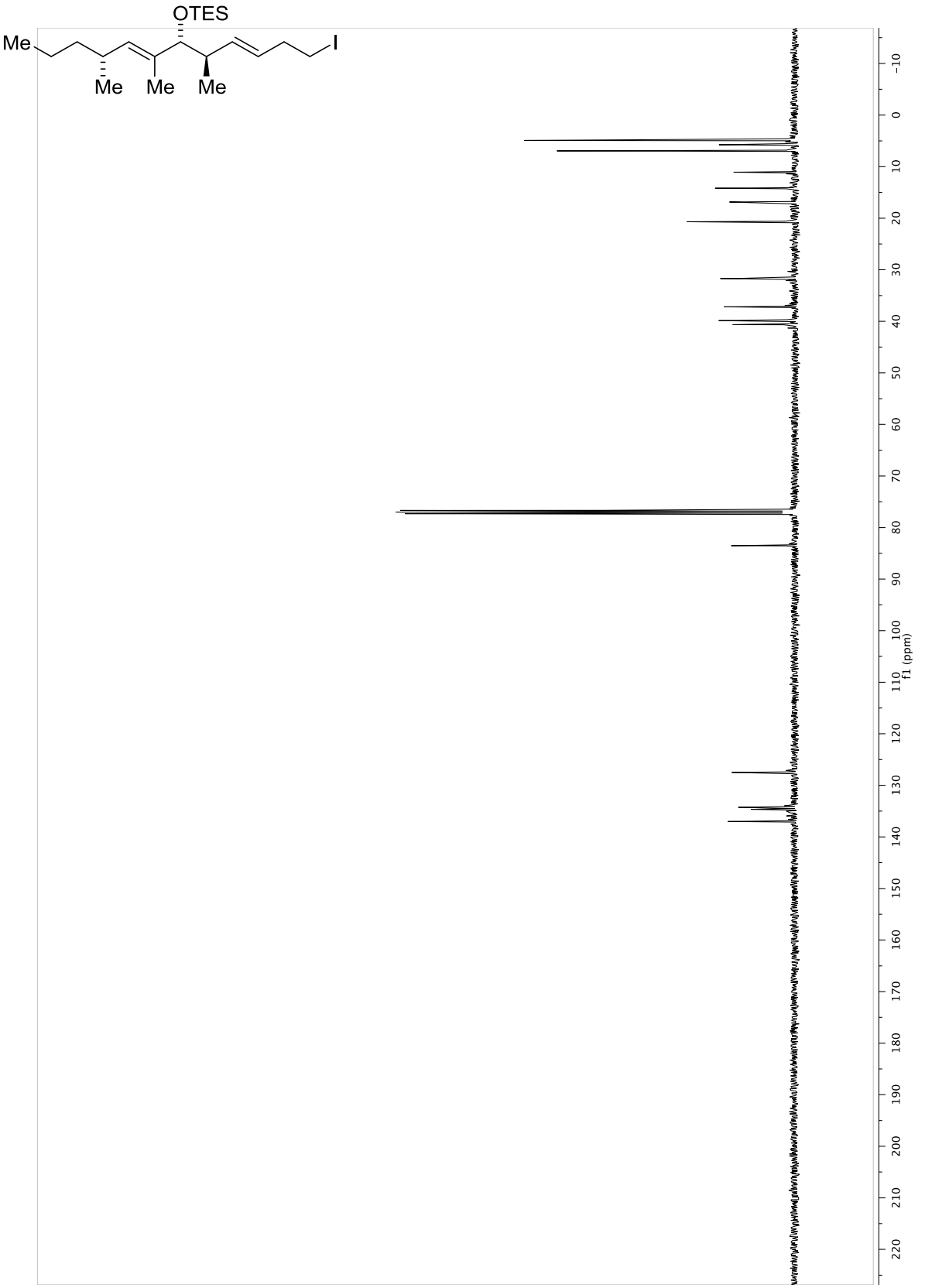
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.56 (ddt, *J* = 15.2, 7.2, 1.2, 1H), 5.38-5.28 (m, 1H), 5.00 (d, *J* =9.2 Hz, 1H), 3.59 (d, *J* = 8.3 Hz, 1H), 3.18-3.07 (m, 2H), 2.64-2.46 (m, 2H), 2.40-2.32 (m, 1H), 2.27-2.19 (m, 1H), 1.54 (td, *J* = 8.4, 1.6 Hz, 3H), 1.28-1.16 (m, 4H), 0.94-0.84 (m, 15H), 0.81 (d, *J* = 6.8 Hz, 3H), 0.57-0.50 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 137.0, 134.6, 134.3, 127.5, 83.5, 40.7, 39.9, 37.2, 31.7, 20.70, 20.68, 16.9, 14.2, 11.1, 6.9, 5.8, 4.9.

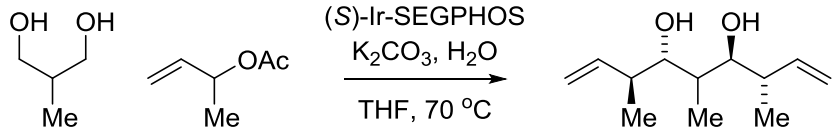
FTIR (neat): 2955, 2874, 1456, 1238, 1061, 1006, 867, 815, 740, 687 cm^{-1}.

HRMS: (ESI, *m/z*) for $C_{21}H_{41}INaOSi^+$ calculated 487.1864, found 487.1866.


OTES
Me
Me
Me
Me
I
f1 (ppm)


OTES
Me
Me
Me
Me
I
f1 (ppm)

(3*S*,4*S*,6*S*,7*S*)-3,5,7-Trimethylnona-1,8-diene-4,6-diol (2b)



An oven-dried sealed tube under an atmosphere of argon was charged with 2-methyl-1,3-propanediol (**1b)** (0.985 g, 10.93 mmol), (*S*)-Ir-SEGPHOS catalyst (283 mg, 0.273 mmol, 2.5 mol%), K_2CO_3 (3.021g, 21.86 mmol, 200 mol%), H_2O (0.78 mL, 43.72 mmol, 400 mol%) and THF (10.9 mL). Freshly distilled crotyl acetate (6.238 g, 54.65 mmol, 500 mol%) was added and the mixture was sparged with Ar for 2 min. The reaction was heated to 70 °C for 168 hr. The reaction mixture was cooled to room temperature and the volatiles were removed *via* rotary evaporation. The resulting residue was subjected to flash column chromatography (SiO_2; hexanes/EtOAc 80:20—70:30) to afford diol **2b** (1.104 g, 5.574 mmol, 51%) as a 6:1 mixture of diastereoisomers and as a colorless viscous oil which solidified on standing. The major diastereomer could be separated by flash column chromatography. The spectral data were identical to those reported.[12]

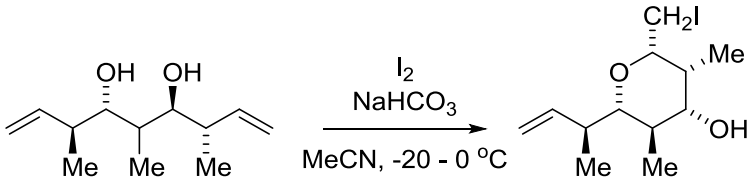
TLC (SiO_2): R_f = 0.31 (hexanes/EtOAc 75:25).

$[\alpha]_D^{20}$: –19.0 (*c* 0.41, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$): δ5.85–5.73 (m, 2H), 5.15–5.09 (m, 4H), 3.65 (d, *J* = 9.6 Hz, 1H), 3.39–3.37 (m, 1H), 2.80 (s, 1H), 2.54 (d, *J* = 4.0 Hz, 1H), 2.46–2.40 (m, 1H), 2.31–2.25 (m, 1H), 1.89–1.86 (m, 1H), 1.03 (d, *J* = 7.2 Hz, 3H), 1.01 (d, *J* = 6.8 Hz, 1H), 0.94 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ142.2, 141.0, 116.5, 116.0, 79.3, 73.9, 42.3, 42.0, 34.8, 17.2, 16.5, 10.7.

(2*S*,3*R*,4*R*,5*R*,6*S*)-2-((*S*)-But-3-en-2-yl)-6-(iodomethyl)-3,5-dimethyltetrahydro-2H-pyran-4-ol (7)



A solution of diol **2b** (535 mg, 2.70 mmol) and $NaHCO_3$ (566.6 mg, 6.74 mmol, 250 mol%) in MeCN (54.0 mL) was cooled to –20 °C. To this solution was added iodine (2.054 g, 8.09 mmol, 300 mol%) in one portion. The reaction was stirred at –20 °C for 1 h. The reaction mixture was warmed to 0 °C and was allowed to stir at this temperature for 6 h. Saturated aqueous $Na_2S_2O_3$ was added and the reaction mixture was allowed to stir until the solution became colorless. The reaction mixture was transferred to a separatory funnel and the aqueous phase was extracted with EtOAc (3 × 30 mL). The combined organic extracts were dried over $MgSO_4$, filtered and the volatiles were removed *via* rotary evaporation. The residue was subjected to flash column chromatography (SiO_2, hexanes/EtOAc 10:1) to afford iodoether **7** (656.5 mg, 2.025 mmol, 75%) as a colorless oil in >20:1 dr. The spectral data was identical to those reported.[12]

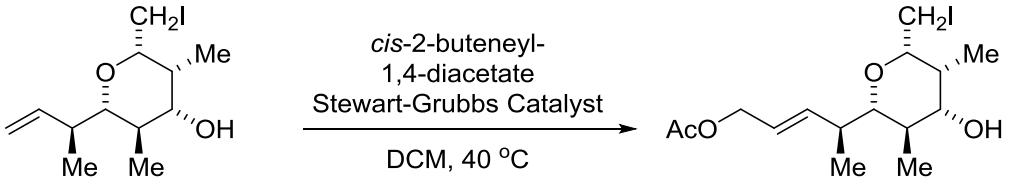
TLC (SiO_2): R_f = 0.52 (hexanes/EtOAc 75:25).

$[\alpha]_D^{20}$: +37.2 (*c* 0.46, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.87–5.78 (m, 1H), 5.02–4.97 (m, 2H), 3.54–3.50 (m, 1H), 3.40 (dd, *J* = 10.8, 4.8 Hz, 1H), 3.25 (dd, *J* = 10.0, 7.6 Hz, 1H), 3.08 (dd, *J* = 10.0, 6.0 Hz, 1H), 2.88 (dd, *J* = 10.0, 2.0 Hz, 1H), 2.44–2.37 (m, 1H), 2.19–2.13 (m, 1H), 1.56-1.49 (m, 2H), 1.16 (d, *J* = 6.8 Hz, 3H), 0.90 (d, *J* = 6.8 Hz, 3H), 0.80 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 139.2, 115.2, 85.1, 78.7, 76.4, 39.9, 38.2, 34.6, 18.8, 12.2, 6.2, 4.6.

(*S*,*E*)-4-((2*S*,3*R*,4*R*,5*R*,6*S*)-4-Hydroxy-6-(iodomethyl)-3,5-dimethyltetrahydro-2H-pyran-2-yl)pent-2-en-1-yl acetate (S9)



A flame-dried round bottom flask was charged with Stewart–Grubbs catalyst (94 mg, 0.164 mmol, 8.5 mol%) and purged with argon for 10 min. A solution of iodoether **7** (626 mg, 1.91 mmol) in CH_2Cl_2 that was sparged with Ar (8 mL, 0.25 M) was added slowly, followed by (*Z*)-but-2-ene-1,4-diyl diacetate (2.15 mL, 13.52 mmol, 700 mol%). The resulting mixture was heated to 40 °C and stirred for a total period of 24 h. The reaction was allowed to cool to room temperature and the volatiles were removed *via* rotary evaporation. The residue was subjected to flash column chromatography (SiO_2, hexanes/EtOAc 80:20) to afford acetate **S9** (620 mg, 1.57 mmol, 81%) as a colorless oil.

TLC (SiO_2): R_f = (hexanes/EtOAc 95:5).

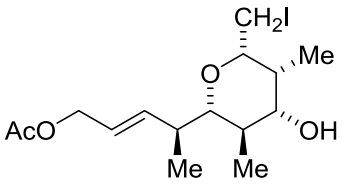
$[\alpha]_D^{20}$: +53.0 (*c* 1.0, CH_2Cl_2).

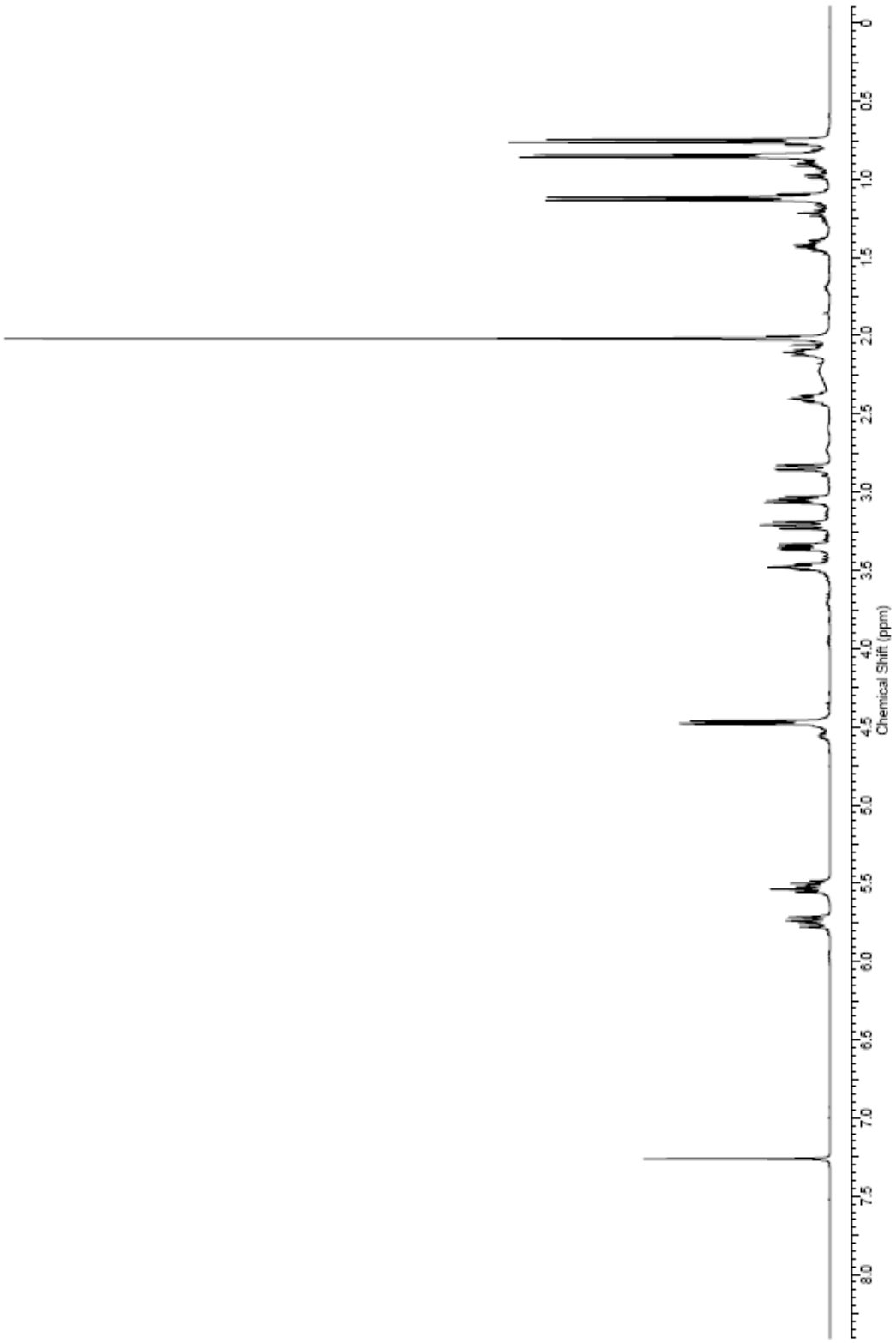
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.75 (dd, *J* = 15.5, 9.2 Hz, 1H), 5.57–5.47 (m, 1H), 4.47 (d, *J* =6.3 Hz, 2H), 3.48 (ddd, *J* = 7,9, 6.0, 1.8 Hz, 1H), 3.35 (dd, *J* = 10.6, 4.7 Hz, 1H), 3.21 (dd, *J* = 10.0, 8.0 Hz, 1H), 3.05 (dd, *J* = 10.2, 5.9 Hz, 1H), 2.84 (dd, *J* = 10.0, 1.8 Hz, 1H), 2.40 (m, 1H), 2.10 (m, 1H), 2.02 (s, 3H), 1.42 (m, 1H), 1.12 (d, *J* = 7.0 Hz, 3H), 0.85 (d, *J* = 6.7 Hz, 3H), 0.75 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 170.9, 136.2, 124.7, 84.9, 78.6, 76.1, 65.0, 38.2, 38.1, 34.4, 21.0, 18.8, 12.3, 6.1, 4.5.

FTIR (neat): 3500–3300, 2965, 1736, 1457, 1364, 1229, 1131, 1098, 1012, 977, 732 cm^{-1}.

HRMS: (ESI, *m/z*) for $C_{15}H_{25}INaO_4$ calculated 419.0690, found 419.0630.


CH2I
Me
O
AcO
OH
Me
Me


Chemical Shift (ppm)
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6.0
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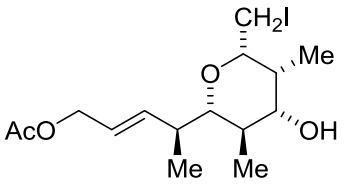
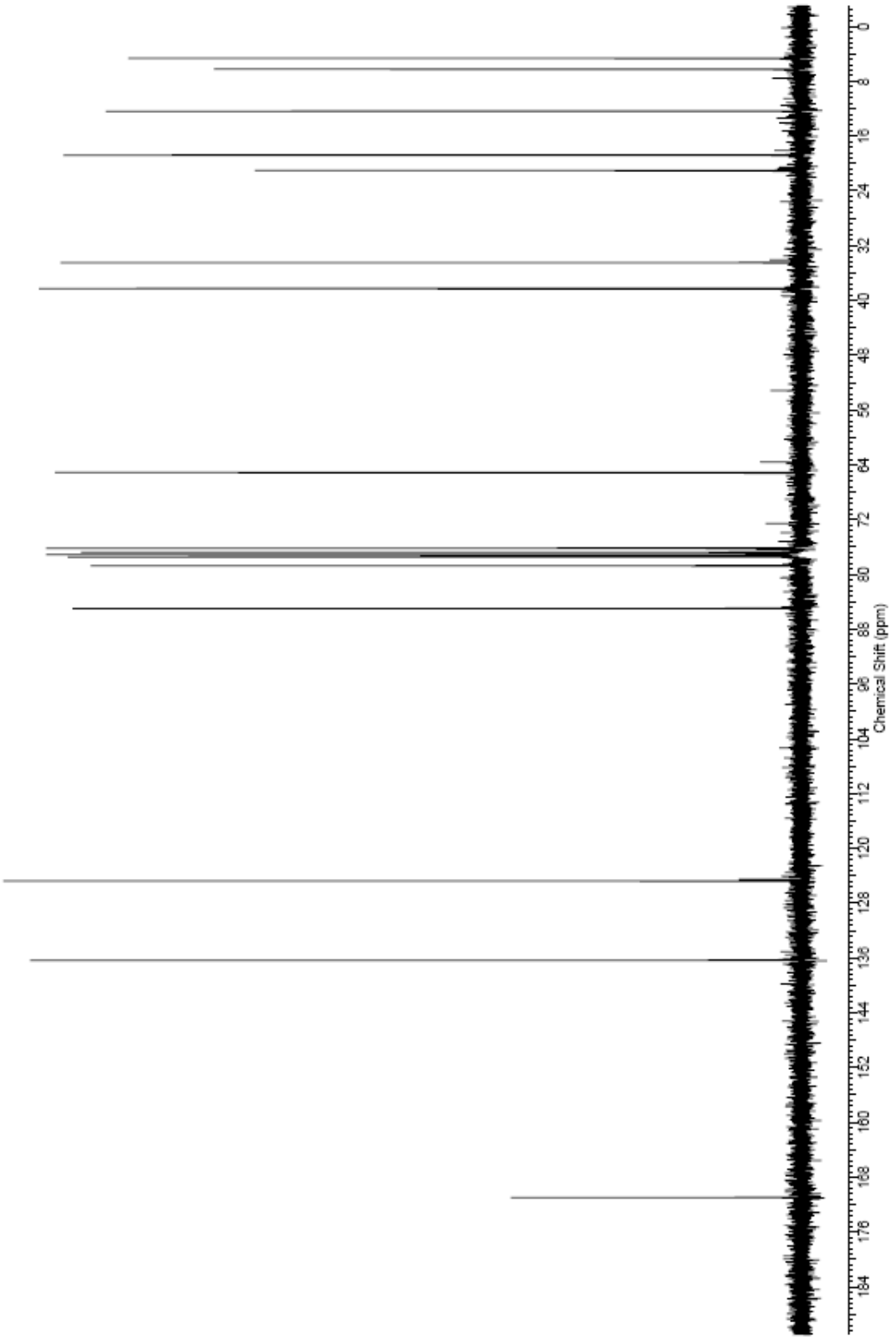
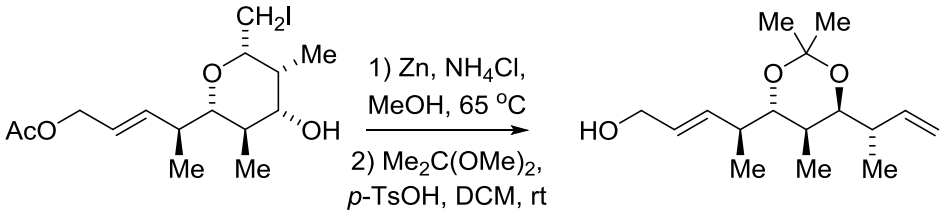
7.0
7.5
8.0


CH2I
Me
O
AcO
OH
Me
Me


Chemical Shift (ppm)

(*S*,*E*)-4-((4*S*,5*R*,6*S*)-6-((*S*)-But-3-en-2-yl)-2,2,5-trimethyl-1,3-dioxan-4-yl)pent-2-en-1-ol (8)



To a stirred solution of acetate **S9** (400 mg, 1.01 mmol) in MeOH (10.1 mL) in a glass pressure vessel were added activated zinc dust (994 mg, 15.2 mmol, 1500 mol%) and NH_4Cl (540 mg, 10.1 mmol, 1000 mol%) in one portion. The resulting suspension was heated to 65 °C and stirred vigorously until the TLC analysis indicated complete cleavage of the iodoether and acetate ester (8–12 h). The mixture was allowed to cool to room temperature and filtered through a short plug of SiO_2. The volatiles were removed *via* rotary evaporation. The residue was dissolved in CH_2Cl_2 (10 mL), causing a white solid to precipitate, which was removed *via* gravity filtration. The filtrate was concentrated *via* rotary evaporation to afford crude triol.

To a solution of crude triol in CH_2Cl_2 (10 mL) was added 2,2-dimethoxypropane (1.24 mL, 10.1 mmol, 1000 mol%), followed by *p*-TsOH·H_2O (38 mg, 0.20 mmol, 20 mol%). The resulting mixture was stirred for 3 hrs before MeOH (1.0 mL) was added and the resulting mixture was stirred vigorously until the TLC analysis indicated complete cleavage of primary acetal (usually 5–10 min). A saturated aqueous solution of $NaHCO_3$ (5.0 mL) was added and the layers were separated. The aqueous layer was extracted with EtOAc (3 × 5.0 mL) and the combined organic extracts were washed with brine (10 mL), dried over $MgSO_4$, filtered and the volatiles were removed *via* rotary evaportation. The residude was subjected to flash column chromatography (SiO_2, hexanes/EtOAc 80:20) to afford alcohol **8** (195 mg, 0.727 mmol, 72% over 2 steps) as a colorless oil.

TLC (SiO_2): R_f = 0.60 (hexanes/EtOAc 70:30).

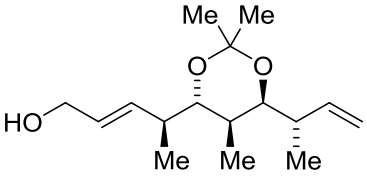
$[\alpha]_D^{20}$: +36.6 (*c* 1.0, CH_2Cl_2).

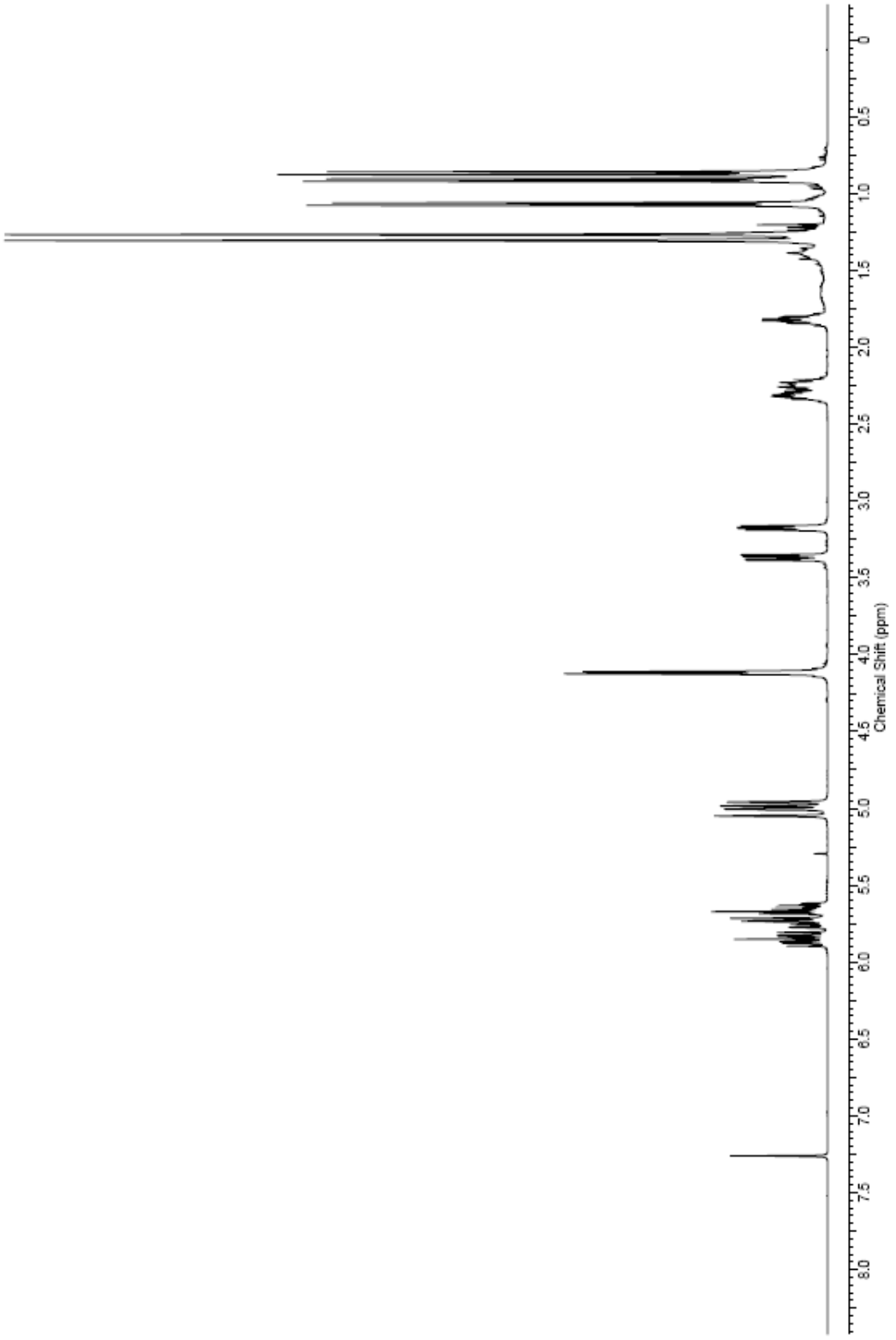
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.85 (ddd, *J* = 17.3, 10.5, 6.7 Hz, 1H), 5.74 (dd, *J* = 15.7, 7.8 Hz, 1H), 5.64 (m, 1H), 5.08–4.92 (m, 2H), 4.12 (d, *J* = 5.5 Hz, 2H), 3.37 (dd, *J* = 10.6, 4.3 Hz, 1H), 3.18 (dd, *J* = 7.0, 3.9 Hz, 1H), 2.37–2.18 (m, 2H), 1.82 (m, 1H), 1.30 (s, 3H), 1.27 (s, 3H), 1.07 (d, *J* = 6.7 Hz, 3H), 0.91 (d, *J* = 6.7 Hz, 3H), 0.87 (d, *J* = 6.7 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 142.2, 134.5, 129.6, 113.4, 100.6, 78.3, 73.2, 63.8, 40.0, 37.0, 35.1, 25.0, 23.4, 17.3, 15.7, 12.2.

FTIR (neat): 3500–3300, 2971, 2933, 1457, 1377, 1223, 1181, 997, 976, 909, 888 cm^{-1}.

HRMS: (ESI, *m/z*) for $C_{16}H_{28}NaO_3$ calculated 291.1931, found 291.1932.


Me
Me
O
O
HO
Me
Me
Me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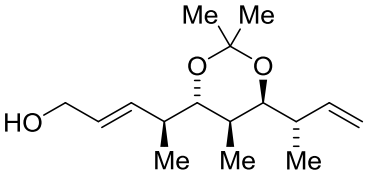
7.0
7.5
8.0
Chemical Shift (ppm)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HO
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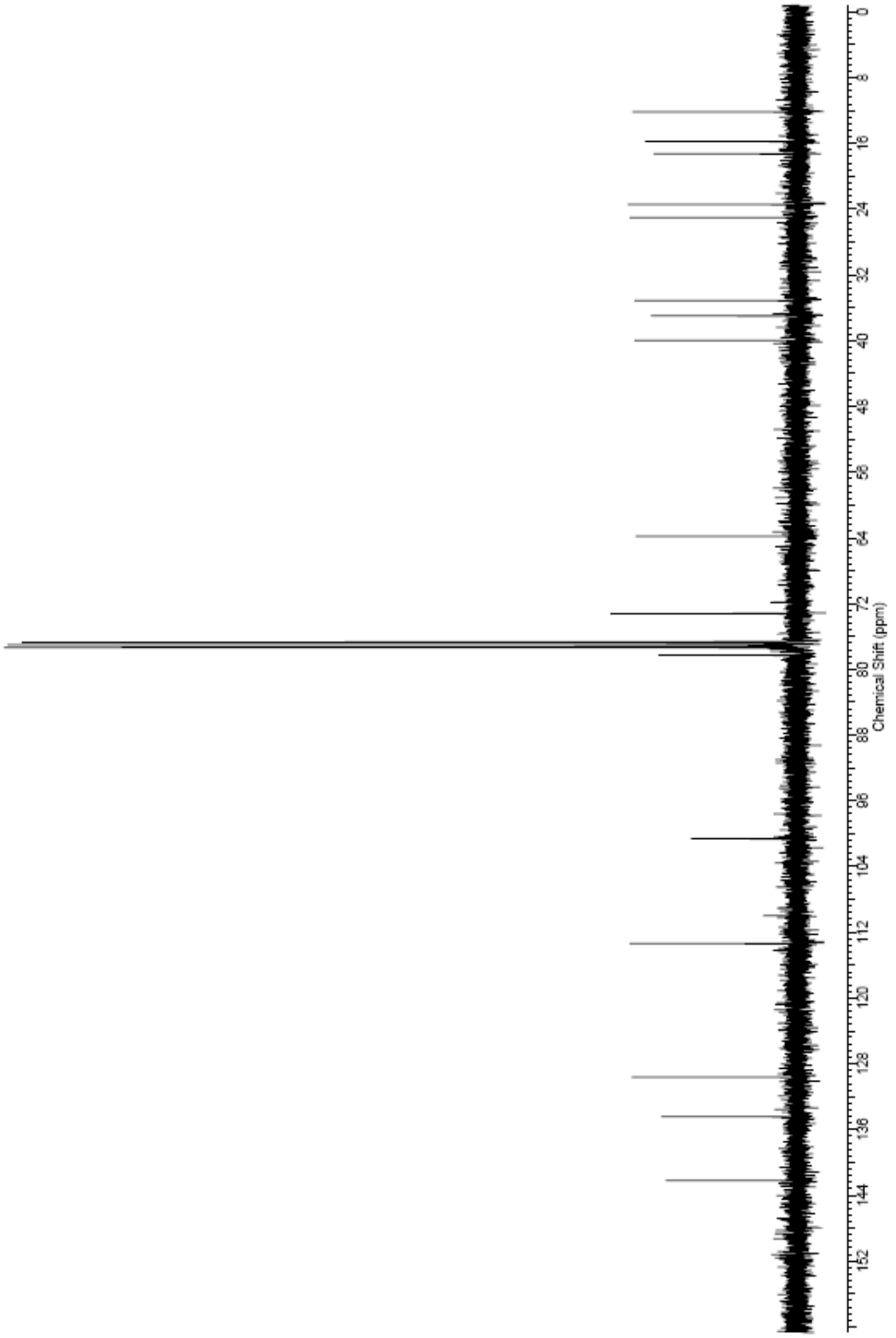
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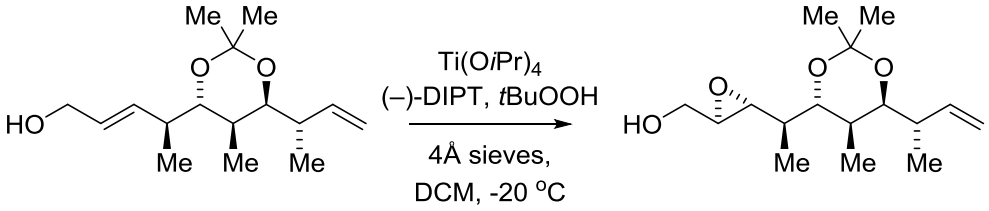
144
152

((2*R*,3*R*)-3-((*R*)-1-((4*R*,5*R*,6*S*)-6-((*S*)-But-3-en-2-yl)-2,2,5-trimethyl-1,3-dioxan-4-yl)ethyl)oxiran-2-yl)methanol (S10)



A round bottomed flask equipped with stir bar was charged with powdered 4Å molecular sieves (2.77g) and flamed dried three times under vacuum. The flask was back-filled with argon and CH_2Cl_2 (13 mL) was added followed by (−)-diisopropyl tartarate (396 mg, 1.69 mmol, 130 mol%). The mixture was cooled to −20 °C and $Ti(O^iPr)_4$ (0.423 mL, 1.43 mmol, 110 mol%) was slowly added. The resulting mixture was stirred for 20 min. *tert*-Butyl hydrogen peroxide (5.5 M in decane, 0.473 mL, 2.60 mmol, 200 mol%) was added dropwise and the mixture was stirred at −20 °C for 30 min before a solution of alcohol **8** (350 mg, 1.30 mmol) in CH_2Cl_2 (13 mL) was added dropwise. After stirring for 2 hrs, additional *tert*-butyl hydrogen peroxide (5.5 M in decane, 0.473 mL, 2.60 mmol, 200 mol%) was added, and the mixture was stirred at −20 °C for a further 2 hrs. The reaction mixture was diluted with EtOAc (50 mL) and quenched with MeOH (10 mL) and H_2O (5.0 mL). The resulting mixture was filtered through a plug of celite and the filtrate was washed with H_2O (2 × 20 mL). The organic phase was dried over $MgSO_4$, filtered and the volatiles were removed *via* rotary evaporation. The residue was subjected to flash column chromatography (SiO_2, hexanes/actone 85:15) to afford epoxide **S10** (315 mg, 1.11 mmol, 85%) as a colorless oil in >20:1 dr.

TLC (SiO_2): R_f = 0.45 (hexanes/EtOAc 70:30).

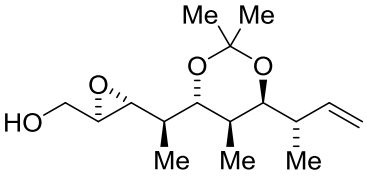
$[\alpha]_D^{20}$: +56.0 (*c* 1.0, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.83 (ddd, *J* = 17.5, 10.5, 6.7 Hz, 1H), 5.06–4.88 (m, 2H), 3.87 (dd, *J* = 12.5, 2.7 Hz, 1H), 3.56 (dd, *J* = 12.5, 5.1 Hz, 1H), 3.46 (dd, *J* = 10.4, 4.1 Hz, 1H), 3.23 (dd, *J* = 7.4, 3.5 Hz, 1H), 3.06 (dd, *J* = 7.8, 2.3 Hz, 1H), 2.88 (td, *J* = 4.9, 2.6 Hz, 1H), 2.24 (m, 1H), 2.12 (m, 1H), 1.56 (dquin, *J* = 7.1, 3.5 Hz, 1H), 1.27 (s, 3H), 1.26 (s, 3H), 0.96 (d, *J* = 7.0 Hz, 3H), 0.92 (d, *J* = 7.0 Hz, 3H), 0.85 (d, *J* = 6.7 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 142.1, 113.4, 100.7, 77.3, 73.2, 62.1, 56.7, 56.5, 38.7, 37.0, 34.8, 24.9, 23.4, 15.7, 13.6, 12.0.

FTIR (neat): 3550–3200, 2967, 2922, 1459, 1377, 1087, 973, 911, 675 cm^{-1}.

HRMS: (ESI, *m/z*) for $C_{16}H_{28}NaO_4$ calculated 307.1880, found 307.1884.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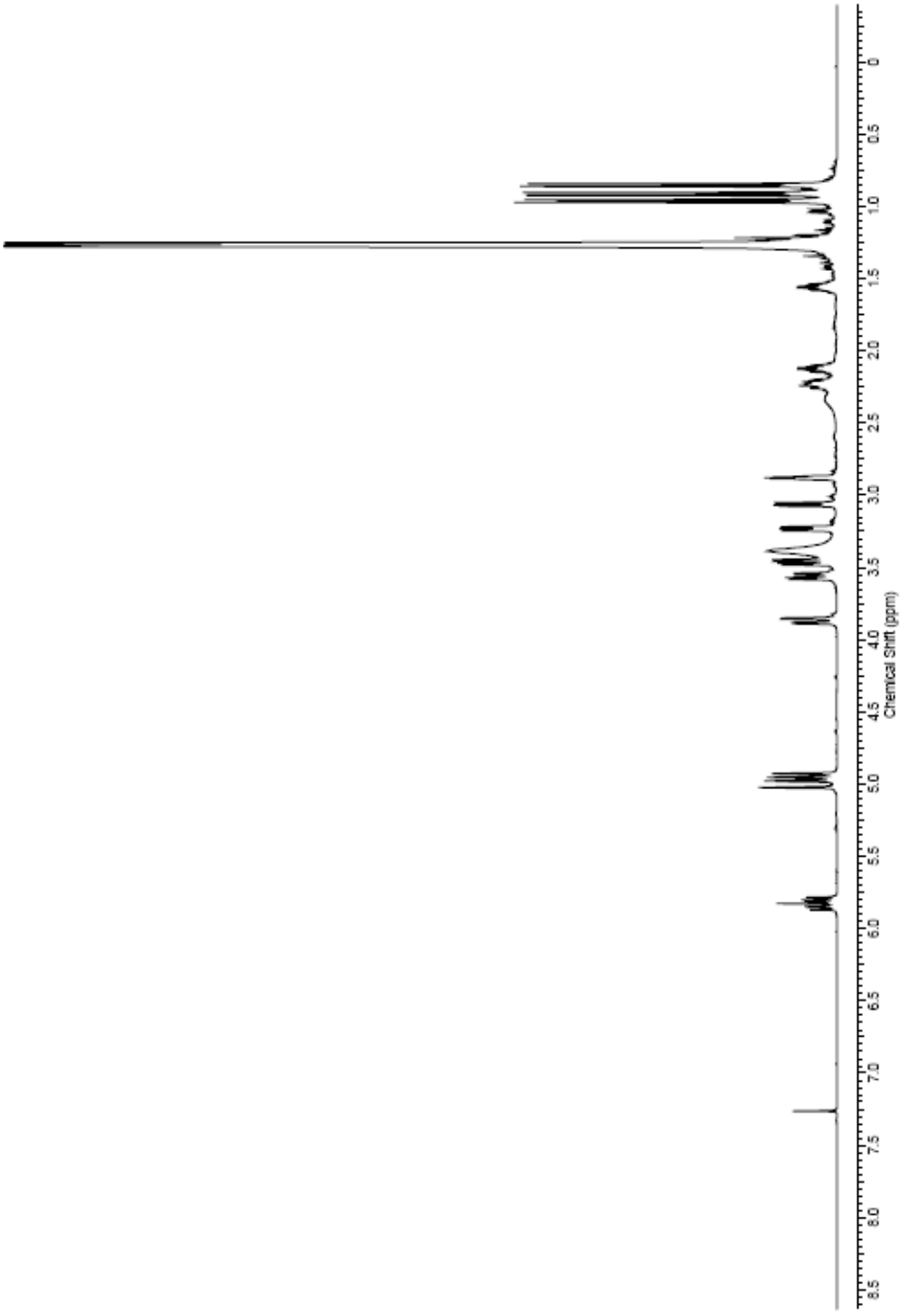
HO
Me
Me
Me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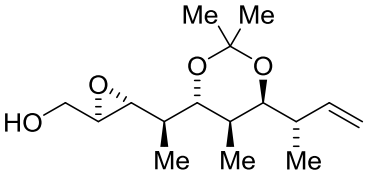
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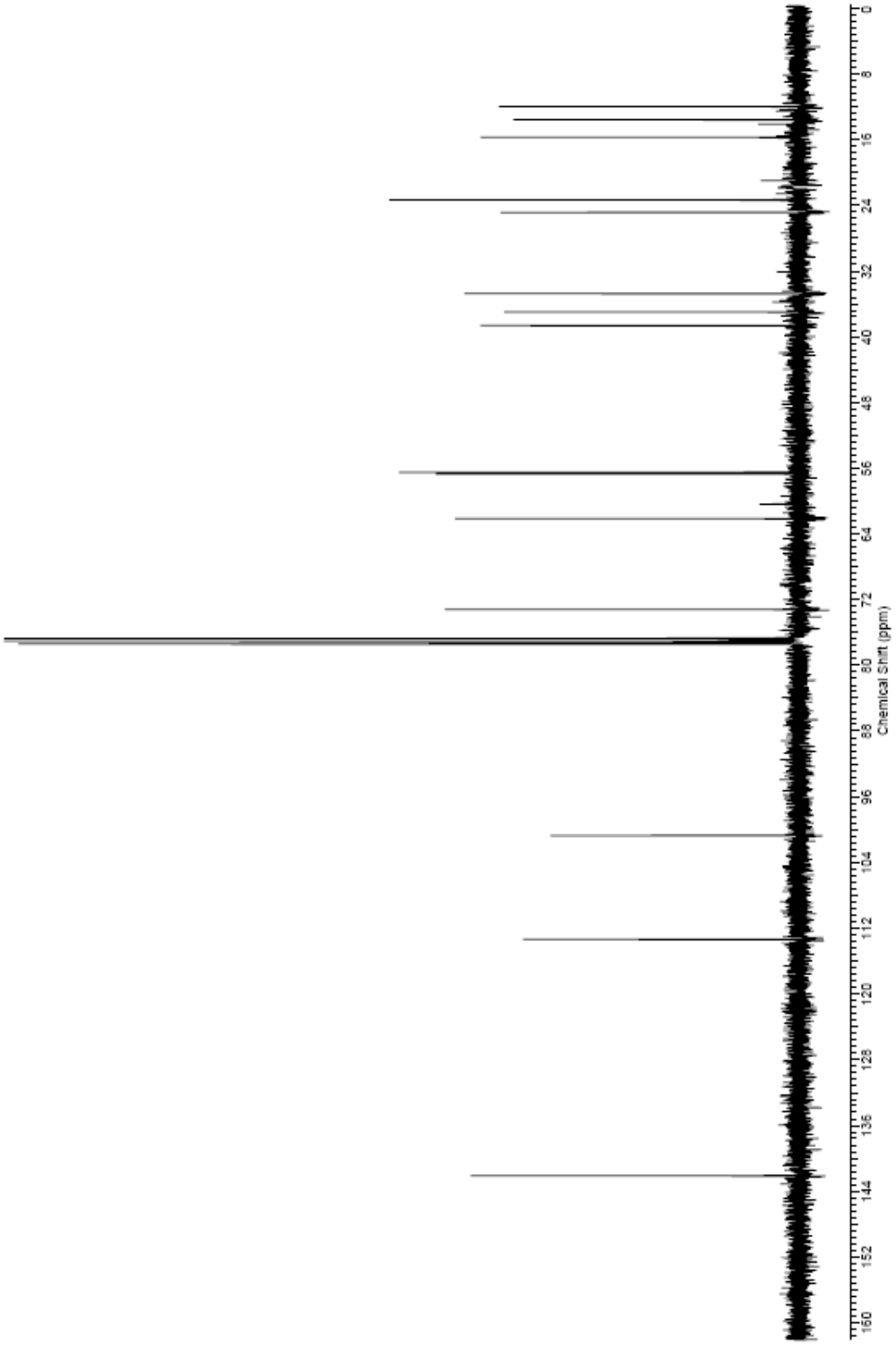
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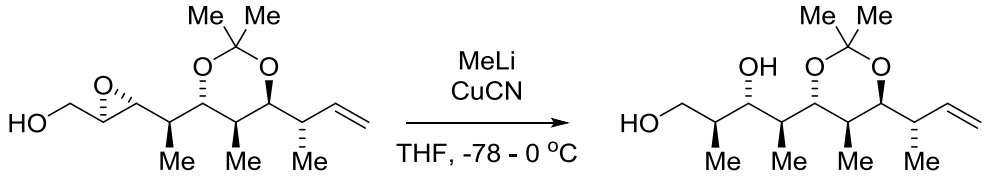
144
152
160

(2*S*,3*S*,4*S*)-4-((4*S*,5*R*,6*S*)-6-((*S*)-But-3-en-2-yl)-2,2,5-trimethyl-1,3-dioxan-4-yl)-2-methylpentane-1,3-diol (9)



To a stirred suspension of CuCN (1.99 g, 22.2 mmol, 2000 mol%) in THF (10.1 mL) at −78 °C was added MeLi (1.6 M in Et_2O, 27.8 mL, 44.4 mmol, 4000 mol%) dropwise over 15 min. The resulting mixture was warmed to 0 °C and stirred for 45 min before being cooled to −78 °C. A solution of epoxide **S10** (315 mg, 1.11 mmol) in THF (10.1 mL) was added dropwise and the reaction was stirred at this temperature for 3 hrs before being warmed to 0 °C and stirred for a further 12 hrs. The reaction mixture was poured slowly to a 3:1 mixture of a saturated aqueous solution of NH_4Cl and NH_4OH (200 mL) and the resultant mixture was stirred vigorously for 2 hrs. The layers were partitioned and the aqueous layer was extracted with Et_2O (3 × 100 mL). The combined organics were washed with brine (100 mL), dried over $MgSO_4$, filtered, and the volatiles were removed *via* rotary evaporation. The residue was subjected to flash column chromatography (SiO_2, hexanes/acetone 85:15—70:30) to afford diol **9** (300 mg, 1.00 mmol, 90%) as a colorless oil and a single regioisomer.

TLC (SiO_2): R_f = 0.30 (hexanes/EtOAc 70:30).

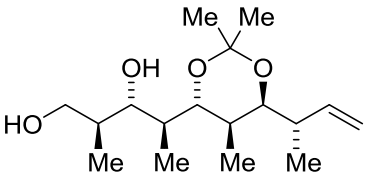
$[\alpha]_D^{20}$: +17.1 (*c* 0.50, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.83 (ddd, *J* = 17.3, 10.5, 6.7 Hz, 1H), 5.08–4.93 (m, 2H), 3.88 (dd, *J* = 11.0, 3.1 Hz, 1H), 3.60–3.51 (m, 2H), 3.48 (dd, *J* = 10.4, 3.7 Hz, 1H), 3.35 (t, *J* = 7.0 Hz, 1H), 2.25 (td, *J* = 10.5, 6.7 Hz, 1H), 1.98–1.80 (m, 3H), 1.36 (s, 3H), 1.28 (s, 3H), 1.12 (d, *J* = 7.0 Hz, 3H), 0.94 (d, *J* = 6.7 Hz, 3H), 0.92 (d, *J* = 6.7 Hz, 3H), 0.88 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 141.7, 113.7, 100.9, 81.9, 80.9, 73.1, 65.0, 41.5, 37.0, 36.8, 36.0, 25.5, 23.5, 15.5, 15.2, 13.3, 12.8.

FTIR (neat): 3500–3200, 2970, 2934, 2879, 1458, 1377, 1224, 1182, 1107, 1019, 1002, 910, 883 cm^{-1}.

HRMS: (ESI, *m/z*) for $C_{17}H_{32}NaO_4$ calculated 323.2193, found 323.2202.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Me
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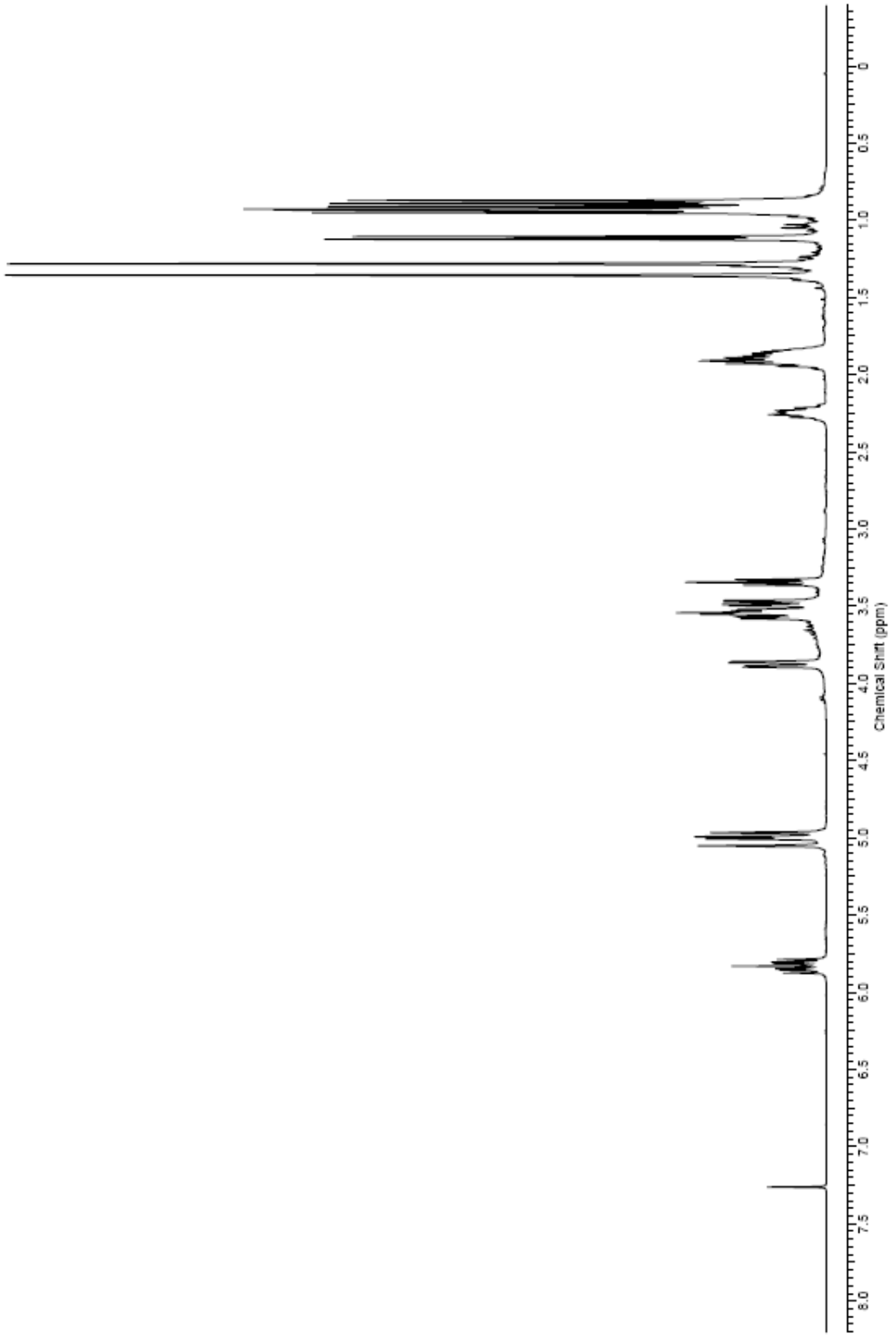
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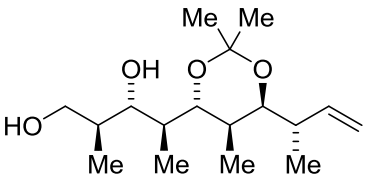
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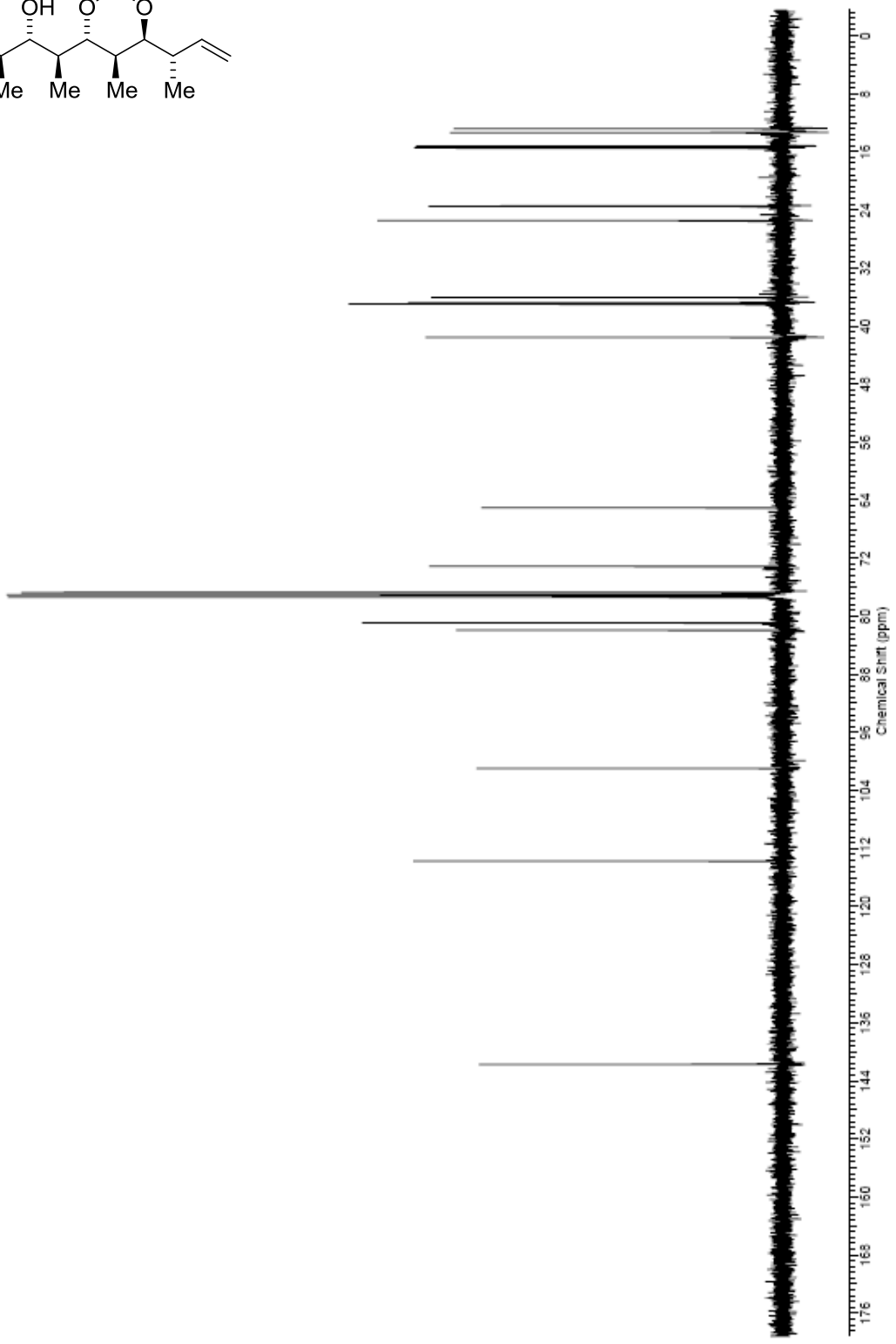
Chemical Shift (ppm)
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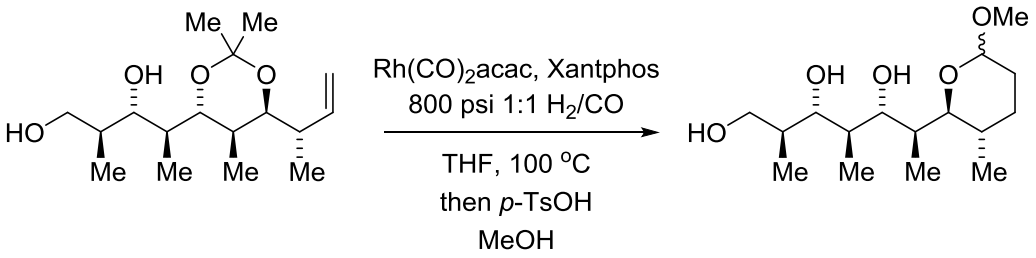
144
152
160
168
176

(2*S*,3*S*,4*S*,5*S*,6*S*)-6-((2*S*,3*S*,6*S*)-6-Methoxy-3-methyltetrahydro-2H-pyran-2-yl)-2,4-dimethylheptane-1,3,5-triol (10)



A solution of diol **9** (119 mg, 0.396 mmol), Xantphos (17 mg, 0.030 mmol, 7.5 mol%) and Rh(acac)$(CO)_2$ (5.1 mg, 0.020 mmol, 5 mol%) in THF (22 mL) in a 50 mL flat bottom flask was placed in a high pressure Parr bomb and the pressure gauge/gas inlet was assembled. The bomb was charged to 50 psi with CO gas and the pressure was carefully released. This procedure was repeated twice before the bomb was charged to 400 psi CO and then with another 400 psi H_2 (800 psi total) and heated to 100 °C (sand bath, external temperature). The reaction mixture was stirred for 48 hrs before being cooled to room temperature. The pressure was carefully released.

The mixture was diluted with MeOH (7.8 mL, 0.05M), and *p*-TsOH•H_2O (7.5 mg, 0.040 mmol, 10 mol%) was added at ambient temperature. The reaction was allowed to stir for 6 hr before another portion of *p*-TsOH•H_2O (3.8 mg, 0.020 mmol, 5 mol%) was added. The reaction was allowed to stir for an additional 3 hrs before the reaction was quenched with 1 mL Et_3N. The volatiles were then removed *via* rotary evaporation, and the residue was subjected to flash column chromatography (SiO_2, CH_2Cl_2/EtOAc 50:50) to afford triol **10** (73 mg, 0.240 mmol, 61% over 2 steps) as a colorless oil. The major diastereomer could be separated from the minor diastereomer and is characterized below.

TLC (SiO_2): R_f = 0.30 (CH_2Cl_2/EtOAc 50:50).

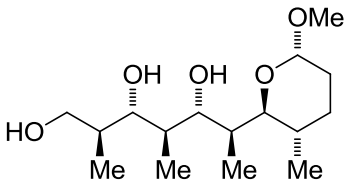
$[\alpha]_D^{20}$: +11.1 (*c* 0.25, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.71 (d, *J* = 2.0 Hz, 1H), 4.03 (dd, *J* = 11.0, 2.5 Hz, 1H), 3.95 (dd, *J* = 10.2, 1.4 Hz, 1H), 3.69 (dd, *J* = 9.0, 2.0 Hz, 1H), 3.61–3.51 (m, 2H), 3.48 (s, 3H), 2.18–2.04 (m, 2H), 1.88 (dt, *J* = 6.6, 2.7 Hz, 1H), 1.80–1.61 (m, 3H), 1.58–1.46 (m, 2H), 1.23 (d, *J* = 7.0 Hz, 3H), 1.13 (d, *J* = 7.2 Hz, 3H), 0.82 (d, *J* = 6.5 Hz, 3H), 0.73 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 98.9, 84.6, 83.1, 75.0, 64.3, 56.3, 38.9, 35.3, 32.6, 31.5, 30.2, 26.3, 17.3, 15.5, 13.1, 11.2.

FTIR (neat): 3500–3300, 2936, 1653, 1459, 1382, 1158, 1123, 1034, 1010, 815, 685 cm^{-1}.

HRMS: (ESI, *m/z*) for $C_{16}H_{32}NaO_5$ calculated 327.2142, found 327.2149.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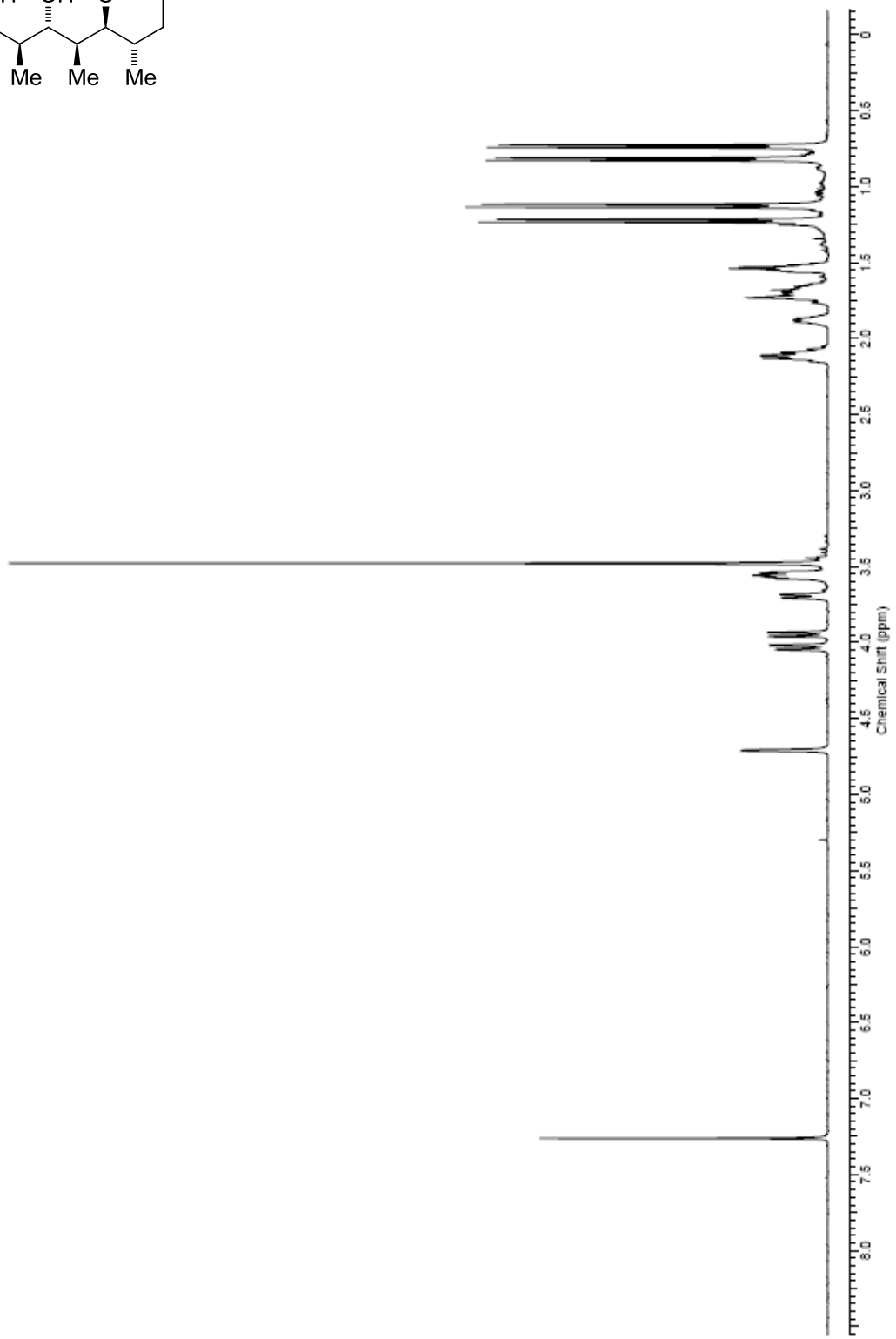
HO
Me
Me
Me
Me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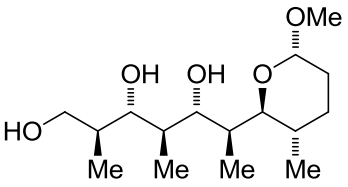
Chemical Shift (ppm)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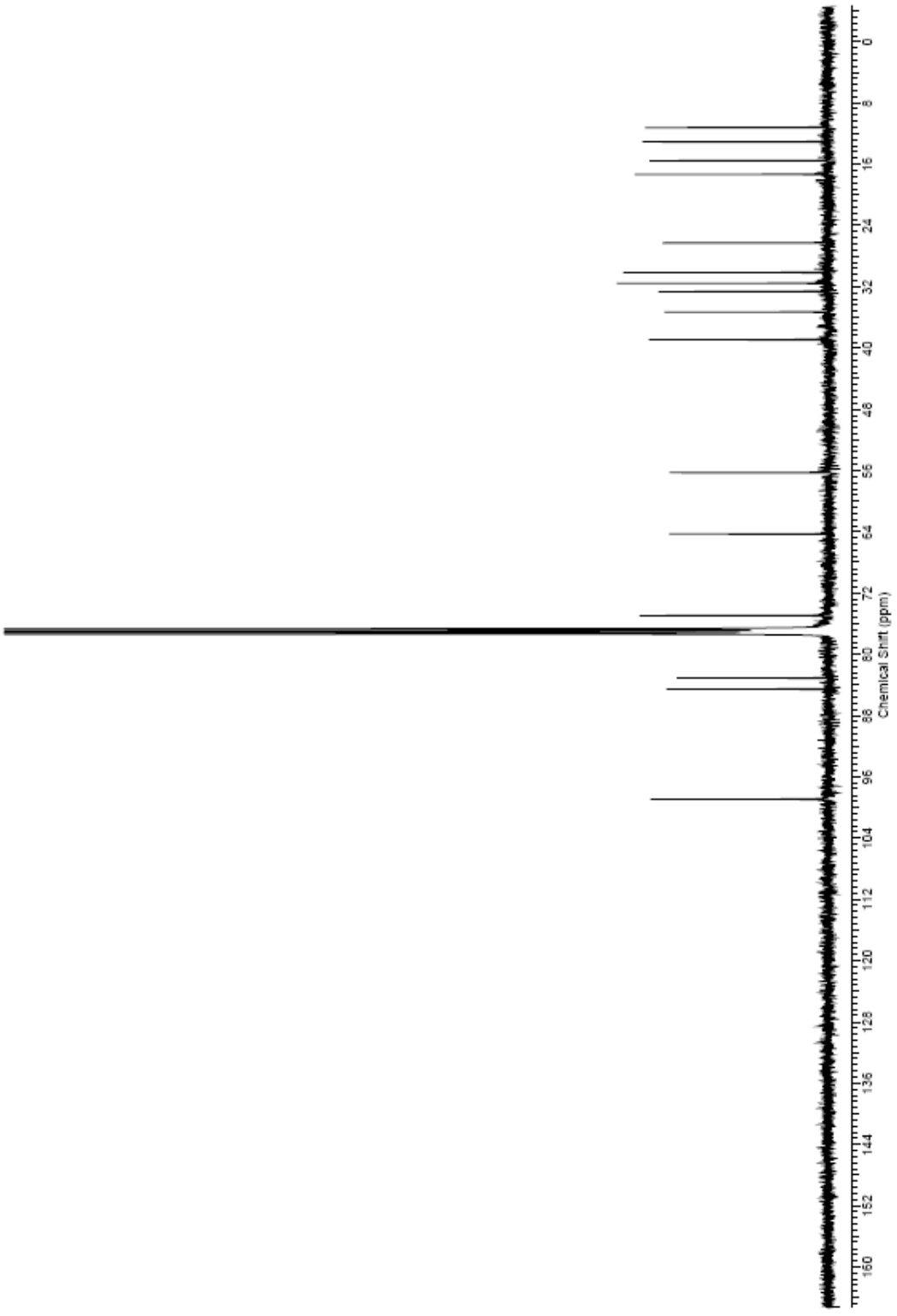
Me
Me
Me
Me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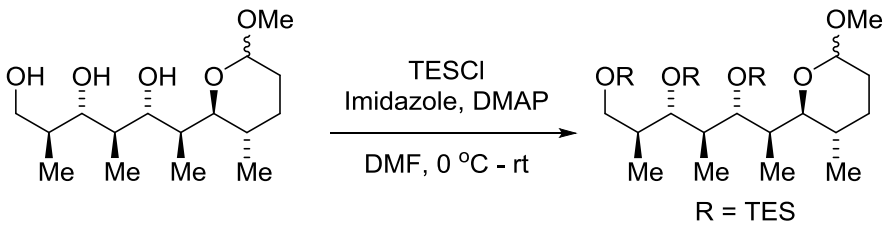
152
160

(5*R*,6*S*,7*S*,8*S*)-3,3,11,11-Tetraethyl-5-((*R*)-1-((2*S*,3*S*,6*S*)-6-methoxy-3-methyltetrahydro-2H-pyran-2-yl)ethyl)-6,8-dimethyl-7-((triethylsilyl)oxy)-4,10-dioxa-3,11-disilatridecane (S11)



To a stirred solution of triol **10** as a mixture of diastereomers from the previous step (51.0 mg, 0.168 mmol) in DMF (0.84 mL) was added imidazole (172 mg, 2.52 mmol, 1500 mol%), followed by DMAP (20.5 mg, 0.168 mmol, 100 mol%). The resultant mixture was cooled to 0 °C and chlorotriethylsilane (282 μL, 1.68 mmol, 1000 mol%) was slowly added. The reaction mixture was allowed to slowly warm to room temperature and was stirred for 24 hrs before being cooled 0 °C and quenched by the dropwise addition of a saturated aqueous solution of $NaHCO_3$. The mixture was then extracted with Et_2O (3 × 1.0 mL) and the combined organic extracts were washed with brine (2.0 mL), dried over $MgSO_4$, filtered and the volatiles were removed *via* rotary evaporation. The residue was subjected to flash column chromatography (SiO_2, hexanes/Et_2O 99:1) to afford ether **S11** (95.8 mg, 0.148 mmol, 88%) as a colorless oil. The major diastereomer could be separated from the minor diastereomer and is characterized below.

TLC (SiO_2): R_f = 0.80 (hexanes/Et_2O 95:5).

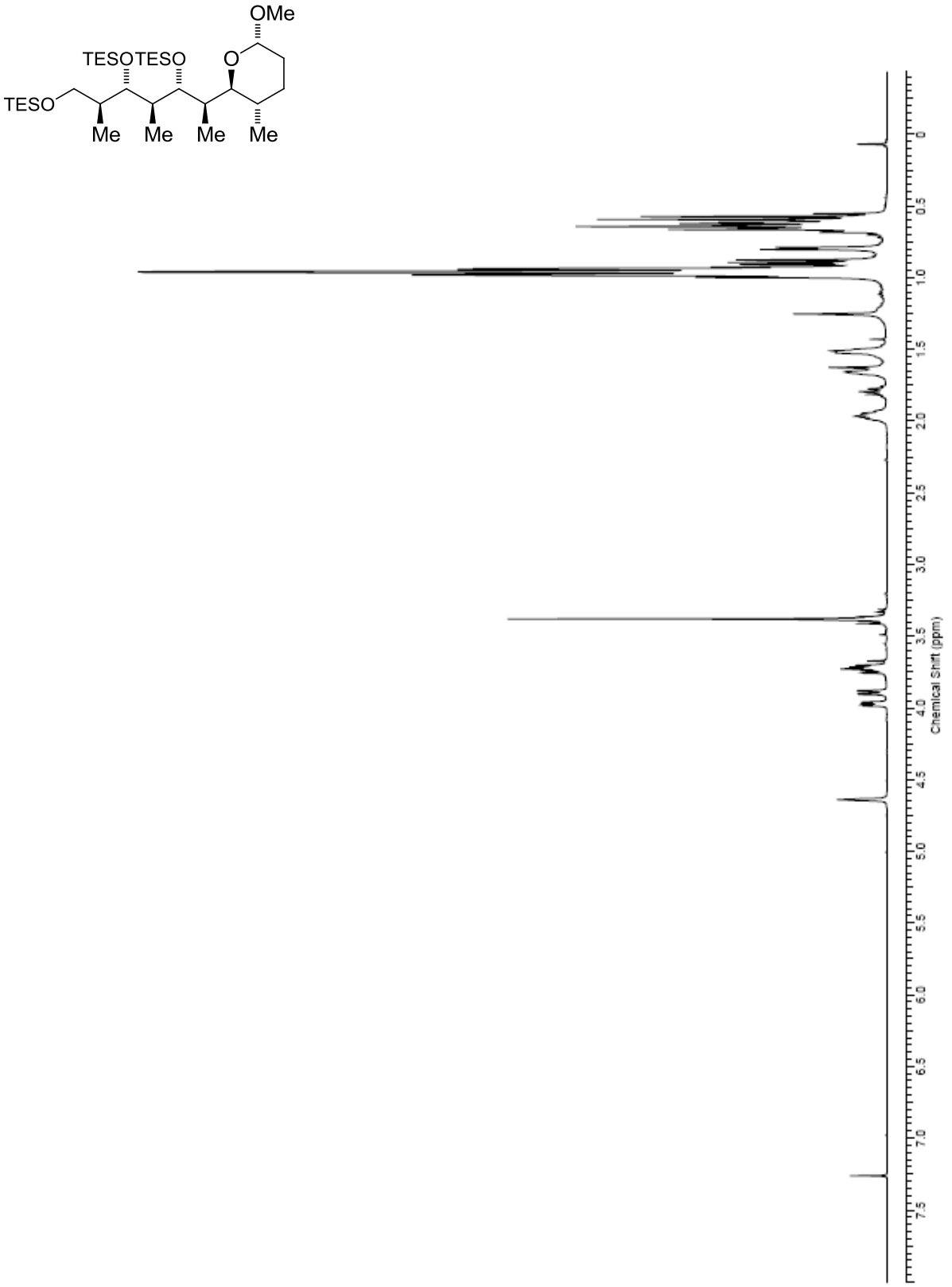
$[\alpha]_D^{20}$: −21.3 (*c* 0.50, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.64 (t, *J* =2.3 Hz, 1H), 3.97 (dd, *J* = 7.4, 3.5 Hz, 1H), 3.89 (dd, *J* = 8.6, 2.0 Hz, 1H), 3.73 (td, *J* = 10.2, 5.1 Hz, 2H), 3.42–3.36 (m, 4H), 2.02–1.91 (m, 2H), 1.79 (quin, *J* = 7.1 Hz, 1H), 1.71–1.61 (m, 2H), 1.58–1.46 (m, 3H), 1.04–0.85 (m, 33H), 0.80 (d, *J* = 5.9 Hz, 3H), 0.71–0.53 (m, 21H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 98.2, 75.8, 74.5, 73.6, 64.4, 55.2, 44.2, 40.4, 37.9, 31.3, 30.3, 27.3, 18.5, 14.6, 10.8, 10.5, 7.2, 7.1, 6.8, 5.7, 5.5, 4.4.

FTIR (neat): 2953, 2930, 2876, 1458, 1379, 1238, 1082, 1057, 1006, 812, 725 cm^{-1}.

HRMS: (ESI, *m/z*) for $C_{34}H_{74}NaO_5Si_3$ calculated 669.4736, found 669.4733.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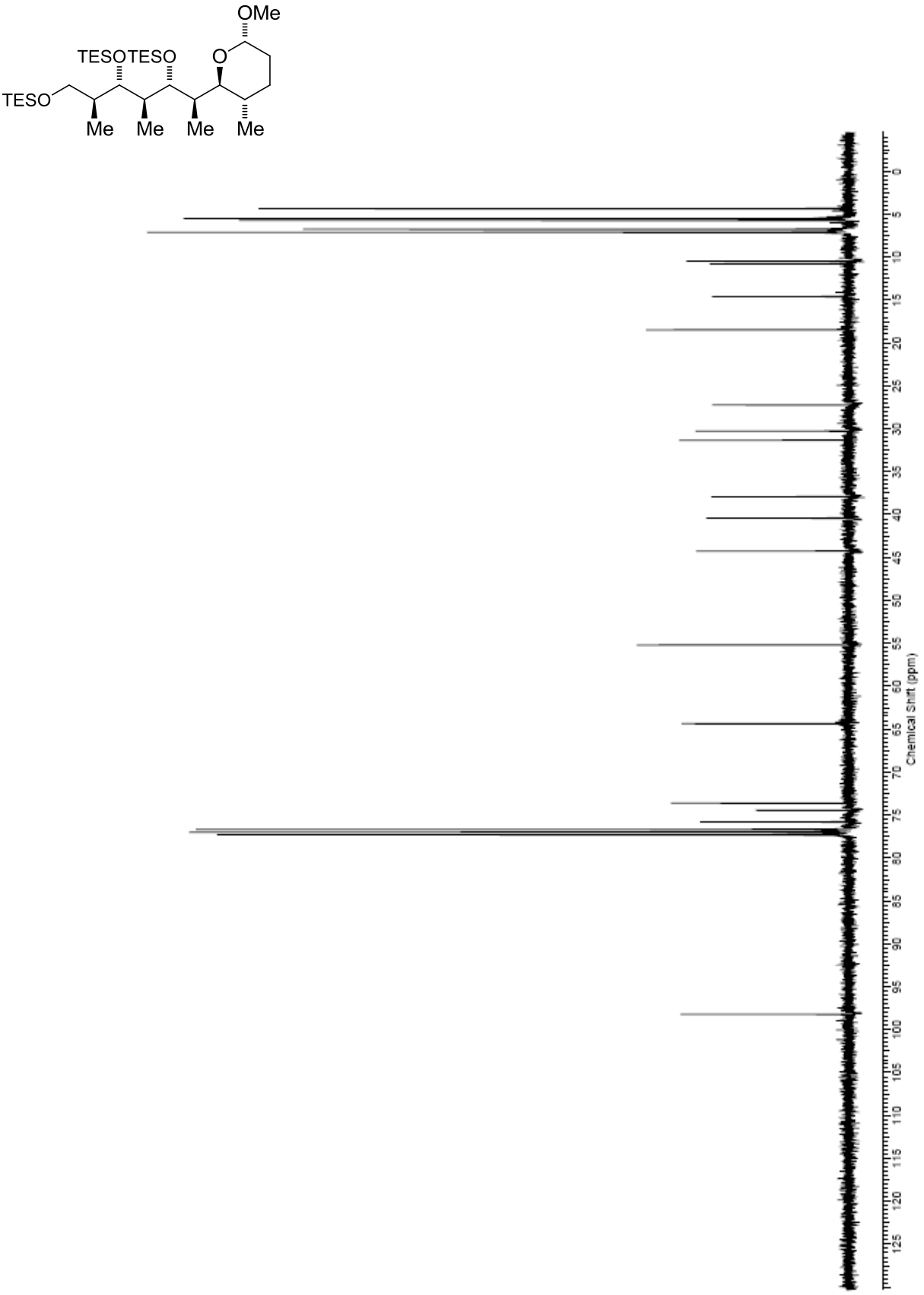
Chemical Shift (ppm)


OMe
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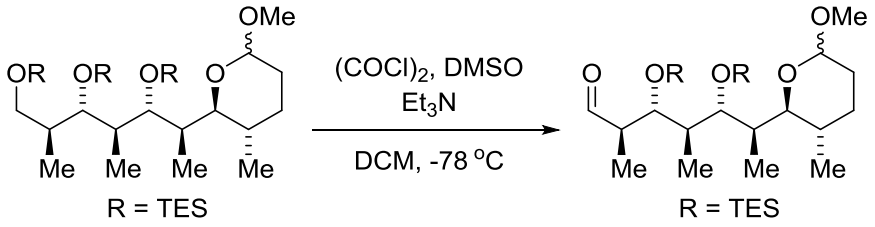
Chemical Shift (ppm)

(2*R*,3*R*,4*R*,5*R*,6*R*)-6-((2*S*,3*S*,6*S*)-6-Methoxy-3-methyltetrahydro-2H-pyran-2-yl)-2,4-dimethyl-3,5-bis((triethylsilyl)oxy)heptanal (Fragment B)



To a stirred solution of oxalyl chloride (31 μL, 0.359 mmol, 250 mol%) in CH_2Cl_2 (0.7 mL) was added DMSO (51 μL, 0.717 mmol, 500 mol%) dropwise at −78 °C. The resultant solution was stirred for 15 min before a solution of ether **S11** (93 mg, 0.143 mmol) in CH_2Cl_2 (0.7 mL) was slowly added and the reaction mixture was stirred at −78 °C for 3 hrs. Triethylamine (200 μL, 1.43 mmol, 1000 mol%) was added dropwise over 10 min and the mixture was stirred for 45 min before being warmed to 0 °C and quenched with a pH=7 buffer (2.0 mL). The layers were separated and the aqueous layer was extracted with Et_2O (3 × 2.0 mL). The combined organics were washed with brine (2.0 mL), dried over $MgSO_4$, filtered, and the volatiles were removed *via* rotary evaporation. The residue was subjected to flash column chromatography (SiO_2, hexanes/Et_2O 95:5) to afford aldehydes **Fragment B** (39 mg, 0.073 mmol, major diastereomer; 23 mg, 0.043 mmol, minor diastereomer, 81% yield) as colorless oils. The diastereomers were completely separated by column chromatography, and the spectral data for both are reported below.

TLC (SiO_2): R_f = 0.50 (major), 0.39 (minor) (hexanes/Et_2O 90:10).

$[\alpha]_D^{20}$: −48.7 (*c* 0.50, CH_2Cl_2,, major), −33.3 (*c* 0.50, $CHCl_3$, minor).

^{1}H NMR (major): (400 MHz, $CDCl_3$): δ 9.82 (d, *J* = 2.0 Hz, 1H), 4.64 (t, *J* = 2.4 Hz, 1H), 4.25 (dd, *J* = 6.0, 1.6 Hz, 1H), 3.79 (dd, *J* = 5.6, 4.4 Hz, 1H), 3.60 (d, *J* = 9.6 Hz, 1H), 3.36 (s, 3H), 2.73 (qt, *J* = 7.2, 2.0 Hz, 1H), 2.17-2.08 (m, 1H), 1.84 (quin., *J* = 6.6 Hz, 1H), 1.70-1.63 (m, 2H), 1.56-1.48 (m, 3H), 1.15 (d, *J* = 7.2 Hz, 3H), 0.99-0.93 (m, 21H), 0.89 (d, *J* = 7.2 Hz, 3H), 0.80 (d, *J* = 6.4 Hz, 3H), 0.67-0.61 (m, 12H).

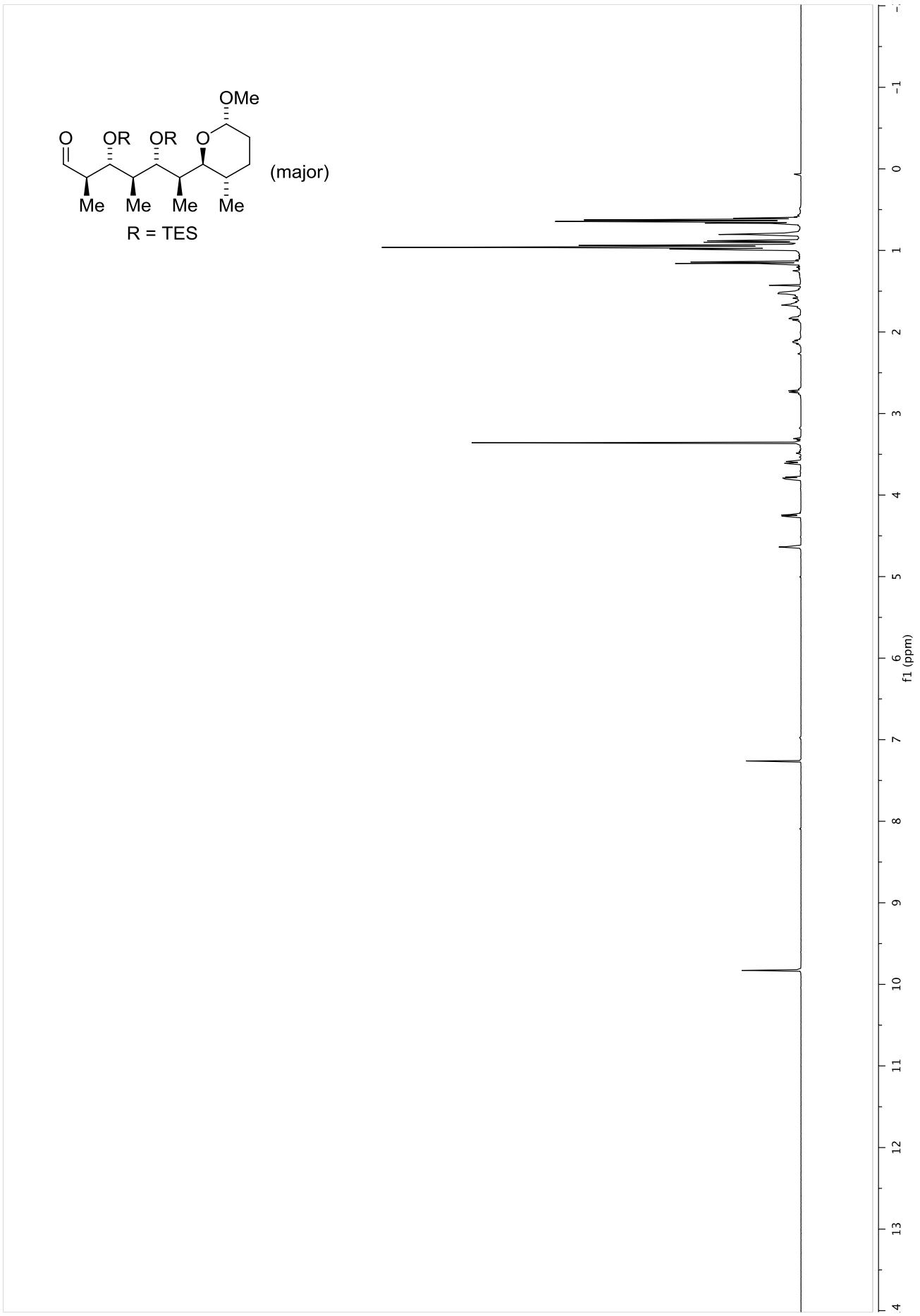
^{13}C NMR (major): (100 MHz, $CDCl_3$): 205.5, 98.3, 77.5, 75.4, 74.1, 55.2, 50.1, 43.2, 38.7, 31.6, 30.1, 27.1, 18.4, 12.5, 12.1, 10.2, 7.1, 7.0, 5.5, 5.2.

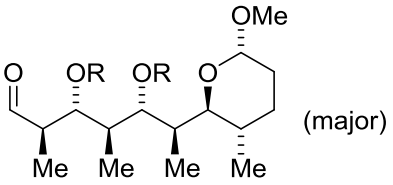
^{1}H NMR (minor): (400 MHz, $CDCl_3$): δ 9.82 (d, *J* = 1.6 Hz, 1H), 4.33 (dd, *J* = 9.4, 2.0 Hz, 1H), 4.24 (dd, *J* = 6.5, 1.8 Hz, 1H), 3.85 (dd, *J* = 9.2, 2.5 Hz, 1H), 3.47 (s, 3H), 3.31 (d, *J* = 9.8 Hz, 1H), 2.83 (q, *J* = 6.8 Hz, 1H), 2.00 (dt, *J* = 6.9, 2.5 Hz, 1H), 1.85–1.73 (m, 3H), 1.51 (m, 1H), 1.40 (m, 1H), 1.20 (m, 1H), 1.14 (d, *J* = 7.0 Hz, 3H), 1.02–0.89 (m, 21H), 0.77 (d, *J* = 6.7 Hz, 3H), 0.72–0.56 (m, 15H).

^{13}C NMR (minor): (100 MHz, $CDCl_3$): δ 204.7, 102.6, 79.6, 76.1, 74.4, 55.8, 50.9, 41.7, 38.8, 31.8, 31.7, 30.9, 17.3, 13.2, 11.3, 9.9, 7.1, 6.9, 5.6, 5.2.

FTIR (neat): 2954, 2877, 1724, 1457, 1381, 1239, 1057, 1022, 1006, 810, 740 cm^{-1}.

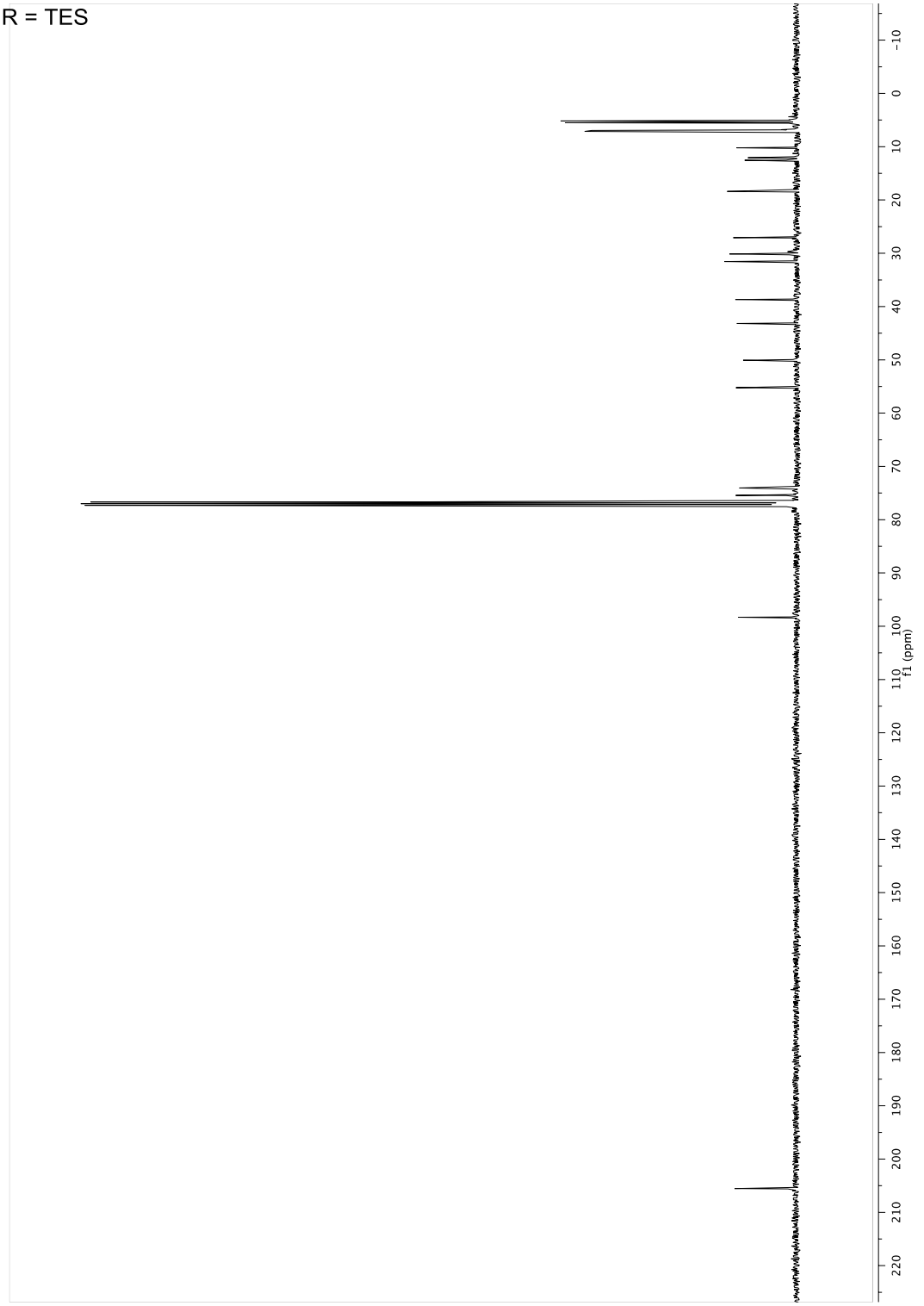
HRMS: (ESI, *m/z*) for $C_{28}H_{58}NaO_5Si_2$ calculated 553.3715, found 553.3718 (major), found 553.3715 (minor).

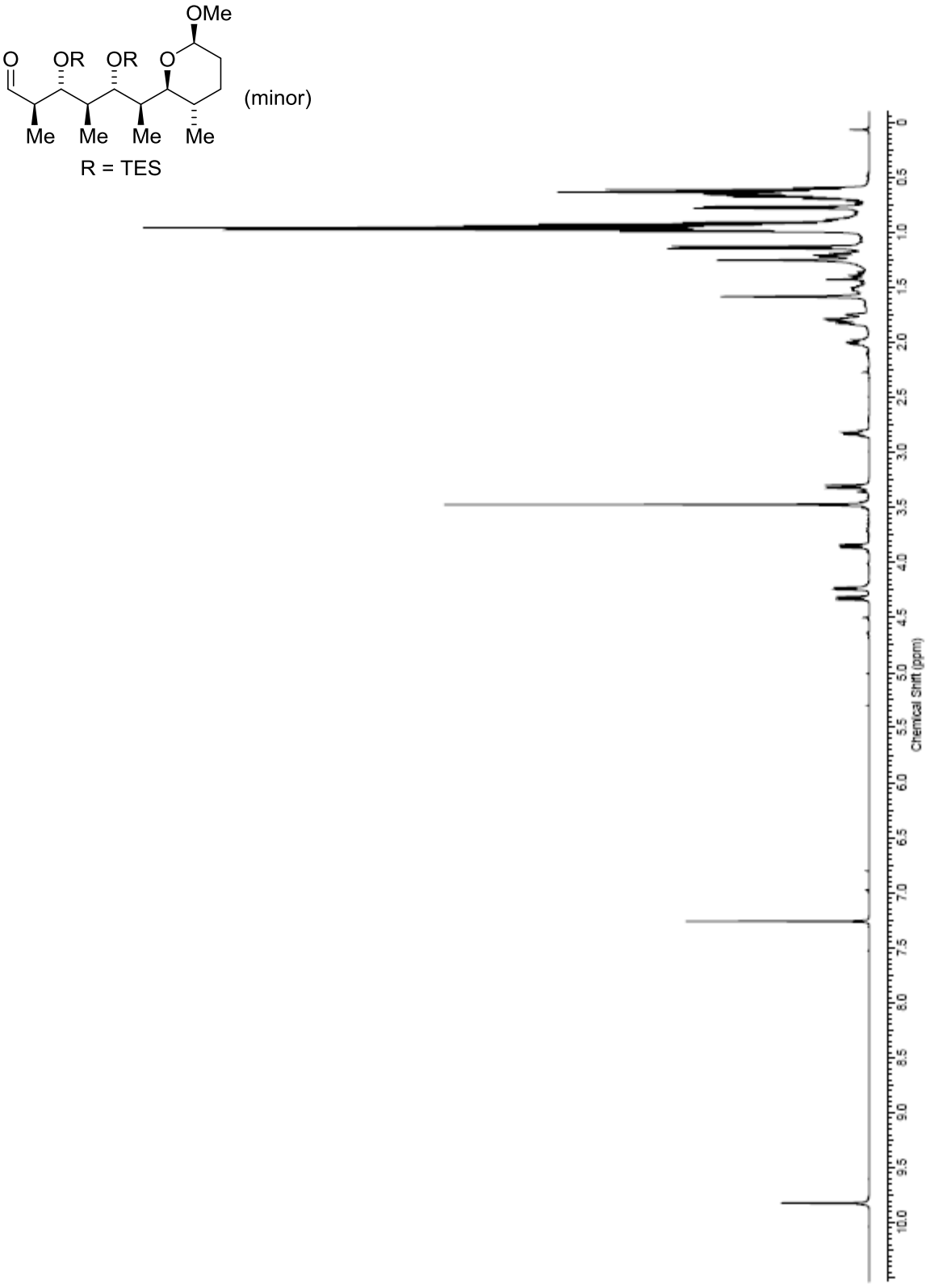

OMe
O
OR
OR
O
Me
Me
Me
Me
R = TES
(major)
f1 (ppm)

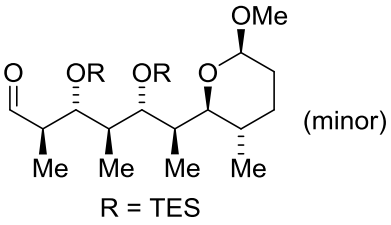


(major)

R = TES



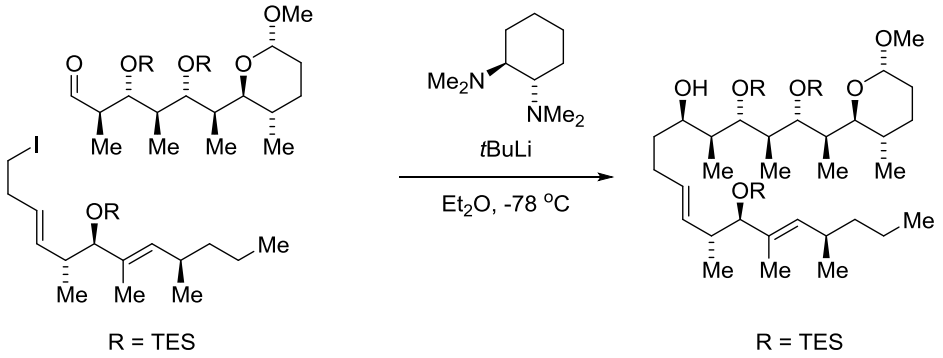

OMe
O
OR
OR
O
Me
Me
Me
Me
R = TES
(minor)
Chemical Shift (ppm)


OMe
O
OR
OR
O
Me
Me
Me
Me
R = TES

(minor)

-10
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220
230
f1 (ppm)

(5*R*,6*S*,7*S*,8*S*,9*R*,14*R*,15*R*,*E*)-3,3,17,17-tetraethyl-5-((*R*)-1-((2*S*,3*S*,6*S*)-6-methoxy-3-methyltetrahydro-2*H*-pyran-2-yl)ethyl)-6,8,14-trimethyl-15-((*R*,*E*)-4-methylhept-2-en-2-yl)-7-((triethylsilyl)oxy)-4,16-dioxa-3,17-disilanonadec-12-en-9-ol (11)



To an oven-dried round bottomed flask equipped with stir bar was added iodide (**Fragment A**) (77 mg, 0.165 mmol, 250 mol%), Et_2O (1.5 mL) and (1*S*,2*S*)-N^1,N^1,N^2,N^2-tetramethylcyclohexane-1,2-diamine (113 mg, 0.659 mmol, 1000 mol%). The solution was cooled to -78 °C and *tert*-butyl lithium (0.70 M in pentane, 235 µL, 0.165 mmol, 250 mol%) was added dropwise. The solution was allowed to stir for 15 minutes at -78 °C before aldehyde (**Fragment B**) (35 mg, 0.066 mmol, 100 mol%) was added in Et_2O (1.0 ml) dropwise. The reaction was allowed to stir at -78 °C for 1.5 hrs, before being quenched with 1 mL pH=7 buffer. The aqueous layer was extracted with Et_2O (3 × 1 mL). The combined organic layers were dried with Na_2SO_4 and filtered. The volatiles were removed *via* rotary evaporation, and the residue was subjected to flash column chromatography (SiO_2, hexanes/ Et_2O 95:5 – 9:1) to afford **11** as a colorless oil in a 3:1 mixture of diastereomers (30 mg (major), 9 mg (minor), 0.045 mmol, 68% yield). The major and minor diastereomers could be separated by column chromatography and the major is characterized below.

TLC (SiO_2): R_f = 0.41 desired, 0.36 undesired (hexanes/Et_2O 9:1).

$[\alpha]_D^{20}$: +20.0 (c 0.50, $CHCl_3$).

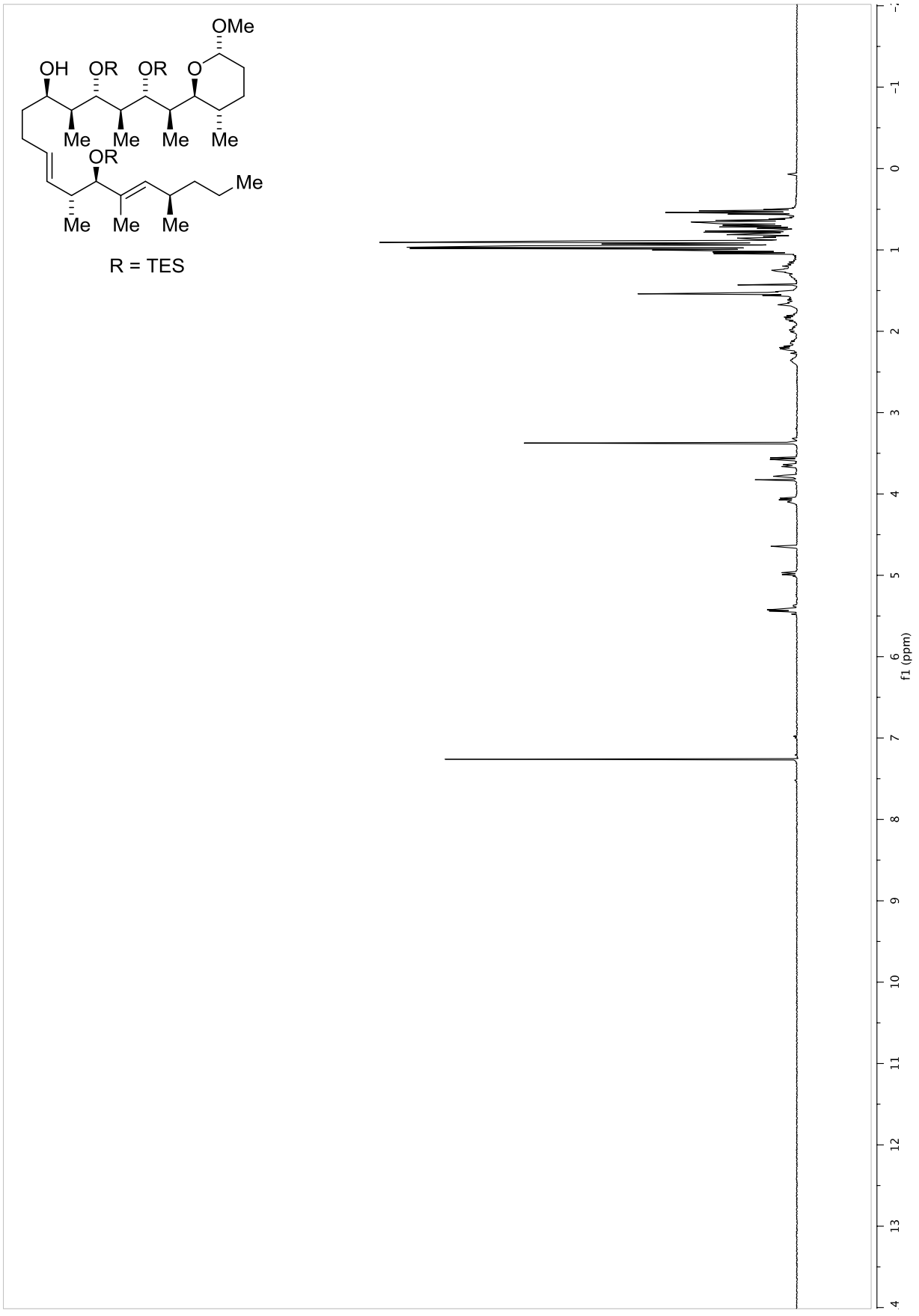
^{1}H NMR (400 MHz, $CHCl_3$): 5.48-5.67 (m, 2H), 4.98 (d, *J* = 9.6 Hz, 1H), 4.64 (t, *J* = 2.0 Hz, 1H), 4.11-4.05 (m, 2H), 3.83 (s, 1H), 3.78 (t, *J* = 5.2 Hz, 1H), 3.65 (d, *J* = 8.8 Hz, 1H), 3.57 (d, *J* = 8.4 Hz, 1H), 3.37 (s, 3H), 2.39-2.32 (m, 2H), 2.25-2.11 (m, 3H), 2.02-1.93 (m, 1H), 1.89-1.78 (m, 2H), 1.71-1.49 (m, 9H), 1.36-1.15 (m, 5H), 1.05-0.84 (m, 41H), 0.81 (d, *J* = 6.0 Hz, 3H), 0.78 (d, *J* = 7.2 Hz, 3H), 0.73-0.62 (m, 12H), 0.56-0.50 (m, 6H).

^{1}H NMR (400 MHz, C_6D_6): δ 5.79-5.65 (m, 2H), 5.06 (d, *J* = 10.4 Hz, 1H), 4.65 f(d, *J* = 2.8 Hz, 1H), 4.43-4.38 (m, 1H), 4.18 (dd, *J* = 7.6, 1.6 Hz, 1H), 4.05 (dd, *J* = 6.4, 4.8 Hz, 1H), 3.90 (d, *J* = 10.4 Hz, 1H), 3.73 (d, *J* = 8 Hz, 1H), 3.62 (s, 1H), 3.41 (s, 3H), 2.65-2.55 (m, 1H), 2.47-2.32 (m, 4H), 2.06-1.89 (m, 3H), 1.73-1.67 (m, 2H), 1.66 (d, *J* = 1.2 Hz, 3H), 1.55-1.48 (m, 3H), 1.39-1.30 (m, 4H), 1.26-0.97 (m, 37 H), 0.92-0.64 (m, 30 H).

^{13}C NMR: (100 MHz, C_6D_6): δ 135.6, 134.4, 134.1, 130.1, 98.7, 84.2, 80.7, 76.6, 74.0, 71.0, 55.3, 44.6, 41.4, 40.3, 38.8, 38.6, 36.1, 32.0, 31.9, 30.6, 30.3, 27.5, 21.1, 21.0, 18.6, 17.3, 14.4, 12.9, 12.0, 11.4, 10.8, 7.5, 7.3, 7.3, 6.2, 5.8, 5.5.

FTIR (neat): 2954, 2876, 1458, 1414, 1375, 1233, 1058, 1003, 964, 815, 724 cm^{-1}.

HRMS: (ESI+, *m/z*) for $C_{49}H_{100}NaO_6Si_3^+$ calculated 891.6720, found 891.6724.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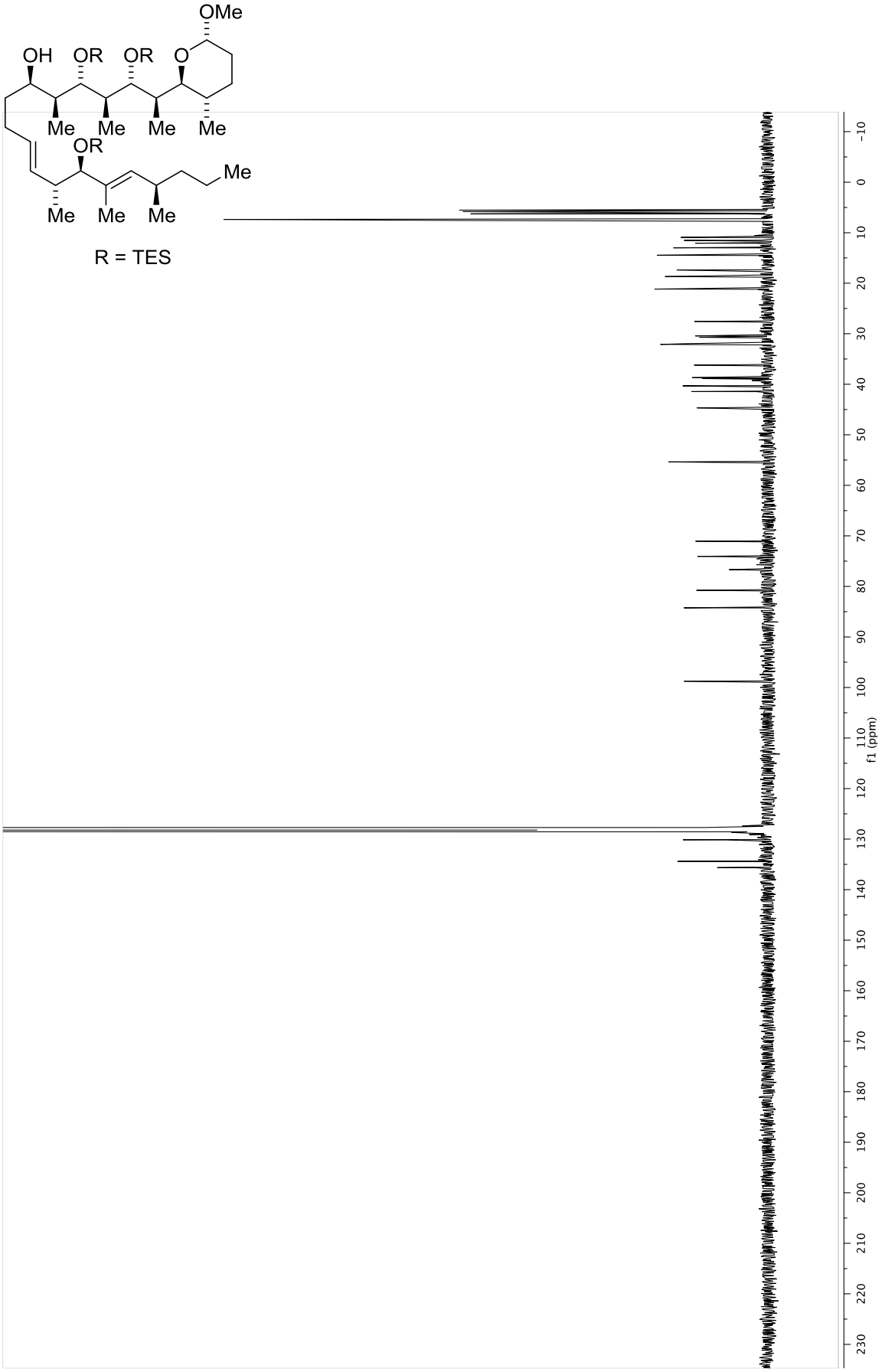
f1 (ppm)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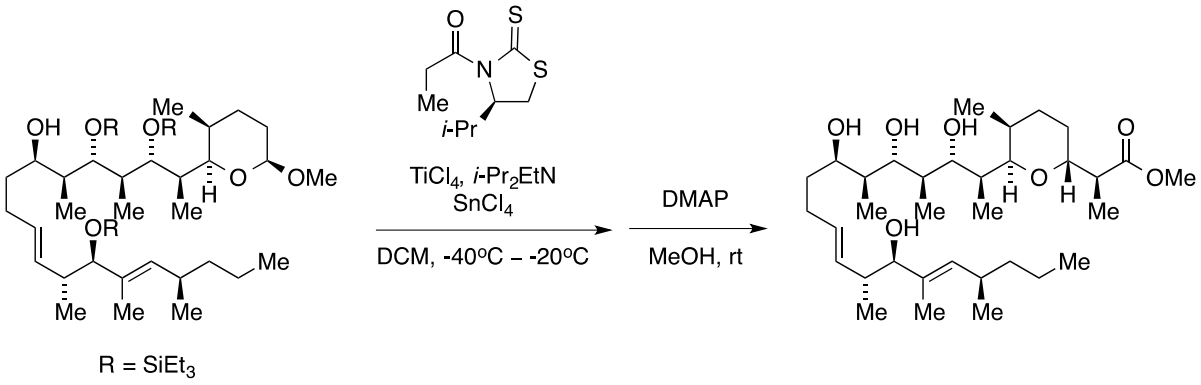
R = TES
f1 (ppm)

Methyl (*S*)-2-((2*R*,5*S*,6*R*)-5-methyl-6-((2*S*,3*S*,4*S*,5*S*,6*S*,7*R*,10*E*,12*R*,13*R*,14*E*,16*R*)-3,5,7,13-tetrahydroxy-4,6,12,14,16-pentamethylnonadeca-10,14-dien-2-yl)tetrahydro-2*H*-pyran-2-yl)propanoate (Zincophorin Methyl Ester)



To an over dried test tube under argon was added a solution of thiazole **S3** (6.0 mg, 0.028 mmol, 400 mol%) in 0.3 ml CH_2Cl_2. At 0 °C $TiCl_4$ (1.0 M in CH_2Cl_2, 28 µL, 0.028 mmol, 400 mol%) was added resulting in yellow heterogeneous solution. The reaction was cooled to -40 °C and *i*-Pr_2EtN was added (1.0 M in in CH_2Cl_2, 28 µL, 0.028 mmol, 400 mol%). The resultant red solution was allowed to stir at -40 °C for 3 hrs. $SnCl_4$ (1.0 M in in CH_2Cl_2, 8 µL, 0.013 mmol, 120 mol%) was then added, immediately after which a solution of **11** (6.0 mg, 0.007 mmol) in 0.2 mL CH_2Cl_2 was added. The reaction was allowed to stir at -40 °C for 1 hr, before being warmed to -20 °C for an additional 12 hrs. The reaction was then cooled to -78 °C before being quenched with pH=7 buffer. The mixture was extracted with EtOAc (3 × 1mL). The combined organic layers were dried with Na_2SO_4, filtered, and the volatiles were removed *via* rotary evaporation. The resulting oil was transferred to a vial with stir bar and diluted with 0.3 mL MeOH. DMAP (0.8 mg, 0.007 mmol, 100 mol%) was then added. The vial was capped and allowed to stir at ambient temperature for 24 hrs. The reaction mixture was then diluted with 1 mL EtOAc and 1mL NH_4Cl (sat., aq.) was added. The aqueous layer was extracted with EtOAc (3 × 1mL). The combined organic layers were dried with Na_2SO_4, filtered, and the volatiles were removed *via* rotary evaporation. The resulting residue was subjected to flash column chromatography (SiO_2, hexanes/ EtOAc 9:1– 4:1 – 7:3) to afford **Zincophorin Methyl Ester (**1.5 mg, 0.0025 mmol, 37% yield over 2 steps).

TLC (SiO_2): R_f = 0.55 (3:2 hexanes/ EtOAc).

$[\alpha]_D^{20}$: +26.7 (*c* 0.15, $CHCl_3$).

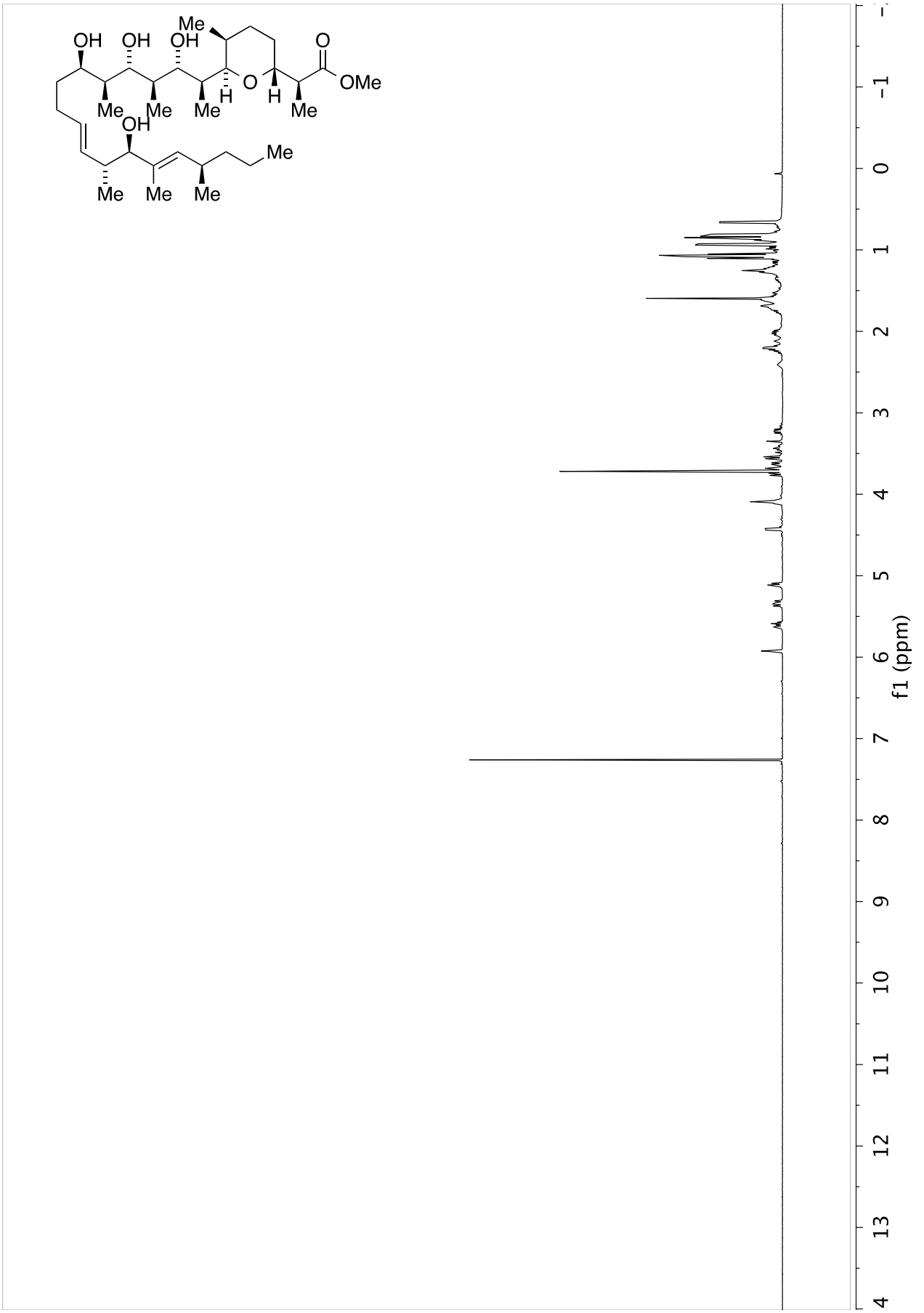
^{1}H NMR (400 MHz, $CHCl_3$): δ 5.92 (s, 1H), 5.61 (dt, *J* = 15.6, 6.8 Hz, 1H), 5.34 (dd, *J* = 15.2, 8.8 Hz, 1H), 5.10 (d, *J* = 8.8 Hz, 1H), 4.43 (d, *J* = 8.0 Hz, 1H), 4.11-4.07 (m, 3H), 3.75 (d, *J* = 9.6 Hz, 1H), 3.72 (s, 3H), 3.63 (dd, *J* = 8.8, 1.6 Hz, 1H), 3.55 (d, *J* = 9.2 Hz, 1H), 3.43 (td, *J* = 8.4, 2.8 Hz, 1H), 3.22 (dq, *J* = 10.8, 7.2 Hz, 1H), 2.44-2.38 (m 1H), 2.27-2.17 (m, 3H), 2.12 (s, 1H), 2.07-1.96 (m, 2H), 1.77-1.61 (m, 4H), 1.60 (d, *J* = 1.2 Hz, 3H), 1.41-1.15 (m, 6H), 1.10 (d, *J* = 7.2 Hz, 3H), 1.08 (d, *J* = 6.8 Hz, 3H), 1.06 (d, *J* = 6.8 Hz, 3H), 0.93 (d, *J* = 6.8 Hz, 3H), 0.89- 0.85 (m, 5H), 0.84 (d, *J* = 6.8 Hz, 3H), 0.81 (d, *J* = 6.4 Hz, 3H), 0.66 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR: (100 MHz, $CHCl_3$): δ 175.6, 135.7, 133.4, 133.3, 133.3*, 84.4, 84.0, 81.9, 76.1, 74.6, 69.0, 52.4, 41.8, 39.9, 39.6, 38.4, 37.5, 34.4, 34.0, 31.8, 31.6, 29.1, 26.3, 25.0, 21.0, 20.6, 17.7, 17.5, 14.8, 14.2, 13.3, 11.3, 11.2, 10.8.

FTIR (neat): 3411, 2954, 2933, 2872, 1737, 1457, 1381, 1278, 1082, 1016, 967 cm^{-1}.

HRMS: (ESI+, *m/z*) for $C_{34}H_{62}NaO_7^+$ calculated 605.4388, found 605.4389.

*The presence of two overlapping olefinic carbons was confirmed by HSQC correlation.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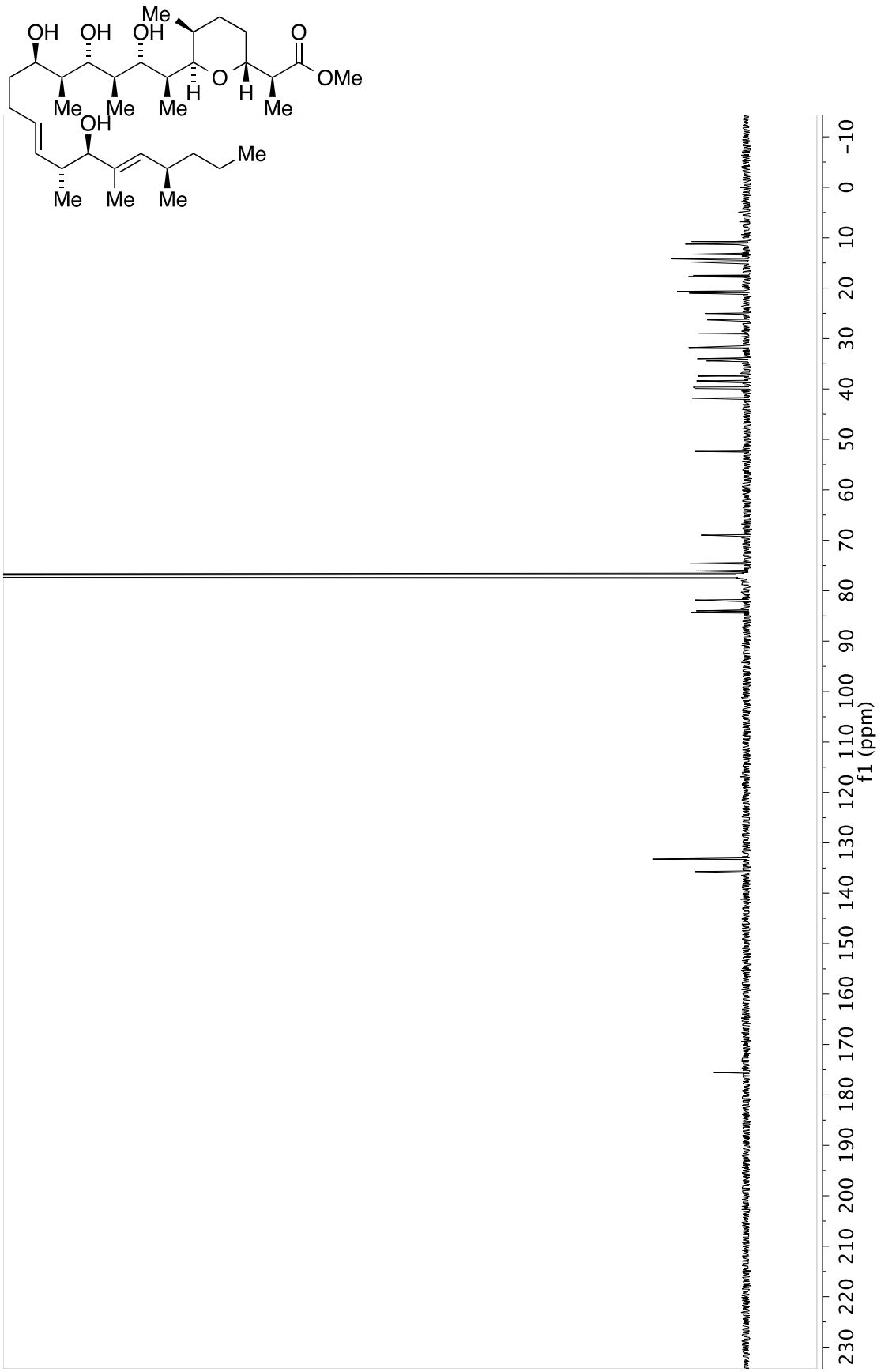
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Me
Me
Me
f1 (ppm)

Comparison to Leighton's Synthetic Zincophorin Methyl Ester (Harrison, T.; Ho, S.; Leighton, J. L. *J. Am. Chem. Soc.* **2011**, *133*, 7308.)

1H (400 MHz)	
δ (ppm)	δ (ppm) Leighton
5.92	5.91
5.61	5.63
5.34	5.34
5.10	5.11
4.43	4.42
4.11-4.07	4.12-4.08
3.75	3.76
3.72	3.72
3.63	3.63
3.55	3.56
3.43	3.43
3.22	3.22
2.44-2.38	2.46-2.37
2.27-2.17	2.29-2.18
2.12	2.11
2.07-1.96	2.03-1.94
1.77-1.61	1.77-1.62
1.60	1.60
1.41-1.15	1.46-1.15
1.10	1.10
1.08	1.08
1.06	1.06
0.93	0.94
0.89-0.85	0.90-0.86
0.84	0.84
0.81	0.82
0.66	0.66

13C (100 MHz)	
δ (ppm)	δ (ppm) Leighton
175.6	175.6
135.7	135.7
133.4	133.4
133.3	133.3
133.3	133.2
84.4	84.4
84.0	84.0
81.9	81.9
76.1	76.1
74.6	74.6
69.0	69.0
52.4	52.4
41.8	41.8
39.9	39.9
39.6	39.7
38.4	38.4
37.5	37.4
34.4	34.5
34.0	34.0
31.8	31.8
31.6	31.6
29.1	29.8
26.3	26.3
25.0	25.0
21.0	21.0
20.6	20.6
17.7	17.7
17.5	17.5
14.8	14.8
14.2	14.2
13.3	13.3
11.3	11.3
11.2	11.2
10.8	10.8

[1] Amarego, W. L. F.; Chai, C. *Purification of Laboratory Chemicals*, 6th ed., Elsevier Inc.: Oxford, UK, 2009.
[2] Still, W. C.; Kahn, M; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
[3] Magens, S.; Ertelt, M.; Jatsch, A.; Plietker, B. *Org. Lett.* **2008**, *10*, 53.
[4] Hodgson, D. M.; Kloesges, J.; Evans, B. *Org. Lett.* **2008**, *10*, 2781.
[5] Galvalez, E.; Romea, P.; Urpi, F. *Org. Synth.* **2009**, *86*, 70.
$\underline{[\alpha]_D^{20}:}$ +34.76 (*c* 1.11, $CHCl_3$) reported for **S3**.
$\underline{[\alpha]_D^{20}:}$ –420.84 (*c* 1.01, $CHCl_3$) reported for **S4**.
[6] Prepared according to Breit: *Angew. Chem. Int. Ed.* **2008**, *47*, 5451, but also commercially available.
[7] Studte, C.; Breit, B. *Angew. Chem. Int. Ed.* **2008**, *47*, 5451.
[8] Lister, T.; Perkins, M. V. *Aust. J. Chem.* **2004**, *57*, 787.
[9] $[\alpha]_D^{20}$: +10.5, (*c* 0.85, $CHCl_3$) reported. Chen, H.-Y.; McDonald, F. E. *J. Am. Chem. Soc.* **2006**, *128*, 4568.
[10] $\underline{[\alpha]_D^{20}:}$ -4.2 (*c* 1.0, $CHCl_3$) reported. (*ref. 8*)

[11] $\underline{[\alpha]_D^{20}:}$ –14.6 (*c* 1.1, $CHCl_3$) reported. (*ref. 8*)
[12] Gao, X.; Han, H.; Krische, M. J. *J. Am. Chem. Soc.* **2011**, *133*, 12795.