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Stereospecific and Stereodivergent Construction of Tertiary and Quaternary Carbon Centers through Switchable Directed/Nondirected Allylic Substitution**

Bernhard Breit,*[a] Peter Demel,[a, b] Daniel Grauer,[a] and Christopher Studte[a]

Abstract: This study introduces the *ortho*-diphenylphosphanylbenzoate (*o*-DPPB)/*o*-DPPB oxide system as a switchable directing/nondirecting leaving group in a copper-mediated allylic substitution with Grignard and organozinc reagents. With this system, the regioselective, stereospecific, and stereodivergent construction of quaternary as well as tertiary carbon centers is possible in a reliable and predictable fashion. Starting from one substrate enantiomer, both optical antipodes of the substitution products are readily available. Hence, this methodology features reversed polarity in comparison to established enolate alkylation chemistry and may be an interesting alternative, particularly for the construction of quaternary stereogenic carbon centers.

Keywords: allylation · asymmetric synthesis · Grignard reagents · organocopper reagents · stereoselectivity

Introduction

Reactions that build the skeleton of organic compounds are the backbone of modern organic synthesis. In this respect, carbon–carbon bond-forming reactions that allow a reliable and predictable as well as a stereospecific construction of tertiary and quaternary carbon centers are extremely desirable but rare. Significant progress has been made employing enantioselective catalytic methods, but still no general solution to this synthetic problem exists.[1]

An attractive alternative strategy is to start from a substrate equipped with an easily accessible stereogenic center, such as a secondary alcohol, which is subsequently transformed in a stereospecific manner into an all-carbon-substituted one. Important examples are sigmatropic processes such as the Claisen rearrangement, which allow a stereospecific 1,3-transposition of a readily available enantiomerically pure secondary or tertiary stereogenic allylic alcohol to a tertiary or quaternary carbon center with excellent levels of 1,3-chirality transfer.[2] However, the nature of the sigmatropic process sets structural limitations on the type of carbon nucleophile that can be transferred. In this respect, allylic substitutions with organometallic carbon nucleophiles could provide a more-general solution, provided that all aspects of selectivity can be controlled. Among the variety of metal-catalyzed and -mediated allylic substitution reactions known, only Cu-,[3] Ir-,[4] and Rh-catalyzed[5] variants display a regio- and stereospecific relation between the stereogenic center carrying the leaving group and the newly formed one. However, both Ir- and Rh-catalyzed allylic substitutions are restricted to the introduction of soft carbon and heteroatom nucleophiles such as malonates, which again sets narrow limitations on the type of carbon nucleophile that can be transferred. For this reason, the copper-catalyzed and -mediated allylic substitutions became of particular interest to us as they allow the introduction of hard nucleophiles, such as alkyl, alkenyl, and aryl groups, into an existing skeleton. Thus, the only limitation with respect to structural flexibility is set in principle by the availability of the corresponding organometallic reagent.

Copper-mediated and -catalyzed allylic substitutions generally proceed by *anti* attack of the nucleophile with respect to the leaving group.[3] Stereoelectronic reasons on the basis of an optimal π(alkene)–Cu(d)–σ*(C leaving group) orbital overlap have been proposed as the origin of the *anti* stereo-

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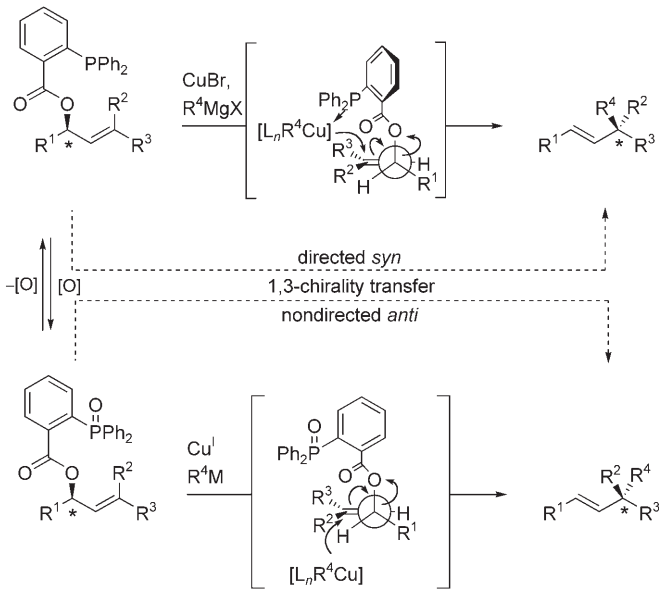
chemical course.[6] However, the simultaneous control of regio- and stereochemistry is a difficult problem to solve, and only a few successful examples are known.[7] Progress has been made in employing substrate direction with the aid of reagent-directing leaving groups, among which carbamates[8] and benzothiazoles[9] have proven useful. However, control over double-bond geometry is often unsatisfactory, and renders the chirality transfer incomplete.[3] Furthermore, in many cases an excess of organometallic reagent has to be used, which is undesirable, particularly if valuable organic residues are to be transferred. We recently found a solution to these problems by employing the *ortho*-diphenylphosphanylbenzoate group (*o*-DPPB) as a new reagent-directing leaving group. Copper-mediated and -catalyzed allylic substitution with only stoichiometric amounts of Grignard reagents could be realized with excellent control of chemo-, regio-, and stereoselectivity and with recovery of the directing group.[10] In an extension of this concept, enantioselective copper-mediated allylic substitution can be achieved by employing a chiral variant of the *o*-DPPB leaving group, the planar chiral *ortho*-diphenylphosphanylferrocene carboxylate.[11]

Herein we report in full detail on the regioselective, stereospecific, and stereodivergent construction of quaternary as well as tertiary carbon stereocenters with *o*-DPPB-directed and copper-mediated allylic substitution with Grignard reagents.[12] Specifically, we show that the stereochemical outcome of these reactions can be reversed by an oxidative on/off switch of the directing power of the *o*-DPPB group. This allows the preparation of both optical antipodes of the substitution product starting from a single substrate enantiomer (Scheme 1).

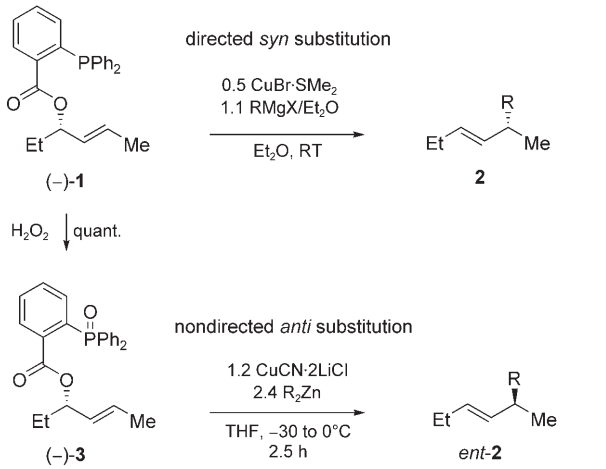


Scheme 1. Concept of stereodivergent allylic substitution with organocopper reagents for the stereospecific construction of quaternary carbon centers by employing a switchable directing/nondirecting leaving group. L_n = unspecified additional ligand(s).

Results and Discussion

We began by probing our concept for the construction of tertiary stereogenic centers. Thus, starting from allylic *o*-DPPB ester (−)-**1**, which is readily available on a multigram scale via a sequence of enzyme resolutions and esterifications as described previously,[2c–e] a series of directed and copper-mediated allylic substitutions with a variety of Grignard reagents was studied (Table 1). The directed allylic substitution proceeded in all cases with excellent regioselectivity and 1,3-chirality transfer (Table 1, entries 1–6). Only in the case of the sterically demanding *tert*-butyl Grignard reagent was the stereoselectivity lower. In all cases, starting from (−)-**1**, the reaction followed the directed *syn*-S_N2' pathway. This was verified upon determination of absolute configuration at the stage of the alcohols **4** obtained from oxi-

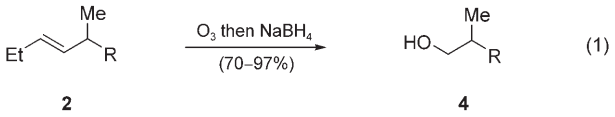
Table 1. Stereospecific and stereodivergent formation of tertiary carbon centers through switchable directed/nondirected allylic substitution.



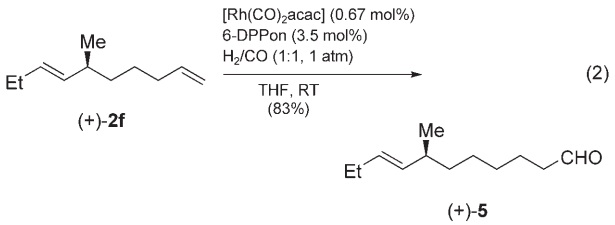
Entry	Substrate	R	S_N2'/ S_N2[a]	Product (*ee* [%])[b]	CT [%][c]	Yield [%][d]
1	(−)-**1**	*n*Bu	98:2	(+)-**2a** (97)	99	96
2	(−)-**1**	3-pentyl	97:3	(+)-**2b** (95)	99	90
3	(−)-**1**	*t*Bu	97:3	(+)-**2c** (80)	82	96
4	(−)-**1**	Ph	98:2	(−)-**2d** (94)	97	94
5	(−)-**1**	Bn	97:3	(+)-**2e** (93)	96	97
6	(−)-**1**	4-pentenyl	95:5	(+)-**2f** (94)	97	80
7	(−)-**3**	*n*Bu	94:6	(−)-**2a** (97)	100	92
8	(−)-**3**	*t*Bu	75:25	(−)-**2c** (74)	76	68
9	(−)-**3**	Ph	93:7	(+)-**2d** (94)	97	86

[a] Determined by GC. The *E*/*Z* ratio was >99:1 in all cases as determined by GC. [b] Determined by chiral GC after derivatization to alcohols **4**. [c] CT = chirality transfer calculated on the basis of 99% *ee* and an *E*/*Z* ratio of 99:1 of the starting material ((−)-**1** and (−)-**3**) determined by HPLC. [d] Yield of isolated product.

dative cleavage of the alkene function of **2** through ozonolysis followed by reductive workup with $NaBH_4$ [Eq. (1)].



In the case of the 4-pentenyl-functionalized substitution product (+)-**2f**, the *ee* value was determined after derivatization to the C_1 chain-elongated aldehyde (+)-**5** ([Eq. (2)]; acac = acetylacetonato). This was achieved upon chemo- and



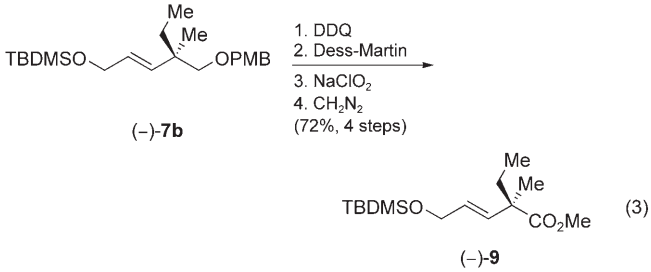
regioselective hydroformylation of the terminal alkene function of (+)-**2f** with our recently developed 6-diphenylphosphanylpyridin-2(1*H*)-one (6-DPPon)/rhodium catalyst at room temperature under syngas atmosphere at ambient pressure.[13]

To gain access to the optical antipodes of the substitution products **2** starting from the same allylic *o*-DPPB ester substrate (−)-**1**, the stereochemistry of the allylic substitution has to be reversed from a directed *syn*-substitution pathway to a nondirected *anti* attack of the nucleophile with respect to the leaving group. For this reason, the directing power of the *o*-DPPB function has to be turned off. Hence, the phosphane function of (−)-**1** was oxidized quantitatively with hydrogen peroxide to the phosphane oxide (−)-**3**, in which the ability of the *o*-DPPB group to coordinate the copper reagent is supressed. Furthermore, changing the *ortho*-phosphino group to a phosphane increases the leaving capability of the benzoate group significantly.

In fact, reaction of (−)-**3** with an organocopper reagent derived in situ from the reaction of CuCN·2LiCl (1.2 equiv) and $Zn(n\mathrm{Bu})_2$ (2.4 equiv) in THF furnished in excellent yield and regio- and stereoselectivity the optical antipode (−)-**2a** (Table 1, entry 7). Hence, the reaction proceeded by a nondirected *anti*-S_N2' substitution mode. Although the transfer of a phenyl group occurred with similar levels of efficiency, the *tert*-butyl substituent again marks a limitation of this methodology (Table 1, entries 8 and 9).

To explore the possibility for stereoselective construction of quaternary carbon centers, the *o*-DPPB esters (−)-**6a** and (−)-**6b** were chosen. These substrates are synthetically interesting for two reasons. First, they are readily available from the chiral pool (D-mannitol),[14] and second, the resulting allylic substitution products are equipped with the appropriate functionalities to allow a flexible incorporation of the quaternary stereocenter into the desired carbon skeleton (Table 2).

The reactions of PMB ether derivative (−)-**6a** with a range of Grignard reagents in the presence of $CuBr{\cdot}SMe_2$ (0.5 equiv) proceeded smoothly with excellent regio- and stereoselectivity (Table 2, entries 1–4). Hence, a perfect chirality transfer was obtained upon construction of quaternary carbon centers (Table 2, entries 2–4). However, when a benzyl Grignard reagent was employed, the chirality transfer decreased slightly to 91% (Table 2, entry 5). The absolute configuration of the substitution products was determined upon transformation of (−)-**7b** to the known ester (−)-**9** ([Eq. (3)]; DDQ = 2,3-dichloro-5,6-dicyano-*p*-benzoquinone).[7b]



Next, allylic substitution with (−)-**6b** was examined. Here the problem of a thermodynamically unfavorable enoate deconjugation combines with that of chemoselectivity caused by the additional ethyl ester functionality (allylic substitution vs. conjugate addition).[3,7a,b] Interestingly, the directed allylic substitution occurred with complete chemo-, regio-, and stereoselectivity and with excellent chirality transfer to give the substitution products (−)-**7g–i** (Table 2, entries 7–9).

To gain access to the optical antipodes (+)-**7g–i**, the *o*-DPPB function was oxidized to the corresponding phosphane oxide (−)-**8** to suppress the directing abilities of the phosphane function and to increase the leaving capability of the benzoate group. Thus, treatment of (−)-**8** with a copper reagent prepared in situ from the appropriate dialkylzinc reagent (2.4 equiv) in the presence of CuCN·2LiCl (1.2 equiv) in THF furnished the *anti*-S_N2' products (+)-**7g–i** in good yield with perfect regioselectivity and excellent 1,3-*anti*-chirality transfer.[15] Interestingly, when (−)-**6b** was subjected to the reaction conditions for entries 10–12 of Table 2, allylic substitution did not occur even after warming to room temperature and prolonged reaction time (24 h). The oxidation of the phosphane function to the phosphane oxide therefore serves two purposes. First, it switches off the directing power of the phosphane function and thus suppresses the directed *syn*-substitution pathway. Second, it enhances the leaving capability of the benzoate group towards the nondirected *anti*-substitution pathway.

Besides acyclic substrates, this methodology is also applicable to cyclic substrates with similar efficiency. This is shown for the stereodivergent directed/nondirected substitution of the six-membered ring systems (−)-**10a,b** and (−)-**11a,b** (Table 3).

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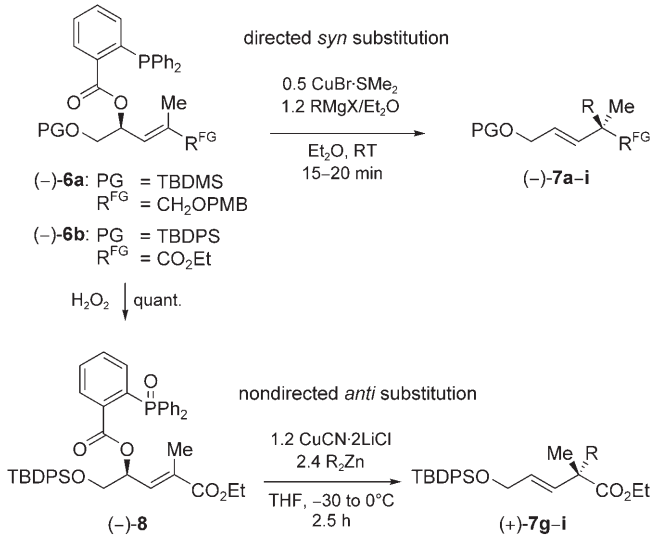
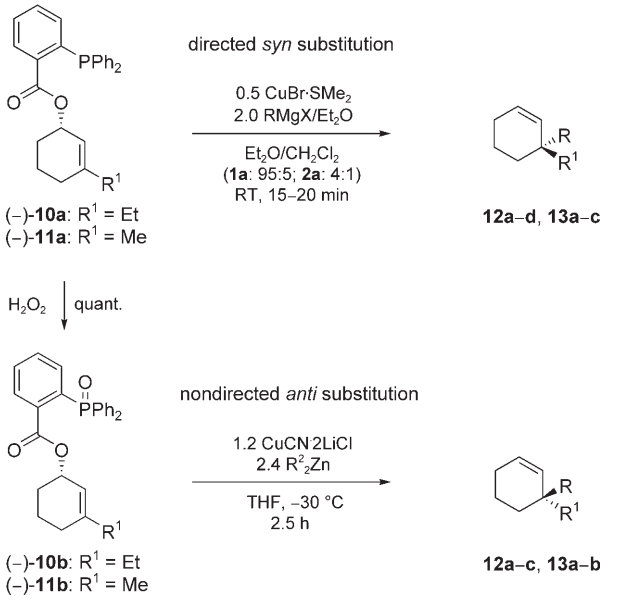
Table 2. Stereospecific and stereodivergent formation of quaternary carbon centers through switchable directed/nondirected allylic substitution of acyclic substrates.



Entry[a]	Substrate (*ee* [%])[b]	R	S_N2'/S_N2[c]	*E*/*Z*[c]	Product (*ee* [%])[c]	CT [%][d]	Yield [%][e]
1	(–)-**6a** (94)	Me	>95:5	>95: 5	**7a**	–	72
2	(–)-**6a** (94)	Et	>99:1	>99: 1	(–)-**7b** (94%)	100	86
3	(–)-**6a** (93)	*n*Bu	>99:1	>99: 1	(–)-**7c** (93%)	100	99
4	(–)-**6a** (93)	*i*Pr	>99:1	>99: 1	(–)-**7d** (93%)	100	89
5[f]	(–)-**6a** (93)	Bn	>99: 1	>99: 1	(–)-**7e** (85%)	91	53
6	(–)-**6a** (92)	*t*Bu	14: 86[g]	80: 20[g]	**7f** (n.d.)	n.d.	90
7	(–)-**6b** (>99)	Et	>99: 1	>99: 1	(–)-**7g** (98%)	98	84
8	(–)-**6b** (>99)	*n*Bu	>99: 1	>99: 1	(–)-**7h** (97%)	98	87
9	(–)-**6b** (>99)	*i*Pr	>99: 1	>99: 1	(–)-**7i** (97%)	98	84
10	(–)-**8** (>99)	Et	>99: 1	>99: 1	(+)-**7g** (99%)	100	85
11	(–)-**8** (>99)	*n*Bu	>98: 2	>98: 2	(+)-**7h** (99%)	100	87
12	(–)-**8** (>99)	*i*Pr	97: 3	>95: 5	(+)-**7i** (>99%)	100	94

[a] All reactions were performed in diethyl ether ($c = 0.05$ M with respect to the *o*-DPPB ester). The Grignard reagents ($c = 0.76$–1.23 M in diethyl ether) were added to the reaction mixture with a syringe pump over a period of 15–20 min. [b] The *o*-DPPB esters were prepared from the corresponding allylic alcohols;[14] see Experimental Section for details. The enantiomeric excess was determined by HPLC analysis after TBDPS deprotection at the stage of the corresponding allylic alcohol (**6a**: Chiralpak-AD; **6b**: Chiralcel-OD-H). [c] Determined by ^{1}H NMR spectroscopy (entry 1) or HPLC analysis (entries 2, 3, 5, 7, 9: Chiralcel-OD-H; entry 4: Chiralpak-AD after removal of the TBDMS group; entries 9, 12: Chiralcel-OD-H after removal of the TBDPS group). [d] CT was calculated as CT = [*ee*(**7**)/*ee*(**6** or **8**)] × 100%. [e] Yield of isolated product after chromatographic purification. [f] c(**6a**) = 0.01 M in ether; the Grignard reagent ($c = 0.07$ M in diethyl ether) was added over a period of 90 min. [g] Product ratios were determined by ^{1}H NMR spectroscopy. PMB = *p*-methoxybenzyl, TBDMS = *tert*-butyldimethylsilyl, TBDPS = *tert*-butyldiphenylsilyl, n.d. = not determined.

Table 3. Stereospecific and stereodivergent formation of quaternary carbon centers through switchable directed/nondirected allylic substitution of cyclic substrates.



Entry	Substrate (*ee* [%])[a]	R	S_N2'/S_N2[b]	Product (*ee* [%])[b]	CT [%][c]	Yield [%][d]
1	(–)-**10a** (97)	Me	99:1	(+)-**12a** (96)	99	>95
2	(–)-**10a** (97)	*n*Bu	>99: 1	(+)-**12b** (96)	99	>95
3	(–)-**10a** (97)	*i*Pr	98: 2	(–)-**12c** (96)	99	>95
4	(–)-**10a** (97)	Ph	40: 60	(–)-**12d** (92)	95	>95
5	(–)-**11a** (94)	Et	96: 4	(–)-**12a** (91)	97	>95
6	(–)-**11a** (94)	*n*Bu	98: 2	(+)-**13a** (94)	100	>95
7	(–)-**11a** (94)	*i*Pr	96: 4	(–)-**13b** (91)	97	>95
8	(–)-**11a** (94)	Ph	41: 59	(+)-**13c** (82)	87	>95
9	(–)-**10b** (97)	Me	99: 1	(–)-**12a** (93)	96	>95
10	(–)-**10b** (97)	*n*Bu	>99: 1	(–)-**12b** (96)	99	>95
11	(–)-**10b** (97)	*i*Pr	97: 3	(+)-**12c** (94)	97	>95
12	(–)-**11b** (94)	Et	>99: 1	(+)-**12a** (93)	99	>95
13	(–)-**11b** (94)	*n*Bu	99: 1	(–)-**13a** (94)	100	>95
14	(–)-**11b** (94)	*i*Pr	99: 1	(+)-**13b** (93)	99	>95

[a] The *o*-DPPB esters were prepared from the corresponding allylic alcohols following an esterification protocol reported previously.[10] The enantiomeric excess was determined by HPLC analysis (**10a**: Chiralpak-AD-H; **11a**: Chiralcel-OD-H). [b] Determined by ^{1}H NMR spectroscopy and GC analysis (see Experimental Section). [c] CT was calculated as CT = [*ee*(**12**)/*ee*(**10** or **11**)] × 100%. [d] Yield from GC.

Conclusions

This study introduces the *o*-DPPB/*o*-DPPB oxide system as a switchable directing/nondirecting leaving group in copper-mediated allylic substitution with Grignard and organozinc reagents. With this system, the regioselective, stereospecific, and stereodivergent construction of quaternary as well as tertiary carbon centers is possible in a reliable and predictable fashion. Hence, starting from one substrate enantiomer, both optical antipodes of the substitution product are readily available. If the allylic substitution reaction is followed by an oxidative cleavage of the alkene function, α-chiral carbonyl derivatives are obtained, which are the typical products of an enolate alkylation. Hence, the stereospecific allyl-

ic substitution reported herein features reversed polarity compared to enolate alkylation methodology and may be an interesting alternative, particularly for the construction of quaternary carbon centers.

Experimental Section

General Remarks

Reactions were performed in flame-dried glassware under argon (purity >99.998%). The solvents were dried by standard procedures, distilled, and stored under argon. All temperatures quoted were not corrected. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AM-400 or Bruker DRX-500 spectrometers with tetramethylsilane (TMS), chloroform ($CHCl_3$), or benzene (C_6H_6) as internal standards. ^{31}P NMR spectra were recorded on a Varian Mercury 300 spectrometer with H_3PO_4 (85%) as external standard. Melting points were determined with a melting-point apparatus by Dr. Tottoli (Büchi). Elemental analyses were performed on an Elementar Vario EL instrument. Flash chromatography was performed over silica gel (Si 60, E. Merck AG, Darmstadt, 40–63 μm). Reversed-phase silica-gel chromatography: Polygoprep 100–50 C18 (Macherey–Nagel).

The following compounds were prepared following literature procedures: *ortho*-diphenylphosphanylbenzoic acid (*o*-DPPBA)[16] and (−)-**1**.[10c,e]

*General Procedure for the Synthesis of o-*DPPB Esters: the Steglich Protocol[17]

o-DPPBA (1 equiv), 4-dimethylaminopyridine (DMAP; 1 equiv), and dicyclohexylcarbodiimide (DCC; 1 equiv) were added successively to a solution of the allylic alcohol (1 equiv) in CH_2Cl_2 (0.5 M). The resulting mixture was stirred at ambient temperature until TLC showed complete consumption of the starting material. The reaction mixture was filtered through a plug of CH_2Cl_2-wetted celite and washed with additional CH_2Cl_2. An appropriate amount of silica gel was added to the filtrate, which was then concentrated to dryness. Flash chromatography with petroleum ether/ethyl acetate provided the *o*-DPPB esters as slightly yellow to colorless, highly viscous oils or solids.

(−)-**6a**: (+)-1-*tert*-Butyldimethylsilanyloxy-5-(4-methoxybenzyloxy)-4-methylpent-3-en-2-ol[14,18] (267 mg, 0.76 mmol, 95% *ee*) gave (−)-**6a** (424 mg, 0.65 mmol, 85%) as a yellowish, highly viscous oil. $[\alpha]_D^{23} = -6.5$ ($c = 1.02$, $CHCl_3$, *ee* = 95%); ^{1}H NMR (300.064 MHz, $CDCl_3$): $\delta = 0.00$ (s, 6H), 0.84 (s, 9H), 1.70 (d, $J = 0.7$ Hz, 3H), 3.54 (dd, $J = 10.5$, 5.4 Hz, 1H), 3.64 (dd, $J = 10.6$, 6.2 Hz, 1H), 3.80 (s, 3H), 3.83 (s, 2H), 4.37 (s, 2H), 5.36 (dq, $J = 8.9$, 1.0 Hz, 1H), 5.73 (dpt, $J = 8.9$, 5.8 Hz, 1H), 6.86 (m, 2H), 6.91 (m, 1H), 7.25 (m, 2H), 7.22–7.33 (m, 10H), 7.37 (m, 2H), 8.08 ppm (m, 1H); ^{13}C NMR (100.614 MHz, $CDCl_3$): $\delta = -5.3$ (2C), 14.7, 18.3, 25.9 (3C), 55.4, 64.5, 71.4, 72.5, 74.8, 113.9 (2C), 122.6, 128.2, 128.4, 128.5 (d, $J_{C,P} = 4.4$ Hz, 2C), 128.5 (d, $J_{C,P} = 4.4$ Hz, 2C), 129.5 (2C), 130.6, 130.8 (d, $J_{C,P} = 8.7$ Hz, 2C), 131.8, 133.9 (d, $J_{C,P} = 2.9$ Hz, 2C), 134.1, 134.4, 135.0 (d, $J_{C,P} = 18.9$ Hz), 138.2, 138.3 (d, $J_{C,P} = 5.8$ Hz), 138.4, 138.6, 140.3 (d, $J_{C,P} = 27.6$ Hz), 159.3, 166.1 ppm; ^{31}P NMR (121.468 MHz, $CDCl_3$): $\delta = -3.9$ ppm; elemental analysis: calcd (%) for $C_{39}H_{47}O_5PSi$ (654.85): C 71.53, H 7.23; found: C 71.31, H 7.18.

rac-**6a**: A mixture of *rac*-1-*tert*-butyldimethylsilanyloxy-5-(4-methoxybenzyloxy)-4-methylpent-3-en-2-ol (prepared from the enantiomerically pure allylic alcohol through sequential oxidation with Dess–Martin periodinane followed by reduction with $NaBH_4$ in MeOH) (70 mg, 0.2 mmol), DMAP (24 mg, 0.2 mmol), *o*-DPPBA (61 mg, 0.2 mmol), and DCC (41 mg, 0.2 mmol) gave *rac*-**6a** (126 mg, 96%).

(−)-**6b**: (−)-(*S*,*E*)-ethyl 5-*tert*-butyldiphenylsilanyloxy-4-hydroxy-2-methylpent-2-enoate[19] (385 mg, 0.93 mmol, >99.5% *ee*) gave (−)-**6b** (619 mg, 95%) as a yellowish glass. $[\alpha]_D^{20} = -11.1$ ($c = 1.62$, $CHCl_3$); ^{1}H NMR (400.136 MHz, $CDCl_3$): $\delta = 1.00$ (s, 9H), 1.29 (t, $J = 6.9$ Hz, 3H), 1.79 (m, 3H), 3.63 (dd, $J = 10.8$, 4.7 Hz, 1H), 3.75 (dd, $J = 10.8$, 6.0 Hz, 1H), 4.19 (m, 2H), 5.81 (dt, $J = 8.6$, 5.6 Hz, 1H), 6.56 (m, 1H), 6.91 (m, 1H), 7.19–7.42 (m, 18H), 7.62 (d, $J = 6.9$ Hz, 4H), 8.08 ppm (m, 1H); ^{13}C NMR (100.624 MHz, $CDCl_3$): $\delta = 13.2$, 14.2, 19.1, 26.7 (3C), 60.7, 64.5, 72.1, 127.7 (2C), 128.1, 128.4 (d, $J_{C,P} = 7.3$ Hz, 4C), 128.5 (2C), 129.7 (4C), 130.8 (d, $J_{C,P} = 2.9$ Hz), 132.0, 132.1, 133.1 (2C), 133.9 (d, $J_{C,P} = 20.3$ Hz, 4C), 134.2 (m), 134.3, 135.4, 135.57 (2C), 135.61 (2C), 138.0 (d, $J_{C,P} = 11.6$ Hz, 2C), 140.6 (d, $J_{C,P} = 27.6$ Hz), 165.8, 167.3 ppm; ^{31}P NMR (121.449 MHz, $CDCl_3$): $\delta = -4.4$ ppm; elemental analysis: calcd (%) for $C_{43}H_{45}O_5PSi$ (700.87): C 73.69, H 6.47; found: C 73.66, H 6.46.

rac-**6b**: A mixture of *rac*-ethyl 5-*tert*-butyldiphenylsilanyloxy-4-hydroxy-2-methylpent-2-enoate (prepared from the enantiomerically pure allylic alcohol through sequential oxidation with pyridinium chlorochromate (PCC) on Al_2O_3 followed by reduction with $NaBH_4$ in MeOH) (131 mg, 0.318 mmol), DMAP (39 mg, 0.318 mmol), *o*-DPPBA (97 mg, 0.318 mmol), and DCC (66 mg, 0.318 mmol) gave *rac*-**6b** (182 mg, 82%).

(−)-**10a**: A mixture of (−)-(*S*)-3-ethylcyclohex-2-en-1-ol[20] (300 mg, 2.38 mmol), *o*-DPPBA (800 mg, 2.61 mmol), DCC (564 mg, 2.73 mmol), and DMAP (291 mg, 2.38 mmol) in CH_2Cl_2 (9.5 mL) with 16 h reaction time followed by purification by flash chromatography with cyclohexane/ethyl acetate (20:1) gave (−)-**10a** (874 mg, 89%, 97% *ee*) as a yellowish, highly viscous oil. $[\alpha]_D^{20} = -99.4$ ($c = 3.5$ in $CHCl_3$); ^{1}H NMR (300.064 MHz, $CDCl_3$): $\delta = 0.98$ (t, $J = 7.4$ Hz, 3H, CH_2CH_3), 1.58–1.75 (m, 4H, 4/6-H, 5-H), 1.89–1.95 (m, 2H, 4/6-H), 1.97 (q, $J = 7.4$ Hz, 2H, CH_2CH_3), 5.40 (m, 2H, 1-H, 2-H), 6.90 (m, 1H, Ar-H), 7.23–7.41 (m, 12H, Ar-H), 8.04 ppm (m, 1H, Ar-H); ^{13}C NMR (75.451 MHz, $CDCl_3$): $\delta = 12.0$ (CH_2CH_3), 19.2 (C5), 28.3 (C4), 28.4 (CH_2CH_3), 30.4 (C6), 70.1 (C1), 118.3 (C2), 128.2 (Ar-C), 128.48 (d, $J_{C,P} = 10.7$ Hz, 2C, Ar-C), 128.49 (d, $J_{C,P} = 10.9$ Hz, 2C, Ar-C), 128.51 (2C, Ar-C), 130.6 (d, $J_{C,P} = 2.9$ Hz, Ar-C), 131.7 (Ar-C), 134.0 (d, $J_{C,P} = 20.4$ Hz, 2C, Ar-C), 134.1 (d, $J_{C,P} = 20.7$ Hz, 2C, Ar-C), 134.3 (Ar-C), 135.6 (Ar-C), 138.30 (d, $J_{C,P} = 11.5$ Hz, Ar-C), 138.32 (d, $J_{C,P} = 11.8$ Hz, Ar-C), 140.1 (d, $J_{C,P} = 26.2$ Hz, Ar-C), 146.1 (C3), 166.8 ppm (d, $J_{C,P} = 2.3$ Hz, Ar-*C*OOR); ^{31}P NMR (121.468 MHz, $CDCl_3$): $\delta = -4.7$ ppm; elemental analysis: calcd (%) for $C_{27}H_{27}O_2P$ (414.48): C 78.24, H 6.57; found: C 78.12, H 6.74; HPLC (DAICEL Chiralpak AD-H, 0.46×25 cm, 0.8 mL min^{-1}, *n*-heptane/isopropanol = 100:1, 40 °C, 260 nm): t_R(+)-**10a**: 14.95 min (1.3%), t_R(−)-**10a**: 15.89 min (98.7%).

rac-**10a**: A mixture of *rac*-3-ethylcyclohex-2-en-1-ol (150 mg, 1.19 mmol), DMAP (145 mg, 1.19 mmol), *o*-DPPBA (400 mg, 1.31 mmol), and DCC (282 mg, 1.37 mmol) in CH_2Cl_2 (5 mL) gave *rac*-**10a** (425 mg, 86%).

(−)-**11a**: A mixture of (−)-(*S*)-3-methylcyclohex-2-en-1-ol[20] (466 mg, 4.15 mmol), *o*-DPPBA (1.35 g, 4.36 mmol), DCC (942 mg, 4.57 mmol), and DMAP (507 mg, 4.15 mmol) in CH_2Cl_2 (17 mL) with 20 h reaction time followed by purification by flash chromatography with cyclohexane/ethyl acetate (20:1) gave (−)-**11a** (1.30 g, 78%, 94% *ee*) as a yellowish, highly viscous oil. $[\alpha]_D^{20} = -109.0$ ($c = 2.33$ in $CHCl_3$); ^{1}H NMR (400.136 MHz, $CDCl_3$): $\delta = 1.50$–1.59 (m, 1H, 6-H^1), 1.67 (s, 3H, 3-CH_3), 1.60–1.77 (m, 3H, 5-H, 6-H^2), 1.82–1.97 (m, 2H, 4-H), 5.37 (m, 1H, 1-H), 5.40 (m, 1H, 2-H), 6.91 (m, 1H, Ar-H), 7.24–7.33 (m, 10H, Ar-H), 7.36 (m, 2H, Ar-H), 8.04 ppm (m, 1H, Ar-H); ^{13}C NMR (100.624 MHz, $CDCl_3$): $\delta = 19.2$ (C5), 23.8 (3-CH_3), 28.0 (C6), 30.0 (C4), 70.0 (C1), 120.1 (C2), 128.2 (Ar-C), 128.5 (d, $J_{C,P} = 7.3$ Hz, 4C, Ar-C), 128.6 (2C, Ar-C), 130.7 (d, $J_{C,P} = 2.9$ Hz, 2C, Ar-C), 131.7 (Ar-C), 134.0 (d, $J_{C,P} = 20.3$ Hz, 2C, Ar-C), 134.1 (d, $J_{C,P} = 20.4$ Hz, 2C, Ar-C), 134.3 (Ar-C), 135.5 (d, $J_{C,P} = 18.9$ Hz, Ar-C), 138.3 (d, $J_{C,P} = 11.6$ Hz, Ar-C), 140.1 (d, $J_{C,P} = 26.2$ Hz, Ar-C), 140.9 (C3), 166.8 ppm (d, $J_{C,P} = 2.3$ Hz, Ar-*C*OOR); ^{31}P NMR (121.468 MHz, $CDCl_3$): $\delta = -4.6$ ppm; elemental analysis: calcd (%) for $C_{26}H_{25}O_2P$ (400.45): C 77.98, H 6.29; found: C 77.75, H 6.11; HPLC (DAICEL Chiralpak OD-H, 0.46×25 cm, 0.8 mL min^{-1}, *n*-heptane/isopropanol = 200:1, 22 °C, 260 nm): t_R(+)-**11a**: 11.07 min (3.0%), t_R(−)-**11a**: 16.19 min (97.0%).

rac-**11a**: A mixture of *rac*-3-methylcyclohex-2-en-1-ol (112 mg, 1.0 mmol), DMAP (122 mg, 1.0 mmol), *o*-DPPBA (337 mg, 1.31 mmol), and DCC (237 mg, 1.37 mmol) in CH_2Cl_2 (4 mL) gave *rac*-**11a** (375 mg, 94%).

*General Procedure for the Preparation of o-*DPPB Oxides

Aqueous H_2O_2 (35%, 10 equiv) was added to a magnetically stirred solution of the corresponding *o*-DPPB ester (1.0 equiv) in dichloromethane (0.1 M) at room temperature. After 2 h, *tert*-butyl methyl ether was added

(40 mL mmol^{-1}), and the organic phase was washed with water until free of H_2O_2 (peroxide test sticks from Merck, Darmstadt). The combined aqueous phases were extracted with *tert*-butyl methyl ether (2× 40 mL mmol^{-1}), and the combined organic phases were dried ($MgSO_4$). Evaporation of the solvent gave the analytically pure phosphane oxides.

(−)-**3**: (−)-(*E*)-hex-4-en-3-ol[10c,e] (2.67 g, 6.95 mmol) gave, after recrystallization from petroleum ether/dichloromethane (1:1), (−)-**3** (2.59 g, 6.48 mmol) as a colorless crystalline solid. $[\alpha]_D^{20} = -4.6$ ($c = 2.0$, $CHCl_3$); ^{1}H NMR (400.130 MHz, $CDCl_3$): $\delta = 0.66$ (t, $^3J = 7.4$ Hz, 3H, 1-CH_3), 1.37 (m, 2H, 2-CH_2), 1.55 (dd, $^3J = 6.4$ Hz, $^4J = 1.6$ Hz, 3H, 6-CH_3), 4.90 (dt, $^3J = 6.8$ Hz, $^3J = 7.0$ Hz, 1H, 3-CH), 5.10 (ddq, $^3J = 15.3$ Hz, $^3J = 7.7$ Hz, $^4J = 1.7$ Hz, 1H, 4-CH), 5.50 (dqd, $^3J = 15.3$ Hz, $^3J = 6.5$ Hz, $^4J = 0.9$, 1H, 5-CH), 7.32–7.38 (m, 4H, Ar-H), 7.40–7.49 (m, 3H, Ar-H), 7.51–7.68 (m, 6H, Ar-H), 7.86–7.90 ppm (m, 1H, Ar-H); ^{13}C NMR (125.741 MHz, $CDCl_3$): $\delta = 9.6$ (C1), 17.7 (C6), 26.9 (C2), 78.0 (C3), 128.2 (d, $J_{C,P} = 2.2$ Hz, 2C, Ar), 128.9 (d, $J_{C,P} = 2.2$ Hz, 2C, Ar), 128.7 (C5), 129.6 (C4), 130.6 (d, $J_{C,P} = 8.7$ Hz, 2C, Ar), 131.0 (d, $J_{C,P} = 11.6$ Hz, 2C, Ar), 131.5, 131.8 (d, $J_{C,P} = 2.7$ Hz, Ar), 131.9 (d, $J_{C,P} = 3.9$ Hz, 2C, Ar), 132.0 (d, $J_{C,P} = 3.6$ Hz, 2C, Ar), 132.8, 132.9 (d, $J_{C,P} = 4.6$ Hz, C_q), 134.0 (d, $J_{C,P} = 4.8$ Hz, C_q), 135.1 (d, $J_{C,P} = 10.1$, 2C, Ar), 136.2 (d, $J_{C,P} = 6.3$, C_q), 165.8 ppm (d, $J_{C,P} = 2.7$ Hz, C=O); ^{31}P NMR (161.976 MHz, $CDCl_3$): $\delta = 31.4$ ppm; elemental analysis: calcd (%) for $C_{25}H_{25}O_3P$ (404.44): C 74.24, H 6.29; found: C 74.11, H 6.23; HPLC (DAICEL Chiralpak AD-H, 0.46×25 cm, 0.8 mL min^{-1}, *n*-heptane/methanol = 100:1, 22 °C, 224 nm): t_R(−)-(*Z*)-**11a**: 41.48 min (0.57%), t_R(+)-(*E*)-**11a**: 44.19 min (1.21%); t_R(−)-(*E*)-**11a**: 48.60 min (98.31%).

(−)-**8**: *o*-DPPB ester (−)-**6b** (1.538 g, 2.19 mmol) gave (−)-**8** (1.556 g, >99%) as a colorless, highly viscous glass. $[\alpha]_D^{20} = -5.0$ ($c = 1.6$ in $CHCl_3$); ^{1}H NMR (400.136 MHz, $CDCl_3$): $\delta = 0.99$ (s, 9H), 1.30 (t, $J = 7.34$ Hz, 3H), 1.74 (s, 3H), 3.47 (dd, $J = 10.7$, 5.6 Hz, 1H), 3.65 (dd, $J = 10.7$, 6.0 Hz, 1H), 4.20 (m, 2H), 5.52 (ptd, $J = 9.0$, 5.6 Hz, 1H), 6.44 (dd, $J = 9.0$, 1.3 Hz, 1H), 7.29–7.44 (m, 12H), 7.59 (m, 10H), 7.76 (m, 1H), 7.94 ppm (m, 1H); ^{13}C NMR (100.624 MHz, $CDCl_3$): $\delta = 13.2$, 14.2, 19.1, 26.7 (3C), 60.7, 64.2, 72.3, 127.67 (2C), 127.70, 128.1 (d, $J_{C,P} = 11.6$ Hz, 4C), 129.8 (4C), 130.6 (d, $J_{C,P} = 8.7$ Hz), 131.2 (d, $J_{C,P} = 11.6$ Hz), 131.4 (d, $J_{C,P} = 2.9$ Hz), 131.7 (d, $J_{C,P} = 2.9$ Hz), 131.85 (d, $J_{C,P} = 10.1$ Hz, 2C), 131.88 (d, $J_{C,P} = 10.1$ Hz, 2C), 132.1, 132.4, 132.8 (d, $J_{C,P} = 5.8$ Hz), 133.1 (2C), 133.4, 133.9 (d, $J_{C,P} = 5.8$ Hz), 135.1–135.6 (m, 2C), 135.55 (2C), 135.61 (2C), 165.5 (d, $J_{C,P} = 2.9$ Hz), 167.3 ppm; ^{31}P NMR (121.474 MHz, $CDCl_3$): $\delta = 31.3$ ppm; elemental analysis: calcd (%) for $C_{43}H_{45}O_6PSi$ (716.87): C 72.04, H 6.33; found (%) C 71.88, H 6.15.

(−)-**10b**: *o*-DPPB ester (−)-**10a** (415 mg, 1.00 mmol, 97% *ee*) gave (−)-**10b** (425 mg, 99%) as a colorless glass. $[\alpha]_D^{20} = -67.1$ ($c = 2.58$, $CHCl_3$); ^{1}H NMR (400.136 MHz, $CDCl_3$): $\delta = 0.95$ (t, $J = 7.3$ Hz, 3H, CH_2CH_3), 1.46–1.65 (m, 4H, 4/6-H, 5-H), 1.83–1.91 (m, 2H, 4/6-H), 1.92 (q, $J = 7.3$ Hz, 2H, CH_2CH_3), 5.10 (m, 1H, 1-H), 5.23 (m, 1H, 2-H), 7.40–7.44 (m, 4H, Ar-H), 7.47–7.55 (m, 3H, Ar-H), 7.59 (m, 1H, Ar-H), 7.67 (m, 4H, Ar-H), 7.75 (m, 1H, Ar-H), 7.88 ppm (m, 1H, Ar-H); ^{13}C NMR (100.624 MHz, $CDCl_3$): $\delta = 12.0$ (CH_2CH_3), 19.2 (C5), 27.9 (CH_2CH_3), 28.3, 30.4, 70.8, 118.1, 128.2 (d, $J_{C,P} = 11.6$ Hz, 4C, Ar-C), 130.4 (d, $J_{C,P} = 8.7$ Hz, 2C, Ar-C), 130.8 (d, $J_{C,P} = 11.6$ Hz, 2C, Ar-C), 131.5 (2C, Ar-C), 131.8 (Ar-C), 132.12 (d, $J_{C,P} = 10.2$ Hz, 2C, Ar-C), 132.16 (d, $J_{C,P} = 10.1$ Hz, 2C, Ar-C), 135.0 (d, $J_{C,P} = 10.2$ Hz, 2C, Ar-C), 136.7 (d, $J_{C,P} = 7.3$ Hz, Ar-C), 146.2, 166.8 ppm (d, $J_{C,P} = 2.9$ Hz, *C*OOR); ^{31}P NMR (121.468 MHz, $CDCl_3$): $\delta = 31.4$ ppm; elemental analysis: calcd (%) for $C_{27}H_{27}O_3P$ (430.48): C 75.33, H 6.32; found: C 75.01, H 6.29.

(−)-**11b**: *o*-DPPB ester (−)-**11a** (400 mg, 1.00 mmol, 94% *ee*) gave (−)-**11b** (413 mg, 99%). $[\alpha]_D^{20} = -82.4$ ($c = 3.07$, $CHCl_3$); ^{1}H NMR (400.136 MHz, $CDCl_3$): $\delta = 1.43$–1.61 (m, 4H, 4/6-H, 5-H), 1.62 (s, 1H, 3-CH_3), 1.76–1.90 (m, 2H, 4/6-H), 5.08 (m, 1H, 1-H), 5.22 (m, 1H, 2-H), 7.42 (m, 4H, Ar-H), 7.51 (m, 3H, Ar-H), 7.59 (m, 1H, Ar-H), 7.66 (m, 4H, Ar-H), 7.72 (m, 1H, Ar-H), 7.89 ppm (m, 1H, Ar-H); ^{13}C NMR (100.624 MHz, $CDCl_3$): $\delta = 19.1$, 23.7, 27.5, 29.9, 70.7, 119.8, 128.2 (d, $J_{C,P} = 11.6$ Hz, 4C, Ar-C), 130.4 (d, $J_{C,P} = 7.3$ Hz, 2C, Ar-C), 130.8 (d, $J_{C,P} = 11.6$ Hz, 2C, Ar-C), 131.5 (2C, Ar-C), 131.8 (Ar-C), 132.1 (d, $J_{C,P} = 10.2$ Hz, 4C, Ar-C), 135.0 (d, $J_{C,P} = 8.7$ Hz, 2C, Ar-C), 136.7 (d, $J_{C,P} = 7.3$ Hz, Ar-C), 140.9, 166.8 ppm (d, $J_{C,P} = 2.9$ Hz, *C*OOR); ^{31}P NMR (121.468 MHz, $CDCl_3$): $\delta = 31.5$ ppm; elemental analysis: calcd (%) for $C_{26}H_{25}O_3P$ (416.45): C 74.99, H 6.05; found: C 74.58, H 6.09.

*General Procedure for the Directed syn-*Allylic Substitution of *o*-DPPB Esters: Copper and Grignard Reagents

Variant A: Copper(I) bromide dimethyl sulfide (0.5 equiv) was added in one portion to a magnetically stirred solution of the *o*-DPPB ester (1.00 equiv) in diethyl ether (0.05 M unless otherwise noted) at room temperature and stirred for a further 5–10 min until a clear yellow solution was formed. The corresponding Grignard reagent in diethyl ether was added to this well-stirred solution within the noted time by a syringe pump, and the mixture was stirred vigorously until TLC showed quantitative consumption of starting material.

Variant B: A solution of the *o*-DPPB ester (1.0 equiv) and copper bromide dimethylsulfide (0.5 equiv) in diethyl ether (0.01 M) was added dropwise to a solution of the corresponding Grignard reagent (0.05 M, 1.1 equiv) by syringe pump during the time indicated.

Workup procedure A: The reaction was quenched by successive addition of a saturated aqueous solution of NH_4Cl (20 mL mmol^{-1}) and an aqueous solution of ammonia (12.5%, 10 mL mmol^{-1}) followed by the addition of diethyl ether (20 mL mmol^{-1}). The mixture was stirred for 10 min, the organic phase was separated, and the aqueous phase was extracted three times with diethyl ether. The combined organic phases were washed with brine, dried ($MgSO_4$), and the solvent was removed in vacuo to give the crude product. Column chromatography (SiO_2, pentane or petroleum ether (PE)/EtOAc) yielded the analytically pure products. Regioisomeric ratios were determined by achiral GC analysis for volatile compounds or by ^{1}H NMR spectroscopic analysis of the crude product. Enantiomeric excess was determined by chiral HPLC analysis and referred to racemic material obtained as described above from the corresponding racemic *o*-DPPB esters.

Workup procedure B: The reaction mixture was quenched with water (20 mmol mmol^{-1} substrate) and filtered with pentane through silica gel. Removal of the solvent (rotavap, normal pressure, 45 °C) furnished the substitution products.

General Procedure for Ozonolysis Followed by Reductive Workup with $NaBH_4$

A stream of ozone was bubbled (1 bubble s^{-1}) through a solution of the alkene (1 equiv) in MeOH/CH_2Cl_2 (1:1, 0.1 M) at −78 °C until quantitative conversion was determined by TLC. Subsequently, excess ozone was removed by bubbling argon through this solution. $NaBH_4$ (10 equiv) was then added at −78 °C, and the mixture was allowed to warm to room temperature overnight. Saturated aqueous NH_4Cl (2 mL mmol^{-1} substrate) was added, and the reaction mixture was extracted with *tert*-butyl methyl ether (3×20 mL mmol^{-1} substrate) and dried ($MgSO_4$). Removal of the solvent in vacuo and purification by column chromatography on silica with PE/*tert*-butyl methyl ether (10:1–5:1) furnished the analytically pure alcohol generally as a colorless oil. The corresponding racemic substrates were treated likewise to obtain a reference for analytical chiral GC.

(+)-**2a** (Table 1, entry 1): Following the general procedure (variant A, workup A), a mixture of (−)-**1** (181 mg, 0.5 mmol), copper(I) bromide dimethyl sulfide (52 mg, 0.25 mmol), and a solution of *n*-butyl magnesium chloride (1.1 mL, 0.55 mmol, 0.5 M, addition time: 20 min) in diethyl ether (10 mL) gave, after column chromatography (pentane), (+)-**2a** (63 mg, 0.45 mmol, 96%) as a colorless oil with 98% regioselectivity (GC, Supelco Wax 10). $[\alpha]_D^{20} = +13.2$ ($c = 1.9$ in $CHCl_3$); ^{1}H NMR (500.13 MHz, $CDCl_3$): $\delta = 0.88$ (t, $^3J = 6.9$ Hz, 3H, 9-CH_3), 0.94 (d, $^3J = 6.6$ Hz, 3H, 5-Me), 0.96 (t, $^3J = 7.1$ Hz, 3H, 1-CH_3), 1.18–1.35 (m, 6H, 6-CH_2, 7-CH_2, 8-CH_2), 1.95–2.07 (m, 3H, 2-CH_2, 5-CH), 5.25 (ddt, $^3J = 15.3$ Hz, $^3J = 7.6$ Hz, $^4J = 1.5$ Hz, 1H, 4-CH), 5.39 ppm (dtd, $^3J = 15.7$ Hz, $^3J = 6.2$ Hz, $^4J = 0.6$ Hz, 1H, 3-CH); ^{13}C NMR (125.76 MHz, $CDCl_3$): $\delta = 14.2$ (C1, C9), 20.9 (5-Me), 22.9 (CH_2), 25.6 (CH_2), 29.7 (CH_2), 36.7 (C2), 37.0 (C5), 130.0 (C3), 135.6 ppm (C4). The analytical data correspond to those reported previously.[21]

(+)-**4a**: Compound (+)-**2a** (35 mg, 0.25 mmol) gave (+)-**4a** (26 mg, 88%, 97% *ee*). $[\alpha]_D^{20} = -15.0$ ($c = 1.8$ in $CHCl_3$) (reference [22]: $[\alpha]_D^{20} =$

−11.6 (c=1.8 in $CHCl_3$)); ^{1}H NMR (400.130 MHz, $CDCl_3$): δ=0.9 (t, ^3J=6.9 Hz, 3H, 6-CH_3), 0.91 (d, ^3J=6.7 Hz, 3H, 2-Me), 1.20–1.45 (m, 6H, 3-CH_2, 4-CH_2, 5-CH_2), 1.60 (m, 1H, 2-CH), 3.42 (dd, ^2J=10.5 Hz, ^3J=6.6 Hz, 1H, 1-CH_2), 3.51 ppm (dd, ^2J=10.5 Hz, ^3J=5.8 Hz, 1H, 1-CH_2); ^{13}C NMR (100.167 MHz, $CDCl_3$): δ=14.2 (C6), 16.7 (CH_2), 23.0 (2-Me), 29.3 (CH_2), 32.9 (CH_2), 35.8 (C2), 68.5 ppm (C1); GC (Hydrodex-β, 65 °C, isotherm, 1.3 bar He): t_R(+)-**4a**=28.12 min (1.5 %), t_R(−)-**4a**=29.90 min (98.5 %).

(+)-**2b** (Table 1, entry 2): Following the general procedure (variant A, workup A), a mixture of (−)-**1** (181 mg, 0.5 mmol), copper(I) bromide dimethyl sulfide (52 mg, 0.25 mmol), and a solution of 3-pentyl magnesium bromide (1.1 mL, 0.55 mmol, 0.5 M, addition time: 20 min) in diethyl ether (10 mL) gave, after column chromatography (pentane), (+)-**2b** (63 mg, 0.45 mmol, 82 %) as a colorless oil with 97 % regioselectivity (GC, Supelco Wax 10). $[\alpha]_D^{20}$=+8.6 (c=1.0 in $CHCl_3$); ^{1}H NMR (400.870 MHz, $CDCl_3$): δ=0.84 (t, ^3J=7.4 Hz, 6H, 2×8-CH_3), 0.91 (d, ^3J=6.8 Hz, 3H, 5-Me), 0.96 (t, ^3J=7.5 Hz, 3H, 1-CH_3), 1.12–1.38 (m, 5H, 6-H, 2×7-CH_2), 1.96–2.09 (m, 3H, 2-CH_2, 5-H), 5.28 (ddt, ^3J=15.3 Hz, ^3J=7.4 Hz, ^4J=1.2 Hz, 1H, 4-H), 5.35 ppm (dtd, ^3J=15.4 Hz, ^3J=6.0 Hz, ^4J=0.8 Hz, 1H, 3-H); ^{13}C NMR (125.741 MHz, $CDCl_3$): δ=12.6 (2×C8), 14.2 (C1), 22.6 (5-Me), 22.7 (2×C7), 25.8 (C2), 37.9 (C5), 43.0 (C6), 130.7 (C3), 133.9 (C4); MS (EI) (70 eV): m/z (%): 154 $[M]^+$ (22), 83 (4), 67 (2), 55 (100), 41 (26).

(−)-**4b**: Compound (+)-**2b** (20 mg, 0.13 mmol) gave (−)-**4b** (15 mg, 74 %, 95 % *ee*). $[\alpha]_D^{20}$=−10.7 (c=1.0 in $CHCl_3$); ^{1}H NMR (499.870 MHz, $CDCl_3$): δ=0.86 (t, ^3J=7.4 Hz, 6H, 2×5-CH_3), 0.99 (d, ^3J=6.8 Hz, 3H, 5-Me), 1.02 (t, ^3J=7.5 Hz, 3H, 1-CH_3), 1.68 (m, 1H, 2-H), 3.46 (dd, ^2J=12.6 Hz, ^3J=7.2 Hz, 1H, 1-CH_2), 3.60 ppm (dd, ^2J=11.4 Hz, ^3J=5.9 Hz, 1H, 1-CH_2); ^{13}C NMR (125.741 MHz, $CDCl_3$): δ=12.9 (2×C5), 23.6 (5-Me), 24.7 (2×C4), 43.0 (C2), 64.3 ppm (C1); GC (Hydrodex-β, 50 °C, isotherm, 1.5 bar He): t_R(−)-**4b**=5.41 min (97.8 %), t_R(+)-**4b**=5.70 min (2.2 %).

(+)-**2c** (Table 1, entry 3): Following the general procedure (variant A, workup A), a mixture of (−)-**1** (78 mg, 0.20 mmol), copper(I) bromide dimethyl sulfide (21 mg, 0.1 mmol), and a solution of *tert*-butyl magnesium bromide (0.5 mL, 0.22 mmol, 0.5 M, addition time: 30 min) in diethyl ether (10 mL) gave, after column chromatography (pentane), (+)-**2c** (30 mg, 0.19 mmol, 90 %) as a colorless oil with 97 % regioselectivity (GC, Supelco Wax 10). $[\alpha]_D^{20}$=+16.1 (c=1.0 in $CHCl_3$); ^{1}H NMR (499.870 MHz, $CDCl_3$): δ=0.83 (s, 9H, $C(CH_3)_3$), 0.88 (t, ^3J=7.4 Hz, 3H, 1-Me), 0.91 (d, ^3J=6.6 Hz, 3H, Me), 1.80–1.87 (m, 1H, 5-H), 1.95–2.12 (m, 1H, 2-H), 5.30–5.41 ppm (m, 2H, 3-H, 4-H); ^{13}C NMR (125.741 MHz, $CDCl_3$): δ=14.2 (CH_3), 15.7 (CH_3), 22.4 (C_q), 25.6, 27.5 ($C(CH_3)_3$), 47.1, 131.6 and 132.6 ppm (C3, C4); MS (EI) (70 eV): m/z (%): 140 $[M]^+$ (3), 82 (3), 67 (4), 57 (100), 41 (26).

(+)-**4c**: Compound (+)-**2c** (28 mg, 0.2 mmol) gave (+)-**4c** (14 mg, 72 %, 80 % *ee*). GC (Hydrodex-β, 50 °C, isotherm, 1.0 bar He): t_R(−)-**4c**=33.48 min (10 %), t_R(+)-**4c**=34.90 min (90 %); $[\alpha]_D^{20}$=+27.5 (c=1.2 in $CHCl_3$); ^{1}H NMR (400.130 MHz, $CDCl_3$): δ=0.88 (s, 9H, *t*Bu), 0.99 (d, ^3J=6.8 Hz, 3H, 2-Me), 1.68 (m, 1H, 2-H), 3.38 (dd, ^2J=10.5 Hz, ^3J=6.4 Hz, 1H, 1-CH_2), 3.44 ppm (dd, ^2J=10.6 Hz, ^3J=5.9 Hz, 1H, 1-CH_2); ^{13}C NMR (100.167 MHz, $CDCl_3$): δ=23.0 (2-Me), 27.5 ($C(CH_3)_3$), 32.1 (C_q), 39.2 (C2), 68.5 ppm (C1). The analytical data correspond to those reported previously.[23]

(−)-**2d**: (Table 1, entry 4): Following the general procedure (variant B, workup B, addition time 2 h), a mixture of (−)-**1** (71 mg, 0.18 mmol), copper(I) bromide dimethyl sulfide (19 mg, 0.09 mmol), and a solution of phenyl magnesium bromide (0.22 mmol, 0.05 M) in diethyl ether gave (−)-**2d** (27 mg, 94 %) as a colorless oil with 98 % regioselectivity. $[\alpha]_D^{20}$=−9.5 (c=1.0 in $CHCl_3$); ^{1}H NMR (499.870 MHz, $CDCl_3$): δ=0.98 (t, ^3J=7.4 Hz, 3H, 1-CH_3), 1.34 (d, ^3J=6.9 Hz, 3H, 5-Me), 2.03 (dqd, ^3J=6.8 Hz, ^3J=7.5 Hz, ^4J=1.0 Hz, 2H, 2-CH_2), 3.42 (m, 1H, 5-H), 5.50 (dtd, ^3J=15.3 Hz, ^3J=6.1 Hz, ^4J=1.0 Hz, 1H, 4-H), 5.54 (ddt, ^3J=15.4 Hz, ^3J=6.6 Hz, ^4J=1.3 Hz, 1H, 3-H), 7.18–7.78 ppm (m, 5H, Ar-H); ^{13}C NMR (125.692 MHz, $CDCl_3$): δ=13.9 (C1), 21.6 (CH_2), 26.9 (5-Me), 42.2 (C5), 125.9 (C-Ar), 127.2 (2×C-Ar), 128.3 (2×C-Ar), 130.8 (C3), 133.9 ppm (C4); HRMS (EI) (70 eV): m/z calcd for $C_{12}H_{16}$: 160.1254; found 168.1252; GC (Hydrodex-β, 50 °C isotherm, 1.0 bar He): t_R(S_N2)=47.82 min (0.8 %), t_R(S_N2)=49.48 min (0.7 %), t_R(−)-**2d**=50.97 min, t_R(+)-**2d**=52.21 min (3.0 %).

(+)-**2e**: (Table 1, entry 5): Following the general procedure (variant B, workup B, addition time 30 min), a mixture of (−)-**1** (78 mg, 0.20 mmol), copper(I) bromide dimethyl sulfide (21 mg, 0.10 mmol), and a solution of benzyl magnesium bromide (0.22 mmol, 0.1 M) in diethyl ether gave (+)-**2e** (33 mg, 97 %) as a colorless oil with 97 % regioselectivity. $[\alpha]_D^{20}$=+17.8 (c=0.6 in $CHCl_3$); ^{1}H NMR (499.870 MHz, $CDCl_3$): δ=0.86 (t, ^3J=7.6 Hz, 3H, 1-CH_3), 0.88 (d, ^3J=6.9 Hz, 3H, 5-Me), 1.90 (m, 2H, 2-CH_2), 2.27–2.35 (m, 1H, 5-H), 2.41 (dd, ^4J=13.2 Hz, ^3J=7.6 Hz, 1H, 6-CH_2), 2.58 (dd, ^4J=13.2 Hz, ^3J=6.6 Hz, 1H, 6-CH_2), 5.06–5.33 (m, 2H, 3-H, 4-H), 7.04–7.14 (m, 3H, Ar-H), 7.16–7.23 ppm (m, 2H, Ar-H); ^{13}C NMR (125.692 MHz, $CDCl_3$): δ=14.0 (C1), 20.1 (C2), 25.7 (5-Me), 38.8 (C5), 43.9 (C6), 125.7 (C-Ar), 128.1 (2×C-Ar), 129.4 (2×C-Ar), 130.5 (C3), 136.6 ppm (C4); HRMS (EI) (70 eV): m/z calcd for $C_{13}H_{18}$: 174.1408; found 168.1404; GC (Hydrodex-β, 60 °C isotherm, 1.5 bar He): t_R(S_N2)=73.2 min, t_R(−)-**2e**=89.50 min (3.5 %), t_R(+)-**2e**=91.24 min (94.1 %).

(+)-**2f**: (Table 1, entry 6): Following the general procedure (variant A, workup B), a mixture of (−)-**1** (194 mg, 0.5 mmol), copper(I) bromide dimethyl sulfide (50 mg, 0.25 mmol), and a solution of 4-pentenyl magnesium bromide (1.1 mL, 0.55 mmol, 0.5 M, addition time: 30 min) gave (+)-**2f** (61 mg, 80 %) as a colorless oil with 98 % regioselectivity (GC, Supelco Wax 10). $[\alpha]_D^{20}$=+10.8 (c=0.8 in $CHCl_3$); ^{1}H NMR (400.130 MHz, $CDCl_3$): δ=0.95 (d, ^3J=6.7 Hz, 3H, 5-Me), 0.95 (t, ^3J=7.3 Hz, 3H, 1-CH_3), 1.22–1.38 (m, 4H, 6-CH_2, 7-CH_2), 1.95–2.10 (m, 5H, 2-CH_2, 5-H, 8-CH_2), 4.90–5.02 (m, ^2J=17.1 Hz, 2H, 10-CH_2), 5.24 (ddt, ^3J=15.3 Hz, ^3J=7.6 Hz, ^4J=1.4 Hz, 1H, 4-H), 5.40 (dtd, ^3J=15.3 Hz, ^3J=6.2 Hz, ^4J=0.9 Hz, 1H, 3-H), 5.81 ppm (ddt, ^3J=17.2 Hz, ^3J=10.1 Hz, ^3J=6.7 Hz, 1H, 9-H); ^{13}C NMR (125.741 MHz, $CDCl_3$): δ=14.2 (C1), 21.0 (5-Me), 25.7 (C2), 26.8 (C7), 34.0 (C6), 36.7 (C5), 114.2 (C10), 130.3 (C3), 135.3 (C4), 139.3 ppm (C9).

(+)-**5**: Caution: Carbon monoxide is toxic and the reaction should be carried out in a well-ventilated fume hood equipped with a CO sensor.[13] $[Rh(CO)_2acac]$ (0.9 mg, 3.5 μmol) and 6-DPPon[24] (4.7 mg, 17.5 μmol) were placed in a Schlenk flask under an atmosphere of argon and dissolved in THF (1 mL). After 5 min, (+)-**2f** (304 mg, 0.52 mmol) was added, and the argon atmosphere was exchanged three times against an atmosphere of synthesis gas (CO/H_2=1:1). The reaction mixture was magnetically stirred with a cross stirrer bar for 24 h, then filtered with dichloromethane through silica. The solvent was removed in vacuo to furnish (+)-**5** (78 mg, 83 %, 94 % *ee*). $[\alpha]_D^{20}$=+14.3 (c=1.2 in $CHCl_3$); ^{1}H NMR (400.130 MHz, $CDCl_3$): δ=0.94 (d, ^3J=6.6 Hz, 3H, CH_3), 0.96 (t, ^3J=7.4 Hz, 3H, CH_3), 1.36–1.66 (m, 6H, 3×CH_2), 1.95–2.07 (m, 5H), 2.41 (dt, ^3J=10.5 Hz, ^3J=3.8 Hz, 2H, 2-CH_2), 5.23 (ddt, ^3J=15.3 Hz, ^3J=7.6 Hz, ^4J=1.4 Hz, 1H, 8-H), 5.38 (dtd, ^3J=15.3 Hz, ^3J=6.2 Hz, ^4J=0.9 Hz, 1H, 9-H), 9.76 ppm (t, ^3J=1.7 Hz, 1H, CHO); ^{13}C NMR (125.741 MHz, $CDCl_3$): δ=14.3 (C1), 21.0, 22.1, 25.7 , 27.0 , 29.3, 36.6, 37.1, 43.9, 130.3, 135.2, 203.1 ppm; HRMS (EI) (70 eV): m/z calcd for $C_{12}H_{22}O$: 182.1671; found 182.1666; GC (Hydrodex-β, 70 °C isotherm, 10 min, 10° min^- to 200 °C, 1.5 bar He): t_R(−)-**5**=18.49 min (3.2 %), t_R(+)-**5**=18.56 min (96.8 %).

7a: (Table 2, entry 1): Following the general procedure (variant A, workup A), a mixture of (−)-**6a** (91 mg, 0.139 mmol), copper(I) bromide dimethyl sulfide (14.4 mg, 0.07 mmol), and a solution of methyl magnesium iodide (0.19 mL, 0.167 mmol, 0.86 M, addition time: 15 min) gave **7a** (38 mg, 72 %) as a colorless oil with >95 % regioselectivity (^{1}H NMR). ^{1}H NMR (300.064 MHz, $CDCl_3$): δ=0.06 (s, 6H), 0.90 (s, 9H), 1.03 (s, 6H), 3.16 (s, 2H), 3.80 (s, 3H), 4.15 (dd, J=5.2, 1.3 Hz, 2H), 4.44 (s, 2H), 5.50 (dt, J=15.7, 5.2 Hz, 1H), 5.67 (dt, J=15.8, 1.3 Hz, 1H), 6.87 (m, 2H), 7.24 ppm (m, 2H); ^{13}C NMR (125.741 MHz, $CDCl_3$): δ=−4.9 (2C), 18.5, 24.7 (2C), 26.1 (3C), 32.2, 55.3, 64.5, 73.0, 79.2, 113.9 (2C), 126.5 (C2), 129.0, 131.0, 138.4, 159.1 ppm; HRMS (EI): m/z calcd for $C_{17}H_{27}O_3Si$: 307.1730 $[M^+-t\text{Bu}]$; found: 307.1728.

(−)-**7b**: (Table 2, entry 2): Following the general procedure (variant A, workup A), a mixture of (−)-**6a** (399 mg, 0.593 mmol, 94 % *ee*), copper(I) bromide dimethyl sulfide (62 mg, 0.3 mmol), and a solution of ethyl magnesium bromide (0.79 mL, 0.712 mmol, 0.9 M, addition time: 20 min) gave

(−)-**7b** (192 mg, 86%) as a colorless oil with >99% regioselectivity and 94% *ee* (HPLC). $[\alpha]_D^{22} = -8.6$ ($c = 1.13$ in $CHCl_3$); ^{1}H NMR (300.064 MHz, $CDCl_3$): $\delta = 0.06$ (s, 6H), 0.77 (t, 3H, $J = 7.6$ Hz), 0.90 (s, 9H), 0.99 (s, 3H), 1.42 (m, 2H), 3.17 (d, 1H, $J = 8.8$ Hz), 3.21 (d, 1H, $J = 8.8$ Hz), 3.80 (s, 3H), 4.15 (dd, 2H, $J = 5.0$, 1.2 Hz), 4.42 (s, 2H), 5.48 (dt, 1H, $J = 15.8$, 5.0 Hz), 5.60 (pd, 1H, $J = 15.8$ Hz), 6.85 (m, 2H), 7.24 ppm (m, 2H); ^{13}C NMR (100.614 MHz, $CDCl_3$): $\delta = -5.0$ (2C), 8.3, 18.4, 21.1, 26.0 (3C), 30.3, 40.1, 55.3, 64.5, 73.0, 77.6, 113.7 (2C), 127.5, 128.9 (2C), 131.1, 136.9, 159.0 ppm; elemental analysis: calcd (%) for $C_{22}H_{38}O_3Si$ (378.62): C 69.79, H 10.12; found: C 69.56, H 10.30; HPLC (2×Chiralcel OD-H, *n*-heptane, 15°C, 0.6 mL min^{-1}, 275 nm): $t_R(R)$-(−)-**7b** = 57.51 min, $t_R(S)$-(+)-**7b** = 61.39 min.

(−)-**7c**: (Table 2, entry 3): Following the general procedure (variant A, workup A), a mixture of (−)-**6a** (69 mg, 0.105 mmol, 93% *ee*), copper(I) bromide dimethyl sulfide (10.3 mg, 0.05 mmol), and a solution of *n*-butyl magnesium bromide (0.11 mL, 0.126 mmol, 1.2 M, addition time: 15 min) gave (−)-**7c** (42 mg, 99%) as a colorless oil with >99% regioselectivity and 93% *ee* (HPLC). $[\alpha]_D^{22} = -5.7$ ($c = 0.615$ in $CHCl_3$); ^{1}H NMR (400.136 MHz, $CDCl_3$): $\delta = 0.06$ (s, 6H), 0.87 (t, $J = 7.3$ Hz, 3H), 0.90 (s, 9H), 1.00 (s, 3H), 1.15 (m, 2H), 1.24 (m, 2H), 1.36 (m, 2H), 3.18 (m, 2H), 3.80 (s, 3H), 4.16 (dd, $J = 5.2$, 1.3 Hz, 2H), 4.42 (s, 2H), 5.47 (dt, $J = 15.9$, 5.2 Hz, 1H), 5.61 (m, 1H), 6.86 (m, 2H), 7.24 ppm (m, 2H); ^{13}C NMR (100.624 MHz, $CDCl_3$): $\delta = -5.0$ (2C), 14.1, 18.4, 21.6, 23.5, 26.0 (3C), 26.2, 37.7, 40.0, 55.3, 64.5, 72.9, 77.8, 113.7 (2C), 127.2, 129.0 (2C), 131.1, 137.3, 159.0 ppm; elemental analysis: calcd (%) for $C_{24}H_{42}O_3Si$ (406.67): C 70.88, H 10.41; found: C 70.89, H 10.42; HPLC (2×Chiralcel OD-H, *n*-heptane, 15°C, 0.5 mL min^{-1}, 275 nm): $t_R(R)$-(−)-**7c** = 57.93 min, $t_R(S)$-(+)-**7c** = 61.25 min.

(−)-**7d**: (Table 2, entry 4): Following the general procedure (variant A, workup A), a mixture of (−)-**6a** (75 mg, 0.115 mmol, 94% *ee*), copper(I) bromide dimethyl sulfide (11.9 mg, 0.058 mmol), and a solution of isopropyl magnesium bromide (0.18 mL, 0.138 mmol, 0.76 M, addition time: 15 min) gave (−)-**7d** (40 mg, 89%) as a colorless oil with >99% regioselectivity (HPLC). $[\alpha]_D^{20} = -13.1$ ($c = 0.93$ in $CHCl_3$); ^{1}H NMR (500.003 MHz, $CDCl_3$): $\delta = 0.06$ (s, 6H), 0.79 (d, $J = 6.9$ Hz, 3H), 0.81 (d, $J = 6.9$ Hz, 3H), 0.90 (s, 9H), 0.95 (s, 3H), 1.81 (psept, $J = 6.9$ Hz, 1H), 3.23 (d, $J = 8.8$ Hz, 1H), 3.25 (d, $J = 8.8$ Hz, 1H), 3.80 (s, 3H), 4.17 (dd, $J = 5.4$, 1.5 Hz, 2H), 4.40 (d, $J = 12.2$ Hz, 1H), 4.42 (d, $J = 12.2$ Hz, 1H), 5.49 (dt, $J = 15.9$, 5.4 Hz, 1H), 5.66 (dt, $J = 15.9$, 1.4 Hz, 1H), 6.86 (m, 2H), 7.24 ppm (m, 2H); ^{13}C NMR (125.741 MHz, $CDCl_3$): $\delta = -5.0$ (2C), 17.2, 17.6, 18.1, 18.4, 26.0 (3C), 32.4, 42.5, 55.3, 64.5, 72.9, 76.8, 113.6 (2C), 127.9, 129.0 (2C), 131.0, 135.7, 159.0 ppm; elemental analysis: calcd (%) for $C_{23}H_{40}O_3Si$ (392.27): C 70.35, H 10.27; found: C 70.45, H 10.25.

(−)-(*R*,*E*)-4,5-dimethyl-4-(4-methoxybenzyloxymethyl)hex-2-en-1-ol: A solution of (−)-**7d** (32 mg, 0.082 mmol) in THF (1 mL) was treated with tetra-*n*-butylammonium fluoride (TBAF; 0.1 mmol, 1 M solution in THF), and the mixture was stirred at room temperature until TLC showed quantitative consumption of the starting material (2 h). The solvents were removed under reduced pressure, and the residue was purified by column chromatography (PE/EtOAc = 9:1) to yield the analytically pure allylic alcohol (22 mg, 96%, 93% *ee*) as a colorless liquid. $[\alpha]_D^{20} = -19.2$ ($c = 1.79$, $CHCl_3$); ^{1}H NMR (400.136 MHz, $CDCl_3$): $\delta = 0.79$ (d, $J = 6.9$ Hz, 3H), 0.81 (d, $J = 6.9$ Hz, 3H), 0.95 (s, 3H), 1.81 (psept, $J = 6.9$ Hz, 1H), 3.23 (d, $J = 8.6$ Hz, 1H), 3.25 (d, $J = 8.6$ Hz, 1H), 3.80 (s, 3H), 4.12 (m, 2H), 4.41 (s, 2H), 5.59 (dt, $J = 15.9$, 5.6 Hz, 1H), 5.71 (d, $J = 15.9$ Hz, 1H), 6.87 (m, 2H), 7.23 ppm (m, 2H) (the signal for OH could not be detected); ^{13}C NMR (100.624 MHz, $CDCl_3$): $\delta = 17.2$, 17.6, 17.8, 32.4, 42.7, 55.3, 64.3, 73.0, 76.6, 113.7 (2C), 127.6, 129.0 (2C), 130.9, 138.1, 159.1 ppm; elemental analysis: calcd (%) for $C_{17}H_{26}O_3$ (278.39): C 73.34, H 9.41; found: 73.07, H 9.41; Chiral HPLC (Chiralpak AD, *n*-heptane/*iso*-propanol = 96:4, 20°C, 1 mL min^{-1}, 275 nm): t_R(+)-alcohol = 15.01 min, t_R(−)-alcohol = 19.29 min.

(−)-**7e** (Table 2, entry 5): Following the general procedure (variant A, workup A), a mixture of (−)-**6a** (45 mg, 0.069 mmol, 93% *ee*), copper(I) bromide dimethyl sulfide (7.1 mg, 0.035 mmol), and a solution of benzyl magnesium bromide (2.0 mL, 0.104 mmol, 0.07 M, addition time: 90 min) gave (−)-**7e** (16 mg, 53%) as a colorless oil with >99% regioselectivity and 85% *ee* (HPLC). $[\alpha]_D^{20} = -4.4$ ($c = 2.51$ in $CHCl_3$); ^{1}H NMR (300.065 MHz, $CDCl_3$): $\delta = 0.05$ (s, 6H), 0.90 (s, 9H), 0.98 (s, 3H), 2.67 (d, $J = 12.9$ Hz, 1H), 2.74 (d, $J = 12.9$ Hz, 1H), 3.12 (d, $J = 12.9$ Hz, 1H), 3.15 (d, $J = 12.9$ Hz, 1H), 3.81 (s, 3H), 4.13 (dd, $J = 5.2$, 1.5 Hz, 2H), 4.44 (s, 2H), 5.42 (dd, $J = 15.9$, 5.2 Hz, 1H), 5.71 (m, 1H), 6.88 (m, 2H), 7.07–7.32 ppm (m, 7H); ^{13}C NMR (75.460 MHz, $CDCl_3$): $\delta = -5.1$ (2C), 18.4, 21.7, 26.0 (3C), 40.9, 43.8, 55.3, 64.2, 72.8, 76.3, 113.7 (2C), 125.8, 127.4, 127.6 (2C), 129.1 (2C), 130.8 (2C), 130.9, 136.5, 138.4, 159.1 ppm; elemental analysis: calcd (%) for $C_{27}H_{40}O_3Si$ (440.69): C 73.59, H 9.15; found: C 73.71, H 9.44; HPLC (Chiralcel OD-H, *n*-heptane, 15°C, 0.8 mL min^{-1}, 275 nm): $t_R(R)$-(−)-**7e** = 33.52 min, $t_R(S)$-(+)-**7e** = 43.01 min.

(−)-**7g** (Table 2, entry 7): Following the general procedure (variant A, workup A), a mixture of (−)-**6b** (76 mg, 0.11 mmol, >99% *ee*), copper(I) bromide dimethyl sulfide (11.3 mg, 0.055 mmol), and a solution of ethyl magnesium bromide (0.13 mL, 0.132 mmol, 1.02 M, addition time: 15 min) gave (−)-**7g** (39 mg, 84%) as a colorless oil with >95% regioselectivity and 98% *ee* (HPLC). $[\alpha]_D^{20} = -4.9$ ($c = 1.74$ in $CHCl_3$); ^{1}H NMR (400.136 MHz, $CDCl_3$): $\delta = 0.84$ (t, $J = 7.3$ Hz, 3H), 1.06 (s, 9H), 1.23 (s, 3H), 1.23 (m, 3H), 1.59 (m, 1H), 1.74 (m, 1H), 4.12 (m, 2H), 4.22 (dd, $J = 4.7$, 1.7 Hz, 2H), 5.58 (dt, $J = 15.9$, 4.7 Hz, 1H), 5.90 (dt, $J = 15.9$, 1.7 Hz, 1H), 7.39 (m, 6H), 7.67 ppm (m, 4H); ^{13}C NMR (100.624 MHz, $CDCl_3$): $\delta = 8.9$, 14.2, 19.3, 20.5, 26.8 (3C), 32.2, 48.0, 60.5, 64.5, 127.6 (4C), 127.9, 129.6 (2C), 133.88 (2C), 133.94, 135.6 (4C), 175.9 ppm; elemental analysis: calcd (%) for $C_{26}H_{36}O_3Si$ (424.6): C 73.54, H 8.54; found: C 73.58, H 8.54; HPLC (2×Chiralcel OD-H, *n*-heptane, 15°C, 0.5 mL min^{-1}, 275 nm): $t_R(R)$-(−)-**7g** = 66.93 min, $t_R(S)$-(+)-**7g** = 71.23 min.

(−)-**7h** (Table 2, entry 8): Following the general procedure (variant A, workup A), a mixture of (−)-**6b** (82 mg, 0.117 mmol, >99% *ee*), copper(I) bromide dimethyl sulfide (12.0 mg, 0.059 mmol), and a solution of *n*-butyl magnesium bromide (0.11 mL, 0.140 mmol, 1.23 M, addition time: 15 min) gave (−)-**7h** (46 mg, 87%) as a colorless oil with >95% regioselectivity and 97% *ee* (HPLC). $[\alpha]_D^{22} = -3.7$ ($c = 1.75$ in $CHCl_3$); ^{1}H NMR (400.136 MHz, $CDCl_3$): $\delta = 0.89$ (t, $J = 7.3$ Hz, 3H), 1.06 (s, 9H), 1.23 (t, $J = 7.3$ Hz, 3H), 1.24 (s, 3H), 1.28 (m, 4H), 1.53 (m, 1H), 1.67 (m, 1H), 4.10 (m, 1H), 4.13 (m, 1H), 4.22 (dd, $J = 5.5$, 1.7 Hz, 2H), 5.58 (m, 1H), 5.90 (dt, $J = 15.9$, 1.7 Hz, 1H), 7.39 (m, 6H), 7.68 ppm (m, 4H); ^{13}C NMR (100.624 MHz, $CDCl_3$): $\delta = 14.0$, 14.2, 19.2, 21.0, 23.1, 26.81 (3C), 26.84, 39.2, 47.6, 60.5, 64.5, 127.60 (4C), 127.64, 129.6 (2C), 133.9, 134.2 (2C), 135.6 (4C), 176.0 ppm; elemental analysis: calcd (%) for $C_{28}H_{40}O_3Si$ (452.70): C 74.29, H 9.01; found: C 74.38, H 8.91; HPLC (Chiralcel OD-H, *n*-heptane, 15°C, 0.8 mL min^{-1}, 227 nm): $t_R(R)$-(−)-**7h** = 14.01 min, $t_R(S)$-(+)-**7h** = 15.80 min.

(−)-**7i** (Table 2, entry 9): Following the general procedure (variant A, workup A), a mixture of (−)-**6b** (127 mg, 0.181 mmol, >99% *ee*), copper(I) bromide dimethyl sulfide (18.5 mg, 0.09 mmol), and a solution of isopropyl magnesium bromide (0.24 mL, 0.181 mmol, 0.75 M, addition time: 15 min) gave (−)-**7h** (67 mg, 84%) as a colorless oil with >95% regioselectivity and 97% *ee* (HPLC), determined at the stage of the deprotected primary alcohol; see below. $[\alpha]_D^{22} = -12.1$ ($c = 1.99$ in $CHCl_3$); ^{1}H NMR (400.136 MHz, $CDCl_3$): $\delta = 0.82$ (d, $J = 6.9$ Hz, 3H), 0.84 (d $J = 6.9$ Hz, 3H,), 1.06 (s, 9H), 1.15 (s, 3H), 1.24 (t, $J = 7.3$ Hz, 3H), 2.13 (psept, $J = 6.9$ Hz, 1H), 4.12 (q, $J = 7.3$ Hz, 1H), 4.13 (q, $J = 7.3$ Hz, 1H), 4.23 (m, 2H), 5.98 (m, 1H), 5.93 (dt, $J = 15.9$, 1.7 Hz, 1H), 7.39 (m, 6H), 7.68 ppm (m, 4H); ^{13}C NMR (100.624 MHz, $CDCl_3$): $\delta = 14.2$, 15.0, 17.3, 17.8, 19.2, 26.8 (3C), 34.5, 51.5, 60.4, 64.5, 127.6 (4C), 128.7, 129.6 (2C), 133.3, 133.86, 133.89, 135.5 (4C), 176.0 ppm; elemental analysis: calcd (%) for $C_{27}H_{38}O_3Si$ (438.67): C 73.92, H 8.73; found: C 73.93, H 8.84.

(*R*,*E*)-4-ethoxycarbonyl-4,5-dimethyl-2-hexen-1-ol:[18b] A solution of (−)-**7i** (10 mg, 0.023 mmol) in THF (0.5 mL) was treated with TBAF (0.03 mmol, 1 M solution in THF) and stirred at room temperature until TLC showed quantitative consumption of the starting material (1 h). The solvents were removed under reduced pressure, and the residue was purified by column chromatography (pentane/diethyl ether = 3:1) to yield the analytically pure primary allylic alcohol (4 mg, 87%, 97% *ee*) as a colorless liquid. ^{1}H NMR (300.066 MHz, $CDCl_3$): $\delta = 0.82$ (d, $J = 6.8$ Hz, 3H), 0.84 (d, $J = 6.8$ Hz, 3H), 0.88 (t, $J = 6.7$ Hz, 3H), 1.18 (s, 3H), 2.14 (psept, $J = 6.8$ Hz, 1H), 4.14 (m, 4H), 5.68 (dt, $J = 15.8$, 5.7 Hz, 1H), 5.89 ppm

(dt, $J=15.8$, 1.3 Hz, 1H) (the OH resonance could not be detected); ^{13}C NMR (100.624 MHz, $CDCl_3$): $\delta=14.2$, 15.1, 17.3, 17.7, 34.9, 51.3, 60.6, 63.7, 129.0, 135.0, 175.9 ppm; elemental analysis: calcd (%) for $C_{11}H_{20}O_3$ (200.27): C 65.97, H 10.07; found: C 66.29, H 10.08; Chiral HPLC (Chiralcel OD-H, *n*-heptane/*iso*-propanol = 95:5, 20 °C, 0.8 mL min^{-1}, 220 nm): t_R(*R*)-alcohol = 10.29 min, t_R(*S*)-alcohol = 11.62 min.

(+)-**12a** (Table 3, entry 1): Following the general procedure (variant B, workup B, addition time 90 min), a mixture of (−)-**10a** (42 mg, 0.10 mmol), copper(I) bromide dimethyl sulfide (10 mg, 0.05 mmol) in Et_2O/CH_2Cl_2 (10 mL, 20:1), and an ethereal solution of methyl magnesium iodide (4.0 mL, 0.22 mmol, 0.05 M) gave (+)-**12a** (17 mg, >95%) as a colorless oil with 99% regioselectivity and 96% *ee* determined by GC. $[\alpha]_D^{20}=+10.1$ ($c=0.80$ in *n*-pentane); ^{1}H NMR (400.136 MHz, $CDCl_3$): $\delta=0.83$ (t, $J=7.5$ Hz, 3H, CH_2CH_3), 0.92 (s, 3H, 3-CH_3), 1.30 (q, $J=7.6$ Hz, 2H, CH_2CH_3), 1.33 (m, 1H, 4-H^1), 1.48 (ddd, $J=13.1$, 8.4, 5.4 Hz, 1H, 4-H^2), 1.60 (m, 2H, 5-H), 1.92 (m, 2H, 6-H), 5.40 (dt, $J=9.9$, 1.9 Hz, 1H, 2-H), 5.59 ppm (dt, $J=9.9$, 3.7 Hz, 1H, 1-H); ^{13}C NMR (125.692 MHz, $CDCl_3$): $\delta=8.4$ (CH_2CH_3), 19.4 (CH_2CH_3), 25.4 (C5), 26.8 (C3-Me), 31.0 (C6), 32.0 (C3), 35.1 (C4), 125.3 (C1), 136.9 ppm (C2); MS (EI) (70 eV): *m/z* (%): 124 $[M]^+$ (18), 109 (5), 95 (100), 79 (7), 67 (31), 55 (6); HRMS (EI) (70 eV): *m/z* calcd for C_9H_{16}: 124.1251; found 124.1252; GC (Betadex 110, 35 °C isotherm, 0.3 bar He): $t_R(S_N2)=132.8$ min (0.8%), $t_R(S_N2)=137.0$ min (0.4%), t_R(−)-**12a** = 150.5 min (2.1%), t_R(+)-**12a** = 154.0 min (96.7%).

(+)-**12b** (Table 3, entry 2): Following the general procedure (variant B, workup B, addition time 90 min), a mixture of (−)-**10a** (42 mg, 0.10 mmol), copper(I) bromide dimethyl sulfide (10 mg, 0.05 mmol) in Et_2O/CH_2Cl_2 (10 mL, 20:1), and an ethereal solution of *n*-butyl magnesium bromide (4.0 mL, 0.20 mmol, 0.05 M) gave (+)-**12b** (21 mg, >95%) as a colorless oil with >99% regioselectivity and 96% *ee* determined by GC. $[\alpha]_D^{20}=+9.4$ ($c=2.57$ in *n*-pentane); ^{1}H NMR (400.136 MHz, $CDCl_3$): $\delta=0.80$ (t, $J=7.4$ Hz, 3H, CH_2CH_3), 0.89 (t, $J=7.1$ Hz, 3H, 3′-CH_3), 1.18–1.38 (m, 6H, 1′-H, 2′-H, 3′-H), 1.30 (q, $J=7.6$ Hz, 2H, CH_2CH_3), 1.41 (pt, $J=6.0$ Hz, 1H, 4-H^1), 1.42 (dd, $J=5.8$, 2.6 Hz, 1H, 4-H^2), 1.59 (pquin, $J=6.0$ Hz, 2H, 5-H), 1.92 (tdd, $J=6.0$, 3.8, 2.2 Hz, 2H, 6-H), 5.42 (dt, $J=10.3$, 2.2 Hz, 1H, 2-H), 5.59 ppm (dt, $J=10.3$, 3.7 Hz, 1H, 1-H); ^{13}C NMR (125.692 MHz, $CDCl_3$): $\delta=8.2$ (CH_2CH_3), 14.2 (C3′-Me), 19.3 (CH_2CH_3), 23.8 (C3′), 25.4 (C5), 26.1 (C2′), 32.0 (C3), 32.1 (C1′), 32.3 (C6), 39.2 (C4), 125.9 (C1), 136.1 ppm (C2); MS (EI) (70 eV): *m/z* (%): 166 $[M]^+$ (17), 137 (59), 109 (100), 95 (30), 81 (67), 67 (72), 55 (8); HRMS (EI) (70 eV): *m/z* calcd for $C_{12}H_{22}$: 166.1722; found: 166.1722; GC (trifluoroacetyl-γ-cyclodextrin, 38 °C isotherm, 1.5 bar He): $t_R(S_N2)=132.3$ min (0.6%), t_R(−)-**12b** = 136.2 min (2.2%), t_R(+)-**12b** = 143.7 min (97.2%).

(−)-**12c** (Table 3, entry 3): Following the general procedure (variant B, workup B, addition time 90 min), a mixture of (−)-**10a** (42 mg, 0.10 mmol), copper(I) bromide dimethyl sulfide (10 mg, 0.05 mmol) in Et_2O/CH_2Cl_2 (10 mL, 20:1), and an ethereal solution of isopropyl magnesium bromide (4.0 mL, 0.20 mmol, 0.05 M) gave (−)-**12c** (19 mg, >95%) as a colorless oil with 98% regioselectivity and 96% *ee* determined by GC. $[\alpha]_D^{20}=-25.5$ ($c=2.17$ in *n*-pentane); ^{1}H NMR (400.136 MHz, $CDCl_3$): $\delta=0.80$ (t, $J=7.5$ Hz, 3H, CH_2CH_3), 0.82 (d, $J=6.9$ Hz, 3H, 1′-CH_3), 0.83 (d, $J=6.9$ Hz, 3H, 1′-CH_3), 1.36 (q, $J=7.3$ Hz, 2H, CH_2CH_3), 1.42 (pq, $J=7.7$ Hz, 1H, 4-H^1), 1.48 (dt, $J=13.8$, 6.0 Hz, 1H, 4-H^2), 1.59 (m, 2H, 5-H), 1.67 (hept, $J=6.9$ Hz, 1H, 1′-H), 1.90 (m, 2H, 6-H), 5.40 (dt, $J=10.3$, 2.4 Hz, 1H, 2-H), 5.69 ppm (dt, $J=10.3$, 3.9 Hz, 1H, 1-H); ^{13}C NMR (100.624 MHz, $CDCl_3$): $\delta=8.3$ (CH_2CH_3), 16.8 (C1′-Me^1), 17.8 (C1′-Me^2), 19.5 (CH_2CH_3), 25.3 (C5), 28.1 (C1′), 32.0 (C3), 33.3 (C6), 37.2 (C4), 126.5 (C1), 135.2 ppm (C2); MS (EI) (70 eV): *m/z* (%): 152 $[M]^+$ (21), 123 (6), 109 (100), 91 (4), 81 (7), 67 (52), 55 (5); HRMS (EI) (70 eV): *m/z* calcd for $C_{11}H_{20}$: 152.1563; found: 152.1565; GC (trifluoroacetyl-γ-cyclodextrin, 60 °C isotherm, 1.3 bar He): $t_R(S_N2)=16.6$ min (1.9%), t_R(+)-**12c** = 23.3 min (2.1%), t_R(−)-**12c** = 24.6 min (96%).

(+)-**12d** (Table 3, entry 4): Following the general procedure (variant B, workup B, addition time 90 min), a mixture of (−)-**10a** (83 mg, 0.20 mmol), copper(I) bromide dimethyl sulfide (21 mg, 0.10 mmol) in Et_2O/CH_2Cl_2 (20 mL, 20:1), and an ethereal solution of phenyl magnesium bromide (8.0 mL, 0.40 mmol, 0.05 M) gave (+)-**12d** (46 mg, >95%) as a colorless oil. $S_N2'/S_N2=40:60$, 92% *ee* determined by GC. $[\alpha]_D^{20}=+10.5$ ($c=1.52$ in *n*-pentane); ^{1}H NMR (400.136 MHz, $CDCl_3$): $\delta=0.75$ (t, $J=7.3$ Hz, 3H, CH_2CH_3), 1.46–1.94 (m, 4H, 4-H, 5-H), 1.74 (q, $J=7.3$ Hz, 2H, CH_2CH_3), 2.01 (m, 2H, 6-H), 5.87 (dt, $J=10.3$, 1.7 Hz, 1H, 2-H), 5.92 (dt, $J=10.3$, 3.0 Hz, 1H, 1-H), 7.15–7.23 (m, 3H, Ar-H), 7.32–7.38 ppm (m, 2H, Ar-H); ^{13}C NMR (75.451 MHz, $CDCl_3$): $\delta=8.7$ (CH_2CH_3), 19.0 (CH_2CH_3), 25.6 (C5), 32.0 (C3), 35.1 (C6), 42.1 (C4), 125.4 (C1), 127.3 (2C, Ar-C), 127.8 (2C, Ar-C), 128.0 (Ar-C), 133.0 (Ar-C), 147.5 ppm (C2); MS (EI) (70 eV): *m/z* (%): 186 $[M]^+$ (15), 157 (100), 142 (6), 129 (30), 115 (8), 91 (35), 79 (6); HRMS (EI) (70 eV): *m/z* calcd for $C_{14}H_{18}$: 186.1409; found: 186.1409; GC (Betadex 110, 100 °C isotherm, 0.8 bar He): t_R(−)-**12d** = 104.8 min (1.7%), t_R(+)-**12d** = 107.6 min (38.3%), $t_R(S_N2)=129.8$ min (24.0%), $t_R(S_N2)=133.6$ min (36.0%).

(−)-**12a** (able 3, entry 5): Following the general procedure (variant B, workup B, addition time 90 min), a mixture of (−)-**11a** (40 mg, 0.10 mmol), copper(I) bromide dimethyl sulfide (10 mg, 0.05 mmol) in Et_2O/CH_2Cl_2 (10 mL, 4:1), and an ethereal solution of ethyl magnesium bromide (4.0 mL, 0.20 mmol, 0.05 M) gave (−)-**12a** (16 mg, >95%) as a colorless oil with 96% regioselectivity and 91% *ee* determined by GC (Betadex 110, 35 °C isotherm, 0.3 bar He); $[\alpha]_D^{20}=-9.2$ ($c=1.76$ in *n*-pentane). Spectroscopic data were identical to those of (+)-**12a** (see above).

(+)-**13a** (Table 3, entry 6): Following the general procedure (variant B, workup B, addition time 90 min), a mixture of (−)-**11a** (40 mg, 0.10 mmol), copper(I) bromide dimethyl sulfide (10 mg, 0.05 mmol) in Et_2O/CH_2Cl_2 (10 mL, 4:1), and an ethereal solution of *n*-butyl magnesium bromide (4.0 mL, 0.20 mmol, 0.05 M) gave (+)-**13a** (19 mg, >95%) as a colorless oil. $S_N2'/S_N2=98:2$, 94% *ee* determined by GC. $[\alpha]_D^{20}=+2.7$ ($c=2.59$ in *n*-pentane); ^{1}H NMR (400.136 MHz, $CDCl_3$): $\delta=0.89$ (t, $J=7.1$ Hz, 3H, 3′-CH_3), 0.93 (s, 3H, 3-CH_3), 1.21–1.33 (m, 6H, 1′-H, 2′-H, 3′-H), 1.35 (dpq, $J=13.0$, 3.5 Hz, 1H, 4-H^1), 1.50 (ddd, $J=12.9$, 8.2, 4.7 Hz, 1H, 4-H^2), 1.61 (m, 2H, 5-H), 1.93 (tdd, $J=6.0$, 3.6, 2.4 Hz, 2H, 6-H), 5.41 (dt, $J=10.3$, 1.9 Hz, 1H, 2-H), 5.58 ppm (dt, $J=10.3$, 3.9 Hz, 1H, 1-H); ^{13}C NMR (75.451 MHz, $CDCl_3$): $\delta=14.2$ (C3′-Me), 19.4 (C3-Me), 23.7 (C3′), 25.3 (C5), 26.3 (C2′), 27.4 (C1′), 32.0 (C3), 35.0 (C6), 42.8 (C4), 125.1 (C1), 137.2 ppm (C2); MS (EI) (70 eV): *m/z* (%): 152 $[M]^+$ (28), 137 (4), 109 (7), 95 (100), 81 (20), 67 (45), 55 (9), 41 (4); HRMS (EI) (70 eV): *m/z* calcd for $C_{11}H_{20}$: 152.1563; found: 152.1565; GC (trifluoroacetyl-γ-cyclodextrin, 40 °C isotherm, 1.3 bar He): t_R(−)-**13a** = 51.3 min (3.1%), t_R(+)-**13a** = 53.3 min (94.5%), $t_R(S_N2)=64.5$ min (2.4%).

(−)-**13b** (Table 3, entry 7): Following the general procedure (variant B, workup B, addition time 90 min), a mixture of (−)-**11a** (20 mg, 0.05 mmol), copper(I) bromide dimethyl sulfide (5 mg, 0.025 mmol) in Et_2O/CH_2Cl_2 (5 mL, 4:1), and an ethereal solution of isopropyl magnesium bromide (2.0 mL, 0.20 mmol, 0.05 M) gave (−)-**13b** (9 mg, >95%) as a colorless oil. $S_N2'/S_N2=96:4$, 91% *ee* determined by GC. $[\alpha]_D^{20}=-36.6$ ($c=2.00$ in *n*-pentane); ^{1}H NMR (400.136 MHz, $CDCl_3$): $\delta=0.84$ (d, $J=6.9$ Hz, 3H, 1′-CH_3), 0.86 (d, $J=6.9$ Hz, 3H, 1′-CH_3), 0.92 (s, 3H, 3-CH_3), 1.44–1.73 (m, 5H, 1′-H, 4-H, 5-H), 1.92 (m, 2H, 6-H), 5.45 (dpq, $J=10.3$, 1.7 Hz, 1H, 2-H), 5.60 ppm (dt, $J=10.3$, 3.9 Hz, 1H, 1-H); ^{13}C NMR (75.451 MHz, $CDCl_3$): $\delta=17.1$ (C1′-Me^1), 17.7 (C1′-Me^2), 19.4 (C3-Me), 24.4 (C1′), 25.3 (C5), 31.2 (C6), 32.0 (C3), 36.9 (C4), 125.3 (C1), 136.8 ppm (C2); MS (EI) (70 eV): *m/z* (%): 138 $[M]^+$ (12), 123 (3), 95 (100), 79 (19), 67 (53), 55 (9); HRMS (EI) (70 eV): *m/z* calcd for $C_{10}H_{18}$: 138.1407; found: 138.1409; GC (trifluoroacetyl-γ-cyclodextrin, 50 °C isotherm, 1.3 bar He): $t_R(S_N2)=15.1$ min (4.4%), t_R(+)-**13b** = 16.5 min (4.3%), t_R(−)-**13b** = 17.4 min (91.3%).

(+)-**13c** (Table 3, entry 8): Following the general procedure (variant B, workup B, addition time 90 min), a mixture of (−)-**11a** (80 mg, 0.20 mmol), copper(I) bromide dimethyl sulfide (21 mg, 0.10 mmol) in Et_2O/CH_2Cl_2 (20 mL, 4:1), and an ethereal solution of phenyl magnesium bromide (8.0 mL, 0.40 mmol, 0.05 M) gave (+)-**13c** (44 mg, >95%) as a colorless oil. $S_N2'/S_N2=41:59$, 82% *ee* determined by GC. $[\alpha]_D^{20}=+7.6$ ($c=2.14$ in cylohexane) (reference [25] for (−)-(*S*)-**13c**: $[\alpha]_D^{20}=-16.6$ ($c=9.37$ in cyclohexane)); ^{1}H NMR (400.136 MHz, $CDCl_3$): $\delta=1.40$ (s, 3H, 3-CH_3), 1.42–1.72 (m, 4H, 4-H, 5-H), 2.04 (m, 2H, 6-H), 5.72 (ddd, $J=10.3$, 3.0, 2.2 Hz, 1H, 2-H), 5.86 (dt, $J=10.3$, 3.9 Hz, 1H, 1-H), 7.15–7.23

(m, 3H, Ar-H), 7.32–7.38 ppm (m, 2H, Ar-H); ^{13}C NMR (100.624 MHz, $CDCl_3$): δ = 24.0 (C1-Me), 25.2 (C5), 30.9 (C6), 32.0 (C3), 42.3 (C4), 125.6 (C1), 127.3 (2C, Ar-C), 127.8 (2C, Ar-C), 128.0 (Ar-C), 135.3 (Ar-C), 147.4 ppm (C2); MS (EI) (70 eV): *m/z* (%): 172 $[M]^+$ (100), 157 (100), 143 (33), 129 (93), 115 (31), 91 (57), 79 (14); HRMS (EI) (70 eV): *m/z* calcd for $C_{13}H_{16}$: 172.1251; found: 172.1252; GC (Betadex 110, 80 °C (180 min), 1 °C min^{-1}, 120 °C (5 min), 0.8 bar He): t_R(−)-**13c** = 188.8 min (3.9%), t_R(+)-**13c** = 190.1 min (37.2%), t_R(S_N2) = 205.0 min (23.6%), t_R-(S_N2) = 207.6 min (35.4%).

General Procedure for the Nondirected anti-Allylic Substitution of *o*-DPPB Oxide Esters

The required dialkylzinc reagent (2.4 equiv) was added slowly to a magnetically stirred and freshly prepared solution of CuCN·2LiCl (1.2 equiv) in THF (1.0 M) at −30 °C. The reaction mixture was maintained for a further 30 min at −30 °C before a solution of the corresponding allylic *o*-DPPB oxide ester (1.0 equiv) in THF (0.07 M) was added during the time indicated (5–30 min). The reaction mixture was warmed over 2.5 h to 0 °C.

Workup variant C: Pentane was added and the reaction mixture was filtered through silica gel. After evaporation of the solvent (rotavap, 800 mbar), the corresponding substitution products were obtained as colorless oils.

Workup variant D: The reaction mixture was quenched upon addition of saturated aqueous NH_4Cl (40 mL mmol^{-1} substrate) and aqueous NH_3 (12.5%, 10 mL mmol^{-1} substrate). Pentane (20 mL mmol^{-1} substrate) was added, the organic phase separated, and the aqueous phase extracted with additional pentane (3 × 20 mL mmol^{-1} substrate). The combined organic phases were washed with aqueous NaOH (10%, 20 mL mmol^{-1} substrate), water (3 × 20 mL mmol^{-1} substrate), and brine (20 mL mmol^{-1} substrate) and dried ($MgSO_4$). Removal of solvents under normal pressure (rotavap, 45 °C) and purification of the crude product by column chromatography furnished the substitution products as colorless oils.

(−)-**2a** (Table 1, entry 7): Following the general procedure, a mixture of (−)-**3** (81 mg, 0.2 mmol, addition time: 30 min) and a solution of Zn(*n*Bu)$_2$ in THF (0.5 M, 0.9 mL, 0.42 mmol,) gave (workup C) (−)-**2a** (51 mg, 92%) as a colorless oil with 94% regioselectivity (GC, Supelco Wax 10). $[\alpha]_D^{20}$ = −14.5 (*c* = 1.9 in $CHCl_3$). Spectroscopic data were identical to those of (+)-**2a**.

(+)-**4a**: Compound (−)-**2a** (35 mg, 0.25 mmol) gave (+)-**4a** (26 mg, 88%, 97% *ee*; GC (Hydrodex-β, 65 °C, isotherm, 1.3 bar He)). Spectroscopic data were identical to those of (−)-**4a**.

(−)-**2c**: (Table 1, entry 8): Following the general procedure, a mixture of (−)-**3** (81 mg, 0.2 mmol, addition time: 30 min) and a solution of Zn(*n*Bu)$_2$ in THF (0.5 M, 0.9 mL, 0.42 mmol,) prepared by the reaction of *t*BuLi with $ZnCl_2$ gave (workup C) (−)-**2c** (20 mg, 68%) as a colorless oil with 75% regioselectivity (GC, Supelco Wax 10). $[\alpha]_D^{20}$ = −12.9 (*c* = 1.9 in $CHCl_3$). Spectroscopic data were identical to those reported for (+)-**2c**.

(−)-**4c**: Compound (−)-**2c** (42 mg, 0.3 mmol) gave (−)-**4c** (30 mg, 86%, 74% *ee*; GC (Hydrodex-β, 50 °C, isotherm, 1.0 bar He)). Spectroscopic data were identical to those of (+)-**4c**.

(+)-**2d**: (Table 1, entry 9): Following the general procedure, a mixture of (−)-**3** (81 mg, 0.2 mmol, addition time: 30 min) and a solution of diphenyl zinc in THF (0.3 M, 1.5 mL, 0.44 mmol) gave (workup C) (+)-**2d** (27 mg, 86%) as a colorless oil with 93% regioselectivity (GC, Supelco Wax 10) and 94% *ee* determined by GC (Hydrodex-β, 50 °C, isotherm, 1.0 bar He). Spectroscopic data were identical to those of (−)-**2d**.

(+)-**7g**: (Table 2, entry 10): Following the general procedure, a mixture of (−)-**8** (48 mg, 0.067 mmol, *E*/*Z* = 98.5:1.5, >99% *ee*) and a solution of diethyl zinc in THF (1.0 M, 0.17 mL, 0.17 mmol) gave (workup D), after column chromatography with PE (60:70)/EtOAc (95:5), (+)-**7g** (24 mg, 85%) as a colorless oil with S_N2'/S_N2 > 99:1, *E*/*Z* > 99:1, 97% *ee* determined by HPLC. $[\alpha]_D^{20}$ = +6.5 (*c* = 0.87 in $CHCl_3$); HPLC (2 × Chiralcel OD-H, 15 °C, 0.5 mL *n*-heptane/min, 227 nm): t_R(−)-**7g** = 70.71 min (1.5%), t_R(+)-**7g** = 74.20 min (98.5%). Spectroscopic data were identical to those of (−)-**7g**.

(+)-**7h** (Table 2, entry 11): Following the general procedure, a mixture of (−)-**8** (31 mg, 0.043 mmol, *E*/*Z* = 98.5:1.5, >99% *ee*) and a solution of Zn(*n*Bu)$_2$ in THF (1.0 M, 0.10 mL, 0.10 mmol) gave (workup D), after column chromatography with PE (60:70)/EtOAc (95:5), (+)-**7h** (17 mg, 87%) as a colorless oil with S_N2'/S_N2 > 99:1, *E*/*Z* > 98:2, 99% *ee* determined by HPLC. $[\alpha]_D^{20}$ = +9.1 (*c* = 0.87 in $CHCl_3$). HPLC (2 × Chiralcel OD-H, 15 °C, 0.5 mL *n*-heptane, 227 nm): t_R(−)-**7h** = 20.01 min (0.5%), t_R(+)-**7h** = 21.90 min (99.5%). Spectroscopic data were identical to those of (−)-**7h**.

(+)-**7i** (Table 2, entry 12): Following the general procedure, a mixture of (−)-**8** (89 mg, 0.124 mmol, *E*/*Z* = 98.5:1.5, >99% *ee*) and a solution of diisopropyl zinc in THF (1.0 M, 0.30 mL, 0.30 mmol) gave (workup D), after column chromatography with PE (60:70)/EtOAc (95:5), (+)-**7i** (51 mg, 94%) as a colorless oil with S_N2'/S_N2 = 97:3, *E*/*Z* > 99:1, 99% *ee* determined by HPLC after TBDPS removal at the stage of the resulting allylic alcohol as described above for (−)-**7i**. Spectroscopic data were identical to those of (−)-**7i**.

(−)-**12a** (Table 3, entry 10): Following the general procedure, a mixture of (−)-**10b** (108 mg, 0.25 mmol, 97% *ee*) and a solution of dimethyl zinc in THF (1.0 M, 0.60 mL, 0.60 mmol) gave (workup D), after column chromatography with pentane, (−)-**12a** (41 mg, >95%) as a colorless oil with S_N2'/S_N2 = 99:1 and 93% *ee* determined by GC (GC method described above for (+)-**12a**). Spectroscopic data were identical to those of (+)-**12a**.

(−)-**12b** (Table 3, entry 9): Following the general procedure, a mixture of (−)-**10b** (108 mg, 0.25 mmol, 97% *ee*) and a solution of dimethyl zinc in THF (1.0 M, 0.60 mL, 0.60 mmol) gave (workup D), after column chromatography with pentane, (−)-**12b** (53 mg, >95%) as a colorless oil with S_N2'/S_N2 > 99:1 and 97% *ee* determined by GC (GC method described above for (+)-**12b**). Spectroscopic data were identical to those of (+)-**12b**.

(+)-**12c** (Table 3, entry 11): Following the general procedure, a mixture of (−)-**10b** (108 mg, 0.25 mmol, 97% *ee*) and a solution of dimethyl zinc in THF (1.0 M, 0.60 mL, 0.60 mmol) gave (workup D), after column chromatography with pentane, (+)-**12c** (48 mg, >95%) as a colorless oil with S_N2'/S_N2 = 97:3 and 94% *ee* determined by GC (GC method described above for (−)-**12c**). Spectroscopic data were identical to those of (−)-**12c**.

(+)-**12a** (Table 3, entry 12): Following the general procedure, a mixture of (−)-**11b** (104 mg, 0.25 mmol, 94% *ee*) and a solution of diethyl zinc in THF (1.0 M, 0.60 mL, 0.60 mmol) gave (workup D), after column chromatography with pentane, (+)-**12a** (40 mg, >95%) as a colorless oil with S_N2'/S_N2 > 99:1 and 93% *ee* determined by GC (GC method described above for (−)-**12a**). Spectroscopic data were identical to those of (−)-**12a**.

(−)-**13a** (Table 3, entry 13): Following the general procedure, a mixture of (−)-**11b** (104 mg, 0.25 mmol, 94% *ee*) and a solution of Zn(*n*Bu)$_2$ in THF (1.0 M, 0.60 mL, 0.60 mmol) gave (workup D), after column chromatography with pentane, (−)-**13a** (53 mg, >95%) as a colorless oil with S_N2'/S_N2 = 99:1 and 94% *ee* determined by GC (GC method described above for (+)-**13a**). Spectroscopic data were identical to those of (+)-**13a**.

(+)-**13b** (Table 3, entry 14): Following the general procedure, a mixture of (−)-**11b** (104 mg, 0.25 mmol, 94% *ee*) and a solution of Zn(*n*Bu)$_2$ in THF (1.0 M, 0.60 mL, 0.60 mmol) gave (workup D), after column chromatography with pentane, (+)-**13b** (44 mg, >95%) as a colorless oil with S_N2'/S_N2 = 99:1 and 93% *ee* determined by GC (GC method described above for (−)-**13b**). Spectroscopic data were identical to those of (−)-**13b**.

(*R*,*E*)-5-(*tert*-butyldimethylsilanyloxy)-2-ethyl-2-methylpent-3-en-1-ol:[28] A solution of (−)-**7b** (188 mg, 0.50 mmol) in dichloromethane/water (20:1, 10 mL) was treated with DDQ (142 mg, 0.63 mmol) in one portion. The resulting green suspension was stirred at room temperature for 45 min, and a saturated aqueous solution of $NaHCO_3$ (40 mL) was added. The aqueous phase was separated and extracted with dichloromethane (4 × 20 mL). The combined organic phases were washed with brine (20 mL), dried ($MgSO_4$), and the solvent was removed under re-

duced pressure. The brown oily residue contained a 1:1 mixture of the deprotected alcohol and 4-methoxybenzaldehyde, and was used for the next step without further purification. ^{1}H NMR (300.064 MHz, $CDCl_3$): $\delta = 0.07$ (s, 6H), 0.82 (t, 3H, $J = 7.5$ Hz), 0.91 (s, 9H), 0.99 (s, 3H), 1.36 (m, 2H), 3.35 (m, 2H), 4.19 (d, 2H, $J = 3.7$ Hz), 5.51 (d, 1H, $J = 16.0$ Hz), 5.58 ppm (m, 1H). The resonance for the OH proton could not be detected.

(−)-(*R*,*E*)-5-(*tert*-butyldimethylsilanyloxy)-2-ethyl-2-methylpent-3-en-1-al:[28] The crude alcohol obtained above (179 mg of the above isolated mixture, which corresponds to ≈116 mg alcohol, 0.46 mmol) in dichloromethane (1 mL) was added to a suspension of Dess–Martin periodinane (229 mg, 0.54 mmol) in dichloromethane (2 mL) over 5 min and stirred at room temperature for 60 min (TLC control). The reaction was quenched with a solution of $Na_2S_2O_3$ in a saturated aqueous solution of $NaHCO_3$ (2.5 g per 10 mL, 20 mL). The aqueous phase was separated and extracted with diethyl ether (3×20 mL), and the combined organic phases were washed with water (10 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure, and the yellow residue was purified by column chromatography (PE/EtOAc = 95:5) to give the product aldehyde (100 mg, 87%). $[\alpha]_D^{21} = -40.2$ ($c = 1.10$ in $CHCl_3$); ^{1}H NMR (300.064 MHz, $CDCl_3$): $\delta = 0.07$ (s, 6H), 0.85 (t, $J = 7.5$ Hz, 3H), 0.91 (s, 9H), 1.15 (s, 3H), 1.63 (m, 2H), 4.2 (d, $J = 2.6$ Hz, 2H), 5.62 (m, 2H), 9.37 ppm (s, 1H).

(−)-**9**:[26,29] $NaClO_2$ (115 mg, 1.27 mmol) and $NaH_2PO_4 \cdot H_2O$ (132 mg, 0.96 mmol) in water (1.15 mL) were added slowly with stirring to a solution of the aldehyde obtained above (38 mg, 0.148 mmol) and 2-methyl-2-butene (0.67 mL) in *tert*-butanol (3 mL) at room temperature. Stirring was continued for 60 min (TLC control). The reaction mixture was evaporated under reduced pressure, diluted with water (10 mL), and acidified with HCl (5% in water) to pH 2–3. Extraction with diethyl ether/dichloromethane (3:1, 6×10 mL), washing of the combined organic phases with brine (10 mL), drying over $MgSO_4$, and removal of the solvent in vacuo furnished the crude carboxylic acid. The crude acid was dissolved in diethyl ether/dichloromethane (3:1, 5 mL) and treated with diazomethane (1 mL, 0.28 mmol, 0.28 M solution in diethyl ether) for 10 min at room temperature. The solvent was removed in vacuo, and the residue was purified by column chromatography (PE/EtOAc = 95:5) to furnish (−)-**9** (35 mg, 83%). $[\alpha]_D^{22} = -5.6$ ($c = 0.54$, $CHCl_3$) (reference [7a]: $[\alpha]_D^{17} = -4.7$ ($c = 0.86$, $CHCl_3$)); ^{1}H NMR (500.003 MHz, $CDCl_3$): $\delta = 0.04$ (s, 6H), 0.81 (t, $J = 7.5$ Hz, 3H), 0.88 (s, 9H), 1.24 (s, 3H), 1.58 (dq, $J = 13.6$, 7.5 Hz, 1H), 1.75 (dq, $J = 13.7$, 7.5 Hz, 1H), 3.66 (s, 3H), 4.18 (d, $J = 5.1$ Hz, 1H), 4.19 (d, $J = 5.1$ Hz, 1H), 5.58 (dpt, $J = 15.7$, 5.1 Hz, 1H), 5.82 ppm (dt, $J = 15.7$, 1.5 Hz, 1H); ^{13}C NMR (125.741 Hz, $CDCl_3$): $\delta = -5.1$ (2C), 9.0, 18.4, 20.4, 25.9 (3C), 32.2, 48.2, 51.8, 63.9, 128.5, 133.7, 176.4 ppm. The analytical data correspond to those reported previously.[26,29]

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[1] a) S. F. Martin, *Tetrahedron* **1980**, *36*, 419–460; b) K. Fuji, *Chem. Rev.* **1993**, *93*, 2037–2066; c) E. J. Corey, A. Guzman-Perez, *Angew. Chem.* **1998**, *110*, 402–415; *Angew. Chem. Int. Ed.* **1998**, *37*, 388–401; d) C. Spino, C. Beaulieu, *Angew. Chem.* **2000**, *112*, 2006–2008; *Angew. Chem. Int. Ed.* **2000**, *39*, 1930–1932; e) J. Christoffers, A. Mann, *Angew. Chem.* **2001**, *113*, 4725–4732; *Angew. Chem. Int. Ed.* **2001**, *40*, 4591–4597; f) J. Christoffers, A. Baro, *Angew. Chem.* **2003**, *115*, 1726–1728; *Angew. Chem. Int. Ed.* **2003**, *42*, 1688–1690; g) *Quaternary Stereocenters: Challenges and Solutions for Organic Synthesis* (Eds.: J. Christophers, A. Baro), Wiley-VCH, Weinheim, **2005**; h) J. Christophers, A. Baro, *Adv. Synth. Catal.* **2005**, *347*, 1473–1482.

[2] a) [3,3′]-Sigmatropic processes: H. Frauenrath, *Methods of Organic Chemistry (Houben-Weyl)*, **1995**, Vol. E21, pp. 3301–3756; b) [2,3′]-sigmatropic processes: J. Kallmerten, *Methods of Organic Chemistry (Houben-Weyl)*, **1995**, Vol. E21, pp. 3757–3809; c) Wittig rearrangement: T. Nakai, K. Mikami, *Chem. Rev.* **1986**, *86*, 885–902.

[3] a) Y. Yamamoto, *Methods of Organic Chemistry (Houben-Weyl)*, **1995**, Vol. E21, pp. 2011–2040 b) *Modern Organocopper Chemistry* (Eds.: B. Breit, P. Demel in N. Krause), Wiley-VCH, Weinheim, **2002**, pp. 188–223; c) N. Krause, A. Gerold, *Angew. Chem.* **1997**, *109*, 194–213; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 186–204; d) B. H. Lipshutz, Z. Sengupta, *Org. React.* **1992**, *41*, 135–601.

[4] R. Takeuchi, *Synlett* **2002**, 1954–1965.

[5] a) P. A. Evans, J. D. Nelson, *J. Am. Chem. Soc.* **1998**, *120*, 5581–5582; B. L. Ashfeld, K. A. Miller, S. F. Martin, *Org. Lett.* **2004**, *6*, 1321–1324.

[6] E. J. Corey, N. W. Boaz, *Tetrahedron Lett.* **1984**, *25*, 3063–3066.

[7] a) T. Ibuka, M. Tanaka, S. Nishii, Y. Yamamoto, *J. Chem. Soc. Chem. Commun.* **1987**, 1596–1598; b) T. Ibuka, N. Akimoto, M. Tanaka, S. Nishii, Y. Yamamoto, *J. Org. Chem.* **1989**, *54*, 4055–4061; c) N. Harrington-Frost, H. Leuser, M. I. Calaza, F. F. Kneisel, P. Knochel, *Org. Lett.* **2003**, *5*, 2111–2114; d) H. Leuser, S. Perrone, F. Liron, F. F. Kneisel, *Angew. Chem.* **2005**, *117*, 4703–4707; *Angew. Chem. Int. Ed.* **2005**, *44*, 4627–4631.

[8] a) C. Gallina, *Tetrahedron Lett.* **1982**, *23*, 3094–3096; b) H. L. Goering, S. S. Kantner; C. C. Tseng, *J. Org. Chem.* **1983**, *48*, 715–721; c) J. H. Smitrovich, K. A. Woerpel, *J. Am. Chem. Soc.* **1998**, *120*, 12998–12999; d) J. H. Smitrovich, K. A. Woerpel, *J. Org. Chem.* **2000**, *65*, 1601–1614.

[9] a) P. Barsanti, V. Calò, L. Lopez, G. Marchese, F. Naso, G. Pesce, *J. Chem. Soc. Chem. Commun.* **1978**, 1085–1086; b) V. Calò, L. Lopez, W. F. Carlucci, *J. Chem. Soc. Perkin Trans. 1* **1983**, 2953–2956; c) S. Valverde, M. Bernabé, S. Garcia-Ochoa, A. M. Gómez, *J. Org. Chem.* **1990**, *55*, 2294–2298.

[10] a) B. Breit, P. Demel, *Adv. Synth. Catal.* **2001**, *343*, 429–432; b) P. Demel, M. Keller, B. Breit, *Chem. Eur. J.* **2006**, *12*, 6669–6683; c) B. Breit, C. Herber, *Angew. Chem.* **2004**, *116*, 3878–3880; *Angew. Chem. Int. Ed.* **2004**, *43*, 3790–3792; d) C. Herber, B. Breit, *Angew. Chem.* **2005**, *117*, 5401–5403; *Angew. Chem. Int. Ed.* **2005**, *44*, 5267–5269; e) C. Herber, B. Breit, *Chem. Eur. J.* **2006**, *12*, 6684–6691.

[11] B. Breit, D. Breuninger, *Synthesis* **2005**, 147–157.

[12] For a preliminary communciation, see: B. Breit, P. Demel, C. Studte, *Angew. Chem.* **2004**, *116*, 3874–3877; *Angew. Chem. Int. Ed.* **2004**, *43*, 3786–3789.

[13] W. Seiche, A. Schuschkowski, B. Breit, *Adv. Synth. Catal.* **2005**, *347*, 1488–1494.

[14] J. H. Hong, M.-Y. Gao, Y. Choi, Y.-C. Cheng, R. F. Schinazi, C. K. Chu, *Carbohydr. Res.* **2000**, *328*, 37–48.

[15] Experiments with magnesium cuprates also led to excellent 1,3-chirality transfer resulting from an *anti*-substitution pathway. However, regioselectivity was incomplete. An excess of zinc reagent had to be used to achieve quantitative conversion.

[16] J. E. Hoots, T. B. Rauchfuss, D.-A. Wrobleski, *Inorg. Synth.* **1982**, *21*, 175–179.

[17] G. Höfle, W. Steglich, H. Vorbrüggen, *Angew. Chem.* **1978**, *90*, 602–615; *Angew. Chem. Int. Ed. Engl.* **1978**, *17*, 569–583.

[18] a) H. Nemoto, A. Satoh, M. Ando, K. Fukumoto, *J. Chem. Soc. Perkin Trans. 1* **1991**, 1309–1314; b) E. J. Corey, A. Venkateswarlu, *J. Am. Chem. Soc.* **1972**, *94*, 6190–6191.

[19] S. Hanessian, P. Lavallee, *Can. J. Chem.* **1975**, *53*, 2975–2977.

[20] G. Carrea, B. Danieli, G. Palmisano, S. Riva, M. Santagostino, *Tetrahedron: Asymmetry* **1992**, *3*, 775–784.

[21] D. Seebach, A. K. Beck, B. Schmitt, Y. M. Wang, *Tetrahedron* **1994**, *50*, 15, 4363–4368.

[22] a) M. Destrut, A. Kergomard, M. Renard, H. Veschambre, *Tetrahedron* **1981**, *37*, 3825–3830; b) C. Fuganti, P. Grasselli, S. Servi, C. Zirotti, *Tetrahedron Lett.* **1982**, *23*, 4269–4272.

[23] B. B. Snider, R. Cordova, R. T. Prive, *J. Org. Chem.* **1982**, *47*, 3643–3646.
[24] B. Breit, W. Seiche, *J. Am. Chem. Soc.* **2003**, *125*, 6608–6609.
[25] A. G. Brook, H. W. Kucera, D. M. MacRae, *Can. J. Chem.* **1970**, *48*, 818–823.
[26] A. B. Smith III, E. G. Nolen, R. Shirai, F. R. Blase, M. Ohta, N. Chida, R. A. Hartz, D. M. Fitch, W. M. Clark, P. A. Sprengeler, *J. Org. Chem.* **1995**, *60*, 7837–7848.
[27] K. Hiruma, T. Kajimoto, G. Weitz-Schmidt, I. Ollmann, C.-H. Wong, *J. Am. Chem. Soc.* **1996**, *118*, 9265–9270.
[28] a) D. B. Dess, J. C. Martin, *J. Org. Chem.* **1983**, *48*, 4155–4156; b) D. B. Dess, J. C. Martin, *J. Am. Chem. Soc.* **1991**, *113*, 7277–7287; c) Synthesis of Dess–Martin periodinanes: R. K. Boeckman, Jr., P. Shao, J. J. Mullins, *Org. Synth.* **2000**, *77*, 141–149.
[29] B. S. Bal, W. E. Childers, H. W. Pinnick, *Tetrahedron* **1981**, *37*, 2091–2096.

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