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Chemical Investigation of the Senegalese Marine Sponge *Luffariella geometrica*

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Abstract

One new γ-hydroxybutenolide (**1**) together with the known compounds (**2-7**) were isolated from the Senegalese marine sponge *Luffariella geometrica*. Their chemical structures were established on the basis of spectroscopic methods 1D and 2D NMR, in addition to mass spectrometry and comparison with literature data.

1. Introduction

Marine organisms are an inexhaustible source of natural compounds that are promising for creation of drugs or biologically active additives, which is closely related to the huge biological diversity of the resources of the World Ocean [1]. Among the marine organisms, sponges are the most profiling source in bioactive compounds with some focusing on compounds with anticancer [2-4] and antibacterial activities [5-7], and effects against other infectious diseases [8-10].

In an effort to explore natural compounds from marine invertebrates, the Senegalese marine sponge *Luffariella geometrica* was found to contain new γ-hydroxybutenolide (**1**) together with known compounds 3-hydroxy-5-methyl-4-phenylfuran-2(5H)-one (**2**),

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clathryimine A (**3**), 3-(hydroxyacetyl)indole (**4**), 2-oxo-3-phenylpropanenitrile (**5**), 2-hydroxydeoxyadenosine (**6**) and thymidine (**7**). Compound **2** has been previously synthesized [11,12] and after isolated from marine fungus *Paradendryphiella salina* [13]. Clathryimine A (**3)** has been found first in the Indo-Pacific sponge *Clathria basilana* [14] and then in the Australian sponge *Luffariella geometrica* [15]. Compound **4** has been reported as a plant growth regulator from the Oregon red algae *Prionitis lanceolata* [16] and encountered in the marine sponge *Tedania ignis* [17] and in the liquid cultures of fungus *Lactarius deliciosus* [18]. The 2-oxo-3-phenylpropanenitrile (**5**) known as synthetic compound [19,20] was isolated for the first time as natural compound as well as nucleoside (**6**) known as a product of radical oxidation of the adenine moiety of nucleoside and DNA [21,22]. Thymidine (**7**) was isolated from starfish *Acanthaster planci* [23] and also isolated from the marine sponges Haliclona sp. [24] and Callyspongia sp. [25].

2. Experimental

2.1. General

Details of general procedures and analytical HPLC conditions have been reported previously [26,27].

2.2. Animal material

The sponge was collected by scuba diving at a depth of 3 m from Ouakam, Senegal in July 2016. The collected material was immediately frozen and kept at -20°C until investigation.

2.3. Extraction and isolation

Sponge specimen was freeze-dried (dry weight 170 g) and extracted with a mixture of MeOH/CH_2Cl_2(1:1, v/v) 3 x 1 L. Solvent was removed in vacuo to give a brown crude extract (21.17 g). The crude extract was fractionated using reverse phase C_{18} flash column chromatography with a decreasing polarity gradient of H_2O/MeOH from 1:0 to 0:1, then MeOH/CH_2Cl_2 from 1:0 to 0:1.

The H_2O/MeOH (1:2, v/v) fraction (434 mg) was then subjected to semi-preparative HPLC-DAD (Macherey-Nagel NUCLEODUR® sphinx RP column 250 x 10 mm id, 5 µm) with a gradient of H_2O/MeCN/Formic acid 90/10/0.1 to 40/60/0.1 in 45 minutes (flow: 3.0 mL.min^{-1}, injection volume: 80 µL). This purification gives compound **1** (15.7 mg, 0.0092 dry weight), compound **2** (2.7 mg, 0.0016% dry weight), clathryimine A (**3**)

(5.0 mg, 0.0029% dry weight), 3-(hydroxyacetyl)indole (**4**) (2.6 mg, 0.0015 dry weight) and compound **5** (4.4 mg, 0.0026% dry weight).

The H_2O/MeOH (2:1, v/v) fraction (1.5 g) was dissolved in MeOH and absorbed on a Diaion HP-20 column (Supleco) and eluted with an MeOH/H_2O system. The MeOH fraction (270 mg) was subjected to a semi-preparative HPLC-DAD (Macherey-Nagel NUCLEODUR® Sphinx RP column, 250 x 10 mm id, 5 µm) using H_2O/MeOH/Formic acid gradient 100:0:0.1 to 95/5/0.1 in 25 minutes to afford compound **6** (7.3 mg, 0.0043% dry weight) and thymidine (**7**) (10.1 mg, 0.0059 dry weight).

3. Results and Discussion

Compound **1** was isolated as a brown amorphous powder. Inspection of its ^1H and ^{13}C NMR spectra showed the presence of a methyl-α-hydroxy-γ-butenolide moiety by comparison with NMR data of compound **2** (Figures 1 and 2). This was inferred from the signals at δ_C171.99 (C-1), 138.13 (C-2) and 142.74 ppm (C-3); δ_H/δ_C4.94/77.85 (C-4) and 1.40/19.89 ppm (C-5). The ^1H NMR and COSY spectra demonstrated the presence of the isopropyl moiety and consisting by the connection between signals at δ_H2.68 (hept, 7 Hz, H-1') and 1.25 (d, 7 Hz, H-2') and 1.21 (d, 7Hz, H-3') (Table).

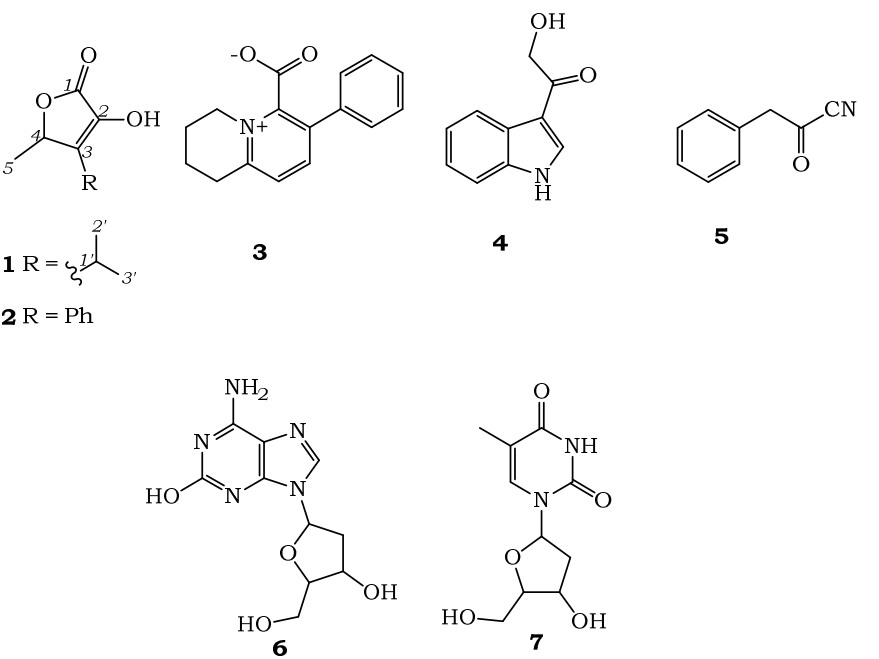

Table. NMR data (500/125 MHz, CD_3OD) of compound **1**.

N°	δ_C (ppm)/	mult.	δ_H (ppm)/ J (Hz)/ mult.			COSY	HMBC
1	171.99	qC					
2	138.13	qC					
3	142.74	qC					
4	77.85	CH	4.94	6.5	q	5	1, 2, 3, 5, 1’
5	19.89	CH_3	1.40	6.5	d	4	3, 4
1’	27.03	CH	2.68	7	hept.	2’, 3’	2, 3, 4, 2’, 3’
2’	21.07	CH_3	1.21	7	d	1’	3, 1’, 3’
3’	20.29	CH_3	1.25	7	d	1’	3, 1’, 2’

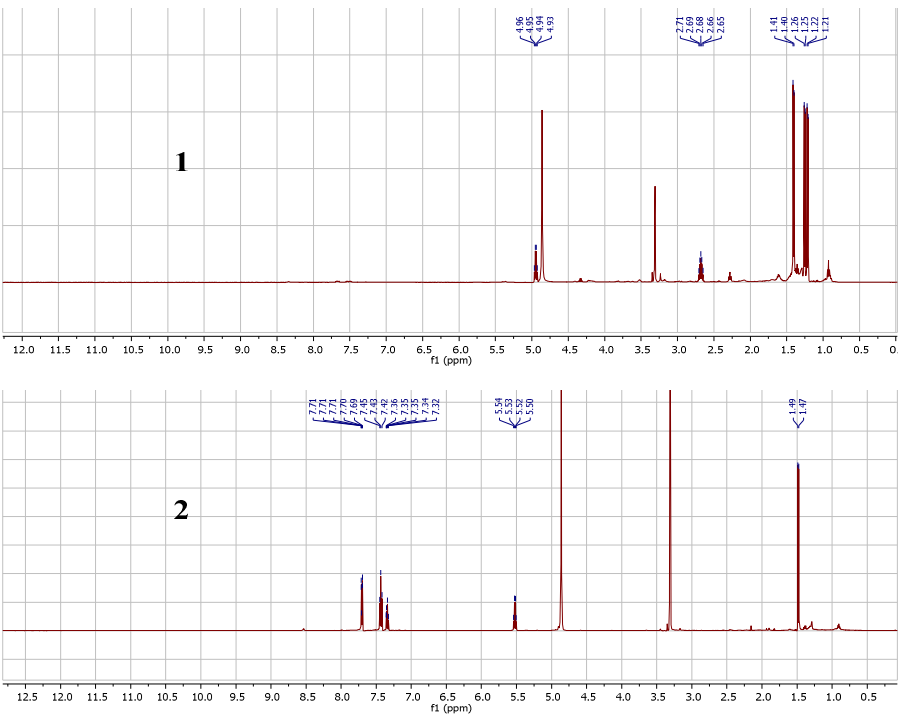

Figure 1. ^{1}H NMR spectra of compound **1** and **2**.

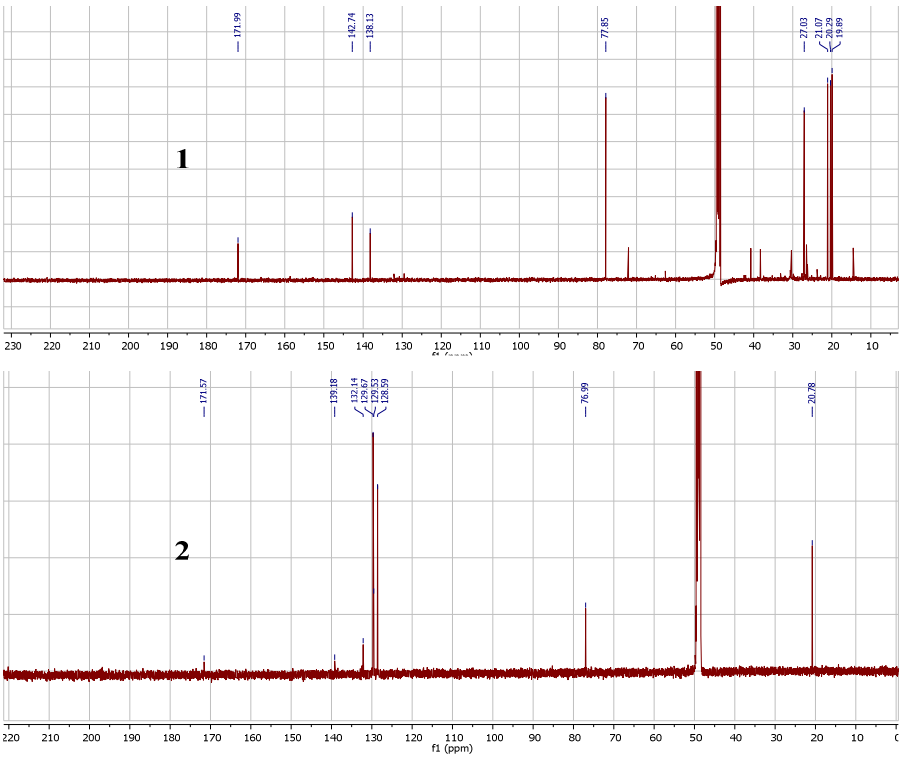

Figure 2. ^{13}C NMR spectra of compound **1** and **2**.

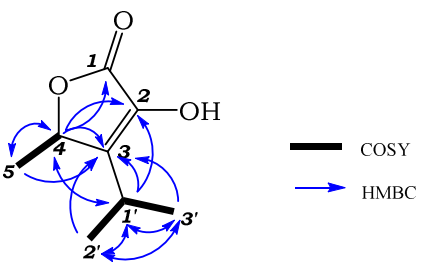

Figure 3. COSY and HMBC correlations of compound **1**.

Signals at δ_H2.68 correlating with carbons at δ_C138.13 (C-2), 142.74 (C-3) and 77.85 (C-4) and at δ_H1.21 and 1.25 correlating with carbon at δ_C142.74 (Figure 3) demonstrated the connection of isopropyl moiety and α-hydroxy-γ-butenolide fragment at C-3-C-1'.

4. Conclusion

Chemical investigation of the hydromethanolic fractions H_2O/MeOH (1:2, v/v) and H_2O/MeOH (2:1, v/v) of the Senegalese marine sponge *Luffariella geometrica* yielded respectively one new and four known compounds and two known nucleosides. Compounds **5** and **6** are isolated for the first time as natural products.

In our continuing to explore bioactive compounds from Senegalese marine organisms, we hope to investigate the other fractions of our sponge to isolate new metabolites of pharmacological interest.

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