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REARRANGED LABDANE DITERPENOIDS FROM *GALEOPSIS ANGUSTIFOLIA*

LAURA PÉREZ-SIRVENT, BENJAMÍN RODRÍGUEZ, GIUSEPPE SAVONA* and ORIETTA SERVETTAZ†

Instituto de Química Orgánica, CSIC, Juan de la Cierva 3, Madrid 6, Spain; *Istituto di Chimica Organica dell'Università, Archirafi 20, 90123 Palermo, Italy; †Istituto di Botanica, Università di Milano, Milano, Italy

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Key Word Index—*Galeopsis angustifolia*; *G. ladanum*; *G. speciosa*; *G. tetrahit*; Labiatae; diterpenoids; rearranged labdane diterpenoids; galeopsitrione; galeolone; galeopsinolone; hispanone.

Abstract—From the aerial part of *Galeopsis angustifolia* collected in Spain, a labdane and three rearranged labdane diterpenoids have been isolated. The structures of these new substances have been established by chemical and spectroscopic means and by correlation with known compounds. A sample of the same species collected in Italy and other species of *Galeopsis* showed some remarkable chemical differences. The taxonomic significance of these results is discussed briefly.

INTRODUCTION

In a previous communication [1], we reported hispanolone (**1**) [2], galeopsin (**2**) and pregaleopsin as the major diterpenoid constituents of *Galeopsis angustifolia* growing in Spain. A study of the minor diterpene constituents of this plant has now allowed the isolation of four new diterpenoids, galeopsitrione (**3**, 15,16-epoxy-8,9-secolabdane-13(16),14-diene-7,8,9-trione), its hemiacetal derivative galeolone (**4**), galeopsinolone (**5**, 15,16-epoxy-6β-hydroxy-8,9-seco-7,11-cyclolabdane-7(11),13(16),14-trien-9-one) and hispanone (**6**, 15,16-epoxylabdane-8,13(16),14-trien-7-one).

RESULTS AND DISCUSSION

The first of the new diterpenoids, galeopsitrione (**3**), $C_{20}H_{28}O_4$, had an IR spectrum which showed strong and broad ketone (1700 cm^{-1}) and furanoid (3150, 3130, 1503, 880 cm^{-1}) absorptions and no hydroxyl bands. The ^1H NMR spectrum showed signals for a β-substituted furan ring (two α-furan protons at δ 7.29 and 7.16, and a β-furan proton at 6.21), three C–Me singlets (δ 1.22, 0.93 and 0.90) and a singlet of a methyl group adjacent to a carbonyl grouping (δ 2.35). Moreover, the ^{13}C NMR spectrum showed signals corresponding to three ketone groups (δ 215.5, 199.0 and 197.1), and typical resonances for a β-substituted furan ring (Table 1). Two of the ketone groups form an α-diketone grouping, compound **3** showing UV absorption at λ_{max} 245 nm ($\log\varepsilon = 3.23$) which changed to λ_{max} 265 ($\log\varepsilon = 3.64$) and 300 nm ($\log\varepsilon = 3.34$) in basic media [3], and it formed a quinoxaline derivative when treated with σ-phenylendiamine. In the ^1H NMR spectrum of this quinoxaline derivative there was a paramagnetic shift ($\Delta\delta + 0.45$) of the signal assigned to the methyl group adjacent to a ketone, thus, a –CO–CO–Me structural moiety was established for galeopsitrione.

Treatment of galeopsitrione (**3**) with aqueous hydrochloric acid in ethanol yielded a unique product, $C_{20}H_{24}O_2$, for which structure **7** was assigned on the basis of its spectroscopic properties (see Experimental). The formation of **7** from galeopsitrione (**3**) may be rationalized in terms of an aldol condensation between C-7 and C-11 followed by an alkylation reaction between C-16 and C-8.

All the above deductions on the structures of galeopsitrione (**3**) and its derivative (**7**), as well as the absolute configuration of these compounds, were confirmed as follows. When galeopsin (**2**) [1] was heated at 190° for 10 min under N_2 and without solvent, a retroaldol

1 R=H
2 R=OAc

3 R=O
8 R=H, OAc

4

	5	9	10	11	12
R^1	βOH,αH	H_2	H_2	O	H_2
R^2	H_2	H,OH	O	H_2	H_2

6

7

reaction occurred to give **8** [1], which on reaction with *t*-BuOK in benzene quantitatively yielded **9** [4, 5]. Oxidation of this compound with chromium trioxide in pyridine gave **10**, which, on treatment with hydrochloric acid in ethanol, was quantitatively transformed into a substance identical in all respects (mp, mmp, $[\alpha]_D$, IR, UV, ^{1}H NMR and mass spectra) with compound **7**. Moreover, no transformation was observed when the hydroxy-ketone, **9**, was treated under the same conditions as the diketone, **10**.

Table 1. ^{13}C NMR data for compounds **3**, **5** and **12** (25.2 MHz, $CDCl_3$, TMS as int. standard)

Carbon No.	3	5	12
1	36.5 *t**	35.9 *t*	33.5 *t*
2	18.1 *t*	18.5 *t*	18.3 *t*
3	40.9 *t*	44.2 *t*	41.6 *t*
4	34.2 *s*	34.6 *s*	33.6 *s*
5	44.2 *d*	51.2 *d*	48.3 *d*
6	37.8 *t**	67.0 *d*	27.7 *t**
7	199.0 *s*†	156.8 *s*	158.0 *s*
8	197.1 *s*†	24.7 *t*	28.0 *t**
9	215.5 *s*	203.8 *s*	204.1 *s*
10	51.6 *s*	44.6 *s*	44.1 *s*
11	33.8 *t*	131.5 *s*	130.5 *s*
12	19.2 *t*	20.8 *t*	20.7 *t*
13	124.0 *s*	123.8 *s*	123.7 *s*
14	110.9 *d*	111.2 *d*	111.0 *d*
15	142.5 *d*	142.5 *d*	142.1 *d*
16	138.9 *d*	139.3 *d*	138.8 *d*
17	23.6 *q*	24.5 *q*	17.1 *q*
18	33.0 *q*	32.1 *q*	32.2 *q*
19	22.6 *q*	22.2 *q*	22.1 *q*
20	17.0 *q*	12.5 *q*	12.3 *q*

*,†These assignments may be interchanged.

The C-7–C-9 hemiacetal of the C-7 enolic form of galeopsitrione (**4**, galeolone) was also present. It showed IR absorptions for hydroxyl (3420 cm^{-1}), furanoid (3150, 1505, 880 cm^{-1}) and α,β-unsaturated ketone (1670, 1650 cm^{-1}) groups. Its ^{1}H NMR spectrum showed signals (see Experimental) for a β-substituted furan ring, three C–Me groups, a methyl group adjacent to an α,β-unsaturated ketone and an AX system attributed to the C-6 and C-5 protons (δ 5.58, *d*, and 3.12, *d*, respectively, $J_{5,6}$ = 11 Hz). Moreover, UV absorptions at λ_{max} 211 nm (furan) and λ_{max} 265 nm (α-ether-α,β-unsaturated ketone) supported structure **4** for this substance. Treatment of galeolone (**4**) with hydrochloric acid in ethanol also yielded compound **7**.

Another diterpenoid isolated from *G. angustifolia*, galeopsinolone (**5**), was a $C_{20}H_{28}O_3$ compound. Its IR spectrum showed hydroxyl (3470 cm^{-1}), furanoid (3150, 3130, 1505, 880 cm^{-1}) and α,β-unsaturated ketone (1650, 1635 cm^{-1}) absorptions. The presence of an α,β-unsaturated ketone in galeopsinolone was also confirmed by its UV absorption at λ_{max} 238 nm ($\log\varepsilon$ = 3.74). The ^{1}H NMR spectrum of this substance showed signals in complete agreement with structure **5**: a β-substituted furan ring, three C–Me singlets (C-18–C-20), an ethyl side chain attached to a fully substituted sp^2 carbon atom (δ1.12, 3H, *t*, *J* = 7.5 Hz, 3H-17, and 2.43, 2H, *q*, *J* = 7.5 Hz, 2H-8), an AB system at δ3.55 and 3.29 (*J* = 15 Hz) due to the C-12 methylene group, and a one-proton doublet at δ 4.58, which must be assigned to the equatorial geminal proton of a C-6β (axial) hydroxyl group, because it is only coupled (*J* = 3.5 Hz) with the C-5α (axial) proton (δ 1.52, *d*, *J* = 3.5 Hz).

Chromium trioxide–pyridine oxidation of galeopsinolone (**5**) yielded the ene-dione derivative **11** (λ_{max} 253.5 nm, $\log\varepsilon$ = 3.98), the ^{1}H NMR spectrum of which showed a singlet at δ 2.50 for its C-5α proton. Furthermore, comparison of the ^{13}C NMR spectra (Table 1) of galeopsinolone (**5**) and compound **12**, a substance previously obtained from hispanolone (**1**) [4, 5], clearly confirmed structure **5** for this new diterpenoid. In particular, the β-effect on C-5 ($\Delta\delta$ + 2.9), the δ-effects on C-1, C-3 and C-17 ($\Delta\delta$ + 2.4, + 2.6 and + 7.4, respectively) and the γ-effects on C-4 and C-8 ($\Delta\delta$ + 1.0 and − 3.3, respectively) rigorously established the existence of a C-6β (axial) hydroxyl group in the molecule of galeopsinolone (**5**).

The last diterpenoid isolated from *G. angustifolia* has been named hispanone and it was identical in all respects with a compound previously obtained by dehydration of hispanolone (**1**) [4, 5]. Thus, hispanone possesses structure **6**.

From a biogenetic point of view, it is important to note that the hydrocarbon skeleton of galeopsitrione (**3**), galeolone (**4**) and galeopsinolone (**5**) must be derived from the labdane skeleton of galeopsin (**2**). A retroaldol reaction produces the 8,9-secolabdanes **3** and **4**, and a subsequent regioselective aldol condensation generates the rearranged labdane **5**.

On completion of this part of the work we had the opportunity of examining some samples of *G. angustifolia* collected in northern Italy. Extraction of the material gave a diterpene fraction containing pregaleopsin [1] and galeolone (**4**), but not the other diterpenoids found in the Spanish samples (compounds **1**–**3**, **5** and **6**). On the contrary, we isolated from the Italian samples the triterpene hederagenin (3β,23-dihydroxy-olean-12-en-28-oic acid) [6] and the flavones salvigenin (5-hydroxy-6,7,4′-trimethoxyflavone) and galangustin (5,7-dihydroxy-8,4′-dimethoxyflavone) [7], i.e. compounds that are absent from the Spanish samples. Therefore, some differences in chemical contents seem to occur between *G. angustifolia* growing in Spain and northern Italy; they could be attributed to varietal differences or to diversities of climate, humidity, soil, etc.

These results led us to carry out a chemotaxonomic survey of other representatives of the genus *Galeopsis*. We examined *G. ladanum* L., *G. speciosa* Miller, *G. terahit* L. subsp. *silvestris* Schlecht and *G. tetrahit* subsp. *reichenbachii* Reuter. None of these plants contained diterpenes, triterpenes or flavonoids. This negative result, however, may be of some chemotaxonomic significance. The genus *Galeopsis* [8, 9] is divided into two subgenera: *Ladanum* (*G. segetum* = *G. dubia* = *G. ochroleuca*, *G. pyrenaica*, *G. ladanum* = *G. intermedia*, *G. angustifolia* and *G. reuteri*) and *Galeopsis* (*G. speciosa*, *G. pubescens*, *G. tetrahit* and *G. bifida*). Only *G. ochroleuca* has been previously studied [10] and reported to contain some flavonoids. The occurrence of diterpenoids only in *G. angustifolia* could suggest the need to relocate this species in a separate subgenus.

Further chemotaxonomic investigation on other species of *Galeopsis* should be useful, also taking into account their possible pharmacological value as evidenced

by the current use of some species in traditional medicines [11].

EXPERIMENTAL

Mps are uncorr. Elemental analyses were carried out in Madrid with the help of an automatic analyser. Assignments of ^{13}C NMR shifts were made with the aid of off-resonance and noise-decoupled ^{13}C NMR spectra. Plant materials of *G. angustifolia* and *G. ladanum* were collected in June 1981 near Molina de Aragón (Guadalajara) and Rodiezmo (León), respectively, both in Spain, and voucher specimens were deposited in the Herbarium of the Faculty of Pharmacy (Madrid, Computense University, Spain). Plant materials of *G. speciosa* were collected in June 1981 in Austria, and of *G. angustifolia*, *G. tetrahit* subsp. *silvestris* and subsp. *reichenbachii* in June 1981 in northern Italy, and voucher specimens were deposited in the Herbarium of the Istituto di Botanica, University of Milano, Italy.

The previously known compounds were identified by their physical (mp, $[\alpha]_D$) and spectroscopic (IR, ^1H NMR, MS) data and by comparison with authentic samples.

Compounds **1**, **2**, **6**, **8** and **12** have been previously described [1, 2, 4, 5].

Isolation of the diterpenoids. Dried and finely powdered aerial parts (2.1 kg) of *G. angustifolia*, collected in Spain, were extracted (× 3) with Me_2CO (10 l.) at room temp. for 1 week. After filtration the extracts were evaporated to dryness under red. pres. and low temp. (26°). The residue (87 g) was chromatographed on a Si gel (Merck, No. 7734, deactivated with 15% H_2O) column (1.5 kg). Elution with *n*-hexane and *n*-hexane–EtOAc (19:1 and 9:1) gave, in order of elution, galeopsitrione (**3**, 240 mg), hispanone (**6**, 150 mg), galeolone (**4**, 36 mg), hispanolone (**1**, 4.3 g) [1, 2], galeopsinolone (**5**, 180 mg), galeopsin (**2**, 2.1 g) [1] and pregaleopsin (2.5 g) [1].

Identical treatment of a sample of *G. angustifolia* collected in Italy yielded galeolone (**4**), pregaleopsin [1], hederagenin [6], salvigenin and galangustin [7]. Samples of *G. speciosa*, *G. ladanum*, *G. tetrahit* subsp. *silvestris* and *G. tetrahit* subsp. *reichenbachii* were also investigated, but none of these plants contained triterpenes or diterpenes or flavonoids in detectable amounts.

Galeopsitrione (**3**). A syrup, $[\alpha]_D^{25}$ 1.5038; $[\alpha]_D^{24} - 7.5°$ ($CHCl_3$; *c* 0.61); IR ν_{max}^{NaCl} cm^{-1}: 3150, 3130, 1700 (*br*), 1503, 1465, 1385, 1355, 1170, 1070, 1027, 880, 790, 730; UV λ_{max}^{MeOH} nm (log ε): 221.5 (3.70), 245 (3.23); $\lambda_{max}^{MeOH+NaOMe}$ nm (log ε): 220 (3.74), 265 (3.64), 300 (3.34); ^1H NMR (90 MHz, $CDCl_3$): see Results and Discussion; ^{13}C NMR (25.2 MHz, $CDCl_3$): see Table 1; EIMS (direct inlet) 75 eV, *m/z* (rel. int.): 332 $[M]^+$ (6), 317 (3), 289 (100), 271 (7), 261 (4), 247 (6), 229 (8), 195 (9), 177 (8), 161 (7), 149 (8), 123 (60), 109 (24), 95 (33), 81 (84), 69 (36), 55 (33), 43 (60), 41 (51). (Found: C, 72.03; H, 8.53. $C_{20}H_{28}O_4$ requires: C, 72.26; H, 8.49%.)

Galeolone (**4**). A syrup, $[\alpha]_D^{20} + 31.4°$ ($CHCl_3$; *c* 0.59); IR ν_{max}^{NaCl} cm^{-1}: 3420, 3150, 2930, 2880, 1670, 1650, 1505, 1450, 1390, 1350, 1240, 1025, 880, 785; UV λ_{max}^{EtOH} nm (log ε): 211 (3.79), 265 (4.01); ^1H NMR (90 MHz, $CDCl_3$): δ 7.27 (1H, *m*, $W_{\frac{1}{2}}$ = 4.5 Hz, H-15 or H-16), 7.17 (1H, *m*, $W_{\frac{1}{2}}$ = 4.5 Hz, H-16, or H-15), 6.22 (1H, *m*, $W_{\frac{1}{2}}$ = 4 Hz, H-14), 5.58 (1H, *d*, *J* = 11 Hz, H-6), 3.12 (1H, *d*, *J* = 11 Hz, H-5), 2.73 (4H, complex signal, 2H-11 and 2H-12), 2.37 (3H, *s*, 3H-17), C–Me singlets at 1.10 (3H), 0.93 (3H) and 0.87 (3H); EIMS (direct inlet) 75 eV, *m/z* (rel. int.): 332 $[M]^+$ (31), 317 (2), 314 (1), 299 (5), 289 (19), 271 (3), 209 (27), 191 (14), 163 (12), 153 (15), 149 (15), 127 (34), 123 (52), 113 (30), 109 (36), 95 (70), 81 (82), 69 (56), 55 (37), 53 (35), 43 (100). (Found: C, 72.08; H, 8.43, $C_{20}H_{28}O_4$ requires: C, 72.26; H, 8.49%.)

Galeopsinolone (**5**). Mp 153–154° (from EtOAc–*n*-hexane); $[\alpha]_D^{21} - 117.9°$ ($CHCl_3$; *c* 0.273); IR ν_{max}^{KBr} cm^{-1}: 3470, 3150, 3130, 2990, 2960, 2930, 2900, 2870, 1650, 1635, 1505, 1455, 1375, 1290, 1210, 1165, 1040, 1025, 995, 950, 880, 770; UV λ_{max}^{MeOH} nm (log ε): 217 (3.72), 238 (3.74); ^1H NMR (90 MHz, $CDCl_3$): δ 7.25 (1H, *m*, $W_{\frac{1}{2}}$ = 4.5 Hz, H-15 or H-16), 7.13 (1H, *m*, $W_{\frac{1}{2}}$ = 4.5 Hz, H-16 or H-15), 6.20 (1H, *m*, $W_{\frac{1}{2}}$ = 4.5 Hz, H-14), 4.58 (1H, *d*, *J* = 3.5 Hz, equatorial H-6), 3.55 and 3.29 (an AB system, *J* = 15 Hz, 2H-12), 2.43 (2H, *br q*, *J* = 7.5 Hz, 2H-8), 1.52 (1H, *d*, *J* = 3.5 Hz, H-5), 1.12 (3H, *t*, *J* = 7.5 Hz, 3H-17), C–Me singlets at 1.38 (3H), 1.35 (3H) and 1.10 (3H). Some of these assignments (H-5, H-6, 2H-8, 2H-12 and 3H-17) were confirmed by double resonance expts. ^{13}C NMR (25.2 MHz, $CDCl_3$): see Table 1; EIMS (direct inlet) 75 eV, *m/z* (rel. int.): 316 $[M]^+$ (90), 301 (16), 298 (2), 287 (28), 283 (10), 269 (12), 255 (12), 231 (17), 219 (15), 203 (16), 192 (25), 164 (32), 109 (32), 91 (43), 81 (100), 69 (50), 55 (80), 53 (60), 43 (75). (Found: C, 75.69; H, 8.96. $C_{20}H_{28}O_3$ requires: C, 75.91; H, 8.92%.)

Hispanone (**6**). Mp 58–60° (from MeOH); $[\alpha]_D^{18} + 38.7°$ ($CHCl_3$; *c* 1.15) (lit. [4, 5]: mp 58–60°, $[\alpha]_D + 39.7°$). The IR, UV, ^1H NMR, ^{13}C NMR and MS of the natural diterpenoid (**6**) were identical with the previously reported data for the synthetic compound [4, 5].

Quinoxaline derivative of galeopsitrione. To a soln of **3** (20 mg) in H_2O–HOAc (9:1, 3 ml) a crystal (*ca* 20 mg) of σ-phenylendiamine was added. The soln was then heated at 100° for 10 min. Work-up in the usual manner yielded the quinoxaline derivative (23 mg, after two crystallizations from MeOH), mp 101–103°; IR ν_{max}^{KBr} cm^{-1}: 3150, 3080, 2940, 2880, 1695, 1575, 1505, 1495, 1445, 1397, 1390, 1030, 880, 770, 730; UV λ_{max}^{MeOH} nm (log ε): 237.5 (4.23), 308 sh (3.66), 319 (3.75), 330 sh (3.61); ^1H NMR (90 MHz, $CDCl_3$): δ 8.10–7.45 (4H, complex signal, aromatic protons), 7.17 (1H, *m*, $W_{\frac{1}{2}}$ = 5 Hz, H-15 or H-16), 6.80 (1H, *m*, $W_{\frac{1}{2}}$ = 4 Hz, H-16 or H-15), 5.90 (1H, *m*, $W_{\frac{1}{2}}$ = 4 Hz, H-14), 2.80 (3H, *s*, 3H-17), C–Me singlets at 1.53 (3H), 1.07 (3H) and 1.03 (3H); EIMS (direct inlet) 75 eV, *m/z* (rel. int.): 404 $[M]^+$ (55), 389 (15), 281 (100), 254 (8), 252 (10), 171 (30), 158 (85), 123 (45), 102 (10), 95 (15), 81 (70), 69 (20), 41 (50). (Found: C, 77.26; H, 7.83; N, 7.08. $C_{26}H_{32}O_2N_2$ requires: C, 77.19; H, 7.97; N, 6.93%.)

Compound **7** *from galeopsitrione* (**3**) *and galeolone* (**4**). To a soln of **3** (50 mg) in EtOH (10 ml) conc. HCl (1 ml) was added, and the soln heated under reflux for 5 hr. The soln was then cooled, diluted with H_2O and extracted with $CHCl_3$. Evaporation of the solvent yielded pure **7** (42 mg), mp 107–108° (from MeOH); $[\alpha]_D^{20} - 4.4°$ ($CHCl_3$; *c* 0.86); IR ν_{max}^{KBr} cm^{-1}: 3160, 3130, 3015, 3005, 2980, 2960, 2920, 2880, 2850, 1680, 1620, 1590, 1540, 1460, 1390, 1380, 1335, 1305, 1200, 1135, 1085, 1035, 910, 880, 790, 775, 740, 700; UV λ_{max}^{MeOH} nm (log ε): 236.5 (4.52), 258 (3.76), 272 (3.62), 310 (3.06); ^1H NMR (90 MHz, $CDCl_3$): δ 8.20 (1H, *s*, H-12), 7.60 (1H, *d*, *J* = 2.4 Hz, H-15), 6.79 (1H, *d*, *J* = 2.4 Hz, H-14), 3.05 (1H, *dd*, part A of an ABX system, J_{AB} = 17 Hz, J_{AX} = 5 Hz, H-6α), 2.83 (1H, *dd*, part B of an ABX system, J_{BX} = 11 Hz, H-6β), 2.49 (3H, *s*, 3H-17), 2.07 (1H, *dd*, part X of an ABX system, H-5), C–Me singlets at 1.13 (6H) and 1.06 (3H); EIMS (direct inlet), 75 eV, *m/z* (rel. int.): 296 $[M]^+$ (100), 281 (55), 255 (45), 213 (36), 211 (35), 186 (36), 144 (18), 128 (15), 115 (20), 55 (22), 41 (40). (Found: C, 80.86; H, 8.26. $C_{20}H_{24}O_2$ requires: C, 81.04; H, 8.16%.)

Identical treatment of galeolone (**4**) also yielded **7**.

Compounds **8** *and* **9** *from galeopsin* (**2**). The preparation of **8** from galeopsin (**2**) has been previously described [1]. Treatment of **8** with *t*-BuOK in C_6H_6 soln, at room temp. for 12 hr quantitatively yielded **9** as an inseparable mixture of the C-8 epimers [1]. Quantitative transformation of galeopsin (**2**) into **9** was achieved by treatment of **2** with 5% ethanolic KOH for 24 hr at room temp. Compound **9** was a syrup, IR ν_{max}^{NaCl} cm^{-1}: 3440, 3150, 2920, 2880, 2860, 1665, 1635, 1503, 1455, 1370, 1150, 1060, 1025, 880, 775; UV λ_{max}^{MeOH} nm (log ε): 218 (3.81), 242 (3.95); ^1H

NMR (90 MHz, $CDCl_3$): δ 7.25 (1H, *m*, $W_{\frac{1}{2}}$ = 4.5 Hz, H-15 or H-16), 7.10 (1H, *m*, $W_{\frac{1}{2}}$ = 4.5 Hz, H-16 or H-15), 6.17 (1H, *m*, $W_{\frac{1}{2}}$ = 4.5 Hz, H-14), 4.93 (1H, *q*, *J* = 6 Hz, H-8), 3.51 and 3.19 (an AB system, *J* = 15 Hz, 2H-12), 1.29 (3H, *d*, *J* = 6 Hz, 3H-17), C–Me singlets at 1.05 (3H), 1.01 (3H) and 0.97 (3H); EIMS (direct inlet), 75 eV, *m/z* (rel. int.): 316 $[M]^+$ (70), 301 (8), 298 (22), 283 (20), 273 (32), 146 (28), 109 (34), 95 (22), 91 (40), 81 (100), 69 (70), 55 (54).

After treatment of **9** with HCl–EtOH as previously described for galeopsitrione (**3**), only the starting material was recovered.

Ene-dione **10**. CrO_3–pyridine oxidation of **9** (300 mg) yielded **10** (290 mg) as a syrup, $[n]_D^{17}$ 1.5317; $[\alpha]_D^{21}$ −72.9° ($CHCl_3$; *c* 0.635); IR ν_{max}^{NaCl} cm^{-1}: 3160, 3150, 2940, 2880, 2860, 1695, 1680, 1505, 1460, 1430, 1360, 1230, 1170, 1030, 880, 780; UV λ_{max}^{MeOH} nm (log ε): 214.5 (3.92), 242 (3.88); ^1H NMR (90 MHz, $CDCl_3$): δ 7.21 (1H, *m*, $W_{\frac{1}{2}}$ = 4.5 Hz, H-15 or H-16), 7.15 (1H, *m*, $W_{\frac{1}{2}}$ = 4.5 Hz, H-16 or H-15), 6.20 (1H, *m*, $W_{\frac{1}{2}}$ = 4.5 Hz, H-14), 3.43 and 3.27 (an AB system, *J* = 14 Hz, 2H-12), 2.31 (3H, *s*, 3H-17), C–Me singlets at 1.03 (3H), 1.00 (3H) and 0.93 (3H); EIMS (direct inlet), 75 eV, *m/z* (rel. int.): 314 $[M]^+$ (66), 299 (22), 285 (7), 271 (5), 147 (12), 109 (10), 91 (16), 81 (28), 69 (18), 55 (23), 43 (100), 41 (40). (Found: C, 76.23; H, 8.49. $C_{20}H_{26}O_3$ requires: C, 76.40; H, 8.34%.)

Compound **7** *from* **10**. Treatment of **10** with HCl–EtOH as previously described for galeopsitrione, quantitatively yielded **7** (identical mp, mmp, TLC, $[\alpha]_D$, IR, UV, ^1H NMR and MS).

CrO_3–*pyridine oxidation of galeopsinolone* (**5**) *to give* **11**. This was performed in the usual manner. Compound **11** is a syrup, $[n]_D^{15}$ 1.5266; $[\alpha]_D^{21}$ −82.3° ($CHCl_3$; *c* 0.35); IR ν_{max}^{NaCl} cm^{-1}: 3150, 2940, 2880, 1690, 1670, 1620, 1505, 1460, 1380, 1240, 1185, 1175, 1025, 995, 880, 780; UV λ_{max}^{MeOH} nm (log ε): 215.5 (3.77), 253.5 (3.98); ^1H NMR (90 MHz, $CDCl_3$): δ 7.27 (1H, *m*, $W_{\frac{1}{2}}$ = 4.5 Hz, H-15 or H-16), 7.17 (1H, *m*, $W_{\frac{1}{2}}$ = 4.5 Hz, H-16 or H-15), 6.18 (1H, *m*, $W_{\frac{1}{2}}$ = 4.5 Hz, H-14), 3.62 and 3.42 (an AB system, *J* = 14 Hz, 2H-12), 2.50 (1H, *s*, H-5), 2.42 (2H, *q*, *J* = 7.5 Hz, 2H-8), 1.00 (3H, *t*, *J* = 7.5 Hz, 3H-17), C–Me singlets at 1.28 (3H) and 1.13 (6H); EIMS (direct inlet), 75 eV, *m/z* (rel. int.): 314 $[M]^+$ (100), 299 (16), 285 (8), 281 (9), 271 (12), 231 (14), 229 (12), 162 (10), 109 (27), 95 (20), 91 (30), 81 (68), 67 (31), 55 (56), 53 (54), 43 (36), 41 (92). (Found: C, 76.23; H, 8.29. $C_{20}H_{26}O_3$ requires: C, 76.40; H, 8.34%.)

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