

THE STRUCTURE OF OCHNAFLAVONE, A NEW TYPE OF BIFLAVONE
AND THE SYNTHESIS OF ITS PENTAMETHYL ETHER

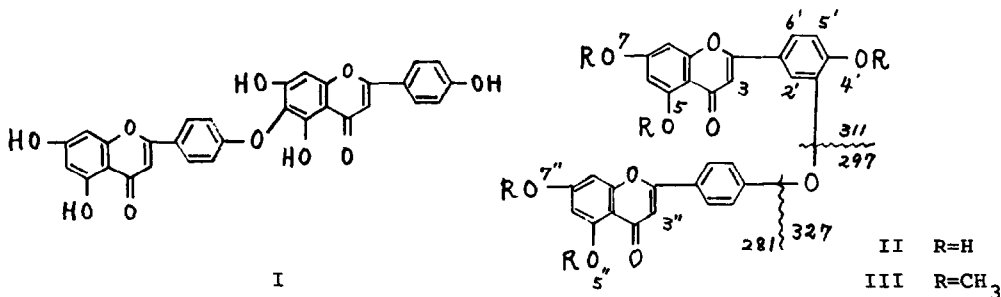
M. Okigawa and N. Kawano*

Faculty of Pharmaceutical Sciences, Nagasaki University, Nagasaki, Japan
and

M. Aqil and W. Rahman

Department of Chemistry, Aligarh Muslim University, Aligarh, India
(Received in Japan 29 March 1973; received in UK for publication 24 April 1973)

Hinokiflavone (I) has been reported¹ as the sole example of naturally occurring biflavonyl ether. We now report a new type of biflavonyl ether isolated from *Ochna squarrosa* Linn. (Ochnaceae) and named ochnaflavone (II). Although biflavones so far isolated have been obtained mostly from gymnosperm, some biflavanoids² such as morelloflavone³ and fukugetin⁴ were isolated from Guttiferae plants. Ochnaceae is a family closely related to Guttiferae.



Extraction of the plant leaves with acetone followed by solvent fractionations and chromatographic separations gave three compounds termed as OSI (m.p. 233-235°), OSII (m.p. 297-299°) and OSIII (m.p. 288-290°). On a silica gel thin layer chromatography (TLC) using benzene-pyridine-formic acid (36:9:5) as a solvent, the three compounds showed R_f values of 0.56, 0.72 and 0.81 respectively. By methylation with dimethyl sulfate and potassium carbonate in boiling acetone, they produced an identical methyl ether (III), m.p. 167-169°, λ max (ethanol): 267 nm (log ε, 4.60) and 328 (4.65). The UV spectra of these compounds are similar to those of apigenin (5,7,4'-trihydroxyflavone) derivatives. The mass spectrum of compound III showed a parent peak, 608 and frag-

* To whom all correspondences should be addressed.

ment peaks, 594, 580, 327, 311, 304 (M^{++}), 297, 281 and so on, quite similar to those of penta-O-methylhinokiflavone. The NMR signals of compound III are listed in Table 1 and show the presence of five methoxy groups in the compound.

Recently, it was reported⁵ that the NMR signals of H-6, 6" of several methylated biflavones, when $\text{Eu}(\text{FOD})_3$ was added, showed a considerable downfield shift in comparison with H-8, 8" and H-3, 3", and that $\text{CH}_3\text{O}-5, 5''$ showed much larger downfield shift values than $\text{CH}_3\text{O}-7, 7''$. Chemical shift changes found in every proton signal of compound III when $\text{Eu}(\text{FOD})_3$ was added, are expressed by S-values⁶ and listed in Table 1. S-values of the five methoxy groups of compound III (10.26, 11.56, 0.80, 0.96 and -0.14) are all compatible with reported⁵ values of $\text{CH}_3\text{O}-5, 5''$, $\text{CH}_3\text{O}-7, 7''$ and a methoxy group in the side phenyl group respectively, meaning that the ether linkage between two apigenin molecules is in neither 5, 5"- nor 7, 7"-positions. Similarly, H-3, 3", 6, 6", 8 and 8" in compound III all showed satisfactory S-values (Table 1). Accordingly, the position of ether linkage between the two flavone molecules will be confined to side phenyl groups.

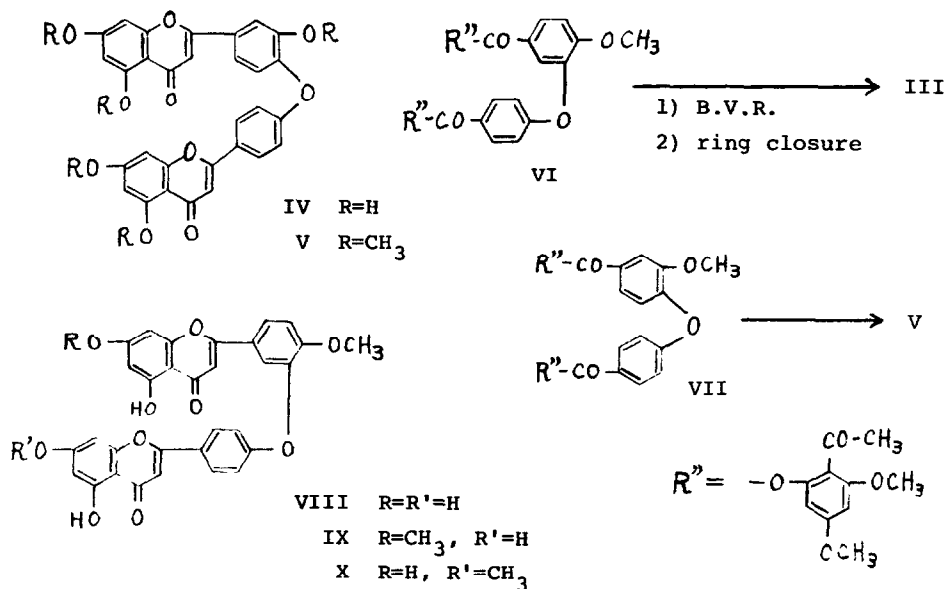
The three compounds, OSI, OSII and OSIII gave acetates termed as OSIA (m.p. 239-241°), OSIIA (m.p. 248-250°) and OSIIIA (m.p. 212-214°) respectively. The NMR signals of these acetates are also listed in Table 1, which shows that OSIA has five acetoxy groups and that OSII and OSIII have one and two methoxy groups respectively. A relatively large upfield shift (7.35 \rightarrow 7.13 ppm) of H-5' in OSIIA from that in OSIA suggested the presence of $\text{CH}_3\text{O}-4'$ in OSIIA. In case of OSIIIA, the presence of $\text{CH}_3\text{O}-7$ (or 7") besides $\text{CH}_3\text{O}-4'$ can be deduced by chemical shift changes of H-6 (6.82 \rightarrow 6.58 ppm) and H-8 (7.29 \rightarrow 6.82 ppm) from those of OSIIA.

Two singlets due to H-3, 3" and four doublets ($J=2.5$ Hz) due to H-6, 8, 6", 8" in each compound support the conclusion that they have an ether linkage between side phenyl groups of apigenin. Two doublets ($J=9.0$ Hz) due to H-3"', 5"' and H-2"', 6"' and three proton signals due to H-2', 5', 6' are very similar to those of amentoflavone derivatives.⁷ These findings led us to structure II for ochnaflavone. Although other structures such as formula IV are also possible for ochnaflavone the chemical shift change of H-5' (7.35 \rightarrow 7.13 ppm) and biosynthetic considerations support structure II.

In order to confirm the structure II for ochnaflavone we synthesized the two compounds III and V (pentamethyl ether of IV) by Baker-Venkataraman rearrangement (B.V.R.)⁸ and subsequent ring closure of compounds VI and VII respectively, which were derived from corresponding diphenyl ether dicarboxylic acids.⁹ The compound III thus synthesized, m.p. 169-171° was identified with the methyl ether of natural ochnaflavone by mixed m.p. 169-171° and by comparisons of UV, IR and NMR spectra, while the NMR spectrum of compound V (m.p. 154-156°) showed

Table 1. The NMR Data of Ochnaflavone Derivatives.

Assigned position	δ -values (ppm from TMS)				S-values by Eu(FOD) ₃
	III	OSIA	OSIIA	OSIIIA	III
4'	3.88 (3H, s)	2.20	3.88	3.88	-0.14
7	3.88 (3H, s)	[2.32]	[2.31]	[3.88]	[0.80]
7"	3.88 (3H, s)	[2.35]	[2.33]	[2.34]	[0.96]
5	3.92 (3H, s)	[2.42]	2.43	2.43	[10.26]
5"	3.92 (3H, s)	[2.44]	2.43	2.43	[11.56]
3	[6.55 (1H, s)]	[6.62]	[6.54]	[6.49]	[0.32]
3"	[6.59 (1H, s)]	[6.57]	[6.58]	[6.57]	[0.24]
6	6.34 (1H, d, J=2.5 Hz)	[6.83]	6.82	[6.58]	[4.86]
6"	6.34 (1H, d, J=2.5 Hz)	[6.84]	6.82	[6.82]	[5.58]
8	[6.51 (1H, d, J=2.5 Hz)]	[7.32]	[7.29]	[6.82]	[1.14]
8"	[6.54 (1H, d, J=2.5 Hz)]	[7.34]	[7.31]	[7.30]	[1.26]
3''', 5'''	7.01 (2H, d, J=9.0 Hz)	7.13	7.02	7.01	-0.12
5'	7.11 (1H, d, J=9.0 Hz)	7.35	7.13	7.12	-0.12
2'	7.60 (1H, d, J=2.5 Hz)	7.58	7.60	7.61	0
6'	7.72 (1H, q, J=2.5 & 9.0)	7.71	7.72	7.72	-0.10
2''', 6'''	7.81 (2H, d, J=9.0 Hz)	7.86	7.81	7.79	-0.10



3.80 ppm (CH_3O), 3.83 ($4 \times \text{CH}_3\text{O}$), 6.27, 6.30 (1H, d each, 6, 6"), 6.47, 6.50 (1H, d each, 8, 8"), 6.53, 6.59 (1H, s each, 3, 3"), 7.01 (2H, d, 3"', 5)'), 7.09 (1H, d, 5'), 7.41 (1H, d, 2'), 7.46 (1H, q, 6') and 7.79 (2H, d, 2"', 6'') signals.

Consequently, structures II and VIII are given for the new compounds OSI and OSII respectively, while OSIII will have alternative structures IX or X. The isolation of these compounds is noteworthy for the following reason: while all other biflavones and flavanoflavones so far isolated have a linkage at ring A of flavone nucleus, ochnaflavone is the first example of biflavones which have a linkage between side phenyls.

Acknowledgement --- The authors are grateful to Dr. Sahni, FRI Dehradun and Mr. Ch. Maqsood and others of HRC Saharanpure, India for the procurement of the plant material. M. Aqil is thankful to CSIR, Govt. of India for its financial assistance.

REFERENCES

1. Y.Fukui and N.Kawano: J. Amer. Chem. Soc., 81, 6331 (1959). N.Kawano, H.Miura and A.C.Waiss, Jr.: Chemistry & Industry (London), 2020 (1964). K.Nakazawa: Chem. Pharm. Bull. (Tokyo), 16, 2503 (1968).
2. B.Jackson, H.D.Lockesley and F.Scheinmann: J. Chem. Soc. (C), 3794 (1971). A.Pelter, R.Warren, K.K.Chexal, B.K.Handa and W.Rahman: Tetrahedron, 27, 1625 (1971).
3. G.G.Karanjgaokar, P.V.Radhakrishnan and K.Venkataraman: Tetrahedron Letters, No. 33, 3195 (1967).
4. M.Konoshima, Y.Ikeshiro, A.Nishinaga, T.Matsuura, T.Kubota and H.Sakamoto: Tetrahedron Letters, No. 2, 121 (1969). Y.Ikeshiro and M.Konoshima: Ibid., No. 43, 4383 (1972).
5. M.Okigawa, N.Kawano, W.Rahman and M.M.Dhar: Tetrahedron Letters, No. 40, 4125 (1972).
6. A.F.Cockerill and D.M.Rackham: Tetrahedron Letters, No. 59, 5149 (1970).
7. A.Pelter, R.Warren, M.Ilyas, J.N.Usmani, S.P.Bhatnagar, R.H.Rizvi, M.Ilyas and W.Rahman: Experientia, 25, 350 (1969).
8. W.Baker: J. Chem. Soc., 1381 (1933). H.S.Mahal and K.Venkataraman: Ibid., 1767 (1934). J.E.Gowan and T.S.Wheeler: Ibid., 1925 (1950). S.Moriyama, M.Okigawa and N.Kawano: Tetrahedron Letters, No. 21, 2105 (1972).
9. E.Späth and J.Pickl: Chem. Ber., 62, 2251 (1929).