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## Covilanone: a new rearranged labdane type diterpene

J. M. L. Rodilla,<sup>a,\*</sup> M. I. Ismael,<sup>a</sup> L. A. Silva,<sup>a</sup> J. P. Cesário Serrano,<sup>a</sup> J. G. Urones<sup>b</sup> and F. Sanz<sup>c</sup>

<sup>a</sup>Departamento de Química, Universidade da Beira Interior, 6200 Covilhã, Portugal

<sup>b</sup>Departamento de Química Orgánica, Facultad de Ciencias Químicas, Universidad de Salamanca, Plaza de los Caidos 1–5, 37008 Salamanca, Spain

<sup>c</sup>Servicio de Difracción de Rayos X, Universidad de Salamanca, 37008 Salamanca, Spain

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**Abstract**—A bicyclic diterpene triol with a new rearranged labdane carbon skeleton was isolated from the aerial parts of *Halimium viscosum* (Willk.) Pinto da Silva (S. João da Pesqueira). Its structure was established by FAB MS and two-dimensional NMR experiments (<sup>1</sup>H/<sup>1</sup>H, <sup>1</sup>H/<sup>13</sup>C) and its stereochemistry by NOE and X-ray study. © 2002 Elsevier Science Ltd. All rights reserved.

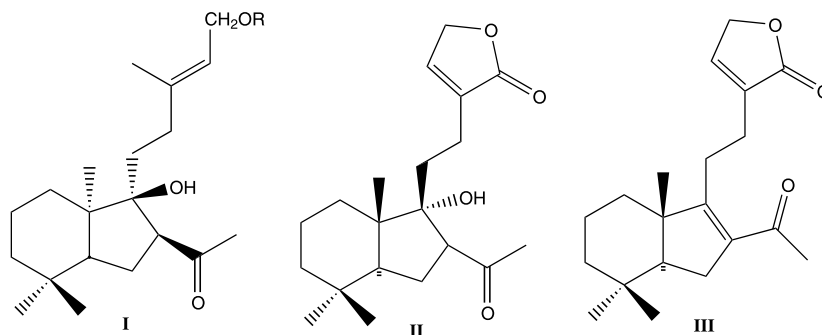
Labdane diterpenes with a [4.3.0]nonane ring B system are quite rare in the literature. Compound **I** isolated from *Gypothamun pinifolium*<sup>1</sup> a β-hydroxyketone with an acetyl group on C-7 of the enantiomeric series and Chapaecoderins B and C (**II** and **III**) isolated from *Echinodorus macrophyllus*<sup>2</sup> with a butenolide ring are between them.

In our studies of Cistaceae components of the Iberian Peninsula, we have isolated from the aerial parts of *Halimium viscosum* (Willk.) P. da Silva<sup>3–6</sup> bicyclic diterpenes with labdane or halimane skeleton or tricyclic diterpenes as valparane and valparolane.

The room temperature ethyl acetate extract of *H. viscosum*, S. João da Pesqueira,<sup>6,7</sup> give several diterpe-

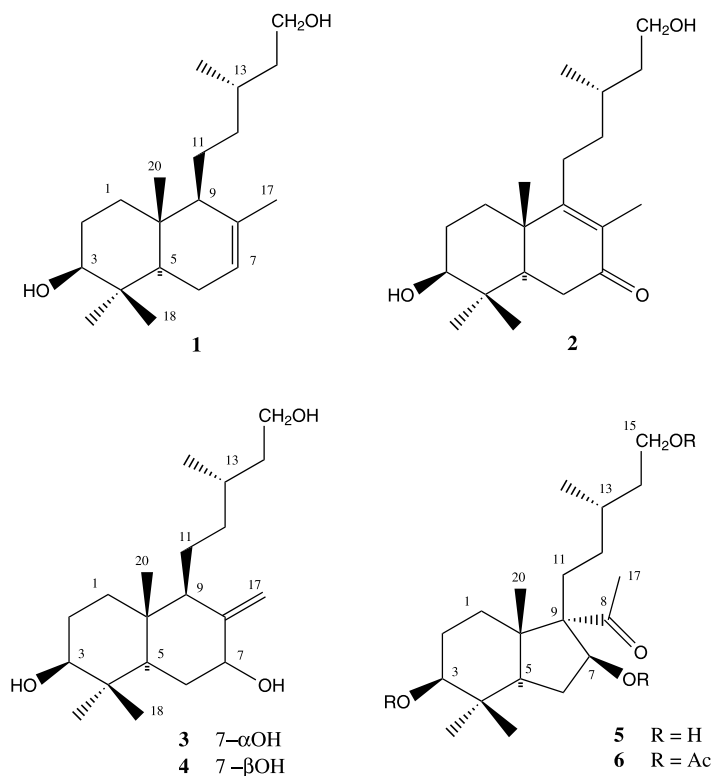
nes, some known such as **1–3**, **4**,<sup>8</sup> epimer on C-7 of **3**, described for the first time and one unknown, compound **5**,<sup>9</sup> purified by chromatography of the acetyl derivative **6** and reverted by hydrolysis in basic conditions.

The <sup>13</sup>C NMR spectrum for the triacetyl derivative **6**<sup>10</sup> C<sub>26</sub>H<sub>42</sub>O<sub>7</sub> shows signals corresponding to 26 carbon atoms, three acetoxy groups, five methyls, seven methylenes, four methines and four quaternary carbons, one of them corresponding to a carbonyl group (ketone). From the <sup>1</sup>H NMR and bidimensional <sup>1</sup>H/<sup>13</sup>C spectra (HMQC) the group -CH<sub>2</sub>-CH<sub>2</sub>OAc and two CHOAc next to methylene and a quaternary carbon (-CH<sub>2</sub>-CHOAc-C-) each, are observed.



**Keywords:** cistaceae; *Halimium viscosum*; covilanone; rearranged labdane.

\* Corresponding author. Fax: 351 275 319888; e-mail: [rodilla@ubista.ubi.pt](mailto:rodilla@ubista.ubi.pt)



The long distance correlation spectra (HMBC) observed for methyls Me-18, Me-19 and Me-20 on quaternary carbon atom (Table 1) suggest the disposition in an annular system analog to ring A of a labdane

with a secondary  $\beta$ -acetoxo group on C-3, except for the correlation between H-1 and C-9, in this case a quaternary carbon atom. H-16 was also correlated with C-12 and H-12 with C-19.

**Table 1.** NMR spectral data for **6**

C	$\delta_C$	Observed HMQC. Proton correlations ( $\delta_H$ ), $J$ Hz	Observed long-range HMBC correlations
1	33.5	1.63 (2H, m)	3, 9, 10
2	24.6	1.80 (2H, m)	3, 4
3	80.5	4.35 (1H, dd, $J_1=10.4$ , $J_2=5.7$ )	C=O(Ac), 4, 19, 18
4	37.1		
5	50.2	1.28 (1H, m)	4, 6, 7, 10, 20
6	31.5	2.38 (2H, m)	4, 5, 7, 9, 10
7	75.1	5.57 (1H, dd, $J_1=8.5$ , $J_2=3.4$ )	C=O(Ac), 8, 10
8	211.3		
9	68.8		
10	46.4		
11	25.8	1.89 (2H, m)	9, 12
12	32.5	1.02 (2H, m)	9
13	31.1		
14	35.3	1.60 (2H, m)	13, 15, 16
15	62.7	4.05 (2H, t, $J=6.5$ )	C=O(Ac), 13, 14
16	19.2	0.91 (3H, d, $J=8.4$ )	12, 13, 14
17	29.8	2.15 (3H, s)	8, 9
18	28.8	0.81 (3H, s)	3, 4, 5, 19
19	16.9	0.93 (3H, s)	3, 4, 5, 18
20	16.1	1.07 (3H, s)	1, 5, 9, 10

The  $3\beta$ -OAc 170.9 and 21.3 (2.03 for  $\delta_H$ ),  $7\beta$ -OAc 169.9 and 20.9 (2.03 for  $\delta_H$ ), 15-OAc 171.1 and 21.1 (2.03 for  $\delta_H$ ).

The new compound has a C-9 as a quaternary carbon atom and the side chain analogue to the other labdanes **1–4**.

The primary structure was deduced by correlation between H-7 with C-8 and C-10. The acetyl group is situated on C-9 and the remaining secondary acetoxy group on a methine next to the methylene C-6.

From the study of the NOE experiments, as observed in Fig. 1, the relative stereochemistry for **5** was established, and corroborated by single X-ray crystal analysis<sup>11</sup> of the molecular structure, and the packing of the molecules is shown in Fig. 2.

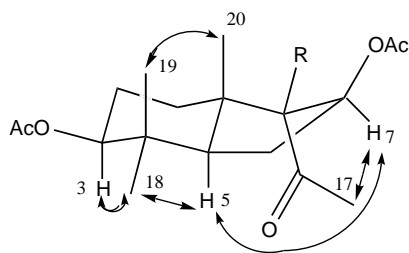


Figure 1.

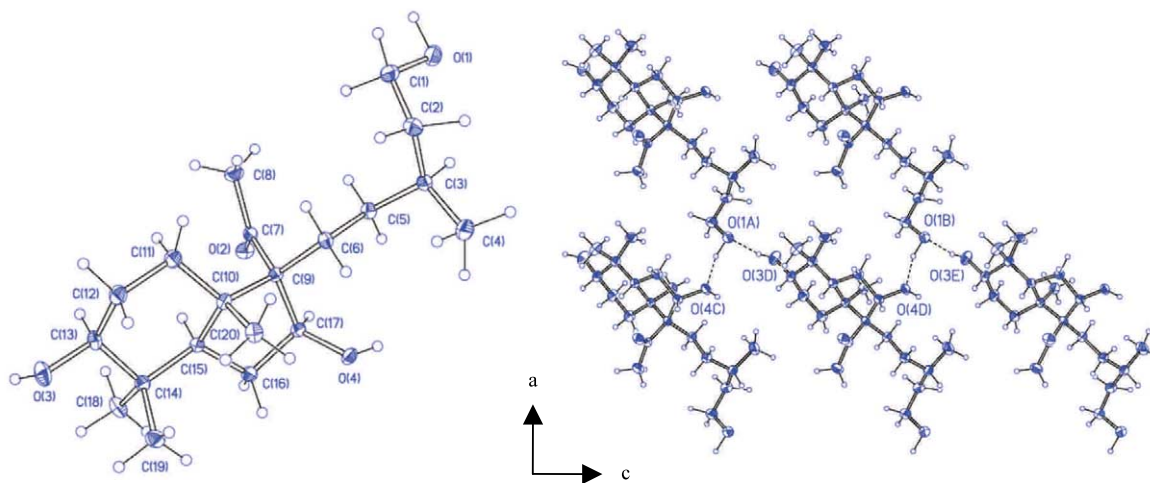
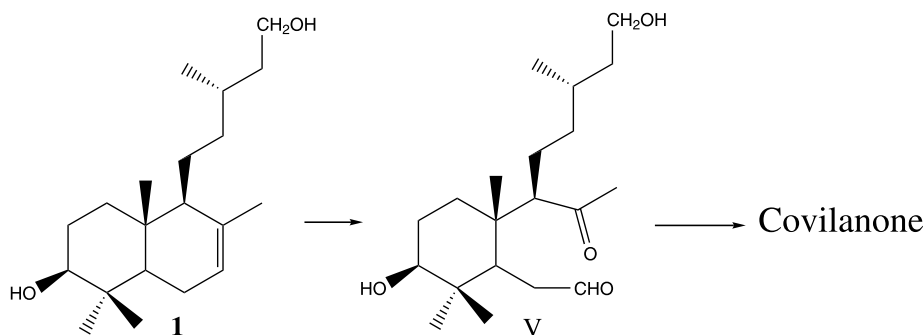


Figure 2.



In the crystal structures the molecules of **5** are connected by intermolecular O–H···O hydrogen bonds [ $O1\cdots O4=2.79(2)$  Å,  $H10\cdots O4=1.73(1)$  Å,  $\angle O1-H10\cdots O4=161(2)^\circ$ ;  $O3\cdots O1=2.83(1)$  Å,  $H3O\cdots O1=1.84(5)$  Å,  $\angle O3-H3O\cdots O1=162(1)^\circ$ ;  $O4\cdots O2=2.80(1)$  Å,  $H4O\cdots O2=1.98(2)$  Å,  $\angle O4-H4O\cdots O2=172(2)^\circ$ ]. No intramolecular interactions were observed for this new compound.

Compound, **5**, called covilanone, shows a carbon skeleton different to the primarily isolated compounds with a [4.3.0]nonane bicyclic system that could be formed from the major component labdendiol **1**, by fragmentation of  $\Delta^7$  and cyclisation of a secoderivative V.

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7. *Halimium viscosum* (Willk) P. da Silva, was collected in São João da Pesqueira, Bragança, Portugal on June 1995 and identified by Dr. Miguel M. de Sequeira. A voucher specimen was deposited at the Herbarium of University de Trás os Montes e Alto Douro, Portugal.
8. Compound **4**:  $[\alpha]_D^{23} = +15.20^\circ$  ( $c = 0.13$ ,  $\text{CHCl}_3$ ). IR  $\nu_{\text{max}}$   $\text{cm}^{-1}$ : 3349, 3019, 1648, 1460, 1030, 898.  $^1\text{H}$  NMR (250 MHz)  $\delta$  5.17 and 4.68 (1H, s, each one), 3.96 (1H, dd,  $J_1 = 11.0$  Hz and  $J_2 = 5.4$  Hz), 3.66 (2H, m), 3.25 (1H, dd,  $J_1 = 11.2$  Hz and  $J_2 = 4.1$  Hz), 1.00 (3H, s), 0.98 (3H, d,  $J = 6.1$  Hz), 0.78 (3H, s) and 0.66 (3H, s).  $^{13}\text{C}$  NMR (62.9 MHz)  $\delta$  C-1 36.8, C-2 27.8, C-3 78.7, C-4 38.9, C-5 52.2, C-6 20.8, C-7 73.8, C-8 150.1, C-9 55.0, C-10 39.1, C-11 33.4, C-12 35.8, C-13 30.2, C-14 39.5, C-15 61.1, C-16 19.8, C-17 103.2, C-18 28.2, C-19 15.4 and C-20 14.4.
9. Compound **5**: Mp 153–154 (*n*-hexane).  $[\alpha]_D^{22} = +20$  ( $c = 0.20$ ,  $\text{CHCl}_3$ ). IR  $\nu_{\text{max}}$   $\text{cm}^{-1}$ : 3400, 1670, 1462, 1387, 1355, 1068, 758.  $^1\text{H}$  NMR (250 MHz)  $\delta$  4.68 (1H, dd,  $J_1 = 8.3$  Hz and  $J_2 = 4.0$  Hz), 3.66 (2H, m), 3.14 (1H, dd,  $J_1 = 8.5$  Hz and  $J_2 = 7.2$  Hz), 2.13 (3H, s), 1.04 (3H, s), 0.92 (3H, d,  $J = 6.5$  Hz), 0.92 (3H, s) and 0.91 (3H, s).  $^{13}\text{C}$  NMR (62.9 MHz)  $\delta$  C-1 33.4, C-2 26.2, C-3 79.5, C-4 38.2, C-5 50.0, C-6 32.5, C-7 72.6, C-8 213.9, C-9 70.0, C-10 46.4, C-11 28.4, C-12 34.3, C-13 31.4, C-14 38.5, C-15 60.6, C-16 20.0, C-17 30.4, C-18 29.2, C-19 16.2 and C-20 16.1.
10. Compound **6**:  $^1\text{H}$  NMR (400 MHz) and  $^{13}\text{C}$  NMR (100. MHz) spectra were measured in  $\text{CDCl}_3$ , see Table 1. EIMS  $m/z$ : 466 [ $\text{M}^+$ ] (1), 406 (40), 363 (11), 346 (65), 303 (100), 271 (62), 229 (75), 203 (25), 161 (39), 121 (85), 107 (41), 81 (50), 69 (60), 55 (70). HRFAB calcd for  $\text{C}_{26}\text{H}_{43}\text{O}_7$ , 467.2931; found 467.3008.
11. Crystal data for **5**:  $\text{C}_{20}\text{H}_{36}\text{O}_4$ ,  $M = 340.49$ , orthorhombic, space group  $P2_12_12_1$  (no. 19).  $a = 9.447(3)$ ,  $b = 9.539(5)$ ,  $c = 21.364(3)$  Å,  $V = 1925.2(3)$  Å<sup>3</sup>,  $Z = 4$ ,  $D_{\text{calcd}} = 1.175$  Mg/m<sup>3</sup>,  $m(\text{Cu-K}\alpha) = 0.631$ ,  $F(000) = 752$ . Data (3210 collected reflections and 2196 observed reflections [ $I > 2\sigma(I)$ ]) were measured on a Seifert 3003 SC rotating anode diffractometer with (Cu-K $\alpha$ ) radiation (graphite monochromator) using  $2\theta-\omega$  scans at 268 K. The structure absolute was determined by direct methods using the SHELXTL™ suite of programs. Hydrogen atoms were placed in calculated positions. Full-matrix least-squares refinement based on  $F^2$  with anisotropic thermal parameters for the non-hydrogen atoms, and isotropic thermal parameters for the hydrogen atoms led to agreement factors  $R_1 = 0.0341$ ,  $wR_2 = 0.0683$ . Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited at the Cambridge Crystallographic Data Centre as supplementary material no. CCDC-179799.