Supporting Information for the Experimental Section

Part 1

Enantioselective Synthesis of the C8-C20 Segment of Curvicollide C

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1. General Experimental Methods

Unless otherwise stated, commercially available reagents were used as purchased without further purification. Solvents were dried by passage through activated alumina columns of a MBRAUN SPS-800 system: tetrahydrofuran (THF), dichloromethane (CH_2Cl_2), and diethylether (Et_2O). Diisopropylamine and pyridine were distilled from CaH_2 and stored over 3 Å molecular sieves. Methanol was distilled from magnesium and stored over activated 3 Å molecular sieves. Dimethylformamide (Fluka, >99.8%, stored over activated 3 Å molecular sieves) and ethanol (Merck, >99.8%) were used as purchased.

n-BuLi (2.5 M in hexanes), K-Selectride (1 M in THF), KHMDS (0.5 M in toluene), MeLi (1.6 M in Et_2O), Hexanoylchloride, and MeMgBr (1 M in THF) were purchased from Acros. Trifluoroethanol (>99%), DIBAH (1 M in CH_2Cl_2), and hydrogen fluoride·pyridine were purchased from Sigma-Aldrich.

Dess-Martin periodinane[1], Chloromethyl triphenylphosphonium chloride[2], copper (I) bromide dimethylsulfide complex[3], (*R*)-4-phenyloxazolidin-2-one[4], and (*S*)-4-isopropyl-oxazolidin-2-one[4] were prepared according to literature.

The concentrations of *n*-BuLi and MeLi were determined employing 4-biphenylmethanol as indicator.[5] All moisture-sensitive reactions were performed in flame-dried septum-sealed glassware under an atmosphere of argon. Reagents were transferred by means of syringe or cannula. Glass pressure tubes with a screw-cap were purchased from Sigma-Aldrich (Ace pressure tube, 35 ml, PTFE bushing, FETFE O-ring, type A). Analytical TLC was performed using pre-coated silica gel foils 60 F_{254} (Merck, 4 cm hight). Visualization was achieved using 365 nm ultraviolet irradiation followed by staining with an anisaldehyde reagent (*p*-anisaldehyde 2.53 vol%, acetic acid 0.096

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[1] (a) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, 48, 4156-4158. (b) Dess, D. B.; Martin, J. C. *J. Am. Chem. Soc.* **1991**, 113, 7277-7287.

[2] Lawrence, N. J.; Liddle, J.; Jackson, D. *J. Chem. Soc., Perkin Trans. 1* **2002**, 2260-2267.

[3] House, H. O.; Chu, C.; Wilkins, J. M.; Umen, M. J. *J. Org. Chem.* **1975**, 40, 1460-1469.

[4] Evans, D. A.; Bartroli, J.; Shih, T. L. *J. Am. Chem. Soc.* **1981**, 103, 2127-2129.

[5] Juaristi, E.; Martinez-Richa, A.; Garcia-Rivera, A.; Cruz-Sanchez, J. S. *J. Org. Chem.* **1983**, *48*, 2603-2606.

vol%, ethanol 93.06 vol%, concd H_2SO_4 0.034 vol%). Flash chromatography was performed using silica gel Merck (particle size 0.032-0.063 mm) supplied by Merck and mixtures of hexanes and ethyl acetate as eluent.

Preparative HPLC was conducted fully automized on a Knauer HPLC (*Smartline* series) with UV detector 2600 (254 nm), peak recognition software (ChromGate® 3.1.6), pump 1800, and autosampler 3900 using Nucleosil 50-7 (32 mm × 250 mm). Analytical HPLC was conducted on a Knauer HPLC (*Smartline* series) with UV detector 2600 (254 nm) using Chiralpak IA (0.46 cm × 25 cm). Ozonolysis was performed on an Ozonizer 301.19 (Erwin Sander instruments).

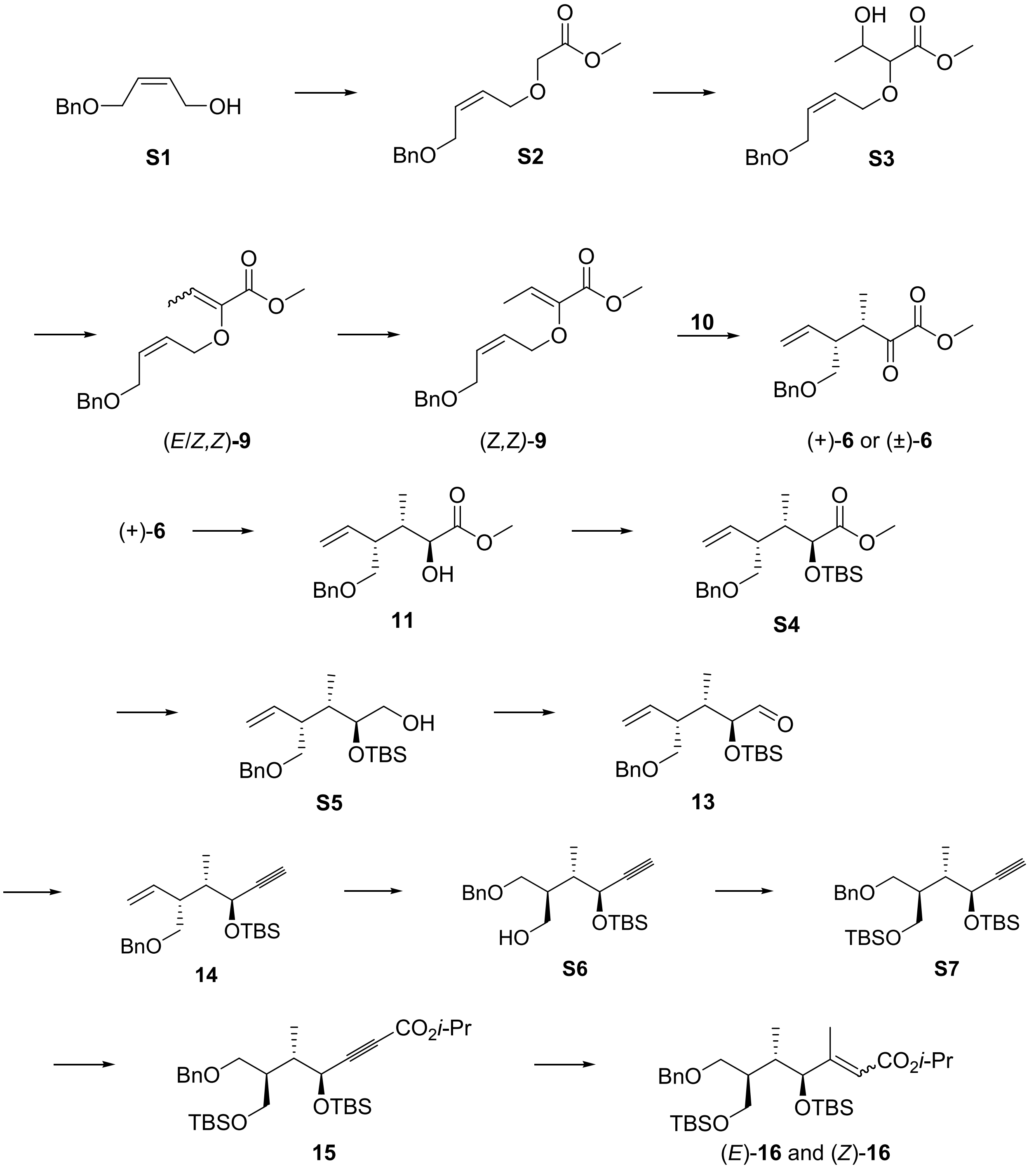
^1H NMR spectra were recorded on different spectrometers at 300 MHz, 400 MHz, 500 MHz, or 600 MHz. Chemical shifts are reported in ppm relative to tetramethylsilane (δ 0 ppm). Signal splitting pattern are labeled by the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, br s = broad singlet, sept = septet, m = multiplet or overlap of non equivalent resonances. ^{13}C NMR spectra were recorded on different spectrometers at 76 MHz, 101 MHz, or 126 MHz. Chemical shifts are reported in ppm relative to $CDCl_3$ (δ 77.0 ppm). The assignment of CH_2 is based on APT (attached proton test) or DEPT experiments. The terms $^{\text{"major"}}$ and $^{\text{"minor"}}$ are used to distinguish between NMR resonances of diastereomers.

Infrared spectra were recorded as a thin film on a KBr disk ("in substance") on a Nicolet Avatar™ E.S.P.™ spectrometer. High resolution mass spectra were recorded on a LTQ-Orbitrap spectrometer by electrospray ionization (ESI) or electron impact (EI).

Molecular formula assignment was confirmed by combustion elemental analysis using an Elemental Analyzer CHNS-932 (Leco instruments).

Melting points were measured with a Büchi B-540 capillary melting point apparatus.

2. Chart of all Synthesized Compounds in Order of their Appearance



S1

S2

S3

(*E*/*Z*,*Z*)-**9**

(Z,*Z*)-**9**

(+)-**6** or (±)-**6**

11

S4

S5

13

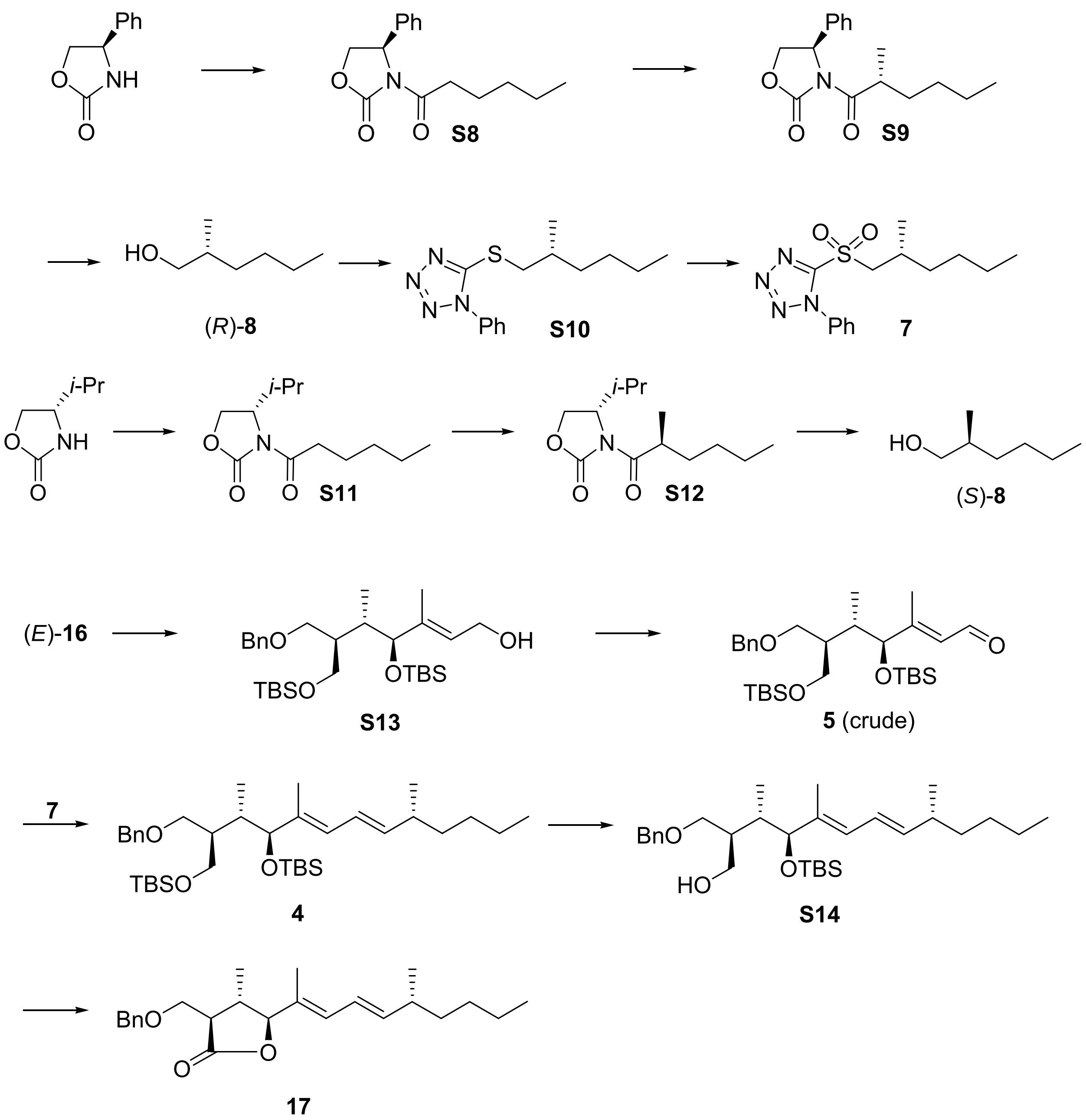
14

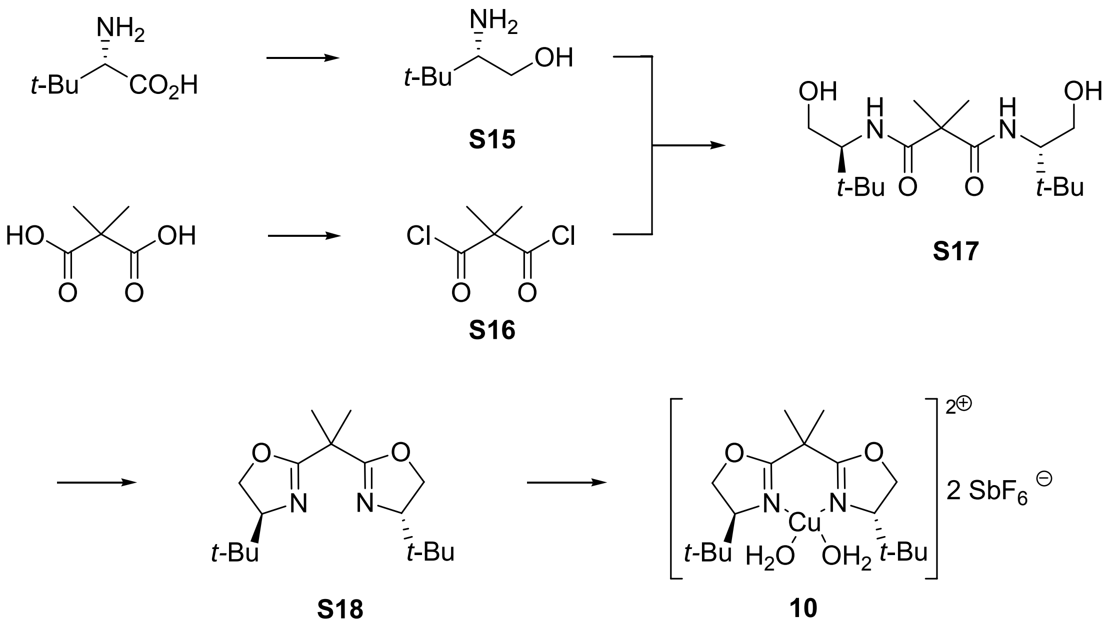
S6

S7

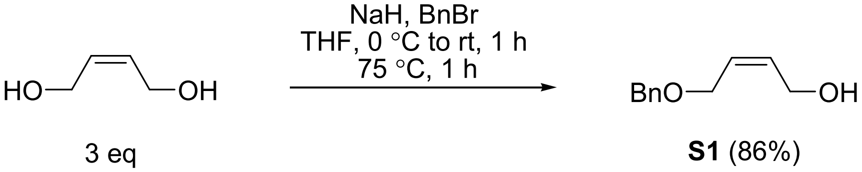
15

(*E*)-**16** and (*Z*)-**16**


Ph
NH
O
S8
S9
HO
(R)-8
S10
7
N
S
Ph
i-Pr
S11
S12
(S)-8
(E)-16
BnO
TBSO
OTBS
OH
S13
5 (crude)
7
4
S14
17

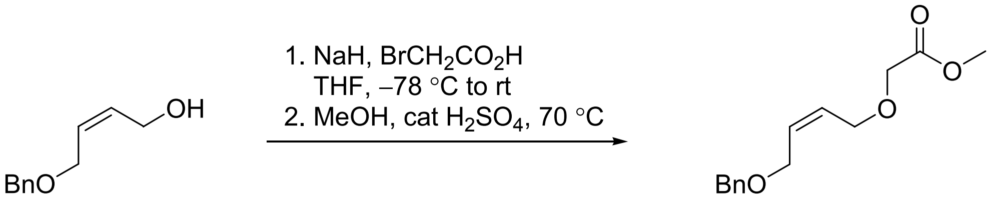

S15
S16
S17
S18
10
NH2
t-Bu
CO2H
OH
HO
Cl
O
N
H
Cu
H2O
OH2
2⊕
2 SbF6 ⊖

3. Experimental Procedures and Analytical Data for Compounds S1-S18, 4-9, 11, 13-17



S1 (86%)

Benzyl Ether S1:[6] To a stirred solution of *cis*-butene-1,4-diol (50 g, 568 mmol, 3 eq) in THF (200 mL, 0.4 mL/mmol diol) was carefully added sodium hydride (7.8 g, 200 mmol, 1.05 eq) at 0 °C. After being stirred for 1 h at room temperature, benzyl bromide (23 mL, 190 mmol, 1 eq) was added, and the resulting mixture was stirred at 75 °C for 1 h. The reaction was then quenched at room temperature by the addition of sat. aqueous NH_4Cl solution and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Flash chromatography (*i*-hexane/ethyl acetate 10/1 to 5/1 to 1/1) afforded the protected diol **S1** (29.2 g, 163 mmol, 86%) as pale yellow oil: R_f 0.44 (*i*-hexane/ethyl acetate 1/1); ^{1}H NMR (300 MHz, $CDCl_3$, δ) 4.18 (d, J = 4.2 Hz, 2H), 4.23 (d, J = 5.9 Hz, 2H), 4.53 (s, 2H), 5.74-5.89 (m, 2H), 7.29-7.35 (m, 5H); ^{13}C NMR (76 MHz, $CDCl_3$, δ) 58.6 (CH_2), 65.6 (CH_2), 72.5 (CH_2), 127.8 (CH=), 127.9 (CH=), 128.1 (2 × CH=), 128.5 (2 × CH=), 132.4 (CH=), 137.9 (C=).



S1

S2 (95%)

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[6] Gao, Y.; Klunder, J. M.; Hanson, R. M.; Masamune, H.; Ko, S. Y.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765-5780.

Ester S2:[7] To a stirred solution of bromoacetic acid (25 g, 180 mmol, 1.1 eq) in THF (300 mL, 1.8 mL/mmol **S1**) at –78 °C was added sodium hydride (19.6 g, 489 mmol, 3 eq). After being stirred for 0.5 h at –78 °C, (*Z*)-4-benzyloxy-but-2-en-1-ol (**S1**) (29.2 g, 163 mmol, 1 eq) in THF (80 mL, 0.5 mL/mmol **S1**) was added, and the resulting mixture was allowed to warm to room temperature over night. The reaction was then quenched by the addition of aqueous 1 M KOH (200 mL). The aqueous phase was acidified by the addition of concd HCl (pH < 4) and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was used for the next step without purification.

^{1}H NMR (300 MHz, $CDCl_3$, δ) 4.07-4.09 (m, 4H), 4.17 (d, *J* = 6.3 Hz, 2H), 4.52 (s, 2H), 5.70-5.90 (m, 2H), 7.24-7.41 (m, 5H); ^{13}C NMR (76 MHz, $CDCl_3$, δ) 65.5 (CH_2), 66.8 (CH_2), 67.1 (CH_2), 72.4 (CH_2), 127.8 (3 × CH=), 128.0 (CH=), 128.4 (2 × CH=), 130.8 (CH=), 137.8 (C=), 173.3 (C=O).

The crude acid (163 mmol, 1 eq) was dissolved in MeOH (100 mL, 0.6 mL/mmol **S1**) and cooled to 0 °C. Concd Sulfuric Acid (3 mL, 56 mmol, 0.3 eq) was added, and the resulting solution was stirred at 70 °C for 3 h. The reaction was then quenched by the addition of H_2O (50 mL) and brine (50 mL) at room temperature. The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. Flash chromatography (*i*-hexane/ethyl acetate 10/1 to 5/1) afforded the ester **S2** (39 g, 155 mmol, 95%) as colorless oil: R_f 0.66 (*i*-hexane/ethyl acetate 3/1); ^{1}H NMR (300 MHz, $CDCl_3$, δ) 3.74 (s, 3H), 4.05 (s, 2H), 4.06 (d, *J* = 5.9 Hz, 2H), 4.14 (d, *J* = 5.9 Hz, 2H), 4.50 (s, 2H), 5.77-5.85 (m, 2H), 7.28-7.37 (m, 5H); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ) 51.8 (CH_3), 65.6 (CH_2), 66.9 (CH_2), 67.2 (CH_2), 72.3 (CH_2), 127.7 (CH=), 127.8 (2 × CH=), 128.4 (2 × CH=), 130.4 (2 × CH=), 138.0 (C=), 170.7 (C=O); IR (in substance): ν 3090-3030, 2950-2850, 1760 cm^{-1}; Anal. Calcd. for $C_{14}H_{18}O_4$: C, 67.2; H, 7.3. Found: C, 67.2; H, 7.3.

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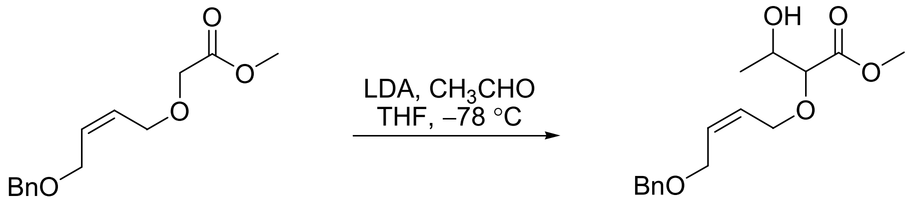
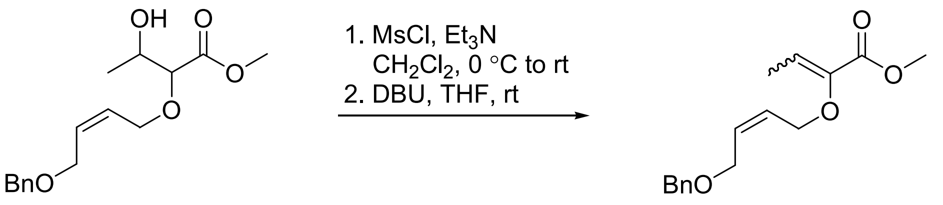
[7] Körner, M.; Hiersemann, M. *Synlett* **2006**, 1, 121-123.



S2 **S3** (87%, dr = 69/31)

β-Hydoxy Ester S3:[**7**] A chilled (−78 °C) solution of **S2** (10 g, 40.0 mmol, 1 eq) in THF (40 mL, 1 mL/mmol **S2**) was added via syringe to a solution of LDA [prepared *in situ* from diisopropylamine (7.3 mL, 52 mmol, 1.3 eq) and *n*-BuLi (2.3 M in *n*-hexanes, 21 mL, 48 mmol, 1.2 eq) in THF (80 mL, 2 mL/mmol **S2**) at −78 °C]. The bright yellow solution was stirred for 15 min at −78 °C. Freshly distilled and chilled (−78 °C) acetaldehyde (4.5 mL, 80 mmol, 2.0 eq) was then added to the reaction mixture at −78 °C. After being stirred for 1 h, sat. aqueous NH_4Cl solution (100 mL) and H_2O (100 mL) were added at −78 °C, and the mixture was warmed to room temperature. The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were dried over $MgSO_4$, and the solvents were removed under reduced pressure. Purification by flash chromatography (*i*-hexane/ethyl acetate 5/1 to 2/1 to 1/1) provided the β-hydroxy ester **S3** (10.2 g, 34.8 mmol, 87%, dr = 69/31 relative configuration not assigned) as a brown oil: R_f 0.23 (*i*-hexane/ethyl acetate 3/1); ^{1}H NMR (300 MHz, $CDCl_3$, δ, mixture of diastereomers) 1.19 (d, J = 6.5 Hz, $3H^{major}$), 1.21 (d, J = 7.4 Hz, $3H^{minor}$), 1.90 (br. s, 1H), 3.71 (d, J = 5.3 Hz, $1H^{minor}$), 3.74 (s, 3H), 3.89 (d, J = 4.4 Hz, $1H^{major}$), 3.97-4.10 (m, 4H), 4.26-4.29 (m, 1H), 4.50 (s, 2H), 5.70-6.86 (m, 2H), 7.27-7.37 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$, δ, mixture of diastereomers) 18.2 (CH_3^{major}), 18.8 (CH_3^{minor}), 51.8 (CH_3^{major}), 51.9 (CH_3^{minor}), 65.4 (CH_2^{minor}), 65.5 (CH_2^{major}), 66.3 (CH_2^{minor}), 66.4 (CH_2^{major}), 68.1 (CH^{major}), 68.2 (CH^{minor}), 72.2 (CH_2^{major}), 72.2 (CH_2^{minor}), 81.9 (CH^{major}), 82.3 (CH^{minor}), 127.6 (CH=), 127.7 (CH=), 128.2 (CH=), 128.3 (CH=), 128.4 (CH=), 130.2 (CH=), 130.4 (CH=), 137.8 ($C=^{major}$), 137.9 ($C=^{minor}$), 171.1 ($C=O^{major}$), 171.3 ($C=O^{minor}$); IR (in substance): ν 3700-3200, 2870-3200, 1740 cm^{-1}; Anal. Calcd. for $C_{16}H_{22}O_5$: C, 65.3; H, 7.5. Found: C, 65.4; H, 7.7.



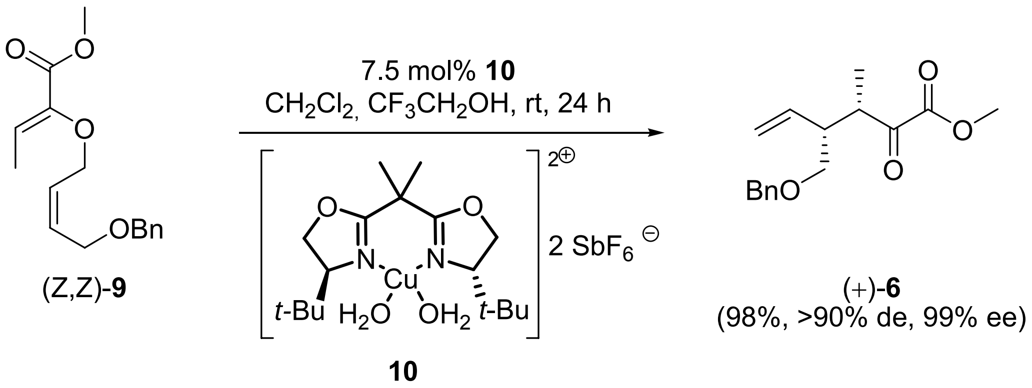
S3

9

(83%, (*E*,*Z*)/(*Z*,*Z*) = 38/62)

Allyl Vinyl Ether 9:[7] To a solution of the diastereomeric β-hydroxy ester **S3** (30 g, 100 mmol, 1 eq) in CH_2Cl_2 (300 mL, 3 mL/mmol **S3**) at 0 °C was added Et_3N (18 mL, 130 mmol, 1.3 eq) and methanesulfonyl chloride (MsCl, 9.3 mL, 120 mmol, 1.2 eq). The reaction mixture was stirred for 1 h at room temperature and then quenched by the addition of sat. aqueous $NaHCO_3$ solution. The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and dried *in vacuu* to afford the crude mesylate, which was dissolved in THF (300 mL, 3 mL/mmol **S3**) and cooled to 0 °C. DBU (45 mL, 300 mmol, 3.0 eq) was added at 0 °C, and the reaction mixture was stirred at room temperature over night (~14 h). The reaction was then quenched by the addition of H_2O (200 mL). The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 200 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (*i*-hexane/ethyl acetate 50/1) provided the allyl vinyl ether **9** (23 g, 83 mmol, 83%) as a mixture of double bond isomers [(*E*,*Z*)/(*Z*,*Z*) = 38/62] as a clear oil: R_f 0.50 (*i*-hexane/ethyl acetate 3/1). The double bond isomers were separated by preparative HPLC, column: 32 × 250 mm, Nucleosil 50-5, 5 μm, solvent: (heptane/ethyl acetate 7/1, flow: 25 mL/min, r_t (*Z*,*Z*)-**9** ~ 11 min, r_t (*E*,*Z*)-**9** ~ 13 min).

(*Z*,*Z*)-**9**: ^1H NMR (300 MHz, $CDCl_3$, δ) 1.76 (d, *J* = 7.1 Hz, 3H), 3.73 (s, 3H), 4.09 (d, *J* = 5.0 Hz, 2H), 4.41 (d, *J* = 5.3 Hz, 2H), 4.50 (s, 2H), 5.76-5.88 (m, 2H), 6.36 (q, *J* = 7.1 Hz, 1H), 7.27-7.34 (m, 5H); ^{13}C NMR (76 MHz, $CDCl_3$, δ) 11.4 (CH_3), 51.7 (CH_3), 65.5 (CH_2), 67.4 (CH_2), 72.2 (CH_2), 124.8 (CH=), 127.6 (2 × CH=), 128.2 (2 × CH=), 128.3 (2 × CH=), 130.2 (CH=), 138.0 (C=), 145.1 (C=), 164.1 (C=O); IR (in substance): ν 3040-3030, 2950-2860, 1725 cm^{-1}; Anal. Calcd. for $C_{16}H_{20}O_4$: C, 69.5; H, 7.3. Found: C, 69.7; H, 7.4.



(Z,Z)-**9**

10

(+)-**6**
(98%, >90% de, 99% ee)

α-Keto Ester (+)-6: To a blue solution of [Cu{(*S*,*S*)-*tert*-Bu-box}]$(H_2O)_2(SbF_6)_2$ **10**[8] (1.06 g, 1.22 mmol, 7.5 mol%) in trifluoroethanol (16 mL, 1 mL/mmol **9**) was added (*Z*,*Z*)-**9** (4.5 g, 16.3 mmol, 1 eq) in CH_2Cl_2 (16 mL, 1 mL/mmol **9**) at room temperature. The solution was stirred at room temperature, until TLC control indicated complete consumption of the starting material (~12 h). The solvents were removed under reduced pressure. The crude product was dissolved in CH_2Cl_2 (5 mL) and the solution was loaded onto a silica gel column for flash chromatography. Purification by flash chromatography (*c*-hexane/ethyl acetate 50/1) provided the α-keto ester (+)-**6** (4.4 g, 15.9 mmol, 98%, >90% de, 99% ee) as a clear oil: R_f 0.59 (*i*-hexane/ethyl acetate 5/1); ^{1}H NMR (300 MHz, $CDCl_3$, δ) 1.08 (d, *J* = 7.0 Hz, 3H), 2.90-3.00 (m, 1H), 3.35-3.41 (m, 1H), 3.45-3.53 (m, 2H), 3.70 (s, 3H), 4.36 (d, *J* = 12.1 Hz, 1H), 4.40 (d, *J* = 12.1 Hz, 1H), 5.04-5.13 (m, 2H), 5.81 (ddd, *J* = 17.3, 10.5, 8.3 Hz, 1H), 7.26-7.34 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$, δ) 11.5 (CH_3), 42.9 (CH), 46.2 (CH), 52.4 (CH_3), 69.9 (CH_2), 72.9 (CH_2), 117.2 (CH_2=), 127.4 (2 × CH=), 127.5 (2 × CH=), 128.1 (CH=), 136.1 (CH=), 137.6 (C=), 161.7 (C=O), 195.4 (C=O); IR (in substance): ν 3070-3000, 2950-2860, 1720 cm^{-1}; Anal. Calcd. for $C_{16}H_{20}O_4$: C, 69.5; H, 7.3. Found: C, 69.6; H, 7.4; $[\alpha]^{25}_D$ +41.3 (*c* 0.60, $CHCl_3$).

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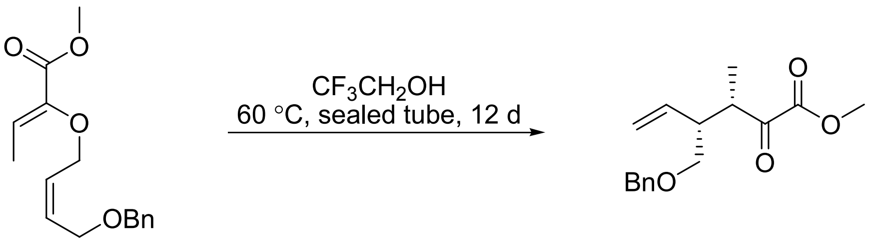
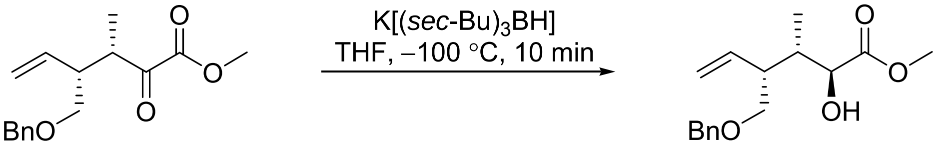
[8] Evans, D. A.; Miller, S. J.; Lectka, T.; Matt, P. v. *J .Am. Chem. Soc.* **1999**, 121, 7559-7573.



(Z,Z)-**9**

(±)-**6**
(91%, >90% de)

α-Keto Ester (±)-6: A solution of the allyl vinyl ether (*Z*,*Z*)-**9** (100 mg, 0.36 mmol) in trifluoroethanol (2 mL, 6 mL/mmol **9**) was heated in a sealed tube (bath temperature 60 °C). After 12 d, the solvent was evaporated, and the crude product was purified by flash chromatography (*i*-hexane/ethyl acetate 50/1) to afford the α-keto ester (±)-**6** (91 mg, 0.33 mmol, 91%, >90% de) as a clear oil: R_f 0.59 (*i*-hexane/ethyl acetate 5/1). Analytical data are identical to the data collected for (+)-**6**.

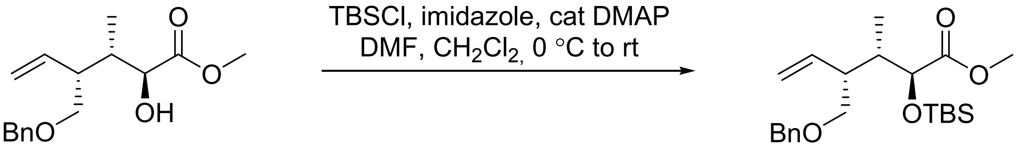


(+)-**6**

11
(94%, >90% de)

α-Hydroxy Ester 11: Four 50 mL septum-sealed round-bottom flasks were each charged with a solution of the α-keto ester (+)-**6** (1.0 g, 3.6 mmol, 1 eq) in THF (20 mL, 5 mL/mmol α-keto ester) under an atmosphere of argon. K-Selectride (1 M in THF, 4.3 mL, 4.3 mmol, 1.2 eq) was slowly added to the solutions at –100 °C. It was pivotal to maintain the low reaction temperature in order to ensure the high diastereoselectivity. After being stirred for 10 min, the reactions were quenched by the addition of sat. aqueous NH_4Cl solution (15 mL) and warmed to room temperature. All batches were then combined, the phases were separated and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (*c*-hexane/ethyl acetate 20/1) provided the α-hydroxy ester **11** (3.8 g, 13.6 mmol, 94%, >90% de) as a clear oil: R_f 0.37 (*i*-hexane/ethyl acetate 3/1); ^{1}H NMR (400 MHz, $CDCl_3$, δ) 0.95 (d, *J* = 7.3 Hz, 3H), 2.15-

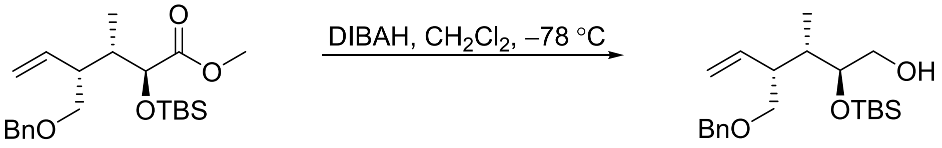
2.23 (m, 1H), 2.44-2.51 (m, 1H), 3.43 (dd, *J* = 9.4, 5.1 Hz, 1H), 3.48 (dd, *J* = 9.4, 7.1 Hz, 1H), 3.73 (s, 3H), 3.83 (d, *J* = 7.5 Hz, 1H), 4.15 (dd, *J* = 7.5, 4.5 Hz, 1H), 4.49 (d, *J* = 12.1 Hz, 1H), 4.54 (d, *J* = 12.1 Hz, 1H), 5.02-5.07 (m, 2H), 5.72 (ddd, *J* = 17.2, 10.4, 8.4 Hz, 1H), 7.26-7.35 (m, 5H); ^{13}C NMR (76 MHz, CDCl$_3$, δ) 12.6 (CH$_3$), 39.4 (CH), 44.4 (CH), 52.0 (CH$_3$), 70.4 (CH$_2$), 73.4 (CH$_2$), 74.3 (CH), 116.5 (CH$_2$=), 127.7 (CH=), 127.8 (CH=), 128.4 (3 × CH=), 137.7 (C=), 138.3 (CH=), 174.9 (C=O); IR (in substance): ν 3700-3050, 3000-2880, 1735 cm^{-1}; Anal. Calcd. for $C_{16}H_{22}O_4$: C, 69.0; H, 8.0. Found: C, 69.1; H, 7.9; $[\alpha]^{25}_{D}$: +47.8 (*c* 1.22, CHCl$_3$).



11

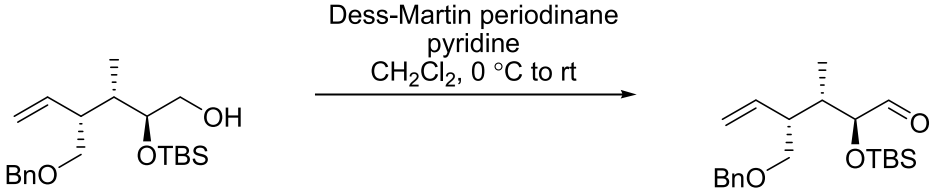
S4 (89%)

Silyl ether S4: To a solution of **11** (3.45 g, 12.4 mmol, 1 eq) in CH$_2$Cl$_2$ (3 mL, 0.25 mL/mmol **11**) and DMF (3 mL, 0.25 mL/mmol **11**) was added DMAP (0.15 g, 1.2 mmol, 0.1 eq), imidazole (2.53 g, 24.8 mmol, 3 eq), and TBSCl (3.74 g, 24.8 mmol, 2 eq) at 0 °C. The reaction mixture was stirred for 4 d at room temperature and then quenched by the addition of sat. aqueous NH$_4$Cl solution. The layers were separated and the aqueous phase was extracted with CH$_2$Cl$_2$ (3 × 10 mL). The combined organic layers were dried over MgSO$_4$ and concentrated under reduced pressure. Purification by flash chromatography (*c*-hexane/ethyl acetate 100/1 to 50/1) provided **S4** (4.39 g, 11.1 mmol, 89%) as a clear oil: R$_f$ 0.66 (*i*-hexane/ethyl acetate 3/1); ^{1}H NMR (500 MHz, CDCl$_3$, δ) 0.03 (s, 3H), 0.04 (s, 3H), 0.90-0.92 (m, 12H), 2.05-2.12 (m, 1H), 2.57-2.63 (m, 1H), 3.49 (dd, *J* = 9.2, 7.1 Hz, 1H), 3.56 (dd, *J* = 9.2, 4.7 Hz, 1H), 3.69 (s, 3H), 4.22 (d, *J* = 5.5 Hz, 1H), 4.47 (d, *J* = 12.2 Hz, 1H), 4.52 (d, *J* = 12.2 Hz, 1H), 5.11-5.14 (m, 2H), 5.83 (ddd, *J* = 17.2, 10.5, 8.5 Hz, 1H), 7.26-7.34 (m, 5H); ^{13}C NMR (126 MHz, CDCl$_3$, δ) –7.0 (CH$_3$), –6.7 (CH$_3$), 11.1 (CH$_3$), 16.5 (C), 24.1 (3 × CH$_3$), 38.4 (CH), 42.6 (CH), 49.6 (CH$_3$), 69.4 (CH$_2$), 71.4 (CH$_2$), 73.4 (CH), 114.6 (CH$_2$=), 125.7 (CH=), 125.9 (2 × CH=), 126.6 (2 × CH=), 136.9 (C=), 137.6 (CH=), 171.9 (C=); IR (in substance): ν 3070-2860, 1755 cm^{-1}; Anal. Calcd. for $C_{22}H_{36}O_4Si$: C, 67.3; H, 9.2. Found: C, 67.3; H, 9.5; $[\alpha]^{25}_{D}$: –3.5 (*c* 1.31, CHCl$_3$).



S4 **S5** (86%)

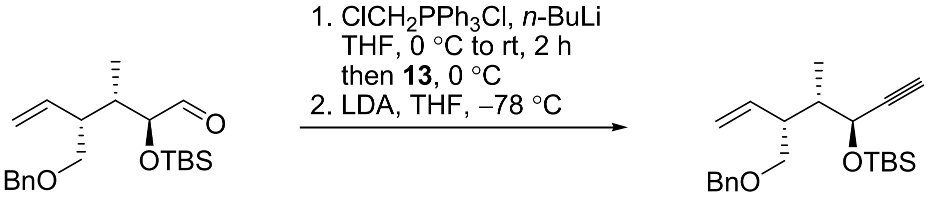
Alcohol S5: To a solution of **S4** (4.39 g, 11.1 mmol, 1 eq) in CH_2Cl_2 (44 mL, 4 mL/mmol **S4**) was added DIBAH (1 M in CH_2Cl_2, 33 mL, 33.2 mmol, 3 eq) at –78 °C. After being stirred for 1 h, the reaction was carefully quenched at –78 °C by the addition of aqueous pH 7 buffer (20 mL) and sat. Rochelle salt solution (40 mL) and then stirred for 30 min at 0 °C. The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (*i*-hexane/ethyl acetate 20/1) provided **S5** (3.48 g, 9.6 mmol, 86%) as a clear oil: R_f 0.50 (*i*-hexane/ethyl acetate 3/1); ^{1}H NMR (300 MHz, $CDCl_3$, δ) 0.00 (s, 3H), 0.01 (s, 3H), 0.82-0.84 (m, 12H), 1.70 (br s, 1H), 1.75-1.87 (m, 1H), 2.18-2.28 (m, 1H), 3.35-3.53 (m, 4H), 3.75 (dt, *J* = 5.8, 3.8 Hz, 1H), 4.39 (d, *J* = 12.2 Hz, 1H), 4.45 (d, *J* = 12.2 Hz, 1H), 4.98-5.06 (m, 2H), 5.73 (ddd, *J* = 17.2, 10.4, 8.8 Hz, 1H), 7.23-7.29 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$, δ) –4.6 (2 × CH_3), 11.3 (CH_3), 17.9 (C), 25.9 (3 ×CH_3), 38.1 (CH), 45.6 (CH), 62.5 (CH_2), 71.4 (CH_2), 73.0 (CH_2), 74.1 (CH), 116.0 (CH_2=), 127.4 (CH=), 128.2 (2 × CH=), 128.3 (2 × CH), 138.4 (C=), 139.6 (CH=); IR (in substance): ν 3650-3200, 3070-2855 cm^{-1}; Anal. Calcd. for $C_{21}H_{36}O_3Si$: C, 69.2; H, 10.0. Found: C, 69.2; H, 10.1; $[\alpha]^{25}_D$: +10.9 (*c* 0.49, $CHCl_3$).



S5 **13** (97%)

Aldehyde 13: To an ice-cooled solution of **S5** (1.0 g, 2.8 mmol, 1 eq) in CH_2Cl_2 (14 mL, 5 mL/mmol **S5**) and pyridine (3 mL, 1 mL/mmol **S5**) was added the Dess-Martin periodinane[1] (1.75 g, 3.7 mmol, 1.5 eq). The mixture was stirred for 2 h at room temperature and was then quenched by the addition of sat. aqueous $Na_2S_2O_3$ solution.

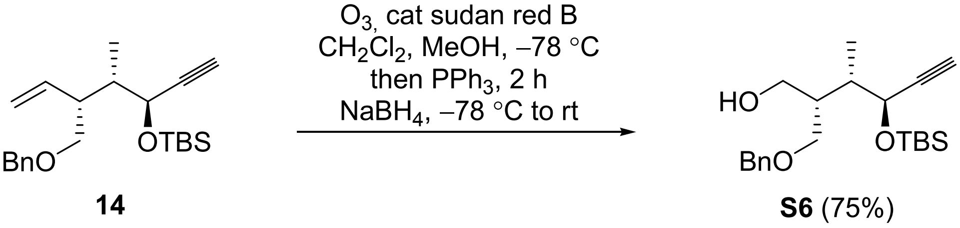
The resulting biphasic solution was stirred vigorously for 20 min. The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (*i*-hexane/ethyl acetate 50/1) provided **13** (0.97 g, 2.6 mmol, 97%) as a clear oil: R_f 0.78 (*i*-hexane/ethyl acetate 3/1); ^{1}H NMR (300 MHz, $CDCl_3$, δ) -0.01 (s, 3H), 0.00 (s, 3H), 0.88 (s, 9H), 0.94 (d, J = 7.1 Hz, 3H), 2.13 (m, 1H), 2.46 (m, 1H), 3.42-3.44 (m, 2H), 3.89 (dd, J = 3.9, 1.5 Hz, 1H), 4.39 (d, J = 12.2 Hz, 1H), 4.46 (d, J = 12.2 Hz, 1H), 5.07-5.12 (m, 2H), 5.70 (ddd, J = 17.1, 10.4, 9.1 Hz, 1H), 7.23-7.32 (m, 5H), 9.53 (d, J = 1.5 Hz, 1H); ^{13}C NMR (76 MHz, $CDCl_3$, δ) -5.0 (CH_3), -4.5 (CH_3), 14.2 (CH_3), 18.1 (C), 25.8 (3 × CH_3), 40.0 (CH), 45.0 (CH), 71.3 (CH_2), 73.1 (CH_2), 80.6 (CH), 117.3 (CH_2=), 127.5 (CH=), 127.6 (2 × CH=), 128.3 (2 × CH=), 138.4 (C=), 140.4 (CH=), 205.2 (C=O); IR (in substance): ν 3070-2860, 1730 cm^{-1}; Anal. Calcd. for $C_{21}H_{34}O_3Si$: C, 69.6; H, 9.5. Found: C, 69.4; H, 9.3; $[\alpha]^{25}_D$: +2.2 (*c* 1.13, $CHCl_3$).



13

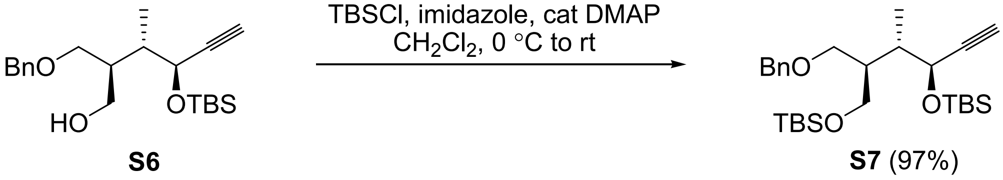
14 (88%)

Alkyne 14: To a suspension of chloromethyl triphenylphosphonium chloride[2] (3.5 g, 9.6 mmol, 3.5 eq) in THF (26 mL, 10 mL/mmol **13**) was added dropwise *n*-BuLi (1.9 M in hexanes, 4.3 mL, 8.2 mmol, 3 eq) at 0 °C to give a dark red solution. After being stirred for 2 h at room temperature, a solution of **13** (0.96 g, 2.6 mmol, 1 eq) in THF (14 mL, 5 mL/mmol **13**) was added at 0 °C. The reaction mixture was stirred for 5 min at 0 °C, and was then filtered through a pentane (200 mL) saturated pad of celite. The organic layers were concentrated under reduced pressure. The crude product was purified by flash chromatography (*c*-hexane/ethyl acetate 20/1) and dried *in vacuu*. The alkene (2.6 mmol, 1 eq) was dissolved in THF (26 mL, 10 mL/mmol alkene), cooled to −78 °C and treated with a solution of LDA [prepared *in situ* from diisopropylamine (1 mL, 7.1 mmol, 2.6 eq), and *n*-BuLi (1.9 M in hexanes, 3.6 mL, 6.7 mmol, 2.5 eq) in THF (9 mL, 3 mL/mmol alkene) at –78 °C]. The resulting orange solution was stirred for 5 min at –78 °C, and then 1 min at 0 °C. The reaction was quenched by the addition of sat. aqueous NH_4Cl solution. The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (*i*-hexane to *i*-hexane/ethyl acetate 100/1 to 50/1) provided **14** (0.84 g, 2.3 mmol, 88%) as a clear oil: R_f 0.51 (*i*-hexane/ethyl acetate 100/1); ^{1}H NMR (400 MHz, $CDCl_3$, δ) 0.04 (s, 3H), 0.09 (s, 3H), 0.87 (s, 9H), 0.98 (d, *J* = 6.8 Hz, 3H), 1.75-1.84 (m, 1H), 2.32 (d, *J* = 2.0 Hz, 1H), 2.34-2.40 (m, 1H), 3.47-3.52 (m, 2H), 4.41 (dd, *J* = 5.3, 2.0 Hz, 1H), 4.44 (d, *J* = 12.3 Hz, 1H), 4.50 (d, *J* = 12.3 Hz, 1H), 5.08-5.13 (m, 2H), 5.79 (ddd, *J* = 17.3, 10.0, 10.0 Hz, 1H), 7.24-7.34 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$, δ) –5.2 (CH_3), –4.7 (CH_3), 11.2 (CH_3), 18.0 (C), 25.7 (3 × CH_3), 40.8 (CH), 45.9 (CH), 65.3 (CH), 71.4 (CH_2), 73.0 (CH_2), 73.2 (CH), 83.4 (C), 116.3 (CH_2=), 127.4 (CH=), 127.5 (2 × CH=), 128.2 (2 × CH=), 138.4 (C=), 139.2 (CH=); IR (in substance): ν 3070-2860, 1730 cm^{-1}; Anal. Calcd. for $C_{22}H_{34}O_2Si$: C, 73.7; H, 9.5. Found: C, 74.0; H, 9.2; $[\alpha]^{25}_D$: +10.2 (*c* 1.09, $CHCl_3$).



Alcohol S6: Through a solution of the olefin **14** (1.5 g, 4.2 mmol, 1 eq) and catalytic amounts of sudan red B in CH_2Cl_2 (8 mL, 2 mL/mmol **14**) and MeOH (24 mL, 6 mL/mmol **14**) at –78 °C was bubbled a stream of ozone, until the red color of sudan red B had been dissapeared (~45 min). The excess ozone was removed by a stream of nitrogen, and PPh_3 (3.3 g, 12.6 mmol, 3 eq) was then added at –78 °C. After being stirred for 2 h at –78 °C, $NaBH_4$ (0.5 g, 12.6 mmol, 3 eq) was added, and the reaction mixture was allowed to warm to room temperature over night (~15 h). The solvents were removed and purification by flash chromatography (*i*-hexane/ethyl acetate 50/1 to 20/1) provided **S6** (1.1 g, 3.1 mmol, 75%) as a clear oil: R_f 0.37 (*i*-hexane/ethyl acetate 5/1); ^{1}H NMR

(400 MHz, $CDCl_3$, δ) 0.07 (s, 3H), 0.11 (s, 3H), 0.87 (s, 9H), 0.97 (d, *J* = 6.5 Hz, 3H), 1.94-2.34 (m, 2H), 2.34 (d, *J* = 2.0 Hz, 1H), 2.66 (br s, 1H), 3.60-3.64 (m, 1H), 3.71-3.74 (m, 2H), 3.77-3.82 (m, 1H), 4.42-4.44 (m, 1H), 4.47 (d, *J* = 12.1 Hz, 1H), 4.51 (d, *J* = 12.1 Hz, 1H), 7.27-7.35 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$, δ) –5.1 (CH_3), –4.7 (CH_3), 12.0 (CH_3), 18.1 (C), 25.7 (3 × CH_3), 38.1 (CH), 41.7 (CH), 65.0 (CH), 65.3 (CH), 71.8 (CH_2), 73.3 (CH_2), 73.5 (CH_2), 83.8 (C), 127.5 (2 × CH=), 127.7 (2 × CH=), 128.4 (CH=), 137.8 (C=); IR (in substance): ν 3600-3350, 3300, 3000-2800, 1250, 1090 cm^{-1}; Anal. Calcd. for $C_{21}H_{34}O_3Si$: C, 69.6; H, 9.5. Found: C, 69.7; H, 9.2; $[\alpha]^{25}_D$: –27.7 (*c* 1.00, $CHCl_3$).

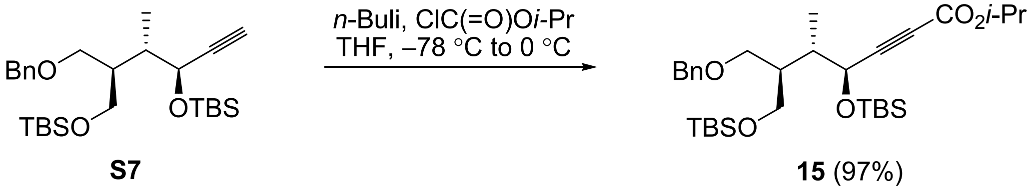


S6

S7 (97%)

Silyl ether S7: To a solution of **S6** (1.14 g, 3.1 mmol, 1 eq) in CH_2Cl_2 (3 mL, 1 mL/mmol **S6**) was added DMAP (40 mg, 0.31 mmol, 0.1 eq), imidazole (0. 64 g, 9.4 mmol, 3 eq), and TBSCl (0.71 g, 4.7 mmol, 1.5 eq) at 0 °C. The reaction mixture was stirred for 2 h at room temperature and then quenched by the addition of sat. aqueous NH_4Cl solution. The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (*c*-hexane to *c*-hexane/ethyl acetate 50/1) provided **S7** (1.46 g, 3.1 mmol, 97%) as a clear oil: R_f 0.37 (*i*-hexane/ethyl acetate 20/1); ^1H NMR (400 MHz, $CDCl_3$, δ) 0.01 (s, 6H), 0.05 (s, 3H), 0.10 (s, 3H), 0.86 (s, 9H), 0.87 (s, 9H), 0.97 (d, *J* = 6.8 Hz, 3H), 1.85-1.91 (m, 1H), 1.93-1.99 (m, 1H), 2.31 (d, *J* = 2.3 Hz, 1H), 3.43 (dd, *J* = 9.0, 7.8 Hz, 1H), 3.58 (dd, *J* = 9.0, 4.4 Hz, 1H), 3.69-3.70 (m, 2H), 4.41-4.50 (m, 3H), 7.20-7.31 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$, δ) –5.4 (2 × CH_3), –5.1 (CH_3), –4.5 (CH_3), 11.7 (CH_3), 18.2 (C), 18.3 (C), 25.8 (3 × CH_3), 26.0 (3 × CH_3), 38.6 (CH), 42.2 (CH), 62.0 (CH_2), 65.6 (CH), 68.7 (CH_2), 73.1 (CH), 73.2 (CH_2), 84.4 (C), 124.4 (CH=), 127.6 (2 × CH=), 128.3 (2 × CH=), 138.8 (C=); IR (in substance): ν 3300, 3000-2800, 1089, 837 cm^{-1}; Anal. Calcd. for $C_{27}H_{48}O_3Si_2$: C, 68.0;

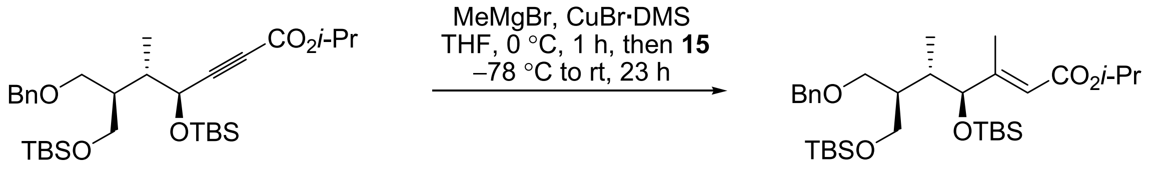
H, 10.2. Found: C, 68.2; H, 10.2; $[\alpha]^{25}_{D}$: −17.1 (*c* 0.67, $CHCl_3$).



S7

15 (97%)

Acetylenic ester 15: To a solution of **S7** (1.0 g, 2.1 mmol, 1.0 eq) in THF (21 mL, 10 mL/mmol **S7**) was added dropwise *n*-BuLi (2.0 M in hexanes, 1.4 mL, 2.7 mmol, 1.3 eq) at −78 °C to give a slightly yellow reaction mixture. After being stirred for 15 min at −78 °C, a solution of isopropyl chloroformate (1 M in toluene, 2.7 mL, 2.7 mmol, 1.3 eq) was then added dropwise at −78 °C and stirred for 1 h at −78 °C. The reaction mixture was warmed to 0 °C over a period of 2 h and was subsequently quenched by the addition of sat. aqueous NH_4Cl solution. The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (*c*-hexane to *c*-hexane/ethyl acetate 100/1) provided **15** (1.1 g, 2.0 mmol, 97%) as a clear oil: R_f 0.56 (*i*-hexane/ethyl acetate 20/1); ^1H NMR (400 MHz, $CDCl_3$, δ) 0.03 (s, 6H), 0.06 (s, 3H), 0.12 (s, 3H), 0.87 (s, 9H), 0.88 (s, 9H), 1.00 (d, *J* = 8.5 Hz, 3H), 1.26 (d, *J* = 6.3 Hz, 6H), 1.94-1.99 (m, 2H), 3.43 (dd, *J* = 8.9, 7.2 Hz, 1H), 3.56 (dd, *J* = 8.9, 4.3 Hz, 1H), 3.65-3.70 (m, 2H), 4.42 (d, *J* = 11.8 Hz, 1H), 4.47 (d, *J* = 11.8 Hz, 1H), 4.62 (d, *J* = 5.5 Hz, 1H), 5.04 (sept, *J* = 6.3 Hz, 1H), 7.24-7.34 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$, δ) −5.6 (CH_3), −5.5 (CH_3) −5.3 (CH_3), −4.7 (CH_3), 11.8 (CH_3), 18.0 (C), 18.1 (C), 21.5 (2 × CH_3), 25.6 (3 × CH_3), 25.8 (3 × CH_3), 38.6 (CH), 41.9 (CH), 61.9 (CH_2), 65.6 (CH), 68.5 (CH_2), 69.6 (CH), 73.1 (CH_2), 77.5 (C), 87.2 (C), 127.4 (CH=), 127.5 (2 × CH=), 128.2 (2 × CH=), 138.4 (C=), 153.0 (C=O); IR (in substance): ν 3000-2850, 2250, 1700, 910, 730 cm^{-1}; Anal. Calcd. for $C_{31}H_{54}O_5Si_2$: C, 66.1; H, 9.7. Found: C, 66.3; H, 9.8; $[\alpha]^{25}_{D}$: −13.4 (*c* 1.19, $CHCl_3$).

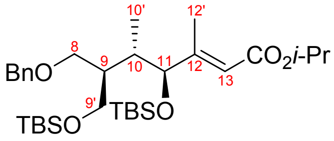


15

(*E*)-**16** (91%, >90% de)

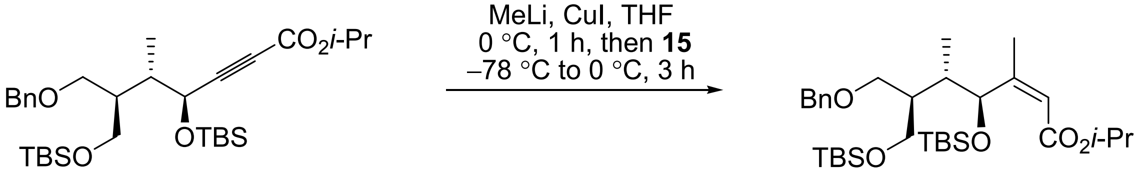
Olefin (*E*)-16: To an ice-cooled suspension of the CuBr·DMS complex[3] (1.43 g, 7.0 mmol, 10 eq) in THF (30 mL, 45 mL/mmol **15**) was added dropwise a MeMgBr solution (1 M in THF, 7 mL, 7.0 mmol, 10 eq). After being stirred for 1 h at 0 °C, the reaction mixture was cooled to –78 °C, and a chilled solution (–78 °C) of **15** (393 mg, 0.7 mmol, 1 eq) in THF (20 mL, 30 mL/mmol **15**) was added. The reaction mixture was slowly warmed to room temperature over a period of 23 h and then quenched by the addition of sat. aqueous NH_4Cl solution (20 mL) and H_2O (10 mL). The resulting biphasic solution was stirred vigorously for 20 min. The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with brine (3 × 30 mL), followed by extraction of the combined aqueous phases with CH_2Cl_2 (3 × 20 mL). The combined organic phases were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (*c*-hexane/ethyl acetate 100/1) afforded (*E*)-**16** (369 mg, 0.64 mmol, 91%) as a single diastereomer (>90% de): R_f 0.51 (*i*-hexane/ethyl acetate 20/1); ^{1}H NMR (400 MHz, $CDCl_3$, δ) –0.09 (s, TBS-C*H*$_3$, 3H), –0.02 (s, TBS-C*H*$_3$, 3H), 0.00 (s, 2 × TBS-C*H*$_3$, 6H), 0.71 (d, *J* = 7.3 Hz, 10'-C*H*$_3$, 3H), 0.84 (s, 3 × TBS-C*H*$_3$, 9H), 0.86 (s, 3 × TBS-C*H*$_3$, 9H), 1.24 (d, *J* = 6.3 Hz, 2 × -O*i*-Pr-C*H*$_3$, 6H), 1.99-2.01 (m, 10-C*H*, 1H), 2.03 (s, 12'-C*H*$_3$, 3H), 2.19-2.23 (m, 9-C*H*, 1H), 3.31 (dd, *J* = 8.6, 8.6 Hz, 8-C*H*$_2$ or 9'-C*H*$_2$, 1H), 3.50-3.55 (m, 8-C*H*$_2$ or 9'-C*H*$_2$, 2H), 3.71 (dd, *J* = 9.9, 5.1 Hz, 8-C*H*$_2$ or 9'-C*H*$_2$, 1H), 4.00 (d, *J* = 7.5 Hz, 11-C*H*, 1H), 4.42 (s, 8'-Ph-C*H*$_2$, 2H), 5.01 (sept, *J* = 6.3 Hz, -O*i*-Pr-C*H*, 1H), 5.81 (s, 13-C*H*=, 1H), 7.25-7.34 (m, 5 × Ph-C*H*, 5H); ^{13}C NMR (101 MHz, $CDCl_3$, δ) –5.6 (CH_3), –5.4 (CH_3), –5.3 (CH_3), –4.7 (CH_3), 11.9 (CH_3), 14.0 (CH_3), 18.0 (C), 18.1 (C), 21.9 (2 × CH_3), 25.7 (3 × CH_3), 25.8 (3 × CH_3), 35.2 (CH), 39.4 (CH), 63.1 (CH_2), 66.7 (CH), 68.2 (CH_2), 73.0 (CH_2), 81.1 (CH), 117.2 (CH=), 127.3 (CH=), 127.4 (2 × CH=), 128.2 (2 × CH=), 138.7 (C=), 159.4 (C=), 166.1 (C=O); IR (in substance): ν 3000-2850, 1715, 1385, 1100 cm^{-1}; Anal. Calcd. for $C_{32}H_{58}O_5Si_2$: C, 66.4; H, 10.1. Found: C, 66.6; H, 10.5; $[\alpha]^{25}_D$: –14.3 (*c* 1.07, $CHCl_3$).

Table S1. NOESY ($CDCl_3$, 600 MHz) studies on (*E*)-**16**.



(*E*)-**16**

entry	irradiated	NOE observed to	conclusion
1	13-H (5.81 ppm)	11-H (4.00 ppm)	(12*E*)



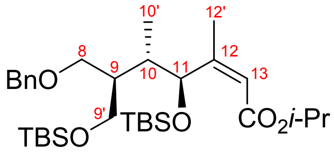
15

(*Z*)-**16** (70%, >90% de)

Olefin (*Z*)-16: To an ice-cooled suspension of CuI (0.31 g, 1.6 mmol, 3 eq) in THF (5 mL, 10 mL/mmol **15**) was added dropwise MeLi (1.5 M in Et_2O, 2.1 mL, 3.2 mmol, 6 eq) to give a clear solution. After being stirred for 1 h at 0 °C, the reaction mixture was cooled to –78 °C, and a chilled solution (–78 °C) of **15** (300 mg, 0.53 mmol, 1 eq) in THF (5 mL, 10 mL/mmol **15**) was added. The bright yellow solution was slowly warmed to 0 °C over a period of 3 h and was then quenched by the addition of sat. Aqueous NH_4Cl solution (5 mL) and H_2O (5 mL). The resulting biphasic solution was stirred vigorously for 20 min. The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with brine (3 × 20 mL), followed by extraction of the combined aqueous phases with CH_2Cl_2 (3 × 20 mL). The combined organic phases were then dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (*c*-hexane/ethyl acetate 50/1) afforded **16** (260 mg, 0.45 mmol, 85%) as mixture of double bond isomers (*E*/*Z* = 4/96). The double bond isomers were separated by flash chromatography (*i*-hexane/ethyl acetate 100/1) to obtain (*Z*)-**16** (212 mg, 0.37 mmol, 70%) as a clear oil: R_f 0.54 (*i*-hexane/ethyl acetate 20/1); ^{1}H NMR (500 MHz, $CDCl_3$, δ) –0.04 (s, TBS-CH_3, 3H), 0.03 (s, TBS-CH_3, 3H), 0.04 (s, TBS-CH_3, 3H), 0.06 (s, TBS-CH_3, 3H), 0.65 (d, *J* = 7.5 Hz, 10'-CH_3, 3H), 0.88

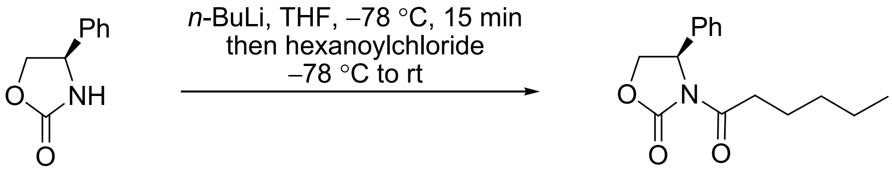
(s, 6 × TBS-CH_3, 18H), 1.24 (d, *J* = 6.2 Hz, 2 × -O*i*-Pr-CH_3, 6H), 1.88 (s, 12’-CH_3, 3H), 1.97-2.03 (m, 10-C*H*, 1H), 2.31-2.39 (m, 9-C*H*, 1H), 3.36 (dd, *J* = 9.1, 9.1 Hz, 8-CH_2 or 9’-CH_2, 1H), 3.59-3.63 (m, 8-CH_2 or 9’-CH_2, 2H), 3.82 (dd, *J* = 9.1, 4.5 Hz, 8-CH_2 or 9’-CH_2, 1H), 4.45 (d, *J* = 12.0 Hz, 8’-Ph-CH_2, 1H), 4.52 (d, *J* = 12.0 Hz, 8’-Ph-CH_2, 1H), 5.01 (sept, *J* = 6.2 Hz, -O*i*-Pr-C*H*, 1H), 5.51 (d, *J* = 9.7 Hz, 11-C*H*, 1H), 5.72 (s, 13-C*H*=, 1H), 7.28-7.33 (m, 5 × Ph-C*H*, 5H); ^{13}C NMR (101 MHz, $CDCl_3$, δ) –5.6 (CH_3), –5.4 (CH_3), –5.3 (CH_3), –5.0 (CH_3), 10.1 (CH_3), 17.9 (C), 18.1 (C + CH_3), 21.8 (6 × CH_3), 25.8 (2 × CH_3), 35.9 (CH), 39.8 (CH), 63.1 (CH_2), 66.8 (CH), 67.7 (CH_2), 70.5 (CH), 73.1 (CH_2), 118.3 (CH=), 127.1 (CH=), 127.4 (2 × CH=), 128.1 (2 × CH=), 138.9 (C=), 160.0 (C=), 165.4 (C=O); IR (in substance): ν 3000-2850, 1700, 1385, 910, 735 cm^{-1}; Anal. Calcd. for $C_{32}H_{58}O_5Si_2$: C, 66.4; H, 10.1. Found: C, 66.8; H, 9.9; $[\alpha]^{25}_{D}$: –4.5 (*c* 1.57, $CHCl_3$).

Table S2. NOESY ($CDCl_3$, 600 MHz) studies on (*Z*)-**16**.



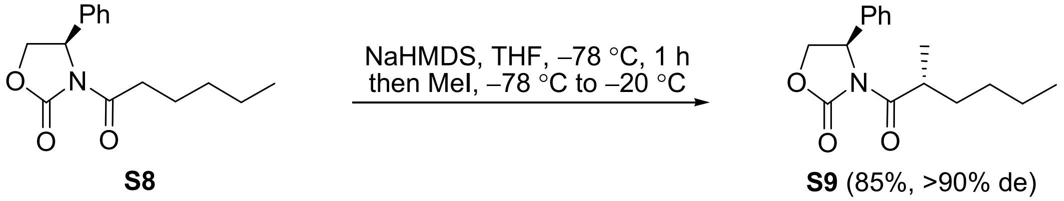
(*Z*)-**16**

entry	irradiated	NOE observed to	conclusion
1	13-H (5.72 ppm)	12’-CH_3 (1.88 ppm)	(12*Z*)
2	12’-CH_3 (1.88 ppm)	13-H (5.72 ppm)	(12*Z*)



S8 (87%)

(4*R*)-3-Hexanoyl-4-phenyloxazolidin-2-one S8:[9] To a solution of (*R*)-4-phenyloxazolidin-2-one[4] (5.6 g, 34.1 mmol, 1 eq) in THF (100 mL, 3 mL/mmol oxazolidinone) was added dropwise *n*-BuLi (2.3 M in hexanes, 16.3 mL, 37.5 mmol, 1.1 eq) at –78 °C to give a slightly yellow solution. After being stirred for 15 min at –78 °C, a solution of hexanoylchloride (5.8 mL, 40.9 mmol, 1.2 eq) was added dropwise at –78 °C and stirred for 15 min at –78 °C. The reaction mixture was warmed to room temperature over a period of 1 h and then quenched by the addition of sat. Aqueous NH_4Cl solution. The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (*c*-hexane/ethyl acetate 20/1) provided **S8** (7.7 g, 29.5 mmol, 87%) as a white solid: R_f 0.23 (*c*-hexane/ethyl acetate 5/1); ^{1}H NMR (400 MHz, $CDCl_3$, δ) 0.83 (t, *J* = 6.9 H, 3H), 1.24-1.27 (m, 4H), 1.54-1.61 (m, 2H), 2.89 (m, 2H), 4.23 (dd, *J* = 8.9, 3.6 Hz, 1H), 4.65 (t, *J* = 8.9 Hz, 1H), 5.39 (dd, *J* = 8.9, 3.6 Hz, 1H), 7.25-7.39 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$, δ) 13.8 (CH_3), 22.3 (CH_2), 23.7 (CH_2), 31.0 (CH_2), 35.4 (CH_2), 57.4 (CH), 69.8 (CH_2), 125.8 (2 × CH=), 128.6 (2 × CH=), 129.1 (CH=), 139.1 (C=), 153.7 (C=O), 172.8 (C=O); IR (in substance): ν 3000-2950, 1780, 1700, 1215, 760 cm^{-1}; Anal. Calcd. for $C_{15}H_{19}NO_3$: C, 68.9; H, 7.3; N, 5.4. Found: C, 69.1; H, 7.6; N, 5.2; $[\alpha]^{25}_D$: –58.7 (*c* 1.0, $CHCl_3$).



(*R*)-3-((*R*)-2-methylhexanoyl)-4-phenyloxazolidin-2-one S9: To a solution of **S8** (8.6 g, 33 mmol, 1 eq) in THF (66 mL, 2 mL/mmol **S8**) was added dropwise NaHMDS (2.0 M in THF, 20 mL, 40 mmol, 1.2 eq) at –78 °C to give a slightly yellow reaction mixture. After being stirred for 1 h at –78 °C, a solution of MeI (5.1 mL, 83 mmol, 2.5 eq) was

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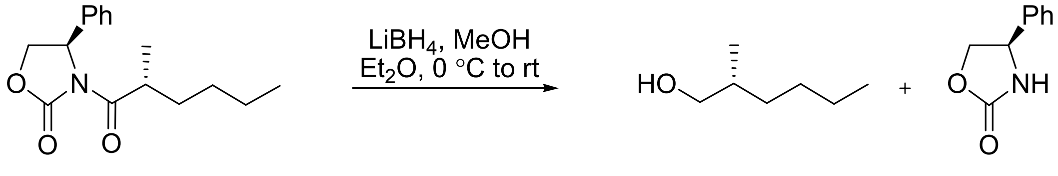
[9] Feroci, M.; Orsini, M.; Palombi, L.; Sotgiu, G.; Colapietro, M.; Inesi, A. *J. Org. Chem.* **2004**, 69, 487-494.

added and stirred for 30 min at –78 °C. The reaction mixture was then warmed to –20 °C over a period of 2 h, and was subsequently quenched by the addition of sat. Aqueous NH_4Cl solution. The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (*c*-hexane/ethyl acetate 20/1) provided **S9** (7.7 g, 27.8 mmol, 85%, >90% de) as a white solid: R_f 0.34 (*c*-hexane/ethyl acetate 5/1); ^{1}H NMR (400 MHz, $CDCl_3$, δ) 0.86 (t, *J* = 6.9 H, 3H), 1.07 (d, *J* = 7.0 Hz, 3H), 1.24-1.35 (m, 5H), 1.64-1.68 (m, 1H), 3.66-3.76 (m, 1H), 4.23 (dd, *J* = 8.9, 3.8 Hz, 1H), 4.66 (t, *J* = 8.9 Hz, 1H), 5.41 (dd, *J* = 8.9, 3.6 Hz, 1H), 7.24-7.37 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$, δ) 13.9 (CH_3), 17.2 (CH_3), 22.6 (CH_2), 29.3 (CH_2), 32.6 (CH_2), 37.7 (CH), 57.6 (CH), 69.6 (CH_2), 125.6 (2 × CH=), 128.5 (CH=), 129.1 (2 × CH=), 139.2 (C=), 153.3 (C=O), 176.6 (C=O); IR (in substance): ν 3000-2850, 1780, 1700, 1380, 700 cm^{-1}; Anal. Calcd. for $C_{16}H_{21}NO_3$: C, 69.8; H, 7.7; N, 5.1. Found: C, 69.9; H, 7.5; N, 5.1; $[\alpha]^{25}_D$: –100.2 (*c* 1.1, $CHCl_3$).



S9

(*R*)-**8** (74%)

(79%)

Alcohol (*R*)-8:[10] To an ice-cooled solution of **S9** (2.0 g, 7.3 mmol, 1 eq) in Et_2O (73 mL, 10 mL/mmol **S9**) and MeOH (0.9 mL, 21.9 mmol, 3 eq) was added $LiBH_4$ (0.48 g, 21.9 mmol, 3 eq), and the reaction mixture was stirred for 1.5 h at room temperature. The reaction was then quenched by the slow addition of sat. Aqueous Rochelle salt solution (30 mL) and the resulting biphasic solution was stirred vigorously for 30 min. The layers were separated and the aqueous phase was extracted with Et_2O (4 × 30 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure (700 mbar, 40 °C bath temperature). The crude product was then dissolved in 20/1 pentane/Et_2O (3 × 3 mL), followed by decantation to remove most of the crystalline

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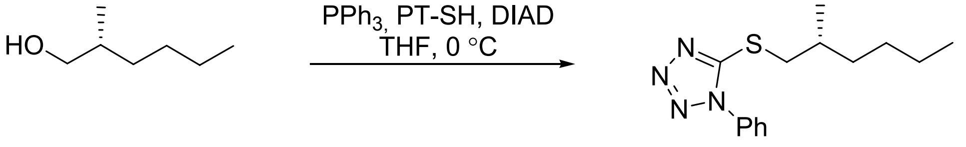
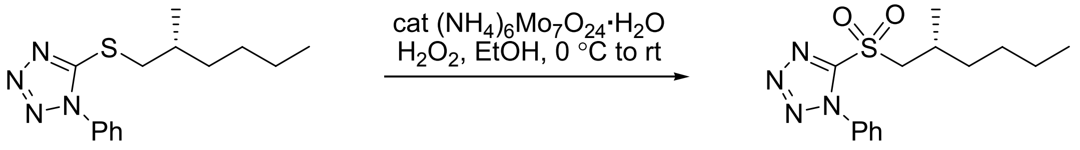
[10] Goldstein, S. W.; Overman, L. E.; Rabinowitz, M. H. *J. Org. Chem.* **1992**, 57, 1179-1190.

oxazolidinone. Concentration under reduced pressure (700 mbar, 40 °C bath temperature) and kugelrohr distillation (20 mbar, 100 °C) afforded (*R*)-**8** (0.64 g, 5.5 mmol, 79%) as a colorless liquid and (*R*)-4-phenyloxazolidin-2-one (0.87 g, 5.3 mmol, 74%) as white crystals. (*R*)-**8:** R_f 0.31 (*c*-hexane/ethyl acetate 5/1); ^{1}H NMR (400 MHz, $CDCl_3$, δ) 0.87 (t, *J* = 6.9 Hz, 3H), 0.89 (d, *J* = 6.8 Hz, 3H), 1.04-1.12 (m, 1H), 1.19-1.40 (m, 6H), 1.53-1.62 (m, 1H), 3.39 (dd, *J* = 10.5 Hz, 6.5 Hz, 1H), 3.48 (dd, *J* = 10.5 Hz, 5.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$, δ) 14.0 (CH_3), 16.5 (CH_3), 22.9 (CH_2), 29.1 (CH_2), 32.7 (CH_2), 35.6 (CH), 68.3 (CH_2); IR (in substance): ν 3700-3100, 3000-2850, 1465, 1260 cm^{-1}; Anal. Calcd. for $C_7H_{16}O$: C, 72.4; H, 13.9. Found: C, 72.4; H, 13.9; $[\alpha]^{25}_D$: +12.4 (*c* 1.0, $CHCl_3$).



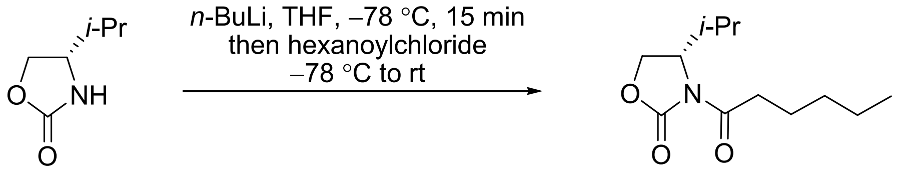
(*R*)-**8** **S10** (92%)

Phenyl-1*H*-tetrazole S10: To an ice-cooled solution of the alcohol (*R*)-**8** (0.71 g, 6.1 mmol, 1.0 eq) in THF (6 mL, 1 mL/mmol alcohol) was added PPh_3 (1.9 g, 7.3 mmol, 1.2 eq), 1-phenyl-1*H*-tetrazole-5-thiol (PT-SH, 1.6 g, 9.1 mmol, 1.5 eq), and diisopropylazodicarboxylate (DIAD, 1.6 mL, 7.9 mmol, 1.3 eq). After being stirred for 1 h at 0 °C, sat. Aqueous $NaHCO_3$ solution was added. The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (*c*-hexane/ethyl acetate 50/1) provided **S10** (1.5 g, 5.6 mmol, 92%) as a yellow oil: R_f 0.26 (*c*-hexane/ethyl acetate 10/1); ^{1}H NMR (400 MHz, $CDCl_3$, δ) 0.87 (t, *J* = 6.9 Hz, 3H), 1.01 (d, *J* = 6.8 Hz, 3H), 1.23-1.33 (m, 5H), 1.42-1.49 (m, 1H), 1.86-1.95 (m, 1H), 3.24 (dd, *J* = 12.6, 7.5 Hz, 1H), 3.44 (dd, *J* = 12.6, 5.7 Hz, 1H), 7.50-7.58 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$, δ) 13.9 (CH_3), 18.9 (CH_3), 22.6 (CH_2), 28.8 (CH_2), 32.7 (CH), 35.4 (CH_2), 40.3 (CH_2), 123.6 (2 × CH=), 129.6 (2 × CH=), 129.9 (CH=), 133.6 (C=), 154.5 (C=N); IR (in substance): ν 3000-2850, 1500, 1385 cm^{-1}; HRMS (ESI) Calcd. for $C_{14}H_{21}N_4S$ ($[M + H]^+$): 277.1482. Found: 277.1482; $[\alpha]^{25}_D$: –2.1 (*c* 1.75, $CHCl_3$).



S10 **7** (93%)

Sulfone 7: To an ice-cooled solution of **S10** (1.0 g, 3.6 mmol, 1.0 eq) in EtOH (36 mL, 10 mL/mmol **S10**) was added a solution of $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$ (45 mg, 0.36 mmol, 0.1 eq) in H_2O_2 (35% in H_2O, 3.5 mL, 36 mmol, 10.0 eq). The reaction mixture was stirred at room temperature for 12 h and then quenched by the addition of brine. The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (*c*-hexane/ethyl acetate 100/1 to 50/1) provided **7** (1.0 g, 3.4 mmol, 93%) as a pale yellow oil: R_f 0.66 (*i*-hexane/ethyl acetate 5/1); ^{1}H NMR (400 MHz, $CDCl_3$, δ) 0.87 (t, *J* = 6.9 Hz, 3H), 1.13 (d, *J* = 6.5 Hz, 3H), 1.23-1.38 (m, 5H), 1.47-1.56 (m, 1H), 2.26-2.35 (m, 1H), 3.56 (dd, *J* = 14.6, 8.0 Hz, 1H), 3.79 (dd, *J* = 14.6, 4.8 Hz, 1H), 7.55-7.61 (m, 3H), 7.65-7.67 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$, δ) 13.9 (CH_3), 19.6 (CH_3), 22.4 (CH_2), 28.1 (CH), 28.3 (CH_2), 36.1 (CH_2), 61.7 (CH_2), 125.0 (2 × CH=), 129.6 (2 × CH=), 131.3 (CH=), 132.9 (C=), 154.0 (C=N); IR (in substance): ν 3000-2900, 2360-2340, 1500, 1340, 1150, 760 cm^{-1}; HRMS (ESI) Calcd. for $C_{14}H_{21}N_4SO_2$ ($[M+H]^+$): 309.1380. Found: 309.1380; $[\alpha]^{25}_D$: +2.1 (*c* 1.90, $CHCl_3$).



S11 (92%)

(4*S*)-3-Hexanoyl-4-isopropyloxazolidin-2-one S11:[11] To a solution of (*S*)-4-isopropyl-oxazolidin-2-one[4] (8.5 g, 65.9 mmol, 1 eq) in THF (200 mL, 3 mL/mmol oxazolidinone) was added dropwise *n*-BuLi (2.1 M in hexanes, 35 mL, 72.5 mmol, 1.1 eq) at –78 °C to

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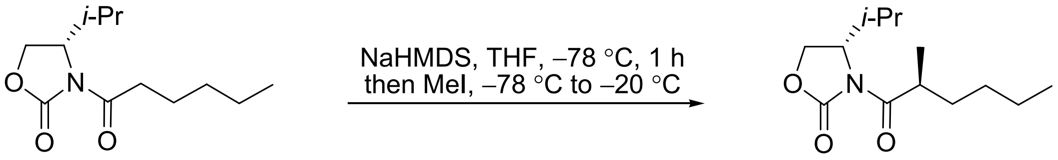
[11] Ager, D. J.; Babler, S.; Froen, D. E.; Laneman, S. A.; Pantaleone, D. P.; Prakash, I.; Zhi, B. *Organic Process Research & Development* **2003**, *7*, 369-378.

give a slightly yellow solution. After being stirred for 15 min at –78 °C, a solution of hexanoylchloride (11.2 mL, 79.1 mmol, 1.2 eq) was added dropwise at –78 °C and stirred for 15 min at –78 °C. The reaction mixture was warmed to room temperature over a period of 1 h and then quenched by the addition of sat. Aqueous NH_4Cl solution. The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (*c*-hexane/ethyl acetate 20/1) provided **S11** (13.8 g, 60.6 mmol, 92%) as a clear oil: R_f 0.33 (*c*-hexane/ethyl acetate 5/1); ^1H NMR (400 MHz, $CDCl_3$, δ) 0.83-0.89 (m, 9H), 1.28-1.32 (m, 4H), 1.58-1.65 (m, 2H), 2.30-2.38 (m, 1H), 2.82 (ddd, *J* = 16.3 Hz, 8.2 Hz, 7.4 Hz, 1H), 2.95 (ddd, *J* = 16.3 Hz, 8.2 Hz, 7.0 Hz, 1H), 4.17 (dd, *J* = 9.0 Hz, 3.0 Hz, 1H), 4.23 (dd, *J* = 9.0 Hz, 9.0 Hz, 1H), 4.41 (dt, J = 8.0 Hz, 3.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$, δ) 13.8 (CH_3), 14.5 (CH_3), 17.9 (CH_3), 22.3 (CH_2), 24.0 (CH_2), 28.2 (CH), 31.2 (CH_2), 35.4 (CH_2), 58.3 (CH), 63.2 (CH_2), 154.0 (C=O), 173.3 (C=O); $[\alpha]^{25}_D$: +79.7 (*c* 1.0, $CHCl_3$).

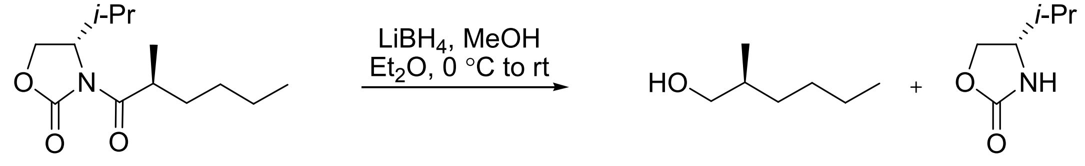


S11

S12 (93%, >90% de)

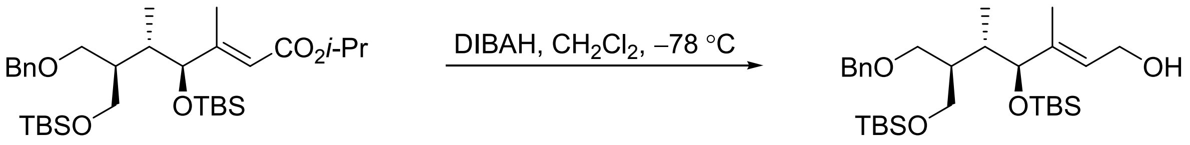
(*S*)-4-Isopropyl-3-((*S*)-2-methylhexanoyl)oxazolidin-2-one S12:[11] To a solution of **S11** (11.6 g, 51 mmol, 1 eq) in THF (100 mL, 2 mL/mmol **S11**) was added dropwise NaHMDS (2.0 M in THF, 31 mL, 62 mmol, 1.2 eq) at –78 °C to give a slightly yellow reaction mixture. After being stirred for 1 h at –78 °C, a solution of MeI (8 mL, 127 mmol, 2.5 eq) was added and stirred for 30 min at –78 °C. The reaction mixture was then warmed to –20 °C over a period of 2 h and subsequently quenched by the addition of sat. Aqueous NH_4Cl solution. The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (*c*-hexane/ethyl acetate 20/1) provided **S12** (11.4 g, 47.3 mmol, 93%, >90% de) as a clear oil: R_f 0.50 (*c*-hexane/ethyl acetate 10/1); ^1H NMR (400 MHz, $CDCl_3$, δ) 0.84-0.90

(m, 9H), 1.17 (d, *J* = 6.8 Hz, 3H), 1.20-1.40 (m, 5H), 1.65-1.74 (m, 1H), 2.29-2.37 (m, 1H), 3.66-3.74 (m, 1H), 4.17 (dd, *J* = 9.0 Hz, 3.0 Hz, 1H), 4.24 (dd, *J* = 9.0 Hz, 9.0 Hz, 1H), 4.41-4.45 (m, 1H); ^{13}C NMR (101 MHz, CDCl$_3$, δ) 14.0 (CH$_3$), 14.7 (CH$_3$), 17.9 (2 × CH$_3$), 22.7 (CH$_2$), 28.4 (CH), 29.5 (CH$_2$), 32.8 (CH$_2$), 37.7 (CH), 58.4 (CH), 63.2 (CH$_2$), 153.7 (C=O), 177.3 (C=O); IR (in substance): ν 3000-2870, 1780, 1700, 1385, 1200 cm^{-1}; Anal. Calcd. for $C_{13}H_{23}NO_3$: C, 64.7; H, 9.6; N, 5.8. Found: C, 64.9; H, 9.5; N, 5.5. $[\alpha]^{25}_{D}$: +96.4 (*c* 1.0, CHCl$_3$).



S12 (*S*)-**8** (90%) (91%)

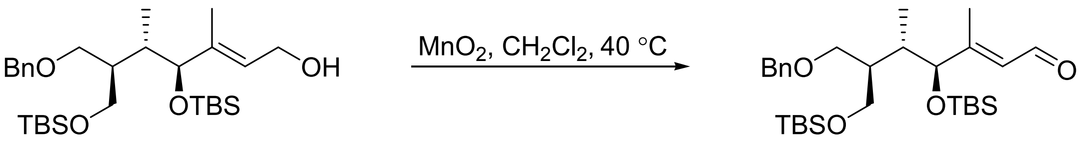
Alcohol (*S*)-8:[10] To an ice-cooled solution of **S12** (1.82 g, 7.5 mmol, 1 eq) in Et$_2$O (75 mL, 10 mL/mmol **S12**) and MeOH (0.9 mL, 22.6 mmol, 3 eq) was added LiBH$_4$ (0.49 g, 22.6 mmol, 3 eq), and the reaction mixture was stirred for 1.5 h at room temperature. The reaction was then quenched by the slow addition of sat. Aqueous Rochelle salt solution (40 mL) and the resulting biphasic solution was stirred vigorously for 30 min. The layers were separated and the aqueous phase was extracted with Et$_2$O (3 × 30 mL). The combined organic layers were dried over MgSO$_4$ and concentrated under reduced pressure (700 mbar, 40 °C bath temperature). The crude product was purified by kugelrohr distillation (20 mbar, 100 °C) to afforded the alcohol (*S*)-**8** (0.79 g, 6.8 mmol, 90%) as a colorless liquid and (*S*)-4-isopropyloxazolidin-2-one (0.89 g, 6.9 mmol, 91%) as distillation residue. (*S*)-**8:** R$_f$ 0.31 (*c*-hexane/ethyl acetate 5/1); ^{1}H NMR (400 MHz, CDCl$_3$, δ) 0.87 (t, *J* = 6.9 Hz, 3H), 0.89 (d, *J* = 6.5 Hz, 3H), 1.04-1.12 (m, 1H), 1.19-1.40 (m, 6H), 1.53-1.62 (m, 1H), 3.39 (dd, *J* = 10.5 Hz, 6.5 Hz, 1H), 3.49 (dd, *J* = 10.5 Hz, 5.8 Hz, 1H); ^{13}C NMR (101 MHz, CDCl$_3$, δ) 14.0 (CH$_3$), 16.5 (CH$_3$), 22.9 (CH$_2$), 29.1 (CH$_2$), 32.7 (CH$_2$), 35.6 (CH), 68.3 (CH$_2$); IR (in substance): ν 3700-3100, 3000-2850, 1465, 1380 cm^{-1}; HRMS (EI) Calcd. for $C_7H_{16}O$ (M$^+$): 116.1196. Found: 116.1177; $[\alpha]^{25}_{D}$: −13.1 (*c* 1.0, CHCl$_3$).



(*E*)-**16**

S13 (93%)

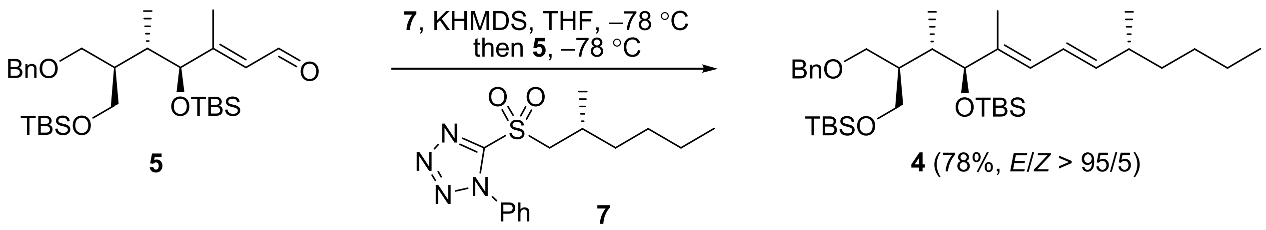
Alcohol S13: To a solution of (*E*)-**16** (184 mg, 0.32 mmol, 1 eq) in CH_2Cl_2 (3 mL, 10 mL/mmol ester) was added DIBAH (1 M in CH_2Cl_2, 1.1 mL, 1.1 mmol, 3.5 eq) at –78 °C. After being stirred for 1 h, the reaction mixture was warmed to 0 °C. It was then carefully quenched by the addition of aqueous pH 7 buffer (2 mL) and sat. Rochelle salt solution (3 mL) and subsequently stirred for additional 30 min. The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (*i*-hexane/ethyl acetate 20/1 to 10/1) provided **S13** (153 mg, 0.29 mmol, 93%) as a clear oil: R_f 0.40 (*i*-hexane/ethyl acetate 5/1); ^{1}H NMR (400 MHz, $CDCl_3$, δ) –0.08 (s, 3H), –0.02 (s, 3H), 0.00 (s, 6H), 0.65 (d, *J* = 7.3 Hz, 3H), 0.84 (s, 9H), 0.85 (s, 9H), 1.55 (s, 3H), 1.61 (br s, 1H), 1.91-1.94 (m, 1H), 2.24-2.28 (m, 1H), 3.32 (dd, *J* = 8.7, 8.7 Hz, 1H), 3.49-3-55 (m, 2H), 3.72 (dd, *J* = 9.8, 5.3 Hz, 1H), 3.84 (d, *J* = 8.3 Hz, 1H), 4.16 (m, 2H), 4.41 (d, *J* = 12.3 Hz, 1H), 4.44 (d, *J* = 12.3 Hz, 1H), 5.48 (t, *J* = 6.4 Hz, 1H), 7.26-7.33 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$, δ) –5.6 (CH_3), –5.4 (CH_3), –5.3 (CH_3), –4.5 (CH_3), 11.3 (CH_3), 11.8 (CH_3), 18.0 (C), 18.1 (C), 25.8 (6 × CH_3), 35.1 (CH), 39.4 (CH), 59.1 (CH_2), 63.3 (CH_2), 68.3 (CH_2), 73.1 (CH_2), 80.9 (CH), 125.7 (CH=), 127.2 (2 × CH=), 127.4 (CH=), 128.1 (2 × CH=), 138.7 (C=), 140.2 (C=); IR (in substance): ν 3000-2850, 1385, 1085, 835 cm^{-1}; Anal. Calcd. for $C_{29}H_{54}O_4Si_2$: C, 66.6; H, 10.4. Found: C, 66.4; H, 10.3; $[\alpha]^{25}_{D}$: –12.2 (*c* 1.09, $CHCl_3$).



S13

5 (crude)

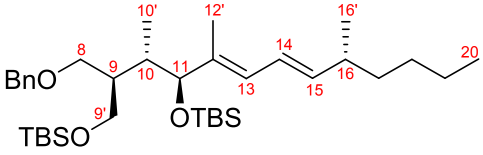
Aldehyde 5: To a solution of **S13** (100 mg, 0.19 mmol, 1 eq) in CH_2Cl_2 (4 mL, 20 mL/mmol **S13**) was added MnO_2 (196 mg, 1.9 mmol, 10 eq) at room temperature. The mixture was refluxed for 3.5 h and then filtered through a pad of celite. The solvent was removed under reduced pressure to provide the crude aldehyde **5**, which was used for the next step without further purification: R_f 0.48 (*i*-hexane/ethyl acetate 10/1); ^{1}H NMR (400 MHz, $CDCl_3$, δ) –0.11 (s, 3H), –0.01 (s, 3H), 0.00 (s, 6H), 0.72 (d, *J* = 7.0 Hz, 3H), 0.85 (s, 9H), 0.86 (s, 9H), 2.02-2.07 (m, 1H), 2.07 (s, 3H), 2.15-2.25 (m, 1H), 3.31 (dd, *J* = 8.7, 8.7 Hz, 1H), 3.47-3.54 (m, 2H), 3.71 (dd, *J* = 9.9, 5.1 Hz, 1H), 4.03 (d, *J* = 7.3 Hz, 1H), 4.41 (s, 2H), 5.94 (d, *J* = 8.0 Hz, 1H), 7.25-7.34 (m, 5H), 10.02 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$, δ) –5.6 (CH_3), –5.4 (CH_3), –5.2 (CH_3). –4.7 (CH_3), 11.8 (CH_3), 12.8 (CH_3), 18.0 (C), 18.1 (C), 25.7 (3 × CH_3), 25.8 (3 × CH_3), 35.1 (CH), 39.5 (CH), 63.0 (CH_2), 68.2 (CH_2), 73.1 (CH_2), 80.7 (CH), 127.3 (CH=), 127.4 (2 × CH=), 127.5 (CH=), 128.2 (2 × CH=), 138.5 (C=), 163.9 (C=), 191.3 (C=O); IR (in substance): ν 3000-2850, 1673, 1385, 1075, 910, 740 cm^{-1}.



Alkene 4: To a solution of the sulfon **7** (106 mg, 0.33 mmol, 1.8 eq) in THF (2 mL, 10 mL/mmol **5**) at –78 °C was added KHMDS (0.5 M in toluene, 0.7 mL, 0.33 mmol, 1.8 eq) and the resulting mixture was stirred for 30 min. A chilled (–78 °C) solution of the aldehyde **5** (0.19 mmol, 1 eq) in THF (4 mL, 20 mL/mmol **5**) was then added, and the mixture was warmed to room temperature overnight (~17 h). The resulting slurry was diluted with water (3 mL) and brine (3 mL). The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 3 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (*i*-hexane to *i*-hexane/ethyl acetate 100/1) provided **4** (90 mg, 0.15 mmol, 78%) as a pale yellow oil: R_f 0.57 (*i*-hexane/ethyl acetate 20/1); ^{1}H NMR (400 MHz, $CDCl_3$, δ) –0.11 (s, TBS-C*H*$_3$, 3H), 0.04 (s, TBS-C*H*$_3$, 3H), 0.00 (s, 2 × TBS-C*H*$_3$, 6H), 0.64 (d, *J* = 7.3 Hz, 10'-C*H*$_3$, 3H), 0.87-0.86 (m, 6 × TBS-C*H*$_3$ and 20-C*H*$_3$, 21H), 0.97 (d, *J* = 6.5 Hz, 16'-C*H*$_3$, 3H), 1.24-1.27 (m, 17-, 18- and 19-C*H*$_2$, 6H), 1.60 (s, 12'-

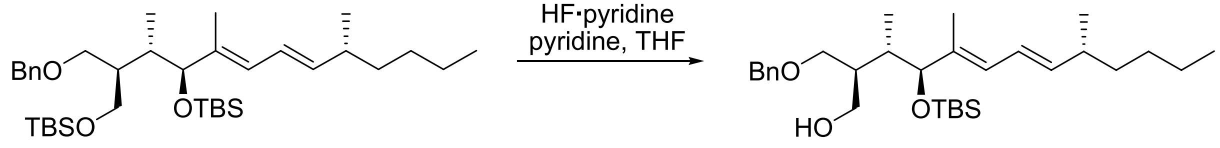
CH_3, 3H), 1.90-1.98 (m, 10-C*H*, 1H), 2.10-2.15 (m, 16-C*H*, 1H), 2.26-2.32 (m, 9-C*H*, 1H), 3.34 (dd, *J* = 8.4, 8.4 Hz, 8-CH_2 or 9’-CH_2, 1H), 3.51 (dd, *J* = 4.6, 4.6 Hz, 8-CH_2 or 9’-CH_2, 1H), 3.55 (dd, *J* = 9.8, 7.8 Hz, 8-CH_2 or 9’-CH_2, 1H), 3.73 (dd, *J* = 10.0, 5.3 Hz, 8-CH_2 or 9’-CH_2, 1H), 3.85 (d, *J* = 8.5 Hz, 11-C*H*, 1H), 4.41 (d, *J* = 12.0 Hz, 8’-Ph-CH_2, 1H), 4.45 (d, *J* = 12.0 Hz, 8’-Ph-CH_2, 1H), 5.45 (dd, *J* = 14.9, 7.7 Hz, 15-C*H*=, 1H), 5.85 (d, *J* = 10.7 Hz, 13-C*H*=, 1H), 6.17 (dd, *J* = 14.9, 10.7 Hz, 14-C*H*=, 1H), 7.35-7.27 (m, 5 × Ph-C*H*, 5H); ^{13}C NMR (126 MHz, $CDCl_3$, δ) –5.1 (CH_3), –4.9 (CH_3), –4.8 (CH_3), –4.2 (CH_3), 12.0 (CH_3), 12.3 (CH_3), 14.5 (CH_3), 18.6 (C), 18.7 (C), 21.0 (CH_3), 23.2 (CH_2), 26.3 (6 × CH_3), 30.0 (CH_2), 36.1 (CH), 37.3 (CH_2), 37.4 (CH), 40.1 (CH), 63.9 (CH_2), 68.9 (CH_2), 73.5 (CH_2), 81.9 (CH), 124.6 (CH=), 127.6 (CH=), 127.7 (CH=), 127.9 (2 × CH=), 128.6 (2 × CH=), 137.0 (C=), 139.4 (C=), 140.5 (CH=); IR (in substance): ν 3000-2850, 1385, 1255, 1050, 835 cm^{-1}; Anal. Calcd. for $C_{36}H_{66}O_3Si_2$: C, 71.7; H, 11.0. Found: C, 71.9; H, 10.7; $[\alpha]^{25}_{D}$: –3.9 (*c* 1.49, $CHCl_3$).

Table S3. NOESY ($CDCl_3$, 600 MHz) studies on **4**.



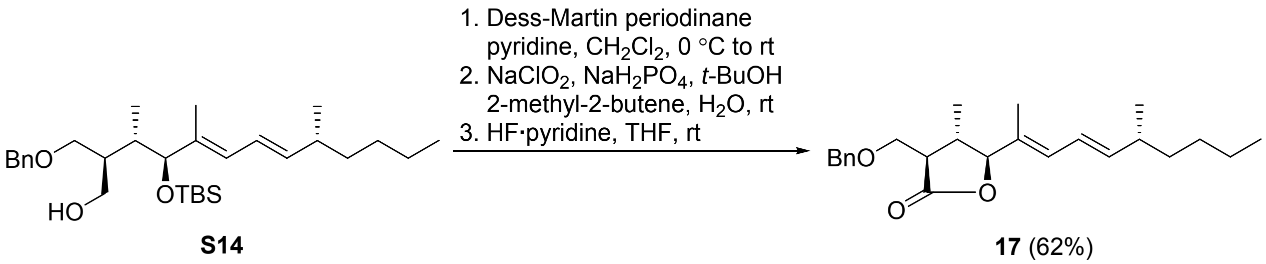
4

entry	irradiated	NOE observed to	conclusion
1	13-H (5.85 ppm)	15-CH_3 (5.45 ppm)	(14*E*)
2	13-H (5.85 ppm)	11-H (3.85 ppm)	(12*E*)
3	14-H (6.17 ppm)	12’-CH_3 (1.62 ppm)	(12*E*)
4	14-H (6.17 ppm)	16’-CH_3 (1.00 ppm)	(14*E*)
5	14-H (6.17 ppm)	16-H (2.15 ppm)	(14*E*)



4 **S14** (84%)

Alkohol S14: Alkene **4** (78 mg, 0.13 mmol, 1 eq) was dissolved in THF (4 mL, 30 mL/mmol **4**) in a polyethylene vial. After being cooled to 0 °C, a solution of hydrogen fluoride•pyridine (0.26 mL, 2.0 mL/mmol), pyridine (0.41 mL, 3.2 mL/mmol), and THF (1 mL, 10 mL/mmol) was added. The cooling bath was then removed and the solution was stirred at room temperature for 6 h. The reaction was carefully quenched by the addition of sat. aqueous $NaHCO_3$ solution and diluted with CH_2Cl_2. The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 3 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (*i*-hexane/ethyl acetate 50/1 to 20/1) provided **S14** (53 mg, 0.11 mmol, 84%) as a pale yellow oil: R_f 0.51 (*c*-hexane/ethyl acetate 50/1); ^{1}H NMR (400 MHz, $CDCl_3$, δ) –0.09 (s, 3H), –0.02 (s, 3H), 0.63 (d, *J* = 7.3 Hz, 3H), 0.85 (m, 12H), 0.98 (d, *J* = 6.8 Hz, 3H), 1.20-1.30 (m, 6H), 1.60 (s, 3H), 1.77-1.80 (m, 1H), 2.12-2.15 (m, 1H), 2.31-2.37 (m, 1H), 2.72 (br s, 1H), 3.52 (dd, *J* = 9.2, 9.2 Hz, 1H), 3.57-3.60 (m, 1H), 3.67-3.70 (m, 2H), 3.83 (dd, *J* = 10.4, 8.4 Hz, 1H), 4.48 (s, 2H), 5.47 (dd, *J* = 14.8 Hz, 7.8 Hz, 1H), 5.81 (d, *J* = 10.8 Hz, 1H), 6.12 (dd, *J* = 14.8, 10.8 Hz, 1H), 7.26-7.34 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$, δ) –5.4 (CH_3), –4.7 (CH_3), 11.5 (CH_3), 12.4 (CH_3), 14.0 (CH_3), 18.1 (C), 20.4 (CH_3), 22.7 (CH_2), 25.8 (3 × CH_3), 29.5 (CH_2), 36.7 (CH_2), 36.7 (CH), 36.9 (CH), 39.8 (CH), 67.1 (CH_2), 71.4 (CH_2), 73.5 (CH_2), 81.2 (CH), 123.8 (CH=), 127.5 (2 × CH=), 127.6 (2 × CH=), 128.3 (2 × CH=), 135.6 (C=), 137.9 (C=), 140.6 (CH=); IR (in substance): ν 3500-3100, 3000-2850, 1385, 1250, 1050, 835 cm^{-1}; HRMS (ESI) Calcd. for $C_{30}H_{52}O_3NaSi$ ($[M + Na]^+$): 511.3578. Found: 511.3580; $[\alpha]^{25}_D$: –7.5 (*c* 1.0, $CHCl_3$).



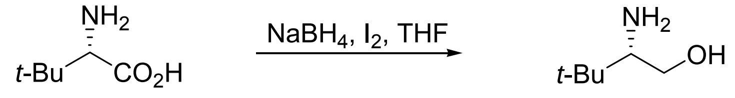
Lacton 17: To an ice-cooled solution of **S14** (59 mg, 0.121 mmol, 1 eq) in CH_2Cl_2 (2.5 mL, 20 mL/mmol **S14**) and pyridine (0.2 mL, 2 mL/mmol **S14**) was added the Dess-Martin periodinane[1] (0.15 g, 0.363 mmol, 3 eq). The mixture was stirred for 4 h at room temperature and was then quenched by the addition of sat. aqueous $Na_2S_2O_3$ solution. The resulting biphasic solution was stirred vigorously for 10 min. The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 4 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was passed through a 4 × 0.5 cm plug of silica gel using *c*-hexane/ethyl acetate 50/1 as eluent to provide the aldehyde (58 mg, 0.121 mmol, 100%) as a colorless oil [R_f 0.66 (*c*-hexane/ethyl acetate 5/1)] that was immediately used after purification.

To a solution of the aldehyde (58 mg, 0.121 mmol, 1 eq) in *t*-BuOH (1.2 mL, 10 mL/mmol aldehyde) and 2-methyl-2-butene (1.2 mL, 10 mL/mmol aldehyde) was added a solution of $NaClO_2$ (0.14 g, 1.2 mmol, 10 eq) and $NaH_2PO_4{\cdot}H_2O$ (0.12 g, 0.85 mmol, 7 eq) in water (2.4 mL, 20 mL/mmol aldehyde). The reaction mixture was stirred for 16 h at room temperature, diluted with water (2 mL) and extracted with CH_2Cl_2 (3 × 2 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (*i*-hexane/ethyl acetate 10/1 to 5/1) provided the acid (45 mg, 0.090 mmol, 74%) as a pale green oil (R_f 0.28 *c*-hexane/ethyl acetate 5/1) that was used in the next step without characterization.

The acid (45 mg, 0.090 mmol, 1 eq) was dissolved in THF (4 mL, 45 mL/mmol acid) in a polyethylene vial. After being cooled to 0 °C, a solution of hydrogen fluoride·pyridine (0.35 mL, 4.0 mL/mmol) was added and stirred for 19 h at room temperature. The reaction was carefully quenched by the addition of sat. aqueous $NaHCO_3$ solution. The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 4 mL).

The combined organic layers were dried with $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (*i*-hexane/ethyl acetate 20/1) provided **17** (28 mg, 0.076 mmol, 84%) as a pale yellow oil: R_f 0.45 (*c*-hexane/ethyl acetate 5/1); ^{1}H NMR (500 MHz, $CDCl_3$, δ) 0.89 (t, *J* = 7.1 Hz, 3H), 1.01 (d, *J* = 6.7 Hz, 3H) 1.11 (d, *J* = 6.2 Hz, 3H), 1.23-1.33 (m, 6H), 1.73 (s, 3H), 2.16-2.22 (m, 1H), 2.41-2.51 (m, 2H), 3.76 (dd, *J* = 9.9 Hz, 3.4 Hz, 1H), 3.82 (dd, *J* = 9.9 Hz, 4.6 Hz, 1H), 4.28 (d, *J* = 9.2 Hz, 1H), 4.53 (d, *J* = 12.0 Hz, 1H), 4.60 (d, *J* = 12.0 Hz, 1H), 5.65 (dd, *J* = 15.2 Hz, 8.0 Hz, 1H), 6.05 (d, *J* = 10.7 Hz, 1H), 6.20 (dd, *J* = 15.2 Hz, 10.7 Hz, 1H), 7.28-7.36 (m, 5H); ^{13}C NMR (126 MHz, $CDCl_3$, δ) 11.3 (CH_3), 14.0 (CH_3), 15.6 (CH_3), 20.4 (CH_3), 22.8 (CH_2), 29.5 (CH_2), 36.6 (CH_2), 37.0 (CH), 48.9 (CH), 49.0 (CH), 67.0 (CH_2), 73.4 (CH_2), 90.5 (CH), 123.4 (CH=), 127.4 (2 × CH=), 127.6 (CH=), 128.3 (2 × CH=), 129.6 (CH=), 130.0 (C=), 138.0 (C=), 143.2 (CH=), 176.3 (C=O); IR (in substance): ν 3000-2870, 1777, 1172, 1114, 968 cm^{-1}; Anal. Calcd. for $C_{24}H_{34}O_3$: C, 77.8; H, 9.3. Found: C, 78.0; H, 9.4; HRMS (ESI) Calcd. for $C_{24}H_{35}O_3$ ($[M + H]^+$): 371.2581. Found: 371.2577; $[\alpha]^{25}_D$: –8.2 (*c* 1.0, $CHCl_3$).

4. General Procedure for Preparation of Catalyst 10[12]



S15 (82%)

Amino Alcohol S15: To an ice-cooled solution of (*S*)-*t*-leucine (65.6 g, 500 mmol, 1.0 eq) and sodium borohydride (45.4 g, 1200 mmol, 2.4 eq) in THF (500 mL, 1 mL/mmol) was slowly added a solution of iodine (126.9 g, 500 mmol, 1.0 eq) in THF (250 mL, 0.5 mL/mmol) over a period of 1.5 h (vigorous H_2 formation!). The reaction mixture was warmed to room temperature and stirred for 30 min. The reaction mixture was subsequently refluxed for 19 h, cooled to 0 °C and then carefully treated with MeOH (150 mL, 0.3 mL/mmol). The solvents were removed under reduced pressure and the crude product was dissolved in 20% aqueous KOH (1 L, 2 mL/mmol). After stirring for 6 h at room temperature, the reaction mixture was extracted with CH_2Cl_2 (3 × 800 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Kugelrohr distillation (80 °C, 2.0 mbar) afforded (*S*)-*t*-leucinol (**S15**) (47.9 g, 409 mmol, 82%) as colorless oil that solidified upon cooling to room temperature: R_f 0.14 (ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$, δ) 0.87 (s, 9H), 1.67 (br s, 3H), 2.47 (dd, *J* = 10.2 Hz, 3.9 Hz, 1H), 3.17 (t, *J* = 10.2 Hz, 1H), 3.68 (dd, *J* = 10.2, 3.9 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$, δ) 26.1 (3 × CH_3), 33.2 (C), 61.7 (CH), 62.2 (CH_2); $[\alpha]^{25}_D$: +39.0 (*c* 1.18, $CHCl_3$).

S16 (86%)

Malonyl dichloride S16: To an ice-cooled solution of 2,2-dimethyl malonic acid (7.5 g, 56.8 mmol, 1.0 eq) and DMF (0.6 mL, 7.4 mmol, 0.13 eq) in CH_2Cl_2 (60 mL, 1 mL/mmol

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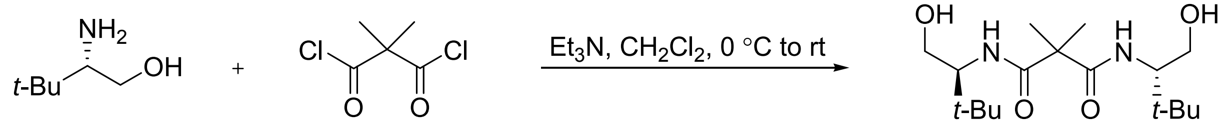
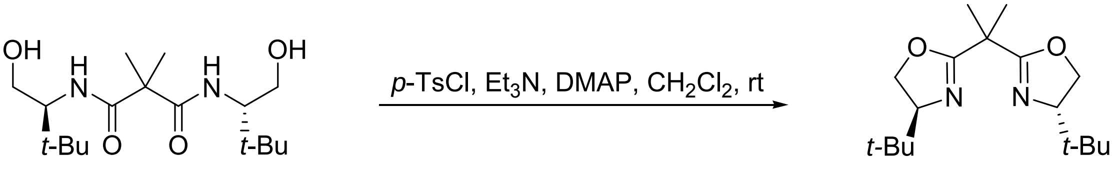
[12] Evans, D. A.; Burgey, C. S.; Paras, N. A.; Vojkovsky, T.; W. Tregay, S. W. *J .Am. Chem. Soc.* **1998**, 120, 5824-5825.

acid) was added dropwise oxalyl chloride (16.2 mL, 170 mmol, 3.0 eq) over a period of 1 h. The reaction mixture was warmed to room temperature, stirred for 18 h and was concentrated under reduced pressure. The crude product was purified by distillation (77 °C, 80 mbar) to afford the malonyl dichloride (**S16**) (8.2 g, 48.5 mmol, 86%) as a colorless liquid: ^{1}H NMR (400 MHz, $CDCl_3$, δ) 1.66 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$, δ) 23.1 (2 × CH_3), 77.2 (C), 171.9 (2 × C=O).



S15 **S16** **S17** (69%)

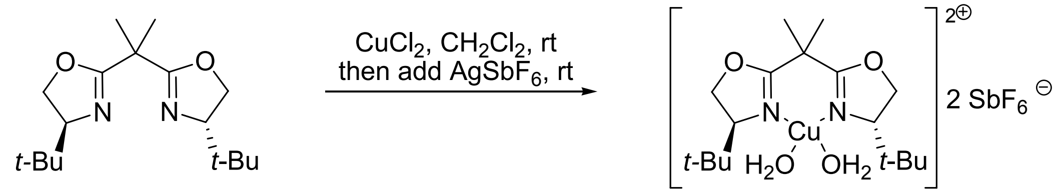
Bis(amide) S17: To an ice-cooled solution of (*S*)-*t*-leucinol (**S15**) (12.6 g, 108 mmol, 2.25 eq) in CH_2Cl_2 (50 mL, 1 mL/mmol **S16**) was added Et_3N (33.4 mL, 240 mmol, 5.0 eq) and a solution of **S16** (8.1 g, 50 mmol, 1.0 eq) in CH_2Cl_2 (50 mL, 1 mL/mmol **S16**) over a period of 20 min. The reaction mixture was warmed to room temperature, stirred for 35 min and diluted with CH_2Cl_2 (400 mL, 8 mL/mmol **S16**). The layers were separated and the organic layer was washed with aqueous 1N HCl (60 mL), sat. aqueous $NaHCO_3$ solution (60 mL), and brine (60 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Recrystallisation of the crude product from ethyl acetate provided the (*S*,*S*)-bis(amide) **S17** (10.8 g, 32.8 mmol, 69%) as a white solid: R_f 0.23 (ethyl acetate); mp = 160 °C; ^{1}H NMR (400 MHz, $CDCl_3$, δ) 0.91 (s, 18H), 1.49 (s, 6H), 1.58 (br s, 2H), 3.43 (t, *J* = 10.5 Hz, 2H), 3.80-3.89 (m, 4H), 6.35 (br d, *J* = 10.5 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$, δ) 23.6 (2 × CH_3), 26.7 (6 × CH_3), 33.3 (2 × C), 50.2 (C), 59.4 (2 × CH), 62.2 (2 × CH_2), 174.6 (2 × C=O); IR (in substance): ν 3335, 3000-2850, 1645, 1525, 1470, 1370, 1045 cm^{-1}; Anal. Calcd. for $C_{17}H_{34}N_2O_4$: C, 61.6; H, 10.4; N, 8.5. Found: C, 61.7; H, 10.9; N, 8.4.



S17

S18 (72%)

Bis(oxazoline) S18: To an ice-cooled solution of the (*S*,*S*)-bis(amide) **S17** (5.2 g, 15.7 mmol, 1 eq) and DMAP (0.2 g, 1.6 mmol, 0.1 eq) in CH_2Cl_2 (60 mL, 3.8 mL/mmol **S17**) was added Et_3N (13.3 mL, 94.4 mmol, 6 eq) and a solution of *para*-toluene sulfonyl chloride (*p*-TsCl, 6.0 g, 31.5 mmol, 2 eq) in CH_2Cl_2 (30 mL, 2 mL/mmol **S17**). The cooling bath was then removed and the solution was stirred at room temperature for 3 d. The reaction was quenched by the addition of sat. aqueous NH_4Cl solution (50 mL). The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 60 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (*i*-hexane/ethyl acetate 20/1 to 10/1) provided **S18** (3.3 g, 11.3 mmol, 72%) as a white solid: R_f 0.15 (*i*-hexane/ethyl acetate 1/1); mp = 82 °C; ^1H NMR (300 MHz, $CDCl_3$, δ) 0.86 (s, 18H), 1.50 (s, 6H), 3.83 (dd, J = 10.1 Hz, 6.9 Hz, 2H), 4.07 (dd, J = 8.6 Hz, 6.9 Hz, 2H), 4.13 (dd, J = 11.5 Hz, 10.1 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$, δ) 24.3 (2 × CH_3), 25.5 (6 × CH_3), 33.8 (2 × C), 38.5 (C), 68.9 (2 × CH), 75.2 (2 × CH_2), 168.5 (2 × C=O); IR (in substance): ν 3000-2850, 1660, 1480, 1450, 1385, 1365, 1140, 1120 cm^{-1}; Anal. Calcd. for $C_{17}H_{30}N_2O_2$: C, 69.4; H, 10.3; N, 9.5. Found: C, 69.5; H, 10.2; N, 9.5; $[\alpha]^{25}_D$: +93.6 (*c* 1.75, $CHCl_3$).



S18

10 (99%)

Catalyst 10: To a solution of **S18** (2.1 g, 7.3 mmol, 1 eq) in CH_2Cl_2 (29 mL, 4 mL/mmol **S18**) was added $CuCl_2$ (1.0 g, 7.3 mmol, 1 eq) at room temperature. The clear green solution was stirred for 3.5 h at room temperature. The solution was then filtered through a cotton pad and diluted with CH_2Cl_2 (7 mL, 1 mL/mmol **S18**). $AgSbF_6$ (5.0 g, 14.6 mmol, 2 eq) was then added and the resulting blue suspension was stirred at room temperature for 2 h in the dark. The reaction mixture was filtered through a pad of Celite and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 (5 mL) and filtered through a 2 μm PTFE syringe filter. The clear blue green solution was slowly concentrated under reduced pressure to afford **10** (6.2 g, 7.2 mmol, 99%) as a blue solid: IR (in substance): ν 3700-3000 (br, w, OH), 2970 (w, CH), 1740 (w), 1650 (w, N=C), 1480 (w), 1370 (w), 1250 (w, C-O), 1140 (m, C-N), 1070 (w), 971 (w), 946 (w), 653 (s), 640 (s) cm^{-1}.