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Dulxanthone E: a pyranoxanthone from the leaves of *Garcinia dulcis*

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Abstract

A pyranoxanthone, dulxanthone E isolated from *Garcina dulcis*, was elucidated as 5,9,10,12-tetramethoxy-2,2-dimethyl-2H-pyrano[5,6-b]xanthen-6-one by various NMR techniques and confirmed by X-ray crystallography.

Keywords: *Garcina dulcis*; Guttiferae; Xanthone; 5,9,10,12-Tetramethoxy-2,2-dimethyl-2H-pyrano[5,6-b]xanthen-6-one

1. Introduction

Species belonging to the genus *Garcina* are a rich source of aromatic metabolites, e.g., flavonoids, benzophenones and xanthones. The bark, branches, leaves and roots of *Garcina dulcis* (Roxb.) Kurz were previously reported to contain flavonoids, xanthones and benzophenone–xanthone dimers (Harrison, Leong, Leong, Sia, Sim & Tan, 1994; Iinuma, Ito, Tosa & Tanaka, 1996a,b,c; Ito, Miyamoto, Nakayama, Kawai, Rao, & Furukawa, 1997; Likhitwittayawuid, Chanmahasathien, Ruangrugsi, & Krungkra, 1998). In Indonesia, the leaves and seeds of this plant have been used for the treatment of lymphatitis, parotitis and struma (Likhitwittayawuid et al., 1998). We report herein the investigation of the leaves of this plant which resulted in the isolation of a minor pyranoxanthone, dulxanthone E, and friedelin.

2. Results and discussion

Dulxanthone E, isolated from the chromatographic separation of the hexane extract of the leaves of *G. dulcis* as yellow cubic crystals, mp 191–192°C, $C_{22}H_{22}O_7$ (*m*/*z* 398.13612), had UV [272 (4.20), 320 (3.75) nm] and IR (1654, 1612, 1589, 1475, 1429, 1288 cm^{-1}) spectral data, which were suggestive of a xanthone derivative. In the ^{1}H-NMR spectrum, two one-proton doublets (δ 6.96 and 7.99 ppm, each $J =$ 9.1 Hz) were observed in addition to four methoxyl singlets (δ 3.91, 3.98, 4.00 and 4.08 ppm). The spectrum further showed the presence of two methyl groups in a singlet (1.53 ppm) and two *cis*-olefinic protons as doublets (δ 5.72 and 6.74 ppm, each $J = 10.1$ Hz), implying the presence of a dimethylchromene ring. All protonated carbons of dulxanthone E were assigned by the HMQC spectrum. In the HMBC spectrum, one of two *ortho*-coupled protons at 7.99 ppm was correlated to the two *O*-function quaternary carbons at δ 156.7 and 151.2 ppm and the carbonyl carbon at δ 174.7 ppm, and the other at δ 6.96 ppm was also correlated to two quaternary carbons at δ 117.3 and 136.2 ppm. The methoxyl groups at δ 4.00 and

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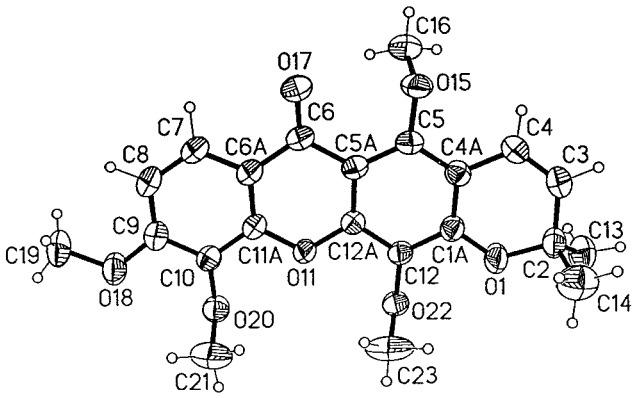
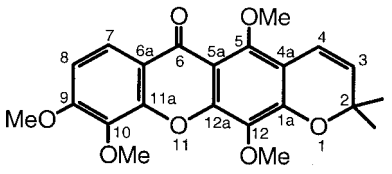


Fig. 1. X-ray structure of dulxanthone E.

4.08 ppm showed a ^3J correlation to the quaternary carbons at 156.7 and 136.2 ppm, respectively. These results indicated that dulxanthone E is a 5,6-dimethoxyxanthone derivative, which was further supported by NOE results. Irradiation of the methoxyl singlet at 4.00 ppm caused NOE enhancements of one of *ortho*-coupled protons at 6.96 ppm and the methoxyl singlet at 4.08 ppm. The other aromatic ring, therefore, bears two methoxyl groups and the dimethylpyran ring. Irradiation of the methoxyl group at δ 3.91 ppm caused an NOE enhancement of the more deshielded pyran proton at 6.74 ppm. Saturation of H-4 caused NOE enhancements of the methoxyl group at δ 3.91 ppm and the less deshielded pyran proton at δ 5.72 ppm (H-3), indicating that the pyran ring was fused in a linear form to the xanthone nucleus. Therefore, the two methoxyl groups at δ 3.91 ppm and 3.98 ppm were attached to C_5 and C_{12} giving either **1** or **2** as the structure for dulxanthone E. Structure **1** with the phloroglucinol substitution pattern of ring A of xanthones is favoured on biogenetic grounds and this was confirmed by a single crystal X-ray crystallographic study (Fig. 1).



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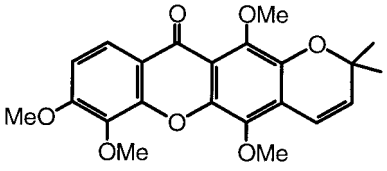

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Table 1
NMR data for compound **1**

Position	H[a]	^{13}C[b]	DEPT	HMBC[c]	NOE
2		77.8	C		
3	5.72 *d* (10.1)	130.1	CH	2, 4a	4, 2-Me
4	6.74 *d* (10.1)	121.8	CH	1a, 2, 5	3, 5-OMe
4a		112.4	C		
5		151.5	C		
5a		110.0	C		
6		174.7	C		
6a		117.3	C		
7	7.99 *d* (9.1)	108.4	CH	6a, 10	7, 9-OMe
8	6.96 *d* (9.1)	116.2	CH	6, 9, 11a	8
9		156.7	C		
10		136.2	C		
11a		151.2	C		
12a		156.7	C		
12		132.8	C		
1a		151.3	C		
2-Me	1.53 *s*	28.2	CH_3	2, 3	3
5-OMe	3.91 *s*	56.3	CH_3	5	4
9-OMe	4.00 *s*	61.3	CH_3	9	8, 10-OMe
10-OMe	4.08 *s*	61.3	CH_3	10	9-OMe
12-OMe	3.98 *s*	62.7	CH_3	12	

[a] Recorded in $CDCl_3$ at 300 MHz.
[b] Recorded in $CDCl_3$ at 75 MHz.
[c] Carbons that correlate with the proton resonance.

3. Experimental

3.1. General

EIMS were determined on a Micromass VG 7035 mass spectrometer at 70 eV. NMR spectra were recorded on Bruker ACF 300 [300 MHz (^{1}H) and 75 MHz (^{13}C)] and AMX 500 [500 MHz (^{1}H) and 125 MHz (^{13}C) instruments using $CDCl_3$ solutions with TMS as an internal standard. IR spectra were recorded on a Bio-Rad FTIR spectrophotometer and UV spectra were recorded on a Hewlett-Packard 8452A diode array spectrophotometer. Chromatographic separations were carried out on silica gel 60 (63–100 μm).

3.2. Plant material

The leaves of *Garcina dulcis* were collected in Bogor, Indonesia in 1997. A voucher specimen is deposited in the Chemistry Department of the University of Indonesia.

3.3. Extraction and isolation

The air-dried leaves (1 kg) were soaked in *n*-hexane for a week and the extract was removed. This was repeated twice and the combined hexane extracts were concentrated to give a green residue (37.2 g) which was fractionated into an acidic and a neutral fraction

(14.5 g). Column chromatography of the neutral fraction on silica gel yielded friedelin (0.10 g), characterised by comparison with an authentic specimen, and a yellow crystalline solid, dulxanthone E (0.25 g) which was recrystallised from ethyl acetate to give dulxanthone E (**1**), yellow cubes, mp 191–2°C. EI-HRMS: m/z 398.13612, $C_{22}H_{22}O_7$ requires 398.13657. EIMS m/z: 398 $[M]^+$ (69.8%), 383 (100%), 368 (42.0%), 366 (49.6%), 352 (59.0%), 339 (18.8%), 231 (11.2%), 184 (54.3%), 117 (25.1%). IR (KBr) V_{max} 1654, 1612, 1589, 1475, 1429, 1288 cm^{-1}. UV (MeOH) λ_{max} (log ε) 272 (4.20), 320 (3.75) nm. ^{1}H- and ^{13}C-NMR, Table 1.

*3.3.1. Crystal data for dulxanthone E (**1**)*

$C_{22}H_{22}O_7$, $M = 398.4$, monoclinic, space group P2(1)/c, a = 10.5579(3), b = 15.4847(5), c = 12.3094(4) Å, $\beta = 104.743(1)$, $V = 1946.1(1)$ $Å^3$ ($\lambda = 0.71073$ Å), $Z = 4$, $D_{calc} = 1.360$ g cm^3, $F(000) = 840$, $\mu = 0.102$ mm^{-1}. Crystal size was $0.5 \times 0.43 \times 0.23$ mm^3. Frame data were collected at 293(2) K in the range 2.63 to 29.12° ($-13 \leqslant h \leqslant 13$; $-20 \leqslant k \leqslant 17$: $-16 \leqslant l \leqslant 9$) on a Siemens SMART CCD system and processed. The processed hkl data were absorption corrected using the program SADABS. Anisotropic thermal parameters were refined for all the non-hydrogen atoms. All the hydrogen atoms were located in the difference Fourier routines. The positional and individual isotropic thermal parameters were refined for all the hydrogen atoms. In the least squares-refinement cycles on F^2, the model converged $R_1 = 0.0430$, $wR_2 = 0.1114$ and GOF = 1.054 for 3492 reflections with $F_o > 4\sigma(F_o)$ and 351 parameters. In the final difference Fourier synthesis, the electron density fluctuates in the range 0.266 to -0.249e $Å^{-3}$. Atomic coordinates, bond lengths and angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC 132629).

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