Further Synthetic Studies Towards the Austrodorane Skeleton: Synthesis of Austrodoral

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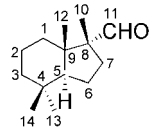
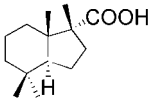
The synthesis of austrodoral (**1**), a marine *nor*-sesquiterpene that contains a unique bicyclic skeleton, has been achieved. The synthetic strategy is based on the ring contraction of a suitable optically active drimanic epoxy derivative, obtained from commercially available (+)-sclareolide (**4**). Fluorosulfonic acid was found to promote the ring contraction efficiently. The *nor*-sesquiterpene hydrocarbon **13**, a key intermediate in the synthesis of sesquiterpene hydroquinones, has also been prepared in optically active form.

Introduction

Austrodoral (**1**) is a *nor*-sesquiterpene recently isolated together with its oxidised work-up derivative **2** from the skin of the marine opisthobranch mollusc *Austrodoris kerguelenensis*.[1] These compounds are characterised by a unique carbon skeleton based on a bicyclic hydrindane template. In order to establish the absolute stereochemistry of these molecules, and also to provide larger amounts of austrodoral (**1**) for evaluating its biological activity, we planned synthetic studies towards this carbon framework. The first approach considered in this project led to the formation of austrodoric acid (**2**) in nine steps with an overall yield of 8%, as described recently.[2] This synthetic strategy is based on the ring contraction of a suitable homodrimanic epoxide, followed by side-chain cleavage. However the conversion of compound **2**, or of the corresponding methyl ester, into austrodoral (**1**) did not occur as expected, most probably due to steric hindrance of the tertiary carboxyl group. So, with the aim of obtaining the aldehyde **1** we decided to explore two different approaches starting from the easily available drimane starting material **3**. We report here the results of this investigation.



austrodoral (**1**)



austrodoric acid (**2**)

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Results and Discussion

The retrosynthetic analysis (Scheme 1) assumed two different pathways (a) and (b), both starting from the drimane hydroxyacetate **3**, which is easily available from the commercial (+)-sclareolide (**4**) by a known procedure.[3]

According to approach (a), hydroxy acetate **3** should be transformed into albicanol (**5**) as reported in the literature[4] and subsequently degraded to *nor*-drimane epoxide **6** to give the desired aldehyde **1** after a ring-contraction step. In approach (b), aldehyde **1** should be obtained by ring contraction of drimane epoxide **7** formed from hydroxy acetate **3** via drimenol acetate **8**.

Approach (a) was considered first. Albicanol (**5**), which was obtained according to the literature procedure,[4] was submitted to mesylation to give derivative **9**, which was subsequently reduced to give the hydrocarbon sesquiterpene **10** (Scheme 2). Hydroxylation of the double bond and cleavage of the resulting diol was performed with osmium tetroxide/sodium periodate in a one-pot procedure, as reported in the literature.[5] Ketone **11** was reduced with sodium borohydride to afford a mixture of epimeric alcohols **12a** and **12b** (**12a/12b** = 2:1). This unresolved mixture was dehydrated with diethyl azodicarboxylate in refluxing tetrahydrofuran[5] to give (+) *nor*-sesquiterpene **13** as the main product, which was identified by comparison of its spectroscopic data with those reported in the literature for the racemic form obtained as an intermediate in the synthesis of fungitoxic sesquiterpene hydroquinones.[6]

According to a literature procedure,[6] compound **13** was subsequently treated with buffered *m*-chloroperbenzoic acid to give a mixture of diastereoisomeric epoxides **6a** and **6b** (**6a/6b** = 4:1). This mixture was then submitted, without purification, to the following key step involving ring contraction in the presence of different acid promoters under

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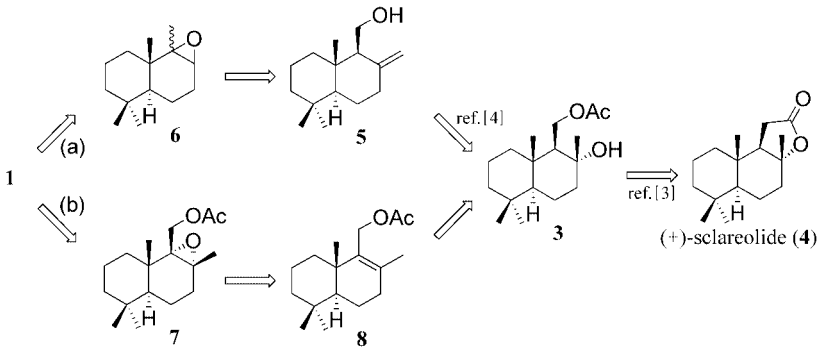
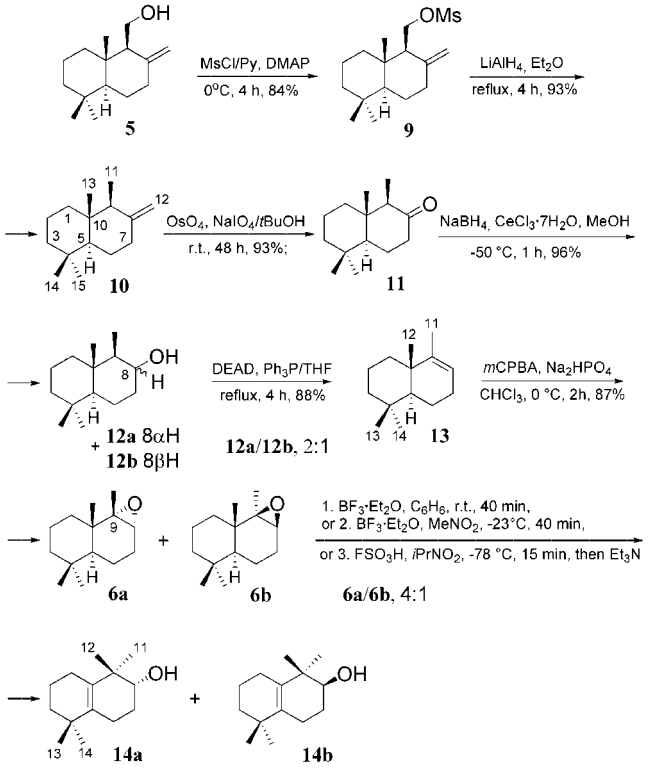


Scheme 1. Retrosynthetic analysis of austrodoral (**1**).

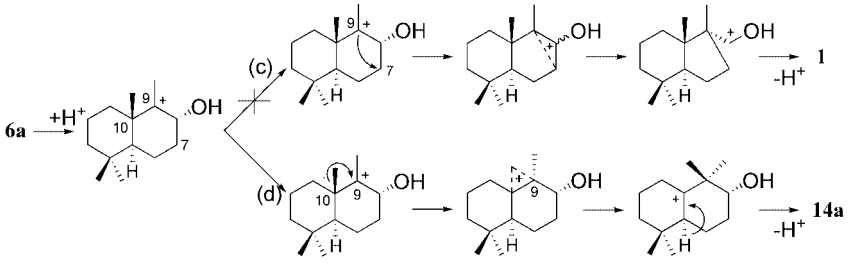


Scheme 2. Pathway (a) leading to compound **14** without ring contraction.

different conditions.[7–9] By analogy with the synthesis of austrodoric acid (**2**),[2] we expected that the epoxides **6a** and **6b**, after opening, would provide the contraction product, aldehyde **1**, however, the secondary alcohol **14** (**a** and **b** enantiomers) was obtained as the main reaction product (Scheme 2).

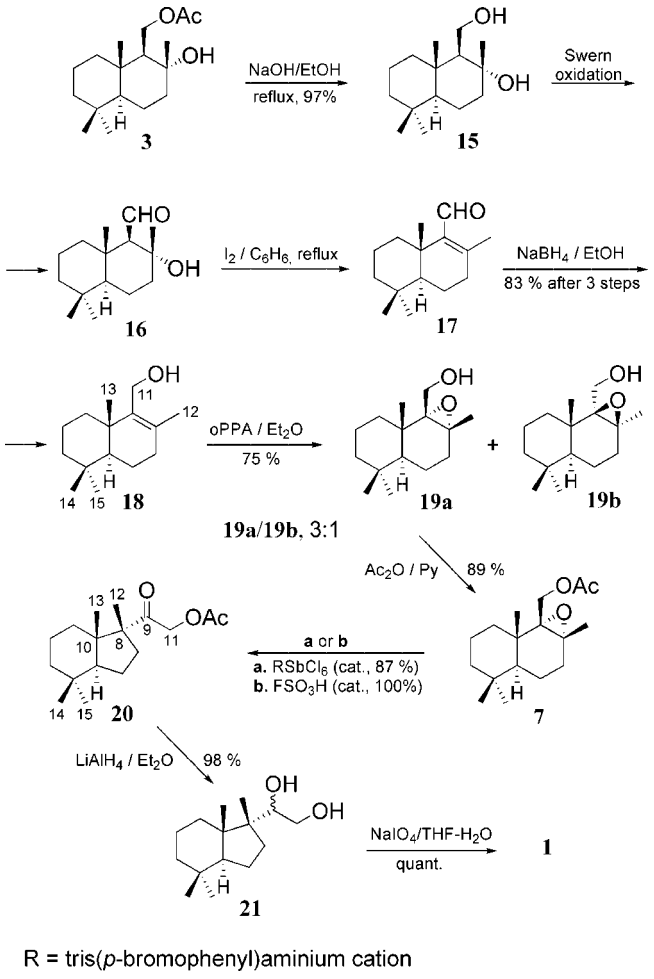
The formation of compound **14** can be rationalised in terms of stabilization of the carbocation at C-9, which is formed by opening of the epoxide ring. The probable reaction mechanism for the formation of the enantiomer **14a** from main α-epoxide **6a** is depicted in Scheme 3. The expected interaction between the carbonium ion at C-9 and the β-carbon C-7 depicted in pathway (c) does not occur, whereas the stabilization of the carbocation at C-9 occurs by migration of the β-methyl group at C-10 [pathway (d)]. In order to confirm the (*R*) absolute stereochemistry at C-8 of the major enantiomer **14a**, the advanced Mosher method[10,11] was applied to the reaction product **14**. According to the MTPA determination rule, the observed values of the ^{1}H NMR chemical shifts of the main (*S*)- and (*R*)-esters formed (from the major enantiomer **14a**, see Exp. Sect.) were in agreement with this absolute configuration.

These results prompted us to consider the approach (b) (Scheme 1), which employs as key step the ring contraction of drimanic epoxide **7** and subsequent cleavage of the side chain. We used as initial starting material the readily available hydroxy acetate **3**[3] (Scheme 4). In order to generate the tetrasubstituted double bond between C-8 and C-9, we tried to perform a dehydration with iodine in refluxing benzene, using the same conditions as those used for the synthesis of austrodoric acid (**2**).[2] However, in this case the dehydration reaction did not occur. Although different refluxing conditions were investigated, the desired tetrasubstituted acetate was not formed. At lower refluxing temperatures (heating bath temperature from 85 °C to 110 °C) the initial starting material remained intact, and at the highest



Scheme 3. Probable reaction mechanism for the formation of **14a**.

reflux temperature (127 °C) a complex mixture of products was formed. We therefore decided to perform the dehydration reaction with a different drimane starting material, the hydroxy aldehyde **16**, which was prepared from 8α,11-drimane diol (**15**) by Swern oxidation (Scheme 4).



Scheme 4. Preparation of austrodoral (**1**) according to pathway (b) of the retrosynthetic analysis.

It has already been reported that aldehyde **16** can be easily dehydrated to the corresponding α,β-unsaturated aldehyde **17** in the presence of *p*-toluenesulfonic acid in refluxing toluene,[12] with a moderate yield of 58%. With the aim of increasing the yield for this step, we decided to use iodine in refluxing benzene as an alternative dehydrating agent. Refluxing **16** for two hours at 95 °C (heating bath temperature) with iodine in benzene provided compound **17** almost quantitatively. Reduction of **17** with sodium borohydride at 0 °C in ethanol afforded bicyclofarnesol (**18**). The overall yield of compound **18** was 83% after three steps. The subsequent epoxidation of **18** with a solution of monoperphthalic acid in diethyl ether provided a mixture of two isomeric epoxy alcohols **19a** and **19b** (**19a**/**19b** = 3:1), which were separated by chromatography and analysed by NMR spectroscopy. The relative stereochemistry of the epoxide group in the two compounds was established by comparing ^{1}H and ^{13}C NMR values of **19a** and **19b** with previously reported related molecules.[2] Particularly diagnostic were the chemical shifts of C-5 and C-7 ($\delta_{C\text{-}5}$ = 43.1 and $\delta_{C\text{-}7}$ = 29.3 ppm in **19a**; $\delta_{C\text{-}5}$ = 53.6 and $\delta_{C\text{-}7}$ = 35.7 ppm in **19b**), due to the steric effect of the α-oriented epoxide group in **19a**, as well as the chemical-shift value of H-5, which resonates at δ = 1.42 ppm in **19a** and at δ = 0.85 ppm in **19b** according to the proposed orientation. The α-epoxide **19a** was acetylated to the corresponding derivative **7**. This compound was used as the starting material for the ring-contraction reaction, which was first carried out with tris(*p*-bromophenyl)aminium hexachloroantimonate ($RSbCl_6$), the same reagent used in the synthesis of austrodoric acid (**2**).[2] Treatment of **7** with a catalytic amount of $RSbCl_6$ in dichloromethane at room temperature provided the desired acetoxy ketone **20** (yield 87%). However, in order to improve the yield of the ring-contraction step, we decided to carry out the reaction with fluorosulfonic acid (FSO_3H), an agent that we have employed widely in our laboratories to perform acid-induced isomerizations of terpenoids at low temperatures. Treatment of **7** with a catalytic amount of FSO_3H in 2-nitropropane at –78 °C provided acetoxy ketone **20** quantitatively. The subsequent conversion of compound **20** to austrodoral (**1**) comprised the reduction with lithium aluminium hydride and cleavage of the resulting mixture of diols **21** with sodium periodate.

The spectral data of synthetic austrodoral (**1**) (^{1}H NMR, ^{13}C NMR, MS, $[\alpha]_D$) were identical with those of the natural product.[1] Synthetic austrodoral (**1**) has been submitted to a preliminary evaluation of its biological activity by assaying ichthyotoxicity in the *Gambusia affinis* test.[13,14] It was found to be very toxic at 10 ppm.

Conclusions

A new synthetic method towards the austrodorane skeleton has been elaborated. It comprises a new, highly selective synthesis of bicyclofarnesol (**18**), followed by epoxidation and ring contraction. Natural austrodoral (**1**) was synthesised starting from 8α,11-drimane diol (**15**), which is readily available from commercial (+)-sclareolide (**4**), in an overall yield of 44% after eight synthetic steps. In addition, fluorosulfonic acid was found to be a new agent for promoting the ring contraction of suitable epoxides efficiently under very mild temperature conditions (–78 °C) and in catalytic amounts. Finally, *nor*-sesquiterpene hydrocarbon **13**, a key intermediate in the synthesis of natural sesquiterpene hydroquinones,[6] has also been prepared in optically active form.

Experimental Section

General: IR spectra were recorded on a Bio-Rad FTS 7 spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on Bruker AM 400 and Bruker WM 300 spectrometers; chemical shifts are reported in ppm and are referenced to chloroform ($CHCl_3$) as internal standard (δ = 7.26 ppm for proton and δ = 77.0 ppm for carbon). Optical rotations were measured in chloroform on a Jasco

DIP 370 polarimeter, using a 10 cm cell and CD curves were recorded on Jasco 710 spectropolarimeter, using a 1 cm cell. Low resolution EI mass spectra were recoreded at 70 eV on a HP-GC 5890 series II mass spectrometer. High resolution ESIMS was performed on a Micromass Q-TOF Micro™. Usual work-up of the reaction mixtures includes exhaustive extraction with diethyl ether, washing successively with 10% sulfuric acid aqueous solution, brine, saturated sodium hydrogencarbonate solution, brine, drying over anhydrous sodium sulfate, filtration, and removal of the solvent under reduced pressure. Commercial Merck Si gel 60 (70–230 mesh ASTM) was used for flash chromatography, and Merck precoated Si gel plates were used for TLC. The chromatograms were sprayed with 0.1% cerium(IV) sulfate in 2 N sulfuric acid and heated at 80 °C for 5 min to detect the spots. All air- and water-sensitive reactions were performed in flasks flame-dried and cooled under a positive flow of argon and conducted under an atmosphere of argon. Benzene and tetrahydrofuran were dried by refluxing with sodium and distillation. Dichloromethane was refluxed over phosphorus pentoxide and distilled. All reagents were purchased from Aldrich and used as received.

Albicanyl Mesylate (9): Mesyl chloride (0.7 mL, 9.04 mmol) and 4-(dimethylamino)pyridine (24.0 mg, 0.20 mmol) were added to a cooled solution (at 0 °C) of albicanol (**5**; 241.5 mg, 1.09 mmol) in dry pyridine (10 mL). The mixture was stirred for 4 h at this temperature, then warmed to room temperature and stirred for another 12 h. The reaction was quenched with ice, and pyridine was removed in vacuo. The residue was dissolved in diethyl ether, worked-up as usual and the residue (312 mg) was purified by flash chromatography (2% diethyl ether/light petroleum ether) to give compound **9** (275 mg, 0.91 mmol, 84%). R_f = 0.17 (20% ethyl acetate/light petroleum ether). $[\alpha]_D^{25}$ = +16.9 (c = 0.40, $CHCl_3$). IR (film): $\tilde{\nu}$ = 1357 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.76 [s, 3 H, C(13)-H], 0.82 [s, 3 H, C(14)-H], 0.89 [s, 3 H, C(15)-H], 1.14 [dd, $J_{H,H}$ = 13, 3 Hz, 1 H, C(5)-H], 1.20 [m, 1 H, C(3)-Ha], 1.30 [m, 1 H, C(1)-Ha], 1.34 [apparent dq, $J_{H,H}$ = 4, 13 Hz, 1 H, C(6)-Ha], 1.42 [m, 1 H, C(3)-Hb], 1.53 [m, 2 H, C(2)-H], 1.72 [m, 1 H, C(1)-Hb], 1.77 [m, 1 H, C(6)-Hb], 2.03 [ddd, $J_{H,H}$ = 13, 13, 4 Hz, 1 H, C(7)-Ha], 2.15 [m, 1 H, C(9)-H], 2.42 [ddd, $J_{H,H}$ = 13, 4, 2 Hz, 1 H, C(7)-Hb], 2.98 [s, 3 H, $-OSO_2CH_3$], 4.34 [dd, $J_{H,H}$ = 10, 10 Hz, 1 H, C(11)-Ha], 4.49 [dd, $J_{H,H}$ = 10, 4 Hz, 1 H, C(11)-Hb], 4.62 [bs, 1 H, C(12)-Ha], 4.91 [bs, 1 H, C(12)-Hb] ppm.^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 15.2 (q, C-13), 19.1 (t, C-2), 21.7 (q, C-14), 23.8 (t, C-6), 33.2 (s, C-4), 33.6 (q, C-15), 37.4 (t, C-7), 37.5 (q, $-OSO_2CH_3$), 39.1 (t, C-1), 39.5 (s, C-10), 41.7 (t, C-3), 55.0 (d, C-5 or C-9), 55.1 (d, C-9 or C-5), 66.6 (t, C-11), 107.7 (t, C-12), 145.6 (s, C-8) ppm. MS (EI): m/z (%) = 300 (3) [M^+], 285 (10), 257 (5), 244 (8), 204 (51), 189 (38), 161 (21), 137 (100), 123 (72), 93 (80), 81 (72), 55 (49). HRMS (ESI) $[M + Na]^+$: m/z = 323.2604. $(C_{16}H_{28}O_3S+Na)^+$ requires 323.2596.

Drim-8(12)-ene (10): Lithium aluminium hydride (540 mg, 14.21 mmol) was added under argon to a solution of mesylate **9** (1.41 g, 4.69 mmol) in anhydrous diethyl ether (35 mL). The reaction mixture was refluxed for 4 h. The mixture was worked-up as usual and the product obtained (0.92 g) was purified by flash chromatography (light petroleum ether) to give compound **10** (904.5 mg, 4.36 mmol, 93%). R_f = 0.93 (2% ethyl acetate/light petroleum ether). $[\alpha]_D^{25}$ = –10.3 (c = 0.57, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 0.67 [s, 3 H, C(13)-H], 0.82 [s, 3 H, C(14)-H], 0.88 [s, 3 H, C(15)-H], 0.89 [d, $J_{H,H}$ = 7 Hz, 3 H, C(11)-H], 1.05 [ddd, $J_{H,H}$ = 13, 13, 4 Hz, 1 H, C(1)-Ha], 1.11 [dd, $J_{H,H}$ = 13, 3 Hz, 1 H, C(5)-H], 1.18 [ddd, $J_{H,H}$ = 13, 13, 4 Hz, 1 H, C(3)-Ha], 1.33 [apparent dq, $J_{H,H}$ = 4, 13 Hz, 1 H, C(6)-Ha], 1.40 [m, 1 H, C(3)-Hb], 1.45 [m, 2 H, C(2)-H], 1.66 [m, 1 H, C(1)-Hb], 1.70 [m, 1 H, C(6)-Hb], 1.81 [m, 1 H, C(9)-H], 2.05 [ddd, $J_{H,H}$ = 13, 13, 4 Hz, 1 H, C(7)-Ha], 2.38 [ddd, $J_{H,H}$ = 13, 4, 2 Hz, 1 H, C(7)-Hb], 4.51 [dd, $J_{H,H}$ = 3.4, 1.7 Hz, 1 H, C(12)-Ha], 4.71 [dd, $J_{H,H}$ = 3.4, 1.7 Hz, 1 H, C(12)-Hb] ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 10.4 (q, C-11), 13.3 (q, C-13), 19.4 (t, C-2), 21.8 (q, C-14), 23.9 (t, C-6), 33.6 (q, C-15), 33.9 (s, C-4), 37.4 (t, C-7), 39.4 (t, C-1), 39.7 (s, C-10), 42.3 (t, C-3), 50.3 (d, C-9), 55.4 (d, C-5), 105.7 (t, C-12), 145.6 (s, C-8) ppm. MS (EI): m/z (%) = 206 (23) [M^+], 191 (34), 177 (13), 163 (11), 150 (16), 137 (100), 123 (31), 121 (28), 109 (31), 95 (47), 81 (39), 69 (23), 55 (16).

12-*nor*-Driman-8-one (11): Acetic acid (1.4 mL), a 2.5% solution of osmium tetroxide (13.7 mg) in *tert*-butyl alcohol (0.55 mL), and a solution of sodium periodate (694 mg, 3.24 mmol) in water (2.0 mL) were added to a solution of hydrocarbon **10** (304 mg, 1.48 mmol) in dry dioxane (29 mL). The reaction mixture was stirred at room temperature for 24 h, then additional aliquots of a 2.5% solution of osmium tetroxide (13.7 mg) in *tert*-butyl alcohol (0.55 mL), and a solution of sodium periodate (694 mg, 3.24 mmol) and water (2.0 mL) were added. The reaction mixture was stirred for a further 48 h and monitored by TLC. At the end of this period the reaction was complete. The mixture was worked-up as usual and the product recovered (308 mg) was purified by silica-gel flash chromatography (2% diethyl ether/light petroleum ether) to give compound **11** (285.5 mg, 1.37 mmol, 93%). R_f = 0.70 (30% ethyl acetate/light petroleum ether). $[\alpha]_D^{25}$ = –50.3 (c = 0.89, $CHCl_3$). IR (film): $\tilde{\nu}$ = 1711 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.73 [s, 3 H, C(12)-H], 0.87 [s, 3 H, C(14)-H], 0.89 [d, $J_{H,H}$ = 7 Hz, 3 H, C(11)-H], 0.97 [s, 3 H, C(13)-H], 1.15 [m, 1 H, C(1)-Ha], 1.26 [m, 1 H, C(3)-Ha], 1.47 [m, 1 H, C(7)-Hb], 1.49 [m, 1 H, C(5)-H], 1.50 [m, 2 H, C(2)-H], 1.69 [m, 1 H, C(1)-Hb], 1.69 [m, 1 H, C(6)-Ha] 2.02 [m, 1 H, C(6)-Hb], 2.20 [q, $J_{H,H}$ = 7 Hz, 1 H, C(9)-H], 2.29 [ddd, $J_{H,H}$ = 14, 14, 7 Hz, 1 H, C(7)-Ha], 2.42 [ddd, $J_{H,H}$ = 14, 5, 2 Hz, 1 H, C(7)-Hb] ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 6.9 (q, C-11), 13.8 (q, C-12), 18.9 (t, C-2), 21.7 (q, C-13), 23.5 (t, C-6), 33.5 (q, C-14), 33.6 (s, C-4), 39.4 (t, C-1), 41.5 (s, C-10), 41.8 (t, C-3 or C-7), 42.0 (t, C-7 or C-3), 54.1 (d, C-5), 58.0 (d, C-9), 213.1 (s, C-8) ppm. MS (EI): m/z (%) = 208 (67) [M^+], 193 (18), 175 (18), 166 (28), 147 (10), 137 (100), 123 (87), 121 (43), 109 (44), 95 (61), 81 (47), 69 (29), 55 (20).

Compounds 12a and **12b:** Cerium(III) chloride heptahydrate (250 mg, 0.67 mmol) was added to a solution of ketone **11** (193 mg, 0.93 mmol) in MeOH (8.9 mL). The suspension was stirred at room temperature for 10 min and then cooled to –50 °C. Sodium borohydride ($NaBH_4$, 105.3 mg, 2.79 mmol) was added in small portions and the reaction was stirred at –20 °C for 1 h. The reaction was quenched with 10% sulfuric acid aqueous solution. The mixture was worked up as usual and the product (190 mg) was purified by silica-gel flash chromatography (diethyl ether/light petroleum ether gradient). The main diastereoisomer **12a** (118.0 mg, 0.57 mmol, 61%) was eluted with 2% diethyl ether/light petroleum ether, whereas the minor diastereoisomer **12b** (68.1 mg, 0.32 mmol, 35%) was recovered with 3% diethyl ether/light petroleum ether.

12-*nor*-Driman-8β-ol (12a): R_f = 0.64 (30% ethyl acetate/light petroleum ether). $[\alpha]_D^{25}$ = +1.07 (c = 0.47, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3649 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.86 [s, 3 H, C(13)-H], 0.87 [m, 1 H, C(1)-Ha], 0.88 [s, 3 H, C(14)-H], 0.89 [m, 1 H, C(5)-H], 0.94 [d, $J_{H,H}$ = 7 Hz, 3 H, C(11)-H], 0.99 [s, 3 H, C(12)-H], 1.15 [ddd, $J_{H,H}$ = 13, 13, 4 Hz, 1 H, C(3)-Ha], 1.25 [m, 1 H, C(9)-H], 1.40 [m, 1 H, C(2)-Ha], 1.41 [m, 1 H, C(3)-Hb], 1.58 [m, 3 H, C(6)-H and C(7)-Ha], 1.60 [m, 1 H, C(2)-Hb], 1.65 [m, 1 H, C(1)-Hb], 1.91 [m, 1 H, C(7)-Hb], 3.76 [m, $w_{½}$ = 7 Hz, 1 H, C(8)-H] ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 11.7 (q, C-11), 15.2 (q, C-12), 17.1 (q, C-3), 18.3 (t, C-2), 21.7 (q, C-13), 33.2 (s, C-4),

33.6 (q, C-14), 35.3 (t, C-8), 39.4 (t, C-1 and s, C-10), 42.2 (t, C-3), 48.7 (d, C-9), 56.0 (d, C-5), 72.9 (d, C-8) ppm. MS (EI): *m*/*z* (%) = 210 (11) [M^+], 192 (33), 177 (91), 163 (13), 149 (20), 137 (67), 124 (100), 109 (87), 95 (79), 81 (77), 69 (66), 55 (49).

12-*nor*-Driman-8α-ol (12b): R_f = 0.54 (30% ethyl acetate/light petroleum ether). $[\alpha]_D^{25}$ = –15.0 (*c* = 0.33, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3650 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.77 [s, 3 H, C(12)-H], 0.82 [s, 3 H, C(13)-H], 0.87 [s, 3 H, C(14)-H], 0.90 [d, $J_{H,H}$ = 7 Hz, 3 H, C(11)-H], 0.92 [m, 2 H, C(1)-Ha and C(5) -H], 1.03 [m, 1 H, C(9)-H], 1.13 [ddd, $J_{H,H}$ = 13, 13, 4 Hz, 1 H, C(3)-Ha], 1.25 [m, 1 H, C(7)-Ha], 1.42 [m, 1 H, C(3)-Hb], 1.45 [m, 2 H, C(2)-H], 1.63 [m, 2 H, C(6)-H], 1.69 [m, 1 H, C(1)-Hb], 2.09 [m, 1 H, C(7)-Hb], 3.37 [ddd, $J_{H,H}$ = 10, 10, 5 Hz, 1 H, C(8)-H] ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 9.95 (q, C-11), 13.6 (q, C-12), 18.6 (t, C-2), 20.9 (t, C-6), 21.8 (q, C-13), 33.5 (s, C-4), 33.5 (q, C-14), 36.8 (t, C-7), 37.3 (s, C-7), 39.3 (t, C-1), 42.0 (t, C-3), 52.8 (d, C-9), 54.7 (d, C-5), 72.2 (d, C-8) ppm. MS (EI): *m*/*z* (%) = 210 (8) [M^+], 192 (23), 177 (75), 163 (10), 149 (13), 137 (44), 124 (100), 109 (82), 95 (47), 81 (41), 69 (38), 55 (18).

12-*nor*-Driman-8(9)-ene (13): Triphenylphosphane (871.2 mg, 3.33 mmol) and diethyl azodicarboxylate (DEAD, 586 mg, 3.37 mmol) were added to a solution of alcohols **12a** and **12b** (120 mg, 0.57 mmol) in anhydrous tetrahydrofuran (17.5 mL). The reaction mixture was refluxed for 4 h and then worked-up as usual. The product obtained (105 mg) was purified by silica-gel flash chromatography (light petroleum ether) to give compound **13**[6] (96.7 mg, 0.50 mmol, 88%). R_f = 0.95 (2% ethyl acetate/light petroleum ether). $[\alpha]_D^{25}$ = +64.0 (*c* = 0.27, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 0.86 [s, 3 H, C(13)-H], 0.89 [s, 3 H, C(14)-H], 1.01 [s, 3 H, C(12)-H], 1.12 [m, 1 H, C(1)-Ha], 1.18 [m, 1 H, C(3)-Ha], 1.19 [m, 1 H, C(5)-H], 1.42 [m, 1 H, C(3)-Hb], 1.45 [m, 2 H, C(2)-Ha and C(6)-Ha], 1.58 [bs, 3 H, C(11)-H], 1.60 [m, 1 H, C(6)-Hb], 1.65 [m, 1 H, C(2)-Hb], 1.72 [m, 1 H, C(1)-Hb], 2.03 [m, 2 H, C(7)-H], 5.17 [sharp m, 1 H, C(8)-H] ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 18.1 (q, C-11), 18.6 (t, C-2), 18.9 (t, C-6), 19.6 (q, C-12), 21.6 (q, C-13), 26.8 (t, C-7), 33.3 (s, C-4), 33.3 (q, C-14), 36.8 (t, C-1), 37.9 (s, C-9), 41.9 (t, C-3), 51.6 (d, C-5), 120.4 (d, C-8), 144.3 (s, C-9) ppm. MS (EI): *m*/*z* (%) = 192 (15) [M^+], 177 (13), 149 (100), 123 (44), 107 (39), 95 (34), 81 (38).

Mixture of Epoxides 6a and **6b:** Sodium hydrogen phosphate (Na_2HPO_4, 187 mg, 1.32 mmol) was added to a solution of 3-chloroperbenzoic acid (*m*-CPBA, 137 mg, 0.79 mmol) in reagent grade chloroform (3 mL).[6] The mixture was cooled to 0 °C (ice bath) and alkene **13** (96 mg, 0.50 mmol) in chloroform (1 mL) was added dropwise. After stirring for 2 h, sodium hydrogen phosphate was filtered and washed with chloroform. The combined chloroform layers were washed with a 5% solution of sodium hydroxide (5 mL), water (3 × 5 mL), brine (5 mL), dried with sodium sulfate, filtered, and the solvents evaporated in vacuo to give 97 mg of crude epoxides **6a** and **6b**.[6] This residue was purified by flash chromatography (2% diethyl ether/light petroleum ether) to give the mixture of epoxides **6a** and **6b** (91.2 mg, 0.43 mmol, 87%; ratio **6a**/**6b**, 4:1). Selected ^1H NMR of main diastereoisomer, 12-*nor*-driman-8(9)-α-epoxide (**6a**) (300 MHz, $CDCl_3$): δ = 0.81 [s, 3 H, C(14)-H], 0.84 [s, 3 H, C(13)-H], 1.06 [s, 3 H, C(12)-H], 1.19 [s, 3 H, C(11)-H], 2.85 [sharp m, 1 H, C(8)-H] ppm.

Compounds 14. Procedure A:[7] Boron trifluoride–diethyl ether ($BF_3{\cdot}Et_2O$, 12.3 mg, 0.09 mmol) was added to a stirred solution of epoxides **6a** and **6b** (18.0 mg, 0.09 mmol) in benzene (1.0 mL) at room temperature. The mixture was stirred at room temperature for 40 min and poured into water (2 mL). Usual work-up gave a residue (17.4 mg), which was submitted to flash chromatography. Elution with 2% diethyl ether/light petroleum ether gave compound **14** (9.0 mg) as the major reaction product.

Procedure B.[8] Boron trifluoride–diethyl ether ($BF_3{\cdot}Et_2O$, 6.5 mg, 0.046 mmol) was added to a stirred solution of epoxides **6a** and **6b** (9.0 mg, 0.043 mmol) in nitromethane (0.7 mL) at –23 °C. The mixture was stirred for 1 h and subsequently poured into water (1 mL). After usual work-up, the crude reaction product (8.7 mg), containing alcohol **14** as the main compound, was recovered.

Procedure C.[9] A solution of fluorosulfonic acid (FSO_3 H, 24.8 mg, 0.25 mmol) in 2-nitropropane (0.23 mL) was added to a solution of epoxides **6a** and **6b** (10.3 mg, 0.049 mmol) in 2-nitropropane (0.7 mL) cooled to –78 °C, whilst stirring vigorously. After 15 min of stirring at the same temperature, the mixture was quenched by adding an excess of triethylamine (Et_3N) in *n*-hexane (1:1, 0.35 mL). The cooling bath was removed and water (1 mL) was added carefully to the reaction mixture. Usual work-up gave the crude product (9.8 mg), the main component of which was compound **14**.

4,4,9,9-Tetramethylhexahydronaphtha-5(10)-en-8-ol (14): R_f = 0.47 (20% ethyl acetate/light petroleum ether). IR (film): $\tilde{\nu}$ = 3655 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.96 [s, 3 H, C(14)-H], 0.97 [s, 6 H, C(12)-H and C(13)-H], 1.02 [s, 3 H, C(11)-H], 1.42 [m, 2 H, C(3)-H], 1.58 [m, 2 H, C(2)-H], 1.66 [m, 1 H, C(7)-Ha], 1.78 [m, 1 H, C(7)-Hb], 1.93 [m, 2 H, C(1)-H], 2.04 [m, 1 H, C(6)-Ha], 2.12 [m, 1 H, C(6)-Hb], 3.46 [dd, $J_{H,H}$ = 9, 3 Hz, 1 H, C(8)-H] ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 19.8 (t, C-2), 21.2 (q, C-12), 22.6 (t, C-6), 25.7 (q, C-11), 25.9 (t, C-1), 26.8 (t, C-7), 28.0 (q, C-13 or C-14), 28.5 (q, C-14 or C-13), 34.1 (s, C-4), 39.3 (s, C-9), 39.6 (t, C-3), 76.0 (d, C-8), 132.7 (s, C-10), 133.5 (s, C-5) ppm. MS (EI): *m*/*z* (%) = 208 (20) [M^+], 190 (28), 175 (100), 149 (29), 133 (10), 119 (21), 105 (26), 79 (7).

Absolute Stereochemistry of 14a: (*S*)- and (*R*)-2-Methoxy-2-phenyl-2-(trifluoromethyl)acetates (Mosher esters) of alcohol **14a** were prepared by treatment of **14** (2 mg for each ester) with *R*-(–)- and *S*-(+)-2-methoxy-2-phenyl-2-(trifluoromethyl)acetyl chloride (0.05 mL), respectively, in dry pyridine (0.5 mL) at room temperature for 16 h. For each reaction, the main diastereoisomeric corresponding ester (from **14a** enantiomer) was obtained and purified. Assignment of the ^1H NMR signals of the esters was achieved by analysing ^1H-^1H COSY NMR experiments.

Selected ^1H NMR chemical shifts for *S*-(+)-Mosher ester (400 MHz, $CDCl_3$): δ = 0.92 [s, 3 H, C(12)-H], 0.94 [s, 3 H, C(11)-H], 0.95 [s, 3 H, C(14)-H], 0.97 [s, 3 H, C(13)-H], 1.80 [m, 1 H, C(7)-Ha], 1.92 [m, 1 H, C(7)-Hb], 1.97 [m, 2 H, C(6)-H] ppm

Selected ^1H NMR chemical shifts for *R*-(–)-Mosher ester (400 MHz, $CDCl_3$): δ = 0.89 [s, 3 H, C(14)-H], 0.96 [s, 6 H, C(12)-H and C(13)-H], 1.01 [s, 3 H, C(11)-H], 1.76 [m, 1 H, C(7)-Ha], 1.83 [m, 1 H, C(7)-Hb], 1.92 [m, 2 H, C(1)-H], 2.05 [m, 2 H, C(6)-H] ppm.

8α,11-Drimanediol (15): A solution of sodium hydroxide (441 mg, 11.01 mmol) in water (several drops) and ethanol (2 mL) was added to a solution of 11-acetoxy-8α-drimanol (**3**; 619 mg, 2.20 mmol) in ethanol (3 mL). The resulting reaction mixture was stirred at gentle reflux (heating bath temperature 87 °C) for 2 h. Then, dilution with water (20 mL) and usual work-up gave crude compound **15**[15] (520 mg, 2.18 mmol), which was used in the next step without purification. R_f = 0.13 (30% ethyl acetate/light petroleum ether). $[\alpha]_D^{25}$ = +1.22 (*c* = 0.3, $CHCl_3$). $[\alpha]_D^{25}$ lit.[15] = +1.6 (*c* = 0.63, $CHCl_3$). Selected ^1H NMR (300 MHz, $CDCl_3$): δ = 0.79 [s, 6 H, C(13)-H and C(14)-H], 0.88 [s, 3 H, C(15)-H], 1.35 [s, 3 H, C(12)-H], 3.93 [d, $J_{H,H}$ = 6.5 Hz, 2 H, C(11)-H] ppm.

8α-Hydroxydrimanal (16): A solution of dimethyl sulfoxide (0.68 mL, 9.57 mmol) in dichloromethane (15 mL) was added dropwise to a stirred solution of oxalyl chloride (0.42 mL, 4.79 mmol) in dichloromethane (17.5 mL) cooled to –60 °C. After 3 min of stirring at this temperature, a solution of compound **15** (520 mg, 2.18 mmol) in dichloromethane (15 mL) was added dropwise. After 20 min of stirring (–60 °C) triethylamine (3.36 mL, 23.94 mmol) was added to the reaction mixture, and after another 15 min the cooling bath was removed and water (25 mL) was added at room temperature. After separation of the phases, the aqueous phase was extracted with dichloromethane (3×25 mL) and the combined organic phase was subsequently washed with a 20% sulfuric acid solution, a saturated sodium hydrogencarbonate solution, brine, and dried with sodium sulfate. Evaporation of the solvent under reduced pressure gave crude hydroxy aldehyde **16**[16] (550 mg), which was used in the next step without purification. R_f = 0.41 (30% ethyl acetate/light petroleum ether). Selected ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.83 [s, 3 H, C(14)-H], 0.89 [s, 3 H, C(15)-H], 1.12 [s, 3 H, C(13)-H], 1.38 [s, 3 H, C(12)-H], 10.02 [d, $J_{H,H}$ = 1.1 Hz, 1 H, C(11)-H] ppm.

Isoalbicanal (17): Crude hydroxy aldehyde **16** (515 mg, 2.l6 mmol) was dissolved in dry benzene (110 mL), and sublimed iodine (442 mg, 1.741 mmol) was added to the resulting solution whilst stirring under argon. The reaction mixture was refluxed for 2 h in an oil bath (95 °C). After that, the reaction mixture was quenched with a 5% sodium thiosulfate solution ($Na_2S_2O_3$, 50 mL). Separation of the phases and the extraction of the aqueous phase with diethyl ether (3×25 mL) gave the combined organic phase, which was dried with sodium sulfate. Evaporation of the solvent under reduced pressure gave crude α,β-unsaturated aldehyde **17** (467 mg), which was used in the next step without purification. A small portion of crude aldehyde **17** was subjected to flash chromatography and the spectroscopic data of pure **17** were found to be in agreement with literature data.[12,17] R_f = 0.73 (30% ethyl acetate/light petroleum ether). $[\alpha]_D^{25}$ = +19.2 (c = 0.7, $CHCl_3$). $[\alpha]_D^{25}$ ref.[17] = +46.2 (c = 0.65, $CHCl_3$). Selected ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.85 [s, 3 H, C(14)-H], 0.90 [s, 3 H, C(15)-H], 1.18 [s, 3 H, C(13)-H], 2.03 [s, 3 H, C(12)-H], 2.26 [m, 1 H, C(7)-Ha], 2.55 [m, 1 H, C(7)-Hb], 10.04 [s, 1 H, C(11)-H] ppm.

(+)-11-Hydroxydrim-8-ene (Bicyclofarnesol, 18): Crude aldehyde **17** (467 mg, 2.l2 mmol) was dissolved in ethanol (15 mL) and sodium borohydride (165 mg, 4.4 mmol) was added to this solution whilst stirring at 0 °C. After 2 h of stirring at this temperature, the reaction mixture was carefully quenched by addition of 20% sulfuric acid solution to an acidic pH. Usual work-up gave a crude product (399 mg), which was submitted to flash chromatography (5% ethyl acetate/light petroleum ether) to give pure compound **18**[18] (401 mg, 1.80 mmol, 83% after 3 steps). R_f = 0.43 (20% ethyl acetate/light petroleum ether). $[\alpha]_D^{25}$ = +92.2 (c = 0.1, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3323 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.84 [s, 3 H, C(14)-H], 0.89 [s, 3 H, C(15)-H], 0.96 [s, 3 H, C(13)-H], 1.13 [br. d, $J_{H,H}$ = 13 Hz, 1 H, C(5)-H], 1.16 [ddd, $J_{H,H}$ = 13, 13, 4 Hz, 1 H, C(3)-Ha], 1.25 [ddd, $J_{H,H}$ = 13, 13, 4 Hz, 1 H, C(1)-Ha], 1.41 [m, 2 H, C(2)-Ha and C(3)-Hb], 1.51 [m, 1 H, C(6)-Ha], 1.62 [m, 1 H, C(6)-Hb], 1.66 [m, 1 H, C(2)-Hb], 1.72 [s, 3 H, C(12)-H], 1.87 [m, 1 H, C(1)-Hb], 2.06 [m, 2 H, C(7)-H], 4.04 [d, $J_{H,H}$ = 11.5 Hz, 1 H, C(11)-Ha], 4.20 [d, $J_{H,H}$ = 11.5 Hz, 1 H, C(11)-Hb] ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 18.9 (t, C-2), 18.9 (t, C-6), 18.9 (q, C-12), 20.7 (q, C-13), 21.6 (q, C-14), 33.2 (s, C-4), 33.2 (q, C-15), 33.7 (t, C-7), 36.8 (t, C-1), 38.0 (s, C-10), 41.6 (t, C-3), 51.7 (d, C-5), 58.3 (t, C-11), 132.4 (s, C-8), 141.0 (s, C-9) ppm. MS (EI): m/z (%) = 222 (13) [M$^+$], 204 (7), 191 (26), 177 (5), 161 (8), 147 (7), 135 (11), 124 (43), 121 (21), 109 (100), 95 (28), 81 (18), 69 (18), 55 (16). HRMS (ESI) [M + Na]$^+$: m/z = 245.1877; $(C_{15}H_{26}O+Na)^+$ requires 245.1882.

Epoxides 19a and 19b: Compound **18** (275 mg, 1.24 mmol) was dissolved in diethyl ether (10 mL) and treated with an ethereal solution of monoperphthalic acid (6.52 mL, 2.48 mmol) at 0 °C. The reaction mixture was stirred overnight at this temperature. After this time TLC showed complete conversion of the initial starting material. The reaction mixture was washed with a 5% solution of sodium hydroxide, then with brine to neutral pH. Drying with sodium sulfate and subsequent evaporation of the solvent gave a crude reaction product, which was submitted to flash chromatography (7.5% ethyl acetate/light petroleum ether) to give epoxide **19a** (221 mg, 0.93 mmol, 75%) and epoxide **19b** (75 mg, 0.32 mmol, 26%).

11-Hydroxydrim-8(9)-α-epoxide (19a): R_f = 0.23 (20% ethyl acetate/light petroleum ether). $[\alpha]_D^{25}$ = +60.5 (c = 0.21, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3481, 1459, 1382, 1032 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.80 [s, 3 H, C(14)-H], 0.84 [s, 3 H, C(15)-H], 0.96 [s, 3 H, C(13)-H], 1.16 [ddd, $J_{H,H}$ = 13, 13, 5 Hz, 1 H, C(3)-Ha], 1.29 [s, 3 H, C(12)-H], 1.37 [m, 1 H, C(1)-Ha], 1.38 [m, 1 H, C(3)-Hb], 1.40 [m, 2 H, C(6)-H], 1.42 [m, 1 H, C(5)-H], 1.54 [m, 2 H, C(2)-H], 1.79 [m, 1 H, C(1)-Hb], 1.85 [m, 1 H, C(7)-Ha], 1.98 [m, 1 H, C(7)-Hb], 3.54 [d, $J_{H,H}$ = 11 Hz, 1 H, C(11)-Ha], 3.86 [dd, $J_{H,H}$ = 12 Hz, 1 H, C(11)-Hb] ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 16.1 (q, C-13), 17.3 (t, C-6), 18.3 (t, C-2), 21.4 (q, C-14), 21.5 (q, C-12), 29.3 (t, C-7), 32.9 (s, C-4), 33.3 (q, C-15), 33.9 (t, C-1), 37.1 (s, C-10), 41.3 (t, C-3), 43.1 (d, C-5), 56.8 (t, C-11), 64.5 (s, C-8), 71.2 (s, C-9) ppm. MS (EI): m/z (%) = 238 (25) [M$^+$], 220 (3), 207 (8), 180 (20), 177 (13), 163 (7), 137 (13), 123 (13), 109 (15), 95 (15), 85 (100), 69 (16), 55 (18). HRMS (ESI) [M + Na]$^+$: m/z = 245.1839; $(C_{15}H_{26}O_2+Na)^+$ requires 261.1831.

11-Hydroxydrim-8(9)-β-epoxide (19b): R_f = 0.16 (20% ethyl acetate/light petroleum ether). $[\alpha]_D^{25}$ = +32.3 (c = 1.15, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3468, 1461, 1382, 1027 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.79 [s, 3 H, C(14)-H], 0.84 [s, 3 H, C(15)-H], 0.85 [m, 1 H, C(5)-H], 1.08 [s, 3 H, C(13)-H], 1.21 [m, 1 H, C(6)-Ha], 1.33 [m, 1 H, C(6)-Hb], 1.37 [s, 3 H, C(12)-H], 1.42 [m, 1 H, C(3)-Ha], 1.48 [m, 1 H, C(1)-Ha], 1.57 [m, 1 H, C(2)-Ha], 1.65 [m, 1 H, C(7)-Ha], 1.70 [m, 1 H, C(3)-Hb], 1.71 [m, 1 H, C(2)-Hb], 1.86 [m, 1 H, C(1)-Hb], 2.00 [m, 1 H, C(7)-Hb], 3.74 [d, $J_{H,H}$ = 12 Hz, 1 H, C(11)-Ha], 3.82 [d, $J_{H,H}$ = 12 Hz, 1 H, C(11)-Hb] ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 16.7 (t, C-6), 16.7 (q, C-13), 19.4 (t, C-2), 20.0 (q, C-12), 21.8 (q, C-14), 33.1 (q, C-15), 33.7 (s, C-4), 35.4 (t, C-1), 35.8 (t, C-7), 37.7 (s, C-10), 41.2 (t, C-3), 53.6 (d, C-5), 61.1 (d, C-11), 64.8 (s, C-8), 71.7 (s, C-9) ppm. MS (EI): m/z (%) = 238 (15) [M$^+$], 220 (3), 205 (8), 192 (21), 179 (13), 177 (48), 163 (15), 149 (18), 137 (34), 123 (56), 109 (100), 95 (79), 81 (62), 69 (69), 55 (59).

11-Acetoxydrim-8(9)-α-epoxide (7): Pure epoxy alcohol **19a** (203 mg, 0.85 mmol) was dissolved in pyridine (2 mL) and treated with acetic anhydride (0.5 mL). The reaction mixture was left overnight and than quenched with ice. Dilution with water and usual work-up gave a crude product (227 mg), which was submitted to flash chromatography (3% ethyl acetate/light petroleum ether) to afford pure epoxy acetate **7** (207 mg, 0.74 mmol, 87%). R_f = 0.54 (20% ethyl acetate/light petroleum ether). $[\alpha]_D^{25}$ = +27.8 (c = 0.27, $CHCl_3$). IR (film): $\tilde{\nu}$ = 1744, 1240 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.80 [s, 3 H, C(14)-H], 0.82 [s, 3 H, C(15)-H], 1.05 [s, 3 H, C(13)-H], 1.15 [ddd, $J_{H,H}$ = 13, 13, 5 Hz, 1 H, C(3)-Ha], 1.29 [s, 3 H, C(12)-Ha], 1.35 [m, 4 H, C(1)-Ha, C(3)-Hb and C(6)-H], 1.45 [dd, $J_{H,H}$ = 13, 2.5 Hz,1 H, C(5)-H], 1.52 [m, 2 H, C(2)-Hb], 1.69 [m, 1 H, C(1)-Hb], 1.82 [dd, $J_{H,H}$ = 15, 8 Hz, 1 H, C(7)-Ha], 1.93 [m, 1 H, C(7)-Hb], 2.05 [s, 3 H, -OCOCH$_3$], 4.03 [d, $J_{H,H}$ =

12 Hz, 1 H, C(11)-Ha], 4.47 [d, $J_{H,H}$ = 12 Hz, 1 H, C(11)-Hb] ppm. ^{13}C NMR (75.5 MHz, $CDCl_{33}$): δ = 16.9 (q, C-13), 17.1 (t, C-6), 18.3 (t, C-2), 21.0 (q, –OCO*CH*$_3$), 21.4 (q, C-14), 22.0 (q, C-12), 29.3 (t, C-7), 32.9 (s, C-4), 33.6 (q, C-15), 34.6 (t, C-1), 37.4 (s, C-10), 41.2 (t, C-3), 42.7 (d, C-5), 63.2 (s, C-8), 63.2 (t, C-11), 68.9 (s, C-9), 170.5 (s, –*O*C*O*CH$_3$) ppm. MS (EI): *m*/*z* (%) = 238 (92) [M – $COCH_3$] $^+$, 220 (67), 205 (25), 177 (93), 166 (53), 149 (38), 143 (49), 123 (94), 101 (100), 81 (50), 69 (54), 55 (38). HRMS [M + Na]$^+$: *m*/*z* = 303.1946; ($C_{17}H_{28}O_3$+Na)$^+$ requires 303.1936.

(5*S*,8*R*,10*S*)-9-(Acetoxymethyl)austrodor-9-one (20). Procedure A: Pure epoxy acetate **7** (78 mg, 0.28 mmol) was dissolved in dichloromethane (3 mL) and treated with tris-(*p*-bromophenyl)aminium hexachloroantimonate (4.6 mg, 0.0056 mmol). The reaction mixture was stirred at room temperature for 2 h. The solvent was then evaporated at reduced pressure and the crude product was submitted to flash chromatography (4% ethyl acetate/light petroleum ether) to give pure acetoxy ketone **20** (68 mg, 0,24 mmol, 87%).

Procedure B: Pure epoxy acetate **7** was dissolved (39.7 mg, 0.14 mmol) in 2-nitropropane (0.7 mL) and a solution of fluorosulfonic acid (FSO_3H, 0.82 µL, 0.014 mmol, 0.1 equiv.) in 2-nitropropane (0.3 mL) was added under argon to the resulting solution at –78 °C. After 30 min of stirring, the reaction mixture was quenched with a solution of triethylamine (0.1 mL) in light petroleum ether (0.1 mL). Removal of the cooling bath, dilution with brine (10 mL), and usual work-up gave crude acetoxy ketone **20** (39 mg).

20: R_f = 0.55 (20% ethyl acetate/light petroleum ether). $[\alpha]_D^{25}$ = –30.9 (*c* = 0.23, $CHCl_3$). CD (*n*-hexane) θ_{211} = +416, θ_{291} = –2458. IR (film): $\tilde{\nu}$ = 1717, 1653, 1541 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 [s, 3 H, C(15)-H], 0.87 [s, 3 H, C(13)-H or C(14)-H], 0.88 [s, 3 H, C(14)-H or C(13)-H], 0.99 [m, 1 H, C(3)-Ha], 1.04 [m, 1 H, C(1)-Ha], 1.20 [s, 3 H, C(12)-H], 1.28 [m,1 H, C(7)-Ha], 1.35-1.60 [m, 2 H, C(2)-H], 1.38 [m, 1 H, C(3)-Hb], 1.40 [m, 1 H, C(6)-Ha], 1.58 [m, 1 H, C(1)-Hb], 1.67 [m, 1 H, C(6)-Hb], 2.16 [s, 3 H, -OCOCH$_3$], 2.19 [m, 1 H, C(7)-Hb] 4.66 [d, $J_{H,H}$ = 17 Hz, 1 H, C(11)-Ha], 4.96 [d, $J_{H,H}$ = 17 Hz, 1 H, C(11)-Hb] ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 16.1 (q, C-13), 19.1 (q, C-12), 20.0 (t, C-2), 20.6 (q, –OCO*CH*$_3$), 21.5 (q, C-14), 21.8 (t, C-6), 33.2 (s, C-4), 33.2 (t, C-7), 33.7 (q, C-15), 35.2 (t, C-1), 40.7 (t, C-3), 47.4 (s, C-10), 52.2 (d, C-5), 59.9 (s, C-8), 67.8 (7, C-11), 170.4 (s, –*O*C*O*CH$_3$), 208.9 (s, C-9) ppm. MS (EI): *m*/*z* (%) = 280 (3) [M$^+$], 220 (15), 205 (5), 179 (49), 143 (100), 123 (90), 109 (38), 101 (84), 81 (21), 69 (28), 55 (13). HRMS (ESI) [M + Na]$^+$: *m*/*z* = 303.1940; ($C_{17}H_{28}O_3$+Na)$^+$ requires 303.1936.

Mixture of Diols 21: Acetoxy ketone **20** (38 mg, 0.14 mmol) was dissolved in dry diethyl ether (3 mL) and the resulting solution was treated with lithium aluminium hydride (21 mg, 0.54 mmol) at 0 °C. After stirring for 3 h at room temperature, the reaction mixture was quenched with water and usual work-up gave the crude reaction product, which was submitted to flash chromatography (20% ethyl acetate/light petroleum ether) to give a mixture of diols [(5*S*,8*R*,10*S*)-9-(hydroxymethyl)austrodor-9-ol, **21**] (32 mg, 0.13 mmol, 98%). Selected ^{1}H NMR chemical shifts (400 MHz, $CDCl_3$): δ = 3.40–4.00 [C(9)-H, C(11)-H] ppm.

Austrodoral (1): A sample of diols **21** (12 mg, 0.05 mmol) was dissolved in a mixture of tetrahydrofuran (0.5 mL) and water (0.3 mL) and the resulting solution was treated, whilst stirring, with sodium periodate (32 mg, 0.15 mmol). After stirring for 3 h at room temperature, the reaction mixture was worked-up as usual to afford pure austrodoral (**1**)[1] (10.5 mg, 0.05 mmol). R_f = 0.70 (20% ethyl acetate/light petroleum ether). $[\alpha]_D^{25}$ = +18.3 (*c* = 0.45, $CHCl_3$). $[\alpha]_D^{25}$ ref.[1] = +5 (*c* = 0.3, $CHCl_3$). CD (*n*-hexane) θ_{303} = +997. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 [s, 3 H, C(13)-H], 0.88 [s, 3 H, C(12)-H], 0.89 [s, 3 H, C(14)-H], 0.97 [ddd, $J_{H,H}$ = 13, 13, 4 Hz, 1 H, C(3)-Ha], 1.04 [s, 3 H, C(10)-H], 1.20 [m, 1 H, C(1)-Ha], 1.25 [m, 1 H, C(5)-H], 1.30 [m, 1 H, C(7)-Ha], 1.41 [m, 1 H, C(6)-Ha], 1.42 [m, 1 H, C(3)-Hb], 1.51 [m, 1 H, C(2)-Ha], 1.60 [m, 1 H, C(2)-Hb], 1.65 [m, 1 H, C(1)-Hb], 1.68 [m, 1 H, C(6)-Hb], 2.16 [ddd, $J_{H,H}$ = 13, 10, 6 Hz, 1 H, C(7)-Hb], 9.68 [s, 1 H, C(11)-Ha] ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 15.9 (q, C-12), 16.4 (q, C-10), 19.6 (t, C-2), 21.4 (q, C-14), 21.4 (t, C-6), 28.6 (t, C-7), 33.1 (t, C-1), 33.2 (s, C-4), 33.6 (q, C-13), 41.2(t, C-3), 46.6 (s, C-8), 54.7 (d, C-5), 58.3 (s, C-9), 207.9 (s, C-11) ppm. MS (EI): *m*/*z* (%) = 208 (10) [M$^+$], 191 (13), 177 (11), 150 (5), 137 (75), 123 (100), 95 (66), 81 (47), 67 (34).

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