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ent-Clerodane diterpenes and other constituents from the liverwort *Adelanthus lindenbergianus* (Lehm.) Mitt.

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Abstract

Eleven *ent*-clerodanes, 13-hydroxy-*cis*-*ent*-cleroda-3,14-diene, 15-hydroxy-*cis*-*ent*-cleroda-3,13(*E*)-diene, 1β,12:15,16-diepoxy-*cis*-*ent*-cleroda-13(16),14-dien-18α,6α-olide, 8β,12:15, 16-diepoxy-*cis*-*ent*-cleroda-13(16),14-dien-18α,6α-olide, 1β,16:15,16-diepoxy-*cis*-*ent*-cleroda-12,14-dien-18α,6α-olide, 7β,12:8β,12-diepoxy-15-hydroxy-*cis*-*ent*-cleroda-13-en-16,15:18α,6α-diolide, 7β,12:8β,12-diepoxy-16-hydroxy-*cis*-*ent*-cleroda-13-en-15,16:18α,6α-diolide, 1α-acetoxy-8β,12-epoxy-15-hydroxy-*cis*-*ent*-cleroda-13-en-16,15:18α,6α-diolide, 1β,12-epoxy-16-hydroxy-*cis*-*ent*-cleroda-13-en-15,16:18α,6α-diolide, 8β,12-epoxy-15-hydroxy-*trans*-cleroda-13-en-16,15:18α,6α-diolide, 8β,12-epoxy-16-hydroxy-*trans*-cleroda-13-en-15,16:18α,6α-diolide along with the known clerodane diterpenes anastreptin and orcadensin have been isolated from the liverwort *Adelanthus lindenbergianus* (Lehm.) Mitt. Furthermore, three eudesmane sesquiterpenes together with the known (−)-1β,10-epoxyaristolan, 3,4-*seco*-4(23),20(29)-lupadien-3,28-dicarboxylic acid dimethyl ester and two acetophenone derivatives were identified by spectroscopic methods, essentially MS and NMR experiments.

Keywords: *Adelanthus lindenbergianus*; Adelanthaceae; Liverwort; Clerodane; Aristolane; Eudesmane; *seco*-Lupane; Chromene; Acetophenone

1. Introduction

Liverworts have been reported as a rich source of rare and novel compounds, partly with unique skeletons and a broad range of biological activities (Zinsmeister et al., 1991; Asakawa, 1995). In the course of our chemical studies of liverworts, we investigated *Adelanthus lindenbergianus* (Lehm.) Mitt. (Adelanthaceae) from Tierra del Fuego, Patagonia. Belonging to a genus found largely in the southern hemisphere, *A. lindenbergianus* is one of the most widespread liverworts throughout the Chilean–Patagonian region (Grolle, 1972). The only previous report of a chemical study of *A. lindenbergianus* is restricted to GC-MS studies with some carbohydrates and sterols identified. The major component was an "unidentified diterpene-like compound" with a molecular weight of 344 (Asakawa and Inoue, 1984). In fact, the investigation of the Patagonian species yielded two diterpenes with molecular ion peaks at *m*/*z* 344, anastreptin and orcadensin, the *cis*-clerodanes known from the liverwort *Anastrepta orcadensis* (Huneck and Overton, 1971). Furthermore, the present report describes the isolation and structure elucidation of 11 new clerodanes along with a variety of further constituents from *A. lindenbergianus*.

2. Results and discussion

A combination of size exclusion chromatography (Sephadex LH-20), vacuum liquid chromatography (VLC) and HPLC of the diethyl ether extract, the ethyl acetate soluble phase as well as the butanol soluble phase of the methanolic extract of *A. lindenbergianus* resulted in the isolation of anastreptin (**3**), orcadensin (**4**), eleven new clerodanes (**1, 2, 5**–**13**) including three mixtures of epimers, a *cis*-stereoisomer (**1**) of kolavelool (Seaman et al.,1990; Anthonson and McCrindle, 1969), a *cis*-stereoisomer (**2**) of kolavenol (Misra et al., 1964), three eudesmanes (**15**–**17**), a *seco*-lupane triterpene (**18**) together with an unusual spiroacetal acetophenone derivative (**20**). Furthermore, the extracts yielded β-(−)-1,10-epoxyaristolan (**14**), already known from the sea pen *Scytalium splendens* (Do and Erickson, 1983), and 2,4,6-trihydroxyacetophenone-3,5-di-*C*-glucoside (**19**), known from *Melicope pteleifolia* (Chen et al., 1994) and the liverworts *Scapania nemorea* (Geis, 1999) and *Lepicolea ochroleuca* (Cullmann and Becker, 1999).

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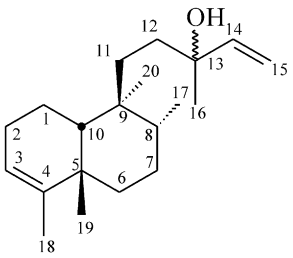

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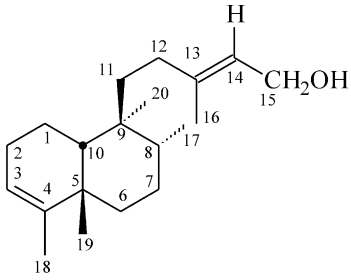

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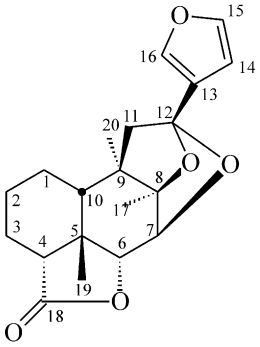

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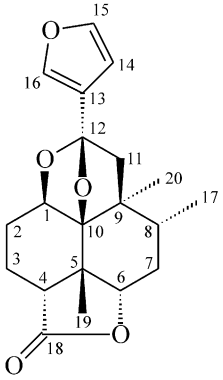

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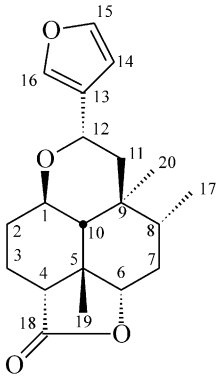

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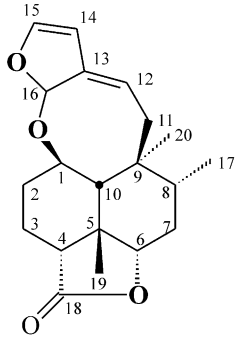

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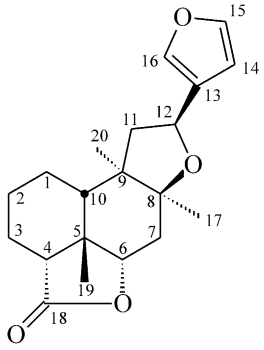

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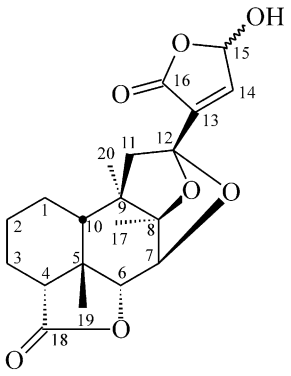

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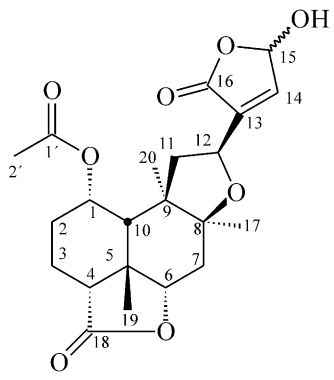

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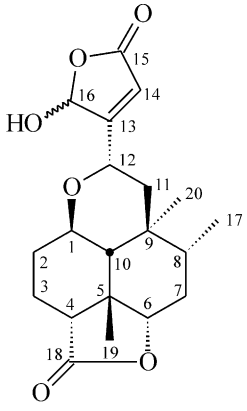

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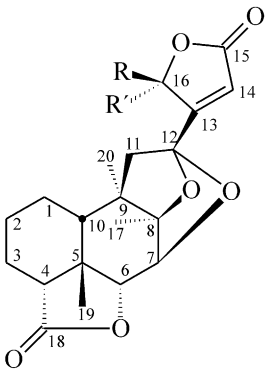

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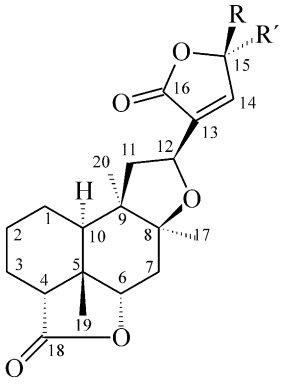
11b R=OH, R′=H



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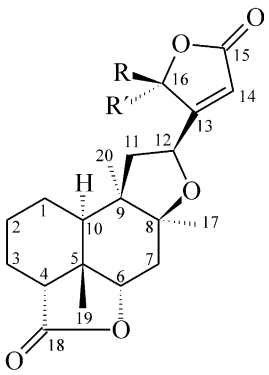

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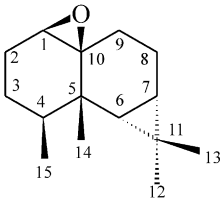
13b R=OH, R′=H



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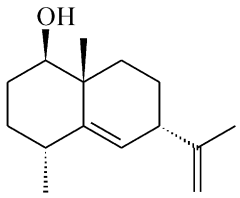

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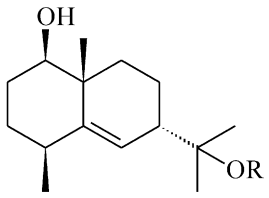
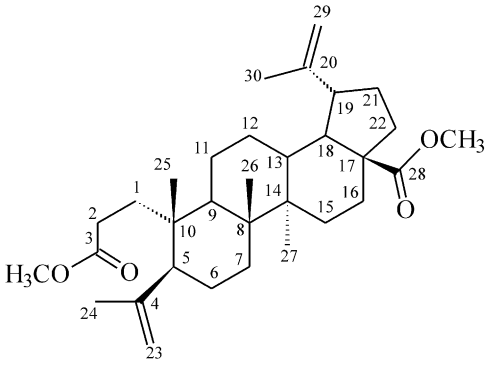


16 R = H
17 R = CH_3



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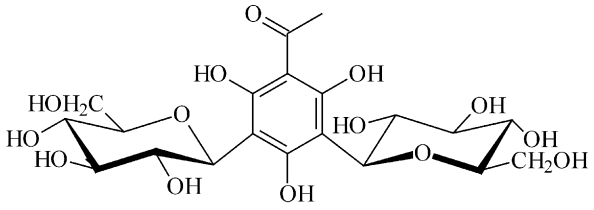
The mass spectrum of compound **1** showed the molecular ion peak at *m*/*z* 290, suggesting a molecular formula of $C_{20}H_{34}O$. Its ^1H NMR spectrum displayed a vinylic proton (δ_H 5.23, *brs*, H-3) of a trisubstituted double bond and three vinylic protons of an ABX spin system with δ_X 5.88 (*dd*, $J = 10.4$, 17.3 Hz), δ_A 5.18 (*dd*, $J = 1.2$, 17.3 Hz) and δ_B 5.02 (*dd*, $J = 1.2$, 10.4 Hz). Also noted in the ^1H NMR spectrum were signals for five methyls, four tertiary and one secondary. Two singlet signals of the four tertiary methyls showed a low field shift indicating a vinyl or oxygen bearing carbon. The ^1H and ^{13}C NMR assignments together with the results of the ^1H–^1H COSY, HSQC, HMBC and NOESY experiments led for **1** to a cleroda-3,14-diene with a hydroxyl group at C-13. The problematic aspect of the structure elucidation was the assignment at the four asymmetric centers, C-5, C-8, C-9 and C-10. The *cis*-stereochemistry at the junction of the rings A and B could be deduced from the chemical shift of C-19 (33.0, *q*) when compared to that of the methyl of *cis*- (δ_C 15.7) and *trans*-methyldecalin (δ_C 28.1). The NOESY experiment confirmed the proposed *cis*-configuration of the decalin moiety, since a correlation between H-19 and H-10 could be observed. Except for C-13, the NOESY revealed the complete relative stereochemistry of **1** with methyl H-17 (δ_H 0.71) and H-20 (δ_H 0.77) at one side of



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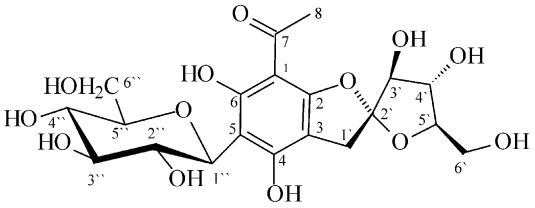

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the bicyclic moiety and H-10 (δ_H 1.29) and methyl H-19 (δ_H 1.00) at the opposite side (Fig. 1). As shown by Seaman et al. (1990) for such *cis*-clerodanes even the absolute stereochemistry can be established from the ^{1}H NMR. 5α,10α-*cis*- and 5β,10β-*cis*-clerodanes, differ in the orientation of methyl H-20 and therefore in its chemical shifts. In 5α,10α-*cis*-clerodanes (*cis-normal*-clerodanes) methyl H-20 shows an equatorial orientation and produces a chemical shift (δ_H 1.08) which is downfield from the axial methyl H-20 (δ_H 0.84) of the 5β,10β-*cis*-clerodanes (*cis-ent*-clerodanes). Therefore **1** belongs to the *ent*-clerodane series and represents the epimer of the *trans*-clerodane kolavelool which has been described from some higher plants and from the liverwort *Jungermannia paroica* (Harrison et al., 1992).

Compound **2**, a colourless oil, was assigned to the molecular formula $C_{20}H_{34}O$ (EIMS, *m/z* 290 $[M]^+$). The ^{1}H and ^{13}C NMR spectra were similar to those of **1**, revealing an *cis-ent*-clerodane, but showed a trisubstituted double bond in the side chain instead of the allylic pattern found in **1**. The ^{13}C and DEPT spectra revealed a hydroxylic methylene at δ_C 59.4 (*t*, C-15) corresponding to δ_H 4.13 (2H, *d*, *J* = 7.0 Hz, H-15) in the HSQC spectrum. The coupling constant *J* = 7.0 Hz of a

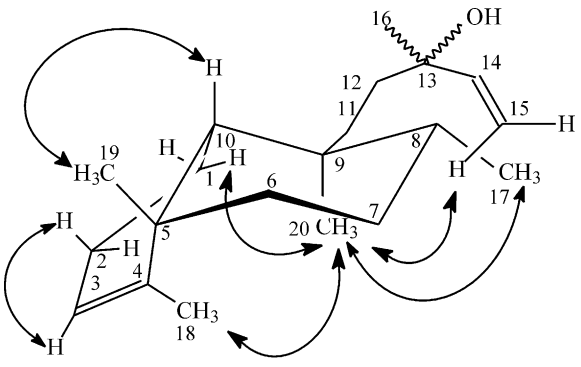

Fig. 1. Significant NOESY correlations of **1**.

vinylic triplet proton δ_H 5.41 (H-14) explained its vicinity to the methylene H-15. Correlations between H-12β/H-14 and H-15/H-16 in the NOESY spectrum led to an *E*-configuration for the side chain double bond. Therefore, the structure of **2** has been established as 15-hydroxy-*cis-ent*-cleroda-3,13(*E*)-diene, the *cis*-isomer of kolavenol, known from *Hardwickia pinnata* (Misra et al., 1964).

Compound **3** and **4**, both (EIMS) *m/z* at 344 $[M]^+$, were identified as the bitter tasting *cis*-clerodane furanoditerpene lactones anastreptin (**3**) and orcadensin (**4**), already known from the liverwort *Anastrepta orcadensis* (Huneck and Overton, 1971). As mentioned above, anastreptin was the major component of *A. lindenbergianus* from Chile (Asakawa and Inoue, 1984). Remarkably, the structures of **3** and **4** both contain cyclic ketal functions with oxygen bridges from C-12 with different positions of the decalin moiety. Their relative configuration had been elucidated by extensive NMR studies (Rycroft, 1990).

The molecular formula of clerodane **5**, $C_{20}H_{26}O_4$, was assumed from the molecular ion peak at *m/z* 330 in the EI mass spectrum. The ^{13}C NMR spectrum contained the signals of three methyls, four methylenes, nine methines and four quarternary carbons indicating a γ-lactone (δ_C 178.2, *s*; 81.9, *d*) and a β-substituted furan moiety (δ_C 128.7, *s*; 108.8, *d*; 143.1, *d*; 138.3, *d*; see also Table 2) as found in **3** for anastreptin. Instead of a ketal function the ^{13}C NMR spectrum of **5** included two methines δ_C 67.7 and 68.7 revealing the presence of an ether, presumably cyclic. Based on ^2J and ^3J HMBC correlations from the corresponding low field proton at δ_H 5.10 (H-12) to C-13 and C-16 of the furan moiety and cross peaks between the proton H-1 and H-10 from a ^{1}H-^{1}H COSY experiment the ether had to be positioned from C-12 to C-1. Thus, compound **5** was an analogue of gymnocolin, firstly known from the liverwort *Gymnocolea inflata* (Huneck et al., 1983). The NOESY correlations (Fig. 2) confirmed the stereochemistry of **5**.

In agreement with compound **5**, the ^{13}C and ^{1}H NMR spectra of compound **6** showed signals assignable to a *cis*-fused decalin with a γ-lactone moiety from C-18 to C-6. Furthermore the ^{13}C NMR and DEPT spectra contained signals of a secondary alcohol (δ_C 72.6, *d*, C-1), an acetal (δ_C 103.2, *d*, C-16), and a trisubstituted enol double bound (δ_C 151.2, *d*, C-15; 104.8, *d*, C-14) in conjugation with a second olefin (δ_C 145.3, *s*, C-13, 116.1, *d*, C-12). A HMBC experiment revealed two sequences C(11)H_2-C(12)H-C(13)-C(14)H-C(15)H-O-C(16)H-O-C(1)H and C(13)-C(16)H. All together concluded in 1β,16:15,16-diepoxy-*cis-ent*-cleroda-12,14-dien-18,6α-olide as structure of compound **6**.

The ^{1}H and ^{13}C NMR of **7** ($[M]^+ = m/z$ 330) revealed typical signals of a *cis*-clerodane with a γ-lactone and a furan moiety along with a cyclic ether in analogy to

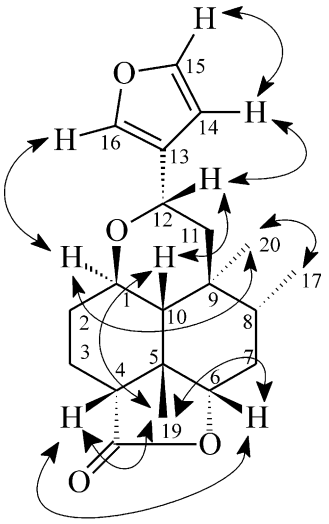

Fig. 2. Significant NOESY correlations of **5**.

compound **5**. However, the position of the ether had changed from 1β,12 in **5** to 8β,12 in **7**. This clearly followed by the comparison of the ^{1}H and ^{13}C NMR data of **5** and **7** as well as the HMBC, ^{1}H-^{1}H COSY and NOESY experiments. In contrast to the earlier mentioned structures methyl H-20 (δ_H 1.14) shows an perceptible downfield shift ($\Delta\delta_H \sim +0.4$) as a consequence of the ether function at C-8, which is therefore no longer an unambiguously marker for a 5β,10β-*cis*-decalin system. Nevertheless, based on the occurence of the above mentioned clerodanes, we assumed that **7** belongs to the *ent*-series as well.

The molecular formula of compound **8**, $C_{20}H_{24}O_7$, was obtained from the CI mass spectrum (*m*/*z* 377 $[M+H]^+$). The ^{1}H and ^{13}C NMR spectra were rather similar to those of anastreptin (**3**) clearly indicating a 18,6α-olide moiety and a cyclic ketal structure with C-12 as ketal carbon (δ_C 103.5, *s*) with ether linkages to C-7 (77.8, *s*) and C-8 (85.6, *s*). The spectroscopic data of **3** and **8** mainly differed by the absence of the signals of the furan moiety. Instead, signals of a 16,15-γ-butenolide appeared in the spectra. It was substituted with an additional hydroxyl at C-15 to give a hemiacetal, since a correlation was observed from a low field shifted singlet proton at δ_H 6.41 to the methine δ_C 96.6 in the HSQC spectrum. HMBC, ^{1}H-^{1}H COSY and NOESY experiments confirmed the suggested structure elements and established the structure of **8** as 7β,12:8β,12-diepoxy-15-hydroxy-*cis*-*ent*-cleroda-13-en-16,15:18α,6α-diolide. The relative position of the hydroxyl group at C-15 remained uncertain.

The mass spectrum of **9** (CIMS, *m*/*z* 421 $[M+H]^+$) indicated an acetylated diterpene. The NMR data revealed a hydroxylated 16,15-butenolide moiety (δ_H 6.72, H-14; 5.99, H-15) and a *cis*-fused clerodane skeleton with a cyclic ether between C-12 and C-8 since there were only signals of tertiary methyls in the ^{1}H NMR spectrum, two of them at lower field (H-17 and H-19: δ_H 1.29, *s*). Furthermore, the observed low field resonance of H-1 (δ_H 4.90) clearly indicated that the acetyl and not the ether bridge was positioned at C-1. The relative stereochemistry followed from the observed NOEs (Fig. 3). The angular H-10β gave effects with H-1β, H-14 and the overlapped signals of H-19 and/or H-17. Though we could not distinguish between the interactions of the methyl H-17 and H-19 we suggested the *cis*-configuration from the low field shift of methyl C-19 (δ_C 28.9). Furthermore, NOEs between H-1β and H-11β supported the α-orientation of the acetyl. Compound **9** has been established as 1α-acetoxy-8β,12-epoxy -15-hydroxy-*cis*-*ent*-cleroda-13-en-16,15:18α,6α-diolide.

Compound **10**, a colourless oil, was assigned the molecular formula $C_{20}H_{26}O_6$ (CIMS, *m*/*z* 363 $[M+H]^+$). The spectral data were close to those of compound **5** except from the signals of the furan moiety. Those were replaced by signals of a 16-hydroxy-15,16-γ-butenolide with isocronic signals for H-14 and H-16 (both δ_H 6.06, both *s*). The ^{13}C NMR signals, taken from the HMBC and the HSQC projections, gave further proof for the mentioned structure elements. The relative configuration of **10** was confirmed by HMBC, ^{1}H-^{1}H COSY and NOESY experiments leading to the structure of 1β,12-epoxy-16-hydroxy-*cis*-*ent*-cleroda-13-en-15,16:18α,6α-diolide.

Adelanthus lindenbergianus also contained three 1:1 mixtures (**I**–**III**) of epimers of clerodane diterpenes. The molecular ion peak *m*/*z* 377 $[M+H]^+$ of mixture **I** (**11a**,**b**) and the ^{1}H and ^{13}C spectra exhibited the presence of an analogue of **8** in which the 15-hydroxy-16,15-butenolide was replaced by a 16-hydroxy-15,16-γ-lactone moiety. The typical high field shift of signal H-14 (δ_H 6.23/6.25) in comparison to the corresponding signal of **8** (δ_H 7.37) gave additional support for the presence of a 15,16-butenolide in mixture **I**. Hence, compounds **11a,b** are substituted at C-16 with either an α (**11a**)- or β (**11b**)-oriented hydroxyl group.

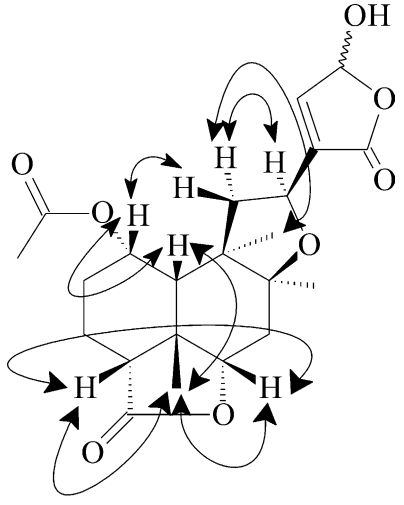

Fig. 3. Significant NOESY correlations of **9**.

Mixture **II** (**12a**,**b**), a colourless oil, was assigned the molecular formula $C_{20}H_{26}O_6$ (CIMS, *m*/*z* 363 $[M+H]^+$) and required eight double bond equivalents. The ^1H and ^{13}C NMR spectra displayed signals for a clerodane with a 6,18-γ-lactone, a 15α- and 15β-hydroxy-16,15-butenolide moiety along with a cyclic ether, proposed between C-8 and C-12. The spectral data of **12a** and **b** were rather consistent with the data of the already described clerodanes but differed in the resonance of the angular methyl group C-19 (δ_C 23.0/23.1). The high field methyl C-19 indicated a *trans*-fused configuration of the decalin moiety and the NOESY showed no correlation between H-5 and H-10, as it would be expected for a *cis* orientation. The 5β,10α orientation of the bicyclic moiety derived from the NOESY correlations between the methyls H-17 and H-20 and H-20 and proton H-10 and the correlations between H-20, H-11α and H-12 led to proposed β-orientation of the 16,15-γ-butenolide.

Again, the ^1H and ^{13}C NMR spectra of mixture **III** (**13a**,**b**) contained double sets of signals of a 1:1 mixture of epimers. The ^{13}C NMR chemical shifts were rather similar to those of **12a** and **b**. Comparison of the spectral data from mixture II and III resulted in the assumption that the 15-hydroxy-16,15-butenolide as found in **12a** and **b** was replaced by the 16-hydroxy-15,16-butenolide moiety with either α (**13a**)- or β (**13b**)-orientation of H-16.

The major component of the sesquiterpene fraction was β-(−)-1,10-epoxyaristolane (**14**), already known from the sea pen *Scytalium splendens* (Do and Erickson, 1983). In the same paper, the eudesmanes 1β,11-dihydroxy-5-eudesmene (**16**) and 1β-hydroxy,11-methoxy-5-eudesmene (**17**) were published as products of **14** after treatment with formic acid and *p*-toluene sulfonic, respectively. We also found **16** and **17** in the ether extract of *A. lindenbergianus*. Taken into account the results of Do and Erickson (1983), both are most probably not genuine constituents

The EIMS spectrum of **15** showed the molecular ion peak at *m*/*z* 220 amu. The ^{13}C NMR spectrum displayed signals of an eudesmane skeleton and resembled that of **16** and **17**. However, the isopropyl alcohol group had changed to an isopropylene moiety (δ_C 148.3, *s*, C-11; δ_C 111.2, *t*, C-12; δ_C/22.0, *q*, C-13). Therefore **15** is 1β-hydroxy-eudesma-5,11-diene.

The EIMS spectrum of **18** (*m*/*z* = 498 $[M]^+$) suggested a dimethylated triterpene with the molecular formula $C_{32}H_{50}O_4$. The ^1H and ^{13}C NMR spectra were close to those of the known canaric acid (De Pascual Teresa et al., 1987), a ring-A-fissioned (3,4-*seco*)-lupane-3, 28-dioyl-3-methyl ester. The NMR spectra of **18** revealed two methyl ester groups (δ_C 176.0, *s*, C-28; 174.5, *s*, C-3; 51.4 and 51.2, both *q*, both OCH_3) and is therefore the 28-methyl ester of canaric acid.

The spectral data of **19** were in agreement with 2,4,6-trihydroxyacetophenone-3,5-di-C-glucoside (Geis, 1999).

The ^{13}C NMR spectrum of **20** showed similarity to that of **19** except for the absence of one glucose moiety. Instead, there were six signals, one quarternary carbon δ_C 122.5 (*s*), two methylenes δ_C 32.5 (*t*), 62.8 (*t*) and three oxygen bearing methines δ_C 82.7, 78.8, 86.3 (each *d*) of another carbohydrate. The ^1H–^1H COSY experiment revealed the sequence CH_2(6′)-CH(5′)-CH(4′)-CH(3′), all carbons bearing an oxygen. Since H-3′ showed no further couplings, e.g. toward the methylene protons of C-1′ (δ_C 32.5), we favoured a 1-desoxyfuranose moiety, connected at C-3 of the acetophenone via C-1′. The molecular formula of **20**, $C_{20}H_{26}O_{13}$, indicating eight double bond equivalents, required an additional cyclus for the molecule. The only possibility was an ether between C-2′ of the sugar moiety and C-2 or C-4 of the acetophenone. The observed chemical shift δ_C 122.5 is in good accordance with the resulting spiroketal function for C-2′. As there were NOE correlations between methyl H-8 and H-3′ and H-5′, the relative position of the spiro-moiety could be established at C-2/C-3 of the acetophenone and not at C-3/C-4. The furanose moiety was found to be α-D-fructopyranose as the were no other NOÉs in addition to H-3′ and H-5′ within the whole carbohydrate moiety.

3. Experimental

3.1. General

NMR-spectroscopy: BRUKER, $CDCl_3$, ambient temperature, 400 MHz (^1H), 100 MHz (^{13}C) for one-dimensional, 500 and 125 MHz for two-dimensional techniques, respectively; chemical shifts are given in δ values (ppm) from TMS, $CHCl_3$ for optical rotation, MeOH for UV spectroscopy; mass spectroscopy: VARIAN MAT 311, 70 eV; GC-MS was performed on a HP-1 capillary column with a G 1800A GCD system (HP).

3.2. Plant material

Adelanthus lindenbergianus (Lehm.) Mitt. was collected at the Paso Garibaldi, Tierra del Fuego in March 1997 and identified by Professor Dr. R. Mues and Professor Dr. U. Drehwald. A voucher specimen is deposited at Herbarium SAAR (No. 5336).

3.3. Extraction and isolation

The extraction scheme followed standard procedures of our group (Cullmann et al., 1993; Adam and Becker, 1994; Bungert et al., 1998). Powdered air dried plant material (600 g) was subsequently extracted with Et_2O and MeOH. The Et_2O extract (14.0 g) was chromatographed on

Sephadex LH-20 (150 × 2.5 cm i.d.) with MeOH–CH_2Cl_2 (1:1) as eluent to give five fractions. Fraction II (1.7 g) was subjected to VLC on silica (silica gel 15 μm, 60 × 35 mm i.d., stepwise with a *n*-hexane–EtOAc gradient) to yield compound **18** (4–6% EtOAc, 20 mg). Fraction III (3.5 g) was separated in the same way to yield nine fractions (III-3 (2–6% EtOAc, 239 mg), III-4 (6–12% EtOAc, 157 mg), III-5 (12–18% EtOAc, 662 mg), III-6 (18–25% EtOAc, 394 mg), fraction III-7 (25–50% EtOAc, 422 mg) and fraction III-8 (50–100% EtOAc, 222 mg). Fraction III-3, III-4 and III-6 were further purified by HPLC on silica gel (LiChrospher Si 60, 5 μm, 4 × 250), fraction III-5 and III-7 on diol-modified silica gel (LiChrospher diol 100, 5 μm, 4 × 250) and fraction III-8 on cyano-modified silicagel (Spherisorb CN. 5 μm, 4.6 × 240). Fraction III-3 gave compound **1** (74 mg, CH_2Cl_2–*n*-hexane 40:60), III-4 compound **2** (7 mg, *n*-hexane–EtOAc 90:10), III-5 compound **3** (46 mg) and **4** (5 mg) (*n*-hexane–TBME 82:18), III-5 compound **5** (16 mg) and **7** (2 mg) (*n*-hexane–EtOAc 70:30) and III-7 compound **6** (147 mg, *n*-hexane–EtOAc 70:30). Fraction III-8 gave compound **16** (6 mg) (*n*-hexane–EtOAc 60:40). Fraction IV (2.4 g) was separated by VLC on silica to yield fractions IV-2 (1.5–2% EtOAc, 255 mg), IV-3 (2–3% EtOAc, 107 mg) and IV-5 (4–9% EtOAc, 80 mg). Fractions IV-2, IV-4, IV-5 were further purified by HPLC on silica gel (LiChrospher Si 60, 5 μm, 4 × 250): *n*-hexane–CH_2Cl_2 (55:45) for **14** (102 mg) and *n*-hexane–EtOAc (89:11) for **15** (12 mg) and **17** (9 mg). The methanolic extract was evaporated in vacuo and distributed between EtOAc and H_2O. The organic layer (6.0 g) was chromatographed on Sephadex LH-20. For the EtOAc soluble fraction of the methanol extract MeOH–CH_2Cl_2 (4:1) was used as eluent to yield three fractions. Fraction II (2.1 g) was chromatographed on diol-modified silica gel via VLC with a *n*-hexane–EtOAc-gradient to three fractions II-2 (30–50% EtOAc, 335 mg) and II-3 (50–100% EtOAc, 294 mg). Fraction II-2 was further purified by HPLC on diol-modified silica gel (LiChrospher diol 100, 5 μm, 4 × 250): *n*-hexane–EtOAc (60:40) for **8** (28 mg), **9** (4 mg) and **11** (18 mg), fraction II-3: *n*-hexane–EtOAc–HCOOH (50:49:1) for **10** (3 mg), **12** (24 mg) and **13** (15 mg).

The aqueous portion of the methanolic extract was further distributed between *n*-butanol and H_2O. The organic layer (2.6 g) was chromatographed on Sephadex LH-20 with MeOH to give three fractions, I (1.71 g), II (1.80 g), III (254 mg). Fraction II was separated on diol-modified silicagel via VLC with an EtOAc–MeOH-gradient to yield four fractions (II-1–II-4). Fraction II-3 (20–35% MeOH, 415 mg) was further purified by HPLC on reversed phase (LiChrospher RP18, 5 μm, 4 × 250): MeOH–H_2O–HCOOH (89:10:1) for compound **19** (4 mg). Fraction III (254 mg) was separated by HPLC on reversed phase (LiChrospher RP18 endc., 5 μm, 250 × 4 mm): H_2O–MeOH–HCOOH (89:10:1) for **20** (21 mg).

3.3.1. 13-Hydroxy-cis-ent-cleroda-3,14-diene (1)

$[\alpha]_D^{20} = -5.2°$ ($CHCl_3$; *c* 0.5); EIMS *m/z* (rel. int.) = 290 (2) $[M]^+$, 272 (1), 257 (7), 229 (7), 191 (37), 175 (19), 161 (13), 121 (52), 107 (90), 95 (100), 81 (57), 71 (47), 55 (43); IR ν_{max}^{KBr} cm^{-1}: 3355, 2930, 2890 ; ^1H NMR ($CDCl_3$): Table 1; ^{13}C NMR ($CDCl_3$): Table 2.

3.3.2. 15-Hydroxy-cis-ent-cleroda-3,13(E)-diene (2)

$[\alpha]_D^{20} = -11.1°$ ($CHCl_3$; *c* 0.6); EIMS *m/z* (rel. int.) = 290 (1) $[M]^+$, 272 (2), 257 (3), 229 (2), 189 (3), 175 (17), 133 (21), 121 (50), 107 (100), 95 (97), 81 (48), 69 (31), 55 (40); IR ν_{max}^{KBr} cm^{-1}: 3430, 2950, 2880; ^1H NMR ($CDCl_3$): Table 1; ^{13}C NMR ($CDCl_3$): Table 2.

3.3.3. 1β,12:15,16-Diepoxy-cis-ent-cleroda-13(16),14-dien-18α,6α-olide (5)

$[\alpha]_D^{20} = -69.0°$ ($CHCl_3$; *c* 1.0) ; EIMS *m/z* (rel. int.) = 330 (8) $[M]^+$, 315 (8), 219 (4), 173 (28), 165 (12), 147 (10), 119 (11), 109 (14), 94 (100), 79 (23), 55 (14); IR ν_{max}^{KBr} cm^{-1}: 3400, 2950, 1760, 1450, 1250, 1150, 900, 850; UV λ_{max} nm: 212 (MeOH); ^1H NMR ($CDCl_3$): Table 1; ^{13}C NMR ($CDCl_3$): Table 2.

3.3.4. 1β,16:15,16-Diepoxy-cis-ent-cleroda-12,14-dien-18α,6α-olide (6)

$[\alpha]_D^{20} = -13.2°$ ($CHCl_3$; *c* 1.0); EIMS *m/z* (rel. int.) = 330 (1) $[M]^+$, 220 (18), 205 (28), 173 (61), 159 (24), 133 (16), 105 (24), 94 (100), 79 (16), 77 (14), 55 (15); IR ν_{max}^{KBr} cm^{-1}: 3500, 2950, 1775, 1500, 1400, 1250, 1000, 870; ^1H NMR ($CDCl_3$): Table 1; ^{13}C NMR ($CDCl_3$): Table 2.

3.3.5. 8β,12:15,16-Diepoxy-cis-ent-cleroda-13(16),14-dien-18α,6α-olide (7)

$[\alpha]_D^{20} = -33.8°$ ($CHCl_3$; *c* 0.012); EIMS *m/z* (rel. int.) = 330 (5) $[M]^+$, 315 (11), 219 (17); 173 (12); 147 (11), 121 (100), 95 (30), 81 (22), 67 (12), 55 (14); ^1H NMR ($CDCl_3$): Table 1; ^{13}C NMR ($CDCl_3$): Table 2.

3.3.6. 7β,12:8β,12-Diepoxy-15-hydroxy-cis-ent-cleroda-13-en-16,15:18α,6α-diolide (8)

$[\alpha]_D^{20} = +\ 10.1°$ ($CHCl_3$; *c* 1.0); CI MS *m/z* (rel. int.) = 377 (61) $[M+H]^+$, 376 (100), 358 (55), 315 (22), 249 (16), 232 (55), 217 (43), 189 (33), 145 (41), 123 (62), 110 (67), 95 (78), 81 (37); IR ν_{max}^{KBr} cm^{-1}: 3400, 2950, 1780, 1450, 1000, 800; UV λ_{max} nm: 213.5 (MeOH); ^1H NMR ($CDCl_3$): Table 1; ^{13}C NMR ($CDCl_3$): Table 2.

3.3.7. 1α-Acetoxy-8β,12-epoxy-15-hydroxy-cis-ent-cleroda-13-en-16,15:18α,6α-diolide (9)

$[\alpha]_D^{20} = -14.4°$ ($CHCl_3$; *c* 0.103); CI MS *m/z* (rel. int.) = 421 (33) $[M+H]^+$, 405 (100), 361 (56), 345 (55), 328 (25), 218 (23), 173 (20), 97 (15), 83 (15); IR ν_{max}^{KBr}

Table 1
^{1}H NMR spectral data of compounds **1**, **2**, **5**–**13**

H	**1**	**2**	**5**	**6**	**7**	H	**8**	**9**	**10**	H	**11a, b**	**12a, b**	**13a, b**
H-1α	1.92 *n.r.*[a]	1.95 *n.r.*	3.69 *dt* (3.6, 10.0)	4.07 *ddd* (2.5, 7.5,10)	1.34 *n.r.*[b]	H-1α	1.01 *n.r.*	—	3.66 *dt* (3.5, 11.5)	H-1α	1.00 *n.r.*	1.54 *n.r.*	1.59 *n.r.*
H-1β	1.72 *n.r.*	1.70 *n.r.*	—	—	1.80 *n.r.*[b]	H-1β	1.67 *n.r.*	4.90 *brs*	—	H-1β	1.72 *n.r.*	1.68 *n.r.*	1.73 *n.r*
H-2α	1.93 *n.r.*	1.96 *n.r.*	1.62 *n.r.*	1.67 *n.r.*	1.30 *n.r.*[b]	H-2α	1.44 *n.r.*	1.60 *n.r.*	1.59 *n.r.*	H-2α	1.43 *n.r.*	1.45 *n.r.*	1.50 *n.r.*
H-2β	2.08 *n.r.*	2.11 *n.r.*	1.81 *n.r.*	2.00 *n.r.*	1.65 *n.r.*[b]	H-2β	1.92 *n.r.*	1.76 *n.r.*	1.86 *n.r.*	H-2β	1.90 *n.r.*	1.77 *n.r.*	1.82 *n.r.*
H-3α	5.23 *brs*	5.26 *brs*	2.00 *n.r.*	1.35 *n.r.*	1.71 *n.r.*[b]	H-3α	1.70 *n.r.*	2.00-2.20 *n.r.*	2.10 *n.r.*	H-3α	1.70 *n.r.*	1.47 *n.r.*	1.46 *n.r.*
H-3β			2.21 *n.r.*	2.11 *n.r.*	1.90 *n.r.*[b]	H-3β	2.15 *n.r.*	2.00-2.20 *n.r.*	2.20 *n.r.*	H-3β	2.14 *n.r.*	1.88 *n.r.*	1.90 *n.r.*
H-4α	—	—	—	—	—	H-4α	—	—	—	H-4α	—	—	—
H-4β	—	—	2.33 *dd* (2.5; 11.2)	2.51 *t* (9.6)	2.30 *t* (7.0)	H-4β	2.33 *dd* (2.5, 5.2)	2.47 *d* (11.0)	2.37 *dd* (2.5, 11.2)	H-4β	2.33 *dd* (2.5, 5.2)	2.40 *n.r.*	2.40 *n.r.*
H-6α	1.03 *n.r.*	1.01 *n.r.*	—	—	—	H-6α	—	—	—	H-6α	—	—	—
H-6b	1.96 *n.r.*	2.01 *n.r.*	4.19 *d* (8.5)	4.21 *dd* (2.2, 8.0)	4.40 *dd* (3.6, 8.0)	H-6β	4.61 *d* (3.3)	4.14 *n.r.*	4.23 *d* (8.5)	H-6β	4.60 *d* (3.3), 4.62 *d* (3.3)	4.50 *n.r.*	4.47 *n.r*
H-7α	1.05 *n.r.*[b]	1.03 *n.r.*[b]	1.71 *n.r.*	1.63 *n.r.*	2.02 *n.r.*	H-7α	4.10 *d* (3.3)	2.40 *n.r.*	1.78 *n.r.*	H-7α	4.11 *d* (3.3), 4.12 *d* (3.3)	1.71 *n.r.*	1.73 *n.r.*
H-7β	1.15 *n.r.*[b]	1.18 *n.r.*[b]	2.10 *n.r.*	2.13 *n.r.*	2.24 *n.r.*	H-7β	—	—	2.15 *n.r.*	H-7β	—	2.40 *n.r.*	2.40 *n.r.*
H-8β	1.39 *n.r.*	1.43 *n.r.*	1.49 *n.r.*	1.60 *n.r.*	—	H-8	—	—	1.53 *n.r.*	H-8	—	—	1.53 *n.r.*
H-10β	1.29 *n.r.*	1.34 *n.r.*	1.50 *n.r.*	2.01 *n.r.*	1.70 *n.r.*	H-10	1.69 *n.r.*	1.93 *n.r.*	1.51 *n.r.*	H-10	1.70 *n.r.*	1.57 *n.r.*, 1.51 *n.r.*	1.49 *n.r.*, 1.50 *n.r.*
H-11α	1.44 *n.r.*[b]	1.55 *n.r.*[b]	1.80 *n.r.*	2.15 *dd* (14.0, 10.0)	1.89 *dd* (6.0, 12.5)	H-11α	1.98 *n.r.*	2.10 *n.r.*	1.82 *n.r.*	H-11α	1.71 *d* (13), 2.01 *d* (13)	1.95 *dd*, 1.90 *dd* (4.0, 13.5)	2.16 *n.r.*, 2.22 *n.r.*
H-11β	1.22 *n.r.*[b]	1.20 *n.r.*[b]	1.94 *d* (13.0)	2.24 *dd* (14.0, 8.0)	2.20 *n.r.*	H-11β	2.58 *n.r.*	2.63 *dd* (13.7, 6.2)	1.90 *n.r.*	H-11β	2.70 *d* (13), 2.50 *d* (13)	2.17 *dd* (10.5, 13.5)	1.85 *n.r.*, 2.10 *n.r.*
H-12α	1.41 *n.r.*	1.86 *n.r.*	—	5.46 *ddd* (1.8, 8.0, 10)	4.85 *dd* (6.0, 9.3)	H-12α	—	4.67 *brs*	4.91 *dd* (6.0, 9.3)	H-12α	—	4.74 *dd*, 4.70 *dd* (1.8, 10.3)	4.90 *dd*, 4.80 *dd* (10.0, 4.0)
H-12β	1.41 *n.r.*	1.86 *n.r.*	5.10 *d* (7.0)	—	—	H-12β	—	—	—	H-12β	—	—	—
H-14	5.88 *dd* (17.3, 10.7)	5.41 *t* (7.0)	6.21 *s*	5.50 *dd* (1.8, 2.6)	6.33 *s*	H-14	7.37 *s*	6.72 *s*	6.06 *s*	H-14	6.23 *s*, 6.25 *s*	6.90 *s*	5.95 *s*, 5.92 *s*
H-15a	5.02 *dd* (1.2, 10.4)	4.13 *d* (7.0)	7.33 *s*	6.72 *d* (2.6)	7.37 *s*	H-15	6.41 *s*	5.99 *brs*	—	H-15	—	6.12 *s*, 6.10 *s*	—
H-15b	5.18 *dd* (1.2, 17.3)	—	—	—	—	H-16	—	—	6.06 *s*	H-16	6.21 *s*, 6.23 *s*	—	6.11 *s*, 5.96 *s*
H-16	1.26 *s*	1.67 *s*	7.24 *s*	5.90 *s*	7.36 *s*	H-17	1.43 *s*	1.29 *s*	0.88 *d* (6.6)	H-17	1.44 *s*, 1.45 *s*	1.18 *s*	1.20 *s*, 1.19 *s*
H-17	0.71 *d* (6.6)	0.76 *d* (6.6)	0.85 *d* (6.6)	0.93 *d* (6.6)	1.31 *s*	H-19	1.57 *s*	1.29 *s*	1.40 *s*	H-19	1.55 *s*, 1.56 *s*	1.03 *s*, 1.02 *s*	1.07 *s*, 1.06 *s*
H-18	1.64 *s*	1.66 *s*	—	—	—	H-20	1.08 *s*	0.98 *s*	0.91 *s*	H-20	1.13 *s*, 1.14 *s*	1.11 *s*	1.15 *s*, 1.14 *s*
H-19	1.00 *s*	1.01 *s*	1.37 *s*	1.31 *s*	1.31 *s*	OAc	—	2.01 *s*	—	OAc	—	—	—
H-20	0.77 *s*	0.76 *s*	0.76 *s*	0.75 *s*	1.14 *s*								

[a] *n.r.* means not resolved due to overlapping of signals.
[b] α and β may be interchanged in vertical columns.

Table 2
^{13}C NMR spectral data of compounds **1**, **2**, **5**–**13**

C	1	2	5	6	7	8	9	10	11a, b	12 a, b	13 a, b
C-1	17.6 *t*	17.7 *t*	67.7 *d*	72.6 *d*	25.2 *t*	22.7 *t*	72.5 *d*	68.5 *d*	22.6 *t*	20.7 *t*	20.7 *t*
C-2	24.0 *t*	24.0 *t*	25.7 *t*	26.7 *t*	21.2 *t*	19.6 *t*	24.5 *t*	25.8 *t*	19.5 *t*	23.0 *t*	23.0 *t*
C-3	123.1 *d*	123.1 *d*	17.8 *t*	19.8 *t*	23.5*t*	15.1 *t*	14.6 *t*	17.8 *t*	15.1 *t*	18.4 *t*	18.5 *t*
C-4	139.8 *s*	139.8 *s*	45.9 *d*	46.7 *d*	48.9 *d*	50.9 *d*	46.3 *d*	45.9 *d*	50.9 *d*	42.1 *d*	42.1 *d*
C-5	36.8 *s*	36.9 *s*	40.2 *s*	39.5 *s*	39.6 *s*	40.0 *s*	39.6 *s*	40.1 *s*	39.9 *s*	40.4 *s*	40.3 *s*
C-6	37.7 *t*	37.7 *t*	81.9 *d*	83.8 *d*	83.1 *d*	82.4 *d*	83.4 *d*	81.9 *d*	82.1 *d*	82.6, 82.7 *d*	82.3, 82.4 *d*
C-7	28.7 *t*	28.8 *t*	29.9 *t*	31.2 *t*	39.6 *t*	77.8 *s*	35.6 *t*	29.9 *t*	77.9, 78.0 *s*	32.8 *t*	32.8 *t*
C-8	37.2 *d*	37.3 *d*	37.6 *d*	32.5 *d*	82.8 *s*	85.6 *s*	84.2 *s*	37.5 *d*	85.8, 85.9 *s*	85.7, 85.8 *s*	85.5, 85.8 *s*
C-9	39.8 *s*	40.1 *s*	35.2 *s*	38.4 *s*	48.2 *s*	42.3 *s*	47.5 *s*	35.3 *s*	42.2, 42.4 *s*	44.7, 45.1 *s*	45.9, 46.1 *s*
C-10	44.5 *d*	44.6 *d*	55.5 *d*	52.1 *d*	44.6 *d*	45.8 *d*	43.8 *d*	55.5 *d*	45.7, 45.8 *d*	43.8, 44.0 *d*	43.8, 44.0 *d*
C-11	31.5 *t*	36.5 *t*	45.1 *t*	38.6 *t*	50.3 *t*	51.3 *t*	45.1 *t*	43.5 *t*	52.3, 53.1 *t*	45.4, 45.8 *t*	44.6, 44.9 *t*
C-12	35.1 *t*	32.7 *t*	68.7 *d*	116.1 *d*	68.7 *d*	103.5 *s*	68.3 *d*	69.9 *d*	104.4, 104.5 *s*	69.3 *d*	70.0, 70.5 *d*
C-13	73.4 *s*	141.1 *s*	128.7 *s*	145.3 *s*	126.7 *s*	132.7 *s*	139.5 *s*	169.8 *s*	159.6, 159.8 *s*	140.4 *s*	168.8 *s*
C-14	145.2 *d*	122.8 *d*	108.8 *d*	104.8 *d*	108.6 *d*	148.4 *d*	140.4 *d*	117.6 *d*	120.7, 121.9 *d*	142.1, 142.3 *d*	116.2, 117.0 *d*
C-15	111.7 *t*	59.4 *t*	143.1 *d*	151.2 *d*	143.4 *d*	96.6 *d*	97.6 *d*	171.7 *s*	169.3, 169.5 *s*	97.0, 97.3 *d*	169.8, 169.9 *s*
C-16	27.6 *q*	16.5 *q*	138.3 *d*	103.2 *d*	139.1 *d*	167.9 *s*	170.0 *s*	97.0 *d*	97.3, 97.5 *d*	169.7 *s*	97.2, 97.3 *d*
C-17	15.8 *q*	15.9 *q*	14.2 *q*	17.7 *q*	26.0 *q*	16.1 *q*	25.3 *q*	14.2 *q*	16.1 *q*	23.4, 23.5 *q*	23.3, 23.4 *q*
C-18	19.7 *q*	19.7 *q*	178.2 *s*	178.0 *s*	178.7 *s*	178.1 *s*	177.6 *s*	178.0 *s*	177.9 *s*	176.4, 176.6 *s*	176.1, 176.2 *s*
C-19	33.0 *q*	33.0 *q*	32.1 *q*	35.5 *q*	31.0 *q*	30.0 *q*	28.9 *q*	31.9 *q*	30.0, 30.1 *q*	23.0, 23.1 *q*	23.0, 23.1 *q*
C-20	17.3 *q*	17.2 *q*	13.9 *q*	17.9 *q*	22.7 *q*	25.9 *q*	21.1 *q*	13.9 *q*	26.0, 26.1 *q*	19.7 *q*	19.7 *q*
OAc	–	–	–	–	–	–	21.8 *q* /172.2 *s*	–	–	–	–

cm^{-1}; UV λ_{max} nm: 214.0 (MeOH); ^{1}H NMR ($CDCl_3$): Table 1; ^{13}C NMR ($CDCl_3$): Table 2.

3.3.8. 1β,12-Epoxy-16-hydroxy-cis-ent-cleroda-13-en-15,16:18α,6α-diolide (**10**)

$[\alpha]_D^{20} = -21.2°$ ($CHCl_3$; *c* 0.033); CI MS *m*/*z* (rel. int.) = 363 (100) $[M+H]^+$, 335 (28), 234 (15), 219 (18), 205 (9), 173 (31), 159 (8), 94 (9), 81 (6), 55 (10); IR ν_{max}^{KBr} cm^{-1}: UV λ_{max} nm: 212.5 (MeOH); ^{1}H NMR ($CDCl_3$): Table 1; ^{13}C NMR ($CDCl_3$): Table 2.

3.3.9. Mixture I: 7β,12:8β,12-diepoxy-16α-hydroxy-cis-ent-cleroda-13-en-15,16:18α,6α-diolide (**11a**); 7β,12:8β,12-diepoxy-16β-hydroxy-cis-ent-cleroda-13-en-15,16:18α,6α-diolide (**11b**)

$[\alpha]_D^{20} = +2.1°$ ($CHCl_3$; *c* 1.0); CI MS *m*/*z* (rel. int.) = 377 (55) $[M+H]^+$, 376 (33), 358 (74), 315 (20), 249 (23), 232 (100), 217 (44), 145 (33), 123 (70),110 (66), 95 (68), 81 (22); IR ν_{max}^{KBr} cm^{-1}: 3400, 2950, 1780, 1450, 1200, 900; UV λ_{max} nm: 213.0 (MeOH); ^{1}H NMR ($CDCl_3$): Table 1; ^{13}C NMR ($CDCl_3$): Table 2.

3.3.10. Mixture II: 8β,12-epoxy-15α-hydroxy-trans-cleroda-13-en-16,15:18α,6α-diolide (**12a**); 8β,12-epoxy-15β-hydroxy-trans-cleroda-13-en-16,15:18α,6α-diolide (**12b**)

$[\alpha]_D^{20} = -4.4°$ ($CHCl_3$; *c* 1.0); CI MS *m*/*z* (rel. int.) = 363 (27) $[M+H]^+$, 347 (46), 263 (27), 233 (31), 220 (100), 175 (36), 149 (39), 133 (23), 95 (46); IR ν_{max}^{KBr} cm^{-1}: UV λ_{max} nm: 214.0 (MeOH); ^{1}H NMR ($CDCl_3$): Table 1; ^{13}C NMR ($CDCl_3$): Table 2.

3.3.11. Mixture III: 8β,12-epoxy-16α-hydroxy-trans-cleroda-13-en-16,15:18α,6α-diolide (**13a**); 8β,12-epoxy-16β-hydroxy-trans-cleroda-13-en-16,15:18α,6α-diolide (**13b**)

$[\alpha]_D^{20} = -12.0°$ ($CHCl_3$; *c* 1.0); CI MS *m*/*z* (rel. int.) = 363 (30) $[M+H]^+$, 347 (100), 235 (8), 220(10), 173 (5), 149 (6), 133 (4), 95 (11); IR ν_{max}^{KBr} cm^{-1}: UV λ_{max} nm: 213.5 (MeOH); ^{1}H NMR ($CDCl_3$): Table 1; ^{13}C NMR ($CDCl_3$): Table 2.

3.3.12. 1β-Hydroxy-eudesma-5,11-diene (**15**)

Colourless oil; $[\alpha]_D^{20} = -10.5°$ ($CHCl_3$; *c* 0.818); EIMS *m*/*z* (rel. int.) = 220 (7) $[M]^+$, 202 (11), 187 (29), 176 (15), 159 (35), 145 (33), 125 (68), 107 (100), 96 (79), 79 (47), 55 (46); IR ν_{max}^{KBr} cm^{-1} : ^{1}H NMR ($CDCl_3$): δ_H 5.30 (1H, *d*, *J* = 4.0 Hz, H-6), 4.78 (1H, *brs*, H-12), 4.58 (1H, *brs*, H-12), 3.24 (1H, *dd*, *J* = 4.0, 11.5 Hz, H-1α), 2.60 (1H, *m*, H-7), 2.43 (1H, *n.r.*, H-4), 1.81 and 1.62 (2H, *n.r.*, H-2), 1.54 (2H, *n.r.*, H-3), 1.65 and 1.55 (2H, *n.r.*, H-8), 1.57 and 1.38 (2H, *n.r.*, H-9), 1.76 (3H, *s*, H-13), 1.12 (3H, *d*, *J* = 7.9 Hz, H-15), 1.09 (3H, *s*, H-14); ^{13}C NMR ($CDCl_3$): δ_C 148.3 (*s*, C-11), 146.6 (*s*, C-5), 125.4 (*d*, C-6), 111.2 (*t*, C-12), 80.1 (*d*, C-1), 41.6 (*d*, C-7), 40.2 (*s*, C-10), 38.0 (*d*, C-4), 33.4 (*t*, C-9), 30.6 (*t*, C-3), 26.3 (*t*, C-2), 22.5 (*q*, C-15), 22.4 (*t*, C-8), 22.0 (*q*, C-13), 19.9 (*q*, C-14).

3.3.13. 1β,11-Dihydroxy-5-eudesmene (**16**)

Colourless oil; $[\alpha]_D^{20} = -21.5°$ ($CHCl_3$; *c* 0.6); ^{1}H NMR ($CDCl_3$): δ_H 5.55 (1H, *d*, *J* = 3.0 Hz, H-6), 3.30 (1H, *dd*, *J* = 4.0, 11.5 Hz, H-1α), 2.42 (1H, *n.r.*, H-4), 2.02 (1H,

n.r., H-7β), 1.80 and 1.65 (2H, *n.r.*, H-2), 1.55 (2H, *n.r.*, H-3), 1.65 and 1.58 (2H, *n.r.*, H-8), 1.65 and 1.51 (2H, *n.r.*, H-9), 1.18 (6H, *s*, H-12,H-13), 1.13 (3H, *d*, $J=7.9$ Hz, H-15), 1.07 (3H, *s*, H-14); ^{13}C NMR ($CDCl_3$): δ_C 148.9 (*s*, C-5), 123.4 (*d*, C-6), 78.3 (*d*, C-1), 73.3 (*s*, C-11), 45.5 (*d*, C-7), 40.0 (*s*, C-10), 38.6 (*d*, C-4), 34.8 (*t*, C-9), 30.8 (*t*, C-3), 27.9 (*q*, C-13), 27.1 (*q*, C-12), 26.5 (*t*, C-2), 22.2 (*q*, C-15), 20.6 (*q*, C-14), 20.1 (*t*, C-8).

3.3.14. 1β-Hydroxy-11-methoxy-5-eudesmene (17)

Colourless oil; $[\alpha]_D^{20}=-53.6^\circ$ ($CHCl_3$; *c* 0.606); ^{1}H NMR ($CDCl_3$): δ_H 5.47 (1H, *d*, $J=3.0$ Hz, H-6), 3.31 (1H, *dd*, $J=4.0$, 11.5 Hz, H-1α), 3.17 (3H, *s,* OMe), 2.42 (1H, *n.r.*, H-4), 2.22 (1H, *n.r.*, H-7β), 1.80 and 1.64 (2H, *n.r.*, H-2), 1.54 (2H, *n.r.*, H-3), 1.55 and 1.50 (2H, *n.r.*, H-8), 1.62 and 1.49 (2H, *n.r.*, H-9), 1.08 (6H, *s*, H-12, H-13), 1.12 (3H, *d*, $J=7.9$ Hz, H-15), 1.06 (3H, *s*, H-14); ^{13}C NMR ($CDCl_3$): δ_C 147.6 (*s*, C-5), 124.1 (*d*, C-6), 77.9 (*d*, C-1), 77.2 (*s*, C-11), 48.8 (*q,* OMe) 41.8 (*d*, C-7), 40.0 (*s*, C-10), 38.5 (*d*, C-4), 34.9 (*t*, C-9), 30.9 (*t*, C-3), 26.5 (*t*, C-2), 22.8 (2*q*, C-12, C-13), 22.2 (*q*, C-15), 20.8 (*q*, C-14), 19.7 (*t*, C-8).

3.3.15. 3,4-Seco-lupa-4(23),20(29)-dien-3,28-dicarboxylic acid dimethyl ester (18)

Colourless oil; $[\alpha]_D^{20}=+\ 10.3^\circ$ ($CHCl_3$; *c* 1.0); EIMS *m/z* (rel. int.) = 498 (40) $[M]^+$, 417 (69), 357 (51), 327 (15), 279 (34), 229 (27), 201 (20), 189 (64), 149 (100), 121 (64)104 (51), 84 (83), 67 (76), 55 (97); IR ν_{max}^{KBr} cm^{-1}: 3500, 2950, 1750, 1650, 1450, 1180, 1000, 850; ^{1}H NMR ($CDCl_3$): δ_H 4.81 (1H, *brs*, H-23a), 4.71, 1H, *brs*, H-29a), 4.61 (1H, *brs*, H-23b); 4.58 (1H, *brs*, H-29b), 3.64 (3H, *s*, OMe), 3.62 (3H, *s*, OMe), 1.69 (3H, *s*, H-24), 1.66 (3H, *s*, H-30), 0.95 (3H, *s*, H-26), 0.93 (3H, *s*, H-27), 0.80 (3H, *s*, H-25); ^{13}C NMR ($CDCl_3$): 176.0 (*s*, C-28), 174.5 (*s*, C-3), 150.4 (*s*, C-20), 147.5 (*s*, C-4), 113.3 (*t*, C-23), 109.6 (*t*, C-29), 56.6 (*s*, C-17), 51.4 (*q*, OMe), 51.2 (*q*, OMe), 50.4 (*d*, C-9), 49.4 (*d*, C-19), 46.9 (*d*, C-18), 42.8 (*s*, C-14), 40.8 (*d*, C-5), 40.4 (*s*, C-8), 39.3 (*s*, C-10), 38.3 (*d*, C-13), 36.9 (*t*, C-22), 34.1 (*t*, C-7), 32.9 (*t*, C-2), 32.1 (*t*, C-16), 30.6 (*t*, C-15), 29.7 (*t*, C-21), 28.4 (*t*, C-6), 25.5 (*t*, C-12), 24.6 (*t*, C-1), 23.2 (*q*, C-24), 21.5 (*t*, C-11), 20.1 (*q*, C-25), 19.4 (*q*, C-30), 15.9 (*q*, C-26), 14.6 (*q*, C-27).

3.3.16. 2,4,6-Trihydroxyacetophenone-2-O-(2′), 3-C-(1′)1′-desoxy-β-D-fructofuranoside-5-C-α-D-glucopyranoside (20)

Colourless crystals; FAB$^+$ MS *m/z* (rel. int.) = 475 (21) $[M+H]^+$, 440 (5), 402 (15), 302 (16), 241 (26), 208 (100); UV λ_{max} nm: 229.7, 286.3, 333.7 ($MeOH/H_2O$: 20/80); ^{1}H NMR ($CDCl_3$): δ_H 4.87 (1H, *d*, $J=9.8$ Hz, H-1″), 4.19 (1H, *d*, $J=3.0$ Hz, H-3′), 4.07 (1H, *n.r.*, H-5′), 4.01 (1H, *dd*, $J=3.0$, 5.5 Hz, H-4′), 3.87 (1H, *n.r.*, H-2″), 3.82 (2H, *n.r.*, H-6″), 3.70 (2H, *n.r.*, H-6′), 3.50–3.40 (3H, *n.r.*, H-3″, H-4″, H-5″), 3.43 (1H, *d*, $J=16.0$ Hz, H-1′α), 2.93 (1H, *d*, $J=16.0$ Hz, H-1′β), 2.59 (3H, *s*, H-8); ^{13}C NMR ($CDCl_3$): δ_C 203.5 (*s*, C-7), 163.9 (*s*, C-6), 162.1 (*s*, C-2), 160.6 (*s*, C-4), 122.5 (*s*, C-2′), 105.3 (*s*, C-5), 104.6 (*s*, C-3), 102.3 (*s*, C-1), 86.3 (*d*, C-5′), 82.7 (*d*, C-3′), 82.5 (*d*, C-5″), 79.7 (*d*, C-3″), 78.8 (*d*, C-4′), 76.3 (*d*, C-1″), 73.8 (*d*, C-2″), 71.3 (*d*, C-4″), 62.8 (*t*, C-6′), 62.2 (*t*, C-6″), 32.5 (*t*, C-1′), 31.4 (*q*, C-8).

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