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Acid-Induced Rearrangement of Epoxygermacra-8,12-olides: Synthesis and Absolute Configuration of Guaiane and Eudesmane Derivatives from Artemisiifolin

Sergio Rosselli,[a] Antonella Maggio,[a] Rosa Angela Raccuglia,[a] and Maurizio Bruno*[a]

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A study on the acid-induced rearrangement of 4,5-epoxy- and 1,10-epoxygermacra-8,12-olides was carried out. From a 4,5-epoxy derivative, guaianes were obtained, whereas 1,10-epoxy derivatives furnished, depending on the stereochemistry of the C-1/C-10 epoxy ring, *trans*-5β,10α- or *trans*-5α,10β-eudesmanolides.

Introduction

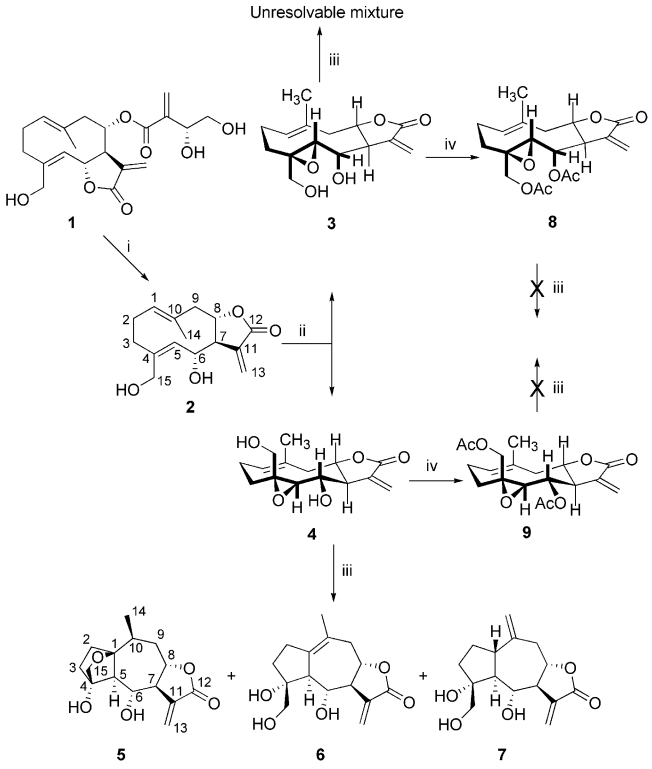
Sesquiterpene lactones (SQLs) are an important class of plant secondary metabolites with antitumoural, phytotoxic, antimicrobial and other biological properties.[1–3] Inside this class, germacranolides are considered to be the precursors of the other skeletal types of SQLs such as elemanolides, eudesmanolides and guianolides.[1] Acid-induced cyclization of germacranolides or that of their corresponding monoepoxides is generally accepted to be biomimetic and represents the biosynthesis of eudesmane and guaiane sesquiterpene lactones.[4–11] In the frame of our ongoing research[12,13] aimed to synthesize natural compound derivatives with potential antitumour activity, some years ago we published a paper on the synthesis of elemane and heliangolane derivatives,[14] and we recently reported on the reactivity of epoxy derivatives and their cytotoxic properties,[15] all prepared starting from cnicin (**1**), which is a 6,12-germacranolide commonly found in species of *Centaurea*, whose antibacterial, cytotoxic and antifungal properties have been investigated.[16–18] In that work, it was shown that acid treatment of the 1β,10α-epoxide results in the formation of eudesmanolides, whereas when the 4α,5β-epoxide was treated similarly, no transformation was obtained. As continuation of our studies on cyclization reactions of germacranolides, we investigated the acid-induced cyclization of the monoepoxides of artemisiifolin, a natural germacrane-8,12-olide isolated from *Ambrosia artemisiifolia*[19] and obtained by us from cnicin by basic hydrolysis. NMR spectra of artemisiifolin show broad or even additional signals, indicating the existence of four conformers in solution as described previously.[20] A smooth epoxidation of one double bond in *E*,*E*-germacran-8,12-olides decreases the conformational flexibility of the 10-membered ring, and the stereochemistry of the resulting epoxides should be affected by the relative abundance of the equilibrating conformers. The epoxy group can be described as a conformational "anchor". Because the regiochemistry and stereochemistry of epoxides play a pivotal role in the outcome of the acid-induced cyclization, our aim was to rationalize the consequences of the conformational equilibrium existing for artemisiifolin on biomimetic cyclizations of its epoxides by experimental data. The lack of such data is pointed out in many theoretical work.[21]

[a] Dipartimento di Chimica Organica, Università di Palermo,
Viale delle Scienze,
90128 Palermo, Italy
Fax: +39-091-596825
E-mail: bruno@dicpm.unipa.it

Results and Discussion

Cnicin (**1**) was isolated in large amounts from *Centaurea napifolia*,[22] providing us with enough starting material to plan this study. Strong basic treatment[23] of cnicin (**1**) resulted in the hydrolysis of the side chain and in relactonization of the C-8 position to afford artemisiifolin (**2**; Scheme 1). Epoxidation of compound **2** with *meta*-chloroperbenzoic acid (*m*-ClPBA) in pyridine gave 4,5-epoxides **3** and **4** in a 3:1 ratio. The major product was 4β,5α-epoxyartemisiifolin (**3**), as clearly indicated by the 5-H/6-H coupling constant (J = 3.3 Hz) and by the chemical shifts of 6-H (δ_H = 4.12 ppm) and 9^B-H (δ_H = 1.99 ppm).[24] Similar considerations allowed us to assign the structure of 4α,5β-epoxyartemisiifolin to compound **4**. Compounds **3** and **4** arise from the epoxidation of the four conformers of artemisiifolin, and their stereochemistry and relative abundance are in perfect agreement with theoretical calculations.[20]

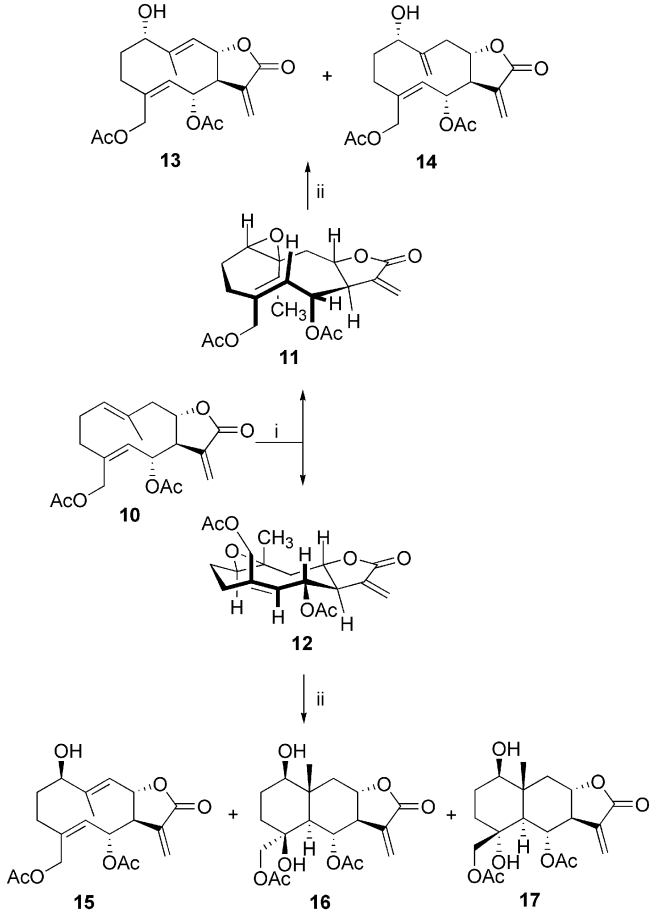
Epoxide **4** was treated with $HCl/CHCl_3$ to yield guaianolides **5**–**7**. The ^1H NMR, ^{13}C NMR and 2D spectra of compound **5** showed, apart from the signals of the lactone, the presence of an α-proton at δ_H = 1.88 ppm (d, 5-H) coupling with 6-H (J = 8.7 Hz), two quaternary oxygenated carbon atoms at δ_C = 88.5 and 83.0 ppm involved in the formation of a tetrahydrofuran ring (C-1, C-5, C-4, C-15) and a



Scheme 1. Reagents and conditions: (i) KOH, H_2O, room temp., 4 h, 77%; (ii) *m*-ClPBA, THF, room temp., 24 h; (iii) $CHCl_3$, HCl/$CHCl_3$(sat.), room temp., 96 h; (iv) Ac_2O, pyridine, room temp., 2 h, 100%.

methyl group at δ_H = 1.15 ppm (d, J = 7.4 Hz, 3 H, 14-H_3) coupling with 10-H, whose stereochemistry was assessed to be β as indicated by the coupling constants of 9-H^A and 9-H^B with 10-H. Compound **6**, on the other hand, had instead of the tetrahydrofuran ring a hydroxymethyl group (δ_H = 3.93 ppm, d, J = 11.1 Hz, 15-H_A; δ_H = 3.63 ppm, d, J = 11.1 Hz, 15-H_B; δ_C = 64.2 ppm, t, C-15) and a tetrasubstituted double bond (δ_C = 126.3 ppm, s, C-1; δ_C = 131.6 ppm, s, C-10). The spectroscopic data of compound **7** indicate that it was a double-bond isomer of triol **6**. In fact, in this case, there were signals for an exocyclic double bond (δ_C = 144.7 ppm, s, C-10; δ_C = 112.4 ppm, t, C-14) and another allylic proton (δ_H = 2.17 ppm, 1-H). The stereochemistry of 1-H was assigned to β by the value of the coupling constant with 5-H (J = 11.0).[25,26] On the other hand, acidic treatment of compound **3** gave an irresolvable, complex mixture of products. Acetylation of compounds **3** and **4** furnished diacetyl epoxides **8** and **9**, respectively, and when these were treated with HCl/$CHCl_3$, they were recovered unaltered.

The presence of two free hydroxy groups in artemisiifolin (**2**) induced selective epoxidation of the C-4/C-5 double bond. Consequently, we tried to direct the epoxidation on the other double bond (C-1/C-10) by transforming artemisiifolin (**2**) into diacetyl derivative **10**.[27] Therefore, by epoxidation of diacetyl artemisiifolin (**10**) only diastereoisomeric 1,10-epoxides **11** and **12** (15-acetoxypyrethrosin),[28] in a 1:1 ratio, were obtained (Scheme 2). The stereochemistry of the epoxy ring in compounds **11** and **12** was easily deduced by the chemical shifts of 14-H_3, 7-H and the two protons on C-9.[24] Acid treatment of 1α,10β-epoxide **11** gave the isomeric germacratrienes **13** and **14**. The difference between the two compounds was the position of the double bond: C-9/C-10 in the former (δ_C = 126.0 ppm, d, C-9; δ_C = 142.8 ppm, s, C-10) and C-10/C-14 (δ_C = 146.6 ppm, s, C-10; δ_C = 115.8 ppm, t, C-14) in the latter. The same reaction, performed on 1β,10α-epoxide **12**, afforded germacrane **15**, the C-1 epimer of compound **13**, and eudesmanolides **16** and **17**. The structure of the most abundant one (i.e., **17**) was elucidated by extensive 1D and 2D NMR experiments, and the stereochemistry of the stereogenic centres was determined by NOESY (Figure 1). In fact, the correlations of 6-H (δ_H = 5.65 ppm) with 14-H_3 (δ_H = 1.06 ppm) and 15-H^A (δ_H = 4.38 ppm) and the correlation of 8-H (δ_H = 4.01 ppm) with both 15-H protons (δ_H = 4.38 and 4.35 ppm) indicated the β orientation of the methyl 14-H_3 group and the acetoxymethylene group at C-15, whereas the correlation between the α-axial proton 1-H (δ_H = 3.53 ppm, dd, J = 10.7, 5.0 Hz) with 5-H (δ_H = 2.03 ppm) showed the *trans* fusion of the decalin moiety. In similar way, compound **16** was showed to be the C-4 epimer of eudesmanolide **17**.



Scheme 2. Reagents and conditions: (i) *m*-ClPBA, THF, room temp., 48 h; (ii) $CHCl_3$, HCl/$CHCl_3$ (sat.), room temp., 24 h.

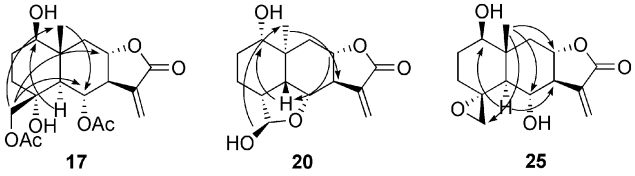
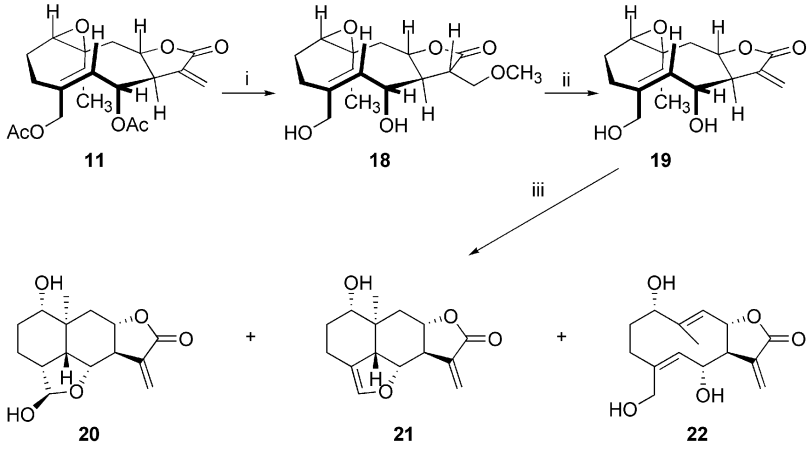
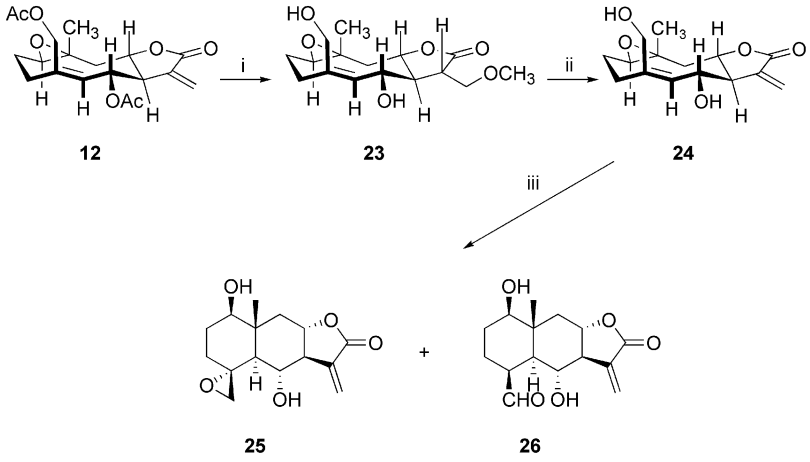


Figure 1. NOESY correlations of compounds **17**, **20** and **25**.

In order to exploit the influence of the acetoxy groups in the cyclization reaction of 1,10-epoxygermacranolides, we tried to hydrolyze the ester moieties of compound **11** by treating it with CH_3OH and $NaHCO_3$. The reaction resulted in the removal of the two acetyl groups but also in the addition of a methoxy group at C-13 to afford quantitatively compound **18** (Scheme 3). The restoration of the C-11/C-13 exocyclic double bond was easily achieved by treating compound **18** with *t*BuOK to give diol **19**. Reaction of compound **19** with HCl yielded eudesmanolides **20** and **21** and germacranolide **22**, which was the most abundant and which was identified as the deacetyl derivative of compound **13**. Compound **20** showed signals for an axial proton at δ_H = 3.51 ppm (dd, J = 9.4, 5.6 Hz, 1-H), an emiacetalic moiety at δ_H = 5.43 ppm (d, J = 6.0 Hz, 15-H; δ_C = 104.8 ppm, d, C-15) and an angular methine at δ_H = 2.05 ppm (dd, J = 5.5, 2.2 Hz, 5-H) coupling with 4-H at δ_H = 2.26 ppm and 6-H at δ_H = 4.57 ppm. The stereochemistry of the stereogenic centres was determined by NOESY (Figure 1). In fact, the correlation of 14-H_3 (δ_H = 1.27 ppm) with 7-H (δ_H = 3.38 ppm) indicated the α orientation of the methyl 14-H_3 group, whereas the correlation between 5-H (δ_H = 2.05 ppm) with the β-axial proton 1-H (δ_H = 3.51 ppm) and 8-H (δ_H = 4.09 ppm) showed the β orientation of 5-H and the 5β,10α-*trans* fusion of the decalin moiety. Finally, the correlation between 15-H (δ_H = 5.43 ppm) and 14-H_3 (δ_H = 1.27 ppm) assessed an α stereochemistry for the emiacetalic proton. Compound **21** was the dehydratation derivative of **20** as easily recognized by the absence of the emiacetalic signals and the presence of a trisubstituted double bond (δ_H = 6.18 ppm, m, 15-H; δ_C = 112.6 ppm, s, C-4; δ_C = 138.1 ppm, d, C-15) involved in a dihydrofuran moiety.



Scheme 3. Reagents and conditions: (i) $NaHCO_3$, CH_3OH, room temp., 24 h, 90%; (ii) *t*BuOK, THF, room temp., 10 min, 56%; (iii) $CHCl_3$, HCl/$CHCl_3$ (sat.), room temp., 24 h.



Scheme 4. Reagents and conditions: (i) $NaHCO_3$, CH_3OH, room temp., 24 h, 96%; (ii) *t*BuOK, THF, room temp., 10 min, 61%; (iii) $CHCl_3$, HCl/$CHCl_3$ (sat.), room temp., 24 h.

Also diacetyl 1β,10α-epoxide **12** was subjected to basic hydrolytic conditions to afford methoxy derivative **23** (Scheme 4), which was easily transformed (*t*BuOK) into diol **24**. The acidic rearrangement of compound **24** gave, in this case, only eudesmanolides **25** and **26**. The NMR spectra of compound **25** indicated the presence of an axial proton at δ_H = 3.59 ppm (dd, J = 10.5, 5.0 Hz, 1-H), a *trans* diaxial relationship between 5-H (δ_H = 1.86 ppm, d, J = 9.6 Hz) and 6-H (δ_H = 3.85 ppm, dd, J = 9.6, 9.6 Hz) and the presence of an epoxide (δ_H = 3.20 ppm, dd, J = 3.6, 1.2 Hz, 15-H_A; δ_H = 2.86 ppm, d, J = 3.6 Hz, 15-H_B; δ_C = 60.9 ppm, C-4; δ_C = 51.9 ppm, C-15), α-orientated, as indicated by the long-range coupling constant (J = 1.2 Hz) between 15-H^A and H-3^A.[29,30] NOESY experiments confirmed the stereochemistry of the chiral centres (Figure 1). In fact, 14-H_3 (δ_H = 1.00 ppm) correlated with 6-H, 8-H (δ_H = 3.96 ppm) and both 15-H protons, whereas the correlation between 5-H with the α-axial proton 1-H and 7-H (δ_H = 2.54 ppm) showed the α orientation of 5-H and the *trans* fusion of the decalin moiety. Compound **26** had a similar framework with respect to epoxide **25**. The only differences were the absence of the epoxy ring and the presence of an aldehyde (δ_H = 9.85 ppm, br. s, 15-H; δ_C = 204.7 ppm). The β-orientation of the aldehyde group was evident by the very small coupling constant with 4-H (<1 Hz), as reported for other compounds with a similar moiety.[7,31]

Finally, because the absolute stereochemistries of cnicin (**1**) and artemisiifolin (**2**) were determined by X-ray analysis,[20,32] in this paper, the absolute configurations of compounds **3**–**26** were ascertained.

Conclusions

The studied acid-catalyzed cyclizations of epoxygermacrane follow the well-established rule that 1,10-epoxygermacranolides cyclize into eudesmanolides[33,34] under acid catalysis, whereas 4,5-epoxygermacranolides yield guainolides,[35] but interesting information concerning the stereochemistry of the epoxides and the presence of substituents can be deducted.

In these cyclizations, it is extremely important to consider the conformational features of the germacranolide ring; in fact cyclization of 4α,5β-epoxyinunolide[36] produces *cis*-fused guaianes, whereas epoxide **4**, with analogous stereochemistry, gives among other products, guaiane **7**, with a *trans*-fused junction, because **4** arises from epoxidation of two conformers[20] of artemisiifolin (**2**) that can give the 4α,5β-epoxy group, and one of these conformers has the suitable geometry for the *trans* fusion observed.

It is worthy to note that 1α,10β-epoxy germacranolide **11** does not cyclize into eudesmanolide. On the contrary 1β,10α-epoxide **12** gives eudesmanolides. When acetoxy groups are removed from scaffold, the acid-catalyzed cyclization of 1α,10β-epoxy germacranolide **19** produces eudesmanolides **20** and **21**, probably because the two acetoxy groups induce strain in the conformation of the germacrane ring, forcing the two reactive carbon atoms (C-5 and C-10) apart. An additional aspect to rationalize the cyclization of diol **19** in contrast to diacetate **11** is the more nucleophilic 4,5 double bond in compound **19**.

Experimental Section

General: IR spectra were obtained with a Perkin–Elmer 1310 spectrometer. ^{1}H NMR spectra were recorded in $CDCl_3$ or CD_3OD solution by using a Bruker Avance series 300 MHz spectrometer, and chemical shifts are reported with respect to residual $CHCl_3$ (δ = 7.27 ppm) or CD_3OD (δ = 3.31 ppm). The term o.s. signifies overlapped signals. ^{13}C NMR spectra were recorded in $CDCl_3$ or CD_3OD solution on the same apparatus at 75.3 MHz, and chemical shifts are reported with respect to solvent signals ($CDCl_3$: δ_C = 77.00 ppm; CD_3OD: δ_C = 49.00 ppm). ^{13}C NMR multiplicities were determined by DEPT spectra. ^{1}H–^{1}H COSY, HSQC, HMBC and NOESY experiments were carried out with the same apparatus. Mass spectra (ESI) were recorded with a Shimadzu GC–MS-QP2010 Plus spectrometer and exact mass measurements were determined with a Micromass Autospec mass spectrometer at 70 eV. Optical rotations were recorded with a Jasco P-1010 polarimeter. Elemental analysis was carried out with a Perkin–Elmer 240 apparatus. Merck silica gel (70–230 mesh), deactivated with 15% H_2O, was used for column chromatography.

Isolation of (6*R*,7*S*,8*S*,1′′*R*)-8-[(1′′,2′′-Dihydroxyethyl)acroyloyl]-15-hydroxygermacra-1(10),4,11(13)-trien-6,12-olide(cnicin) (1): Cnicin (**1**) was isolated from *Centaurea napifolia* collected in June 2007 at Lascari, 60 km east of Palermo, Italy, and the purification procedures have been previously reported.[22]

(6*R*,7*S*,8*S*)-6,15-Dihydroxy-germacra-1(10),4,11(13)-trien-8,12-olide (artemisiifolin) (2): Cnicin (5 g, 13.2 mmol) was dissolved in aqueous 10% KOH (500 mL) and stirred for 4 h. The reaction mixture was quenched with 10% H_2SO_4 and then extracted with EtOAc a few times. The combined organic extracts were dried with Na_2SO_4 (anhydrous) and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel; petroleum ether/ethyl acetate, 3:7) to give artemisiifolin (2.7 g, 77%). The physical and spectroscopic data were identical to those reported in the literature.[19,20]

(4*R*,5*S*,6*S*,7*S*,8*S*)-4,5-Epoxy-6,15-dihydroxygermacra-1(10),11(13)-dien-8,12-olide (3) and (4*S*,5*R*,6*S*,7*S*,8*S*)-4,5-Epoxy-6,15-dihydroxygermacra-1(10),11(13)-dien-8,12-olide (4): *m*-ClPBA (870 mg, 5.7 mmol) was added to a solution of artemisiifolin (**2**; 1 g, 3.8 mmol) in THF (50 mL) and pyridine (3.3 mL). The reaction mixture was stirred at room temperature for 24 h, quenched with a saturated aqueous solution of NH_4Cl and extracted with EtOAc. The organic layer was dried with anhydrous Na_2SO_4. After removal of the solvent, the residue was purified by column chromatography (silica gel; petroleum ether/EtOAc, 1:1) to give compounds **3** (560 mg, 53%) and **4** (160 mg, 15%). Data for **3**: Colourless oil. $[\alpha]_D^{24}$ = +98.4 (c = 0.43, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3421, 2928, 2862, 1757, 1277, 1144, 1013, 734 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.38 (m, 1 H, 1-H), 2.38 (o.s., 2 H, 2-H^A and 2-H^B), 2.52 (ddd, J = 12.9, 3.6, 3.6 Hz, 1 H, 3-H^A), 1.12 (ddd, J = 12.9, 9.9, 9.9 Hz, 1 H, 3-H^B), 2.77 (o.s., 1 H, 5-H), 4.12 (dd, J = 10.8, 3.3 Hz, 1 H, 6-H), 2.77 (o.s., 1 H, 7-H), 4.42 (m, 1 H, 8-H), 2.77 (o.s., 1 H, 9-H^A), 1.99 (m, 1 H, 9-H^B), 6.44 (d, J = 2.0 Hz, 1 H, 13-H^A), 6.13 (d, J = 1.2 Hz, 1 H, 13-H^B), 1.76 (s, 3 H, 14-H_3), 4.14 (d, J = 12.6 Hz, 1 H, 15-H^A), 3.87 (d, J = 12.6 Hz, 1 H, 15-H^B) ppm. ^{13}C

Table 1. ^{13}C NMR spectroscopic data for compounds **3**–**9** and **11**–**17** in $CDCl_3$.

	3	4	5	6	7	8	9	11	12	13	14	15	16	17
C-1	127.3 (d)	126.9 (d)	88.5 (s)	126.3(s)	43.0 (d)	127.8 (d)	126.8 (d)	61.7 (d)	65.4 (d)	67.2 (d)	70.8 (d)	78.4 (d)	77.7 (d)	77.9 (d)
C-2	22.9 (t)	22.5 (t)	33.8 (t)	29.7 (t)	36.5 (t)	23.0 (t)	22.6 (t)	23.6 (t)	23.1 (t)	27.9 (t)	29.7 (t)	28.1 (t)	25.6 (t)	27.4 (t)
C-3	32.5 (t)	31.5 (t)	33.2 (t)	34.1 (t)	26.7 (t)	31.7 (t)	30.9 (t)	29.5 (t)	32.0 (t)	32.3 (t)	41.8 (t)	33.9 (t)	35.0 (t)	34.8 (t)
C-4	64.7 (s)	69.9 (s)	83.0 (s)	83.5 (s)	83.0 (s)	62.3 (s)	62.8 (s)	139.3 (s)	137.6 (s)	135.9 (s)	136.7 (s)	136.2 (s)	72.0 (s)	73.5 (s)
C-5	65.6 (d)	66.6 (d)	57.9 (d)	58.8 (d)	67.0 (d)	60.5 (d)	66.0 (d)	128.7 (d)	129.1 (d)	130.3 (d)	130.6 (d)	131.7 (d)	52.0 (d)	56.1 (d)
C-6	68.3 (d)	69.7 (d)	70.2 (d)	70.8 (d)	73.2 (d)	68.5 (d)	70.4 (d)	72.3 (d)	71.1 (d)	62.2 (d)	71.9 (d)	69.6 (d)	69.5 (d)	69.4 (d)
C-7	46.8 (d)	48.8 (d)	51.6 (d)	54.9 (d)	48.8 (d)	44.5 (d)	47.5 (d)	46.4 (d)	51.4 (d)	49.2 (d)	48.2 (d)	51.1 (d)	53.8 (d)	54.1 (d)
C-8	77.2 (d)	80.7 (d)	79.2 (d)	77.0 (d)	76.8 (d)	77.2 (d)	80.3 (d)	77.3 (d)	76.5 (d)	74.0 (d)	78.3 (d)	76.4 (d)	76.6 (d)	75.9 (d)
C-9	43.4 (t)	44.3 (t)	36.6 (t)	39.9 (t)	40.3 (t)	43.5 (t)	44.5 (t)	44.2 (t)	46.6 (t)	126.0 (d)	31.4 (t)	125.8 (d)	41.5 (t)	43.4 (t)
C-10	130.0 (s)	130.5 (s)	33.5 (d)	131.6 (s)	144.7 (s)	130.2 (s)	130.3 (s)	56.7 (s)	57.9 (s)	142.8 (s)	146.6 (s)	149.0 (s)	42.1 (s)	41.4 (s)
C-11	134.3 (s)	133.8 (s)	137.7 (s)	137.6 (s)	136.6 (s)	133.8 (s)	133.3 (s)	135.0 (s)	134.8 (s)	136.7 (s)	135.6 (s)	136.7 (s)	136.7 (s)	136.3 (s)
C-12	170.0 (s)	170.0 (s)	170.2 (s)	170.1 (s)	170.2 (s)	168.7 (s)	168.3 (s)	168.4 (s)	168.6 (s)	169.1 (s)	169.0 (s)	169.2 (s)	169.7 (s)	169.5 (s)
C-13	128.2 (t)	128.9 (t)	124.1 (t)	124.3 (t)	126.6 (t)	127.7 (t)	127.5 (t)	126.4 (t)	126.6 (t)	122.9 (t)	125.5 (t)	121.8 (t)	118.9 (t)	119.3 (t)
C-14	19.0 (q)	19.0 (q)	20.5 (q)	23.6 (q)	112.4 (t)	19.6 (q)	18.7 (q)	21.4 (q)	17.4 (q)	16.7 (q)	115.8 (t)	12.0 (q)	15.4 (q)	16.8 (q)
C-15	59.6 (t)	61.4 (t)	73.0 (t)	64.2 (t)	66.1 (t)	61.6 (t)	62.6 (t)	62.7 (t)	61.6 (t)	61.7 (t)	62.2 (t)	60.6 (t)	71.4 (t)	64.7 (t)
Ac						170.7 (s)	170.2 (s)	169.5 (s)	170.5 (s)	170.8 (s)	169.6 (s)	170.6 (s)	172.2 (s)	170.9 (s)
Ac						168.7 (s)	168.9 (s)	170.5 (s)	169.3 (s)	169.8 (s)	170.6 (s)	169.6 (s)	171.0 (s)	170.4 (s)
						20.8 (q)	20.5 (q)	20.8 (q)	20.9 (q)	20.9 (q)	20.8 (q)	20.9 (q)	21.6 (q)	21.5 (q)
						20.5 (q)	20.4 (q)	20.8 (q)	20.9 (q)	20.9 (q)	20.8 (q)	20.9 (q)	20.9 (q)	20.8 (q)

NMR (75.3 MHz, $CDCl_3$): see Table 1. HRMS (ESI): calcd. for $C_{15}H_{20}O_5Na$ 303.12084; found 303.12078. Data for **4**: Colourless oil. $[\alpha]_D^{24}$ = +21.1 (*c* = 1.26, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3420, 2928, 2866, 1747, 1653, 1356, 1244, 1149, 1034, 918, 816 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 5.36 (m, 1 H, 1-H), 2.33 (o.s., 2 H, 2-H^A and 2-H^B), 2.33 (o.s., 1 H, 3-H^A), 1.15 (m, 1 H, 3-H^B), 2.76 (d, *J* = 9.1 Hz, 1 H, 5-H), 3.76 (dd, *J* = 9.1, 9.1 Hz, 1 H, 6-H), 2.91 (m, 1 H, 7-H), 3.97 (m, 1 H, 8-H), 2.70 (br. d, *J* = 13.1 Hz, 1 H, 9-H^A), 2.17 (dd, *J* = 13.1, 11.3 Hz, 1 H, 9-H^B), 6.41 (d, *J* = 1.8 Hz, 1 H, 13-H^A), 6.18 (br. s, 1 H, 13-H^B), 1.77 (s, 3 H, 14-H_3), 3.78 (d, *J* = 12.3 Hz, 1 H, 15-H^A), 3.57 (d, *J* = 12.3 Hz, 1 H, 15-H^B) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): see Table 1. HRMS (ESI): calcd. for $C_{15}H_{20}O_5Na$ 303.12084; found 303.12125.

(1*S*,4*R*,5*S*,6*R*,7*S*,8*S*,10*S*)-1,15-Epoxy-4,6-dihydroxyguaian-11(13)-en-8,12-olide (5), (4*R*,5*S*,6*R*,7*S*,8*S*)-4,6,15-Trihydroxyguaian-1(10),11(13)-dien-8,12-olide (6) and (1*R*,4*R*,5*S*,6*R*,7*S*,8*S*)-4,6,15-Trihydroxyguaian-10(14),11(13)-dien-8,12-olide (7): To a solution of **4** (50 mg, 0.18 mmol) dissolved in $CHCl_3$ (4 mL) was added a solution of $CHCl_3$ saturated with gaseous HCl (1 mL), at room temperature. After 4 d the solvent was evaporated and the mixture was subjected to column chromatography (silica gel; petroleum ether/EtOAc, 3:7) to give, in order of increasing polarity, compounds **5** (5 mg, 10%), **6** (10 mg, 20%) and **7** (12 mg, 25%). Data for **5**: Colourless oil. $[\alpha]_D^{24}$ = –29.3 (*c* = 0.08, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3397, 2925, 1752, 1636, 1341, 1278, 1018, 966 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.89 (m, 1 H, 2-H^A), 1.86 (m, 1 H, 2-H^B), 2.01 (m, 1 H, 3-H^A), 1.72 (m, 1 H, 3-H^B), 1.88 (d, *J* = 8.7 Hz, 1 H, 5-H), 4.18 (dd, *J* = 10.2, 8.7 Hz, 1 H, 6-H), 2.97 (dddd, *J* = 10.2, 10.2, 3.0, 3.0 Hz, 1 H, 7-H), 4.27 (ddd, *J* = 10.2, 10.2, 4.2 Hz, 1 H, 8-H), 2.38 (ddd, *J* = 13.8, 6.3, 4.2, Hz, 1 H, 9-H^A), 1.66 (ddd, *J* = 13.8, 10.2, 6.6 Hz, 1 H, 9-H^B), 2.12 (m, 1 H, 10-H), 6.29 (d, *J* = 3.0 Hz, 1 H, 13-H^A), 6.28 (d, *J* = 3.0 Hz, 1 H, 13-H^B), 1.15 (d, *J* = 7.4 Hz, 3 H, 14-H_3), 3.87 (dd, *J* = 7.2, 3.3 Hz, 1 H, 15-H^A), 3.70 (d, *J* = 7.2 Hz, 1 H, 15-H^B) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): see Table 1. MS (ESI+): *m*/*z* (%) = 319 (14) $[M + K]^+$, 303 (100) $[M + Na]^+$, 281 (4.5) $[M + H]^+$. $C_{15}H_{20}O_5$ (280.1311): calcd. C 64.27, H 7.19; found C 64.30, H 7.17. Data for **6**: Colourless oil. $[\alpha]_D^{24}$ = +98.4 (*c* = 0.43, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3321, 2910, 1758, 1635, 1260, 1055 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.49 (o.s., 1 H, 2-H^A), 2.09 (o.s., 1 H, 2-H^B), 2.09 (o.s., 1 H, 3-H^A), 1.56 (m, 1 H, 3-H^B), 2.73 (br. d, *J* = 9.9 Hz, 1 H, 5-H), 3.89 (dd, *J* = 9.9, 9.9 Hz, 1 H, 6-H), 2.83 (dddd, *J* = 9.9, 9.9, 2.9, 2.9 Hz, 1 H, 7-H), 3.83 (ddd, *J* = 10.8, 9.9, 3.0 Hz, 1 H, 8-H), 2.61 (dd, *J* = 15.0, 3.0 Hz, 1 H, 9-H^A), 2.49 (o.s., 1 H, 9-H^B), 6.33 (d, *J* = 2.9 Hz, 1 H, 13-H^A), 6.28 (d, *J* = 2.9 Hz, 1 H, 13-H^B), 1.75 (br. s, 3 H, 14-H_3), 3.93 (d, *J* = 11.1 Hz, 1 H, 15-H^A), 3.63 (d, *J* = 11.1 Hz, 1 H, 15-H^B) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): see Table 1. MS (ESI+): *m*/*z* (%) = 319 (24) $[M + K]^+$, 303 (100) $[M + Na]^+$. $C_{15}H_{20}O_5$ (280.1311): calcd. C 64.27, H 7.19; found C 64.24, H 7.21. Data for **7**: Amorphous solid. $[\alpha]_D^{24}$ = –48.2 (*c* = 0.19, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3318, 2921, 1756, 1640, 1265, 1041, 736 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.17 (m, 1 H, 1-H), 2.05 (m, 1 H, 2-H^A), 1.68 (m, 1 H, 2-H^B), 1.81 (m, 1 H, 3-H^A), 1.65 (m, 1 H, 3-H^B), 1.86 (dd, *J* = 11.0 Hz, 9.9, 1 H, 5-H), 3.98 (dd, *J* = 9.9, 9.9 Hz, 1 H, 6-H), 2.80 (dddd, *J* = 9.9, 9.3, 3.1, 3.1 Hz, 1 H, 7-H), 4.38 (ddd, *J* = 11.1, 9.3, 6.3 Hz, 1 H, 8-H), 3.16 (br. dd, *J* = 15.3, 6.3, Hz, 1 H, 9-H^A), 2.53 (dd, *J* = 15.3, 11.1 Hz, 1 H, 9-H^B), 6.37 (m, 2 H, 13-H^A and 13-H^B), 5.18 (d, *J* = 2.1 Hz, 14_A-H), 5.03 (d, *J* = 1.5 Hz, 14_A-H), 3.78 (d, *J* = 11.6 Hz, 1 H, 15-H^A), 3.63 (d, *J* = 11.6 Hz, 1 H, 15-H^B) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): see Table 1. MS (ESI+): *m*/*z* (%) = 319 (13) $[M + K]^+$, 303 (100) $[M + Na]^+$. $C_{15}H_{20}O_5$ (280.1311): calcd. C 64.27, H 7.19; found C 64.24, H 7.16.

(4*R*,5*S*,6*S*,7*S*,8*S*)-4,5-Epoxy-6,15-diacetoxygermacra-1(10),11(13)-dien-8,12-olide (8): To a stirred solution of compound **3** (100 mg, 0.36 mmol) in acetic anhydride (2 mL) was added, at room temperature, pyridine (2 mL). After 2 h, the reaction was concentrated and subjected to column chromatography (silica gel; petroleum ether/EtOAc, 7:3) to give compound **8** in quantitative yield. Colourless oil. $[\alpha]_D^{24}$ = +16.7 (*c* = 0.53, $CHCl_3$). IR (film): $\tilde{\nu}$ = 2919, 2853, 1737, 1749, 1456, 1398, 1375, 1251, 1152, 1014, 968 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 5.32 (m, 1 H, 1-H), 2.33 (o.s., 2 H, 2-H^A and 2-H^B), 2.37 (m, 1 H, 3-H^A), 1.00 (m, 1 H, 3-H^B), 2.78 (o.s., 1 H, 5-H), 5.24 (dd, *J* = 11.4, 3.0 Hz, 1 H, 6-H), 2.80 (o.s., 1 H, 7-H), 4.52 (m, 1 H, 8-H), 2.78 (o.s., 1 H, 9-H^A), 1.94 (m, 1 H, 9-H^B), 6.26 (d, *J* = 1.8 Hz, 1 H, 13-H^A), 5.76 (d, *J* = 1.2 Hz, 1 H, 13-H^B), 1.69 (s, 3 H, 14-H_3), 4.30 (d, *J* = 12.3 Hz, 1 H, 15_A-H), 4.25 (d, *J* = 12.3 Hz, 1 H, 15_B-H), 2.04 (s, 3 H, Ac-H_3), 2.00 (s, 3 H, Ac-H_3) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): see Table 1. MS (ESI+): *m*/*z* (%) = 403 (19) $[M + K]^+$, 387 (100) $[M + Na]^+$. $C_{19}H_{24}O_7$ (364.1522): calcd. C 62.63, H 6.64; found C 62.67, H 6.68.

(4*S*,5*R*,6*S*,7*S*,8*S*)-4,5-Epoxy-6,15-diacetoxygermacra-1(10),11(13)-dien-8,12-olide (9): Acetic anhydride (2 mL) was added to a solution of compound **4** (100 mg, 0.36 mmol) in pyridine (2 mL) at room temperature. After 2 h, the reaction was concentrated and subjected to column chromatography (silica gel; petroleum ether/EtOAc, 7:3) to give compound **9** in quantitative yield. Colourless oil. $[\alpha]_D^{24}$ = +55.5 (*c* = 0.18, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3502, 2926, 2868, 1732, 1653, 1439, 1372, 1339, 1224, 1122, 984, 816 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 5.35 (br. dd, *J* = 7.2, 7.2 Hz, 1 H, 1-H), 2.32 (o.s., 2 H, 2-H^A and 2-H^B), 2.32 (o.s., 1 H, 3-H^A), 1.24 (m, 1 H, 3-H^B), 2.83 (d, *J* = 9.3 Hz, 1 H, 5-H), 4.94 (dd, *J* = 9.3, 9.3 Hz, 1 H, 6-H), 3.12 (dddd, *J* = 9.3, 4.2, 2.4, 2.4 Hz, 1 H, 7-H), 4.08 (ddd, *J* = 10.5, 4.2, 1.8 Hz, 1 H, 8-H), 2.70 (br. d, *J* = 10.5, Hz, 1 H, 9-H^A), 2.23 (br. dd, *J* = 10.5, 10.5 Hz, 1 H, 9-H^B), 6.39 (d, *J* = 2.4 Hz, 1 H, 13-H^A), 5.83 (d, *J* = 2.4 Hz, 1 H, 13-H^B), 1.83 (s, 3 H, 14-H_3), 4.54 (d, *J* = 12.0 Hz, 1 H, 15-H^A), 3.84 (d, *J* = 12.0 Hz, 1 H, 15-H^B), 2.11 (s, 3 H, Ac-H_3), 2.07 (s, 3 H, Ac-H_3) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): see Table 1. MS (ESI+): *m*/*z* (%) = 403 (14) $[M + K]^+$, 387 (100) $[M + Na]^+$, 365 (2) $[M + H]^+$. $C_{19}H_{24}O_7$ (364.1522): calcd. C 62.63, H 6.64; found C 62.59, H 6.62.

(6*R*,7*S*,8*S*)-6,15-Diacetoxygermacra-1(10),4,11(13)-trien-8,12-olide (dicetylartemisiifolin) (10): Artemisiifolin (1.6 g, 6.1 mmol) was dissolved in pyridine (25 mL) and acetic anhydride (30 mL) was added at room temperature. After 1 h, the mixture was concentrated and subjected to column chromatography (silica gel; petroleum ether/EtOAc, 6:4) to give **10** in quantitative yield.[25] Colourless oil. $[\alpha]_D^{24}$ = +147.6 (*c* = 1.72, $CHCl_3$). HRMS (ESI): calcd. for $C_{19}H_{24}O_6Na$ 371.14706; found 371.14686.

(1*S*,6*R*,7*S*,8*S*,10*S*)-1,10-Epoxy-6,15-diacetoxygermacra-4,11(13)-dien-8,12-olide (11) and (1*R*,6*R*,7*S*,8*S*,10*R*)-1,10-Epoxy-6,15-diacetoxygermacra-4,11(13)-dien-8,12-olide (12): To a solution of dicetylartemisiifolin (**10**; 1.6 g, 4.6 mmol) dissolved in THF (35 mL) was added *m*-ClPBA (870 mg, 5.0 mmol) and pyridine (3 mL). The mixture was stirred for 48 h at room temperature and then washed in turn with saturated aqueous $NaHCO_3$ and NH_4Cl. The organic layer was separated, dried with Na_2SO_4 anhydrous and concentrated. The residue was purified by TLC plates eluted a few times with petroleum ether/diethyl ether (1:4) to give compounds **11** (420 mg, 25%) and **12** (490 mg, 29%). Data for **11**: Colourless oil. $[\alpha]_D^{24}$ = +128.2 (*c* = 0.63, $CHCl_3$). IR (film): $\tilde{\nu}$ = 2933, 1764, 1738, 1373, 1234, 1147, 1026 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.69 (dd, *J* = 10.2, 1.5 Hz, 1 H, 1-H), 2.14 (m, 1 H, 2-H^A), 1.65 (m, 1 H, 2-H^B), 2.53 (ddd, *J* = 15.4, 7.0, 3.0 Hz, 1 H, 3-H^A), 2.34 (ddd, *J* = 15.4, 9.3, 7.5 Hz, 1 H, 3-H^B), 5.32 (o.s., 1 H, 5-H), 5.33 (o.s., 1 H, 6-H), 3.19 (m, 1 H, 7-H), 4.32 (ddd, *J* = 7.8, 7.8, 4.8 Hz, 1 H, 8-H), 2.10 (o.s., 2 H, 9-H^A and 9-H^B), 6.38 (d, *J* = 2.6 Hz, 1 H, 13-H^A), 5.91 (d, *J* = 2.2 Hz, 1 H, 13-H^B), 1.47 (s, 3 H, 14-H_3), 4.96 (d, *J* = 12.6 Hz, 1 H, 15-H^A), 4.59 (d, *J* = 12.6 Hz, 1 H, 15-H^B), 2.10 (s, 6 H, Ac-H_3) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): see Table 1. HRMS (ESI): calcd. for $C_{19}H_{24}O_7Na$ 387.14197; found 387.14266. Data for **12**: Colourless oil: $[\alpha]_D^{24}$ = +12.0 (*c* = 0.42, $CHCl_3$). IR (film): $\tilde{\nu}$ = 2935, 1762, 1740, 1375, 1275, 1149, 1026, 960, 735 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.71 (br. d, *J* = 9.5 Hz, 1 H, 1-H), 2.10 (m, 1 H, 2-H^A), 1.48 (m, 1 H, 2-H^B), 2.46 (br. dd, *J* = 13.0, 3.4 Hz, 1 H, 3-H^A), 2.34 (ddd, *J* = 13.0, 6.2, 6.0 Hz, 1 H, 3-H^B), 5.31 (d, *J* = 9.6 Hz, 1 H, 5-H), 5.42 (dd, *J* = 9.8, 9.8 Hz, 1 H, 6-H), 3.07 (dddd, *J* = 9.8, 7.8, 2.8, 1.8 Hz, 1 H, 7-H), 4.15 (br. dd, *J* = 9.0, 7.8 Hz, 1 H, 8-H), 2.70 (br. d, *J* = 14.0 Hz, 1 H, 9-H^A), 1.57 (dd, *J* = 14.0, 9.0 Hz, 1 H, 9-H^B), 6.37 (d, *J* = 2.8 Hz, 1 H, 13-H^A), 5.92 (d, *J* = 1.6 Hz, 1 H, 13-H^B), 1.31 (s, 3 H, 14-H_3), 4.79 (s, 2 H, 15-H^A and 15-H^B), 2.10 (s, 3 H, Ac-H_3), 2.09 (s, 3 H, Ac-H_3) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): see Table 1. HRMS (ESI): calcd. for $C_{19}H_{24}O_7Na$ 387.14197; found 387.14254.

(1*S*,6*R*,7*S*,8*S*)-1-Hydoxy-6,15-diacetoxygermacra-4,9,11(13)-trien-8,12-olide (13) and (1*S*,6*R*,7*S*,8*S*)-1-Hydoxy-6,15-diacetoxygermacra-4,10(14),11(13)-trien-8,12-olide (14): To a solution of **11** (190 mg, 0.52 mmol) dissolved in $CHCl_3$ (15 mL) was added a solution of $CHCl_3$ saturated with gaseous HCl (4 mL), at room temperature. After 24 h the solvent was evaporated and the mixture was subjected to column chromatography (silica gel; petroleum ether/EtOAc, 7:3) to give compounds **13** (95 mg, 50%) and **14** (20 mg, 10%). Data for **13**: Amorphous solid. $[\alpha]_D^{24}$ = –6.65 (*c* = 0.41, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3447, 2949, 2866, 1740, 1236, 1138, 1020, 735 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.49 (dd, *J* = 10.1, 4.8 Hz, 1 H, 1-H), 1.95 (o.s., 1 H, 2-H^A) 1.75 (m, 1 H, 2-H^B), 2.52 (m, 1 H, 3-H^A), 1.95 (o.s., 1 H, 3-H^B), 5.10 (d, *J* = 9.6 Hz, 1 H, 5-H), 5.47 (dd, *J* = 9.6, 9.6 Hz, 1 H, 6-H), 3.06 (m, 1 H, 7-H), 4.77 (dd, *J* = 9.6, 9.6 Hz, 1 H, 8-H), 5.32 (d, *J* = 9.6 Hz, 1 H, 9-H), 6.29 (d, *J* = 3.0 Hz, 1 H, 13-H^A), 5.75 (d, *J* = 3.0 Hz, 1 H, 13-H^B), 1.84 (s, 3 H, 14-H_3), 4.99 (d, *J* = 12.8 Hz, 1 H, 15-H^A), 4.81 (d, *J* = 12.8 Hz, 1 H, 15-H^B), 2.12 (s, 3 H, Ac-H_3), 2.09 (s, 3 H, Ac-H_3) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): see Table 1. MS (ESI+): *m*/*z* (%) = 751 (100) $[2M + Na]^+$, 403 (16) $[M + K]^+$, 387 (60) $[M + Na]^+$. $C_{19}H_{24}O_7$ (364.1522): calcd. C 62.63, H 6.64; found C 62.67, H 6.69. Data for **14**: Colourless oil. $[\alpha]_D^{24}$ = +84.6 (*c* = 0.09, $CHCl_3$). IR (film): $\tilde{\nu}$ = 2924, 1736, 1496, 1234, 1150, 1026 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.90 (dd, *J* = 7.6, 7.6 Hz, 1 H, 1-H), 2.10 (o.s., 1 H, 2-H^A) 1.26 (m, 1 H, 2-H^B), 2.40 (m, 1 H, 3-H^A), 2.27 (o.s., 1 H, 3-H^B), 5.19 (o.s., 1 H, 5-H), 5.24 (o.s., 1 H, 6-H), 3.04 (m, 1 H, 7-H), 4.16 (m, 1 H, 8-H), 2.27 (o.s., 1 H, 9-H^A), 2.10 (o.s., 1 H, 9-H^B), 6.38 (d, *J* = 2.9 Hz, 1 H, 13-H^A), 5.89 (d, *J* = 2.5 Hz, 1 H, 13-H^B), 5.21 (o.s., 2 H, 14-H^A and 14-H^B), 4.83 (d, *J* = 13.0 Hz, 1 H, 15-H^A), 4.68 (d, *J* = 13.0 Hz, 1 H, 15-H^B), 2.11 (s, 3 H, Ac-H_3), 2.09 (s, 3 H, Ac-H_3) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): see Table 1. MS (ESI+): *m*/*z* (%) = 751 (100) $[2M + Na]^+$, 403 (40) $[M + K]^+$, 387 (68) $[M + Na]^+$. $C_{19}H_{24}O_7$ (364.1522): calcd. C 62.63, H 6.64; found C 62.61, H 6.62.

(1*R*,6*R*,7*S*,8*S*)-1-Hydoxy-6,15-diacetoxygermacra-4,9,11(13)-trien-8,12-olide (15), (1*R*,4*S*,5*S*,6*R*,7*S*,8*S*,10*R*)-1,4-Dihydoxy-6,15-diacetoxyeudesma-11(13)-en-8,12-olide (16) and (1*R*,4*R*,5*S*,6*R*,7*S*,8*S*,10*R*)-1,4-Dihydoxy-6,15-diacetoxyeudesma-11(13)-en-8,12-olide (17): A solution of $CHCl_3$ saturated with gaseous HCl (4 mL) was added to a solution of compound **12** (220 mg, 0.60 mmol) in $CHCl_3$ (15 mL) whilst stirring. After 24 h the solvent was evaporated and the mixture was subjected to column chromatography (silica gel; petroleum ether/EtOAc, 2:3) to give compounds **15** (11 mg, 0.03 mmol, 5%), **16** (31 mg, 0.08 mmol, 13%) and **17** (100 mg, 0.26 mmol, 43%). Data for **15**: Colourless oil. $[\alpha]_D^{24}$ = +17.0 (*c* = 0.12, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3435, 2924, 2854, 1718, 1375, 1256, 1142, 1036 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.38 (dd, *J* = 10.0, 5.0 Hz, 1 H, 1-H), 1.77 (o.s., 2 H, 2-H^A and 2-H^B), 2.52 (m, 1 H, 3-H^A), 2.19 (m, 1 H, 3-H^B), 5.03 (br. d, *J* = 10.3 Hz, 1 H, 5-H), 5.51 (dd, *J* = 10.3, 10.3 Hz, 1 H, 6-H), 3.02 (dddd, *J* = 10.3, 10.0, 3.4, 3.0 Hz, 1 H, 7-H), 4.60 (dd, *J* = 10.0, 9.5 Hz, 1 H, 8-H), 5.36 (d, *J* = 9.5 Hz, 1 H, 9-H), 6.28 (d, *J* = 3.4 Hz, 1 H, 13-H^A), 5.72 (d, *J* = 3.0 Hz, 1 H, 13-H^B), 1.78 (s, 3 H, 14-H_3), 4.83 (d, *J* = 13.2 Hz, 1 H, 15-H^A), 4.69 (d, *J* = 13.2 Hz, 1 H, 15-H^B), 2.11 (s, 3 H, Ac-H_3), 2.10 (s, 3 H, Ac-H_3) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): see Table 1. MS (ESI+): *m*/*z* (%) = 403 (8) $[M + K]^+$, 387 (100) $[M + Na]^+$. $C_{19}H_{24}O_7$ (364.1522): calcd. C 62.63, H 6.64; found C 62.70, H 6.63. Data for **16**: Amorphous solid. $[\alpha]_D^{24}$ = –4.9 (*c* = 0.22, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3398, 2923, 2854, 1743, 1716, 1653, 1458, 1259, 1064 cm^{-1}. ^1H NMR

(300 MHz, $CDCl_3$): δ = 3.43 (dd, J = 11.5, 4.0 Hz, 1 H, 1-H), 1.98 (m, 1 H, 2-H^A), 1.65 (m, 1 H, 2-H^B), 1.87 (m, 1 H, 3-H^A), 1.63 (o.s., 1 H, 3-H^B), 1.76 (d, J = 10.4 Hz, 1 H, 5-H), 5.64 (dd, J = 10.4, 10.4 Hz, 1 H, 6-H), 2.80 (dddd, J = 11.9, 10.4, 2.9, 2.9 Hz, 1 H, 7-H), 4.11 (ddd, J = 11.9, 11.9, 3.9 Hz, 1 H, 8-H), 2.58 (dd, J = 11.9, 3.9 Hz, 1 H, 9-H^A), 1.45 (dd, J = 11.9, 11.9 Hz, 1 H, 9-H^B), 6.12 (d, J = 2.9 Hz, 1 H, 13-H^A), 5.35 (d, J = 2.9 Hz, 1 H, 13-H^B), 1.23 (s, 3 H, 14-H_3), 3.85 (s, 2 H, 15-H^A and 15-H^B), 2.20 (s, 3 H, Ac-H_3), 2.11 (s, 3 H, Ac-H_3) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): see Table 1. MS (ESI+): m/z (%) = 421 (55) $[M + K]^+$, 405 (100) $[M + Na]^+$. $C_{19}H_{26}O_8$ (382.1628): calcd. C 59.68, H 6.85; found C 59.72, H 6.81. Data for **17**: Amorphous solid. $[\alpha]_D^{24}$ = –4.1 (c = 0.66, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3445, 2945, 2875, 1732, 1670, 1369, 1251, 1138, 735 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.53 (dd, J = 10.7, 5.0 Hz, 1 H, 1-H), 1.71 (m, 2 H, 2-H^A and 2-H^B), 1.97 (ddd, J = 13.4, 3.4, 3.4 Hz, 1 H, 3-H^A), 1.46 (o.s., 1 H, 3-H^B), 2.03 (d, J = 10.4 Hz, 1 H, 5-H), 5.65 (dd, J = 10.4, 10.4 Hz, 1 H, 6-H), 2.83 (dddd, J = 11.9, 10.4, 2.9, 2.9 Hz, 1 H, 7-H), 4.01 (ddd, J = 11.9, 11.9, 3.7 Hz, 1 H, 8-H), 2.59 (dd, J = 11.9, 3.7 Hz, 1 H, 9-H^A), 1.51 (dd, J = 11.9, 11.9 Hz, 1 H, 9-H^B), 6.13 (d, J = 2.9 Hz, 1 H, 13-H^A), 5.38 (d, J = 2.9 Hz, 1 H, 13-H^B), 1.06 (s, 3 H, 14-H_3), 4.38 (d, J = 11.9 Hz, 1 H, 15-H^A), 4.35 (d, J = 11.9 Hz, 1 H, 15-H^B), 2.16 (s, 3 H, Ac-H_3), 2.12 (s, 3 H, Ac-H_3) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): see Table 1. MS (ESI+): m/z (%) = 421 (56) $[M + K]^+$, 405 (100) $[M + Na]^+$, 383 (43) $[M + H]^+$. $C_{19}H_{26}O_8$ (382.1628): calcd. C 59.68, H 6.85; found C 59.65, H 6.87.

(1*S*,6*R*,7*S*,8*S*,10*S*,11*S*)-1,10-Epoxy-6,15-dihydroxy-13-methoxygermacra-4-en-8,12-olide (18): To a solution of **11** (208 mg, 0.57 mmol) dissolved in CH_3OH (10 mL) was added $NaHCO_3$ (240 mg, 2.8 mmol). The mixture was stirred for 24 h at room temperature, quenched with water and extracted with EtOAc. The combined organic layers were dried with Na_2SO_4 and evaporated to give compound **18** (160 mg, 0.51 mmol, 90%). Colourless oil. $[\alpha]_D^{24}$ = +86.5 (c = 0.27, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3396, 2930, 2870, 1751, 1424, 1387, 1197, 1029, 756 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.79 (dd, J = 10.5, 2.7 Hz, 1 H, 1-H), 2.14 (o.s., 1 H, 2-H^A), 1.53 (m, 1 H, 2-H^B), 2.35 (o.s., 1 H, 3-H^A), 2.35 (o.s., 1 H, 3-H^B), 5.36 (d, J = 8.1 Hz, 1 H, 5-H), 4.34 (dd, J = 9.9, 8.1, 10.4 Hz, 1 H, 6-H), 2.53 (ddd, J = 8.1, 5.7, 5.7 Hz, 1 H, 7-H), 4.32 (m, 1 H, 8-H), 2.16 (dd, J = 13.6, 11.1 Hz, 1 H, 9-H^A), 1.99 (dd, J = 13.6, 4.5 Hz, 1 H, 9-H^B), 2.89 (ddd, J = 5.7, 5.7, 3.7 Hz, 1 H, 11-H), 3.72 (dd, J = 9.0, 3.7 Hz, 1 H, 13-H^A), 3.67 (dd, J = 9.0, 5.7 Hz, 1 H, 13-H^B), 1.43 (s, 3 H, 14-H_3), 4.23 (d, J = 13.2 Hz, 1 H, 15-H^A), 4.14 (d, J = 13.2 Hz, 1 H, 15-H^B), 3.42 (s, 3 H, OCH_3-H_3) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): see Table 2. MS (ESI+): m/z (%) = 351 (7) $[M + K]^+$, 335 (100) $[M + Na]^+$. $C_{16}H_{24}O_6$ (312.1573): calcd. C 61.52, H 7.74; found C 61.55, H 7.70.

(1*S*,6*R*,7*S*,8*S*,10*S*)-1,10-Epoxy-6,15-dihydroxygermacra-4,11(13)-dien-8,12-olide (19): To a solution of **18** (155 mg, 0.50 mmol) dissolved in dry THF (8 mL) was added *t*BuOK (66 mg, 0.60 mmol). The mixture was stirred for 10 min at room temperature, then quenched with a saturated solution of NH_4Cl and extracted with EtOAc. The combined organic layers were dried with Na_2SO_4 and evaporated to give compound **19** (80 mg, 0.28 mmol, 56%). Data for **19**: Colourless oil. $[\alpha]_D^{24}$ = +161.5 (c = 1.49, CH_3OH). IR (film): $\tilde{\nu}$ = 3415, 3340, 1761, 1458, 1280, 1159, 1034, 1017 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.82 (dd, J = 10.2, 2.1 Hz, 1 H, 1-H), 2.15 (o.s., 1 H, 2-H^A), 1.53 (m, 1 H, 2-H^B), 2.34 (o.s., 1 H, 3-H^A), 2.34 (o.s., 1 H, 3-H^B), 5.47 (d, J = 7.8 Hz, 1 H, 5-H), 4.32 (o.s., J = 10.4 Hz, 1 H, 6-H), 3.12 (m, 1 H, 7-H), 4.35 (o.s., 1 H, 8-H), 2.07 (o.s., 1 H, 9-H^A), 2.07 (o.s., 1 H, 9-H^B), 6.37 (d, J = 2.4 Hz, 1 H, 13-H^A), 6.15 (br. s, 1 H, 13-H^B), 1.44 (s, 3 H, 14-H_3), 4.24 (s, 2 H, 15_A-H and 15_B-H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): see Table 2. MS (ESI+): m/z (%) = 319 (8) $[M + K]^+$, 303 (100) $[M + Na]^+$. $C_{15}H_{20}O_5$ (280,1311): calcd. C 64.27, H 7.19; found C 64.31, H 7.16.

(1*S*,4*R*,5*R*,6*R*,7*S*,8*S*,10*S*,15*R*)-1,15-Dihydoxy-6,15-epoxyeudesma-11(13)-en-8,12-olide (20), (1*S*,5*R*,6*R*,7*S*,8*S*,10*S*)-1-Hydoxy-6,15-epoxyeudesma-4(15),11(13)-dien-8,12-olide (21) and (1*S*,6*R*,7*S*,8*S*)-1,6,15-Trihydroxygermacra-9,11(13)-dien-8,12-olide (22): A solution of $CHCl_3$ saturated with gaseous HCl (2 mL) was added to a solution of compound **19** (80 mg, 0.29 mmol) in $CHCl_3$ (8 mL), whilst stirring. After 24 h, the solvent was evaporated, and the mixture was subjected to column chromatography (silica gel; petroleum ether/EtOAc, 3:7) to give compounds **20** (11 mg, 0.04 mmol, 14%), **21** (5 mg, 0.02 mmol, 6%) and **22** (28 mg, 0.1 mmol, 34%), whereas **19** (15 mg, 0.05 mmol) was also recovered. Data for **20**: Colourless oil. $[\alpha]_D^{24}$ = –10.13 (c = 0.25, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3413, 2924, 1750, 1455, 1254, 1135, 1029, 737 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.51 (dd, J = 9.4, 5.6 Hz, 1 H, 1-H), 1.82 (m, 1 H, 2-H^A), 1.62 (m, 1 H, 2-H^B), 1.95 (m, 1 H, 3-H^A), 1.27 (o.s., 1 H, 3-H^B), 2.26 (o.s., 1 H, 4-H), 2.05 (dd, J = 5.5, 2.2 Hz, 1 H, 5-H), 4.57 (dd, J = 7.2, 5.0 Hz, 1 H, 6-H), 3.38 (dddd, J = 12.6, 7.2, 3.5, 3.0 Hz, 1 H, 7-H), 4.09 (ddd, J = 12.6, 9.6, 8.4 Hz, 1 H, 8-H), 2.26 (dd, J = 13.4, 8.4 Hz, 1 H, 9-H^A), 1.83 (dd, J = 13.4, 9.6 Hz, 1 H,

Table 2. ^{13}C NMR spectroscopic data for compounds **18**–**26** in $CDCl_3$.

	18	**19**	**20**	**21**	**22**[a]	**23**	**24**[b]	**25**	**26**[b]
C-1	59.2 (d)	61.6 (d)	77.2 (d)	77.8 (d)	68.0 (d)	66.5 (d)	65.5 (d)	77.2 (d)	77.2 (d)
C-2	24.2 (t)	23.8 (t)	27.9 (t)	30.4 (t)	29.0 (t)	23.4 (t)	23.0 (t)	29.1 (t)	26.3 (t)
C-3	30.8 (t)	30.6 (t)	19.5 (t)	20.4 (t)	32.9 (t)	31.8 (t)	31.9 (t)	32.8 (t)	22.6 (t)
C-4	140.6 (s)	140.0 (s)	44.1 (d)	112.6 (s)	138.1 (s)	131.2 (s)	138.4 (s)	60.9 (s)	43.3 (d)
C-5	129.2 (d)	128.9 (d)	47.0 (d)	51.3 (d)	133.9 (d)	139.4 (d)	131.8 (d)	51.5 (d)	54.2 (d)
C-6	71.5 (d)	69.6 (d)	78.4 (d)	80.3 (d)	70.6 (d)	69.4 (d)	68.8 (d)	67.8 (d)	66.4 (d)
C-7	51.0 (d)	49.7 (d)	46.6 (d)	45.2 (d)	53.5 (d)	55.8 (d)	53.8 (d)	54.3 (d)	55.3 (d)
C-8	78.7 (d)	77.5 (d)	75.9 (d)	75.8 (d)	76.4 (d)	78.1 (d)	77.0 (d)	76.0 (d)	77.7 (d)
C-9	44.4 (t)	43.9 (t)	38.4 (t)	35.3 (t)	127.4 (d)	45.9 (t)	46.3 (t)	40.8 (t)	41.2 (t)
C-10	61.7 (s)	57.2 (s)	37.4 (s)	39.0 (s)	143.7 (s)	58.0 (s)	58.1 (s)	43.0 (s)	41.3 (s)
C-11	47.5 (d)	135.5 (s)	138.2 (s)	138.2 (s)	140.2 (s)	47.5 (d)	135.8 (s)	136.9 (s)	137.5 (s)
C-12	176.1 (s)	170.0 (s)	170.2 (s)	170.1 (s)	172.3 (s)	174.7 (s)	170.0 (s)	170.2 (s)	171.0 (s)
C-13	72.3 (t)	126.4 (t)	119.6 (t)	120.4 (t)	122.9 (t)	71.6 (t)	126.9 (t)	120.6 (t)	119.7 (t)
C-14	21.1 (q)	20.7 (q)	21.2 (q)	19.0 (q)	17.0 (q)	17.5 (q)	17.2 (q)	14.3 (q)	14.8 (q)
C-15	61.7 (t)	61.0 (t)	104.8 (d)	138.1 (d)	59.8 (t)	60.4 (t)	59.8 (t)	51.9 (t)	204.7 (d)
OCH_3	57.2 (q)					59.2 (q)			

[a] In MeOD. [b] In $CDCl_3$/MeOD, 9:1.

9-H^B), 6.21 (d, J = 3.5 Hz, 1 H, 13-H^A), 5.76 (d, J = 3.0 Hz, 1 H, 13-H^B), 1.27 (s, 3 H, 14-H$_3$), 5.43 (d, J = 6.0 Hz, 1 H, 15-H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): see Table 2. MS (ESI+): m/z (%) = 303 (3) $[M + Na]^+$, 285 (100) $[M - H_2O + Na]^+$. $C_{15}H_{20}O_5$ (280.1311): calcd. C 64.27, H 7.19; found C 64.30, H 7.17. Data for **21**: Colourless oil. $[\alpha]_D^{24}$ = –32.34 (c = 0.15, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3416, 2926, 1767, 1666, 1453, 1256, 1192, 1024, 737 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.52 (o.s., 1 H, 1-H), 1.79 (m, 1 H, 2-H^A), 1.49 (m, 1 H, 2-H^B), 2.47 (m, 1 H, 3-H^A), 2.24 (m, 1 H, 3-H^B), 2.35 (br. d, J = 9.2 Hz, 1 H, 5-H), 4.50 (dd, J = 9.2, 9.2 Hz, 1 H, 6-H), 3.55 (o.s., 1 H, 7-H), 4.04 (ddd, J = 12.3, 9.3, 8.8 Hz, 1 H, 8-H), 2.20 (dd, J = 13.4, 8.8 Hz, 1 H, 9-H^A), 1.92 (dd, J = 13.4, 9.3 Hz, 1 H, 9-H^B), 6.24 (d, J = 3.0 Hz, 1 H, 13-H^A), 5.77 (d, J = 3.0 Hz, 1 H, 13-H^B), 1.12 (s, 3 H, 14-H$_3$), 6.18 (m, 1 H, 15-H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): see Table 2. MS (ESI+): m/z (%) = 301 (57) $[M + K]^+$, 285 (100) $[M + Na]^+$. $C_{15}H_{18}O_4$ (262.1205): calcd. C 68.68, H 6.92; found C 68.70, H 6.89. Data for **22**: Colourless oil. $[\alpha]_D^{24}$ = –49.85 (c = 0.50, CH_3OH). IR (film): $\tilde{\nu}$ = 3420, 3333, 1763, 1275, 1165, 1040 cm^{-1}. ^{1}H NMR (300 MHz, CD_3OD): δ = 4.52 (dd, J = 12.0, 5.1 Hz, 1 H, 1-H), 2.02 (m, 1 H, 2-H^A) 1.74 (m, 1 H, 2-H^B), 2.58 (br. dd, J = 12.6, 6.3 Hz, 1 H, 3-H^A), 1.87 (o.s., 1 H, 3-H^B), 5.06 (d, J = 10.8 Hz, 1 H, 5-H), 4.57 (dd, J = 10.8, 9.0 Hz, 1 H, 6-H), 2.79 (dddd, J = 9.0, 9.0, 3.3, 3.0 Hz, 1 H, 7-H), 4.78 (dd, J = 10.3, 9.0 Hz, 1 H, 8-H), 5.31 (dd, J = 10.3, 1.3 Hz, 1 H, 9-H), 6.17 (o.s., 1 H, 13-H^A), 6.17 (o.s., 1 H, 13-H^B), 1.83 (br. s, 3 H, 14-H$_3$), 4.28 (d, J = 12.6 Hz, 1 H, 15-H^A), 4.15 (d, J = 12.6 Hz, 1 H, 15-H^B) ppm. ^{13}C NMR (75.3 MHz, CD_3OD): see Table 2. MS (ESI+): m/z (%) = 303 (100) $[M + Na]^+$. $C_{15}H_{20}O_5$ (280.1311): calcd. C 64.27, H 7.19; found C 64.24, H 7.23.

(1*R*,6*R*,7*S*,8*S*,10*R*,11*S*)-1,10-Epoxy-6,15-dihydroxy-13-methoxygermacra-4-en-8,12-olide (23): To a solution of **12** (110 mg, 0.30 mmol) dissolved in CH_3OH (40 mL) was added $NaHCO_3$ (125 mg, 1.48 mmol). The mixture was stirred at room temperature for 24 h, quenched with water and extracted with EtOAc. The combined organic layers were dried with Na_2SO_4 and evaporated to give compound **23** (90 mg, 0.29 mmol, 96%). Colourless oil. $[\alpha]_D^{24}$ = –8.39 (c = 0.20, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3384, 2930, 1761, 1450, 1364, 1299, 1160, 935, 754 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.74 (dd, J = 11.1, 2.1 Hz, 1 H, 1-H), 2.08 (m, 2 H, 2-H^A), 1.38 (m, 1 H, 2-H^B), 2.50 (ddd, J = 12.9, 5.4, 2.7 Hz, 1 H, 3-H^A), 2.28 (m, 1 H, 3-H^B), 5.31 (d, J = 9.6 Hz, 1 H, 5-H), 4.51 (dd, J = 9.6, 9.6 Hz, 1 H, 6-H), 2.38 (ddd, J = 9.6, 9.6, 9.6 Hz, 1 H, 7-H), 4.20 (br. dd, J = 9.6, 9.6 Hz, 1 H, 8-H), 2.67 (br. d, J = 14.1 Hz, 1 H, 9-H^A), 1.52 (dd, J = 14.1, 9.6 Hz, 1 H, 9-H^B), 2.92 (ddd, J = 9.6, 6.6, 3.3 Hz, 1 H, 11-H), 3.94 (dd, J = 9.0, 3.3 Hz, 1 H, 13-H^A), 3.59 (dd, J = 9.0, 6.6 Hz, 1 H, 13-H^B), 1.20 (s, 3 H, 14-H$_3$), 4.35 (d, J = 12.9 Hz, 1 H, 15-H^A), 4.01 (d, J = 12.9 Hz, 1 H, 15-H^B), 3.44 (s, 3 H, OCH$_3$-H$_3$) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): see Table 2. MS (ESI+): m/z (%) = 351 (30) $[M + K]^+$, 335 (100) $[M + Na]^+$. $C_{16}H_{24}O_6$ (312.1573): calcd. C 61.52, H 7.74; found C 61.48, H 7.75.

(1*R*,6*R*,7*S*,8*S*,10*R*)-1,10-Epoxy-6,15-dihydroxygermacra-4,11(13)-dien-8,12-olide (24): To a solution of **23** (72 mg, 0.23 mmol) dissolved in dry THF (6 mL) was added *t*BuOK (30 mg, 0.26 mmol). The mixture was stirred for 10 min at room temperature. The reaction was quenched by adding a solution of phosphate buffer (pH 5) and extracted with EtOAc. The combined organic layers were dried with Na_2SO_4 and evaporated; the mixture was subjected to column chromatography (silica gel; petroleum ether/EtOAc, 3:7) to give compound **24** (40 mg, 0.14 mmol, 61%). Colourless oil. $[\alpha]_D^{24}$ = –26.79 (c = 0.74, CH_3COCH_3). IR (film): $\tilde{\nu}$ = 3403, 1772, 1653, 1267, 1146 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$/MeOD, 9:1): δ = 2.72 (dd, J = 11.1, 2.4 Hz, 1 H, 1-H), 2.06 (m, 2 H, 2-H^A), 1.39 (m, 1 H, 2-H^B), 2.45 (ddd, J = 12.9, 5.7, 3.0 Hz, 1 H, 3-H^A), 2.25 (m, 1 H, 3-H^B), 5.31 (d, J = 9.3 Hz, 1 H, 5-H), 4.45 (dd, J = 9.3, 9.3 Hz, 1 H, 6-H), 2.82 (dddd, J = 9.3, 6.6, 3.0, 3.0 Hz, 1 H, 7-H), 4.08 (br. dd, J = 9.3, 6.6 Hz, 1 H, 8-H), 2.61 (br. d, J = 14.1 Hz, 1 H, 9-H^A), 1.50 (dd, J = 14.1, 9.6 Hz, 1 H, 9-H^B), 6.31 (d, J = 3.0 Hz, 1 H, 13-H^A), 6.26 (d, J = 3.0 Hz, 1 H, 13-H^B), 1.22 (s, 3 H, 14-H$_3$), 4.27 (d, J = 12.9 Hz, 1 H, 15-H^A), 3.93 (d, J = 12.9 Hz, 1 H, 15-H^B) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$/MeOD, 9:1): see Table 2. MS (ESI+): m/z (%) = 319 (24) $[M + K]^+$, 303 (100) $[M + Na]^+$. $C_{15}H_{20}O_5$ (280,1311): calcd. C 64.27, H 7.19; found C 64.29, H 7.15.

(1*R*,4*S*,5*S*,6*R*,7*S*,8*S*,10*R*)-1,6-Dihydoxy-4(15)-epoxyeudesma-11(13)-en-8,12-olide (25) and (1*R*,4*S*,5*S*,6*R*,7*S*,8*S*,10*R*)-1,6-Dihydoxy-15-oxoeudesma-11(13)-en-8,12-olide (26): A solution of $CHCl_3$ saturated with gaseous HCl (1.5 mL) was added to a solution of **24** (40 mg, 0.14 mmol) in $CHCl_3$ (4 mL), whilst stirring. After 4 h, the solvent was evaporated and the mixture was subjected to column chromatography (silica gel; DCM/MeOH, 24:1) to give compounds **25** (5 mg, 0.02 mmol, 14%) and **26** (11 mg, 0.04 mmol, 29%). Data for **25**: Colourless oil. $[\alpha]_D^{24}$ = –122.43 (c = 0.07, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3420, 1632 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.59 (dd, J = 10.5, 5.0 Hz, 1 H, 1-H), 2.01 (m, 1 H, 2-H^A), 1.81 (m, 1 H, 2-H^B), 2.11 (m, 1 H, 3-H^A), 1.39 (ddd, J = 13.2, 4.8, 2.4 Hz 1 H, 3-H^B), 1.86 (d, J = 9.6 Hz, 1 H, 5-H), 3.85 (dd, J = 9.6, 9.6 Hz, 1 H, 6-H), 2.54 (dddd, J = 11.7, 9.6, 3.0, 3.0 Hz, 1 H, 7-H), 3.96 (ddd, J = 11.7, 11.7, 3.6 Hz, 1 H, 8-H), 2.49 (dd, J = 11.7, 3.6 Hz, 1 H, 9-H^A), 1.55 (dd, J = 11.7, 11.7 Hz, 1 H, 9-H^B), 6.15 (d, J = 3.0 Hz, 1 H, 13-H^A), 5.97 (d, J = 3.0 Hz, 1 H, 13-H^B), 1.00 (s, 3 H, 14-H$_3$), 3.20 (dd, J = 3.6, 1.2 Hz, 1 H, 15-H^A), 2.86 (d, J = 3.6 Hz, 1 H, 15-H^B) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): see Table 2. MS (ESI+): m/z (%) = 319 (28) $[M + K]^+$, 303 (100) $[M + Na]^+$. $C_{15}H_{20}O_5$ (280,1311): calcd. C 64.27, H 7.19; found C 64.30, H 7.19. Data for **26**: Colourless oil. $[\alpha]_D^{24}$ = –8.58 (c = 0.25, CH_3OH). IR (film): $\tilde{\nu}$ = 3393, 1631, 1248, 992 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$/MeOD, 9:1): δ = 3.24 (dd, J = 10.8, 5.1 Hz, 1 H, 1-H), 1.62 (o.s., 1 H, 2-H^A), 1.53 (m, 1 H, 2-H^B), 2.31 (m, 1 H, 3-H^A), 1.36 (o.s., 1 H, 3-H^B), 2.87 (m, 1 H, 4-H), 1.60 (dd, J = 10.2, 5.4 Hz, 1 H, 5-H), 4.26 (dd, J = 10.2, 10.2 Hz, 1 H, 6-H), 2.45 (dddd, J = 12.2, 10.2, 3.0, 3.0 Hz, 1 H, 7-H), 3.91 (ddd, J = 12.2, 11.7, 3.7 Hz, 1 H, 8-H), 2.37 (dd, J = 11.7, 3.7 Hz, 1 H, 9-H^A), 1.36 (dd, J = 11.7, 11.7 Hz, 1 H, 9-H^B), 6.08 (d, J = 3.0 Hz, 1 H, 13-H^A), 5.94 (d, J = 3.0 Hz, 1 H, 13-H^B), 0.72 (s, 3 H, 14-H$_3$), 9.85 (br. s, 1 H, 15-H) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$/MeOD, 9:1): see Table 2. MS (ESI+): m/z (%) = 319 (35) $[M + K]^+$, 303 (100) $[M + Na]^+$. $C_{15}H_{20}O_5$ (280.1311): calcd. C 64.27, H 7.19; found C 64.24, H 7.21.

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