Synthesis of Drimanes from (+)-Larixol

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Abstract: The selective transformation of the side chain of larixol **1** to a functionalized one-carbon moiety leads to 6,8-diacetoxydrimenal **13**, which was converted to the drimanes (−)-albrassitriol (**2**), (−)-drimenol (**3**), (−)-uvidin C (**4**) and (−)-*epi*-albrassitriol (**5**).

Key words: drimane sesquiterpenoids, natural product synthesis, (+)-larixol, (−)-albrassitriol, (−)-uvidin C, (−)-*epi*-albrassitriol

The biological activities of some drimane sesquiterpenoids have greatly stimulated the development of new synthetic routes to this class of compounds, and many syntheses of drimanes have appeared in the last twenty years.[1–3]

The oleoresin of larch (*Larix decidua*, *L. europea*)[4,5] contains large amounts of the labdane diterpene larixol **1** (>10 weight%), which can be easily isolated from larix turpentine in pure form.[5] In view of its availability and its chemical structure, larixol seems to be a suitable starting material for the synthesis of isoprenoids possessing a 4,4,10−trimethyldecalin skeleton. The higher functionalized drimane sesquiterpenoids are especially attractive target molecules for syntheses starting from larixol. Since larixol has a hydroxyl group at C-6 as a characteristic structural element, it is particularly suited as chiral starting material for the syntheses of drimanes that have a functional group at the same position.

In this paper we report the first semisynthesis of (−)-albrassitriol (**2**)[6] and the enantioselective synthesis of (−)-drimenol (**3**),[7] which is an intermediate in the synthesis of the well-known drimanes (−)-polygodial[8] and (−)-warburganal[9] (Figure 1). These drimanes have generated considerable interest because of their potent antifeedant and molluscicidal activities.[10–12] Moreover, (−)-uvidin C (**4**)[13–17] and (−)-*epi*-albrassitriol (**5**),[18] which exhibits weak antiviral activity in in vitro tests against influenza A- and myxovirus (MIC 44.4 μg/mL; dosis tolerata maxima 133.3 μg/mL) were prepared (Figure 1).

For the conversion of larixol **1** into drimanes, first a selective oxidative degradation of the side chain has to take place. The methodology developed for sclareol[19–21] seemed appropriate and when applied to larixol acetate, the diacetate **9** was obtained in high yield. Thus, the exocyclic double bond of larixol **1** was selectively epoxidized[22] to the epoxide **6**, which was subsequently reduced to 6α-hydroxysclareol **7** with lithium aluminium hydride.[23] After selective protection of the (C-6)-secondary alcohol with acetic anhydride in pyridine,[24] the oxidation of **8** with osmium tetroxide−sodium periodate[19-21] yielded acetoxyaldehyde **9** in one step (84%) (Scheme 1).

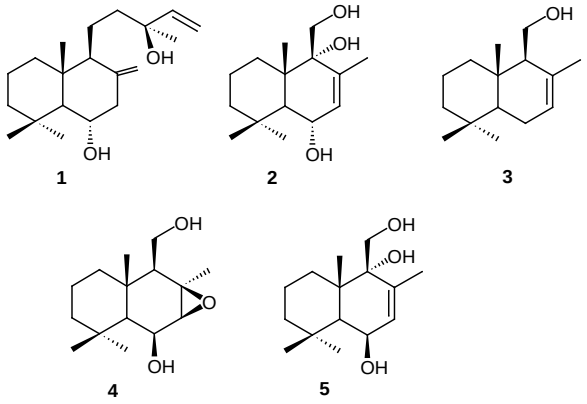
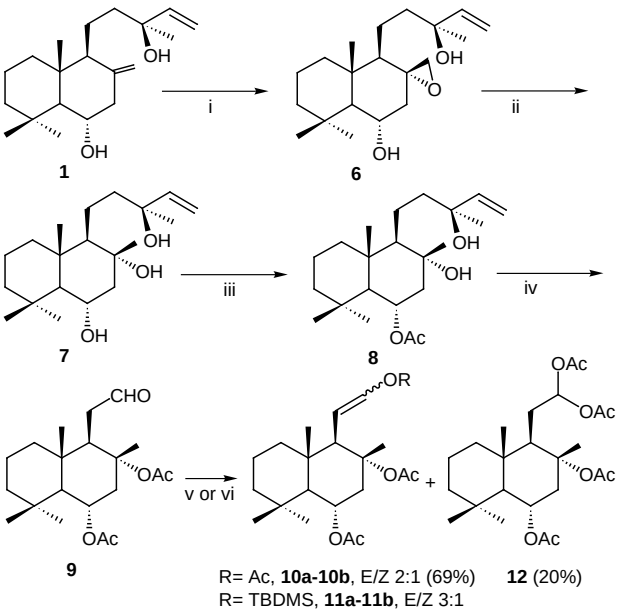


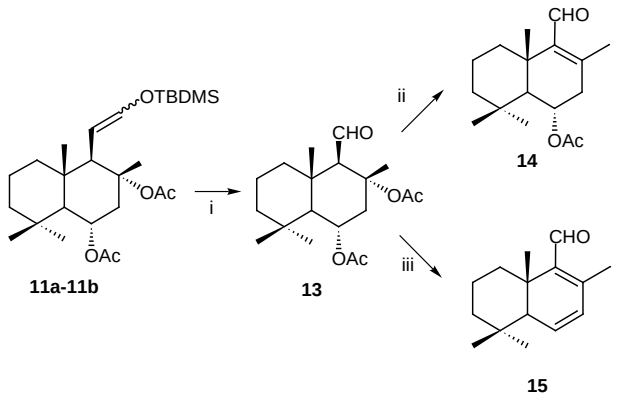
Figure 1



Reagents and conditions: (i) oxone, CH_2Cl_2, acetone, H_2O, $NaHCO_3$, 18-crown-6, 0−3 °C, 81%; (ii) $LiAlH_4$, THF, r.t., 94%; (iii) Ac_2O, pyridine, r.t., 99%; (iv) OsO_4, $NaIO_4$, THF, H_2O, 45 °C, 84%; (v) Ac_2O, Et_3N, 4-DMAP, THF, reflux, 89% or (vi) TBDMSCl, NaH, THF, r.t., 96%.

Scheme 1

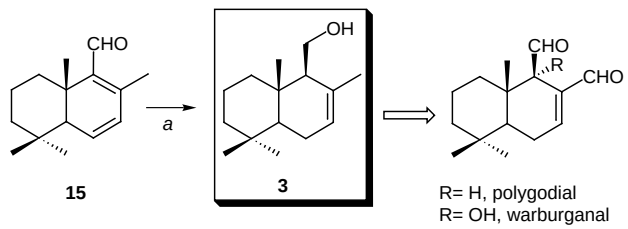
A further breakdown of the side chain of **9** can be performed by the oxidative degradation of the corresponding enol derivatives **10** or **11**. The enol acetates **10a**, **10b** (*ratio* E/Z 2:1) and the tetraacetate **12** were prepared from **7** with acetic anhydride in the presence of triethylamine.[20] To avoid the formation of byproducts such as **12**, it proved to be more convenient to convert the acetoxyaldehyde **9** into its silyl enol ether[20,25] and a mixture of **11a** and **11b** was obtained in 96% yield (Scheme 1). Next, an ozonolysis of these silyl enol ethers with dimethyl sulfide[20,25] as reducing agent was carried out to give aldehyde **13**, as key intermediate for the synthesis of these drimanes. The acetoxyaldehyde **13** underwent a regioselective elimination of the (C-8)-acetate by heating with collidine[25] to give a moderate yield of **14**. The diene **15** was obtained as a second product (*vide infra*). The elimination of both acetates from aldehyde **13** could be achieved in high yield in a more concentrated collidine solution (Scheme 2).[25]



Reagents and conditions: (i) O_3, CH_2Cl_2–MeOH (3:2), −78 ºC; Me_2S, r.t., 78%; (ii) collidine, 200 ºC, 15 min, 41%; (iii) collidine, 200 ºC, 1h 30, 77%.

Scheme 2

The reduction of the obtained diene aldehyde **15** with sodium borohydride[25] proceeded smoothly and unexpectedly yielded (−)-drimenol (**3**) in high yield. (−)-Drimenol has been used before as a starting material in the synthesis of (−)-polygodial[8] and (−)-warburganal[9] (Scheme 3).



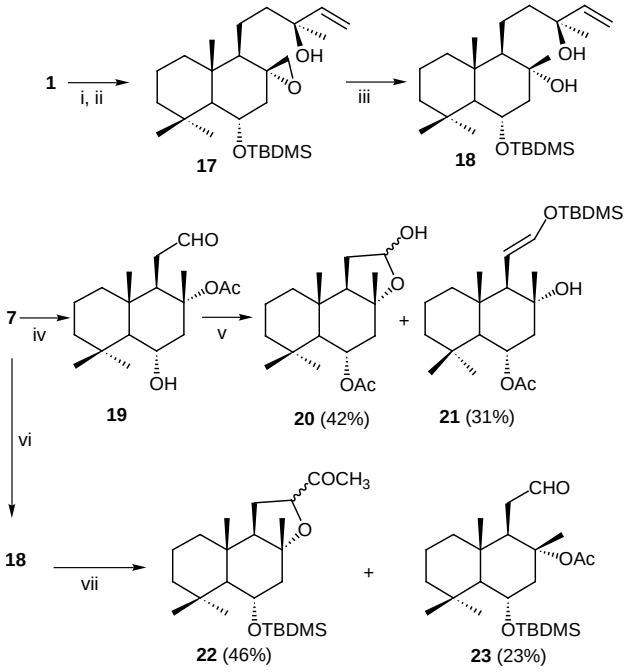
Reagents and conditions: (i) $NaBH_4$, EtOH, 0 ºC to r.t., 89%.

Scheme 3

For the synthesis of albrassitriol (**2**), we first tried to improve the selectivity of the elimination of the (C-8)-acetate in **13** and to optimize the yield of aldehyde **14**. Some reaction sequences were investigated in which the leaving group capability of the substituent at C-6 was diminished by protection as its *t*-butyldimethylsilyl derivative or by just maintaining it as an unprotected hydroxy group.

The secondary alcohol of **1** was first protected as the *t*-butyldimethylsilyl ether **16**.[26] Its epoxidation with oxone[22] gave the requisite epoxide **17** but now in a moderate 30% yield, and epoxidation of the 14,-15 double bond was a competing side reaction (29%). The reduction of the epoxide **17** with lithium aluminium hydride[23] furnished the diol **18** (Scheme 4).

Because of the poor selectivity and yield of the epoxidation of **16**, the utility of triol **7** as starting material was investigated as well. Exposure of **7** to osmium tetroxide and sodium periodate[19–21] readily afforded the acetoxyaldehyde **19** but also in a moderate yield (40–45%). Treatment of **19** with *t*-butyldimethylsilyl chloride gave unexpectedly **20** together with the silyl enol ether **21**. In both compounds, the acetate had moved to the undesired C-6 position, thus promoting the wrong hydroxy group to the better leaving group (Scheme 4).



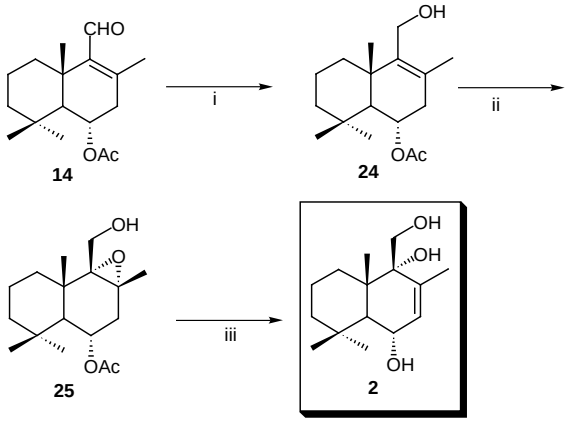
Reagents and conditions: (i) TBDMSCl, imidazole, DMF, 60 ºC, 91%; (ii) oxone, CH_2Cl_2, acetone, H_2O, $NaHCO_3$, 18-crown-6, 0–3 ºC, 30%; (iii) $LiAlH_4$, THF, r.t., 68%; (iv) OsO_4, $NaIO_4$, THF, H_2O, 45 ºC, 40-45%; (v) TBDMSCl, NaH, THF, r.t., 73%; (vi) TBDMSCl, imidazole, DMF, 60 ºC, 79%; (vii) OsO_4, $NaIO_4$, THF, H_2O, 45 ºC, 69%.

Scheme 4

Since the oxidation of **7** with osmium tetroxide gave a low yield of **19**, we decided to also test compound **18**, obtained

after conversion of **7** into its silyl enol ether. However, treatment of **18** with osmium tetroxide[19–21] gave compound **22** as the major compound in a moderate yield together with **23** (Scheme 4). It became clear that seemingly small changes of the functional groups in the molecule at the C-6 position could have a profound and unpredictable influence on the course and results of the reactions.

Therefore the moderate yield of **14** was accepted and its conversion into (−)-albrassitriol (**2**) was investigated. Treatment of **14** with sodium borohydride[25] afforded the allylic alcohol **24**, which was epoxidized[27] to the α-epoxide **25** in 95% yield. This epoxide was then converted into (−)-albrassitriol (**2**) by treatment with lithium diethylamide[28,29] (Scheme 5).

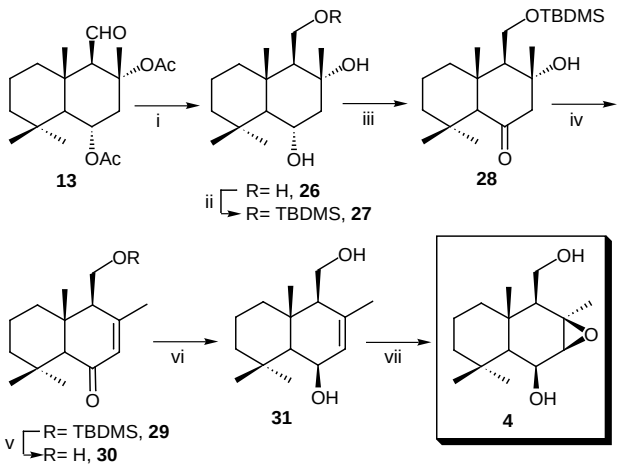


Reagents and conditions:(i) $NaBH_4$, EtOH, −8 ºC to r.t., 94%; (ii) *m*-CPBA, CH_2Cl_2, r.t., 95%; (iii) Et_2NLi, anhyd Et_2O, 0 ºC to r.t., N_2, 43%.

Scheme 5

Another important and attractive target to synthesize is (−)-uvidin C (**4**), which was obtained from the 6,8-diacetoxydrimenal **13** in seven steps. Reduction of **13** with lithium aluminium hydride[23] gave the triol **26** as the only product. After monoprotection of **26** with *t*-butyldimethylsilyl chloride,[26] the oxidation with PCC[30,31] yielded ketone **28**, which underwent a regioselective elimination of the (C-8)-alcohol by treatment with thionyl chloride in pyridine[32] to give the expected unsaturated ketone **29** in a slow reaction. Compound **30** could be obtained in pure form after deprotection of the primary alcohol in 60% yield, by stirring the mixture with TBAF[33] (Scheme 6).

Reduction of **30** with Dibal-H[34] gave the 6β-alcohol **31** (J_{5-6} = 4.2 Hz) in high yield. The high stereoselectivity in the reduction of the oxo function can be readily explained by the steric hindrance of the β-face of this ketone by the axial methyl substituent, favouring hydride delivery from the bottom face of the carbonyl group. Treatment with *m*-chloroperbenzoic acid in dichloromethane[27] afforded exclusively the β-epoxide, thus completing the synthesis of (−)-uvidin C (**4**) (Scheme 6).



Reagents and conditions: (i) $LiAlH_4$, THF, r.t., 70%; (ii) TBDMSCl, imidazole, r.t., 1h, 94%; (iii) PCC, CH_2Cl_2, 3Å molecular sieves, AcOH, r.t., 1h, 78%; (iv) $SOCl_2$, pyridine, 0 ºC to r.t., 71%; (v) TBAF, r.t., 60%, (vi) Dibal-H, dry THF, N_2, 0 ºC to r.t., 1h, 94%; (vii) *m*-CPBA, CH_2Cl_2, r.t., 1h, 95%.

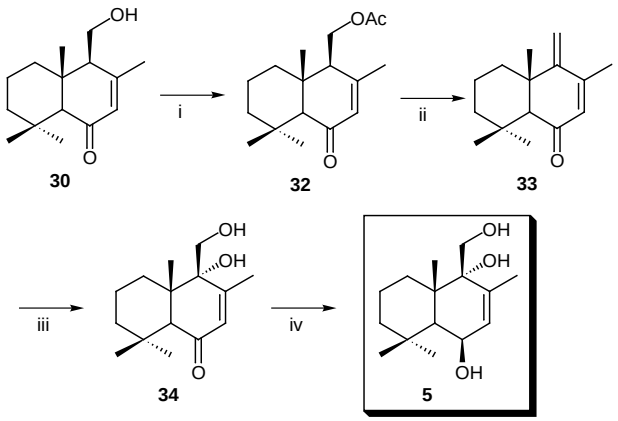
Scheme 6

An efficient route to (−)-*epi*-albrassitriol (**5**) has been developed via acetylation of **30** with acetic anhydride in pyridine[24] to afford compound **32** (Scheme 7). For the synthesis of (−)-*epi*-albrassitriol (**5**), our plan was to introduce the 9-α hydroxy group before the reduction of the ketone at the C-6 position to the corresponding 6β-hydroxyl.

Exposure of **32** to DBU readily afforded the known dienone **33**, which was submitted to osmylation.[34] This reaction proceeded smoothly, and as expected at the most nucleophilic 9,-11 double bond from the less hindered α side. The stereochemistry at C-9 is supported by the shift of the proton H-5 (δ 2.9) in comparison with the corresponding signal for the enone **32**. This downfield shift can be attributed to the *cis*-1,3-diaxial interaction of H-5 with the free C-9 hydroxyl group. Reduction of **34** with Dibal-H[34] afforded the 6β-alcohol **5** again arising from hydride delivery from the least hindered α face of the carbonyl group (Scheme 7).

In conclusion, the utility of larixol as natural chiral starting material[35–37] for the synthesis of highly functionalized drimane sesquiterpenoids was demonstrated by the first semisynthesis of (−)-albrassitriol (**2**) and (−)-*epi*-albrassitriol (**5**) and by its conversion into (−)-drimenol (**3**) and (−)-uvidin C (**4**).

Optical rotations were determined on a Perkin-Elmer 241 polarimeter with a 1 dm microcell, using $CHCl_3$ as solvent (concentration expressed in g/ 100 mL). IR spectra were obtained on a BIORAD FTS-7 spectrometer with samples between NaCl. ^{1}H NMR spectra were recorded on a Bruker AC 200 spectrometer. Chemical shifts are given in ppm values with $CHCl_3$ as reference (set at δ 7.24 ppm), unless otherwise stated, and coupling constants in Hz. Abbreviations: s, singlet, d, doublet, t, triplet, dd, doublet of doublets, dt, doublet of triplets, m, multiplet. ^{13}C NMR spectra were measured in $CDCl_3$ or C_6D_6 and recorded on a Bruker AC 200. Mass spectra



Reagents and conditions: (i) Ac_2O, pyridine, r.t., 85%; (ii) DBU, anhyd benzene, reflux, 66%; (iii) OsO_4, pyridine, r.t., N_2, 88%; (iv) Di-bal-H, anhyd THF, N_2, 0 ºC to r.t., 1h, 83%.

Scheme 7

(MS) data were obtained on an AEI MS 902 spectrometer. Melting points (mp) were determined in capillary tubes. For analytical TLC, Merck silica gel 60G in 0.25 mm-thick layers was used. Chromatographic separations were carried out on Merck silica gel 60 using petroleum ether (boiling range 40−60 °C)−EtOAc mixtures of increasing polarity. Ozonization reactions were carried out with a mixture of ozone−oxygen provided by an oxygen-feed Fischer apparatus. All solvents were purified and dried by standard techniques just before use. Aqueous solutions were usually extracted with an organic solvent. The combined organic extracts were washed with brine and dried ($MgSO_4$), and the volatiles were evaporated under reduced pressure. Compound **1** was isolated from the oleoresin of *Larix decidua*.[4]

(1*S*,4*S*,4a*R*,8a*S*)-4-[(3*S*)-3-Hydroxy-3-methylpent-4-enyl]-4a,8,8-trimethyl-3-methylenedecahydronaphthalen-1-ol (1)

The oleoresin of *Larix decidua* (25 g) was dissolved in hexane (100 mL) and a solution of 1M KOH (50 mL) was added. A precipitate appeared and the mixture was filtered on Celite. The organic solution was separated and washed with a solution of 1N NaOH. The organic solution was dried ($MgSO_4$) and concentrated to yield the crude product as a yellow oil which was dissolved in a solution of 0.1N KOH in EtOH (300 mL). The solution was heated at reflux for 3 h. After cooling, the solution was concentrated to 150 mL. Water was added (100 mL) and the solution was concentrated to yield an insoluble product, which was dissolved in Et_2O (100 mL). The aqueous solution was extracted with Et_2O and the combined organic solutions were dried ($MgSO_4$) and the solvent was evaporated. The yellow oil was crystallized in cyclohexane (30 mL) to yield **1** (3.47g, 14% w/w) as white crystals; mp 100 °C (lit.: 102 °C,[38] 101 °C[24]).

$[\alpha]_D^{25}$ +52.9 (*c* = 0.59, $CHCl_3$).

HRMS: *m*/*z* calcd for $C_{20}H_{34}O_2$ (M^+) 306.2559, found 306.2848.

IR (film): ν = 3590, 1644, 925, 890 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): δ = 5.9 (X part of an ABX system, J_{cis} = 10.9 Hz, J_{trans} = 16.4 Hz, 1H), 5.2, 5.05 (AB part of an ABX system, J_{cis} = 10.9 Hz, J_{trans} = 16.4 Hz, *J* = 1.3 Hz, 2H), 4.9, 4.6 (2s, 2H), 3.8 (dt, *J* = 10.7 Hz, *J* = 5.4 Hz, 1H), 2.65 (dd, *J* = 5.4 Hz, *J* = 10.7 Hz, 1H), 2.0 (t, *J* = 10.9 Hz, 1H), 1.8-0.6 (m), 1.2 (s, 3H), 1.1 (s, 3H), 1.0 (s, 3H), 0.7 (s, 3H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 145.6 (s), 145.2 (d), 111.7 (t), 108.4 (t), 73.6 (s), 71.7 (d), 60.6 (d), 56.5 (d), 49.2 (t), 43.8 (t), 41.3 (t), 39.6 (s), 39.3 (t), 36.7 (q), 33.9 (s), 27.8 (q), 22.4 (q), 19.1 (t), 18.0 (t), 16.1 (q).

Epoxidation of (1*S*,4*S*,4a*R*,8a*S*)-4-[(3*S*)-3-Hydroxy-3-methylpent-4-enyl]-4a,8,8-trimethyl-3-methylenedecahydronaphthalen-1-ol (1)

To a stirred solution of larixol **1** (6.08 g, 19.85 mmol) in CH_2Cl_2 (100 mL) at 0−3 °C were added acetone (100 mL), H_2O (100 mL), 18-crown-6 (605 mg), $NaHCO_3$ (24.2 g) and a solution of oxone (18 g in 100 mL of H_2O). The mixture was stirred for 2.5 h, and sat. $NaHCO_3$ was added. The mixture was extracted with EtOAc/Et_2O (2×). The combined organic solutions were dried ($MgSO_4$) and concentrated to yield the crude product (8.93 g) as a yellow oil. The oil was purified by chromatography over silica gel (eluent: petroleum ether−EtOAc 1:1) to afford white crystals of **6** (5.19 g, 81%); mp 100 °C.

$[\alpha]_D^{25}$ +19.5 (*c* = 0.19, $CHCl_3$).

HRMS: *m*/*z* calcd for $C_{20}H_{34}O_3$ (M^+) 322.2508 and 304.2402 for $(M-H_2O)^+$, found 304.2403.

IR (film): ν = 3417, 2931, 2867, 1649, 1218, 921 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): δ = 5.8 (X part of an ABX system, J_{cis} = 10.8 Hz, J_{trans} = 17.4 Hz, 1H), 5.2, 5.0 (AB part of an ABX system, J_{cis} = 10.8 Hz, J_{trans} = 17.4 Hz, *J* = 1.4 Hz, 2H), 3.9 (dt, *J* = 4.8 Hz, 1H), 2.8 (dd, *J* = 4.2 Hz, 1H), 2.5 (d, *J* = 4.2 Hz, 1H), 2.1-0.77 (m), 1.2 (s, 3H), 1.15 (s, 3H), 1.0 (s, 3H), 0.8 (s, 3H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 144.9 (d), 111.7 (t), 73.5 (s), 69.8 (d), 60.3 (d), 57.7 (s), 53.6 (d), 51.2 (t), 46.9 (t), 43.7 (t), 43.6 (t), 40.2 (s), 39.1 (t), 36.6 (q), 33.7 (s), 28.1 (q), 22.2 (q), 18.3 (t), 15.9 (t), 15.7 (q).

(1*S*,3*R*,4*R*,4a*R*,8a*S*)-4-[(3*S*)-3-Hydroxy-3-methylpent-4-enyl]-3,4a,8,8-tetramethyldecahydronaphthalene-1,3-diol (7)

To a stirred solution of $LiAlH_4$ (694 mg, 18.26 mmol, 2 equiv) in anhyd THF (28 mL) under N_2 was added **6** (2.94 g, 9.12 mmol). After stirring overnight, the excess of $LiAlH_4$ was quenched with Et_2O and a solution of 1M HCl. The mixture was then extracted with EtOAc/Et_2O. The organic solution was washed with brine, dried ($MgSO_4$) and concentrated to afford white crystals of **7** (3.0 g), which were recrystallized from EtOAc/CH_2Cl_2 (2.77 g, 94%); mp 176 °C.

$[\alpha]_D^{25}$ +48.9 (*c* = 0.09, $CHCl_3$).

HRMS: *m*/*z* calcd for $C_{20}H_{36}O_3$ (M^+) 324.2664, found 291.2325.

IR (film): ν = 3355, 2939, 914 cm^{-1}.

^1H NMR ($CDCl_3$+DMSO, 200 MHz): δ = 5.8 (X part of an ABX system, J_{cis} = 10.6 Hz, J_{trans} = 17.4 Hz, 1H), 5.1, 5.0 (AB part of an ABX system, J_{cis} = 10.6 Hz, J_{trans} = 17.4 Hz, *J* = 2.0 Hz, 2H), 3.7 (dt, *J* = 10.8 Hz, *J* = 3.8 Hz, 1H), 2.0 (dd, *J* = 12.0 Hz, *J* = 3.8 Hz, 1H), 1.65-0.7 (m), 1.2 (s, 3H), 1.1 (s, 3H), 1.0 (s, 3H), 0.9 (s, 3H), 0.7 (s, 3H).

^{13}C NMR ($CDCl_3$+DMSO, 50 MHz): δ = 144.4 (d), 111.9 (t), 74.0 (2 × s), 68.7 (d), 61.0 (2 × d), 53.6 (t), 44.4 (t), 43.7 (t), 39.7 (t), 39.4 (s), 36.2 (q), 33.6 (s), 29.1 (q), 25.2 (q), 21.8 (q), 18.9 (t), 18.2 (t), 16.2 (q).

1-(1*S*,3*R*,4*R*,4a*S*,8a*S*)-3-Hydroxy-4-[(3*S*)-3-hydroxy-3-methylpent-4-enyl]-3,4a,8,8-tetramethyldecahydronaphthalen-1-yl Acetate (8)

To a solution of **7** (1.01 g, 3.1 mmol) in pyridine (4.3 mL, 30.8 mmol, 9.9 equiv) was added Ac_2O (1.4 mL, 15.1 mmol, 4.8 equiv). The mixture was stirred overnight and then it was diluted with water. The mixture was extracted with CH_2Cl_2 and the organic solution

was dried ($MgSO_4$) and concentrated to yield the crude product (1.58 g) as a yellow oil. The oil was purified by chromatography over silica gel (eluent: petroleum ether−EtOAc 2:1) to afford white crystals of **8** (1.13 g, 99%); mp 120 °C.

$[\alpha]_D^{25}$ +46.0 (*c* = 0.35, CH_3Cl).

HRMS: *m*/*z* calcd for $C_{22}H_{38}O_4$ (M^+) 336.2770 and 348.2664 for $(M\text{-}18)^+$, found 348.2655.

IR (film): ν = 3499, 2929, 1724, 1711, 1369, 1247, 1028, 919 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): δ = 5.8 (X part of an ABX system, J_{cis} = 10.6 Hz, J_{trans} = 17.2 Hz, 1H), 5.2, 5.0 (AB part of an ABX system, J_{cis} = 10.8 Hz, J_{trans} = 17.2 Hz, *J* = 1.2 Hz, 2H), 5.0 (dt, *J* = 4.0 Hz, 1H), 2.1−0.8 (m), 2.0 (s, 3H), 1.2 (s, 2 × 3H), 1.0 (s, 3H), 0.83 (s, 3H), 0.8 (s, 3H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 170.2 (s), 145.1 (d), 112.0 (t), 74.3 (s), 74.1 (s), 70.9 (d), 60.9 (d), 58.4 (d), 50.0 (t), 44.2 (t), 43.5 (t), 39.7 (s), 39.5 (t), 36.1 (q), 33.3 (s), 29.1 (q), 25.7 (q), 22.0 (q), 21.9 (q), 19.0 (t), 18.05 (t), 16.2 (q).

(1*S*,3*R*,4*R*,8a*S*)-4-(Acetyloxy)-2,5,5,8a-tetramethyl-1-(2-oxoethyl)decahydronaphthalen-1-yl Acetate (9)

To a solution of **8** (630 mg, 1.72 mmol) in THF (51 mL) and H_2O (13 mL) were added $NaIO_4$ (13.9 g, 65 mmol, 37.8 equiv) and OsO_4 (0.26 mL of a 2.5% wt solution in *t*-BuOH). The mixture was stirred at 45 °C overnight. Then it was cooled and diluted with EtOAc. The organic solution was washed with aq Na_2SO_3, dried ($MgSO_4$) and concentrated, to yield the crude product (850 mg) as an orange oil. The oil was chromatographed on silica gel (eluent: petroleum ether−EtOAc acetate 3:2) to afford **9** (510 mg, 84%) as white crystals; mp 100−110 °C.

$[\alpha]_D^{25}$ +37.4 (*c* = 1.47, $CHCl_3$).

HRMS: *m*/*z* calcd for $C_{20}H_{32}O_5$ (M^+) 337.2015 for $(M-15)^+$, found 337.2017.

^1H NMR (C_6D_6, 200 MHz): δ = 9.4 (t, *J* = 1.8 Hz, 1H), 5.2 (dt, *J* = 11.2 Hz, *J* = 3.8 Hz, 1H), 3.15 (dd, *J* = 12.2 Hz, *J* = 4.0 Hz, 1H), 2.15−0.5 (m), 1.62 (s, 3H), 1.6 (s, 3H), 1.4 (s, 3H), 1.0 (s, 3H), 0.8 (s, 3H), 0.5 (s, 3H).

^{13}C NMR (C_6D_6, 50 MHz): δ = 199.9 (d), 169.1 (s), 168.6 (s), 83.8 (s), 69.2 (d), 57.4 (d), 52.0 (d), 45.4 (t), 43.0 (t), 40.1 (t), 39.3 (t), 38.2 (s), 35.8 (q), 33.0 (s), 21.8 (q), 21.7 (q), 21.1 (q), 21.0 (q), 17.8 (t), 16.5 (q).

(1*S*,3*R*,4*R*,8a*S*)-4-(Acetyloxy)-4-[(*E*/*Z*)-2-(acetyloxy)ethenyl]-3,4a,8,8-tetramethyldecahydronaphthalen-1-yl Acetate (10a and 10b)

To a stirred solution of **9** (40 mg, 0.11mmol) in THF (0.6 mL) were added Et_3N (55 μL, 0.4 mmol, 3.6 equiv), Ac_2O (77 μL, 0.82 mmol, 7.45 equiv) and 4-DMAP (1 mg). The mixture was refluxed for 1 day under N_2. Then, the solvent was evaporated and the residue was dissolved in Et_2O. The organic solution was washed with sat. $NaHCO_3$ and H_2O, dried ($MgSO_4$) and concentrated to yield the crude product (60 mg) as a yellow oil. The oil was purified by chromatography over silica gel (eluent: petroleum ether−EtOAc 6:1) to afford a mixture of **10a** and **10b** (30 mg, 69%, E/Z 2:1) and **12** (10 mg, 20%).

10a and **10b**: oil, $[\alpha]_D^{25}$ +70 (*c* = 0.025, $CHCl_3$).

HRMS: *m*/*z* calcd for $C_{22}H_{34}O_6$ (M^+) 394.2355, found 334.2143 and 274.1930.

IR (film): ν = 2929, 1765, 1730, 1664, 1250, 929 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): signals assigned to **10a** and **10b** δ = 5.1 (dt, 1H), 2.55 (dd, 1H), 2.0 (s, 3H), 1.4 (s, 3H), 0.94 (s, 3H), 0.8 (s, 3H); **10a**: δ = 7.0 (d, *J* = 12.2 Hz, 1H), 5.3 (t, *J* = 11.2 Hz, *J* = 12.2 Hz, 1H), 2.3 (d, *J* = 11.0 Hz, 1H), 2.06 (s, 3H), 1.9 (s, 3H), 0.97 (s, 3H); **10b**: δ = 7.1 (d, *J* = 6.8 Hz, 1H), 4.8 (dd, *J* = 6.8 Hz, *J* = 11.2 Hz, 1H), 3.15 (d, *J* = 11.0 Hz, 1H), 2.1 (s, 3H), 1.7 (s, 3H), 1.0 (s, 3H).

^{13}C NMR ($CDCl_3$, 50 MHz): **10a**: δ = 170.2 (s), 170.1 (s), 168.0 (s), 138.1 (d), 109.8 (d), 83.5 (s), 69.9 (d), 56.95 (d), 56.3 (d), 43.6 (t), 43.2 (t), 40.1 (t), 37.8 (s), 35.8 (q), 33.3 (s), 22.8 (q), 22.7 (q), 22.2 (q), 22.1 (q), 20.8 (q), 18.0 (t), 17.0 (q); **10b**: δ = 170.2 (s), 170.1 (s), 168.1 (s), 137.0 (d), 109.8 (d), 83.9 (s), 70.1 (d), 56.95 (d), 52.1 (d), 43.6 (t), 43.2 (t), 40.5 (t), 38.3 (s), 35.8 (q), 33.3 (s), 22.8 (q), 22.7 (q), 22.2(q), 22.1 (q), 20.8 (q), 18.0 (t), 16.6 (q).

12: oil, $[\alpha]_D^{25}$ +64 (*c* = 0.05, $CHCl_3$).

HRMS: *m*/*z* calcd for $C_{24}H_{38}O_8$ (M^+) 454.2567, 394.2355 and 334.2144, found 394.2146, 394.2361.

IR (film): ν = 1770, 1725, 1250 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): δ = 6.9 (t, *J* = 6.2 Hz, 1H), 5.05 (dt, *J* = 11.2 Hz, *J* = 4.0 Hz, 1H), 2.5 (dd, *J* = 12.0 Hz, *J* = 4.0 Hz, 1H), 2.1 (s, 3H), 2.08 (s, 3H), 2.06 (s, 3H), 1.9 (s, 3H), 1.4 (s, 3H), 0.9 (s, 3H), 0.8 (s, 3H), 0.7 (s, 3H).

(1*S*,3*R*,4*R*,8a*S*)-3-(Acetyloxy)-4-{(*E*/*Z*)-2-[[*tert*-butyl(dimethyl)silyl]oxy)ethenyl}-3,4a,8,8-tetramethyldecahydronaphthalen-1-yl Acetate (11a and 11b)

To a solution of **9** (900 mg, 2.55 mmol) in anhyd THF (25 mL) at 0−3 °C under N_2 were added TBDMSCl (461 mg, 3.06 mmol, 1.2 equiv) and NaH (477 mg of 60% reagent in mineral oil, 19.9 mmol, 7.8 equiv). The mixture was allowed to warm to r.t. and stirred for 4 h. Then it was filtered through silica gel (eluent: THF) and the solvent was evaporated to give a mixture of **11a** and **11b** (1.1 g, 96%, *E*/*Z* 3:1) as an oil, which was not further purified.

11a and **11b**: $[\alpha]_D^{25}$ +34.8 (*c* = 0.135, $CHCl_3$).

HRMS: *m*/*z* calcd for $C_{27}H_{46}O_5$ (M^+) 450.3345, found 346.2691.

IR (film): ν = 2961, 1730, 1661, 1365, 1244, 839 cm^{-1}.

^1H NMR (C_6D_6, 200 MHz): signals assigned to **11a** δ = 6.25 (d, *J* = 11.6 Hz, 1H), 5.3 (dt, *J* = 10.8 Hz, *J* = 4.4 Hz, 1H), 5.0 (t, *J* = 11.0 Hz, 1H), 2.8 (dd, *J* = 12.2 Hz, *J* = 4.2 Hz, 1H), 2.4 (t, *J* = 10.8 Hz, 1H), 2.38 (d, *J* = 10.8 Hz, 1H), 2.1−0.0 (m), 1.7 (s, 3H), 1.65 (s, 3H), 1.5 (s, 3H), 1.1 (s, 3H), 0.95 (s, 3 × 3H), 0.9 (s, 3H), 0.7 (s, 3H), 0.1 (s, 2 × 3H).

^{13}C NMR (C_6D_6, 50 MHz): δ = 169.1 (2 × s), 143.3 (d), 106.5 (d), 84.0 (s), 69.8 (d), 57.1 (d), 56.0 (d), 44.0 (t), 43.4 (t), 41.1 (t), 37.9 (s), 35.9 (q), 33.2 (s), 25.5 (3 × q), 22.8 (q), 22.3 (q), 22.0 (q), 21.1 (q), 18.1 (t), 16.8 (q), −5.3 (2 × q).

(1*S*,3*R*,4*R*,4a*S*,8a*S*)-3-(Acetyloxy)-4-formyl-3,4a,8,8-tetramethyldecahydronaphthalen-1-yl Acetate (13)

To a stirred solution of **11a** and **11b** (30 mg, 0.07 mmol) in anhyd CH_2Cl_2−MeOH (3:2) (2 mL) was slowly added an O_3/ O_2 mixture for 10 min at −78 °C. Then, Me_2S (0.9 mL) was added and the mixture was stirred overnight at r.t. The solvent was evaporated affording the crude product (30 mg) as an oil. The oil was purified by chromatography over silica gel (eluent: petroleum ether−ethyl-acetate 3:1) to afford **13** (18 mg, 78%); mp 105 °C.

$[\alpha]_D^{25}$+53.3 (*c* = 0.075, $CHCl_3$).

HRMS: *m*/*z* calcd for $C_{19}H_{30}O_5$ (M^+) 338.4385, found 236.1747 and 252.1729.

IR (film): ν = 2936, 1720, 1250 cm^{-1}.

^1H NMR (C_6D_6, 200 MHz): δ = 9.7 (d, *J* = 4.0 Hz, 1H), 5.2 (dt, *J* = 9.6 Hz, *J* = 4.4 Hz, 1H), 2.6 (dd, *J* = 12.8 Hz, *J* = 4.4 Hz, 1H), 2.45 (d, *J* = 4 Hz, 1H), 2.0 (t, *J* = 9.6 Hz, 1H), 1.9−0.5 (m), 1.7 (s, 3H), 1.6 (s, 2 × 3H), 0.93 (s, 3H), 0.9 (s, 3H), 0.8 (s, 3H).

^{13}C NMR (C_6D_6, 50 MHz): δ = 202.0 (d), 169.05 (2 x s), 81.9 (s), 69.1 (d), 67.4 (d), 56.3 (d), 45.6 (t), 43.3 (t), 39.7 (t), 38.15 (s), 35.5 (q), 33.0 (s), 22.9 (q), 21.8 (q), 21.7 (q), 20.95 (q), 17.6 (q), 17.6 (t).

(1*R*,4a*S*)-4-Formyl-3,4a,8,8-tetramethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl Acetate (14)

A stirred solution of **13** (350 mg, 1.03 mmol) in 2,4,6-collidine (2 mL, 15 mmol, 14 equiv) was heated at 200 °C for 15 min. After cooling, the mixture was diluted with Et_2O. The organic solution was washed with 1M HCl and brine, dried ($MgSO_4$) and the solvent removed in vacuo to afford the crude product (160 mg) as a yellow oil. The oil was purified by chromatography over silica gel (eluent: petroleum ether−EtOAc 1:1) to afford **14** (120 mg, 41%) as an oil.

$[\alpha]_D^{25}$+80 (*c* = 0.005, $CHCl_3$).

HRMS: *m*/*z* calcd for $C_{17}H_{26}O_3$ (M^+) 278.1882, found 249.1848 and 234.1616.

IR (film): ν = 2931, 1780, 1720, 1590, 1365, 1244 cm^{-1}.

^{1}H NMR (C_6D_6, 200 MHz): δ = 9.8 (s, 1H), 5.3 (m, 1H), 2.4 (dd, *J* = 19.0 Hz, *J* = 6.4 Hz, 1H), 1.9−0.7 (m), 1.7 (s, 3H), 1.4 (s, 3H), 1.2 (s, 3H), 1.1 (s, 3H), 0.9 (s, 3H).

^{13}C NMR (C_6D_6, 50 MHz): δ = 190.7 (d), 169.3 (s), 147.7 (s), 142.9 (s), 69.2 (d), 53.2 (d), 42.9 (t), 42.3 (t), 40.1 (s), 36.0 (q, t), 33.1 (s), 22.1 (q), 21.15 (q), 21.0 (q), 18.6 (t), 17.7 (q).

(4a*S*,8a*S*)-2,5,5,8a-Tetramethyl-4a,5,6,7,8,8a-hexahydronaphthalene-1-carbaldehyde (15)

A stirred solution of **13** (60 mg, 0.18 mmol) in 2,4,6-collidine (1 mL, 7.6 mmol, 42 equiv) was heated at 200 °C for 1.5 h. After cooling, the mixture was diluted with Et_2O. The organic solution was washed with 1M HCl and brine, dried ($MgSO_4$) and the solvent removed in vacuo to afford the crude product (70 mg) as a yellow oil. The oil was chromatographed on silica gel (eluent: petroleum ether−EtOAc 8:1) to give **15** (30 mg, 77%) as a yellow oil.

IR (film): ν = 3011, 2954, 2873, 1730, 1680, 1244, 757 cm^{-1}.

^{1}H NMR (C_6D_6, 200 MHz): δ = 10.0 (s, 1H), 5.9 (dd, *J* = 9.6 Hz, *J* = 3.2 Hz, 1H), 5.6 (dd, *J* = 9.4 Hz, *J* = 3.0 Hz, 1H), 1.9 (t, *J* = 3.0 Hz, 1H), 1.7−0.75 (m), 1.7 (s, 3H), 1.1 (s, 3H), 0.8 (s, 3H), 0.8 (s, 3H).

^{13}C NMR (C_6D_6, 50 MHz): δ = 190.8 (d), 144.2 (s), 142.9 (s), 136.5 (d), 130.2 (d), 52.6 (d), 40.7 (t), 39.1 (s), 35.1 (t), 32.4 (q), 31.9 (s), 22.45 (2 × q), 18.8 (t), 15.8 (q).

(−)-Drimenol (3)

To a stirred solution of **15** (10 mg, 0.046 mmol) in EtOH (0.4 mL) was added $NaBH_4$ (3 mg, 0.082mmol, 1.8 equiv) at −8 °C. After 15 min, the mixture was stirred at r.t. for an additional 2 h, diluted with H_2O and extracted with Et_2O. The organic solution was washed with H_2O and brine, dried ($MgSO_4$) and the solvent removed to afford the crude product (10 mg) as an oil. The oil was purified by chromatography over silica gel (eluent: petroleum ether−EtOAc 8:1) to afford (**3**) (9 mg, 89%) as white crystals; mp 98 °C (lit.:[7] 96−97 °C).

HRMS: *m*/*z* calcd for $C_{15}H_{26}O$ (M^+) 222.1984, found 204.1513.

IR (film): ν = 3400, 2929, 1715, 1154 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 5.8 (m, 1H), 4.2 (m, *J* = 11.6 Hz, 2H), 2.1−0.7 (m), 1.8 (s, 3H), 0.9 (s, 3H), 0.85 (s, 3H), 0.8 (s, 3H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 140.0 (s), 129.3 (d), 58.0 (t), 55.2 (d), 53.0 (d), 41.0 (t), 38.6 (t), 38.2 (s), 35.2 (t), 32.9 (s), 32.5 (q), 32.1 (q), 22.8 (q), 18.9 (t), 16.5 (q).

(2S)-2-(2[(1*S*,4*S*,4a*S*,8a*R*)-4-({[*tert*-Butyl(dimethyl)silyl]oxy}-5,5,8a-trimethyl-2-methylenedecahydronaphthalen-1-yl)ethyl]but-3-en-2-ol (16)

To a stirred solution of **1** (130 mg, 0.42 mmol) in DMF (3 mL) were added TBDMSCl (633 mg, 4.2 mmol, 10 equiv) and imidazole (572 mg, 8.4 mmol, 20 equiv). The mixture was stirred at 60 °C for 3 days, and sat. $NaHCO_3$ was added. The mixture was extracted with Et_2O. The organic solution was washed with brine, dried ($MgSO_4$) and concentrated to yield the crude product which was purified by chromatography over silica gel (eluent: petroleum ether−EtOAc 4:1) to give **16** (160 mg, 91%) as white crystals.

IR (film): ν = 3400, 2951, 1476, 1395, 1388, 834 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 5.8 (X part of an ABX system, J_{cis} = 10.8 Hz, J_{trans} = 17.4 Hz, 1H), 5.05, 5.0 (AB part of an ABX system, J_{cis} = 10.8 Hz, J_{trans} = 17.4 Hz, *J* = 1.2 Hz, 2H), 4.7, 4.4 (2s, 2H), 4.4 (s, 1H), 3.8 (dt, *J* = 10.4 Hz, *J* = 5.6 Hz, 1H), 2.5 (dd, *J* = 4.8 Hz, *J* = 12.4 Hz, 1H), 1.9 (t, *J* = 11.2 Hz, 1H), 1.6−0.1 (m), 1.15 (s, 3H), 1.0 (s, 3H), 0.88 (s, 3 × 3H), 0.7 (s, 3H), 0.6 (s, 3H), 0.06 (s, 2 × 3H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 146.1 (s), 145.1 (d), 111.6 (t), 108.0 (t), 73.6 (s), 72.6 (d), 60.0 (d), 56.5 (d), 49.7 (t), 44.1 (t), 41.3 (t), 39.6 (t), 39.4 (s), 36.5 (q), 33.6 (s), 27.7 (q), 26.1 (3 × q), 22.3 (q), 19.0 (t), 18.1 (s), 17.9 (t), 16.1 (q), −3.6 (2 × q).

Epoxidation of (2S)-2-(2[(1*S*,4*S*,4a*S*,8a*R*)-4-{[*tert*-butyl(dimethyl)silyl]oxy}-5,5,8a-trimethyl-2-methylenedecahydronaphthalen-1-yl)-ethyl]but-3-en-2-ol (16)

To a stirred solution of **16** (160 mg, 0.38 mmol), in CH_2Cl_2 (5 mL) at 0−3°C were added acetone (5 mL), H_2O (5 mL), 18-crown-6 (12 mg), $NaHCO_3$ (463 mg) and a solution of oxone (627 mg in 3.5 mL of H_2O). The mixture was stirred for 1.5 h, and sat. $NaHCO_3$ was added. The mixture was extracted with EtOAc/ Et_2O. The organic solution was dried ($MgSO_4$) and concentrated to yield the crude product (100 mg) as a yellow oil, which was purified by chromatography over silica gel (eluent: petroleum ether−EtOAc 1:1) to afford white crystals of **17** (50 mg, 30%), mp 110 °C. $[\alpha]_D^{25}$ + 22.7 (c = 0.075, $CHCl_3$).

IR (film): ν = 3463, 2967, 2851, 1470, 1391, 1254, 1084, 879 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 5.8 (X part of an ABX system, J_{cis} = 10.6 Hz, J_{trans} = 17.2 Hz, 1H), 5.1, 5.0 (AB part of an ABX system, J_{cis} = 10.6 Hz, J_{trans} = 17.2 Hz, *J* = 1.4 Hz, 2H), 4.0 (dt, *J* = 10.8 Hz, *J* = 4.6 Hz, 1H), 2.8 (dd, *J* = 2.0 Hz, *J* = 4.0 Hz, 1H), 2.5 (d, *J* = 4.2 Hz, 1H), 2.0 (t, *J* = 9.4 Hz, 1H), 1.9−0.04 (m), 1.2 (s, 3H), 1.1 (s, 3H), 1.0 (s, 3H), 0.9 (s, 3 × 3H), 0.8 (s, 3H), −0.06 (s, 2 × 3H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 144.9 (d), 111.7 (t), 73.6 (s), 70.5 (d), 59.8 (d), 57.8 (s), 53.5 (d), 51.2 (t), 47.3(t), 44.1 (t), 43.6 (t), 40.0 (s), 39.5 (t), 36.4 (q), 33.5 (s), 28.1 (q), 26.0 (3 × q), 22.1 (q), 18.2 (t), 18.2 (s), 15.9 (q, t), −3.6 (q), −4.0 (q).

(1*R*,2*R*,4*S*,4a*S*,8a*R*)-4-{[*tert*-Butyl(dimethyl)silyl]oxy}-1-[(3*S*)-3-hydroxy-3-methylpent-4-enyl]-2,5,5,8a-tetramethyldecahydronaphthalen-2-ol (18)

To a stirred solution of $LiAlH_4$ (129 mg, 3.4 mmol, 2 equiv) in anhyd THF (16 mL) under N_2 was added **17** (740 mg, 1.7 mmol). After stirring overnight, the excess of $LiAlH_4$ was quenched with Et_2O and a solution of 1M HCl and the mixture was extracted with EtOAc/ Et_2O. The organic solution was washed with brine, dried ($MgSO_4$) and concentrated to afford the crude product (700 mg) as white crystals. The crude product was purified by chromatography over silica gel (eluent: petroleum ether−EtOAc 4:1) to afford white crystals of **18** (510 mg, 68%); mp 160−162 °C.

$[\alpha]_D^{25}$ +49.1 (*c* = 0.11, $CHCl_3$).

HRMS: *m*/*z* calcd for $C_{26}H_{50}O_3Si$ (M^+) 438.3424, found 363.2716.

IR (film): ν = 3437, 2957, 1724, 1454, 945, 779 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 5.9 (X part of an ABX system, J_{cis} = 10.8 Hz, J_{trans} = 17,4 Hz, 1H), 5.1, 5.0 (AB part of an ABX system, J_{cis} = 10.6 Hz, J_{trans} = 17.2 Hz, *J* = 1.2 Hz, 2H), 3.9 (dt, *J* = 10.4 Hz, *J* = 3.6 Hz, 1H), 2.0 (dd, *J* = 12.0 Hz, *J* = 3.4 Hz, 1H), 1.7−0.07 (m), 1.3 (s, 3H), 1.2 (s, 3H), 1.1 (s, 3H), 0.93 (s, 3H), 0.9 (s, 3 × 3H), 0.8 (s, 3H), 0.1 (2s, 2 × 3H).

^{13}C NMR ($CDCl_3$, 50 Hz): δ = 144.9 (d), 112.0 (t), 74.3 (s), 74.2 (s), 69.8 (d), 61.7 (d), 60.9 (d), 54.5 (t), 44.6 (t), 44.2 (t), 40.1 (s), 39.4 (t), 36.3 (q), 33.5 (s), 29.3 (q), 26.1 (3 × q), 25.5 (q), 21.9 (q), 19.0 (t), 18.1 (t, s), 16.4 (q), −3.5 (q), −3.9 (q).

(1*R*,2*R*,4*S*,4a*S*,8a*S*)-4-Hydroxy-2,5,5,8a-tetramethyl-1-(2-oxoethyl)decahydronaphthalen-2-yl Acetate (19)

To a solution of **7** (300 mg, 0.92 mmol) in THF (27 mL) and H_2O (6.8 mL) were added $NaIO_4$ (7.98 g, 37.3 mmol, 40.5 equiv) and OsO_4 (140 μL of a 2.5% wt solution in *t*-BuOH). The mixture was stirred at 45 °C overnight, and then it was cooled and diluted with EtOAc. The organic solution was washed with aq Na_2SO_3, dried ($MgSO_4$) and concentrated to yield the crude product (310 mg) as an orange oil. The oil was purified by chromatography over silica gel (eluent: petroleum ether−EtOAc 3:1) to afford **19** (129 mg, 45%) as white crystals; mp 100 °C.

$[\alpha]_D^{25}$ −6.1 (*c* = 0.065, $CHCl_3$).

HRMS: *m*/*z* calcd for $C_{18}H_{30}O_4$ (M^+) 310.4284 and 232.1827, found 304.2403 and 232.1825.

^{1}H NMR (C_6D_6, 200 MHz): δ = 9.4 (m, 1H), 3.5 (dt, *J* = 10.8 Hz, 1H), 3.0 (dd, *J* = 12.2 Hz, *J* = 4.0 Hz, 1H), 2.1−0.4 (m), 1.65 (s, 3H), 1.35 (s, 3H), 1.3 (s, 3H), 1.0 (s, 3H), 0.5 (s, 3H).

^{13}C NMR (C_6D_6, 50 MHz): δ = 200.4 (d), 168.9 (s), 84.4 (s), 67.5 (d), 59.5 (d), 52.5(d), 49.7 (t), 43.3 (t), 40.25 (t), 39.5 (t), 37.9 (s), 36.3 (q), 33.5 (s), 21.9 (2 × q), 21.1 (q), 18.1 (t), 16.7 (q).

(1*S*,3*R*,4*R*,4a*R*,8a*S*)-4-(*(E)*-2-{[*tert*-Butyl(dimethyl)silyl]oxy}-ethenyl)-3-hydroxy-3,4a,8,8-tetramethyldecahydronaphthalen-1-yl Acetate (21)

To a solution of **19** (70 mg, 0.23 mmol) in anhyd THF (4.8 mL) under N_2 were added TBDMSCl (43 mg, 0.28 mmol, 1.2 equiv) and NaH (62 mg of 60% reagent in mineral oil, 2.58 mmol, 11.2 equiv). The mixture was allowed to warm to r.t. and stirred for an additional 4 h. Then it was filtered through silica gel (eluent: THF) and the solvent was evaporated to give the crude product (80 mg) as an oil. The oil was purified by chromatography over silica gel (eluent: petroleum ether−EtOAc 3:1) to afford **20** (30 mg, 42%) and **21** (31 mg, 31%).

20: oil.

HRMS: *m*/*z* calcd for $C_{18}H_{30}O_4$ (M^+) 310.2144, found 349.2558 and 250.1932.

IR (film): ν = 3595, 1072, 1024, 943 cm^{-1}.

^{1}H NMR (C_6D_6, 200 MHz): δ = 5.3 (t, *J* = 5.0 Hz, 1H), 5.1 (dt, *J* = 11.2 Hz, *J* = 3.6 Hz, 1H), 2.1−0.7 (m), 1.95 (s, 3H), 1.2 (s, 3H), 0.9 (s, 3H), 0.8 (s, 3H), 0.74 (s, 3H).

^{13}C NMR (C_6D_6, 50 MHz): δ = 170.2 (s), 101.8 (d), 79.6 (s), 71.4 (d), 59.85 (d), 59.4 (d), 47.0 (t), 43.7 (t), 39.7 (t), 39.6 (s), 35.8 (q), 33.3 (s), 30.7 (t), 25.7 (q), 22.0 (q), 21.75 (q), 18.0 (t), 16.3 (q) **21**: oil, HRMS: *m*/*z* calcd for $C_{24}H_{44}O_4Si$ (M^+) 424.3009, found 364.2800.

IR (film): ν = 3580, 2940, 1725, 1650, 1370, 1253, 974 cm^{-1}.

^{1}H NMR (C_6D_6, 200 MHz): δ = 6.25 (d, *J* = 11.6 Hz, 1H), 5.3 (dt, *J* = 11.2 Hz, *J* = 4.0 Hz, 1H), 5.0 (t, *J* = 9.4 Hz, 1H), 2.35 (dd, *J* = 12.0 Hz, *J* = 3.8 Hz, 1H), 1.8−0.7 (m), 1.7 (s, 3H), 1.1 (s, 3H), 1.0 (s, 3H), 0.9 (s, 3 × 3H), 0.9 (s, 3H), 0.75 (s, 3H), 0.1 (s, 2 × 3H).

^{13}C NMR (C_6D_6, 50 MHz): δ = 169.2 (s), 143.9 (d), 106.3 (d), 70.5 (s), 70.4 (d), 60.8 (d), 58.3 (d), 48.7 (t), 43.5 (t), 40.9 (t), 37.9 (s), 36.2 (q), 33.3 (s), 26.0 (q), 25.6 (3 × q), 22.0 (q), 21.2 (q), 18.3 (t), 16.5 (q), −5.4 (2 × q).

(1*R*,2*R*,4*S*,4a*S*,8a*R*)-4-{[*tert*-Butyl(dimethyl)silyl]oxy}-1-[(3*S*)-3-hydroxy-3-methylpent-4-enyl]-2,5,5,8a-tetramethyldecahydronaphthalen-2-ol (18)

To a stirred solution of **7** (189 mg, 0.58 mmol) in DMF (15 mL) were added TBDMSCl (879 mg, 5.8 mmol, 10 equiv) and imidazole (790 mg, 11.6 mmol, 20 equiv). The mixture was stirred at 60 °C for 1 day, and sat. $NaHCO_3$ was added. The mixture was extracted with Et_2O. The organic solution was washed with brine, dried ($MgSO_4$) and concentrated to yield the crude product. The residue was purified by chromatography over silica gel (eluent: petroleum ether−EtOAc 1:1) to afford **18** (200 mg, 79%) as white crystals.

1-((3a*R*,5*S*,5a*S*,9a*R*,9b*R*)-5-{[*tert*-Butyl(dimethyl)silyl]oxy}-3a,6,6,9a-tetramethyldodecahydronaphtho[2,1-*b*]furan-2-yl)ethanone (22)

To a solution of **18** (150 mg, 0.34 mmol) in THF (10 mL) and H_2O (2 mL) were added $NaIO_4$ (2.74 g, 12.8 mmol, 37.6 equiv) and OsO_4 (50 μL of a 2.5% wt solution in *t*-BuOH). The mixture was stirred at 45 °C for 5 h. Then it was cooled and diluted with EtOAc and washed with aq Na_2SO_3. The organic solution was dried ($MgSO_4$) and concentrated to yield the crude product (100 mg) as a brown oil. The oil was purified by chromatography over silica gel (eluent: petroleum ether−EtOAc 5:1) to afford **22** (66 mg, 46%) and **23** (33 mg, 23%).

22: oil, HRMS: *m*/*z* calcd for $C_{24}H_{44}O_3Si$ (M^+) 408.3060, found 365.2873 and 393.2825.

IR (film): ν = 2930, 1724, 1244 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 4.4 (dd, *J* = 10.0 Hz, *J* = 2.8 Hz, 1H), 4.0 (dt, *J* = 10.8 Hz, *J* = 4.0 Hz, 1H), 2.2 (dd, *J* = 12.8 Hz, 1H), 2.2 (s, 3H), 2.3−0.8 (m), 1.2 (s, 3H), 1.1 (s, 3H), 1.0 (s, 3H), 0.93 (s, 3 × 3H), 0.9 (s, 3H), 0.16 (s, 3H), 0.14 (s, 3H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ 211.2 (s), 81.7 (s, d), 71.4 (d), 62.2 (d), 59.6 (d), 51.4 (t), 44.7 (t), 40.7 (t), 36.5 (q), 35.6 (s), 33.9 (s), 27.5 (t), 27.2 (q), 26.5 (3 × q), 23.1 (q), 21.9 (q), 18.4 (t), 16.5 (q), −3.0 (q), −3.6 (q).

23: oil, HRMS, *m*/*z* calcd for $C_{24}H_{44}O_4Si$ (M^+) 424.3009, 365.2545 and 393.2825, found 365.2545 and 393.2764.

IR (film): ν = 2930, 1720, 1398, 1366, 1244 cm^{-1}.

^{1}H NMR ($CDCl_3$, 200 MHz): δ = 9.5 (t, *J* = 2.4 Hz, 1H), 3.8 (dt, *J* = 11.0 Hz, 1H), 2.9 (dd, *J* = 12.4 Hz, *J* = 3.6 Hz, 1H), 2.4−0.7 (m), 1.8 (s, 3H), 1.4 (s, 3H), 1.0 (s, 3H), 0.8 (s, 3H), 0.78 (s, 4 × 3H), 0.04 (s, 3H), 0.0 (s, 3H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 202.2 (d), 169.5 (s), 84.7 (s), 69.0 (d), 60.2 (d), 53.0 (d), 49.8 (t), 43.7 (t), 40.5 (2 × t), 38.2 (s), 36.2 (q), 33.4 (s), 26.1 (3 × q), 22.5 (q), 21.8 (q), 21.2 (q), 18.1 (s), 17.9 (t), 17.2 (q), −3.6 (q), −4.0 (q).

(1*S*,4a*S*,8a*S*)-4-(Hydroxymethyl)-3,4a,8,8-tetramethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl Acetate (24)

To a stirred solution of **14** (40 mg, 0.14 mmol) in EtOH (8 mL) was added solid $NaBH_4$ (9 mg, 0.24 mmol, 1.7 equiv) at −8 °C. After 20 min, the mixture was warmed to r.t. and stirred for an additional 45 min, and then diluted with H_2O. The solvent was evaporated and the mixture was extracted with EtOAc. The organic solution was washed with H_2O and brine, dried ($MgSO_4$) and the solvent was removed in vacuo to afford the crude product (40 mg) as a yellow oil. The oil was purified by chromatography over silica gel (eluent: petroleum ether−EtOAc 4:1) to afford white crystals of **24** (37 mg, 94%).$[\alpha]_D^{25}$+106.7 (*c* = 0.015, $CHCl_3$).

HRMS: *m/z* calcd for $C_{17}H_{28}O_3$ (M^+) 280.2038, found 249.1854.

IR (film): ν = 3701, 1720, 1650, 1540, 1260, 1015 cm^{-1}.

^1H NMR (C_6D_6, 200 MHz): δ = 5.5 (m, 1H), 3.95 (AB system, *J* = 11.6 Hz, 2H), 2.6 (dd, *J* = 6.6 Hz, *J* = 17.6 Hz, 1H), 2.2−0.8 (m), 1.9 (s, 3H), 1.5 (s, 3H), 1.2 (s, 3H), 1.04 (s, 3H), 1.02 (s, 3H).

^{13}C NMR (C_6D_6, 50 MHz): δ = 169.7 (s), 140.9 (s), 129.15 (s), 70.5 (d), 57.8 (t), 54.0 (d), 43.5 (t), 40.7 (t), 36.9 (t, s), 36.2 (q), 33.4 (s), 22.3 (q), 21.9 (q), 21.4 (q), 18.9 (t), 18.7 (q).

Epoxidation of (1*S*,4a*S*,8a*S*)-4-(Hydroxymethyl)-3,4a,8,8-tetramethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl Acetate (24)

To a stirred solution of **24** (20 mg, 0.071 mmol) in CH_2Cl_2 (4 mL) was added *m*-CPBA (31 mg, 0.18 mmol, 2.5 equiv). The mixture was stirred for 2 h, and H_2O was added. The mixture was extracted with EtOAc/ Et_2O. The organic solution was dried ($MgSO_4$) and concentrated to yield the crude product (30 mg) as a yellow oil. The oil was purified by chromatography over silica gel (eluent: petroleum ether−EtOAc 2:1) to afford **25** (20 mg, 95%) as an oil. $[\alpha]_D^{25}$ +60.0 (*c* = 0.005, $CHCl_3$).

HRMS: *m/z* calcd for $C_{17}H_{28}O_4$ (M^+) 296.1988 and 236.1776, found 236.1771.

IR (film): ν = 3600, 1720, 1250, 900, 805 cm^{-1}.

^1H NMR (C_6D_6, 200 MHz): δ = 5.1 (m, 1H), 3.6 (AB system, *J* = 11.6 Hz, 2H), 2.3 (dd, *J* = 7.4 Hz, *J* = 6.0 Hz, 1H), 2.05 (d, *J* = 10.2 Hz, 1H), 1.85 (dd, *J* = 16.0 Hz, *J* = 5.0 Hz, 1H), 1.8−0.8 (m), 1.7 (s, 3H), 1.04 (s, 3H), 1.0 (s, 3H), 0.9 (s, 3H), 0.8 (s, 3H).

^{13}C NMR (C_6D_6, 50 MHz): δ = 169.8 (s), 69.6 (s), 68.6 (d), 62.4 (s), 58.1 (t), 47.6 (d), 42.7 (t), 38.05 (s), 37.4 (t), 35.3 (t), 35.0 (q), 33.5 (s), 22.4 (q), 21.3 (q), 20.1 (q), 18.4 (t), 18.2 (q).

(−)-Albrassitriol (2)

To an ice-cold solution of lithium diethylamide (20 mg, 0.25 mmol, 2.5 equiv) in anhyd Et_2O (2 mL) was added **25** (30 mg, 0.1 mmol) in anhyd Et_2O (2 mL). The mixture was stirred at r.t. for 3 h. Then it was poured into H_2O and the mixture was extracted with EtOAc/ Et_2O. The organic solution was washed successively with 1M HCl, sat. $NaHCO_3$ and H_2O. The solution was dried ($MgSO_4$) and concentrated to yield the crude product (30 mg) as a yellow oil. The oil was purified by chromatography over silica gel (eluent: petroleum ether−EtOAc 2:1) to afford (**2**) (11 mg, 43%) as an oil.

HRMS: *m/z* calcd for $C_{15}H_{26}O_3$ (M^+) 254.1882, found 254.1878.

^1H NMR ($CDCl_3$, 200 MHz): δ = 5.3 (m, 1H), 4.0 (dd, *J* = 11.4 Hz, 1H), 3.6 (dd, *J* = 11.6 Hz, 1H), 3.5 (dd, 1 H), 2.5 (s, 1H), 2.2−1.5 (m), 1.3 (s, 3H), 1.05 (s, 3H), 0.8 (s, 3H), 0.6 (s, 3H).

^{13}C NMR (C_6D_6, 50 MHz): δ = 128.9 (s), 124.3 (d), 76.0 (s), 68.4 (d), 59.0 (t), 50.3 (d), 42.6 (t), 42.4 (t), 38.05 (s), 34.6 (s), 32.4 (q), 22.4 (q), 20.1 (q), 18.4 (t), 18.2 (q).

(1*S*,3*R*,4*S*,4a*S*,8a*S*)-4-(Hydroxymethyl)-3,4a,8,8-tetramethyldecahydronaphthalene-1,3-diol (26)

To a stirred solution of $LiAlH_4$ (425 mg, 11.18 mmol, 6 equiv) in anhyd THF (17 mL) under N_2 was added **13** (630 mg, 1.86 mmol). After stirring overnight, the excess of $LiAlH_4$ was quenched with Et_2O and a solution of 1M HCl. The mixture was then extracted with EtOAc/Et_2O. The organic solution was washed with brine, dried ($MgSO_4$) and concentrated to afford white crystals (400 mg). The crude product was purified by chromatography over silica gel (eluent: EtOAc) to afford **26** (332 mg, 70%) as white crystals; mp 150 °C. $[\alpha]_D^{25}$ +26.2 (c = 0.08, EtOH).

HRMS: *m/z* calcd for $C_{15}H_{28}O_3$ (M^+) 256.2038 and 220.1827, found 241.1803 and 220.1829.

IR (film): ν = 3397, 2957, 1711, 1454, 1209, 748 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): δ = 3.9 (m, 2H), 3.8 (dt, *J* = 4.0 Hz, *J* = 10.4 Hz, 1H), 2.1 (dd, *J* = 3.8 Hz, *J* = 12.2 Hz, 1H), 2.0−0.7 (m), 1.4 (s, 3H), 1.1 (s, 3H), 1.0 (s, 3H), 0.8 (s, 3H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 74.5(s), 68.6 (d), 61.1 (d), 59.8 (d), 53.9 (t), 43.1 (t), 40.2 (t), 38.2 (s), 36.3 (t), 33.7 (q, s), 25.7 (q), 22.3 (q), 18.4 (t), 18.2 (q).

(1*S*,3*R*,4*S*,4a*S*,8a*S*)-4-({[*tert*-Butyl(dimethyl)silyl]oxy}methyl)-3,4a,8,8-tetramethyldecahydronaphthalene-1,3-diol (27)

To a stirred solution of **26** (260 mg, 1.01 mmol) in DMF (26 mL) were added TBDMSCl (182 mg, 1.2 mmol, 1.2 equiv) and imidazole (202 mg, 2.9 mmol, 2.9 equiv). The mixture was stirred at r.t. for 1 h, and H_2O was added. The mixture was extracted with Et_2O. The organic solution was washed with brine, dried ($MgSO_4$) and concentrated to yield the crude product. The product was purified by chromatography over silica gel (eluent: petroleum ether−EtOAc 1:1) to afford **27** (350 mg, 94%) as white crystals; mp 114-115 °C.

$[\alpha]_D^{25}$ +58.9 (*c* = 0.09, $CHCl_3$).

HRMS: *m/z* calcd for $C_{21}H_{42}O_3Si$ (M^+) 370.2903 and 295.2093, found 295.2095 and 262.1933.

IR (film): ν = 3383, 2950, 1736, 1470, 1049 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): δ = 3.8 (dt, 1H), 3.6 (m, 2H), 2.0 (dd, *J* = 3.6 Hz, *J* = 12.4 Hz, 1H), 1.6−0.7 (m), 1.2 (s, 3H), 1.0 (s, 3H), 0.9 (s, 3H), 0.8 (s, 3 × 3H), 0.7 (s, 3H), −0.4 (s, 6H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 73.0 (s), 67.9 (d), 62.0 (t), 60.6 (d), 58.5 (d), 52.9 (t), 43.1 (t), 40.3 (t), 37.8 (s), 36.5 (q), 33.45 (s), 26.0 (q), 25.7 (3 × q), 22.2 (q), 17.9 (t), 17.86 (s), 16.95 (q), −5.7 (2 × q).

(3*R*,4*S*,4a*R*,8a*S*)-4-({[*tert*-Butyl(dimethyl)silyl]oxy}methyl)-3-hydroxy-3,4a,8,8-tetramethyloctahydronaphthalen-1(2*H*)-one (28)

To a solution of **27** (350 mg, 0.94 mmol) in CH_2Cl_2 (7.5 mL), with 3Å molecular sieves was added PCC (304 mg, 1.42 mmol, 1.5 equiv). After 40 min, the mixture was diluted with Et_2O and filtered through silica gel (eluent: Et_2O). After evaporation of the solvents, the green oil (280 mg) was purified by chromatography over silica gel (eluent: petroleum ether−EtOAc 4:1) to afford **28** (270 mg, 78%) as white crystals; mp 108−109 °C. $[\alpha]_D^{25}$ +54.5 (*c* = 0.055, $CHCl_3$).

HRMS: *m/z* calcd for $C_{21}H_{40}O_3Si$ (M^+) 368.2747 and 311.2032, found 311.2032.

IR (film): ν = 3488, 2936, 1715, 1475, 1140, 829 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): 3.9 (m, 2H), 2.6 (m, 2H), 2.3 (s, 1H), 2.2−0.8 (m), 1.3 (s, 3H), 1.2 (s, 3H), 0.92 (s, 3H), 0.9 (s, 3 × 3H), 0.8 (s, 3H), 0.1 (s, 2 × 3H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 208.9 (s), 76.0 (s), 65.5 (d), 61.8 (t), 59.2 (d), 59.1 (t), 42.1 (t), 40.1 (t), 39.9 (s), 32.5 (q), 32.1 (s), 26.0 (q), 25.7 (3 × q), 21.7 (q), 18.2 (t), 17.9 (s), 16.7 (q), −5.7 (2 × q).

(4*S*,4a*R*,8a*S*)-4-({[*tert*-Butyl(dimethyl)silyl]oxy}methyl)-3,4a,8,8-tetramethyl-4a,5,6,7,8,8a-hexahydronaphthalen-1(4*H*)-one (29)

To a solution of **28** (270 mg, 0.73 mmol) in pyridine (4.3 mL, 53 mmol, 73 equiv) was added 4-DMAP (88 mg) and $SOCl_2$ (250 μL, 3.4 mmol, 4.7 equiv). After 5 h at r.t., ice was added and the pyridine was evaporated in vacuo. The mixture was extracted with Et_2O (2×) and the organic solution was washed successively with H_2O, sat. $NaHCO_3$ and brine. The organic solution was dried ($MgSO_4$) and concentrated to yield the crude product (300 mg) as a yellow oil. The oil was purified by chromatography over silica gel (eluent:

petroleum ether−EtOAc 9.5:0.5) to afford **29** (182 mg, 71%) as an oil.

$[\alpha]_D^{25}$ −17.1 (*c* = 0.035, $CHCl_3$).

HRMS: *m*/*z* calcd for $C_{21}H_{38}O_2Si$ (M^+) 350.2641 and 263.1467, found 263.1829.

IR (film): ν = 3301, 2930, 1455, 1010 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): δ = 5,8 (s, 1H), 3.8 (m, 2H), 2.25 (m, 1H), 2.0 (s, 1H), 1.9−0.8 (m), 1.2 (s, 3H), 1.15 (s, 3H), 1.1 (s, 3H), 0.9 (s, 3H), 0.85 (s, 3 × 3H), 0.02 (s, 2 × 3H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 200.5 (s), 158.2 (s), 129.1 (d), 63.2 (d), 59.8 (t), 58.1 (d), 43.3 (t), 42.4 (s), 39.4 (t), 33.6 (q), 32.3 (s), 25.8 (3 × q), 22.0 (q), 21.7 (q), 18.3 (t), 18.2 (s), 16.05 (q), −5.5 (2 × q).

(4*S*,4a*R*,8a*S*)-4-(Hydroxymethyl)-3,4a,8,8-tetramethyl-4a,5,6,7,8,8a-hexahydronaphthalen-1(4*H*)-one (30)

To a solution of **29** (150 mg, 0.43 mmol) in THF (5.4 mL) was added TBAF (124 μL, 0.43 mmol). After 1 h, the mixture was diluted with H_2O and extracted with CH_2Cl_2. The organic solution was washed with brine, dried ($MgSO_4$) and concentrated to yield the crude product (180 mg) as a yellow oil. The oil was purified by chromatography over silica gel (eluent: EtOAc) to afford **30** (62 mg, 60%) as an oil.

$[\alpha]_D^{25}$ +60.0 (*c* = 0.005, $CHCl_3$).

HRMS: *m*/*z* calcd for $C_{15}H_{24}O_2$ (M^+) 236.1776, found 236.1775.

^1H NMR ($CDCl_3$, 200 MHz): δ = 5.8 (m, 1H), 3.95 (m, 2H), 2.2 (m, 1H), 2.05 (s, 1H), 2.0−0.9 (m), 2.0 (s, 3H), 1.1 (s, 3H), 1.1 (s, 3H), 0.9 (s, 3H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 200.3 (s), 157.5 (s), 129.0 (d), 63.0 (d), 59.9 (t), 58.2 (d), 43.0 (t), 42.1 (s), 39.3 (t), 33.6 (q), 32.3 (s), 22.0 (q), 21.7 (q), 18.2 (t), 15.9 (q).

(1*R*,4*S*,4a*R*,8a*S*)-4-(hydroxymethyl)-3,4a,8,8-tetramethyl-1,4,4a,5,6,7,8,8a-octahydronaphthalen-1-ol (31)

To a solution of **30** (30 mg, 0.13 mmol) in anhyd THF (1.2 mL) at 0 °C under N_2 was added Dibal-H (0.42 mL of a 1.5M solution in toluene, 0.6 mmol, 4.6 equiv). After stirring for 1 h, the excess of Dibal-H was quenched with EtOAc and a solution of 5% H_2SO_4. The mixture was then extracted with EtOAc/ Et_2O. The organic solution was washed with brine, dried ($MgSO_4$) and concentrated to afford **31** (29 mg, 94%) as white crystals. The residue was not purified, but directly converted into **4**.

IR (film): ν = 3301, 2930, 1455, 1010 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): δ = 5.7 (m, 1H), 4.4 (m, 1H), 3.8 (m, 2H), 1.8−0.85 (m), 1.8 (s, 3H), 1.1 (s, 3H), 1.0 (s, 3H), 0.85 (s, 3H).

(−)-Uvidin C (4)

To a solution of **31** (20 mg, 0.08 mmol) in CH_2Cl_2 (5 mL) was added *m*-CPBA (36 mg, 0.21 mmol, 2.5 equiv). The mixture was stirred for 25 min, and H_2O was added. The mixture was extracted with EtOAc/ Et_2O. The organic solution was washed with 10% $Na_2S_2O_3$, sat. $NaHCO_3$ and brine. The organic solution was dried ($MgSO_4$) and concentrated to yield the crude product (30 mg) as an oil. The oil was purified by chromatography over silica gel (eluent: petroleum ether−EtOAc 2:1) to afford **4** (20 mg, 95%) as an oil.

IR (film): ν = 3428, 2932, 1705, 1010 cm^{-1}.

^1H NMR (C_6D_6, 200 MHz): δ = 4.3 (dd, *J* = 5.4 Hz, *J* = 4.6 Hz, 1H), 3.7 (d, *J* = 3.4 Hz, 2H), 2.9 (d, *J* = 5.8 Hz, 1H), 2.05 (s, 1H), 2.0−0.4 (m), 1.5 (s, 3H), 1.35 (s, 3H), 1.15 (s, 3H), 1.1 (s, 3H), 0.5 (d, *J* = 4.0 Hz, 1H).

^{13}C NMR (C_6D_6, 50 MHz): δ = 65.2 (d), 63.2 (s, d), 60.8 (t), 55.2 (d), 54.3 (d), 44.5 (t), 43.2 (t), 35.7 (s), 34.3 (s), 33.3 (q), 24.7 (q), 22.85 (q), 19.0 (q), 18.8 (t).

((1*S*,4a*S*,8a*R*)-2,5,5,8a-Tetramethyl-4-oxo-1,4,4a,5,6,7,8,8a-octahydronaphthalen-1-yl)methyl Acetate (32)

To a solution of **30** (15 mg, 0.13 mmol) in pyridine (2.1 mL) was added Ac_2O (850 μL, 9.05 mmol). The mixture was stirred for 3 h at r.t. Then it was diluted with H_2O and extracted with CH_2Cl_2. The organic solution was dried ($MgSO_4$) and concentrated to yield the crude product (50 mg) as a yellow oil. The oil was purified by chromatography over silica gel (eluent: petroleum ether−EtOAc 2:1) to afford white crystals of **32** (30 mg, 85%); mp 55−60 °C. $[\alpha]_D^{25}$ +31.4 (*c* = 0.035, $CHCl_3$).

HRMS: *m*/*z* calcd for $C_{17}H_{26}O_3$ (M^+) 278.1882, found 278.1886.

IR (film): ν = 3428, 2932, 1705, 1010 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): δ = 5.8 (m, 1H), 4.35, 4.3 (m, 2H), 2.45 (br s, 1H), 2.05 (s, 1H), 2.0 (s, 3H), 1.9−0.9 (m), 1.9 (s, 3H), 1.15 (s, 3H), 1.1 (s, 3H), 0.9 (s, 3H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 199.6 (s), 170.8 (s), 155.4 (s), 129.4 (d), 63.0 (d), 61.7 (t), 54.6 (d), 42.85 (t), 42.2 (s), 39.1 (t), 33.5 (q), 32.2 (s), 21.7 (q), 21.55 (q), 21.1 (q), 18.1 (t), 15.6 (q).

(4a*S*)-3,4a,8,8-Tetramethyl-4-methylene-4a,5,6,7,8,8a-hexahydronaphthalen-1(4*H*)-one (33)

To a solution of **32** (40 mg, 0.14 mmol) in anhyd benzene (2 mL) was added DBU (128 ml, 0.86 mmol). The mixture was stirred for 3.5 h at reflux under N_2. After evaporation of the solvent, the residue was purified by chromatography over silica gel (eluent: petroleum ether−EtOAc 3:1) to afford **33** (20 mg, 66%) as an oil. $[\alpha]_D^{25}$ −101.3° (*c* = 0.075, $CHCl_3$).

IR (film): ν = 3428, 2932, 1705, 1010 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): δ = 5.8 (s, 1H), 5.2 (d, *J* = 12.0 Hz, 2H), 2.2 (s, 1H), 2.0−0.75 (m), 2.0 (s, 3H), 1.15 (s, 3H), 1.1 (s, 2 × 3H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 199.6 (s), 156.2 (s), 150.0 (s), 128.0 (d), 111.8 (t), 61.1 (d), 43.1 (t), 42.9 (s), 37.8 (t), 33.3 (q), 32.75 (s), 23.3 (q), 21.75 (q), 20.4 (t), 18.4 (q).

(4*R*,4a*S*,8a*S*)-4-Hydroxy-4-(hydroxymethyl)-3,4a,8,8-tetramethyl-4a,5,6,7,8,8a-hexahydronaphthalen-1(4*H*)-one (34)

To a solution of **33** (20 mg, 0.09 mmol) in anhyd pyridine (0.6 mL) under N_2 was added OsO_4 (1.07 g of a 2.5% wt solution in *t*-BuOH, 0.1 mmol). The mixture was stirred at r.t. overnight. Then it was diluted with aq. 10% $Na_2S_2O_3$ and stirred for 1 h. The mixture was extracted with Et_2O. The organic solution was washed with brine, dried ($MgSO_4$) and concentrated to yield the crude product (60 mg) as a black oil. The oil was chromatographed on silica gel (eluent: EtOAc−MeOH 9:1) to afford **34** (20 mg, 88%) as white crystals; mp 142 °C.

HRMS: *m*/*z* calcd for $C_{15}H_{24}O_3$ (M^+) 252.1725, found 191.1434.

IR (film): ν = 3500, 2969, 2947, 1676, 1450, 970, 833 cm^{-1}.

^1H NMR ($CDCl_3$, 200 MHz): δ = 5.6 (m, 1H), 4.7 (AB system, *J* = 11.2 Hz, 2H), 3.2 (s, 1H), 2.0−0.8 (m), 2.0 (s, 3H), 1.15 (s, 3H), 1.12 (s, 3H), 1.1 (s, 3H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ = 201.1 (s), 157.0 (s), 128.0 (d), 92.2 (s), 84.5 (t), 55.0 (d), 46.5 (s), 43.2 (t), 33.6 (q), 32.2 (s), 31.45 (t), 21.8 (q), 20.9 (q), 18.1 (t), 14.2 (q).

(−)-*epi*-Albrassitriol (5)

To a solution of **34** (15 mg, 0.06 mmol) in anhyd THF (0.6 mL) at 0°C under N_2 was added Dibal-H (0.21 mL of a 1.5M solution in

toluene, 0.31 mmol, 5.1 equiv). After stirring 1h, the excess of Dibal-H was quenched with aq NH_4Cl. The mixture was then extracted with EtOAc/ Et_2O. The organic solution was washed with sat. $NaHCO_3$, dried ($MgSO_4$) and concentrated to yield the crude product as an oil. The oil was purified by chromatography over silica gel (eluent: EtOAc-MeOH 9:1) to afford (**5**) (14 mg, 83%) as an oil.

^{1}H NMR (acetone-d_6, 200 MHz): δ = 5.35 (m, 1H), 4.7 (m, 2H), 4.16 (t, 1H), 2.0−1.0 (m), 1.35 (s, 3H), 1.06 (s, 3H), 1.05 (s, 3H).

^{13}C NMR (acetone-d_6, 50 MHz): δ = 141.0 (s), 127.4 (d), 74.5 (s), 67.2 (t), 63.3 (d), 48.3 (d), 46.3 (t), 41.0 (s), 33.8 (s), 33.1 (q), 33.0 (t), 25.1 (q), 20.4 (q), 19.3 (t), 18.2 (q).

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