SYNTHESIS OF (+)-METHYL DIHYDROEPIJASMONATE

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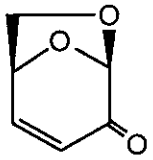
Abstract-------(+)-Methyl dihydroepijasmonate (**2**) was synthesized starting from levoglucosenone (**1**) in an optically pure state.

Levoglucosenone [1,6-anhydro-3,4-dideoxy-β-D-glycero-hex-3-eno-pyranos-2-ulose (**1**)][1] is widely known as a pyrolytic product of cellulose. It is very useful chiral source for synthesizing natural products[2] owing to its highly functionalized structure containing essentially one chiral center. The synthesis of useful compounds starting from levoglucosenone (**1**) and their applications as useful chiral building blocks have been reported.[3]

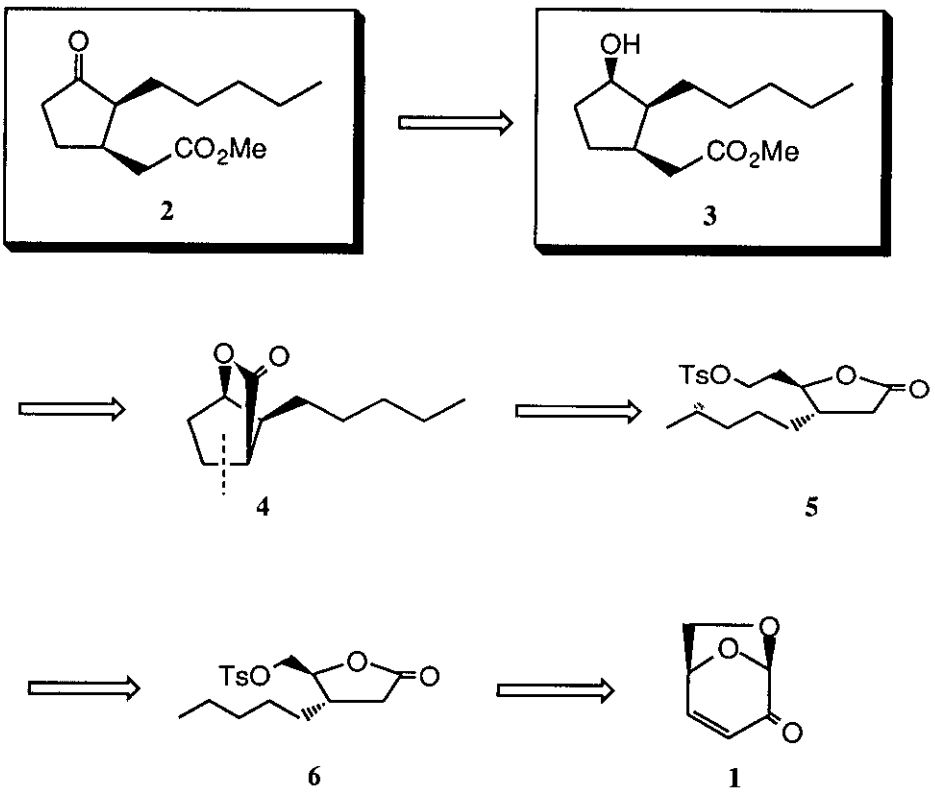


Levoglucosenone **(1)**

Attention is now being derected to new applications for synthesizing substituted cyclopentane derivatives. This paper reports the synthesis of (+)-methyl dihydroepijasmonate (**2**), an important synthetic fragrance. A very recent investigation showed that **2** and its reduced derivative (**3**) possessed potent plant hormone activities such as potato tuber formation[4] and plant growth regulation.[5] It was also definitively shown that the *cis* configurations of all substituents in **2** and **3** were important to reveal those activities. Although racemic compounds (**2**) and (**3**) were synthesized,[5,6] the stereoselective synthesis of optically active **2** and **3** has so far not been reported.

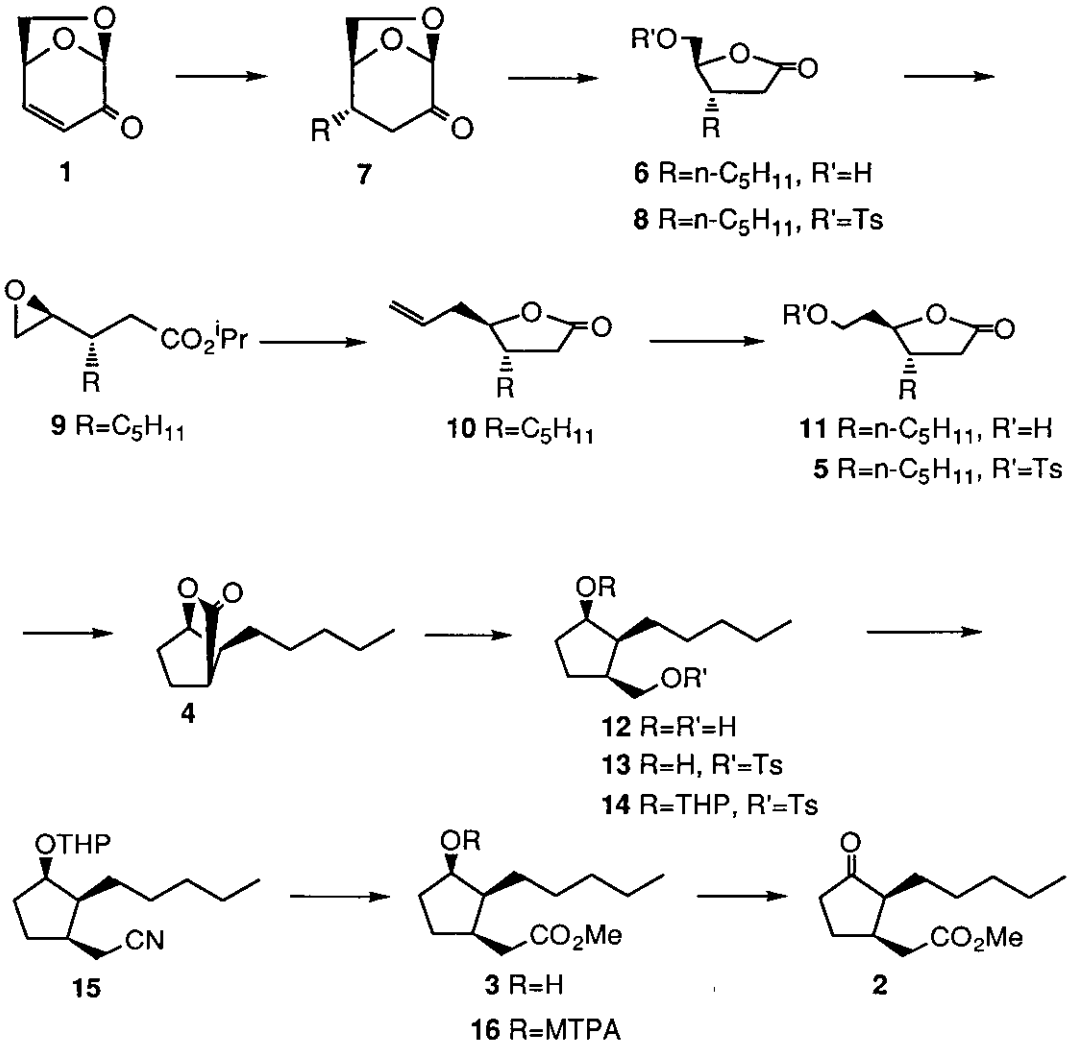
Our synthetic plan is shown in Scheme 1. It should be an easy process to convert the hydroxy compound (**3**) to **2** by oxidation. The main problem is how to set up all substituents in their correct configurations. We chose the bicyclic γ-lactone (**4**) as the precursor for this purpose. Compound (**4**) may be derived from the tosylate (**5**) by

cyclization reaction. The precursor of **5** should be compound (**6**) easily derivable from levoglucosenone (**1**). Thus, cyclization reaction (**5**→**4**) should be a key step.



Scheme 1

Our synthesis is illustrated in Scheme 2. The first quarter of the synthesis was essentially the same synthetic sequence as that for whisky lactone, which was previously reported.[3i] That is, treatment of levoglucosenone (**1**) with lithium dipentylcuprate gave adduct (**7**) in 81 % yield. This compound was shown to be 100 % diastereomerically pure when analyzed by glc and ^{1}H nmr. Compound (**7**) was thus oxidized with peracetic acid followed by the usual work up to give **6** in 90.5 % yield.[3a] Lactone (**6**) was converted to the corresponding tosylate (**8**) in 86.6 % yield under the usual condition. Tosylate (**8**) was treated with potassium carbonate in isopropyl alcohol to give epoxide (**9**) in 77.7 % yield. Treatment of epoxide (**9**) with vinylcuprate[7] gave lactone (**10**) in 70.8 % yield. Lactone (**10**) was ozonized and then reduced with diborane[8] to give **11** in 81.9 % yield,



Scheme 2

which was converted to the corresponding tosylate (**5**) in 82.3 % yield. The next step is the key step of the synthesis. This compound (**5**) could be easily cyclized by treatment with lithium bis(trimethylsilyl)amide to give the expected compound (**4**) in 85.6 % yield. This reaction was clean and rapid. γ-Lactone (**4**) was reduced with lithium aluminum hydride to give diol (**12**) in 83.7 % yield. Selective tosylation of the primary alcohol of **12** was achieved by treatment with one equivalent of tosyl chloride to give the desired monotosylate (**13**) in 61.7 % yield. After protection of the secondary alcohol of compound (**13**) as a THP ether, the product (**14**) was treated

with sodium cyanide for the required one carbon elongation to give nitrile (**15**) in 58.2 % yield. The cyano group was hydrolyzed and then treated with diazomethane to give hydroxy ester (**3**) in 90.3 % yield.[9] MTPA ester (**16**) was prepared from **3** by the standard manner.[10] Optical purity of **3** was shown to be 100 % e.e. by hplc analysis. Finally, the secondary alcohol was oxidized with PDC[11] to give (+)-methyl dihydroepijasmonate (**2**) in 62.6 % yield {$[\alpha]_D^{24}$ +83.4° ($CHCl_3$)}. Our synthetic (+)-methyl dihydroepijasmonate (**2**) was shown to be 100 % diastereomerically pure when analyzed by hplc and ^{13}C nmr.

In conclution, (+)-methyl dihydroepijasmonate (**2**) can thus be synthesized starting from levoglucosenone (**1**) in an optically pure state. The overall yield was 4.1 % in 17 steps.

EXPERIMENTAL

All bps and mps were uncorrected. Ir spectra were measured with a Jasco FT/IR 5000 spectrophotometer and ^1H nmr spectra were recorded at 300 MHz and ^{13}C nmr at 75 MHz, with TMS as the internal standard on a Brucker AC-300P spectrometer. Optical rotations were measured on a Jasco DIP-370 digital polarimeter. Glc analyses were performed on a Shimadzu GC-14A gas chromatograph.

1,6-Anhydro-3,4-dideoxy-4-C-pentyl-β-D-erythro-hexopyranos-2-ulose (**7**).

A solution of pentyllithium (0.8 N, 75 ml, 60 mmol) was added dropwise to a stirred suspension of CuI (5.72 g, 30 mmol) in dry ether (15 ml) at -60°C under Ar. The mixture was warmed until clear and then cooled to -60°C. To this was added dropwise a solution of levoglucosenone (**1**) (3.15 g, 25 mmol) in dry ether (10 ml). After stirring for 30 min at -60°C, the reaction temperature was gradually raised to 0°C during 3 h. The reaction mixture was poured into a mixture of saturated NH_4Cl solution and ice, and stirred for 30 min and filtered to remove the insoluble material. The filtrate was extracted with CH_2Cl_2. The organic layer was washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was chromatographed over SiO_2 (Kieselgel 60, 100 g). Elution with *n*-hexane-ether (10:1-2:1) yielded **7** which was purified by distillation to give 4.01 g (81.0 %) of **7**, bp 132-134°C / 0.2 mm Hg, n_D^{23} 1.4674, $[\alpha]_D^{23}$ -206° (c 0.664, $CHCl_3$); ir (film) 2962 (s), 2930 (s), 2862 (s), 1740 (s), 1129 (m), 1114 (s), 913 (s), ^1H-nmr ($CDCl_3$) δ: 0.89 (3H, t, *J*=7.0 Hz), 1.20-1.72 (8H, m), 2.01-2.22 (2H, m), 2.80 (1H, dd, *J*=7.8 and 16.3 Hz), 3.92-4.06 (2H, m), 4.50-4.59 (1H, m), 5.06 (1H, s); glc: [column, CBP 10, 0.25 mm x 25 m; temperature, 100-200°C (2°C/min); Carrier gas, He, 1.1 kg/cm^2]; t_R 34.9 min (single); Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.79; H, 9.07.

(3S,4S)-5-Hydroxy-3-pentylpentan-4-olide (**6**).

To a solution of **7** (7.51 g, 37.9 mmol) in acetic acid (37 ml), peracetic acid (6.7 ml, 249 mmol, 40 % in acetic acid) was added dropwise slowly at 20°-30°C. The mixture was stirred overnight at room temperature. Then dimethyl sulfide (2.4 g, 38.7 mmol) was added to the mixture. After stirring for 30 min at room temperature, the reaction mixture was concentrated *in vacuo*. The residue was dissolved in methanol (30 ml) and then ten drops of conc. HCl were added to this solution. After stirring for 6 h at 50°C, the reaction mixture was concentrated *in vacuo*. The residue was chromatographed over SiO_2 (Kieselgel 60, 30 g). Elution with *n*-hexane-ethyl acetate (1:1-1:3) yielded 6.38 g (90.5 %) of **6** as an oil, n_D^{23} 1.4616, $[\alpha]_D^{27}$ +64.1° (c 1.08, $CHCl_3$); ir (film) 3422 (brs), 2958 (s), 2932 (s), 2862 (m), 1779 (s), 1218 (m), 1183 (m), 936 (m), ^{1}H-nmr ($CDCl_3$) δ: 0.90 (3H, t, *J*=6.9 Hz), 1.10-1.62 (9H, m), 2.22 (1H, dd, *J*=8.7 and 17.3 Hz), 2.35-2.52 (1H, m), 2.75 (1H, dd, *J*=8.6 and 17.3 Hz), 3.61-3.74 (1H, m), 3.85-3.96 (1H, m), 4.19-4.29 (1H, m). Anal. Calcd for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74. Found: C, 64.12; H, 9.64.

(3S, 4S)-3-Pentyl-5-tosyloxypentan-4-olide (**8**).

TsCl (2.32 g, 12.2 mmol) was added to a solution of **7** (1.51 g, 8.12 mmol) in dry pyridine (10 ml) with stirring and ice-cooling. Stirring was continued for 3.5 h at room temperature before the mixture was poured into ice-cooled diluted HCl solution and extracted with ether. The extract was successively washed with water, saturated $CuSO_4$ and brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was chromatographed over SiO_2 (Kieselgel 60, 100 g). Elution with *n*-hexane-ethyl acetate (10:1-5:1) gave 2.39 g (86.6 %) of **8** as an oil; ir (film) 3032(w), 2960 (s), 2932 (s), 2862 (m), 1789 (s), 1601 (m), 1365 (s), 1191 (s), 1180 (s), 977 (s), ^{1}H-nmr ($CDCl_3$) δ: 0.90 (3H, t, *J*=6.9 Hz), 1.20-1.61 (8H, m), 2.21 (1H, dd, *J*=8.1 and 17.4 Hz), 2.30-2.53 (4H, m, containing 3H, s at 2.46), 2.73 (1H, dd, *J*=8.6 and 17.4 Hz), 4.10-4.34 (3H, m), 7.39 (2H, d, *J*=8.5 Hz), 7.80 (2H, d, *J*=8.5 Hz). This was employed in the next step without further purification.

Isopropyl (3S, 4S)-4,5-epoxy-3-pentylpentanoate (**9**).

Powdered anhydrous potassium carbonate (1.34 g, 9.71 mmol) was added to a stirred solution of **8** (3.00 g, 8.82 mmol) in isopropyl alcohol (50 ml) and the mixture was stirred overnight at 50°C. The reaction mixture was filtered to remove the insoluble material, and the filtrate was concentrated *in vacuo*. The residue was chromatographed over SiO_2 (Kieselgel 60, 30 g). Elution with *n*-hexane-ethyl acetate (10:1-5:1) yielded **9** which was purified by distillation to give 1.53 g (76.1 %) of **9**, bp 122-123°C / 4 mm Hg, n_D^{23} 1.4362, $[\alpha]_D^{22}$ -7.75°

(c 1.02, $CHCl_3$); ir (film) 3050 (w), 2962 (s), 2932 (s), 1734 (s), 1259 (m), 1201 (m), 1180 (m), 1110 (s), ^{1}H-nmr ($CDCl_3$) δ: 0.89 (3H, t, *J*=6.9 Hz), 1.15-1.50 (15H, m), 2.32 (1H, dd, *J*=8.3 and 15.3 Hz), 2.49 (1H, dd, *J*=7.8 and 15.3 Hz), 2.52-2.60 (1H, m), 2.75-2.86 (2H, m), 4.96-5.10 (1H, m); hrms Calcd for $C_{13}H_{25}O_3$ (M^++1): 229.1826. Found: 229.1815.

(3S, 4R)-3-Pentyl-6-hepten-4-olide (**10**).

A solution of vinylmagnesium bromide (1.0 N, 3.71 ml, 3.71 mmol) was added dropwise slowly to the stirred and cooled suspension of **9** (770 mg, 3.38 mmol) and CuI (129 mg, 0.68 mmol) in dry ether (25 ml) at -20°C. After stirring for 30 min at -20°C, the reaction mixture was poured into a mixture of saturated NH_4Cl solution and ice, and stirred for 30 min and filtered to remove the insoluble material. The filtrate was extracted with ether. The ethereal solution was washed with water and brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was dissolved in methanol (5 ml) and 10 % aqueous sodium hydroxide solution (5 ml). This mixture was stirred for 3 h at room temperature and then concentrated *in vacuo*. The residue was diluted with water and washed with ether to remove neutral impurities. The aqueous layer was acidified with diluted HCl to pH<1 and extracted with ether. The extract was dried over $MgSO_4$ and concentrated *in vacuo*. The residue was chromatographed over SiO_2 (Kieselgel 60, 20 g). Elution with *n*-hexane-ether (10:1-5:1) yielded **10** which was purified by distillation to give 469 mg (70.8 %) of **5**, bp 95-97°C / 0.22 mm Hg, n_D^{24} 1.4581, $[\alpha]_D^{21}$ +63.2° (c 0.95, $CHCl_3$); ir (film) 3082 (w), 2960 (s), 2932 (s), 2862 (s), 1781 (s), 1212 (s), 1176 (s), 982 (s), 915 (m), ^{1}H-nmr ($CDCl_3$) δ: 0.89 (3H, t, *J*=6.7 Hz), 1.17-1.65 (8H, m), 2.12-2.28 (2H, m), 2.33-2.54 (2H, m), 2.68 (1H, dd, *J*=11.5 and 20.5 Hz), 4.17 (1H, dd *J*=6.5 and 11.5 Hz), 5.12-5.22 (2H, m), 5.74-5.90 (1H,m). Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.32; H, 10.26.

(3S, 4S)-6-Hydroxy-3-pentyl-4-hexanolide (**11**).

Into a solution of **10** (327 mg, 1.67 mmol) in dry CH_2Cl_2 (40 ml), ozone gas was bubbled at -78°C until the blue color of unreacted ozone was noticeable. The reaction mixture was allowed to warm to room temperature and dry nitrogen was bubbled through it for 10 min. Borane-dimethyl sulfide complex (10 M, 0.584 ml, 5.84 mmol) was added dropwise, and the reaction mixture was stirred at room temperature for 20 h. 5 % HCl aqueous solution (1 ml) was added and resulting mixture was vigorouslly stirred for 1 h. Solid $NaHCO_3$ was added until the aqueous layer became basic, and anhydrous $MgSO_4$ was added. This was filtered and the filtrate was concentrated *in vacuo*. The residue was chromatographed over SiO_2 (Kieselgel 60, 10 g). Elution with *n*-

hexane-ethyl acetate (10:1-3:1) gave 272 mg (81.9 %) of **11** as an oil, n_D^{24} 1.4637, $[\alpha]_D^{24}$ +86.1° (c 1.01, $CHCl_3$); ir (film) 3430 (brs), 2958 (s), 2930 (s), 2862 (s), 1775 (s), 1216 (m), 1054 (s), 971 (m), ^{1}H-nmr ($CDCl_3$) δ: 0.90 (3H, t, *J*=6.8 Hz), 1.21-1.66 (7H, m), 1.76-2.30 (6H, m), 2.61-2.79 (1H, m), 3.74-3.89 (2H, m), 4.25-4.36 (1H, m). Anal. Calcd for $C_{11}H_{20}O_3$: C, 65.97; H, 10.07. Found: C, 65.94; H, 10.17.

(3S, 4S)-3-Pentyl-6-tosyloxyhexan-4-olide (**5**).

TsCl (1.61 g, 8.44 mmol) was added to a solution of **11** (1.12 mg, 5.63 mmol) in dry pyridine (40 ml) with stirring and ice-cooling. Stirring was continued overnight at room temperature before the mixture was poured into ice-cooled diluted HCl solution and extracted with ether. The extract was successively washed with water, saturated $CuSO_4$ and brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was chromatographed over SiO_2 (Kieselgel 60, 70 g). Elution with *n*-hexane-ethyl acetate (10:1-5:1) gave 1.63 g (82.3 %) of **5** as an oil; ir (film) 3028(w), 2960 (m), 2932 (s), 2862 (m), 1781 (s), 1601 (m), 1363 (s), 1191 (s), 1178 (s), 973 (m), ^{1}H-nmr ($CDCl_3$) δ: 0.90 (3H, t, *J*=6.8 Hz), 1.18-1.59 (8H, m), 1.80-1.93 (1H, m), 2.03-2.27 (3H, m), 2.56 (3H, s), 2.65 (1H, dd, *J*=8.0 and 16.9 Hz), 4.06-4.26 (3H, m), 7.38 (2H, d, *J*=8.5 Hz), 7.79 (2H, d, *J*=8.5 Hz). This was employed in the next step without further purification.

(1R, 4S, 7S)-7-Pentyl-2-oxabicyclo[2. 2. 1]heptan-3-one (**4**).

A solution of lithium bis(trimethylsilyl)amide (1N, 3.97 ml, 3.97 mmol) in tetrahydrofuran was added dropwise to a stirred solution of **5** (1.40 g, 3.97 mmol) in dry tetrahydrofuran (25 ml) at -78°C under Ar. The reaction temperature was gradually raised to room temperature during 1 h. The reaction mixture was poured into saturated NH_4Cl solution and extracted with ether. The ethereal solution was washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was chromatographed over SiO_2 (Kieselgel 60, 50 g). Elution with *n*-hexane-ether (20:1-5:1) gave 619 mg (85.6 %) of **4** as an oil, n_D^{23} 1.4628, $[\alpha]_D^{23}$ +26.5° (c 1.02, $CHCl_3$); ir (film) 2958 (s), 2932 (s), 2862 (s), 1779 (s), 1466 (m), 1336 (m), 1178 (m), 1100 (m), 1042 (m), 949 (m), ^{1}H-nmr ($CDCl_3$) δ: 0.90 (3H, t, *J*=6.8 Hz), 1.19-1.60 (9H, m), 1.62-1.80 (1H, m), 1.81-2.06 (3H, m), 2.68-2.75 (1H, m), 4.60-4.68 (1H, m); ^{13}C-nmr ($CDCl_3$) δ: 13.92, 22.43, 23.19, 25.95, 27.93, 28.62, 31.67, 46.50, 52.44, 83.04, 178.35. Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96. Found: C, 72.59; H, 9.95.

(1R, 2S,3R)-3-Hydroxymethyl-2-pentyl-1-cyclopentanol (**12**).

A solution of **11** (747 mg, 4.10 mmol) in dry ether (10 ml) was added to a stirred suspension of $LiAlH_4$ (234 mg, 6.16 mmol) in dry ether (10 ml) at 0°C. The stirring was continued for 1 h at room temperature. The excess $LiAlH_4$ was decomposed by the successive addition of water (0.5 ml), 2N NaOH solution (1 ml) and water (0.5 ml) to the stirred and ice-cooled mixture. After stirring for 1 h, the mixture was filtered and the solid was washed with ether. The combined filtrate and washings were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was chromatographed over SiO_2 (Kieselgel 60, 40 g). Elution with *n*-hexane:ethyl acetate (10:1-1:1) gave 639 mg (83.7 %) of **12** as an oil, n_D^{23} 1.4725, $[\alpha]_D^{23}$ -10.0° (c 1.05, $CHCl_3$); ir (film) 3265(brs), 2958 (s), 2928 (s), 2864 (s), 1466 (m), 1025 (m), 944 (m), 758 (m), ^{1}H-nmr ($CDCl_3$) δ: 0.89 (3H, t, *J*=6.6 Hz), 1.21-1.60 (6H, m), 1.67-1.98 (5H, m), 2.16-2.29 (1H, m), 3.42-3.73 (4H, m), 4.05-4.14 (1H, m). Anal. Calcd for $C_{11}H_{22}O_2$: C, 70.92; H, 11.90. Found: C, 70.68; H, 11.93.

(1R, 2S, 3R)-3-Tosyloxymethyl-2-pentyl-1-cyclopentanol (**13**).

A solution of TsCl (175 mg, 0.92 mmol) and pyridine (218 mg, 2.76 mmol) in dry CH_2Cl_2 (5 ml) was added dropwise to a stirred solution of **12** (171 mg, 0.92 mmol) at -20°C. After stirring for 9 h at 0°C, the mixture was diluted with brine (10 ml) and extracted with ether. The extract was successively washed with saturated $CuSO_4$ solution and brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was chromatographed over SiO_2 (Kieselgel 60, 10 g). Elution with *n*-hexane:ethyl acetate (10:1-1:1) gave 241 mg (61.7 %) of **13** as an oil, ir (film) 3410 (br), 2960 (s), 2930 (s), 2862 (m), 1601 (m), 1361 (m), 1189 (s), 1178 (s), 949 (m), ^{1}H-nmr ($CDCl_3$) δ: 0.87 (3H, t, *J*=6.8 Hz), 1.18-1.40 (7H, m), 1.52-1.85 (7H, m), 2.24-2.38 (1H, m), 2.45 (3H, s), 3.99-4.17 (3H, m), 7.34 (2H, m), 7.79 (2H, m). This was employed in the next step without further purification.

(1R, 2S, 3R)-2-Pentyl-1-tetrahydropyranyloxy-3-tosyloxymethylcyclopentane (**14**).

PPTS (30 mg, 0.12 mmol) was added to a stirred solution of **13** (230 mg, 0.54 mmol) and dihydropyran (140 mg, 1.6 mmol) in dry CH_2Cl_2 (20 ml) at room temperature. After stirring at room temperature overnight, the reaction mixture was diluted with ether (30 ml) and 50 % saturated brine and extracted with ether. The extract was dried over MgSO4 and concentrated *in vacuo*. The residue was chromatographed over SiO_2 (Kieselgel 60, 20 g). Elution with *n*-hexane:ether (10:1-2:1) gave 253 mg (91.7 %) of **14** as an oil, ir (film) 2938 (s), 2864 (m), 1601 (m), 1365 (m), 1189 (s), 1178 (s), 1025 (s), 955 (s), ^{1}H-nmr ($CDCl_3$) δ: 0.87 (3H, t, *J*=6.7 Hz), 1.19-2.00 (19H, m), 2.22-2.39 (1H, m), 2.44 (3H, s), 3.39-3.50 (1H, m), 3.62-3.80 (1H, m), 3.87-4.19 (3H,

m), 4.51-4.59 (1H, m), 7.31-7.37 (2H, m), 7.75-7.84 (2H, m). This was employed in the next step without further purification.

(1R, 2S, 3R)-3-Cyanomethyl-2-pentyl-1-tetrahydropyranyloxycyclopentane (**15**).

NaCN (58 mg, 1.18 mmol) and Bu_4NBr (32 mg, 0.1 mmol) were added to a stirred solution of **14** (200 mg, 0.39 mmol) in dry DMF (10 ml) at room temperature. The reaction mixture was stirred overnight at 100°C, before the cooled reaction mixture was poured into water and extracted with ether. The extract was washed with saturated $NaHCO_3$ solution, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was chromatographed over SiO_2 (Kieselgel 60, 10 g). Elution with *n*-hexane:ether (20:1-5:1) gave 82.9 mg (58.0 %) of **15** as an oil, n_D^{23} 1.4736, $[\alpha]_D^{23}$+26.1° (c 1.25, $CHCl_3$); ir (film) 2938 (s), 2862 (s), 2250 (m), 1458 (m), 1344 (m), 1201 (m), 1156 (m), 1135 (s), 1116 (s), 1079 (s), 1025 (s), 988 (s), ^{1}H-nmr ($CDCl_3$) δ: 0.89 (3H, t, *J*=6.9 Hz), 1.20-2.05 (18H, m), 2.28-2.55 (3H, m), 3.45-3.56 (1H, m), 3.75-3.90 (1H, m), 3.97-4.03 (0.7H, m), 4.14-4.19 (0.3H, m),4.52-4.59 (0.7H, m), 4.63-4.68 (0.3H, m); Anal. Calcd for $C_{17}H_{29}O_2N$: C, 73.07; H, 10.46; N, 5.01. Found: C,72.92; H, 10.33; N, 4.98.

(1R, 2S, 3R)-1-Hydroxy-3-methoxycarbonylmethyl-2-pentylcyclopentane (**3**).

A mixture of **15** (83 mg, 0.23 mmol) and NaOH (100 mg, 2.5 mmol) in 50 % aqueous 2-methoxyethanol (2 ml) was stirred overnight under reflux. After cooling, the reaction mixture was poured into diluted H_2SO_4 solution and stirred for 1 h. The mixture was extracted with CH_2Cl_2. The extract was washed with water and brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was dissolved in MeOH (2 ml) and 10 % aqueous NaOH solution (2 ml). This was stirred for 3 h at room temperature and then concentrated *in vacuo*. The residue was diluted with water and washed with ether to remove neutral impurities. The aqueous layer was acidified with diluted H_2SO_4 to pH 3 and extracted with CH_2Cl_2. The extract was dried over Na_2SO_4 and concentrated *in vacuo*. The residue was finally treated with an ethereal solution of CH_2N_2 for 1 h at 0°C. The reaction mixture was concentrated *in vacuo*. The residue was chromatographed over SiO_2 (Kieselgel 60, g). Elution with *n*-hexane:ethyl acetate (10:1) gave 47.1 mg (90.3 %) of **3** as an oil, n_D^{24} 1.4656, $[\alpha]_D^{24}$ +24.6° (c 1.60, $CHCl_3$); ir (film) 3480 (br), 2956 (s), 2930 (s), 2862 (s), 1740 (s), 1723 (s), 1462 (m), 1437 (m), 1257 (m), 1203 (m), 1176 (m), 1021 (m), ^{1}H-nmr ($CDCl_3$) δ: 0.90 (3H, t, *J*=7.0 Hz), 1.10-2.45 (17H, m), 3.66 (3H, s), 4.13-4.27 (1H, m); ^{13}C-nmr ($CDCl_3$) δ: 14.05, 22.60, 25.09, 28.30, 29.48, 32.22, 33.66, 36.33, 36.58, 47.61, 51.37, 74.76, 174.75; Anal. Calcd for $C_{13}H_{24}O_3$: C, 68.38; H, 10.59. Found: C, 68.13; H, 10.51.

Determionation of the enantiomeric purity of **3**.

3 was converted into corresponding (R)- and (S)-MTPA ester (**16**) in the usual manner. Both the diastereomers were analyzed by hplc to give the result that the enantiomeric purity of **3** was 100 % e.e. Operating conditions: column, silica-2251-N, 25 cm x 6 mm; n-hexane:THF 60:1; flow rate; 1 ml/min, detected at 254 nm: t_R (R)-MTPA ester; 43.87 (min), (S)-MTPA ester; 46.15 (min).

(2S, 3R)-3-Methoxycarbonylmethyl-2-pentyl-1-cyclopentanone (methyl dihydroepijasmonate (**2**)).

To a stirred suspension of pyridinium dichromate (490 mg, 1.30 mmol) in dry CH_2Cl_2 (20 ml) was added a solution of **3** (200mg, 0.88 mmol) in dry CH_2Cl_2 (10 ml). The mixture was stirred for 3 h at room temperature. It was then diluted with ether and filtered through a short pad of Florisil. The filtrate was concentrated *in vacuo* and the residue was chromatographed over SiO_2 (30 g). Elution with *n*-hexane:ether (10:1-5:1) gave 124 mg (62.6 %) of **2** as an oil, n_D^{24} 1.4567, $[\alpha]_D^{24}$ +83.4° (c 0.585, $CHCl_3$); ir (film) 2960 (s), 2934 (s), 2864 (m), 1742 (s), 1462 (m), 1437 (m),1410 (m), 1381 (m), 1315 (m), 1265 (m), 1197 (m), 1104 (w), 1017 (w), 917 (m), 810 (s), ^{1}H-nmr ($CDCl_3$) δ: 0.88 (3H, t, *J*=6.9 Hz), 1.16-1.41 (8H, m), 1.56-1.65 (1H, m), 1.81 (1H, ddd, *J*=4.4, 8.8 and 13.2 Hz), 1.97-2.06 (1H, m), 2.09 (1H, dd, *J*=10 and 15 Hz), 2.15-2.29 (2H, m), 2.38 (1H, dd, *J*=5 and 15 Hz), 2.78-2.83 (1H, m), 3.69 (3H, s); ^{13}C-nmr ($CDCl_3$) δ: 13.97, 22.42, 24.63, 25.65, 27.13, 31.83, 33.70, 35.11, 35.72, 51.65, 52.67, 172.94, 198.20; hplc (column, nucleosil 100-5, 4.6 mm x 500 mm; n-hexane:ethyl acetate 8:1; flow rate, 3 ml/min; refractive index detection) t_R 23.3 min (single); Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 68.71; H, 9.77.

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