GARCIPYRAN, A NOVEL 6-ARYL-1,2-BENZOPYRAN DERIVATIVE FROM *GARCINIA KOLA*

Masatake Niwa,[a*] Junko Ito,[a] Kenji Terashima,[a] and Muhd Aqil[b]

[a]Faculty of Pharmacy, Meijo University, Tempaku, Nagoya 468, Japan
[b]Department of Chemistry, Faculty of Science, University of Maiduguri,
P. M. B. 1069, Maiduguri, Nigeria

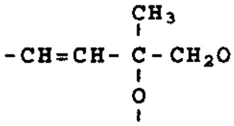
Abstract ----- A novel 6-aryl-1,2-benzopyran derivative named garcipyran was isolated from the roots of *Garcinia kola* (Guttiferae) and the structure was elucidated by spectroscopic and chemical methods. The plausible biogenetic pathways of 6-aryl-1,2-benzopyran (garcipyran) and 5-arylbenzofuran (garcifuran-B) were also discussed.

The studies on the constituents of plants of *Garcinia* genus (Guttiferae) have recently received more attention than before in the points of view of natural medicinal resources.[1~3] In the previous papers,[4,5] we also reported the isolation and structures of two novel 5-arylbenzofurans named garcifuran-A (**1**) and garcifuran-B (**2**) from the roots of *Garcinia kola* Heckel collected in Nigeria. Our continuous study on the constituents of the above plant led to the isolation of a novel arylbenzopyran derivative named garcipyran (**3**). In the present paper we wish to describe the structure of garcipyran (**3**) and to discuss the biogenetic relationship between garcifuran-B (**2**) and garcipyran (**3**).

Isolation The chloroform soluble fraction of the methanol extract described in the previous paper[5] was separated by column chromatography on silica gel using a mixture of chloroform and ethyl acetate. More polar fraction than one including garcifurans-A and B gave crude garcipyran. The crude material was purified by repeated preparative thin layer chromatographies (tlc) on silica gel to give garcipyran (**3**) in 0.033% yield.

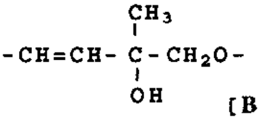
Structure of Garcipyran (3) Garcipyran (**3**) was found to have the molecular formula $C_{18}H_{18}O_5$ by the high resolution EIms. The ir and uv spectra showed the presence of both hydroxy and aromatic groups. In the ^{1}H-nmr of **3**, two singlet signals at δ_H 1.40 and 3.93 ppm were assigned to a methyl group attached on fully substituted carbon bearing oxygen and a methoxyl group on a benzene ring, respectively.

In the H-H COSY spectrum of garcipyran (**3**), three correlations were observed between the signals at δ 6.83 (H-8) and δ 7.28 (H-7), the signals at δ 7.14 (H-5) and δ 7.28 (H-7), and the signals at δ 6.62 (H-2') and δ 6.77 (H-6'). The strong resemblance of the chemical shift values of C-1' to C-6' carbons in the ^{13}C-nmr spectrum of **2**[5] to those of **3** (see Table 1) suggested garcipyran to have such a substituted biphenyl structure as shown in garcifuran-B (**2**). Moreover, the nmr data; δ_H 5.63 (1H, d, *J*=10.3 Hz), 6.52 (1H, d, *J*=10.3 Hz), 3.64 (1H, d, *J*=11.7 Hz), 3.74 (1H, d, *J*=11.7 Hz), 1.40 (3H, s), and δ_C 127.2 (d), 124.9 (d), 79.6 (s), 68.8 (t), 22.7 (q) suggested the presence of the following partial structure **A** or **B**.



$$-CH{=}CH-\overset{\displaystyle CH_3}{\underset{\displaystyle \overset{|}{O}-}{\overset{|}{\underset{|}{C}}}}-CH_2OH$$

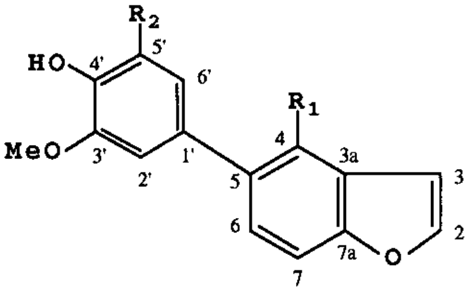
[A]



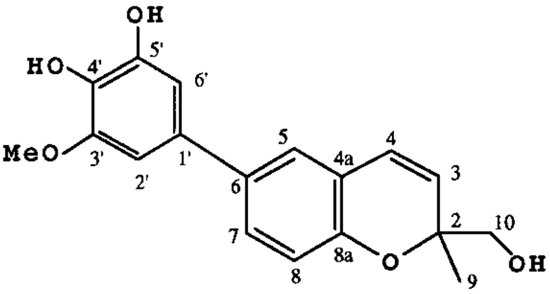
$$-CH{=}CH-\overset{\displaystyle CH_3}{\underset{\displaystyle OH}{\overset{|}{\underset{|}{C}}}}-CH_2O-$$

[B]

Treatment of garcipyran with acetic anhydride in pyridine gave the corresponding triacetate (**4**). The low field shifts of the methylene protons of **3** from δ_H 3.64 and 3.74 ppm to δ_H 4.14 and 4.23 ppm on acetylation indicated garcipyran to have the partial structure **A**.



Garcifuran-A (1); R_1=OH, R_2=OMe
Garcifuran-B (2); R_1=H, R_2=OH



Garcipyran (3)

Table 1. ^{1}H and ^{13}C Nmr data of garcifuran-B (**2**) and garcipyran (**3**)[a,b]

Garcifuran-B (2)			**Garcipyran (3)**		
Position	^{1}H	^{13}C	Position	^{1}H	^{13}C
2	7.65 d (2.2)	145.6	2	-	79.6
3	6.80 dd (2.2, 0.7)	106.7	3	5.63 d (10.3)	127.2
4	7.72 d (1.7)	119.3	4	6.52 d (10.3)	124.9
5	-	136.4	5	7.14 near s	125.0
6	7.46 dd (8.6, 1.7)	123.7	6	-	133.1
7	7.53 dd (8.6, 0.7)	111.4	7	7.28 near d (8.3)	127.7
			8	6.83 d (8.3)	116.4
			9	1.40 s	22.7
			10	3.64 d (11.7)	68.8
				3.74 d (11.7)	
3a	-	127.9	4a	-	121.0
7a	-	154.4	8a	-	151.8
1'	-	134.1	1'	-	134.3
2'	6.71 d (1.7)	102.6	2'	6.62 near s	101.9
3'	-	144.1	3'	-	144.1
4'	-	131.7	4'	-	131.7
5'	-	147.1	5'	-	147.1
6'	6.87 d (1.7)	108.0	6'	6.77 near s	107.3
3'-OMe	3.96 s	56.2	3'-OMe	3.93 s	56.2

a: All assignments were confirmed by H-H COSY, C-H COSY and HMBC spectra.

b: Coupling constants are given (J in Hz) in parentheses

From the evidence mentioned above, the structure of garcipyran should be represented as 2-hydroxymethyl-2-methyl-6-(4',5'-dihydroxy-3'-methoxyphenyl)-1,2-benzopyran (**3**). This was supported by NOE experiments. Namely, 9.6% enhancement of the signal H-5 was observed on irradiation at the signal H-4, and 4.5% enhancement of the signal H-3 was also observed on irradiation at the signal H-9. The absolute stereo-structure at the C_2-position remains unsettled.

Biogenetic Pathways We finally discuss the plausible biogenetic pathway of garcifuran-B (**2**) and garcipyran (**3**). The co-occurrence and their structural resemblance suggest that both compounds (**2**)and(**3**) are biosynthesized from the common precursor, a prenylated biphenyl compound(**5**)as shown in Figure 1.[6] Garicifuran-B (**2**) would be derived from the precursor (**5**) by a series of reactions; epoxidation, cyclization and fragmentation, and garcipyran (**3**) would also be derived from by a series of reactions; dehydration, epoxidation and cyclization.

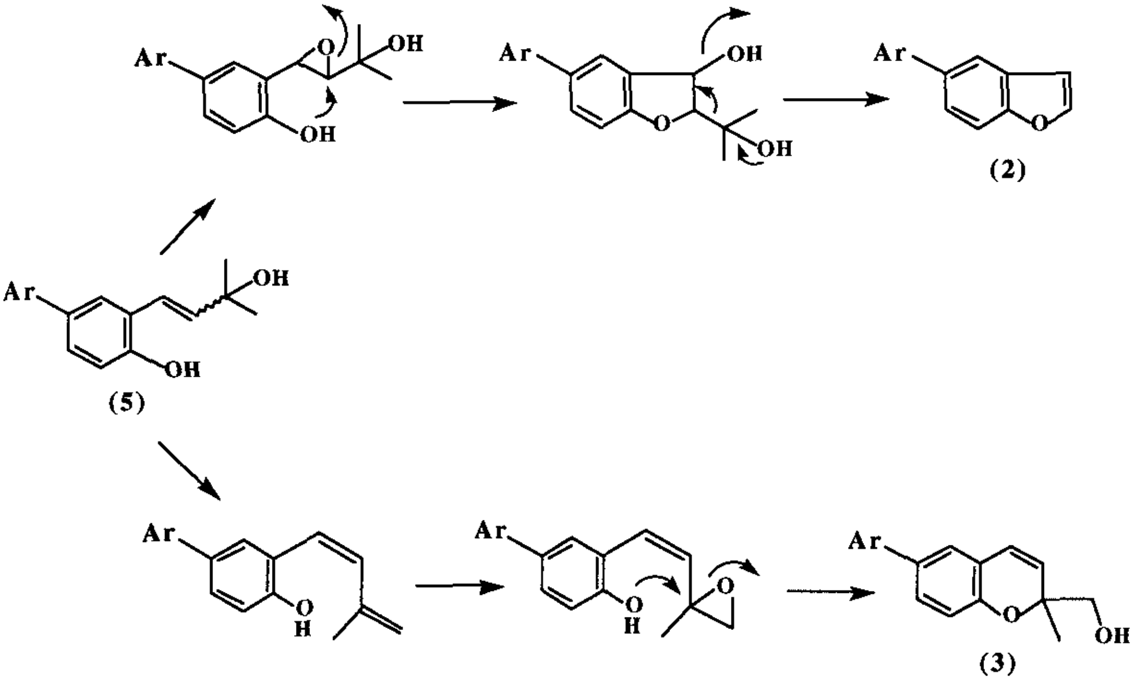


Figure 1. Plausible biogenetic pathways of garcifuran-B (**2**) and garcipyran (**3**)

EXPERIMENTAL

Ir spectra were taken on a JASCO FT/IR-5000 infrared spectrophotometer. Uv spectrum was recorded on a JASCO UVIDEC-610 spectrophotometer. Optical rotation was recorded on a JASCO DIP-181 polarimeter at 25°C. ^{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_H and δ_C (ppm) with $CHCl_3$ (7.26 and 77.0 ppm, respectively) in the solvent $CDCl_3$ as an internal standard. Coupling constants are given (*J* in Hz) in parentheses. Mass spectra were recorded on a Hitachi M-80 spectrometer.

Isolation

The last fraction (76 mg) separated by CC on silica gel with $CHCl_3$ - EtOAc(10 : 1) described in the previous paper[4] was subjected to CC on silica gel (Katayama Chemical, Osaka, K70 3.0 g) with a mixture of $CHCl_3$ - EtOAc(10 : 0 to 7: 3) to give 4 fractions (Fr. 1; 4 mg, Fr. 2; 21 mg, Fr. 3; 13 mg, Fr. 4; 24 mg). The second fraction (21 mg) was purified by preparative tlc on silica gel (Merck 5744) with benzene - EtOAc (3 : 1) and then hexane - EtOAc (1 : 1) to give garcipyran (**3**) in 7 mg yield.

Garcipyran (**3**)

Colorless oil. $[\alpha]_D$ -2.2 ° (*c* 0.12, $CHCl_3$, cell length; 100 mm). HRms, *m/z* 314.1124 [M$^+$] ($C_{18}H_{18}O_5$ requires: 314.1152). LRms, *m/z* 314 (M$^+$, 27), 283 (100), 268 (27). Uv (MeOH) λ_{max} nm (ε): 229 (36500), 256 (22900), 288 sh (12100). Ir (film) ν 3400 br. cm^{-1}. ^{1}H and ^{13}C nmr : see Table 1.

Acetylation of garcipyran (**3**)

A mixture of **3** (2.5 mg), acetic anhydride (0.3 ml) and pyridine (0.3 ml) was stirred at room temperature over night. After evaporation, the residue was subjected to preparative tlc on silica gel (Merck 5715) with $CHCl_3$ - EtOAc(4 : 1) to give triacetylgarcipyran (**4**) (2.7 mg).

Triacetylgarcipyran (**4**)

$C_{24}H_{24}O_8$. LRms, *m/z* 440 (M$^+$, 14), 367 (M$^+$-CH_2OCOCH_3, 100), 325 (82), 283 (22). Ir (film) ν 1775, 1746 cm^{-1}. ^{1}H nmr, δ_H ($CDCl_3$) 1.46 (3H, s), 2.02 (3H, s), 2.30 (3H, s), 2.32 (3H, s), 3.89 (3H, s), 4.14 (1H, d, *J*=11.7 Hz), 4.23 (1H, d, *J*=11.7 Hz), 5.59 (1H, d, *J*=10.0 Hz), 6.50 (1H, d, *J*=10.0 Hz), 6.84 (1H, d, J=8.3 Hz), 6.91 (1H, d, J=2.0 Hz), 6.97 (1H, d, J=2.0 Hz), 7.15 (1H, d, J=2.4 Hz), 7.30 (1H, dd, J=8.3, 2.4 Hz) ppm. ^{13}C nmr, δ_C ($CDCl_3$) 20.3 (q), 20.7 (q), 20.8 (q), 23.6 (q), 56.3 (q), 68.5 (s), 77.5 (t), 108.4 (d), 113.4 (d), 116.5 (d), 120.8 (s), 124.7 (d), 125.2 (d), 126.3 (d), 128.2 (d), 130.8 (s), 133.1 (s), 139.5 (s), 143.4 (s), 152.4 (s), 152.7 (s), 168.0 (s), 168.4 (s), 170.8 (s) ppm.

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, Professor S. Kosemura of Keio University (Yokohama, Japan) for HMBC and HRMS measurements.

REFERENCES

1. Y. Fukuyama, A. Kamiyama, Y. Mima, and M. Kodama, *Phytochemistry*, 1991, **30**, 3433.
2. Y. Fukuyama, A. Kaneshi, N. Tani, and M. Kodama, *Phytochemistry*, 1993, **33**, 483.
3. M. Yoshikawa, E. Harada, A. Miki, K. Tsukamoto, S. Liang, J. Yamahara, and N. Murakami, *Yakugaku Zasshi*, 1994, **114**, 129.
4. M. Niwa, K. Terashima, and M. Aqil, *Heterocycles*, 1993, **36**, 671.
5. M. Niwa, K. Terashima, J. Ito, and M. Aqil, *Heterocycles*, 1994, **38**, 1071.
6. R. D. H. Murray, J. Mendez, and S. A. Brown, 'The Natural Coumarins: Occurrence, Chemistry and Biochemistry,' John Wiley & Sons Ltd., Chichester, 1982, pp. 173 - 176.

Received, 13th April, 1994