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# Sesquiterpene phenols from marine sponge *Smenospongia cerebriformis*

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**Abstract**

Using various chromatography methods, four sesquiterpene phenols, dictyoceratin C (**1**), polyfibrospongol A (**2**), polyfibrospongol B (**3**), and 19-hydroxy-polyfibrospongol B (**4**) were isolated from the methanol extract of the Vietnamese marine sponge *Smenospongia cerebriformis*. Their structures were determined by 1D-, 2D-NMR spectra, HR-ESI-MS and in comparison with those reported in the literature.

**Keywords.** *Smenospongia cerebriformis*, sponge, sesquiterpene phenol.

## 1. INTRODUCTION

Sesquiterpenes were found as a main components of the genus *Smenospongia*. These compounds represent a prominent class of biologically active metabolites. Several chemical investigations have been focused on the marine sponge *Smenospongia cerebriformis*. The components of this genus were identified as sesquiterpenes [1, 2], indole alkaloids [2-4] and phenyl alkene [5]. They exhibited some biological activities such as anti-human cancer [1, 5] and anti-depressant [2]. We reported herein the isolation and structure elucidation of four sesquiterpene phenols from the Vietnamese marine sponge *Smenospongia cerebriformis*.

## 2. MATERIALS AND METHODS

### 2.1. Sponge materials

The sponge *Smenospongia cerebriformis* (Duchassaing & Michelotti, 1864) was collected in Vinhmoc, Quangtri in August 2015 and identified by Assoc. Prof. Do Cong Thung, Institute of Marine Environment and Resources, VAST. A voucher specimen (HM08.2015-2) was deposited at the Institute of Marine Biochemistry, VAST.

### 2.2. General experimental procedures

The $^{1}$H-NMR (500 MHz) and $^{13}$C-NMR (125 MHz) spectra were recorded on a Bruker AM500 FT-NMR spectrometer and TMS was used as an internal standard. Column chromatography was performed using a silica gel (Kieselgel 60, 70-230 mesh and 230-400 mesh, Merck, Whitehouse Station, NJ) or RP-18 resins (30-50 μm, Fuji silysia Chemical Ltd.), and thin layer chromatography (TLC) using pre-coated silica-gel 60 $F_{254}$ (0.25 mm, Merck) and RP-18 $F_{254S}$ plates (0.25 mm, Merck).

### 2.3. Extraction and isolation

Frozen dried samples of sponge *Smenospongia cerebriformis* (15.0 kg) were well grinded and sonicated with hot MeOH three times and then concentrated under reduced pressure to give MeOH extract (SP, 360g). This extract was suspended in water and then partitioned with $CH_2Cl_2$ to give the $CH_2Cl_2$ (SPD, 102 g) and water (SPW, 250 g) extracts after removal of the solvents *in vacuo*. Fraction SPD (100 g) was subjected to silica gel column chromatography and eluted with an *n*-hexane – acetone stepwise gradient to give five fractions SPD1 (39.0 g), SPD2 (5.8 g), SPD3 (12.9 g), SPD4 (20.0 g), and SPD5 (2.8 g). SPD2 was chromatographed on a RP-18 column eluting with acetone – water (1.5:1, v/v) to give four smaller fractions, SPD2A-D. Fraction SPD2D was applied to a silica gel column eluting with *n*-hexane-acetone (7:1, v/v) to give **4** (ASP12, 22 mg). SPD3 was chromatographed on a RP-18 column using

*n*-hexane-ethyl acetate (3:1, v/v) as eluent to give five smaller fractions, SPD3A (2.4 g), SPD3B (1.5 g), SPD3C (3.2 g), SPD3D (2.2 g) and SPD3E (1.8 g). Furthermore, fraction SPD3A (2.4 g) was chromatographed on a silica gel column and eluted with *n*-hexane – acetone (7:1, v/v) to yield **3** (ASP6, 22.0 mg). Fraction SPD3E (1.8 g) was chromatographed on a RP-18 column eluting with acetone -water (1:1, v/v) to yield two fractions SPD3E1-2. Compound **1** (ASP26, 33.0 mg) was obtained by using a RP-18 column chromatography with acetone-water (1:1, v/v) from fraction SPD3E2. Fraction SPD5 (2.8 g) was chromatographed on a silica gel column and eluted with dichloromethane-ethyl acetate (10:1, v/v) to yield five fractions SPD5A-E. Fraction SPD5B was chromatographed on a RP-18 column and eluted with acetone-water (2.0:1, v/v) give two fractions SPD5B1-2. Finally, compound **2** (ASP21, 22 mg) was obtained from the SPD5B2 fraction using a silica gel column and eluted with dichloromethane-ethyl acetate (7:1, v/v).

**Dictyoceratin C (1):** White amorphous powder; $[\alpha]_D^{25}$: +20.5 (*c* = 0.1, in $CDCl_3$); $^1$H- and $^{13}$C-NMR ($CDCl_3$), see table 1.

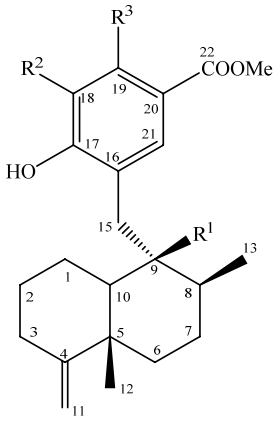
**Polyfibrospongol A (2):** White amorphous powder; $[\alpha]_D^{25}$: +34.6 (*c* = 0.1, in $CDCl_3$); $^1$H- and $^{13}$C-NMR ($CDCl_3$), see table 1.

**Polyfibrospongol B (3):** White amorphous powder; $[\alpha]_D^{25}$: +21.2 (*c* = 0.1, in $CDCl_3$); $^1$H- and $^{13}$C-NMR ($CDCl_3$), see table 2.

**19-Hydroxy-polyfibrospongol B (4):** White amorphous powder; $[\alpha]_D^{25}$: +25.7 (*c* = 0.1, in $CDCl_3$); $^1$H- and $^{13}$C-NMR ($CDCl_3$), see table 2.

## 3. RESULTS AND DISCUSSION

Compound **1** was isolated as a white amorphous powder. $^1$H NMR and HSQC spectroscopic analysis of **1** showed the presence of three methyl groups comprising two tertiary methyl groups ($\delta_H$ 0.88 and 1.06; each 3H, s) and a secondary methyl group at $\delta_H$ 1.02 (d, *J* = 6.5 Hz), exocyclic methylene signals ($\delta_H$ 4.37 and 4.41; each 1H, br s), and two benzylic methylene protons at $\delta_H$ 2.63 and 2.67 (each 1H, d, *J* = 14.0 Hz). In addition, the $^1$H-NMR spectrum of **1** showed the presence of a 1,2,4-trisubstituted benzene ring [$\delta_H$ 6.75 (1H, d, *J* = 8.0 Hz), 7.75 (1H, d, *J* = 8.0 Hz), 7.76 (1H, s)], a methoxy group at $\delta_H$ 3.87, and a singlet signal of hydroxyl group at $\delta_H$ 5.94. The $^{13}$C NMR of **1** revealed signals of 23




| | $R^1$ | $R^2$ | $R^3$ |
|---|---|---|---|
| **1** | $CH_3$ | H | H |
| **2** | $CH_3$ | OMe | H |
| **3** | $CH_2OH$ | OMe | H |
| **4** | $CH_2OH$ | OMe | OH |

*Figure 1:* Chemical structures of compounds **1-4**

carbons which were classified by DEPT as seven non-protonated carbons, five methines, seven methylenes, and four methyl carbons. Of these, carbon signals at $\delta_C$ 167.4 and 51.9 were assigned for a carboxyl functional group and a methoxy group, respectively. The HMBC correlations between proton H-11 ($\delta_H$ 4.37, 4.41) and carbons C-3 ($\delta_C$ 33.0)/C-4 ($\delta_C$ 160.0)/C-5 ($\delta_C$ 40.2) suggested an exocyclic olefinic methylene forming at C-11/C-4. Methyl proton H-12 ($\delta_H$ 1.06) was observed to have HMBC correlations with carbons C-4/C-5/C-6 ($\delta_C$ 36.6)/C-10 ($\delta_C$ 48.1), indicating the location of a methyl group at C-5. The HMBC correlations between proton H-14 ($\delta_H$ 0.88) and carbons C-8 ($\delta_C$ 36.4)/C-9 ($\delta_C$ 42.1)/C-10/C-15 ($\delta_C$ 37.1) confirmed the methyl group at C-9. In addition, the secondary methyl group located at C-8 which was indicated by HMBC correlations between H-13 ($\delta_H$ 1.02) and carbons C-7 ($\delta_C$ 27.7)/C-8/C-9. Continuously, HBMC correlations between methylene protons H-15 ($\delta_H$ 2.65, 2.70) and carbons C-16 ($\delta_C$ 125.2)/C-17 ($\delta_C$ 159.2)/C-20 ($\delta_C$ 121.7) suggested the phenol moiety binding with the sesquiterpene skeleton at C-15. The presence of a hydroxy group at C-17 was confirmed by the HMBC correlations between hydroxy proton ($\delta_H$ 5.94) and carbons C-16/C-17/C-18 ($\delta_C$ 115.3) and deshielded carbon signal of C-17 ($\delta_C$ 159.2). The HMBC correlations between protons H-19 ($\delta_H$ 7.75), H-21 ($\delta_H$ 7.76) and C-20 ($\delta_C$ 121.7) and carbonyl carbon ($\delta_C$ 167.4) as well as between methoxy proton and carbonyl carbon ($\delta_C$ 167.4) confirmed that the -$COOCH_3$ group linked at C-20. Consequently, structure of **1** was identified as dictyoceratin C, a sesquiterpene phenol previously isolated from the sponge *Spongia sp.* [6]. Its $^1$H and $^{13}$C NMR data133.7)/C-19 ($\delta_C$ 153.0)/C-20 ($\delta_C$ 105.3), and of were identical with those reported in the literature (table 1) and found to match well [6].

*Table 1:* $^{1}$H- and $^{13}$C-NMR data for **1-2** and reference compounds

| C | **1** | | | **2** | | |
|---|---|---|---|---|---|---|
| | $\delta_C^{\#,a}$ | $\delta_C^{a,b}$ | $\delta_H^{a,c}$ (mult., *J* in Hz) | $\delta_C^{\%,a}$ | $\delta_C^{a,b}$ | $\delta_H^{a,c}$ (mult., *J* in Hz) |
| 1 | 23.2 | 23.3 | 1.57 (m)/2.08 (br d, 13.5) | 23.1 | 23.1 | 1.55 (m)/2.12 (br d, 12.5) |
| 2 | 27.8 | 27.9 | 1.40 (m)/1.91 (m) | 27.9 | 28.0 | 1.40 (m)/1.92 (m) |
| 3 | 33.0 | 33.0 | 2.08 (br d, 13.5)<br>2.33 (ddd, 5.5, 13.5, 13.5) | 33.1 | 33.1 | 2.09 (br d, 13.5)<br>2.32 (ddd, 5.5, 13.5, 13.5) |
| 4 | 159.9 | 160.0 | - | 160.3 | 160.3 | - |
| 5 | 40.1 | 40.2 | - | 40.2 | 40.2 | - |
| 6 | 36.5 | 36.6 | 1.21 (m)/1.46 (ddd, 3.0, 3.0, 12.5) | 36.6 | 36.6 | 1.22 (m)/1.46 (ddd, 3.5, 3.5, 14.0) |
| 7 | 27.6 | 27.7 | 1.40 (m) | 27.7 | 27.7 | 1.38 (m) |
| 8 | 36.3 | 36.4 | 1.30 (m) | 36.4 | 36.4 | 1.30 (m) |
| 9 | 42.0 | 42.1 | - | 42.1 | 42.2 | - |
| 10 | 47.9 | 48.1 | 0.96 (dd, 1.0, 11.5) | 48.0 | 48.1 | 0.95 (dd, 2.0, 12.0) |
| 11 | 102.8 | 102.8 | 4.37 (br s)/4.41 (br s) | 102.6 | 102.6 | 4.36 (br s)/4.41 (br s) |
| 12 | 20.6 | 20.6 | 1.06 (s) | 20.6 | 20.7 | 1.06 (s) |
| 13 | 17.6 | 17.6 | 1.02 (d, 6.5) | 17.6 | 17.6 | 1.03 (d, 6.5) |
| 14 | 17.6 | 17.6 | 0.88 (s) | 17.7 | 17.7 | 0.88 (s) |
| 15 | 37.0 | 37.1 | 2.63 (d, 14.5)/2.67 (d, 14.5) | 36.8 | 36.9 | 2.68 (s) |
| 16 | 125.1 | 125.2 | - | 124.4 | 124.4 | - |
| 17 | 159.0 | 159.2 | - | 149.2 | 149.3 | - |
| 18 | 115.3 | 115.3 | 6.75 (d, 8.0) | 145.8 | 145.9 | - |
| 19 | 129.2 | 129.3 | 7.75 (d, 8.0) | 109.0 | 109.1 | 7.38 (d, 1.5) |
| 20 | 121.7 | 121.7 | - | 120.4 | 120.4 | - |
| 21 | 135.0 | 135.0 | 7.76 (s) | 127.5 | 127.6 | 7.45 (d, 1.5) |
| 22 | 167.3 | 167.4 | - | 167.2 | 167.2 | - |
| 18-OMe | | | | 56.1 | 56.1 | 3.93 (s) |
| 22-OMe | 51.9 | 51.9 | 3.87 (s) | 51.9 | 51.9 | 3.87 (s) |
| 17-OH | | | 5.94 (s) | | | 6.12 (s) |

Measured in $^{a)}CDCl_3$, $^{b)}$125 MHz, $^{c)}$500 MHz. $^{\#)}\delta_C$ of dictyoceratin C [6], $^{\%)}\delta_C$ of polyfibrospongol A [7].

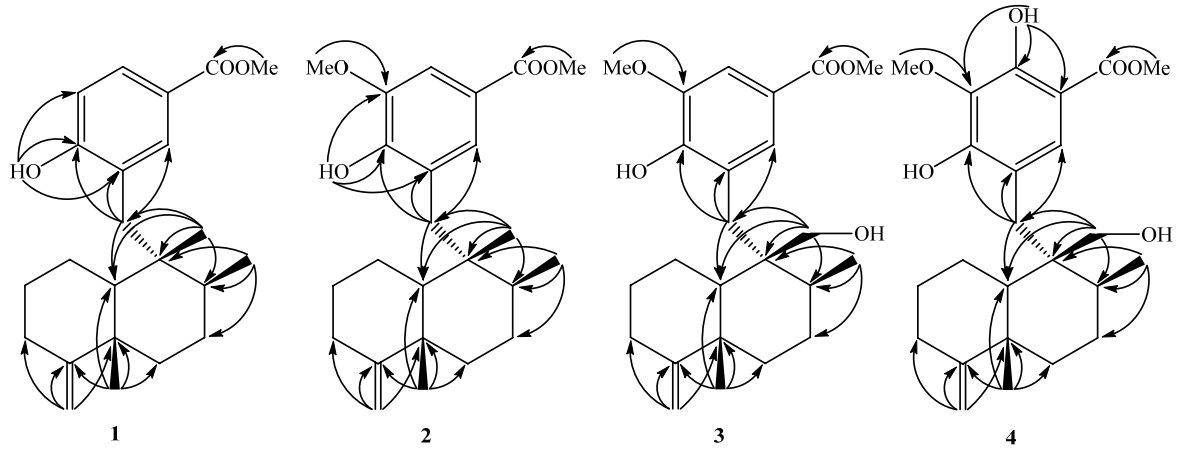



*Figure 2:* The key HMBC correlations of compounds **1-4**

Compound **2** was isolated as a white amorphous powder. The $^{1}$H and $^{13}$C NMR spectra of **2** were similar to those of **1** except for signals belonging to phenol moiety (1,3,4,5-tetrasubstituted benzene ring) and an additional methoxy group ($\delta_H$ 3.93/$\delta_C$ 56.1). The above evidence implied that the structure of **2** was similar to **1** except for an additional methoxy group at the phenol moiety. Moreover, a pair of meta-coupled proton signals in the $^{1}$H NMR of **2** ($\delta_H$ 7.38 and 7.45, each doublet *J* = 1.5 Hz) differed

from an ABX coupled system in the $^1$H NMR of **1**, suggesting that the additional methoxy group substituted at C-18 in **2** instead of a proton in **1**. The location of this methoxy group was further confirmed by HMBC correlations between methoxy proton ($\delta_H$ 3.93) and H-19 ($\delta_H$ 7.38) and C-18 ($\delta_C$ 145.9). The remaining NMR spectral signals of **2** were assigned by analysis of its HSQC and HMBC spectral data and by comparison with the correspoding data of compound **1** and shown in table 1. Thus, compound **2** was determined to be polyfibrospongol A, a known compound previously isolated from the sponge *Polyfibrospongia australis* [7]. The $^1$H and $^{13}$C NMR spectral data of **2** were found to match with those reported in the literature [7].

*Table 2:* $^1$H- and $^{13}$C-NMR data for **3-4** and reference compounds

| C | **3** | | | **4** | | |
|---|---|---|---|---|---|---|
| | $\delta_C^{\$,a}$ | $\delta_C^{a,b}$ | $\delta_H^{a)}$ (mult., *J* in Hz) | $\delta_C^{\&,a}$ | $\delta_C^{a,b}$ | $\delta_H^{a)}$ (mult., *J* in Hz) |
| 1 | 24.1 | 24.2 | 1.59 (m)/2.16 (br d, 13.5) | 24.1 | 24.1 | 1.60 (m)/2.11 (br d, 13.0) |
| 2 | 28.3 | 28.3 | 1.29 (m)/1.89 (m) | 28.3 | 28.3 | 1.24 (m)/1.88 (m) |
| 3 | 33.1 | 33.2 | 2.10 (ddd, 2.0, 2.0, 13.5)<br>2.31 (ddd, 5.0, 13.5, 13.5) | 33.2 | 33.2 | 2.09 (br d, 14.0)<br>2.31 (ddd, 5.0, 14.0, 14.0) |
| 4 | 159.8 | 159.8 | - | 159.7 | 159.7 | - |
| 5 | 40.1 | 40.1 | - | 40.0 | 40.0 | - |
| 6 | 36.9 | 36.9 | 1.29 (m)/1.52 (ddd, 3.5, 3.5, 13.5) | 36.9 | 36.9 | 1.30 (m)<br>1.53 (ddd, 3.5, 3.5, 13.0) |
| 7 | 28.0 | 28.0 | 1.44 (m)/1.50 (m) | 27.9 | 27.9 | 1.45 (m)/1.48 (m) |
| 8 | 36.7 | 37.3 | 1.39 (m) | 37.1 | 37.1 | 1.35 (m) |
| 9 | 46.6 | 46.6 | - | 46.2 | 46.2 | - |
| 10 | 49.5 | 49.5 | 1.09 (dd, 2.0, 12.0) | 49.2 | 49.2 | 1.05 (dd, 2.0, 10.5) |
| 11 | 103.2 | 103.2 | 4.40 (br s)/4.43 (br s) | 103.3 | 103.3 | 4.42 (br s)/4.45 (br s) |
| 12 | 20.9 | 20.9 | 1.06 (s) | 20.9 | 20.9 | 1.06 (s) |
| 13 | 19.0 | 19.0 | 1.11 (d, 6.5) | 18.9 | 18.9 | 1.09 (d, 7.0) |
| 14 | 64.5 | 64.5 | 3.81 (d, 12.0)/3.90 (d, 12.0) | 64.5 | 64.5 | 3.79 (d, 11.5)/3.89 (d, 11.5) |
| 15 | 37.3 | 31.6 | 2.85 (d, 14.0)/3.10 (d, 14.0) | 31.0 | 30.9 | 2.75 (d, 14.5)/3.00 (d, 14.5) |
| 16 | 124.3 | 124.4 | - | 116.4 | 116.3 | - |
| 17 | 149.2 | 149.3 | - | 154.2 | 154.2 | - |
| 18 | 146.0 | 146.1 | - | 133.7 | 133.7 | - |
| 19 | 109.3 | 109.3 | 7.40 (d, 2.0) | 153.0 | 153.0 | - |
| 20 | 120.6 | 120.7 | - | 105.3 | 105.3 | - |
| 21 | 127.8 | 127.7 | 7.51 (d, 2.0) | 128.6 | 128.6 | 7.36 (s) |
| 22 | 167.1 | 167.1 | - | 170.7 | 170.7 | - |
| 18-OMe | 56.1 | 56.1 | 3.94 (s) | 60.8 | 60.8 | 3.96 (s) |
| 22-OMe | 51.2 | 51.9 | 3.87 (s) | 52.1 | 52.0 | 3.90 (s) |
| 19-OH | | | | | | 10.87 (s) |

Measured in $^{a)}CDCl_3$, $^{b)}$125 MHz, $^{c)}$500 MHz. $^{\$)}\delta_C$ of polyfibrospongol B [7], $^{\&)}\delta_C$ of 19-hydroxy-polyfibrospongol B [8].

Compound **3** had a molecular formula $C_{24}H_{34}O_5$ which was elucidated from a pseudo-molecular ion $[M-H]^-$ peak at *m/z* 401.2326 (calcd. for $C_{24}H_{33}O_5$, 401.2328) in the HR-ESI-MS and in conjunction with $^{13}$C NMR data. The NMR spectra of **3** were very similar to those of **2** except for the changed signals at C-14, suggesting the additional oxygenated methylene in compound **3** ($\delta_H$ 3.81, 3.90; $\delta_C$ 64.5) instead of tertiary methyl group (C-14, $\delta_H$ 0.88/$\delta_C$ 17.7) in compound **2**. These findings indicated that compound **3** had an additional free hydroxyl group at C-14, which was further confirmed by the HMBC correlations between H-14 ($\delta_H$ 3.81, 3.90) and carbons C-8 ($\delta_C$ 37.3)/C-9 ($\delta_C$ 46.6)/C-10 ($\delta_C$ 49.5)/C-15 ($\delta_C$ 31.6). Thus, chemical structure of compound **3** was established and identified to be polyfibrospongol B. Comparing the NMR data of **3** with those of polyfibrospongol B in the previous report revealed that $^{13}$C-NMR signal of C-15 ($\delta_C$ 31.6) in **3** differed from that reported in the

literature ($\delta_C$ 37.3) [7]. Therefore, the chemical shift value at C-15 was carefully reconfirmed by 2D-NMR spectra. Clear HSQC correlations between H-15 and C-15 together with HMBC correlations between H-15 ($\delta_H$ 2.85, 3.10) and C-8/C-9/C-10/C-14 ($\delta_C$ 64.5)/C-16 ($\delta_C$ 124.4)/C-17 ($\delta_C$ 149.3)/C-21 ($\delta_C$ 127.7) led to undoubtedly determine the chemical shift values at C-15 ($\delta_H$ 2.85, 3.10; $\delta_C$ 31.6), as the same C-15 chemical shift values reported for 19-hydroxy-polyfibrospongol B [8].

Compound **4** was isolated as a white amorphous powder. The molecular formula $C_{24}H_{34}O_6$ was deduced on the basis of HR-ESI-MS (*m/z*: 417.2299, $[M-H]^-$; calcd. for $C_{24}H_{33}O_6$, 417.2277) and $^{13}C$-NMR analysis. The $^1H$ and $^{13}C$ NMR data of **4** were close with those of **3** (table 2). Molecular weight of **4** showed 16 atomic mass unit greater than that of **3**, together with the presence of only one aromatic proton signal at $\delta_H$ 7.36 and a deuterium exchangeable signal at $\delta_H$ 10.87 indicating an additional hydroxyl substitution on the aromatic ring in the structure of **4** compared to **3**. Furthermore, HMBC correlations of hydroxyl proton ($\delta_H$ 10.87) with C-18 ($\delta_C$ proton H-21 ($\delta_H$ 7.36) with C-16 ($\delta_C$ 116.3)/C-17 ($\delta_C$ 154.2)/C19/C-20/C-22 ($\delta_C$ 170.7) (Figure 2) confirmed the structure of a pentasubstituted phenolic moiety and the location of the hydroxyl group at C-19. In addition, the $^1H$- and $^{13}C$-NMR data of **4** were identical with those of 19-hydroxy-polyfibrospongol B, a compound isolated from sponge *Dysidea arenaria* [8] and found to mach. Consequently, the structure of **4** was established.

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REFERENCES

1. Park S. et al. *Ilimaquinone and ethylsmenoquinone, marine sponge metabolites, suppress the proliferation of multiple myeloma cells by down-regulating the level of β-catenin*, Mar. Drugs, **12(6)**, 3231-3244 (2014).
2. Kochanowska A. J. et al. *Secondary Metabolites from Three Florida Sponges with Antidepressant Activity*, J. Nat. Prod., **71(2)**, 186-189 (2008).
3. Dai J. et al. *Dictazoles: Potential Vinyl Cyclobutane Biosynthetic Precursors to the Dictazolines*, J. Org. Chem., **75(7)**, 2399-2402 (2010).
4. Dai J. et al. *Dictazolines A and B, Bisspiroimidazolidinones from the Marine Sponge Smenospongia cerebriformis*, J. Nat. Prod., **71(7)**, 1287-1290 (2008).
5. Hwang I. H. et al. *A novel natural phenyl alkene with cytotoxic activity*, Tetrahedron Lett., **54(29)**, 3872-3876 (2013).
6. Shugeng C. et al. *Marine Sesquiterpenoids that Inhibit the Lyase Activity of DNA Polymerase β.* Journal of Natural Products, **67**, 1716-1718 (2004).
7. Shen Y. C. and P. W. Hsieh. *New Sesquiterpene Hydroquinones from a Taiwanese Marine sponge Polyfibrospongia australis*, Journal of Natural Products, **60**, 93-97 (1997).
8. Yan Q. and M. W. Xiu. *A New Sesquiterpenoid Hydroquinone from the Marine Sponge Dysidea arenaria*, Molecules, **13**, 1275-1281 (2008).

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