Lobocalone: A Novel Secondary Metabolite from the Soft Coral Lobophytum caledonense

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LOBOCALONE: A NOVEL SECONDARY METABOLITE FROM THE SOFT CORAL *LOBOPHYTUM CALEDONENSE*

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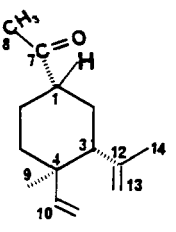
ABSTRACT.—A novel secondary metabolite, lobocalone [**1**], was isolated from the soft coral *Lobophytum caledonense* collected off the South China Sea. Its structure and relative stereochemistry were established mainly by 1D and 2D nmr and NOESY as (1*R**,3*R**,4*R**)-3-(1-methyl)-4-methyl-4-vinylcyclohexyl methyl ketone.

Many cembranoid diterpenes have been isolated from soft corals of the genus *Lobophytum* (1–5). We have previously reported the isolation and structure elucidation of two cembranoid diterpenes from Chinese *Lobophytum* (6,7). Recently, in our research on *Lobophytum caledonense* Tix Dur (Alcyonaceae), we have isolated the new secondary metabolite lobocalone [**1**]. We report herein the isolation, structural elucidation, and relative stereochemistry of lobocalone [**1**].

An EtOH extract of dried *L. caledonense* was partitioned between EtOAC and H_2O. Si gel chromatography of the EtOAc extract followed by purification with hplc afforded lobocalone [**1**].

Lobocalone [**1**] was isolated as a colorless oil, $[\alpha]^{20}D$ +18.5°. Its ir spectrum indicated the presence of a carbonyl group (1709 cm^{-1}) and terminal double bonds (1638, 898 cm^{-1}). A molecular ion at *m/z* 206 and fourteen signals in its ^{13}C-nmr DEPT spectrum established the molecular formula as $C_{14}H_{22}O$ with four degrees of unsaturation. The ^1H- and ^{13}C-nmr signals at δ 2.16 and 211.7 and the fragment ion at *m/z* 163 $[M-O=CMe]^+$ clearly indicated the presence of a methyl keto group. The 600 MHz ^1H-nmr spectrum showed five vinyl proton signals at δ 4.90, 4.92, 4.60, 4.85, and 5.79. A vinylic methyl signal at δ 1.71 together with four signals of sp^2 carbons at δ 149.6, 112.6, 146.9, and 110.2 established two terminal double bonds: one is a vinyl group, the other is an isopropenyl group. Based on the data above, **1** must be a monocarbocyclic compound with multifunctionalities.



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The ^1H-^1H correlations observed in a 2D ^1H-^1H COSY spectrum enabled us to establish a subunit -CH_2-CH_2-CH-CH_2-CH<. The downfield signal of H-1 (δ 2.39) indicated that the methyl keto group should be linked to C-1. The downfield signal of H-3 (δ 1.98) indicated that C-3 must be connected to one of the double bonds, either the vinyl group or the isopropenyl group. The clear AB splitting of H-10 in its 600 MHz ^1H-nmr spectrum indicated that the vinyl group must be connected with a quaternary carbon (C-4), so C-3 must be connected to the isopropenyl group. Considering the requirement of ring-forming, it was reasonable to assemble the quaternary carbon (C-4) into a six-membered ring with both the vinyl group and the remaining methyl group attached to it. Thus the structure of lobocalone was deduced as **1**. The correlation between

H-3 and the C-14 methyl group observed in the 2D ^{1}H-^{1}H TOCSY spectrum and the ms fragmentation (Scheme 1) also confirmed this deduction.

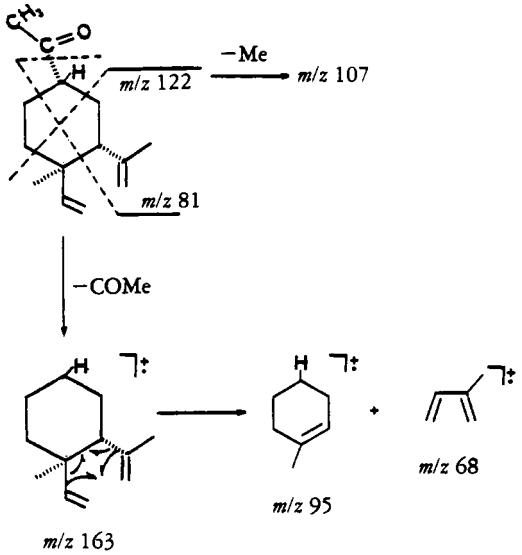
EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Their spectrum was measured in $CDCl_3$ with a Nico-let 5DX-FT spectrometer. ^{1}H- and ^{13}C-nmr, ^{1}H-^{1}H COSY, ^{1}H-^{1}H TOCSY, and ^{1}H-^{1}H NOESY spectra were recorded with a Bruker AMX-600 spectrometer. Optical rotations were recorded in MeOH with a Perkin-Elmer 241 polarimeter. Eims was determined at 70 eV on a ZAB-HS spectrometer. Hplc was performed on a Waters 510 liquid chromatograph with a Lambda-Max LC spectrometer, using a μPorasil Si gel column.

BIOLOGICAL MATERIAL.—The soft coral *L. caledonense* was collected off the South China Sea in May 1990. A voucher specimen was deposited in the Research Center of Organic Natural Products, Zhongshan University, Guangzhou, China.

EXTRACTION AND ISOLATION.—The sun-dried material (930 g) was extracted by EtOH. The extract was evaporated in vacuo to give a dark brown syrup (119.1 g). Then it was partitioned between EtOAc and H_2O. The EtOAc-soluble fraction was evaporated in vacuo to give a brown syrup (43.4 g), which was subjected to flash chromatography (8, 9), using solvents of gradually increasing polarity. The fraction that was eluted with petroleum ether-EtOAc (90:10) was purified by preparative tlc and then by hplc, giving lobocalone [**1**] (10 mg).

Lobocalone [**1**].—Colorless oil: $[\alpha]^{20}D$ +18.5° (c=0.13, MeOH); ir ν max (KBr) 3082, 2988, 2882, 1709, 1638, 1411, 1374, 898 cm^{-1}; ^{1}H and



SCHEME 1. Mass spectral fragmentation of lobocalone [**1**].

The relative stereochemistry of three chiral carbons in the molecule was determined by a ^{1}H-^{1}H NOESY experiment (Figure 1). A strong nOe between H-1, H-3, and H-5 indicated their diaxial positions; thus both the substituents on C-1 and C-3 must be equatorial. Also a strong nOe between Me-9 and H-2, H-6 was observed, which revealed that Me-9 was axial. Other evidence such as the nOe between H-10 and H-5, H-3 corroborated that Me-9 was axial. As a result, the relative stereochemistry at C-1, C-3, and C-4 was established as 1*R**,3*R**,4*R**.

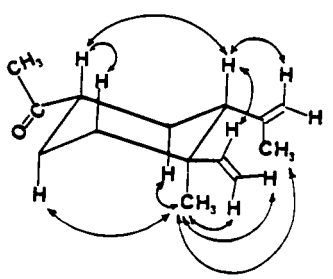


FIGURE 1. Representation of lobocalone [**1**] showing ^{1}H-^{1}H NOESY correlations.

TABLE 1. ^{1}H- and ^{13}C-nmr Data of Lobocalone [**1**].[a]

Position	^{13}C[b]	^{1}H	^{1}H-^{1}H COSY
1	51.95 (d)	2.39 (m)	H_a-6, H-2
2	29.36 (t)	1.88 (dt, 11, 2.1)	H-3, H-1
3	51.86 (d)	1.98 (dd, 11, 2.9)	H-2
4	39.64 (s)		
5	39.07 (t)	1.49 (dt, 11, 2.4)	H_a-6
6a	23.75 (t)	1.57 (m)	H_b-6, H-5, H-1
6b		1.75 (dd, 11, 2.4)	H_a-6
7	211.7 (s)		
8	28.19 (q)	2.16 (s)	
9	24.74 (q)	1.00 (s)	
10	149.62 (d)	5.79 (dd, 12, 9)	H_a-11, H_b-11
11a	112.84 (t)	4.90 (dd, 9, 2.4)	H-10
11b		4.92 (dd, 12, 2.4)	H-10
12	146.92 (s)		
13a	110.2 (t)	4.61 (d, 1.0)	
13b		4.85 (d, 1.0)	
14	16.46 (q)	1.71 (s)	

[a]Measured at 600 MHz in $CDCl_3$. Chemical shifts are reported as δ values (ppm) relative to TMS. Multiplicity and *J* values (Hz) given in parentheses.
[b]Multiplicities were determined by DEPT experiment.

^{13}C nmr see Table 1; eims (70 eV) *m/z* (rel. int.) 206(14), 191(12), 173(7), 163(79), 148(12), 127(31), 121(49), 107(61), 95(100), 81(76), 77(25), 71(35), 68(47), 55(45), 53(34), 51(8).

ACKNOWLEDGMENTS

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