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NOVEL XANTHONES FROM *GARCINIA MANGOSTANA*, STRUCTURES OF BR-XANTHONE-A AND BR-XANTHONE-B*

KRISHNAMOORTHI BALASUBRAMANIAN and KRISHNAMOORTHI RAJAGOPALAN

Department of Organic Chemistry, University of Madras, Guindy Campus, Madras, 600 025, India

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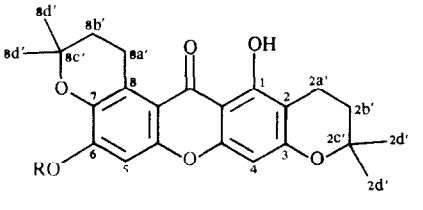
Key Word Index—*Garcinia mangostana*, Guttiferae, BR-xanthone-A, BR-xanthone-B, xanthones

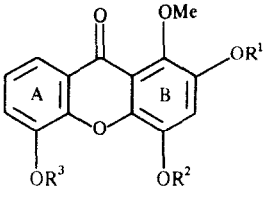
Abstract—The chemical examination of the dry fruit hulls of *Garcinia mangostana* yielded, in addition to known xanthones, two new xanthones, a bis-pyrano xanthone, BR. xanthone-*A* and 1-methoxy-2,4,5-trihydroxyxanthone, BR-xanthone-B Evidence of their structures is presented

INTRODUCTION

Garcinia mangostana Linn (Guttifereae) is a tree, fairly widespread in India, Sri Lanka, Burma and known for its sweet fruits called mangosteen. In the ayurvedic system of medicine, the fruit hull of this plant finds wide application, mainly as an anti-inflammatory agent and in the treatment of diarrhoea In general, xanthones and their derivatives were shown to be effective as an allergy inhibitor and bronchodialator in treatment of asthma [1] Antileukemic xanthones have also been isolated from plants belonging to the Guttiferae family [2]. The chemistry of xanthones isolated from various plant families has been reviewed by Sultanbawa *et al.* [3]. We report now the isolation and characterization of two new xanthones from the hulls of *Garcinia mangostana*, in addition to the already reported xanthones–mangostin, gartanins and garcinones [4, 5].



1 R = H
1a R = Ac
1b R = Me



2 $R^1 = R^2 = R^3 = H$
2a $R^1 = R^2 = R^3 = Me$

* Part 1 in the series 'Studies as Indigenous Medicinal Plants'

RESULTS AND DISCUSSION

In the literature there appears to be no report on X-ray crystallographic studies on either mangostin or its derivatives. It is with this primary objective in mind, that the investigation of this plant was undertaken. The combined petrol and benzene extracts of the powdered fruit hulls, after careful column chromatography over silica gel (Experimental), afforded a novel xanthone BR-Xanthone-*A* (**1**) as a low polar material in addition to several other known xanthones The acetone extract of the defatted hulls, on column chromatography (Experimental) furnished another new xanthone, BR-xanthone-*B* (**2**).

BR-Xanthone *A* (**1**) was crystallized from petrol–benzene (1:1) as pale yellow needles (mp 181–182°) and was found to have a molecular formula of $C_{23}H_{24}O_6$ (based on the high resolution mass spectrum). It gave all the standard tests for xanthones Its UV spectrum had bands at 243, 259, 319 nm.

The effect of added sodium acetate, sodium hydroxide and aluminium chloride in the UV spectrum of the parent xanthone was valuable in ascertaining the hydroxylation pattern. The absence of any significant bathochromic shift with sodium acetate indicated the absence of a free hydroxyl group at C-3 of the xanthone nucleus. The IR spectrum showed a strong absorption at 1640 cm^{-1} (hydrogen bonded carbonyl) with a broad band around 3400 cm^{-1}, showing the presence of a hydroxyl group.

The ^1H NMR spectrum (360 MHz) $CDCl_3$ had a peak at δ13.72 indicating a chelated hydroxyl group at C-1 or C-8 and a singlet at δ6.36 for a phenolic hydroxyl which was exchanged with D_2O thus confirming the presence of two free hydroxyl groups in the xanthone (Table 1). The facile formation of a mono-acetate or mono-methyl ether of the xanthone confirmed the presence of a relatively free hydroxyl group. Two singlets were seen in the ^1H NMR spectrum at δ6.77 and 6.23 and two carbon doublets were observed at δ93.93 and 100 43 in the ^{13}C NMR spectrum. The INEPT technique in the ^{13}C NMR ($J=\pi/2$) spectrum gave a clear indication of the presence of two CH signals and two Me signals and four CH_2 signals, revealing that the nucleus contained two aromatic CH carbons and two types of methyl group and four different CH_2 carbons. The INEPT technique of CH↑ ($J=3\pi/4$) alone confirmed the above fact and it facilitated the assignment of the structure with the help of ^1H NMR data. The molecular formula $C_{23}H_{24}O_6$ entails a double bond equivalent (DBE) of 12. Of these the xanthone nucleus will account for 10 leaving two DBE which can be either two double bonds or two rings. The absence of any vinyl protons or vinyl methyls in the ^1H NMR spectrum as well as the absence of any olefinic carbon in the ^{13}C NMR spectrum clearly indicated that the remaining two DBE can only be accounted for by two rings The presence of two saturated pyran rings was confirmed by the appearance of four triplets in the ^1H NMR spectrum and four methylene carbon triplets in the ^{13}C NMR spectrum and by the INEPT technique. Benzylic methylene and the aliphatic methylene protons were identified by decoupling studies.

Confirmatory evidence for the structure of BR. Xanthone *A*, was obtained by comparing it with the cyclization product obtained by heating mangostin with hydrogen iodide [6] (mmp, identical IR and ^1H NMR spectra) Yates *et al.* [6] report the formation of two pyranoxanthones from mangostin on refluxing with hydrogen iodide under different conditions. One of these xanthones obtained when pure hydrogen iodide (free of iodine) was used for this reaction was found to be identical with the BR-xanthone 1. This xanthone was established to have one pyran ring linearly fused and another angularly fused which are rather novel features Similar naturally occurring saturated pyrano xanthones with one pyran ring are toxyl xanthone [7, 8] and cordato oblongue xanthone [9]

BR-Xanthone B (1-methoxy-2,4,5-trihydroxy xanthone, **2**) was obtained as a greenish yellow solid, (mp 308–310°) having the molecular formula $C_{14}H_{10}O_6$ (high resolution mass spectrum). The standard tests confirmed it to be a xanthone. The UV spectrum (EtOH) showed absorptions at 222, 244, 313 and 357 nm. The pattern in the UV spectrum obtained did not correspond with any other known xanthones. The 10 double bond equivalents according to the molecular formula $C_{14}H_{10}O_6$ confirmed that it contained only the xanthone nucleus and no other ring or unsaturation. Hence the formula could be written as $C_{13}H_8O_2$–CH_2OH. The ^1H NMR spectrum (360 MHz) showed the presence of a methoxyl group at

Table 1 ^1H NMR spectral data for compounds **1**, **1a** and **1b**

Proton no	δvalues		
	1	**1a**	**1b**
C-1 OH	13 72 *s*	13 67 *s*	13 65 *s*
H-5	6.77 *s*	6.70 *s*	6.63 *s*
C-6 OH	6.36 *s*	—	—
H-4	6.23 *s*	6 14 *s*	6 14 *s*
C-6 OMe	—	—	3 8 *s*
H_2-8*a*′	3 40 *t* ($J=2$ Hz)	3 43 *t* ($J=2$ Hz)	3 42 *t* ($J=2$ Hz)
H_2-2*a*′	2 7 *t* ($J=2$ Hz)	2 63 *t* ($J=2$ Hz)	2.63 *t* ($J=2$ Hz)
C-6 Ac	—	2.24 *s*	
H_2-8b′	1 87 *t* ($J=2$ Hz)	1.74 *t* ($J=2$ Hz)	1 76 *t* ($J=2$ Hz)
H_2-2*b*′	1.82 *t* ($J=2$ Hz)	1 74	1 76
H_3-8d′	1 37 *s*	1 26 *s*	1.31 *s*
H_3-2d′	1 35 *s*	1 26 *s*	1.29 *s*

δ3.97 as a singlet The other three oxygens could be hydroxyl groups. The IR (KBr) spectrum showed the carbonyl absorption at 1650 cm^{-1} which did not alter even when the compound was methylated The D_2O exchanged spectrum, methylation experiment and the ^1H NMR spectrum of the compound confirmed these conclusions The absence of any signal around δ12–14 indicated the absence of a C-1 or C-8 hydroxy group. The aromatic region of the ^1H NMR spectrum showed four protons, a singlet at δ6 63, a multiplet at 7 27–7 34 and a *dd* at 7 73 with $J = 8$ Hz and 2 Hz and 2 Hz which suggested that three of the four hydrogens were present in the same ring (with a proton having both *ortho*- and *meta*-coupling). The hydroxylation pattern was arrived at by comparison with the ^1H NMR spectral pattern of known xanthones [10] and decoupling studies Hence the B ring of the xanthone nucleus had three hydroxyl substitutions and the other ring had one

The positions of methoxyl and the hydroxyl groups were fixed on the basis of the sodium acetate induced shift of the xanthone [6] Hence, the structure of BR xanthone-B (**2**) was assigned as 1-methoxy-2,4,5-trihydroxyxanthone This xanthone is hitherto unreported from *G. mangostana* The X-ray crystallography and the pharmacological studies on the compound are in progress

EXPERIMENTAL

Mps uncorr ^1H and ^{13}C NMR spectra were run at 360 MHz and on a 90 MHz Jeol FX 90Q instrument with solvents $CDCl_3$ and CD_3OD with TMS as int standard. High resolution mass spectra were recorded on a VG mass spectrometer at 70 eV at elevated temp with peak to peak data comparison Petrol refers to bp 60–80° Silica gel G grade (without binder) was used

Plant material Dried fruit hulls supplied by M/s IMCOPS, Adyar, Madras 20, India, were used for the extraction

Isolation of components from powdered fruit hulls of G mangostana Plant material (2 kg) was extracted successively with petrol (3 × 3 l) with C_6H_6 (3 × 3 l) and finally with Me_2CO (3 × 3 l) Petrol and C_6H_6 extracts were found to be identical on TLC and so were combined It showed low polar components on TLC along with known compounds CC of the combined extract (2 g) over silica gel (40 g) gave on elution with petrol–C_6H_6 (1 19) BR-xanthone-A as a mixture with some low melting waxes Rechromatography and further purification of the above mixture yielded BR-xanthone A (R_f 0 8), as a homogenous material Purity of the material was checked by TLC using either pure C_6H_6 or C_6H_6–MeOH (100 1) for development

The gummy solid from the Me_2CO extract after careful CC using silica gel gave mangostin (eluent C_6H_6–petrol 1 1, mixture of gartamins) Elution with C_6H_6–$CHCl_3$ (1 1) gave mangostin, gartonins, the known xanthones, along with a polar material as a mixture Separation of BR-xanthone B (greenish yellow solid) from this mixture was achieved using flash chromatographic technique over silica gel (G) without binder The first few fractions using petrol as eluent gave a mixture of products and elution with petrol–C_6H_6 (1 1) gave the desired xanthone

BR-Xanthone A (**1**) Pale yellow crystalline solid mp 181–182° High resolution mass spectrum Found [M^+] 396 16, Calc 396 15 $C_{23}H_{24}O_6$ UV λ_{max}^{EtOH} nm (logε), 243 (4 54), 259 (4 43), 319 (4 37) and 367 (3 85) (+NaOH), 242, 260, 376 (+NaOAc) 242, 259, 321 and 371 (+$AlCl_3$) 237, 269, 343, and 411 IR ν_{max}^{KBr} cm^{-1}, 3400 (OH), 1640 (C=O), 1580 (aromatic) ^1H NMR (360 MHz), see Table 1 ^{13}CNMR 75 42 (*s*, C-8C'), 75 81 (*s*, C-2C'), 103 05 (*s*, C-8b'), 103 48 (*s*, C-8a'), 111 20 (*s*, C-2), 121 34 (*s*, C-8), 137 75 (*s*, C-4b'), 151 51 (*s*, C-4a'), 153 26 (*s*, C-3), 154 93 (*s*, C-7), 160 43 (*s*, C-6), 160 50 (*s*, C-1), 182 60 (C=O) 93 93 (*d*, C-4), 100 43 (*d*, C-5) (indicating the 2 aromatic carbons having the protons) 16 (*t*, C-2b'), 22 27 (*t*, C-8b'), 31 94 (*t*, C-2a), 32 90 (*t*, C-8a) 26 69 and 26 41, (*q*'s, C-2d' and C-8d') MS *m/z* (rel int) 397 15 [M + 1] (24), 396 15 ([M]$^+$ (100), 381 13, [M − Me]$^+$ (14 3), 353 10 [M − 43] (88 7), 340 09 (35.9), 325 07 (13), 297 03 (27)

BR-Xanthone A monoacetate (**1a**) Compound 1 (15 mg) was acetylated under mild conditions and after the usual work-up gave a homogenous solid mp 166–167° IR ν_{max}^{KBr} cm^{-1}, 3640 (–OH), 1750 (Ac), 1640 (C=O), 1580 (aromatic), ^1H NMR see Table 1

BR-Xanthone A monomethyl ether (**1b**) Compound **1** (15 mg was methylated by refluxing in dimethyl sulphate and K_2CO_3 in Me_2CO The product was purified by CC using petrol–EtOAc (49 1) to give a white solid mp 215–216° IR ν_{max}^{KBr} cm^{-1} 3640 (–OH), 1640 (C=O), 1580 (aromatic) ^1H NMR see Table 1

BR-xanthone B (**2**) Greenish yellow crystalline solid mp 308–310 Molecular formula $C_{14}H_{10}O_6$ (high resolution mass spec) Found [M^+] 274 04, calcd 274 04 UV λ_{max}^{EtOH} nm (logε), 272 (4 38), 244 (4 53), 313 (4 19) and 357 (3 80) (+NaOH) 233, 254, 291 and 353 (+NaOAc) 210, 355 (+$AlCl_3$) 222, 244, 265, 281, 341 and 412 IR ν_{max}^{KBr} cm^{-1} 3300, 1650, 1590 ^1H NMR (360 MHz) δ3 97 (3H, *s*, OMe), 6 63 (1H, *s*, ArH_3), 7 27–7 34 (2H, *m*, H-6, H-7), 7 73 (1H, *dd*, $J = 8$ Hz, *J*) MS *m/z* (rel int) 273.04 [M]$^+$ (100), 259 02 [M − 15]$^+$ (96 5), 231 03 (73 1), 228 04 (10 6), 137 02 (13 1)

BR-xanthone-B tetramethyl ether (**2a**) Compound **2** (10 mg) was refluxed with dimethyl sulphate and K_2CO_3 in Me_2CO to yield the product on usual work-up as a white solid mp 156–158° IR ν_{max}^{KBr} cm^{-1} 1650, 1590 ^1H NMR (360 MHz), δ3 9–4 1 (12H, or *s*, OMe), 6 9 (1H, *s*, ArH_3), 7 2–7 4 (2H, *br*, H-6, H-7) MS *m/z* (rel int) 316 1 (23 5%), 301 15 (75 5%), 1 273 (13 7%), 258 (18 7%), 151 05 (32 1%), 149 05 (33 7%), 129 1 (16 0%)

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