Dulxanthones F−H, Three New Pyranoxanthones from *Garcinia dulcis*

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Three new pyranoxanthones, dulxanthones F−H (**1**−**3**), have been isolated from the leaves of *Garcinia dulcis*. Their structures have been determined on the basis of extensive NMR studies.

Extensive phytochemical studies have shown that *Garcinia* species are rich in a variety of oxygenated and prenylated xanthones.[1] Some of these exhibit a wide range of biological and pharmacological activities, for example, cytotoxic,[2,3] antimicrobial,[4] antifungal,[5,6] antioxidant,[7,8] antimalarial,[9,10] and HIV-1 protease inhibitory activity.[11] The bark, branches, leaves, and roots of *Garcinia dulcis* (Roxb.) were previously reported to contain flavonoids, xanthones, and benzophenone−xanthone dimers.[10,12−16] In Indonesia, the leaves and seeds of this plant have been used for the treatment of lymphatitis, parotitis, and struma.[10] Further investigation on the hexane extract of the leaves of *G. dulcis* has resulted in the isolation of three new pyranoxanthones, dulxanthones F (**1**), G (**2**), and H (**3**). The structure elucidation of these three pyranoxanthones is reported herein.

Compound **1**, dulxanthone F, obtained as a yellow powder, mp 152.0−153.0 °C, $C_{21}H_{20}O_7$ (*m*/*z* 384.11928), had UV and IR spectral data suggestive of a xanthone derivative. In the ^{1}H NMR spectrum, one chelated phenolic hydroxyl group [δ 13.64 (1 H, s, 5-OH)] and two one-proton aromatic singlets [δ 6.36 (1 H, s, 12-H) and 6.39 (1 H, s, 8-H)] were observed, in addition to three methoxyl groups [δ 3.91 ppm (3 H, s, 10-OMe) and 4.01 (6 H, s, 7-, 9-OMe)]. The spectrum further showed the presence of two methyl groups in a singlet (δ 1.52) and two *cis*-olefinic protons in doublets [(δ 6.71 (1 H, d, J = 10.0 Hz, 4-H) and 5.57 (1 H, d, J = 10.0 Hz, 3-H)], implying the presence of a dimethylchromene ring. Irradiation of one of the dimethylchromene protons at δ 6.74 caused an NOE enhancement of the chelated hydroxyl group at δ 13.64. This suggested that the dimethylpyran ring was fused in a linear fashion to the xanthone nucleus. The orientation of the dimethylchromene ring was precisely determined by 2D NMR techniques (HMQC and HMBC). In the HMBC spectrum (Table 1), cross-peaks between the chelated hydroxyl group and C-5 (δ 157.82), C-4a (δ 104.81), and C-5a (δ 103.42) and between C-4a and the *cis*-olefinic protons were observed; C_{1a} (δ 160.06) was correlated not only with one of the *cis*-olefinic protons at δ 6.71 but also with the aromatic singlet at δ 6.34. The positioning of the three methoxyl groups on the xanthone ring was deduced as follows. An NOE was observed between the methoxyl group at δ 4.01 and the aromatic singlet at δ 6.39. On the other hand, in the HMBC spectrum, cross-peaks between the aromatic singlet at δ 6.39 and C-7 (δ 157.40), C-9 (δ 158.07), C-6a (δ 105.45), and C-10 (δ 130.29) were observed. Dulxanthone F was thus characterized as 5-hydroxy-7,9,10-trimethoxy-2,2-dimethyl-2-H-pyrano[5,6-b]xanthen-6-one.

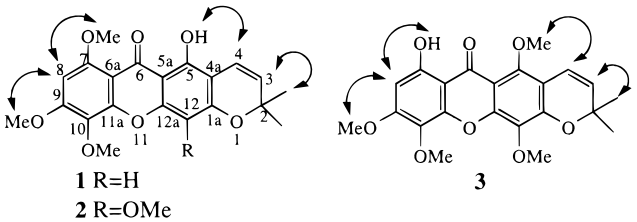

Figure 1. Selected NOE correlations for compounds **1**, **2**, and **3**.

Dulxanthone G (**2**), isolated as yellow needles, mp 182.5−184.0 °C, had a molecular formula $C_{22}H_{22}O_8$ on basis of its HREIMS (414.13365; calcd 414.13147). UV and IR data suggested that **2** also had a xanthone skeleton. A comparison of the ^{1}H and ^{13}C NMR data of **2** with those of **1** revealed that the only difference was the substituent at C-12, the proton in **1** replaced by the methoxyl group in **2**. This structure assignment was confirmed by its HMBC (Table 1) and NOE difference (Figure 1) spectra.

Compound **3**, dulxanthone H, $C_{22}H_{22}O_8$ (*m*/*z* 414.1337), also had spectral characteristics of a chromenoxanthone. Its ^{1}H and ^{13}C NMR spectra were very similar to those of **2**. Irradiation of the aromatic singlet at δ 6.37, however, caused NOE enhancements of the chelated hydroxyl group at δ 13.22 and the methoxyl group at δ 3.94, which suggested that the chelated hydroxyl group at δ 13.22 must be attached to C-7 with two methoxyl groups at C-9 and C-10 and one aromatic singlet at C-8. The other aromatic ring, therefore, bears the other two methoxyl groups and the dimethylpyran ring. Irradiation of the methoxyl group at δ 3.91 caused an NOE enhancement of one of the dimethylchromene protons at δ 6.73, indicating that the dimethylpyran ring is fused in a linear fashion to the xanthone nucleus. Comparison of the NMR data of **3** with those of dulxanthone E, whose structure had been confirmed by X-ray crystallography,[16] showed both compounds to have the same aromatic-ring substituent pattern. Therefore, dulxanthone H can be assigned as 7-hydroxy-5,9,10,12-tetramethoxy-2,2-dimethyl-2-H-pyrano[5,6-*b*]xanthen-6-one.

Experimental Section

General Experimental Procedures. 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

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Table 1. NMR Data for Dulxanthone F (**1**), G (**2**), and H (**3**)

	dulxanthone F (**1**)		dulxanthone G (**2**)		dulxanthone H (**3**)	
position	H[a]	HMBC[b]	H[a]	HMBC[b]	H[a]	HMBC[b]
3	5.57 d (10.0)	2, 4a	5.59 d (10.0)	2, 4a	5.73 d (10.0)	2, 4a
4	6.71 d (10.0)	1a, 2, 5	6.74 d (10.0)	1a, 2	6.73 d (10.0)	1a, 2, 5
8	6.39 s	6a, 7, 9, 10	6.39 s	6a, 7, 9, 10	6.37 s	6a, 7, 9
12	6.36 s	1a				
2-Me	1.52 s	2	1.52 s	2	1.54 s	2
5-OH or5-OMe	13.64 s	4a, 5, 5a	13.34 s	4a, 5, 5a	3.91 s	5
7-OMeor 7-OH	4.01 s	7	4.02 s	7	13.22 s	6a, 7, 8
9-OMe	4.01 s	9	4.02 s	9	3.94 s	9
10-OMe	3.91 s	10	3.95 s	10	4.00 s	10
12-OMe			3.98 s	12	3.96 s	12

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

Table 2. ^{13}C NMR Assignment for Dulxanthones F (**1**), G (**2**), and H (**3**)[a]

c	**1**	**2**	**3**
1a	160.06	152.99	152.21
2	78.00	78.28	78.23
3	127.21	127.30	130.38
4	115.63	115.79	116.01
4a	104.81	104.94	112.64
5	157.82	153.35	151.21
5a	103.42	103.00	108.66
6	180.72	180.79	180.23
6a	105.45	105.29	103.16
7	157.40	157.84	159.10
8	91.46	91.60	94.84
9	158.07	157.30	159.10
10	130.29	130.57	130.38
11a	151.53	148.53	148.31
12a	156.03	151.43	151.34
12	94.63	127.96	132.86
2-Me	28.36	28.28	28.34
5-OH or 5-OMe			61.45
7-OMe or 7-OH	56.40	56.40	
9-OMe	56.40	56.40	56.31
10-OMe	61.59	61.54	61.45
12-OMe		61.54	62.88

[a] All spectra recorded in $CDCl_3$ at 75 MHz.

Hewlett-Packard 8452A diode array spectrophotometer. Chromatographic separations were carried out on Si gel 60 (63−100 μm).

Plant Material. The leaves of *G. dulcis* (Guttiferae) were collected in Bogor, Indonesia, in 1997. A voucher specimen (GDT-99) has been deposited in the Chemistry Department of the University of Indonesia.

Extraction and Isolation. The air-dried leaves (600 g) were soaked in *n*-hexane for a week, and the extract was concentrated to give a residue (12.0 g) that was subjected to column chromatography on Si gel with hexane−ethyl acetate (85:15) to afford four yellow pyranoxanthones, dulxanthone E (30 mg),[16] a mixture (40 mg) of dulxanthone F and dulxanthone G, and dulxanthone H (**3**) (6 mg). The mixture (20 mg) was separated on Si gel preparative TLC to give dulxanthone F (**1**) (9 mg) and dulxanthone G (**2**) (8 mg).

Dulxanthone F (1): yellow needles (EtOAc); mp 152.0−153.0 °C; UV (MeOH) λ_{max} (log ϵ) 216 (4.90), 235 (4.83), 276 (5.05), 333 (4.77) nm; IR (KBr) ν_{max} 3434, 1654, 1637, 1605, 1568, 1515, 1466, 1295, 1183, 1089 cm^{-1}; EIMS *m/z* 384 $[M]^+$, 369, 339, 325, 240, 177, 163, 93, 43; HREIMS *m/z* 384.11928 (calcd for $C_{21}H_{20}O_7$, 384.12091); ^1H and ^{13}C NMR assignments are found in Tables 1 and 2.

Dulxanthone G (2): yellow needles (EtOAc); mp 182.5−184.0 °C; UV (MeOH) λ_{max} (log ϵ) 222 (5.38), 276 (5.65), 342 (5.39) nm; IR (KBr) ν_{max} 3461, 1659, 1647, 1618, 1569, 1516, 1474, 1319, 1265, 1159 cm^{-1}; EIMS *m/z* 414 $[M]^+$, 399, 369, 353, 339, 311, 192, 177, 69, 40; HREIMS *m/z* 414.13365 (calcd for $C_{22}H_{22}O_8$, 414.13147); ^1H and ^{13}C NMR assignments are found in Tables 1 and 2.

Dulxanthone H (3): yellow cubes (EtOAc); mp 195.9−196.5 °C; UV (MeOH) λ_{max} (log ϵ) 207 (5.78), 274 (6.04), 286 (5.97), 327 (5.57) nm; IR (KBr) ν_{max} 3426, 1653, 1637, 1579, 1480, 1436, 1263, 1162, 1148, 1064 cm^{-1}; EIMS *m/z* 414 $[M]^+$, 399, 369, 354, 348, 325, 271, 192, 163, 69, 40; HREIMS *m/z* 414.13375 (calcd for $C_{22}H_{22}O_8$, 414.13147); ^1H and ^{13}C NMR assignments are found in Tables 1 and 2.

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