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Phytochemistry, Vol. 23, No. 12, pp. 2958–2959, 1984.
Printed in Great Britain.

0031-9422/84 $3.00 + 0.00

GALEUTERONE AND PREGALEUTERONE, LABDANE DITERPENOIDS FROM *GALEOPSIS REUTERI*

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(*Received* 13 *March* 1984)

Key Word Index—*Galeopsis reuteri*; Labiatae; diterpenoids; furanic and prefuranic labdane derivatives; galeuterone; pregaleuterone.

Abstract—From the aerial part of *Galeopsis reuteri* a furanic labdane diterpenoid, galeuterone, and its prefuranic derivative, pregaleuterone, have been isolated. The structures of these substances have been established mainly by spectroscopic means.

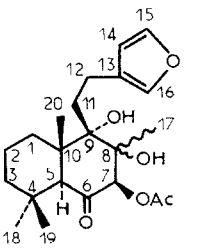
INTRODUCTION

In our search for new natural diterpenoids in the Labiatae plants belonging to the genus *Galeopsis* [1, 2], we have examined the aerial part of *G. reuteri* Reichenb. From this source two diterpenes, galeuterone (**1**) and pregaleuterone (**2**), have been isolated and their structures established mainly by spectroscopic means.

RESULTS AND DISCUSSION

Galeuterone (**1**) has a molecular formula $C_{22}H_{32}O_6$ and its IR spectrum showed hydroxyl (3570, 3510, 3460 cm^{-1}), furanic (3145, 1505, 875 cm^{-1}), acetate (1740, 1255 cm^{-1}) and ketone (1725 cm^{-1}) absorptions. The ^1H NMR spectrum of this diterpenoid showed signals in agreement with a structure such as **1**: δ7.35 (1H, *t*, $J_{15,14} = J_{15,16} = 1.8$ Hz, H-15), 7.30 (1H, *m*, $W_{1/2} = 3$ Hz, H-16), 6.30 (1H, *dd*, $J_{14,15} = 1.8$ Hz, $J_{14,16} = 0.6$ Hz, H-14), 5.31 (1H, *d*, $^4J_{7\alpha,5\alpha} = 0.8$ Hz, H-7α), 2.90 (1H, *d* (*br*), $^4J_{5\alpha,7\alpha} = 0.8$ Hz, H-5α), 2.18 (3H, *s*, OAc), 1.33 (3H, *s*, Me-17), 1.25 (3H, *s* (*br*), Me-20), 1.02 and 0.92 (3H each, *s*, Me-18 and Me-19). In addition, the ^1H NMR spectrum of **1** showed two one proton singlets at δ2.21 and 1.98 which disappeared after addition of D_2O and were assigned to the C-8 and C-9 tertiary hydroxyl groups. Double resonance experiments confirmed all the above assignments and established that the H-5α proton was coupled with the H-7 proton and the Me-20 group [3], because irradiation at δ2.90 transformed the H-7 doublet signal at δ5.31 into a singlet and caused a noticeable narrowness of the signal at δ1.25. The observed coupling between the H-5α and H-7 protons ($^4J = 0.8$ Hz) can only be explained if ring B of galeuterone adopts a boat conformation in which the Me-20–C-8β-substituent 1,3-diaxial interactions are minimized. In this conformation the pseudoequatorial C-7α proton is coupled through the C-6 carbonyl group with the C-5α pseudoaxial proton [4]. Thus establishing a C-7β configuration for the acetoxyl group of galeuterone (**1**).

A less probable alternative structure for galeuterone, with the acetoxyl group at the C-6β position and the



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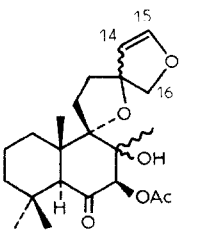

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ketone at the C-7 position was discarded for the following reasons. In labdane derivatives with C-6β hydroxyl and C-7 keto groups, such as leosibirin [5] and ballotenol [6], the C-5α proton appears as a doublet ($J_{5\alpha,6\alpha}$ = 3 Hz) at δ2.00 and 1.92, respectively, whereas in compounds with a C-6 keto and C-7β hydroxyl isomeric structure, such as isoleosibirin [5] and isoballotenol [6], the C-5α proton shows a broad singlet signal at δ3.29 and 3.20, respectively. Thus, the data of galeuterone ($\delta_{H\text{-}5\alpha}$ 2.90, *d* (*br*), *J* = 0.8 Hz) are in agreement with a 6-keto-7-acetoxy arrangement (**1**). Moreover, the ^{13}C NMR spectrum of galeuterone (Table 1) showed carbon atom resonances in complete agreement with structure **1** for this diterpenoid. In particular, the observed $\delta_{C\text{-}5}$ and $\delta_{C\text{-}10}$ values (56.6 and 49.8, respectively, see Table 1) are almost identical (δ55.7 and 48.4, respectively) with those calculated for 7β-acetoxy-8ξ,9α-dihydroxy-6-ketolabdane derivatives from the reported data of closely related structures [1, 5–8] and very different from those calculated for the 6β-acetoxy-7-keto isomeric arrangement (δ50.0 and 44.7, respectively).

The other diterpenoid isolated from *G. reuteri*, pregaleuterone (**2**), also has a molecular formula $C_{22}H_{32}O_6$. Its ^{1}H NMR spectrum was very similar to that of galeuterone (**1**), the differences being consistent with the occurrence in **2** of a β,β-disubstituted dihydrofuran [δ6.51 and 5.26 (1H each, *d*, *J* = 2.7 Hz, H-15 and H-14, respectively), 4.53 and 4.13 (AB system, *J* = 10.5 Hz, 2H-16)] instead of the β-monosubstituted furan ring of galeuterone (**1**). This assignment was confirmed by the ready conversion of pregaleuterone (**2**) to galeuterone (**1**) by mild acidic reagents.

The stereochemistry at C-8 and the absolute configuration of these diterpenoids (**1** and **2**) were not ascertained. However, on biogenetic grounds we suppose that galeuterone (**1**) and pregaleuterone (**2**) belong to the normal labdane series, since this absolute configuration has been found in all the diterpenoids isolated from *Galeopsis* species [1, 2].

EXPERIMENTAL

For general details on experimental, see refs [1, 2]. Plant materials were collected in July 1983, at Val di Gesso, Alpi Marittime, Italy, and voucher specimens were deposited in the herbarium of the Dipartimento di Biologia, University of Milan, Italy.

Extraction and isolation of the diterpenoids. Dried and finely powdered *G. reuteri* aerial parts (120 g) were extracted with Me_2CO (1 l. × 3) at room temp. for 3 days. The extracts were evaporated to dryness under red. pres. and low temp. (26°). The residue (7 g) was chromatographed on a silica gel (Merck. No. 7734, deactivated with 15% H_2O) column (200 g). Elution with petrol–EtOAc (7:3) gave in order of elution, galeuterone (**1**, 50 mg) and pregaleuterone (**2**, 250 mg).

Galeuterone (**1**). Mp 187–189° (from EtOAc–*n*-hexane); $[\alpha]_D^{19}$ +88.1° ($CHCl_3$; *c* 0.36); IR ν_{max}^{KBr} cm^{-1}: 3570, 3510, 3460, 3145, 3010, 2930, 2880, 1740, 1725, 1505, 1470, 1385, 1275, 1255, 1240, 1155, 1060, 1025, 930, 875, 720; ^{1}H NMR (90 MHz, $CDCl_3$): see discussion of results; ^{13}C NMR (75.4 MHz, $CDCl_3$): see Table 1; EIMS (direct inlet) 75 eV, *m/z* (rel. int.): 392 $[M]^+$ (4), 377 (2), 374 (3), 332 (6), 317 (4), 315 (4), 275 (10), 225 (6), 209 (23), 183 (16), 168 (8), 151 (24), 123 (14), 109 (15), 95 (21), 85 (40), 82 (20), 81 (47), 69 (17), 55 (13), 43 (100). (Found: C, 67.60; H, 8.49. $C_{22}H_{32}O_6$ requires: C, 67.32; H, 8.22%.)

Pregaleuterone (**2**). A syrup; $[\alpha]_D^{19}$ +36.0° ($CHCl_3$; *c* 0.33); IR ν_{max}^{NaCl} cm^{-1}: 3500, 3100, 3010, 2940, 2880, 1740, 1725, 1620, 1470, 1380, 1240, 1150, 1020, 950, 920, 900, 855; ^{1}H NMR (90 MHz, $CDCl_3$): δ6.51 (1H, *d*, *J* = 2.7 Hz, H-15), 5.28 (1H, *d*, $J_{7\alpha,5\alpha}$ = 0.8 Hz, H-7α), 5.26 (1H, *d*, *J* = 2.7 Hz, H-14), 4.53 and 4.13 (an AB system, *J* = 10.5 Hz, 2H-16), 2.73 (1H, *d* (*br*), $J_{5\alpha,7\alpha}$ = 0.8 Hz, H-5α), 2.20 (3H, *s*, OAc), 2.04 (1H, *s*, disappeared after addition of D_2O, hydroxyl proton at C-8), 1.25 (6H, *s*, Me-17 and Me-20), 1.01 (3H, *s*) and 0.93 (3H, *s*) C-18 and C-19 methyl groups; EIMS (direct inlet) 75 eV, *m/z* (rel. int.): 392 $[M]^+$ (13), 377 (1), 374 (1), 359 (1), 332 (11), 275 (23), 225 (17), 209 (43), 183 (34), 168 (16), 153 (29), 123 (30), 109 (31), 95 (42), 85 (83), 82 (100), 81 (84), 69 (31), 55 (26), 43 (90). $C_{22}H_{32}O_6$ MW 392.

Galeuterone (**1**) *from pregaleuterone* (**2**). A suspension of pregaleuterone (**2**, 40 mg), CH_2Cl_2 (10 ml) and Amberlite IR-120 (H^+ form, 150 mg) was stirred at room temp. for 1 hr. The soln was filtered, the solvent removed and the residue crystallized from EtOAc–*n*-hexane yielding galeuterone (**1**, 32 mg), identical with the sample previously isolated (mp, mmp, $[\alpha]_D$, IR, ^{1}H NMR, MS and TLC).

Table 1. ^{13}C NMR data of galeuterone (**1**) (75.4 MHz, $CDCl_3$, TMS as int. standard)

Carbon No.	δ	Carbon No.	δ
1	32.2 *t**	11	28.8 *t*
2	17.8 *t*	12	21.5 *t*
3	42.1 *t*	13	124.6 *s*
4	32.4 *s*	14	110.8 *d*
5	56.6 *d*	15	143.3 *d*
6	80.8 *d*	16	138.8 *d*
7	204.1 *s*	17	18.0 *q*
8	83.3 *s*	18	32.5 *q*
9	78.4 *s*	19	22.2 *q*†
10	49.8 *s*	20	22.7 *q*†
OAc	169.7 *s*, 20.7 *q*		

*SFORD multiplicity.

†These assignments may be reversed.

Acknowledgements—We thank Miss M. D. Casado and Mrs. M. Plaza, Madrid, for recording the ^{1}H and ^{13}C NMR spectra. This work was supported by the 'Istituto C.N.R. per lo Studio delle Sostanze Naturali di Interesse Alimentare e Chimico-Farmaceutico', Catania, Italy, and by the Spanish 'Comisión Asesora de Investigación Científica y Técnica' (grant No. 11/1981).

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