# Sarcophytolides G – L, New Biscembranoids from the Soft Coral *Sarcophyton elegans*

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Six new biscembranoids, namely, sarcophytolides G – L (**1** – **6**, resp.), together with six known analogs, were isolated from a marine soft coral *Sarcophyton elegans*. The structures of the new compounds were established on the basis of 1D- and 2D-NMR (COSY, HSQC, HMBC, and NOESY) spectroscopic analysis together with the aid of MS, CD, and IR data. The unusual isobiscembranoid sarcophytolide G (**1**) was found for the first time in the genus *Sarcophyton*.

**Introduction.** – Dimeric cembranoids, termed biscembranoids, belong to an emerging group of natural products that are considered to be biogenetically derived from a probable *Diels–Alder* cycloaddition between a cembranoid-diene and cembranoid-dienophiles [1]. This biogenetic hypothesis is partly supported by the isolation of methyl tetrahydrosarcoate and methyl sarcoate as precursors from soft corals [2]. The number of these uncommon tetraterpenoids have rapidly increased in recent years [3 – 8]. With their complex and unique skeleton and significant bioactivities, biscembranoids also attracted much attention in synthetic chemistry. Soft corals, belonging to the genus *Sarcophyton* (Alcyoniidae), are well-recognized as a rich source of macrocyclic cembrane-type diterpenoids and biscembranoids. Chemical structures of diverse cembranoids from the genus *Sarcophyton* vary significantly due to the geographic location and species differentiation [8]. Thus, it is a challenge to uncover new natural products from known species of marine organisms distributed in new locations. In our continuing search for the chemical diversity from the soft corals in various locations of South China Sea, soft coral *Sarcophyton elegans* was collected. Primary HPLC/ESI-MS and $^1$H-NMR experiments on the AcOEt extracts revealed the the presence of a diverse array of terpenoids. Further chromatographic separation and purification experiments resulted in the isolation of twelve biscembranoids (*Fig. 1*). Herein, we report the structure elucidation of the new compounds and the primary bioactivities of the isolated compounds.

**Results.** – The molecular formula of sarcophytolide G (**1**) was established as $C_{41}H_{64}O_9$ based on the HR-ESI-MS data (*m*/*z* 723.4442 $[M+Na]^+$), requiring ten degrees of unsaturation. The $^1$H- and $^{13}$C-NMR data (*Tables 1* and *2*) were character-

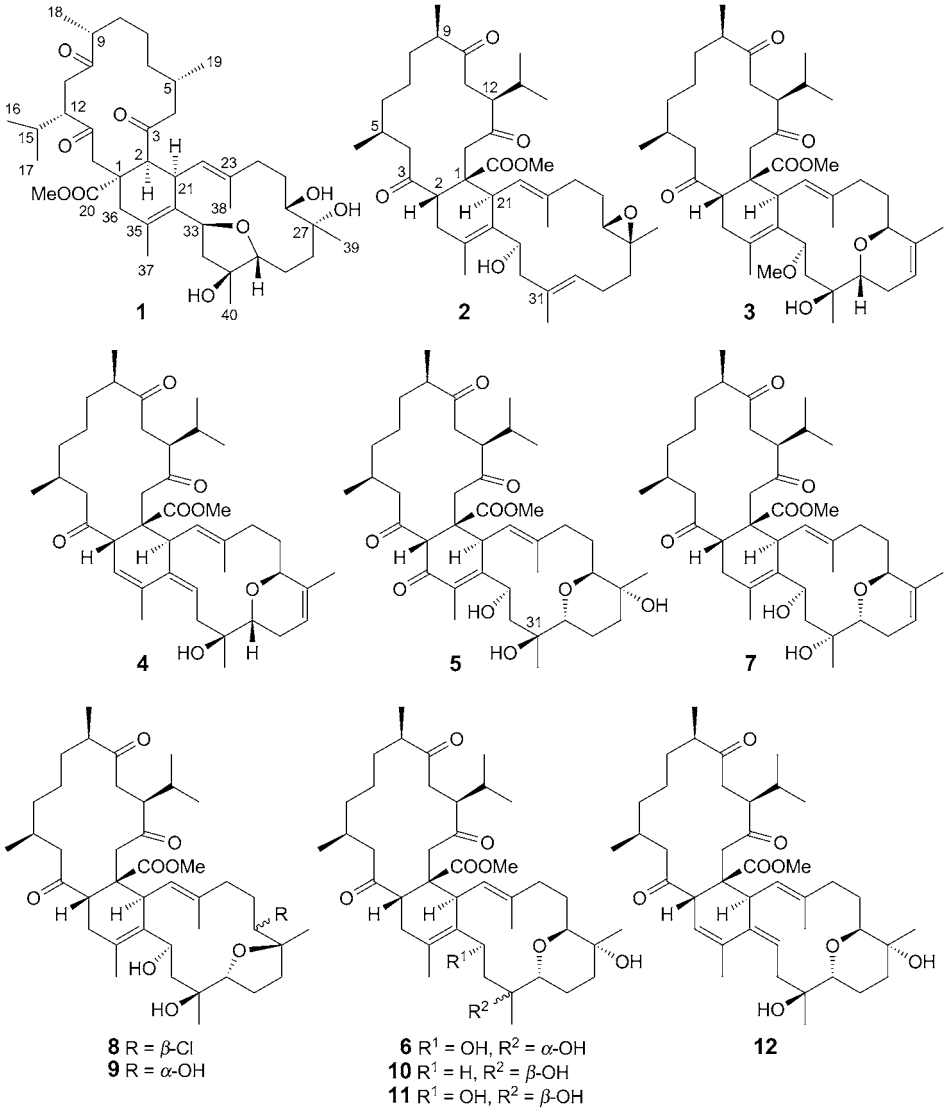


Fig. 1. *Structures of Isobiscembranoid* **1** *and Biscembranoids* **2**–**12**

istic of a biscembranoid-type tetraterpenoid [9]. The COSY correlation of H–C(21) ($\delta$(H) 3.27 ($dd, J = 10.5, 11.0$)) to H–C(22) ($\delta$(H) 4.56 ($d, J = 11.0$)) and H–C(2) ($\delta$(H) 4.22 ($d$, $J = 10.5$)), revealed **1** as an isobiscembranoid. Its NMR data exhibited the signal features closely related to those of lobophytones F and G, the isobiscembranoids from soft coral *Lobophytum pauciflorum* [9]. According to the 2D-NMR data, **1** shares the same substructure regarding rings *A* and *B* of lobophytone F. Concerning the ring *C*, 2D-NMR examination (COSY, HMQC, and HMBC) was conducted to establish a

Table 1. *$^1$H-NMR Data* (500 MHz; ($D_6$)DMSO) *for* **1**–**6**. $\delta$ in ppm, $J$ in Hz. Atom numbering as indicated in *Fig. 1*.

| H-Atom | **1** | **2** | **3** | **4** | **5** | **6** |
|---|---|---|---|---|---|---|
| H–C(2) | 4.22 (*d*, *J* = 10.5) | 3.91 (*dd*, *J* = 5.5,8.5) | 3.70 (*dd*, *J* = 8.5, 9.0) | 3.96 (*s*) | 4.47 (*s*) | 3.50 (*dd*, *J* = 5.0, 9.0) |
| $CH_2$(4) | 1.91–1.84 (*m*), 2.15–2.07 (*m*) | 3.02 (*dd*, *J* = 8.5, 20.0), 2.45 (*d*, *J* = 20.0) | 2.40–2.34 (*m*), 2.43–2.39 (*m*) | 3.06 (*dd*, *J* = 10.5, 20.5), 2.53 (*d*, *J* = 20.5) | 3.06–3.00 (*m*), 2.34–2.27 (*m*) | 3.07–3.01 (*m*), 2.37–2.30 (*m*) |
| H–C(5) | 1.93–1.87 (*m*) | 1.83–1.77 (*m*) | 1.75–1.67 (*m*) | 1.66–1.60 (*m*) | 1.72–1.65 (*m*) | 1.68–1.62 (*m*) |
| $CH_2$(6) | 1.88–1.80 (*m*), 2.09–1.99 (*m*) | 1.03–0.96 (*m*), 1.10–1.04 (*m*) | 1.06–0.98 (*m*), 1.10–1.04 (*m*) | 1.62–1.55 (*m*), 1.30–1.23 (*m*) | 0.90–0.85 (*m*), 1.02–0.97 (*m*) | 0.99–0.93 (*m*), 1.10–1.04 (*m*) |
| $CH_2$(7) | 0.85–0.78 (*m*), 1.10–1.03 (*m*) | 1.09–1.02 (*m*), 1.31–1.26 (*m*) | 2.01–1.93 (*m*), 1.30–1.23 (*m*) | 0.85–0.80 (*m*), 1.11–1.04 (*m*) | 1.78–1.71 (*m*), 1.30–1.24 (*m*) | 1.83–1.77 (*m*), 1.40–1.34 (*m*) |
| $CH_2$(8) | 0.55–0.49 (*m*), 1.25–1.19 (*m*) | 1.52–1.45 (*m*), 1.31–1.26 (*m*) | 1.38–1.31 (*m*), 1.55–1.47 (*m*) | 1.39–1.32 (*m*), 1.55–1.49 (*m*) | 1.47–1.40 (*m*), 1.36–1.29 (*m*) | 1.52–1.47 (*m*), 1.40–1.35 (*m*) |
| H–C(9) | 2.30–2.23 (*m*) | 2.44–2.38 (*m*) | 2.27–2.20 (*m*) | 2.27–2.21 (*m*) | 2.34–2.28 (*m*) | 2.32–2.28 (*m*) |
| $CH_2$(11) | 2.57 (*d*, *J* = 15.5), 2.72 (*dd*, *J* = 7.0, 15.5) | 2.23–2.17 (*m*), 1.95–1.89 (*m*) | 1.75–1.69 (*m*), 2.11–2.07 (*m*) | 1.90–1.84 (*m*), 2.87–2.80 (*m*) | 2.76–2.70 (*m*), 1.87–1.81 (*m*) | 2.80–2.75 (*m*), 1.90–1.82 (*m*) |
| H–C(12) | 2.67–2.58 (*m*) | 3.06–3.01 (*m*) | 2.85–2.78 (*m*) | 2.86–2.79 (*m*) | 2.87–2.80 (*m*) | 2.85–2.80 (*m*) |
| $CH_2$(14) | 3.17 (*d*, *J* = 19.5), 3.06 (*d*, *J* = 19.5) | 3.12 (*d*, *J* = 19.0), 3.18 (*d*, *J* = 19.0) | 2.75 (*d*, *J* = 18.0), 3.00 (*d*, *J* = 18.0) | 2.77 (*d*, *J* = 19.0), 2.79 (*d*, *J* = 19.0) | 2.82 (*d*, *J* = 19.0), 2.84 (*d*, *J* = 19.0) | 2.76 (*d*, *J* = 19.0), 2.78 (*d*, *J* = 19.0) |
| H–C(15) | 1.65–1.57 (*m*) | 2.20–2.15 (*m*) | 2.10–2.02 (*m*) | 2.27–2.20 (*m*) | 2.20–2.14 (*m*) | 2.31–2.27 (*m*) |
| $CH_3$(16) | 0.81 (*d*, *J* = 7.0) | 0.77 (*d*, *J* = 6.5) | 0.65(*d*, *J* = 6.7) | 0.63 (*d*, *J* = 6.5) | 0.89 (*d*, *J* = 6.7) | 0.95 (*d*, *J* = 6.7) |
| $CH_3$(17) | 0.78 (*d*, *J* = 7.0) | 0.96 (*d*, *J* = 6.5) | 0.91(*d*, *J* = 6.7) | 0.94 (*d*, *J* = 6.5) | 0.70 (*d*, *J* = 6.7) | 0.62 (*d*, *J* = 6.7) |
| $CH_3$(18) | 1.13 (*d*, *J* = 7.0) | 1.15 (*d*, *J* = 6.5) | 1.06 (*d*, *J* = 6.8) | 1.05 (*d*, *J* = 7.0) | 1.07 (*d*, *J* = 6.8) | 1.06 (*d*, *J* = 6.8) |
| $CH_3$(19) | 0.71 (*d*, *J* = 6.0) | 0.86 (*d*, *J* = 6.5) | 0.81(*d*, *J* = 6.8) | 0.82 (*d*, *J* = 6.5) | 0.81 (*d*, *J* = 6.8) | 0.81 (*d*, *J* = 6.8) |
| H–C(21) | 3.27 (*dd*, *J* = 10.5, 11.0) | 3.43 (*d*, *J* = 11.0) | 3.46 (*d*, *J* = 10.7) | 3.40 (*d*, *J* = 11.0) | 3.40 (*d*, *J* = 10.7) | 3.20 (*d*, *J* = 10.6) |
| H–C(22) | 4.56 (*d*, *J* = 11.0) | 5.02 (*d*, *J* = 11.0) | 4.90 (*d*, *J* = 10.7) | 4.68 (*d*, *J* = 11.0) | 4.89 (*d*, *J* = 10.7) | 4.81 (*d*, *J* = 10.6) |
| $CH_2$(24) | 1.90–1.88 (*m*), 2.05–1.99 (*m*) | 2.22–2.17 (*m*), 2.25–2.19 (*m*) | 1.75–1.69 (*m*) | 2.25–1.98 (*m*), 2.26–2.20 (*m*) | 1.67–1.60 (*m*), 2.50–2.42 (*m*) | 2.23–2.17 (*m*), 1.58–1.51 (*m*) |
| $CH_2$(25) | 1.19–1.12 (*m*), 1.65–1.59 (*m*) | 1.45–1.38 (*m*), 2.17–2.10 (*m*) | 0.93–0.87 (*m*), 1.76–1.70 (*m*) | 1.25–1.19 (*m*), 1.70–1.65 (*m*) | 1.74–1.68 (*m*), 1.72–1.65 (*m*) | 1.71–1.66 (*m*), 1.69–1.62 (*m*) |
| H–C(26) | 3.06 (br. *d*, *J* = 9.5) | 2.90 (*dd*, *J* = 5.0,7.5) | 3.84–3.78 (*m*) | 3.84 (br. *d*, *J* = 9.5) | 3.43–3.37 (*m*) | 3.11–3.05 (*m*) |
| $CH_2$(28)/ H–C(28) | 1.55–1.47 (*m*), 1.70–1.63 (*m*) | 0.97–0.89 (*m*), 2.00–1.93 (*m*) | 5.41–5.37 (*m*) | 5.46 (*dd*, *J* = 2.0, 2.0) | 1.66–1.60 (*m*), 1.80–1.73 (*m*) | 1.64–1.58 (*m*) |

*Table 1* (cont.)

| H-Atom | **1** | **2** | **3** | **4** | **5** | **6** |
|---|---|---|---|---|---|---|
| $CH_2$(29) | 1.20–1.12 (*m*), 1.50–1.40 (*m*) | 1.97–1.90 (*m*), 2.25–2.18 (*m*) | 1.75–1.70 (*m*), 1.95–1.88 (*m*) | 1.80–1.73 (*m*), 1.95–1.88 (*m*) | 1.65–1.60 (*m*), 1.25–1.19 (*m*) | 1.63–1.56 (*m*), 1.30–1.23 (*m*) |
| H–C(30) | 3.76 (*d*, *J* = 12.0) | 4.82 (*dd*, *J* = 7.3,7.5) | 3.38–3.30 (*m*) | 3.17 (*dd*, *J* = 4.0,11.0) | 3.20–3.14 (*m*) | 3.10–3.04 (*m*) |
| $CH_2$(32) | 2.02–1.96 (*m*), 1.80–1.74 (*m*) | 2.30 (*dd*, *J* = 2.0, 13.0), 2.35 (*dd*, *J* = 10.0, 13.0) | 1.31–1.27 (*m*), 1.88–1.81 (*m*) | 2.01 (br.*d*, *J* = 15.0), 2.50 (*dd*, *J* = 10.5, 15.0) | 1.40–1.33 (*m*), 1.89–1.82 (*m*) | 2.35–2.30 (*m*), 1.10–1.04 (*m*) |
| H–C(33) | 3.86 (*dd*, *J* = 8.5, 8.5) | 4.96 (*dd*, *J* = 2.0, 10.0) | 4.42 (*dd*, *J* = 6.5, 7.5) | 5.80 (br. *d*, *J* = 10.5) | 4.92 (*dd*, *J* = 9.5, 9.5) | 4.66 (br.*d*, *J* = 10.5) |
| $CH_2$(36)/ H–C(36) | 1.95 (*d*, *J* = 16.5), 2.22 (*d*, *J* = 16.5) | 2.30 (*dd*, *J* = 5.5, 14.0), 2.40 (*dd*, *J* = 8.5, 14.0) | 2.02–1.96 (*m*), 2.30–2.25 (*m*) | 5.08 (br. *s*) | | 2.25–2.20 (*m*), 2.05–1.98 (*m*) |
| Me(37) | 1.84 (*s*) | 1.70 (*s*) | 1.70 (*s*) | 1.79 (*s*) | 1.81 (*s*) | 1.72 (*s*) |
| Me(38) | 1.63 (*s*) | 1.69 (*s*) | 1.66 (*s*) | 1.77 (*s*) | 1.72 (*s*) | 1.53 (*s*) |
| Me(39) | 0.92 (*s*) | 1.27 (*s*) | 1.58 (*s*) | 1.54 (*s*) | 0.98 (*s*) | 0.94 (*s*) |
| Me(40) | 1.18 (*s*) | 1.62 (*s*) | 0.93 (*s*) | 1.05 (*s*) | 1.02 (*s*) | 0.88 (*s*) |
| MeO | 3.46 (*s*) | 3.52 (*s*) | 3.43 (*s*) | 3.46 (*s*) | 3.39 (*s*) | 3.39 (*s*) |
| MeO | | | 3.15 (*s*) | | | |

Table 2. *$^{13}$C-NMR Data* (125 MHz; ($D_6$)DMSO) *of* **1**–**6**. $\delta$ in ppm. Atom numbering as indicated in *Fig. 1*.

| C-Atom | **1** | **2** | **3** | **4** | **5** | **6** |
|---|---|---|---|---|---|---|
| 1 | 46.6 (*s*) | 50.0 (*s*) | 48.9 (*s*) | 49.5 (*s*) | 50.6 (*s*) | 49.8 (*s*) |
| 2 | 47.8 (*d*) | 44.8 (*d*) | 44.7 (*d*) | 48.1 (*d*) | 61.0 (*d*) | 43.8 (*d*) |
| 3 | 210.8 (*s*) | 213.7 (*s*) | 213.4 (*s*) | 212.9 (*s*) | 213.7 (*s*) | 213.8 (*s*) |
| 4 | 52.2 (*t*) | 52.9 (*t*) | 52.5 (*t*) | 53.8 (*t*) | 53.7 (*t*) | 54.2 (*t*) |
| 5 | 24.0 (*d*) | 27.1 (*d*) | 27.0 (*d*) | 27.3 (*d*) | 26.0 (*d*) | 27.5 (*d*) |
| 6 | 35.9 (*t*) | 37.3 (*t*) | 36.9 (*t*) | 37.7 (*t*) | 36.6 (*t*) | 37.7 (*t*) |
| 7 | 22.6 (*t*) | 25.7 (*t*) | 25.6 (*t*) | 25.1 (*t*) | 30.1 (*t*) | 30.7 (*t*) |
| 8 | 31.3 (*t*) | 34.2 (*t*) | 33.3 (*t*) | 34.3 (*t*) | 33.0 (*t*) | 34.2 (*t*) |
| 9 | 46.1 (*d*) | 47.7 (*d*) | 47.4 (*d*) | 48.3 (*d*) | 46.7 (*d*) | 47.9 (*d*) |
| 10 | 214.1 (*s*) | 213.5 (*s*) | 223.4 (*s*) | 212.9 (*s*) | 212.6 (*s*) | 213.6 (*s*) |
| 11 | 40.0 (*t*) | 30.9 (*t*) | 26.7 (*t*) | 30.8 (*t*) | 31.2 (*t*) | 30.7 (*t*) |
| 12 | 51.1 (*d*) | 50.9 (*d*) | 51.4 (*d*) | 51.0 (*t*) | 51.2 (*d*) | 51.6 (*d*) |
| 13 | 213.8 (*s*) | 210.6 (*s*) | 211.1 (*s*) | 209.8 (*s*) | 209.9 (*s*) | 210.2 (*s*) |
| 14 | 52.1 (*t*) | 48.1 (*t*) | 46.6 (*t*) | 45.8 (*t*) | 44.5 (*t*) | 45.8 (*t*) |
| 15 | 30.1 (*d*) | 28.9 (*d*) | 29.2 (*d*) | 28.8 (*d*) | 28.6 (*d*) | 28.8 (*d*) |
| 16 | 20.3 (*q*) | 17.7 (*q*) | 18.4 (*q*) | 17.7 (*q*) | 18.3 (*q*) | 21.6 (*q*) |
| 17 | 20.4 (*q*) | 21.2 (*q*) | 21.1 (*q*) | 21.5 (*q*) | 21.0 (*q*) | 17.5 (*q*) |
| 18 | 15.6 (*q*) | 17.5 (*q*) | 18.4 (*q*) | 17.7 (*q*) | 17.2 (*q*) | 17.5 (*q*) |
| 19 | 22.0 (*q*) | 21.9 (*q*) | 22.5 (*q*) | 22.9 (*q*) | 22.5 (*q*) | 23.0 (*q*) |
| 20 | 175.0 (*s*) | 174.8 (*s*) | 174.5 (*s*) | 174.2 (*s*) | 173.4 (*s*) | 174.8 (*s*) |
| 21 | 39.6 (*d*) | 42.8 (*d*) | 43.0 (*d*) | 46.7 (*d*) | 47.9 (*d*) | 43.7 (*d*) |
| 22 | 127.7 (*d*) | 123.1 (*d*) | 123.5 (*d*) | 122.5 (*d*) | 121.9 (*d*) | 125.2 (*d*) |
| 23 | 134.7 (*s*) | 133.5 (*s*) | 136.4 (*s*) | 138.1 (*s*) | 139.8 (*s*) | 137.0 (*s*) |
| 24 | 35.9 (*t*) | 34.2 (*t*) | 33.3 (*t*) | 37.8 (*t*) | 36.4 (*t*) | 38.2 (*t*) |
| 25 | 24.0 (*t*) | 26.0 (*t*) | 21.7 (*t*) | 28.8 (*t*) | 24.8 (*t*) | 25.8 (*t*) |
| 26 | 68.4 (*d*) | 62.0 (*d*) | 78.5 (*d*) | 79.3 (*d*) | 83.0 (*d*) | 79.1(*d*) |
| 27 | 73.1 (*s*) | 59.5 (*s*) | 134.9 (*s*) | 134.9 (*s*) | 68.9 (*s*) | 69.7 (*s*) |
| 28 | 36.9 (*t*) | 39.2 (*t*) | 120.1 (*d*) | 119.9 (*d*) | 33.7 (*t*) | 34.2 (*t*) |
| 29 | 20.4 (*t*) | 25.8 (*t*) | 33.1 (*t*) | 19.8 (*t*) | 25.6 (*t*) | 25.7 (*t*) |
| 30 | 91.9 (*d*) | 124.8 (*d*) | 68.4 (*d*) | 67.7 (*d*) | 73.0 (*d*) | 80.1(*d*) |
| 31 | 79.5 (*s*) | 131.6 (*s*) | 73.0 (*s*) | 73.0 (*s*) | 72.8 (*s*) | 73.8 (*s*) |
| 32 | 48.4 (*t*) | 44.2 (*t*) | 42.0 (*t*) | 37.7 (*t*) | 40.5 (*t*) | 42.6 (*t*) |
| 33 | 78.6 (*d*) | 67.1 (*d*) | 78.4 (*d*) | 124.9 (*d*) | 68.5 (*d*) | 63.9 (*d*) |
| 34 | 131.9 (*s*) | 131.4 (*s*) | 132.9 (*s*) | 130.7 (*s*) | 159.6 (*s*) | 133.5 (*s*) |
| 35 | 130.5 (*s*) | 131.2 (*s*) | 126.0 (*s*) | 135.7 (*s*) | 129.1 (*s*) | 126.4 (*s*) |
| 36 | 40.0 (*t*) | 33.0 (*t*) | 33.2 (*t*) | 123.6 (*d*) | 196.4 (*s*) | 32.7 (*t*) |
| 37 | 20.9 (*q*) | 18.0 (*q*) | 19.2 (*q*) | 19.4 (*q*) | 11.8 (*q*) | 19.1 (*q*) |
| 38 | 15.2 (*q*) | 18.0 (*q*) | 19.6 (*q*) | 20.2 (*q*) | 19.2 (*q*) | 15.4 (*q*) |
| 39 | 23.5 (*q*) | 16.0 (*q*) | 20.4 (*q*) | 20.5 (*q*) | 26.3 (*q*) | 22.7 (*q*) |
| 40 | 26.0 (*q*) | 15.9 (*q*) | 25.3 (*q*) | 17.7 (*q*) | 24.8 (*q*) | 23.0 (*q*) |
| MeO | 51.9 (*q*) | 51.2 (*q*) | 51.3 (*q*) | 51.0 (*q*) | 51.2 (*q*) | 51.1 (*q*) |
| MeO | | | 55.8 (*q*) | | | |

14-membered ring in which a C(22)=C(23) bond and an ether bridge between C(30) and C(33) were confirmed. In addition, the presence of two OH-bearing C-atoms, *i.e.*, C(26) ($\delta$(C) 68.4) and C(27) ($\delta$(C) 73.1), to replace the epoxy C-atoms of lobophytone F was indicated by the chemical-shift difference in association with the molecular

formula of **1** containing one $H_2O$ unit more than the latter. Thus, the gross structure of **1** was assumed to be a 26,27-dihydroxylated lobophytone F. The NOE correlations between H–C(21) and H–C(2), and from Me(33) to H–C(38) and a weak correlation to Me(40), as observed in lobophytone F, allowed assignment of $\alpha$-orientation of H–C(21), H–C(2), H–C(33), and Me(40). In addition, the NOE correlations from H–C(26) to Me(38) and H–C(33), and from H–C(30) to Me(37) and Me(39), further indicated $\alpha$-orientation of H–C(26), whereas H–C(30) and Me(39) were $\beta$-oriented. The absolute configuration of C(26) was determined *via Mosher* method. Analyses of the chemical-shift differences ($\Delta\delta(RS) = \delta(R) - \delta(S)$) of the 2-methoxy-2-phenyl-2-(trifluoromethyl)acetate (MTPA) diastereoisomers (*Fig. 2*) disclosed (26*S*)-configuration. Thus, the configurations of the remaining stereogenic centers in ring *C* are assumed as (2*S*,21*R*,27*R*,31*R*,32*S*,34*S*).

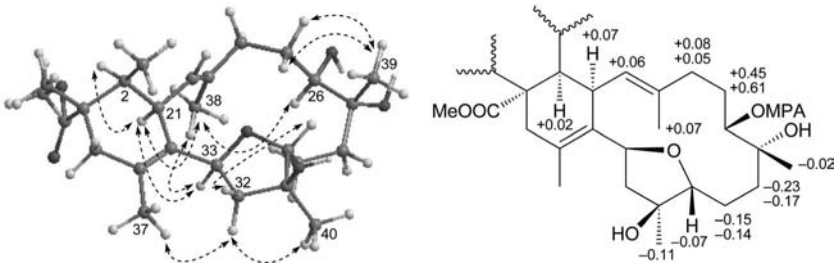


Fig. 2. *Key NOE Correlations and* $\Delta\delta$(RS) *Values of* **1**

The molecular formula of sarcophytolide H (**2**; $C_{41}H_{62}O_7$), determined on the basis of the HR-ESI-MS (*m/z* 689.4388 $[M + Na]^+$) and NMR data, was the same as that of lobophytone S [6]. Comparison of the NMR data disclosed that both compounds have the same partial structure regarding rings *A* and *B*. The NMR data for ring *C* of both compounds were quite similar, indicating the presence of a 14-membered carbocyclic ring bearing two C=C bonds, an epoxy group, and a hydroxylated C-atom. The H-atom H–C(33) ($\delta$(H) 4.96 (*dd*, $J = 2.0, 10.0$)) showed HMBCs to C(21) ($\delta$(C) 42.8), C(31) ($\delta$(C) 131.6), and C(35) ($\delta$(C) 131.2) and COSY correlation with $CH_2$(32) ($\delta$(H) 2.30, 2.35) evidenced a C(30)=C(31) bond, while C(33) ($\delta$(C) 67.1) was hydroxylated. The second C=C bond was positioned between C(22) and C(23) on the basis of the COSY relationship between H–C(21) ($\delta$(H) 3.43 (*d*, $J = 11.0$)) and the olefinic H-atom H–C(22) ($\delta$(H) 5.02 (*d*, $J = 11.0$)) in addition to their HMBC interactions. Additional HMBC interaction from Me(39) ($\delta$(H) 1.27 (*s*)) to the epoxy C-atoms C(26) ($\delta$(C) 62.0) and C(27) ($\delta$(C) 59.5) in association with the COSY correlations between H–C(26) ($\delta$(H) 2.90 (*dd*, $J = 5.0, 7.5$)) and $CH_2$(25) ($\delta$(H) 1.45 – 1.38, 2.17 – 2.10), and between $CH_2$(25) and $CH_2$(24) ($\delta$(H) 2.22 – 2.17, 2.25 – 2.19) allowed us to locate an epoxy group between C(26) and C(27). Thus, the structure of **2** differed from that of lobophytone S in the positions of the epoxy group and a C=C bond. The relative configurations of the stereogenic centers in **2** were determined on the basis of NOE relationships and *J* values. The NOE relationship between H–C(2) ($\delta$(H) 3.91) and MeO was attributed to *cis*-fusion of rings *A* and *B*. The exclusive $\beta$-face of the methyl

ester group, as found in all known biscembranoids, led to the biogenetical assignment of the methyl ester at C(1) to be $\beta$-oriented. The obvious NOE correlations between H–C(22) ($\delta$(H) 5.02), and H–C(2) and H–C(26), and between H–C(21) ($\delta$(H) 3.43) and Me(38) ($\delta$(H) 1.69) revealed H–C(26) to be $\beta$-oriented, whereas H–C(21) was $\alpha$-oriented. In addition, the NOE relationship between H–C(26) and $H_a$–C(28) ($\delta$(H) 0.97 – 0.89) indicated a *trans* geometry of the epoxy group. The $\beta$-orientation of H–C(33) was evident from the NOE correlation between H–C(33) and H–C(22). In addition, the (*E*)-geometries of the C(22)=C(23) and C(30)=C(31) bonds were determined *via* the additional NOEs Me(38)/H–C(21) and Me(40)/$CH_2$(29) together with the $^{13}$C-NMR data of the olefinic Me groups.

The molecular formula of sarcophytolide I (**3**) was determined as $C_{42}H_{64}O_8$ based on its HR-ESI-MS (*m/z* 697.4677 $[M+H]^+$) data. Its $^1$H- and $^{13}$C-NMR data were mostly identical to those of lobophytone H [5], except for the presence of a MeO group ($\delta$(C) 55.8, $\delta$(H) 3.15). The HMBC relationship of MeO H-atoms with C(33) ($\delta$(C) 78.4, CH) enabled us to locate the MeO group at C(33). The similar NOE relationships for **3** and lobophytone H, such as the interactions between H–C(2), and ester Me H-atoms and H–C(22), and between H–C(21) and Me(38) indicated the same geometries of ring *C* and the spatial fusion of rings *A* and *B*. Thus, the NOE interactions between H–C(22), and H–C(33) ($\delta$(H) 4.42 (*dd*, $J = 6.5, 7.5$)) and H–C(30) ($\delta$(H) 3.38 – 3.30) indicated $\beta$-orientation of H–C(33) and H–C(30), while the configurations of the remaining stereogenic centers in **3** were the same as those of lobophytone H based on their similar NMR and NOE data.

The HR-ESI-MS data of sarcophytolide J (**4**) provided the molecular formula $C_{41}H_{60}O_7$ (*m/z* 665.4427 ($[M+H]^+$), 687.4231 ($[M+Na]^+$)), implying twelve degrees of unsaturation. Analysis of 2D-NMR (COSY, HMQC, and HMBC) data revealed that the structure of **4** was closely related to methyl tortuoate A [10], except for the presence of an additional C=C bond in ring *C*. The location of a C=C bond between C(27) and C(28) was determined on the basis of the HMBC relationships between Me(39) ($\delta$(H) 1.54 (*s*)), and C(27) ($\delta$(C) 134.9) and C(28) ($\delta$(C) 119.9), together with the COSY correlations. The HMBC relationship between H–C(30) ($\delta$(H) 3.17) and C(26) ($\delta$(C) 79.3) revealed the presence of an ether bridge between C(26) and C(30). The NOE interactions between H–C(22) and H–C(2), and between H–C(21) ($\delta$(H) 3.40 (*d*, $J = 11.0$)) and Me(38) were indicative of $H_\beta$–C(2) and $H_\alpha$–C(21). The (22*E*)-geometry was determined from the NOE relationship between H–C(22) and $CH_2$(24), whereas the (27*Z*)- and (33*Z*)-geometries were evident from the NOESY cross-peaks H–C(33)/H–C(21), H–C(32)/Me(37), and H–C(28)/Me(39). Moreover, the NOE correlations between H–C(26), Me(38), and OH–C(31), and between H–C(30) and Me(40) indicated $H_\beta$–C(30) and $H_\alpha$–C(26), while HO–C(31) was $\alpha$-oriented. Thus, compound **4** was determined as a 27-dehydrated analog of methyl tortuoate A.

The molecular formula of sarcophytolide K (**5**) was determined as $C_{41}H_{62}O_{10}$ based on the HR-ESI-MS (*m/z* 737.4235 ($[M+Na]^+$)) data. A comparison of the NMR data indicated the structure of sarcophytolide K (**5**) to be closely related to that of lobophytone U [7]. The difference was found only in ring *B*, where compound **5** had a C(36)=O replacing a $CH_2$ group of the known analog. This assignment was confirmed with the HMBC interactions between Me(37), and C(34) ($\delta$(C) 159.6), C(35) ($\delta$(C) 129.1), and C(36) ($\delta$(C) 196.4), in association with the molecular weight of **5** with

14 amu higher than that of lobophytone U. The configurations of the stereogenic centers of **5** were determined to be the same as those of lobophytone U based on closely similar NMR and NOE data.

The molecular formula of sarcophytolide L (**6**) was determined as $C_{41}H_{64}O_9$ on the basis of HR-ESI-MS (*m/z* 723.4464 ($[M+Na]^+$)) data. Analysis of 1D- and 2D-NMR (COSY, HMQC, and HMBC) data indicated that compound **6** had the same gross structure as lobophytone U [7]. The distinction was due to the signal of C(30) ($\delta$(C) 80.1) in **6** that was significantly shifted downfield in comparison with the corresponding signal of the latter ($\delta$(C) 74.9 (C(30))), indicating that **6** was a stereoisomer. Examinations of NOE interactions revealed that Me(40) ($\delta$(H) 0.88 (*s*)) correlated to H–C(22) ($\delta$(H) 4.81 (*d*)), H–C(33) ($\delta$(H) 4.66 (br. *d*)), and H–C(26) ($\delta$(H) 3.11–3.05 (*m*)), indicating $\beta$-orientation for Me(40), whereas the remaining NOE interactions were the same as those of lobophytone U. Thus, the structure of **6** was determined as the C(31)-epimer of lobophytone U. The downfield shifted C(30) signal was induced by the gauche effect of the equatorial HO–C(31).

Based on the comparison of the spectroscopic data with those reported in literature, six known biscembranoids were identified as lobophytones H, Q, K, W, U (**7**–**11**, resp.) [5–7], and methyl sartortuoate (**12**) [10][11].

All compounds showed weak cytotoxic activities against a panel of tumor cell lines including human colon carcinoma HCT-8, human hepatoma Bel7402, human gastric carcinoma BGC823, human lung adenocarcinoma A549, and human ovarian carcinoma A2780 with $IC_{50}$ values $>10$ μM.

**Discussion.** – It is noted that most known biscembranoids display the same partial structure in the left part of cembranoid-dienophile, while the variation mainly occurs in ring *C*, followed by oxidation and ring rearrangement. The co-occurrence of isobiscembranoid and biscembranoids in the specimen was recognized in the genus *Sarcophyton* for the first time. Methyl tetrahydrosarxoate is assumed as a dienophile precursor reacting with a diene to form biscembranoids and isobiscembranoids *via Diels–Alder* condensation. The finding that rich analogs and high contents of biscembranoids in comparison with those of isobiscembranoids implied the formation of biscembranoids to be a favored. The weak cytotoxicities of biscembranoids indicate that they rather play a chemoecological role. Indeed, our previous work revealed that the weakly cytotoxic biscembranoids possess antifouling activities [5–7].

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## Experimental Part

*General.* Low-pressure column chromatography (CC): silica gel ($SiO_2$; 160–200 and 200–300 mesh). TLC: $GF_{254}$ silica gel (*Qingdao Marine Chemistry Co. Ltd.*). Optical rotations: *Perkin-Elmer 243B* polarimeter. IR Spectra: *Thermo Nicolet Nexus 470* FTIR spectrometer, in $cm^{-1}$. $^1H$-, $^{13}C$-, and 2D-NMR spectra: *Avance-500 FT* 500 MHz NMR spectrometer; TMS as an internal standard; $\delta$ values in ppm, and *J* values in Hz. HR-ESI-MS: *Bruker APEX IV* instrument.

*Animal Material.* The soft coral *Sarcophyton elegans* was collected from Xidao Island, Hainan, P. R. China, in 2002, and kept frozen until extraction. The specimen was identified by Dr. *Leen van Ofwegen*

(National Museum of National History, Naturalis). The soft coral (HSE-17) was deposited with the State Key Laboratory of Natural and Biomimetic Drugs, Peking University, P. R. China.

*Extraction and Isolation.* The frozen soft coral *Sarcophyton elegans* (3.5 kg, wet weight) was homogenized and was extracted with EtOH (2 × 3 h). The concentrated extract was desalted through dissolving in MeOH to yield a residue (100 g). This residue was defatted by partitioning between $H_2O$ and petroleum ether (PE), and then the $H_2O$ fraction was extracted with AcOEt. The AcOEt fraction (7.4 g) was subjected to CC ($SiO_2$; gradient of PE/acetone) to give eight subfractions, *SF1* – *SF8*). *SF3* (1.0 g) was subjected to CC ($SiO_2$; PE/AcOEt 5 : 1) to yield **2** (5.0 mg) and **6** (5.0 mg). As described for *SF3*, **5** (3.6 mg), **1** (3.0 mg), **2** (7.1 mg), **3** (4.0 mg), and **4** (3.3 mg) were isolated from *SF4* (560 mg) by CC ($SiO_2$; PE/$CH_2Cl_2$/AcOEt 5 : 5 : 1). *SF5* (320 mg) was separated by semiprep. HPLC ($C_{18}$ (5 μm); MeOH/$H_2O$ 70 : 30) to afford **7** (11.5 mg), **12** (8.9 mg), **9** (18.3 mg), **8** (5.6 mg), **11** (7.8 mg), and **10** (3.5 mg).

*Bioassays.* The 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2*H*-tetrazolium bromide (MTT) assay was used for evaluation *in vitro* cytotoxicity to HCT-8, Bel-7402, BGC-823, A549, and A2780 tumor cell lines.

*Sarcophytolide G* (= *Methyl (1*E,*5*S,*6*R,*9*R,*10*S,*12*S,*14a*R,*17*S,*20*R,*24*S,*26a*S,*26b*R*)-4,5,6,7,8,9,10,11, 12,14,15,16,17,18,19,20,21,22,23,24,25,26,26a,26b-Tetracosahydro-5,6,10-trihydroxy-2,6,10,13,20,24-hexamethyl-16,19,26-trioxo-17-(propan-2-yl)-9,12-epoxybenzo[1,2*-a *:3,4*-a′*]di[14]annulene-14a(3*H*)-carboxylate*; **1**). Colorless, amorphous. $[\alpha]_D^{25} = +68.6$ ($c = 0.7$, $CHCl_3$). IR (KBr): 3413, 2924, 1704, 1427, 1157, 1068. $^1$H- and $^{13}$C-NMR: *Tables 1* and *2*, resp. HR-ESI-MS: 723.4442 ($[M+Na]^+$, $C_{41}H_{64}NaO_9^+$; calc. 723.4440).

*Sarcophytolide H* (= *Methyl (1a*S,*4*E,*7*R,*9a*S,*12*S,*16*R,*19*S,*21a*S,*21b*S,*22*E,*25a*S*)-2,3,6,7,9,9a,10,11,12, 13,14,15,16,17,18,19,20,21,21b,24,25,25a-Docosahydro-7-hydroxy-1a,5,8,12,16,23-hexamethyl-10,17,20-trioxo-19-(propan-2-yl)cyclotetradeca[3′,4′]benzo[1′,2′:9,10]cyclotetradeca[1,2-*b*]oxirene-21a(1a*H*)-carboxylate*; **2**). Colorless, amorphous. $[\alpha]_D^{25} = +176.4$ ($c = 1.1$, $CHCl_3$). IR (KBr): 3447, 2929, 1741, 1708, 1458, 1205, 1067. $^1$H- and $^{13}$C-NMR: *Tables 1* and *2*, resp. HR-ESI-MS: 689.4388 ($[M+Na]^+$, $C_{41}H_{62}NaO_7^+$; calc. 689.4387).

*Sarcophytolide I* (= *Methyl (1*E,*5*S,*9*R,*10*S,*12*R,*14a*S,*17*S,*21*R,*24*S,*26a*S,*26b*S*)-3,5,8,9,10,11,12,14,14a, 15,16,17,18,19,20,21,22,23,24,25,26,26b-Docosahydro-10-hydroxy-12-methoxy-2,6,10,13,17,21-hexamethyl-15,22,25-trioxo-24-(propan-2-yl)-5,9-epoxybenzo[1,2*-a *:3,4*-a′*]di[14]annulene-26a(4*H*)-carboxylate*; **3**). Colorless, amorphous. $[\alpha]_D^{25} = +48.0$ ($c = 1.2$, $CHCl_3$). IR (KBr): 3443, 2960, 2920, 1739, 1710, 1632, 1462, 1021. $^1$H- and $^{13}$C-NMR: *Tables 1* and *2*, resp. HR-ESI-MS: 697.4677 ($[M+H]^+$, $C_{42}H_{65}O_8^+$; calc. 697.4679).

*Sarcophytolide J* (= *Methyl (1*E,*5*S,*9*R,*10*S,*12*Z,*14a*S,*17*S,*21*R,*24*S,*26a*S,*26b*S*)-3,5,8,9,10,11,14a,15,16, 17,18,19,20,21,22,23,24,25,26,26b-Icosahydro-10-hydroxy-2,6,10,13,17,21-hexamethyl-15,22,25-trioxo-24-(propan-2-yl)-5,9-epoxybenzo[1,2*-a *:3,4*-a′*]di[14]annulene-26a(4*H*)-carboxylate*; **4**). Colorless, amorphous. $[\alpha]_D^{25} = +62.3$ ($c = 1.2$, $CHCl_3$). IR (KBr): 3419, 2923, 1704, 1458, 1167. $^1$H- and $^{13}$C-NMR: *Tables 1* and *2*, resp. HR-ESI-MS: 687.4231 ($[M+Na]^+$, $C_{41}H_{60}NaO_7^+$; calc. 687.4237).

*Sarcophytolide K* (= *Methyl (1*E,*5*S,*6*R,*9*R,*10*S,*12*R,*14a*S,*17*S,*21*R,*24*S,*26a*S,*26b*S*)-3,5,6,7,8,9,10,11, 12,14,14a,15,16,17,18,19,20,21,22,23,24,25,26,26b-Tetracosahydro-6,10,12-trihydroxy-2,6,10,13,17,21-hexamethyl-14,15,22,25-tetraoxo-24-(propan-2-yl)-5,9-epoxybenzo[1,2*-a *:3,4*-a′*]di[14]annulene-26a(4*H*)-carboxylate*; **5**). Colorless, amorphous. $[\alpha]_D^{25} = +8.7$ ($c = 4.0$, $CHCl_3$). IR (KBr): 3431, 2954, 2929, 1731, 1711, 1665, 1458, 1372, 1210, 1069. $^1$H- and $^{13}$C-NMR: *Tables 1* and *2*, resp. HR-ESI-MS: 737.4235 ($[M+Na]^+$, $C_{41}H_{62}NaO_{10}^+$; calc. 737.4235).

*Sarcophytolide L* (= *Methyl (1*E,*5*S,*6*R,*9*R,*10*R,*12*R,*14a*S,*17*S,*21*R,*24*S,*26a*S,*26b*S*)-3,5,6,7,8,9,10,11, 12,14,14a,15,16,17,18,19,20,21,22,23,24,25,26,26b-Tetracosahydro-6,10,12-trihydroxy-2,6,10,13,17,21-hexamethyl-15,22,25-trioxo-24-(propan-2-yl)-5,9-epoxybenzo[1,2*-a *:3,4*-a′*]di[14]annulene-26a(4*H*)-carboxylate*; **6**). Colorless, amorphous. $[\alpha]_D^{25} = +22.9$ ($c = 2.8$, $CHCl_3$). IR (KBr): 3423, 2954, 2926, 1739, 1456, 1253, 1203, 1069. $^1$H- and $^{13}$C-NMR: *Tables 1* and *2*, resp. HR-ESI-MS: 723.4464 ($[M+Na]^+$, $C_{41}H_{64}NaO_9^+$; calc. 723.4442).

Mosher *Reaction.* Compound **1** (0.01 mmol) together with DMAP (4-(dimethylamino)pyridine, 0.01 mmol) and DCC (dicyclohexylcarbodiimide, 0.01 mmol) were dissolved in $CH_2Cl_2$ (2 ml) at 0°, and then (*R*)- or (*S*)-2-methoxy-2-phenyl-2-(trifluoromethyl)acetic acid (MTPA) (0.01 mmol) was added to the soln. After stirring at r.t. for 24 h, the mixture was evaporated under reduced pressure to obtain a

residue, which was separated by a reversed phase (RP) semiprep. HPLC (95% MeCN/$H_2O$) to yield (*R*)-MTPA or (*S*)-MTPA ester, resp.

## REFERENCES

[1] A. Bishara, A. Rudi, Y. Benayahu, Y. Kashman, *J. Nat. Prod.* **2007**, *70*, 1951.
[2] M. O. Ishitsuka, T. Kusumi, H. Kakisawa, *Tetrahedron Lett.* **1991**, *32*, 2917.
[3] R. Jia, Y.-W. Guo, P. Chen, Y.-M. Yang, E. Mollo, M. Gavagnin, G. Cimino, *J. Nat. Prod.* **2007**, *70*, 1158.
[4] R. Jia, Y.-W. Guo, E. Mollo, M. Gavagnin, G. Cimino, *Helv. Chim. Acta* **2008**, *91*, 2069.
[5] P. Yan, Z. Deng, L. van Ofwegen, P. Proksch, W. Lin, *Chem. Pharm. Bull.* **2010**, *58*, 1591.
[6] P. Yan, Z. Deng, L. van Ofwegen, P. Proksch, W. Lin, *Marine Drugs* **2010**, *8*, 2837.
[7] P. Yan, Z. Deng, L. van Ofwegen, P. Proksch, W. Lin, *Chem. Biodiversity* **2011**, *8*, 1724.
[8] M. Koh, T. Iwanaga, M. Hatanaka, A. Nakano, K. Morihara, K. Takemura, *Biosci., Biotechnol., Biochem.* **2000**, *64*, 858.
[9] P. Yan, Y. Lv, L. van Ofwegen, P. Proksch, W. Lin, *Org. Lett.* **2010**, *12*, 2484.
[10] L.-M. Zeng, W.-J. Lan, J.-Y. Su, G.-W. Zhang, X.-L. Feng, Y.-J. Liang, X.-P. Yang, *J. Nat. Prod.* **2004**, *67*, 1915.
[11] W.-J. Lan, J.-Y. Su, L.-M. Zeng, *Chin. J. Org. Chem.* **2005**, *25*, 1465.

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