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Anthraquinones and Xanthones from *Cratoxylum glaucum* (Guttiferae)

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ABSTRAK

Dalam pencarian berterusan untuk sebatian xanton dan kuinon daripada famili Guttiferae, kami telah membuat keputusan untuk meneliti genus *Cratoxylum*. Satu kajian kimia teliti ke atas *Cratoxylum glaucum* telah menghasilkan dua triterpenoid iaitu friedelin (**1**) dan stigmasterol (**2**) dua antrakuinon 1,8-dihidroksi-3-metil-6-metoksiantrakuinon (**3**) dan vismiakuinon (**4**) and satu xanton dimetilmangostin (**5**). Sebatian-sebatian ini telah dikenal pasti menggunakan Spektroskopi RMN 1D dan 2D. Ini adalah laporan pertama mengenai ciri kimia *Cratoxylum glaucum*.

ABSTRACT

In a continuing search for xanthones and quinones from the Guttiferae family, we decided to look at the genus *Cratoxylum*. A detailed chemical study on *Cratoxylum glaucum* has led to the isolation of two triterpenoids, friedelin(**1**) and stigmasterol (**2**), two anthraquinones 1,8-dihydroxy-6-methyl-3-methoxyanthraquinone (**3**) and vismiaquinone(**4**) and one xanthone dimethylmangostin(**5**). These compounds were identified using the 1D and 2D NMR spectroscopy. This is the first report done on the chemistry of *Cratoxylum glaucum*.

Keywords: *Cratoxylum glaucum*, Guttiferae, anthraquinones, xanthones, triterpenoids

INTRODUCTION

The genus *Cratoxylum* which consists of a total of six species is a small genus of South East Asian trees belonging to Guttiferae, which it is sometimes categorized under the family of Hypericaceae. The stem bark of *Cratoxylum* species is known to be used in traditional medicine (Bennet *et al.*, 1993). The wood of *Cratoxylum glaucum* is used for house and farm hut construction. Poles from moderately big trees are used as beams, joists, rafters and posts in the farm hut construction (Pearce *et al.*, 1987). The bark, roots and leaves are reported to be used in folk medicine to treat fevers, cough, diarrhoea, itches, ulcers and abdominal complaints (Lien *et al.*, 1998). There are not many reports on the chemistry of the *Cratoxylum* species. However, some phytochemical studies on this genus have revealed it to be rich in xanthones, triterpenoids and tocotrienols (Iinuma *et al.*, 1996; Bennett *et al.*, 1993; Sia *et al.*, 1995; Nguyen *et al.*, 1998; Bennett and Lee, 1989). This paper describes the isolation and identification of anthraquinones and xanthones from the not-so-common *Cratoxylum glaucum*.

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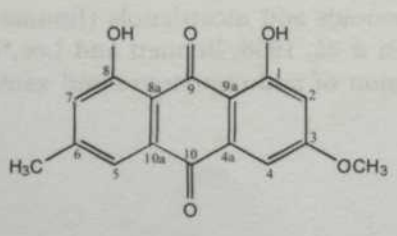
MATERIALS AND METHOD

Plant Material – The stem bark of the *Cratoxylum glaucum* was collected from Sri Aman Sarawak, Malaysia. The plant materials were identified by Ms Runi Sylvester from the Herbarium of Sarawak Forestry Department, Kuching, Sarawak, Malaysia.

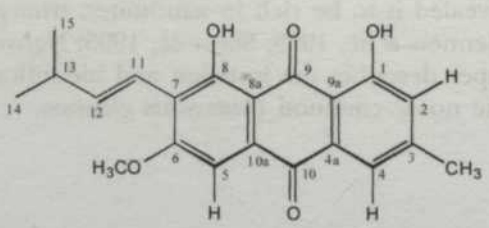
General – Infrared spectra were measured in KBr/NaCl pellet on a Perkin-Elmer FTIR Spectrum BX spectrometer. EIMS were recorded on a Shimadzu GCMS-QP5050A spectrometer. NMR spectra were obtained using a Unity INOVA 500MHz NMR/ JEOL 400MHz FT NMR spectrometer using tetramethylsilane (TMS) as the internal standard. Ultra violet spectra were recorded in $CHCl_3$ on a Shimadzu UV-160A, UV-Visible Recording Spectrophotometer.

Extraction and Isolation – The air-dried and powdered stem bark of the *Cratoxylum glaucum* (1.0 kg) was extracted successively with hexane, chloroform, ethyl acetate and methanol at room temperature. The extracts were evaporated to dryness under a reduced pressure to yield 16.4 g of crude hexane extract, 15.3 g of crude chloroform extract, 16.8 g of crude ethyl acetate extract and 18.7 g of crude methanol extract. Each of the crude extracts was subjected to a series of column chromatography over silica gel columns using a stepwise gradient system (hexane/chloroform, chloroform/ethyl acetate and ethyl acetate/methanol). The elements were collected in a range volume of 50 to 250 ml, depending on the size of the columns used. The column chromatography of the hexane extract gave two terpenoids, friedelin (**1**) (20mg) and stigmasterol (**2**) (15 mg). The ethyl acetate extract yielded 1,8-dihydroxy-3-methyl-6-methoxyanthraquinone (**3**) (10 mg) while the chloroform extract gave vismiaquinone (**4**) (20 mg). The methanol extract gave 10 mg of dimethylmangostin (**5**).

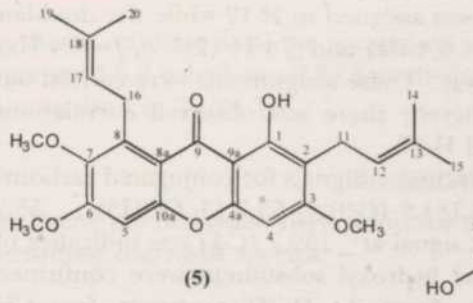
1,8-Dihydroxy-3-methyl-6-methoxyanthraquinone (**3**): Orange crystals, m.p. 209-210 °C (Lit. 208-209 °C, Hofle, 1977). UV (EtOH) λ_{max} nm (log ε): 287 (0.73), 266 (0.75); IR ν_{max} cm^{-1} (KBr): 3418 (broad, OH), 2924 (C-H stretching), 1676 (C=O), 1622 (C=O), 1564 (C=C), 1480 (CH_2 bending), 1316 (CH_3 bending), 1158 (C-O); EI-MS m/z (rel. int.): 284 (100), 255 (18), 241 (16), 213 (12), 128 (18); ^{1}H NMR (400 MHz, $CDCl_3$): δ12.28 (1H, s, OH-1), δ12.05 (1H, s, OH-8), δ7.56 (1H, brs, H-7), δ7.29 (1H, d, J = 2.8 Hz, H-4), δ7.05 (1H, brs, H-5), δ6.62 (1H, d, J = 2.8 Hz, H-2), δ3.87 (1H, s, OCH_3), δ2.38 (1H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ190.7 (C-9), δ182.0 (C-10), δ166.6 (C-3), δ165.2 (C-1), δ162.5 (C-8), δ148.4 (C-6), δ135.2 (C-10a), δ133.2 (C-4a), δ124.5 (C-7), δ121.3 (C-5), δ110.2 (C-8a), δ113.5 (C-9a), δ108.2 (C-4), δ106.8 (C-2), δ56.1 (OCH_3), δ22.2 (CH_3).



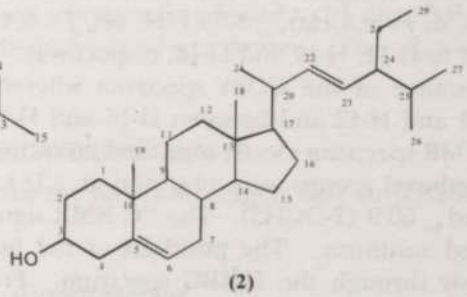
(3)



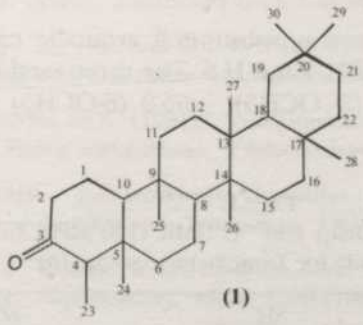
(4)



(5)



(2)



(1)

Vismiaquinone (**4**): Dark reddish crystals, m.p. 201-203 °C (Lit. 202-204 °C, Goncalves *et al.*, 1981). UV (EtOH) λ_{max} nm (log ε): 294 (0.84), 263 (0.57). IR ν_{max} cm^{-1} (KBr): 3440 (broad, OH), 2952 (C-H stretching), 1626 (C=O), 1560 (C=C), 1482 (CH_2 bending), 1374 (CH_3 bending), 1174 (C-O); EI-MS m/z (rel. int.): 352 [M^+, 48], 337 (20), 309 (100), 297 (31), 161 (11); ^{1}H NMR (400 MHz, $CDCl_3$): _12.86 (OH-1, s), _12.02 (OH-8, s), δ 7.52 (1H, s, H-4), _7.30 (1H, s, H-5), _7.05 (1H, s, H-2), _6.99 (1H, dd, *J* = 16.0 Hz & 6.4 Hz, H-12), _6.61 (1H, dd, *J* = 16.0 Hz, H-11), _3.99 (3H, s, OCH_3-6), _ 2.49 (1H, m, H-13), _2.40 (3H, s, H-3), _1.11 (6H, d, *J* = 6.5 Hz, H-14 & H-15); ^{13}C NMR (100 MHz, $CDCl_3$): δ191.2 (C-9), δ181.7 (C-10), δ162.9 (C-6), _162.4 (C-8), _162.0 (C-1), _148.4 (C-3), _146.7 (C-12), _133.1 (C-4a), _131.9 (C-10a), _124.3 (C-2), _121.0 (C-4), _119.9 (C-7), _115.7 (C-11), _113.6 (C-9a), _110.4 (C-8a), _103.3 (C-5), _56.26 (6-OMe), _33.4 (C-13), _22.4 (C-14 & C15), _22.1 (3-CH_3).

RESULTS AND DISCUSSIONS

Dimethylmangostin (**5**) was isolated as pale yellow crystals with a melting point of 111-113 °C (Lit. 110-106 °C, Yates *et al.*, 1958). It has a molecular formula of $C_{26}H_{30}O_6$ as established by EI mass spectrometry (m/z 438 [M^+]). A positive test with alcoholic FeCl3 revealed its phenolic nature. The UV spectrum exhibited the characteristic absorption bands of a xanthone at 312.0, 294.0 and 247.0 nm. The IR spectrum also indicated the presence of the chelated hydroxyl and conjugated carbonyl group characteristic of a xanthone at 3446 and 1600 cm^{-1}.

The ^{1}H NMR spectrums showed the presence of a low field chelated hydroxyl group at δ 13.46 (OH-1) which is attached to C-1. Two aromatic proton singlets observed at δ

6.27 and δ 6.69 were assigned to H-4 and H-5, respectively. Meanwhile, three methoxy groups which show a three hydrogen singlet each were present at δ 3.87, δ 3.93 and δ 3.77, respectively. A signal at _ 5.20 (1H, brs) was assigned to H-12 while the doublets at _ 3.32 (2H, d, J = 6.4 Hz), _ 5.23 (1H, brt, J = 6.4 Hz) and _ 4.11 (2H, d, J = 6.4 Hz) were assigned to H-11, H-17 and H-16, respectively. These assignments were carried out with the assistance of the COSY spectrum whereby there was observed correlations between H-11 and H-12 and between H-16 and H-17.

The ^{13}C NMR spectrum clearly indicated 26 carbons. Signals for conjugated carbonyl and three methoxyl groups were observed at _ 181.9 (C-9), _ 55.7 (3- OCH3) , _ 55.9 (6-OCH3) and _ 60.9 (7-OCH3). The ^{13}C NMR signal at _ 159.7 (C-1) was indicative of an oxygenated xanthone. The positions of the hydroxyl substituent were confirmed unambiguously through the HMBC spectrum. From the DEPT spectrum, four CH groups, two CH_2 groups, three methoxy group and four CH_3 groups were revealed to be present in the molecule.

In the HSQC spectrum, the two unsubstituted aromatic carbons of C-4 and C-5 showed linkages to their protons of H-4 and H-5. The three methoxy groups were linked to the assigned carbon at _ 55.7 (3- OCH3), _ 55.9 (6-OCH3) and _ 60.9 (7-OCH3).

TABLE 1
^{1}H (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) assignments for Dimethylmangostin (5)

Position	δH	δC
1	13.46 (1H, s)	159.7
2		111.4
3		163.3
4	6.27 (1H,s)	88.6
4a		155.2
5	6.69 (1H, s)	98.1
6		157.9
7		143.9
8		137.2
8a		112.0
9		181.9
9a		103.9
10a		155.1
11	3.32 (2H, d, J=6.4 Hz)	21.3
12	5.20 (1H, brs)	122.3
13		131.6
14	1.83 (3H, s)	17.8
15	1.78 (3H, s)	25.8
16	4.11 (2H, d, J= 6.4 Hz)	26.1
17	5.23 (1H, brt, J=6.4Hz)	123.2
18		131.7
19	1.66 (6H, s)	18.2
20	1.66 (6H, s)	25.9
3-OCH3	3.87 (3H, s)	55.7
6-OCH3	3.93 (3H, s)	55.9
7-OCH_3	3.77 (3H, s)	60.9

From the HMBC experiment, the chelated hydroxyl functional of OH-1 group gave linkages to the carbons of C-1, C-2 and C-9a, thus supporting the location of the OH at C-1.

Based on these data, the compound was therefore found to be dimethylmangostin, 1-hydroxy-3,6,7-trihydroxy-2,8-(3-methylbut-2-enyl)-xanthone. The spectral data are summarized in Table 1.

ACKNOWLEDGEMENTS

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