VIETNAM JOURNAL OF CHEMISTRY VOL. 53(2) 240-242 APRIL 2015
DOI: 10.15625/0866-7144.2015-00122

SESQUITERPENES FROM MARINE SPONGE *Dysidea fragilis*

Nguyen Thi Cuc[1], Dan Thi Thuy Hang[1], Duong Thi Dung[1], Nguyen Xuan Nhiem[1], Hoang Le Tuan Anh[1], Pham Hai Yen[1], Do Cong Thung[2], Chau Van Minh[1], Phan Van Kiem[1*]

[1]*Institute of Marine Biochemistry, Vietnam Academy of Science and Technology (VAST)*

[2]*Institute of Marine Environment and Resources, VAST*

Received 10 April 2015; Accepted for publication 20 April 2015

Abstract

By various chromatographic separations, three sesquiterpenes, furodysinin lactone (**1**), *O*-methyl furodysinin lactone (**2**) and *O*-methyl-9-oxofurodysinin lactone (**3**) were isolated from Vietnamese marine sponge *Dysidea fragilis*. Their structures were determined by 1D-, 2D-NMR spectra and in comparison with the reported data. Compound **3** was reported from sponge *D. fragilis* for the first time.

Keywords. *Dysidea fragilis*, sesquiterpene

1. INTRODUCTION

Sesquiterpenes were found as a main components of the genus *Dysidea* (Dysideidae). These compounds represent a prominent class of biologically active metabolites. Several chemical investigations have been focused on the marine sponge *Dysidea fragilis*. The components of this genus were identified as sesquiterpenes [1-3], steroids [4], and diketopiperazines [5]. They exhibited various biological activities such as anti-inflammatory [1] and cytotoxic activities [4]. We reported herein the isolation and structure elucidation of three sesquiterpenes from the sponge *D. fragilis*.

2. MATERIAL AND METHODS

2.1. Sponge materials

The sponge *Dysidea fragilis* was collected in Vandon, Quang Ninh in August 2014 and identified by one of our authors, Prof. Do Cong Thung. A voucher specimen (HM06) was deposited at Institute of Marine Biochemistry, VAST.

2.2. General experimental procedures

Optical rotations were determined on a Jasco DIP-370 automatic polarimeter. 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, Fujisilisa Chemical Ltd.), and thin layer chromatography (TLC) using pre-coated silica-gel 60 F254 (0.25 mm, Merck) and RP-18 F254S plates (0.25 mm, Merck).

2.3. Extraction and isolation

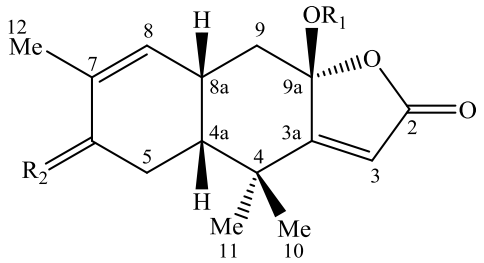
Fresh frozen dried samples of *D. fragilis* (2.0 kg) were well grinded and extracted with hot MeOH three times and then concentrated under reduced pressure to give MeOH extract (DF, 120 g). This extract was suspended in water and then partitioned with CH_2Cl_2 to give the CH_2Cl_2 (DF1, 50.0 g) and water (DF2, 75 g) extracts after removal of the solvents *in vacuo*. DF1 (45 g) was chromatographed on a silica gel column and eluted with a gradient elution of *n*-hexane – acetone (40:1 → 0:1, v/v) to yield five fractions, DF1A (6.0 g), DF1B (4.2 g), DF1C (2.5 g), DF1D (10.5 g), and DF1E (20.0 g). DF1C was chromatographed on a silica gel column eluted with *n*-hexane – CH_2Cl_2 – acetone (1:1:0.05, v/v/v) to give four smaller fractions, DF1C1 (250.0 mg), DF1C2 (500 mg), DF1C3 (400 mg), and DF1C4 (450 mg). Furthermore, DF1C3 was chromatographed on a RP-18 column eluted with acetone – water (2.0:1, v/v) to yield **2** (30.0 mg) and **3** (30.0 mg). DF1D was chromatographed on a silica gel column eluted with *n*-hexane – CH_2Cl_2 – acetone (1:1:0.3, v/v/v) to give four fractions, DF1D1–DF1D4. Finally, compound **1** was obtained from the

DF1D3 fraction using a RP-18 column and eluted with acetone – water (4:1, v/v).

Furodysinin lactone (1): White amorphous powder; $[\alpha]_D^{25}$: +20.0 (*c* 0.1, MeOH), ^{1}H- and ^{13}C-NMR (CD_3OD), see table 1.

O-Methyl furodysinin lactone (2): White amorphous powder; $[\alpha]_D^{25}$: –80.5 (*c* 0.1, MeOH), ^{1}H- and ^{13}C-NMR ($CDCl_3$), see table 1.

O-Methyl-9-oxofurodysinin lactone (3): White amorphous powder; $[\alpha]_D^{25}$: –64.1 (*c* 0.1, MeOH), ^{1}H- and ^{13}C-NMR ($CDCl_3$), see table 1.



	$\mathbf{R_1}$	$\mathbf{R_2}$
1	H	H,H
2	Me	H,H
3	Me	O

Figure 1: Chemical structures of compounds **1-3**

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

C	**1**			**2**		**3**		
	δ_C[#]	δ_C[a]	δ_H[a] (mult., *J* = Hz)	δ_C[b]	δ_H[b] (mult., *J* = Hz)	δ_C[$]	δ_C[b]	δ_H[b] (mult., *J* = Hz)
2	170.8	172.71	-	169.57	-	168.8	168.86	-
3	114.9	115.71	5.75 (s)	117.27	5.81 (s)	118.7	118.73	5.92 (s)
3a	177.0	177.00	-	173.03	-	171.0	171.01	-
4	38.6	39.61	-	38.70	-	38.6	38.58	-
4a	47.3	48.77	1.72 (m)	47.74	1.68 (m)	47.1	47.08	2.26 (dt, 4.5, 14.5)
5	**31.0**	**19.75**	1.20 (m, α) 1.72 (m, β)	18.48	1.16 (m, α) 1.68 (m, β)	35.0	35.03	2.05 (dd, 14.5, 17.5, β) 2.46 (dd, 4.5, 17.5, α)
6	**18.7**	**32.01**	2.03 (m)	30.91	1.97 (m)	198.1	198.07	-
7	134.3	135.34	-	134.26	-	135.8	135.84	-
8	123.6	124.92	5.41 (d, 5.0)	123.54	5.36 (d, 5.0)	146.5	146.53	6.74 (d, 6.5)
8a	30.4	31.92	2.81 (m)	30.18	2.77 (m)	31.0	31.03	3.08 (m)
9	40.9	42.15	1.52 (dd, 13.5, 13.5, α) 2.27 (dd, 3.5, 13.5, β)	40.25	1.52 (dd, 13.5, 13.5, α) 2.34 (dd, 3.5, 13.5, β)	37.6	37.65	1.64 (dd, 13.5, 13.5, α) 2.48 (m, β)
9a	105.5	107.50	-	107.51	-	106.8	106.85	-
10	26.8	27.32	1.42 (s)	25.70	1.37 (s)	25.0	24.97	1.40 (s)
11	25.3	25.70	1.26 (s)	25.24	1.24 (s)	24.7	24.71	1.22 (s)
12	23.3	23.34	1.65 (s)	23 10	1.62 (s)	15.6	15.61	1.78 (s)
9a-OMe				50.35	3.17 (s)	50.6	50.58	3.20 (s)

[a)]recorded in CD_3OD, [b)]$CDCl_3$, [#]δ_C of furodysinin lactone [6], [$]$\delta_C$ O-methyl-9-oxofurodysininlactone [7].

3. RESULTS AND DISCUSSION

Compound **1** was obtained as a white amorphous powder. The ^{1}H-NMR of **1** showed the presence of two olefinic protons at δ_H 5.41 (d, *J* = 5.0 Hz) and 5.75 (s); three tertiary methyl groups at δ_H 1.26 (s), 1.42 (s) and 1.65 (s). The ^{13}C-NMR and DEPT revealed 15 carbons, including one carbonyl at δ_C 172.71; four non-protonated at δ_C 39.61, 107.50, 135.34 and 177.00; four methine at δ_C 31.92, 48.77, 115.71 and 124.92; three methylene at δ_C 19.75, 32.01 and 42.15; three methyl carbons at δ_C 23.34, 25.70 and 27.32. The ^{1}H- and ^{13}C-NMR data of **1** were very similar to those of furodysinin lactone [6]. The HMBC correlations between H-10 (δ_H 1.42)/H-11 (δ_H 1.26) and C-3a (δ_C 177.00)/C-4 (δ_C 39.61)/C-4a (δ_C 48.77); H-3 (δ_H 5.75) and C-2 (δ_C 172.71)/C-3a (δ_C 177.00)/C-9a (δ_C 107.50); H-12 (δ_H 1.65) and

C-6 (δ_C 32.01)/C-7 (δ_C 135.34)/C-8 (δ_C 124.92) confirmed the positions of two double bonds at C-3/C-3a and C-7/C-8. The ^{13}C-NMR chemical shifts of C-5 (δ_C 19.75) and C-6 (δ_C 32.01) (Table 1) should be exchanged due to HMBC correlation from H-12 (δ_H 1.65) to C-6 (δ_C 32.01) was observed as well as high chemical shift of H-6 (δ_H 2.03) [6] . Based on the above evidence, the structure of **1** was elucidated as furodysinin lactone [6], a known compound from the sponge *D. fragilis* [3].

The ^{1}H-NMR spectrum of **2** exhibited two olefinic protons at δ_H 5.36 (d, J = 5.0 Hz) and 5.81 (s); one methoxy group at δ_H 3.17 (s); three tertiary methyl groups at δ_H 1.24 (s), 1.37 (s), and 1.62 (s). The ^{13}C-NMR and DEPT spectra of **2** showed 16 carbon signals including one carbonyl, four non-protonated, four methine, three methylene, and four methyl carbons. ^{1}H- and ^{13}C-NMR data of **2** indicated that structure of **2** was similar to that of **1**. Detailed analysis of the 1D-NMR together with

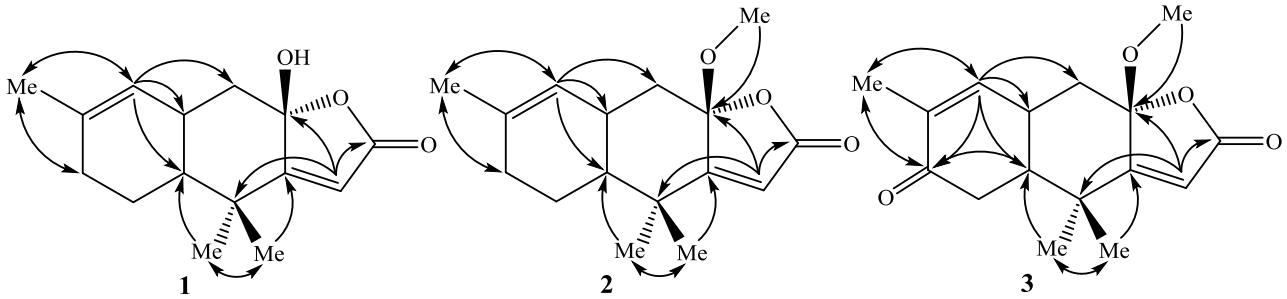


Figure 2: The key HMBC correlations of compounds **1** and **2**

HSQC and HMBC data revealed the additional methoxy group at C-9a of **2** comparing to **1**. This was further confirmed by HMBC correlation from methoxy protons (δ_H 3.17) to C-9a (δ_H 107.52). The remaining positions in **2** were also built by HSQC and HMBC spectral data. Thus, the structure of **2** was determined to be *O*-methyl furodysinin lactone [3].

Compound **3** also obtained as a white amorphous powder. The ^{1}H- and ^{13}C-NMR data of **3** were very similar to those of **2** except for an addition of ketone group at C-6. This was further confirmed by HMBC correlations from H-12 (δ_H 1.78) to C-6 (δ_C 198.07)/C-7 (δ_C 135.84)/C-8 (δ_C 146.53). Moreover, the position of methoxy group at C-9a was proved by HMBC correlations from methoxy (δ_H 3.17) to C-9a (δ_H 107.52). Thus, the structure of **3** were defined as *O*-methyl-9-oxofurodysinin lactone (**3**) [7]. To the best of our knowledge, this is the first report of this compound from the sponge of *Dysidea* genus.

Acknowledgement. *This research was supported by Vietnam Academy of Science and Technology under grant number VAST.TĐ.ĐAB.01/13-15.*

REFERENCES

1. W.-H. Jiao, T.-T. Xu, F. Zhao, H. Gao, G.-H. Shi, J. Wang, L.-L. Hong, H.-B. Yu, Y.-S. Li, F. Yang, H.-W. Lin. *Dysifragilones A–C, unusual sesquiterpene aminoquinones and inhibitors of NO production from the South China Sea sponge Dysidea fragilis.* European Journal of Organic Chemistry, **2015**, 960-966 (2015).
2. Z. G. Yu, J. Li, Z. Y. Li, Y. W. Guo. *Two new unprecedented acetonyl-bearing sesquiterpenes from the hainan sponge Dysidea fragilis.* Chemistry Biodiversity, **6**, 858-863 (2009).
3. N. S. Reddy, U. Venkatesham, T. P. Rao, Y. Venkateswarlu. *New sesquiterpenes from the marine sponge Dysidea fragilis.* Indian Journal of Chemistry -Section B, **39B**, 393-395 (2000).
4. A. Aiello, E. Fattorusso, M. Menna, R. Carnuccio, T. Iuvone. *New cytotoxic steroids from the marine sponge Dysidea fragilis coming from the lagoon of Venice.* Steroids, **60**, 666-673 (1995).
5. J.-Y. Su, Y.-L. Zhong, L.-M. Zeng, S. Wei, Q.-W. Wang, T. C. W. Mak, Z.-Y. Zhou. *Three new diketopiperazines from a marine sponge Dysidea fragilis.* Journal of Natural Products, **56**, 637-642 (1993).
6. G.-W. Zhang, C.-Z. Liao, X.-S. Yao, H. Kurihara, J.-Y. Su, L.-M. Zeng. *8β-Hydroxy-2,6,6-trimethyl-5βH,10βH-eudesma-1,7(11)-dien-12,8-olide.* Acta Crystallographica Section E, **61**, o172-o173 (2005).
7. E. J. Dumdei, J. Kubanek, J. E. Coleman, J. Pika, R. J. Andersen, J. R. Steiner, J. Clardy. *New terpenoid metabolites from the skin extracts, an egg mass, and dietary sponges of the Northeastern Pacific dorid nudibranch Cadlina luteomarginata.* Canadian Journal of Chemistry, **75**, 773-789 (1997).

Corresponding author: **Phan Van Kiem**
Institute of Marine Biochemistry, Vietnam Academy of Science and Technology
18 Hoang Quoc Viet, Cau Giay, Hanoi, Vietnam
E-mail: phankiem@yahoo.com.