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# 19-HYDROXYGALEOPSIN, A LABDANE DITERPENOID FROM *LEONURUS CARDIACA*

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**Key Word Index**—*Leonurus cardiaca*; Lamiaceae; labdane derivatives; 19-hydroxygaleopsin.

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**Abstract**—A new labdane diterpene, 19-hydroxygaleopsin, has been isolated from *Leonurus cardiaca*. Its structure was established by $^1$H and $^{13}$C NMR studies, and by examination of its acetate. © 1997 Elsevier Science Ltd

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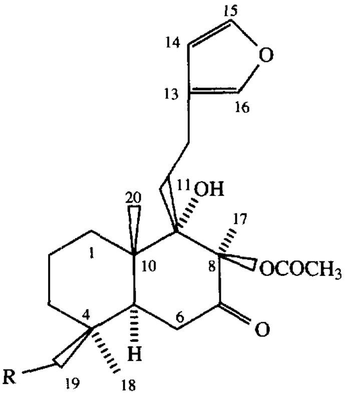
## INTRODUCTION

*Leonurus cardiaca* L. is widespread in Bulgaria and has been used in folk medicine for the treatment of tachycardia, hypertonia and nervous disorders [1]. We have described the isolation of a number of new labdane diterpenoids [2–4]. A study of another fraction of the same plant material has now allowed the isolation of a new labdane diterpenoid, 19-hydroxygaleopsin (**1**). Its structure was established by spectroscopic methods as well as by examination of its acetate.

## RESULTS AND DISCUSSION

19-Hydroxygaleopsin (**1**) had a molecular formula $C_{22}H_{32}O_6$. Its IR spectrum showed typical absorptions for alcoholic (3543, 1156 and 1056 cm$^{-1}$), furan (3136, 1500 and 873 cm$^{-1}$), an ester group and broad ketone (1724 cm$^{-1}$ *br*). Its $^1$H NMR spectrum (Table 1) was consistent with a $\beta$-substituted furan partial structure (two $\alpha$-furan protons at $\delta$ 6.30 and 7.26 and one $\beta$-furan proton at $\delta$ 7.38), a primary hydroxyl group attached to a fully substituted sp$^3$ carbon atom (an AB system at $\delta$ 3.59 and 3.68, 1H each, *d*, $J = 10.9$ Hz, 2H-19), an acetoxyl group (at $\delta$ 2.08, 3H, *s*) and also with three tertiary methyl groups (at $\delta$ 1.00, 3H, *s*, Me-18; 1.22, *s*, 3H, Me-20 and 1.49, 3H, *s*, Me-17). The C-8 atom must have two fully substituted carbon atoms attached to it. These data suggested that the keto group should be at the C-7 position. The $^{13}$C NMR data (Table 1) confirmed all of the above assignments, which were very similar to those reported for related compounds [5].



**1** R = OH
**2** R = OAc

The relative stereochemistry of **1** was also in agreement with its NOESY spectrum, which showed cross-peaks of NOEs between the Me-17 protons ($\delta$ 1.49 *s*) and the equatorial H-6 ($\delta$ 2.44 *br t*), as well as between the H-6$\alpha$ and the Me-18 protons ($\delta$ 1.00 *s*). Therefore the configuration of the tertiary methyl on C-8 must be equatorial. The axial C-19 protons ($\delta$ 3.59 *d* and 3.68 *d*) displayed NOEs with the Me-18 and Me-20 ($\delta$ 1.22 *s*) protons and the axial H-6$\beta$ ($\delta$ 2.68 *dd*). Moreover, the acetoxyl group at $\delta$ 2.08 *s* showed NOEs interactions with the Me-17 and Me-20 protons.

Treatment of compound **1** with acetic anhydride in pyridine in mild conditions, afforded **2** ($C_{24}H_{34}O_7$). The spectroscopic properties of **2** revealed the presence of a diacetate ($\delta$ 2.05, 3H, *s* and 2.09, 3H, *s*). The acetylation caused noticeable para-magnetic shifts for the C-19 protons ($\Delta\delta$+0.29 and 0.55 ppm, respectively). The IR spectrum of **2** was devoid of hydroxyl

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Table 1. $^1H$ and $^{13}C$ NMR spectral data for compounds **1** and **2** (250 MHz, $CDCl_3$ and 62.9 MHz, $CDCl_3$)

| H | 1 | 2 | C | 1 | 2 |
|---|---|---|---|---|---|
| 1 | 1.48* | — | 1 | 35.5 *t* | 35.4 *t* |
| | 1.70* | — | 2 | 17.6 *t* | 17.8 *t* |
| 2 | 1.60* | — | 3 | 35.5 *t* | 35.8 *t* |
| | 1.72* | — | 4 | 44.5 *s* | 44.4 *s* |
| 3 | 1.08* | — | 5 | 50.0 *d* | 49.7 *d* |
| | 1.52* | — | 6 | 36.3 *t* | 36.1 *t* |
| 5α | 1.89 *dd* | 1.87 *dd* | 7 | 206.9 *s* | 206.4 *s* |
| 6α | 2.44 *dd* | 2.45 *dd* | 8 | 88.3 *s* | 88.2 *s* |
| 6β | 2.68 *dd* | 2.65 *dd* | 9 | 81.7 *s* | 81.7 *s* |
| 11α | 2.53 *br t* | 2.52 *br t* | 10 | 44.4 *s* | 44.5 *s* |
| 11β | 2.10 *dd* | 2.11 *dd* | 11 | 32.2 *t* | 32.0 *t* |
| 12(2H) | 2.15 *m** | 2.19 *m** | 12 | 21.3 *t* | 21.3 *t* |
| 14 | 6.30 *m* | 6.31 *m* | 13 | 124.6 *s* | 124.5 *s* |
| 15 | 7.38 *m* | 7.38 *m* | 14 | 110.8 *d* | 110.7 *s* |
| 16 | 7.26 *m* | 7.32 *m* | 15 | 143.2 *d* | 143.2 *d* |
| 17 | 1.49 *s* | 1.49 *s* | 16 | 138.8 *d* | 138.7 *d* |
| 18 | 1.00 *s* | 1.00 *s* | 17 | 26.8 *q* | 25.7 *q* |
| 19 A | 3.59 *d* | 3.89 *d* | 18 | 17.1 *q* | 17.2 *q* |
| 19 B | 3.68 *d* | 4.23 *d* | 19 | 65.9 *t* | 67.0 *t* |
| 20 | 1.22 *s* | 1.22 *s* | 20 | 15.1 *q* | 15.0 *q* |
| OAc | 2.08 *s* | 2.05 *s* | $OCO\underline{C}H_3$ | 21.4 *q* | 21.3 *q* |
| OAc | — | 2.09 *s* | $O\underline{C}OMe$ | 169.1 *s* | 169.1 *s* |
| | | | $OCOCH_3$ | — | 21.2 *q* |
| | | | $O\underline{C}OMe$ | — | 171.2 *s* |

*J* (Hz): 5α,6α = 2.4; 5α,6β = 14.3; 6α,6β = 11.8; 11α,12β = 8.3; 11α,12α = 2.2; 11α,11β = 7.2; 19A,19B = 10.9.

* The multiplicity of these signals is due to overlapping.

absorptions but showed the characteristic absorptions due to acetate (1739 and 1245 cm$^{-1}$).

The absolute stereochemistry of compound **1** was not ascertained. However it is reasonable to assume that it belongs to the normal-labdane series, like galeopsin [5].

## EXPERIMENTAL

Mps: uncorr. Plant material was collected near the town of Burgas (eastern Bulgaria) in June 1995 and voucher specimens were deposited in the Herbarium of the Higher Institute of Agriculture at Plovdiv, Bulgaria.

*Extraction and isolation of the diterpenoid.* Dried and powdered aerial parts of *Leonurus cardiaca* L. (2.7 kg) were extracted with $Me_2CO$ (3 × 7 l) at room temp. for 1 week. After filtration, the solvent was evapd to dryness under red. pres. and low temp. (35°) yielding a residue (72 g), which was dissolved in MeOH (1 l) and extracted with petrol (6 × 200 ml). The petrol phase was concd giving a residue (50 g) which was subjected to CC (silica gel Merck N7734, deactivated with 15% $H_2O$, 250 g). Elution with $CH_2Cl_2$ gave pure 19-hydroxygaleopsin (**1**, 60 mg).

*19-Hydroxygaleopsin* (**1**). Mp 167–169°; $[\alpha]_D^{20}$ +13.29° ($CHCl_3$, *c* 0.43). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3543, 3136, 3113, 3003, 2973, 2945, 2920, 2872, 2851, 1724, 1671, 1606, 1591, 1500, 1471, 1448, 1439, 1373, 1339, 1265, 1208, 1194, 1181, 1156, 1103, 1088, 1056, 1036, 1024, 982, 945, 905, 873, 846, 834, 813, 783, 771, 728, 673, 638, 613, 602, 577, 538, 516, 503, 457. $^1H$ and $^{13}C$ NMR (Table 1). EIMS (70 eV, direct inlet) *m*/*z* (rel. int.): 392 $[M]^+$ (0.5), 374 (4), 350 (5), 332 (7), 305 (16), 290 (8), 279 (9), 191 (10), 179 (18), 173 (12), 123 (100), 121 (12), 109 (50), 107 (10), 95 (15), 93 (9), 82 (35), 81 (25), 67 (15). Found: C, 67.44; H, 8.21, $C_{22}H_{32}O_6$, requires: C, 67.35; H, 8.16.

*Acetylation of* **1**. A soln of **1** (15 mg) in pyridine (0.2 ml) was treated with $Ac_2O$ (0.2 ml) for 3 hr at room temp. After the usual work-up, 16 mg of **2** was obtained, mp 66–68°, $[\alpha]_D^{20}$ +14.03 (3.9 mg, $CHCl_3$). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3538, 3139, 2931, 2874, 1739, 1642, 1605, 1497, 1469, 1446, 1373, 1245, 1158, 1114, 1087, 1026, 984, 953, 908, 874, 850, 787, 733, 697, 677, 635, 602. $^1H$ and $^{13}C$ NMR (Table 1). MS, *m*/*z*: 434 $[M]^+$, 391 $[M\text{-}CH_3CO]^+$, 374 $[M\text{-}CH_3CO_2H]^+$. Found:

C, 66.41; H, 7.86, $C_{24}H_{34}O_7$, requires: C, 66.36 H, 7.83.

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