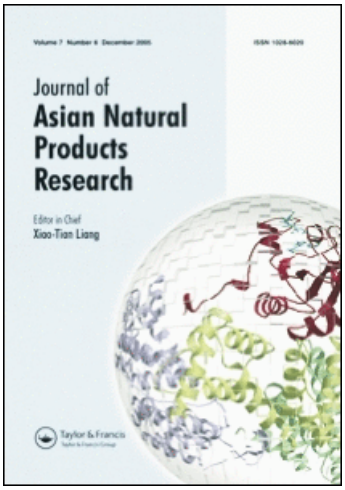


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# Trocheliophorin: A novel rearranged sesquiterpenoid from the Indian Ocean soft coral *Sarcophyton trocheliophorum*

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A novel rearranged sesquiterpenoid, trocheliophorin (**1**) has been isolated from the soft coral *Sarcophyton trocheliophorum* besides the known compounds, sarcophytin, methyl arachidonate, and two polyhydroxy steroids (24*S*)-24-methylcholestane-3β,5α,6β,25-tetrol-25-monoacetate and (24*S*)-24-methylcholestane-3β,5α,6β,25-tetrol. The structure of the new sesquiterpenoid was elucidated by a study of its spectral data.

**Keywords:** soft coral; *Sarcophyton trocheliophorum*; rearranged sesquiterpenoid; trocheliophorin



## 1. Introduction

Soft corals (family, Alcyoniidae) are known to produce a variety of polyhydroxy steroids, sesquiterpenoids, diterpenoids, and even tetraterpenoids [1,2]. In our continuing program on the secondary metabolities of the soft corals of the Indian Ocean and in particular those of the *Sarcophyton* genus [3], including *S. crassocaule* [4,5], *S. elegans* [6–9], and *S. buitendijki* [10], we have undertaken the chemical examination of *Sarcophyton trocheliophorum* (family, Alcyoniidae) collected from the Mandapam coast (9°16′ N, 79°12′ E). This species, which occurs in different sea waters, has been chemically examined [11–14]. The present chemical examination of this Indian species furnished a novel carboxylic acid, trocheliophorin (**1**), along with the known diterpenoid sarcophytin (**3**) [6], methyl arachidonate, and two polyhydroxy steroids, (24*S*)-24-methylcholestane-3β,5α,6β,25-tetrol-25-mono acetate and (24*S*)-24-methylcholestane-3β,5α,6β,25-tetrol. The structure of the novel acid was elucidated by a study of its physical and spectral ($^1$H, $^{13}$C, APT, $^1$H–$^1$H COSY; HMQC, HMBC and Mass) data.

## 2. Results and discussion

The residue (26 g) from the ethyl acetate extract was subjected to chromatographic separation over a column of silica gel to furnish a new sesquiterpenoid trocheliophorin (**1**, 8 mg), as the minor constituent. It was isolated as a colorless oil, $[\alpha]_D^{30} + 0.356$ (*c* 0.04, in $CHCl_3$), and its molecular formula was established as $C_{16}H_{20}O_5$ from elemental analysis (C and H analysis; required C, 65.75%; H, 6.84% and found C, 65.57%; H, 6.85%). The mass ions at *m/z* 310.2 $[M + NH_4]$, 602.5 $[2M + NH_4]^+$ in the positive FAB mass spectrum. Its IR spectrum showed absorption bands at 3430, 1700 and 1738 $cm^{-1}$ (the —COOH and the ester groupings, respectively). It showed strong UV absorptions at 226 and 291 nm.

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Table 1. $^{1}H$ and $^{13}C$ NMR assignments and HMBC and $^{1}H-^{1}H$ COSY correlations of (**1**).

| Position | $^{1}H$ | $^{13}C^{a}$ | HMBC | $^{1}H-^{1}H$ COSY |
|---|---|---|---|---|
| 1 | | 180.4 | | |
| 2 | 3.04 (1H, m) | 46.1 | C-1, C-4, C-3, C-11, C-12, C-13 | 11-H, 3-H |
| 3 | 3.00 (1H, m) | 37.0 | C-4, C-11, C-1, C-2 | 2-H |
| | 3.50 (1H, dd, $J = 14$, 8 Hz) | | | |
| 4 | | 197.8 | | |
| 5 | | 136.8 | | |
| 6 | 8.40 (1H, s) | 126.4 | C-4, C-14, C-5, C-7, C-8, C-10 | 8-H, 10-H |
| 7 | | 130.5 | | |
| 8 | 8.04 (1H, s) | 134.6 | C-14, C-6, C-10, C-15, C-7 | 10-H, 15-$H_3$ |
| 9 | | 138.9 | | |
| 10 | 7.94 (1H, s) | 132.7 | C-4, C-8, C-6, C-15 | |
| 11 | 2.16 (m) | 29.9 | C-12, C-13, C-3, C-2, C-1 | 12-$H_3$, 13-$H_3$ |
| 12 | 1.02 (3H, d, $J = 6$ Hz) | 20.2 | C-2, C-11, C-13 | 11-H |
| 13 | 1.04 (3H, d, $J = 6$ Hz) | 19.6 | C-2, C-11, C-12 | 11-H |
| 14 | | 166.5 | | |
| 15 | 2.45 (3H, s) | 21.1 | C-8, C-9, C-10 | |
| OMe | 3.94 (3H, s) | 52.3 | C-14 | |

Chemical shifts in δ from TMS (multiplicity, $J$ in Hz) in $CDCl_3$.
[a]Assignments made using the HMQC and HMBC techniques.



The $^{1}H$ and $^{13}C$ NMR spectral data (Table 1) of **1** suggested that it might be a novel sesquiterpenoid methyl ester containing an aromatic ring. Its $^{1}H$ NMR spectrum showed the presence of a carbomethoxyl group (—COOMe) ($\delta$ 3.94, 3H, s), an aromatic methyl group ($\delta$ 2.45, 3H, s), an isopropyl group ($\delta$ 1.02, 3H, d, $J = 6.0$ Hz), ($\delta$ 1.04, 3H, d, 6.0 Hz), and ($\delta$ 2.16, 1H, m). In the aromatic region, three protons were seen each as a singlet at $\delta$ 7.94, 8.04, and 8.40, respectively. The aromatic pattern of the protons suggested that compound **1** contained a 1,3,5-tri-substituted benzene system. In the aliphatic region, the $^{1}H$ NMR spectrum showed the presence of a methylene group ($\delta$ 3.00, 1H, m, $\delta$ 3.50, 1H, dd, 14.8 Hz) and a methine proton ($\delta$ 3.04, 1H, m). These two systems are mutually coupled vicinal protons as they exhibited $^{1}H-^{1}H$ COSY correlations. The methine proton showed a $^{1}H-^{1}H$ COSY correlation (Table 1) not only with the neighboring methylene protons but also with the isopropyl proton that appeared at $\delta$ 2.16. The isopropyl proton in turn showed $^{1}H-^{1}H$ COSY correlations with the two isopropyl methyls. The molecule might, therefore, contain a partial structure (A). Three aromatic protons in the *meta* positions showed mutual $^{1}H-^{1}H$ COSY correlations, besides two of them also showing COSY correlations with the aromatic methyl.

The molecular formula of trocheliophorin requires seven double bond equivalences, out of which the aromatic ring accounts for four and the carbonyl groups the remaining three. From the foregoing information, two tentative structures (**1**,**2**) can be drawn up for trocheliophorin.

The $^{13}C$ NMR spectrum showed all the 16 carbon signals (Table 1) including four methyls, one methylene, five methine, and six quaternary carbons with the help of the APT experiment. The chemical shifts of the respective carbons were assigned based on a comparison with the literature values and HMQC spectral data. The carboxyl carbon appeared at $\delta$ 180.4 and the ester carbonyl carbon at $\delta$ 166.5 with the keto carbonyl at $\delta$ 197.8. The six aromatic carbons were at $\delta$ 136.8, 126.4, 130.5, 134.6, 138.9, and 132.7. The $^{13}C$ NMR spectral data, though supporting the gross structure of the molecule, cannot distinguish between the two alternative structures (**1** and **2**) proposed.

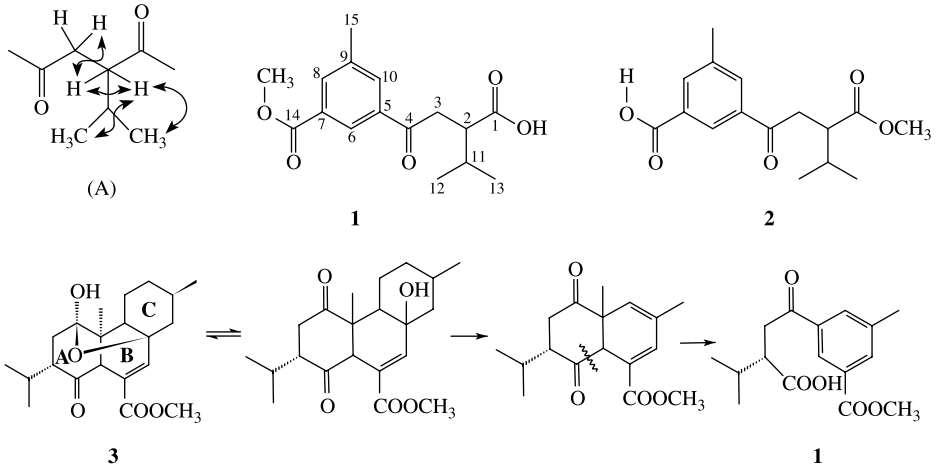


Figure 1. The structure and proposed biogenetic pathway of **1**.

The structure of trocheliophorin could be established by the HMBC correlations. The H-2 at $\delta$ 3.04 showed correlation with the carboxyl carbon but not with the carbomethoxyl carbon indicating that the carboxyl is in its vicinity. The H-2 also showed correlations with C-3 and C-11, and C-1 and H-3 showed correlations with C-1, C-2, C-4, and C-11 carbons. The methoxyl protons of the ester carbonyl showed correlation only with its carbonyl carbon C-14. The aromatic methyl protons at $\delta$ 2.45 showed correlations with C-8, C-9, and C-10 as expected. The above HMBC correlations established clearly that the carboxyl is at the end of the chain and the carbomethoxyl is attached to the aromatic ring as in structure **1**.

The novel structure of trocheliophorin could thus be established as 2-isopropyl-4-keto-4-(3-carbomethoxy-5-methyl) phenyl-butanoic acid (**1**). Although, the structure might be considered as a sequiterpenoid methyl ester with an aromatic ring, its formation cannot be explained on the basis of sequiterpenoid biogenetic considerations. It might, therefore, be considered as an artifact found by the rearrangement and degradation of a larger terpenoid. Looking in this perspective, it can be related to the diterpenoid sarcophytin (**3**) with which it is co-occurring (Figure 1).

It might be presumed that ring B of sarcophytin **(3)** aromatizes with dehydration and elimination of a ring junction methyl and ring C, followed by breaking of ring A to give rise to trocheliophorin (**1**).

## 3. Experimental

### *3.1 General experimental procedures*

Optical rotations were determined using a Roudalph Autopol-III polarimeter. Melting points were obtained using a VEB-Analytic Dreader HMK hot plate and are uncorrected. IR spectra were recorded using a Perkin-Elmer-841 IR spectrometer in $CHCl_3$ solution. UV spectra were recorded using a Milton Roy Spectronic 1201 spectrometer in $CHCl_3$. $^1H$ NMR spectra were obtained using Bruker Advance DRX 300 and JEOL JNM EX-90 spectrometers. $^{13}C$ NMR spectra were obtained using a Bruker advance DRX 300 spectrometer at 75 MHz and JEOL JNM Ex-90 spectrometer at 22.5 MHz using $CDCl_3$ as the solvent and tetramethylsilane as the internal reference. Elemental analyses were done using a Carlo Erba 1108 instrument and mass spectra were obtained using a JEOL JMS-300 spectrometer.

### *3.2 Animal material*

The organism was collected in June 1999 from Kurside Island off the Mandapam coast.

The material was kindly identified by Dr V. Jayashree, Scientist, NIO, Goa. Voucher specimens (code AU1-070) are deposited at the marine museums of the School of Chemistry, Andhra University and National Institute of Oceanography, Goa.

### 3.3 Extraction and isolation

The organism (5.5 kg) after collection was percolated with methanol (10 l) at room temperature every 3 days. This process was repeated until the residue became colorless (eight times). The combined methanolic extract was concentrated under reduced pressure, and the concentrate was extracted with ethyl acetate. The ethyl acetate extract was distilled under reduced pressure to leave a gummy residue (25 g). A part of the above residue (16 g) was chromatographed over a column (85 mm × 100 cm) of silica gel (160 g, 100–200 mesh Acme) using eluents of increasing polarity beginning with hexane (60–80°C) through ethyl acetate to methanol, followed by further purification which furnished a novel rearranged sesquiterpenoid trochelioporin (8 mg) along with sarcophytin (3 mg), and two polyhydroxy steroids (24*S*)-24-methylcholestane-3β,5α,6β,25-tetrol-25-monoacetate (26 mg) and (24*S*)-24-methylcholestane-3β,5α,6β,25-tetrol (25 mg). The fatty gummy residue (1.8 g) from the column fractions 51–63 (hexane:EtOAc, 8.0:2.0) showed a single spot with a little trailing on the TLC plate. It was re-chromatographed by passing through a small column of silica gel using hexane:EtOAc as the eluent. Further purification over a column of silica gel impregnated with silver nitrate (20%) gave a colorless oil (**1**, 8 mg).

#### 3.3.1 Trocheliophorin (1)

The title compound showed $[\alpha]_D^{30} + 0.356$ (*c* 0.04, in $CHCl_3$) and its molecular formula was established as $C_{16}H_{20}O_5$ from elemental analysis (C and H analysis; required C, 65.75%; H, 6.84% and found C, 65.57%; H, 6.85%). The mass ions at *m*/*z* 310.2 $[M + NH_4]$, 602.5 $[2M + NH_4]^+$ in the positive FAB mass spectrum. Its IR spectrum showed absorption bands at 3430 and 1738 $cm^{-1}$ (the carbonyl and ester groups, respectively). It showed strong UV absorptions at 226 and 291 nm. See Table 1 or $^1H$ and $^{13}C$ spectral data.

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