SHORT PAPER

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A novel chalcone from *Garcinia nervosa*

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A novel chalcone 5′-bromo-2′-hydroxy-4,4′,6′-trimethoxy-chalcone, isoliquiritigenin-4,4′-dimethyl ether (2′-hydroxy-4,4′-dimethoxy chalcone) and 2′-hydroxy-3,4,4′,6′-tetramethoxy dihydrochalcone have been isolated from the leaves of *Garcinia nervosa.* Their structure have been elucidated on the basis of chemical and spectral evidences (^{1}H NMR, ^{13}C NMR, HMQC, NOE, IR, UV and mass spectra).

Keywords: chalcone, *Garcinia nervosa*

Garcinia species are known for their medicinal properties such as antiinflammatory[1] anti-immunosuppressive and antimicrobial[2] activity and for their use in healing skin infections and wounds[3]. This led to our interest in carrying out a comprehensive investigation of the leaves of *Garcinia nervosa*. The present paper deals with the isolation and characterisation of a novel chalcone, 5′-bromo-2′-hydroxy-4′,4,6′-trimethoxy-chalcone (**2a**) along with isoliquiritigenin-4,4′-dimethylether (2′-hydroxy-4,4′-dimethoxychalcone[4,5a] (**1**) and 2′-hydroxy-3,4,4′,6′-tetramethoxy dihydrochalcone (**3**)[6]. To the best of our knowledge halogenated natural products have been reported from marine plants only.[7,8] However, the occurrence of bromochalcone in non-marine plants is surprising and being reported for the first time. The occurrence may be because of environment of the area from where the plant was collected.

Powdered leaves of *Garcinia nervosa* after being defatted with hot petroleum ether (b.p. 40–60°C), were extracted with ethanol. The residue which was obtained after the complete removal of the solvent, was extracted with chloroform. The chloroform extract was chromatographed over silica gel. Repeated column chromatography followed by fractional crystallisation with chloroform–methanol afforded three crystalline compounds, GNA, GNB and GNC. The compound GNA was characterised as isoliquiritigenin-4, 4′-dimethylether (**1**) by comparison of its spectral data with the literature[4,5a], while GNB was characterised as a novel chalcone 5′-bromo-2′-hydroxy-4,4′,6′-trimethoxychalcone (**2a**) and GNC as 2′-hydroxy-3,4,4′,6′-tetramethoxy dihydrochalcone[6] (**3**).

GNB (**2a**): Crystallised from $CHCl_3$–MeOH as yellow shining crystals m.p. 180 °C, and analysed for $C_{18}H_{17}O_5Br$. It gave a red colour with conc. H_2SO_4 and orange to red colour with aq. NaOH, suggesting it was a chalcone[9]. It showed a molecular ion peak at *m*/*z* 392/394. These isotopic peaks with equal intesitities indicated the presence of bromine in the compound, further confirmed by the Bielstein test. The IR spectrum showed characteristic bands at 2949 (br, chelated OH), 1684 (C=O) and 1462 (C=C) cm^{-1}. Its UV spectrum showed the maximum absorption at 365 nm and minimum absorption at 235 nm. A bathochromic shift of 40 nm with $AlCl_3$/HCl showed the presence of 2′-hydroxyl group[5c] which was further confirmed by the signal at δ_H13.65 in the ^{1}H NMR spectrum and greenish brown colour with $FeCl_3$.

In the ^{1}H NMR spectrum, the three independent singlets of three protons each at δ3.80, 3.86 and 3.94, were assigned to three methoxyl groups. A pair of ortho-coupled doublets at δ 6.95 (*J*=9Hz) and δ 7.65 (*J*=9Hz), each integrating for two protons were attributed to H-3, 5 and H-2,6. A sharp one-proton singlet at δ 6.4 could be assigned to either H-3′ or H-5′. The possibility that it was H-5′ was ruled out as it gave a negative Gibb's test[10] which indicated that the carbon para to the hydroxyl is substituted. Thus, the bromine is placed at 5′-position. This was further supported by the NOE spectrum in which the solitary proton interacted with only one methoxyl group which is possible only when the proton is at 3′-position. Hence, the bromine is placed at 5′-position flanked by two methoxyl groups. Therefore, the singlet at δ 6.4 was assigned to H-3′. The remaining two protons singlet at δ 7.89 was ascribed to the α,β-protons of a chalcone[5b,11]. These were resolved into two independent doublets of one proton each at δ 6.96 (*J*=16Hz) for H-α and 7.43 (*J*=16Hz) for H-β in its acetate (**2b**). In the HMQC, spectrum, the singlet at δ 6.4 for H-3′ showed a one bond correlation with δ 98, while the δ 7.8 signal showed two correlations at δ 123 and δ 145, indicating that the singlet at δ 7.8 has two different C-H overlaping. Hence, this showed that singlet at δ 7.8 has two chalcone α, β-protons *i.e.* 123 for C-α and 145 for C-β.

The ^{13}C NMR spectrum of GNB (**2a**) showed the downfield shift of C-5′ at δ 114.60 due to Br while the assignments of other carbons are given in Table 1.

Table 1 ^{13}C NMR chemical shift [δc values (ppm)] of GNB (**2a**)

Carbon no.	Assignments
C	
1′	127.9
2′	161.96
3′	97.45
4′	162.07
5′	114.60
6′	165.92
α	123.46
β	144.43
1	129.19
3,5	114.59
2,6	130.45
4	159.94
C=O	192.63
OCH_3	55.44
OCH_3	56.62
OCH_3	62.27

The above assigned structure was supported by the mass spectrum (Scheme 1) which showed the molecular ion peak at *m*/*z* 392/394. The fragment ion at *m*/*z* 134 supported the presence of *p*-methoxyphenyl ring, and the Retro-Diels–Aider

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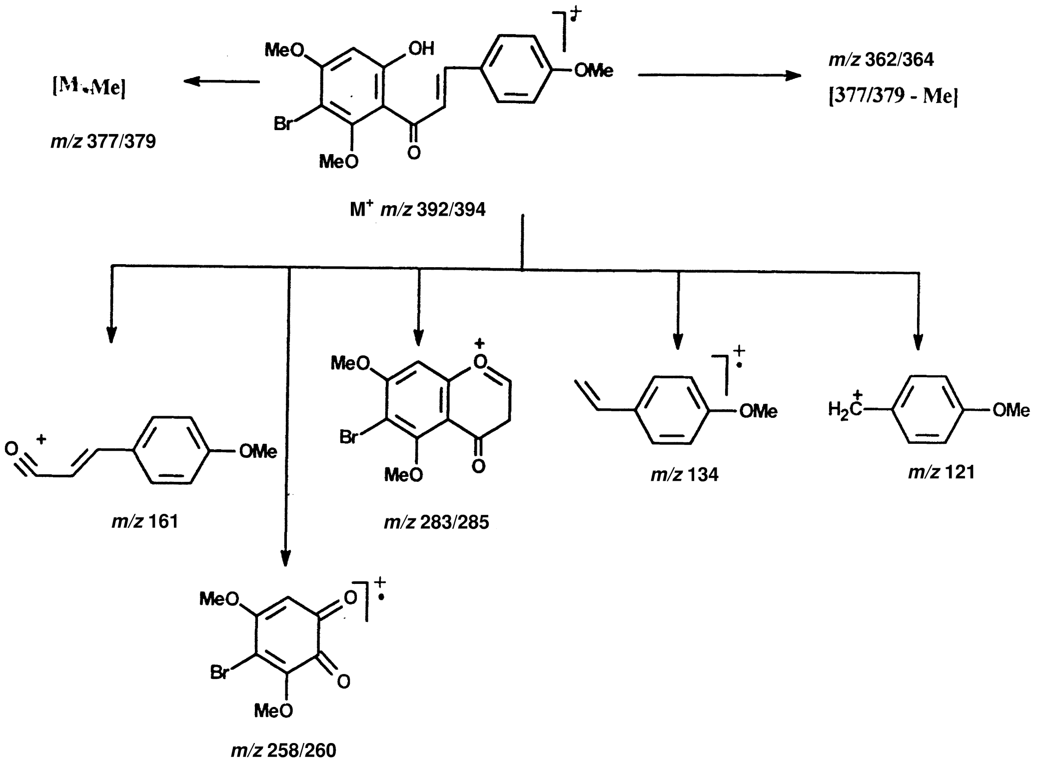
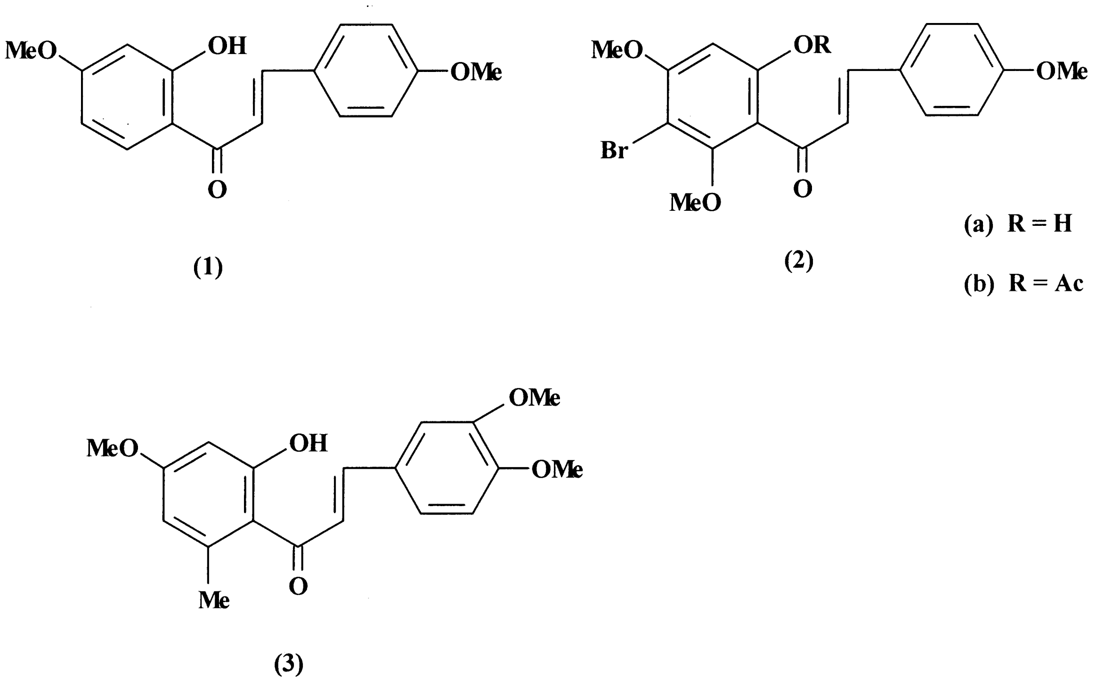
† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*



Scheme 1



Scheme 2

cleavage representing ring A at *m*/*z* 258/260 (due to Br). Further, more, the fragments at *m*/*z* 283/285 (again due to Br) corresponded to the loss of the *p*-methoxyphenyl from M^+. The other fragments are shown in Scheme 1.

On the basis of above, the compound GNB was characterised as 5′-bromo-2′-hydroxy-4,4′,6′-trimethoxychalcone (**2a**); the first such report.

Experimental

All melting points were uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ on Bruker WM-400. Chemical shifts were quoted in δ ppm scale with TMS as internal standard. The MS were obtained by direct inlet method at 70 eV ionisation potential on JEOL JMS-300 mass spectrometer. UV spectra were recorded on Pye

Univcam PU-8800 spectrophotometer and IR were measured on Shimadzu IR-408.

Plant material: Leaves of *Garcinia nervosa* were procured from Zaria, Nigeria. The plant was growing near the hospital where all the chemicals and waste materials were dumped.

Extraction and isolation: Air dried powdered leaves of *G. nervosa* after being defatted with hot petroleum ether (40–60°C), were extracted exhaustively with EtOH. The ethanol extracts was concentrated under vacuum. The residue obtained was extracted with chloroform. The chloroform extract was chromatographed over silica gel column. Elution of the column with benzene–chloroform (9:1-1:1) and chloroform gave the fractions which on repeated column chromatography followed by fractional crystallisation with $CHCl_3$-MeOH afforded two crystalline compounds. GNA, GNB and GNC.

GNA (1): Yellow needle shaped crystals (100 mg) m.p. 123 °C (Found C, 71.6, H, 5.7, $C_{17}H_{16}O_4$ requires C, 71.8, H, 5.6%). It gave a greenish-brown colour with $FeCl_3$, red colour with conc. H_2SO_4 and orange to red colour with aq. NaOH. UV. $\lambda_{max/nm}$(MeOH); 236.4 and 364.8. IR $\nu_{max/cm}$–1(KBr); 2930 (br, OH), 1670 (C=O), 1465 (C=C); ^{1}H NMR ($CDCl_3$) : 3.88 (6H, s, 2 x OMe), 6.46 ((1H,d,*J*=2.5 Hz, H-3′), 6.51 (1H, dd, *J*=2.5 and 9 Hz, H-5′), 6.95 (2H, d *J*=9 Hz, H-3,5), 7.49 (1H, d, *J*=16 Hz, H-α), 7.61 (2 H, d, *J*=9 Hz, H-2, 6), 7.81 (1H, d, *J*=9 Hz, H-6′), 7.89 (1 H, d, *J* =16 Hz, H-β), 13.56 (1H, s, 2′-OH), MS *m*/*z* (rel. int): 284 $[M]^+$ (82.8), 269 $[M\text{-}Me]^+$ (10.3), 256 $[M\text{-}CO]^+$ (5.9), 254 $[269\text{-}Me]^+$ (5.1), 177 (21), 161 (18.1), 151 (27.3), 134 (100), 121 (56.4).

GNB (**2a**)*:* Yellow shining crystals (120 mg) m.p. 180 °C, [Found C 55.0, H 4.31, $C_{18}H_{17}O_5$ Br requires C 55.1, H 4.33%]. It gave +ve Bielstein test, red colour with conc. H_2SO_4, orange to red colour with aq. NaOH and a greenish-brown with $FeCl_3$. IR $\nu_{max/cm}$–1(KBr); 2949 (br, OH), 1684, (C=O), 1606, 1462 (C=C), 1392, 1344, 879, 833. UV $\lambda_{max/nm}$(MeOH); 235, 365; +$AlCl_3$, 231, 304 sh, 405; +$AlCl_3$/HCl, 232, 301sh, 406; +NaOAc, 235, 307sh, 405; +NaOMe, 237 308 sh, 415. δH ($CDCl_3$); 3.80 (3H, s, OMe), 3.86 (3H, s, OMe), 3.94 (3H, s, OMe), 6.4 (1H, s, H-3′), 6.95 (2H, d, *J*=9 Hz, H-3, 5), 7.65 (2H, d, *J*=9 Hz, H-2, 6), 7.89 (2H, s, H-α, β), 13.65 (1H, s 2′-OH). ^{13}C NMR ($CDCl_3$): 55.44 (OMe), 56.92 (OMe), 62.27 (OMe), 97.45 (C-3′), 114.0 (C-Br, C-5), 114.59 (C-3, 5), 123.46 (α-C), 127.9 (C-1′), 130.45 (C-2, 6), 144.43 (β-C), 159.94 (C-4), 161.96 (C-2′), 162.07 (C-4′), 165.92 (C-6′), 192.63 (C=O). Ms *m*/*z* (rel. int): 392/394 $[M]^+$ (46.5, 44.8), 377/379 $[M\text{-}Me]^+$ (7, 5.5), 362/364 $[377/379\text{-}Me]^+$ (9.3, 10.5), 283/285 (12, 10.5), 258/260 (21.1, 20.5), 161 (13.9), 134 (100), 121 (74.8).

Acetylation of GNB (**1a**)*:* GNB (20mg) was acetylated with pyridine (1ml) and acetic anhydride (2ml) by heating on waterbath for 2 h. After usual work up, it was crystallised with $CHCl_3$–EtOH as grannular crystals (2b) m.p. 120–122 °C. ^{1}H NMR ($CDCl_3$): δ 2.19 (3 H, s, OAc), 3.81 (3 H, s, OMe), 3.86 (3H, s, OMe), 3.96 (3 H, s, OMe), 6.56 (1 H, s, H-3′), 6.91 (2H, d, *J*=9 Hz, H-3, 5), 6.96 (1 H, d, *J*=16 Hz, H-α), 7.43 (1 H, d, *J*=16 Hz, H-β), 7.51 (2H, d, *J*=9 Hz, H-2, 6).

GNC(**3**)*:* Yellow shining crystals (70 mg), m.p. 132°C, (Found: C, 65.78; H, 6.43, $C_{19}H_{22}O_6$ requires C, 65.89; H, 6.32%). It gave a greenish brown colour with $FeCl_3$. IR $\nu_{max/cm}$–1 3320(OH), 1690 (C=O), 1465 (C=C). ^{1}H NMR ($CDCl_3$), δ 2.80-3.26 (4H, m, CH_2-CH_2), 3.83 (6H, s, 2 × OMe), 3.87 (6H, s, 2 × OMe), 6.09 (1H, d, *J* = 2.5 Hz, H-3′), 6.20 (1H, d, *J* = 2.5 Hz, H-5′), 6.78-6.80 (3H, br, m, H-2, 5,6), 13.5 (1H, s, 2′-OH).

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