Bryophyte Constituents; 5: Synthesis of Taylorione

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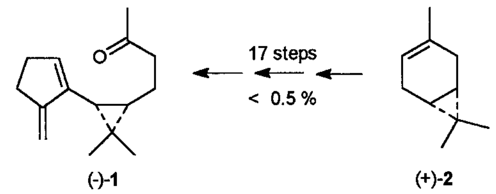
Dedicated to Prof. Dr. Manfred Regitz on the occasion of his 60th birthday

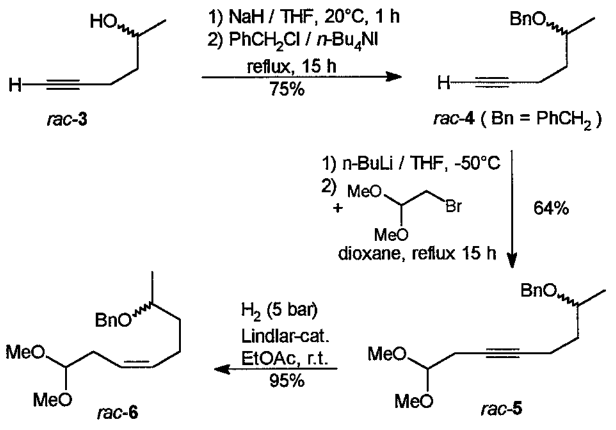
An efficient total synthesis of the sesquiterpene ketone taylorione (**1**) from *Mylia taylorii* is described starting from readily available hex-5-yn-2-ol (**3**) and leading to the natural product in its racemic form.

The sesquiterpene (−)-taylorione (**1**) with a unique carbon skeleton was isolated from the liverwort *Mylia taylorii (Hock.) S. Gray* of the *Jungermanniaceae.*[1,2] A multistep synthesis of (−)-**1** starting from (+)-3-carene (**2**) has been reported,[3] but gave the enantiopure natural product in only low yield. This prompted us to develop an efficient and expeditious route to taylorione (**1**) in the course of our interdisciplinary investigations on bryophyte constituents.[4]



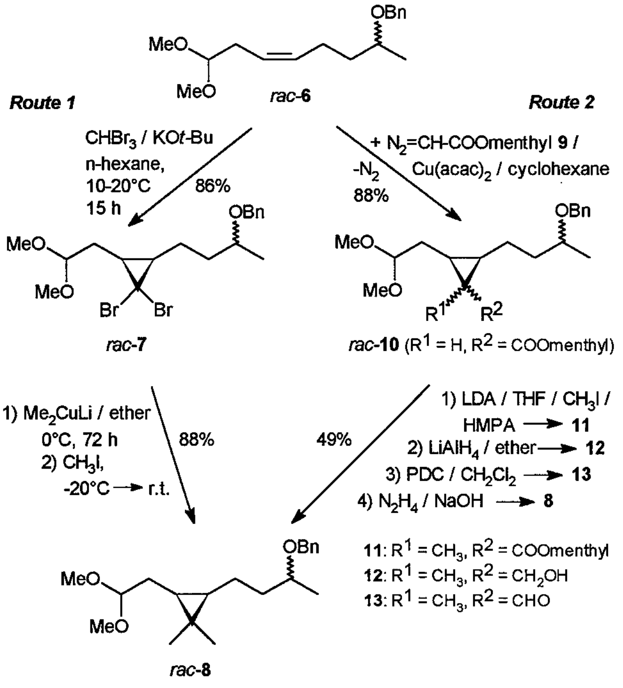
Scheme 1

The synthetic strategy is based on the stereoselective construction of the cyclopropane moiety of **1** by addition of dimethylcarbene equivalents to a *cis*-olefin of appropriate substitution pattern, namely **6**. This olefin was obtained (three steps, see Scheme 2) from the readily available racemic hex-5-yn-2-ol (**3**)[5] by *O*-benzylation (to give **4**), alkylation of the terminal alkyne function with bromoacetaldehyde dimethyl acetal[6] (to give **5**), and *cis*-hydrogenation of the triple bond[7] in the presence of Lindlar catalyst (to give **6**). The protected hydroxy function was introduced as a masked carbonyl group required for the further transformations (see Scheme 4).



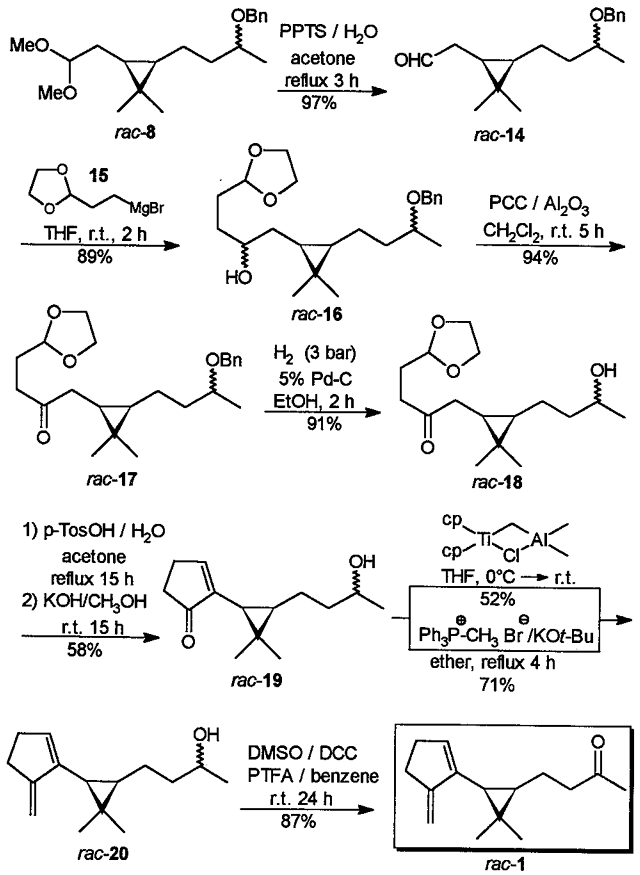
Scheme 2

The olefin **6** was used as a substrate for two different routes that introduced the cyclopropane moiety: stereospecific *syn*-addition of dibromocarbene[8] (Scheme 3, route 1) gave the dibromocyclopropane **7**, whose geminal bromine atoms were substituted by methyl groups using lithium dimethylcuprate–iodomethane[9] yielding *rac*-**8**. Alternatively, cyclopropanation of **6** to **8** was achieved by *syn*-addition of menthyl diazoacetate **9**[10] in the presence of copper(II) acetylacetonate (Scheme 3, route 2), and four-step transformation (via **11**–**13**) of the cyclopropanecarboxylic ester **10** to give *rac*-**8**, although in a smaller overall yield.



Scheme 3

Cyclopropane *rac*-**8** served as a key intermediate in the present synthesis. Acid hydrolysis of the dimethyl acetal and addition of the Grignard reagent **15** from 2-(2-bromoethyl)-1,3-dioxolane[11] to the aldehyde **14** resulted in a chain elongation to the secondary alcohol **16**. After oxidation to the ketone **17** and hydrogenolytic cleavage of the benzyl ether, the dioxolane protective group in **18** was removed by hydrolysis with acid and the cyclopentenone **19** was obtained by intramolecular aldol condensation in basic medium. Methylenation of the carbonyl function in **19** with the Tebbe reagent[12] or by Wittig reaction[13] resulted in formation of the methylenecyclopentene **20**, which was transformed to racemic taylorione (*rac*-**1**) by oxidation of the secondary OH-function according to the Pfitzner–Moffat procedure[14] (Scheme 4).



Scheme 4

Thus, the total synthesis of racemic taylorione (*rac*-**1**) was achieved from the *cis*-olefin **6** via the key intermediate *rac*-**8** in 10 steps with an overall yield of 20% according to route 1, or in 13 steps with 11% according to route 2. Route 2 in principle offers the possibility of an enantioselective approach to the target molecule **1** by performing the cyclopropanation of *rac*-**6** in the presence of a chiral catalyst system.[15] This route is currently under investigation.

^1H and ^{13}C NMR (TMS as internal standard): Bruker AM 400. IR: Beckmann Acculab 8. UV: Varian DMS 80. MS: Finnigan MAT 90. The purity of all products was monitored by capillary gas chromatography (Varian GC 3400 fitted with a fused silica capillary column Macherey-Nagel Permabond OV-1, 25 m × 0.25 mm, injection: split, detection: FID). All new compounds gave satisfactory microanalyses performed with Leco CHNS-932 (C ± 0.3, H ± 0.3). All reactions sensitive to air or moisture were carried out under N_2. Anhydrous solvents were dried by conventional methods. Column chromatography was performed on silica gel (J.T. Baker 0.063–0.200 mm) monitored by GC and TLC (Merck aluminium roll silica gel 60 F_{254} pre-coated).

5-Benzyloxyhex-1-yne (4):

To a stirred solution of hex-5-yn-2-ol (*rac*-**3**) (98.1 g, 1.00 mol) in anhydr. THF (1700 mL) was slowly added NaH (24.0 g, 1.00 mol) at 0–10 °C over 1 h. After stirring for 1 h at r.t. hydrogen evolution was finished. Benzyl chloride (127 g, 1.00 mol) and tetrabutylammonium iodide (7.40 g, 20.0 mmol) were added. The mixture was refluxed for 15 h, volatile compounds were removed at reduced pressure and the residue was taken up in Et_2O (200 mL) and H_2O (200 mL). The aqueous layer was extracted with Et_2O (2 × 100 mL), the combined organic layers were washed with sat. aq NaCl (2 × 100 mL) and dried ($MgSO_4$). After evaporation of the solvent the residue was distilled in vacuo to yield 141 g (75%) of *rac*-**4** as a colourless oil, bp 79 °C/1 mbar.

IR (film): ν = 3295, 3020, 2960, 2100, 735, 695 cm^{-1}.

^1HNMR ($CDCl_3$): δ = 7.35–7.25 (m, 5 H), 4.58, 4.44 (2 d, J = 11.6 Hz, 2 H), 3.66 (m_c, 1 H), 2.30 (m_c, 2 H), 1.91 (t, J = 2.7 Hz, 1 H), 1.80–1.65 (m, 2 H), 1.20 (d, J = 6.2 Hz, 3 H).

^{13}CNMR ($CDCl_3$): δ = 139.0, 128.4, 127.7, 127.5, 84.36, 68.27, 73.25, 70.67, 35.61, 19.44, 14.79.

MS (CI, 120 eV): m/z (%) = 188 (10) [M^+], 171 (25), 111 (100) [$M^+ - C_6H_5$], 91 (31) [$C_7H_7^+$].

7-Benzyloxyoct-3-ynal Dimethyl Acetal (5):

To a solution of the alkyne *rac*-**4** (94.1 g, 0.50 mol) in anhydr. THF (250 mL) was slowly added BuLi (200 mL, 2.5 M in n-hexane, 0.50 mol) at less than −50 °C. After stirring for 30 min at r.t., bromoacetaldehyde dimethyl acetal (84.5 g, 0.50 mol) and anhydr. dioxane (300 mL) were added. THF and *n*-hexane were completely distilled off. The mixture was refluxed for 15 h (precipitation of LiBr). After cooling to r.t. water (200 mL) and Et_2O (200 mL) were added. The aqueous layer was extracted with Et_2O (2 × 200 mL), the combined organic layers were washed with sat. aq NaCl (3 × 100 mL) and dried ($MgSO_4$). After evaporation of the solvent the residue was distilled in vacuo to yield 84.4 g (64%) of *rac*-**5** as a colourless oil, bp 115 °C/0.001 mbar.

IR (film): ν = 3075, 3025, 2925, 1125, 1070, 1040 cm^{-1}.

^1HNMR ($CDCl_3$): δ = 7.35–7.25 (m, 5 H), 4.58, 4.45 (2 d, J = 11.6 Hz, 2 H), 4.47 (t, J = 5.6 Hz, 1 H), 3.65 (m_c, 1 H), 3.35 (s, 6 H), 2.47, 2.29 (2 m_c, 4 H), 1.80–1.60 (m, 2 H), 1.20 (d, J = 6.2 Hz, 3 H).

^{13}CNMR ($CDCl_3$): δ = 139.1, 128.3, 127.7, 127.4, 103.0, 81.70, 75.02, 73.72, 70.61, 53.34, 35.98, 24.06, 19.48, 15.23.

MS (CI, 120 eV): m/z (%) = 277 (2) [$M^+ + 1$], 245 (26) [$M^+ - OCH_3$], 213 (26), [$M^+ - 2OCH_3$], 91 (11) [$C_7H_7^+$], 75 (100) [$CH(OMe)_2^+$].

***cis*-7-Benzyloxyoct-3-enal Dimethyl Acetal (6):**

In a hydrogenation apparatus, a mixture of the alkyne *rac*-**5** (69.1 g, 0.25 mol), Lindlar catalyst [5% Pd on $CaCO_3$, poisoned with 3.5% $Pb(OAc)_2$, 1.0 g] quinoline (10 drops) and EtOAc (200 mL) was hydrogenated at 3 bar until an equimolar amount of H_2 was absorbed. The mixture was filtered, washed with sat. aq NaCl (2 × 100 mL) and dried ($MgSO_4$). After evaporation of the solvent the residue was distilled in vacuo to yield 66.1 g (95%) of *rac*-**6** as a colourless oil, bp 110 °C/0.001 mbar.

IR (film): ν = 3055, 3015, 2925, 1125, 1065 cm^{-1}.

^1HNMR ($CDCl_3$): δ = 7.35–7.25 (m, 5 H), 5.50–5.35 (m, 2 H), 4.56, 4.44 (2 d, J = 11.7 Hz, 2 H), 4.36 (t, J = 5.8 Hz, 1 H), 3.52 (sext, J = 6.1 Hz, 1 H), 3.31 (s, 6 H), 2.37 (t, J = 6.1 Hz, 2 H), 2.20–2.10 (m, 2 H), 1.70–1.45 (m, 2 H), 1.20 (d, J = 6.1 Hz, 3 H).

^{13}CNMR ($CDCl_3$): δ = 139.1, 128.3, 127.6, 127.4, 132.0, 123.8, 104.3, 74.42, 70.37, 52.95, 36.52, 31.05, 23.58, 19.6.

MS (CI, 120 eV): m/z (%) = 278 (3) [M^+], 247 (100) [$M^+ - OCH_3$], 215 (39) [$M^+ - 2OCH_3$), 197 (26), 141 (11), 139 (16).

[3-(3-Benzyloxy-1-butyl)-2,2-dibromo-1-cyclopropyl]acetaldehyde Dimethyl Acetal (7):

Bromoform (30.3 g, 0.12 mol) in anhydr. *n*-hexane (100 mL) was added dropwise to a rapidly stirred slurry of the olefin *rac*-**6** (11.1 g, 40.0 mmol), potassium *tert*-butoxide (13.5 g, 0.12 mol) and anhydr. *n*-hexane (30 mL) at 5–10 °C. The mixture was stirred for 8 h at r.t. and diluted with water (200 mL). The aqueous layer was extracted with petroleum ether (2 × 100 mL), the combined organic layers were washed with sat. aq NaCl (2 × 100 mL) and dried ($MgSO_4$). After evaporation of the solvent (1 mbar for removing the excess of bromoform) the residue was purified by column chromatography (Et_2O/cyclohexane, 1 : 10, monitored by GC) to yield 15.5 g (86%) of *rac*-**7** as a yellow unstable oil.

IR (film): ν = 3060, 3025, 2930, 1130, 1070, 735, 700 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 7.35–7.25 (m, 5 H), 4.58, 4.46 (2 dd, J = 11.8, 2.2 Hz, 2 H), 4.49 (t, J = 5.9 Hz, 1 H), 3.55 (sext, J = 6.2 Hz, 1 H), 3.38/3.36 (2 s, 6 H), 1.80–1.30 (comb. m, 8 H), 1.22 (d, J = 6.2 Hz, 3 H).

^{13}C NMR ($CDCl_3$): δ = 139.0, 128.3, 127.6, 127.4, 103.6, 74.35/74.10, 70.35/70.25, 53.92/53.38, 36.83/36.71, 35.13/34.81, 33.93/33.25, 30.71, 29.36, 23.47/23.22, 19.67/19.56.

MS (CI, 120 eV): m/z (%) = 451–458 [M^+], 417–421 (4–48) [$M^+ - OMe$], 91 (35) [$C_7H_7^+$], 75 (100) [$CH(OMe)_2^+$].

[3-(3-Benzyloxy-1-butyl)-2,2-dimethyl-1-cyclopropyl]acetaldehyde Dimethyl Acetal (*rac*-8) (Route 1):

In a carefully dried three-necked flask CuI (38.1 g, 0.20 mol) was suspended in anhydr. Et_2O (100 mL) and MeLi (1.4 M in Et_2O, 250 mL, 0.40 mol) was added at less than -50 °C over 1 h. The heterogeneous mixture was allowed to warm to -20 °C for 10 min giving a clear solution of the cuprate and recooled to -50 °C. Dibromide **7** (9.00 g, 20.0 mmol) in Et_2O (30 mL) was added and stirring was continued for 72 h at 0 °C. Iodomethane (10 mL) was added dropwise at -20 °C. The mixture was allowed to warm to r.t. within 24 h and poured into sat. aq NH_4Cl (300 mL). Insoluble copper salts were filtered off and washed with sat. aq NH_4Cl (200 mL) and Et_2O (100 mL). The filtrate was separated and the aqueous layer extracted with Et_2O (2 × 200 mL). The combined organic layers were washed with 10% NH_4Cl in conc. NH_3 (3 × 200 mL), sat. aq $NaHCO_3$ (2 × 100 mL) and sat. aq NaCl (2 × 100 mL), and dried ($MgSO_4$). After evaporation of the solvent the residue was purified by column chromatography (Et_2O/cyclohexane, 1:10) to yield 5.65 g (88%) of *rac*-**8** as a colourless oil.

IR (film): ν = 3060, 2930, 1460, 1380, 1130, 1065 cm^{-1}.

^{1}H NMR (C_6D_6): δ = 7.34 (d, J = 7.6 Hz, 2 H), 7.15 (t, J = 7.5 Hz, 2 H), 7.10 (t, J = 7.3 Hz, 1 H), 4.46, 4.32 (2 d, J = 12.1 Hz, 2 H), 4.44 (t, J = 5.7 Hz, 1 H), 3.38 (sext, J = 6.1 Hz, 1 H), 3.20 (s, 6 H, OCH_3), 1.75–1.20 (comb. m, 6 H), 1.10 (d, J = 6.1 Hz, 3 H), 1.051/1.045 (2 s, 3 H), 0.93 [s, 3 H, $C(CH_3)_2$], 0.69, 0.45 (2 q, J = 7.3 Hz, *cis*-coupling, 2 H, cyclopropyl-H).

^{13}C NMR ($CDCl_3$): δ = 139.2, 128.3, 127.6, 127.3, 105.4, 74.81, 70.24, 53.03, 37.04, 29.31, 28.00, 26.32, 21.57, 20.53, 19.67, 16.73, 14.96.

MS (CI, 120 eV): m/z (%) = 320 (1) [M^+], 289 (100) [$M^+ - OCH_3$], 257 (21) [$M^+ - 2OCH_3$], 197 (23), 91 (21) [$C_7H_7^+$], 75 (51) [$CH(OMe)_2^+$].

(±)Menthyl 2-(3-Benzyloxy-1-butyl)-3-(2,2-dimethoxyethyl)cyclopropane-1-carboxylate (10):

A solution of the olefin *rac*-**6** (8.35 g, 30.0 mmol) and copper(II) acetylacetonate (235 mg, 0.90 mmol) in anhydr. cyclohexane (5 mL) was heated to 60–70 °C with vigorous stirring under a nitrogen atmosphere and a few drops of a solution of D,L(*rac*)-menthyl diazoacetate **9**[10] (20.2 g, 90.0 mmol) in anhydr. cyclohexane (20 mL) were added to initiate the reaction evidenced by evolution of nitrogen. Then the temperature was lowered to 40 °C and the remainder of the solution of the diazoester was added dropwise (1–2 drops per minute). The mixture was cooled and separated by column chromatography (monitored by GC). Dimenthyl fumarate and dimenthyl maleate were eluted with Et_2O/cyclohexane, 1:10, the desired *rac*-**10** was eluted with Et_2O/cyclohexane, 1:7, yielding 12.5 g (88%) of a yellow oil.

IR (film): ν = 3020, 2950, 1720, 1455, 1170.

^{1}H NMR ($CDCl_3$): δ = 7.35–7.20 (m, 5 H), 4.65 (td, J = 10.7, 4.2 Hz, 1 H), 4.57 (dd, J = 11.8, 3.0 Hz, 1 H), 4.43 (d, J = 11.8 Hz, 1 H), 4.40 (superimposed, 1 H), 3.54 (m_c, 1 H), 3.334/3.330/3.325 (3 s, 6 H), 2.00–1.30 (comb. m, 13 H), 1.19 (d, J = 6.0 Hz, 3 H), 0.89 (d, J = 6.8 Hz, 6 H), 0.76 (d, J = 6.9 Hz, 3 H), 1.15–0.80 (comb. m, 5 H).

^{13}C NMR ($CDCl_3$): δ = 173.6, 139.0, 128.3, 127.6, 127.4, 104.8, 74.39/74.29, 74.00, 70.41, 53.51/53.21, 47.31, 41.14, 36.57/36.49, 34.40, 31.44, 31.02, 26.94/26.46, 26.81/26.66, 23.69/23.54, 23.20, 23.00, 22.73, 22.04, 20.75, 19.66, 19.53.

MS (CI, 120 eV): m/z (%) = 475 (11) [M^+], 443 (100) [$M^+ - OCH_3$], 319 (6), 305 (18), 287 (12), 91 (19) [$C_7H_7^+$], 75 (100) [$CH(OMe)_2^+$].

[3-(3-Benzyloxy-1-butyl)-2,2-dimethyl-1-cyclopropyl]acetaldehyde Dimethyl Acetal (*rac*-8) (Route 2):

(a) Methylation of the Cyclopropanecarboxylic Ester **10**:

At -70 °C the ester *rac*-**10** (11.9 g, 25.0 mmol) in anhydr. THF (20 mL) was added slowly to LDA (75.0 mmol) in THF (45 mL), prepared (4 °C, 15 min) by treatment of diisopropylamine (7.60 g, 75.0 mmol) with butyllithium (75.0 mmol, 2.5 M in *n*-hexane). The enolate solution was allowed to warm to -10 °C for 3 h and recooled to -70 °C. Iodomethane (17.7 g, 7.80 mL, 0.125 mol) in HMPA (16.8 g, 16.4 mL, 0.125 mol) was added dropwise and the mixture was allowed to warm to r.t. over 15 h. Sat. aq NH_4Cl (125 mL) was added and stirring was continued for 30 min. The phases were separated and the aqueous layer was extracted with Et_2O (2 × 100 mL). The combined organic layers were washed with sat. aq NH_4Cl (100 mL), sat. aq $NaHCO_3$ (100 mL) and sat. aq NaCl (100 mL) and dried ($MgSO_4$). After evaporation of the solvent, the residue was purified by short column chromatography (Et_2O/cyclohexane, 1:7) to yield 9.00 g (74%) of *rac*-**11** as a yellow oil. GC analysis showed **11** to be a 40:60 mixture of the *E*/*Z* methylated esters.

(b) Reduction of the Carboxylic Ester **11**:

The carboxylic ester *rac*-**11** (8.80 g, 18.0 mmol) in anhydr. Et_2O (70 mL) was added to a stirred slurry of $LiAlH_4$ (680 mg, 18.0 mmol) in anhydr. Et_2O (70 mL). The mixture was refluxed for 3 h, cooled and poured into an ice-cold sat. aq K-Na-tartrate solution (150 mL). The phases were separated and the aqueous layer was extracted with Et_2O (2 × 75 mL). The combined organic layers were washed with sat. aq NaCl (2 × 75 mL) and dried ($MgSO_4$). After evaporation of the solvent the residue was purified by column chromatography (short column, monitored by GC). Menthol was eluted with Et_2O/cyclohexane, 1:7, the desired product was eluted with Et_2O/cyclohexane, 1:1 to 3:1, yielding 5.05 g (83%) of *rac*-**12** as a colourless oil, identified by GC analysis as a 40:60 mixture of the *E*/*Z* cyclopropyl carbinols.

(c) Oxidation of the Cyclopropyl Carbinol **12**:

To the alcohol *rac*-**12** (5.05 g, 15.0 mmol) in anhydr. CH_2Cl_2 (40 mL) was added PDC (8.50 g, 22.5 mmol). After stirring for 15 h at r.t., the mixture was filtered and the solvent removed at 20 °C. The residue was taken up in Et_2O/cyclohexane, 1:1, and purified by column chromatography (short column; same eluent, 1:1) yielding 4.55 g (90%) of *rac*-**13** as a colourless oil, identified by GC analysis as a 40:60 mixture of the *E*/*Z* aldehydes.

(d) Reduction of the Aldehyde **13** *According to the Wolff–Kishner Procedure:*

A mixture of the aldehyde *rac*-**13** (4.50 g, 13.5 mmol), hydrazine hydrate (6.75 g, 135 mmol) and NaOH (5.40 g, 135 mmol) in triethylene glycol (120 mL) was heated to 150 °C (bath temperature) for 2 h. The reflux condenser was displaced by a Liebig condenser and the temperature increased to 220 °C (nitrogen evolution) while an excess of hydrazine hydrate and water was distilled off over 2 h. The residue was cooled, diluted with water (100 mL) and extracted with Et_2O (3 × 75 mL). The combined organic layers were washed with sat. aq NaCl (2 × 75 mL) and dried ($MgSO_4$). After evaporation of the solvent the residue was purified by column chromatography (short column; Et_2O/cyclohexane, 1:10) yielding 3.80 g (88%) of *rac*-**8**, identical in all spectroscopic data to the product obtained according to route 1.

[3-(3-Benzyloxy-1-butyl)-2,2-dimethyl-1-cyclopropyl]acetaldehyde (14):

A mixture of the dimethyl acetal *rac*-**8** (16.0 g, 50.0 mmol), PPTS (3.75 g, 15.0 mmol), acetone (320 mL) and water (160 mL) was refluxed for 3 h. Acetone was removed in vacuo and the residue was saturated with NaCl and extracted with Et_2O (3 × 100 mL). The combined organic layers were washed with sat. aq $NaHCO_3$ (2 × 100 mL) and sat. aq NaCl (100 mL) and dried ($MgSO_4$). The residue obtained after evaporation of the solvent was pure aldehyde *rac*-**14**; yield 13.3 g (97%) of a yellow oil.

IR (film): ν = 3025, 2930, 2715, 1730, 1460, 1380, 1075, 740, 700 cm^{-1}.

^{1}H NMR (CDCl$_3$): δ = 9.78 (t, J = 2.1 Hz, 1 H), 7.35–7.25 (m, 5 H), 4.56, 4.44 (2 d, J = 11.8 Hz, 2 H), 3.51 (sext, J = 6.1 Hz, 1 H), 2.33 (m$_c$, 2 H), 1.70–1.10 (comb. m, 4 H), 1.19 (d, J = 6.1 Hz, 3 H), 1.074, 0.92 [2 s, 3 H, C(CH$_3$)$_2$], 0.78, 0.59 (2 q, J = 8.7 Hz, *cis*-coupling, 2 H, cyclopropyl-H).

^{13}C NMR (CDCl$_3$): δ = 202.5, 139.2, 128.3, 127.6, 127.4, 74.62, 70.27, 39.63, 36.85, 29.00, 26.45, 20.51, 19.62, 17.10, 14.96.

MS (CI, 120 eV): *m*/*z* (%) = 275 (12) [M$^+$ + 1], 183 (3), 167 (16), 149 (16), 123 (20), 95 (27), 91 (93) [C$_7$H$_7^+$], 85 (100).

5-[3-(3-Benzyloxy-1-butyl)-2,2-dimethyl-1-cyclopropyl]-4-hydroxypentanal Ethylene Acetal (16):

To Grignard reagent **15**, prepared from Mg (1.60 g, 65.0 mmol, 5 mL anhydr. THF) and 2-(2-bromoethyl)-1,3-dioxolane (12.2 g, 67.5 mmol in 50 mL anhydr. THF; 35 °C, 1 h) was added the aldehyde *rac*-**14** (13.2 g, 48.0 mmol) in THF (15 mL) at 0 °C. Stirring was continued for 2 h at r.t. and the mixture was poured into ice-cold sat. aq NH$_4$Cl (50 mL) and separated. The aqueous layer was extracted with Et$_2$O (3 × 50 mL) and the combined organic layers were washed with sat. aq NaHCO$_3$ (2 × 50 mL) and sat. aq NaCl (50 mL), and dried (MgSO$_4$). The residue obtained after evaporation of the solvent was purified by column chromatography (short column; Et$_2$O/cyclohexane, 2:1) yielding 16.1 g (89 %) of *rac*-**16** as a colourless oil.

IR (film): ν = 3460, 3025, 2930, 1455, 1380, 1100, 740, 700 cm^{-1}.

^{1}H NMR (CDCl$_3$): δ = 7.35–7.25 (m, 5 H), 4.89 (t, J = 4.5 Hz, 1 H), 4.56, 4.45 (2 d, J = 11.8 Hz, 2 H), 4.00–3.80 (m, 4 H), 3.63 (m$_c$, 1 H), 3.51 (sext, J = 6.1 Hz, 1 H), 2.28 (s, 1 H, OH), 1.90–1.20 (comb. m, 10 H), 1.19 (d, J = 6.1 Hz, 3 H), 1.030/1.023 (2 s, 3 H), 0.916/0.906 [2 s, 3 H, C(CH$_3$)$_2$], 0.60–0.40 (m, 2 H, cyclopropyl-H).

^{13}C NMR (CDCl$_3$): δ = 139.2, 128.3, 127.6, 127.3, 104.6, 74.79, 72.28/71.96, 70.20, 64.90, 37.05/36.97, 32.36/32.26, 31.14, 30.14, 29.38/29.29, 26.45/26.34, 22.93, 20.63/20.54, 19.64, 16.87/16.72, 15.14/15.00.

MS (CI, 120 eV): *m*/*z* (%) = 377 (9) [M$^+$ + 1], 35 (5), 315 (45), 207 (33), 189 (21), 131 (23), 91 (100) [C$_7$H$_7^+$], 85 (44), 73 (44) [C$_3$H$_5$O$_2^+$].

5-[3-(3-Benzyloxy-1-butyl)-2,2-dimethyl-1-cyclopropyl]-4-oxopentanal Ethylene Acetal (17):

To the alcohol *rac*-**16** (15.1 g, 40.0 mmol) in CH$_2$Cl$_2$ (300 mL) was added pyridinium chlorochromate (PCC) on Al$_2$O$_3$ (100 g, 100 mmol) and vigorous stirring was continued for 5 h. The slurry was filtered and eluted with CH$_2$Cl$_2$ (100 mL). The solvent was removed at 30 °C, the residue was taken up in Et$_2$O/cyclohexane (2:1; 50 mL) and purified by filtration through silica gel and elution with the same solvent to give 14.0 g (94 %) of *rac*-**17** as a nearly colourless oil.

IR (film): ν = 3020, 2925, 1720, 1140, 735, 695 cm^{-1}.

^{1}H NMR (CDCl$_3$): δ = 7.35–7.25 (m, 5 H), 4.90 (t, J = 4.4 Hz, 1 H), 4.56, 4.44 (2 d, J = 11.9 Hz, 2 H), 3.95–3.75 (m, 4 H), 3.50 (sext, J = 6.1 Hz, 1 H), 2.55 (t, J = 7.5 Hz, 2 H), 2.45–2.25 (m, 2 H), 1.97 (td, J = 7.5, 4.4 Hz, 2 H), 1.70–1.20 (comb. m, 4 H), 1.19 (d, J = 6.1 Hz, 3 H), 1.057 (s, 3 H), 0.89 [s, 3 H, C(CH$_3$)$_2$], 0.80, 0.53 (2 q, J = 7.3 Hz, *cis*-coupling, 2 H, cyclopropyl-H).

^{13}C NMR (CDCl$_3$): δ = 210.1, 139.2, 128.3, 127.6, 127.4, 103.4, 74.67, 70.21, 64.96, 38.52, 36.88/36.84, 36.09, 28.98, 27.72, 26.25, 21.37/21.32, 20.54/20.49, 19.64, 16.99, 14.88.

MS (CI, 120 eV): *m*/*z* (%) = 375 (11) [M$^+$ + 1], 313 (2), 283 (5), 267 (12), 223 (6), 203 (33), 141 (38), 129 (14) [α-cleavage], 91 (20) [C$_7$H$_7^+$], 79 (11), 73 (100) [C$_3$H$_5$O$_2^+$], 59 (18), 45 (18) [C$_2$H$_5$O$^+$].

5-[3-(3-Hydroxy-1-butyl)-2,2-dimethyl-1-cyclopropyl]-4-oxopentanal Ethylene Acetal (18):

In a hydrogenation apparatus, a mixture of the benzyl ether *rac*-**17** (13.2 g, 35.0 mmol), 5 % Pd–C (5.25 g) and EtOH (200 mL) was hydrogenated at 3 bar until an equimolar amount of H$_2$ was absorbed. The mixture was filtered and the solvent removed. The residue was taken up in Et$_2$O (100 mL), washed with sat. aq NaCl (2 × 100 mL) and dried (MgSO$_4$). The crude material obtained after evaporation of the solvent was the alcohol *rac*-**18** (95 % according to GC analysis, satisfactorily pure for further transformation), yield 9.05 g (91 %) of a nearly colourless oil. An analytical sample could be obtained by column chromatography (Et$_2$O/cyclohexane, 3:1).

IR (film): ν = 3455 (OH), 2925, 1720 (C=O), 1140 cm^{-1}.

^{1}H NMR (CDCl$_3$): δ = 4.92 (t, J = 4.3 Hz, 1 H), 4.00–3.80 (m, 4 H), 3.77 (sext, J = 6.2 Hz, 1 H), 2.58 (t, J = 7.2 Hz, 2 H), 2.37 (d, J = 7.1 Hz, 2 H), 2.24 (s, 1 H, OH), 2.00–1.95 (m, 2 H), 1.50–1.20 (comb. m, 4 H), 1.19 (d, J = 6.2 Hz, 3 H), 1.07, 0.90 [2 s, 6 H, C(CH$_3$)$_2$], 0.80, 0.53 (2 q, J = 7.3 Hz, *cis*-coupling, 2 H, cyclopropyl-H).

^{13}C NMR (CDCl$_3$): δ = 210.3, 103.4, 67.86/67.63, 64.96, 39.69/39.58, 38.45, 36.14, 28.96, 27.72, 26.26, 23.66/23.57, 21.46/21.40, 20.88/20.63, 17.01/16.93, 14.90.

MS (CI, 120 eV): *m*/*z* (%) = 285 (15) [M$^+$ + 1], 267 (27) [M$^+$ − OH], 223 (36), 129 (36) [α-cleavage], 123 (28), 104 (28), 85 (32), 73 (100) [C$_3$H$_5$O$_2^+$], 45 (100) [C$_2$H$_5$O$^+$].

2-[3-(3-Hydroxy-1-butyl)-2,2-dimethyl-1-cyclopropyl]-cyclopenten-2-one (19):

A mixture of dioxolane *rac*-**18** (8.50 g, 30.0 mmol), *p*-TosOH · H$_2$O (5.70 g, 30.0 mmol), acetone (180 mL) and water (90 mL) was refluxed for 15 h. Acetone was removed in vacuo, the residue was saturated with NaCl and extracted with Et$_2$O (3 × 100 mL). The combined organic layers were washed with sat. aq NaHCO$_3$ (2 × 100 mL) and sat. aq NaCl (100 mL), and dried (MgSO$_4$). The residue obtained after evaporation of the solvent was taken up in methanol (500 mL), KOH (1.10 g, 20.0 mmol) was added and the mixture was stirred at r.t. for 15 h. Water (50 mL) was added and the methanol removed in vacuo. The residue was extracted with Et$_2$O (3 × 100 mL) and the combined organic layers were washed with sat. aq NaCl (2 × 50 mL) and dried (MgSO$_4$). After evaporation of the solvent the crude material was purified by column chromatography (Et$_2$O/cyclohexane, 3:1) yielding 3.90 g (58 %) of *rac*-**19** as a yellow oil.

IR (film): ν = 3440 (OH), 3070, 2920, 1705 (C=O), 1690 (C=C) cm^{-1}.

^{1}H NMR (CDCl$_3$): δ = 7.27 (m$_c$, 1 H), 3.78 (sext, J = 6.2 Hz, 1 H), 2.58 (m$_c$, 2 H), 2.36 (m$_c$, 2 H), 2.05 (s, 1 H, OH), 1.55–1.20 (comb. m, 5 H), 1.18 (d, J = 6.2 Hz, 3 H), 1.17, 0.98 [2 s, 6 H, C(CH$_3$)$_2$], 0.90 (m$_c$, 1 H).

^{13}C NMR (CDCl$_3$): δ = 211.1, 156.1, 143.4, 67.75, 39.49, 33.76, 29.34, 29.20, 26.66, 23.59/23.55, 22.30/22.25, 21.41/21.34, 20.30, 15.67.

MS (CI, 120 eV): *m*/*z* (%) = 223 (97) [M$^+$ + 1], 205 (100) [M$^+$ − OH], 161 (41), 149 (46), 133 (31), 120 (34), 109 (44), 105 (30), 91 (30).

4-[2,2-Dimethyl-3-(5-methylenecyclopent-1-en-1-yl)-1-cyclopropyl]-butan-2-ol (20):

(a) By Tebbe Reaction:

To a solution of the cyclopentenone *rac*-**19** (1.78 g, 8.00 mmol) in anhydr. THF (20 mL) at 0 °C was added a toluene solution of Tebbe reagent (16.0 mL of 0.5 M solution, 8.00 mmol). The mixture was allowed to warm to r.t. and after 15 min Et$_2$O (120 mL) was added. Then 60–80 drops of aq. NaOH (0.1 M) were added while stirring the mixture until gas evolution ceased. The orange mixture was dried (MgSO$_4$) and filtered using a silica gel layer. The crude product obtained after evaporation of the solvent was purified by column chromatography (Et$_2$O/cyclohexane, 1:5) yielding 920 mg (52 %) of *rac*-**20** as a nearly colourless oil.

(b) By Wittig Reaction:

To a rapidly stirred slurry of potassium *tert*-butoxide (5.05 g, 45.0 mmol) in anhydr. Et$_2$O (75 mL) was added methyl triphenylphosphonium bromide (16.1 g, 45.0 mmol) and the yellow mixture was heated to reflux for 30 min. Cyclopentenone **19** (3.30 g, 15.0 mmol) in anhydr. Et$_2$O (10 mL) was added dropwise (exothermic reaction) and heating was continued for 4 h. To the cooled mixture were added petroleum ether (50 mL) and water (50 mL). The phases were separated, the aqueous layer extracted with petroleum ether (2 × 25 mL) and the combined organic layers washed with water (3 × 25 mL) and dried ($MgSO_4$). After concentration (triphenylphosphine oxide was removed by filtration) the crude product was purified as in (a) yielding 2.35 g (71 %) of *rac*-**20**.

IR (film): ν = 3350 (OH), 3070, 2925, 1630 (C=C), 1460, 850 cm^{-1}.

UV (ethanol): λ = 241 nm (ε = 10185).

^1H NMR ($CDCl_3$): δ = 5.92, 4.85, 4.75 (3 s, each 1 H), 3.79 (m_c, 1 H), 2.54, 2.40 (2 m_c, each 1 H), 1.70–1.25 (comb. m, 5 H), 1.18 (d, J = 6.2 Hz, 3 H), 1.17, 0.93 (2 s, 6 H), 1.08, 0.75 (2 m_c, 2 H, cyclopropyl-H).

^{13}C NMR ($CDCl_3$): δ = 156.9, 142.0, 135.4, 100.2, 68.14, 40.18, 30.53, 29.40, 28.38, 24.60, 23.58, 22.29, 18.78, 15.88.

MS (CI, 120 eV): m/z (%) = 220 (30) [M^+], 202 (14) [$M^+ - OH$], 187 (21), 177 (17), 162 (29), 147 (100) [$M^+ - C_4H_9$], 131 (36), 119 (73), 105 (58), 91 (48), 85 (26), 79 (21) [$C_6H_7^+$].

4-[2,2-Dimethyl-3-(5-methylenecyclopent-1-en-1-yl)-1-cyclopropyl]-butan-2-one (*rac*-Taylorione) (1):

Tayloriol (*rac*-**20**) (2.20 g, 10.0 mmol) was dissolved in anhydr. benzene (30 mL) and DMSO (30 mL). Pyridinium trifluoroacetate (970 mg, 5.00 mmol) and DCC (6.20 g, 30.0 mmol) were added and the mixture was stirred at r.t. for 24 h. Et_2O (200 mL) was added followed by a solution of oxalic acid (3.80 g, 30.0 mmol of dihydrate) in methanol (30 mL). After gas evolution had ceased, water (200 mL) was added and the insoluble dicyclohexyl urea was removed by filtration. The aqueous phase was extracted with Et_2O (2 × 50 mL) and the combined organic layers were washed with sat. aq $NaHCO_3$ (2 × 100 mL) and sat. aq NaCl (2 × 100 mL), and dried ($MgSO_4$). After concentration the crude product was purified by column chromatography (Et_2O/cyclohexane, 1 : 10); yield 950 mg (87 %) of *rac*-**1** as a colourless oil.

IR (film): ν = 3075, 2970, 2925, 2855, 1725 (C=O), 1635 (C=O), 1460, 1430, 1375, 1365, 1300, 1275, 1265, 1230, 1200, 1165, 1140, 1085, 1020, 960, 930, 855, 785, 740 cm^{-1}.

UV (ethanol): λ = 243 nm (ε = 11200).

^1H NMR ($CDCl_3$): δ = 5.91, 4.84, 4.74 (3 s, each 1 H, vinyl-H), 2.60–2.30 (comb. m, 6 H, active methylene-H), 2.13 (s, 3 H), 1.77 (ddt, J = 14.0, 8.8, 7.0 Hz, 1 H), 1.47 (dtd, J = 14.0, 7.0, 6.0 Hz, 1 H), 1.16 (s, 3 H), 1.10 (m_c, 1 H), 0.94 (s, 3 H), 0.74 (ddd, J = 8.8, 8.8, 6.0 Hz, 1 H). NOE: 1.77, 1.47, 1.16, 1.10, 0.94, 0.74 ppm.

^{13}C NMR ($CDCl_3$): δ = 208.7, 156.8, 141.6, 135.6, 100.3, 44.38, 30.53, 29.90, 29.38, 29.35, 27.70, 24.67, 20.65, 18.86, 15.84.

MS (CI, 120 eV): m/z (%) = 218 (14) [M^+], 203 (5), 185 (8), 175 (17), 160 (85), 145 (100) [$M^+ - C_4H_8O$], 131 (15), 119 (27), 105 (29), 91 (17).

All spectroscopic data were identical with the literature.[1,2]

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