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THE STRUCTURES OF SCANDENIN AND LONCHOCARPIC ACID.

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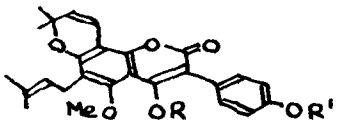
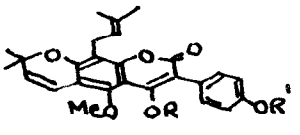
We have recently been able to assign formulae (Ia) or (IIa) to scandenin (1,2) an extractive from the root of D. scandens. This compound is therefore a representative of the new class of natural product, the 4-hydroxy-3-phenylcoumarins or isoflavonols, and it remained only to decide between these two formulae.



(I)

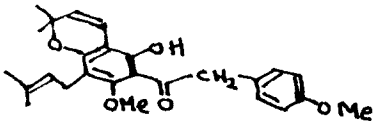


(II)

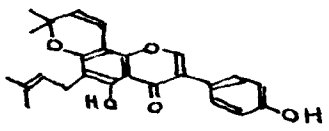
(a) R = R' = H

(b) R = H, R' = Me

(c) R = R' = Me.



(III)



(IV)

The problem was readily settled when di-O-methylosajetin (III) became available to us*. Reaction of this deoxybenzoin with ethyl chloroformate in the presence of potassium carbonate in acetone (3) gave the 4-hydroxy-4',5-dimethoxy-3-phenylcoumarin (Ib) m.p. 195-197°, in high yield. Methylation with diazomethane produced di-O-methylscandenin (Ic) m.p.129°, identical in all respects with the product from the direct methylation of scandenin. In particular the mixed melting point was not depressed and the I.R. and N.M.R. spectra were absolutely superimposable. With di-O-methyllonchocarpic acid, on the contrary, the mixed melting point was depressed, the I.R. spectrum differed in many bands in the finger-print region and in the N.M.R. spectrum one olefinic proton of the 2,2-dimethylchromene ring system was found at a different τ value for the two compounds.

Osajin has been shown to have the constitution (IV), and di-O-methylosajetin is therefore (III). On this basis scandenin must be expressed by the formula (Ia), being the isoflavonol corresponding to the isoflavone 5-O-methylosajin.

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* We wish to express our thanks to Professor Wolfrom for his generous gift of a sample of this compound.

Acetylation of one of the fractions obtained by ether extraction of the roots of D.scandens, followed by chromatography on neutral alumina yielded a product m.p. 151°, the subsequent transformations of which showed it to be di-O-acetyllonchocarpic acid (5,6). Mild hydrolysis gave lonchocarpic acid, with the typical double melting points of 206° and 219° previously noted for this compound. Methylation then gave di-O-methyl-lonchocarpic acid m.p. 148-150°. In each case the mixed melting point with the corresponding compound of the scandenin series was depressed, but these melting points correspond very well with those reported for lonchocarpic acid and its derivatives by Jones (5). Clarke (6) has previously reported that lonchocarpic acid occurs in D. scandens although Seshadri (2) was unable to confirm this.

There have been previous suggestions (6,7) that scandenin and lonchocarpic acid belong to the same, then unknown, family of natural product and we have recently commented on this ourselves (4). The compounds are isomeric, of formula $C_{26}H_{26}O_6$, give the same colour reactions, occur in the same plant, give p-hydroxybenzoic acid on oxidation with alkaline hydrogen peroxide and contain an extremely acidic hydroxyl group.

Spectral data confirm these suggestions, and taken together with formula (Ia) for scandenin lead unequivocally to formula (IIa) for lonchocarpic acid.

A comparison of the N.M.R. spectra of scandenin and lonchocarpic acid is shown below, and indicates the same substituents to be present in both compounds.

Group.	Scandenin. τ	Lonchocarpic Acid. τ
ββ-Dimethylallyl	8.26(3H) 8.19(3H), 6.7, 6.6(2H), 4.81(1H) multiplet.	8.32(3H), 8.14(3H), 6.57, 6.45(2H) 4.74(1H) multiplet.
2,2-Dimethylchromene.	8.51(6H), Doublets at 4.31(1H), 3.08(1H) (J=10.2c/s).	8.54(6H), Doublets at 4.20(1H), 3.42(1H) (J=10.2c/s).
Methoxyl.	6.06(3H)	6.05(3H)
Hydroxyl.	3.95(1H), -0.22(1H)	3.89(1H), -0.04(1H)
Aromatic protons.	Two doublets centred at 3.1(2H) 2.55(2H)	Two doublets centred at 3.12(2H) 2.57(2H)

Only one significant difference is shown here, the olefinic proton of the 2,2-dimethylchromene ring which showed at the abnormally low value of τ 3.08 in scandenin is now at the more normal value of τ 3.42 in lonchocarpic acid. This difference is not found in the acetates whose N.M.R. spectra are strikingly similar.

Group.	Scandenin Acetate τ	Lonchocarpic Acid. Acetate τ
ββ-Dimethylallyl.	8.31(3H), 8.13(3H), 6.55 6.43(2H) 4.76(1H) Multiplet.	8.29(3H), 8.13(3H), 6.54, 6.42(2H), 4.78(1H) Multiplet.
2,2-Dimethylchromene.	8.54(6H) Doublets at 4.27(1H), 3.37(1H) (J=10.2c/s)	8.53(6H) Doublets at 4.26(1H), 3.37(1H) (J=10.1c/s).
Methoxyl.	6.22(3H)	6.21(3H)
Acetyl.	7.89(3H), 7.70(3H)	7.85(3H), 7.68(3H)
Aromatic protons.	Two doublets at 2.81(2H) and 2.52(2H) (J=8.7c/s).	Two doublets at 2.83(2H) and 2.52(2H) (J=8.7c/s).

That the same groupings are present in both scandenin and lonchocarpic acid cannot be in doubt, and further, ring B of lonchocarpic acid must contain a 4'-hydroxyl group to give rise to both the pattern of aromatic protons shown and to the position of these protons being affected to the same degree in lonchocarpic acid and scandenin on acetylation.

In the I.R. spectrum lonchocarpic acid shows a carbonyl stretching frequency at 1664 cm^{-1}, moving to 1704 cm^{-1} in di-O-methyllonchocarpic acid. The grouping $HO-(C=C)_n-CO$ is indicated, and that n = 1 is shown by the identity of the breakdown pattern of scandenin and lonchocarpic acid in the mass spectrometer, in each case the characteristic, unique splitting of the 4-hydroxy-3-phenylcoumarin series being shown (1,4). The U.V. spectra of lonchocarpic acid

and its derivatives are also fully consistent with this formulation.

That the methoxyl group of lonchocarpic acid must be placed in the 5-position, as in scandenin and robustic acid (4) is shown by its low position in the N.M.R. spectrum at τ 6.05 being shifted to τ 6.17 in the methyl ether, a property characteristic of a 5-methoxyl group in this series. Further on acetylation an identical shift upfield of τ 0.16 is shown by this group in both scandenin and lonchocarpic acid, indicating the same environment in both. Therefore, lonchocarpic acid must be that isomer of scandenin represented by (IIa) and is another member of the new class of flavonoid, the isoflavonols.

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