

## A novel tribrominated indole nucleoside from the Senegalese marine sponge *Diplastrella* sp.

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### Abstract:

Chemical investigation of the hydromethanolic fraction of ethanolic crude extract of *Diplastrella* sp. collected from Senegalese coast yielded a new tribrominated indole nucleoside. The compound was identified using HRMS and 1D and 2D NMR spectroscopic.

**Keywords:** Marine sponge, *Diplastrella* sp., indole nucleoside, marine metabolite.

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### I. Introduction

Sponges are sessile invertebrates; they do not have an innate immune system and cannot move and lack physical defenses, they are highly susceptible to marine predators. Thus, it is not surprising that sponges have developed a wide suite of defensive chemicals (metabolites) to deter predators<sup>[1-2]</sup>. Such metabolites, biosynthesis by sponges, present promising pharmacological properties<sup>[3]</sup>, they proved to have antibacterial<sup>[4]</sup>, antiviral<sup>[5]</sup>, antifungal<sup>[6]</sup>, antimalarial<sup>[7]</sup>, antitumor<sup>[8]</sup>, immunosuppressive<sup>[9]</sup>, and cardiovascular activity<sup>[10]</sup>.

In our pursuit in bioactive natural products from Senegalese marine sponges, the chemical investigation of a hydromethanolic fraction of marine sponge *Diplastrella* sp., family *Spirastrellidea* was carried out. The study resulted in the isolation and identification of the new tribrominated indole nucleoside. Herein, the purification and the structure determination will be discussed.

### II. Experimental section

#### General procedure

All the organic solvents used for material extraction were of analytical grade and purchased from Sigma Aldrich (France). High-resolution mass spectra (HRMS) were recorded with an Thermo LCQ Advantage. NMR spectra were obtained in DMSO on a 400 and 500 MHz Bruker Avance. NMR chemical shifts were expressed in parts per million (ppm) referenced to residual DMSO solvent signals ( $\delta_H 2.50$  for <sup>1</sup>H and  $\delta_C 39.52$  for <sup>13</sup>C).

HPLC-PDA-ELSD analyses were performed with a Waters Alliance 2695 HPLC system (Waters

Corporation, Milford, MA) coupled with a Waters 996 photodiode array detector and a Sedex55 evaporative light-scattering detector (SEDERE, France), using a bifunctional Macherey-Nagel

NUCLEODUR® Sphinx RP column (250 x 4.6 mm, 5 μm) consisting of a balanced ratio of propylphenyl and C18 ligands. The mobile phase was composed of water (H<sub>2</sub>O + 0.1% formic acid) and acetonitrile (MeCN + 0.1% formic acid) and the following gradient was used: H<sub>2</sub>O:MeCN 90:10 for 5 min, H<sub>2</sub>O:MeCN 90:10 to 0:100 for 30 min, 0:100 for 5 min, 0:100 to 90:10 for 15 min (flow: 1.0 mL.min<sup>-1</sup>, injection volume: 20 μL). Chromatograms were extracted at the following detection wavelengths for visual inspection: 214, 254, and 280 nm.

#### Biological materials

The marine sponge *Diplastrella* sp. (**Figure 1**) was collected off 14° 43' 30'' north and 17° 16' 15'' west using scuba diving at a depth of 5 m.



**Figure 1:** *Diplastrella sp.* photography.

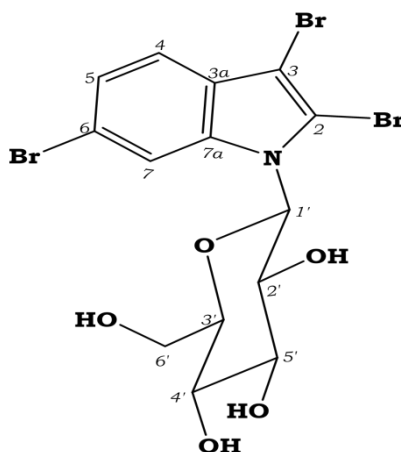
The collected material was immediately frozen and kept at -20 °C until investigation. The sponge was identified by Dr. Michelle Kelly (National Institute of Water and Atmospheric Research, Wellington, New Zealand).

### Extraction and isolation

The frozen sponge material (400 g) was extracted thawed at room temperature with EtOH followed by a mixture of MeOH/CH<sub>2</sub>Cl<sub>2</sub> (1:1, v/v) in an ultrasonic bath to yield 24.88 g of the ethanolic and 3.17 g of the MeOH/CH<sub>2</sub>Cl<sub>2</sub> crude extracts after concentration under reduced pressure. The ethanolic crude extract was fractionated by RP-C18 flash chromatography (elution with a decreasing polarity gradient of H<sub>2</sub>O/MeOH from 1:0 to 0:1, then MeOH/CH<sub>2</sub>Cl<sub>2</sub> from 1:0 to 0:1). The H<sub>2</sub>O/MeOH (2:1, v/v) fraction (365 mg) was then subjected to semi-preparative HPLC-DAD (Macherey-NagelNUCLEODUR® SphinxRP column, 250 x 10 mm id, 5 μm) with a gradient of H<sub>2</sub>O/MeCN/Formic acid 90:10:0.1 to 0:100:0.1 (flow: 3.0 mL.min<sup>-1</sup>, injection volume: 100 μL) to afford the tribrominated indole nucleoside (7.5 mg). The compound was identified by a combination of spectroscopic methods (1D and 2D NMR, MS) and comparison with the literature data<sup>[11-17]</sup>.

### III. Results And Discussion

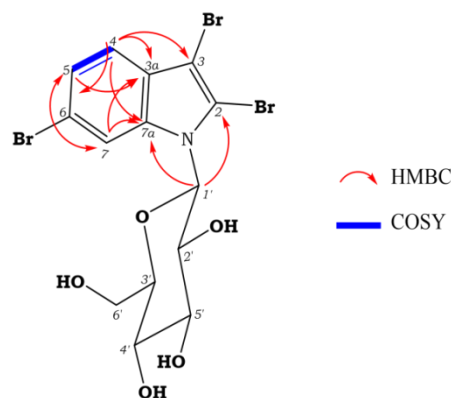
The compound (**Figure 2**) was isolated and purified as a colorless amorphous solid. The (+)-LRESIMS of the compound exhibited an isotopic cluster ions [M + H]<sup>+</sup> at *m/z* 513, 515, 517, and 519 in the ratio 1:3:3:1, indicating the presence of three bromine atoms. The molecular formula of the compound was determined to be C<sub>14</sub>H<sub>14</sub>Br<sub>3</sub>NO<sub>5</sub> by a pseudomolecular ion peak in the (+)-HRESIMS spectrum at *m/z* 513.8495.



**Figure 2:** Structure of the tribrominated indole nucleoside.

Analysis of the <sup>13</sup>C NMR and HSQC spectra (table) indicated the molecule contained fourteen C-atoms, including five quaternary carbons, eight methines, and one methylene groups. From the spectral data (table), it was suggested that our compound is an *N-glycoside* consisting of a deoxy sugar moiety and a chromophore of an indole derivative.

COSY and HMBC correlations (Figure 3) of the indole moiety comparison with the reported NMR data of the known compounds<sup>[11, 12]</sup> suggested that it's an 2,3,6-tribromoindole.



**Figure 3:** HMBC correlations and COSY connectivities of compound.

The presence of N-glycopyranosyl moiety in the structure was inferred from signals in the  $^1\text{H}$  and  $^{13}\text{C}$  spectra at  $\delta_{\text{H}}/\delta_{\text{C}}$  5.43/88.02 (C-1'), 3.81/70.90 (C-2'), 3.42/77.10 (C-3'), 3.42/69.50 (C-4'), 3.42/80.28 (C-5') and 3.74, 3.55/60.70 (C-6') and couplings observed in the COSY and HMBC spectra (table).

**Table.** NMR data (400, 500/100 MHz, DMSO- $d_6$ ) for tribrominated indole nucleoside

N <sup>o</sup>	$\delta_{\text{C}}$ (ppm)/	type	$\delta_{\text{H}}$ (ppm)/ $J$ (Hz)/ mult.			COSY	HMBC
2	116.50	qC					1'
3	93.68	qC					4
3a	126.45	qC					4, 5, 7
4	120.01	CH	7.43-7.34		m	5	
5	124.44	CH	7.43-7.34		m	4, 7	7
6	115.75	qC					4
7	115.70	CH	7.82	1.5	d	5	5
7a	134.59	qC					4, 5, 7, 1'
1'	88.02	CH	5.43	9.1	d	2'	2', 2'-OH
2'	70.90	CH	3.81	8.8, 5.3	td	1', 3', 2'-OH	1', 2'-OH
3'	77.10	CH	3.42		m	2', 4', 3'-OH	1', 2', 2'-OH, 3'-OH
4'	69.50	CH	3.42		m	3', 5', 4'-OH	3', 5', 3'-OH, 4'-OH
5'	80.28	CH	3.42		m		4', 6'
6'	60.70	CH <sub>2</sub>	3.74	12.0, 5.7, 1.8	ddd		5', 6'-OH
			3.55	11.6, 5.5	dt		5', 6'-OH
2'-OH		OH	5.36	5.4	d	2'	
3'-OH		OH	5.16	4.9	d	3'	
4'-OH		OH	5.16	4.9	d	4'	
6'-OH		OH	4.68	5.6	t	6'	

The large  $^1\text{H}$ - $^1\text{H}$  coupling constant for H-1' (9.1 Hz) indicated  $\alpha\beta$ -glycoside configuration, by comparison with N-glycosyl indoles and derivatives previously reported<sup>[13-17]</sup>.

The long-range H-C coupling of the anomeric proton H-1' with C-2 and C-7a in the HMBC experiment indicated the N-C-1' connection of indole nucleus and glycopyranosyl moiety.

It's a first time that indole nucleoside is isolated from marine sponge.

#### IV. Conclusion

In conclusion, our search for marine-derived bioactive compounds has led to the investigation of specimen of the Senegalese marine sponge *Diplastrella* sp. One new tribrominated indole nucleoside, was isolated and its chemical structure was assigned using spectroscopic studies.

N-glycosyl indoles are of high importance in medicinal chemistry and commonly found in many compounds of practical importance, ranging from natural compounds to pharmaceutical agents<sup>[13-17]</sup>. The next step in our work would be to study isolated compound for research possible biological activities.

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