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PHENOLIC CONSTITUENTS OF *SEMECARPUS ANACARDIUM*

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Key Word Index—*Semecarpus anacardium*; Anacardiaceae; vesicant catechol derivatives; bhilawanols; biflavanoids; 8,3′-binaringenin; 8,8′-biliquiritigenin.

Abstract—GLC-MS analysis of methylated bhilawanol from *S. anacardium* nuts and its oxidation product, the methyl ester of an aromatic carboxylic acid, conclusively proved that it contains more than seven closely related compounds. Two of them are major components which were isolated and shown to be 1-pentadec-$\Delta^{8'}$-enyl-2,3-dimethoxybenzene (I) and 1-pentadeca-$\Delta^{7',10'}$-dienyl-1,3-dimethoxybenzene (IV). Three related biflavanoids *A*, *B* and *C* have been also isolated from defatted nuts of *S. anacardium*. The first of these has been characterized as its methyl ethers, A_1 and A_2, for which biflavanone structures (VI) and (VII) are suggested on the basis of chemical and spectral evidence. The biflavanones *B* and *C* have been also characterized as their methyl ethers. Suggested structures are *O*-methyl derivatives of a IB-3′, IIA-8-binaringenin (XIV) for the former and IB-3′, IIA-8-biliquiritigenin (XV) for the latter.

RESULTS

The Alkenyl Catechols

IN VIEW of a recent publication[1] on the phenolic constituents of *S. anacardium*, we wish to present the results* of our investigation on the topic. The phenolic oil was named bhilawanol by Pillay and Siddiqui,[2] and these as well as later investigators[3,4] recognized that it was a mixture of several long chain alkenyl catechols. Our preliminary investigation[5] also confirmed this. A study of the methylated bhilawanol, b.p. 212–218°/3 mm was, therefore made using GLC with a 1·5% SE30 column at 200° coupled to a mass spectrometer and Table 1 gives these data.

The GLC analysis indicates more than seven components in the methylated bhilawanol, of which the major component has M^+ 346 (together with a trace of M^+ 344) and formed 83%. The remaining constituents totalled only 17% with M^+ varying from 358 to 168. The fragmentation patterns revealed identical ions at *m/e* 165, 152, 151 in most of these components, derived from the common methylated catechol nucleus of bhilawanols, but the extent of unsaturation cannot be easily assessed from the remaining fragments.

In a further study, the methylated bhilawanol indicated an overall unsaturation of three double bonds in iodine number, peracid estimation and in hydrogenation. Mild oxidation

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* These results were included in the Ph.D. thesis of N. S. P. Rao submitted to Andhra University, in July 1971.

[1] T. R. GOVINDACHARI, B. S. JOSHI, V. N. KAMAT and N. VISWANATHAN, *Indian J. Chem.* **9**, 1044 (1971).

[2] P. P. PILLAY and S. SIDDIQUI, *J. Indian Chem. Soc.* **III**, 517 (1931).

[3] H. S. MASON, *J. Am. Chem. Soc.* **67**, 418 (1945).

[4] B. LOEV, *Nature, Lond.* **186**, 389, 435 (1960); W. S. SYMES and C. R. DAWSON, *J. Am. Chem. Soc.* **75**, 4952 (1953).

[5] N. S. P. RAO and L. R. ROW, *Curr. Sci.* **39**, 207 (1970).

with permanganate in acetone for 30 min was used to provide information regarding the aromatic moiety and the position of double bonds. The products contained the steam-volatile *n*-heptanoic and valeric acids only and no butyric acid (see Ref. 1) could be detected. The non-steam volatile fraction contained the aromatic acids, which were esterified with diazomethane and the methyl esters (b.p. 184°/1 mm) examined by GLC–MS using a 8% PEGA column at 200°. The data (Table 2) were very informative.

TABLE 1. GCL–MS ANALYSIS OF THE METHYLATED BHILAWANOL

Fraction	M^+	*m/e*
1	358(356 minor)	366(341, 328(326), 165(163)
2	346(344 major)	165, 152, 151, 137, 136, 123·3*, 122·5*
3	296	265, 264, 235·6*, 165
4	270	239, 227, 191*, 165, 143
5	222	165, 152, 151
6	208	165, 152, 151
7	168	153, 152, 139·5*

* Metastable.

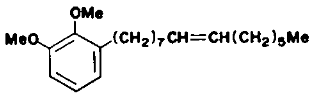
It is quite obvious that the steam non-volatile methyl esters are a mixture of five homologous components which differ in having four to eight methylene groups and they in turn indicate alkenyl catechols in bhilawanol differing in the position of the first double bond from Δ^5 and Δ^9. But there are two major constituents which possess the double bond at Δ^7 and Δ^8 giving rise to two non-volatile aromatic methyl esters of M^+ 280 and 294 respectively in a total yield of 90%. Considering the mild conditions of oxidation, successive degradation of the alkyl side chain of the aromatic acid is unlikely. Therefore, the position of the first double bond in the alkenyl catechols of bhilawanol might vary as indicated.

TABLE 2. GLC–MS ANALYSIS OF THE CARBOXYLIC ACID METHYL ESTER

Comp.	R_t (sec)	M^+	*m/e*	$Ar(CH_2)_nCO_2Me$ (*n*)		Approximate %
1	424	252	152, 151	4	5	1·8
2	615	266	152, 151	5	6	6·2
3	825	280	152, 151	6	7	30·8
4	1100	294	152, 151	7	8	59·4
5	1458	308	152, 151	8	9	1·9

An attempt was, therefore, made to fractionate the methylated bhilawanol on a silica gel column impregnated with 30% silver nitrate. Careful elution with hexane yielded two fractions, bhilawanols *A* and *B* (70 and 10%). These were purified by redistillation and analysed; bhilawanol *A* (b.p. 205°/1 mm, $C_{23}H_{40}O_2$) and bhilawanol *B* (b.p. 196°/1 mm, $C_{23}H_{38}O_2$). Their spectral properties indicated one double bond in *A* and two unconjugated double bonds in *B*.

The MS and NMR spectral characteristics of bhilawanol *A* agree with dimethoxyphenyl-pentadec-$\Delta^{8'}$-ene. Oxidation with neutral permanganate followed by steam distillation yielded *n*-heptanoic acid and a non-volatile aromatic acid (methyl ester M^+ 294, $C_{17}H_{26}O_4$). The MS of both *O*-methylbhilawanol *A* and the methyl ester contained identical peaks at *m*/*e* 165, 152, 151, 136 and 121.[6] In particular, the *m*/*e* 151/152 ratio was about 1·2, which suggested that *meta* stabilization of *m*/*e* 152 and *ortho* or *para* stabilization of *m*/*e* 151 were both occurring, and the methoxyl groups were 2,3 or 3,4. The formation of *n*-heptanoic acid and also *n*-heptanal in ozonolysis confirms the position of the double bond in the side chain. Drastic oxidation of the methyl ester using aqueous alkaline permanganate for 18 hr under reflux furnished a small quantity of *o*-veratric acid (III) which finally settled the 1,2,3-substitution pattern in the aromatic nucleus. Bhilawanol *A* and the derived methyl ester may, therefore, be represented by (I) and (II) which supports the earlier results.[1,2]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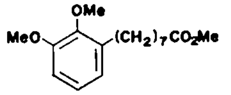
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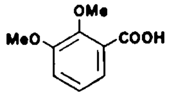
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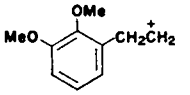
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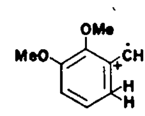
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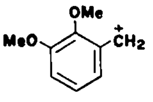
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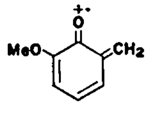
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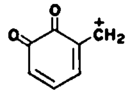
m/e 121

Similar permangante oxidation of bhilawanol *B* furnished the steam volatile *n*-valeric acid (b.p. 185–187°) and a non-volatile aromatic acid whose methyl ester (V) (M^+ 280, $C_{16}H_{22}O_4$) is the next lower homologue of (II). The NMR spectrum of *B* at 100 MHz exhibited a complex pattern similar to those of (I) and (II) for the aromatic protons; four olefinic protons appears as a triplet in the olefinic region (δ 5·31–5·38) and suggested two double bonds which the UV spectrum showed to be unconjugated. Further, six protons appeared as an unresolved multiplet at δ 1·8–2·12 suggesting three allylic methylenes. All these facts can be accommodated in structure (IV) for bhilawanol *B* which is, therefore, 1-pentadeca-$\Delta^{7',10'}$-dienyl-2,3-dimethoxybenzene. The NMR data of both methylated bhilawanols *A* and *B* are given in Table 3.

TABLE 3. NMR DATA OF METHYLATED BHILAWANOLS *A* AND *B* AT 100 MHz IN $CDCl_3$

Methylated bhilawanol *A* δ values	Methylated bhilawanol *B* δ values	No. of protons	Assignment
0·75–0·92(t)	0·8–1·2(t)	3	$-C\underline{H}_3$
1·25–1·27(a)	1·35(b)	(a) = 18	(a) = $-(C\underline{H}_2)_9$
		(b) = 12	(b) = $-(C\underline{H}_2)_6$
1·80–2·14 (m)(a)	1·8–2·14 (m)(b)	(a) = 4	(a) = $C\underline{H}_2-CH=CH-C\underline{H}_2-$
		(b) = 6	(b) = $C\underline{H}_2-CH=CH-C\underline{H}_2-CH=CH-C\underline{H}_2-$
2·40–2·60(m)	2·53–2·9(m)	2	$Ar-C\underline{H}_2$
3·73, 3·76	3·82, 3·85	6	$Ar-(OC\underline{H}_3)_2$
5·17–5·32(t)(a)	5·30–5·47(t)(b)	(a) = 2	(a) = $C\underline{H}=C\underline{H}-$
		(b) = 4	(b) = $C\underline{H}^7=C\underline{H}-CH_2-CH^{10}=CH-$
6·48–6·75(m)	6·68–6·98(m)	3	$Ar-(\underline{H})_3$

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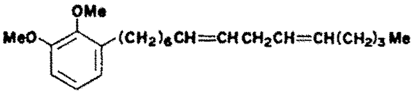
[6] J. L. OCCOLOWITZ, *Analyt. Chem.* 36, 2177 (1964).

The *cis* or *trans* nature of the double bonds in either of the two bhilawanols *A* and *B*, could not be ascertained from the NMR spectra alone. Loev[4] suggested on the basis of hydroxylation studies, that a portion of bhilawanol could be a mixture of *cis*- and *trans*-isomers of 3-(*n*-pentadec-8-enyl)-catechol.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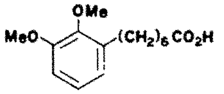
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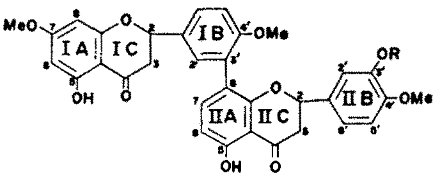
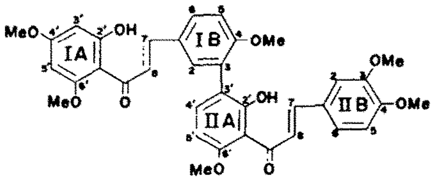

(VII) A_2, R = Me
(VI) A_1, R = H


(VIII)

We could not isolate the fraction *B* reported by Govindachari *et al.*[1] in which the double bonds are situated at carbon atoms 8 and 11. Also, there was no indication of any homologue higher than C_{16}. The GLC–MS indicated the presence of two compounds with M^+ 358 and 356 which could, possibly, be $C_{24}H_{38}O_2$ and $C_{24}H_{36}O_2$ containing two and three double bonds respectively.

TABLE 4. BIFLAVANOIDS OF *Semecarpus anacardium*

Biflavanoids	m.p. (°)	Formula	No. of functional groups OH	OMe	Colour reactions NaBH$_4$	FeCl$_3$	IR ν_{max}^{Nujol} cm^{-1}	UV λ_{max}^{EtOH} nm (ϵ)
O-Trimethyl biflavanone A_1	158–160	$C_{33}H_{28}O_{10}$	3	3	Pink	Brown	3490, 1640	226 (84, 780) 288 (55, 900) 331 (2, 513)
O-Tetramethyl biflavanone A_2	138–140	$C_{34}H_{30}O_{10}$	2	4	Pink	Brown	3490, 1640	226 (84, 690) 288 (54, 800) 331 (2, 500)
O-Hexamethyl bichalcone *A*	238–240	$C_{36}H_{34}O_{10}$	2	6	—	—	3500, 1630	222 289 362
O-Dimethyl biflavanone *B*	180–182	$C_{32}H_{26}O_{10}$	4	2	Pink	Brown	3490, 3385 1640	215 280 310
O-Heptamethyl bichalcone B_1	156–158	$C_{37}H_{36}O_{10}$	1	7	—	—	3500, 1670, 1640–30	300 (25, 450) 353 (48, 650)
O-Hexamethyl bichalcone B_2	218	$C_{36}H_{34}O_{10}$	2	6	—	—	3500, 1630	223 296 348
O-Tetramethyl biflavanone *C*	128–130	$C_{34}H_{30}O_8$	—	4	Pink	—	1640	232 (82, 490) 292 (42, 790) 330 (1, 842)

The Biflavanoids

After removing the vesicant oil, the bruised nuts of *S. anacardium* were powdered and extracted with warm methanol. The extract was distilled under vacuum and the light yellowish brown residue (0·006%) appeared to be flavanoid in character (Table 4). It was methylated with diazomethane and the methyl ether fractionally crystallized from acetone to yield a crystalline compound *B*, m.p. 180–182°. The remaining material was subjected to preparative TLC from which three compounds (A_1, A_2 and *C*) were separated in pure condition. These are closely related new biflavanoids (Table 4) and are designated biflavanones *A*, *B* and *C*.

O-Methyl biflavanones A_1 *and* A_2. These are different methyl ethers of the same biflavanone *A*, since A_1 can be converted into A_2 by further methylation with large excess of diazomethane. Their NMR spectra bring out clearly their close relationship (Table 5).

TABLE 5. NMR SPECTRA OF *O*-METHYL BIFLAVANONES A_1, A_2 AND *C* AT 60 MHz IN $CDCl_3$

Assignment		Biflavanone	Biflavanone	Biflavanone *C*	
Rings	Position	A_1	A_2	$CDCl_3$	Acetone
IA	5–OH	14·41(*s*, 1H)	14·28(*s*, 1H)	Nil	Nil
IIA	5–OH	14·55(*s*, 1H)	14·43(*s*, 1H)	Nil	Nil
IIB	3–OH	7·15(*s*, 1H)*	Nil	Nil	Nil
IA	C–6,8	6·1(*s*, 2H)	6·1(*s*, 2H)	6·0(*s*, 2H)	5·45(*s*, 2H)
IIA	C–6 or 8	6·3(*s*, 1H)	6·25(*s*, 1H)	6·16(*s*, 1H)	5·65(*s*, 1H)
IIA IB IIB	C–7 C–2,5,6 C–2,5,6	6·8–7·3 (*m*, 7H)	6·80–7·18 (*m*, 4H) 7·31(*s*, 3H)	6·75–7·30 (*m*, 9H)	6·10–6·28 (*d*, 2H)*J* 8 Hz 6·58–6·71 (*d*, 2H)*J* 8 Hz 6·40–6·52 (*t*, 1H) 6·72(*s*, 4H) (IA–5 and IIA–5 Protons also)
IC IIC	C–2	5·2–5·6 (*b*, 2H)	5·2–5·6 (*b*, 2H)	5·1–5·5 (*b*, 2H)	—
IC IIC	C–3	2·8–3·2 (*b*, 4H)	2·8–3·15 (*b*, 4H)	2·8–3·0 (*b*, 4H)	—
OMe		3·85(*s*, 9H)	3·85(*s*, 12H)	3·75(*s*, 12H)	—

* Better resolution of the aromatic protons in A_1 was secured in acetone solution. The signals are given as follows after allowing for the shift (0·4 ppm) due to solvent. δ 6·58, 6·72, 6·76, 6·86 (3H); 7·06, 7·10, 7·19 (4H) and δ 7·1–7·2 (b) (1H, exchange with D_2O) due to unchelated hydroxyl at IIB–3′.

A_1 is a trimethyl ether containing two chelated hydroxyls (δ 14·43 and 14·55) and an unchelated hydroxyl (δ 7·1–7·2). The position of the unchelated hydroxyl is clearly revealed when the NMR spectrum is taken in acetone. Biflavanone A_2 on the other hand, contained four methoxyls and two chelated hydroxyls. All the ten oxygens in A_2 are accounted for by the four methoxyls, two hydroxyls and four pyranone oxygens. Consequently, the two flavanone units must be linked by a C–C linkage only, which is placed tentatively at IB-3′–IIA-8 from the following facts and hence *O*-methyl biflavanones A_1 and A_2 may be represented by (VI) and (VII) respectively.

The two hydroxyls in A_2 appear at δ 14·55 and 14·41 unlike the 7″-OH in ginkgetin[7] (δ 10·90). They are chelated and should be placed at IA-5 and IIA-5. Since permanganate oxidation of A_1 and A_2 afforded only veratric acid, the diphenyl system contains only one methoxyl which is placed by analogy and from NMR (Table 5) at IB-4′ leaving IIA-7

[7] T. J. BATTERHAM and R. J. HIGHET, *Austral. J. Chem.* **17**, 428 (1964).

unoccupied. There is no reliable method for distinguishing the C–C linkage between IB-3′ and IIA- or -8, but we would prefer IB-3′ and IIA-8 linkage from several existing analogies. The aromatic protons in A_2 integrate to a total of ten and after allowing C–C linkage at IB-3′ and IIA-6 or -8 and a veratryl ring system in ring IIB, four protons have to be located in rings IA and IIA. The doublet signal at δ 6·1–6·3 integrate to three protons, two of them being *meta* coupled protons of ring IA. The extra proton (δ 6·1, unresolved) is now shown to belong to IIA-6 (or -8) position and couples with an *ortho* proton at IIA-7. These assignments point out clearly that the linkage is likely to be between IB-3′ and IIA-6 or -8 leaving the IIA-7 position free without any substituent.

TABLE 6. NMR DATA OF *O*-METHYL BICHALCONES A, B_1 AND B_2 IN $CDCl_3$

Assignment Rings	Position	A*	B_1*	B_2†
IA	C-2′-OH	14·14 (*s*, 1H)	Nil	14·14 (*s*, 1H)
IIA	C-2′-OH	14·33 (*s*, 1H)	14·32 (*s*, 1H)	14·33 (*s*, 1H)
IA	C-3′, 5′	5·91 (*d*, 1H) *J* 2·5 Hz	5·89 (*d*, 1H) *J* 2·5 Hz	5·99 (*d*, 1H) *J* 2·5 Hz
		6·06 (*d*, 1H) *J* 2·5 Hz	6·07 (*d*, 1H) *J* 2·5 Hz	6·26 (*d*, 1H) *J* 2·5 Hz
IIA	C-3′ or 5′	6·095 (*d*, 1H) *J* 10 Hz	6·37 (*s*, 1H)	6·45 (*s*, 1H)
	C-4′	7·04 (*d*, 1H) *J* 10 Hz	—	—
IB IIB	C-2, 5, 6 C-2, 5, 6	7·46 (*d*, 2H) *J* 2·5 Hz	7·62 (*d*, 2H) *J* 2·5 Hz	7·30–7·70 (*m*, 4H)
		7·55 ($_2$, 2H) *J* 2·5, 8 Hz	7·46 ($_2$, 2H) *J* 2·5, 9·5 Hz	
		6·90 (*d*, 2H) *J* 8 Hz	6·75 (*d*, 3H)‡ *J* 9·5 Hz	6·96 (*d*, 3H)‡ *J* 9·0 Hz
IB IIB	C-7, 8 C-7, 8	7·78 (*s*, 4H)	6·82–6·91 (*b*, 1H) 7·40–7·63 (*b*, 1H) 7·76 (*s*, 2H)	7·88 (*s*, 4H)
OMe		3·78 3·81 (15H) 3·83	3·78 (*s*, 18H)	3·82 3·95 (15H)
		4·02 (3H)	3·36 (3H)	3·5 (3H)

* At 100 MHz. † At 60 MHz. ‡ Contains IIB-3 proton also.

This assignment receives support from the NMR spectrum (Table 6) of *O*-methyl bichalcone A (VIII) obtained by drastic methylation of *O*-methyl biflavanones A_1 or A_2, with dimethylsulphate and K_2CO_3 in acetone. The *O*-methyl bichalcone A is bright yellow, m.p. 236–238° ($FeCl_3$-light brown; Mg–HCl-negative). It analysed for $C_{36}H_{34}O_{10}$, M^+ 626; IR $\nu_{max}^{CHCl_3}$ 3500 (OH), 1630 (C=O) cm^{-1}. It gave on oxidation with neutral permanganate only veratric acid and no anisic acid.

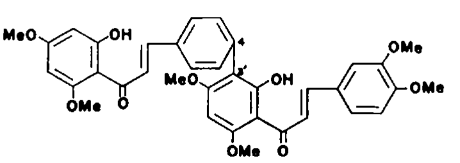
The NMR spectrum of *O*-methyl bichalcone A (Table 6) indicates six methoxyls and two chelated hydroxyls at IA-2′ and IIA-2′ (δ 14·14 and 14·33). Similarly, the four olefinic protons appear as a singlet at δ 7·78, as was noticed by Batterham *et al.*[7] in 2′-hydroxy-4,4′-dimethoxychalcone. The aromatic protons can be grouped into those that belong to the phloroglucinol unit (IA-3′ δ 5·90 and IA-5′ δ 6·05) and the rest occurring between δ 6·86–7·59. Of these, the peaks at δ 6·86, 6·94 (*J* 8 Hz), δ 7·51 and 7·59 (*J* 8 Hz) along with the signal at δ 7·46 together integrate for two *A B C* systems assignable to rings IB and IIB as indicated in Table 6. The remaining two doublets at δ 7·04 and 6·095 (*J* 10 Hz) clearly indicate an *ortho* coupled system in ring IIA, unlike in the parent *O*-methyl biflavanone A_2, placeable at IIA-4′ and 5′ (chalcone numbering) corresponding to IIA-6 and -7 in (VI).

TABLE 7. MS OF *O*-METHYL BICHALCONE *A*

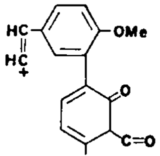
Fragment	% Abundance	Elemental composition	Fragment	% Abundance	Elemental composition
M^+ 626	43	$C_{36}H_{34}O_{10}$	*m/e* 445	23	$C_{27}H_{25}O_8$
m/e 463	12	$C_{26}H_{23}O_8$	281	26	$C_{17}H_{13}O_4$
461	12	$C_{26}H_{21}O_8$	207	23	$C_{11}H_{11}O_4$
			181	100	$C_9H_9O_4$

The other alternate structure (IX) resulting from positioning the two methoxyls in ring C has also been considered, but a IB-4–IIA-3′ linkage is biogenetically much less likely.

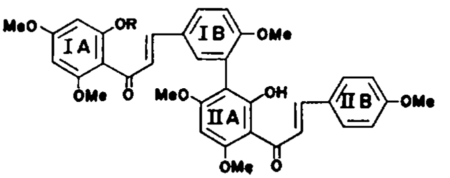
The MS of *O*-methylbichalcone *A* is consistent with the above structure (VIII) (Table 7). The fragmentation is probably similar to that described by Jackson *et al.*[8,9] Perhaps the most significant feature is the formation of the central fragment *m/e* 281 (X), which indicates that the linkage is between rings IB and IIA. Overall, the fragmentation exhibits a close similarity to that of morelloflavone.[10]



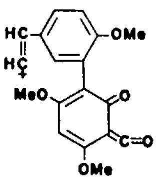
(IX)



m/e 281
(X)



(XI) B_1; R = Me
(XII) B_2; R = H



m/e 311
(XIII)

Biflavanone B *methyl ether* is colourless, m.p. 180–182°, ($C_{32}H_{26}O_{10}$; M^+ 570). Like its predecessor it is also a biflavanoid (red, $NaBH_4$ reaction) containing free hydroxyls (IR ν_{max}^{Nujol} 3490, 3385, 1640 cm^{-1}). Upon acetylation, it yielded a tetraacetate ($C_{40}H_{34}O_{14}$, m.p. 150–152°), whose NMR revealed the presence of four acetoxyls (δ 2·00–2·39) and two methoxyls (δ 3·72 and δ 3·75).

As the methyl ether was insoluble in most solvents, complete methylation with diazomethane could not be accomplished. Further methylation of *O*-methyl biflavanone *B* with

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[8] B. JACKSON, H. D. LOCKSLEY, F. SCHEINMANN and W. A. WOLSTENHOLME, *Tetrahedron Letters* **9**, 787 (1967); *ibid. J. Chem. Soc.* 3791 (1971).

[9] S. NATARAJAN, V. V. S. MURTI and T. R. SESHADRI, *Indian J. Chem.* **7**, 751 (1969).

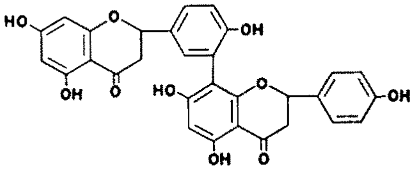
[10] C. G. KARANJGAOKAR, P. V. RADHAKRISHNAN and K. VENKATARAMAN, *Tetrahedron Letters* **33**, 3195 (1967).

dimethyl sulphate and K_2CO_3 in acetone was carried out whereby two *O*-methyl bichalcones B_1 (70%; Mg–HCl-negative, m.p. 158°) and B_2 (10% Mg–HCl-negative, m.p. 218°) were secured. Oxidation of bichalcone B_2 with neutral permanganate yielded anisic acid and phloroglucinol carboxylic acid, 2,4-dimethyl ether and bichalcone B_1 gave anisic acid only. The NMR spectra of bichalcones B_1 and B_2 were similar (Table 6).

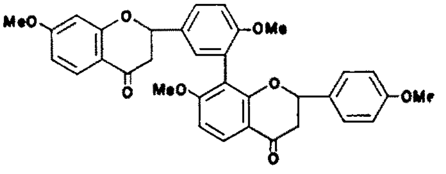
As in any chalcone,[8] the four olefinic protons at 7,8 in B_2 appeared at δ 7·86–7·90 as a singlet and in B_1 their pattern has been complicated by the extra methoxyl group at IA-2′. It is also clear that the pair of doublets (2H) at δ 5·98–6·03 and 6·24–6·28 (*J* 2·5 Hz) in bichalcone B_2 and at δ 5·88–5·905 and 6·06–6·085 (*J* 2·5 Hz) in bichalcone B_1 indicate the presence of an *O*-dimethylphloroglucinol unit now assigned to ring IA (XI). Further, the singlet at δ 6·45 can be assigned to the IIA-5′ proton, thus leaving IIA-3′ for linkage. The NMR showed 6 methoxyls in B_2 and 7-methoxyls in B_1. There is an upfield methoxyl at δ 3·50 in bichalcone B_2 and at δ 3·36 in bichalcone B_1 which was assigned to IIA-4′ methoxyl, compare isocorydine methocloride.[12]

There is also a three proton multiplet at δ 6·88–7·03 (*J* 9 Hz) which can be assigned to IB-5 and IIB-3,5 and the signals between δ 7·30–7·70 are assignable to IB-2,6 and IIB-2,6 protons. This assignment leaves IB-3 for the linkage with IIA-3′ and hence the bichalcones B_1 and B_2 are assigned structure (XI) and (XII) with a linkage at IB-3 and IIA-3′.

The MS of bichalcone B_1 heptamethyl ether showed a molecular ion at M^+640, $C_{37}H_{36}O_{10}$. The peak at *m/e* 612 is significant in the spectrum formed by the extrusion of a CO group. The ion at *m/e* 311 is assignable to a diphenyl fragment (XIII) containing three methoxyls as indicated in the NMR spectrum. The fragment at *m/e* 121 can of course be assigned to the anisyl cation.



(XIV)



(XV)

The above NMR and MS studies indicate the structures (XI) and (XII) respectively for bichalcones B_1 and B_2. The corresponding flavanone may be given the structure (XIV) which would correspond to a novel IB-3′–IIA-8-binaringenin.

O-Tetramethyl biflavanone C was isolated as colourless needles ($C_{34}H_{30}O_8$, m.p. 128–130°) in a very low yield. Its flavanone character was evident from the red colouration with $NaBH_4$ and its extreme instability to alkali. Oxidation with $KMnO_4$ yielded anisic acid only and no other product could be recognized. The compound did not contain any hydroxyl (IR; $FeCl_3$ negative) and its NMR spectrum confirms that it is a biflavanoid containing four methoxyls at δ 3·75 and no free hydroxyl. The facile methylation with diazomethane indicates that the molecule contains no chelated hydroxyl. Therefore, the methoxyls may be placed at IA-7, IB-4′, IIA-7, IIB-4′. Further, the NMR spectrum (Table 5) suggests that it could be a dimer related to liquiritigenin.[11]

The presence of four methylene protons at δ 2·8–3·0 and two benzylic methine protons at δ 5·1–5·5 confirms that the linkage is not through the pyranone ring systems. The assign-

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[11] J. SHINODA and S. UEEDA, *Chem. Ber.* 67, 434 (1934).

[12] I. R. C. BICK, J. HARLEY-MASON, N. SHEPPARD and M. J. VERNENGO, *J. Chem. Soc.* 1896 (1961).

ment of aromatic protons was made from the spectrum taken in acetone solution when the line separation was better. It would seem (Table 5) that the linkage is between IB and IIA ring systems at the 3′ and 8 positions. Biflavanoid *C* is, therefore, to be represented as IA3′-IIA 8 biliquiritigenin tetramethyl ether (XV).

EXPERIMENTAL

Isolation of alkenyl phenols. Nuts (2 kg) of Semecarpus anacardium, obtained from the Forest Department, Elamanchili, Andhra Pradesh, India, were cut into pieces and extracted with alcohol by cold percolation. The total extract (5 l.) was concentrated, dried, filtered and evaporated. The oil was distilled under high vacuum, b.p. 212–218°/3 mm., yield 60 g. It gave a brown $FeCl_3$ colour and a yellow colour with conc. H_2SO_4. On exposure to air it turned black; a dark red precipitate was formed with 1% aq. alkali. It decolourized bromine.

Methylation of the phenolic oil. O-*methyl bhilawanol.* (a) The oil (30 g) was refluxed for 8 hr with Me_2SO_4 (25 ml) and K_2CO_3 (65 g) in acetone (300 ml). The methyl ether distilled as a pale yellow liquid, b.p. 196–198°/1 mm, yield 30 g. IR. ν_{max}^{liquid} 2940 (s), 2860 (s), 1590 (w), 1490 (w), 1280 (s), 1228 (s), 1900 (s), 1020 (s) and 750 (m) cm^{-1}. (Found: C, 79·34; H, 11·05. $C_{23}H_{38}O_2$ requires: C, 79·71; H, 11·05%.) It gave a negative ferric reaction and yellow colour with conc. H_2SO_4. It decolourized bromine; iodine value 112·6 and perbenzoic acid value 2·872 mol. The methylated oil was fractionated under high vacuum and two fractions were collected. *Fraction* A. b.p. 156°/2·3 × 10^{-3} mm. It decolourized bromine. IR. ν_{max}^{liquid} 2940 (s), 2860 (s), 1590 (w), 1490 (s), 1280 (s), 1230 (s), 1090 (s), 1028 (s) and 750 (s) cm^{-1}. UV. λ_{max}^{EtOH} 221 and 272 nm. (Found: C, 79·34; H, 11·05. $C_{23}H_{38}O_2$ requires: C, 79·71; H, 11·05%.) *Fraction* B. b.p. 189–190°/2·3 × 10^{-3} mm. It decolourized bromine. IR. ν_{max}^{liquid} 2640 (s), 2860 (s), 1590 (w), 1490 (s), 1280 (s), 1230 (s), 1090 (s), 1028 (s) and 750 (s) cm^{-1}. UV. λ_{max}^{EtOH} 221 and 272 nm. (Found: C, 79·34; H, 11·05. $C_{23}H_{38}O_2$ requires: C, 79·71; H, 11·05%.) TLC on 15% $AgNO_3$ impregnated silica gel G using *n*-hexane–benzene (1:1) showed four spots for both fractions. The R_f were the same for both the fractions (R_f 0·68, 0·53, 0·42 and 0·23).

Chromatography of the methylated oil. The redistilled methylated oil, b.p. 196°/1 mm, (1 g), was chromatographed on silica gel column impregnated with 30% $AgNO_3$. The column was set in *n*-hexane and eluted with mixtures of *n*-hexane and benzene and finally with Et_2O. The column was monitored through TLC on silica gel G impregnated with 15% $AgNO_3$ using *n*-hexane–benzene (1:1). Elution with *n*-hexane–benzene (3:1) gave pure methylated bhilawanol *A* (500 mg; R_f 0·68) and *n*-hexane–benzene (5:3) gave methylated bhilawanol *B* (50 mg; R_f 0·53). Elution with *n*-hexane–benzene (5:2 and 1:1) and finally with ether gave mixtures. It was collected and re-chromatographed over silica gel and eluted with *n*-hexane, *n*-hexane–benzene (5:3, 1:1) and benzene. In hexane–benzene (5:3) a small quantity (20 mg) of methylated bhilawanol *B* was obtained. In other eluates, the oil was found to be a mixture on TLC and therefore, was not examined further.

Methylated bhilawanol A. Distilled under high vacuum b.p. 205°/1 mm (external) TLC single spot (R_f 0·68). It gave a negative ferric reaction, yellow colour with conc. H_2SO_4, and decolourized bromine. IR. ν_{max}^{liquid} 2940 (s), 2860 (s), 1590 (w), 1490 (s), 1280 (s), 1230 (s), 1090 (s), 1028 (s) and 750 (s) cm^{-1}. UV. λ_{max}^{EtOH} 221 and 272 nm. (Found: C, 79·26; N, 11·05. $C_{23}H_{38}O_2$ requires: C, 79·71; H, 11·05%.)

Oxidation of methylated bhilawanol A. (a) *With neutral permanganate.* Methylated bhilawanol A (500 mg) was oxidized with $KMnO_4$ in acetone (50 ml). The steam-volatile product was extracted with Et_2O and distilled, b.p. 223°. It formed an anilide, m.p. 71°, and was identified to be *n*-heptoic acid. (Found: C, 64·08; H, 10·23. $C_7H_{14}O_2$ requires: C, 64·58; H, 10·84%.)

The steam non-volatile acid (100 mg) was esterified with ethereal diazomethane (100 ml). The ester distilled at 182°/1 mm. (Found: C, 68·64; H, 9·08; OMe, 29·4. $C_{17}H_{26}O_4$ requires: C, 69·36; H, 8·9%.) It gave a negative ferric reaction and yellow colour with conc. H_2SO_4. It did not decolourize bromine. It was identified as 8-(2:3-dimethoxyphenyl)-octanoic acid (II, R=H) by NMR and MS. (M^+ 294; NMR δ values: 1·5*s* ($10\underline{H}$, $-(C\underline{H}_2)_5-$), 2·21*t* ($2\underline{H}$, $-C\underline{H}_2CO_2-$), 2·55*t* (2H, $Ar-C\underline{H}_2-$), 3·58*s* (3H, $-CO_2C\underline{H}_3$), 3·74, 3·80 (6H, $Ar-(OC\underline{H}_3)_2$, 6·54–6·81 m (3H, $Ar-(\underline{H})_3$). (b) *Ozonolysis.* Ozone was passed into a $CHCl_3$ solution of methylated bhilawanol *A* (1 g) at −5° to 0° for 4 hr and the ozonide was decomposed with 8% H_2SO_4 by refluxing on an H_2O bath for 1·5 hr. The steam volatile fraction was collected as a yellow crystalline 2,4-dinitrophenylhydrazone (10 mg), needles from hexane, m.p. 108°. It was identified as *n*-heptanaldehyde 2,4-dinitrophenylhydrazone by admixture with an authentic sample. (Found: C, 52·96; H, 6·68. $C_{13}H_{18}N_4O_4$ requires: C, 53·41; H, 6·16%.)

Oxidation of methylated bhilawanol B. *With* $KMnO_4$. Methylated bhilawanol *B* (50 mg) was oxidized with neutral $KMnO_4$ in acetone (50 ml). The steam volatile fraction gave *n*-valeric acid, b.p. 185–187° which was identified as its anilide, m.p. 63°. (Found: C, 58·75; H, 8·96. $C_5H_{10}O_2$ requires: C, 58·80; H, 9·82%.)

The steam non-volatile fraction (50 mg) was methylated with CH_2N_2 in Et_2O. The product, after chromatography on silica gel with benzene, was obtained as a colourless compound (25 mg). TLC on $AgNO_3$ impregnated silica gel showed a single spot (benzene–hexane (1:1). IR. ν_{max}^{liquid} 1600, 1590, 1250 cm^{-1} NMR δ values. 1·5 (10H, –$(CH_2)_4$), 2·20 (2H, –CH_2CO), 2·54*t* (2H, Ar–C$\underline{H}_2$–), 3·58*s* (3H, –COOMe), 3·74*s* (3H, Ar–OMe), 3·80*s* (3H, Ar–OMe) and 6·57–6·87*n* (Ar–H), M^+ 280. (Found: C, 68·52, H, 8·60. $C_{16}H_{24}O_4$ requires: C, 68·55; H, 8·63%.)

Oxidation of methylated bhilawanol. Methylated bhilawanol (10 g) was oxidized with $KMnO_4$ in acetone (400 ml). The steam volatile fraction, after purification, distilled between 185 and 187° and was identified as *n*-valeric acid. The steam non-volatile fraction was extracted with Et_2O and washed with 5% aq. Na_2CO_3. The Na_2CO_3 extract was neutralized, extracted with Et_2O, dried and esterified with CH_2N_2. The methyl ester distilled at 178–182°/1 mm. It gave a negative ferric reaction and yellow colour with conc. H_2SO_4. (Found: C, 68·84; H, 9·18. $C_{17}H_{26}O_4$ requires: C, 69·36; H, 8·9%.) This compound was found to be a mixture of 5 components by combined GLC–MS.

Oxidation of the steam non-volatile fraction. The steam non-volatile acid (1 g) was oxidized with alkaline $KMnO_4$ under reflux. A compound was obtained as colourless needles from benzene m.p. 121–122°, identical with an authentic sample of *o*-veratric acid by m.m.p. and IR. IR. $\nu_{max}^{CHCl_3}$ 3350 (b), 1690 (s), 1600 (s), 1250 (s) cm^{-1}. (Found: C, 59·30; H, 5·28. C $H_{10}O_4$ requires: C, 59·54; H, 5·53%.)

Isolation of biflavanoids. The pierced nuts (2 kg) of *Semecarpus anacardium* L., after removing the phenolic oil by cold percolation with hexane, were powdered and extracted with hot alcohol. The extract was concentrated under vacuum and *n*-hexane (2 l.) was added, when a dark coloured gum separated out. The *n*-hexane layer was decanted and the gum was washed 2 × with portions (200 ml) of *n*-hexane. The residual gummy material was extracted in a Soxhlet with *n*-hexane, benzene, $CHCl_3$ and EtoAc. The EtOAc extract afforded a dark red gum which gave a positive pink Mg–HCl reaction. Yield: 3 g.

Chromatography of the flavanoid mixture. The dark red gum (30 g) was adsorbed on silica gel (30 g) and transferred over to a column of silica gel (150 g) set with *n*-hexane. The column was eluted successively with *n*-hexane benzene, $CHCl_3$, Et_2O and EtOAc. The Et_2O eluate which contained the flavanoids gave a light yellow compound, which sintered at 146° and melted at 241°, 2 g. This showed only one spot with a tailing on TLC R_f 0·53 (silica–$CHCl_3$–EtOAc, 1:1). It gave a pink colour with Mg–HCl and with $NaBH_4$ and a brown ferric reaction. Attempts to crystallize it were unsuccessful. After purification through preparative TLC ($CHCl_3$–EtOAc, 1:1) the compound gave a molecular ion at M^+ 542.

Methylation of the biflavanoid mixture. With diazomethane. The mixture (500 mg) in MeOH (10 ml) was added to an ethereal solution of CH_2N_2 (100 ml) and kept in refrigerator for 12 hr. CH_2N_2 (4 × 100 ml) was added at 6-hr intervals. The solvent was evaporated and the product on examination by TLC on silica gel in $CHCl_3$ showed four spots R_f 0·8, 0·65, 0·43 and 0·27. These compounds were then separated by preparative TLC ($CHCl_3$) and named biflavanone methyl ethers A_1, A_2, *B* and *C*.

Biflavanone A_1 *trimethyl ether* (VI). It was crystallized from MeOH as a colourless microcrystalline powder, m.p. 158–160°, yield 70 mg. It gave a positive Mg–HCl reaction, a brown ferric reaction and was a deep orange colour in aq. NaOH. It gave a red colour with alcoholic $NaBH_4$. IR. ν_{max}^{Nujol} 3490 (b), 1640 (s), 1595–85 (s), 1310 (s), 1290 (w), 1265 (w), 1250 (w), 1200 (s), 1180 (w), 1155 (s), 1105 (m), 1090 (w), 1025 (w), 855 (m), 830 (m), 763 (s) cm^{-1}. UV. λ_{max}^{EtOH} 226, 288, 331 nm. (Found: C, 67·52; H, 4·76. $C_{33}H_{28}O_{10}$ requires: C, 67·80; H, 4·83%.) Methylation with excess ethereal CH_2N_2 yielded *O*-tetramethyl biflavanone A_2.

Biflavanone A_2 *tetramethyl ether* (VII) was crystallized from MeOH as colourless needles, m.p. 138–140°, yield 30 mg. It gave the same colour reactions as (VI). IR. ν_{max}^{Nujol} 3480 (b), 1640 (s), 1590 (m), 1575 (m), 1310 (s), 1290 (w), 1265 (w), 1250 (w), 1200 (s), 1180 (w), 1160 (s), 1105 (m), 1909 (w), 1025 (w), 855 (m), 840–830 (m), 740 (m) cm^{-1}. UV. λ_{max}^{EtOH} 226, 288, 331 nm. (Found: C, 68·00; H, 4·95. $C_{34}H_{30}O_{10}$ requires: C, 68·22; H, 5·05%.)

Methylation of O*-timethyl biflavanone* A_1. *O*-Trimethyl biflavanone A_1 (100 mg) was refluxed with Me_2SO_4 (0·5 ml) and K_2CO_3 (1 g) in dry acetone (50 ml) for 8 hr. After several crystallizations from $CHCl_3$–MeOH *O*-hexamethyl bichalcone was obtained as an orange–red compound, m.p. 238–240° (80 mg), (Silica-$CHCl_3$, R_f 0·81 Mg–HCl, negative $FeCl_3$ light brown in alkali). IR. $\nu_{max}^{CHCl_3}$ 3500 (b), 3150 (b), 1630 (s), 1590 (s), 1580 (s), 1470 (w), 1330 (b), 1130–1120, 980 cm^{-1}. UV. λ_{max}^{EtOH} 222 and 362 nm M^+ 626. (Found: C, 68·77; H, 5·42. $C_{36}H_{34}O_{10}$ requires: C, 69·00; H, 5·47%.) In a similar methylation, *O*-methyl biflavanone A_2 afforded bichalcone *A* hexamethyl ether.

Oxidation of O*-tetramethyl biflavanone* A_2. Biflavanone A_2 (50 mg) was oxidized with $KMnO_4$ in acetone (50 ml) for 0·5 hr. The residue was crystallized from benzene when a crystalline solid, m.p. 178–180° (5 mg) identical with authentic veratric acid was obtained.

Oxidation of O*-hexamethyl bichalcone* A. The bichalcone *A* (250 mg) was oxidized with $KMnO_4$ in acetone (50 ml) for 0·5 hr. The residue was extracted with hot benzene, and concentrated when a crystalline solid separated out, m.p. 179–180° (15 mg) identical with authentic veratric acid m.m.p. and IR). The residual solid was crystallized from MeOH when a colourless solid separated out, m.p. 152–154° (10 mg); methyl ester, m.p. 107–109° identical with 2-hydroxy-4,6-dimethoxybenzoic acid (m.m.p. and IR).

Biflavanone B *dimethyl ether.* Crystallized from acetone when it separated as colourless crystalline solid, m.p. 180–182°. It gave a pink Mg–HCl reaction, brown ferric reaction and a deep orange-yellow in aq, NaOH. It gave a positive $NaBH_4$ reaction. IR. ν_{max}^{Nujol} 3485 (w), 3385 (w), 1640 (s), 1595 (w), 1305 (m), 1285 (m), 1208 (s), 1150 (s), 1095 (m), 1070 (m), 835 (m) cm^{-1}. UV. λ_{max}^{EtOH} 215, 280 and 310 nm, yield 250 mg. (Found: C, 67·00; H, 4·59. $C_{32}H_{26}O_{10}$ requires: C, 67·37; H, 4·59%.) The acetate separated from MeOH as a powder, m.p. 150–152°. IR. $\nu_{max}^{CHCl_3}$ 2840 (w), 1730 (s), 1630 (s), 1595 (m), 885 (m) cm^{-1}. UV. λ_{max}^{EtOH} 215, 280 and 310 nm. NMR δ values: 2·00–2·32 (12H,(–OCOMe))$_4$ and 3·85 (6H, (–OMe))$_2$. (Found: C, 64·99; H, 4·5. $C_{40}H_{34}O_{14}$ requires: C, 65·03; H, 4·6%.)

Methylation of O-*dimethyl biflavanone* B. Methylated with Me_2SO_4 and K_2CO_3 in acetone. TLC (silica–$CHCl_3$) showed the presence of two components R_f 0·88 and 0·59. They were separated by preparative TLC to give the pure ethers of bichalcone B_1 and bichalcone B_2.

Bichalcone B_1 *heptamethyl ether.* Crystallized as bright yellow needles, m.p. 156–158°. It did not respond to Mg–HCl and gave a light brown ferric reaction. One spot on TLC (silica–$CHCl_3$, R_f 0·59). IR. $\nu_{max}^{CHCl_3}$ 3500 (b), 3180–3120 (b), 1670, 1640–1630, 1590, 1470, 1460–1450, 1353, 1330, 1110, 980 cm^{-1}. UV. λ_{max}^{EtOH} 220, 350 nm. (Found: C, 68·94; H, 5·06. $C_{37}H_{36}O_{10}$ requires: C, 69·36; H, 5·66%.)

Bichalcone B_2 *hexamethyl ether.* Crystalllized from $CHCl_3$ as bright yellow needles, m.p. 218°. It did not respond to Mg–HCl, gave a brown ferric reaction and was soluble in alkali. IR. $\nu_{max}^{CHCl_3}$ 3500 (b), 2840 (m) 2660–2560 (b), 1630 (s), 1590 (s), 1340 (s), 1150 (m), 1115–1105 (m), 985 (s), 890 (w) cm^{-1}. UV. λ_{max}^{EtOH} 223 348 nm. (Found: C, 68·82; H, 5·4. $C_{36}H_{34}O_{10}$ requires: C, 69·00; H, 5·4%.)

Oxidation of bichalcone B_2 *hexamethyl ether.* Bichalcone B_2 (50 mg) in acetone (10 ml) was refluxed with $KMnO_4$ and gave anisic acid, m.p. 186° (4 mg) and 2-hydroxy-4,6-dimethoxybenzoic acid, m.p. 154° (5 mg). From *O*-heptamethyl bichalcone B_2, only anisic acid was secured in a similar oxidation.

Biflavanone C *tetramethyl ether* crystallized from MeOH as colourless needles, m.p. 128–130°. It gave a pink Mg–HCl reaction and was soluble in aq. alkali giving a deep orange red solution. It gave a negative ferric reaction and a pink $NaBH_4$ reaction.

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