

A PREFURANIC LABDANE DITERPENE FROM *LEONURUS* *CARDIACA*

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(Received 24 February 1997)

Key Word Index—*Leonurus cardiaca*; Labiatae; diterpenoid; prefuranic labdane derivative; 19-acetoxypregaleopsin.

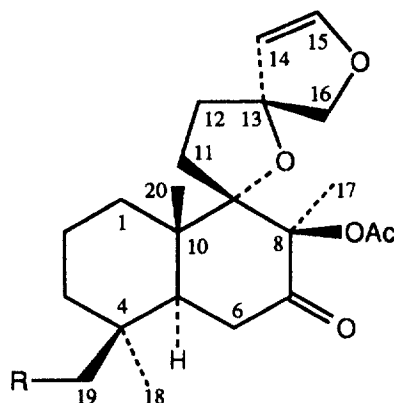
Abstract—A new diterpenoid, 19-acetoxypregaleopsin, has been isolated from the aerial parts of *Leonurus cardiaca*. Its structure, [(13*R*)-8β,19-diacetoxy-9α,13; 15,16-diepoxy]labd-14-en-7-one] was established by spectroscopic means. © 1998 Elsevier Science Ltd. All rights reserved

INTRODUCTION

Several furanic and prefuranic labdane diterpenes have been isolated from some species of *Leonurus* [1–5]. Recently [6], four known diterpenoids, leosibirin, leosibiricin [1], preleosibirin [7] and isoballotenol acetate [8], have been identified in an acetone extract of shoot cultures of *L. cardiaca*, a species from which a *neo-clerodane* diterpenoid was isolated some years ago [9]. Now, an investigation of an acetone extract of the aerial parts of a wild plant of this species allowed the isolation of a new prefuranic labdane diterpene, 19-acetoxypregaleopsin, whose structure (**1**) was established by spectroscopic means and by comparison with closely related compounds.

RESULTS AND DISCUSSION

The IR spectrum of the new diterpenoid (19-acetoxypregaleopsin, **1**, C₂₄H₃₄O₇) showed acetate (1740, 1735, 1250 cm⁻¹), ketone (1725 cm⁻¹) and vinyl ether (3120, 1610 cm⁻¹) [1, 2, 7] absorptions but did not show hydroxyl bands. Its ¹H and ¹³C NMR spectra (Table 1) were very similar to those of pregaleopsin (**2**) [10] and almost identical to those of the *p*-bromobenzoate derivative (**3**) of 4β-hydroxymethylpregaleopsin (**4**), a diterpenoid found in *L. persicus* whose structure, including its absolute configuration, was established by an X-ray diffraction analysis of **3**



- 1** R=OAc
- 2** R=H
- 3** R=*p*-OCOC₆H₄Br
- 4** R=OH

[4]. The slight differences observed between the ¹H and ¹³C NMR spectra of **1** (Table 1) and **3** [4] were consistent with the presence in the former of a C-19 acetoxyl group instead of the *p*-bromobenzoate of the latter.‡

The relative stereochemistry of **1** was also in agreement with its NOESY spectrum, which showed NOE cross-peaks between the Me-17 protons (δ 1.33 s) and one of the C-16 methylene protons (δ 4.48 d) and between the H-14 (δ 5.10 d) and Me-20 (δ 1.16 s) protons, as well as between the axial C-19 protons (δ 3.84 d and 4.20 d) and the Me-18 (δ 0.97 s) and Me-20 protons. Moreover, the acetoxyl group at δ 2.06 displayed a NOE with the Me-17 and Me-20 protons,

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‡ In ref. [4], the numbering system for defining the substituents of the C-4 carbon is not correct and must be reversed (see Connolly, J. D. and Hill, R. A., *Dictionary of Terpenoids*, Vol. 1. Chapman and Hall, London, 1991, p. 32).

Table 1. ^1H and ^{13}C NMR spectral data for compound **1***

H	1	H	1	C	1	C	1
1	1.45† 1.69†	14 15	5.10 <i>d</i> 6.41 <i>d</i>	1 2	33.7 <i>t</i> 17.8 <i>t</i>	13 14	94.7 <i>s</i> 106.8 <i>d</i>
2	1.60† 1.70†	16A 16B	4.04 <i>d</i> 4.48 <i>d</i>	3 4	35.9 <i>t</i> 37.9 <i>s</i>	15 16	148.5 <i>d</i> 80.3 <i>t</i>
3	1.15† 1.66†	Me-17 Me-18	1.33 <i>s</i> 0.97 <i>s</i>	5 6	50.5 <i>d</i> 35.7 <i>t</i>	17 18	15.8 <i>q</i> 26.8 <i>q</i>
5 α	1.81 <i>dd</i>	19A	3.84 <i>d</i>	7	205.1 <i>s</i>	19	66.9 <i>t</i>
6 α	2.41 <i>dd</i>	19B	4.20 <i>d</i>	8	87.5 <i>s</i>	20	18.2 <i>q</i>
6 β	2.53 <i>dd</i>	Me-20	1.16 <i>s</i>	9	96.7 <i>s</i>	8-OAc	169.0 <i>s</i>
11	2.10† 2.26†	8-OAc‡ 19-OAc‡	2.06 <i>s</i> 2.03 <i>s</i>	10 11	42.9 <i>s</i> 28.9 <i>t</i>		21.4 <i>q</i> 171.2 <i>s</i>
12	2.14 (2H)†			12	38.4 <i>t</i>	19-OAc	20.9 <i>q</i>

$J_{\text{H,H}}$ (Hz): 5 α ,6 α = 2.6; 5 α ,6 β = 14.3; 6 α ,6 β = 11.7; 14,15 = 2.6; 16A,16B = 10.6; 19A,19B = 11.0.

* 400 MHz (^1H) and 100.57 MHz (^{13}C), CDCl_3 . Chemical shifts (δ values) are relative to residual CHCl_3 for ^1H (δ 7.25) and to the solvent for ^{13}C (δ_{CDCl_3} , 77.00). The multiplicities of the carbons were assigned from the HMQC and DEPT spectra.

† The multiplicity of these signals is unclear due to overlapping.

‡ These assignments are in agreement with the NOESY spectrum.

whereas, the acetate at δ 2.03 showed NOE interactions with the Me-18 and Me-20 protons, thus allowing the assignment of the acetates (Table 1). All these NOESY data confirmed [7, 10, 11] the relative configuration depicted in **1** for 19-acetoxypregaleopsin.

The absolute stereochemistry of **1** was not ascertained. However, it is reasonable to assume that it belongs to the normal-labadane series, like **3**, because both substances possessed specific rotations of the same sign and identical magnitude: **1** $[\alpha]_{\text{D}}^{19}$ -56.8° (CHCl_3 ; c 0.137); **3** $[\alpha]_{\text{D}}^{25}$ -56.0° (CHCl_3 ; c 0.1) [4].

EXPERIMENTAL

General. Mp: uncorr. Plant materials were collected in June 1995 near Burgas, Bulgaria, and voucher specimens are 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 no. 7734, deactivated with 15% H_2O , 250 g). Elution with a petrol- CH_2Cl_2 gradient provided nine frs. The fr. (1.7 g) eluted with petrol- CH_2Cl_2 (1:1) was decoloured by filtration through a pad of a mixt. (1:1) of activated charcoal and celite and then rechromatographed (CC, silica gel, 15 g) eluting with Et_2O -petrol (4:1) giving pure 19-acetoxypregaleopsin (**1**) 27 mg.

19-Acetoxypregaleopsin (**1**). Mp $202-204^\circ$ (EtOAc - n -hexane); $[\alpha]_{\text{D}}^{19}$ -56.8° (CHCl_3 ; c 0.137). IR $\nu_{\text{max}}^{\text{KBr}}$

cm^{-1} : 3120, 1610 (enol ether), 1740, 1735, 1250 (OAc), 1725 (ketone), 2990, 2960, 2930, 1460, 1375, 1360, 1140, 1105, 1060, 1050, 1025, 1015, 945, 850, 765; ^1H and ^{13}C NMR: Table 1; EIMS (70 eV, direct inlet) m/z (rel. int.): 434 $[\text{M}]^+$ (0.6), 392 $[\text{M}-\text{CH}_2\text{CO}]^+$ (28), 375 $[\text{M}-\text{OAc}]^+$ (4), 374 $[\text{M}-\text{HOAc}]^+$ (1), 332 (9), 279 (9), 191 (11), 179 (19), 163 (13), 123 (39), 121 (13), 109 (29), 107 (11), 95 (22), 93 (10), 82 (34), 81 (58), 67 (18), 55 (16), 43 (100), 41 (12). (Found: C, 66.41; H, 7.93. $\text{C}_{24}\text{H}_{34}\text{O}_7$ requires: C, 66.34; H, 7.89%).

Acknowledgements—This work was supported by the Bulgarian Ministry of Education and Science ('Funds for Scientific Research') and the Spanish 'Dirección General de Investigación Científica y Técnica' (grants PB93-0154 and PB94-0104).

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