# Supporting Information I

# Stereoselective Synthesis of a Monocyclic Peloruside A Analog

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## Contents

# General Information

All solvents used for reactions were purchased as anhydrous grade from Fluka (puriss.; dried over molecular sieves; $H_2O$ <0.005%) and used without further purification. Solvents for extractions, flash column chromatography (FC) and thin layer chromatography (TLC) were purchased as commercial grade and distilled prior to use. All non-aqueous reactions were performed under an argon atmosphere using flame-dried glassware and standard syringe/septa techniques. All other commercially available reagents were used without further purification, unless otherwise noted. In general, reactions were magnetically stirred and monitored by TLC performed on Merck TLC aluminum sheets (silica gel 60 $F_{254}$). Spots were visualized with UV light ($\lambda$ = 254 nm) or through staining with $Ce_2(SO_4)_3$/phosphomolybdic acid/$H_2SO_4$ or $KMnO_4/K_2CO_3$. Chromatographic purification of products (FC) was performed using Fluka silica gel 60 for preparative column chromatography (particle size 40–63 μm).

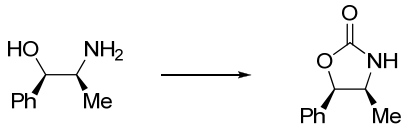
Melting points were obtained in open capillary tubes using a Büchi melting point apparatus B-540 and are uncorrected. $^1$H- and $^{13}$C-NMR spectra were recorded in $CDCl_3$ (unless otherwise noted) on a Bruker AV-400 400 MHz at room temperature. Chemical shifts ($\delta$) are reported in ppm and are referenced to added tetramethyl silane as an internal standard (otherwise to chloroform; $\delta$ 7.26 ppm for $^1$H, $\delta$ 77.16 ppm for $^{13}$C). All $^{13}$C-NMR spectra were measured with complete proton decoupling. Data for NMR spectra are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, quint. = quintet, sext. = sextet, m = multiplet, br = broad signal, J = coupling constant in Hz.

Infrared spectra (IR) were recorded on a Jasco FT/IR-6200 instrument. Resonance frequencies are given as wavenumbers in $cm^{-1}$. Data for IR spectra are reported as follows: w = weak, m = medium, s = strong, br = broad signal.

Optical rotations were measured on a Jasco P-1020 polarimeter. Mass spectra were recorded by the ETH Zürich MS service; HRMS (ESI) spectra were obtained on a Varian IonSpec spectrometer.

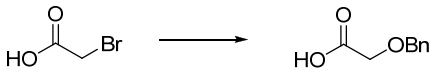
# Experimental Procedures

## Synthesis of carboxylic acid **6**




**(4*S*,5*R*)-4-Methyl-5-phenyl-1,3-oxazolidin-2-one (A).**[1] To a suspension of diphosgene (Acros 99%, 0.780 ml, 6.47 mmol, 0.970 equiv) and activated charcoal (Hänseler AG, 50 mg) in 40 ml THF was added (1*R*,2*S*)-(–)-norephedrine (Aldrich 99%, 1.01 g, 6.68 mmol, 1.00 equiv). The reaction mixture was stirred at room temperature for 15 h and then filtered through Celite. The filtrate was treated with 25 ml sat. aq. $NaHCO_3$ and then extracted with $Et_2O$ (3 × 20 ml). The combined organic layers were washed with 20 ml sat. aq. NaCl, dried over $MgSO_4$ and concentrated. FC ($SiO_2$, AcOEt/hexane 2:1; d = 2.4 cm; h = 18 cm) gave the desired product **A** as a white crystalline solid (925 mg, 78%).

**$R_f$** (AcOEt/hexane 2:1) 0.28. **M.p.:** 108–109 °C. **$[\alpha]_D^{23}$**: –156° (c 0.953, $CHCl_3$). **IR** (film): 3289m (br, 3450–3150), 2982w, 1756s, 1713s, 1698s, 1457m, 1416m, 1385s, 1358m, 1243s, 1037s, 1017s, 948s. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.42–7.29 (m, 5 H); 6.12 (br s, 1 H); 5.71 (d, J = 8.0, 1 H); 4.21 (br dq, J = 7.6, 6.9, 1 H); 0.82 (d, J = 6.6, 3 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 159.54; 134.93; 128.52 (2 C); 128.50; 125.97 (2 C); 81.03; 52.44; 17.55.




**2-(Benzyloxy)acetic acid (B).**[2,3] To a cooled (0 °C) suspension of NaH (Aldrich, 60% in mineral oil, 7.46 g, 187 mmol, 2.57 equiv) in 350 ml THF was added a solution of bromoacetic acid (Fluka purum 98%, 10.1 g, 72.7 mmol, 1.00 equiv) in 50 ml THF. The suspension was warmed to room temperature and stirred until the evolution of hydrogen stopped (*ca*. 5 min). Benzyl alcohol (Fluka purum 98.0%, 7.65 ml, 73.9 mmol, 1.02 equiv) was then added dropwise at 0 °C and the resulting grey/milky suspension was stirred at room temperature until the evolution of hydrogen stopped again. After addition of tetrabutylammonium iodide (Aldrich 98%, 1.61 g, 4.36 mmol, 0.0600 equiv) the resulting white/milky reaction mixture was heated at reflux temperature for 3½ h and then cooled to 0 °C. EtOH (30 ml) was added and the mixture was concentrated to give a light-yellow oil, which was diluted with 200 ml sat. aq. $NaHCO_3$ and 200 ml $Et_2O$. The phases were separated and the organic layer was extracted with sat. aq. $NaHCO_3$ (2 × 200 ml). The combined aqueous extracts were then acidified to pH 2 with 10% sulfuric acid (ca. 200 ml) and 2 M aq. HCl (ca. 50 ml) and extracted with $Et_2O$ (3 × 200 ml). The combind organic extracts were once washed with 200 ml sat. aq. NaCl, dried over $MgSO_4$ and concentrated under reduced pressure, which gave the crude product **B** as a yellow oil (12.8 g, directly used for the next step without further purification).

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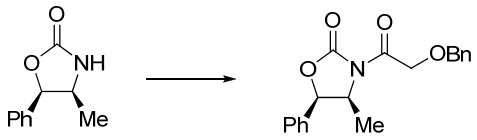
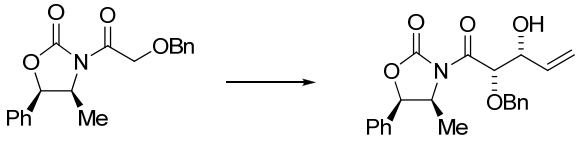
[1] Alouane, N.; Boutier, A.; Baron, C.; Vrancken, E.; Mangeney, P. *Synthesis* **2006**, 885–889.
[2] Yu, H.; Ballard, C. E.; Boyle, P. D.; Wang, B. *Tetrahedron* **2002**, *58*, 7663–7679.
[3] Solladié, G.; Adamy, M.; Colobert, F. *J. Org. Chem*. **1996**, *61*, 4369–4373.

**$R_f$** (AcOEt/hexane 1:2) 0.00–0.15 (broad spot). **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 10.17 (br s, 1 H); 7.37–7.29 (m, 5 H); 4.65 (s, 2 H); 4.14 (s, 2 H). **$^1$H-NMR** (400 MHz, $CD_3OD$): δ 7.38–7.27 (m, 5 H); 4.93 (br s, 1 H); 4.60 (s, 2 H); 4.09 (s, 2 H).




**(4*S*,5*R*)-3-(2-(Benzyloxy)acetyl)-4-methyl-5-phenyl-1,3-oxazolidin-2-one (12).** To a cooled (–78 °C) solution of crude 2-(benzyloxy)acetic acid (**B**) (5.00 g, ca. 30 mmol, ca. 1.2 equiv) in 200 ml THF was added pivaloyl chloride (Fluka purum 98.0%, 4.00 ml, 32.5 mmol, 1.29 equiv) followed by triethylamine (Fluka puriss p.a. 99.5%, 6.30 ml, 45.2 mmol, 1.80 equiv). The resulting white suspension (quite viscous) was stirred for 10 min at –78 °C and 1 h at room temperature, to form the mixed anhydride, and then again cooled to –78 °C. In a separate flask oxazolidinone **A** (4.45 g, 25.1 mmol, 1.00 equiv) was dissolved in 40 ml THF and cooled to –78 °C. Then *n*-BuLi (Fluka, 1.6 M in hexane, 17.3 ml, 27.6 mmol, 1.10 equiv) was added. The deep-red colored solution was stirred for 20 min and then transferred to the mixed anhydride *via* cannula/syringe and the mixture was stirred for 3 h at –78 °C and then allowed to warm to room temperature overnight (12 h; cooling bath slowly warmed to rt). After quenching of the reaction with 150 ml sat. aq. $NH_4Cl$, the organic phase was separated and the aqueous phase extracted with AcOEt (3 × 150 ml). The combined organic extracts were successively washed with 200 ml of 1 M aq. NaOH, 200 ml sat. aq. NaCl, dried over $MgSO_4$, filtered and concentrated. The resulting yellow oil (11.4 g) was purified by FC ($SiO_2$, hexane/AcOEt 5:1 → 3:1 → 2:1; d = 5.4 cm; h = 17 cm) affording the desired acyloxazolidinone **12** as a white solid (7.23 g, 88% from **A**).

**$R_f$** (AcOEt/hexane 1:2) 0.45. **M.p.:** 95–96 °C. **$[\alpha]_D^{24}$:** –29.4° (c 1.19, $CHCl_3$). **IR** (film): 3033w, 1777s, 1715s, 1456w, 1415w, 1369m, 1349s, 1261m, 1219m, 1201m, 1150m, 1123m. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.44–7.28 (m, 10 H); 5.73 (d, J = 7.4, 1 H); 4.79 (quint., J = 6.9, 1 H); 4.75 (d, J = 17.8, 1 H); 4.70 (d, J = 17.8, 1 H); 4.69 (s, 2 H); 0.93 (d, J = 6.6, 3 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 169.90; 152.95; 137.20; 133.01; 128.93; 128.78 (2 C); 128.52 (2 C); 128.10 (2 C); 128.03; 125.63 (2 C); 80.05; 73.54; 69.75; 54.57; 14.59. **HRMS** (ESI): 348.1176 (56, $[M + Na]^+$, $C_{19}H_{19}NNaO_4$, calcd. 348.1206).




**(4*S*,5*R*)-3-((2*S*,3*R*)-2-(Benzyloxy)-3-hydroxypent-4-enoyl)-4-methyl-5-phenyl-1,3-oxazolidin-2-one (13).**[4] To a cooled (–78 °C) solution of *N*-glycolylimide **12** (4.00 g, 12.3 mmol, 1.00 equiv) in 100 ml $CH_2Cl_2$ was added $TiCl_4$ (Fluka puriss. 99.0%, 1.41 ml, 12.9 mmol, 1.05 equiv) dropwise (immediate very intense yellow-coloration) and stirred for 15 min. Then Hünig's base (Aldrich redist. 99.5%, 5.35 ml, 30.7 mmol, 2.50 equiv) was added dropwise (little smoke emission observed) and the dark-colored solution was stirred for 2 h at –78 °C.

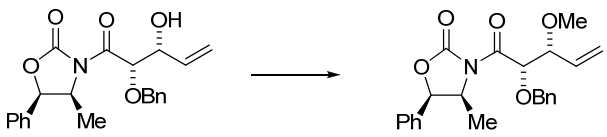
[4] Bierstedt, A.; Roels, J.; Zhang, J.; Wang, Y.; Fröhlich, R.; Metz, P. *Tetrahedron Lett.* **2003**, *44*, 7867–7870. (The crystal structure of *ent*-**13** is reported in ref. 4, but no other analytical data are available).

After addition of *N*-methyl-2-pyrrolidinone[5] (Fluka 99.5%, 1.18 ml, 12.3 mmol, 1.00 eq.) at –78 °C the mixture was stirred for additional 10 min followed by the addition of acrolein (Fluka puriss 99.0%, 2.46 ml, 36.9 mmol, 3.00 equiv). The very dark reaction mixture was stirred for 1¼ h at –78 °C (TLC: starting material fully converted) and then quenched with 100 ml half-saturated aq. $NH_4Cl$. The organic layer was separated and the aqueous layer was extracted with $CH_2Cl_2$ (3 × 75 ml). The combined organic extracts were washed with 100 ml sat. aq. NaCl, then dried over $Na_2SO_4$ and concentrated to yield a yellow oil. Purification of this material by FC ($SiO_2$, hexane/AcOEt 3:1 → 2:1 → 1:1; d = 4.6 cm; h = 16 cm) afforded **13** as a viscous, colorless oil (3.25 g, 69%, dr = 14:2:1).

**$R_f$** (AcOEt/hexane 1:2) 0.26. **$[\alpha]_D^{24}$:** –34.8 ° (c 1.01, $CHCl_3$). **IR** (film): 3475w (br, 3650–3250), 3033w, 1774s, 1708s, 1455m, 1365s, 1342s, 1197s, 1147s, 1120s, 1066m, 1030m, 989m, 698s. **$^1$H-NMR** (400 MHz, $CDCl_3$): (Data for major isomer **13**) δ 7.44–7.27 (m, 10 H); 5.99 (ddd, J = 17.2, 10.5, 5.8, 1 H); 5.66 (d, J = 7.1, 1 H); 5.39 (dt, J = 17.2, 1.4, 1 H); 5.29–5.27 (m, 1.5 H); 5.25 (t, J = 1.4, 0.5 H); 4.72 (quint., J = 6.7, 1 H); 4.69 (d, J = 11.5, 1 H); 4.57 (d, J = 11.5, 1 H); 4.49–4.43 (m, 1 H); 2.65 (d, J = 7.9, 1 H); 0.86 (d, J = 6.6, 3 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): data of major isomer **13** δ 170.04; 153.04; 136.95; 136.56; 132.89; 128.91; 128.79 (2 C); 128.47 (2 C); 128.44 (2 C); 128.21; 125.61 (2 C); 117.13; 79.92; 79.75; 73.77; 73.35; 55.34; 14.41. **HRMS** (ESI): 404.1448 (100, $[M + Na]^+$, $C_{22}H_{23}NNaO_5$, calcd. 404.1468).

**Alternative procedure with $Bu_2BOTf$**: To a cooled (–78 °C) solution of *N*-glycolylimide **12** (300 mg, 0.922 mmol, 1.00 equiv) in 5 ml $CH_2Cl_2$ was added triflic acid dibutylboryl ester[6] (Fluka 1 M in $CH_2Cl_2$, 1.01 ml, 1.01 mmol, 1.10 equiv) and $NEt_3$ (Fluka puriss. p.a. 99.5%, 0.15 ml, 1.11 mmol, 1.20 equiv). The solution was stirred for 30 min at –78 °C (colorless solution) and for 1¾ h at 0 °C (yellow solution). After recooling to –78 °C, acrolein (Fluka puriss 99.0%, 0.10 ml, 1.50 mmol, 1.63 equiv) was added in one portion. After 2 h at –78 °C (TLC showed conversion <50%) the yellow solution was allowed to warm to 0 °C and then stirred for 15 min at this temperature. Then 1.2 ml of pH 7 phosphate buffer and 4 ml MeOH were added at 0 °C, and the resulting mixture was stirred vigorously in an ice bath as 1.2 ml of 30% aq. $H_2O_2$ were added dropwise. The mixture was stirred for 1 h at 0 °C and then partitioned between 5 ml $H_2O$ and 5 ml $CH_2Cl_2$. The organic layer was separated, the aq. solution was extracted with $CH_2Cl_2$ (3 × 10 ml) and the combined org. phases were washed with 20 ml sat. aq. $NaHCO_3$, 20 ml sat. aq. NaCl, dried over $Na_2SO_4$ and concentrated. The oily residue was purified by FC ($SiO_2$; hexane/AcOEt 3:1 → 2:1 → 1:1; d = 2.4 cm; h = 17 cm) to afford the desired product **13** as a viscous, colorless oil (51 mg, 15%, enantiomerically pure).

Enploying this procedure, significant variations in yield were obtained between individual experiments (15–72%).

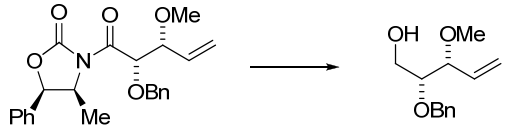



**(4*S*,5*R*)-3-((2*S*,3*R*)-2-(Benzyloxy)-3-methoxypent-4-enoyl)-4-methyl-5-phenyl-1,3-oxazolidin-2-one (C).** To a solution of trimethyloxonium tetrafluoroborate (Fluka purum 98.0%, 3.41 g, 23.1 mmol, 10.7 equiv) in 35 ml

[5] Crimmins, M. T.; She, J. *Synlett* **2004**, 1371–1374.
[6] Crimmins, M. T.; Choy, A. L. *J. Am. Chem. Soc*. **1999**, *121*, 5653–5660.

$CH_2Cl_2$ was added a solution of alcohol **13** (dr = 14:2:1, 820 mg, 2.15 mmol, 1.00 equiv) and 1,8-bis(dimethylamino)-naphthalene[7] (Acros 99%, 4.20 g, 19.6 mmol, 9.12 equiv) in 5 ml $CH_2Cl_2$ in one portion. The orange suspension was stirred for 40 h at room temperature. Then 30 ml sat. aq. $NH_4Cl$ were added and the organic layer was separated. The aq. layer was extracted with $CH_2Cl_2$ (3 × 25 ml), the combined organic extracts were successively washed with 50 ml 0.5 M aq. HCl and 50 ml sat. aq. NaCl, dried over $MgSO_4$ and then concentrated *in vacuo*. The residue (8.88 g of an orange/red solid) was purified by FC (applied to the column as a concentrated solution in $CH_2Cl_2$: $SiO_2$, hexane/AcOEt 5:1 → 2:1; d = 4.4 cm; h = 11 cm) to afford the desired product **C** as a single isomer as a colorless oil (576 mg, 68%).[8]

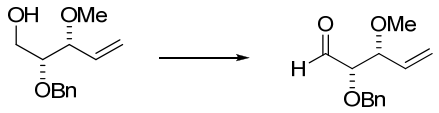
**$R_f$** (AcOEt/hexane 1:2) 0.41. **$[\alpha]_D^{22}$:** –37.3° (c 1.14, $CHCl_3$). **IR** (film): 3032w, 2985w, 2934w, 2825w, 1775s, 1708m, 1455m, 1341s, 1234m, 1195s, 1146m, 1119s, 1088s, 1030m, 988m, 936m, 840w, 810w, 751s, 698s, 666m. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.44–7.23 (m, 10 H); 5.91 (ddd, J = 17.4, 10.3, 7.7, 1 H); 5.61 (d, J = 7.0, 1 H); 5.39 (d, J = 5.0, 1 H); 5.39–5.33 (m, 2 H); 4.685 (d, J = 11.6, 1 H); 4.680 (quint, J = 6.7, 1 H); 4.61 (d, J = 11.9, 1 H); 4.04 (ddt, J = 7.7, 5.0, 0.8, 1 H); 3.33 (s, 3 H); 0.82 (d, J = 6.6, 3 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 169.92; 152.94; 137.44; 134.09; 133.04; 128.89; 128.81 (2 C); 128.46 (2 C); 128.37 (2 C); 127.98; 125.64 (2 C); 119.89; 83.12; 79.61; 79.53; 73.61; 57.29; 55.44; 14.45. **HRMS** (ESI): 418.1618 (100, $[M + Na]^+$, $C_{23}H_{25}NNaO_5$, calcd. 418.1625).




**(2*R*,3*R*)-2-(Benzyloxy)-3-methoxypent-4-en-1-ol (14).** To a cooled (0 °C) solution of **C** (585 mg, 1.48 mmol, 1.00 equiv) in 20 ml THF and MeOH (0.08 ml, 1.85 mmol, 1.25 equiv) was added $LiBH_4$ (Aldrich, 2 M in THF, 0.93 ml, 1.85 mmol, 1.25 equiv) dropwise. After stirring for ½ h at 0 °C, the reaction was carefully quenched with 20 ml 1 M aq. NaOH and the solution stirred until clear phases were obtained. The organic phase was separated and the aqueous solution was extracted with AcOEt (3 × 20 ml). The combined organic extracts were washed with sat. aq. NaCl (40 ml), dried over $MgSO_4$ and concentrated. The residue (light-yellow oil) was purified by FC ($SiO_2$, AcOEt/hexane 1:3 → 1:2 → 1:1; d = 2.4 cm; h = 15 cm) to yield the desired product **14** as a colorless oil (262 mg, 80%).

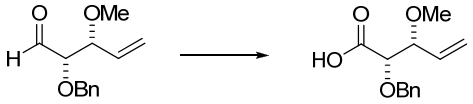
**$R_f$** (AcOEt/hexane 2:1) 0.53; **$R_f$** (AcOEt/hexane 1:4) 0.16. **$[\alpha]_D^{22}$:** +11.0° (c 1.77, $CHCl_3$). **IR** (film): 3448w (br, 3600–3200), 2981w, 2931w, 2881w, 2824w, 1497w, 1455m, 1420w, 1403w, 1355w, 1208w, 1122s, 1089s, 1048s, 995m, 930m, 738m. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.36–7.24 (m, 5 H); 5.80–5.71 (m, 1 H); 5.32–5.30 (m, 1 H); 5.28–5.27 (m, 1 H); 4.75 (d, J = 11.7, 1 H); 4.63 (d, J = 11.7, 1 H); 3.76 (ddt, J = 7.6, 5.6, 1.0, 1 H); 3.72–3.68 (m, 1 H); 3.59–3.51 (m, 2 H); 3.30 (s, 3 H); 2.51 (br t, J = 5.6, 1 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 138.43; 134.53; 128.46 (2 C); 127.91 (2 C); 127.79; 119.11; 84.20; 80.88; 73.32; 62.06; 56.80. **HRMS** (ESI): 245.1141 (100, $[M + Na]^+$, $C_{13}H_{18}NaO_3$, calcd. 245.1148); 223.1320 (18, $[M + H]^+$, $C_{13}H_{19}O_3$, calcd. 223.1329).

[7] Evans, D. A.; Ratz, A. M.; Huff, B. E.; Sheppard, G. S. *Tetrahedron Lett.* **1994**, *35*, 7171–7172.
[8] When diastereomerically pure **13** was converted to **C** under this conditions, the yield was 75%.




**(2*S*,3*R*)-2-(Benzyloxy)-3-methoxypent-4-enal (D).** To a cooled (0 °C) solution of alcohol **14** (301 mg, 1.35 mmol, 1.00 equiv) in 15 ml $CH_2Cl_2$ was added *Dess-Martin* periodinane (Acros 15-wt% in $CH_2Cl_2$, 3.17 ml, 1.49 mmol, 1.10 equiv) and the mixture was stirred for 3 h at 0 °C and for 50 min at room temperature. Subsequently, the white suspension was cooled to 0 °C, 10 ml sat. aq. $Na_2S_2O_3$ and 15 ml sat. aq. $NaHCO_3$ were added and the resulting mixture was stirred for 5 min. The organic phase was then removed and the aq. solution was extracted with $CH_2Cl_2$ (3 × 10 ml). The combined organic solutions were washed with 15 ml sat. aq. NaCl, dried over $MgSO_4$ and concentrated. The residue (yellow oil) was purified by FC (applied to the column as a concentrated solution in $CH_2Cl_2$: $SiO_2$, AcOEt/hexane 1:10 → 1:5; d = 2.4 cm; h = 13.5 cm) yielding the desired product **D** as an oil (208 mg, 70%).

**$R_f$** (AcOEt/hexane 1:4) 0.55. **$[\alpha]_D^{22}$:** –41.1° (c 1.31, $CHCl_3$). **IR** (film): 2978w, 2931w, 2899w, 2825w, 1733m, 1455m, 1085s, 933m, 738m, 698m. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 9.68 (d, J = 1.6, 1 H); 7.35–7.26 (m, 5 H); 5.91–5.82 (m, 1 H); 5.36–5.34 (m, 1 H); 5.32–5.31 (m, 1 H); 4.73 (d, J = 12.0, 1 H); 4.62 (d, J = 12.0, 1 H); 3.97 (ddt, J = 7.6, 3.8, 0.9, 1 H); 3.79 (dd, J = 3.8, 1.6, 1 H); 3.26 (s, 3 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 202.83; 137.03; 133.77; 128.49 (2 C); 128.21 (2 C); 128.14; 119.56; 85.10; 82.92; 73.55; 57.02. **HRMS** (ESI): 243.0989 (12, $[M + Na]^+$, $C_{13}H_{16}NaO_3$, calcd. 243.0992).

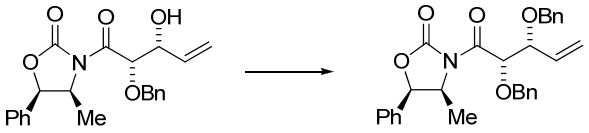



**(2*S*,3*R*)-2-(Benzyloxy)-3-methoxypent-4-enoic acid (6).** To a solution of aldehyde **D** (206 mg, 0.935 mmol, 1.00 equiv) in 20 ml *t*-BuOH/$H_2O$ 4:1 was added 2-methyl-2-butene (Acros 99%, 4.00 ml, 37.8 mmol, 40.4 equiv), $NaH_2PO_4$•$H_2O$ (Fluka puriss. p.a. 99%, 323 mg, 2.34 mmol, 2.50 equiv), followed by sodium chlorite (Fluka puriss p.a. 80%, 423 mg, 3.74 mmol, 4.00 equiv). After stirring at room temperature for ¾ h the reaction mixture was cooled to 0 °C and carefully (exothermic!) quenched by the addition of 10 ml sat. aq. $Na_2S_2O_3$ and 15 ml sat. aq. $NH_4Cl$, acidified to pH 2–3 with *ca*. 6 ml 2 M aq. HCl and then extracted with $Et_2O$ (3 × 10 ml). The combined organic extracts were dried over $Na_2SO_4$ and concentrated. The resulting residue (251 mg of a yellow oil) was diluted with 5 ml sat. aq. $NaHCO_3$ and the solution was washed with $Et_2O$ (5 ml). The ether layer was extracted twice with 5 ml sat. aq. $NaHCO_3$. The combined aq. extracts were acidified to pH 2–3 with 1 M aq. HCl (*ca*. 15 ml) and extracted with $Et_2O$ (3 × 10 ml); the combined organic extracts were dried over $Na_2SO_4$ and concentrated to yield crude **6** as a yellow oil (197 mg, 89%).

Alternatively, the material obtained after quenching, acidification, and extraction was purified by FC ($SiO_2$, AcOEt/hexane/AcOH 50:50:1 → 100:0:1; d = 2.4 cm; h = 15 cm) to yield the desired product **6** as a colorless oil (107 mg, 70%, after co-evaporation with toluene (3 times)). This work-up was performed only for the generation of a pure analytical sample and did not lead to better results in the Yamaguchi esterification reaction (*vide infra*: **5** + **6** → **Y**).

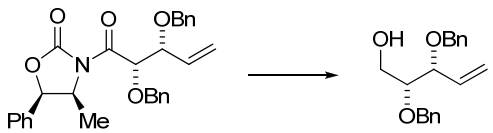
**$R_f$** (AcOEt/hexane 1:4) 0.00; $R_f$ (AcOEt/hexane 1:0) 0.00; $R_f$ (AcOEt/AcOH 100:1) 0.44; $R_f$ (AcOEt/hexane/AcOH 50:50:1) 0.22. **$[\alpha]_D^{22}$:** –57.9° (c 1.07, $CHCl_3$). **IR** (film): 3100w (br, 3650–2500), 3064w, 3032w, 2983w, 2933m, 2897w, 2829w, 1733s, 1456m, 1338m, 1209m, 1127s, 1089s, 1027m, 996m, 935m,

742m, 699s. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 10.04 (br s, 1 H); 7.35–7.25 (m, 5 H); 5.92–5.82 (m, 1 H); 5.37–5.31 (m, 2 H); 4.80 (d, J = 11.9, 1 H); 4.50 (d, J = 11.9, 1 H); 4.03–4.00 (m, 2 H); 3.30 (s, 3 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 174.50; 136.77; 133.70; 128.42 (2 C); 128.26 (2 C); 128.10; 119.91; 83.01; 80.34; 73.46; 57.12. **HRMS** (ESI, negative polarity): 235.0972 (100, $[M - H]^-$, $C_{13}H_{15}O_4$, calcd. 235.0976).



**(4*S*,5*R*)-3-((2*S*,3*R*)-2,3-Bis(benzyloxy)pent-4-enoyl)-4-methyl-5-phenyl-1,3-oxazolidin-2-one (E).** To a stirred solution of secondary alcohol **13** (14:2:1 diastereomeric mixture, 176 mg, 0.461 mmol, 1.00 equiv) in 4.5 ml cyclohexane/$CH_2Cl_2$ 2:1 was added benzyl 2,2,2-trichloroacetimidate (Aldrich, 0.11 ml, 0.60 mmol, 1.30 equiv) followed by dropwise addition of a solution of trifluoromethanesulfonic acid (Fluka puriss. >99.0%, 2.0 µl, 0.023 mmol, 0.050 equiv) in 0.1 ml $CH_2Cl_2$ over a period of 3 h at room temperature. The reaction mixture was then filtered through a short pad of silica ($SiO_2$, AcOEt/hexane 1:2; d = 2.4 cm; h = 5 cm), the filtrate was evaporated, and the residue was purified by FC ($SiO_2$, AcOEt/hexane 1:10 → 1:5 → 1:3; d = 2.4 cm; h = 14.5 cm) to afford the desired product **E** as a *ca*. 10:1 mixture of diastereomers as a colorless oil (154 mg, 71%).

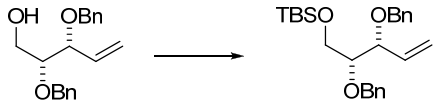
**$R_f$** (AcOEt/hexane 1:2) 0.56. **$[\alpha]_D^{22}$:** –32.7° (c 5.10, $CHCl_3$). **IR** (film): 3064w, 3029w, 2985w, 2930w, 2870w, 1776s, 1710m, 1496w, 1455w, 1366m, 1341m, 1196m, 1119m, 1066m, 1028m, 989m, 747s, 697s, 666m. **$^1$H-NMR** (400 MHz, $CDCl_3$): (Data for major isomer **E**). δ 7.42–7.18 (m, 15 H); 6.00 (ddd, J = 17.2, 10.5, 7.4, 1 H); 5.43–5.41 (m, 1 H); 5.39 (d, J = 0.7, 1 H); 5.35 (d, J = 4.0, 1 H); 4.99 (d, J = 7.0, 1 H); 4.72 (d, J = 11.6, 1 H); 4.69 (d, J = 12.0, 1 H); 4.55 (d, J = 11.9, 1 H); 4.40 (quint., J = 6.7, 1 H); 4.32 (d, J = 12.4, 1 H); 4.19 (ddt, J = 7.4, 4.0, 0.9, 1 H); 0.78 (d, J = 6.6, 3 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): (Data for major isomer **E**). δ 169.56; 152.81; 138.36; 137.31; 134.06; 132.96; 128.73; 128.70 (2 C); 128.57 (2 C); 128.37 (2 C); 128.33 (2 C); 128.28 (2 C); 127.87; 127.75; 125.43 (2 C); 119.69; 79.60; 79.30; 79.22; 73.47; 70.19; 55.35; 14.25. **HRMS** (ESI): 472.2125 (36, $[M + H]^+$, $C_{29}H_{30}NO_5$, calcd. 472.2118); 489.2392 (100, $[M + NH_4]^+$, $C_{29}H_{33}N_2O_5$, calcd. 489.2384); 494.1946 (8, $[M + Na]^+$, $C_{29}H_{29}NNaO_5$, calcd. 494.1938).



**(2*R*,3*R*)-2,3-Bis(benzyloxy)pent-4-en-1-ol (15).**[9,10] To a cooled (0 °C) solution of **E** (191 mg, 0.405 mmol, 1.00 equiv) in 6 ml THF and MeOH (Fluka puriss., absolute, over MS, 0.0200 ml, 0.506 mmol, 1.25 equiv) was added $LiBH_4$ (Aldrich 2 M in THF, 0.250 ml, 0.506 mmol, 1.25 equiv) dropwise. After stirring for 2 h at 0 °C, the reaction was carefully quenched with 7 ml 1 M aq. NaOH. The organic phase was separated; the aqueous layer was extracted with AcOEt (3 × 6 ml), and the combined organic layers were then washed with 10 ml sat. aq. NaCl, dried over $MgSO_4$, and concentrated. This residue (colorless oil) was purified by FC ($SiO_2$, AcOEt/hexane 1:5 → 1:3; d = 2.4 cm; h = 16 cm) yielding the desired product **15** as a colorless oil (77 mg, 64%).

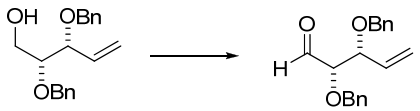
[9] Heo, J.-N.; Micalizio, G. C.; Roush, W. R. *Org. Lett.* **2003**, *5*, 1693–1696.
[10] Diastereomer of **15**: Bravo, F.; Castillón, S. *Eur. J. Org. Chem.* **2001**, 507–516.

**$R_f$** (AcOEt/hexane 1:2) 0.40; $R_f$ (AcOEt/hexane 1:10) 0.06; $R_f$ (AcOEt/hexane 1:5) 0.13. **$[\alpha]_D^{24}$:** –6.44° (c 1.33, $CHCl_3$). **IR** (film): 3440w (br, 3650–3150), 3030w, 2926w, 2871m, 1496w, 1455m, 1394w, 1352w, 1207w, 1067s, 1028s, 995m, 931m, 736s, 697s. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.36–7.25 (m, 10 H); 5.88–5.80 (m, 1 H); 5.34 (ddd, J = 10.6, 1.5, 0.7; 1 H); 5.33 (ddd, J = 16.9, 1.6, 1.0, 1 H); 4.79 (d, J = 11.6, 1 H); 4.65 (d, J = 11.8, 1 H); 4.63 (d, J = 11.6, 1 H); 4.39 (d, J = 11.9, 1 H); 4.00 (ddt, J = 7.5, 5.9, 0.8, 1 H); 3.75–3.69 (m, 1 H); 3.62–3.54 (m, 2 H); 2.13 (br s, 1 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 138.37; 138.16; 134.62; 128.44 (2 C); 128.41 (2 C); 127.93 (2 C); 127.80 (2 C); 127.79; 127.66; 119.26; 81.37; 81.03; 73.43; 70.62; 62.04. **HRMS** (ESI): 321.1460 (67, $[M + Na]^+$, $C_{19}H_{22}NaO_3$, calcd. 321.1461); 299.1639 (36, $[M + H]^+$, $C_{19}H_{23}O_3$, calcd. 299.1642).




**((2*R*,3*R*)-2,3-Bis(benzyloxy)pent-4-enyloxy)(*tert*-butyl)dimethylsilane (16).**[9] To a cooled (0 °C) solution of alcohol **15** (50 mg, 0.168 mmol, 1.00 equiv) in 1.5 ml dry $CH_2Cl_2$ were added successively 2,6-lutidine (Aldrich 99%, 0.060 ml, 0.50 mmol, 3.0 equiv) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (ABCR 98%, 0.060 ml, 0.25 mmol, 1.5 equiv). The reaction mixture was stirred for 75 min at 0 °C (TLC showed complete conversion) and the reaction quenched by the addition of 2 ml sat. aq. $NH_4Cl$. The organic phase was removed and the aq. phase was extracted with $CH_2Cl_2$ (2 × 3 ml). The combined organic extracts were once washed with 4 ml sat. aq. NaCl and dried over $MgSO_4$. The residue (colorless oil) was purified by FC ($SiO_2$, AcOEt/hexane 1:50 → 1:20 → 1:10; d = 2.4 cm; h = 16 cm) to yield the desired product **16** as a colorless oil (60 mg, 87%).

**$R_f$** (AcOEt/hexane 1:10) 0.62. **$[\alpha]_D^{25}$:** –9.43° (c 1.67, $CHCl_3$). **IR** (film): 2952w, 2927w, 2882w, 2856w, 1496w, 1455m, 1253m, 1090s, 1073s, 1028m, 928m, 835s, 776s, 733s, 696s. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.36–7.23 (m, 10 H); 5.87 (ddd, J = 17.5, 10.4, 7.4, 1 H); 5.29 (ddd, J = 17.4, 1.8, 1.2, 1 H); 5.26 (ddd, J = 10.4, 1.8, 0.8, 1 H); 4.73 (d, J = 11.8, 1 H); 4.69 (d, J = 11.9, 1 H); 4.62 (d, J = 12.0, 1 H); 4.39 (d, J = 12.0, 1 H); 3.95 (ddt, J = 7.4, 5.0, 1.2, 1 H); 3.79 (dd, J = 10.7, 4.2, 1 H); 3.66 (dd, J = 10.7, 6.3, 1 H); 3.53 (ddd, J = 6.4, 4.6, 4.6, 1 H); 0.88 (s, 9 H); 0.02 (s, 6 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$):[11] δ 138.94; 138.56; 135.52; 128.23 (2 C); 128.17 (2 C); 127.91 (2 C); 127.78 (2 C); 127.39 (2 C); 118.11; 82.39; 80.32; 73.58; 70.72; 63.24; 25.91 (3 C); 18.25; –5.37; –5.41. **HRMS** (ESI): 435.2330 (71, $[M + Na]^+$, $C_{25}H_{36}NaO_3Si$, calcd. 435.2326).



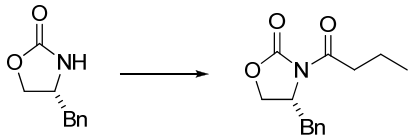

**(2*S*,3*R*)-2,3-bis(benzyloxy)pent-4-enal (17).**[9] To a cooled (0 °C) solution of alcohol **15** (52 mg, 0.174 mmol, 1.00 equiv) in 2 ml $CH_2Cl_2$ was added a solution of *Dess-Martin* periodinane (Acros, 15-wt% in $CH_2Cl_2$, 0.41 ml, 0.19 mmol, 1.10 equiv) and the mixture was stirred for 1 h at 0 °C and for 45 min at room temperature. Subsequently, the white suspension was cooled to 0 °C, 1.5 ml sat. aq. $Na_2S_2O_3$ and 1.5 ml sat. aq. $NaHCO_3$ were added and the resulting mixture was stirred for 5 min. The organic phase was then removed and the aq. phase was extracted with $CH_2Cl_2$ (3 × 3 ml). The combined organic extracts were washed with 5 ml sat. aq.

[11] A $^{13}$C signal at δ 145.4 ppm is reported in ref. 9. No signals above 140 ppm were observable in the $^{13}$C spectrum of our preparation of **16**.

NaCl, dried over $MgSO_4$ and concentrated. The residue (yellow oil) was purified by FC ($SiO_2$, AcOEt/hexane 1:5; d = 2.4 cm; h = 13.5 cm) affording the desired product **17** as an oil (28 mg, 54%).

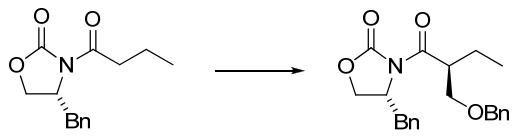
**$R_f$** (AcOEt/hexane 1:5) 0.33. **$[\alpha]_D^{25}$:** –49.9° (c 1.40, $CHCl_3$). **IR** (film): 3064w, 3031w, 2925w, 2866w, 1733m, 1684w, 1496w, 1455m, 1207w, 1067s, 1027m, 996m, 933m, 736s, 697s. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 9.68 (d, J = 1.5, 1 H); 7.34–7.25 (m, 10 H); 5.94 (ddd, J = 17.2, 10.4, 7.6, 1 H); 5.37 (ddd, J = 10.3, 1.4, 0.7, 1 H); 5.34 (ddd, J = 17.3, 1.5, 1.0, 1 H); 4.75 (d, J = 12.0, 1 H); 4.63 (d, J = 12.0, 1 H); 4.62 (d, J = 12.0, 1 H); 4.35 (d, J = 12.0, 1 H); 4.17 (ddt, J = 7.6, 4.1, 0.9, 1 H); 3.83 (dd, J = 4.2, 1.5, 1 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 202.50; 137.54; 137.06; 133.80; 128.48 (2 C); 128.37 (2 C); 128.16 (2 C); 128.12; 127.93 (2 C); 127.77; 119.87; 85.14; 79.93; 73.45; 70.66. **HRMS** (ESI): 314.1751 (39, $[M + NH_4]^+$, $C_{19}H_{24}NO_3$, calcd. 314.1751).

## Synthesis of vinyl iodide **7**




**(*R*)-4-Benzyl-3-butyryl-1,3-oxazolidin-2-one (F).**[12] To a cooled (–78 °C) solution of (*R*)-4-benzyl-1,3-oxazolidin-2-one (XinChem Corporation, 10.3 g, 58.1 mmol, 1.00 equiv) in 150 ml THF was added *n*-BuLi (Fluka, 1.6 M in hexane, 38.1 ml, 61.0 mmol, 1.05 equiv) dropwise over a period of 30 min, resulting in the development of a deep-orange coloration. Then butyryl chloride (Fluka purum, 6.08 ml, 58.1 mmol, 1.00 equiv) was added in one portion (leading to immediate decolorization), and the light-yellow solution was stirred at –78 °C for further 30 min (reaction complete, as indicated by TLC) and then warmed to ambient temperature. Saturated aq. $NH_4Cl$ (75 ml) was added and the organic phase was separated. The aq. solution was extracted with AcOEt (3 × 50 ml) and the combined organic extracts were washed successively with 100 ml 1 M aq. NaOH, 100 ml sat. aq. NaCl, dried over $MgSO_4$ and then concentrated, to leave a light yellow oil (15.8 g). This material was purified by FC ($SiO_2$, hexane/AcOEt 20:1 → 5:1 → 3:1; d = 5.8 cm; h = 14.5 cm) to give the desired product **F** as a colorless oil (13.5 g, 94%).

**$R_f$** (AcOEt/hexane 1:1) 0.68; $R_f$ (AcOEt/hexane 1:3) 0.40; $R_f$ ($Et_2O$/toluene 1:3) 0.56. **$[\alpha]_D^{23}$**: –57.1° (c 1.14, $CHCl_3$). **IR** (film): 2965w, 2933w, 2875w, 1775s, 1698s, 1455w, 1386s, 1351m, 1316w, 1290w, 1209s, 1092m, 762m, 748m, 702m. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.36–7.20 (m, 5 H); 4.68 (ddt, J = 9.6, 7.3, 3.3, 1 H); 4.22–4.15 (m, 2 H); 3.30 (dd, J = 13.3, 3.2, 1 H); 3.00–2.84 (m, 2 H); 2.77 (dd, J = 13.4, 9.6, 1 H); 1.73 (sext.d, J = 7.4, 1.7, 2 H); 1.01 (t, J = 7.4, 3 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 173.34; 153.58; 135.45; 129.53 (2 C); 129.05 (2 C); 127.44; 66.27; 55.24; 38.05; 37.48; 17.82; 13.79.

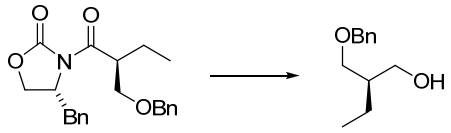



**(*R*)-4-benzyl-3-((*S*)-2-(benzyloxymethyl)butanoyl)-1,3-oxazolidin-2-one (18).**[13] To a stirred solution of (*R*)-4-benzyl-3-butyryl-1,3-oxazolidin-2-one (**F**) (17.5 g, 70.8 mmol, 1.09 equiv) in 250 ml $CH_2Cl_2$ was added $TiCl_4$

[12] (*S*)-enantiomer of **F**: Evans, D. A.; Rieger, D. L.; Jones, T. K.; Kaldor, S. W. *J. Org. Chem.* **1990**, *55*, 6260–6268.
[13] (*S*)-enantiomer of **18**: Ihara, M.; Katsumata, A.; Setsu, F.; Tokunaga, Y.; Fukumoto, K. *J. Org. Chem.* **1996**, *61*, 677–684.

(Fluka puriss., 7.76 ml, 70.8 mmol, 1.09 equiv) at 0 °C. The resulting yellow reaction mixture was stirred for 5 min at 0 °C and for 5 min at room temperature (formation of a yellow suspension, followed by the complete solidification). Dropwise addition of $NEt_3$ (Fluka puriss. p.a., 9.86 ml, 70.8 mmol, 1.09 equiv) to the solid reaction mixture at 0 °C gave a dark-colored solution which was stirred for 30 min at 0 °C. Benzyloxy methylchloride (12.0 ml, 64.9 mmol, 1.00 equiv) was added (the reaction mixture remained dark) and the mixture was further stirred for 4 h at 0 °C, when the reaction was quenched by the addition of 150 ml of sat. aq. $NH_4Cl$. The organic phase was separated and the aq. phase extracted once with 100 ml $CH_2Cl_2$. The combined extracts were washed with 100 ml sat. aq. $NaHCO_3$, dried over $Na_2SO_4$ and then concentrated to a yellow oil. The residue was purified by FC ($SiO_2$, AcOEt/hexane 1:20 → 1:5 → 1:3; d = 5.8 cm; h = 14.5 cm) to yield the target compound **18** as a colorless oil (23.7 g, 91%).

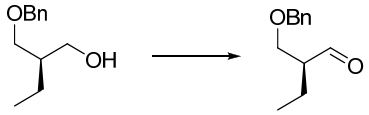
**$R_f$** (AcOEt/hexane 1:3) 0.40; $R_f$ ($Et_2O$/toluene 1:3) 0.61. **M.p.:** 73 °C. **$[\alpha]_D^{24}$:** –39.1° (c 0.963, $CHCl_3$). **IR** (film): 2966w, 2929w, 2875w, 1773s, 1695s, 1454m, 1387m, 1350m, 1210s, 1097s, 736s, 698s. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.34–7.17 (m, 10 H); 4.77–4.69 (m, 1 H); 4.56 (d, J = 12.2, 1 H); 4.52 (d, J = 12.2, 1 H); 4.21–4.14 (m, 2 H); 4.11 (dd, J = 9.0, 3.1, 1 H); 3.81 (dd, J = 9.1, 8.2, 1 H); 3.66 (dd, J = 9.1, 5.0, 1 H); 3.22 (dd, J = 13.5, 3.3, 1 H); 2.70 (dd, J = 13.5, 9.2, 1 H); 1.81–1.70 (m, 1 H); 1.64–1.54 (m, 1 H); 0.93 (t, J = 7.5, 3 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 175.05; 153.23; 138.25; 135.35; 129.49 (2 C); 128.87 (2 C); 128.34 (2 C); 127.64 (2 C); 127.56; 127.23; 73.15; 71.08; 65.82; 55.22; 44.83; 37.73; 22.14; 11.53.




**(*R*)-2-(Benzyloxymethyl)butan-1-ol (19).**[14,15] To a cooled (0 °C) suspension of (*R*)-4-benzyl-3-((*S*)-2-(benzyloxymethyl)butanoyl)-1,3-oxazolidin-2-one (**18**) (23.7 g, 67.8, 1.00 equiv) in 250 ml $Et_2O$ containing EtOH (4.76 ml, 81.4 mmol, 1.20 equiv) was added $LiBH_4$ (Aldrich, 2 M in THF, 40.7 ml, 81.4 mmol, 1.20 equiv) dropwise over a period of 15 min. After stirring for ½ h at 0 °C the reaction was carefully quenched with 1 M aq. NaOH (75 ml). The organic layer was separated and the aqueous layer extracted with $Et_2O$ (2 × 150 ml), the combined organic layers were washed with sat. NaCl (150 ml), dried over $MgSO_4$ and concentrated. The residue (23.4 g, colorless oil) was purified by FC ($SiO_2$, AcOEt/hexane 1:5 → 1:3 → 1:2; d = 5.8 cm; h = 14 cm) to yield alcohol **19** as a colorless oil (11.5 g, 87%).

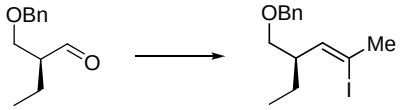
**$R_f$** (AcOEt/hexane 1:3) 0.23; $R_f$ (AcOEt/hexane 1:4) 0.15. **$[\alpha]_D^{24}$:** +19.1° (c 3.67, $CHCl_3$). **IR** (film): 3395w (br, 3600–3100), 2961w, 2927w, 2874w, 1454m, 1364w, 1206w, 1093s, 1029m, 735s, 696s, 610m. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.33–7.22 (m, 5 H); 4.49 (d, J = 12.0, 1 H); 4.45 (d, J = 12.0, 1 H); 3.69–3.62 (m, 1 H); 3.60 (br d, J = 6.9, 1 H); 3.56 (dd, J = 9.2, 4.5, 1 H); 3.45 (dd, J = 9.1, 7.3, 1 H); 2.96 (br s, 1 H); 1.78–1.69 (m, 1 H); 1.37–1.26 (m, 2 H); 0.89 (t, J = 7.4, 3 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 138.14; 128.35 (2 C); 127.59; 127.51 (2 C); 73.30; 73.14; 65.06; 42.33; 20.92; 11.59. **HRMS** (ESI): 195.1374 (100, $[M + H]^+$, $C_{12}H_{19}O_2$, calcd. 195.1380).

[14] Bell, L.; Brookings, D. C.; Dawson, G. J.; Whitby, R. J.; Jones, R. V. H.; Standen, M. C. H. *Tetrahedron* **1998**, *54*, 14617–14634.
[15] Sefkow, M.; Neidlein, A.; Sommerfeld, T.; Sternfeld, F.;Maestro, M. A.; Seebach, D. *Liebigs Ann. Chem.* **1994**, 719–729.




**(*S*)-2-(Benzyloxymethyl)butanal (G).** To a cooled (–78 °C) solution of oxalyl chloride (Fluka puriss., 1.08 ml, 12.8 mmol, 1.10 equiv) in 50 ml $CH_2Cl_2$ was added DMSO (2.06 ml, 29.1 mmol, 2.50 equiv) dropwise. After stirring at –78 °C for 30 min a solution of alcohol **19** (2.26 g, 11.6 mmol, 1.00 equiv) in 15 ml $CH_2Cl_2$ was added dropwise over a period of 20 min. The resulting white suspension was stirred for 30 min, then triethylamine (Fluka puriss. p.a., 7.27 ml, 52.2 mmol, 4.50 equiv) was added slowly, whereby a clear solution was obtained. The reaction mixture was allowed to warm to 0 °C and leading to the reappearance of a suspension. The reaction was quenched by the addition of 40 ml sat. aq. $NH_4Cl$. The aq. layer was separated and extracted with $CH_2Cl_2$ (2 × 30 ml). The combined organic extracts were then washed successively with 40 ml sat. aq. $NH_4Cl$ and 40 ml sat. aq. NaCl, dried over $MgSO_4$ and concentrated. The resulting yellow oil (2.28 g) was used for the next step without further purification.

**$R_f$** (AcOEt/hexane 1:20) 0.20; $R_f$ (AcOEt/hexane 1:4) 0.53. **$[\alpha]_D^{22}$:** +17.7° (c 1.94, $CHCl_3$). **IR** (film): 2966w, 2933w, 2865w, 1726s, 1496w, 1455m, 1362m, 1204w, 1098s, 1028m, 739s, 698s. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 9.66 (d, J = 2.2, 1 H); 7.33–7.22 (m, 5 H); 4.49 (d, J = 12.1, 1 H); 4.46 (d, J = 12.1, 1 H); 3.67 (dd, J = 9.5, 6.9, 1 H); 3.62 (dd, J = 9.5, 4.9, 1 H); 2.48–2.41 (m, 1 H); 1.76–1.65 (m, 1 H); 1.58–1.47 (m, 1 H); 0.91 (t, J = 7.5, 3 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 203.86; 138.00; 128.38 (2 C); 127.67; 127.55 (2 C); 73.21; 68.23; 53.63; 18.95; 11.39. **HRMS** (ESI): 193.1222 (28, $[M + H]^+$, $C_{12}H_{17}O_2$, calcd. 193.1223).



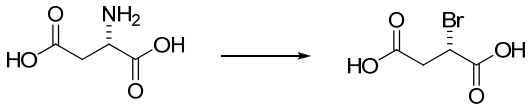

**(*R,Z*)-((2-Ethyl-4-iodopent-3-enyloxy)methyl)benzene (7).** To a yellow suspension of 2-iodoethyl-2-triphenylphosphonium iodide[16] (7.62 g, 14.0 mmol, 1.21 equiv) in 50 ml THF was added LiHMDS (Acros, 1 M in THF/PhEt, 14.0 ml, 14.0 mmol, 1.21 equiv) dropwise at room temperature and the resulting deep-red suspension was stirred for 15 min. The mixture was then cooled to –78 °C and a solution of crude aldehyde **G** (2.23 g, 11.6 mmol, 1.00 equiv) in 20 ml THF was added dropwise. The reaction mixture was stirred at –78 °C for 1½ h before being allowed to warm to 0 °C. The reaction was quenched by the addition of 40 ml sat. aq. $NH_4Cl$ and extracted with AcOEt (3 × 40 ml). The comb. org. layers were washed with 40 ml sat. aq. NaCl, dried over $MgSO_4$ and concentrated. The residue (red solid) was dissolved in $CH_2Cl_2$ and the solution was filtered through a short pad of silica ($SiO_2$; hexane/EtOAc 20:1; d = 3.4 cm; h = 10.5 cm) to yield, after evaporation of the solvent, 2.14 g of a yellow oil, which was purified by FC ($SiO_2$; hexane/toluene 1:0 → 3:1 → 2:1; d = 3.4 cm; h = 18 cm) to yield the desired product **7** as a 10:1 mixture of *Z*/*E* diastereomers as a light yellow oil (1.50 g, 40% over two steps).

**$R_f$** (AcOEt/hexane 1:20) 0.54; **$R_f$** (AcOEt/hexane 1:10) 0.86. **$[\alpha]_D^{22}$:** –48.5° (c 1.07, $CHCl_3$). **IR** (film): 3029w, 2960s, 2926s, 2857s, 2361w, 1496w, 1454s, 1427w, 1378w, 1362m, 1101s, 1060s, 1029m, 774w, 735s, 697s. **$^1$H-NMR** (400 MHz, $CDCl_3$): (Data of major *Z*-isomer **7**) δ 7.33–7.22 (m, 5 H); 5.26 (dq, J = 8.9, 1.4, 1 H); 4.52

[16] (a) Chen, J.; Wang, T.; Zhao, K. *Tetrahedron Lett.* **1994**, *35*, 2827–2828. (b) Smith, A. B., III; Beauchamp, T. J.; LaMarche, M. J.; Kaufman, M. D.; Qiu, Y.; Arimoto, H.; Jones, D. R.; Kobayashi, K. *J. Am. Chem. Soc.* **2000**, *122*, 8654 –8664.

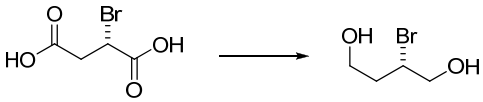
(d, J = 12.1, 1 H); 4.48 (d, J = 12.1, 1 H); 3.43 (dd, J = 9.4, 5.8, 1 H); 3.37 (dd, J = 9.4, 6.2, 1 H); 2.57–2.49 (m, 1 H); 2.50 (d, J = 1.4, 3 H); 1.66–1.56 (m, 1 H); 1.43–1.31 (m, 1 H); 0.90 (t, J = 7.4, 3 H). Minor *E*-isomer (only clearly distinguishable signals listed): δ 5.96 (dq, J = 10.0, 1.5, 1 H); 3.34–3.31 (m, 2 H); 2.39 (d, J = 1.5, 3 H); ca. 1.6–1.52 (m, 1 H); 1.28–1.17 (m, 1 H); 0.87 (t, J = 7.4, 3 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): Data for major *Z*-isomer **7**). δ 138.57; 136.93; 128.27 (2 C); 127.50 (2 C); 127.42; 101.69; 72.86; 72.23; 48.51; 33.81; 24.15; 11.43. Data of minor *E*-isomer: δ 142.78; 138.44; 128.33; 127.50; 127.46; 95.00; 73.02; 72.78; 43.30; 28.16; 24.50; 11.51. **HRMS** (ESI): 348.0822 (100, $[M + NH_4]^+$, $C_{14}H_{23}INO$, calcd. 348.0819).

## Synthesis of aldehyde **8**




**(*S*)-2-Bromosuccinic acid (H).**[17] A 1000 ml 3-necked round-bottomed flask (charged with 2 washing bottles connected in series with the first one empty and the second one filled with 2 M NaOH) was charged with (*S*)-L-(+)-aspartic acid (Fluka >99%, 18.8 g, 141 mmol, 1.00 equiv) and KBr (Fluka puriss. p.a. 99.5%, 72.5 g, 609 mmol, 4.32 equiv). 300 ml of a 2.5 M aq. solution of $H_2SO_4$ were added in one portion and then the solution was cooled to –5 °C. A solution of sodium nitrite (Fluka puriss. p.a. 99.0%, 16.8 g, 243 mmol, 1.72 equiv) in 40 ml $H_2O$ was added with careful temperature monitoring, such that the reaction temperature was maintained below 0 °C for the entire 90 min addition period. After completion of the addition of $NaNO_2$ the resulting dark brown reaction mixture was stirred for 2 h at –5 °C and then extracted with AcOEt (4 × 100 ml; clear aq. phase, dark red/brown organic phase). The combined organic extracts were washed with 100 ml half sat. aq. NaCl, then dried over $Na_2SO_4$ and concentrated under reduced pressure to yield the desired product **H** as a white solid (24.6 g, 88%).

**$R_f$** (AcOEt/hexane 1:1 containing 5% AcOH) 0.52; $R_f$ (AcOEt/hexane/MeOH 6:6:1) 0.00–0.18. **M.p.:** 166–167 °C. **$[\alpha]_D^{24}$:** –35.0° (c 8.12, $H_2O$). **IR** (film): 3328m (br, 3700–3000), 2946m, 2833m, 2640w, 2552w, 2528w, 1702s, 1415m, 1304m, 1185m, 1020s, 935m, 759m, 648s. **$^1$H-NMR** (400 MHz, $CD_3OD$): δ 4.97 (br s, 2 H); 4.56 (dd, J = 8.6, 6.2, 1 H); 3.19 (dd, J = 17.2, 8.7, 1 H); 2.95 (dd, J = 17.2, 6.2, 1 H). **$^{13}$C-NMR** (100 MHz, $CD_3OD$): δ 173.20; 172.38; 40.78; 40.11.

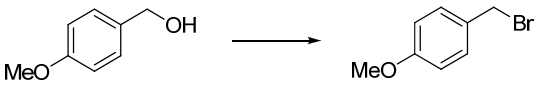



**(*S*)-2-Bromobutane-1,4-diol (I).**[17] To a cooled (0 °C) solution of (*S*)-2-bromosuccinic acid (**H**) (23.9 g, 121 mmol, 1.00 equiv) in 250 ml THF was added borane•THF (Aldrich, 1 M in THF, 364 ml, 364 mmol, 3.00 equiv) over a period of 1 h. After the addition, the cooling bath was removed and the light-yellow solution was stirred for 15 min, resulting in the formation of a thick, milky-white suspension. Stirring was continued at room temperature for 3 h, when the reaction mixture was cooled to 0 °C and the excess borane quenched by dropwise (!) addition of 5 ml $H_2O$ (formation of a clear solution). $K_2CO_3$ (5.0 g) was then added to the reaction mixture

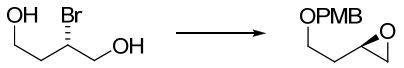
[17] Frick, J. A.; Klassen, J. B.; Bathe, A.; Abramson, J. M.; Rapoport, H. *Synthesis* **1992**, 621.

and solids were removed by decantation (filtration was not possible). The solid residue was washed with $Et_2O$ (3 × 40 ml) and the combined original supernatant and $Et_2O$ washes were concentrated to an oily, yellow residue. This material was triturated with $Et_2O$ (4 × 40 ml) and borate salts removed by filtration. The combined filtrates were dried over $MgSO_4$, filtered, and evaporated to a thick, yellow oil (38.5 g), which was purified by FC ($SiO_2$, AcOEt/hexane/MeOH 6:6:1; d = 7 cm; h = 15 cm) to give the desired product **I** as a white foam (18.3 g, 89%).

**$R_f$** (AcOEt/hexane/MeOH 6:6:1) 0.34; $R_f$ (AcOEt/hexane 1:1 & 5% AcOH) 0.00–0.24. **$[\alpha]_D^{24}$:** –35.1° (c 11.8, $CHCl_3$). **IR** (film): 3328m (br, 3600–3000), 2935w, 2886w, 2362w, 1635w, 1420w, 1266w, 1164w, 1052s, 1025s, 909m, 731s, 644s, 536m. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 4.30 (dtd, J = 8.2, 5.4, 5.1, 1 H); 3.90–3.76 (m, 4 H); 3.47 (br s, 1 H); 3.03 (br s, 1 H); 2.21–2.04 (m, 2 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 67.09; 60.02; 54.64; 37.84.




**1-(Bromomethyl)-4-methoxybenzene (J).** To a cooled (0 °C) solution of *p*-methoxybenzyl alcohol (Fluka purum 98%, 19.3 g, 140 mmol, 1.00 equiv) in 250 ml $CH_2Cl_2$ was added phosphorus tribromide (Fluka purum, 98%, 17.0 ml, 180 mmol, 1.29 equiv) over a period of 15 min. After stirring at 0 °C for another 45 min, the reaction was quenched by the addition of ice. The muddy org. layer was separated, once washed with 100 ml sat. aq. $NaHCO_3$ (kept at 0 °C), dried over $MgSO_4$ and then concentrated under reduced pressure, yielding crude PMBBr (**J**) as yellow oil (27.4 g).

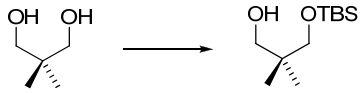



**(*R*)-2-(2-(4-Methoxybenzyloxy)ethyl)oxirane (10).** To a cooled (–5 °C) suspension of NaH (Aldrich, 60% in mineral oil, 12.8 g, 319 mmol, 3.00 equiv) in 140 ml THF was added a solution of (*S*)-2-bromobutane-1,4-diol (**I**) (18.0 g, 106 mmol, 1.00 equiv) in 60 ml THF over 15 min. After 2¼ h of stirring at –5 °C, a solution of crude *para*-methoxybenzyl bromide (**J**) (27.4 g, 136 mmol, 1.28 equiv) in 100 ml DMF was added in one portion and the white/yellow suspension was stirred for further 5 min at –5 °C. Then the reaction mixture was warmed to room temperature and the reaction was left to proceed for further 2½ h. Sat. aq. $NH_4Cl$ (100 ml) was then added carefully (warming!; ice was added carefully to cool the mixture), the organic layer was separated and the aqueous solution was extracted with AcOEt (3 × 100 ml). The combined organic extracts were washed successively with 100 ml $H_2O$ and 100 ml sat. aq. NaCl, dried over $Na_2SO_4$ and concentrated. The residue (29.8 g of a orange-yellow oil) was purified by FC ($SiO_2$, AcOEt/hexane 1:4 → 1:2 → 1:1; d = 8.8 cm; h = 10 cm) to give the desired product **10** as a colorless oil (14.1 g, 64%).

**$R_f$** (AcOEt/hexane 1:4) 0.28; $R_f$ (AcOEt/toluene 1:4) 0.36. **$[\alpha]_D^{24}$:** +12.1° (c 0.607, $CHCl_3$) (Lit.[18] $[\alpha]_D^{25}$: +10.6°; lit.[19] $[\alpha]_D^{25}$: –13.1° for (*S*)-enantiomer; lit.[20] $[\alpha]_D^{25}$: –10.6° for (*S*)-enantiomer).[21] **IR** (film): 2998w, 2926w,

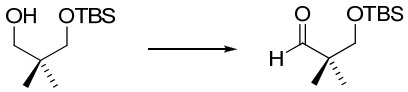
[18] Mohapatra, D. K.; Das, P. P.; Reddy, D. S.; Yadav, J. S. *Tetrahedron Lett*. **2009**, *50*, 5941–5944.
[19] Gaunt, M. J.; Jessiman, A. S.; Orsini, P.; Tanner, H. R.; Hook, D. F.; Ley, S. V. *Org. Lett*, **2003**, *5*, 4819–4822.
[20] Fürstner, A.; Albert, M.; Mlynarski, J.; Matheu, M.; DeClercq, E. *J. Am. Chem. Soc.* **2003**, *125*, 13132-13142 (Cpd. **S-3** in Supplementary Information).
[21] In line with our own data for the optical rotation of **10** and those in refs. 18-20, a negative sign of the optical rotation of (*S*)-2-(2-(4-methoxybenzyloxy)ethyl)oxirane (***ent*-10**) is indicated in: Smith, A. B., III; Boldi, A. M. *J. Am. Chem. Soc.* **1997**, *119*, 6925; Smith, A. B., III; Pitram, S. M.; Boldi, A. M.; Gaunt, M. J.; Sfouggatakis, C.; Moser, W. H. *J. Am. Chem. Soc.* **2003**, *125*, 14435. In contrast, an $[\alpha]_D^{20}$ of -12.3 ° has been reported for **10** by Marshall *et al*. (Marshall, J. A.; Schaaf, G.; Nolting, A. *Org. Lett.* **2005**, *7*, 5331–5333). The compound

2858w, 2839w, 1712w, 1612m, 1586w, 1513s, 1464w, 1362w, 1302m, 1246s, 1173m, 1090s, 1032s, 907w, 821s. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.28–7.24 (m, 2 H); 6.90–6.86 (m, 2 H); 4.46 (s, 2 H); 3.80 (s, 3 H); 3.63–3.55 (m, 2 H); 3.07–3.03 (m, 1 H); 2.77 (dd, J = 4.9, 4.3, 1 H); 2.51 (dd, J = 5.0, 2.7, 1 H); 1.93–1.85 (m, 1 H); 1.80–1.72 (m, 1 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 159.24; 130.42; 129.25 (2 C); 113.84 (2 C); 72.77; 66.75; 55.28; 50.09; 47.09; 32.97. **HRMS** (ESI): 231.0992 (5, $[M + Na]^+$, $C_{12}H_{16}NaO_3$, calcd. 231.0992).




**3-(*tert*-Butyldimethylsilyloxy)-2,2-dimethylpropane-1-ol (K).**[22] To a cooled (0 °C) suspension of NaH (Aldrich, 60% in mineral oil, 610 mg, 15,3 mmol, 1.00 equiv) in 20 ml THF was added a solution of 2,2-dimethylpropane-1,3-diol (Fluka purum 98%, 1.59 g, 15.3 mmol, 1.00 equiv) in 10 ml THF over a period of 10 min. The resulting thick slurry was warmed to room temperature and stirred for 1 h. It was then again cooled to 0 °C and TBSCl (ABCR GmbH 98%, 2.28 g, 15.1 mmol, 0.99 equiv) was added in one portion, resulting in an immediate thinning of the slurry. The cooling bath was removed and the reaction was stirred at room temperature for further 40 min. Then the reaction mixture was diluted with 15 ml AcOEt and 15 ml 10% aq. $K_2CO_3$, the organic phase was separated and the aq. solution was extracted once with 15 ml AcOEt. The combined organic extracts were washed with 15 ml sat. aq. NaCl, dried over $Na_2SO_4$ and concentrated to provide crude **K** as a colorless oil (3.41 g, directly used for the next step without further purification).

**$R_f$** (AcOEt/hexane 1:10) 0.42. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 3.47–3.45 (m, 2 H); 3.46 (s, 2 H); 2.85 (br t, J = 5.3, 1 H); 0.90 (s, 9 H); 0.88 (s, 6 H); 0.07 (s, 6 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 72.69; 72.19; 36.42; 25.85 (3 C); 21.45 (2 C); 18.18; –5.65 (2 C).




**3-(*tert*-Butyldimethylsilyloxy)-2,2-dimethylpropanal (L).**[22] To a cooled (–78 °C) solution of oxalyl chloride (Fluka puriss 99.0%, 1.42 ml, 16.8 mmol, 1.10 equiv) in 50 ml $CH_2Cl_2$ was added dimethyl sulfoxide (2.72 ml, 38.3 mmol, 2.50 equiv) dropwise. The solution was stirred for 30 min, then a solution of crude alcohol **K** (3.41 g, 15.3 mmol, 1.00 equiv) in 10 ml $CH_2Cl_2$ was added dropwise over a period of 20 min. The resulting white suspension was again stirred for 30 min, then triethylamine (Fluka puriss. p.a., 9.60 ml, 68.9 mmol, 4.50 equiv) was slowly added, whereby a clear solution was obtained. The reaction mixture was allowed to warm to room temperature and again a suspension formed. The reaction was quenched by the addition of 30 ml sat. aq. $NH_4Cl$, the organic layer was separated and the aq. solution was extracted with $CH_2Cl_2$ (2 × 30 ml). The combined

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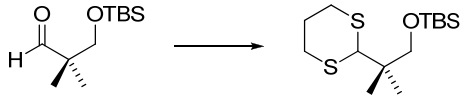
was prepared by hydrolytic kinetic resolution (HKR) of the racemic epoxide with Jacobsen's (1*R*,2*R*)-(salen)Co$^{III}$(OAc) catalyst. However, the description of the experiment is not entirely consistent. While the structural drawing of the target compound is for **10**, the procedure states that "The (*S*)-PMB epoxy ether [i. e. ***ent*-10**] was removed by careful bulb-to-bulb distillation (0.05 mm/Hg, 160 °C) from the reaction mixture…" HKR was also employed for the preparation of **10** in ref. 18 ((1*R*,2*R*)-(salen)Co$^{III}$(OAc) catalyst); likewise, Fürstner's synthesis of ***ent*-10** (ref. 20) is based on HRK with the corresponding 1*S*,2*S* catalyst. Marshall's group has also reported the preparation of the ***benzyl*** analog of ***ent*-10** ((-)-(*S*)-(2-benzyloxyethyl)oxirane) using HRK, employing the 1*S*, 2*S* Jacobsen catalyst (Marshall, J. A., Sabatini, J. J. *Org. Lett.* **2005**, 7, 4819-4822). The $[\alpha]_D^{20}$ of this compound is given as -14.5 ° (c 1.50 $CHCl_3$), which is in perfect agreement with Fürstner's data for ***ent*-10**, but seems to be in conflict with a negative sign of the optical rotation for **10**.

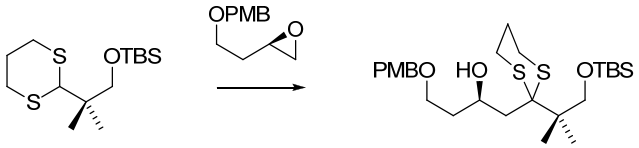
[22] (a) Wender, P. A.; Baryza, J. L.; Bennett, C. E.; Bi, F. C.; Brenner, S. E.; Clarke, M. O.; Horan, J. C.; Kan, C.; Lacôte, E.; Lippa, B.; Nell, P. G.; Turner, T. M. *J. Am. Chem. Soc*. **2002**, *124*, 13648–13649. (b) Brandau, S.; Hoppe, D. *Tetrahedron* **2005**, *61*, 12244–12255.

organic extracts were washed with 30 ml sat. aq. $NH_4Cl$ and 40 ml sat. aq. NaCl, dried over $MgSO_4$ and then concentrated, to yield crude **L** as a yellow oil (3.43 g, directly used for the next step without further purification). **$R_f$** (AcOEt/hexane 1:20) 0.65; $R_f$ (toluene) 0.64; $R_f$ (AcOEt/hexane 1:10) 0.73; $R_f$ (AcOEt/hexane 1:2) 0.82. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 9.57 (s, 1 H); 3.60 (s, 2 H); 1.04 (s, 6 H); 0.87 (s, 9 H); 0.04 (s, 6 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 206.08; 68.38; 48.07; 25.77 (3 C); 18.56 (2 C); 18.20; –5.62 (2 C).




**(2-(1,3-Dithian-2-yl)-2-methylpropoxy)(*tert*-butyl)dimethylsilane (11).** To a cooled (0 °C) yellow suspension of crude aldehyde **L** (3.31 g, 15.3 mmol, 1.00 equiv) and $MgBr_2$•$Et_2O$ (Fluka purum 98%, 5.08 g, 19.7 mmol, 1.29 equiv) in 60 ml $Et_2O$ was added 1,3-propanedithiol (ABCR GmbH, 1.86 ml, 18.4 mmol, 1.20 equiv) in one portion. The reaction mixture was warmed to room temperature and stirred for 90 min. The remaining 1,3-propanedithiol was then quenched by the addition of 1,3,5-trioxane (Fluka purum 99%, 1.20 g, 13.3 mmol, 0.87 equiv), which produced an immediate color change and the formation of a milky-yellow, cloudy suspension that was stirred further for 30 min. 40 ml 1 M aq. NaOH were then added and the organic phase was separated. The aq. solution was then extracted with $Et_2O$ (3 × 35 ml) and the combined organic extracts were washed with 40 ml sat. aq. NaCl, dried over $MgSO_4$ and concentrated. The residue (4.49 g of a yellow oil) was purified by FC ($SiO_2$, AcOEt/hexane 1:50 → 1:20; d = 3.4 cm; h = 22 cm) to yield the dithiane **11** as a colorless oil (3.80 g, 80% over three steps).

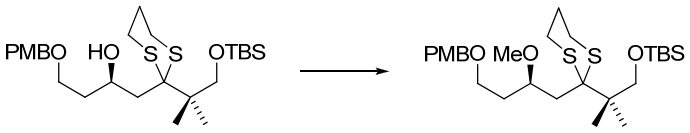
**$R_f$** (AcOEt/toluene 1:4) 0.82; $R_f$ (AcOEt/hexane 1:4) 0.91; $R_f$ (AcOEt/hexane 1:20) 0.66; $R_f$ (toluene) 0.78. **IR** (film): 2953w, 2928w, 2896w, 2856w, 1470m, 1421w, 1363w, 1251m, 1096s, 1005w, 850s, 835s, 774s, 667w. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 4.21 (s, 1 H); 3.46 (s, 2 H); 2.86 (dd, J = 7.8, 3.4, 4 H); 2.06 (dquint., J = 14.0, 3.4, 1 H); 1.80 (dquint., J = 14.0, 7.6, 1 H); 1.03 (s, 6 H); 0.89 (s, 9 H); 0.04 (s, 6 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 69.29; 57.72; 40.51; 31.45 (2 C); 26.27; 25.89 (3 C); 22.36 (2 C); 18.30; –5.49 (2 C). **HRMS** (ESI): 329.1394 (100, $[M + Na]^+$, $C_{14}H_{30}NaOS_2Si$, calcd. 329.1400).




**(*R*)-1-(2-(1-(*tert*-Butyldimethylsilyloxy)-2-methylpropan-2-yl)-1,3-dithian-2-yl)-4-(4-methoxybenzyloxy)butan-2-ol (M).** To a solution of (2-(1,3-dithian-2-yl)-2-methylpropoxy)(*tert*-butyl)dimethylsilane (**11**) (1.31 g, 4.27 mmol, 1.80 equiv) in 15 ml THF was added *n*-BuLi (Fluka, 1.6 M in hexane, 2.67 ml, 4.27 mmol, 1.80 equiv) over a period of 15 min at room temperature (the temperature of the reaction mixture was kept below 35 °C throughout the addition). After stirring at room temperature for 10 min, a solution of (*R*)-2-(2-(4-methoxybenzyloxy)ethyl)oxirane (**10**) (493 mg, 2.37 mmol, 1.00 equiv) in 5 ml THF was added dropwise to the light orange solution of the dithiane anion, which was accompanied by warming of the mixture. Stirring at room temperature was continued for 30 min, when the reaction was quenched by the addition of 20 ml sat. aq. $NH_4Cl$ and the mixture was extracted with AcOEt (3 × 15 ml). The combined organic extracts were washed with 20 ml sat. aq. NaCl, dried over $MgSO_4$ and concentrated. The residue (1.96 g of a yellow oil)

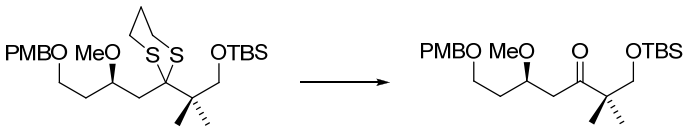
was purified by FC ($SiO_2$, AcOEt/hexane 1:5 → 1:2; d = 3.4 cm; h = 15 cm) to yield the desired product **M** as a yellowish oil (1.19 g, 93%).

**$R_f$** (AcOEt/toluene 1:4) 0.50; $R_f$ (AcOEt/hexane 1:4) 0.28. **$[\alpha]_D^{22}$:** +2.36° (c 0.818, $CHCl_3$). **IR** (film): 3460w (br, 3580–3350), 2952m, 2928m, 2856m, 1613w, 1514s, 1471m, 1362w, 1302w, 1249s, 1173w, 1092s, 1037m, 836s, 776m. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.28–7.25 (m, 2 H); 6.88–6.85 (m, 2 H); 4.45 (s, 2 H); 4.42–4.36 (m, 1 H); 4.07 (br s, 1 H); 3.80 (s, 3 H); 3.73 (d, J = 9.7, 1 H); 3.70 (d, J = 9.7, 1 H); 3.63 (t, J = 6.4, 2 H); 3.06–2.99 (m, 1 H); 2.96–2.89 (m, 1 H); 2.81–2.73 (m, 2 H); 2.27 (dd, J = 15.7, 8.4, 1 H); 2.17 (dd, J = 15.7, 1.7, 1 H); 2.01–1.85 (m, 2 H); 1.84–1.70 (m, 2 H); 1.15 (s, 3 H); 1.14 (s, 3 H); 0.90 (s, 9 H); 0.04 (s, 6 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 159.15; 130.63; 129.27 (2 C); 113.77 (2 C); 72.76; 68.20; 68.00; 67.41; 61.05; 55.28; 47.32; 45.19; 38.24; 27.27; 27.08; 25.95 (3 C); 23.45; 21.32; 21.14; 18.31; –5.45 (2 C). **HRMS** (ESI): 537.2501 (30, [*M* + Na]$^+$, $C_{26}H_{46}NaO_4S_2Si$, calcd. 537.2499).



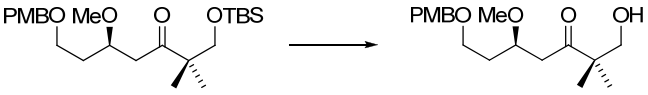

**(*R*)-*tert*-Butyl(2-(2-(2-methoxy-4-(4-methoxybenzyloxy)butyl)-1,3-dithian-2-yl)-2-methylpropoxy)dimethylsilane (20).** To a cooled (0 °C) suspension of NaH (Aldrich, 60% in mineral oil, 3.88 g, 97.1 mmol, 5.00 equiv) in 60 ml THF was added a solution of alcohol **M** (10.0 g, 19.4 mmol, 1.00 equiv) in 50 ml THF, 15-crown-5 (ABCR GmbH 98%, 4.04 ml, 20.4 mmol, 1.05 equiv) and iodomethane (Fluka purum 99.0%, 10.9 ml, 175 mmol, 9.00 equiv) each in one portion. The white, milky suspension was stirred for 2 h at 0 °C and for 14 h at room temperature (ice bath slowly warmed up overnight). The mixture was then again cooled to 0 °C and the reaction was carefully quenched by the addition of 60 ml sat. aq. $NaHCO_3$. The solution was then extracted with AcOEt (3 × 50 ml), the comb. organic extracts were washed once with 100 ml sat. aq. $NaHCO_3$ and once with 100 ml sat. aq. NaCl, dried over $MgSO_4$ and concentrated *in vacuo*. The residue (12.0 g of a yellow oil) was purified by FC ($SiO_2$, AcOEt/hexane 1:5; d = 5.6 cm; h = 14.5 cm) to afford the desired product **20** as a yellowish oil (9.68 g, 94%).

**$R_f$** (AcOEt/hexane 1:4) 0.50; $R_f$ (AcOEt/toluene 1:4) 0.65. **$[\alpha]_D^{22}$:** +6.02° (c 0.743, $CHCl_3$). **IR** (film): 2952w, 2928m, 2855w, 1613w, 1513m, 1463w, 1362w, 1302w, 1247s, 1173w, 1086s, 1037m, 1006w, 835s, 774s, 669w. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.29–7.25 (m, 2 H); 6.89–6.85 (m, 2 H); 4.46 (d, J = 11.5, 1 H); 4.43 (d, J = 11.5, 1 H); 3.80 (s, 3 H); 3.79–3.71 (m, 3 H); 3.59 (dd, J = 6.9, 1.4, 1 H); 3.58 (br d, J = 7.0, 1 H); 3.31 (s, 3 H); 3.04 (ddd, J = 14.1, 10.1, 4.0, 1 H); 2.91–2.83 (m, 1 H); 2.74–2.61 (m, 2 H); 2.30 (d, J = 4.3, 2 H); 2.09–2.01 (m, 1 H); 1.95–1.88 (m, 1 H); 1.87 –1.78 (m, 2 H); 1.13 (s, 3 H); 1.12 (s, 3 H); 0.90 (s, 9 H); 0.04 (s, 6 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 159.16; 130.70; 129.25 (2 C); 113.77 (2 C); 77.44; 72.73; 68.24; 66.52; 60.57; 56.09; 55.30; 46.94; 43.34; 34.93; 27.29; 27.18; 25.97 (3 C); 24.44; 21.07; 20.94; 18.32; –5.38; –5.41. **HRMS** (ESI): 551.2653 (23, [*M* + Na]$^+$, $C_{27}H_{48}NaO_4S_2Si$, calcd. 551.2655).



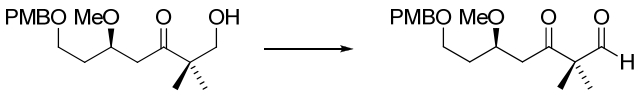

**(*R*)-1-(*tert*-Butyldimethylsilyloxy)-5-methoxy-7-(4-methoxybenzyloxy)-2,2-dimethylheptan-3-one (N).** To a solution of 1,3-dithiane **20** (7.86 g, 14.9 mmol, 1.00 equiv) in 150 ml MeCN were added 75 ml sat. aq. $NaHCO_3$. This mixture was cooled to 0 °C and iodine (Fluka puriss. p.a. 99.8%, 15.1 g, 59.4 mmol, 4.00 equiv) was added portionwise over a period of 15 min. The reaction was then allowed to warm to room temperature and stirred for 20 min before cooling to 0 °C and quenching of the reaction with 75 ml sat. aq. $NaHCO_3$ and 75 ml sat. aq. $Na_2S_2O_3$. The mixture was extracted with AcOEt (3 × 100 ml) and the combined organic extracts were washed with 150 ml sat. aq. NaCl, dried over $MgSO_4$ and concentrated. The residue (7.26 g of an orange-red oil) was purified by FC (material applied to column as a concentrated solution in small volume of $CH_2Cl_2$; $SiO_2$, AcOEt/hexane 1:10 → 1:5 → 1:3; d = 5.8 cm; h = 17.5 cm) to afford the desired product **N** as a yellowish oil (5.39 g, 83%).

**$R_f$** (AcOEt/toluene 1:4) 0.56; $R_f$ (AcOEt/hexane 1:1) 0.73. **$[\alpha]_D^{22}$:** +2.14° (c 0.906, $CHCl_3$). **IR** (film): 2953w, 2929m, 2857w, 1705m, 1613w, 1514m, 1464w, 1362w, 1248s, 1095s, 1038m, 837s, 776m, 758s. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.27–7.24 (m, 2 H); 6.88–6.85 (m, 2 H); 4.44 (d, J = 11.5, 1 H); 4.40 (d, J = 11.5, 1 H); 3.90–3.84 (m, 1 H); 3.80 (s, 3 H); 3.60–3.51 (m, 4 H); 3.29 (s, 3 H); 2.86 (dd, J = 17.6, 6.5, 1 H); 2.55 (dd, J = 17.6, 5.6, 1 H); 1.85–1.70 (m, 2 H); 1.075 (s, 3 H); 1.072 (s, 3 H); 0.86 (s, 9 H); 0.02 (s, 6 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 212.98; 159.15; 130.71; 129.26 (2 C); 113.78 (2 C); 74.39; 72.57; 69.93; 66.59; 57.42; 55.29; 49.63; 43.11; 34.62; 25.83 (3 C); 21.35; 21.33; 18.21; –5.60 (2 C). **HRMS** (ESI): 461.2713 (100, $[M + Na]^+$, $C_{24}H_{42}NaO_5Si$, calcd. 461.2694).



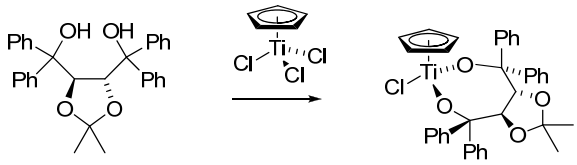

**(*R*)-1-Hydroxy-5-methoxy-7-(4-methoxybenzyloxy)-2,2-dimethylheptan-3-one (O).** To a solution of TBS-ether **N** (5.06 g, 11.5 mmol, 1.00 equiv) in 110 ml THF/MeOH 1:10 was added *para*-toluenesulfonic acid monohydrate (Fluka puriss., 2.33 g, 12.2 mmol, 1.06 equiv) in one portion. The reaction mixture was stirred at room temperature for 3 h. Then 50 ml sat. aq. $NaHCO_3$ and 50 ml $H_2O$ were added and the solution was extracted with AcOEt (4 × 50 ml). The combined organic extracts were washed once with 100 ml sat. aq. NaCl, dried over $Na_2SO_4$ and concentrated. The yellow-colored biphasic oily residue (5.53 g) was purified by FC ($SiO_2$, AcOEt/hexane 1:1 → 2:1; d = 4.6 cm; h = 16 cm) to afford the desired product **O** as a colorless oil (3.54 g, 95%).

**$R_f$** (AcOEt/hexane 1:1) 0.22. **$[\alpha]_D^{22}$:** –14.9° (c 1.95, $CHCl_3$). **IR** (film): 3455w (br, 3600–3100), 2933w, 2871w, 1701m, 1612m, 1513s, 1465m, 1364m, 1302m, 1246s, 1174m, 1085s, 1034s, 820m, 756w. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.26–7.23 (m, 2 H); 6.89–6.85 (m, 2 H); 4.42 (s, 2 H); 3.95–3.88 (m, 1 H); 3.80 (s, 3 H); 3.62 (dd, J = 11.4, 6.3, 1 H); 3.52 (t, J = 6.2, 2 H); 3.49 (dd, J = 11.4, 7.4, 1 H); 3.29 (s, 3 H); 2.90 (dd, J = 16.6, 8.1, 1 H); 2.80 (dd, J = 7.2, 6.6, 1 H); 2.45 (dd, J = 16.6, 4.6, 1 H); 1.88–1.75 (m, 2 H); 1.11 (s, 6 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 214.81; 159.23; 130.40; 129.33 (2 C); 113.81 (2 C); 75.66; 72.71; 69.73; 66.19; 57.46; 55.28; 49.95; 42.36; 33.58; 21.06; 21.01. **HRMS** (ESI): 347.1844 (100, $[M + Na]^+$, $C_{18}H_{28}NaO_5$, calcd. 347.1829).



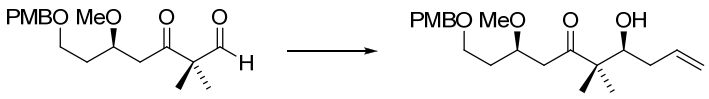

**(*R*)-5-Methoxy-7-(4-methoxybenzyloxy)-2,2-dimethyl-3-oxoheptanal (9).** To a cooled (–78 °C) solution of oxalyl chloride (Fluka puriss. 99.0%, 0.32 ml, 3.80 mmol, 1.10 equiv) in 18 ml $CH_2Cl_2$ was added dimethyl sulfoxide (0.61 ml, 8.63 mmol, 2.50 equiv) dropwise. The solution was stirred for 30 min, then a solution of hydroxy ketone **O** (1.12 g, 3.45 mmol, 1.00 equiv) in 9 ml $CH_2Cl_2$ was added dropwise over a period of 20 min. The resulting white suspension was stirred for 50 min, when triethylamine (Fluka pruss. p.a., 2.00 ml, 14.4 mmol, 4.17 equiv) was slowly added, whereby a clear solution was obtained. The reaction mixture was allowed to warm to 0 °C, which resulted in the reappearance of a suspension. The reaction was quenched by the addition of 20 ml sat. aq. $NH_4Cl$, and the aq. layer was separated and extracted with $CH_2Cl_2$ (2 × 20 ml). The combined organic extracts were washed with 30 ml sat. aq. $NH_4Cl$ and 30 ml sat. aq. NaCl, dried over $MgSO_4$ and concentrated. The residue (yellow oil) was purified by FC ($SiO_2$, AcOEt/hexane 1:2; d = 3.6 cm; h = 17 cm) to afford the desired keto aldehyde **9** as a colorless oil (1.05 g, 94%).

**$R_f$** (AcOEt/hexane 1:2) 0.38. **$[\alpha]_D^{25}$:** –2.26° (c 0.925, $CHCl_3$). **IR** (film): 2969w, 2934w, 2863w, 2837w, 1731m, 1702s, 1613m, 1513s, 1465m, 1366m, 1302m, 1247s, 1174m, 1087s, 1035s, 822m, 754m. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 9.56 (s, 1 H); 7.26–7.22 (m, 2 H); 6.89–6.85 (m, 2 H); 4.41 (s, 2 H); 3.89–3.83 (m, 1 H); 3.79 (s, 3 H); 3.50 (t, J = 6.2, 2 H); 3.27 (s, 3 H); 2.77 (dd, J = 16.9, 7.6, 1 H); 2.51 (dd, J = 16.9, 4.7, 1 H); 1.85–1.72 (m, 2 H); 1.291 (s, 3 H); 1.286 (s, 3 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 207.90; 200.88; 159.22; 130.45; 129.29 (2 C); 113.80 (2 C); 74.88; 72.66; 66.14; 60.51; 57.43; 55.26; 44.02; 33.75; 19.00; 18.94. **HRMS** (ESI, dissolved in $CH_2Cl_2$/MeOH): 377.1934 (100, $[M + Na + MeOH]^+$, $C_{19}H_{30}NaO_6$, calcd. 377.1935); 345.1671 (8, $[M + Na]^+$, $C_{18}H_{26}NaO_5$, calcd. 345.1672).



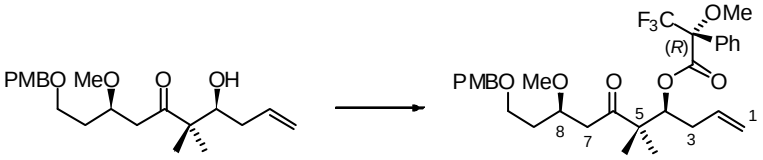

**Formation of the Duthaler-Hafner reagent (P).**[23] A yellow solution/suspension of freshly sublimed cyclopentadienyltitanium trichloride (Acros 99%, 1.34 g, 6.13 mmol, 1.00 equiv) in 100 ml cyclohexane (Acros 99.5%, extra dry, over MS) was treated with (–)-(*R*,*R*)-Taddol (TCI, 97.0%, 2.86 g, 6.13 mmol, 1.00 equiv) under argon. The reaction flask was fitted with a Soxhlet extractor containing 6 g of MgO (activated for 3 h at 300 °C, 5 mbar) and the mixture was stirred at reflux temperature (oil bath 130 °C) for 17 h. After cooling to room temperature (leading to the formation of a yellow precipitate) the solvent was evaporated (rotary evaporator vented with argon prior to use). Crude **P** was obtained as a yellow/orange solid that was dissolved in 70 ml ether and used for the next step without further purification.

[23] Hafner, A.; Duthaler, R. O.; Marti, R.; Rib, G.; Rothe-Streit, P.; Schwarzenbach, F. *J. Am. Chem. Soc.* **1992**, *114*, 2321–2336.




**(3*R*,7*S*)-7-Hydroxy-3-methoxy-1-(4-methoxybenzyloxy)-6,6-dimethyldec-9-en-5-one (21).** Allylmagnesium bromide (Aldrich, 0.8 M in $Et_2O$, 6.13 ml, 4.90 mmol, 1.79 equiv) was added dropwise to the solution of the Duthaler-Hafner reagent **P** (6.13 mmol, 2.25 equiv, orange solution/suspension as described above) in 70 ml $Et_2O$ at 0 °C over a period of 10 min. After stirring at 0 °C for 1.5 h, the orange-red suspension (clear orange-red solution with precipitate, formed already after 5 min) was cooled to –78 °C and a solution of *β*-keto aldehyde **9** (879 mg, 2.73 mmol, 1.00 equiv) in 10 ml $Et_2O$ was added over 2 min, which was accompanied by the formation of a yellow suspension. After 2¼ h at –78 °C the reaction was treated with 30 ml 45% aq. $NH_4F$ solution, then warmed to room temperature and stirred for 18 h. It was then filtered through celite and extracted with $Et_2O$ (3 × 50 ml). The combined organic extracts were washed once with 50 ml sat. aq. NaCl, dried over $MgSO_4$ and concentrated. The oily residue was purified by FC ($SiO_2$, AcOEt/hexane 1:5 → 1:2 → 1:1; d = 4.6 cm; h = 17 cm) to afford homoallylic alcohol **21** as an oil (892 mg, 90%, dr = 70:1) and the recovered Taddol as solid (2.3 g, ca. 80%).

**$R_f$** (AcOEt/hexane 1:2) 0.26; $R_f$ (AcOEt/hexane 1:1) 0.55. **$[\alpha]_D^{23}$**: –8.10° (c 0.958, $CHCl_3$). **IR** (film): 3460w (br, 3600–3200), 2974w, 2935w, 2874w, 2837w, 1702m, 1640w, 1613m, 1513s, 1466m, 1365m, 1302m, 1247s, 1174m, 1086s, 1035s, 993m, 915m, 822m. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.27–7.23 (m, 2 H); 6.88–6.85 (m, 2 H); 5.90–5.79 (m, 1 H); 5.12 (dq, J = 18.7, 1.4, 1 H); 5.10 (dq, J = 10.3, 1.0, 1 H); 4.43 (d, J = 11.6, 1 H); 4.40 (d, J = 11.6, 1 H); 3.93–3.87 (m, 1 H); 3.79 (s, 3 H); 3.74 (ddd, J = 10.2, 4.2, 2.2, 1 H); 3.52 (td, J = 6.2, 1.3, 2 H); 3.29 (s, 3 H); 2.86 (dd, J = 17.2, 7.3, 1 H); 2.65 (d, J = 4.6, 1 H); 2.57 (dd, J = 17.1, 5.1, 1 H); 2.26–2.21 (m, 1 H); 2.02 (dddt, J = 14.1, 10.3, 7.8, 1.0, 1 H); 1.80 (qd, J = 6.4, 1.2, 2 H); 1.14 (s, 3 H); 1.08 (s, 3 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 214.39; 159.18; 135.82; 130.44; 129.31 (2 C); 117.55; 113.77 (2 C); 75.37; 75.03; 72.64; 66.27; 57.45; 55.24; 51.89; 43.06; 36.29; 33.67; 21.32; 18.70. **HRMS** (ESI): 387.2133 (100, [*M* + Na]$^+$, $C_{21}H_{32}NaO_5$, calcd. 387.2142).

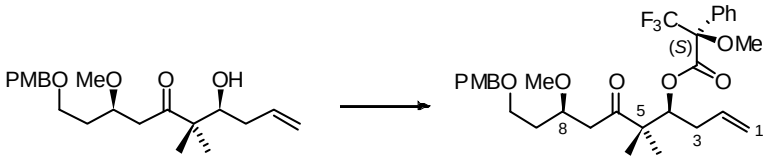



**(*R*)-((4*S*,8*R*)-8-Methoxy-10-(4-methoxybenzyloxy)-5,5-dimethyl-6-oxodec-1-en-4-yl) 3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (Q).** To a solution of **21** (dr ca. 10:1,[24] 57.0 mg, 0.156 mmol, 1.00 equiv) in 2.5 ml $CH_2Cl_2$ was added pyridine (Fluka puriss., 0.050 ml, 0.62 mmol, 4.0 equiv) followed by (*S*)-(+)-3,3,3-trifluoro-2-methoxy-2-phenylpropionyl chloride (ABCR 98%, 50.0 mg, 0.198 mmol, 1.27 equiv) in 0.5 ml $CH_2Cl_2$ and 4-dimethylamino pyridine (Aldrich 99%, 23.0 mg, 0.188 mmol, 1.21 equiv). The solution was stirred for 26 h at room temperature (only ca. 60% conversion on TLC). Then 3 ml sat. aq. $NH_4Cl$ were added and the reaction mixture was extracted with $CH_2Cl_2$ (3 × 3 ml). The combined organic extracts were washed with 8 ml sat. aq. $NH_4Cl$, dried over $MgSO_4$ and concentrated. The residue (yellow oil) was purified by FC ($SiO_2$,

[24] This starting material **21** with dr 10:1 was derived from a different batch than the one described for the reaction **9** → **21** which gave a dr of 70:1.

AcOEt/hexane 1:3 → 1:2; d = 1.4 cm; h = 16 cm) to afford the Mosher ester **Q** as a colorless oil (12 mg, 13%, dr ca. 10:1).

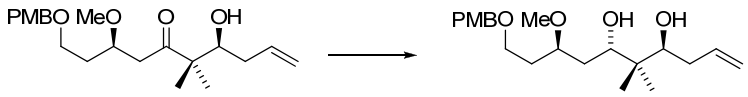
**$R_f$** (AcOEt/hexane 1:2) 0.46. **$[\alpha]_D^{23}$**: +20.1° (c 0.600, $CHCl_3$). **IR** (film): 2930w, 2855w, 1747m, 1707m, 1613w, 1513m, 1467w, 1368w, 1248s, 1170s, 1103s, 1084s, 1016m, 994m, 922w, 821m, 764m, 720m. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.57–7.50 (m, 2 H); 7.39–7.35 (m, 3 H); 7.27–7.23 (m, 2 H); 6.89–6.86 (m, 2 H); 5.79–5.69 (m, 1 H); 5.59 (dd, J = 9.3, 3.1, 1 H); 5.06–5.01 (m, 2 H); 4.43 (d, J = 11.7, 1 H); 4.40 (d, J = 11.6, 1 H); 3.86–3.81 (m, 1 H); 3.80 (s, 3 H); 3.53 (q, J = 0.9, 3 H); 3.51 (t, J = 6.3, 2 H); 3.25 (s, 3 H); 2.75 (dd, J = 17.4, 7.6, 1 H); 2.44 (dd, J = 17.4, 4.8, 1 H); 2.37–2.30 (m, 1 H); 2.29–2.20 (m, 1 H); 1.77 (q, J = 6.0, 2 H); 1.06 (s, 3 H); 1.05 (s, 3 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 210.80; 165.91; 159.22; 134.17; 132.08; 130.54; 129.58; 129.31 (2 C); 128.24 (2 C); 127.63 (2 C); 123.40 (q, J = 287 Hz); 118.12; 113.81 (2 C); 84.45 (q, J = 27.4 Hz); 79.04; 74.61; 72.69; 66.34; 57.49; 55.29 (2 C); 51.61; 43.15; 35.56; 33.88; 21.29; 19.16. **HRMS** (ESI): 603.2541(100, [*M* + Na]$^+$, $C_{31}H_{39}F_3NaO_7$, calcd. 603.2540).




**(*S*)-((4*S*,8*R*)-8-Methoxy-10-(4-methoxybenzyloxy)-5,5-dimethyl-6-oxodec-1-en-4-yl) 3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (R).** To a solution of **21** (dr ca. 10:1,[24] 53.0 mg, 0.145 mmol, 1.00 equiv) in 2.5 ml $CH_2Cl_2$ was added pyridine (Fluka puriss., 0.050 ml, 0.62 mmol, 4.3 equiv) followed by (*R*)-(–)-3,3,3-trifluoro-2-methoxy-2-phenylpropionyl chloride (ABCR 98%, 50.0 mg, 0.198 mmol, 1.37 equiv) in 0.5 ml $CH_2Cl_2$ and 4-dimethylamino pyridine (Aldrich 99%, 56.0 mg, 0.458 mmol, 3.16 equiv). The solution was stirred for 40 h at room temperature. Then 3 ml sat. aq. $NH_4Cl$ were added and the reaction mixture was extracted with $CH_2Cl_2$ (3 × 3 ml). The combined organic layers were washed with 8 ml sat. aq. $NH_4Cl$, dried over $MgSO_4$ and concentrated. The residue (yellow oil) was purified by FC ($SiO_2$, AcOEt/hexane 1:3 → 1:2; d = 1.4 cm; h = 17 cm) to afford the desired product **R** as a colorless oil (48 mg, 57%, dr ca. 10:1).

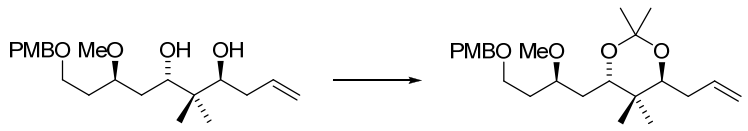
**$R_f$** (AcOEt/hexane 1:2) 0.46. **$[\alpha]_D^{23}$**: +1.85° (c 2.40, $CHCl_3$). **IR** (film): 2979w, 2935w, 2854w, 1745m, 1708m, 1613w, 1514m, 1467w, 1452w, 1368w, 1247s, 1170s, 1084s, 1014m, 990m, 820m, 765m, 720m. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.53–7.51 (m, 2 H); 7.39–7.37 (m, 3 H); 7.26–7.24 (m, 2 H); 6.88–6.86 (m, 2 H); 5.73–5.62 (m, 1 H); 5.56 (dd, J = 9.4, 3.0, 1 H); 5.01–4.95 (m, 2 H); 4.41 (s, 2 H); 3.88–3.82 (m, 1 H); 3.79 (s, 3 H); 3.51 (t, J = 6.3, 2 H); 3.46 (q, J = 0.9, 3 H); 3.26 (s, 3 H); 2.80 (dd, J = 17.3, 7.8, 1 H); 2.45 (dd, J = 17.3, 4.4, 1 H); 2.33–2.27 (m, 1 H); 2.24–2.15 (m, 1 H); 1.77 (q, J = 6.1, 2 H); 1.11 (s, 6 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 210.84; 165.93; 159.21; 133.77; 131.75; 130.55; 129.62; 129.31 (2 C); 128.35 (2 C); 127.90 (2 C); 123.38 (q, J = 286 Hz); 118.20; 113.81 (2 C); 84.79 (q, J = 27.6 Hz); 78.97; 74.67; 72.68; 66.33; 57.53; 55.28 (2 C); 51.53; 43.15; 35.34; 33.86; 21.04; 19.55. **HRMS** (ESI): 603.2542(80, [*M* + Na]$^+$, $C_{31}H_{39}F_3NaO_7$, calcd. 603.2540).

Data for Mosher ester analysis: C8–O*Me* for (*S*)-ester **R**: 3.26 ppm; for (*R*)-ester **Q**: 3.25 ppm. C7–H for (*S*)-**R**: 2.80, 2.45; for (*R*)-**Q**: 2.75, 2.44. C5–*Me* for **R**: 1.11 (2×); for **Q**: 1.06, 1.05. C3–H for **R**: 2.33–2.27, 2.24–2.15; for **Q**: 2.37–2.30, 2.29–2.20. C2–H for **R**: 5.73–5.62; for **Q**: 5.79–5.69. C1–H for **R**: 5.01–4.95, for **Q**: 5.06–5.01.




**(4*S*,6*S*,8*R*)-8-Methoxy-10-(4-methoxybenzyloxy)-5,5-dimethyldec-1-ene-4,6-diol (S).** A solution of tetramethylammonium triacetoxyborohydride[25] (Fluka purum >95.0%, 9.38 g, 35.7 mmol, 11.6 equiv) in 15 ml MeCN and 15 ml anhydrous acetic acid (Fluka puriss p.a. ACS; >99.8%) was stirred at room temperature for 15 min and then cooled to –25 °C. A solution of β-hydroxy ketone **21** (1.12 g, 3.07 mmol, 1.00 equiv) in 15 ml MeCN was added dropwise at –25 °C (the solution of **21** has to be added immediately after cooling, in order to prevent the MeCN/AcOH 1:1 solvent mixture from freezing). The temperature was then raised to –20 °C and the reaction mixture was stirred for 4 days (94 h). After warming to ambient temperature and stirring for further 15 min the reaction was quenched by the addition of 4.0 ml 4-hydroxy-2-butanone (TCI, >95%) and the mixture was stirred for 30 min (slight warming). It was then diluted with 25 ml MeCN and 25 ml glycerol and stirred for additional 30 min. The pH of the cooled (0 °C) mixture was adjusted to basic (pH 10–11) by the addition of ca. 70 ml sat. aq. $K_2CO_3$ and the aq. layer was separated and extracted with $Et_2O$ (3 × 50 ml, after each extraction a small amount of NaCl was added to the aq. layer). The combined organic extracts were washed once with 100 ml sat. aq. NaCl, dried over $Na_2SO_4$ and then concentrated. The residue (yellow oil) was purified by FC ($SiO_2$, AcOEt/hexane 1:1; d = 3.4 cm; h = 19 cm) to afford unreacted **21** (55 mg, 5%) as well as the desired product **S** as a colorless oil (1.01 g, 90%, dr. 10:1).

**$R_f$** (AcOEt/hexane 1:2) 0.17; $R_f$ (AcOEt/hexane 1:1) 0.40; $R_f$ (AcOEt/hexane 1:4) 0.06. **$[\alpha]_D^{23}$:** –21.8° (c 0.826, $CHCl_3$). **IR** (film): 3401w (br, 3600–3150), 2935m, 2873w, 2837w, 1613m, 1513s, 1466m, 1366w, 1302m, 1247s, 1174m, 1085s, 1036s, 913w, 821m, 758m. **$^1$H-NMR** (400 MHz, $CDCl_3$): (Data for major isomer) δ 7.26–7.23 (m, 2 H); 6.89–6.86 (m, 2 H); 5.96–5.86 (m, 1 H); 5.16–5.09 (m, 2 H); 4.43 (s, 2 H); 3.88 (d, J = 3.1; 1 H); 3.82–3.78 (m, 1 H); 3.80 (s, 3 H); 3.72–3.66 (m, 1 H); 3.58–3.50 (m, 3 H); 3.45 (d, J = 3.8, 1 H); 3.36 (s, 3 H); 2.29–2.25 (m, 1 H); 2.19–2.11 (m, 1 H); 2.01–1.93 (m, 1 H); 1.85–1.73 (m, 2 H); 1.51 (ddd, J = 14.4, 5.9, 1.4, 1 H); 0.91 (s, 3 H); 0.85 (s, 3 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): (Data for major isomer) δ 159.26; 136.65; 130.42; 129.35 (2 C); 117.08; 113.83 (2 C); 77.37; 77.24; 75.81; 72.75; 66.52; 57.39; 55.29; 39.86; 36.63; 33.90; 33.35; 21.27; 20.61. Data of minor isomer: δ 159.26; 136.87; 130.32; 129.32 (2 C); 116.81; 113.84 (2 C); 80.60; 79.76; 77.89; 72.81; 66.17; 56.53; 55.29; 40.71; 36.48; 35.59; 33.44; 21.04; 14.94. **HRMS** (ESI): 389.2296 (100, [*M* + Na]$^+$, $C_{21}H_{34}NaO_5$, calcd. 389.2298).

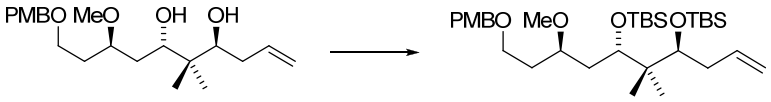



**(4*S*,6*S*)-4-Allyl-6-((*R*)-2-methoxy-4-(4-methoxybenzyloxy)butyl)-2,2,5,5-tetramethyl-1,3-dioxane (T).** To a solution of 1,3-diol **S** (119 mg, 0.325 mmol, 1.00 equiv) in 2,2-dimethoxypropane (Fluka purum 98%, 2.00 ml, 16.3 mmol, 50.2 equiv) was added (+)-camphor-10-sulfonic acid (β) (Fluka purum >98%, 2.1 mg, 0.0090 mmol, 0.028 equiv), and the mixture was stirred at room temperature for 19 h. The reaction was quenched by the addition of 0.08 ml $Et_3N$ (Fluka puriss. p.a. >99.5%). After filtration through a short pad of silica (AcOEt as

[25] Evans, D. A.; Chapman, K. T.; Carreira, E. M. *J. Am. Chem. Soc.* **1988**, *110*, 3560–3578.

eluent; d = 2.4 cm; h = 7 cm), the solution was concentrated *in vacuo* and purified by FC ($SiO_2$, AcOEt/hexane 1:10 → 1:5; d = 2.4 cm; h = 13 cm) yielding the desired product **T** as a colorless oil (100 mg, 76%).

**$R_f$** (AcOEt/hexane 1:2) 0.77; $R_f$ (AcOEt/hexane 1:5) 0.45. **$[\alpha]_D^{22}$:** –20.0° (c 1.28, $CHCl_3$). **IR** (film): 2984w, 2954w, 2934m, 2872w, 2837w, 1613w, 1513s, 1465m, 1379m, 1360m, 1302w, 1247s, 1224s, 1172s, 1090s, 1037s, 940m, 910m, 820m. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.28–7.24 (m, 2 H); 6.89–6.85 (m, 2 H); 5.90–5.80 (m, 1 H); 5.09 (dm, J = 17.2, 1 H); 5.01 (dm, J = 10.3, 1 H); 4.45 (d, J = 12.2, 1 H); 4.42 (d, J = 12.2, 1 H); 3.80 (s, 3 H); 3.64–3.61 (m, 1 H); 3.53 (td, J = 6.9, 1.0, 2 H); 3.50–3.44 (m, 1 H); 3.37 (dd, J = 8.2, 5.0, 1 H); 3.33 (s, 3 H); 2.14–2.10 (m, 1 H); 2.11 (dt, J = 6.7, 1.3, 1 H); 1.91–1.77 (m, 2 H); 1.44–1.40 (m, 2 H); 1.36 (s, 3 H); 1.31 (s, 3 H); 0.77 (s, 3 H); 0.76 (s, 3 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 159.13; 136.56; 130.70; 129.17 (2 C); 115.85; 113.77 (2 C); 100.96; 76.17; 75.16; 72.62; 72.06; 66.52; 56.78; 55.28; 39.04; 34.41; 33.89; 33.42; 24.01; 23.96; 19.60; 19.21. **HRMS** (ESI): 429.2616 (100, $[M + Na]^+$, $C_{24}H_{38}NaO_5$, calcd. 429.2611).

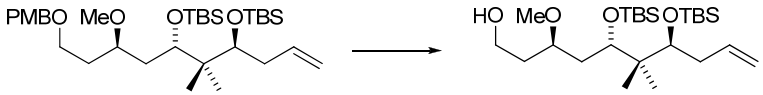



**(5*S*,7*S*)-5-Allyl-7-((*R*)-2-methoxy-4-(4-methoxybenzyloxy)butyl)-2,2,3,3,6,6,9,9,10,10-decamethyl-4,8-dioxa-3,9-disilaundecane (22).** To a cooled (–78 °C) solution of 1,3-diol **S** (309 mg, 0.843 mmol, 1.00 equiv) in 12 ml $CH_2Cl_2$ were added successively 2,6-lutidine (Aldrich 99%, 0.29 ml, 2.53 mmol, 3.00 equiv) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (ABCR GmbH, 0.41 ml, 1.77 mmol, 2.10 equiv). The reaction mixture was stirred for 1 h at –78 °C and then slowly warmed to room temperature over a period of 3 h, and further stirred for 16 h at room temperature ((thawing ice-bath overnight; the starting material was not fully consumed at this point). The reaction was then quenched by the addition of 10 ml sat. aq. $NH_4Cl$, the organic phase was separated and the aq. phase extracted with $CH_2Cl_2$ (2 × 10 ml). The comb. org. phases were once washed with 15 ml sat. aq. NaCl and dried over $MgSO_4$. The residue (light yellow oil) was purified by FC ($SiO_2$, AcOEt/hexane 1:20 → 1:10; d = 2.4 cm; h = 16.5 cm) to afford the desired product **22** as a colorless oil (344 mg, 69%; ca. 10:1 mixture of diasteroisomers).

**Alternative procedure.** To a solution of 1,3-diol **S** (979 mg, 2.67 mmol, 1.00 equiv) in 20 ml DMF were added imidazole (Fluka puriss p.a. >99.5%, 1.64 g, 24.0 mmol, 9.00 equiv), DMAP (Aldrich 99%, 652 mg, 5.34 mmol, 2.00 equiv), and TBSCl (TCI >98.5%, 2.51 g, 16.7 mmol, 6.25 equiv) and the reaction mixture was stirred at room temperature for 20 h (formation of mono-TBS-ethers; no doubly-protected species observable by TLC). Sat. aq. $NH_4Cl$ (20 ml) was then added and the solution was extracted with AcOEt (3 × 20 ml). The combined organic extracts were washed with 30 ml sat. aq. NaCl, dried over $MgSO_4$ and concentrated. The residue was partially purified by FC ($SiO_2$, AcOEt/hexane 1:3; d = 3.4 cm; h = 10 cm); the fractions containing the mono-protected TBS ethers (NMR showed a 7:2-mixture of mono-TBS-protected species) were combined and concentrated under reduced pressure. After addition of 30 ml $CH_2Cl_2$ the solution was cooled to –78 °C and 2,6-lutidine (Aldrich 98%, 0.93 ml, 8.01 mmol, 3.00 equiv) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (ABCR 98%, 0.80 ml, 3.47 mmol, 1.30 equiv) were added. The cooling bath was removed and the solution was stirred at room temperature for 2½ h (conversion after 1½ h was already >85%). At this point more *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.18 ml, 0.801 mmol, 0.30 equiv) was added to the cooled (–78 °C) reaction mixture and stirring at room temperature was continued for 1 h. The reaction was then quenched by

the addition of 30 ml sat. aq. $NH_4Cl$, the organic phase was separated and the aq. solution was extracted with $CH_2Cl_2$ (3 × 30 ml). The combined organic extracts were once washed with 40 ml sat. aq. NaCl, dried over $MgSO_4$ and evaporated. The residue (light yellow oil) was purified by FC ($SiO_2$, AcOEt/hexane 0:1 → 1:20 → 1:10; d = 3.4 cm; h = 19 cm) to give *bis*-TBS ether **22** as a colorless oil (1.28 g, 81%; ca. 10:1 mixture of diasteroisomers (*vide supra*)).

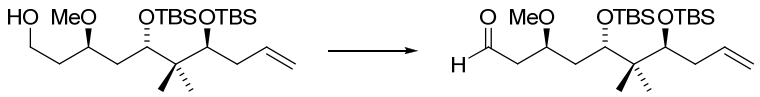
**$R_f$** (AcOEt/hexane 1:4) 0.73; $R_f$ (AcOEt/hexane 1:10) 0.44. **$[\alpha]_D^{22}$:** –14.6° (c 1.24, $CHCl_3$). **IR** (film): 2953w, 2928m, 2885w, 2856w, 1514m, 1471w, 1463w, 1361w, 1249s, 1066s, 1039m, 1005m, 909m, 833s, 772s. **$^1$H-NMR** (400 MHz, $CDCl_3$): (Data for major isomer) δ 7.28–7.24 (m, 2 H); 6.89–6.85 (m, 2 H); 5.96–5.85 (m, 1 H); 5.04–4.95 (m, 2 H); 4.44 (d, J = 11.6, 1 H); 4.41 (d, J = 11.5, 1 H); 3.80 (s, 3 H); 3.80–3.77 (m, 1 H); 3.58–3.46 (m, 4 H); 3.32 (s, 3 H); 2.38–2.31 (m, 1 H); 2.23–2.16 (m, 1 H); 1.95–1.87 (m, 1 H); 1.75–1.67 (m, 1 H); 1.62–1.56 (m, 1 H); 1.37 (ddd, J = 14.7, 8.6, 1.8, 1 H); 0.90 (s, 9 H); 0.89 (s, 9 H); 0.86 (s, 3 H); 0.81 (s, 3 H); 0.08 (s, 3 H); 0.07 (s, 3 H); 0.04 (s, 3 H); 0.03 (s, 3 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): (Data for major isomer) δ 159.12; 137.68; 130.58; 129.20 (2 C); 115.62; 113.74 (2 C); 76.97; 75.37; 74.43; 72.70; 66.57; 55.96; 55.25; 44.15; 39.02; 37.48; 33.69; 26.34 (3 C); 26.16 (3 C); 20.35; 20.28; 18.60; 18.40; –3.08; –3.22; –3.31; –3.97. Minor isomer (only clearly distinguishable signals listed): δ 137.55; 130.62; 129.32; 115.75; 75.74; 74.37; 72.76; 66.48; 56.70; 44.41; 37.78; 34.14; 26.20; 18.36; –2.98; –3.16; –3.87; –4.19. **HRMS** (ESI): 617.4003 (100, [*M* + Na]$^+$, $C_{33}H_{62}NaO_5Si_2$, calcd. 617.4028).




**(3*R*,5*S*,7*S*)-5,7-Bis(*tert*-butyldimethylsilyloxy)-3-methoxy-6,6-dimethyldec-9-en-1-ol (U).** A cooled (0 °C) solution of 4-methoxybenzyl ether **22** (724 mg, 1.22 mmol, 1.00 equiv) in 20 ml $CH_2Cl_2$ and 1.4 ml $H_2O$ was treated with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (Aldrich 98%, 290 mg, 1.28 mmol, 1.05 equiv) in one portion. The dark greenish/brownish reaction mixture was stirred vigorously at 0 °C for 2¼ h. 10 ml 40% aq. $NaHSO_3$ and 15 ml $H_2O$ were then added to the reaction mixture (at 0 °C), which was extracted with $CH_2Cl_2$ (3 × 20 ml). The combined organic extracts were washed once with 20 ml sat. aq. NaCl, dried over $Na_2SO_4$, filtered and then concentrated under reduced pressure. The residue (red oil) was purified by FC ($SiO_2$, AcOEt/hexane 1:10 → 1:5 → 1:3; d = 2.4 cm; h = 20 cm) to afford (due to similar $R_f$-values) a 1:1-mixture (621 mg of an oil) of the desired product **U** (483 mg, 84%) and 4-methoxybenzaldehyde (138 mg, 84%; separation after next step).

**$R_f$** (AcOEt/hexane 1:4) 0.31; $R_f$ (AcOEt/hexane 1:10) 0.10. **$[\alpha]_D^{22}$:** –10.5° (c 1.83, $CHCl_3$; 47.184 mg of the 1:1 mixture corresponding to 36.67 mg (c = 1.834) of product and 10.51 mg (c = 0.5255) of anisaldehyde as impurity). **IR** (film, 1:1-mixture with anisaldehyde): 3400*w* (br, 3600–3250), 2954m, 2929m, 2886w, 2856w, 1699w, 1684w, 1601w, 1578w, 1511w, 1472w, 1463w, 1388w, 1361w, 1255s, 1160m, 1065s, 1005m, 938w, 910m, 833s, 806m, 772s. **$^1$H-NMR** (400 MHz, $CDCl_3$). (1:1-mixture of **U** and anisaldehyde; signals for **U** only). δ 5.94–5.86 (m, 1 H); 5.04–4.97 (m, 2 H); 3.85–3.78 (m, 2 H); 3.72–3.67 (m, 1 H); 3.62–3.57 (m, 2 H); 3.38 (s, 3 H); 2.38–2.32 (m, 2 H); 2.20 (quint, J = 7.5, 1 H); 1.93–1.85 (m, 1 H); 1.79–1.67 (m, 2 H); 1.34 (ddd, J = 14.7, 8.4, 2.2, 1 H); 0.91 (s, 9 H); 0.90 (s, 9 H); 0.87 (s, 3 H); 0.83 (s, 3 H); 0.09 (s, 3 H); 0.08 (s, 3 H); 0.053 (s, 3 H); 0.049 (s, 3 H). Signals for anisaldehyde: δ 9.88 (s, 1 H); 7.85–7.82 (m, 2 H); 7.02–6.99 (m, 2 H); 3.89 (s, 3 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$, 1:1-mixture of **U** and anisaldehyde): data of **U** δ 137.57; 115.72; 76.97; 76.80; 74.66; 59.86; 56.10; 44.23; 38.38; 37.54; 35.16; 26.29 (3 C); 26.16 (3 C); 20.30; 20.24; 18.61; 18.41; –3.05; –

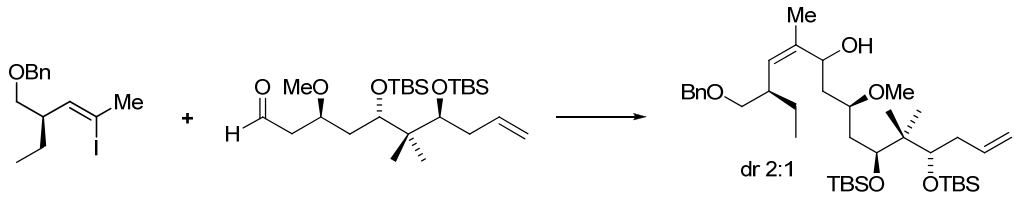
3.21; –3.26; –3.96. Signals for anisaldehyde: δ 190.77; 164.64; 131.99 (2 C); 130.01; 114.33 (2 C); 55.56. **HRMS** (ESI): 497.3442 (58, $[M + Na]^+$, $C_{25}H_{54}NaO_4Si_2$, calcd. 497.3453).




**(3*S*,5*S*,7*S*)-5,7-Bis(*tert*-butyldimethylsilyloxy)-3-methoxy-6,6-dimethyldec-9-enal (8).** To a cooled (0 °C) solution of a 1:1-mixture of alcohol **U** and 4-methoxybenzaldehyde (291 mg of the 1:1-mixture, 227 mg of **U**, 0.480 mmol, 1.00 equiv) in 6 ml $CH_2Cl_2$ was added *Dess-Martin* periodinane (Acros 15wt% in $CH_2Cl_2$, 1.11 ml, 0.524 mmol, 1.10 equiv) and the mixture was stirred at room temperature for 50 min. The white suspension was then cooled to 0 °C, 4 ml sat. aq. $Na_2S_2O_3$ and 8 ml sat. aq. $NaHCO_3$ were added and the resulting mixture stirred for 5 min. The organic phase was separated and the aq. solution was extracted with $CH_2Cl_2$ (3 × 10 ml). The combined organic extracts were washed with 15 ml sat. aq. NaCl, dried over $MgSO_4$ and concentrated. The residue (yellow oil) was purified by FC (material applied to the column as a concentrated solution in a small volume of $CH_2Cl_2$; $SiO_2$, AcOEt/hexane 1:20 → 1:10; d = 2.4 cm; h = 16.5 cm) to afford aldehyde **8** as an oil (192 mg, 85%).

**$R_f$** (AcOEt/hexane 1:10) 0.42. **$[\alpha]_D^{22}$:** –16.6° (c 0.810, $CHCl_3$). **IR** (film): 2955m, 2930m, 2886m, 2857m, 1728m, 1472m, 1388w, 1361w, 1255m, 1068s, 1005m, 937w, 910w, 835s, 804m, 773s. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 9.82 (t, J = 2.5, 1 H); 5.95–5.85 (m, 1 H); 5.04–4.97 (m, 2 H); 3.95–3.89 (m, 1 H); 3.82 (dd, J = 8.6, 0.8, 1 H); 3.55 (dd, J = 6.6, 3.6, 1 H); 3.35 (s, 3 H); 2.66 (ddd, J = 15.9, 5.1, 2.6, 1 H); 2.56 (ddd, J = 15.9, 6.0, 2.4, 1 H); 2.37–2.31 (m, 1 H); 2.22–2.15 (m, 1 H); 1.74 (ddd, J = 14.7, 10.6, 0.8, 1 H); 1.39 (ddd, J = 14.7, 8.7, 2.2, 1 H); 0.904 (s, 9 H); 0.903 (s, 9 H); 0.87 (s, 3 H); 0.82 (s, 3 H); 0.11 (s, 3 H); 0.09 (s, 3 H); 0.05 (s, 3 H); 0.04 (s, 3 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 200.90; 137.53; 115.77; 77.11; 74.13; 73.20; 56.27; 48.06; 44.12; 39.50; 37.52; 26.29 (3 C); 26.16 (3 C); 20.35; 20.34; 18.61; 18.41; –3.07; –3.20; –3.33; –3.96. **HRMS** (ESI): 473.3485 (13, $[M + H]^+$, $C_{25}H_{53}O_4Si_2$, calcd. 473.3477); 579.2457 (3, $[M + Ag]^+$, $C_{25}H_{52}AgO_4Si_2$, calcd. 579.2450).

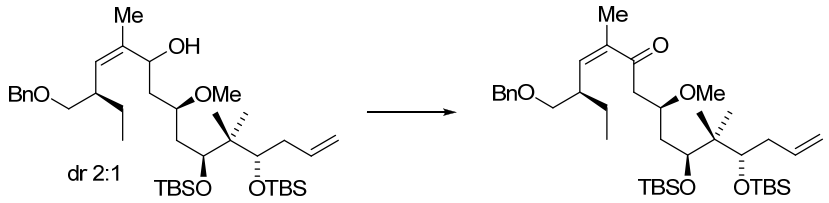
## Assembly of target structure **4**




**(3*R*,6*S*,8*R*,10*S*,12*S*,*Z*)-3-(Benzyloxymethyl)-10,12-bis(*tert*-butyldimethylsilyloxy)-8-methoxy-5,11,11-trimethylpentadeca-4,14-dien-6-ol (5) and (3*R*,6*R*,8*R*,10*S*,12*S*,*Z*)-3-(benzyloxymethyl)-10,12-bis(*tert*-butyldimethylsilyloxy)-8-methoxy-5,11,11-trimethylpentadeca-4,14-dien-6-ol (23) as a 2:1 mixture.** To a cooled (–78 °C) solution of (*Z*)-vinyl iodide **7** (677 mg, 2.05 mmol, 2.50 equiv) in 12 ml $Et_2O$ was added *t*-BuLi (Acros, 1.6 M in pentane, 2.20 ml, 3.52 mmol, 4.29 equiv) dropwise. The slightly orange-colored solution was stirred at –78 °C for 30 min, then a solution of aldehyde **8** (388 mg, 0.821 mmol, 1.00 equiv) in 6 ml $Et_2O$ was added dropwise over a period of 30 min and the slightly yellow reaction mixture was stirred at –78 °C for 15 h. The reaction mixture was then quenched by the addition of 20 ml sat. aq. $NH_4Cl$ and extracted with $Et_2O$ (3 × 20

ml). The combined organic extracts were washed with 40 ml sat. aq. NaCl, dried over $Na_2SO_4$ and concentrated. The residue (yellow oil) was purified by FC ($SiO_2$, AcOEt/hexane 1:20 → 1:10 → 1:5; d = 2.4 cm; h = 20 cm) to afford a mixture of the two diastereoisomers **5**/**23** as a colorless, viscous oil (467 mg, 84%, dr = 2:1).

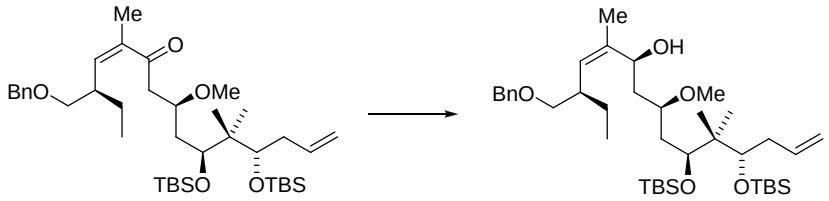
**$R_f$** (AcOEt/hexane 1:10) 0.19. **$[\alpha]_D^{22}$:** –26.2° (c 1.08, $CHCl_3$). **IR (**film): 3450w (br, 3600–3300), 2955m, 2928m, 2885m, 2856m, 1472m, 1462m, 1361m, 1254m, 1087s, 1069s, 1005m, 908m, 835s, 773s, 735m, 697m. **$^1$H-NMR** (400 MHz, $CDCl_3$): (Data for major isomer **5**) δ 7.35–7.26 (m, 5 H); 5.97–5.86 (m, 1 H); 5.05–4.94 (m, 3 H); 4.53 (dd, J = 8.6, 3.6, 1 H); 4.49 (s, 2 H); 3.80 (d, J = 7.5, 1 H); 3.60 (dd, J = 6.6, 3.6, 1 H); 3.57–3.52 (m, 1 H); 3.45–3.40 (m, 1 H); 3.35 (s, 3 H); 3.13 (t, J = 9.0, 1 H); 2.71 (s, 1 H); 2.70–2.61 (m, 1 H); 2.39–2.33 (m, 1 H); 2.25–2.16 (m, 1 H); 2.00 (ddd, J = 13.9, 8.9, 4.8, 1 H); 1.75 (d, J = 1.3, 3 H); 1.65 (dd, J = 15.0, 10.4, 1 H); 1.43–1.37 (m, 3 H); 1.20–1.12 (m, 1 H); 0.91 (s, 9 H); 0.90 (s, 9 H); 0.87 (s, 3 H); 0.84 (t, J = 7.4, 3 H); 0.83 (s, 3 H); 0.11 (s, 3 H); 0.07 (s, 3 H); 0.04 (s, 3 H); 0.03 (s, 3 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): (Data for major isomer **5**) δ 139.88; 137.91; 137.69; 130.45; 128.44 (2 C); 127.77 (2 C); 127.74; 115.65; 76.94; 75.94; 74.29; 73.74; 73.24; 65.82; 55.61; 44.27; 39.49; 39.42; 38.05; 37.53; 26.35 (3 C); 26.18 (3 C); 24.90; 20.31; 20.22; 18.57; 18.41; 18.26; 11.85; –3.06 (2 C); –3.38; –3.97. Minor isomer **23** (only clearly distinguishable signals are listed): δ 138.56; 128.33; 127.56; 127.50; 73.04; 72.66; 46.01; 36.35; 30.44; 24.39; 11.35. **HRMS** (ESI): 699.4823 (100, $[M + Na]^+$, $C_{39}H_{72}NaO_5Si_2$, calcd. 699.4810).




**(3*R*,8*S*,10*S*,12*S*,*Z*)-3-(Benzyloxymethyl)-10,12-bis(tert-butyldimethylsilyloxy)-8-methoxy-5,11,11-trimethylpentadeca-4,14-dien-6-one (V).** To a cooled (0 °C) solution of the 2:1-mixture of diastereoisomers **5**/**23** (167 mg of 2:1-mixture, 0.247 mmol, 1.00 equiv) in 6 ml $CH_2Cl_2$ was added *Dess-Martin* periodinane reagent (Acros 15-wt% in $CH_2Cl_2$, 0.58 ml, 0.271 mmol, 1.10 equiv) and the mixture was stirred for 3 h at 0 °C (nearly complete conversion) and for 60 min at room temperature. Subsequently the reaction mixture was cooled to 0 °C, 6 ml sat. aq. $Na_2S_2O_3$ and 6 ml sat. aq. $NaHCO_3$ were added and the resulting mixture was stirred for 5 min. The organic phase was separated and the aq. phase extracted with $CH_2Cl_2$ (3 × 10 ml). The combined organic extracts were washed with 10 ml sat. aq. NaCl, dried over $MgSO_4$ and concentrated. The residue was purified by FC ($SiO_2$, AcOEt/hexane 1:50 → 1:20; d = 2.4 cm; h = 15.5 cm) to afford the desired product **V** as an oil (109 mg, 65%).

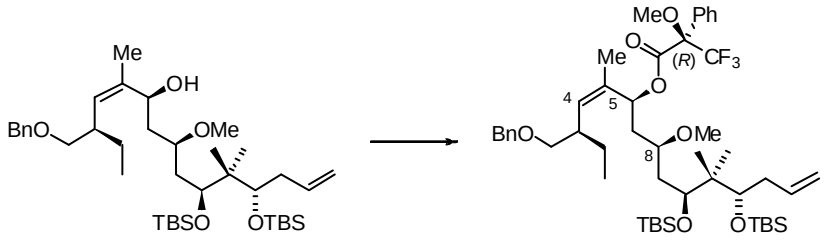
**$R_f$** (AcOEt/hexane 1:10) 0.46. **$[\alpha]_D^{22}$:** –48.0° (c 0.759, $CHCl_3$). **IR** (film): 2957s, 2929s, 2901m, 2856m, 1689w, 1472m, 1462m, 1377m, 1361m, 1254m, 1068s, 1006m, 835s, 807m, 773s. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.34–7.23 (m, 5 H); 5.95–5.85 (m, 1 H); 5.45 (dd, J = 10.4, 1.4, 1 H); 5.03–4.96 (m, 2 H); 4.48 (s, 2 H); 4.00–3.94 (m, 1 H); 3.81 (d, J = 7.6, 1 H); 3.57 (dd, J = 6.5, 3.6, 1 H); 3.40 (d, J = 5.9, 2 H); 3.30 (s, 3 H); 2.91–2.84 (m, 1 H); 2.88 (dd, J = 16.3, 5.7, 1 H); 2.55 (dd, J = 16.3, 5.8, 1 H); 2.37–2.31 (m, 1 H); 2.22–2.15 (m, 1 H); 1.95 (d, J = 1.4, 3 H); 1.67–1.55 (m, 2 H); 1.39–1.23 (m, 2 H); 0.91 (s, 9 H); 0.90 (s, 9 H); 0.86 (s, 3 H); 0.85 (t, J = 7.5, 3 H); 0.81 (s, 3 H); 0.15 (s, 3 H); 0.08 (s, 3 H); 0.04 (s, 3 H); 0.03 (s, 3 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 203.90; 138.82; 138.70; 137.61; 137.31; 128.27 (2 C); 127.51 (2 C); 127.41; 115.68; 76.99; 74.07; 73.96; 73.41;

72.84; 56.54; 47.08; 44.21; 40.78; 39.85; 37.49; 26.36 (3 C); 26.17 (3 C); 24.94; 20.84; 20.28; 20.19; 18.60; 18.40; 11.63; –3.06; –3.12; –3.37; –3.96. **HRMS** (ESI): 697.4656 (55, [*M* + Na]$^+$, $C_{39}H_{70}NaO_5Si_2$, calcd. 697.4654).




**(3*R*,6*S*,8*R*,10*S*,12*S*,*Z*)-3-(Benzyloxymethyl)-10,12-bis(*tert*-butyldimethylsilyloxy)-8-methoxy-5,11,11-trimethylpentadeca-4,14-dien-6-ol (5).** To a cooled (–78 °C) solution of (*Z*)-enone **V** (69.0 mg, 0.102 mmol, 1.00 equiv) in 6 ml toluene was added (*R*)-*B*-Me-CBS-oxazaborolidine catalyst (ABCR GmbH, 1 M in toluene, 0.15 ml, 0.15 mmol, 1.5 equiv) dropwise. After 5 min, catecholborane (Acros, 1 M in THF, 0.20 ml, 0.20 mmol, 2.0 equiv) was added dropwise and the reaction mixture was stirred for 22 h at –78 °C. The reaction was quenched by the addition of 0.5 ml MeOH followed by 2.5 ml $H_2O$ and 3 ml $Et_2O$ and the mixture was warmed to room temperature. Then 5 ml $H_2O$ and 5 ml $Et_2O$ were added, the organic phase was separated and the aq. solution was extracted with $Et_2O$ (3 × 4 ml). The combined organic extracts were washed with 6 ml sat. aq. NaCl, dried over $Na_2SO_4$ and concentrated. The residue was purified by FC ($SiO_2$, AcOEt/hexane 1:20 → 1:10 → 1:5; d = 1.4 cm; h = 18.5 cm) to afford the desired product **5** as a s single isomer as a colorless oil (49 mg, 71%).

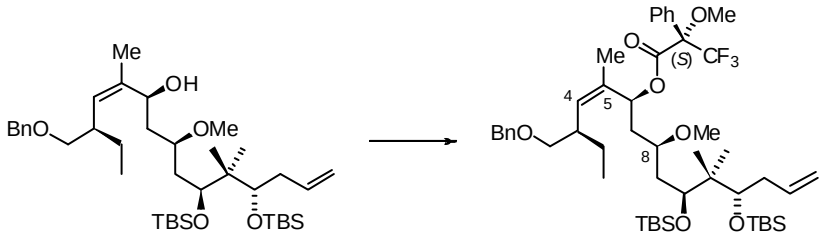
**$R_f$** (AcOEt/hexane 1:10) 0.19. **$[\alpha]_D^{22}$:** –27.6° (c 0.512, $CHCl_3$). **IR** (film): 3450w (br, 3500–3300), 2956s, 2929s, 2886m, 2857m, 1472m, 1462m, 1379m, 1361m, 1254m, 1067s, 1006m, 907w, 835s, 802m, 773s. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.35–7.25 (m, 5 H); 5.97–5.86 (m, 1 H); 5.05–4.94 (m, 3 H); 4.53 (dd, J = 8.8, 3.1, 1 H); 4.49 (s, 2 H); 3.80 (d, J = 7.7, 1 H); 3.60 (dd, J = 6.6, 3.6, 1 H); 3.58–3.52 (m, 1 H); 3.42 (dd, J = 8.7, 4.6, 1 H); 3.35 (s, 3 H); 3.13 (t, J = 9.0, 1 H); 2.71 (s, 1 H); 2.70–2.61 (m, 1 H); 2.39–2.33 (m, 1 H); 2.25–2.17 (m, 1 H); 2.00 (ddd, J = 13.9, 8.9, 4.8, 1 H); 1.75 (d, J = 1.3, 3 H); 1.65 (dd, J = 14.4, 10.2, 1 H); 1.43–1.37 (m, 3 H); 1.20–1.12 (m, 1 H); 0.91 (s, 9 H); 0.90 (s, 9 H); 0.87 (s, 3 H); 0.84 (t, J = 7.4, 3 H); 0.83 (s, 3 H); 0.11 (s, 3 H); 0.08 (s, 3 H); 0.04 (s, 3 H); 0.03 (s, 3 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 139.89; 137.90; 137.68; 130.44; 128.43 (2 C); 127.77 (2 C); 127.74; 115.65; 76.94; 75.93; 74.29; 73.74; 73.24; 65.80; 55.60; 44.27; 39.49; 39.42; 38.04; 37.53; 26.35 (3 C); 26.18 (3 C); 24.90; 20.31; 20.22; 18.57; 18.41; 18.26; 11.85; –3.06 (2 C); –3.38; –3.97. **HRMS** (ESI): 783.3947 (100, [*M* + Ag]$^+$, $C_{39}H_{72}AgO_5Si_2$, calcd. 783.3964); 699.4795 (97, [*M* + Na]$^+$, $C_{39}H_{72}NaO_5Si_2$, calcd. 699.4810).




**(*R*)-((3*R*,6*S*,8*R*,10*S*,12*S*,*Z*)-3-(Benzyloxymethyl)-10,12-bis(*tert*-butyldimethylsilyloxy)-8-methoxy-5,11,11-trimethylpentadeca-4,14-dien-6-yl) 3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (W).** To a solution of **5**

(10.0 mg, 0.0148 mmol, 1.00 equiv) in 0.5 ml dry $CH_2Cl_2$ was added pyridine (Fluka puriss, 0.010 ml, 0.12 mmol, 8.3 equiv) followed by (*S*)-(+)-3,3,3-trifluoro-2-methoxy-2-phenylpropionyl chloride (ABCR 98%, 50.0 mg, 0.198 mmol, 13.4 equiv) in 0.5 ml $CH_2Cl_2$ and 4-dimethylamino pyridine (Aldrich 99%, 7.0 mg, 0.059 mmol, 4.0 equiv). The solution was stirred for 21 h at room temperature (only about 60% conversion by TLC). Then 2 ml sat. aq. $NH_4Cl$ were added and the reaction mixture was extracted with $CH_2Cl_2$ (3 × 3 ml). The combined organic extracts were washed with 8 ml sat. aq. $NH_4Cl$, dried over $MgSO_4$ and concentrated. The residue (yellow oil) was purified by FC ($SiO_2$, AcOEt/hexane 0:1 → 1:50 → 1:20; d = 1.4 cm; h = 14 cm) to afford Mosher ester **W** as an oil that was not entirely pure (6 mg, 45%).

**$R_f$** (AcOEt/hexane 1:10) 0.56. **$[\alpha]_D^{22}$:** +11.0° (c 0.300, $CHCl_3$). **IR** (film): 2954s, 2928s, 2856s, 1745m, 1472m, 1455m, 1387w, 1362w, 1255s, 1188s, 1172s, 1080s, 1070s, 1006m, 915m, 836s, 805m, 773s, 698m. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.51–7.24 (m, 10 H); 5.96 (dd, J = 8.0, 4.0, 1 H); 5.94–5.84 (m, 1 H); 5.23 (dd, J = 10.3, 1.3, 1 H); 5.03–5.00 (m, 2 H); 4.52 (d, J = 12.4, 1 H); 4.48 (d, J = 12.4, 1 H); 3.78 (d, J = 7.8, 1 H); 3.57 (dd, J = 6.7, 3.5, 1 H); 3.51 (q, J = 0.9, 3 H); 3.51–3.45 (m, 1 H); 3.46 (dd, J = 9.4, 4.9, 1 H); 3.36 (dd, J = 9.4, 6.4, 1 H); 3.29 (s, 3 H); 2.89–2.79 (m, 1 H); 2.36–2.29 (m, 1 H); 2.26–2.14 (m, 2 H); 1.72–1.60 (m, 3 H); 1.52 (d, J = 1.2, 3 H); 1.41–1.28 (m, 2 H); 0.90 (s, 9 H); 0.88 (s, 9 H); 0.862 (t, J = 7.4, 3 H); 0.856 (s, 3 H); 0.80 (s, 3 H); 0.06 (s, 3 H); 0.03 (s, 6 H); 0.02 (s, 3 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$, $CF_3$ and $C$–$CF_3$ not observable, due to the limited amount of material available for analysis): δ 165.29; 138.85; 137.57; 133.12; 132.20; 132.15; 130.11; 129.46; 128.70; 128.25 (2 C); 127.51 (2 C); 127.33; 126.92; 115.77; 77.23; 76.85 (impurity?); 74.17; 73.80; 73.05; 72.82; 72.32; 55.36; 54.39; 44.26; 39.33; 38.87; 37.47; 36.73; 26.30 (3 C); 26.16 (3 C); 24.91; 20.20; 20.13; 18.51; 18.41; 17.74; 11.76; –3.05; –3.09; –3.41; –4.00. **HRMS** (ESI): 915.5165 (45, $[M + Na]^+$, $C_{49}H_{79}F_3NaO_7Si_2$, calcd. 915.5209); 910.5615 (38, $[M + NH_4]^+$, $C_{49}H_{83}F_3NO_7Si_2$, calcd. 910.5655).

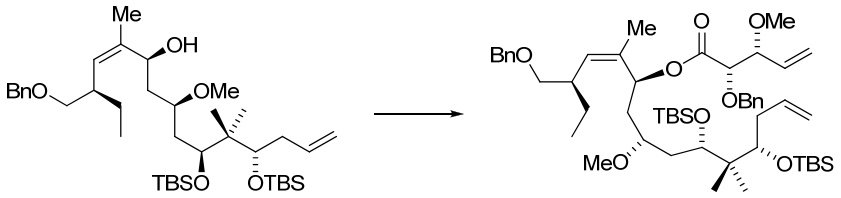



**(*S*)-((3*R*,6*S*,8*R*,10*S*,12*S*,*Z*)-3-(Benzyloxymethyl)-10,12-bis(*tert*-butyldimethylsilyloxy)-8-methoxy-5,11,11-trimethylpentadeca-4,14-dien-6-yl) 3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (X).** To a solution of **5** (10.0 mg, 0.0148 mmol, 1.00 equiv) in 0.5 ml dry $CH_2Cl_2$ was added pyridine (Fluka puriss, 0.010 ml, 0.12 mmol, 8.3 equiv) followed by (*R*)-(+)-3,3,3-trifluoro-2-methoxy-2-phenylpropionyl chloride (ABCR 98%, 50.0 mg, 0.198 mmol, 13.4 equiv) in 0.5 ml $CH_2Cl_2$ and 4-dimethylamino pyridine (Aldrich 99%, 7.0 mg, 0.059 mmol, 4.0 equiv). The solution was stirred for 16 h at room temperature (only about 80% conversion by TLC). Then 2 ml sat. aq. $NH_4Cl$ were added and the reaction mixture was extracted with $CH_2Cl_2$ (3 × 3 ml). The combined organic layers were washed with 8 ml sat. aq. $NH_4Cl$, dried over $MgSO_4$ and concentrated. The residue (yellow oil) was purified by FC ($SiO_2$, AcOEt/hexane 1:50 → 1:20 → 1:10; d = 1.4 cm; h = 13 cm) to afford Mosher ester **X** as a slightly impure oil (7 mg, 53%).

**$R_f$** (AcOEt/hexane 1:10) 0.56. **$[\alpha]_D^{22}$:** –23.1° (c 0.350, $CHCl_3$). **IR** (film): 2955s, 2927s, 2855s, 1746m, 1471m, 1463m, 1361w, 1254s, 1185m, 1171m, 1068s, 1016m, 911m, 835s, 774s, 698m. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.48–7.23 (m, 10 H); 6.01 (dd, J = 7.7, 4.8, 1 H); 5.94–5.82 (m, 1 H); 5.29 (dd, J = 10.3, 1.2, 1 H); 5.04–4.95 (m,

2 H); 4.47 (d, J = 12.2, 1 H); 4.43 (d, J = 12.3, 1 H); 3.78 (d, J = 7.7, 1 H); 3.57 (dd, J = 6.8, 3.6, 1 H); 3.47 (q, J = 0.9, 3 H); 3.47–3.42 (m, 1 H); 3.41 (dd, J = 9.3, 5.0, 1 H); 3.34 (dd, J = 9.3, 6.2, 1 H); 3.23 (s, 3 H); 2.89–2.79 (m, 1 H); 2.36–2.29 (m, 1 H); 2.21–2.13 (m, 2 H); 1.70–1.57 (m, 3 H); 1.67 (d, J = 1.2, 3 H); 1.39–1.30 (m, 2 H); 0.90 (s, 9 H); 0.89 (s, 9 H); 0.86 (t, J = 7.3, 3 H); 0.85 (s, 3 H); 0.81 (s, 3 H); 0.06 (s, 3 H); 0.05 (s, 3 H); 0.04 (s, 3 H); 0.03 (s, 3 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$, $CF_3$ not observable, due to limited amount of material available for analysis): δ 165.53; 138.84; 137.59; 133.58; 132.38; 132.22; 129.50; 128.33 (2 C); 128.24 (2 C); 127.65 (2 C); 127.48 (2 C); 127.31; 115.77; 84.45 (q, J = 27.9); 77.22; 76.86 (impurity?); 73.74; 73.69; 73.13; 72.77; 72.06; 55.10; 53.94; 44.25; 39.35; 38.62; 37.49; 36.54; 26.32 (3 C); 26.16 (3 C); 24.88; 20.23; 20.16; 18.52; 18.41; 17.98; 11.74; –3.06; –3.12; –3.43; –3.97. **HRMS** (ESI): 915.5188 (100, $[M + Na]^+$, $C_{49}H_{79}F_3NaO_7Si_2$, calcd. 915.5209); 910.5640 (35, $[M + NH_4]^+$, $C_{49}H_{83}F_3NO_7Si_2$, calcd. 910.5655).

Data for Mosher ester analysis: C4–H for (*S*)-ester **X**: 5.29 ppm; for (*R*)-ester **W**: 5.23 ppm. C5–*Me* for (*S*)-**X**: 1.67; for (*R*)-**W**: 1.52. C8–O*Me* for **X**: 3.23; for **W**: 3.29.

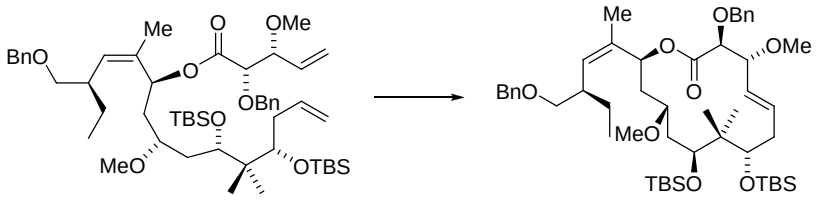



**(2*S*,3*R*)-((3*R*,6*S*,8*R*,10*S*,12*S*,*Z*)-3-(Benzyloxymethyl)-10,12-bis(*tert*-butyldimethylsilyloxy)-8-methoxy-5,11,11-trimethylpentadeca-4,14-dien-6-yl) 2-(benzyloxy)-3-methoxypent-4-enoate (Y).** To a solution of carboxylic acid **6** (15.0 mg, 0.0635 mmol, 1.87 equiv) and $NEt_3$ (Fluka puriss. p.a. 99.5%, 0.019 ml, 0.136 mmol, 4.00 equiv) in 1.5 ml toluene was added 2,4,6-trichlorobenzoyl chloride[26] (Aldrich 97%, 0.016 ml, 0.102 mmol, 3.00 equiv) dropwise. The reaction mixture was stirred for 1 h, then a solution of alcohol **5** (23 mg, 0.0340 mmol, 1.00 equiv) in 1.0 ml toluene and 4-dimethylaminopyridine (Aldrich 99%, 9.1 mg, 0.075 mmol, 2.2 equiv) were added; a suspension formed immediately after the addition of DMAP. The resultant white/grey suspension was stirred at room temperature for 16 h, when the reaction was quenched with 4 ml sat. aq. $NaHCO_3$,which was followed by the addition of 8 ml $Et_2O$. The organic layer was separated and the aq. solution was extracted with $Et_2O$ (3 × 4 ml). The combined org. extracts were washed once with 10 ml sat. aq. NaCl, dried over $Na_2SO_4$ and concentrated under reduced pressure. The residue was purified by FC ($SiO_2$, AcOEt/hexane 1:20 → 1:10; d = 1.4 cm; h = 17.5 cm) to afford ester **Y** as an oil (26 mg, 85%).

**$R_f$** (AcOEt/hexane 1:10) 0.39; $R_f$ (AcOEt/hexane 1:5) 0.65. **$[\alpha]_D^{22}$:** –45.4° (c 1.98, $CHCl_3$). **IR** (film): 2955m, 2928m, 2884w, 2856m, 1744w, 1472w, 1455w, 1360w, 1254m, 1092s, 1068s, 1004m, 935m, 835s, 773s. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.35–7.21 (m, 10 H); 5.95–5.82 (m, 3 H); 5.29 (br d, J = 18.0, 1 H); 5.28 (br d, J = 10.2, 1 H); 5.20 (dd, J = 10.2, 1.0, 1 H); 5.02 (br d, J = 17.8, 1 H); 4.98 (br d, J = 11.0, 1 H); 4.82 (d, J = 11.9, 1 H); 4.52 (d, J = 12.2, 1 H); 4.48 (d, J = 12.2, 1 H); 4.39 (d, J = 11.8, 1 H); 4.00–3.89 (m, 2 H); 3.80 (d, J = 7.9, 1 H); 3.59 (dd, J = 6.6, 3.5, 1 H); 3.53–3.45 (m, 1 H); 3.51 (dd, J = 9.4, 4.4, 1 H); 3.34 (dd, J = 9.4, 6.8, 1 H); 3.30 (s, 3 H); 3.23 (s, 3 H); 2.86–2.77 (m, 1 H); 2.37–2.30 (m, 1 H); 2.22–2.15 (m, 2 H); 1.76–1.66 (m, 2 H); 1.73 (d, J = 1.2, 3 H); 1.58 (ddd, J = 14.8, 5.9, 4.7, 1 H); 1.38 (ddd, J = 14.7, 8.4, 1.8, 1 H); 1.36–1.24 (m, 1 H); 0.90 (s, 9 H); 0.89 (s, 9 H); 0.87 (t, J = 7.4, 3 H); 0.86 (s, 3 H); 0.83 (s, 3 H); 0.07 (s, 6 H); 0.04 (s, 3 H); 0.03 (s, 3 H). **$^{13}$C-**

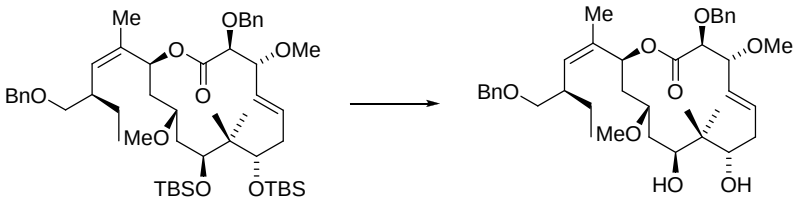
[26] Ding, F.; Jennings, M. P. *Org. Lett.* **2005**, *7*, 2321–2324.

**NMR** (100 MHz, $CDCl_3$): δ 168.86; 139.03; 137.56; 137.53; 134.29; 132.99; 131.93; 128.21 (4 C); 127.97 (2 C); 127.69; 127.51 (2 C); 127.24; 119.51; 115.77; 83.20; 80.79; 76.85; 74.17; 73.85; 73.05; 72.94; 72.75; 70.58; 56.74; 54.22; 44.23; 39.27; 38.70; 37.51; 36.99; 26.36 (3 C); 26.17 (3 C); 24.85; 20.35; 20.13; 18.56; 18.40; 18.13; 11.79; –2.90; –3.04; –3.48; –3.93. **HRMS** (ESI): 912.6190 (44, $[M + NH_4]^+$, $C_{52}H_{90}NO_8Si_2$, calcd. 912.6199).



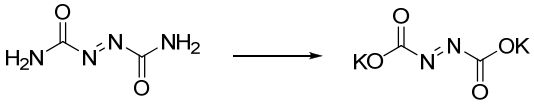

**(3*S*,4*R*,8*S*,10*S*,12*R*,14*S*,*E*)-3-(Benzyloxy)-14-((*R*,*Z*)-4-(benzyloxymethyl)hex-2-en-2-yl)-8,10-bis(*tert*-butyldimethylsilyloxy)-4,12-dimethoxy-9,9-dimethyl-1-oxacyclotetradec-5-en-2-one (24).** To a solution of triene **Y** (78 mg, 0.0871 mmol, 1.00 equiv) in 100 ml 1,2-dichloroethane (*ca*. 0.9 mM) was added a solution of Grubbs second generation catalyst (Aldrich, 3.54 mg, 0.00417 mmol, 0.0479 equiv) in 1 ml 1,2-dichloroethane. The solution was stirred for 30 min at 80 °C; additional catalyst was added (6.88 mg, 0.00810 mmol, 0.0930 equiv) in 1 ml 1,2-dichloroethane and stirring at 80 °C was continued for an additional hour. The reddish solution was then cooled to room temperature and 50 ml sat. aq. $NaHCO_3$ were added. The organic layer was separated and the aq. solution was extracted with $CH_2Cl_2$ (2 × 15 ml). The combined organic extracts were dried over $Na_2SO_4$ and concentrated under reduced pressure. The residue (dark colored oil) was purified by FC ($SiO_2$, AcOEt/hexane 1:20 → 1:10; d = 2.4 cm; h = 16 cm) to afford macrolactone **24** as an oil (56 mg, 65%).

**$R_f$** (AcOEt/hexane 1:5) 0.55; $R_f$ (AcOEt/hexane 1:1) 0.87. **$[\alpha]_D^{22}$:** –44.8° (c 1.10, $CHCl_3$). **IR** (film): 2955m, 2928m, 2886w, 2856m, 1732m, 1471w, 1456w, 1361w, 1253m, 1078s, 1060s, 1005m, 976m, 937m, 834s, 772s, 752s, 697m, 667w. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.35–7.22 (m, 10 H); 6.01–5.92 (m, 2 H); 5.41 (dd, J = 15.4, 8.6, 1 H); 5.16 (dd, J = 10.6, 0.9, 1 H); 4.62 (d, J = 11.4, 1 H); 4.51 (d, J = 12.2, 1 H); 4.48 (d, J = 12.2, 1 H); 4.39 (d, J = 11.3, 1 H); 4.15 (d, J = 5.2, 1 H); 3.80 (dd, J = 8.4, 5.2, 1 H); 3.71 (dd, J = 8.4, 2.3, 1 H); 3.59–3.55 (m, 2 H); 3.51 (t, J = 4.0, 1 H); 3.40–3.32 (m, 1 H); 3.36 (s, 3 H); 3.33 (s, 3 H); 2.88–2.80 (m, 1 H); 2.40 (ddd, J = 14.2, 9.5, 3.2, 1 H); 2.13–1.99 (m, 3 H); 1.92 (ddd, J = 14.9, 7.5, 2.0, 1 H); 1.75–1.65 (m, 1 H); 1.68 (d, J = 1.0, 3 H); 1.36–1.23 (m, 2 H); 0.92 (s, 9 H); 0.89 (s, 3 H); 0.872 (s, 9 H); 0.865 (s, 3 H); 0.84 (t, J = 7.4, 3 H); 0.14 (s, 3 H); 0.13 (s, 3 H); –0.05 (s, 3 H); –0.11 (s, 3 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 169.43; 139.07; 137.63; 135.96 (br, well observable in HSQC); 133.68; 130.80; 128.32 (2 C); 128.20 (2 C); 127.82 (2 C); 127.80; 127.51 (2 C); 127.23; 126.01; 83.22; 80.43; 77.68; 76.44; 74.51; 73.08; 72.84; 72.54; 69.57; 56.78; 56.51; 44.17; 40.03; 39.44; 37.17; 35.08; 26.46 (3 C); 25.99 (3 C); 24.95; 22.1 (very br, but sharp signal in HSQC); 20.30; 18.76; 18.44; 18.19; 11.77; –3.31; –3.55; –3.81; –4.43. **HRMS** (ESI): 884.5894 (100, $[M + NH_4]^+$, $C_{50}H_{86}NO_8Si_2$, calcd. 884.5886).



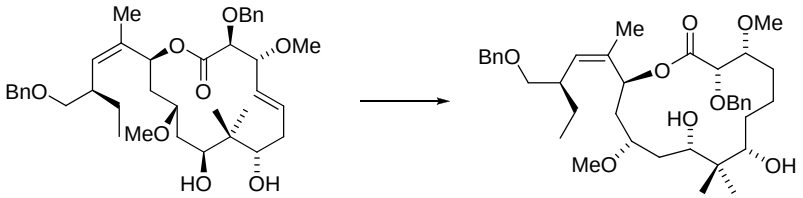

**(3*S*,4*R*,8*S*,10*S*,12*S*,14*S*,*E*)-3-(Benzyloxy)-14-((*R*,*Z*)-4-(benzyloxymethyl)hex-2-en-2-yl)-8,10-dihydroxy-4,12-dimethoxy-9,9-dimethyl-1-oxacyclotetradec-5-en-2-one (Z).** To a solution of fully protected macrolactone **24** (55 mg, 0.0634 mmol, 1.00 equiv) in 3 ml THF (in a 15 ml plastic tube) was added dropwise HF•pyridine (Aldrich 70% HF, 0.35 ml, ca. 12 mmol) at 0 °C and the mixture was stirred at room temperature for 7 h (additional 0.20 ml HF•pyridine were added after 1 h and again after 2¼ h, bringing the total to 0.75 ml, ca. 26 mmol). The reaction was quenched by ml-wise addition of the reaction mixture to a stirred solution of 50 ml sat. aq. $NaHCO_3$ and 10 ml $Et_2O$. The organic phase was separated and the aq. solution was extracted with $Et_2O$ (3 × 5 ml). The combined organic extracts were washed with sat. aq. $CuSO_4$ (2 x 10 ml). The combined aq. $CuSO_4$ extracts were re-extracted with $Et_2O$ (2 × 5 ml) and the combined organic extracts were dried over $Na_2SO_4$ and concentrated under reduced pressure. The residue was purified by FC ($SiO_2$, AcOEt/hexane 1:1; d = 1.4 cm; h = 13.0 cm) to afford the partially protected macrolactone **Z** as an oil (32 mg, 79%).

**$R_f$** (AcOEt/hexane 1:1) 0.26. **$[\alpha]_D^{22}$:** –69.2° (c 1.25, $CHCl_3$). **IR** (film): 3450w (br, 3650–3250), 2960w, 2929m, 2872w, 1730m, 1455m, 1362w, 1256m, 1193m, 1092s, 1029m, 976m, 914m, 749s, 698s, 666w. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 7.35–7.23 (m, 10 H); 6.02–5.95 (m, 2 H); 5.39 (dd, J = 15.5, 8.8, 1 H); 5.16 (d, J = 9.8, 1 H); 4.63 (d, J = 11.5, 1 H); 4.52 (d, J = 12.1, 1 H); 4.48 (d, J = 12.1, 1 H); 4.45 (d, J = 11.5, 1 H); 4.16 (d, J = 5.6, 1 H); 3.91 (br d, J = 7.4, 1 H); 3.86 (dd, J = 8.6, 5.6, 1 H); 3.68–3.62 (m, 1 H); 3.54 (dd, J = 9.2, 4.5, 1 H); 3.46 (br q, J = 5.0, 1 H); 3.36–3.31 (m, 1 H); 3.35 (s, 3 H); 3.34 (s, 3 H); 2.88 (br s, 1 H); 2.78–2.69 (m, 1 H); 2.49 (br s, 1 H); 2.42–2.39 (m, 2 H); 2.26 (ddd, J = 14.8, 10.2, 2.3, 1 H); 1.86–1.65 (m, 4 H); 1.70 (d, J = 1.3, 3 H); 1.29–1.18 (m, 1 H); 0.95 (s, 3 H); 0.90 (s, 3 H); 0.84 (t, J = 7.5, 3 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 169.51; 138.89; 137.38; 135.43; 133.35; 131.20; 128.35 (2 C); 128.24 (2 C); 127.87; 127.64 (3 C); 127.56 (2 C); 127.32; 83.05; 81.28; 78.04; 76.33; 73.50; 73.16; 72.89; 72.70; 70.69; 56.80; 56.72; 42.07; 39.66; 37.17; 35.90; 34.71; 25.03; 21.3 (very br, but sharp signal in HSQC); 20.7 (very br, but sharp signal in HSQC); 18.95; 11.94. **HRMS** (ESI): 656.4142 (31, $[M + NH_4]^+$, $C_{38}H_{58}NO_8$, calcd. 656.4157).



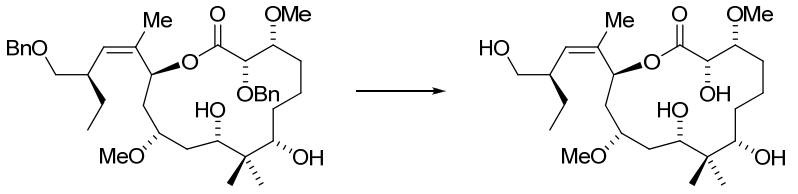

**Dipotassium azo-1,2-dicarboxylate (AA).**[27] To a cooled (0 °C) 40% aq. KOH solution (6.6 ml) was added azodicarbonamide (1.07 g, 9.22 mmol, 1.00 equiv) in small portions over a period of 2 h. The temperature was always kept below 8 °C during each addition. After stirring for an additional hour, the bright yellow solid product was filtered off using a Büchner funnel, and the solid was washed 10 times with 2 ml of precooled (0 °C) MeOH (more of the desired product precipitated from the filtrate and was isolated by re-filtration). Drying in HV gave 1.71 g (95%) of the title compound **AA** as a yellow solid.

[27] Groves, J. T.; Ma, K. W. J. *Am. Chem. Soc.* **1977**, *99*, 4076–4082.




**(3*S*,4*R*,8*S*,10*S*,12*S*,14*S*)-3-(benzyloxy)-14-((*R*,*Z*)-4-(benzyloxymethyl)hex-2-en-2-yl)-8,10-dihydroxy-4,12-dimethoxy-9,9-dimethyl-1-oxacyclotetradecan-2-one (AB).** To a solution of diene **Z** (30 mg, 0.047 mmol, 1.0 equiv) and dipotassium azo-1,2-dicarboxylate **AA**[28] (346 mg, 1.78 mmol, 37.9 equiv) in 3.5 ml $CH_2Cl_2$ was added a solution of acetic acid (Fluka puriss. p.a. 99.8%, 0.020 ml, 0.35 mmol, 7.4 equiv) in 0.10 ml $CH_2Cl_2$ dropwise at reflux. The reaction mixture was stirred at reflux temperature for a total of 17 h, with small amounts of acetic acid (0.010 ml) in 0.05 ml $CH_2Cl_2$ being added after about every hour; additional **AA** was added after 11 h (161 mg) and 13½ h (225 mg). In total 732 mg (3.8 mmol, 80 equiv) **AA** and 0.17 ml (3.0 mmol, 63 eq.) acetic acid were added. The grey suspension was cooled to room temperature and filtered through a plug of silica gel (d = 1.4 cm; h = 7 cm), which was eluted with AcOEt (ca. 25 ml). The eluent was concentrated under reduced pressure and the residue purified by FC ($SiO_2$, AcOEt/hexane 1:2 → 1:1 → 2:1; d = 1.4 cm; h = 14 cm) to afford macrolactone **AB** as an oil (27 mg, 90%).

**$R_f$** (AcOEt/hexane 2:1) 0.45. **$[\alpha]_D^{22}$:** –70.7° (c 1.25, $CHCl_3$). **IR** (film): 3470w (br 3700–3200), 2956m, 2932m, 2872m, 1730m, 1455m, 1378w, 1362m, 1260m, 1092s, 1028m, 953m, 928m, 738m, 698m. **$^1$H-NMR** (400 MHz, $CDCl_3$):[29] δ 7.36–7.23 (m, 10 H); 5.66 (d, J = 11.2, 1 H); 5.17 (dd, J = 10.4, 1.0, 1 H); 4.60 (d, J = 11.7, 1 H); 4.55 (d, J = 12.1, 1 H); 4.51 (d, J = 12.1, 1 H); 4.45 (d, J = 11.7, 1 H); 3.87–3.83 (m, 1 H); 3.81 (d, J = 8.6, 1 H); 3.78–3.69 (m, 2 H); 3.63 (s, 3 H); 3.61–3.56 (m, 2 H); 3.51 (br d, J = 10.6, 1 H); 3.41 (s, 3 H); 3.36 (dd, J = 9.0, 7.1, 1 H); 2.81–2.73 (m, 1 H); 2.36 (ddd, J = 13.7, 12.7, 1.3, 1 H); 1.87–1.73 (m, 4 H); 1.71 (d, J = 1.2, 3 H); 1.61–1.50 (m, 4 H); 1.35–1.18 (m, 3 H); 1.04 (s, 3 H); 0.84 (t, J = 7.4, 3 H); 0.76 (s, 3 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 170.65; 138.86; 137.62; 133.27; 131.05; 128.37 (2 C); 128.26 (2 C); 127.73; 127.54 (2 C); 127.51 (2 C); 127.37; 85.46; 82.24; 78.20; 76.22; 73.21; 72.94; 72.83; 72.75; 70.38; 60.83; 56.20; 40.84; 39.86; 35.92; 33.95; 32.24; 31.18; 25.03; 22.10; 18.73; 18.20; 18.03; 12.09. **HRMS** (ESI): 663.3893 (100, $[M + Na]^+$, $C_{38}H_{56}NaO_8$, calcd. 663.3867).




**(3*S*,4*R*,8*S*,10*S*,12*S*,14*S*)-3,8,10-trihydroxy-14-((*R*,*Z*)-4-(hydroxymethyl)hex-2-en-2-yl)-4,12-dimethoxy-9,9-dimethyl-1-oxacyclotetradecan-2-one (4).** To 43 mg Pd/C (Acros 10%) was added a solution of **AB** (25.0 mg, 0.0390 mmol, 1.00 equiv) in 7 ml AcOEt and hydrogen gas was bubbled through the reaction mixture with stirring at atmospheric pressure and room temperature for 1¼ h. The reaction mixture was then filtered through Celite, the catalyst was washed with AcOEt and the combined filtrates were evaporated. Purification of the

[28] Biswas, K.; Lin, H.; Njardarson, J. T.; Chappell, M. D.; Chou, T.-C.; Guan, Y.; Tong, W. P.; He, L.; Horwitz, S. B.; Danishefsky, S. J. *J. Am. Chem. Soc*. **2002**, *124*, 9825–9832.

[29] Only 55 H-atoms (integral) out of the expected total of 56 could be clearly observed in the spectrum of **AB**. The missing proton is assumed to be an O-*H*, since all C–H correlations in the HSQC spectrum match with the $^1$H integrals in the corresponding parts of the $^1$H-spectrum.

residue by FC ($SiO_2$, AcOEt/MeOH 95:5 → 9:1; d = 1.4 cm; h = 16.5 cm) afforded the final target product **4** as a colorless oil (13.1 mg, 73%).

**$R_f$** (AcOEt/hexane 1:0) 0.12; $R_f$ (AcOEt/MeOH 9:1) 0.39. **$[\alpha]_D^{22}$:** –49.1° (c 0.466, $CHCl_3$). **IR** (film): 3420m (br 3600–3100), 2929s, 2874m, 1732m, 1718m, 1457m, 1385m, 1262m, 1222m, 1092s, 1053m, 998m, 966m, 924m, 756s. **$^1$H-NMR** (400 MHz, $CDCl_3$): δ 5.61 (dd, J = 11.1, 1.7, 1 H); 5.06 (d, J = 10.3, 1 H); 4.03 (dd, J = 6.6, 4.8, 1 H); 3.84–3.77 (m, 2 H); 3.72 (ddd, J = 8.4, 6.7, 4.1, 1 H); 3.66–3.60 (m, 2 H); 3.59–3.56 (m, 1 H); 3.54 (s, 3 H); 3.50 (br d, J = 11.0, 1 H); 3.41 (s, 3 H); 3.34 (td, J = 9.7, 3.0, 1 H); 2.89 (d, J = 4.8, 1 H); 2.73–2.69 (m, 1 H); 2.59–2.50 (m, 1 H); 2.31 (ddd, J = 14.3, 11.6, 1.6, 1 H); 1.87–1.83 (m, 2 H); 1.83–1.76 (m, 2 H); 1.75 (d, J = 1.3, 3 H); 1.68–1.53 (m, 3 H); 1.49–1.39 (m, 2 H); 1.35–1.29 (m, 1 H); 1.20–1.11 (m, 1 H); 1.06 (s, 3 H); 0.86 (t, J = 7.4, 3 H); 0.81 (s, 3 H). **$^{13}$C-NMR** (100 MHz, $CDCl_3$): δ 172.23; 135.65; 131.51; 81.70; 77.23; 76.01; 74.80; 72.66; 72.47; 66.90; 58.64; 56.46; 43.32; 41.07; 35.67; 33.96; 30.80; 29.10; 24.57; 21.86; 19.09; 18.86; 17.95; 12.28. **HRMS** (ESI): 483.2924 (82, $[M + Na]^+$, $C_{24}H_{44}NaO_8$, calcd. 483.2928).