Stereospecific Synthesis of (+)-β-Sesquiphellandrene

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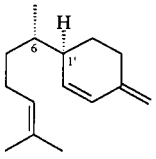
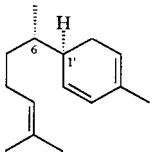
The structure and absolute configuration of (−)-β-Sesquiphellandrene ((−)-**1a**) is shown to be (6*S*)-2-methyl-6-[(1′*R*)-4-methylidenecyclohex-2-enyl]hept-2-ene by stereospecific synthesis of its enantiomer ((+)-**1a**) and of a further (6*S*,1′*S*)-diastereoisomer ((+)-**1b**). Characteristic spectroscopic differences in both diastereoisomeric series are discussed.

Introduction. – In 1965, *Connell* and *Sutherland* [1] described the isolation of the bisabolatriene (−)-**1a** as one of the minor components of ginger oil (from *Zingiber officinale* ROSCOE). The constitution of the monocyclic sesquiterpene named β-sesquiphellandrene was deduced by comparison of its spectral data with the data of (−)-zingiberene ((−)-**2**), the structure of which was established by *Eschenmoser* and *Schinz* [2].

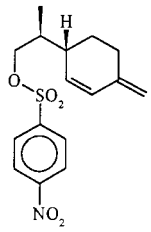


(−)-**1a**

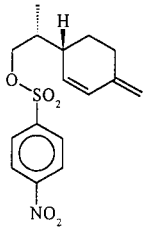


(−)-**2**

The observation that the isomerization product of (−)-**1a** furnished the same *Diels-Alder* adduct (of unknown structure) as (−)-**2**, in our view, does not finally establish the absolute configuration of (−)-**1a**. In the meantime, β-sesquiphellandrene has been reported to be a constituent of various plants (*Iva xanthifolia*, *Senecio amplexicaulis*, and *Rugelia nudicaulis* by *Bohlmann et al.* [3–5], *Marchantia chenopoda* by *Tori* and *Aoki* [6], and *Fitzroya cupressoides* by *Cool* [7]), but stereochemical determination by stereospecific synthesis is still lacking. In our previous paper [8], we depicted the preparation of the two monoterpene derivatives **3a** and **3b**, both in a diastereoisomeri-



3a

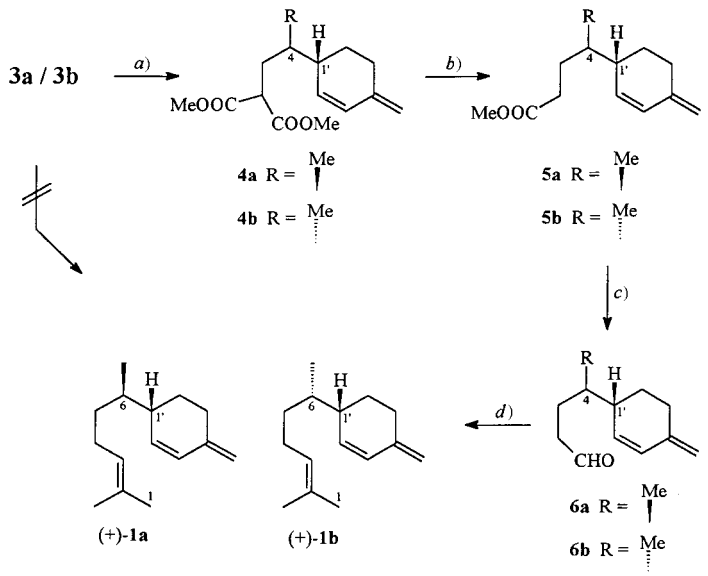


3b

cally pure and an enantiomerically enriched form (60% ee and >90% ee, resp.). With these building blocks of well-defined configuration at our hands, β-sesquiphellandrene became an attractive synthetic target molecule.

Results. – Unexpectedly, the direct substitution of the *p*-nitrobenzenesulfonate group with lithio prenylcopper reagents [9], which would have been the most straightforward synthetic approach to the sesquiphellandrenes, proved completely unsuccessful. Instead, we found that the formation of the side-chain could be initiated by nucleophilic displacement of the nosylate by sodium dimethoxymalonate (*Xu et al.* [10] and *Kato* and *Takeshita* [11]). Thereafter, monodecarbomethoxylation was cleanly achieved without any detectable attack on the conjugated diene system, in a mild procedure employing LiI · 3 H_2O/NaCN in DMF at 125° according to the procedure of *Fiaud* and *Legros* [12]. Subsequent DIBAH reduction of the monoester in toluene at −85° (*Garner* and *Park* [13], *Stevens et al.* [14]) furnished the aldehydes **6a** and **6b** in good yields (*Scheme*). In the final step of our synthesis, we had to use a large excess of the isopropylidene *Wittig* reagent to obtain acceptable yields of the β-sesquiphellandrenes (+)-**1a** and (+)-**1b**. Both were prepared in a diastereoisomerically pure form.

Scheme



a) $CH_2(COOMe)_2$, NaH, KI, THF/DMF, 0° → 80°. *b*) LiI · 3 H_2O, NaCN, DMF, 125°. *c*) DIBAH, $PhCH_3$, −85°. *d*) $Ph_3PCH(CH_3)_2I$, BuLi, THF.

Discussion. – In *Fig. 1*, ^{1}H-NMR spectrum of (+)-**1a** is displayed. In *Tables 1* and *2*, ^{1}H-NMR chemical shifts of the Me−C(7) group, and ^{13}C-NMR data of (+)-**1a** and (+)-**1b** (400 and 100 MHz, resp., $CDCl_3$, assignment by H,H-COSY, C,H correlation (HMQC), C,H long-range correlation (HMBC)) are compared with the data of natural (−)-β-sesquiphellandrene isolated from *Marchantia chenopoda* (400 and 100 MHz,

resp., $CDCl_3$, *Tori* and *Aoki* [6]), with a 1:1 mixture of synthetic diastereoisomers (200 and 50 MHz, resp., $CDCl_3$, *Flisak* and *Hall* [15]), and with the diastereoisomerically pure synthetic racemate of **1a** (75 and 300 MHz, resp., $CDCl_3$, *Schulte-Göcking* [16]). NMR Spectra of (+)-**1a** are obviously in very good agreement with those of the natural product. By such a comparison, the relative configuration of natural β-sesquiphellandrene at the adjacent chirality centers is established as of **1a**.

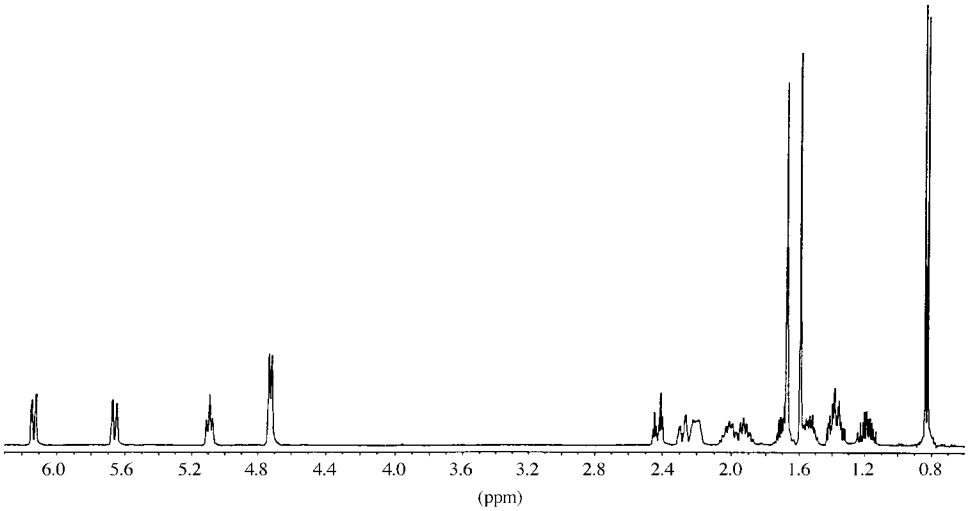


Fig. 1. *^{1}H-NMR Spectrum* (400 MHz, $CDCl_3$) *of (+)-***1a**

Table 1. *^{1}H-NMR Chemical Shifts of the Me–C(7) Group of Compounds (+)-***1a** *and (+)-***1b**

(+)-**1a**	(+)-**1b**	Natural compound [6]	All diastereoisomers [15]	*rac*-**1a** [16]
0.83	0.87	0.84	0.84/0.88	0.84

Characteristic differences between (+)-**1a** and its diastereoisomer (+)-**1b** become even more obvious when details of their ^{13}C-NMR spectra and the corresponding multiplicities (DEPT) are compared directly, as presented in *Fig. 2*.

Considering that optical rotations reported for natural β-sesquiphellandrene are negative $[\alpha]_D^{29} = -3.99$ (in substance) [1] and $[\alpha]_D = -7.48$ ($c = 0.82$, $CHCl_3$ [6]), while our material of established (6*R*,1′*S*)-configuration displayed positive values ($[\alpha]_D^{22} = +5.95$ ($c = 1.71$, $CHCl_3$; 60% ee determined)), (+)-**1a** must be the synthetic enantiomer of the natural product. Therefore, the absolute configuration of natural (−)-β-sesquiphellandrene is (6*S*,1′*R*).

Table 2. *^{13}C-NMR Chemical Shifts of the Compounds (+)-***1a** *and (+)-***1b**

(+)-**1a**	(+)-**1b**	Natural compound [6]	All diastereoisomers [15]	*rac*-**1a** [16]
15.87 (*q*, C(7))	16.43 (*q*, C(7))	15.9	15.91/16.47	15.9 (*q*)
17.66 (*q*, C(1))	17.66 (*q*, C(1))	17.7	17.65	17.7 (*q*)
24.41 (*t*, C(6′))	26.23 (*t*, C(6′))	24.4	24.52/26.32	24.4 (*t*)
25.73 (*q*, *Me*−C(2))	25.73 (*q*, *Me*−C(2))	25.7	25.71	25.7 (*q*)
26.05 (*t*, C(4))	26.06 (*t*, C(4))	26.1	26.10	26.0 (*t*)
30.35 (*t*, C(5′))	30.50 (*t*, C(5′))	30.4	30.41/30.53	30.5 (*t*)
34.27 (*t*, C(5))	33.88 (*t*, C(5))	34.3	33.96/34.32	34.3 (*t*)
36.58 (*d*, C(6))	36.50 (*d*, C(6))	36.6	36.56/36.67	36.5 (*d*)
40.54 (*d*, C(1′))	41.02 (*d*, C(1′))	40.6	40.63/41.07	40.7 (*d*)
109.86 (*t*, CH_2=C(4′))	109.96 (*t*, CH_2=C(4′))	109.9	109.89/109.98	109.9 (*t*)
124.76 (*d*, C(3))	124.80 (*d*, C(3))	124.8	124.84	124.7 (*d*)
129.47 (*d*, C(3′))	129.81 (*d*, C(3′))	129.5	129.58/129.90	129.7 (*d*)
131.27 (*s*, C(2))	131.27 (*s*, C(2))	131.3	131.18	131.2 (*s*)
135.24 (*d*, C(2′))	133.99 (*d*, C(2′))	135.3	133.87/135.09	134.0 (*d*)
143.76 (*s*, C(4′))	143.77 (*s*, C(4′))	143.8	143.71	143.7 (*s*)

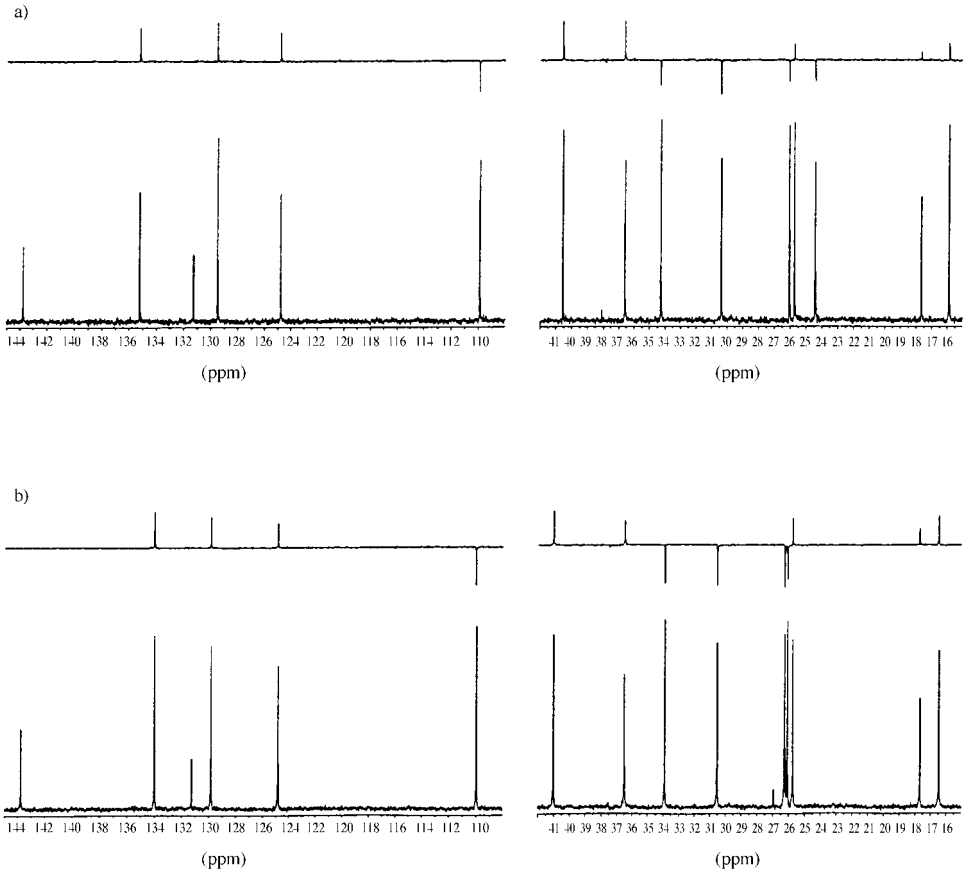


Fig. 2. *^{13}C-NMR and DEPT spectra* (100 MHz, $CDCl_3$) a) *of (+)-***1a** *and* b) *of (+)-***1b**

Experimental Part

General. All reagents and solvents were commercially available and used without further purification. Abs. THF was destilled twice from KOH and once from CaH_2. Solns. were dried with Na_2SO_4. TLC: *Merck* silica gel *60* F_{254} plates (Art. No. 5554); detection with UV, phosphomolybdic acid, $KMnO_4$, I_2, or anisic aldehyde. Column chromatography (CC): silica gel *60* (230–400 mesh) of *Merck Co*. Optical rotations: *Perkin-Elmer-141* automatic polarimeter ($CHCl_3$ at 22°, 10-cm, 1-ml, or 5-ml cell). UV Spectra: *Hitachi U-2000* spectrophotometer. IR Spectra: *Shimadzu-470* spectrometer; films, $\tilde{\nu}$ in cm^{-1}. NMR Spectra: *Bruker-DRX-400* spectrometer (^1H: 400.13 MHz, ^{13}C: 100.61 MHz); solvent: $CDCl_3$; δ [ppm] rel. to internal Me_4Si (= 0.00 ppm, ^1H) and $CDCl_3$ (= 77.02 ppm, ^{13}C); *J* in Hz. MS: *Finnigan Mat-8230* spectrometer (70 eV); *m*/*z* (rel. %).

*(6*R*)-2-Methyl-6-[(1*S*)-4-methylidenecyclohex-2-enyl]hept-2-ene* ((+)-**1a**). To a slurry of Ph_3PCHMe_3I (12.15 g, 28.1 mmol) in THF (90 ml) at 0°, BuLi (11.2 ml 2.5M soln. in hexanes, 28.0 mmol) was added slowly *via* syringe. The resulting red soln. was stirred for 30 min at r.t. Thereafter, a soln. of **6a** (975 mg, 5.48 mmol) in THF (45 ml) was added dropwise within 10 min, stirring was continued at r.t. for 2 h and at 50° for 1 h. H_2O (100 ml) was added at r.t., followed by cyclohexane (500 ml), the mixture was washed with sat. aq. NH_4Cl, H_2O and brine. Drying, evaporation, and purification by CC provided (+)-**1a** (593 mg, 53%). Colorless oil. R_f (cyclohexane) 0.70. $[\alpha]_D = +5.95$ ($c = 1.71$). UV (MeOH): 18400 (231.2). IR: 3077 (C=CH_2), 3021 (C=C–H), 2962, 2928, 2858 (C–H), 1636, 1597 (C=C), 876 (C=CH_2). ^{1}H-NMR: 0.83 (*d*, $^3J = 6.8$, 3 H–C(7)); 1.13–1.24 (*m*, H–C(5)); 1.32–1.43 (*m*, H–C(5), H–C(6′)); 1.48–1.59 (*m*, H–C(6)); 1.59 (*s*, 3 H–C(1)); 1.67 (*d*, $^4J =$ 1.2, Me–C(2)); 1.67–1.74 (*m*, H–C(6′)); 1.87–2.08 (*m*, 2 H–C(4)); 2.16–2.32 (*m*, H–C(1′), H–C(5′)); 2.39–2.46 (*dt*-like, $^2J = 14.8$, H–C(5′)); 4.72 (*m*, CH_2=C(4′)); 5.09 (*m*, H–C(3)); 5.66 (*d*, $^3J = 10.0$, H–C(2′)); 6.13 (*dd*, $^3J = 10.0$, $^4J = 2.6$, H–C(3′)). ^{13}C-NMR: see *Table 2* (assignment of NMR data by H,H-COSY, C,H correlation (HMQC), and C,H long-range correlation (HMBC)). MS: 204 (37, M^+), 161 (47), 133 (32), 120 (25), 109 (23), 93 (44), 92 (37), 91 (29), 71 (26), 69 (100).

*(6*S*)-2-Methyl-6-[(1*S*)-4-methylidenecyclohex-2-enyl]hept-2-ene* ((+)-**1b**). Compound **6b** (180 mg, 1.01 mmol) was treated as described above. Purification by CC yielded (+)-**1b** (93 mg, 45%). R_f (cyclohexane) 0.70. $[\alpha]_D = +39.58$ ($c = 0.43$). UV (MeOH): 12700 (231.0). IR: 3077 (C=CH_2), 3023 (C=C–H), 2964, 2928, 2858 (C–H), 1635, 1596 (C=C), 877 (C=CH_2). ^{1}H-NMR: 0.87 (*d*, $^3J = 7.0$, 3 H–C(7)); 1.11–1.24 (*m*, H–C(5)); 1.35–1.45 (*m*, H–C(5), H–C(6′)); 1.45–1.55 (*m*, H–C(6)); 1.59 (*s*, 3 H–C(1)); 1.67 (*d*, $^4J =$ 1.2, Me–C(2)); 1.70–1.80 (*m*, H–C(6′)); 1.88–2.10 (*m*, 2 H–C(4)); 2.16–2.25 (*m*, H–C(1′)); 2.25–2.37 (*m*, H–C(5′)); 2.40–2.50 (*dt*-like, $^2J = 14.7$, H–C(5′)); 4.73 (*m*, CH_2=C(4′)); 5.09 (*m*, H–C(3)); 5.69 (*d*, $^3J =$ 10.1, H–C(2′)); 6.14 (*dd*, $^3J = 10.1$, $^4J = 2.3$, H–C(3′)). ^{13}C-NMR: see *Table 2* (assignment of NMR data by H,H-COSY, C,H correlation (HMQC), and C,H long-range correlation (HMBC)). MS: 204 (35, M^+), 161 (38), 133 (36), 120 (29), 119 (31), 105 (27), 93 (63), 92 (34), 91 (45), 79 (22), 77 (26), 69 (100).

*Methyl (4*R*)-2-(Methoxycarbonyl)-4-[(1*S*)-4-methylidenecyclohex-2-enyl]pentanoate* (**4a**). To a stirred slurry of NaH (1.65 g, 68.9 mmol) in a mixture of THF (150 ml) and DMF (150 ml), dimethyl malonate (8.48 g, 68.9 mmol) was added slowly *via* syringe. After stirring at r.t. for 15 min, KI (3.05 g, 18.4 mmol) was added, followed by a soln. of **3a** (4.65 g, 13.8 mmol) in a mixture of THF (90 ml) and DMF (90 ml). The resulting mixture was heated at 80° for 2 h. Sat. aq. NH_4Cl soln. (300 ml) was added at r.t. After extraction with Et_2O, the combined org. layers were washed with sat. aq. NH_4Cl soln., H_2O, brine, dried, and evaporated. Excess of dimethyl malonate was removed at 50°/0.05 mbar to furnish the crude diester **4a** (3.45 g, 94%). Pure samples were obtained by CC. R_f (cyclohexane/AcOEt 10:1) 0.45. $[\alpha]_D = +5.72$ ($c = 1.17$). IR: 3077 (C=CH_2), 3020 (C=C–H), 2955, 2936, 2876 (C–H), 1755, 1737 (C=O), 1636, 1597 (C=C), 1245, 1155 (C–O), 880 (C=CH_2). ^{1}H-NMR: 0.82 (*d*, $^3J = 7.0$, 3 H–C(5)); 1.30–1.42 (*m*, 1 H), 1.44–1.53 (*m*, 1 H), 1.64–1.72 (*m*, 2 H), 1.96–2.05 (*m*, 1 H) (2 H–C(3), H–C(4), 2 H–C(6′)); 2.15–2.28 (*m*, 2 H), 2.36–2.44 (*m*, 1 H) (H–C(1′), 2 H–C(5′)); 3.41 (*dd*, $^3J = 9.4$, $^3J = 6.1$, H–C(2)); 3.69 (*s*, 3 H), 3.70 (*s*, 3 H) (2 COOMe); 4.71 (*m*, CH_2=C(4′)); 5.57 (*d*, $^3J =$ 9.8, H–C(2′)); 6.11 (*dd*, $^3J = 9.8$, $^4J = 2.5$, H–C(3′)). ^{13}C-NMR: 15.38 (*q*, C(5)); 24.15 (*t*, C(6′)); 30.10 (*t*, C(5′)); 33.10 (*t*, C(3)); 34.84 (*d*, C(4)); 40.34 (*d*, C(1′)); 49.89 (*d*, C(2)); 52.43, 52.47 (2*q*, 2 COOMe); 110.35 (*t*, CH_2=C(4′)); 130.07 (*d*, C(3′)); 133.68 (*d*, C(2′)); 143.18 (*s*, C(4′)); 169.79/169.99 (*s*, C(1), COOMe)). MS: 266 (19, M^+), 134 (100), 120 (49), 113 (30), 109 (19), 93 (43), 91 (30), 77 (19).

*Methyl (4*S*)-2-(Methoxycarbonyl)-4-[(1*S*)-4-methylidenecyclohex-2′-enyl]pentanoate* (**4b**). Compound **3b** (750 mg, 2.22 mmol) was treated as described above to yield **4b** (539 mg, 91%). Pure samples were obtained by CC. R_f (cyclohexane/AcOEt 10:1) 0.45. $[\alpha]_D = +25.36$ ($c = 0.56$). IR: 3077 (C=CH_2), 3022 (C=C–H), 2955, 2935, 2876 (C–H), 1755, 1738 (C=O), 1635, 1596 (C=C), 1260, 1155 (C–O), 879 (C=CH_2). ^{1}H-NMR: 0.87 (*d*, $^3J = 7.0$, 3 H–C(5)); 1.36–1.52 (*m*, 2 H), 1.64–1.75 (*m*, 2 H), 1.99–2.08 (*m*, 1 H) (2 H–C(3), H–C(4), 2 H–C(6′)); 2.15–2.30 (*m*, 2 H), 2.36–2.45 (*m*, 1 H) (H–C(1′), 2 H–C(5′)); 3.43 (*dd*, $^3J = 9.8$, $^3J = 5.8$,

H–C(2)); 3.70 (*s*, 3 H), 3.71 (*s*, 3 H) (COOMe); 4.73 (*m*, CH_2=C(4′)); 5.63 (*d*, ^3J = 9.8, H–C(2′)); 6.14 (*dd*, ^3J = 9.8, ^4J = 2.5, H–C(3′)). ^{13}C-NMR: 16.12 (*q*, C(5)); 25.63 (*t*, C(6′)); 30.21 (*t*, C(5′)); 32.73 (*t*, C(3)); 34.77 (*d*, C(4)); 40.84 (*d*, C(1′)); 49.95 (*d*, C(2)); 52.44, 52.53 (2*q*, 2 COO*Me*); 110.49 (*t*, *C*H_2=C(4′)); 130.41 (*d*, C(3′)); 132.77 (*d*, C(2′)); 143.27 (*s*, C(4′)); 169.83, 170.10 (2*s*, C(1), 2-*C*OOMe)). MS: 266 (17, M^+), 134 (100), 120 (73), 113 (34), 109 (23), 93 (48), 91 (36), 77 (24).

*Methyl (4*R*)-[(1*S*)-4-Methylidenecyclohex-2-enyl]pentanoate* (**5a**). A soln. of **4a** (3.35 g, 12.6 mmol), LiI · $3H_2O$ (11.8 g, 63.0 mmol) and NaCN (617 mg, 12.6 mmol) in DMF (50 ml) was heated to 125° for 8 h. Et_2O (500 ml) was added at r.t., the mixture was washed with H_2O, brine, dried, and evaporated. CC furnished **5a** (1.62 g, 62%). Colorless oil. R_f (cyclohexane/AcOEt 20 : 1) 0.45. $[\alpha]_D$ = + 7.34 (*c* = 1.08). IR: 3077 (C=*C*H_2), 3021 (C=*C*–*H*), 2951, 2934, 2872 (C–H), 1737 (C=O), 1636, 1597 (C=C), 1271, 1172 (C–O), 878 (C=*C*H_2). ^{1}H-NMR: 0.81 (*d*, ^3J = 6.5, 3 H–C(5)); 1.31–1.55 (*m*, 3 H), 1.64–1.75 (*m*, 2 H) (2 H–C(3), H–C(4), 2 H–C(6′)); 2.15–2.43 (*m*, H–C(1′), 2 H–C(2), 2 H–C(5′)); 3.63 (*s*, COOMe); 4.71 (*m*, CH_2=C(4′)); 5.61 (*d*, ^3J = 9.9, H–C(2′)); 6.11 (*dd*, ^3J = 9.9, ^4J = 2.6, H–C(3′)). ^{13}C-NMR: 15.53 (*q*, C(5)); 24.26 (*t*, C(6′)); 29.15 (*t*, C(3)); 30.13 (*t*, C(5′)); 32.28 (*t*, C(2)); 36.53 (*d*, C(4)); 40.29 (*d*, C(1′)); 51.44 (*q*, COO*Me*); 110.16 (*t*, *C*H_2=C(4′)); 129.81 (*d*, C(3′)); 134.25 (*d*, C(2′)); 143.35 (*s*, C(4′)); 174.20 (*s*, C(1)). MS: 208 (35, M^+), 134 (27), 121 (26), 115 (25), 93 (100), 91 (41), 83 (28), 79 (22), 77 (29), 74 (36), 73 (32).

*Methyl (4*S*)-[(1*S*)-4-Methylidenecyclohex-2-enyl]pentanoate* (**5b**). Compound **4b** (510 mg, 1.92 mmol) was treated as described above. CC furnished **5a** (264 mg, 66%). Colorless oil. R_f (cyclohexane/AcOEt 20 : 1). 0.45 $[\alpha]_D$ = + 20.40 (*c* = 0.35). IR: 3077 (C=*C*H_2), 3022 (C=*C*–*H*), 2959, 2933, 2872 (C–H), 1742 (C=O), 1635, 1596 (C=C), 1258, 1170 (C–O), 877 (C=*C*H_2). ^{1}H-NMR: 0.86 (*d*, ^3J = 6.6, 3 H–C(5)); 1.35–1.62 (*m*, 3 H), 1.68–1.78 (*m*, 2 H) (2 H–C(3), H–C(4), 2 H–C(6′)); 2.15–2.45 (*m*, H–C(1′), 2 H–C(2), 2 H–C(5′)); 3.64 (*s*, COOMe); 4.73 (*m*, CH_2=C(4′)); 5.66 (*d*, ^3J = 9.9, H–C(2′)); 6.11 (*d*, ^3J = 9.9, ^4J = 2.4, H–C(3′)). ^{13}C-NMR: 16.23 (*q*, C(5)); 25.95 (*t*, C(6′)); 28.80 (*t*, C(3)); 30.32 (*t*, C(5′)); 32.35 (*t*, C(2)); 36.53 (*d*, C(4)); 40.83 (*d*, C(1′)); 51.51 (*q*, COO*Me*); 110.31 (*t*, *C*H_2=C(4′)); 130.15 (*d*, C(3′)); 133.26 (*d*, C(2′)); 143.47 (*s*, C(4′)); 174.31 (*s*, C(1)). MS: 208 (28, M^+), 134 (24), 121 (26), 115 (24), 93 (100), 91 (52), 83 (26), 79 (30), 77 (42), 74 (33), 73 (35).

*(4*R*)-4-[(1*S*)-4-Methylidenecyclohex-2-enyl]pentanal* (**6a**). A soln. of **5a** (1.60 g, 7.68 mmol) in toluene (80 ml) was cooled to − 85°, and DIBAH (7.7 ml 1.0M soln. in hexane) was added *via* syringe. After stirring for 30 min, further DIBAH (7.7 ml 1.0M soln. in hexane) was added. After 1.5 h, MeOH (50 ml) was added slowly, the mixture was warmed to − 30° and hydrolized with sat. aq. NH_4Cl soln. (100 ml). Extraction with Et_2O, washing the combined org. layers with sat. aq. NH_4Cl soln., H_2O, and brine, and evaporation gave the crude aldehyde (1.30 g, 95%). Pure samples were obtained by CC. R_f (cyclohexane/AcOEt = 20 : 1) 0.35. $[\alpha]_D$ = + 5.01 (*c* = 1.20). IR: 3077 (C=*C*H_2), 3021 (C=*C*–*H*), 2958, 2934, 2872 (C–H), 2718 (O=*C*–*H*), 1726 (C=O), 1635, 1596 (C=C), 878 (C=*C*H_2). ^{1}H-NMR: 0.83 (*d*, ^3J = 6.5, 3 H–C(5)); 1.32–1.57 (*m*, 3 H), 1.65–1.76 (*m*, 2 H) (H–C(3), H–C(4), H–C(6′)); 2.15–2.29 (*m*, 2 H), 2.33–2.51 (*m*, 3 H) (H–C(1′), 2 H–C(2), 2 H–C(5′)); 4.72 (*m*, CH_2=C(4′)); 5.61 (*d*, ^3J = 9.9, H–C(2′)); 6.13 (*dd*, ^3J = 9.9, ^4J = 2.2, H–C(3′)); 9.74 (*m*, H–C(1)). ^{13}C-NMR: 15.68 (*q*, C(5)); 24.32 (*t*, C(6′)); 26.12 (*t*, C(3)); 30.09 (*t*, C(5′)); 36.55 (*d*, C(4)); 40.35 (*d*, C(1′)); 42.15 (*t*, C(2)); 110.33 (*t*, *C*H_2=C(4′)); 129.94 (*d*, C(3′)); 134.07 (*d*, C(2′)); 143.30 (*s*, C(4′)); 202.57 (*d*, C(1)). MS: 178 (32, M^+), 145 (18), 136 (18), 134 (16), 119 (13), 105 (11), 93 (100), 91 (45), 79 (21), 77 (38).

*(4*S*)-4-[(1*S*)-4-Methylidenecyclohex-2-enyl]pentanal* (**6b**). Compound **5b** (250 mg, 1.20 mmol) was treated as described above to yield **4b** (190 mg, 89%). Pure samples were obtained by CC. R_f (cyclohexane/AcOEt 20 : 1) 0.35. $[\alpha]_D$ = + 14.63 (*c* = 0.25). IR: 3077 (C=*C*H_2), 3022 (C=*C*–*H*), 2962, 2929, 2859 (C–H), 2715 (O=*C*–*H*), 1727 (C=O), 1635, 1596 (C=C), 875 (C=*C*H_2). ^{1}H-NMR: 0.87 (*d*, ^3J = 6.5, 3 H–C(5)); 1.35–1.55 (*m*, 3 H), 1.65–1.80 (*m*, 2 H) (2 H–C(3), H–C(4), 2 H–C(6′)); 2.15–2.50 (*m*, H–C(1′), 2 H–C(2), 2 H–C(5′)); 4.73 (*m*, CH_2=C(4′)); 5.66 (*d*, ^3J = 9.6, H–C(2′)); 6.15 (*dd*, ^3J = 9.9, ^4J = 2.6, H–C(3′)); 9.74 (*m*, H–C(1)). ^{13}C-NMR: 16.37 (*q*, C(5)); 25.76 (*t*, C(3)); 25.91 (*t*, C(6′)); 30.30 (*t*, C(5′)); 36.54 (*d*, C(4)); 40.85 (*d*, C(1′)); 42.20 (*t*, C(2)); 110.46 (*t*, *C*H_2=C(4′)); 130.29 (*d*, C(3′)); 133.05 (*d*, C(2′)); 143.34 (*s*, C(4′)); 202.58 (*d*, C(1)). MS: 178 (27, M^+), 145 (25), 136 (14), 134 (11), 119 (10), 93 (100), 91 (73), 79 (32), 77 (53).

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