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STRUCTURES OF ISOMBAMICHALCONE AND LOPHIROCHALCONE, BI- AND TETRA-FLAVONOIDS FROM *LOPHIRA LANCEOLATA*

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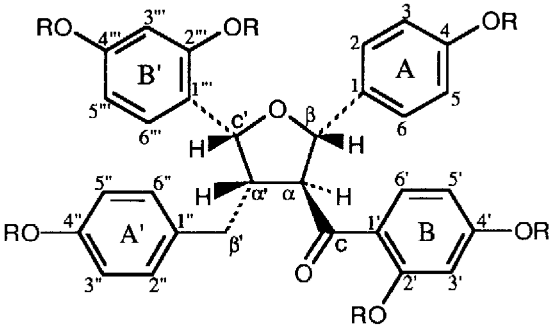
Summary: From the stem bark of *Lophira lanceolata* two new flavonoids, a chalcone dimer, isombamichalcone **1**, and a tetraflavonoid, lophirochalcone **4** have been isolated .

The stem bark of the Cameroonian medicinal plant, *Lophira lanceolata*(*Ochnaceae*) has been shown to be rich in biflavonoids with marked structural particularities [1-3]. From the polar fraction of the AcOEt extract, we have isolated isombamichalcone, and a tetraflavonoid lophirochalcone, for which structures **1** and **4** respectively have been assigned from spectroscopic and chemical evidences. Both compounds were obtained after purification by repeteated column chromatography on silica gel with eluent mixture (1- CH_2Cl_2/AcOEt gradient; 2- CH_2Cl_2/MeOH, 10:1), and showed positive flavonoid test.

1 : R = H
2 : R = CO CH_3
3 : R = CH_3



Isombamichalcone, **1** ($C_{30}H_{26}O_8$), amorphous colorless powder, $[\alpha]_D^{20} = -129°$ (c 0.5, Me_2CO) gave $[M+H]^+$ ion at *m/z* 515 in CIMS, confirming a MW of 514 and showed IR absorption bands (KBr disc) $\upsilon_{cm}{}^{-1}$: 3345 (OH), 1625 (conjugated and chelated C=O), 1618, 1515 (aromatic ring). Complete acetylation (Ac_2O/Py) of **1** gave an amorphous hexa-acetate **2** ($C_{42}H_{38}O_{14}$, M:766), whose ^1H NMR spectrum (Me_2CO-d_6) had six sharp singlet signals (each 3H) at 2.293, 2.273, 2.269, 2.260, 2.217 and 2.153 ppm, indicative of six OH groups in **1**. Permethylation of **1** with CH_3I/K_2CO_3 in dry acetone afforded a hexa-

TABLE 1. ^{13}C and ^{1}H NMR data for isombamichalcone **1** and lophirochalcone **4**.

	1				**4, [I]**				**4, [II]**			
C	δ_C	(*m*)	δ_H	(*m*) J	δ_C	(*m*)	δ_H	(*m*) J	δ_C	(*m*)	δ_H	(*m*) J
1'	113.5	s			116.3	s			110.3	s		
2'	166.6	s			*167.5	s			*166.8	s		
3'	103.3	d	6.177	d 2.4	103.8	d	6.351	d 2.4	103.4	d	6.186	d 2.4
4'	165.5	s			*165.6	s			*165.7	s		
5'	108.3	d	5.909	dd 8.9;2.4	109.2	d	6.560	dd 9.0;2.4	108.5	d	5.958	dd 9.1;2.4
6'	133.7	d	6.444	d 8.9	133.2	d	7.920	d 9.0	133.8	d	6.410	d 9.1
C	205.5	s			192.6	s			205.5	s		
α	59.6	d	3.796	dd 6.5;3.7	117.9	d	7.284	d 15.2	60.1	d	3.702	dd 6.5;3.5
β	84.0	d	5.169	d 6.5	145.6	d	7.684	d 15.2	84.4	d	5.138	d 6.5
1	133.3	s			128.3	s			131.8	s		
2	128.2	d	7.310	m	126.4	d	7.011	d 1.8	128.3	d	7.166	m
3	116.2	d	6.841	m	132.7	s			116.3	d	6.837	m
4	157.7	s			•157.0	s			°157.9	s		
5	116.2	d	6.841	m	110.3	d	6.844	d 6.8	116.3	d	6.837	m
6	128.2	d	7.310	m	132.4	d	7.512	d 6.8;1.8	128.3	d	7.166	m
1'''	117.3	s			121.3	s			117.3	s		
2'''	155.6	s			163.5	s			155.7	s		
3'''	103.2	d	6.425	d 2.4	103.8	d	6.440	d 2.4	103.8	d	6.521	s
4'''	158.3	s			°158.3	s			154.1	s		
5'''	107.3	d	6.423	dd 9.0;2.4	108.0	d	6.505	dd 8.4;2.4	109.2	s		
6'''	128.9	d	7.430	d 9.0	131.7	d	7.390	d 8.4	128.6	d	7.768	s
C'	81.0	d	5.491	d 6.0	42.8	d	4.884	d 11.8	81.8	d	5.287	d 6.0
α'	51.9	d	3.191	dddd 13.1;6.0; 4.4;3.7	52.8	d	4.708	dd 11.8;3.1	52.4	d	3.205	m
β'	36.5	t	2.414 2.241	dd -13.4;4.4 dd -13.4;13.1	90.7	d	5.581	d 3.1	36.7	t	2.479 2.147	dd 13.6;4.1 dd 13.6;13.6
1''	131.4	s			128.6	s			134.1	s		
2''	130.9	d	6.758	m	128.3	d	7.086	m	131.2	d	6.782	m
3''	116.1	d	6.563	m	116.3	d	6.791	m	116.3	d	6.598	m
4''	156.4	s			°157.9	s			•156.6	s		
5''	116.1	d	6.563	m	116.3	d	6.791	m	116.3	d	6.598	m
6''	130.9	d	6.758	m	128.3	d	7.086	m	131.2	d	6.782	m
OH			12.860	s			13.612	s			12.853	s

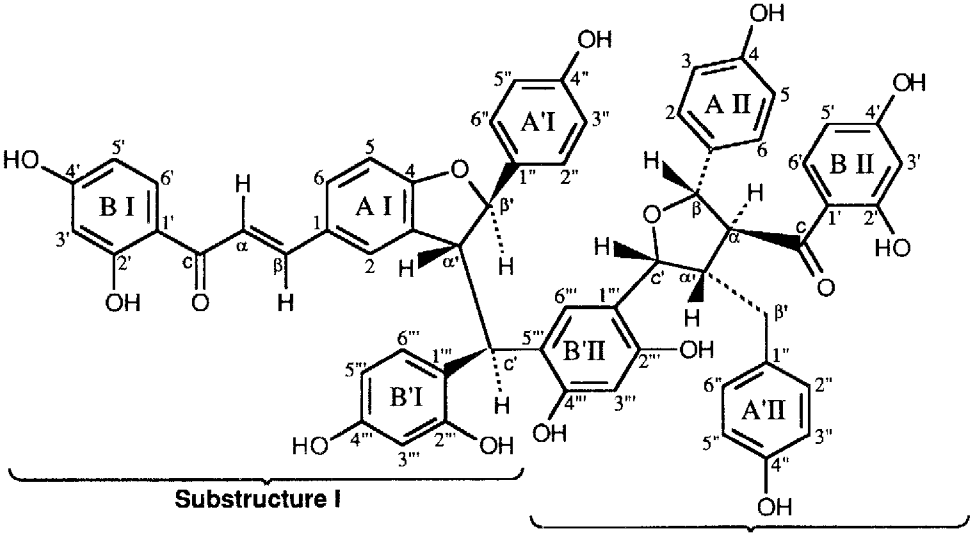
(*,°,• may be reversed; δ ppm; J Hz; *m*: multiplicity).

methyl ether derivative **3** (^{1}H NMR, Me_2CO-d_6, δ_{CH_3O}: 3.859, 3.809, 3.806, 3.802, 3.616, and 3.336 ppm), confirming that all the six hydroxyl groups are phenolic.

The ^{13}C NMR spectrum of **1** had signals of all 30 carbon atoms in the molecule, among which 1 carbonyl, 24 aromatic, and 5 aliphatic (2 >CHO, 2 >CH and 1 CH_2) carbons (Table 1). Its ^{1}H NMR spectra (1D and 2D COSY) revealed four benzene rings (a *p*-hydroxyphenyl, a 2,4-dihydroxyphenyl, a *p*-hydroxybenzyl and a 2,4-dihydroxybenzoyl groups) and a 2,3,4,5-tetrasubstituted tetrahydrofuran ring. A singlet signal at 12.860 ppm collapsing slowly with D_2O addition was assigned to a strongly chelated hydroxyl group. The ^{13}C NMR INADEQUATE spectrum of **1** showed connections between these rings: the benzoyl carbonyl carbon atom (δ_C = 205.5 ppm) was linked to both the quaternary carbon, C-1' (δ_C 113.5) and the methine carbon C-α (δ_C 59.6) while the methylene carbon C-β' (δ_C 36.5) had correlations with the quaternary carbon C-1" (δ_C 131.4) and the methine carbon C-α' (δ_C 51.9). Finally the methine carbons C-β (δ_C 84.0) and C-c' (δ_C 81.0) were connected to C-1 (δ_C 133.3) and C-1"' (δ_C 117.3) respectively leading to structure **1** for isombamichalcone.

The relative configuration of the tetrahydrofuran ring substituents of **1** was determined from ^1H NOE measurements as *trans-trans-cis*, since low values were observed between the vicinal protons α-H and α'-H (0.5%), α-H and β-H (2.9%) and higher values between c'-H and both α'-H (8.2%) and β-H (11.5%). This compound is thus an isomer of mbamichalcone in which the substituents have an all *trans* relative disposition [3].

Lophirochalcone, **4** , amorphous brown solid, $[\alpha]_D^{25}$: +181° (c 0.6, Me_2CO) gave $[M-H]^-$ ion at *m/z* 1007 in $FAB^{(-)}$ MS consistent with molecular formula $C_{60}H_{48}O_{15}$. IR absorptions were indicative of hydroxyl (3409 cm^{-1}), conjugated and chelated C=O, (1626 cm^{-1}), and aromatic ring (1515 cm^{-1}). The presence of eleven hydroxyl groups in **4** was evident from the fact that its complete acetylation (Ac_2O/Py) gave an undeca-acetate ($C_{82}H_{70}O_{26}$), the ^1H NMR of which showed eleven methyl signals from AcO at 2.310, 2.302, 2.274, 2.264, 2.243, 2.195, 2.171, 2.164, 2.152, 2.048, and 2.037 ppm.



4

The spin systems identified from ^{13}C and ^1H NMR (1D and 2D COSY) spectra of **4** (Table 1) were eight benzene rings (one 1,2,4,5-tetrasubstituted, three 1,2,4-trisubstituted, three 1,4-disubstituted phenyls and a dihydrobenzofuran ring), a tetrasubstituted tetrahydrofuran ring, a methine and a methylene groups, a disubstituted *trans* double bond and two carbonyls. Singlet signals at δ_H: 12.853 ppm (1H) and 13.612 ppm (1H) were assigned to two hydroxyl groups *peri* to carbonyl groups.

Chemical shifts and coupling constants from ^{1}H NMR spectrum of **4** were very similar to those for isombamichalcone (**1**) and lophirone C [2]. Examination of the long range ^{1}H-^{1}H COSY spectrum of **4** established two substructures (I and II): I is similar to lophirone C, but has the carbonyl carbon c' reduced to a >CH- group, while **II** is basically isombamichalcone, except that it has only two protons (3"' and -6"')-H on the **B'-II** ring. Cross peaks observed between 6"'(ring **B'-II**) -H and the methine proton (c',**I**)-H at δ_H = 4.884 show that the interflavonoid bond is between the carbons C-c' from substructure **I** and C-5"' from substructure **II**.

NOE difference experiments and the ^{1}H NOESY spectrum of lophirochalcone **4** allowed its relative stereochemistry to be defined. In substructure **I**, a weak NOE effect between β'-H and α'-H (2.9%) indicated their *trans* disposition on the dihydrofuran ring. No NOE was observed between α'-H and C'-H confirming that they are in a favoured *anti* conformation, in agreement with the large value (11.8 Hz) of their mutual coupling constant. But strong NOEs were measured between C'-H and β'-H (7.8%) which are nearby in space and also between α'(**I**)-H and each of the three protons (2",6")(**A'-I**)-H (8.8%), 6"'(**B'-I**)-H (7.4%) and 6"'(**B'-II**)-H (6.8%). A NOE effect (1.6%) observed between 6"'(**B'-II**)-H and β'(**I**)-H implies that they are *gauche* and thus allows assignment of ring **B'-I** and **B'-II** respective positions. The relative stereochemistry of the tetrahydrofuran ring (substructure **II**) was deduced from the strong NOEs observed between c'(**II**)-H and both α'(**II**)-H (10.0%) and β(**II**)-H (8.3%) that are all *cis*, whereas α(**II**)-H was placed *trans* because it gave a weak NOE (1.2%) with β(**II**)-H. Thus the relative stereochemistry of substructures **I** and **II** is the same as in lophirone C and **1** respectively. Significant NOEs observed between aromatic protons (2",6")(**A'-I**)-H and the methylene protons β' (0.9 and 1.6%) of substructure **II** imply their spatial proximity and can be only explained by the relative stereochemistry of substructure **I** as compared to that of substructure **II** depicted in **4**. These results were confirmed by analysis of the ^{1}H NOESY spectrum which showed in addition strong cross peaks between (2,6)-H of ring (**A-II**) and (2",6")-H of ring (**A'-I**); this data also favoured the relative stereochemistry between substructures I and **II** indicated in structure **4**.

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