Enantioselective Synthesis and Determination of the Absolute Configuration of Natural (−)-Elegansidiol

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The enantioselective synthesis and determination of the absolute configuration of the title compound (–)-**1** has been carried out starting from karahana lactone (+)-**2** as an enantiopure building block. The structure was confirmed by single crystal X-ray diffraction analysis and the optical purity of (–)-(1*S*,3*R*)-elegansidiol (–)-**1** verified by chiral HPLC.

In 1999, Barrero et al.[1] isolated a new sesquiterpene, elegansidiol (−)-**1** {*cis*-3-[(*E*)-5-hydroxy-3-methyl-3-pentenyl]-2,2-dimethyl-4-methylenecyclohexanol} (Figure 1), from the hexane extracts of the aerial parts of *Santolina elegans.* They established its structure on the basis of its spectroscopic properties and confirmed the structural assignments by a racemic chemical synthesis, although the absolute configuration of (−)-elegansidiol {$[\alpha]_D$ = −4.0 (*c* = 1, $CHCl_3$)}, still remained unknown.

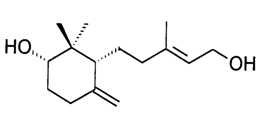
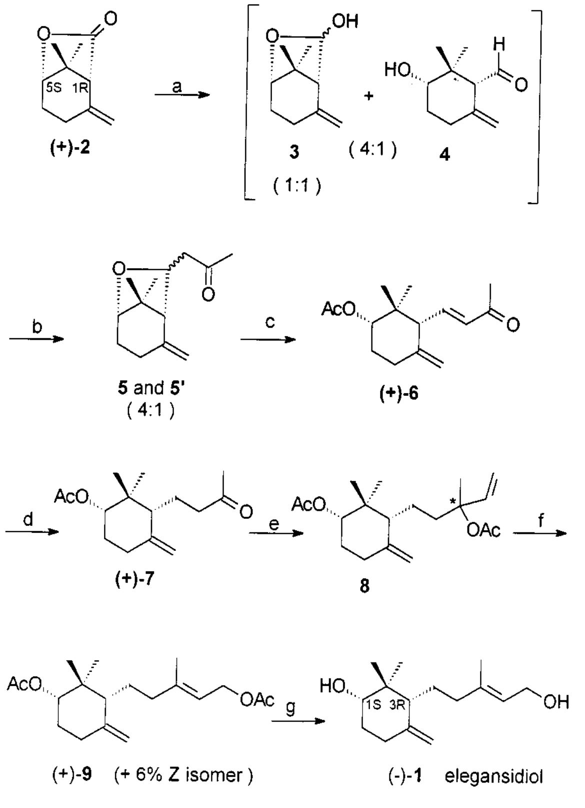


Figure 1. Structure of (−)-elegansidiol, (−)-**1**

We describe herein the first straightforward enantioselective synthesis of (−)-**1** based on an original approach and starting from an enantiopure building block for the introduction and determination of the absolute stereochemistry. Our methodology is outlined in Scheme 1.



Scheme 1. Reagents and conditions: (a) Dibal-H, toluene, −70 °C, 95%; (b) $(EtO)_2P(O)CH_2COMe$, $Ba(OH)_2$, THF, room temp., 92%; (c) Ac_2O, PPTS, toluene, reflux, 81%; (d) $HSnBu_3$, $Pd(PPh_3)_4$, $ZnCl_2$, THF, room temp., 88%; (e) (i) $CH_2{=}CHMgBr$, THF, −20 °C; (ii) Ac_2O, Et_3N, DMAP, THF, reflux, 85%; (f) $Cl_2Pd^{II}(MeCN)_2$, THF, room temp., 95%; (g) (i) K_2CO_3, MeOH, room temp., quant.; (ii) recrystallization from Et_2O/petroleum ether

We recently reported the synthesis of the required starting enantiopure building block, (1*R*,5*S*)-8,8-dimethyl-2-methylene-6-oxabicyclo[3.2.1]octan-7-one, (+)-**2** (karahana lactone).[2] Reduction of (+)-**2** with diisobutylaluminum hydride in toluene formed a 4:1 mixture of diastereomeric lactols **3** (1:1) and aldehyde **4** in 95% yield. Numerous examples where the Horner−Wadsworth−Emmons (HWE) reaction is used for the coupling of β-ketophosphonates with aldehydes have been reported, and various modifications have been developed.[3] Among them, the barium-hydroxide-promoted HWE reaction is a mild and efficient method for epimerizable, base-sensitive aldehydes.[3e] This procedure, applied to the isomeric (**3** + **4**) mixture, using the barium derivative of diethyl 2-oxopropylphosphonate in THF at room temperature, afforded 92% of a 4:1 mixture of (**5** + **5′**) as the only products resulting from the intramolecular domino[4] oxa-conjugate addition of the hydroxyl group to the intermediate enone system generated by the HWE reaction. As shown in Scheme 2, in the aa/ee conformations of the intermediate HWE products (not isolated), once the hydroxyl group and enone system are juxtaposed in the synaxial disposition, the rate of the Michael-initiated ring closure is, for entropic reasons, very high and the equilibrium very favorable to the highly stabilized bicyc-

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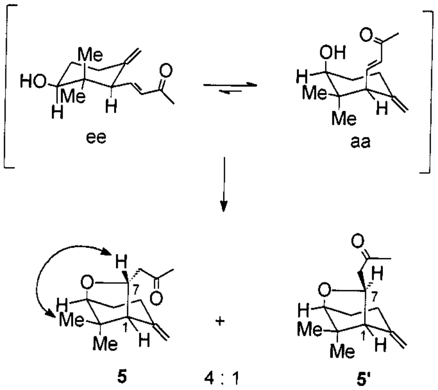
lic compounds **5** and **5′**. When a lower temperature was applied (0 °C for 24 h), no HWE reaction occurred.



Scheme 2. Conformations of the intermediate HWE reaction products (not isolated) and cyclized (**5** + **5′**)

The stereochemistry of **5** and **5′** were assigned as depicted in Scheme 2 by the magnitude of the vicinal coupling constants based on the Karplus relationship in the ^{1}H NMR spectrum. The torsional angle (Dreiding models) is ca. 45° between 1-H and 7-H in **5** [$J_{(1\text{-H}/7\text{-H})} = 3.5$ Hz) and ca. 90° in **5′** [$J_{(1\text{-H}/7\text{-H})} = 1.8$ Hz). In support of these assignments, the NOESY plots were characterized by a strong cross-peak between H7 and Me$_{eq}$ ($\delta = 1.10$) in **5**.

Acetylation of (**5** + **5′**) by heating under reflux with acetic anhydride and PPTS produced crystalline (+)-**6** (m.p. 76 °C) as a single *E* stereoisomer ($^3J_{\text{trans}} = 15.9$ Hz) in 81% yield by an irreversible retro-Michael addition process.[5] The conjugate reduction of α,β-unsaturated carbonyl compounds is an active area of organic synthesis and the arsenal of relevant synthetic tools has been strikingly enriched.[6] After several attempts, the best chemoselective 1,4-conjugate reduction of the α,β-enone system of (+)-**6** was achieved with Bu_3SnH/palladium catalyst in the presence of anhydrous $ZnCl_2$ as the reducing system[7] to afford an 88% yield of solid (+)-**7** (m.p. 40 °C). Subsequent exposure of (+)-**7** to vinylmagnesium bromide and treatment of the crude alcohols with acetic anhydride/triethylamine in the presence of DMAP (dimethylaminopyridine) yielded 85% of diastereomeric diacetates **8**. Soluble palladium(II) salts are effective catalysts in promoting the highly *E*-stereoselective rearrangement of tertiary allylic acetates.[8] Treatment of acetates **8** with dichlorobis(acetonitrile)palladium(II),[9] afforded diacetate (+)-**9** (95% yield, a 94:6 *E*/*Z* mixture, by GLC analysis). Treatment of (+)-**9** with excess K_2CO_3 in methanol at room temperature caused cleavage of the acetates and produced elegansidiol (−)-**1** quantitatively as a white solid (a 94:6 *E*/*Z* mixture, by GLC analysis). Two successive recrystallizations from Et_2O/petroleum ether furnished pure elegansidiol (−)-**1** {m.p. 82 °C, $[\alpha]_D^{25} = -14.8$ (c = 1.0, $CHCl_3$)}. The IR, ^{1}H and ^{13}C NMR spectra of our synthetic sample were in complete agreement with those of the literature.[1] However, the crystalline nature of (−)-elegansidiol has not been reported,[1,10] consequently the structure was secured by a single crystal X-ray diffraction analysis[11] and the high optical purity of (−)-(1*S*, 3*R*)-**1** was verified by HPLC (Figure 2).

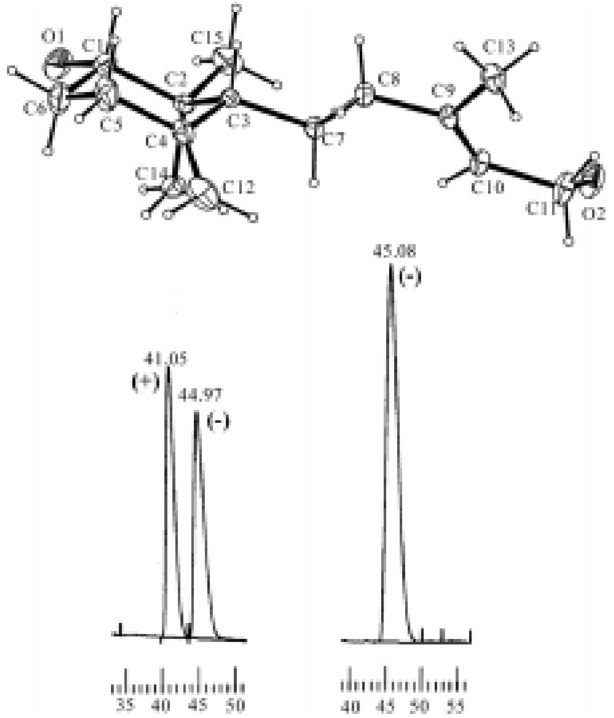


Figure 2. ORTEP view of (−)-**1** (the ellipsoids are drawn at the 30% probability level) and chiral HPLC diagrams of *rac*-**1** and (−)-**1** (conditions of analyses in Exp. Section).

In conclusion, an asymmetric synthesis of (−)-elegansidiol has been achieved, and the absolute configuration determined, using (+)-karahana lactone as the source of chirality. The merits of this synthesis are high-yielding reaction steps and secured absolute stereochemistry. The nonnatural enantiomer (+)-**1** can be synthesized from the available (−)-karahana lactone[2] following the reaction sequence detailed above.

Experimental Section

General: ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ solution on a Bruker AM-400, Bruker AM-300 or Bruker AM-200 spectrometer. Infrared spectra were obtained as films or KBr pellets using a Perkin−Elmer 1600 FTIR spectrophotometer. Routine monitoring of reactions was performed using Merck Silica gel 60 F_{254}, aluminum-supported TLC plates. Column chromatography was performed with silica gel 60 (230−400 mesh) and gradients of pentane/ether as eluent, unless otherwise stated. GC analyses were carried out on a Chrompack 9001 equipped with a WCOT fused-silica column (25 m × 0.32 mm i.d.; CP-Wax-52 CB stationary phase; N_2 carrier gas: 50 kPa). HPLC experiments were performed at 29 °C with a Merck-Hitachi LiChrograph model L-6000 HPLC pump and L-4000 UV detector operating at 221 nm, and a Merck D-2500 recorder. The chiral separation was performed using a commercial column from Daisel: CHIRALCEL OD-H® (250 × 4.6 mm; 10 μm) with hexane/*i*PrOH (98:2 v/v) and a flow rate of 1 mL/min. Optical rotations were measured on a Perkin−Elmer

341 polarimeter. Microanalyses were performed at our University. Melting points are uncorrected. Unless otherwise stated, solutions were dried over magnesium sulfate and the solvents evaporated in a rotary evaporator under reduced pressure.

8,8-dimethyl-2-methylene-6-oxabicyclo[3.2.1]octan-7-ol (3) and 3-hydroxy-2,2-dimethyl-6-methylenecyclohexanecarbaldehyde (4): A 600 mg portion (3.60 mmol) of (+)-**2** was dissolved in 40 mL of anhydrous toluene, and a 1 M toluene solution of diisobutylaluminum hydride (7.2 mL, 7.20 mmol) was added dropwise at −70 °C under an argon atmosphere. The reaction mixture was stirred for 45 minutes at this temperature, quenched with $Na_2SO_4 \cdot 10H_2O$ (4 g) and celite (5 g), and allowed to rise to room temp. Filtration through a pad of $MgSO_4$, concentration, and purification by flash chromatography gave, in the same spot, a 1:1:0.5 mixture (^1H NMR determination) of lactols **3** and aldehyde **4** as a clear oil (577 mg, 95% yield). − IR (neat): $\tilde{\nu}$ = 3400, 3068, 1715, 1652, 1023, 928 cm^{-1}. − ^1H NMR (200 MHz, $CDCl_3$): δ = 0.91 (s, 6 H, **3**), 0.98 (s, 3 H, **4**), 1.13 (s, 6 H, **3** and **4**), 1.33 (s, 3 H, **3**), 1.55−1.95 (m, 3 H, **3** and **4**), 2.10−2.45 (m, 6 H, **3** and **4**), 2.50−2.70 (m, 6 H, **3** and **4**), 2.78 (d, *J* = 3.3 Hz, 1 H, **4**), 3.40−3.52 (m, 1 H, **4**), 3.86 (d, *J* = 3.2 Hz, 1 H, **3**), 4.06 (broad s, 1 H, **3**), 4.64 (s, 1 H, **3**), 4.72 (s, 1 H, **3**), 4.74 (s, 1 H, **3**), 4.80 (s, 1 H, **4**), 4.95 (s, 1 H, **3**), 5.03 (s, 1 H, **4**), 5.33 (d, *J* = 4.8 Hz, 1 H, **3**), 5.64 (dd, *J* = 7.4, 3.8 Hz, 1 H, **3**), 9.75 (d, *J* = 3.3 Hz, 1 H, **4**). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = 202.5 (C, **4**), 146.1 (C, **3**), 144.8 (C, **3**), 141.7 (C, **4**), 113.8 (CH_2, **4**), 112.1 (CH_2, **3**), 109.0 (CH_2, **3**), 101.1 (CH, **3**), 98.8 (CH, **3**), 85.4 (CH, **3**), 83.6 (CH, **3**), 78.9 (CH, **4**), 65.9 (CH, **4**), 60.3 (CH, **3**), 57.9 (CH, **3**), 42.8 (C, **3**), 41.0 (C, **3**), 39.8 (C, **4**), 29.9 (CH_2, **4**), 27.5 (CH_2, **4**), 27.2 (CH_2, **3**), 26.9 (CH_2, **3**), 26.8 (CH_3, **3**), 26.5 (CH_3, **4**), 26.2 (CH_2, **3**), 26.1 (CH_2, **3**), 25.8 (CH_3, **3**), 21.9 (CH_3, **3**), 21.6 (CH_3, **3**). This mixture was used for the next reaction without further purification.

1-(8,8-dimethyl-2-methylene-6-oxabicyclo[3.2.1]oct-7-yl)acetone (5) and (5′): A mixture of diethyl 2-oxopropylphosphonate (1.32 g, 6.79 mmol) and $Ba(OH)_2 \cdot 8H_2O$ (855 mg, 2.71 mmol, heated at 140 °C for 2 h under a flux of argon before use) in THF (6 mL) was stirred at room temp. for 30 min. under an argon atmosphere. A solution of (**3** + **4**; 570 mg, 3.39 mmol) in wet THF (6 mL, 40:1 THF/H_2O) was then added at this temperature. After being stirred for 24 h, the reaction mixture was diluted with CH_2Cl_2, and washed with aqueous $NaHCO_3$ and brine. The organic extract was dried ($MgSO_4$), filtered, and concentrated. Purification by flash chromatography gave an inseparable mixture of diastereomers **5** and **5′** (4:1) as a colorless oil (650 mg, 92% yield). − IR (neat): $\tilde{\nu}$ = 3068, 1722, 1652, 1067, 1043, 925 cm^{-1}. − ^1H NMR (200 MHz, $CDCl_3$): δ = 0.86 (s, 6 H, **5** and **5′**), 1.10 (s, 3 H, **5**), 1.12 (s, 3 H, **5′**), 1.46−1.79 (m, 4 H, **5** and **5′**), 2.11 (s, 3 H, **5**), 2.13 (s, 3 H, **5′**), 2.17 (d, *J* = 1.8 Hz, 1 H, **5′**), 2.21 (d, *J* = 3.5 Hz, 1 H, **5**), 1.95−2.40 (m, 4 H, **5** and **5′**), 2.47 and 2.73 (ABX, *J* = 17.0, 7.0, 6.3 Hz, 2 H, **5**), 2.62 and 2.92 (ABX, *J* = 16.0, 7.9, 6.3 Hz, 2 H, **5′**), 3.74 (broad d, *J* = 2.7 Hz, 2 H, **5** and **5′**), 4.38 (broad t, *J* = 6.6 Hz, 1 H, **5′**), 4.51−4.59 (m partially overlapped, 1 H, **5**), 4.54 (m partially overlapped, 2 H, **5** and **5′**), 4.74 (m, 2 H, **5** and **5′**). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = 207.2 (C, **5**), 145.8 (C, **5**), 111.6 (CH_2, **5**), 107.4 (CH_2, **5′**), 83.7 (CH, **5′**), 82.7 (CH, **5**), 78.1 (CH, **5′**), 74.6 (CH, **5**), 58.6 (CH, **5′**), 56.8 (CH, **5**), 50.3 (CH_2, **5′**), 45.2 (CH_2, **5**), 42.1 (C, **5**), 30.7 (CH_3, **5**), 30.5 (CH_3, **5′**), 27.9 (CH_2, **5′**), 27.2 (CH_3, **5′**), 27.1 (CH_2, **5**), 25.6 (CH_2, **5**), 25.5 (CH_3, **5**), 25.5 (CH_2, **5′**), 22.1 (CH_3, **5′**), 21.9 (CH_3, **5**). − $C_{13}H_{20}O_2$ (208.15, **5** + **5′** mixture): calcd. C 74.96, H 9.68; found C 75.25, H 9.71.

(1*S*,3*R*)-2,2-dimethyl-4-methylene-3-[(1*E*)-3-oxobut-1-enyl]cyclohexyl Acetate (+)-6: A solution of (**5** + **5′**; 650 mg, 3.12 mmol) and Ac_2O (956 mg, 9.36 mmol) in toluene (10 mL) was treated with PPTS (235 mg, 0.94 mmol) and heated at 110 °C for 7 h. After being cooled to 25 °C, the reaction mixture was diluted with Et_2O, washed with aqueous $NaHCO_3$ and brine, and dried ($MgSO_4$). After concentration, flash chromatography gave (+)-**6** (633 mg, 81% yield) as colorless crystals, m.p. 76 °C, $[\alpha]_D^{25}$ = +22.9 (*c* = 1.0, $CHCl_3$). − IR (KBr): $\tilde{\nu}$ = 3087, 3018, 1734, 1665, 1237, 909 cm^{-1}. − ^1H NMR (200 MHz, $CDCl_3$): δ = 0.90 (s, 6 H), 1.63−1.76 (m, 1 H), 1.78−1.91 (m, 1 H), 2.07 (s, 3 H), 2.10−2.25 (m, 1 H), 2.27 (s, 3 H), 2.34−2.47 (m, 1 H), 2.64 (d, *J* = 9.6 Hz, 1 H), 4.60 (s, 3 H), 4.72 (dd, *J* = 8.7, 3.6 Hz, 1 H), 4.87 (s, 3 H), 6.08 (d, *J* = 15.9 Hz, 1 H), 6.97 (dd, *J* = 15.9, 9.6 Hz, 1 H). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = 197.8 (C), 170.3 (C), 145.9 (C), 145.4 (CH), 132.9 (CH), 111.0 (CH_2), 77.7 (CH), 55.8 (CH), 38.9 (C), 31.1 (CH_2), 27.5 (CH_2), 27.2 (CH_3), 26.2 (CH_3), 21.1 (CH_3), 17.8 (CH_3). − $C_{15}H_{22}O_3$ (250.16): calcd. C 71.97, H 8.86; found C 71.69, H 8.89.

(1*S*,3*R*)-2,2-dimethyl-4-methylene-3-(3-oxobutyl)cyclohexyl Acetate (+)-7: Tributyltin hydride (1.05 g, 3.60 mmol) was added to a solution of (+)-**6** (600 mg, 2.40 mmol), $ZnCl_2$ (490 mg, 3.60 mmol), and $Pd(PPh_3)_4$ (56 mg, 0.05 mmol) in dry THF (10 mL) at 25 °C under an argon atmosphere. After stirring for 15 min., the reaction mixture was concentrated and the residue purified by flash chromatography to give (+)-**7** (533 mg, 88% yield) as a whitish solid, m.p. 40 °C, $[\alpha]_D^{25}$ = +21.7 (*c* = 1.0, $CHCl_3$). − IR (KBr): $\tilde{\nu}$ = 3081, 1740, 1715, 1646, 1243, 1029, 897 cm^{-1}. − ^1H NMR (200 MHz, $CDCl_3$): δ = 0.83 (s, 3 H), 0.96 (s, 3 H), 1.49−2.05 (m, 6 H), 2.05 (s, 3 H), 2.10 (s, 3 H), 2.15−2.35 (m, 2 H), 2.40−2.59 (m, 1 H), 4.55 (s, 3 H), 4.66 (dd, *J* = 7.7, 3.9 Hz, 1 H), 4.87 (s, 3 H). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = 208.8 (C), 170.4 (C), 146.5 (C), 109.6 (CH_2), 77.9 (CH), 51.6 (CH), 42.5 (CH_2), 38.9 (C), 30.3 (CH_2), 29.9 (CH_3), 28.3 (CH_2), 26.2 (CH_3), 21.1 (CH_3), 19.7 (CH_2), 18.5 (CH_3). − $C_{15}H_{24}O_3$ (252.17): calcd. C 71.39, H 9.52; found C 71.71, H 9.48.

1-{2-[3-(acetyloxy)-2,2-methyl-6-methylenecyclohexyl]ethyl}-1-methylprop-2-enyl Acetate 8: To a solution of (+)-**7** (500 mg, 1.98 mmol) in THF (5 mL) at −20 °C under an argon atmosphere, was added dropwise vinylmagnesium bromide (1 M in THF, 3 mL, 3.0 mmol). The mixture was stirred at −20 °C for 15 min., allowed to warm to 0 °C and the resulting orange solution then quenched with aqueous NH_4Cl. After warming to 25 °C, the reaction mixture was extracted with Et_2O. The organic layer was dried ($MgSO_4$), and concentrated to give the crude allylic alcohols as a yellow oil, which was utilized for the next step without further purification. The solution of allylic alcohols in THF (5 mL) was treated with Et_3N (610 mg, 6.0 mmol), DMAP (50 mg, 0.4 mmol), Ac_2O (615 mg, 6.0 mmol), and heated under reflux for 24 h. After being cooled to 25 °C, the reaction mixture was diluted with Et_2O, washed with aqueous $NaHCO_3$ and brine, and dried ($MgSO_4$). Concentration and purification by flash chromatography gave an inseparable mixture of diastereomers **8** as a colorless oil (543 mg, 85% yield from **7**). − IR (neat): $\tilde{\nu}$ = 3087, 1740, 1652, 1250, 1023, 889 cm^{-1}. − ^1H NMR (200 MHz, $CDCl_3$): δ = 0.80 (s, 3 H), 0.95 (s, 3 H), 1.53 (s, 3 H), 1.50−2.10 (m, 8 H), 2.01 (s, 3 H), 2.05 (s, 3 H), 2.15−2.35 (m, 1 H), 4.61 (s, 1 H), 4.67 (dd, *J* = 8.3, 3.9 Hz, 1 H), 4.88 (s, 1 H), 5.12 (d, *J* = 11.0 Hz, 1 H), 5.13 (d, *J* = 17.1 Hz, 1 H), 5.95 (dd, *J* = 17.1, 11.0 Hz, 1 H), 5.96 (dd, *J* = 17.1, 11.0 Hz, 1 H, minor). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = 170.5 (C), 169.9 (C), 146.6 (C), 141.9 (CH), 113.1 (CH_2), 113.0 (CH_2, minor), 109.5 (CH_2), 83.2 (C, minor), 83.1 (C, major), 78.4 (CH), 52.4 (CH, major), 52.3 (CH, minor), 39.2 (C), 39.0 (CH_2), 31.1 (CH_2), 28.5 (CH_2), 26.1 (vinylic CH_3, major), 23.6 (CH_3), 23.4 (vinylic CH_3, minor), 22.1 (CH_3), 21.2 (CH_3), 19.5 (CH_2), 18.0 (CH_3). This mixture did not give correct analytical data.

(1*S*,3*R*)3-[(3*E*)-4-(acetyloxy)-3-methylbut-3-enyl]-2,2-dimethyl-4-methylenecyclohexyl Acetate 9: To a solution of (+)-**8** (500 mg, 1.55 mmol) in dry THF (5 mL) at 25 °C under an argon atmosphere was added dichlorobis(acetonitrile)palladium(II) (10 mg, 0.04 mmol). The reaction was monitored by GLC and, upon consumption of the starting material (2 h), the solution mixture was filtered through a pad of silica gel, and concentrated to give a yellow oil. This oil was purified by flash chromatography to give (+)-**9** as a colorless oil (475 mg, 95% yield, a 94:6 *E*/*Z* mixture, by GLC analysis). − $[\alpha]_D^{25} = +12.0$ (c = 1.0, $CHCl_3$). − IR (neat): $\tilde{\nu}$ = 3081, 1734, 1646, 1244, 1020, 890 cm^{-1}. − ^1H NMR (200 MHz, $CDCl_3$): δ = 0.78 (s, 3 H), 0.93 (s, 3 H), 1.67 (s, 3 H), 2.03 (s, 3 H), 1.50−2.15 (m, 7 H), 2.24−2.35 (m, 1 H), 4.56 (d, J = 6.9 Hz, 1 H), 4.65 (dd, J = 8.6, 4.0 Hz, 1 H), 4.58 (s, 1 H), 4.87 (s, 1 H), 5.30 (t, J = 6.9 Hz, 1 H). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = 171.1 (C), 170.6 (C), 146.5 (C), 142.4 (C), 119.4 (CH, minor), 118.3 (CH, major), 109.4 (CH_2), 78.4 (CH), 61.3 (CH_2), 51.4 (CH), 39.1 (C), 38.2 (CH_2), 31.2 (CH_2), 30.7 (CH_2, minor), 29.6 (CH_2, minor), 28.5 (CH_2), 26.1 (vinylic CH_3), 26.0 (vinylic CH_3, minor), 23.8 (CH_2, minor), 23.5 (CH_2), 21.2 (CH_3), 21.0 (CH_3), 17.9 (CH_3), 16.4 (CH_3). − $C_{19}H_{30}O_4$ (322.21; *E*/*Z* mixture): calcd. C 70.77, H 9.38; found C 71.04, H 9.35.

(1*S*,3*S*)-3-[(3*E*)-5-hydroxy-3-methylpent-3-enyl]-2,2-dimethyl-4-methylenecyclohexanol, Elegansidiol (−)-1: A solution of (+)-**9** (400 mg, 1.24 mmol) in MeOH (2 mL) at 25 °C was treated with K_2CO_3 (1.60 g, 12.40 mmol) and stirred for 24 h. The mixture was concentrated to remove MeOH, diluted with Et_2O, filtered and concentrated. Purification by flash chromatography gave (−)-**1** as a white solid (296 mg, quantitative yield, a 94:6 *E*/*Z* mixture, by GLC analysis). After two successive recrystallizations from Et_2O/petroleum ether, pure elegansidiol (−)-**1** (GLC analysis) was obtained as white crystals, m.p. 82 °C, $[\alpha]_D^{25} = -14.8$ (c = 1.0, $CHCl_3$). − IR (KBr): $\tilde{\nu}$ = 3521, 3288, 3075, 1646, 1016, 890 cm^{-1}. − ^1H NMR (400 MHz, $CDCl_3$): δ = 0.71 (s, 3 H), 1.01 (s, 3 H), 1.44−1.56 (m, 2 H), 1.56−1.64 (m, 2 H partially overlapped), 1.66 (s, 3 H), 1.77−1.87 (m, 2 H), 1.94−2.01 (m, 1 H), 2.09−2.15 (m, 1 H), 2.29−2.35 (dt, J = 13.1, 4.8 Hz, 1 H), 3.40 (dd, J = 9.6, 4.0 Hz, 1 H), 4.11 (d, J = 7.1 Hz, 1 H), 4.58 (broad s, 1 H), 4.86 (broad s, 1 H), 5.38 (broad t, J = 6.8 Hz, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 147.1 (C), 140.2 (C), 123.1 (CH), 108.5 (CH_2), 77.2 (CH), 59.4 (CH_2), 51.2 (CH), 40.5 (C), 38.5 (CH_2), 32.8 (CH_2), 32.1 (CH_2,), 25.9 (CH_3), 23.6 (CH_2), 16.3 (CH_3), 15.7 (CH_3). − $C_{15}H_{26}O_2$ (238.19): calcd. C 75.58, H 10.99; found C 75.33, H 11.02.

Crystallographic Data for (−)-1: Orthorhombic crystals, space group $P2_12_12$, a = 13.836(1), b = 17.630(1), c = 6.0609(3) Å, V = 1478.4(2) $Å^3$, Z = 4, 1666 independent reflections, 1148 with $I \geq 3\sigma(I)$; R(on F) = 0.081; Rw = 0.064.

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[10] Unfortunately, we were unable to obtain an authentic sample of (−)-**1**. The difference observed in the numerical value of the specific rotation (−14.0 versus −4.0) seems to imply that natural (−)-elegansidiol is partially racemic.

[11] Crystallographic data (excluding structure factors) for (−)-elegansidiol, (−)-**1** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-153743. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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