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A New Phloroglucinol Derivative from *Syzygium brachyantherum*

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Summary: A new phloroglucinol derivative, (*Z*)-1-(2,4-dihydroxy-6-methoxy phenyl) -octadec-9-en-1-one (**1**), along with a known analogue, 1-(2,4,6-trihydroxyphenyl)-1-hexadecanone (**2**), were isolated from the leaves of *Syzygium brachyantherum*. Their structures were elucidated on the basis of the spectroscopic data and comparison with the values reported. To the best of our knowledge, this is the first example of the constituents from *S. brachyantherum*.

Keywords: Myrtaceae, *Syzygium brachyantherum*, Leaves, Phloroglucinol derivative, Structural elucidation.

Introduction

The genus *Syzygium*, belonging to family Myrtaceae, comprises about 500 species, which is mainly distributed in the tropic and subtropical regions of the world [1]. Many of them have been used as edible and medicinal plants in Southeast Asian [2]. Previous reports revealed that triterpenes, hydrolysable tannins, anthocyannins, flavonoids, chromone derivatives, phenylpropanoids, and phloroglucinols derivatives are the main constituents of genus *Syzygium* [1, 3-5]. *Syzygium brachyantherum*, a shrub or small tree, is grown in Guangdong, Hainan, Guangxi, and Yunnan Provinces, People's Republic of China [6]. To the best of our knowledge, the research on the chemical constituents of *S. brachyantherum* has not been previously reported to date. Aiming to search for new bioactive compounds, the ethyl acetate extract of the leaves of *S. brachyantherum* has been studied and led to a new phloroglucinol derivative, (*Z*)-1-(2,4-dihydroxy-6-methoxy phenyl)-1-octadec -9-en-1-one (**1**) and a known analogue, 1-(2,4,6-trihydroxyphenyl)-1-hexadecanone (**2**). Herein, we present the isolation and structure elucidation of the new compound.

Experimental

General Experimental

UV spectra were acquired in MeOH with a Shimadzu UV-2401PC UV-vis spectrophotometer. IR spectra were measured on a Bruker Tensor 27 FTIR Spectrometer with KBr disks. NMR spectra were recorded on a Bruker Avance III-600 and a Bruker AM-400 instruments with TMS as internal standard. ESI-MS spectra were recorded on a Waters Xevo TQ-S UPLC Triple Quadrupole Mass Spectrometer Column chromatography was performed using silica gel (Qingdao Marine Chemical Factory, China, * 200–300 mesh), Sephadex LH-20 (Pharmacia Biotech Ltd., Sweden). Thin-layer chromatography (TLC) was performed using precoated silica gel GF_{254} plates (Qingdao Marine Chemical Factory). (Qingdao Marine Chemical Factory). Semipreparative HPLC was performed on a Hitachi Chromaster system (Hitachi, Ltd., Japan) equipped with an YMC-Triart C_{18} column (250 mm × 10 mm i.d., 5 μm, YMC Corporation, Japan), using a flow rate of 3.0 mL/min at a column temperature of 25 °C, and detection was performed with a DAD detector.

Plant Material

The leaves of *Syzygium brachyantherum* Merr. et Perry were collected in October 2012 from Xishuang Banna Prefecture, Yunnan Province, People's Republic of China, and were authenticated by Mr. Shun-Cheng Zhang, Xishuang Banna Tropical Botanical Garden, Chinese Academy of Sciences. A voucher specimen (No. Zhang 201201013) was deposited at Kunming Institute of Botany, Chinese Academy of Sciences.

Isolation

The leaves of *S. brachyantherum* (2.0 kg) were extracted with 70% aqueous acetone (8 L × 3) at

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room temperature. The extracts were concentrated by rotary evaporator under reduced pressure to remove organic solvent. The aqueous residue was then partitioned with petroleum ether (4 × 1 L), EtOAc (4 × 1 L), and n-BuOH (4 × 1 L), sequentially. The EtOAc extract (25.0 g) was subjected to silica gel column chromatography (CC) using a gradient system of $CHCl_3$-CH_3OH (1:0−0:1) to afford three fractions (Fr A−C).

Fraction B (5.4 g) was further chromatographed on silica gel column using a gradient system of petroleum ether (PE)-Me_2CO (20:1−1:1) to afford three subfractions Fr B1−B3, then fraction B1 (1.3 g) was separated by silica gel column using a isocratic system of $CHCl_3$-CH_3OH (3:2) to get two subfractions Fr B1-1−2. Fr B1-1-1 (0.6 g) was further purified by semipreparative HPLC (MeOH–H_2O 90:10) to yield compound **1** (21.0 mg, t_R = 61.0 min). Fr B2 (1.1 g) was chromatographed on Sephadex LH-20 column ($CHCl_3$-MeOH, 3:2), followed by semipreparative HPLC (MeOH–H_2O 87:13) to give compound **2** (4.0 mg, t_R = 47.5 min).

Results and Discussion

Compound **1** was isolated as a red gum. The HR-ESI-MS (*m/z* 403.2854 [M - H]$^-$, calcd. 403.2854) gave its molecular formula $C_{25}H_{40}O_4$. Strong UV absorptions at 206 nm and 289 nm implied it had a large conjugated system. IR spectrum displayed the presence of hydroxyl (3291 cm^{-1}), alkyl (2923 and 2853 cm^{-1}), and aromatic ring (1624 cm^{-1}). The ^{1}H NMR experiment disclosed two aromatic hydrogens (δ_H 6.04, s; 5.96, s), a terminal methyl (δ_H 0.87, t, J = 6.8 Hz), and a methoxy group (δ_H 3.90, s). Combining the olefinic signals at δ_H 5.35 (2H, m) in the ^{1}H NMR spectrum with the olefinic signals at δ_C 130.7 and 130.6 in the ^{13}C NMR spectrum indicated the existence of two monosubstituted sp^2 methines. Additionally, a significant down-fielded signal of hydroxyl (δ_H 13.99, s) caused by the intramolecular hydrogen bond suggested a hydroxyl at C-2' (Fig1). The ^{13}C NMR spectra demonstrated 25 carbon signals, including a ketonic carbon (δ_C 206.2), two olefinic carbons (δ_C 130.7 and 130.6), six aromatic carbons (δ_C 91.9, 96.9, 105.8, 164.6, 165.5, and 168.6), fourteen methylenes (δ_C 23.4−44.8), a methoxyl (δ_C 56.2), and a methyl (δ_C 14.4). Moreover, an octadecanoyl side chain in **1** was detected by NMR and MS data. The position of substituents were assigned as shown (Fig 2) based on the 2D NMR (HSQC, COSY, and HMBC) correlations from H-3′ (δ_H 5.96) to C-1′ (δ_C 105.8), C-4′ (δ_C 165.5), and C-5′ (δ_C 91.9), from H-5′ (δ_H 6.04) to C-1′ (δ_C 105.8) and C-3′ (δ_C 96.9), from OMe (δ_H 3.90) to C-6′ (δ_C 164.6), and from H-2 (δ_H 2.98) and H-3 (δ_H 1.64) to C-1 (δ_C 206.2), combining with the resonance of C-1′ (δ_C 105.8), revealing that the aliphatic chain was fixed at C-1′ [2]. All NMR data of **1** resemble those of the known compound, jambone C [2], except for the occurrence of two olefinic carbons (δ_C 130.7 and 130.6) in **1** instead of four olefinic ones (δ_C 129.0−130.8) in jambone C. The location of the double bond at C-9 and C-10 in the aliphatic chain in **1** was deduced by the HMBC cross peaks (Fig 2) from H-7 (δ_H 1.33) to C-9 (δ_C 130.7), and from H-12 (δ_H 1.33) to C-10 (δ_C 130.6). The correlations of H-18/H-17/H-16, H-8/H-9/H-10/H-11, and H-2/H-3 observed in the ^{1}H-^{1}H correlation spectroscopy (COSY) experiment (Fig 2) confirmed the above deductions. The geometry of the olefinic bond was presumed to be *Z* configuration, which was proved by the resonances of carbons C-8 (δ_C 27.9) and C-11 (δ_C 27.9). Generally, the chemical shift of carbons next to a *cis* double bond arise at δ_C 27−28, whereas those of a *trans* ones appear at δ_C 32−33 [7, 8]. Consequently, the structure of **1** was assigned as (*Z*)-1-(2,4-dihydroxy-6- methoxyphenyl)-1-octadec-9-en-1-one.

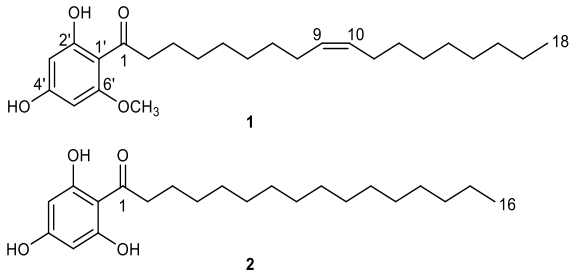
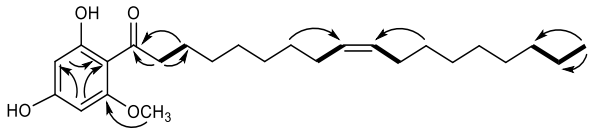


Fig. 1: The chemical structures of compounds **1−2.**



COSY —— HMBC H ⌒ C

Fig. 2: Key 2D NMR correlations of **1**.

Known compound was identified to be 1-

(2,4,6-trihydroxyphenyl)-1-hexadecanone (**2**) [9] by comparing its spectroscopic data with those reported values.

(Z)-1-(2,4-dihydroxy-6-methoxyphenyl)-1-octadec-9-en-1-one (**1**)

Red gum (CH_3OH). IR (KBr): 3291, 3006, 2923, 2853, 1624, 1568, 1493, 1453, 1273, 1204, 1161, 1116, 955, 824 cm^{-1}; UV λ_{max} (MeOH) nm (log ε): 206 (3.45), 221 (3.48), 289 (3.59); HR-ESI-MS: *m/z* 403.2854 $[M - H]^-$ ($C_{25}H_{40}O_4$ – H, calcd. 403.2854); ^1H NMR (400 MHz, acetone-*d*) and ^{13}C NMR (100 MHz, acetone-*d*) Table-1.

Table-1: ^1H, ^{13}C NMR and HMBC Data for compound 1 in acetone-*d* (δ ppm).

C	δ_C[a]	δ_H[b]	HMBC
1	206.2 s		
2	44.8 t	2.98 (t, 2H, *J* = 6.9 Hz)	C-1,3
3	25.7 t	1.64 (m, 2H)	C-1,2,4
4 ~ 7	29.4 ~ 30.6 t	1.29 ~ 1.35 (m, 8H)	
8	27.9 t	2.06 (m, 2H)	C-9,10
9	130.7 d	5.36 (m, 1H)	C-7,8,11
10	130.6 d	5.36 (m, 1H)	C-8,11,12
11	27.9 t	2.06 (m, 2H)	C-9,10
12 ~ 15	29.4 ~ 30.6 t	1.29 ~ 1.35 (m, 8H)	
16	32.7 t	1.27 (m, 2H)	C-17,18
17	23.4 t	1.29 (m, 2H)	C-16,18
18	14.4 q	0.87 (t, 3H, *J* = 6.9 Hz)	C-16,17
1'	105.8 s		
2'	168. 6 s		
3'	96.9 d	5.96 (s, 1H)	C-1',5'
4'	165.5 s		
5'	91.9 d	6.04 (s, 1H)	C-1',3'
6'	164.6 s		
OCH_3	56.2 q	3.90 (s, 3H)	C-6'
2'-OH		13.99 (s, 1H)	

[a] Recorded at 100 MHz. [b] Recorded at 400 MHz.

1-(2,4,6-trihydroxyphenyl)-1-hexadecanone (**2**)

Red gum (CH_3OH). ESI-MS: *m/z* 363 $[M - H]^-$ ($C_{22}H_{36}O_4$ – H); ^1H NMR (600 MHz, acetone-*d*) δ: 5.92 (2H, s, H-3',5'), 3.05 (2H, t, *J* = 7.4 Hz, H-2), 1.27 ~ 1.33 (24H, m, H-4 ~ 15), 1.65 (2H, m, H-3), 0.86 (3H, t, *J* = 6.8 Hz, H-16); ^{13}C NMR (150 MHz, acetone-*d*) δ: 206.2 (C-1), 165.0 (C-2',6'), 164.9 (C-4'), 105.0 (C-1'), 95.6 (C-3', 5'), 44.4 (C-2), 32.6 (C-14), 29.4-30.3 (C-4 ~ 14), 25.5 (C-3), 23.3 (C-15), 14.3 (C-16).

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