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Palmosalides A-C, New Sesquiterpenoids from the Indian Ocean Telestacean Octocoral *Coelogorgia palmosa*

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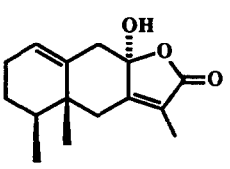
Summary: Three new sesquiterpenoid lactones, palmosalides A-C (**1-3**), possessing both eremophilane and bakkane carbon skeletons, have been isolated from the Indian Ocean telestacean octocoral *Coelogorgia palmosa* Milne Edwards & Haime. The structure determinations of the new eremophilanes, palmosalides A and B, were accomplished by NMR methods, while the structure of palmosalide C was assigned by X-ray analysis. Palmosalide C (**3**) belongs to the rare bakkane class of sesquiterpenoids, but it is epimeric to the known terrestrial bakkenolides at the C-7 spiro center. This is only the second telestacean to be investigated chemically, and the first report of sesquiterpenoid synthesis in this rare class of marine invertebrates.

Marine octocorals of the order Telastaceae are rare coelenterates found mainly in tropical marine environments. Because of their limited scope and distribution, these soft-corals have received less chemical study than other octocorals, such as the gorgonians, alcyonaceans (true soft-corals) and stoloniferans. Only one genus, *Telesto,* has thus far been investigated. Studies have shown that *Telesto spp.* produce unprecedented halogenated prostaglandin derivatives and truncated steroids.[2] During an expedition to the tropical reefs of Aldabra Atoll, Indian Ocean, we encountered a gorgonian-like invertebrate which was later identified as *Coelogorgia palmosa* , a true telestacean octocoral. In subsequent studies, we found this invertebrate to be a rich source of several new sesquiterpene lactones, palmosalides A-C (**1-3**), the structures of which are reported here.



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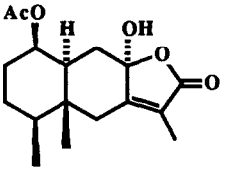

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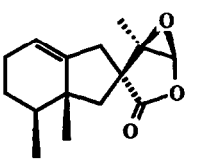

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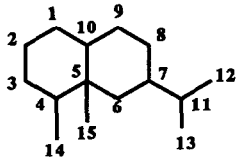
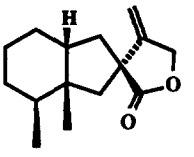
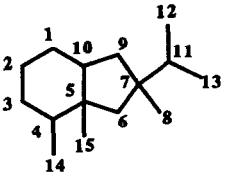


eremophilane



4, bakkenolide-A



bakkane

NMR Data for Palmosalides A-C (1-3)*

C#	1 ^{13}C	1 ^{1}H	2 ^{13}C	2 ^{1}H	3 ^{13}C	3 ^{1}H
1	126.7 (CH)	5.60 (m)	73.1 (CH)	5.01 (m)	118.9 (CH)	5.40(m)
2	25.8 (CH_2)	2.12 (m) 2.00 (m)	30.6 (CH_2)	nr	25.2 (CH_2)[a]	2.15 (m)
3	27.2 (CH_2)	1.46 m	26.0 (CH_2)	nr	26.7 (CH_2)[a]	1.4-1.65 (m)
4	40.6 (CH)	1.70 (ddq, J=4.6, 10.2, 6.8)	42.7 (CH)	nr	38.8 (CH)	1.4-1.56 (m)
5	41.2 (C)	---	40.9 (C)	---	42.9 (C)	---
6	37.3 (CH_2)	ax 2.74 (d, J=13) eq 2.15 (dd, J=13, 1.4)	38.3 (CH_2)[a]	ax 2.62 (d, J=13) eq 2.05 (d, J=13)	38.5 (CH_2)[b]	2.04 (AB dd, J=15)
7	159.4 (C)	---	158.7 (C)	---	52.3 (C)	---
8	103.7 (C)	4.00 (br, OH, exchange)	103.5 (C)	---	180.1 (C)	---
9	45.0 (CH_2)	ax 2.80 (d, J=14) eq 2.48 (ddd, J=14, 5.4, 2.8)	38.4 (CH_2)[a]	nr	46.6 (CH_2)[b]	2.75 (m) 2.40 (d, J=15)
10	136.6 (C)	---	44.0 (CH)	1.65 (m)	144.4 (C)	---
11	122.8 (C)	---	123.4 (C)	---	63.9 (C)	---
12	172.9 (C)	---	172.3 (C)	---	82.6 (CH)	5.41 (s)
13	8.1 (CH_3)	1.71 (d, J=1.4)	8.1 (CH_3)	1.80 (s)	20.9 (CH_3)	1.58 (s)
14	15.9 (CH_3)	1.00 (d, J=6.8)	15.4 (CH_3)[b]	0.96 (d, J=6.1)	16.7 (CH_3)[c]	0.92 (d, J=6.8)
15	17.8 (CH_3)	0.84 (s)	12.8 (CH_3)[b]	0.77 (s)	12.7 (CH_3)[c]	1.01 (s)
OAc			170.6 (C) 21.2 (CH_3)	2.00 (s)		

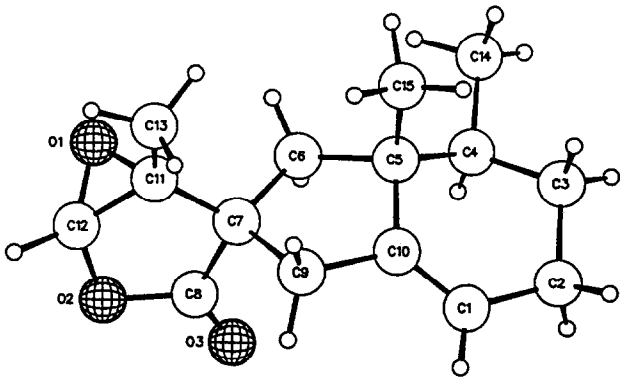
* ^{1}H NMR spectra were recorded in $CDCl_3$ solution at 360 MHz. ^{13}C NMR spectra were recorded in $CDCl_3$ solution at 75 MHz. Proton assignments were aided by single frequency decoupling and COSY measurements. Carbon assignments and proton correlations for **1** were made on the basis of XHCORR and COLOC experiments, and those of **2** and **3** were made by analogy. The notations a,b, etc. within a column denote that assignments are insecure and may be interchanged. The notation "nr" indicates that the signal was not resolved.

Collections of *C. palmosa* were stored in isopropyl alcohol and subsequently extracted with mixtures of methylene chloride and ethyl acetate. The combined organic extracts were reduced to a concentrated tar and chromatographed by vacuum flash methods over TLC grade silica gel, eluting with various mixtures of ethyl acetate in hexane. HPLC purification of medium polarity fractions (20% ethyl acetate / hexane) yielded palmosalides A-C (**1-3**). Palmosalide A, mp 172-174°, analyzed for $C_{15}H_{20}O_3$ by combined HRMS and NMR methods.[3] Infrared absorption at 1755 cm^{-1} and UV absorption at 221 nm, coupled with the observation of a ^{13}C NMR carbonyl band at 172.9 ppm illustrated that **1** was an α,β-unsaturated-γ-lactone. An additional ^{13}C hemi-ketal carbon at 103.7 ppm, in conjunction with no other oxygen bearing carbon resonances, further illustrated that the lactone was γ-hydroxylated. The full assignment of the structure of palmosalide A was subsequently accomplished by NMR experiments involving DEPT, XHCORR and COLOC experiments (Table and ref. 3). Particularly diagnostic were the geminal couplings found in the ^{1}H NMR spectrum for the vicinally isolated protons at C-6 and C-9. The extended coupling of the equitorial C-9 proton was illustrated as allylic to the C-1 proton and homoallylic to one of the C-2 protons. The downfield shift of the axial (α) C-9 proton indicated it was eclipsed with the adjacent hydroxyl group. Similarly, the equitorial C-6 proton showed homoallylic coupling to the olefinic C-13 methyl group. The methyl group at C-4 was placed in an equitorial position on the basis of the large, 10.2 Hz (axial-axial), couplings observed for the proton at that position. The bridgehead

methyl group at C-5 was placed in a β (axial) position by analogy to **3**, by comparison with other eremophilanes, and to accommodate the overall deshielding and pronounced homoallylic couplings observed from the eremophilane bicyclic ring system. Comprehensive ^{1}H -^{13}C NMR correlation experiments confirmed the relationship of all protons to their adjacent carbons leading to the structure shown in **1**.[3]

Palmosalide B (**2**), an oil, analyzed for $C_{17}H_{24}O_5$ by HRMS and ^{13}C NMR methods.[3] Comparison of all spectral data with those of **1** allowed the structure of **2** to be formulated as the acetic acid *trans*-addition product at the C-1 C-10 olefinic position. ^{13}C and ^{1}H NMR coupling constant and chemical shift data further suggested a *trans* decalin structure. The C-1 acetoxyl group was placed in an axial orientation because of the small coupling constants observed for the C-1 equitorial proton (< 4 Hz for each of 3 couplings).

Palmosalide C (**3**), mp 147-149°, analyzed for $C_{15}H_{20}O_3$, also by combined HRMS and NMR methods.[3] However, the spectral data for this compound were not in accord with those of palmosalides A and B. In particular, the infrared spectrum showed a saturated lactone carbonyl band at 1800 cm^{-1}, and the ^{13}C NMR spectrum a corresponding carbonyl band at 180.1 ppm. NMR spectral measurements illustrated that the olefin-containing A ring was intact, but the presence of a quaternary carbon at 52.3 ppm in the ^{13}C NMR spectrum of **3** showed that significant modification to the eremophilane skeleton had taken place.



The structure of this compound was subsequently solved by single crystal X-ray analysis. An X-ray perspective drawing of palmosalide C is shown in the figure with relative stereochemical assignments only. Palmosalide C is related to bakkenolide A (**4**), the first reported member of the bakkane (fukinane) class of sesquiterpenoids. However, the relative stereochemistry of the C-7 spirocarbon center in this compound is inverted to that assigned to the bakkane sesquiterpenoids.[4] Palmosalide C crystallized in the orthorhombic space group $P2_12_12_1$ with the unit cell dimensions of a=5.808(2), b=13.763(4), c=16.336(5) A. Density considerations indicated that one molecule of the composition $C_{15}H_{20}O_3$ formed the asymmetric unit. All unique intensity data with $2\theta < 114°$ were collected on a computer controlled four-circle diffractometer using graphite monochromated Cu Kα radiation (1.542 Å) and variable speed, one degree ω-scans. Of the 1061 total reflections collected, 904 (85.2%) were judged observed ($|Fo|>3\sigma(Fo)$).[5] A phasing model was found by standard direct methods and extended with Fourier refinement. Following partial refinement, the hydrogens were located through difference Fourier synthesis. Block diagonal least squares refinements with anisotropic nonhydrogen atoms and isotropic hydrogens converged to a convential crystallographic residual of 0.0599 for the observed reflections.

Bakkane spiro-sesquiterpenoids are of limited distribution, isolated mainly from two genera of composite plants.[4] Because eremophilanes are generally isolated from the same extracts, the biosynthetic interconversion of these two carbon skeletons has been the subject of discussion and experiments involving biomimetic interconversions[6]. Although the planar structure of palmosalide C (**3**) is of the bakkane skeleton, this compound is epimeric to the terrestrial bakkanes at the C-7 spiro center. Related spirolactones, possessing different carbon skeletons, have also been

isolated from the marine stoloniferan *Tubipora musica*[7], from the sponges *Dysidea etheria*[8] *and Spongia officinalis*[9], and from the liverwort *Ptychanthus striatus*.[10]

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References and Notes

1. On leave from the Department of Chemistry, University of Iowa, Iowa City, IA 52242

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3. Additional spectral data; For **1**: HRMS (EI) M^+ m/z = 248.1406 (+0.5 mmu), IR ($CHCl_3$) 3020, 2965, 2925, 1755, 1210(br) cm^{-1}, UV (MeOH) 221 nm (ε=18,600), $[\alpha]_D$ =155° (c 1.1 $CHCl_3$), COLOC correlations H-3 to C4, C-5, H-6ax to C-7, C-8, C-10, H-6eq to C-5, H-9ax to C-1, C-5, H-9eq to C-10, C-8, H-13 to C-12, C-7, H-14 to C-5, H-15 to C-10, C-5; for **2**: HRMS (EI) M^+ m/z= 308.1636 (-1.4 mmu), IR ($CHCl_3$) 3400, 2950, 2910, 2860, 1760 1740, 1240 cm^{-1}, UV (MeOH) 218 nm (ε=9400), $[\alpha]_D$ =52.8° (c 1.5 $CHCl_3$); for **3**: HRMS (EI) M= m/z 248.1410 (+0.1 mmu), IR ($CHCl_3$) 3020, 2960, 2935, 1800, 1455, 1380, 1300, 1140, 1070, 980, 880 cm^{-1}, $[\alpha]_D$ = 3° (c 1.5 $CHCl_3$)

4. See the recent synthesis paper by Greene *et al.* for comprehensive literature citations of the isolation of bakkenolide (fukinolide) sesquiterpenoids. A. E. Greene, J.-P. Depres, F. Coelho and T. J. Brocksom, *J. Org. Chem.*, **50**, 3945 (1985).

5. All crystallographic calculations were performed on a PRIME 9950 computer operated by the Cornell Computing Facility. The primary programs utilized were: REDUCE and UNIQUE data reduction programs, by M. E. Leonowicz, Cornell University, 1978; MULTAN 80 and RANTAN 80, computer programs for the automatic solution of crystal structures from X-ray diffraction data, by P. Main, S. E. Hull, L. Lessinger, G. Germain, J. P. Declercq and M. M. Woolfson, University of York, England, 1980; BLS78A, an anisotropic block diagonal least squares refinement program written by K. Hirotsu and E. Arnold, Cornell University, 1980; PLUTO 78, a modified crystallographic illustration program by W. D. S. Motherwell, Cambridge Crystallographic Data Centre, 1978; and BOND, a program to calculate molecular parameters and prepare tables, by K. Hirotsu and G. Van Duyne, Cornell University, 1985.

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