3. Stereoselective Syntheses of (±)-epi-β-Santalene and (±)-epi-β-Santalol

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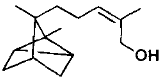
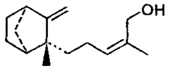
Summary

Stereoselective syntheses of (±)-epi-β-santalene (**1**) and (±)-epi-β-santalol (**2**), minor constituents of East Indian sandalwood oil, are described. The starting material for both syntheses is the tricyclic hemiacetal **4**, readily accessible in two steps from norbornene.

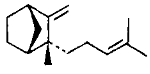
Introduction. - East Indian sandalwood oil is used in large quantities by the perfume industry and over the past few years the increasing scarcity of this oil coupled with rising prices have made its odourific components attractive targets for synthesis [1a-d]. The major components, (+)-α-santalol and (−)-β-santalol [2], are considered to be responsible for the main odour character but, as yet, no economical process has been developed for their large-scale manufacture. Attention has thus been turned towards the synthesis of the minor components of sandalwood oil, several of which, structurally related to α- and β-santalol, also possess interesting olfactory properties [3]. We now report efficient syntheses of the racemates of two of these minor components, (+)-epi-β-santalene (**1**)¹) and (+)-epi-β-santalol (**2**)²).



(+)-α-santalol



(−)-β-santalol



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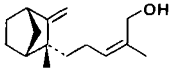

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Synthetic strategy *(Scheme 1)*. - Retrosynthetic analysis indicates that the tricyclic hemiacetal **4**, which allows the possibility of introducing functionality at C(4)³), is a logical intermediate for the stereoselective synthesis of both (±)-epi-β-santalene (**1**) and (±)-epi-β-santalol (**2**). For the former, a *Wittig* reaction can

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¹) For previous syntheses, see [1d] [4] and references cited therein.

²) Recently isolated from East Indian sandalwood oil [5]; during the preparation of our manuscript the first stereoselective synthesis was published [1d].

³) For previous examples of cyclic hemiacetals being used as bifunctional C_5-synthons see [4] [6].

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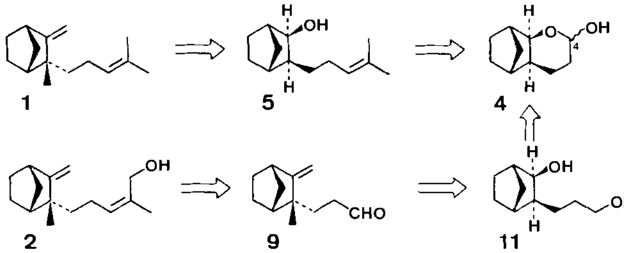
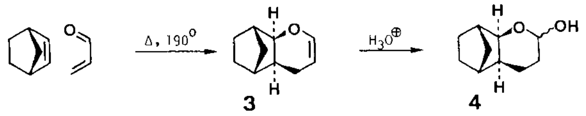
directly introduce in **4** the required isopropylidene group to give bicyclic alcohol **5** which may then be transformed to **1**. For the latter, the (Z)-5-hydroxy-4-methyl-3-pentenyl side chain may be introduced *via* bicyclic aldehyde **9** which would be derived from **4** *via* bicyclic diol **11**.

Scheme 1 (retrosynthetic)



Preparation of tricyclic hemiacetal **4** *(Scheme 2).* The stereospecific hetero *Diels-Alder* reaction of an excess of norbornene with acrolein[4], followed by the acid-catalyzed addition of water to the intermediate diexotricyclic enol ether **3** afforded

Scheme 2



crystalline hemiacetal **4** in 44% overall yield. Despite this only moderate yield the commercial availability and cheapness of the starting materials allow the preparation of **4** on a kilogram scale.

*Preparation of (±)-*epi*-β-santalene* (**1**) *(Scheme 3).* Treatment of the hemiacetal **4** with isopropylidenetriphenylphosphorane in toluene, in the presence of an excess of *t*-BuOK afforded the bicyclic alcohol **5** in excellent yield (96%). CrO_3-oxidation under basic conditions gave ketone **6** (91%) whose enolate was stereoselectively methylated [8] on the less hindered *exo* face of the molecule to give ketone **7** in 97% yield. Finally, methylidenation of the hindered keto-group afforded **1** as a colourless oil in 75% yield. Structural confirmation was obtained by analytical and spectral comparison with a sample of a 60:40 mixture of natural *β*-santalene and *epi-β*-santalene isolated from the volatile fraction of sandalwood oil. Conclusive proof was provided by the conversion of **1** to (±)-*epi-β*-santalol (**2**) (see *Scheme 3*).

Preparation of bicyclic aldehyde **9** *(Scheme 3).* For the preparation of bicyclic aldehyde **9** [1d] two synthetic approaches were investigated: a) *Route A.* Selective hydroxylation of the trisubstituted double bond of **1** followed by oxidative cleavage of the intermediate diol **8** furnished **9** in 65% yield (from **1**); b) *Route B.* Hemiacetal **4** was smoothly converted to the diol **11** (94%) and the differentiation between the primary and secondary alcohol functions was achieved by the slow addition of *t*-butyldimethylchlorosilane to a solution of **11** and imidazole in DMF, furnishing the hydroxysilyl ether **12** in high yield (85%). Oxidation under buffered conditions gave ketone **13** (83%) whose enolate was *exo*-methylated to afford ketone **14** in 80%

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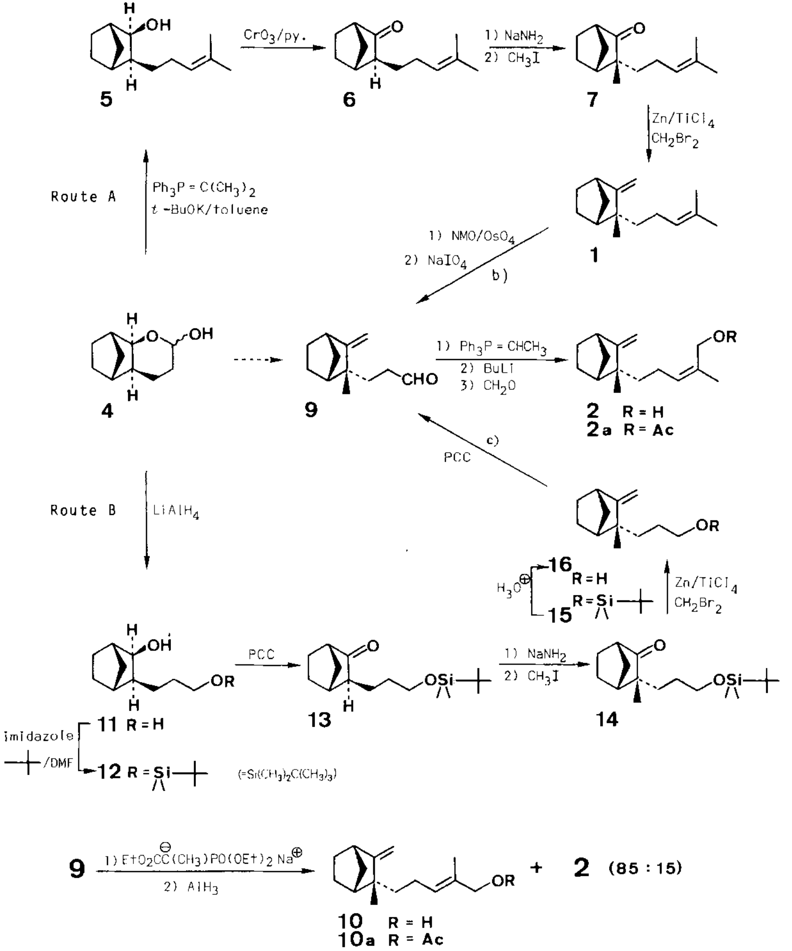
[4] For a review of the *Diels-Alder* reactions of *α,β*-unsaturated carbonyl compounds see [7].

yield. Methylidenation, mild acidic cleavage of the resulting silyl ether **15** and oxidation of the intermediate alcohol **16** finally gave **9** in 72% overall yield (from **14**).

Scheme 3[a])



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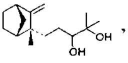
[a]) All compounds exhibit spectral data (IR., ^{13}C- and ^{1}H-NMR., MS.) in accordance with their structures.

[b]) The intermediate diol **8**,  , was isolated as a diastereoisomeric mixture, see Experimental Part.

[c]) PCC = Pyridinium chlorochromate.

Preparation of (±)-epi-*β-santalol* (**2**) *(Scheme 3).* Treatment of a solution of ethylidenetriphenylphosphorane in THF with **9**, followed by sequential addition of butyllithium at −78° and excess of formaldehyde at 0–25° [9] afforded, after chromatography and distillation, **2** in 47% yield. Structural confirmation, already indicated by the analytical and spectral data and by the manner of its preparation, was provided by comparison of the ^{13}C-NMR. data of the acetate of **2** (**2a**), with those of the acetate derived from natural *epi-β*-santalol [5].

The total stereoselectivity of the formation of **2** from **9** was demonstrated by independently preparing a 85:15 mixture of (±)-*epi*-(*E*)-β-santalol (**10**)[5]) and (±)-*epi*-β-santalol (**2**) starting from **9** (61% overall yield). *Wittig* reaction of **9** [10] with sodium triethylphosphonopropionate in THF was followed by a regiospecific reduction of the ester group (AlH_3/ether) [11] *(cf. Scheme 3)*. Analytical and spectral (GC. and ^{13}C-NMR.) comparison was then made between the 85:15 mixture of the *E*- and *Z*-acetates **10a** and **2a** and the previously prepared **2a**.

In conclusion, the olfactory properties of (±)-*epi*-β-santalol (**2**) and (±)-*epi*-(*E*)-β-santalol (**10**) were studied. Contrary to the pronounced odour of (−)-β-santalol, which is part of the odoriferous principle of sandalwood oil *(Santalum album* L.*)*, the faint woody odour of **2** only vaguely recalls the essential oil; **10** is hardly perceptible.

Experimental Part

General. - All solvents were dried and distilled before use. Each reaction was followed to completion by TLC. and GC. analysis. Work-up refers to: successive washing of the combined organic phase with H_2O, sat. aq. $NaHCO_3$-solution and sat. aq. NaCl-solution; drying of the organic phase (anhydrous Na_2SO_4) and removal of the solvent i.V. Thin layer chromatography (TLC., cyclohexane/ethyl acetate 7:3 unless otherwise stated) was performed using *Merck* 0.25 mm (60F254) silica gel plates. Preparative chromatography was carried out on silica gel (*(Merck)* 0.06-0.20 mm). Gas chromatography (GC.): 4 atm N_2; glass columns (3 mm ID 3 m), stationary phases on chromosorb W (acid washed, 80-100 mesh). Column 1: 5% Carbowax; column 2: 5% SE 30; retention time in min. Melting points (m.p.) are not corrected. IR. spectra (*Perkin-Elmer* A21 spectrometer): liquid film unless specified otherwise, $\tilde{\nu}_{max}$ in cm^{-1}. NMR. spectra: in $CDCl_3$, internal standard tetramethylsilane ($\delta = 0$ ppm); abbreviations: *s* = singlet, *d* = doublet, *t* = triplet, *qa* = quadruplet, *m* = multiplet, br. = broad; *J* = spin-spin coupling constant (Hz). ^{1}H-NMR. at 60 MHz (*Varian* A-60) or 360 MHz (*Bruker* WH 360). ^{13}C-NMR. at 90.5 MHz. Mass spectra (MS.) (*Atlas* CH 4; electron energy 70 eV) signals are given in *m/z* (rel. %).

3-Oxatricyclo[6.2.1.0^{2,7}]undec-4-ene (diexo) (**3**). Norbornene (56.4 g, 0.6 mol), acrolein (16.8 g, 0.3 mol) and hydroquinone (0.5 g) were introduced, under N_2, into an autoclave which was then heated at 190° during 15 h. The autoclave was cooled and the contents were poured into 250 ml of sat. aq. $NaHCO_3$-solution. Extraction (ether), work-up and distillation gave **3** as a colourless oil (21.8 g, 48%), b.p. 102-108°/15 Torr. - IR.: 3100, 1725, 1645, 1475, 1455, 1355. - ^{1}H-NMR.: 0.90-2.50 (11 H); 3.70 (*d*, $J = 5$, 1 H); 5.00 (*m*, 1 H); 6.4 (*d*×*d*, $J = 2$ and 5.5, 1 H). - MS.: 150 (36, $C_{10}H_{14}O^+$), 122 (20), 121 (18), 106 (11), 94 (12), 66 (100).

3-Oxatricyclo[6.2.1.0^{2,7}]undecan-4-ol (diexo) (**4**). A solution of **3** (14.5 g, 0.096 mol) in 200 ml of H_2O, 600 ml of acetone and conc. sulfuric acid (4.2 g, 0.042 mol) was stirred at 50° during 2 h. The solution was cooled and extracted (ether). Work-up and recrystallisation from petroleum ether (b.p. 30-50°) gave **4** as a white crystalline solid (12.2 g, 91%), m.p. 55-56°. - IR.: 3410, 1449, 1230, 1200, 1015, 845. - ^{1}H-NMR.: 0.90-2.30 (13 H); 3.86 (*d*, $J = 5$, 1 H); 4.86 (br. *d*, $J = 5$, 1 H), (D_2O exchange removes this signal); 5.17 (*m*, 2 H). - MS.: 168 (1.4, $C_{10}H_{16}O_2^+$), 150 (22), 140 (16), 122 (63), 107 (100), 94 (77).

*3*exo*-(4-Methyl-3-pentenyl)-bicyclo[2.2.1]heptan-2*exo*-ol* (**5**). Potassium *t*-butoxide (21 g, 0.18 mol) was added portionwise to a stirred slurry of isopropyltriphenylphosphonium iodide (26 g, 60 mmol) in 300 ml of toluene at 20° under N_2. The mixture was stirred at RT. during 15 h (deep-red colour) and then a solution of **4** (8.4 g, 50 mmol) in 50 ml of toluene was added dropwise during 30 min. After 20 h at RT. the orange reaction mixture was poured into 200 ml of cold aq. 1N HCl. Basification with solid $NaHCO_3$, extraction (ether) and work-up gave the crude product to which was added 200 ml of petroleum ether (b.p. 30-50°). Filtration through *Celite*, removal of solvent by distillation, column

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[5]) For the only previous stereoselective synthesis of **10**, see [1d].

chromatography (cyclohexane/ethyl acetate 7:3) and fractional distillation afforded **5** as a colourless oil (9.3 g, 96%), b.p. 74-80°/0.05 Torr. - TLC.: Rf 0.49. - GC. (column 1, 175°): 12.0. - IR.: 3390, 2941, 1449, 1115, 1056, 1008. - ^{1}H-NMR.: 0.90-2.30 (20 H); 3.72 (*d*, J=6, 1 H); 5.14 (*m*, 1 H). - MS.: 194 (0, $C_{13}H_{22}O^+$), 176 (27), 133 (17), 109 (24), 93 (27), 82 (100), 67 (69).

3exo-*(4-Methyl-3-pentenyl)-bicyclo[2.2.1]heptan-2-one* (**6**). CrO_3 (20.6 g, 0.206 mol) was added cautiously, under N_2, to stirred pyridine (500 ml) at 10-15° [12]. The mixture was stirred during 1 h at RT. to give a beige slurry. A solution of **5** (10 g, 51.5 mmol) in 150 ml of pyridine was added dropwise during 15 min. The reaction mixture was stirred at RT. during 15 h and was then poured into a mixture of conc. sulfuric acid (250 g) and ice (1 kg). Filtration through *Celite* (after which the *Celite* was washed with H_2O and ether) and saturation of the filtrate with solid NaCl was followed by extraction (ether), work-up and fractional distillation to give **6** as a sweet-smelling colourless oil (9 g, 91%), b.p. 65-70°/0.05 Torr. - TLC.: Rf 0.52. - GC. (column 1, 175°): 8.0. - IR.: 2985, 1739, 1449, 1376, 1171, 1075. - ^{1}H-NMR.: 1.20-2.60 (19 H); 5.09 (*m*, 1 H). - MS.: 192 (4, $C_{13}H_{20}O^+$), 110 (13), 95 (5), 82 (100), 67 (15), 41 (29).

3exo-*Methyl-3-(4-methyl-3-pentenyl)-bicyclo[2.2.1]heptan-2-one* (**7**). A solution of **6** (4.4 g, 23 mmol) in 5 ml of THF was added dropwise to a stirred slurry of sodium amide (1.4 g, 35.8 mmol) in 40 ml of THF at RT. under N_2 [8]. The reaction was boiled under reflux during 2 h under a stream of N_2 (to remove the NH_3 formed), and then a solution of methyl iodide (31 g, 0.218 mol) in 30 ml of THF was added. Reflux was continued for a further 48 h and the reaction mixture was cooled. Removal of the solvent by distillation gave a residue which was taken up into 200 ml of ether and filtered through *Celite*. Work-up and fractional distillation afforded **7** as a pale yellow oil (4.3 g, 97%), b.p. 70-75°/0.1 Torr (lit. [8]: 95°/0.8 Torr). - TLC.: Rf 0.50. - GC. (column 1, 175°): 10.0. - IR.: 2941, 1739, 1449, 1370, 1087, 1055. - ^{1}H-NMR.: 1.03 (*s*, 3 H); 1.15-2.60 (18 H); 5.09 (*m*, 1 H). - MS.: 206 (4, $C_{14}H_{22}O^+$), 124 (52), 109 (9), 96 (100), 69 (38), 55 (15), 41 (41).

2exo-*Methyl-2-(4-methyl-3-pentenyl)-3-methylidene-bicyclo[2.2.1]heptane* (epi-*β-santalene*, **1**). A solution of $TiCl_4$ (4 g, 21 mmol) in 21 ml of CH_2Cl_2 was added dropwise to a stirred slurry of zinc dust (5.7 g, 87.2 mmol) and CH_2Br_2 (5.1 g, 29.3 mmol) in 100 ml of THF at RT. under N_2 [13]. After 30 min a solution of **7** (4 g, 19.4 mmol) in 20 ml of THF was added dropwise, during 10 min, and the mixture was stirred at RT. for 48 h. Filtration through *Celite*, acidification with 1N HCl, extraction (ether), work-up, column chromatography (cyclohexane/ethyl acetate 7:3) and distillation gave **1** as a colourless oil (2.95 g, 75%), b.p. 50-55°/0.05 Torr (lit. [1d]: 105-110°/5 Torr). - TLC.: Rf 0.73. - GC. (column 2, 150°): 9.8. - IR.: 2941, 1661, 1449, 1376, 1103, 876. - ^{1}H-NMR.: 1.00 (*s*, 3 H); 1.15-2.10 (11 H); 2.66 (*m*, 1 H); 4.47 and 4.70 (2*s*, 2 H); 5.13 (*m*, 1 H). - MS.: 204 (4, $C_{15}H_{24}^+$), 122 (44), 94 (100), 79 (22), 69 (18), 55 (16), 41 (39). - GC.-coinjection with a sample of a 60:40 mixture of natural *β*-santalene (GC. (column 2, 150°): 10.3) and epi-*β*-santalene confirmed the structure.

*2-Methyl-5-(2*exo*-methyl-3-methylidene-bicyclo[2.2.1]hept-2-yl)pentane-2,3-diol* (**8**). A solution of **1** (10 g, 49 mmol) was added to a solution of *N*-methylmorpholine-*N*-oxide (NMO) (7.4 g, 55 mmol) in 50 ml of *t*-BuOH containing osmium tetroxide [14] (100 mg, 0.39 mmol) and the mixture was stirred at RT. during 8 h. After addition of a solution of 1.5 g of $NaHSO_3$ in 10 ml of H_2O the mixture was filtered through *Celite*. Removal of the solvent by distillation gave a residue which was continuously extracted (ether) after saturation of the aq. phase with sat. aq. NaCl-solution. Work-up and distillation afforded **8** as a viscous oil (8.9 g, 76%), b.p. 115-120°/0.5 Torr. - TLC.: Rf 0.10. - IR. (in $CDCl_3$): 3448, 2985, 1661, 1466, 1370, 1160. - ^{1}H-NMR.: 1.0 (*s*, 3 H); 1.16 and 1.22 (2*s*, 6 H); 1.10-2.10 (11 H); 2.70 (br. *s*, 2 H; D_2O exchange removes this signal); 2.70 (*m*, 1 H); 3.30 (*m*, 1 H); 4.47 and 4.72 (2*s*, 2 H).

*3-(2*exo*-Methyl-3-methylidene-bicyclo[2.2.1]hept-2-yl)propanal* (**9**). A solution of **8** (8.8 g, 37 mmol) in 80 ml of MeOH was added dropwise to a stirred solution of $NaIO_4$ (12 g, 56 mmol) in 600 ml of $MeOH/H_2O$ 1:1 at RT. After 2 h the mixture was filtered and the solvent was removed by distillation. Extraction (ether) of the residue, work-up (including washing the organic phase with 2N NaOH) and distillation afforded **9** as a colourless oil (5.6 g, 85%), b.p. 45-50°/0.05 Torr (lit. [1d]: 75-85°/1 Torr). - TLC. (CH_2Cl_2): Rf 0.68. - GC. (column 1, 150°): 9.4. - IR.: 3100, 2740, 1730, 1665, 1415, 1370, 1105. - ^{1}H-NMR.: 0.97 (*s*, 3 H); 1.10-2.80 (12 H); 4.50 and 4.75 (2*s*, 2 H); 9.78 (*m*, 1 H). - ^{13}C-NMR.: 202.1*d*, 165.5*s*, 100.2*t*, 46.8*d*, 45.2*d*, 44.3*s*, 40.4*t*, 37.0*t*, 30.8*t*, 29.0*t*, 25.3*qa*, 23.7*t*. - MS.: 178 (5, $C_{12}H_{18}O^+$), 160 (20), 145 (24), 131 (21), 91 (100).

(Z)-*2-Methyl-5-(2*exo*-methyl-3-methylidene-bicyclo[2.2.1]hept-2-yl)-2-penten-1-ol* (epi-*β-santalol,* **2**). A solution of butyllithium in hexane (21 ml, 27 mmol) was added dropwise to a stirred suspension of ethyltriphenylphosphonium iodide (11.3 g, 27 mmol) in 220 ml of THF at 0° under N_2 [9]. The resultant red solution was cooled to $-76°$ and a solution of **9** (4.8 g, 27 mmol) in 25 ml of THF was added dropwise, during 15 min, to give an orange colour. After 15 min at $-78°$ a solution of butyllithium in hexane (21 ml, 27 mmol) was added and the mixture was allowed to attain 0° during 3 h. Dry paraformaldehyde ($(CH_2O)_n$, 5 g, 0.167 mol) was added in one portion to the deep-red homogeneous solution. After 20 h at RT. the mixture was poured into 10 ml of sat. aq. NH_4Cl-solution. Extraction (CH_2Cl_2), work-up, column chromatography (CH_2Cl_2) and distillation gave **2** as a colourless oil (2.8 g, 47%), b.p. 90-95°/0.05 Torr (lit. [1d]: 110-120°/0.3 Torr). - TLC. (CH_2Cl_2): Rf 0.27. - GC. (column 1, 200°): 15.0. - IR.: 3300, 3100, 1665, 1380, 1000, 872. - ^{1}H-NMR.: 0.97 (*s*, 3 H); 0.80-2.30 (11 H); 1.40 (br. *s*, 3 H); 2.60 (*m*, 1 H); 4.10 (2 H); 4.40 and 4.65 (2*s*, 2 H); 5.27 (1 H). - ^{13}C-NMR.: 166.6*s*, 134.0*s*, 128.9*d*, 99.4*t*, 61.6*t*, 46.8*d*, 45.4*d*, 45.0*s*, 39.5*t*, 37.0*t*, 29.1*t*, 25.3*qa*, 23.8*t*, 23.8*t*, 21.2*qa*. - MS.: 220 (1, $C_{15}H_{24}O^+$), 202 (10), 161 (12), 145 (11), 134 (17), 121 (61), 94 (100).

(Z)-*2-Methyl-5-(2*exo*-methyl-3-methylidene-bicyclo[2.2.1]hept-2-yl)-2-pentenyl acetate* (**2a**). A solution of **2** (220 mg, 1 mmol) and Ac_2O (122 mg, 1.2 mmol) in 1 ml of pyridine was stirred at RT. during 5 h. The mixture was then poured into 20 ml of 1N HCl and extracted (ether). Work-up and distillation (130-140° (bath)/0.1 Torr) gave **2a** (240 mg, 92%) as a colourless oil. - TLC. (CH_2Cl_2): Rf 0.76. - GC. (column 1, 200°): 7.3. - IR.: 3070, 1725, 1362, 1220, 1020, 880. - ^{1}H-NMR.: 1.00 (*s*, 3 H); 1.10-2.20 (15 H); 2.67 (*m*, 1 H); 4.43 and 4.70 (2*s*, 2 H); 4.58 (*s*, 2 H); 5.40 (*m*, 1 H). - ^{13}C-NMR.: 170.9*s*, 166.5*s*, 131.3*d*, 129.6*s*, 99.6*t*, 63.2*t*, 46.9*d*, 45.4*d*, 45.0*s*, 39.3*t*, 37.2*t*, 29.2*t*, 25.3*qa*, 23.9*t*, 23.9*t*, 21.6*qa*, 20.9*qa*. - MS.: 262 (0.6, $C_{17}H_{26}O_2^+$), 220 (6), 205 (42), 187 (13), 134 (74), 122 (100).

(E)-*2-Methyl-5-(2*exo*-methyl-3-methylidene-bicyclo[2.2.1]hept-2-yl)-2-penten-1-ol* (epi-(E)-*β-santalol,* **10**). Triethylphosphonopropionate (12 g, 50 mmol), was added dropwise, during 5 min, to a stirred slurry of NaH (1.2 g, 50 mmol) in 180 ml of THF at RT. under N_2 [10]. After 45 min at RT. a solution of **9** (7 g, 39.9 mmol) in 20 ml of THF was added dropwise, during 15 min, and the reaction was stirred for a further 30 min at RT. The mixture was poured into 250 ml of sat. aq. NH_4Cl-solution, extracted (ether) and distilled to give a colourless oil (6.9 g), b.p. 95-105°/0.05 Torr, a 85:15 mixture of (*E*)- and (*Z*)-ethyl 2-methyl-5-(2*exo*-methyl-3-methylidene-bicyclo[2.2.1]hept-2-yl)-2-pentenoate (**A**). These two double bond isomers were separated (on a mg scale) by prep. GC. and characterised.

*(*E*)-Isomer of* A: GC. (column 1, 200°): 7.1. - IR.: 1710, 1660, 1370, 1212, 1140, 873. - ^{1}H-NMR.: 1.02 (*s*, 3 H); 1.32 (*t*, $J=7$, 3 H); 1.10-2.80 (15 H); 4.20 (*qa*, $J=7$, 2 H); 4.47 and 4.70 (2 *s*, 2 H); 5.90 (*m*, 1 H).

*(*Z*)-Isomer of* A: GC. (column 1, 200°): 3.9. - IR.: 1710, 1663, 1455, 1370, 1025, 873. - ^{1}H-NMR.: 1.04 (*s*, 3 H); 1.28 (*t*, $J=7$, 3 H); 1.10-2.50 (14 H); 2.70 (*m*, 1 H); 4.18 (*qa*, $J=7$, 2 H); 4.48 and 4.72 (2 *s*, 2 H); 6.76 (*m*, 1 H).

Solid powdered $AlCl_3$ (2.2 g, 16.5 mmol) was added portionwise to a stirred slurry of $LiAlH_4$ (1.9 g, 50 mmol) in 200 ml of ether under N_2 at 0° [11]. After 30 min at 0° a solution of the foregoing mixture of esters (6.5 g, 24.8 mmol) in 20 ml of ether was added dropwise, during 15 min, and the mixture was stirred for a further 30 min at 0°. Successive cautious addition of 2 ml of H_2O, 2 ml of 4N NaOH and 6 ml of H_2O followed by filtration through *Celite*, removal of the solvent and distillation afforded **10**6) as a colourless oil (5 g, 61% from **10**), b.p. 95-105°/0.05 Torr (lit. [1d]: 120-130°/0.3 Torr). - TLC. (CH_2Cl_2): Rf 0.26. - GC. (column 1, 200°): 17.8. - IR.: 3330, 1660, 1370, 1102, 1010, 873. - ^{1}H-NMR.: 1.01 (*s*, 3 H); 1.10-2.30 (15 H); 2.69 (*m*, 1 H); 3.99 (br. *s*, 2 H); 4.43 and 4.72 (2 *s*, 2 H); 5.42 (*m*, 1 H). - ^{13}C-NMR.: 166.6*s*, 134.4*s*, 126.7*d*, 99.4*t*, 68.8*t*, 46.9*d*, 45.4*d*, 45.0*s*, 38.9*t*, 37.2*t*, 29.2*t*, 25.3*qa*, 23.8*t*, 23.8*t*, 13.7*qa*. - MS.: 220 (1, $C_{15}H_{24}O^+$), 202 (5), 161 (6), 122 (37), 107 (15), 94 (100).

(E)-*2-Methyl-5-(2*exo*-methyl-3-methylidene-bicyclo[2.2.1]hept-2-yl)-2-pentenyl acetate* (**10a**). A solution of **10** (1.1 g, 5 mmol) and Ac_2O (612 mg, 6 mmol) in 10 ml of pyridine was stirred at RT. during 5 h. The mixture was then poured into 200 ml of 1N H_2SO_4 and extracted (ether). Work-up and distillation gave **10a** as a colourless oil (1.25 g, 95%), b.p. 95-100°/0.05 Torr. - TLC. (CH_2Cl_2): Rf 0.75. - GC. (column 1, 200°): 9.4. - IR.: 3075, 1735, 1660, 1450, 1235, 880. - ^{1}H-NMR.: 1.01 (*s*, 3 H); 1.10-2.20 (14 H); 2.05 (*s*, 3 H); 2.67 (*m*, 1 H); 4.44 (*s*, 2 H); 4.44 and 4.70 (2 *s*, 2 H); 5.47 (*m*, 1 H). - ^{13}C-NMR.: 170.5*s*, 166.2*s*, 130.0*d*, 129.7*s*, 99.6*t*, 70.1*t*, 46.8*d*, 45.4*d*, 44.8*s*, 38.5*t*, 37.0*t*, 29.1*t*,

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6) Contains *ca.* 15% of the (Z)-isomer.

25.2*qa*, 23.8*t*, 23.8*t*, 20.8*qa*, 13.8*qa*. - MS.: 262 (0, $C_{17}H_{26}O_2^{+\cdot}$), 205 (8), 170 (42), 134 (13), 126 (26), 113 (42), 94 (100).

*3*exo*-(3-Hydroxypropyl)-bicyclo[2.2.1]heptan-2*exo*-ol* (**11**). A solution of **4** (1.68 g, 10 mmol) in 50 ml of ether was added dropwise, during 20 min, to a stirred slurry of $LiAlH_4$ (380 mg, 10 mmol) in 150 ml of ether at 0° under N_2. After 1 h the mixture was poured onto ice, acidified to pH 2 (1 N HCl) and extracted (ethyl acetate). Work-up and distillation (130-140° (bath)/0.05 Torr) afforded **11** as a colourless oil (1.6 g, 94%). - TLC. (CH_2Cl_2/ethyl acetate 1:1): Rf 0.18. - GC. (column 1, 120°): 11.0. - IR.: 3400, 1450, 1290, 1200, 1050, 1020. - ^{1}H-NMR.: 0.90-2.20 (13 H); 2.80 (br. *s*, 2 H; D_2O exchange removes this signal); 3.65 (3 H). - MS.: 170 (0, $C_{10}H_{18}O_2^{+\cdot}$), 122 (18), 108 (31), 93 (47), 80 (100), 67 (97), 57 (61).

*3*exo*-(3-*t*-Butyldimethylsilyloxypropyl)-bicyclo[2.2.1]heptan-2*exo*-ol* (**12**). A solution of *t*-butyldimethylchlorosilane (1.51 g, 10 mmol) in 15 ml of DMF was added dropwise, during 30 min, to a stirred solution of **11** (1.53 g, 9 mmol) and imidazole (1.36 g, 20 mmol) in 50 ml of DMF at RT. under N_2 [15]. After 1 h the mixture was poured into 100 ml of sat. aq. NH_4Cl-solution. Extraction (ether), work-up, chromatography (CH_2Cl_2, then CH_2Cl_2/ethyl acetate 9:1) and distillation (120-130° (bath)/0.04 Torr) gave **12** as a colourless oil (2.18 g, 85%). - TLC. (CH_2Cl_2): Rf 0.15. - GC. (column 1, 210°): 5.6. - IR.: 3450, 1390, 1360, 1250, 1100, 960. - ^{1}H-NMR.: 0.10 (*s*, 6 H); 0.90 (*s*, 9 H); 1.00-2.20 (13 H); 1.90 (br. *s*, 1 H; D_2O exchange removes this signal); 3.70 (3 H). - MS.: 284 (0, $C_{16}H_{32}O_2Si^{+}$), 135 (89), 121 (18), 107 (43), 93 (81), 75 (100), 67 (98).

*3*exo*-(3-*t*-Butyldimethylsilyloxypropyl)-bicyclo[2.2.1]heptan-2-one* (**13**). A solution of **12** (1.99 g, 7 mmol) in 10 ml of CH_2Cl_2 was added rapidly to a stirred slurry of pyridinium chlorochromate (PCC) (4.3 g, 20 mmol) in 350 ml of CH_2Cl_2 containing anhydrous NaOAc (2.52 g, 30 mmol). After 45 min the mixture was poured into ether (1000 ml). Filtration through *Celite* was followed by successive washing of the organic phase with 2N NaOH (3×), 2N HCl, sat. aq. $NaHCO_3$-solution (2×) and sat. aq. NaCl-solution. Work-up, column chromatography (CH_2Cl_2 then CH_2Cl_2/ethyl acetate 9:1) and distillation (130° (bath)/0.5 Torr) gave **13** (oil, 1.63 g, 83%). - TLC. (CH_2Cl_2): Rf 0.32. - GC. (column 1, 210°): 5.8. - IR.: 1740, 1390, 1360, 1250, 1105, 1005. - ^{1}H-NMR.: 0.05 (*s*, 6 H); 0.55 (*s*, 9 H); 1.20-2.00 and 2.35-2.60 (13 H); 3.60 (2 H). - MS.: 282 (0, $C_{16}H_{30}O_2Si^{+}$), 225 (100), 145 (30), 133 (15), 105 (28), 91 (94), 75 (78).

*3*endo*-(3-*t*-Butyldimethylsilyloxypropyl)-3-methyl-bicyclo[2.2.1]heptan-2-one* (**14**). A solution of **13** (2.2 g, 7.8 mmol) in 2 ml of THF was added dropwise to a stirred slurry of sodium amide (390 mg, 10 mmol) in 40 ml of THF at RT. under N_2 [8]. The mixture was then refluxed during 2½ h, cooled to RT. and methyl iodide (8.52 g, 60 mmol) was added dropwise. The mixture was again refluxed during 72 h and poured into 40 ml of cold sat. aq. NH_4Cl-solution. Extraction (ether), work-up, column chromatography (CH_2Cl_2) and distillation (120-125° (bath)/0.4 Torr) afforded **14** (oil, 1.85 g, 80%). - TLC. (CH_2Cl_2): Rf 0.33. - GC. (column 1, 210°): 6.8. - IR.: 1745, 1470, 1360, 1250, 1090, 1005. - ^{1}H-NMR.: 0.06 (*s*, 6 H); 0.92 (*s*, 9 H); 1.05 (*s*, 3 H); 1.20-2.70 (12 H); 3.65 (2 H). - MS.: 296 (0, $C_{17}H_{32}O_2Si^{+}$), 239 (13), 225 (17), 183 (100), 105 (29), 94 (55), 75 (70).

*2*endo*-(3-*t*-Butyldimethylsilyloxypropyl)-2-methyl-3-methylidene-bicyclo[2.2.1]heptane* (**15**). A solution of $TiCl_4$ (990 mg, 5.2 mmol) in 10 ml of CH_2Cl_2 was added dropwise to a slurry of zinc dust (1.36 g, 21.1 mmol) and CH_2Br_2 (1.2 g, 7.05 mmol) in 25 ml of THF at RT. under N_2 [14]. After 15 min a solution of **14** (1.4 g, 4.7 mmol) in 10 ml of THF was added dropwsie and the reaction was stirred at RT. during 20 h. Filtration through *Celite*, addition of 50 ml of sat. aq. NH_4Cl-solution, extraction (ether), work-up, column chromatography (CH_2Cl_2) and distillation (150-160° (bath)/0.2 Torr) gave **15** (oil, 1.3 g, 93%). - TLC. (hexane): Rf 0.35. - IR.: 1440, 1375, 1250, 1085, 940, 835. - ^{1}H-NMR.: 0.01 (*s*, 6 H); 0.83 (*s*, 9 H); 0.93 (*s*, 3 H); 1.00-2.05 (11 H); 2.60 (*m*, 1 H); 3.54 (*m*, 2 H); 4.40 and 4.65 (2 *s*, 2 H). - MS.: 294 (0, $C_{18}H_{34}OSi^{+}$), 237 (100), 171 (18), 161 (58), 143 (61), 133 (12), 101 (21).

*3-(2*exo*-Methyl-3-methylidene-bicyclo[2.2.1]hept-2-yl)propan-1-ol* (**16**). A solution of **15** (1.25 g, 4.2 mmol) in 25 ml of AcOH/THF/H_2O (3:1:1) was stirred at RT. during 20 h [15]. The mixture was poured into 100 ml of sat. aq. $NaHCO_3$-solution. Extraction (CH_2Cl_2), work-up, column chromatography (CH_2Cl_2) and distillation (120-130° (bath)/0.3 Torr) gave **16** (oil, 718 mg, 94%). - TLC. (CH_2Cl_2): Rf 0.23. - IR.: 3300, 3070, 1660, 1368, 1052, 872. - ^{1}H-NMR.: 1.00 (*s*, 3 H); 1.10-2.10 (11 H); 1.90 (br. *s*, 1 H; D_2O exchange removes this signal); 2.70 (br. *s*, 1 H); 3.65 (2 H); 4.46 and 4.70 (2 *s*, 2 H). - MS.: 180 (1.5, $C_{12}H_{20}O^{+}$), 136 (15), 121 (100), 105 (23), 93 (92), 79 (58).

9. A solution of **16** (630 mg, 3.5 mmol) in 6 ml of CH_2Cl_2 was rapidly added to a stirred slurry of PCC (1.2 g, 6 mmol) and anhydrous NaOAc (588 mg, 7 mmol) in 120 ml of CH_2Cl_2 at RT. under N_2 [16]. After 2 h the mixture was poured into 300 ml of ether. Work-up as described for **13** and distillation (120-130° (bath)/0.2 Torr) afforded **9** (oil, 510 mg, 82%). This compound was identical in all respects with previously prepared material.

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