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Sundaixanthone A from the stem bark of *Calophyllum sundaicum* P. F. Stevens

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Abstract

Sundaixanthone A, a new compound from the class of xanthone was isolated from *Calophyllum sundaicum* collected in Sarawak, Malaysia. The compound was characterized using NMR techniques, and identified as 12-(2,3-dihydroxy-3-methylbutyl)-5,10-dihydroxy-2,2-dimethyl-2H,6H-pyrano [3,2-*b*] xanthen-6-one.

1. Introduction

The *Calophyllum sundaicum* P.F. Stevens tree belongs to the *Calophyllum* genus, one of the largest genera within the Calophyllaceae family. It is a tall tree commonly found in low ground peat swamps up to 40 meters above sea level. The name 'sundaicum' originates from the areas where *C. sundaicum* was frequently found, previously part of Sundaland. Additionally, Malaysian locals refer to this species as 'bintangor batu' (Stevens, 1980). This evergreen tree is mainly distributed in Southern Peninsula Malaysia, Singapore, Borneo (Sarawak, Brunei, West Kalimantan), and Sumatera Island (Stevens, 1980); (Gunawan et al., 2012); (Randi et al., 2014); (Zamri & Slik, 2018); (Seah et al., 2019). It blooms between June and September, bearing greenish fruits in March and May (Stevens, 1980).

Previous scientific studies on this species have reported the isolation of two new polyprenylated acylphloroglucinol derivatives from the leaves, named sundaicumones A and B, found as colorless oil. Both compounds exhibited weak activity towards the glucocorticoid receptor (Cao et al., 2006).

The research conducted on the stem bark of *C. sundaicum* P. F. Stevens, gathered from Sarawak, Malaysia, is focused in exploring its chemical composition. This investigation resulted in the identification of a novel compound named sundaixanthone A (Fig. 1). The structure of the compound was determined through detailed analysis using 1D and 2D NMR techniques.

2. Result and Discussion

Sundaixanthone A was isolated as a pale yellow amorphous. The ^{1}H NMR spectra (Figure S1) showed signals for a chelated hydroxyl group (δH 13.19), and a broad singlet belongs to lone OH (δH 9.10). The two olefinic protons (δH 5.78 and 6.73) and two singlet protons (δH 1.51 and 1.52) formed a 2,2-dimethylpyran ring. A system of three mutually coupled aromatic protons at δH 7.29, 7.33, and 7.66 which was also observed in the COSY spectrum (Figure S2). A comparison (Table 1) was made between the 1D NMR spectral data of sundaixanthone A and trapezifolixanthone, suggesting that the new compound has a similar skeleton to trapezifolixanthone. The remaining protons were assigned to a 2,3-dihydroxy-3-methylbutyl chain and was further proven by the HSQC and HMBC experiments. In addition, the spectral data of 2,3-dihydroxy-3-methylbutyl chain was compared with literature (Table 1), confirming the presence of this moiety.

The C = O signal was observed as the most shifted quartenary carbon peak at δC 181.2 in the ^{13}C NMR spectrum (Figure S3). The DEPT (45, 135) experiments indicated a total of twelve quartenary carbons, six

methine carbons, a methylene carbon and four methyl carbons which in accordance with molecular formula $C_{23}H_{24}O_7$. Correlations among the protons and their corresponding carbons were established in the COSY and HMBC spectra (Fig. 2). The protons were assigned to their respective carbons according to HSQC spectrum (Figure S4).

The HMBC spectrum of sundaixanthone A illustrated in Figure S5 shows the connectivity between the protons and carbons in the range of two to four bonds. The aromatic proton appearing at δH 7.33 (H-6) was correlated with carbons at δC 116.1 (C-8), 145.9 (C-5a), and 147.1 (C-5), while the proton appearing at δH 7.29 (C-7) was correlated with δC 116.1 (C-8), 121.9 (C-8a), 121.4 (C-6), 145.9 (C-5a), and 147.1 (C-5). Meanwhile, the proton at δH 7.66 (H-8) gave correlation with C-6, C-5a, and C-9, thus, establishing the nature of the ring. The cross-peaks of respective H-10 with C-1, C-2, and C-3, and H-11 with C-2 agreed with a linear arrangement of the pyrano unit.

The signal of the chelated OH group at δH 13.19 with carbons at δC 104.0, 105.1, and 156.6 suggested its location at C-1. The correlation between proton H-1' with C-3, C-4, C-4a allowed the position of the 2,3-dihydroxy-3-methylbutyl chain at C-4 of the xanthone moiety. Thus, this compound was established as 12-(2,3-dihydroxy-3-methylbutyl)-5,10-dihydroxy-2,2-dimethyl-2*H*,6*H*-pyrano[3,2-*b*] xanthen-6-one, with a trivial name, sundaixanthone A.

Table 1

Comparison of ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectral data of **sundaixanthone A** in acetone-d_6 with trapezifolixanthone skeleton (*) and 2,3-dihydroxy-3-methylbutyl chain (**).

No.	δ ^{13}C (ppm)	δ ^{13}C (ppm)*	δ ^{13}C (ppm)**	δ ^{1}H (Mult. *J* Hz. int)	δ ^{1}H (Mult. *J* Hz. int)*	δ ^{1}H (Mult. *J* Hz. int)**
1	156.6	156.0		13.19 (*s*, 1H, -OH)	13.33 (*s*, OH)	
2	105.1	104.7				
3	159.4	158.2				
4	107.9	107.4				
4a	155.5	153.7				
5	147.1	144.4		9.10 (*s*, 1H, -OH)	9.24 (*s*, OH)	
5a	145.9	144.2				
6	121.4	119.7		7.33 (*dd*, 1.9, 7.8, 1H)	7.39 (*dd*, 1.5, 7.9, 1H)	
7	125.0	123.9		7.29 (*t*, 7.8, 1H)	7.28 (*d*, 7.9, 1H)	
8	116.1	116.8		7.66 (*dd*, 1.9, 7.8, 1H)	7.69 (*dd*, 1.5, 7.9, 1H)	
8a	121.9	120.9				
9	181.2	181.1				
9a	104.0	103.3				
10	116.1	115.7		6.73 (*d*, 10.0, 1H)	6.71 (*d*, 10.0, 1H)	
11	128.8	127.4		5.78 (*d*, 10.0, 1H)	5.77 (*d*, 10.0, 1H)	
12	79.2	78.3				
13	28.6	28.3		1.51 (*s*, 3H)	1.51 (*s*, 3H)	
14	28.5	28.3		1.52 (*s*, 3H)	1.51 (*s*, 3H)	
1'	26.2		26.0	2.99 (*dd*, 8.7, 13.5, 1H) 3.21 (*d*, 13.5, 1H)		2.61 (*dd*, 10.0, 15.0, 1H) 3.37 (*d*, 15.0, 1H)

No.	δ ^{13}C (ppm)	δ ^{13}C (ppm)*	δ ^{13}C (ppm)**	δ ^{1}H (Mult. *J* Hz. int)	δ ^{1}H (Mult. *J* Hz. int)*	δ ^{1}H (Mult. *J* Hz. int)**
2'	79.3		80.6	3.74 (*m*, 1H) 4.20 (*s*, 1H, -OH)		3.74 (*dd*, 7.0,8.0, 1H)
3'	74.0		73.2			
4'	26.6		26.7	1.33 (*s*, 3H)		1.36 (*s*, 3H)
5'	24.7		22.2	1.33 (*s*, 3H)		1.49 (*s*, 3H)

Lizazman et al., 2023*; measured in acetone-d_6, 400 MHz (^{1}H) and 100 MHz (^{13}C)

Guilet et al., 2001**; measured in $CDCl_3$, 500 MHz (^{1}H) and 67.5 MHz (^{13}C)

3. Experiment Section

3.1. General

The NMR spectra were recorded on BRUKER spectrophotometer in acetone-d_6 at 400 (^{1}H), 100 (^{13}C) MHz with TMS as the internal standard. The column chromatography and radial chromatography were carried out using silica gel 60 Cat. No. 1093851000 (Merck) and silica gel 60 Cat. No. 1077491000 (Merck). Thin layer chromatography was carried out using TLC silica gel 60 F254 aluminium sheet Cat. No. 1055540001 (Merck). The TLC plate was visualized under UV light at 254 nm and 365 nm.

3.2. Plant Material

The stem bark of *C. sundaicum* P. F. Stevens was collected in 2021 from Semengok, Sarawak, Malaysia. The plant was identified by Mr. Tinjan anak Kuda, a botanist from the Forest Department, Sarawak.

3.3. Extraction and Isolation

Approximately 1.5 kg of powdered stem bark from *C. sundaicum* was extracted three times with 6 L of *n*-hexane at room temperature over a period of 72 hours. The resulting combined *n*-hexane extract was concentrated under reduced pressure using a BUCHI rotavapor R-215, resulting in 27.7 g of dried crude extract. The crude extract was then subjected to silica gel column chromatography (CC) using *n*-hexane as the initial solvent, followed by elution with mixtures of *n*-hexane and EtOAc (ranging from 90:10 to 0:100), resulting in 11 fractions (CSuH1-11). Fraction CSuH7-8 was further isolated using Sephadex LH-20 CC and eluted with 100% MeOH to obtain 6 subfractions (CSuH78A-F). Purification of subfractions CSuH78D-F using chromatotron elution with 100% dichloromethane yielded 4.3 mg of sundaixanthone A in the form of pale yellow amorphous.

4. Conclusion

The isolation of the *n*-hexane extract from *C. sundaicum* stem bark has led to the discovery of a new compound, sundaixanthone A. The unique structure of the compound makes it a promising subject for further investigation.

Declarations

Conflict of Interest:

The authors declare no conflict of interest.

Author Contributions:

MAL has contributed to writing - original draft preparation resources, and VJYM conceptualization writing - review, supervision, and funding acquisition.

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Figures

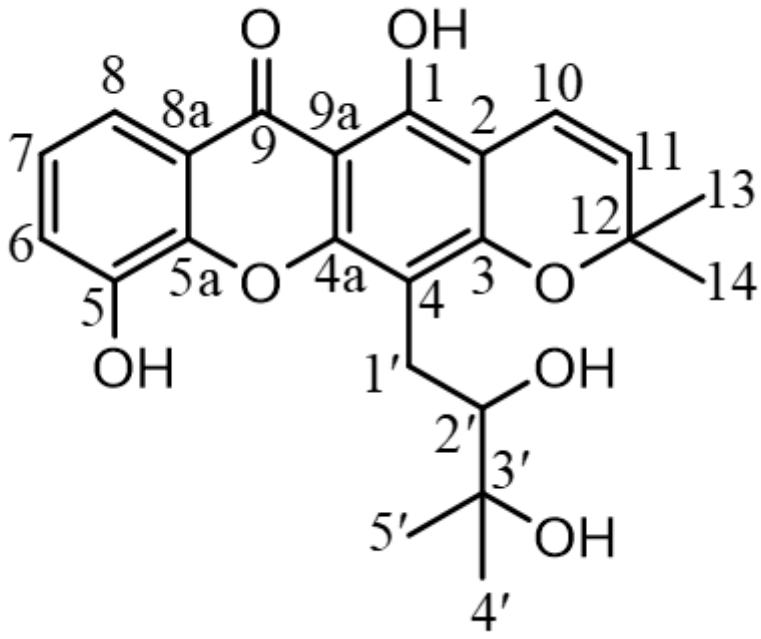


Figure 1

The structure of sundaixanthone A

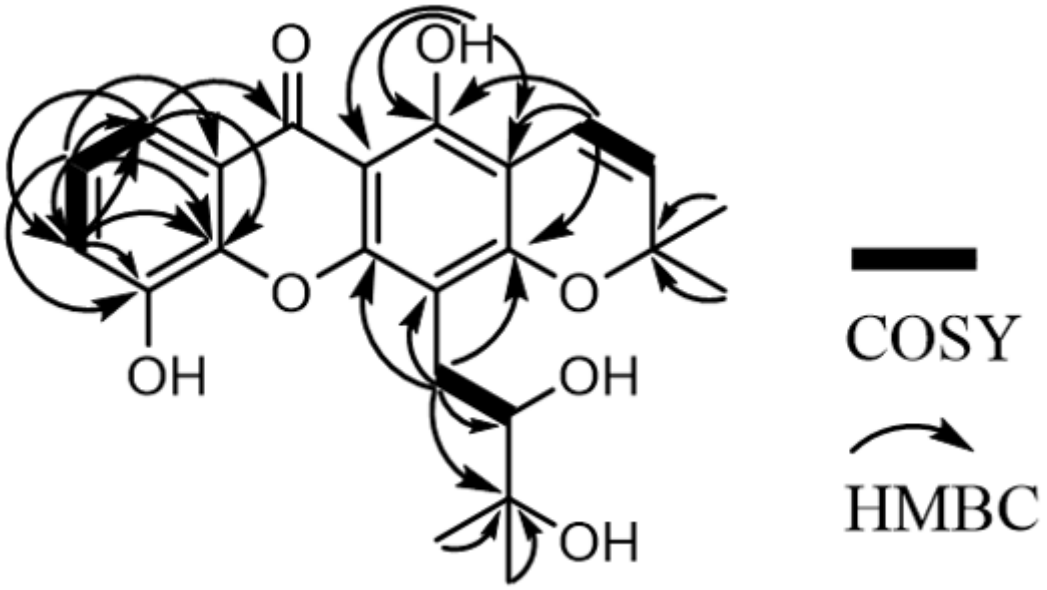


Figure 2

HMBC correlations and COSY couplings for sundaixanthone A

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