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A NEW CARYOPHYLLENE-BASED DITERPENE FROM THE  
SOFT CORAL, *CESPITULARIA* SP.<sup>1</sup>

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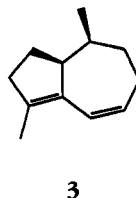
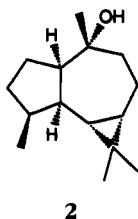
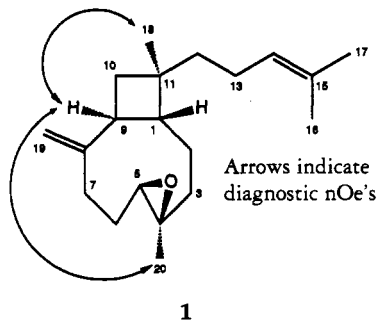
ABSTRACT.—From a sample of the soft coral *Cespitularia* sp., a new caryophyllene-based diterpene **1** was isolated and characterized. This is the first report of this structural class in animals of the genus *Cespitularia*.

Soft corals obtained from the Great Barrier Reef, Australia have proven to be a rich source of terpenoid compounds belonging to many structural classes (1–3). Reports relating to the secondary metabolite chemistry of the genus *Cespitularia* (family Xeniidae) are, however, scarce. This is partly due to difficulties relating to the preservation and thus taxonomic identification of animals of this and related (e.g., *Efflatounaria*) genera. To date, isolates from *Cespitularia* species comprise sesquiterpenes with the aromadendrane skeleton: palustrol, alloaromadendrene, viridiflorol [**2**], and ledol (4–6), a trinorsesquiterpene **3** (7) whose structure was recently shown to have been that of the previously published compound clavukerin A (8), cubebol (7), for which complete nmr data have recently been fully assigned for the first time (9), and sesquiterpene furans (10), as well as diterpenes possessing the cembrane (11,12) or dolabellane (12) skeleton.

The current report describes the isolation and structure elucidation of a new caryophyllene-based diterpenoid **1**. This is the first report of a caryophyllene derivative in *Cespitularia*. This structural class is, however, characteristic for animals of the soft coral genus *Xenia* (13), which is closely related to the genus *Cespitularia*.

The CH<sub>2</sub>Cl<sub>2</sub> extract of the freeze-dried soft coral was separated using vlc over Si gel. Fractions eluting with hexane contained compound **1**, which was further purified by normal-phase hplc.

Compound **1** was obtained as a yellow oil. Its hrms and nmr spectroscopic data indicated a molecular formula of C<sub>20</sub>H<sub>32</sub>O. The presence of four sp<sup>2</sup> carbon resonances in the <sup>13</sup>C-nmr spectrum of **1** for two carbon-carbon double bonds and the absence of any further multiple bonds dictated the molecule to be tricyclic. <sup>1</sup>H- and <sup>13</sup>C-nmr data allowed deduction of the presence of an unsaturated *gem*-dimethyl grouping (δ 17.6 q, 25.7 q, 131.1 s, 124.9 d; 1.60 s, 1.67 s, 5.08 t), two methyl groups on quaternary carbon atoms (δ 18.9 q, 17.1 q, 1.03 s, 1.19 s), a



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1,1-disubstituted double bond ( $\delta$  112.9 t, 151.9 s, 4.85 s, 4.97 s), and an ether, most probably a three-membered epoxy ring ( $\delta$  59.8 s, 63.9 d, 2.89 dd).

From the result of an HMQC measurement ( $J=150$  Hz) and the outcome of a  $^1\text{H}$ - $^1\text{H}$  COSY experiment, three proton spin systems could be discerned, one for the C-12 to C-17 side-chain; the methyl groups at C-16 ( $\delta$  1.60 s) and C-17 ( $\delta$  1.67 s) showed a long range coupling to H-14 ( $\delta$  5.08 t) which further coupled to the methylene protons at C-13 ( $\delta$  1.90 m), and from there an additional coupling to the methylene protons at C-12 ( $\delta$  1.35 m) was evident. The second spin system related the proton at C-5 ( $\delta$  2.89 dd) to those of the C-6 methylene group ( $\delta$  2.24 m, 1.30 m), which further coupled to the methylene protons at C-7 ( $\delta$  2.28 m, 2.15 m). The third and most extensive  $^1\text{H}$ - $^1\text{H}$  spin system within **1** could be traced from the resonance of the bridgehead proton H-1 ( $\delta$  1.84 m) through to H<sub>2</sub>-3 ( $\delta$  2.07 dd, 0.90 m) on one side, and, on the other side to the second bridgehead proton H-9 ( $\delta$  2.64 ddd), and from there to the methylene protons at C-10 ( $\delta$  1.65 m). A long range coupling observed from H-9 ( $\delta$  2.64 ddd) to the *exo*-methylene protons at C-19 ( $\delta$  4.97 s, 4.85 s) clearly positioned the latter functionality. The previous results combined with HMBC measurements ( $J=8.3$  Hz), which showed  $^1\text{H}$ - $^{13}\text{C}$  couplings from the protons of the C-20 methyl-group ( $\delta$  17.1 q, 1.19 s) to C-3 (39.0 t), C-4 (59.8 s), and C-5 (63.9 t), and from the protons of the C-18 methyl group to C-12 (44.1 t), C-11 (37.1 s); C-10 (38.6 t), and C-1 (49.4 d), and from the *exo*-methylene protons H<sub>2</sub>-19 to C-7 (29.6 t) established the basic structure of **1** unambiguously.

The relative stereochemistry of the five chiral centers within **1** was proposed on the basis of the results of a NOESY measurement, which showed diagnostic nOe effects between H<sub>3</sub>-18/H-9 and H-9/H<sub>3</sub>-20, and by comparison of the  $^{13}\text{C}$ -

nmr data of **1** with those of similar compounds (13,14). Compound **1** is thus 4 $\beta$ ,5 $\beta$ -epoxyxeniaphylla-8(19),14-diene.

## EXPERIMENTAL

**GENERAL EXPERIMENTAL PROCEDURES.**—Optical rotations were recorded with a Perkin-Elmer 141 polarimeter using  $\text{CHCl}_3$  as solvent. Ir spectra were measured on a Perkin-Elmer 781 infrared spectrometer as liquid films.  $^1\text{H}$ - and  $^{13}\text{C}$ -nmr spectra and 2D-correlated spectroscopy were measured at 300 and 75.5 MHz, respectively, with a Bruker AMX-300 spectrometer in  $\text{CDCl}_3$ , with residual  $\text{CHCl}_3$  ( $\delta$  7.26 and 77.0) as the internal standard. Hplc was performed using a Waters 6000A solvent delivery system connected to a Rheodyne hplc injector and a Knauer differential refractometer. Hplc columns were from Knauer (250 mm  $\times$  8 mm, LiChrosorb Si60, 5  $\mu\text{m}$ ). Silica (tlc-Silica 60 GF 15  $\mu\text{m}$ , Merck) was used for vlc, while aluminium-backed sheets coated with silica 60F<sub>254</sub>, 0.2 mm thick (Merck) were used for tlc. All solvents were hplc grade.

**ANIMAL MATERIAL.**—The coral was obtained from Old Reef, Great Barrier Reef, Queensland, Australia in 1983. Animals growing at 6–9 m depth were collected, deep frozen, and prior to investigation, freeze-dried. A voucher specimen is deposited at the Northern Territory Museum of Arts and Science, Darwin, N.T. 0801, Australia, voucher number NTMC11658. The specimen has three rows of approximately 17 pinnules down each side of the tentacles. The sclerites are 0.042 mm long. There is no species described as such and it is probable that NTMC11658 is a new species of *Cespitularia*.

**EXTRACTION AND ISOLATION.**—The dry tissue (17.6 g) was exhaustively extracted with 2 liters of  $\text{CH}_2\text{Cl}_2$  and 2 liters of MeOH to yield 1.4 g of  $\text{CH}_2\text{Cl}_2$ -soluble material. Vlc of the crude extract over Si gel, using hexane containing increasing proportions of EtOAc as eluent, afforded eight fractions, each 100 ml. Tlc and  $^1\text{H}$ -nmr examination of these fractions indicated that fraction 3 was of further interest.

Hplc separation of fraction 3 from the vlc with hexane as eluent afforded compound **1** as a clear oil (5 mg, 0.03%):  $[\alpha]^{22}_{\text{D}} +2.7^\circ$  ( $\text{CHCl}_3$ ,  $c=0.07$ ); ir  $\nu$  max (film) 2930, 1380, 1050  $\text{cm}^{-1}$ ;  $^1\text{H}$  nmr ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  0.9 (m, 1H, H-3), 1.03 (s, 3H, H-18), 1.19 (s, 3H, H-20), 1.30 (m, 1H, H-6), 1.35 (m, 2H, H-12), 1.45 (m, 1H, H-2), 1.60 (s, 3H, H-16), 1.65 (m, 2H, H-10), 1.67 (m, 1H, H-2), 1.67 (s, 3H, H-17), 1.84 (m, 1H, H-1), 1.90 (m, 2H, H-13), 2.07 (m, 1H, H-3), 2.15 (m, 1H, H-7), 2.24 (m, 1H, H-6), 2.28 (m, 1H, H-7), 2.64 (ddd,  $J=9.5, 9.5, 9.5$  Hz, 1H, H-9), 2.89 (dd,  $J=3.9, 10.7$  Hz, 1H, H-5), 4.85 (br

s, 1H, H-19), 4.97 (br s, 1H, H-19), 5.08 (br t,  $J=7.4$ , 1H, H-14);  $^{13}\text{C}$  nmr ( $\text{CDCl}_3$ , 75.5 MHz) 17.1 (q, C-20), 17.6 (q, C-16), 18.9 (q, C-18), 22.8 (t, C-13), 25.8 (q, C-17), 27.8 (t, C-2), 29.6 (t, C-7), 30.2 (d, C-6), 37.1 (s, C-11), 38.6 (t, C-10), 39.0 (t, C-3), 44.1 (t, C-12), 48.8 (d, C-9), 49.5 (d, C-1), 59.8 (s, C-4), 63.9 (d, C-5), 112.9 (t, C-19), 124.9 (d, C-14), 131.1 (s, C-15), 151.9 (s, C-8) ppm; eims  $m/z$  (rel. int.)  $[\text{M}]^+$  288 (1), 273 (3), 245 (4), 227 (4), 171 (22), 205 (3), 187 (4), 177 (6), 149 (14), 123 (62), 107 (37), 93 (40), 81 (57), 69 (100), 55 (35), 41 (93), hrms 288.2442 (calcd for  $\text{C}_{20}\text{H}_{32}\text{O}$ , 288.2455).

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