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A New Sesquiterpene Tetronic Acid Derivative from the Marine Sponge *Smenospongia* sp.

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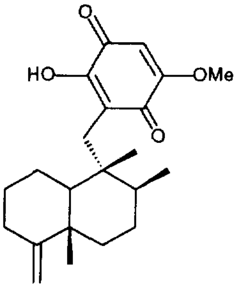
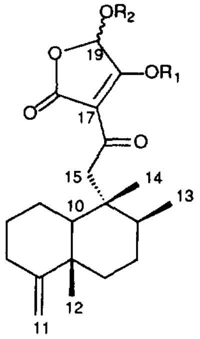
Abstract: A new sesquiterpene tetronic acid derivative, named smenotronic acid 2 was isolated from the Red Sea marine sponge *Smenospongia* sp. Its structure was assigned by detailed spectroscopic analysis.

Marine sponges of the genus *Smenospongia* have yielded a variety of indole [1,2] and terpene [3,4] derivatives. We have previously isolated from the Red Sea *Smenospongia* sp. several antibiotic and cytotoxic sesquiterpene quinones or hydroquinone [5,6] with the known ilimaquinone **1**. From the same species we now report the isolation and structure elucidation of a new sesquiterpene coupled to a tetronic acid, named smenotronic acid **2**.

We recently found that the magnesium salt of ilimaquinone, specifically disassembled dynamically unstable microtubules in fibroblasts and various epithelial cells lines [7]. In order to isolate more ilimaquinone in a continuing biological study, we re-investigated the CH_2Cl_2 extract of *Smenospongia sp.* (8g). Successive chromatographies on Silica gel (CH_2Cl_2/acetone: 98/2, then hexane/AcOEt 70/30) yielded compound **2** in very small amount (0.0025% dry weight).



1



2 R1 = Me and R2 = H
3 R1 = H and R2 = Me

Compound **2** was obtained as a colorless solid. The molecular formula $C_{21}H_{30}O_5$ was determined on the basis of the FABMS (MH^+, 363.2172 Δmmu -0.1), indicating seven degrees of insaturation. The fragment ion at *m/z* 191 in the EIMS spectrum and characteristic resonances in the ^1H NMR spectrum ($CDCl_3$), such as two methyl singlets (δ 0.74, 1.00 ppm), a methyl doublet (δ 0.76 ppm) and an exocyclic olefin signal (δ 4.5 ppm) indicated the presence of a rearranged drimane skeleton, which was confirmed with 2D NMR studies (Table). In addition, the carbons at δ 91.2, 98.4, 169.6 and 176.8 ppm suggested the presence of a tetronic acid moiety [8] and the carbon at δ 60.0 ppm that of one methoxyl group. The hypothesis of a tetronic acid moiety was confirmed by the IR (3414, 1795, 1770, 1722 and 1643 cm^{-1}) and the UV [224 nm (ε: 18180)] data [8].

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A carbonyl group was observed at 202.1 ppm only in the ^{13}C NMR spectrum recorded in C_5D_5N[9], which allowed to obtain informations for structure elucidation of the tetronic acid moiety. The chemical shift of methylene CH_2-15 at δ 43.1 ppm suggested that it might be adjacent to a carbonyl group[10] and then fixed the carbonyl at C16. Additional evidence came from HMBC correlations between protons H15 and the carbons at δ 41.4 and 202.1 ppm. HMBC correlations between the methoxyl group (δ 3.80 ppm) and the carbon at δ 178.8 ppm located the methoxyl group at C-18. Finally, HMBC correlations between proton H19 (δ 5.63 ppm) and the carbons resonating at δ 103.2 and 170.3 ppm and the chemical shift of carbon C17 at δ 103.2 ppm[10] unequivocally confirmed structure of compound **2**. Concerning the relative configuration, a NOESY spectrum indicated that methyls C12, C13 and C14 are oriented on the same side. The axial position of H10 (12.2, 2.2 Hz) was deduced from its coupling constants observed in ^1H NMR spectrum recorded in $CDCl_3$.

During storage of the sample in C_5D_5N solution, epimerization occured as deduced from duplication of several signals in the ^1H NMR spectrum. It gave a 1:1 mixture of the two C19-epimers, which are isomers of dactyltronic acids **3**, previously reported from the sponge *Dactylospongia elegans*[10]. To the best of our knowledge, smenotronic acid **2** is the first compound of this series isolated in a single form (α or β).

Table : ^{13}C (75 Mhz), ^1H (300 MHz) NMR data [δ ppm, (mult.), *J* in Hz] and HMBC correlations of **2**.

n°	^{13}C $CDCl_3$	^1H $CDCl_3$	^1H C_5D_5N	^{13}C C_5D_5N	^1H -^{13}C HMBC C_5D_5N
1	22.7	1.46 (m)	1.46 (m)	22.5	
2	28.3	1.82 (m)	1.82 (m)	28.5	
3	32.8	2.30 (dd) 13.8, 5.3	2.23 (dd) 13.8, 5.3	32.9	C2, C4, C11
		2.06 (dd) 13.8, 1.5	2.12 (dd) 13.8, 1.5		
4	159.6			160.8	
5	40.1			40.2	
6	36.7	1.60 (m)		37.1	C5, C7, C8, C10, C12
7	27.3	1.43 (m)		27.4	C5, C6, C9, C13
8	37.2	1.94 (m)		37.0	
9	41.6			41.4	
10	48.2	1.67 (dd) 12.2, 2.2		48.2	
11	103.0	4.50 (d) 1.5	4.61 (d) 1.5	102.9	C3,C5
12	20.2	1.00 (s)	0.98 (s)	19.5	C6, C7, C10
13	16.5	0.76 (d) 7	0.83 (d) 7	16.4	C7, C8, C9
14	17.3	0.74 (s)	0.72 (s)	17.8	C5, C7, C8, C9, C10
15	41.3	2.60 (d) 19	3.18 (d) 19	43.1	C8, C9, C10, C14, C16
		2.46 (d) 19, AB syst	2.95 (d) 19, AB syst		
16	n.o.			202.1	
17	98.4			103.2	
18	176.8			178.8	
19	91.2	5.26 (s)	5.63 (s)	90.9	C17, C20
20	169.6			170.3	
OCH_3	60.0	3.89 (s)	3.80 (s)	59.7	C20

n.o.: not observable in this solvent.

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