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Sarcophytin, A Novel Tetracyclic Diterpenoid From The Indian Ocean Soft Coral *Sarcophyton elegans*

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Abstract : A novel tetracyclic diterpenoid, sarcophytin (**1**) has been reported from the soft coral, *Sarcophyton elegans* and its structure elucidated by 2D NMR spectral data and supported by X-ray analysis.

In continuation of our interest on the bioactive secondary metabolites of the soft corals of the Indian Ocean,[1,2] we have undertaken the chemical examination of the species *Sarcophyton elegans* collected from Havellock (12° 19'N, 93° 48'E) Island of the Andaman and Nicobar group of Islands of the Indian Ocean. Chemical examination of this species occurring in different regions of the Pacific Ocean has been reported to yield polyhydroxysteroids[3-6] and cembranoid diterpenoids.[7] We now report the isolation of a novel tetracyclic diterpenoid, named sarcophytin (**1**), and its structure elucidation by spectral data including X-ray analysis.

The residue from the ethyl acetate extract of the organism on column chromatography over silica gel furnished sarcophytin (**1**, 150 mg, 0.005%), mp 162-63°C, $[\alpha]_D^{25}$ + 0.238 (c, 0.08, $CHCl_3$). Its molecular formula was assigned as $C_{21}H_{30}O_5$ by elemental analysis and M$^+$ 362 in its EIMS. The presence of hydroxylic absorption (3520 cm^{-1}) and two carbonyls; an α:β-unsaturated ester (1708 cm^{-1}) and a six membered saturated ketone (1720 cm^{-1}) was inferred from its IR spectrum. Its UV absorption at 219 nm indicated conjugation

It exhibited all the 21 carbon signals in its ^{13}C NMR spectrum, which were analysed by the DEPT spectrum as five methyls, four methylenes, six methines and six quaternary carbons. The chemical shifts of the respective carbons were assigned based on the connctivities noticed in its 2D NMR (^{13}C - ^1H COSY) spectrum (Table I). The keto (δ 210.0, s) and the ester (COOMe, δ 165.9 and COOMe, δ 3.73, s) carbonyls were evident from the ^{13}C and ^1H NMR spectra. It also showed a trisubstituted double bond (δ 146.0, d and 130.9, s) supported by the presence of the corresponding olefinic proton at δ 7.10 as a singlet corresponding to a β-proton of an α,β-unsaturated ester. Its ^{13}C NMR spectrum showed two oxygenated carbons; one at δ105.6 (s) assignable to a doubly oxygenated cyclicketal carbon and the other at δ 79.2 (s) as a tertiary carbon. All the five oxygens of the molecule could thus be accounted for. The molecular formula requiring seven double bond equivalence, three of them being accounted for in the two carbonyl functionalities and a double bond, indicated its tetracyclic nature. Its ^1H NMR spectrum revealed its diterpenoid nature by showing five methyl groups,one as carbomethoxyl (δ 3.73, s), two in isopropyl group (δ 0.84, d, J = 7 Hz, 12 & 13-H_3 & 13-H_3), one

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as a secondary methyl (δ 1.06, d, J = 5.5 Hz, 15-H_3) and the remaining as a tertiary methyl (δ 1.10, s, 14-H_3). The presence of an isopropyl group, indicated it to be a tetracyclic diterpenoid derived from the fourteen membered carbocyclic cembranoid skeleton.

A survey of literature revealed that only four tetracyclic derivatives have been reported so far and that too from soft coral species. Three of these are from the species of *Simularia* genus (mandapamate from *S. dissecta*,[8] isomandapamate from *S. maxima*[2] and one more from *S. dissecta*[9]) and the fourth, chatancin (**2**), a PAF antagonist from a soft coral species of *Sarcophyton* genus[10].

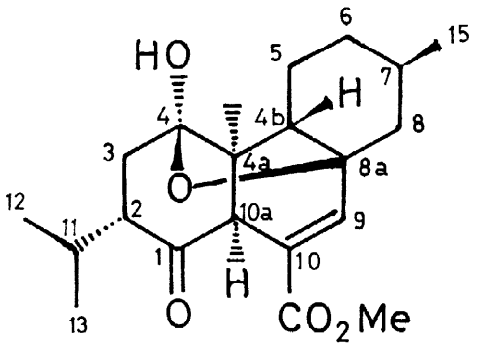

Table I. NMR spectral data of sarcophytin (**1**) [^{13}C (22.5 MHz : δ in PPM multiplicity)] and chatancin (**2**) and ^1H NMR [90 MHz : δ in PPM (multiplicity, J in Hz)]. 2D NMR [^1H-^1H & ^1H-^{13}C COSY and NOESY in 90 MHz] spectral data of sarcophytin (**1**).

Assignment	δc		δH	^1H-^1H COSY	^1H-^{13}C COSY	NOESY
	1	**2**	**1**	**1**	**1**	**1**
1.	210.0, s	99.9				
2.	56.0, d	50.8	2.10 (m)		1-H-C_1	
3.	40.9, t	19.3	2.35 & 1.85 (m)		3-H-C_3	
4.	105.6, s	30.0				
4a.	51.9, s	37.3				
4b.	48.8, d	49.1	2.45 (m)	5-H	4b-H-C_{4b}	
5.	21.3, t	28.5	1.45 (m)	6-H	5-H-C_5	
6.	33.8, t	36.0	1.66 (m)	5-H	6-H=C_6	
7.	29.9, d	30.9	0.98 (m)	15-H		15-H
8	43.7, t	43.5	2.10 (m)		8-H-C_8	
8a	79.2, s	77.1				
9.	146.0, d	144.5	7.10 (s)	10a-H	9-H-C_9	10a-H
10.	130.9, s	137.0				
10a	49.8, d	54.4	2.98 (d, 2)	9-H	10a-H-C_{10a}	9-H
11.	25.9, d	26.4		12 & 13-H_3	11-H-C_{11}	
12.	19.0, q	18.7	0.84 (d, 6)	11-H	12-H-C_{12}	
13.	21.3, q	23.5	0.84 (d, 6)	11-H	13-H-C_{13}	
14.	16.9, q	24.4	1.10 (s)		14-H-C_{14}	
15.	22.2, q	22.8	1.06 (d, 5.5)	7-H	15-H-C_{15}	
16.	169.9, s	167.2				
17.	51.3, q	52.8	3.73 (s)		17-H_3-C_{17}	

The structural features and spectral characteristics of sarcophytin (**1**) find greater similarity with those of chatancin (**2**) (Table I), except for the difference that sarcophytin has a keto functionality. Assuming a similar structure for sarcophytin (**1**) to that of chatancin (**2**) with a perhydrophenanthrene skeleton, the nature as well as the position of cyclicketal ring need to be fixed. Some information could be derived from its 2D NMR (^{1}H-^{1}H COSY) spectral data. The important connectivities noticed were between the olefinic proton at δ 7.10 and the allylic proton C_{10a}-H at δ 2.98 which showed no further connectivity suggesting that this should be an isolated proton at the tertiary carbon and the keto function to be possibly present at C_1. In chataincin (**2**) this carbon happened to be hemiketal carbon making a six membered pyran ring. The highly deshielded carbon-13 value of 4a (δ 51.9) compared to that of δ 37.3 in the latter suggested the presence of oxygenated carbon in its vicinity and hence the hemiketal system in (**1**) to be at C_4. A similar down field shift noticed in carbon-3 (δ 40.9, t) - is consistent with the location of the ketal system at C_4 and so also a shielding effect (δ 24.8 to 16.9) of the β-oxygen on C_{14}. Thus sarcophytin (**1**) differed from chatancin (**2**) in having a five membered heterocyclic ring instead of a six membered one in the latter. A difference of ≈ 7 PPM was noticed in the chemical shifts in C_5 and C_{10} and this might be possibly due to the position of oxygenated bridge. The structure of the molecule was supported by the partial connectivities (Table I). The NOESY spectrum of the molecule showed the following connectivities C_9-H (δ 7.10) with C_{10a}-H (δ 2.98), the C_2-H (δ 2.10) with the 3β-H (δ 1.85) and the 3β-H with 3α-H (δ 2.35). The structure, relative stereochemistry and probable absolute configuration of sarcophytin were finally established by its X-ray analysis as depicted in the structure (**1**). A few pertinent details of X-ray analysis are given below.

Single crystal X-ray analysis of (**1**). Data were acquired with a Siemens R3m/V diffractometer, Cu K_α radiation (λ = 1.5418 Å), graphite monochromator. $C_{21}H_{30}O_5$ (362.45), crystal size 0.35 x 0.10 x 0.08 mm, monoclinic, space group $P2_1$, 293 K, a = 12.299(2), b = 6.563(1), c = 12.607(2) A, β = 102.09(1)°, V = 995.0(3) Å^3, D_c = 1.210 g/cm^3, Z = 2, F(000) = 392, μ = 0.689 mm^{-1}. A total of 1454 reflections were collected in the 3° < 2θ < 110° range using variable speed (2-29°/m) ω/2θ-scans. 1378 reflections were unique, and from these, 1267 were assumed as observed ($F_o > 4\sigma(F_o)$). Lorentz and polarization but not absorbtion corrections were applied. Three standard reflections monitored every 97 reflections indicated no significant intensity variation. The structure was solved by direct methods (SHELXS-86 [1]). Hydrogen atoms were set in calculated positions. The structure was refined by full-matrix least-squares on F^2 (SHELXL-93 [2]) using anisotropic thermal parameters for all non-hydrogen atoms and riding hydrogens. The refinement converged to R_1 = 3.65%, wR_2 = 9.28%, GOF = 1.082 and a final difference map revealed no peaks greater than 0.14 e/Å^3.

Complete details of the structure investigation are available at request from the Cambridge crystal Data Centre, 12 Union Road, Cambridge CB2 1EZ, England.

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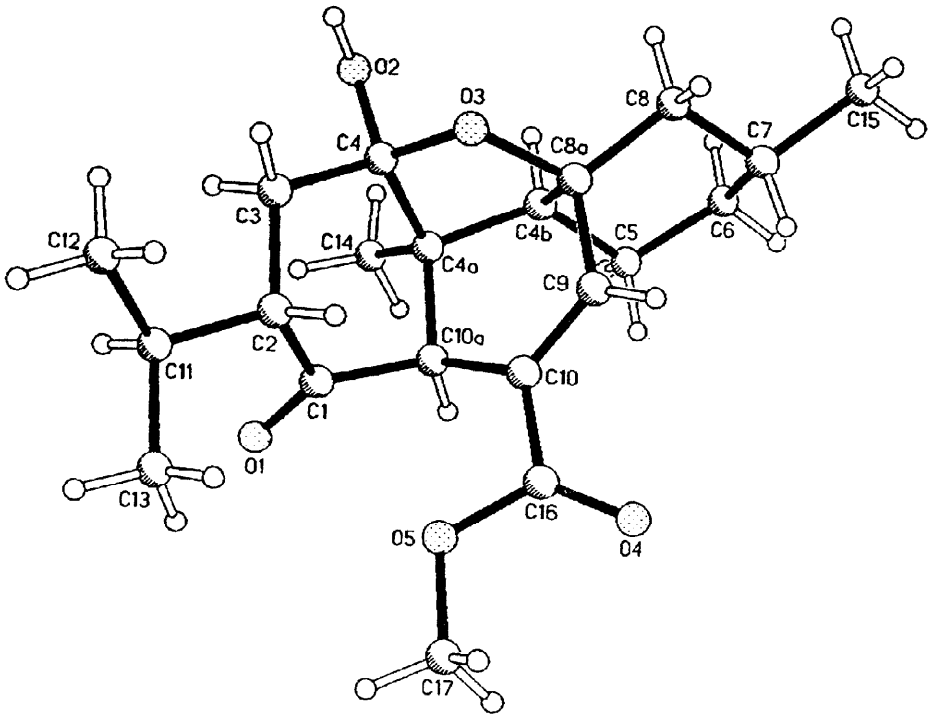

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