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Synthesis of 9-Oxyfunctionalized Eudesmanes from Artemisin

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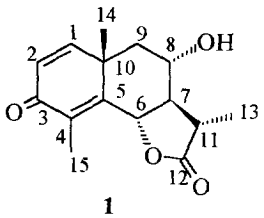
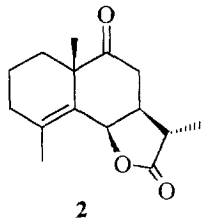
Abstract: Artemisin (**1**) was transformed into two natural sesquiterpenoids **2** and **3** in a sequence which involves functionality transfer from C_8 to C_9 and further elaboration of the A ring and the lactone moiety.

Sesquiterpenes constitute a group of natural compounds widely distributed in the vegetable kingdom.[1] This kind of compounds exhibit considerable biological activities such as antiinflamatory,[2] ichtyotoxic and cytotoxic,[3] seed germination inhibitory[4] and molluscicidal activities,[4,5] and consequently efficient synthesis of these compounds are a synthetic challenge that has received much attention during the last decade.[6]

In recent years a number of 9-oxyfunctionalized eudesmanes have been isolated from natural sources. However the synthesis of this particular kind of compounds have received little attention. In previous papers,[7] starting from artemisin (**1**), we developed an efficient methodology for the synthesis of eudesmanes bearing an oxygenated function on C_9 and used it in the synthesis of two natural *trans* 6α,12-eudesmanolides which structures, proposed on the basis of NMR analysis, proved erroneous.[7] These facts, together with our interest on the synthesis of sesquiterpenes[8] prompted us to undertake the synthesis of other eudesmanes functionalized on this particular position. In this paper we report on the chemical transformation of artemisin (**1**) into *cis* 6β,12-eudesmanolides, such as the naturally occurring 9-oxo-6,7αH,11βH-eudesm-4-en-6,12-olide (**2**), and reduction products at C_6, such as the natural (11*S*)-3-oxo-7αH-eudesm-4-en-9β,12-diol (**3**). These compounds were first isolated from *Artemisia tournefortiana*,[9] and *Cassinia uncata*[10] respectively and the chemical transformations described in this paper constitute the first synthesis of both compounds.



1



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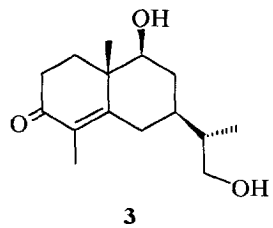
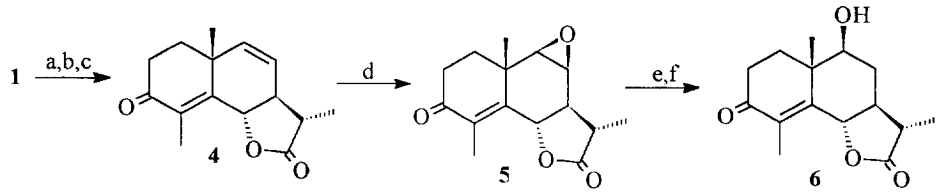


3

RESULTS AND DISCUSSION

The synthesis of compounds **2** and **3** from artemisin (**1**) required the hydroxyl group transfer from C_8 to C_9, which was carried out as we have recently described,[7] by 1,2-hydrogenation and dehydration of the hydroxyl group at C_8 to give **4**, C_8-C_9 epoxidation to furnish **5** and finally opening of the oxirane ring and elimination of the phenylselenenyl group to yield the 9-hydroxy-6,12-eudesmanolide **6**. However, a modification of the previously reported method was used in the preparation of compound **5.** In the new procedure the use of dimethyldioxirane-acetone solutions for the epoxidation of **4** to **5** has been substituted by the generation of the reagent *in situ* with oxone and acetone in phase transfer conditions (see experimental), which avoids the tedious and expensive preparation of the reagent solutions with comparable results in yield and chemo- and stereoselectivity.



Reagents: (a) H_2, Wilkinson catalyst; (b) Triflic anhydride.; (c) Li_2CO_3; (d) Oxone, acetone; (e) PhSeNa; (g) Raney Ni

Once the hydroxyl group was transferred from C_8 to C_9, the synthesis of compound **2** required the epimerization at C_6, followed by deoxygenation of C_3 and oxidation of the hydroxyl group present at C_9.

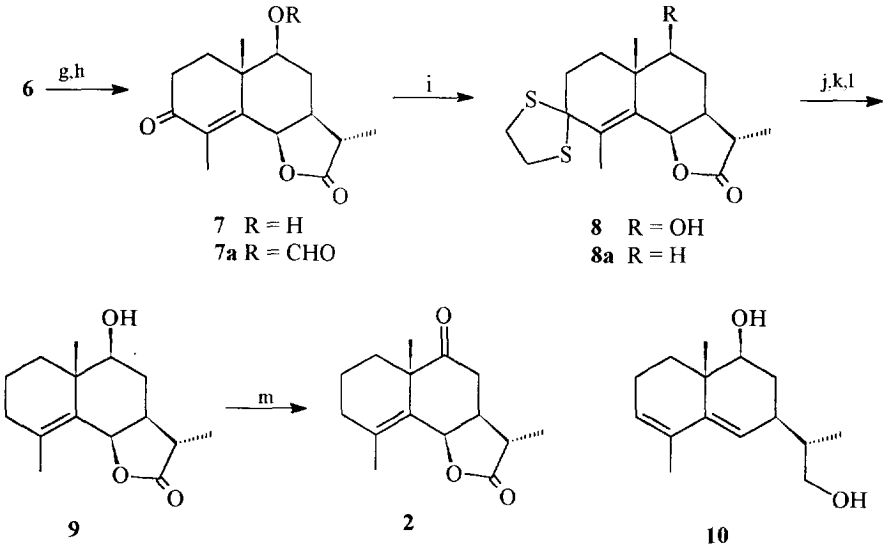
A procedure by Piers and Cheng[11] has been successfully applied for the first purpose in sesquiterpene lactones with structures analogues to **6**. The method involves the treatment of enone-lactones in DMF containing 5-10% dry HCl. However, when this method has been used with hydroxylated substrates[12] the yield is lower than 60%. In our case, treatment of **6** in these conditions yielded the desired *cis*-lactone **7** with a 55% yield only, although a less-polar product was isolated (16%) and identified as the formate **7a** by its spectroscopical features. Compound **7a** probably arises out from the nucleophilic attack of the hydroxyl group at C_9 to an HCl-activated form of DMF.[13] Compound **7a** was found to hydrolyze smoothly on treatment with aqueous acid to give compound **7**. Therefore, and in order to simplify the experimental procedure, we carried out the hydrolysis of **7a** without separation of the original mixture, and in this way we could obtain the lactone **7** with 70% yield from **6**.

For the deoxygenation of C_3, the thioketalization-desulfurization method that we had used with good results in earlier synthesis was chosen.[7] However, a first attempt to obtain the thioketal **8** using ethanedithiol in AcOH-BF_3·Et_2O gave rise to a complex mixture from which the desired compound **8** could be isolated only with a low yield of 18%. By changing the solvent to CH_2Cl_2 and reducing the amount of BF_3·Et_2O the yield of **8** raised to 57%. Finally we obtained the best results by using benzene and a very small amount of BF_3·Et_2O ($2.3\ 10^{-4}$ eq.) for several days at room temperature. In this way we could obtain **8** with a 72% yield, together with a 12% of unreacted starting material.

In the direct desulfurization of 6-*epi*-dihydrosantonin thioketal (**8a**) with Raney nickel,[14] the hydrogenolysis of the C_6-O bond takes place yielding acid material of undetermined structure, while desulfurization of the potassium salt of the lactone yield the normal desulfurizated product (40%). Consequently, we subjected lactone **8** to saponification with ethanolic KOH, and the resulting salt was treated

with Raney nickel at 0°C. After re-lactonization with 10% HCl, a product with the expected spectroscopical constants for **9** was obtained with a yield of 36%. A second extraction of the mother liquors allowed the isolation of a product (19%) which structure was assigned as **10**. Compound **10** is likely formed by dehydration of the C_6-OH group with concomitant migration[15] of the C_4-C_5 double bond to form a conjugate diene during the acidic treatment. Finally, oxidation of **9** with pyridinium chlorochromate (PCC) buffered with NaOAc[16] gave compound **2** with a 66% yield.

It is interesting to note that while the thioketalization-desulfurization method gives good results for the deoxigenation of C_3 in *trans*-6α,12-eudesmanolides,[7] compound **7** is very sensitive to both reaction conditions and presents many problems associated with the presence of a *cis*-6β,12-eudesmanolide moiety on its structure.



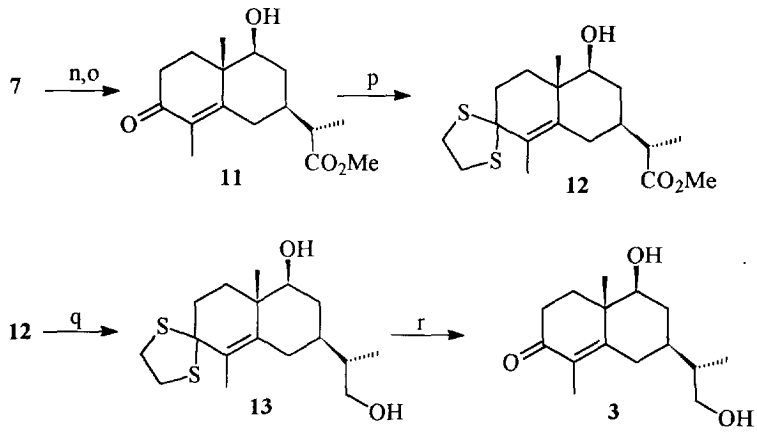
Reagents: (g) HCl/DMF; (h) HCl/MeOH; (i) $(CH_2SH)_2$; (j) KOH; (k) Raney Ni; (l) HCl; (m) PCC

For the synthesis of compound **3**, a reductive cleavage of the C_6-O bond and a refunctionalization of the lateral chain on C_7 were required.

In order to carry out the first transformation we took advantage of the situation of the C_6-O bond in γ to an α,β-unsaturated carbonyl group in compound 7. It is known that good leaving groups on those positions undergo elimination on treatment with reductive metals.[11] Thus, treatment of **7** with Zn dust in MeOH-AcOH gave an acid that was esterified with excess of diazomethane to give the corresponding methyl ester **11** in 61% yield.

On the other hand, the reduction of the methyl ester on C_{12} required the previous protection of the ketone on C_3. This was protected as its thioketal **12** (85%) by treatment with excess of ethanedithiol in AcOH-BF_3·Et_2O without any of the problems mentioned above for **7**.

Once the ketone was protected, reduction of **12** with $LiAlH_4$ afforded alcohol **13** quantitatively, which, upon hydrolysis of the thioketal with periodic acid[17] gave **3** in 71% yield.



Reagents: (n) Zn/MeOH; (o) Diazomethane; (p) $(CH_2SH)_2$; (q) $LiAlH_4$; (r) H_5IO_6

The physical and spectroscopical constants of the synthetic products were fully consistent with structures **2** and **3** and identical with literature data for the natural products isolated from *Artemisia tournefortiana*[9] and *Cassinia uncata*.[10]

EXPERIMENTAL

Melting points were determined in capillary tubes with a Büchi apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 281 spectrometer, as liquid films for oils and in KBr disk for solids. NMR spectra were run on a Brucker AC-200 instrument (200.1 MHz for ^1H and 50.3 MHz for ^{13}C) or a Varian Unity 400 (399.95 MHz for ^1H and 100.58 MHz for ^{13}C) in $CDCl_3$ solutions. The carbon type (methyl, methylene, methine, or quaternary) was determined by DEPT experiments. Mass spectra were recorded at 70 eV. Optical rotations were determined on a Polartronic D (Schmidt and Haensch) polarimeter as solutions in $CHCl_3$. Flash chromatography was carried out on SDS Chromagel 60 silica gel.

8,9β-Epoxy-3-oxo-7αH,6,11βH-eudesm-4-en-6,12-olide (5)

A solution containing compound **4** (200 mg, 0.81 mmol), $NaHCO_3$ (2.22 g, 26.4 mmol), 18-crown-6 (37 mg), H_2O (11 mL), acetone (11 mL) and CH_2Cl_2 (11 mL) was cooled at 0°C. To this solution, three portions of Oxone® (2 x 652 mg, 2 x 2.11 mmol, and 326 mg, 1.06 mmol) in water (2 x 2.4 mL and 1.2 mL) were added at intervals of 1 h. One hour after the last addition, aqueous $NaHCO_3$ was added and the mixture extracted with CH_2Cl_2. The organic layer was washed with 10% Na_2SO_3 and aqueous $NaHCO_3$, and dried over Na_2SO_4. Work up and chromatography gave 3 mg (1.4%) of starting material, and 200 mg (94%) of the epoxide **5** with the physical and spectroscopical features described in the literature.[7]

Table 1. ^{13}C NMR Data of Compounds 3, 7-9, and 11-13

	7[c]	7a	8[d]	9	11	12[d]	13[d]	3[c]
C_1	33.9	33.5	35.0	35.4[a]	33.3[a]	35.0	35.1	33.5
C_2	33.5	33.2	41.8	17.8	33.3[a]	41.0	41.0	33.4
C_3	198.7	197.8	71.2	33.1[a]	198.9	71.9	72.1	198.9
C_4	138.4[a]	138.9	132.7[a]	140.7	130.4	128.8[a]	128.2[a]	130.3
C_5	150.1[a]	148.4	141.2[a]	128.1	159.1	138.6[a]	139.6[a]	160.1
C_6	75.0	76.0	76.0[b]	76.4[b]	33.0[a]	33.2	32.1	31.7
C_7	41.4	41.0	41.6	41.8	44.5[b]	44.6	40.0	35.6
C_8	31.2	27.6	31.3	31.6	31.4	30.5	30.6	31.8
C_9	75.1	74.5	75.8[b]	75.4[b]	77.6	78.4	78.8	78.3
C_{10}	39.8	38.4	38.7	38.6	41.4	40.0	40.2	41.5
C_{11}	43.5	43.3	43.8	44.0	37.2[b]	37.9	36.3	39.9
C_{12}	179.1	178.6	179.6	180.0	175.8	176.1	66.0	65.8
C_{13}	14.9	14.8	14.9	14.8	13.9	14.0	13.0	12.9
C_{14}	16.0	17.4	17.1[c]	18.1	15.6	16.6[b]	16.7[b]	15.7
C_{15}	11.4	11.4	17.6[c]	20.1	11.2	17.2[b]	17.3[b]	11.4
$-OCH_3$	-	-	-	-	51.6	51.5	-	-
-CHO	-	160.2	-	-	-	-	-	-

[a-b] These signals may be interchangeable within the corresponding spectrum.
[c] Assignement by heteronuclear ^1H-^{13}C NMR correlation.
d $(CH_2S)_2$ group 39.2 and 39.8 ppm for compound **8**, 39.3 and 39.7 ppm for compound **12**, and 39.4 and 39.8 ppm for compound **13**.

9β-Hydroxy-3-oxo-6,7αH,11βH-eudesm-4-en-6,12-olide (7)

A solution of compound **6** (100 mg, 0.38 mmol) in 0.9 mL of DMF containing 10% dry HCl was heated under argon at 85°C for 1h. Then, the mixture was poured into water and extracted with EtOAc. The combined organic layer were washed with brine, dried, and concentrated. The resulting oil was dissolved in methanol (8.6 mL) and treated with 1.7 mL of water and 1 mL of 2M HCl. After stirring overnight at rt, the reaction mixture was diluted with water and extracted with EtOAc. Usual work up followed by chromatography eluting with hexane-ether (1:1 to 0:1) allowed to obtain 70 mg (70%) of compound **7** as an oil; $[\alpha]_D^{25}$ -57° (*c* 0.55); MS *m/e* 264 (100, M^+), 191 (12), 173 (12), 154 (50), 135 (12), 123 (17), 105 (12), 123 (17); HRMS 264.1361, $C_{15}H_{20}O_4$ required 264.1361; IR ν_{max} 3650-3150, 1770, 1670, cm^{-1}; ^1H NMR δ 1.20 (s, 3H, H-14), 1.38 (d, J = 8.0 Hz, 3H, H-13), 1.69 (ddd, J = 12.0, 12.6, 13.2 Hz, 1H, H-8β), 1.77 (ddd, J = 5.2, 13.6, 14.4 Hz, 1H, H-1α), 1.89 (ddd, J = 3.6, 6.4, 13.2 Hz, 1H, H-8α), 1.93 (s, 3H, H-15), 2.20 (ddd, J = 2.8, 5.2, 13.6, 1H, H-1β), 2.32 (ddd, J = 5.2, 6.4, 12.6 Hz, 1H, H-7), 2.53 (ddd, J = 2.8, 5.2, 18.0 Hz, 1H, H-2α), 2.53 (q, J = 8.0 Hz, 1H, H-11), 2.63 (ddd, J = 5.2, 14.4, 18.0 Hz, 1H, H-2β), 3.44 (dd, J = 3.6, 12.0 Hz, 1H, H-9), 5.38 (d, J = 5.2 Hz, 1H, H-6);

3,3-(1,2-Ethanedithio)-9β-hydroxy-6,7αH,11βH-eudesm-4-en-6,12-olide (8).

A solution of compound **7** (61 mg, 0.23 mmol), 99% ethanedithiol (0.18 mL, 2.2 mmol), and boron trifluoride etherate (6.3 μL) in dry benzene (4.8 mL) was stirred under argon at rt for 4 d. After this time, the reaction mixture was poured into water and extracted with EtOAc. The combined organic layer was washed with saturated aqueous $NaHCO_3$ and brine, and dried over Na_2SO_4. Filtration and solvent removal followed by chromatography eluting with mixtures of hexane-ether gave compound **8** (112 mg, 72%) and unreacted starting material (15 mg, 12%). Compound **8**: an oil, $[\alpha]_D^{25}$ -33° (*c* 0.66); MS *m/e* 341 (13, M^++1), 340 (71,

M^+), 323 (13), 322 (59), 294 (28), 281 (29), 280 (100), 261 (32), 230 (13), 229 (13), 189 (30); HRMS 340.1170, $C_{17}H_{24}O_3S_2$ required 340.1167; IR ν_{max} 3477, 1738 cm^{-1}; ^1H NMR δ 1.06 (s, 3H, H-14), 1.37 (d, J = 8.0 Hz, 3H, H-13), 1.57 (q, J = 12.6 Hz, 1H, H-8β), 1.6-1.7 (m, H-1), 1.8-1.9 (m, 2H, H-1 and H-8α), 2.10 (s, 3H, H-15), 2.21 (ddd, J = 5.1, 6.6, 12.6, 1H, H-7), 2.2- 2.4 (m, 2H, 2 H-2), 2.46 (q, J = 8.0 Hz, 1H, H-11), 3.2-3.5 (m, 5H, 2-CH_2S and H-9), 5.33 (d, J = 5.1 Hz, 1H, H-6);

9β-Hydroxy-6,7αH,11βH-eudesm-4-en-6,12-olide (9).

A solution of compound **8** (49 mg, 0.145 mmol) in 96% aqueous ethanol (3 mL) was treated with KOH (81 mg, 1.45 mmol) at room temperature under argon. After 50 min, the reaction mixture was cooled at 0°C and 0.9 mL of a pre-cooled ethanolic suspension of Raney nickel W-2 were added. After 10 min, the solution was filtered to remove the reagent, and the filtrate was acidified with 6 mL of 10% aqueous HCl for 30 min. Then, the mixture was extracted with CH_2Cl_2 and the organic layer washed with saturated aqueous $NaHCO_3$ and brine. After usual work up and chromatography with hexane-ether (1:1 to 0:1) compound **9** (13 mg, 36%) was obtained.

A second extraction of the water layer with EtOAc allowed to obtain after concentration under reduced pressure of the organic layer 7 mg (19%) of compound **10**.

Compound **9**: oil, $[\alpha]_D^{25}$ -40° (*c* 0.61); MS *m/e* 251 (14, M^++1), 250 (99, M^+), 236 (11), 235 (74), 232 (42), 206 (94), 159 (31), 139 (100), 133 (37); HRMS 250.1572, $C_{15}H_{22}O_3$ required 250.1569; IR ν_{max} 3467, 1757 cm^{-1}; ^1H NMR δ 1.03 (s, 3H, H-14), 1.27 (td, J = 4.8, 12.8 Hz, 1H, H-1α), 1.33 (d, J = 7.6 Hz, 3H, H-13), 1.45 (brd, J = 4.0 Hz, 1H, OH), 1.60 (q, J = 12.8 Hz, 1H, H-8β), 1.6-1.7 (m, 2H, 2 H-2), 1.80 (s, 3H, H-15), 1.8-1.9 (m, 2H, H-1 and H-8α), 2.08 (dd, J = 5.2, 7.2 Hz, 2H, 2 H-3), 2.13 (ddd, J = 5.2, 6.8, 12.8 Hz, 1H, H-7), 2.45 (q, J = 7.6 Hz, 1H, H-11), 3.30 (td, J = 4.0, 12.0 Hz, 1H, H-9), 5.37 (d, J = 5.2 Hz, 1H, H-6);

Compound **10**: IR ν_{max} 3500-3100, 3400-2700, 1700 cm^{-1}, ^1H NMR δ 0.92 (s, 3H, H-14), 1.11 (d, J = 7.0 Hz, 3H, H-13), 1.2-1.3 (m, 1H, H-1'), 1.63 (q, J = 12.0 Hz, 1H, H-8β), 1.75 (s, 3H, H-15), 1.6-1.8 (m, 1H, H-8α), 1.92 (dd, J = 4.9, 12.9 Hz, 1H, H-1), 2.0-2.2 (m, 2H, 2H-2), 2.57 (dq, J = 5.9, 7.0 Hz, 1H, H-11), 2.7-2.9 (m, 1H, H-7), 3.57 (dd, J = 4.1, 11.8 Hz, 1H, H-9), 5.28 (brs, 1H, H-6), 5.54 (brs, 1H, H-3).

9-Oxo-6,7αH,11βH-eudesm-4-en-6,12-olide (2).

A mixture of PCC (6.5 mg, 0.03 mmol), NaOAc (0.5 mg, $6 \cdot 10^{-3}$ mmol) and compound **9** (5 mg, 0.02 mmol) in CH_2Cl_2 (0.1 mL) was stirred under argon for 6 h. After this time, ether was added and the overfloating solution was taken. The remaining residue was washed several times with ether. The joined solutions and washings were chromatographed on silica gel eluting with ether to give 3.3 mg (66%) of compound **2**: an oil, $[\alpha]_D^{25}$ +35° (*c* 0.24) [lit[9] $[\alpha]_D^{24}$ +49° (*c* 0.62); MS *m/e* 248 (90, M^+), 233 (85), 230 (7), 220 (15), 206 (43), 205 (88), 187 (60), 175 (70), 161 (64), 159 (75); HRMS 248.1417, $C_{15}H_{20}O_3$ required 248.1412; IR ν_{max} cm^{-1}; ^1H NMR δ 1.27 (s, 3H, H-14), 1.35 (d, J = 7.5 Hz, 3H, H-13), 1.4-1.8 (m, 4 H, 2H-1 and 2H-2), 1.85 (s, 3H, H-15), 2.12 (br dd, J = 4.5, 7.8 Hz, 2H, 2 H-3), 2.35 (dd, J = 4.2, 13.5 Hz, 1H, H-8'), 2.41 (dq, J = 4.8, 7.5 Hz, 1H, H-11), 2.63 (dd, J = 6.9, 13.5 Hz, 1 H, H-8), 2.71 (dddd, J = 4.2, 4.8, 6.9, 7.8 Hz, 1H, H-7), 5.68 (d, J = 7.8 Hz, 1H, H-6).

Methyl (11S)-9β-hydroxy-3-oxo-7αH-eudesm-4-en-12-oate (11).

To a solution of compound **7** (40 mg, 0.15 mmol) in methanol (0.75 mL) containing AcOH (16 μL, 3.68 mmol), activated Zn dust (95 mg, 1.45 mmol) was added. After refluxing under argon for 15 m, the reaction mixture was cooled at rt and filtered through silica gel. The resulting solution was treated with an excess of ethereal diazomethane. After allowing the excess of diazomethane to evaporate, the mixture was filtered through a short pad of Celite, concentrated *in vacuo* and eventually chromatographed with hexane-EtOAc to

give compound **11** with the following features: oil, $[\alpha]_D^{23}$+98° (*c* 1.9); MS *m/e* 281 (13, M^++1), 280 (9, M^+), 193 (37), 175 (34), 174 (12), 157 (24), 138 (100), 123 (29); HRMS 280.1677, $C_{16}H_{24}O_4$ required 280.1675; IR ν_{max} 3600-3300, 1730, 1660 cm^{-1}; ^1H NMR δ 1.14 (s, 3H, H-14), 1.19 (d, J = 6.8 Hz, 3H, H-13), 1.47 (q, J = 12.0 Hz, 1H, H-8β), 1.75 (d, J = 0.8 Hz, 3H, H-15), 1.7-1.8 (m, 2H, H-7 and OH), 1.78 (dt, J = 9.6, 13.6 Hz, 1H, H-1'), 1.88 (dddd, J = 2.0, 3.6, 4.4, 12.0 Hz, 1H, H-8α), 1.90 (dt, J = 1.6, 14.0 Hz, 1H, H-6β), 2,11 (dt, J = 4.4, 13.6 Hz, 1H, H-1), 2.43 (dq, J = 6.8, 7.6 Hz, 1H, H-11), 2.43 (dd, J = 4.4, 9.6, 2H, 2H-2 overlapped with H-11), 2.59 (ddd, J= 2.0, 3.6, 14.0 Hz, 1H, H-6α), 3.44 (dt, J = 4.4, 11.2 Hz, 1H, H-9), 3.70 (s, 3H, MeO).

Methyl (11S)-3,3-(1,2-ethanedithio)-9β-hydroxy-7αH-eudesm-4-en-12-oate (12)

A solution of compound **11** (36 mg, 0.129 mmol), 99% ethanedithiol (77 μL, 0.91 mmol) and boron trifluoride etherate (9 μL) in AcOH (0.5 mL) was stirred at rt for 28 h. After this time, the reaction mixture was diluted with EtOAc, washed with saturated aqueous $NaHCO_3$ and brine, and dried over $MgSO_4$. Solvent removal followed by chromatography with hexane-EtOAc (1:1) gave compound **12** (39 mg, 85%): mp 95-96°C (hexane-EtOAc); $[\alpha]_D^{24}$+92° (*c* 1.7); MS *m/e* 357 (20, M^++1), 356 (100, M^+), 338 (90), 310 (38), 296 (84), 245 (29), 214 (57), 190 (49), 189 (30), 157 (63); HRMS 356.1479, $C_{18}H_{28}O_3S_2$ required 356.1479; IR ν_{max} 3600-3300, 1735 cm^{-1}; ^1H NMR δ 0.99 (s, 3H, H-14), 1.14 (d, J = 7.2 Hz, 3H, H-13), 1.33 (q, J = 12.0 Hz, 1H, H-8β), 1.6-1.7 (m, 2H, H-6β and H-7), 1.72 (ddd, J = 4.0, 11.2, 13.6 Hz, 1 H, H-1α), 1.77 (ddd, J = 3.2, 5.6, 13.6 Hz, 1H, H-1β), 1.85 (s, 3H, H-15), 1.8-1.9 (m, 1H, H-8α), 2.15 (ddd, J = 3.2, 11.2, 14.0 Hz, 1 H, H-2), 2.21 (ddd, J = 4.0, 5.6, 14.0 Hz, 1 H, H-2), 2.32 (m, 1H, H-6α), 2.34 (dq, J = 6.8, 7.2 Hz, 1H, H-11), 3.2-3.4 (m, 5H, CH_2S and H-9), 3.67 (s, 3H, MeO);

(11S)-3,3-(1,2-Ethanedithio)-7αH-eudesm-4-en-9β,12-diol (13)

A solution of compound **12** (34 mg, 0.10 mmol) in THF (7.5 mL) was added to a suspension of $LiAlH_4$ (21 mg, 0.54 mmol) in THF (0.7 mL) at 0°C under argon. After 25 min at this temperature, the reaction was quenched with aqueous NH_4Cl and the mixture extracted with EtOAc. Usual work up yielded 31 mg (100%) of diol **13**: oil, $[\alpha]_D^{23}$+73° (*c* 0.78); MS *m/e* 329 (20, M^++1), 328 (100, M^+),311 (11), 310 (53), 282 (28), 268 (45), 259 (15), 217 (22), 214 (47); HRMS 328.1531, $C_{17}H_{28}O_2S_2$ required 328.1531; IR ν_{max} 3600-3125 cm^{-1}; ^1H NMR δ 0.92 (d, J = 6.8 Hz, 3H, H-13), 1.00 (s, 3H, H-14), 1.37 (q, J = 12.0 Hz, 1H, H-8β), 1.4-1.5 (m, 1H, H-7), 1.61 (m, 1H, H-11), 1.8-1.9 (m, 3H, H-1', H-8α and H-6β), 1.83 (ddd, J = 3.6, 5.2, 14.0 Hz, 1 H, H-1), 1.89 (d, J = 1.2, 3H, H-15), 2.17 (ddd, J = 3.2, 10.8, 13.4 Hz, 1 H, H-2'), 2.22 (ddd, J = 4.0, 5.2, 13.4 Hz, 1 H, H-2), 2.38 (ddd, J = 2.0, 3.2, 14.0 Hz, 1 H, H-6α), 3.30 (dd, J = 4.5, 11.4 Hz, 1H, H-9), 3.2-3.4 (m, 4H, CH_2S), 3.51 (dd, J = 6.6, 10.4 Hz, 1 H, H-12'), 3.61 (dd, J = 6.0, 10.4 Hz, 1H, H-12).

(11S)-3-Oxo-7αH-eudesm-4-en-9β,12-diol (3)

To a solution of compound **13** (20 mg, 0.061 mmol) in CH_2Cl_2-MeOH (1:1) at rt, H_5IO_6 (12.6 mg, 0.055 mmol) dissolved in the minimal amount of water was added. After 10 min, aqueous $NaHSO_3$ was added, and the mixture extracted with AcOEt. The organic layer was washed with aqueous $NaHCO_3$ and brine, and dried. After solvent removal, chromatography eluting with hexane-AcOEt gave 11 mg (71%) of compound **3**: mp 135-137°C (hexane-EtOAc); $[\alpha]_D^{23}$+103° (*c* 0.58); MS *m/e* 252 (38, M^+), 175 (11), 138 (100), 123 (20), 91 (14), 81 (21); HRMS 252.1725, $C_{15}H_{24}O_3$ required 252.1725; IR ν_{max} 3312, 3437, 1640 cm^{-1}; ^1H NMR δ 0.95 (d, J = 6.8 Hz, 3H, H-13), 1.14 (s, 3H, H-14), 1.48 (q, J = 12.0 Hz, 1H, H-8β), 1.6-1.7 (m, 2H, H-7 and H-11), 1.77 (d, J = 0.8 Hz, 3H, H-15),1.7-1.9 (m, 1 H, H-8α), 1.80 (dd, J = 9.2, 13.2 Hz, 1 H, H-1'), 1.96 (ddd, J = 0.8, 11.2, 14.4 Hz, 1 H, H-6β), 2.11 (dt, J = 4.4, 13.2 Hz, 1 H, H-1), 2.43 (dd, J = 4.4, 9.2 Hz, 2 H, 2 H-2), 2.61 (ddd, J = 2.0, 3.2, 14.4 Hz, 1 H, H-6α), 3.43 (dd, J = 4.5, 11.6 Hz, 1H, H-9), 3.5 (dd, J = 6.0, 10.4 Hz, 1 H, H-12'), 3.62 (dd, J = 6.4, 10.4 Hz, 1H, H-12).

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