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DITERPENOIDS FROM *SALVIA CANDELABRUM*

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Key Word Index—*Salvia candelabrum*; Labiatae; abietane diterpenoids; 19(4→3)-*abeo*-abietane derivative; 3,4-*seco*-abietane derivative; candesalvones A and B.

Abstract—From the aerial parts of *Salvia candelabrum* two new rearranged abietane diterpenoids, candesalvones A and B, have been isolated besides β-sitosterol, nepeticin [lup-20(29)-ene-3β,11α-diol], candelabrone [11,12,14-trihydroxy-8,11,13-abietatriene-3,7-dione) and large amounts of ursolic and oleanolic acids. The structures of candesalvone A[11,12,14-trihydroxy-19(4→3)-*abeo*-3,8,11,13-abietatetraen-7-one] and candesalvone B [11,12,14-trihydroxy-7-oxo-3,4-*seco*-4(18),8,11,13-abietatetraen-3-oic acid] were established by chemical and spectroscopic means. In addition, the root bark of the same species afforded the previously known abietane derivatives 7α-acetoxyroyleanone, 12-*O*-methylpisiferic acid and sugiol.

INTRODUCTION

In continuation of our studies on diterpene constituents from the genus *Salvia* [1–3], we have now investigated *Salvia candelabrum* Boiss., a species from which the abietane derivative candelabrone (**1**) has recently been isolated [4]. From the acetone extract of the root bark of this plant, we have isolated the known diterpenoids, 7α-acetoxyroyleanone (7α-acetoxy-12-hydroxy-8,12-abietadiene-11,14-dione) [5, 6], 12-*O*-methylpisiferic acid (12-methoxy-8,11,13-abietatrien-20-oic acid) [7–9] and sugiol [12-hydroxy-8,11,13-abietatrien-7-one) [10–12]. The acetone extract of the aerial parts of *S. candelabrum* afforded β-sitosterol, large amounts (3.87% on dry plant material) of a mixture of ursolic and oleanolic acids, and the rare triterpene nepeticin [lup-20(29)-ene-3β,11α-diol], previously found in *Nepeta hindostana* [13] and *Salvia pinnata* [14]. In addition, the abietane derivative candelabrone (**1**), recently isolated from the leaves of *S. candelabrum* [4], and two new diterpenoids, candesalvones A and B, were also found in the same extract. The structures of candesalvones A and B (**3** and **5**, respectively) were established by chemical and spectroscopic means.

Since we observed that some of these abietane derivatives were unstable in the chromatographic process over silica gel and were very difficult to purify (see Experimental), the structure of candesalvone A (**3**) was established from its 12-*O*-methyl derivative **4**, a stable compound which was obtained by ethereal diazomethane treatment of the chromatographic fractions containing impure candesalvone A. Furthermore, candelabrone (**1**), which has already been purified by means of chromatography on polyamide CC-6 [4], was now identified as its derivative **2**, a compound not previously reported.

RESULTS AND DISCUSSION

Candelabrone 12-methyl ether (compound 2) showed ^{1}H and ^{13}C NMR spectra (see Tables 1 and 2, respectively) almost identical with those reported [4] for candelabrone (**1**). The only differences were consistent with the presence in **2** of a methoxyl group (δ 3.81, 3H, *s*; δ_{OMe} 62.14, *q*) instead of one of the phenolic functions of compound **1**. The location of the methyl ether grouping of compound **2** at the C-12 position was firmly supported by the following facts. The ^{1}H NMR spectrum of compound **2** (Table 1) showed signals of two hydroxyl protons at δ 5.77 (*s*) and 13.13 (*s*). The very deshielded resonance of the last hydroxyl proton, together with its slow exchange with D_2O, confirmed the existence of a phenolic group at the C-14 position, forming a strong intramolecular hydrogen bond with the C-7 ketone function [4, 15]. The IR absorptions of compound **2** at 1635 cm^{-1} (C-7 ketone) and 3200–2300 cm^{-1} (C-14 phenolic group) were also in agreement with this conclusion. Thus, the methoxyl group of compound **2** must be at the C-11 or C-12 position.

In NOE experiments irradiation of the methoxyl protons (δ 3.81, *s*) gave a clear NOE enhancement (5%) in the signal of the H-15 proton (δ 3.32, *septet*). This result firmly established an *ortho* relationship between the methoxyl and the isopropyl groups and, consequently, compound **2** possesses its methyl ether grouping at the C-12 position of an abietane hydrocarbon skeleton.

The UV spectrum of compound **2** (Table 3) was identical with that reported for inuroyleanol (**6**), an

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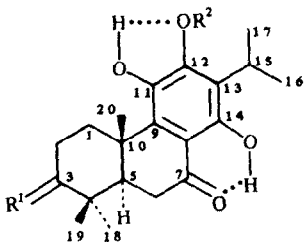
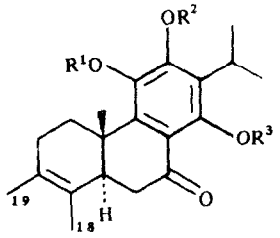
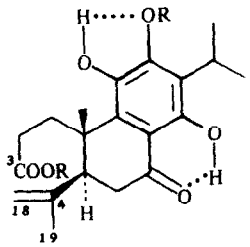


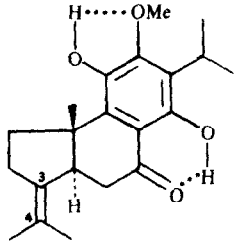
	R^1	R^2
1	O	H
2	O	Me
6	H_2	Me



	R^1	R^2	R^3
3	H	H	H
4	H	Me	H
8	Ac	Me	H
9	Ac	Me	Ac



5 R=H
11 R=Me



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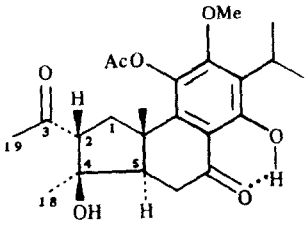

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Scheme 1

abietane diterpenoid possessing a 2,5-dihydroxy-3-isopropyl-4-methoxyphenylketone moiety [16]. The well known regioselectivity of the methylation at the C-12 hydroxyl group in the reaction of 11,12,14-trihydroxy-8,11,13-abietatrien-7-one derivatives with diazomethane [17], also supported the above conclusion on the structure **2** assigned to the *O*-methyl derivative of candelabrone.

The first of the new diterpenoids isolated from *S candelabrum*, candesalvone A (**3**), was purified as its 12-*O*-methyl derivative **4**. Compound **4** had a molecular formula $C_{21}H_{28}O_4$ and its ^1H and ^{13}C NMR spectra (Tables 1 and 2, respectively) showed signals attributable to a structural moiety identical with the rings B and C of compound **2**. The unambiguous location of the methoxyl group (δ 3.80, 3H, *s*) at the C-12 position was established by NOE experiments, as in the case of the derivative **2** (see above). Moreover, the UV spectra of compounds **2** and **4** (Table 3) were almost identical, thus confirming the existence of the same chromophore in both compounds.

In addition, the ^1H NMR spectrum of compound **4** showed the signals of two methyl groups attached to a fully substituted olefinic double bond (methyl resonances at δ 1.67, *br s*, $W_{1/2} = 4.5$ Hz, and δ 1.63, *br s*, $W_{1/2} = 5.0$ Hz; no signals of olefinic protons) and a (C)CH_2CH_2(C) structural part (see Table 1, resonances of the C-1 and C-2 protons). Double resonance experiments and the homonuclear 2D map of compound **4** revealed the existence of homoallylic couplings between the H-5α proton (δ 2.74, *br dd*, $J_{5\alpha,6\alpha} = 3.1$ Hz, $J_{5\alpha,6\beta} = 14.9$ Hz) and the methyl group at δ 1.67, as well as between the other allylic methyl group (δ 1.63) and two protons (δ 2.02 and 2.24) belonging to a methylene grouping ($J_{gem} = 17.9$ Hz, see also Table 1).

All the above data established the structure depicted in **4** for the *O*-methyl derivative of candesalvone A. This conclusion was also supported by the rather deshielded position of the H-1β proton of **4** (δ 3.33, *ddd*), which is due [4, 18] to its coplanarity with the aromatic ring C and its close proximity to the oxygen lone pairs of the C-11 hydroxyl group.

However, an alternative structure such as **7** may also be considered for the *O*-methyl derivative of candesalvone A, although it is less probable taking into account the

Table 1 ^{1}H NMR spectral data of compounds **2**, **4**, **8–10** (300 MHz, $CDCl_3$, TMS as int. standard*

	2	4	8	9†	10
H-1α	1.99 *dt*	1 58 *td*	1.72 *td*	1.77 *td*	2.30 *m*
H-1β	3 37 *dt*	3 33 *ddd*	2.70 *ddd*	2.67 *ddd*	
H-2α	2 62 *m*	2 02 *br ddd*	2.02 *br ddd*	2.01 *br ddd*	—
H-2β		2.24 *m*	2.21 *m*	2 20 *m*	3.48 *br t*
H-5α	2 41 *dd*	2 74 *br dd*	2.75 *br dd*	2.79 *br dd*	2 02 *dd*
H-6α	2.55 *dd*	2.87 *dd*	2.91 *dd*	2 82 *dd*	2.60 *dd*
H-6β	2.74 *dd*	2.53 *dd*	2.52 *dd*	2 37 *dd*	2 85 *dd*
H-15	3.32 *septet*	3.32 *septet*	3.42 *septet*	3.36 *septed*	3 43 *septet*
Me-16‡	1.40 *d*	1.41 *d*	1.37 *d*	1.33 *d*	1 36 *d*
Me-17‡	1.39 *d*	1.39 *d*	1 36 *d*	1.25 *d*	1 34 *d*
Me-18	1.172 *s*‡	1.63 *br s*	1.62 *br s*	1.57 *br s*	1.31 *s*
Me-19	1.169 *s*	1.67 *br s*	1.66 *br s*	1.66 *br s*	2 31 *br s*
Me-20	1.44 *s*	1.21 *s*	1.15 *br s*	1 15 *s*	1 23 *s*
OH-11§	5 77 *s*	5.67 *s*	—	—	—
OH-14¶	13.13 *s*	13.36 *s*	13 82 *s*	—	13.53 *s*
OAc-11	—	—	2.33 *s*	2.33 *s*‡	2.32 *s*
OAc-14	—	—	—	2 36 *s*‡	—
PhOMe	3 81 *s*	3.80 *s*	3.75 *s*	3.78 *s*	3 76 *s*
J (Hz)					
1α,1β	14 1	12.6	12.9	12 4	‖
1α,2α	8.5	6 7	6.3	6.4	—
1α,2β	8.5	12.6	12.9	12.4	9.4
1β,2α	6.5	1.8	1 3	1 8	—
1β,2β	6.5	6 9	8.1	6 1	9.4
2α,2β	‖	17.9	17 0	17 0	—
5α,6α	3.2	3.1	3.4	4 8	4.1
5α,6β	14.4	14.9	14.6	10.5	14 3
6α,6β	16.4	16.8	17 4	18.7	18 0
15,Me-16 (Me-17)	7.0	7.0	7 0	7.0	7 1
Me-18,2α	—	‖	1.1	1.1	—
Me-18,2β	—	‖	1.7	1.7	—
Me-19,5α	—	1.8	1.8	1.7	—

*Spectral parameters were obtained by first order approximation All these assignments have been confirmed by doublet resonance experiments and ^{1}H-^{1}H 2D COSY spectra

†At 45°, see discussion of results.

‡Interchangeable assignments

§Rapidly interchangeable with D_2O.

¶Slowly interchangeable with D_2O

‖Not measured

observed coupling values between the C-1 and C-2 protons (see Table 1, compound **4**). Exclusion of this alternative structural possibility (**7**) and final proof on the structure **4** assigned to the new diterpenoid was achieved as follows.

Treatment of compound **4** with acetic anhydride–pyridine at room temperature for a week yielded a 4:1 mixture of the acetates **8** and **9**, respectively. The major product was the 11-acetyl derivative **8**, since its ^{1}H NMR spectrum (Table 1) showed the C-14 phenolic proton at δ 13.82 and diamagnetically shifted the signal of the H-1β equatorial proton ($\Delta\delta$ −0.63). Moreover, irradiation at δ 3.75 (methoxyl protons) caused NOE enhancements in the signals of the H-15 (δ 3.42, 8% enhancement), acetoxyl (δ 2.33, 3%), and Me-16 and Me-17 (δ 1.37 and 1.36, 0.5%) protons, thus confirming that the 12-*O*-methyl group was placed between the 13-isopropyl and the 11-acetoxyl groups. The diacetyl derivative **9** was the minor product of the reaction, since the acetylation of a C-14 phenolic group in 8,11,13-abietatrien-7-one derivatives is very difficult [16] due to steric hindrance. This was clearly revealed by the fact that the ^{1}H NMR spectrum of compound **9** showed broad and unresolved signals of the H-15, Me-16, Me-17, 12-methoxyl and 14-acetoxyl protons when it was registered at 21°, whereas at 45° (Table 1) all these signals appeared sharp and those of H-15, Me-16 and Me-17 also with splitting, due to the disappearance of the restricted rotation of these substituents.

Reaction of the monoacetate **8** with osmium tetroxide followed by treatment with periodic acid gave a single product, $C_{23}H_{30}O_7$, the ^{1}H NMR spectrum of which (compound **10**, Table 1) revealed the existence of a methyl ketone side chain (δ_{Me} 2.31, *br s*; ν_{CO} 1710 cm^{-1}) attached to a methine grouping (methine proton at δ 3.48, *br t*, J = 9.4 Hz), which was placed between a methylene group (δ 2.30, 2H, *m*) and a fully substituted sp^3 carbon atom.

Table 2 ^{13}C NMR chemical shifts of compounds **2**, **4** and **11** ($CDCl_3$, TMS as internal standard)*

C	2	4	11
1	36 26 *t*†	31.89 *t*	32 20 *t*
2	34 48 *t*	29.88 *t*	29 82 *t*
3	215 75 *s*	126.29 *s*	174.29 *s*
4	46 95 *s*	123 94 *s*	144 16 *s*
5	48 90 *d*	44 36 *d*	46.63 *d*
6	35 50 *t*	37 95 *t*	40.05 *t*
7	204 33 *s*	205.50 *s*	204 29 *s*
8	112 02 *s*	112.76 *s*	113 24 *s*
9	138 93 *s*	139 14 *s*	138 88 *s*
10	38 95 *s*	38.00 *s*	41 37 *s*
11	133 38 *s*	134 11 *s*	129 83 *s*
12	152 49 *s*	152 36 *s*	152 24 *s*
13	126.87 *s*	127 25 *s*	126 86 *s*
14	158 15 *s*	158 69 *s*	158 21 *s*
15	26 10 *d*	26 09 *d*	26 02 *d*
16‡	20.31 *q*	20 44 *q*	20 33 *q*
17‡	20 31 *q*	20 36 *q*	20 30 *q*
18	26 98 *q*	15 55 *q*	116 24 *t*
19	20 86 *q*	19 22 *q*	21 19 *q*§
20	17 50 *q*	16 12 *q*	22 79 *q*§
PhOMe	62 14 *q*	62 03 *q*	62.03 *q*
COOMe	—	—	51 49 *q*

*Assignments of carbons bearing hydrogen atoms were confirmed by ^{1}H-^{13}C2D COSY spectra
†SFORD and DEPT multiplicity
‡Interchangeable assignments
§These assignments may be interchanged.

Moreover, this last carbon was attached to a methyl (δ 1.31, *s*), a hydroxyl (ν_{OH} 3470 cm^{-1}) and the C-5 methine (δ_{H-5} 2.02, *dd*, $J_{5\alpha,6\alpha}$ = 4.1 Hz, $J_{5\alpha,6\beta}$ = 14.3 Hz) groups. Thus, this compound possessed the structure **10** and must be formed from the derivative **8** by initial hydroxylation at C-3 and C-4 positions, followed by cleavage of the C-3–C-4 bond and subsequent regio- and stereoselective aldol condensation. The C-4β configuration of the tertiary hydroxyl group of compound **10** was in agreement [19] with the observed variations in the chemical shifts of its H-6α ($\Delta\delta$ −0 31), H-6β ($\Delta\delta$ + 0.33) and Me-20 ($\Delta\delta$ + 0.08) protons with respect to compound **8** (see Table 1). Furthermore, the *cis* relationship between the C-4β hydroxyl group and the hydrogen atom at the C-2β position was firmly supported by the low-field resonance of this proton (δ 3.48) [19] and the lack in the reaction of the corresponding 2,4-dehydro-3-oxo-derivative, which should be easily formed when the tertiary hydroxyl group and the hydrogen α to the carbonyl function are *trans*

All the above data established the structure depicted in **4** for the 12-*O*-methyl derivative of candesalvone A The 19 (4→3)-*abeo*-abietane hydrocarbon skeleton of this new diterpenoid has been found in some natural products, one of which is 19(4→3)-*abeo*-*O*-demethylcryptojaponol [11,12-dihydroxy-19(4→3)-*abeo*-4(18),8,11,13-abietatetraen-7-one], recently isolated from *Salvia pubescens* [20].

The other of the new diterpenoids isolated from the aerial parts of *S candelabrum*, candesalvone B ($C_{20}H_{26}O_6$), was an amorphous solid which decomposed in storage and also in spectroscopic deuteriochloroform solution Treatment of the natural compound (**5**) with an ethereal solution of diazomethane quantitatively yielded a stable dimethyl derivative, $C_{22}H_{30}O_6$, to which the structure of methyl 11,14-dihydroxy-12-methoxy-7-oxo-3,4-seco-4(18),8,11,13-abietatetraen-3-oate (**11**) was assigned on the basis of the following reasons.

The ^{1}H and ^{13}C NMR spectra of the derivative **11** (Tables 4 and 2, respectively) showed characteristic signals for a 11,14-dihydroxy-12-methoxy-8,11,13-abietatrien-7-one structural moiety identical with that of compounds **2** and **4**. The identical UV absorption of these three substances (**2**, **4** and **11**, see Table 3) further confirmed this point.

In addition, compound **11** possessed an isopropenyl group [IR. ν_{max} 3080, 908 cm^{-1}; ^{1}H NMR: δ 4.80 (1H, *br d*, J = 1.2 Hz, H_A-18), 5.03 (1H, *quintuplet*, J = 1.2 Hz, H_B-18), 1.77 (3H, *d*, J = 1.2 Hz, Me-19); ^{13}C NMR: δ 144 16, *s* (C-4), 116 24 *t* (C-18), 21.19, *q* (Me-19)], a carbomethoxyl function [IR ν_{max} 1740 cm^{-1}; ^{1}H NMR: δ 3.63 (3H, *s*); ^{13}C NMR: δ 174.29, *s* (COOMe), 51 49, *q* (COOMe)] and two methylene groups, probably forming a (C)CH_2CH_2(C) structural moiety (overlapped signals of 4H between δ 2.03 and 2.80; δ 32.20, *t*, and 29 82, *t*), besides the Me-20 (δ 1.42, *s*), the H-5α (δ 2.77, *br dd*, $J_{5\alpha,6\alpha}$ = 3.0 Hz, $J_{5\alpha,6\beta}$ = 12.0 Hz) and the C-6 methylene ($\delta_{H-6\alpha}$ 2.60, *dd*; $\delta_{H-6\beta}$ 2.89, *dd*, J_{gem} = 15 9 Hz) protons almost identical with those found in compounds **2** and **4**.

The preceding data pointed towards a biogenetic plausible structure such as **11** for the dimethyl derivatve of candesalvone B, and this was rigorously confirmed as follows.

Double resonance experiments showed that on irradiation at δ 4.80 (*br d*, J = 1.2 Hz, H_A-18), the signal of the H-5α proton (δ 2.77, *br dd*) appeared as a sharp double doublet, whereas on irradiation at δ 2.77 (H-5α proton) the H_A-18 signal was transformed into a sharp doublet (J = 1.2 Hz), thus establishing that the isopropenyl group was attached to the C-5 position.

The base peak in the mass spectrum of compound **11** appeared at *m/z* 303, by loss of a fragment $C_4H_7O_2$ from the molecular ion (*m/z* 390), which is due to the known β-fragmentation [21] of aliphatic methyl esters. In consequence, compound **11** had a $-CH_2CH_2COOMe$ side

Table 3 UV spectra of compounds **2**, **4**, **8**–**11** [MeOH, λ_{max} nm (log ε)]

2	4	8	9	10	11
238 (4.07)	239 (3.92)	222 (3.93)	223 (4.15)	223 (4.11)	238 (3 91)
277 (4 06)	279 (3.92)	275 (3 75)	265 (3.92)	277 (4 00)	277 (3 90)
369 (3 81)	372 (3.66)	344 (3.40)	300 (sh) (3 35)	343 (3 64)	370 (3 64)

Table 4. ^{1}H NMR spectral data of compounds **5** and **11** ($CDCl_3$, TMS as int. standard)

	5*	11†
H5α	‡	2.77 *br dd*
H-6α	‡	2.60 *dd*
H-6β	‡	2 89 *dd*
H-15	3 40 *sept*	3.32 *sept*
Me-16	1.31 *d*	1.40 *d*
Me-17		
H_A-18	4 82 *br s*	4.80 *br d*
H_B-18	5 02 *br s*	5.03 *quin*
Me-19	1.75 *br s*	1.77 *d*
Me-20	1.40 *s*	1.42 *s*
OH-11§	‖	5 77 *br s*
OH-14¶	‖	13.23 *s*
PhOMe	—	3.79 *s*
COOMe	—	3.63 *s*
J(Hz)		
5α, 6α	‡	3.0
5α, 6β	‡	12.0
6α, 6β	‡	15.9
18A, 18B	‖	1.2
18A, Me-19	‖	0.0
18B, Me-19	‖	1.2
15,Me-16 (Me-17)	7.0	6.9

*At 90 MHz.

†At 300 MHz. Spectral parameters were obtained by first order approximation. All these assignments have been confirmed by double resonance experiments and ^{1}H–^{1}H 2D COSY spectrum The C-1 and C-2 protons of this compound appeared at δ2.03–2.80 as overlapped signals.

‡Overlapped signal.

§Rapidly interchangeable with D_2O.

¶Slowly interchangeable with D_2O.

‖Not measured.

chain. Finally, the ^{1}H and ^{13}C NMR data of the 3,4-*seco*-ring A part of compound **11** (see above) were in complete agreement with those reported [22–24] for the 3,4-*seco*-derivatives of *ent*-pimarane, *ent*-beyerane and cleistanthane diterpenoids having a C-3 carboxyl or carbomethoxyl group and a C-4–C-18 double bond. To our knowledge, candesalvone B (**5**) is the first example of a 3,4-*seco*-abietane diterpenoid isolated from a natural source.

The absolute configuration of candesalvones A (**3**) and B (**5**) must be *normal* (the one depicted in the formulae), since their derivatives **4** and **11** showed specific rotations of positive sign and increasing values between 589 and 436 nm (Table 5) as candelabrone (**1**) and other diterpenoids possessing an aryl ketone chromophore at C-7 [4]. This conclusion was also supported on biogenetic grounds, because all the other abietane derivatives co-occurring in *S. candelabrum* (7α-acetoxyroyleanone, sugiol, 12-*O*-methylpisiferic acid and candelabrone) belong to the *normal* series [4,5–12].

EXPERIMENTAL

Mps uncorr Plant materials were collected in June 1987 at Boquete de Zafarraya (Granada, Spain) and voucher specimens were deposited in the Herbarium of the Royal Botanic Garden of Madrid, Spain.

Extraction and isolation of the diterpenoids from the root bark. Dried and finely powdered *Salvia candelabrum* root bark (830 g) was extracted (× 3) with Me_2CO (5.1) at room temp. for 3 days. The extract (14 1 g) was subjected to flash chromatography on a silica gel column (Merck, No. 81538, 600 g) eluted with *n*-hexane–EtOAc (32:1), which successively yielded 7α-acetoxyroyleanone (890 mg) [5, 6], 12-*O*-methylpisiferic acid (200 mg) [7–9] and sugiol (30 mg) [10–12] The previously known compounds were identified by their physical (mp, $[\alpha]_D$) and spectroscopic (IR, UV, ^{1}H and ^{13}C NMR, MS) data and by comparison (mmp, TLC) with authentic samples

Extraction and isolation of the compounds from the aerial parts Dried and finely powdered *S. candelabrum* aerial parts (1.5 kg) were extracted (× 3) with Me_2CO (10 l.) at room temp. for 3 days with stirring. The extract (134 g) was digested with hot EtOAc (300 ml) leaving an insoluble residue of a mixture of ursolic and oleanolic acids (52 g), which were identified by the ^{13}C NMR spectrum of the mixture of their methyl ester derivatives. The fraction soluble in EtOAc (82 g) was chromatographed on a silica gel column (Merck, No. 7734, deactivated with 10% H_2O, 1 kg). Elution with *n*-hexane and *n*-hexane–EtOAc mixtures gave the following compounds in order of elution: impure candesalvone A (**3**, 720 mg), β-sitosterol (250 mg), nepeticin (15 mg) [13, 14], impure candelabrone (**1**, 220 mg) [4] and candesalvone B (**5**, 80 mg), besides additional quantities (6 g) of the mixture of ursolic and oleanolic acids. Nepeticin and β-sitosterol were identified by their physical (mp, $[\alpha]_D$) and spectroscopic (IR, ^{1}H NMR, MS) data and, in the case of β-sitosterol, by comparison with an authentic sample. Candelabrone (**1**) and candesalvone A (**3**) were purified as their 12-*O*-methyl derivatives (compounds **2** and **4**, respectively) after treatment of the impure samples with ethereal diazomethane.

12-*O*-*Methylcandelabrone* (**2**) Mp 191–193° (yellow needles from MeOH); $[\alpha]$ see Table 5; IR ν_{max}^{KBr} cm^{-1}: 3360 (OH), 3200–2300 (*br*, chelated OH at C-14), 1700 (ketone at C-3), 1635 (chelated aryl ketone at C-7), 1615, 1530 (aromatic); UV see

Table 5 Specific rotations of compounds **2**, **4**, **8**–**11** (values in degrees, $CHCl_3$ solution)

Compound	Temperature (°)	*c*	$[\alpha]_{D(589)}$	$[\alpha]_{578}$	$[\alpha]_{546}$	$[\alpha]_{436}$
2	20	0 310	+160.9	+170.3	+205.2	+516.1
4	20	0.308	+71.1	+76.0	+95.1	+278 9
8	20	0.709	+49.4	+52.0	+64 3	+193.5
9	20	0.479	+65.6	+69.9	+87.9	+294.4
10	22	0.223	+54.3	+57.4	+67 3	+145.3
11	21	0.159	+100.0	+104.4	+126 4	+383.6

Table 3, ^{1}H NMR (300 MHz, $CDCl_3$): see Table 1; ^{13}C NMR (50 3 MHz, $CDCl_3$): see Table 2; EIMS (70 eV, direct inlet) *m/z* (rel int.). 360 $[M]^+$ (9), 345 (5), 183 (40), 141 (40), 137 (13), 113 (22), 111 (100), 93 (20), 83 (15), 69 (16), 68 (13), 43 (26), 41 (19). (Found. C, 70.05, H, 8 00 $C_{21}H_{28}O_5$ requires C, 69 97, H, 7.83%)

12-O-*Methylcandesalvone A* (**4**). Mp 209–212° (yellow plates from MeOH), [α] see Table 5; IR ν_{max}^{KBr} cm^{-1} 3300 (OH), 3200–2200 (*br*, chelated OH at C-14), 1615 (chelated aryl ketone at C-7), 1560 (aromatic), UV see Table 3, ^{1}H NMR (300 MHz, $CDCl_3$) see Table 1, ^{13}C NMR (50 3 MHz, $CDCl_3$) see Table 2, EIMS (direct inlet) *m/z* (rel. int.) 344 $[M]^+$ (100), 329 (91), 326 (3), 314 (3), 311 (4), 301 (5), 287 (6), 249 (6), 235 (23), 209 (21), 91 (8), 55 (7), 43 (12), 41 (9) (Found C, 72 98, H, 8 38 $C_{21}H_{28}O_4$ requires C, 73 22; H, 8.19%)

Acetylation of 12-O-*methylcandesalvone A* (**4**) *to give compounds* **8** *and* **9** Ac_2O–pyridine treatment of **4** (500 mg) for a week at room temp yielded a mixture of compounds **8** and **9** This mixture was chromatographed (silica gel column, *n*-hexane–EtOAc 19 1 as eluent) to give compounds **8** (408 mg, less polar constituent) and **9** (96 mg).

Compound **8** Mp 193°–194° (colourless needles from MeOH), [α]: see Table 5, IR ν_{max}^{KBr} cm^{-1}. 3200–2200 (*br*, chelated OH at C-14), 1772 (acetate), 1630 (chelated aryl ketone at C-7), 1595, 1565, 1505 (aromatic), UV see Table 3, ^{1}H NMR (300 MHz, $CDCl_3$) see Table 1, EIMS (70 eV, direct inlet) *m/z* (rel int) 386 $[M]^+$ (16), 344 (100), 329 (55), 326 (2), 311 (3), 235 (9), 209 (9), 43 (16) (Found C, 71 27, H, 8 02 $C_{23}H_{30}O_5$ requires C, 71 48, H, 7 82%)

Compound **9** Mp 146–150° (colourless needles from MeOH), [α] see Table 5, ν_{max}^{KBr} cm^{-1}. 1780, 1775 (acetates), 1683 (aryl ketone at C-7), 1585, 1550 (aromatic), UV see Table 3, ^{1}H NMR (300 MHz, $CDCl_3$) see Table 1 and discussion of results; EIMS (70 eV, direct inlet) *m/z* (rel int) 428 $[M]^+$ (7), 386 (22), 344 (100), 329 (31), 326 (2), 316 (1), 313 (2), 301 (1), 43 (18) (Found. C, 70 14, H, 7 41 $C_{25}H_{32}O_6$ requires C, 70 07, H, 7 53%)

Compound **10** *from* 11-*acetyl*-12-O-*methylcandesalvone A* (**8**) To a soln of compound **8** (200 mg) in dioxane (40 ml), OsO_4 (200 mg) was added and the reaction was left at room temp for 3 days Then, a soln of $NaHSO_3$ (500 mg in 10 ml of water) was added and the reaction mixture vigorously stirred for 6 hr After addition of H_2O (100 ml) the reaction was extracted with $CHCl_3$ Work-up in the usual manner yielded a residue (180 mg) which showed one spot (TLC) more polar than the starting material (**8**) This residue, without characterization, was treated with a soln of H_5IO_6 (400 mg) in EtOH–H_2O (4 1, v/v, 50 ml) at room temp. for 36 hr Work-up in the usual manner gave compound **10**, which was crystallized from EtOAc–*n*-hexane (140 mg, colourless needles) mp 192°–194°, [α] see Table 5, IR ν_{max}^{KBr} cm^{-1} 3470 (OH at C-4), 3200–2300 (*br*, chelated OH at C-14), 1773 (acetate), 1710 (ketone at C-3), 1620 (chelated aryl ketone at C-7), 1580, 1560 (aromatic), UV see Table 3, ^{1}H NMR (300 MHz, $CDCl_3$) see Table 1, EIMS (70 eV, direct inlet) *m/z* (rel. int) 418 $[M]^+$ (11), 403 (0 4), 401 (0.5), 400 (0 5), 376 (100), 343 (18), 315 (27), 301 (17), 263 (28), 245 (5), 231 (6), 43 (40). (Found C, 65 92, H, 7 32. $C_{23}H_{30}O_7$ requires C, 66 01, H, 7 23%)

Candesalvone B (**5**) An amorphous powder, ^{1}H NMR (90 MHz, $CDCl_3$), see Table 4, EIMS (70 eV, direct inlet) *m/z* (rel. int) 362 $[M]^+$ (0 1), 330 (10), 253 (13), 210 (12), 149 (16), 140 (25), 123 (35), 108 (13), 107 (11), 99 (79), 83 (100), 55 (61), 43 (36), 42 (50), 41 (43), $C_{20}H_{26}O_6$ M_r 362

12-O-*Methylcandesalvone B methyl ester* (**11**) Treatment of candesalvone B (**5**) with an Et_2O soln of CH_2N_2 for 5 hr quantitatively yielded the derivative **11**, mp 85–87° (spontaneously on cooling, yellow needles). [α] see Table 5, IR ν_{max}^{KBr} cm^{-1} 3520, 3440, 3100–2400 (phenolic groups at C-11 and C-14), 3080, 908 (terminal methylene), 1740 (ester), 1630 (chelated aryl ketone at C-7); UV see Table 3, ^{1}H NMR (300 MHz, $CDCl_3$) see Table 4, ^{13}C NMR (50.3 MHz, $CDCl_3$) see Table 2, EIMS (70 eV, direct inlet) *m/z* (rel int.) 390 $[M]^+$ (46), 375 (1), 372 (1), 358 (7), 303 (100), 263 (12), 261 (18), 229 (12), 218 (5), 187 (8), 69 (6), 55 (6), 43 (9), 41 (6) (Found C, 67 49, H, 7 83 $C_{22}H_{30}O_6$ requires C, 67 67, H, 7 74%)

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