New and Convenient Synthesis of (*R*)-(+)-4,5-Dihydro-4-methyl-2(3*H*)-furanone and (*R*)-(–)-4-Bromo-3-methyl-1-*O*-*tert*-butyldimethylsilylbutan-1-ol

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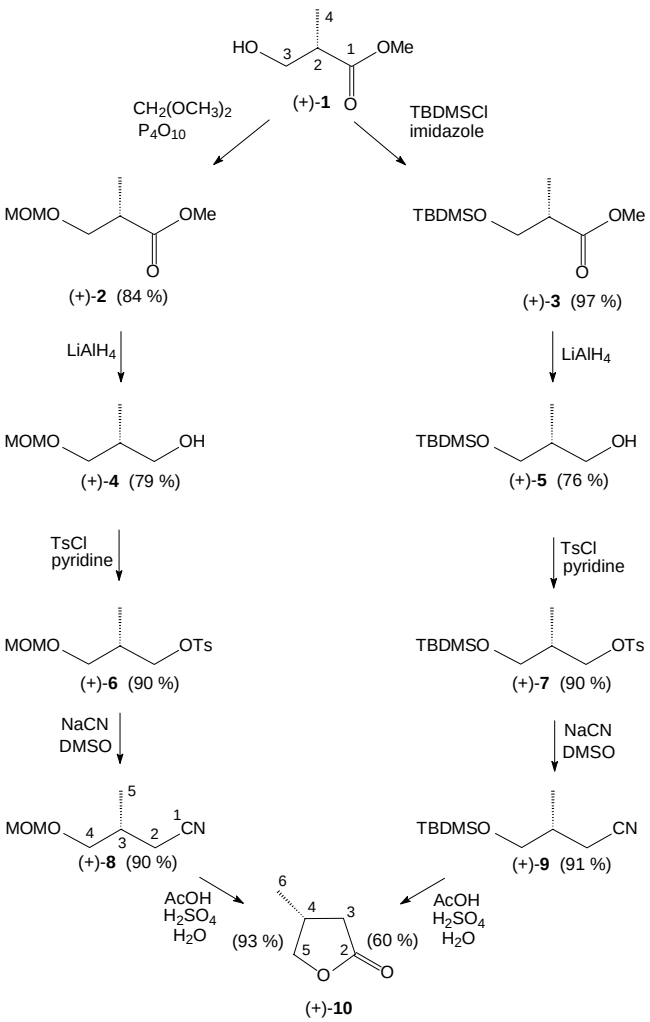
Abstract. A convenient partial synthesis of the lactone (+)-**10** is reported starting from the readily available methyl (*S*)-(+)-3-hydroxy-2-methylpropanoate (+)-**1**. Furthermore, an efficient three step route to the optically active saturated isoprene unit (–)-**13** in high yield starting from the lactone (+)-**10** is reported for the first time.

During our investigations on the enantioselective total synthesis of labdane diterpenes [1, 2] we required the optically active saturated isoprene building block (–)-**13**. This compound can readily be prepared starting from the (*R*)-enantiomer of the β-substituted γ-butyrolactone (+)-**10** adopting a convenient three step sequence developed by Schmid and Barner [3, 4].

While the (*S*)-(–)-enantiomer of lactone **10** is commercially available (Fluka Chemie AG, Buchs, Switzerland), no effective method for the preparation of the corresponding (*R*)-(+)-enantiomer has been reported, although (*R*)-(+)-**10** is known to be a useful chiral synthon for the synthesis of different natural products like mammalian dolichols [5] or various labdane diterpenes [1, 2, 6, 7, 8]. There is only reported the resolution of the racemic lactone (±)-**10** with (*R*)-(+)-α-phenylethylamine as the chiral auxiliary [1, 5] using the method of Helmchen and Nill [9] and a multistep asymmetric total synthesis starting from (*E*)-(2*R*,3*S*)-6-ethylidene-3,4-dimethyl-2-phenylperhydro-1,4-oxazepine-5,7-dione for the preparation of (*R*)-(+)-**10** [10, 11]. (*S*)-(–)-**10** was synthesized by Mori [12] starting from methyl (*R*)-(–)-3-hydroxy-2-methylpropanoate ((–)-**1**) in five steps with a total yield of 17%.

In this communication we report a convenient partial synthesis of (+)-**10** starting from commercial methyl (*S*)-(+)-3-hydroxy-2-methylpropanoate ((+)-**1**), Fluka Chemie AG, Buchs, Switzerland) with a total yield up to 49%. Furthermore, an efficient three step route to the optically active saturated isoprene unit (–)-**13** in high yield starting from the lactone (+)-**10** is reported for the first time.

To avoid by-products it was necessary to protect the hydroxy group of the starting compound (+)-**1** as its MOM- or TBDMS-ether (+)-**2** and (+)-**3**, respectively. (+)-**2** and (+)-**3** can be transferred by means of $LiAlH_4$ reduction to the corresponding alcohols (+)-**4** and (+)-**5**. In order to receive a better leaving group for the next step of the synthesis, alcohols (+)-**4** and (+)-**5** were treated with *p*-tosyl chloride in pyridine yielding the tosylates (+)-**6** and (+)-**7**. Introduction of a cyano group extended the carbon chain for one unit affording the



Scheme 1

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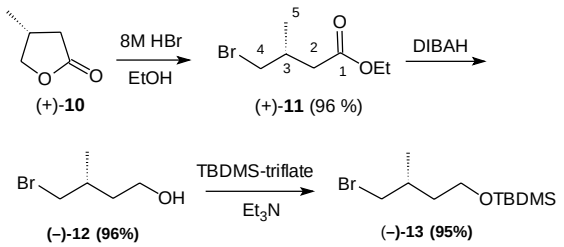
nitriles (+)-**8** and (+)-**9** in almost quantitative yield. Finally cyclization of (+)-**8** and (+)-**9** under acidic conditions afforded lactone (+)-**10** in very good overall yield (up to 49%).

The synthesis of the optically active saturated isoprene building block (–)-**13** was achieved by transesterification of lactone (+)-**10** with 8M HBr in ethanol leading to the γ-bromoester (+)-**11**. DIBAH-reduction of (+)-**11** and protection of the hydroxy group of the resulting alcohol (–)-**12** as TBDMS ether afforded the side chain building block (–)-**13**, synthesized for the first time and in high overall yield.



Scheme 2

Experimental

^{1}H and ^{13}C NMR spectra were taken on a Bruker AC 300 spectrometer. Chemical shifts are given in ppm (δ-scale), coupling constants (J) in Hertz. ^{1}H-chemical shifts (300 MHz) were referenced to the residual $CHCl_3$ signal (7.24). ^{13}C-chemical shifts (75 MHz) were referenced to $CDCl_3$ (77.0). MS were recorded at 70 eV on a Varian MAT-313 spectrometer. Optical rotations were measured on a Perkin Elmer 241 polarimeter. IR-spectra were taken on a Perkin Elmer 1420 ratio recording spectrometer, 1–2% solution in $CHCl_3$.

Thin layer chromatography was carried out on precoated plates of Polygram® SILG/UV$_{254}$ (layer thickness 0.25 mm, Macherey-Nagel). Spots were visualized by UV (254 nm) and spraying with phosphomolybdic acid reagent followed by heating to about 200 °C. MPLC was performed on Merck silica gel 60 (70–230 mesh ASTM).

Methyl (*S*)-(+)-3-hydroxy-2-methylpropanoate was purchased from Fluka Chemie AG (Buchs, Switzerland). All reactions were carried out under nitrogen. Solvents were distilled under nitrogen before use: CH_2Cl_2 and $CHCl_3$ from P_2O_5, ether from Na/benzophenone.

Preparation of 8M HBr in EtOH: Bromine was slowly added to a stirred mixture of tetrahydronaphthalene (dried over Na_2SO_4 and distilled) and some Fe-shavings (as catalyst) at r.t. The resulting HBr gas was bubbled through tetrahydronaphthalene and a gas trap (cooled to –60 °C) to remove rests of bromine and tetrahydronaphthalene. The purified HBr gas was bubbled through anhydrous ethanol (100 g), until the mass increased about 65 g. The resulting solution can be stored at –20 °C for several weeks under exclusion of moisture.

Methyl (S)-(+)-2-methyl-3-methoxymethyloxypropanoate (+)-**2**

7.10 g (50 mmol) P_2O_5 was added to a mixture of 5.33 g (45.1 mmol) of methyl (*S*)-(+)-3-hydroxy-2-methylpropanoate ((+)-**1**) and 34.25 g (450 mmol) methylal in 100 ml of $CHCl_3$. The mixture was stirred overnight at r.t. The solution was decanted. 100 ml of $CHCl_3$ and some crushed ice were added to the residue, and the mixture was neutralized with 2N K_2CO_3-solution. The organic phase was separated, and the aqueous layer was extracted twice with 50 ml of $CHCl_3$. The organic phase was washed with $NaHCO_3$ aq, water and brine, dried (Na_2SO_4) and concentrated *in vacuo* to give 6.14 g (37.9 mmol, 84%) of (+)-**2** as a colourless oil. R_f = 0.56 (cyclohexane/EtOAc, 2:1). $[\alpha]_D^{25}$ = + 11.9° (c = 1.03, $CHCl_3$). – IR: ν/cm^{-1} = 2950, 2880, 1730, 1460, 1440, 1390, 1140, 1110, 1040. – ^{1}H NMR: δ/ppm = 2.65 (m, H-2), 3.55 (m, 2H-3), 1.08 (d, J = 7.1, 3H-4), 3.59 (s, C$\underline{H}_3$O), 4.50 (s, CH$_3$OC$\underline{H}_2$), 3.23 (s, C$\underline{H}_3$OCH$_2$). – ^{13}C NMR: δ/ppm = 174.9 (C-1), 40.0 (C-2), 69.4 (C-3), 13.7 (C-4), 51.5 (C$\underline{H}_3$O), 96.3 (CH$_3$O$\underline{C}$H$_2$), 55.0 ($\underline{C}$H$_3$OCH$_2$). – MS: *m/z* (%) = 147 (10) [M$^+$-15], 131 (7), 103 (11), 69 (100), 45 (10).

Methyl (S)-(+)-2-methyl-3-tert-butyldimethylsilyloxypropanoate (+)-**3**

5.36 g (45.1 mmol) methyl (*S*)-(+)-3-hydroxy-2-methylpropanoate ((+)-**1**) was added to a solution of 6.13 g (90 mmol) imidazole and 10.2 g (67.7 mmol) of TBDMSCl in 100 ml of *N*,*N*-dimethylformamide. The mixture was stirred overnight at 60 °C. The solution was diluted with 100 ml of water and 100 ml of ether, and the organic layer was separated. The aqueous layer was extracted three times with 30 ml of ether. The organic layer was washed twice with 25 ml of water and brine, dried (Na_2SO_4) and concentrated *in vacuo*. The crude product was purified by MPLC (hexane/EtOAc, 2:1) to yield 10.17 g (43.7 mmol, 97%) of (+)-**3** as a colourless liquid. R_f = 0.71 (cyclohexane/EtOAc, 2:1). $[\alpha]_D^{25}$ = + 17.2° (c = 2.51, $CHCl_3$). – IR: ν/cm^{-1} = 2970, 2945, 2875, 1736, 1465, 1261, 1104, 841. – ^{1}H NMR: δ/ppm = 2.60 (m, H-2), 3.66 (m, 2H-3), 1.10 (d, J = 7.0, 3H-4), 3.62 (s, C$\underline{H}_3$O), –0.01(s, (C$\underline{H}_3$)$_2$Si)), 0.83 (s, (C$\underline{H}_3$)$_3$C). – ^{13}C NMR: δ/ppm = 175.3 (C-1), 42.5 (C-2), 65.2 (C-3), 13.4 (C-4), 51.4 ($\underline{C}$H$_3$O), –5.6 (($\underline{C}$H$_3$)$_2$Si), 25.7 (($\underline{C}$H$_3$)$_3$C), 18.1 ((CH$_3$)$_3\underline{C}$). – MS: *m/z* (%) = 201 (10) [M$^+$–31], 175 (24) [M$^+$–57], 101 (100) [M$^+$–131], 89 (18), 75 (16), 73 (16), 59 (14).

(R)-(+)-2-Methyl-3-methoxymethyloxypropan-1-ol (+)-**4**

A solution of 4.90 g (30.2 mmol) (+)-**2** in anhydrous ether (25 ml) was added dropwise to a stirred suspension of $LiAlH_4$ (750 mg) in anhydrous ether (25 ml) at 0–5 °C. The stirring was continued for 4 h at r.t. The excess of $LiAlH_4$ was destroyed by successive careful addition of water (10 ml) and 10% KOH aq (2ml) to the stirred mixture. After stirring for 2 h the suspension was filtered, and the solid was washed three times with 25 ml of ether. The combined filtrates and washings were washed with brine, dried (Na_2SO_4) and concentrated *in vacuo* to give 3.20 g (23.9 mmol, 79%) of (+)-**4**. R_f = 0.26 (cyclohexane/EtOAc, 2:1). $[\alpha]_D^{25}$ = + 10.9° (c = 1.65, $CHCl_3$). – IR: ν/cm^{-1} = 3490, 2995, 2930, 2875, 1460, 1410, 1140, 1040, 1005. – ^{1}H NMR (DMSO-D$_6$): δ/ppm = 3.24 (m, 2H-1), 1.75 (m, H-2), 3.36 (m, 2H-3), 0.84 (d, J = 6.8, 3H-4), 4.52 (s, CH$_3$OC$\underline{H}_2$), 3.22 (s, C$\underline{H}_3$OCH$_2$), 4.41 (t, J = 5.3, OH). – ^{13}C NMR (DMSO-D$_6$): δ/ppm = 69.6 (C-1), 36.1 (C-2), 63.3 (C-3), 14.1 (C-4), 95.8 (CH$_3$O$\underline{C}$H$_2$), 54.4 ($\underline{C}$H$_3$OCH$_2$). – MS: *m/z* (%) = 133 (2) [M$^+$–1], 115 (24) [M$^+$–1–18], 89 (17), 73 (10), 63 (35), 55 (19), 45 (100), 43 (20).

(R)-(+)-2-Methyl-3-tert-butyldimethylsilyloxypropan-1-ol (+)-**5**

Compound (+)-**5** was synthesized as described for compound (+)-**4** starting from 9.78 g (42.0 mmol) (+)-**3** in 50 ml of ether. After work up the reaction yielded 6.95 g (34.0 mmol) of crude (+)-**5**. Purification by MPLC (hexane/EtOAc, 2:1 – 1:1) finally yielded 6.52 g (31.9 mmol, 76%) of (+)-**5** as a colourless liquid. R_f = 0.39 (cyclohexane/EtOAc, 5:1). $[\alpha]_D^{25}$= + 5.9° (c = 1.13, $CHCl_3$). – IR: ν/cm^{-1} = 3475, 3000, 2950, 2925, 2852, 1462, 1255, 1082, 1060, 1022, 835. – ^{1}H NMR: δ/ppm = 3.54 (m, 2H-1), 1.83 (m, H-2), 3.52 (m, 2H-3), 0.76 (d, J = 6.9, 3H-4)), –0.01(s, ($C\underline{H}_3)_2$Si)), 0.82 (s, ($C\underline{H}_3)_3$C), 3.08 (br s, OH). – ^{13}C NMR: δ/ppm = 68.0 (C-1), 37.2 (C-2), 67.4 (C-3), 13.0 (C-4),), –5.7 (($\underline{C}H_3)_2$Si), 25.7 (($\underline{C}H_3)_3$C), 18.1 ($(CH_3)_3\underline{C}$). – MS: *m/z* (%) = 203 (2) [M$^+$–1], 189 (5) [M$^+$–15], 147 (30), 115 (5), 105 (67), 75 (100), 73 (47), 59 (14), 55 (25), 45 (13).

(S)-(+)- 2-Methyl-3-methoxymethyloxypropan-1-yl-tosylate (+)-**6**

4.50 g (23.6 mmol) *p*-TsCl was added to a stirred solution of 3.10 g (23.0 mmol) (+)-**4** in 25 ml anhydrous pyridine at 0–5 °C. The mixture was left to stand overnight in a refrigerator, then poured in ice-water and extracted three times with 25 ml of ether. The ether solution was washed with water, $CuSO_4$ solution, water and brine, dried (Na_2SO_4) and concentrated *in vacuo* to afford 5.95 g (20.6 mmol, 90%) (+)-**6** as a colourless oil. R_f = 0.42 (cyclohexane/EtOAc, 2:1). $[\alpha]_D^{25}$ = + 3.5° (c = 1.04, $CHCl_3$). – IR: ν/cm^{-1} = 3015, 2975,1645, 1610, 1500, 1472, 1365, 1180, 1130, 1045, 985, 955, 820. – ^{1}H NMR: δ/ppm = 3.97 (m, 2H-1), 2.03 (m, H-2), 3.35 (m, 2H-3), 0.87 (d, J = 6.9, 3H-4), 4.45 (s, $CH_3OC\underline{H}_2$), 3.25 (s, $C\underline{H}_3OCH_2$), 7.75 (d, J = 8.0, H-2', H-6'), 7.30 (d, J = 8.0, H-3', H-5'), 2.41 (s, 3H-7'). – ^{13}C NMR: δ/ppm = 71.9 (C-1), 33.3 (C-2), 68.3 (C-3), 13.3 (C-4), 96.2 ($CH_3O\underline{C}H_2$), 54.9 ($\underline{C}H_3OCH_2$), 132.7 (C-1'), 129.6 (C-2', C-6'), 127.6 (C-3', C-5'), 144.6 (C-4'), 21.3 (C-7'). – MS: *m/z* (%) = 288 (2) [M$^+$], 243 (8) [M$^+$–15], 227 (16), 155 (98), 105 (7), 91(100), 45 (100).

(S)-(+)- 2-Methyl-3-tert-butyldimethylsilyloxypropan-1-yl-tosylate (+)-**7**

Compound **7** was synthesized as described for compound (+)-**6** starting from 4.70 g (23.0 mmol) of (+)-**5** in 25 ml of pyridine. After work up the reaction yielded 5.95 g (20.6 mmol, 90%) of (+)-**7** as a colourless oil. R_f = 0.49 (cyclohexane/EtOAc, 5:1). $[\alpha]_D^{25}$ = + 2.6° (c = 0.99, $CHCl_3$). – IR: ν/cm^{-1} = 3041, 2965, 2949, 2865, 1605, 1475, 1366, 1261, 1182, 1105,1051, 980, 945, 843. – ^{1}H NMR: δ/ppm = 3.93 (m, 2H-1), 1.90 (m, H-2), 3.41 (m, 2H-3), 0.84 (d, J = 6.9, 3H-4), 7.75 (d, J = 8.0, H-2', H-6'), 7.29 (d, J = 8.0, H-3', H-5'), 2.40 (s, 3H-7'), –0.06 (s, ($C\underline{H}_3)_2$Si), 0.78 (s, ($C\underline{H}_3)_3$C). – ^{13}C NMR: δ/ppm = 72.1 (C-1), 35.6 (C-2), 63.7 (C-3), 13.1 (C-4), 133.1 (C-1'), 129.7 (C-2', C-6'), 127.8 (C-3', C-5'), 144.5 (C-4'), 21.5 (C-7'), –5.7 (($\underline{C}H_3)_2$Si), 25.7 (($\underline{C}H_3)_3$C), 18.1 ($(CH_3)_3\underline{C}$). – MS: *m/z* (%) = 301 (3) [M$^+$–57], 271 (4), 229 (100), 203 (2), 149 (9), 131 (3), 115 (4), 91 (11).

(R)-(+)- 3-Methyl-4-methoxymethyloxybutanenitrile (+)-**8**

1.34 g (27.3 mmol) NaCN was added to a solution of 5.00 g (17.3 mmol) (+)-**6** in 15 ml of DMSO. The mixture was stirred overnight at 50 °C, diluted with 100 ml of water and extracted three times with 25 ml of pentane. The organic extract was washed with water and brine, dried (Na_2SO_4), and the pentane was evaporated *in vacuo* to give 2.18 g (15.2 mmol, 90%) (+)-**8** as a slightly yellow oil. R_f = 0.37 (cyclohexane/EtOAc, 2:1). $[\alpha]_D^{25}$ = + 27.8° (c = 0.64, $CHCl_3$). – IR: ν/cm^{-1} = 2925, 2880, 2250, 1455, 1420, 1390, 1140, 1105, 1040, 970, 920. – ^{1}H NMR: δ/ppm = 3.39 (m, 2H-2), 2.09 (m, H-3), 3.38 (m, 2H-4), 1.03 (d, J = 6.9, 3H-5), 4.55 (s, $CH_3OC\underline{H}_2$), 3.31 (s, $C\underline{H}_3OCH_2$). – ^{13}C NMR: δ/ppm = 118.4 (C-1), 21.2 (C-2), 30.9 (C-3), 70.4 (C-4), 16.1 (C-5), 96.4 ($CH_3O\underline{C}H_2$), 55.1 ($\underline{C}H_3OCH_2$). – MS: *m/z* (%) = 142 (2) [M$^+$-1], 113 (5), 98 (2), 82 (15), 61 (7), 55 (13), 45 (100).

(R)-(+)-3-Methyl-4-tert-butyldimethylsilyloxybutanenitrile (+)-**9**

735 mg (15 mmol) NaCN was added to a solution of 3.55 g (9.9 mmol) (+)-**7** in 10 ml DMSO. The mixture was stirred overnight at 50 °C, diluted with 100 ml of water and extracted three times with 25 ml of pentane. The organic extract was washed with water and brine, dried (Na_2SO_4), and the pentane was evaporated *in vacuo* to give 1.92 g (8.99 mmol, 91%) of (+)-**9** as a slightly yellow oil. R_f = 0.67 (cyclohexane/EtOAc, 1:1). $[\alpha]_D^{25}$ = + 11.7° (c = 1.75, $CHCl_3$). – IR: ν/cm^{-1} = 2950, 2925, 2855, 2250, 1465, 1390, 1255, 1100, 1030, 840. – ^{1}H NMR: δ/ppm = 3.32 (m, 2H-2), 1.98 (m, H-3), 3.47 (m, 2H-4), 1.00 (d, J = 6.8, 3H-5), –2 (s, ($C\underline{H}_3)_2$Si), 0.86 (s, ($C\underline{H}_3)_3$C). – ^{13}C NMR: δ/ppm = 18.8 (C-1), 20.8 (C-2), 33.2 (C-3), 65.9 (C-4), 13.0 (C-5), –5.6 (($\underline{C}H_3)_2$Si), 25.7 (($\underline{C}H_3)_3$C), 18.1 ($(CH_3)_3\underline{C}$). – MS: *m/z* (%) = 212 (2) [M$^+$–1], 198 (11) [M$^+$–15], 156 (100), 131 (3), 129 (19), 115 (25), 98 (22), 89 (10), 75 (62), 73 (26), 59 (9), 45 (4).

(R)-(+)-4,5-Dihydro-4-methyl-2(3H)-furanone (+)-**10**

A: Cyclization of (+)-**8**

1.90 g (13.3 mmol) of (+) **8** was added to a mixture of 15 ml of conc. H_2SO_4/conc. AcOH/water (1:1:1). The mixture was stirred and heated under reflux for 1.5 h. After pouring onto ice the mixture was neutralized with 10% NaOH aq, extracted three times with ether (25 ml) and then with CH_2Cl_2 (25 ml). The combined organic phases were washed with 5% $KHCO_3$-solution and brine, dried (Na_2SO_4) and concentrated *in vacuo* to yield 1.24 g (12.4 mmol, 93%) of (+)-**10** as a colourless liquid.

B: Cyclization of (+)-**9**

Compound (+)-**10** was synthesized as described under A starting from 1.82 g (8.53 mmol) (+)-**9**. After work up the reaction yielded 512 mg (5.12 mmol, 60%) of (+)-**10** as a colourless oil. R_f = 0.59 (cyclohexane/EtOAc, 1:1). $[\alpha]_D^{25}$ = + 23° (c = 4.00, MeOH) [5] $[\alpha]_D^{26}$= + 25.7° (c = 4.0, MeOH). – IR: ν/cm^{-1} = 2996, 2990, 1779, 1365, 1170, 1020. – ^{1}H NMR: δ/ppm = 2.01 (m, H-3), 2.46 (m, H-3), 2.52 (m, H-4), 3.71 (m, H-5), 4.25 (m, H-5), 1.11 (d, J = 5.9, 3H-6). – ^{13}C NMR: δ/ppm = 177.0 (C-2), 35.7 (C-3), 30.0 (C-4), 74.4 (C-5), 17.5 (C-6). – MS: *m/z* (%) = 100 (21) [M$^+$], 56 (69), 42 (100), 41 (87).

Ethyl (R)-(+)-4-Bromo-3-methylbutanoate (+)-**11**

1.06 g (10.6 mmol) (+)-**10** was added dropwise to a solution of 8M HBr in anhydrous ethanol (15 ml) at r.t. After the

addition was complete, the mixture was stirred for 16 h at r.t. The reaction mixture was poured onto ice, and, after addition of water (50 ml), extracted with ether (3 × 25 ml). The combined organic layers were washed successively with $NaHCO_3$ solution and brine, dried (Na_2SO_4), and the solvent was evaporated *in vacuo* at r.t. to afford 2.13 g (10.2 mmol, 96%) of (+)-**11** as a colourless liquid. R_f = 0.55 (cyclohexane/EtOAc, 8:1). $[\alpha]_D^{25}$ = +2.8° (c = 4.34, $CHCl_3$) [3] (–)-**11** $[\alpha]_D^{26}$ = –2.3° (c = 4.0, $CHCl_3$). – IR: ν/cm^{-1} = 2960, 2925, 2875, 1715, 1450, 1370, 1290, 1135, 1020. – ^{1}H NMR: δ/ppm = 2.16–2.51 (m, 2H-2), 2.28 (m, H-3), 3.39 (m, 2H-4), 1.03 (d, J = 6.6, 3H-5), 4.09 (q, J = 7.1, (OC$\underline{H}_2$CH$_3$), 1.21 (t, J = 7.1, OCH$_2$C$\underline{H}_3$). – ^{13}C NMR: δ/ppm = 171.9 (C-1), 39.2 (C-2), 32.0 (C-3), 40.0 (C-4), 18.6 (C-5), 60.3 (O$\underline{C}$H$_2$CH$_3$), 14.0 (OCH$_2\underline{C}$H$_3$). – MS: *m/z* (%) = 165/163 (16/15), 137/135 (6/5), 129 (8), 88 (100), 60 (30), 55 (46), 41 (35).

R-(–)-4-Bromo-3-methyl-1-butanol (–)-**12**

To 25 ml of a solution of 1M DIBAH in hexane was added dropwise (+)-**11** (2.43 g, 11.6 mmol) in hexane (10 ml) at 0 °C. After the addition was complete, the mixture was allowed to stand at –20 °C for 12 h. Excessive DIBAH was destroyed by adding MeOH at 0 °C, and then the mixture was poured onto ice. The mixture was treated with 2N H_2SO_4 until pH 3–4 was reached, and extracted with ether (3 × 25 ml). The combined organic layers were washed successively with 5% aqueous $NaHCO_3$ solution (20 ml) and brine (20 ml), dried (Na_2SO_4), and the solvent was evaporated *in vacuo* at r.t. to give 1.87 g (11.3 mmol, 96%) of (–)-**12** as a pale yellow liquid. R_f = 0.42 (cyclohexane/EtOAc, 1:1). $[\alpha]_D^{25}$ = –2.5° (c = 2.75, $CHCl_3$). – IR: ν/cm^{-1} = 3400, 2960, 2940, 2855, 1465, 1380, 1275, 1235, 1093, 725. – ^{1}H NMR: δ/ppm = 3.70 (m, 2H-1), 1.45 (m, H-2), 1.69 (m, H-2), 1.99 (m, H-3), 3.36 (J = 5.1, 1.1, 2H-4), 1.01 (d, J = 6.7, 3H-5), 2.44 (br.s, OH). – ^{13}C NMR: δ/ppm = 58.9 (C-1), 37.1 (C-2), 31.6 (C-3), 41.2 (C-4), 18.5 (C-5). – MS: *m/z* (%) = 150/148 (9/8), 122/120 (30/31), 69 (91), 56 (52), 41 (100).

R-(–)-4-Bromo-3-methyl-1-O-tert.-butyldimethylsilylbutan-1-ol (-)-**13**

To a solution of (–)-**12** (1.95 g, 11.6 mmol) and triethylamine (3.54 g, 34.5 mmol) in CH_2Cl_2 (50 ml) was added dropwise TBDMS-triflate (5.85 g, 23 mmol) at 0 °C. After the addition was complete, the mixture was stirred for 1 h at 0 °C and was then allowed to stand at –20 °C for 12 h. The solvent was evaporated, and ether (100 ml) was added to the residue. The ether solution was washed successively with 5% $NaHCO_3$ aq. solution (25 ml), water (20 ml) and brine (20 ml), dried (Na_2SO_4), and the solvent was evaporated *in vacuo* to yield 3.10 g (11.0 mmol, 95%) of (–)-**13** as a colourless oil. R_f = 0.77 (cyclohexane/EtOAc, 2:1). $[\alpha]_D^{25}$ = –2.5° (c = 1.62, $CHCl_3$). – IR: ν/cm^{-1} = 2957, 2931, 2858, 1472, 1388, 1256, 1100, 837. – ^{1}H NMR: δ/ppm = 3.63 (m, 2H-1), 1.43 (m, H-2), 1.64 (m, H-2), 1.98 (m, H-3), 3.38 (m, 2H-4), 1.01 (d, J = 6.7, 3H-5), –0.03 (s, (C$\underline{H}_3$)$_2$Si), 0.87 (s, (C$\underline{H}_3$)$_3$C). – ^{13}C NMR: δ/ppm = 60.7 (C-1), 37.6 (C-2), 31.9 (C-3), 41.6 (C-4), 18.7 (C-5), –5.4 ((C$\underline{H}_3$)$_2$Si), 25.9 ((C$\underline{H}_3$)$_3$C), 18.2 ((CH$_3$)$_3\underline{C}$). – MS: *m/z* (%) = 225/223(9/10), 169/167 (69/70), 139/137 (53/55), 73 (32), 69 (100), 59 (16), 41 (62).

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