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Enantioselective Total Synthesis and Determination of the Absolute Configuration of the 4,6,8,10,16,18-Hexamethyldocosane from *Antitrogus parvulus*

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The absolute and relative configuration of the hexamethyldocosane (**1**) isolated from the cuticula of *Antitrogus parvulus* was determined based on the total synthesis of both diastereomers **1a** and **1b** in enantiomerically pure form. The synthesis demonstrates the utility of the *o*-DPPB-directed and copper-mediated allylic *syn*-substitution reaction with Grignard reagents for iterative deoxypropionate construction (*o*-DPPB = *ortho*-diphenylphosphanylbenzoyl). Additionally, the synthetic power of copper catalyzed sp^3–sp^3 cross coupling reactions by twofold employment for building block construction and as the final fragment coupling step in the course of a convergent total synthesis is shown.

Introduction

Larvae of the cane beetle *Antitrogus parvulus* (known as cane grubs) are the source of major damage in sugar cane crops in Australia.[1] In order to control population of these species, current plant protection strategies rely on the use of inseticides. In this context, ongoing research on a more environmentally benign plant protection strategy has focused on identification of sex pheromones of the cane beetle as an alternative handle to control population of this species. As a result, complex hydrocarbons such as 4,6,8,10,16-penta- and 4,6,8,10,16,18-hexamethyldocosanes (**1**) featuring an unprecedented *anti*-*anti*-*anti*-configuration in the 4,6,8,10-methyltetrad have been isolated from the cuticula of the cane beetle *Antitrogus parvulus*.[2] Unfortunately, the small amount of material isolated from natural sources did not allow determining their biological role yet. Combined spectroscopic and synthetic investigations have elucidated the relative *anti*-configuration of the four methyl-bearing stereocenters in the tetrad part of **1** and the relative *syn*-configuration within the methyl diad region. However, the stereochemical relation between the *all*-*anti* tetrad and the *syn*-diad remained unknown (**1a** or **1b**), as did the absolute configuration (Scheme 1).[2]

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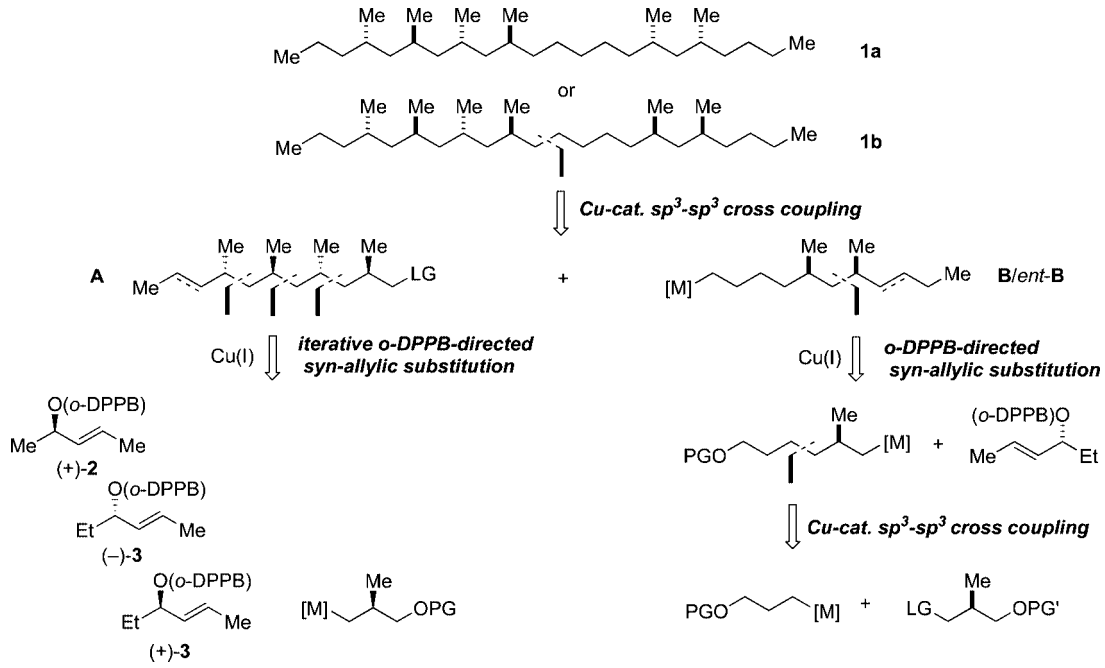
Results and Discussion

We herein report in detail on the total synthesis of both diastereomers **1a** and **1b** in enantiomerically pure form, thus enabling the determination of the relative and the absolute configuration of the natural product.[3,4] The synthesis demonstrates the utility of our recently developed *o*-DPPB-directed and copper-mediated allylic *syn*-substitution reaction with Grignard reagents for iterative deoxypropionate synthesis (*o*-DPPB = *ortho*-diphenylphosphanylbenzoyl).[5] Additionally, the power of copper-catalyzed sp^3–sp^3 cross coupling reactions by twofold employment for building block construction and as the final fragment coupling step in the course of a convergent total synthesis is highlighted.

Our synthetic plan is outlined in Scheme 1. As the fragment coupling of the methyl tetrad and the methyl diad we envisioned to explore the utility of a catalytic sp^3–sp^3 cross coupling reaction.[6] This should be an attractive final step of the synthesis, which would allow the flexible construction of both diastereomers **1a** and **1b**. Comparison of spectroscopic data of **1a** and **1b** with a natural sample should allow the determination of relative configuration of the natural product. Furthermore, comparison of the optical rotation with the natural sample would allow assigning the absolute configuration.

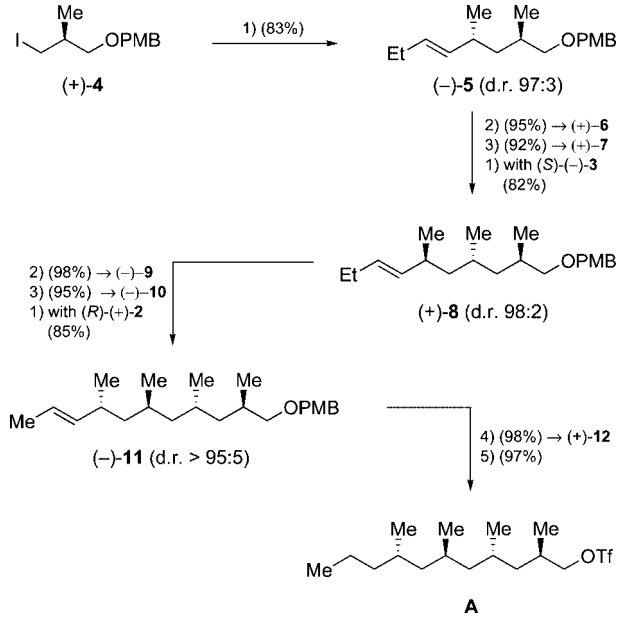
The required tetradeoxypropionate building block **A** could be assembled employing our iterative deoxypropionate synthetic strategy using enantiomerically pure allylic *o*-DPPB building blocks **2** and **3** as propionate-acetate and



Scheme 1. Synthetic plan for **1a** and **1b**. PG = protecting group, LG = leaving group, M = metal.

propionate units, respectively.[5] Relying on similar chemistry the two optical antipodes **B**/*ent*-**B** of the methyl diad building block could be readily accessible.

The synthesis began with construction of the tetrad building block **A**. Thus, iodide (+)-**4** (available in three steps from the Roche ester)[7] was transformed into a Grignard reagent and subjected to the conditions of the *o*-DPPB-directed *syn*-allylic substitution with allylic *o*-DPPB ester (*R*)-(+)-**3** in the presence of 0.5 equiv. of copper bromide–dimethyl sulfide to give the dideoxypropionate (–)-**5** with complete 1,3-chirality transfer.[5] Two iterations, each consisting of the three steps: alkene ozonolysis with reductive work-up ($NaBH_4$), transformation to the iodide, and directed allylic *syn*-substitution with (*S*)-(–)-**3** and (*R*)-(+)-**2**, respectively, furnished the tetradeoxypropionate (–)-**11** with all carbon atoms and stereocenters in place. Alkene hydrogenation and reductive PMB ether cleavage occurred upon subjection to heterogeneous catalytic hydrogenation. The thus derived building block **A** was stored as the alcohol and activated prior to fragment coupling as the corresponding triflate (Scheme 2).



Scheme 2. Synthesis of tetradeoxypropionate building block **A**. 1) 2 *t*BuLi, $MgBr_2{\cdot}OEt_2$ then (*R*)-(+)-**3**, CuBr·SMe_2, Et_2O; 2) O_3, $NaBH_4$, MeOH; 3) PPh_3I_2, imidazole, CH_2Cl_2; 4) PtO_2, H_2 (5 bar), MTBE, then $Pd(OH)_2$; 5) Tf_2O, NEt_3, CH_2Cl_2, –78 °C. Tf = trifluoromethylsulfonyl.

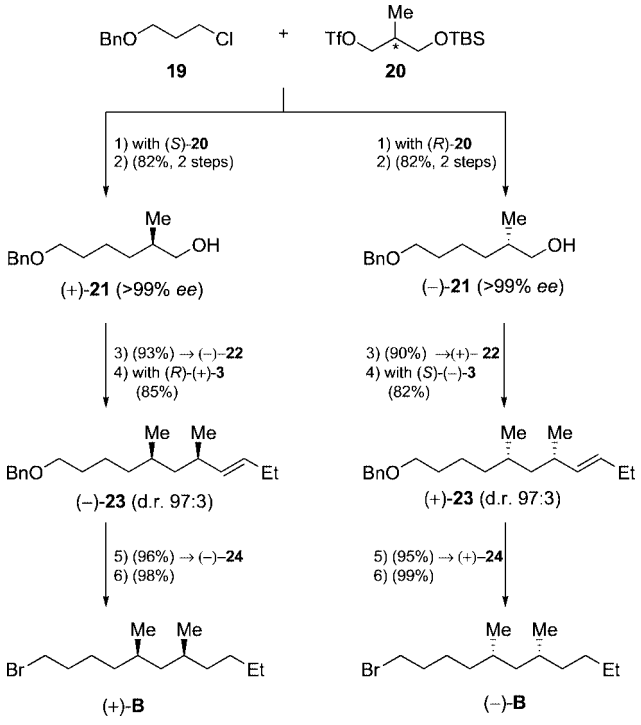
Synthesis of the dideoxypropionate building blocks **B** commenced from chloride **19** (Scheme 3).[8] For carbon skeleton expansion we chose a copper-catalyzed sp^3–sp^3 cross coupling with a three carbon electrophile of type **20** derived from the Roche ester.[9] Orienting experiments with the corresponding bromide and iodide derivatives, however, showed that significant chemoselectivity problems occurred due to elimination and *trans*-magnesiation. Therefore a model system was studied first in order to identify optimal reaction conditions for the copper-catalyzed sp^3–sp^3 coupling reaction. Representative results of these exploratory studies are summarized in Table 1.

According to previous investigations of Cahiez et al.,[10] clean copper-catalyzed sp^3–sp^3 cross-coupling should proceed with Grignard reagents employing alkyl bromides and tosylates as electrophiles. Unfortunately, using similar reaction conditions in order to effect a cross coupling reaction between an *n*-butyl Grignard reagent and the β-branched substrate **13**, low chemoselectivity was observed (Table 1, entry 1). Thus, in addition to the desired cross-coupling product **15**, 38% of by-products, namely the reduction product **16**, the homo-coupling product **17**, and the elimi-

Table 1. Copper-catalyzed sp^3–sp^3 cross coupling with β-branched electrophiles (LG = leaving group).

Entry	Substrate	Equiv. *n*BuMgX	X	*T* [°C]	C (%)[a]	**15** (%)[a]	**16** (%)[a]	**17** (%)[a]	**18** (%)[a]
1	**13**	1.3	Cl	r.t.	99	62	15	16	7
2	**13**	1.3	Br	r.t.	85	61	17	4	19
3	**13**	1.3	Cl	–78 → r.t.	10	n.d.	n.d.	n.d.	n.d.
4[b]	**14**	2.0	Cl	–20	100	100	0	0	0

[a] The experiments were performed on a 1.0 mmol scale; reaction time > 12 h; n.d. = not determined. area-% GC-MS analysis. [b] Without NMP.

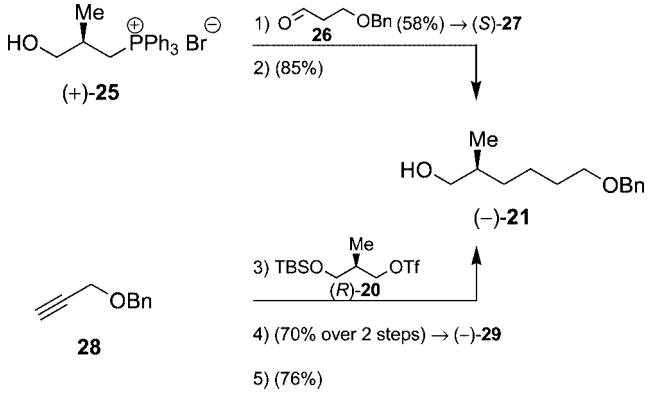


Scheme 3. Synthesis of the enantiomeric dideoxypropionate building blocks (+)-**B**/(–)-**B**. 1) Mg, THF, 4 mol-% Li_2CuCl_4; 2) 5% HCl in MeOH; 3) PPh_3I_2, imidazole, CH_2Cl_2; 4) 2 *t*BuLi, $MgBr_2{\cdot}OEt_2$ then **3**, $CuBr{\cdot}SMe_2$, Et_2O; 5) H_2, PtO_2, ethyl acetate, 12 h; then H_2, Pd/C 10% 24 h; 6) PPh_3, NBS, CH_2Cl_2. Bn = benzyl, TBS = *tert*-butyldimethylsilyl, NBS = *N*-bromosuccinimide.

nation product **18** were detected. Employing the Grignard reagent obtained from *n*-butyl bromide did not bring about any improvement (Table 1, entry 2). Lowering the reaction temperature to –78 °C (Table 1, entry 3) resulted in low conversion (10%). Driven by the hope to achieve higher chemoselectivity at lower reaction temperatures, we needed a more reactive electrophile. Hence triflate **14** was selected. With this electrophile, in fact, a very clean cross coupling reaction with *n*-butylmagnesium chloride occurred in the presence of 4 mol-% of Li_2CuCl_4 as the catalyst (Table 1, entry 4). The cross-coupling product **15** was obtained in almost quantitative yield.[9,11] With these optimal conditions for sp^3–sp^3 cross coupling in hand we turned towards the synthesis of the dideoxypropionate building blocks **B** and *ent*-**B** (Scheme 3).

Starting from triflates (+)-**20** and (–)-**20**,[9] copper catalyzed cross-coupling at –20 °C with the Grignard reagent derived from chloride **19**[6] followed by desilylation of the crude coupling products with methanolic hydrogen chloride gave alcohols (+)-**21** and (–)-**21** in 82% isolated yield each (two steps). Mukaiyama redox condensation furnished the corresponding iodides which were subjected to the protocol for the directed *syn*-allylic substitution with (*R*)-(+)-**3** and (*S*)-(–)-**3**, respectively, to furnish the dideoxypropionates (–)-**23** and (+)-**23** in excellent yield with complete diastereoselectivity. Minimal standard functional group manipulation led to building blocks (+)-**B** and (–)-**B**.

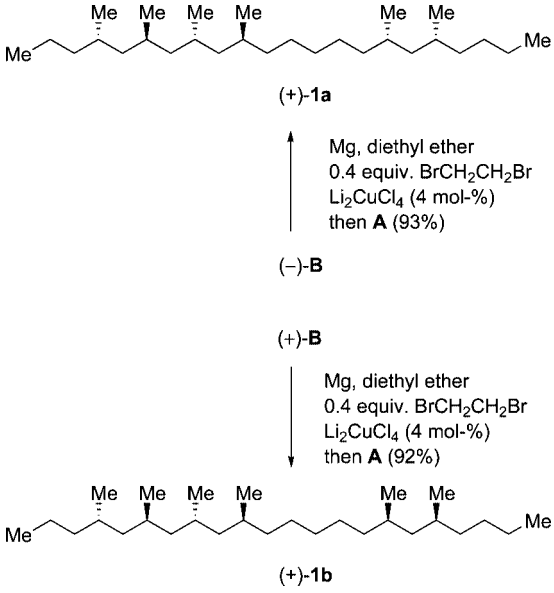
Additionally, two alternative approaches to alcohols **21** have been explored (Scheme 4). Thus, Wittig olefination of aldehyde **26** with the known Wittig ylide **25**,[12] and subsequent olefin hydrogenation of (*S*)-**27** furnished (–)-**21**. Another alternative access to (–)-**21** provides the alkylation of the lithium acetylide derived from propargyl ether **28** with triflate **20**. Notably, neither the bromide **13** nor the corresponding iodide derivative gave significant amounts of the



Scheme 4. Alternative approaches to alcohol (–)-**21**. 1) *n*BuLi, THF, –78 °C; TMSCl; **26**; 2) H_2, PtO_2, TBME, 12 h; 3) *n*BuLi, THF, –78 °C; (*R*)-**20** to 0 °C; DMSO to room temp.; 4) 5% HCl in MeOH; 5) H_2, PtO_2, cyclohexane, 4 d. Bn = benzyl; Tf = trifluoromethylsulfonyl.

desired coupling product. After silyl ether deprotection and hydrogenolytic reduction of the alkyne function of (–)-**29**, alcohol (–)-**21** was obtained in good overall yield.

The final fragment coupling step (Scheme 5) employing a copper-catalyzed sp^3–sp^3 cross coupling of the Grignard reagent derived from (+)/(–)-**B** with the triflate **A** required some optimization because of problems which arose from the small scale of the reaction (0.1 mmol). It was found that Grignard reagent generation at this small scale worked fine in the presence of an excess of dibromoethane. However, the thus formed excess of dibromomagnesium reacted also with the triflate electrophile to yield the corresponding bromide as a side product (which unfortunately did not undergo further cross-coupling). This problem could be circumvented by adding an ethereal solution of the triflate **A** together with 4 mol-% of the catalyst Li_2CuCl_4 to the ethereal Grignard reagent solution derived from **B**. Under these conditions excellent yields of both diastereomers **1a** and **1b** were obtained.



Scheme 5. Fragment coupling through Cu-catalyzed sp^3–sp^3 cross coupling. Synthesis of (+)-**1a** and (+)-**1b**.

In order to prove identity of natural and synthetic material ^{13}C NMR spectra of **1a** and **1b** were measured in NMR tubes which were equipped each with a capillary of a $CDCl_3$ solution of a sample of the natural product.[13] Comparison of these spectra showed a perfect match for diastereomer **1b**. Finally, comparison of the optical rotation of the natural material {$[\alpha]_D^{20}$ = +10.7 (*c* = 0.44, $CHCl_3$)} and synthetic **1b** {$[\alpha]_D^{20}$ = +8.5 (*c* = 1.21, $CHCl_3$)} allowed to determine the absolute configuration of the natural product to be that depicted in Scheme 5.

Conclusions

In conclusion, enantioselective total synthesis of the (4*S*,6*R*,8*R*,10*S*,16*R*,18*S*)-hexamethyldocosane (**1b**) from *Antitrogus parvulus* has been accomplished, thus enabling the determination of the relative and the absolute configuration of the natural product. The successful enantioselective synthesis of **1b** (and its diastereomer **1a**) highlights the synthetic power of our recent methodology for deoxypropionate construction relying on an *o*-DPPB-directed and copper mediated allylic substitution with Grignard reagents. Furthermore, the synthetic utility of copper-catalyzed sp^3–sp^3 cross coupling for fragment coupling in a total synthesis has been demonstrated.

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 are not corrected. ^1H, ^{13}C NMR spectra: Bruker AM-400, Bruker DRX-500 with tetramethylsilane (TMS), chloroform ($CHCl_3$) or benzene (C_6H_6) as internal standards. ^{31}P-NMR spectra: Varian Mercury 300 with 85% H_3PO_4 as external standard. Signal multiplicities in NMR spectra are abbreviated as s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublet), pt (pseudo triplet) etc. Melting points: apparatus by Dr. Tottoli (Büchi). Elemental analyses: Elementar Vario EL. Flash chromatography: silica gel Si 60, E. Merck AG, Darmstadt, 40–63 μm. Reversed-phase silica gel Polygoprep 100–50 C18 from Macherey–Nagel. *tert*-Butyllithium was purchased from Aldrich, Li_2CuCl_4 from Acros.

(2*R*,4*R*,5*E*)-1-(4-Methoxybenzyloxy)-2,4-dimethyloct-5-ene [(–)-5]: To a solution of iodide (+)-**4**[7] (160 mg, 0.500 mmol) in diethyl ether (1.0 mL) was added dropwise *t*BuLi (0.6 mL, 1.66 M in pentane, 1.0 mmol, 2.0 equiv.) at –100 °C. After 15 min TLC showed complete conversion of the starting material. Then a freshly prepared ethereal solution of $MgBr_2{\cdot}OEt_2$ (from 1.00 mmol Mg, 0.65 mmol dibromoethane, 0.7 mL Et_2O) was added and the solution was slowly warmed to room temp. (30 min). The resulting colorless Grignard reagent solution was added dropwise at room temp. via a transfer needle within 30 min to a solution of the *o*-DPPB ester (+)-**3** (214 mg, 0.550 mmol, 1.1 equiv.), $CuBr{\cdot}SMe_2$ (56 mg, 0.275 mmol, 0.55 equiv.) in diethyl ether (11 mL). The resulting suspension was stirred overnight. Then saturated NH_4Cl solution (3.5 mL), aqueous NH_3 solution (12.5%, 1.3 mL) and CH_2Cl_2 (11 mL) were added and stirred until two clear phases were obtained. The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic phases were dried (Na_2SO_4). An appropriate amount of silica gel was added to the filtrate, which was then concentrated to dryness. Flash chromatography of the residue (50:1 petroleum ether/*tert*-butyl methyl ether) yielded the title compound (–)-**5** as a colorless oil (114.7 mg, 83%, *dr* 97:3). HPLC: Macherey–Nagel EC 250/4 Nucleosil 100-5, 0.4 × 25 cm, 0.8 mL/min, 200:0.3 *n*-heptane/ethyl acetate, 25 °C, 275 nm. $[\alpha]_D^{20}$ = –18.9 (*c* = 0.88 in $CHCl_3$). ^1H NMR (499.873 MHz, $CDCl_3$): δ = 0.91 (d, ^3J = 6.8 Hz, 3 H, CH_3), 0.92 (d, ^3J = 6.8 Hz, 3 H, CH_3), 0.95 (t, ^3J = 7.5 Hz, 3 H, CH_3), 1.08 (dt, ^2J = 13.5, ^3J = 7.5 Hz, 1 H, CH_2), 1.29 (m_c, 1 H, CH_2), 1.81 (m_c, 1 H, CH), 1.98 (m_c, 2 H, CH_2), 2.14 (m_c, 1 H, CH), 3.18 (dd, ^2J = 9.1, ^3J = 7.1 Hz, 1 H, CH_2), 3.32 (dd, ^2J = 9.1, ^3J = 5.4 Hz, 1 H, CH_2), 3.80 (s, 3 H, O-CH_3), 4.41 (d, ^2J = 11.7 Hz, 1 H, CH_2-Ar), 4.44 (d, ^2J = 11.7 Hz, 1 H, CH_2-Ar), 5.25 (ddt, ^3J = 15.3, 7.6, ^4J = 1.4 Hz, 1 H, CH), 5.38 (dtd, ^3J = 15.3, 6.2, ^4J = 0.9 Hz, 1 H, CH), 6.87 (m, 2 H, Ar-H), 7.26 (m, 2 H, Ar-H) ppm. ^{13}C NMR (125.709 MHz, $CDCl_3$): δ = 17.7 (CH_3), 17.9 (C-7), 20.7 (CH_3),

31.0 (C-2), 34.1 (C-4), 41.2 (C-3), 55.3 (OCH_3), 72.6 (CH_2Ar), 75.6 (C-1), 113.7 (2× C-3′), 122.6 (C-6), 129.1 (2× C-2′), 131.0 (C-1′), 137.9 (C-5), 159.0 (C-4′) ppm; signal assignment based on C/H-COSY NMR experiments. $C_{18}H_{28}O_2$ (276.41): calcd. C 78.21, H 10.21; found C 78.07, H 10.21.

(2*R*,4*R*)-5-(4′-Methoxybenzyloxy)-2,4-dimethylpentan-1-ol [(+)-6]: Through a solution of (–)-**5** (276 mg, 1.00 mmol) in MeOH (10 mL) at –78 °C was bubbled a stream of ozone (1 bubble/s) until a quantitative conversion was observed by TLC. Subsequently, the ozone was removed by bubbling argon through this solution. $NaBH_4$ (189 mg, 5.00 mmol, 5.0 equiv.) was added at –78 °C and then the mixture was slowly warmed to room temp. NH_4Cl solution (10 mL) was added, the solution was extracted with ethyl acetate (3 × 10 mL), and dried (Na_2SO_4). An appropriate amount of silica gel was added to the filtrate, which was then concentrated to dryness. Flash chromatography (20:1 petroleum ether/*tert*-butyl methyl ether) furnished alcohol (+)-**6** (240 mg, 0.950 mmol, 95%) as a colorless oil. $[\alpha]_D^{20}$ = +13.5 (*c* = 2.72 in $CHCl_3$). ^{1}H NMR (499.873 MHz, $CDCl_3$): δ = 0.89 (pt, *J* = 6.2 Hz, 6 H, CH_3), 1.21 (m_c, 2 H, 3-CH_2), 1.60 (br. t, 1 H, OH), 1.74 (m_c, 1 H, 2- or 4-CH), 1.88 (m_c, 1 H, 2- or 4-CH), 3.24 (dd, ^2J = 9.0, ^3J = 6.4 Hz, 1 H, CH_2), 3.27 (dd, ^2J = 8.9, ^3J = 6.4 Hz, 1 H, CH_2), 3.42 (m_c, 2 H, CH_2), 3.80 (s, 3 H, O-CH_3), 4.43 (pt, *J* = 11.9 Hz, 2 H, CH_2-Ar), 6.88 (m, 2 H, 3′-CH), 7.25 (m, 2 H, 2′-CH) ppm. ^{13}C NMR (125.709 MHz, $CDCl_3$): δ = 16.3 (CH_3), 17.0 (CH_3), 30.5 (CH), 33.0 (CH), 37.3 (C-3), 55.2 (O-CH_3), 68.8 (C-1), 72.7 (-*C*H_2-Ar), 76.3 (C-5), 113.7 (2× C-3′), 129.1 (2× C-2′), 130.7 (C-1′), 159.1 (C-4′) ppm. $C_{15}H_{24}O_3$ (252.35): calcd. C 71.39, H 9.59; found C 71.09, H 9.53.

(2*R*,4*R*)-5-Iodo-1-(4′-methoxybenzyloxy)-2,4-dimethylpentane [(+)-7]: To PPh_3I_2[5b] (1.30 g, 2.52 mmol, 1.2 equiv.) and imidazole (345 mg, 5.07 mmol, 2.4 equiv.) in CH_2Cl_2 (9 mL) was added dropwise a solution of the alcohol (+)-**6** (530 mg, 2.10 mmol) in CH_2Cl_2 (4 mL) at room temp. under exclusion of light. The suspension was stirred overnight. TLC showed a quantitative conversion of the starting material. The suspension was concentrated in vacuo. Flash chromatography (20:1 petroleum ether/*tert*-butyl methyl ether) furnished the title compound (+)-**7** (699 mg, 1.93 mmol, 92%) as a colorless oil which was stored at –20 °C under exclusion of light. $[\alpha]_D^{20}$ = +7.6 (*c* = 1.36 in $CHCl_3$). ^{1}H NMR (400.136 MHz, $CDCl_3$): δ = 0.91 (d, ^3J = 6.9 Hz, 3 H, CH_3), 0.95 (d, ^3J = 6.4 Hz, 3 H, CH_3), 1.16–1.33 (m, 2 H, 3-CH_2), 1.61 (m_c, 1 H, CH), 1.82 (m_c, 1 H, CH), 3.14 (dd, ^2J = 9.5, ^3J = 6.0 Hz, 1 H, 5-CH_2), 3.18–3.25 (m, 2 H, CH_2), 3.27 (dd, ^2J = 9.0, ^3J = 6.0 Hz, 1 H, 1-CH_2), 3.80 (s, 3 H, O-CH_3), 4.42 (pt, *J* = 12.3 Hz, 2 H, CH_2-Ar), 6.87 (m, 2 H, 3′-CH), 7.25 (m, 2 H, 2′-CH) ppm. ^{13}C NMR (100.624 MHz, $CDCl_3$): δ = 17.1 (CH_3), 18.3 (CH_3), 20.3 (C-5), 31.1 (CH), 32.3 (CH), 40.8 (C-3), 55.3 (O-CH_3), 72.7 (*C*H_2-Ar), 75.9 (C-1), 113.8 (2× C-3′), 129.1 (2× C-2′), 130.8 (C-1′), 159.1 (C-4′) ppm. $C_{15}H_{23}IO_2$ (362.25): calcd. C 49.73, H 6.40; found C 50.00, H 6.28.

(2*R*,4*S*,6*S*,7*E*)-1-(4′-Methoxybenzyloxy)-2,4,6-trimethyldec-7-ene [(+)-8]: The procedure was analogous to that used for the preparation of (–)-**5**. From *o*-DPPB ester (–)-**3** (214 mg, 0.550 mmol, 1.1 equiv.), CuBr·SMe_2 (56 mg, 0.275 mmol, 0.55 equiv.) and iodide (+)-**7** (181 mg, 0.500 mmol) was obtained alkene (+)-**8** (131 mg, 0.410 mmol, 82%, *dr* 98:2) as a colorless oil after chromatographic purification [flash chromatography (50:1 petroleum ether/MTBE) followed by reversed phase chromatography (75:25, 80:20 acetonitrile/water, the product fractions were first concentrated in vacuo, then extracted with CH_2Cl_2 and dried with $CaCl_2$]. GC (CP-SIL 5 Lowbleed/MS; 30 m × 0.32 mm × 0.25 μm: 50 °C (5 min isothermal), → 150 °C (25 °C/min, 10 min isothermal), → 170 °C (25 °C/min, 30.2 min isothermal), 2.5 mL/min He. $[\alpha]_D^{20}$ = +25.3 (*c* = 0.93 in $CHCl_3$). ^{1}H NMR (499.873 MHz, $CDCl_3$): δ = 0.82 (d, ^3J = 6.6 Hz, 3 H, CH_3), 0.87 (d, ^3J = 6.6 Hz, 3 H, CH_3), 0.91 (d, ^3J = 6.6 Hz, 3 H, CH_3), 0.95 (t, ^3J = 7.4 Hz, 3 H, 10-CH_3), 1.07–1.13 (m, 4 H, 3- and 5-CH_2), 1.54 (m_c, 1 H, 4-CH), 1.84 (m_c, 1 H, 2-CH), 1.98 (m_c, 2 H, 9-CH_2), 2.16 (m_c, 1 H, 6-CH), 3.18 (dd, ^2J = 9.0, ^3J = 6.9 Hz, 1 H, 1-CH_2), 3.26 (dd, ^2J = 9.1, ^3J = 5.9 Hz, 1 H, 1-CH_2), 3.79 (s, 3 H, O-CH_3), 4.41 (d, ^2J = 11.7 Hz, 1 H, CH_2-Ar), 4.44 (d, ^2J = 11.7 Hz, 1 H, CH_2-Ar), 5.21 (ddt, ^3J = 15.3, 7.9, ^4J = 1.4 Hz, 1 H, 7-CH), 5.38 (dtd, ^3J = 15.3, 6.3, ^4J = 0.8 Hz, 1 H, 8-CH), 6.87 (m, 2 H, 3′-CH), 7.26 (m, 2 H, 2′-CH) ppm. ^{13}C NMR (125.709 MHz, $CDCl_3$): δ = 14.1 (C-10), 16.8 (CH_3), 19.8 (CH_3), 21.0 (CH_3), 25.6 (C-9), 27.3 (C-4), 30.9 (C-2), 34.0 (C-6), 40.7 (C-3), 45.7 (C-5), 55.2 (O-CH_3), 72.6 (*C*H_2-Ar), 76.5 (C-1), 113.7 (2× C-3′), 129.1 (2× C-2′), 129.9 (C-8), 131.0 (C-1′), 135.6 (C-7), 159.0 (C-4′) ppm. $C_{21}H_{34}O_2$ (318.49): calcd. C 79.19, H 10.76; found C 79.07, H 10.77.

(2*S*,4*S*,6*R*)-7-(4′-Methoxybenzyloxy)-2,4,6-trimethyl-1-heptanol [(–)-9]: The procedure was analogous to that used for the preparation of (+)-**6**. From alkene (+)-**8** (360 mg, 1.13 mmol) and $NaBH_4$ (214 mg, 5.65 mmol, 5.0 equiv.) was obtained alcohol (–)-**9** (326 mg, 1.11 mmol, 98%) as colorless oil. $[\alpha]_D^{20}$ = –3.1 (*c* = 1.30 in $CHCl_3$). ^{1}H NMR (400.136 MHz, $CDCl_3$): δ = 0.81 (d, ^3J = 6.9 Hz, 3 H, CH_3), 0.86 (d, ^3J = 6.9 Hz, 3 H, CH_3), 0.88 (d, ^3J = 6.4 Hz, 3 H, CH_3), 0.98–1.07 (m, 2 H, CH_2), 1.11–1.22 (m, 2 H, CH_2), 1.38 (br. s, 1 H, OH), 1.58 (m_c, 1 H, CH), 1.69 (m_c, 1 H, CH), 1.84 (m_c, 1 H, CH), 3.17 (dd, ^2J = 9.0, ^3J = 6.9 Hz, 1 H, 7-CH_2), 3.26 (dd, ^2J = 9.0, ^3J = 5.6 Hz, 1 H, 7-CH_2), 3.36 (dd, ^2J = 10.3, ^3J = 6.4 Hz, 1 H, 1-CH_2), 3.45 (dd, ^2J = 10.3, ^3J = 5.4 Hz, 1 H, 1-CH_2), 3.78 (s, 3 H, O-CH_3), 4.41 (pt, ^2J = 12.3 Hz, 2 H, CH_2-Ar), 6.85 (m, 2 H, 3′-CH), 7.23 (m, 2 H, 2′-CH) ppm. ^{13}C NMR (100.624 MHz, $CDCl_3$): δ = 16.4 (CH_3), 17.1 (CH_3), 19.1 (CH_3), 27.1 (CH), 30.8 (CH), 33.2 (CH), 41.4 (CH_2), 42.0 (CH_2), 55.2 (O-CH_3), 68.9 (C-1), 72.6 (*C*H_2-Ar), 76.2 (C-7), 113.7 (2× C-3′), 129.1 (2× C-2′), 130.9 (C-1′), 159.1 (C-4′) ppm. $C_{18}H_{30}O_3$ (294.43): calcd. C 73.43, H 10.27; found C 73.08, H 10.28.

(2*R*,4*S*,6*S*)-7-Iodo-1-(4′-methoxybenzyloxy)-2,4,6-trimethyl-1-heptane [(–)-10]: The procedure was analogous to that used for the preparation of (+)-**7**. From the alcohol (–)-**9** (174 mg, 0.594 mmol), PPh_3I_2[5b] (368 mg, 0.713 mmol, 1.2 equiv.) and imidazole (98 mg, 1.4 mmol, 2.4 equiv.) was obtained iodide (–)-**10** (229 mg, 0.567 mmol, 95%) as a colorless oil. $[\alpha]_D^{20}$ = –0.5 (*c* = 2.04 in $CHCl_3$). ^{1}H NMR (400.136 MHz, C_6D_6): δ = 0.73 (d, ^3J = 6.4 Hz, 3 H, CH_3), 0.75 (d, ^3J = 6.9 Hz, 3 H, CH_3), 0.91 (d, ^3J = 6.9 Hz, 3 H, CH_3), 0.92–1.08 (m, 3 H, CH_2), 1.16–1.32 (m, 2 H, CH, CH_2), 1.43 (m_c, 1 H, CH), 1.85 (m_c, 1 H, CH), 2.77 (dd, ^2J = 9.5, ^3J = 6.0 Hz, 1 H, 7-CH_2), 2.83 (dd, ^2J = 9.5, ^3J = 4.7 Hz, 1 H, 7-CH_2), 3.14 (dd, ^2J = 9.0, ^3J = 6.4 Hz, 1 H, 1-CH_2), 3.19 (dd, ^2J = 9.0, ^3J = 6.0 Hz, 1 H, 1-CH_2), 3.32 (s, 3 H, O-CH_3), 4.36 (pt, ^2J = 12.3 Hz, 2 H, CH_2-Ar), 6.82 (m, 2 H, 3′-CH), 7.25 (m, 2 H, 2′-CH) ppm. ^{13}C NMR (100.624 MHz, $CDCl_3$): δ = 17.3 (CH_3), 18.0 (CH_3), 19.4 (CH_3), 20.3 (C-7), 27.6 (CH), 31.3 (CH), 32.3 (CH), 41.9 (CH_2), 44.9 (CH_2), 54.8 (O-CH_3), 72.9 (*C*H_2-Ar), 76.2 (C-1), 114.1 (2× C-3′), 129.3 (2× C-2′), 131.5 (C-1′), 159.7 (C-4′) ppm. $C_{18}H_{29}IO_2$ (404.33): calcd. C 53.47, H 7.23; found C 53.64, H 7.26.

(2*R*,4*S*,6*S*,8*R*,9*E*)-1-(4′-Methoxybenzyloxy)-2,4,6,8-tetramethylundec-9-ene [(–)-11]: The procedure was analogous to that used for the preparation of (+)-**8**. From *o*-DPPB ester (+)-**2** (171 mg, 0.457 mmol, 1.1 equiv.), CuBr·SMe_2 (46.4 mg, 0.226 mmol, 0.55 equiv.) and iodide (–)-**10** (167 mg, 0.413 mmol) was obtained alkene (–)-**11** (121 mg, 0.350 mmol, 85%, *dr* >95:5, NMR) as a colorless oil. $[\alpha]_D^{20}$ = –16.1 (*c* = 1.32 in $CHCl_3$). ^{1}H NMR

(499.873 MHz, $CDCl_3$): δ = 0.77 (pt, ^3J = 6.7 Hz, 6 H, CH_3), 0.89 (d, ^3J = 6.5 Hz, 6 H, CH_3), 0.91–1.03 (m, 2 H, CH_2), 1.05–1.11 (m, 3 H, CH_2), 1.12–1.19 (m, 1 H, CH_2), 1.47–1.60 (m, 2 H, 4- and 6-CH), 1.62 (ddd, ^3J = 6.2, ^4J = 1.4, ^5J = 0.6 Hz, 3 H, 11-CH_3), 1.83 (m_c, 1 H, 2-CH), 2.14 (m_c, 1 H, 8-CH), 3.16 (dd, ^2J = 9.0, ^3J = 7.1 Hz, 1 H, 1-CH_2), 3.26 (dd, ^2J = 9.1, ^3J = 5.7 Hz, 1 H, 1-CH_2), 3.79 (s, 3 H, O-CH_3), 4.40 (d, ^2J = 11.8 Hz, 1 H, CH_2-Ar), 4.43 (d, ^2J = 11.7 Hz, 1 H, CH_2-Ar), 5.25 (ddq, ^3J = 15.2, 7.6, ^4J = 1.4 Hz, 1 H, 9-CH), 5.34 (dqd, ^3J = 15.2, 6.3, ^4J = 0.8 Hz, 1 H, 10-CH), 6.86 (m, 2 H, 3′-CH), 7.24 (m, 2 H, 2′-CH) ppm. ^{13}C NMR (125.709 MHz, $CDCl_3$): δ = 17.1 (CH_3), 17.9 (C-11), 19.2 (CH_3), 20.0 (CH_3), 20.8 (CH_3), 27.2 and 27.5 (C-4 and C-6), 30.8 (C-2), 34.1 (C-8), 42.1 and 45.4 and 45.6 (C-3 and C-5 and C-7), 55.3 (O-CH_3), 72.6 (CH_2-Ar), 76.3 (C-1), 113.7 (2× C-3′), 122.4 (C-10), 129.1 (2× C-2′), 131.0 (C-1′), 138.0 (C-9), 159.0 (C-4′) ppm. $C_{23}H_{38}O_2$ (346.55): calcd. C 79.71, H 11.05; found C 79.54, H 11.31.

(2*R*,4*S*,6*R*,8*S*)-2,4,6,8-Tetramethylundecan-1-ol [(+)-12]: To a solution of ether (–)-**11** (504 mg, 1.45 mmol) in MTBE (5 mL) in a stainless-steel autoclave with glass inlet was added under argon PtO_2 (21 mg, 5 mol-%) at room temp. The argon atmosphere was replaced by hydrogen (5 bar) and the reaction mixture was stirred overnight. Completion of conversion was insured by GC-MS analysis. Subsequently, $Pd(OH)_2$ (ca. 81%, 53 mg, 5 mol-%) was added and the suspension was stirred for further 24 h under a hydrogen pressure of 5 bar. TLC analysis showed complete conversion of the starting material. The suspension was filtered and washed with MTBE (30 mL). An appropriate amount of silica gel was added to the filtrate, which was then concentrated to dryness. Flash chromatography (20:1 to 1:1 petroleum ether/MTBE) furnished alcohol (+)-**12** (324 mg, 1.42 mmol, 98%) as colorless oil. $[a]_D^{20}$ = +22.7 (c = 1.01 in $CHCl_3$). ^{1}H NMR (499.873 MHz, $CDCl_3$): δ = 0.78 (d, ^3J = 6.6 Hz, 3 H, CH_3), 0.797 (d, ^3J = 6.6 Hz, 3 H, CH_3), 0.802 (d, ^3J = 6.6 Hz, 3 H, CH_3), 0.85 (t, ^3J = 7.2 Hz, 3 H, 11-CH_3), 0.88 (d, ^3J = 6.8 Hz, 3 H, 2-CH-CH_3), 0.95–1.35 (m, 11 H), 1.47 (m_c, 1 H), 1.57 (m_c, 2 H), 1.70 (m_c, 1 H, 2-CH), 3.38 (dd, ^2J = 9.9, ^3J = 6.9 Hz, 1 H, 1-CH_2), 3.46 (dd, ^2J = 10.2, ^3J = 5.4 Hz, 1 H, 1-CH_2) ppm. ^{13}C NMR (125.709 MHz, $CDCl_3$): δ = 14.4 (C-11), 16.4 (2-CH-CH_3), 19.4 (CH_3), 19.5 (CH_3), 19.6 (CH_3), 20.1, 27.2, 27.3, 29.7, 33.2 (2-CH), 40.2, 41.3, 45.5, 46.5, 69.0 (C-1) ppm. $C_{15}H_{32}O$ (228.41): calcd. C 78.87, H 14.12; found C 78.75, H 13.92.

(2*R*,4*S*,6*R*,8*S*)-2,4,6,8-Tetramethylundecyl Trifluoromethanesulfonate (A): To a solution of alcohol (+)-**12** (22.8 mg, 100 μmol) in CH_2Cl_2 (1.0 mL) at –78 °C was added triethylamine (24.3 mg, 240 μmol, 2.4 equiv.) followed by trifluoromethanesulfonic acid anhydride (33.9 mg, 120 μmol, 1.2 equiv.). The mixture was stirred for 20 min at this temperature. TLC analysis showed complete conversion of the starting material. The reaction was quenched by addition of one drop of methanol. Then the solution was filtered over Alox N (deactivated with 20% water) and $MgSO_4$ and concentrated in vacuo. The triflate **A** (35 mg, 97 μmol, 97%) was obtained as a colorless oil which was used directly in the fragment coupling step without further characterization. ^{1}H NMR (300.066 MHz, $CDCl_3$): δ = 0.81 (d, ^3J = 6.4 Hz, 3 H, CH_3), 0.83 (t, ^3J = 6.0 Hz, 6 H, CH_3), 0.89 (d, ^3J = 7.0 Hz, 3 H, CH_3), 1.00 (d, ^3J = 6.7 Hz, 3 H, 2-CH-CH_3), 1.00–1.68 (m, 13 H), 2.06 (m_c, 1 H), 4.29 (dd, ^2J = 9.4, ^3J = 6.7 Hz, 1 H, 1-CH_2), 4.38 (dd, ^2J = 9.5, ^3J = 5.6 Hz, 1 H, 1-CH_2) ppm.

6-Benzyloxy-2-methyl-1-hexanol (21): To freshly activated magnesium[14] (972 mg, 40.0 mmol, 5.0 equiv.) was added under argon THF (1 mL) followed by the first half of chloride **19**[8] (dried with CaH_2, 4.0 mmol of totally 8.0 mmol, 2.0 equiv.) and dibromoethane (20 μL). The reaction mixture was heated to reflux until an exothermic reaction could be observed without heating. Subsequently, the remaining half of chloride **19** (739 mg, 4.00 mmol) dissolved in THF (7 mL) was added directly under additional heating to reflux. The suspension was stirred at this temperature for further 30 min.

The thus-obtained Grignard reagent solution was added dropwise to a solution of triflate **20**[9] (1.35 g, 4.00 mmol), Li_2CuCl_4 (0.1 M in THF, 3.2 mL, 0.32 mmol, 4 mol-% related to the Grignard reagent) in THF (16 mL) at –20 °C. The reaction solution turned from orange over nearly colorless to dark gray. After stirring for 15 h at –20 °C the color of the reaction solution was black. The reaction was quenched by addition of water (6 mL) and the reaction mixture was extracted with MTBE (3 × 20 mL). The combined organic phases were dried (Na_2SO_4), an appropriate amount of silica gel was added and the mixture was concentrated to dryness in vacuo. Flash chromatography (20:1 petroleum ether/MTBE) yielded the silylated product (3.56 mmol, 89%) together with hydrolyzed Grignard reagent.

To this product mixture dissolved in MTBE (13 mL) was added HCl (5% in MeOH, 10 mL) and the solution was stirred for 30 min at room temp. The solvents were removed in vacuo and flash chromatography (10:1 to 1:1 petroleum ether/MTBE) delivered alcohol **21** (729 mg, 3.28 mmol, 82% over 2 steps, >99%*ee*) as a colorless oil. HPLC (dAICEL Chiralcel-OD-H, 0.46 × 25 cm, 0.8 mL/min, eluent: 95:5 *n*-heptane/*i*PrOH, room temp., 254 nm, t_R(*S*)-**21**: 13.5 min, t_R(*R*)-**21**: 14.8 min). [(*R*)-(+)-**21**] $[a]_D^{20}$ = +6.4 (c = 1.48 in $CHCl_3$). [(*S*)-(–)-**21**] $[a]_D^{20}$ = –6.2 (c = 2.01 in $CHCl_3$). ^{1}H NMR (400.136 MHz, $CDCl_3$): δ = 0.90 (d, ^3J = 6.9 Hz, 3 H, 2-CH-CH_3), 1.08–1.18 (m, 1 H), 1.32–1.48 (m, 4 H), 1.55–1.65 (m, 3 H), 3.39 (dd, ^2J = 10.8, ^3J = 6.5 Hz, 1 H, 1-CH_2), 3.46 (t, 2 H, 6-CH_2), 3.47 (dd, ^2J = 10.1, ^3J = 6.2 Hz, 1 H, 1-CH_2), 4.49 (s, 2 H, CH_2-Ar), 7.24–7.38 (m, 5 H, Ar-H) ppm. ^{13}C NMR (100.624 MHz, $CDCl_3$): δ = 16.5 (CH_3), 23.6, 30.0, 32.9, 35.7, 68.2 (C-1), 70.3 (C-6), 72.9 (-CH_2-Ar), 127.5 (Ar-*C*), 127.6 (2× Ar-*C*), 128.3 (2× Ar-*C*), 138.7 (Ar-*C*) ppm. $C_{14}H_{22}O_2$ (222.32): calcd. C 75.63, H 9.97; found [(*S*)-(–)-**21**] C 75.43, H 9.98; found [(*R*)-(+)-**21**] C 75.37, H 10.11. The analytical and spectroscopic data correspond to those reported previously.[15]

6-Benzyloxy-1-iodo-2-methylhexane (22): The procedure employed was analogous to that used for the preparation of (+)-**7**. From alcohol (+)-**21** (1.04 g, 4.66 mmol), PPh_3I_2[5b] (2.98 g, 5.77 mmol, 1.24 equiv.) and imidazole (786 mg, 11.5 mmol, 2.48 equiv.) was obtained iodide (–)-**22** (1.44 g, 4.33 mmol, 93%) as a colorless oil. A similar experiment with (–)-**21** furnished the enantiomeric iodide (+)-**22** in 90% yield. [(*R*)-(–)-**22**] $[a]_D^{20}$ = –2.4 (c = 2.40 in $CHCl_3$). [(*S*)-(+)-**22**] $[a]_D^{20}$ = +1.8 (c = 2.20 in $CHCl_3$). ^{1}H NMR (400.136 MHz, $CDCl_3$): δ = 0.96 (d, ^3J = 6.4 Hz, 3 H, 2-CH-CH_3), 1.16–1.28 (m, 2 H), 1.30–1.50 (m, 3 H), 1.59 (m_c, 2 H), 3.13 (dd, ^2J = 9.5, ^3J = 6.0 Hz, 1 H, 1-CH_2), 3.20 (dd, ^2J = 9.9, ^3J = 4.7 Hz, 1 H, 1-CH_2), 3.46 (t, ^3J = 6.4 Hz, 2 H, 6-CH_2), 4.48 (s, 2 H, -CH_2-Ar), 7.25–7.33 (m, 5 H, Ar-H) ppm. ^{13}C NMR (100.624 MHz, $CDCl_3$): δ = 17.7 (CH_3), 20.5 (C-1), 23.6, 29.8, 34.7, 36.2, 70.2 (C-6), 72.9 (CH_2-Ar), 127.5 (Ar-*C*), 127.6 (2× Ar-*C*), 128.3 (2× Ar-*C*), 138.6 (Ar-*C*) ppm. $C_{14}H_{21}IO$ (332.22): calcd. C 50.61, H 6.37; found [(*R*)-(–)-**22**] C 50.57, H 6.39; found [(*S*)-(+)-**22**] C 50.90, H 6.50.

(3*E*)-11-Benzyloxy-5,7-dimethylundec-3-ene (23): The procedure was analogous to that used for the preparation of (+)-**8**. From *o*-DPPB ester (+)-**3** (1.22 g, 3.16 mmol, 0.9 equiv.), $CuBr{\cdot}SMe_2$ (325 mg, 1.58 mmol, 0.45 equiv.) and iodide (–)-**22** (1.17 g,

3.51 mmol) was obtained alkene (–)-**23** (860 mg, 2.98 mmol, 83%, *dr* 97:3) as a colorless oil. A similar experiment with (+)-**22** and (–)-**3** yielded the enantiomeric alkene (+)-**23** in 82% yield. GC [CP-SIL 5 Lowbleed/MS; 30 m × 0.32 mm × 0.25 μm, 50 °C (2 min) to 180 °C (5 °C/min)]. (–)-**23** $[\alpha]_D^{20}$ = –9.9 (*c* = 2.76 in $CHCl_3$). (+)-**23** $[\alpha]_D^{20}$ = +9.9 (*c* = 2.03 in $CHCl_3$). ^{1}H NMR (499.873 MHz, $CDCl_3$): δ = 0.81 (d, ^3J = 6.6 Hz, 3 H, 7-CH-CH_3), 0.92 (d, ^3J = 6.8 Hz, 3 H, 5-CH-CH_3), 0.95 (t, ^3J = 7.5 Hz, 3 H, 1-CH_3), 0.90–1.01 (m, 1 H), 1.05–1.45 (m, 6 H), 1.52–1.63 (m, 2 H), 1.97 (m_c, 2 H, 2-CH_2), 2.14 (m_c, 1 H, 5-CH), 3.45 (t, ^3J = 6.6 Hz, 2 H, 11-CH_2), 4.49 (s, 2 H, CH_2-Ar), 5.17 (ddt, ^3J = 15.3, 8.1, ^4J = 1.5 Hz, 1 H, 4-CH), 5.38 (dtd, ^3J = 15.3, 6.3, ^4J = 0.8 Hz, 1 H, 3-CH), 7.24–7.35 (m, 5 H, Ar-H) ppm. ^{13}C NMR (125.708 MHz, $CDCl_3$): δ = 14.1 (C-1), 19.5 (CH_3), 21.9 (CH_3), 23.5, 25.6 (C-2), 30.1, 30.2, 34.3 (C-5), 37.3, 44.8, 70.5 (C-11), 72.8 (*C*H_2-Ar), 127.4 (Ar-*C*), 127.6 (2× Ar-*C*), 128.3 (2× Ar-*C*), 130.1 (C-3), 135.2 (C-4), 138.7 (Ar-*C*) ppm. $C_{20}H_{32}O$ (288.47): calcd. C 83.27, H 11.18; found (–)-**23** C 83.17, H 11.23; found (+)-**23** C 83.01, H 11.12.

5,7-Dimethylundecan-1-ol (24): To a solution of the alkene (–)-**23** (108 mg, 0.374 mmol) in ethyl acetate (1.5 mL) was added at room temp. under argon PtO_2 (5 mg, 5 mol-%). Subsequently, the argon atmosphere was replaced by hydrogen (balloon technique) and the suspension was stirred overnight. Completenes of conversion was checked by GC-MS analysis. Subsequently, Pd/C (10%, 20 mg, 5 mol-%) was added and the reaction mixture was stirred for further 24 h. TLC analysis showed complete conversion of the starting material. The reaction mixture was poured directly on a flash column. Flash chromatography (10:1 to 1:1 petroleum ether/MTBE) furnished alcohol (–)-**24** (71.9 mg, 0.359 mmol, 96%) as a colorless oil. A similar experiment with (+)-**23** furnished the enantiomeric alcohol (+)-**24** in 95% yield. (–)-**24** $[\alpha]_D^{20}$ = –1.1 (*c* = 2.44 in $CHCl_3$). (+)-**24** $[\alpha]_D^{20}$ = +0.8 (*c* = 3.30 in $CHCl_3$). ^{1}H NMR (499.873 MHz, $CDCl_3$): δ = 0.81 (d, ^3J = 6.9 Hz, 3 H, CH_3), 0.82 (d, ^3J = 6.9 Hz, 3 H, CH_3), 0.82–1.60 (m, 20 H), 3.62 (t, ^3J = 6.7 Hz, 2 H, 1-CH_2) ppm. ^{13}C NMR (125.708 MHz, $CDCl_3$): δ = 14.1 (C-11), 20.2 (CH_3), 20.3 (CH_3), 23.0, 23.1, 29.1, 30.01, 30.04, 33.2, 36.5, 36.7, 45.2, 63.1 (C-1) ppm. $C_{13}H_{28}O$ (200.36): calcd. C 77.93, H 14.09; found (–)-**24** C 77.71, H 14.05; found (+)-**24** C 77.63, H 14.05.

1-Bromo-5,7-dimethylundecane (B): To a solution of alcohol (–)-**24** (54.0 mg, 270 μmol) in CH_2Cl_2 (1.5 mL) was added triphenylphosphane (92.0 mg, 351 μmol, 1.30 equiv.). The solution was cooled to 0 °C and then *N*-bromosuccinimide (63.0 mg, 354 μmol, 1.31 equiv.) was added, and the reaction was warmed to room temp. overnight. The resulting brown reaction mixture was poured on a flash column (20:1 petroleum ether/MTBE) to furnish bromide (+)-**B** (70.0 mg, 266 μmol, 98%) as a colorless liquid. A similar experiment with (+)-**24** yielded the enantiomeric bromide (–)-**B** in 99% yield. (+)-**B** $[\alpha]_D^{20}$ = +1.7 (*c* = 2.50 in $CHCl_3$). (–)-**B** $[\alpha]_D^{20}$ = –2.5 (*c* = 2.00 in $CHCl_3$). ^{1}H NMR (499.873 MHz, $CDCl_3$): δ = 0.82 (d, ^3J = 6.8 Hz, 3 H, CH_3), 0.83 (d, ^3J = 6.6 Hz, 3 H, CH_3), 0.86–1.53 (m, 17 H), 1.77–1.89 (m, 2 H), 3.39 (td, ^3J = 6.8, ^4J = 0.6 Hz, 2 H, 1-CH_2) ppm. ^{13}C NMR (125.708 MHz, $CDCl_3$): δ = 14.2 (C-11), 20.2 (CH_3), 20.3 (CH_3), 23.1, 25.5, 29.2, 29.9, 30.0, 33.2, 34.0, 35.9, 36.5, 45.1. $C_{13}H_{27}Br$ (263.26): calcd. C 59.31, H 10.34; found (+)-**B** C 59.42, H 10.00; found (–)-**B** C 59.11, H 10.14.

(2*S*)-6-Benzyloxy-2-methylhex-3-en-1-ol [(*S*)-27]: To a suspension of phosphonium salt (+)-**25**[12] (415 mg, 1.00 mmol, 1.25 equiv.) in THF (4 mL) was added at –78 °C *n*BuLi (1.3 mL, 1.54 M in hexane, 2.0 mmol, 2.5 equiv.) dropwise. The reaction mixture was warmed slowly to room temperature (color change to red). After cooling of the reaction mixture to –78 °C again, TMSCl (108 mg, 1.00 mmol, 1.25 equiv.) was added dropwise followed by warming to room temperature. After cooling to –78 °C aldehyde **26**[16] (132 mg, 0.800 mmol) was added. The resulting orange suspension was warmed overnight to room temperature. The reaction was quenched by addition of HCl_{aq} (3 mL, 1 M, 3 mmol), and the mixture was stirred for further 3 h. The aqueous phase was separated, and extracted with MTBE (3 × 15 mL). The combined organic phases were dried with sodium sulfate and concentrated in vacuo. Flash chromatography (5:1 petroleum ether/MTBE) furnished the alcohol (*S*)-**27** (101 mg, 0.460 mmol, 58%, *E*/*Z* mixture) as a colorless oil. ^{1}H NMR (400.136 MHz, $CDCl_3$): δ = 0.92 (d, ^3J = 6.9 Hz, 3 H, 2-CH-CH_3), 0.97 (d, ^3J = 6.9 Hz, 3 H, 2-CH-CH_3), 2.14 (br. s, 2 H, OH), 2.23–2.37 (m, 4 H), 2.50 (m_c, 1 H), 2.72 (m_c, 1 H), 3.26–3.37 (m, 2 H), 3.41–3.54 (m, 6 H), 4.49 (s, 2 H, CH_2-Ar), 4.50 (s, 2 H, CH_2-Ar), 5.24 (dd, $^3J_{cis}$ = 10.1, ^3J = 9.9 Hz, 1 H, 3-CH), 5.34 (dd, $^3J_{trans}$ = 15.5, ^3J = 8.6 Hz, 1 H, 3-CH), 5.48–5.58 (m, 2 H, 4-CH), 7.24–7.38 (m, 10 H, Ar-H) ppm. ^{13}C NMR (100.624 MHz, $CDCl_3$): δ = 16.4 and 17.0 (CH_3), 28.4, 33.1, 34.8, 39.7, 67.2 and 67.7 (C-1), 69.4 and 69.8 (C-6), 72.9 and 73.0 (*C*H_2-Ar), 127.54 (Ar-*C*), 127.58 (2× Ar-*C*), 127.62 (Ar-*C*), 127.69 (2× Ar-*C*), 128.1, 128.29, 128.33 (4× Ar-*C*), 134.5, 134.6, 138.2 (Ar-*C*), 138.4 (Ar-*C*) ppm. $C_{14}H_{20}O_2$ (220.31): calcd. C 76.33, H 9.15; found C 76.20, H 9.01.

(–)-21 via Alkene 27: To a solution of the alcohol (*S*)-**27** (881 mg, 4.00 mmol) in MTBE (16 mL) was added PtO_2 (45 mg, 0.20 mmol, 5 mol-%) and the suspension was stirred under a hydrogen atmosphere (balloon) overnight. Subsequently, the reaction mixture was filtered through celite. Flash chromatography (5:1 petroleum ether/MTBE) furnished alcohol (–)-**21** (756 mg, 3.40 mmol, 85%) as a colorless oil.

(2*S*)-6-Benzyloxy-2-methyl-4-hexyn-1-ol [(–)-29]: To a solution of **28**[17] (249 mg, 1.70 mmol, 1.8 equiv.) in THF (3.4 mL) was added *n*BuLi (0.94 mL, 1.6 M in hexane, 1.5 mmol, 1.6 equiv.) at –78 °C and the mixture was stirred for 20 min, warmed to 0 °C and stirred for 20 min at this temperature. Then the mixture was cooled to –78 °C again and the triflate (*R*)-**20** (313 mg, 0.930 mmol) was added. The reaction mixture was warmed to 0 °C, DMSO (3.5 mL) was added and warmed to room temperature overnight. The reaction was stopped by addion of water (1 mL). The reaction mixture was extracted with petroleum ether (3 × 5 mL). To the combined organic phases was added HCl (5% in MeOH, 5 mL) and the resulting solution was stirred for 1 h. Subsequently, the solution was washed with saturated aqueous $NaHCO_3$ solution and the phases were separated. The aqueous phase was extracted with MTBE (3 × 50 mL) and the combined organic phases were washed again with saturated $NaHCO_3$ and brine, dried (Na_2SO_4) and concentrated in vacuo. Flash chromatography (20:1 to 1:1 petroleum ether/MTBE) furnished the alcohol (–)-**29** (142 mg, 0.65 mmol, 70%) as a slightly yellow oil. $[\alpha]_D^{20}$ = –8.1 (*c* = 1.08 in $CHCl_3$). ^{1}H NMR (400.136 MHz, $CDCl_3$): δ = 1.01 (d, ^3J = 6.9 Hz, 3 H, 2-CH-CH_3), 1.69 (br. s, 1 H, OH), 1.88 (oct, ^3J = 8.8 Hz, 1 H, 2-CH), 2.25 (ddt, ^2J = 16.8, ^3J = 6.4, ^4J = 2.1 Hz, 1 H, 3-CH_2), 2.33 (ddt, ^2J = 16.7, ^3J = 6.4, ^4J = 2.2 Hz, 1 H, 3-CH_2), 3.55 (d, ^3J = 6.0 Hz, 2 H, 1-CH_2), 4.16 (t, ^5J = 2.1 Hz, 2 H, 6-CH_2), 4.58 (s, 2 H, CH_2-Ar), 7.24–7.38 (m, 5 H, Ar-*H*) ppm. ^{13}C NMR (100.624 MHz, $CDCl_3$): δ = 16.2 (2-CH-*C*H_3), 22.6 (C-3), 26.9 (C-4 or C-5), 35.1 (C-2), 57.7 (C-6), 66.9 (C-1), 71.4 (*C*H_2-Ar), 85.1 (C-4 or C-5), 127.7 (Ar-*C*), 128.0 (2× Ar-*C*), 128.4 (2× Ar-*C*), 137.6 (Ar-*C*) ppm. $C_{14}H_{18}O_2$ (218.29): calcd. C 77.03, H 8.31; found C 76.76, H 8.29.

(–)-21 via Alkyne 29: To a solution of the alcohol (–)-**29** (22.0 mg, 100 μmol) in cyclohexane (0.4 mL) was added PtO_2 (0.6 mg) and the suspension was stirred under a hydrogen atmosphere (balloon

technique) for 4 d at room temperature. Subsequently, the suspension was filtered through celite to furnish alcohol (–)-**21** (16.9 mg, 76 μmol, 76%) as colorless oil.

(4*S*,6*R*,8*R*,10*S*,16*S*,18*R*)-2,6,8,10,16,18-Hexamethyldocosane [(+)-1a]: To magnesium (24 mg) was added under argon an ethereal solution (0.65 mL) of bromide (+)-**B** (266 μmol, 2.7 equiv.) and dibromoethane (106 μmol, 1.1 equiv.). The suspension was maintained at reflux for further 30 min. Then the Grignard reagent was cooled to –50 °C. The triflate **A** (97 μmol, 1.0 equiv.) was dissolved in benzene following an azeotropic distillation (rotary evaporator) to remove water traces. Then ether (0.5 mL) and Li_2CuCl_4[18] (0.1 M in THF, 106 μL, 10.6 μmol, 4 mol-% rel. to the bromide) were added to the triflate. This orange solution was added dropwise to the Grignard reagent at –30 °C resulting in a black solution containing a gray solid. The suspension was slowly warmed to –20 °C and stirred at this temperature for 18 h. The reaction was quenched by the addition of water (100 μL) and extracted with MTBE (5 × 2 mL). To the crude product solution was added an appropriate amount of silica gel, which was then concentrated to dryness. Flash chromatography (100:1 petroleum ether/MTBE) delivered the product (+)-**1a** together with hydrolyzed Grignard reagent which was removed by bulb-to-bulb distillation (100 °C, 20 mbar). A final HPLC separation delivered the product (+)-**1a** (35.6 mg, 90.2 μmol, 93%) as a colorless oil. HPLC: (Macherey–Nagel, Nucleosil 100-7 C18; eluent: *i*PrOH/H_2O 91:9 to 93:7 in 20 min, 9 mL/min). A similar experiment with (–)-**B** yielded the diastereomeric docosane (+)-**1b** in 92% yield. (+)-**1a** $[\alpha]_D^{20}$ = +7.7 (*c* = 1.29 in $CHCl_3$). (+)-**1b** $[\alpha]_D^{20}$ = +8.5 (*c* = 1.21 in $CHCl_3$). ^{1}H NMR (499.873 MHz, $CDCl_3$, (+)-**1a**): δ = 0.78 (d, ^3J = 6.6 Hz, 6 H, CH_3), 0.81 (pt, ^3J = 7.1 Hz, 12 H, CH_3), 0.86 (pt, ^3J = 7.2 Hz, 6 H, CH_3), 0.95–1.35 (m, 28 H), 1.45 (m_c, 4 H, CH), 1.55 (m_c, 2 H, CH) ppm. ^{13}C NMR (125.708 MHz, $CDCl_3$, (+)-**1a**): δ = 14.181 and 14.389 (C-1 and C-22), 19.553 (CH_3), 19.570 (CH_3), 19.589 (CH_3), 19.647 (CH_3), 20.080, 20.302 (16-CH-CH_3, 18-CH-CH_3), 23.072, 26.928, 27.063, 27.294 (2 C), 29.175, 29.715, 29.982 (2 C), 29.995, 30.346, 36.573, 36.876, 37.876, 40.222, 45.225, 45.552, 45.579, 46.535 ppm. ^{1}H NMR (499.873 MHz, $CDCl_3$, (+)-**1b**): δ = 0.78 (d, ^3J = 6.6 Hz, 6 H, CH_3), 0.81 (pt, ^3J = 7.1 Hz, 12 H, CH_3), 0.86 (pt, ^3J = 7.2 Hz, 6 H, CH_3), 0.95–1.35 (m, 28 H), 1.45 (m_c, 4 H, CH), 1.55 (m_c, 2 H, CH) ppm. ^{13}C NMR (125.708 MHz, $CDCl_3$, (+)-**1b**): δ = 14.181 and 14.389 (C-1 and C-22), 19.553 (CH_3), 19.570 (CH_3), 19.589 (CH_3), 19.649 (CH_3), 20.080 and 20.302 (16-CH-*C*H_3 and 18-CH-*C*H_3), 23.072, 26.940, 27.070, 27.294 (2 C), 29.175, 29.715, 29.982 (2 C), 30.002, 30.365, 36.570, 36.878, 37.885, 40.222, 45.222, 45.550, 45.562, 46.537 ppm. HR-MS analysis for $C_{28}H_{58}$ (394.76): calcd. 394.453850; found for (+)-**1a** 394.454844; found for (+)-**1b** 394.455080.

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