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The use of solvent induced methoxy shifts as a guide to hinokiflavone structure.

Andrew Pelter, R. Warren, J.N. Usmani, M. Ilyas and W. Rahman

University of Manchester, U.K. and Muslim University of Aligarh, India.

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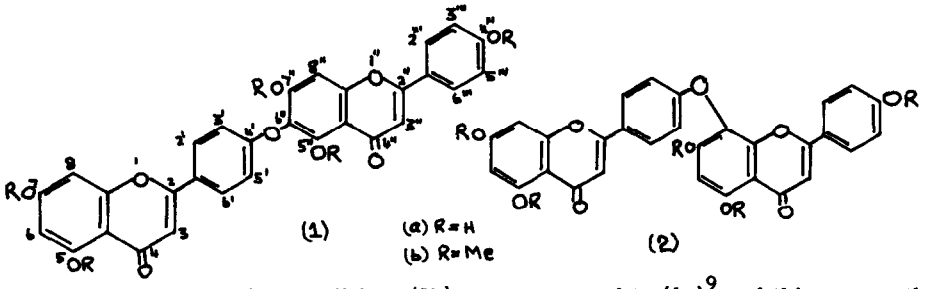
Despite the large amount of work that has been devoted to the elucidation of the structure of hinokiflavone[1,2,3] and its derivatives[4,5,6,7,8] the structure of only one sample has been fully settled. The elegant total synthesis of hinokiflavone pentamethyl ether by Nakazawa[9] proved that the sample produced by Kawano[10] had the 4' -O-6 ether linkage (Ib). Previously the compound had been assigned the 4' -O-8 ether linkage (2b) on the basis of spectral and degradative evidence[2,11,12]. A comparative study[13] of the position in the p.m.r. spectrum of the methoxy groups of hinokiflavone pentamethyl ether as compared with corresponding monomeric flavone methyl ethers also indicated structure (2b).



Under demethylating conditions (2b) was converted to (1a)[9] and this means that syntheses of these compounds in which at any stage demethylation occurs, cannot be looked upon as unambiguous. Such a synthesis is that of (2b) by Seshadri et al[14], who records that he was unable to distinguish isomers (Ib) and (2b) by standard chemical means, and although the p.m.r. spectra differ in details (Table 1) it is difficult to use these diagnostically.

Table I[*]

Proton	(Ib)	(2b)
2‴ (6‴)	2.20d. J=9	2.56d. J=9
3‴ (5‴)	3.06d. "	3.19d. "
2' (6')	2.12 "	2.16 "
3' (5')	2.98 "	2.94 "
3, 3"	3.38, 3.41	3.41, 3.44
6"		3.49
8"	2.95	
6	3.45, 3.63 J=2	3.51, 3.64 J=2
8		
OMe	6.06, 6.09	5.95, 6.02, 6.05, 6.10, 6.21.

[*]All spectra run at 100H$_3$ in CDCl$_3$ (TMS internal standard = τ 10.0) Values of J in c/s.

In these circumstances it is by no means clear that all the various samples called hinokiflavone are, in fact, identical and a simple and unambiguous test to distinguish the isomers would be of use.

Sterically hindered methoxy groups in flavonoids may be distinguished by means of solvent induced methoxy shifts[15a,b] and criteria that lay down the limits of the method have been established[15b]. It has been shown that the 6-8 linked agathisflavone series may readily be distinguished from the 8, 8-linked cuppressuflavone series and the 3', 8-linked amentoflavone series[16]. The method might well be applicable in the present case.

An authentic sample of (2b) was produced by a modification of the Nakazawa synthesis and the methoxy shifts of this compound are presented in Fig. 1. They are precisely as expected[15b] from a compound with five methoxy groups unhindered to solvation by benzene.

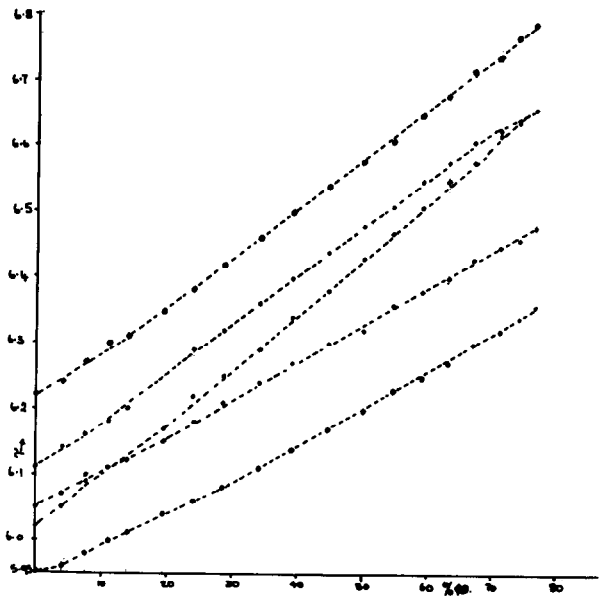


Fig. 1

Three samples of "hinokiflavone" were isolated[*] from (i) Taxodium mucronatum, (ii) Juniperis chinensis and (iii) Thuja orientalis. The pentamethyl ether of each sample gave the same shifts of the methoxy groups, as shown in Fig. 2. The shifts from 0% C_6D_6 to 80% C_6D_6/20% $CDCl_3$ were 34c/s, 54c/s, 57c/s, 64c/s and 1c/s.

These shifts are well within the range for four unhindered methoxy groups and one hindered methoxy group and show that the three samples isolated all have structure (Ia). The difference between Fig. 1 and Fig. 2 is clear and seems to meet the requirements for a simple test to distinguish between the 4-O-6 linked series and the 4-O-8 linked compounds.

The positions of the methoxy groups of the 4-O-6 isomer (Ib) in the p.m.r. spectrum run in pyridine have been reported by Kawano et al[8]. We confirm their figures, the 5" methoxy group being found at τ5.88, a downfield methoxy shift. The methoxy groups of (2b)

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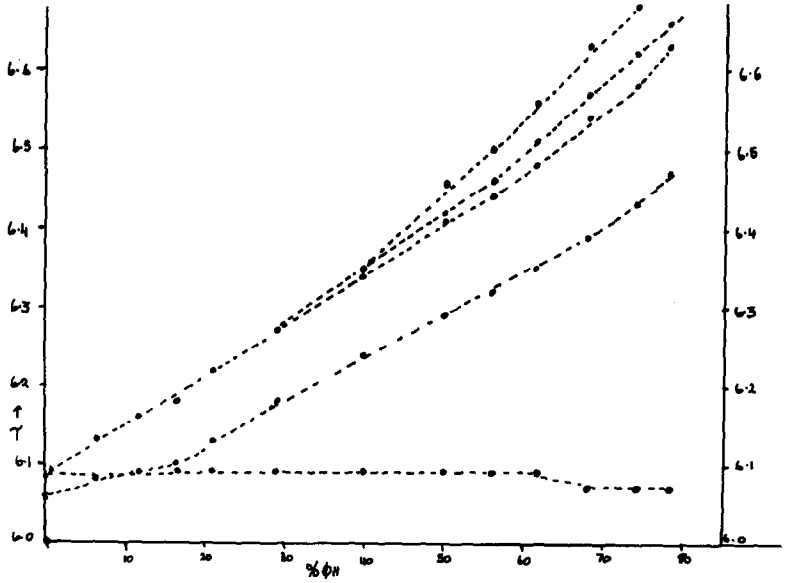

Fig. 2

show at τ6.03, 6.13, 6.19, 6.22 and 6.40 in this solvent.

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