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Two highly oxygenated eudesmanes and 10 lignans from *Achillea holosericea*

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Abstract

Two new highly oxygenated eudesmanes and 10 known lignans were isolated from the aerial parts of *Achillea holosericea*. Their structures were elucidated by extensive application of one- and two-dimensional ^{1}H and ^{13}C NMR spectroscopy. © 2002 Elsevier Science Ltd. All rights reserved.

Keywords: *Achillea holosericea*; Asteraceae; Sesquiterpenes; Eudesmanes; Lignans

1. Introduction

Members of the genus *Achillea* (family Asteraceae, tribe Anthemideae, subtribe Achilleinae) are common in the Mediterranean area, Eurasia and North Africa. Several species are occasionally cultivated and a few species, e.g. *Achillea millefolium* L., are naturalized in the western hemisphere (Anderberg, 1995). Aerial parts of different species of this genus are widely used in folk medicine for the preparation of herbal teas with anti-phlogostic and spasmolytic activity (Wichtl, 1994); extracts exhibit pharmacological activities including anti-bacterial (Mishurova et al., 1985), anti-inflammatory (Goldberg et al., 1969) and antiallergic (Orkiszewska et al., 1985) properties. Many species have been examined chemically for flavonoids (Valant-Vetschera and Wollenweber, 1988; Ahmed et al., 1989) and sesquiterpene lactones (Linde and Ragab, 1967; Rustaiyan et al., 1987; Stefanovic et al., 1989; Rucker et al., 1990; Ulubelen et al., 1990).

In a continuation of our chemical investigation of the genus *Achillea* (Ahmed et al., 1990, 1995; Balboul et al., 1997), we studied the secondary metabolites constituents of *Achillea holosericea* Sibth. & Sm. collected from Greece.

2. Results and discussion

Fractionation of the MeOH–CH_2Cl_2 (1:1) extract of the aerial parts of this species on silica gel and Sephadex LH-20 columns afforded two new highly oxygenated eudesmanes (**1**, **2**) and 10 known lignans. One of the new sesquiterpene derivatives (**1**) (3β-acetoxy,5α,11,12,13-tetrahydroxyeudesm-4(15)-ene) was obtained after fractionation on a Sephadex LH-20 column and found to have a molecular formula $C_{17}H_{28}O_6$ as calculated from high resolution negative FABMS spectrum, *m*/*z* 327.18145. Acetylation of **1** yielded the corresponding 3β,12,13-triacetyl derivative (**1a**). High resolution FABMS of **1a** supported the $C_{21}H_{32}O_8$ molecular formula $[M+H]^+$ *m*/*z* 413.21592 (calc. 413.21754). For structure elucidation of the sesquiterpene **1** we used the acetylated derivative **1a**. The ^{1}H NMR spectrum indicated the following groups: four CH_3 groups (three adjacent to carbonyl group), two OCH_2 groups and one

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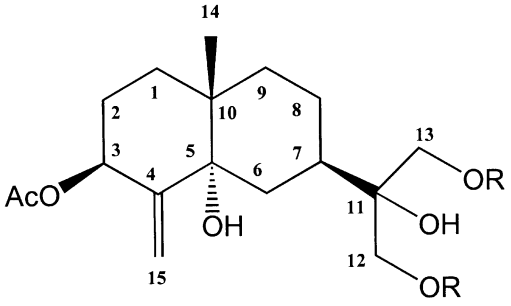
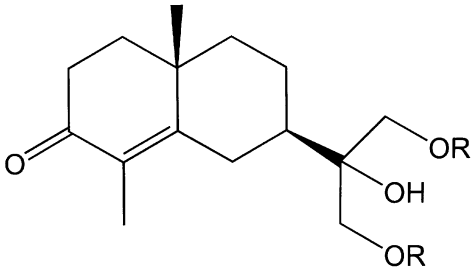
terminal $=CH_2$, together with 12 additional methylene and methine protons. The ^{13}C NMR spectrum indicated the presence of four CH_3, seven sp^3 CH_2 (two of them connected to oxygen atoms), one sp^2 CH_2, one sp^3 CH and one sp^3 OCH groups. The signals of the seven quaternary carbon atoms can be easily assigned to the three O-acetyl C=O groups, one sp^2 carbon, two oxygenated sp^3 carbons and one shielded sp^3 carbon. These data and the molecular formula indicate a structure with two rings as depicted in Fig. 1. Unambiguous ^1H and ^{13}C NMR signal assignments were achieved on the basis of ^1H–^1H COSY, HMQC and HMBC (optimized for 7 Hz long-range couplings) measurements. The differentiation between the two oxygenated quaternary carbon signals (74.2 and 76.2) was assigned on the basis of HMBC responses CH_3-14/C-5 and $H_2C(12)$/C-11, respectively. The *trans* ring junction was proven from NOESY responses of the Me-14 protons with H_{ax}-2, H_{ax}-6, H_{ax}-8, respectively. The NOESY crosspeaks OH/H-3 and OH/H-7 revealed the equatorial positions of the substituents attached to C-3 and C-7. Similarly, the ^1H and ^{13}C NMR spectral data of compound **1** were assigned by $^1H-^1H$ COSY, HMQC and HMBC.

The high resolution CIMS of compound **2** displayed the $[M+H]^+$ ion at m/z 269.17564, (calc. 269.17528),



1 R = H

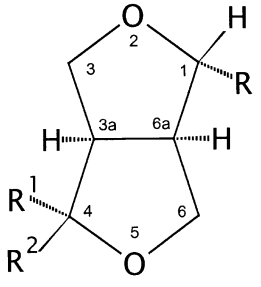
1a R = Ac

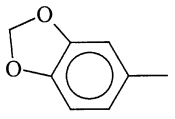


2 R = H

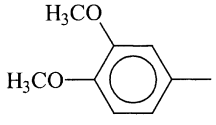
2a R = Ac

	R (')	R^1 (")	R^2 (")	trivial name
3	Ar^1	Ar^2	H	-
4	Ar^1	H	Ar^4	-
5	Ar^1	Ar^4	H	Ashantin
6	Ar^3	H	Ar^4	Episesartemin B
7	Ar^3	Ar^4	H	Sesartemin
8	Ar^2	H	Ar^2	Epieudesmin
9	Ar^4	H	Ar^4	Epiyangambin
10	Ar^4	Ar^4	H	Yangambin
11	Ar^4	Ar^2	H	-
12	Ar^4	H	Ar^2	-

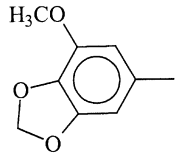




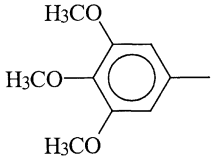
Ar^1



Ar^2



Ar^3



Ar^4

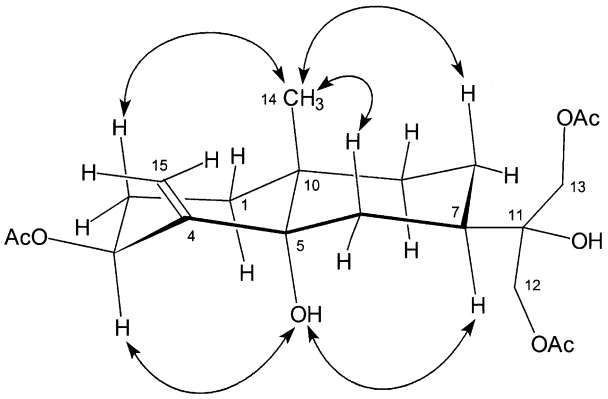


Fig. 1. Stereo projection of **1a**. Double arrows on the formula indicate significant proximities.

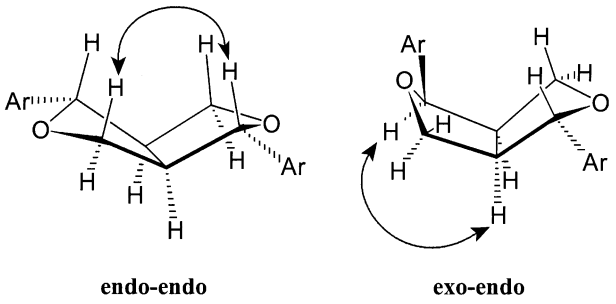


Fig. 2. Stereochemistry of *cis*- and *trans*-1,4-diaryltetrahydrofurofurans. Double arrows indicate NOE interactions.

which correlated with a molecular formula of $C_{15}H_{24}O_4$ for **2**. The ^1H NMR indicated two CH_3 moieties and two OCH_2 groups, whereas the ^{13}C NMR showed two methyl groups, one sp^3 CH, seven sp^3 CH_2 (two of them connected to oxygen atoms), and five quaternary carbon atoms. The signals at δ 199.2, 129.0 and 162.0 are characteristic for an α,β-unsaturated ketone, whereas the signals at δ 36.1 and 74.7, respectively, were in accordance with two sp^3 carbon atoms. The latter should be oxygen substituted. The ^1H and ^{13}C NMR assignments are supported with ^1H–^1H COSY, HMQC and HMBC measurements. The H-7 signal showed two $J(H_{ax,}H_{ax})$ couplings in accord with the equatorial position of the substituent at C-7. Comparison of the chemical shift of C-8 (22.1) with the corresponding value of 20.9 measured for C-8 in **1**, strongly supported the *cis* arrangement of CH_3-14 and the substituent attached to C-7. Acetylation of **2** gave the diacetyl derivative **2a**. Its NMR data are given in Section 3.

The structures of the ten lignans were deduced from their complete ^1H and ^{13}C NMR signal assignment, moreover stereochemistry were determined utilizing ^1H, ^1H–COSY, HMQC, HMBC and NOESY experiments. In the 1,4-diaryl-tetrahydrofurans the individual oxolane rings adopt envelope conformations where the oxygens are the out-of-plane atoms. The bulky aryl groups are pseudo-equatorial disposed. The stereochemistry of the *cis*-1,4-diaryl-lignans **3**, **5**, **7**, **10** and **11** corresponds to an "endo–endo" structure, i.e. endo positions for both oxygen atoms relative to the second fused five-ring. In the case of the corresponding "endo–exo" *trans* isomers **4**, **6**, **8**, **9** and **12** one oxygen is endo to the second ring, the second one exo. Besides, the ^1H chemical shifts, $^3J(H,H)$ couplings and the NOESY responses proved to be very useful for the differentation of *cis* and *trans* isomers. The H-4/H-6a cross-peak in the NOESY spectra proved the *trans* "endo–exo" structure of compounds **5**, **7**, **11**, **12** and **15** (Fig. 2). Data not previously reported are given in Section 3.

3. Experimental

3.1. General

NMR spectra were recorded in $CDCl_3$ and acetone-d_6 at 300 K using a Bruker Avance DRX-500 spectrometer. Chemical shifts are given on the δ-scale. The pulse programs of the NMR experiments were taken from the Bruker software library. MS measurements were run on Finnigan MAT 8430 and Micromass VG-ZAB-E instruments.

3.2. Plant material

The plant material of *A. holosericea* was collected during the flowering stage, in July 1996, on the mountain Parnitha at Attiki, Greece. Voucher specimens were identified by Dr. T. Constantinids, Institute of Botany, University of Patras and are deposited in the Laboratory Pharmacognosy, University of Athens. (No. OT-6 and OT-7, respectively).

3.3. Extraction and isolation

The aerial parts of *A. holosericea* (800 g) were extracted with methanol-dichloromethane (1:1, 4 l, 24 h) and the solvent was evaporated under reduced pressure. The extract (25 g, 31%) was fractionated by column chromatography on silica gel eluted with dichloromethane-*n*-hexane step gradient. The first two fractions (*n*-hexane 100%, 2 l, 8 g) and (*n*-hexane-dichloro-methane 75:25, 2 l, 4 g) contained hydrocarbons. While the third fraction (*n*-hexane-dichloromethane 1:1, 2 l, 2.5 g) was purified on a Sephadex LH-20 column (*n*-hexane-dichloromethane-methanol 6:5:1) to give a complex mixture of lignans which was separated by seven TLC runs (*n*-hexane-diethyl ether 1:1), to give compound **3** (12 mg; Greger and Hofer, 1980), compound **4** (10 mg; Hofer and Scholm, 1981), ashantin **5** (13 mg; Greger and Hofer, 1980), sesartermin B **6** (9 mg) and episesartemin B **7** (16 mg; Greger and Hofer, 1980), epieudesmin **8** (12 mg; Nishibe et al., 1984), epiyangambin **9** (11 mg; Greger and Hofer,

1980), The fourth fraction (*n*-hexane-dichloromethane 1:3, 2 l) gave yangambin **10** (18 mg; Tsukamoto et al., 1984), compound **11** (12 mg) and **12** (10 mg; Miyazawa et al., 1992, 1995), which were isolated by TLC (*n*-hexane-diethyl ether 1:2, double run). The last fraction (dichloromethane 100%, 2 l) was subjected to further fractionation on a Sephadex LH-20 column to give **1** (18 mg) and an impure fraction, which was purified on HPLC (methanol–water 3:1) to give **2** (12 mg).

3.3.1. 3β-Acetoxy,5α,11,12,13-tetrahydroxy-eudesm-4(15)-ene (*1*)

$[\alpha]_D^{25}$ + 6.9° ($CHCl_3$, $c = 0.42$); IR ($CHCl_3$) cm^{-1}: 3431, 2929, 1647, 1377, 1258, 1045; ^1H NMR ($CDCl_3$, 500 MHz) δ: 5.72 (1H, *dd*, *J* = 6, 10 Hz, H-3), 4.82 (1H, *s*, H-15), 4.78 (1H, *s*, H-15′), 3.64 (4H, *m*, H-12, H-13), 2.17 (1H, *m*, H-7), 2.11 (3H, *s*, 3-OAc), 1.94 (1H, *dd*, *J* = 10, 9 Hz, H_{ax}-1), 1.90 (1H, *m*, H_{ax}-2), 1.73 (1H, *t*, *J* = 10 Hz, H_{ax}-9), 1.64 (3H, *m*, H_{eq}-2, H-6), 1.49 (1H, *m*, H_{eq}-8), 1.39 (1H, *m*, H_{ax}-8), 1.19 (1H, *d*, *J* = 10 Hz, H_{eq}-9), 1.11 (1H, *d*, *J* = 10 Hz, H_{eq}-1), 0.82 (3H, *s*, CH_3-14); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 171.1 (*s*, 3-OAc), 150.3 (*s*, C-4), 104.7 (*t*, C-15), 76.4 (*s*, C-5), 76.0 (*s*, C-11), 72.9 (*d*, C-3), 64.5 (*t*, C-12, C-13), 37.9 (*s*, C-10), 35.9 (*d*, C-7), 33.9 (*t*, C-9), 33.3 (*t*, C-1), 30.6 (*t*, C-6), 28.6 (*t*, C-2), 21.4 (*q*, 3-OAc), 20.9 (*t*, C-8), 20.1 (*q*, C-14); negative HRCIMS $[M–H]^+$ *m*/*z* 327.18145 (calc for $C_{17}H_{27}O_6$, 327.18076).

3.3.2. 3β,12,13-Triacetoxy-5α,11-dihydroxy-eudesm-4(15)-ene (*1a*)

IR ($CHCl_3$) cm^{-1}: 3445, 2956, 1738, 1650, 1462, 1376, 1244, 1040; ^1H NMR ($CDCl_3$, 500 MHz) δ: 5.72 (1H, *dd*, *J* = 6, 12 Hz, H-3), 4.87 (1H, *d*, *J* = 2 Hz, H-15), 4.80 (1H, *d*, *J* = 2 H, H-15′), 4.22-4.13 (4H, *m*, H-12, H-13), 2.84 (1H, *s*, 5-OH), 2.30 (1H, *tt*, *J* = 4, 12 Hz, H-7), 2.13 (3H, *s*, 3-OAc), 2.12 (6H, *s*, 12-OAc,13-OAc), 1.99 (1H, *tm*, *J* = 13 Hz, H_{ax}-1), 1.93 (1H, *tm*, *J* = 13 Hz, H_{eq}-2), 1.80 (1H, *t*, *J* = 12 Hz, H_{ax}-6), 1.78 (1H, *td*, *J* = 4, 13 Hz, H_{ax}-9), 1.68 (1H, *qd*, *J* = 3, 12 Hz, H_{ax}-2), 1.62 (1H, *dd*, *J* = 4, 12 Hz, H_{eq}-6), 1.48 (2H, *m*, H-8), 1.25 (1H, *dd*, *J* = 4, 13 Hz, H_{eq}-9), 1.16 (1H, *tm*, *J* = 13.Hz, H_{eq}-1), 0.86 (3H, *s*, CH_3-14); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 171.3 (*s*, 12-OAc, 13-OAc), 170.6 (*s*, 3-OAc), 149.7 (*s*, C-4), 105.4 (*t*, C-15), 76.2 (*s*, C-5), 74.2 (*s*, C-11), 72.5 (*d*, C-3), 65.9 (*t*, C-12, C-13), 37.9 (*s*, C-10), 36.5 (*d*, C-7), 33.7 (*t*, C-9), 33.3 (*t*, C-1), 30.9 (*t*, C-6), 28.7 (*t*, C-2), 21.4 (*q*, 3-OAc), 21.1 (*q*, 12-OAc, 13-OAc), 21.0 (*t*, C-8), 20.1 (*q*, C-14); HRFABMS $[M+H]^+$ *m*/*z* 413.21592 (calc for $C_{21}H_{33}O_8$, 413.21754).

3.3.3. 3-Oxo,11,12,13-trihydroxy-eudesm-4-ene (*2*)

$[\alpha]_D^{25}$ + 21.8° ($CHCl_3$, $c = 0.17$); IR ($CHCl_3$) cm^{-1}: 3443, 1710, 1462, 1377, 1260, 1045; ^1H NMR ($CDCl_3$, 500 MHz) δ: 3.65–3.60 (4H, *m*, H-12, H-13), 2.83 (1H, *tm*, *J* = 13 Hz, H_{eq}-6), 2.51 (1H, d*dd*, *J* = 7, 13, 17 Hz, H_{ax}-2), 2.39 (1H, *dt*, *J* = 4, 17 Hz, H_{eq}-2), 1.99 (1H, *tm*, *J* = 13 Hz, H_{ax}-6), 1.77 (3H, *s*, CH_3-15), 1.75 (2H, *m*, H-1), 1.70 (1H, *dd*, *J* = 3, 12 Hz, H_{eq}-9), 1.66 (1H, *tm*, *J* = 12 Hz, H_{eq}-8), 1.65 (1H, *tm*, *J* = 13 Hz, H-7), 1.56 (1H, *qm*, *J* = 12 Hz, H_{ax}-8), 1.37 (1H, *td*, *J* = 3, 12 Hz, H_{ax}-9), 1.20 (3H, *s*, CH_3-14); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 199.4 (*s*, C-3), 162.2 (*s*, C-5), 129.2 (*s*, C-4), 74.7 (*s*, C-11), 66.2 (*t*, C-13), 65.7 (*t*, C-12), 43.5 (*d*, C-7), 42.0 (*t*, C-9), 37.5 (*t*, C-1), 36.1 (*s*, C-10), 33.9 (*t*, C-2), 28.1 (*t*, C-6), 22.6 (*q*, C-14), 22.1 (*t*, C-8), 11.1 (*q*, C-15); HRCIMS $[M+H]^+$ *m*/*z* 269.17564 (calc. for $C_{15}H_{25}O_6$, 269.17528).

3.3.4. 3-Oxo,12,13-diacetoxy,11-hydroxy-eudesm-4-ene (*2a*)

IR ($CHCl_3$) cm^{-1} : 3490, 1745, 1715, 1260; ^1H NMR ($CDCl_3$, 500 MHz) δ: 4.25–4.15 (4H, *m*, H-12, H-13), 2.82 (1H, *tm*, *J* = 13 Hz, H_{eq}-6), 2.51 (1H, d*dd*, *J* = 7, 13, 17 Hz, H_{ax}-2), 2.40 (1H, *dt*, *J* = 4, 17 Hz, H_{eq}-2), 2.10 (6H, *s*, 12-OAc, 13-OAc), 1.78 (3H, *s*, CH_3-15), 1.22 (3H, *s*, CH_3-14); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 199.2 (*s*, C-3), 161.4 (*s*, C-5), 129.4 (*s*, C-4), 73.9 (*s*, C-11), 42.8 (*d*, C-7), 41.9 (*t*, C-9), 37.4 (*t*, C-1), 36.0 (*s*, C-10), 33.9 (*t*, C-2), 27.8 (*t*, C-6), 22.5 (*q*, C-14), 21.7 (*t*, C-8), 20.0 (*q*, OAc), 11.1 (*q*, C-15); HRFABMS $[M+H]^+$ *m*/*z* 353.19607 (calc. for $C_{19}H_{29}O_6$, 353.19641).

3.3.5. (*3*)

^1H NMR ($CDCl_3$, 500 MHz) δ: 6.90–6.80 (6H, *m*, H-2′, H-5′, H-6′, H-2″, H-5″, H-6″), 5.96 (2H, *s*, OCH_2O), 4.75 (1H, *d*, *J* = 4.4 Hz, H-4), 4.74 (1H, *d*, *J* = 4.4 Hz, H-1), 4.26 (2H, *dd*, *J* = 6.9, 9.2 Hz, $H_α$-3, $H_α$-6), 3.91 (3H, *s*, 3″-OCH_3), 3.89 (3H, *s*, 4″-OCH_3), 3.89 (2H, *dd*, *J* = 3.6, 9.2 Hz, $H_β$-3, $H_β$-6), 3.09 (2H, *m*, H-3a, H-6a); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 149.5 (*s*, C-3″), 148.9 (*s*, C-4″), 148.2 (*s*, C-3′), 147.3 (*s*, C-4′), 135.3 (*s*, C-1′), 133.7 (*s*, C-1″), 119.6 (*d*, C-6′), 118.5 (*d*, C-6″), 111.3 (*d*, C-5″), 109.4 (*d*, C-2″), 108.4 (*d*, C-5′), 106.7 (*d*, C-2′), 101.3 (*t*, OCH_2O), 86.0 (*d*, C-1, C-4), 72.0 (*t*, C-6), 71.9 (*t*, C-3), 56.2 (*q*, 4″-OCH_3), 56.1 (*q*, 3″-OCH_3), 54.6 (*d*, C-6a), 54.4 (*d*, C-3a).

3.3.6. (*4*)

^1H NMR ($CDCl_3$, 500 MHz) δ: 6.90–6.80 (3H, *m*, H-2′, H-5′, H-6′), 6.59 (2H, *s*, H-2″,6″), 5.96 (2H, *s*, OCH_2O), 4.86 (1H, *d*, *J* = 5.6 Hz, H-4), 4.44 (1H, *d*, *J* = 7.0 Hz, H-1), 4.13 (1H, *dd*, *J* = 0.9, 9.4 Hz, $H_β$-6), 3.89 (6H, *s*, 3″, 5″-OCH_3), 3.86 (3H, *s*, 4″-OCH_3), 3.85 (2H, *m*, $H_α$-3, $H_α$-6), 3.36 (1H, *m*, H-3a), 3.34 (1H, *m*, $H_β$-3), 2.89 (1H, *m*, H-6a); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 153.5 (*s*, C-3″, C-5″), 148.2 (*s*, C-3′), 147.4 (*s*, C-4′), 137.2 (*s*, C-4″), 135.3 (*s*, C-1′), 134.3 (*s*, C-1″), 119.8 (*d*, C-6′), 108.4 (*d*, C-5′), 106.7 (*d*, C-2′), 102.8 (*d*, C-2″,6″), 101.3 (*t*, OCH_2O), 87.9 (*d*, C-1), 82.4 (*d*, C-4), 71.2 (*t*, C-6), 70.0 (*t*, C-3), 61.1 (*q*, 4″-OCH_3), 56.4 (*q*, 3″, 5″-OCH_3), 54.7 (*d*, C-6a), 50.3 (*d*, C-3a).

*3.3.7. Ashantin (**5**)*

^{1}H NMR ($CDCl_3$, 500 MHz) δ: 6.86 (1H, *d*, *J* = 1.5 Hz, H-2′), 6.81 (1H, *dd*, *J* = 1.5, 8.0 Hz, H-6′), 6.79 (1H, *d*, *J* = 8.0 Hz, H-5′), 6.57 (2H, *s*, H-2″,6″), 5.96 (2H, *s*, OCH_2O), 4.75 (2H, *d*, *J* = 4.5 Hz, H-1, H-4), 4.29 (1H, *dd*, *J* = 6.7, 9.2 Hz, $H_α$-3), 4.27 (1H, *dd*, *J* = 6.7, 9.2 Hz, $H_α$-6), 3.92 (1H, *dd*, *J* = 3.6, 9.2 Hz, $H_β$-3), 3.90 (1H, *dd*, *J* = 3.6, 9.2 Hz, $H_β$-6), 3.88 (6H, *s*, 3″, 5″-OCH_3), 3.84 (3H, *s*, 4″-OCH_3), 3.08 (2H, *m*, H-3a, H-6a); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 153.6 (*s*, C-3″, C-5″), 148.2 (*s*, C-3′), 147.3 (*s*, C-4′), 137.7 (*s*, C-4″), 137.0 (*s*, C-1″), 135.2 (*s*, C-1′), 119.5 (*d*, C-6′), 108.4 (*d*, C-5′), 106.7 (*d*, C-2′), 103.0 (*d*, C-2″,6″), 101.3 (*t*, OCH_2O), 86.2 (*d*, C-4), 85.9 (*d*, C-1), 72.2 (*t*, C-3), 71.9 (*t*, C-6), 61.0 (*q*, 4″-OCH_3), 56.4 (*q*, 3″, 5″-OCH_3), 54.6 (*d*, C-3a), 54.4 (*d*, C-6a).

*3.3.8. Episesartemin B (**6**)*

^{1}H NMR ($CDCl_3$, 500 MHz) *δ:* 6.58 (2H, *s*, H-2″, 6″), 6.57 (1H, *d*, *J* = 1.4, Hz, H-6′), 6.56 (1H, *d*, *J* = 1.5 Hz, H-2′), 5.97 (2H, *s*, OCH_2O), 4.86 (1H, *d*, *J* = 5.6 Hz, H-4), 4.42 (1H, *d*, *J* = 7.0 Hz, H-1), 4.14 (1H, *dd*, *J* = 0.9, 9.4 Hz, $H_β$-6), 3.93 (3H, *s*, 5′-OCH_3), 3.89 (6H, *s*, 3″, 5″-OCH_3), 3.88 (2H, *m*, $H_α$-3, $H_α$-6), 3.87 (3H, *s*, 4″-OCH_3), 3.36 (1H, *m*, H-3a), 3.34 (1H, *m*, $H_β$-3), 2.89 (1H, *m*, H-6a); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 153.4 (*s*, C-3″, C-5″), 149.3 (*s*, C-3′), 143.9 (*s*, C-5′), 137.1 (*s*, C-4″), 136.0 (*s*, C-1′), 135.0 (*s*, C-4′), 134.2 (*s*, C-1″), 105.8 (*d*, C-6′), 102.8 (*d*, C-2″,6″), 101.7 (*t*, OCH_2O), 100.4 (*d*, C-2′), 87.9 (*d*, C-1), 82.4 (*d*, C-4), 71.3 (*t*, C-6), 70.0 (*t*, C-3), 61.1 (*q*, 4″-OCH_3), 56.9 (*q*, 5′-OCH_3), 56.4 (*q*, 3″, 5″-OCH_3), 54.8 (*d*, C-6a), 50.2 (*d*, C-3a).

3.3.9. Sesartemin (7)

^{1}H NMR ($CDCl_3$, 500 MHz) δ: 6.57 (2H, *s*, H-2″, H-5″), 6.55 (1H, *d*, *J* = 1.5, Hz, H-6′), 6.53 (1H, *d*, *J* = 1.5 Hz, H-2′), 5.97 (2H, *s*, OCH_2O), 4.74 (2H, *d*, *J* = 4.5 Hz, H-1, H-4), 4.30 (1H, *dd*, *J* = 6.7, 9.2 Hz, $H_α$-3), 4.27 (1H, *dd*, *J* = 6.7, 9.2 Hz, $H_α$-6), 3.93 (3H, *s*, 5′-OCH_3), 3.93 (1H, *dd*, *J* = 3.6, 9.2 Hz, $H_β$-3), 3.90 (1H, *dd*, *J* = 3.6, 9.2 Hz, $H_β$-6), 3.88 (6H, *s*, 3″, 5″-OCH_3), 3.85 (3H, *s*, 4″-OCH_3), 3.08 (2H, *m*, H-3a, H-6a); ^{13}C NMR ($CDCl_3$, 125 MHz) *δ:* 153.4 (*s*, C-3″, C-5″), 149.1 (*s*, C-3′), 143.6 (*s*, C-5′), 137.5 (*s*, C-4″), 136.7 (*s*, C-1″), 135.8 (*s*, C-1′), 134.6 (*s*, C-4′), 105.6 (*d*, C-6′), 102.8 (*d*, C-2″), 101.5 (*t*, OCH_2O), 100.0 (*d*, C-2′), 86.0 (*d*, C-1), 85.8 (*d*, C-4), 72.0 (*t*, C-3), 71.8 (*t*, C-6), 60.8 (*q*, 4″-OCH_3), 56.7 (*q*, 5′-OCH_3), 56.2 (*q*, 3″, 5″-OCH_3), 54.3 (*d*, C-3a, C-6a).

*3.3.10. Epieudesmin (**8**)*

^{1}H NMR ($CDCl_3$, 500 MHz) δ: 6.98-6.85 (6H, *s*, H-2′, H-5′, H-6′, H-2″, H-5″, H-6″), 4.89 (1H, *d*, *J* = 5.6 Hz, H-4), 4.46 (1H, *d*, *J* = 7.0 Hz, H-1), 4.14 (1H, *dd*, *J* = 0.9, 9.5 Hz, $H_β$-6), 3.92-3.89 (12H, *s*, 3′, 4′, 3″, 4″-OCH_3), 3.86 (2H, *m*, $H_α$-3, $H_α$-6), 3.36 (1H, *m*, H-3a), 3.33 (1H, *m*, $H_β$-3), 2.93 (1H, *m*, H-6a); *δ:* ^{13}C NMR ($CDCl_3$, 125 MHz) *δ:* 149.5 (*s*, C-3′), 149.1 (*s*, C-3″), 149.0 (*s*, C-4′), 148.2 (*s*, C-4″), 133.9 (*s*, C-1′), 131.2 (*s*, C-1″), 118.7 (*d*, C-6′), 117.9 (*d*, C-6″), 111.2 (*d*, C-5′, C-5″), 109.4 (*d*, C-2′), 109.2 (*d*, C-2″), 87.9 (*d*, C-1), 82.3 (*d*, C-4), 71.2 (*t*, C-6), 70.0 (*t*, C-3), 56.1 (*q*, 3′, 4′, 3″, 4″-OCH_3), 54.7 (*d*, C-6a), 50.4 (*d*, C-3a).

*3.3.11. Epiyangambin (**9**)*

^{1}H NMR ($CDCl_3$, 500 MHz) δ: 6.60 (4H, *s*, H-2′, H-6′, H-2″, H-6″), 4.87 (1H, *d*, *J* = 5.6 Hz, H-4), 4.45 (1H, *d*, *J* = 7.0 Hz, H-1), 4.17 (1H, *dd*, *J* = 0.9, 9.5 Hz, $H_β$-6), 3.89-3.84 (18H, *s*, 3′, 4′, 5′, 3″, 4″, 5″-OCH_3), 3.90 (2H, *m*, $H_α$-3, $H_α$-6), 3.37 (1H, *m*, H-3a), 3.36 (1H, *m*, $H_β$-3), 2.93 (1H, *m*, H-6a); *δ:* ^{13}C NMR ($CDCl_3$, 125 MHz) *δ:* 153.4 (*s*, C-3′, C-5′), 153.2 (*s*, C-3″, C-5″), 137.6 (*s*, C-4′), 137.0 (*s*, C-4″), 136.8 (*s*, C-1′), 134.0 (*s*, C-1″), 103.0 (*d*, C-2′,6′), 102.6 (*d*, C-2″,6″), 87.8 (*d*, C-1), 82.2 (*d*, C-4), 71.1 (*t*, C-6), 69.8 (*t*, C-3), 60.8 (*q*, 4′, 4″-OCH_3), 56.2 (*q*, 3′, 5′, 3″, 5″-OCH_3), 54.5 (*d*, C-6a), 50.0 (*d*, C-3a).

*3.3.12. Yangambin (**10**)*

^{1}H NMR ($CDCl_3$, 500 MHz) δ: 6.58 (4H, *s*, H-2′,6′, H-2″,6″), 4.76 (2H, *d*, *J* = 4.Hz, H-1, H-4), 4.32 (2H, *dd*, *J* = 6.9, 9.2 Hz, $H_α$-3, $H_α$-6), 3.95 (2H, *dd*, *J* = 3.6, 9.2 Hz, $H_β$-3, $H_β$-6), 3.88 (12H, *s*, 3′, 3″, 5′, 5″-OCH_3), 3.85 (6H, *s*, 4′, 4″-OCH_3), 3.11 (2H, *m*, H-3a, H-6a); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 153.7 (*s*, C-3′, C-3″, C-5′, C-5″), 137.0 (*s*, C-1′, C-1″), 103.1 (*d*, C-2′,6′, C-2″,6″), 86.2 (*d*, C-1, C-4), 72.2 (*t*, C-3, C-6), 61.1 (*q*, 4′, 4″-OCH_3), 56.4 (*q*, 3′, 3″, 5′, 5″-OCH_3), 54.6 (*d*, C-3a, C-6a).

*3.3.13. (**11**)*

^{1}H NMR ($CDCl_3$, 500 MHz) δ: 6.92–6.86 (3H, *m*, H-2″, H-5″, H-6″), 6.58 (2H, *s*, H-2′,6′), 4.76 (*q*, 4′-OCH_3), 56.2 (*q*, 3′, 5′, 3″, 4″-OCH_3), 5.44 (*d*, C-6a), 5.41 (*d*, C-3a), (2H, *d*, *J* = 4.5 Hz, H-1, H-4), 4.30 (2H, *m*, $H_α$-3, $H_α$-6), 3.93 (2H, *m*, $H_β$-3, $H_β$-6), 3.91 (3H, *s*, 4″-OCH_3), 3.89 (9H, *s*, 3′, 5′, 3″-OCH_3), 3.84 (3H, *s*, 4′-OCH_3), 3.13 (2H, *m*, H-3a, H-6a); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 153.3 (*s*, C-3′, C-5′), 149.2 (*s*, C-4″), 148.7 (*s*, C-3″), 137.6 (*s*, C-4′), 136.8 (*s*, C-1′), 133.5 (*s*, C-1′), 118.2 (*d*, C-6″), 111.1 (*d*, C-5″), 109.2 (*d*, C-2″), 102.8 (*d*, C-2′,6′), 85.9 (*d*, C-1), 85.8 (*d*, C-4), 71.9 (*t*, C-3), 71.8 (*t*, C-6), 60 (*q*, 4′, 4″-OCH_3).

*3.3.14. (**12**)*

^{1}H NMR ($CDCl_3$, 500 MHz) δ: 6.95–6.87 (3H, *m*, H-2″, H-5″, H-6″), 6.60 (2H, *s*, H-2′,6′), 4.89 (1H, *d*, *J* = 5.6 Hz, H-4), 4.46 (1H, *d*, *J* = 7.0 Hz, H-1), 4.16 (1H, *dd*, *J* = 0.9, 9.5 Hz, $H_β$-6), 3.90-3.85 (15H, *s*, 3′, 4′, 5, 3″, 4″-OCH_3), 3.88 (2H, *m*, $H_α$-3, $H_α$-6), 3.35 (1H, *m*, H-3a), 3.34 (1H, *m*, $H_β$-3), 2.93 (1H, *m*, H-6a); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 153.7 (*s*, C-3′, C-5′), 149.1 (*s*, C-4″), 148.3 (*s*, C-3″), 137.8 (*s*, C-4′), 137.1 (*s*, C-1′), 131.1 (*s*, C-1″), 118.0 (*d*, C-6″), 111.3 (*d*, C-5″), 109.3 (*d*, C-2″), 103.2 (*d*, C-2′,6′), 88.1 (*d*, C-1), 82.3 (*d*, C-4), 70.0 (*t*, C-

3, C-6), 61.1 (*q*, 4′-OCH_3), 56.4 (*q*, 3′, 3″, 4″-OCH_3), 56.1 (*q*, 5′-OCH_3), 54.9 (*d*, C-6a), 50.3 (*d*, C-3a).

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