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Total Synthesis of (+)-Balanitol and of (+)-Selin-4-(15)-ene-1β,11-diol

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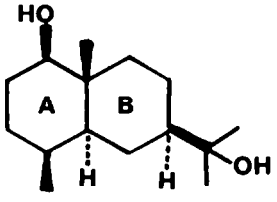
Abstract: (+)-Balanitol (1) and (+)-selin-4-(15)-ene-1β,11-diol (2), two recently-isolated naturally occurring eudesmanoid bicyclic sesquiterpene alcohols, have been synthesized stereoselectively by a route involving a [2 +2] photocycloaddition of a cyclobutene and a suitably structured 2-cyclohexenone. The structure and stereochemistry of the compounds are thereby corroborated.

(+)-Balanitol is a bicyclic sequiterpene alcohol belonging to the eudesmane subgroup, which was isolated in 1978 from the bark of the Indian tree Balanites roxburghii by Polonsky and collaborators.[1] It was shown to be 1β-hydroxydihydroeudesmol (1) by chemical transformations and spectral analysis. Some four years later a dehydro-derivative of balanitol, (+)-selen-4(15)-ene-1β,11-diol (2), was isolated from the root of the Indian shrub Pterocarpus marsupium by Syamasundar and Adinarayana; its structure and stereochemistry were settled by similar means.[2] The racemic variety of the former compound had been synthesized by Heathcock and Ratcliffe[3] in 1970 as an intermediate in the synthesis of α-bulnesene and bulnesol, before the (+)-form had been encountered as a natural product. We describe here a stereoselective synthesis of both these natural sesquiterpenoids.



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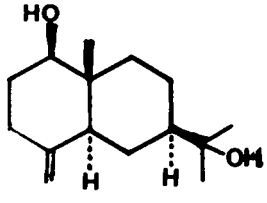

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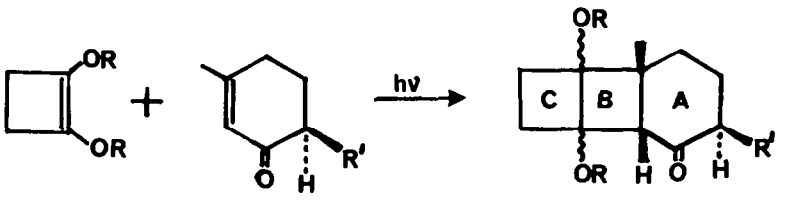
We investigated a route employing a possible [2 + 2] photocycloaddition between a suitably functionalized cyclobutene (3) and an appropriate 2-cyclohexenone (4), to arrive at the tricyclic structure 5. Examples of this type of reaction have been described by several workers,[4] but especially by Vandewalle and associates.[5] Accordingly, a reaction between 1,2-bistrimethylsilyloxycyclobutene (3, R = $OSiMe_3$), prepared from diethyl succinate,[6] and (+)-isopiperitenone (4, R'= $C(CH_3)=CH_2$) obtainable by Jones oxidation of (+)-2,8-p-menthadien-1-ol, (6) was first investigated. The latter compound, obtained commercially, was a mixture cis- and trans-isomers, the absolute configurations of which have been shown to be 6a and 6b respectively.[7] It could be expected with confidence to yield (+)-isopiperitenone (4, R' = $C(CH_3)=CH_2$) on Jones oxidation with carbonyl transposition (see Experimental); this ketone has the desired 6β orientation for the isopropenyl group.



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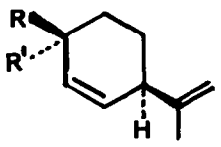
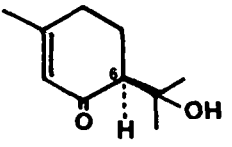


6a R = CH_3, R' = OH
6b R = OH, R' = CH_3



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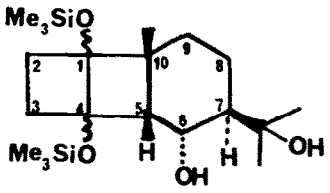
The desired cycloaddition between (3, R = $OSiMe_3$) and (4, R' = $C(CH_3)=CH_2$) did indeed occur, leading to the A/B cis tricyclic structure 5 (R = $OSiMe_3$, R' = $C(CH_3)=CH_2$) but the optimum yield achieved was only 24%. GLC monitoring of the progress of the reaction revealed that most of the enone was being consumed in an undesirable side reaction, probably intramolecular photocycloaddition, even when a large excess of the cyclobutene was used. The cycloaddition reaction was therefore modified in that the cyclohexenone 7, prepared from (+)-isopiperitenone (4, R' = $C(CH_3)=CH_2$), by successive side-chain epoxidation, reduction, and re-oxidation of the secondary alcohol group, was used in the photoaddition. This reaction furnished the tricyclic ketoalcohol 5 (R = $OSiMe_3$, R' = Me_2COH) as a mixture of cis A/B diastereomers, but with the desired cis relationship between the angular methyl and isopropanol substituents, in 75% yield. The former stereochemistry was assigned on the basis of precedent[5] and from the NMR chemical shift of the angular methyl group.[8] Elaboration of this product towards the target structures 1 and 2 was effected as follows.

Reduction of 5 (R = $OSiMe_3$, R' = Me_2COH) ($LiAlH_4$) afforded the corresponding secondary alcohol 8, the 6α configuration resulting from attack by the AlH_4^- ion on the less hindered (β) (exo) face of the molecule. This diol (8) was exposed in methanol solution to gaseous oxygen, when it suffered desilylation and oxidation to the diketodiol 9, in which the cis A/B ring junction had been retained. This compound was inverted to the A/B. trans isomer 10 by exposure to silica gel; however, attempts to effect a partial dehydration of 10 to the enedione 11 by several procedures resulted mainly in the formation of the dienedione 12. Eventually it was found that the A/B cis diol 9 could be satisfactorily partially dehydrated to the enedione 11 by stirring in ethyl acetate at reflux in the presence of Florisil.[9] A small amount of unwanted dienedione 12 was also encountered, but the two were easily separated by flash chromatography, to yield pure, crystalline 11. An earlier attempt to effect the desired dehydration to 11 by refluxing the diol in benzene with a trace of p-toluenesulfonic acid resulted in exclusive formation of dienedione 12.

Regiospecific, stereoselective reduction of 11 to the 1β alcohol 13 was achieved by sodium borohydride in ethanol at -45° C using a limited amount of reductant and a short time of reaction. This diol was reduced catalytically and stereospecifically to the A/B trans diol 14, which appeared as a monohydrate. It was subjected to a Wittig reaction with methylenetriphenylphosphorane, which furnished the desired crystalline 4-methylenediol 2. This product proved to be identical in all respects with an authentic sample of natural (+)-selin-4(15)-ene-1β,11-diol.[2]

Catalytic hydrogenation of the foregoing product[10] resulted in exclusive formation of the crystalline 4β-methyldiol 1, the physical and chemical properties of which proved to be identical with those reported[1] for natural (+)-balanitol (an authentic sample was not available). The PMR and mass spectra were identical with those of a specimen of (±)-balanitol,[3] and the specific rotation agreed with that reported for (+)-balanitol.[1]

An attempt was made to extend this synthetic pathway towards a synthesis of (+)-brasudol (15), a feeding deterrent isolated from the digestive glands of the mollusk Aplysia brasiliana.[11] Firstly an attempt was made to replace the 1β-hydroxyl group in 2 directly by bromine, with retention of configuration, using thionyl bromide.[12] This proved to be unsatisfactory because of addition of the HBr liberated to the double bond and because of partial oxidation of the secondary alcoholic group. Next, 2 was selectively converted into its mesylate, which was then displaced by sodium benzeneselenide[13,14] to yield the selenide 16 with stereochemical inversion. The latter compound reacted with triethylamine dibromide[13,14] to yield a dark, complex mixture, rather than the desired bromide 15.



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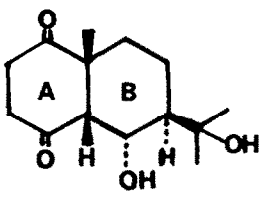

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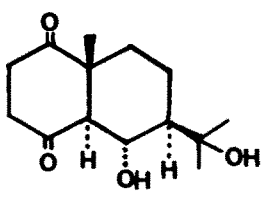

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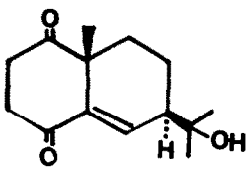

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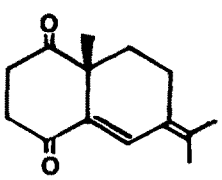

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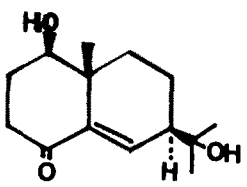

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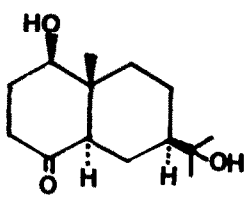

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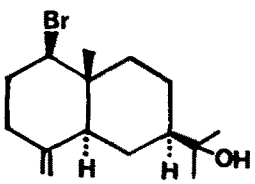

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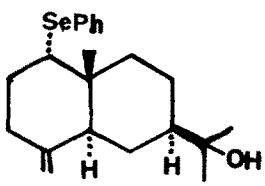

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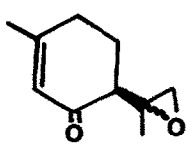

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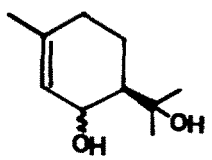

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Experimental

^{1}H NMR spectra were recorded on JEOL FX90Q and Hitachi-Perkin-Elmer R-24 instruments, and ^{13}C NMR spectra on the former instrument, both using Me_4Si as internal standard (δ = 0). UV spectra were measured on a Perkin-Elmer 202 spectrometer. IR spectra were recorded on a Perkin-Elmer 1310 instrument. Mass spectra were taken on a Hewlett-Packard 5840A GC-MS instrument. Melting points are uncorrected. Elemental analyses were performed by Atlantic Microlab, Inc., Atlanta, GA. Flash chromatography was effected with Woelm silica gel 32-63.

(+)-Isopiperitenone [3-Methyl-6R-(2'-propenyl)-2-cyclohexenone] (4, R' = $C(CH_3)=CH_2$) Initially we prepared this compound from commercial (-)-isopulegol by sequential oxidation, bromination and dehydrobromination.[15] Subsequently a superior procedure was found to be oxidation of (+)-2,8-p-menthadien-1-ol as follows.[16] The dienol (30.0 g, 0.197 mol) in ether (200 mL) was stirred mechanically during the addition of Jones reagent (188 mL of 4N) at a rate sufficient to maintain a gentle reflux of the solvent. The mixture was stirred at room temperature for 12 h, then separated and the aqueous layer extracted thrice with ether. The combined ether layers were washed with aqueous $NaHCO_3$ and brine, then dried

($MgSO_4$). Removal of the solvent *in vacuo* afforded a yellow oil which distilled at 65° C (0.35 torr) (24.6 g, 83%): IR (neat) 3060, 2920, 1660, 1430, 1375, 1200, 890 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.74 (s, 3 H, $H_2C=C\underline{CH_3}$), 1.95 (s, 3 H, 3-CH_3), 2.95 (dd, 1 H, J = 6.8 Hz, 8.3 Hz, 6-H), 4.75 (s, 1 H, =CH), 4.94 (s, 1 H, $=CH_2$), 5.88 (s, 1 H, 2-H); ^{13}C NMR ($CDCl_3$) (proton noise decoupled) δ 199, 161.7, 143.1, 126.4, 113.3, 53.6, 30.0, 27.4, 23.9, 20.4; UV λ_{max}^{EtOH} 232 nm (ε 8500); MS $^m/_z$ 150 (M^+) ($C_{10}H_{14}O$ calc. 150); $[\alpha]_D^{21}$ + 63.4° (ethanol, c = 1.35).

1,2-Bistrimethylsilyloxycyclobutene (3, R = $OSiMe_3$). This compound was prepared from diethyl succinate by reaction with powdered sodium followed by chlorotrimethylsilane.[6] It distilled at 50° C (0.75 torr) (85%); IR (neat) 2940, 1715, 1300, 1250, 1190, 1070, 940, 860 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.01 [s, 9 H, $Si(CH_3)_3$], 1.94 (s, 4 H, CH_2); ^{13}C NMR ($CDCl_3$) (proton noise decoupled) δ 0.33 [$Si(CH_3)_3$], 26.0 (C_3, C_4), 120.0 (C_1, C_2); MS $^m/_z$ 230 (M^+) ($C_{10}H_{22}O_2Si_2$ calc. 230), 215, 147, 133, 73.

cis, *syn*, *cis* and *cis*, *anti*, *cis*-5β-1,4-Bistrimethylsilyloxy-10β-methyl-7β-(2'-propenyl) tricyclo[4.4.0.$0^{1,4}$]decan-6-one (5, R = $OSiMe_3$, R' = $C(CH_3)=CH_2$). (+)-Isopiperitenone (0.5 g, 3.3 mmol), the foregoing cyclobutene 3 (R = $OSiMe_3$) (3.83 g, 16.7 mmol) and degassed pentane (50 mL) were placed in an Ace photochemical reactor and irradiated at room temperature with a 250 w Hg immersion lamp. Progress of the reaction was monitored by GC. When the peak corresponding to isopiperitenone had disappeared (3.5 h) the solvent was removed *in vacuo* and the residue distilled, bp 120° C (0.1 torr). The distillate was subjected to flash chromatography (30/60 petroleum containing 5% ethyl acetate), yielding the desired cycloadduct (0.31 g, 24%); IR (neat) 3060, 2940, 1720, 1450, 1270, 1180, 870 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.06 [s, 9 H, $Si(CH_3)_3$], 0.10 [s, 9 h, $Si(CH_3)_3$], 0.99 (s, 3 H, angular CH_3), 1.62 (s, 3 H, vinylic CH_3), 2.43 (s, 1 H, C_5-H), 2.83 (dd, 1 H, J = 6.3, 10.7 Hz, C_7-H); MS $^m/_z$ (M^+) ($C_{20}H_{36}O_3Si_2$ calc. 380), 270, 269, 223, 208, 194, 179, 156, 147, 73.

6-[2'-(1',2'-Epoxypropyl)]-3-methyl-2-cyclohexenone (17). (+)-Isopiperitenone (5.44 g, 36.3 mmol) in chloroform (40 mL) was added dropwise, with stirring, to a solution of *m*-chloroperbenzoic acid (8.22 g of 80%, 38.1 mmol) in chloroform (110 mL). After 6 h at room temperature the solution was washed with aqueous $NaHCO_3$ and brine, then dried (Na_2SO_4). The solvent was removed *in vacuo* and the residual oily epoxide was distilled, bp 80° C (0.15 torr) (5.63 g, 94%); IR (neat) 3020, 2920, 1655, 1425, 1385, 1200, 880, 840, 790 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.26, 1.43 (2s, each 3 H, 2'-CH_3), 1.95 (s, 3 H, vinylic CH_3), 5.86 (s, 1 H, vinylic H).

6-(1'-Hydroxyisopropyl)-3-methyl-2-cyclohexenol (18). The foregoing epoxide (18.0 g, 0.108 mol) in dry ether (100 mL) was added dropwise, with stirring, to a suspension of lithium aluminum hydride (6.18 g, 0.163 mol) in dry ether (350 mL), at 5° C. On completion of the addition the suspension was stirred at room temperature for 16 h, then cooled in ice and decomposed by the gradual addition of water (20 mL) and 10% aqueous NaOH (17 mL). After 7 hours' stirring at room temperature the mixture was filtered and the filtrate dried (Na_2SO_4). Evaporation of the solvent left a turbid, viscous syrup (18.04 g, 98%), which was used without further purification; NMR analysis showed it to be a mixture of *cis* and *trans* isomers; IR (neat) 3400, 3300, 2960, 1450, 1375, 1180, 950, 900 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.19, 1.23, 1.28, 1.38 (4 s, each 3 H, isopropyl CH_3), 1.70 (s, 3 H, vinylic CH_3), 3.73 (m, 1 H, C<u>H</u>OH), 5.34 s, 1 H, vinylic H), 5.61 (d, J = 5.3 Hz, vinylic H), 4.45 (broad s, 1 H, OH).

6β-(2'-Hydroxyisopropyl)-3-methyl-2-cyclohexenone (7). Finely powdered pyridinium dichromate (12.0 g, 31.65 mmol) was suspended in methylene chloride (35 mL) and to the stirred suspension was added dropwise the foregoing diol mixture (3.6 g, 21.1 mmol) in the same solvent (35 mL) at room temperature, during several minutes. Stirring was continued for 8 h, then the mixture was diluted with ether (175 mL) and filtered through Florisil. Evaporation of the dried filtrate left the yellowish ketonic product which distilled at 90° C (0.18 torr). Flash chromatography (30/60 petroleum-ethyl acetate, 5:1) provided the desired ketol, which was further distilled (2.04 g, 58%). The distillate solidified on cooling and separated from pentane in white needles, mp 38-40° C; IR (neat) 3440, 2940, 1640, 1375, 1210, 1180, 930 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.21 [s, 6 H, $C(CH_3)_2$], 1.97 (s, 3 H, vinylic CH_3), 5.25 (s, 1 H, OH), 5.87 (broad s, 1 H, vinylic H); MS $^m/_z$ 110, 82, 67, 54; UV λ_{max}^{EtOH} 238 nm (ε 17,000. Anal. Calcd.

for $C_{10}H_{16}O_2$:C, 71,39; H, 9.59. Found: C, 71.29; H, 9.60.

cis, syn, cis- and cis, anti, cis-5β-1,4-Bistrimethylsilyloxy-7β-(2'-hydroxyisopropyl)-10β-methyltricyclo[4.4.0.0^{1,4}]decan-6-one (5, R = $OSiMe_3$, R' = Me_2COH). The foregoing ketol (3.0 g, 17.9 mmol) and 1,2-bistrimethylsilyloxycyclobutene (6.2 g, 27.0 mmol) were mixed in dry, degassed pentane (250 mL) and irradiated as described above for 8 h at room temperature, The solvent was evaporated and the residue chromatographed on silica gel (35 g), with elution by 30/60 petroleum containing increasing amounts of ethyl acetate. Most of the product (5.3 g, 75%) appeared in the petroleum and petroleum-ethyl acetate (5%) fraction. It was used in the next step without further purification; IR (neat) 3485, 2950, 1740, 1680, 1290, 1250, 840 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.14 [s, 9 H $Si(CH_3)_3$], 0.16 [s, 9 H, $Si(CH_3)_3$], 1.05 (s, 3 H, angular CH_3), 1.17, 1.20 (2s, each 3 H, isopropanol methyls), 2.44 (s, 1 H, C_5-H), 4.74 (s, 1 H, OH): MS $^m/_z$ 340, 270, 269, 230, 222, 207, 193, 183, 147, 73.

cis, syn, cis- and cis, anti, cis-5β-1,4-Bistrimethylsilyloxy-6α-hydroxy-7β-(2'-hydroxyisopropyl)-10β-methyltricyclo[4.4.0.0^{1,4}]decane (8). The above cycloadduct (10.27 g, 25.8 mmol) in dry ether (100 mL) was added gradually to a stirred suspension of lithium aluminum hydride (1.46 g, 38.4 mmol) in dry ether (330 mL) at 5° C. The mixture was stirred at room temperature for a further 8 h, then decomposed at 0° C cautiously by the addition of water (28.5 mL) and dilute HCl (15 mL of 2N). After 8 hours' stirring at room temperature the mixture was filtered and the filtrate concentrated in vacuo. The residual diol (8.9 g, 86%) was used without further purification; IR (neat) 3380, 2950, 1170, 890, 840 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.12 [s, 9 H, $Si(CH_3)_3$], 0.25 [s, 9 H, $Si(CH_3)_3$], 0.99 (s, 3 H, angular CH_3), 1.13, 1.21 (2s, each 3 H, isopropanol methyls), 4.00 (m, 1 H, CHOH).

5β-H-6α-Hydroxy-7β-(1-hydroxy-1-methylethyl-10β-methylbicyclo[4.4.0]decan-1,4-dione (9). The foregoing crude diol (8.9 g, 22.3 mmol) in methanol (250 mL) was stirred at room temperature for 24 h whilst oxygen was bubbled through the solution, then for the same period without the gas bubbling. The solvent was evaporated in vacuo and the residue purified by flash chromatography (ethyl acetate - 30/60 petroleum, 3:2). Evaporation of the solvents left a syrup (5.33 g, 94%); IR (neat) 3400, 2960, 1710, 1378, 1260, 1175, 1100, 910 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.19 (s, 3 H, angular CH_3) 1.25, 1.27 (2s, each 3 H, $C(CH_3)_2$], 2.61-2.88 (m, 4 H, CH_2s), 3.08 (d, 1 H, J = 4.4 Hz, C_5-H), 4.1 (dd, 1 H, J = 4.7, 10.55 Hz, CHOH); ^{13}C NMR ($CDCl_3$) (proton noise decoupled) δ 19.4, 21.6, 22.9, 27.7, 30.7, 34.6, 35.8, 47.7, 47.9, 55.5, 70.2, 72.8, 210.5, 213.1; MS $^m/_z$ 218, 178, 163, 135, 121, 120, 59.

5α-H-6α-Hydroxy-7β(1-hydroxy-1-methylethyl)-10β-methylbicyclo[4.4.0]decane-1,4-dione (10). The above A/B cis diketodiol (100 mg) in ethyl acetate (5 mL) was stirred at ambient temperature with silica gel (0.8 g, Woelm 63-200) for 3 days. The suspension was filtered and the residue well washed with ethyl acetate. Evaporation of the filtrate in vacuo afforded the crystalline trans isomer in quantitative yield. It separated from ether in fine needles, mp 174° C; IR (KBr) 3510, 3430, 2970, 2910, 1695, 1410, 1195, 1179 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.03 (s, 3 H, angular CH_3), 1.18, 1.26 [s, each 3 H, $C(CH_3)_2$], 2.70-2.80 (m, 4 H, α-methylenes), 4.03 (bs, 1 H, OH), 4.31 (t, 1 H, J = 10.0 Hz, CHOH), 4.64 (bs, 1 H, OH); MS $^m/_z$ 218, 178, 163, 136, 135, 121, 120, 118, 105, 94, 93, 91, 79, 77, 59.
Anal. Calcd. for $C_{14}H_{22}O_4$: C, 66.10; H, 8.74. Found: C, 65.93; H, 8.74. Attempts to effect a partial dehydration of this compound to 11 led mainly to the unwanted dienedione (12).

7β-(1-Hydroxy-1-methylethyl)-10β-methylbicyclo[4.4.0]dec-5-ene-1,4-dione (11). Florisil (4.0 g, 60-100 mesh) was added to a solution of the above A/B cis diol (0.234 g, 0.922 mmol) in ethyl acetate (25 mL). The mixture was stirred at 80° C for 11 h. After being kept at 0° C overnight additional Florisil (3.0 g) was added and the heating repeated for a further 9 h. The cooled suspension was filtered and the residue washed thoroughly with the solvent. Evaporation in vacuo afforded the crude product (0.174 g), TLC of which showed the presence of two components which were separated by flash chromatography (ethyl acetate - 30/60 petroleum, 3:2), yielding the desired enedione (11) (0.135 g, 62%) and the unwanted dienedione (12) (38.6 mg, 19%). The former separated from 30/60 petroleum-ethyl acetate (9:2) in waxy plates, mp 139-141° C; IR (KBr) 3240, 3140, 1715, 1696, 1618, 1262, 1160 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.23

(s, 3 H, angular CH_3), 1.30 [s, 6 H, $C(CH_3)_2$], 2.76 (s, 4 H, α-methylenes), 7.06 (s, 1 H, vinylic H): UV λ_{max}^{EtOH} = 249 nm (ε 5,140); MS $^{m}/_{z}$ (CI) 238 $(M+2)^+$, 220, 219, 179, 178, 161; (EI) 221, 178, 163, 161, 136, 135, 121, 120, 93, 91, 77, 59. Anal. Calcd. for $C_{14}H_{20}O_3$: C, 71.14; H, 8.55; Found: C, 71.08; H, 8.58.

7-(1-Methylethylidene)-10β-methylbicyclo[4.4.0]dec-5,7(11)-diene-1,4-dione (12). To the cis-diketodiol (9) above (97.6 mg, 0.38 mmol) in benzene (30 mL) was added p-toluenesulfonic acid (7 mg). The solution was refluxed 3 h, then concentrated in vacuo. A yellow solid (83 mg) remained; it proved to be the unwanted dienedione (12); UV λ_{max}^{EtOH} 321 nm (ε 10,850); IR (KBr) 2978, 1712, 1678, 1612, 1570, 1310, 1275, 1172 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.87, 1.99 (2s, each 3 H, vinylic methyls), 2.76 (s, 4 H, α-methylenes), 7.67 (s, 1 H, vinylic H).

7β-(1-Hydroxy-1-methylethyl)-1β-hydroxy-10β-methylbicyclo[4.4.0]dec-5-en-4-one (13). A solution of the above enedione (11) (0.535 g, 2.26 mmol) in 95% ethanol (50 mL) was stirred with sodium borohydride (43 mg, 1.13 mmol) at -45° C for 25 min, then quenched with acetone (2-3 mL). The reaction mixture was poured into aqueous ammonium chloride, and the product extracted with methylene chloride (4 x 30 mL). The combined, dried ($MgSO_4$) extracts afforded on evaporation in vacuo a crystalline residue (0.543 g, 100%) which separated from 30/60 petroleum-ethyl acetate (6:1) in cubes, mp 154-156° C; IR (KBr) 3495, 3325, 2970, 1675, 1610, 1365, 1260, 1126, 1060 cm^{-1}; UV λ_{max}^{EtOH} 246 nm (ε 7,000); ^1H NMR ($CDCl_3$) δ 1.01 (s, 3 H, angular CH_3), 1.21, 1.26 [2s, each 3 H, $C(CH_3)_2$], 1.74 (s, 2 H, α-CH_2), 3.73 (dd, 1 H, J = 7.4, 8.4 Hz, CHOH), 6.64 (s, 1 H, vinylic H); MS $^{m}/_{z}$ (CI) 239 (M+1), 221, 203, 181, 180, 163, 161; (EI) 180, 162, 147, 136, 121, 105, 91, 77, 59, 43. Anal. Calcd. for $C_{14}H_{22}O_3$: C, 70.54; H, 9.32. Found: C, 70.43; H, 9.32.

5α-H,7β-(1-Hydroxy-1-methylethyl)-1β-hydroxy-10β-methylbicyclo[4.4.0] decan-4-one (14). The foregoing enone-diol (31.3 mg, 0.132 mmol) in methanol (5 mL) was shaken in hydrogen in the presence of 10% Pd-C catalyst (3.5 mg) under ambient conditions for 60 min. The catalyst was removed by filtration and the filtrate freed of solvent in vacuo. The viscous residue (30 mg, 96%) gradually crystallized; it separated from 30/60 petroleum-ethyl acetate (6:1) in needles, mp 75-78° C; IR (KBr) 3470, 3370, 2980, 1705, 1390, 1180, 1050, 920 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.74 (s, 3 H, angular CH_3), 1.19 [s, 6 H, $C(CH_3)_2$], 3.80 (dd, 1 H, J = 4.8, 11.0 Hz, CHOH); ^{13}C NMR ($CDCl_3$) (proton noise decoupled) δ 10.9, 21.0, 21.6, 26.7, 27.0, 30.1, 36.9, 38.7, 42.1, 47.7, 54.4, 72.5, 77.0, 211.6. The product proved to be a monohydrate. Anal. Calcd. for $C_{14}H_{22}O_3 \cdot H_2O$: C, 65.08; H, 10.14. Found: C, 65.33; H, 10.33.

5α-H,7β-(1-Hydroxy-1-methylethyl)-1β-hydroxy-10β-methyl-bicyclo[4.4.0]-dec-4(15)-ene (2). Sodium hydride (67.7 of 60% pure, 1.69 mmol) was washed thrice by decantation with 30/60 petroleum, then treated with dimethyl sulfoxide (2.0 mL). The mixture was heated under dry N_2 at 75° C for 45 min, then cooled. A solution of methyltriphenylphosphonium bromide (60.3 mg, 1.69 mmol) in dry DMSO (1.5 mL) was added all at once via a syringe, and the mixture was stirred at room temperature for 30 min. Ylid formation was evidenced by the development of a deep orange-red color. The foregoing ketol (40.6 mg, 0.169 mmol) in DMSO (1.5 mL) was added via a syringe, with stirring at room temperature for 1½ hr, then at 65° C for the same period, and finally at 30° C overnight. Water (125 mL) was added and the product was isolated by ether extraction (4 x 30 mL). The combined extracts were washed with water, dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash chromatography with elution by ethyl acetate-30/60 petroleum, 3:2), which yielded the desired product (2) (25 mg, 63%). It separated from 30/60 petroleum-ethyl acetate (8:1) in needles, mp 152° C, alone or admixed with a sample of the natural compound;[2] $[\alpha]_D^{25°}$ + 55.8° (c = 1.5, $CHCl_3$). IR (KBr) 3330, 3070, 2940, 2870 1645, 1380, 1200, 1135, 1085, 1015, 885 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.67 (s, 3 H, angular CH_3), 1.20 [s, 6 H, $C(CH_3)_2$], 3.40 (dd, 1 H, J = 4.8, 11.0 Hz, CHOH), 4.52, 4.76 (2s, each 1 H, vinylic H); ^{13}C NMR ($CDCl_3$) (proton noise decoupled) δ 10.2, 22.1, 24.4, 26.9, 27.0, 31.4, 34.2, 36.9, 40.1, 47.4, 48.9, 72.6, 79.2, 106.7, 148.8, MS $^{m}/_{z}$ (CI) 239 (M + 1), 222, 221, 203, 180, 162, 147. Anal. Calcd. for $C_{15}H_{26}O_2$: C, 75.56; H, 11.01. Found: C, 75.64; H, 11.04.

5α-H,7β-(1-Hydroxy-1-methylethyl),1β-hydroxy-4β,10β-dimethylbicyclo[4.4.0]decane [(+)-Balanitol] (1). The previous olefinic product (21.1 mg, 0.87 mmol) in methanol (2 mL), along with pre-reduced Adams catalyst (from 102 mg PtO_2), was shaken in hydrogen at room temperature

until uptake of gas ceased (55 min). The suspension was filtered and the filtrate concentrated in vacuo. The residue (20.9 mg, 98.5%) was crystallized from benzene, from which it separated in white needles, mp 156-158° C (natural balanitol mp 158-160° C);[1] $[\alpha]_D^{25°}$ + 10.5° (C = 0.84, $CHCl_3$). Its spectral properties (see below) proved to be in excellent agreement with those reported for the (±)-compound,[3] and for the natural product.[1] IR (KBr) 3300, 2925, 2860, 1380, 1205, 1140, 1085, 1025, 920 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (d, 3 H, J = 6.7 Hz, C-4 CH_3), 0.90 (s, 3 H, angular CH_3), 1.20 [s, 6 H, $C(CH_3)$, 3.22 (m, 1 H, CHOH); ^{13}C NMR ($CDCl_3$) (proton noise decoupled) δ 14.0, 14.8, 22.6, 26.5, 27.0, 27.4, 31.6, 33.3, 39.3, 40.3, 46.0, 49.8, 72.8, 80.6, MS $^m/_z$ (CI) 240 (M^+), 223, 221, 206, 205, 165, 150, 149, 135. Anal. Calcd. for $C_{15}H_{28}O_2$: C, 74.95; H, 11.74. Found: C, 74.78; H, 11.73.

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