A New Route to 2,7- and 7-Functionalized Labdanes

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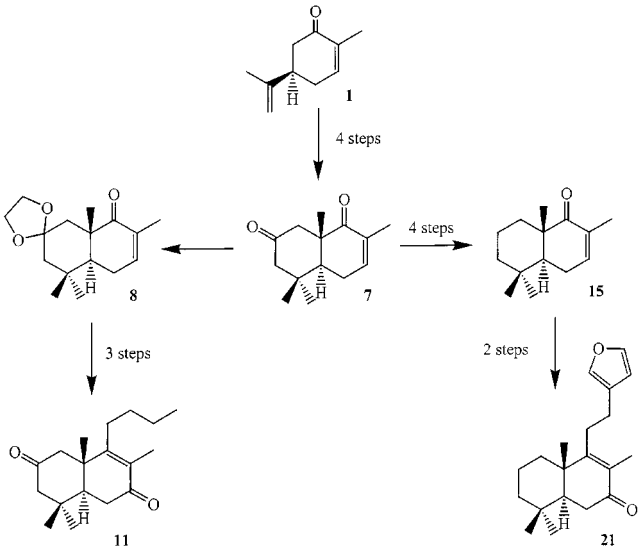
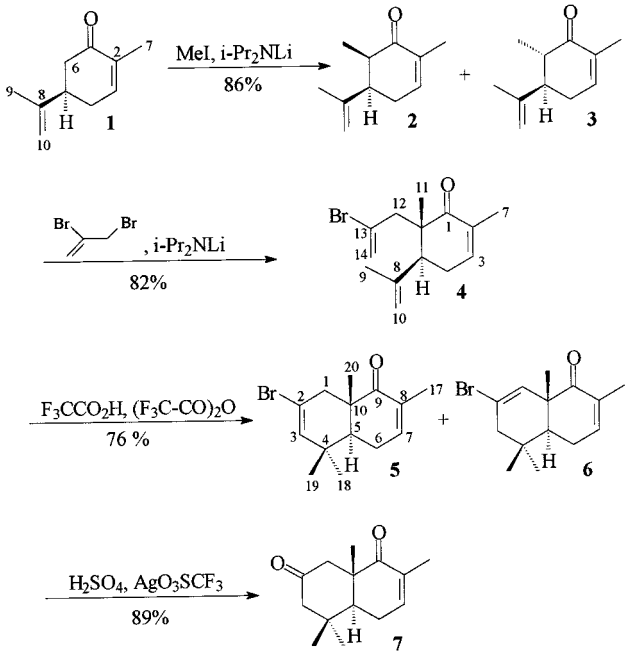
A new route for the synthesis of 2,7- and 7-functionalized labdanes starts from (*R*)-carvone (**1**). 11-Nordrim-7-en-9-one (**15**) is an appropriate starting material for the total synthesis of hispanone (**21**), a biologically active furolabdane isolated from the Mediterranean medicinal plant *Ballota saxatilis*.

Introduction

(*R*)-Carvone (**1**) and its enantiomer are part of the chiral pool. They have already been used for many syntheses of natural products,[1–10] especially labdanes.[11–13] The synthesis of 11-nordrim-7-ene-2,9-dione (**7**) (Scheme 2) and 11-nordrim-7-en-9-one (**15**) has previously been described by Gesson et al.[14,15] We used the monoprotected dione **8** for the first synthesis of the 2,7-functionalized bisnorlabdane (**11**). The vinyl ketone **15** represents an appropriate starting material for the synthesis of hispanone (**21**) (Scheme 1), a fungicidal and bactericidal furolabdane, which was first obtained by the transformation of hispanolone,[16,17] and has also been isolated from the plants *Ballota saxatilis*[18] (Lamiaceae) and *Galeopsis angustifolia*[19] (Labiatae).



Scheme 1. Synthetic routes



Scheme 2. Synthesis of 11-nordrim-7-ene-2,9-dione (**7**)

Results and Discussion

(5*S*,6*S*)-6-(2-Bromoallyl)-6-methylcarvone (**4**) was obtained by the two-fold alkylation of (*R*)-carvone (**1**) in position 6 with MeI (compounds **2** and **3**) and then with 2,3-dibromopropene.[15] The configuration in position 6 of **2** and **3** was assigned according to Gesson et al.[15] The ^{1}H NMR signal of the axial methyl group 3H-11 of **2** was observed at a higher field (δ = 0.86) than the signal of the equatorial methyl group of **3** (δ = 0.95). The ratio of diastereomers **2** and **3** was determined by the integration of the signal of 3H-11 and was found to be 43:57. Treatment of **2** and **3** with LiN*i*Pr$_2$ gave the expected enolate which reacted diastereoselectively with 2,3-dibromopropene to give (5*S*,6*S*)-6-(2-bromoallyl)-6-methylcarvone (**4**). The diastereoselectivity of this reaction is a consequence of the steric hindrance by the isopropenyl group on one side of

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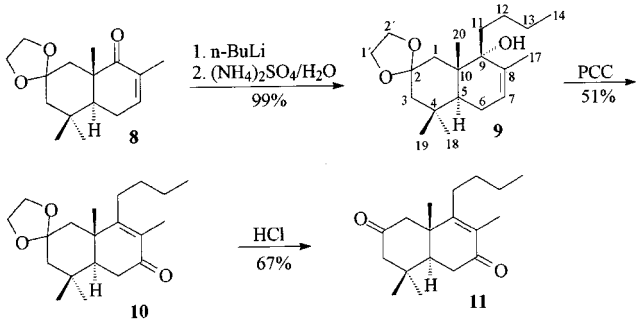
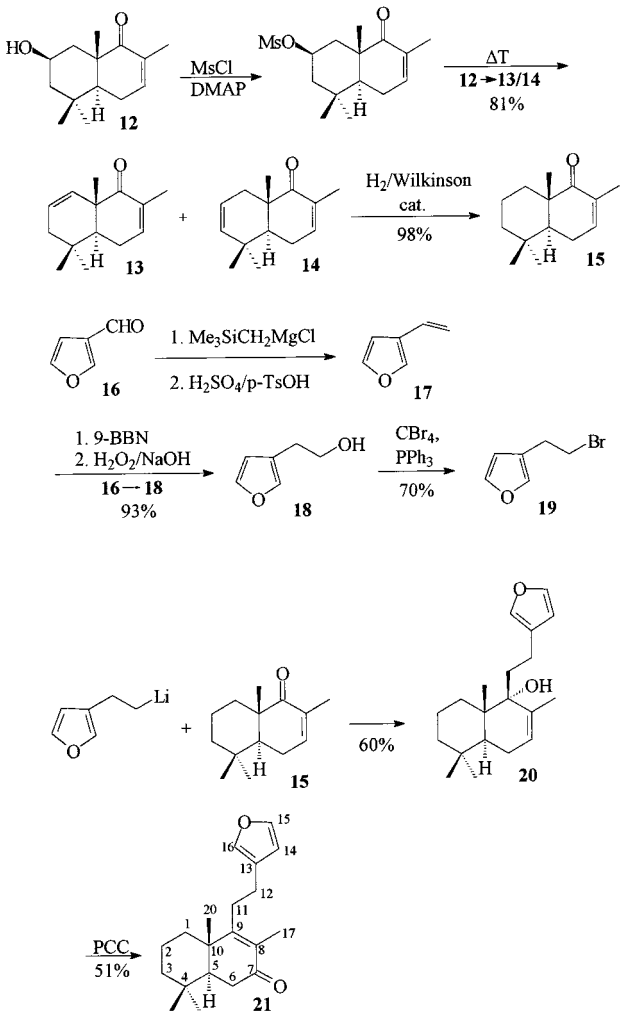
the enolate. The published ^{1}H NMR spectroscopic data of (5*S*,6*S*)-6-(2-bromoallyl)-6-methylcarvone show good agreement with **4** and not with (5*S*,6*R*)-6-(2-bromoallyl)-6-methylcarvone,[15] which could not be detected in the ^{1}H and ^{13}C NMR spectrum of **4**. When **4** was heated for 3 days at 65 °C in 85% phosphoric acid a mixture of the bicyclic bromo ketones **5/6** (38%) and 11-nordrim-7-ene-2,9-dione (**7**) (49%) was produced. The yield of this reaction could be improved to 76% (related to turnover 80%) by cyclization of **4** to 2-bromo-11-nordrima-2,7-dien-9-one (**5**) and 2-bromo-11-nordrima-1,7-dien-9-one (**6**) with TFAA. The mixture of **5** and **6** could not be separated by column chromatography on silica gel. The reaction of **5/6** with 80% sulfuric acid for 24 h at room temperature gave 11-nordrim-7-ene-2,9-dione (**7**) (35%) and unreacted **5** (20%). The hydrogenation of **5/6** under a hydrogen atmosphere at normal pressure with Pd/C as catalyst in ethyl acetate/methanol (4:1) as solvent gave (8*R*)-2-bromo-11-nordrim-2-en-9-one (40%) and **6** (16%). In this way pure samples of **5** and **6** could be obtained and were used for the determination of the spectroscopic data. Compounds **5** and **6** were transformed in a yield of 89% to 11-nordrim-7-ene-2,9-dione (**7**) by means of AgO_3SCF_3 in 80% H_2SO_4 for 10 min at room temperature (Scheme 2).

The 2-oxo-group of **7** was selectively protected as its ethylene ketal to form **8**, which is a new and appropriate building block for labdanes with functionalization in the 2 position. The reaction of **8** with *n*BuLi gave (9*R*)-2,2-ethylenedioxy-15,16-bisnorlabd-7-en-9-ol (**9**), which was transformed to 2,2-ethylenedioxy-15,16-bisnorlabd-8(9)-en-7-one (**10**) by rearrangement and oxidation by PCC in CH_2Cl_2. The (9*R*)-configuration of **9** was determined by a ROESY NMR experiment in [D_6]DMSO. The 9-OH proton showed cross peaks with H_{ax}-1 and H_{ax}-5 which prove the axial orientation of the 9-OH group. After removal of the protecting group 15,16-bisnorlabd-8(9)-ene-2,7-dione (**11**) was obtained (Scheme 3).



Scheme 3. Synthesis of 15,16-bisnorlabd-8(9)-ene-2,7-dione (**11**)

The 2-oxo-group of **7** can be effectively removed to obtain 11-nordrim-7-en-9-one (**15**) in a total yield of 57%. Compound **15** is a useful starting material for the synthesis of labdanes with a double bond in position 8 and no functionalization in ring A. The value of this bicyclic ketone **7** is demonstrated by its use for the synthesis of hispanone



Scheme 4. Synthesis of hispanone (**21**)

(**21**) (Scheme 4). The 2-keto-group of **7** was diastereoselectively reduced with $NaBH_4$ to (2*R*)-2-hydroxy-11-nordrim-7-en-9-one (**12**). (2*S*)-2-Hydroxy-11-nordrim-7-en-9-one could not be detected in the ^{1}H and ^{13}C NMR spectra of **12**. The hydroxy-group of **12** was transformed into the mesylate and eliminated. The selective hydrogenation of the double bond in ring A of the isomers **13** and **14** was tried without success in benzene/methanol (1:1) as solvent in the presence of Wilkinson′s catalyst under a hydrogen atmosphere at normal pressure. In contrast, the yield of the hydrogenation was 98% under a hydrogen pressure of 50 bar at room temperature for 3 days and the above conditions (Scheme 4).

The side chain, 3-(2-bromoethyl)furan (**19**), could be synthesized by two routes. The Diels–Alder reaction of 4-phenyloxazole with 3-butyn-1-ol gave 2-(3-furyl)ethanol (**18**) in a yield of 61%. The methylenation of furan-3-carbaldehyde (**16**) according to Peterson led to **17**, which was hydroborated and oxidized to the alcohol **18** in a total yield of 93%. Compound **18** was transformed to the bromide **19** by reaction with CBr_4 and PPh_3 (Scheme 4). Similar to the synthesis of 15,16-bisnorlabd-8(9)-ene-2,7-dione (**11**), compound **19** was lithiated and coupled to **15**. The tertiary allyl

alcohol **20** was formed in 60% yield. (9*R*)-15,16-Epoxylabda-7,13(16),14-trien-9-ol (**20**) has been obtained before by reaction of 8,9α;15,16-diepoxylabda-13(16),14-dien-7-one with hydrazine.[17] In our hands, it was rearranged and oxidized with PCC to hispanone (**21**) (Scheme 4). A comparison of melting point, optical rotation and spectroscopic data (MS, NMR) of synthetic **21** with natural **21**[16] shows good agreement.

For the first time a bisnorlabdane with keto-groups in the positions 2 and 7 was synthesized starting from (*R*)-carvone. In this way a possible synthetic route for the synthesis of labdanes with functionalization in position 2 and 2/7 was illustrated. The first total synthesis of the 7-functionalized hispanone (**21**) started with the key compound 11-nordrim-7-en-9-one (**15**).

Experimental Section

General Remarks: All solvents were dried and purified prior to use. – THF and diethyl ether were dried by distillation from Na/K under N_2. Column chromatography: Merck silica gel 60, 0.040–0.063 mm (230–400 mesh). – IR: Perkin–Elmer 1420 Ratio Recording Spectrometer; solvent: $CHCl_3$. – Optical rotation values: Perkin–Elmer Polarimeter 241 (589 nm). – MS: Finnigan MAT 8500 and Finnigan MAT SS 300; 70 eV. – NMR: Bruker AC 300 and Bruker DRX 500, $CDCl_3$/$CHCl_3$ as internal standard. – MPLC: Büchi B688 pump and Büchi B687 gradient former; column 17980 with silica gel 60, Lichroprep 15–25 mm. – For TLC runs, precoated silica-gel foils 60 F_{254} (5 × 10 cm) from Merck were used. Spots were visualized by irradiation under an UV lamp or by treatment with the phosphomolybdic acid test spray.

(5*R*,6*R*)-6-Methylcarvone (2): Under an N_2 atmosphere abs. *i*Pr_2NH (5.85 mL, 41.4 mmol) was dissolved in 20 mL of abs. THF and cooled to –15 °C. During 20 min, *n*BuLi (26 mL; 1.6 M in hexane) was added and stirred for 30 min. Over a period of 90 min a solution of (*R*)-carvone (5 mL, 32.0 mmol) in 40 mL of abs. THF was added and stirred for 2 h. Then 10 mL of MeI was added in one go and stirred for 5 d. The solution was acidified with 50 mL of HCl (2.5% in water) and extracted three times with 50 mL of Et_2O. The organic layer was washed twice with 100 mL of NaOH (2 M). The water layer was reextracted twice with 50 mL of Et_2O. The combined organic extracts were dried with Na_2SO_4, concentrated in vacuo, and the residue was purified by MPLC (eluent: gradient hexane/ethyl acetate). 6-Methylcarvone (**2/3**; 4.54 g, 27.6 mmol) was obtained as yellow liquid (86% yield). The diastereomeric mixture of **2** and **3** (4.37 g) could be separated by column chromatography on silica gel (438 g, eluent: cyclohexane/ethyl acetate = 19:1) to give **2** (894 mg), **3** (469 mg) and a mixture of **2** and **3** (2.21 g). R_f = 0.32 (CH/EA = 19:1). – $[\alpha]_D^{22}$ = +37 (*c* = 1.6, $CHCl_3$). – IR ($CHCl_3$): $\tilde{\nu}$ = 3020, 2980, 2930, 1660, 1450, 1380, 1240, 900 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 0.86 (d, *J* = 7.2 Hz, 3 H, 11-H), 1.64 (s, 3 H, 9-H), 1.71–1.73 (m, 3 H, 7-H), 2.26–2.68 (m, 4 H, 4-H, H-5, 6-H), 4.68 (d, *J* = 1.0 Hz, 1 H, 10-H), 4.86 (d, *J* = 1.0 Hz, 1 H, 10-H), 6.64–6.67 (m, 1 H, 3-H). – ^{13}C NMR ($CDCl_3$): δ = 10.4 (C-11), 15.9 (C-7), 21.8 (C-9), 26.2 (C-4), 42.9 (C-6), 44.7 (C-5), 111.4 (C-10), 133.6 (C-2), 143.9 (C-3), 144.8 (C-8), 203.4 (C-1). – EI-MS: *m*/*z* (%) = 164 (10) [M^+·], 149 (8), 121 (9), 108 (45), 107 (38), 98 (30), 93 (24), 82 (100), 67 (11), 54 (16), 41 (13). – HRMS ($C_{11}H_{16}O$): calcd. 164.1201; found: 164.1201.

(5*R*,6*S*)-6-Methylcarvone (3): Prepared as above for **2**. R_f = 0.39 (CH/EA = 19:1). – M.p. 38–40 °C. (ref.[15] M.p. 38 °C). – $[\alpha]_D^{22}$ = +21 (*c* = 1.7, $CHCl_3$). – IR ($CHCl_3$): $\tilde{\nu}$ = 3020, 2980, 2930, 2900, 1660, 1450, 1380, 1240, 1010, 900 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 0.95 (dd, *J* = 6.5 Hz, *J* = 1.7 Hz, 3 H, 11-H), 1.60 (s, 3 H, 9-H), 1.67 (s, 3 H, 7-H), 2.13–2.39 (m, 4 H, 4-H, 5-H, 6-H), 4.70 (s, 2 H, 10-H), 6.58 (dd, *J* = 4.1 Hz, *J* = 1.7 Hz, 1 H, 3-H). – ^{13}C NMR ($CDCl_3$): δ = 12.3 (C-11), 16.0 (C-7), 18.0 (C-9), 31.0 (C-4), 44.1 (C-5), 50.4 (C-6), 113.0 (C-10), 134.6 (C-2), 143.2 (C-3), 145.5 (C-8), 201.5 (C-1). – EI-MS: *m*/*z* (%) = 164 (8) [M^+·], 149 (8), 107 (16), 82 (100), 67 (17), 54 (17), 43 (35), 41 (18), 39 (16). – HRMS ($C_{11}H_{16}O$): calcd. 164.1201; found: 164.1201.

(5*S*,6*S*)-6-(2-Bromoallyl)-6-methylcarvone (4): Under an N_2 atmosphere abs. *i*Pr_2NH (12.1 mL, 85.6 mmol) was dissolved in 75 mL of abs. THF and cooled to –20 °C. *n*BuLi (53.5 mL, 85.6 mmol, 1.6 M in hexane) was added slowly and stirred for 30 min. Over a period of 45 min a solution of 6-methylcarvone (**2/3**; 10.2 g, 62.1 mmol) in 100 mL of abs. THF was added and stirred for 12 h. Then 2,3-dibromopropene (18.2 mL, 186.3 mmol) was added in one go and stirred for 24 h. The solution was acidified with 100 mL of HCl (2.5% in water) and extracted three times with Et_2O (80 mL). The combined organic extracts were dried with Na_2SO_4 and concentrated in vacuo. The residue was purified by MPLC (eluent: gradient hexane/ethyl acetate) to give **4** (14.4 g, 50.7 mmol) as a colourless liquid (82% yield), R_f = 0.75 (CH/EA = 2:1). – $[\alpha]_D^{22}$ = +2 (*c* = 2.9, $CHCl_3$) {ref.[15] $[\alpha]_D$= +3.7 (*c* = 0.5, $CHCl_3$)}. – IR ($CHCl_3$): $\tilde{\nu}$ = 2940, 2910, 1660, 1440, 1430, 1370, 890 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 1.07 (s, 3 H, 11-H), 1.58 (dd, *J* = 1.4 Hz, *J* = 0.7 Hz, 3 H, 9-H), 1.78 (dd, *J* = 3.5 Hz, *J* = 2.0 Hz, 3 H, 7-H), 2.22–2.33 (m, 1 H, 4-H), 2.64–2.75 (m, 1 H, 4-H), 2.70 (dd, *J* = 15.1 Hz, *J* = 0.7 Hz, 1 H, 12-H), 2.82 (dd, *J* = 15.1 Hz, *J* = 1.0 Hz, 1 H, 12-H), 2.89 (dd, *J* = 6.1 Hz, *J* = 4.4 Hz, 1 H, 5-H), 4.71–4.72 (m, 1 H, 10-H), 4.75–4.77 (m, 1 H, 10-H), 5.45–5.46 (m, 1 H, 14-H), 5.55 (d, *J* = 1.9 Hz, 1 H, 14-H), 6.55–6.58 (m, 1 H, 3-H). – ^{13}C NMR ($CDCl_3$): δ = 16.4 (C-7), 19.4 (C-11), 21.9 (C-9), 28.4 (C-4), 48.0 (C-6), 48.7 (C-12), 49.3 (C-5), 114.4 (C-10), 121.0 (C-14), 128.4 (C-13), 134.4 (C-2), 141.3 (C-3), 145.7 (C-8), 202.4 (C-1). – EI-MS: *m*/*z* (%) = 284 (4) [M^+·], 283 (17), 282 (2), 281 (9), 203 (99) [M^+· – Br], 145 (64), 119 (50), 105 (55), 91 (73), 82 (74), 79 (50), 69 (54), 57 (55), 55 (53), 43 (100), 41 (55). – HRMS ($C_{14}H_{19}BrO$): calcd. 282.0619; found: 282.0619.

2-Bromo-11-nordrima-2,7-dien-9-one (5): To 20 mL of trifluoroacetic acid (98%) under an argon atmosphere was added trifluoroacetic acid anhydride (4 mL) and the mixture stirred for 10 min. It was then cooled to 0 °C, compound **4** (4.84 g, 17.09 mmol) added and stirred for 3 d at room temperature. The reaction mixture was then diluted with 40 g of ice and neutralized by slow addition of 18 g of Na_2CO_3. The reaction mixture was extracted three times with 200 mL of Et_2O. The combined organic extracts were washed with 50 mL of sat. NaCl solution, filtered through Na_2SO_4 and silica gel and concentrated in vacuo. The resulting mixture of **5** and **6** (4.85 g) was purified by silica gel chromatography (pentane/Et_2O = 30:1) to give **5/6** (3.67 g, 13.0 mmol; yield: 76%, relative to turnover 80%) and **4** (246 mg, 0.87 mmol; yield: 5%). Pure samples of **5** and **6** were obtained as described above and used for the determination of the spectroscopic data. R_f = 0.42 (CH/EA = 5:1). – IR ($CHCl_3$): $\tilde{\nu}$ = 3010, 2970, 2930, 1730, 1660, 1460, 1430, 1370, 1250, 1040, 1020 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 0.98 (s, 3 H, 18-H), 1.01 (s, 3 H, 19-H), 1.07 (s, 3 H, 20-H), 1.71 (dd, *J* = 3.4 Hz, *J* = 1.8 Hz, 3 H, 17-H), 1.86 (dd, *J* = 8.8 Hz, *J* = 7.5 Hz, 1 H, 5-H), 2.55 (d, *J* = 1.5 Hz, 2 H, 1-H), 2.27–2.32 (m, 2 H, 6-H), 5.74 (t, *J* = 1.5 Hz, 1 H, 3-H), 6.71–6.74 (m, 1 H, 7-H). – ^{13}C NMR ($CDCl_3$): δ = 16.2 (C-17), 17.7 (C-20), 24.0 (C-6), 24.1 (C-19), 30.9 (C-18), 38.4 (C-4), 43.2 (C-1), 45.4 (C-5), 46.7 (C-10), 118.4 (C-2),

133.4 (C-8), 137.2 (C-3), 143.8 (C-7), 203.1 (C-9). – EI-MS: *m/z* (%) = 284 (52) [$M^{+\cdot}$], 282 (54), 269 (28), 267 (29), 241 (99), 239 (100), 203 (45), 187 (51), 161 (28), 159 (60), 145 (25), 121 (26), 105 (34), 91 (43), 82 (34), 43 (27) – HRMS ($C_{14}H_{19}BrO$): calcd. 282.0619; found: 282.0619.

2-Bromo-11-nordrima-1,7-dien-9-one (6): For preparation see **5** above. R_f = 0.59 (CH/EA = 2:1). – IR ($CHCl_3$): $\tilde{\nu}$ = 2970, 2940, 1720, 1440, 1380, 1130, 1080, 1010, 1000, 960 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 0.95 (s, 3 H, 18-H), 1.05 (s, 3 H, 19-H), 1.14 (s, 3 H, 20-H), 1.87 (dd, *J* = 11.0 Hz, *J* = 4.4 Hz, 1 H, 5-H), 1.73–1.76 (m, 3 H, 17-H), 2.23- 2.39 (m, 2 H, 6-H), 2.17–2.28 (m, 1 H, 3-H), 2.30–2.39 (m, 1 H, 3-H), 6.51 (d, *J* = 2.4 Hz, 1 H, 1-H), 6.67–6.70 (m, 1 H, 7-H). – ^{13}C NMR ($CDCl_3$): δ = 16.4 (C-17), 18.2 (C-20), 23.0 (C-19), 24.0 (C-6), 29.9 (C-18), 35.4 (C-4), 46.0 (C-5), 49.5 (C-10), 50.7 (C-3), 120.5 (C-2), 131.3 (C-1), 133.1 (C-8), 143.3 (C-7), 200.9 (C-9). – EI-MS: *m/z* (%) = 284 (60) [$M^{+\cdot}$], 282 (59), 202 (66), 200 (71), 187 (94),185 (100), 121 (60), 120 (40), 106 (62), 105 (41), 91 (53), 83 (65), 82 (61), 77 (35), 55 (48), 43 (46), 41 (58). – HRMS ($C_{14}H_{19}BrO$): calcd. 282.0619; found: 282.0619.

11-Nordrim-7-ene-2,9-dione (7): Compound **4** (5.1 g, 18.0 mmol) was slowly added to 19 mL of H_3PO_4 (85%) and stirred for 3 d at 65 °C. After cooling to 0 °C the reaction mixture was added to 150 mL of sat. $NaHCO_3$ solution. The organic layer was separated and the water layer was extracted twice with 50 mL of Et_2O. The combined organic extracts were dried with Na_2SO_4 and concentrated in vacuo. The residue (5.0 g) was flash-chromatographed over 1.2 kg of silica gel (gradient: cyclohexane/ethyl acetate = 7:1 → 3:1) to give **7** (1.9 g, 8.8 mmol; yield: 49%) and **5/6** (1.9 g, 6.8 mmol; yield: 38%).

To a mixture of **5/6** (520 mg, 1.84 mmol) and AgO_3SCF_3 (454 mg, 1.87 mmol) was added 6 mL of sulfuric acid (80%) and stirred for 10 min. The reaction mixture was then diluted with 30 g of ice and extracted twice with 100 mL of Et_2O. The combined organic extracts were washed with 30 mL of sat. $KHCO_3$ solution and 30 mL of sat. NaCl solution, filtered through Na_2SO_4 and silica gel and concentrated in vacuo. The residue was purified by silica gel chromatography (pentane/Et_2O = 2:1) to give **7** (359 mg; yield: 89%). R_f = 0.42 (CH/EA = 2:1). – M.p. 63–66 °C. (ref.[15] m.p. 61–62 °C). – $[\alpha]_D^{22}$ = –50 (*c* = 1.1, $CHCl_3$) {ref.[15] $[\alpha]_D$= –49.3 (*c* = 1.2, $CHCl_3$)}. – IR ($CHCl_3$): $\tilde{\nu}$ = 3010, 2960, 1710, 1670, 1450, 1430, 1370, 1360, 1290, 1240, 1050, 1010 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 0.84 (s, 3 H, 19-H), 0.86 (s, 3 H, 20-H), 0.93 (s, 3 H, 18-H), 1.62 (m, 3 H, 17-H), 1.97 (dd, *J* = 12.8 Hz, *J* = 2.0 Hz, 5-H), 2.00 (dd, *J* = 10.7 Hz, *J* = 4.9 Hz, 1 H, 3-H), 2.16–2.22 (m, 1 H, 3-H), 2.25–2.34 (m, 2 H, 6-H), 2.29–2.41 (m, 2 H, 1-H), 6.61 (m, 1 H, 7-H). – ^{13}C NMR ($CDCl_3$): δ = 16.0 (C-17), 17.9 (C-20), 22.7 (C-19), 24.4 (C-6), 31.4 (C-18), 39.1 (C-4), 48.4 (C-5), 48.6 (C-1), 49.1 (C-10), 55.7 (C-3), 132.7 (C-8), 143.0 (C-7), 202.3 (C-9), 210.2 (C-2). – EI-MS: *m/z* (%) = 220 (17) [$M^{+\cdot}$], 205 (2) [$M^{+\cdot}$ – 15], 176 (3), 163 (8), 148 (3), 135 (13), 134 (8), 121 (13), 107 (7), 93 (12), 91 (9), 83 (11), 81 (100), 69 (9), 55 (8), 54 (9), 53 (7), 41 (17). – HRMS ($C_{14}H_{20}O_2$): calcd. 220.1463; found: 220.1463.

2,2-Ethylenedioxy-11-nordrim-7-en-9-one (8): Compound **7** (0.431 g, 1.96 mmol) was stirred for 18 h under reflux with *p*-TsOH (7.0 mg) and ethylene glycol (1.3 mL, 22.4 mmol) of in benzene with a Dean-Stark-trap. A sat. $KHCO_3$ solution (25 mL) was added in one go. The organic layer was separated and the water layer extracted once with ethyl acetate. The combined organic extracts were washed with 30 mL of sat. NaCl solution, dried over Na_2SO_4 and concentrated in vacuo to give **8** (0.517 g, 1.96 mmol; yield: 100%). R_f = 0.52 (CH/EA = 2:1). – $[\alpha]_D^{22}$ = –43 (*c* = 1.9, $CHCl_3$). – IR ($CHCl_3$): $\tilde{\nu}$ = 3010, 2960, 2920, 1660, 1470, 1450, 1430, 1370, 1360, 1100, 1080, 1070, 1020, 960, 930, 840 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 0.90 (s, 3 H, 18-H), 1.09 (s, 3 H, 19-H), 1.15 (d, *J* = 0.6 Hz, 3 H, 20-H), 1.41 (d, *J* = 13.8 Hz, 1 H, 3-H), 1.55 (d, *J* = 13.8 Hz, 1 H, 3-H), 1.56–1.64 (m, 1 H, 5-H), 1.61 (d, *J* = 14.8 Hz, 1 H, 1-H), 1.71 (m, 3 H, 17-H), 2.03 (dd, *J* = 14.8 Hz, *J* = 2.9 Hz, 1 H, 1-H), 2.25–2.32 (m, 2 H, 6-H), 3.76–3.97 (m, 4 H, 1′-H, 2′-H), 6.62–6.65 (m, 1 H, 7-H). – ^{13}C NMR ($CDCl_3$): δ = 16.0 (C-17), 16.9 (C-20), 22.3 (C-19), 24.1 (C-6), 32.7 (C-18), 34.8 (C-4), 40.0 (C-1), 46.3 (C-10), 48.0 (C-3), 48.6 (C-5), 62.6, 64.5 (C-1′, C-2′), 108.9 (C-2), 132.6 (C-8), 142.8 (C-7), 204.2 (C-9). – EI-MS: *m/z* (%) = 264 (83) [$M^{+\cdot}$], 249 (8), 207 (20), 182 (87), 167 (68), 127 (100), 113 (14), 86 (16). – HRMS ($C_{16}H_{24}O_3$): calcd. 264.1725; found: 264.1725.

(9*R*)-2,2-Ethylenedioxy-15,16-bisnorlabd-7-en-9-ol (9): Under an argon atmosphere dry **8** (212.1 mg, 0.80 mmol) was dissolved in 10 mL of abs. Et_2O, cooled to –20 °C and *n*BuLi (1.2 equiv., 0.48 mL, 0.96 mmol, 2 M in pentane) was added in one go. After stirring for 5 h, 10 mL of sat. $(NH_4)_2SO_4$ solution was added. The organic layer was separated and the water layer extracted twice with 30 mL of Et_2O and once with 30 mL of ethyl acetate. The combined organic extracts were washed with 10 mL of sat. $KHCO_3$ solution, twice with 10 mL of H_2O and finally with 10 mL of sat. NaCl solution. The combined organic extracts were dried with Na_2SO_4 and concentrated in vacuo to give **9** (255.7 mg, 0.79 mmol; yield: 99%). R_f = 0.40 (CH/EA = 4:1). – M.p. 73–77 °C. – $[\alpha]_D^{22}$ = –51 (*c* = 3.6, $CHCl_3$). – IR ($CHCl_3$): $\tilde{\nu}$ = 3600, 3480, 3000, 2950, 1730, 1470, 1450, 1380, 1360, 1100, 1080, 910 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 0.87 (t, *J* = 7.0 Hz, 3 H, 14-H), 0.88 (s, 3 H, 18-H), 1.05 (s, 3 H, 19-H), 1.06 (s, 3 H, 20-H), 1.17–1.31 (m, 2 H, 13-H), 1.25–1.35 (m, 2 H, 12-H), 1.44 (d, *J* = 13.6 Hz, 1 H, 3-H_{ax}), 1.54–1.70 (m, 2 H, 11-H), 1.62 (d, *J* = 13.6 Hz, 1 H, 3-H_{eq}), 1.62–1.75 (m, 2 H, 1-H), 1.64–1.70 (m, 1 H, 5-H), 1.68 (m, 3 H, 17-H), 1.81–2.04 (m, 2 H, 6-H), 3.81–3.88, 3.96–4.01 (m, 4 H, 1′-H, 2′-H), 5.42 (m, 1 H, 7-H). – ^{13}C NMR ($CDCl_3$): δ = 14.1 (C-14), 15.4 (C-20), 19.4 (C-17), 22.2 (C-19), 23.86 (C-6), 23.95 (C-13), 28.3 (C-12), 33.9 (C-18), 34.7 (C-4), 38.2 (C-11), 38.8 (C-1), 43.0 (C-10), 43.5 (C-5), 48.3 (C-3), 62.6, 64.7 (C-1′, C-2′), 79.7 (C-9), 109.6 (C-2), 122.9 (C-7), 137.0 (C-8). – EI-MS: *m/z* (%) = 322 (2) [$M^{+\cdot}$], 307 (2) [$M^{+\cdot}$ – 15], 266 (14), 265 (100), 183 (10), 179 (17), 140 (9), 127 (12), 87 (12). – HRMS ($C_{20}H_{34}O_3$): calcd. 322.2508; found: 322.2508.

2,2-Ethylenedioxy-15,16-bisnorlabd-8(9)-en-7-one (10): Under an N_2 atmosphere PCC (165.5 mg, 0.77 mmol) was suspended in 1 mL of abs. CH_2Cl_2 and stirred vigorously. A solution of **9** (76.1 mg, 0.24 mmol) in 2 mL of abs. CH_2Cl_2, was added in one go. After stirring for 4 h at room temperature the reaction mixture was diluted with 25 mL of Et_2O and filtered through 2.9 g of silica gel. After washing the column with 50 mL of Et_2O, the combined organic extracts were washed twice with 10 mL of NaOH (7%) and twice with 5 mL of sat. $NaHCO_3$ solution, dried with Na_2SO_4 and concentrated in vacuo. The residue was purified by preparative TLC [2 plates, developed twice with cyclohexane/ethyl acetate (4:1) and eluted with ethyl acetate] to give **10** (38.5 mg, 0.12 mmol; yield: 51%, 73% related to the turnover) and **9** (23.5 mg, 0.07 mmol; yield: 31%). R_f = 0.60 (CH/EA = 2:1). – $[\alpha]_D^{22}$ = +56 (*c* = 1.8, $CHCl_3$). – IR ($CHCl_3$): $\tilde{\nu}$ = 3000, 2950, 2870, 1640, 1600, 1380, 1350, 1330, 1100, 1080, 1010 cm^{-1}. – ^1H NMR ($CDCl_3$): δ = 0.88 (s, 3 H, 18-H), 0.90 (t, *J* = 6.9 Hz, 3 H, 14-H), 1.01 (s, 3 H, 19-H), 1.20 (s, 3 H, 20-H), 1.33–1.40 (m, 4 H, 12-H, 13-H), 1.41 (d, *J* = 13.9 Hz, 1 H, 3-H), 1.62 (d, *J* = 13.2 Hz, 1 H, 1-H), 1.66 (d, *J* = 13.9 Hz, 1 H, 3-H), 1.70 (s, 3 H, 17-H), 1.73 (dd, *J* = 13.6 Hz, *J* = 4.1 Hz, 1 H, 5-H), 2.00 (dd, *J* = 13.2 Hz, *J* = 2.4 Hz, 1 H, 1-H), 2.08–2.20

(m, 2 H, 11-H), 2.36 (dd, J = 17.5 Hz, J = 13.6 Hz, 1 H, 6-H_{ax}), 2.49 (dd, J = 17.5 Hz, J = 4.1 Hz, 1 H, 6-H_{eq}), 3.83–3.87, 3.94–4.05 (m, 4 H, 1′-H, 2′-H). – ^{13}C NMR ($CDCl_3$): δ = 11.3 (C-17), 13.7 (C-14), 18.6 (C-20), 21.3 (C-19), 23.6 (C-13), 29.4 (C-11), 31.2 (C-12), 33.1 (C-18), 34.2 (C-4), 34.9 (C-6), 42.0 (C-10), 43.1 (C-1), 47.7 (C-3), 49.4 (C-5), 62.8/64.8 (C-1′, C-2′), 109.0 (C-2), 129.4 (C-8), 168.2 (C-9), 199.9 (C-7). – EI-MS: m/z (%) = 320 (7) [$M^{+\cdot}$], 305 (5) [$M^{+\cdot}$ – 15], 264 (11), 263 (18), 141 (4), 139 (5), 128 (5), 127 (100), 113 (4), 32 (5). – HRMS ($C_{20}H_{32}O_3$): calcd. 320.2351; found: 320.2351.

15,16-Bisnorlabd-8(9)-ene-2,7-dione (11): To a solution of **10** (38.5 mg, 0.12 mmol) in 10 mL of THF was added 5 mL of HCl (5%) and the mixture stirred for 6 h at room temperature. It was then neutralised with 15 mL of sat. $KHCO_3$ solution. The organic layer was separated and the water layer extracted three times with 20 mL of Et_2O. The combined organic extracts were washed twice with 30 mL of sat. $KHCO_3$ solution and once with 30 mL of sat. NaCl solution, dried with Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel chromatography (gradient: CH → CH/EE = 9:1) to give **11** (22.9 mg, 0.08 mmol; yield: 67%). R_f = 0.49 (CH/EA = 2:1). – M.p. 140–144 °C. – $[\alpha]_D^{23}$ = +91 (c = 0.47, $CHCl_3$). – IR ($CHCl_3$): $\tilde{\nu}$ = 3010, 2960, 2870, 1710, 1650, 1380, 1330, 1280, 1260, 1090 cm^{-1}. – ^{1}H NMR ($CDCl_3$): δ = 0.90 (t, J = 7.0 Hz, 3 H, 14-H), 0.93 (s, 3 H, 19-H), 1.05 (s, 3 H, 18-H), 1.05 (s, 3 H, 20-H), 1.30–1.45 (m, 4 H, 12-H, 13-H), 1.75 (s, 3 H, 17-H), 2.01–2.22 (m, 2 H, 11-H), 2.18–2.26 (m, 1 H, 3-H), 2.20–2.26 (m, 1 H, 5-H), 2.34–2.40 (m, 1 H, 3-H), 2.34–2.44 (m, 1 H, 6-H), 2.47–2.62 (m, 2 H, 1-H), 2.55–2.62 (m, 1 H, 6-H). – ^{13}C NMR ($CDCl_3$): δ = 11.4 (C-17), 13.7 (C-14), 19.2 (C-20), 22.5 (C-19), 23.5 (C-13), 29.4 (C-11), 31.2 (C-12), 32.3 (C-18), 35.1 (C-6), 38.2 (C-4), 45.1 (C-10), 49.6 (C-5), 51.4 (C-1), 56.0 (C-3), 130.5 (C-8), 165.3 (C-9), 198.8 (C-7), 209.5 (C-2). – EI-MS: m/z (%) = 276 (12) [$M^{+\cdot}$], 261 (8) [$M^{+\cdot}$ – 15], 234 (5), 220 (31), 219 (28), 191 (6), 177 (15), 165 (7), 163 (10), 149 (8), 139 (10), 135 (100), 125 (9), 123 (17), 121 (9), 107 (10), 97 (9), 91 (6), 69 (8), 55 (8), 41 (6). – HRMS ($C_{18}H_{28}O_2$): calcd. 276.2089; found: 276.2089.

(2*R*)-2-Hydroxy-11-nordrim-7-en-9-one (12): Under an N_2 atmosphere **7** (1.01 g, 4.58 mmol) was dissolved in 20 mL of methanol, cooled to 0 °C, and $NaBH_4$ (76 mg, 2.01 mmol) added in one go. After stirring for 3 h at room temperature the reaction was quenched with 10 mL of H_2O and the methanol evaporated in vacuo. The residue was twice partitioned between 100 mL of ethyl acetate and 25 mL of sat. NH_4Cl solution. The combined organic extracts were washed with 25 mL of sat. NaCl solution, filtered through Na_2SO_4 and silica gel and concentrated in vacuo. The residue was purified on 95 g silica gel (pentane/ethyl acetate = 4:1) to give **12** (734 mg, 3.30 mmol) as a colourless solid (yield: 72%). R_f = 0.41 (CH/EA = 2:1). – M.p. 122–124 °C (CH) (ref.[15] M.p. 105–107 °C). – $[\alpha]_D^{23}$ = –41 (c = 0.3, $CHCl_3$) {ref.[15] $[\alpha]_D$ = –41.6 (c = 1.0, $CHCl_3$)}. – IR ($CHCl_3$): $\tilde{\nu}$ = 3610, 3470, 3010, 2960, 2920, 1660, 1450, 1430, 1370, 1100, 1050, 960 cm^{-1}. – ^{1}H NMR ($CDCl_3$): δ = 0.89 (s, 3 H, 18-H), 1.21 (s, 3 H, 19-H), 1.29 (d, J = 0.6 Hz, 3 H, 20-H), 1.38 (dd, J = 14.8 Hz, J = 3.3 Hz, 1 H, 3-H), 1.61–1.64 (m, 1 H, 5-H), 1.61–1.68 (m, 1 H, 1-H), 1.66–1.68 (m, 1 H, 3-H), 1.72 (dd, J = 3.2 Hz, J = 1.9 Hz, 3 H, 17-H), 2.07 (m, J = 15.1 Hz, J = 2.7 Hz, 1 H, 1-H), 2.31–2.37 (m, 2 H, 6-H), 4.27–4.31 (m, 1 H, 2-H_{eq}), 6.65–6.68 (m, 1 H, 7-H). – ^{13}C NMR ($CDCl_3$): δ = 16.4 (C-17), 19.1 (C-20), 24.29 (C-19), 24.31 (C-6), 33.0 (C-4), 33.1 (C-18), 38.8 (C-1), 44.6 (C-10), 46.3 (C-3), 49.1 (C-5), 67.9 (C-2), 132.5 (C-8), 143.4 (C-7), 205.4 (C-9). – EI-MS: m/z (%): 222 (100) [$M^{+\cdot}$], 204 (24) [$M^{+\cdot}$ – 18], 189 (31), 163 (36), 161 (32), 148 (25), 147 (28), 135 (40), 123 (38), 109 (24), 96 (21), 82 (75), 41 (21). – HRMS ($C_{14}H_{22}O_2$): calcd. 222.1619; found: 222.1619.

11-Nordrima-1,7-dien-9-one (13): A mixture of **12** (606 mg, 2.73 mmol), pyridine (0.66 mL, 8.18 mmol), *N*,*N*-dimethyl-4-aminopyridine (33 mg, 0.27 mmol) and trifluoromethanesulfonyl chloride (0.42 mL, 5.45 mmol) in 40 mL of CH_2Cl_2 was stirred for 2 h at room temperature. The solvent was evaporated in vacuo, and 2 mL of THF and 40 mL of cyclohexane were added. The mixture was stirred for 15 h under reflux. After cooling to room temperature 25 mL of HCl (5%) was added and the reaction mixture extracted with 300 mL of ethyl acetate. The organic layer was washed with 50 mL of sat. $KHCO_3$ solution and 50 mL of sat. NaCl solution and filtered through Na_2SO_4 and silica gel. The solvent was evaporated in vacuo and the residue chromatographed through 100 g of silica gel (pentane/Et_2O = 30:1) to give **13/14** (ratio 1/2; NMR) (425 mg, 2.08 mmol) as a clear oil (yield: 81%). R_f = 0.48 (pentane/Et_2O = 15:1). – IR of **13/14** ($CHCl_3$): $\tilde{\nu}$ = 3019, 2960, 2925, 2880, 1660, 1465, 1450, 1430, 1365, 1015, 845 cm^{-1}. – ^{1}H NMR ($CDCl_3$): δ = 0.89 (s, 3 H, 18-H), 0.94 (s, 3 H, 19-H), 1.08 (s, 3 H, 20-H), 1.71 (m, 3 H, 17-H), 1.77 (m, 1 H, 3-H), 1.85 (m, 1 H, 3-H), 1.86 (m, 1 H, 5-H), 2.29 (m, 2 H, 6-H), 5.59 (ddd, J = 10.3 Hz, J = 5.3 Hz, J = 2.3 Hz, 1 H, 2-H), 6.03 (d, J = 10.3 Hz, 1 H, 1-H), 6.63 (m, 1 H, 7-H). – ^{13}C NMR ($CDCl_3$): δ = 16.3 (C-17), 18.4 (C-20), 22.7 (C-19), 24.1 (C-6), 30.2 (C-18), 32.1 (C-4), 41.1 (C-3), 46.4 (C-10), 47.1 (C-5), 124.5 (C-2), 129.8 (C-1), 133.0 (C-8), 143.3 (C-7), 202.9 (C-9).

11-Nordrima-2,7-dien-9-one (14): For preparation see **13** above. R_f = 0.48 (pentane/Et_2O = 15/1). – ^{1}H NMR ($CDCl_3$): δ = 0.94 (s, 3 H, H-18), 0.96 (s, 3 H, H-19), 1.00 (s, 3 H, H-20), 1.71 (m, 3 H, H-17), 1.89 (m, 1 H, H-5), 2.04 (m, 1 H, H-1), 2.17 (m, 1 H, H-1), 2.29 (m, 2 H, H-6), 5.31 (m, 1 H, H-3), 5.49 (ddd, J = 10.1 Hz, J = 5.7 Hz, J = 2.2 Hz, 1 H, H-2), 6.72 (m, 1 H, H-7). – ^{13}C NMR ($CDCl_3$): δ = 16.2 (C-17), 17.5 (C-20), 22.4 (C-19), 24.2 (C-6), 31.3 (C-18), 33.3 (C-1), 34.8 (C-4), 44.0 (C-10), 46.6 (C-5), 121.2 (C-2), 133.3 (C-8), 136.6 (C-3), 144.0 (C-7), 204.9 (C-9).

11-Nordrim-7-en-9-one (15): The mixture of **15/16** (2.82 g, 13.8 mmol) and $(Ph_3P)_3Rh^ICl$ (172 mg, 0.19 mmol) were dissolved in 10 mL of benzene and 10 mL of methanol. The mixture was hydrogenated for 3 d at room temperature (pressure: 50 bar) and then concentrated in vacuo. The residue was dissolved in 30 mL of pentane/Et_2O (1:1) and filtered through silica gel. The solvent was evaporated in vacuo and the residue chromatographed through 100 g of silica gel (pentane/Et_2O = 30:1) to give **8** (2.80 g, 13.6 mmol) as colourless needles (yield: 98%). R_f = 0.47 (pentane/Et_2O = 15:1). – M.p. 82–84 °C (ref.[15] M.p. 83.5–84 °C). – $[\alpha]_D^{22}$ = –74 (c = 0.7, $CHCl_3$) {ref.[15] $[\alpha]_D^{17}$ = –75.8 (c = 3.5, $CHCl_3$)}. – IR ($CHCl_3$): $\tilde{\nu}$ = 3000, 2925, 2860, 1660, 1455, 1365, 1050, 1010, 960, 850 cm^{-1}. – ^{1}H NMR ($CDCl_3$): δ = 0.85 (s, 3 H, 18-H), 0.93 (s, 3 H, 19-H), 0.98 (s, 3 H, 20-H), 1.11 (m, 1 H, 3-H_{ax}), 1.27 (ddd, J = 18.1 Hz, J = 13.4 Hz, J = 5.8 Hz, 1 H, 1-H_{ax}), 1.38 (d, J = 13.2 Hz, 1 H, 3-H_{eq}), 1.50 (m, 2 H, 2-H), 1.53 (m, 1 H, 5-H), 1.69 (m, 3 H, 17-H), 1.84 (d, J = 13.4 Hz, 1 H, 1-H_{eq}), 2.11–2.34 (m, 2 H, 6-H), 6.62 (m, 1 H, 7-H). – ^{13}C NMR ($CDCl_3$): δ = 17.1 (C-20), 18.1 (C-2), 16.4 (C-17), 22.2 (C-19), 24.3 (C-6), 32.3 (C-18), 33.2 (C-1), 33.6 (C-4), 45.0 (C-10), 41.5 (C-3), 49.3 (C-5), 132.9 (C-8), 143.3 (C-7), 205.8 (C-9). – EI-MS: m/z (%) = 206 (100) [$M^{+\cdot}$], 191 (32), 163 (36), 149 (17), 135 (60), 123 (39), 121 (44), 109 (39), 95 (25), 82 (84), 41 (28). – HRMS ($C_{14}H_{22}O$): calcd. 206.1671; found: 206.1671.

3-Ethenylfuran (17): Mg (763 mg, 31.4 mmol) was suspended in 20 mL of abs. Et_2O and activated with ultrasound. After the addition of chloromethyltrimethylsilane (4.24 mL, 30.5 mmol) the mixture was stirred for 1 h under reflux. Furan-3-carbaldehyde (2.74 g, 28.5 mmol) was then dissolved in 24 mL of Et_2O and added to the

mixture. Stirring was continued for 30 min at room temperature. A sat. NH_4Cl solution (10 mL) was then added, and the reaction mixture was poured into a cooled (0 °C) mixture of *p*-TsOH (16 g), 1.5 mL of sulfuric acid and 30 mL of Et_2O and stirred for 10 min at room temperature. Pentane (100 mL) and 5 g of Na_2SO_4 were then added, and stirring was continued until the solution became clear. The mixture was then filtered through K_2CO_3, Na_2SO_4 and silica gel and concentrated to 25 mL. Distilled pentane (50 mL) was then added and the mixture was concentrated again to 25 mL. This solution was used without further purification. ^{1}H NMR ($CDCl_3$): δ = 5.08 (dd, *J* = 10.9 Hz, *J* = 1.1 Hz, 1 H, 7-H_{cis}), 5.41 (dd, *J* = 17.4 Hz, *J* = 1.1 Hz, 1 H, 7-H_{trans}), 6.50 (s, 1 H, 4-H), 6.51 (dd, *J* = 17.4 Hz, *J* = 10.9 Hz, 1 H, 6-H), 7.31 (s, 1 H, 2-H), 7.36 (s, 1 H, 5-H). – ^{13}C NMR ($CDCl_3$): δ = 107.1 (C-4), 113.2 (C-7), 124.8 (C-3), 126.5 (C-6), 140.5 (C-2), 143. 4 (C-5).

2-(3-Furyl)ethanol (18): To a solution of **17** (2.68 g, 28.5 mmol) in 20 mL of pentane under an Ar-atmosphere 62 mL (31 mmol) of 9-BBN (0.5 M in THF) was added and stirred for 1 h under reflux. After cooling to room temperature 18 mL of ethanol, 6 mL of NaOH solution (6 N) and 12 mL of H_2O_2 solution (30%) were added and stirring continued for 1 h at 35 °C. The reaction mixture was washed with 25 mL of sat. NH_4Cl solution and 25 mL of NaCl solution. The combined water phases were reextracted with 50 mL of ethyl acetate. The combined organic extracts were filtered through Na_2SO_4 and silica gel, concentrated in vacuo, and the residue was separated on 280 g of silica gel (cyclohexane/ethyl acetate = 2/1). 2.98 g (26.6 mmol) of **18** was obtained as colourless liquid (yield: from **16** to **18**, 93%). R_f = 0.51 (CH/EE 1:1). – IR ($CHCl_3$): $\tilde{\nu}$ = 3620, 3475, 3010, 2950, 2880, 1500, 1070, 1050, 1025, 875 cm^{-1}. – ^{1}H NMR: ($CDCl_3$) δ = 2.67 (t, *J* = 6.5 Hz, 2 H, 7-H), 3.76 (t, *J* = 6.5 Hz, 2 H, 6-H), 6.31 (1 H, 4-H), 7.31 (1 H, 5-H), 7.37 (1 H, 2-H). – ^{13}C NMR: ($CDCl_3$) δ = 28.1 (C-6), 62.2 (C-7), 110.9 (C-4), 121.3 (C-3), 139.6 (C-2), 142.8 (C-5). EI-MS: *m*/*z* (%): 112 (47) [M^+·], 94 (6), 84 (7), 82 (39), 81 (100), 54 (13), 53 (60), 51 (11).

3-(2-Bromoethyl)furan (19): Under an Ar-atmosphere **18** (2.98 g, 26.6 mmol) and CBr_4 (13.23 g, 39.9 mmol) were dissolved in 20 mL of CH_2Cl_2. PPh_3 (7.56 g, 28.8 mmol) was dissolved in 20 mL of CH_2Cl_2 and added during 40 min. After stirring for 15 min at room temperature 15 g of silica gel was added and the solvent evaporated in vacuo. The residue was chromatographed through 250 g of silica gel (pentane) to give **19** (3.24 g, 18.5 mmol) as a colourless oil (yield: 70%) which must be stored at –18 °C. R_f = 0.48 (pentane). – IR ($CHCl_3$): $\tilde{\nu}$ = 2960, 2925, 2860, 1570, 1495, 1275, 1160, 1070, 1020, 875 cm^{-1}. – ^{1}H NMR ($CDCl_3$): δ = 2.99 (t, *J* = 7.3 Hz, 2 H, 6-H), 3.49 (t, *J* = 7.3 Hz, 2 H, 7-H), 6.31 (s, 1 H, 4-H), 7.31(s, 1 H, 2-H), 7.37 (s, 1 H, 5-H). – ^{13}C NMR ($CDCl_3$): δ = 28.6 (C-6), 32.2 (C-7), 110.5 (C-4), 122.1 (C-3), 143.0 (C-5), 139.6 (C-2). – EI-MS: *m*/*z* (%) = 176 (68) [M^+·], 174 (70), 95 (82), 94 (28), 81 (100), 67 (29), 65 (34), 53 (51), 41 (89).

(9*R*)-15,16-Epoxylabda-7,13(16),14-trien-9-ol (20): Compound **19** (320 mg, 1.83 mmol) was dissolved in 5 mL of abs. Et_2O and cooled to –78 °C. *t*BuLi (1.08 mL, 1.83 mmol, 1.7 M in pentane) was then added while keeping the temperature below –65 °C. After 10 min **15** (126 mg, 0.61 mmol) was dissolved in 4 mL of abs. Et_2O and added to the reaction mixture, stirring for 45 min at –78 °C. The reaction was quenched with 10 mL of sat. NH_4Cl solution. The organic layer was separated and the water layer extracted three times with 10 mL of Et_2O. The combined organic extracts were dried with Na_2SO_4, concentrated in vacuo and chromatographed through 40 g of silica gel (cyclohexane/ethyl acetate = 12:1) to give **20** (110 mg, 0.364 mmol; yield: 60%, 94% related to the turnover). R_f = 0.49 (CH/EE 5:1). – $[\alpha]_D^{22}$ = –55 (*c* = 0.22, $CHCl_3$) {ref.[17] $[\alpha]_D^{22}$ = –53.7 (*c* = 0.27, $CHCl_3$)}. – IR ($CHCl_3$): $\tilde{\nu}$ = 3625, 2930, 2875, 1500, 1160, 1460, 1380, 1065, 1025 cm^{-1}. – ^{1}H NMR ($CDCl_3$): δ = 0.86 (s, 3 H, 18-H), 0.93 (s, 3 H, 19-H), 0.95 (s, 3 H, 20-H), 1.16 (m, 1 H, 3-H), 1.45 (m, 1 H, 3-H), 1.47 (m, 1 H, 1-H), 1.49 (m, 1 H, 2-H), 1.51 (m, 1 H, 2-H), 1.53 (m, 1 H,1-H), 1.63 (dd, *J* = 11.2 Hz, *J* = 6.1 Hz, 1 H, 5-H), 1.75 (m, 3 H, 17-H), 1.86 (m, 1 H, 6-H), 1.93 (m, 2 H, 11-H), 2.02 (m, 1 H, 6-H), 2.53 (m, 2 H, 12-H), 6.29 (s, 1 H, 14-H), 5.45 (m, 1 H, 7-H), 7.23 (s, 1 H, 16-H), 7.34 (s, 1 H, 15-H). – ^{13}C NMR ($CDCl_3$): δ = 15.4 (C-20), 18.7 (C-2), 19.7 (C-17), 21.4 (C-12), 21.5 (C-6), 22.0 (C-19), 32.0 (C-1), 33.5 (C-4), 33.7 (C-18), 38.8 (C-11), 41.8 (C-10), 42.3 (C-3), 44.4 (C-5), 79.3 (C-9), 111.0 (C-14), 123.3 (C-7), 125.9 (C-13), 137.2 (C-8), 138.7 (C-16), 142.7 (C-15). – EI-MS: *m*/*z* (%) = 302 (2) [M^+·], 284 (2), 208 (17), 207 (100), 189 (9), 160 (21), 149 (17), 119 (21), 109 (21), 95 (20), 81 (27), 69 (14), 43 (16). – HRMS ($C_{20}H_{30}O_2$): calcd. 302.2246; found: 302.2246.

Hispanone, 15,16-Epoxylabda-8(9),13(16),14-trien-7-one (21): Under an argon atmosphere PCC (1.26 g, 5.85 mmol) and $CaCO_3$ (250 mg) were suspended in 70 mL of CH_2Cl_2 and stirred for 30 min at room temperature. Compound **20** (177 mg, 0.59 mmol) was then added and stirring was continued for 12 h. After the addition of 400 mL of pentane the reaction mixture was filtered through silica gel. The solution was then concentrated in vacuo and the residue chromatographed through 100 g of silica gel (cyclohexane/ethyl acetate = 15:1) to give **21** (90 mg, 0.30 mmol; yield: 51%) as a colourless oil, which was crystallized from MeOH. R_f = 0.49 (CH/EE 5:1). – M.p. 58–60.5 °C (MeOH) (ref.[16] M.p. 58–60 °C). – $[\alpha]_D^{22}$ = +39 (*c* = 0.5, $CHCl_3$) {ref.[16] $[\alpha]_D^{20}$ = +39.7 (*c* = 1.1, $CHCl_3$)}. – IR ($CHCl_3$): $\tilde{\nu}$ = 3000, 2975, 2950, 2860, 1645, 1600, 1500, 1460, 1375, 1325, 1020, 875 cm^{-1}. – ^{1}H NMR ($CDCl_3$): δ = 0.88 (s, 3 H, 18-H), 0.91 (s, 3 H, 19-H), 1.09 (s, 3 H, 20-H), 1.22 (m, 1 H, 3-H), 1.37 (m, 1 H, 1-H), 1.48 (m, 1 H, 3-H), 1.58 (m, 1 H, 2-H), 1.69 (m, 1 H, 2-H), 1.71 (m, 1 H, 5-H), 1.78 (s, 3 H, 17-H), 1.95 (m, 1 H, 1-H), 2.35 (m, 1 H, 6-H), 2.42 (m, 2 H, 11-H), 2.50 (m, 1 H, 6-H), 2.54 (m, 2 H, 12-H), 6.29 (s, 1 H, 14-H), 7.25 (s, 1 H, 16-H), 7.36 (s, 1 H, 15-H). – ^{13}C NMR ($CDCl_3$): δ = 11.4 (C-17), 18.1 (C-20), 18.6 (C-2), 21.3 (C-19), 24.2 (C-12), 30.2 (C-11), 32.5 (C-18), 33.1 (C-4), 35.2 (C-6), 35.8 (C-1), 40.9 (C-10), 41.3 (C-3), 50.2 (C-5), 110.5 (C-14), 124.5 (C-13), 130.3 (C-8), 138.6 (C-16), 143.0 (C-15), 167.0 (C-9), 200.3 (C-7). – EI-MS: *m*/*z* (%) = 300 (29) [M^+·], 285 (17), 282 (9), 267 (9), 205 (11), 177 (28), 176 (74), 161 (13), 135 (36), 123 (14), 109 (13), 95 (10), 82 (22), 81 (100), 69 (13), 53 (15), 41 (16). – HRMS ($C_{20}H_{28}O_2$): calcd. 300.2089; found: 300.2089.

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