

## Flavonoids from *Artocarpus teysmanii* Miq.

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**ABSTRACT** Phytochemical studies on barks of *Artocarpus teysmanii* Miq. (Moraceae) have resulted in the isolation of four compounds, xanthone-lactone derivative, artonol B **1**, furanodihydrobenzoxanthone derivatives, cycloartobiloxanthone **2** and artobiloxanthone **3** and isoprenylated flavone, artonin E **4**.

**ABSTRAK** Kajian fitokimia ke atas kulit batang *Artocarpus teysmanii* Miq. (Moraceae) telah mengasingkan empat sebatian, terbitan xanton-lakton, artonol B **1**, terbitan furanodihydrobenzoxanton, iaitu sikloartobiloxanton **2**, artobiloxanton **3** dan isoprenilflavon, artonin E **4**.

(*Artocarpus teysmanii* Miq., bark, xanthone derivatives, flavonoid)

### INTRODUCTION

*Artocarpus* is a small genus of Moraceae. It is represented by 20 species in the flora of Peninsular Malaysia including the cultivated species, *A. communis*, *A. heterophyllus* and *A. integer*, which are cultivated throughout the country for their fruits [1,2]. The phytochemicals of several species of this genus have been reviewed. This genus is recognized as rich source of prenylated phenolic compounds, including flavonoids, xanthenes and chalcones which have some pharmacological and biological interests [3]. As part of our continuing work on isolation and identification of chemical constituents of Malaysian *Artocarpus* species, we have studied the dichloromethane and ethyl acetate extracts of *Artocarpus teysmanii* Miq. Four known flavonoids, namely artonol B **1**, cycloartobiloxanthone **2**, artobiloxanthone **3** and artonin E **4** have been isolated. The structures of these secondary metabolites were established using spectroscopic methods. In this paper, we would like to report the isolation and structural identification of **1** and **2**. Structural elucidation of **3** and **4** have been published earlier [4].

### EXPERIMENTAL

#### General

Mps. (uncorr.) were determined using electrothermal Southenol SS2 5PH Model. UV were recorded on Shimadzu UV-1601PC spectrophotometer in methanol. IR spectra were recorded on Perkin Elmer 1650 FTIR spectrometer. Mass spectra were obtained on VG Autospec mass spectrometer (EI mode). <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on JEOL JNH A500 Spectrometer measured at 500MHz and 125MHz, respectively. VLC and CC were carried out using silica gel (230-400 mesh, Merck 9385 and 70-230 mesh, Merck 7734).

#### Plant Material

Sample of the barks of *A. teysmanii* were collected in August 2002 from UKM Reserve Forest, Bangi, Selangor. A voucher specimen (AZ7086) has been deposited at the Herbarium of Department of Biology, UKM, Bangi, Selangor.

#### Extraction and Isolation

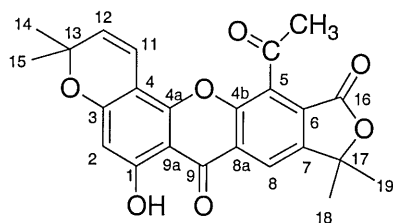
The dried ground barks (1 kg) were soaked sequentially with hexane, dichloromethane, ethyl acetate and methanol, for three days each.

The dichloromethane extract was fractionated by VLC (hexane, hexane-ethyl acetate and ethyl acetate) into six major fractions. Column chromatographic purification of fraction four using hexane-ethyl acetate as a solvent system gave artonol B **1** (48 mg), while purification of fraction six using the same technique afforded cycloartobiloxanthone **2** (80 mg), artobiloxanthone **3** (120 mg) and artonin E **4** (310 mg). Further purification of the ethyl acetate extract afforded artonin E **4** (2 g) as the major compound.

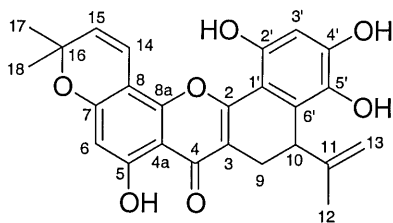
**Artonol B 1.** Orange powder; m.p. 189-192°C, lit. [5] 265-267°C and lit. [6] 189-196°C; IR (KBr)  $\nu_{\max}$  (cm<sup>-1</sup>): 3404 (OH), 1773 ( $\gamma$ -lactone C=O), 1717 (ketone C=O), 1651 (chelated C=O); UV  $\lambda_{\max}$  (MeOH) nm (log  $\epsilon$ ) 360.6 (3.48), 268.2 (3.35), 203.8 (3.23); UV  $\lambda_{\max}$  (MeOH + AlCl<sub>3</sub>) nm (log  $\epsilon$ ) 480.2 (3.14), 356.4 (3.42), 278.8 (4.12), 206.4 (4.10); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500MHz)  $\delta$  12.50 (s, 1-OH), 8.30 (1H, s, H-8), 6.60 (1H, d, *J*=10Hz, H-11), 6.32 (1H, s, H-2), 5.63 (1H, d, *J*=10Hz, H-12), 2.80 (3H, s, CH<sub>3</sub>CO), 1.75 (6H, s, H-18 & H-19), 1.50 (6H, s, H-14 & H-15); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125MHz)  $\delta$  198.4 (-COCH<sub>3</sub>), 179.1 (C-9), 166.7 (C-16), 163.2 (C-1), 162.3 (C-3), 151.3 (C-4a), 151.1 (C-4b), 148.6 (C-7), 130.2 (C-5), 128.2 (C-12), 126.5 (C-6), 125.2

(C-8a), 119.2 (C-8), 114.2 (C-11), 103.5 (C-9a), 101.2 (C-4), 100.2 (C-2), 86.5 (C-17), 79.1 (C-13), 32.3 (-COCH<sub>3</sub>), 28.5 (C-4 & (C-15), 27:6 (C-18 & C-19); EIMS *m/e* [M<sup>+</sup>] 420.

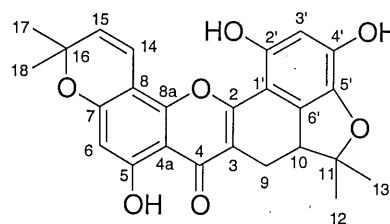
**Cycloartobiloxanthone 2.** Yellow powder; m.p. 284-287°C, lit. [5] 285-288°C and lit. [7] 285-287°C; IR (KBr)  $\nu_{\max}$  (cm<sup>-1</sup>): 3404 (OH), 1651 (ketone C=O); UV (MeOH)  $\lambda_{\max}$  (log  $\epsilon$ ) 386.0 (3.53), 271.0 (3.37), 201.8 (3.24) nm; no bathochromic shift upon addition of NaOAc-H<sub>3</sub>BO<sub>3</sub>; <sup>1</sup>H NMR (MeOH-*d*, 500 MHz)  $\delta$  6.90 (1H, d, *J*=10Hz, H-14), 6.23 (1H, s, H-3'), 6.13 (1H, s, H-6), 5.62 (1H, d, *J*=10Hz, H-15), 3.40 (1H, dd, *J*=9 & 15 Hz, H-9b), 3.15 (1H, dd, *J*=9 & 15 Hz, H-10), 2.35 (1H, t, *J*=15Hz, H-9a), 1.66 (3H, s, H-13), 1.46 (6H, s, H-14 & C-15), 1.32 (3H, s, H-12); <sup>13</sup>C NMR (MeOH-*d*, 125MHz)  $\delta$  180.6 (C-4), 161.2 (C-7), 161.1 (C-2), 158.8 (C-8a), 151.2 (C-5), 151.2 (C-2'), 146.5 (C-4'), 136.7 (C-5'), 132.5 (C-6'), 126.8 (C-15), 115.0 (C-14), 111.3 (C-1'), 104.3 (C-3'), 103.7 (C-8), 104.0 (C-4a), 101.2 (C-3), 99.0 (C-6), 93.0 (C-11), 77.8 (C-16), 46.6 (C-10), 28.1 (C-17), 28.1 (C-18), 27.9 (C-12), 22.7 (C-13), 19.9 (C-9); EIMS *m/e* [M<sup>+</sup>] 434.



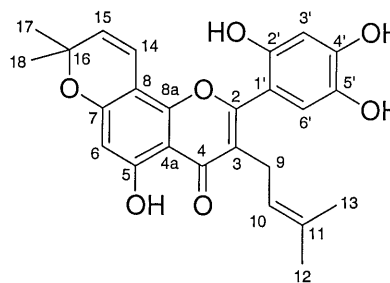
**1**



**3**



**2**



**4**

## RESULTS AND DISCUSSION

The hexane extract of *A. teysmanii* was found to contain a mixture of hydrocarbons and sterols, which was not investigated further. Silica gel VLC and repeated column chromatography of the dichloromethane extract of the bark have afforded four pure compounds, i.e. artonol B **1**, cycloartobiloxanthone **2**, artobiloxanthone **3** and artonin E **4**. Compounds **3** and **4** have previously been isolated from the bark of *Artocarpus scortechinii* King [4].

Artonol B **1** was isolated as an orange powder, m.p. 189-192°C, lit. [5] 265-267°C and lit. [6] 189-196°C, exhibited positive ferric chloride reaction suggesting a polyoxygenated compound. The compound revealed a molecular ion peak,  $[M^+]$  at  $m/e$  420 in the mass spectrum which was analysed for the molecular formula  $C_{24}H_{20}O_7$ . The IR spectrum of **1** disclosed the absorption bands due to the hydroxyl ( $3404\text{ cm}^{-1}$ ),  $\gamma$ -lactone carbonyl ( $1773\text{ cm}^{-1}$ ), ketone carbonyl ( $1717\text{ cm}^{-1}$ ), and chelated carbonyl ( $1651\text{ cm}^{-1}$ ) groups. The UV spectrum showed the absorption maxima at and 203.8, 268.2 and 360.6, which was similar to those of xanthenes [7]. The  $^1\text{H}$  NMR spectrum of **1** showed signals for protons in a 2,2-dimethylpyran ring, i.e. singlet at  $\delta$  1.50 for protons H-14 and H-15, two doublets at  $\delta$  5.63 ( $J=10\text{Hz}$ ) and  $\delta$  6.60 ( $J=10\text{Hz}$ ) for H-12 and H-11, respectively. The methyl signals for H-18 and H-19 appeared as one singlet at  $\delta$  1.75. The acetyl group was shown by a singlet at  $\delta$  2.80 which was integrated for three protons. The two isolated aromatic protons appeared at  $\delta$  6.32 and  $\delta$  8.30 for H-2 and H-8 respectively. A singlet at  $\delta$  12.50 was attributable to a proton in a hydrogen-bonded hydroxyl group (1-OH). The  $^{13}\text{C}$  NMR spectrum of **1** indicated the presence of twenty four carbons (Table 1). The most downfield signal ( $\delta$  198.4) was assigned to the carbonyl carbon in the acetyl group. Signal at  $\delta$  179.1 was attributable to the chelated carbonyl (C-9) while signal at  $\delta$  166.7 was assigned to the lactone carbonyl carbon. The full

assignments of the carbons signal were carried out by using the  $^1\text{H}$ - $^1\text{H}$  COSY,  $^1\text{H}$ - $^{13}\text{C}$  HMQC, HMBC, and comparison with literature data [5, 6]. Based on the spectral evidence and comparison with literatures, **1** was found to be artonol B. Artonol B has also been reported to be found in *A. communis* [6].

Compound **2** was obtained as a yellow powder, m.p. 284-287°C, lit. [5] 285-288°C and lit. [7] 285-287°C, also exhibited positive ferric chloride reaction. The mass spectrum of compound **2** showed a molecular ion peak at  $m/e$  434 which corresponded to molecular formula  $C_{25}H_{22}O_7$ . The IR spectrum showed absorption bands due to the hydroxyl ( $3404\text{ cm}^{-1}$ ) and ketone carbonyl ( $1651\text{ cm}^{-1}$ ) groups. The UV spectrum showed the absorption maxima at 201.8, 271.0 and 386.0 and does not undergo a bathochromic shift in the presence of boric acid and sodium acetate, showing that the hydroxyls at ring B are not in the *ortho* position to each other [7]. The  $^1\text{H}$  NMR spectrum showed two signals for two methyl groups at  $\delta$  1.66 and 1.32 (3H each) and an ABX type of signals at  $\delta$  2.35 (1H, t,  $J=15\text{Hz}$ , H-9a), 3.40 (1H, dd,  $J=9$  and  $15\text{ Hz}$ , H-9b) and 3.15 (1H, dd,  $J=9$  and  $15\text{Hz}$ , H-10). Two singlets at  $\delta$  6.13 and 6.23 were assigned to the isolated aromatic protons, H-6 and H-3'. The presence of a 2,2-dimethylchromene moieties was shown by doublet signals at  $\delta$  6.90 ( $J=10\text{Hz}$ ) and  $\delta$  5.62 ( $J=10\text{Hz}$ ) for protons H-14 and H-15, respectively. The methyl groups signal was observed as a singlet at  $\delta$  1.46 (6H, H-18 and H-19). The full assignments for the protons and carbons signal was tabulated in Table 2. Compound **2** was identified as cycloartobiloxanthone based on the 1D and 2D NMR spectral data and comparison with literatures [5, 7]. The occurrence of this compound was also reported from *A. nobilis* [7], *A. communis* [8], *A. rigida* [9], and *A. rotunda* [10].

**Table 1.** <sup>1</sup>H and <sup>13</sup>C NMR chemical shifts (δ) of compound 1

Carbon	Compound 1		Artonol B [6]	
	<sup>13</sup> C NMR	<sup>1</sup> H NMR (CDCl <sub>3</sub> )	<sup>13</sup> C NMR	<sup>1</sup> H NMR (CDCl <sub>3</sub> )
1	163.2	12.50 (s, OH)	163.2	12.49 (s, OH)
2	100.2	6.32 (s)	100.2	6.31 (s)
3	162.3	-	162.3	-
4	101.2	-	101.4	-
4a	151.3	-	151.3	-
4b	151.1	-	151.1	-
5	130.2	-	130.2	-
6	126.5	-	126.5	-
7	148.6	-	148.6	-
8	119.2	8.30 (s)	119.2	8.30 (s)
8a	125.2	-	125.2	-
9	179.1	-	179.2	-
9a	103.5	-	103.6	-
11	114.2	6.60 (d, <i>J</i> 10Hz)	114.2	6.60 (d, <i>J</i> 10 Hz)
12	128.2	5.63 (d, <i>J</i> 10Hz)	128.2	5.63 (d, <i>J</i> 10 Hz)
13	79.1	-	79.1	-
14	28.5	1.50 (3H, s)	28.5	1.50 (3H, s)
15	28.5	1.50 (3H, s)	28.5	1.50 (3H, s)
16	166.7	-	166.7	-
17	86.5	-	86.6	-
18	27.6	1.75 (3H, s)	27.6	1.76 (3H, s)
19	27.6	1.75 (3H, s)	27.6	1.76 (3H, s)
-COCH <sub>3</sub>	198.4	-	198.5	-
-COCH <sub>3</sub>	32.3	2.80 (3H, s)	32.3	2.81 (3H, s)

**Table 2.** <sup>1</sup>H and <sup>13</sup>C NMR chemical shifts (δ) of compound 2

Carbon	Compound 2		Cycloartobioxanthone [5]	
	<sup>13</sup> C NMR	<sup>1</sup> H NMR (MeOH- <i>d</i> )	<sup>13</sup> C NMR	<sup>1</sup> H NMR (CDCl <sub>3</sub> )
2	161.1	-	160.8	-
3	101.2	-	103.6	-
4	180.6	-	180.6	-
4a	104.0	-	104.5	-
5	151.2	-	150.9	-
6	99.0	6.13 (1H, s)	101.2	6.25 (1H, s)
7	161.2	-	160.7	-
8	103.7	-	99.6	-
8a	158.8	-	158.6	-
9	19.9	3.40 (1H, dd, <i>J</i> 9 & 15Hz) 2.35 (1H, t, <i>J</i> 15Hz)	19.5	3.40 (1H, dd, <i>J</i> 7 & 15Hz) 2.40 (1H, t, <i>J</i> 15Hz)
10	46.6	3.15 (1H, dd, <i>J</i> 9 & 15Hz)	46.4	3.20 (1H, dd, <i>J</i> 7 & 15Hz)
11	93.0	-	93.4	-
12	27.9	1.32 (3H, s)	22.3	1.35 (3H, s)
13	22.7	1.66 (3H, s)	27.7	1.58 (3H, s)
14	115.0	6.90 (1H, d, <i>J</i> 10Hz)	114.9	6.85 (1H, d, <i>J</i> 10Hz)
15	126.8	5.62 (1H, d, <i>J</i> 10Hz)	127.0	5.58 (1H, d, <i>J</i> 10Hz)
16	77.8	-	77.8	-
17	28.1	1.46 (3H, s)	27.7	1.47 (3H, s)
18	28.1	1.46 (3H, s)	27.8	1.48 (3H, s)
1'	111.3	-	111.4	-
2'	151.2	-	150.4	-
3'	104.3	6.23 (1H, s)	103.8	6.25 (1H, s)
4'	146.5	-	145.9	-
5'	136.7	-	136.6	-
6'	132.5	-	132.1	-

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