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Enantioselective Synthesis of the Unnatural Enantiomers of the Fungal Sesquiterpenoids Acorenone and Trichoacorenol

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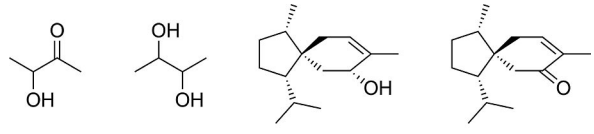
The volatiles released by several strains of *Trichoderma* fungi were collected using a closed-loop stripping apparatus and analysed by GC–MS. Most of the investigated strains released the two structurally related spirocyclic sesquiterpenoids trichoacorenol, previously identified in *Trichoderma koningii* (Huang et al., 1995), and acorenone. A new enantioselective synthesis of the enantiomer of the natural spirocyclic sesquiterpene acorenone and the first enantioselective synthesis of the related compound *ent*-trichoacorenol have been completed by a chiral-pool approach starting from (+)-(*R*)-pulegone using ring-closing metathesis as the key step. The absolute configuration of natural trichoacorenol from *Trichoderma harzianum* sp. 714 has been assigned by chiral GC–MS analysis and is the same as that in *T. koningii*.

Introduction

Trichoderma spp. are asexually reproducing fungi common in soil, root, and foliar ecosystems. In addition, marine representatives have frequently been isolated especially from sediments or sponges.[1] In soil, *Trichoderma* belong to the most frequently occurring fungi that are present in nearly all temperate and tropical regions. The sexual teleomorph is classified as the genus *Hypocrea*, but many strains do not have a known sexual stage. The individuals of the asexual form can exhibit an exceptionally high level of genetic diversity resulting in the production of a wide range of small-molecule secondary metabolites with antibiotic activities and extracellular enzymes such as chitinases.[2]

These metabolites and exoenzymes provide the molecular basis for interactions between the plants and *Trichoderma* as opportunistic, avirulent plant symbionts. The symbiotic system is characterized by enhanced plant root growth and thereby crop productivity as a result of an interaction of the fungi with the plant's nutrient-uptake system.[3] *Trichoderma* can solubilize nutrients otherwise unavailable to plants such as metal oxides and calcium phosphate by reduction or release of siderophores as iron chelators.[4] Further, the symbiont is beneficial to the plants by a mycoparasitic effect towards a range of plant-pathogenic fungi, as the extracellular chitinases released by *Trichoderma* are toxic to the pathogen.[2] In addition, *Trichoderma* prevents the penetration of leaf surfaces by plant-pathogenic fungi such as *Botrytis cinerea* by inhibiting or degrading the enzymes involved such as pectinases.[5] Besides these direct effects, *Trichoderma* is able to induce localized or systemic resistance to fungal pathogens in plants.[6]

To date, little information has accumulated regarding the molecular elicitors that participate in the interaction between the plants and their microbial symbionts. Some details are known for the symbiotic system between plants and plant growth-promoting rhizobacteria that also have the potential to induce systemic resistance. Herein, plant-growth promotion is mediated by the volatiles acetoin (**1**) and 2,3-butanediol (**2**, Figure 1).[7]



1 **2** **3a** **4**

Figure 1. Plant-growth-promoting volatiles from rhizobacteria (**1** and **2**) and structures of trichoacorenol (**3a**) and acorenone (**4**).

This example demonstrates that volatiles can play important roles with respect to interspecies communication. However, most research on secondary metabolites includes the preparation of culture extracts from laboratory liquid cultures followed by concentration steps during which volatile metabolites are easily lost, and as a consequence volatiles are frequently overlooked. The analysis of volatile metabolites is a promising approach to identify new bioactive compounds even from strains that are otherwise well studied in terms of their secondary metabolism. These considerations provided the motivation to analyse the volatiles released by several strains of *Trichoderma*. Most of the strains investigated produced two structurally related spirocyclic sesquiterpenes, trichoacorenol (**3a**) and acorenone (**4**).

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Compound (–)-**3a** has been previously isolated from *Trichoderma koningii*, and its relative configuration has been determined by NOE experiments[8] and correlation of its oxidation product acorenone with synthetic references.[9,10] The absolute configuration of (–)-**3a** has been correlated from its oxidation product (–)-**4** to natural (–)-acorenone from *Acorus calamus*.[11] Several synthetic approaches to prepare racemic **4**[12] and also a few enantioselective routes[13] have been published. In addition, the racemic alcohol *rac*-**3a** has been obtained during a formal synthesis of *rac*-**4** from its epimer acorenone B.[14] However, an enantioselective synthesis of **3a** has not been performed. Furthermore, the structurally related compound α-acoradiene, the major aggregation pheromone of *Gnatocerus cornutus*, has been synthesized, and its structure was revised after total synthesis.[15–17] This clearly demonstrates the need for total syntheses of natural products to fully and unambiguously determine their structures. Here we report a new enantioselective synthesis of the optical antipodes of natural trichoacorenol and acorenone from (*R*)-pulegone. The synthetic material was used to assign the relative and absolute configurations of natural trichoacorenol from *T. harzianum*, which is in agreement with the published structure of (–)-**3a** from *T. koningii*.

Results and Discussion

The volatiles emitted from agar plate cultures of different *Trichoderma* strains were collected using a closed-loop stripping apparatus (Figure S1, Supporting Information) and analysed by GC–MS. These analyses resulted in the identification of two sesquiterpenoids produced in large amounts by several *Trichoderma* strains, which were identified by comparison of their mass spectra to spectral libraries as **3a** and **4**. Especially large amounts of these compounds were emitted by *Trichoderma harzianum* 714 (Figure 2). The full results of the analyses and investigations on the biosynthesis of **3a** by feeding experiments with deuterated mevalonolactone isotopomers have been published recently.[18,19]

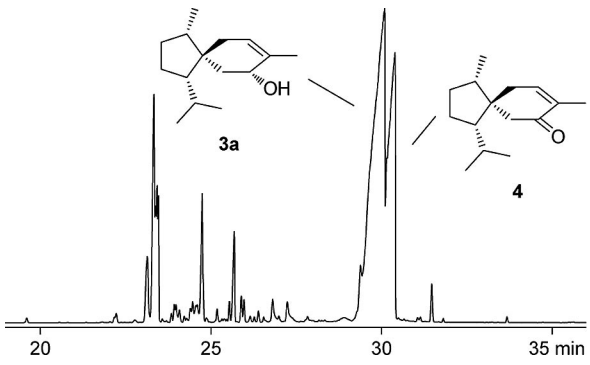
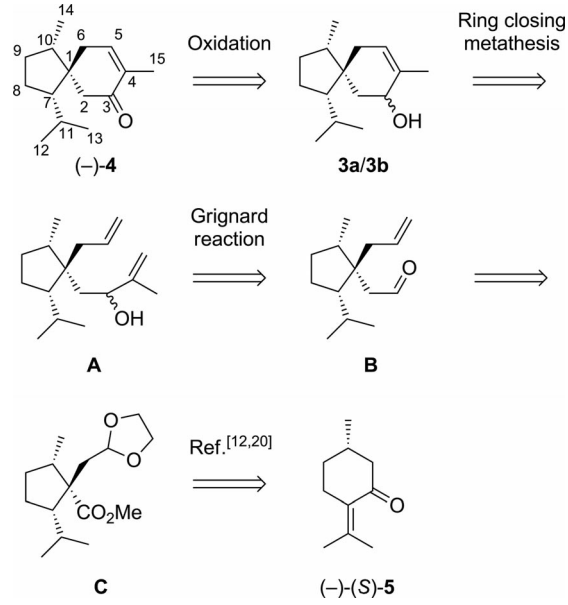


Figure 2. Total ion chromatogram of a headspace extract from *Trichoderma harzianum* 714.

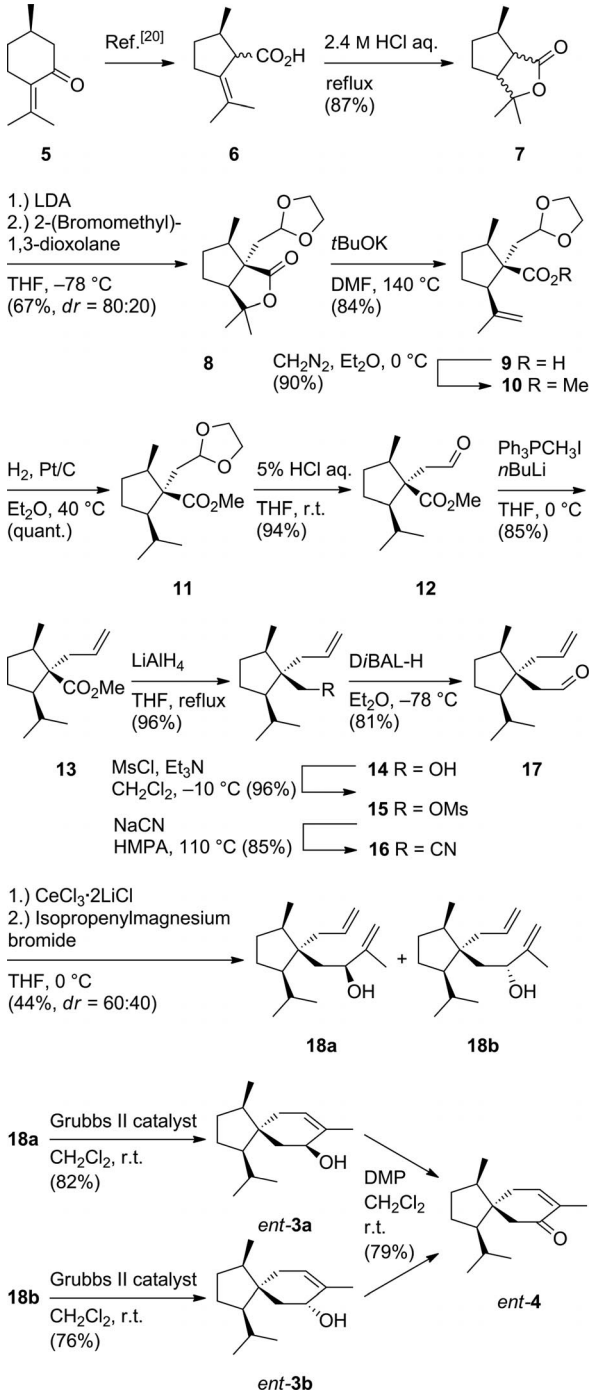
For the unambiguous identification and complete structural elucidation with respect to the relative and absolute configurations of the tentatively identified compounds, an enantioselective total synthesis was carried out. Scheme 1 shows the retrosynthetic analysis for **3a** and **4**. The ketone **4** can be obtained by the oxidation of **3a** or its epimer **3b** that are both available from ring-closing metathesis of the diastereomeric dienes **A**. A mixture of these diastereomeric alcohols can arise from the aldehyde **B** through a Grignard reaction. Compound **B** is a hydrogenated and twofold one-carbon-elongated homologue of the methyl ester **C**, which can be constructed in analogy to literature methods starting from (–)-(*S*)-pulegone.[12,20]



Scheme 1. Retrosynthetic analysis of **3a** and **4**.

As (+)-(*R*)-pulegone (ca. 3 € per g) is much cheaper than (–)-(*S*)-pulegone (ca. 200 € per g), the synthesis of the enantiomers *ent*-**3a** and *ent*-**4** was approached. The synthetic route to these sesquiterpenes was carried out as shown in Scheme 2. The known pulegenic acid [**6**, diastereomeric ratio (1*R*,2*R*)/(1*S*,2*R*) = 60:40] derived from (+)-(*R*)-pulegone (**5**) was converted into puleganolide [**7**, diastereomeric ratio (3a*S*,6a*R*)/(3a*R*,6a*S*) = 60:40] under acidic conditions.[20] Alkylation of the lactone **7** with lithium diisopropylamide (LDA) and commercially available 2-(bromomethyl)-1,3-dioxolane gave **8** in a diastereomeric ratio of (3a*S*,6a*R*)/(3a*R*,6a*S*) = 80:20. The diastereoisomers were separated by column chromatography, and the required diastereoisomer (3a*S*,6a*R*)-**8** was converted into the acid **9** by ring opening of the lactone moiety by treatment with potassium *tert*-butoxide (KO*t*Bu) in boiling *N*,*N*-dimethylformamide (DMF). The acid **9** was esterified with diazomethane to afford the corresponding methyl ester **10**, which was hydrogenated with a platinum catalyst on charcoal to give **11**. Deprotection under acidic conditions released the aldehyde **12**, which was converted to **13** by a Wittig methylenation. The alcohol **14** was afforded by reduction with $LiAlH_4$ and transfomed into the mesylate **15**.

The nucleophilic substitution with sodium cyanide in hexamethylphosphoric triamide at 110 °C yielded **16**, which was reduced to the aldehyde **17** with diisobutylaluminium hydride (D*i*BAL-H). The alcohols **18a** and **18b** (diastereomeric ratio 60:40) were obtained by a $CeCl_3$-mediated Grignard reaction with isopropenylmagnesium bromide and were separated by column chromatography.[21] Subsequent ring-closing metathesis of both diastereomeric alcohols was performed with a Grubbs–Hoveyda II catalyst and resulted in the formation of *ent*-**3a** and its epimer *ent*-**3b**, which were both oxidized with Dess–Martin periodinane (DMP) to *ent*-**4**. This route included 14 steps for the synthesis of *ent*-**4** with an overall yield of 5% based on **6**.



Scheme 2. Synthesis of *ent*-**3a** and *ent*-**4**.

The relative configurations of the hydroxy groups of *ent*-**3a** and *ent*-**3b** were determined by 2D NMR spectroscopy. Figure 3 shows the key NOESY correlations for both synthetic diastereomers (for NOESY spectra and carbon numbering of *ent*-**3a** and *ent*-**3b** see Supporting Information). The configuration at C-3 of compound (3*S*)-*ent*-**3a** was deduced from the NOESY couplings of 3-H with the isopropyl group (12-H, 13-H). Additional cross peaks are visible with the OH proton, the H_R proton at C-2, and the methyl group bonded to C-4 (11-H). In contrast, the 3-H proton of (3*R*)-*ent*-**3b** shows a strong NOESY coupling with the methyl group bonded to C-10 (15-H), and additionally to the H_S proton at C-2, the methyl protons 11-H, and OH.

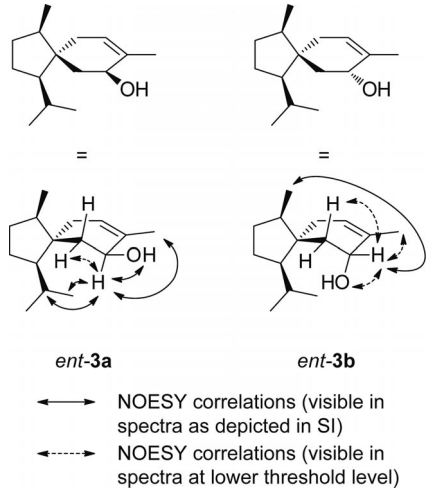


Figure 3. Key NOESY correlations of *ent*-**3a** and *ent*-**3b**.

To determine the absolute configuration of natural **3a**, *rac*-**3a** was synthesized using the same approach as for *ent*-**3a** starting from *rac*-citronellal that was converted into *rac*-pulegone by a literature procedure.[22] GC–MS analyses of the natural and the synthetic compounds on a chiral stationary phase are presented in Figure 4. The enantiomers of *rac*-**3a** were separated on a chiral Hydrodex-6-TBDMS fused-silica capillary column (Figure 4A). Synthetic *ent*-**3a** proved to be the second enantiomer eluted (Figure 4B), whereas **3a** from *T. harzianum* eluted with the same retention time as the first enantiomer (Figure 4C). This was confirmed by analysis of a mixture of the racemic and the natural compound (Figure 4D), and a mixture of enantiomerically pure *ent*-**3a** and the natural product (Figure 4E). In conclusion, the synthetic material is the opposite enantiomer to natural **3a**, clearly establishing the absolute configuration of trichoacorenol from *T. harzianum* as (1*S*,3*R*,7*S*,10*S*)-**3a** by correlation of *ent*-**3a** to (*R*)-pulegone.

To confirm that **3a** from *T. harzianum* has the same absolute configuration as trichoacorenol from *T. koningii*, the specific rotation of *ent*-**3a** was measured. The reported op-

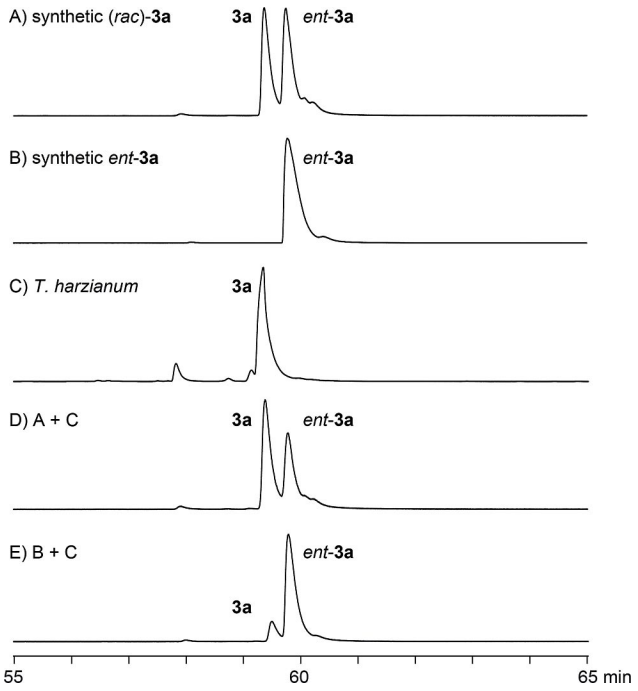


Figure 4. Determination of the absolute configuration of natural **3a** from *T. harzianum* by chiral GC. The chromatograms show analyses of (A) synthetic (*rac*)-**3a**, (B) synthetic *ent*-**3a**, (C) a headspace extract from *T. harzianum*, (D) a mixture of synthetic (*rac*)-**3a** and a headspace extract from *T. harzianum*, and (E) synthetic *ent*-**3a** and a headspace extract from *T. harzianum*.

tical rotation for natural **3a** from *T. koningii* is $[\alpha]_D^{26} = -5.2$ ($c = 0.12$, $CHCl_3$),[8] and the specific rotation of the synthetic material *ent*-**3a** is $[\alpha]_D^{17} = +5.5$ ($c = 0.12$, $CHCl_3$), confirming that both species produce the same enantiomer of **3a**. Furthermore, the specific rotation of synthetic *ent*-**4**, $[\alpha]_D^{17} = +44.0$ ($c = 0.02$, $CHCl_3$), exhibited the opposite sign as reported for the oxidation product **4** obtained from natural **3a** from *T. koningii*, $[\alpha]_D^{26} = -22.0$ ($c = 0.047$, $CHCl_3$), and for natural **4** isolated from *Acorus calamus*, $[\alpha]_D^{25} = -28$ (CCl_4).[8,13c]

Conclusions

The enantioselective synthesis of the unnatural enantiomers of the two main compounds in the headspace extract of *Trichoderma harzianum* and other fungal species from this genus, (–)-acorenone and (–)-trichoacorenol, has been accomplished starting from (+)-(*R*)-pulegone. As the key step in the formation of the spirocyclic carbon backbone an olefin metathesis was used. The same synthesis was performed to prepare the racemic compound. The enantiomers of the racemate of trichoacorenol were separated on a chiral GC phase, and by comparison of the natural compound from *T. harzianum* with the synthetic material the absolute configuration of the natural product was unambiguously established as (+)-trichoacorenol, which is the same as that from *T. koningii*.[8]

Experimental Section

General Synthetic Methods: Chemicals were purchased from Acros Organics (Geel, Belgium) or Sigma–Aldrich Chemie GmbH (Steinheim, Germany) and used without further purification. Solvents were purified by distillation and dried according to standard methods. Oxygen- and/or moisture-sensitive reactions were carried out under N_2 in vacuum-heated flasks with dry solvents. TLC was performed on 0.20 mm Macherey–Nagel silica gel plates (Polygram SIL G/UV_{254}). Column chromatography was performed with Merck silica gel 60 (0.040–0.063 mm) using standard flash-chromatographic methods. NMR spectra were recorded with Bruker DRX-400 (400 MHz), AV III-400 (400 MHz), and AV II-600 (600 MHz) spectrometers and were referenced against TMS (δ = 0.00 ppm) for ^{1}H NMR and $CHCl_3$ (δ = 77.16 ppm) for ^{13}C NMR spectroscopy. Chemical shifts are reported in parts per million (ppm), multiplicities are abbreviated as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br. = broad, and coupling constants *J* are given in Hertz (Hz). IR spectra were recorded with a Bruker Tensor 27 ATR spectrometer. UV spectra were recorded with a Varian Cary 100 Bio spectrometer. Specific rotations were measured using a Dr. Kernchen Propol Digital Automatic Polarimeter. GC–MS analyses for the synthetic compounds were carried out with an HP6890 GC system connected to an HP5973 Mass Selective Detector fitted with a BPX-5 fused-silica capillary column (25 m × 0.22 mm i.d., 0.25 μm film, SGE Inc., Melbourne, Australia) under the following conditions: inlet pressure: 77.1 kPa, He 23.3 mL min^{-1}; injection volume: 1 μL; injector: 250 °C; transfer line: 300 °C; electron energy: 70 eV. The GC was programmed as follows: 50 °C (5 min isothermic), increasing at 10 °C min^{-1} to 320 °C, and operated in split mode; carrier gas (He): 1.0 mL min^{-1}. Retention indices *I* were determined from a homologous series of *n*-alkanes (C_8 – C_{32}). Polar compounds with adverse chromatographical behaviour were transformed into their trimethylsilyl derivatives by treatment with *N*-methyl-*N*-(trimethylsilyl)trifluoroacetamide (MSTFA)[23] prior to GC analysis. Chiral GC analyses were performed using a Hydrodex-6-TBDMS fused-silica capillary column (30 m × 0.25 mm i.d., 0.25 μm film, Macherey–Nagel). The GC was programmed as follows: 10 min at 50 °C increasing with 2 °C min^{-1} to 160 °C and then with 10 °C min^{-1} to 220 °C.

(2*R*)-2-Methyl-5-(propan-2-ylidene)cyclopentanecarboxylic Acid (6):[20] To a suspension of (+)-(*R*)-pulegone [(*R*)-**5**] (12.2 g, 80.1 mmol, 1.0 equiv.) and $NaHCO_3$ (2.04 g) in dry Et_2O (200 mL) was added Br_2 (12.7 g, 79.6 mmol, 1.0 equiv.) at 0 °C. After stirring at 0 °C for 30 min, the mixture was concentrated in vacuo. An aqueous KOH solution (0.8 M, 350 mL) was added, and the mixture was stirred under reflux for 3 h. The reaction mixture was washed with ethyl acetate, acidified with an aqueous H_2SO_4 solution (2 M), extracted with diethyl ether, dried with $MgSO_4$, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 5:1) to give the acid **6** {diastereomeric mixture [(1*R*,2*R*)/(1*S*,2*R*) = 60:40], 4.79 g, 28.5 mmol, 36%} as a colorless oil. R_f = 0.41; *I* = 1348 (major), 1326 (minor). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 11.43 (br. s, 2 H, 2× COOH), 3.40 (d, $^3J_{H,H}$ = 8.0 Hz, 1 H, CH), 2.97 (d, $^3J_{H,H}$ = 5.1 Hz, 1 H, CH), 2.48 – 2.18 (m, 5 H, 2× CH, 2× CH_2), 2.05 – 1.97 (m, 1 H, CH_2), 1.85 – 1.70 (m, 2 H, CH_2), 1.68 (s, 3 H, CH_3), 1.67 (s, 3 H, CH_3), 1.647 (s, 3 H, CH_3), 1.645 (s, 3 H, CH_3), 1.33 – 1.15 (m, 2 H, CH_2), 1.092 (d, $^3J_{H,H}$ = 6.9 Hz, 3 H, CH_3), 1.086 (d, $^3J_{H,H}$ = 6.8 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 182.1 (C_q), 180.5 (C_q), 134.5 (C_q), 133.8 (C_q), 126.7 (C_q), 126.5 (C_q), 55.4 (CH), 52.7 (CH), 40.8 (CH), 38.9 (CH), 33.7 (CH_2), 32.6

(CH_2), 30.3 (CH_2), 30.2 (CH_2), 21.5 (CH_3), 21.3 (CH_3), 21.2 (CH_3), 21.1 (CH_3), 19.8 (CH_3), 15.6 (CH_3) ppm. MS (EI) (major): *m*/*z* (%) = 240 (17) [M^+], 225 (16), 122 (59), 117 (4), 107 (22), 91 (7), 81 (11), 75 (17), 73 (100), 67 (3), 55 (3), 45 (6), 41 (5). MS (EI) (minor): *m*/*z* (%) = 240 (18) [M^+], 225 (19), 122 (57), 117 (4), 107 (21), 91 (7), 81 (11), 75 (17), 73 (100), 67 (3), 55 (3), 45 (5), 41 (5).

(6*R*)-3,3,6-Trimethylhexahydro-1*H*-cyclopenta[*c*]furan-1-one (7): A suspension of **3** (diastereomeric mixture, 6.09 g, 36.2 mmol) in aqueous HCl (2.4 M, 50 mL) was stirred under reflux for 2 h. The product was extracted with diethyl ether, successively washed with water and a saturated aqueous $NaHCO_3$ solution, dried with $MgSO_4$, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 5:1) to give **7** {diastereomeric mixture [(3a*S*,6*R*,6a*R*)/(3a*R*,6*R*,6a*S*) = 60:40], 5.26 g, 31.3 mmol, 87%} as a colorless oil. R_f = 0.38; *I* = 1366 (major), 1344 (minor). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.12 (t, $^3J_{H,H}$ = 8.6 Hz, 1 H, CH), 2.76 (dd, $^3J_{H,H}$ = 8.8, $^3J_{H,H}$ = 4.1 Hz, 1 H, CH), 2.63 (td, $^3J_{H,H}$ = 9.0, $^3J_{H,H}$ = 4.1 Hz, 1 H, CH), 2.59 (td, $^3J_{H,H}$ = 9.1, $^3J_{H,H}$ = 7.7 Hz, 1 H, CH), 2.41 – 2.32 (m, 1 H, CH), 2.30 – 2.22 (m, 1 H, CH), 1.94 – 1.74 (m, 4 H, 2× CH_2), 1.70 – 1.60 (m, 1 H, CH_2), 1.58 – 1.50 (m, 1 H, CH_2), 1.40 (s, 3 H, CH_3), 1.39 (s, 6 H, 2× CH_3), 1.38 (s, 3 H, CH_3), 1.27 – 1.13 (m, 2 H, CH_2), 1.22 (d, $^3J_{H,H}$ = 7.1 Hz, 3 H, CH_3), 1.15 (d, $^3J_{H,H}$ = 6.9 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.9 (C_q), 176.8 (C_q), 84.1 (C_q), 84.0 (C_q), 53.7 (CH), 50.1 (CH), 49.7 (CH), 49.5 (CH), 38.2 (CH), 37.9 (CH), 35.4 (CH_2), 34.3 (CH_2), 31.0 (CH_3), 29.8 (CH_3), 27.9 (CH_2), 27.3 (CH_2), 23.8 (CH_3), 23.6 (CH_3), 21.2 (CH_3), 15.4 (CH_3) ppm. MS (EI) (major): *m*/*z* (%) = 153 (35), 109 (31), 81 (100), 80 (14), 67 (48), 59 (8), 53 (7), 43 (32), 41 (16). MS (EI) (minor): *m*/*z* (%) = 168 (10) [M^+], 153 (48), 139 (5), 123 (15), 113 (10), 109 (29), 95 (6), 91 (4), 81 (100), 79 (13), 67 (63), 59 (12), 53 (10), 43 (42) 41 (22).

(3a*S*,6*R*,6a*R*)-6a-[(1,3-Dioxolan-2-yl)methyl]-3,3,6-trimethylhexahydro-1*H*-cyclopenta[*c*]furan-1-one (8): To a solution of diisopropylamine (7.48 g, 74.1 mmol, 1.5 equiv.) in dry THF (60 mL) was added *n*BuLi (1.6 M in hexane, 46.2 mL, 74.0 mmol, 1.5 equiv.) at 0 °C. After stirring at 0 °C for 1 h, a solution of **7** (diastereomeric mixture, 8.28 g, 49.3 mmol, 1.0 equiv.) in dry THF (40 mL) was added to the mixture at –78 °C. The mixture was stirred at –40 °C for 2.5 h. 2-(Bromomethyl)-1,3-dioxolane (14.8 g, 88.7 mmol, 1.8 equiv.) was added at –78 °C, and the mixture was warmed to room temperature overnight. The reaction was quenched with a saturated aqueous NH_4Cl solution, the mixture extracted with ethyl acetate, dried with $MgSO_4$, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 5:1) to give the alkylation product (8.36 g, 32.9 mmol, 67%, 60% *de*) as a colorless oil. The desired diastereoisomer **8** was separated by column chromatography (5.00 g). R_f = 0.20; *I* = 1861. $[\alpha]_D^{23}$ = –58.7 (*c* = 0.30, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 4.95 (t, $^3J_{H,H}$ = 5.0, CH, $^1J_{C,H}$ = 164.6 Hz, 1 H, 11-H), 4.00 – 3.94 (m, 2 H, 2× CH_2, 12-H, 13-H), 3.87 – 3.81 (m, 2 H, 2× CH_2, 12-H, 13-H), 2.81 (d, $^3J_{H,H}$ = 8.6, $^1J_{C,H}$ = 136.8 Hz, 1 H, CH, 3a-H), 2.20 (dd, $^2J_{H,H}$ = 14.6, $^3J_{H,H}$ = 4.7, $^1J_{C,H}$ = 110.9 Hz, 1 H, CH_2, 10-H), 2.04 – 1.98 (m, 1 H, CH, 6-H), 2.01 (dd, $^2J_{H,H}$ = 14.6, $^3J_{H,H}$ = 5.1 Hz, 1 H, CH_2, 10-H), 1.91 (ddt, $^2J_{H,H}$ = 13.6, $^3J_{H,H}$ = 5.8, $^4J_{H,H}$ = 1.3 Hz, 1 H, CH_2, *pro-R* 4-H), 1.80 (dt, $^2J_{H,H}$ = 11.9, $^3J_{H,H}$ = 6.0 Hz, 1 H, CH_2, *pro-S* 5-H), 1.63 (tdd, $^2J_{H,H}$ = 13.3, $^3J_{H,H}$ = 8.6, $^3J_{H,H}$ = 6.1 Hz, 1 H, CH_2, *pro-S* 4-H), 1.43 (s, $^1J_{C,H}$ = 126.8 Hz, 3 H, CH_3, 7-H), 1.35 (s, $^1J_{C,H}$ = 126.8 Hz, 3 H, CH_3, 8-H), 1.14 (qd, $^3J_{H,H}$ = 12.4, $^3J_{H,H}$ = 5.7 Hz, 1 H, CH_2, *pro-R* 5-H), 1.10 (d, $^3J_{H,H}$ = 7.0, $^1J_{C,H}$ = 126.6 Hz, 3 H, CH_3, 9-H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 177.9 (C_q, C-1), 102.2 (CH, C-11), 83.8 (C_q, C-3), 64.6 (CH_2, C-12), 64.4 (CH_2, C-13), 56.6 (C_q, C-6a), 51.5 (CH, C-3a), 45.3 (CH, C-6), 39.9 (CH_2, C-10), 34.5 (CH_2, C-5), 31.9 (CH_3, C-7), 28.3 (CH_2, C-4), 24.1 (CH_3, C-8), 14.7 (CH_3, C-9) ppm. IR (ATR): $\tilde{\nu}$ = 2970, 2877, 1748, 1456, 1388, 1372, 1258, 1227, 1196, 1112, 1041, 966, 950, 819, 761, 656, 609 cm^{-1}. MS (70 eV): *m*/*z* (%) = 239 (9), 167 (8), 149 (3), 123 (3), 107 (3), 95 (3), 87 (18), 79 (5), 73 (100), 67 (3), 55 (3), 45 (11), 41 (5). HRMS (APCI$^+$): calcd. for $C_{14}H_{23}O_4$ [MH^+] 255.15909, found 255.15918.

(1*R*,2*R*,5*R*)-1-[(1,3-Dioxolan-2-yl)methyl]-5-methyl-2-(prop-1-en-2-yl)cyclopentanecarboxylic Acid (9): To a solution of *t*BuOK (4.57 g, 40.8 mmol, 1.2 equiv.) in dry DMF (125 mL) was added a solution of **8** (8.63 g, 34.0 mmol, 1.0 equiv.) in dry DMF (125 mL) at 120 °C. After stirring at 140 °C for 6 h, the reaction was quenched with iced water, the mixture washed with diethyl ether, acidified with an aqueous HCl solution (1 M), extracted with $CHCl_3$, dried with $MgSO_4$, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 3:1) to give **9** (7.22 g, 28.4 mmol, 84%) as a colorless oil. R_f = 0.25; *I* (MSTFA) = 1876. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 11.8 (br. s, 1 H, COOH), 4.99 (dd, $^3J_{H,H}$ = 5.0, $^3J_{H,H}$ = 4.3 Hz, 1 H, CH), 4.83 – 4.82 (m, 1 H, CH_2), 4.78 – 4.76 (m, 1 H, CH_2), 4.02 – 3.91 (m, 2 H, 2× CH_2), 3.87 – 3.79 (m, 2 H, 2× CH_2), 2.74 (dd, $^3J_{H,H}$ = 11.4, $^3J_{H,H}$ = 8.8 Hz, 1 H, CH), 2.34 – 2.24 (m, 1 H, CH_2), 2.31 (dd, $^2J_{H,H}$ = 15.1, $^3J_{H,H}$ = 4.2 Hz, 1 H, CH_2), 2.09 (qd, $^3J_{H,H}$ = 11.8, $^3J_{H,H}$ = 5.2 Hz, 1 H, CH), 1.95 (dd, $^2J_{H,H}$ = 15.1, $^3J_{H,H}$ = 5.1 Hz, 1 H, CH_2), 1.95 – 1.88 (m, 1 H, CH_2), 1.86 – 1.76 (m, 1 H, CH_2), 1.71 (s, 3 H, CH_3), 1.69 – 1.59 (m, 1 H, CH_2), 1.03 (d, $^3J_{H,H}$ = 6.8 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.8 (C_q), 143.9 (C_q), 112.7 (CH_2), 102.6 (CH), 64.7 (CH_2), 64.5 (CH_2), 56.9 (C_q), 56.3 (CH), 42.1 (CH), 38.1 (CH_2), 31.0 (CH_2), 28.1 (CH_2), 21.9 (CH_3), 15.2 (CH_3) ppm. IR (ATR): $\tilde{\nu}$ = 2956, 2879, 1723, 1691, 1431, 1377, 1231, 1127, 1024, 945, 890, 725, 664 cm^{-1}. MS (EI, MSTFA): *m*/*z* (%) = 326 [M^+, 1], 271 (13), 253 (7), 240 (43), 223 (8), 212 (6), 209 (13), 193 (7), 163 (3), 155 (5), 147 (33), 133 (5), 125 (7), 121 (10), 105 (14), 91 (6), 87 (6), 79 (6), 73 (100), 67 (4), 55 (4), 45 (16), 41 (4). HRMS (ESI$^+$): calcd. for $C_{14}H_{23}O_4$ [MH^+] 255.15909, found 255.15928.

Methyl (1*R*,2*R*,5*R*)-1-[(1,3-Dioxolan-2-yl)methyl]-5-methyl-2-(prop-1-en-2-yl)cyclopentanecarboxylate (10): To a solution of Diazald® (17.1 g, 80.0 mmol, 5.6 equiv.) in diethyl ether (40 mL) and 1-methoxy-2-(2-methoxyethoxy)ethane (40 mL) was added a solution of KOH (16.0 g) in water (40 mL) and MeOH (40 mL). The emerging diazomethane was introduced into diethyl ether (250 mL) at –78 °C. After completion of the gas formation, a solution of **9** (7.18 g, 28.3 mmol, 1.0 equiv.) in diethyl ether (50 mL) was added at –0 °C, and the mixture was warmed to room temperature overnight. The reaction was quenched with AcOH, the mixture neutralized with a saturated aqueous $NaHCO_3$ solution, extracted with diethyl ether, dried with $MgSO_4$, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 5:1) to give **10** (6.78 g, 25.3 mmol, 90%) as a colorless oil. R_f = 0.39; *I* = 1787. $[\alpha]_D^{23}$ = –12.0 (*c* = 0.30, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 4.96 (dd, $^3J_{H,H}$ = 5.0, $^3J_{H,H}$ = 4.4 Hz, 1 H, CH, 9-H), 4.81 – 4.80 (m, 1 H, CH_2, 12-H), 4.69 – 4.68 (m, 1 H, CH_2, 12-H), 4.00 – 3.92 (m, 2 H, 2× CH_2, 10-H, 11-H), 3.85 – 3.79 (m, 2 H, 2× CH_2, 10-H, 11-H), 3.63 (s, $^1J_{C,H}$ = 146.8 Hz, 3 H, CH_3, 7-H), 2.71 (dd, $^3J_{H,H}$ = 11.4, $^3J_{H,H}$ = 8.9 Hz, 1 H, CH, 2-H), 2.31 (dd, $^2J_{H,H}$ = 15.1, $^3J_{H,H}$ = 4.3 Hz, 1 H, CH_2, 8-H), 2.26 (ddq, $^3J_{H,H}$ = 9.8, $^3J_{H,H}$ = 9.8, $^3J_{H,H}$ = 6.7 Hz, 1 H, CH, 5-H), 2.05 (dddd, $^2J_{H,H}$ = 12.5, $^3J_{H,H}$ = 11.8, $^3J_{H,H}$ = 11.4, $^3J_{H,H}$ = 5.4 Hz, 1 H, CH_2, *pro-S* 3-H), 1.99 (dd, $^2J_{H,H}$ = 15.1, $^3J_{H,H}$ = 5.1 Hz, 1 H, CH_2, 8-H), 1.92 (dddd, $^2J_{H,H}$ = 12.6, $^3J_{H,H}$ = 9.5, $^3J_{H,H}$ = 9.5, $^3J_{H,H}$ = 5.4 Hz, 1 H, CH_2, *pro-S* 4-H), 1.82 (dddd,

$^2J_{H,H}$ = 12.7, $^3J_{H,H}$ = 9.0, $^3J_{H,H}$ = 9.0, $^3J_{H,H}$ = 3.9 Hz, 1 H, CH_2, *pro-R* 3-H), 1.66 (m, 3 H, CH_3, 14-H), 1.65 (dddd, $^2J_{H,H}$ = 12.2, $^3J_{H,H}$ = 9.9, $^3J_{H,H}$ = 9.9, $^3J_{H,H}$ = 4.2, $^1J_{C,H}$ = 126.1 Hz, 1 H, CH_2, *pro-R* 4-H), 0.95 (d, $^3J_{H,H}$ = 6.8, $^1J_{C,H}$ = 125.5 Hz, 3 H, CH_3, 15-H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 174.7 (C_q, C-6), 144.3 (C_q, C-13), 112.2 (CH_2. C-12), 102.6 (CH, C-9), 64.6 (CH_2, C-10), 64.4 (CH_2, C-11), 57.0 (C_q, C-1), 55.7 (CH, C-2), 50.8 (CH_3, C-7), 42.0 (CH, C-5), 38.0 (CH_2, C-8), 31.0 (CH_2, C-4), 28.1 (CH_2, C-3), 21.9 (CH_3, C-14), 15.2 (CH_3, C-15) ppm. IR (ATR): $\tilde{\nu}$ = 2950, 2877, 1721, 1458, 1434, 1376, 1214, 1126, 1065, 1033, 1005, 982, 944, 893, 661 cm^{-1}. MS (EI): *m*/*z* (%) = 268 [M^+, 1], 237 (3), 225 (4), 213 (4), 209 (10), 182 (22), 165 (7), 157 (11), 147 (48), 139 (4), 135 (4), 131 (4), 125 (11), 121 (27), 113 (10), 105 (24), 91 (10), 87 (12), 79 (11), 73 (100), 67 (10), 59 (5), 55 (7), 45 (21), 41 (9). HRMS (EI): calcd. for $C_{15}H_{24}O_4$ [M^+] 268.16691, found 268.16699.

Methyl (1*R*,2*R*,5*R*)-1-[(1,3-Dioxolan-2-yl)methyl]-2-isopropyl-5-methylcyclopentanecarboxylate (11): A suspension of Pt/C (5% Pt, 4.58 g, 1.18 mmol, 5 mol-%) and **10** (6.61 g, 24.7 mmol) in diethyl ether (180 mL) was stirred under H_2 (35 bar) at 40 °C for 1 h. The reaction mixture was filtered and concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 5:1) to give **11** (6.65 g, 24.6 mmol, quant.) as a colorless oil. R_f = 0.43; *I* = 1776. $[a]_D^{23}$ = 2.4 (*c* = 0.27, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 4.97 (t, $^3J_{H,H}$ = 4.7 Hz, 1 H, CH, 9-H), 4.00 – 3.93 (m, 2 H, 2× CH_2, 10-H, 11-H), 3.85 – 3.78 (m, 2 H, 2× CH_2, 10-H, 11-H), 3.66 (s, 3 H, CH_3, 7-H), 2.28 (dd, $^2J_{H,H}$ = 15.3, $^3J_{H,H}$ = 4.4 Hz, 1 H, CH_2, 8-H), 2.26 (ddq, $^3J_{H,H}$ = 10.3, $^3J_{H,H}$ = 8.9, $^3J_{H,H}$ = 6.8 Hz, 1 H, CH, 5-H), 2.11 (dd, $^2J_{H,H}$ = 15.3, $^3J_{H,H}$ = 4.9 Hz, 1 H, CH_2, 8-H), 1.90 – 1.83 (m, 2 H, CH, CH_2, 2-H, 3-H), 1.83 – 1.77 (m, 1 H, CH_2, 4-H), 1.69 – 1.61 (m, 2 H, CH, CH_2, 3-H, 13-H), 1.61 – 1.54 (m, 1 H, CH_2, 4-H), 0.92 (d, $^3J_{H,H}$ = 6.8 Hz, 3 H, CH_3, 12-H), 0.88 (d, $^3J_{H,H}$ = 6.8 Hz, 3 H, CH_3, 15-H), 0.83 (d, $^3J_{H,H}$ = 6.6 Hz, 3 H, CH_3, 14-H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 175.1 (C_q, C-6), 102.7 (CH, C-9), 64.5 (2× CH_2, C-10, C-11), 57.1 (C_q, C-1), 54.0 (CH, C-2), 50.7 (CH_3, C-7), 42.4 (CH, C-5), 38.0 (CH_2, C-8), 30.90 (CH_2, C-4), 30.87 (CH, C-13), 28.3 (CH_2, C-3), 22.5 (CH_3, C-12), 21.7 (CH_3, C-14), 15.0 (CH_3, C-15) ppm. IR (ATR): $\tilde{\nu}$ = 2953, 2874, 1721, 1462, 1433, 1378, 1221, 1189, 1162, 1130, 1059, 1033, 1005, 984, 944, 922, 902, 882, 663 cm^{-1}. MS (EI): *m*/*z* (%) = 182 (5), 155 (5), 139 (6), 123 (4), 107 (4), 95 (3), 87 (10), 81 (5), 73 (100), 55 (3), 45 (9), 41 (5). HRMS (ESI^+): calcd. for $C_{14}H_{23}O_4$ [MH^+] 271.19039, found 271.19040.

Methyl (1*R*,2*R*,5*R*)-2-Isopropyl-5-methyl-1-(2-oxoethyl)cyclopentanecarboxylate (12): A solution of **11** (0.379 g, 1.40 mmol) in aqueous HCl (5%, 20 mL) and THF (20 mL) was stirred at room temperature for 4 h. The reaction was quenched with solid $NaHCO_3$, the mixture extracted with diethyl ether, washed with a saturated aqueous $NaHCO_3$ solution, dried with $MgSO_4$, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 10:1) to give **12** (0.299 g, 1.32 mmol, 94%) as a colorless oil. Due to its instability this compound was immediately used in the next step. R_f = 0.16; *I* = 1538. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.91 (dd, $^3J_{H,H}$ = 3.5, $^3J_{H,H}$ = 2.3 Hz, 1 H, CH), 3.72 (s, $^1J_{C,H}$ = 147.1 Hz, 3 H, CH_3), 2.96 (dd, $^2J_{H,H}$ = 15.6, $^3J_{H,H}$ = 2.3, $^1J_{C,H}$ = 126.6 Hz, 1 H, CH_2), 2.58 (dd, $^2J_{H,H}$ = 15.7, $^3J_{H,H}$ = 3.5, $^1J_{C,H}$ = 128.6 Hz, 1 H, CH_2), 2.18 – 2.11 (m, 1 H, CH_2), 1.91 – 1.57 (m, 6 H, 3× CH, 2× CH_2), 0.94 (d, $^3J_{H,H}$ = 7.1, $^1J_{C,H}$ = 124.8 Hz, 3 H, CH_3), 0.92 (d, $^3J_{H,H}$ = 6.9, $^1J_{C,H}$ = 125.6 Hz, 3 H, CH_3), 0.85 (d, $^3J_{H,H}$ = 6.5, $^1J_{C,H}$ = 125.2 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 202.9 (CH), 174.3 (C_q), 57.7 (C_q), 56.6 (CH), 51.1 (CH_3), 50.3 (CH_2), 44.6 (CH), 31.1 (CH_2), 30.6 (CH), 28.0 (CH_2), 22.7 (CH_3), 21.4 (CH_3), 15.4 (CH_3) ppm. IR (ATR): $\tilde{\nu}$ = 3035, 2956, 2875, 2744, 1702, 1457, 1409, 1381, 1336, 1226, 1190, 1163, 1040, 988, 965, 909, 826, 719, 662 cm^{-1}. MS (EI): *m*/*z* (%) = 195 (6), 183 (89), 171 (4), 167 (12), 155 (70), 151 (22), 140 (13), 139 (100), 135 (17), 123 (80), 115 (5), 111 (60), 107 (55), 101 (6), 95 (85), 91 (18), 83 (30), 81 (74), 77 (23), 69 (27), 67 (39), 59 (23), 55 (48), 53 (31), 43 (34), 41 (64).

Methyl (1*R*,2*R*,5*R*)-1-Allyl-2-isopropyl-5-methylcyclopentanecarboxylate (13): To a solution of methyltriphenylphosphonium iodide (5.78 g, 14.4 mmol, 1.5 equiv.) in dry THF (100 mL) was added *n*BuLi (1.6 M in hexane, 8.4 mL, 13.4 mmol, 1.4 equiv.) at 0 °C. After stirring at room temperature for 1 h, a solution of **12** (2.16 g, 9.55 mmol, 1.0 equiv.) in dry THF (50 mL) was added at 0 °C, and the mixture was stirred at room temperature for 6 h. The reaction was quenched with a saturated aqueous NH_4Cl solution, the mixture extracted with hexane, dried with $MgSO_4$, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 10:1) to give **13** (1.82 g, 8.10 mmol, 85%) as a colorless oil. R_f = 0.48; *I* = 1419. $[a]_D^{25}$ = –15.4 (*c* = 0.14, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 5.82 (ddt, $^3J_{H,H}$ = 17.0, $^3J_{H,H}$ = 10.1, $^3J_{H,H}$ = 7.4 Hz, 1 H, CH, 9-H), 5.10 [ddt, $^3J_{H,H}$ = 10.2, $^2J_{H,H}$ = 2.3, $^4J_{H,H}$ = 1.0 Hz, 1 H, CH_2, (*E*) 10-H], 5.07 [ddt, $^3J_{H,H}$ = 17.0, $^2J_{H,H}$ = 2.3, $^4J_{H,H}$ = 1.4 Hz, 1 H, CH_2, (*Z*) 10-H], 3.67 (s, $^1J_{C,H}$ = 146.6 Hz, 3 H, CH_3, 7-H), 2.57 (ddt, $^2J_{H,H}$ = 14.8, $^3J_{H,H}$ = 7.6, $^4J_{H,H}$ = 1.0 Hz, 1 H, CH_2, 8-H), 2.53 (ddt, $^2J_{H,H}$ = 14.7, $^3J_{H,H}$ = 7.4, $^4J_{H,H}$ = 1.2 Hz, 1 H, CH_2, 8-H), 2.03 (ddq, $^3J_{H,H}$ = 10.5, $^3J_{H,H}$ = 8.9, $^3J_{H,H}$ = 6.9 Hz, 1 H, CH, 5-H), 1.82 (dddd, $^2J_{H,H}$ = 11.8, $^3J_{H,H}$ = 9.2, $^3J_{H,H}$ = 9.2, $^3J_{H,H}$ = 5.1 Hz, 1 H, CH_2, 3-H), 1.78 – 1.72 (m, 1 H, CH_2, 4-H), 1.72 (dd, $^2J_{H,H}$ = 17.9, $^3J_{H,H}$ = 9.1 Hz, 1 H, CH, 2-H), 1.67 – 1.59 (m, 2 H, CH, CH_2, 3-H, 12-H), 1.59 – 1.52 (m, 1 H, CH_2, 4-H), 0.92 (d, $^3J_{H,H}$ = 6.7, $^1J_{C,H}$ = 124.2 Hz, 3 H, CH_3, 11-H), 0.84 (d, $^3J_{H,H}$ = 6.8, $^1J_{C,H}$ = 125.1 Hz, 3 H, CH_3, 14-H), 0.83 (d, $^3J_{H,H}$ = 6.0, $^1J_{C,H}$ = 125.1 Hz, 3 H, CH_3, 13-H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 175.7 (C_q, C-6), 134.8 (CH, C-9), 118.3 (CH_2, C-10), 58.5 (C_q, C-1), 52.3 (CH, C-2), 50.7 (CH_3, C-7), 41.5 (CH, C-5), 37.4 (CH_2, C-8), 31.1 (CH, C-12), 30.6 (CH_2, C-4), 28.5 (CH_2, C-3), 22.3 (CH_3, C-13), 22.0 (CH_3, C-11), 14.7 (CH_3, C-14) ppm. IR (ATR): $\tilde{\nu}$ = 3076, 2954, 2873, 1723, 1462, 1435, 1380, 1219, 1186, 1159, 993, 913, 705 cm^{-1}. MS (EI): *m*/*z* (%) = 224 (2) [M^+], 209 (4), 192 (5), 181 (41), 169 (11), 165 (17), 154 (7), 149 (26), 141 (56), 137 (11), 125 (14), 123 (52), 114 (18), 109 (85), 107 (36), 101 (4), 95 (36), 93 (46), 83 (10), 81 (90), 77 (41), 69 (35), 67 (38), 59 (32), 55 (50), 53 (32), 41 (100). HRMS ($APCI^+$): calcd. for $C_{14}H_{23}O_2$ [MH^+] 225.18491, found 225.15489.

[(1*R*,2*R*,5*R*)-1-Allyl-2-isopropyl-5-methylcyclopentyl]methanol (14): To a solution of **13** (0.172 g, 0.77 mmol, 1.0 equiv.) in dry THF (15 mL) was added $LiAlH_4$ (0.018 g, 0.47 mmol, 0.6 equiv.). After stirring the mixture under reflux for 2 h, the reaction was quenched with water, the mixture extracted with diethyl ether, dried with $MgSO_4$, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 5:1) to give **14** (0.145 g, 0.74 mmol, 96%) as a colorless oil. R_f = 0.47; *I* = 1476. $[a]_D^{25}$ = –4.3 (*c* = 0.18, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 5.85 (dddd, $^3J_{H,H}$ = 17.1, $^3J_{H,H}$ = 10.0, $^3J_{H,H}$ = 7.7, $^3J_{H,H}$ = 7.2 Hz, 1 H, CH, 8-H), 5.07 [ddt, $^3J_{H,H}$ = 10.1, $^2J_{H,H}$ = 2.3, $^4J_{H,H}$ = 0.9 Hz, 1 H, CH_2, (*E*) 9-H], 5.03 [ddt, $^3J_{H,H}$ = 17.0, $^2J_{H,H}$ = 2.3, $^4J_{H,H}$ = 1.4 Hz, 1 H, CH_2, (*Z*) 9-H], 3.64 (d, $^2J_{H,H}$ = 11.5, $^1J_{C,H}$ = 140.2 Hz, 1 H, CH_2, 6-H), 3.58 (d, $^2J_{H,H}$ = 11.5, $^1J_{C,H}$ = 140.3 Hz, 1 H, CH_2, 6-H), 2.23 (dd, $^2J_{H,H}$ = 14.2, $^3J_{H,H}$ = 7.1 Hz, 1 H, CH_2, 7-H), 2.14 (dd, $^2J_{H,H}$ = 14.2, $^3J_{H,H}$ = 7.9 Hz, 1 H, CH_2, 7-H), 1.89 – 1.82 (m, 1 H, CH, 5-H), 1.80 – 1.69 (m, 3 H, 1× CH, 2× CH_2, 3-H, 4-H, 11-H), 1.53 – 1.49 (m, 1 H, CH, 2-H), 1.46 – 1.39 (m, 1 H, CH_2, 3-H), 1.35 – 1.25 (m, 1 H, CH_2, 4-H), 1.20 (s,

1 H, OH), 1.03 (d, $^3J_{H,H}$ = 6.7, $^1J_{C,H}$ = 124.4 Hz, 3 H, CH_3, 10-H), 0.97 (d, $^3J_{H,H}$ = 7.0, $^1J_{C,H}$ = 124.4 Hz, 3 H, CH_3, 13-H), 0.90 (d, $^3J_{H,H}$ = 6.6, $^1J_{C,H}$ = 124.7 Hz, 3 H, CH_3, 12-H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 135.0 (CH, C-8), 117.5 (CH_2, C-9), 64.6 (CH_2, C-6), 51.0 (CH, C-2), 49.6 (C_q, C-1), 40.2 (CH, C-5), 37.3 (CH_2, C-7), 30.3 (CH_2, C-4), 29.8 (CH, C-11), 27.4 (CH_2, C-3), 23.2 (CH_3, C-12), 22.6 (CH_3, C-10), 14.6 (CH_3, C-13) ppm. IR (ATR): $\tilde{\nu}$ = 3403, 3075, 2951, 2871, 1638, 1461, 1380, 1366, 1035, 1028, 997, 911, 713, 534 cm^{-1}. MS (EI): *m*/*z* (%) = 165 (10), 155 (4), 137 (61), 123 (27), 109 (35), 107 (14), 95 (79), 93 (32), 81 (100), 79 (44), 69 (49), 67 (42), 57 (21), 55 (61), 53 (22), 41 (91). HRMS (APCI$^+$): calcd. for $C_{13}H_{25}O$ [MH$^+$] 197.18999, found 197.18991.

[(1*R*,2*R*,5*R*)-1-Allyl-2-isopropyl-5-methylcyclopentyl]methyl Methanesulfonate (15): To a solution of **14** (4.06 g, 20.7 mmol, 1.0 equiv.) and methanesulfonyl chloride (2.97 g, 25.9 mol, 1.2 equiv.) in dry CH_2Cl_2 (125 mL) was added triethylamine (5.30 g, 52.4 mmol, 2.5 equiv.) at –10 °C. After stirring at –10 °C for 2 h, the reaction was quenched with a saturated aqueous $NaHCO_3$ solution, the mixture extracted with CH_2Cl_2, dried with $MgSO_4$, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 5:1) to give **15** (5.45 g, 19.9 mmol, 96%) as a colorless oil. R_f = 0.34; *I* = 1855. $[\alpha]_D^{23}$ = –9.3 (*c* = 0.18, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 5.81 (dddd, $^3J_{H,H}$ = 17.0, $^3J_{H,H}$ = 10.1, $^3J_{H,H}$ = 7.8, $^3J_{H,H}$ = 7.0 Hz, 1 H, CH, 9-H), 5.12 [ddt, $^3J_{H,H}$ = 10.1, $^2J_{H,H}$ = 2.2, $^4J_{H,H}$ = 0.9 Hz, 1 H, CH_2, (*E*) 10-H], 5.07 [ddt, $^3J_{H,H}$ = 16.9, $^2J_{H,H}$ = 2.2, $^4J_{H,H}$ = 1.4 Hz, 1 H, CH_2, (*Z*) 10-H], 4.14 (d, $^2J_{H,H}$ = 9.8, $^1J_{C,H}$ = 148.5 Hz, 1 H, CH_2, 6-H), 4.12 (d, $^2J_{H,H}$ = 9.7, $^1J_{C,H}$ = 148.4 Hz, 1 H, CH_2, 6-H), 3.01 (s, $^1J_{C,H}$ = 138.7 Hz, 3 H, CH_3, 7-H), 2.32 (ddt, $^2J_{H,H}$ = 14.3, $^3J_{H,H}$ = 7.0, $^4J_{H,H}$ = 1.1 Hz, 1 H, CH_2, 8-H), 2.20 (ddt, $^2J_{H,H}$ = 14.3, $^3J_{H,H}$ = 7.9, $^4J_{H,H}$ = 1.0 Hz, 1 H, CH_2, 8-H), 1.93 (ddq, $^3J_{H,H}$ = 10.9, $^3J_{H,H}$ = 8.8, $^3J_{H,H}$ = 7.1 Hz, 1 H, CH, 5-H), 1.84 – 1.74 (m, 2 H, 2× CH_2, 3-H, 4-H), 1.71 (dsept., $^3J_{H,H}$ = 8.4, $^3J_{H,H}$ = 6.6 Hz, 1 H, CH, 12-H), 1.62 – 1.55 (m, 1 H, CH, 2-H), 1.45 – 1.37 (m, 1 H, CH_2, 3-H), 1.33 – 1.25 (m, 1 H, CH_2, 4-H), 1.04 (d, $^3J_{H,H}$ = 6.7, $^1J_{C,H}$ = 124.4 Hz, 3 H, CH_3, 11-H), 0.95 (d, $^3J_{H,H}$ = 7.1, $^1J_{C,H}$ = 125.0 Hz, 3 H, CH_3, 14-H), 0.89 (d, $^3J_{H,H}$ = 6.5, $^1J_{C,H}$ = 126.7 Hz, 3 H, CH_3, 13-H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 133.5 (CH, C-9), 118.6 (CH_2, C-10), 70.5 (CH_2, C-6), 50.9 (CH, C-2), 48.5 (C_q, C-1), 40.2 (CH, C-5), 37.2 (CH_3, C-7), 36.9 (CH_2, C-8), 29.71 (CH_2, C-4), 29.67 (CH, C-12), 27.2 (CH_2, C-3), 22.9 (CH_3, C-11), 22.7 (CH_3, C-13), 14.2 (CH_3, C-14) ppm. IR (ATR): $\tilde{\nu}$ = 3076, 2954, 2874, 1473, 1463, 1353, 1335, 1173, 948, 921, 836, 752 cm^{-1}. MS (EI): *m*/*z* (%) = 178 (3), 165 (11), 137 (61), 121 (23), 107 (27), 95 (72), 93 (56), 81 (74), 79 (100), 69 (32), 67 (43), 65 (14), 55 (50), 53 (20). HRMS (ESI$^+$): calcd. for $C_{14}H_{26}NaO_3S$ [MNa$^+$] 297.14949, found 297.14960.

2-[(1*R*,2*R*,5*R*)-1-Allyl-2-isopropyl-5-methylcyclopentyl]acetonitrile (16): A suspension of **15** (1.072 g, 3.88 mmol, 1.0 equiv.) and NaCN (2.852 g, 58.20 mmol, 15.0 equiv.) in dry hexamethylphosphoramide (50 mL) was stirred at 110 °C for 7 d. The reaction was quenched with a saturated aqueous $NaHCO_3$ solution, the mixture extracted with hexane, dried with $MgSO_4$, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 5:1) to give **16** (0.679 g, 3.31 mmol, 85%) as a colorless oil. R_f = 0.58; *I* = 1574. $[\alpha]_D^{23}$ = –15.8 (*c* = 0.14, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 5.80 (dddd, $^3J_{H,H}$ = 17.0, $^3J_{H,H}$ = 10.1, $^3J_{H,H}$ = 7.9, $^3J_{H,H}$ = 6.9 Hz, 1 H, CH, 9-H), 5.13 [ddt, $^3J_{H,H}$ = 10.2, $^2J_{H,H}$ = 2.1, $^4J_{H,H}$ = 0.9 Hz, 1 H, CH_2, (*E*) 10-H], 5.10 [ddt, $^3J_{H,H}$ = 16.9, $^2J_{H,H}$ = 2.1, $^4J_{H,H}$ = 1.4 Hz, 1 H, CH_2, (*Z*) 10-H], 2.44 (ddt, $^2J_{H,H}$ = 14.3, $^3J_{H,H}$ = 6.9, $^4J_{H,H}$ = 1.0 Hz, 1 H, CH_2, 8-H), 2.34 (ddt, $^2J_{H,H}$ = 14.3, $^3J_{H,H}$ = 8.0, $^4J_{H,H}$ = 1.0 Hz, 1 H, CH_2, 8-H), 2.19 (d, $^2J_{H,H}$ = 17.1 Hz, 1 H, CH_2, 6-H), 2.17 (d, $^2J_{H,H}$ = 16.8 Hz, 1 H, CH_2, 6-H), 1.93 (ddq, $^3J_{H,H}$ = 10.9, $^3J_{H,H}$ = 8.6, $^3J_{H,H}$ = 7.0 Hz, 1 H, CH, 5-H), 1.85 – 1.75 (m, 2 H, 2× CH_2, 3-H, 4-H), 1.70 (sept.d, $^3J_{H,H}$ = 6.6, $^3J_{H,H}$ = 1.6 Hz, 1 H, CH, 12-H), 1.58 (dt, $^3J_{H,H}$ = 10.6, $^3J_{H,H}$ = 8.5 Hz, 1 H, CH, 2-H), 1.44 – 1.36 (m, 1 H, CH_2, 3-H), 1.32 – 1.24 (m, 1 H, CH_2, 4-H), 1.06 (d, $^3J_{H,H}$ = 6.6, $^1J_{C,H}$ = 124.7 Hz, 3 H, CH_3, 11-H), 0.97 (d, $^3J_{H,H}$ = 7.0, $^1J_{C,H}$ = 124.7 Hz, 3 H, CH_3, 14-H), 0.91 (d, $^3J_{H,H}$ = 6.5, $^1J_{C,H}$ = 125.1 Hz, 3 H, CH_3, 13-H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 133.1 (CH, C-9), 119.7 (C_q, C-7), 118.9 (CH_2, C-10), 51.1 (CH, C-2), 47.8 (C_q, C-1), 40.6 (CH, C-5), 39.6 (CH_2, C-8), 29.6 (CH, C-12), 28.9 (CH_2, C-4), 26.4 (CH_2, C-3), 22.9 (CH_3, C-11), 22.6 (CH_3, C-13), 18.2 (CH_2, C-6), 14.1 (CH_3, C-14) ppm. IR (ATR): $\tilde{\nu}$ = 3077, 2956, 2875, 2242, 1639, 1468, 1420, 1384, 1367, 995, 916 cm^{-1}. MS (EI): *m*/*z* (%) = 205 (1) [M$^+$], 190 (17), 176 (3), 164 (50), 148 (18), 134 (6), 123 (100), 120 (61), 107 (30), 95 (48), 93 (34), 81 (62), 79 (71), 69 (37), 67 (33), 65 (17), 55 (36), 53 (24), 41 (80). HRMS (APCI$^+$): calcd. for $C_{14}H_{24}N$ [MH$^+$] 206.19033, found 206.19046.

2-[(1*R*,2*R*,5*R*)-1-Allyl-2-isopropyl-5-methylcyclopentyl]acetaldehyde (17): To a solution of **16** (0.679 g, 3.31 mmol, 1.0 equiv.) in dry Et_2O (40 mL) was added D*i*BAL-H (1 M in toluene, 8.5 mL, 8.50 mmol, 2.6 equiv.) at –78 °C. After stirring at –78 °C for 2 h, the mixture was warmed to 0 °C and quenched with MeOH and water, the mixture extracted with Et_2O, dried with $MgSO_4$, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 10:1) to give **17** (0.559 g, 2.69 mmol, 81%) as a colorless oil. Due to its instability this compound was immediately used in the next step. R_f = 0.47; *I* = 1534. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.98 (t, $^3J_{H,H}$ = 3.4, $^1J_{C,H}$ = 170.8 Hz, 1 H, CH), 5.88 (dddd, $^2J_{H,H}$ = 17.0, $^3J_{H,H}$ = 10.1, $^3J_{H,H}$ = 7.9, $^3J_{H,H}$ = 6.9, $^1J_{C,H}$ = 151.4 Hz, 1 H, CH), 5.12 – 5.03 (m, 2 H, CH_2), 2.50 (ddt, $^2J_{H,H}$ = 14.3, $^3J_{H,H}$ = 6.9, $^4J_{H,H}$ = 1.1 Hz, 1 H, CH_2), 2.38 (ddt, $^2J_{H,H}$ = 14.3, $^3J_{H,H}$ = 7.9, $^4J_{H,H}$ = 0.9 Hz, 1 H, CH_2), 2.27 (dd, $^2J_{H,H}$ = 14.8, $^3J_{H,H}$ = 3.5 Hz, 1 H, CH_2), 2.24 (dd, $^2J_{H,H}$ = 14.8, $^3J_{H,H}$ = 3.3 Hz, 1 H, CH_2), 1.97 – 1.87 (m, 1 H, CH_2), 1.86 – 1.71 (m, 2 H, CH, CH_2), 1.66 – 1.52 (m, 2 H, 2× CH), 1.31 – 1.11 (m, 2 H, 2× CH_2), 1.03 (d, $^3J_{H,H}$ = 6.4 Hz, 3 H, CH_3), 0.90 (d, $^3J_{H,H}$ = 6.9 Hz, 3 H, CH_3), 0.89 (d, $^3J_{H,H}$ = 6.3 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 204.1 (CH), 134.0 (CH), 118.2 (CH_2), 51.7 (CH), 49.8 (C_q), 45.7 (CH_2), 41.0 (CH), 40.0 (CH_2), 30.1 (CH), 29.2 (CH_2), 27.0 (CH_2), 22.7 (CH_3), 22.6 (CH_3), 14.5 (CH_3) ppm. IR (ATR): $\tilde{\nu}$ = 3076, 2953, 2874, 2740, 1714, 1468, 1414, 1382, 997, 913 cm^{-1}. MS (EI): *m*/*z* (%) = 208 (2) [M$^+$], 193 (3), 190 (3), 164 (28), 149 (46), 137 (9), 123 (100), 121 (41), 109 (18), 107 (27), 105 (20), 95 (44), 93 (51), 81 (58), 79 (53), 67 (41), 55 (45), 53 (21), 41 (86). HRMS (APCI$^+$): calcd. for $C_{14}H_{25}O$ [MH$^+$] 209.18999, found 209.19064.

(*S*)-1-[(1*R*,2*R*,5*R*)-1-Allyl-2-isopropyl-5-methylcyclopentyl]-3-methylbut-3-en-2-ol (18a) and (*R*)-1-[(1*R*,2*R*,5*R*)-1-Allyl-2-isopropyl-5-methylcyclopentyl]-3-methylbut-3-en-2-ol (18b): To a solution of **17** (0.199 g, 0.957 mmol) in dry THF (1 mL) was added a solution of $CeCl_3$·2LiCl (0.33 M in THF, 3.0 mL, 1.000 mmol, freshly prepared as described in ref.[21]). After stirring at room temperature for 1 h, isopropenylmagnesium bromide (0.5 M in THF, 2.2 mL, 1.100 mmol) was added to the reaction mixture at 0 °C, and the stirring was continued at 0 °C for 2 h, and at room temperature overnight. The reaction was quenched with a saturated aqueous NH_4Cl solution, the mixture extracted with Et_2O, dried with $MgSO_4$, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 10:1) to give **18a** (0.062 g, 0.248 mmol, 26%) and **18b** (0.042 g, 0.168 mmol, 18%) as colorless oils. **18a**: R_f = 0.38; *I* = 1716. $[\alpha]_D^{23}$ = –16.7 (*c* = 0.20, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.89

(dddd, $^2J_{H,H}$ = 16.9, $^3J_{H,H}$ = 10.3, $^3J_{H,H}$ = 8.0, $^3J_{H,H}$ = 6.7 Hz, 1 H, CH, 12-H), 5.07 – 5.01 (m, 2 H, CH_2, 13-H), 4.93 – 4.92 (m, 1 H, CH_2, 9-H), 4.76 – 4.75 (m, 1 H, CH_2, 9-H), 4.35 (dd, $^3J_{H,H}$ = 6.8, $^3J_{H,H}$ = 2.7 Hz, 1 H, CH, 7-H), 2.62 (dd, $^2J_{H,H}$ = 14.5, $^3J_{H,H}$ = 6.7 Hz, 1 H, CH_2, 11-H), 2.35 (dd, $^2J_{H,H}$ = 14.5, $^3J_{H,H}$ = 8.1 Hz, 1 H, CH_2, 11-H), 1.89 – 1.79 (m, 1 H, CH, 5-H), 1.78 (t, $^4J_{H,H}$ = 1.0 Hz, 3 H, CH_3, 10-H), 1.77 – 1.59 (m, 3 H, CH, 2× CH_2, 3-H, 4-H,15-H), 1.51 – 1.41 (m, 2 H, CH_2, 6-H), 1.39 (br. s, 1 H, OH), 1.28 – 1.14 (m, 2 H, 2× CH_2, 3-H, 4-H), 1.04 (d, $^3J_{H,H}$ = 6.7 Hz, 3 H, CH_3, 14-H), 0.91 (d, $^3J_{H,H}$ = 7.0 Hz, 3 H, CH_3, 17-H), 0.88 (d, $^3J_{H,H}$ = 6.6 Hz, 3 H, CH_3, 16-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.7 (C_q, C-8), 135.7 (CH, C-12), 117.2 (CH_2, C-13), 110.2 (CH_2, C-9), 73.3 (CH, C-7), 51.7 (CH, C-2), 47.4 (C_q, C-1), 41.2 (CH, C-5), 37.9 (CH_2, C-11), 34.8 (CH_2, C-6), 30.0 (CH, C-15), 29.1 (CH_2, C-4), 26.9 (CH_2, C-3), 22.9 (CH_3, C-16), 22.4 (CH_3, C-14), 17.6 (CH_3, C-10), 14.8 (CH_3, C-17) ppm. IR (ATR): $\tilde{\nu}$ = 3458, 3073, 2950, 2871, 1638, 1463, 1371, 1049, 1030, 997, 903, 536 cm^{-1}. MS (EI): *m*/*z* (%) = 232 (37), 217 (23), 204 (4), 189 (100), 175 (14), 164 (15), 161 (24), 147 (55), 145 (14), 143 (4), 136 (14), 135 (66), 133 (59), 131 (18), 128 (10), 121 (65), 119 (56), 117 (22), 109 (50), 107 (71), 105 (90), 95 (64), 93 (70), 91 (90), 81 (63), 79 (57), 69 (56), 67 (36), 65 (16), 55 (49), 53 (20), 41 (78). HRMS (APCI$^+$): calcd. for $C_{17}H_{29}$ [$MH^+ - H_2O$] 233.22638, found 233.22645. **18b**: R_f = 0.34; *I* = 1710. $[\alpha]_D^{23}$ = 12.0 (*c* = 0.21, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.87 (dddd, $^2J_{H,H}$ = 16.9, $^3J_{H,H}$ = 10.3, $^3J_{H,H}$ = 8.1, $^3J_{H,H}$ = 6.6, $^1J_{C,H}$ = 150.6 Hz, 1 H, CH, 12-H), 5.07 – 5.00 (m, 2 H, CH_2, 13-H), 4.94 – 4.93 (m, 1 H, CH_2, 9-H), 4.78 – 4.77 (m, 1 H, CH_2, 9-H), 4.39 – 4.35 (m, 1 H, CH, 7-H), 2.53 (dd, $^2J_{H,H}$ = 14.5, $^3J_{H,H}$ = 6.7 Hz, 1 H, CH_2, 11-H), 2.31 (dd, $^2J_{H,H}$ = 14.5, $^3J_{H,H}$ = 8.1 Hz, 1 H, CH_2, 11-H), 1.83 – 1.75 (m, 1 H, CH, 5-H), 1.78 (dd, $^4J_{H,H}$ = 1.4, $^4J_{H,H}$ = 0.9 Hz, 3 H, CH_3, 10-H), 1.77 – 1.59 (m, 3 H, CH, 2× CH_2, 3-H, 4-H, 15-H), 1.52 – 1.32 (m, 3 H, CH, CH_2, 2-H, 6-H), 1.30 – 1.12 (m, 2 H, 2× CH_2, 3-H, 4-H), 1.07 (d, $^3J_{H,H}$ = 6.6 Hz, 3 H, CH_3, 14-H), 0.91 (d, $^3J_{H,H}$ = 6.9 Hz, 3 H, CH_3, 17-H), 0.87 (d, $^3J_{H,H}$ = 6.5 Hz, 3 H, CH_3, 16-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.8 (C_q, C-8), 135.4 (CH, C-12), 117.3 (CH_2, C-13), 110.4 (CH_2, C-9), 73.4 (CH, C-7), 52.1 (CH, C-2), 47.6 (C_q, C-1), 41.3 (CH, C-5), 38.3 (CH_2, C-11), 34.7 (CH_2, C-6), 30.2 (CH, C-15), 28.8 (CH_2, C-4), 26.9 (CH_2, C-3), 23.1 (CH_3, C-16), 22.9 (CH_3, C-14), 17.5 (CH_3, C-10), 13.8 (CH_3, C-17) ppm. IR (ATR): $\tilde{\nu}$ = 3408, 3073, 2950, 2871, 1638, 1465, 1378, 1095, 1054, 997, 899, 562, 543 cm^{-1}. MS (EI): *m*/*z* (%) = 232 (28), 217 (20), 204 (3), 189 (79), 187 (9), 175 (13), 173 (5), 163 (10), 161 (22), 159 (8), 153 (3), 147 (52), 145 (19), 143 (7), 136 (12), 135 (52), 133 (56), 131 (23), 128 (14), 121 (58), 119 (56), 117 (24), 109 (44), 107 (67), 105 (94), 95 (61), 93 (69), 91 (100), 81 (64), 79 (62), 69 (63), 67 (40), 65 (19), 55 (58), 53 (24), 41 (99). HRMS (APCI$^+$): calcd. for $C_{17}H_{29}$ [$MH^+ - H_2O$] 233.22638, found 233.22657.

***ent*-Trichoacorenol (*ent*-3a):** A solution of **18a** (0.056 g, 0.22 mmol, 1.0 equiv.) and Grubbs–Hoveyda II catalyst (0.011 g, 7.5 mol-%) in dry CH_2Cl_2 (25 mL) was stirred at room temperature for 12 h. The reaction mixture was concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 10:1) to give *ent*-**3a** (0.039 g, 0.18 mmol, 82%) as a colorless oil. R_f = 0.19; *I* = 1706. $[\alpha]_D^{17}$ = +5.5 (*c* = 0.12, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.49 – 5.45 (m, 1 H, CH, 5-H), 4.28 (m, 1 H, CH, 3-H), 2.17 – 2.09 (m, 1 H, CH_2, 6-H), 1.82 – 1.53 (m, 6 H, 2× CH, 4× CH_2, 2-H, 6-H, 8-H, 9-H, 10-H, 13-H), 1.78 (s, 3 H, CH_3, 11-H), 1.48 (br. s, 1 H, OH), 1.47 – 1.37 (m, 1 H, CH_2, 8-H), 1.28 – 1.12 (m, 3 H, CH, 2× CH_2, 2-H, 7-H, 9-H), 0.91 (d, $^3J_{H,H}$ = 6.6, $^1J_{C,H}$ = 124.3 Hz, 3 H, CH_3, 12-H), 0.85 (d, $^3J_{H,H}$ = 6.5, $^1J_{C,H}$ = 124.8 Hz, 3 H, CH_3, 14-H), 0.84 (d, $^3J_{H,H}$ = 6.8, $^1J_{C,H}$ = 124.3 Hz, 3 H, CH_3, 15-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.6 (C_q, C-4), 125.1 (CH, C-5), 68.7 (CH, C-3), 59.9 (CH, C-7), 46.6 (CH, C-10), 45.0 (C_q, C-1), 35.3 (CH_2, C-6), 32.3 (CH_2, C-2), 30.2 (CH, C-13), 28.9 (CH_2, C-9), 26.5 (CH_2, C-8), 23.4 (CH_3, C-12), 23.0 (CH_3, C-14), 19.0 (CH_3, C-11), 14.2 (CH_3, C-15) ppm. IR (ATR): $\tilde{\nu}$ = 3257, 2946, 2868, 2425, 1462, 1432, 1367, 1333, 1308, 1038, 965, 924, 834, 791, 753, 713, 547 cm^{-1}. MS (EI): *m*/*z* (%) = 222 (48) [M^+], 207 (10), 189 (3), 179 (31), 166 (27), 161 (21), 151 (100), 138 (96), 137 (31), 133 (9), 123 (33), 119 (33), 111 (22), 109 (68), 107 (23), 105 (40), 95 (66), 91 (44), 84 (87), 81 (44), 69 (36), 67 (29), 55 (52), 53 (20), 43 (51), 41 (69). HRMS (APCI$^+$): calcd. for $C_{17}H_{29}$ [$MH^+ - H_2O$] 205.19508, found 205.19513.

***ent-epi*-Trichoacorenol (*ent*-3b):** A solution of **18b** (0.062 g, 0.25 mmol, 1.0 equiv.) and Grubbs–Hoveyda II catalyst (0.012 g, 7.5 mol-%) in dry CH_2Cl_2 (25 mL) was stirred at room temperature for 12 h. The reaction mixture was concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 10:1) to give *ent*-**3b** (0.042 g, 0.19 mmol, 76%) as a colorless oil. R_f = 0.15; *I* = 1721. $[\alpha]_D^{26}$ = 19.9 (*c* = 0.25, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.47 – 5.44 (m, 1 H, CH, 5-H), 4.30 – 4.27 (m, 1 H, CH, 3-H), 2.33 – 2.27 (m, 1 H, CH_2, 6-H), 1.99 (ddd, $^2J_{H,H}$ = 13.2, $^3J_{H,H}$ = 6.3, $^4J_{H,H}$ = 1.7 Hz, 1 H, CH, 2-H), 1.78 – 1.59 (m, 5 H, 2× CH, 3× CH_2, 6-H, 8-H, 9-H, 10-H, 13-H), 1.75 (dd, $^4J_{H,H}$ = 2.6, $^4J_{H,H}$ = 1.1 Hz, 3 H, CH_3, 11-H), 1.48 (br. s, 1 H, OH), 1.44 (dd, $^2J_{H,H}$ = 13.2, $^3J_{H,H}$ = 9.9 Hz, 1 H, CH_2, 2-H), 1.42 – 1.23 (m, 3 H, CH, 2× CH_2, 7-H, 8-H, 9-H), 0.95 (d, $^3J_{H,H}$ = 6.7, $^1J_{C,H}$ = 124.4 Hz, 3 H, CH_3, 12-H), 0.93 (d, $^3J_{H,H}$ = 7.1, $^1J_{C,H}$ = 124.3 Hz, 3 H, CH_3, 15-H), 0.87 (d, $^3J_{H,H}$ = 6.6, $^1J_{C,H}$ = 124.5 Hz, 3 H, CH_3, 14-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.1 (C_q, C-4), 124.6 (CH, C-5), 69.2 (CH, C-3), 57.0 (CH, C-7), 46.3 (C_q, C-1), 46.2 (CH, C-10), 38.1 (CH_2, C-6), 34.3 (CH_2, C-2), 30.7 (CH_2, C-9), 29.1 (CH, C-13), 26.2 (CH_2, C-8), 23.7 (CH_3, C-12), 21.9 (CH_3, C-14), 19.0 (CH_3, C-11), 16.4 (CH_3, C-15) ppm. IR (ATR): $\tilde{\nu}$ = 3312, 2948, 2870, 1453, 1368, 1303, 1271, 1052, 1023, 932, 814 cm^{-1}. MS (EI): *m*/*z* (%) = 222 (37) [M^+], 207 (8), 189 (3), 179 (25), 166 (22), 161 (19), 151 (100), 138 (82), 137 (26), 133 (9), 123 (30), 119 (35), 111 (20), 109 (60), 105 (41), 95 (63), 91 (48), 84 (82), 81 (45), 79 (39), 69 (38), 67 (32), 55 (58), 53 (23), 43 (66), 41 (82). HRMS (APCI$^+$): calcd. for $C_{17}H_{29}$ [$MH^+ - H_2O$] 205.19508, found 205.19502.

***ent*-Acorenone (*ent*-4):** A solution of *ent*-**3a** (0.030 g, 0.14 mmol, 1.0 equiv.) and Dess–Martin periodinane (0.076 g, 0.18 mmol, 1.3 equiv.) in CH_2Cl_2 (2 mL) was stirred at room temperature for 2 h. The reaction mixture was concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 10:1) to give *ent*-**4** (0.024 g, 0.11 mmol, 79%) as a colorless oil. Using the same procedure, a mixture of *ent*-**3a** and *ent*-**3b** was oxidized to give *ent*-**4** in similar yields. R_f = 0.39; *I* = 1722. $[\alpha]_D^{17}$ = 44.0 (*c* = 0.02, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.67 – 6.64 (m, 1 H, CH, 5-H), 2.66 (ddq, $^2J_{H,H}$ = 19.7, $^3J_{H,H}$ = 3.2, $^5J_{H,H}$ = 2.4 Hz, 1 H, CH_2, 6-H), 2.35 (d, $^2J_{H,H}$ = 16.8 Hz, 1 H, CH_2, 2-H), 2.31 (dd, $^2J_{H,H}$ = 16.8, $^4J_{H,H}$ = 0.7 Hz, 1 H, CH_2, 2-H), 2.13 (ddq, $^2J_{H,H}$ = 19.7, $^3J_{H,H}$ = 5.0, $^5J_{H,H}$ = 1.0 Hz, 1 H, CH_2, 6-H), 1.79 – 1.57 (m, 4 H, 2× CH, 2× CH_2, 8-H, 9-H, 10-H, 13-H), 1.77 – 1.76 (m, 3 H, CH_3, 11-H), 1.47 – 1.23 (m, 3 H, CH, 2× CH_2, 7-H, 8-H, 9-H), 0.97 (d, $^3J_{H,H}$ = 6.7 Hz, 3 H, CH_3, 12-H), 0.86 (d, $^3J_{H,H}$ = 6.6 Hz, 3 H, CH_3, 15-H), 0.83 (d, $^3J_{H,H}$ = 6.5 Hz, 3 H, CH_3, 14-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.7 (C_q, C-3), 144.8 (CH, C-5), 134.7 (C_q, C-4), 56.8 (CH, C-7), 47.9 (C_q, C-1), 47.3 (CH, C-10), 38.7 (CH_2, C-6), 37.7 (CH_2, C-2), 29.9 (CH_2, C-9), 29.1 (CH, C-13), 25.5 (CH_2, C-8), 24.0 (CH_3, C-12), 21.7 (CH_3, C-14), 16.3 (CH_3, C-11), 15.7 (CH_3, C-15) ppm. IR (ATR): $\tilde{\nu}$ = 2953, 2872, 1671, 1453, 1430, 1366, 1244, 1118, 1092,

924 cm^{-1}. UV (CH_2Cl_2): λ_{max} (ε) = 240 (7350 $L\,mol^{-1}\,cm^{-1}$) nm. MS (EI): *m*/*z* (%) = 220 (36) [M^+], 205 (13), 191 (11), 177 (46), 164 (24), 163 (16), 159 (5), 150 (60), 149 (34), 135 (93), 133 (6), 121 (61), 109 (100), 107 (53), 105 (21), 95 (24), 93 (63), 91 (63), 82 (86), 79 (49), 69 (25), 67 (23), 55 (33), 53 (25), 41 (57). HRMS (APCI$^+$): calcd. for $C_{15}H_{25}O$ [MH^+] 221.18999, found 221.18989.

Supporting Information (see footnote on the first page of this article): Schematic experimental setup of a closed-loop stripping apparatus and copies of the ^1H and ^{13}C NMR spectra of all synthetic compounds.

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