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ABIETANE DITERPENOIDS FROM THE ROOT OF *SALVIA LAVANDULAEFOLIA*

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Key Word Index—*Salvia lavandulaefolia*; Labiatae; diterpenoids; abietane derivatives; 7α-ethoxyroyleanone; 7α-ethoxy-12-*O*-methyl-royleanone.

Abstract—Two new derivatives of royleanone, 7α-ethoxyroyleanone and 7α-ethoxy-12-*O*-methyl-royleanone, besides the previously known diterpenes royleanone, 6,7-dehydroroyleanone, 7α-acetoxyroyleanone and inuroyleanol, have been isolated from the root of *Salvia lavandulaefolia*. The triterpenoid *O*-acetyloleanolic aldehyde has also been obtained from the same source.

INTRODUCTION

In a continuation of our studies on the diterpenoid compounds from *Salvia* spp. [1–3], we have now investigated the root of *S. lavandulaefolia* Vahl., a species from the aerial part of which ursolic acid and the known abietane diterpenoid galdosol have been isolated [4]. The presence in the root of this plant of unidentified derivatives of the abietane diterpenoid royleanone has also been reported [5]. Now, from the root of *S. lavandulaefolia*, six diterpenoid compounds have been isolated, four of which are the previously known royleanone (**1**) [6, 7], its 6,7-dehydroderivative [6, 8], inuroyleanol (11,14-dihydroxy-12-methoxy-abieta-8,11,13-trien-7-one) [9] and 7α-acetoxyroyleanone (**2**) [6]. The other two diterpenoids are new substances, whose structures were established as 7α-ethoxy-12-hydroxy-abieta-8,12-diene-11,14-dione (**3**, 7α-ethoxyroyleanone) and 7α-ethoxy-12-methoxy-abieta-8,12-diene-11,14-dione (**4**, 7α-ethoxy-12-*O*-methyl-royleanone). In addition, the rare triterpenoid *O*-acetyloleanolic aldehyde [10, 11] was also isolated from the same source.

RESULTS AND DISCUSSION

Compound **3**, molecular formula $C_{22}H_{32}O_4$, had very similar UV properties (Table 1) to those of royleanone (**1**), thus establishing the presence of an identical chromophore in both substances (**1** and **3**). Moreover, the ^1H NMR spectrum of compound **3** (Table 2) was identical with that of horminone (**5**) [12], except for the presence of three additional signals which were assigned to an ethoxyl group (δ 1.21, 3H, *t*, $J = 7.1$ Hz; 3.71, 1H, and 3.68, 1H, both *dq*, $J_{gem} = 8.9$ Hz, $J_{vic} = 7.1$ Hz), instead of the hydroxyl proton of horminone (**5**). From the above data it was clear that compound **3** was the 7α-ethoxy derivative of royleanone, since an alternative structure with a hydroxyl function at the C-7α position and the ethoxyl group in C-12 was firmly discarded on the basis of the UV data (see Table 1).

The other new diterpenoid isolated from the root of *S. lavandulaefolia* was a $C_{23}H_{34}O_4$ substance, the ^1H NMR spectrum of which was identical with that of compound **3** (Table 2), except for the presence of a three-proton singlet signal at δ 3.82 instead of the phenolic one-proton singlet

Table 1. UV spectra of compounds 3 and 4 [λ_{max} nm (log ε)]

Compound	MeOH (3) or EtOH (4)	+ NaOMe	+ $AlCl_3$	+ $AlCl_3$- HCl
3	271.5 (4.04) 410 (2.48)	273 (3.88) 514 (3.08)	289 (3.92) 520 (2.60)	277 (3.94) 295 sh (3.70) 366 sh (2.60)
4	269 (4.00) 364 (2.70)	*	*	*

*No change was observed.

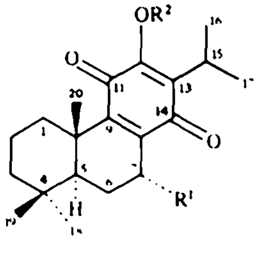
Table 2. ^{1}H NMR data of compounds 3 and 4 (300 MHz, $CDCl_3$, TMS as int. standard)*

H	3	4
1β†	2.68 *ddd*	2.55 *ddd*
	$J_{1\beta,1\alpha} = 12.0$ Hz; $J_{1\beta,2} = 4.0$ Hz; $J_{1\beta,2} = 2.0$ Hz	$J_{1\beta,1\alpha} = 12.7$ Hz; $J_{1\beta,2} = 4.0$ Hz; $J_{1\beta,2} = 2.0$ Hz
5α†	1.63 *dd*	1.58 *dd*
	$J_{5\alpha,6\beta} = 12.9$ Hz; $J_{5\alpha,6\alpha} = 1.5$ Hz	$J_{5\alpha,6\beta} = 12.8$ Hz; $J_{5\alpha,6\alpha} = 1.2$ Hz
6α†	2.01 *ddd*	2.00 *ddd*
	$J_{6\alpha,6\beta} = 14.1$ Hz; $J_{6\alpha,7\beta} = 1.8$ Hz	$J_{6\alpha,6\beta} = 12.8$ Hz; $J_{6\alpha,7\beta} = 1.7$ Hz
6β†	1.37 *ddd*	1.40 *td*
	$J_{6\beta,7\beta} = 3.5$ Hz	$J_{6\beta,7\beta} = 3.7$ Hz
7β†	4.42 *dd*	4.41 *dd*
15†	3.17 *septet*	3.17 *septet*
	$J_{15,16} = J_{15,17} = 7.0$ Hz	$J_{15,16} = J_{15,17} = 7.0$ Hz
Me-16, Me-17†	1.23 *d*	1.21 *d*
	1.19 *d*	1.17 *d*
Me-18, Me-19	0.94 *s*	0.92 *s*
	0.91 *s*	0.91 *s*
Me-20	1.21 *s*	1.26 *s*
OCH_2Me†	3.71 *dq*	3.68 *q*
	3.68 *dq*	
	$J_{gem} = 8.9$ Hz; $J_{vic} = 7.1$ Hz	$J_{vic} = 7.0$ Hz
OCH_2Me†	1.21 *t*	1.20 *t*
OMe	··	3.82 *s*
OH	7.13 *s*	—

*Spectral parameters were obtained by first order approximation.
†These assignments were confirmed by double resonance experiments.

at δ7.13 of substance 3. Since ethereal diazomethane treatment of compound 3 yielded a substance (4) identical (mp, mmp, [α]$_D$, IR, UV, ^{1}H NMR and MS) in all respects with the $C_{23}H_{34}O_4$ substance isolated from *S. lavandulaefolia*, it was clear that this last compound possesses a structure such as 4.

Since ethoxy compounds are very rare as natural products, it was just conceivable that diterpenoids 3 and 4 were artefacts arising from ethanol impurities in the organic solvents used in the extraction process (acetone) or/and in the chromatography (ethyl acetate). In fact, when 7α-acetoxyroyleanone (2) or horminone (5) were refluxed in ethanol solution containing a trace of *p*-toluenesulphonic acid, minor quantities of the ethoxy derivative 3 were obtained. Therefore, compounds 3 and 4 could be artefacts.



	R¹	R²
1	H	H
2	OAc	H
3	OEt	H
4	OEt	Me
5	OH	H

EXPERIMENTAL

Mps are uncorr. For general details on methods see refs [1-3]. Plant materials were collected in August 1984, near Ablanque, Guadalajara (Spain), and voucher specimens were deposited in the Herbarium of the Faculty of Pharmacy (Madrid 'Complutense' University).

Extraction and isolation of the diterpenoids. Dried and finely powdered *S. lavandulaefolia* Vahl. roots (1240 g) were extracted with Me_2CO (5 l.) at room temp. for 5 days. After filtration, the solvent was evaporated yielding a red gum (22 g) which was subjected to dry CC over silica gel (500 g, Merck No. 7734, deactivated with 10% H_2O). Elution with *n*-hexane and *n*-hexane–EtOAc mixtures yielded the following compounds in order of elution: royleanone (**1**, 260 mg) [6, 7], 6,7-dehydroroyleanone (40 mg) [6, 8], inuroyleanol (80 mg) [9], 7α-ethoxy-12-*O*-methyl-royleanone (**4**, 11 mg), 7α-ethoxyroyleanone (**3**, 50 mg), *O*-acetyloleanolic aldehyde (38 mg) [10, 11] and 7α-acetoxyroyleanone (**2**, 2.1 g) [6]. The previously known compounds were identified by their physical (mp, $[\alpha]_D$) and spectroscopic (IR, UV, ^{1}H NMR, MS) data and, in some cases, by comparison (mmp, TLC) with authentic samples.

7α-Ethoxyroyleanone (**3**). Mp 103–104° (from *n*-hexane); $[\alpha]_D^{21}$ $-69.4°$ ($CHCl_3$; *c* 0.321); IR ν_{max}^{KBr} cm^{-1}: 3380, 2970, 2940, 2880, 1675, 1655, 1635, 1600, 1460, 1395, 1290, 1250, 1135, 1070, 960, 900, 765, 755; UV: see Table 1; ^{1}H NMR: see Table 2; EIMS (direct inlet) 75 eV, *m/z* (rel. int.): 360 $[M]^+$ (50), 345 (22), 331 (71), 316 (100), 314 (20), 299 (28), 245 (20), 231 (17), 220 (18), 187 (10), 109 (15), 91 (17), 83 (20), 69 (24), 55 (35), 43 (40). (Found: C, 73.45; H, 8.89. $C_{22}H_{32}O_4$ requires: C, 73.30; H, 8.95%.)

7α-Ethoxy-12-O-methyl-royleanone (**4**). Mp 142–145° (*n*-hexane); $[\alpha]_D^{21}$ $-175.1°$ ($CHCl_3$; *c* 0.185); IR ν_{max}^{KBr} cm^{-1}: 2960, 2910, 2870, 1663, 1650, 1603, 1448, 1390, 1375, 1290, 1245, 1140, 1070, 890, 835, 760; UV: see Table 1; ^{1}H NMR: see Table 2; EIMS (direct inlet) 75 eV, *m/z* (rel. int.): 374 $[M]^+$ (35), 359 (15), 345 (43), 330 (100), 328 (50), 315 (20), 313 (52), 259 (29), 119 (15), 115 (16), 105 (15), 91 (23), 83 (19), 69 (30), 55 (41), 43 (36). (Found: C, 73.68; H, 9.22. $C_{23}H_{34}O_4$ requires: C, 73.76; H, 9.15%.)

Compound **4** *from compound* **3**. Ethereal CH_2N_2 treatment of **3** for 3 hr at 7° yielded a compound identical (mp, mmp, $[\alpha]_D$, TLC, UV, IR, ^{1}H NMR and MS) in all respects with natural **4**.

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