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Total Synthesis and Structure Revision of (–)-Avicennone C

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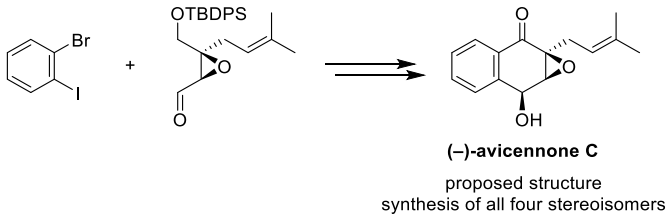
Supporting Information Placeholder



ABSTRACT: All four possible stereoisomers of the natural product (–)-avicennone C were synthesized using two different methods for ring closure. The absolute stereochemistry was elucidated unambiguously by comparison of the analytical data with those of the reported natural product and by single X-ray crystal diffraction of synthetic intermediates. The proposed structure needed to be revised with regard to the absolute configuration of the stereogenic center bearing the secondary hydroxyl group. The reported synthesis offers a flexible, selective, and efficient access to all possible stereoisomers and may be of value for the stereoselective synthesis of other epoxyquinone natural products.

INTRODUCTION

Epoxyquinone natural products (NPs)[1] such as (+)-ambuic acid (**1**), (–)-jesterone (**2**), and (–)-cycloepoxydon (**3**) (Figure 1) display promising biological activities and have attracted interest due to their structural novelty. (+)-Ambuic acid[2], which shows antimicrobial activity[3], and (–)-jesterone[4], possessing antimycotic activity, were isolated from the fungus *Pestalotiopsis* spp. (–)-Cycloepoxydon[5], inhibiting the activation of the transcription factor NF-kB, was obtained from a Deuteromycete strain.

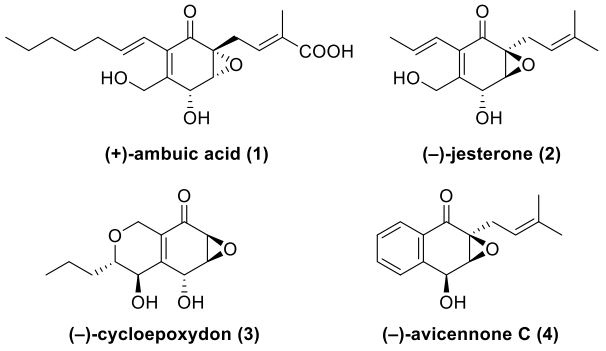
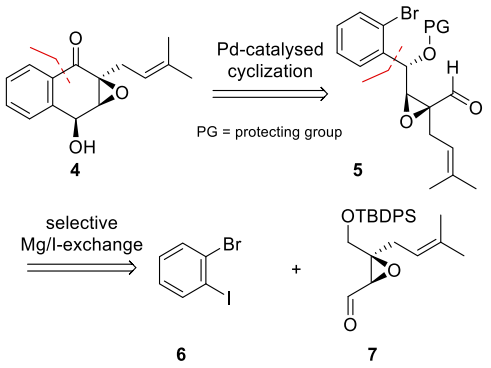


Figure 1. **Selected epoxyquinone NPs.**

For epoxyquinone NPs, elucidation of the absolute stereochemistry has shown no clear preference for one specific stereoisomer. Since challenging total syntheses are required in most cases to unambiguously determine the absolute stereoconfiguration, a flexible, selective, and efficient synthetic pathway to all possible stereoisomers would be desirable.[6] We chose (–)-avicennone C (**4**)[7,8] as model system, because in contrast to the compounds **1**, **2**, and **3** neither biological activities nor a total synthesis have been reported. Avicennone C was isolated from mangrove tree *Avicennia marina* and its absolute stereochemistry was proposed based on NMR and CD data as well as molecular modeling by Sattler and Lin *et al*.[7]

Scheme 1. **Retrosynthetic analysis.**

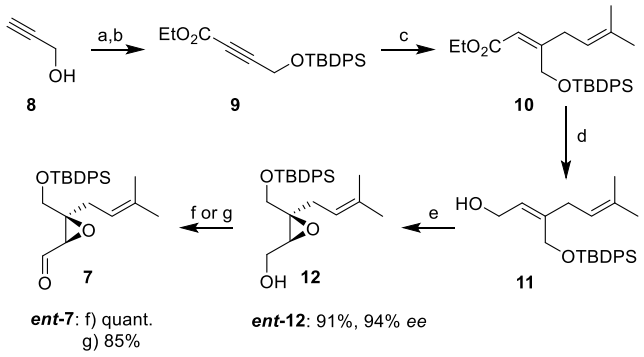


Our retrosynthetic analysis of **4** led to a final disconnection between the ketone and the aryl moiety (Scheme 1). For the ring closure we envisaged a palladium-catalyzed intramolecular cyclization similar to a published method of Muratake *et al*.[9] Aldehyde **5** should be accessible by addition of a Grignard reagent derived from 1-bromo-2-iodobenzene (**6**) to the highly functionalized epoxy aldehyde **7**[10], followed by protecting group manipulations and oxidation.

RESULTS AND DISCUSSION

Synthesis of epoxy aldehyde **7** (Scheme 2) was performed analogously to a described reaction sequence from Barrett *et al*.[10] The use of a prenyl cuprate, generated from freshly prepared prenyl Grignard reagent[11], represents the significant difference. Key feature of this sequence is the stereoselective formation of the epoxide *via* Sharpless epoxidation.[12] Both enantiomers **7** and ***ent*-7** were obtained in excellent yields and enantiomeric excesses (*ee*) over six steps on a 4–5 gram scale. The final oxidation was performed either under Swern conditions without further purification or with Dess–Martin periodinane (DMP) followed by a filtration over silica.

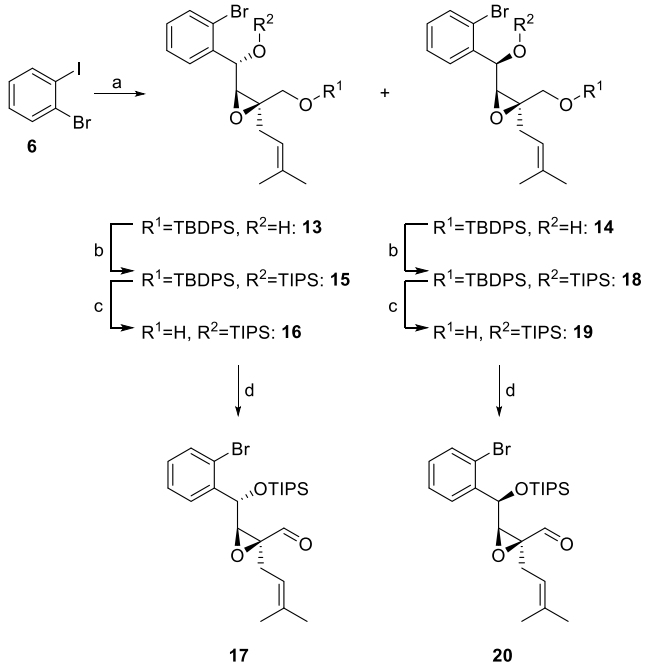
Scheme 2. **Synthesis of the epoxy aldehydes 7 and *ent*-7.[a]**



[a]Conditions: (a) TBDPSCl, imidazole, CH_2Cl_2, 99%; (b) *n*-BuLi, THF, –78 °C, 30 min; EtOCOCl, 94%; (c) CuBr·SMe_2, prenylMgCl, THF, –40 °C, 40 min; **9**, –78 °C, 90 min, 94%; (d) DIBALH, PhMe, –78 °C, 92%; (e) Ti(O*i*-Pr)$_4$, L-(+)-DET, *t*-BuOOH, 4 Å MS, CH_2Cl_2, –20 °C, 3 d, 88%, 93% *ee*; (f) $(COCl)_2$, DMSO, CH_2Cl_2, –78 °C, 15 min; **12**, –78 °C, 90 min; DIPEA, –78 °C to 0 °C, 30 min, quant. used as a crude; g) DMP, CH_2Cl_2, 76%.

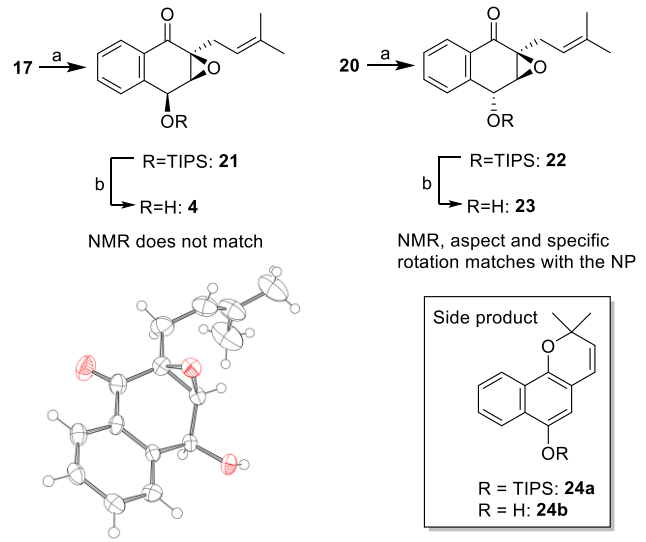
The preparation of the two diastereomeric alcohols **13** and **14** was first achieved by using 1,2-dibromobenzene and Knochel's turbo Grignard reagent.[13] However, the reaction was hampered by slow formation of the aryl Grignard reagent, incomplete conversion, side reactions, and low isolated yields. A possible explanation is the tendency of 1,2-dibrombenzene to form benzyne *via* 1,2-elimination rather than forming the desired Grignard reagent.[13] Switching to 2-bromo-1-iodobenzene (**6**) enabled complete Grignard formation with *i*-PrMgCl at low temperature and resulted in full conversion of the epoxy aldehyde **7** (Scheme 3). The resulting diastereomers were separated by careful flash chromatography and were isolated in good yields with a ratio of approx. 1:1, which could be expected from similar reactions described in literature.[14,10] The assignment of the absolute stereochemistry of **13** and **14** was only possible retrospectively by deduction from the crystal structure of **4** (Scheme 4). After TIPS protection, the envisaged selective cleavage of the TBDPS group of **15** and **18** was achieved in only moderate yields with ammonium fluoride in methanol since significant double deprotection occurred.[15] The oxidation to aldehydes **17** and **20** worked smoothly with DMP followed by a filtration over silica.

Scheme 3. **Synthesis of aldehydes 17 and 20.[a]**



[a]Conditions: (a) *i*-PrMgCl, THF, –40 °C, 45 min; **7**, –40 °C, 45 min; 42% for **13**, 42% for **14**; (b) TIPSOTf, 2,6-lutidine, CH_2Cl_2; 82% for **15**, 92% for **18**; (c) NH_4F, MeOH/THF 12:1; (d) DMP, CH_2Cl_2; 54% for **16**, 56% for **19**.

Scheme 4. **Palladium-catalyzed cyclization[a] and thermal ellipsoid plot of the molecular structure of 4.[b]**

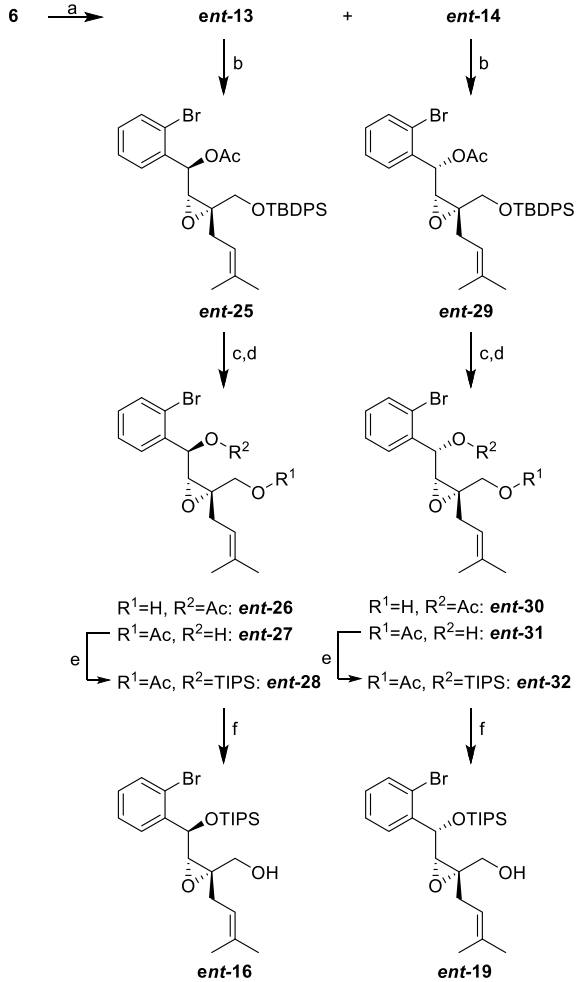


[a]Conditions: (a) $PdCl_2(PPh_3)_2$ (0.1 eq.), Cs_2CO_3, toluene, reflux[7]; 46% for **21**, 48% for **22**; (b) TBAF, HOAc, THF; 87%, 94% *ee* for **4**, 83%, 94% *ee* for **23**.[16]

[b]Thermal ellipsoid probability set to 50%, only one molecule of the asymmetric unit shown.

The final cyclization of aldehydes **17** and **20** was performed under the palladium-catalyzed conditions described by Muratake *et al*[9](Scheme 4). There are only few examples for an intramolecular palladium-catalyzed ketone synthesis by α-arylation with an aldehyde[17], whilst intermolecular couplings of this type have been reported by Xiao *et al*.[18] The conversions of **17** and **20** to the desired products **21** and **22** proceeded relatively slowly and were accompanied by side product formation. However, it was possible to isolate **21** and **22** in moderate yields contaminated with minor amounts of their double bond isomers.[19] As a side product **24a** was isolated[20] and identified as TIPS protected NP hemitectol (**24b**).[21] Final deprotection of **21** and **22** yielded **4** and its hydroxyl epimer **23** in good yields. Both stereoisomers showed very similar NOE correlations, which made it impossible to determine their relative stereochemistry. The absolute stereochemistry of compound **4** was unambiguously determined by single X-ray crystal diffraction and exhibited to be the proposed structure for NP (–)-avicennone C. However, the reported NMR spectra, aspect and specific rotation[7] of (–)-avicennone C matched with compound **23**. Therefore, our results support a revision of the reported stereochemistry of the NP (–)-avicennone C (Scheme 4).

Scheme 5. **Alternative protecting group strategy.[a]**



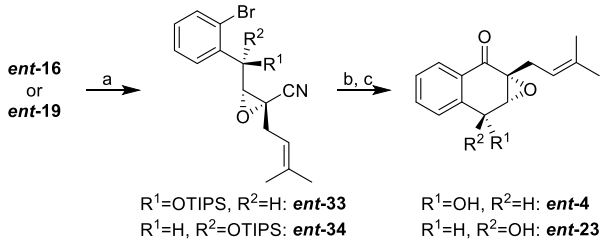
[a]Conditions: (a) *i*-PrMgCl, THF, –40 °C, 45 min; ***ent*-7**, –40 °C, 45 min; 39% for ***ent*-13**, 45% for ***ent*-14**; (b) Ac_2O, pyridine, DMAP (0.1 eq.), CH_2Cl_2; 93% for ***ent*-25**, quant. for ***ent*-29**; (c) TBAF, HOAc, THF; (d) DBU, CH_2Cl_2; 91% over two steps for ***ent*-27**/***ent*-26**[22], 94% over two steps for ***ent*-31**/***ent*-30**[22]; (e) TIPSOTf, 2,6-lutidine, CH_2Cl_2; 74% for ***ent*-28**, 74% for ***ent*-32**; (f) LiOH, THF/H_2O 5:1, 79% for ***ent*-16**, 85% for ***ent*-19**.

For the synthesis of the corresponding enantiomers a different protecting group strategy was applied in order to obtain improved yields (Scheme 5). The hydroxyl functions of ***ent*-13** and ***ent*-14**, obtained from **6** and ***ent*-7**, were acetate protected. During TBDPS deprotection of the primary hydroxyl group a partial acetate migration was observed even though the TBAF solution was buffered with acetic acid. Treatment of the prepurified mixture of regioisomers with DBU in anhydrous CH_2Cl_2 resulted in almost full conversion to compounds ***ent*-27** and ***ent*-31**.[22] ***Ent*-16** and ***ent*-19** were obtained by TIPS protection followed by saponification.

Besides final product **4**, in the entire synthetic pathways we were only able to obtain single crystals for ***ent*-32**.[23] The absolute configurations determined were in complete alignment.

For the final cyclization a different method with less side product formation, shorter reaction times, and no isomerization of the prenyl double bond would be desirable. An alternative cyclization strategy could start with a selective lithium-bromine exchange at low temperature followed by an addition of the lithium-species to a carboxylic acid[24], an ester[25], or an amide[26]. This approach requires mild oxidation of the primary hydroxyl group to the carboxylic acid and subsequent ester or amide formation. During our literature search for suitable reaction conditions a one-pot hydroxyl to nitrile oxidation procedure described by Vatéte attracted our attention.[27] The oxidation of ***ent*-16** and ***ent*-19** to the corresponding nitriles proceeded smoothly. For the lithium-bromine exchange a solution of ***ent*-33** or ***ent*-34** in anhydrous THF was cooled to –100 °C and a stoichiometric amount of *n*-BuLi solution was added. Within a few minutes complete conversion to the desired products was detected *via* LCMS and TLC. A slightly acidic aqueous work-up ensured full hydrolysis of the intermediate imines to liberate ketones ***ent*-21** and ***ent*-22**. The final products ***ent*-4** and ***ent*-23** were obtained by cleavage of the TIPS protection group (Scheme 6).

Scheme 6. **Alternative cyclization for *ent*-avicennones.[a]**

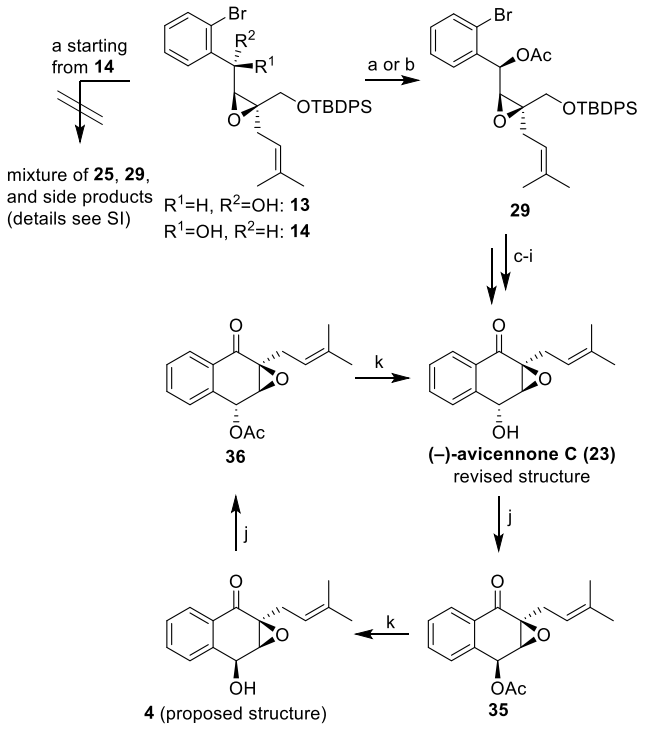


[a]Conditions: (a) TEMPO (0.2 eq.), NH_4OAc, BAIB, MeCN/H_2O 9:1; 63% for ***ent*-33**, 68% for ***ent*-34**; (b) *n*-BuLi, THF, –100 °C, 5 min; 80% for ***ent*-21**, 95% for ***ent*-22**; (c) TBAF, HOAc, THF; 79% for ***ent*-4**, 93% *ee*; 93% for ***ent*-23**, 92% *ee*.

For our goal of an efficient and flexible access to any specific stereoisomer of the epoxyquinoids, the unselective Grignard ad-

dition remained the final optimization parameter. To circumvent the loss of material due to formation of undesired stereoisomers, Mitsunobu inversions were attempted for **13** and **14**. Whilst acetate **29** was obtained in good yields and full inversion of the stereocenter from **13**, the Mitsunobu reaction of **14** resulted in a mixture of both stereoisomers **25** and **29** as well as side product formation.[28] From common intermediate **29**, (–)-avicennone C (**23**) was finalized in 7 steps with an overall yield of 31% under optimized conditions. In contrast to the failed inversion of **14**, the Mitsunobu reaction of **23** and **4** worked successfully and subsequent saponification of acetates **35** and **36** yielded the fully inverted products in good yields (Scheme 7).

Scheme 7. **Recycling strategy for undesired hydroxy isomers.**[a]



[a]Conditions: (a) for **13**: PPh_3, HOAc, DIAD, THF; 70%; (b) for **14**: Ac_2O, pyridine, DMAP (0.1 eq.), CH_2Cl_2; 97%; (c) TBAF, HOAc, THF; (d) DBU, CH_2Cl_2; 98% over two steps; (e) TIPSOTf, 2,6-lutidine, CH_2Cl_2; 66%; (f) LiOH, THF/H_2O 5:1, 85%; (g) TEMPO (0.2 eq.), NH_4OAc, BAIB, MeCN/H_2O 9:1; 69%; (h) *n*-BuLi, THF, –100 °C, 5 min; 92%; (i) TBAF, HOAc, THF; 89%; (j) PPh_3, HOAc, DIAD, THF; 90% for **35**, 73% for **36**; (k) LiOH, THF/H_2O 5:1, 90% for **4**, 93% for **23**.

CONCLUSION

We synthesized all four possible stereoisomers of avicennone C following two different pathways and revised the reported stereochemistry of (–)-avicennone C (**23**) unambiguously. Besides elegant protecting group manipulation utilizing an acetate group, the most significant synthetic achievement was realized by an alcohol to nitrile oxidation-cyclization sequence providing high yields as well as avoiding side product formation. Furthermore, a step-neutral Mitsunobu inversion approach enabled us to also recycle the undesired diastereomer **13**. Based on this concept we established a robust and scalable total synthesis route towards epoxyquinone NPs in general and provided sufficient amounts of all four avicennone C stereoisomers for follow-up biological and physico-chemical profiling, which is currently ongoing. Finally, this study demonstrates that even the structure elucidation of relatively small NPs such as (–)-avicennone C bears the risk of misassignments and emphasizes the importance of total synthesis not only for material supply and generation of analogs, but also for unambiguous structure determination.

EXPERIMENTAL SECTION

General Information. All chemicals and solvents/anhydrous solvents were commercially supplied and used without further purification. For heating of reaction mixtures, aluminium flask carriers in different sizes from IKA were used. Reactions were monitored using thin layer chromatography (TLC) or using one of the following LCMS systems: 1100 HPLC (Agilent) with DAD and ELSD equipped with MSD (Agilent) ESI quadrupole MS, 1100 HPLC (Agilent) with DAD equipped with Amazon (Bruker) ESI trap MS, 1290 UPLC (Agilent) with DAD or ELSD equipped with micrOTOF (Bruker) ESI TOF MS or 1290 UPLC (Agilent) with DAD and ELSD equipped with maXis II (Bruker) ESI TOF MS. TLC was performed on pre-coated silica gel glass plates (Merck TLC Silica gel 60 F254) and compounds were detected under UV light (254 nm) and/or by staining with an aqueous solution of $KMnO_4$ with K_2CO_3 and NaOH followed by heating with a heat gun. Products were purified by flash column chromatography using silica gel 60 M (Macherey-Nagel) or by using an automated flash column chromatography system (Biotage® SP4 with ISOLUTE® Flash SI II) equipped with ISOLUTE® Flash SI II columns of different sizes from Biotage or PF-15SIHC flash columns of different sizes from Interchim (eluants are given in parentheses). NMR spectra were recorded on a Bruker AVANCE II WB spectrometer (400 MHz), a AVANCE III HD spectrometer (400 MHz) or a AVANCE III HD spectrometer (600 MHz) with $CDCl_3$ or CD_3OD as solvent with chemical shifts (δ) quoted in parts per million (ppm) and referenced to the solvent signal ($\delta^1H/^{13}C$: $CDCl_3$ 7.26/77.1, MeOD 3.31/49.0) or TMS (δ = 0 ppm in $CDCl_3$). Assignment was confirmed based on COSY, HSQC, HMBC, and NOESY correlations. The absolute configuration of compounds **4** and ***ent*-32** was assigned by X-ray diffraction analysis (for details regarding solvent and method for crystal growth see experimental section and Supporting Information). High resolution mass spectrometry was performed on the maXis II (Bruker) ESI TOF MS. Specific rotation was measured by a polarimeter (P 3000 series) from Krüss. For SI structures with complete analytical data see Supporting Information.

Ethyl 4-[*tert*-butyl(diphenyl)silyl]oxybut-2-ynoate (9). The synthesis of **9** was performed according to literature known procedure starting from propargyl alcohol in two steps. The analytical data are in accordance to the reported data in literature.[10] **^{1}H-NMR** ($CDCl_3$, 400 MHz): 7.71–7.67 (m, 4H, aryl-*H*), 7.48–7.37 (m, 6H, aryl-*H*), 4.40 (s, 2H, alkyne-CH_2), 4.23 (q, 2H, *J* = 7.1 Hz, Me-CH_2), 1.32 (t, 3H, *J* = 7.1 Hz, CH_3), 1.06 (s, 9H, ^{t}Bu-CH_3); **^{13}C-NMR** ($CDCl_3$, 100 MHz): 153.5 (*C*=O), 135.7 (Ar-*C*), 132.5 (Ar-C_q), 130.2 (Ar-*C*), 128.0 (Ar-*C*), 85.5 (alkyne-*C*), 76.9 (alkyne-*C*), 62.1 (Me-CH_2), 52.4 (alkyne-CH_2), 26.8 (^{t}Bu-CH_3), 19.3 (^{t}Bu-C_q), 14.2 (CH_3); **HRMS (ESI)** m/z

calcd. for $C_{22}H_{26}O_3SiNa$: $(M+Na)^+$, 389.1543; found: 389.1544 $(M+Na)^+$; **R_f** (*n*-heptane/ethyl acetate 10:1): 0.38.

Ethyl (2*Z*)-3-[[*tert*-butyl(diphenyl)silyl]oxymethyl]-6-methyl-hepta-2,5-dienoate (10). The Grignard formation was performed in oven-dried glassware under argon atmosphere. To a suspension of Mg turnings (10.6 g, 437 mmol, 4.00 eq.) in anhydrous THF (28 mL) a small crystal of I_2 was added. Prenyl chloride (12.3 mL, 109 mmol, 1.00 eq.) was dissolved in anhydrous THF (185 mL) and the chloride solution was added dropwise over a period of 8 h to the reaction mixture. After 5 min stirring at room temperature the Grignard solution was cooled until the end of the addition with an ice-water bath. After complete addition of the chloride, the reaction mixture was allowed to get to room temperature and it was stirred overnight under inert atmosphere. The supernatant layer was transferred *via* cannula to an oven-dried two-neck round-bottom flask. The Grignard-solution was titrated according to a literature known procedure.[29] Cuprate addition was carried out in moisture-free glassware under inert atmosphere. To a suspension of CuBr·Me_2S (6.13 g, 29.8 mmol, 2.10 eq.) in anhydrous THF (20 mL) the Grignard solution (3.00 eq.) was added at −40 ºC. The suspension was stirred for 40 min. After this time, the mixture was cooled to −78 ºC and a solution of alkyne **9** (5.20 g, 14.2 mmol, 1.00 eq.) in anhydrous THF (20 mL) was added dropwise over a period of 30 min. The resulting mixture was stirred at −78 °C for 1 h and remaining cuprate was quenched with saturated aqueous NH_4Cl (200 mL). The mixture was extracted with Et_2O (3 x 300 mL) and the combined organic layers were washed with saturated aqueous NaCl (200 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (100% DCM) to give addition product **10** (5.84 g, 13.4 mmol, 94%) as colorless oil.
^{1}H-NMR ($CDCl_3$, 400 MHz): 7.71–7.62 (m, 4H, aryl-*H*), 7.45–7.33 (m, 6H, aryl-*H*), 5.59 (m, 1H, alkene-C*H*), 5.20 (m, 1H, Me_2C=C*H*), 4.87 (m, 2H, TBDPSO-CH_2), 4.01 (q, 2H, *J* = 7.1 Hz, Me-CH_2), 3.13 (d, 2H, *J* = 7.4 Hz, CH-CH_2), 1.75 (s, 3H, *E*-CH_3), 1.61 (s, 3H, *Z*-CH_3), 1.16 (t, 3H, *J* = 7.1 Hz, CH_2-CH_3), 1.08 (s, 9H, ^{t}Bu-CH_3); **^{13}C-NMR** ($CDCl_3$, 100 MHz): 166.4 (*C*=O), 162.0 (CH=C_q), 135.8 (Ar-*C*), 135.1 ($C_q$$Me_2$), 133.7 (Ar-$C_q$), 129.9 (Ar-*C*), 127.9 (Ar-*C*), 120.3 (*C*H=CMe_2), 114.9 (O=C-*C*H), 63.1 (TBDPSO-*C*H_2), 60.0 (Me-*C*H_2), 32.8 (CH-*C*H_2), 27.2 (^{t}Bu-*C*H_3), 26.1 (*E*-*C*H_3), 19.6 (^{t}Bu-C_q), 18.0 (*Z*-*C*H_3), 14.4 (CH_2-*C*H_3); **HRMS (ESI)** m/z calcd. for $C_{27}H_{37}O_3Si$: $(M+H)^+$, 437.2506; found: 437.2501 $(M+H)^+$; **R_f** (*n*-heptane/ethyl acetate 10:1): 0.44.

(2*Z*)-3-[[*tert*-Butyl(diphenyl)silyl]oxymethyl]-6-methyl-hepta-2,5-dien-1-ol (11). Under inert atmosphere DIBAl-H in toluene (1.20 M; 43.5 mL, 52.2 mmol, 3.90 eq.) was added slowly to ester **10** (5.84 g, 13.4 mmol, 1.00 eq.) dissolved in anhydrous toluene (140 mL) at −78 °C. The resulting mixture was stirred at this temperature for 1.5 h. Excess of DIBAL-H was quenched carefully with MeOH (6 mL) and afterwards saturated aqueous Rochelle's salt solution (140 mL) was added. The resulting suspension was left to warm up to room temperature and was stirred vigorously for 4 h. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (3 x 100 mL). The combined organic layers were washed with saturated aqueous NaCl (100 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (0–30% ethyl acetate in *n*-heptane) to give alcohol **11** (4.88 g, 12.4 mmol, 92%) as colorless oil. **^{1}H-NMR** ($CDCl_3$, 400 MHz): 7.72–7.66 (m, 4H, aryl-*H*), 7.47–7.36 (m, 6H, aryl-*H*), 5.46 (t, 1H, *J* = 6.9 Hz, alkene-C*H*), 5.13 (m, 1H, Me_2C=C*H*), 4.17 (s, 2H, TBDPSO-CH_2), 3.95 (d, 2H, *J* = 7.0 Hz, HO-CH_2), 2.84 (d, 2H, *J* = 7.2 Hz, Me_2C=CH-CH_2), 1.71 (s, 3H, *E*-CH_3), 1.60 (s, 3H, *Z*-CH_3), 1.40 (s, br, 1H, O*H*), 1.05 (s, 9H, ^{t}Bu-CH_3); **^{13}C-NMR** ($CDCl_3$, 100 MHz): 141.4 (CH=C_q), 135.8 (Ar-*C*), 133.7 ($C_q$$Me_2$ or Ar-C_q), 133.5 ($C_q$$Me_2$ or Ar-C_q), 129.9 (Ar-*C*), 127.8 (Ar-*C*), 125.7 (CH_2-*C*H=C_q), 121.5 (*C*H=CMe_2), 61.9 (TBDPSO-*C*H_2), 58.9 (HO-*C*H_2), 33.4 (Me_2C=CH-*C*H_2), 26.9 (^{t}Bu-*C*H_3), 25.9 (*E*-*C*H_3), 19.3 (^{t}Bu-C_q), 17.8 (*Z*-*C*H_3); **HRMS (ESI)** m/z calcd. for $C_{25}H_{34}O_2SiNa$: $(M+Na)^+$, 417.2220; found: 417.2214 $(M+Na)^+$; **R_f** (*n*-heptane/ethyl acetate 4:1): 0.25.

[(2*S*,3*R*)-3-[[*tert*-Butyl(diphenyl)silyl]oxymethyl]-3-(3-methylbut-2-enyl)oxiran-2-yl]methanol (12). The reaction was carried out in oven-dried glassware under argon atmosphere. To a suspension of 4 Å molecular sieve in anhydrous DCM (25 mL) L-(+)-diethyl tartrate (0.156 mL, 0.910 mmol, 0.12 eq.) and $Ti(OiPr)_4$ (0.225 mL, 0.760 mmol, 0.10 eq.) were added at −30 °C followed by addition of anhydrous *tert*-butyl hydroperoxide in dodecane (5.5 M; 2.22 mL, 12.1 mmol, 1.60 eq.). The resulting mixture was stirred carefully for 40 min. After this time, allyl alcohol **11** (3.01 g, 7.62 mmol, 1.00 eq.) dissolved in anhydrous DCM (10 mL) was added to the suspension dropwise. The resulting suspension was allowed to stay at −28 °C in the freezer for 3 days. After this time, 10% aqueous NaOH solution saturated with NaCl (30 mL) was added at −20 °C and the suspension was allowed to stir for 1.5 h at 0 °C. After filtration over a frit with Celite® (4 x 7 cm), which was flushed with DCM (500 mL), the solvent was reduced *in vacuo* to a volume of 250 mL and the residue was washed with saturated aqueous NaCl (100 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (0–40% ethyl acetate in *n*-heptane) to give epoxy alcohol **12** (2.75 g, 5.09 mmol, 88%) as colorless oil. **^{1}H-NMR** ($CDCl_3$, 400 MHz): 7.71–7.61 (m, 4H, aryl-*H*), 7.49–7.35 (m, 6H, aryl-*H*), 5.07 (m, 1H, Me_2C=C*H*), 3.82 (d, 1H, *J* = 11.0 Hz, TBDPSO-CH_2), 3.65 (t, 2H, *J* = 6.1 Hz, HO-CH_2), 3.61 (d, 1H, *J* = 11.1 Hz, TBDPSO-CH_2), 3.09 (t, 1H, *J* = 5.9 Hz, epoxy-C*H*), 2.52 (dd, 1H, *J* = 15.1, 7.5 Hz, Me_2C=CH-CH_2), 2.42 (dd, 1H, *J* = 15.0, 7.2 Hz, Me_2C=CH-CH_2), 1.89–1,79 (m, 1H, O*H*), 1.69 (s, 3H, *E*-CH_3), 1.60 (s, 3H, *Z*-CH_3), 1.07 (s, 9H, ^{t}Bu-CH_3); **^{13}C-NMR** ($CDCl_3$, 100 MHz): 135.9/135.7 (Ar-*C*), 135.4 ($C_q$$Me_2$), 133.0/132.8 (Ar-$C_q$), 130.1 (Ar-*C*), 128.0/127.9 (Ar-*C*), 117.9 (*C*H=CMe_2), 64.7 (TBDPSO-*C*H_2), 63.7 (epoxy-C_q), 61.4 (HO-*C*H_2 or epoxy-*C*H), 61.3 (HO-*C*H_2 or epoxy-*C*H), 32.0 (Me_2C=CH-*C*H_2), 27.0 (^{t}Bu-*C*H_3), 25.9 (*E*-*C*H_3), 19.4 (^{t}Bu-C_q), 18.1 (*Z*-*C*H_3); **HRMS (ESI)** m/z calcd. for $C_{25}H_{34}O_3SiNa$: $(M+Na)^+$, 433.2169; found: 433.2167 $(M+Na)^+$; **R_f** (*n*-heptane/ethyl acetate 2:1): 0.38; **Chiral HPLC** (Chiralpak IC; hexane:isopropyl alcohol 94:6): **12** (Rt = 7.2 min) : ***ent*-12** (Rt = 6.3 min) 96.3 : 3.7 (93% *ee*); **Specific rotation** $[\alpha]_D^{22.6}$ = − 7.4 (c = 1.08; $CHCl_3$).

[(2*R*,3*S*)-3-[[*tert*-Butyl(diphenyl)silyl]oxymethyl]-3-(3-methylbut-2-enyl)oxiran-2-yl]methanol (*ent*-12). ***Ent*-12** (1.18 g, 2.88 mmol, 91%) was synthesized in analogous manner with D-(-)-diethyl tartrate instead of L-(+)-diethyl tartrate. The NMR data are identical to the ones reported for **12**. **HRMS (ESI)** m/z calcd. for $C_{25}H_{34}O_3SiNa$: $(M+Na)^+$, 433.2169; found:

433.2173 $(M+Na)^+$; **R_f** (*n*-heptane/ethyl acetate 2:1): 0.38; **Chiral HPLC** (Chiralpak IC; hexane:isopropyl alcohol 94:6): ***ent*-12** (Rt = 6.6 min) : **12** (Rt = 7.7 min) 96.9 : 3.1 (94% *ee*); **Specific rotation** $[\alpha]_D^{22.6}$ = + 6.0 (c = 1.32; $CHCl_3$).

(2*R*,3*R*)-3-[[*tert*-Butyl(diphenyl)silyl]oxymethyl]-3-(3-methylbut-2-enyl)oxirane-2-carbaldehyde (7). Condition 1: Epoxy alcohol **12** (2.06 g, 5.01 mmol, 1.00 eq.) was dissolved in anhydrous DCM (30 mL) and Dess–Martin periodinane (15% in DCM, 20.8 mL, 10.0 mmol, 2.00 eq.) was added. After stirring for 4 h at room temperature, the TLC showed complete conversion of the starting material. The reaction solution was flash chromatographed (100% DCM) to give epoxy aldehyde **7** (1.56 g, 3.81 mmol, 76%) as colorless oil. Condition 2: The reaction was carried out in moisture-free glassware under inert atmosphere. To a solution of $(COCl)_2$ (0.365 mL, 4.26 mmol, 1.60 eq.) in anhydrous DCM (15 mL) anhydrous DMSO (0.605 mL, 8.52 mmol) was added carefully at −78 °C. After stirring for 15 min, epoxy alcohol **12** (1.09 g, 2.66 mmol, 1.00 eq.) dissolved in anhydrous DCM (12 mL) was added. The reaction mixture was stirred for 1.5 h at −78 °C. Then DIPEA (2.32 mL, 13.3 mmol, 5.00 eq.) was added and the solution was stirred for 30 min at −78 °C and for further 30 min without cooling bath. A mixture of cooled toluene/saturated aqueous NH_4Cl (3:1, 120 mL, pre-cooled to 0 °C) was added to the reaction mixture. The aqueous layer was separated and the organic layer was washed again with saturated aqueous NH_4Cl (3 x 30 mL, pre-cooled to 0 °C), with saturated aqueous $NaHCO_3$ (30 mL, pre-cooled to 0 °C), and with brine (30 mL, pre-cooled to 0 °C). The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure to yield epoxy aldehyde **7** (1.09 g, 1.66 mmol, quant.) as slightly yellow oil which was used in the next stage without further purification. **^{1}H-NMR** ($CDCl_3$, 400 MHz): 9.47 (d, 1H, *J* = 4.9 Hz, C*H*O), 7.72–7.61 (m, 4H, aryl-*H*), 7.49–7.36 (m, 6H, aryl-*H*), 5.03 (m, 1H, Me_2C=C*H*), 3.82 (q, 2H, *J* = 12.0 Hz, TBDPSO-CH_2), 3.25 (d, 1H, *J* = 4.6 Hz, epoxy-C*H*), 2.52 (dd, 1H, *J* = 15.1, 7.9 Hz, Me_2C=CH-CH_2), 2.35 (dd, 1H, *J* = 15.2, 6.8 Hz, Me_2C=CH-CH_2), 1.68 (s, 3H, *E*-CH_3), 1.57 (s, 3H, *Z*-CH_3), 1.04 (s, 9H, ^{t}Bu-CH_3); **^{13}C-NMR** ($CDCl_3$, 100 MHz): 198.8 (*C*HO), 136.6 ($C_q$$Me_2$), 135.7/135.7 (Ar-*C*), 132.6/132.6 (Ar-C_q), 130.1 (Ar-*C*), 128.0/128.0 (Ar-*C*), 116.8 (*C*H=CMe_2), 68.6 (epoxy-C_q), 63.3 (TBDPSO-CH_2), 62.4 (epoxy-*C*H), 31.5 (Me_2C=CH-CH_2), 26.9 (^{t}Bu-*C*H_3), 25.9 (*E*-*C*H_3), 19.3 (^{t}Bu-C_q), 18.1 (*Z*-*C*H_3); **HRMS (ESI)** m/z calcd. for $C_{25}H_{32}O_3SiNa$: $(M+Na)^+$, 431.2013; found: 431.2013 $(M+Na)^+$; **R_f** (*n*-heptane/ethyl acetate 10:1): 0.31; **Specific rotation** $[\alpha]_D^{22.6}$ = + 18.9 (c = 1.59; $CHCl_3$).

(2*S*,3*S*)-3-[[*tert*-Butyl(diphenyl)silyl]oxymethyl]-3-(3-methylbut-2-enyl)oxirane-2-carbaldehyde (*ent*-7). ***Ent*-7** (1.09 g, 2.66 mmol, quant.) was synthesized in analogous manner to condition 2 starting from ***ent*-12** (1.09 g, 2.66 mmol). The NMR data are identical to the ones reported for **7**. Yield for condition 1: 85%. **HRMS (ESI)** m/z calcd. for $C_{25}H_{32}O_3SiNa$: $(M+Na)^+$, 431.2013; found: 431.2016 $(M+Na)^+$; **R_f** (*n*-heptane/ethyl acetate 10:1): 0.31; **Specific rotation** $[\alpha]_D^{22.6}$ = − 17.3 (c = 1.27; $CHCl_3$).

(*R*)-(2-Bromophenyl)-[(2*S*,3*R*)-3-[[*tert*-butyl(diphenyl)silyl]oxymethyl]-3-(3-methylbut-2-enyl)oxiran-2-yl]methanol (14) and (*S*)-(2-bromophenyl)-[(2*S*,3*R*)-3-[[*tert*-butyl(diphenyl)silyl]oxymethyl]-3-(3-methylbut-2-enyl)oxiran-2-yl]methanol (13). The reaction was carried out in moisture-free glassware under inert atmosphere. To a solution of 1-bromo-2-iodobenzene (**6**, 0.436 mL, 3.40 mmol, 1.60 eq.) dissolved in anhydrous THF (13 mL) *i*-PrMgCl in THF (2.0 M, 1.59 mL, 3.19 mmol, 1.50 eq.) was added dropwise at −40 °C. After stirring for 45 min, epoxy aldehyde **7** (0.868 g, 2.12 mmol, 1.00 eq.) in anhydrous THF (7 mL) was added. The reaction mixture was stirred for 45 min at −40 °C and was then diluted with saturated aqueous NH_4Cl (30 mL). The mixture was extracted with ethyl acetate (2 x 100 mL) and the combined organic layers were washed with saturated aqueous NaCl (50 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (0–20% ethyl acetate in *n*-heptane) to give addition products **14** (0.498 g, 0.880 mmol, 42% over two steps) and **13** (0.500 g, 0.880 mmol, 42% over two steps) as colorless oils. For **14**: **^{1}H-NMR** ($CDCl_3$, 400 MHz): 7.72–7.63 (m, 4H, aryl-*H*), 7.55 (dd, 1H, *J* = 7.9, 1.7 Hz, Br-aryl-*H*), 7.50 (dd, 1H, *J* = 8.1, 1.2 Hz, Br-aryl-*H*), 7.48–7.36 (m, 6H, aryl-*H*), 7.33 (td, 1H, *J* = 7.5, 1.2 Hz, Br-aryl-*H*), 7.15 (td, 1H, *J* = 7.7, 1.7 Hz, Br-aryl-*H*), 5.02 (m, 1H, Me_2C=C*H*), 4.88 (dd, 1H, *J* = 6.1, 3.6 Hz, C*H*-OH), 3.91 (d, 1H, *J* = 11.5 Hz, TBDPSO-CH_2), 3.81 (d, 1H, *J* = 11.6 Hz, TBDPSO-CH_2), 3.11 (d, 1H, *J* = 6.1 Hz, epoxy-C*H*), 2.72 (dd, 1H, *J* = 14.8, 7.9 Hz, Me_2C=CH-CH_2), 2.59 (d, 1H, *J* = 4.0 Hz, O*H*), 2.28 (dd, 1H, *J* = 14.9, 6.8 Hz, Me_2C=CH-CH_2), 1.66 (s, 3H, *E*-CH_3), 1.58 (s, 3H, *Z*-CH_3), 1.07 (s, 9H, ^{t}Bu-CH_3); **^{13}C-NMR** ($CDCl_3$, 100 MHz): 140.6 (Br-Ar-C_q), 136.0 (Ar-*C*), 135.8 (Ar-*C*), 135.5 ($C_q$$Me_2$), 133.3/133.2 (Ar-$C_q$), 132.9 (Br-Ar-*C*), 130.0/129.9 (Ar-*C*), 129.6 (Br-Ar-*C*), 128.2 (Br-Ar-*C*), 127.9 (Br-Ar-*C*), 127.9/127.8 (Ar-*C*), 122.2 (Br-C_q), 117.8 (*C*H=CMe_2), 69.3 (*C*-OH), 65.5 (epoxy-C_q), 64.7 (epoxy-*C*H), 64.2 (TBDPSO-*C*H_2), 31.4 (Me_2C=CH-*C*H_2), 27.0 (^{t}Bu-*C*H_3), 25.9 (*E*-*C*H_3), 19.4 (^{t}Bu-C_q), 18.1 (*Z*-*C*H_3); **HRMS (ESI)** m/z calcd. for $C_{31}H_{36}BrO_2Si$: $(M+H-H_2O)^+$, 547.1662; found: 547.1660 $(M+H-H_2O)^+$; **R_f** (*n*-heptane/ethyl acetate 4:1): 0.34; **Specific rotation** $[\alpha]_D^{24.0}$ = − 3.4 (c = 1.46; $CHCl_3$). For **13**: **^{1}H-NMR** ($CDCl_3$, 400 MHz): 7.75–7.68 (m, 4H, aryl-*H*), 7.58 (dd, 1H, *J* = 7.7, 1.6 Hz, Br-aryl-*H*), 7.54 (dd, 1H, *J* = 8.1, 1.1 Hz, Br-aryl-*H*), 7.51–7.37 (m, 6H, aryl-*H*), 7.37–7.32 (m, 1H, Br-aryl-*H*), 7.15 (td, 1H, *J* = 7.8, 1.7 Hz, Br-aryl-*H*), 5.08 (dd, 1H, *J* = 7.8, 2.5 Hz, C*H*-OH), 5.03 (m, 1H, Me_2C=C*H*), 4.02 (d, 1H, *J* = 11.2 Hz, TBDPSO-CH_2), 3.84 (d, 1H, *J* = 10.9 Hz, TBDPSO-CH_2), 3.15 (d, 1H, *J* = 7.8 Hz, epoxy-C*H*), 3.02 (d, 1H, *J* = 2.5 Hz, O*H*), 2.45 (d, 2H, *J* = 7.2 Hz, Me_2C=CH-CH_2), 1.65 (s, 3H, *E*-CH_3), 1.56 (s, 3H, *Z*-CH_3), 1.12 (s, 9H, ^{t}Bu-CH_3); **^{13}C-NMR** ($CDCl_3$, 100 MHz): 140.2 (Br-Ar-C_q), 136.0/135.8 (Ar-*C*), 135.5 ($C_q$$Me_2$), 133.0 (Br-Ar-*C*), 132.7/132.5 (Ar-C_q), 130.2/130.2 (Ar-*C*), 129.6 (Br-Ar-*C*), 128.2 (Br-Ar-*C*), 128.1/128.0 (Ar-*C*), 128.0 (Br-Ar-*C*), 123.0 (Br-C_q), 117.8 (*C*H=CMe_2), 70.8 (*C*-OH), 65.4 (TBDPSO-*C*H_2), 64.7 (epoxy-*C*H), 63.9 (epoxy-C_q), 32.1 (Me_2C=CH-*C*H_2), 27.1 (^{t}Bu-*C*H_3), 25.9 (*E*-*C*H_3), 19.4 (^{t}Bu-C_q), 18.1 (*Z*-*C*H_3); **HRMS (ESI)** m/z calcd. for $C_{31}H_{36}BrO_2Si$: $(M+H-H_2O)^+$, 547.1662; found: 547.1659 $(M+H-H_2O)^+$; **R_f** (*n*-heptane/ethyl acetate 4:1): 0.37; **Specific rotation** $[\alpha]_D^{24.0}$ = − 16.2 (c = 0.93; $CHCl_3$).

(*S*)-(2-Bromophenyl)-[(2*R*,3*S*)-3-[[*tert*-butyl(diphenyl)silyl]oxymethyl]-3-(3-methylbut-2-enyl)oxiran-2-yl]methanol (*ent*-14) and (*R*)-(2-bromophenyl)-[(2*R*,3*S*)-3-[[*tert*-butyl(diphenyl)silyl]oxymethyl]-3-(3-methylbut-2-enyl)oxiran-2-yl]methanol (*ent*-13). ***Ent*-14** (0.928 g 1.64 mmol, 45% over two steps) and ***ent*-13** (0.802 g, 1.42 mmol, 39% over two steps) were synthesized in analogous manner starting from epoxy aldehyde ***ent*-7** (1.49 g, 3.65 mmol). The NMR data are identical

to the ones reported for **14** and **13**. For ***ent*-14**: **HRMS (ESI)** m/z calcd. for $C_{31}H_{36}BrO_2Si$: $(M+H-H_2O)^+$, 547.1662; found: 547.1660 $(M+H-H_2O)^+$; $\mathbf{R_f}$ (*n*-heptane/ethyl acetate 4:1): 0.34; **Specific rotation** $[\alpha]_D^{22.2}$ = + 1.8 (c = 1.12; $CHCl_3$). For ***ent*-13**: **HRMS (ESI)** m/z calcd. for for $C_{31}H_{36}BrO_2Si$: $(M+H-H_2O)^+$, 547.1662; found: 547.1659 $(M+H-H_2O)^+$; $\mathbf{R_f}$ (*n*-heptane/ethyl acetate 4:1): 0.37; **Specific rotation** $[\alpha]_D^{22.2}$ = + 13.5 (c = 0.82; $CHCl_3$).

[(*R*)-(2-Bromophenyl)-[(2*S*,3*R*)-3-[[*tert*-butyl(diphenyl)silyl]oxymethyl]-3-(3-methylbut-2-enyl)oxiran-2-yl]methoxy]-triisopropyl-silane (18). 2,6-Lutidine (0.751 mL, 6.47 mmol, 6.00 eq.) and then TIPS triflate (0.870 mL, 3.24 mmol, 3.00 eq.) were added to a solution of alcohol **14** (0.610 g, 1.08 mmol, 1.00 eq.) in anhydrous DCM (25 mL) at 0 °C. The reaction mixture was allowed to stir at room temperature for 1.5 h. Because the TLC showed remaining starting material, 2,6-lutidine (6.00 eq.) and then TIPS triflate (3.00 eq.) were added a second time at 0 °C. After 2.5 h stirring at room temperature, the TLC showed complete conversion. Saturated aqueous NH_4Cl (30 mL) was added. The mixture was extracted with ethyl acetate (2 x 75 mL) and the combined organic layers were washed with saturated aqueous NaCl (40 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (0–4% ethyl acetate in *n*-heptane) to give **18** (0.714 g, 0.99 mmol, 92%) as a colorless oil. **^{1}H-NMR** ($CDCl_3$, 400 MHz): 7.73–7.62 (m, 4H, aryl-*H*), 7.48–7.32 (m, 8H, aryl-*H*, Br-aryl-*H*), 7.30–7.24 (m, 1H, Br-aryl-*H*), 7.07 (ddd, 1H, *J* = 8.0, 7.3, 1.7 Hz, Br-aryl-*H*), 4.83 (m, 1H, Me_2C=C*H*), 4.81 (d, 1H, *J* = 4.8 Hz, C*H*-OTIPS), 3.78 (d, 1H, *J* = 11.5 Hz, TBDPSO-CH_2), 3.67 (d, 1H, *J* = 11.5 Hz, TBDPSO-CH_2), 3.17 (d, 1H, *J* = 7.8 Hz, epoxy-C*H*), 2.90 (dd, 1H, *J* = 14.7, 8.2 Hz, Me_2C=CH-CH_2), 1.99 (dd, 1H, *J* = 14.6, 6.5 Hz, Me_2C=CH-CH_2), 1.56 (s, 3H, *E*-CH_3), 1.48 (s, 3H, *Z*-CH_3), 1.07 (s, 9H, ^{t}Bu-CH_3), 1.04–0.85 (m, 21H, TIPS-*H*); **^{13}C-NMR** ($CDCl_3$, 100 MHz): 141.3 (Br-Ar-C_q), 135.9/135.8 (Ar-*C*), 134.6 (C_qMe$_2$), 133.8/133.4 (Ar-C_q), 132.7 (Br-Ar-*C*), 129.7/129.7 (Ar-*C*), 129.7 (Ar-*C*), 129.3 (Br-Ar-*C*), 127.7 (Br-Ar-*C*), 127.6 (Br-Ar-*C*), 121.4 (Br-C_q), 118.7 (*C*H=CMe$_2$), 72.5 (*C*-OTIPS), 67.1 (epoxy-*C*H), 66.1 (TBDPSO-*C*H$_2$), 65.1 (epoxy-C_q), 31.2 (Me_2C=CH-*C*H$_2$), 27.0 (^{t}Bu-*C*H$_3$), 25.8 (*E*-*C*H$_3$), 19.5 (^{t}Bu-C_q), 18.1 (*Z*-*C*H$_3$), 18.0/17.9/12.3 (TIPS-*C*); **HRMS (ESI)** m/z calcd. for $C_{40}H_{57}BrO_3Si_2Na$: $(M+Na)^+$, 743.2922; found: 743.2929 $(M+Na)^+$; $\mathbf{R_f}$ (*n*-heptane/ethyl acetate 10:1): 0.68; **Specific rotation** $[\alpha]_D^{23.0}$ = + 13.4 (c = 1.20; $CHCl_3$).

[(*S*)-(2-Bromophenyl)-[(2*S*,3*R*)-3-[[*tert*-butyl(diphenyl)silyl]oxymethyl]-3-(3-methylbut-2-enyl)oxiran-2-yl]methoxy]-triisopropyl-silane (15). 15 (0.613 g, 0.85 mmol, 82%) was synthesized in analogous manner to **18** starting from **13** (0.584 g, 1.03 mmol) and was obtained as colorless oil. **^{1}H-NMR** ($CDCl_3$, 400 MHz): 7.75–7.66 (m, 4H, aryl-*H*), 7.57–7.48 (m, 1H, Br-aryl-*H*), 7.48–7.33 (m, 7H, aryl-*H*, Br-aryl-*H*), 7.29 (td, 1H, *J* = 7.6, 0.7 Hz, Br-aryl-*H*), 7.09 (td, 1H, *J* = 7.7, 1.5 Hz, Br-aryl-*H*), 5.09 (m, 1H, Me_2C=C*H*), 5.02 (d, 1H, *J* = 7.0 Hz, C*H*-OTIPS), 4.14 (d, 1H, *J* = 11.2 Hz, TBDPSO-CH_2), 3.90 (d, 1H, *J* = 11.1 Hz, TBDPSO-CH_2), 3.00 (d, 1H, *J* = 8.1 Hz, epoxy-C*H*), 2.93 (dd, 1H, *J* = 14.5, 7.9 Hz, Me_2C=CH-CH_2), 2.08 (dd, 1H, *J* = 14.5, 7.0 Hz, Me_2C=CH-CH_2), 1.66 (s, 3H, *E*-CH_3), 1.59 (s, 3H, *Z*- CH_3), 1.10 (s, 9H, ^{t}Bu-CH_3), 0.91–0.81 (m, 21H, TIPS-*H*); **^{13}C-NMR** ($CDCl_3$, 100 MHz): 142.0 (Br-Ar-C_q), 136.0/135.9 (Ar-*C*), 134.7 (C_qMe$_2$), 133.7/133.2 (Ar-C_q), 132.5 (Br-Ar-*C*), 129.8/129.8 (Ar-*C*), 129.2 (Br-Ar-*C*), 129.1 (Br-Ar-*C*), 127.8 (Ar-*C*), 127.7 (Br-Ar-*C*), 122.4 (Br-C_q), 118.8 (*C*H=CMe$_2$), 69.7 (*C*-OTIPS), 65.9 (epoxy-*C*H), 65.4 (epoxy-C_q), 64.5 (TBDPSO-*C*H$_2$), 31.2 (Me_2C=CH-*C*H$_2$), 27.1 (^{t}Bu-*C*H$_3$), 25.9 (*E*-*C*H$_3$), 19.5 (^{t}Bu-C_q), 18.1 (*Z*-*C*H$_3$), 17.9/17.8/12.3 (TIPS-*C*); **HRMS (ESI)** m/z calcd. for $C_{40}H_{57}BrO_3Si_2Na$: $(M+Na)^+$, 743.2922; found: 743.2928 $(M+Na)^+$; $\mathbf{R_f}$ (*n*-heptane/ethyl acetate 10:1): 0.59; **Specific rotation** $[\alpha]_D^{23.0}$ = − 8.1 (c = 1.30; $CHCl_3$).

[(2*R*,3*S*)-3-[(*R*)-(2-Bromophenyl)-triisopropylsilyloxy-methyl]-2-(3-methylbut-2-enyl)oxiran-2-yl]methanol (19). Condition 1: To a solution of **18** (0.714 g, 0.990 mmol, 1.00 eq.) in MeOH/THF (23.5 mL/1.5 mL) NH_4F (0.366 g, 9.89 mmol, 10.00 eq.) was added. The reaction mixture stirred for 5 h at 40 °C. Because the TLC only showed a slow conversion of the starting material, the reaction was allowed to stir overnight at room temperature and then saturated aqueous $NaHCO_3$ (50 mL) was added. The mixture was extracted with ethyl acetate (2 x 100 mL) and the combined organic layers were washed with saturated aqueous NaCl (75 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (0–20% ethyl acetate in *n*-heptane) to give the desired product **19** (0.267 g, 0.550 mmol, 56%) and side product **SI1** (0.080 g, 0.250 mmol, 25%) as colorless oils. Condition 2: To a solution of **32** (0.174 g, 0.330 mmol, 1.00 eq.) in THF/H_2O (5:1, 8.0 mL/1.6 mL) LiOH · H_2O (0.028 g, 0.66 mmol, 2.00 eq.) was added. The reaction mixture stirred over night at room temperature. After the TLC showed a complete conversion the next day, saturated aqueous $NaHCO_3$ (20 mL) was added. The mixture was extracted with ethyl acetate (2 x 30 mL) and the combined organic layers were washed with saturated aqueous NaCl (20 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (0–25% ethyl acetate in *n*-heptane) to give **19** (0.137 g, 0.280 mmol, 85%) as a colorless oil. **^{1}H-NMR** ($CDCl_3$, 400 MHz): 7.60 (dd, 1H, *J* = 7.7, 1.7 Hz, aryl-*H*), 7.52 (dd, 1H, *J* = 8.1, 1.1 Hz, aryl-*H*), 7.39–7.33 (m, 1H, aryl-*H*), 7.16 (ddd, 1H, *J* = 8.9, 6.5, 1.8 Hz, aryl-*H*), 5.17 (d, 1H, *J* = 7.8 Hz, C*H*-OTIPS), 4.94 (m, 1H, Me_2C=C*H*), 3.80 (dd, 1H, *J* = 12.1, 6.5 Hz, CH_2-OH), 3.67 (dd, 1H, *J* = 12.2, 6.7 Hz, CH_2-OH), 3.25 (d, 1H, *J* = 7.9 Hz, epoxy-C*H*), 2.47 (dd, 1H, *J* = 14.8, 7.7 Hz, Me_2C=CH-CH_2), 2.15 (dd, 1H, *J* = 14.8, 7.2 Hz, Me_2C=CH-CH_2), 1.66 (t, 1H, *J* = 6.7 Hz, O*H*), 1.61 (s, 3H, *E*-CH_3), 1.50 (s, 3H, *Z*-CH_3), 1.07–0.92 (m, 21H, TIPS-*H*); **^{13}C-NMR** ($CDCl_3$, 100 MHz): 141.3 (Ar-C_q), 135.5 (C_qMe$_2$), 132.9 (Ar-*C*), 129.8 (Ar-*C*), 129.6 (Ar-*C*), 128.0 (Ar-*C*), 121.5 (Br-C_q), 117.9 (*C*H=CMe$_2$), 72.4 (*C*-OTIPS), 68.0 (epoxy-*C*H), 64.9 (epoxy-C_q), 63.3 (*C*H$_2$-OH), 32.0 (Me_2C=CH-*C*H$_2$), 25.8 (*E*-*C*H$_3$), 18.0 (*Z*-*C*H$_3$), 18.0/17.9/12.4 (TIPS-*C*); **HRMS (ESI)** m/z calcd. for $C_{24}H_{38}BrO_2Si$: $(M+H-H_2O)^+$, 465.1819; found: 465.1819 $(M+H-H_2O)^+$; $\mathbf{R_f}$ (*n*-heptane/ethyl acetate 4:1): 0.42; **Specific rotation** $[\alpha]_D^{21.3}$ = − 15.4 (c = 0.97; $CHCl_3$).

[(2*R*,3*S*)-3-[(*S*)-(2-Bromophenyl)-triisopropylsilyloxy-methyl]-2-(3-methylbut-2-enyl)oxiran-2-yl]methanol (16). 16 (0.223 g, 0.460 mmol, 54%) was synthesized in analogous manner to **19** (condition 1) starting from **15** (0.612 g, 0.850 mmol). **16** and side product **SI2** (0.103 g, 0.310 mmol, 37%) were obtained as colorless oils. **^{1}H-NMR** ($CDCl_3$, 400 MHz): 7.63 (dd, 1H, *J* = 7.9, 1.7 Hz, aryl-*H*), 7.51 (dd, 1H, *J* = 8.1, 1.6 Hz, aryl-*H*), 7.36 (td, 1H, *J* = 7.6, 0.9 Hz, aryl-*H*), 7.15 (ddd, 1H, *J* =

7.9, 7.4, 1.7 Hz, aryl-*H*), 5.37 (d, 1H, *J* = 7.0 Hz, C*H*-OTIPS), 5.09 (m, 1H, Me_2C=C*H*), 4.03 (dd, 1H, *J* = 12.0, 5.2 Hz, CH_2-OH), 3.93 (dd, 1H, *J* = 12.0, 8.1 Hz, CH_2-OH), 3.10 (d, 1H, *J* = 6.8 Hz, epoxy-C*H*), 2.67 (dd, 1H, *J* = 14.6, 8.0 Hz, Me_2C=CH-CH_2), 2.06 (dd, 1H, *J* = 14.5, 6.8 Hz, Me_2C=CH-CH_2), 1.81 (dd, 1H, *J* = 7.9, 5.1 Hz, O*H*), 1.68 (s, 3H, *E*-CH_3), 1.61 (s, 3H, *Z*-CH_3), 1.03–0.95 (m, 21H, TIPS-*H*); **^{13}C-NMR** ($CDCl_3$, 100 MHz): 141.9 (Ar-C_q), 135.6 ($C_q$$Me_2$), 132.6 (Ar-*C*), 129.5 (Ar-*C*), 129.0 (Ar-*C*), 127.9 (Ar-*C*), 122.3 (Br-C_q), 118.1 (*C*H=CMe_2), 69.8 (*C*-OTIPS), 67.6 (epoxy-*C*H), 65.6 (epoxy-C_q), 62.3 (*C*H_2-OH), 32.4 (Me_2C=CH-*C*H_2), 25.9 (*E*-*C*H_3), 18.0 (*Z*-*C*H_3), 18.0/17.9/12.3 (TIPS-*C*); **HRMS (ESI)** m/z calcd. for $C_{24}H_{38}BrO_2Si$: $(M+H-H_2O)^+$, 465.1819; found: 465.1826 $(M+H-H_2O)^+$; **R$_f$** (*n*-heptane/ethyl acetate 4:1): 0.41; **Specific rotation** $[\alpha]_D^{27.6}$ = + 10.1 (c = 0.20; $CHCl_3$).

[(2*S*,3*R*)-3-[(*S*)-(2-Bromophenyl)-triisopropylsilyloxy-methyl]-2-(3-methylbut-2-enyl)oxiran-2-yl]methanol (*ent*-19) and [(2*S*,3*R*)-3-[(*R*)-(2-Bromophenyl)-triisopropylsilyloxy-methyl]-2-(3-methylbut-2-enyl)oxiran-2-yl]methanol (*ent*-16). *Ent*-19 (0.427 g, 0.880 mmol, 85%) and ***ent*-16** (0.346 g, 0.720 mmol, 79%) were synthesized according to **19** (condition 2) starting from ***ent*-32** (0.542 g, 1.03 mmol) and ***ent*-28** (0.822 g, 1.47 mmol). The NMR data are identical to the ones reported for **19** and **16**. For ***ent*-19**: **HRMS (ESI)** m/z calcd. for $C_{24}H_{38}BrO_2Si$: $(M+H-H_2O)^+$, 465.1819; found: 465.1822 $(M+H-H_2O)^+$; **R$_f$** (*n*-heptane/ethyl acetate 4:1): 0.42; **Specific rotation** $[\alpha]_D^{22.0}$ = + 21.7 (c = 0.97; $CHCl_3$). For ***ent*-16**: **HRMS (ESI)** m/z calcd. for $C_{24}H_{39}BrO_3SiNa$: $(M+Na)^+$, 505.1744; found: 505.1752 $(M+Na)^+$; **R$_f$** (*n*-heptane/ethyl acetate 4:1): 0.41; **Specific rotation** $[\alpha]_D^{21.2}$ = − 35.8 (c = 1.17; $CHCl_3$).

(2*S*,3*S*)-3-[(*R*)-(2-Bromophenyl)-triisopropylsilyloxy-methyl]-2-(3-methylbut-2-enyl)oxirane-2-carbaldehyde (20). Alcohol **19** (0.259 g, 0.540 mmol, 1.00 eq.) was dissolved in DCM (10 mL) and Dess–Martin periodinane (15% in DCM, 2.24 mL, 1.07 mmol, 2.00 eq.) was added. After stirring for 4 h at room temperature, the TLC showed a complete conversion of the starting material. The reaction solution was filtered through a short silica column (100% DCM, 20 g silica) and was then purified *via* flash column chromatography (0–5% ethyl acetate in *n*-heptane) to give epoxy aldehyde **20** (0.200 g, 0.420 mmol, 77%) and recovered starting material **19** (0.019 g, 0.040 mmol, 7%) as colorless oils. **^{1}H-NMR** ($CDCl_3$, 400 MHz): 9.55 (s, 1H, CHO), 7.60 (dd, 1H, *J* = 7.8, 1.8 Hz, aryl-*H*), 7.50 (dd, 1H, *J* = 8.1, 1.2 Hz, aryl-*H*), 7.36 (td, 1H, *J* = 7.6, 1.1 Hz, aryl-*H*), 7.17 (ddd, 1H, *J* = 8.0, 7.4, 1.7 Hz, aryl-*H*), 5.38 (d, 1H, *J* = 6.8 Hz, C*H*-OTIPS), 4.95 (m, 1H, Me_2C=C*H*), 3.46 (d, 1H, *J* = 6.6 Hz, epoxy-C*H*), 2.50 (dd, 1H, *J* = 15.2, 7.4 Hz, Me_2C=CH-CH_2), 2.40 (dd, 1H, *J* = 15.3, 7.4 Hz, Me_2C=CH-CH_2), 1.63 (s, 3H, *E*-CH_3), 1.51 (s, 3H, *Z*-CH_3), 1.16–0.92 (m, 21H, TIPS-*H*); **^{13}C-NMR** ($CDCl_3$, 100 MHz): 198.9 (C=O), 140.2 (Ar-C_q), 136.2 ($C_q$$Me_2$), 132.8 (Ar-*C*), 129.9 (Ar-*C*), 129.5 (Ar-*C*), 127.9 (Ar-*C*), 121.4 (Br-C_q), 116.6 (*C*H=CMe_2), 71.2 (*C*-OTIPS), 68.1 (epoxy-*C*H), 67.4 (epoxy-C_q), 28.3 (Me_2C=CH-*C*H_2), 25.8 (*E*-*C*H_3), 18.0 (*Z*-*C*H_3), 18.0/17.9/12.3 (TIPS-*C*); **HRMS (ESI)** m/z calcd. for $C_{24}H_{37}BrO_3SiNa$: $(M+Na)^+$, 503.1588; found: 503.1582 $(M+Na)^+$; **R$_f$** (*n*-heptane/ethyl acetate 4:1): 0.75; **Specific rotation** $[\alpha]_D^{25.6}$ = − 41.9 (c = 0.93; $CHCl_3$).

(2*S*,3*S*)-3-[(*S*)-(2-Bromophenyl)-triisopropylsilyloxy-methyl]-2-(3-methylbut-2-enyl)oxirane-2-carbaldehyde (17). **17** (0.162 g, 0.340 mmol, 75%) was synthesized in analogous manner to **20** starting from **16** (0.218 g, 0.450 mmol). It was obtained as colorless oil. Starting material **16** (0.021 g, 0.040 mmol, 8%) was also recovered. **^{1}H-NMR** ($CDCl_3$, 400 MHz): 9.84 (s, 1H, CHO), 7.52 (dd, 1H, *J* = 8.0, 0.9 Hz, aryl-*H*), 7.41–7.32 (m, 2H, aryl-*H*), 7.17 (ddd, 1H, *J* = 8.0, 7.0, 2.0 Hz, aryl-*H*), 5.64 (d, 1H, *J* = 2.9 Hz, C*H*-OTIPS), 4.98 (m, 1H, Me_2C=C*H*), 3.29 (d, 1H, *J* = 2.8 Hz, epoxy-C*H*), 2.54 (dd, 1H, *J* = 15.1, 7.5 Hz, Me_2C=CH-CH_2), 2.31 (dd, 1H, *J* = 15.2, 7.4 Hz, Me_2C=CH-CH_2), 1.62 (s, 3H, *E*-CH_3), 1.43 (s, 3H, *Z*-CH_3), 1.12–0.92 (m, 21H, TIPS-*H*); **^{13}C-NMR** ($CDCl_3$, 100 MHz): 200.5 (C=O), 140.3 (Ar-C_q), 136.4 ($C_q$$Me_2$), 132.6 (Ar-*C*), 129.8 (Ar-*C*), 129.1 (Ar-*C*), 128.3 (Ar-*C*), 121.8 (Br-C_q), 116.7 (*C*H=CMe_2), 70.1 (*C*-OTIPS), 67.7 (epoxy-*C*H), 66.6 (epoxy-C_q), 29.2 (Me_2C=CH-*C*H_2), 25.8 (*E*-*C*H_3), 17.8 (*Z*-*C*H_3), 17.9/17.8/12.3 (TIPS-*C*); **HRMS (ESI)** m/z calcd. for $C_{24}H_{37}BrO_3SiNa$: $(M+Na)^+$, 503.1588; found: 503.1583 $(M+Na)^+$; **R$_f$** (*n*-heptane/ethyl acetate 4:1): 0.77; **Specific rotation** $[\alpha]_D^{25.6}$ = + 5.8 (c = 0.87; $CHCl_3$).

(1a*S*,7*R*,7a*S*)-1a-(3-Methylbut-2-enyl)-7-triisopropylsilyloxy-7,7a-dihydronaphtho[2,3-b]oxiren-2-one (22). Condition 1: Aldehyde **20** (0.141 g, 0.293 mmol, 1.00 eq.) was dissolved in toluene (15 mL). The solution was degassed with Argon for 15 min and Cs_2CO_3 (0.286 g, 0.878 mmol, 3.00 eq.) as well as $PdCl_2(PPh_3)_2$ (0.021 g, 0.029 mmol, 0.10 eq.) were added. The reaction mixture was refluxed for 5 h. As the TLC showed remaining starting material, further $PdCl_2(PPh_3)_2$ (0.10 eq.) was added. The reaction mixture was stirred overnight at 100 °C. After the TLC showed a complete conversion of the starting material the next day, the reaction solution was filtered through a short silica gel column (*n*-heptane/ ethyl acetate 10:1, 10 g silica) and was then purified *via* flash column chromatography (0–4% ethyl acetate in *n*-heptane) to give **22** (0.056 g, 0.139 mmol, 48%) as a yellowish oil. Product **22** was contaminated with approx. 20% inseparable isomerization product, which was characterized after deprotection to **23**. The formation of further side products was observed. TIPS protected natural product hemitectol[21] (0.005 g, 0.013 mmol, 4%) **24a** was isolated and fully characterized. Condition 2: The halogen-lithium exchange was carried out in a moisture-free glassware under argon atmosphere. To a solution of nitrile **34** (0.053 g, 0.110 mmol, 1.00 eq.) in anhydrous THF (5 mL) prediluted *n*-BuLi solution (0.110 mmol, 1.00 eq.) was added at −100 ºC.[30] The obtained yellow solution was stirred for 20 min at −100 ºC and for 5 min without cooling bath. During this time, the reaction solution turned from yellow to orange. For hydrolysis of the intermediate imine, aqueous citric acid (10%, 15 mL) was added and the mixture was extracted with ethyl acetate (50 mL). The organic layer was separated, washed with saturated aqueous $NaHCO_3$ (15 mL) as well as with saturated aqueous NaCl (20 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (0–15% ethyl acetate in *n*-heptane) to give ketone **22** (0.041 g, 0.100 mmol, 92%) as colorless oil. **^{1}H-NMR** ($CDCl_3$, 400 MHz): 7.92 (dd, 1H, *J* = 7.8, 1.2 Hz, aryl-*H*), 7.56 (td, 1H, *J* = 7.5, 1.4 Hz, aryl-*H*), 7.44 (td, 1H, *J* = 7.6, 1.1 Hz, aryl-*H*), 7.35 (d, br, 1H, *J* = 7.6 Hz, aryl-*H*), 5.37 (d, 1H, *J* = 2.4 Hz, C*H*-OTIPS), 5.16 (m, 1H, Me_2C=C*H*), 3.77 (d, 1H, *J* = 2.6 Hz, epoxy-C*H*), 3.02 (dd, 1H, *J* = 15.3, 7.8 Hz, Me_2C=CH-CH_2), 2.55 (dd, 1H, *J* = 15.3, 6.8 Hz, Me_2C=CH-CH_2), 1.72 (s, 3H, *E*-CH_3), 1.68 (s, 3H, *Z*-CH_3), 1.14–0.94 (m, 21H, TIPS-*H*); **^{13}C-NMR** ($CDCl_3$, 100 MHz): 195.3 (C=O), 140.0 (Ar-C_q), 135.8 ($C_q$$Me_2$), 133.6 (Ar-*C*), 130.5 (Ar-C_q-CO), 129.6 (Ar-*C*),

129.2 (Ar-*C*), 127.6 (Ar-*C*), 117.2 (*C*H=CMe$_2$), 68.2 (*C*-OTIPS), 60.5 (epoxy-C_q), 60.1 (epoxy-*C*H), 26.9 (Me$_2$C=CH-*C*H$_2$), 26.0 (*E*-*C*H$_3$), 18.1 (*Z*-*C*H$_3$), 18.2/18.1/12.7 (TIPS-*C*); **HRMS (ESI)** m/z calcd. for $C_{24}H_{37}O_3Si$: $(M+H)^+$, 401.2506; found: 401.2505 $(M+H)^+$; **R$_f$** (*n*-heptane/ethyl acetate 10:1): 0.44; **Specific rotation** $[\alpha]_D^{24.2} = -140.4$ (c = 0.71; $CHCl_3$).

(2,2-Dimethylbenzo[h]chromen-6-yl)oxy-triisopropylsilane (24a). **^{1}H-NMR** ($CDCl_3$, 400 MHz): 8.14 (m, 2H, *H*-5, *H*-8), 7.42 (m, 2H, *H*-6, *H*-7), 6.55 (s, 1H, *H*-3), 6.35 (d, 1H, *J* = 9.7 Hz, *H*-1'), 5.64 (d, 1H, *J* = 9.6 Hz, *H*-2'), 1.49 (s, 6H, *H*-4', *H*-5'), 1.44–1.31 (m, 3H, *H*-11), 1.18–1.11 (m, 18H, *H*-12); **^{13}C-NMR** ($CDCl_3$, 100 MHz): 145.5 (*C*-4), 142.2 (*C*-1), 130.0 (*C*-2'), 128.2 (*C*-9), 126.2 (*C*-10), 125.7 (*C*-6), 125.4 (*C*-7), 123.1 (*C*-1'), 122.8 (*C*-5), 121.9 (*C*-8), 115.1 (*C*-2), 110.2 (*C*-3), 76.3 (*C*-3'), 27.7 (*C*-4', *C*-5'), 18.3 (*C*-12), 13.2 (*C*-11); **HRMS (ESI)** m/z calcd. for $C_{24}H_{35}O_2Si$: $(M+H)^+$, 383.2401; found: 383.2399 $(M+H)^+$; **R$_f$** (*n*-heptane/ethyl acetate 10:1): 0.78.

(1a*S*,7*S*,7a*S*)-1a-(3-Methylbut-2-enyl)-7-triisopropylsilyloxy-7,7a-dihydronaphtho[2,3-b]oxiren-2-one (21). 21 (0.039 g, 0.100 mmol, 46%) was synthesized in analogous manner to **22** (condition 1) starting from **17** (0.100 g, 0.210 mmol). It was obtained as colorless oil and contaminated with inseparable isomerization product (approx. 16%), which was characterized after deprotection to **4**. Formation of TIPS protected NP hemitectol **24a** was also observed, but the compound was not isolated. **^{1}H-NMR** ($CDCl_3$, 400 MHz): 7.86 (dd, 1H, *J* = 7.8, 1.2 Hz, aryl-*H*), 7.68 (d, br, 1H, *J* = 7.7 Hz, aryl-*H*), 7.62 (td, 1H, *J* = 7.5, 1.2 Hz, aryl-*H*), 7.43–7.35 (m, 1H, aryl-*H*), 5.31 (s, br, 1H, C*H*-OTIPS), 5.12 (m, 1H, Me$_2$C=C*H*), 3.77 (d, 1H, *J* = 1.6 Hz, epoxy-C*H*), 2.93 (dd, 1H, *J* = 15.3, 8.0 Hz, Me$_2$C=CH-C*H*$_2$), 2.62 (dd, 1H, *J* = 15.3, 6.9 Hz, Me$_2$C=CH-C*H*$_2$), 1.73 (s, 3H, *E*-C*H*$_3$), 1.68 (s, 3H, *Z*-C*H*$_3$), 1.35–1.13 (m, 21H, TIPS-*H*); **^{13}C-NMR** ($CDCl_3$, 100 MHz): 195.2 (C=O), 140.4 (Ar-C_q), 136.3 (C_qMe$_2$), 134.0 (Ar-*C*), 129.3 (Ar-C_q-CO), 128.0 (Ar-*C*), 127.3 (Ar-*C*), 126.6 (Ar-*C*), 117.0 (*C*H=CMe$_2$), 67.8 (*C*-OTIPS), 61.8 (epoxy-C_q), 58.7 (epoxy-*C*H), 26.3 (Me$_2$C=CH-*C*H$_2$), 25.9 (*E*-*C*H$_3$), 18.4/18.3 (TIPS-*C*), 18.2 (*Z*-*C*H$_3$), 12.9 (TIPS-*C*); **HRMS (ESI)** m/z calcd. for $C_{24}H_{36}O_3SiNa$: $(M+Na)^+$, 423.2326; found: 423.2330 $(M+Na)^+$; **R$_f$** (*n*-heptane/ethyl acetate 10:1): 0.51; **Specific rotation** $[\alpha]_D^{25.8} = -80.9$ (c = 1.04; $CHCl_3$).

(1a*R*,7*S*,7a*R*)-1a-(3-Methylbut-2-enyl)-7-triisopropylsilyloxy-7,7a-dihydronaphtho[2,3-b]oxiren-2-one (*ent*-22) and (1a*R*,7*R*,7a*R*)-1a-(3-Methylbut-2-enyl)-7-triisopropylsilyloxy-7,7a-dihydronaphtho[2,3-b]oxiren-2-one (*ent*-21). *Ent*-22 (0.129 g, 0.320 mmol, 95%) and ***ent*-21** (0.053 g, 0.130 mmol, 80%) were synthesized according to **22** (condition 2) starting from ***ent*-34** (0.162 g, 0.340 mmol) and ***ent*-33** (0.079 g, 0.170 mmol). The NMR data are identical to the ones reported for **22** and **21**. No side product formation was observed. For ***ent*-22**: **HRMS (ESI)** m/z calcd. for $C_{24}H_{37}O_3Si$: $(M+H)^+$, 401.2506; found: 401.2509 $(M+H)^+$; **R$_f$** (*n*-heptane/ethyl acetate 10:1): 0.44; **Specific rotation** $[\alpha]_D^{21.3} = +138.5$ (c = 0.61; $CHCl_3$). For ***ent*-21**: **HRMS (ESI)** m/z calcd. for $C_{24}H_{37}O_3Si$: $(M+H)^+$, 401.2506; found: 401.2501 $(M+H)^+$; **R$_f$** (*n*-heptane/ethyl acetate 10:1): 0.51; **Specific rotation** $[\alpha]_D^{21.3} = +139.3$ (c = 1.14; $CHCl_3$).

(1a*S*,7*R*,7a*S*)-7-Hydroxy-1a-(3-methylbut-2-enyl)-7,7a-dihydronaphtho[2,3-b]oxiren-2-one (23). In a 50 mL falcon tube TBAF in THF (1 M, 0.245 mL, 0.250 mmol, 1.20 eq.), followed by acetic acid glacial (0.012 mL, 0.200 mmol, 1.00 eq.) were added to a solution of **22** (0.082 g, 0.200 mmol, 1.00 eq.) in THF (7 mL). After 2 h reaction time, the TLC showed a complete conversion of the starting material. The reaction mixture was loaded on silica and filtered through a small silica column (*n*-heptane/ ethyl acetate 3:1, 10 g silica) and was then purified *via* flash column chromatography (0–40% ethyl acetate in *n*-heptane) to give **23** (0.044 mg, 0.180 mmol, 89%) as a colorless oil. Material **22**, which was obtained from condition 1, was contaminated with some isomerization product. After complete deprotection **23** (0.019 g, 0.080 mmol, 83%) was obtained (sum of collected fractions with different amount of **SI3** after two times careful chromatography; in total the content of **SI3** was estimated to be maximum 16% by analysis of the NMR spectra). An almost pure sample of **23** was obtained for full characterization. **SI3** was isolated enriched in a mixture with product **23** (ratio **SI3**:**23** approx. 2:1; analytical data see Supporting Information). **^{1}H-NMR** ($CDCl_3$, 600 MHz): 7.94 (dd, 1H, *J* = 7.8, 1.1 Hz, aryl-*H*), 7.62 (td, 1H, *J* = 7.5, 1.3 Hz, aryl-*H*), 7.47 (td, 1H, *J* = 7.6, 1.3 Hz, aryl-*H*), 7.44 (dd, 1H, *J* = 7.6, 1.2 Hz, aryl-*H*), 5.24 (d, br, 1H, *J* = 3.9 Hz, C*H*-OH), 5.14 (m, 1H, Me$_2$C=C*H*), 3.83 (d, 1H, *J* = 2.1 Hz, epoxy-C*H*), 2.95 (dd, 1H, *J* = 15.5, 8.0 Hz, Me$_2$C=CH-C*H*$_2$), 2.64 (dd, 1H, *J* = 15.3, 6.8 Hz, Me$_2$C=CH-C*H*$_2$), 2.04 (d, 6.5 Hz, O*H*), 1.73 (s, 3H, *E*-C*H*$_3$), 1.70 (s, 3H, *Z*-C*H*$_3$); **^{13}C-NMR** ($CDCl_3$, 100 MHz): 194.4 (C=O), 139.6 (Ar-C_q), 136.4 (C_qMe$_2$), 134.4 (Ar-*C*), 129.9 (Ar-*C*), 129.8 (Ar-C_q-CO), 129.7 (Ar-*C*), 127.8 (Ar-*C*), 116.7 (*C*H=CMe$_2$), 67.2 (*C*-OH), 60.6 (epoxy-C_q), 60.1 (epoxy-*C*H), 26.8 (Me$_2$C=CH-*C*H$_2$), 26.0 (*E*-*C*H$_3$), 18.2 (*Z*-*C*H$_3$); **HRMS (ESI)** m/z calcd. for $C_{15}H_{17}O_3$: $(M+H)^+$, 245.1172; found: 245.1171 $(M+H)^+$; **R$_f$** (*n*-heptane/ethyl acetate 2:1): 0.31; **Chiral HPLC** (Chiralpak IC; hexane:isopropyl alcohol 95:5): **23** (Rt = 8.3 min) : ***ent*-23** (Rt = 9.2 min) 96.8 : 2.9 (94% *ee*); **Specific rotation** $[\alpha]_D^{24.7} = -193.6$ (c = 0.70; $CHCl_3$).

(1a*S*,7*S*,7a*S*)-7-Hydroxy-1a-(3-methylbut-2-enyl)-7,7a-dihydronaphtho[2,3-b]oxiren-2-one (4). 4 (0.021 g, 0.080 mmol, 87%) was synthesized in analogous manner to **23** starting from **21** (0.039 g, 0.100 mmol) which was only obtained from condition 1. It was obtained as colorless solid (sum of collected fractions with different amount of **SI4** after two times careful chromatography; in total the content of **SI4** was estimated to be maximum 12% by analysis of the NMR spectra). A sufficiently pure sample of **4** was obtained for full characterization. **SI4** was isolated enriched in a mixture with product **4** (ratio **SI4**:**4** approx. 2:1; analytical data see Supporting Information). In a 4 mL Vial, a small portion of **4** was dissolved in DCM (1 mL) and *n*-heptane (1.5 mL) was added. The system was left at room temperature for one night. A crystal was obtained for determination by single X-ray crystal diffraction (see Supporting Information for further details). **^{1}H-NMR** ($CDCl_3$, 600 MHz): 7.92 (dd, 1H, *J* = 7.9, 1.0 Hz, aryl-*H*), 7.69 (m, 2H, aryl-*H*), 7.42 (m, 1H, aryl-*H*), 5.14–5.05 (m, 2H, Me$_2$C=C*H*, C*H*-OH), 3.86 (d, 1H, *J* = 2.2 Hz, epoxy-C*H*), 2.94 (dd, 1H, *J* = 15.4, 7.9 Hz, Me$_2$C=CH-C*H*$_2$), 2.62 (dd, 1H, *J* = 15.4, 7.0 Hz, Me$_2$C=CH-C*H*$_2$), 2.33 (d or s, br., 1H, *J* = 11.2 Hz, O*H*), 1.73 (s, 3H, *E*-C*H*$_3$), 1.68 (s, 3H, *Z*-C*H*$_3$); **^{13}C-NMR** ($CDCl_3$, 100 MHz): 194.0 (C=O), 140.0 (Ar- C_q), 136.4 (C_qMe$_2$), 134.4 (Ar-*C*), 129.1 (Ar-C_q-CO), 128.6 (Ar-*C*), 127.5 (Ar-*C*), 127.2 (Ar-*C*), 116.6 (*C*H=CMe$_2$), 66.4 (*C*-OH), 62.4 (epoxy-C_q), 59.4 (epoxy-*C*H), 26.7 (Me$_2$C=CH-*C*H$_2$), 26.0 (*E*-*C*H$_3$), 18.2 (*Z*-

CH_3); **HRMS (ESI)** m/z calcd. for $C_{15}H_{17}O_3$: $(M+H)^+$, 245.1172; found: 245.1172 $(M+H)^+$; $\mathbf{R_f}$ (*n*-heptane/ethyl acetate 2:1): 0.36; **Chiral HPLC** (Chiralpak IC; hexane:isopropyl alcohol 95:5): **4** (Rt = 12.4 min) : ***ent*-4** (Rt = 10.8 min) 97.0 : 3.0 (94% *ee*); **Specific rotation** $[\alpha]_D^{23.7}$ = − 241.3 (c = 1.18; $CHCl_3$).

(1a*R*,7*S*,7a*R*)-7-Hydroxy-1a-(3-methylbut-2-enyl)-7,7a-dihydronaphtho[2,3-b]oxiren-2-one (*ent*-23) and (1a*R*,7*R*,7a*R*)-7-Hydroxy-1a-(3-methylbut-2-enyl)-7,7a-dihydronaphtho[2,3-b]oxiren-2-one (*ent* -4). *Ent*-23 (0.023 g, 0.100 mmol, 93%) and ***ent*-4** (0.027 g, 0.110 mmol, 79%) were synthesized in analogous manner to **23** starting from ***ent*-22** (0.041 g, 0.100 mmol) and ***ent*-21** (0.055 g, 0.140 mmol). The NMR data are identical to the ones reported for **23** and **4**. For ***ent*-23**: **HRMS (ESI)** m/z calcd. for $C_{15}H_{17}O_3$: $(M+H)^+$, 245.1172; found: 245.1175 $(M+H)^+$; $\mathbf{R_f}$ (*n*-heptane/ethyl acetate 2:1): 0.31; **Chiral HPLC** (Chiralpak IC; hexane:isopropyl alcohol 95:5): ***ent*-23** (Rt = 9.2 min) : **23** (Rt = 8.3 min) 96.2 : 3.8 (92% *ee*); **Specific rotation** $[\alpha]_D^{25.1}$ = + 177.1 (c = 1.10; $CHCl_3$). For ***ent*-4**: **HRMS (ESI)** m/z calcd. for $C_{15}H_{17}O_3$: $(M+H)^+$, 245.1172; found: 245.1172 $(M+H)^+$; $\mathbf{R_f}$ (*n*-heptane/ethyl acetate 2:1): 0.36.; **Chiral HPLC** (Chiralpak IC; hexane:isopropyl alcohol 95:5): ***ent*-4** (Rt = 10.8 min) : **4** (Rt = 12.4 min) 96.3 : 3.7 (93% *ee*); **Specific rotation** $[\alpha]_D^{25.1}$ = + 218.8 (c = 1.26; $CHCl_3$).

[(*S*)-(2-Bromophenyl)-[(2*R*,3*S*)-3-[[*tert*-butyl(diphenyl)silyl]oxymethyl]-3-(3-methylbut-2-enyl)oxiran-2-yl]methyl] acetate (*ent*-29). To a solution of alcohol ***ent*-14** (0.900 g, 1.59 mmol, 1.00 eq.) in anhydrous DCM (23 mL) anhydrous pyridine (0.385 mL, 4.77 mmol, 3.00 eq.), acetic anhydride (0.451 mL, 4.77 mmol, 3.00 eq.) and 4-dimethylaminopyridine (0.019 g, 0.160 mmol, 0.10 eq.) were added. The reaction mixture was stirred for 2 h until the TLC showed complete conversion. Toluene (20 mL) was added and the reaction mixture was concentrated *in vacuo*. The crude product was purified by flash column chromatography (0–30% ethyl acetate in *n*-heptane) to give ***ent*-29** (0.964 g, 1.59 mmol, quant.) as a colorless oil. **^{1}H-NMR** ($CDCl_3$, 400 MHz): 7.68–7.57 (m, 4H, aryl-*H*), 7.49 (dd, 1H, *J* = 8.0, 1.1 Hz, Br-aryl-*H*), 7.46–7.32 (m, 7H, aryl-*H*, Br-aryl-*H*), 7.28 (td, 1H, *J* = 4.4, 1.1 Hz, Br-aryl-*H*), 7.14 (td, 1H, *J* = 7.8, 1.7 Hz, Br-aryl-*H*), 5.87 (d, 1H, *J* = 7.9 Hz, C*H*-OAc), 4.92 (m, 1H, Me_2C=C*H*), 3.81 (d, 1H, *J* = 16.8 Hz, TBDPSO-CH_2), 3.77 (d, 1H, *J* = 16.8 Hz, TBDPSO-CH_2), 3.34 (d, 1H, *J* = 7.9 Hz, epoxy-C*H*), 2.70 (dd, 1H, *J* = 14.9, 7.9 Hz, Me_2C=CH-CH_2), 2.24 (dd, 1H, *J* = 15.0, 6.8 Hz, Me_2C=CH-CH_2), 2.03 (s, 3H, CO-CH_3), 1.63 (s, 3H, *E*-CH_3), 1.53 (s, 3H, *Z*-CH_3), 1.04 (s, 9H, ^{t}Bu-CH_3); **^{13}C-NMR** ($CDCl_3$, 100 MHz): 169.5 (*C*=O), 137.0 (Br-Ar-C_q), 135.9/135.8 (Ar-*C*), 135.4 (C_qMe_2), 133.5 (Br-Ar-*C*), 133.5/133.1 (Ar-C_q), 130.1 (Br-Ar-*C*), 129.9/129.8 (Ar-*C*), 129.2 (Br-Ar-*C*), 127.8/127.8 (Ar-*C*), 127.7 (Br-Ar-*C*), 123.0 (Br-C_q), 117.9 (*C*H=CMe_2), 73.5 (*C*-OAc), 64.9 (TBDPSO-CH_2), 64.8 (epoxy-C_q), 62.5 (epoxy-*C*H), 30.9 (Me_2C=CH-CH_2), 27.0 (^{t}Bu-CH_3), 25.9 (*E*-CH_3), 21.0 (CO-CH_3), 19.4 (^{t}Bu-C_q), 18.1 (*Z*-CH_3); **HRMS (ESI)** m/z calcd. for $C_{33}H_{40}BrO_4Si$: $(M+H)^+$, 607.1874; found: 607.1861 $(M+H)^+$; $\mathbf{R_f}$ (*n*-heptane/ethyl acetate 4:1): 0.37; **Specific rotation** $[\alpha]_D^{18.7}$ = − 8.4 (c = 1.19; $CHCl_3$).

[(*R*)-(2-Bromophenyl)-[(2*R*,3*S*)-3-[[*tert*-butyl(diphenyl)silyl]oxymethyl]-3-(3-methylbut-2-enyl)oxiran-2-yl]methyl] acetate (*ent*-25). *Ent*-25 (0.762 g, 1.25 mmol, 93%) was synthesized in analogous manner to ***ent*-29** starting from ***ent*-13** (0.766 g, 1.35 mmol). It was obtained as colorless oil. **^{1}H-NMR** ($CDCl_3$, 400 MHz): 7.73–7.65 (m, 4H, aryl-*H*), 7.51 (dd, 1H, *J* = 8.1, 1.0 Hz, Br-aryl-*H*), 7.46–7.33 (m, 7H, aryl-*H*, Br-aryl-*H*), 7.30 (td, 1H, *J* = 7.5, 1.2 Hz, Br-aryl-*H*), 7.15 (td, 1H, *J* = 7.7, 1.7 Hz, Br-aryl-*H*), 5.95 (d, 1H, *J* = 7.6 Hz, C*H*-OAc), 5.06 (m, 1H, Me_2C=C*H*), 4.01 (d, 1H, *J* = 11.2 Hz, TBDPSO-CH_2), 3.88 (d, 1H, *J* = 11.4 Hz, TBDPSO-CH_2), 3.20 (d, 1H, *J* = 7.7 Hz, epoxy-C*H*), 2.71 (dd, 1H, *J* = 15.0, 7.6 Hz, Me_2C=CH-CH_2), 2.37 (dd, 1H, *J* = 15.0, 7.0 Hz, Me_2C=CH-CH_2), 1.98 (s, 3H, CO-CH_3), 1.69 (s, 3H, *E*-CH_3), 1.61 (s, 3H, *Z*-CH_3), 1.08 (s, 9H, ^{t}Bu-CH_3); **^{13}C-NMR** ($CDCl_3$, 100 MHz): 169.1 (*C*=O), 137.4 (Br-Ar-C_q), 135.9/135.8 (Ar-*C*), 135.3 (C_qMe_2),.133.4/133.2 (Ar-C_q), 133.2 (Br-Ar-*C*), 129.9 (Br-Ar-*C*), 129.8 (Ar-*C*), 128.8 (Br-Ar-*C*), 127.9/127.8 (Ar-*C*), 127.8 (Br-Ar-*C*), 123.7 (Br-C_q), 118.1 (*C*H=CMe_2), 71.3 (*C*-OAc), 65.3 (epoxy-C_q), 64.1 (TBDPSO-CH_2), 62.4 (epoxy-*C*H), 31.3 (Me_2C=CH-CH_2), 27.0 (^{t}Bu-CH_3), 25.9 (*E*-CH_3), 20.9 (CO-CH_3), 19.4 (^{t}Bu-C_q), 18.2 (*Z*-CH_3); **HRMS (ESI)** m/z calcd. for $C_{33}H_{40}BrO_4Si$: $(M+H)^+$, 607.1874; found: 607.1879 $(M+H)^+$; $\mathbf{R_f}$ (*n*-heptane/ethyl acetate 4:1): 0.40; **Specific rotation** $[\alpha]_D^{18.7}$ = + 10.0 (c = 1.20; $CHCl_3$).

[(2*S*,3*R*)-3-[(*S*)-(2-Bromophenyl)-hydroxy-methyl]-2-(3-methylbut-2-enyl)oxiran-2-yl]methyl acetate (*ent*-31). In a 50 mL falcon tube, acetic acid glacial (0.124 mL, 2.16 mmol, 1.40 eq.) followed by TBAF in THF (1 M, 1.85 mL, 1.85 mmol, 1.20 eq.) were added to a solution of TBDPS-protected ***ent*-29** (0.939 g, 1.55 mmol, 1.00 eq.) in THF (19 mL). After 4 h, a second portion of acetic acid (0.60 eq.) and TBAF (0.50 eq.) were added to complete conversion which was monitored by TLC. The reaction mixture was loaded on silica and was then flash chromatographed (*n*-heptane / ethyl acetate 3:1) to give a mixture of ***ent*-30** and ***ent*-31**. To complete the acetate migration, the product mixture was dissolved in anhydrous DCM (25 mL) and DBU (0.204 mL, 1.36 mmol, 0.90 eq.) was added. After stirring at room temperature for 2.5 h, the LC-MS showed a nearly complete migration (a stagnation of migration with remaining 5–10% of **30** was observed). Saturated aqueous NH_4Cl (30 mL) was added. The mixture was extracted with ethyl acetate (2 x 75 mL) and the combined organic layers were washed with saturated aqueous NaCl (75 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure to yield ***ent*-31** (0.534 g, 1.45 mmol, 94% over two steps)[22] as colorless oil, which was pure enough to be used in the next stage without further purification. **^{1}H-NMR** ($CDCl_3$, 400 MHz): 7.60 (dd, 1H, *J* = 7.7, 1.6 Hz, aryl-*H*), 7.57 (dd, 1H, *J* = 8.0, 1.0 Hz, aryl-*H*), 7.38 (td, 1H, *J* = 7.7, 1.1 Hz, aryl-*H*), 7.20 (td, 1H, *J* = 7.7, 1.6 Hz, aryl-*H*), 5.08–5.01 (m, 2H, C*H*-OH, Me_2C=C*H*), 4.35 (d, 1H, *J* = 12.0 Hz, CH_2-OAc), 4.28 (d, 1H, *J* = 12.1 Hz, CH_2-OH), 3.19 (d, 1H, *J* = 6.4 Hz, epoxy-C*H*), 2.73 (d, br, 1H, *J* = 3.4 Hz, O*H*), 2.56 (dd, 1H, *J* = 14.9, 8.1 Hz, Me_2C=CH-CH_2), 2.21 (dd, 1H, *J* = 14.8, 7.1 Hz, Me_2C=CH-CH_2), 2.06 (s, 3H, CO-CH_3), 1.69 (s, 3H, *E*-CH_3), 1.57 (s, 3H, *Z*-CH_3); **^{13}C-NMR** ($CDCl_3$, 100 MHz): 170.7 (*C*=O), 140.2 (Ar-C_q), 136.3 (C_qMe_2), 133.1 (Ar-*C*), 129.9 (Ar-*C*), 128.3 (Ar-*C*), 128.1 (Ar-*C*), 122.3 (Br-C_q), 117.0 (*C*H=CMe_2), 69.8 (*C*-OH), 65.0 (epoxy-*C*H), 64.3 (*C*H_2-OAc), 63.2 (epoxy-C_q), 32.0 (Me_2C=CH-*C*H_2), 25.9 (*E*-CH_3), 20.9 (CO-CH_3), 18.0 (*Z*-CH_3); **HRMS (ESI)** m/z calcd. for $C_{17}H_{21}BrO_4Na$: $(M+Na)^+$, 391.0515; found: 391.0516 $(M+Na)^+$; $\mathbf{R_f}$ (*n*-heptane/ethyl acetate 2:1): 0.40; **Specific rotation** $[\alpha]_D^{18.7}$ = + 7.3 (c = 0.82; $CHCl_3$).

[(2*S*,3*R*)-3-[(*R*)-(2-Bromophenyl)-hydroxy-methyl]-2-(3-methylbut-2-enyl)oxiran-2-yl]methyl acetate (*ent*-27). ***Ent*-27** (0.411 g, 1.11 mmol, 91% over two steps)[22] was synthesized in analogous manner to ***ent*-31** starting from ***ent*-25** (0.423 g, 1.14 mmol). It was obtained as colorless oil. **^{1}H-NMR** ($CDCl_3$, 400 MHz): 7.60 (dd, 1H, *J* = 7.8, 1.7 Hz, aryl-*H*), 7.56 (dd, 1H, *J* = 8.1, 1.1 Hz, aryl-*H*), 7.37 (td, 1H, *J* = 7.5, 1.1 Hz, aryl-*H*), 7.18 (td, 1H, *J* = 7.6, 1.7 Hz, aryl-*H*), 5.22 (dd, 1H, *J* = 7.6, 1.7 Hz, C*H*-OH), 5.09 (m, 1H, Me_2C=C*H*), 4.40 (d, 1H, *J* = 12.1 Hz, CH_2-OAc), 4.35 (d, 1H, *J* = 12.1 Hz, CH_2-OH), 3.21 (d, 1H, *J* = 7.6 Hz, epoxy-C*H*), 3.19–3.14 (m, 1H, O*H*), 2.36 (d, br, 2H, *J* = 7.6 Hz, Me_2C=CH-CH_2), 2.13 (s, 3H, CO-CH_3), 1.70 (s, 3H, *E*-CH_3), 1.60 (s, 3H, *Z*-CH_3); **^{13}C-NMR** ($CDCl_3$, 100 MHz): 171.5 (*C*=O), 139.9 (Ar-C_q), 136.0 (C_qMe_2), 133.1 (Ar-*C*), 129.7 (Ar-*C*), 128.3 (Ar-*C*), 128.0 (Ar-*C*), 122.9 (Br-C_q), 117.3 (*C*H=CMe_2), 69.8 (*C*-OH), 65.2 (epoxy-*C*H), 63.5 (*C*H_2-OAc), 62.0 (epoxy-C_q), 32.2 (Me_2C=CH-*C*H_2), 26.0 (*E*-*C*H_3), 21.0 (CO-*C*H_3), 18.1 (*Z*-*C*H_3); **HRMS (ESI)** m/z calcd. for $C_{17}H_{21}BrO_4Na$: $(M+Na)^+$, 391.0515; found: 391.0517 $(M+Na)^+$; **R_f** (*n*-heptane/ethyl acetate 2:1): 0.43; **Specific rotation** $[\alpha]_D^{18.7}$ = − 16.0 (c = 1.03; $CHCl_3$).

[(2*S*,3*R*)-3-[(*S*)-(2-Bromophenyl)-triisopropylsilyloxy-methyl]-2-(3-methylbut-2-enyl)oxiran-2-yl]methyl acetate (*ent*-32). 2,6-Lutidine (1.00 mL, 8.56 mmol, 6.00 eq.) followed by TIPS triflate (1.15 mL, 4.28 mmol, 3.00 eq.)were added to a solution of alcohol ***ent*-31** (0.527 g, 1.43 mmol, 1.00 eq.) in anhydrous DCM (20 mL) at 0 °C. The reaction mixture was allowed to stir at room temperature for 2 h. After this time, the TLC showed remaining starting material. Therefore a second portion of 2,6-lutidine (2.00 eq.) and TIPS triflate (1.00 eq.) were added at 0°C. After stirring at room temperature for additional 3 h, the TLC showed a complete conversion. Saturated aqueous NH_4Cl (30 mL) was added. The mixture was extracted with ethyl acetate (2 x 100 mL) and the combined organic layers were washed with saturated aqueous NaCl (70 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was prepurified by flash column chromatography (0–20% ethyl acetate in *n*-heptane) and finally purified by flash column chromatography (0–20% ethyl acetate in *n*-heptane) to give ***ent*-32** (0.555 g, 1.06 mmol, 74%) as a colorless solid. In a 4 mL Vial, a small portion of ***ent*-32** was dissolved in DCM (1 mL) and *n*-heptane (1.5 mL) was added. The system was left at room temperature for one night. A crystal was obtained for determination by single X-ray crystal diffraction (see Supporting Information for further details). **^{1}H-NMR** ($CDCl_3$, 400 MHz): 7.58 (dd, 1H, *J* = 7.8, 1.7 Hz, aryl-*H*), 7.51 (dd, 1H, *J* = 8.1, 1.1 Hz, aryl-*H*), 7.36 (td, 1H, *J* = 7.5, 1.0 Hz, aryl-*H*), 7.16 (td, 1H, *J* = 7.7, 1.7 Hz, aryl-*H*), 5.06 (d, 1H, *J* = 7.7 Hz, C*H*-OTIPS), 4.90 (m, 1H, Me_2C=C*H*), 4.23 (d, 1H, *J* = 11.9 Hz, CH_2-OAc), 4.12 (d, 1H, *J* = 11.9 Hz, CH_2-OAc), 3.24 (d, 1H, *J* = 7.7 Hz, epoxy-C*H*), 2.42 (dd, 1H, *J* = 14.9, 7.8 Hz, Me_2C=CH-CH_2), 2.10 (dd, 1H, *J* = 14.8, 7.2 Hz, Me_2C=CH-CH_2), 2.01 (s, 3H, CO-CH_3), 1.61 (s, 3H, *E*-CH_3), 1.47 (s, 3H, *Z*-CH_3), 1.16–0.91 (m, 21H, TIPS-*H*); **^{13}C-NMR** ($CDCl_3$, 100 MHz): 170.8 (*C*=O), 141.4 (Ar-C_q), 135.6 (C_qMe_2), 132.9 (Ar-*C*), 129.8 (Ar-*C*), 129.6 (Ar-*C*), 127.9 (Ar-*C*), 121.8 (Br-C_q), 117.5 (*C*H=CMe_2), 72.5 (*C*H-OTIPS), 67.6 (epoxy-*C*H), 65.3 (*C*H_2-OAc), 62.2 (epoxy-C_q), 32.1 (Me_2C=CH-*C*H_2), 25.8 (*E*-*C*H_3), 20.9 (CO-*C*H_3), 17.9 (*Z*-*C*H_3), 18.0/17.8/12.4 (TIPS-*C*); **HRMS (ESI)** m/z calcd. for $C_{26}H_{41}BrO_4SiNa$: $(M+Na)^+$, 547.1850; found: 547.1853 $(M+Na)^+$; **R_f** (*n*-heptane/ethyl acetate 4:1): 0.52; **Specific rotation** $[\alpha]_D^{21.6}$ = + 15.8 (c = 0.95; $CHCl_3$).

[(2*S*,3*R*)-3-[(*R*)-(2-Bromophenyl)-triisopropylsilyloxy-methyl]-2-(3-methylbut-2-enyl)oxiran-2-yl]methyl acetate (*ent*-28). ***Ent*-28** (0.484 g, 0.920 mmol, 74%) was synthesized in analogous manner to ***ent*-32** starting from ***ent*-27** (0.404 g, 1.09 mmol). It was obtained as colorless oil. **^{1}H-NMR** ($CDCl_3$, 400 MHz): 7.59 (dd, 1H, *J* = 7.8, 1.6 Hz, aryl-*H*), 7.50 (dd, 1H, *J* = 8.0, 1.1 Hz, aryl-*H*), 7.35 (td, 1H, *J* = 7.5, 1.0 Hz, aryl-*H*), 7.15 (td, 1H, *J* = 7.7, 1.7 Hz, aryl-*H*), 5.38 (d, 1H, *J* = 5.9 Hz, C*H*-OTIPS), 4.99 (m, 1H, Me_2C=C*H*), 4.53 (d, 1H, *J* = 11.8 Hz, CH_2-OAc), 4.46 (d, 1H, *J* = 11.8 Hz, CH_2-OAc), 3.10 (d, 1H, *J* = 5.9 Hz, epoxy-C*H*), 2.57 (dd, 1H, *J* = 14.6, 8.1 Hz, Me_2C=CH-CH_2), 2.12 (s, 3H, CO-CH_3), 2.06 (dd, 1H, *J* = 14.6, 7.1 Hz, Me_2C=CH-CH_2), 1.64 (s, 3H, *E*-CH_3), 1.52 (s, 3H, *Z*-CH_3), 1.12–0.94 (m, 21H, TIPS-*H*); **^{13}C-NMR** ($CDCl_3$, 100 MHz): 170.9 (*C*=O), 141.4 (Ar-C_q), 135.7 (C_qMe_2), 132.6 (Ar-*C*), 129.5 (Ar-*C*), 128.9 (Ar-*C*), 127.9 (Ar-*C*), 122.1 (Br-C_q), 117.7 (*C*H=CMe_2), 69.8 (*C*H-OTIPS), 65.9 (epoxy-*C*H), 64.1 (*C*H_2-OAc), 62.7 (epoxy-C_q), 32.1 (Me_2C=CH-*C*H_2), 25.9 (*E*-*C*H_3), 21.0 (CO-*C*H_3), 17.9 (*Z*-*C*H_3), 17.9/17.9/12.3 (TIPS-*C*); **HRMS (ESI)** m/z calcd. for $C_{26}H_{41}BrO_4SiNa$: $(M+Na)^+$, 547.1850; found: 547.1832 $(M+Na)^+$; **R_f** (*n*-heptane/ethyl acetate 4:1): 0.53; **Specific rotation** $[\alpha]_D^{21.6}$ = − 21.0 (c = 1.38; $CHCl_3$).

(2*S*,3*R*)-3-[(*S*)-(2-Bromophenyl)-triisopropylsilyloxy-methyl]-2-(3-methylbut-2-enyl)oxirane-2-carbonitrile (*ent*-34). Alcohol ***ent*-19** (0.409 g, 0.850 mmol, 1.00 eq.) was dissolved in MeCN/H_2O 9:1 (30 mL/3.3 mL) and NH_4OAc (0.261 g, 3.39 mmol, 4.00 eq.), BIAB (0.818 g, 2.54 mmol, 3.00 eq.), and TEMPO (0.027 g, 0.170 mmol, 0.20 eq.) were added. The reaction solution was allowed to stir 8.5 h at room temperature, until the TLC and the LC-MS showed a complete conversion to the nitrile (n.b. the starting material is first converted to the intermediate aldehyde and then converted to the nitrile in a two-step fashion). Saturated aqueous Na_2SO_3 (30 mL) was added. The mixture was extracted with ethyl acetate (100 mL) and the separated organic layer was washed with saturated aqueous NaCl (30 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified *via* flash column chromatography (0–5% ethyl acetate in *n*-heptane) to give nitrile ***ent*-34** (0.277 g, 0.580 mmol, 68%) as a colorless solid. **^{1}H-NMR** ($CDCl_3$, 400 MHz): 7.61 (dd, 1H, *J* = 7.8, 1.7 Hz, aryl-*H*), 7.57 (dd, 1H, *J* = 8.0, 1.0 Hz, aryl-*H*), 7.34 (td, 1H, *J* = 7.5, 1.0 Hz, aryl-*H*), 7.20 (td, 1H, *J* = 7.7, 1.7 Hz, aryl-*H*), 5.19 (d, 1H, *J* = 7.6 Hz, C*H*-OTIPS), 5.04 (m, 1H, Me_2C=C*H*), 3.39 (d, 1H, *J* = 7.6 Hz, epoxy-C*H*), 2.50 (dd, 1H, *J* = 14.9, 7.6 Hz, Me_2C=CH-CH_2), 2.41 (dd, 1H, *J* = 15.0, 7.4 Hz, Me_2C=CH-CH_2), 1.69 (s, 3H, *E*-CH_3), 1.54 (s, 3H, *Z*-CH_3), 1.18–0.94 (m, 21H, TIPS-*H*); **^{13}C-NMR** ($CDCl_3$, 100 MHz): 139.6 (Ar-C_q), 138.7 (C_qMe_2), 133.4 (Ar-*C*), 130.2 (Ar-*C*), 130.0 (Ar-*C*), 127.8 (Ar-*C*), 122.0 (Br-C_q), 117.5 (*C*N), 114.6 (*C*H=CMe_2), 73.6 (*C*H-OTIPS), 65.9 (epoxy-*C*H), 53.8 (epoxy-C_q), 33.1 (Me_2C=CH-*C*H_2), 25.9 (*E*-*C*H_3), 18.2 (*Z*-*C*H_3), 18.0/17.9/12.4 (TIPS-*C*); **HRMS (ESI)** m/z calcd. for $C_{24}H_{37}BrNO_2Si$: $(M+H)^+$, 478.1771; found: 478.1778 $(M+H)^+$; **R_f** (*n*-heptane/ethyl acetate 10:1): 0.52; **Specific rotation** $[\alpha]_D^{21.7}$ = + 14.6 (c = 1.17; $CHCl_3$).

(2*S*,3*R*)-3-[(*R*)-(2-Bromophenyl)-triisopropylsilyloxy-methyl]-2-(3-methylbut-2-enyl)oxirane-2-carbonitrile (*ent*-33).

***Ent*-33** (0.201 g, 0.420 mmol, 63%) was synthesized in analogous manner to ***ent*-24** starting from ***ent*-16** (0.322 g, 0.670 mmol). It was obtained as a colorless oil. **^{1}H-NMR** ($CDCl_3$, 400 MHz): 7.73 (dd, 1H, *J* = 7.8, 1.3 Hz, aryl-*H*), 7.54 (dd, 1H, *J* = 8.0, 1.0 Hz, aryl-*H*), 7.39 (td, 1H, *J* = 7.6, 1.0 Hz, aryl-*H*), 7.19 (td, 1H, *J* = 7.7, 1.7 Hz, aryl-*H*), 5.50 (d, 1H, *J* = 5.5 Hz, C*H*-OTIPS), 5.07 (m, 1H, Me_2C=C*H*), 3.18 (d, 1H, *J* = 5.4 Hz, epoxy-C*H*), 2.58 (dd, 1H, *J* = 14.9, 7.8 Hz, Me_2C=CH-CH_2), 2.39 (dd, 1H, *J* = 15.0, 7.3 Hz, Me_2C=CH-CH_2), 1.70 (s, 3H, *E*-CH_3), 1.57 (s, 3H, *Z*-CH_3), 1.20–0.98 (m, 21H, TIPS-*H*); **^{13}C-NMR** ($CDCl_3$, 100 MHz): 140.2 (Ar-C_q), 138.7 ($C_q$$Me_2$), 132.8 (Ar-*C*), 129.9 (Ar-*C*), 129.1 (Ar-*C*), 128.0 (Ar-*C*), 122.2 (Br-C_q), 117.4 (*C*N), 114.8 (*C*H=CMe_2), 70.2 (*C*H-OTIPS), 65.5 (epoxy-*C*H), 53.0 (epoxy-C_q), 33.3 (Me_2C=CH-*C*H_2), 25.9 (*E*-*C*H_3), 18.1 (*Z*-*C*H_3), 18.0/17.9/12.3 (TIPS-*C*); **HRMS (ESI)** m/z calcd. for $C_{24}H_{37}BrNO_2Si$: $(M+H)^+$, 478.1771; found: 478.1772 $(M+H)^+$; **R_f** (*n*-heptane/ethyl acetate 4:1): 0.64; **Specific rotation** $[\alpha]_D^{21.4}$ = + 4.6 (c = 0.88; $CHCl_3$).

General procedure for a Mitsunobu inversion. Alcohol **13** (0.206 g, 0.370 mmol, 1.00 eq.) was dissolved in anhydrous THF (8 mL). PPh_3 (0.143 g, 0.550 mmol, 1.50 eq.) and HOAc (0.063 mL, 1.09 mmol, 3.00 eq.) were added. Then DIAD (0.107 mL, 0.550 mmol, 1.50 eq.) was added at 0 °C. The reaction solution was allowed to stir at room temperature. Every 1-2 h were added further PPh_3 (1.5 eq.), HOAc (3.00 eq.) and DIAD (1.50 eq.) at 0 °C until the LC-MS showed a complete conversion (n.b. reaction control by TLC is not possible because the starting material and the product showed the same R_f value). In total 6 eq. of DIAD had to be added for a complete conversion. The reaction mixture was loaded on silica and was then purified *via* flash column chromatography (0–20% ethyl acetate in *n*-heptane) to give **29** (0.154 g, 0.25 mmol, 70%) as colorless oil. All analytical data matched with the ones of **29** described in the paragraph "Resynthesis of Avicennone C".

[(*S*)-(2-Bromophenyl)-[(2*S*,3*R*)-3-[[*tert*-butyl(diphenyl)silyl]oxymethyl]-3-(3-methylbut-2-enyl)oxiran-2-yl]methyl] acetate (25). The Mitsunobu reaction of **14** (0.166 g, 0.290 mmol, 1.00 eq.) resulted in a mixture of **25** (0.020 g, 0.030 mmol, 11%), **29** (0.026 g, 0.040 mmol, 15%) and side products **SI5** (0.051 g, 0.080 mmol, 26%) as well as **SI6** (0.028 g, 0.090 mmol, 32%). For both side products (**SI5** and **SI6**) NMR spectra indicated formation of only one specific diastereomer each. However, from analysis of the 2D NMR data it was not possible to unambiguously determine the stereochemistry. For analytical data of **29** see aforementioned synthetic procedure of **29**. The NMR data of **25** are identical to the ones reported for ***ent*-25**. **HRMS (ESI)** m/z calcd. for $C_{33}H_{40}BrO_4Si$: $(M+H)^+$, 607.1874; found: 607.1879 $(M+H)^+$; **R_f** (*n*-heptane/ethyl acetate 4:1): 0.40; **Specific rotation** $[\alpha]_D^{24.7}$ = – 8.7 (c = 0.97; $CHCl_3$).

Resynthesis of Avicennone C under improved conditions.

[(*R*)-(2-Bromophenyl)-[(2*S*,3*R*)-3-[[*tert*-butyl(diphenyl)silyl]oxymethyl]-3-(3-methylbut-2-enyl)oxiran-2-yl]methyl] acetate (29). 29 (0.210 g, 0.350 mmol, 97%) was synthesized in analogous manner to ***ent*-29** starting from **14** (0.201 g, 0.360 mmol). The NMR data are identical to the ones reported for ***ent*-29**. **HRMS (ESI)** m/z calcd. for $C_{33}H_{40}BrO_4Si$: $(M+H)^+$, 607.1874; found: 607.1880 $(M+H)^+$; **R_f** (*n*-heptane/ethyl acetate 4:1): 0.37; **Specific rotation** $[\alpha]_D^{22.3}$ = + 6.7 (c = 0.91; $CHCl_3$).

[(2*R*,3*S*)-3-[(*R*)-(2-Bromophenyl)-hydroxy-methyl]-2-(3-methylbut-2-enyl)oxiran-2-yl]methyl acetate (31). 31 (0.185 g, 0.500 mmol, 98% over two steps)[22] was synthesized in analogous manner to ***ent*-31** starting from **29** (0.187 g, 0.510 mmol). The NMR data are identical to the ones reported for ***ent*-31**. **HRMS (ESI)** m/z calcd. for $C_{17}H_{21}BrO_4Na$: $(M+Na)^+$, 391.0515; found: 391.0520 $(M+Na)^+$; **R_f** (*n*-heptane/ethyl acetate 2:1): 0.40; **Specific rotation** $[\alpha]_D^{26.6}$ = – 10.9 (c = 0.69; $CHCl_3$).

[(2*R*,3*S*)-3-[(*R*)-(2-Bromophenyl)-triisopropylsilyloxy-methyl]-2-(3-methylbut-2-enyl)oxiran-2-yl]methyl acetate (32). 32 (0.174 g, 0.330 mmol, 66%) was synthesized in analogous manner to ***ent*-32** starting from **31** (0.185 g, 0.500 mmol). The NMR data are identical to the ones reported for ***ent*-32**. **HRMS (ESI)** m/z calcd. for $C_{26}H_{41}BrO_4SiNa$: $(M+Na)^+$, 547.1850; found: 547.1849 $(M+Na)^+$; **R_f** (*n*-heptane/ethyl acetate 2:1): 0.67; **Specific rotation** $[\alpha]_D^{21.6}$ = – 20.8 (c = 0.48; $CHCl_3$).

(2*R*,3*S*)-3-[(*R*)-(2-Bromophenyl)-triisopropylsilyloxy-methyl]-2-(3-methylbut-2-enyl)oxirane-2-carbonitrile (34). 34 (0.106 g, 0.220 mmol, 69%) was synthesized in analogous manner to ***ent*-34** starting from **19** (0.157 g, 0.320 mmol). The NMR data are identical to the ones reported for ***ent*-34**. **HRMS (ESI)** m/z calcd. for $C_{24}H_{37}BrNO_2Si$: $(M+H)^+$, 478.1771; found: 478.1768 $(M+H)^+$; **R_f** (*n*-heptane/ethyl acetate 10:1): 0.52; **Specific rotation** $[\alpha]_D^{23.1}$ = – 11.0 (c = 1.18; $CHCl_3$).

(1a*S*,7*R*,7a*S*)-1a-(3-Methylbut-2-enyl)-7-triisopropylsilyloxy-7,7a-dihydronaphtho[2,3-b]oxiren-2-one (22). See aforementioned synthetic procedure for **22** (conditions 2).

(1a*S*,7*R*,7a*S*)-7-Hydroxy-1a-(3-methylbut-2-enyl)-7,7a-dihydronaphtho[2,3-b]oxiren-2-one (23). See aforementioned synthetic procedure for **23**.

[(1a*S*,7*S*,7a*S*)-1a-(3-methylbut-2-enyl)-2-oxo-7,7a-dihydronaphtho[2,3-b]oxiren-7-yl] acetate (35). Alcohol **23** (0.044 g, 0.180 mmol, 1.00 eq.) was dissolved in anhydrous THF (10 mL). PPh_3 (0.142 g, 0.540 mmol, 3.00 eq.) and HOAc (0.062 mL, 1.09 mmol, 6.00 eq.) were added. Then DIAD (0.107 mL, 0.54 mmol, 3.00 eq.) was added at 0 °C. The reaction solution was allowed to stir at room temperature. The TLC showed a complete conversion after 1 h reaction time. The reaction mixture was loaded on silica and purified *via* flash column chromatography (0–40% ethyl acetate in *n*-heptane) to give **35** (0.046 g, 0.16 mmol, 90%) as colorless oil. **^{1}H-NMR** ($CDCl_3$, 400 MHz): 7.96 (dd, 1H, *J* = 7.8, 1.2 Hz, aryl-*H*), 7.61 (td, 1H, *J* = 7.6, 1.3 Hz, aryl-*H*), 7.45 (m, 1H, aryl-*H*), 7.30 (d, 1H, *J* = 7.8 Hz, aryl-*H*), 6.34 (s, 1H, C*H*-OAc), 5.09 (m, 1H, Me_2C=C*H*,), 3.87 (d, 1H, *J* = 2.0 Hz, epoxy-C*H*), 2.95 (dd, 1H, *J* = 15.5, 7.9 Hz, Me_2C=CH-CH_2), 2.64 (dd, 1H, *J* = 15.5, 6.8 Hz, Me_2C=CH-CH_2), 2.33 (s, 3H, CO-CH_3), 1.73 (s, 3H, *E*-CH_3), 1.68 (s, 3H, *Z*-CH_3); **^{13}C-NMR** ($CDCl_3$, 100 MHz): 193.6 (C=O), 171.1 (*C*O-CH_3), 136.7 ($C_q$$Me_2$), 135.7 ($C_q$-CHOAc), 134.1 (Ar-*C*H), 129.7 (epoxy-C_q-CO-C_q), 128.9 (Ar-*C*H), 127.9 (Ar-*C*H), 126.3 (Ar-*C*H), 116.3 (*C*H=CMe_2), 67.8 (*C*H-OAc), 61.4 (epoxy-C_q), 56.2 (epoxy-*C*H), 26.5 (Me_2C=CH-*C*H_2), 26.0 (*E*-*C*H_3), 21.2 (CO-*C*H_3), 18.2 (*Z*-*C*H_3); **HRMS (ESI)** m/z calcd. for $C_{17}H_{19}O_4$: $(M+H)^+$, 287.1278; found: 287.1276 $(M+H)^+$; **R_f** (*n*-heptane/ethyl acetate 2:1): 0.48; **Specific rotation** $[\alpha]_D^{23.6}$ = – 244.5 (c = 1.82; $CHCl_3$).

(1a*S*,7*S*,7a*S*)-7-Hydroxy-1a-(3-methylbut-2-enyl)-7,7a-dihydronaphtho[2,3-b]oxiren-2-one (4). To a solution of **35** (0.046 g, 0.160 mmol, 1.00 eq.) in THF/H_2O (5:1, 6.0 mL/1.2 mL) LiOH · H_2O (0.014 g, 0.32 mmol, 2.00 eq.) was added. The TLC showed a complete conversion after 1.5 h reaction time.

Saturated aqueous $NaHCO_3$ (20 mL) was added. The mixture was extracted with ethyl acetate (2 x 30 mL) and the combined organic layers were washed with saturated aqueous NaCl (20 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (0–30% ethyl acetate in *n*-heptane) to give **4** (0.036 g, 0.150 mmol, 90%) as a colorless solid. For analytical data see aforementioned synthetic procedure of **4**.

[(1a*S*,7*R*,7a*S*)-1a-(3-methylbut-2-enyl)-2-oxo-7,7a-dihydronaphtho[2,3-b]oxiren-7-yl] acetate (36). Alcohol **4** (0.036 g, 0.150 mmol, 1.00 eq.) was dissolved in anhydrous THF (8 mL). PPh_3 (0.115 g, 0.440 mmol, 3.00 eq.) and HOAc (0.050 mL, 0.880 mmol, 6.00 eq.) were added. Then DIAD (0.086 mL, 0.440 mmol, 3.00 eq.) was added at 0 °C. The reaction solution was allowed to stir at room temperature. Since TLC showed incomplete conversion after 2 h, the addition of the same portions of the reagents was repeated three times after 1 h each and one time the next day. 1 h after the last addition of reagents, the reaction mixture was loaded on silica and purified *via* flash column chromatography (0–50% ethyl acetate in *n*-heptane) to give **36** (0.031 g, 0.110 mmol, 73%) as colorless oil and recovered starting material **4** (0.006 g, 0.020 mmol, 16%) as colorless solid.[31] **^{1}H-NMR** ($CDCl_3$, 400 MHz): 7.95 (dd, 1H, *J* = 7.7, 1.2 Hz, aryl-*H*), 7.59 (td, 1H, *J* = 7.5, 1.5 Hz, aryl-*H*), 7.50 (dt, 1H, *J* = 7.6, 1.2 Hz, aryl-*H*), 7.46 (d, br, 1H, *J* = 7.6 Hz, aryl-*H*), 6.46 (d, 1H, *J* = 2.4 Hz, C*H*-OAc), 5.12 (m, 1H, Me_2C=C*H*,), 3.75 (d, 1H, *J* = 2.4 Hz, epoxy-C*H*), 2.91 (dd, 1H, *J* = 15.5, 7.7 Hz, Me_2C=CH-CH_2), 2.70 (dd, 1H, *J* = 15.5, 6.8 Hz, Me_2C=CH-CH_2), 2.05 (s, 3H, CO-CH_3), 1.73 (s, 3H, *E*-CH_3), 1.68 (s, 3H, *Z*-CH_3); **^{13}C-NMR** ($CDCl_3$, 100 MHz): 194.3 (C=O), 170.2 (*C*O-CH_3), 136.4 ($C_q$$Me_2$), 135.5 ($C_q$-CHOAc), 134.1 (Ar-*C*H), 131.0 (epoxy-C_q-CO-C_q), 130.6 (Ar-*C*H), 130.1 (Ar-*C*H), 127.6 (Ar-*C*H), 116.5 (*C*H=CMe_2), 67.8 (*C*H-OAc), 60.4 (epoxy-C_q), 57.1 (epoxy-*C*H), 26.4 (Me_2C=CH-*C*H_2), 26.0 (*E*-*C*H_3), 21.1 (CO-*C*H_3), 18.1 (*Z*-*C*H_3); **HRMS (ESI)** m/z calcd. for $C_{17}H_{19}O_4$: $(M+H)^+$, 287.1278; found: 287.1280 $(M+H)^+$; **R_f** (*n*-heptane/ethyl acetate 2:1): 0.53; **Specific rotation** $[\alpha]_D^{22.8}$ = – 239.3 (c = 1.00; $CHCl_3$).

(1a*S*,7*R*,7a*S*)-7-Hydroxy-1a-(3-methylbut-2-enyl)-7,7a-dihydronaphtho[2,3-b]oxiren-2-one (23). To a solution of **36** (0.031 g, 0.110 mmol, 1.00 eq.) in THF/H_2O (5:1, 4.0 mL/0.8 mL) LiOH · H_2O (0.009 g, 0.21 mmol, 2.00 eq.) was added. The TLC showed a complete conversion after 1 h reaction time. Saturated aqueous $NaHCO_3$ (20 mL) was added. The mixture was extracted with ethyl acetate (2 x 30 mL) and the combined organic layers were washed with saturated aqueous NaCl (20 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (0–50% ethyl acetate in *n*-heptane) to give **23** (0.024 g, 0.100 mmol, 93%) as a colorless oil. For analytical data see aforementioned synthetic procedure of **23**.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at http://pubs.acs.org. Detailed experimental procedures including spectroscopic data and crystallographic data as well as determination of enantiomeric excess (PDF).

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[19] The isomerization side products have been characterized after deprotection to **4** and **23**, data and spectra can be found in the Supporting Information.

[20] **24a** is most likely a secondary product of **21** and **22**, respectively, since it occurred after prolonged heating. A hypothesis for a potential reaction mechanism is provided in the Supporting Information.

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[22] The DBU treatment resulted in *ent*-**27** and *ent*-**31**, which are both accompanied by <10% *ent*-**26** and *ent*-**30**. The minor regioisomer was removed after the saponification.

[23] Thermal ellipsoid plot of the molecular structure of ***ent*-32** see Supporting Information.

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[30] A 2.5 M solution of *n*-BuLi in hexane from a commercially supplier was diluted by a factor of four at −78 °C with anhydrous THF for a better handling. For the −100 °C cooling bath a mixture of ethanol and liquid N_2 was used.

[31] No traces of diastereomer **35** were detected, which indicates a full inversion of stereochemistry. The reaction time of the Mitsunobu inversion of **4** to **36** was significantly slower than the conversion of **23** to **35** and required more reagents. After 24 h the reaction was stopped even though traces of starting material were detected *via* TLC.