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WB1 AND W11, THE FIRST OPTICALLY ACTIVE BIFLAVONES.

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Following our previous work on biflavonoids[1,2] we report the isolation of two optically active biflavones from Araucaria cunninghamii and A.cookii.

The powdered leaves gave an acetone extract that on column chromatography (magnesium silicate) followed by preparative TLC (silica gel) yielded several biflavonoids. Among these was WB1, m.p.151°, $C_{34}H_{26}O_{10}$ (594.1535), dimethyl ether WB1(a), m.p.161° (622.182034), diacetate WB1(b), m.p.156° (678.176231). WB1 had $\lambda_{max.}$ 273(19,300), very similar to that of acacetin, apigenin and genkwanin. The behaviour with aluminium chloride was characteristic of flavones with a 5-OH group[3] and a 5,7,4'-oxygenation pattern was suggested.

The mass spectrum of WB1 was dominated by the molecular ion at 594(100), the only other significant peaks being at m/e 593(5) and m/e 297.0722(7), $(C_{17}H_{15}O_5)$. This is therefore a highly stable molecule, the pattern suggesting a biflavone[4] breaking down to its units. The high intensity (45%) of the M-1 peak in WB1(b) is also characteristic of flavones[4,5].

The P.M.R. spectra of WB1, WB1(a) and WB1(b) are shown in the Table.

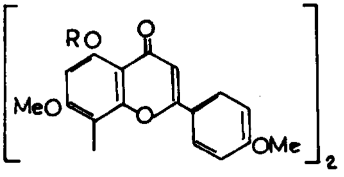
TABLE*

	WB1	WB1(a)	WB1(b)
H-3	3.42(4H)s.	3.41(2H)s.	3.51(2H)s.
H-6		3.43(2H)s.	3.19(2H)s.
H-2',6'	2.56(4H)d.J = 9 c/s.	2.70(4H)d. J = 9 c/s.	2.75(4H)d. J = 9 c/s.
H-3',5'	3.16(4H)d.J = 9 c/s.	3.23(4H)d. J = 9 c/s.	3.22(4H)d. J = 9 c/s.
-OMe	6.19(12H)	5.88(6H) 6.14(6H) 6.22(6H)	6.20, 6.26(12H)
-OH	-3.18(2H)	-	-
-O.CO.CH_3	-	-	7.51(6H)
TOTAL	26H	30H	30H

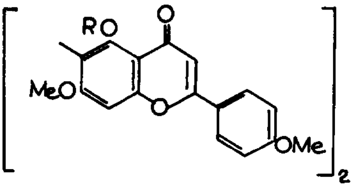
*Spectra run in $CDCl_3$ at 100Mc., $SiMe_4$ as internal standard.

For all three compounds the spectra are such that the molecules must have an axis of symmetry. In WB1(a) and WB1(b), H-3 and H-6 are distinguished, the former proton appearing at the characteristic position for the H-3 of a flavone[6]. The low field value of the proton of the hydroxy group in WB1 showed it was hydrogen-bonded (C-5) and the A_2B_2 pattern of H-2'6' and H-3'5', invariant on acetylation, showed there was a 4'-methoxy group throughout. In WB1(a), the two new 5-methoxy groups are below τ6.0. This may be characteristic of such groups in an 8,8''-linked biflavone. 5-Methoxy groups in the related armentoflavone series studied by us do not appear at such low field.

To meet the requirements of symmetry and of the P.M.R. spectra the structures I(a), (b) (c) [8,8''-linked] or II(a) (b) (c) (6,6''-linked) are possible.



I(a), R=H
(b), R=Me
(c), R=Ac



II(a), R=H
(b), R=Me
(c), R=Ac

In the armentoflavone series, with both H-8 and H-6 present, sciadiopitysin has H-6 at τ3.54, H-8 at 3.62, ginkgetin has H-6 at τ3.56, H-8 at 3.63[7]. Whilst I(a) is indicated by this, better evidence comes from the shift of τ0.23 of the aromatic proton at τ3.42 in WB1 to τ3.19 in WB1(b). Massicot[6] has shown that in a flavone with a 5,7,4'-oxygenation pattern, acetylation of a 5-OH group moves H-6 downfield by τ0.22-0.29 and H-8 by τ0.33-0.49 Hence I(a) is indicated for WB1. However, I(a) has been assigned to cupressuflavone tetramethyl ether[1,8], recorded as having m.p.259-261°, the dimethyl ether has m.p.295-297° and the diacetate has m.p.168-170°. We have confirmed these melting points on authentic samples.

The assignment of an 8,8''-linkage to cupressuflavone was based originally on an Ullman coupling of 8-iodo,5,7,4'-trimethylapigenin. However in the key reaction demethylation occurred and a rearrangement to yield a 6,6''-biflavone was not out of the question.

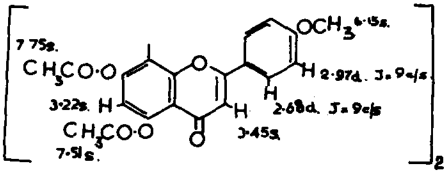
An attempt to resolve the situation was made by using the solvent-induced shifts of the methoxy groups of WB1(b)[9,10] In a substance of structure I(b) all three methoxy groups should shift. In II(b), the 5-OMe group, clear at τ5.88, should not move. In fact, solvent change from $CDCl_3$ to C_6H_6 caused the following shifts in WB1(b); 5-OMe, 53 c/s; 7-OMe, 75 c/s; 4'-OMe, 49 c/s. The P.M.R. spectra and the solvent-induced shifts of cupressuflavone hexamethyl ether were indistinguishable from those of WB1(b).

The 8,8''-linkage for both compounds seemed sure and the only explanation for the discrepant melting points was that whereas all previously isolated biflavones were racemic compounds, WB1 must be optically active. Measurement showed that WB1 had $[\alpha]_{600}-10^\circ$, $[\alpha]_{545}-0^\circ$, $[\alpha]_{500}+35^\circ$, $[\alpha]_{450}+210^\circ$, $[\alpha]_{425}+590^\circ$, $[\alpha]_{400}+1770^\circ$, $[\alpha]_{395}+2090^\circ$.

WB1 is thus (-)-4,4''',7,7''-tetra-O-methylcupressuflavone, the first optically active biflavone.

A further compound isolated was W11, m.p.301-4°, $C_{32}H_{22}O_{10}$ (566.120997), $[\alpha]_D^{32}$ (pyridine/ethanol), + 65°, tetra-acetate W11(a), $C_{40}H_{30}O_{14}$.

Similar considerations to those given for WB1 lead to the formulation of W11 as 4',4'''-di-O-methylcupressuflavone. The figures for the protons for W11(a) are given below in structure (III). There is an almost exact correlation between the figures given and those quoted[6] for 5,7-diacetoxy-4'-methoxyflavone, with the exception of the 2'-H. W11 itself is therefore (+)-4',4'''-di-O-methylcupressuflavone.



(III)

This assignment allows the methoxy groups of WB1 to be separated, and leads to the inference that it is the 7-OMe group that shows the large solvent shift of 75 c/s, possibly a diagnostic test for this grouping. The chirality of these compounds will be discussed in a full paper.

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