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SESQUITERPENOIDS FROM THE FAR-EASTERN GORGONARIA *Stenogorgia* SP.

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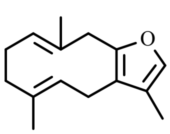
In continuation of the search for biologically active natural compounds in marine coelenterates, we investigated the composition of the sesquiterpenoid fraction from the Far-Eastern Gorgonaria *Stenogorgia* sp. [1, 2].

The Gorgonaria was collected in August 2008 near Urup Island (Kuril Islands) from gravelly ground by a bottom trawler at a depth of 350 m. Ground animal was extracted with EtOH. The evaporated extract was dissolved in water and extracted with hexane.

Compounds **1** and **2** were isolated from the hexane extract by column chromatography over Sephadex LH-20 (EtOH) and silica gel (KSK, 50-160 μm) using a hexane:EtOAc gradient (100:0–90:10) with subsequent HPLC on an Altex Ultrasphere^{TM} Si column (5 μm, 4.6 × 250 mm, hexane). Compound **3** was obtained by a series of chromatographic procedures including an LH-20 column (EtOH), silica gel (hexane:EtOAc, 92:8), and monocratic HPLC on Ultrasphere^{TM} Si (5 μm, 4.6 × 250 mm, hexane:EtOAc, 3.5:1) and Agilent Hypersil ODS (5 μm, 4.0 × 250 mm, EtOH:H_2O, 7:3) columns.



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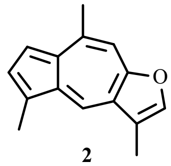

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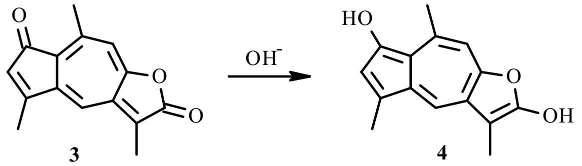

3 4

Isofuranodiene (1) (11.7 mg, 0.003% of dry animal mass), colorless oil, R_f 0.65 (silica gel, hexane). The molecular formula $C_{15}H_{20}O$ was confirmed by high-resolution mass spectrometry with electron ionization (calcd for $[M]^+$ 216.1514 *m/z*; found, 216.1516 *m/z*). The structure of **1** was identified using NMR spectroscopy (^1H, ^{13}C, DEPT, COSY, NOESY, HSQC, HMBC). Compound **1** was isolated previously from *Curcuma zedoaria* Roscoe (Zingiberaceae) collected in Japan [3] and was found later in soft coral of the genera *Cespitularia* and *Efflatounaria* (Australia) [4], invertebrate *Leminda millecra* (South Africa) [5], and Gorgonaria *Dasystenella acanthita* (Antarctica) [6].

Linderazulene (2) (13.2 mg, 0.004%), amorphous violet compound, R_f 0.63 (silica gel, hexane). The structure of **2** was identified by comparison of mass and NMR spectra with those in the literature for linderazulene from Gorgonariae *Paramuricea chamaeleon* [7], *Echinogorgia complexa* [8], and *Platogorgia* sp. [9].

Ketolactone (3) (17.3 mg, 0.005%), amorphous yellow compound. The structure of **3** was identified using NMR spectra (^1H, ^{13}C, DEPT, COSY, NOESY, HSQC, HMBC). The high-resolution mass spectrum showed a peak for $[M]^+$ at 240.0780 *m/z*; calcd for $C_{15}H_{12}O_3$, 240.07864. UV spectrum ($CHCl_3$:MeOH, 1:1, λ_{max}, nm): 240, 271, 281, 291, 417, 434, 461. Compound **3** was described in the literature first as a photo-artefact formed from **2** [9] and later as a native metabolite from Gorgonaria *Placogorgia* sp. [10].

We observed a previously unknown property of **3**. It behaves as an indicator, changing color from yellow to red upon making the solution basic with KOH. Thus, its UV spectrum changed after a solution of **3** in MeOD was stirred and treated with several drops of KOH solution in MeOD. A long-wavelength maximum appeared at 503 nm [UV spectrum (λ_{max}, nm): 244, 271, 291, 337, 375, 391, 503]. The NMR spectrum (500 MHz, δ, MeOD) of the product, which we assigned structure **4**, had three 1H singlets at 6.41, 7.31, and 7.90 ppm and three 3H singlets at 2.05, 2.22, and 2.31 ppm whereas the spectrum of **3** (500 MHz, MeOD, δ, ppm) showed the corresponding resonances at 6.24 (1H, s), 6.67 (1H, s), 7.12 (1H, s) and 2.15 (3H, s),

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2.36 (3H, s), 2.67 (3H, s). These results confirmed that the chain of conjugated multiple bonds had changed, which could be related to enolization of both carbonyls in **3**. Compound **4** was unstable. The color of the solution gradually faded upon standing.

Thus, known sesquiterpenoids **1**–**3** were found for the first time in the Kuril Gorgonaria *Stenogorgia* sp., which had not been studied chemically before. It was shown that **3** has the ability to change the conjugation system of multiple bonds in basic medium.

Furthermore, we established by the literature method [11] that **1**–**3** exhibit weak cytotoxicity against HeLa tumor cells (IC_{50} = 237.5, 411.8, and 150 μM, respectively).

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