XYLOKETAL G, A NOVEL METABOLITE FROM THE MANGROVE FUNGUS *Xylaria sp.* 2508

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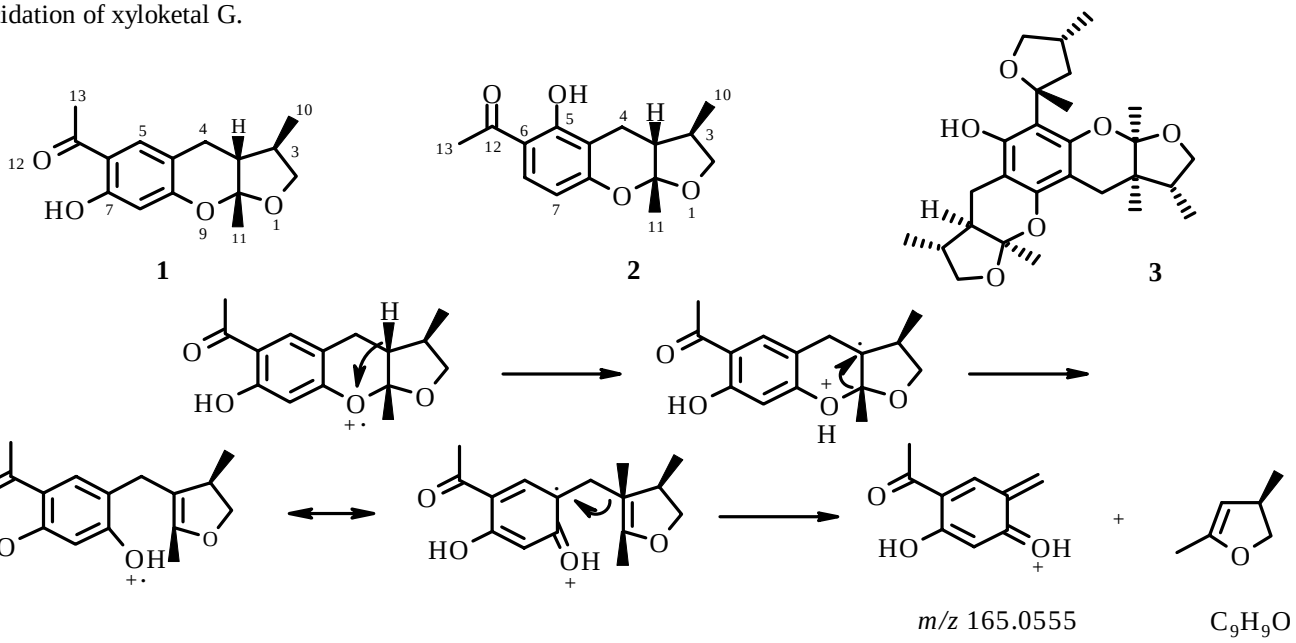
*A novel metabolite **1**, named xyloketal G, was isolated from cultures of marine derived mangrove fungus* Xylaria sp. *2508. Its structure was elucidated by analysis of spectroscopic data.*

Key words: xyloketal, marine, fungus, mangrove, xylaria.

Microorganisms are the third most widely distributed among marine natural products [1]. Among them, the marine mangrove fungus has have attracted much researches due to its importance in ecology [2–8]. Xyloketals are a group of metabolites from the mangrove fungus *Xylaria sp*. 2508 [6], which have attracted two research groups to their synthesis since they were reported [9–11]. In the ongoing research on metabolites from the fungus we isolated another novel compound (1-(7-hydroxy-3,9a-dimethyl-2,3,3a,9a-tetrahydro-4H-1,9-dioxacyclopenta[b]naphthalen-6-yl)-ethanone (**1**), xyloketal G, $C_{15}H_{18}O_4$, M^+ 262.1190, mp 144°C. $[\alpha]^{25}_D$ –111° (*c* 0.1, $CHCl_3$). In this paper we describe the isolation and structure elucidation of xyloketal G.



Cultures of marine derived fungus *Xylaria* sp. 2508 isolated from the seeds of an angiosperm tree in Mai Po in Hong Kong were filtered through cheesecloth; the filtrate was concentrated below 50°C and extracted with ethyl acetate. Repeated chromatography afforded xyloketal D as colorless blocks. The mixture of **1** and xyloketal D was purified by HPLC to give colorless blocks **1**.

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TABLE 1. NMR Data of **1** ($CDCl_3$, δ, ppm, J/Hz)

Atom	δ_c (DEPT)	δ_H	COSY	HMBC	ROESY
2	74.2 (CH_2)	4.16 (t, J = 8.5)	H-3	H-10, 3	H-3a
		3.55 (t, J = 8.5)			
3	34.6 (CH)	2.15-2.00 m	H-2, 3a, 10	H-10, 3a, 4, 2	H-10, 3a, 2
3a	48.2 (CH)	1.98 (ddd, J = 11.5, 6.0, 2.0)	H-3, 4	H-10, 11, 3, 2	H-2, 3, 4, 10
4	23.8 (CH_2)	2.98 (ddd, J = 16.5, 6.0, 1.5)	H-3a	H-3a, 3, 5	H-3a
		2.75 (dd, J = 16.5, 1.5)			
4a	110.3 (C)			H-8, 4, 3a	
5	132.0 (CH)	7.45 s		H-4	H-13
6	114.5 (C)			H-13, 8, OH	
7	163.3 (C)			H-5, 8, OH	
8	104.6 (CH)	6.36 s		OH	
8a	160.3 (C)			H-8, 5, 4	
9a	108.9 (C)			H-11, 4, 3a, 2	
10	16.0 (CH_3)	1.07 (d, J = 7.0)	H-3	H-3a, 2	H-3, 3a, 2, 11
11	23.4 (CH_3)	1.57 s		H-3a	H-10
12	202.2 (C)			H-13, 5	
13	26.1 (CH_3)	2.55 s			H-5
7-OH		12.35 s			

High-resolution MS of **1** indicated a molecular weight of $C_{15}H_{18}O_4$ (M^+ 262.1190, calc. 262.1205) and showed a significant peak $(M\text{-}C_6H_9O)^+$, which was the major ion peak in the MS of other xyloketals. The proposed cleavage of C_6H_9O was shown in the scheme. The ^1H and ^{13}C NMR spectral data of **1** and xyloketal D are similar, and they have the same molecular weight. This suggests that **1** is the stereoisomer of xyloketal D (**2**). Instead of two doublets due to aromatic protons in xyloketal D, the two singlets due to aromatic protons shows that they are in *para*-position to each other. The downfield signal of the OH at 12.35 indicates that it is located on the *ortho*-position of the acetyl group. In the HMBC spectrum of **1**, the correlations between H-5 and both C(12) and C(4) define the position of the two substituents on the benzene ring. The ROESY showed the correlations of H-10 and both H-3a and H-11, implying the same stereochemistry at C(3)R*, C(3a) R* and C(9a)R*. The $[\alpha]_D^{25}$ of **1** was –111°, showing a similar negative Cotton effect as xyloketal D ($[\alpha]_D^{25}$ –119.5°), the absolute structure (3R, 3aR, 9aR) of which has been confirmed by quantum mechanical calculations [6] and synthesis [9–11], so it is reasonable that the absolute configuration of **1** was also all R. All H- and C- atoms in xyloketal G are completely assigned as shown in Table 1.

According to the significant cleavage of C_6H_9O (97.0635, calc. 97.0613) shown in the scheme and the 2,4-dimethyl-tetrahydrofuran fragment found in xyloketal E (3), we speculate that the biosynthetic route for xyloketals is via *ortho*-quinone methide. The synthesis of xyloketal D via *ortho*-quinone methide was successfully performed by Wilson and co-workers [10].

EXPERIMENTAL

M.p.: uncorrected. IR: KBr pellets; in cm^{-1}. ^1H-, ^{13}C-, DEPT, $^1H,^1H$-COSY, ROESY, HMQC, HMBC NMR: Varian Inova 500 NB spectrometer, δ in ppm, J in Hz. UV: Shimadzu UV-2501PC spectrophotometer. MS: VG-ZAB-HS mass spectrometer. HRMS: VG Autospec-500 mass spectrometer.

Fungus Material and Purification. A strain of the fungus *Xylaria* sp. (no. 2508) was isolated from the seeds of an angiosperm tree in Mai Po, Hong Kong. Starter cultures were maintained on cornmeal seawater agar. Plugs of agar supporting mycelial growth were cut and transferred aseptically to a 250 mL Erlenmeyer flask containing 100 mL of liquid medium (glucose 10g/L, Peptone 2 g/L, yeast extract 1 g/L, NaCl 30 g/L). The flask was incubated at 30°C on a rotary shaker for 5–7 days. The mycelium was aseptically transferred to a 300-L fermenter containing 170 L of GYT medium, incubated at 30°C for 80 h. The 170 L cultures were filtered through cheesecloth. The filtrate was concentrated to 3.5 L below 50°C and extracted

five times by shaking with an equal volume of ethyl acetate. The combined extracts were chromatographed repeatedly on silica gel using gradient elution from petroleum to ethyl acetate to obtain xyloketal D (30 mg) and a mixture of xyloketal D and **1** from the ethyl acetate–petroleum ether (8:92) fraction. The mixture of xyloketal D and **1** was purified by reverse phase HPLC with MeOH to give colorless blocks **1** (5 mg), (1-(7-hydroxy-3,9a-dimethyl-2,3,3a,9a-tetrahydro-4H-1,9-dioxa-cyclopenta[b]naphthalen-6-yl)-ethanone, xyloketal G (**1**), $C_{15}H_{18}O_4$, M^+ 262.1190, mp 144°C. $[\alpha]_D^{25}$ –111° (*c* 0.1, $CHCl_3$).

IR spectrum (KBr, ν, cm^{-1}): 3417 (OH), 3052, 2961, 2933, 2868, 1646 (C=O), 1616, 1494 (Ph), 1367, 1286, 1205, 1166, 1136, 1002, 873, 850, 807. ^1H, ^{13}C NMR see Table 1.

Mass spectrum (FAB^+, *m/z*; I_{rel}, %): 263 (100) $[M+1]^+$, 262 (100), 247 (29), 205 (20), 203 (18), 165 (100), 147 (35), 111 (36), 97 (32), 83 (62), 55 (20). Mass spectrum (HR-ACPI) ($ACPI^+$, *m/z*; I_{rel}, %): Found: 262.1190 (50) M^+ (calc. for $C_{15}H_{18}O_4$, 262.1205), 165.0555 (100).

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