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NOVEL CEMBRANOIDS WITH A 13-MEMBERED CARBOCYCLIC SKELETON FROM A SOFT CORAL, *SARCOPHYTON* SPECIES

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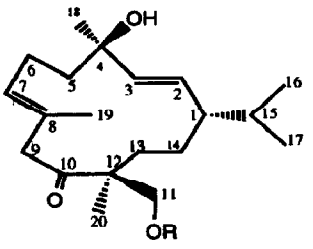
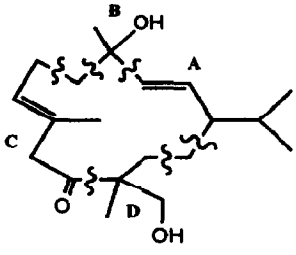
Abstract: Absolute structures of sarcotol and sarcotol acetate, novel irregular cembranoids possessing a 13-membered carbocyclic skeleton from a soft coral, *Sarcophyton* sp., have been determined by spectroscopic and single crystal X-ray analyses.

Soft corals are well-known to be a rich source of cembrane diterpenes possessing a 14-membered carbocyclic ring.[1] Recently, other cembranoids with a 12-membered carbon skeleton or a 13-membered variants have been discovered from Gorgonacea and Alyconacea.[1] During our investigations on biologically active constituents from marine animals collected in the Kagoshima area of southern Japan, we have isolated two novel 13-membered carbocyclic cembranoids, named sarcotol (**1**) and sarcotol acetate (**2**) from an unidentified *Sarcophyton* species.

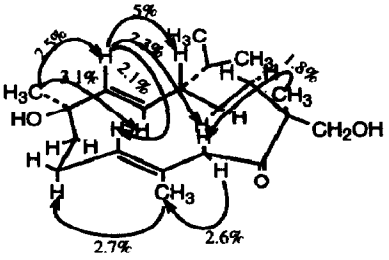
Sarcotol **1**,[2] $C_{20}H_{34}O_3$, was isolated as needles from the dichloromethane soluble portion of methanol extract. The ^{1}H-NMR spectrum showed signals corresponding to six methyls: an isopropyl [δ0.81 and 0.85 (3H each, d, J=6.6 Hz), 1.53 (1H, m)], a tertiary methyl [δ1.16 (s)], a tertiary methyl on a carbon carrying an oxygen function [δ1.31 (s)], an olefinic methyl [δ1.65 (br s)], and a hydroxymethyl group [δ3.48 (1H, dd, J=6.2 and 11.4 Hz) and 3.73 (1H, dd, J=5.9 and 11.4 Hz)]. This indicated that **1** is a rearranged cembranoid.



1 R=H
2 R=Ac
3 R=*p*-BrPhCO



1a



1b

The partial structures of **A** - **D** could be deduced from the ^{1}H-^{1}H and ^{13}C-^{1}H COSY spectra and their connectivity was determined by the COLOC experiments as depicted in **1a**. The geometries of the olefinic bonds at C-2 and C-7 were determined to be *E* by the coupling constant (J=15.8 Hz) between H-2 and H-3 and the chemical shift of the methyl at C-19 (δ15.9), respectively. The relative stereochemistry of the chiral centers except for C-4 were elucidated from the observed NOE shown in **1b**. Final confirmation of the structure was

provided by X-ray analysis on sarcotol 11-*O*-*p*-bromobenzoate.[3] A computer-generated perspective drawing of the final X-ray model of **3** is given in Figure 1.[4]

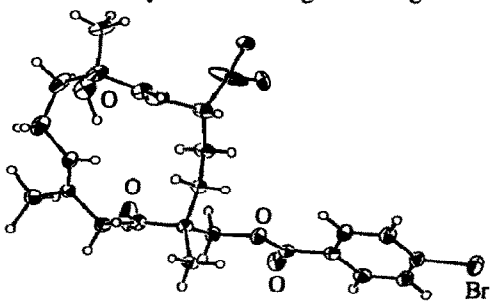


Figure 1. ORTEP representation of **3**

Spectral data of sarcotol acetate (**2**),[5] $C_{22}H_{36}O_4$ were identical with those of an acetate obtained by acetylation of **1** and established sarcotol acetate **2** as the 11 acetyl derivative of sarcotol.

Sarcotol and sarcotol acetate may be formed by rearrangement of a cembrane with an epoxide between C-11 and C-12 as well as in the case of lobophytol.[6]

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REFERENCES AND NOTES

1. Faulkner, D. *J. Nat. Prod.* **1992**, 323 and references therein.
2. Sarcotol **1**: Needles, mp 113°, $[\alpha]_D$ -189.7°; ^{1}H-NMR ($CDCl_3$): δ0.81 and 0.85 (3H each, d, J=6.6 Hz, isopropyl Me), 0.98 (1H, m, H-14_{endo}), 1.16 (3H, s, H-20), 1.31 (1H, m, H-13), 1.31 (3H, s, H-18), 1.40 (H-14_{exo}), 1.53 (3H, m, H-15), 1.60 (1H, m, H-1), 1.53 (1H, m, H-15), 1.65 (3H, br s, H-19), 1.72-1.85 (3H, m, H-5 x 2 and H-13_{endo}), 2.18 (2H, m, H-6), 2.66 (1H, br d, J=12.1 Hz, H-9α), 3.48 (1H, dd, J=6.2 and 11.4 Hz, H-11), 3.53 (1H, d, J=12.1 Hz, H-9β), 3.73 (1H, dd, J=5.9 and 11.4 Hz, H-11), 5.23 (1H, dd, J=9.2 and 15.8 Hz, H-2), 5.29 (1H, br t, J=6.6 Hz, H-7), 5.47 (1H, d, J=15.8 Hz, H-3); ^{13}C-NMR ($CDCl_3$): δ15.9 (C-19), 19.8 and 16.7 (C-16, and 17), 20.4 (C-20), 23.4 (C-6), 25.8 (C-14), 27.6 (C-18), 32.6 (C-15), 34.9 (C-13), 43.1 (C-5), 49.0 (C-9), 50.2 (C-1), 53.7 (C-11), 66.1 (C-11), 73.1 (C-4), 128.6 (C-8), 129.9 (C-2), 131.3 (C-7), 137.8 (C-3), 214.3 (C-10), 212.3 (C10); HREIMS *m/z*: 322.2524 ($C_{20}H_{34}O_3$ requires 322.2508).
3. Sarctotol 11-*O*-*p*-bromobenzoate **3**. Prisms, mp 119-120°; ^{1}H-nmr (CD_3OD): δ0.81 (3H, d, J=7.0 Hz, H-16 or 17) and 0.84 (3H, d, J=6.6 Hz, H-17 or 16), 0.98 (1H, m, H-14_{exo}), 1.24 (3H, s, H-18), 1.27 (3H, s, H-20), 1.42 (1H, m, H-14_{endo}), 1.48-1.57 (2H, m, H-13 and H-15), 1.64 (3H, s, H-19), 1.64 (1H, m, H-1), 1.71 (1H, m, H-5_{exo}), 1.80 (1H, dt, J=3.1 and 9.0 Hz, H-5endo), 2.03 (1H, dt, J=4.2 and 13.8 Hz, H-13_{endo}), 2.19 (1H, m, H-6β), 2.74 (1H, br d, J=12.1 Hz, H-9α), 3.63 (1H, d, J=12.1 Hz, H-9β), 4.33 and 4.65 (AB, J=11.0 Hz, H-11), 5.18 (1H, dd, J=8.8 and 15.6 Hz, H-2), 5.40 (1H, br t, J=6.2 Hz, H-7), 5.48 (1H, d, J=16.2 Hz, H-3), 7.65 and 7.83 (A_2B_2, J=8.8 Hz, arom-H); HR EIMS *m/z* 486.1783 ($C_{27}H_{37}O_4Br$-H_2O requires 486.17870).
4. X-ray analysis of **3**. Crystal data: $C_{27}H_{37}O_4Br$, Mr=$C_{27}H_{37}O_4Br$,Mr=505.49, monoclinic, P21, a=5.854(2), b=10.816(2), c=20.088(2) Å, β=92.97(2)°, V=1270.1(4) $Å^3$, Z=2, Dx=1.322 g/cm^3, F(000)=532, μ(Cu Kα)=24.38 cm^{-1}. Intensity data were collected at 200K on a Rigaku AFC5R diffractometer using graphite monochromatized Cu Kα radiation (λ=1.54178 Å) up to 2θ=120°. Of the total 2011 unique reflections, 1878 were observed [I>3σ(I)]. The structure was solved by a heavy atom method and refined by full-matrix least-squares techniques to R=0.035 and Rw=0.054. The absolute configuration of the molecule was determined based on the Bijvoet inequality relationships mainly due to the anomalous dispersion of the bromine atom (Δf'=-0.676, Δf"=1.281): Bijvoet differences of Fo and Fc were compared for 36 pairs with |ΔFcl/σ(Fo)>1.0, those of 33 pairs exhibiting the same inequality signs. Detailed atomic coordinates, bond distances and angles have been deposited at the Cambridge Crystallographic Data Center.
5 Sarcotol acetate **2**. Oil, $[\alpha]_D$ -182.4°; ^{1}H-nmr ($CDCl_3$): δ0.79 (3H, d, J=7.0 Hz, H-16 or H-17), 0.83 (3H, d, J=6.6 Hz, H-17 or H-16), 0.92 (1H, m, H-14_{exo}), 1.18 (3H, s, H-20), 1.31 (3H, s, H-18), *ca* 1.3(1H, m, H-14_{endo}), 1.35 (1H, m, H-11exo), 1.52 (1H, oct, J=6.6 Hz, H-15), 1.60 (1H, m, H-1), 1.68 (3H, s, H-19), 1.79 (2H, m, H-5), 1.89 (1H, dt, J=3.7 and 14.0 Hz, H-endo), 2.02 (3H, s, OAc), 2.18 (2H, m, H-6), 2.75 (1H, br d, J=12.5 Hz, H-9α), 3.44 (1H, d, J=12.5 Hz, H-9β), 4.11 and 4.22 (AB, J=11.0 Hz, H-11), 5.24 (1H, dd, J=8.4 and 15.8 Hz, H-2), ca 5.24 (1H, obscured, H-7), 5.43 (1H, d, J=15.8 Hz, H-3); ^{13}C-NMR ($CDCl_3$): δ16.2 (C-19), 19.7 (C-16 or 17), 20.2 (C-17 or 16), 20.8 (C-20), 20.9 (OCOCH3), 23.6 (C-6), 25.5 (C-14), 28.1 (C-18), 32.5 (C-15), 34.3 (C-13), 42.8 (C-5), 48.6 (C-9), 49.1 (C-10, 51.6 (C-11), 67.0 (C-12), 73.2 (C-4), 128.8 (C-8), 129.5 (C-2), 131, 2 (C-7), 137.6 (C-3), 170.9 (OCOCH3); HREIMS *m/z* 364.2622 ($C_{22}H_{36}O_4$ requires 364.2614).
6. Iguchi, K: Kitade, M: Yamada, Y: Ichikawa, A: Ohtani, I: Kusumi, T: Kakisawa, H. *Chemistry Lett.* **1991**, 319.

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