Pergamon

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Tetrahedron Letters 44 (2003) 5939–5942

TETRAHEDRON LETTERS

Caminatal, an aldehyde sesterterpene with a novel carbon skeleton from the Antarctic sponge *Suberites caminatus*

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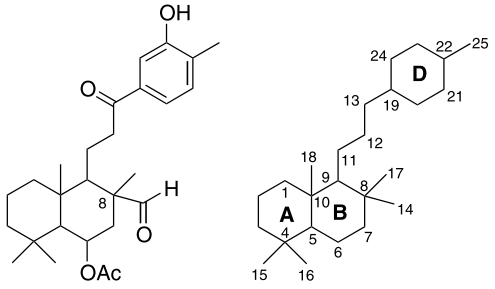
Received 10 March 2003; revised 21 April 2003; accepted 22 April 2003

Abstract—A new sesterterpene, caminatal **1**, containing a bicyclic terpenoid moiety with an aldehyde appendage in combination with an isolated isoprenic aromatic ring leading to a novel carbon skeleton has been obtained from the Antarctic sponge *Suberites caminatus*. Its structure and relative stereochemistry were established by spectroscopic evidence and biogenetic considerations.

Marine sponges from tropical and subtropical areas are a prolific source of an impressive array of novel natural compounds, covering almost all structural types. A plentiful number of genera and species has been chemically studied for new chemical and biological activities.[1] However, sponges from high latitudes such as the Antarctic and other temperate water environments are far from receiving the same attention despite the interesting metabolites discovered.[2]

At present, 15 species of Antarctic sponges, belonging to 14 genera, have been chemically investigated. *Dendrilla membranosa*, an Antarctic sponge studied quite early,[3,4] proved to be rich in metabolites and, consequently, has been intensively investigated for bioactive compounds.[5–8] Nevertheless, a variety of structural types of new metabolites have also been isolated from other genera, for example: steroids from *Homaxinela*,[9] *Artemisina*,[10] *Cinachyra* and *Xestospongia*;[11] alkaloids from *Kirkpatrickia*,[12–14] *Latrunculia*,[15,16] *Psammopemma*,[17] *Isodictya*,[18,19] and *Negombata*;[15] polyenes from *Leucetta*;[20] sesterterpenes from *Suberites*;[21] sesquiterpenes from an unknown species of sponge;[22] diterpenes from *Lissodendoryx*,[23] and *Dendrilla*,[5–8] and metabolites from sponge-associated microorganisms.[24]

In this work, we report on a biogenetically interesting sesterterpene **1** isolated from the Antarctic sponge *Suberites caminatus*. The compound possesses a bicyclic moiety containing an unusual aldehyde appendage at C-8 together with an isoprenoid aromatic ring leading to a novel tricyclic carbon skeleton for which we propose the trivial name caminatane **2**.



Compound **1** was isolated as a colorless oil[25] from the hexane–ethyl acetate (90:20) fraction of the vacuum flash chromatography of the ethyl acetate extract of *S. caminatus* after gel filtration and purification by HPLC. The EIMS spectrum showed a peak at m/z 442 that corresponds to the molecular formula $C_{27}H_{38}O_5$ $[M]^+$ (HRMS) (nine unsaturation degrees). Absorbances for hydroxyl and carbonyl groups were observed at 3422, 1657 and 1637 cm^{-1}, respectively, in the IR spectrum.

The ^{13}C NMR spectrum (Table 1) displayed signals for 27 carbons whose multiplicities were determined from the DEPT spectrum: six methyl groups (one acetate

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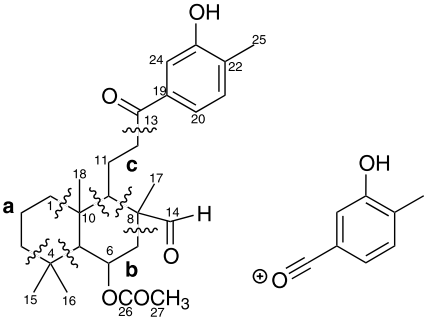
0040-4039/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/S0040-4039(03)01426-6

methyl group); six methylenes; six methine carbons (three olefinic and one bearing oxygen); one aldehyde and eight nonprotonated carbons (two carbonyl, and three olefinic, suggesting the presence of a trisubstituted aromatic ring, and three sp^3 quaternary carbons). The ^{1}H NMR spectrum showed the following downfield signals: an aldehydic proton at δ 9.31 (s); two *ortho*-coupled aromatic protons at δ 7.37 (dd, 1.6, 7.8) and at δ 7.18 (d, 7.8); a *meta*-coupled aromatic proton at δ 7.29 (d, 1.6); and a proton geminal to an acetate group at δ 5.57 (dd, 3.0, 5.7). In the upfield region appeared signals for an aromatic methyl group at δ 2.30 (s); acetate methyl group at δ 2.06 (s); and four methyl groups at δ 0.96 (s, 3H), 1.01 (s, 3H), 1.30 (s, 6H).

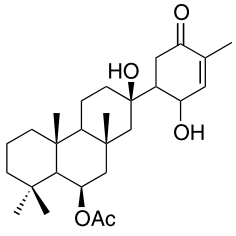
The molecule possesses only five isoprenic methyl groups, including the aromatic one, suggesting that the lacking methyl group, characteristic of a sesterterpene structure, could be oxidized to aldehyde. As the degree of unsaturation indicated that the molecule must be tricyclic, it did not seem at this point that the lacking methyl group could be involved in a ring formation.

From the ^{1}H–^{1}H COSY NMR spectrum it was clearly possible to differentiate three discrete spin systems (H_2-1–H_2-2–H_2-3; H-5–H-6–H_2-7 and H-9–H_2-11–H_2-12) that correspond to fragments **a**–**c** as shown in **1**. HMBC experiments confirmed these fragments. The HMBC correlations of H_3-15/C-3, C-4, C-5, C-16; H_3-16/C-3, C-4, C-5, C-15 and H-6 and H_3-27 with C-26 allowed fragments **a** and **b** to be connected through C-4 and confirmed the presence of the acetate group at C-6. Correlation between H_3-18 with C-1, C-5, C-9 and C-10 placed Me-18 at C-10 and allowed closure of ring A. Correlation between H_3-17 with C-7, C-8, C-9 and C-14 placed Me-17 and the aldehyde at C-8 and allowed us to close ring B.



1

A *m/z* 135



Suberitenone B, **3**

Table 1. ^{1}H, ^{13}C and HMBC NMR data of compound **1** [500 MHz, δ ppm, (*J*) Hz]

	δ_H[a]	δ_C[a]	δ_H[b]	δ_C[b]	HMBC
1	1.03 m; 1.80 m	42.3	0.73 m; 1.57 m	42.0	H-2; H_3-18
2	1.50 m; 1.60 m	18.6	1.50 m; 1.50 m	18.9	H-5
3	1.22 m; 1.41 m	44.2	0.92 m; 1.16 m	44.3	H_3-15; H_3-16
4		34.4		34.4	H_3-15; H_3-16
5	1.11 d (2.2)	56.2	0.70 d (2.2)	55.8	H_3-15; H_3-16; H_3-18
6	5.57 dd (3.0, 5.7)	68.4	5.54 dd (3.0, 5.9)	68.3	
7	1.68 m; 1.68 m	37.4	1.20 m; 1.40 m	37.4	H-5; H_3-20
8		38.8		38.9	H-6; H_3-17
9	1.54 m	52.5	1.19 m	52.3	H_3-17
10		50.5		50.4	H-6; H_2-11; H-14; H_3-17
11	1.50 m; 1.98 m	21.5	1.50 m; 1.97 m	21.5	
12	2.73 ddd (5.4, 10.8, 16.2)	40.1	2.60 ddd (5,4, 10.7, 16.3)	40.3	
	2.94 ddd (5.3, 11.2, 16.4)		2.90 ddd (5.4, 10.7, 16.3)		
13		199.5		198.7	H_2-11; H-20; H-24
14	9.31 s	206.2	9.02 s	206.5	H_3-17
15	0.96 s	33.5	0.90 s	33.5	H_3-16
16	1.01 s	23.4	0.95 s	23.7	H-5; H_3-15
17	1.30 s	17.5	1.20 s	17.6	
18	1.30 s	16.4	1.14 s	16.4	
19		130.7		130.8	H_3-25
20	7.37 dd (1.6, 7.8)	121.0	7.50 dd (1.5, 7.7)	121.2	H-24
21	7.18 d (7.8)	131.5	6.93 d (7.7)	131.8	H-20
22		136.2		136.9	H-21
23		154.5		155.3	H-21; H_3-25
24	7.29 d (1.6)	114.3	7.28 d (1.5)	114.5	H-20
25	2.30 s	16.4	2.09 s	16.4	H-21
26		170.0		169.7	H_3-27
27	2.06 s	22.1	1.61 s	22.0	

[a] $CDCl_3$.
[b] C_6D_6.

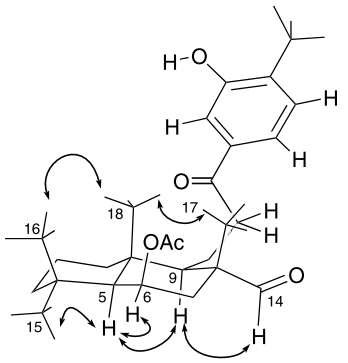


Figure 1. Selected NOEs and relative stereochemistry of **1**.

Since the position of the aldehyde group was located, the remaining fragment **c** of the molecule linked to C-13 was easily deducted assuming that the aldehyde group could be derived from suberitenone B, **3**,[21] by oxidative cleavage and aromatization of ring D. This was corroborated by HMBC correlations (Table 1) as well as the MS of **1** which showed a peak at m/z 135 (base peak) corresponding to fragment A. This completed the planar structure of **1**.

Chemical shift evidences and 2D NOESY experiments established the relative configurations of the chiral centers of the decaline system. Due to the overlapping of Me-17 and Me-18 signals in the ^{1}H NMR spectra taken in $CDCl_3$, 2D NOESY experiments were taken in C_6D_6. The small values observed for the coupling constants of H-6 with H-5 and H_2-7 (Table 1) indicated that the acetoxy group on C-6 must be axial. In addition, the following NOEs, Figure 1, were observed: H-5 with H-6, H-9 and H_3-15; H_3-18 with H_3-16 and H_3-17; and H-14 with H-9. These indicated that the acetate group, Me-16, Me-17, M-18 and the side chain must be on the same side of the molecule, and also that the A/B ring fusion must be *trans*. This allowed us to propose for **1** the relative stereochemistry shown in Figure 1.

Unlike other sesterterpene skeletons, caminatane has some peculiarities: (a) it possesses an irregular carbon appendage at C-8, probably derived from oxidative cleavage of ring C of **6**, Figure 2. Ring C could be produced by cyclization involving an exomethylene in the isoprenic chain precursor **4**, (b) it contains an isolated cyclohexane ring D which appears to be obtained from a discrete intermediate **5** in an overall non-synchronized annulation pathway. An array of possible new metabolites generated from this unusual oxidative pathway could be expected.

Acknowledgements

This work was supported by Ministerio de Ciencia y Tecnología (MCYT), projects: REN2002-10485-E/ANT and PPQ2002-02494), Instituto Antártico Chileno (INACH), and DGUI (Gobierno de Canarias: PI2002/044). A.R.D.-M. acknowledges an I3P grant from the CSIC and E.D. acknowledges a fellowship (FPI) from the CICYT.

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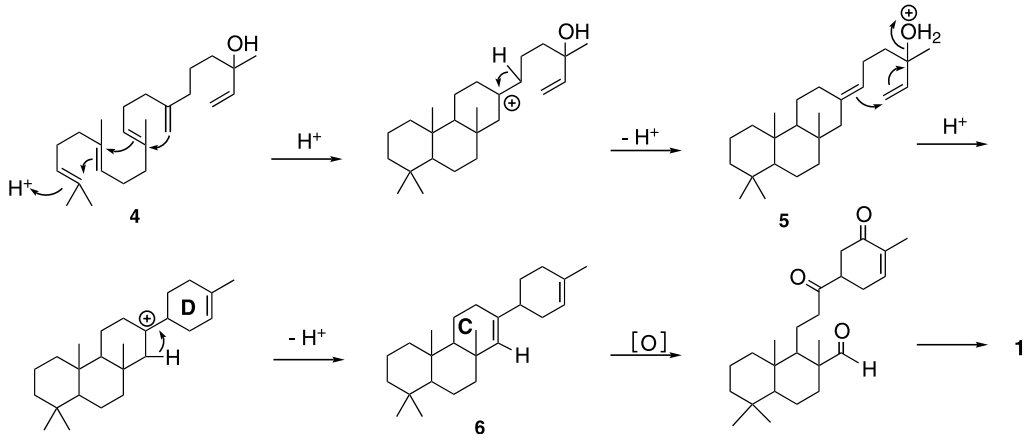

Figure 2. Possible biogenesis of caminatal **1**.

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25. **Compound 1**: colorless oil; $[\alpha]_D^{20}$ +167 (*c*, 0.12, $CHCl_3$); IR ν_{max} (film) 3422, 1657 and 1637 cm^{-1}; ^1H and ^{13}C NMR, see Table 1; EIMS *m*/*z* 442 $[M]^+$ (<1), 424 $[M-H_2O]^+$ (<1), 382 $[M-AcOH]^+$ (2), 364 $[M-H_2O-AcOH]^+$ (13), 135 (100); HREIMS $[M]^+$ 442.2745 (calcd for $C_{27}H_{38}O_5$, 442.2719).