

Chapter X:

Experimental

10.1. General Information

^1H and ^{13}C NMR spectra were recorded at room temperature with a Bruker Avance 300 operating at a frequency of 300 MHz for ^1H and 75 MHz for ^{13}C . In cases of ambiguous assignments, spectra were recorded with a Bruker 500. ^1H NMR spectra were recorded in CDCl_3 , unless otherwise specified, and referenced to CHCl_3 ($\delta = 7.26$ ppm) as an internal standard. ^{13}C NMR spectra were referenced to the CDCl_3 ($\delta = 77.16$ ppm) signal. ^1H NMR data are shown as follows: δ in ppm (multiplicity, coupling constant, integration, attribution). The multiplicity is described as follows: m (multiplet), *b* (broad), s (singlet), d (doublet), t (triplet), q (quartet),... dd (doublet of doublet),... ^{13}C NMR data are shown as follows: δ ppm (attribution).

Mass spectra were recorded using Varian Matt 44S, Finnigan-Matt TSQ-70 or a systems exactive HCD ThermoFisher Scientific. **High-resolution mass** data were obtained with a Kratos MS50TC instrument or with a systems exactive HCD ThermoFisher Scientific.

Infrared spectra were recorded in cm^{-1} on a SHIMATZU-FTIR-8400S.

Melting points were determined by Büchi 545 and Büchi SMP-20.

DCM was distilled from CaH_2 . THF and Et_2O were distilled from Na/benzophenone.

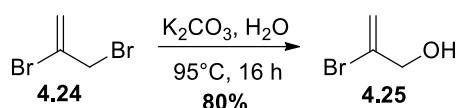
The term “room temperature” indicates an uncontrolled temperature that might reach 18°C in winter and 25°C in summer.

Experimental

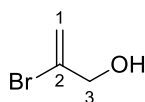
10.2. Procedures and spectral data

10.2.1. Ene-IMSC

2-bromoprop-2-en-1-ol

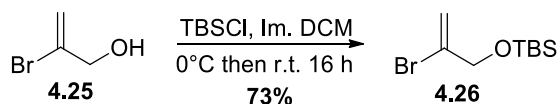


A 500 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with 2,3-dibromopropene (7.3 mL, 75 mmol, 1 eq.) and an aqueous solution (120 mL) of K_2CO_3 (11.4 g, 82.5 mmol, 1.1 eq.). Resulting heterogeneous mixture was stirred and heated at $95^\circ C$ for 16 h. After cooling down of the solution, the latter was treated with HCl (1M, 50 mL). The aqueous phase was then extracted with diethyl ether (3 x 100 mL). Combined organic fractions were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by distillation under vacuum to afford alcohol **4.25** as a yellow oil (8.1 g, 80%). $R_f = 0.44$ (PE/AcOEt 3:1).

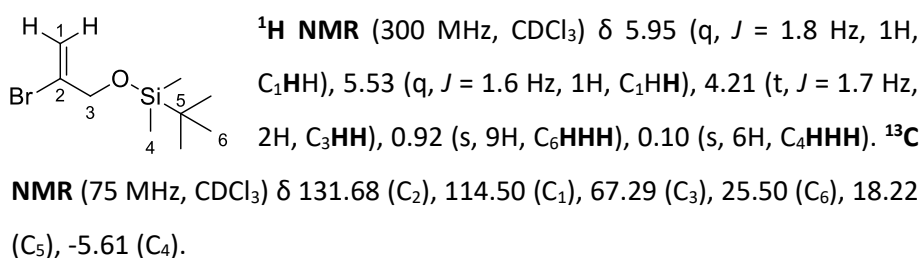


^1H NMR (300 MHz, $CDCl_3$) δ 5.94 (dd, $J = 3.4, 1.5$ Hz, 1H, C_1HH), 5.58 (dt, $J = 2.0, 1.0$ Hz, 1H, C_1HH), 4.23 (bs, 2H, C_3HH), 2.11 (m, 1H, C_3OH). ^{13}C NMR (75 MHz, $CDCl_3$) δ 132.37 (C_2), 116.23 (C_1), 67.45 (C_3).

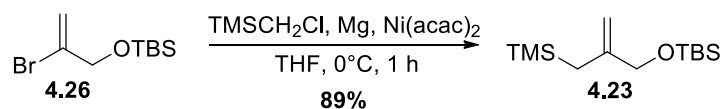
((2-bromoallyl)oxy)(tert-butyl)dimethylsilane



A 2 L round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with allylic alcohol **4.25** (88.0 g, 640 mmol, 1 eq.), imidazole (87.47 g, 1.28 mol, 2 eq.) and DCM (640 mL). Resulting mixture was cooled to 0°C in a bath of ice and water, before adding TBSCl (144.69 g, 960 mmol, 1.5 eq.) in one portion. The heterogeneous mixture was stirred at room temperature for 16 h, then diluted with water (400 mL). The two layers were separated and the aqueous phase was extracted with DCM (3 x 300 mL). Combined organic fractions were concentrated under reduced pressure. Finally, the residue was purified by distillation under reduced pressure (15 mBar, 60 - 80°C) to afford silyl enoether **4.26** as a colorless oil (117.38 g, 73%). R_f = 0.82 (PE/AcOEt 3:1).



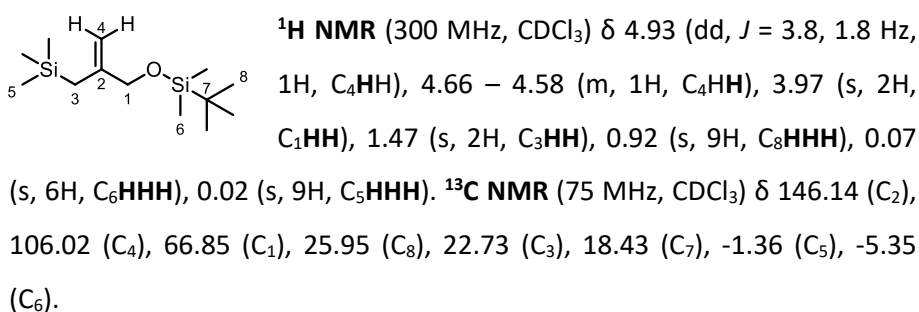
tert-butyl dimethyl((2-((trimethylsilyl)methyl)allyl)oxy)silane



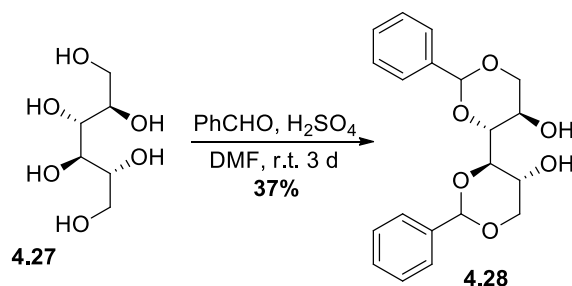
Mg (5 g) was washed with an aqueous solution of HCl (1M, 3 x 50 mL), *i*PrOH (3 x 50 mL) and diethyl ether (3 x 50 mL). Activated Mg was then added to a 500 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer and a cooling tower. A single iodine crystal, THF (30 mL) and TMSCl (0.1 mL) were added subsequently. Resulting orange mixture was stirred for 10 minutes, followed by careful addition of TMSCH₂Cl (10.7 mL, 76.9 mmol, 1.5 eq.) to the mixture. A very exothermic reaction was

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observed. At that moment, the black Grignard solution was transferred to a stirred solution of vinylbromide **4.26** (12.88 g, 53.1 mmol, 1 eq.) and Ni(acac)₂ (0.078 g, 0.308 mmol, 0.002 eq.) in THF (150 mL) at 0°C. The latter was left stirring for 1 h at 0°C prior to addition of a saturated aqueous solution of NaHCO₃ (50 mL). After separation, the aqueous phase was extracted with diethyl ether (3 x 50 mL). Combined organic fractions were dried over MgSO₄, concentrated under reduced pressure and the residue was purified by distillation (0.6 mBar, 58-64°C) to afford allylsilane **4.23** as a colorless oil (12.18 g, 89%). R_f = 0.78 (PE/AcOEt 10:1).

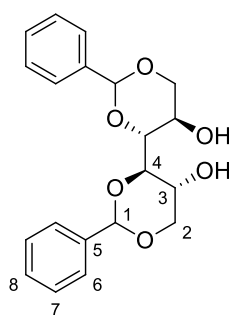


(4*R*,4'*R*,5*R*,5'*R*)-2,2'-diphenyl-[4,4'-bi(1,3-dioxane)]-5,5'-diol



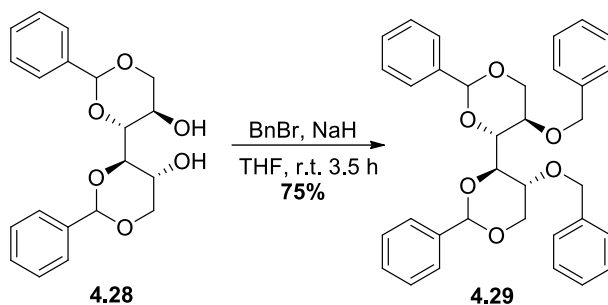
A 1 L round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with concentrated sulfuric acid (19.9 mL, 373 mmol, 0.68 eq.), D-mannitol **4.27** (100 g, 549 mmol, 1 eq.), benzaldehyde (120 mL, 1.19 mol,

2.16 eq.) and DMF (300 mL). Resulting mixture was stirred at room temperature for 3 days, prior to addition to a mixture of ice, K₂CO₃ (30 g), water (3 L) and PE (300 mL). The obtained white precipitate was filtered and washed with PE (70 mL). Crude product was recrystallized from DCM to afford diol **4.28** as a white solid (73.64 g, 37%). R_f = 0.37 (PE/AcOEt 1:2).



¹H NMR (300 MHz, CDCl₃) δ 7.46 – 7.32 (m, 10H, C₆H, C₇H, C₈H), 5.51 (s, 2H, C₁H), 4.39 (dd, *J* = 10.9, 5.0 Hz, 2H, C₂HH), 4.28 – 4.12 (m, 4H, C₃H, C₄H), 3.65 (dd, *J* = 10.8, 9.4 Hz, 2H, C₂HH). ¹³C NMR (75 MHz, CDCl₃) δ 137.16 (C₅), 129.47, 128.62, 126.10 (C₆, C₇, C₈), 101.70 (C₁), 80.64 (C₄), 70.73 (C₂), 61.75 (C₃).

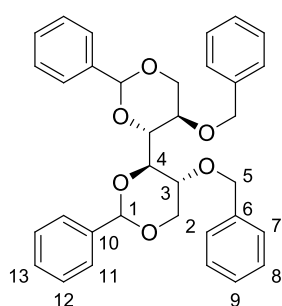
(4*R*,4'*R*,5*R*,5'*R*)-5,5'-bis(benzyloxy)-2,2'-diphenyl-4,4'-bi(1,3-dioxane)



A 2 L round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with diol **4.28** (66.42 g, 185 mmol, 1 eq.) and THF (500 mL) prior to addition of NaH (60% in mineral oil, 22.2 g, 555 mmol, 3 eq.). Resulting mixture was left stirring for 30 minutes, before adding benzyl bromide (48.5 mL, 408 mmol, 2.2 eq.). After 24 h, the solution was treated with brine (300 mL). After separation, the aqueous phase was extracted with DCM (2 x 50 mL). Combined organic fractions were dried over MgSO₄

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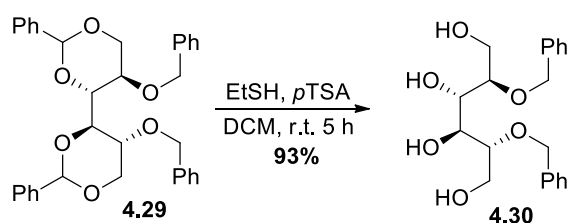
and purified by flash column chromatography on silica gel (PE/AcOEt 20: 1 to 15: 1) to afford **4.29** as a white solid (81.01 g, 75%). R_f = 0.76 (PE/AcOEt 4:1).



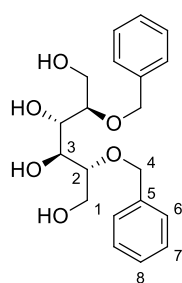
^1H NMR (300 MHz, CDCl_3) δ 7.55 – 7.19 (m, 8H, C_7H , C_8H , C_9H , C_{11}H , C_{12}H , C_{13}H), 5.41 (s, 2H, C_1H), 4.60 (d, J = 12.7 Hz, 2H, C_5HH), 4.56 (d, J = 12.7 Hz, 2H, C_5HH), 4.35 (dd, J = 10.6, 4.8 Hz, 2H, C_2HH), 4.06 (d, J = 9.8 Hz, 2H, C_4H), 4.05 – 3.94 (m, 2H, C_3H), 3.67 (t, J = 10.2 Hz, 1H, C_2HH). ^{13}C

NMR (75 MHz, CDCl_3) δ 138.04, 137.81 (C_6 , C_{10}), 128.97, 128.60, 128.26, 128.13, 128.08, 126.34 (C_7 , C_8 , C_9 , C_{11} , C_{12} , C_{13}), 101.13 (C_1), 77.55 (C_4), 72.80 (C_5), 69.74 (C_2), 66.93 (C_3).

(2*R*,3*S*,4*S*,5*R*)-2,5-bis(benzyloxy)hexane-1,3,4,6-tetraol

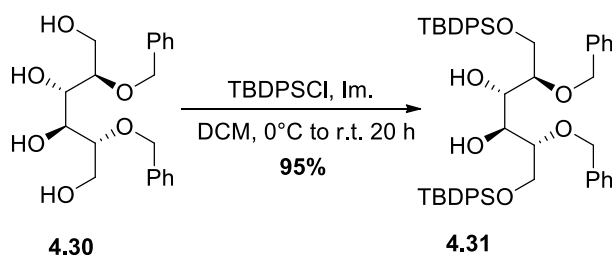


A 2 L round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with intermediate **4.29** (81.0 g, 150 mmol, 1 eq.), DCM (600 mL), ethanethiol (44.5 mL, 602 mmol, 4 eq.) and $p\text{TSA}$ (2.86 g, 15 mmol, 0.1 eq.). Resulting mixture was left stirring at room temperature during 5 h prior to filtration of the obtained white solid. The residue was washed with PE (2 x 50 mL). A recrystallization from DCM furnished tetraol **4.30** as a white solid (50.55 g, 93%). R_f = 0.2 (AcOEt).



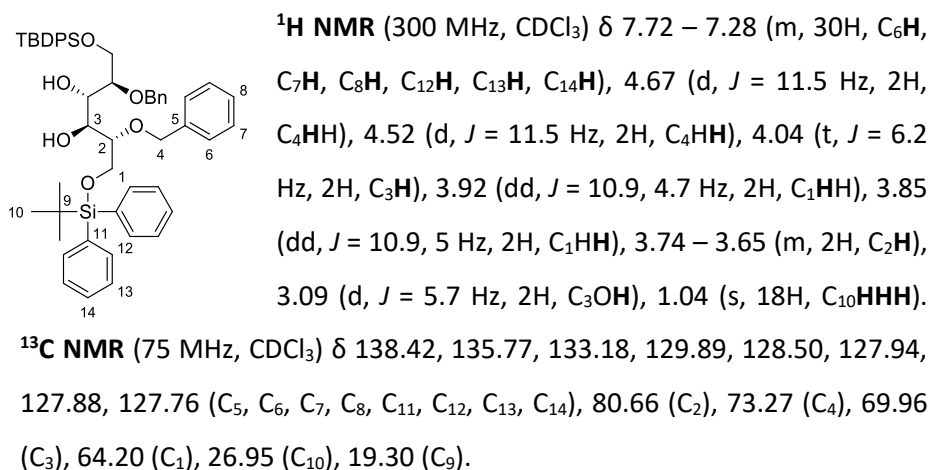
^1H NMR (300 MHz, CDCl_3) δ 7.43 – 7.27 (m, 10H, C_6H , C_7H , C_8H), 4.66 (d, J = 11.5 Hz, 2H, C_4HH), 4.58 (d, J = 11.6 Hz, 2H, C_4HH), 3.96 (t, J = 6.2 Hz, 2H, C_3H), 3.90 – 3.73 (m, 4H, C_1HH), 3.60 (dt, J = 6.4, 4.5 Hz, 2H, C_2H), 2.83 (d, J = 6.3 Hz, 2H, C_3OH), 2.26 (dd, J = 7.4, 5.0 Hz, 2H, C_1OH). **^{13}C NMR** (75 MHz, CDCl_3) δ 137.70 (C_5), 128.65, 128.16, 128.04 (C_6 , C_7 , C_8), 79.69 (C_2), 72.67 (C_4), 70.02 (C_1), 61.41 (C_3).

(6*R*,7*S*,8*S*,9*R*)-6,9-bis(benzyloxy)-2,2,13,13-tetramethyl-3,3,12,12-tetraphenyl-4,11-dioxo-3,12-disilatetradecane-7,8-diol

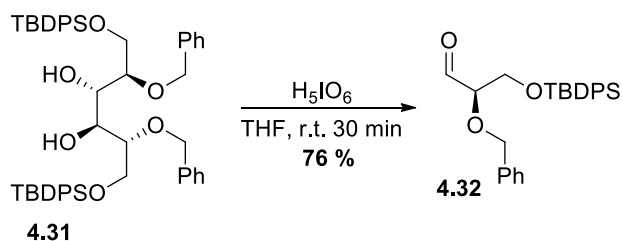


A 500 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with tetraol **4.30** (11.32 g, 31.22 mmol, 1 eq.), imidazole (6.37 g, 93.7 mmol, 3 eq.), TBDPSCI (16.44 mL, 64.0 mmol, 2.05 eq.) and DCM (130 mL) at 0°C. Resulting solution was stirred at room temperature for 20 h prior to addition of a saturated aqueous solution of NaHCO_3 (250 mL) at 0°C. The layers were separated and the aqueous phase was extracted with DCM (2 x 50 mL). Combined organic fractions were dried over MgSO_4 , concentrated under reduced pressure and the residue was purified by flash column chromatography on silica gel (PE/AcOEt 20: 1) to furnish diol **4.31** as a sticky oil (24.98 g, 95%). R_f =0.80 (PE/AcOEt 4:1).

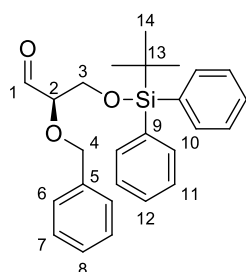
Experimental



(*R*)-2-(benzyloxy)-3-((tert-butyldiphenylsilyl)oxy)propanal

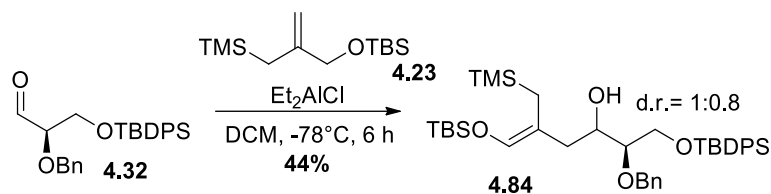


A 1 L round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with diol **4.31** (27.12 g, 32.32 mmol, 1 eq.) and THF (220 mL). Periodic acid (8.11 g, 35.55 mmol, 1.1 eq.) was then added in one portion to the reaction mixture which was left stirring for 30 minutes prior to addition of a saturated aqueous solution of NaHCO₃ (150 mL). The layers were separated and the aqueous phase was extracted with diethyl ether (2 x 100 mL). Combined organic fractions were washed with brine, dried over MgSO₄ and concentrated under reduced pressure. The obtained white solid was recrystallized from DCM to afford aldehyde **4.32** (10.28 g, 76%). *M*_p = 75–76°C. *R*_f = 0.68 (PE/AcOEt 4:1).



^1H NMR (300 MHz, CDCl_3) δ 9.76 (d, J = 1.2 Hz, 1H, C_1H), 7.71 – 7.32 (m, 15H, C_6H , C_7H , C_8H , C_9H , C_{10}H , C_{11}H , C_{12}H), 4.69 (d, J = 11.9 Hz, 1H, C_4HH), 4.64 (d, J = 11.9 Hz, 1H, C_4HH), 3.99 – 3.96 (m, 2H, C_3HH), 3.89 (ddd, J = 5.6, 4.3, 1.4 Hz, 1H, C_2H), 1.07 (s, 9H, C_{14}HHH). **^{13}C NMR** (125 MHz, CDCl_3) δ 203.0 (C_1), 137.83 (C_5), 136.13 (C_{10}), 136.07 ($\text{C}_{10'}$), 133.37 (C_9), 133.32 (C_9'), 130.32 (C_{12}), 128.46–128.24 (C_6 , C_7 , C_8), 84.42 (C_2), 72.98 (C_4), 63.8 (C_3), 27.20 (C_{14}), 19.7 (C_{13}).

(6*R*,*Z*)-6-(benzyloxy)-2,2,12,12,13,13-hexamethyl-3,3-diphenyl-9-((trimethylsilyl)methyl)-4,11-dioxa-3,12-disilatetradec-9-en-7-ol

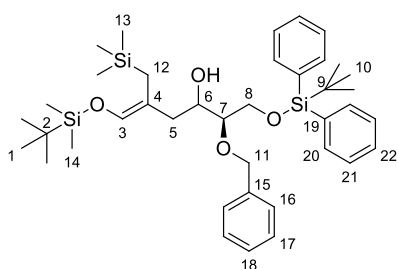


A 25 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with allylsilane **4.23** (0.15 g, 0.597 mmol, 1 eq.), aldehyde **4.32** (0.25 g, 0.597 mmol, 1 eq.) and DCM (6 mL). Resulting mixture was stirred and cooled to -78°C in a bath of dry ice and acetone prior to dropwise addition of diethyl aluminium chloride (1M in hexane, 0.9 mL, 1.5 eq.). After 6 h at that temperature, a saturated aqueous solution of Potassium sodium tartrate was added (10 mL) and the heterogeneous mixture was stirred for another hour at room temperature. The two layers were then separated and the aqueous phase was extracted with DCM (3 x 15 mL). Combined organic fractions were dried over MgSO_4 , concentrated under reduced pressure and the residue was purified by column chromatography on silica

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gel (PE then PE/AcOEt 5:1) to afford allylsilane **4.84** as a mixture of two diastereoisomeres (178 mg, 44%, d.r.= 1:0.8).

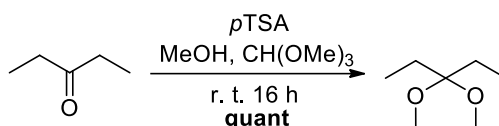
Analyses carried out on the major diastereoisomer (relative stereochemistry could not be assigned)



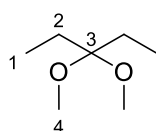
¹H NMR (300 MHz, CDCl₃) δ 7.69 – 7.20 (m, 15H, C₁₆H, C₁₇H, C₁₈H, C₂₀H, C₂₁H, C₂₂H), 6.06 (s, 1H, C₃H), 4.68 (d, *J* = 11.6 Hz, 1H, C₁₁HH), 4.48 (d, *J* = 11.6 Hz, 1H, C₁₁HH), 3.87 (m, 3H, C₈HH et C₆H), 3.44 (td, *J* = 5.4, 3.0 Hz, 1H, C₇H), 2.06 (d, *J* =

6.7 Hz, 2H, C₅HH), 1.57 (d, *J* = 13.5 Hz, 1H, C₁₂HH), 1.43 (d, *J* = 13.4 Hz, 1H, C₁₂HH), 1.06 (s, 9H, C₁₀HHH), 0.91 (s, 9H, C₁HHH), 0.08 (s, 6H, C₁₄HHH), 0.01 (s, 9H, C₁₃HHH). **¹³C NMR** (75 MHz, CDCl₃) δ 135.66 (C ar.), 135.61 (C ar.), 134.01 (C₃), 129.75 (C ar.), 129.72 (C ar.), 129.64 (C ar.), 128.52 (C ar.), 128.30 (C ar.), 128.19 (C ar.), 127.77 (C ar.), 127.73 (C ar.), 114.98 (C₄), 80.67 (C₇), 73.00 (C₁₁), 68.85 (C₆), 63.69 (C₈), 37.73 (C₅), 26.84 (C₁₀), 25.74 (C₁₂), 25.65 (C₁), 19.17 (C₉), 17.14 (C₂), -0.99 (C₁₃), -5.16 (C₁₄). **IR** (neat, cm⁻¹) 3500, 2953, 2930, 2856, 1660, 1472, 1427, 1248, 1200, 1157, 1103. **MSMS** (p ESI), *m/z* (%): 675.33 (41); 347.18 (7); 273.13 (9); 247.11 (23); 167.06 (43); 91.05 (100). **HRMS** *m/z*: calculated for C₃₉H₆₀O₄Si₃Na [M+23]: 699.3692. Found: 699.3689.

3,3-dimethoxypentane



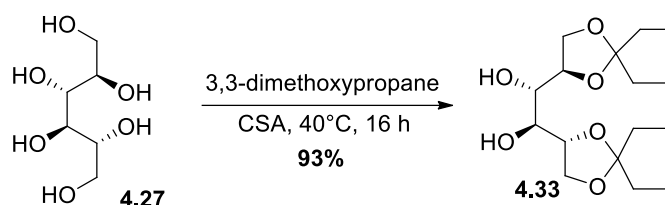
A 500 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with 3-pentanone (47 mL, 440 mmol, 1 eq.), trimethyl orthoformate (73 mL, 670 mmol, 1.5 eq.), methanol (55 mL) and *p*-toluenesulfonic acid monohydrate (0.77 g, 4.48 mmol, 0.1 eq.). Resulting mixture was left stirring at 0°C for one hour, then at room temperature over night. Crude reaction mixture was treated with a saturated aqueous solution of NaHCO₃ (100 mL). After separation, the organic phase was extracted with pentane (3 x 100 mL). Combined organic layers were dried over Na₂SO₄ and concentrated under reduced pressure to give a colorless volatile residue. Ketal was used without further purification for the next step.



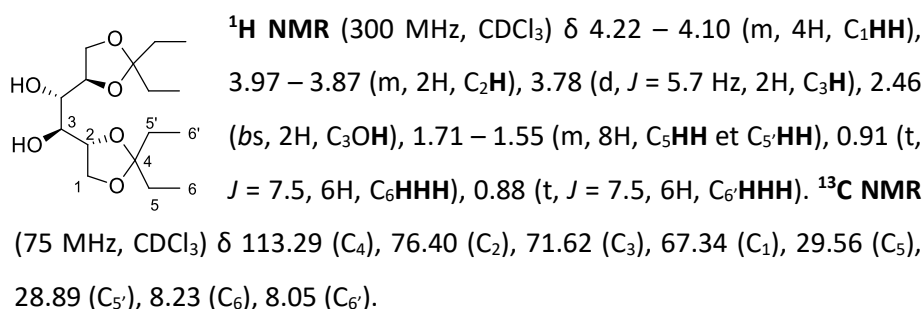
¹H NMR (300 MHz, CDCl₃) δ 3.15 (s, 6H, C₄HHH), 1.59 (q, *J* = 7.5 Hz, 4H, C₂HH), 0.82 (t, *J* = 7.5 Hz, 6H, C₁HHH). **¹³C NMR** (75 MHz, CDCl₃) δ 104.17 (C₃), 47.65 (C₄), 24.24 (C₂), 7.88 (C₁).

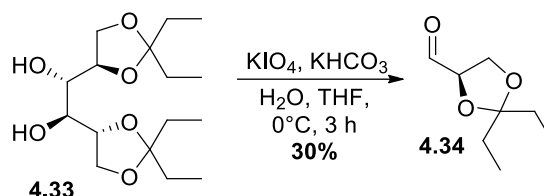
Experimental

(1*S*,2*S*)-1,2-bis((*R*)-2,2-diethyl-1,3-dioxolan-4-yl)ethane-1,2-diol

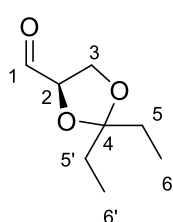


A 100 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with D-mannitol **4.27** (5.35 g, 0.029 mol, 1eq.), CSA (0.1 g, 0.015 eq.) and DMF (25 mL) prior to addition of 3,3-dimethoxypropane (8.15 g, 0.062 mol, 2.1 eq.). Resulting mixture was left stirring over night at 40°C before adding NEt₃ (0.3 mL). The volatiles were then removed under reduced pressure and the crude residue was treated with AcOEt (50 mL) and water (70 mL). After separation, the organic layer was washed with brine, dried over MgSO₄, filtered and concentrated under reduced pressure to afford **4.33** as a white solid. The latter was recrystallized from AcOEt (8,611 g, 93%). R_f = 0.36 (PE/AcOEt 6:4.)



(R)-2,2-diethyl-1,3-dioxolane-4-carbaldehyde

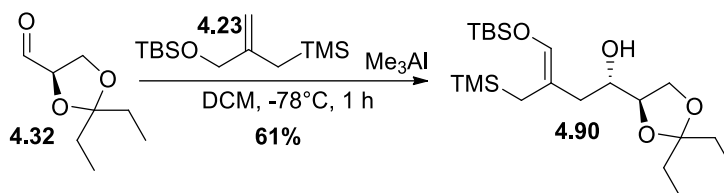
A 250 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with an aqueous solution (35 mL) of potassium periodate (12.52 g, 0.054 mol, 2 eq.) and potassium hydrogen carbonate (5.4 g, 0.054 mol, 2 eq.), and a solution of 1,2:5,6-Di-O-(3-pentylidene)-D-mannitol **4.33** (8.665 g, 0.027 mol, 1 eq.) in THF (50 mL). Resulting mixture was left stirring for 3 h at 0 °C, filtered through celite® which was washed with ethyl acetate (3 x 20 mL). The obtained solution was treated with brine (50 mL). After phase separation, the aqueous layer was extracted with ethyl acetate (5 x 30 mL). Combined organic fractions were then dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by distillation (10 mBar, 180°C) to furnish aldehyde **4.34** as a colorless liquid (2,56 g, 30%).



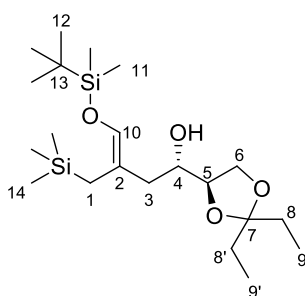
¹H NMR (300 MHz, CDCl₃) δ 9.68 (d, *J* = 1.8 Hz, 1H, C₁H), 4.38 – 4.28 (m, 1H, C₂H), 4.13 (t, *J* = 8.1 Hz, 1H, C₃HH), 4.00 (ddd, *J* = 8.6, 5.4, 0.4 Hz, C₃HH), 1.72 – 1.56 (m, 4H, C₅HH), 0.88 (q, *J* = 7.4 Hz, 6H, C₆HHH, C_{6'}HHH). **¹³C NMR** (75 MHz, CDCl₃) δ 201.48 (C₁), 115.15 (C₄), 79.87 (C₂), 65.58 (C₃), 29.15 (C₅), 28.71 (C_{5'}), 7.99 (C₆), 7.81 (C_{6'}).

Experimental

(*S,Z*)-4-((*tert*-butyldimethylsilyl)oxy)-1-((*R*)-2,2-diethyl-1,3-dioxolan-4-yl)-3-((trimethylsilyl)methyl)but-3-en-1-ol



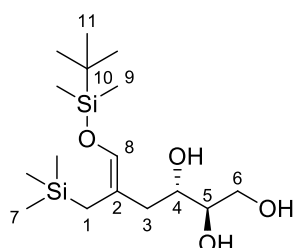
A 250 mL round-bottom flask, equipped with a Teflon-coated magnetic stirrer was charged with allylsilane **4.23** (0.15 g, 0.597 mmol, 1 eq.), aldehyde **4.32** (0.094 g, 0.597 mmol, 1 eq.) and DCM (6 mL). Resulting mixture was cooled to -78°C prior to dropwise addition of trimethylaluminium (2M in toluene, 0.3 mL, 3 eq.). After 1 h at the same temperature, a saturated aqueous solution of Potassium sodium tartrate (10 mL) was added and resulting mixture was left stirring for another hour at room temperature. The two layers were then separated and the aqueous phase was extracted with DCM (3 x 15 mL). Combined organic fractions were collected, dried over MgSO_4 , concentrated under reduced pressure and the residue was purified by flash column chromatography on silica gel (PE/ AcOEt 5%) to afford allylsilane **4.90** as a colorless oil (152 mg, 61%).



$^1\text{H NMR}$ (300 MHz, CDCl_3) δ 6.08 (s, 1H, C_{10}H), 4.10 – 4.01 (m, 1H, C_6HH), 3.97 – 3.86 (m, 2H, C_6HH , C_5H), 3.70 (dt, $J = 8.5, 4.1$ Hz, 1H, C_4H), 2.20 (dd, $J = 14.0, 3.8$ Hz, 1H, C_3HH), 1.91 (bs, 1H, C_4OH), 1.86 (dd, $J = 14.0, 9.3$ Hz, 1H, C_3HH), 1.72 (d, $J = 13.2$ Hz, 2H, C_1HH), 1.63 (m, 4H,

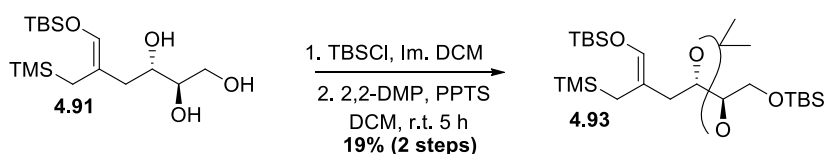
C_8HH , C_8HH), 1.29 (d, $J = 13.4$ Hz, 1H, C_1HH), 0.98 – 0.84 (m, 15H, C_9HHH , C_{12}HHH), 0.10 (s, 6H, C_{11}HHH), 0.02 (s, 9H, C_{14}HHH). $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 134.34 (C_{10}), 114.15 (C_2), 112.89 (C_7), 78.57 (C_4), 68.87 (C_5), 66.44

Experimental



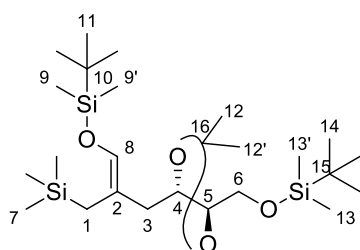
¹H NMR (300 MHz, CDCl₃) δ 6.13 (s, 1H, C₈H), 3.89 – 3.78 (m, 2H, C₆HH), 3.78 – 3.73 (m, 1H, C₅H), 3.62 (dd, *J* = 8.9, 5.0 Hz, 1H, C₄H), 2.21 (dd, *J* = 12.9, 3.1 Hz, 1H, C₃HH), 1.93 (dd, *J* = 13.9, 10.2 Hz, 1H, C₃HH), 1.80 (d, *J* = 13.4 Hz, 1H, C₁HH), 1.63 (bs, 3H, OH), 1.24 (d, *J* = 13.3 Hz, 1H, C₁HH), 0.94 (s, 9H, C₁₁HHH), 0.14 (s, 6H, C₉HHH), 0.04 (s, 9H, C₇HHH). **¹³C NMR** (75 MHz, CDCl₃) δ 134.65 (C₈), 114.08 (C₂), 73.79 (C₄), 69.89 (C₅), 63.47 (C₆), 37.25 (C₃), 25.67 (C₁₁), 18.11 (C₁₀), 16.88 (C₁), -0.71 (C₇), -5.17 (C₉), -5.31 (C₉). **IR** (neat, cm⁻¹) 3360, 2953, 2930, 2889, 2885, 1661, 1472, 1412, 1248, 1200, 1157, 1099, 1067, 1028. **MS** (p ESI), *m/z* (%): 371.20 (100); 347.21 (15); 217.13 (45). **HRMS**, *m/z*: calculated for C₁₆H₃₆O₄Si₂Na [M + 23]: 371.2044. Found: 371.2038.

tert-butyl(((4*R*,5*S*)-5-((*Z*)-3-((tert-butyldimethylsilyl)oxy)-2-((trimethylsilyl)methyl)allyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methoxy)dimethylsilane



A 25 mL round-bottom flask was charged with triol **4.91** (124 mg, 0.36 mmol, 1 eq.), imidazole (72 mg, 1.1 mmol, 3 eq.), TBSCl (53 mg, 0.36 mmol, 1 eq.) and DCM (5 mL). Resulting mixture was left stirring at room temperature for 5 h prior to addition of a saturated aqueous solution of NH₄Cl (20 mL) and DCM (20 mL). After separation, the aqueous layer was extracted with DCM (3 x 15 mL). Organic fractions were collected, dried over MgSO₄ and concentrated under reduced pressure. Resulting crude diol

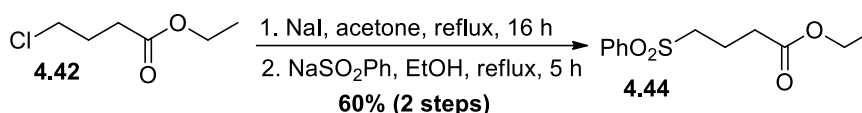
(35 mg, 0.076 mmol, 1 eq.) was then dissolved without further purification in DCM (3 mL) and 2,2-DMP (79 mg, 0.76 mmol, 10 eq.). PPTS (8 mg, 0.03 mmol, 0.4 eq.) was added in one portion and the mixture was left stirring at room temperature for another 5 h before adding DCM (15 mL) and a saturated aqueous solution of NaHCO₃ (15 mL). After separation, the aqueous layer was extracted with DCM (3 x 15 mL). Combined organic fractions were dried over MgSO₄, concentrated under reduced pressure and resulting residue was purified by flash column chromatography on silica gel (PE/AcOEt 10:1) to furnish **4.93** as a colorless oil (16 mg, 19% on the 2 steps). *R*_f = 0.83 (PE/AcOEt 4:1, Vanillin).



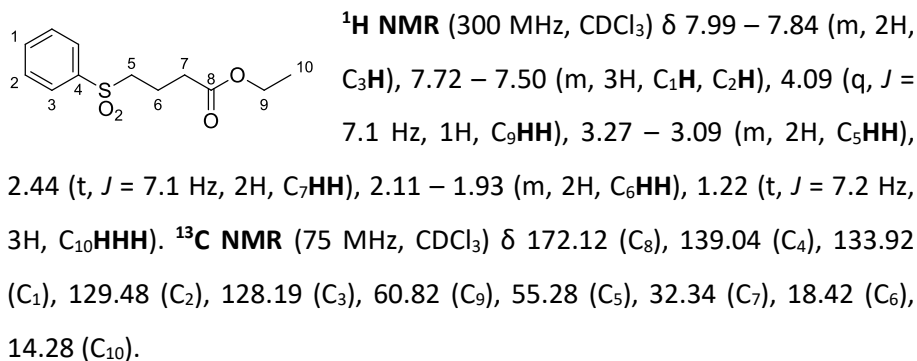
¹H NMR (300 MHz, CDCl₃) δ 6.09 (s, 1H, C₈H), 4.24 (ddd, *J* = 9.5, 5.8, 4.0 Hz, 1H, C₄H), 4.07 (dd, *J* = 12.4, 5.7 Hz, 1H, C₅H), 3.72 – 3.59 (m, 2H, C₆HH), 2.11 (dd, *J* = 14.5, 6.1 Hz, C₃HH), 2.06 (dd, *J* = 14.8, 9.0 Hz, 1H, C₃HH), 1.67 (d, *J* = 13.6 Hz, 1H, C₁HH), 1.46 (d, *J* = 13.9 Hz, 1H, C₁HH), 1.42 (s, 3H, C₁₂HHH), 1.32 (s, 3H, C₁₂'HHH), 0.92 (s, 9H, C₁₁HHH or C₁₄HHH), 0.89 (s, 9H, C₁₁HHH or C₁₄HHH), 0.10 (s, 6H, C₉HHH or/and C₁₃HHH or/and C₉'HHH or/and C₁₃'HHH), 0.06 (s, 6H, C₉HHH or/and C₁₃HHH or/and C₉'HHH or/and C₁₃'HHH), 0.01 (s, 9H, C₇HHH). **¹³C NMR** (75 MHz, CDCl₃) δ 133.55 (C₈), 115.45 (C₂), 107.90 (C₁₆), 78.15 (C₅), 76.16 (C₄), 62.12 (C₆), 33.19 (C₃), 28.41 (C₁₂), 26.07, 25.91, 25.79 (C₁₁, C₁₄, C₁₂'), 18.43, 18.32, (C₁₀, C₁₅), 17.65 (C₁), -0.45 (C₇), -5.06, -5.21, -5.25 (C₉, C₉', C₁₃, C₁₃'). **IR** (neat, cm⁻¹): 2953, 2930, 2885, 2856, 1664, 1464, 1364, 1250, 1217, 1159, 1097. **MS** (p ESI), *m/z* (%): 525.32 (21), 485.29 (20), 411.24 (100), 371.20 (32), 331.21 (50), 313.20 (20). **HRMS**, *m/z*: calculated for C₂₅H₅₄O₄Si₃Na [*M* + 23]: 525.3222. Found: 525.3222.

Experimental

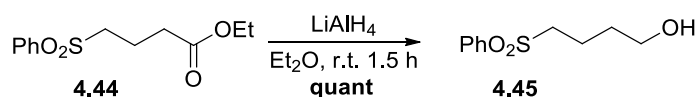
ethyl 4-(phenylsulfonyl)butanoate



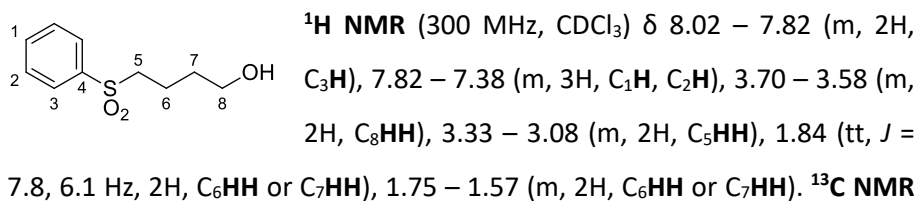
A 500 mL round-bottom flask equipped with a magnetic Teflon-coated stirrer and a cooling tower was charged with ester **4.42** (15 g, 0.099 mol, 1 eq.) and acetone (150 mL, distilled from K₂CO₃). NaI (25.37 g, 0.169 mol, 1.7 eq.) was then added in one portion and resulting mixture was left stirring at reflux for 16 h. Formation of a white precipitate was then observed and the volatiles were removed under reduced pressure. The residue was dissolved in water (40 mL) and Et₂O (40 mL). After separation, the aqueous layer was extracted with Et₂O (2 x 30 mL). Combined organic fractions were dried over MgSO₄ and concentrated under reduced pressure with the aid of a rotary evaporator to furnish a yellow oil. The iodinated ester was dissolved in EtOH (185 mL) together with NaSO₂Ph (17.79 g, 0.11 mol, 1.1 eq.). The mixture was left stirring at reflux for 5 h before being allowed to cool down to room temperature. Water (60 mL) was then added and the volatiles were again removed under reduced pressure. Resulting aqueous layer was extracted with Et₂O (3 x 50 mL) and combined organic fractions were dried over MgSO₄, concentrated under reduced pressure with a rotary evaporator and purified by flash column chromatography on silica gel (PE/AcOEt 4:1 to 1:1) to afford **4.44** as a colorless oil (11.866 g, 47% of pure ester) and 3.386 g of a 2:1 mixture of the desired ester and the O-addition product.



4-(phenylsulfonyl)butan-1-ol



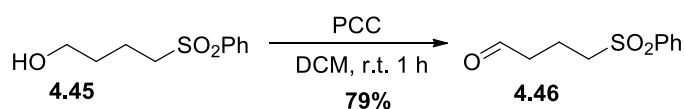
A 500 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with sulfone **4.44** (3.71 g, 0.015 mol, 1 eq.) and Et₂O (150 mL). Resulting mixture was left stirring at 0°C prior to dropwise addition of LiAlH₄ (4 M in THF, 2 mL, 0.008 mol, 0.5 eq.). After 1 h 30 at 0°C, a saturated aqueous solution of potassium sodium tartrate (100 mL) was added to the mixture and stirring was continued for another hour. At that moment, the heterogeneous mixture was filtered through celite®. After phase separation, the aqueous layer was extracted with AcOEt (3 x 50 mL). Combined organic fractions were dried over MgSO₄ and concentrated under reduced pressure with the rotary evaporator. Alcohol **4.45** was used without further purification. R_f = 0.4 (AcOEt, KMnO₄, UV).



Experimental

(75 MHz, CDCl_3) δ 139.17 (C_4), 133.86, 129.45, 128.19 (C_1 , C_2 , C_3), 62.06 (C_8), 56.12 (C_5), 31.07, 19.61 (C_6 , C_7). IR (neat, cm^{-1}) 3430, 2945, 2874, 1447, 1286, 1141, 1084, 1068, 1061, 1024.

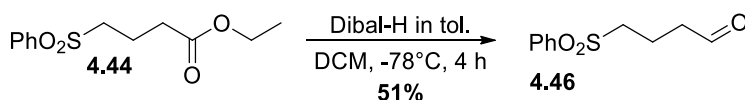
4-(phenylsulfonyl)butanal



A 1 L round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with alcohol **4.45** (6.69 g, 0.031 mol, 1 eq.), DCM (300 mL) and PCC (10.1 g, 0.047 mol, 1.5 eq.). Reaction mixture was left stirring at room temperature for 1 h, before adding celite® (30 g). Stirring was continued for 1 h, then resulting mixture was filtered on silica gel. The latter was washed several times with DCM (3 x 100 mL). Crude product was concentrated under reduced pressure and could be used without further purification (5.19 g, 79%).

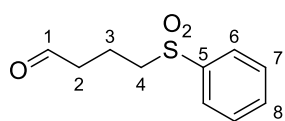
Analyses: see below

Alternative route



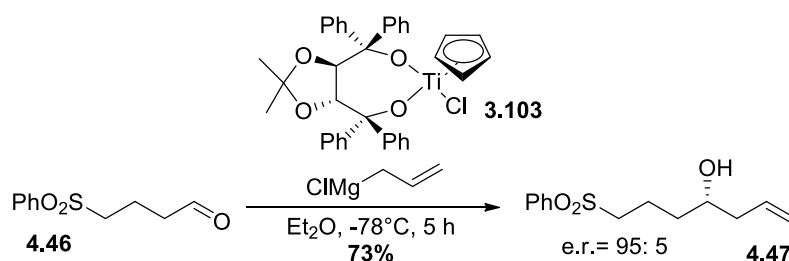
A 2 L round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with ester **4.44** (26.70 g, 0.104 mol, 1 eq.) and DCM (500 mL). Resulting mixture was cooled to -78°C prior to slow addition of Dibal-H (17.78 g, 0.125 mol, 1.2 eq.) in toluene (48 mL). After a total reaction time of 4 h, a saturated aqueous solution of potassium sodium tartrate (300 mL) was added carefully to the mixture. After phase separation, the aqueous layer was extracted with DCM (3 x 200 mL). Combined organic fractions

were dried over MgSO_4 , concentrated under reduced pressure and purified by flash column chromatography on silica gel (PE/AcOEt 3:1) to afford aldehyde **4.46** as a colorless oil (11.24 g, 51%).



^1H NMR (300 MHz, CDCl_3) δ 9.75 (s, 1H, C_1H), 7.91 (dd, $J = 7.2, 1.2$ Hz, 2H, C_6H), 7.71 – 7.51 (m, 3H, C_7H et C_8H), 3.19 – 3.11 (t, $J = 7.6$ Hz, 2H, C_4HH), 2.69 (t, $J = 6.9$ Hz, 2H, C_2HH), 2.04 (p, $J = 6.9$ Hz, 2H, C_3HH). ^{13}C NMR (75 MHz, CDCl_3) δ 200.21 (C_1), 138.87 (C_5), 133.86, 129.38, 128.02 ($\text{C}_6, \text{C}_7, \text{C}_8$), 54.90 (C_4), 41.71 (C_2), 15.51 (C_3). IR (neat, cm^{-1}) 2926, 2833, 2731, 1720, 1447, 1304, 1288, 1136, 1086, 1072.

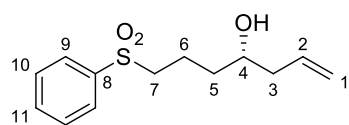
7-(phenylsulfonyl)hept-1-en-4-ol (via Duthaler allylation)



A 250 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with (*S,S*)-**3.103** (2.01 g, 3.26 mmol, 1.4 eq.) and Et_2O (35 mL). The mixture was left stirring and was cooled to 0°C . Allyl Magnesium chloride (2M in THF, 1.39 mL, 2.75 mmol, 1.18 eq.) was then added slowly over 5 minutes which resulted in a brown reaction mixture changing then slowly to a dark-green color. After 2 h at that temperature, the mixture was allowed to cool down to -78°C prior to addition of

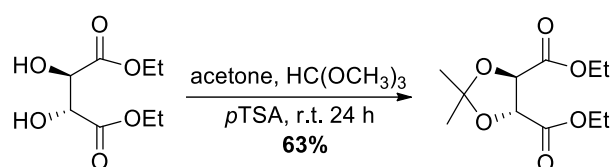
Experimental

aldehyde **4.46** (494 mg, 2.33 mmol, 1 eq.) dissolved in Et₂O (11 mL). The mixture turned orange and stirring was maintained for 5 h at -78°C. When TLC showed full conversion, H₂O (20 mL) was added dropwise at -78°C. The acetone/CO₂ bath was removed and the mixture was allowed to heat to room temperature over night. At that moment, the heterogeneous green/yellow mixture was filtered through celite®, that was washed afterwards with Et₂O (3 x 30 mL). After separation, the aqueous layer was extracted with Et₂O (3 x 30 mL). Combined organic fractions were dried over MgSO₄, then concentrated under reduced pressure. Resulting residue was purified by flash column chromatography on silica gel (PE/AcOEt 4:1 to 1:1) to afford alcohol **4.47** as a colorless oil (431 mg, 73%, e.r. =95:5 by SFC).

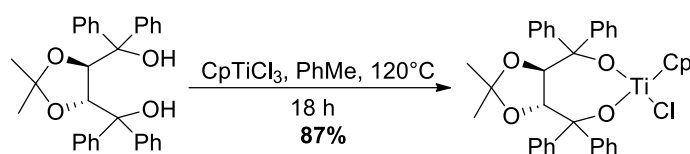


¹H NMR (300 MHz, CDCl₃) δ 7.97 – 7.85 (m, 2H, C₉H), 7.74 – 7.50 (m, 3H, C₁₀H, C₁₁H), 5.77 (dddd, *J* = 16.8, 10.5, 7.9, 6.4 Hz, 1H, C₂H), 5.22 – 5.05 (m, 2H, C₁HH), 3.61 (dq, *J* = 12.3, 4.1 Hz, 1H, C₄H), 3.19 – 3.12 (m, 2H, C₇HH), 2.31 – 2.21 (m, 1H, C₃HH), 2.17 – 2.04 (m, 1H, C₃HH), 1.98 – 1.74 (m, 2H, C₆HH), 1.66 – 1.42 (m, 3H, C₅HH et C₄OH). ¹³C NMR (75 MHz, CDCl₃) δ 139.13 (C₈), 134.11 (C₂), 133.66, 129.28, 128.06 (C₉, C₁₀, C₁₁), 118.78 (C₁), 69.87 (C₄), 56.12 (C₇), 42.03 (C₃), 34.88 (C₅), 19.32 (C₆). IR (neat, cm⁻¹): 3460, 2918, 1447, 1304, 1286, 1140, 1086. MS (p ESI), *m/z* (%): 277.08 (85), 255.10 (10), 95.09 (12). HRMS, *m/z*: calculated for C₁₃H₁₉O₃S [M + 1]: 255.1048. Found: 255.1049.

Duthaler allylation complex



A 250 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with acetone (180 mL), diol (71.00 g, 0.344 mol, 1 eq.), trimethylorthoformate (54.76 g, 0.516 mol, 1.5 eq.) and *p*TSA (1.00 g). Resulting mixture was left stirring at r.t for 24 h prior to washing the mixture with brine (50 mL). Resulting yellow oil was purified by distillation (1.5 mBar, *b_p* 105-110°C) to furnish the dioxolane as a yellow liquid (53.00 g, 63%).

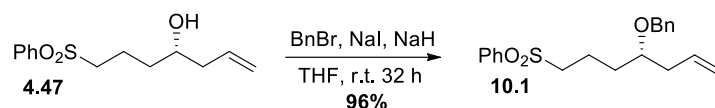


A 2-necked 500 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer and a condenser was charged with toluene (distilled from CaH_2 , 180 mL) and CpTiCl_3 (5 g, 23 mmol, 1 eq.). Resulting mixture was heated to reflux (120°C). After 5 minutes at 120°C, heating was stopped and 5 minutes later, Taddol (10.85 g, 23.25 mmol, 1.02 eq.) was added in one portion and heating was restarted. Argon was then allowed to bubble through the solution with the aid of a needle. The septum on top of the condenser was then removed and exchanged for a small gas outlet. HCl_g formation could be observed at that outlet. Argon bubbling was maintained for 18 h till no HCl_g formation was observed anymore. At that moment, heating was stopped and the reaction mixture was allowed to cool down to room temperature during one hour. Then, the mixture was transferred to a 500 mL round-bottom flask and concentrated under reduced pressure. The sticky brown oil was dissolved in dry Et_2O (60 mL) and hexane (180 mL,

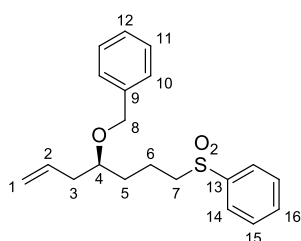
Experimental

freshly distilled from CaH_2). A green/yellow precipitate was forming immediately. This mixture was stirred for 1 h 30, then the precipitate was filtered and washed with hexane (distilled, 3 x 15 mL). Resulting solid was dried under a light argon flow for 4 h to afford (*S,S*)-**3.103** as a slightly yellow solid (12.297 g, 87%).

(*S*)-((4-(benzyloxy)hept-6-en-1-yl)sulfonyl)benzene



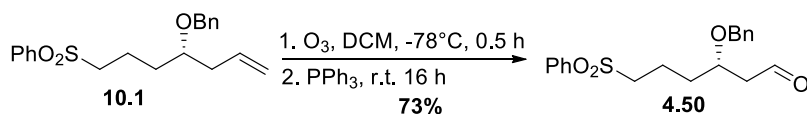
A 100 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with alcohol **4.47** (0.431 g, 1.7 mmol, 1 eq.) and THF (17 mL). NaH (60% in mineral oil, 0.136 g, 5.1 mmol, 3 eq.) was then added carefully at 0°C (exothermic reaction was observed). After 10 min of stirring, NaI (tip of spatula) and BnBr (0.48 mL, 4.08 mmol, 2.4 eq.) were added to the flask and resulting mixture was left stirring at room temperature for 32 h, before adding a saturated aqueous solution of NH_4Cl . After separation, the aqueous layer was extracted with Et_2O (3 x 20 mL). Combined organic fractions were dried over MgSO_4 and concentrated under reduced pressure. Resulting residue was purified by flash column chromatography on silica gel (PE/AcOEt 8:1 to 5:1) to afford the benzylated alcohol **10.1** as a colorless oil (0.561 g, 96%). R_f = 0.68 (PE/AcOEt 1:1, Vanillin, UV).



^1H NMR (300 MHz, CDCl_3) δ 7.95 – 7.83 (m, 2H, C_{10}H), 7.73 – 7.49 (m, 3H, C_{11}H , C_{12}H), 7.39 – 7.19 (m, 5H, C_{14}H , C_{15}H , C_{16}H), 5.88 – 5.65 (m, 1H, C_2H), 5.12 – 5.00 (m, 1H, C_1HH), 4.56 (d, J = 11.5 Hz, 1H, C_8HH), 4.38 (d, J = 11.5 Hz, 1H, C_8HH),

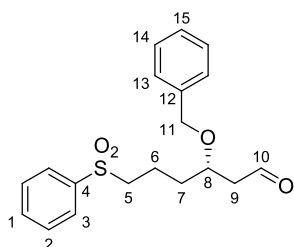
3.50 – 3.32 (m, 1H, C₄H), 3.20 – 2.96 (m, 2H, C₇HH), 2.42 – 2.18 (m, C₃HH), 1.95 – 1.66 (m, 2H, C₆HH), 1.64 – 1.49 (m, 2H, C₅HH). ¹³C NMR (75 MHz, CDCl₃) δ 139.14, 138.38 (C₉, C₁₃), 134.11 (C₂), 133.59, 129.22, 128.40, 128.07, 127.78, 127.66 (C₁₀, C₁₁, C₁₂, C₁₄, C₁₅, C₁₆), 117.53 (C₁), 70.98 (C₈), 56.18 (C₇), 37.93 (C₃), 32.29 (C₅), 19.04 (C₆). IR (neat, cm⁻¹) 2920, 2864, 1447, 1306, 1146, 1086, 1070. MSMS (p ESI), m/z (%): 203.14 (100), 185.13 (26), 143.09 (14), 129.07 (13), 177.07 (53), 109.05. HRMS, m/z: calculated for C₂₀H₂₅O₃S [M + 1]: 345.1519. Found: 345.1520.

3-(benzyloxy)-6-(phenylsulfonyl)hexanal



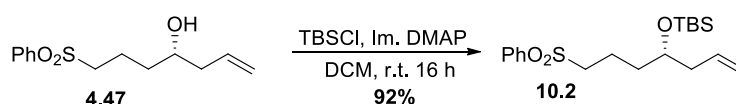
A 3-necked 500 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with olefin **10.1** (9.00 g, 26 mmol, 1 eq.) and DCM (230 mL). The mixture was then cooled to -78°C and stirred while ozone was bubbled through the solution using a Pasteur pipet. After 30 minutes, the solution was flushed with argon in order to eliminate excess ozone and was allowed to heat up to room temperature. PPh₃ (7.54 g, 28 mmol, 1.1 eq.) was then added and the mixture was stirred over night at room temperature. The crude reaction mixture was then concentrated under reduced pressure and the residue was purified by column chromatography on silica gel (PE/AcOEt 3:1 to 1:1) to furnish aldehyde **4.50** as a yellow oil (6.567, 73%).

Experimental



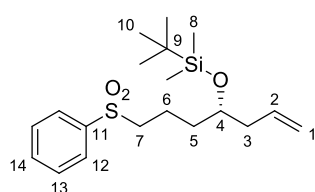
^1H NMR (300 MHz, CDCl_3) δ 9.76 (t, J = 1.9 Hz, 1H, C_{10}H), 7.89 (m, 2H, C_3H), 7.73 – 7.60 (m, 1H, C_1H), 7.61 – 7.52 (m, 2H, C_3H), 7.40 – 7.17 (m, 5H, C_{13}H , C_{14}H , C_{15}H), 4.51 (d, J = 11.4 Hz, 1H, C_{11}HH), 4.44 (d, J = 11.4 Hz, 1H, C_{11}HH), 4.01 – 3.87 (m, 1H, C_8H), 3.09 (dd, J = 11.6, 4.2 Hz, 2H, C_5HH), 2.71 (ddd, J = 16.7, 6.5, 2.1 Hz, 1H, C_9HH), 2.54 (ddd, J = 16.7, 5.4, 1.6 Hz, 1H, C_9HH), 1.93 – 1.75 (m, 2H, C_6HH), 1.74 – 1.54 (m, 2H, C_7HH). **^{13}C NMR** (75 MHz, CDCl_3) δ 200.83 (C_{10}), 139.15 (C_4), 137.82 (C_{12}), 133.88 (C_1), 129.46 (C_2), 128.65, 128.19, 128.07, 128.00 (C_3 , C_{13} , C_{14} , C_{15}), 73.33 (C_8), 71.65 (C_{11}), 56.06 (C_5), 48.15 (C_9), 33.03 (C_7), 18.86 (C_6). **IR** (neat, cm^{-1}) 2926, 2874, 2847, 1720, 1447, 1437, 1304, 1292, 1140, 1117, 1086, 1070, 1026. **MSMS** (p ESI), m/z (%): 369.11 (100), 91.05 (37). **HRMS**, m/z : calculated for $\text{C}_{19}\text{H}_{22}\text{O}_4\text{SNa}$ [$M + 23$]: 369.1131. Found: 369.1131.

(*S*)-tert-butyldimethyl((7-(phenylsulfonyl)hept-1-en-4-yl)oxy)silane



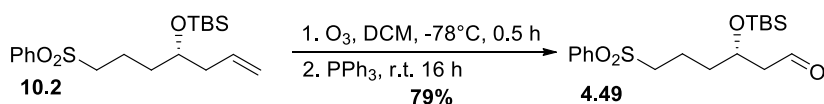
A 500 mL round bottom-flask equipped with a Teflon-coated magnetic stirrer was charged with alcohol **4.47** (2.063 g, 0.008 mol, 1 eq.), DCM (100 mL), imidazole (1.65 g, 0.0243 mol, 3 eq.), DMAP (0.001 eq.) and TBSCl (3.66 g, 0.0243 mol, 3 eq.). Resulting white mixture was stirred at room temperature for 16 h, before adding a saturated aqueous solution of NH_4Cl (100 mL). After separation, the aqueous phase was extracted with DCM (3 x 100 mL). Combined organic fractions were dried over MgSO_4 , concentrated under reduced pressure and purified by flash column chromatography on

silica gel (PE/AcOEt 6:1) to furnish protected alcohol **10.2** as a colorless oil (3.393 g, 92%). $R_f = 0.50$ (PE/AcOEt 4:1, Vanillin, UV).



$^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.96 – 7.85 (m, 2H, C_{12}H), 7.73 – 7.51 (m, 3H, C_{13}H , C_{14}H), 5.71 (ddt, $J = 18.0, 10.8, 7.2$ Hz, 1H, C_2H), 5.05 – 4.92 (m, 2H, C_1HH), 3.70 – 3.59 (m, 1H, C_4H), 3.20 – 2.91 (m, 2H, C_7HH), 2.16 (t, $J = 6.4$ Hz, 2H, C_3HH), 1.88 – 1.61 (m, 2H, C_6HH), 1.61 – 1.35 (m, 2H, C_5HH), 0.81 (s, 9H, C_{10}HHH), 0.01 (s, 3H, C_8HHH), -0.04 (s, 3H, C_8HHH). $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 138.98 (C_{11}), 134.43 (C_2), 133.60, 129.24 (C_{13} , C_{14}), 128.11 (C_{12}), 117.26 (C_1), 71.12 (C_4), 56.45 (C_7), 41.82 (C_3), 34.92 (C_5), 25.79 (C_{10}), 19.24 (C_6), 17.98 (C_9), -4.37 (C_8), -4.70 (C_8').

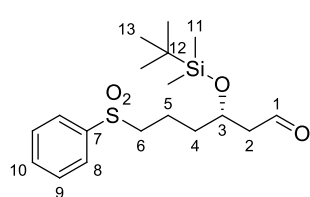
(S)-3-((tert-butyldimethylsilyl)oxy)-6-(phenylsulfonyl)hexanal



A 3-necked 250 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with olefin **10.2** (3.839, 0.01 mol, 1 eq.) and DCM (75 mL). The mixture was cooled to -78°C and stirred while ozone was bubbled through the solution using a Pasteur pipet. The reaction was monitored by TLC and after 0.5 h all the starting material was consumed. After flushing the solution with argon to eliminate excess ozone, the solution was allowed to heat up to room temperature. At that moment, PPh_3 (3.04 g, 0.011 mol, 1.1 eq.) was added in one portion and the mixture was left stirring over night. The crude reaction mixture was then concentrated under reduced pressure and purified by flash column

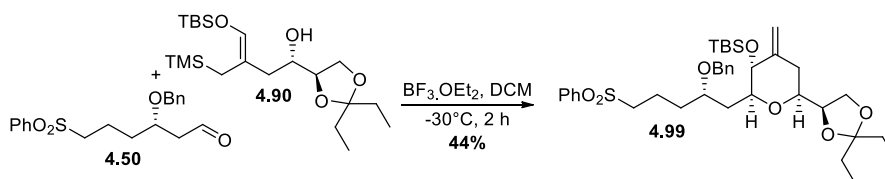
Experimental

chromatography on silica gel (PE/AcOEt 4:1 to 1:1) to afford aldehyde **4.49** as a white solid (3.658 g, 79%). R_f = 0.50 (PE/AcOEt 1:1).



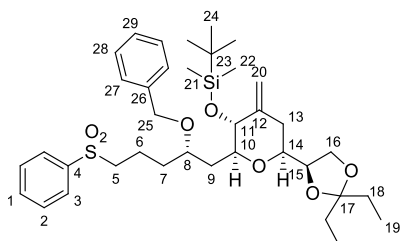
^1H NMR (300 MHz, CDCl_3) δ 9.75 (t, J = 2.1 Hz, 1H, C_1H), 7.90 (dd, J = 5.3, 3.3 Hz, 2H, C_8H), 7.72 – 7.51 (m, 3H, C_9H , C_{10}H), 4.16 (p, J = 5.7 Hz, 1H, C_3H), 3.10 (ddd, J = 8.8, 7.0, 1.9 Hz, 2H, C_6HH), 2.52 (dt, J = 5.7, 2.2 Hz, 2H, C_2HH), 1.86 – 1.67 (m, 2H, C_5HH), 1.63 – 1.53 (m, 2H, C_4HH), 0.81 (s, 9H, C_{13}HHH), 0.02 (s, 3H, C_{11}HHH), -0.00 (s, 3H, $\text{C}_{11'}\text{HHH}$). **^{13}C NMR** (75 MHz, CDCl_3) δ 201.19 (C_1), 138.99 (C_7), 133.73, 129.32 (C_9 , C_{10}), 128.07 (C_8), 67.12 (C_3), 56.14 (C_6), 50.77 (C_2), 36.00 (C_4), 25.66 (C_{13}), 18.85 (C_5), 17.87 (C_{12}), -4.64 (C_{11}), -4.67 ($\text{C}_{11'}$). **IR** (neat, cm^{-1}) 2953, 2930, 2856, 1722, 1447, 1306, 1142, 1086.

(((2*S*,3*R*,6*S*)-2-((*S*)-2-(benzyloxy)-5-(phenylsulfonyl)pentyl)-6-((*R*)-2,2-diethyl-1,3-dioxolan-4-yl)-4-methylenetetrahydro-2H-pyran-3-yl)oxy)(tert-butyl)dimethylsilane



A 100 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with aldehyde **4.50** (1.252 g, 3.6 mmol, 1 eq.), allylsilane **4.90** (1.506 g, 3.6 mmol, 1 eq.) and DCM (36 mL) and was then cooled to -78°C. At that moment, $\text{BF}_3\cdot\text{OEt}_2$ (0.511 g, 3.6 mmol, 1 eq.) dissolved in DCM (2.5 mL) was added dropwise over a period of 5 min at -78°C. The reaction

mixture was then allowed to heat up to -35°C . This temperature was maintained for another hour, before adding water (40 mL). The aqueous layer was extracted with DCM (3 x 40 mL). Combined organic fractions were dried over MgSO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (PE/AcOEt 10:1) to furnish THP **4.99** as a colorless oil (1.062 g, 44%).



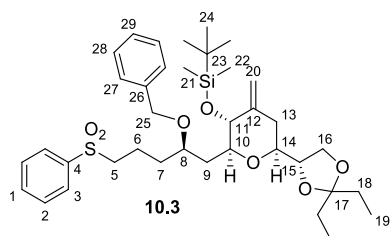
^1H NMR (300 MHz, CDCl_3) δ 8.02 – 7.75 (m, 2H, C_3H), 7.64 (tt, $J = 7.4, 2.2$ Hz, 1H, C_1H), 7.54 (t, $J = 7.5$ Hz, 2H, C_2H), 7.40 – 7.09 (m, 5H, C_{27}H , C_{28}H , C_{29}H), 5.04 (s, 1H, C_{20}HH), 4.88 (d, $J = 1.3$ Hz, 1H, C_{20}HH), 4.54 (d, $J = 11.5$ Hz, 1H, C_{25}HH), 4.30 (d, $J = 11.5$ Hz, 1H, C_{25}HH), 4.02 (dd, $J = 7.7, 6.5$ Hz, 1H, C_{16}HH), 3.92 (dd, $J = 13.1, 6.4$ Hz, 1H, C_{15}H), 3.70 (m, 2H, C_{16}HH , C_{11}H), 3.55 – 3.45 (m, 1H, C_8H), 3.20 (ddd, $J = 11.0, 6.9, 2.1$ Hz, 1H, C_{14}H), 3.10 – 3.01 (m, 3H, C_{10}H , C_5HH), 2.61 (dd, $J = 13.2, 2.1$ Hz, 1H, $\text{C}_{13}\text{H-eq}$), 2.17 – 2.06 (t, $J = 13.5$ Hz, 1H, $\text{C}_{13}\text{H-ax}$), 1.97 (ddd, $J = 13.9, 8.9, 1.7$ Hz, 1H, C_9HH), 1.74 (dd, $J = 10.4, 3.4$ Hz, 2H, C_6HH), 1.69 – 1.56 (m, 6H, C_{18}HH , C_9HH , C_7HH), 1.55 – 1.44 (m, 1H, C_7HH), 0.94 – 0.85 (m, 15H, C_{24}HHH , C_{19}HHH), 0.07 (s, 3H, C_{21}HHH), 0.04 (s, 3H, C_{22}HHH). ^{13}C NMR (75 MHz, CDCl_3) δ 146.08 (C_{12}), 139.24, 138.57 (C_4 , C_{26}), 133.70 (C_1), 129.35 (C_2), 128.51, 128.22, 127.97, 127.76 (C_3 , C_{27} , C_{28} , C_{29}), 113.54 (C_{17}), 107.40 (C_{20}), 80.38 (C_{10}), 79.76 (C_{14}), 78.12 (C_{15}), 75.52 (C_8), 74.46 (C_{11}), 70.71 (C_{25}), 67.92 (C_{16}), 56.29 (C_5), 38.26 (C_{13}), 36.18 (C_9), 32.66 (C_7), 29.79 (C_{18}), 29.31 ($\text{C}_{18'}$), 26.01 (C_{24}), 19.38 (C_6), 18.26 (C_{23}), 8.33 (C_{19}), 8.19 ($\text{C}_{19'}$), -4.22 (C_{21}), -4.55 (C_{22}). IR (neat, cm^{-1}) 2951, 2928, 2883, 2856, 1462, 1447, 1306, 1252, 1146, 1111, 1086, 1028. MS (p ESI), m/z (%): 695.34 (48), 627.28 (100), 605.30

Experimental

(17), 541.26 (32), 473.20 (28). **HRMS**, m/z : calculated for $C_{37}H_{57}O_7SSi$ [$M + 1$]: 673.3589. Found: 673.3588.

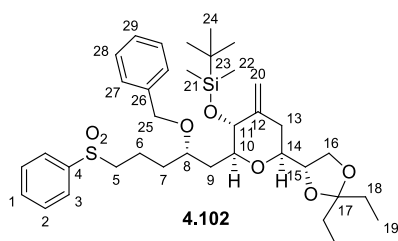
N.B. For unknown reasons, we observed the following two epimerized products **4.102** and **10.3** in one case out of 13.

Minor diastereoisomer:



¹³C NMR (75 MHz, CDCl₃) δ 146.18 (C₁₂), 139.20, 138.67 (C₄, C₂₆), 133.73 (C₁), 129.38 (C₂), 128.49, 128.21, 127.86, 127.70 (C₃, C₂₇, C₂₈, C₂₉), 109.70 (C₁₇), 107.30 (C₂₀), 80.45 (C₁₀), 79.46 (C₁₄),

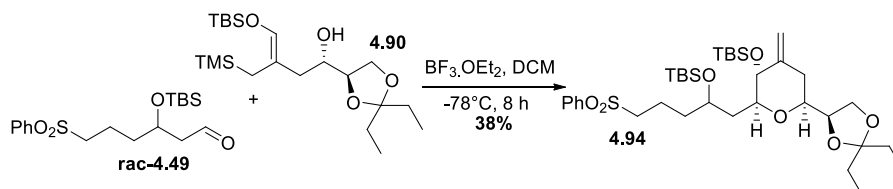
77.80 (C₁₅), 75.00 (C₈), 74.57 (C₁₁), 71.42 (C₂₅), 67.16 (C₁₆), 56.43 (C₅), 37.76 (C₉), 37.57 (C₁₃), 33.38 (C₇), 26.72 (C₁₈), 26.03 (C₂₄, C₁₉, C_{19'}), 25.39 (C_{18'}), 18.84 (C₆), 18.31 (C₂₃), -4.19 (C₂₁), -4.52 (C₂₂). **MSMS** (p APCI), m/z (%): 541.26 (5), 229.05 (27), 211.04 (52), 177.13 (27), 149.13 (17), 121.10 (19), 91.05 (100). **HRMS**, m/z : calculated for $C_{37}H_{57}O_7SSi$ [$M + 1$]: 673.3589. Found: 673.3617.

Major diastereoisomer

¹³C NMR (75 MHz, CDCl₃) δ 145.93 (C₁₂), 138.44 (C₄, C₂₆), 133.56 (C₁), 129.22 (C₂), 128.38, 128.09, 127.84, 127.62 (C₃, C₂₇, C₂₈, C₂₉), 109.59 (C₁₇), 107.32 (C₂₀), 80.31 (C₁₀), 79.48 (C₁₄), 77.72 (C₁₅), 75.37 (C₈),

74.33 (C₁₁), 70.57 (C₂₅), 67.13 (C₁₆), 56.17 (C₅), 37.67 (C₁₃), 36.05 (C₉), 32.52 (C₇), 26.64 (C₁₈), 25.89 (C₂₄, C₁₉, C_{19'}), 25.33 (C_{18'}), 19.26 (C₆), 18.15 (C₂₃), -4.34 (C₂₁), -4.67 (C₂₂).

tert-butyl(((2*S*,3*R*,6*S*)-2-(2-((tert-butyldimethylsilyl)oxy)-5-(phenylsulfonyl)pentyl)-6-((*R*)-2,2-diethyl-1,3-dioxolan-4-yl)-4-methylenetetrahydro-2H-pyran-3-yl)oxy)dimethylsilane

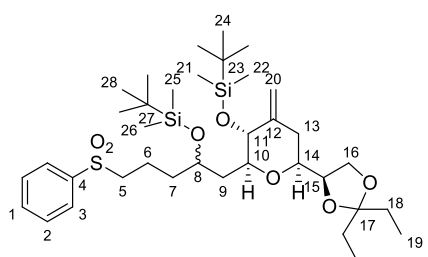


A 100 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with aldehyde **4.49** (89 mg, 0.24 mmol, 1 eq.), allylsilane **4.90** (100 mg, 0.24 mmol, 1 eq.) and DCM (3 mL) and was then cooled to -78°C. At that moment, BF₃.OEt₂ (0.033 mL, 0.26 mmol, 1.1 eq.) dissolved in DCM (1 mL) was added dropwise over a period of 5 min at -78°C. The reaction mixture was left stirring at -78°C for 8 hours, before adding water (10 mL). The aqueous layer was extracted with DCM (3 x 10 mL). Combined organic fractions were dried over MgSO₄ and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (PE/AcOEt 10:1) to furnish tetrahydropyran **4.94** as a colorless oil

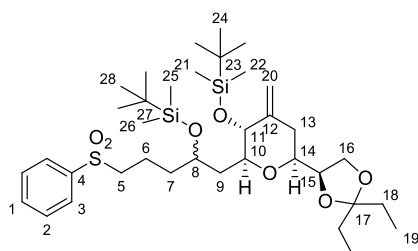
Experimental

and as a 1:1 mixture of two diastereoisomers (63 mg, 38% + 47% **4.90** recovery).

Diastereoisomer 1 (unknown stereochemistry at C₈)



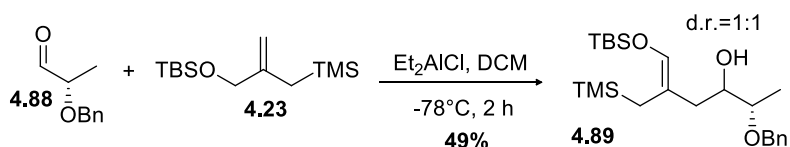
¹H NMR (300 MHz, CDCl₃) δ 7.90 (dd, J = 7.0, 1.4 Hz, 2H, C₃H), 7.72 – 7.48 (m, 3H, C₂H, C₁H), 5.01 (s, 1H, C₂₀HH), 4.84 (s, 1H, C₂₀HH), 4.04 (dd, J = 7.8, 6.3 Hz, 1H, C₁₆HH), 3.91 (q, J = 6.4 Hz, 1H, C₁₅H), 3.82 (m, 1H, C₈H), 3.76 (dd, J = 7.8, 6.5 Hz, 1H, C₁₆HH), 3.59 (d, J = 8.8 Hz, 1H, C₁₁H), 3.19 (ddd, J = 11.0, 7.0, 2.1 Hz, 1H, C₁₄H), 3.13 – 3.02 (m, 3H, C₅HH, C₁₀H), 2.59 (dd, J = 13.2, 2.0 Hz, 1H, C₁₃H-*eq*), 2.08 (t, J = 12.2 Hz, 1H, C₁₃H-*ax*), 1.93 (ddd, J = 13.7, 8.9 Hz, 1 Hz, 1H, C₉HH), 1.76 – 1.67 (m, 2H, C₆HH), 1.62 (ddd, J = 10.0, 7.4, 4.1 Hz, 4H, C₁₈HH), 1.51 (dd, J = 9.8, 4.9 Hz, 2H, C₇HH), 1.33 – 1.27 (m, 1H, C₉HH), 0.96 – 0.84 (m, 15H, C₁₉HHH, C₂₄HHH), 0.77 (s, 9H, C₂₈HHH), 0.03 (s, 3H, C₂₆HHH or C₂₅HHH), 0.02 (s, 3H, C₂₆HHH or C₂₅HHH), -0.03 (s, 3H, C₂₁HHH or C₂₂HHH), -0.07 (s, 3H, C₂₁HHH or C₂₂HHH). **¹³C NMR** (75 MHz, CDCl₃) δ 146.10 (C₁₂), 138.97 (C₄), 133.57 (C₃), 129.23 (C₁), 128.08 (C₂), 113.35 (C₁₇), 107.04 (C₂₀), 80.17 (C₁₄), 79.36 (C₁₀), 78.10 (C₁₅), 73.93 (C₁₁), 67.80 (C₁₆), 67.75 (C₈), 56.61 (C₅), 39.93 (C₉), 38.14 (C₁₃), 36.68 (C₇), 29.59 (C₁₈), 29.28 (C_{18'}), 25.82, 25.71 (C₂₈, C₂₄), 18.08 (C₆), 18.03, 17.86 (C₂₇, C₂₃), 8.21 (C₁₉), 7.94 (C_{19'}), -4.23, -4.27, -4.71 (C₂₆, C₂₅, C₂₂, C₂₁). **IR** (neat, cm⁻¹) 2955, 2928, 2856, 1462, 1305, 1252, 1146, 1122, 1086. **MS** (p ESI), m/z (%): 719.38 (100), 565.30 (25). **HRMS**, m/z : calculated for C₃₆H₆₅O₇SSi₂ [M + 1]: 697.3984. Found: 697.3986. **[α]_D²⁰**: -19.8 (CHCl₃, 19 mg/mL, Perkin Elmer Polarimeter 343).

Diastereoisomer 2 (Unknown stereochemistry at C₈)¹H NMR (300 MHz, CDCl₃) δ 7.93 – 7.86(m, 2H, C₃H), 7.70 – 7.50 (m, 3H, C₂H,C₁H), 5.02 (d, J = 1.1 Hz, 1H, C₂₀HH),4.86 (d, J = 1.6 Hz, 1H, C₂₀HH), 4.03(dd, J = 7.8, 6.3 Hz, 1H, C₁₆HH), 3.89 (q,

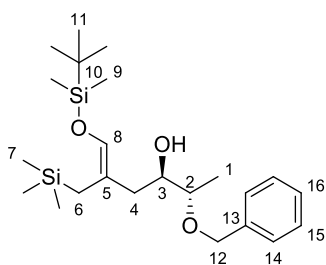
J = 6.5 Hz, 1H, C₁₅H), 3.82 – 3.74 (m, 1H, C₈H), 3.73 (dd, J = 7.8, 6.6 Hz, 2H, C₁₆HH), 3.62 (d, J = 8.9 Hz, 1H, C₁₁H), 3.19 (ddd, J = 11.0, 6.8, 2.2 Hz, 1H, C₁₄H), 3.09 (m, 2H, C₅HH), 2.96 (ddd, J = 10.9, 8.9, 2.0 Hz, 1H, C₁₀H), 2.59 (dd, J = 13.2, 2.3 Hz, 1H, C₁₃H-*eq*), 2.07 (t, J = 12.2 Hz, 1H, C₁₃H-*ax*), 1.87 (ddd, J = 13.4, 9.7, 2.0 Hz, 1H, C₉HH), 1.68 – 1.57 (m, 6H, C₁₈HH, C₆HH), 1.56 – 1.50 (m, 3H, C₉HH, C₇HH), 0.92 (s, 9H, C₂₄HHH), 0.94 – 0.84 (m, 6H, C₁₉HHH), 0.80 (s, 9H, C₂₈HHH), 0.05 (s, 3H, C₂₆HHH or C₂₅HHH), 0.02 (s, 3H, C₂₆HHH or C₂₅HHH), -0.00 (s, 3H, C₂₁HHH or C₂₂HHH), -0.05 (s, 3H, C₂₁HHH or C₂₂HHH). ¹³C NMR (75 MHz, CDCl₃) δ 146.00 (C₁₂), 138.95 (C₄), 133.58 (C₃), 129.23 (C₁), 128.14 (C₂), 113.34 (C₁₇), 107.12 (C₂₀), 80.43 (C₁₄), 79.50 (C₁₀), 78.04 (C₁₅), 73.93 (C₁₁), 68.65 (C₈), 67.80 (C₁₆), 56.50 (C₅), 40.81 (C₉), 38.33 (C₁₃), 34.50 (C₇), 29.65 (C₁₈), 29.16 (C_{18'}), 25.87, 25.78 (C₂₈, C₂₄), 19.30 (C₆), 18.14, 17.94 (C₂₇, C₂₃), 8.16 (C₁₉), 8.05 (C_{19'}), -4.41, -4.43, -4.75 (C₂₆, C₂₅, C₂₂, C₂₁). IR (neat, cm⁻¹) 2955, 2928, 2856, 1462, 1305, 1252, 1146, 1122, 1086. MS (p ESI), m/z (%): 719.38 (100), 565.30 (25). HRMS, m/z: calculated for C₃₆H₆₅O₇SSi₂ [M + 1]: 697.3984. Found: 697.3986. [α]_D²⁰: -22.6 (CHCl₃, 19 mg/mL, Perkin Elmer Polarimeter 343).

Experimental

(2*S*,*Z*)-2-(benzyloxy)-6-((tert-butyldimethylsilyl)oxy)-5-((trimethylsilyl)methyl)hex-5-en-3-ol

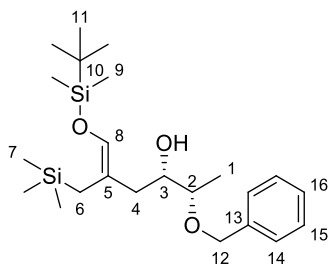


A 500 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with aldehyde **4.88** (7.13 g, 0.044 mol, 1 eq.), allylsilane **4.23** (11.51 g, 0.044 mol, 1 eq.) and DCM (220 mL). Resulting mixture was cooled to -78°C in a bath of acetone and dry ice. At that moment, diethylaluminium chloride (1M in hexane, 53 mL, 0.053 mol, 1.2 eq.) was added dropwise and resulting mixture was left stirring for 30 min at that temperature. A saturated aqueous solution of Rochelle's salt (200 mL) was then added and the mixture was left stirring for 1 h. The layers were separated and the aqueous phase was extracted with DCM (100 mL). Organic fractions were dried over MgSO₄, concentrated under reduced pressure and purified by flash column chromatography on silica gel (PE/AcOEt 20:1) to afford alcohol **4.89** as a sluggish 1:1 diastereomeric mixture (9.33 g, 49%, d.r.=1:1). R_f = 0.66, 0.88 (PE/AcOEt 4:1).

Diastereoisomer 1:

¹H NMR (300 MHz, CDCl₃) δ 7.37 – 7.27 (m, 5H, C₁₄H, C₁₅H, C₁₆H), 6.09 (s, 1H, C₈H), 4.66 (d, J = 11.6 Hz, 1H, C₁₂HH), 4.48 (d, J = 11.6 Hz, 1H, C₁₂HH), 3.58 (*bs*, 1H, C₃H), 3.53 – 3.42 (m, 1H, C₂H), 2.21 (d, J = 2.6 Hz, 1H, C₃OH),

2.08 (ddd, J = 14.1, 4.1, 1.2 Hz, 1H, C₄HH), 1.96 (dd, J = 14.0, 8.8 Hz, 1H, C₄HH), 1.70 (d, J = 13.4 Hz, 1H, C₆HH), 1.33 (d, J = 13.8 Hz, 1H, C₆HH), 1.22 (d, J = 6.2 Hz, 3H, C₁HHH), 0.92 (s, 9H, C₁₁HHH), 0.10 (s, 3H, C₉HHH), 0.09 (s, 3H, C₉HHH), 0.01 (s, 9H, C₇HHH).

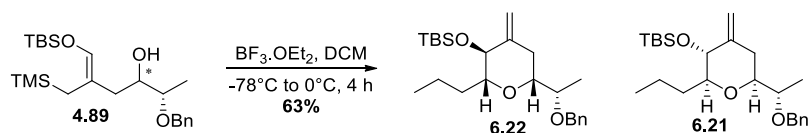
Diastereoisomer 2:

¹H NMR (300 MHz, CDCl₃) δ 7.41 – 7.27 (m, 5H, C₁₄H, C₁₅H, C₁₆H), 6.09 (s, 1H, C₈H), 4.63 (d, J = 11.8 Hz, 1H, C₁₂HH), 4.52 (d, J = 11.8 Hz, 1H, C₁₂HH), 3.78 – 3.68 (m, 1H, C₃H), 3.56 – 3.42 (m, 1H, C₂H), 2.16 (dd, J = 14.0, 3.0 Hz, 1H, C₄HH), 1.91 (dd, J = 14.9, 5.5 Hz, 1H, C₄HH), 1.69 (d, J = 13.4 Hz, 1H, C₆HH), 1.30 (d, J = 13.5 Hz, 1H, C₆HH), 1.21 (d, J = 6.3 Hz, 3H, C₁HHH), 0.92 (s, 9H, C₁₁HHH), 0.10 (s, 3H, C₉HHH), 0.10 (s, 1H, C₉HHH), 0.02 (s, 9H, C₇HHH).

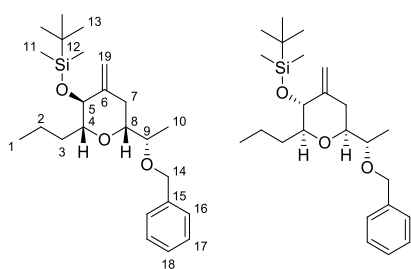
IR (film, cm⁻¹) 3794, 2940, 1454, 1362, 1248, 1204, 1161, 1099, 1074. (mixture of the two diastereoisomers).

Experimental

(((2*S*,3*R*,6*S*)-6-((*S*)-1-(benzyloxy)ethyl)-4-methylene-2-propyltetrahydro-2*H*-pyran-3-yl)oxy)(tert-butyl)dimethylsilane



A 250 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with butanal (1.36 g, 1.81 mmol, 2 eq.), allylsilane **4.89** (384, 0.95 mmol, 1 eq.) and DCM (100 mL) and was then cooled to -78°C . At that moment, $\text{BF}_3 \cdot \text{OEt}_2$ (1.35 g, 0.95 mmol, 1 eq.) dissolved in DCM (1 mL) was added dropwise over a period of 5 min at -78°C . The reaction mixture was left stirring at -78°C for 2 hours, before adding brine (100 mL). The aqueous layer was extracted with DCM (3 x 100 mL). Combined organic fractions were dried over MgSO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (PE/AcOEt 4:1) to furnish tetrahydropyran **6.21** and **6.22** as a colorless oil and as a 1:1 mixture of two diastereoisomers (243 mg, 63%).

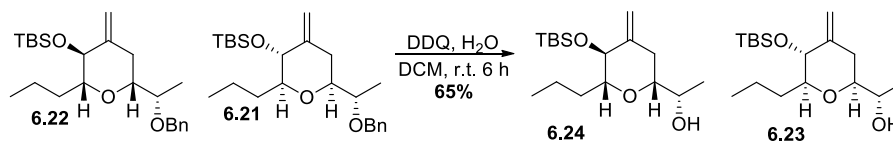


^1H NMR (300 MHz, CDCl_3) δ 7.40 – 7.27 (m, 10H, C_{16}H , C_{17}H , C_{18}H , $\text{C}_{16'}\text{H}$, $\text{C}_{17'}\text{H}$, $\text{C}_{18'}\text{H}$), 5.03 (s, 2H, C_{19}HH , $\text{C}_{19'}\text{HH}$), 4.86 (d, $J = 1.8$ Hz, 2H, C_{19}HH , $\text{C}_{19'}\text{HH}$), 4.83 – 4.53 (m, 4H, C_{14}HH , $\text{C}_{14'}\text{HH}$), 3.72 (d, $J =$

9.1 Hz, 1H, C_5H or $\text{C}_5'\text{H}$), 3.69 (d, $J = 9.1$ Hz, 1H, C_5H or $\text{C}_5'\text{H}$), 3.59 – 3.45 (m, 2H, C_9H , $\text{C}_9'\text{H}$), 3.38 – 3.30 (m, 1H, C_8H or $\text{C}_8'\text{H}$), 3.20 (ddd, $J = 11.1$, 6.3, 2.3 Hz, 1H, C_8H or $\text{C}_8'\text{H}$), 3.05 (t, $J = 8.9$ Hz, 2H, C_4H , $\text{C}_4'\text{H}$), 2.67 (dd, $J = 13.1$, 2.3 Hz, 1H, C_7HH or $\text{C}_7'\text{HH}$), 2.28 (d, $J = 6.4$ Hz, 2H, C_7HH or $\text{C}_7'\text{HH}$), 2.13 (t, $J = 12.2$ Hz, 1H, C_7HH or $\text{C}_7'\text{HH}$), 1.86 – 1.72 (m, 2H, C_3HH or $\text{C}_3'\text{HH}$), 1.69 – 1.58 (m, 2H, C_3HH or $\text{C}_3'\text{HH}$), 1.49 – 1.31 (m, 4H, C_2HH , $\text{C}_2'\text{HH}$), 1.25 (d, $J = 6.3$ Hz,

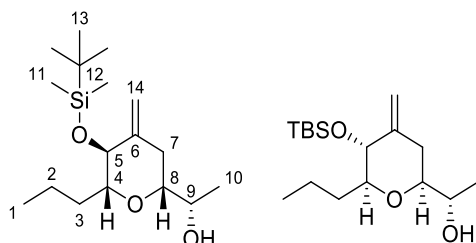
3H, C₁₀HHH or C_{10'}HHH), 1.21 (d, *J* = 6.3 Hz, 3H, C₁₀HHH or C_{10'}HHH), 0.99 – 0.85 (m, 24H, C₁₃HHH, C_{13'}HHH, C₁HHH, C_{1'}HHH), 0.10– 0.06 (m, 12H, C₁₁HHH, C_{11'}HHH). ¹³C NMR (75 MHz, CDCl₃) δ 147.76, 147.48 (C₆, C_{6'}), 139.06, 138.92 (C₁₅, C_{15'}), 128.45, 128.39, 127.91, 127.62, 127.58 (C₁₆, C_{16'}, C₁₇, C_{17'}, C₁₈, C_{18'}), 106.55 (C₁₉, C_{19'}), 83.30, 83.19 (C₄, C_{4'}), 82.05, 81.94 (C₈, C_{8'}), 74.90, 74.84 (C₅, C_{5'}), 71.49, 71.08 (C₁₄, C_{14'}), 37.58, 37.13 (C₇, C_{7'}), 34.79 (C₃, C_{3'}), 25.84 (C₁₃, C_{13'}), 18.98, 18.92 (C₂, C_{2'}), 18.37 (C₁₂, C_{12'}), 16.84, 15.82 (C₁₀, C_{10'}), 14.06 (C₁, C_{1'}), -4.09, -4.61 (C₁₁, C_{11'}). IR (neat, cm⁻¹) 2957, 2930, 2895, 2856, 1651, 1462, 1454, 1362, 1252, 1111. MSMS (p APCI): *m/z* (%) 91.05 (100), 107.05 (8), 147.12 (6), 165.13 (10), 181.12 (5), 229.16 (8), 297.22 (7). HRMS, *m/z*: calculated for C₂₄H₄₁O₃Si [M+1]: 405.2817. Found: 405.2820.

(S)-1-((2*R*,5*S*,6*R*)-5-((tert-butyldimethylsilyl)oxy)-4-methylene-6-propyltetrahydro-2*H*-pyran-2-yl)ethanol



A 50 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with the diastereomeric mixture **6.21** and **6.22** (0.25 g, 0.62 mmol, 1 eq.), DDQ (0.28 g, 1.24 mmol, 2 eq.), DCM (6 mL) and phosphate buffer (pH=8.2, 0.2 mL). The reaction mixture was left stirring at room temperature for 6 hours, before adding brine (10 mL). The aqueous layer was extracted with DCM (3 x 10 mL). Combined organic fractions were dried over MgSO₄ and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (PE/AcOEt 9:1) to furnish the two separated tetrahydropyrans **6.23** and **6.24** (126 mg, 65%).

Experimental



Diastereoisomer 1

¹H NMR (300 MHz, CDCl₃) δ 5.04 (dd, *J* = 3.4, 1.9 Hz, 1H, C₁₄HH), 4.84 (dd, *J* = 3.5, 1.7 Hz, 1H, C₁₄HH), 3.67 (d, *J* = 8.7 Hz, 1H, C₅H), 3.64 – 3.56 (m, 1H, C₉H), 3.08 (dtd, *J* = 11.6, 7.1, 2.5 Hz, 2H, C₄H, C₈H), 2.62 (d, *J* = 2.8 Hz, 1H, C₉OH), 2.34 (dd, *J* = 13.0, 2.4 Hz, 1H, C₇HH), 2.08 (t, *J* = 12.4 Hz, 1H, C₇HH), 1.93 – 1.75 (m, 1H, C₃HH), 1.62 – 1.46 (m, 1H, C₂HH), 1.45 – 1.27 (m, 2H, C₃HH, C₂HH), 1.17 (d, *J* = 6.3 Hz, 3H, C₁₀HHH), 1.00 – 0.81 (m, 12H, C₁HHH, C₁₃HHH), 0.08 (s, 3H, C₁₁HHH), 0.04 (s, 3H, C_{11'}HHH). **¹³C NMR** (75 MHz, CDCl₃) δ 146.77 (C₆), 107.20 (C₁₄), 82.98, 82.92 (C₄, C₈), 74.67 (C₅), 70.50 (C₉), 37.56 (C₇), 34.81 (C₃), 26.04 (C₁₃), 19.01 (C₁₂), 18.59 (C₂), 18.36 (C₁₀), 14.19 (C₁), -4.16, -4.63 (C₁₁).

Diastereoisomer 2

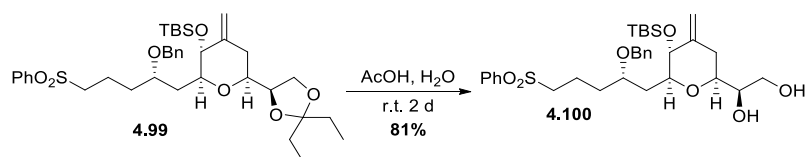
¹H NMR (300 MHz, CDCl₃) δ 5.02 (d, *J* = 1.2 Hz, 1H, C₁₄HH), 4.83 (d, *J* = 1.4 Hz, 1H, C₁₄HH), 3.91 – 3.79 (m, 1H, C₉H), 3.65 (d, *J* = 8.9 Hz, 1H, C₅H), 3.19 (ddd, *J* = 11.2, 3.7, 2.6 Hz, 1H, C₈H), 3.07 (td, *J* = 8.9, 2.5 Hz, 1H, C₄H), 2.36 (dd, *J* = 13.1, 2.4 Hz, 1H, C₇HH), 2.27 – 2.12 (m, 2H, C₇HH, C₉OH), 1.86 – 1.73 (m, 1H, C₃HH), 1.62 – 1.20 (m, 3H, C₂HH, C₃HH), 1.15 (d, *J* = 6.5 Hz, 3H, C₁₀HHH), 1.00 – 0.79 (m, 12H, C₁HHH, C₁₃HHH), 0.07 (s, 3H, C₁₁HHH), 0.04 (s, 3H, C_{11'}HHH). **¹³C NMR** (75 MHz, CDCl₃) δ 146.77 (C₆), 106.88 (C₁₄), 83.13,

81.69 (C₄, C₈), 74.81 (C₅), 69.24 (C₉), 34.83, 34.80 (C₇, C₃), 26.05 (C₁₃), 18.85 (C₁₂), 18.40 (C₂), 18.20 (C₁₀), 14.27 (C₁), -4.10, -4.63 (C₁₁, C_{11'}). **IR** (neat, cm⁻¹) 3500, 2955, 2928, 2912, 2899, 1462, 1252, 1112, 1067. **MS** (p ESI) *m/z* (%): 337.21 (100), 183.14 (35). **HRMS**, *m/z*: calculated for C₁₇H₃₄O₃SiNa [M + 23]: 337.2169. Found: 337.2169.

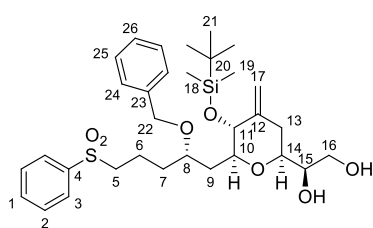
Experimental

10.2.2. Cupration

(*R*)-1-((2*S*,5*R*,6*S*)-6-((*S*)-2-(benzyloxy)-5-(phenylsulfonyl)pentyl)-5-((tert-butyldimethylsilyl)oxy)-4-methylenetetrahydro-2*H*-pyran-2-yl)ethane-1,2-diol



A 50 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with tetrahydropyran **4.99** (318 mg, 0.0005 mol, 1 eq.), AcOH (12 mL) and H₂O (1 mL). Resulting mixture was left stirring at room temperature for 2 days. The crude reaction mixture was then treated with DCM (20 mL) and a saturated aqueous solution of NaHCO₃ (20 mL). After phase separation, the aqueous layer was extracted with DCM (3 x 20 mL). Combined organic fractions were dried over MgSO₄, concentrated under reduced pressure and resulting residue was purified by flash column chromatography on silica gel (PE/AcOEt 2:3) to afford diol **4.100** as a colorless oil (230 mg, 81%).

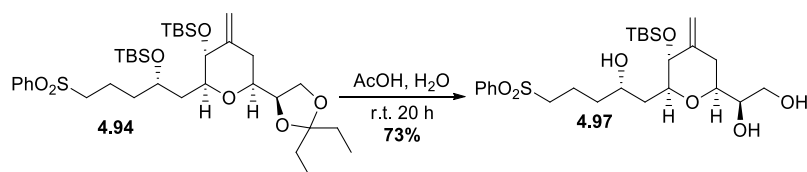


¹H NMR (300 MHz, CDCl₃) δ 7.91 – 7.82 (m, 2H, C₃H), 7.69 – 7.61 (m, 1H, C₁H), 7.60 – 7.49 (m, 2H, C₂H), 7.37 – 7.21 (m, 5H, C₂₄H, C₂₅H, C₂₆H), 5.04 (d, *J* = 1.0 Hz, 1H, C₁₇HH), 4.87 (d, *J* = 1.6 Hz, 1H, C₁₇HH), 4.55 (d, *J* =

11.6 Hz, 1H, C₂₂HH), 4.34 (d, *J* = 11.6 Hz, 1H, C₂₂HH), 3.79 – 3.64 (m, 3H, C₁₁H, C₁₆HH), 3.64 – 3.50 (m, 2H, C₈H, C₁₅H), 3.41 – 3.30 (m, 1H, C₁₄H), 3.15 – 3.07 (m, 1H, C₁₀H), 3.03 (dd, *J* = 11.2, 4.4 Hz, 2H, C₅HH), 2.53 (dd, *J* = 13.2, 2.2 Hz, 1H, C₁₃H *eq*), 2.17 (t, *J* = 12.2 Hz, 1H, C₁₃H *ax*), 1.99 (ddd, *J* = 13.9,

8.7, 1.9 Hz, 1H, C₉HH), 1.78 (m, 4H, C₇HH, C₉HH, C₆HH), 1.53 (dt, *J* = 14.0, 7.9 Hz, 1H, C₇HH), 0.93 (s, 9H, C₂₁HHH), 0.08 (s, 3H, C₁₈HHH), 0.04 (s, 3H, C₁₉HHH). ¹³C NMR (75 MHz, CDCl₃) δ 146.18 (C₁₂), 139.31, 138.54 (C₄, C₂₃), 133.89 (C₁), 129.42 (C₂), 128.56, 128.13, 128.05, 127.78 (C₃, C₂₄, C₂₅, C₂₆), 107.65 (C₁₇), 80.60 (C₁₀), 79.48 (C₁₄), 75.31 (C₈), 74.48 (C₁₁), 73.75 (C₁₅), 70.84 (C₂₂), 63.04 (C₁₆), 56.05 (C₅), 37.37 (C₁₃), 36.28 (C₉), 32.55 (C₇), 26.10 (C₂₁), 19.31 (C₆), 18.22 (C₂₀), -4.29 (C₁₈), -4.61 (C₁₉). IR (neat, cm⁻¹) 3500, 2955, 2928, 2856, 1446, 1306, 1252, 1144, 1107, 1086. MSMS (p APCI), *m/z* (%): 261.15 (45), 229.05 (23), 211.04 (38), 183.12 (21), 143.09 (16), 91.06 (100). HRMS, *m/z*: calculated for C₃₂H₄₉O₇SSi [M + 1]: 605.2963. Found: 605.2977.

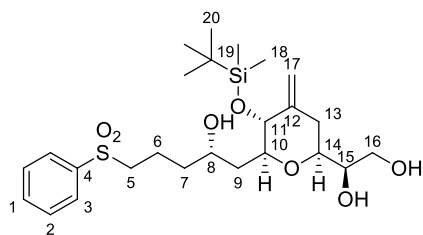
(R)-1-((2S,5R,6S)-5-((tert-butyldimethylsilyl)oxy)-6-((S)-2-hydroxy-5-(phenylsulfonyl)pentyl)-4-methylenetetrahydro-2H-pyran-2-yl)ethane-1,2-diol



A 25 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with tetrahydropyran **4.94** (91 mg, 0.2 mmol, 1 eq.), AcOH (3 mL) and H₂O (0.5 mL). Resulting mixture was left stirring at room temperature for 20 hours. The crude reaction mixture was then treated with DCM (20 mL) and a saturated aqueous solution of NaHCO₃ (20 mL). After phase separation, the aqueous layer was extracted with DCM (3 x 20 mL). Combined organic fractions were dried over MgSO₄, concentrated under reduced pressure and resulting residue was purified by flash column

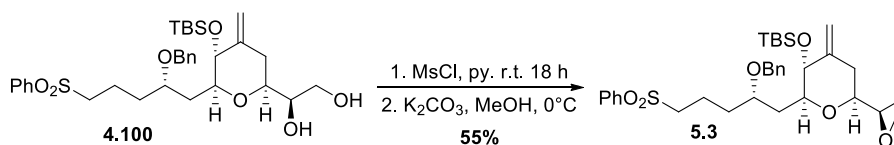
Experimental

chromatography on silica gel (AcOEt) to afford triol **4.97** as a colorless oil (75 mg, 73%). R_f = 0.29 (AcOEt).



(300 MHz, $CDCl_3$) δ 7.95 – 7.88 (m, 1H, C_3H), 7.71 – 7.61 (m, 1H, C_1H), 7.56 (dd, J = 8.1, 6.6 Hz, 2H, C_2H), 5.05 (d, J = 1.5 Hz, 1H, $C_{17}HH$), 4.89 (d, J = 1.5 Hz, 1H, $C_{17}HH$), 3.85 – 3.73 (m, 1H, C_8H), 3.67 (m, 4H, $C_{11}H$, $C_{15}H$, $C_{16}HH$), 3.48 (d, m, 1H, $C_{14}H$), 3.29 (t, J = 8.8, 1.9 Hz, 1H, $C_{10}H$), 3.22 – 3.11 (m, 2H, C_5HH), 2.60 (bs, 1H, C_9OH), 2.50 (dd, J = 13.3, 2.2 Hz, 1H, $C_{13}H-eg$), 2.29 – 2.15 (m, J = 13.3 Hz, 1H, $C_{13}H-ax$), 1.98 (d, J = 14.3 Hz, 1H, C_9HH), 1.91 – 1.77 (m, 2H, C_6HH), 1.58 – 1.38 (m, 2H, C_7HH), 0.92 (s, 9H, $C_{20}HHH$), 0.06 (s, 3H, $C_{18}HHH$), 0.04 (s, 3H, $C_{18'}HHH$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.35 (C_{12}), 139.15 (C_4), 133.71 (C_1), 129.27 (C_2), 128.06 (C_3), 107.84 (C_{17}), 84.59 (C_{10}), 79.64 (C_{14}), 74.05 (C_{11}), 73.33 (C_{15}), 71.19 (C_8), 62.99 (C_{16}), 56.19 (C_5), 39.26 (C_9), 36.53 (C_7), 35.84 (C_{13}), 25.82 (C_{20}), 19.08 (C_6), 18.16 (C_{19}), -4.33, -4.70 (C_{18} , $C_{18'}$). IR (neat, cm^{-1}) 3412, 2951, 2928, 2856, 1462, 1447, 1306, 1292, 1252, 1142, 1086.

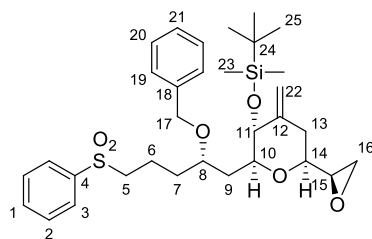
(((3*R*)-2-(2-(benzyloxy)-5-(phenylsulfonyl)pentyl)-4-methylene-6-((*R*)-oxiran-2-yl)tetrahydro-2H-pyran-3-yl)oxy)(tert-butyl)dimethylsilane



A 250 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with diol **4.100** (1.670 g, 2.8 mmol, 1 eq.), MsCl (300 mg, 2.6 mmol, 0.95 eq.) and pyridine (50 mL). Resulting mixture was left stirring at 0°C and after 1 h, allowed to heat up to room temperature.

Stirring was continued for 17 h. At that moment, AcOEt (50 mL) and H₂O (50 mL) were added to the mixture. After separation, the aqueous phase was extracted with AcOEt (3 x 40 mL). Combined organic fractions were dried over MgSO₄ and concentrated under reduced pressure. This crude primary mesylate was transferred without further purification into a 500 mL round-bottom flask containing K₂CO₃ (3.87 g, 28 mmol, 10 eq.) and MeOH (120 mL) at 0°C. Resulting mixture was left stirring at 0°C for 1 h before adding AcOEt (120 mL) and H₂O (120 mL). After separation, the organic phase was extracted with AcOEt (3 x 80 mL). Combined organic fractions were dried over MgSO₄, concentrated under reduced pressure and resulting residue was purified by flash column chromatography on silica gel (PE/AcOEt 5:1) to afford epoxide **5.3** as a colorless oil (910 mg, 55%). R_f=0.25 (PE/AcOEt 4:1).

Major diastereoisomer



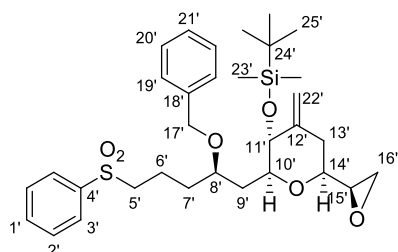
¹H NMR (300 MHz, CDCl₃) δ 7.89 – 7.84 (m, 2H, C₃H), 7.68 – 7.59 (m, 1H, C₁H), 7.59 – 7.50 (m, 2H, C₂H), 7.37 – 7.21 (m, 5H, C₁₉H, C₂₀H, C₂₁H), 5.04 (d, *J* = 1.2 Hz, 1H, C₂₂HH), 4.86 (d, *J* = 1.6 Hz, 1H, C₂₂HH),

4.55 (d, *J* = 11.6 Hz, 1H, C₁₇HH), 4.33 (d, *J* = 11.6 Hz, 1H, C₁₇HH), 3.70 (d, *J* = 8.8 Hz, 1H, C₁₁H), 3.55 (ddd, *J* = 11.5, 8.0, 3.3 Hz, 1H, C₈H), 3.29 - 3.25 (m, 2H, C₁₄H, C₁₀H), 3.06 (ddd, *J* = 13.7, 8.9, 3.3 Hz, 2H, C₅HH), 2.98 (td, *J* = 4.1, 2.7 Hz, 1H, C₁₅H), 2.76 (dd, *J* = 5.0, 4.1 Hz, 1H, C₁₆HH), 2.64 (dd, *J* = 5.1, 2.7 Hz, 1H, C₁₆HH), 2.41 (dd, *J* = 13.1, 2.5 Hz, 1H, C₁₃HH-*eq*), 2.19 (t, *J* = 12.2 Hz, 1H, C₁₃HH-*ax*), 1.98 (ddd, *J* = 14.0, 8.4, 2.0 Hz, 1H, C₉HH), 1.88 – 1.42 (m, 5H, C₆HH, C₇HH, C₉HH), 0.93 (s, 9H, C₂₅HHH), 0.07 (s, 3H, C₂₃HHH), 0.03 (s, 3H, C_{23'}HHH). **¹³C NMR** (75 MHz, CDCl₃) δ 145.77 (C₁₂), 139.24, 138.62 (C₄, C₁₈), 133.69 (C₁), 129.34, 128.48, 128.21, 128.06, 127.73 (C₂, C₃, C₁₉, C₂₀, C₂₁),

Experimental

107.65 (C₂₂), 80.43 (C₁₀), 77.77 (C₁₄), 75.47, 74.33 (C₈, C₁₁), 70.72 (C₁₇), 56.26 (C₅), 53.28 (C₁₅), 45.04 (C₁₆), 37.19 (C₁₃), 36.16 (C₉), 32.79 (C₇), 26.01 (C₂₅), 19.39 (C₆), 18.27 (C₂₄), -4.23, -4.54 (C₂₃).

Minor diastereoisomer



¹H NMR (300 MHz, CDCl₃) δ 7.91 – 7.84

(m, 2H, C_{3'}H), 7.68 – 7.60 (m, 1H, C_{1'}H),

7.59 – 7.50 (m, 2H, C_{2'}H), 7.36 – 7.20 (m,

5H, C_{19'}H, C_{20'}H, C_{21'}H), 5.04 (s, 2H,

C_{22'}HH), 4.85 (s, 2H, C_{22'}HH), 4.44 (d, J =

11.6 Hz, 1H, C_{17'}HH), 4.39 (d, J = 11.6 Hz, 1H, C_{17'}HH), 3.73 – 3.52 (m, 2H,

C_{8'}H, C_{11'}H), 3.24 – 3.16 (m, 1H, C_{14'}H), 3.14 – 3.00 (m, 3H, C_{10'}H, C_{5'}HH), 2.93

(td, J = 4.1, 2.7 Hz, 1H, C_{15'}H), 2.75 (dd, J = 9.1, 4.6 Hz, 1H, C_{16'}HH), 2.59 (dd,

J = 5.1, 2.6 Hz, 1H, C_{16'}HH), 2.44 – 2.36 (m, 1H, C_{13'}HH), 2.25 – 2.14 (m, 1H,

C_{13'}HH), 2.16 – 2.06 (m, 1H, C_{9'}HH), 1.88 – 1.31 (m, 5H, C_{6'}HH, C_{7'}HH, C_{9'}HH),

0.94 (s, 9H, C_{25'}HHH), 0.05 (s, 3H, C_{23'}HHH), 0.03 (s, 3H, C_{23'}HHH). ¹³C NMR

(75 MHz, CDCl₃) δ 145.85 (C_{12'}), 139.30, 138.76 (C_{4'}, C_{18'}), 133.70 (C_{1'}),

129.37, 128.49, 128.22, 127.94, 127.71 (C_{2'}, C_{3'}, C_{19'}, C_{20'}, C_{21'}), 107.57 (C_{22'}),

80.46, (C_{10'}), 77.71 (C_{14'}), 74.93, 74.52, (C_{8'}, C_{11'}), 71.43 (C_{17'}), 56.43 (C_{5'}),

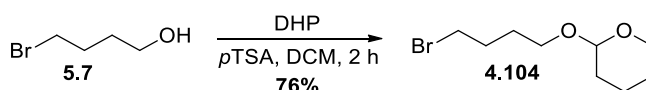
53.31 (C_{15'}), 45.01 (C_{16'}), 37.76 (C_{13'}), 33.51 (C_{9'}), 32.82 (C_{7'}), 26.04 (C_{25'}),

18.86 (C_{6'}), 18.32 (C_{24'}), -4.20, -4.51 (C_{23'}).

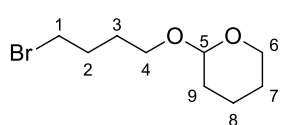
Following analyses were carried out on the 1: 1 mixture of the two diastereoisomers:

IR (neat, cm^{-1}) 2991, 2926, 2851, 1447, 1306, 1252, 1144, 1107, 1086, 1070, 1028. **MSMS** (p ESI), m/z (%): 455.18 (10), 437.17 (15), 419.16 (12), 347.13 (30), 329.12 (13), 267.16 (16), 243.13 (21), 229.05 (56), 211.04 (34), 183.04 (24), 143.04 (25). **HRMS**, m/z : calculated for $\text{C}_{32}\text{H}_{47}\text{O}_6\text{Si}$ [$M + 1$]: 587.2857. Found: 587.2867.

2-(4-bromobutoxy)tetrahydro-2H-pyran

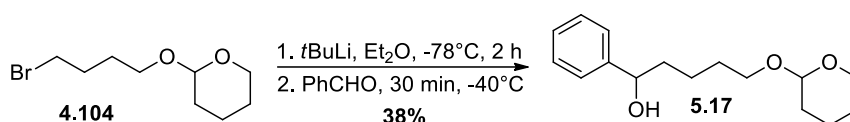


A 250 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with alcohol **5.7** (8.7 g, 57 mmol, 1 eq.), DHP (6.22 g, 74 mmol, 2.6 eq.), DCM (110 mL) and *p*TSA monohydrate (1 mol%). Resulting mixture was left stirring at room temperature for 2 h. A saturated aqueous solution of NaHCO_3 (60 mL) was then added to the mixture and after separation of the phases, the aqueous layer was extracted with DCM (3 x 60 mL). Combined organic fractions were dried over MgSO_4 , concentrated under reduced pressure and purified by flash column chromatography on silica gel (PE/AcOEt 10:1) to afford protected alcohol **4.104** as a yellow oil (10.22 g, 76%).

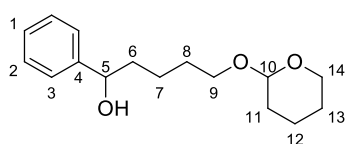
 **^1H NMR** (300 MHz, CDCl_3) δ 4.57 (t, $J = 3.4$ Hz, 1H, C_5H), 3.90 – 3.71 (m, 2H), 3.56 – 3.35 (m, 4H), 2.03 – 1.91 (m, 2H), 1.86 – 1.65 (m, 4H), 1.64 – 1.45 (m, 4H). **^{13}C NMR** (75 MHz, CDCl_3) δ 99.00 (C_5), 66.61, 62.51 (C_4 , C_6), 33.91, 30.84, 29.96, 28.51, 25.58, 19.75 (C_1 , C_2 , C_3 , C_7 , C_8 , C_9).

Experimental

1-phenyl-5-((tetrahydro-2H-pyran-2-yl)oxy)pentan-1-ol

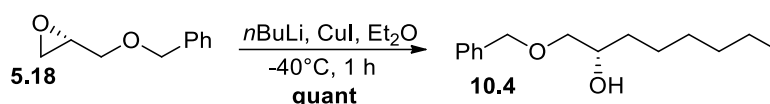


A 25 mL round-bottom flask (25 mL) equipped with a Teflon-coated magnetic stirrer was charged with bromide **4.104** (0.1 g, 0.42 mmol, 1 eq.) and Et₂O (1 mL). Resulting mixture was left stirring and cooled down to -78°C. At that moment, *t*-BuLi (1.7M in pentane, 0.52 mL, 0.886 mmol, 2.1 eq.) was added slowly over a period of 3 minutes. Resulting mixture was left stirring for another 2 hours, then allowed to heat up to -40°C prior to addition of benzaldehyde (0.42 mmol, 44 mg, 1 eq.) dissolved in Et₂O (2 mL). The solution was left stirring for 30 minutes at -40°C then, a saturated aqueous solution of NH₄Cl (60 mL) was added to the mixture and after separation of the phases, the aqueous layer was extracted with DCM (3 x 60 mL). Combined organic fractions were dried over MgSO₄, concentrated under reduced pressure and purified by flash column chromatography on silica gel (PE/AcOEt 1:1) to afford alcohol **5.17** as colorless oil and as a mixture of two diastereoisomers (42 mg, 38%). *R*_f = 0.20 (PE/AcOEt 4:1).

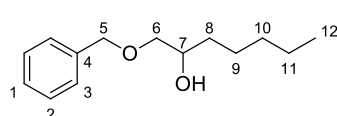


¹H NMR (300 MHz, CDCl₃) δ 7.41 – 7.26 (m, 5H, C₁H, C₂H, C₃H), 4.72 – 4.65 (m, 1H, C₅H), 4.55 (m, 1H, C₁₀H), 3.89 – 3.78 (m, 1H, C₁₄HH or C₉HH), 3.73 (dt, *J* = 9.6, 6.6 Hz, 1H, C₁₄HH or C₉HH), 3.54 – 3.43 (m, 1H, C₉HH), 3.37 (dtd, *J* = 9.6, 6.4, 1.1 Hz, 1H, C₁₄HH), 1.93 – 1.31 (m, 14H, C₆HH, C₇HH, C₈HH, C₁₁HH, C₁₂HH, C₁₃HH). ¹³C NMR (75 MHz, CDCl₃) δ 144.96 (C₄), 128.71, 128.57, 127.80, 127.64, 127.12, 126.00 (C₁, C_{1'}, C₂, C_{2'}, C₃, C_{3'}), 99.02 (C₁₀), 74.67 (C₅), 67.55, 62.50 (C₁₄, C₁₉), 39.01, 30.87, 29.66, 25.61, 22.72, 19.81 (C₆, C₇, C₈, C₁₁, C₁₂, C₁₃).

1-(benzyloxy)octan-2-ol



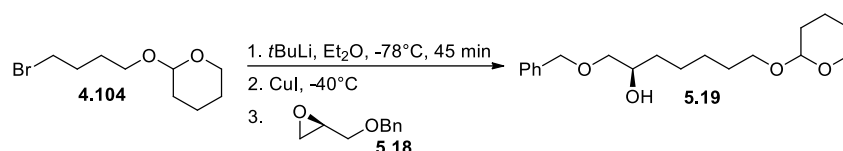
A 50 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with CuI (0.580 g, 3.05 mmol, 5 eq.) and Et₂O (16 mL). The heterogeneous mixture was cooled down to -50°C and *n*BuLi (2.5M in pentane, 2.4 mL, 6.1 mmol, 10 eq.) was added dropwise. The solution turned black and was allowed to heat up to -30°C for 10 minutes, before being cooled down to -40°C again. At that temperature, epoxide **5.18** (100 mg, 0.61 mmol, 1 eq.) in Et₂O (0.5 mL) was added dropwise and the mixture was left stirring for 1h30, prior to dilution with a saturated aqueous solution of NH₄Cl (20 mL). The layers were separated and the aqueous phase was extracted with AcOEt (30 mL). Combined organic fractions were then dried over MgSO₄ and concentrated under reduced pressure. Further purification was not necessary (136 mg, quant.). *R*_f = 0.74 (PE/AcOEt 1:1).



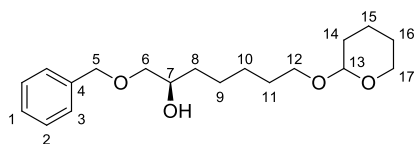
¹H NMR (300 MHz, CDCl₃) δ 7.40 – 7.29 (m, 5H, C₁H, C₂H, C₃H), 4.56 (s, 2H, C₅HH), 3.86 – 3.76 (m, 1H, C₇H), 3.51 (dd, *J* = 9.4, 2.9 Hz, 1H, C₆HH), 3.32 (dd, *J* = 9.3, 8.0 Hz, 1H, C₆HH), 1.93 (*bs*, 1H, C₇OH), 1.50 – 1.15 (m, 8H, C₈HH, C₉HH, C₁₀HH, C₁₁HH), 0.88 (t, *J* = 6.7 Hz, 3H, C₁₂HHH). **¹³C NMR** (75 MHz, CDCl₃) δ 138.16 (C₄), 128.61, 127.93, 127.88 (C₁, C₂, C₃), 74.80, 73.48, 70.60 (C₅, C₆, C₇), 33.24 (C₈), 32.01 (C₉), 25.34 (C₁₀), 22.72 (C₁₁), 14.18 (C₁₂).

Experimental

(2R)-1-(benzyloxy)-7-((tetrahydro-2H-pyran-2-yl)oxy)heptan-2-ol



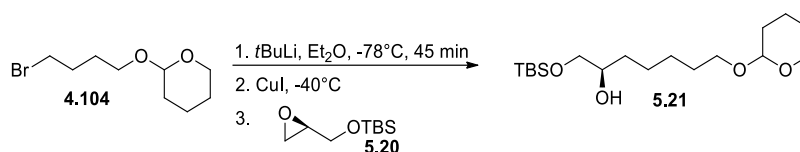
A 25 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with $t\text{BuLi}$ (1.7M in pentane, 1.6 mL, 2.7 mmol, 21 eq.) and Et_2O (2.5 mL) at -78°C and was left stirring for 10 minutes at that temperature. Neat bromide **4.104** (300 mg, 1.3 mmol, 10 eq.) was then added to the mixture at 0°C and stirred for another 45 minutes. A white precipitate was observed. A second 25 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was then charged with CuI (0.124 g, 0.7 mmol, 5 eq.) and Et_2O (4 mL). The heterogeneous mixture was cooled down to -50°C and the freshly prepared lithiated species was transferred to the latter heterogeneous mixture. Resulting mixture turned black and was allowed to heat up to -30°C for 10 minutes, before being again cooled down to -40°C . At that temperature, epoxide **5.18** (21 mg, 0.13 mmol, 1 eq.) in Et_2O (0.5 mL) was added dropwise to the mixture, which was left stirring for 30 minutes. At that moment, a saturated aqueous solution of NH_4Cl (10 mL) was added. The layers were separated and the aqueous phase was extracted with AcOEt (30 mL). Combined organic fractions were dried over MgSO_4 , concentrated under reduced pressure and resulting residue was purified by flash column chromatography on silica gel (PE/ AcOEt 3:1 to AcOEt 100%) to afford alcohol **5.19** as a yellow oil (31 mg, 74%). R_f = 0.42 (PE/ AcOEt 1:1).



$^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.40 – 7.27 (m, 5H, C_1H , C_2H , C_3H), 4.58 – 4.54 (m, 3H, C_5HH , C_{13}H), 3.91 – 3.77 (m, 2H, C_7H , C_{17}HH or C_{12}HH), 3.73 (dt, J = 9.6,

6.8 Hz, 1H, C₁₇HH or C₁₂HH), 3.50 (dd, $J = 9.4, 3.1$ Hz, 1H, C₆HH), 3.44 – 3.55 (m, 1H, C₁₇HH or C₁₂HH) 3.38 (dt, $J = 9.6, 6.5$ Hz, 1H, C₁₇HH or C₁₂HH), 3.32 (dd, $J = 9.4, 7.9$ Hz, 1H, C₆HH), 2.34 (*bs*, 1H, C₇OH), 1.90 – 1.21 (m, 14H, C₈HH, C₉HH, C₁₀HH, C₁₁HH, C₁₃HH, C₁₄HH, C₁₅HH). ¹³C NMR (75 MHz, CDCl₃) δ 138.13 (C₄), 128.60, 127.93, 127.88 (C₁, C₂, C₃), 99.01 (C₁₃), 74.76, 73.48, 70.48, 67.67, 62.51 (C₅, C₆, C₇, C₁₂, C₁₇), 33.20, 30.91, 29.79, 26.42, 25.62, 25.49, 19.84 (C₈, C₉, C₁₀, C₁₁, C₁₄, C₁₅, C₁₆).

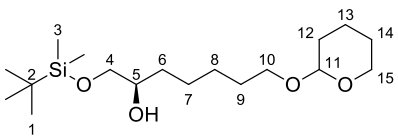
(2R)-1-((tert-butyldimethylsilyl)oxy)-7-((tetrahydro-2H-pyran-2-yl)oxy)heptan-2-ol



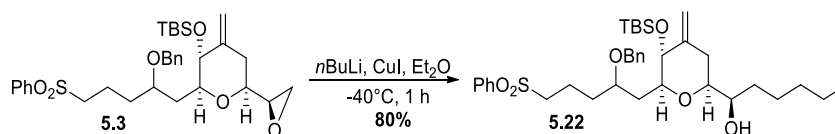
A 500 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with *t*BuLi (1.7M in pentane, 51 mL, 87 mmol, 8.2 eq.) and Et₂O (85 mL) at -78°C and was left stirring for 10 minutes at that temperature. Neat bromide **4.104** (10.05 g, 42 mmol, 4 eq.) was then added to the mixture at the same temperature and stirring was continued for 45 minutes. A white precipitate was forming. A second 1 L round-bottom flask was charged with CuI (4.04 g, 21 mmol, 2 eq.) and Et₂O (120 mL). The heterogeneous mixture was cooled down to -50°C and the freshly prepared lithiated species was transferred to the solution. The solution turned black and was allowed to heat up to -30°C for 10 minutes, prior to being cooled down to -40°C again. At that temperature, the epoxide (2.0 g, 11 mmol, 1 eq.) in Et₂O (5 mL) was added dropwise, the mixture was left stirring for 30 minutes, then treated with a saturated aqueous solution of NH₄Cl (100 mL). The layers were separated and the aqueous phase was extracted with AcOEt (80 mL). Combined organic fractions were dried over MgSO₄ and concentrated under reduced pressure. Resulting residue was purified by

Experimental

flash column chromatography on silica gel (PE/AcOEt 3:1 to AcOEt 100%) to afford alcohol **5.21** as a yellow oil (710 mg, 20%). R_f = 0.42 (PE/AcOEt 1:1, Vanillin).

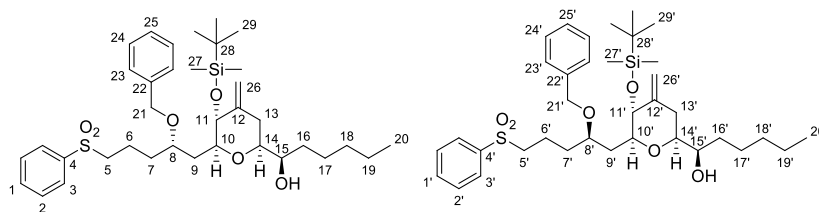
 ^1H NMR (300 MHz, CDCl_3) δ 4.56 (t, J = 3.5 Hz, 1H, C_{11}H), 3.93 – 3.32 (m, 7H, C_4HH , C_5H , C_{10}HH , C_{15}HH), 1.91 – 1.12 (m, 14H, C_6HH , C_7HH , C_8HH , C_9HH , C_{12}HH , C_{13}HH , C_{14}HH), 0.89 (s, 9H, C_1HHH), 0.06 (s, 6H, C_3HHH). ^{13}C NMR (75 MHz, CDCl_3) δ 98.86 (C_{11}), 71.75, 67.55, 67.27, 62.37 (C_4 , C_5 , C_{10} , C_{15}), 32.74, 30.78, 29.67, 26.36, 25.49, 25.45, 19.71 (C_6 , C_7 , C_8 , C_9 , C_{12} , C_{13} , C_{14}), 25.89 (C_1), 18.29 (C_2), -5.33, -5.39 (C_3 , C_3'). IR (neat, cm^{-1}) 3500, 2926, 2897, 2856, 1464, 1362, 1252, 1119, 1099, 1078, 1022. MSMS (p ESI) m/z (%): 245.19 (100), 113.10 (75), 95.09 (83). HRMS, m/z : calculated for $\text{C}_{18}\text{H}_{39}\text{O}_4\text{Si}$ [$M + 1$]: 347.2612. Found: 347.2615.

(1*R*)-1-((5*R*)-6-(2-(benzyloxy)-5-(phenylsulfonyl)pentyl)-5-((tert-butyldimethylsilyl)oxy)-4-methylenetetrahydro-2H-pyran-2-yl)hexan-1-ol



A 250 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with CuI (1.28 g, 6.7 mmol, 5 eq.) and Et_2O (35 mL). The heterogeneous mixture was cooled down to -50°C and $n\text{BuLi}$ (2.5M in pentane, 5.4 mL, 13.5 mmol, 10 eq.) was added dropwise via a syringe. The solution turned black and was allowed to heat up to -30°C for 10 minutes, before being again cooled down to -40°C . At that temperature, epoxide **5.3** (0.79 g, 0.097 mmol, 1 eq.) in Et_2O (5 mL) was added dropwise, the mixture

was stirred for 30 minutes, then diluted in a saturated aqueous solution of NH_4Cl (40 mL). The layers were separated and the aqueous phase was extracted with AcOEt (3 x 30 mL). Combined organic fractions were dried over MgSO_4 , concentrated under reduced pressure and resulting residue was purified by flash column chromatography on silica gel (PE/AcOEt 3:1 to AcOEt 100%) to afford alcohol **5.22** as a one to one mixture of two separable diastereoisomers (700 mg, 83%). R_f = 0.31; 0.29 (PE/AcOEt 4:1).

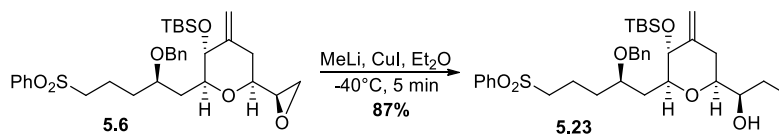


^1H NMR (300 MHz, CDCl_3) δ 7.88 (ddd, J = 6.2, 3.6, 1.3 Hz, 4H, C_3H , $\text{C}_3'\text{H}$), 7.64 (m, 2H, C_1H , $\text{C}_1'\text{H}$), 7.60 – 7.49 (m, 4H, C_2H , $\text{C}_2'\text{H}$), 7.35 – 7.18 (m, 10H, C_{23}H , $\text{C}_{23}'\text{H}$, C_{24}H , $\text{C}_{24}'\text{H}$, C_{25}H , $\text{C}_{25}'\text{H}$), 5.03 (s, 2H, C_{26}HH , $\text{C}_{26}'\text{HH}$), 4.85 (s, 2H, C_{26}HH , $\text{C}_{26}'\text{HH}$), 4.54 (d, J = 11.6 Hz, 1H, C_{21}HH), 4.42 (s, 2H, C_{21}HH), 4.33 (d, J = 11.6 Hz, 1H, C_{21}HH), 3.71 – 3.48 (m, 6H, C_8H , $\text{C}_8'\text{H}$, C_{11}H , $\text{C}_{11}'\text{H}$, C_{15}H , $\text{C}_{15}'\text{H}$), 3.31 – 2.99 (m, 8H, C_5HH , $\text{C}_5'\text{HH}$, C_{10}H , $\text{C}_{10}'\text{H}$, C_{14}H , $\text{C}_{14}'\text{H}$), 2.38 – 2.20 (m, 3H, C_9HH , C_{13}HH , $\text{C}_{13}'\text{HH}$), 2.12 (m, 2H, C_{13}HH , $\text{C}_{13}'\text{HH}$), 1.97 – 1.27 (m, 19H, C_9HH , $\text{C}_9'\text{HH}$, C_{16}HH , $\text{C}_{16}'\text{HH}$, C_{17}HH , $\text{C}_{17}'\text{HH}$, C_{18}HH , $\text{C}_{18}'\text{HH}$, C_{19}HH , $\text{C}_{19}'\text{HH}$), 1.02 – 0.83 (m, 24H, C_{20}HHH , $\text{C}_{20}'\text{HHH}$, C_{29}HHH , $\text{C}_{29}'\text{HHH}$), 0.12 – 0.01 (m, 12H, C_{27}HHH , $\text{C}_{27}'\text{HHH}$). ^{13}C NMR (75 MHz, CDCl_3) δ 146.82, 146.71 (C_{12} , C_{12}'), 139.28, 138.71, 138.58 (C_4 , C_4' , C_{22} , C_{22}'), 133.71, 129.38, 129.35, 128.52, 128.47, 128.20, 128.01, 127.92, 127.78, 127.70 (C_1 , C_1' , C_2 , C_2' , C_3 , C_3' , C_{23} , C_{23}' , C_{24} , C_{24}' , C_{25} , C_{25}'), 107.29, 107.15 (C_{26} , C_{26}'), 81.14, 81.01, 80.41, 80.37 (C_{10} , C_{10}' , C_{14} , C_{14}'), 75.51, 74.90, 74.72, 74.57 (C_8 , C_8' , C_{11} , C_{11}'), 73.19, 73.15 (C_{15} , C_{15}'), 71.29, 70.76 (C_{21} , C_{21}'), 56.43, 56.34 (C_5 , C_5'), 37.81, 36.34, 34.41, 34.28, 33.44, 32.77, 32.45, 32.39, 32.02, 26.04, 25.78, 25.72, 22.76,

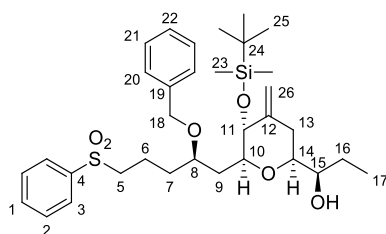
Experimental

19.34, 18.80 (C₆, C_{6'}, C₇, C_{7'}, C₉, C_{9'}, C₁₃, C_{13'}, C₁₆, C_{16'}, C₁₇, C_{17'}, C₁₈, C₁₈, C₁₉, C_{19'}, C₂₉, C_{29'}), 18.33, 18.29 (C₂₈, C_{28'}), 14.34, 14.20 (C₂₀, C_{20'}), -4.20, -4.51 (C₂₇, C_{27'}). IR (neat, cm⁻¹) 3500, 2955, 2932, 2856, 1447, 1379, 1305, 1252, 1148, 1111, 1088, 1070, 1026. MSMS (p ESI), m/z (%): 387.20 (12), 229.05 (99), 211.04 (63), 183.05 (30), 143.01 (18), 99.08 (13), 91.05 (100). HRMS, m/z: calculated for C₃₆H₅₇O₆SSi [M + 1]: 645.3640. Found: 645.3628.

(R)-1-((2S,5R,6S)-6-((R)-2-(benzyloxy)-5-(phenylsulfonyl)pentyl)-5-((tert-butylidimethylsilyl)oxy)-4-methylenetetrahydro-2H-pyran-2-yl)propan-1-ol



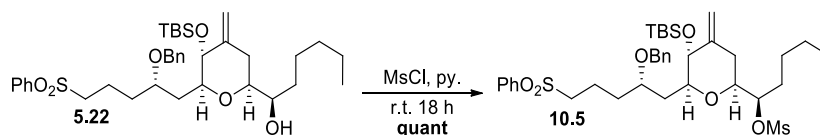
A 250 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with Cul (0.650 g, 3.4 mmol, 5 eq.) and Et₂O (75 mL). The heterogeneous mixture was cooled down to -40°C and MeLi (1.6 M in Et₂O, 4.2 mL, 6.8 mmol, 10 eq.) was added dropwise via a syringe. At that temperature, epoxide **5.6** (0.40 g, 0.68 mmol, 1 eq.) in Et₂O (5 mL) was added dropwise, the mixture was stirred for 5 min, then diluted in a saturated aqueous solution of NH₄Cl (40 mL). The layers were separated and the aqueous phase was extracted with AcOEt (3 x 30 mL). Combined organic fractions were dried over MgSO₄, concentrated under reduced pressure and resulting residue was purified by flash column chromatography on silica gel (PE/AcOEt 4:1 to AcOEt 100%) to afford alcohol **5.23** (356 mg, 87%). R_f = 0.20 (PE/AcOEt 4:1).



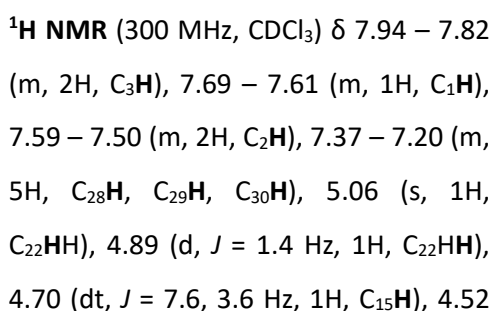
^1H NMR (300 MHz, CDCl_3) δ 7.88 (t, J = 6.1 Hz, 2H, C_3H), 7.69 – 7.46 (m, 3H, C_1H , C_2H), 7.37 – 7.19 (m, 5H, C_{20}H , C_{21}H , C_{22}H), 5.03 (s, 1H, C_{26}HH), 4.84 (s, 1H, C_{26}HH), 4.42 (s, 2H, C_{18}HH), 3.72 – 3.44

(m, 3H, C_8H , C_{11}H , C_{15}H), 3.30 – 2.98 (m, 4H, C_5HH , C_{10}H , C_{14}H), 2.38 – 1.29 (m, 10H, C_6HH , C_7HH , C_9HH , C_{13}HH , C_{16}HH), 1.03 – 0.86 (m, 12H, C_{25}HHH , C_{17}HHH), 0.05 (s, 3H, C_{23}HHH), 0.03 (s, 3H, $\text{C}_{23'}\text{HHH}$). ^{13}C NMR (75 MHz, CDCl_3) δ 146.64 (C_{12}), 139.10, 138.53 (C_4 , C_{19}), 133.61, 129.26, 128.34, 128.06, 127.81, 127.58 (C_1 , C_2 , C_3 , C_{20} , C_{21} , C_{22}), 107.04 (C_{26}), 80.56, 80.25 (C_{10} , C_{14}), 75.34, 74.77, 74.44 (C_8 , C_{11} , C_{15}), 71.15 (C_{18}), 56.29 (C_5), 36.19, 34.21 (C_9 , C_{13}), 25.90 (C_{25}), 25.28, 19.22, 18.67, 18.19 (C_6 , C_7 , C_{16} , C_{24}), 10.33 (C_{17}), -4.33, -4.65 (C_{23} , $\text{C}_{23'}$). IR (neat, cm^{-1}) 3500, 2957, 2930, 2856, 1447, 1306, 1252, 1143, 1111, 1088. MS (p ESI), m/z (%): 625.30 (61), 603.32 (56), 471.22 (100). HRMS, m/z : calculated for ($\text{C}_{33}\text{H}_{51}\text{O}_6\text{SSi}$) [$\text{M} + 1$]: 603.3170. Found: 603.3164.

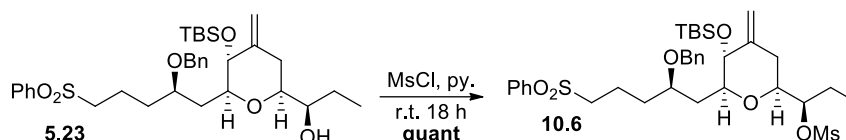
(*R*)-1-((2*S*,5*R*,6*S*)-6-((*S*)-2-(benzyloxy)-5-(phenylsulfonyl)pentyl)-5-((tert-butyldimethylsilyl)oxy)-4-methylenetetrahydro-2H-pyran-2-yl)hexyl methanesulfonate



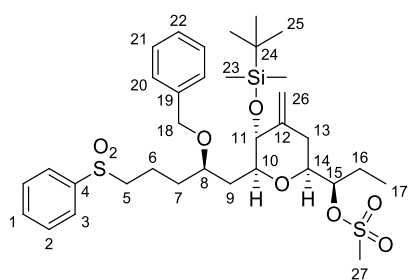
A 25 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with alcohol **5.22** (50 mg, 0.8 mmol, 1 eq.), MsCl (10 mg, 0.85 mmol, 1.1 eq.) and pyridine (3 mL). Resulting mixture was left stirring at



(*R*)-1-((2*S*,5*R*,6*S*)-6-((*R*)-2-(benzyloxy)-5-(phenylsulfonyl)pentyl)-5-((tert-butylidimethylsilyl)oxy)-4-methylenetetrahydro-2*H*-pyran-2-yl)propyl methanesulfonate



A 25 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with alcohol **5.23** (410 mg, 0.68 mmol, 1 eq.), MsCl (85 mg, 0.75 mmol, 1.1 eq.) and pyridine (5 mL). Resulting mixture was left stirring at room temperature for 18 h. After complete conversion, the mixture was treated with a saturated aqueous solution of CuSO₄ (10 mL) and DCM (10 mL). After separation of the phases, the aqueous layer was extracted with DCM (10 mL). Combined organic fractions were dried over MgSO₄, concentrated under reduced pressure and purified by flash column chromatography on silica gel (PE/AcOEt 4:1) to yield tetrahydropyran **10.6** (46 mg, quant). *R*_f = 0.15 (PE/AcOEt 4:1).



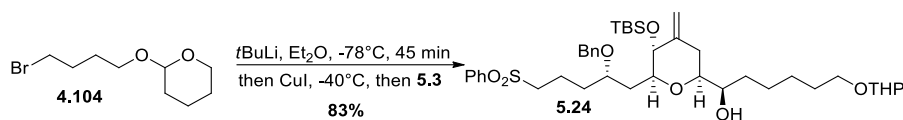
¹H NMR (300 MHz, CDCl₃) δ 7.93 – 7.84 (m, 2H, C₃H), 7.73 – 7.60 (m, 1H, C₁H), 7.61 – 7.47 (m, 2H, C₂H), 7.41 – 7.19 (m, 5H, C₂₀H, C₂₁H, C₂₂H), 5.07 (s, 1H, C₂₆HH), 4.87 (s, 1H, C₂₆HH), 4.54 – 4.46 (m, 1H, C₁₅H), 4.45 (d, *J* = 11.5 Hz,

1H, C₁₈HH), 4.40 (d, *J* = 11.8 Hz, 1H, C₁₈HH), 3.69 – 3.50 (m, 2H, C₈H, C₁₁H), 3.33 – 2.96 (m, 7H, C₅HH, C₁₀H, C₁₄H, C₂₇HHH), 2.40 (t, *J* = 12.5 Hz, 1H, C₁₃HH-ax), 2.30 – 1.43 (m, 9H, C₆HH, C₇HH, C₉HH, C₁₃HH, C₁₆HH), 1.00 (t, *J* = 7.4 Hz, 3H, C₁₇HHH), 0.95 (s, 9H, C₂₅HHH), 0.06 (s, 3H, C₂₃HHH), 0.04 (s, 3H, C₂₃HHH). ¹³C NMR (75 MHz, CDCl₃) δ 145.51 (C₁₂), 139.20, 138.58 (C₄, C₁₉),

Experimental

133.66, 129.34, 128.41, 128.11, 127.94, 127.66 (C₁, C₂, C₃, C₂₀, C₂₁, C₂₂), 107.99 (C₂₆), 85.48 (C₁₅), 80.42, 78.46 (C₁₀, C₁₄), 74.52, 74.41, 71.09 (C₈, C₁₁, C₁₈), 56.14 (C₅), 38.83 (C₂₇), 37.76 (C₉), 35.04 (C₁₃), 33.11, 25.94, 24.23, 18.61, 18.23 (C₆, C₇, C₁₆, C₂₄, C₂₅), 9.95 (C₁₇), -4.27, -4.58 (C₂₃, C_{23'}). **IR** (neat, cm⁻¹) 2953, 2928, 2856, 1460, 1447, 1348, 1306, 1252, 1175, 1146, 1113, 1086. **MSMS** (p ESI), m/z (%): 441.14 (26), 345.15 (100), 211.04 (40), 91.05 (46). **HRMS**, m/z: calculated for (C₃₄H₅₃O₈S₂Si) [M + 1]: 681.2946. Found: 681.29156.

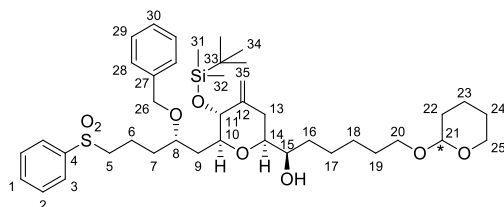
(1*R*)-1-((2*S*,5*R*,6*S*)-6-((*S*)-2-(benzyloxy)-5-(phenylsulfonyl)pentyl)-5-((tert-butyltrimethylsilyl)oxy)-4-methylenetetrahydro-2*H*-pyran-2-yl)-6-((tetrahydro-2*H*-pyran-2-yl)oxy)hexan-1-ol



A 25 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with *t*BuLi (1.7M in pentane, 1.2 mL, 2.04 mmol, 21 eq.) and Et₂O (2 mL) and was then left stirring at -78°C for 10 minutes. Neat bromide **4.104** (265 mg, 0.97 mmol, 10 eq.) was then added to the mixture at the same temperature and the solution was stirred for another 45 minutes. A white precipitate was forming. A second 25 mL-round bottom flask was charged with CuI (0.092 g, 0.485 mmol, 5 eq.) and Et₂O (3 mL). The heterogeneous mixture was cooled down to -50°C and the freshly prepared alkyl lithium was added dropwise via a syringe. The solution turned black and was allowed to heat up to -30°C for 10 minutes, prior to being cooled down again to -40°C. At that temperature, epoxide **5.3** (57 mg, 0.097 mmol, 1 eq.) in Et₂O (0.5 mL) was added dropwise, the mixture was stirred for 30 min, then treated with a saturated aqueous solution of NH₄Cl (10 mL). The layers were separated and the aqueous phase was extracted with AcOEt (30

mL). Combined organic fractions were dried over MgSO_4 , concentrated under reduced pressure and resulting residue was purified by flash column chromatography on silica gel (PE/AcOEt 3:1 to AcOEt 100%) to afford alcohol **5.24** as a one to one mixture of two separable diastereoisomers (60 mg, 83%). R_{f1} = 0.35 (PE/AcOEt 1:1, Vanillin, purple). R_{f2} = 0.70 (PE/AcOEt 1:1, Vanillin, brown).

Diastereoisomer 1: R_f = 0.70



^1H NMR (300 MHz, CDCl_3) δ

7.92 – 7.84 (m, 2H, C_3H), 7.70 –

7.61 (m, 1H, C_1H), 7.54 (dd, J =

8.1, 6.8 Hz, 2H, C_2H), 7.41 –

7.20 (m, 5H, C_{28}H , C_{29}H , C_{30}H),

5.02 (s, 1H, C_{35}HH), 4.85 (s, 1H, C_{35}HH), 4.60 – 4.51 (m, 2H, C_{21}H , C_{26}HH),

4.33 (d, J = 11.6 Hz, 1H, C_{26}HH), 3.92 – 3.81 (m, 1H, C_{25}HH or C_{20}HH), 3.75

(dt, J = 9.1, 6.7 Hz, 1H, C_{20}HH or C_{25}HH), 3.65 (d, J = 8.6 Hz, 2H, C_{11}H , C_{15}H),

3.58 – 3.45 (m, 1H, C_{20}HH or C_{25}HH), 3.38 (ddd, J = 16.9, 8.4, 5.4 Hz, 1H,

C_{20}HH or C_{25}HH), 3.20 (dt, J = 10.2, 3.4 Hz, 1H, C_{10}H or C_{14}H), 3.14 – 2.97 (m,

3H, C_{10}H or C_{14}H , C_5HH), 2.37 – 2.23 (m, 2H, C_{13}HH), 2.05 – 1.90 (m, 1H,

C_9HH), 1.90 – 1.09 (m, 19H, C_6HH , C_7HH , C_9HH , C_{16}HH , C_{17}HH , C_{18}HH , C_{19}HH ,

C_{22}HH , C_{23}HH , C_{24}HH), 0.92 (s, 9H, C_{34}HHH), 0.07 (s, 3H, C_{31}HHH), 0.03 (s, 3H,

C_{32}HHH). ^{13}C NMR (75 MHz, CDCl_3) δ 146.64 (C_{12}), 139.22, 138.55 (C_4 , C_{27}),

133.72 (C_1), 129.36 (C_2), 128.52, 128.21, 128.01, 127.79 (C_3 , C_{28} , C_{29} , C_{30}),

107.33 (C_{35}), 99.07 (C_{21}), 81.09, 80.38 (C_{10} , C_{14}), 75.47 (C_8), 74.51 (C_{11}), 73.05

(C_{15}), 70.75 (C_{26}), 67.65, 62.58 (C_{20} , C_{25}), 56.31 (C_5), 36.31 (C_9), 34.27 (C_{13}),

32.74, 32.29, 30.92, 29.83, 26.47, 26.43, 25.61, 19.89 (C_7 , C_{16} , C_{17} , C_{18} , C_{19} ,

C_{22} , C_{23} , C_{24}), 26.02 (C_{34}), 19.32 (C_6), 18.28 (C_{33}), -4.22, -4.54 (C_{31} , C_{32}). IR

Experimental

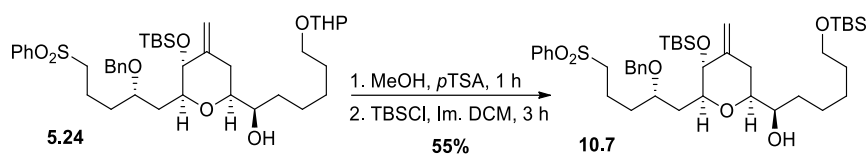
(neat, cm^{-1}) 3500, 2930, 2856, 1447, 1306, 1254, 1182, 1142, 1113, 1087.

MSMS (p ESI), m/z (%): 767.40 (75), 683.34 (83), 625.39 (22), 535.34 (13), 91.05 (100). **HRMS**, m/z : calculated for $\text{C}_{41}\text{H}_{64}\text{O}_8\text{SSiNa}$ [$M + 23$]: 767.3983. Found: 767.3985.

Diastereoisomer 2: $R_f = 0.35$

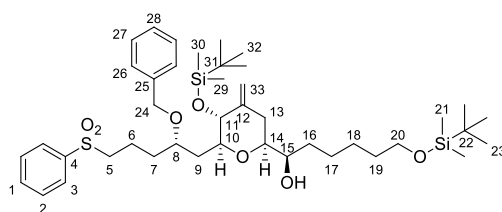
^1H NMR (300 MHz, CDCl_3) δ 7.95 – 7.77 (m, 2H, C_3H), 7.72 – 7.42 (m, 3H, C_1H , C_2H), 7.39 – 7.16 (m, 5H, C_{28}H , C_{29}H , C_{30}H), 5.01 (s, 1H, C_{35}HH), 4.84 (s, 1H, C_{35}HH), 4.65 – 4.48 (m, 2H, C_{26}HH , C_{21}H), 4.33 (d, $J = 11.6$ Hz, 1H, C_{26}HH), 3.93 – 3.81 (m, 2H, C_{25}HH or C_{20}HH), 3.82 – 3.70 (m, 2H, C_{20}HH or C_{25}HH), 3.66 (dd, $J = 10.6, 4.7$ Hz, 2H, C_{11}H , C_{15}H), 3.48 (ddd, $J = 8.9, 8.1, 4.8$ Hz, 1H, C_{20}HH or C_{25}HH), 3.40 (ddd, $J = 9.6, 6.5, 2.4$ Hz, 1H, C_{20}HH or C_{25}HH), 3.18 (dd, $J = 12.3, 8.8$ Hz, 1H, C_{10}H or C_{14}H), 3.05 (dt, $J = 10.7, 8.2$ Hz, 3H, C_{10}H or C_{14}H , C_5HH), 2.39 – 2.20 (m, 2H, C_{13}HH), 2.12 – 1.05 (m, 20H, C_6HH , C_7HH , C_9HH , C_{16}HH , C_{17}HH , C_{18}HH , C_{19}HH , C_{22}HH , C_{23}HH , C_{24}HH), 0.92 (s, 9H, C_{34}HHH), 0.06 (s, 3H, C_{31}HHH), 0.02 (s, 3H, C_{32}HHH). **MSMS** (p ESI), m/z (%): 767.40 (100), 683.34 (95), 625.39 (25), 535.34 (12). **HRMS**, m/z : calculated for $\text{C}_{41}\text{H}_{64}\text{O}_8\text{SSiNa}$ [$M + 23$]: 767.3983. Found: 767.3980.

(*R*)-1-((2*S*,5*R*,6*S*)-6-((*S*)-2-(benzyloxy)-5-(phenylsulfonyl)pentyl)-5-((tert-butyltrimethylsilyl)oxy)-4-methylenetetrahydro-2H-pyran-2-yl)-6-((tert-butyltrimethylsilyl)oxy)hexan-1-ol



A 50 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with tetrahydropyran **5.24** (276 mg, 0.37 mmol, 1 eq.), MeOH (5 mL) and *p*TSA (cat. amount). Resulting mixture was left stirring at room temperature for 1 h. After complete conversion, the mixture was treated with DCM (15 mL) and a saturated aqueous solution of NaHCO₃ (15 mL). After separation of the phases, the aqueous layer was extracted with DCM (2 x 15 mL). Combined organic fractions were dried over MgSO₄ and concentrated under reduced pressure to the primary yield alcohol as a colorless oil (200 mg, 82%). The latter was used without further purification. A 50 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with the prepared alcohol (193 mg, 0.29 mmol, 1 eq.), DCM (3 mL), imidazole (40 mg, 0.58 mmol, 2 eq.) and TBSCl (44 mg, 0.29 mmol, 1 eq.). Resulting mixture was left stirring at room temperature for 3 h. After complete conversion, the mixture was treated with DCM (15 mL) and a saturated aqueous solution of NH₄Cl (15 mL). After separation of the phases, the aqueous layer was extracted with DCM (2 x 15 mL). Combined organic fractions were dried over MgSO₄, concentrated under reduced pressure and resulting residue was purified by flash column chromatography on silica gel (PE/AcOEt 3:1) to yield tetrahydropyran **10.7** as a colorless oil (145 mg, 64%).

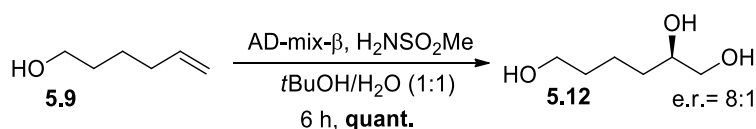
Experimental



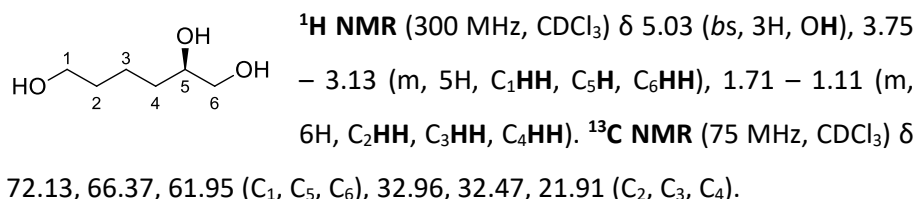
¹H NMR (300 MHz, CDCl₃) δ 7.91 – 7.84 (m, 2H, C₃H), 7.69 – 7.60 (m, 1H, C₁H), 7.60 – 7.50 (m, 2H, C₂H), 7.38 – 7.20 (m, 5H, C₂₆H, C₂₇H, C₂₈H), 5.03 (s,

1H, C₃₃HH), 4.85 (s, 1H, C₃₃HH), 4.54 (d, J = 11.6 Hz, 1H, C₂₄HH), 4.33 (d, J = 11.6 Hz, 1H, C₂₄HH), 3.75 – 3.51 (m, 5H, C₈H, C₁₁H, C₁₅H, C₂₀HH), 3.22 (m, 1H, C₁₀H or C₁₄H), 3.16 – 2.95 (m, 3H, C₁₀H or C₁₄H, C₅HH), 2.40 – 2.20 (m, 2H, C₁₃HH), 1.98 (m, 1H, C₉HH), 1.91 – 1.45 (m, 13H, C₉HH, C₆HH, C₇HH, C₁₆HH, C₁₇HH, C₁₈HH, C₁₉HH), 0.93 (s, 9H, C₂₃HHH or C₃₂HHH), 0.89 (s, 9H, C₂₃HHH or C₃₂HHH), 0.05 (m, 12H, C₂₁HHH, C_{21'}HHH, C₂₉HHH, C₃₀HHH). **¹³C NMR** (75 MHz, CDCl₃) δ 146.65 (C₁₂), 139.24, 138.55 (C₄, C₂₅), 133.69, 129.33, 128.49, 128.18, 127.98, 127.75 (C₁, C₂, C₃, C₂₆, C₂₇, C₂₈), 107.29 (C₃₃), 81.09, 80.38 (C₁₀, C₁₄), 75.47, 74.51, 73.08 (C₈, C₁₁, C₁₅), 70.73 (C₂₄), 63.27 (C₂₀), 56.30 (C₅), 36.30 (C₉), 34.26 (C₁₃), 32.91, 32.71, 32.35, 26.11, 26.01, 25.92 (C₇, C₁₆, C₁₇, C₁₈, C₁₉, C₂₃, C₃₂), 19.29 (C₆), 18.49, 18.26 (C₂₂, C₃₁), -4.24, -4.55, -5.12 (C₂₁, C_{21'}, C₂₉, C₃₀). **IR** (film, cm⁻¹) 2928, 2893, 2883, 2856, 1462, 1447, 1305, 1254, 1146, 1099, 1088, 1070, 1028, 1005. **MSMS** (p ESI), m/z (%): 229.05 (68), 211.04 (100), 183.05 (20), 143.08 (20), 91.05 (73). **HRMS**, m/z : calculated for C₄₂H₇₁O₇SSi₂ [M + 1]: 775.4454. Found: 775.4445.

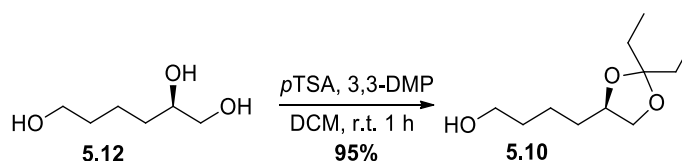
(*R*)-hexane-1,2,6-triol



A 1 L round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with AD-mix- β (42 g), methylsulfoneamide (2.85 g, 30 mmol, 1 eq.), *t*BuOH (150 mL), H₂O (150 mL) and olefin **5.9** (3.005 g, 30 mmol, 1 eq.) and was left stirring at room temperature for 6 h. At that moment, the crude reaction mixture was treated with Na₂SO₃ (45 g) and was left stirring for another hour prior to addition of AcOEt (200 mL). After phase separation, the aqueous layer was extracted with AcOEt (2 x 100 mL). Combined organic fractions were washed with a 1M aqueous solution of KOH (3 x 20 mL), dried over MgSO₄ and concentrated under reduced pressure. Triol **5.12** was used without further purification for the next step.



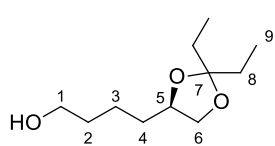
(*R*)-4-(2,2-diethyl-1,3-dioxolan-4-yl)butan-1-ol



A 100 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with triol **5.12** (4.025 g, 30 mmol, 1 eq.), 3,3-DMP (25.05 g, 150 mmol, 5 eq.) and DCM (25 mL). Resulting mixture was left stirring at room temperature for 1 h, prior to addition of a saturated aqueous solution of NaHCO₃ (25 mL). After phase separation, the aqueous layer was extracted with DCM (3 x 25 mL). Combined organic fractions were dried over MgSO₄, concentrated under reduced pressure and resulting residue was purified by flash column chromatography on silica gel

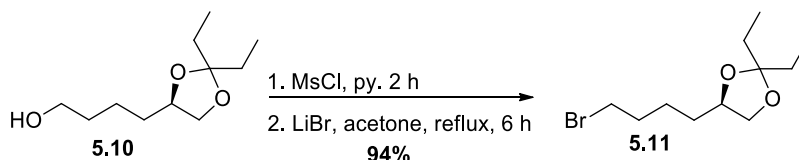
Experimental

(PE/AcOEt 4:1) to afford alcohol **5.10** as a colorless oil (5.76 g, 95%). $R_f = 0.50$ (PE/ AcOEt 1:1)



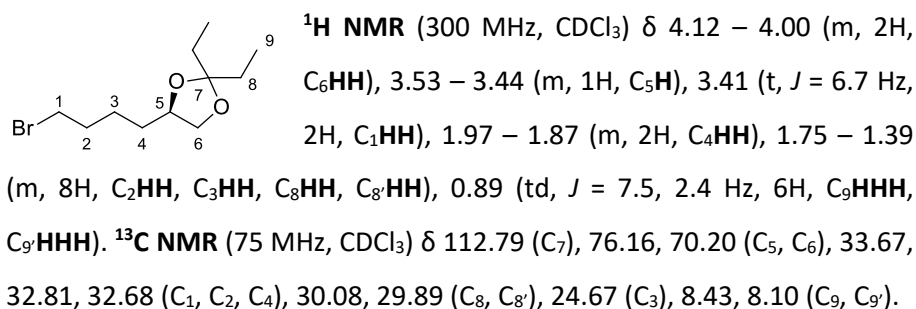
^1H NMR (300 MHz, CDCl_3) δ 4.12 – 4.01 (m, 2H, C_6HH), 3.65 (t, $J = 6.4$ Hz, 2H, C_1HH), 3.53 – 3.40 (m, 1H, C_5H), 1.78 – 1.32 (m, 10H, C_2HH , C_3HH , C_4HH , C_8HH , $\text{C}_8'\text{HH}$), 0.89 (td, $J = 7.5, 2.5$ Hz, 6H, C_9HHH , $\text{C}_9'\text{HHH}$). ^{13}C NMR (75 MHz, CDCl_3) δ 112.70 (C_7), 76.40, 70.26, 62.82 (C_1 , C_5 , C_6), 33.23, 32.78 (C_2 , C_4), 30.08, 29.92 (C_8 , C_8'), 22.27 (C_3), 8.42, 8.08 (C_9 , C_9').

(R)-4-(4-bromobutyl)-2,2-diethyl-1,3-dioxolane

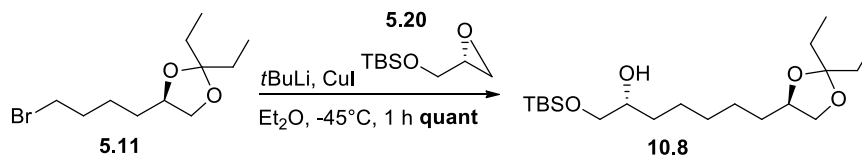


A 25 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with alcohol **5.10** (5.057 g, 25 mmol, 1 eq.), MsCl (3.72 g, 32.5 mmol, 1.3 eq.) and pyridine (10 mL). Resulting mixture was left stirring for 2 h at room temperature prior to addition of DCM (30 mL) and a saturated aqueous solution of CuSO_4 . After phase separation, the organic fraction is dried over MgSO_4 and concentrated under reduced pressure. The crude mesylate is then transferred to a 100 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer, and a saturated solution of LiBr in acetone (50 mL). Resulting mixture was refluxed for 6 h prior to addition of H_2O (50 mL) and Et_2O (100 mL). After phase separation, the aqueous layer was extracted with Et_2O (2 x 40 mL). Combined organic fractions were then dried over MgSO_4 , concentrated under reduced pressure and resulting residue was purified by flash column chromatography on silica gel (PE/

AcOEt 4:1) or by distillation (1.5 mBar, 110°C) to afford bromide **5.11** as a colorless oil (6.30 g, 94%). R_f = 0.76 (PE/AcOEt 1:1).



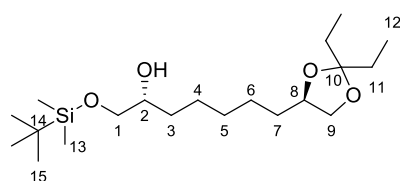
(*R*)-1-((*tert*-butyldimethylsilyl)oxy)-7-((*R*)-2,2-diethyl-1,3-dioxolan-4-yl)heptan-2-ol



A 500 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with $t\text{BuLi}$ (1.7M in pentane, 51 mL, 87 mmol, 8.2 eq.) and Et_2O (85 mL) at -78°C and was left stirring for 10 min at that temperature. Neat bromide **5.11** (10.05 g, 42 mmol, 4 eq.) was then added to the mixture at the same temperature and stirring was continued for 45 min. A white precipitate was forming. A second 1 L round-bottom flask was charged with CuI (4.04 g, 21 mmol, 2 eq.) and Et_2O (120 mL). The heterogeneous mixture was cooled down to -50°C and the freshly prepared lithiated species was transferred to the solution. The solution turned black and was allowed to heat up to -30°C for 10 min, prior to being cooled down to -40°C again. At that temperature, the epoxide **5.20** (2 g, 11 mmol, 1 eq.) in Et_2O (5 mL) was added dropwise, the mixture was left stirring for 30 min, then treated with a saturated aqueous solution of NH_4Cl (100 mL). The

Experimental

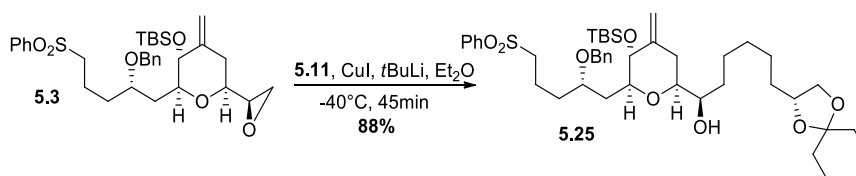
layers were separated and the aqueous phase was extracted with AcOEt (80 mL). Combined organic fractions were dried over MgSO₄ and concentrated under reduced pressure. Resulting residue was purified by flash column chromatography on silica gel (PE/AcOEt 3:1 to AcOEt 100%) to afford alcohol **10.8** as a yellow oil (394 mg, quant).



¹H NMR (300 MHz, CDCl₃) δ 4.07 – 3.97 (m, 2H, C₉HH), 3.65 – 3.56 (m, 2H, C₁HH), 3.50 – 3.27 (m, 2H, C₂H, C₈H), 2.43 (d, *J* = 3.1 Hz, 1H, OH), 1.70 – 1.55

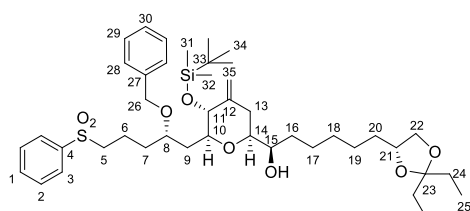
(m, 4H, C₁₁HH, C_{11'}HH), 1.55 – 1.20 (m, 10H, C₃HH, C₄HH, C₅HH, C₆HH, C₇HH), 1.00 – 0.80 (m, 15H, C₁₂HHH, C_{12'}HHH, C₁₅HHH), 0.06 (s, 6H, C₁₃HHH).
¹³C NMR (75 MHz, CDCl₃) δ 112.59 (C₁₀), 76.48, 71.90, 70.34, 67.40 (C₁, C₂, C₈, C₉), 33.51, 32.81, 30.11, 29.97, 29.89 (C₃, C₄, C₅, C₆, C₇), 26.02 (C₁₅), 25.89, 25.62 (C₁₁, C_{11'}), 18.44 (C₁₄), 8.43, 8.10 (C₁₂, C_{12'}), -5.20, -5.25 (C₁₃, C_{13'}).

(*R*)-1-((2*S*,5*R*,6*S*)-6-((*S*)-2-(benzyloxy)-5-(phenylsulfonyl)pentyl)-5-((tert-butyl dimethylsilyl)oxy)-4-methylenetetrahydro-2H-pyran-2-yl)-6-((*R*)-2,2-diethyl-1,3-dioxolan-4-yl)hexan-1-ol



A 100 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with *t*BuLi (1.87M in pentane, 16.8 mL, 32 mmol, 21 eq.) and Et₂O (36 mL) and was then stirred at -78°C for 10 min. Neat

bromide **5.11** (4.06 g, 15 mmol, 10 eq.) was then added to the mixture at the same temperature and stirring was continued for another 45 min. A second 250 mL round-bottom flask equipped with a Teflon coated magnetic stirrer was charged with CuI (1.46 g, 7.7 mmol, 5 eq.) and Et₂O (48 mL). The heterogeneous mixture was cooled down to -50°C and the freshly prepared alkyl lithium was added dropwise via a syringe. The solution turned black and was allowed to heat up to -30°C for 10 min, before being again cooled down to -40°C. At that temperature, epoxide **5.3** (900 mg, 1.5 mmol, 1 eq.) in Et₂O (4 mL) was added dropwise, the mixture was stirred for 45 min, then diluted in a saturated aqueous solution of NH₄Cl (80 mL). The layers were separated and the aqueous phase was extracted with AcOEt (40 mL). Combined organic fractions were dried over MgSO₄, concentrated under reduced pressure and resulting residue was purified by flash column chromatography on silica gel (PE/AcOEt 5:1 to 3:1) to afford alcohol **5.25** as a colorless oil (1.020 g; 88%). R_f = 0.46 (PE/AcOEt 1:1).



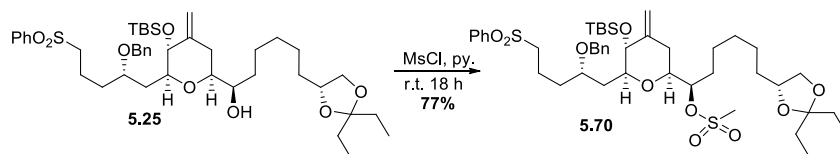
¹H NMR (300 MHz, CDCl₃) δ 7.95 – 7.80 (m, 2H, C₃H), 7.70 – 7.59 (m, 1H, C₁H), 7.61 – 7.46 (m, 2H, C₂H), 7.39 – 7.14 (m, 5H, C₂₈H, C₂₉H, C₃₀H), 5.03 (s, 1H, C₃₅HH),

4.85 (s, 1H, C₃₅HH), 4.54 (d, *J* = 11.5 Hz, 1H, C₂₆HH), 4.33 (d, *J* = 11.5 Hz, 1H, C₂₆HH), 4.10 – 3.97 (m, 2H, C₂₂HH), 3.72 – 3.39 (m, 4H, C₈H, C₁₁H, C₁₅H, C₂₁H), 3.30 – 3.15 (m, 1H, C₁₀H or C₁₄H), 3.15 – 2.97 (m, 3H, C₅HH, C₁₄H or C₁₀H), 2.39 – 1.21 (m, 23H, C₂₂H, C₆HH, C₇HH, C₉HH, C₁₃HH, C₁₆HH, C₁₇HH, C₁₈HH, C₁₉HH, C₂₀HH, C₂₄HH, C_{24'}HH), 1.01 – 0.82 (m, 15H, C₂₅HHH, C_{25'}HHH, C₃₄HHH), 0.07 (s, 3H, C₃₂HHH), 0.03 (s, 3H, C₃₁HHH). ¹³C NMR (75 MHz, CDCl₃) δ 146.65 (C₁₂), 139.25, 138.56 (C₄, C₂₆), 133.73 (C₁), 129.36 (C₂), 128.53, 128.20, 128.01, 127.80 (C₃, C₂₈, C₂₉, C₃₀), 112.60 (C₂₃), 107.35 (C₃₅),

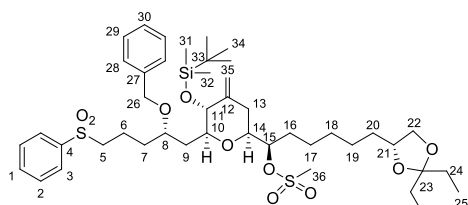
Experimental

81.10, 80.40 (C₁₀, C₁₄), 76.46 (C₂₁), 75.49 (C₈), 74.52 (C₁₁), 73.08 (C₁₅), 70.75 (C₂₆), 70.32 (C₂₂), 56.31 (C₅), 36.31 (C₉), 34.25 (C₁₃), 35.72, 33.54, 32.74, 32.26, 29.88, 25.93 (C₇, C₁₆, C₁₇, C₁₈, C₁₉, C₂₀), 30.11, 29.95 (C₂₄, C_{24'}), 26.02 (C₃₄), 19.33 (C₆), 18.28 (C₃₃), 8.44, 8.10 (C₂₅, C_{25'}), -4.22, -4.54 (C₃₁, C₃₂). **IR** (neat, cm⁻¹) 3500, 2964, 2928, 2880, 2858, 1462, 1306, 1144, 1103, 1072, 1059, 1040, 1028. **MSMS** (p APCI), m/z (%): 229.05 (43), 211.04 (100), 183.05 (22), 143.02 (12), 95.09 (18), 91.05 (76). **HRMS**, m/z: calculated for (C₄₃H₆₉O₈SSi) [M + 1]: 773.4477. Found: 773.4460.

(R)-1-((2S,5R,6S)-6-((S)-2-(benzyloxy)-5-(phenylsulfonyl)pentyl)-5-((tert-butyl)dimethylsilyl)oxy)-4-methylenetetrahydro-2H-pyran-2-yl)-6-((R)-2,2-diethyl-1,3-dioxolan-4-yl)hexyl methanesulfonate



A 50 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with alcohol **5.25** (1000 mg, 1.3 mmol, 1 eq.), MsCl (163 mg, 1.4 mmol, 1.1 eq.) and pyridine (15 mL). Resulting mixture was left stirring at room temperature for 18 h. After complete conversion, the mixture was treated with a saturated aqueous solution of CuSO₄ (25 mL) and DCM (50 mL). After separation of the phases, the aqueous layer was extracted with DCM (50 mL). Combined organic fractions were dried over MgSO₄ and concentrated under reduced pressure to yield mesylate **5.70** as a colorless oil (850 mg, 77%). R_f = 0.31 (PE/AcOEt 4:1).



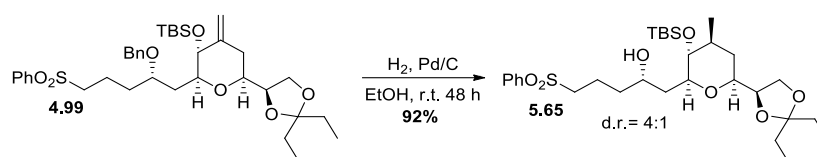
^1H NMR (300 MHz, CDCl_3) δ 7.92 – 7.84 (m, 2H, C_3H), 7.65 (t, $J = 7.3$ Hz, 1H, C_1H), 7.55 (t, $J = 7.5$ Hz, 2H, C_2H), 7.37 – 7.19 (m, 5H, C_{28}H , C_{29}H , C_{30}H), 5.07 (s, 1H, C_{35}HH), 4.89 (s, 1H, C_{35}HH), 4.76 – 4.66 (m, 1H, C_{15}H), 4.52 (d, $J = 11.6$ Hz, 1H, C_{26}HH), 4.33 (d, $J = 11.7$ Hz, 1H, C_{26}HH), 4.03 (dd, $J = 11.1$, 7.1 Hz, 2H, C_{22}HH), 3.71 – 3.36 (m, 4H, C_8H , C_{11}H , C_{14}H , C_{21}H), 3.16 – 2.96 (m, 3H, C_5HH , C_{10}H), 3.02 (s, 3H, C_{36}HHH), 2.39 (dd, $J = 13.1$, 2.2 Hz, 1H, $eq\text{-C}_{13}\text{HH}$), 2.31 – 2.19 (m, 1H, $ax\text{-C}_{13}\text{HH}$), 2.09 – 1.10 (m, 20H, C_6HH , C_7HH , C_9HH , C_{16}HH , C_{17}HH , C_{18}HH , C_{19}HH , C_{20}HH , C_{24}HH , $\text{C}_{24'}\text{HH}$), 1.00 – 0.80 (m, 15H, C_{34}HHH , C_{25}HHH , $\text{C}_{25'}\text{HHH}$), 0.07 (s, 3H, C_{32}HHH), 0.03 (s, 3H, C_{31}HHH).

^{13}C NMR (75 MHz, CDCl_3) δ 145.46 (C_{12}), 139.32, 138.50 (C_4 , C_{27}), 133.71 (C_1), 129.36, 128.56, 128.18, 127.95, 127.81 (C_2 , C_3 , C_{28} , C_{29} , C_{30}), 112.61 (C_{23}), 108.22 (C_{35}), 84.31 (C_{15}), 80.56, 79.07 (C_{10} , C_{14}), 76.36 (C_{21}), 75.42 (C_8), 74.38 (C_{11}), 70.84 (C_{26}), 70.28 (C_{22}), 56.05 (C_6), 38.94 (C_{36}), 36.32 (C_9), 34.98 (C_{13}), 33.44, 32.48, 31.02, 30.09, 29.93, 29.48, 25.99, 25.80, 25.44 (C_7 , C_{16} , C_{17} , C_{18} , C_{19} , C_{20} , C_{24} , $\text{C}_{24'}$, C_{34}), 19.17 (C_6), 18.26 (C_{33}), 8.43, 8.10 (C_{25} , $\text{C}_{25'}$), -4.30, -4.61 (C_{31} , C_{32}). **IR** (neat, cm^{-1}) 2934, 2881, 2858, 1462, 1447, 1352, 1306, 1254, 1175, 1146, 1111, 1086, 1059, 1028. **MSMS** (p APCI), m/z (%): 537.26 (20), 429.21 (100), 421.20 (23), 325.21 (46), 239.07 (22), 229.07 (46), 211.04 (90), 183.05 (24), 143.02 (34), 91.05 (74). **HRMS**, m/z : calculated for ($\text{C}_{44}\text{H}_{71}\text{O}_{10}\text{S}_2\text{Si}$) [$\text{M} + 1$]: 851.4252. Found: 851.4244.

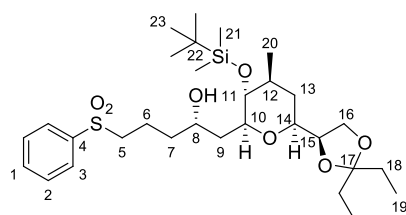
Experimental

10.2.3. Hydrogenation

(S)-1-((2S,3R,4S,6S)-3-((tert-butyldimethylsilyl)oxy)-6-((R)-2,2-diethyl-1,3-dioxolan-4-yl)-4-methyltetrahydro-2H-pyran-2-yl)-5-(phenylsulfonyl)pentan-2-ol



A 100 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with **4.99** (1.83 g, 2.7 mmol, 1 eq.), Pd/C (catalytic amount) and EtOH (35 mL). Resulting mixture was left stirring at room temperature for 2 days. After complete conversion, the mixture was filtered through celite®. The latter was washed with AcOEt (5 x 25 mL). Combined organic fractions were concentrated under reduced pressure to yield tetrahydropyran **5.65** as white sticky oil (1.45 g, 92%). R_f = 0.83 (PE/AcOEt 1:1).

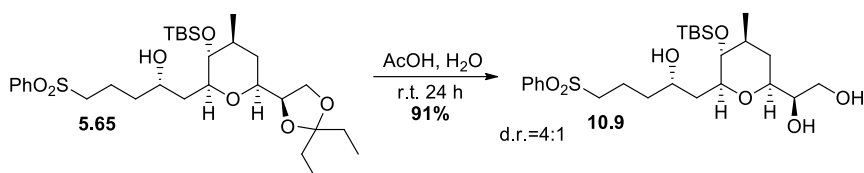


^1H NMR (300 MHz, CDCl_3) δ 7.94 – 7.87 (m, 2H, C_3H), 7.69 – 7.61 (m, 1H, C_1H), 7.61 – 7.49 (m, 2H, C_2H), 4.04 – 3.95 (m, 1H, C_{16}HH), 3.86 (dt, J = 11.0, 5.6 Hz, 1H, C_{15}H), 3.79 – 3.68 (m, 3H,

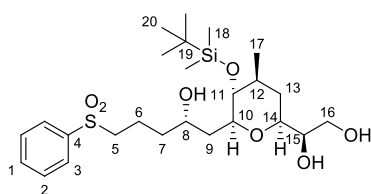
C_8H , C_{14}H , C_{16}HH), 3.31 (t, J = 9.8 Hz, 1H, C_{10}H), 3.20 – 3.11 (m, 2H, C_5HH), 2.89 (t, J = 9.0 Hz, 1H, C_{11}H), 1.84 – 1.31 (m, 9H, C_6HH , C_7HH , C_9HH , C_{12}H , C_{13}HH), 0.98 (d, J = 6.5 Hz, 3H, C_{20}HHH), 0.87 (s, 9H, C_{23}HHH), 0.06 (s, 3H, C_{21}HHH), 0.02 (s, 3H, C_{21}HHH). **^{13}C NMR** (75 MHz, CDCl_3) δ 139.28 (C_4), 133.70 (C_1), 129.37 (C_2), 128.23 (C_3), 113.49 (C_{17}), 83.90 (C_{10}), 77.89 (C_{15}), 77.36 (C_{11}), 71.63 (C_{14}), 71.40 (C_8), 67.13 (C_{16}), 56.41 (C_5), 37.70, 36.18,

36.09 (C₁₃, C₁₂, C₉), 31.84 (C₇), 29.73, 26.97 (C₁₈, C_{18'}), 26.16 (C₂₃), 19.52, 19.41 (C₆, C₂₂), 18.37 (C₂₀), 8.33, 8.27 (C₁₉), -3.08, -3.12 (C₂₁, C₂₁). IR (film, cm⁻¹) 3520, 2953, 2930, 2881, 2858, 1462, 1447, 1306, 1290, 1252, 1148, 1122, 1061.

(*R*)-1-((2*S*,4*S*,5*R*,6*S*)-5-((*tert*-butyldimethylsilyl)oxy)-6-((*S*)-2-hydroxy-5-(phenylsulfonyl)pentyl)-4-methyltetrahydro-2H-pyran-2-yl)ethane-1,2-diol



A 25 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with tetrahydropyran **5.65** (783 mg, 1.3 mmol, 1 eq.), AcOH (10 mL) and H₂O (3 mL). Resulting mixture was left stirring at room temperature for 24 hours. The crude reaction mixture was then treated with DCM (20 mL) and a saturated aqueous solution of NaHCO₃ (20 mL). After phase separation, the aqueous layer was extracted with DCM (3 x 20 mL). Combined organic fractions were dried over MgSO₄, concentrated under reduced pressure and resulting residue was purified by flash column chromatography on silica gel (AcOEt) to afford triol **10.9** as a colorless oil (611 mg, 91%, d.r.= 4:1). R_f= 0.82 (PE/AcOEt 1:1).

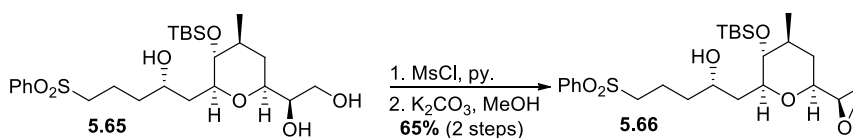


¹H NMR (300 MHz, CDCl₃) δ 7.98 – 7.83 (m, 2H, C₃H), 7.72 – 7.47 (m, 3H, C₁H, C₂H), 3.86 – 3.72 (m, 1H, C₈H), 3.72 – 3.43 (m, 4H, C₁₄H, C₁₅H, C₁₆HH), 3.30 (t, *J* = 8.8 Hz, 1H, C₁₀H), 3.21 – 3.10 (m, 2H, C₅HH), 2.89 (t, *J* = 9.0 Hz, 1H, C₁₁H), 2.00 –

Experimental

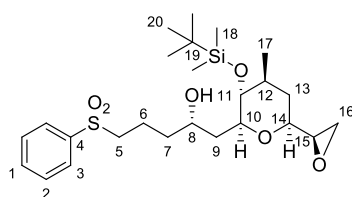
1.71 (m, 4H, C₆HH, C₇HH, C₉HH), 1.62 – 1.43 (m, 3H, C₁₂H, C₁₃HH), 1.39 – 1.31 (m, 1H, C₉HH), 1.27 – 1.22 (m, 1, C₇HH), 0.98 (d, *J* = 6.5 Hz, 3H, C₁₇HHH), 0.87 (s, 9H, C₂₀HHH), 0.07 (s, 3H, C₁₈HHH), 0.02 (s, 3H, C_{18'}HHH). ¹³C NMR (75 MHz, CDCl₃) δ 139.23 (C₄), 133.77 (C₁), 129.41 (C₂), 128.21 (C₃), 83.65 (C₁₀), 78.34 (C₁₄), 77.36 (C₁₁), 73.50 (C₁₅), 71.65 (C₈), 63.23 (C₁₆), 56.30 (C₅), 39.07 (C₉), 37.83 (C₁₃), 36.03 (C₁₂), 35.00 (C₇), 26.16 (C₂₀), 19.59, 19.24 (C₆, C₁₉), 18.36 (C₁₇), -3.10 (C₁₈). IR (film, cm⁻¹) 3430, 2955, 2928, 2883, 2858, 1304, 1258, 1146, 1086, 1024, 1007. HRMS, *m/z*: calculated for (C₂₅H₄₅O₇SSi) [*M* + 1]: 517.2650. Found: 517.2656.

(*S*)-1-((2*S*,3*R*,4*S*,6*S*)-3-((*tert*-butyldimethylsilyl)oxy)-4-methyl-6-((*R*)-oxiran-2-yl)tetrahydro-2H-pyran-2-yl)-5-(phenylsulfonyl)pentan-2-ol



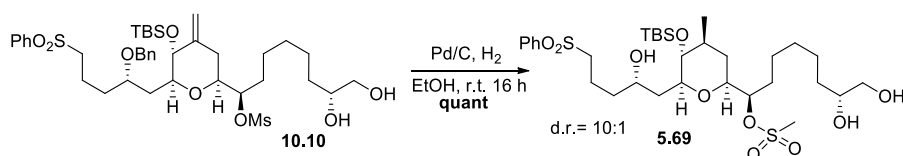
A 25 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with triol **5.65** (0.335 g, 0.65 mmol, 1 eq.), MsCl (70 mg, 0.62 mmol, 0.95 eq.) and pyridine (5 mL). Resulting mixture was left stirring at 0°C and after 1 h, allowed to heat up to room temperature. Stirring was continued for 17 h. At that moment, AcOEt (5 mL) and H₂O (5 mL) were added to the mixture. After separation, the aqueous phase was extracted with AcOEt (3 x 10 mL). Combined organic fractions were dried over MgSO₄ and concentrated under reduced pressure. This crude primary mesylate was transferred without further purification into a 50 mL round-bottom flask containing K₂CO₃ (0.830 g, 6.2 mmol, 10 eq.) and MeOH (10 mL) at 0°C. Resulting mixture was left stirring at 0°C for 1 h before adding AcOEt (10 mL) and H₂O (10 mL). After separation, the organic phase was extracted with AcOEt (3 x 10 mL). Combined organic fractions were dried over MgSO₄,

concentrated under reduced pressure and resulting residue was purified by flash column chromatography on silica gel (PE/AcOEt 5:1) to afford epoxide **5.66** as a colorless oil (210 mg, 65 %). R_f = 0.75 (AcOEt).



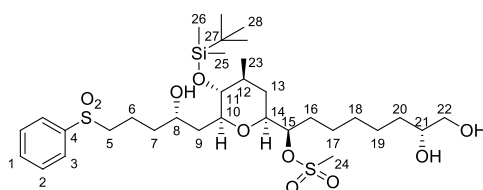
^1H NMR (300 MHz, CDCl_3) δ 8.00 – 7.81 (m, 2H, C_3H), 7.76 – 7.39 (m, 3H, C_1H , C_2H), 3.79 – 3.69 (m, 1H, C_8H), 3.52 – 3.44 (m, 1H, C_{14}H), 3.30 (t, J = 9.8 Hz, 1H, C_{10}H), 3.21 – 3.10 (m, 2H, C_5HH), 2.94 – 2.85 (m, 2H, C_{15}H , C_{11}H), 2.70 (dd, J = 7.9, 3.9 Hz, 1H, C_{16}HH), 2.68 – 2.60 (m, 1H, C_{16}HH), 1.96 – 1.30 (m, 9H, C_6HH , C_7HH , C_9HH , C_{12}H , C_{13}HH), 0.99 (d, J = 6.5 Hz, 3H, C_{17}HHH), 0.87 (s, 9H, C_{20}HHH), 0.06 (s, 3H, C_{18}HHH), 0.02 (s, 3H, C_{18}HHH). **^{13}C NMR** (75 MHz, CDCl_3) δ 139.25 (C_4), 133.70 (C_1), 129.37 (C_2), 128.23 (C_3), 83.85 (C_{10}), 77.36 (C_{11}), 71.74 (C_8), 70.36 (C_{14}), 56.39 (C_5), 53.03 (C_{15}), 44.50 (C_{16}), 39.00 (C_9), 37.65 (C_{13}), 36.17 (C_{12}), 35.65 (C_7), 26.14 (C_{20}), 19.46, 19.39 (C_6 , C_{19}), -3.12, -3.16 (C_{18} , C_{18}'). **IR** (film, cm^{-1}) 3500, 1447, 1360, 1306, 1252, 1175, 1146, 1086, 1007. **HRMS**, m/z : calculated for $(\text{C}_{25}\text{H}_{43}\text{O}_6\text{SSi})$ [$\text{M} + 1$]: 499.2544. Found: 499.2545.

(1*R*,7*R*)-1-((2*S*,4*S*,5*R*,6*S*)-5-((tert-butyldimethylsilyl)oxy)-6-((*S*)-2-hydroxy-5-(phenylsulfonyl)pentyl)-4-methyltetrahydro-2*H*-pyran-2-yl)-7,8-dihydroxyoctyl methanesulfonate



Experimental

A 10 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with diol **10.10** (186 mg, 0.24 mmol, 1 eq.), Pd/C (10mol%, 20 mg) and EtOH (5 mL). Resulting mixture was left stirring at room temperature for 36 h. After complete conversion, the mixture was filtered through celite®. The latter was washed with AcOEt (5 x 25 mL). Combined organic fractions were concentrated under reduced pressure to yield tetrahydropyran **5.69** as white sticky oil (164 mg, quant). $R_f = 0.33$ (AcOEt).



$^1\text{H NMR}$ (300 MHz, CDCl_3) δ

7.92 – 7.84 (m, 2H, C_3H), 7.68 –

7.50 (m, 3H, C_1H , C_2H), 4.72 (d, J

= 8.8 Hz, 1H, C_{15}H), 3.83 – 3.26

(m, 8H, C_8H , C_{10}H , C_{14}H , C_{21}H , C_{22}HH , OH), 3.14 (t, J = 7.9 Hz, 2H, C_5HH), 3.08

– 3.00 (m, 3H, C_{24}HHH), 2.85 (t, J = 8.8 Hz, 1H, C_{11}H), 2.07 – 1.09 (m, 19H,

C_6HH , C_7HH , C_9HH , C_{12}H , C_{13}HH , C_{16}HH , C_{17}HH , C_{18}HH , C_{19}HH , C_{20}HH), 0.99

(d, J = 6.3 Hz, 3H, C_{23}HHH), 0.86 (s, 9H, C_{28}HHH), 0.06 (s, 3H, C_{25}HHH), 0.02

(s, 3H, C_{26}HHH). $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 139.18 (C_4), 133.76 (C_1), 129.39,

128.17 (C_2 , C_3), 83.99, 83.59 (C_{10} , C_{15}), 77.96 (C_{14}), 77.36 (C_{11}), 72.16, 71.36

(C_8 , C_{21}), 66.82 (C_{22}), 56.29 (C_5), 39.51, 39.03, 37.64, 36.06, 32.83, 32.78,

30.13, 28.95, 26.10, 25.21, 25.16 (C_7 , C_9 , C_{12} , C_{13} , C_{16} , C_{17} , C_{18} , C_{19} , C_{20} , C_{24} ,

C_{28}), 19.52 (C_{23}), 19.28 (C_6), 18.31 (C_{27}), -3.12, -3.15 (C_{25} , C_{26}). IR (neat, cm^{-1})

3500, 2930, 2910, 2856, 1462, 1447, 1339, 1306, 1256, 1173, 1146, 1086,

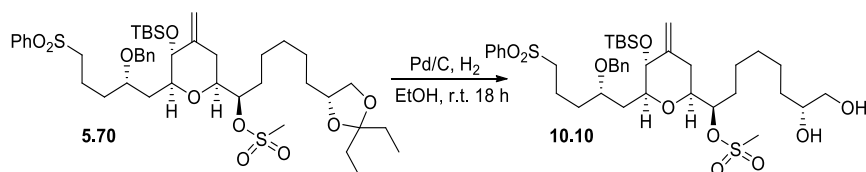
1024. MSMS (p ESI), m/z (%): 563.32 (15), 449.24 (71), 431.23 (100), 413.21

(43), 393.19 (35), 293.12 (25), 279.10 (20), 133.10. HRMS, m/z : calculated

for ($\text{C}_{32}\text{H}_{58}\text{O}_{10}\text{S}_2\text{SiNa}$) [$\text{M} + 23$]: 717.3133; found: 717.3128. $[\alpha]_{20}^D$: -68.8 ($c=9$

mg/mL, DCM).

NB. Sometimes when **5.70** was subjected to the hydrogenation conditions, we first observed the cleavage of the dioxolane (An explanation of this behaviour can be found in **Chapter IV**):

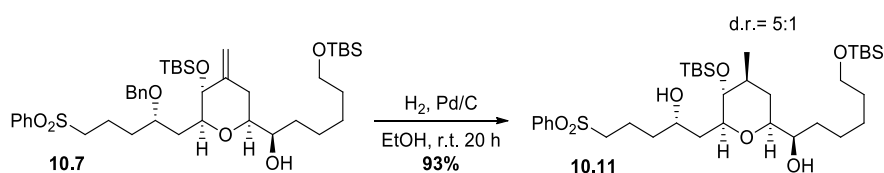


¹H NMR (300 MHz, CDCl₃) δ 7.88 (d, *J* = 7.2 Hz, 2H, C₃H), 7.66 (t, *J* = 7.3 Hz, 1H, C₁H), 7.56 (t, *J* = 7.5 Hz, 2H, C₂H), 7.42 – 7.15 (m, 5H, C₂₅H, C₂₆H, C₂₇H), 5.07 (s, 1H, C₂₉HH), 4.90 (s, 1H, C₂₉HH), 4.78 – 4.64 (m, 1H, C₁₅H), 4.53 (d, *J* = 11.7 Hz, 1H, C₂₃HH), 4.33 (d, *J* = 11.6 Hz, 1H, C₂₃HH), 3.79 – 3.42 (m, 6H, C₈H, C₁₁H, C₁₄H, C₂₁H, C₂₂HH), 3.21 – 2.93 (m, 6H, C₅HH, C₂₈HHH, C₁₀H), 2.49 – 1.20 (m, 18H, C₆HH, C₇HH, C₉HH, C₁₃HH, C₁₆HH, C₁₇HH, C₁₈HH, C₁₉HH, C₂₀HH), 0.98 – 0.83 (m, 9H, C₃₃HHH), 0.08 (s, 3H, C₃₁HHH), 0.04 (s, 3H, C₃₀HHH). **¹³C NMR** (75 MHz, CDCl₃) δ 145.45 (C₁₂), 138.57, 138.48 (C₄, C₂₄), 133.80 (C₁), 129.42, 128.60, 128.20, 128.01, 127.87 (C₂, C₃, C₂₅, C₂₆, C₂₇), 108.23 (C₂₉), 84.14 (C₁₅), 80.53, 77.36 (C₁₀, C₁₄), 75.44 (C₈), 74.41 (C₁₁), 72.14 (C₂₁), 70.86 (C₂₃), 66.98 (C₂₂), 56.08 (C₅), 38.97 (C₂₈), 36.31 (C₉), 33.04, 32.51, 31.01, 29.25, 28.32, 26.17, 26.00, 25.90 (C₇, C₁₃, C₁₆, C₁₇, C₁₈, C₁₉, C₂₀, C₃₃), 19.28 (C₆), 18.22 (C₃₂), -4.22, -4.54 (C₃₀, C₃₁). **IR** (neat, cm⁻¹) 3500, 2930, 2858, 1350, 1319, 1306, 1252, 1173, 1144, 1109, 1070. **MSMS** (p ESI), *m/z* (%): 783.36 (66), 687.33 (100), 537.27 (53), 447.22 (33), 439.21 (45), 393.30 (23), 343.23 (50), 239.07 (15), 229.06 (34), 211.04 (42), 183.05 (13), 143.02 (20), 91.05 (90).

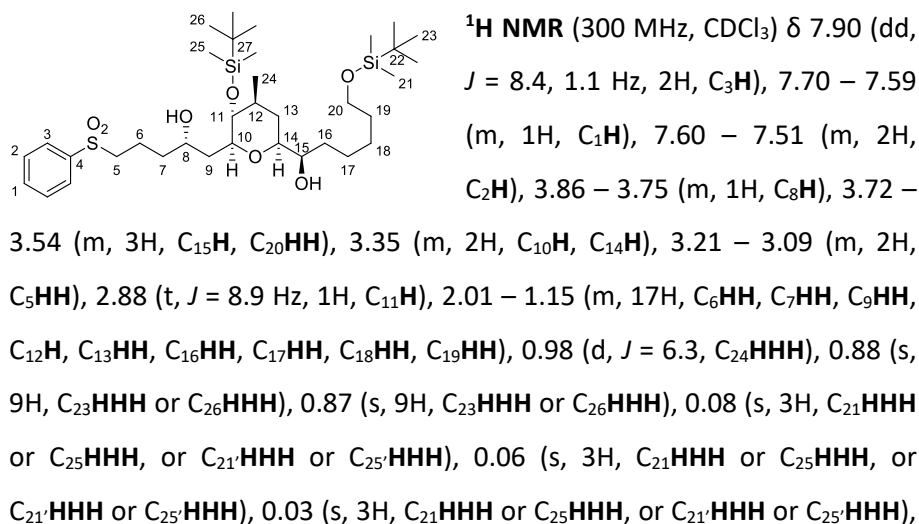
Experimental

HRMS, m/z : calculated for (C₃₉H₆₂O₁₀S₂SiNa) [M + 23]: 805.3446. Found: 805.3434.

(*R*)-6-((tert-butyldimethylsilyl)oxy)-1-((2*S*,4*S*,5*R*,6*S*)-5-((tert-butyldimethylsilyl)oxy)-6-((*S*)-2-hydroxy-5-(phenylsulfonyl)pentyl)-4-methyltetrahydro-2H-pyran-2-yl)hexan-1-ol



A 10 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with alcohol **10.7** (150 mg, 0.22 mmol, 1 eq.), Pd/C (10%, 20 mg) and EtOH (5 mL). Resulting mixture was left stirring at room temperature for 20 h. After complete conversion, the mixture was filtered through celite®. The latter was washed with AcOEt (5 x 25 mL). Combined organic fractions were concentrated under reduced pressure to yield tetrahydropyran **10.11** as white sticky oil (139 mg, quant.).

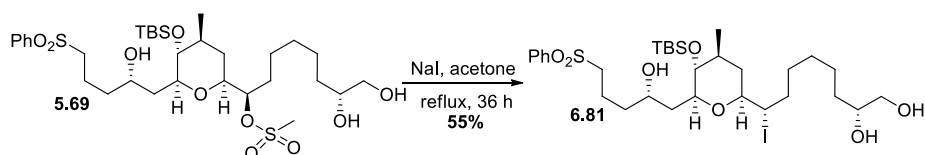


0.02 (s, 3H, C₂₁HHH or C₂₅HHH, or C_{21'}HHH or C_{25'}HHH). ¹³C NMR (75 MHz, CDCl₃) δ 139.25 (C₄), 133.73, 129.38, 128.21 (C₁, C₂, C₃), 83.95, 80.10 (C₁₀, C₁₄), 77.30 (C₁₁), 73.19 (C₁₅), 71.86 (C₈), 62.81 (C₂₀), 56.36 (C₅), 38.92 (C₉), 37.65 (C₁₂), 35.99, 32.77, 32.63, 32.47, 26.16, 25.92, 25.78 (C₆, C₇, C₁₃, C₁₆, C₁₇, C₁₈, C₁₉), 25.72, 25.59 (C₂₃, C₂₆), 19.67 (C₂₄), 19.28, 18.35, (C₂₂, C₂₇), -3.10, -3.49 (C₂₁, C₂₅, C_{21'}, C_{25'}).

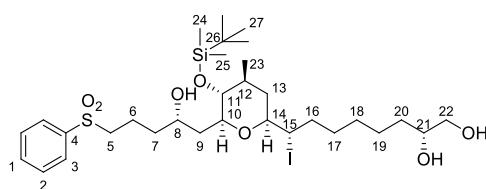
Experimental

10.2.4. Fragmentation and dihydroxylation

(2*R*,8*S*)-8-((2*S*,4*S*,5*R*,6*S*)-5-((tert-butyldimethylsilyl)oxy)-6-((*S*)-2-hydroxy-5-(phenylsulfonyl)pentyl)-4-methyltetrahydro-2*H*-pyran-2-yl)-8-iodooctane-1,2-diol



A 10 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with mesylate **5.69** (50 mg, 0.07 mmol, 1 eq.), NaI (162 mg, 1.05 mmol, 15 eq.) and acetone (5 mL). Resulting mixture was left stirring at reflux for 36 h. The crude reaction mixture was then concentrated under reduced pressure and resulting residue was purified by flash column chromatography on silica gel (PE/AcOEt 1:1 to AcOEt 100%) to afford triol **6.81** as a colorless oil (29 mg, 55%). R_f = 0.48 (AcOEt).



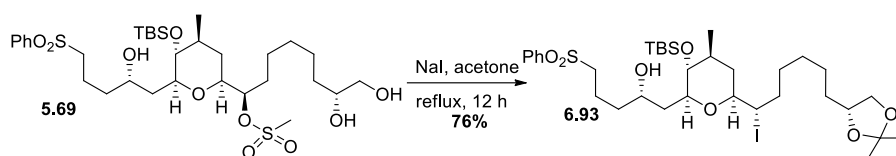
^1H NMR (300 MHz, CDCl_3) δ 7.91

(d, J = 7.7 Hz, 2H, C_3H), 7.65 (t, J = 6.8 Hz, 1H, C_1H), 7.56 (t, J = 7.6 Hz, 2H, C_2H), 3.89 – 2.99 (m, 8H,

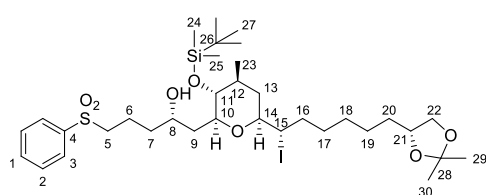
C_5HH , C_8H , C_{10}H , C_{14}H , C_{21}H , C_{22}H), 2.90 (t, J = 8.9 Hz, 1H, C_{11}H), 2.08 – 1.08 (m, 19H, C_6HH , C_7HH , C_9HH , C_{12}H , C_{13}HH , C_{16}HH , C_{17}HH , C_{18}HH , C_{19}HH , C_{20}HH), 0.99 (d, J = 6.4 Hz, 3H, C_{23}HHH), 0.87 (s, 9H, C_{27}HHH), 0.07 (s, 3H, C_{25}HHH), 0.03 (s, 3H, C_{24}HHH). IR (neat, cm^{-1}) 3500, 2930, 2856, 1462, 1447, 1306, 1254, 1148, 1088, 1026, 1007. MSMS (p ESI), m/z (%): 727.36 (34), 559.14 (23), 449.23 (41), 431.22 (100), 413.21 (55), 395.20 (38), 269.08 (33), 251.07 (75), 239.07 (42), 213.06 (22), 161.13 (28), 143.02 (35), 133.10

(56). **HRMS**, m/z : calculated for $(C_{31}H_{55}O_7I\text{SSiNa})$ $[M + 23]$: 749.2375. Found: 749.2360.

(S)-1-((2S,3R,4S,6S)-3-((tert-butyldimethylsilyl)oxy)-6-((S)-6-((R)-2,2-dimethyl-1,3-dioxolan-4-yl)-1-iodohexyl)-4-methyltetrahydro-2H-pyran-2-yl)-5-(phenylsulfonyl)pentan-2-ol



A 10 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with mesylate **5.69** (85 mg, 0.085 mmol, 1 eq.), NaI (457 mg, 3.05 mmol, 25 eq.) and acetone (6 mL). Resulting mixture was left stirring at reflux for 12 h. The crude reaction mixture was then concentrated under reduced pressure and resulting residue was purified by flash column chromatography on silica gel (PE/AcOEt 2:1) to give alcohol **6.93** as a colorless oil (51 mg, 76%). R_f = 0.94 (AcOEt, UV or Vanillin, blue).



^1H NMR (300 MHz, CDCl_3) δ 8.02

– 7.83 (m, 2H, C_3H), 7.69 – 7.49

(m, 3H, C_1H , C_2H), 4.11 – 3.98 (m,

3H, C_{15}H , C_{22}HH), 3.96 – 3.22 (m,

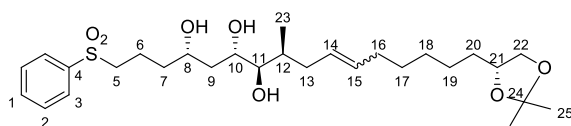
4H, C_8H , C_{10}H , C_{14}H , C_{21}H), 3.22 – 3.10 (m, 2H, C_5HH), 2.89 (t, J = 9.0 Hz, 1H,

C_{11}H), 2.02 – 1.16 (m, 19H, C_6HH , C_7HH , C_9HH , C_{12}H , C_{13}HH , C_{16}HH , C_{17}HH ,

C_{18}HH , C_{19}HH , C_{20}HH), 0.98 (d, J = 6.5 Hz, 3H, C_{23}HHH), 0.87 (s, 9H, C_{27}HHH),

0.06 (s, 3H, C_{24}HHH), 0.03 (s, 3H, C_{25}HHH). **^{13}C NMR** (75 MHz, CDCl_3) δ

139.25 (C_4), 133.70 (C_1), 129.37, 128.21 (C_2 , C_3), 108.78 (C_{28}), 83.87 (C_{10}),

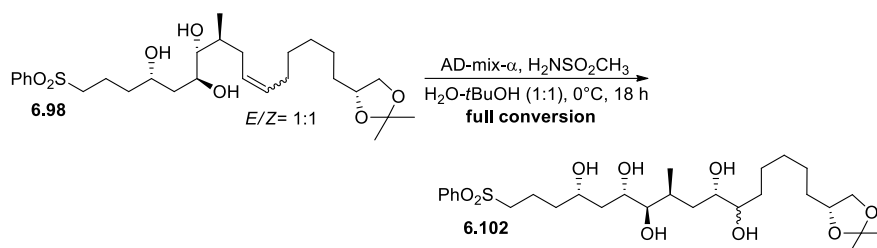


^1H NMR (300 MHz, CDCl_3) δ 7.91 (d, $J = 7.2$ Hz, 2H, C_3H), 7.66 (t, $J =$

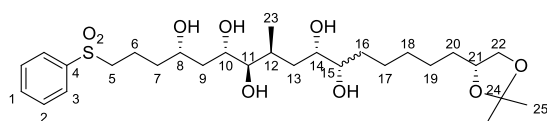
7.4 Hz, 1H, C_1H), 7.57 (t, $J = 7.4$ Hz, 2H, C_2H), 5.51 – 5.31 (m, 2H, C_{14}H , C_{15}H), 4.12 – 3.99 (m, 2H, C_{21}H , C_{22}HH), 3.97 – 3.83 (m, 2H, C_8H , C_{10}H), 3.49 (t, $J = 6.9$ Hz, 1H, C_{22}HH), 3.42 – 3.35 (m, 1H, C_{11}H), 3.20 – 3.11 (m, 2H, C_5HH), 2.11 – 1.18 (m, 25H, C_6HH , C_7HH , C_9HH , C_{12}H , C_{13}HH , C_{16}HH , C_{17}HH , C_{18}HH , C_{19}HH , C_{20}HH , C_{25}HHH , $\text{C}_{25'}\text{HHH}$), 0.96 (d, $J = 7.6$ Hz, 1H, C_{23}HHH for the *Z* or *E* isomer), 0.95 (d, $J = 6.6$ Hz, 3H, C_{23}HHH for the *Z* or *E* isomer). **^{13}C NMR** (75 MHz, CDCl_3) δ 139.22 (C_4), 133.90 (C_1), 132.85, 131.75 (C_{14} and/or C_{15} *E* and/or *Z* isomer), 129.49 (C_2), 128.17 (C_3), 127.77, 127.41 (C_{14} and/or C_{15} *E* and/or *Z* isomer), 108.76 (C_{24}), 77.36 (C_{11}), 76.25 (C_{21}), 71.59 (C_8 , C_{10}), 69.63 (C_{22}), 56.15 (C_5), 37.77, 36.85, 36.54, 34.57, 34.32, 33.71, 32.58, 32.07, 31.32, 29.85, 29.57, 29.51, 29.41, 29.25, 27.35, 27.11, 25.90, 25.77, 25.71, 22.84, 18.90 (C_6 , C_7 , C_9 , C_{12} , C_{13} , C_{16} , C_{17} , C_{18} , C_{19} , C_{20} , C_{25} , $\text{C}_{25'}$ for the *E* and the *Z* isomers), 14.45, 14.35 (C_{23} *E* and *Z* isomer). **MSMS** (p ESI), m/z (%): 487.36 (76), 433.24 (100), 397.22 (37), 270.06 (39), 239.07 (45), 213.06 (80), 143.02 (60), 135.12 (50). **HRMS**, m/z : calculated for $(\text{C}_{28}\text{H}_{47}\text{O}_7\text{S})$ [$\text{M} + 1$]: 527.3037. Found: 527.3037.

Experimental

(4*S*,6*S*,7*R*,8*S*,10*S*)-16-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-8-methyl-1-(phenylsulfonyl)hexadecane-4,6,7,10,11-pentaol



A 10 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with triol **6.98** (10 mg, 0.02 mmol, 1 eq.), AD-mix- α (27 mg, 0.02 mmol, 1 eq.), H_2O (0.1 mL), $t\text{BuOH}$ (0.1 mL), methylsulfonamide (2 mg, 0.02 mmol, 1 eq.) and a droplet of an aqueous solution of OsO_4 (5%w). Resulting mixture was left stirring at 0°C for 18 h. Then Na_2SO_3 (29 mg) was added to the crude reaction mixture and stirring was continued for another hour. At that moment, AcOEt (5 mL) and H_2O (5 mL) were added. After separation, combined organic fractions were dried over MgSO_4 , concentrated under reduced pressure and purified by flash column chromatography on silica gel (AcOEt 100% to DCM/MeOH 9:1) to furnish polyol **6.102** (quant). R_f = 0.11 (DCM/MeOH 9:1, UV or Vanillin, blue).



^1H NMR (300 MHz, CDCl_3) δ

7.91 (d, J = 7.2 Hz, 2H, C_3H),

7.67 (t, J = 7.4 Hz, 1H, C_1H),

7.57 (t, J = 7.4 Hz, 2H, C_2H), 4.12 – 3.99 (m, 2H, C_{21}H , C_{22}HH), 3.91 – 3.36 (m,

6H C_8H , C_{10}H , C_{11}H , C_{14}H , C_{15}H , C_{22}HH), 3.15 (t, J = 7.7 Hz, 2H, C_5HH), 1.95 –

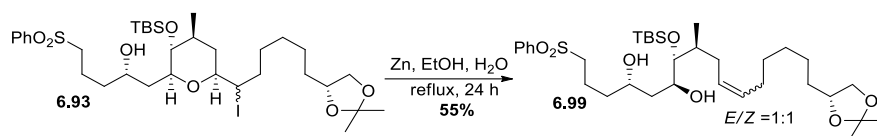
1.23 (m, 17H, C_6HH , C_7HH , C_9HH , C_{12}H , C_{16}HH , C_{17}HH , C_{18}HH , C_{19}HH , C_{20}HH),

1.40 (s, 3H, C_{25}HHH), 1.35 (s, 3H, C_{25}HHH), 0.99 (d, J = 6.8, 3H, C_{23}HHH), 0.98

(d, J = 6.8, 3H, C_{23}HHH other isomer). **MSMS** (p ESI), m/z (%): 431.22 (100),

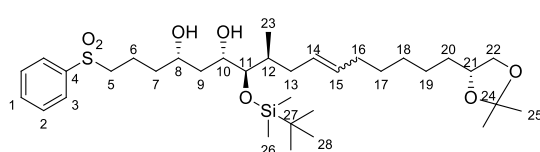
413.21 (36), 393.12 (57), 237.18 (45), 213.06 (60). **HRMS**, m/z : calculated for (C₂₈H₄₉O₉S) [M + 1]: 561.3092. Found: 561.3089.

(4*S*,6*S*,7*R*,8*S*)-7-((tert-butyldimethylsilyl)oxy)-16-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-8-methyl-1-(phenylsulfonyl)hexadec-10-ene-4,6-diol



Zinc activation: Zinc dust was washed subsequently with HCl aq 1M (3 x 20 mL), H₂O (3 x 20 mL), Et₂O (3 x 20 mL) and finally dried in vacuo.

A 10 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with iodate **6.93** (47 mg, 0.06 mmol, 1 eq.), activated zinc dust (120 mg, 1.80 mmol, 30 eq.), H₂O (0.2 mL) and EtOH (4 mL). Resulting mixture was left stirring at reflux for 24 h. The crude reaction mixture was filtered on silica gel, then purified by flash column chromatography on silica gel (PE/AcOEt 1:1 to AcOEt 100%) to furnish polyol **6.99**. (20 mg isolated, 55% estimated by ¹H NMR). R_f = 0.54 (AcOEt/PE 1:1, UV or Vanillin, blue).



¹H NMR (300 MHz, CDCl₃) δ

7.91 (d, J = 7.1 Hz, 2H, C₃H),

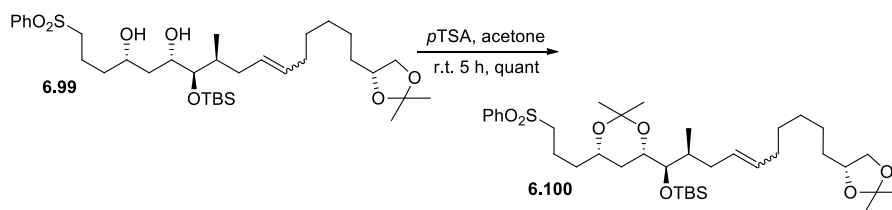
7.65 (t, J = 7.3 Hz, 1H, C₁H),

7.56 (t, J = 7.4 Hz, 2H, C₂H), 5.49 – 5.24 (m, 2H, C₁₄H, C₁₅H), 4.13 – 3.98 (m, 2H, C₂₁H, C₂₂HH), 3.94 – 3.75 (m, 2H, C₈H, C₁₀H), 3.49 (t, J = 6.7 Hz, 2H, C₁₁H, C₂₂HH), 3.20 – 3.10 (m, 2H, C₅HH), 2.13 – 1.04 (m, 25H, C₆HH, C₇HH, C₉HH, C₁₂H, C₁₃HH, C₁₆HH, C₁₇HH, C₁₈HH, C₁₉HH, C₂₀HH, C₂₅HHH, C₂₅HHH), 0.96 – 0.85 (m, 12H, C₂₃HHH, C₂₈HHH), 0.11 – 0.04 (m, 6H, C₂₆HHH). **MSMS** (p

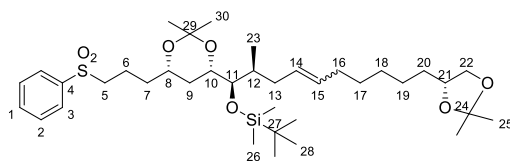
Experimental

APCI, m/z (%): 641.27 (20), 433.24 (100), 397.22 (60), 213.06 (97), 187.15 (45), 143.02 (46). **HRMS**, m/z : calculated for $(C_{34}H_{61}O_7SSi)$ $[M + 1]$: 641.3902. Found: 641.3898.

tert-butyl(((1R,2S)-10-((R)-2,2-dimethyl-1,3-dioxolan-4-yl)-1-((4S,6S)-2,2-dimethyl-6-(3-(phenylsulfonyl)propyl)-1,3-dioxan-4-yl)-2-methyldec-4-en-1-yl)oxy)dimethylsilane



A 10 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with diol **6.99** (10 mg), acetone (1 mL) and $pTSA$ (1 single crystal). Resulting mixture was left stirring at room temperature for 5 h. The crude reaction mixture was immediately purified by flash column chromatography on silica gel (PE/AcOEt 3:1) to furnish olefin **6.100** (8 mg isolated, quant). R_f = 0.65 (AcOEt /PE 1:1, UV or Vanillin, blue).



^1H NMR (300 MHz, $CDCl_3$) δ

7.91 (d, J = 7.1 Hz, 2H, C_3H),

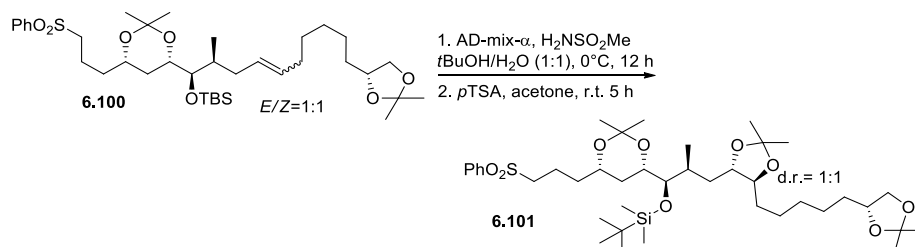
7.66 (t, J = 7.4 Hz, 1H, C_1H), 7.57

(t, J = 7.4 Hz, 2H, C_2H), 5.48 –

5.24 (m, 2H, $C_{14}H$, $C_{15}H$), 4.14 – 3.95 (m, 2H, $C_{21}H$, $C_{22}HH$), 3.76 (ddd, J = 11.3, 5.8, 2.6 Hz, 2H, C_8H , $C_{10}H$), 3.53 – 3.46 (m, 1H, $C_{22}HH$), 3.46 – 3.38 (m, 1H, $C_{11}H$), 3.23 – 3.01 (m, 2H, C_5HH), 2.12 – 1.08 (m, 31H, C_6HH , C_7HH , C_9HH , $C_{12}H$, $C_{13}HH$, $C_{16}HH$, $C_{17}HH$, $C_{18}HH$, $C_{19}HH$, $C_{20}HH$, $C_{25}HHH$, $C_{25'}HHH$,

C_{30} HHH, $C_{30'}$ HHH), 1.02 – 0.87 (m, 9H, C_{28} HHH), 0.84 (d, J = 6.8 Hz, 3H, C_{23} HHH), 0.09 – -0.00 (m, 6H, C_{26} HHH). ^{13}C NMR (75 MHz, CDCl_3) δ 139.27 (C_4), 133.76 (C_1), 141.49 (C_{14} or C_{15}), 129.40 (C_2), 128.75 (C_{14} or C_{15}), 128.21 (C_3), 108.73 (C_{24}), 98.47 (C_{29}), 78.38 (C_{11}), 76.26 (C_{21}), 70.36 (C_{10} or C_8), 69.66 (C_{22}), 68.47 (C_{10} or C_8), 56.29 (C_5), 36.55, 36.39, 34.98, 33.72, 32.85, 32.66, 31.61, 30.06, 29.84, 29.28, 27.10, 26.28, 25.90, 25.77, 19.78, 18.97 (C_6 , C_7 , C_9 , C_{12} , C_{13} , C_{16} , C_{17} , C_{18} , C_{19} , C_{20} , C_{25} , $C_{25'}$, C_{28} , C_{30} , $C_{30'}$), 18.88 (C_{27}), 14.39 (C_{23}), -3.30, -4.05 (C_{26} , $C_{26'}$). **MSMS** (p ESI), m/z (%): 703.40 (100), 645.36 (40), 235.04 (20). **HRMS**, m/z : calculated for ($C_{37}H_{64}O_7SSiNa$) [$M + 23$]: 703.4034. Found: 703.4027.

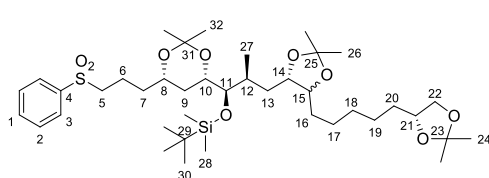
tert-butyl((1*R*,2*S*)-3-((4*S*,5*S*)-5-(5-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)pentyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-1-((4*S*,6*S*)-2,2-dimethyl-6-(3-(phenylsulfonyl)propyl)-1,3-dioxan-4-yl)-2-methylpropoxy)dimethylsilane



A 5 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with olefin **6.100** (5 mg, 0.007 mmol, 1 eq.), AD-mix- α (10 mg, 0.007 mmol, 1 eq.), H_2O (0.1 mL), $t\text{BuOH}$ (0.1 mL), methylsulfonamide (1 crystal) and a droplet of an aqueous solution of OsO_4 (5%w). Resulting mixture was left stirring at 0°C for 12 h. Then Na_2SO_3 (10 mg) was added to the crude reaction mixture and stirring was continued for 1 h. At that moment, AcOEt (5 mL) and H_2O (5 mL) were added. After separation,

Experimental

combined organic fractions were dried over MgSO_4 , concentrated under reduced pressure and used without further purification. A 5 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with crude diol, acetone (1 mL) and *p*TSA (1 single crystal). Resulting mixture was left stirring at room temperature for 5 h. The crude reaction mixture was immediately purified by column chromatography (PE/AcOEt 3:1) to furnish **6.101** as a 0.4: 0.6 mixture of two diastereoisomers. R_f = 0.51 (AcOEt/PE 2:1, UV or Vanillin, blue).



^1H NMR (500 MHz, CDCl_3) δ 7.91

(d, J = 7.2 Hz, 2H, C_3H), 7.66 (t, J =

7.4 Hz, 1H, C_1H), 7.57 (t, J = 7.7

Hz, 2H, C_2H), 4.14 – 4.00 (m, 3H,

C_{21}H , C_{22}HH , C_{14}H or C_{15}H), 3.81 – 3.70 (m, 2H, C_8H , C_{10}H), 3.56 – 3.37 (m,

3H, C_{11}H , C_{14}H or C_{15}H , C_{22}H), 3.19 – 3.06 (m, 2H, C_5HH), 2.03 – 1.01 (m,

C_6HH , C_7HH , C_9HH , C_{12}H , C_{13}HH , C_{16}HH , C_{17}HH , C_{18}HH , C_{19}HH , C_{20}HH , C_{24}HHH ,

$\text{C}_{24'}\text{HHH}$, C_{26}HHH , $\text{C}_{26'}\text{HHH}$, C_{32}HHH , $\text{C}_{32'}\text{HHH}$), 0.93 – 0.85 (m, 12H, C_{27}HHH ,

C_{30}HHH), 0.07 (s, 3H, C_{28}HHH), 0.04 (s, 3H, C_{30}HHH). IR (neat, cm^{-1}) 2924,

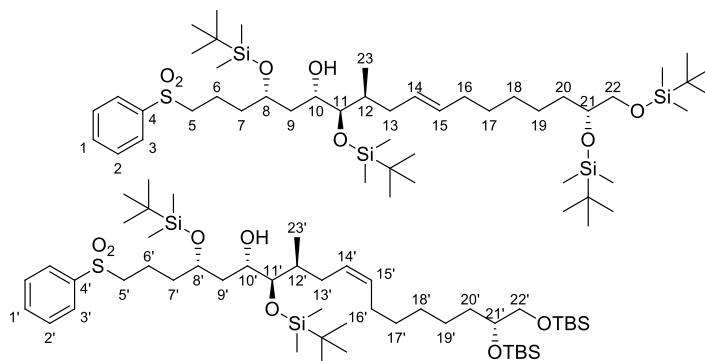
2854, 1462, 1448, 1379, 1369, 1308, 1290, 1256, 1148, 1086, 1072. MS (p

APCI), m/z (%): 715.42 (80), 675.40 (55), 639.38 (36), 507.28 (60), 449.24

(63), 391.28 (100), 227.07 (26), 149.02 (37). HRMS, m/z : calculated for

($\text{C}_{40}\text{H}_{71}\text{O}_9\text{SiS}$) [$\text{M} + 1$]: 755.4583. Found: 755.4591.

Experimental



Pure *E* olefin

¹H NMR (500 MHz, CDCl₃) δ 7.90 (d, *J* = 7.2 Hz, 2H, C₃H), 7.65 (t, *J* = 7.5 Hz, 1H, C₁H), 7.56 (t, *J* = 7.7 Hz, 2H, C₂H), 5.40 (td, *J* = 15.1, 6.7 Hz, 1H, C₁₄H), 5.31 (td, *J* = 15.1, 6.7 Hz, 1H, C₁₅H), 3.91 – 3.86 (m, 1H, C₁₀H), 3.69 – 3.60 (m, 2H, C₈H, C₂₁H), 3.50 (dd, *J* = 9.9, 5.6 Hz, 1H, C₂₂HH), 3.43 – 3.40 (m, 1H, C₁₁H), 3.39 (dd, *J* = 9.9, 6.3 Hz, 1H, C₂₂HH), 3.10 (dt, *J* = 9.7, 5.9 Hz, 2H, C₅HH), 2.50 (d, *J* = 2.6 Hz, 1H, OH), 2.06 – 1.15 (m, 19H, C₆HH, C₇HH, C₉HH, C₁₂H, C₁₃HH, C₁₆HH, C₁₇HH, C₁₈HH, C₁₉HH, C₂₀HH), 0.90 – 0.82 (m, 39H, C₂₃HHH, Si-C(CH₃)₃), 0.07 (s, 3H, Si-CH₃), 0.05 (s, 6H, Si-CH₃), 0.04 (s, 3H, Si-CH₃), 0.04 (s, 3H, Si-CH₃), -0.00 (s, 3H, Si-CH₃).

Pure *Z* olefin

¹H NMR (500 MHz, CDCl₃) δ 7.90 (dd, *J* = 8.4, 1.2 Hz, 2H C₃H), 7.65 (t, *J* = 7.5 Hz, 1H, C₁H), 7.56 (t, *J* = 7.7 Hz, 2H, C₂H), 5.45 – 5.23 (m, 2H, C₁₄H, C₁₅H), 3.92 – 3.85 (m, 1H, C₁₀H), 3.70 – 3.60 (m, 2H, C₈H, C₂₁H), 3.50 (dd, *J* = 9.9, 5.6 Hz, 1H, C₂₂HH), 3.42 (dd, *J* = 4.6, 3.6 Hz, 1H, C₁₁H), 3.39 (dd, *J* = 10, 6.3 Hz, 1H, C₂₂HH), 3.15 – 3.05 (m, 2H, C₅HH), 2.56 (d, *J* = 2.4 Hz, 1H, OH), 2.06 – 1.19 (m, 19H, C₆HH, C₇HH, C₉HH, C₁₂H, C₁₃HH, C₁₆HH, C₁₇HH, C₁₈HH, C₁₉HH, C₂₀HH), 0.94 – 0.77 (m, 39H, C₂₃HHH, Si-C(CH₃)₃), 0.07 (s, 3H, Si-CH₃), 0.07 (s, 3H, Si-CH₃), 0.07 (s, 3H, Si-CH₃), 0.07 (s, 3H, Si-CH₃).

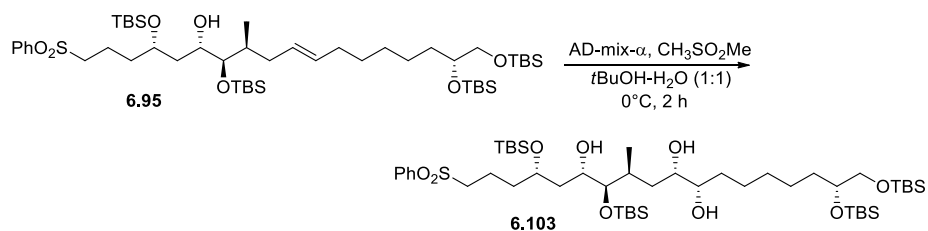
0.07 (s, 3H, Si-CHHH), 0.05 (s, 6H, Si-CHHH), 0.05 (s, 6H, Si-CHHH), 0.04 (s, 3H, Si-CHHH), 0.04 (s, 3H, Si-CHHH), -0.00 (s, 3H, Si-CHHH), -0.00 (s, 3H, Si-CHHH).

Following analyses were carried out on the 1: 1 mixture

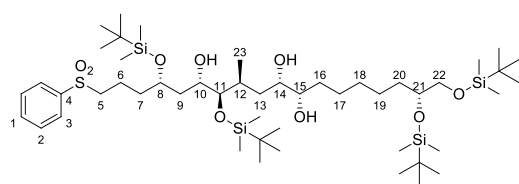
¹³C NMR (126 MHz, CDCl₃) δ 139.07 (C₄, C_{4'}), 133.79 (C₁, C_{1'}), 132.38, 131.35 (C₁₄ and/or C_{14'} and/or C₁₅ and/or C_{15'}), 129.41 (C₂, C_{2'}), 128.69, 128.31 (C₁₄ and/or C_{14'} and/or C₁₅ and/or C_{15'}), 128.26 (C₃, C_{3'}), 78.61, 78.28, 73.29, 71.95, 71.83, 71.01, 70.92 (C₈, C_{8'}, C₁₀, C_{10'}, C₁₁, C_{11'}, C₂₁, C_{21'}), 67.63 (C₂₂, C_{22'}), 56.56 (C₅, C_{5'}), 39.18, 37.84, 35.75, 35.62, 35.58, 34.46, 32.78, 32.43, 29.83, 29.81, 29.74, 29.55, 27.72 (C₆, C_{6'}, C₇, C_{7'}, C₉, C_{9'}, C₁₂, C_{12'}, C₁₃, C_{13'}, C₁₆, C_{16'}, C₁₇, C_{17'}, C₁₈, C_{18'}, C₁₉, C_{19'}, C₂₀, C_{20'}), 26.19, 26.15, 26.07, 25.94 (4 x Si-C(CHHH)₃), 19.13, 19.08, 18.55, 18.49, 18.32 (4 x Si-C(CHHH)₃), 14.63, 14.48 (C₂₃, C_{23'}), -3.66, -3.69, -4.03, -4.09, -4.37, -4.55, -5.13, -5.20 (Si-CHHH). **IR** (cm⁻¹, neat) 2928, 2883, 2854, 1462, 1447, 1406, 1367, 1360, 1319, 1306, 1254, 1146, 1088, 1025. **MS** (p ESI), m/z (%): 965.60 (92), 943.62 (100), 829.53 (30), 811.52 (20), 679.42 (20), 547.33 (20). **HRMS**, m/z: calculated for (C₄₉H₉₉O₇SSi₄) [M + 1]: 943.6183. Found: 943.6180.

Experimental

**(5*S*,7*S*,8*R*,9*S*,11*S*,12*S*,18*R*)-7,8,18-tris((tert-butyldimethylsilyl)oxy)-
2,2,3,3,9,21,21,22,22-nonamethyl-5-(3-(phenylsulfonyl)propyl)-4,20-
dioxo-3,21-disilatricosane-11,12-diol**



A 5 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with *E*-olefin **6.95** (5 mg, 0.005 mmol, 1 eq.), AD-mix- α (6 mg, 0.005 mmol, 1 eq.) H_2O (0.3 mL), *t*BuOH (0.3 mL) and MeSO_2NH_2 (1 mg). Resulting mixture was left stirring at 0°C for 2 h. The crude reaction mixture was treated with AcOEt (20 mL) and water (20 mL). After phase separation, the aqueous layer was extracted with AcOEt (20 mL). Combined organic fractions were washed with NaOH 5M (3 x 5 mL), then dried over MgSO_4 and concentrated in vacuo to afford polyol **6.103**.



^1H NMR (300 MHz, CDCl_3) δ

7.90 (d, $J = 7.1$ Hz, 2H, C_3H),

7.64 (d, $J = 7.2$ Hz, 1H, C_1H),

7.56 (t, $J = 7.4$ Hz, 2H, C_2H),

3.98 – 3.86 (m, 1H, C_{10}H), 3.77 – 3.58 (m, 3H, C_8H , C_{21}H , C_{14}H or C_{15}H), 3.51

(dd, $J = 9.9, 5.4$ Hz, 1H, C_{22}HH), 3.54 – 3.48 (m, 1H, C_{14}H or C_{15}H), 3.45 – 3.35

(m, 2H, C_{11}H , C_{22}HH), 3.10 (d, $J = 7.7$ Hz, 2H, C_5HH), 2.07 – 1.03 (m, 37H,

C_6HH , C_7HH , C_9HH , C_{12}H , C_{13}HH , C_{16}HH , C_{17}HH , C_{18}HH , C_{19}HH , C_{20}HH), 0.99 –

0.75 (m, 39H, C_{23}HHH , OSi-C(CHHH)_3), 0.10 – -0.03 (m, 24H, OSi(CHHH)_2).

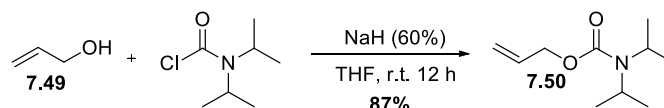
^{13}C NMR (75 MHz, CDCl_3) δ 139.43 (C_4), 133.83 (C_1), 129.45, 128.22 (C_2 , C_3),

79.79, 75.50, 73.28, 72.74, 72.04, 71.23 (C₈, C₁₀, C₁₁, C₁₄, C₁₅, C₂₁), 67.60 (C₂₂), 56.52 (C₅), 38.98 (C₉), 34.46 (C₇), 33.03 (C₁₂), 26.15, 26.07, 25.92 (OSi-C(CH₃)₃), 22.85 (C₆), 18.63 (OSi-C(CH₃)₃), 14.27 (C₂₃), -3.69, -3.79, -3.95, -4.08, -4.28, -4.44, -4.55, -5.14, -5.20 (OSi-CH₃) Remaining carbons: 38.55, 35.83, 33.85, 30.16, 25.77, 25.26, (C₁₃, C₁₆, C₁₇, C₁₈, C₁₉, C₂₀). **IR** (neat, cm⁻¹) 3500, 2955, 2926, 2856, 1462, 1379, 1362, 1306, 1256, 1086, 1072, 1005. **HRMS**, m/z: calculated for (C₄₉H₁₀₁O₉SSi₄) [M + 1]: 977.6238. Found: 977.6238.

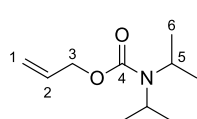
Experimental

10.2.5. Tin allylation

Allyl diisopropylcarbamate



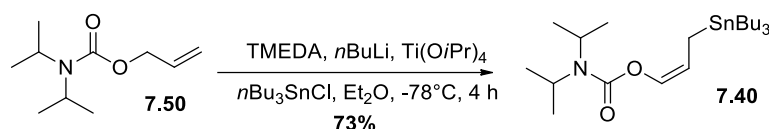
A 1 L round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with NaH (60%, 4.90 g, 122.64 mmol, 1.3 eq.) and THF (650 mL). Resulting mixture was left stirring at 0°C prior to careful addition of allylic alcohol **7.49** (5.93 g, 102.2 mmol, 1 eq.). Finally, carbamoyl chloride (20 g, 122.64 mmol, 1.2 eq.) was added slowly (exothermic reaction) and the reaction mixture was left stirring at room temperature for 12 h. At that moment, the crude mixture was diluted with a saturated aqueous solution of NaHCO₃ (400 mL). After separation, the aqueous layer was extracted with Et₂O (3 x 200 mL). Organic fractions were collected, dried over MgSO₄, concentrated under vacuum and purified by flash column chromatography on silica gel (PE/AcOEt 15:1) to furnish **7.50** (16.41 g, 87% yield). R_f = 0.70 (PE/AcOEt 5:1).



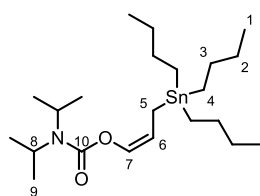
¹H NMR (300 MHz, CDCl₃) δ 5.95 (ddt, J = 17.1, 10.8, 5.5 Hz, 1H, C₂H), 5.30 (dq, J = 17.2, 1.6 Hz, 1H, C₁H-*trans*), 5.19 (ddd, J = 10.5, 2.7, 1.3 Hz, 1H, C₁H-*cis*), 4.59 (dt, J = 5.5, 1.5

Hz, 2H, C₃H), 3.92 (m, 2H, C₅H), 1.21 (d, J = 6.8 Hz, 12H, C₆H). **¹³C NMR** (75 MHz, CDCl₃) δ 155.21 (C₄), 133.38 (C₂), 116.80 (C₁), 65.19 (C₃), 45.71 (C₅), 22.57 (C₆), 20.89 (C_{6'}).

3-(tributylstannyl)prop-1-en-1-yl diisopropylcarbamate



A 1 L round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with a solution of freshly distilled TMEDA (12.54 g, 108 mmol, 2 eq.) in Et₂O (100 mL) at -78°C. Resulting mixture was left stirring at that temperature prior to careful addition of *n*BuLi (43.21 mL, 108 mmol, 2 eq.). After an additional 30 min at -78°C, carbamate **7.50** (10 g, 54 mmol, 1 eq.) in Et₂O (100 mL) was added dropwise to the homogeneous mixture. Resulting yellow mixture was left stirring for 30 min at the same temperature at which point Ti(O*i*Pr)₄ (39.97 mL, 135 mmol, 2.5 eq.) was added in one portion which resulted in a deep brown color. Finally, the solution was left stirring for 30 min prior to addition of *n*Bu₃SnCl (36.62 mL, 135 mmol, 2.5 eq.) in Et₂O (100 mL). The solution was left stirring for a last 30 min period at 0°C. After complete conversion, an aqueous solution of HCl 1M (300 mL) was added slowly. Resulting mixture was filtered on celite® prior to phase separation. The aqueous layer was extracted with Et₂O (3 x 300 mL). Organic fractions were collected, dried over MgSO₄, concentrated under vacuum and purified by flash column chromatography on silica gel (PE/DCM 5:1) to furnish allylstannane **7.40** (18.68 g, 73% yield). R_f = 0.85 (PE/AcOEt 10:1).

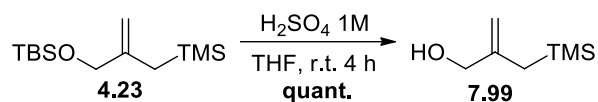


¹H NMR (300 MHz, CDCl₃) δ 6.82 (dt, *J* = 6.2, 1.0 Hz, 1H, C₇H), 4.88 (td, *J* = 9.2, 6.2 Hz, 1H, C₆H), 3.96 (bs, 2H, C₈H), 1.75 (dd, *J* = 9.3, 1.1 Hz, 2H, C₅HH), 1.53 – 1.40 (m, 12H, C₂HH, C₃HH), 1.26 (d, *J* = 6.7 Hz, 12H,

Experimental

C₉HHH), 0.93 – 0.80 (m, 15H, C₄HH, C₁HHH). ¹³C NMR (75.47 MHz, CDCl₃) δ 153.59 (C₁₀), 133.28 (C₇), 112.02 (C₆), 45.80 (C₈), 29.25 (C₃), 27.46 (C₂), 20.96 (C₉), 13.85 (C₁), 9.34 (C₄), 7.97 (C₅).

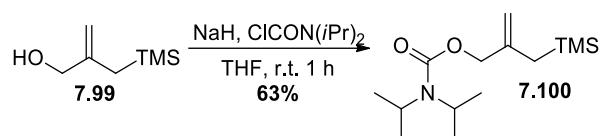
2-((trimethylsilyl)methyl)prop-2-en-1-ol



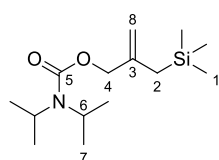
A 50 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with allylsilane **4.23** (3.00 g, 0.0117 mol, 1 eq.), THF (20 mL) and H₂SO₄ (2.3 mL, 1M, 2.3 mmol, 0.2 eq.). Resulting mixture was left stirring at room temperature for 12 h. The crude reaction mixture was treated with a saturated aqueous solution of NaHCO₃ (20 mL). After phase separation, the aqueous layer was extracted with Et₂O (3 x 50 mL). Combined organic phases were dried over MgSO₄, concentrated and purified by flash column chromatography on silica gel (PE/AcOEt 9:1, 1% Et₃N) to yield **7.99** as a colorless liquid (1.68 g, quant). R_f = 0.4 (PE/AcOEt 9:1, Vanillin).

¹H NMR (300 MHz, CDCl₃) δ 4.90 (s, 1H, C₃HH), 4.67 (s, 1H, C₃HH), 3.99 (s, 2H, C₁HH), 1.66 (bs, 1H, OH), 1.53 (s, 2H, C₄HH), 0.03 (s, 9H, C₇HHH). ¹³C NMR (75 MHz, CDCl₃) δ 147.01 (C₂), 106.73 (C₃), 67.16 (C₁), 23.38 (C₄), -1.30 (C₅).

2-((trimethylsilyl)methyl)allyl diisopropylcarbamate



A 100 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with allylsilane **7.99** (3.591 g, 0.025 mol, 1 eq.), Et₂O (50 mL) and NaH (60% in mineral oil, 1.99 g, 0.05 mol, 2 eq.) Carbamoyl chloride (6.14 g, 0.0375 mmol, 2 eq.) was then added by small portions and reaction mixture was left warming to room temperature and stirred further for 1 h. The crude solution was treated with a saturated aqueous solution of NH₄Cl (30 mL). After phase separation, the aqueous layer was extracted with Et₂O (3 x 50 mL). Combined organic phases were dried over MgSO₄, concentrated and purified by flash column chromatography on silica gel (PE/AcOEt 20:1, 1% Et₃N) to yield **7.100** as a colorless liquid (4.262 g, 63%). R_f = 0.55 (PE/AcOEt 9:1, Vanillin).

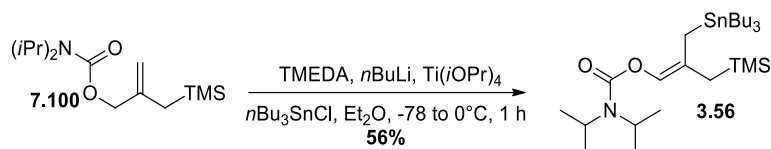


¹H NMR (300 MHz, CDCl₃) δ 4.88 (s, 1H, C₈HH), 4.69 (s, 1H, C₈HH), 4.45 (s, 2H, C₄HH), 3.94 (bs, 2H, C₆H), 1.55 (s, 2H, C₂HH), 1.22 (d, *J* = 6.7 Hz, 12H, C₇HHH), 0.04 (s, 9H, C₁HHH). ¹³C NMR (75 MHz, CDCl₃) δ 155.96 (C₅), 143.47

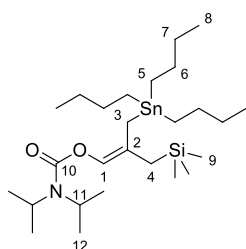
(C₃), 109.24 (C₈), 68.67 (C₄), 46.58 (C₆), 24.37 (C₂), 21.73 (C₇), -0.76 (C₁).

Experimental

(Z)-3-(tributylstannyl)-2-((trimethylsilyl)methyl)prop-1-en-1-yl diisopropylcarbamate



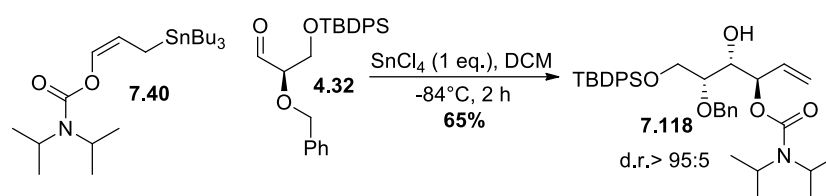
A 250 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with a solution of freshly distilled TMEDA (1.10 mL, 7.4 mmol, 2 eq.) in Et₂O (11 mL) at -78°C. Resulting mixture was left stirring at that temperature prior to careful addition of *n*BuLi (2.5 M in cyclohexane/hexane, 2.96 mL, 7.4 mmol, 2 eq.). After an additional 30 min at -78°C, carbamate **7.100** (1.00 g, 3.7 mmol, 1 eq.) in Et₂O (8 mL) was added dropwise to the homogeneous mixture. Resulting yellow mixture was left stirring for 30 min at the same temperature at which point Ti(*Oi*Pr)₄ (3.26 mL, 11 mmol, 3 eq.) was added in one portion which resulted in a deep brown color. Finally, the solution was left stirring for 30 min prior to addition of *n*Bu₃SnCl (3.0 mL, 11 mmol, 3 eq.) in Et₂O (5 mL). The solution was left stirring for a last 30 min period at 0°C. After complete conversion, a saturated aqueous solution of NaHCO₃ (50 mL) was added slowly. Resulting mixture was filtered on celite® prior to phase separation. The aqueous layer was extracted with Et₂O (3 x 50 mL). Organic fractions were collected, dried over MgSO₄, concentrated under vacuum and purified by flash column chromatography on silica gel (PE/AcOEt 30:1) to furnish allylstannane **3.56** (1.16 g, 56% yield). R_f=0.79 (DCM).



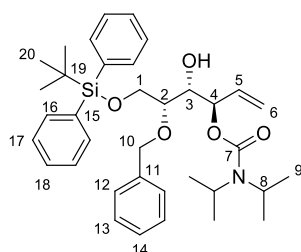
¹H NMR (300 MHz, CDCl₃) δ 6.53 (s, 1H, C₁H), 3.94 (m, 2H, C₁₁H), 1.73 (s, 2H, C₃HH), 1.53 – 1.40 (m, 6H, C₆H), 1.36 – 1.27 (m, 6H, C₇H), 1.24 (m, 14H, C₁₂HHH, C₄HH), 0.92 – 0.82 (m, 15H, C₅HH, C₈HHH), 0.04 (s, 9H, C₉HHH). **¹³C NMR** (75 MHz, CDCl₃) δ 153.31 (C₁₀),

126.39 (C₁), 120.54 (C₂), 46.11 (C₁₁), 29.30 (C₆), 27.55 (C₇), 23.10 (C₄), 20.91 (C₁₂), 14.11 (C₃), 13.85 (C₈), 9.82 (C₅), -0.94 (C₉).

(3*R*,4*R*,5*R*)-5-(benzyloxy)-6-((*tert*-butyldiphenylsilyl)oxy)-4-hydroxyhex-1-en-3-yl diisopropylcarbamate



A 1 L round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with olefin **7.40** (7.14 g, 0.015 mol, 1.05 eq.) and DCM (240 mL). Resulting mixture was left stirring at -78°C for 10 min before adding dropwise SnCl₄ (3.92 g, 0.015 mol, 1.05 eq.). After another 10 min, the mixture is cooled down to -85°C and the aldehyde (6.00 g, 0.014 mol, 1 eq.) in DCM (10 mL) was added carefully. After 2 h, DCM (100 mL) and a saturated aqueous solution of NaHCO₃ (200 mL) were added. After separation, combined organic fractions were dried over MgSO₄, concentrated under reduced pressure and resulting milky residue was purified by column chromatography (PE 100% to PE/ AcOEt 15:1) to furnish **7.118** (5.49 g, 65%). R_f = 0.43 (PE/AcOEt 4:1).

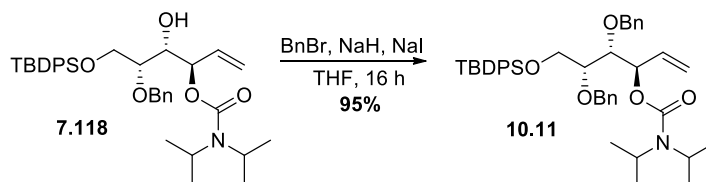


¹H NMR (300 MHz, CDCl₃) δ 7.66 – 7.27 (m, 15H, C₁₂H, C₁₃H, C₁₄H, C₁₆H, C₁₇H, C₁₈H), 6.08 – 5.94 (m, 1H, C₅H), 5.40 – 5.26 (m, 3H, C₆HH, C₄H), 4.62 (d, *J* = 11.2 Hz, 1H, C₁₀HH), 4.51 (d, *J* = 11.1 Hz, 1H, C₁₀HH), 4.04 (bs, 1H, C₈H), 3.87 (td, *J* = 7.9, 2.1 Hz, 1H, C₃H), 3.85 (dd, *J* = 10.2, 6.6 Hz, 1H, C₁HH), 3.77 (dd, *J*

Experimental

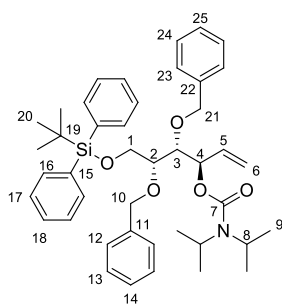
= 10.3, 5.2 Hz, 2H, C₁HH, C₈H), 3.73 – 3.63 (m, 1H, C₂H), 2.52 (d, *J* = 8.2 Hz, 1H, C₃OH), 1.27 – 1.15 (m, 12H, C₉H), 1.04 (s, 9H, C₂₀HHH). ¹³C NMR (125.76 MHz, CDCl₃) δ 154.45 (C₇), 138.03 (C₁₁), 135.73 (C₁₆), 135.66 (C₁₆), 135.01 (C₅), 133.33 (C₁₅), 133.17 (C₁₅), 129.91 (C₁₈), 129.88 (C₁₈), 128.50 (C₁₂), 128.32 (C ar), 127.94 (C ar), 127.88 (C ar), 118.16 (C₆), 77.62 (C₂), 74.73 (C₄), 73.34 (C₁₀), 72.32 (C₃), 63.05 (C₁), 46.55 (C₈), 45.58 (C₈), 26.90 (C₂₀), 21.77 (C₉), 20.76 (C₉), 19.27 (C₁₉). IR (film, cm⁻¹) 3458, 3070, 3053, 3029, 2997, 2960, 2931, 2883, 2856, 1679, 1647, 1471, 1427, 1367, 1299, 1284, 1251, 1190, 1132, 1105, 1047, 1029. MS (D-ESI+), *m/z* (%): 626.11 (80), 603.84 (68), 242.35 (100), 128.11 (5). HRMS, *m/z*: calculated for (C₃₆H₄₉NO₅NaSi) [M + 23]: 626.3278. Found (C₃₆H₄₉NO₅NaSi): 626.3283.

(3*R*,4*R*,5*R*)-4,5-bis(benzyloxy)-6-((*tert*-butyldiphenylsilyl)oxy)hex-1-en-3-yl diisopropylcarbamate



A 100 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with alcohol **7.118** (2.09 g, 3.4 mmol, 1 eq.) and THF (34 mL). NaH (60% in mineral oil, 0.206 g, 5.1 mmol, 1.5 eq.) was then added carefully at 0°C (exothermic reaction was observed). After 10 min of stirring, NaI (tip of spatula) and BnBr (0.63 g, 3.7 mmol, 1.1 eq.) were added to the flask and resulting mixture was left stirring at room temperature for 16 h, before adding a saturated aqueous solution of NH₄Cl. After separation, the aqueous layer was extracted with Et₂O (3 x 20 mL). Combined organic fractions were dried over MgSO₄ and concentrated under reduced pressure. Resulting residue was purified by flash column

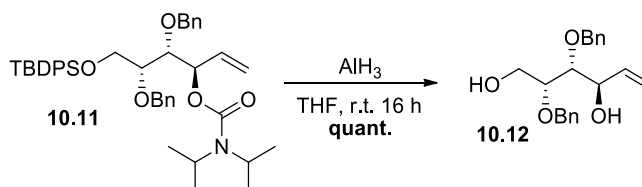
chromatography on silica gel (PE/AcOEt 15:1) to afford the benzylated product **10.11** as a colorless oil (2.24 g, 95%). R_f = 0.87 (PE/AcOEt 4:1, Vanillin, UV).



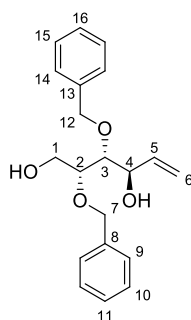
$^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.83 – 7.13 (m, 20H, C_{12}H , C_{13}H , C_{14}H , C_{16}H , C_{17}H , C_{18}H , C_{23}H , C_{24}H , C_{25}H), 6.07 (ddd, J = 17.1, 10.6, 6.3 Hz, 1H, C_5H), 5.51 (t, J = 5.8 Hz, 1H, C_4H), 5.32 (d, J = 17.4 Hz, 1H, $\text{C}_6\text{HH-trans}$), 5.23 (d, J = 10.6 Hz, 1H, $\text{C}_6\text{HH-cis}$), 4.72 (d, J = 11.0 Hz, 1H, C_{10}HH), 4.62 (d, J = 11.1 Hz, 1H, C_{10}HH), 4.56 (d, J = 11.3 Hz, 1H, C_{21}HH), 4.51 (d, J = 11.6 Hz, 1H, C_{21}HH), 3.99 – 3.65 (m, 6H, C_1HH , C_2H , C_3H , C_8H , C_8H), 1.31 – 1.14 (m, 12H, C_9HHH), 1.03 (s, 9H, C_{20}HHH). $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 154.29, 138.64, 138.59, 135.73, 134.94 (C ar), 134.86 (C_5), 133.5, 133.4, 129.68, 129.81, 128.34, 128.31, 128.01, 127.86, 127.85, 127.63, 127.58 (C ar), 117.76 (C_6), 80.83 (C_2), 80.13 (C_3), 74.77, 74.72 (C_4 , C_{21}), 73.69 (C_{10}), 63.03 (C_1), 45.83 (C_8), 26.97 (C_{20}), 21.6 (C_9), 20.89 (C_9), 19.3 (C_{19}). **IR** (film, cm^{-1}) 3069, 3047, 3030, 2997, 2962, 2930, 2887, 2856, 1693, 1472, 1454, 1427, 1310, 1296, 1111, 1086, 1074, 1047, 1028. **MS** (D-APCI+), m/z (%): 693.7 (93), 662.96 (29), 585.99 (88), 440.92 (100), 388.93 (70), 363.03 (23), 282.12 (96), 129.04 (14), 91 (54). **HRMS**, m/z : calculated for ($\text{C}_{43}\text{H}_{55}\text{NO}_5\text{Si}$) [$\text{M} + 1$]: 693.9860. Found ($\text{C}_{43}\text{H}_{55}\text{NO}_5\text{Si}$): 693.987. $[\alpha]_D^{20}$: -6.3 ($c=2.3$, CHCl_3).

Experimental

(2R,3R,4R)-2,3-bis(benzyloxy)hex-5-ene-1,4-diol



A 25 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with carbamate **10.11** (2.25 g, 3.2 mmol, 1 eq.), Et_2O (15 mL) and a solution of AlH_3 in Et_2O (This solution was prepared prior to addition by treating 214 mg of AlCl_3 in 10 mL of Et_2O with 1.2 mL of a 4M solution of LiAlH_4 in Et_2O). Resulting mixture was left stirring at room temperature for 16 h. The crude reaction mixture was then treated carefully with a saturated aqueous solution of NH_4Cl (25 mL). After separation, the aqueous layer was extracted with Et_2O (2 x 30 mL). Combined organic fractions were dried over MgSO_4 , concentrated under reduced pressure and resulting residue was purified by flash column chromatography on silica gel (Et_2O 100%) to give diol **10.12** as a colorless oil (1.05 g, quant). R_f = 0.43 (Et_2O).

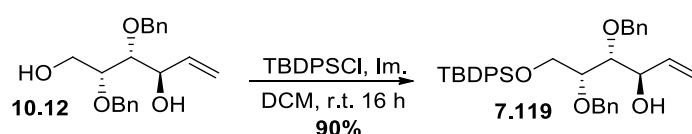


^1H NMR (300 MHz, CDCl_3) δ 7.41 – 7.24 (m, 10H, C_9H , C_{10}H , C_{11}H , C_{14}H , C_{15}H , C_{16}H), 5.94 (ddd, J = 17.1, 10.5, 5.6 Hz, 1H, C_5H), 5.39 (dt, J = 17.2, 1.6 Hz, 1H, $\text{C}_6\text{HH-trans}$), 5.24 (dt, J = 10.5, 1.5 Hz, 1H, $\text{C}_6\text{HH-cis}$), 4.73 (d, J = 11.5 Hz, 1H, C_7HH), 4.66 (d, J = 11.4 Hz, 1H, C_{12}HH), 4.62 (d, J = 10.7 Hz, 1H, C_7HH), 4.61 (d, J = 11.4 Hz, 1H, C_{12}HH), 4.42

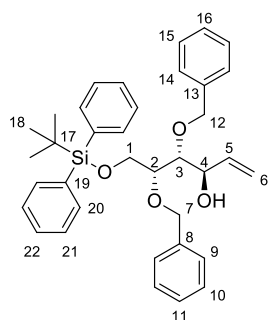
(q, J = 5.6 Hz, 1H, C_4H), 3.85 (m, 1H, C_1HH), 3.78 – 3.63 (m, 2H, C_1HH , C_2H), 3.59 (dd, J = 5.3, 4.1 Hz, 1H, C_3H), 3.10 (d, J = 5.9 Hz, 1H, C_4OH), 2.98 (bs, 1H, C_1OH). **^{13}C NMR** (75 MHz, CDCl_3) δ 137.78 (C_8), 137.70 (C_{13}), 137.54 (C_5), 128.64, 128.62, 128.27, 128.25, 128.15, 128.10 (C_9 , C_{10} , C_{11} , C_{14} , C_{15} , C_{16}), 116.57 (C_6), 80.75 (C_3), 79.41 (C_2), 73.20 (C_7), 72.70 (C_{12}), 72.29 (C_4), 61.47

(C₁). IR (neat, cm⁻¹): 3421, 2920, 2870, 1645, 1454, 1427, 1398, 1350, 1325, 1302, 1259, 1209, 1090, 1074, 1049, 1028. [α]_D²⁰: -14.5 (5.44, CHCl₃).

(3*R*,4*R*,5*R*)-4,5-bis(benzyloxy)-6-((tert-butyldiphenylsilyl)oxy)hex-1-en-3-ol



A 50 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with diol **10.12** (490 mg, 1.5 mmol, 1 eq.), TBDPSCI (431 mg, 1.6 mmol, 1.05 eq.), imidazol (258 mg, 3.8 mmol, 2.5 eq.) and DCM (15 mL). Resulting mixture was left stirring at room temperature for 16 h. The crude reaction mixture was then treated carefully with a saturated aqueous solution of NH₄Cl (25 mL). After separation, the aqueous layer was extracted with DCM (2 x 30 mL). Combined organic fractions were dried over MgSO₄, concentrated under reduced pressure and resulting residue was purified by flash column chromatography on silica gel (PE/AcOEt 20:1) to give alcohol **7.119** as a colorless oil (0.764 g, 90%). R_f = 0.4 (PE/AcOEt 4:1, Vanillin).

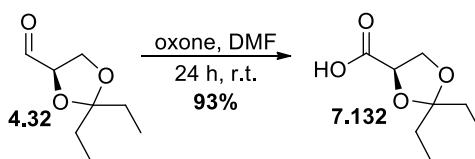


¹H NMR (300 MHz, CDCl₃) δ 7.77 – 7.18 (m, 20H, C₉H, C₁₀H, C₁₁H, C₁₄H, C₁₅H, C₁₆H, C₂₀H, C₂₁H, C₂₂H), 5.87 (ddd, *J* = 17.2, 10.5, 5.3 Hz, 1H, C₅H), 5.32 (dt, *J* = 17.2, 1.6 Hz, 1H, C₆HH), 5.18 (dt, *J* = 10.5, 1.6 Hz, 1H, C₆HH), 4.66 (d, *J* = 11.6 Hz, 1H, C₁₂HH), 4.61 (d, *J* = 11.6 Hz, 1H, C₇HH), 4.57 (d, *J* = 11.6 Hz, 2H, C₁₂HH), 4.44 (d, *J* = 11.5 Hz, 1H, C₇HH), 4.41 – 4.34 (m, 1H, C₄H), 3.94 – 3.82 (m, 2H, C₁HH), 3.79 – 3.72 (m, 1H, C₂H), 3.59 (dd, *J* = 5.6, 3.5 Hz, 1H,

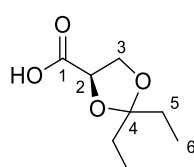
Experimental

C₃H), 1.05 (s, 9H, C₁₈HHH). ¹³C NMR (125 MHz, C₆D₆) δ 139.07 (C₈ or C₁₃), 138.97 (C₅), 138.88 (C₈ or C₁₃), 136.08 (C₂₀), 133.75 (C₁₉), 133.73 (C_{19'}), 130.13 (C₂₂), 130.10 (C_{22'}), 128.63, 128.55, 128.35, 128.20, 128.18, 128.12, 127.71 (C ar), 115.64 (C₆), 80.91 (C₃), 80.88 (C₂), 73.43, 73.28 (C₁₂, C₇), 72.42 (C₄), 63.56 (C₁), 27.12 (C₁₈), 19.44 (C₁₇). IR (neat, cm⁻¹) 3394, 3068, 3047, 3029, 3010, 2929, 2887, 2856, 1645, 1427, 1110, 1087, 1072. MS (D-APCI⁺), m/z (%): 566.6 (10), 563.05 (39), 488.64 (93), 380.76 (21), 220.88 (36), 212.96 (100). HRMS, m/z: calculated for (C₃₆H₄₂O₄NaSi) [M + 23]: 589.2750. Found: 589.2722. [α]_D²⁰: -2.27 (c=0.73, DCM)

(R)-2,2-diethyl-1,3-dioxolane-4-carboxylic acid

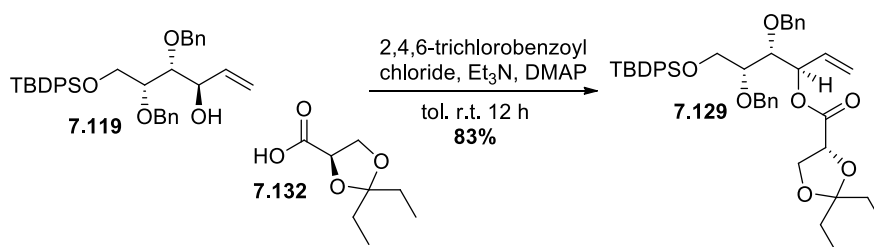


A 50 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with aldehyde **4.32** (300 mg, 1.9 mmol, 1 eq.), oxone (317 mg, 2.1 mmol, 1.1 eq.) and DMF (20 mL). Resulting mixture was left stirring at room temperature for 24 h. The crude reaction mixture was then treated carefully with a saturated aqueous solution of CuSO₄ (25 mL). After separation, the aqueous layer was extracted with AcOEt (2 x 30 mL). Combined organic fractions were dried over MgSO₄, concentrated under reduced pressure and resulting residue was used without further purification.



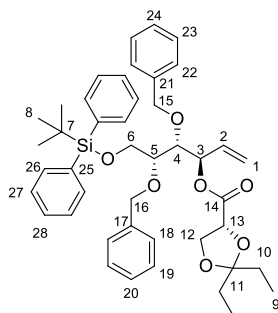
¹H NMR (300 MHz, CDCl₃) δ 4.62 (dd, *J* = 7.6, 6.0 Hz, 1H, C₃HH), 4.33 (m, 1H, C₂H), 4.11 (dd, *J* = 8.6, 6.0 Hz, 1H, C₃HH), 1.76 (q, *J* = 7.5 Hz, 2H, C₅HH), 1.67 (q, *J* = 7.5 Hz, 2H, C₅HH), 1.04 – 0.82 (m, 6H, C₆HHH). **¹³C NMR** (75 MHz, CDCl₃) δ 174.25 (C₁), 116.19 (C₄), 73.86 (C₂), 67.57 (C₃), 29.15, 28.67 (C₅), 8.23, 8.12 (C₆).

(*R*)-(3*R*,4*R*,5*R*)-4,5-bis(benzyloxy)-6-((*tert*-butyldiphenylsilyl)oxy)hex-1-en-3-yl 2,2-diethyl-1,3-dioxolane-4-carboxylate



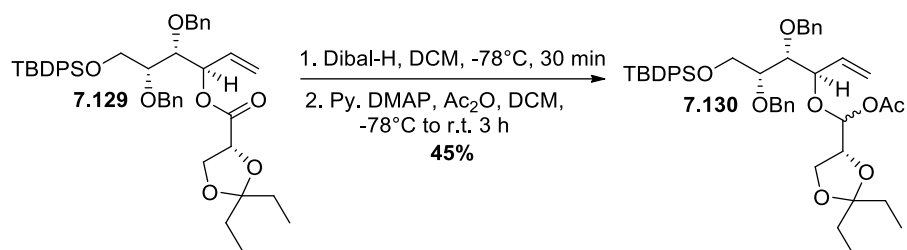
A 25 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with carboxylic acid **7.132** (800 mg, 4.56 mmol, 4.2 eq.), acyl chloride (880 mg, 4.36 mmol, 4 eq.), Et₃N (220 mg, 4.72 mmol, 8 eq.) and toluene (12 mL). Resulting mixture was left stirring at room temperature for 3 h, prior to addition of alcohol **7.119** (160 mg, 1.09 mmol, 1 eq.) in toluene (5 mL). After 1 h, the crude reaction mixture was treated carefully with a saturated aqueous solution of NH₄Cl (25 mL). After separation, the aqueous layer was extracted with DCM (2 x 30 mL). Combined organic fractions were dried over MgSO₄, concentrated under reduced pressure and resulting residue was purified by flash column chromatography on silica gel (PE/AcOEt 10:1) to give ester **7.129** as a colorless oil (659 mg, 83%). *R*_f = 0.47 (PE/AcOEt 4:1, Vanillin).

Experimental



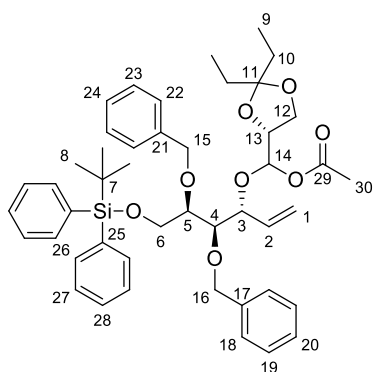
^1H NMR (300 MHz, CDCl_3) δ 7.79 – 7.23 (m, 20H, C_{18}H , C_{19}H , C_{20}H , C_{22}H , C_{23}H , C_{24}H , C_{26}H , C_{27}H , C_{28}H), 6.02 (ddd, $J = 17.4, 10.5, 6.9$ Hz, 1H, C_2H), 5.65 (dd, $J = 6.7, 4.8$ Hz, 1H, C_3H), 5.40 – 5.32 (m, 1H, C_1HH), 5.32 – 5.27 (m, 1H, C_1HH), 4.85 – 4.43 (m, 5H, C_{13}H , C_{15}HH , C_{16}HH), 4.18 – 4.10 (m, 1H, C_{12}HH), 3.97 – 3.78 (m, 4H, C_{12}HH , C_6HH , C_4H or C_5H), 3.64 (dd, $J = 10.2, 5.3$ Hz, 1H, C_4H or C_5H), 1.71 (dq, $J = 12.4, 7.4$ Hz, 4H, C_{10}HH), 1.16 – 1.03 (m, 9H, C_8HHH), 0.99 – 0.90 (m, 6H, C_9HHH). **^{13}C NMR** (75 MHz, CDCl_3) δ 169.81 (C_{14}), 138.38, 138.26 (C_{17} , C_{21}), 135.76, 134.92 (Car), 133.27 (C_{25} , $\text{C}_{25'}$), 132.90 (C_2), 129.93, 129.87, 129.78, 128.37, 128.20, 128.16, 127.90, 127.85 (C ar), 119.56 (C_1), 115.51 (C_{11}), 79.95, 79.80 (C_4 , C_5), 75.28 (C_{13} or C_{15} or C_{16}), 74.57 (C_3), 74.50, 73.34 (C_{13} and/or C_{15} and/or C_{16}), 67.51 (C_{12}), 62.91 (C_6), 29.35, 29.00 (C_{10} , $\text{C}_{10'}$), 26.69 (C_8), 19.28 (C_7), 8.35, 8.08 (C_9 , $\text{C}_{9'}$). **MSMS** (p ESI), m/z (%): 745.36 (14), 571.27 (14), 481.22 (16), 389.16 (41), 373.16 (23), 320.12 (15), 239.05 (19), 179.05 (18), 91.06 (100). **HRMS**, m/z : calculated for $(\text{C}_{44}\text{H}_{54}\text{O}_7\text{NaSi}) [\text{M} + 23]$: 745.3531. Found: 745.3525.

(((3*R*,4*R*,5*R*)-4,5-bis(benzyloxy)-6-((tert-butyldiphenylsilyl)oxy)hex-1-en-3-yl)oxy)((*R*)-2,2-diethyl-1,3-dioxolan-4-yl)methyl acetate



A 10 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with ester **7.129** (100 mg, 0.14 mmol, 1 eq.) in DCM (1 mL) at -78°C. Resulting mixture was left stirring at that temperature and Dibal-H (1M in hexane, 0.28 mL, 0.276 mmol, 2 eq.) was added. After 30 min, pyridine (0.03 mL, 0.415 mmol, 3 eq.) and DMAP (34 mg, 0.276 mmol, 3 eq.) in DCM (1 mL) were added. Finally, acetic anhydride (0.08 mL, 0.83 mmol, 6 eq.) was added dropwise and resulting mixture was stirred at -78°C for 30 min, then allowed to heat up to room temperature and agitation was continued for 3 h. At that moment, the crude reaction mixture was treated carefully with a saturated aqueous solution of Rochelle's salt (10 mL) and DCM (10 mL). After separation, the aqueous layer was extracted with DCM (2 x 10 mL). Combined organic fractions were dried over MgSO₄, concentrated under reduced pressure and resulting residue was purified by flash column chromatography on silica gel (PE/AcOEt 10:1 + 1% Et₃N) to give α-acetoxy ether **7.130** (48 mg, 45%).

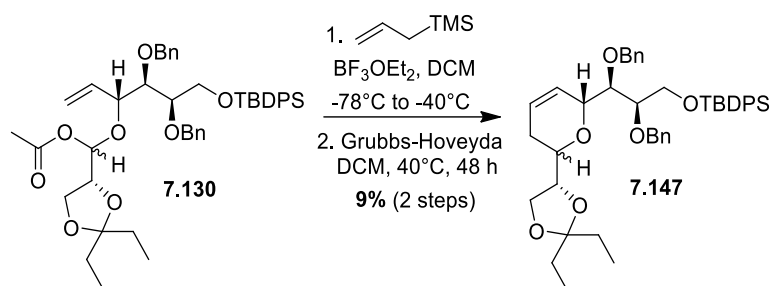
Experimental



¹H NMR (300 MHz, CDCl₃) δ 7.75 —7.16 (m, 16H, C₁₈H, C₁₉H, C₂₀H, C₂₂H, C₂₃H, C₂₄H, C₂₆H, C₂₇H, C₂₈H), 6.16 — 5.78 (m, 2H, C₂H, C₁₄H), 5.67 — 5.54 (m, 1H, C₃H), 5.38 — 5.20 (m, 2H, C₁HH), 4.88 — 4.54 (m, 4H, C₁₅HH, C₁₆HH), 4.52 — 3.52 (m, 7H, C₄H, C₅H, C₆HH, C₁₂HH, C₁₃H), 2.07 (s, 3H, C₃₀HHH), 1.52 (m, 4H, C₁₀HH, C₁₀HH), 1.04 (s, 9H,

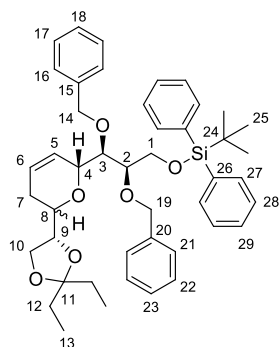
C₈HHH), 0.90 (m, 6H, C₉HHH, C₉HHH). **¹³C NMR** (75 MHz, CDCl₃) δ 169.52 (C₂₉), 138.38, 138.32 (C₁₇, C₂₁), 135.76, 135.47, 133.63, 133.36, 133.31 (C ar.), 132.69 (C₂), 129.83, 128.35, 128.27, 128.21, 127.86, 127.83, 127.80, 127.72, 127.66 (C ar.), 119.12 (C₁), 115.62 (C₁₁), 98.74 (C₁₄), 79.82, 79.68, 79.62 (C₄, C₅, C₁₃), 75.13 (C₃), 74.51, 73.16 (C₁₅, C₁₆), 67.44 (C₁₂), 63.88 (C₆), 26.73 (C₈), 20.83 (C₁₀), 19.36 (C₇), 19.17 (C₃₀), 8.12 (C₉). **HRMS**, m/z: calculated for (C₄₆H₅₈O₈NaSi) [M + 23]: 789.3793. Found: 789.3790. **IR** (film, cm⁻¹) 2972, 2934, 1745, 1455, 1427, 1364, 1232, 1205, 1105, 1087.

((2*R*,3*R*)-2,3-bis(benzyloxy)-3-((2*R*)-6-((*R*)-2,2-diethyl-1,3-dioxolan-4-yl)-5,6-dihydro-2*H*-pyran-2-yl)propoxy)(tert-butyl)diphenylsilane



A 10 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with α -acetoxy ether **7.130** (50 mg, 0.07 mmol, 1 eq), trimethylallylsilane (0.11 mL, 0.7 mmol, 10 eq.) and DCM (2 mL). Resulting mixture was cooled down to -78°C and $\text{BF}_3\cdot\text{OEt}_2$ (0.025 mL, 0.20 mmol, 3 eq.) was added dropwise. The reaction mixture was allowed to heat up to -40°C and agitation was continued for another two hours. At that moment, a saturated aqueous solution of NH_4Cl (5 mL) and DCM (5 mL) were added to the reaction vessel. After phase separation, the aqueous layer was extracted with DCM (2 x 10 mL). Combined organic fractions were dried over MgSO_4 , concentrated under reduced pressure and purified by flash column chromatography on silica gel (PE/AcOEt 20:1 to 15:1) to give corresponding diene (17%). A 10 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was then charged with diene (17 mg, 0.02 mmol, 1 eq.), Grubbs-Hoveyda catalyst (catalytic amount) and DCM (12 mL). Resulting mixture was left stirring at 40°C for 48 h, prior to filtration on celite®. Resulting residue was purified by flash column chromatography on silica gel (PE/AcOEt 15:1) to give DHP **7.147** as a colorless oil (5 mg, 53% for the metathesis step, 9% over two steps). $R_f = 0.47$ (PE/AcOEt 10:1, Vanillin).

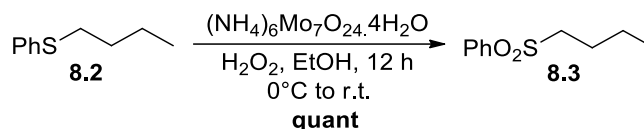
Experimental



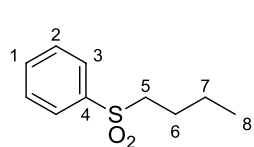
^1H NMR (300 MHz, CDCl_3) δ 7.67 – 7.11 (m, 20H, C_{16}H , C_{17}H , C_{18}H , C_{21}H , C_{22}H , C_{23}H , C_{27}H , C_{28}H , C_{29}H), 6.01 – 5.73 (m, 2H, C_5H , C_6H), 4.62 – 4.38 (m, 4H, C_{14}HH , C_{19}HH), 4.35 – 4.27 (m, 1H, C_4H), 3.97 (dd, $J = 7.9, 6.3$ Hz, 1H, C_{10}HH), 3.94 – 3.58 (m, 5H, C_1HH , C_2H , C_9H , C_{10}HH), 3.50 (ddd, $J = 10.6, 7.1, 3.9$ Hz, 1H, C_3H), 3.42 (ddd, $J = 10.6, 7.1, 3.9$ Hz, 1H, C_8H), 2.21 – 2.14 (m, 1H, C_7HH), 2.09 – 2.01 (m, 1H, C_7HH), 1.62 – 1.50 (m, 4H, C_{12}HH , $\text{C}_{12'}\text{HH}$), 0.97 (s, 9H, C_{25}HHH), 0.89 – 0.75 (m, 6H, C_{13}HHH , $\text{C}_{13'}\text{HHH}$). **^{13}C NMR** (75 MHz, CDCl_3) δ 138.85, 138.58 (C_{15} , C_{20}), 135.76, 133.55, 133.51, 129.82, 128.46, 128.30, 128.10, 127.94, 127.84, 127.63 (C_5 or C_6 , C_{16} , C_{17} , C_{18} , C_{21} , C_{22} , C_{23} , C_{27} , C_{28} , C_{29}), 124.77 (C_5 or C_6), 113.27 (C_{11}), 81.00 (C_3), 79.83 (C_2), 78.66 (C_9), 75.03, 74.95 (C_4 , C_8), 74.66, 73.69 (C_{14} , C_{19}), 68.06 (C_{10}), 63.29 (C_1), 29.91, 29.46 (C_{12} , $\text{C}_{12'}$), 28.39 (C_7), 27.01 (C_{25}), 19.30 (C_{24}), 8.36, 8.22 (C_{13} , $\text{C}_{13'}$). **IR** (film, cm^{-1}) 2930, 2901, 2856, 1454, 1427, 1111, 1080, 1028. **HRMS**, m/z : calculated for ($\text{C}_{45}\text{H}_{57}\text{O}_6\text{Si}_1$): [$\text{M} + 1$]: 721.3919. Found 721.3918.

10.2.6. Julia olefination

(butylsulfonyl)benzene



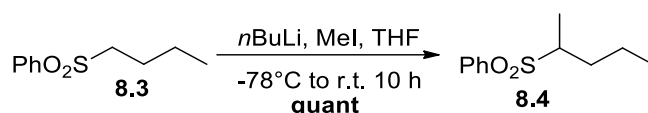
A 100 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with thioether **8.2** (1.00 g, 6 mmol, 1 eq.), Molybdenum catalyst (1.48 g, 1.2 mmol, 0.2 eq.), H₂O₂ (30%, 7 mL) and EtOH (30 mL) at 0°C. Resulting mixture was left stirring and allowed to heat up to room temperature for 12 h. The crude reaction mixture was then treated carefully with H₂O/AcOEt (1:1, 60 mL). After separation, the aqueous layer was extracted with AcOEt (2 x 30 mL). Combined organic fractions were dried over MgSO₄, concentrated under reduced pressure and resulting residue was purified by flash column chromatography on silica gel (AcOEt 100%) to give sulfone **8.3** as a colorless oil (1.19 g, quant.) R_f = 0.55 (AcOEt 100%, Vanillin, white).



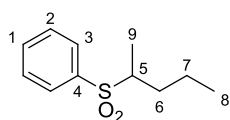
¹H NMR (300 MHz, CDCl₃) δ 8.04 – 7.78 (m, 2H, C₃H), 7.76 – 7.44 (m, 3H, C₁H, C₂H), 3.13 – 3.04 (m, 2H, C₅HH), 1.76 – 1.62 (m, 2H, C₆HH), 1.38 (dq, *J* = 14.7, 7.3 Hz, 2H, C₇HH), 0.88 (t, *J* = 7.3 Hz, 3H, C₈HHH). **¹³C NMR** (75 MHz, CDCl₃) δ 137.17 (C₄), 128.95, 128.94, 125.75 (C₁, C₂, C₃), 33.38 (C₅), 31.35 (C₆), 22.10 (C₇), 13.78 (C₈).

Experimental

(pentan-2-ylsulfonyl)benzene

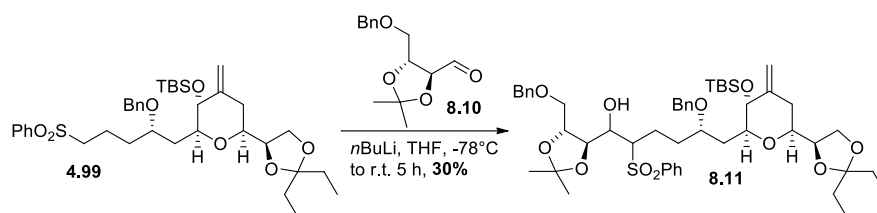


A 50 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with sulfone **8.3** (2.36 g, 1.24 mmol, 1 eq.) and THF (13 mL) at -78°C . $n\text{BuLi}$ (2.5M, 0.52 mL, 1.05 eq.) was then added dropwise and a yellow solution was observed immediately. After 30 min at that temperature, MeI (2 mmol, 0.13 mL, 1.6 eq.) was added in one portion and the yellow color disappeared. Mixture was left stirring for 10 h while being allowed to heat up to room temperature. The crude reaction mixture was then treated carefully with a saturated aqueous solution of NH_4Cl (20 mL). After separation, the aqueous layer was extracted with AcOEt (2 x 30 mL). Combined organic fractions were dried over MgSO_4 , concentrated under reduced pressure and resulting residue was purified by flash column chromatography on silica gel (AcOEt 100%) to give sulfone **8.4** as a colorless oil (2.54 g, quant.)

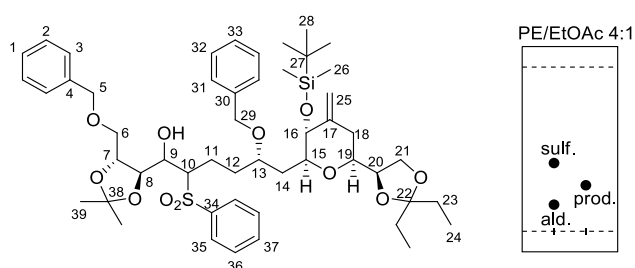


^1H NMR (300 MHz, CDCl_3) δ 7.91 – 7.83 (m, 2H, C_3H), 7.73 – 7.61 (m, 1H, C_1H), 7.61 – 7.51 (m, 2H, C_2H), 3.10 – 2.96 (m, 1H, C_5H), 2.00 – 1.85 (m, 1H, C_6HH), 1.74 – 1.18 (m, 6H, C_6HH , C_7HH , C_9HHH), 0.89 (t, $J = 7.1$ Hz, 3H, C_8HHH). **^{13}C NMR** (75 MHz, CDCl_3) δ 137.45 (C_4), 133.66, 129.17 (C_1 , C_2 , C_3), 60.13 (C_5), 31.19 (C_6), 19.97 (C_7), 13.86, 13.27 (C_8 , C_9).

(5S)-5-(benzyloxy)-1-((4R,5R)-5-((benzyloxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-6-((2S,3R,6S)-3-((tert-butyldimethylsilyl)oxy)-6-((R)-2,2-diethyl-1,3-dioxolan-4-yl)-4-methylenetetrahydro-2H-pyran-2-yl)-2-(phenylsulfonyl)hexan-1-ol



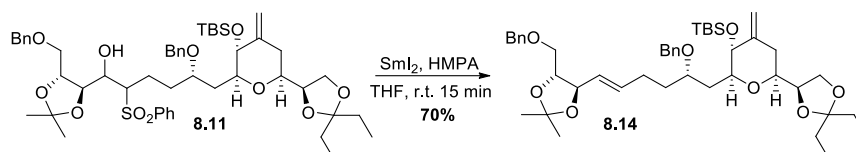
A 10 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with sulfone **4.99** (200 mg, 0.3 mmol, 1 eq.) and THF (4 mL) at -78°C . $n\text{BuLi}$ (2.4 M, 0.13 mL, 1.1 eq.) was then added dropwise and a yellow solution was observed immediately. After 15 min at that temperature, aldehyde **8.10** (78 mg, 0.33 mmol, 1.05 eq.) was added in one portion and the yellow color disappeared. Mixture was left stirring and allowed to heat up to room temperature for 5 h. The crude reaction mixture was then treated carefully with a saturated aqueous solution of NH_4Cl (10 mL). After separation, the aqueous layer was extracted with Et_2O (2 x 10 mL). Combined organic fractions were dried over MgSO_4 , concentrated under reduced pressure and resulting residue was purified by flash column chromatography on silica gel (PE/AcOEt 12:1) to give β -hydroxy sulfone **8.11** as a colorless oil (30% ^1H NMR yield)



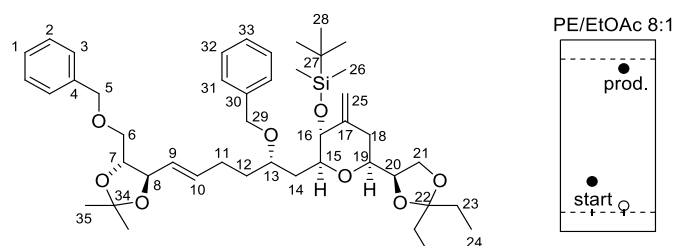
Experimental

¹H NMR (300 MHz, CDCl₃) δ 8.05 – 7.82 (m, 2H, C₃₅H), 7.72 – 7.09 (m, 13H, C₁H, C₂H, C₃H, C₃₁H, C₃₂H, C₃₃H, C₃₆H, C₃₇H), 5.05 (d, *J* = 6.5 Hz, 1H, C₂₅HH), 4.88 (d, *J* = 4.4 Hz, 1H, C₂₅HH), 4.64 – 4.33 (m, 4H, C₅HH, C₂₉HH), 4.20 – 3.44 (m, 10H, C₆HH, C₇H, C₈H, C₉H, C₁₃H, C₁₆H, C₂₀H, C₂₁HH), 3.42 – 2.95 (m, 3H, C₁₀H, C₁₅H, C₁₉H), 2.71 – 2.52 (m, 1H, C₁₈HH-*eq*), 2.26 – 1.83 (m, 2H, C₁₄HH, C₁₈HH-*ax*), 1.83 – 1.45 (m, 10H, C₁₁HH, C₁₂HH, C₁₄HH, C₂₃HHH, C₂₃HHH), 1.55 – 1.04 (m, 7H, C₁₂HH, C₃₉HHH, C₃₉HHH), 1.03 – 0.82 (m, 15H, C₂₄HHH, C₂₄HHH, C₂₈HHH), 0.08 (s, 3H, C₂₆HHH), 0.04 (s, 3H, C₂₆HHH). **¹³C NMR** (75 MHz, CDCl₃) δ 146.20 (C₁₇), 138.95, 138.04, 137.73 (C₄, C₃₀, C₃₄), 133.88 (C₃₇), 129.37, 129.29, 129.23, 129.14, 128.92, 128.61, 128.53, 128.40, 127.92, 127.81, 127.48 (C₁, C₂, C₃, C₃₁, C₃₂, C₃₃, C₃₅, C₃₆ + diastereoisomers), 113.51 (C₂₅), 110.14 (C₃₈), 107.37 (C₂₂), 80.48, 80.33, 79.82, 78.15, 75.56, 74.56, 73.61, 71.01, 70.29, 68.13, 65.67, 65.31 (C₅, C₆, C₇, C₈, C₉, C₁₀, C₁₃, C₁₅, C₁₆, C₁₉, C₂₀, C₂₁, C₂₉), 38.39, 36.11, 29.79, 29.32, 27.29, 26.63 (C₁₁, C₁₂, C₁₄, C₁₈, C₂₃, C₂₃', C₃₉, C₃₉'), 26.05 (C₂₈), 18.27 (C₂₇), 8.34, 8.20 (C₂₄, C₂₄'), -4.22, -4.52 (C₂₆, C₂₆'). **IR** (neat, cm⁻¹) 3500, 2893, 1447, 1371, 1304, 1252, 1211, 1167, 1144, 1028. **MSMS** (p ESI), *m/z* (%): 945.46 (15), 803.45 (100), 717.38 (21), 583.34 (10), 477.22. **HRMS**, *m/z*: calculated for (C₅₁H₇₄O₁₁SiNa) [*M* +23]: 945.46133. Found: 945.46062.

((2*S*,3*R*,6*S*)-2-((*S*,*E*)-2-(benzyloxy)-6-((4*R*,5*R*)-5-((benzyloxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)hex-5-en-1-yl)-6-((*R*)-2,2-diethyl-1,3-dioxolan-4-yl)-4-methylenetetrahydro-2*H*-pyran-3-yl)oxy)(tert-butyl)dimethylsilane



A 10 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with β -hydroxy sulfone **8.11** (200 mg, 0.1 mmol, 1 eq.) and THF (1 mL) at room temperature. A 0.1 M Sml_2 (4 mL, 0.4 mmol, 4 eq.)/HMPA (1.6 mmol, 16 eq.) was added in one portion at room temperature. After 15 min at that temperature, the deep purple coloration of the solution turned yellow/grey and the crude reaction mixture was then treated carefully with a saturated aqueous solution of NH_4Cl (10 mL). After separation, the aqueous layer was extracted with Et_2O (2 x 10 mL). Combined organic fractions were dried over MgSO_4 , concentrated under reduced pressure and resulting residue was purified by flash column chromatography on silica gel (PE/AcOEt 20:1) to give olefin **8.14** as a 1:1 mixture of the two olefinic geometries (70% ^1H NMR yield).



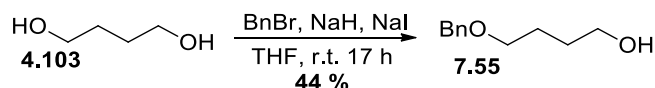
^1H NMR (300 MHz, CDCl_3) δ 7.35 – 7.24 (m, 10H, C_1H , C_2H , C_3H , C_{31}H , C_{32}H , C_{33}H), 5.80 – 5.65 (m, 1H, C_{10}H), 5.50 – 5.35 (m, 1H, C_9H), 5.05 (s, 1H, C_{25}HH), 4.88 (s, 1H, C_{25}HH), 4.62 – 4.51 (m, 3H, C_5HH , C_{29}HH), 4.38 (d, J = 11.6 Hz, 1H, C_{29}HH), 4.37 (d, J = 11.7 Hz, 1H, $\text{dia-C}_{29}\text{HH}$), 4.15 (td, J = 8.1, 2.3 Hz, 1H, C_8H), 4.03 (ddd, J = 7.9, 6.3, 1.6 Hz, 1H, C_{21}HH), 3.96 – 3.81 (m, 2H,

Experimental

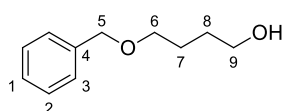
C₂₀H, C₇H), 3.76 – 3.67 (m, 2H, C₁₆H, C₂₁HH), 3.62 – 3.50 (m, 3H, C₁₃H, C₆HH), 3.20 (ddd, $J = 11.0, 7.3, 2.2$ Hz, 1H, C₁₉H), 3.09 (t, $J = 9.6$ Hz, 1H, C₁₅H), 2.62 (d, $J = 15.0$ Hz, 1H, C₁₈HH), 2.62 (d, $J = 11.1$ Hz, 1H, dia-C₁₈HH), 2.31 – 1.94 (m, 4H, C₁₁HH, C₁₂HH, C₁₄HH, C₁₈HH), 1.80 – 1.53 (m, 5H, C₁₁HH, C₁₂HH, C₂₃HH, C₁₄HH), 1.43 (s, 6H, C₃₅HHH), 0.94 (s, 9H, C₂₈HHH), 0.89 (t, $J = 7.5$ Hz, 6H, C₂₄HHH), 0.09 (s, 3H, C₂₆HHH), 0.04 (s, 3H, C_{26'}HHH). ¹³C NMR (126 MHz, CDCl₃) δ 146.25 (C₁₇), 139.01, 138.20 (C₄, C₃₀), 136.61 (C₁₀), 128.49, 128.47, 127.90, 127.83, 127.76, 127.63 (C₁, C₂, C₃, C₃₁, C₃₂, C₃₃), 127.10, 126.90 (E-C₈, Z-C₈), 113.52 (C₃₄), 109.24 (C₂₂), 107.37 (C₂₅), 80.62, 80.28 (C₆, C₁₅), 79.88 (C₈), 79.27 (C₁₉), 78.18 (C₂₀), 75.80, 75.74 (C₁₃, C₁₃ dia), 74.60 (C₁₆), 73.65 (C₅), 70.74, 70.69 (C₂₉), 69.53 (C₇), 68.11 (C₂₁), 38.45 (C₁₈), 36.35 (C₁₄), 33.30, 33.16 (C₁₁, C₁₁ dia), 29.82, 29.34 (C₂₂, C_{22'}), 28.35, 28.24 (C₁₂, C₁₂ dia), 27.24, 27.13 (C₃₅, C_{35'}), 26.06 (C₂₈), 18.31 (C₂₇), 8.36, 8.22 (C₂₃, C_{23'}), -4.18, -4.49 (C₂₆, C_{26'}). IR (neat, cm⁻¹) 2930, 2899, 2883, 1454, 1369, 1252, 1207, 1169, 1086, 1028, 1007. MSMS (p ESI), m/z (%): 787.46 (100), 729.41 (15), 701.38 (18), 461.23 (12). HRMS, m/z : calculated for (C₄₅H₆₈O₈SiNa) [M + 23]: 787.45757. Found: 787.45695.

10.2.7. Synthesis of the polyol fragment by tin allylation

4-(benzyloxy)butan-1-ol



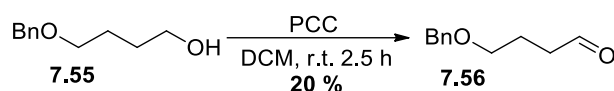
A 500 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with butane-1,4-diol (29.50 mL, 333 mmol, 1 eq.), THF (350 mL), sodium hydride (8.66 g, 216 mmol, 0.65 eq.) and sodium iodide (0.002 g, 16.7 mmol, 0.05 eq.) and was left stirring at 0°C for 30 min. At that moment, benzylbromide (19.81 mL, 167 mmol, 0.5 eq.) was added in one portion and resulting heterogeneous mixture was stirred at room temperature for 17 h. The latter was then treated with an aqueous solution of NH₄Cl (1M, 50 mL). After separation, the aqueous phase was extracted with diethyl ether (3 x 100 mL). Organic fractions were collected, dried over MgSO₄ and concentrated under vacuum. The crude product was purified by flash column chromatography on silica gel (PE/AcOEt 1:1) to afford **7.55** as a slightly yellow oil (26.39 g, 44%).



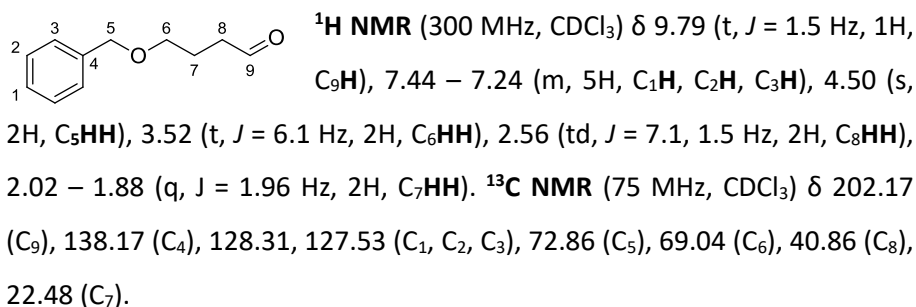
¹H NMR (300 MHz, CDCl₃) δ 7.40 – 7.20 (m, 5H, C₁H, C₂H, C₃H), 4.48 (s, 2H, C₅HH), 3.61 (t, *J* = 5.8 Hz, 2H, C₆HH or C₉HH), 3.49 (t, *J* = 5.8 Hz, 2H, C₆HH or C₉HH), 2.53 (bs, 1H, C₁₁OH), 1.83 – 1.50 (m, 4H, C₇HH, C₈HH). **¹³C NMR** (75 MHz, CDCl₃) δ 138.17 (C₄), 128.38, 127.68, 127.61 (C₁, C₂, C₃), 73.00 (C₅), 70.31, 62.57 (C₆, C₉), 30.03, 26.61 (C₇, C₈).

Experimental

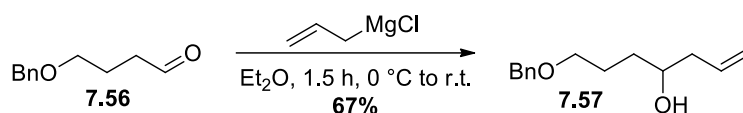
4-(benzyloxy)butanal



A 500 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with alcohol **7.55** (26.39 g, 159 mmol, 1 eq.), DCM (320 mL) and pyridinium chlorochromate (34.23 g, 159 mmol, 1 eq.). Resulting heterogeneous mixture was stirred at room temperature for 2.5 h. The latter was then treated with celite[®] (30 g). Solids were filtered off and the brown solution was concentrated under vacuum. The crude product was purified by flash column chromatography on silica gel (AcOEt/PE 1:5) to afford **7.56** as a slightly brown oil (5.58 g, 20%).

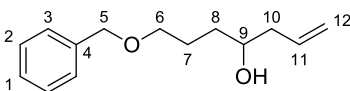


7-(benzyloxy)hept-1-en-4-ol

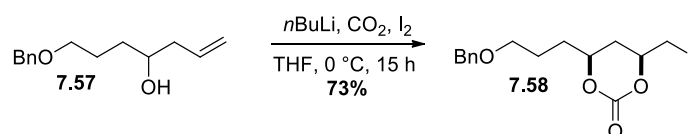


A 250 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with aldehyde **7.56** (5.58 g, 31.3 mmol, 1 eq.) and Et₂O (63 mL). Allylmagnesium chloride (23.94 mL, 40.7 mmol, 1.3 eq.) was then added dropwise. Resulting heterogeneous mixture was stirred at 0 °C for

1.5 h. The mixture was then treated with an aqueous saturated solution of NH_4Cl (50 mL). The aqueous phase was subsequently extracted with PE (3 x 50 mL). Organic fractions were washed with brine, dried over MgSO_4 and concentrated under vacuum. The crude product was purified by flash column chromatography on silica gel (PE/AcOEt 1:5) to afford **7.57** as a slightly yellow oil (4.63 g, 67%).

 **^1H NMR** (300 MHz, CDCl_3) δ 7.52 – 6.93 (m, 5H, C_1H , C_2H , C_3H), 5.96 – 5.70 (m, 1H, C_{11}H), 5.17 – 5.07 (m, 2H, C_{12}HH), 4.52 (s, 2H, C_5HH), 3.66 (ddt, $J = 12.2$, 8.3, 4.1 Hz, 1H, C_9H), 3.51 (t, $J = 6.0$ Hz, 2H, C_6HH), 2.44 (d, $J = 3.9$ Hz, 1H, C_9OH), 2.34 – 2.11 (m, 2H, C_{10}HH), 1.87 – 1.42 (m, 4H, C_7HH , C_8HH). **^{13}C NMR** (75 MHz, CDCl_3) δ 138.24 (C_4), 135.05 (C_{11}), 128.39, 127.69, 127.61 (C_1 , C_2 , C_3), 117.70 (C_{12}), 73.00, 70.55, 70.45 (C_5 , C_6 , C_9), 41.99 (C_{10}), 34.00, 26.20 (C_7 , C_8).

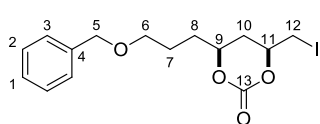
(4S,6S)-4-(3-(benzyloxy)propyl)-6-(iodomethyl)-1,3-dioxan-2-one



A 250 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with alcohol **7.57** (3.33 g, 15.09 mmol, 1 eq.), THF (35 mL) and fluorene as indicator. The resulting homogeneous mixture was cooled to 0 °C prior to dropwise addition of a solution of *n*butyllithium (2M) until the mixture turned permanently yellow. CO_2 was allowed to bubble into that mixture for 1 h at room temperature. Afterwards, a THF solution of iodine (33 mL, 33.19 mmol) was added and the resulting mixture was

Experimental

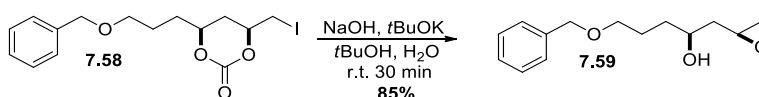
allowed to stir for 15 h at room temperature. The latter was finally diluted with AcOEt (30 mL) and with a saturated aqueous solution of $\text{Na}_2\text{S}_2\text{O}_3$ (30 mL) until the coloration disappeared. After separation of the layers, the collected organic fractions were dried over MgSO_4 and concentrated under vacuum. The crude product was purified by flash column chromatography on silica gel (PE/AcOEt 4:1) to afford **7.58** as a slightly yellow oil (4.32 g, 73%).



^1H NMR (300 MHz, CDCl_3) δ 7.66 – 7.17 (m, 5H, C_1H , C_2H , C_3H), 4.63 – 4.31 (m, 2H, C_9H , C_{11}H), 4.52 (s, 2H, C_5HH), 3.55 (bs, 2H, C_6HH), 3.33

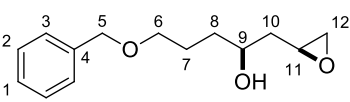
(ddd, $J = 18.0, 10.5, 5.8$ Hz, 2H, C_{12}HH), 2.50 – 2.22 (m, 2H, C_{10}HH), 1.97 – 1.54 (m, 4H, C_7HH , C_8HH). **^{13}C NMR** (75 MHz, CDCl_3) δ 138.26 (C_4), 128.44, 127.68 (C_1 , C_2 , C_3), 78.21 (C_9 , C_{11}), 73.00 (C_5), 69.30 (C_6), 33.26 (C_{10}), 32.14, 24.73 (C_7 , C_8), 5.29 (C_{12}).

(S)-5-(benzyloxy)-1-((S)-oxiran-2-yl)pentan-2-ol

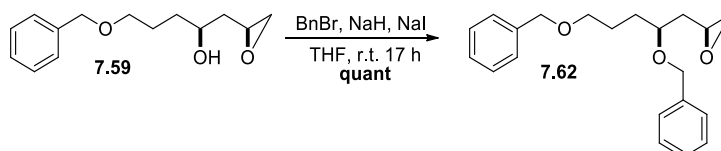


A 50 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with carbonate **7.58** (4.32 g, 11 mmol, 1 eq.), *t*butanol (22 mL), water (10 mL) and sodium hydroxide (4.43 g, 111 mmol, 10 eq.). Resulting heterogeneous mixture was stirred at room temperature for 30 min. The latter was then treated with a saturated aqueous solution of NH_4Cl and then with HCl (1M) until the pH was adjusted to 7. After separation, the aqueous phase was extracted with PE (3 x 30 mL). Organic fractions were dried over MgSO_4 and concentrated under vacuum. The crude product was

purified by flash column chromatography on silica gel (PE/AcOEt 1:1) to afford **7.59** as a slightly yellow oil (2.22 g, 85%).

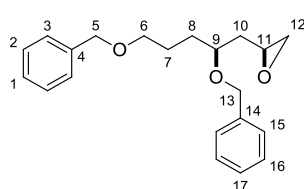
 **¹H NMR** (300 MHz, CDCl₃) δ 7.49 – 7.18 (m, 5H, C₁H, C₂H, C₃H), 4.53 (s, 2H, C₅HH), 3.91 (m, 1H, C₉H), 3.53 (t, J = 5.7 Hz, 2H, C₆HH), 3.18 – 3.02 (m, 1H, C₁₁H), 2.89 (m, 1H, C₉OH), 2.83 – 2.46 (m, 2H, C₁₂HH), 1.96 – 1.45 (m, 6H, C₇HH, C₈HH, C₁₀HH). **¹³C NMR** (75 MHz, CDCl₃) δ 138.10 (C₄), 128.42, 127.72, 127.68 (C₁, C₂, C₃), 73.06 (C₅), 70.41 (C₆), 69.91 (C₉), 50.42 (C₁₁), 46.67 (C₁₂), 39.82 (C₁₀), 34.77, 26.14 (C₇, C₈). **IR** (film, cm⁻¹) 3392, 2921, 2914, 1454, 1363, 1093, 1027. **MSMS** (p ESI), m/z (%): 71.05 (14), 91.05 (100), 129.09 (19). **HRMS**, m/z : calculated for (C₁₄H₂₁O₃) [M+1]: 237.1485. Found: 237.1484.

2-(5-(benzyloxy)-2-phenoxypropyl)oxirane



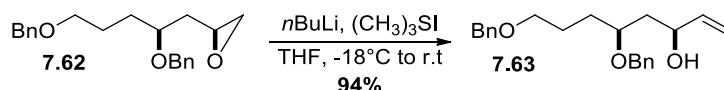
A 25 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with **7.59** (0.5 g, 2.12 mmol, 1 eq.), THF (8.5 mL), sodium hydride (0.11 g, 2.73 mmol, 1.3 eq.) and sodium iodide (0.016 g, 0.11 mmol, 0.05 eq.) at 0°C. After 30 min at that temperature, benzylbromide (0.25 mL, 2.12 mmol, 1 eq.) was added in one portion and resulting heterogeneous mixture was stirred at room temperature for 17 h. The latter was then treated with an aqueous solution of NH₄Cl (1M, 10 mL). After separation, the aqueous phase was extracted with diethyl ether (3 x 10 mL). Organic fractions were dried over MgSO₄ and concentrated under vacuum. The crude product was purified by flash column chromatography on silica gel (PE/AcOEt 4:1) to afford **7.62** as a slightly yellow oil (0.710 g, quant).

Experimental

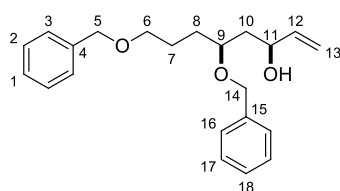


¹H NMR (300 MHz, CDCl₃) δ 7.37 – 7.27 (m, 10H, C₁H, C₂H, C₃H, C₁₅H, C₁₆H, C₁₇H), 4.53 (s, 2H, C₅HH), 4.50 (s, 2H, C₁₃HH), 3.73 – 3.55 (m, 1H, C₉H), 3.54 – 3.43 (m, 2H, C₆HH), 3.14 – 3.00 (m, 1H, C₁₁H), 2.77 – 2.44 (m, 2H, C₁₂HH), 1.94 – 1.62 (m, 6H, C₇HH, C₈HH, C₁₀HH). **¹³C NMR** (75 MHz, CDCl₃) δ 138.55 (C₄, C₁₄), 132.97, 128.37, 127.74, 127.64, 127.57, 127.53 (C₁, C₂, C₃, C₁₅, C₁₆, C₁₇), 72.90 (C₅, C₁₃), 70.86 (C₆), 70.24 (C₉), 49.54 (C₁₁), 46.89 (C₁₂), 36.80 (C₁₀), 30.69, 25.65 (C₇, C₈). **IR** (film, cm⁻¹) 2920, 2854, 1496, 1454, 1361, 1093, 1068, 1027. **MSMS** (p ESI), m/z (%): 71.05 (10), 91.05 (100), 127.07 (22), 129.09 (19), 181.10 (100). **HRMS**, m/z: calculated for (C₂₁H₂₇O₃) [M+1]: 327.1955. Found: 327.1955.

(3S,5S)-5,8-bis(benzyloxy)oct-1-en-3-ol

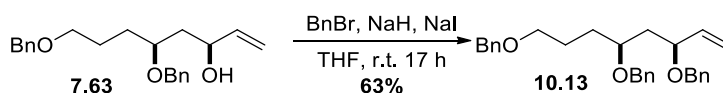


A 25 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with trimethylsulfonium iodide (0.875 g, 4.29 mmol, 4 eq.) and THF (6 mL). After cooling to -20 °C, a solution of *n*butyllithium (2.04 mL, 4.07 mmol, 3.8 eq.) was added dropwise and resulting mixture was allowed to stir for 1 h at -20 °C. A solution of epoxide **7.62** (0.350 g, 1.07 mmol, 1 eq.) in THF (1.5 mL) was then added to the reaction mixture which was allowed to stir once again for 1 h at -20 °C and finally to heat up slowly to room temperature. The homogeneous mixture was then diluted with water (10 mL). After separation, the aqueous phase was extracted with AcOEt (3 x 10 mL). Organic fractions were dried over MgSO₄ and concentrated under vacuum. The crude product was purified by flash column chromatography on silica gel (PE/AcOEt 3:1) to afford **7.63** as a slightly yellow oil (0.344 g, 94%).



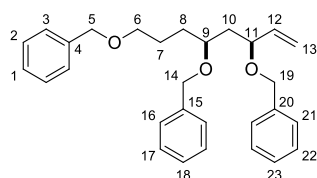
¹H NMR (300 MHz, CDCl₃) δ 7.40 – 7.26 (m, 10H, C₁H, C₂H, C₃H, C₁₆H, C₁₇H, C₁₈H), 5.90 – 5.76 (m, 1H, C₁₂H), 5.15 (m, 2H, C₁₃HH), 4.67 – 4.41 (m, 4H, C₅HH, C₁₄HH), 4.29 (m, 1H, C₁₁H), 3.80 – 3.69 (m, 1H, C₉H), 3.49 (t, J = 5.9 Hz, 2H, C₆HH), 3.31 (d, J = 1.9 Hz, 1H, C₁₁OH), 1.86 – 1.61 (m, 6H, C₇HH, C₈HH, C₁₀HH). **¹³C NMR** (75 MHz, CDCl₃) δ 140.68 (C₁₂), 138.50, 137.97 (C₄, C₁₅), 128.52, 128.38, 127.93, 127.80, 127.63, 127.57 (C₁, C₂, C₃, C₁₆, C₁₇, C₁₈), 114.25 (C₁₃), 78.80 (C₁₁), 72.92, 72.32 (C₅, C₁₄), 70.63, 70.24 (C₆, C₉), 41.05 (C₁₀), 29.98, 24.84 (C₇, C₈). **IR** (film, cm⁻¹) 3450, 2854, 1496, 1454, 1361, 1205, 1093, 1066, 1027. **MSMS** (p ESI), m/z (%): 71.05 (100), 91.05 (24), 181.10 (14). **HRMS**, m/z : calculated for (C₂₂H₂₉O₃) [M+1]: 341.2111. Found: 341.2111.

(3S, 5S)-3,5,8-tri(benzyloxy)-oct-1-ene



A 25 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with **7.63** (0.344 g, 1.01 mmol, 1 eq.), THF (4 mL), sodium hydride (0.053 g, 1.31 mmol, 1.3 eq.) and sodium iodide (0.008 g, 0.051 mmol, 0.05 eq.) at 0°C. After 30 min at that temperature, benzylbromide (0.12 mL, 1.01 mmol, 1 eq.) was added in one portion and resulting heterogeneous mixture was stirred at room temperature for 17 h. The latter was then treated with an aqueous solution of NH₄Cl (1M, 5 mL). After separation, the aqueous phase was extracted with diethyl ether (3 x 10 mL). Organic fractions were dried over MgSO₄ and concentrated under vacuum. The crude product was purified by flash column chromatography on silica gel (PE/AcOEt 4:1) to afford **10.13** as a slightly yellow oil (0.274 g, 63%).

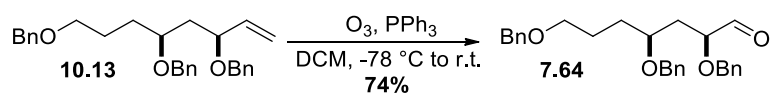
Experimental



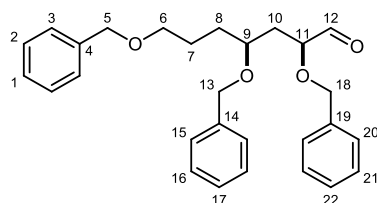
^1H NMR (300 MHz, CDCl_3) δ 7.43 – 7.21 (m, 15H, C₁H, C₂H, C₃H, C₁₆H, C₁₇H, C₁₈H, C₂₁H, C₂₂H, C₂₃H), 5.71 (ddd, J = 17.2, 10.3, 8.0 Hz, 1H, C₁₂H), 5.18 (m, 2H, C₁₃HH), 4.61 – 4.28 (m, 6H, C₅HH, C₁₄HH, C₁₉HH), 3.90 (dd, J = 14.6, 6.9 Hz, 1H, C₁₁H), 3.58 – 3.49 (m, 1H, C₉H), 3.48 – 3.40 (m, 2H, C₆HH), 2.14 – 1.56 (m, 6H, C₇HH, C₈HH, C₁₀HH).

^{13}C NMR (75 MHz, CDCl_3) δ 138.81, 138.72, 138.60 (C₄, C₁₂, C₁₅, C₂₀), 128.34, 128.31, 127.82, 127.60, 127.49, 127.44 (C₁, C₂, C₃, C₁₆, C₁₇, C₁₈, C₂₁, C₂₂, C₂₃), 117.75 (C₁₃), 77.84 (C₁₁), 75.52, 72.80, 70.55, 70.38, 70.04 (C₅, C₆, C₁₄, C₉, C₁₉), 40.08 (C₁₀), 30.37, 25.37 (C₇, C₈). **IR** (film, cm^{-1}) 2921, 2856, 1496, 1454, 1361, 1205, 1093, 1066, 1027. **MSMS** (p ESI), m/z (%): 71.05 (100), 91.05 (31), 181.10 (31). **HRMS**, m/z : calculated for (C₂₉H₃₅O₃) [M+1]: 431.2581. Found: 431.2583.

(2S,4S)-2,4,7-tris(benzyloxy)heptanal

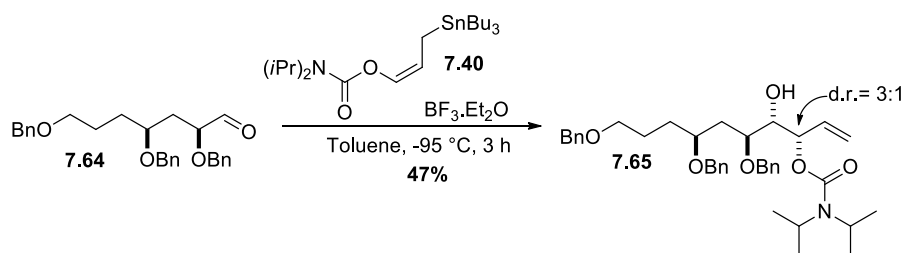


A 25 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with olefin **10.13** (0.274 g, 0.636 mmol, 1 eq.) and DCM (5 mL). After cooling to $-78\text{ }^\circ\text{C}$, ozone was bubbled for 15 min through the solution. The resulting mixture was then treated with triphenylphosphine (0.250 g, 0.0955 mmol, 1.5 eq.) and was subsequently allowed to stir for 17 h at room temperature. After concentration under vacuum, the crude product was purified by flash column chromatography on silica gel (PE/AcOEt 4:1) to afford **7.64** as a slightly yellow oil (0.203 g, 74%).



^1H NMR (300 MHz, CDCl_3) δ 9.63 (d, $J = 1.0$ Hz, 1H, C₁₂H), 7.42 – 7.24 (m, 15H, C₁H, C₂H, C₃H, C₁₅H, C₁₆H, C₁₇H, C₂₀H, C₂₁H, C₂₂H), 4.75 – 4.45 (m, 6H, C₅HH, C₁₃HH, C₁₈HH), 3.92 (t, $J = 5.3$ Hz, 1H, C₁₁H), 3.78 – 3.64 (m, 1H, C₉H), 3.46 (t, $J = 5.5$ Hz, 2H, C₆HH), 2.18 – 1.90 (m, 2H, C₁₀HH), 1.77 – 1.60 (m, 4H, C₇HH, C₈HH). **^{13}C NMR** (75 MHz, CDCl_3) δ 202.57 (C₁₂), 138.50, 138.33, 137.44 (C₄, C₁₄, C₁₉), 128.51, 128.37, 128.33, 128.00, 127.88, 127.62, 127.54 (C₁, C₂, C₃, C₁₅, C₁₆, C₁₇, C₂₀, C₂₁, C₂₂), 80.57 (C₁₁), 74.37, 72.88, 72.23, 70.93, 70.22 (C₅, C₆, C₉, C₁₃, C₁₈), 35.68 (C₁₀), 30.20, 25.26 (C₇, C₈). **IR** (film, cm^{-1}) 2921, 2858, 1731, 1496, 1454, 1361, 1205, 1087, 1060, 1027, 1002, 991. **MSMS** (p ESI), m/z (%): 91.05 (39), 181.10 (100). **HRMS**, m/z : calculated for (C₂₈H₃₃O₄) [M+1]: 433.2373. Found: 433.2374.

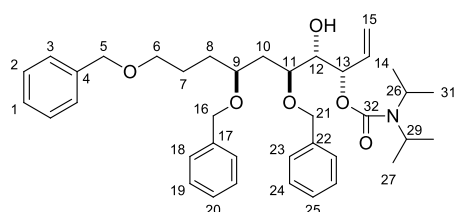
**(4*S*,5*S*,7*S*)-5,7,10-tris(benzyloxy)-4-hydroxydec-1-en-3-yl
diisopropylcarbamate**



A 25 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with aldehyde **7.64** (0.203 g, 0.469 mmol, 1 eq.), diisopropylcarbamate **7.40** (0.223 g, 0.469 mmol, 1 eq.) and toluene (5 mL). After cooling to $-94\text{ }^{\circ}\text{C}$, $\text{BF}_3\cdot\text{Et}_2\text{O}$ (0.06 mL, 0.469 mmol, 1 eq.) was added dropwise slowly and the resulting homogeneous mixture was allowed to

Experimental

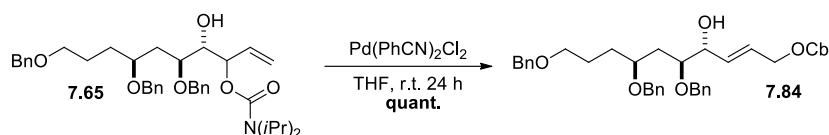
stir for 3 h at -94°C . The mixture was then diluted with an aqueous saturated solution of NaHCO_3 . After separation, the aqueous phase was extracted with DCM (2 x 10 mL). Organic fractions were dried over MgSO_4 and concentrated under vacuum. The crude product was purified by flash column chromatography on silica gel (PE/AcOEt 4:1) to afford **7.65** as a colorless oil (0.135 g, 47 %, d.r.= 3:1).



^1H NMR (300 MHz, CDCl_3) δ 7.40 – 7.26 (m, 15H, C_1H , C_2H , C_3H , C_{18}H , C_{19}H , C_{20}H , C_{23}H , C_{24}H , C_{25}H), 5.99 – 5.84 (m, 1H, C_{14}H), 5.57 – 5.37 (m,

1H, C_{13}H), 5.36 – 5.15 (m, 2H, C_{15}HH), 4.58 – 4.39 (m, 6H, C_5HH , C_{16}HH , C_{21}HH), 4.07 – 3.65 (m, 2H, C_{26}H , C_{29}H), 3.84 – 3.75 (m, 1H, C_{12}H or C_{11}H or C_9H), 3.75 – 3.66 (m, 1H, C_{12}H or C_{11}H or C_9H), 3.56 (dd, $J = 7.7, 3.9$ Hz, 1H, C_{12}H or C_{11}H or C_9H), 3.50 – 3.39 (m, 2H, C_6HH), 3.31 – 3.20 (bs, 1H, C_{12}OH), 2.03 – 1.80 (m, 2H, C_{10}HH), 1.74 – 1.60 (m, 4H, C_7HH , C_8HH), 1.41 – 1.09 (m, 12H, C_{27}HHH , C_{31}HHH). ^{13}C NMR (75 MHz, CDCl_3) δ 155.14 (C_{32}), 138.73, 138.29, 138.16, 135.32 (C_{14} , C_4 , C_{17} , C_{22}), 128.60, 128.54, 128.25, 127.93, 127.78, 127.71 (C_1 , C_2 , C_3 , C_{18} , C_{19} , C_{20} , C_{23} , C_{24} , C_{25}), 117.42 (C_{15}), 76.58, 75.34, 74.80, 74.14, 73.04, 72.07, 71.05, 70.40 (C_5 , C_6 , C_9 , C_{11} , C_{12} , C_{13} , C_{16} , C_{21}), 33.97 (C_{10}), 30.25, 25.23 (C_7 , C_8), 21.73, 20.84 (b , C_{27} , C_{31}). IR (film, cm^{-1}) 2925, 1731, 1496, 1473, 1454, 1436, 1367, 1340, 1288, 1217, 1132, 1093, 1049, 1027. MSMS (p ESI), m/z (%): 91.05 (100), 113.06 (10), 165.09 (13), 181.10 (67), 257.15 (17). HRMS, m/z : calculated for ($\text{C}_{38}\text{H}_{52}\text{O}_6\text{N}$) [$\text{M}+1$]: 618.3789. Found: 618.3786.

**(4*R*,5*S*,7*S*,*E*)-5,7,10-tris(benzyloxy)-4-hydroxydec-2-en-1-yl
diisopropylcarbamate**



A 10 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with diisopropylcarbamate **7.65** (0.439 g, 0.711 mmol, 1 eq.), THF (3 mL) and bis(benzonitrile)palladium (II) chloride (0.002 g, 0.0356 mmol, 0.05 eq.). Resulting homogeneous mixture was stirred at room temperature for 24 h. The latter was then filtered through celite® which was subsequently washed with dichloromethane (2 x 5 mL). Organic fractions were concentrated under vacuum. The crude product was purified by flash column chromatography on silica gel (PE/AcOEt 2:1) to afford **7.84** as a slightly yellow oil (0.435 g, quant).

¹H NMR (300 MHz, CDCl₃) δ 7.37 – 7.23 (m, 15H, C₃H, C₄H, C₅H, C₁₈H, C₁₉H, C₂₀H, C₂₃H, C₂₄H, C₂₅H), 5.94 – 5.70 (m, 2H, C₁₃H, C₁₄H), 4.63 – 4.40 (m, 8H, C₁HH, C₁₆HH, C₂₁HH, C₁₅HH), 4.31 – 4.22 (m, 1H, C₁₂H), 4.07 – 3.65 (m, 2H, C₂₇H, C₂₉H), 3.64 – 3.59 (m, 1H, C₉H or C₁₁H), 3.57 – 3.50 (m, 1H, C₉H or C₁₁H), 3.49 – 3.38 (m, 2H, C₆HH), 1.79 – 1.55 (m, 6H, C₁₀HH, C₈HH, C₇HH), 1.19 (d, *J* = 6.8 Hz, 12H, C₂₈HHH, C₃₀HHH). **¹³C NMR** (75 MHz, CDCl₃) δ 155.46 (C₂₆), 138.71, 138.47, 138.37 (C₂, C₁₇, C₂₂), 131.93, 129.69 (C₁₃, C₁₄), 128.55, 128.52, 128.09, 128.01, 127.91, 127.78, 127.69, 127.48 (C₃, C₄, C₅, C₁₈, C₁₉, C₂₀, C₂₃, C₂₄, C₂₅), 79.40, 75.49 (C₉, C₁₁), 73.02, 72.45, 71.85, 70.80, 70.40, 64.75 (C₁, C₆, C₁₆,

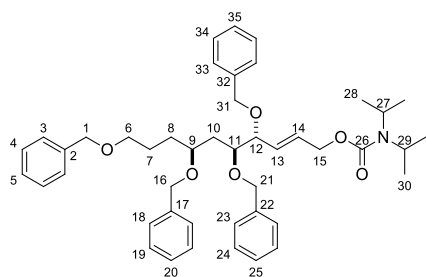
Experimental

C₂₁, C₁₂, C₁₅), 45.96 (*b* C₂₇, C₂₉), 33.70 (C₁₀), 30.38, 25.40 (C₇, C₈), 21.16 (*b* C₂₈, C₃₀). **IR** (film, cm⁻¹) 3400, 2931, 2864, 1681, 1496, 1475, 1452, 1442, 1367, 1307, 1292, 1215, 1191, 1155, 1134, 1089, 1064, 1049, 1027. **MSMS** (p ESI), *m/z* (%): 91.06 (100), 128.11 (15), 113.06 (10), 165.09 (13), 181.10 (75), 257.15 (16). **HRMS**, *m/z*: calculated for (C₃₈H₅₂O₆N) [M+1]: 618.3789. Found: 618.3789.

(4*R*,5*S*,7*S*,*E*)-4,5,7,10-tetrakis(benzyloxy)dec-2-en-1-yl diisopropylcarbamate

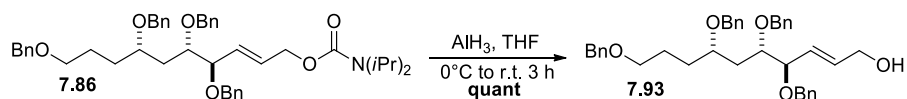


A 10 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with diisopropylcarbamate **7.84** (0.150 g, 0.244 mmol, 1 eq.), DMF (8 mL) and sodium hydride (0.020 g, 0.488 mmol, 2 eq.) at 0°C. After 30 min, benzylbromide (0.046 g, 0.268 mmol, 1.1 eq.) was added in one portion to the stirred solution. Resulting heterogeneous mixture was stirred at room temperature for 5 h. The latter was then diluted with a saturated aqueous solution of NH₄Cl (1M, 5 mL). After separation, the aqueous phase was extracted with diethyl ether (3 x 10 mL). Organic fractions were dried over MgSO₄ and concentrated under vacuum. The crude product was purified by flash column chromatography on silica gel (PE/AcOEt 4:1) to afford **7.86** as a slightly yellow oil (0.143 g, 83 %). *R*_f = 0.83 (PE/AcOEt 2:1).



^1H NMR (300 MHz, CDCl_3) δ 7.41 – 7.26 (m, 20H, C_3H , C_4H , C_5H , C_{18}H , C_{19}H , C_{20}H , C_{23}H , C_{24}H , C_{25}H , C_{33}H , C_{34}H , C_{35}H), 5.79 – 5.70 (m, 2H, C_{13}H , C_{14}H), 4.68 – 4.22 (m, 11H, C_1HH , C_{16}HH , C_{21}HH , C_{31}HH , C_{12}H , C_{15}HH), 4.15 – 3.64 (m, 3H, C_9H , C_{27}H , C_{29}H), 3.58 (dt, $J = 7.9, 4.1$ Hz, 1H, C_{11}H), 3.45 – 3.26 (m, 2H, C_6HH), 1.95 – 1.31 (m, 6H, C_7HH , C_8HH , C_{10}HH), 1.22 (d, $J = 6.8$ Hz, 12H, C_{28}HHH , C_{30}HHH). **^{13}C NMR** (75 MHz, CDCl_3) δ 155.32 (C_{26}), 138.86, 138.71, 138.65, 138.53 (C_2 , C_{17} , C_{22} , C_{32}), 130.39, 130.32, 128.35, 128.29, 128.27, 128.07, 128.01, 127.84, 127.63, 127.49, 127.47, 127.43 (C_3 , C_4 , C_5 , C_{18} , C_{19} , C_{20} , C_{23} , C_{24} , C_{25} , C_{33} , C_{34} , C_{35} , C_{13} , C_{14}), 81.89, 78.21, 75.93, 72.81, 72.52, 70.60, 70.37, 70.34, 64.39 (C_1 , C_6 , C_9 , C_{11} , C_{12} , C_{15} , C_{16} , C_{21} , C_{31}), 46.09 (*b* C_{29} , C_{27}), 35.77 (C_{10}), 30.44, 25.52 (C_7 , C_8), 21.19 (*b* C_{28} , C_{30}). **IR** (film, cm^{-1}) 2960, 2931, 2920, 2860, 1693, 1496, 1452, 1442, 1367, 1309, 1288, 1215, 1190, 1153, 1132, 1089, 1066, 1027. **MSMS** (p ESI), m/z (%): 91.05 (100), 128.11 (35), 181.10 (86), 600.37 (21). **HRMS**, m/z : calculated for ($\text{C}_{45}\text{H}_{58}\text{O}_6\text{N}$) [$\text{M}+1$]: 708.4259. Found: 708.4255.

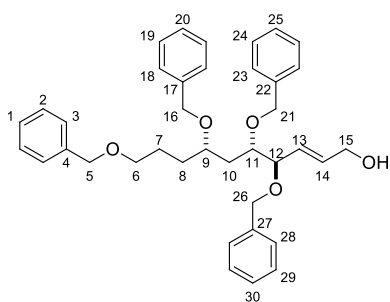
(4*R*,5*S*,7*S*,*E*)-4,5,7,10-tetrakis(benzyloxy)dec-2-en-1-ol



A 25 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with aluminium (III) chloride (0.190 g, 1.41 mmol, 10 eq.) and THF (8.9 mL). After cooling to 0 °C, a diethyl ether solution of LiAlH_4 (1.1 mL,

Experimental

4.24 mmol, 30 eq.) was added slowly and the resulting heterogeneous mixture was allowed to stir for 30 min at 0 °C. At that moment, a solution of diisopropylcarbamate **7.86** (0.100 g, 0.14 mmol, 1 eq.) in THF (5 mL) was added to the mixture which was allowed to stir for 3 h at room temperature. The resulting mixture was then diluted with an aqueous solution of NH₄Cl (10 mL) and an aqueous saturated solution of Rochelles' salt (10 mL). After separation, the aqueous phase was extracted with diethylether (2 x 10 mL). Organic fractions were dried over MgSO₄ and concentrated under vacuum. The crude product was purified by flash column chromatography on silica gel (PE/AcOEt 1:1) to afford **7.93** as a slightly yellow oil (82 mg, quant).

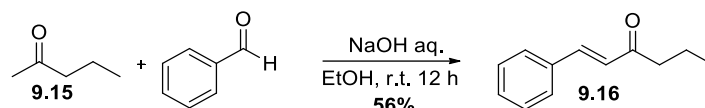


¹H NMR (300 MHz, CDCl₃) δ 7.39 – 7.01 (m, 20H, C₁H, C₂H, C₃H, C₁₈H, C₁₉H, C₂₀H, C₂₃H, C₂₄H, C₂₅H, C₂₈H, C₂₉H, C₃₀H), 5.88 – 5.55 (m, 2H, C₁₃H, C₁₄H), 4.74 – 4.20 (m, 9H, C₅HH, C₁₂H, C₁₆HH, C₂₁HH, C₂₆HH), 4.07 – 3.96 (m, 2H, C₁₅HH), 3.82 (dd, *J* =

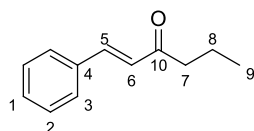
7.3, 3.2 Hz, 1H, C₉H), 3.62 – 3.54 (m, 1H, C₁₁H), 3.49 – 3.24 (m, 2H, C₆HH), 1.96 – 1.22 (m, 6H, C₇HH, C₈HH, C₁₀HH). **¹³C NMR** (75 MHz, CDCl₃) δ 138.99, 138.82, 138.79, 138.71 (C₄, C₁₇, C₂₂, C₂₇), 134.16, 130.41, 130.35, 128.48, 128.42, 128.40, 128.38, 128.15, 127.91, 127.76, 127.66, 127.58, 127.55, 127.51 (C₁₃, C₁₄, C₁, C₂, C₃, C₁₈, C₁₉, C₂₀, C₂₃, C₂₄, C₂₅, C₂₈, C₂₉, C₃₀), 82.07, 78.44, 76.09, 72.95, 72.54, 70.71, 70.66, 70.50, 63.12 (C₅, C₆, C₉, C₁₆, C₁₁, C₂₁, C₁₂, C₂₆, C₁₅), 35.74, 30.44, 25.53 (C₇, C₈, C₁₀). **IR** (film, cm⁻¹) 3400, 2925, 2912, 2856, 1496, 1454, 1361, 1205, 1091, 1066, 1027, 1000. **HRMS**, *m/z*: calculated for C₃₈H₄₅O₅ [M+1]: 581.3262. Found: 581.3263.

10.2.8. Formal synthesis of Herbarumine I

(E)-1-phenylhex-1-en-3-one



A 500 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with ketone **9.15** (22.7 mL, 213 mmol, 1.13 eq.), aldehyde (19.1 mL, 188 mmol, 1 eq.), NaOH (2.32 g, 47 mmol, 0.25 eq.), H₂O (50 mL) and EtOH (100 mL). Resulting mixture was left stirring at room temperature for 12 h. After total conversion, the volatiles were removed under reduced pressure with the aid of a rotary evaporator. Resulting aqueous layer was extracted with Et₂O (2 x 50 mL). Combined organic fractions were dried over MgSO₄ and concentrated under reduced pressure to afford enone **9.16** that was used without further purification (18.11 g, 56%). R_f = 0.32 (PE/AcOEt 8:1).

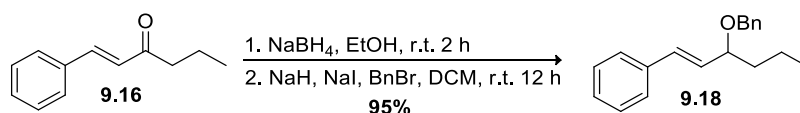


¹H NMR (300 MHz, CDCl₃) δ 7.59 – 7.16 (m, 5H, C₁H, C₂H, C₃H), 7.55 (d, *J* = 16.2 Hz, 1H, C₅H), 6.74 (d, *J* = 16.3 Hz, 1H, C₆H), 2.65 (t, *J* = 7.3 Hz, 2H, C₇HH), 1.73

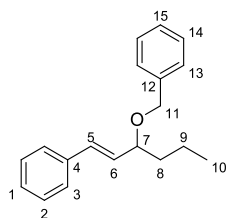
(dt, *J* = 14.8, 7.4 Hz, 2H, C₈HH), 0.98 (t, *J* = 7.4 Hz, 3H, C₉HHH). ¹³C NMR (75 MHz, CDCl₃) δ 200.59 (C₁₀), 138.68 (C₄), 132.33 (C₅), 130.93 (C₆), 128.65, 128.18, 128.13 (C₁, C₂, C₃), 38.19 (C₇), 18.88 (C₈), 14.18 (C₉).

Experimental

(E)-(3-(benzyloxy)hex-1-en-1-yl)benzene



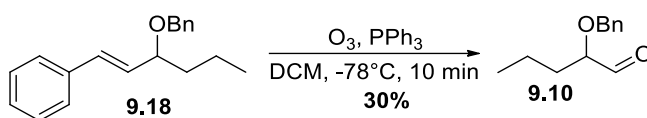
A 500 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with enone **9.16** (18.48 g, 106 mmol, 1 eq.), NaBH₄ (5.24 g, 138 mmol, 1 eq.) and EtOH (200 mL) at 0°C. Resulting mixture was left stirring at room temperature for 2 h prior to addition of a saturated aqueous solution of NH₄Cl (150 mL). After separation, the aqueous phase was extracted with AcOEt (2 x 100 mL). Combined organic fractions were dried over MgSO₄, concentrated under reduced pressure and purified by flash column chromatography on silica gel (PE/AcOEt 10:1) to furnish corresponding alcohol which is immediately introduced into a 250 mL round bottom flask equipped with a Teflon-coated magnetic stirrer, NaH (60%, 8.48 g, 221 mmol, 1 eq.) and DCM (200 mL). Resulting mixture was left stirring at 0°C for 15 min prior to addition of NaI (1.1 g, 7.4 mmol, 0.1 eq.) and benzyl bromide (16.28 g, 95.8 mmol, 1.3 eq.). Resulting mixture was left stirring at room temperature for 12 h. At that stage, reaction mixture was treated with a saturated aqueous solution of NH₄Cl (150 mL). After separation, the aqueous phase was extracted with DCM (2 x 100 mL). Combined organic fractions were dried over MgSO₄, concentrated under reduced pressure and purified by flash column chromatography on silica gel (PE/AcOEt 12:1) to furnish benzyl ether **9.18** (26.58, 95%). R_f = 0.6 (PE/AcOEt 4:1).



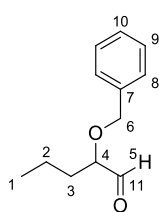
¹H NMR (300 MHz, CDCl₃) δ 7.44 – 7.24 (m, 10H, C₁H, C₂H, C₃H, C₁₃H, C₁₄H, C₁₅H), 6.54 (d, *J* = 16.0 Hz, 1H, C₅H), 6.14 (dd, *J* = 16.0, 8.0 Hz, 1H, C₆H), 4.62 (d, *J* = 11.9 Hz, 1H, C₁₁HH), 4.41 (d, *J* = 11.9 Hz, 1H, C₁₁HH), 3.93 (m, 1H, C₇H), 1.76 (m, 1H, C₈HH), 1.65 – 1.50 (m,

1H, C₈HH), 1.50 – 1.33 (m, 2H, C₉HH), 0.96 – 0.84 (m, 3H, C₁₀HHH). ¹³C NMR (75 MHz, CDCl₃) δ 138.68 (C₄), 136.83 (C₁₂) 132.33 (C₅), 130.93 (C₆), 129.18, 128.57, 128.48, 127.89, 127.55, 126.62 (C₁, C₂, C₃, C₁₃, C₁₄, C₁₅), 80.10 (C₇), 70.26 (C₁₁), 38.19 (C₈), 18.88 (C₉), 14.18 (C₁₀).

2-(benzyloxy)pentanal



A 3-necked 500 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with olefin **9.18** (5 g, 18.8 mmol, 1 eq.) and DCM (300 mL). The mixture was cooled to -78°C and stirred while ozone was bubbled through the solution using a Pasteur pipet. The reaction was monitored by TLC and after 10 min, all the starting material was consumed. After flushing the solution with argon to eliminate excess ozone, the solution was allowed to heat up to room temperature. At that moment, PPh₃ (14.76 g, 56 mol, 3 eq.) was added in one portion and the mixture was left stirring over night. The crude reaction mixture was then concentrated under reduced pressure and purified by flash column chromatography on silica gel (PE/AcOEt 10:1) to afford aldehyde **9.10** (1.082 g, 30%). R_f = 0.34 (PE/AcOEt 3:1).

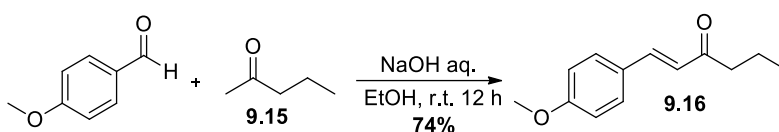


¹H NMR (300 MHz, CDCl₃) δ 9.66 (d, J = 2.2 Hz, 1H, C₅H), 7.41 – 7.28 (m, 5H, C₈H, C₉H, C₁₀H), 4.69 (d, J = 11.7 Hz, 1H, C₆HH), 4.54 (d, J = 11.7 Hz, 1H, C₆HH), 3.77 (ddd, J = 7.6, 5.7, 2.2 Hz, 1H, C₄H), 1.74 – 1.61 (m, 2H, C₃HH), 1.53 – 1.39 (m, 2H, C₂HH), 0.92 (t, J = 7.3 Hz, 3H, C₁HHH). ¹³C NMR (75 MHz, CDCl₃) δ 204.02 (C₁₁), 137.53 (C₇), 128.65, 128.18, 128.13 (C₈, C₉, C₁₀), 83.45

Experimental

(C₄), 72.66 (C₆), 32.21 (C₃), 18.25 (C₂), 14.00 (C₁). IR (neat, cm⁻¹) 2960, 2933, 2871, 1731, 1454, 1128, 1091, 1060.

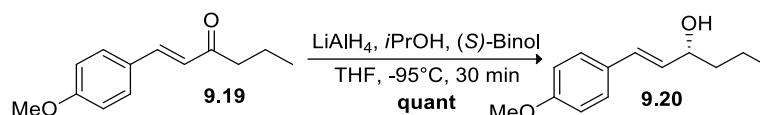
(E)-1-(4-methoxyphenyl)hex-1-en-3-one



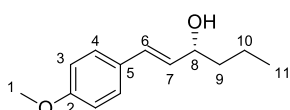
A 250 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with ketone **9.15** (17.39 g, 202 mmol, 1.1 eq.), aldehyde (25 g, 183 mmol, 1 eq.), NaOH (1.83 g, 46 mmol, 0.25 eq.), H₂O (50 mL) and EtOH (100 mL). Resulting mixture was left stirring at room temperature for 12 h. After total conversion, the volatiles were removed under reduced pressure with the aid of a rotary evaporator. Resulting aqueous layer was extracted with Et₂O (2 x 50 mL). Combined organic fractions were dried over MgSO₄, concentrated under reduced pressure and purified by flash column chromatography on silica gel (PE/AcOEt 6:1) to afford enone **9.16** (30.49 g, 74%).

¹H NMR (300 MHz, CDCl₃) δ 7.55 – 7.46 (m, 4H, C₃H, C₄H), 6.94 – 6.88 (m, 2H, C₆H), 6.63 (d, *J* = 16.1 Hz, 1H, C₇H), 3.84 (s, 3H, C₁HHH), 2.62 (dd, *J* = 8.7, 6.0 Hz, 2H, C₉HH), 1.79 – 1.62 (m, 2H, C₁₀HH), 1.04 – 0.92 (m, 3H, C₁₁HHH). ¹³C NMR (75 MHz, CDCl₃) δ 200.59 (C₈), 161.48 (C₂), 142.10 (C₆), 129.93 (C₇), 127.23 (C₅), 124.15 (C₄), 114.38 (C₃), 55.40 (C₁), 42.71 (C₉), 17.95 (C₁₀), 13.91 (C₁₁).

(E)-1-(4-methoxyphenyl)hex-1-en-3-ol



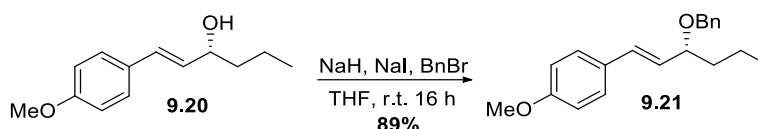
A 25 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with LiAlH_4 in THF (4M, 550 μL , 2.2 mmol, 3 eq.) and *i*PrOH (132 mg, 2.2 mmol, 3 eq.). Resulting mixture was left stirring at room temperature for 10 min prior to addition of a solution of (*S*)-Binol (631 mg, 2.2 mmol, 3 eq.) in THF (3 mL). A second 25 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with enone **9.19** (150 mg, 0.734 mmol, 1 eq.) and THF (3 mL). Resulting mixture was left stirring at -95°C for 15 min prior to dropwise addition of the freshly prepared solution of Binol over a period of 15 min. Resulting mixture was left stirring for another 30 min at that temperature. At that stage, reaction mixture was treated with a 1M aqueous solution of HCl (10 mL) and Et_2O (20 mL). After separation, the aqueous phase was extracted with Et_2O (2 x 10 mL). Combined organic fractions were dried over MgSO_4 , concentrated under reduced pressure and purified by flash column chromatography on silica gel (PE/AcOEt 9:1) to furnish alcohol **9.20** as a 1:5 enantiomeric mixture (151 mg, quant).



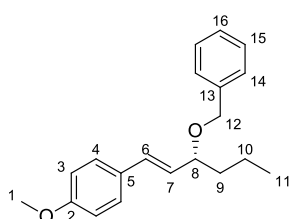
^1H NMR (300 MHz, CDCl_3) δ 7.44 – 7.13 (m, 2H, C_4H), 6.93 – 6.81 (m, 2H, C_3H), 6.49 (d, $J = 15.9$ Hz, 1H, C_6H), 6.06 (dd, $J = 15.9, 7.1$ Hz, 1H, C_7H), 5.61 (bs, 1H, C_8OH), 4.27 – 4.16 (m, 1H, C_8H), 3.81 (s, 3H, C_1HHH), 1.68 – 1.50 (m, 2H, C_9HH), 1.50 – 1.34 (m, 2H C_{10}HH), 0.96 (t, $J = 7.2$ Hz, 3H C_{11}HHH). **^{13}C NMR** (75 MHz, CDCl_3) δ 159.21 (C_2), 130.45 (C_6), 129.81 (C_7), 129.50 (C_5), 127.62 (C_4), 113.98 (C_3), 73.05 (C_8), 55.30 (C_1), 39.55 (C_9), 18.74 (C_{10}), 14.06 (C_{11}).

Experimental

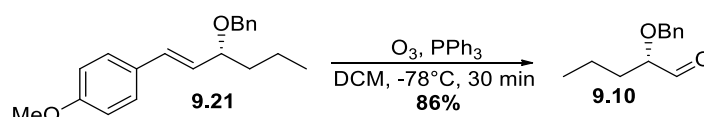
(E)-1-(3-(benzyloxy)hex-1-en-1-yl)-4-methoxybenzene



A 100 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with alcohol **9.20** (8.93 g, 43.3 mmol, 1 eq.), NaH (60%, 3.12 g, 129.9 mmol, 1 eq.) and THF (50 mL). Resulting mixture was left stirring at 0°C for 15 min prior to addition of NaI (650 mg, 4.33 mmol, 0.1 eq.) and benzyl bromide (16.28 g, 95.8 mmol, 1.3 eq.). Resulting mixture was left stirring at room temperature for 16 h. At that stage, reaction mixture was treated with a saturated aqueous solution of NH₄Cl (50 mL). After separation, the aqueous phase was extracted with DCM (2 x 50 mL). Combined organic fractions were dried over MgSO₄, concentrated under reduced pressure and purified by flash column chromatography on silica gel (PE/AcOEt 19:1) to furnish benzyl ether **9.21** (10.71 g, 89%).

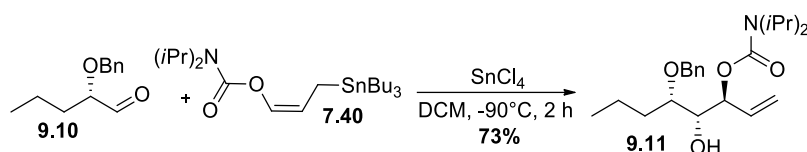


¹H NMR (300 MHz, CDCl₃) δ 7.45 – 7.29 (m, 7H, C₁₄H, C₁₅H, C₁₆H, C₄H), 6.94 (d, J = 8.5 Hz, 2H, C₃H), 6.55 (d, J = 15.9 Hz, 1H, C₆H), 6.13 – 5.99 (dd, J = 15.9, 6.2 Hz, 1H, C₇H), 4.70 (d, J = 12.0 Hz, 1H, C₁₂H), 4.47 (d, J = 12.0, 1H, C₁₂H), 3.96 (dd, J = 12.7, 6.2 Hz, 1H, C₈H), 3.86 (s, 3H, C₁HHH), 1.91 – 1.73 (m, 2H, C₉HH), 1.71 – 1.37 (m, 2H, C₁₀HH), 1.03 – 0.94 (m, 2H, C₁₁HHH). **¹³C NMR** (75 MHz, CDCl₃) δ 159.41 (C₂), 139.07 (C₁₃), 131.88 (C₆), 129.17 (C₇), 128.67, 128.45, 127.87, 127.78 (C₅, C₁₄, C₁₅, C₁₆), 127.50 (C₄), 114.14 (C₃), 80.26 (C₁₂), 70.11 (C₈), 55.47 (C₁), 38.27 (C₉), 18.92 (C₁₀), 14.19 (C₁₁).

2-(benzyloxy)pentanal

A 3-necked 500 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with olefin **9.21** (11.45 g, 38.68 mmol, 1 eq.) and DCM (380 mL). The mixture was cooled to -78°C and stirred while ozone was bubbled through the solution using a Pasteur pipet. The reaction was monitored by TLC and after 30 min, all the starting material was consumed. After flushing the solution with argon to eliminate excess ozone, the solution was allowed to heat up to room temperature. At that moment, PPh_3 (30 g, 116 mmol, 1.5 eq.) was added in one portion and the mixture was left stirring over night. The crude reaction mixture was then concentrated under reduced pressure and purified by flash column chromatography on silica gel (PE/AcOEt 14:1) to afford aldehyde **9.10** (6.39 g, 86%).

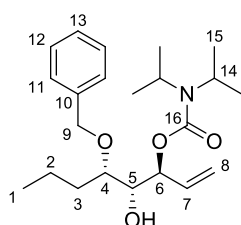
Analyses: see above

(3*S*,4*R*,5*S*)-5-(benzyloxy)-4-hydroxyoct-1-en-3-yl diisopropylcarbamate

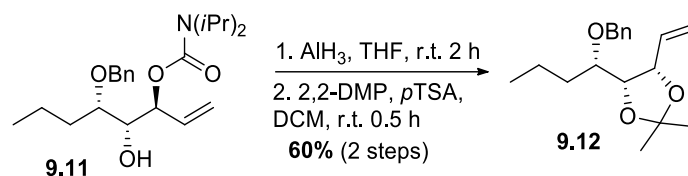
A 250 mL round bottom flask equipped with a Teflon-coated magnetic stirrer was charged with olefin **7.40** (2.13 g, 4.5 mmol, 1.05 eq.) and DCM (70 mL). Resulting mixture was left stirring at -78°C for 10 min before adding dropwise SnCl_4 (0.52 mL, 4.5 mmol, 1.05 eq.). After another 10 min, the mixture was cooled down to -85°C and the aldehyde **9.10** (0.91 g, 4.05

Experimental

mmol, 1 eq.) in DCM (30 mL) was added carefully. After 2 h, DCM (50 mL) and a saturated aqueous solution of NaHCO_3 (50 mL) were added. After separation, combined organic fractions were dried over MgSO_4 , concentrated under reduced pressure and resulting milky residue was purified by flash column chromatography on silica gel (PE 100% to PE/AcOEt 15:1) to furnish **9.11** (1.12 g, 73%). R_f = 0.3 (PE/AcOEt 5:1).

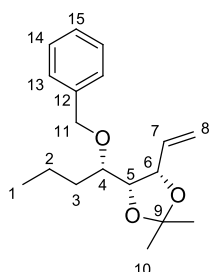


^1H NMR (300 MHz, CDCl_3) δ 7.44 – 7.23 (m, 5H, C_{11}H , C_{12}H , C_{13}H), 6.03 (ddd, J = 17.2, 10.6, 6.6 Hz, 1H, C_7H), 5.37 – 5.21 (m, 3H, C_6H , C_8HH), 4.61 (d, J = 11.0 Hz, 1H, C_9HH), 4.55 (d, J = 11.0 Hz, 1H, C_9HH), 3.98 (bs, 1H, C_{14}H), 3.86 (bs, 1H, $\text{C}_{14'}\text{H}$), 3.66 (ddd, J = 7.5, 6.5, 3.5 Hz, 1H, C_5H), 3.49 (td, J = 6.2, 3.6 Hz, 1H, C_4H), 2.50 (d, J = 7.6 Hz, 1H, C_5OH), 1.74 – 1.60 (m, 2H, C_3HH), 1.41 (td, J = 14.8, 7.3 Hz, 2H, C_2HH), 1.27 – 1.14 (m, 12H, C_{15}HHH , $\text{C}_{15'}\text{HHH}$), 0.93 (t, J = 7.3 Hz, 3H, C_1HHH). **^{13}C NMR** (75 MHz, CDCl_3) δ 154.55 (C_{16}), 138.31 (C_{10}), 134.62 (C_7), 128.52, 128.21, 127.88 (C_{11} , C_{12} , C_{13}), 118.19 (C_8), 77.92 (C_4), 75.27 (C_6), 74.14 (C_5), 72.76 (C_9), 46.35 (C_{14}), 45.77 ($\text{C}_{14'}$), 33.17 (C_3), 21.57 (C_{15}), 20.86 ($\text{C}_{15'}$), 18.71 (C_2), 14.34 (C_1). **IR** (neat, cm^{-1}) 3500, 2962, 2933, 2873, 1693, 1304, 1284, 1049. **MS** (ES+), m/z (%): 400.25 (100), 349.18 (5), 243.12 (7), 206.96 (5), 202.97, (26).

(4*R*,5*S*)-4-((*S*)-1-(benzyloxy)butyl)-2,2-dimethyl-5-vinyl-1,3-dioxolane

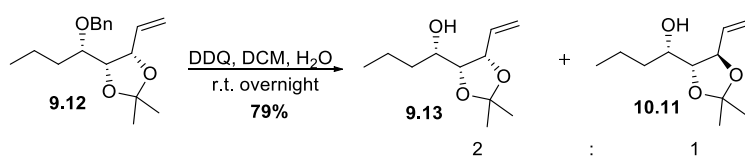
A 10 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with aluminium (III) chloride (689 mg, 5.23 mmol, 0.33 eq.) and THF (1 mL). After cooling to 0 °C, a 4M diethyl ether solution of LiAlH_4 (0.6 mL, 15.69 mmol, 1 eq.) was added slowly and the resulting heterogeneous mixture was allowed to stir for 30 min at 0 °C. At that moment, a solution of diisopropylcarbamate **9.11** (5.92 g, 15.69 mmol, 1 eq.) in THF (15 mL) was added to the mixture which was allowed to stir for 3 h at room temperature. The resulting mixture was then diluted with an aqueous solution of NH_4Cl (25 mL) and an aqueous saturated solution of Rochelle's Salt (10 mL). After separation, the aqueous phase was extracted with diethylether (2 x 30 mL). Organic fractions were dried over MgSO_4 and concentrated under vacuum. The crude product was used without further purification. A 25 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was then charged with corresponding diol (410 mg, 1.63 mmol, 1 eq.), DCM (4 mL), 2,2-DMP (1.697 g, 16.3 mmol, 10 eq.) and *p*TSA (catalytic amount). The mixture was left stirring at room temperature for 30 min. At that moment, the crude mixture was diluted with an aqueous solution of NaHCO_3 (15 mL) and DCM (10 mL). After separation, the aqueous phase was extracted with DCM (2 x 30 mL). Organic fractions were dried over MgSO_4 , concentrated under vacuum and purified by flash column chromatography on silica gel (PE/AcOEt 20:1) to afford a diastereomeric mixture of olefin **9.12** (2.96 g, 65%).

Experimental



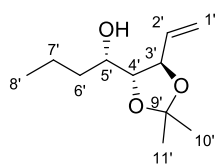
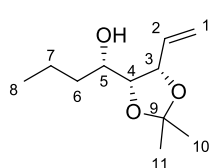
¹H NMR (300 MHz, CDCl₃) δ 7.43 – 7.23 (m, 5H, C₁₃H, C₁₄H, C₁₅H), 5.88 (ddd, J = 17.2, 10.1, 8.6 Hz, 1H, C₇H), 5.31 – 5.26 (m, 2H, C₈HH), 4.83 (d, J = 11.5 Hz, 1H, C₁₁HH), 4.59 (d, J = 11.5 Hz, 1H, C₁₁HH), 4.44 (dd, J = 8.6, 6.0 Hz, 1H, C₆H), 4.21 (dd, J = 8.0, 6.0 Hz, 1H, C₅H), 3.43 (td, J = 7.8, 3.5 Hz, 1H, C₄H), 1.53 (s, 3H, C₁₀HHH), 1.42 (s, 3H, C_{10'}HHH), 1.41 (m, 4H, C₂HH, C₃HH), 0.86 (t, J = 7.1 Hz, 3H, C₁HHH). **¹³C NMR** (75.47 MHz, CDCl₃) δ 139.25 (C₁₂), 134.70 (C₇), 128.34, 127.99, 127.47 (C₁₃, C₁₄, C₁₅), 118.98 (C₈), 108.97 (C₉), 81.79 (C₅), 79.54 (C₆), 77.42 (C₄), 73.05 (C₁₁), 33.32 (C₃), 28.29 (C₁₀), 25.83 (C_{10'}), 18.71 (C₂), 14.14 (C₁). **IR** (neat, cm⁻¹) 2983, 2958, 2933, 2871, 1706, 1454, 1429, 1379, 1369, 1307, 1288, 1247, 1217, 1153, 1145, 1097, 1076, 1039. **MS** (p ESI) m/z (%): 313.18 (100), 279.09; 219.18; 180.05; 140.01. **HRMS**, m/z: calculated for (C₁₈H₂₆O₃Na) [M+23]: 313.1780. Found: 313.1782.

(S)-1-((4R,5S)-2,2-dimethyl-5-vinyl-1,3-dioxolan-4-yl)butan-1-ol



A 25 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with olefin **9.12** (846 mg, 2.91 mmol, 1 eq.), DCM (15 mL), H₂O (1 mL) and DDQ (1.98 g, 8.71 mmol, 3 eq.). The mixture was left stirring at room temperature for 16 h. At that moment, the crude mixture was diluted with a saturated aqueous solution of NaHCO₃ (15 mL) and DCM (10 mL) prior to filtration on celite®. After separation, the aqueous phase was extracted with DCM (2 x 30 mL). Organic fractions were dried over MgSO₄,

concentrated under vacuum and purified by flash column chromatography on silica gel (PE/AcOEt 7:1) to afford a 2:1 diastereomeric mixture of olefin **9.13** (460 mg, 79%).



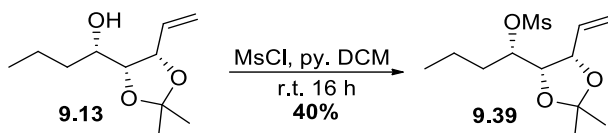
¹H NMR (300 MHz, CDCl₃) δ 5.98 (ddd, *J* = 17.2, 10.2, 8.1 Hz, 1H, C₂H), 5.88 (ddd, *J* = 16.4, 10.6, 5.3 Hz, 1H, C₂H), 5.37 (tt, *J* = 9.2, 1.5 Hz, 1H, C₁HH), 5.33 – 5.23 (m, 3H, C₁HH, C₁'HH), 4.57 (dd, *J* = 7.8, 7.0 Hz, 2H, C₃H, C₃'H), 4.01 (dd, *J* = 6.7, 5.4 Hz, 2H, C₄H, C₄'H), 3.58 (dd, *J* = 10.9, 6.0 Hz, 2H, C₅H, C₅'H), 1.52 (s, 3H, C₁₀H), 1.40 (s, 6H, C₁₁H, C₁₀'H), 1.39 (s, 3H, C₁₁'H), 1.67 – 1.35 (m, 4H, C₆H, C₆'H), 1.32 – 1.19 (m, 4H, C₇H, C₇'H), 0.96 – 0.87 (m, 6H, C₈H, C₈'H).

Following analyses were carried out on the major diastereoisomer:

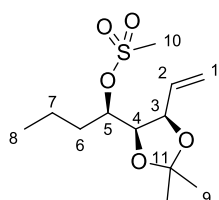
¹³C NMR (75.47 MHz, CDCl₃) δ 134.26 (C₂), 119.41 (C₁), 108.69 (C₉), 80.88 (C₄), 79.27 (C₃), 69.50 (C₅), 36.11 (C₆), 27.61, 25.20 (C₁₀, C₁₁), 18.84 (C₇), 14.11 (C₈). **IR** (neat, cm⁻¹) 3429, 2955, 1682, 1458, 1377, 1304, 1254, 1215, 1169, 1068, 1030. **MS** (p ESI) *m/z* (%): 223.13 (100), 102.13 (50). **HRMS**, *m/z*: calculated for (C₁₁H₂₀O₃Na) [*M*+23]: 223.1347. Found: 223.1350.

Experimental

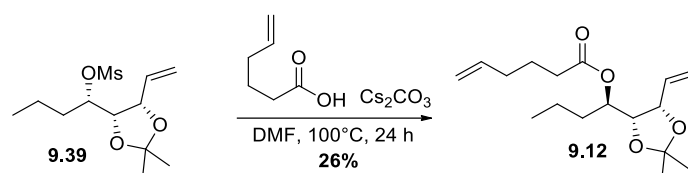
(S)-1-((4S,5S)-2,2-dimethyl-5-vinyl-1,3-dioxolan-4-yl)butylmethanesulfonate



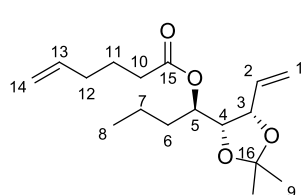
A 25 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with alcohol **9.13** (200 mg, 1.00 mmol, 1 eq.), DCM (2 mL), pyridine (284 mg, 3.00 mmol, 3 eq.) and MsCl (137 mg, 1.20 mmol, 1.2 eq.). The mixture was left stirring at room temperature for 16 h. At that moment, the crude mixture was diluted with a saturated aqueous solution of NH_4Cl (15 mL) and DCM (10 mL). After separation, the aqueous phase was extracted with DCM (2 x 30 mL). Organic fractions were dried over MgSO_4 , concentrated under vacuum and purified by flash column chromatography on silica gel (PE/AcOEt 4:1) to afford **9.39** (111 mg, 40%).



^1H NMR (300 MHz, CDCl_3) δ 5.84 (ddd, $J = 17.3, 13.5, 8.8$ Hz, 1H, C_2H), 5.35 (d, $J = 5.7$ Hz, 1H, C_1HH), 5.34 – 5.27 (m, 1H, C_1HH), 4.62 (td, $J = 8.9, 2.7$ Hz, 1H, C_5H), 4.47 (dd, $J = 8.7, 6.0$ Hz, 1H, C_3H), 4.23 (dd, $J = 9.1, 6.0$ Hz, 1H, C_4H), 3.10 (s, 3H, C_{10}HHH), 1.60 – 1.51 (m, 2H, C_6HH), 1.50 (s, 3H, C_9HHH), 1.37 (s, 3H, $\text{C}_9'\text{HHH}$), 0.97-0.86 (m, 5H, $\text{C}_7\text{HH}, \text{C}_8\text{HHH}$). **^{13}C NMR** (75 MHz, CDCl_3) δ 133.12 (C_2), 120.42 (C_{11}), 109.32 (C_1), 82.31 (C_5), 78.92 (C_4), 78.89 (C_3), 38.95 (C_{10}), 33.17 (C_6), 28.01 (C_9), 25.69 ($\text{C}_{9'}$), 18.01 (C_7), 13.63 (C_8).

(*R*)-1-((4*R*,5*S*)-2,2-dimethyl-5-vinyl-1,3-dioxolan-4-yl)butyl hex-5-enoate

A 25 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with Cs_2CO_3 (351 mg, 1.07 mmol, 3 eq.), MeOH (10 mL) and hexenoic acid (41 mg, 0.357 mmol, 1 eq.). The mixture was left stirring at room temperature for 1 h. At that moment, the crude mixture was concentrated under vacuum to afford the cesium carboxylate. A 50 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was then charged with the freshly prepared cesium salt, mesylate **9.39** (100 mg, 0.36 mmol, 1 eq.) and DMF (8 mL). The mixture was left stirring at 100°C for 24 h. At that moment, the crude mixture was diluted with a saturated aqueous solution of NH_4Cl (15 mL) and DCM (10 mL). After separation, the aqueous phase was extracted with DCM (2 x 30 mL). Organic fractions were dried over MgSO_4 , concentrated under vacuum and purified by flash column chromatography on silica gel (PE/AcOEt 25:1) to afford diene **9.12** (28 mg, 26%).

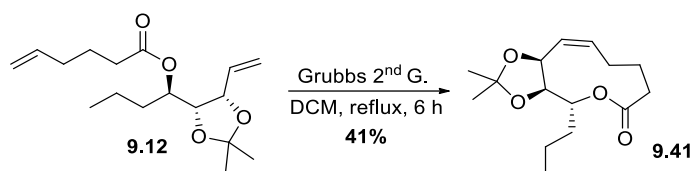


^1H NMR (300 MHz, CDCl_3) δ 5.88 – 5.69 (m, 2H, C_2H , C_{13}H), 5.33 (d, $J = 17.0$ Hz, 1H, C_1HH or C_{14}HH), 5.21 (d, $J = 10.3$ Hz, 1H, C_1HH or C_{14}HH), 5.07 – 4.96 (m, 2H, C_1HH , C_{14}HH), 4.93 (td, $J = 7.6, 3.8$ Hz, 1H, C_5H), 4.60 (t, $J = 7.0$ Hz, 1H, C_4H), 4.18 (dd, $J = 7.3, 6.7$ Hz, 1H, C_3H), 2.25 (td, $J = 7.5, 3.6$ Hz, 2H, C_{12}HH), 2.14 – 2.02 (m, 2H, C_6HH), 1.81 – 1.52 (m, 4H, C_{10}HH , C_{11}HH), 1.48 (s, 3H, C_9HHH), 1.37 (s, 3H, C_9HHH), 1.34 – 1.22 (m, 2H, C_7HH), 0.90 (t, $J = 7.3$ Hz, 3H, C_8HHH). **^{13}C NMR** (75.47 MHz, CDCl_3) δ 172.5 (C_{15}), 137.6 (C_{13}), 133.3 (C_2), 118.4 (C_1), 115.3 (C_{14}), 108.7

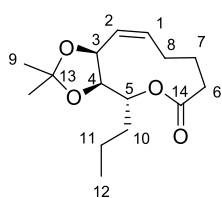
Experimental

(C₁₆), 78.9 (C₃), 78.4 (C₄), 71.6 (C₅), 33.7 (C₁₂), 33.4 (C₁₀), 33.0 (C₆), 27.5 (C₉), 25.2 (C_{9'}), 23.9 (C₁₁), 17.9 (C₇), 14.0 (C₈). **IR** (film, cm⁻¹) 3078, 2954, 2867, 1738, 1640, 1430, 1254, 1215. **MS** (p ESI) m/z (%): 319.19 (100), 279.09 (47), 233.11 (28). **HRMS**, m/z: calculated for (C₁₇H₂₈O₄Na) [M+23]: 319.1880. Found: 319.1883.

(3a*R*,4*R*,11a*S*,*Z*)-2,2-dimethyl-4-propyl-3a,4,7,8,9,11a-hexahydro-6H-[1,3]dioxolo[4,5-*c*]oxecin-6-one



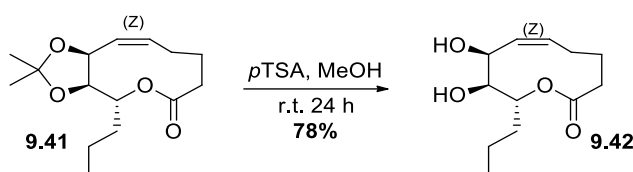
A 100 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with diene **9.12** (28 mg, 0.095 mmol, 1 eq.), DCM (45 mL) and Grubbs' second generation catalyst (6 mg, 0.0095 mmol, 0.1 eq.). The mixture was left stirring at 58°C for 6 h and every hour, 10 mol% of catalyst were added. At that moment, the crude mixture was filtered on celite®, concentrated under vacuum and purified by flash column chromatography on silica gel (PE/AcOEt 9:1) to afford lactone **9.41** (10 mg, 41%).



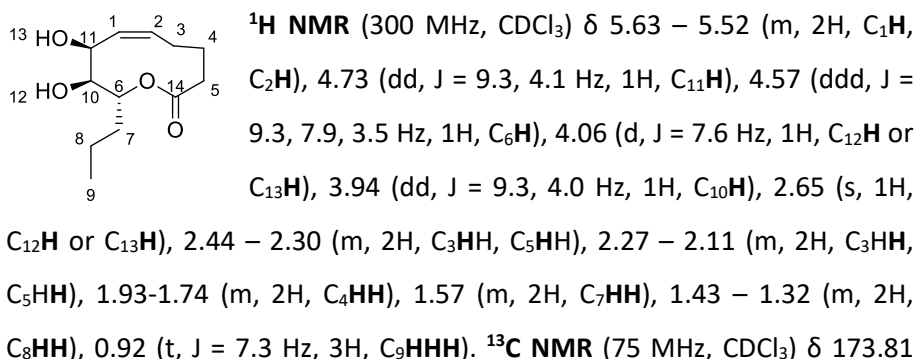
¹H NMR (300 MHz, CDCl₃) δ 5.51 – 5.32 (m, 2H, C₁H, C₂H), 4.96 (dd, *J* = 8.7, 6.2 Hz, 1H, C₃H), 4.68 (ddd, *J* = 10.1, 7.6, 3.6 Hz, 1H, C₅H), 4.22 (dd, *J* = 10.0, 6.2 Hz, 1H, C₄H), 2.38 – 2.28 (m, 2H, C₆HH), 2.23 – 2.12 (m, 2H, C₈HH), 1.88 – 1.72 (m, 2H, C₇HH and/or C₁₀HH and/or C₁₁HH), 1.65 – 1.52 (m, 2H, C₇HH and/or C₁₀HH and/or C₁₁HH), 1.49 (s, 3H, C₉HHH), 1.46 – 1.39

(m, 2H, C₇HH and/or C₁₀HH and/or C₁₁HH), 1.37 (s, 3H, C₉HHH), 0.93 (t, *J* = 7.3 Hz, 3H, C₁₂HHH). ¹³C NMR (75 MHz, CDCl₃) δ 173.34 (C₁₄), 133.69 (C₂), 127.85 (C₁), 110.09 (C₁₃), 79.04 (C₄), 77.21 (C₃), 74.64 (C₅), 72.40 (C₆), 35.74 (C₁₀), 35.03 (C₇), 28.27 (C₈), 27.01 (C₉), 25.83 (C₉'), 17.96 (C₁₁), 14.16 (C₁₂).

(*Z*)-Herbarumine I



A 25 mL round-bottom flask equipped with a Teflon-coated magnetic stirrer was charged with acetonide **9.41** (10 mg, 0.037 mmol, 1 eq.), *p*TSA (catalytic amount) and MeOH (5 mL). Resulting mixture was left stirring at room temperature for 24 h. At that moment, the crude mixture was diluted with a saturated aqueous solution of NaHCO₃ (15 mL) and DCM (40 mL). After separation, the aqueous phase was extracted with DCM (2 x 30 mL). Organic fractions were dried over MgSO₄, concentrated under vacuum and purified by flash column chromatography on silica gel (PE/AcOEt 1:1) to afford diol **9.42** (6 mg, 78%).



Experimental

(C₁₄), 134.45 (C₁), 126.30 (C₂), 74.30 (C₁₀), 74.07 (C₆), 66.84 (C₁₁), 35.62 (C₅),
35.45 (C₇), 27.61 (C₄), 25.50 (C₃), 18.11 (C₈), 14.09 (C₉).