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LETTERS

Covilanone: a new rearranged labdane type diterpene

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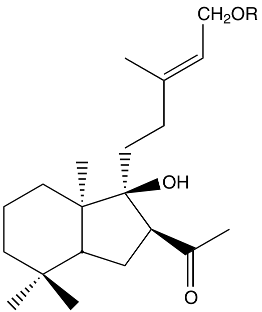
Abstract—A bicyclic diterpene triol with a new rearranged labdane carbon skeleton was isolated from the aerial parts of *Halimium viscosum* (Willk.) Pinto da Silva (S. João da Pesqueira). Its structure was established by FAB MS and two-dimensional NMR experiments ($^1H/^1H$, $^1H/^{13}C$) and its stereochemistry 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*[1] 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 macrophillus*[2] with a butenolide ring are between them.

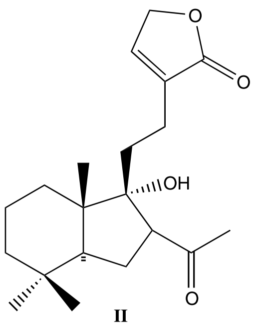
In our studies of Cistaceae components of the Iberian Peninsulae, we have isolated from the aerial parts of *Halimium viscosum* (Willk.) P. da Silva[3–6] bicyclic diterpenes with labadane or halimane skeleton or tricyclic diterpenes as valparane and valparolane.

The room temperature ethyl acetate extract of *H. viscosum*, S. João da Pesqueira,[6,7] give several diterpenes, some known such as **1**–**3**, **4**,[8] epimer on C-7 of **3**, described for the first time and one unknown, compound **5**,[9] purified by chromatography of the acetyl derivative **6** and reverted by hydrolysis in basic conditions.

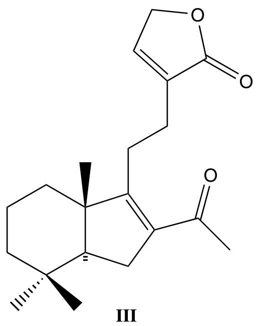
The ^{13}C NMR spectrum for the triacetyl derivative **6**[10] $C_{26}H_{42}O_7$ shows signals corresponding to 26 carbon atoms, three acetoxy groups, five methyls, seven methylenes, four methines and four quaternary carbons, one of them corresponding to a carbonyl group (ketone). From the ^1H NMR and bidimensional $^1H/^{13}C$ spectra (HMQC) the group $-CH_2-CH_2OAc$ and two CHOAc next to methylene and a quaternary carbon ($-CH_2-CHOAc-C-$) each, are observed.



I



II



III

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

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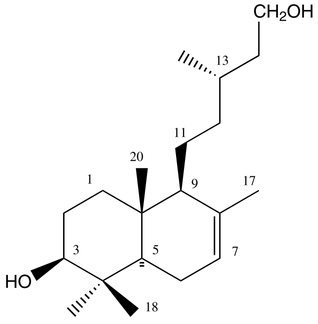
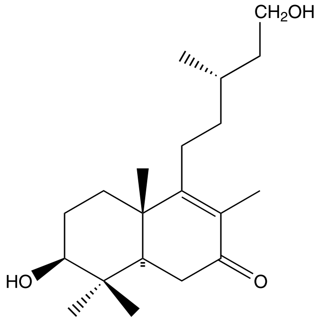


1



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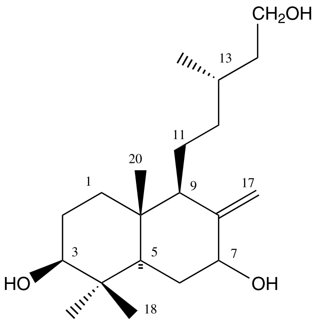
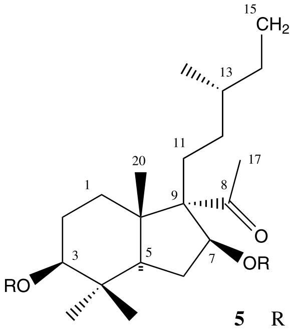


3 7–αOH
4 7–βOH



5 R = H
6 R = Ac

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 β-acetoxy 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	δ_C	Observed HMQC. Proton correlations (δ_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 3β-OAc 170.9 and 21.3 (2.03 for δ_H), 7β-OAc 169.9 and 20.9 (2.03 for δ_H), 15-OAc 171.1 and 21.1 (2.03 for δ_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[11] of the molecular structure, and the packing of the molecules is shown in Fig. 2.

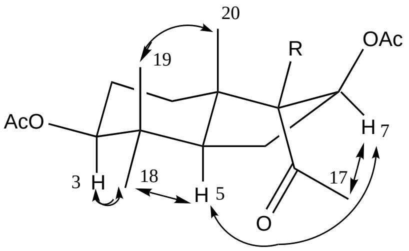


Figure 1.

In the crystal structures the molecules of **5** are connected by intermolecular O–H···O hydrogen bonds [O1···O4 = 2.79(2) Å, H1O···O4 = 1.73(1) Å, <O1–H1O···O4> = 161(2)°; O3···O1 = 2.83(1) Å, H3O···O1 = 1.84(5) Å, <O3–H3O···O1> = 162(1)°; O4···O2 = 2.80(1) Å, H4O···O2 = 1.98(2) Å, <O4–H4O···O2> = 172(2)°]. 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 Δ^7 and cyclisation of a secoderivative V.

Acknowledgements

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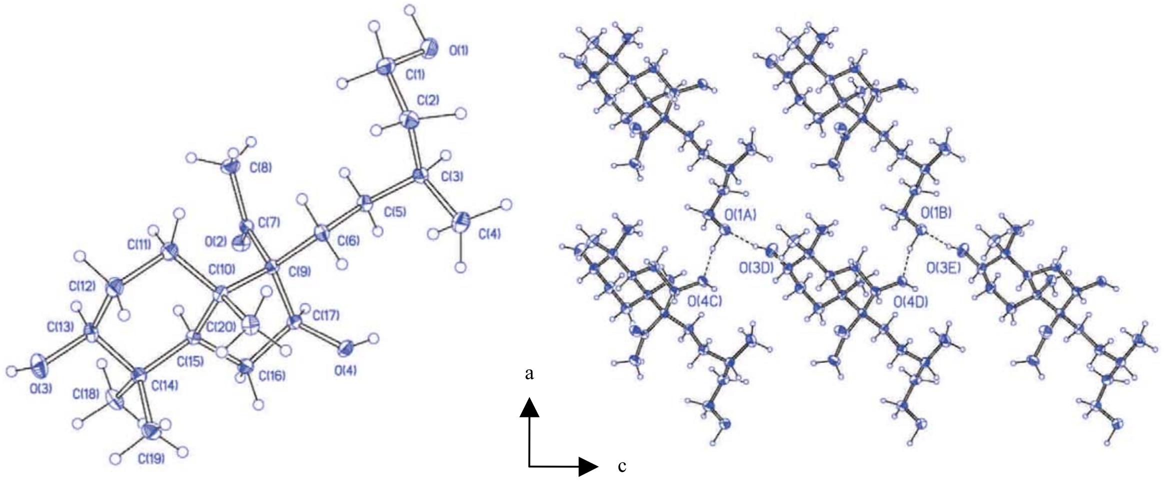
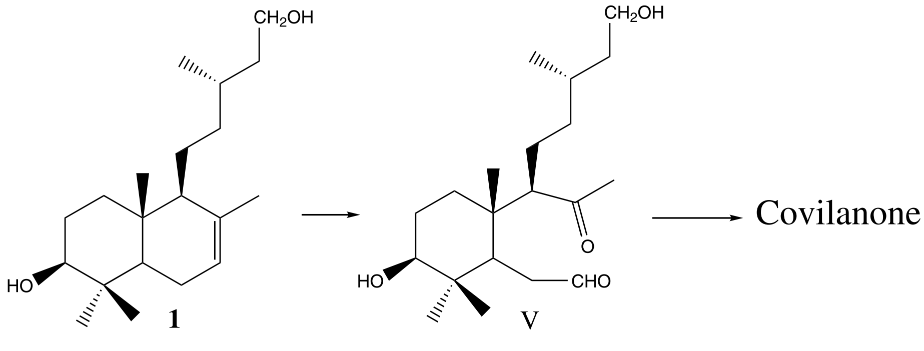


Figure 2.



References

1. Zdero, C.; Bohlmann, F.; Niemeyer, H. M. *Phytochemistry* **1988**, *27*, 2953–2959.
2. Kobayashi, J.; Sekiguchi, M.; Shigemori, H.; Ohsaki, A. *J. Nat. Prod.* **2000**, *63*, 375–377.
3. Rodilla, J. M. L.; de Mendonça, D. I. M.; Lithgow, A. M.; Marcos, I. S. *Phytochemistry* **1997**, *44*, 1301–1307.
4. Rodilla, J. M. L.; de Mendonça, D. I. M.; Urones, J. G.; Moro, R. F.; Willians, D. J. *Phytochemistry* **1998**, *47*, 1545–1549.
5. Rodilla, J. M. L.; de Mendonça, D. I. M.; Urones, J. G.; Moro, R. F. *Phytochemistry* **1998**, *49*, 817–822.
6. Rodilla, J. M. L.; de Mendonça, D. I. M.; Ismael, M. I. G.; Figueiredo, J. A.; Silva, M. L. A.; Lopes, E. *Nat. Prod. Lett.* **2001**, *15*, 401–409.
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**: $[\alpha]^{23}_{D}=+15.20°$ ($c=0.13$, $CHCl_3$). IR ν_{max} cm^{-1}: 3349, 3019, 1648, 1460, 1030, 898. ^{1}H NMR (250 MHz) δ 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}C NMR (62.9 MHz) δ 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). $[\alpha]^{22}_{D}=+20$ ($c=0.20$, $CHCl_3$). IR ν_{max} cm^{-1}: 3400, 1670, 1462, 1387, 1355, 1068, 758. ^{1}H NMR (250 MHz) δ 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}C NMR (62.9 MHz) δ 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}H NMR (400 MHz) and ^{13}C NMR (100. MHz) spectra were measured in $CDCl_3$, see Table 1. EIMS *m*/*z*: 466 [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 $C_{26}H_{43}O_7$, 467.2931; found 467.3008.
11. Crystal data for **5**: $C_{20}H_{36}O_4$, $M=340.49$, orthorhombic, space group $P2_12_12_1$ (no. 19). $a=9.447(3)$, $b=9.539(5)$, $c=21.364(3)$ A, $V=1925.2(3)$ A^3, Z=4, $D_{calcd}=1.175$ Mg/m^3, $m=$(Cu-Kα)$=0.631$, $F(000)=752$. Data (3210 collected reflections and 2196 observed reflections [$I>2\sigma(I)$]) were measured on a Seifert 3003 SC rotating anode diffractometer with (Cu-Kα) 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.