TWO NOVEL ARYLBENZOFURANS, GARCIFURAN-A AND GARCIFURAN-B FROM *GARCINIA KOLA*[1,2]

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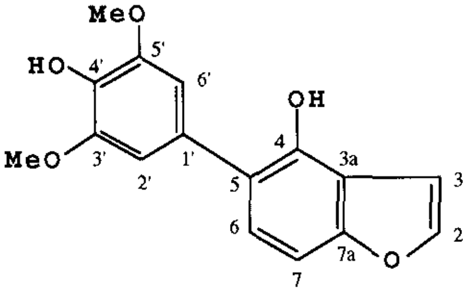
Abstract ----- Two novel arylbenzofurans, garcifuran-A and garcifuran-B were isolated from the roots of *Garcinia kola* (Guttiferae) and the structures were determined by spectroscopic methods

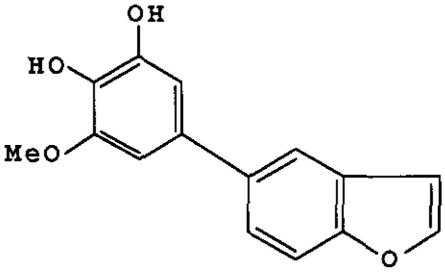
Garcinia species (Guttiferae) are well known as a source of biflavonoids,[3,4] xanthones,[5,6] benzophenones[6] and polyprenylated phloroglucinols.[7] In the course of our search for C-3/C-3"-biflavanones,[8,9] we have studied the chemical constituents of the roots of *G. kola* Heckel collected in Nigeria and isolated two novel arylbenzofuran derivatives named garcifuran-A (**1**)[1,2] and garcifuran-B (**2**) which possess a novel 5-arylbenzofuran skeleton. In the present paper, we wish to report the isolation and structures of garcifuran-A (**1**) and garcifuran-B (**2**).

Isolation The methanol extract of the plant material was partitioned between chloroform and water, and then the organic layer was subjected to column chromatography on silica gel using a mixture of chloroform and ethyl acetate (10 : 1) to give a mixture of garcifurans-A and B. The mixture was further separated by column chromatography on silica gel using a mixture of benzene and methanol (10 : 1) followed by preparative thin layer chromatography (tlc) [silica gel, hexane - ethyl acetate (2 : 1)] to give garcifurans-A (**1**) and B (**2**) in 0.076 and 0.019% yields, respectively.

Structure of Garcifuran-A (1) Garcifuran-A was found to have the molecular formula $C_{16}H_{14}O_5$ determined by the high resolution EIms. The ir and uv spectra showed the presence of both hydroxy and aromatic groups. In the ^{1}H-nmr of **1**, the AB-type signals at δ_H 7.04 and 7.17 ppm having *J*=8.4 Hz were assigned to *ortho*-located aromatic protons on a benzene ring and the AB-type signals at δ_H 6.96 and 7.62 ppm



Garcifuran-A (1)



Garcifuran-B (2)

having J=2.2 Hz were assigned to *vicinal*-located protons on a furan ring. Furthermore, the small coupling constant (J=0.7 Hz) between a proton at δ_H 6.96 ppm and a proton at δ_H 7.04 ppm indicated the characteristic long range coupling between the 3- and 7-protons on a benzofuran ring.[10] These data suggested **1** to be 4,5-disubstituted benzofuran. This was further supported by HMBC experiment as follows. The correlations were observed between H-2 and C-3a, H-2 and C-7a, H-3 and C-7a, H-6 and C-4, H-6 and C-7a, H-7 and C-3a, and H-7 and C-5, respectively. Two substituents, a hydroxy group and a phenyl group at C-4 and 5 were determined as follows. The nmr data (δ_H 3.86 (6H, s) and 6.80 ppm (2H, s)) coupled with both experiments of HMBC and NOE indicated the substituent at C-5 to be a 4-hydroxy-3,5-dimethoxyphenyl group. The correlation between H-2' and C-5, and the enhancements of the signals (19.2% at δ 3.86 ppm (MeO) and 5.0% at δ 7.17 ppm (H-6)) on irradiation of the signal at δ 6.80 ppm (H-2' (6')) were observed in HMBC and NOE experiments, respectively.[11] This led the substituent located at C-4 to be a hydroxy group. Thus, the structure of garcifuran-A should be 4-hydroxy-5-(4'-hydroxy-3',5'-dimethoxyphenyl)benzofuran (**1**).[1]

Structure of Garcifuran-B (2) Garcifuran-B was found to have the molecular formula $C_{15}H_{12}O_4$ determined by the high resolution EIms The ir and uv spectra showed close similarity with those of garcifuran-A (**1**). In the ^{1}H-nmr of **2**, two AB-type signals at δ_H 7.46 and 7.53 ppm (J=8.6 Hz) assigned to *ortho*-located aromatic protons on a benzene ring (H-6 and H-7) and at δ_H 6.80 and 7.65 ppm (J=2.2 Hz) assigned to *vicinal*-located protons on a furan ring (H-3 and H-2). Furthermore, the characteristic long range coupling (J=0.7 Hz) between a proton at δ_{H-3} 6.80 ppm and a proton at δ_{H-7} 7.53 ppm was observed as shown in **1**.[10] The signal

Table 1. ^{1}H and ^{13}C Nmr data of garcifuran-A (**1**) and garcifuran-B (**2**)

	Garcifuran-A (1) [a,b]		**Garcifuran-B (2)** [a,c]	
Position	^{1}H	^{13}C	^{1}H	^{13}C
2	7.62 d (2.2)*	145.8	7.65 d (2.2)*	145.6
3	6.96 dd (2.2, 0.7)	105.9	6.80 dd (2.2, 0.7)	106.7
4	-	149.0	7.72 d (1.7)	119.3
5	-	124.5	-	136.4
6	7.17 d (8.4)	129.0	7.46 dd (8.6, 1.7)	123.7
7	7.04 dd (8.4, 0.7)	105.0	7.53 dd (8.6, 0.7)	111.4
3a	-	119.6	-	127.9
7a	-	157.9	-	154.4
1'	-	131.9	-	134.1
2'	6.80 s	109.2	6.71 d (1.7)	102.6
3'	-	149.8	-	144.1
4'	-	136.4	-	131.7
5'	-	149.8	-	147.1
6'	6.80 s	109.2	6.87 d (1.7)	108.0
3'-OMe	3.86 s	57.6	3.96 s	56.2
5'-OMe	3.86 s	57.6	-	-

a. All assignments were confirmed by H-H COSY, C-H COSY and HMBC
b The spectra were taken in CD_3OD
c· The spectra were taken in $CDCl_3$
* Coupling constans are given (J in Hz) in parentheses

at δ_H 7.46 ppm was further coupled with the signal at $\delta_{H\text{-}4}$ 7.72 ppm (J=1.7 Hz). These data suggested **2** to be a 5-substituted benzofuran. This was further supported by HMBC experiment showing the correlations between H-4 and C-6, H-4 and C-7a, and H-6 and C-4, respectively. A methoxyl group (δ 3.96 ppm (3H, s)), two unsymmetrical *meta*-coupling protons ($\delta_{H\text{-}2'}$ 6.71 (1H, d, J=1.7 Hz) and $\delta_{H\text{-}6'}$ 6.87 (1H, d, J=1.7 Hz)), and two protons due to two hydroxy groups (δ 5.40 ppm (2H, s)) indicated the subsituent at C-5 to be a 4,5-dihydroxy-3-methoxyphenyl group. The enhancements of the signals (9.1% at δ 3.96 ppm (MeO) on irradiation of the signal at δ 6.71 ppm (H-2') and 5.0 % at δ 7.72 ppm (H-4)) on irradiation of the signal at δ 6.87 ppm (H-6'), respectively were observed in NOE experiments.

Thus, the structure of garcifuran-B was characterized as 5-(4',5'-dihydroxy-3'-methoxyphenyl)benzofuran (**2**). Garcifuran-A (**1**) and garcifuran-B (**2**) are the first examples of 5-arylbenzofuran.

EXPERIMENTAL

Ir spectra were recorded on a JASCO FT/IR-5000 infrared spectrophotometer. Uv spectra were taken on a JASCO UVIDEC-610 spectrophotometer. ^{1}H and ^{13}C nmr spectra were recorded on a JEOL GX-400 (400 and 100 MHz, respectively) spectrometer. Chemical shifts are presented in terms of δ (ppm) with $CHCl_3$ (7.26 ppm) in the solvent $CDCl_3$ as an internal standard.

Plant material

The roots of *G kola* Heckel (450 g) collected in Kogi State of Nigeria were identified by Mr. J. Phillip, Principal Forest Officer, Ankpa Local Government, Kogi State, Nigeria.

Extraction and Isolation

The dried and powdered roots (450 g) of *G. kola* Heckel were extracted with MeOH (5 l x 2) under reflux (3 h). The extract was treated with EtOAc and H_2O to give an EtOAc soluble fraction (58 g). A part of the fraction (21 g) was further partitioned between $CHCl_3$ and H_2O to give a $CHCl_3$ soluble fraction (211 mg). The $CHCl_3$ soluble fraction (211 mg) was fractionated by CC on silica gel (Katayama Chemical, Osaka, K230 6.0 g) with $CHCl_3$ - EtOAc (10 : 1) to give 4 fractions (Fr. 1; 25mg, Fr. 2; 75 mg, Fr. 3; 15 mg, Fr. 4; 76 mg). The second fraction (75 mg) was further separated by CC on silica gel (K230 7.0 g) with benzene - MeOH (10 : 1) to give the crude compounds. Each crude compound was purified by preparative tlc on silica gel (Merck 5744) with hexane - AcOEt (10 : 1) to give pure garcifuran-A (**1**) and garcifuran-B (**2**) in 4 mg and 16 mg yields, respectively.

Garcifuran-A (**1**)

Colorless oil. HRms, *m/z* 286.0848 [M$^+$] ($C_{16}H_{14}O_5$ requires: 286.0840). LRms, *m/z* 286 (M$^+$, 100), 271 (10), 239 (39), 211 (42). Uv (MeOH) λ_{max} nm (ε). 218 (26600), 245 (19800), 250 sh (14800), 268 sh (7700). Ir (film) ν 3400 br cm^{-1}. ^{1}H and ^{13}C nmr : see Table 1.

Garcifuran-B (**2**)

Colorless oil. HRms, *m/z* 256.0725 [M$^+$] ($C_{15}H_{12}O_4$ requires: 256.0734). LRms, *m/z* 256 (M$^+$, 100), 241 (20), 213 (43). Uv (MeOH) λ_{max} nm (ε): 218 (31200), 244 (16700), 256 sh (12500), 267 sh (8100). Ir (film) ν 3400 br cm^{-1}. ^{1}H and ^{13}C nmr : see Table 1.

ACKNOWLEDGEMENT

We are thankful to Professor M. B. Ahmed of University of Maiduguri (Maiduguri, Nigeria) for his encouragement, Mr. J. Phillip of Ankpa Local Government (Kogi State, Nigeria) for procurement of the plant material, Dr. C. Ito of Meijo University (Nagoya, Japan) for the HMBC measurement, and Dr. S. Kosemura of Keio University (Yokohama, Japan) for HRMS measurement and valuable suggestion.

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Received, 27th December, 1993