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Stereoselective total synthesis of the parthenolides indicates target selectivity for tubulin carboxypeptidase activity

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Supporting Information

Table of content

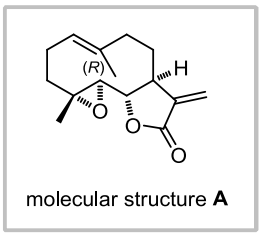
Figures, Schemes and Tables

1 Correct molecular structure of (–)-parthenolide

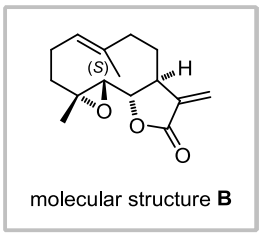
There are several reported molecular structures of (–)-parthenolide varying in the epoxide's stereochemistry, although the published X-ray crystal structures show the stereochemistry clearly to be 4*R*,5*R*,6*S*,7*S* (see also manuscript).[S1] Beside molecular structure **A** (see Scheme S1 below), which is used throughout this manuscript and by others,[S1c, 2] the wrong variant **B** frequently occurs and was also featured in Wikipedia.[S3] It may be that the depiction issue arose from projecting the 3D (crystal) structure that features basically all rings in the same plane to a 2D represenation without losing the appearance of the characteristic all-*trans* stereochemistry.[S1b] For a step by step construction of the correct epoxide's stereochemistry depiction, the starting point is the epoxidation of a *trans* alkene **X1** from the backside (Scheme S1), as realized during the biosynthesis of (–)-parthenolide from (+)-costunolide.[S4] The molecular structure of the epoxide **X2** shown is close to a 3D representation and includes the carbon chain's *trans* geometry as well as the right epoxide geometry, drawn with the oxygen above the carbon chain. More commonly, the oxygen atom is placed below the carbon chain (**X3**), as shown in the correct parthenolide structure **A**. Another variant which we ourselves used in a previous publication (**X4**)[S5] shows even more clearly the correct stereochemistry (see **X5**), but with an impossible conformation. Therefore, we chose structure **A** for using in this manuscript and recommend its usage furtheron. The entry in Wikipedia has been adapted accordingly.

The common structure **B** uses an epoxide depiction (**X6**) which would also correspond to an impossible conformation (**X7**), but in fact resolving to a *cis* stereochemistry (**X8**) with incorrect 5*S* configuration.

■ **comparison of two molecular structures of (–)-parthenolide**

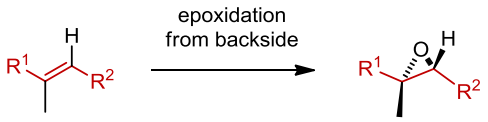


molecular structure **A**



molecular structure **B**

■ **generation of the epoxide's stereochemistry by alkene epoxidation**



X1 **X2**

3D depiction
trans geometry retained

■ **correct 2D depiction (two possibilities):**

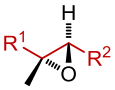
X3 **X4**

comprehensable	unambiguous stereochemistry
but	*but*
uncommon tetrahedral geometry depiction	impossible conformation

■ **correct tetrahedral depiction next to R^2:**

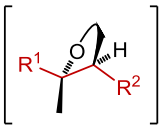
X5

■ **wrong 2D depiction:**



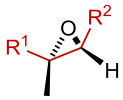
X6

would correspond to:



X7

being in fact the *cis* stereochemistry:



X8

Scheme S1. Correct and wrong stereochemistry depictions of parthenolide.

2 General information

2.1 Instrumentation (Chemistry)

NMR spectra were recorded on one of the following Bruker spectrometers: Avance I (250 MHz, probe: BBO), Fourier (300 MHz, probe: Dual $^{1}H/^{13}C$), Avance I (400 MHz, probe: BBO), Avance II [400 MHz, probes: BBFO, BBO (+ATM)], Avance III HD [500 MHz, probe: BBO (Prodigy)] or Avance III [600 MHz, probes: TCPI (+ATM), PAQXI (+ATM), BBO (+ATM)]. $^{1}H,^{13}C$ ASAP–HSQC and Multiplicity-edited ASAP–HSQC (denoted as HSQC/DEPT) spectra were recorded as described by Luy and co-workers.[S6] Chemical shifts (δ) are expressed in parts per million (ppm) with respect to the solvent signal (^{13}C NMR, δ: C_6D_6 128.06, $CDCl_3$ 77.16), the residual nondeuterated solvent signal (^{1}H NMR, δ: C_6D_5H 7.16, $CHCl_3$ 7.26) or an external standard (^{11}B NMR: $BF_3{\times}OEt_2$, ^{119}Sn: $SnMe_4$ in $CDCl_3$).[S7] Signals were assigned on the basis of 2D NMR experiments.

RP-HPLC analyses were conducted on a Shimadzu system fitted with a Macherey-Nagel EC 125/4 Nucleodur C18 Gravity column (5 µm, 125 × 10 mm ID). Linear MeCN/H_2O gradients were employed at 1 mL/min flow rate. **Chiral HPLC** analyses and separations were conducted on a Shimadzu system with an analytical Daicel Chiralpak-IA (5 µm, 250 × 4.6 mm ID) or a semi-preperative Daicel Chiralpak-OJ column (10 µm, 250 × 10 mm ID), eluting with isocratic *n*-hexane/EtOH mixtures (see experimental procedures for details).

GC–MS (low resolution) analyses were conducted on a HP 6890 system with a SGE BPX5 column (0.25µm, 25 m × 0.22 mm ID) and a HP 5973 mass selective detector (single quadrupol) in EI mode, using He as carrier gas (1 mL/min flow rate). High resolution mass spectra (**HRMS**) were recorded on one of the following machines: Bruker Maxis Impact (QTOF) in ESI mode, Thermo Scientific Q Exactive Plus (Orbitrap) in ESI or APCI mode or Thermo Q Exactive GC (Orbitrap) in EI mode.

FT-IR spectra were recorded on a Shimadzu IRAffinity-1 machine in ATR mode. The following notations indicate the intensity of the absorption bands: *s* = strong, *m* = medium, *w* = weak.

Melting points were determined with a Büchi B-540 apparatus.

Optical rotations were recorded with a Jasco P-2000 polarimeter at 589 nm. The path length of the cuvette was d = 10 mm. Specific rotations ($[\alpha]$) are expressed in deg × mL × g^{-1} × dm^{-1}, but reported without the unit. Corresponding concentrations (c) are given in g/(100mL).

2.2 Methods and materials (Chemistry)

Unless otherwise stated, all reactions were carried out using standard Schlenk techniques under a positive pressure of nitrogen or argon. Analytical thin layer chromatography (**TLC**) was performed on silica gel 60 F_{254} on aluminum sheets. Substances were detected by UV quenching (254 nm) or staining ($KMnO_4$ in aq. K_2CO_3 solution). **Silica gel** 60 (40–63 μm) was used for flash column chromatography (approx. 0.3 bar positive pressure).[S8] **(–)-Parthenolide** was purchased from Tokyo Chemical Industry Co., Ltd. as a reference (Lot. NM8FA-CT).

Reagents available from commercial sources were used without further purification, with the following exceptions: Anhydrous amines (**Et_3N**, **pyridine**, **2,6-lutidine**) and anhydrous **TMSCl** were obtained by distillation from CaH_2. Anhydrous **CH_2Cl_2** and **1,2-dibromoethane** were obtained by distillation from CaH_2 or by treating HPLC grade material with 3 Å molecular sieves (MS 3Å) for min. 24 h. Anhydrous **DMF** and **PhMe** were obtained from a solvent purification system prior to use (HPLC grade solvents, N_2 atmosphere, MS 3Å or activated alumina, respectively). Anhydrous **Et_2O** and **THF** were obtained by distilling peroxide free (KOH) and pre-dried ($CaCl_2$) material from purple Na/benzophenone. **MeOH**, **EtOH**, and **MeCN** (HPLC grade) were dehydrated by treatment with MS 3Å (min. 48 h). **$CDCl_3$** was passed through a short plug of activated basic Al_2O_3 (63–200 μm, activity grade I) directly before use. **C_6D_6** was stored with MS 3Å. **LiBr** was dried under vacuum by slowly heating the solid to 160 °C (20°C/h) and keeping it at this temperature for 5 h.

pH 7 phosphate buffer (0.5 M) was prepared by dissolving 58.8 g $Na_3PO_4 \times 12\ H_2O$ (144 mmol), 42.7 g NaH_2PO_4 (356 mmol) and 113 mg NaN_3 (1.74 mmol) in 900 mL water and filling up to a total volume of 1 L. **Na_2EDTA** (0.5 M, pH 8) **solution** was prepared by suspending 186 g $Na_2EDTA \times 3H_2O$ in 900 mL water and slowly adding NaOH pellets until dissolution was complete and pH 8 was reached. It was filled up to a total volume of 1 L.

The concentration of BuLi solutions was determined by threefold titration using 4-biphenyl acetic acid in anhydrous THF at room temperature.[S9]

The following substances were prepared according to the published procedures:

Homoallyloxy acetaldehyde **SI-1**[S10], allyl alcohol **SI-2**[S11], $MgBr_2 \times OEt_2$ (as 0.8 M solution in 4:1 Et_2O/C_6H_6)[S12], aldehyde (±)-**SI-3**[S13], aldehyde (±)-**SI-4**[S14] and PMB–Br[S15].

2.3 Methods and materials (biology)

2.3.1 DRG neuron cultures and immunocytochemical stainings

Cultures were prepared as described previously.[S16] DRG neurons were harvested from adult C57BL/6j mice as described previously.[S16] Isolated DRGs (T8–L6) were incubated in 0.25% trypsin/EDTA (GE Healthcare, Chalfont St Giles, UK) and 0.3% collagenase type IA (Sigma) in DMEM (Life Technologies, Carlsbad, US-CA) at 37 °C and 5% CO_2 for 45 min and mechanically dissociated. Cells were resuspended in DMEM containing 10% fetal bovine serum (GE Healthcare) and penicillin/streptomycin (500 U/mL; Merck Millipore, Billerica, US-MA) and cultured at 37 °C and 5% CO_2 on poly-D-lysine (PDL, 0.1 mg/mL, molecular weight <300,000 kDa; Sigma) and laminin (20 µg/mL; Sigma)-coated plates (Sarstedt, Germany). Cells were either treated with vehicle (DMSO), 1 nM (−)-parthenolide (Sigma-Aldrich, USA, MO), 0.5–50 nM (−)-**1**, 0.5–50 nM (+)-**1**, 0.5–50 nM (−)-**22** or 0.5–50 nM (+)-**22**.

Axonal growth was determined 48 h upon incubation by fixation in 4% PFA (Sigma) and immunocytochemical staining with antibodies against βIII-tubulin (1:2,000; Covance, Princeton, US-NJ). Imaging and quantification of total axon length and neuron numbers per well were automatically performed with the Olympus VS120 microscope system (BD, Franklin Lakes, US-NJ) and ImageJ NeuriteTracer plugin, avoiding experimenter-induced quantification bias. Average axon length per neuron and neuron counts per experimental group were normalized to control groups. Data represent means ± SEM of 3 replicate wells per experiment and two independent experiments. Significances of intergroup differences were evaluated using either one- or two-way analysis of variance (ANOVA) followed by the Holm-Sidak post hoc test.

Microtubule detyrosination in axon tips was evaluated two days in culture using antibodies against βIII-tubulin (1:2,000; Covance) and detyrosinated tubulin (1:2,000; Millipore) as described previously.[S16] Axon tips were defined as the last 15 µm of βIII-tubulin positive neurite extensions and determined positive with a gray value above 30 after background subtraction. Data represent means ± SEM of three replicate wells with 20 tips per well from at least two independent experiments. Significances of intergroup differences were evaluated using either one-way analysis of variance (ANOVA) followed by Holm-Sidak post hoc test.

2.3.2 Monocyte isolation and polarization of macrophages

Leukocyte concentrates from freshly withdrawn peripheral blood of male and female healthy adult human donors (age 18–65 years) with written informed consent were provided by the Institute of Transfusion Medicine at the University Hospital Jena, Germany. The experimental protocol was approved by the ethical committee of the University Hospital Jena. All methods were performed in accordance with the relevant guidelines and regulations. Peripheral blood mononuclear cells (PBMC) were separated using dextran sedimentation, followed by centrifugation on lymphocyte separation medium (Histopaque®-1077, Sigma-Aldrich). PBMC were seeded in RPMI 1640 (Sigma-Aldrich) containing 10% (v/v) heat-inactivated fetal calf serum (FCS), 100 U/mL penicillin, and 100 µg/mL streptomycin in cell culture flasks (Greiner Bio-one, Frickenhausen, Germany) for 1.5 h at 37 °C and 5% CO_2 for adherence of monocytes. For differentiation of monocytes to macrophages and polarization towards M1, published criteria were used.[S17] M1 were generated by incubating monocytes with 20 ng/mL granulocyte-macrophage colony-stimulating factor (GM-CSF; Peprotech, Hamburg, Germany) for 6 days in RPMI 1640 supplemented with 10% FCS, 2 mmol/L glutamine (Biochrom/Merck, Berlin, Germany), and penicillin-streptomycin (Biochrom/Merck), followed by treatment with 100 ng/mL lipopolysaccharide (LPS) and 20 ng/mL interferone (INF)-γ (Peprotech).

2.3.3 Determination of cell viability

The viability of M1 macrophages was assessed by MTT assay as described.[S18] Briefly, macrophages after 6 days of differentiation of monocytes were pre-incubated with test compounds for 15 min at 37 °C (5% CO_2), LPS (100 ng/mL, Peprotech) and INF-γ (20 ng/mL, Peprotech) were added, and cells were incubated for 48 h. Staurosporine (1 µM, Sigma-Aldrich), a pan-kinase inhibitor and inducer of apoptosis, was used as positive control. MTT solution was added, cells were further incubated for 4 h, and lysed in a buffer containing 10% (w/v) SDS.

2.3.4 SDS-PAGE and Western blot

Unpolarized macrophages were treated with test compounds or vehicle (0.1% DMSO) 15 min before cells were polarized to M1 for 6 h. Cell lysates, corresponding to 2×10^6 macrophages, were separated on 10% polyacrylamide gels, and blotted onto nitrocellulose membranes (Amersham Protran Supported 0.45 µm nitrocellulose, GE Healthcare, Freiburg, Germany). The membranes were incubated with the primary antibodies: rabbit polyclonal anti-COX-2,

1:1000 (4842S, Cell Signaling) and mouse monoclonal anti-*β*-actin, 1:1000 (3700S, Cell Signaling). Immunoreactive bands were stained with IRDye 800CW Goat anti-Rabbit IgG (H+L), 1:15,000 (926 32211, LI-COR Biosciences) and IRDye 680LT Goat anti-Mouse IgG (H+L), 1:40,000 (926-68020, LI-COR Biosciences), and visualized by an Odyssey infrared imager (LI-COR Biosciences). Data from densitometric analysis were background corrected.

2.3.5 Determination of cytokine levels

Unpolarized macrophages were treated with test compounds or vehicle (0.1% DMSO) 15 min before cells were polarized to M1 for 48 h. For measurement of extracellular cytokine levels, supernatants were collected by centrifugation (2000 g, 4 °C, 10 min). TNF-α was analyzed by in-house made ELISA kits (R&D system, Bio-Techne, MN, USA).

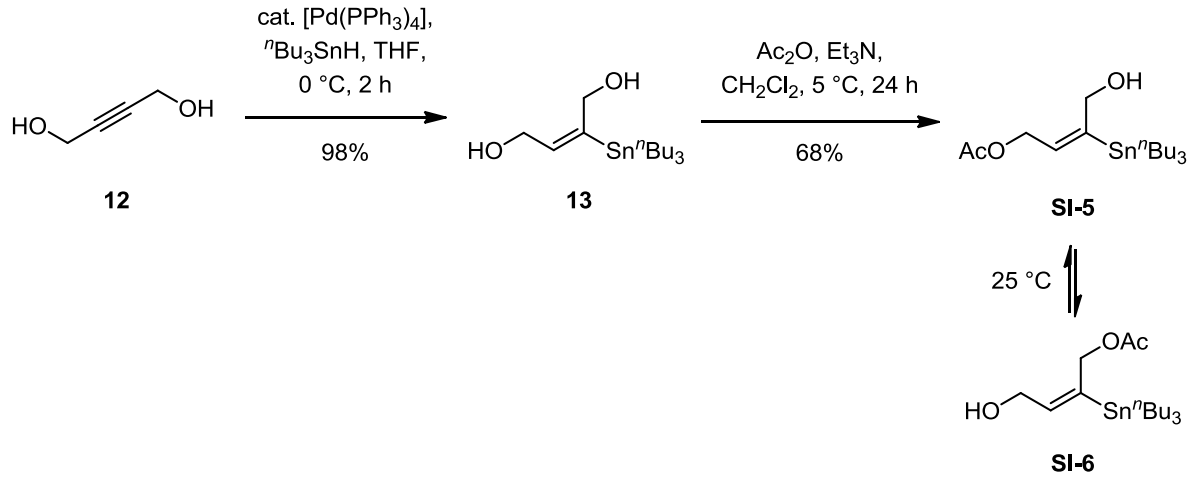
2.4 Abbreviations

15-c-5 = 15-crown-5, acac = acetylacetonate, *α*M*γ*B = *α*-methylene-*γ*-butyrolactone, Ar = aryl, brsm = (yield) based on recovered starting material, COX = cyclooxygenase, CSA = camphorsulfonic acid, DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, detyr = detyrosinated, DIPT = diisopropyl tartrate, DMP = Dess–Martin periodinane, *dr* = diastereomeric ratio, DRG = dorsal root ganglion, EWG = electron withdrawing group, IFN = interferone, Im = imidazole, KHMDS = potassium hexamethyldisilazide, LPS = lipopolysaccharide, MS = molecular sieves, Ms = methanesulfonyl, MTBE = methyl *tert*-butyl ether, NBS = *N*-bromosuccinimide, PE = petroleum ether (bp. 35–70 °C), pin = pinacolate [2,3-dimethylbutane-2,3-bis(olate)], PMB = *p*-methoxy benzyl, PTL = parthenolide, rt = room temperature (20–25 °C), SEM = standard error mean, stau = staurosporine, TBAF = tetra-*n*-butylammonium fluoride, TBS = *tert*-butyldimethyl-silyl, TCP = tubulin carboxypeptidase, TEMPO = 2,2,6,6-Tetramethylpiperidine-1-oxyl, Tf = trifluoromethanesulfonate, TNF = tumor necrosis factor, tub = tubulin, unpol = unpolarized, veh = vehicle.

3 Experimental

3.1 Preparation of 2-(silyloxymethyl)allylboronates

(*E*)-4-Hydroxy-3-(tri-*n*-butylstannyl)but-2-en-1-yl acetate (SI-5)



To a stirred solution of 2-butyne-1,4-diol (**12**, 5.0 g, 58.0 mmol, 1 equiv.) in anhydrous THF (100 mL) at 0 °C was added [$Pd(PPh_3)_4$] (670 mg, 0.58 mmol, 0.01 equiv.), followed by dropwise addition of $^{n}Bu_3SnH$ (15.9 mL, 17.2 g, 59.0 mmol, 1.02 equiv.) over the course of 1.5 h (0.18 mL/min) by using a syringe pump. After additional 30 min (TLC control, PE/EtOAc, 1:1) the solvent was evaporated. Column chromatography of the residue (PE/EtOAc, 10:1→5:1→1:1, 8 × 15 cm) provided the stannane **13** (21.3 g, 56.6 mmol, 98%) as a slightly yellow oil.

TLC: R_f = 0.45 (PE/EtOAc, 1:1).

Stannane **13** was dissolved in anhydrous CH_2Cl_2 (180 mL) and cooled to 0 °C with stirring. Et_3N (10.2 mL, 7.44 g, 73.5 mmol, 1.3 equiv.) was added, followed by Ac_2O (6.95 mL, 7.50 g, 73.5 mmol, 1.3 equiv.). The solution was kept at 5 °C. After 24 h (TLC control, PE/EtOAc, 2:1) MeOH (20 mL) was added and the mixture was stirred at rt for 1 h. The solution was then washed with a 1.0 M HCl solution (2 × 100 mL), sat. $NaHCO_3$ solution (100 mL) and brine (100 mL), dried with $MgSO_4$, filtered and concentrated *in vacuo*. Column chromatography of the residue (PE/Et_2O, 4:1→2:1, 8 × 20 cm) provided the acetoxy stannane **SI-5** (16.1 g, 38.4 mmol, 68%) as a colorless oil, which slowly isomerizes partially to acetoxy stannane **SI-6** at ~25 °C.[S19] Evaporation was carried out at 0–10 °C, in order to suppress isomerization.

SI-5:

TLC: R_f = 0.51 (PE/Et_2O, 3:2).

^{1}H NMR (400 MHz, C_6D_6, mixture of **SI-5** (major) and **SI-6**, **SI-5** assigned): δ = 5.81 (*tt*, 1H, $^{3,4}J_{H,H}$ = 6.3, 2.2 Hz, =C<u>H</u>; $^3J_{H,Sn}$ = 67.0 Hz), 4.57–4.48 (*m*, 2H, CH_2O), 4.21–4.07 (*m*, 2H, CH_2O; $^3J_{H,Sn}$ = 34.7 Hz), 1.68–1.53 (*m*, 9H, 3 × CH_2), 1.46–1.31 (*m*, 6H, 3 × CH_2), 1.15–0.90 (*m*, 15H, 3 × CH_2 + 3 × CH_3).

^{13}C{^{1}H} NMR (101 MHz, C_6D_6, mixture of **SI-5** (major) and **SI-6**, **SI-5** assigned): δ = 170.2 (C=O),

153.1 (=CSn, $^1J_{C,Sn}$ = 370.8 Hz), 131.7 (=CH, $^2J_{C,Sn}$ = 22.5 Hz), 63.4 (CH_2O, $^3J_{C,Sn}$ = 17.2 Hz), 61.4 (CH_2O, $^3J_{C,Sn}$ = 61.7 Hz), 29.6 (CH_2, $^3J_{C,Sn}$ = 19.5 Hz), 27.8 (CH_2, $^2J_{C,Sn}$ = 57.6 Hz), 20.5 (C(O)<u>C</u>H_3), 14.0 (CH_3), 10.6 (CH_2, $^1J_{C,Sn}$ = 326.8 Hz).

^{119}Sn{^{1}H} (149 MHz, C_6D_6): δ = –40.2 (*s*).

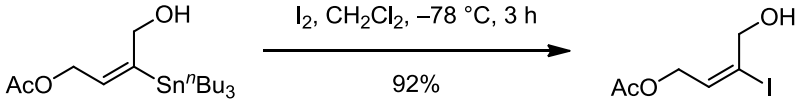
IR (ATR): $\tilde{\nu}$ = 3441 (*w*), 3000–2800 (*m*), 1744 (*s*), 1728 (*m*), 1458 (*m*), 1377 (*m*), 1226 (*s*), 1026 (*s*), 1038 (*s*), 690 (*m*), 864 (*m*), 663 (*m*) cm^{-1}.

HRMS (ESI, TOF): m/z calc'd for $C_{18}H_{36}O_3Sn$ $[M+Na]^+$ 443.1579; observed 443.1584.

SI-6

TLC: R_f = 0.30 (PE/Et_2O, 3:2).

(*E*)-4-Hydroxy-3-iodobut-2-en-1-yl acetate (SI-7)



SI-5 **SI-7**

To a stirred solution of stannane **SI-5** (9.51 g, 22.7 mmol, 1.0 equiv.) in anhydrous CH_2Cl_2 (70 mL) at –78 °C I_2 (6.04 g, 23.8 mmol, 1.05 equiv.) was added in one portion. After 3 h at this temperature (TLC control, Et_2O/PE, 3:1) the cooling bath was removed and semi-sat. $Na_2S_2O_3$ solution (70 mL) was added. Stirring was continued for 10 min. The colorless organic layer was separated, washed with sat. $NaHCO_3$ solution (70 mL) and brine (70 mL), dried with $MgSO_4$, filtered and concentrated *in vacuo*. The residue was taken up in MeCN (100 mL) and washed with PE (100 mL). The PE layer was then extracted with MeCN (3 × 30 mL). The combined MeCN extracts were concentrated *in vacuo*. After column

chromatography (PE/MTBE, 1:1, 6 × 20 cm) the vinyl iodide **SI-7** (5.35 g, 20.9 mmol, 92%) was obtained as a colorless oil.

TLC: R_f = 0.30 (PE/MTBE, 1:1).

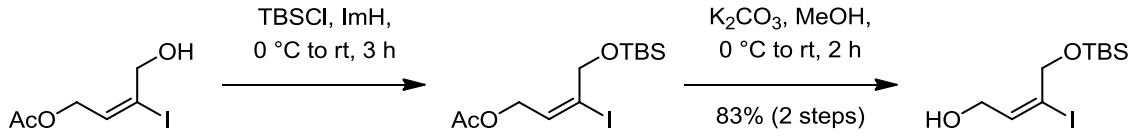
^{1}H NMR (300 MHz, C_6D_6): δ = 6.19 (*tt*, 1H, $^{3,4}J_{H,H}$ = 7.2, 0.9 Hz, =CH), 4.25 (*d*, 2H, $^3J_{H,H}$ = 7.3 Hz, CH_2), 4.02 (*d*, 2H, $^3J_{H,H}$ = 4.4 Hz, CH_2), 2.77 (*br s*, 1H, OH), 1.54 (*s*, 3H, CH_3).

^{13}C{^{1}H} NMR (75 MHz, C_6D_6): δ = 170.6 (C=O), 136.2 (=CH), 109.6 (=CI), 66.5 (CH_2OH), 61.2 (CH_2OAc), 20.4 (CH_3).

IR (ATR): $\tilde{\nu}$ = 3433 (*w*), 3000–2800 (*m*), 1736 (*s*), 1636 (*w*), 1439 (*w*), 1377 (*m*), 1362 (*m*), 1223 (*s*), 1115 (*m*), 1026 (*s*), 964 (*m*), 814 (*w*), 737 (*w*), 606 (*m*) cm^{-1}.

HRMS (ESI, TOF): m/z calc'd for $C_6H_9IO_3$ $[M+Na]^+$ 278.9489; observed 278.9492.

(*E*)-4-[(*tert*-Butyldimethylsilyl)oxy]-3-iodobut-2-en-1-ol (14)



SI-7 **SI-8** **14**

To a stirred solution of alcohol **SI-7** (7.46 g, 29.1 mmol, 1.0 equiv.) in anhydrous CH_2Cl_2 (100 mL) at 0 °C was added imidazole (2.97 g, 43.7 mmol, 1.5 equiv.), followed by TBSCl (6.14 g, 40.7 mmol, 1.4 equiv.). After 10 min the cooling bath was removed and the suspension was stirred for 3 h at rt (TLC control, PE/MTBE, 1:1). The mixture was filtered through a plug of silica (6 × 6 cm, PE/MTBE, 3:1). The solvent was removed *in vacuo* and the residual oil (**SI-8**) was taken to the next step.

TLC: R_f = 0.79 (PE/MTBE, 3:1).

The crude protected diol **SI-8** was dissolved in anhydrous MeOH (100 mL) and cooled to 0 °C with stirring. K_2CO_3 (8.04 g, 58.2 mmol, 2.0 equiv.) was added and after 10 min the cooling bath was removed. The suspension was stirred at rt for 2 h (TLC control, PE/MTBE, 5:1), then filtered through a plug of Celite, followed by addition of sat. NH_4Cl solution (100 mL). The mixture was extracted with MTBE (200 mL). The organic layer was separated

and washed with brine (100 mL), dried with $MgSO_4$, filtered and concentrated *in vacuo*. Column chromatography of the residue (PE/MTBE, 3:1→2:1, 8 × 15 cm) provided the allyl alcohol **14** (7.93 g, 24.2 mmol, 83% over 2 steps) as a colorless oil.

TLC: R_f = 0.26 (PE/MTBE, 5:1).

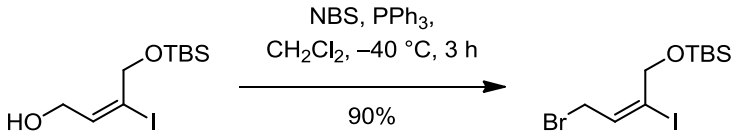
^{1}H NMR (300 MHz, C_6D_6): δ = 6.31 (*t*, 1H, $^3J_{H,H}$ = 6.5 Hz, =CH), 4.08 (*s*, 2H, CH_2OSi), 3.77 (*d*, 2H, $^3J_{H,H}$ = 6.0 Hz, $C\underline{H}_2OH$), 1.68 (*br s*, 1H, OH), 0.94 (*s*, 9H, $SiC(CH_3)_3$), 0.04 (*s*, 6H, $Si(CH_3)_2$).

^{13}C{^{1}H} NMR (75 MHz, C_6D_6): δ = 142.0 (=CH), 105.1 (=CI), 66.7 (CH_2OSi), 60.5 (CH_2OH), 26.1 ($SiC(\underline{C}H_3)_3$), 18.5 ($Si\underline{C}(CH_3)_3$), –5.0 ($Si(CH_3)_2$).

IR (ATR): $\tilde{\nu}$ = 3379 (*w*), 3000–2800 (*m*), 2280 (*w*), 1634 (*w*), 1470 (*w*), 1362 (*w*), 1254 (*m*), 1107 (*m*), 1003 (*m*), 941 (*w*), 833 (*s*), 814 (*m*), 775 (*s*), 741 (*w*), 671 (*w*) cm^{-1}.

HRMS (ESI, TOF): m/z calc'd for $C_{10}H_{21}IO_2Si$ $[M+Na]^+$ 351.0248; observed 351.0251.

(*E*)-[(4-Bromo-2-iodobut-2-en-1-yl)oxy](*tert*-butyl)dimethylsilane (15)



14 **15**

To a stirred solution of alcohol **14** (7.93 g, 24.2 mmol, 1.0 equiv.) in anhydrous CH_2Cl_2 (100 mL) at –40 °C was added PPh_3 (9.52 g, 36.3 mmol, 1.5 equiv.). After 10 min NBS (6.03 g, 33.9 mmol, 1.4 equiv.) was added in 6 portions at 3 min intervals. The mixture was stirred at this temperature for 6 h (TLC control, PE/MTBE, 3:1). Anhydrous MeOH (1 mL) was added and stirring was continued for 20 min. The cooling bath was removed, the mixture was diluted with PE (50 mL) and filtered through a plug of silica (d × h = 7 × 5 cm, PE/CH_2Cl_2, 3:1). The filtrate was concentrated and purified by column chromatography (PE/CH_2Cl_2, 15:1, 7 × 15 cm). Allyl bromide **15** (8.48 g, 21.7 mmol, 90%) was obtained as slightly pink oil, which was stored at –25 °C for months without detectable decomposition.

TLC: R_f = 0.38 (PE/CH_2Cl_2, 9:1).

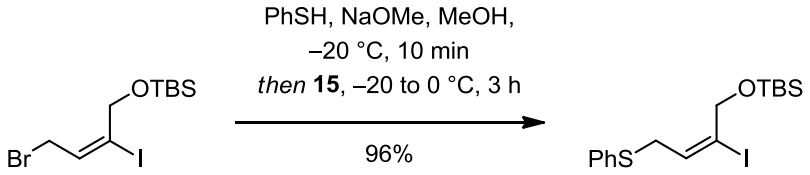
^{1}H NMR (300 MHz, C_6D_6): δ = 6.22 (*tt*, 1H, $^{3,4}J_{H,H}$ = 8.6, 1.2 Hz, =CH), 4.03 (*s*, 2H, CH_2OSi), 3.42 (*d*, 2H, $^3J_{H,H}$ = 8.7 Hz, CH_2Br), 0.93 (*s*, 9H, $SiC(CH_3)_3$), 0.01 (*s*, 6H, $Si(CH_3)_2$).

$^{13}C\{^1H\}$ NMR (75 MHz, C_6D_6): δ = 136.9 (=CH), 109.3 (=CI), 66.2 (CH_2OSi), 27.1 (CH_2Br), 26.0 ($SiC(\underline{C}H_3)_3$), 18.4 ($Si\underline{C}(CH_3)_3$), –5.1 ($Si(CH_3)_2$).

IR (ATR): $\tilde{\nu}$ = 3000–2800 (*m*), 2280 (*w*), 1620 (*w*), 1470 (*w*), 1330 (*w*), 1261 (*m*), 1203 (*w*), 1103 (*m*), 1064 (*w*), 1007 (*w*), 833 (*s*), 813 (*m*), 779 (*m*), 737 (*s*), 706 (*w*) cm^{-1}.

HRMS (ESI, TOF): m/z calc'd for $C_{10}H_{20}BrIOSi$ $[M+Na]^+$ 412.9404; observed 412.9406.

(*E*)-*tert*-Butyl{[2-iodo-4-(phenylthio)but-2-en-1-yl]oxy}dimethylsilane (SI-9)



15 **SI-9**

To a stirred solution of PhSH (1.11 mL, 1.20 g, 10.9 mmol, 1.05 equiv.) in anhydrous MeOH (80 mL) at –20 °C was added a NaOMe solution (2.50 mL, 10.9 mmol, 1.05 equiv., 4.36 M in MeOH). After stirring for 10 min a solution of the allyl bromide **15** (4.06 g, 10.4 mmol, 1.0 equiv.) in anhydrous MeOH (20 mL) was added and the reaction mixture was allowed to warm to 0 °C over 2 h and stirred at 0 °C for another hour (TLC control, PE/CH_2Cl_2, 4:1). After completion of the reaction the cooling bath was removed, pH 7 phosphate buffer (150 mL, 0.5 M) and MTBE (150 mL) were added, and the organic layer was separated. The organic extract was washed with sat. $NaHCO_3$ solution (2 × 50 mL) and brine (100 mL), dried with $MgSO_4$, filtered and concentrated *in vacuo*. Column chromatography of the residue (PE/CH_2Cl_2, 8:1→4:1→2:1, 6 × 15 cm) provided the allyl sulfide **SI-9** (4.18 g, 9.94 mmol, 96%) as a slightly yellow oil.

TLC: R_f = 0.22 (PE/CH_2Cl_2, 8:1).

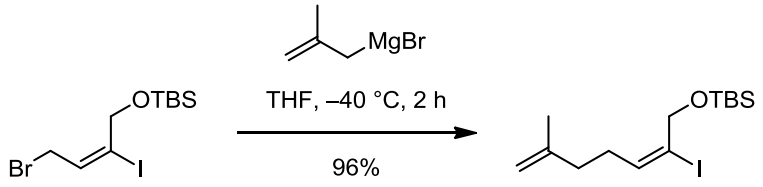
^{1}H NMR (300 MHz, C_6D_6): δ = 7.26–7.21 (*m*, 2H, CH, Ph), 6.99–6.87 (*m*, 3H, CH, Ph), 6.28 (*tt*, 1H, $^{3,4}J_{H,H}$ = 8.1, 1.0 Hz, HC=), 3.81 (*s*, 2H, CH_2O), 3.16 (*d*, 2H, $^3J_{H,H}$ = 8.1 Hz, SCH_2), 0.95 (*s*, 9H, $SiC(CH_3)_3$), 0.02 (*s*, 6H, $Si(CH_3)_2$).

$^{13}C\{^1H\}$ NMR (75 MHz, C_6D_6): δ = 137.1 (SC_{quart}), 135.5 (HC═), 132.0 (CH, Ph), 129.2 (CH, Ph), 127.3 (CH, Ph), 106.5 (═CI), 65.5 (CH_2O), 34.8 (CH_2S), 26.1 ($SiC(\underline{C}H_3)_3$), 18.5 ($Si\underline{C}(CH_3)_3$), –5.0 ($Si(CH_3)_2$).

IR (ATR): $\tilde{\nu}$ = 3902 (*w*), 3855 (*w*), 3749 (*w*), 3650 (*w*), 3567 (*w*), 2928 (*m*), 2855 (*m*), 2362 (*w*), 1745 (*w*), 1622 (*w*), 1579 (*w*), 1469 (*m*), 1363 (*m*), 1254 (*s*), 1169 (*w*), 1098 (*s*), 939 (*w*), 835 (*s*), 749 (*s*), 691 (*m*) cm^{-1}.

HRMS (ESI, Orbitrap): m/z calc'd for $C_{16}H_{25}IOSSi$ $[M–H]^-$ 419.0356; observed 419.0348.

(*E*)-*tert*-Butyl[(2-iodohepta-2,6-dien-1-yl)oxy]dimethylsilane (SI-10)



15 **SI-10**

To a stirred solution of allyl bromide **15** (170 mg, 0.43 mmol, 1.0 equiv.) in anhydrous THF (3.6 mL) at –40 °C was added a solution of methallylmagnesium bromide (0.75 mL, 0.52 mmol, 1.2 equiv, 0.7 M in THF), prepared from methallyl bromide and Mg (3.0 equiv.) in anhydrous THF at 0 °C. After 1.5 h at –40 °C (TLC control, PE/Et_2O, 20:1) the cooling bath was removed, sat. NH_4Cl solution (20 mL) was added and the mixture was extracted with MTBE (20 mL). The organic layer was separated, washed with brine (20 mL), dried with $MgSO_4$, filtered and all volatiles were removed *in vacuo*. Column chromatography of the residue (PE/MTBE, 99:1, 1 × 18 cm) gave the vinyl iodide **SI-10** (148 mg, 0.40 mmol, 94%) as a colorless oil.

TLC: R_f = 0.25 (PE).

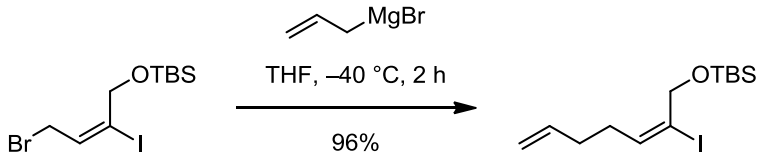
^1H NMR (300 MHz, C_6D_6): δ = 6.17 (*t*, 1H, $^3J_{H,H}$ = 7.5 Hz, ═CH), 4.78–4.68 (*m*, 1H, ═C(H)$\underline{H}$'), 4.70–4.58 (*m*, 1H, ═C($\underline{H}$)H'), 4.14 (*s*, 2H, CH_2OSi), 2.10–1.90 (*m*, 2H, CH_2), 1.85–1.68 (*m*, 2H, CH_2), 1.51 (*s*, 3H, ═C(R)CH_3), 1.00 (*s*, 9H, $SiC(CH_3)_3$), 0.09 (*s*, 6H, $Si(CH_3)_2$).

$^{13}C\{^1H\}$ NMR (75 MHz, C_6D_6): δ = 144.2 (═C_q), 142.1 (═CH), 111.1 (═CH_2), 103.1 (═CI), 65.7 (CH_2OSi), 37.0 (CH_2), 29.5 (CH_2), 26.1 ($SiC(\underline{C}H_3)_3$), 22.3 (CH_3), 18.6 ($Si\underline{C}(CH_3)_3$), –4.9 ($Si(CH_3)_2$).

IR (ATR): $\tilde{\nu}$ = 3300–3000 (*w*), 3000–2800 (*m*), 1651 (*w*), 1632 (*w*), 1462 (*m*), 1369 (*w*), 1253 (*m*), 1107 (*m*), 1080 (*m*), 1006 (*w*), 941 (*w*), 887 (*m*), 833 (*s*), 775 (*s*), 667 (*m*), 613 (*w*) cm^{-1}.

HRMS (ESI, TOF): m/z calc'd for $C_{14}H_{27}IOSi$ $[M+Na]^+$ 389.0768; observed 389.0769.

(*E*)-*tert*-Butyl[(2-iodohepta-2,6-dien-1-yl)oxy]dimethylsilane (SI-11)



15 **SI-11**

To a stirred solution of allyl bromide **15** (3.0 g, 7.67 mmol, 1.0 equiv.) in anhydrous THF (70 mL) at –40 °C was added a solution of allylmagnesium bromide (14.0 mL, 11.5 mmol, 1.5 equiv., 0.82 M in Et_2O), prepared from allyl bromide and Mg (3.0 equiv.) in anhydrous Et_2O at 0 °C. After 2 h at –40 °C (TLC control, PE/Et_2O, 20:1) EtOH (1 mL) was added and the cooling bath was removed. Sat. NH_4Cl solution (100 mL) was added and the mixture was extracted with MTBE (100 mL). The organic layer was separated, washed with brine (100 mL), dried with $MgSO_4$, filtered and all volatiles were removed *in vacuo*. Column chromatography of the residue (PE/CH_2Cl_2, 9:1, 4 × 15 cm) gave the vinyl iodide **SI-11** (2.59 g, 7.35 mmol, 96 %) as a colorless oil.

TLC: R_f = 0.36 (PE/CH_2Cl_2, 8:1),

^{1}H NMR (300 MHz, C_6D_6): δ = 6.14 (*t*, 1H, $^3J_{H,H}$ = 7.4 Hz, HC═CI), 5.62–5.48 (*m*, 1H, HC═), 4.93–4.91 (*m*, 1H, ═C(H)H'), 4.89–4.85 (*m*, 1H, ═C(H)H'), 4.11 (*s*, 2H, CH_2OSi), 1.95–1.85 (*m*, 2H, CH_2), 1.82–1.74 (*m*, 2H, CH_2), 0.99 (*s*, 9H, $SiC(CH_3)_3$), 0.08 (*s*, 6H, $Si(CH_3)_2$).

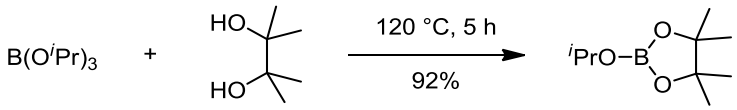
^{13}C{^{1}H} NMR (101 MHz, C_6D_6): δ = 141.8 (HC═), 137.3 (HC═), 115.6 (═CH_2), 103.4 (═CI), 65.7 (CH_2OSi), 33.2 (CH_2), 30.7 (CH_2), 26.1 ($SiC(\underline{C}H_3)_3$), 18.5 ($Si\underline{C}(CH_3)_3$), –4.9 ($Si(CH_3)_2$).

IR (ATR): $\tilde{\nu}$ = 3078 (*w*), 2929 (*m*), 2856 (*m*), 2194 (*w*), 2045 (*w*), 1926 (*w*), 1710 (*w*), 1639 (*w*), 1465 (*m*), 1361 (*m*), 1254 (*s*), 1099 (*s*), 1002 (*s*), 913 (*m*), 835 (*s*), 777 (*s*), 670 (*s*) cm^{-1}.

MS (GC, EI): m/z 295.0 $[M-{}^tBu]^+$.

HRMS: No molecular ion peak detectable (collected HPLC fraction, ionization modes: ESI, APCI, EI).

2-Isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (SI-12)



SI-12

A published procedure was modified in the following way:[S20] Pinacol (10.0 g, 84.2 mmol, 1.0 equiv.) and B(O^{i}Pr)$_3$ (19.4 mL, 15.8 g, 84.2 mmol, 1.0 equiv.) were stirred in a distillation apparatus at 120 °C and 900 mbar for 5 h. After that time the pressure was reduced to 100 mbar over 30 min followed by increasing the heating to 150 °C. After vacuum distillation ^{i}PrOB(pin) (14.4 g, 77.5 mmol, 92%) was obtained as colorless oil, which was stored under anhydrous N_2 atmosphere.

Bp.: 104–106 °C (100 mbar).

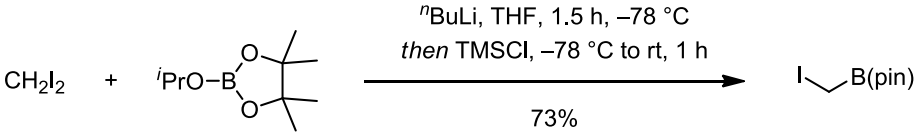
^{1}H NMR (400 MHz, C_6D_6): δ = 4.47 (*sept*, 1H, $^3J_{H,H}$ = 6.2 Hz, $\underline{H}(CH_3)_2$), 1.17 (*d*, 6H, $^3J_{H,H}$ = 6.2 Hz, CH_3), 1.06 (*s*, 12H, CH_3, pin).

^{13}C{^{1}H} NMR (101 MHz, C_6D_6): δ = 82.2 (OC_{quart}), 67.3 ($\underline{C}H(CH_3)_2$), 24.7 (CH_3), 24.6 (CH_3), 24.6 (CH_3).

^{11}B{^{1}H} NMR (128 MHz, C_6D_6): δ = 22.2 (s).

The NMR data matched published data.[S21]

2-(Iodomethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (SI-13)



SI-12 **SI-13**

A published procedure was modified in the following way:[S21] To a stirred solution of CH_2I_2 (5.62 mL, 18.7 g, 69.7 mmol, 1.0 equiv., dehydrated by passing through a plug of activated neutral alumina before usage) and ^{i}PrOB(pin) (**SI-12**, 15.0 mL, 13.0 g, 69.7 mmol, 1.0 equiv.) in anhydrous THF (50 mL) at –78 °C was added a ^{n}BuLi solution (27.9 mL, 69.7 mmol, 1.0 equiv., 2.5 M in hexanes) dropwise over 1 h using a syringe pump. The initially yellow

suspension was stirred for a further 30 min at –78 °C, then TMSCl (8.87 mL, 7.57 g, 69.7 mmol, 1.0 equiv.) was added, the cooling bath was removed and the solution was allowed to reach rt and stirred for an additional hour. Hexane (80 mL) was added and the suspension was filtered through Celite (PE). All volatiles were removed *in vacuo*. The residual oil was rapidly filtered through a plug of silica (d × h = 5 × 4 cm; MTBE/PE, 1:1) and the filtrate was concentrated *in vacuo*. After distillation of the residue (3–4 mbar, bath temperature: 110 °C) the boronate **SI-13** (13.7 g, 51.1 mmol, 73%) was obtained as a colorless oil, which solidifies below –25 °C.

TLC: R_f = 0.33 (PE/MTBE, 9:1).

Bp.: 60–64 °C (3–4 mbar).

^{1}H NMR (400 MHz, C_6D_6): δ = 1.96 (*s*, 2H, CH_2), 1.00 (*s*, 12H, CH_3).

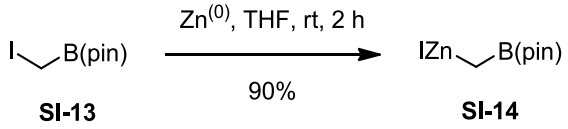
^{13}C{^{1}H} NMR (75 MHz, C_6D_6): δ = 82.0 (C_{quart}), 22.5 (CH_3).

the carbon (CH_2) adjacent to boron was not observed, due to quadrupolar coupling with ^{11}B (I = 3/2) and ^{10}B (I = 3), resulting in very weak signals and fast relaxation.

^{11}B{^{1}H} NMR (128 MHz, C_6D_6): δ = 31.8 (s).

The NMR data matched published data.[S22]

[(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)methyl]zinc(II) iodide [IZnCH$_2$B(pin), SI-14]



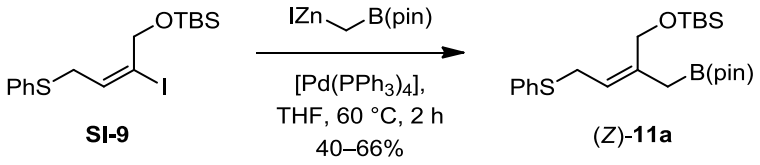
SI-13 **SI-14**

According to Knochel's procedure,[S23] zinc powder (5.17 g, 79.1 mmol, 2.0 equiv.) was suspended in anhydrous THF (30 mL) and anhydrous 1,2-dibromoethane (0.34 mL, 744 mg, 3.96 mmol, 0.1 equiv.) was added under vigorous stirring. The solution was brought to reflux for a minute and then allowed to cool to rt. TMSCl (0.10 mL, 86.0 mg, 0.80 mmol, 0.02 equiv.) was added and the mixture was again refluxed for a minute and cooled to rt. After 15 min a solution of ICH$_2$B(pin) (**SI-13**, 10.6 g, 39.6 mmol, 1.0 equiv.) in anhydrous THF (10 mL) was added over 30 min. The stirring was stopped after additional 2 h and the solids were allowed to settle over 36–48 h at 5 °C. The clear, colorless supernatant containing

SI-14 was titrated against I_2 (1.0 equiv.) in THF to determine its concentration (0.76 M, ~90% yield).

The reagent solution with the settled, excess zinc was stored at 5 °C under nitrogen for 2–3 weeks without noticeable decomposition and decrease in concentration.

(*Z*)-*tert*-Butyldimethyl{{4-(phenylthio)-2-[(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl]but-2-en-1-yl}oxy}silane [(*Z*)-11a]



To a stirred solution of $[Pd(PPh_3)_4]$ (274 mg, 0.24 mmol, 0.1 equiv.) in anhydrous THF (15 mL) at rt was added a solution of alkylzinc reagent **SI-14** (7.60 mL, 4.76 mmol, 2.0 equiv., 0.62 M in THF), followed by a solution of vinyl iodide **SI-9** (1.00 g, 2.38 mmol, 1.0 equiv.) in anhydrous THF (10 mL). The flask was immersed in a preheated 60 °C oil bath and stirred for 3 h (GC–MS control). The oil bath was removed and the mixture was cooled to 0 °C whereupon it was added to a stirred pH 6 phosphate buffer (75 mL, 0.5 M) at 0 °C. The mixture was extracted with MTBE (70 mL) and the extract was washed with brine (70 mL). The organic extract was dried with $MgSO_4$, filtered and the solvent was removed *in vacuo*. Rapid (10 min) column chromatography of the residue (PE/Et_2O, 40:1, 4 × 10 cm) provided the allylboronate (*Z*)-**11a** (680 mg, 1.56 mmol, 66%) as a colorless oil which solidified below –25 °C.

[Note: The allylboronate decomposes on silica gel, therefore prolonged contact (>15 min) should be avoided]

TLC: R_f = 0.26 (PE/CH_2Cl_2, 6:1).

^{1}H NMR (300 MHz, C_6D_6): δ = 7.36–7.27 (*m*, 2H, CH, Ph), 7.07–6.96 (*m*, 2H, CH, Ph), 6.94–6.85 (*m*, 1H, CH, Ph), 5.47 (*t*, 1H, $^3J_{H,H}$ = 7.8 Hz, HC═), 4.27 (*s*, 2H, CH_2O), 3.47 (*d*, 2H, $^3J_{H,H}$ = 7.8 Hz, $PhSCH_2$), 1.98 (*s*, 2H, CH_2B), 1.02 (*s*, 12H, CH_3, pin), 0.96 (*s*, 9H, $SiC(CH_3)_3$), 0.06 (*s*, 6H, $Si(CH_3)_2$).

^{13}C{^{1}H} NMR (75 MHz, C_6D_6): δ = 140.6 (SC_{quart}), 137.8 (R_2C═), 130.1 (CH, Ph), 129.0 (CH, Ph), 126.1 (CH, Ph), 120.7 (HC═), 83.1 ($\underline{C}(CH_3)_2$, pin), 61.9 (CH_2O), 31.9 (CH_2S), 26.2 ($SiC(\underline{C}H_3)_3$), 24.9 (CH_3, pin), 18.6 ($Si\underline{C}(CH_3)_3$), –5.1 ($Si(CH_3)_2$).

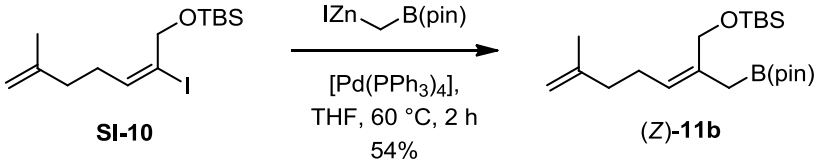
The carbon atom (CH_2) adjacent to boron was concealed, due to quadrupolar coupling with ^{11}B (I = 3/2) and ^{10}B (I = 3).

$^{11}B\{^1H\}$ NMR (128 MHz, C_6D_6): δ = 33.4 (s).

IR (ATR): $\tilde{\nu}$ = 3947 (*w*), 3903 (*w*), 3855 (*w*), 3748 (*w*), 3650 (*w*), 3567 (*w*), 3059 (*w*), 2929 (*w*), 2856 (*w*), 2362 (*w*), 1745 (*w*), 1651 (*w*), 1581 (*w*), 1471 (*w*), 1317 (*m*), 1260 (*m*), 1143 (*m*), 1072 (*m*), 966 (*m*), 835 (*s*), 749 (*s*), 690 (*m*) cm^{-1}.

HRMS (APCI, Orbitrap): m/z calc'd for $C_{23}H_{39}BO_3SSi$ $[M+H]^+$ 435.2555; observed 435.2553.

(*Z*)-*tert*-Butyldimethyl({6-methyl-2-[(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl]hepta-2,6-dien-1-yl}oxy)silane [(*Z*)-11b]



SI-10 (*Z*)-**11b**

Following the procedure described for the synthesis of boronate (*Z*)-**11a** the reaction of vinyl iodide **SI-10** (1.38 g) and $IZnCH_2B(pin)$ (**SI-14**, 14.3 mL, 0.53 M) in the presence of $[Pd(PPh_3)_4]$ (563 mg) in anhydrous THF (50 mL) at 60 °C for 2 h yielded 54% of boronate (*Z*)-**11b** (770 mg) after rapid column chromatography.

[Note: The allylboronate decomposes on silica gel, therefore prolonged contact (>15 min) should be avoided]

TLC: R_f = 0.22 (PE/CH_2Cl_2, 4:1).

^1H NMR (400 MHz, C_6D_6): δ = 5.34 (*t*, 1H, $^3J_{H,H}$ = 7.0 Hz, HC═), 4.79 (*s*, 2H, ═CH_2), 4.46 (*s*, 2H, CH_2O), 2.27–2.19 (*m*, 2H, CH_2), 2.11 (*s*, 2H, CH_2B), 2.05–2.02 (*m*, 2H, CH_2), 1.62 (*s*, 3H, CH_3), 1.07 (*s*, 12H, CH_3, pin), 1.01 (*s*, 9H, $SiC(CH_3)_3$), 0.14 (*s*, 6H, $Si(CH_3)_2$).

$^{13}C\{^1H\}$ NMR (101 MHz, C_6D_6): δ = 145.1 (R_2C═), 136.2 (R_2C═), 124.9 (RC(H)═), 110.2 (═CH_2), 82.5 ($\underline{C}(CH_3)_2$, pin), 61.7 (CH_2O), 38.1 (CH_2), 26.1 (CH_2), 25.8 ($SiC(\underline{C}H_3)_3$), 24.6 (CH_3, pin), 22.2 ($\underline{C}H_3C$═), 18.7 (CH_2B, B-decoupled, from HSQC), 18.6 ($Si\underline{C}(CH_3)_3$), –5.4 ($Si(CH_3)_2$).

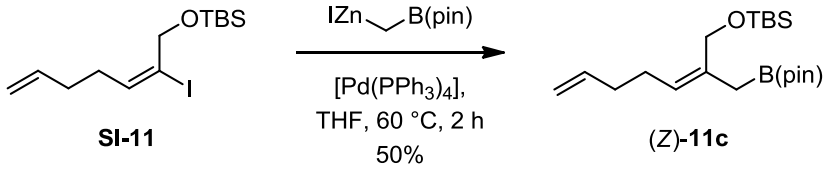
The carbon atom (CH_2) adjacent to boron was concealed, due to quadrupolar coupling with ^{11}B (I = 3/2) and ^{10}B (I = 3).

$^{11}B\{^1H\}$ NMR (128 MHz, C_6D_6): δ = 33.6 (s).

IR (ATR): $\tilde{\nu}$ = 3000–2800 (*m*), 1651 (*w*), 1462 (*w*), 1344 (*m*), 1319 (*m*), 1253 (*m*), 1215 (*w*), 1146 (*s*), 1072 (*m*), 1006 (*w*), 968 (*m*), 883 (*m*), 837 (*s*), 775 (*s*), 671 (*m*) cm^{-1}.

HRMS (ESI, TOF): m/z calc'd for $C_{21}H_{41}BO_3Si$ $[M+Na]^+$ 403.2810; observed 408.2813.

(*Z*)-*tert*-butyldimethyl{{2-[(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl]hepta-2,6-dien-1-yl}oxy}silane [(*Z*)-11c]



SI-11 (*Z*)-**11c**

Following the procedure described for the synthesis of boronate (*Z*)-**11a** the reaction of vinyl iodide **SI-11** (774 mg) and $IZnCH_2B(pin)$ (**SI-14**, 2.95 mL, 0.82 M) in the presence of $[Pd(PPh_3)_4]$ (127 mg, 5 mol-%) in anhydrous THF (11 mL) at 60 °C for 4 h yielded 50% of boronate (*Z*)-**11c** (403 mg) after rapid (10 min) column chromatography (PE/Et_2O, 30:1, 5 × 10 cm).

TLC: R_f = 0.29 ($PE/CH_2Cl_2/Et_2O$, 29:5:1).

^{1}H NMR (400 MHz, C_6D_6): δ = 5.78 (*ddt*, 1H, $^3J_{H,H}$ = 16.7, 10.2, 6.5 Hz, C(H)═), 5.29 (*t*, 1H, $^3J_{H,H}$ = 7.1 Hz, $\underline{H}C{=}C_{quart}$), 5.04–4.93 (*m*, 2H, ═$CH_2$), 4.41 (*s*, 2H, CH_2OSi), 2.18–1.96 (*m*, 6H, 3 × CH_2), 1.06 (*s*, 12H, CH_3, pin), 0.99 (*s*, 9H, $SiC(CH_3)_3$), 0.12 (*s*, 6H, $Si(CH_3)_2$).

^{13}C{^{1}H} NMR (75 MHz, C_6D_6): δ = 138.7 (HC═), 136.9 (R_2C═), 125.0 (R$\underline{C}$(H)═), 114.8 (═CH_2), 82.9 ($\underline{C}(CH_3)_2$, pin), 62.1 (CH_2O), 34.6 (CH_2), 27.6 (CH_2), 26.3 ($SiC(\underline{C}H_3)_3$), 25.0 (CH_3, pin), 18.6 ($Si\underline{C}(CH_3)_3$), –5.0 ($Si(CH_3)_2$).

The carbon atom (CH_2) adjacent to boron was concealed, due to quadrupolar coupling with ^{11}B (I = 3/2) and ^{10}B (I = 3).

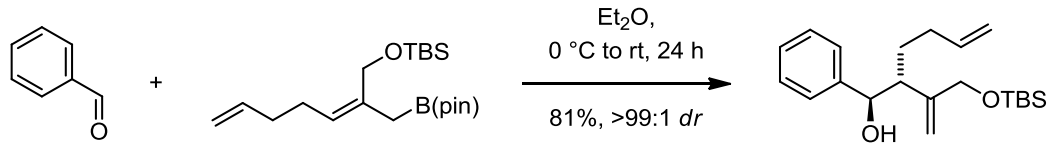
^{11}B{^{1}H} NMR (128 MHz, C_6D_6): δ = 33.5 (s).

IR (ATR): $\tilde{\nu}$ = 2932 (*m*), 2859 (*m*), 2363 (*w*), 1735 (*m*), 1641 (*w*), 1437 (*s*), 1373 (*m*), 1301 (*m*), 1256 (*m*), 1148 (*s*), 952 (*m*), 833 (*s*), 782 (*s*), 674 (*s*) cm^{-1}.

HRMS (ESI, TOF): m/z calc'd for $C_{20}H_{39}BO_3Si$ $[M+Na]^+$ 389.2654; observed 389.2658.

3.2 Preparation of carbonyl compounds and allylboration reactions

(1*R,2*R**)-2-{3-[(*tert*-Butyldimethylsilyl)oxy]prop-1-en-2-yl}-1-phenylhex-5-en-1-ol [(±)-16a]**



(*Z*)-**11c** (±)-**16a**

Freshly distilled benzaldehyde (7.0 µl, 7.3 mg, 68.8 µmol, 1.2 equiv.) was added to a stirred solution of boronate (*Z*)-**11c** (21.0 mg, 57.3 µmol, 1.0 equiv.) in anhydrous Et_2O (0.6 mL) at 0 °C. The solution was allowed to reach rt over 2 h. After 24 h at this temperature (TLC control, PE/Et_2O, 6:1) the complete mixture was directly subjected to column chromatography (PE/Et_2O, 8:1, 1.5 × 20 cm) to obtain the homoallyl alcohol (±)-**16a** (16.1 mg, 46.5 µmol, 81%) as a colorless oil.

TLC: R_f = 0.39 (PE/Et_2O, 6:1).

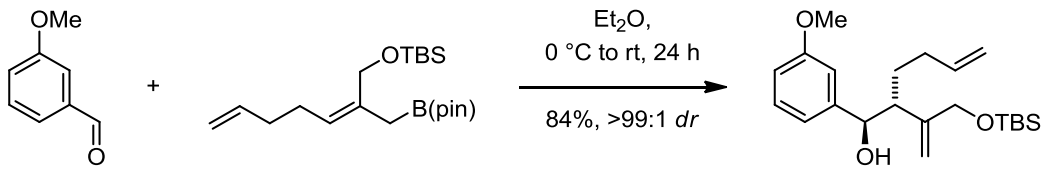
^{1}H NMR (300 MHz, C_6D_6): δ = 7.35–7.30 (*m*, 2H, 2 × CH, Ph), 7.22–7.06 (*m*, 3H, 3 × CH, Ph, overlapped with solvent signal), 5.59 (*ddt*, 1H, $^3J_{H,H}$ = 16.9, 10.2, 6.6 Hz, C(H)═), 5.31 (*d*, 1H, $^2J_{H,H}$ = 1.4 Hz, ═C(H)H'), 4.97–4.87 (*m*, 3H, ═C(H)H' + ═CH_2), 4.53 (*dd*, 1H, $^3J_{H,H}$ = 7.6, 3.7 Hz, C(H)OH), 4.05 (*d*, 1H, $^3J_{H,H}$ = 13.1 Hz, C(H)H'OSi), 3.93 (*d*, 1H, $^3J_{H,H}$ = 13.1 Hz, C(H)H'OSi), 2.75 (*d*, 1H, $^3J_{H,H}$ = 3.7 Hz, OH), 2.45–2.33 (*m*, 1H, C(H)C(R)═CH_2), 2.09–1.91 (*m*, 1H, C(H)H'), 1.91–1.72 (*m*, 1H, C(H)H'), 1.58–1.37 (*m*, 2H, CH_2), 0.98 (*s*, 9H, $SiC(CH_3)_3$), 0.08–0.04 (*m*, 6H, $Si(CH_3)(CH_3)$').

^{13}C{^{1}H} NMR (75 MHz, C_6D_6): δ = 148.1 (C_{quart}, Ph), 144.4 (R_2C═), 138.7 (C(H)═), 128.2 (CH, Ph), 127.6 (CH, Ph), 127.2 (CH, Ph), 114.9 (═CH_2), 114.1 (═CH_2), 77.4 (C(H)OH), 66.3 (CH_2OSi), 51.9 (C(H)C(R)═CH_2), 31.9 (CH_2), 30.4 (CH_2), 26.1 ($SiC(CH_3)_3$), 18.5 ($SiC(CH_3)_3$), –5.3 ($Si(CH_3)(CH_3)$'), –5.3 ($Si(CH_3)(CH_3)$').

IR (ATR): $\tilde{\nu}$ = 3904 (*w*), 3737 (*w*), 3422 (*w*), 3070 (*w*), 2929 (*m*), 2856 (*m*), 1641 (*w*), 1452 (*m*), 1390 (*m*), 1253 (*m*), 1191 (*w*), 1048 (*s*), 908 (*s*), 836 (*s*), 776 (*s*), 700 (*s*) cm^{-1}.

HRMS (ESI, TOF): m/z calc'd for $C_{21}H_{34}O_2Si$ $[M+Na]^+$ 369.2220; observed 369.2222.

(1*R,2*R**)-2-{3-[(*tert*-Butyldimethylsilyl)oxy]prop-1-en-2-yl}-1-(3-methoxyphenyl)hex-5-en-1-ol [(±)-16b]**



(*Z*)-**11c** (±)-**16b**

m-Anisaldehyde (6.8 µl, 7.62 mg, 56.0 µmol, 1.2 equiv.) was added to a stirred solution of boronate (*Z*)-**11c** (17.1 mg, 46.7 µmol, 1.0 equiv.) in anhydrous Et_2O (0.6 mL) at 0 °C. The solution was allowed to reach rt over 2 h. After 24 h at this temperature (TLC control, PE/Et_2O, 5:1) the complete mixture was directly subjected to column chromatography (PE/Et_2O, 7:1, 1.5 × 20 cm) to obtain the homoallyl alcohol (±)-**16b** (14.7 mg, 39.0 µmol, 84%) as a colorless oil.

TLC: R_f = 0.34 (PE/Et_2O, 7:1).

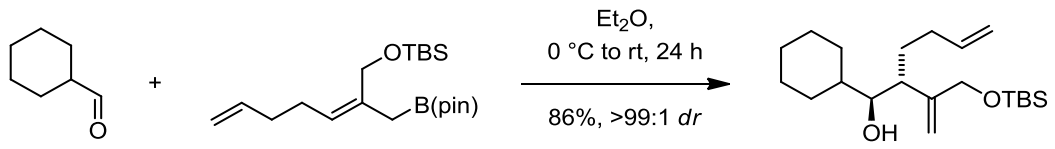
^{1}H NMR (300 MHz, C_6D_6): δ = 7.14–7.10 (*m*, 2H, CH, Ar), 6.95 (*d*, 1H, $^3J_{H,H}$ = 7.6 Hz, CH, Ar), 6.73 (*dd*, 1H, $^{3,4}J_{H,H}$ = 8.1, 2.5 Hz, CH, Ar), 5.61 (*ddt*, 1H, $^3J_{H,H}$ = 16.9, 10.2, 6.6 Hz, C(H)═), 5.31 (*d*, 1H, $^2J_{H,H}$ = 1.1 Hz, ═C(H)H'), 4.99–4.86 (*m*, 3H, ═C(H)H' + ═CH_2), 4.55 (*dd*, 1H, $^3J_{H,H}$ = 7.5, 3.5 Hz, C(H)OH), 4.06 (*d*, 1H, $^3J_{H,H}$ = 13.1 Hz, C(H)H'OSi), 3.94 (*d*, 1H, $^3J_{H,H}$ = 13.1 Hz, C(H)H'OSi), 3.37 (*s*, 3H, OCH_3), 2.78 (*d*, 1H, $^3J_{H,H}$ = 3.7 Hz, OH), 2.48–2.40 (*m*, 1H, C(H)C(R)═CH_2), 2.08–1.94 (*m*, 1H, C(H)H'), 1.89–1.76 (*m*, 1H, C(H)H'), 1.55–1.45 (*m*, 2H, CH_2), 0.98 (*s*, 9H, $SiC(CH_3)_3$), 0.07–0.05 (*m*, 6H, $Si(CH_3)(CH_3)$').

^{13}C{^{1}H} NMR (75 MHz, C_6D_6): δ = 160.3 (COMe, Ar), 148.2 (C_{quart}, Ar), 146.1 (R_2C═), 138.7 (C(H)═), 129.3 (CH, Ar), 119.6 (CH, Ar), 114.9 (═CH_2), 114.0 (═CH_2), 113.0 (CH, Ar), 113.0 (CH, Ar), 77.4 (C(H)OH), 66.4 (CH_2OSi), 54.7 ($COCH_3$, Ar), 51.7 (C(H)C(R)═CH_2), 31.9 (CH_2), 30.5 (CH_2), 26.1 ($SiC(CH_3)_3$), 18.5 ($SiC(CH_3)_3$), –5.3 ($Si(CH_3)(CH_3)$'), –5.3 ($Si(CH_3)(CH_3)$').

IR (ATR): $\tilde{\nu}$ = 3437 (*w*), 3075 (*w*), 2930 (*m*), 2857 (*m*), 2358 (*w*), 1600 (*m*), 1461 (*m*), 1254 (*s*), 1043 (*s*), 908 (*m*), 836 (*s*), 775 (*s*), 699 (*m*) cm^{-1}.

HRMS (ESI, TOF): m/z calc'd for $C_{22}H_{36}O_3Si$ $[M+Na]^+$ 399.2326; observed 399.2326.

(1*S,2*R**)-2-{3-[(*tert*-Butyldimethylsilyl)oxy]prop-1-en-2-yl}-1-cyclohexylhex-5-en-1-ol [(±)-16c]**



(*Z*)-**11c** (±)-**16c**

Freshly distilled cyclohexanecarboxaldehyde (7.61 µl, 7.05 mg, 62.9 µmol, 1.2 equiv.) was added to a stirred solution of boronate (*Z*)-**11c** (19.2 mg, 52.4 µmol, 1.0 equiv.) in anhydrous Et_2O (0.6 mL) at 0 °C. The solution was allowed to reach rt over 2 h. After 24 h at this temperature (TLC control, PE/Et_2O, 20:1) the complete mixture was directly subjected to column chromatography (PE/Et_2O, 20:1, 1.5 × 20 cm) to obtain the homoallyl alcohol (±)-**16c** (15.9 mg, 45.1 µmol, 86%) as a colorless oil.

TLC: R_f = 0.32 (PE/Et_2O, 20:1).

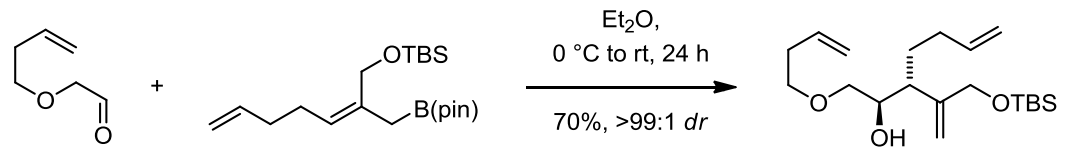
^{1}H NMR (300 MHz, C_6D_6): δ = 5.78 (*ddt*, 1H, $^3J_{H,H}$ = 17.0, 10.2, 6.6 Hz, C(H)═), 5.25 (*d*, 1H, $^2J_{H,H}$ = 1.5 Hz, ═C(H)H'), 5.10–4.92 (*m*, 3H, ═C(H)H' + ═CH_2), 4.15 (*d*, 1H, $^3J_{H,H}$ = 13.0 Hz, C(H)H'OSi), 3.98 (*d*, 1H, $^3J_{H,H}$ = 13.0 Hz, C(H)H'OSi), 3.27 (*dd*, 1H, $^3J_{H,H}$ = 6.2, 6.0 Hz, C(H)OH), 2.46–2.35 (*m*, 1H, OH), 2.14–1.88 (*m*, 3H, C(H)C(R)═CH_2 + CH_2), 1.83–1.14 (*m*, 13H, 6 × CH_2 + R_2CH), 0.96 (*s*, 9H, $SiC(CH_3)_3$), 0.07–0.03 (*m*, 6H, $Si(CH_3)(CH_3)$').

^{13}C{^{1}H} NMR (75 MHz, C_6D_6): δ = 148.6 (R_2C═), 139.0 (C(H)═), 115.1 (═CH_2), 114.9 (═CH_2), 77.8 (C(H)OH), 65.6 (CH_2OSi), 47.1 (C(H)C(R)═CH_2), 41.3 (CH), 32.1 (CH_2), 30.9 (CH_2), 30.4 (CH_2), 27.5 (CH_2), 27.1 (CH_2), 26.9 (CH_2), 26.7 (CH_2), 26.1 ($SiC(CH_3)_3$), 18.5 ($SiC(CH_3)_3$), –5.3 ($Si(CH_3)(CH_3)$'), –5.3 ($Si(CH_3)(CH_3)$').

IR (ATR): $\tilde{\nu}$ = 3442 (*w*), 3076 (*w*), 2926 (*s*), 2855 (*m*), 2712 (*w*), 2543 (*w*), 2361 (*w*), 1641 (*w*), 1450 (*w*), 1392 (*w*), 1254 (*m*), 1186 (*w*), 1050 (*m*), 908 (*m*), 836 (*s*), 775 (*s*), 667 (*m*) cm^{-1}.

HRMS (ESI, TOF): m/z calc'd for $C_{21}H_{40}O_2Si$ $[M+Na]^+$ 375.2690; observed 375.2694.

(2*R,3*R**)-1-(But-3-en-1-yloxy)-3-{3-[(*tert*-butyldimethylsilyl)oxy]prop-1-en-2-yl}hept-6-en-2-ol [(±)-16d]**



SI-1 (*Z*)-**11c** (±)-**16d**

Homoallyloxy acetaldehyde **SI-1** (90.2 mg, 0.79 mmol, 1.84 equiv., used as a 2:1 molar mixture with CH_2Cl_2) was added to a stirred solution of boronate (*Z*)-**11c** (160 mg, 0.43 mmol, 1.0 equiv.) in anhydrous Et_2O (3.0 mL) at 0 °C. The solution was allowed to reach rt over 6 h. After 24 h at this temperature (TLC control, PE/Et_2O, 7:1) the complete mixture was directly subjected to column chromatography (PE/Et_2O, 7:1, 3 × 15 cm) to obtain the homoallyl alcohol (±)-**16d** (105 mg, 0.30 mmol, 70%) as a colorless oil.

TLC: R_f = 0.27 (PE/Et_2O, 7:1).

^{1}H NMR (300 MHz, C_6D_6): δ = 5.87–5.66 (*m*, 2H, 2 × C(H)═), 5.37 (*s*, 1H, ═C(H)H'), 5.09–4.96 (*m*, 5H, 2 × ═CH_2 + ═C(H)H'), 4.25 (*d*, 1H, $^3J_{H,H}$ = 13.9 Hz, C(H)H'OSi), 4.10 (*d*, 1H, $^3J_{H,H}$ = 13.9 Hz, C(H)H'OSi), 3.84–3.73 (*m*, 1H, $OCH_2C(H)OH$), 3.38–3.19 (*m*, 4H, CH_2OCH_2), 2.72 (*d*, 1H, $^3J_{H,H}$ = 4.7 Hz, OH), 2.38–2.29 (*m*, 1H, C(H)C(R)═CH_2), 2.25–1.90 (*m*, 4H, 2 × CH_2), 1.72–1.59 (*m*, 2H, CH_2), 0.98 (*s*, 9H, $SiC(CH_3)_3$), 0.08 (*s*, 6H, $Si(CH_3)_2$).

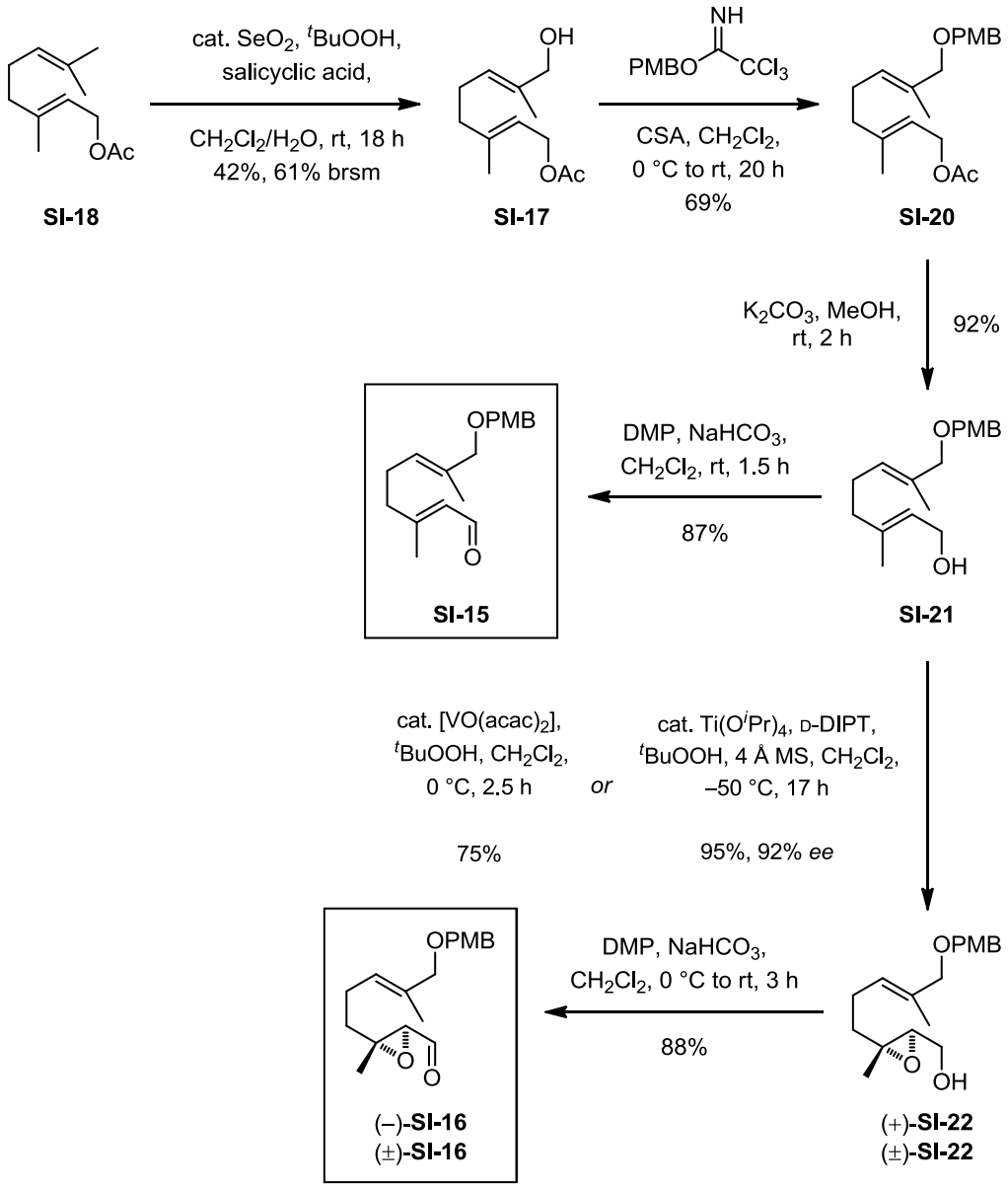
^{13}C{^{1}H} NMR (75 MHz, C_6D_6): δ = 148.1 (R_2C═), 139.0 (C(H)═), 135.7 (C(H)═), 116.4 (═CH_2), 114.8 (═CH_2), 113.4 (═CH_2), 74.0 ($OCH_2C(H)OH$), 72.5 ($OCH_2C(H)OH$), 70.7 (CH_2OCH_2), 65.5 (CH_2OSi), 46.5 (C(H)C(R)═CH_2), 34.6 (CH_2), 32.0 (CH_2), 29.8 (CH_2), 26.1 ($SiC(CH_3)_3$), 18.6 ($SiC(CH_3)_3$), –5.2 ($Si(CH_3)(CH_3)$'), –5.3 ($Si(CH_3)(CH_3)$').

IR (ATR): $\tilde{\nu}$ = 3903 (*w*), 3854 (*w*), 3737 (*w*), 3568 (*w*), 3422 (*w*), 3078 (*w*), 2930 (*m*), 2859 (*m*), 2361 (*w*), 1641 (*w*), 1461 (*w*), 1362 (*w*), 1254 (*m*), 1103 (*s*), 994 (*m*), 907 (*s*), 836 (*s*), 774 (*s*), 668 (*m*) cm^{-1}.

HRMS (ESI, TOF): m/z calc'd for $C_{20}H_{38}O_3Si$ $[M+Na]^+$ 377.2482; observed 377.2482.

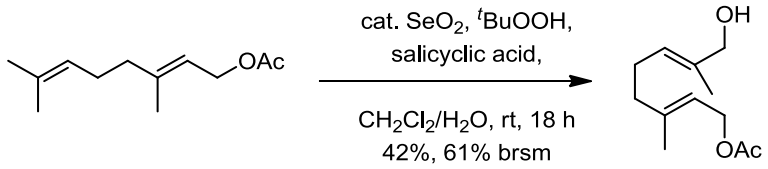
Synthesis scheme for the *α,β*-unsaturated aldehyde SI-15 and *α,β*-epoxy aldehydes (–)-/(±)-SI-16.

Experimental conditions see below scheme.



Scheme S2. Synthesis of *α*,*β*-unsaturated aldehyde **SI-15** and *α*,*β*-epoxy aldehydes (–)-/(±)-**SI-16**.

(2*E*,6*E*)-8-Hydroxy-3,7-dimethylocta-2,6-dien-1-yl acetate (SI-17)



SI-18 **SI-17**

Salicylic acid (544 mg, 3.94 mmol, 0.1 equiv.), SeO_2 (131 mg, 1.18 mmol, 0.03 equiv.) and ^{t}BuOOH (13.5 mL, 98.5 mmol, 2.5 equiv, ~70*w*-% in water) were dissolved in CH_2Cl_2 (50 mL) open to air and stirred for 15 min. Then geranyl acetate[S24] (**SI-18**, 7.74 g, 39.4 mmol, 1.0 equiv.) was added as a solution in CH_2Cl_2 (50 mL). After 18 h (TLC control, PE/acetone, 6:1) the solution was washed with a 1.0 M NaOH solution (4 × 30 mL) and brine (50 mL). The organic extract was dried with $MgSO_4$, filtered and concentrated *in vacuo*. Column chromatography of the residue (PE/acetone, 6:1→2:1, 7 × 25 cm) gave in order of elution remaining starting material (2.32 g, 11.8 mmol, 30%) and the allyl alcohol **SI-17** (3.54 g, 16.7 mmol, 42%, 61% brsm), both as colorless oils.

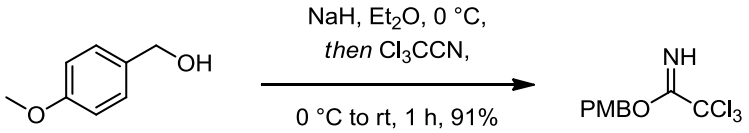
TLC: R_f = 0.24 (PE/acetone, 6:1).

^{1}H NMR (300 MHz, C_6D_6): δ = 5.51–5.44 (*m*, 1H, C(H)═), 5.41–5.34 (*m*, 1H, C(H)═), 4.67 (*d*, 2H, $^3J_{H,H}$ = 7.1 Hz, CH_2OAc), 3.92 (*s*, 2H, ═C(CH_2)OH), 2.18–2.09 (*m*, 2H, CH_2), 2.06–1.98 (*m*, 2H, CH_2), 1.80 (*s*, 3H, OC(O)CH_3), 1.62 (*s*, 3H, CH_3), 1.59 (*s*, 3H, CH_3), 1.42 (*br s*, 1H, OH).

^{13}C{^{1}H} NMR (75 MHz, C_6D_6): δ = 170.4 (O<u>C</u>(O)CH_3), 141.3 (R_2C═), 135.9 (R_2C═), 124.6 (HC═), 119.7 (HC═), 68.7 (CH_2OH), 61.3 (CH_2OAc), 39.4 (CH_2), 25.9 (CH_2), 20.6 (OC(O)<u>C</u>H_3), 16.3 (CH_3), 13.7 (CH_3).

The NMR data matched published data.[S25]

4-Methoxybenzyl 2,2,2-trichloroacetimidate (SI-19)



SI-19

A published procedure was modified in the following way:[S26] NaH (1.20 g, 30.0 mmol, 0.14 equiv., 60*w*-% in mineral oil) was suspended in anhydrous Et_2O (200 mL) at 0 °C under stirring. After 10 min *p*-methoxybenzyl alcohol (27.0 mL, 30.0 g, 217 mmol, 1.0 equiv.) was added and stirring was continued for 15 min. Then trichloroacetonitrile (24.0 mL, 34.5 g, 239 mmol, 1.1 equiv.) was added dropwise over 30 min using a syringe pump (0.8 mL/min). The solution was allowed to warm to rt over 1 h and kept at rt for additional 30 min. All volatiles were removed *in vacuo* and the residual oil was taken up in *n*-hexane (25 mL). MeOH (1.40 mL, 32.6 mmol, 0.15 equiv.) was added and the mixture was stirred vigorously for 15 min, followed by filtration of the suspension through Celite (*n*-hexane). The filtrate was concentrated *in vacuo* and purified by column chromatography (PE/EtOAc, 9:1 + 2% Me_2NEt, 9 × 15 cm) to obtain the PMB trichloroacetimidate **SI-19** (55.6 g, 197 mmol, 91%) as a slightly yellow oil, which solidified below –25 °C.

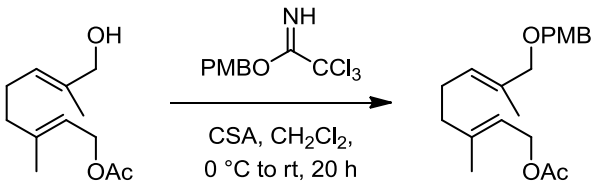
TLC: R_f = 0.41 (PE/EtOAc, 4:1)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.37 (*br s*, 1H, NH), 7.42–7.33 (*m*, 2H, CH, Ar), 6.97–6.84 (*m*, 2H, CH, Ar), 5.28 (*s*, 2H, CH_2O), 3.82 (*s*, 3H, OCH_3).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ = 162.7 (C═NH), 159.8 ($\underline{C}OCH_3$), 129.8 (CH, Ar), 127.6 ($OCH_2\underline{C}$, Ar), 114.0 (CH, Ar), 91.6 (CCl_3), 70.8 (CH_2O), 55.4 (CH_3).

The NMR data matched published data.[S26]

(2*E*,6*E*)-8-[(4-Methoxybenzyl)oxy]-3,7-dimethylocta-2,6-dien-1-yl acetate (SI-20)



SI-17 **SI-20**

To a stirred solution of allyl alcohol **SI-17** (3.32 g, 15.6 mmol, 1.0 equiv.) in anhydrous CH_2Cl_2 (60 mL) at 0 °C was added PMB trichloroacetimidate (5.30 g, 18.8 mmol, 1.2 equiv.), followed by (+)-CSA (725 mg, 3.12 mmol, 0.2 equiv.). The solution was stirred at 0 °C for 1 h and then allowed to warm to rt. After 19 h (TLC control, PE/acetone, 6:1) the brown suspension was filtered. The filtrate was washed with sat. $NaHCO_3$ solution (60 mL) and brine (60 mL), dried with $MgSO_4$, filtered and the solvent was removed *in vacuo*. Column

chromatography of the residue (PE/MTBE, 4:1, 7 × 20 cm) provided the PMB ether **SI-20** (3.58 g, 10.8 mmol, 69%) as a slightly yellow oil.

TLC: R_f = 0.34 (PE/MTBE, 4:1).

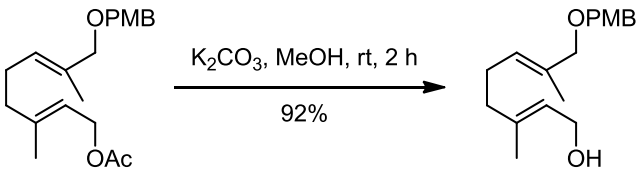
^{1}H NMR (300 MHz, C_6D_6): δ = 7.30–7.23 (*m*, 2H, CH, Ar), 6.85–6.79 (*m*, 2H, CH, Ar), 5.44–5.34 (*m*, 2H, 2 × C(H)═), 4.59 (*d*, 2H, $^3J_{H,H}$ = 6.7 Hz, CH_2OAc), 4.35 (*s*, 2H, OCH_2Ar), 3.84 (*s*, 2H, ═$C(CH_2)O$), 3.32 (*s*, 3H, OCH_3), 2.12–2.01 (*m*, 2H, CH_2), 1.96–1.90 (*m*, 2H, CH_2), 1.69 (s, 3H, $OC(O)CH_3$), 1.63 (*s*, 3H, CH_3), 1.49 (*s*, 3H, CH_3).

^{13}C{^{1}H} NMR (75 MHz, C_6D_6): δ = 170.1 ($OC(O)CH_3$), 159.7 ($COCH_3$, Ar), 141.3 (R_2C═), 133.2 (R_2C═), 131.4 (OCH_2C, Ar), 129.4 (CH, Ar), 127.0 (HC═), 119.7 (HC═), 114.1 (CH, Ar), 75.9 (CH_2OR), 71.4 (CH_2OR), 61.2 (CH_2OAc), 54.8 (OCH_3), 39.4 (CH_2), 26.1 (CH_2), 20.6 ($OC(O)CH_3$), 16.3 (CH_3), 14.0 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2913 (*w*), 2841 (*w*), 2361 (*m*), 2060 (*w*), 1869 (*w*), 1735 (*m*), 1612 (*m*), 1512 (*m*), 1442 (*m*), 1364 (*m*), 1231 (*s*), 1031 (*s*), 952 (*m*), 819 (*s*), 751 (*s*), 607 (*m*) cm^{-1}.

HRMS (ESI, TOF): m/z calc'd for $C_{20}H_{28}O_4$ $[M+Na]^+$ 355.1880; observed 355.1878.

(2*E*,6*E*)-8-[(4-Methoxybenzyl)oxy]-3,7-dimethylocta-2,6-dien-1-ol (SI-21)



SI-20 **SI-21**

To a stirred solution of acetate **SI-20** (3.48 g, 10.5 mmol, 1.0 equiv.) in anhydrous MeOH (40 mL) at rt was added K_2CO_3 (2.90 g, 21.0 mmol, 2.0 equiv.). After 2 h (TLC control, PE/MTBE, 1:1) the suspension was cooled to 0 °C, a NaCl saturated 1.0 M HCl solution (45 mL) was added and after 10 min the mixture was extracted with EtOAc (80 mL). The organic layer was separated and washed with brine (80 mL). The organic extract was dried with $MgSO_4$, filtered and concentrated *in vacuo*. Column chromatography of the residue (PE/MTBE, 1:1, 7 × 12 cm) provided the alcohol **SI-21** (2.82 g, 9.71 mmol, 92%) as a colorless oil.

TLC: R_f = 0.44 (PE/MTBE, 1:1).

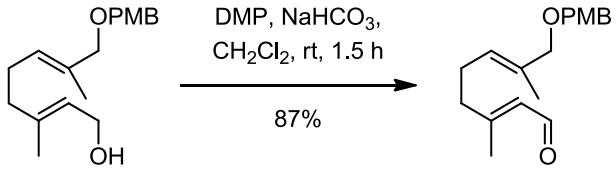
^{1}H NMR (300 MHz, C_6D_6): δ = 7.32–7.22 (*m*, 2H, CH, Ar), 6.86–6.78 (*m*, 2H, CH, Ar), 5.46–5.37 (*m*, 2H, 2 × C(H)═), 4.35 (*s*, 2H, OCH_2Ar), 4.02 (*d*, 2H, $^3J_{H,H}$ = 6.7 Hz, C<u>H</u>$_2$OH), 3.84 (*s*, 2H, ═C(CH_2)O), 3.32 (*s*, 3H, OCH_3), 2.15–2.06 (*m*, 2H, CH_2), 2.01–1.93 (*m*, 2H, CH_2), 1.66 (*s*, 3H, CH_3), 1.47 (*s*, 3H, CH_3), 1.34 (*s*, 1H, OH).

^{13}C{^{1}H} NMR (75 MHz, C_6D_6): δ = 159.7 (<u>C</u>OCH_3), 137.5 (R_2C═), 133.1 (R_2C═), 131.4 (OCH_2<u>C</u>, Ar), 129.5 (CH, Ar), 127.4 (HC═), 125.4 (HC═), 114.1 (CH, Ar), 76.0 (CH_2O), 71.5 (CH_2O), 59.3 (CH_2O), 54.8 (OCH_3), 39.4 (CH_2), 26.3 (CH_2), 16.1 (CH_3), 14.1 (CH_3).

IR (ATR): $\tilde{\nu}$ = 3736 (*w*), 3393 (*w*), 2914 (*m*), 2851 (*m*), 2361 (*m*), 2137 (*w*), 1944 (*w*), 1869 (*w*), 1669 (*w*), 1612 (*m*), 1512 (*s*), 1457 (*m*), 1361 (*m*), 1302 (*m*), 1245 (*s*), 1173 (*m*), 1032 (*s*), 819 (*s*), 751 (*s*), 616 (*m*) cm^{-1}.

HRMS (ESI, TOF): m/z calc'd for $C_{18}H_{26}O_3$ $[M+Na]^+$ 313.1774; observed 313.1775.

(2*E*,6*E*)-8-[(4-Methoxybenzyl)oxy]-3,7-dimethylocta-2,6-dienal (SI-15)



SI-21 **SI-15**

To a stirred solution of allyl alcohol **SI-21** (200 mg, 0.69 mmol, 1.0 equiv.) and $NaHCO_3$ (290 mg, 3.45 mmol, 5.0 equiv.) in anhydrous CH_2Cl_2 (7.0 mL) at rt was added DMP (352 mg, 0.83 mmol, 1.2 equiv.) in one portion. After 1.5 h (TLC control, MTBE/PE, 2:1) the suspension was poured into a mixture of sat. $NaHCO_3$ (10 mL) and sat. Na_2SO_3 (10 mL) and stirred for 30 min. The organic layer was separated, washed with sat. $NaHCO_3$ (20 mL) and brine (20 mL), dried with $MgSO_4$, filtered and concentrated *in vacuo*. Column chromatography of the residue (PE/MTBE, 3:1→2:1, 2.5 × 30 cm) provided the *α,β*-unsaturated aldehyde **SI-15** (174 mg, 0.60 mmol, 87%) as a colorless oil.

TLC: R_f = 0.34 (PE/MTBE, 2:1)

^{1}H NMR (300 MHz, C_6D_6): δ = 9.86 (*d*, 1H, $^3J_{H,H}$ = 7.7 Hz, CHO), 7.33–7.24 (*m*, 2H, CH, Ar), 6.88–6.80 (*m*, 2H, CH, Ar), 5.81 (*dq*, 1H, $^{3,4}J_{H,H}$ = 7.7, 2.4, 1.2 Hz, ═C(<u>H</u>)CHO), 5.30–5.20 (*m*, 1H, C(H)═), 4.34 (*s*, 2H, CH_2O), 3.79 (*s*, 2H, CH_2O), 3.32 (*s*, 3H, OCH_3), 1.90 (*dt*,

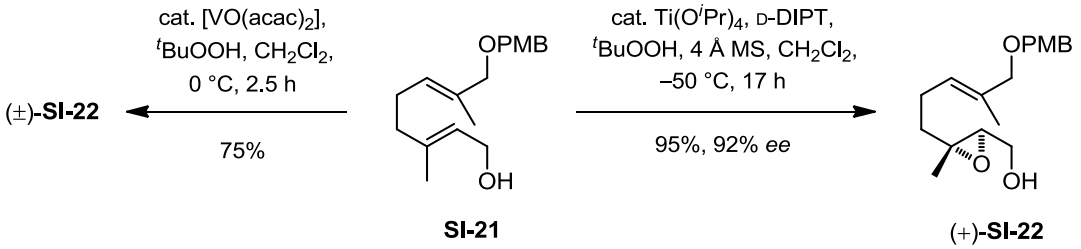
2H, $^{3}J_{H,H}$ = 7.7, 7.2 Hz, C$\underline{H}_2$C(H)═), 1.78–1.70 (*m*, 2H, CH_2), 1.56 (*s*, 3H, CH_3), 1.50 (*d*, 3H, $^{4}J_{H,H}$ = 1.2 Hz, CH_3).

^{13}C{^{1}H} NMR (75 MHz, C_6D_6): δ = 189.8 (CHO), 161.2 (C_{quart}), 159.8 (C_{quart}), 131.3 ($OCH_2\underline{C}$, Ar), 129.4 (CH, Ar), 125.6 (HC═), 114.2 (CH, Ar), 75.6 (CH_2O), 71.6 (CH_2O), 54.8 (OCH_3), 40.0 (CH_2), 25.4 (CH_2), 16.9 (CH_3), 14.0 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2914 (*m*), 2849 (*m*), 2342 (*w*), 2109 (*w*), 2008 (*w*), 1669 (*s*), 1612 (*m*), 1512 (*s*), 443 (*m*), 1380 (*m*), 1303 (*m*), 1245 (*s*), 1176 (*m*), 1033 (*s*), 818 (*s*), 614 (*m*) cm^{-1}.

HRMS (ESI, TOF): m/z calc'd for $C_{18}H_{24}O_3$ $[M+Na]^+$ 311.1618; observed 311.1619.

{(2*R*,3*R*)-3-{(*E*)-5-[(4-Methoxybenzyl)oxy]-4-methylpent-3-en-1-yl}-3-methyloxiran-2-yl}methanol [(+)-SI-22 and (±)-SI-22]



Racemic conditions:

To a stirred solution of allyl alcohol **SI-21** (4.00 g, 13.8 mmol, 1.0 equiv.) in anhydrous CH_2Cl_2 (100 mL) at 0 °C was added $[VO(acac)_2]$ (729 mg, 2.75 mmol, 0.2 equiv.), followed by an anhydrous ^{t}BuOOH solution (3.32 mL, 16.6 mmol, 1.2 equiv., 5.0 M in decane with 4 Å molecular sieves). The deep red solution was stirred at 0 °C for 2.5 h (TLC control, MTBE/PE, 2:1) after which a 1:1 mixture of sat. Na_2SO_3 solution and sat. $NaHCO_3$ solution (50 mL) was added. The cooling bath was removed and the mixture was stirred for 30 min until the color changed to light green. The organic layer was separated, washed with sat. $NaHCO_3$ solution (100 mL), brine (100 mL), dried with $MgSO_4$, filtered and concentrated *in vacuo*. Column chromatography of the residue (MTBE/PE, 1:1→2:1, 6 × 15 cm) provided the epoxy alcohol (±)-**SI-22** (3.18 g, 10.4 mmol, 75%) as a colorless oil.

*Enantioselective conditions for (2R,3R)-(+)-**SI-22**:*

Freshly activated powdered 4 Å molecular sieves (1.60 g) were suspended in anhydrous (MeOH-free) CH_2Cl_2 (40 mL) with stirring. D-(–)-DIPT (0.41 mL, 464 mg, 1.98 mmol, 0.25 equiv.) was added and the mixture was stirred for 20 min after which it was cooled to –20 °C. $Ti(O^{i}Pr)_4$ (0.47 mL, 449 mg, 1.58 mmol, 0.20 equiv.) was added and stirring was

continued for 15 min. Anhydrous ^{t}BuOOH solution (3.16 mL, 15.8 mmol, 2.0 equiv., 5.0 M in decane with 4 Å molecular sieves) was added and after additional 30 min the mixture was cooled to –50 °C. Then allyl alcohol **SI-21** (2.30 g, 7.92 mmol, 1.0 equiv.) was added as a solution in anhydrous CH_2Cl_2 (10 mL). After 17 h at this temperature (TLC control, MTBE/PE, 2:1) the cooling bath was removed and the mixture was filtered through a plug of silica (d × h = 5 × 4 cm, Et_2O). The filtrate was washed with a 1:1 mixture of sat. Na_2SO_3 solution and sat. $NaHCO_3$ solution (80 mL), followed by brine (80 mL), dried with $MgSO_4$, filtered and concentrated *in vacuo*. Column chromatography of the residue (MTBE/PE, 1:1→2:1, 4 × 20 cm) gave the enantioenriched epoxy alcohol (+)-**SI-22** (2.31 g, 7.54 mmol, 95%) as a colorless oil (92% *ee*, chiral HPLC see below).

TLC: R_f = 0.43 (MTBE/PE, 2:1).

$[\alpha]_D^{25}$ = +4.64 (*c* = 1.0, THF, 92% *ee*).

^{1}H NMR (300 MHz, C_6D_6): δ = 7.30–7.24 (*m*, 2H, CH, Ar), 6.85–6.79 (*m*, 2H, CH, Ar), 5.37 (*t*, 1H, $^{3}J_{H,H}$ = 7.2 Hz, C(H)═), 4.35 (*s*, 2H, CH_2O), 3.80 (*s*, 2H, CH_2O), 3.55–3.49 (*m*, 2H, CH_2O), 3.31 (*s*, 3H, OCH_3), 2.83 (*t*, 1H, $^{3}J_{H,H}$ = 5.5 Hz, C(O)CH, epoxide), 2.03 (*dt*, 2H, $^{3}J_{H,H}$ = 7.5, 7.5 Hz, CH_2), 1.87 (*br s*, 1H, OH), 1.62 (*s*, 3H, CH_3), 1.60–1.51 (*m*, 1H, C(H)H'), 1.36 (*dt*, 1H, $^{2,3}J_{H,H}$ = 13.7, 8.2 Hz, C(H)H'), 1.06 (*s*, 3H, CH_3).

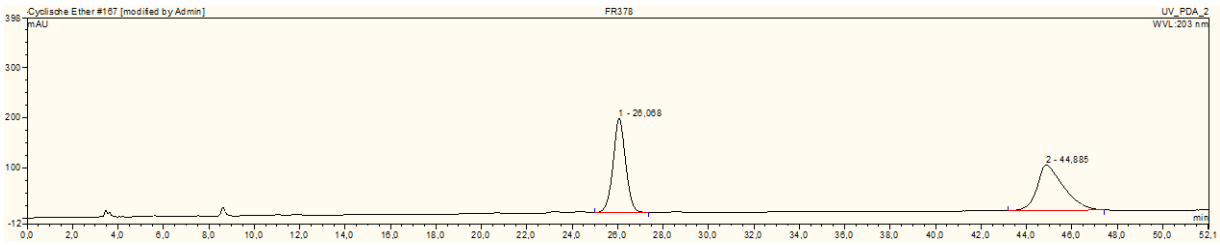
^{13}C{^{1}H} NMR (75 MHz, C_6D_6): δ = 159.8 ($\underline{C}OCH_3$), 133.2 (R_2C═), 131.2 ($OCH_2\underline{C}$, Ar), 129.6 (CH, Ar), 127.0 (HC═), 114.1 (CH, Ar), 75.9 (CH_2O), 71.7 (CH_2O), 63.0 (C(O)CH, epoxide), 61.4 (C(O)CH, epoxide), 60.2 (CH_2O), 54.8 (OCH_3), 38.4 (CH_2), 23.7 (CH_2), 16.7 (CH_3), 14.1 (CH_3).

IR (ATR): $\tilde{\nu}$ = 3738 (*w*), 3649 (*w*), 3420 (*w*), 2918 (*m*), 2853 (*m*), 2361 (*m*), 1611 (*m*), 1512 (*m*), 1456 (*m*), 1383 (*m*), 1245 (*s*), 1174 (*m*), 1031 (*s*), 818 (*s*), 751 (*s*), 686 (*m*), 614 (*m*) cm^{-1}.

HRMS (ESI, TOF): m/z calc'd for $C_{18}H_{26}O_4$ $[M+H]^+$ 307.1904; observed 307.1904.

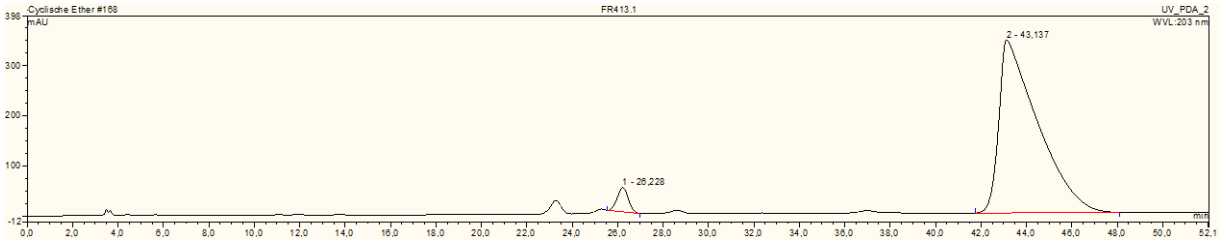
Chiral HPLC [Daicel Chiralcel-IA column (5 µm, 253 × 4.6 mm ID) with guard cartridge, *n*-Hexan/EtOH, 95:5, 1 mL/min, 25 °C, 203 nm]:

a. (±)-**SI-22**



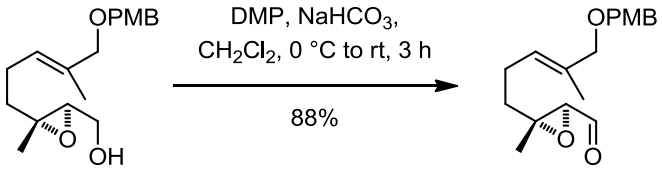
No.	Ret. time / min	Area / mAU×min	Height / mAU	Rel. area / %	Resolution
1	26.1	120.0	187.3	49.5	12.5
2	44.9	122.5	90.9	50.5	–

b. (2*R*,3*R*)-(+)-**SI-22**; t_R = 26.1, 44.0 min (major), *er* = 96:4, *ee* = 92%.



No.	Ret. time / min	Area / mAU×min	Height / mAU	Rel. area / %	Resolution
1	26.2	27.5	48.5	3.86	8.55
2	43.1	684.9	345.0	96.14	–

(2*R*,3*R*)-3-{(*E*)-5-[(4-Methoxybenzyl)oxy]-4-methylpent-3-en-1-yl}-3-methyloxirane-2-carbaldehyde [(–)-SI-16 and (±)-SI-16]



(+)-**SI-22**
(±)-**SI-22**

(–)-**SI-16**
(±)-**SI-16**

To a stirred solution of epoxy alcohol (±)-**SI-22** (1.06 g, 3.46 mmol, 1.0 equiv.) and $NaHCO_3$ (581 mg, 6.92 mmol, 2.0 equiv.) in anhydrous CH_2Cl_2 (30 mL) at 0 °C was added DMP

(1.91 g, 4.50 mmol, 1.3 equiv.) in one portion. The mixture was allowed to warm to rt over 1 h. After additional stirring at rt for 2 h (TLC control, MTBE/PE, 2:1) the complete mixture was directly subjected to column chromatography (PE/MTBE, 2:1, 4 × 20 cm) to give epoxy aldehyde (±)-**SI-16** (928 mg, 3.05 mmol, 88%) as a colorless oil. The product slowly decomposed at rt and was stored at –25 °C until usage.

Under the same conditions epoxy alcohol (+)-**SI-22** (2.30 g, 7.50 mmol) was converted to epoxy aldehyde (–)-**SI-16**, yielding 2.12 g (6.96 mmol, 93%) of a colorless oil.

TLC: R_f = 0.32 (PE/MTBE, 2:1).

$[\alpha]_D^{25}$ = –48.5 (*c* = 1.0, THF, 92% *ee*).

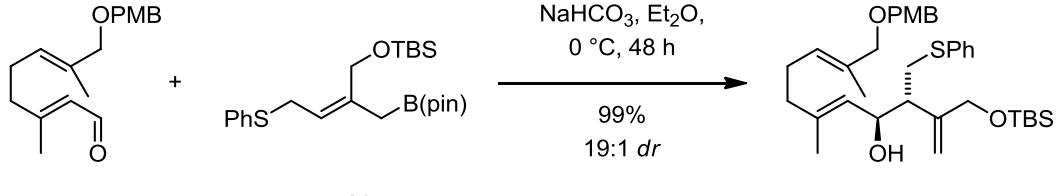
^{1}H NMR (300 MHz, C_6D_6): δ = 9.13 (*d*, 1H, $^3J_{H,H}$ = 5.0 Hz, C(O)H), 7.32–7.24 (*m*, 2H, CH, Ar), 6.87–6.78 (*m*, 2H, CH, Ar), 5.27 (*tq*, 1H, $^{3,4}J_{H,H}$ = 7.2, 1.2 Hz, C(H)═), 4.36 (*s*, 2H, CH_2O), 3.81 (*s*, 2H, CH_2O), 3.31 (*s*, 3H, OCH_3), 2.84 (*d*, 1H, $^3J_{H,H}$ = 5.0 Hz, C(O)CH, epoxide), 1.86 (*dt*, 2H, $^3J_{H,H}$ = 7.6 Hz, CH_2), 1.56 (*s*, 3H, CH_3), 1.37–1.15 (*m*, 2H, CH_2), 0.95 (*s*, 3H, CH_3),

^{13}C{^{1}H} NMR (75 MHz, C_6D_6): δ = 198.6 (CHO), 159.8 ($\underline{C}OCH_3$), 133.8 (R_2C═), 131.3 ($OCH_2\underline{C}$, Ar), 129.4 (CH, Ar), 125.7 (HC═), 114.1 (CH, Ar), 75.7 (CH_2O), 71.7 (CH_2O), 63.4 (C(O)$\underline{C}$H, epoxide), 54.8 ($\underline{C}$(O)CH, epoxide), 37.9 (CH_2), 23.2 (CH_2), 16.9 (CH_3), 14.0 (CH_3).

IR (ATR): $\tilde{\nu}$ = 3735 (*w*), 3649 (*w*), 3567 (*w*), 3421 (*w*), 2915 (*m*), 2841 (*m*), 2361 (*m*), 2061 (*w*), 1989 (*w*), 1719 (*m*), 1611 (*m*), 1512 (*s*), 1456 (*m*), 1383 (*m*), 1244 (*s*), 1174 (*m*), 1032 (*s*), 818 (*s*), 751 (*s*), 613 (*m*) cm^{-1}.

HRMS (APCI, Orbitrap): m/z calc'd for $C_{18}H_{24}O_4$ $[M–H]^-$ 303.1602; observed 303.1601.

(3*R,4*S**,5E,9E)-2-{[(*tert*-Butyldimethylsilyl)oxy]methyl}-11-[(4-methoxybenzyl)oxy]-6,10-dimethyl-3-[(phenylthio)methyl]undeca-1,5,9-trien-4-ol [(±)-16e]**



SI-15 (*Z*)-**11a** (±)-**16e**

Boronate (*Z*)-**11a** (135 mg, 0.31 mmol, 1.0 equiv.) was added to a stirred solution of aldehyde **SI-15** (100 mg, 0.35 mmol, 1.10 equiv.) and $NaHCO_3$ (1.30 mg, 15.5 μmol, 0.05 equiv.) in anhydrous Et_2O (2.0 mL) at 0 °C. After 48 h at this temperature (TLC control, PE/MTBE, 3:1) the complete mixture was directly subjected to column chromatography (PE/MTBE, 3:1, 2.5 × 20 cm), to obtain the isomerically pure allyl/homoallyl alcohol (±)-**16e** (175 mg, 0.29 mmol, 94%) as a colorless oil. A second isomer was detected by HPLC–MS (19:1 *dr* major:minor), but not isolated.

TLC: R_f = 0.37 (PE/MTBE, 3:1).

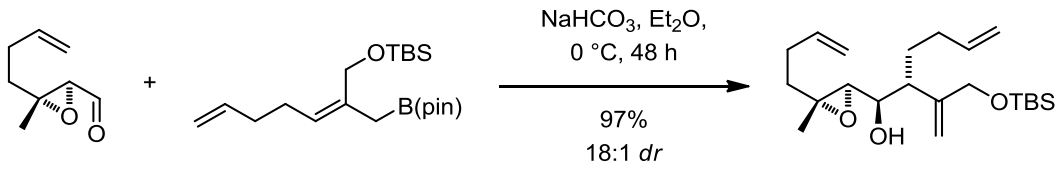
^{1}H NMR (300 MHz, C_6D_6): δ = 7.38–7.31 (*m*, 2H, CH, Ar), 7.31–7.25 (*m*, 2H, CH, Ar), 7.07–6.98 (*m*, 2H, CH, Ar), 6.95–6.86 (*m*, 1H, CH, Ar), 6.85–6.78 (*m*, 2H, CH, Ar), 5.43 (*td*, 1H, $^{3,4}J_{H,H}$ = 6.9, 1.1 Hz, $CH_2C(\underline{H}){=}CR_2$), 5.36 (*d*, 1H, $^3J_{H,H}$ = 1.4 Hz, ═C(H)H'), 5.30 (*dd*, 1H, $^{3,4}J_{H,H}$ = 8.7, 1.1 Hz, C(H)═C(H)OH), 5.06 (*d*, 1H, $^3J_{H,H}$ = 0.7 Hz, ═C(H)H'), 4.61 (*ddd*, 1H, $^3J_{H,H}$ = 8.7, 5.7, 4.9 Hz, C(H)OH), 4.37 (*s*, 2H, CH_2O), 4.23 (*d*, 1H, $^3J_{H,H}$ = 13.2 Hz, C(H)H'OSi), 4.10 (*d*, 1H, $^3J_{H,H}$ = 13.2 Hz, C(H)H'OSi), 3.85 (*s*, 2H, CH_2O), 3.39–3.25 (*m*, 4H, OCH_3 + C(H)H'S), 3.13–2.99 (*m*, 1H, C(H)H'S), 2.53 (*ddd*, 1H, $^3J_{H,H}$ = 9.2, 5.9, 5.9 Hz, C(H)C(R)═CH_2), 2.41 (*d*, 1H, $^3J_{H,H}$ = 4.9 Hz, OH), 2.17–2.07 (*m*, 2H, CH_2), 2.01–1.93 (*m*, 2H, CH_2), 1.66 (*s*, 3H, CH_3), 1.56 (*d*, 3H, $^4J_{H,H}$ = 1.2 Hz, CH_3), 0.95 (*s*, 9H, $SiC(CH_3)_3$), 0.06 (*m*, 6H, $Si(CH_3)(CH_3)$').

^{13}C{^{1}H} NMR (75 MHz, C_6D_6): δ = 159.7 ($\underline{C}OCH_3$), 147.2 (R_2C═), 138.0 (R_2C═), 137.7 (R_2C═), 133.3 (C_{quart}, Ar), 131.4 (C_{quart}, Ar), 129.5 (CH, Ar), 129.2 (CH, Ar), 129.1 (CH, Ar), 127.7 ($\underline{C}(H){=}CR_2$, overlayed by C_6D_5H (HMBC)), 127.2 ($\underline{C}(H){=}CR_2$), 125.9 (CH, Ar), 115.1 (═CH_2), 114.1 (CH, Ar), 76.0 (CH_2O), 71.6 (CH_2O), 69.8 (C(H)OH), 66.3 (CH_2OSi), 54.8 (OCH_3), 50.2 ($\underline{C}(H)C(R){=}CH_2$), 39.6 ($CH_2$), 35.1 ($CH_2S$), 26.3 ($CH_2$), 26.1 ($SiC(\underline{C}H_3)_3$), 18.5 ($Si\underline{C}(CH_3)_3$), 16.8 ($CH_3$), 14.2 ($CH_3$), –5.2 ($Si(\underline{C}H_3)(CH_3)$'), –5.3 ($Si(CH_3)(\underline{C}H_3)$').

IR (ATR): $\tilde{\nu}$ = 3738 (*w*), 3442 (*w*), 2928 (*m*), 2854 (*m*), 2361 (*w*), 1612 (*m*), 1512 (*s*), 1440 (*m*), 1360 (*m*), 1247 (*s*), 1173 (*m*), 1036 (*s*), 835 (*s*), 745 (*s*), 690 (*s*) cm^{-1}.

HRMS (ESI, TOF): m/z calc'd for $C_{35}H_{52}O_4SSi\,[M+Na]^+$ 619.3248; observed 619.3249.

(1*R,2*R**)-1-[(2*R**,3*R**)-3-(But-3-en-1-yl)-3-methyloxiran-2-yl]-2-{3-[(*tert*-butyldimethylsilyl)oxy]prop-1-en-2-yl}hex-5-en-1-ol [(±)-16f]**



(±)-**SI-3** (*Z*)-**11c** (±)-**16f**

Boronate (*Z*)-**11c** (20 mg, 54.6 μmol, 1.0 equiv.) was added to a stirred solution of aldehyde (±)-**SI-3** (8.42 mg, 60.1 μmol, 1.1 equiv.) and $NaHCO_3$ (0.23 mg, 2.73 μmol, 0.05 equiv.) in anhydrous Et_2O (0.5 mL) at 0 °C. After 48 h at this temperature (TLC control, PE/MTBE, 5:1) the complete mixture was directly subjected to column chromatography (PE/MTBE, 10:1, 2 × 20 cm), to obtain the isomerically pure homoallyl alcohol (±)-**16f** (19.1 mg, 50.2 μmol, 92%) as a colorless oil. A second isomer was detected by GC–MS (18:1 *dr* major:minor), but not isolated.

TLC: R_f = 0.36 (PE/MTBE, 10:1).

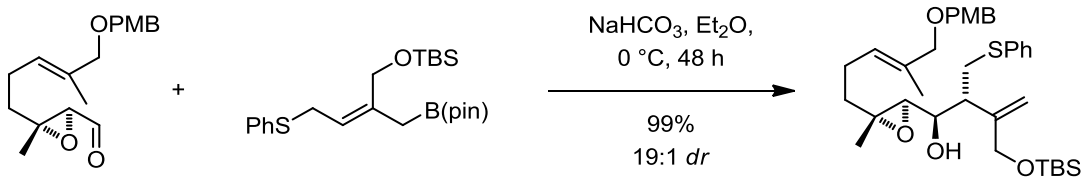
^{1}H NMR (300 MHz, C_6D_6): δ = 5.85–5.70 (*m*, 2H, 2 × C(H)═), 5.21 (*s*, 1H, ═C(H)H'), 5.10–4.99 (*m*, 3H, ═C(H)H' + ═CH_2), 4.97–4.92 (*m*, 2H, ═CH_2), 4.08 (*d*, 1H, $^3J_{H,H}$ = 12.3 Hz, C(H)H'OSi), 3.95 (*d*, 1H, $^3J_{H,H}$ = 12.3 Hz, C(H)H'OSi), 3.54–3.41 (*m*, 1H, C(H)OH), 3.22 (*d*, 1H, $^3J_{H,H}$ = 5.5 Hz, C(H)OH), 2.76 (*d*, 1H, $^3J_{H,H}$ = 8.4 Hz, C(O)CH, epoxide), 2.58–2.48 (*m*, 1H, C(H)C(R)═CH_2), 2.17–1.84 (*m*, 5H, 2 × CH_2 + C(H)H'), 1.80–1.42 (*m*, 3H, CH_2 + C(H)H'), 1.32 (*s*, 3H, CH_3), 0.93 (*s*, 9H, $SiC(CH_3)_3$), 0.06–0.00 (*m*, 6H, $Si(CH_3)(CH_3)$').

^{13}C{^{1}H} NMR (75 MHz, C_6D_6): δ = 147.1 (R_2C═), 138.8 (C(H)═), 138.5 (C(H)═), 116.9 (═CH_2), 115.0 (═CH_2), 114.8 (═CH_2), 72.8 (C(H)OH), 65.8 (CH_2OSi), 64.9 (C(O)CH, epoxide), 60.2 (C(O)CH, epoxide), 49.9 (C(H)C(R)═CH_2), 38.4 (CH_2), 32.0 (CH_2), 30.0 (CH_2), 29.4 (CH_2), 26.0 ($SiC(CH_3)_3$), 18.5 ($SiC(CH_3)_3$), 17.2 (CH_3), –5.4 ($Si(CH_3)(CH_3)$'), –5.4 ($Si(CH_3)(CH_3)$'),

IR (ATR): $\tilde{\nu}$ = 3102 (*w*), 3088 (*w*), 2911 (*m*), 2877 (*m*), 2352 (*w*), 1532 (*w*), 1470 (*m*), 1366 (*m*), 1381 (*m*), 1244 (*m*), 1088 (*m*), 1078 (*m*), 990 (*m*), 912 (*s*), 827 (*s*), 769 (*s*), 673 (*m*) cm^{-1}.

HRMS (ESI, TOF): m/z calc'd for $C_{22}H_{40}O_3Si$ $[M+Na]^+$ 403.2639; observed 403.2642.

(1*R*,2*R*)-3-{[(*tert*-Butyldimethylsilyl)oxy]methyl}-1-{(2*R*,3*R*)-3-{(*E*)-5-[(4-methoxybenzyl)oxy]-4-methylpent-3-en-1-yl}-3-methyloxiran-2-yl}-2-[(phenylthio)methyl]but-3-en-1-ol [(+)-16g and (±)-16g]



(–)-**SI-16**
(±)-**SI-16**

(*Z*)-**11a**

(+)-**16g**
(±)-**16g**

Boronate (*Z*)-**11a** (1.51 g, 3.48 mmol, 1.00 equiv.) was added to a stirred solution of aldehyde (±)-**SI-16** (1.16 g, 3.82 mmol, 1.10 equiv.) and $NaHCO_3$ (14.3 mg, 0.17 mmol, 0.05 equiv.) in anhydrous Et_2O (18 mL) at 0 °C. After 48 h at this temperature (TLC control, PE/MTBE, 4:1) sat. $NaHCO_3$ solution (30 mL) and Et_2O (15 mL) were added and the biphasic mixture was stirred for 5 min. Then the organic layer was separated and washed with brine (30 mL). The organic extract was dried with $MgSO_4$, filtered and concentrated *in vacuo*. Column chromatography of the residue (PE/MTBE, 3:1, 7 × 35 cm) provided the isomerically pure homoallyl alcohol (±)-**16g** (2.02 g, 3.29 mmol, 94%) as colorless oil. A second isomer was detected by HPLC–MS (19:1 *dr* major:minor), but not isolated.

Under the same conditions the reaction of boronate (*Z*)-**11a** (1.65 g, 3.79 mmol) and epoxy aldehyde (–)-**SI-16** (1.27 g, 4.18 mmol) gave 2.11 g (3.44 mmol, 91%) of the homoallyl alcohol (+)-**16g** as a colorless oil.

TLC: R_f = 0.60 (PE/MTBE, 2:1).

$[\alpha]_D^{23}$ = +6.44 (*c* = 1.0, THF, 92% *ee*).

^{1}H NMR (300 MHz, C_6D_6): δ = 7.39–7.34 (*m*, 2H, CH, Ar), 7.31–7.25 (*m*, 2H, CH, Ar), 7.05–6.98 (*m*, 2H, CH, Ar), 6.93–6.86 (*m*, 1H, CH, Ar), 6.85–6.80 (*m*, 2H, CH, Ar), 5.41 (*t*, 1H, $^3J_{H,H}$ = 6.8 Hz, $CH_2C(\underline{H}){=}CR_2$), 5.30 (*d*, 1H, $^3J_{H,H}$ = 0.9 Hz, ═C(H)H'), 5.19 (*d*, 1H, $^3J_{H,H}$ = 0.9 Hz, ═C(H)H'), 4.35 (*s*, 2H, CH_2O), 4.21 (*d*, 1H, $^3J_{H,H}$ = 12.4 Hz, C(H)H'OSi), 4.06 (*d*, 1H, $^3J_{H,H}$ = 12.3 Hz, C(H)H'OSi), 3.81 (*s*, 2H, CH_2O), 3.78–3.69 (*m*, 1H, C(H)OH), 3.54–3.43 (*m*, 1H, C(H)H'S), 3.31 (*s*, 3H, OCH_3), 3.18 (*dd*, 1H, $^{2,3}J_{H,H}$ = 12.8, 9.4 Hz, C(H)H'S), 2.93–2.85 (*m*, 1H, C(H)C(R)═CH_2), 2.79 (*d*, 1H, $^3J_{H,H}$ = 8.5 Hz, C(O)CH, epoxide), 2.12 (*td*, 2H, $^3J_{H,H}$ = 7.5, 7.4 Hz, CH_2), 1.70–1.56 (*m*, 4H, CH_3 + C(H)H'), 1.51–

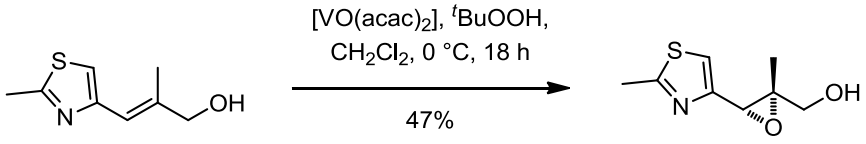
1.38 (*m*, 1H, C(H)H'), 1.31 (*s*, 3H, CH_3), 0.92 (*s*, 9H, $SiC(CH_3)_3$), 0.02 (*m*, 6H, $Si(CH_3)(CH_3)$').

$^{13}C\{^1H\}$ NMR (75 MHz, C_6D_6): δ = 159.8 ($\underline{C}OCH_3$), 146.0 ($R_2C{=}$), 137.4 ($R_2C{=}$), 133.2 (C_{quart}, Ar), 131.3 (C_{quart}, Ar), 129.5 (CH, Ar), 129.5 (CH, Ar), 129.2 (CH, Ar), 127.2 ($CH_2\underline{C}(H){=}CR_2$), 126.1 (CH, Ar), 117.5 ($={CH_2}$), 114.1 (CH, Ar), 76.0 (CH_2O), 71.6 (CH_2O), 71.3 (C(H)OH), 66.0 (CH_2OSi), 64.5 (C(O)$\underline{C}$H, epoxide), 60.8 ($\underline{C}$(O)CH, epoxide), 54.8 (OCH_3), 49.0 ($\underline{C}(H)C(R){=}CH_2$), 38.6 ($CH_2$), 34.8 ($CH_2S$), 26.0 ($SiC(\underline{C}H_3)_3$), 23.9 ($CH_2$), 18.5 ($Si\underline{C}(CH_3)_3$), 17.1 ($CH_3$), 14.1 ($CH_3$), –5.4 ($Si(\underline{C}H_3)(CH_3)$'), –5.4 ($Si(CH_3)(\underline{C}H_3)$').

IR (ATR): $\tilde{\nu}$ = 3855 (*w*), 3739 (*w*), 3650 (*w*), 3567 (*w*), 3383 (*w*), 3072 (*w*), 2929 (*m*), 2855 (*m*), 2362 (*m*), 2166 (*w*), 1990 (*w*), 1921 (*w*), 1869 (*w*), 1612 (*m*), 1512 (*m*), 1460 (*m*), 1362 (*m*), 1248 (*s*), 1173 (*m*), 1035 (*s*), 908 (*m*), 836 (*s*), 748 (*s*), 691 (*m*) cm^{-1}.

HRMS (ESI, TOF): m/z calc'd for $C_{35}H_{52}O_5SSi\,[M+H]^+$ 613.3377; observed 613.3378.

[(2*S,3*S**)-2-methyl-3-(2-methylthiazol-4-yl)oxiran-2-yl]methanol [(±)-SI-23]**



SI-2 (±)-**SI-23**

The allyl alcohol **SI-2** (97.0 mg, 0.57 mmol, 1.0 equiv.) and $[VO(acac)_2]$ (29.2 mg, 0.1 mmol, 0.2 equiv.) were dissolved in anhydrous CH_2Cl_2 (6.0 mL). The turquoise-green solution was cooled to 10 °C and an anhydrous ^{t}BuOOH solution (178 µl, 0.89 mmol, 1.5 equiv., 5.0 M in decane with 4 Å molecular sieves) was added. After 18 h at this temperature (TLC control, EtOAc/PE, 4:1) the red solution was concentrated *in vacuo*. Column chromatography of the residue (EtOAc/PE, 4:1, 3 × 20 cm) delivered epoxide (±)-**SI-23** (50.0 mg, 0.27 mmol, 47%) as a slightly yellow oil.

TLC: R_f = 0.30 (EtOAc/PE, 4:1).

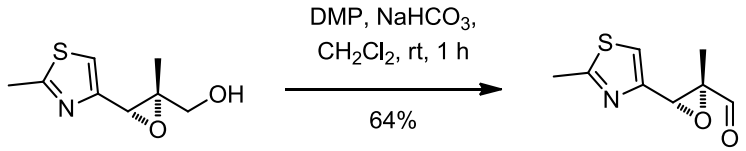
^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.98 (*d*, 1H, $^4J_{H,H}$ = 0.8 Hz, CH, Ar), 4.25 (*s*, 1H, HC(O)C, epoxide), 3.86–3.70 (*m*, 2H, $C\underline{H}_2OH$), 2.71 (*s*, 3H, CH_3, Ar), 2.39 (*s*, 1H, OH), 1.21 (*s*, 3H, $C(O)C(CH_3)$).

$^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ = 166.7 (C_{quart}, Ar), 151.5 (C_{quart}, Ar), 115.3 (CH, Ar), 65.1 (CH_2OH), 64.0 (HC(O)C, epoxide), 58.2 (HC(O)C, epoxide), 19.3 (CH_3), 13.7 (CH_3).

IR (ATR): $\tilde{\nu}$ = 3339 (*m*), 3122 (*m*), 2927 (*m*), 2865 (*m*), 2362 (*w*), 2234 (*w*), 2143 (*w*), 2002 (*w*), 1944 (*w*), 1870 (*w*), 1715 (*w*), 1653 (*w*), 1439 (*m*), 1381 (*m*), 1275 (*m*), 1188 (*s*), 1136 (*m*), 1035 (*s*), 904 (*m*), 758 (*s*), 651 (*s*) cm^{-1}.

HRMS (ESI, TOF): m/z calc'd for $C_8H_{11}NO_2S$ $[M+H]^+$ 186.0583; observed 186.0584.

(2*S,3*R**)-2-Methyl-3-(2-methylthiazol-4-yl)oxirane-2-carbaldehyde [(±)-SI-24]**



(±)-**SI-23** (±)-**SI-24**

To a stirred solution of epoxy alcohol (±)-**SI-23** (41.0 mg, 0.22 mmol, 1.0 equiv.) and $NaHCO_3$ (37.0 mg, 0.44 mmol, 2.0 equiv.) in anhydrous CH_2Cl_2 (2.5 mL) at rt was added DMP (113 mg, 0.27 mmol, 1.2 equiv.). After 1 h (TLC control, EtOAc/PE, 4:1) a 1:1 mixture of sat. $Na_2S_2O_3$ solution and sat. $NaHCO_3$ solution (4 mL) was added and the biphasic mixture was stirred for 10 min. Then the organic layer was separated and washed with brine (4 mL). The organic extract was dried with $MgSO_4$, filtered and concentrated *in vacuo*. Column chromatography of the residue (PE/EtOAc, 1:1, 2 × 15 cm) provided the aldehyde (±)-**SI-24** (25.0 mg, 0.14 mmol, 64%) as colorless oil.

TLC: R_f = 0.28 (PE/EtOAc, 2:1).

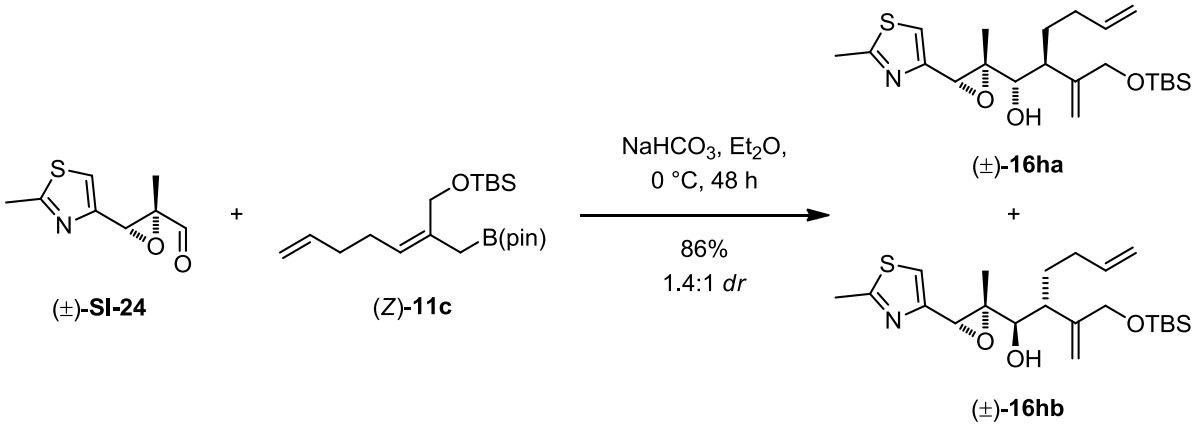
^1H NMR (300 MHz, $CDCl_3$): δ = 9.05 (*s*, 1H, CHO), 7.07 (*d*, 1H, $^4J_{H,H}$ = 0.7 Hz, CH, Ar), 4.40 (*s*, 1H, HC(O)C, epoxide), 2.72 (*s*, 3H, CH_3), 1.33 (*s*, 3H, CH_3).

$^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ = 198.4 (CHO), 167.3 (C_{quart}, Ar), 148.8 (C_{quart}, Ar), 116.6 (CH, Ar), 65.0 (HC(O)C, epoxide), 58.2 (HC(O)C, epoxide), 19.3 (CH_3), 9.5 (CH_3).

IR (ATR): $\tilde{\nu}$ = 3903 (*w*), 3735 (*w*), 3119 (*w*), 2931 (*w*), 2851 (*w*), 2362 (*w*), 2112 (*w*), 1944 (*w*), 1870 (*w*), 1726 (*s*), 1439 (*m*), 1380 (*m*), 1272 (*m*), 1184 (*m*), 1134 (*m*), 1031 (*s*), 893 (*m*), 753 (*s*), 662 (*s*) cm^{-1}.

HRMS (EI, Orbitrap): m/z calc'd for $C_8H_9NO_2S$ $[M-H]^+$ 182.0270; observed 182.071.

(1*S,2*S**)-2-{3-[(*tert*-Butyldimethylsilyl)oxy]prop-1-en-2-yl}-1-[(2*R**,3*R**)-2-methyl-3-(2-methylthiazol-4-yl)oxiran-2-yl]hex-5-en-1-ol [(±)-16ha] and (1*R**,2*R**)-2-{3-[(*tert*-Butyldi-methylsilyl)oxy]prop-1-en-2-yl}-1-[(2*R**,3*R**)-2-methyl-3-(2-methylthiazol-4-yl)oxiran-2-yl]hex-5-en-1-ol [(±)-16hb]**



Aldehyde (±)-**SI-24** (27.5 mg, 150 µmol, 1.1 equiv.) was added to a stirred solution of boronate (*Z*)-**11c** (50.0 mg, 136 µmol, 1.0 equiv.) and $NaHCO_3$ (0.57 mg, 6.82 µmol, 0.05 equiv.) in anhydrous Et_2O (0.7 mL) at 0 °C. After 48 h at this temperature (TLC control, PE/EtOAc, 2:1) the complete mixture was directly subjected to column chromatography (PE/EtOAc, 3:1, 3 × 25 cm), to obtain the following products in order of elution: Homoallyl alcohol (±)-**16ha** (21.0 mg, 49.6 µmol, 36%) and (±)-**16hb** (29.0 mg, 68.4 µmol, 50%), both as colorless oils.

Major isomer was assigned as Felkin product, referring to the configuration assignment described in the main text.

16ha:

TLC: R_f = 0.45 (PE/EtOAc, 3:1).

^{1}H NMR (300 MHz, C_6D_6): δ = 6.77 (*s*, 1H, CH, thiazole), 5.82 (*ddt*, 1H, $^3J_{H,H}$ = 16.8, 10.2, 6.5 Hz, C(H)═), 5.40 (*d*, 1H, $^4J_{H,H}$ = 1.3 Hz, ═C(H)H'), 5.13–4.96 (*m*, 3H, ═C(H)H' + ═CH_2), 4.29–4.23 (*m*, 2H, C(H)H'OSi + HC(O)C, epoxide), 4.17 (*d*, 1H, $^4J_{H,H}$ = 13.6 Hz, C(H)H'OSi), 3.51 (*d*, 1H, J = 6.8 Hz, C(H)OH), 3.17 (*br s*, 1H, OH), 2.49 (*ddd*, 1H, $^3J_{H,H}$ = 10.7, 6.8, 4.3 Hz, C(H)C(R)═CH_2), 2.24 (*s*, 3H, CH_3), 2.20–2.09 (*m*, 1H, C(H)H'), 2.08–1.90 (*m*, 2H, C(H)H' + C(H)H'), 1.87–1.72 (*m*, 1H, C(H)H'), 1.30 (*s*, 3H, CH_3), 0.98 (*s*, 9H, $SiC(CH_3)_3$), 0.08 (*s*, 6H, $Si(CH_3)_2$).

^{13}C{^{1}H} NMR (75 MHz, C_6D_6): δ = 166.0 (C_{quart}, thiazole), 152.8 (C_{quart}, thiazole), 148.1 (R_2C═), 138.9 (C(H)═), 115.3 (═CH_2), 115.1 (CH, thiazole), 113.6 (═CH_2), 77.9

(C(H)OH), 66.4 (CH_2O), 64.9 (HC(O)C, epoxide), 59.2 (HC(O)C, epoxide), 45.8 (C(H)C(R)=CH_2), 31.9 (CH_2), 30.3 (CH_2), 26.2 (SiC(CH_3)$_3$), 18.8 (SiC(CH_3)$_3$), 18.6 (CH_3), 12.5 (CH_3), –5.2 (Si(CH_3)(CH_3)'), –5.3 (Si(CH_3)(CH_3)').

IR (ATR): $\tilde{\nu}$ = 3077 (*w*), 2930 (*m*), 2857 (*m*), 2362 (*w*), 1717 (*w*), 1642 (*w*), 1459 (*m*), 1387 (*m*), 1254 (*m*), 1186 (*m*), 1105 (*m*), 1053 (*m*), 907 (*m*), 835 (*s*), 774 (*s*), 668 (*m*) cm^{-1}.

HRMS (ESI, TOF): m/z calc'd for $C_{22}H_{37}NO_3SSi$ $[M+Na]^+$ 446.2156; observed 446.2158.

16hb:

TLC: R_f = 0.35 (PE/EtOAc, 3:1).

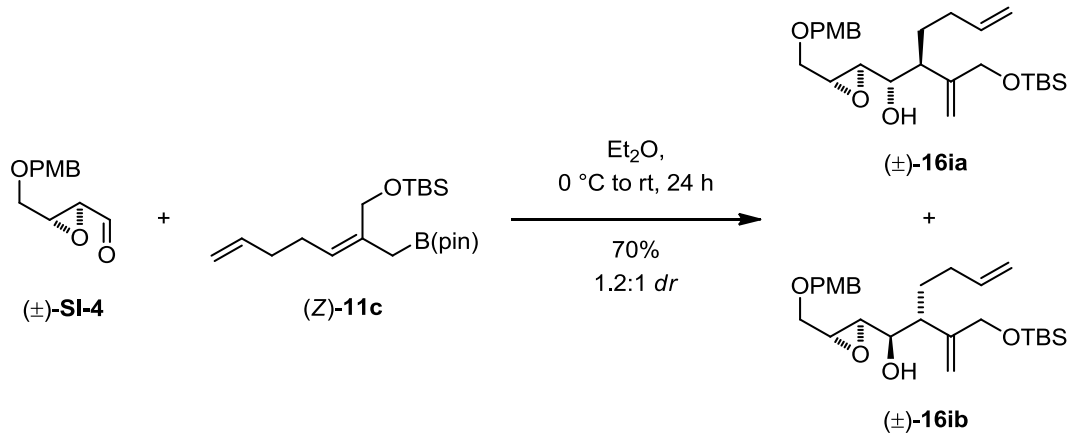
^{1}H NMR (300 MHz, C_6D_6): δ = 6.75 (*d*, 1H, $^4J_{H,H}$ = 0.8 Hz, CH, thiazole), 5.82 (*ddt*, 1H, $^3J_{H,H}$ = 16.7, 10.3, 6.3 Hz, C(H)=), 5.33 (*d*, 1H, $^4J_{H,H}$ = 1.3 Hz, =C(H)H'), 5.14 (*dd*, 1H, $^{3,4}J_{H,H}$ = 17.2, 1.6 Hz, =C(H)H'), 5.05–4.98 (*m*, 1H, =C(H)H'), 4.95 (*s*, 1H, =C(H)H'), 4.26 (*s*, 1H, HC(O)C, epoxide), 4.13 (*s*, 2H, CH_2OSi), 3.38 (*d*, 1H, $^3J_{H,H}$ = 8.7 Hz, C(H)OH), 2.82 (*br s*, 1H, OH), 2.33 (*ddd*, 1H, $^3J_{H,H}$ = 8.9, 8.8, 3.5 Hz, C(H)C(R)=CH_2), 2.23 (*s*, 3H, CH_3), 2.18–2.05 (*m*, 1H, C(H)H'), 2.01–1.85 (*m*, 2H, C(H)H' + C(H)H'), 1.70–1.55 (*m*, 1H, C(H)H'), 1.28 (*s*, 3H, CH_3), 0.98 (*s*, 9H, SiC(CH_3)$_3$), 0.07 (*s*, 6H, Si(CH_3)$_2$).

^{13}C{^{1}H} NMR (75 MHz, C_6D_6): δ = 166.2 (C_{quart}, thiazole), 152.6 (C_{quart}, thiazole), 148.5 (R_2C=), 138.7 (C(H)=), 115.1 (=CH_2), 115.1 (CH, thiazole), 113.0 (=CH_2), 80.0 (C(H)OH), 66.5 (CH_2O), 65.6 (HC(O)C, epoxide), 60.4 (HC(O)C, epoxide), 46.5 (C(H)C(R)=CH_2), 31.5 (CH_2), 29.8 (CH_2), 26.1 (SiC(CH_3)$_3$), 18.8 (SiC(CH_3)$_3$), 18.5 (CH_3), 11.3 (CH_3), –5.3 (Si(CH_3)(CH_3)'), –5.3 (Si(CH_3)(CH_3)').

IR (ATR): $\tilde{\nu}$ = 3567 (*w*), 3395 (*w*), 3123 (*w*), 3076 (*w*), 2929 (*m*), 2855 (*m*), 2362 (*w*), 1795 (*w*), 1731 (*w*), 1641 (*w*), 1458 (*m*), 1385 (*m*), 1253 (*m*), 1185 (*m*), 1063 (*s*), 906 (*s*), 835 (*s*), 773 (*s*), 668 (*m*) cm^{-1}.

HRMS (ESI, TOF): m/z calc'd for $C_{22}H_{37}NO_3SSi$ $[M+Na]^+$ 446.2156; observed 446.2155.

(1*S,2*S**)-2-{3-[(*tert*-Butyldimethylsilyl)oxy]prop-1-en-2-yl}-1-{(2*R**,3*R**)-3-{[(4-methoxybenzyl)oxy]methyl}oxiran-2-yl}hex-5-en-1-ol [(±)-16ia] and (1*R**,2*R**)-2-{3-[(*tert*-Butyldimethylsilyl)oxy]prop-1-en-2-yl}-1-{(2*R**,3*R**)-3-{[(4-methoxybenzyl)oxy]-methyl}oxiran-2-yl}hex-5-en-1-ol [(±)-16ib]**



Aldehyde (±)-**SI-4** (14.0 µl, 13.8 mg, 61.9 µmol, 1.2 equiv.) was added to a stirred solution of boronate (*Z*)-**11c** (18.9 mg, 51.6 µmol, 1.0 equiv.) in anhydrous Et_2O (0.6 mL) at 0 °C. The solution was allowed to reach rt over 8 h. After 24 h at this temperature (TLC control, PE/Et_2O, 20:1) the complete mixture was directly subjected to column chromatography (PE/MTBE, 4:1, 1.5 × 20 cm), to obtain the homoallyl alcohols (±)-**16ia,b** (16.7 mg, 36.1 µmol, 70%) as a colorless oil and as an inseparable 1.2:1 mixture of diastereomers.

Major isomer was assigned as Felkin product, referring to the configuration assignment described in the main text.

TLC: R_f = 0.41 (PE/MTBE, 2:1).

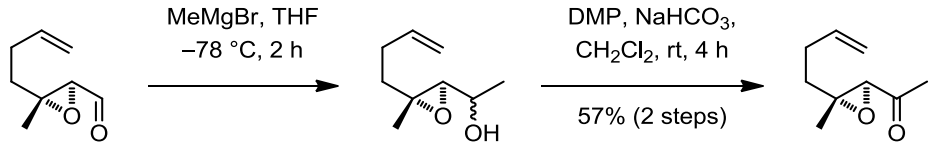
^{1}H NMR (300 MHz, C_6D_6; mixture of diastereomers, integrals given for each): δ = 7.25–7.20 (*m*, 4H, CH, Ar), 6.83–6.76 (*m*, 4H, CH, Ar), 5.84–5.67 (*m*, 2H, 2 × C(H)═), 5.28 (*dd*, 2H, $^{3,4}J_{H,H}$ = 6.0, 1.5 Hz, 2 × ═C(H)H'), 5.09–4.89 (*m*, 6H, 2 × ═C(H)H' + 2 × ═CH_2), 4.40 (*s*, 2H, CH_2O), 4.36 (*d*, 2H, $^4J_{H,H}$ = 4.0 Hz, CH_2O), 4.15–3.96 (*m*, 4H, 2 × CH_2OSi), 3.60 (*dd*, 1H, $^{3,4}J_{H,H}$ = 11.4, 2.7 Hz, OC(H)H'C(O)C), 3.49 (*dd*, 1H, $^{3,4}J_{H,H}$ = 11.3, 3.3 Hz, OC(H)H'C(O)C), 3.45–3.27 (*m*, 10H, $OCH_2C(O)C$, 2 × C(H)OH, 2 × OCH_3), 3.23–3.13 (*m*, 2H, 2 × HC(O)CH, epoxide), 2.90–2.84 (*m*, 2H, 2 × HC(O)CH, epoxide), 2.75 (*d*, 1H, $^3J_{H,H}$ = 5.1 Hz, OH), 2.53 (*d*, 1H, $^3J_{H,H}$ = 6.4 Hz, OH), 2.44–2.34 (*m*, 1H, C(H)C(R)═CH_2), 2.27 (*dt*, 1H, $^3J_{H,H}$ = 10.7, 5.5 Hz, C(H)C(R)═CH_2), 2.11–1.83 (*m*, 4H, 2 × CH_2), 1.80–1.50 (*m*, 4H, 2 × CH_2), 0.99–0.93 (*m*, 18H, 2 × $SiC(CH_3)_3$), 0.10–0.06 (*m*, 6H, $Si(CH_3)(CH_3)$'), 0.04 (*s*, 6H, $Si(CH_3)_2$).

$^{13}C\{^1H\}$ NMR (75 MHz, C_6D_6; mixture of diastereomers, assignment: * or #): δ = 159.5* (COMe, Ar), 159.4# (COMe, Ar), 147.4* (R_2C═), 146.9# (R_2C═), 138.4*# (C(H)═), 130.4* (C_{quart}, Ar), 130.4# (C_{quart}, Ar), 129.2* (CH, Ar), 129.1# (CH, Ar), 114.6* (═CH_2), 114.6# (═CH_2), 113.8* (CH, Ar), 113.7# (CH, Ar), 113.2*# (═CH_2), 72.7*# (OCH_2Ar), 72.8* (C(H)OH), 72.6# (C(H)OH), 69.7* (OCH_2), 69.6# (OCH_2), 65.6* (OCH_2), 65.3# (OCH_2), 57.6* (C(O)C, epoxide), 56.8# (C(O)C, epoxide), 55.3* (C(O)C, epoxide), 54.4# (C(O)C, epoxide), 54.7*# ($COCH_3$, aryl), 47.7* (CH_2), 47.3# (CH_2), 31.5* (CH_2), 31.4# (CH_2), 29.3* (CH_2), 29.0# (CH_2), 25.7* ($SiC(CH_3)_3$), 25.7# ($SiC(CH_3)_3$), 18.2* ($SiC(CH_3)_3$), 18.1# ($SiC(CH_3)_3$), –5.6* ($Si(CH_3)(CH_3)'$), –5.7# ($Si(CH_3)(CH_3)'$), –5.8*# ($Si(CH_3)_2$).

IR (ATR): $\tilde{\nu}$ = 3073 (*w*), 2929 (*m*), 2856 (*m*), 2712 (*w*), 2542 (*w*), 2361 (*w*), 2213 (*w*), 2033 (*w*), 1990 (*w*), 1612 (*m*), 1512 (*s*), 1460 (*m*), 1362 (*m*), 1248 (*s*), 1174 (*m*), 1096 (*s*), 1036 (*s*), 905 (*s*), 836 (*s*), 774 (*s*), 670 (*m*) cm^{-1}.

HRMS (ESI, TOF): m/z calc'd for $C_{26}H_{42}O_5Si$ $[M+Na]^+$ 485.2694; observed 485.2693.

1-[(2*S,3*R**)-3-(But-3-en-1-yl)-3-methyloxiran-2-yl]ethanone [(±)-SI-25]**



(±)-**SI-3** (±)-**SI-26** (±)-**SI-25**

Epoxy aldehyde (±)-**SI-3** (200 mg, 1.43 mmol, 1.0 equiv.) was added dropwise over 30 min to a solution of MeMgBr (0.52 mL, 1.57 mmol, 1.1 equiv., 3.0 M in Et_2O) in anhydrous THF (14 mL) at –78 °C. After 2 h at –78 °C (TLC control, PE/MTBE, 2:1) the cooling bath was removed and a sat. NH_4Cl solution (20 mL) was added and the mixture was stirred for 10 min. Then brine (20 mL) and MTBE (40 mL) were added and the organic layer was separated after extraction. The organic extract was dried with $MgSO_4$, filtered and the solvent was removed *in vacuo*.

The residual oil (**SI-26**) was dissolved in anhydrous CH_2Cl_2 (15 mL). $NaHCO_3$ (140 mg, 1.67 mmol, 1.2 equiv.) was added at rt, followed by DMP (667 mg, 1.57 mmol, 1.1 equiv.). The mixture was stirred for 4 h (TLC control, heptanes/MTBE, 2:1). Semi-sat. $Na_2S_2O_3$ (10 mL) was added and the suspension was stirred until all solids dissolved (15–30 min). The organic layer was separated, washed with brine (40 mL), dried with $MgSO_4$, filtered and

concentrated *in vacuo*. Column chromatography of the residue (PE/MTBE, 8:3, 3 × 25 cm) provided the epoxy ketone (±)-**SI-25** (126 mg, 0.82 mmol, 57% over 2 steps) as a colorless oil.

TLC: R_f = 0.35 (PE/MTBE, 4:1).

^{1}H NMR (400 MHz, C_6D_6): δ = 5.65–5.54 (*m*, 1H, C(H)═), 4.94–4.92 (*m*, 1H, ═C(H)H'), 4.91–4.87 (*m*, 1H, ═C(H)H'), 2.95 (*s*, 1H, C(O)CH, epoxide), 1.93–1.82 (*m*, 2H, CH_2), 1.74 (*s*, 3H, CH_3), 1.50–1.36 (*m*, 1H, C(H)H'), 1.32–1.21 (*m*, 1H, C(H)H'), 0.96 (*s*, 3H, CH_3).

^{13}C{^{1}H} NMR (101 MHz, C_6D_6): δ = 203.0 (C═O), 137.7 (RC(H)═), 115.2 (═CH_2), 64.5 (C(O)CH, epoxide), 62.2 (C(O)CH, epoxide), 37.5 (CH_2), 29.5 (CH_2), 27.5 (CH_3), 16.4 (CH_3).

IR (ATR): $\tilde{\nu}$ = 3078 (*w*), 2926 (*m*), 2858 (*m*), 2361 (*m*), 2195 (*w*), 2113 (*w*), 2066 (*w*), 1719 (*s*), 1641 (*m*), 1355 (*m*), 1243 (*m*), 1184 (*m*), 1071 (*m*), 995 (*m*), 914 (*s*), 836 (*m*), 750 (*s*), 611 (*s*) cm^{-1}.

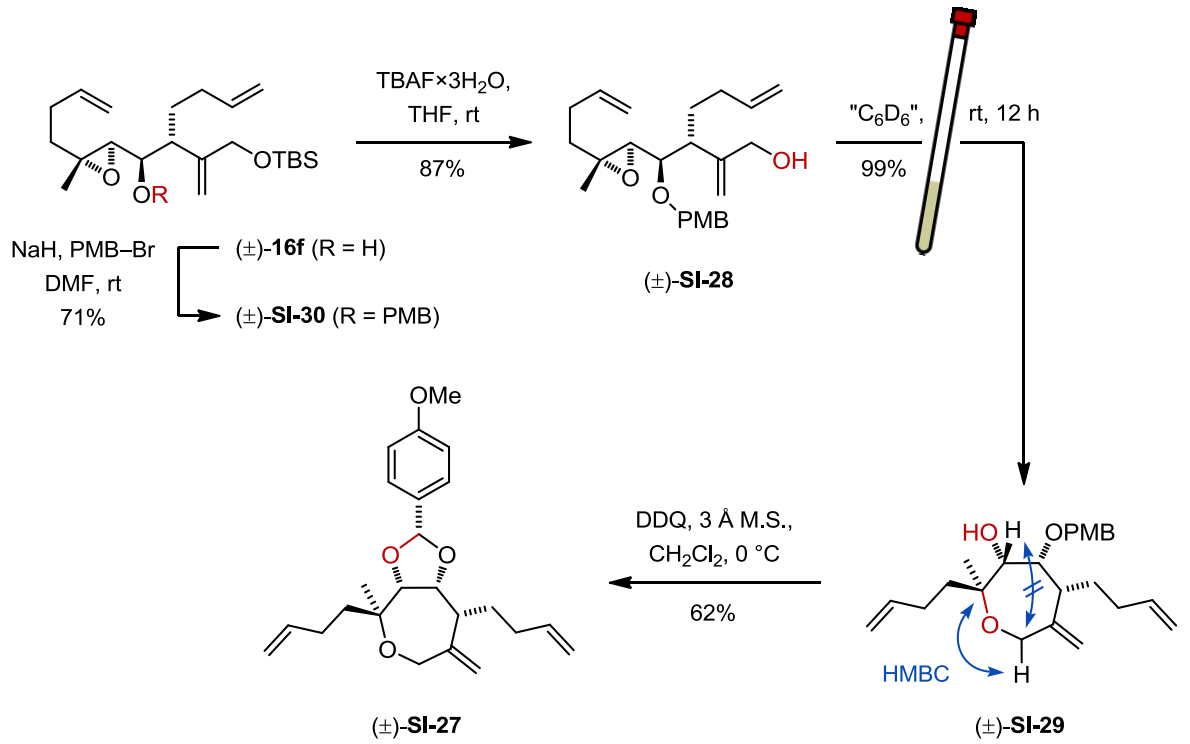
HRMS (ESI, TOF): m/z calc'd for $C_9H_{14}O_2$ $[M+Na]^+$ 177.0886; observed 177.0888.

3.3 Structure elucidation of allylboration products

To determine the stereochemistry of the epoxy alcohol (±)-**16f** we planned to transform it to a bicyclic compound by intramolecular epoxide opening and by bridging the newly formed alcohol moiety with the existing (protected) one. This bicycle (±)-**SI-27** should be rigid enough for ^{1}H,^{1}H-NOESY experiments.

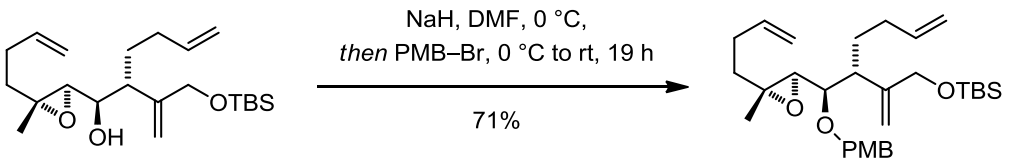
The synthesis is depicted in Scheme S3. Epoxy alcohol (±)-**SI-28** underwent a clean, regioselective epoxide opening during an overnight NMR measurement to form (±)-**SI-29**. The connectivity was determined by a ^{1}H,^{13}C-HMBC experiment and shown to be the product of a formal acid induced opening, with attack of the nucleophile at the higher substituted position.

After signal assignment by HSQC/DEPT and HMBC experiments, the NOESY analysis of (±)-**SI-27** (see below reaction conditions) confirmed the configuration that corresponds to Felkin control in the allylboration. (Additional confirmation of the formation of the Felkin product was gained by X-ray crystal structure analysis of allyl bromide (±)-**2**).



Scheme S3. Epoxide opening and oxidative cyclization of an allylboration product for structure elucidation by NMR

{{(*R)-3-{(*R**)-[(2*R**,3*R**)-3-(But-3-en-1-yl)-3-methyloxiran-2-yl][(4-methoxybenzyl)-oxy]methyl}-2-methylenehept-6-en-1-yl}oxy}(*tert*-butyl)dimethylsilane [(±)-SI-30]**



(±)-**16f** (±)-**SI-30**

To a stirred solution of alcohol (±)-**16f** (48.0 mg, 126 μmol, 1.0 equiv.) in anhydrous DMF (1.2 mL) at 0 °C was added NaH (7.60 mg, 190 μmol, 1.5 equiv., 60*w*-% in mineral oil) in 5 portions. After 20 min freshly purified PMB–Br (38.2 mg, 190 μmol, 1.5 equiv.) was added and the suspension was allowed to warm to rt. After 19 h (TLC control, heptanes/MTBE, 7:1) the mixture was cooled to 0 °C, pH 7 phosphate buffer (10 mL) and MTBE (10 mL) were added and the organic layer was separated. The organic extract was washed with brine (2 × 20 mL), dried with $MgSO_4$, filtered and concentrated *in vacuo*. Column chromatography of the residue (PE/Et_2O, 15:1, 2 × 20 cm) provided the PMB ether (±)-**SI-30** (45.0 mg, 89.9 μmol, 71%) as a colorless oil.

TLC: R_f = 0.34 (PE/Et_2O, 15:1).

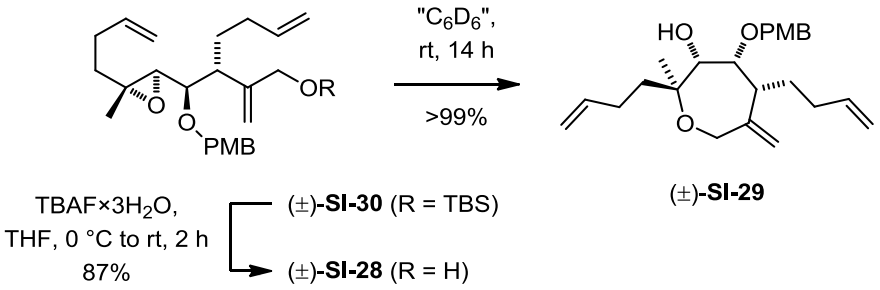
^{1}H NMR (300 MHz, C_6D_6): δ = 7.27–7.21 (*m*, 2H, CH, Ar), 6.85–6.78 (*m*, 2H, CH, Ar), 5.87–5.60 (*m*, 3H, 2 × C(H)═ + ═C(H)H'), 5.44 (*d*, 1H, $^2J_{H,H}$ = 1.9 Hz, ═C(H)H'), 5.06 (*dd*, 1H, $^{3,2}J_{H,H}$ = 17.1, 1.8 Hz, ═C(H)H'), 5.01–4.90 (*m*, 3H, ═C(H)H' + ═CH_2), 4.52–4.36 (*m*, 3H, OCH_2Ar + OC(H)H'C═), 4.24 (*d*, 1H, $^2J_{H,H}$ = 11.3 Hz, OC(H)H'C═), 3.34–3.28 (*m*, 4H, C(H)OPMB + OCH_3), 2.85 (*d*, 1H, $^3J_{H,H}$ = 8.6 Hz, C(O)CH, epoxide), 2.54–2.46 (*m*, 1H, OCH_2C(═C)CH), 2.24–2.09 (*m*, 1H, C(H)H'), 2.08–1.85 (*m*, 4H, C(H)H' + CH_2 + C(H)H'), 1.80–1.67 (*m*, 1H, C(H)H'), 1.60–1.48 (*m*, 1H, C(H)H'), 1.46–1.34 (*m*, 1H, C(H)H'), 1.13 (*s*, 3H, CH_3), 1.00 (*s*, 9H, $SiC(CH_3)_3$), 0.12–0.11 (*m*, 6H, $Si(CH_3)(CH_3)$').

^{13}C{^{1}H} NMR (75 MHz, C_6D_6): δ = 159.8 ($COCH_3$, Ar), 148.0 (OCH_2C═), 139.0 (C(H)═), 138.3 (C(H)═), 131.2 (C_{quart}, Ar), 129.2 (CH, Ar), 114.9 (═CH_2), 114.9 (═CH_2), 114.1 (CH, Ar), 111.8 (OCH_2C═CH_2), 78.8 (C(H)OPMB), 71.8 (OCH_2C═), 65.9 (OCH_2Ar), 62.9 (C(O)CH, epoxide), 61.1 (C(O)CH, epoxide), 54.8 (OCH_3), 46.0 (OCH_2C(═C)CH), 38.0 (CH_2), 32.1 (CH_2), 30.9 (CH_2), 29.7 (CH_2), 26.2 ($SiC(CH_3)_3$), 18.7 ($SiC(CH_3)_3$), 17.7 (CH_3), –5.2 ($Si(CH_3)_2$).

IR (ATR): $\tilde{\nu}$ = 3075 (*w*), 2929 (*m*), 2855 (*m*), 2362 (*w*), 2169 (*w*), 2066 (*w*), 1944 (*w*), 1828 (*w*), 1612 (*w*), 1512 (*m*), 1458 (*m*), 1385 (*m*), 1248 (*s*), 1172 (*m*), 1083 (*s*), 907 (*s*), 835 (*s*), 774 (*s*), 669 (*m*) cm^{-1}.

HRMS (APCI, Orbitrap): m/z calc'd for $C_{30}H_{48}O_4Si$ $[M+H]^+$ 501.3395; observed 501.3397.

(2*S,3*R**,4*R**,5*R**)-2,5-Di(but-3-en-1-yl)-4-[(4-methoxybenzyl)oxy]-2-methyl-6-methyleneoxepan-3-ol [(±)-SI-29]**



To a stirred solution of TBS protected alcohol (±)-**SI-30** (40.2 mg, 80.3 µmol, 1.0 equiv.) in anhydrous THF (1.0 mL) at 0 °C was added a TBAF×$3H_2O$ solution (0.08 mL, 84.3 µmol, 1.05 equiv., 1.0 M in THF). After 15 min at 0 °C to solution was allowed to stir at rt for 2 h (TLC control, PE/MTBE, 3:1, **SI-28:** R_f = 0.30). Then the solution was diluted with MTBE (10 mL) and added to a sat. NH_4Cl solution (10 mL). The organic layer was separated and washed with brine (2 × 10 mL). The organic extract was dried with $MgSO_4$, filtered and the solvent was removed *in vacuo*. Column chromatography of the residue (PE/MTBE, 3:1, 2 × 15 cm) gave alcohol **SI-28** (27.1 mg, 70.1 µmol, 87%) as a colorless oil. During NMR measurements (rt, 14 h) the solution of the alcohol (±)-**SI-28** in C_6D_6 (0.6 mL) rearranged quantitatively to alcohol (±)-**SI-29**.

(±)-**SI-29:**

TLC: R_f = 0.43 (PE/MTBE, 5:1).

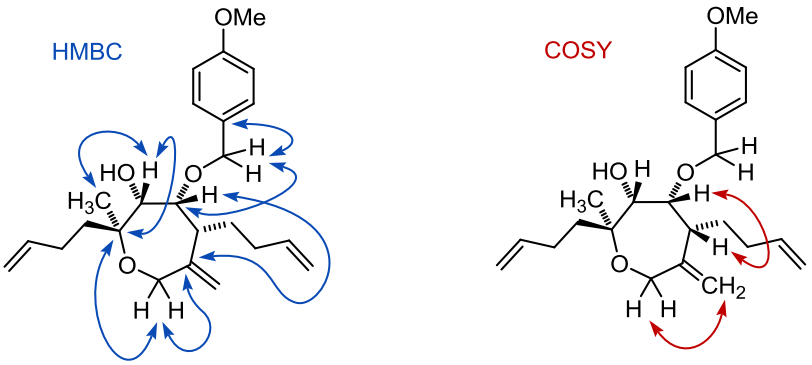
^{1}H NMR (300 MHz, C_6D_6): δ = 7.21–7.13 (*m*, 2H, CH, Ar, overlap with C_6D_5H, see HSQC), 6.82–6.75 (*m*, 2H, CH, Ar), 5.95–5.68 (*m*, 2H, 2 × C(H)═), 5.14–4.96 (*m*, 4H, 2 × ═CH_2), 4.88 (*s*, 1H, OCH_2C═C(H)H'), 4.79 (*s*, 1H, OCH_2C═C(H)H'), 4.48 (*d*, 1H, $^2J_{H,H}$ = 11.3 Hz, OC(H)H'Ar), 4.40–4.29 (*m*, 2H, OC(H)H'Ar + OC(H)H'C═), 4.18 (*d*, 1H, $^2J_{H,H}$ = 14.9 Hz, OC(H)H'C═), 3.65 (*dd*, 1H, $^3J_{H,H}$ = 3.8, 2.5 Hz, C(H)OPMB), 3.55 (*d*, 1H, $^3J_{H,H}$ = 3.8 Hz,

C(H)OH), 3.30 (*s*, 3H, OCH_3), 2.72–2.65 (*m*, 1H, $OCH_2C(=C)CH$), 2.38–2.13 (*m*, 2H, CH_2), 2.12–1.84 (*m*, 4H, 2 × CH_2), 1.82–1.64 (*m*, 2H, CH_2), 1.31 (*s*, 3H, CH_3).

$^{13}C\{^1H\}$ NMR (75 MHz, C_6D_6): δ = 159.9 ($COCH_3$, Ar), 148.0 ($OCH_2C=$), 139.6 (C(H)=), 138.9 (C(H)=), 131.1 (C_{quart}, Ar), 129.3 (CH, Ar), 115.0 ($=CH_2$), 114.3 ($=CH_2$), 114.3 (CH, Ar), 110.1 ($OCH_2C=CH_2$), 82.9 (C(H)OPMB), 79.2 ($C_{quart}CH_3$), 77.9 (C(H)OH), 74.4 (OCH_2Ar), 69.1 ($OCH_2C=$), 54.8 (OCH_3), 44.1 ($OCH_2C(=C)CH$), 40.0 (CH_2), 32.5 (CH_2), 29.9 (CH_2), 28.2 (CH_2), 18.7 (CH_3).

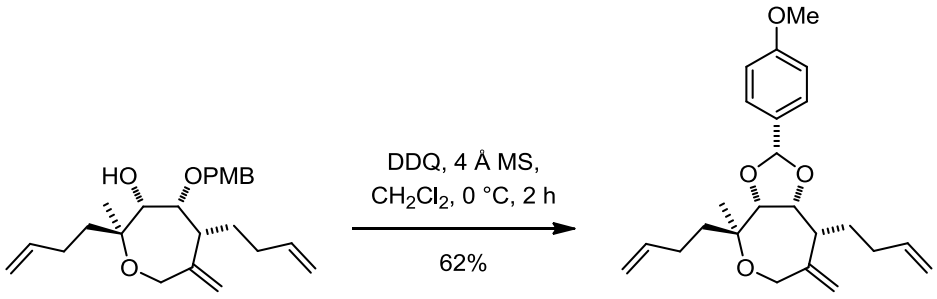
IR (ATR): $\tilde{\nu}$ = 3567 (*w*), 3075 (*w*), 2927 (*m*), 2362 (*m*), 1944 (*w*), 1828 (*w*), 1612 (*m*), 1513 (*m*), 1457 (*m*), 1360 (*m*), 1248 (*s*), 1172 (*m*), 1094 (*s*), 1033 (*s*), 906 (*s*), 821 (*s*), 753 (*s*), 634 (*m*) cm^{-1}.

HRMS (ESI, TOF): m/z calc'd for $C_{24}H_{34}O_4[M+H]^+$ 387.2530; observed 387.2532.



For the corresponding 2D spectra see section 5.

(2*R,3a*R**,4*S**,8*R**,8a*R**)-4,8-Di(but-3-en-1-yl)-2-(4-methoxyphenyl)-4-methyl-7-methylenehexahydro-[1,3]dioxolo[4,5-c]oxepine [(±)-SI-27]**



(±)-**SI-29** (±)-**SI-27**

To a stirred solution of alcohol (±)-**SI-29** (26.0 mg, 67.3 µmol, 1.0 equiv.) and activated powdered 3 Å molecular sieves (70 mg) in anhydrous CH_2Cl_2 (1.5 mL) at 0 °C was added

DDQ (18.3 mg, 80.7 µmol, 1.2 equiv.), whereupon the colorless solution turned first yellow and later green. After 2 h at this temperature (TLC control, PE/MTBE, 10:1) the brown suspension was directly subjected to column chromatography (PE/Et_2O, 10:1, 2 × 15 cm). The acetal (±)-**SI-27** (14.5 mg, 41.6 µmol, 62%) was obtained as colorless oil.

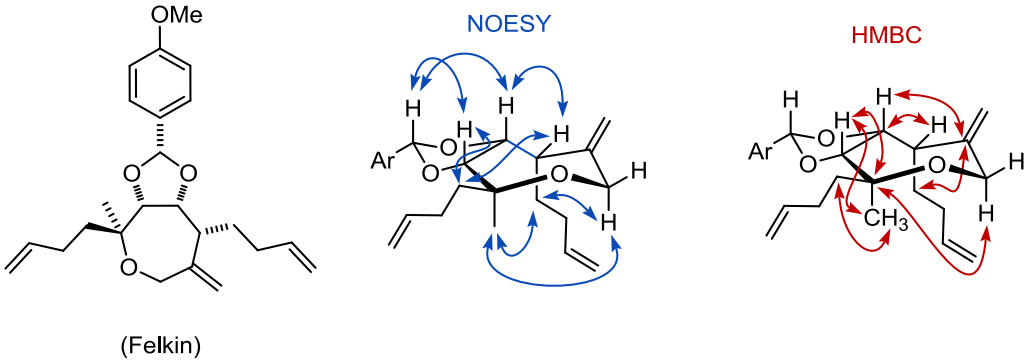
TLC: R_f = 0.30 (PE/Et_2O, 10:1).

^{1}H NMR (300 MHz, C_6D_6): δ = 7.60–7.53 (*m*, 2H, CH, Ar), 6.84–6.77 (*m*, 2H, CH, Ar), 5.92–5.67 (*m*, 2H, 2 × C(H)═), 5.64 (*s*, 1H, $(RO)_2CHAr$), 5.14–4.95 (*m*, 4H, 2 × $=CH_2$), 4.89–4.85 (*m*, 2H, $OCH_2C=C\underline{H}_2$), 4.58 (*d*, 1H, $^2J_{H,H}$ = 15.2 Hz, OC(H)H'C═), 4.24–4.14 (*m*, 2H, OC(H)H'C═ + (═C)CHCHO), 3.76 (*d*, 1H, $^3J_{H,H}$ = 7.1 Hz, $C_{quart}C(H)O$), 3.27 (*s*, 3H, OCH_3), 2.88–2.79 (*m*, 1H, $OCH_2C(=C)C\underline{H}$), 2.37–2.17 (*m*, 2H, $C_{quart}CH_2C\underline{H}_2$), 2.16–2.04 (*m*, 2H, $OCH_2C(=C)CHCH_2C\underline{H}_2$), 1.94–1.80 (*m*, 2H, $OCH_2C(=C)CHC\underline{H}_2$), 1.78–1.54 (*m*, 2H, $C_{quart}CH_2$), 1.33 (*s*, 3H, CH_3).

^{13}C{^{1}H} NMR (75 MHz, C_6D_6): δ = 160.8 ($\underline{C}OCH_3$, Ar), 148.4 ($OCH_2\underline{C}$═), 139.2 (C(H)═), 139.0 (C(H)═), 130.2 (C_{quart}, Ar), 128.8 (CH, Ar), 115.0 ($=CH_2$), 114.6 ($=CH_2$), 113.8 (CH, Ar), 109.4 ($OCH_2C=\underline{C}H_2$), 102.7 $(RO)_2CHAr$), 84.0 ($C_{quart}\underline{C}HO$), 79.2 ((═C)CH$\underline{C}$HO), 77.6 ($\underline{C}_{quart}CH_3$), 68.2 ($O\underline{C}H_2C$═), 54.8 ($OCH_3$), 41.4 ($C_{quart}\underline{C}H_2$), 40.5 ($OCH_2C(=C)\underline{C}H$), 31.8 ($OCH_2C(=C)CHCH_2\underline{C}H_2$), 28.8 ($OCH_2C(=C)$–$CH\underline{C}H_2$), 28.2 ($C_{quart}CH_2\underline{C}H_2$), 20.6 ($CH_3$).

IR (ATR): $\tilde{\nu}$ = 3650 (*w*), 3568 (*w*), 3076 (*w*), 2924 (*m*), 2362 (*m*), 1920 (*w*), 1829 (*w*), 1717 (*w*), 1615 (*m*), 1514 (*m*), 1399 (*m*), 1304 (*m*), 1251 (*s*), 1171 (*m*), 1071 (*s*), 1002 (*s*), 908 (*s*), 827 (*s*), 634 (*m*) cm^{-1}.

HRMS (APCI, Orbitrap): m/z calc'd for $C_{24}H_{32}O_4[M+H]^+$ 385.2373; observed 385.2376.

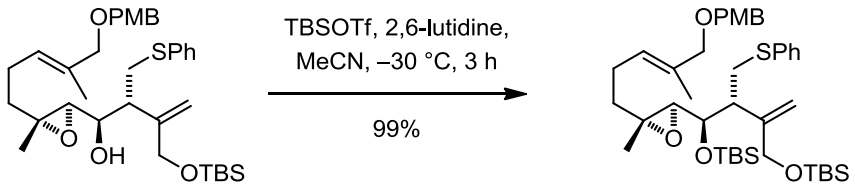


(Felkin)

For the corresponding 2D spectra see section 5.

3.4 Synthesis of parthenolides

(5*R*,6*R*)-5-{(2*R*,3*R*)-3-{(*E*)-5-[(4-Methoxybenzyl)oxy]-4-methylpent-3-en-1-yl}-3-methyloxiran-2-yl}-2,2,3,3,10,10,11,11-octamethyl-7-methylene-6-[(phenylthio)methyl]-4,9-dioxa-3,10-disiladodecane [(+)-17 and (±)-17]



(+)-**16g**
(±)-**16g**

(+)-**17**
(±)-**17**

TBSOTf (0.55 mL, 637 mg, 2.41 mmol, 1.0 equiv.) was added to a stirred solution of 2,6-lutidine (0.84 mL, 776 mg, 7.24 mmol, 3.0 equiv.) in anhydrous MeCN (18 mL) at –30 °C. After 10 min a solution of alcohol (±)-**16g** (1.48 g, 2.41 mmol, 1.0 equiv.) in anhydrous MeCN (6.0 mL) was added dropwise and the solution was allowed to stir for 3 h at this temperature (TLC control, PE/MTBE, 4:1). The solution was added to a stirred sat. $NaHCO_3$ solution (120 mL) at 0 °C and extracted with MTBE (100 mL). The combined organic layers were washed consecutively with sat. $CuSO_4$ solution (3 × 30 mL), a Na_2EDTA solution (2 × 50 mL, 0.2 M, pH 8) and brine (2 × 50 mL). The organic extract was dried with $MgSO_4$, filtered and concentrated *in vacuo*. Column chromatography of the residue (PE/Et_2O, 9:1, 4 × 25 cm) provided TBS ether (±)-**17** (1.74 g, 2.39 mmol, 99%) as a colorless oil.

Under the same conditions alcohol (+)-**16g** (2.09 g, 3.41 mmol) was converted to the TBS ether (+)-**17**, yielding 2.09 g (2.87 mmol, 84%) of a colorless oil.

TLC: R_f = 0.30 (PE/Et_2O, 9:1).

$[\alpha]_D^{23}$ = +14.8 (*c* = 1.0, THF, 92% *ee*).

^{1}H NMR (300 MHz, C_6D_6): δ = 7.38–7.32 (*m*, 2H, CH, Ar), 7.31–7.25 (*m*, 2H, CH, Ar), 7.05–6.97 (*m*, 2H, CH, Ar), 6.93–6.86 (*m*, 1H, CH, Ar), 6.84–6.79 (*m*, 2H, CH, Ar), 5.69 (*d*, 1H, $^2J_{H,H}$ = 1.8 Hz, =C(H)H'), 5.53 (*d*, 1H, $^2J_{H,H}$ = 1.8 Hz, =C(H)H'), 5.40 (*t*, 1H, $^3J_{H,H}$ = 6.6 Hz, $CH_2C(H)=CR_2$), 4.42 (*s*, 2H, CH_2O), 4.36 (*s*, 2H, CH_2O), 4.22 (*dd*, 1H, $^3J_{H,H}$ = 7.9, 2.8 Hz, C(H)OSi), 3.84 (*s*, 2H, CH_2O), 3.39–3.21 (*m*, 5H, OCH_3 + CH_2S), 2.86 (*d*, 1H, $^3J_{H,H}$ = 7.9 Hz, C(O)CH, epoxide), 2.76–2.67 (*m*, 1H, C(H)C(R)=CH_2), 2.19–2.08 (*m*, 2H, CH_2), 1.66 (*s*, 3H, CH_3), 1.64–1.51 (*m*, 1H, C(H)H'), 1.48–1.26 (*m*, 1H, C(H)H'), 1.20 (*s*,

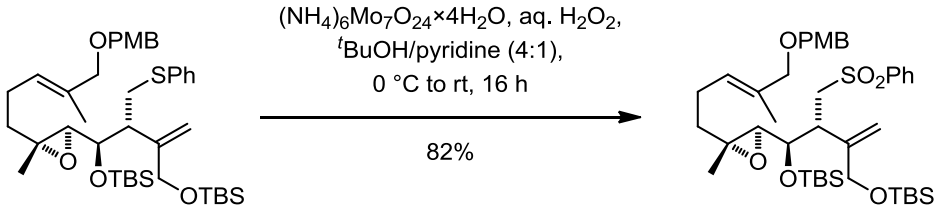
3H, CH_3), 1.00 (*s*, 9H, $SiC(CH_3)_3$), 0.98 (*s*, 9H, $SiC(CH_3)_3$), 0.17 (*s*, 3H, $Si(C\underline{H}_3)(CH_3)$'), 0.13 (*m*, 6H, $Si(CH_3)_2$), 0.08 (*s*, 3H, $Si(CH_3)(C\underline{H}_3)$').

$^{13}C\{^1H\}$ NMR (75 MHz, C_6D_6): δ = 159.7 ($\underline{C}OCH_3$), 147.5 (R_2C═), 137.1 (R_2C═), 133.3 (C_{quart}, Ar), 131.4 (C_{quart}, Ar), 129.6 (CH, Ar), 129.5 (CH, Ar), 129.3 (CH, Ar), 126.9 ($CH_2\underline{C}(H)$═CR_2), 126.2 (CH, Ar), 114.1 (CH, Ar), 112.7 (═CH_2), 75.9 (CH_2O), 71.5 (CH_2O), 69.3 (C(H)OSi), 66.1 (CH_2O), 64.3 (C(O)$\underline{C}$H, epoxide), 61.7 ($\underline{C}$(O)CH, epoxide), 54.8 (OCH_3), 45.1 ($\underline{C}$(H)C(R)═CH_2), 38.0 (CH_2), 36.0 (CH_2S), 26.2 ($SiC(\underline{C}H_3)_3$), 26.1 ($SiC(\underline{C}H_3)_3$), 23.4 (CH_2), 18.6 ($Si\underline{C}(CH_3)_3$), 18.4 ($Si\underline{C}(CH_3)_3$), 17.6 (CH_3), 14.0 (CH_3), –3.8 ($Si(\underline{C}H_3)(CH_3)$'), –4.4 ($Si(CH_3)(\underline{C}H_3)$'), –5.1 ($Si(CH_3)_2$).

IR (ATR): $\tilde{\nu}$ = 3855 (*w*), 3735 (*w*), 3650 (*w*), 3568 (*w*), 3063 (*w*), 2929 (*m*), 2855 (*m*), 2361 (*m*), 1700 (*w*), 1612 (*w*), 1512 (*m*), 1460 (*m*), 1360 (*w*), 1252 (*s*), 1171 (*m*), 1090 (*s*), 938 (*m*), 835 (*s*), 773 (*s*), 690 (*m*) cm^{-1}.

HRMS (APCI, Orbitrap): m/z calc'd for $C_{41}H_{66}O_5SSi_2$ $[M+H]^+$ 727.4242; observed 727.4238.

(5*R*,6*R*)-5-{(2*R*,3*R*)-3-{(*E*)-5-[(4-Methoxybenzyl)oxy]-4-methylpent-3-en-1-yl}-3-methyloxiran-2-yl}-2,2,3,3,10,10,11,11-octamethyl-7-methylene-6-[(phenylsulfonyl)-methyl]-4,9-dioxa-3,10-disiladodecane [(+)-18 and (±)-18]



(+)-**17**
(±)-**17**

(+)-**18**
(±)-**18**

Thioether (±)-**17** (1.74 g, 2.39 mmol, 1.0 equiv.) was dissolved in ^{t}BuOH (12 mL) and pyridine (3.0 mL) open to air and cooled to 0 °C. $(NH_4)_6Mo_7O_{24}\times4H_2O$ (1.77 g, 1.43 mmol, 0.6 equiv.) was added in one portion, followed by aq. H_2O_2 (3.0 mL, ~30*w*-%). The suspension was allowed to warm to rt over 6 h. After additional 10 h (TLC control, PE/EtOAc, 3:1) a mixture of sat. Na_2SO_3 solution (20 mL) and sat. $NaHCO_3$ solution (10 mL) was added slowly to the yellow suspension at 0 °C. EtOAc (40 mL) was added and the biphasic mixture was stirred for 10 min. The organic layer was separated and washed consecutively with sat. $CuSO_4$ solution (2 × 30 mL), a Na_2EDTA solution (2 × 30 mL, 0.2 M, pH 8) and brine (2 × 30 mL). The organic extract was dried with $MgSO_4$, filtered and

concentrated *in vacuo*. Column chromatography of the residue (PE/EtOAc, 7:1→5:1, 3 × 15 cm) provided the sulfone (±)-**18** (1.49 g, 1.96 mmol, 82%) as a colorless oil.

Under the same conditions thioether (+)-**17** (2.07 g, 2.85 mmol) was converted to sulfone (+)-**18**, yielding 2.07 g (2.72 mmol, 95%) of a colorless oil.

TLC: R_f = 0.39 (PE/EtOAc, 5:1).

$[\alpha]_D^{23}$ = +20.1 (*c* = 1.0, THF, 92% *ee*).

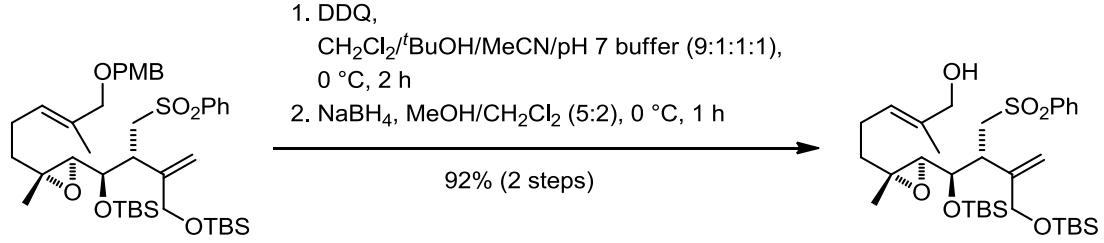
^{1}H NMR (300 MHz, C_6D_6): δ = 7.87–7.80 (*m*, 2H, CH, Ar), 7.32–7.23 (*m*, 2H, CH, Ar), 6.96–6.86 (*m*, 3H, CH, Ar), 6.86–6.79 (*m*, 2H, CH, Ar), 5.53 (*d*, 1H, $^2J_{H,H}$ = 1.7 Hz, ═C(H)H'), 5.44–5.34 (*m*, 2H, $CH_2C(H)$═CR_2 + ═C(H)H'), 4.49 (*dd*, 1H, $^3J_{H,H}$ = 7.8, 2.7 Hz, C(H)OSi), 4.37 (*s*, 2H, CH_2O), 4.35–4.21 (*m*, 2H, CH_2OSi), 3.84 (*s*, 2H, CH_2O), 3.83–3.73 (*m*, 1H, C(H)H'S), 3.31 (*s*, 3H, OCH_3), 3.24–3.14 (*m*, 2H, C(H)H'S + $C(H)C(R)$═CH_2), 2.80 (*d*, 1H, $^3J_{H,H}$ = 7.8 Hz, C(O)CH, epoxide), 2.19–2.08 (*m*, 2H, CH_2), 1.66 (*s*, 3H, CH_3), 1.62–1.52 (*m*, 1H, C(H)H'), 1.46–1.35 (*m*, 1H, C(H)H'), 1.30 (*s*, 3H, CH_3), 0.99 (*s*, 9H, $SiC(CH_3)_3$), 0.96 (*s*, 9H, $SiC(CH_3)_3$), 0.29 (*s*, 3H, $Si(CH_3)(CH_3)$'), 0.11 (*s*, 3H, $Si(CH_3)(CH_3)$'), 0.08–0.07 (*m*, 6H, $Si(CH_3)(CH_3)$').

^{13}C{^{1}H} NMR (75 MHz, C_6D_6): δ = 159.7 ($COCH_3$), 146.6 (R_2C═), 140.8 (SC_{quart}), 133.3 (C_{quart}, Ar), 133.2 (CH, Ar), 131.4 (R_2C═), 129.5 (CH, Ar), 129.2 (CH, Ar), 127.9 (CH, Ar), 126.9 ($CH_2C(H)$═CR_2), 114.1 (CH, Ar), 113.5 (═CH_2), 75.9 (CH_2O), 71.5 (CH_2O), 69.9 (C(H)OSi), 65.8 (CH_2OSi), 64.3 (C(O)CH, epoxide), 62.0 (C(O)CH, epoxide), 57.4 (CH_2S), 54.8 (OCH_3), 40.7 ($C(H)C(R)$═CH_2), 37.9 (CH_2), 26.2 ($SiC(CH_3)_3$), 26.1 ($SiC(CH_3)_3$), 23.4 (CH_2), 18.6 ($SiC(CH_3)_3$), 18.4 ($SiC(CH_3)_3$), 17.6 (CH_3), 14.0 (CH_3), –3.9 ($Si(CH_3)(CH_3)$'), –4.3 ($Si(CH_3)(CH_3)$'), –5.3 ($Si(CH_3)_2$).

IR (ATR): $\tilde{\nu}$ = 3855 (*w*), 3736 (*w*), 3649 (*w*), 3567 (*w*), 2930 (*m*), 2855 (*m*), 2361 (*m*), 1612 (*w*), 1512 (*m*), 1458 (*m*), 1387 (*m*), 1304 (*m*), 1252 (*m*), 1086 (*m*), 908 (*m*), 835 (*s*), 750 (*s*), 689 (*m*) cm^{-1}.

HRMS (APCI, Orbitrap): m/z calc'd for $C_{41}H_{66}O_7SSi_2$ $[M+H]^+$ 759.4141; observed 759.4117.

(*E*)-2-Methyl-5-{(2*R,3*R**)-2-methyl-3-{(5*R**,6*R**)-2,2,3,3,10,10,11,11-octamethyl-7-methylene-6-[(phenylsulfonyl)methyl]-4,9-dioxa-3,10-disiladodecan-5-yl}oxiran-2-yl}pent-2-en-1-ol [(–)-SI-31 and (±)-SI-31]**



(+)-**18**
(±)-**18**

(–)-**SI-31**
(±)-**SI-31**

To a stirred solution of PMB ether (±)-**18** (1.49 g, 1.96 mmol, 1.0 equiv.) in a mixture of CH_2Cl_2 (36 mL), ^{t}BuOH (4.0 mL), MeCN (4.0 mL) and pH 7 phosphate buffer (4.0 mL, 0.5 M) was added DDQ (890 mg, 3.92 mmol, 2.0 equiv.) in 6 portions, every 2 min at 0 °C. After 6 h at this temperature (TLC control, PE/EtOAc, 3:1) the mixture was filtered and the filtrate was stirred with sat. $NaHCO_3$ solution (20 mL) for 20 min until all solids dissolved and the solution turned completely red. Additional sat. $NaHCO_3$ solution (100 mL) was added and the mixture was extracted with MTBE/PE (2:1, 300 mL). The organic layer was washed with sat. $NaHCO_3$ solution (100 mL) and brine (200 mL), dried with $MgSO_4$, filtered and the solvent was removed *in vacuo*. The residual oil was taken up in anhydrous MeOH/CH_2Cl_2 (5:2, 40 mL) and cooled to 0 °C. $NaBH_4$ (111 mg, 2.94 mmol, 1.5 equiv.) was added in one portion under stirring and the mixture was kept at this temperature for 1 h (TLC control, PE/EtOAc, 2:1) followed by addition of sat. NH_4Cl solution (100 mL) and CH_2Cl_2 (100 mL). The organic layer was separated, washed with sat. $NaHCO_3$ solution (100 mL) and brine (100 mL), dried with $MgSO_4$, filtered and concentrated *in vacuo*. Column chromatography of the residue (PE/MTBE, 2:1, 4 × 35 cm) provided the allyl alcohol (±)-**SI-31** (1.15 g, 1.80 mmol, 92%) as a colorless oil.

Under the same conditions PMB protected alcohol (+)-**18** (2.0 g, 2.63 mmol) was converted to alcohol (–)-**SI-31**, yielding 1.54 g (2.41 mmol, 92%) of a colorless oil.

TLC: R_f = 0.26 (PE/EtOAc, 3:1).

$[\alpha]_D^{23}$ = –15.3 (*c* = 1.0, THF, 92% *ee*).

^{1}H NMR (300 MHz, C_6D_6): δ = 7.90–7.77 (*m*, 2H, CH, Ph), 6.97–6.82 (*m*, 3H, CH, Ph), 5.53 (*s*, 1H, =C(H)H'), 5.36 (*s*, 1H, =C(H)H'), 5.26 (*t*, 1H, $^3J_{H,H}$ = 7.0 Hz, $CH_2C(H)=CR_2$),

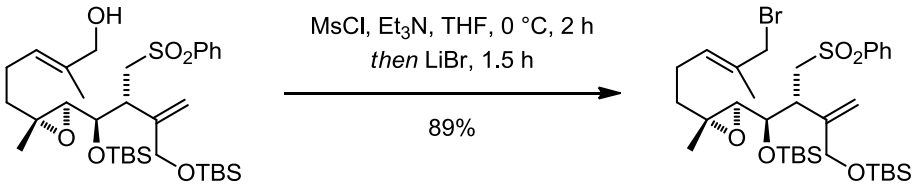
4.51 (*dd*, 1H, $^{3}J_{H,H}$ = 7.8, 2.4 Hz, C(H)OSi), 4.33 (*d*, 1H, $^{2}J_{H,H}$ = 15.0 Hz, C(H)H'OSi), 4.25 (*d*, 1H, $^{2}J_{H,H}$ = 15.0 Hz, C(H)H'OSi), 3.86–3.69 (m, 3H, C(H)H'S + CH_2OH), 3.24–3.11 (m, 2H, C(H)H'S + OH), 2.81 (*d*, 1H, $^{3}J_{H,H}$ = 7.8 Hz, C(O)CH, epoxide), 2.17–1.99 (*m*, 2H, CH_2), 1.61–1.50 (*m*, 4H, CH_3 + C(H)H'), 1.47–1.35 (*m*, 1H, C(H)H'), 1.31 (*s*, 3H, CH_3), 0.99 (*s*, 9H, $SiC(CH_3)_3$), 0.96 (*s*, 9H, $SiC(CH_3)_3$), 0.30 (*s*, 3H, $Si(CH_3)(CH_3)$'), 0.12 (*s*, 3H, $Si(CH_3)(CH_3)$'), 0.08 (*s*, 6H, $Si(CH_3)_2$).

$^{13}C\{^{1}H\}$ NMR (75 MHz, C_6D_6): δ = 146.6 (R_2C═), 140.8 (SC_{quart}), 135.8 (R_2C═), 133.2 (CH, Ph), 129.2 ($CH_2C(H)$═CR_2), 128.2 (CH, Ph), 124.6 (CH, Ph), 113.5 (═CH_2), 69.9 (C(H)OSi), 68.5 (CH_2OH), 65.8 (CH_2OSi), 64.3 (C(O)CH, epoxide), 62.0 (C(O)CH, epoxide), 57.4 (CH_2S), 40.7 (C(H)C(R)═CH_2), 37.9 (CH_2), 26.2 ($SiC(CH_3)_3$), 26.1 ($SiC(CH_3)_3$), 23.3 (CH_2), 18.6 ($SiC(CH_3)_3$), 18.4 ($SiC(CH_3)_3$), 17.7 (CH_3), 13.5 (CH_3), –3.9 ($Si(CH_3)(CH_3)$'), –4.3 ($Si(CH_3)(CH_3)$'), –5.3 ($Si(CH_3)_2$).

IR (ATR): $\tilde{\nu}$ = 3735 (*w*), 3649 (*w*), 3567 (*w*), 2930 (*m*), 2856 (*m*), 2361 (*m*), 2060 (*w*), 1920 (*m*), 1649 (*m*), 1458 (*m*), 1387 (*m*), 1305 (*m*), 1254 (*m*), 1087 (*s*), 1003 (*m*), 909 (*m*), 836 (*s*), 751 (*s*), 689 (*m*) cm^{-1}.

HRMS (ESI, Orbitrap): m/z calc'd for $C_{33}H_{58}O_6SSi_2$ $[M+Na]^+$ 661.3385; observed 661.3370.

(5*R*,6*R*)-5-{(2*R*,3*R*)-3-[(*E*)-5-Bromo-4-methylpent-3-en-1-yl]-3-methyloxiran-2-yl}-2,2,3,3,10,10,11,11-octamethyl-7-methylene-6-[(phenylsulfonyl)methyl]-4,9-dioxa-3,10-disiladodecane [(–)-9 and (±)-9]



(–)-**SI-31**
(±)-**SI-31**

(–)-**9**
(±)-**9**

To a stirred solution of anhydrous Et_3N (0.24 mL, 178 mg, 1.76 mmol, 1.20 equiv.) in anhydrous THF (10 mL) at 0 °C was added MsCl (0.12 mL, 177 mg, 1.54 mmol, 1.05 equiv.). After 5 min a solution of allyl alcohol (±)-**SI-31** (940 mg, 1.47 mmol, 1.0 equiv.) in anhydrous THF (5.0 mL) was added and the suspension was stirred for 2 h. Then anhydrous LiBr (1.28 g, 14.7 mmol, 10.0 equiv.) in anhydrous THF (14.7 mL; stored as 1.0 M stock solution with 4 Å molecular sieves) was added at 0 °C and the mixture was stirred for another 1.5 h (TLC control, PE/EtOAc, 3:1). pH 7 phosphate buffer (30 mL, 0.5 M) was added to

terminate the reaction. The mixture was extracted with MTBE (60 mL) and the extract was washed with brine (2 × 30 mL), dried with $MgSO_4$ and filtered. Toluene (3.0 mL) was added and the solution was concentrated *in vacuo*. Column chromatography of the residue (PE→PE/MTBE, 7:1, 3 × 15 cm) provided the allyl bromide (±)-**9** (922 mg, 1.31 mmol, 89%) as a colorless oil which solidified slowly upon storage at –25 °C to give a colorless solid.
Crystals suitable for X-ray analysis were obtained by slow (complete) evaporation of a saturated solution in *n*-heptane/C_6H_6 (5:1) at rt.

Under the same conditions alcohol (–)-**SI-31** (1.43 g, 2.24 mmol) was converted to bromide (–)-**9**, yielding 1.38 g (1.96 mmol, 88%) of a colorless oil.

TLC: R_f = 0.34 (PE/MTBE, 9:1).

Mp.: 88–90 °C [MTBE, (±)-**9**].

$[\alpha]_D^{23}$ = –10.9 (*c* = 1.0, THF, 92% *ee*).

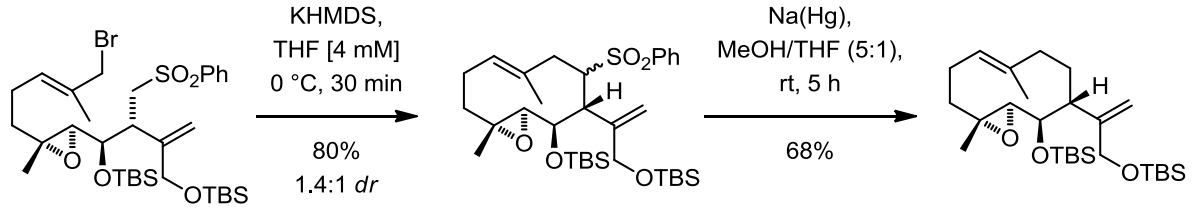
^{1}H NMR (300 MHz, C_6D_6): δ = 7.82 (*dd*, 2H, $^{3,4}J_{H,H}$ = 7.6, 1.6 Hz, CH, Ph), 6.98–6.86 (*m*, 3H, CH, Ph), 5.51 (*d*, 1H, $^4J_{H,H}$ = 1.6 Hz, ═C(H)H'), 5.34 (*d*, 1H, $^4J_{H,H}$ = 1.3 Hz, ═C(H)H'), 5.19 (*t*, 1H, $^3J_{H,H}$ = 7.0 Hz, $CH_2C(H)═CR_2$), 4.46 (*dd*, 1H, $^3J_{H,H}$ = 7.8, 2.7 Hz, C(H)OSi), 4.30 (*d*, 1H, $^2J_{H,H}$ = 15.0 Hz, C(H)H'OSi), 4.22 (*d*, 1H, $^2J_{H,H}$ = 15.0 Hz, C(H)H'OSi), 3.75 (*dd*, 1H, $^{2,3}J_{H,H}$ = 14.8, 10.3 Hz, C(H)H'S), 3.61 (*s*, 2H, CH_2Br), 3.22–3.11 (*m*, 2H, C(H)H'S + $C(H)C(R)═CH_2$), 2.73 (*d*, 1H, $^3J_{H,H}$ = 7.8 Hz, C(O)CH, epoxide), 1.97–1.85 (*m*, 2H, CH_2), 1.55 (*s*, 3H, CH_3), 1.48–1.33 (*m*, 1H, C(H)H'), 1.29–1.14 (*m*, 4H, CH_3 + C(H)H'), 0.99–0.93 (*m*, 18H, 2 × $SiC(CH_3)_3$), 0.28 (*s*, 3H, $Si(CH_3)(CH_3)$'), 0.11–0.04 (*m*, 9H, $Si(CH_3)(CH_3)$' + $Si(CH_3)_2$).

^{13}C{^{1}H} NMR (75 MHz, C_6D_6): δ = 146.5 ($R_2C═$), 140.7 (SC_{quart}), 133.3 (CH, Ph), 132.6 ($R_2C═$), 130.4 ($CH_2C(H)═CR_2$), 129.3 (CH, Ph), 128.2 (CH, Ph), 113.5 ($═CH_2$), 69.9 (C(H)OSi), 65.8 (CH_2OSi), 64.3 (C(O)CH, epoxide), 61.8 (C(O)CH, epoxide), 57.4 (CH_2S), 41.2 (CH_2Br), 40.6 ($C(H)C(R)═CH_2$), 37.1 (CH_2), 26.2 ($SiC(CH_3)_3$), 26.1 ($SiC(CH_3)_3$), 23.8 (CH_2), 18.6 ($SiC(CH_3)_3$), 18.4 ($SiC(CH_3)_3$), 17.6 (CH_3), 14.5 (CH_3), –3.9 ($Si(CH_3)(CH_3)$'), –4.4 ($Si(CH_3)(CH_3)$'), –5.2 ($Si(CH_3)_2$).

IR (ATR): $\tilde{\nu}$ = 3839 (*w*), 3736 (*w*), 3649 (*w*), 3567 (*w*), 2932 (*m*), 2857 (*m*), 2712 (*w*), 2361 (*m*), 1699 (*w*), 1653 (*w*), 1460 (*m*), 1391 (*m*), 1253 (*m*), 1150 (*s*), 1085 (*s*), 1001 (*m*), 936 (*m*), 840 (*s*), 774 (*s*) cm^{-1}.

HRMS (ESI, TOF): m/z calc'd for $C_{33}H_{57}BrO_5SSi_2$ $[M+Na]^+$ 725.2526 (100%), 723.2541 (83%); observed 725.2525 (100%), 723.2539 (83%).

***tert*-Butyl{{2-{(1*R**,2*R**,3*R**,10*R**,*E*)-2-[(*tert*-butyldimethylsilyl)oxy]-6,10-dimethyl-11-oxabicyclo[8.1.0]undec-6-en-3-yl}allyl}oxy}dimethylsilane [(+)-20 and (±)-20]**



(–)-**9**
(±)-**9**

19a,b
(±)-**19a,b**

(+)-**20**
(±)-**20**

To a stirred solution of a KHMDS solution (0.57 mL, 0.57 mmol, 4.0 equiv., 1.0 M in THF) in anhydrous THF (33 mL) at 0 °C was added a solution of sulfone (±)-**9** (110 mg, 0.16 mmol, 1.0 equiv.) in anhydrous THF (7.0 mL) over 15 min using a syringe pump (0.46 mL/min). After another 15 min (TLC control, PE/MTBE, 4:1) the reaction was terminated by addition of sat. NH_4Cl solution (30 mL), followed by Et_2O (90 mL). The organic layer was separated, washed with sat. $NaHCO_3$ solution (90 mL) and brine (90 mL), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. After column chromatography (PE/MTBE, 4:1, 2 × 30 cm) the separable diastereomeric sulfones (±)-**19a** and (±)-**19b** were combined to yield a colorless glass, which was taken further to the next step. Yield in total: 77.8 mg, 0.13 mmol, 80%.

Under the same conditions, but divided into 9 separate transformation, sulfone (–)-**9** (1.37 g, 1.95 mmol) was converted to the ten-membered ring sulfones **19a,b**, yielding 762 mg (1.22 mmol, 63%) of a colorless glass.

19a: TLC: R_f = 0.67 (PE/MTBE, 4:1).

19b: TLC: R_f = 0.31 (PE/MTBE, 4:1).

HRMS (ESI, Orbitrap): m/z calc'd for $C_{33}H_{56}NaO_5SSi_2$ $[M+Na]^+$ 643.3279; observed 643.3274.

To a strongly stirred suspension of the diastereomeric sulfones (±)-**19a** and (±)-**19b** (230 mg, 0.37 mmol, 1.0 equiv.) in a 5:1 mixture of anhydrous MeOH and THF (2.0 mL) at rt was

added 5% Na(Hg) (1.71 g, 3.70 mmol Na, 10.0 equiv.) in one portion *[Note: Consistent yields were obtained with Na(Hg) pieces <3 mm size (hammered)]*. After 1.5 h (TLC control, PE/MTBE, 6:1) the suspension was filtered through a plug of Celite (MTBE, 20 mL) into stirred pH 7 phosphate buffer (20 mL, 0.5 M) at 0 °C. After 5 min the organic layer was separated, washed with sat. $NaHCO_3$ solution (20 mL) and brine (20 mL), dried with $MgSO_4$, filtered and concentrated *in vacuo*. Column chromatography of the residue (PE/MTBE, 15:1, 3 × 25 cm) provided the protected epoxy alcohol (±)-**20** (120 mg, 0.25 mmol, 68%) as a colorless oil.

Under the same conditions sulfones **19a,b** (762 mg, 1.22 mmol) were converted to protected epoxy alcohol (+)-**20**, yielding 411 mg (0.85 mmol, 70%) of a colorless oil.

TLC: R_f = 0.40 (PE/MTBE, 20:1).

$[\alpha]_D^{22}$ = +34.4 (*c* = 1.0, THF, 92% *ee*).

^{1}H NMR (300 MHz, C_6D_6): δ = 5.40 (*s*, 1H, ═C(H)H'), 5.06 (*br s*, 1H, C(H)═), 4.95 (*s*, ═C(H)H'), 4.29 (*d*, 1H, $^2J_{H,H}$ = 13.7 Hz, C(H)H'OSi), 4.21 (*d*, 1H, $^2J_{H,H}$ = 13.7 Hz, C(H)H'OSi), 3.94 (*dd*, 1H, $^3J_{H,H}$ = 10.6, 3.3 Hz, C(H)OSi), 2.51 (*d*, 1H, $^3J_{H,H}$ = 3.3 Hz, C(O)CH, epoxide), 2.14–1.95 (*m*, 3H, CH_2 + C(H)C(R)═CH_2), 1.93–1.83 (*m*, 1H, C(H)H'), 1.80–1.68 (*m*, 1H, C(H)H'), 1.54 (*s*, 3H, CH_3), 1.48–1.38 (*m*, 4H, C(H)H' + CH_3), 1.09–0.99 (*m*, 19H, C(H)H' + 2 × $SiC(CH_3)_3$), 0.33 (*s*, 3H, $Si(CH_3)(CH_3)_2$'), 0.17 (*s*, 3H, $Si(CH_3)(CH_3)_2$'), 0.12 (*s*, 6H, $Si(CH_3)_2$).

The signal for one CH_2 group could not be detected.

^{13}C{^{1}H} NMR (75 MHz, C_6D_6): δ = 153.7 (R_2C═), 135.1 (*br*, R_2C═), 125.2 (*br*, C(H)═CR_2), 110.1 (═CH_2), 74.3 (C(H)OSi), 67.9 (CH_2OSi), 64.9 (C(O)CH, epoxide), 59.6 (C(O)CH, epoxide), 45.6 (C(H)C(R)═CH_2), 38.7 (*br*, CH_2), 32.9 (*br*, CH_2), 26.6 ($SiC(CH_3)_3$), 26.2 ($SiC(CH_3)_3$), 24.2 (*br*, CH_2), 20.1 (*br*, ═C(R)CH_3), 18.9 ($SiC(CH_3)_3$), 18.6 ($SiC(CH_3)_3$), 15.8 (CH_3), –3.3 ($Si(CH_3)(CH_3)_2$'), –4.8 ($Si(CH_3)(CH_3)_2$'), –5.1 ($Si(CH_3)(CH_3)_2$'), –5.2 ($Si(CH_3)(CH_3)_2$').

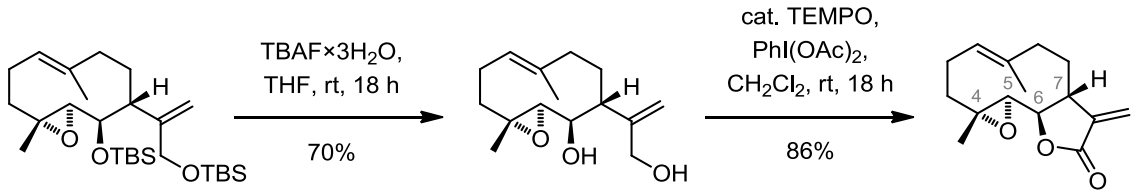
The signal for one CH_2 group could not be detected.

IR (ATR): $\tilde{\nu}$ = 3855 (*w*), 3736 (*w*), 3649 (*w*), 3567 (*w*), 2929 (*m*), 2856 (*m*), 2709 (*w*), 2362 (*m*), 2165 (*w*), 1919 (*w*), 1651 (*m*), 1459 (*m*), 1361 (*m*), 1251 (*m*), 1099 (*m*), 963 (*m*), 835 (*s*), 772 (*s*), 669 (*m*) cm^{-1}.

MS (GC, EI): m/z 423.3 $[M-{}^tBu]^+$.

HRMS: No molecular ion peak detectable (collected HPLC fraction, ionization modes: ESI, APCI, EI).

(4*R*,5*R*,6*R*,7*R*)-*dia*-Parthenolide [(+)-22 and (±)-22]



(+)-**20**
(±)-**20**

21
(±)-**21**

(+)-**22**
(±)-**22**

To a stirred solution of TBS protected diol (±)-**20** (30.0 mg, 62.4 μmol, 1.0 equiv.) in anhydrous THF (2.0 mL) at rt was added a TBAF×3H_2O solution (0.13 mL, 0.13 mmol, 2.0 equiv., 1.0 M in THF). After 18 h (TLC control, MTBE/PE, 2:1) the mixture was diluted with Et_2O (20 mL) and washed with pH 7 phosphate buffer (20 mL), sat. $NaHCO_3$ solution (20 mL) and brine (3 × 10 mL). The organic layer was then dried with $MgSO_4$, filtered and concentrated *in vacuo*. Column chromatography of the residue (MTBE/PE, 3:1, 2 × 20 cm) gave the unstable epoxy diol (±)-**21** (11.0 mg, 43.6 μmol, 70%) as a colorless oil.

TLC: R_f = 0.25 (MTBE/PE, 2:1).

The diol **21** was dissolved in anhydrous CH_2Cl_2 (0.5 mL) and TEMPO (2.05 mg, 13.1 μmol, 0.3 equiv.) was added at rt with stirring, followed by $PhI(OAc)_2$ (41.9 mg, 0.13 mmol, 3.0 equiv.). After 18 h (TLC control, PE/EtOAc, 2:1) the mixture was diluted with PE (1 mL) and directly subjected to column chromatography (PE/EtOAc, 3:1, 2 × 20 cm), obtaining (4*R**,5*R**,6*R**,7*R**)-*dia*-parthenolide[S5] (±)-**22** (9.3 mg, 37.5 μmol, 86%) as a colorless solid. Milligram amounts of the pure enantiomers (4*R*,5*R*,6*R*,7*R*)-**22** and (4*S*,5*S*,6*S*,7*S*)-**22** were obtained by multi-run separation on a HPLC system using an analytical Daicel Chiralcel-IA column, like described below.

Under the same conditions epoxide (+)-**20** (30.0 mg, 62.4 μmol) was converted to diol **21** (13.1 mg, 51.5 μmol), which was directly transformed to (4*R*,5*R*,6*R*,7*R*)-(+)-parthenolide (+)-**22**, yielding 10.2 mg (41.4 μmol, 80%) of a colorless solid.

TLC: R_f = 0.43 (PE/EtOAc, 2:1); 0.34 (CH_2Cl_2/PhMe/MTBE, 10:5:1)[S5].

$[\alpha]_D^{22}$ = +5.4 (*c* = 1.0, THF, >99% *ee*), +4.6 (*c* = 1.0, THF, 92% *ee*) for (4*R*,5*R*,6*R*,7*R*)-**22**.

$[\alpha]_D^{22}$ = –4.9 (*c* = 1.0, THF, >99% *ee*) for (4*S*,5*S*,6*S*,7*S*)-**22**.

NMR:

Table S1. ^{1}H NMR data in comparison to published data of (±)-**22**.[S5]

300 MHz, $CDCl_3$ (Ref. [S5])	Assignment	400 MHz, $CDCl_3$ (this work)
6.23 (*d*, 1H, $^2J_{H,H}$ = 3.4 Hz)	=C(H)H'	6.23 (*d*, 1H, $^2J_{H,H}$ = 3.4 Hz)
5.56 (*d*, 1H, $^2J_{H,H}$ = 3.4 Hz)	=C(H)H'	5.56 (*d*, 1H, $^2J_{H,H}$ = 3.4 Hz)
5.44–5.30 (*m*, 1H)	=C(H)CH_2	5.37 (*br s*, 1H),
4.37 (*dd*, 1H, $^3J_{H,H}$ = 10.2, 3.5 Hz)	C(H)OCO	4.37 (*dd*, 1H, $^3J_{H,H}$ = 10.2, 3.6 Hz)
2.90–2.79 (*m*, 1H)	C(H)C=CH_2	2.89–2.80 (*m*, 1H)
2.75 (*br s*, 1H)	(H)C(O)C, epoxide	2.74 (*br s*, 1H)
2.48–2.36 (*m*, 1H)	C(H)H'	2.47–2.36 (*m*, 1H)
2.34–2.25 (*m*, 1H)	C(H)H'	2.35–2.26 (*m*, 1H),
2.23–2.01 (*m*, 4H)	2 × C(H)H' + 2 × C(H)H'	2.23–2.02 (*m*, 4H),
1.70–1.55 (*m*, 4H)	=C(CH_2)CH_3 + C(H)H'	1.70–1.57 (*m*, 4H)
1.43–1.24 (*m*, 4H)	CH_3 + C(H)H'	1.45–1.28 (*m*, 4H)

Table S2. $^{13}C\{^1H\}$ NMR data in comparison to published data of (±)-**22**.[S5]

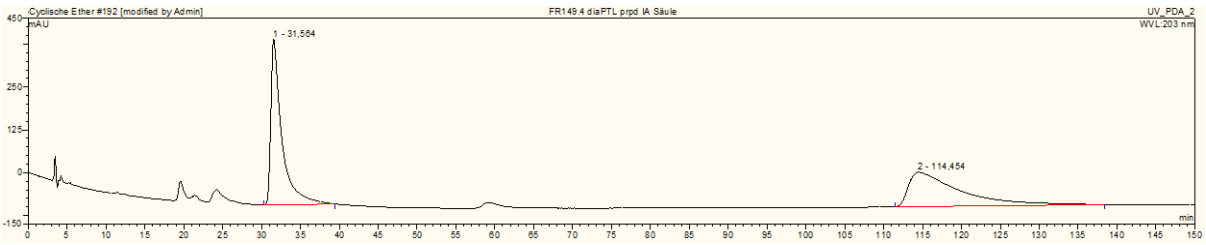
75 MHz, $CDCl_3$ (Ref. [S5])	Assignment	101 MHz, $CDCl_3$ (this work)
169.1	CO_2	169.1
139.5	C=CH_2	139.5
136.7 (*br*)	=C(CH_2)CH_3	137.0 (*br*)
125.0 (*br*)	=C(H)CH_2	124.8 (*br*)
119.1	=CH_2	119.1
79.6	C(H)OCO	79.5
62.4	(H)C(O)C, epoxide	62.3
60.4	(H)C(O)C, epoxide	60.4

75 MHz, $CDCl_3$ (Ref. [S5])	**Assignment**	**101 MHz, $CDCl_3$ (this work)**
44.2	$\underline{C}(H)C{=}CH_2$	44.3
39.4 (*br*)	CH_2	39.4 (*br*)
36.5 (*br*)	CH_2	36.5 (*br*)
25.7 (*br*)	CH_2	25.7 (*br*)
22.5 (*br*)	CH_2	22.5 (*br*)
17.0	$=C(CH_2)\underline{C}H_3$	17.0
16.6	CH_3	16.6

The NMR data matched previously published data.[S5]

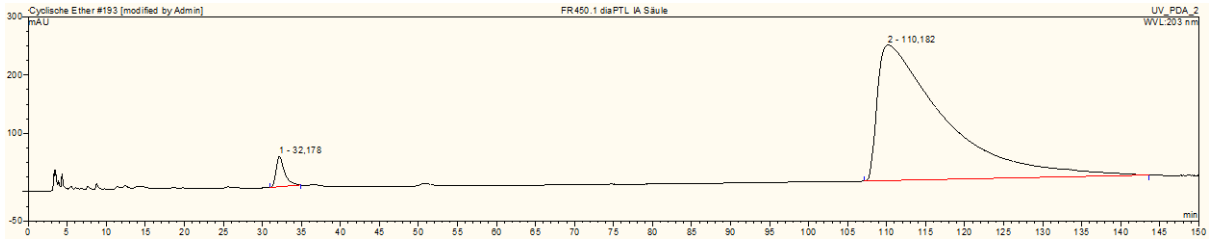
Chiral HPLC [Daicel Chiralcel-IA column (5 µm, 253 × 4.6 mm ID) with guard cartridge, *n*-Hexan/EtOH, 95:5, 1 mL/min, 25 °C, 203 nm]:

a. (±)-**22**



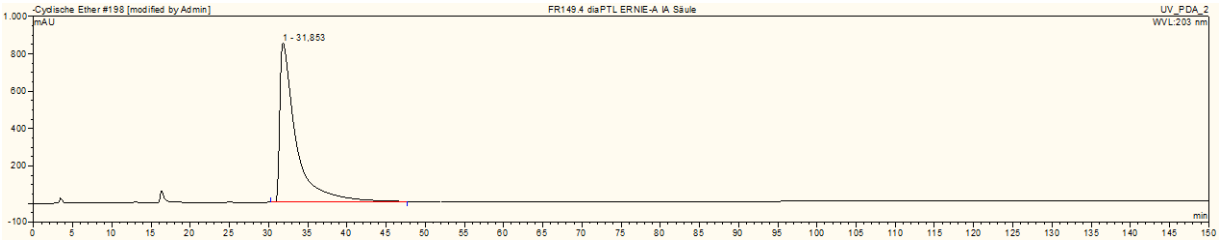
No.	Ret. time / min	Area / mAU×min	Height / mAU	Rel. area / %	Resolution
1	31.6	788.3	482.5	50.8	13.0
2	114.5	763.4	99.9	49.2	–

b. (4*R*,5*R*,6*R*,7*R*)-(+)-**22;** t_R = 31.2, 110.2 min (major), *er* = 97:3, *ee* = 94%.

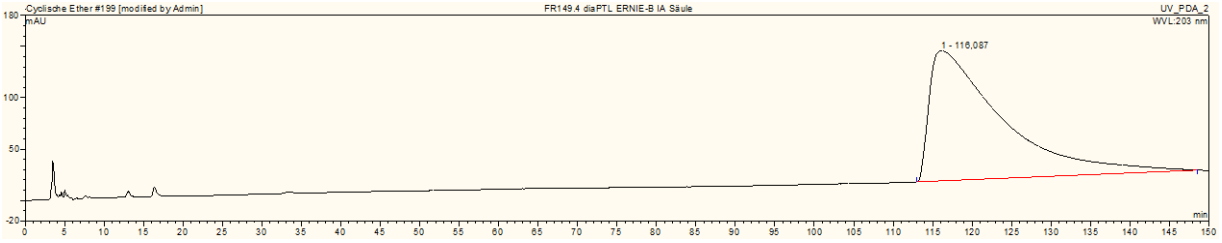


No.	Ret. time / min	Area / mAU×min	Height / mAU	Rel. area / %	Resolution
1	31.2	65.6	52.3	2.78	10.1
2	110.2	2297	232.2	97.2	–

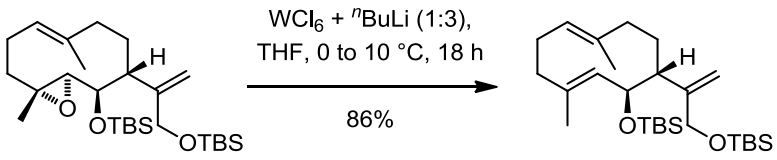
c. (4*S*,5*S*,6*S*,7*S*)-(−)-**22,** >99% *ee* after preparative chiral HPLC.



d. (4*R*,5*R*,6*R*,7*R*)-(+)-**22,** >99% *ee* after preparative chiral HPLC.



***tert*-Butyl{{2-{(1*R*,2*S*,3*E*,7*E*)-2-[(*tert*-butyldimethylsilyl)oxy]-4,8-dimethylcyclodeca-3,7-dien-1-yl}allyl}oxy}dimethylsilane [(−)-23 and (±)-23]**



(+)-**20**
(±)-**20**

(−)-**23**
(±)-**23**

Fresh, blue WCl_6 (333 mg, 0.84 mmol, 4.0 equiv.) was added in one portion to stirred anhydrous THF (2.5 mL) at –78 °C. After 5 min a (alkoxide/hydroxide free) *n*-BuLi solution (1.05 mL, 2.52 mmol, 12.0 equiv., 2.4 M in hexane) was added dropwise over 10 min. The suspension was kept at –78 °C for 10 min and then allowed to warm to 15 °C over 1.5 h, during which several color changes were observed (red, green, yellow, brown, dark brown). The solution was kept at 15 °C for 2 min, cooled again to 0 °C (10 min) and added to a solution of epoxide (±)-**20** (108 mg, 0.21 mmol, 1.0 equiv.) in anhydrous THF (0.5 mL) at 0 °C. The dark brown suspension was kept at this temperature for 3 h and then kept at 10 °C for 15 h (TLC control, PE/CH_2Cl_2, 6:1). The mixture was added into stirred sat. $NaHCO_3$ solution (30 mL) at 0 °C. Et_2O (30 mL) was added and stirring was continued for 10 min. The organic layer was separated and washed sequentially with sat. $NaHCO_3$ solution (2 × 30 mL), a Na_2EDTA solution (30 mL, 0.2 M, pH 8) and brine (30 mL). The extract was dried with $MgSO_4$, filtered and concentrated *in vacuo*. Column chromatography of the residue (PE/CH_2Cl_2, 10:1 + 0.5% Me_2NEt, 3 × 35 cm) provided the germacrene (±)-**23** (69.0 mg, 0.15 mmol, 71%) as a colorless oil.

Under the same conditions epoxide (+)-**20** (200 mg, 0.42 mmol) was converted to germacrene (−)-**23**, yielding 168 mg (0.36 mmol, 86%) of a colorless oil.

TLC: R_f = 0.48 (PE/CH_2Cl_2, 5:1).

$[\alpha]_D^{22}$ = –24.5 (*c* = 1.0, THF, 92% *ee*).

^{1}H NMR (300 MHz, C_6D_6): δ = 5.43–5.27 (*m*, 1H, =C(H)H'), 5.02–4.87 (*m*, 1H, =C(H)H'), 4.75–4.61 (*m*, 2H, 2 × C(H)=), 4.44–4.15 (*m*, 3H, C(H)OSi + CH_2OSi), 2.40–2.22 (*m*, 1H, C(H)H'), 2.18–1.91 (*m*, 5H, C(H)C(R)=CH_2 + 2 × C(H)H' + 2 × C(H)H'), 1.89–1.75 (*m*, 2H, C(H)H' + C(H)H'), 1.72–1.52 (*m*, 1H, C(H)H'), 1.44 (*d*, 3H, $^4J_{H,H}$ = 1.2 Hz, CH_3), 1.33 (*s*, 3H, CH_3), 1.07–0.98 (*m*, 18H, 2 × SiC(CH_3)$_3$), 0.17–0.11 (*m*, 12H, 2 × Si(CH_3)$_2$).

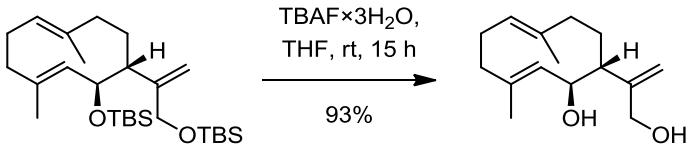
$^{13}C\{^1H\}$ NMR (75 MHz, C_6D_6): δ = 155.1 (R_2C═), 137.5 (R_2C═), 135.6 (C(H)═CR_2), 131.5 (R_2C═), 126.9 (C(H)═CR_2), 107.0 (═CH_2), 73.9 (C(H)OSi), 66.9 (CH_2OSi), 54.7 (C(H)C(R)═CH_2), 42.5 (CH_2), 39.6 (CH_2), 32.9 (CH_2), 26.3 (SiC(CH_3)$_3$), 26.2 (SiC(CH_3)$_3$), 25.8 (CH_2), 18.6 (2 × SiC(CH_3)$_3$), 17.1 (CH_3), 16.5 (CH_3), –3.4 (Si(CH_3)(CH_3)'), –4.6 (Si(CH_3)(CH_3)'), –5.1 (Si(CH_3)(CH_3)'), –5.2 (Si(CH_3)(CH_3)').

IR (ATR): $\tilde{\nu}$ = 3854 (*w*), 3735 (*w*), 3649 (*w*), 3567 (*w*), 2928 (*m*), 2855 (*m*), 2708 (*w*), 2361 (*m*), 2090 (*w*), 1920 (*w*), 1650 (*m*), 1458 (*m*), 1361 (*m*), 1250 (*m*), 1056 (*m*), 833 (*s*), 769 (*s*), 668 (*m*) cm^{-1}.

MS (GC, EI): m/z 464.4 $[M]^{\bullet+}$, 407.3 $[M–^tBu]^+$.

HRMS: No molecular ion peak detectable (collected HPLC fraction, ionization modes: ESI, APCI, EI).

(1*S*,2*E*,6*E*,10*R*)-10-(3-Hydroxyprop-1-en-2-yl)-3,7-dimethylcyclodeca-2,6-dienol [(–)-SI-32 and (±)-SI-32]



(–)-**23** (±)-**23** (–)-**SI-32** (±)-**SI-32**

To a stirred solution of TBS protected diol (±)-**23** (66.0 mg, 0.14 mmol, 1.0 equiv.) in anhydrous THF (1.5 mL) at rt was added a TBAF×3H_2O solution (0.28 mL, 0.28 mmol, 2.0 equiv., 1.0 M in THF). After 15 h at this temperature (TLC control, Et_2O/PE, 4:1) the solution was diluted with Et_2O (20 mL) and washed with pH 7 phosphate buffer (20 mL), followed by sat. $NaHCO_3$ solution (20 mL) and brine (3 × 10 mL). The organic layer was then dried with $MgSO_4$, filtered and concentrated *in vacuo*. Column chromatography of the residue (Et_2O/PE, 4:1 + 0.5% Et_2NMe, 2 × 15 cm) provided the diol (±)-**SI-32** (31.0 mg, 0.13 mmol, 93%) as a colorless oil.

Under the same conditions TBS protected diol (–)-**23** (160 mg, 0.34 mmol) was converted to diol (–)-**SI-32**, yielding 74.3 mg (0.31 mmol, 91%) of a colorless oil.

TLC: R_f = 0.23 (Et_2O/PE, 4:1).

$[\alpha]_D^{23}$ = –68.0 (*c* = 1.0, THF, 92% *ee*).

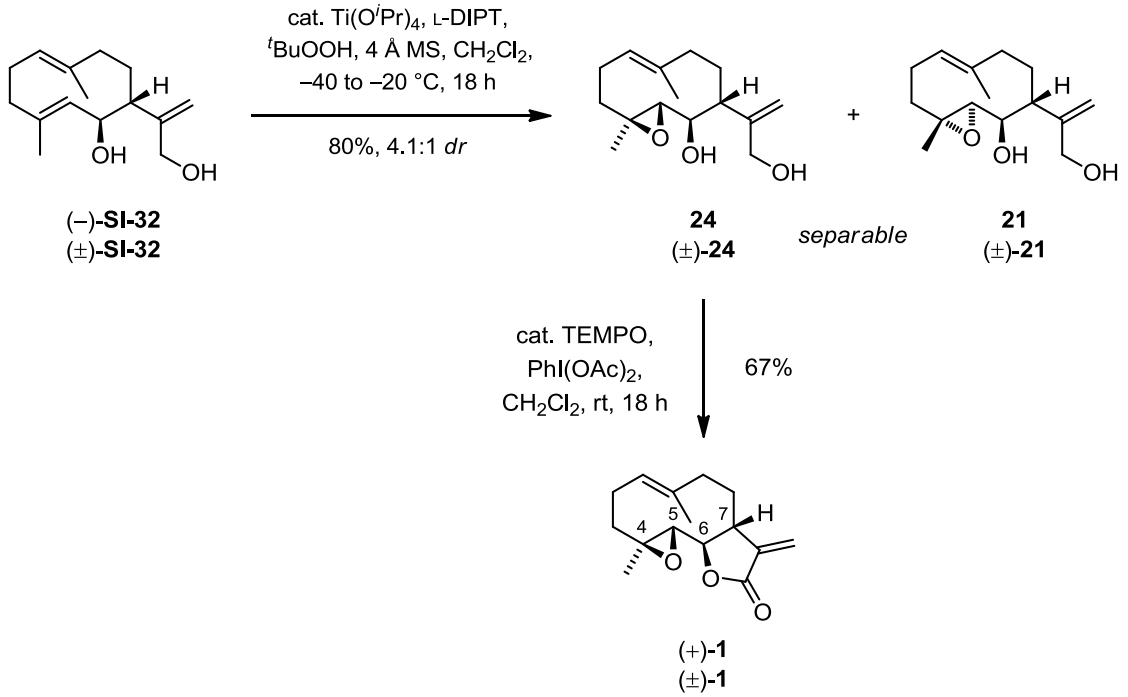
^{1}H NMR (400 MHz, C_6D_6): δ = 5.16 (*s*, 1H, =C(H)H'), 4.93 (*s*, 1H, =C(H)H'), 4.67 (*d*, 1H, $^3J_{H,H}$ = 10.6 Hz, C(H)=), 4.59 (*d*, 1H, $^3J_{H,H}$ = 9.4 Hz, C(H)=), 4.19–4.02 (*m*, 3H, C(H)OH + CH_2OH), 3.32 (*br s*, 1H, OH), 2.51 (*br s*, 1H, OH), 2.27–2.13 (*m*, 2H, C(H)C(R)=CH_2 + C(H)H'), 2.10–1.92 (*m*, 4H, CH_2 + C(H)H' + C(H)H'), 1.90–1.76 (*m*, 1H, C(H)H'), 1.60–1.52 (*m*, 2H, CH_2), 1.46 (*s*, 3H, CH_3), 1.24 (*s*, 3H, CH_3).

^{13}C{^{1}H} NMR (101 MHz, C_6D_6): δ = 153.9 (R_2C=), 137.8 (R_2C=), 134.1 (C(H)=CR_2), 133.5 (R_2C=), 127.0 (C(H)=CR_2), 111.9 (=CH_2), 71.6 (C(H)OH), 65.2 (CH_2OH), 55.6 (C(H)C(R)=CH_2), 41.9 (CH_2), 39.7 (CH_2), 32.5 (CH_2), 26.2 (CH_2), 16.9 (CH_3), 16.4 (CH_3).

IR (ATR): $\tilde{\nu}$ = 3326 (*m*), 2923 (*m*), 2362 (*m*), 2171 (*w*), 2066 (*w*), 1985 (*w*), 1646 (*m*), 1439 (*m*), 1383 (*m*), 1275 (*m*), 1183 (*m*), 1000 (*s*), 898 (*s*), 750 (*m*) cm^{-1}.

HRMS (ESI, TOF): m/z calc'd for $C_{15}H_{24}O_2$ $[M+Na]^+$ 259.1669; observed 259.1670.

(4*S*,5*S*,6*R*,7*R*)-Parthenolide [(+)-1 and (±)-1]



Freshly activated powdered 4 Å molecular sieves (10 mg) were suspended in anhydrous (MeOH-free) CH_2Cl_2 (0.15 mL) with stirring. L-(+)-DIPT (1.29 µl, 1.44 mg, 5.08 µmol, 0.25 equiv.) was added and the mixture was stirred for 20 min after which it was cooled to –20 °C. Ti(O^{i}Pr)$_4$ (1.50 µl, 1.44 mg, 5.08 µmol, 0.20 equiv.) was added and stirring was continued for 15 min. An anhydrous ^{t}BuOOH solution (10.4 µl, 50.8 µmol, 2.0 equiv., 5.0 M

in decane with 4 Å molecular sieves) was added and after additional 30 min the mixture was cooled to –40 °C. Then allyl alcohol (±)-**SI-32** (6.0 mg, 25.4 μmol, 1.0 equiv.) was added as a solution in anhydrous CH_2Cl_2 (0.1 mL) and the temperature was allowed to reach –20 °C over 30 min. After 18 h at this temperature (TLC control, EtOAc/PE, 5:1) the cooling bath was removed and the mixture was filtered through a short plug of silica (d × h = 0.5 × 1 cm, MTBE/PE, 4:1). The filtrate was washed with a 1:2 mixture of sat. Na_2SO_3 solution and sat. $NaHCO_3$ solution (5 mL), followed by sat. $NaHCO_3$ solution (5 mL) and brine (5 mL). The solution was dried with $MgSO_4$, filtered and concentrated *in vacuo*. The following products were obtained after column chromatography of the residue (EtOAc/PE, 3:1→4:1, 2.5 × 40 cm), in order of elution: Epoxy alcohol (±)-**21** (0.83 mg, 3.30 μmol, 13%) and epoxy alcohol (±)-**24** (3.91 mg, 15.5 μmol, 61%), both as colorless glasses which readily decomposed at within several hours.

Under the same conditions allyl alcohol (–)-**SI-32** (58.0 mg, 0.25 mmol) was converted to epoxy alcohol (+)-**21** (9.66 mg, 38.3 μmol, 15%) and epoxy alcohol (+)-**24** (39.6 mg, 0.16 mmol, 64%).

TLC: R_f = 0.37 (EtOAc/PE, 5:1).
HRMS (ESI, TOF): m/z calc'd for $C_{15}H_{24}O_3$ $[M+Na]^+$ 275.1618; observed 275.1619.

The epoxy diol (±)-**24** (1.6 mg, 6.34 μmol) was dissolved in anhydrous CH_2Cl_2 (0.1 mL) and TEMPO (0.30 mg, 1.90 μmol, 0.3 equiv.) was added at rt under stirring, followed by $PhI(OAc)_2$ (6.13 mg, 19.0 μmol, 3.0 equiv.). After 18 h (TLC control, PE/EtOAc, 2:1) the solution was diluted with PE (0.5 mL) and directly subjected to column chromatography (PE/EtOAc, 3:1, 2 × 20 cm), obtaining racemic (4*S**,5*S**,6*R**,7*R**)-parthenolide (±)-**1** (1.10 mg, 4.44 μmol, 70%) as a colorless solid.
Milligram amounts of the pure enantiomers (4*R*,5*R*,6*R*,7*R*)- and (4*S*,5*S*,6*S*,7*S*)-**1** were obtained by multi-run separation on a HPLC system using an semi-preparative Daicel Chiralcel-OJ column, like described below.

Under the same conditions epoxy diol (+)-**24** (13.7 mg, 54.3 μmol) was converted to (4*S*,5*S*,6*R*,7*R*)-(+)-parthenolide (+)-**1**, yielding 9.0 mg (36.2 μmol, 67%) of a colorless solid.

TLC: R_f = 0.34 (PE/EtOAc, 2:1).

$[\alpha]_D^{22}$ = +80.0 (*c* = 1.0, THF, >99% *ee*), +73.6 (*c* = 1.0, THF, 92% *ee*) for (4*S*,5*S*,6*R*,7*R*)-**1**.

$[\alpha]_D^{22}$ = –77.7 (*c* = 1.0, THF, >99% *ee*) for (4*R*,5*R*,6*S*,7*S*)-**1**.

NMR:

Table S3. ^{1}H NMR data of (–)-**1** in comparison with commercial material (TCI).

400 MHz, C_6D_6 (reference)	**Assignment**	**400 MHz, C_6D_6 (this work)**
6.24 (*d*, 1H, $^2J_{H,H}$ = 3.7 Hz)	=C(H)H’	6.23 (*d*, 1H, $^2J_{H,H}$ = 3.7 Hz)
4.94 (*d*, 1H, $^2J_{H,H}$ = 3.3 Hz, 1H)	=C(H)H’	4.94 (*d*, 1H, $^2J_{H,H}$ = 3.3 Hz, 1H)
4.71 (*dd*, 1H, $^{3,4}J_{H,H}$ = 12.0, 2.2 Hz)	=C(H)CH_2	4.66 (*dd*, 1H, $^{3,4}J_{H,H}$ = 12.4, 2.3 Hz)
3.30 (*dd*, 1H, $^3J_{H,H}$ = 8.8, 8.6 Hz)	C(H)OCO	3.25 (*dd*, 1H, $^3J_{H,H}$ = 8.9, 8.6 Hz)
2.31 (*d*, 1H, $^3J_{H,H}$ = 8.9 Hz)	C(O)CH, epoxide	2.23 (*d*, 1H, $^3J_{H,H}$ = 8.9 Hz)
2.09–1.90 (*m*, 2H)	C(H)C=CH_2 + C(H)H’	2.07–1.86 (*m*, 2H)
1.89–1.74 (*m*, 3H)	2 × C(H)H’ + C(H)H’	1.86–1.69 (*m*, 3H)
1.61 (*dd*, 1H, $^3J_{H,H}$ = 18.4, 7.0 Hz)	C(H)H’	1.55 (*dd*, 1H, $^3J_{H,H}$ = 18.4, 7.0 Hz)
1.43 (*dd*, 1H, $^3J_{H,H}$ = 15.2, 6.2 Hz)	C(H)H’	1.38 (*dd*, 1H, $^3J_{H,H}$ = 15.2, 6.2 Hz)
1.27 (*s*, 3H)	CH_3	1.25 (*s*, 3H)
1.04–0.91 (*m*, 5H)	CH_3 + 2 × C(H)H’	1.03–0.82 (*m*, 5H)

The ^{1}H NMR spectra of synthetic and reference material are almost identical, with a chemical shift average deviation of 1.9%, possibly due to impurities (see spectrum). All coupling constants are in good agreement.

Table S4. $^{13}C\{^{1}H\}$ NMR data of (–)-**1** in comparison with commercial material (TCI).

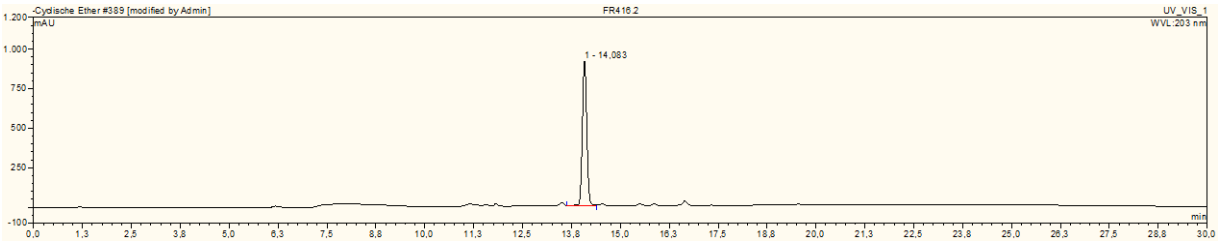
101 MHz, C_6D_6 (reference)	**Assignment**	**101 MHz, C_6D_6 (this work)**
169.1	CO_2	168.9
140.6	$\underline{C}{=}CH_2$	140.6
134.3	$={\underline{C}}(CH_2)CH_3$	134.2
125.3	$={\underline{C}}(H)CH_2$	125.3
119.7	$={\underline{C}}H_2$	119.5
82.1	$\underline{C}(H)OCO$	82.0
66.2	$\underline{C}(O)CH$, epoxide	66.1
60.8	$C(O)\underline{C}H$, epoxide	60.6
47.3	$\underline{C}(H)C{=}CH_2$	47.3
41.1	CH_2	41.1
36.7	CH_2	36.7
30.3	CH_2	30.3
24.3	CH_2	24.2
17.4	$=C(CH_2)\underline{C}H_3$	17.3
16.7	CH_3	16.7

Considering spectrometer accuracy, the $^{13}C\{^{1}H\}$ NMR spectra of synthetic and commercial material were identical.

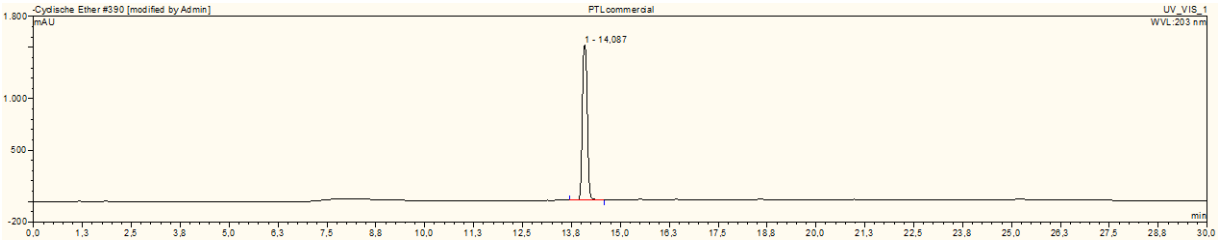
HRMS (ESI, TOF): m/z calc'd for $C_{15}H_{20}O_3$ $[M+Na]^+$ 271.1305; observed 271.1308.

RP-HPLC [Nucleodur C18 Gravity column (5.0 µm, 125 × 10 mm ID) with guard cartridge, gradient (%MeCN in H_2O): $10\%_{1\,min} \xrightarrow{15\ min} 95\%_{5\,min} \xrightarrow{5\ min} 10\%_{4\,min}$, 1 mL/min, 25 °C, 203 nm]:

a. (4*S*,5*S*,6*R*,7*R*)-(+)-**1**

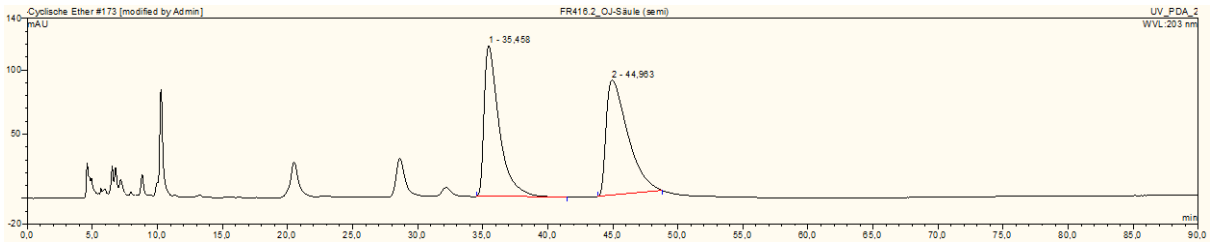


b. co-injection of (4*S*,5*S*,6*R*,7*R*)-(+)-**1** and commercial (–)-parthenolide (TCI)



Chiral HPLC [Daicel Chiralcel-OJ column (10.0 μm, 250 × 10.0 mm ID) with guard cartridge, *n*-Hexan/EtOH, 90:10, 3 mL/min, 25 °C, 203 nm]:

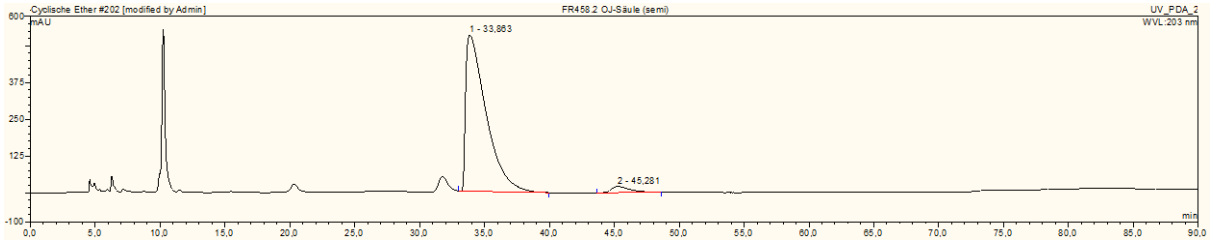
a. (±)-**1** (crude mixture)



No.	Ret. time / min	Area / mAU×min	Height / mAU	Rel. area / %	Resolution
1	35.5	156.4	117.2	47.6	13.0
2	45.0	172.1	89.5	52.4*	–

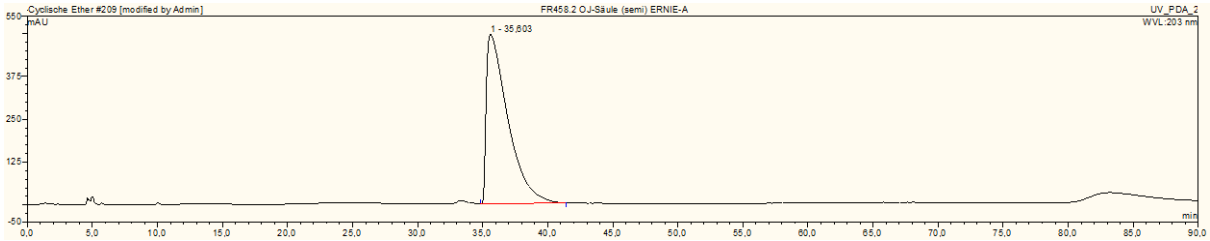
* co-elutes with impurity

b. (4*S*,5*S*,6*R*,7*R*)-(+)-**1;** t_R = 33.9 (major), 45.3, *er* = 96:4, *ee* = 93%.

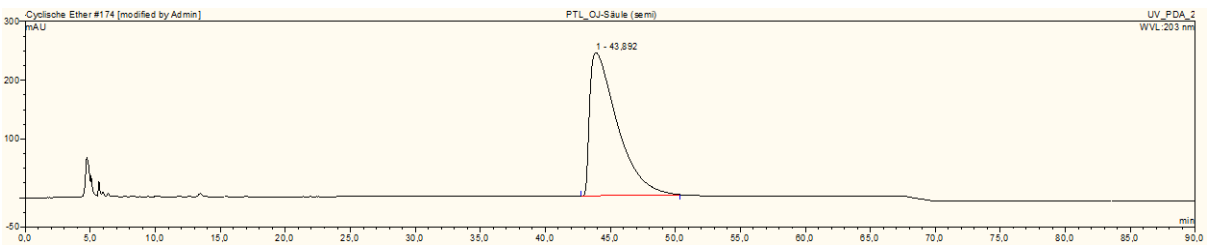


No.	Ret. time / min	Area / mAU×min	Height / mAU	Rel. area / %	Resolution
1	33.9	963.8	531.8	96.54	10.1
2	45.3	34.5	20.4	3.46	–

c. (4*S*,5*S*,6*R*,7*R*)-(+)-**1,** >99% *ee* after preparative chiral HPLC.



d. (4*R*,5*R*,6*S*,7*S*)-(−)-**1** (natural isomer) >99% *ee* after preparative chiral HPLC.



3.5 Single-crystal X-ray structure analysis of bromide (±)-9

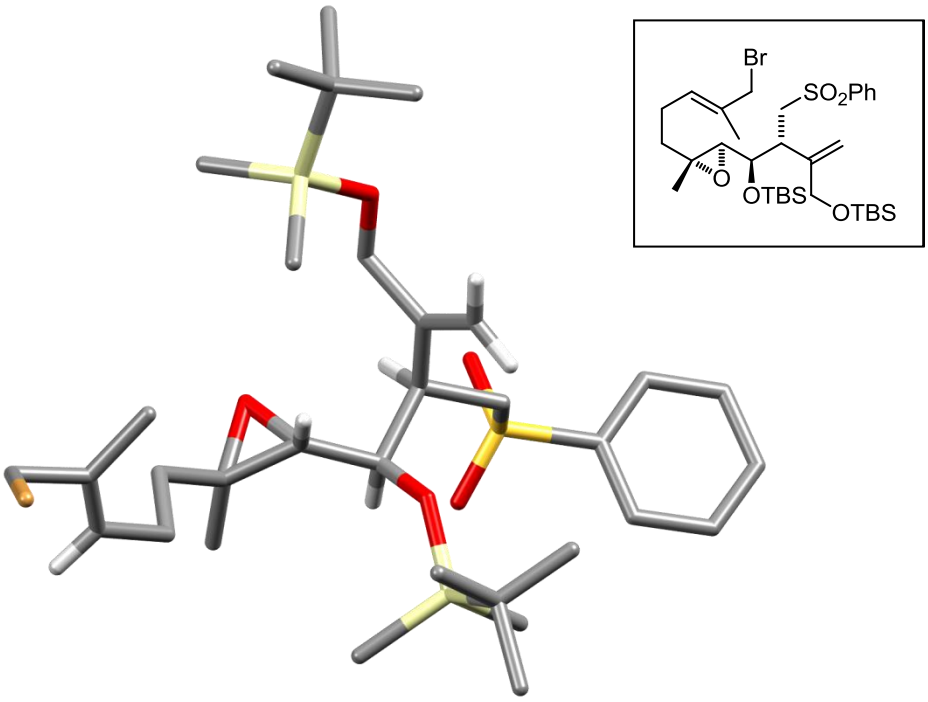


Fig. S1. Molecular structure of bromide (±)-**9** obtained from single-crystal X-ray analysis. Only the (*R*,*R*,*R*,*R*)-enantiomer is depicted. Most of the H atoms are omitted for clarity reasons. C = grey, H = white, Br = orange, O = red, S = bright yellow, Si = pale yellow.

Crystal Structure Determination

The intensity data were collected on a Nonius KappaCCD diffractometer, using graphite-monochromated Mo-K_α radiation. Data were corrected for Lorentz and polarization effects; absorption was taken into account on a semi-empirical basis using multiple-scans.[S27]

The structure was solved by direct methods (SHELXS)[S28] and refined by full-matrix least squares techniques against Fo^2 (SHELXL-97).[S29] The hydrogen atoms bound to the vinylidene-groups of (±)-**9** were located by difference Fourier synthesis and refined isotropically. All other hydrogen atoms were included at calculated positions with fixed thermal parameters. All non-hydrogen atoms were refined anisotropically.[S29] MERCURY[S30] was used for structure representations.

Crystal Data for **(±)-9**: $C_{33}H_{57}BrO_5SSi_2$, Mr = 701.94 $gmol^{-1}$, colourless prism, size 0.122 × 0.112 × 0.108 mm^3, monoclinic, space group P $2_1/n$, a = 28.3329(4), b = 9.8848(2), c = 30.0449(4) Å, β = 118.103(1)°, V = 7422.5(2) $Å^3$, T = –140 °C, Z = 8, $\rho_{calcd.}$ = 1.256 gcm^{-3},

μ (Mo-K_α) = 12.64 cm^{-1}, multi-scan, $trans_{min}$: 0.6697, $trans_{max}$: 0.7456, F(000) = 2992, 70579 reflections in h(–36/35), k(–12/8), l(–39/38), measured in the range $1.36° \leq \Theta \leq 27.48°$, completeness Θ_{max} = 99.9%, 16971 independent reflections, R_{int} = 0.0433, 13131 reflections with $F_o > 4\sigma(F_o)$, 797 parameters, 0 restraints, $R1_{obs}$ = 0.0467, wR^2_{obs} = 0.1043, $R1_{all}$ = 0.0685, wR^2_{all} = 0.1152, GOOF = 1.042, largest difference peak and hole: 2.293/–0.605 e $Å^{-3}$.

Supporting Information Available: Crystallographic data deposited at the Cambridge Crystallographic Data Centre under CCDC-1902988 for (±)-**9** contain the supplementary crystallographic data excluding structure factors; these data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.htmL (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).

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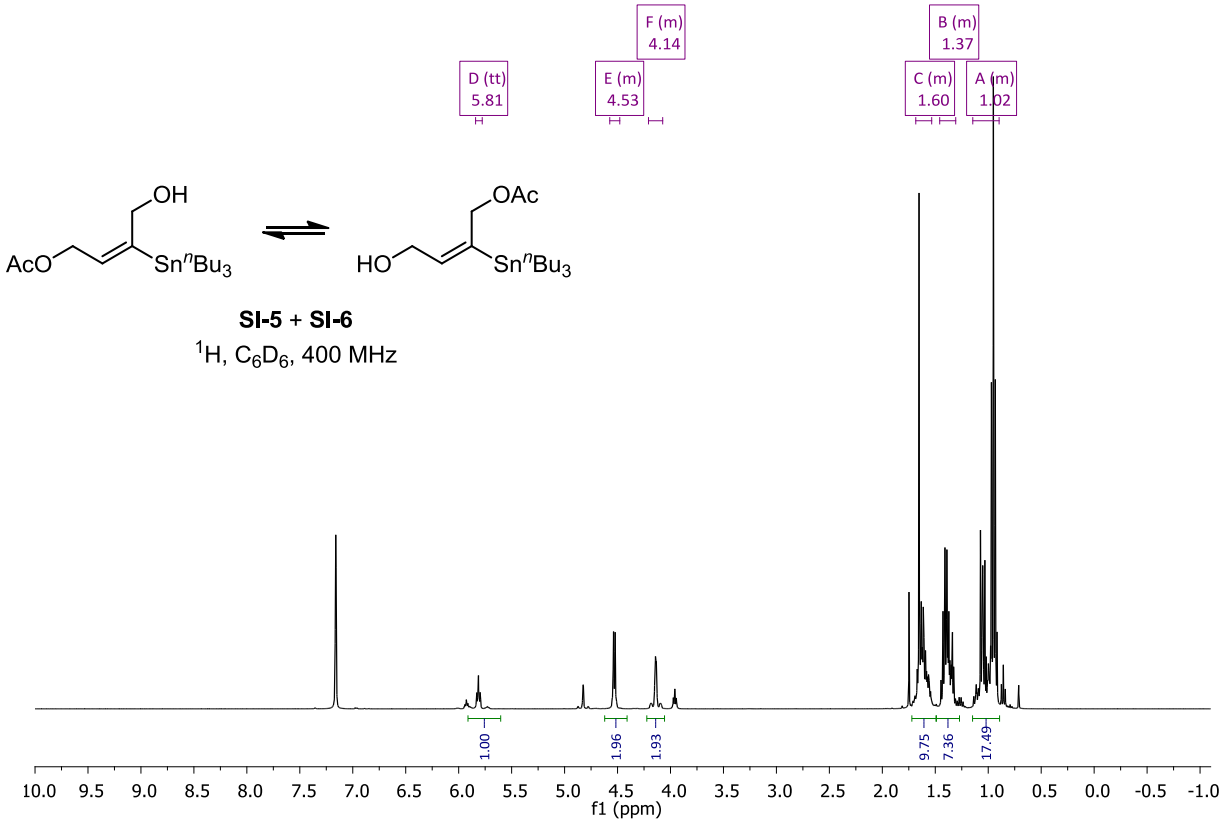
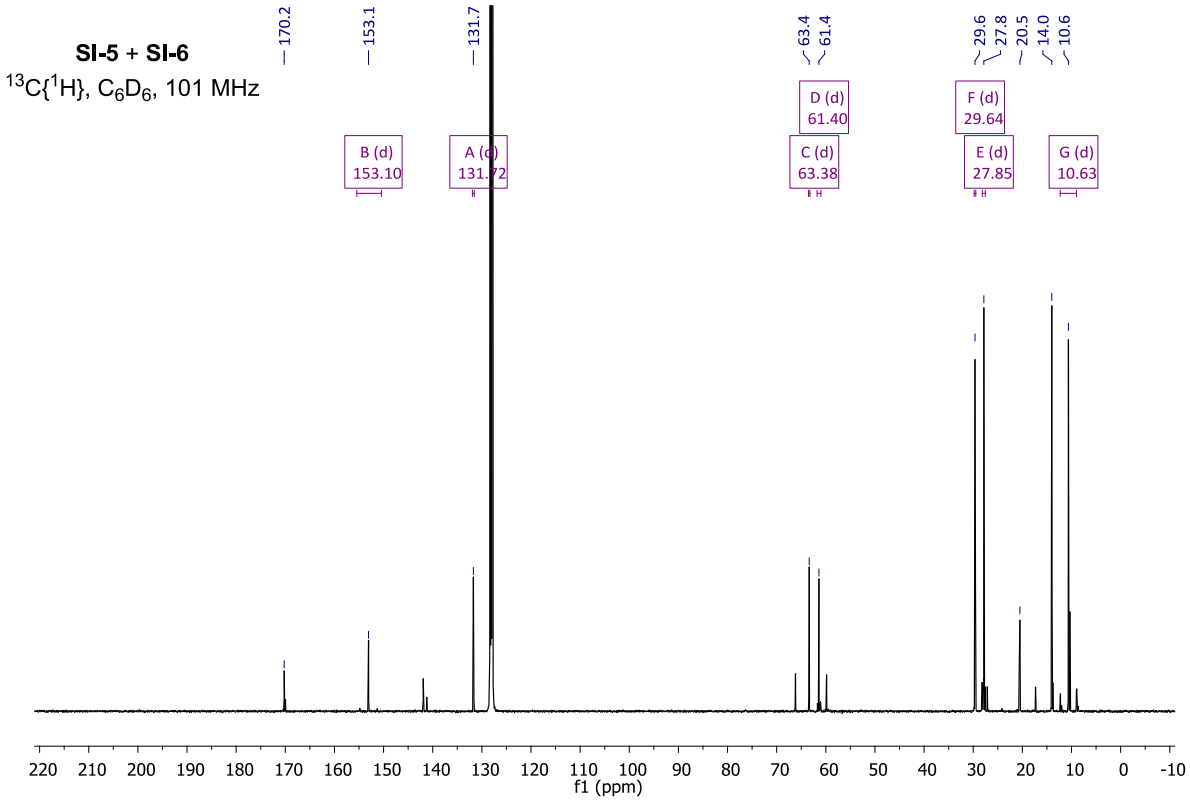
5 NMR spectra of new compounds



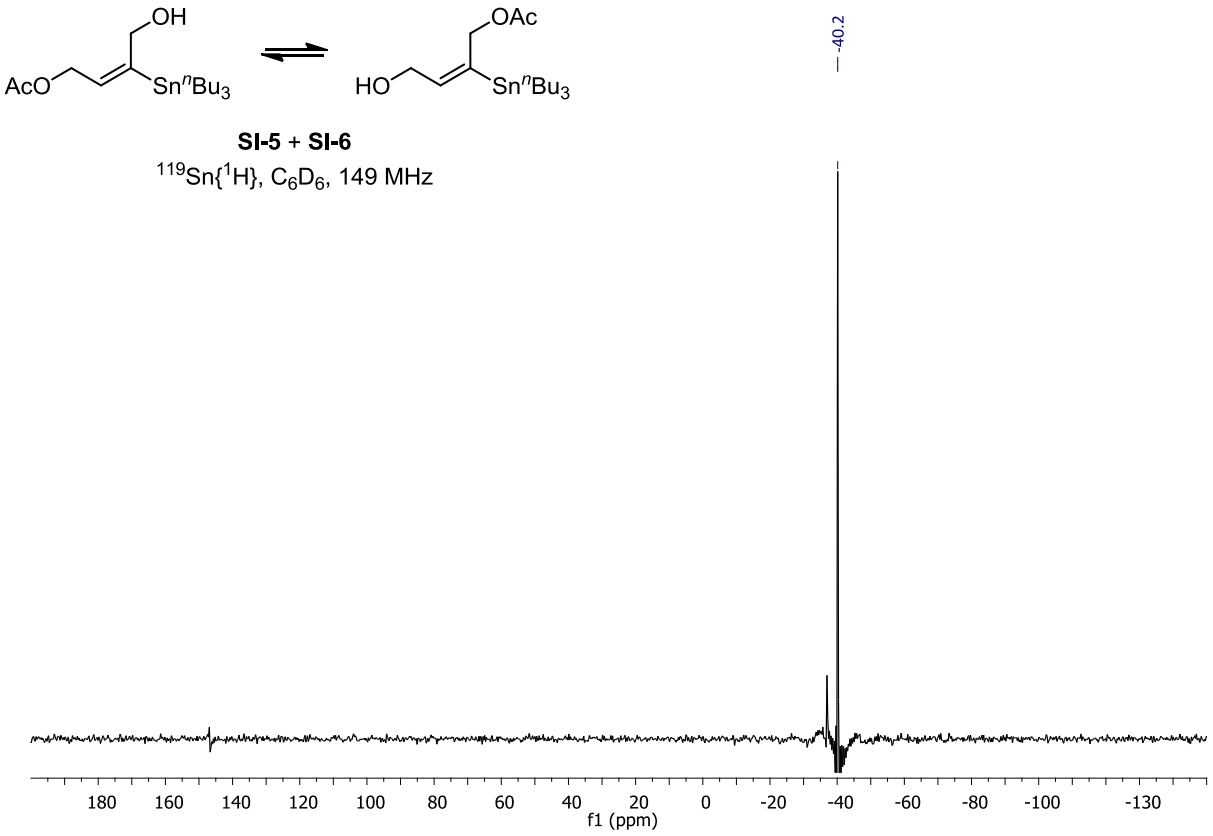
SI-5 + **SI-6**

^{1}H, C_6D_6, 400 MHz



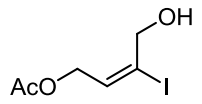
SI-5 + **SI-6**

$^{13}C\{^1H\}$, C_6D_6, 101 MHz



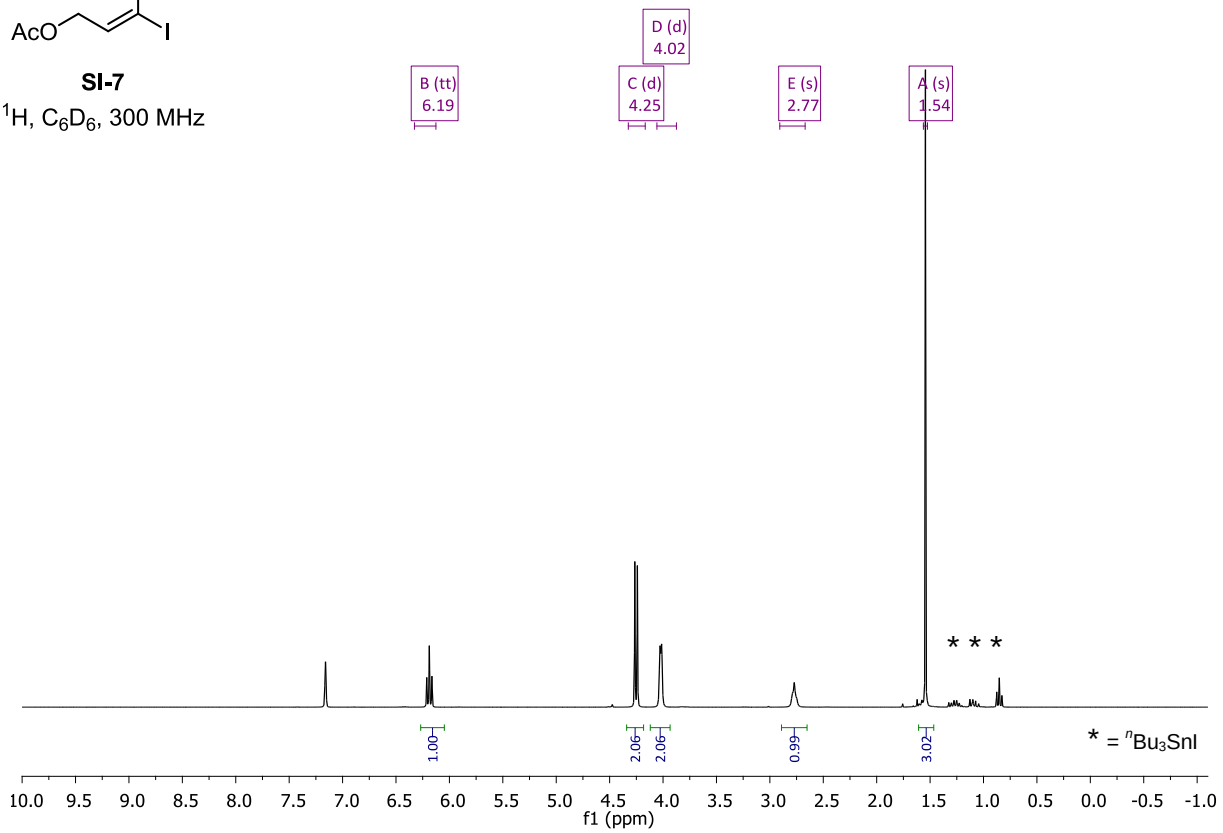
SI-5 + **SI-6**

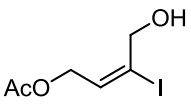
$^{119}Sn\{^1H\}$, C_6D_6, 149 MHz



SI-7

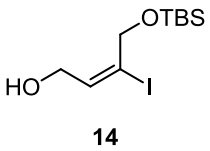
^{1}H, C_6D_6, 300 MHz





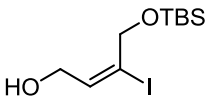
SI-7

$^{13}C\{^{1}H\}$, C_6D_6, 75 MHz



14

^{1}H, C_6D_6, 300 MHz



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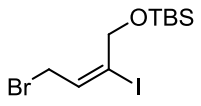
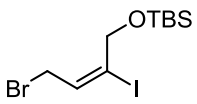


15

^{1}H, C_6D_6, 300 MHz



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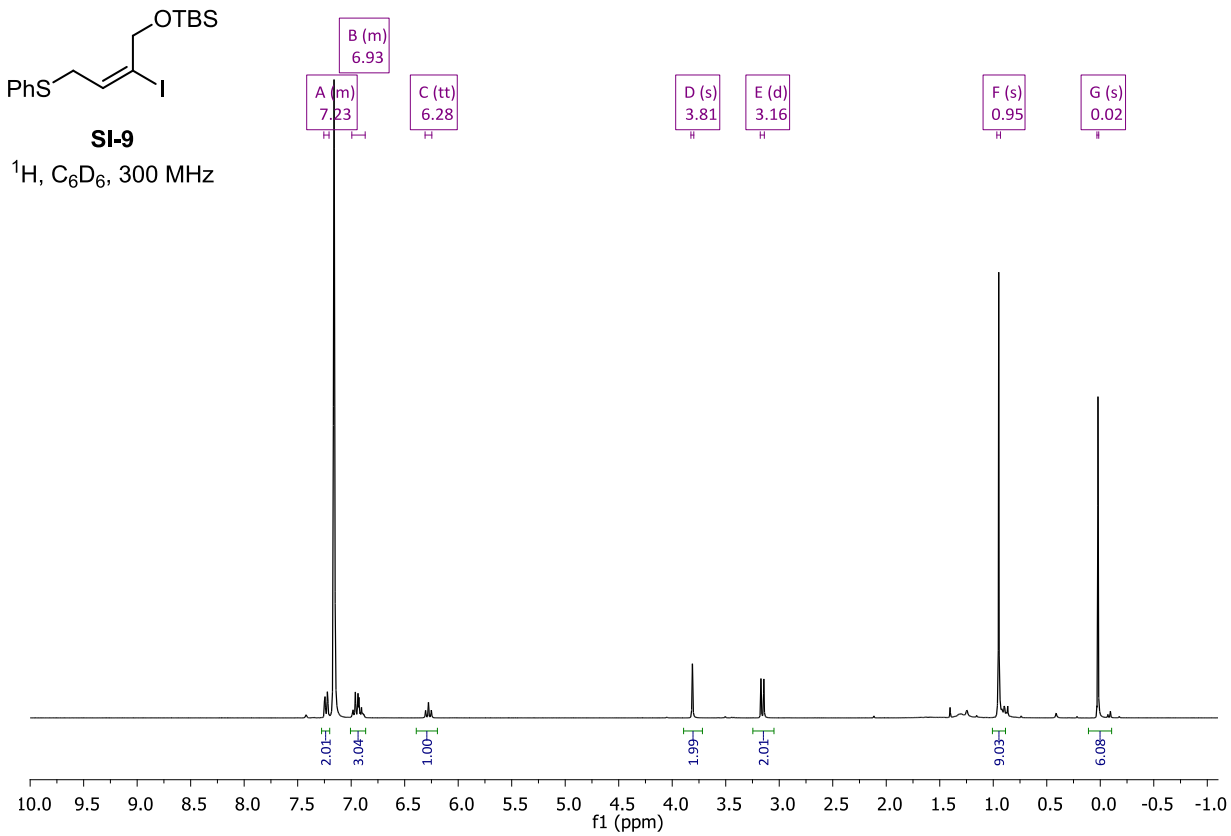
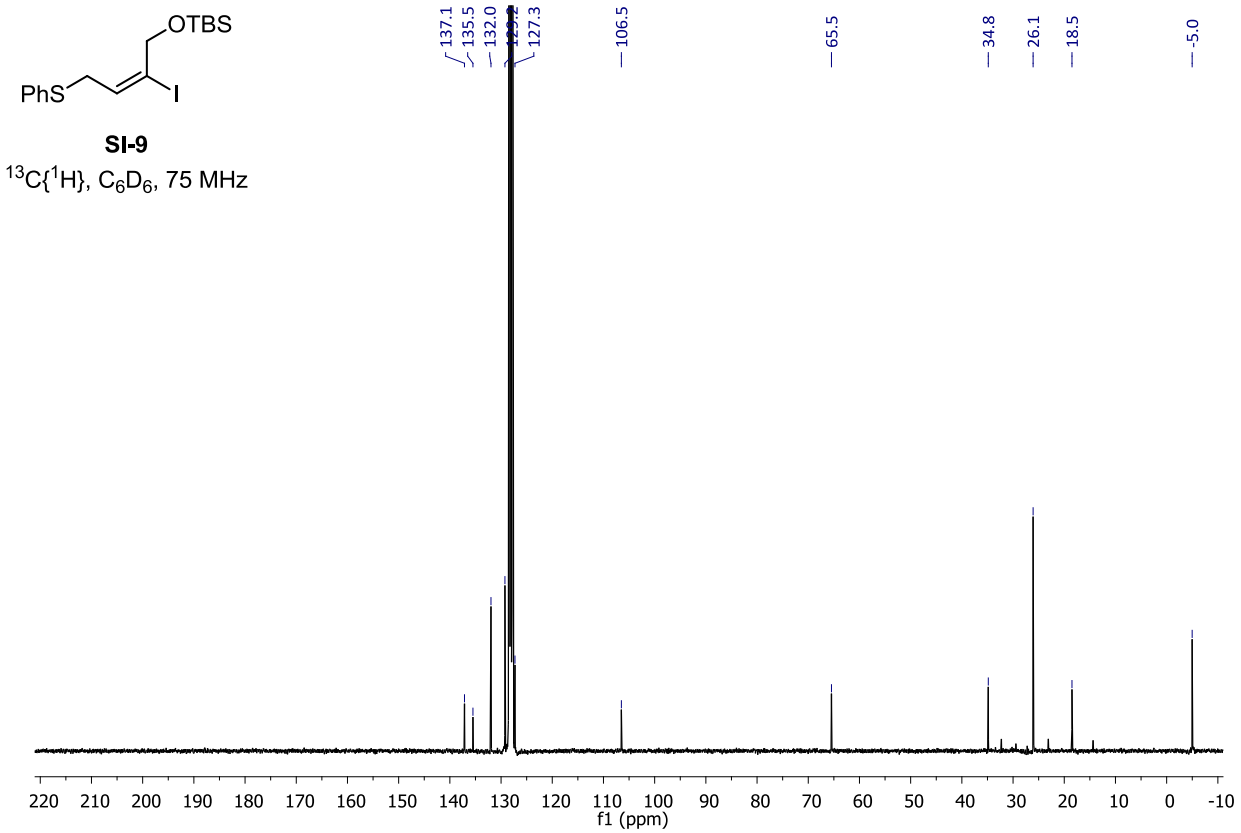
$^{13}C\{^{1}H\}$, C_6D_6, 75 MHz


OTBS
PhS
I
SI-9
1H, C6D6, 300 MHz
B (m) 6.93
A (m) 7.23
C (tt) 6.28
D (s) 3.81
E (d) 3.16
F (s) 0.95
G (s) 0.02
2.01
3.04
1.00
1.99
2.01
9.03
6.08
f1 (ppm)


OTBS
PhS
I
SI-9
13C{1H}, C6D6, 75 MHz
137.1
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106.5
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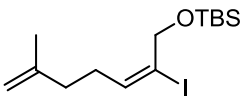
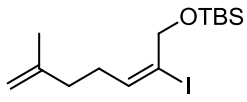
34.8
26.1
18.5
-5.0
f1 (ppm)



SI-10

^{1}H, C_6D_6, 300 MHz



SI-10

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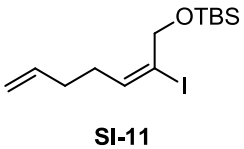
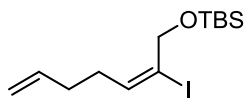


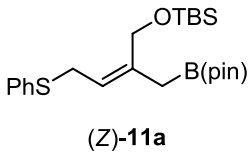
SI-11

^{1}H, C_6D_6, 300 MHz



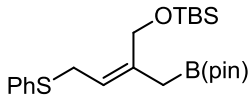
SI-11

$^{13}C\{^{1}H\}$, C_6D_6, 75 MHz



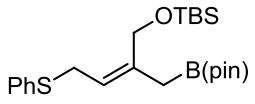
(*Z*)-**11a**

^{1}H, C_6D_6, 300 MHz



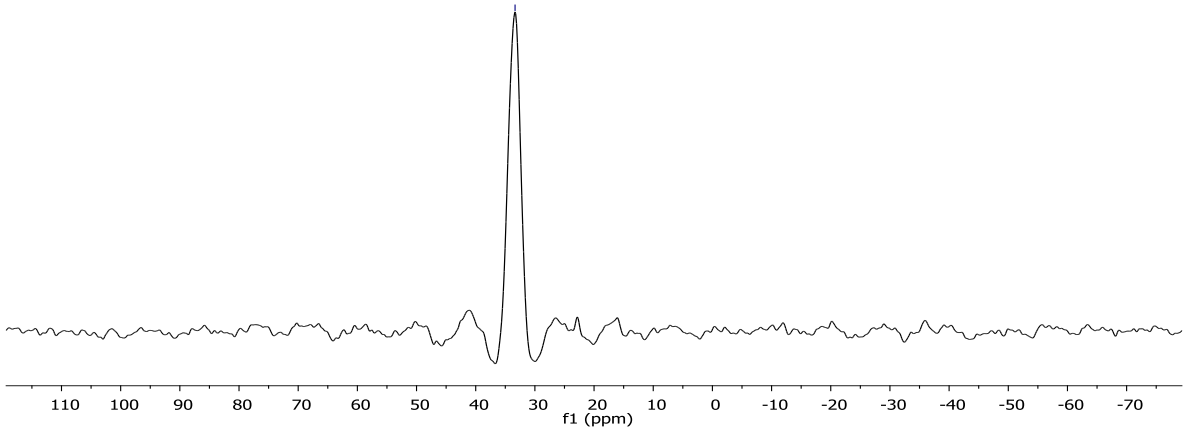
(*Z*)-**11a**

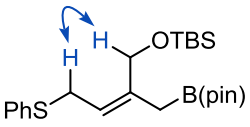
$^{13}C\{^{1}H\}$, C_6D_6, 75 MHz



(*Z*)-**11a**

$^{11}B\{^{1}H\}$, C_6D_6, 128 MHz



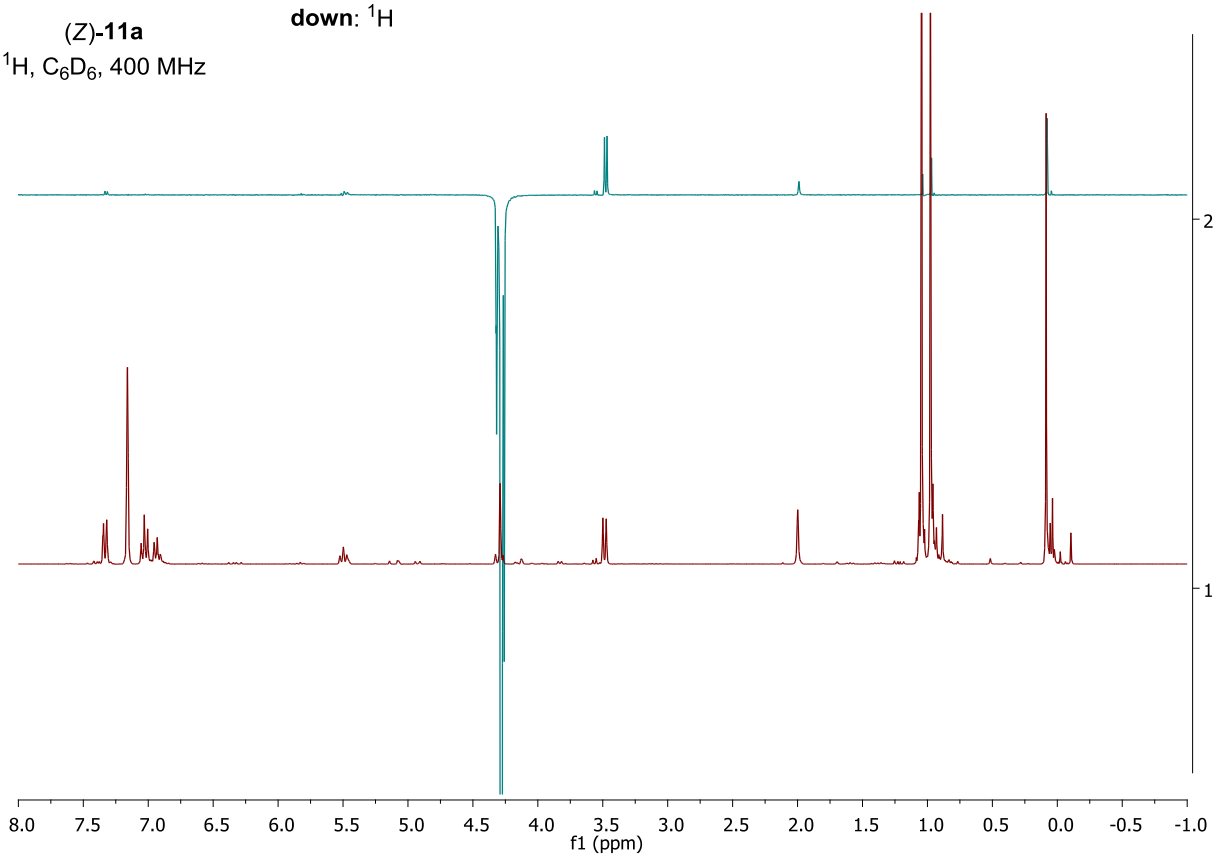


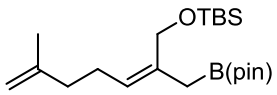
(*Z*)-**11a**

^{1}H, C_6D_6, 400 MHz

up: 1D-NOESY, irrad. at CH_2O signal

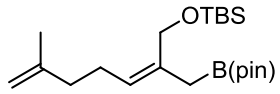
down: ^{1}H





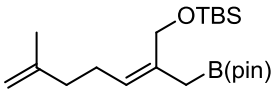
(*Z*)-**11b**

^{1}H, C_6D_6, 400 MHz



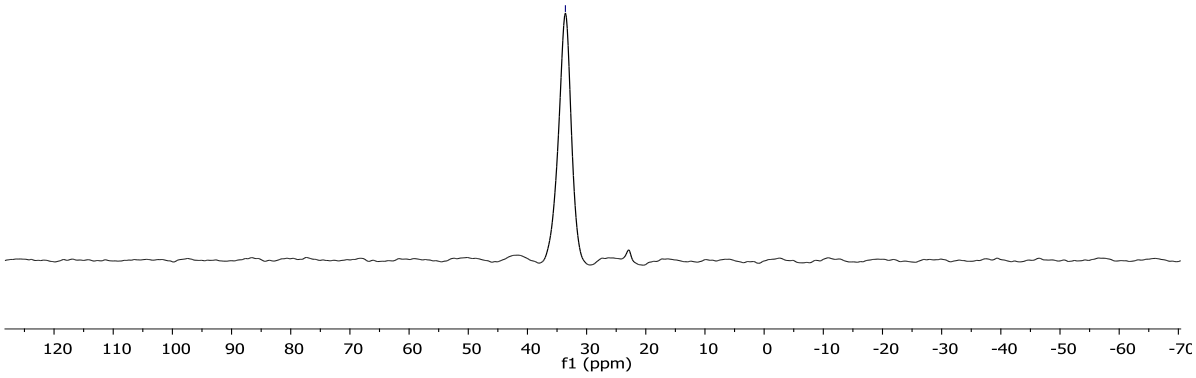
(*Z*)-**11b**

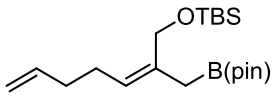
$^{13}C\{^{1}H\}$, C_6D_6, 101 MHz



(*Z*)-**11b**

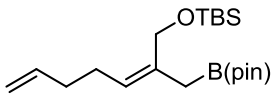
$^{11}B\{^{1}H\}$, C_6D_6, 128 MHz





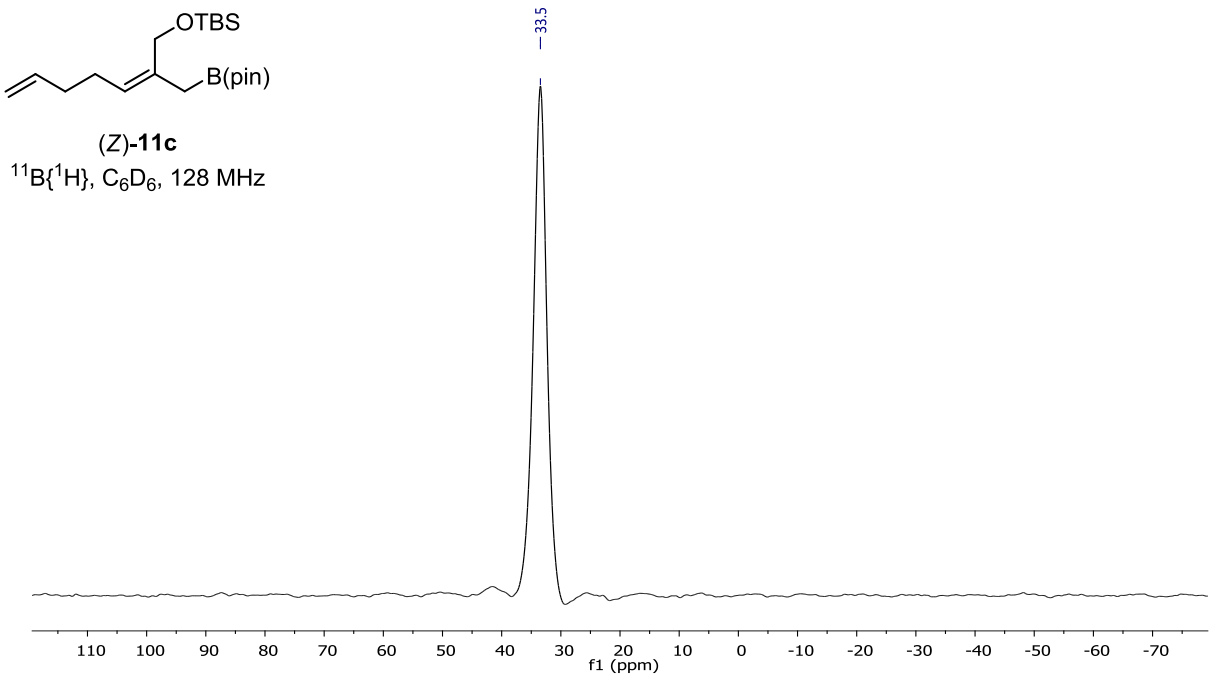
(*Z*)-**11c**

^{1}H, C_6D_6, 400 MHz



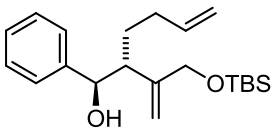
(*Z*)-**11c**

^{13}C{^{1}H}, C_6D_6, 101 MHz



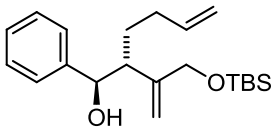
(*Z*)-**11c**

$^{11}B\{^{1}H\}$, C_6D_6, 128 MHz



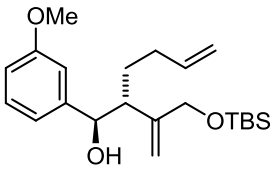
16a

^{1}H, C_6D_6, 300 MHz



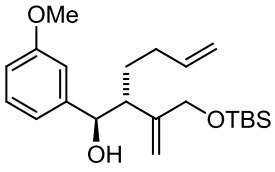
16a

$^{13}C\{^{1}H\}$, C_6D_6, 75 MHz



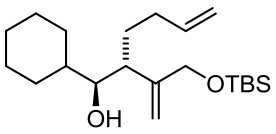
16b

^{1}H, C_6D_6, 300 MHz



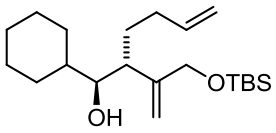
16b

$^{13}C\{^{1}H\}$, C_6D_6, 75 MHz



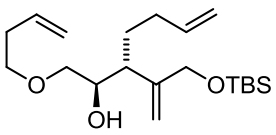
16c

^{1}H, C_6D_6, 300 MHz



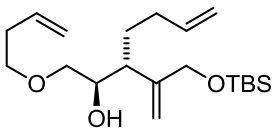
16c

$^{13}C\{^{1}H\}$, C_6D_6, 75 MHz



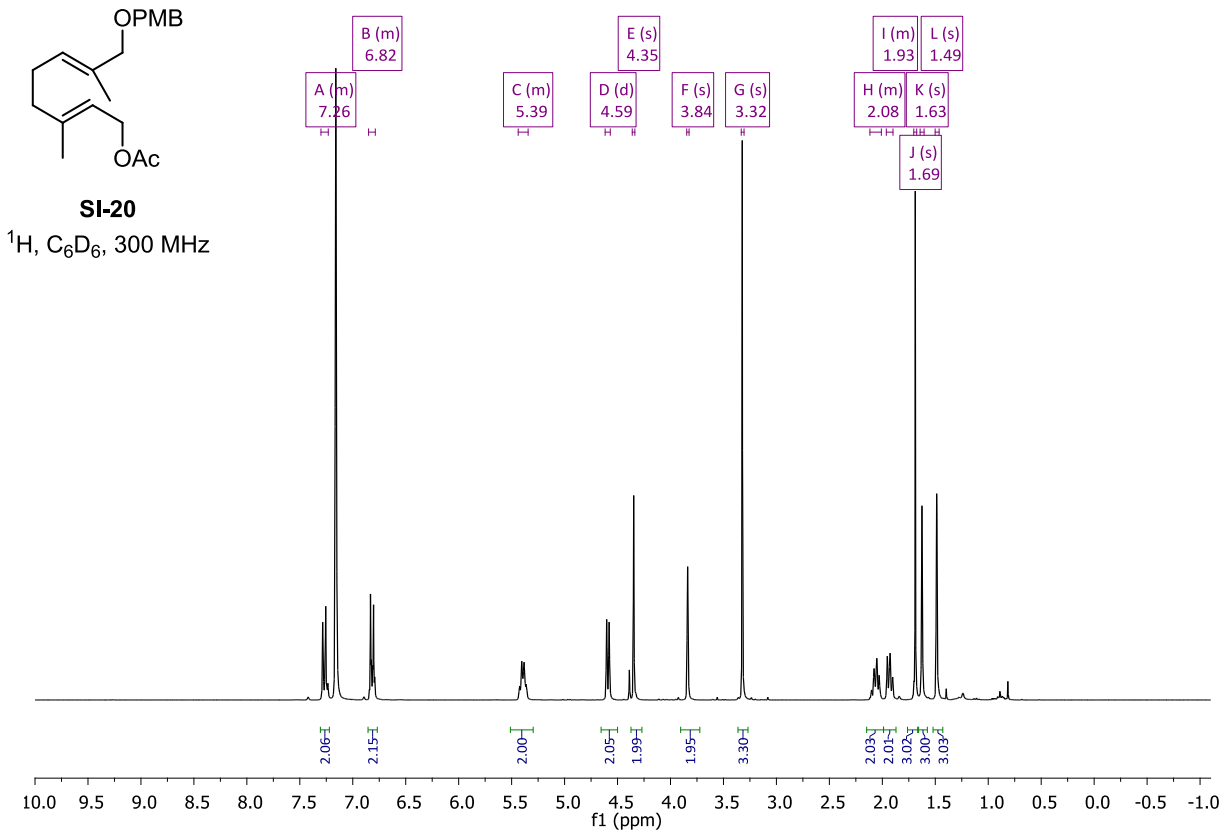
16d

^{1}H, C_6D_6, 300 MHz



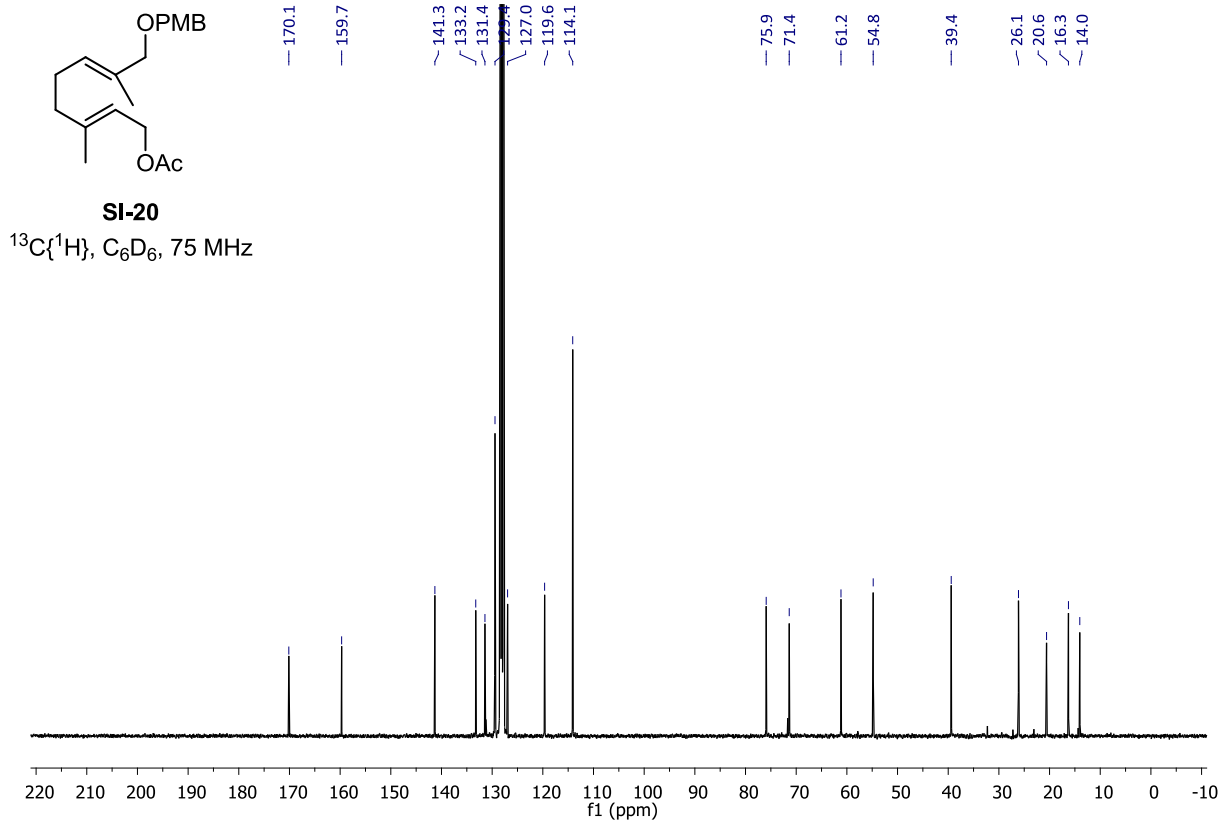
16d

$^{13}C\{^{1}H\}$, C_6D_6, 75 MHz



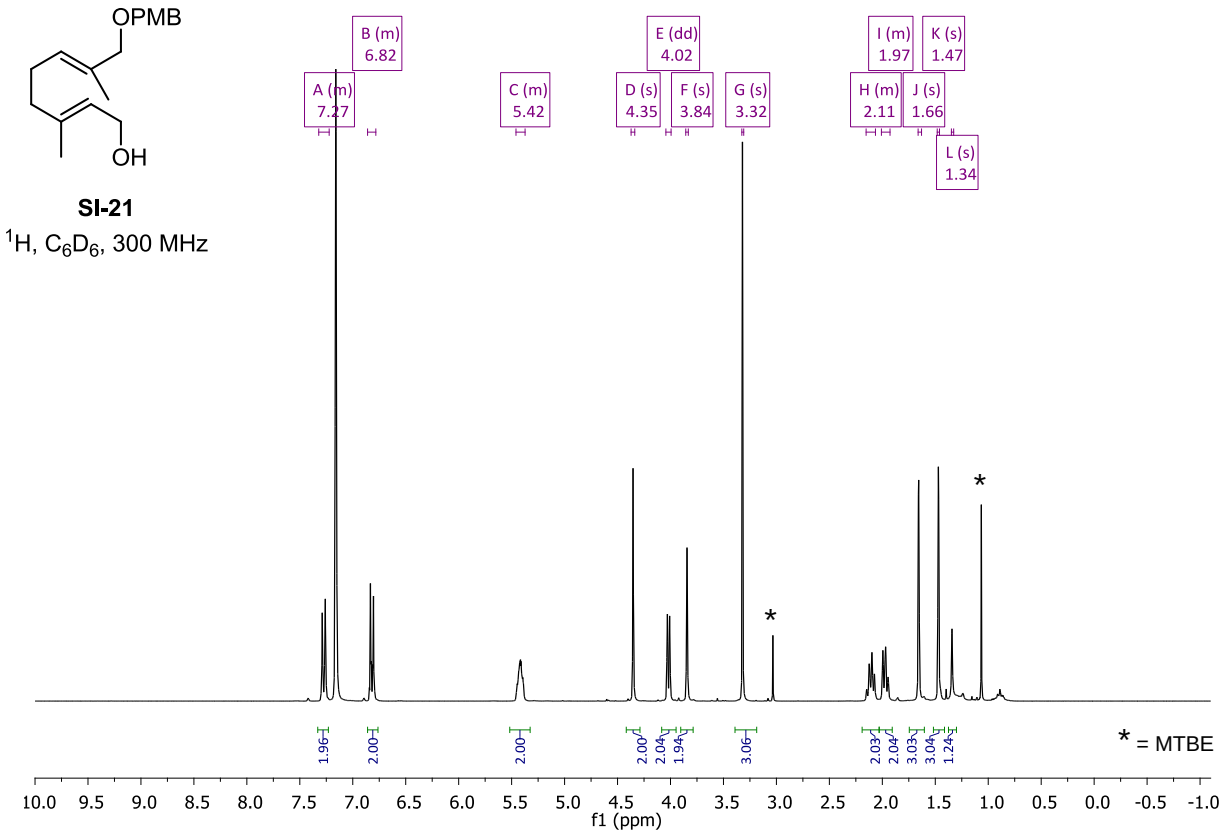
SI-20

^{1}H, C_6D_6, 300 MHz



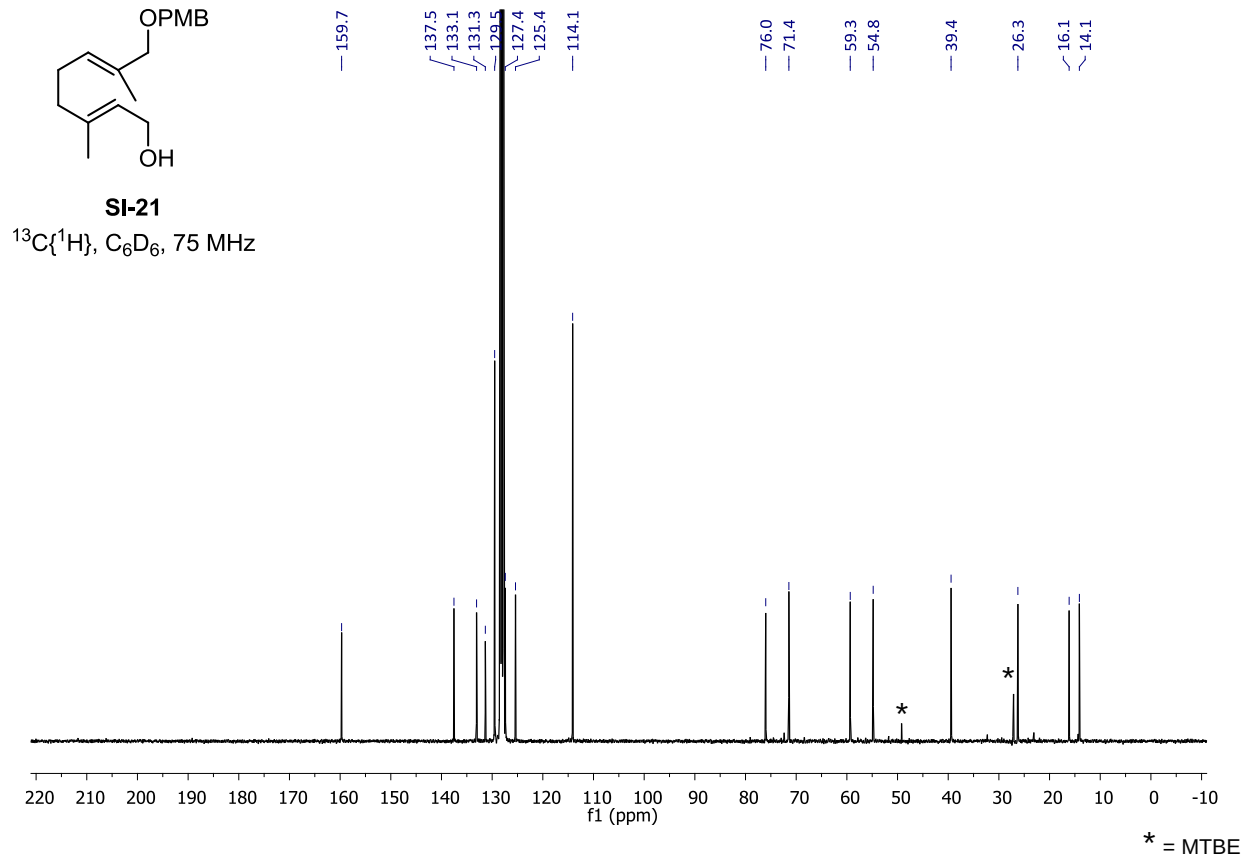
SI-20

$^{13}C\{^{1}H\}$, C_6D_6, 75 MHz



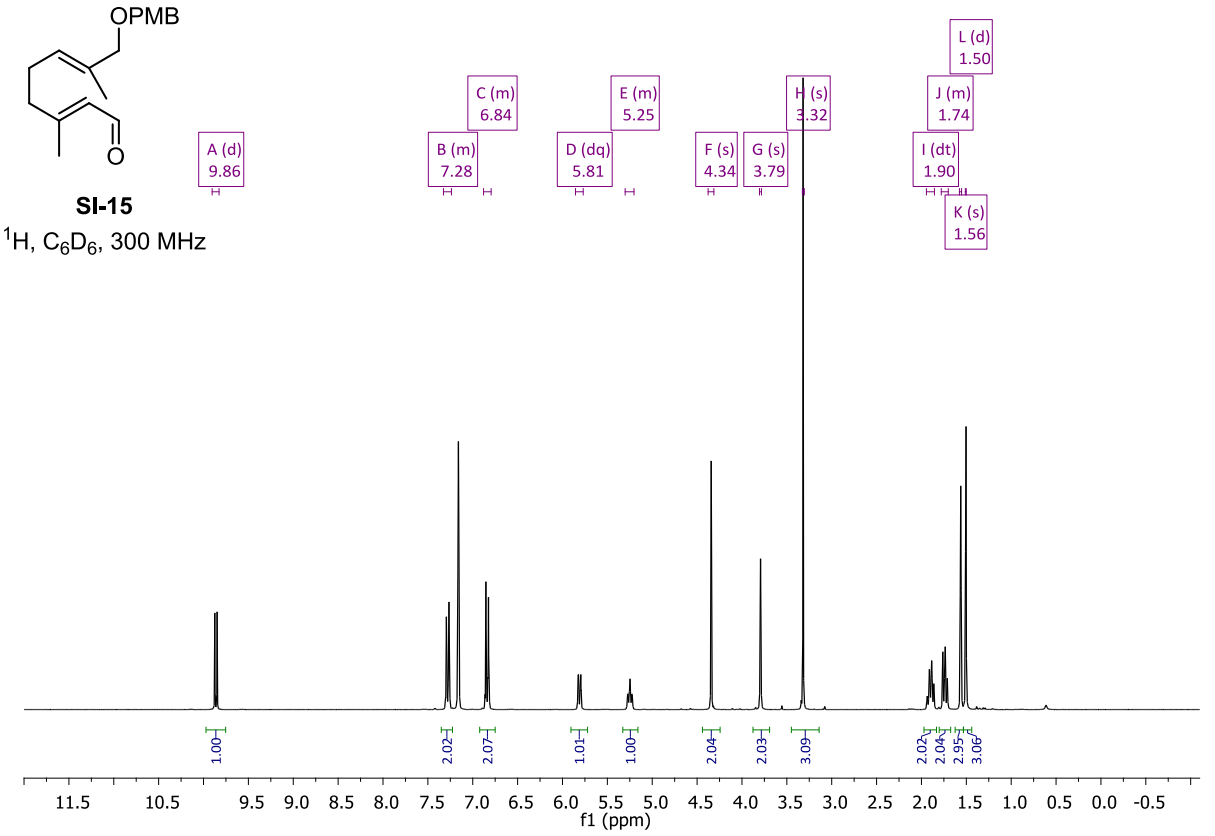
SI-21

^{1}H, C_6D_6, 300 MHz



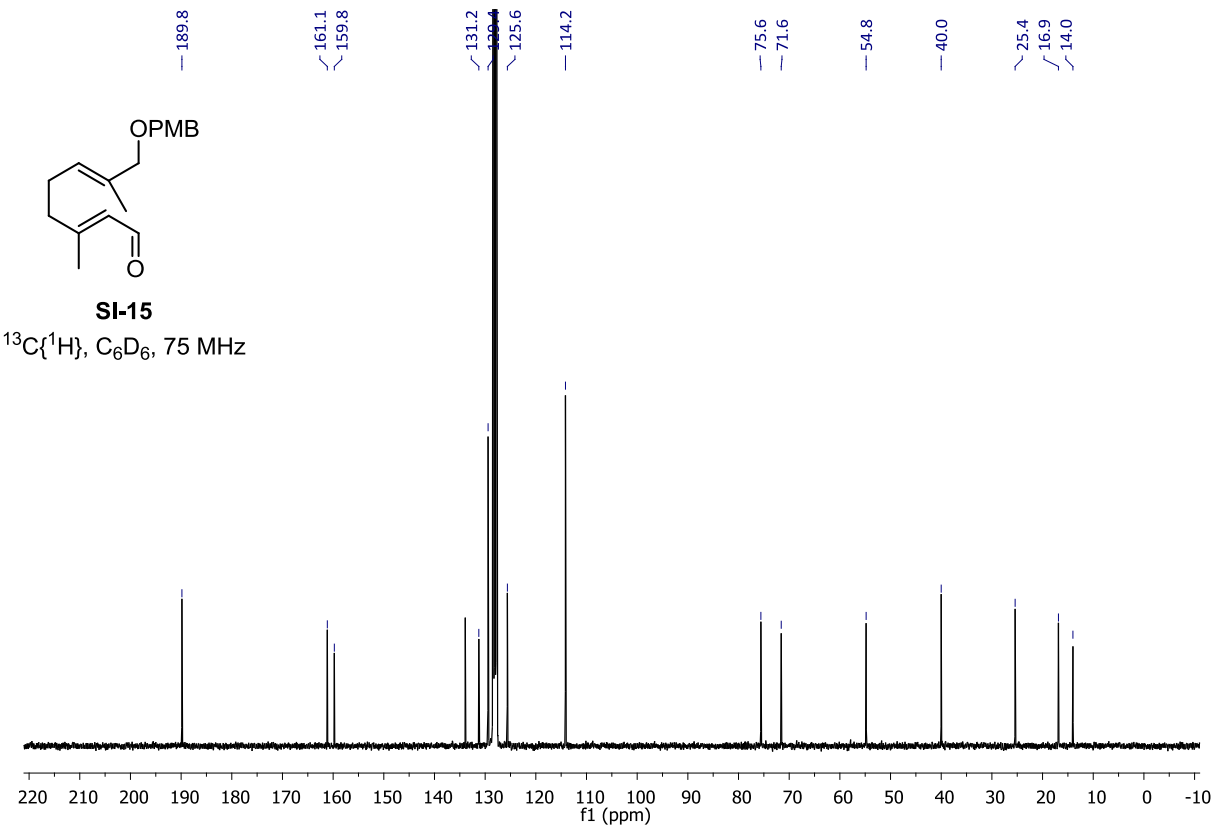
SI-21

$^{13}C\{^{1}H\}$, C_6D_6, 75 MHz



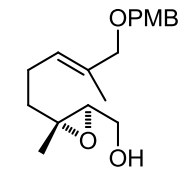
SI-15

^{1}H, C_6D_6, 300 MHz



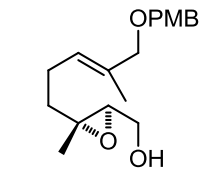
SI-15

$^{13}C\{^{1}H\}$, C_6D_6, 75 MHz



SI-22

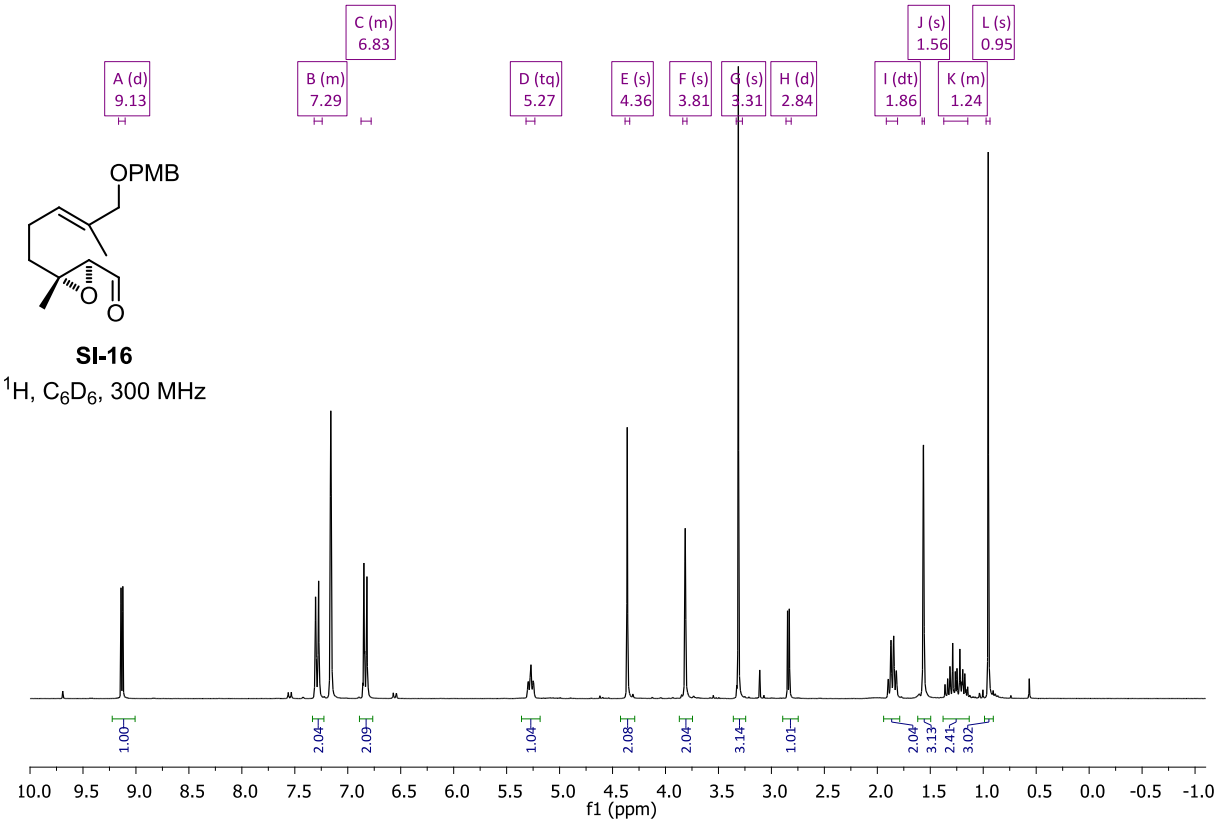
^{1}H, C_6D_6, 300 MHz



SI-22

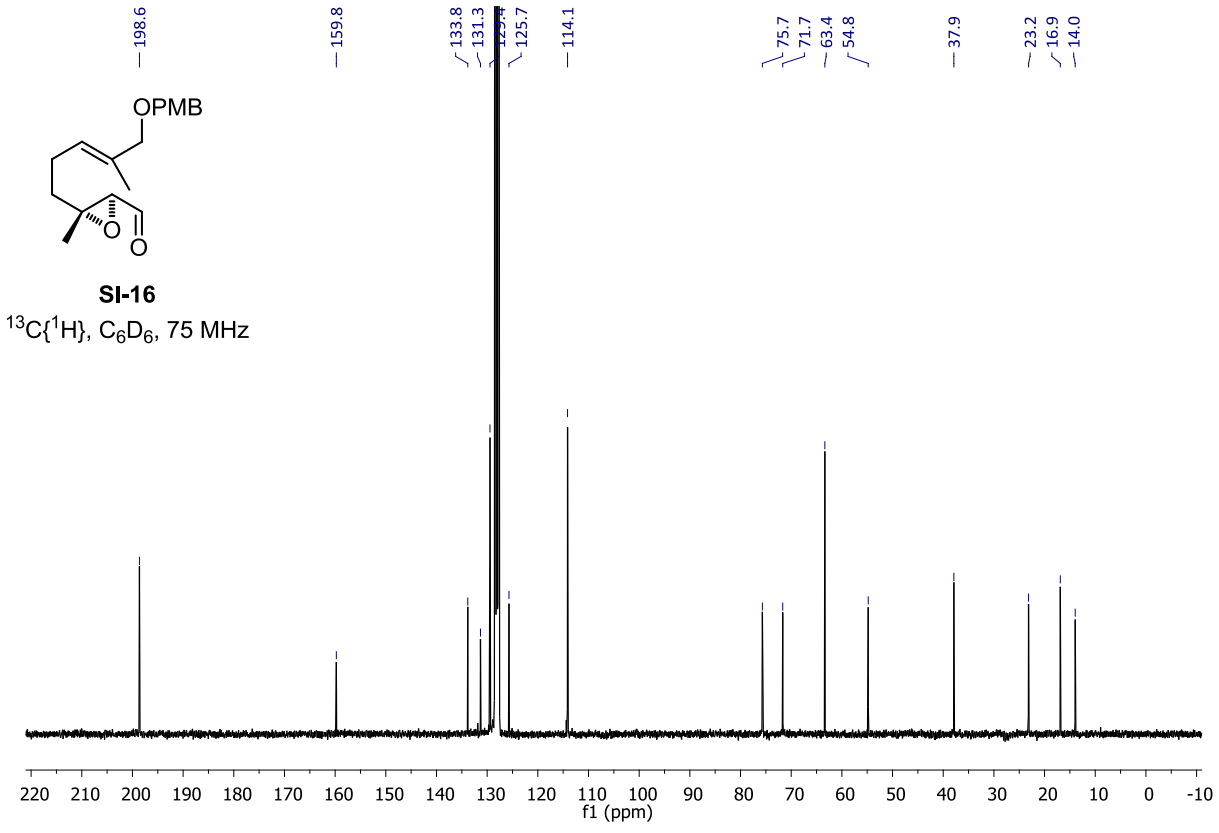
$^{13}C\{^{1}H\}$, C_6D_6, 75 MHz

* = MTBE



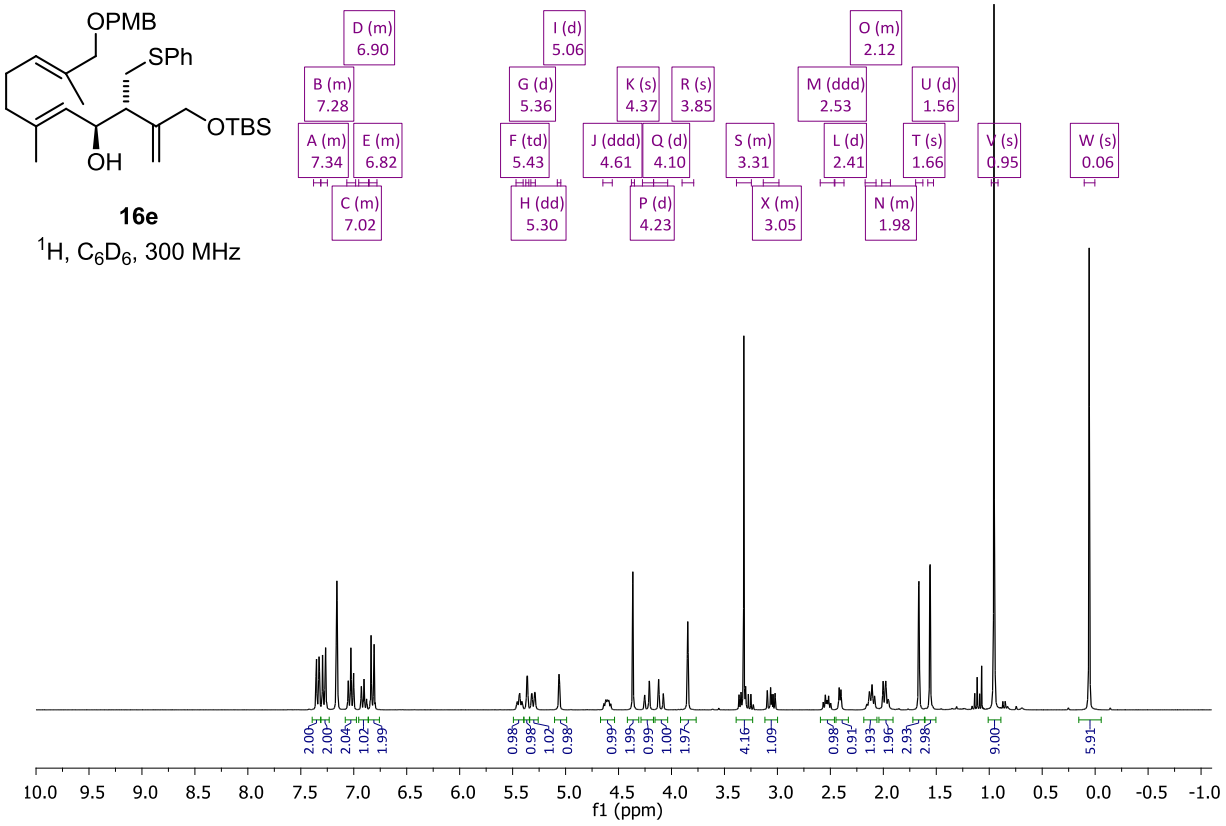
SI-16

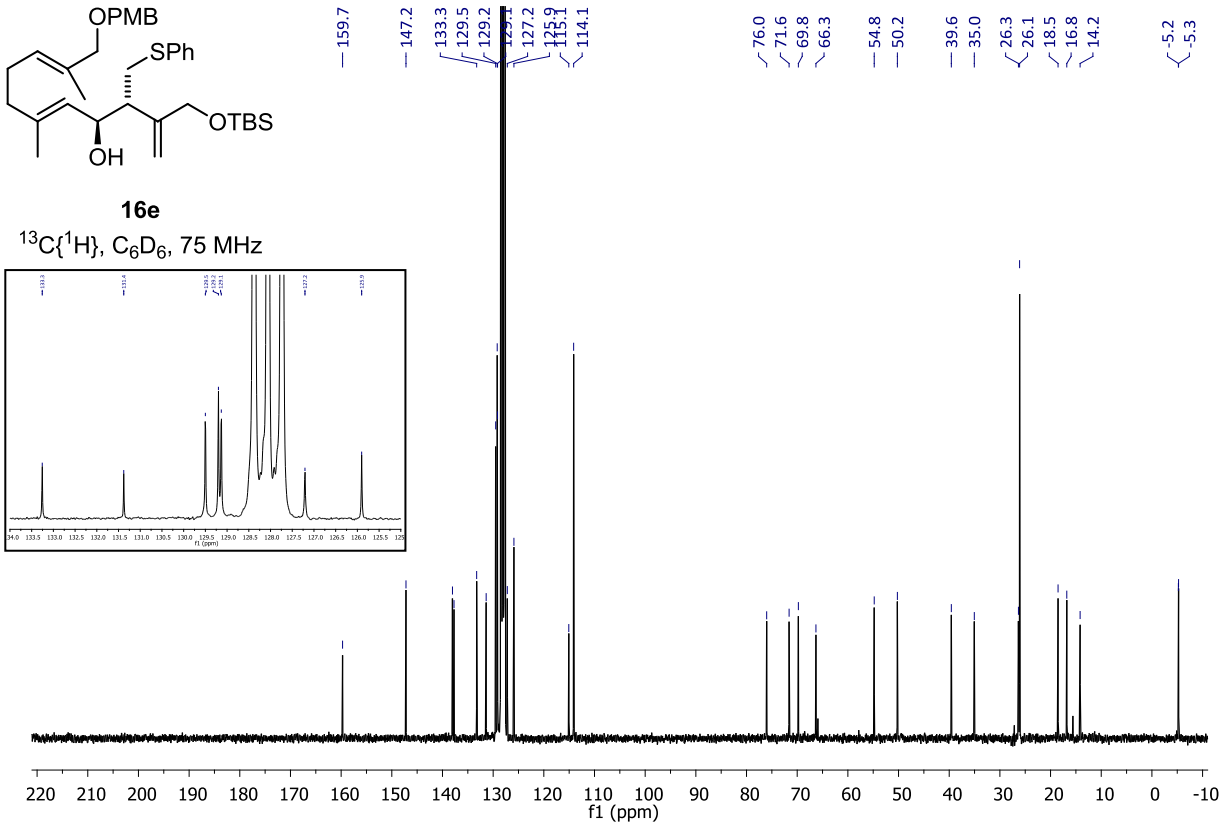
^{1}H, C_6D_6, 300 MHz

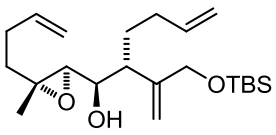


SI-16

$^{13}C\{^{1}H\}$, C_6D_6, 75 MHz

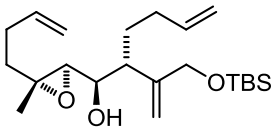

OPMB
SPh
OTBS
OH
16e
1H, C6D6, 300 MHz
D (m) 6.90
B (m) 7.28
A (m) 7.34
E (m) 6.82
C (m) 7.02
I (d) 5.06
G (d) 5.36
F (td) 5.43
H (dd) 5.30
K (s) 4.37
R (s) 3.85
J (ddd) 4.61
Q (d) 4.10
P (d) 4.23
S (m) 3.31
X (m) 3.05
O (m) 2.12
M (ddd) 2.53
L (d) 2.41
N (m) 1.98
U (d) 1.56
T (s) 1.66
V (s) 0.95
W (s) 0.06
f1 (ppm)


OPMB
SPh
OTBS
OH
16e
13C{1H}, C6D6, 75 MHz
159.7
147.2
133.3
129.5
129.2
129.1
127.2
125.9
115.1
114.1
76.0
71.6
69.8
66.3
54.8
50.2
39.6
35.0
26.3
26.1
18.5
16.8
14.2
-5.2
-5.3
f1 (ppm)



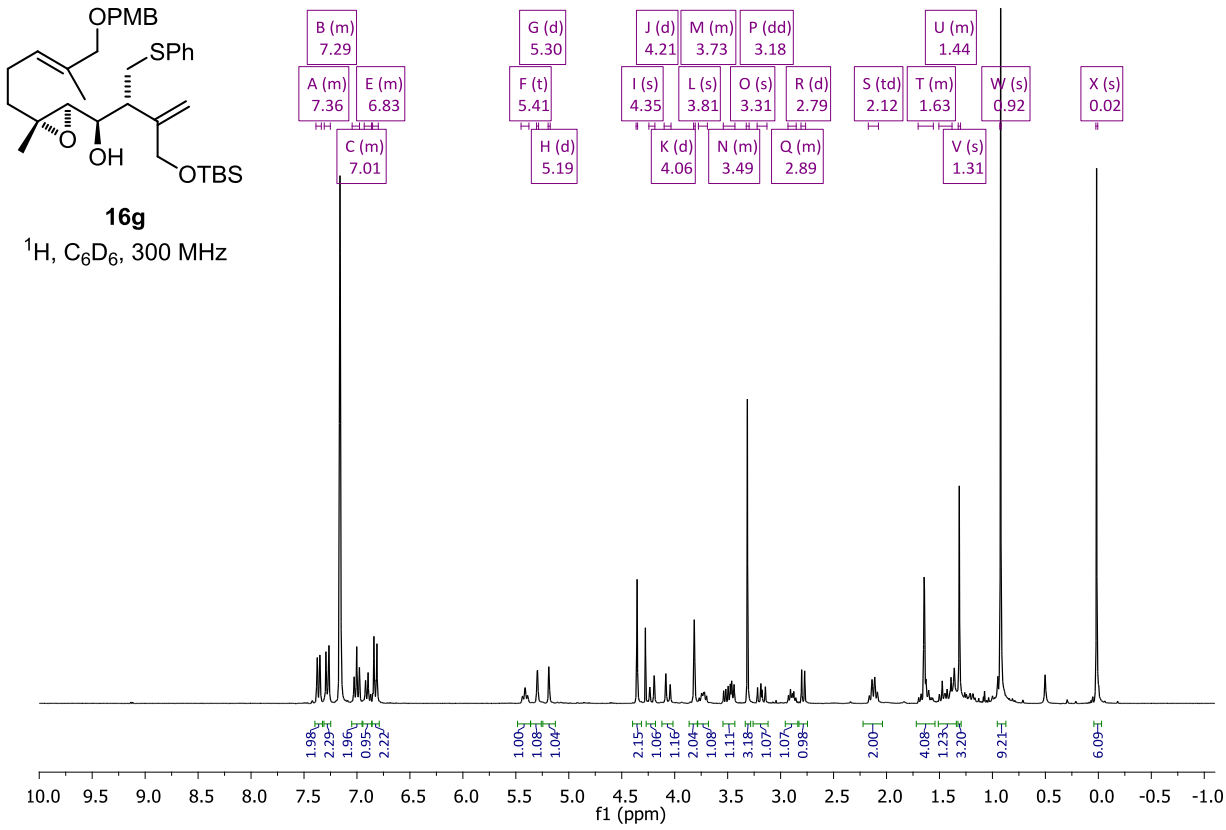
16f

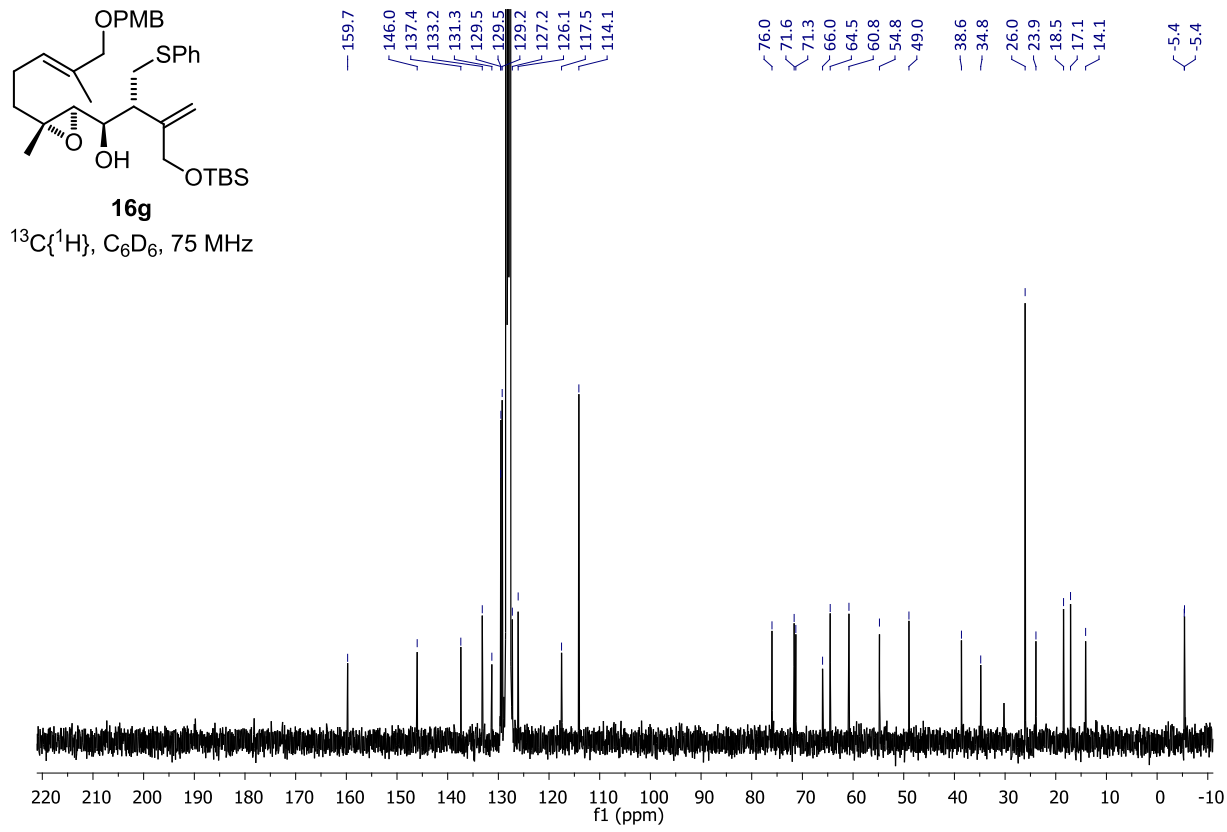
^{1}H, C_6D_6, 300 MHz

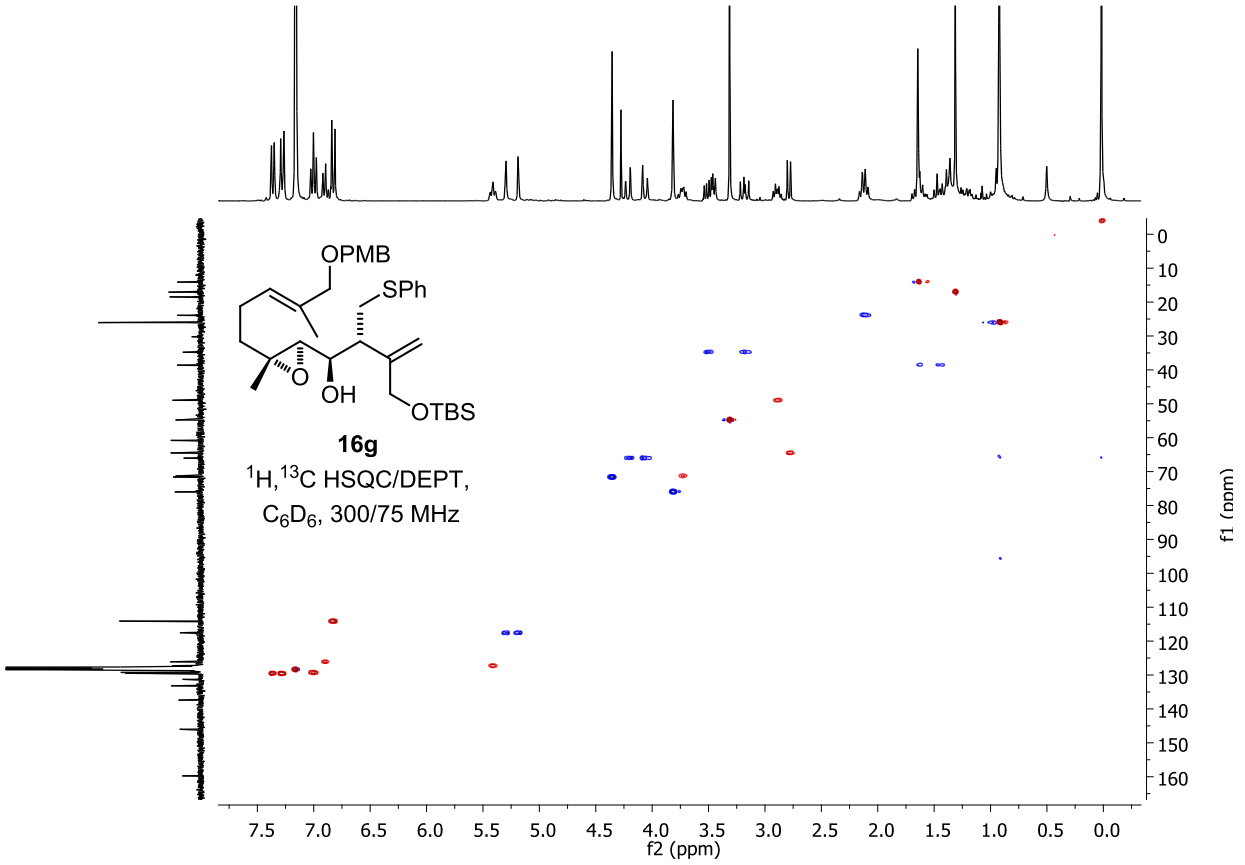


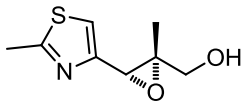
16f

$^{13}C\{^{1}H\}$, C_6D_6, 75 MHz


OPMB
SPh
OH
OTBS
16g
^{1}H, C_6D_6, 300 MHz
B (m) 7.29
A (m) 7.36
E (m) 6.83
C (m) 7.01
G (d) 5.30
F (t) 5.41
H (d) 5.19
J (d) 4.21
M (m) 3.73
P (dd) 3.18
I (s) 4.35
L (s) 3.81
O (s) 3.31
R (d) 2.79
K (d) 4.06
N (m) 3.49
Q (m) 2.89
S (td) 2.12
U (m) 1.44
T (m) 1.63
W (s) 0.92
V (s) 1.31
X (s) 0.02
f1 (ppm)

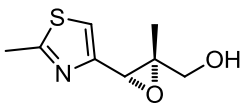

OPMB
SPh
OH
OTBS
16g
^{13}C{^{1}H}, C_6D_6, 75 MHz
159.7
146.0
137.4
133.2
131.3
129.5
129.5
129.2
127.2
126.1
117.5
114.1
76.0
71.6
71.3
66.0
64.5
60.8
54.8
49.0
38.6
34.8
26.0
23.9
18.5
17.1
14.1
-5.4
-5.4
f1 (ppm)


OPMB
SPh
O
OH
OTBS
16g
$^{1}H,^{13}C$ HSQC/DEPT,
C_6D_6, 300/75 MHz
f2 (ppm)
f1 (ppm)



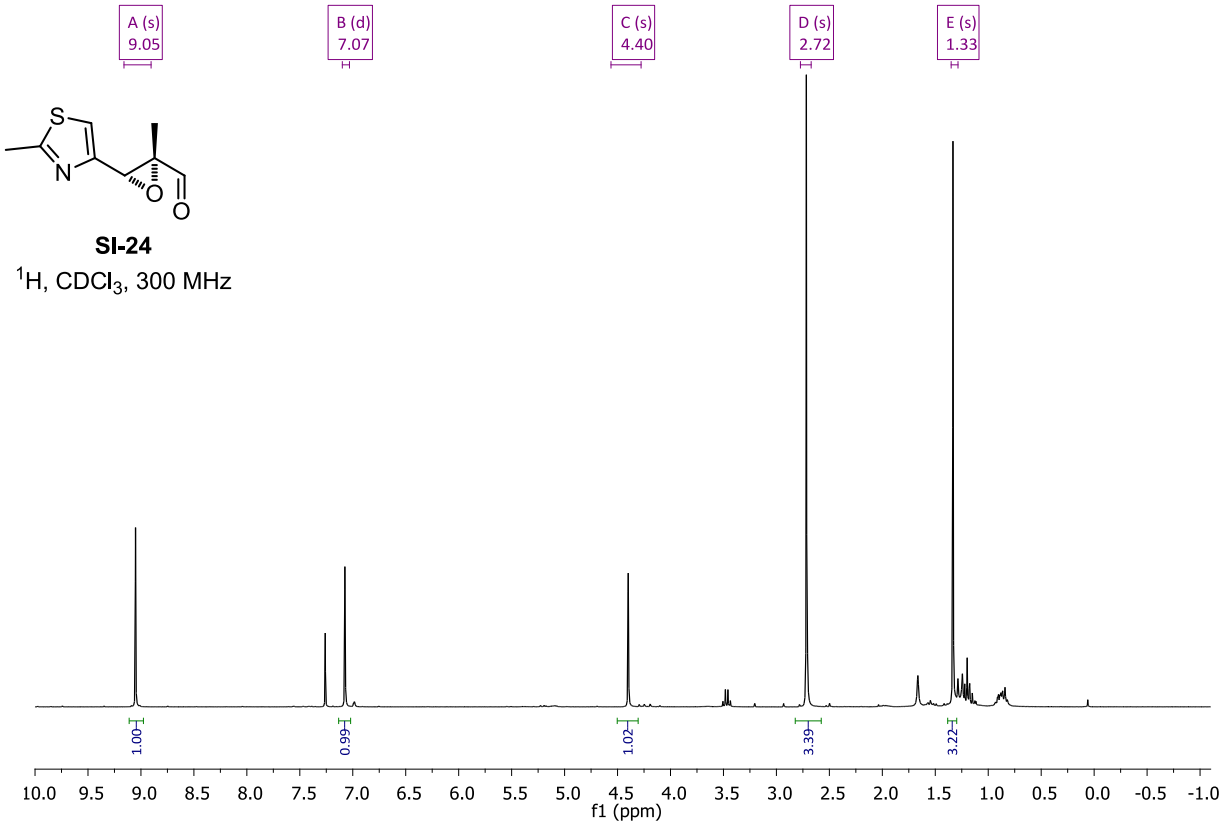
SI-23

^{1}H, $CDCl_3$, 300 MHz



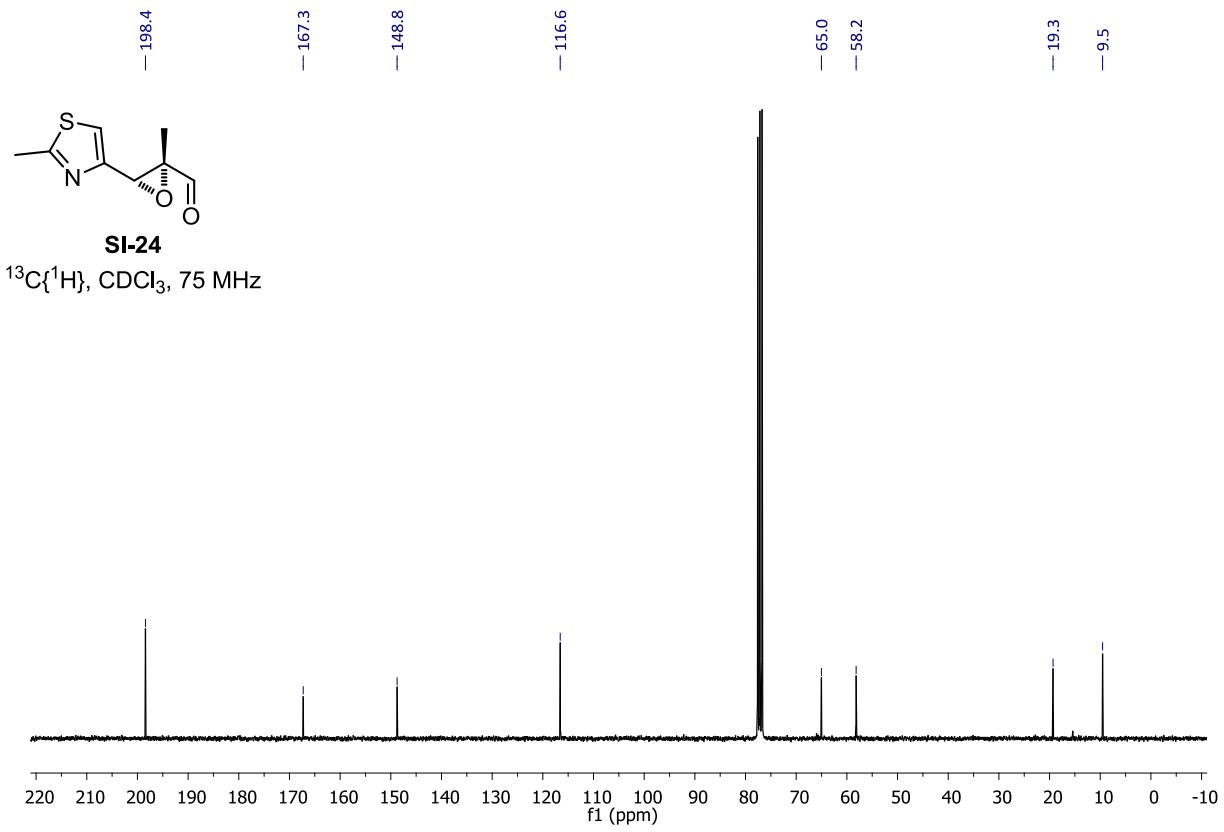
SI-23

$^{13}C\{^{1}H\}$, $CDCl_3$, 75 MHz



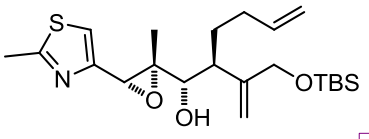
SI-24

^{1}H, $CDCl_3$, 300 MHz



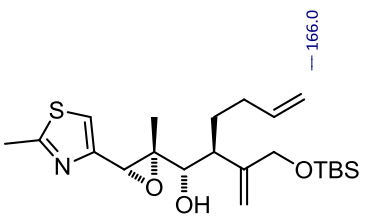
SI-24

$^{13}C\{^{1}H\}$, $CDCl_3$, 75 MHz



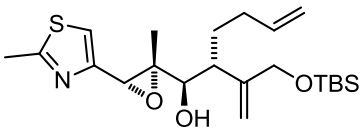
16ha

^{1}H, C_6D_6, 300 MHz



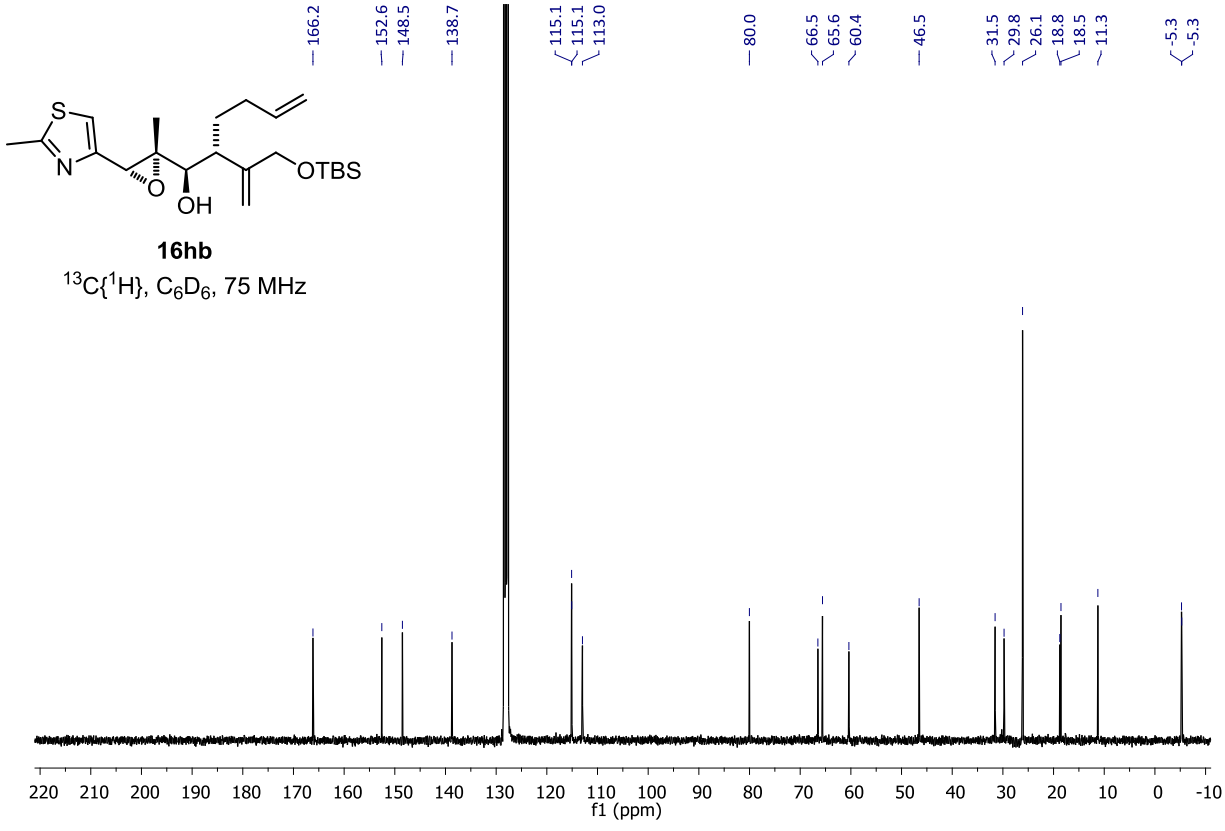
16ha

$^{13}C\{^{1}H\}$, C_6D_6, 75 MHz



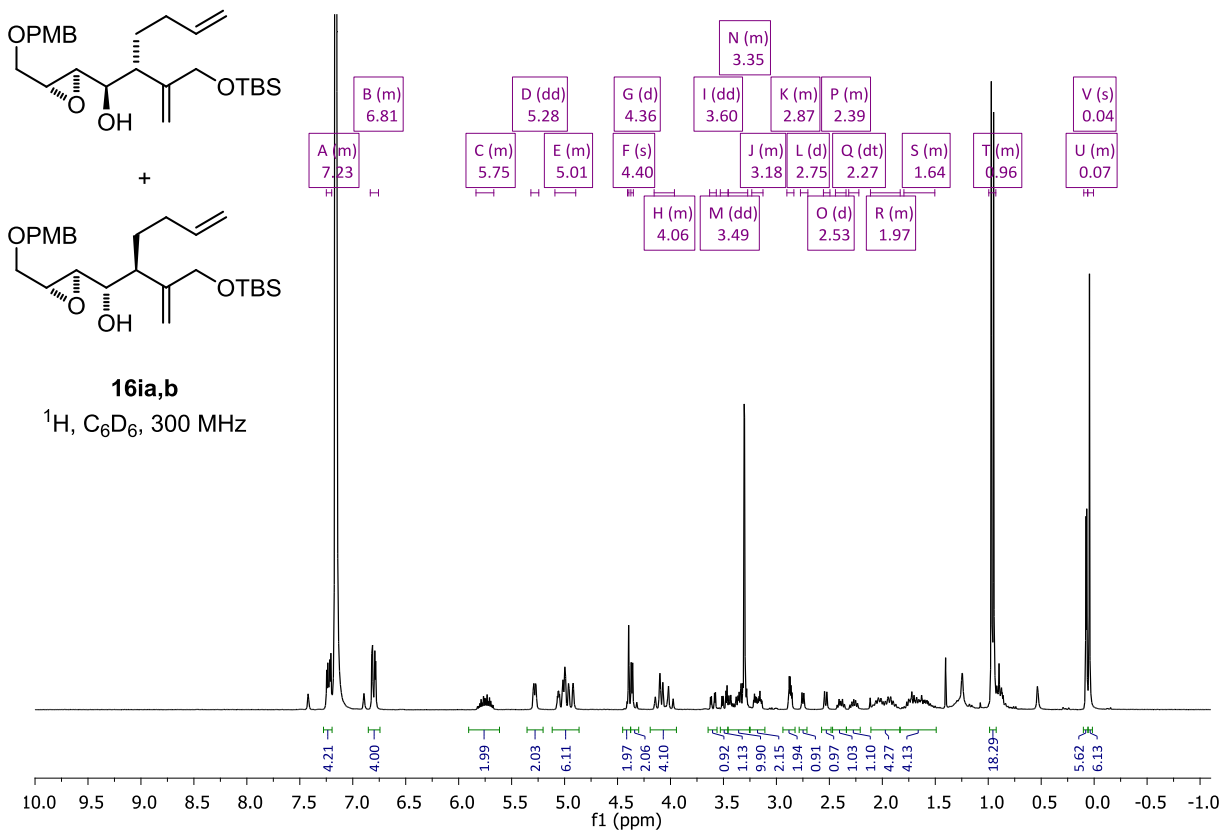
16hb

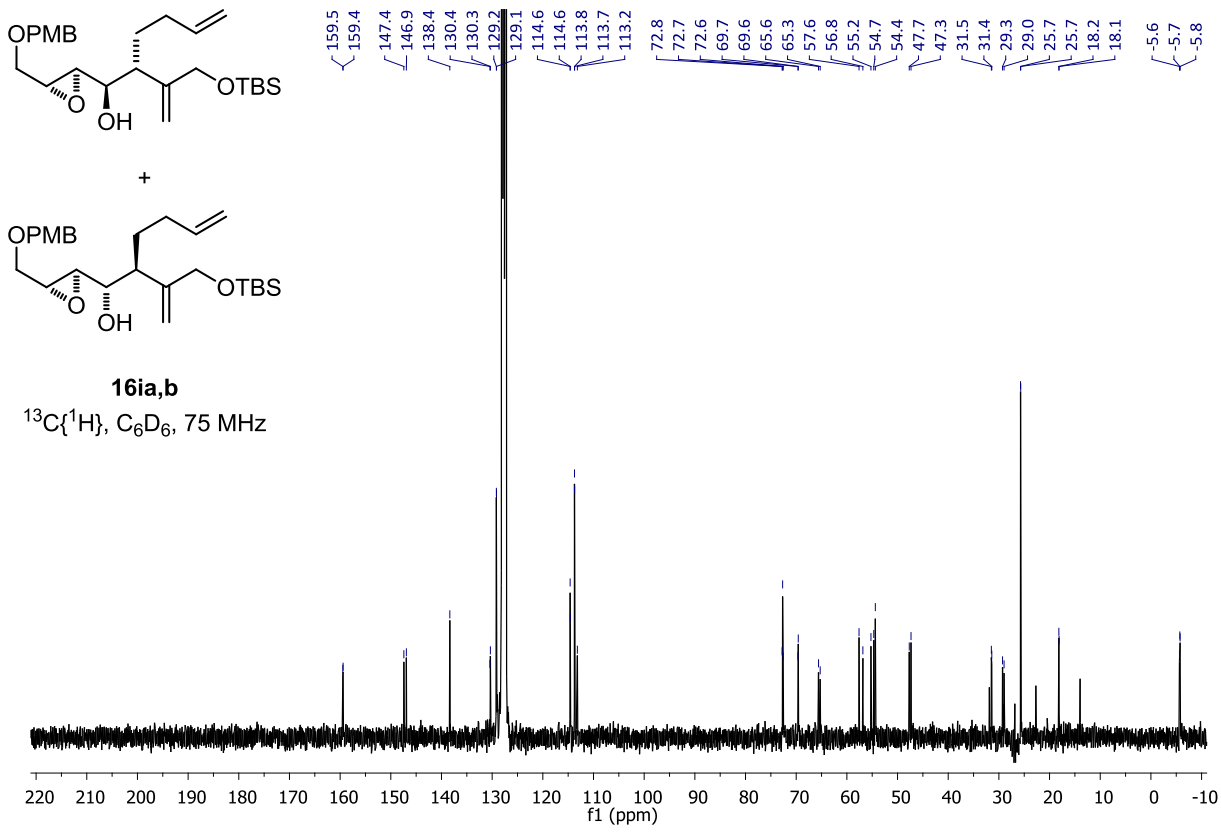
^{1}H, C_6D_6, 300 MHz

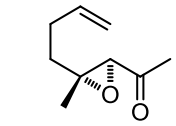


16hb

$^{13}C\{^{1}H\}$, C_6D_6, 75 MHz

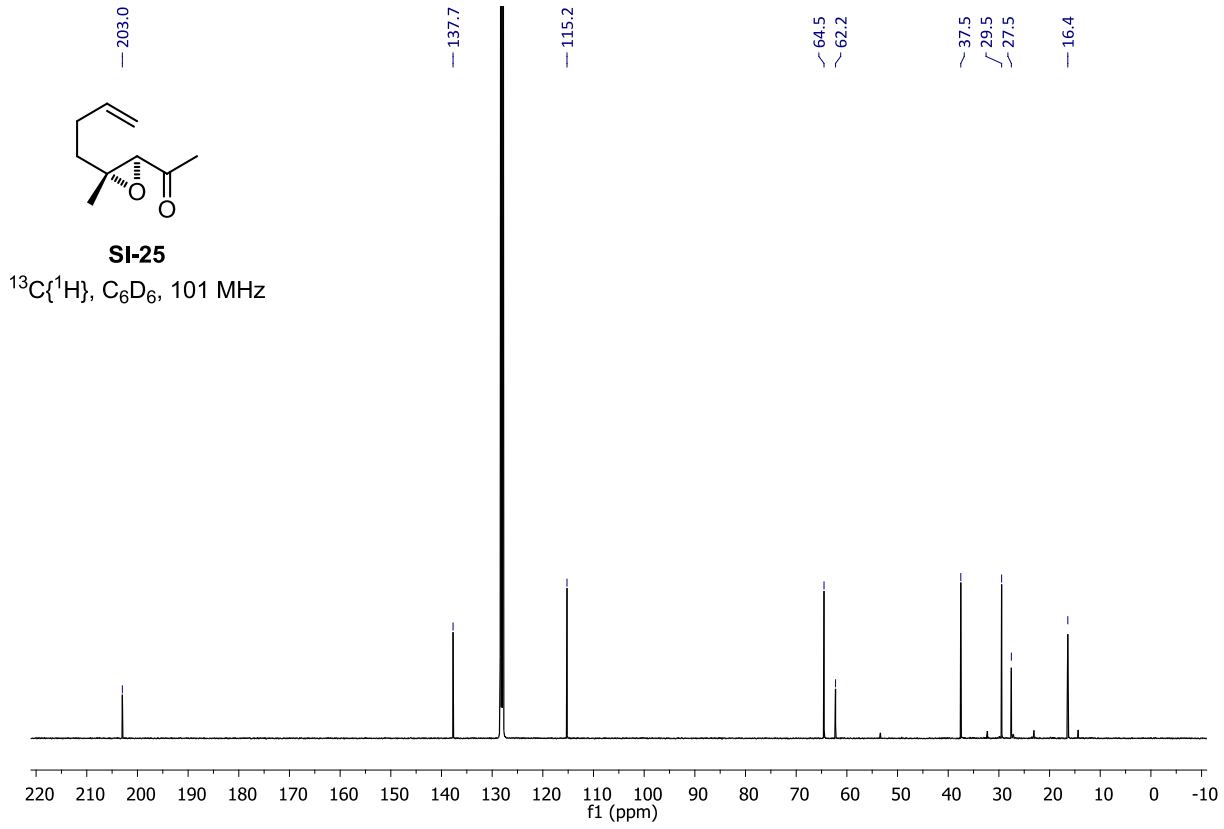

OPMB
OTBS
OH
+
OPMB
OTBS
OH
16ia,b
1H, C6D6, 300 MHz
A (m) 7.23
B (m) 6.81
C (m) 5.75
D (dd) 5.28
E (m) 5.01
F (s) 4.40
G (d) 4.36
H (m) 4.06
I (dd) 3.60
J (m) 3.18
K (m) 2.87
L (d) 2.75
M (dd) 3.49
N (m) 3.35
O (d) 2.53
P (m) 2.39
Q (dt) 2.27
R (m) 1.97
S (m) 1.64
T (m) 0.96
U (m) 0.07
V (s) 0.04
4.21
4.00
1.99
2.03
6.11
1.97
2.06
4.10
0.92
1.13
9.90
2.15
1.94
0.91
0.97
1.03
1.10
4.27
4.13
18.29
5.62
6.13
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 -0.5 -1.0
f1 (ppm)


OPMB
OTBS
OH
+
OPMB
OTBS
OH
16ia,b
13C{1H}, C6D6, 75 MHz
159.5
159.4
147.4
146.9
138.4
130.4
130.3
129.2
129.1
114.6
114.6
113.8
113.7
113.2
72.8
72.7
72.6
69.7
69.6
65.6
65.3
57.6
56.8
55.2
54.7
54.4
47.7
47.3
31.5
31.4
29.3
29.0
25.7
25.7
18.2
18.1
-5.6
-5.7
-5.8
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



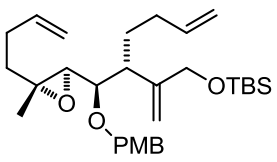
SI-25

^{1}H, C_6D_6, 400 MHz



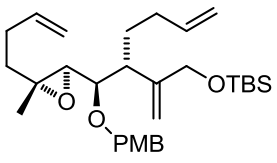
SI-25

$^{13}C\{^{1}H\}$, C_6D_6, 101 MHz



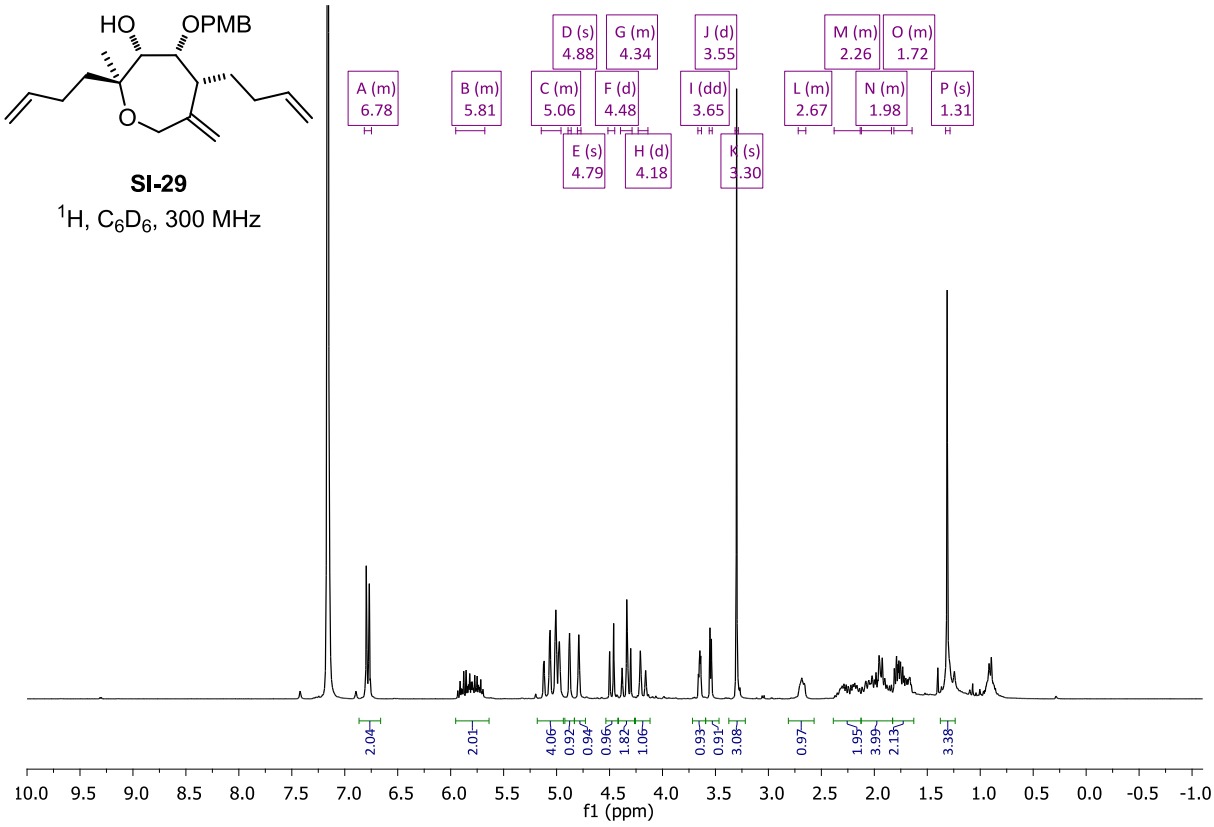
SI-30

^{1}H, C_6D_6, 300 MHz



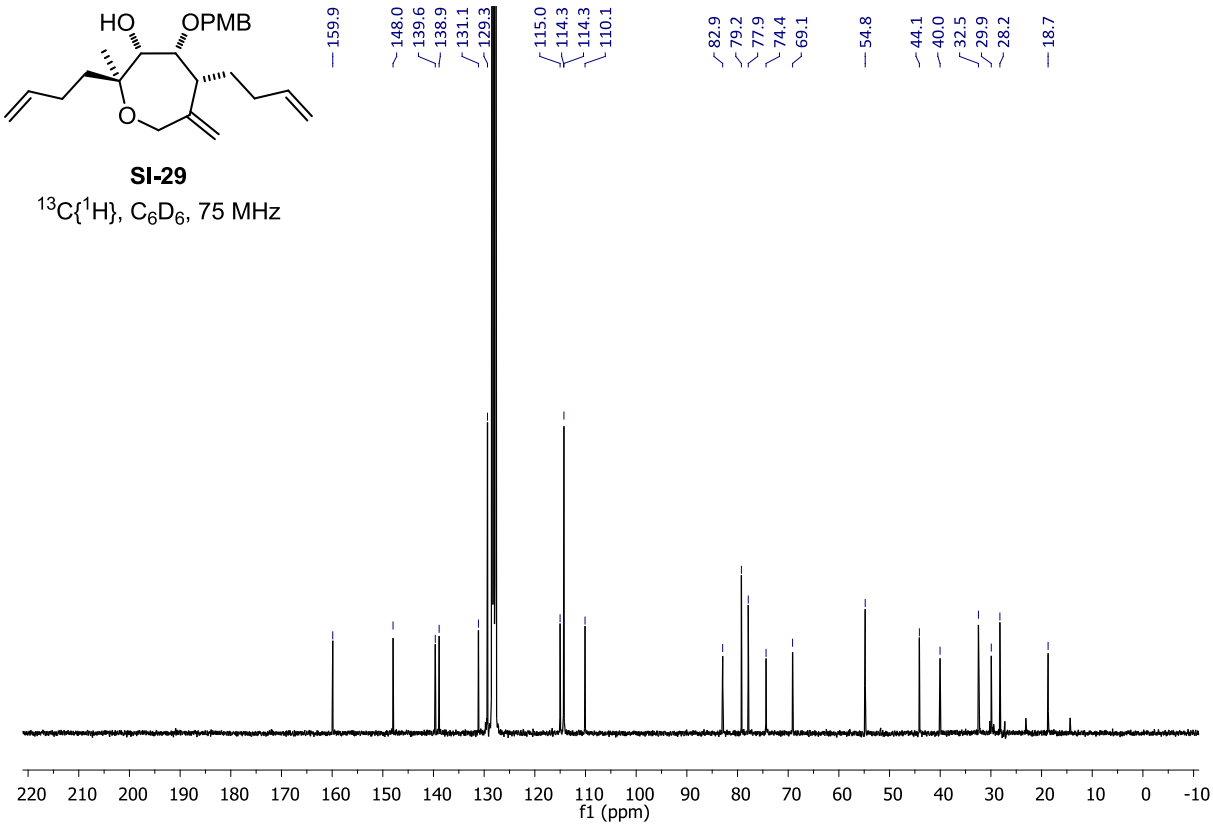
SI-30

$^{13}C\{^{1}H\}$, C_6D_6, 75 MHz



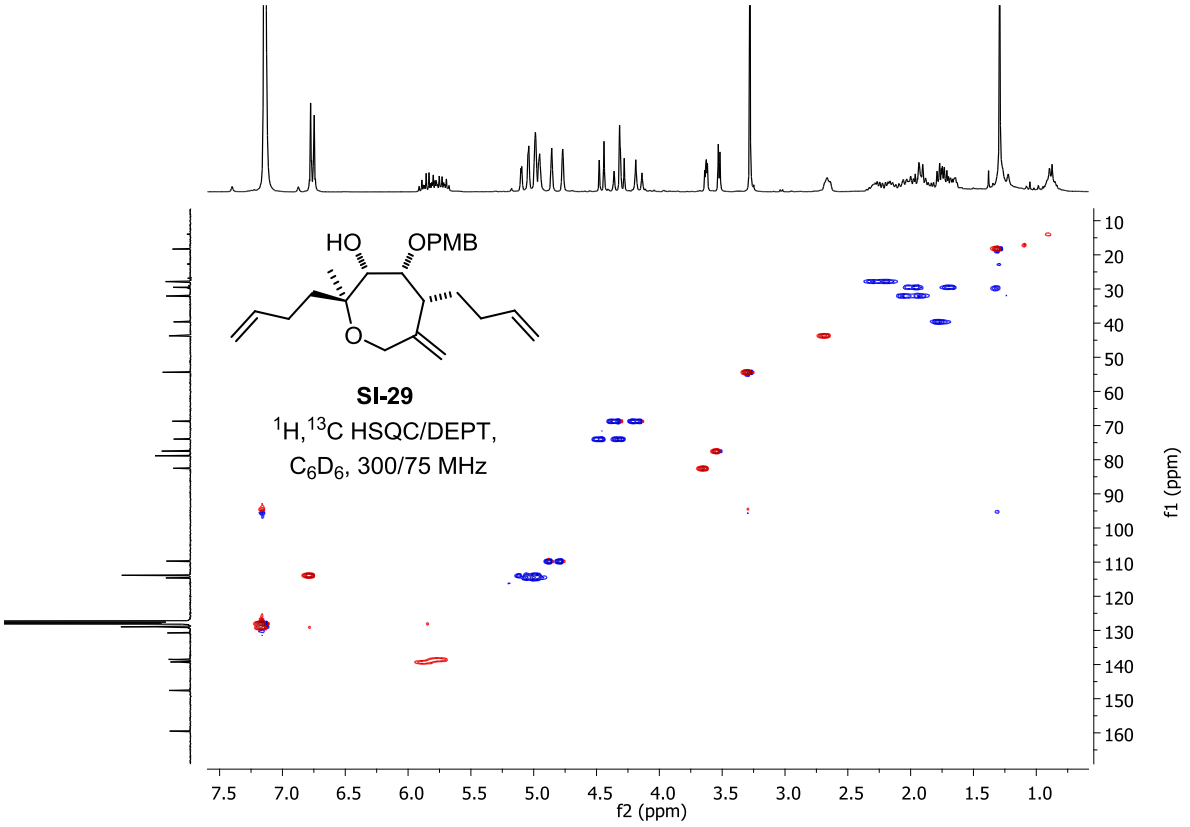
SI-29

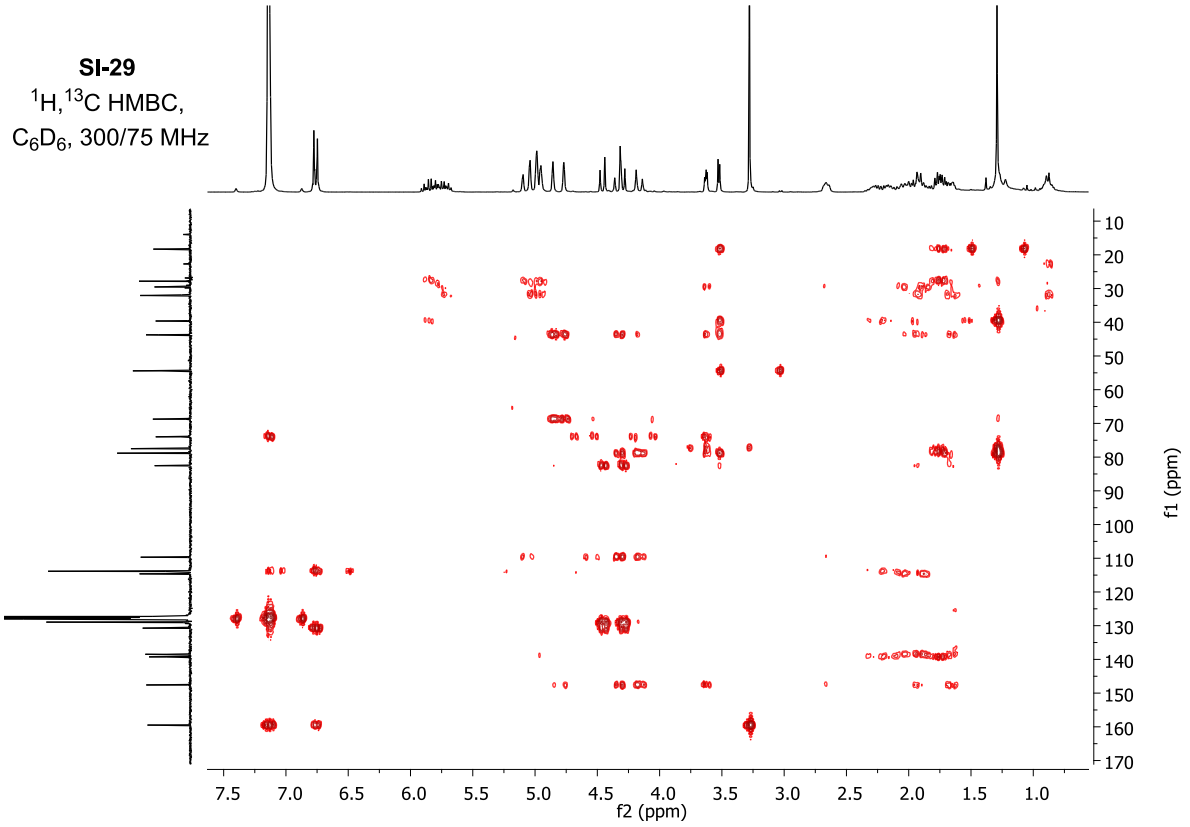
^{1}H, C_6D_6, 300 MHz

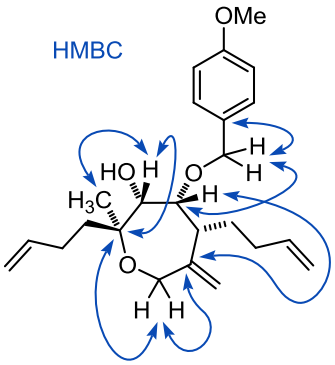


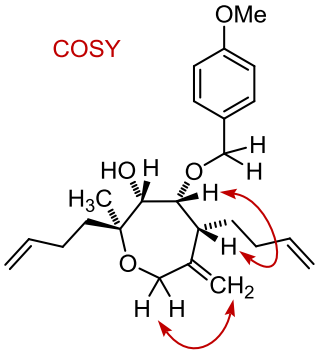
SI-29

$^{13}C\{^{1}H\}$, C_6D_6, 75 MHz


HO
OPMB
O
SI-29
$^{1}H,^{13}C$ HSQC/DEPT,
C_6D_6, 300/75 MHz
f1 (ppm)
f2 (ppm)


SI-29
$^{1}H,^{13}C$ HMBC,
C_6D_6, 300/75 MHz
f1 (ppm)
f2 (ppm)

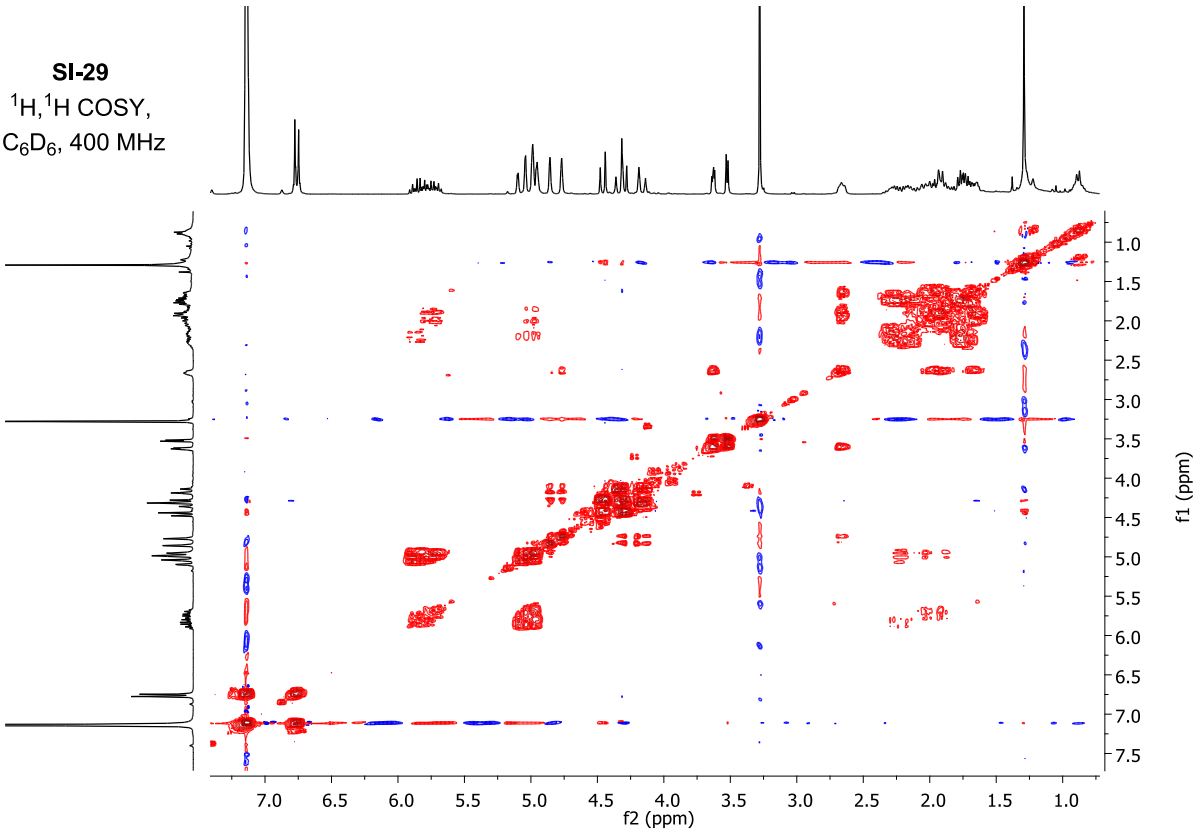


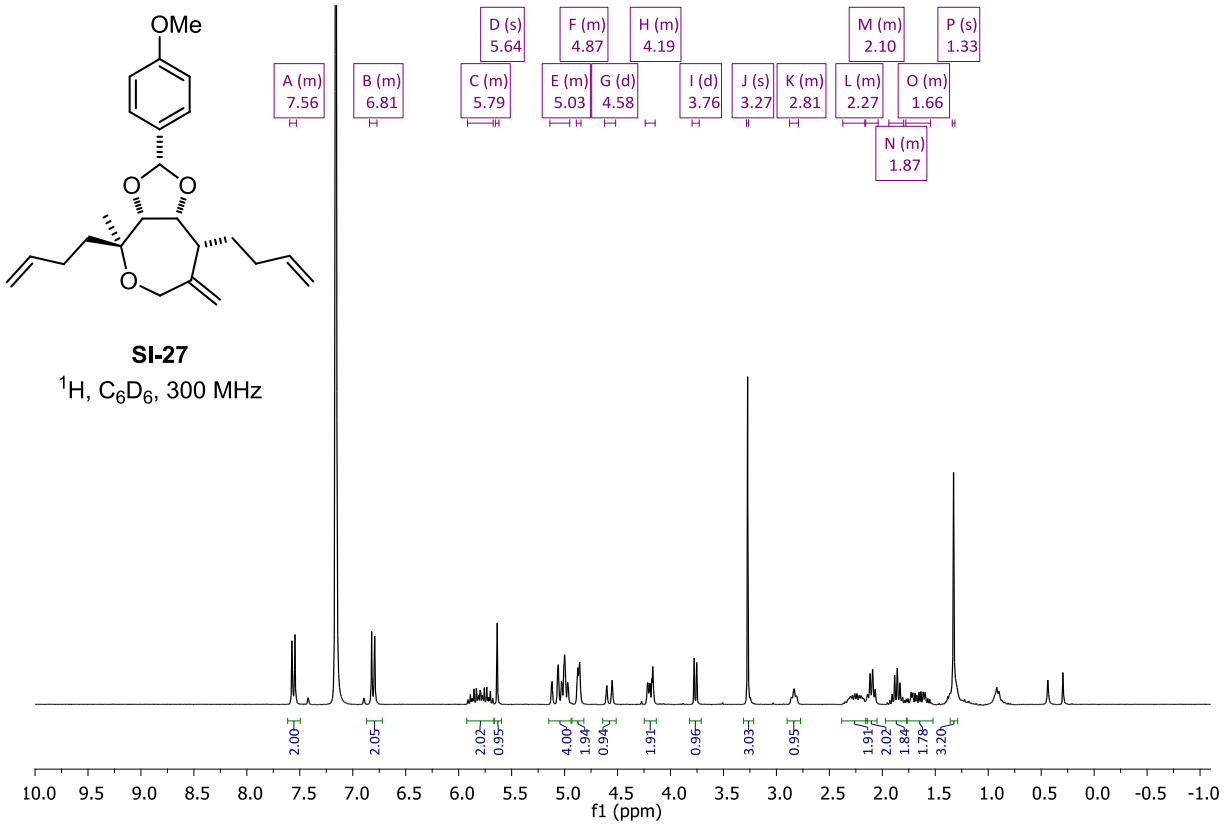


SI-29

$^{1}H,^{1}H$ COSY,

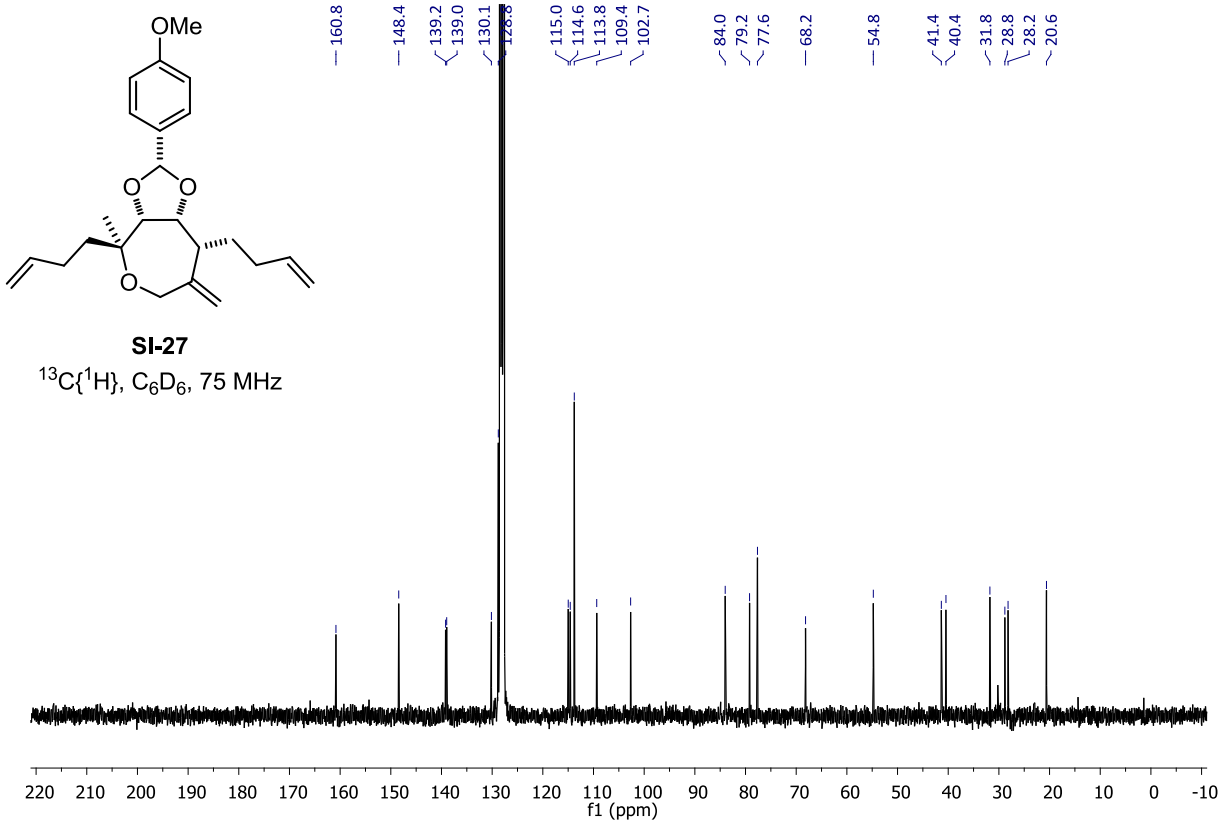
C_6D_6, 400 MHz





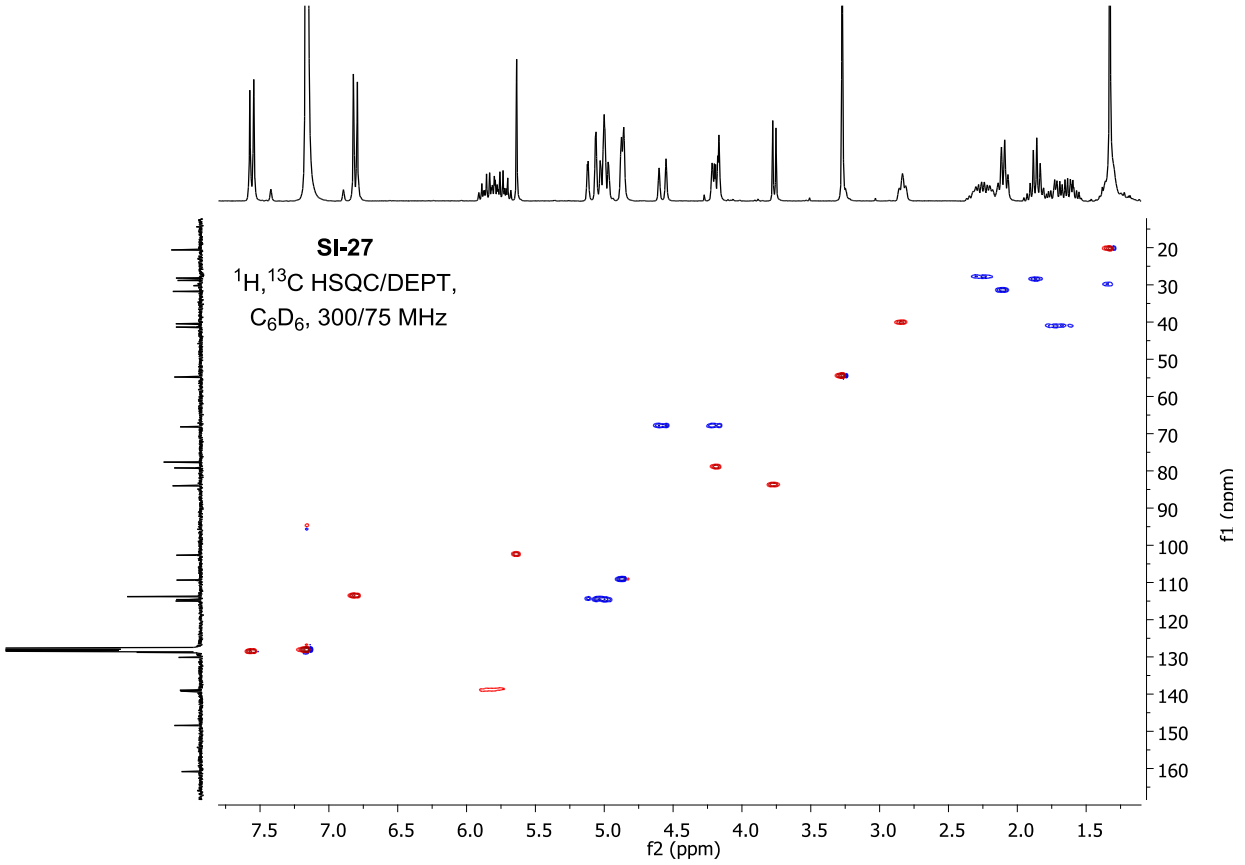
SI-27

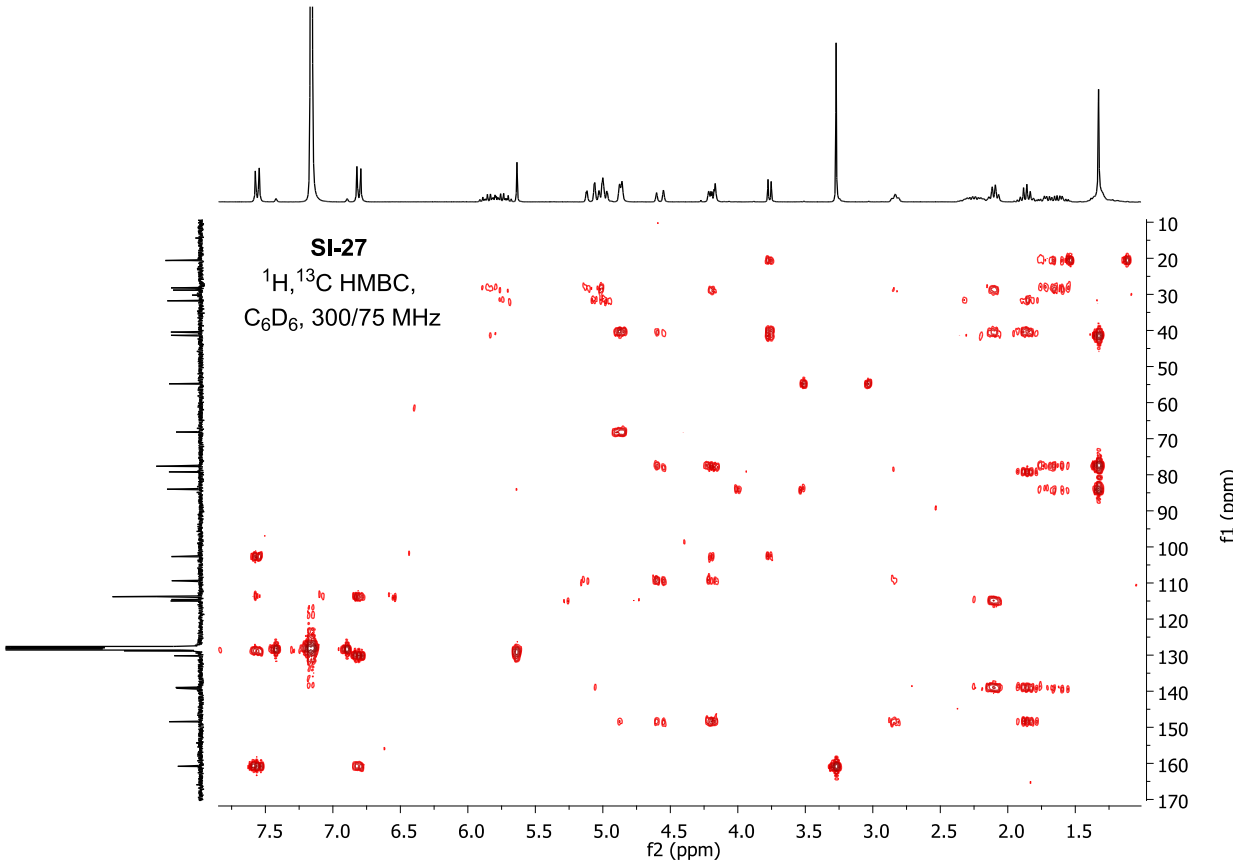
^{1}H, C_6D_6, 300 MHz



SI-27

$^{13}C\{^{1}H\}$, C_6D_6, 75 MHz

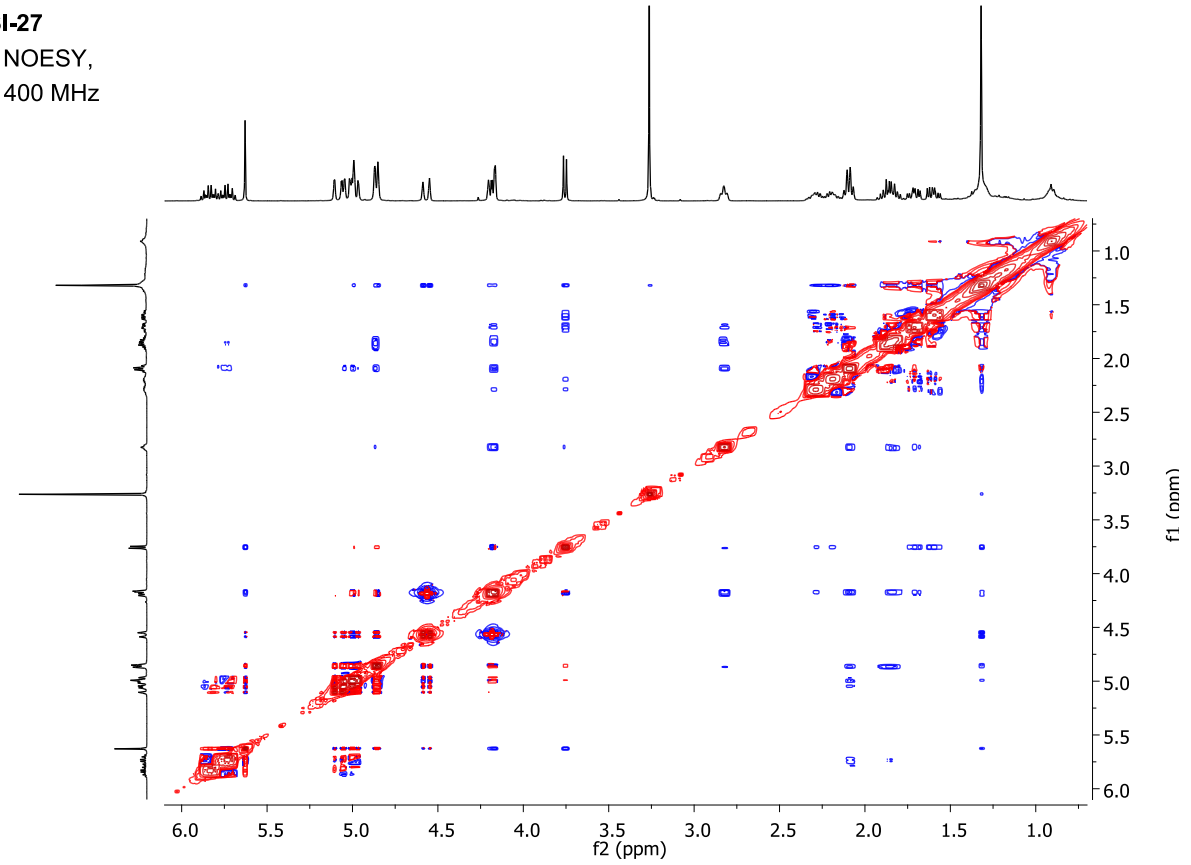

SI-27
$^{1}H,^{13}C$ HSQC/DEPT,
C_6D_6, 300/75 MHz
f2 (ppm)
f1 (ppm)


SI-27
$^{1}H,^{13}C$ HMBC,
C_6D_6, 300/75 MHz
f2 (ppm)
f1 (ppm)

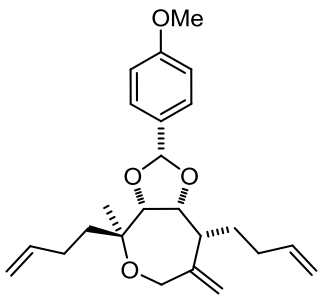
SI-27

$^{1}H,^{1}H$ NOESY,

C_6D_6, 400 MHz

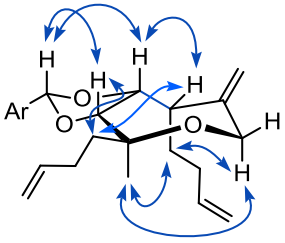


formed

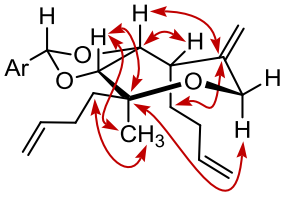


(Felkin)

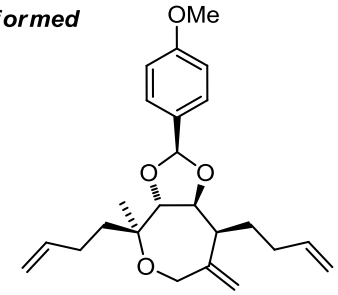
NOESY



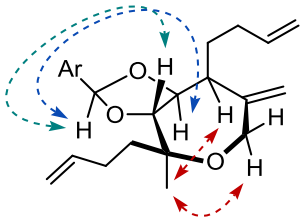
HMBC



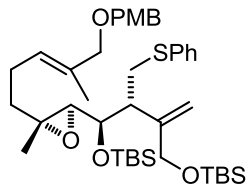
not formed



(*anti*-Felkin)

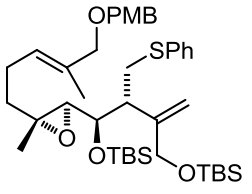


expected nOe correlations for *anti*-Felkin
(coloring for clarity reasons)



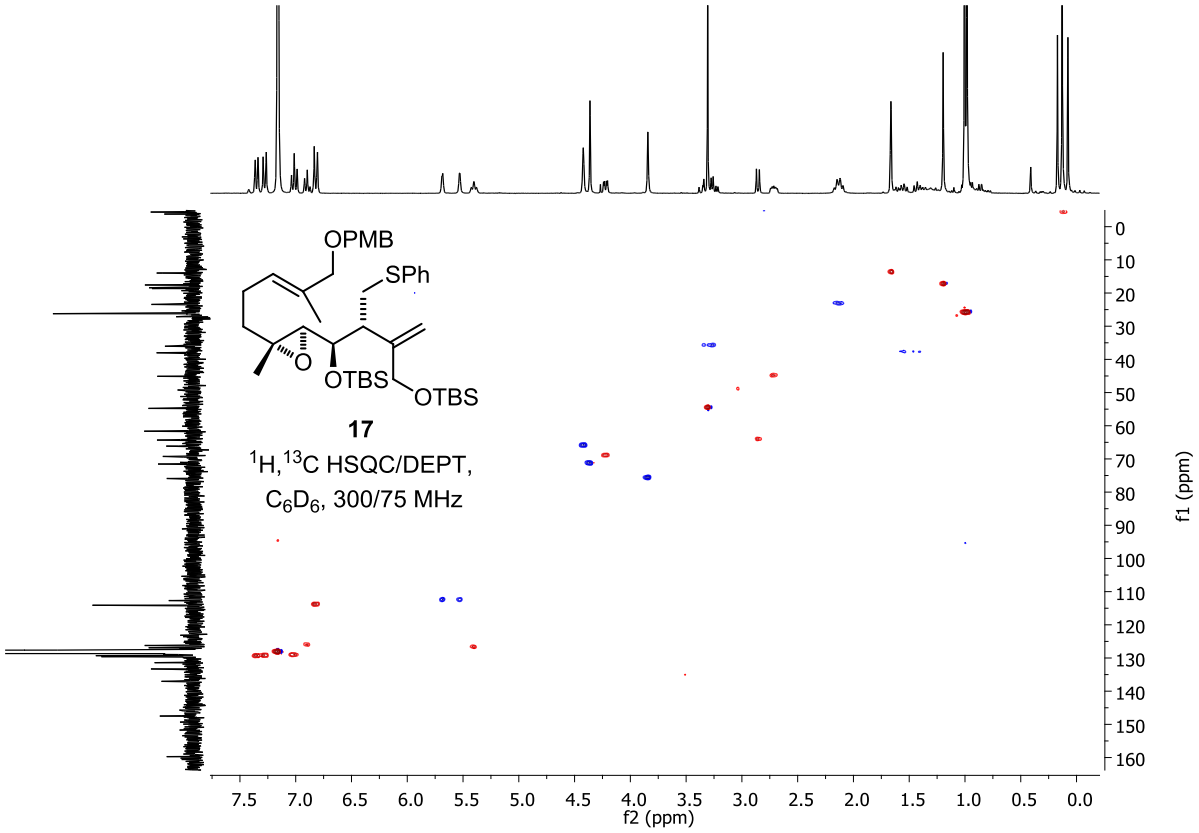
17

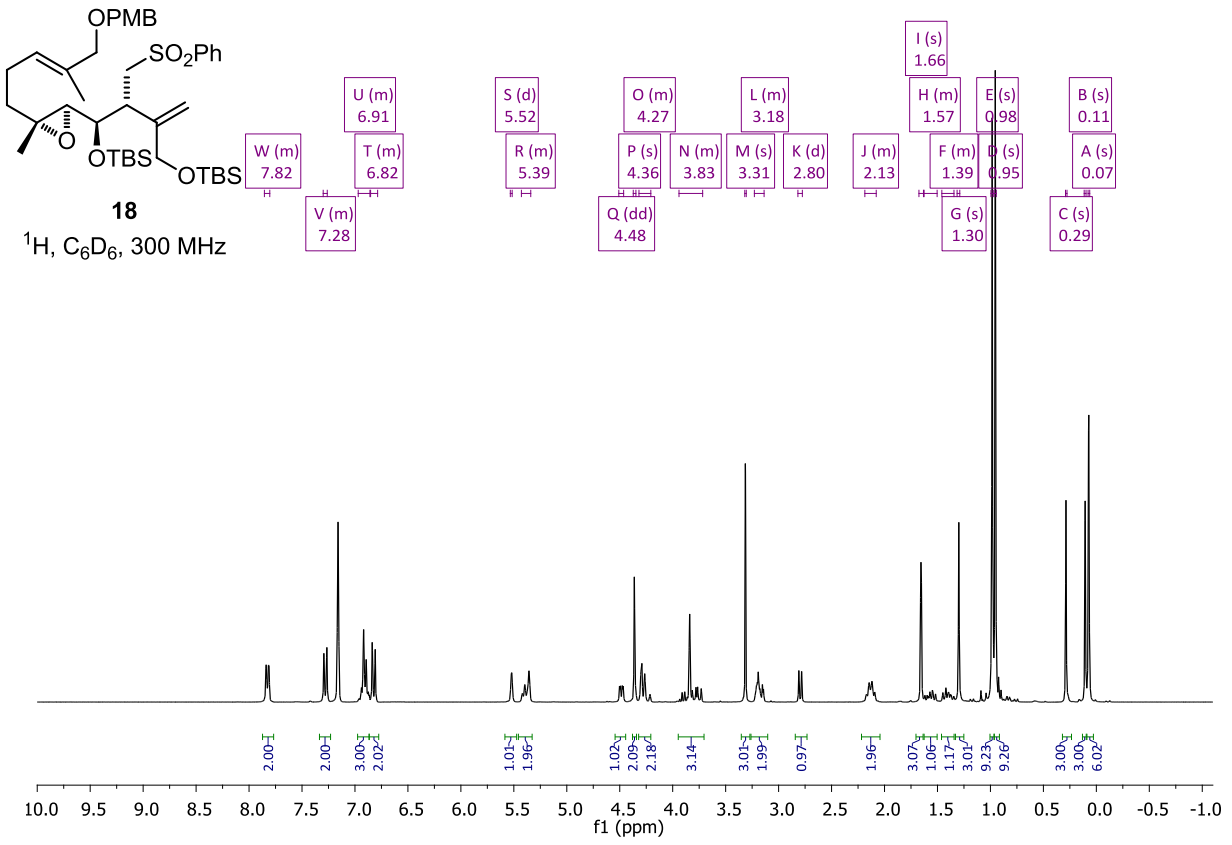
^{1}H, C_6D_6, 300 MHz

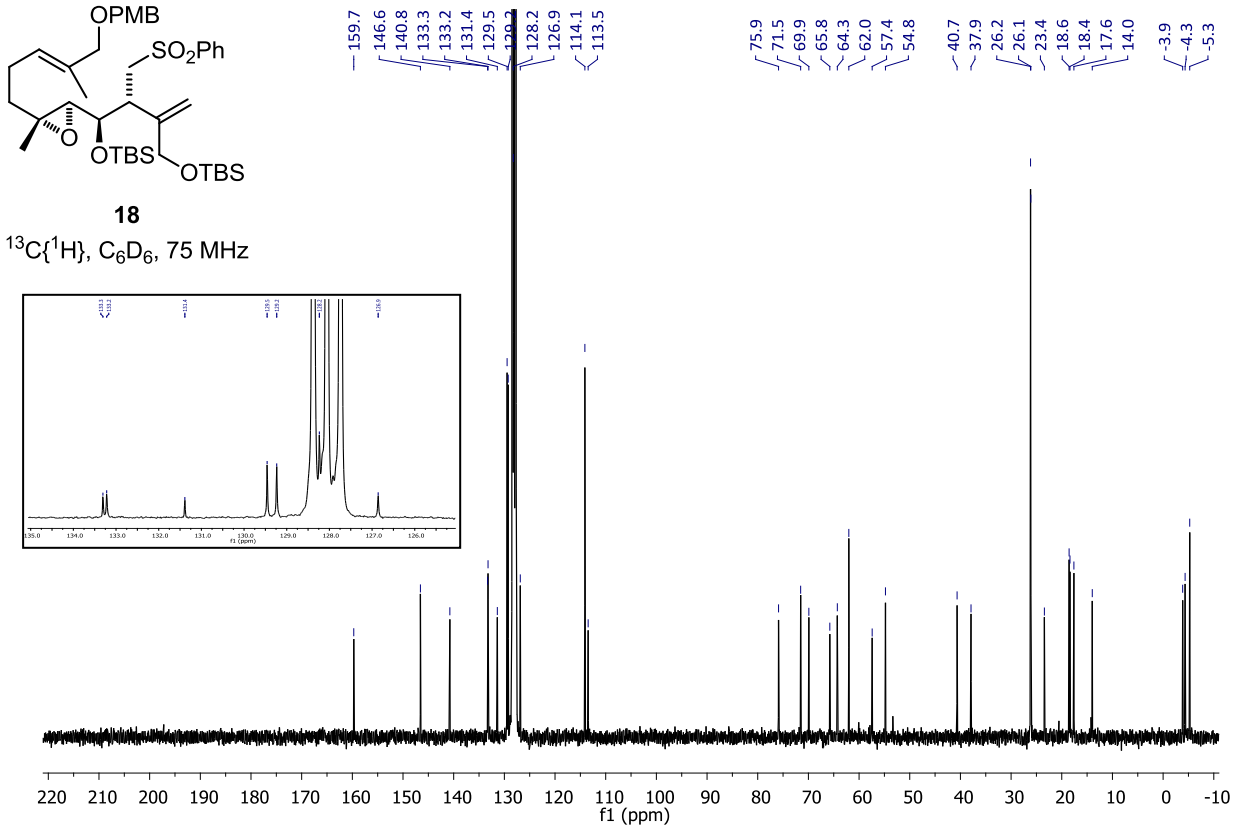


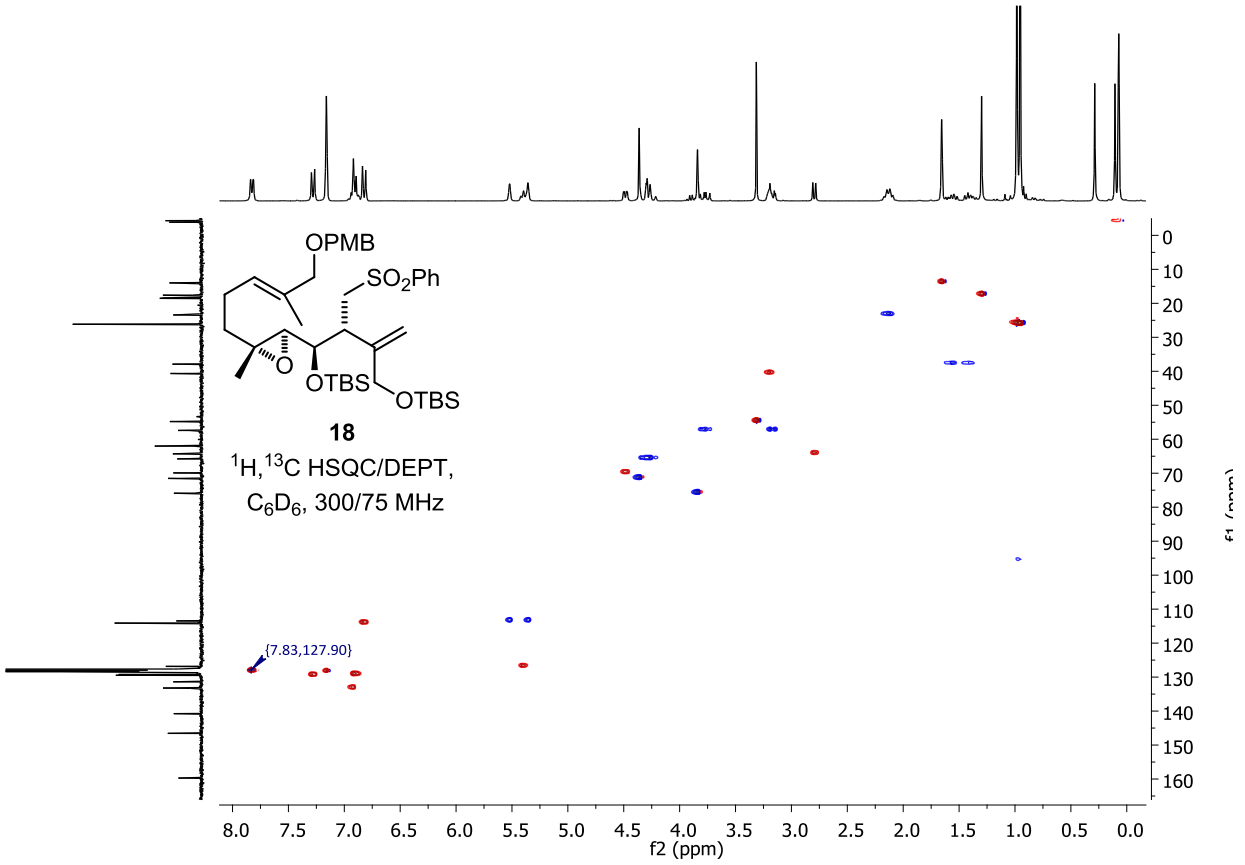
17

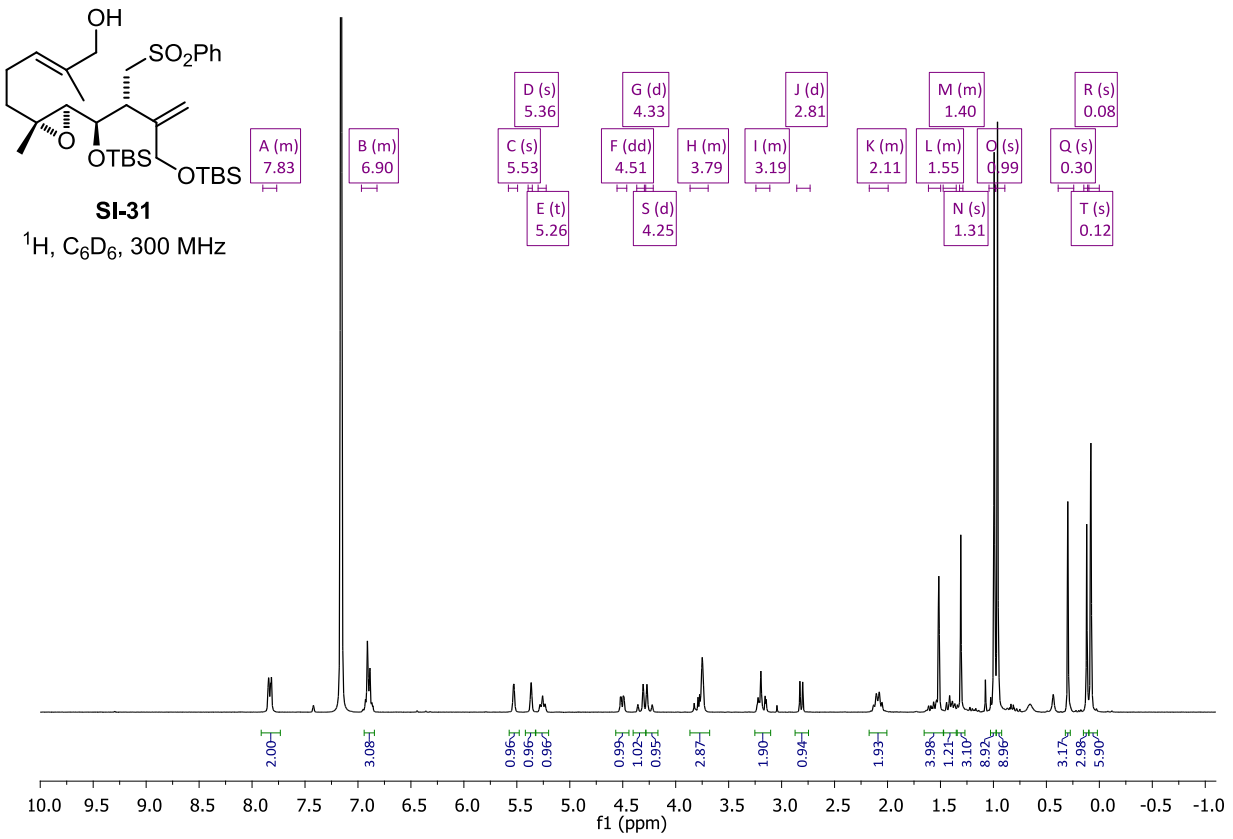
$^{13}C\{^{1}H\}$, C_6D_6, 75 MHz


OPMB
SPh
O
OTBS
OTBS
17
1H,13C HSQC/DEPT,
C6D6, 300/75 MHz
f2 (ppm)
f1 (ppm)


OPMB
SO2Ph
OTBS
OTBS
18
1H, C6D6, 300 MHz
W (m) 7.82
V (m) 7.28
U (m) 6.91
T (m) 6.82
S (d) 5.52
R (m) 5.39
Q (dd) 4.48
P (s) 4.36
O (m) 4.27
N (m) 3.83
M (s) 3.31
L (m) 3.18
K (d) 2.80
J (m) 2.13
I (s) 1.66
H (m) 1.57
G (s) 1.30
F (m) 1.39
E (s) 0.98
D (s) 0.95
C (s) 0.29
B (s) 0.11
A (s) 0.07
f1 (ppm)

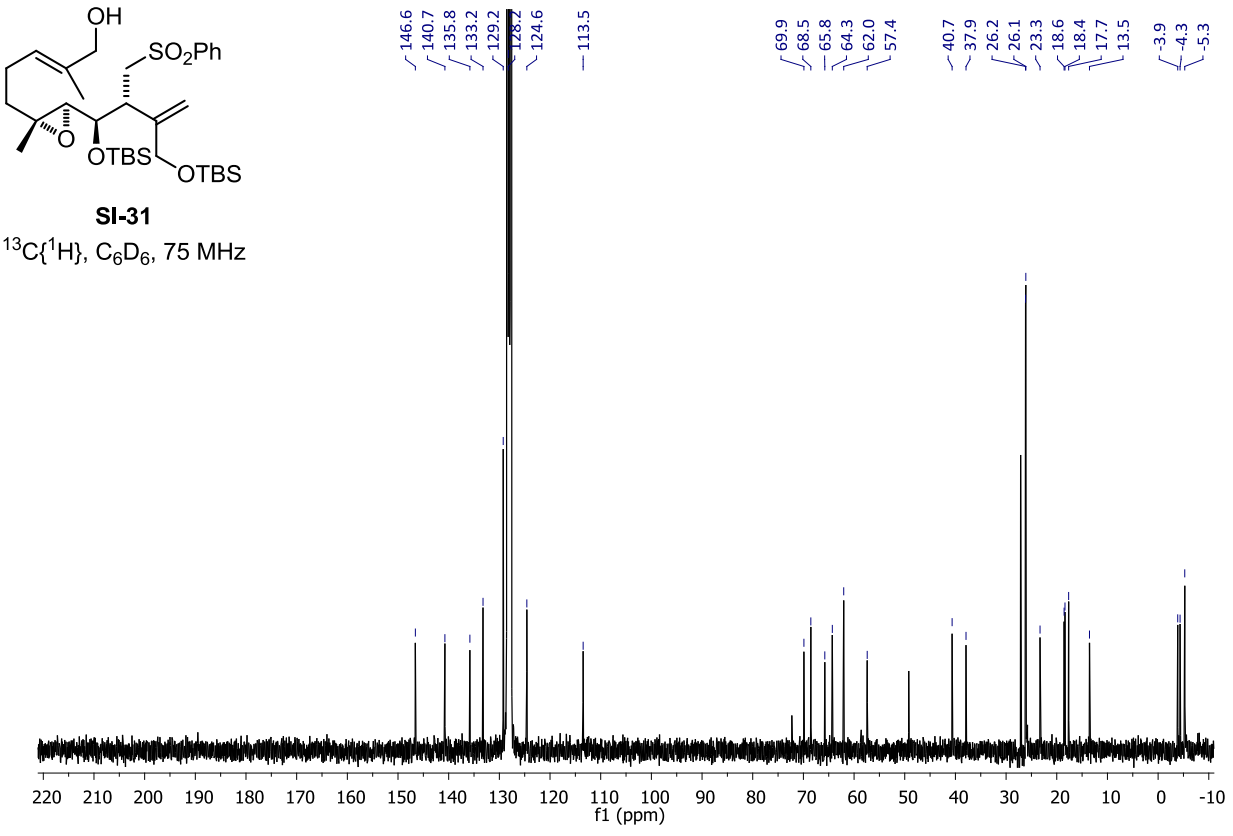

OPMB
SO2Ph
OTBS
OTBS
18
13C{1H}, C6D6, 75 MHz
159.7
146.6
140.8
133.3
133.2
131.4
129.5
129.2
128.2
126.9
114.1
113.5
75.9
71.5
69.9
65.8
64.3
62.0
57.4
54.8
40.7
37.9
26.2
26.1
23.4
18.6
18.4
17.6
14.0
-3.9
-4.3
-5.3
f1 (ppm)


OPMB
SO2Ph
O
OTBS
OTBS
18
1H,13C HSQC/DEPT,
C6D6, 300/75 MHz
{7.83,127.90}
f2 (ppm)
f1 (ppm)



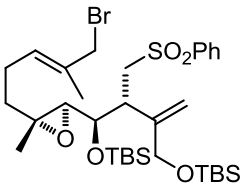
SI-31

^{1}H, C_6D_6, 300 MHz



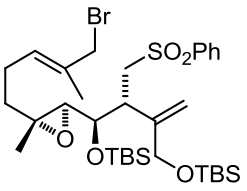
SI-31

$^{13}C\{^{1}H\}$, C_6D_6, 75 MHz



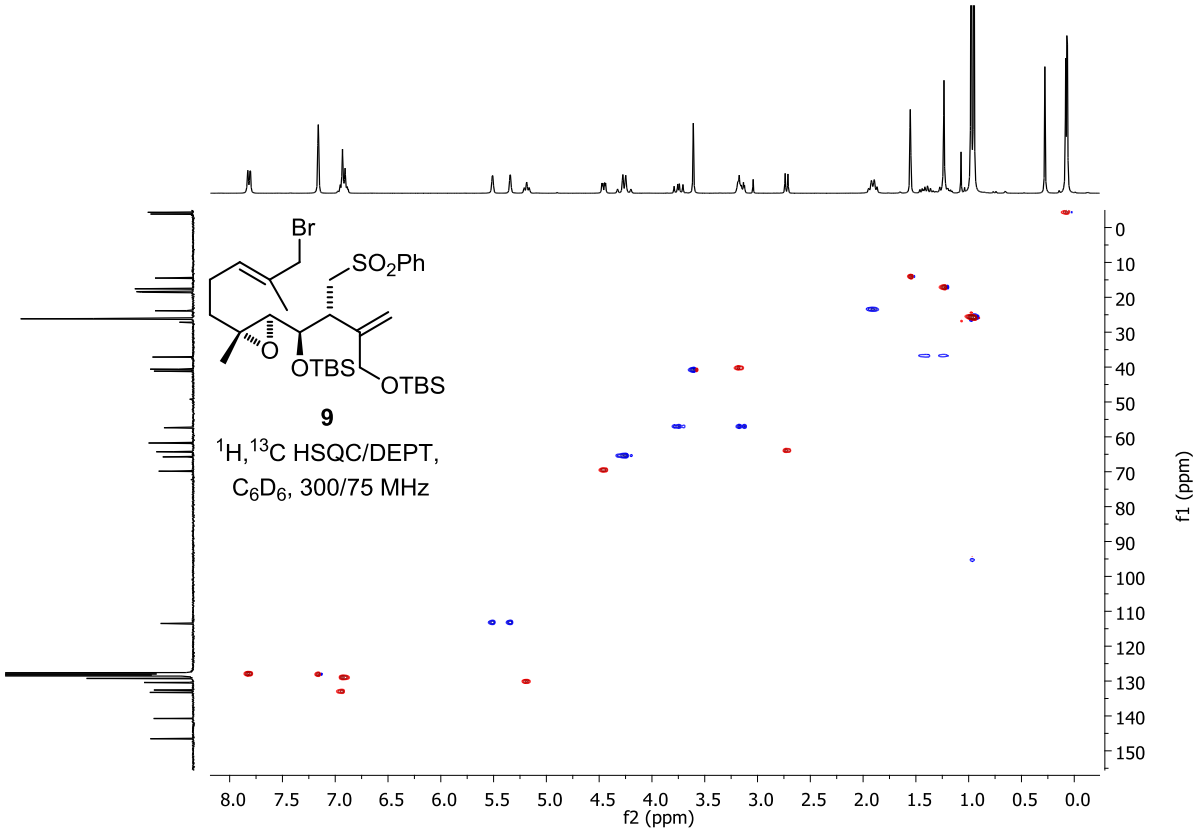
9

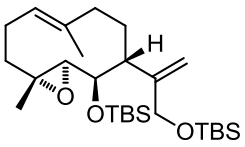
^{1}H, C_6D_6, 300 MHz



9

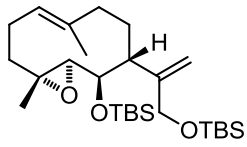
$^{13}C\{^{1}H\}$, C_6D_6, 75 MHz


Br
SO2Ph
O
OTBS
OTBS
9
1H,13C HSQC/DEPT,
C6D6, 300/75 MHz
f2 (ppm)
f1 (ppm)



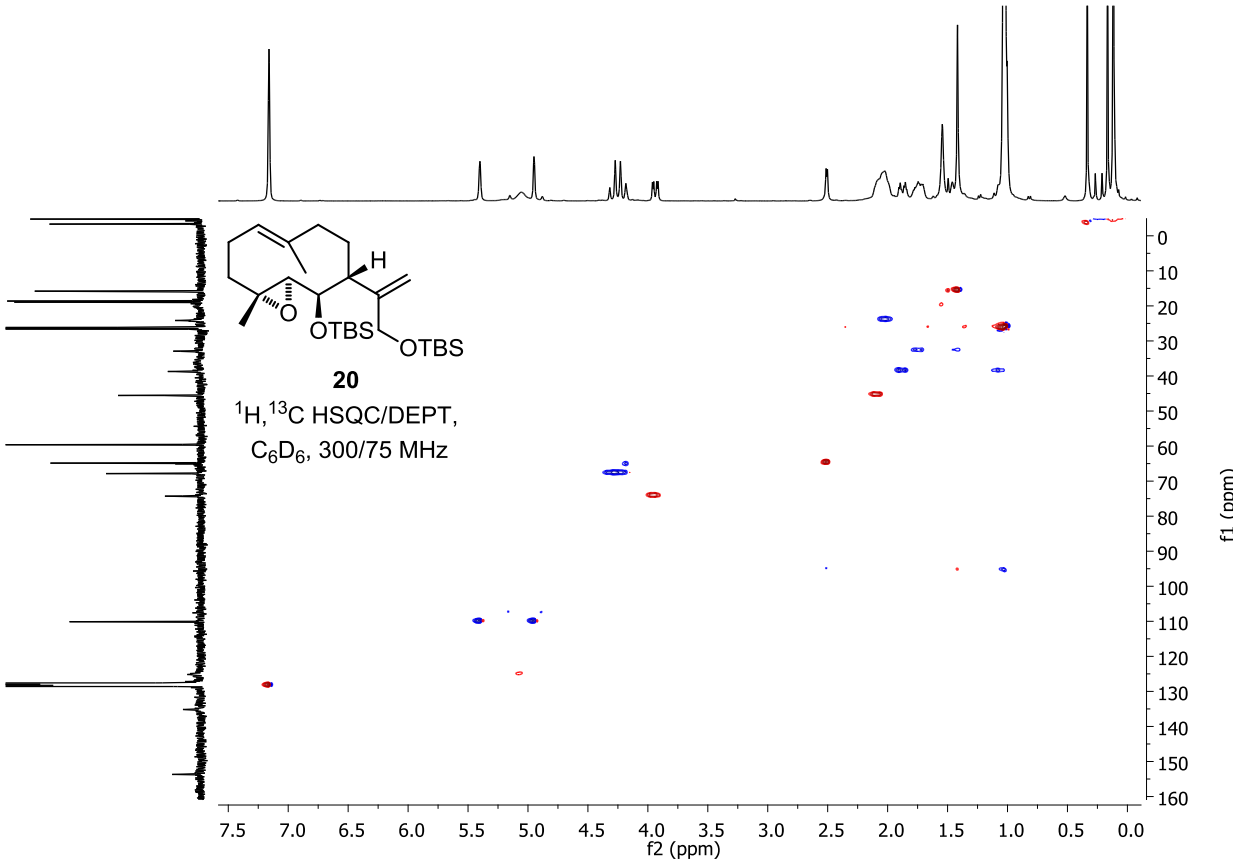
20

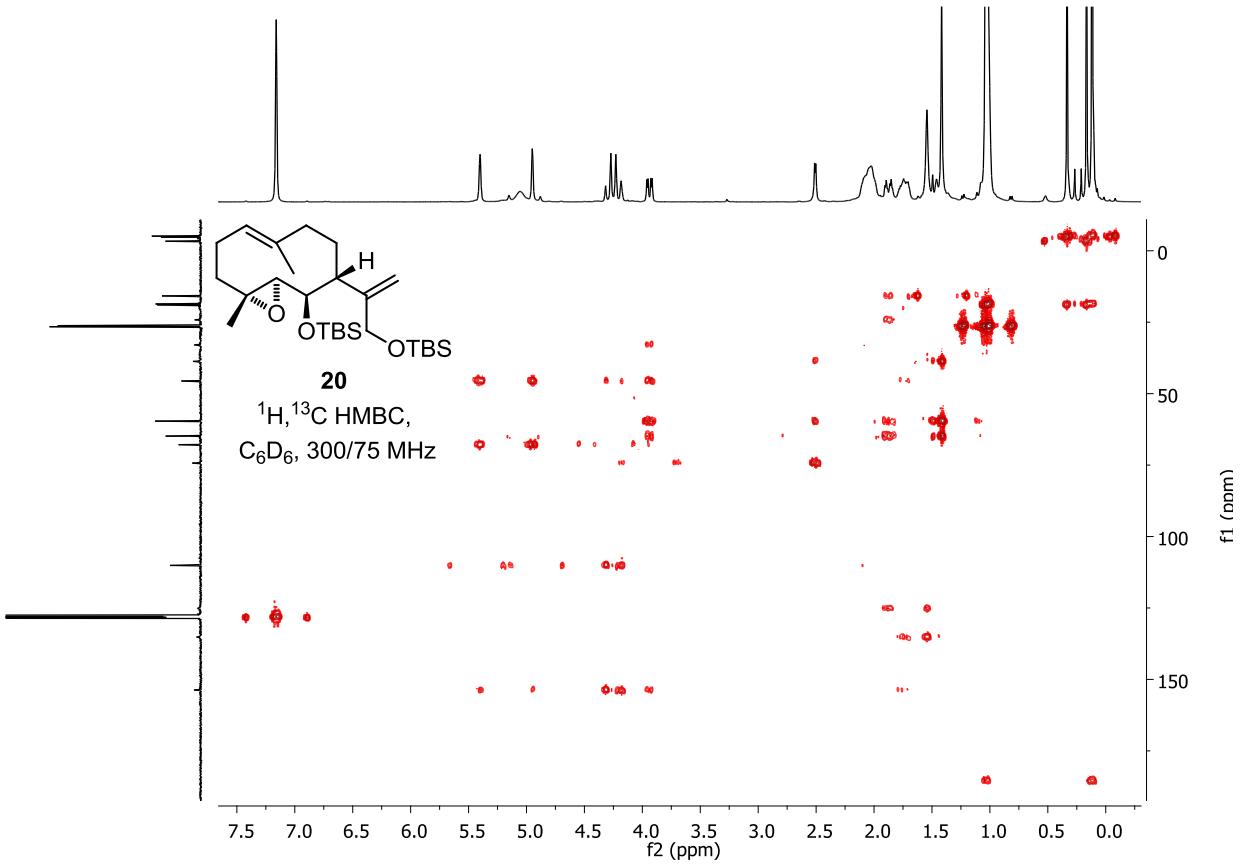
^{1}H, C_6D_6, 300 MHz

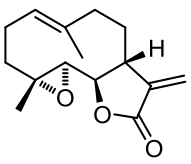


20

$^{13}C\{^{1}H\}$, C_6D_6, 75 MHz

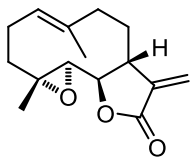

H
O
OTBS
OTBS
20
$^{1}H,^{13}C$ HSQC/DEPT,
C_6D_6, 300/75 MHz
f2 (ppm)
f1 (ppm)


H
O
OTBS
OTBS
20
$^{1}H,^{13}C$ HMBC,
C_6D_6, 300/75 MHz
f2 (ppm)
f1 (ppm)



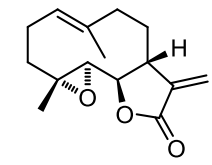
22

^{1}H, $CDCl_3$, 400 MHz



22

$^{13}C\{^{1}H\}$, $CDCl_3$, 101 MHz

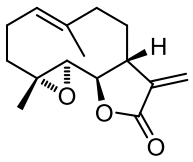


22

^{1}H, $CDCl_3$, 400 MHz

up: this work

down: [ref. S22]
$CDCl_3$, 300 MHz

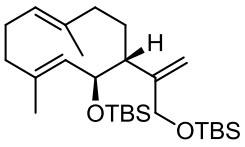


22

$^{13}C\{^{1}H\}$, $CDCl_3$, 101 MHz

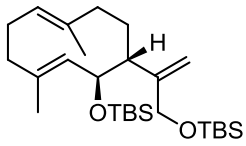
up: this work

down: [ref. S22]
$CDCl_3$, 75 MHz



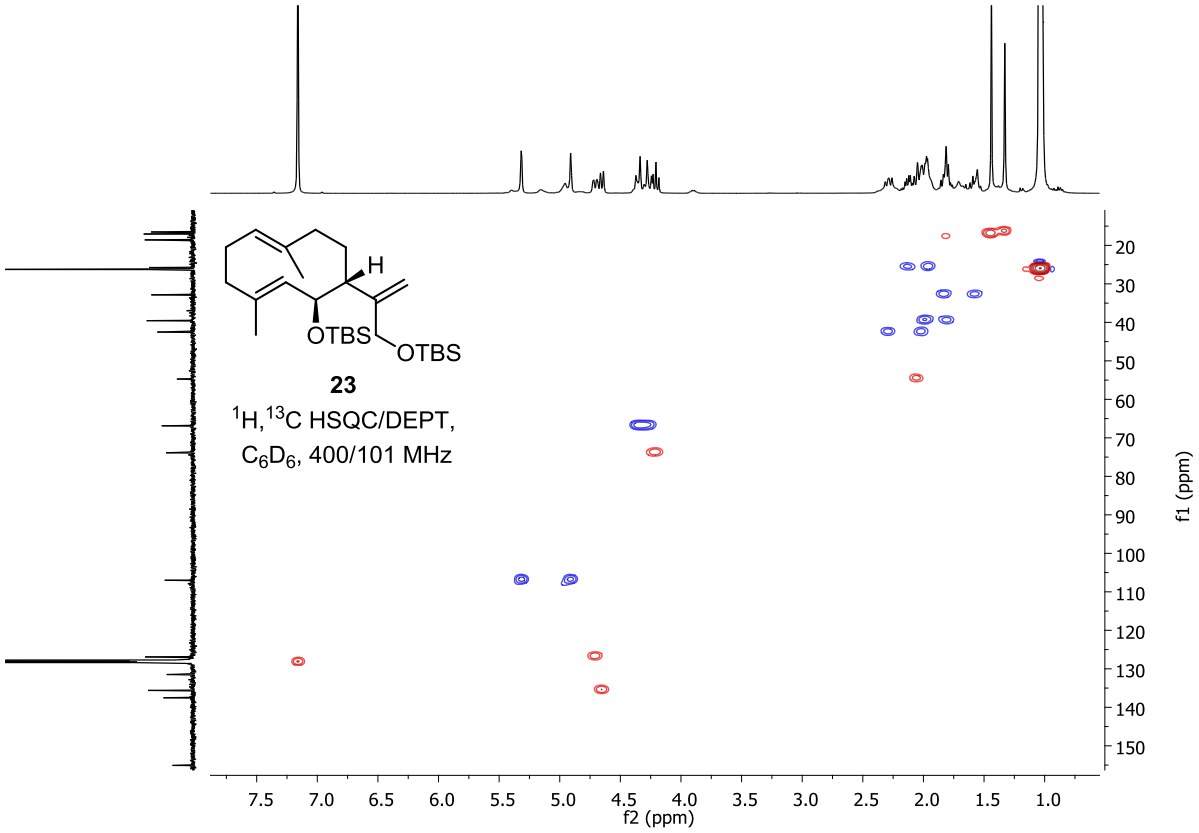
23

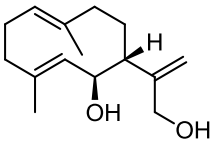
^{1}H, C_6D_6, 300 MHz



23

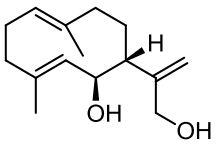
$^{13}C\{^{1}H\}$, C_6D_6, 75 MHz


H
OTBS
OTBS
23
$^{1}H,^{13}C$ HSQC/DEPT,
C_6D_6, 400/101 MHz
f2 (ppm)
f1 (ppm)



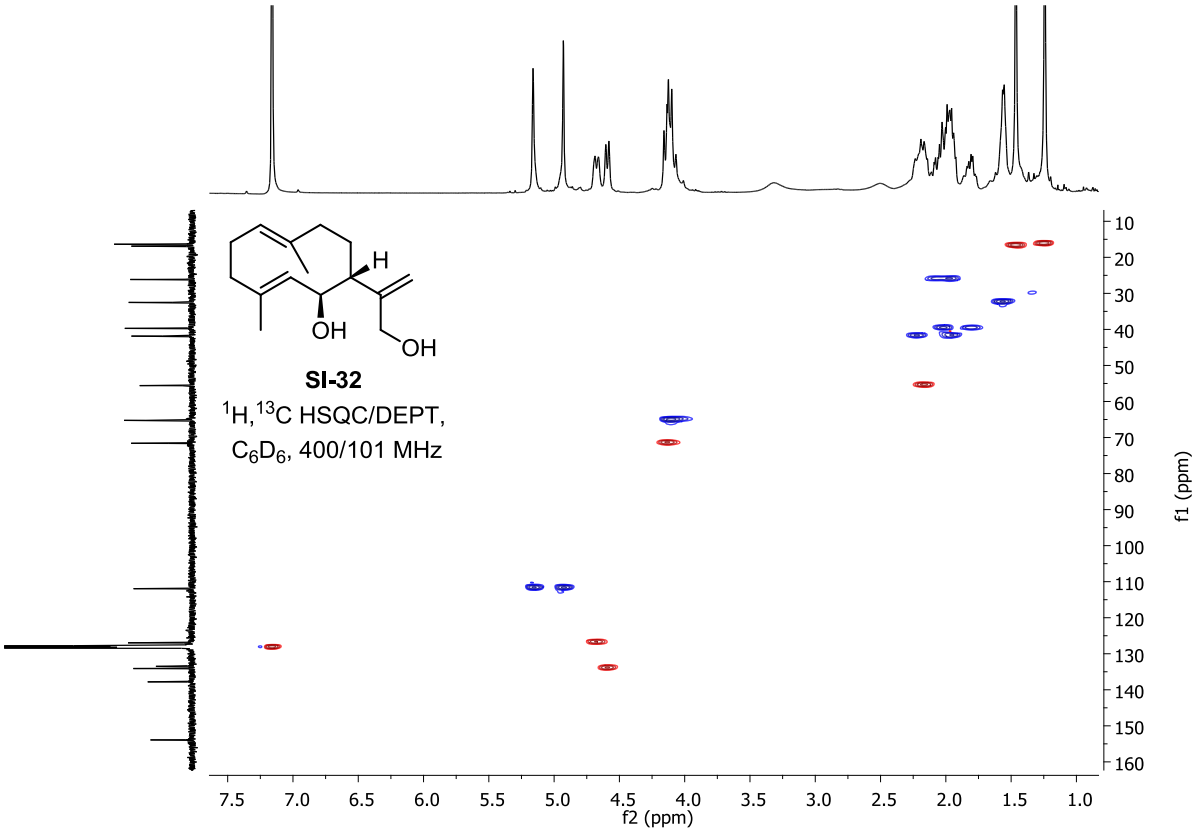
SI-32

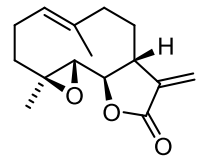
^{1}H, C_6D_6, 400 MHz



SI-32

$^{13}C\{^{1}H\}$, C_6D_6, 101 MHz

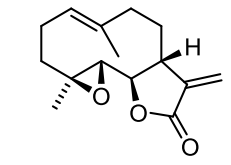

H
OH
OH
SI-32
1H,13C HSQC/DEPT,
C6D6, 400/101 MHz
f2 (ppm)
f1 (ppm)



1

^{1}H, C_6D_6, 400 MHz

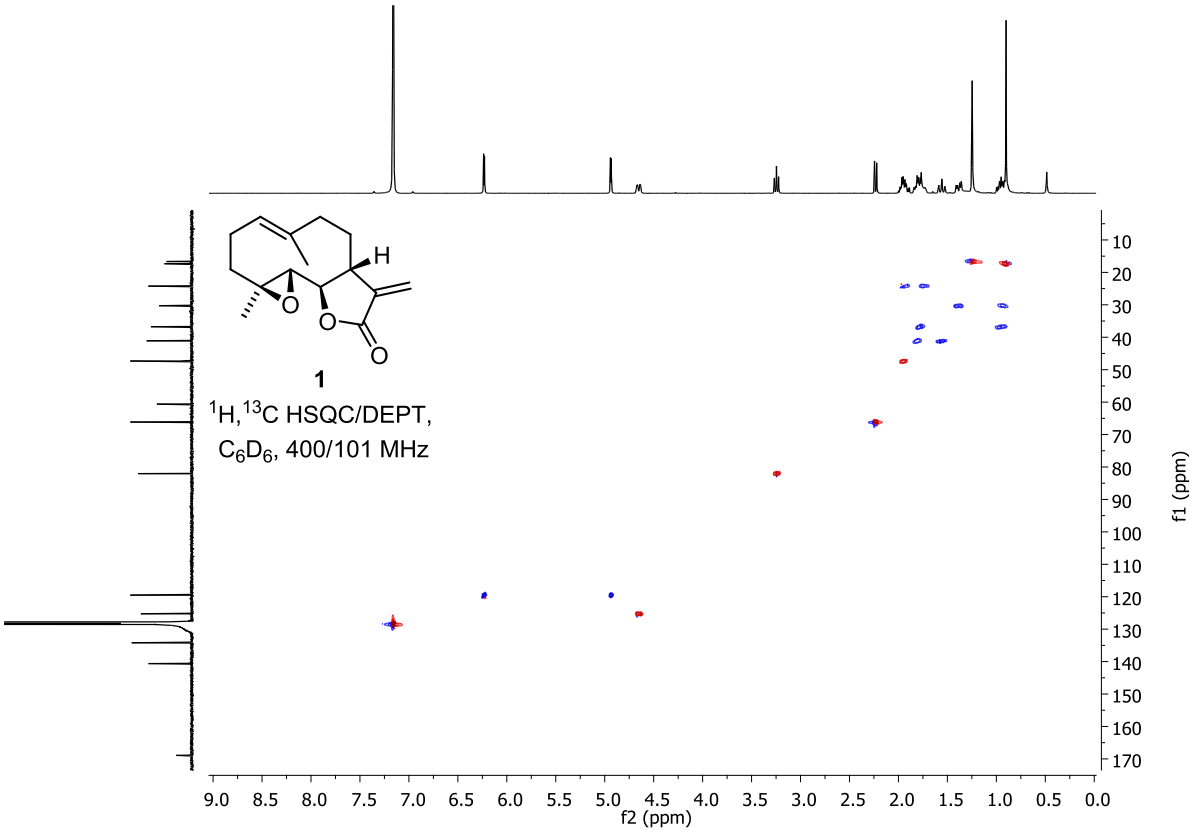
* = impurity from solvent

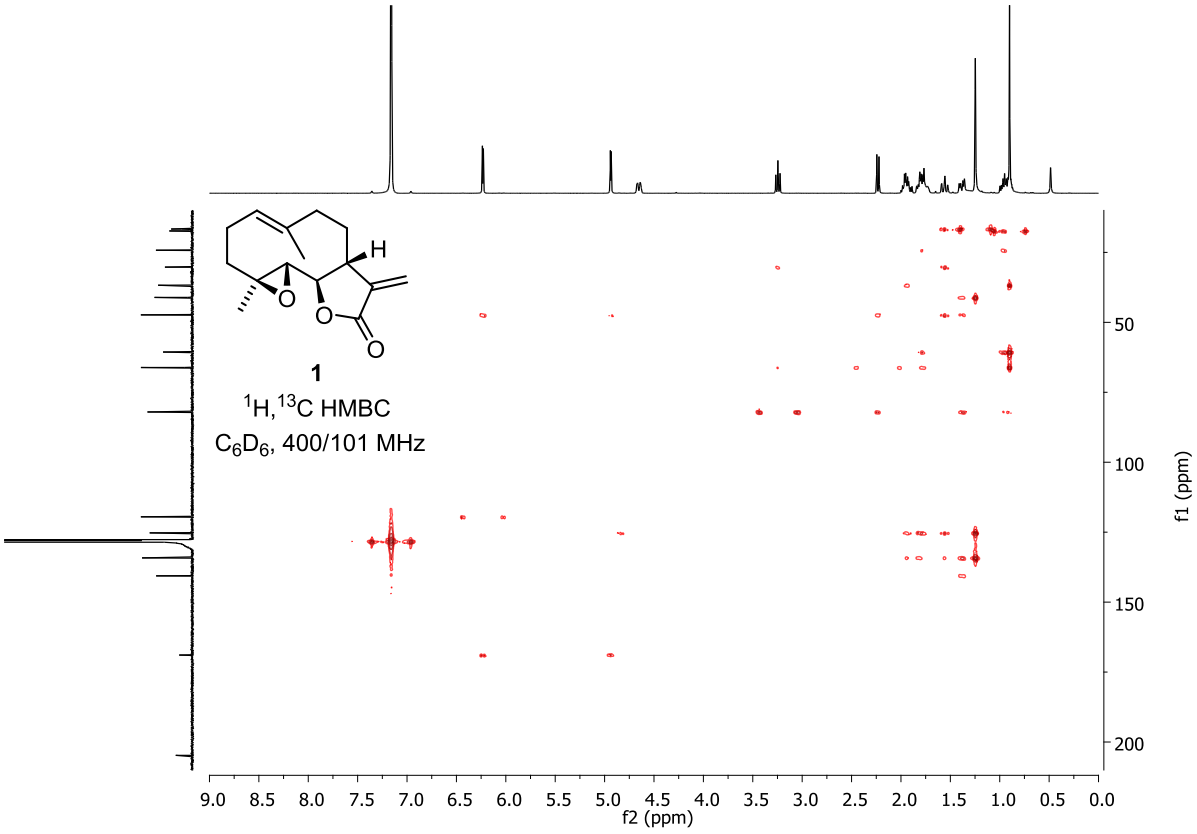


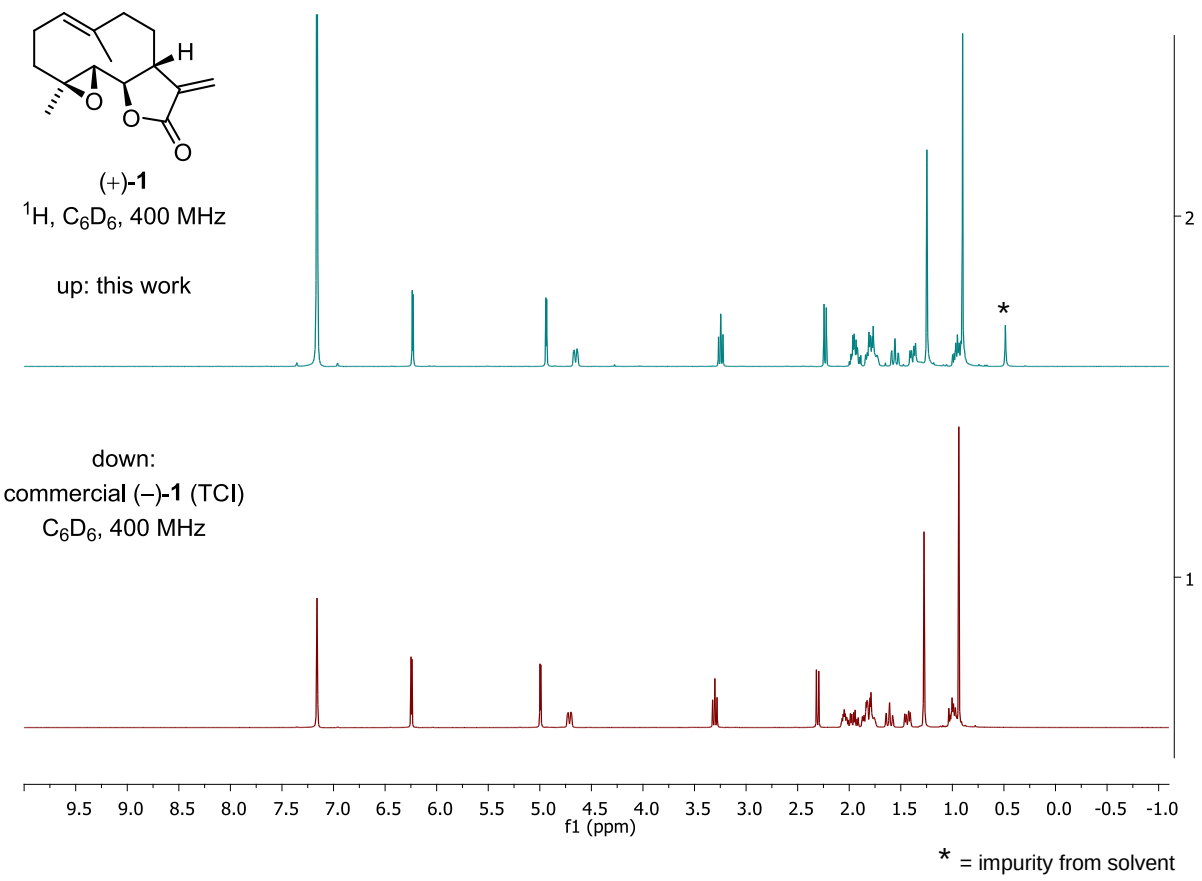
1

^{13}C{^{1}H}, C_6D_6, 101 MHz

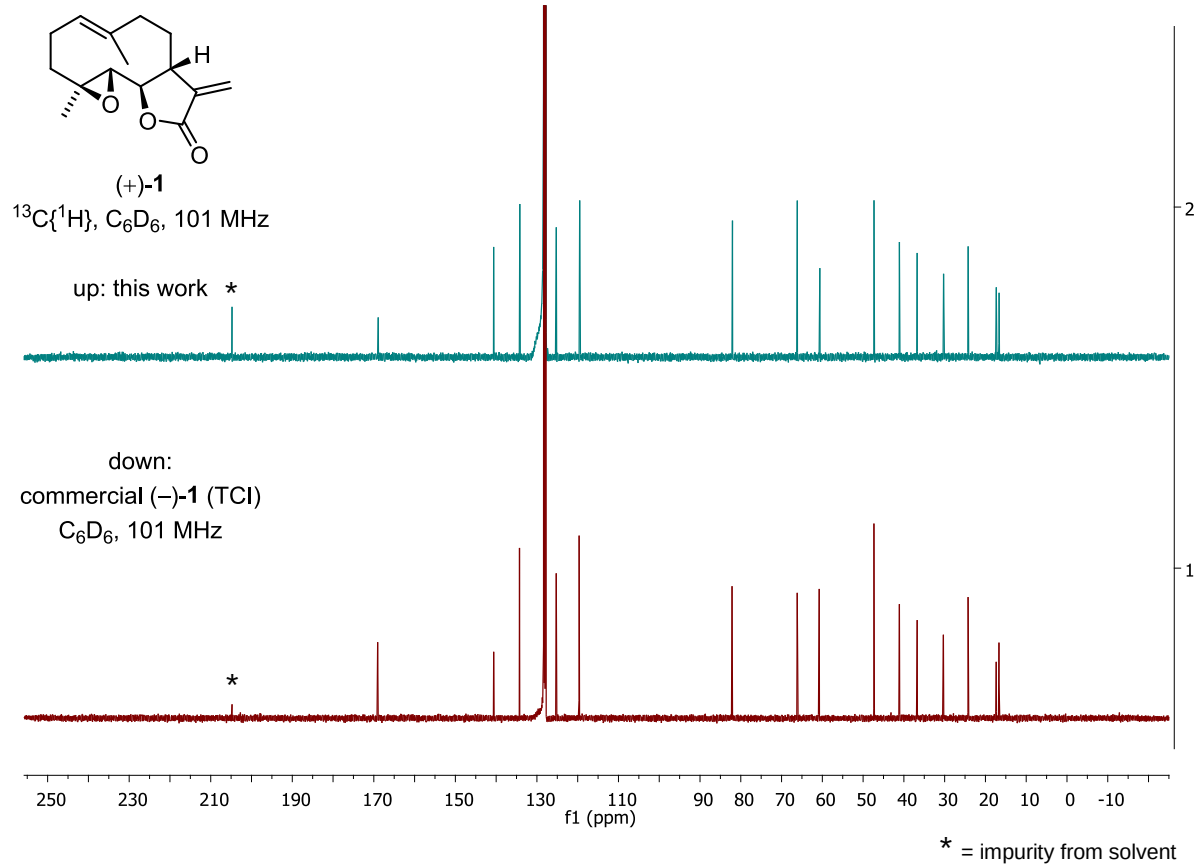
* = impurity from solvent


H
O
O
O
1
^{1}H,^{13}C HSQC/DEPT,
C_6D_6, 400/101 MHz
f1 (ppm)
f2 (ppm)


H
O
O
O
1
^{1}H,^{13}C HMBC
C_6D_6, 400/101 MHz
f1 (ppm)
f2 (ppm)



* = impurity from solvent



* = impurity from solvent