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A NOVEL HEXAFLAVONOID FROM LOPHIRA ALATA.

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Abstract : From the MeOH extract of the stem bark of *Lophira alata* a hexaflavonoid has been isolated, the structure of which has been elucidated by spectroscopic and chemical evidence.

Previous investigations{1,2,3,4}, have shown that the methanolic extract of the stem bark of *Lophiraalata* Banks ex Gaertn contains many very polar new polyflavonoids, some having important antibacterial and antiviral activities. These interesting results made us examine a more polar fraction of the same extract, which after purification by repeated chromatography over silica gel, gave 10mg of an amorphous light brown solid, Azobechalcone **1** the structure of which is reported in this paper.

Azobechalcone **1**, showed a positive flavonoid test and was attributed the molecular formula $C_{90}H_{72}O_{22}$, from HR-FAB$^+$-MS analysis in which the $(M+H)^+$ appeared at m/z 1503.4439 (Calculated $C_{90}H_{73}O_{22}$ requires 1503.4436). Strong absorptions observed in its IR spectrum (KBr paste) at 3460 cm^{-1} (hydroxyl) , 1635cm^{-1} (conjugated and chelated carbonyl) and 1618 cm^{-1} (conjugated aromatic double bonds) are consistent with a flavonoid structure.

Its 300 MHz ^{1}H NMR spectra (1D and 2D COSY) had signals defining the following proton systems: four 1,4 - disubstituted benzene rings; four 1,2,4 - trisubstituted benzene rings; two 1,2,4,5 - tetrasubstituted benzene rings; two benzodihydrofuran rings; one tetrasubstituted tetrahydrofuran ring; two *trans* double bonds; two methine protons; two methylene protons; three strongly chelated hydroxyl groups at 12.761, 13.552 and 13.521 ppm typical of hydroxyl functions *peri* to carbonyl groups.

Azobechalcone has a total of 16 hydroxyl groups since its total methylation (CH_3I/ K_2CO_3) gave a mixture of three compounds among which a major band, recovered by prep.TLC on SiO_2 support showed no residual hydroxyl IR absorption. Its ^{1}H NMR spectrum showed distinct signals for 16 CH_3O groups (δppm: 3.349, 3.581, 3.589, 3.598, 3.611, 3.619, 3.641, 3.658, 3.672, 3.729, 3.752, 3.774, 3.781, 3.869, 3.878, 3.887, each 3H).

Detailed analysis of the COSY LR ^{1}H NMR spectra of Azobechalcone established the fact that three biflavonoid substructures (I, II and III) were implicated in its structure such that I and II are similar to lophirone C {5} while III is closely related to mbamichalcone{1}. Correlation spots observed between proton $H_{6'''}$ (ring B_4, δppm: 7.959) and the proton $H_{c'1}$(δ 4.979 ppm), locates the first interflavonoid bond linking I and II using carbons C'_1(δCppm: 43.4) and $C_{5'''}$(δCppm:

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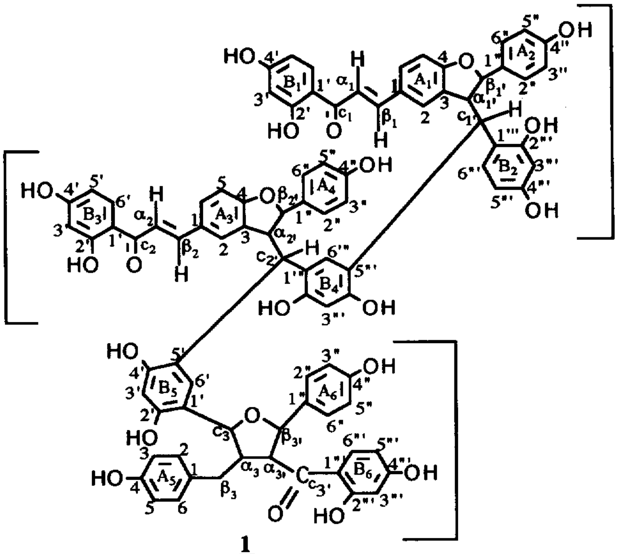
TABLE 1: NMR DATA (^{13}C: 75.6Mz and ^{1}H : 300 Mz with solvent acetone d_6).

Carbon No	δCppm:		δH ppm	J (Hz)	Carbon No	δCppm:		δH ppm	J (Hz)	Carbon No	δCppm:		δH ppm	J (Hz)
1 (A$_1$)	127.9	s	-		1 (A$_3$)	127.4	s	-		1 (A$_5$)	131.5	s	-	
2(A$_1$)	126.0	d	6.641	d(1.8)	2(A$_3$)	125.7	d	6.641	d(1.8)	2(A$_5$)	131.2	d	6.815	m*
3 (A$_1$)	132.6	s	-		3 (A$_3$)	132.6	s	-		3 (A$_5$)	116.0	d	6.572	m*
4 (A$_1$)	162.8	s	-		4 (A$_3$)	163.1	s	-		4 (A$_5$)	156.4	s	-	
5 (A$_1$)	109.0	d	6.762	d(8.2)	5 (A$_3$)	109.8	d	6.652	d(8.1)	5 (A$_5$)	116.0	d	6.572	m*
6 (A$_1$)	132.5	d	7.452	dd(8.2; 1.8)	6 (A$_3$)	133.0	d	7.329	dd(8.1; 1.8)	6 (A$_5$)	131.2	d	6.815	m*
α_1	117.4	d	7.168	d(15.2)	α_2	117.3	d	7.573	d(15.3)	α_3	52.2	d	3.306	dddd(5,1; 8.4; 9.0; 9.1)
β_1	145.4	d	7.720	d(15.2)	β_2	145.5	d	7.066	d(15.3)	β_3	36.7	t	a: 2.564	dd(5,1; 13.9)
													b: 2.146	dd(13,9; 9,1)
c_1	192.2	s	-		c_2	192.3	s	-		c_3	81.8	d	5.543	d(8.4)
1' (B$_1$)	114.3	s	-		1' (B$_3$)	114.4	s	-		1' (B$_5$)	117.6	s	-	
2' (B$_1$)	167.0	s	-		2' (B$_3$)	167.0	s	-		2' (B$_5$)	153.4	s	-	
3' (B$_1$)	103.2	d	6.321	d(2.1)	3' (B$_3$)	103.6	d	6.324	d(2.3)	3' (B$_5$)	103.5	d	6.426	s
4' (B$_1$)	165.3	s	-		4' (B$_3$)	165.3	s	-		4' (B$_5$)	155.5	s	-	
5' (B$_1$)	109.3	d	6.633	dd(8.9; 2.1)	5' (B$_3$)	110.1	d	6.545	dd(8.8; 2.3)	5' (B$_5$)	121.2	s	-	
6' (B$_1$)	133.1	d	7.872	d(8.9)	6' (B$_3$)	133.7	d	7.795	d(8.8)	6' (B$_5$)	127.5	d	7.670	s
1" (A$_2$)	133.0	s	-		1" (A$_4$)	133.7	s	-		1" (A$_6$)	132.3	s	-	
2"(A$_2$)	128.4	d	7.008	m*	2"(A$_4$)	128.7	d	6.970	m*	2"(A$_6$)	128.1	d	7.163	m*
3" (A$_2$)	115.9	d	6.856	m*	3" (A$_4$)	116.2	d	6.544	m*	3" (A$_6$)	116.2	d	6.704	m*
4" (A$_2$)	158.1	s	-		4" (A$_4$)	158.2	s	-		4" (A$_6$)	157.9		-	
5" (A$_2$)	115.9	d	6.856	m*	5" (A$_4$)	116.2	d	6.544	m*	5" (A$_6$)	116.2	d	6.704	m*
6" (A$_2$)	128.4	d	7.008	m*	6" (A$_4$)	128.7	d	6.970	m*	6" (A$_6$)	128.1	d	7.163	m*
α'_1	51.0	d	4.329	dd(4.0; 11.8)	α'_2	53.5	d	4.656	dd(3.0; 11.3)	α'_3	60.0	d	3.738	dd(9.0; 8.2)
β'_1	90.5	d	5.471	d(4.0)	β'_2	90.7	d	5.661	d(3.0)	β'_3	84.6	d	5.269	d(8.2)
c'_1	43.4	d	4.979	d(11.8)	c'_2	40.3	d	4.796	d(11.3)	c'_3	205.3	s	-	
1"' (B$_2$)	121.1	s	-		1"' (B$_4$)	122.2	s	-		1"' (B$_6$)	113.4	s	-	
2"'(B$_2$)	156.2	s	-		2"'(B$_4$)	154.9	s	-		2"'(B$_6$)	166.2	s	-	
3"' (B$_2$)	103.1	d	6.288	d(2.4)	3"' (B$_4$)	103.1	d	6.494	s	3"' (B$_6$)	103.4	d	6.157	d(2.4)
4"' (B$_2$)	157.6	s	-		4"' (B$_4$)	154.9	s	-		4"' (B$_6$)	165.4	s	-	
5"' (B$_2$)	107.7	d	6.288	dd(2.4; 8.0)	5"' (B$_4$)	121.8	s	-		5"' (B$_6$)	108.3	d	5.954	dd(8.9; 2.4)
6"' (B$_2$)	130.1	d	7.069	d(8.0)	6"' (B$_4$)	131.8	d	7.959	s	6"' (B$_6$)	133.7	d	6.459	d(8.9)

* AA'BB' complex; Multiplicity: s= singulet ; d= doublet ; t= triplet ; m= multiplet.

121.8). Connections between proton $H_{6'}$ (ring B_5, δppm:7.670) and proton $H_{c'2}$ (δ 4.796ppm) show that the link with III is with carbons C'_2(δCppm: 40.3) and $C_{5'}$ (ring B_5, δCppm: 121.2) leading to structure **1** for Azobechalcone.



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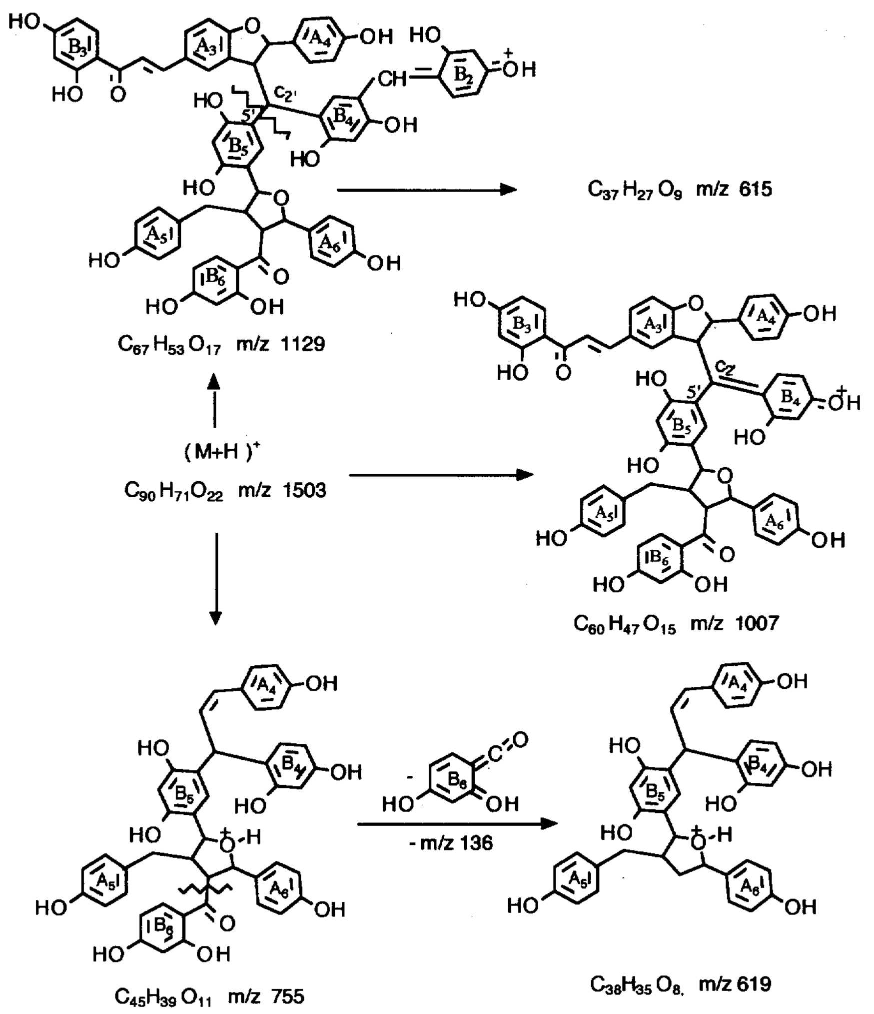
More evidence in support of structure **1**, for Azobechalcone came from its 75.6 MHz CMR spectra in which complete assignments of signals were made using totally decoupled, J-modulated, as well as HMBC spectra. Signals for all 90 carbon atoms in molecular formular gave chemical shifts very similar to corresponding ones in either lophirone C or mbamichalcone. Major differences observed concerned carbons C'_1 and C'_2 carbonyls in lophirone C(δCppm: 201.4 ppm) but reduced in **1** to saturated methine carbons (δCppm: C'_1=43.4 and C'_2=40.3) .

The fragmentation pattern in the MS of Azobechalcone reflects structure **1**. Interflavonoid bond cleavage in $(M+H)^+$ ion at 1503 accounts for abundant ions at m/z 1007 and m/z 615. The base peak at m/z 1129 comes from the rupture of the bond between carbons $\alpha_{1'}$ and $C_{1'}$ while other important ions at m/z 755 and m/z 619 are accounted for in Scheme 1.

An all *trans* stereochemistry of the pentacyclic heterocyclic protons in **1**, was evident as corresponding protons to those in either lophirone C or mbamichalcone having practically the same chemical shifts and coupling constants are in an all *trans* stereochemistry. Confirmation came from NOE differences measurements in which no correlation spots were observed between: $H_{\alpha'1}$ and $H_{\beta'1}$ $H_{\alpha'2}$ and $H_{\beta'2}$; and finally $H_{\beta'2}$ and $H_{c'2}$. Equally, protons H_{c3} and $H_{\alpha3}$; $H_{\alpha3}$ and $H_{\alpha'3}$; $H_{\alpha'3}$ and $H_{\beta'3}$ show very faint enhancements in accord with a *trans* - *trans* - *trans* stereochemistry of the tetrahydrofuran ring.

Biosynthetically, Azobechalcone can be considered to originate from the condensation of a unit each of lophirone C and lophirachalcone {6}.



Scheme 1: Major fragments in MS of **1**

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