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Catalytic asymmetric synthesis of protected α-hydroxy aldehydes and related 1,2-difunctional chiral building blocks. An enantioselective synthesis of (−)-*exo*- and (−)-*endo*-brevicomin

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Abstract: Chiral allylic alcohols which were prepared by the addition of functionalized dialkylzincs to α,β-unsaturated aldehydes in good to excellent enantioselectivity, were converted to protected α-hydroxy aldehydes and 1,2-amino alcohols without loss of enantiomeric purity. *Syn*- or *anti*-1,2-diols can be obtained stereoselectively by a second asymmetric addition to α-silyloxy aldehydes. Functionalized 1,2-diols prepared in this way were converted to enantiomerically pure (−)-*exo*- and (−)-*endo*-brevicomin (>99% *ee*). © 1997 Elsevier Science Ltd. All rights reserved.

Chiral 1,2-difunctional compounds are useful intermediates in the synthesis of more complex chiral molecules.[1] Naturally occurring α-hydroxy carbonyl compounds are widely used as sources of chirality in natural product synthesis.[1,2] Unfortunately, higher homologs bearing a longer carbon chain or further functionalities do not belong to the chiral pool and are therefore less readily available. Our target was the synthesis of chiral α-hydroxy aldehydes which are useful intermediates for the preparation of chiral 1,2-difunctional compounds, e.g. 1,2-amino alcohols or 1,2-diols. These have found numerous applications in natural product synthesis. In many cases, 1,2-difunctional chiral building blocks are obtained by asymmetric transition metal catalyzed reactions like hydrogenation,[3] epoxidation,[4] dihydroxylation[5] and aminohydroxylation[6] which are powerful tools in asymmetric synthesis.

Especially interesting are asymmetric transition metal catalyzed C–C-bond formation reactions which create a new stereocenter.[7] Recently, we have demonstrated that *functionalized* diorganozincs[8] can be added to a wide range of aldehydes which can also bear further oxygen functionalities.[8c–f,j] In the presence of Ti(O*i*-Pr)$_4$ or Ti(O*t*-Bu)$_4$ and catalytic amounts of (*R*,*R*)-1,2-*bis*(trifluoromethylsulfonamido)cyclohexane **1**, chiral secondary alcohols can be obtained with excellent enantioselectivity.[9] Our strategy for the synthesis of chiral nonnatural α-hydroxy aldehydes of type **2** or **3** was to use a double bond as an equivalent of the carbonyl group. This can be generated by simple oxidative cleavage of allylic alcohols **4** (Scheme 1).

Thus, the reaction of α,β-unsaturated aldehydes **6** (R=Ph, Me, *n*-Pr, *t*-Bu) with an excess of diorganozinc (FG-R)$_2$Zn **5** (2.0–2.7 equiv) in the presence of Ti(O*i*-Pr)$_4$ (1.25 equiv) and catalytic amounts of **1** (5 mol%) at −45°C or −45 to −20°C for 2–16 h provides the desired allylic alcohols **4a–q** in 54–93% and 70–97% *ee* (Scheme 2 and Table 1).[8l,10]

The presence of a pivaloxy group at remote position is well tolerated and provides uniformly high enantioselectivities (Table 1). In general pivalates give better results than the corresponding acetates (entries 11, 12 of Table 1) as observed before.[8f] Also secondary pivaloxy groups, difunctional and chloro-substituted organozinc compounds give excellent enantioselectivities (entries 6, 12 and 13). The use of either an aromatic unsaturated aldehyde like cinnamaldehyde **6a** or aliphatic unsaturated aldehydes such as crotonaldehyde **6b** or *E*-2-hexenal **6c** is well suited to the reaction. The steric

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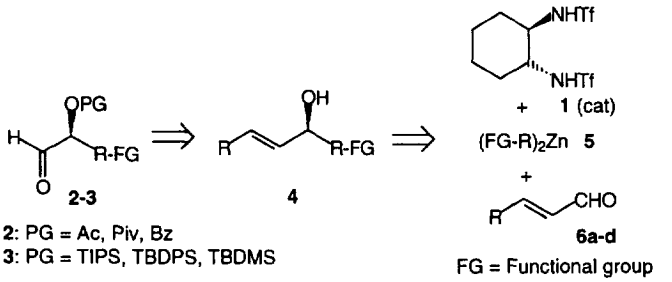
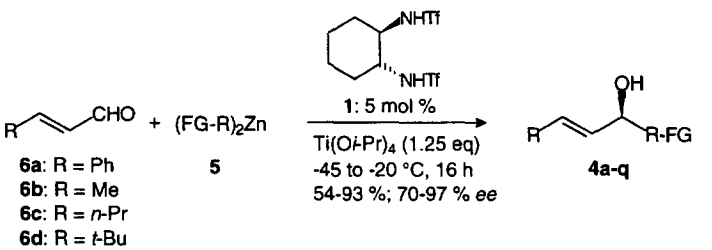


Scheme 1.



Scheme 2.

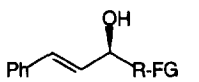
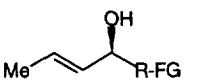
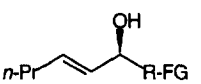
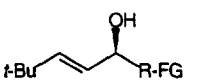
influence of the group R attached in γ-position of the α,β-unsaturated aldehyde **6** is noticeable only when unfunctionalized zinc reagents are added (compare entries 2 and 8). A bulky *t*-butyl group in the γ-position **6d** gives a significantly higher enantioselectivity (up to 97% *ee*), however, the yield decreases from 93% to 61% (compare entries 4 and 12). By replacing $Ti(O\textit{i}\text{-}Pr)_4$ with $Ti(O\textit{t}\text{-}Bu)_4$, a slight increase of the enantioselectivity can be achieved (entries 1 and 7), but slower reaction rates are observed and a higher reaction temperature must be chosen (0°C instead of −45°C).[8d]

The cleavage of the carbon–carbon double bond of products **4** has been carried out in two ways depending on the nature of the protecting group of the hydroxyl function. By using an electron withdrawing protecting group like an ester (R^1COCl, pyridine, CH_2Cl_2, rt, 16 h, R^1=Me, Ph, *t*-Bu), the ozonolysis (CH_2Cl_2, −78°C, DMS; method A; Scheme 3) proceeds in satisfactory overall yields (48–75%, Table 2) furnishing the new α-acyloxy aldehydes **2** without any loss of stereochemistry.[11] The ozonolysis gives higher yields if protected cinnamic alcohols are used instead of crotyl alcohols (entry 2 of Table 2). With an electron donating protecting group like a triisopropylsilyl group (TIPS), the ozonolysis does not proceed cleanly.[12] Better results are obtained in two steps via dihydroxylation and sodium periodate cleavage ((i) $K_2OsO_2(OH)_4$, DABCO, $K_3Fe(CN)_6$, K_2CO_3, *t*-BuOH, H_2O, 35°C, 24 h;[13] (ii) $NaIO_4$ (1.25 equiv), THF, H_2O, rt, 2–16 h; method B) leading to the desired, very stable α-silyloxy aldehydes **3** without racemization of the stereogenic carbon center at the α-position (Scheme 3 and Table 2).[14]

α-Hydroxy aldehydes are reactive key intermediates for the synthesis of other chiral 1,2-difunctional building blocks. They can readily be converted to the corresponding *N*-benzylated 1,2-amino alcohols by reductive amination.[15] Thus, the treatment of aldehydes of type **3** with benzylamine (1 equiv) and $Ti(O\textit{i}\text{-}Pr)_4$ (1.25 equiv) at rt, followed by the addition of $NaBH_3(CN)$ (0.65 equiv, rt, 20 h) furnishes the corresponding amino alcohols **7a–d** in 56–65% yield with almost identical enantiomeric excess as determined by chiral HPLC measurements (Scheme 4).[16,17]

Protected α-hydroxy aldehydes have been widely used as substrates for a further addition of organometallic compounds.[18] The addition reaction of those reagents yielding selectively the *syn*- or *anti*-1,2-diols has been investigated intensively. Especially, the chemoselective organotitanium reagents have been found very useful in chelation or nonchelation controlled addition reactions.[19] Our intention

Table 1. Chiral allylic alcohols **4a–q** obtained by the addition of diorganozincs **5** to the unsaturated aldehydes **6a–d** in the presence of **1** (5 mol%)

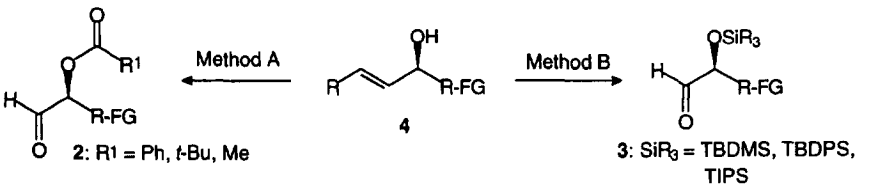
entry	aldehyde **6**	product of type **4** derived from $(FG\text{-}R)_2Zn$ **5** FG-R	yield[a] (%)	*ee*[b] (%)
	6a: R = Ph			
1	**6a**	**4a**: Pent	87 (77)	85 (87)
2	**6a**	**4b**: Oct	76	89
3	**6a**	**4c**: $(CH_2)_3OPiv$	91	90
4	**6a**	**4d**: $(CH_2)_4OPiv$	93	90
5	**6a**	**4e**: $(CH_2)_5OPiv$	91	93
6	**6a**	**4f**: $(CH_2)_3CH(OPiv)CH_2OPiv$	80	93
7	**6a**	**4g**: $(CH_2)_4Cl$	71 (50)	80 (86)
	6b: R = Me			
8	**6b**	**4h**: Oct	73	70
9	**6b**	**4i**: $(CH_2)_3OPiv$	74	92
10	**6b**	**4j**: $(CH_2)_4OPiv$	73	94
11	**6b**	**4k**: $(CH_2)_3CH(OAc)CH_2OAc$	69	83
12	**6b**	**4l**: $(CH_2)_3CH(OPiv)CH_2OPiv$	82	92
	6c: R = *n*-Pr			
13	**6c**	**4m**: $(CH_2)_3CH(OPiv)CH_3$	82	94
14	**6c**	**4n**: $(CH_2)_4OPiv$	82	95
15	**6c**	**4o**: $(CH_2)_4Cl$	68	89
	6d: R = *t*-Bu			
16	**6d**	**4p**: $(CH_2)_4OPiv$	61	97
17	**6d**	**4q**: $(CH_2)_5OPiv$	54	97

(a) Isolated yields of analytically pure products. The yields in parenthesis correspond to the reactions performed in the presence of $Ti(O\textit{t}\text{-}Bu)_4$ instead of $Ti(O\textit{i}\text{-}Pr)_4$. (b) The enantiomeric excess was determined by preparing the (*S*)-(+)-*O*-acetyl-mandelates according to ref. 10.

was to synthesize either the *syn*- or *anti*-diols **8** or **9** selectively via an asymmetric titanium catalyzed addition reaction of dialkylzincs to the functionalized α-silyloxy aldehydes **3** (Scheme 5). The newly formed stereocenter should only depend on the chirality of the catalyst.[20]

The results of the addition of Et_2Zn to several α-chiral aldehydes of type **3** under standard conditions (5 mol% **1**) are shown in Table 3.

The yield of the addition reaction increases the longer the distance between pivaloxy and carbonyl group (entries 1, 2 of Table 3). The *syn*- or *anti*-diols are obtained in good yield and with excellent



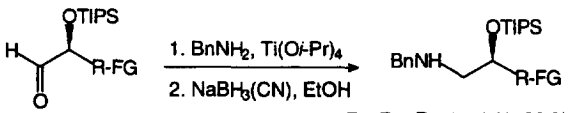
Method A: (i) R^1COCl, pyridine, CH_2Cl_2, rt, 16 h; (ii) O_3, CH_2Cl_2, -78 °C; (iii) Me_2S, -78 to 20 °C, 2 h.
Method B: (i) R_3SiCl, imidazole, DMF, 50 °C, 16 h; (ii) $K_2OsO_2(OH)_4$, DABCO, $K_3Fe(CN)_6$, K_2CO_3, *t*-BuOH, H_2O 35 °C, 24 h; (iii) $NaIO_4$, THF, H_2O, rt, 2-16 h.

Scheme 3.

Table 2. Oxidative cleavage of allylic alcohols of type **4** leading to α-acyloxy aldehydes **2** or α-silyloxy aldehydes **3** according to method A or B

entry	allylic alcohol **4**	method	product **2** or **3**	protective group PG	yield (%)[a]	*ee* (%)[b]
1	**4a**	A	**2a**: FG-R = Pent	Piv	48	87[c]
2	**4b** (**4h**)	A	**2b**: FG-R = Oct	Ac	63 (40)	89[c] (70)
3	**4c**	A	**2c**: FG-R = $(CH_2)_3OPiv$	Bz	72	90
4	**4d**	A	**2d**: FG-R = $(CH_2)_4OPiv$	Bz	75	90
5	**4e**	A	**2e**: FG-R = $(CH_2)_5OPiv$	Bz	68	93[c]
6	**4a**	B	**3a**: FG-R = Pent	TIPS	73	87
7	**4h**	B	**3b**: FG-R = Oct	TIPS	74	70
8	**4g**	B	**3c**: FG-R = $(CH_2)_4Cl$	TIPS	53	86
9	**4i** (**4c**)	B	**3d**: FG-R = $CH_2)_3OPiv$	TIPS	75 (82)	92 (90)
10	**4j** (**4d**)	B	**3e**: FG-R = $(CH_2)_4OPiv$	TIPS	83 (68)	94[d] (90)
11	**4j**	B	**3f**: FG-R = $(CH_2)_4OPiv$	TBDMS	59	94
12	**4j**	B	**3g**: FG-R = $(CH_2)_4OPiv$	TBDPS	39	94
13	**4e**	B	**3h**: FG-R = $(CH_2)_5OPiv$	TIPS	67	93
14	**4k**	B	**3i**: FG-R = $(CH_2)_3CH(OPiv)CH_2OPiv$	TIPS	76	92
15	**4n**	B	**3j**: FG-R = $(CH_2)_3CH(OPiv)CH_3$	TBDMS	69	94

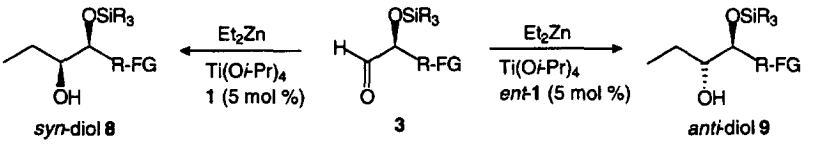
(a) Overall yield of isolated product using either method A or B. (b) Enantiomeric excess of allylic alcohols **4**. (c) See ref. 11. (d) See ref. 14.



7a: R = Pent; 56 %; 89 %*ee*
7b: R = $(CH_2)_3OPiv$; 63 %; 87 %*ee*
7c: R = $(CH_2)_4OPiv$; 65 %; 89 %*ee*
7d: R = $(CH_2)_5OPiv$; 64 %; 91 %*ee*

Scheme 4.

stereocontrol (84:16 to 95:5 diastereoselectivity). No difference between the matched or mismatched case is observed.[21] The reaction is strictly controlled by configuration of the used catalyst. Interestingly the smallest hydroxy protecting group (TBDMS, entry 4) gives the best result. This implies that not only a good shielding of the chelating hydroxy group is necessary for an efficient catalysis, but also



Scheme 5.

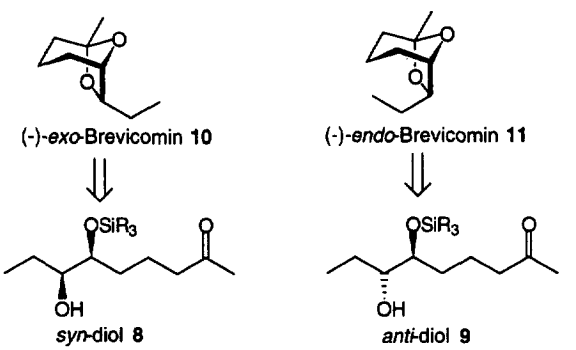
Table 3. Asymmetric catalyzed synthesis of *syn*- and *anti*-diols **8** and **9** from aldehydes **3**

entry	aldehyde 3	R-FG	protecting group		yield (%)	diastereoselectivity[a] *S,S* (*R,S*)-diastereomer
1	**3d**	$(CH_2)_3OPiv$	TIPS	**8a** (**9a**)	63 (52)	88:12 (84:16)
2	**3e**	$(CH_2)_4OPiv$	TIPS	**8b** (**9b**)	78 (76)	84:16 (92:8)
3	**3g**	$(CH_2)_4OPiv$	TBDPS	**8c**	73	93:7
4	**3f**	$(CH_2)_4OPiv$	TBDMS	**8d**	83	95:5

(a) Diastereoselectivity was determined in ^1H- and ^{13}C-NMR.

steric effects play a pivotal role in this ligand accelerated transition metal catalyzed reaction.[22] The sterically less demanding alcoholate is removed faster from the chiral titanium catalyst by the excess of Ti(O*i*Pr)$_4$. This makes the chiral addition much more faster than the competiting racemic addition catalyzed by Ti(O*i*Pr)$_4$.[8h]

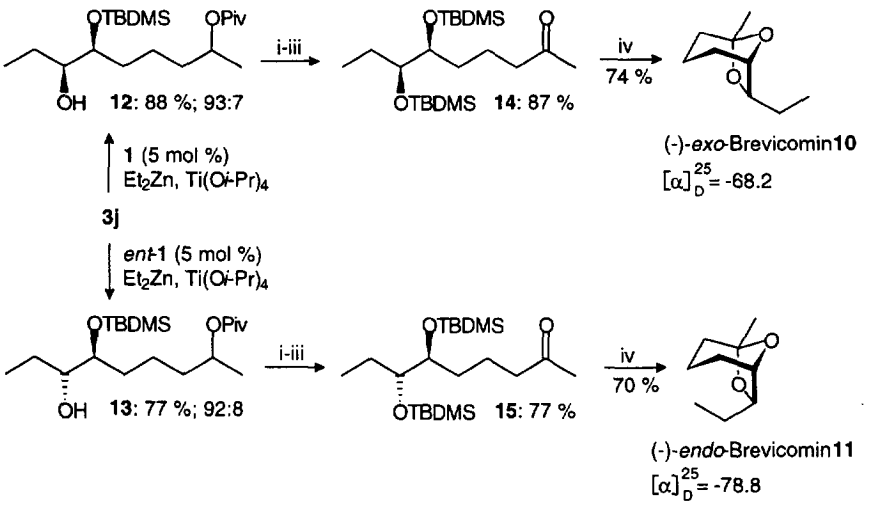
As an application of this method, we have prepared the pine beetle pheromones (−)-*exo*-brevicomin **10** and (−)-*endo*-brevicomin **11**[23,24] in high enantiomeric purity (>99% *ee*) by using α-silyloxy aldehyde **3j** (94% *ee*; entry 15 of Table 2). The retroanalysis of the chiral ketal structures **10** and **11** leads respectively to the corresponding *syn*- and *anti*-diols **8** and **9** (Scheme 6).



Scheme 6.

The addition of diethylzinc to α-silyloxy aldehyde **3j** under the usual reaction conditions (1.5–2 equiv Ti(O*i*-Pr)$_4$) in the presence of the catalyst **1** and *ent*-**1** (5 mol%) gives the two protected 1,2-diols **12** and **13** in high diastereoselectivity (93:7 and 92:8) and 88% and 77% yield (Scheme 7).[25]

These results show that the configuration of the newly formed carbinol only depends on the configuration of the catalyst and is independent of the configuration of the stereogenic center already present in α-position of the starting aldehyde **3j**.[20] Standard protection of the hydroxyl group with *t*-butyldimethylsilyl chloride (1.3 equiv; imidazole, DMF, 50°C, 16 h) followed by deprotection of the pivalic ester (DIBAL-H (3 equiv), −78 to 20°C, 1 h) and oxidation with the Dess–Martin reagent[26] (1.1 equiv, CH_2Cl_2, 0 to 20°C, 1 h) furnishes the cyclization precursors **14** and **15** in 87 and 77% overall yield. These could be deprotected and cyclized under acidic conditions (HF, CH_3CN, −20 to 20°C, 3 h) to the desired (−)-*exo*-brevicomin **10** and (−)-*endo*-brevicomin **11** (Scheme 7).[27] Both isomers



(i) TBDMSCl, imidazole, DMF, 50 °C, 16 h; (ii) DIBAL-H, THF, -78 to 20 °C, 1 h; (iii) Dess-Martin oxidation, CH_2Cl_2, 0 to 20 °C; (iv) HF, CH_3CN, -20 to 20°C, 3 h.

Scheme 7.

are obtained almost diastereomerically pure (99:1) after purification by silica gel chromatography in 74 and 70% yield, respectively. The enantiomeric excess of both natural products was >99% *ee* as shown by GC analysis using a chiral column.[27] With this method all four isomers of brevicomin are available by the same reaction pathway, only a switching of the catalyst enantiomers is necessary.

In summary, we have shown that a range of 1,2-difunctional chiral building blocks can be obtained by using an asymmetric catalytic carbon–carbon bond formation reaction. The readily available chiral allylic alcohols **4** can be converted to α-acyloxy aldehydes **2**, α-silyloxy aldehydes **3** and 1,2-amino alcohols **4** with almost complete retention of configuration. Chiral *syn*- or *anti*-1,2-diols **8** and **9** can be synthesized enantioselectively by a second asymmetric addition of an organozinc compound to α-silyloxy aldehydes **3**. As an application, we have converted the α-silyloxy aldehyde **3j** in 5 steps to either optically pure (−)-*exo*-brevicomin or (−)-*endo*-brevicomin (>99% *ee*) in 57 and 42% overall yield. Both stereocenters of the brevicomins were introduced using an asymmetric catalytic addition of organozincs.[28]

Experimental section

General considerations

All reactions with organometallic reagents were carried out under argon. Solvents (toluene, ether) were dried and freshly distilled from sodium/benzophenone. CH_2Cl_2 and DMF were freshly distilled over CaH_2. Reactions were monitored by gas–liquid-phase chromatography (GC) and thin-layer chromatography (TLC) analysis of hydrolyzed aliquots. ^{1}H- and ^{13}C-NMR were recorded on *Bruker ARX 200* and *AC 300*. IR-spectra were recorded on *Perkin–Elmer 281* and *Nicolet 511*. Optical rotations were measured with *Perkin–Elmer 241*. Mass spectra were recorded on *Varian MAT CH 7 A*. Elemental analyses were performed by the *Microanalytical Service Laboratory of the Fachbereich Chemie* (Marburg).

Starting materials

$Ti(Oi\text{-}Pr)_4$ was distilled before use. The following starting materials were prepared according to literature procedures: Dipentylzinc,[29] $Ti(Ot\text{-}Bu)_4$,[30] (*R,R*)-1,2-*bis*(trifluoromethanesulfonamido)cyclohexane **1**.[9] The alkyl iodides required for the preparation of

the corresponding dialkylzincs were prepared by standard methods: 2-acetoxy-5-iodopentyl acetate,[31] 2-pivaloxy-5-iodopentyl pivalate was prepared in analogy to ref. [31], 3-iodopropyl pivalate,[8h] 4-iodobutyl pivalate,[32] 4-iodopentyl-2-pivalate,[31,32] 5-iodopentyl pivalate,[32] 4-chloro-1-iodobutane[8h] and *E*-3-*t*-butylacrolein was prepared in analogy to ref. [33].

General procedure 1 for the preparation of functionalized dialkyzinc compounds via iodine–zinc-exchange reaction[8a]

A 100 mL two necked-flask with argon inlet, a magnetic stirring bar, a dropping funnel and a septum cap was charged with an iodoalkane (50 mmol) and CuI (29 mg, 0.3 mol%). Diethylzinc (7.7 mL, 75 mmol, 1.5 equiv) was transferred via canula to the dropping funnel (*Caution*: diethylzinc burns immediately in contact to oxygen). Diethylzinc was added dropwise to the iodoalkane at 25°C. The reaction mixture was heated to 40–75°C for several hours (see below for temperature and reaction time). The conversion of the iodoalkane was checked by gaschromatographic analysis (GC) of hydrolyzed and iodolyzed aliquots. Finally, the reaction flask was connected to the vacuum line and the formed ethyl iodide and excess diethylzinc were condensed off in vacuo (0.1 Torr, 55°C) in two cooling traps cooled with liquid nitrogen. After 2 h, decane (1.5 mL) was added and the evaporation was continued. This coevaporation procedure was repeated three times. The resulting dialkylzinc reagent was dissolved in toluene (10 mL) and ready to use.

The distilled diethylzinc collected in cooling traps was quenched by addition of mixtures of hexanes/acetone and warming to rt. *The condensation of liquid oxygen on diethylzinc should be avoided since such mixtures are explosive.*

$(FG\text{-}R)_2Zn$ from FG-RI FG-R	Temperature (°C)	Reaction time (h)
OctI	75	18
$PivO(CH_2)_3I$	55	16
$PivO(CH_2)_4I$	55	16
$PivO(CH_2)_5I$	55	16
$CH_3(PivO)CH(CH_2)_3I$	50	16
$PivOCH_2(PivO)CH(CH_2)_3I$	55	16
$AcOCH_2(AcO)CH(CH_2)_3I$	50	16
$Cl(CH_2)_4I$	40	5[a]

(a) Evaporated below 40 °C.

General procedure 2 for the asymmetric addition of functionalized dialkylzincs **5** *to aldehydes* **6**[8,9]

A 100 mL two-necked flask with an argon inlet and a septum cap was charged with toluene (4 mL), $Ti(O\textit{i}\text{-}Pr)_4$ (3.7 mL, 12.5 mmol, 1.25 equiv) and (*R*,*R*)-1,2-*bis*(trifluoromethanesulfonamido)cyclohexane **1** (567 mg, 5 mol%) and stirred for 0.5 h at 50°C. After cooling to −60°C, a solution of the functionalized dialkylzinc **5** was slowly added (2–2.7 equiv). The mixture was stirred for 0.5–1 h to reach −45°C and aldehyde **6** (10.0 mmol) was added without solvent. The reaction was slowly warmed to −20°C and stirred for 16 h. It was diluted with ether and hydrolyzed with aqueous saturated NH_4Cl and 10% aqueous HCl until a clear solution resulted. The aqueous layer was extracted with ether (3×). The combined organic layer was washed with 2N NaOH to remove the catalyst and dried ($MgSO_4$). After filtration and evaporation of the solvents, the residual oil was purified by flash chromatography (hexanes/ether) affording pure allylic alcohol **4** as colorless oil unless otherwise stated. The enantiomeric excess was determined in ^{1}H-NMR of the corresponding *O*-acetyl-mandelic ester prepared using (*S*)-(+)-*O*-acetyl-mandelic acid and DCC according to Parker's method.[8h,10] Alcohol **4** was also treated with racemic *O*-acetyl-mandelic acid providing a mixture of the two diastereomers and allowing a facile determination of the enantiomeric excess using ^{1}H-NMR spectra analysis.

General procedure 3 for the preparation of α-acyloxy aldehydes 2

Allylic alcohol **4** (1 equiv), pyridine (1.3 equiv) and DMAP (5 mol%) were dissolved in CH_2Cl_2 (1 M) and cooled to 0°C. A solution of the acid chloride (1.3 equiv) in CH_2Cl_2 was slowly added and the reaction mixture was allowed to warm to rt overnight. The mixture was hydrolyzed with 10% aqueous HCl and the aqueous layer was extracted with ether (3×). The combined organic layer was washed with aqueous saturated $NaHCO_3$, brine and dried ($MgSO_4$). After filtration and evaporation of the solvents, the residual oil was dissolved in CH_2Cl_2 (1 M) and cooled to −78°C. Ozone was bubbled through the stirred solution until a slight blue color persisted. Then, nitrogen was bubbled through the reaction mixture and after 5 min, dimethyl sulfide (2 equiv) was added at −78°C and stirred for 1 h and 2 h at rt. The mixture was evaporated and the residual oil was purified by flash chromatography affording the α-acyloxy aldehyde **2** as colorless oil.

General procedure 4 for the preparation of α-silyloxy aldehydes 3

Imidazole (1.06 g, 15.6 mmol, 2.6 equiv) and the corresponding silyl chloride (1.3–1.5 equiv) were added to a solution of allylic alcohol **4** (6.0 mmol) in DMF (2 mL) and stirred for 16 h at 50°C. The reaction mixture was diluted with hexanes/ether (4:1), filtrated over silica and eluated with hexanes/ether (4:1). After evaporation, an oily residue was obtained which was diluted in *t*-BuOH (45 mL)/water (45 mL). In this reaction mixture, $K_3[Fe(CN)_6]$ (5.94 g, 18.0 mmol) and K_2CO_3 (2.49 g, 18.0 mmol) were dissolved successively, followed by DABCO (0.33 g, 5 mol%) and $K_2OsO_2(OH)_4$ (22 mg, 0.06 mmol, 1 mol%). The reaction mixture was vigorously stirred for 24 h at 35°C. After completion of the reaction, Na_2SO_3 (0.1 g) was added and stirred for 0.5 h. Water (50 mL) and ethyl acetate (100 mL) were added and the aqueous layer was extracted with ethyl acetate (3×100 mL). The combined organic layer was washed with 10% aqueous HCl (100 mL) and aqueous saturated $NaHCO_3$ (100 mL) and dried ($MgSO_4$). After filtration, the solvent was removed *in vacuo*, the residual oil was dissolved in THF (60 mL), water (60 mL) and cooled to 0°C. Sodium periodate (1.61 g, 7.5 mmol, 1.25 equiv) was added and the reaction mixture was allowed to warm to rt and was stirred 2–16 h until completion of the reaction as checked by tlc. Ether (150 mL) was added and the aqueous layer was separated and extracted with ether (3×150 mL). The combined organic layer was dried ($MgSO_4$), filtrated and the solvents were evaporated. The pure α-silyloxy aldehyde was obtained after chromatographic purification as colorless oil.

General procedure 5 for the preparation of 1,2-amino alcohols 7[15]

A mixture of aldehyde **3** (1 equiv), Ti(O*i*-Pr)$_4$ (1.25 equiv) and benzylamine (1.25 equiv) was stirred under argon at rt for 0.5 h. Sodium cyanoborohydride (0.64 equiv) was added and the solution stirred for 16 h. Water (0.5 mL/mmol) was added and the resulting precipitate was filtered and washed with ethanol. After evaporation of the solvent, the crude product was purified by chromatography.

General procedure 6 for the asymmetric addition of diethylzinc to aldehydes 3[9]

A 50 mL two-necked flask with an argon inlet and a septum cap was charged with toluene (see below), Ti(O*i*-Pr)$_4$ (1.5–3 equiv) and (*R*,*R*)-1,2-*bis*(trifluoromethanesulfonamido)cyclohexane **1** (5 mol%), stirred for 0.5 h at 50°C and then cooled to −60°C. Diethylzinc (2–3 equiv) was slowly added to the reaction mixture. The mixture was stirred for 0.5 h, was allowed to reach the desired reaction temperature and the corresponding α-silyloxy aldehyde **3** in toluene (1 M) was added. The reaction was stirred for 12–16 h, diluted with ether and hydrolyzed with aqueous saturated NH_4Cl and 10% aqueous HCl until a clear solution resulted. The aqueous layer was extracted with ether (3×). The combined organic layer was washed with 2N NaOH to remove the catalyst and was dried ($MgSO_4$). After filtration and evaporation of the solvents, the residual oil was purified by flash chromatography (hexanes/ether) affording pure alcohol **8** as colorless oil.

Synthesis of chiral allylic alcohols ***4****: asymmetric additions to cinnamaldehyde*

E-*(S)-(+)-1-Phenyloct-1-en-3-ol* ***4a***

(a) Cinnamaldehyde (660 mg, 5.0 mmol) was treated with dipentylzinc (2.0 equiv) following *procedure 2* yielding alcohol **4a** (890 mg, 4.36 mmol, 87%, 85% *ee*) after flash chromatographic purification (hexanes/ether 4:1). Reaction conditions: −45°C, 2 h.

(b) Cinnamaldehyde (1.32 g, 10.0 mmol) was treated with dipentylzinc (2.0 equiv) following procedure 2 (0°C) with $Ti(OtBu)_4$ (2.0 equiv) instead of $Ti(OiPr)_4$ yielding alcohol **4a** (1.59 g, 7.68 mmol, 77%, 87% *ee*). Reaction conditions: 0°C to rt, 16 h. R_f=0.18 (hexanes/ether 4:1); $[\alpha]_D^{25}$=+1.5 (*c* 4.5, C_6H_6, 87% *ee*); IR (neat): 3400 (br), 2920 (s), 2860 (s), 1700 (m), 695 (m); ^{1}H-NMR ($CDCl_3$, 200 MHz): δ=7.27–7.11 (m, 5 H), 6.43 (d, *J*=16.0 Hz, 1 H), 6.09 (dd, *J*=16.0, 6.8 Hz, 1 H), 4.20–4.05 (m, 1 H), 2.24 (s, 1 H), 1.54–1.44 (m, 2 H), 1.33–1.20 (m, 6 H), 0.79 (t, *J*=6.3 Hz, 3 H); ^{13}C-NMR ($CDCl_3$, 50 MHz): δ=136.7, 132.6, 130.0, 128.4, 127.4, 126.3, 72.9, 37.2, 31.7, 25.0, 22.5, 14.0; MS (EI): *m/z* 204 (9), 133 (100), 105 (40), 99 (27), 91 (56), 55 (33); $C_{14}H_{20}O$ (204.313): calcd C 82.30, H 9.87; found C 82.95, H 9.91.

E-*(S)-(+)-1-Phenylundec-1-en-3-ol* ***4b***

Cinnamaldehyde (538 mg, 4.07 mmol) was treated with dioctylzinc (2.5 equiv, prepared via hydrozincation)[34] following *procedure 2* yielding alcohol **4b** (763 mg, 3.10 mmol, 76%, 89% *ee*) after flash chromatographic purification (hexanes/ether 4:1). Reaction conditions: −45°C, 12 h. R_f=0.41 (hexanes/ether 1:1); $[\alpha]_D^{25}$=+3.9 (*c* 2.0, $CHCl_3$); IR (neat): 3340 (br), 2920 (s), 960 (m), 745 (m), 695 (m); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ=7.23 (m, 5 H), 6.42 (d, *J*= 15.9 Hz, 1 H), 6.13 (dd, *J*= 6.8, 15.9 Hz, 1 H), 4.11 (m, 1 H), 2.41 (bs, 1 H), 1.54–1.38 (m, 2 H), 1.37–1.10 (m, 12 H), 0.79 (t, *J*= 6.4 Hz, 3 H); ^{13}C-NMR ($CDCl_3$, 50 MHz): δ=136.7, 132.6, 129.9, 128.4, 127.4, 126.3, 72.9, 37.3, 31.8, 29.52, 29.48, 29.2, 25.4, 22.6, 14.0; MS (EI): *m/z* 246 (M^+, 4), 228 (22), 143 (37), 133 (100), 91 (56); $C_{17}H_{26}O$ (246.394): calcd C 82.87, H 10.64; found C 82.61, H 10.55.

E-*(S)-(+)-4-Hydroxy-6-phenylhex-5-enyl pivalate* ***4c***

(a) Cinnamaldehyde (397 mg, 3.00 mmol) was treated with di(3-pivaloxypropyl)zinc (2.5 equiv) following *procedure 2* yielding alcohol **4c** (754 mg, 2.73 mmol, 91%, 90% *ee*) after flash chromatographic purification (hexanes/ether 4:1 to 1:1). Reaction conditions: −45 to −20°C, 16 h. R_f=0.22 (hexanes/ether 1:1); $[\alpha]_D^{25}$=+3.9 (*c* 2.3, $CHCl_3$); IR (neat): 3420 (br), 2970 (s), 2870 (s), 1725 (s), 1280 (s), 1160 (s); ^{1}H-NMR ($CDCl_3$, 200 MHz): δ=7.30–7.17 (m, 5 H), 6.51 (d, *J*=15.9 Hz, 1 H), 6.14 (dd, *J*=15.9, 6.8 Hz, 1 H), 4.22–4.27 (m, 1 H), 4.02 (t, *J*=6.2 Hz, 2 H), 1.76–1.61 (m, 5 H), 1.13 (s, 9 H); ^{13}C-NMR ($CDCl_3$, 50 MHz): δ=178.6, 136.5, 132.0, 130.7, 128.6, 127.7, 126.4, 72.6, 64.2, 38.7, 33.5, 27.2, 24.7; MS (EI): *m/z* 174 (40), 156 (31), 133 (40), 91 (43), 57 (100); $C_{17}H_{24}O_3$ (276.376): calcd C 73.88, H 8.75; found C 73.74, H 8.52.

E-*(S)-(+)-5-Hydroxy-7-phenylhept-6-enyl pivalate* ***4d***

Cinnamaldehyde (1.32 g, 10.0 mmol) was treated with di(4-pivaloxybutyl)zinc (2.5 equiv) following *procedure 2* yielding alcohol **4d** (2.70 g 9.3 mmol, 93%, 90% *ee*) after flash chromatographical purification (hexanes/ether 4:1 to 1:1). Reaction conditions: −45 to −20°C, 16 h. R_f=0.04 (hexanes/ether 4:1); $[\alpha]_D^{25}$=+8.0 (*c* 2.0, $CHCl_3$); IR (neat): 3410 (br), 2950 (s), 1725 (s), 1290 (s), 1165 (s); ^{1}H-NMR ($CDCl_3$, 200 MHz): δ=7.32–7.16 (m, 5 H), 6.50 (d, *J*=15.8 Hz, 1 H), 6.13 (dd, *J*=15.8, 6.8 Hz, 1 H), 4.22–4.12 (m, 1 H), 3.99 (t, *J*=6.2 Hz, 2 H), 1.73–1.42 (m, 7 H), 1.10 (s, 9 H); ^{13}C-NMR ($CDCl_3$, 50 MHz): δ=178.6, 136.5, 132.2, 130.4, 128.5, 127.6, 126.4, 72.8, 64.1, 38.7, 36.7, 28.5, 27.1, 21.8; MS (EI): *m/z* 290 (1), 188 (46), 170 (50), 133 (52), 91 (47), 57 (100); $C_{18}H_{26}O_3$ (290.403): calcd C 74.45, H 9.02; found C 74.36, H 8.97.

E-*(S)-(+)-6-Hydroxy-8-phenyloct-7-enyl pivalate* **4e**

Cinnamaldehyde (0.66 g, 5.00 mmol) was treated with di(5-pivaloxypentyl)zinc (2.5 equiv) following *procedure 2* yielding alcohol **4e** (1.38 g, 4.55 mmol, 91%, 93% *ee*) after flash chromatographic purification (hexanes/ether 4:1 to 1:1). Reaction conditions: −20°C, 16 h. R_f=0.25 (hexanes/ether 1:1); $[\alpha]_D^{25}$=+5.8 (*c* 2.7, $CHCl_3$); IR (neat): 3380 (br), 2920 (s), 2860 (s), 1710 (s), 1285 (s), 1155 (s); ^{1}H-NMR ($CDCl_3$, 200 MHz): δ=7.29–7.15 (m, 5 H), 6.49 (d, *J*=16.0 Hz, 1 H), 6.14 (dd, *J*=16.0, 6.8 Hz, 1 H), 4.24–4.15 (m, 1 H), 3.97 (t, *J*=6.2 Hz, 2 H), 1.76 (s, 1 H), 1.57–1.31 (m, 8 H), 1.11 (s, 9 H); ^{13}C-NMR ($CDCl_3$, 50 MHz): δ=178.6, 136.6, 132.4, 130.3, 128.5, 127.6, 126.4, 72.9, 64.3, 38.7, 37.2, 28.5, 27.2, 25.9, 25.0; MS (EI): *m/z* 304 (0.2), 156 (57), 133 (26), 91 (55), 57 (100), 41 (23); $C_{19}H_{28}O_3$ (304.430): calcd C 74.96, H 9.27; found C 74.91, H 9.17.

E-*(S)-(+)-6-Hydroxy-8-phenyl-2-pivaloxyoct-7-enyl pivalate* **4f**

Cinnamaldehyde (415 mg, 3.14 mmol) was treated with di(4,5-dipivaloxypentyl)zinc (2.2 equiv) following *procedure 2* yielding alcohol **4f** (1.02 g, 2.51 mmol, 80%, 93% *ee*) as yellowish oil after flash chromatographic purification (hexanes/ether 4:1 to 1:1). Reaction conditions: −45 to −25°C, 16 h. R_f=0.27 (hexanes/ether 1:1); $[\alpha]_D^{25}$=−4.4 (*c* 1.8, $CHCl_3$); IR (neat): 3450 (br), 2970 (m), 1725 (s), 1295 (s), 1150 (s); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ=7.35–7.20 (m, 5 H), 6.53 (d, *J*=15.9 Hz, 1 H), 6.16 (dd, *J*=6.8, 15.9 Hz, 1 H), 5.12–4.98 (m, 1 H), 4.22 (m, 1 H), 4.199/4.195 (dd, *J*=3.3, 11.8 Hz, 1 H), 3.984/3.976 (dd, *J*= 6.6, 11.8 Hz, 1 H), 1.68–1.26 (m, 7 H), 1.15 (s, 9 H), 1.13 (s, 9 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ=178.1, 177.8, 136.6, 132.2, 130.3, 128.5, 127.6, 126.4, 72.6, 72.5, 70.9, 65.0, 38.7, 36.82, 36.77, 30.61, 30.57, 27.0, 20.9, 20.8; MS (EI): *m/z* 404 (0.1, M^+), 146 (11), 131 (26), 85 (28), 57 (100); $C_{24}H_{36}O_5$ (404.547): calcd C 71.26, H 8.97; found C 70.91, H 8.71.

E-*(S)-(+)-7-Chloro-1-phenylhept-1-en-3-ol* **4g**

(a) Cinnamaldehyde (1.45 g, 11.0 mmol) was treated with di(4-chlorobutyl)zinc (2.5 equiv) following *procedure 2* yielding alcohol **4g** (1.76 g, 7.83 mmol, 71%, 80% *ee*) after flash chromatographic purification (hexanes/ether 4:1 to 1:1). Reaction conditions: −45°C, 12 h.

(b) Cinnamaldehyde (780 mg, 5.90 mmol) was treated with di(4-chlorobutyl)zinc (2.7 equiv) following *procedure 2* (0°C) with $Ti(OtBu)_4$ (2.0 equiv) instead of $Ti(OiPr)_4$ yielding alcohol **4g** (660 mg, 2.94 mmol, 50%, 86% *ee*). Reaction conditions: 0°C, 16 h. R_f=0.22 (hexanes/ether 1:1); $[\alpha]_D^{25}$=−14.4 (*c* 0.5, $CHCl_3$); IR (neat): 3400 (br), 2940 (m), 750 (s), 695 (s); ^{1}H-NMR ($CDCl_3$, 200 MHz): δ=7.67–7.18 (m, 5 H), 6.49 (dd, *J*=0.6, 15.7 Hz, 1 H), 6.13 (dd, *J*=6.8, 15.7 Hz, 1 H), 4.25–4.16 (m, 1 H), 3.46 (t, *J*=6.6 Hz, 2 H), 1.80–1.65 (m, 3 H), 1.65–1.35 (m, 4 H); ^{13}C-NMR ($CDCl_3$, 50 MHz): δ=136.5, 132.1, 130.5, 128.6, 127.7, 126.4, 72.8, 44.9, 36.4, 32.4, 22.8; MS (EI): *m/z* 224 (3, M^+), 206 (4), 133 (62), 105 (38), 91 (100); $C_{13}H_{17}OCl$ (224.731): calcd C 69.48, H 7.63; found C 69.30, H 7.42.

Asymmetric additions to crotonaldehyde

(S)-(−)-Dodec-2-en-4-ol **4h**

Crotonaldehyde (854 mg, 12.2 mmol) was treated with dioctylzinc (2.5 equiv, prepared via boron–zinc exchange)[35] following *procedure 2* yielding alcohol **4h** (1.64 g, 8.90 mmol, 73%, 70% *ee*) after flash chromatographic purification (hexanes/ether 4:1 to 1:1). Reaction conditions: −45 to −25°C, 16 h. R_f=0.32 (hexanes/ether 4:1); $[\alpha]_D^{25}$=−5.3 (*c* 0.9, $CHCl_3$); IR (neat): 3320 (br), 2960 (s), 2920 (s), 960 (m); ^{1}H-NMR ($CDCl_3$, 200 MHz): δ=5.61 (dq, *J*=15.2, 6.0 Hz, 1 H), 5.44 (ddq, *J*=15.2, 6.8, 1.0 Hz, 1 H), 3.99 (m, 1 H), 1.68–1.65 (d, *J*=6.0 Hz, 3 H), 1.50–1.17 (m, 15 H), 0.85 (t, *J*=6.0 Hz, 3 H); ^{13}C-NMR ($CDCl_3$, 50 MHz): δ=134.4, 126.5, 73.1, 37.3, 31.8, 29.6 (2 C), 29.2, 25.5, 22.6, 17.6, 14.0; MS (EI): *m/z* 184 (M^+, 0.2), 166 (1), 141 (3), 71 (100); $C_{12}H_{24}O$ (184.323): calcd C 78.20, H 13.12; found C 78.34, H 13.24.

E-*(S)-(−)-4-Hydroxyhept-5-enyl pivalate* ***4i***

Crotonaldehyde (1.06 g, 15.1 mmol) was treated with di(3-pivaloxypropyl)zinc (2.6 equiv) following *procedure 2* yielding alcohol **4i** (2.40 g, 11.2 mmol, 74%, 92% *ee*) as yellowish oil after flash chromatographic purification (hexanes/ether 4:1 to 1:1). Reaction conditions: −45 to −20°C, 16 h. R_f=0.30 (hexanes/ether 1:1); $[\alpha]_D^{25}$=−12.3 (*c* 0.6, $CHCl_3$); IR (neat): 3400 (bs), 2970 (s), 1720 (s), 1260 (s), 1150 (s); ^{1}H-NMR ($CDCl_3$, 200 MHz): δ=5.75 (dq, *J*=15.3, 6.4 Hz, 1 H), 5.51 (ddq, *J*=15.3, 6.4, 1.2 Hz, 1 H), 3.99 (t, *J*=6.2 Hz, 3 H), 2.09 (bs, 1 H), 1.79–1.48 (m, 6 H), 1.07 (s, 9 H); ^{13}C-NMR ($CDCl_3$, 50 MHz): δ=178.3, 133.9, 126.8, 72.3, 63.6, 38.6, 33.4, 27.0, 24.6, 17.5; MS (EI): *m/z* 144 (5), 103 (47), 97 (34), 71 (61), 57 (100); $C_{12}H_{22}O_3$ (214.305): calcd C 67.26, H 10.35; found C 66.97, H 10.65.

E-*(S)-(−)-5-Hydroxyoct-6-enyl pivalate* ***4j***

Crotonaldehyde (0.88 g, 12.4 mmol) was treated with di(4-pivaloxybutyl)zinc (2.4 equiv) following *procedure 2* yielding alcohol **4j** (2.06 g, 9.02 mmol, 73%, 94% *ee*) after flash chromatographic purification (hexanes/ether 4:1 to 1:1). Reaction conditions: −45 to −25°C, 16 h. The dialkylzinc compound was synthesized from 4-iodobutyl pivalate[31] (17.2 g, 60.0 mmol, 55°C, 16 h) using a solution of diethylzinc (9.2 mL, 90 mmol) in *n*-Bu_2O (15.3 mL, 90 mmol, conversion >95%). R_f =0.29 (hexanes/ether 1:1); $[\alpha]_D^{25}$=−1.1 (*c* 2.7, $CHCl_3$); IR (neat): 3400 (br), 2940 (s), 1720 (s), 1290 (s), 1170 (s); ^{1}H-NMR ($CDCl_3$, 200 MHz): δ=5.57 (dqd, *J*=15.3, 6.3, 0.5 Hz, 1 H), 5.40 (ddq, *J*=15.3, 6.3, 1.3 Hz, 1 H), 4.01 (t, *J*=6.5 Hz, 2 H), 4.00–3.80 (m, 1 H), 1.64 (ddd, *J*=6.3, 1.3, 0.5 Hz, 3 H), 1.63–1.38 (m, 6 H), 1.35 (bs, 1 H), 1.14 (s, 9 H); ^{13}C-NMR ($CDCl_3$, 50 MHz): δ=178.6, 134.1, 126.9, 72.8, 64.2, 38.7, 36.7, 28.5, 27.1, 21.8, 17.6; MS (EI): *m/z* 126 (15), 111(21), 101 (43), 71 (62), 57 (100); $C_{13}H_{24}O_3$ (228.332): calcd C 68.38, H 10.59; found C 68.36, H 10.46.

E-*(S)-(+)-6-Hydroxy-2-acetoxynon-7-enyl acetate* ***4k***

Crotonaldehyde (211 mg, 3.01 mmol) was treated with di(4,5-diacetoxypentyl)zinc (2.3 equiv) following *procedure 2* yielding alcohol **4k** (534 mg, 2.07 mmol, 69%, 83% *ee*) as yellowish, oily liquid after flash chromatographic purification (hexanes/ether 4:1 to 1:2). Reaction conditions: −45 to −25°C, 16 h. R_f=0.05 (hexanes/ether 1:1); $[\alpha]_D^{25}$=−5.2 (*c* 1.0, $CHCl_3$); IR (neat): 3470 (br), 2940 (m), 1735 (s), 1235 (s), 1045 (s); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ=5.59 (dqd, *J*=15.1, 6.6, 0.5 Hz, 1 H), 5.40 (ddq, *J*=15.1, 7.1, 0.8 Hz, 1 H), 5.05–4.97 (m, 1 H), 4.16/4.17 (dd, *J*=12.0, 3.2 Hz, 1 H), 4.00–3.93 (m, 2 H), 2.00 (s, 6 H), 1.79 (bs, 1 H), 1.64 (d, *J*=6.5 Hz, 3 H), 1.64–1.30 (m, 6 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ=170.7, 170.5, 134.1, 126.7, 72.5, 71.4, 64.9, 36.8, 30.5, 21.0, 20.6, 17.5; MS (EI): *m/z* 198 (1), 128 (17), 86 (25), 71 (54), 43 (100); $C_{13}H_{22}O_5$ (258.314): calcd C 60.45, H 8.58; found C 60.38, H 8.58.

E-*(S)-(+)-6-Hydroxy-2-pivaloyloxynon-7-enyl pivalate* ***4l***

Crotonaldehyde (225 mg, 3.21 mmol) was treated with di(4,5-dipivaloxypentyl)zinc (2.2 equiv) following *procedure 2* yielding alcohol **4l** (897 mg, 2.62 mmol, 82%, 92% *ee*) as yellowish oil after flash chromatographic purification (hexanes/ether 4:1 to 1:1). Reaction conditions: −45 to −25°C, 16 h. R_f=0.20 (hexanes/ether 1:1); $[\alpha]_D^{25}$=−1.4 (*c* 1.3, $CHCl_3$); IR (neat): 3490 (br), 1730 (s), 1290 (s), 1165 (s), 1150 (s); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ=5.62 (dq, *J*=15.2, 6.4 Hz, 1 H), 5.43 (ddd, *J*=15.2, 7.1, 1.4 Hz, 1 H), 5.09–5.02 (m, 1 H), 4.20/4.21 (dd, *J*=11.8, 3.1Hz, 1 H), 4.02–3.95 (m, 2 H), 1.66 (d, *J*=6.3 Hz, 3 H), 1.65–1.23 (m, 7 H), 1.17 (s, 9 H), 1.16 (s, 9 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ=178.0, 177.7, 134.1, 126.8, 72.6, 71.0, 65.0, 38.7, 36.78, 36.74, 30.63, 30.58, 27.0, 20.9, 20.8, 17.5; MS (EI): *m/z* 170 (5), 138 (6), 125 (7), 85 (39), 57 (100); $C_{19}H_{34}O_5$ (342.476): calcd C 66.64, H 10.01; found C 66.37, H 9.83.

Asymmetric additions to E-*2-hexenal*

E-*(S)-(−)-6-Hydroxyundec-7-enyl-2-pivalate* ***4m***

E-2-Hexenal (1.00 g, 10.2 mmol) was treated with di(4-pivaloxypentyl)zinc (2.4 equiv) following *procedure 2* yielding alcohol **4m** (2.27 g, 8.39 mmol, 82%, 94% *ee*) after flash chromatographic purification (hexanes/ether 4:1 to 1:1). Reaction conditions: −45°C, 20 h, −20°C, 20 h. R_f=0.35 (hexanes/ether 1:1); $[\alpha]_D^{25}$=−3.2 (*c* 2.2, $CHCl_3$); IR (neat): 3420 (br), 2970 (s), 1720 (s), 1280 (s), 1170 (s); ^{1}H-NMR ($CDCl_3$, 200 MHz): δ=5.49 (dt, *J*=15.4, 6.4 Hz, 1 H), 5.30 (dd, *J*=15.4, 6.9 Hz, 1 H), 4.74 (m, 1 H), 3.92 (m, 1 H), 2.33 (bs, 1 H), 1.87 (m, 2 H), 1.41–1.22 (m, 8 H), 1.06 (d, *J*=6.2 Hz, 3 H), 1.06 (s, 9 H), 0.78 (t, *J*=7.3 Hz, 3 H); ^{13}C-NMR ($CDCl_3$, 50 MHz): δ=177.9, 133.0, 131.5, 72.53, 72.50, 70.23, 70.17, 38.4, 36.82, 36.76, 35.58, 35.51, 34.0, 26.9, 22.1, 21.16, 21.02, 19.6, 13.4; MS (EI): *m/z* 125 (44), 115 (26), 103 (100), 99 (44), 57 (93); $C_{16}H_{30}O_3$ (270.413): calcd C 71.07, H 11.18; found C 70.90, H 11.01.

E-*(S)-(−)-5-Hydroxydec-6-enyl pivalate* ***4n***

E-2-Hexenal (1.02 g, 10.4 mmol) was treated with di(4-pivaloxybutyl)zinc (2.4 equiv) following *procedure 2* yielding alcohol **4n** (2.13 g, 8.54 mmol, 82%, 95% *ee*) after flash chromatographic purification (hexanes/ether 4:1 to 1:1). Reaction conditions: −45°C, 12 h. R_f=0.30 (hexanes/ether 1:1); $[\alpha]_D^{25}$=−2.0 (*c* 3.6, $CHCl_3$); IR (neat): 3400 (br), 2930 (s), 2870 (m), 1730 (s), 1270 (s), 1150 (s); ^{1}H-NMR ($CDCl_3$, 200 MHz): δ=5.57 (dt, *J*=15.3, 6.3, 1 H), 5.37 (ddt, *J*=15.3, 6.3, 1.0 Hz, 1 H), 4.01 (t, *J*=6.5 Hz, 2 H), 4.00–3.80 (m, 1 H), 1.95 (q, *J*=6.3, 2 H), 1.60–1.20 (m, 9 H), 1.14 (s, 9 H), 0.85 (t, *J*=7.2, 3 H); ^{13}C-NMR ($CDCl_3$, 50 MHz): δ=178.6, 133.0, 132.1, 72.9, 64.2, 38.7, 36.7, 34.2, 28.5, 27.1, 22.3, 21.6, 13.6; MS (EI): *m/z* 111 (41), 101 (61), 85 (28), 57 (100), 41 (31); $C_{15}H_{28}O_3$ (256.386): calcd C 70.27, H 11.01; found C 70.30, H 11.10.

E-*(S)-(+)-1-Chloro-dec-6-en-5-ol* ***4o***

E-2-Hexenal (0.98 g, 10.0 mmol) was treated with di(4-chlorobutyl)zinc (2.7 equiv) following *procedure 2* yielding alcohol **4o** (1.29 g, 6.8 mmol, 68%, 89% *ee*) after flash chromatographic purification (hexanes/ether 4:1 to 1:1). Reaction conditions: −45 to −25°C, 16 h. R_f =0.41 (hexanes/ether 1:1); $[\alpha]_D^{25}$=+0.9 (*c* 1.2, $CHCl_3$); IR (neat): 3350 (br), 2950 (s), 2880 (s), 970 (s); ^{1}H-NMR ($CDCl_3$, 200 MHz): δ=5.57 (dt, *J*=15.3, 6.3, 1 H), 5.37 (ddt, *J*=15.3, 6.3, 1.0 Hz, 1 H), 4.10–3.95 (m, 1 H), 4.01 (t, *J*=6.6 Hz, 2 H), 1.87–2.05 (m, 2 H), 1.85–1.20 (m, 9 H), 0.86 (t, *J*=7.3, 3 H); ^{13}C-NMR ($CDCl_3$, 50 MHz): δ=132.9, 132.3, 72.9, 44.9, 36.3, 34.2, 32.4, 22.8, 22.2, 13.6; MS (EI): *m/z* 147 (14), 99 (67), 57 (100), 55 (24), 41 (15); $C_{10}H_{19}OCl$ (190.714): calcd C 62.98, H 10.04; found C 62.87, H 10.14.

Asymmetric additions to E-*3-*t*-butylacrolein*

E-*(S)-(+)-8,8-Dimethyl-5-hydroxynon-6-enyl pivalate* ***4p***

E-3-*t*-Butylacrolein (337 mg, 3.00 mmol) was treated with di(4-pivaloxybutyl)zinc (2.5 equiv) following *procedure 2* yielding alcohol **4p** (500 mg, 1.85 mmol, 61%, 97% *ee*) after flash chromatographic purification (hexanes/ether 4:1 to 1:1). Reaction conditions: −45 to 25°C, 16 h. R_f=0.35 (hexanes/ether 1:1); $[\alpha]_D^{25}$=+0.1 (*c* 2.1, $CHCl_3$); IR (neat): 3400 (br), 2960 (s), 1750 (s), 1290 (s), 1160 (s); ^{1}H-NMR ($CDCl_3$, 200 MHz): δ=5.55 (dd, *J*=15.8, 0.8 Hz, 1 H), 5.29 (dd, *J*=15.8, 7.2 Hz, 1 H), 4.02 (t, *J*=6.5 Hz, 1 H), 4.01–3.99 (m, 1 H), 1.63–1.20 (m, 8 H), 1.16 (s, 9 H), 0.97 (s, 9 H); ^{13}C-NMR ($CDCl_3$, 50 MHz): δ=178.6, 143.2, 127.5, 73.2, 64.2, 38.7, 36.9, 32.7, 29.5, 28.5, 27.2, 21.9; MS (EI): *m/z* 213 (3), 111 (97), 101 (70), 57 (100); $C_{16}H_{30}O_3$ (270.413): calcd C 71.07, H 11.18; found C 70.94, H 11.30.

E-*(S)-(+)-9,9-Dimethyl-6-hydroxydec-7-enyl pivalate* ***4q***

E-3-*t*-Butylacrolein (561 mg, 5.00 mmol) was treated with di(5-pivaloxypentyl)zinc (2.7 equiv) following *procedure 2* yielding alcohol **4q** (762 mg, 2.68 mmol, 54%, 97% *ee*) after flash chromatographic purification (hexanes/ether 4:1 to 1:1). Reaction conditions: −45 to −25°C, 16 h. R_f=0.36

(hexanes/ether 1:1); $[\alpha]_D^{25}$=+1.2 (*c* 1.6, $CHCl_3$); IR (neat): 3480 (br), 2940 (s), 2860 (s), 1730 (s), 1290 (m); ^{1}H-NMR ($CDCl_3$, 200 MHz): δ=5.55 (dd, *J*=15.8, 0.8 Hz, 1 H), 5.30 (dd, *J*=15.8, 7.2 Hz, 1 H), 4.00 (t, *J*=6.5 Hz, 1 H), 4.01–3.99 (m, 1 H), 1.50–1.25 (m, 10 H), 1.15 (s, 9 H), 0.97 (s, 9 H); ^{13}C-NMR ($CDCl_3$, 50 MHz): δ=178.6, 143.1, 127.6, 73.2, 64.3, 38.7, 37.2, 32.7, 29.5, 28.6, 27.2, 25.8, 25.1; MS (EI): *m/z* 227 (5), 125 (36), 113 (29), 103 (100), 85 (28), 57 (81); $C_{17}H_{32}O_3$ (284.440): calcd C 71.79, H 11.34; found C 71.64, H 11.18.

Preparation of chiral α-acyloxy aldehydes (2)

(S)-(−)-1-Carboxy-1-hexyl pivalate ***2a***

The reaction was performed with alcohol **4a** (1.50 g, 7.30 mmol, 87% *ee*) following *procedure 3* using pivaloyl chloride yielding aldehyde **2a** (765 mg, 3.54 mmol, 48%) after chromatographic purification (hexanes/ether 4:1 to 1:1). The enantiomeric excess (92% *ee*) was determined with GC using a chiral column (FS-Lipodex E, 50 m x 0.25 mm; temperature 130°C; carrier gas nitrogen; retention time: (*S*)-enantiomer 10.6 min, (*R*)-enantiomer 11.5 min). R_f=0.28 (hexanes/ether 4:1); $[\alpha]_D^{25}$=−30.0 (*c* 3.6, $CHCl_3$); IR (neat): 2960 (s), 2930 (s), 2870 (m), 1730 (s), 1155 (s); ^{1}H-NMR ($CDCl_3$, 200 MHz): δ=9.47 (d, *J*=0.8 Hz, 1 H), 4.94 (ddd, *J*=0.8, 5.6, 8.2 Hz, 1 H), 2.15–1.76 (m, 2 H), 1.31–1.22 (m, 6 H), 1.26 (s, 9 H), 0.82 (t, *J*=6.4 Hz, 3 H); ^{13}C-NMR ($CDCl_3$, 50 MHz): δ=198.6, 178.2, 77.9, 38.8, 31.3, 28.5, 27.1, 24.5, 22.3, 13.9; MS (EI): *m/z* 185 (1), 103 (6), 85 (30), 57 (100); $C_{12}H_{22}O_3$ (214.305): calcd C 67.26, H 10.35; found C 67.18, H 10.51.

(S)-(−)-1-Carboxy-1-nonyl acetate ***2b***

(a) The reaction was performed with alcohol **4b** (256 mg, 1.04 mmol) following *procedure 3* using acetyl chloride yielding aldehyde **2b** (142 mg, 0.66 mmol, 63%) after chromatographic purification (hexanes/ether 4:1 to 1:1). The enantiomeric excess (89% *ee*) was determined with GC using a chiral column (FS-Lipodex E, 50 m×0.25 mm; oven temperature 130°C; carrier gas nitrogen; retention time: (*S*)-enantiomer 27.1 min, (*R*)-enantiomer 25.3 min).

(b) The reaction was performed with alcohol **4h** (580 mg, 2.95 mmol) following *procedure 3* using acetyl chloride yielding aldehyde **2b** (260 mg, 1.21 mmol, 40%). R_f=0.09 (hexanes/ether 4:1); $[\alpha]_D^{25}$=−21.3 (*c* 1.2, $CHCl_3$, 89% *ee*); IR (neat): 2930 (s), 2850 (s), 1745 (s), 1240 (s); ^{1}H-NMR ($CDCl_3$, 200 MHz): δ=9.47 (s, 1 H), 4.95 (dd, *J*=5.0, 8.0 Hz, 1 H), 2.14 (s, 3 H), 1.75–1.67 (m, 2 H), 1.45–1.10 (m, 12 H), 0.84 (t, *J*=6.3 Hz, 3 H); ^{13}C-NMR ($CDCl_3$, 50 MHz): δ=198.3, 170.6, 78.3, 31.7, 29.1, 29.1, 29.0, 28.5, 24.8, 22.5, 20.4, 13.9; MS (EI): *m/z* 201 (4), 141 (27), 71 (21), 57 (49), 43 (100), 28 (45); $C_{12}H_{22}O_3$ (214.305): calcd C 67.26, H 10.35; found C 67.30, H 10.31.

(S)-(−)-4-Benzoyloxy-5-oxopentyl pivalate ***2c***

The reaction was performed with alcohol **4c** (1.36 g, 4.92 mmol) following *procedure 3* using benzoyl chloride yielding aldehyde **2c** (1.09 g, 3.56 mmol, 72%) after chromatographic purification (hexanes/ether 4:1 to 1:1). R_f=0.24 (hexanes/ether 1:1);$[\alpha]_D^{25}$=−26.4 (*c* 3.1, $CHCl_3$); IR (neat): 2955 (m), 1720 (s), 1270 (s), 1160 (s), 1110 (s), 710 (s); ^{1}H-NMR ($CDCl_3$, 200 MHz): δ=9.63 (d, *J*=0.8 Hz, 1 H), 8.12–7.46 (m, 5 H), 5.24 (ddd, *J*=0.8, 5.0, 7.4 Hz, 1 H), 4.15 (t, *J*=6.2 Hz, 2 H), 2.04–1.81 (m, 4 H), 1.17 (s, 9 H); ^{13}C-NMR ($CDCl_3$, 50 MHz): δ=198.1, 178.4, 166.0, 133.6, 129.8, 128.9, 128.5, 78.1, 63.4, 38.7, 27.1, 25.6, 24.3; MS (EI): *m/z* 105 (100), 77 (27), 71 (22), 57 (26); $C_{17}H_{22}O_5$ (306.358): calcd C 66.65, H 7.24; found C 66.52, H 7.25.

(S)-(−)-5-Benzoyloxy-6-oxohexyl pivalate ***2d***

The reaction was performed with alcohol **4d** (2.37 g, 8.16 mmol) following *procedure 3* using benzoyl chloride yielding aldehyde **2d** (1.96 g, 6.12 mmol, 75%) after chromatographic purification (hexanes/ether 4:1 to 1:1). R_f=0.25 (hexanes/ether 1:1); $[\alpha]_D^{25}$=−29.5 (*c* 4.0, $CHCl_3$); IR (neat): 2960 (s), 1725 (s), 1280 (s), 1170 (m), 710 (s); ^{1}H-NMR ($CDCl_3$, 200 MHz): δ=9.63 (d, *J*=0.6 Hz, 1 H), 8.12–7.42 (m, 5 H), 5.22 (ddd, *J*=0.6, 5.4, 7.6 Hz, 1 H), 4.07 (t, *J*=6.2 Hz, 2 H), 1.97–1.57 (m,

6 H), 1.16 (s, 9 H); ^{13}C-NMR ($CDCl_3$, 50 MHz): δ=197.7, 177.9, 165.4, 133.0, 129.2, 128.4, 127.9, 77.8, 63.0, 38.1, 27.9, 27.6, 26.5, 20.9; MS (EI): *m/z* 207 (1), 105 (100), 85 (20), 77 (29), 57 (34); $C_{18}H_{24}O_5$ (320.385): calcd C 67.48, H 7.55; found C 67.13, H 7.66.

(S)-(−)-6-Benzoyloxy-7-oxoheptyl pivalate ***2e***

The reaction was performed with alcohol **4e** (1.10 g, 3.61mmol) following *procedure 3* using benzoyl chloride yielding aldehyde **2e** (818 mg, 2.45 mmol, 68%) after chromatographic purification (hexanes/ether 4:1 to 1:1). The enantiomeric excess (90% *ee*) was determined in ^{1}H-NMR after reduction of the ozonide with $NaBH_4$ in ethanol and derivatization with (*S*)-(+)-*O*-acetyl-mandelic acid. Rf =0.27 (hexanes/ether 1:1); $[\alpha]_D^{25}$=−29.9 (*c* 2.1, $CHCl_3$); IR (neat): 2950 (s), 2870 (m), 1725 (s), 1280 (s), 1160 (s), 715 (s); ^{1}H-NMR ($CDCl_3$, 200 MHz): δ=9.62 (d, *J*=0.8 Hz, 1 H), 8.12–7.43 (m, 5 H), 5.22 (dd, *J*=5.4, 7.6 Hz, 1 H), 4.04 (t, *J*=6.4 Hz, 2 H), 1.93–1.45 (m, 8 H), 1.16 (s, 9 H); ^{13}C-NMR ($CDCl_3$, 50 MHz): δ=198.5, 178.6, 166.1, 133.6, 129.8, 129.1, 128.5, 78.6, 64.0, 38.7, 28.8, 28.4, 27.1, 25.7, 24.7; MS (EI): *m/z* 122 (41), 105 (100), 77 (42), 57 (16); $C_{19}H_{26}O_5$ (334.412): calcd C 68.24, H 7.84; found C 68.22, H 7.85.

Preparation of chiral α-silyloxy aldehydes ***3***

(S)-(−)-2-(Triisopropylsilyloxy)heptanal ***3a***

The reaction was performed with alcohol **4a** (0.79 g, 3.8 mmol) following *procedure 4* using triisopropylsilyl chloride yielding aldehyde **3a** (0.81 g, 2.8 mmol, 73%) after chromatographic purification (hexanes/ether 6:1). R_f=0.75 (hexanes/ether 4:1); $[\alpha]_D^{25}$=−12.4 (*c* 1.4, $CHCl_3$); IR (neat): 2980 (s), 2940 (s), 1730 (s), 1480 (s); ^{1}H-NMR ($CDCl_3$, 200 MHz): δ=9.51 (d, *J*=2.2 Hz, 1 H), 3.96 (dt, *J*=6.0, 2.2 Hz, 1 H), 1.65–1.35 (m, 2 H), 1.30–1.11 (m, 4 H), 1.07–0.85 (m, 21 H), 0.80 (t, *J*=6.7 Hz, 3 H); ^{13}C-NMR ($CDCl_3$, 50 MHz): δ=204.8, 77.7, 32.5, 31.9, 23.6, 22.4, 17.9, 13.9, 12.2; MS (EI): *m/z* 285 (1), 243 (100), 103 (19), 75 (19), 59 (29); $C_{16}H_{34}O_2Si$ (286.513): calcd C 65.63, H 12.48; found C 65.81, H 12.24.

(S)-(−)-2-(Triisopropylsilyloxy)decanal ***3b***

The reaction was performed with alcohol **4h** (246 mg, 1.00 mmol) following *procedure 4* using triisopropylsilyl chloride yielding aldehyde **3b** (244 mg, 0.74 mmol, 74%) after chromatographic purification (hexanes/ether 6:1). R_f=0.76 (hexanes/ether 4:1); $[\alpha]_D^{25}$=−12.2 (*c* 0.5, $CHCl_3$); IR (neat): 2980 (s), 2950 (s), 1730 (m); ^{1}H-NMR ($CDCl_3$, 200 MHz): δ=9.61 (d, *J*=2.2 Hz, 1 H), 4.06 (dt, *J*=5.9, 2.1 Hz, 1 H), 1.76–1.61 (m, 2 H), 1.47–1.16 (m, 14 H), 1.10–0.96 (m, 21 H), 0.86 (t, *J*=5.3 Hz, 3 H); ^{13}C-NMR ($CDCl_3$, 50 MHz): δ=204.7, 77.7, 33.6, 31.9, 30.3, 29.7, 29.4, 29.2, 24.0, 22.7, 17.9, 14.1, 12.0; MS (EI): *m/z* 300 (1.9), 286 (22), 285 (100), 157 (11), 59 (20); $C_{19}H_{40}O_2Si$ (328.613): calcd C 69.45, H 12.27; found C 69.45, H 12.39.

(S)-(−)-6-Chloro-2-(triisopropylsilyloxy)hexanal ***3c***

The reaction was performed with alcohol **4g** (652 mg, 2.90 mmol) following *procedure 4* using triisopropylsilyl chloride yielding aldehyde **3c** (472 mg, 1.54 mmol, 53%) after chromatographic purification (hexanes/ether 6:1). R_f=0.58 (hexanes/ether 4:1); $[\alpha]_D^{25}$=−12.6 (*c* 1.9, $CHCl_3$); IR (neat): 2990 (s), 2950 (s), 1740 (s), 1130 (m), 750 (s); ^{1}H-NMR ($CDCl_3$, 200 MHz): δ=9.60 (d, *J*=2.0 Hz, 1 H), 4.05 (dt, *J*=2.0, 5.5 Hz, 1 H), 3.46 (t, *J*=6.5 Hz, 2 H), 1.82–1.32 (m, 6 H), 1.17–0.90 (m, 21 H); ^{13}C-NMR ($CDCl_3$, 50 MHz): δ=204.4, 77.3, 44.5, 32.5, 21.4, 17.9, 17.5, 12.2; MS (EI): *m/z* 277 (5), 263 (100), 131 (16), 75 (32), 59 (38); $C_{15}H_{31}O_2ClSi$ (306.950): calcd C 58.70, H 10.18; found C 58.83, H 10.16.

(S)-(−)-5-Oxo-4-(triisopropylsilyloxy)pentyl pivalate ***3d***

(a) The reaction was performed with alcohol **4i** (364 mg, 1.70 mmol) following *procedure 4* using triisopropylsilyl chloride yielding aldehyde **3d** (455 mg, 1.27 mmol, 75%) after chromatographic purification (hexanes/ether 6:1).

(b) The reaction was performed with alcohol **4c** (1.11 g, 4.0 mmol) following *procedure 4* using triisopropylsilyl chloride yielding aldehyde **3d** (1.18 g, 3.3 mmol, 82%). R_f=0.66 (hexanes/ether 4:1); $[\alpha]_D^{25}$=−15.8 (*c* 0.5, $CHCl_3$); IR (neat): 2930 (s), 2860 (s), 1725 (s), 1290 (m), 1160 (s); ^{1}H-NMR ($CDCl_3$, 200 MHz): δ=9.60 (d, *J*=1.9 Hz, 1 H), 4.08–4.03 (m, 1 H), 3.99 (t, *J*=6.0 Hz, 2 H), 1.84–1.50 (m, 4 H), 1.13 (s, 9 H), 1.12–0.90 (m, 21 H); ^{13}C-NMR ($CDCl_3$, 50 MHz): δ=204.5, 178.5, 77.0, 63.9, 38.7, 30.0, 27.1, 23.4, 17.9, 12.2; MS (EI): *m/z* 213 (70), 159 (28), 75 (32), 57 (100); $C_{19}H_{38}O_4Si$ (358.595): calcd C 63.64, H 10.68; found C 63.65, H 10.56.

(S)-(−)-6-Oxo-5-(triisopropylsilyloxy)hexyl pivalate ***3e***

(a) The reaction was performed with alcohol **4j** (2.00 g, 8.75 mmol) following *procedure 4* using triisopropylsilyl chloride yielding aldehyde **3e** (2.70 g, 7.25 mmol, 83%) after chromatographic purification (hexanes/ether 6:1). The enantiomeric excess (92% *ee*) was determined in ^{13}C-NMR after reduction with $NaBH_4$ in ethanol and derivatization with (*S*)-(+)-*O*-acetyl-mandelic acid.

(b) The reaction was performed with alcohol **4d** (1.03 g, 3.7 mmol) following *procedure 4* using triisopropylsilyl chloride yielding aldehyde **3e** (0.94 g, 2.5 mmol, 68%). R_f=0.66 (hexanes/ether 4:1); $[\alpha]_D^{25}$=−18.2 (*c* 0.9, $CHCl_3$); IR (neat): 2920 (s), 2860 (s), 1720 (s), 1160 (s); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ=9.61 (d, *J*=2.0 Hz, 1 H), 4.06 (dt, *J*=2.0, 5.8 Hz, 1 H), 4.01 (t, *J*=6.2 Hz, 2 H), 1.72–1.36 (m, 6 H), 1.15 (s, 9 H), 1.14–0.99 (m, 21 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ=204.5, 178.5, 77.4, 63.9, 38.7, 33.1, 28.8, 27.1, 20.6, 17.9, 12.2; MS (EI): *m/z* 343 (5), 329 (20), 227 (48), 85 (28), 57 (100); $C_{20}H_{40}O_4Si$ (372.622): calcd C 64.47, H 10.82; found C 64.49, H 10.86.

(S)-(−)-6-Oxo-5-(t-butyldimethylsilyloxy)hexyl pivalate ***3f***

The reaction was performed with alcohol **4j** (840 mg, 5.59 mmol) following *procedure 4* using *t*-butyldimethylsilyl chloride yielding aldehyde **3f** (860 mg, 2.60 mmol, 59%) after chromatographic purification (hexanes/ether 6:1). R_f=0.29 (hexanes/ether 4:1); $[\alpha]_D^{25}$=−6.9 (*c* 1.4, $CHCl_3$); IR (neat): 2950 (s), 2860 (m), 1720 (s), 1260 (m), 1160 (s), 850 (s); ^{1}H-NMR ($CDCl_3$, 200 MHz): δ=9.56 (d, *J*=1.6 Hz, 1 H), 4.01 (t, *J*=6.2 Hz, 2 H), 3.99 (dt, *J*=1.4, 5.8 Hz, 1 H), 1.70–1.52 (m, 4 H), 1.51–1.35 (m, 2 H), 1.15 (s, 9 H), 0.88 (s, 9 H), 0.05 (s, 3 H), 0.03 (s, 3 H); ^{13}C-NMR ($CDCl_3$, 50 MHz): δ=204.1, 178.5, 77.5, 63.9, 38.7, 32.2, 28.5, 27.1, 25.7, 21.2, 18.1, −4.7, −5.0; MS (EI): *m/z* 301 (5), 171 (31), 159 (46), 75 (46), 73 (42), 57 (100); $C_{17}H_{34}O_4Si$ (330.541): calcd C 61.77, H 10.37; found C 61.56, H 10.29.

(S)-(−)-6-Oxo-5-(t-butyldiphenylsilyloxy)hexyl pivalate ***3g***

The reaction was performed with alcohol **4j** (729 mg, 3.18 mmol) following *procedure 4* (Dihydroxylation 48 h, periodate cleavage 24 h) using *t*-butyldiphenylsilyl chloride yielding aldehyde **3g** (560 mg, 1.20 mmol, 39%) after chromatographic purification (hexanes/ether 4:1). R_f=0.38 (hexanes /ether 4:1); $[\alpha]_D^{25}$=−4.1 (*c* 0.9, $CHCl_3$); IR (neat): 3050 (w), 2960 (m), 2940 (m), 2860 (w), 1720 (s), 1150 (s), 700 (s); ^{1}H-NMR ($CDCl_3$, 200 MHz): δ=9.58 (d, *J*=1.4 Hz, 1 H), 7.66–7.61 (m, 4 H), 7.42–7.37 (m, 6 H), 4.04 (dt, *J*=1.4, 5.8 Hz, 1 H), 3.97 (t, *J*=6.1 Hz, 2 H), 1.77–1.24 (m, 6 H), 1.16 (s, 9 H), 1.07 (s, 9 H);^{13}C-NMR ($CDCl_3$, 50 MHz): δ=203.8, 178.5, 135.76, 135.69, 132.99, 132.87, 130.0, 127.8, 77.7, 63.9, 38.7, 32.5, 28.5, 27.2, 26.9, 20.6, 19.3; MS (EI): *m/z* 397 (9), 283 (53), 227 (32), 199 (100), 57 (77); $C_{27}H_{38}O_4Si$ (454.683): calcd C 71.32, H 8.42; found C 71.26, H 8.44.

(S)-(−)-7-Oxo-6-(triisopropylsilyloxy)heptyl pivalate ***3h***

The reaction was performed with alcohol **4e** (1.29 g, 4.3 mmol) following *procedure 4* using triisopropylsilyl chloride yielding aldehyde **3h** (1.10 g, 2.8 mmol, 67%) after chromatographic purification (hexanes/ether 9:1 to 4:1). R_f=0.26 (hexanes/ether 9:1); $[\alpha]_D^{25}$=−14.1 (*c* 5.1, $CHCl_3$); IR (neat): 2940 (s), 2870 (s), 2790 (w), 1715 (s), 1150 (s); ^{1}H-NMR ($CDCl_3$, 200 MHz): δ=9.61 (d, *J*=2.2 Hz, 1 H), 4.06 (dt, *J*=2.2, 5.9 Hz, 1 H), 4.00 (t, *J*=6.4 Hz, 2 H), 1.80–1.19 (m, 8 H), 1.16 (s, 9 H), 1.03–0.99 (m, 21 H); ^{13}C-NMR ($CDCl_3$, 50 MHz): δ=204.7, 178.5, 77.4, 64.1, 38.7, 33.4, 28.4, 27.1, 26.1, 23.6, 17.9, 12.1; MS (EI): *m/z* 125 (30), 103 (59), 99 (31), 57 (100); $C_{21}H_{42}O_4Si$ (386.649): calcd C 65.24, H 10.95; found C 64.96, H 10.65.

(S)-(−)-7-Oxo-2-pivaloxy-6-(triisopropylsilyloxy)heptyl pivalate ***3i***

The reaction was performed with alcohol **4l** (685 mg, 2.00 mmol) following *procedure 4* using triisopropylsilyl chloride yielding aldehyde **3i** (734 mg, 1.51 mmol, 76%) after chromatographic purification (hexanes/ether 4:1). R_f=0.16 (hexanes/ether 4:1); $[\alpha]_D^{25}$=−7.4 (*c* 1.3, $CHCl_3$); IR (neat): 2900 (s), 1730 (s), 1290 (s), 1160 (s); ^{1}H-NMR ($CDCl_3$, 200 MHz): δ=9.60 (d, *J*=2.0 Hz, 1 H), 5.06–4.99 (m, 1 H), 4.19 (dd, *J*=11.8, 3.3 Hz, 1 H), 4.05 (m, 1 H), 3.95 (dd, *J*=11.8, 6.4 Hz, 1 H), 1.87–1.34 (m, 6 H), 1.33–1.13 (m, 21 H), 1.05 (s, 9 H), 1.03 (s, 9 H); ^{13}C-NMR ($CDCl_3$, 50 MHz): δ=204.4, 178.0, 177.7, 77.3, 70.8, 70.7, 64.9, 64.8, 38.7, 33.2, 30.9, 27.1, 19.6, 17.9, 12.2; MS (EI): *m/z* 457 (1), 239 (29), 215 (20), 85 (21), 57 (100); $C_{26}H_{50}O_6Si$ (486.766): calcd C 64.16, H 10.35; found C 63.92, H 10.30.

(S)-(−)-7-Oxo-6-(t-butyldimethylsilyloxy)heptyl-2-pivalate ***3j***

The reaction was performed with alcohol **4m** (1.63 g, 6.02 mmol) following *procedure 4* using *t*-butyldimethylsilyl chloride yielding aldehyde **3j** (1.44 g, 4.18 mmol, 69%) after chromatographic purification (hexanes/ether 4:1). R_f=0.69 (hexanes/ether 1:1); $[\alpha]_D^{25}$=−11.6 (*c* 1.2, $CHCl_3$); IR (neat): 2950 (s), 2865 (m), 2800 (w), 1720 (s), 1160 (s); ^{1}H-NMR ($CDCl_3$, 200 MHz): δ=9.50 (d, *J*=1.6 Hz, 1 H), 4.83–4.74 (m, 1 H), 3.89 (dt, *J*=5.0, 1.4 Hz, 1 H), 1.60–1.30 (m, 6 H), 1.10 (d, *J*=6.2 Hz, 3 H), 1.10 (s, 9 H), 0.84 (s, 9 H), 0.00 (s, 6 H); ^{13}C-NMR ($CDCl_3$, 50 MHz): δ=203.83, 203.75, 177.85, 77.44, 77.40, 69.99, 69.90, 38.54, 35.79, 35.63, 32.28, 26.99, 25.61, 20.58, 20.47, 19.69, 18.04, −4.78, −5.09; MS (EI): *m/z* 315 (5), 185 (40), 171 (34), 159 (58), 75 (81), 57 (100); $C_{18}H_{36}O_4Si$ (344.568): calcd C 62.74, H 10.53; found C 62.76, H 10.55.

Preparation of 1,2-amino alcohols

(S)-(+)-N-Benzyl-2-(triisopropylsilyloxy)heptylamin ***7a***

The reaction was performed with aldehyde **3a** (0.28 g, 1.0 mmol) following general *procedure 5* yielding amino alcohol **7a** (0.21 g, 0.56 mmol, 56%) after chromatographic purification (hexanes/ether 2:1). HPLC analysis on chiral column (Daicel Chiralcel OD, heptane: isopropanol 98:2, flow 0.6 mL/min) showed 89% *ee* (*S*-enantiomer 6.00 min, *R*-enantiomer 6.32 min). R_f=0.10 (hexanes/ether 2:1); $[\alpha]_D^{25}$=+14.9 (*c* 1.4, $CHCl_3$); IR (neat): 3028 (w), 2944 (s), 2865 (s), 1464 (s), 1058 (s); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ=7.33–7.22 (m, 5 H), 3.95 (m, 1 H), 3.86 (d, *J*=13.4 Hz, 1 H), 3.78 (d, *J*=13.4, 1 H), 2.67 (m, 2 H), 1.65–1.55 (m, 4 H), 1.24–1.20 (m, 5H), 1.06 (s, 21 H), 0.89 (t, *J*=6.9 Hz), 3 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ=140.7, 128.3, 127.9, 126.7, 72.3, 54.4, 54.2, 35.6, 32.1, 24.9, 22.7, 18.2, 14.0, 12.7; MS (EI): m/z 377 (6), 334 (65), 257 (21), 157 (28), 120 (100), 91 (90); $C_{22}H_{43}NOSi$ (365.65): calcd C 73.14, H 11.47, N 3.71; found C 72.67, H 11.36, N 4.10.

(S)-(+)-5-N-Benzylamino-4-(triisopropylsilyloxy)pentyl pivalate ***7b***

The reaction was performed with aldehyde **3d** (0.70 g, 2.0 mmol) following general *procedure 5* yielding amino alcohol **7b** (0.57 g, 1.27 mmol, 63%) after chromatographic purification (hexanes/ether 2:1). HPLC analysis on chiral column (Daicel Chiralcel OD, heptane: isopropanol 98:2, flow 0.9 mL/min) showed 87% *ee* (*S*-enantiomer 5.79 min, *R*-enantiomer 12.41 min). R_f=0.13 (hexanes/ether

2:1); $[\alpha]_D^{25}$=+6.9 (*c* 6.5, $CHCl_3$); IR (neat): 3029 (w), 2945 (s), 2867 (s), 1729 (s), 1457 (m), 1155 (s); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ=7.28–7.18 (m, 5 H), 4.02 (m, 2 H), 3.96 (m, 1 H), 3.80 (d, *J*=13.3 Hz, 1 H), 3.73 (d, *J*=13.3 Hz, 1 H), 2.63 (m, 2 H), 1.72–1.56 (m, 5 H), 1.16 (s, 9H), 1.02 (s, 21 H); ^{13}C-NMR ($CDCl_3$, 75 MHZ): δ=178.5, 140.6, 128.3, 128.0, 126.8, 126.4, 71.7, 64.5, 54.1, 38.7, 31.8, 27.2, 24.4, 18.0; MS (EI), 449 (3), 406 (14), 304 (3), 227 (20), 120 (100), 91 (78); $C_{26}H_{47}NO_3Si$ (449.73): calcd C 69.43, H 10.54, N 3.12; found C 69.33, H 10.71, N 3.34.

*(S)-(+)-6-*N*-Benzylamino-5-(triisopropylsilyloxy)hexyl pivalate* ***7c***

The reaction was performed with aldehyde **3e** (0.23 g, 0.6 mmol) following general *procedure 5* yielding amino alcohol **7c** (0.18 g, 0.38 mmol, 65%) after chromatographic purification (hexanes/ether 2:1). HPLC analysis on chiral column (Daicel Chiralcel OD, heptane: isopropanol 98:2, flow 0.6 mL/min) showed 89% *ee* (*S*-enantiomer 7.92 min, *R*-enantiomer 15.36 min). R_f=0.10 (hexanes/ether 2:1); $[\alpha]_D^{25}$=+6.4 (*c* 4.4, $CHCl_3$); IR (neat): 3030 (w), 2942 (s), 2866 (s), 1728 (s), 1460 (m), 1156 (s); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ=7.30–7.17 (m, 5 H), 4.00 (t, *J*=6.5, 2 H), 3.90 (m, 1 H), 3.78 (d, *J*=13.3 Hz, 1 H), 3.72 (d, *J*=13.3 Hz, 1 H), 2.62 (m, 2H), 1.65–1.52 (m, 5 H), 1.37–1.32 (m, 2 H), 1.20 (s, 9 H), 1.00 (s, 21 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ=178.6, 140.7, 128.3, 128.0, 126.8, 72.1, 64.3, 54.4, 38.7, 35.2, 29.0, 27.2, 22.3, 18.2, 12.7; MS (EI): m/z 463 (1), 420 (15), 120 (100), 91 (81); $C_{27}H_{49}NO_3Si$ (463.75): calcd C 69.92, H 10.65, N 3.02; found C 69.94, H 10.64, N 3.36.

*(S)-(+)-7-*N*-Benzylamino-6-(triisopropysilyloxy)heptyl pivalate* ***7d***

The reaction was performed with aldehyde **3h** (0.60 g, 2.1 mmol) following general *procedure 5* yielding amino alcohol **7d** (0.64 g, 1.34 mmol, 64%) after chromatographic purification (hexanes/ether 2:1). HPLC analysis on chiral column (Daicel Chiralcel OD, heptane: isopropanol 98:2, flow 0.9 mL/min) showed 91% *ee* (*S*-enantiomer 7.91 min, *R*-enantiomer 10.55 min). R_f=0.09 (hexanes/ether 2:1); $[\alpha]_D^{25}$=+5.9 (*c* 4.3, $CHCl_3$); IR (neat): 3030 (w), 2944 (s), 2867 (s), 1725 (s), 1461 (s), 1159 (s); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ=7.26–7.15 (m, 5 H), 3.99 (t, *J*=6.6 Hz, 2 H), 3.87 (m, 1 H), 3.77 (d, *J*=13.4 Hz, 1 H), 3.71 (d, *J*=13.4 Hz, 1 H), 2.60 (m, 2 H), 1.58–1.47 (m, 5 H), 1.34–1.26 (m, 4 H), 1.18, (s, 9 H), 0.98 (s, 21 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ =178.6, 140.7, 128.3, 128.0, 126.8, 72.1, 64.4, 54.2, 38.8, 35.5, 28.7, 27.2, 26.3, 24.8, 18.2, 12.7; MS (EI): m/z 477 (3), 434 (25), 120 (100), 91 (91); $C_{28}H_{51}NO_3Si$ (477.78): calcd C 70.38, H 10.76, N 2.93; found C 70.20, H 10.31, N 2.72.

Preparation of diols ***8*** *and* ***9*** *by asymmetric addition of diethylzinc to aldehydes* ***3***

(5S)-(+)-Hydroxy-(4S)-(triisopropylsilyloxy)heptyl pivalate ***8a***

Aldehyde **3d** (216 mg, 0.60 mmol) was treated with diethylzinc (2.5 equiv), Ti(O*i*-Pr)$_4$ (3.0 equiv) in toluene (1.5 mL) following *procedure 6* yielding alcohol **8a** (146 mg, 0.38 mmol, 63%, diastereoselectivity 88:12) after flash chromatographic purification (hexanes/ether 4:1). Reaction conditions: −40 to −15°C, 16 h. R_f=0.22 (hexanes/ether 4:1); $[\alpha]_D^{25}$=+7.9 (*c* 1.6, $CHCl_3$); IR (neat): 3450 (br), 2860 (s), 1710 (s), 1280 (s), 1150 (s), 650 (s); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ=4.05–3.95 (m, 2 H), 3.73–3.68 (m, 1 H), 3.38–3.30 (m, 1 H), 2.19 (d, *J*=7.3 Hz, 1 H), 1.75–1.43 (m, 6 H), 1.15 (s, 9 H), 1.08–1.00 (m, 21 H), 0.92 (t, *J*=7.8 Hz, 3 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ=178.2, 74.5, 73.7, 64.2, 38.5, 30.2, 26.9, 26.7, 24.0, 17.9, 12.6, 10.2; MS (EI): *m/z* 345 (1), 243 (41), 113 (48), 95 (100), 57 (91); $C_{21}H_{44}O_4Si$ (388.665): calcd C 64.90, H 11.41; found C 64.70, H 11.47.

(5R)-(+)-Hydroxy-(4S)-(triisopropylsilyloxy)heptyl pivalate ***9a***

Aldehyde **3d** (208 mg, 0.58 mmol) was treated with diethylzinc (2.5 equiv), Ti(O*i*-Pr)$_4$ (3.0 equiv) and *ent*-**1** (5 mol%) in toluene (1.5 mL) following *procedure 6* yielding alcohol **9a** (116 mg, 0.30 mmol, 52%, diastereoselectivity 84:16) after flash chromatographic purification (hexanes/ether 4:1). Reaction conditions: −40 to −15°C, 16 h. R_f=0.22 (hexanes/ether 4:1); $[\alpha]_D^{25}$=+5.9 (*c* 1.1, $CHCl_3$); IR (neat): 3450 (br), 2860 (s), 1710 (s), 1280 (s), 1150 (s), 650 (s); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ=4.01 (t, *J*=5.9 Hz, 2 H), 3.83–3.78 (m, 1 H), 3.58–3.54 (m, 1 H), 2.24 (d, *J*=2.9 Hz, 1 H), 1.78–1.37

(m, 6 H), 1.21 (s, 9 H), 1.05–1.01 (m, 21 H), 0.95 (t, J=7.4 Hz, 3 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ=178.3, 75.9, 74.4, 64.3, 38.5, 27.7, 26.9, 24.6, 24.5, 17.9, 12.4, 10.4; MS (EI): *m/z* 345 (5), 243 (71), 227 (38), 113 (62), 95 (100), 57 (87); $C_{21}H_{44}O_4Si$ (388.665): calcd C 64.90, H 11.41; found C 64.73, H 11.63.

(6S)-(+)-Hydroxy-(5S)-(triisopropylsilyloxy)octyl pivalate ***8b***

Aldehyde **3e** (382 mg, 1.03 mmol) was treated with diethylzinc (3.0 equiv), Ti(O*i*-Pr)$_4$ (2.5 equiv) in toluene (1.5 mL) following *procedure 6* yielding alcohol **8b** (322 mg, 0.80 mmol, 78%, diastereoselectivity 84:16) after flash chromatographic purification (hexanes/ether 4:1). Reaction conditions: −40 to −20°C, 16 h. R_f=0.26 (hexanes/ether 4:1); $[\alpha]_D^{25}$=+6.0 (*c* 2.1, $CHCl_3$); IR (neat): 3450 (br), 2860 (s), 1710 (s), 1290 (s), 1155 (s); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ=4.01 (t, J=6.2 Hz, 2 H), 3.67 (m, 1 H), 3.34 (m, 1 H), 2.22 (bs, 1 H), 1.70–1.27 (m, 8 H), 1.16 (s, 9 H), 1.05–1.01 (m, 21 H), 0.95 (t, J=7.3 Hz, 3 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ=178.5, 75.1, 74.0, 64.1, 38.7, 33.6, 29.0, 27.1, 26.9, 21.4, 18.1, 12.8, 10.4; MS (EI): *m/z* 359 (12), 215 (44), 127 (83), 109 (100), 85 (68), 57 (88); $C_{22}H_{46}O_4Si$ (402.692): calcd C 65.62, H 11.51; found C 65.41, H 11.47.

(6R)-(−)-Hydroxy-(5S)-(triisopropylsilyloxy)octyl pivalate ***9b***

Aldehyde **3e** (372 mg, 1.00 mmol) was treated with diethylzinc (3.0 equiv), Ti(O*i*-Pr)$_4$ (2.5 equiv) and *ent*-**1** (5 mol%) in toluene (1.5 mL) following *procedure 6* yielding alcohol **9b** (305 mg, 0.76 mmol, 76%, diastereoselectivity 92:8) after flash chromatographic purification (hexanes/ether 4:1). Reaction conditions: −40 to −20°C, 16 h. R_f=0.26 (hexanes/ether 4:1); $[\alpha]_D^{25}$=−6.4 (*c* 0.8, $CHCl_3$); IR (neat): 3450 (br), 2860 (s), 1710 (s), 1290 (s), 1155 (s); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ=4.00 (t, J=6.2 Hz, 2 H), 3.78–3.75 (m, 1 H), 3.52 (m, 1 H), 2.22 (bs, 1 H), 1.62–1.31 (m, 8 H), 1.13 (s, 9 H), 1.03–0.99 (m, 21 H), 0.93 (t, J=7.4 Hz, 3 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ=178.2, 75.9, 74.9, 63.9, 38.4, 31.0, 28.9, 26.9, 24.4, 21.9, 17.9, 12.5, 10.4; MS (EI): *m/z* 359 (12), 215 (44), 127 (83), 109 (100), 85 (68), 57 (88); $C_{22}H_{46}O_4Si$ (402.692): calcd C 65.62, H 11.51; found C 65.42, H 11.66.

(6S)-(+)-Hydroxy-(5S)-(t-butyldiphenylsilyloxy)octyl pivalate ***8c***

Aldehyde **3g** (490 mg, 1.08 mmol) was treated with diethylzinc (1.85 equiv), Ti(O*i*-Pr)$_4$ (1.85 equiv) in toluene (2 mL) following *procedure 6* yielding alcohol **8c** (380 mg, 0.79 mmol, 73%, diastereoselectivity 93:7) after flash chromatographic purification (hexanes/ether 4:1). Reaction conditions: −50 to −20°C, 16 h. R_f=0.49 (hexanes/ether 1:1); $[\alpha]_D^{25}$=+19.8 (*c* 1.1, $CHCl_3$); IR (neat): 3490 (br), 2950 (s), 1715 (s), 1280 (s), 1160 (s), 1110 (s), 700 (s); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ=7.68–7.65 (m, 4 H), 7.43–7.35 (m, 6 H), 3.84 (t, J=6.3 Hz, 2 H), 3.58 (m, 1 H), 3.38 (m, 1 H), 2.17 (d, J=7.1 Hz, 1 H), 1.65–1.20 (m, 8 H), 1.15 (s, 9 H), 1.06 (s, 9 H), 0.87 (t, J=7.4 Hz, 3 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ=178.4, 135.9, 134.8, 134.0, 129.8, 129.7, 127.7, 127.5, 75.8, 74.3, 64.0, 38.6, 32.9, 28.5, 27.12, 27.10, 26.6, 21.3, 19.5, 10.2; MS (EI): *m/z* 427 (3), 325 (17), 199 (100), 109 (55), 57 (31); $C_{29}H_{44}O_4Si$ (484.753): calcd C 71.85, H 9.15; found C 71.91, H 9.08.

(6S)-(+)-Hydroxy-(5S)-(t-butyldimethylsilyloxy)octyl pivalate ***8d***

Aldehyde **3f** (530 mg, 1.59 mmol) was treated with diethylzinc (2.4 equiv), Ti(O*i*-Pr)$_4$ (2.4 equiv) in toluene (2.5 mL) following *procedure 6* yielding alcohol **8d** (470 mg, 1.31 mmol, 83%, diastereoselectivity 95:5) after flash chromatographic purification (hexanes/ether 4:1). Reaction conditions: −50 to −20°C, 16 h. R_f=0.13 (hexanes/ether 4:1); $[\alpha]_D^{25}$=+8.6 (*c* 1.0, $CHCl_3$); IR (neat): 3500 (br), 2950 (s), 2870 (s), 1725 (s), 1160 (s), 830 (s); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ=4.03 (t, J=6.4, 2 H), 3.44 (m, 1 H), 3.30 (m, 1 H), 2.10 (d, J=7.1 Hz, 1 H), 1.68–1.56 (m, 3 H), 1.54–1.34 (m, 5 H), 1.17 (s, 9 H), 0.95 (t, J=7.4 Hz, 3 H), 0.88 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ=178.4, 74.9, 74.5, 64.3, 38.9, 33.6, 29.2, 27.4, 26.9, 26.1, 21.7, 18.3, 10.6, −4.0,

−4.4; MS (EI): *m/z* 301 (19), 109 (53), 85 (54), 75 (73), 57 (100); $C_{19}H_{40}O_4Si$ (360.611): calcd C 63.28, H 11.18; found C 63.13, H 10.94.

*Synthesis of (−)-*endo-*und (±)-*exo-*brevicomin*

(7S)-(+)-Hydroxy-(6S)-(t-butyldimethylsilyloxy)nonyl-2-pivalate ***12***

Aldehyde **3j** (1.43 g, 4.15 mmol) in toluene (2.5 mL) was treated with diethylzinc (2.0 equiv), Ti(O*i*-Pr)$_4$ (2.0 equiv) in toluene (5 mL) following *procedure 6* yielding alcohol **12** (1.37 g, 3.66 mmol, 88%, diastereoselectivity 93:7) after flash chromatographic purification (hexanes/ether 4:1). Reaction conditions: −45°C, 7 h, −30°C, 16 h. R_f=0.60 (hexanes/ether 1:1); $[\alpha]_D^{25}$=+9.8 (*c* 1.7, $CHCl_3$); IR (neat): 3480 (br), 2950 (s), 2860 (m), 1720 (s), 1160 (s), 840 (s); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ=4.88–4.79 (m, 1 H), 3.50–3.45 (m, 1 H), 3.33–3.25 (m, 1 H), 2.11/2.09 (d, *J*=6.9 Hz, 1 H), 1.58–1.14 (m, 7 H), 1.15 (d, *J*=6.2 Hz, 3 H), 1.15 (s, 9 H), 0.93 (t, *J*=7.2 Hz, 3 H), 0.86 (s, 9 H), 0.043 (s, 3 H), 0.039 (s, 3 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ=178.0, 74.7, 74.23, 74.19, 70.3, 70.1, 38.6, 36.2, 33.7, 33.6, 27.1, 26.8, 25.8, 21.0, 20.8, 19.8, 19.7, 18.1, 10.3, −4.2, −4.7; MS (EI): *m/z* 315 (15), 215 (67), 75 (80), 73 (100), 57 (57); $C_{20}H_{42}O_4Si$ (374.638): calcd C 64.12, H 11.30; found C 63.93, H 11.28.

(7R)-(−)-Hydroxy-(6S)-(t-butyldimethylsilyloxy)nonyl-2-pivalate ***13***

Aldehyde **3j** (1.15 g, 3.34 mmol) in toluene (2 mL) was treated with diethylzinc (2.0 equiv), Ti(O*i*-Pr)$_4$ (1.55 equiv) and *ent*-**1** (5 mol%) in toluene (4 mL) following *procedure 6* yielding alcohol **13** (0.96 g, 2.56 mmol, 77%, diastereoselectivity 92:8) after flash chromatographic purification (hexanes/ether 4:1). Reaction conditions: −45°C, 20 h, −10°C, 12 h. R_f=0.60 (hexanes/ether 1:1); $[\alpha]_D^{25}$=−5.6 (*c* 1.4, $CHCl_3$); IR (neat): 3500 (br), 2950 (s), 2880 (m), 1720 (s), 1160 (s), 830 (s); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ=4.86–4.81 (m, 1 H), 3.60–3.55 (m, 1 H), 3.48–3.44 (m, 1 H), 2.11 (br, 1 H), 1.60–1.31 (m, 8 H), 1.16 (d, *J*=6.1 Hz, 3 H), 1.15 (s, 9 H), 0.94 (t, *J*=7.4 Hz, 3 H), 0.86 (s, 9 H), 0.04 (m, 6 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ=178.1, 76.1, 75.9, 75.1, 75.0, 70.3, 38.7, 36.2, 36.1, 30.6, 30.5, 27.1, 25.8, 24.8, 24.7, 21.7, 21.5, 19.8, 18.0, 10.5, −4.5; MS (EI): *m/z* 315 (8), 215 (41), 171 (42), 123 (43), 75 (100), 57 (58); $C_{20}H_{42}O_4Si$ (374.638): calcd C 64.12, H 11.30; found C 63.95, H 11.05.

*(6S,7S)-(−)-Di(*t*-butyldimethylsilyloxy)-2-nonanone* ***14***

Alcohol **12** (1.73 g, 4.62 mmol) was silylated with *t*-butyldimethylsilyl chloride (*procedure 3*). The reaction was diluted with hexanes (50 mL) and saturated aqueous NH_4Cl (50 mL) was added. The aqueous layer was extracted with hexanes (3×50 mL) and the combined organic layer was treated with brine (50 mL) and dried ($MgSO_4$). The solvent was evaporated and the residual oil was diluted in THF (13 mL). The solution was cooled to −78°C and a solution of DIBAL-H (2.5 mL, 14.0 mmol, 3 equiv) in THF (5 mL) was slowly added. The reaction mixture was warmed to rt and stirred for 45 min. It was cooled to 0°C, ethyl acetate (15 mL) was slowly added and stirring was continued for 20 min at rt. The solution was cooled again to 0°C and Na_2SO_4.10 H_2O (4.6 g) was added in portions. The reaction was allowed to warm to rt and stirred further 45 min. After filtration the residue was washed with ethyl acetate (4×50 mL) and the solvent was evaporated. The alcohol was diluted in CH_2Cl_2 (5 mL) and added to a solution of 1,1,1-triacetoxy-1,1-dihydro-1,2-benziodoxol-3-(1H)-one[26] (2.15 g, 5.08 mmol, 1.1 equiv) in CH_2Cl_2 (15 mL) at 0°C. The reaction mixture was stirred for 10 min at 0°C and 1 h at rt, diluted with CH_2Cl_2 (50 mL) and worked up with 2 N aqueous NaOH (50 mL). The aqueous layer was extracted with CH_2Cl_2 (3×50 mL), the combined organic layer was washed with brine (50 mL) and dried ($MgSO_4$). After evaporation of the solvent, the product was purified by flash chromatography (hexanes/ether 40:1 to 9:1) yielding ketone **14** (2.15 g, 5.08 mmol, 87%) as colorless, oily liquid. R_f=0.31 (hexanes/ether 9:1); $[\alpha]_D^{25}$=−40.8 (*c* 3.9, $CHCl_3$); IR (neat): 2930 (s), 2860 (s), 1715 (s), 1260 (s), 1100 (s), 1070 (s), 1010 (s), 830 (s), 775 (s); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ=3.53 (ddd, *J*=9.6, 4.4, 2.2 Hz, 1 H), 3.44 (ddd, *J*=9.6, 4.0, 2.6 Hz, 1 H), 2.39 (t, *J*=7.3 Hz, 2 H), 2.10 (s, 3 H), 1.80–1.36 (m, 4 H), 1.32–1.12 (m, 2 H), 0.87 (t, *J*=7.3 Hz, 3 H), 0.86 (s, 18 H),

0.03 (m, 12 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ=208.7, 77.0, 75.3, 44.1, 29.8, 29.6, 25.8, 23.0, 21.3, 18.0, 11.4, −4.3, −4.8; MS (EI): *m/z* 345 (8), 229 (52), 173 (29), 147 (46), 73 (100); $C_{21}H_{46}O_3Si_2$ (402.768): calcd C 62.62, H 11.51; found C 62.61, H 11.54.

(6S,7R)-(−)-Di(t-butyldimethylsilyloxy)-2-nonanone ***15***

Alcohol **13** (0.96 g, 2.56 mmol) was treated as above for the preparation of **14** yielding ketone **15** (0.80 g, 1.99 mmol, 78%) as colorless, oily liquid. R_f=0.31 (hexanes/ether 9:1); $[\alpha]_D^{25}$=−4.1 (*c* 1.7, $CHCl_3$); IR (neat): 2940 (s), 2860 (s), 1715 (m), 1250 (s), 1100 (s), 1010 (m), 830 (s), 770 (s); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ=3.53 (m, 1 H), 3.47 (m, 1 H), 2.35 (t, *J*=7.2 Hz, 2 H), 2.08 (s, 3 H), 1.76–1.28 (m, 6 H), 0.84 (s, 18 H), 0.80 (t, *J*=7.3 Hz, 3 H), 0.020 (s, 3 H), 0.012 (s, 3 H), 0.005 (s, 3 H), 0.001 (s, 3 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ=208.6, 77.1, 75.1, 44.1, 32.5, 29.7, 26.0, 25.8, 20.0, 18.19, 18.18, 9.8, −4.22, −4.29, −4.58, −4.60; MS (EI): *m/z* 345 (7), 229 (49), 173 (43), 147 (77), 73 (100); $C_{21}H_{46}O_3Si_2$ (402.768): calcd C 62.62, H 11.51; found C 62.78, H 11.46.

*(1S,5R,7S)-(−)-7-Ethyl-5-methyl-6,8-dioxabicyclo[3.2.1]octan; (±)-*exo*-brevicomin* ***10***

Ketone **14** (1.56 g, 3.87 mmol) was dissolved in acetonitrile (15 mL) and added to a solution of aqueous HF in acetonitrile (5%, 10.5 mL) at −20°C. It was allowed to warm to rt and stirred for 3 h. The reaction mixture was diluted with hexanes (50 mL) and washed with aqueous saturated $NaHCO_3$ (50 mL). The aqueous layer was extracted with hexanes (3×50 mL), the combined organic layer was washed with brine (50 mL) and dried ($MgSO_4$). The solvent was evaporated (50°C, 150 mbar) and the residual liquid was purified by flash chromatography (hexanes/ether 40:1 to 20:1). The solvent was carefully removed (50°C, 110 mbar) yielding pure (−)-*exo*-brevicomin (447 mg, 2.86 mmol, 74%) as colorless liquid. Gas-chromatographical analysis on chiral column (Chrompack Chirasil-DEX CB, 100°C isotherm, carrier gas hydrogen) showed >99:1 diastereoselectivity and >99% *ee*. R_f=0.27 (hexanes/ ether 9:1); $[\alpha]_D^{25}$=−68.2 (*c* 1.4, ether; ref. [24b]: −69.7, *c* 3.6, ether); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ=4.07 (s, br, 1 H), 3.87 (t, *J*=6.5 Hz, 1 H), 1.92–1.67 (m, 2 H), 1.58–1.38 (m, 6 H), 1.36 (s, 3 H), 0.85 (t, *J*=7.5 Hz, 3 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ=107.6, 81.1, 78.2, 34.9, 28.5, 27.9, 24.9, 17.1, 9.7. The spectral data are identical with ref. [24b].

*(1S,5R,7R)-(−)-7-Ethyl-5-methyl-6,8-dioxabicyclo[3.2.1]octan; (±)-*endo*-brevicomin* ***11***

Ketone **15** (494 mg, 1.23 mmol) was treated as described above for the preparation of **10** yielding (−)-*endo*-brevicomin (142 mg, 0.91 mmol, 70%) as colorless liquid. Gas-chromatographic analysis on chiral column showed 99:1 diastereoselectivity and >99% *ee*. R_f=0.21 (hexanes/ether 9:1); $[\alpha]_D^{25}$=−78.8 (*c* 0.8, ether; ref. [24b]: −79.4, *c* 1.4, ether); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ=4.18 (m, 1 H), 2.96 (ddt, *J*=0.6, 4.1, 7.1 Hz, 1 H), 1.98–1.70 (m, 3 H), 1.64–1.47 (m, 5 H), 1.41 (s, 3 H), 0.96 (t, *J*=7.5 Hz, 3 H); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ=107.0, 81.6, 76.5, 34.5, 25.0, 23.7, 21.9, 17.5, 10.9. The spectral data are identical with ref. [24b].

Gas chromatographic analyses of the crude reaction mixtures on chiral column (Chrompack Chirasil-DEX CB, 100°C isotherm, carrier gas hydrogen):

Retention time (min)	Reaction mixture of **14**	**15**	Isomer of Brevicomin
3.96	0.2 %	2.9 %	(1*R*, 5*S*, 7*R*) (+)-*exo*
4.73	94.2 %	4.7 %	(1*S*, 5*R*, 7*S*) (-)-*exo* **10**
5.35	3.5 %	92.4 %	(1*S*, 5*R*, 7*R*) (-)-*endo* **11**
5.59	2.1 %	< 0.1 %	(1*R*, 5*S*, 7*S*) (+)-*endo*

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