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STUDIES OF THE STRUCTURE OF SCANDENIN

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Scandenin, a compound isolated from D.scandens, was first studied by Clarke[1] and Seshadri[2] who assigned to it the formula $C_{26}H_{26}O_6$. It was shown to contain one methoxyl group, two hydroxyl groups and two readily reducible olefinic bonds. On oxidation with alkaline hydrogen peroxide, p-hydroxybenzoic acid was obtained. It did not give the characteristic colour tests of either a rotenoid or a flavonoid and was stated to belong to no known class of compounds. Recently Rao[3,4] has put forward the suggestion that scandenin is a 4'-hydroxy-7-methoxyflavanone substituted in the 3 position by an unknown group containing a chelated hydroxyl grouping.

An accurate determination of the molecular weight of scandenin showed it to be 434.1728, confirming the formula $C_{26}H_{26}O_6$ (434.1729). The result of alkaline hydrogen peroxide oxidation was confirmed, and a pink colour was obtained with magnesium and hydrochloric acid indicating that scandenin was some type of flavonoid.

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[1] E.P.Clarke, J.Org.Chem., 8, 489, (1943).

[2] N.V.Subba Rao and T.R.Seshadri, Proc.Ind.Acad.Sci., A, 24, 465, (1946).

[3] N.V.Subba Rao and W.A.Khan, Ind.J.Chem., 1, 74, (1963).

[4] N.V.Subba Rao and W.A.Khan, Ind.J.Chem., 1, 295, (1963).

The N.M.R. spectrum allowed the groups shown in Fig.1 to be identified.

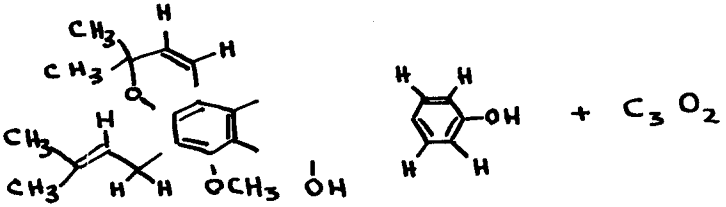

Fig. 1.

A singlet at τ 6.06 (3H) was due to the methoxyl group and two bands at τ 3.95 (1H) and τ - 0.22 (1H) were due to two hydroxyl groups. The ββ-dimethylallyl moiety was identified by the two non equivalent methyl groups at τ 8.26 (3H) and τ 8.19 (3H), together with a doublet at τ 6.6 and τ 6.7 (2H) and a multiplet centred at τ 4.81 (1H). The 2,2-dimethylchromene ring showed a singlet at τ 8.51 (6H) and one doublet centred at τ 4.31 (1H) together with another at τ 3.08 (1H) J = 10.2 c./s.[5] This last doublet, due to the hydrogen on the chromene ring adjacent to the benzene ring, is reminiscent of the corresponding hydrogen in β-toxicarol which shows as a doublet at τ 2.97, J = 10 c./s.[6] That the four C-Me groups were present as two pairs of gem-dimethyl groups was confirmed by Kuhn-Roth analysis, which indicated 1.21 C-Me groups, this low result being typical of such groupings.[7] The four aromatic protons show as two sets of bands centred at τ 3.1 and τ 2.55, all twenty-six hydrogen atoms being accounted for.

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[5] Varian Spectra Catalogue, 1962.

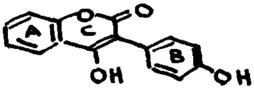
[6] L.Crombie and J.W.Lowrie, J.Chem.Soc., 175, (1962).

[7] B.F.Burrows, W.D.Ollis and L.M.Jackson, Proc.Chem.Soc., 177, (1960).

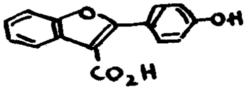
The dissection into a C_{15} unit plus two C_5 units is one fairly commonly met among flavonoids.

The ultraviolet spectrum of scandenin showed maxima at 235 mμ (4.65), 287 mμ (4.19) and 343 mμ (4.27). This last band makes an isoflavone structure unlikely. There was no shift on addition of aluminium chloride, nor on methylation was there any change showing no chelated hydroxyl groups to be present. Sodium acetate produced a hypsochromic shift in the long wavelength absorptions to give maxima at 240 mμ (4.70), 275 mμ (4.29) and 330 mμ (4.18).

In the infrared region the carbonyl stretching frequency of scandenin showed at 1680 cm.$^{-1}$. shifting to 1708 cm.$^{-1}$ on methylation. The sodium salt of scandenin had lost this band completely and instead a new band at 1518 cm.$^{-1}$ appeared. The group HO-(C=C)$_n$-CO- was therefore present, leading to the two possible C_{15} ring structures for scandenin (I) and (II), where n = 1 and 0 respectively.

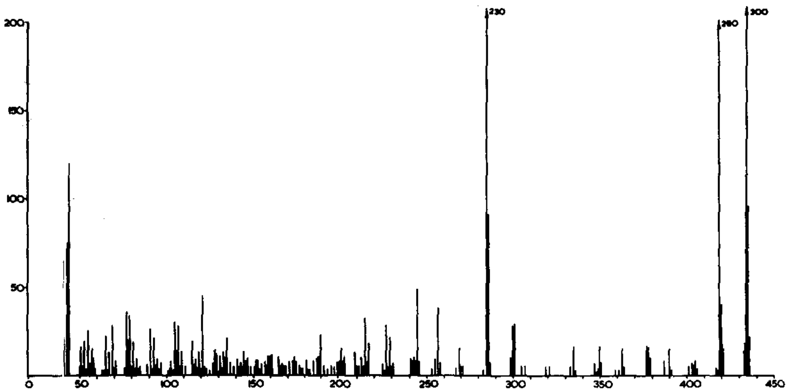


(I)

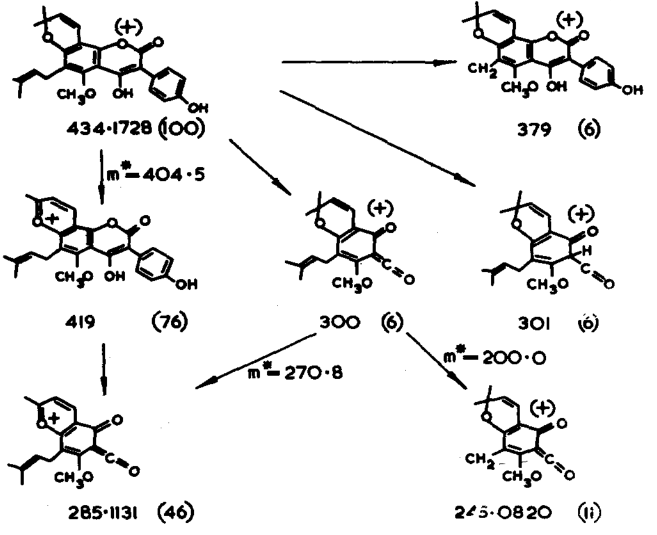


(II)

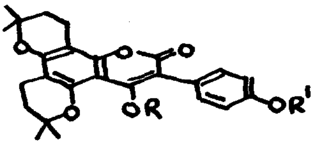
In each case ring A is fully substituted with the two C_5 units and the methoxyl group. A decision in favour of (I) could be made on two criteria. (a) Hydrolysis of scandenin with 10% aqueous sodium hydroxide gave p-hydroxyphenylacetic acid, readily purified and identified by comparison with an authentic sample. (b) The mass spectrum was as shown below.



This is quite incompatible with (II), a partial scheme on the basis of formula (I) is given. A definite formula for scandenin is written for simplicity, but this does not imply that this order of substituents on ring A is proven.

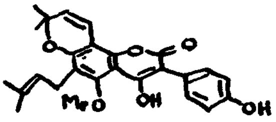


With hydriodic acid, scandenin gave dihydroisonorscandenin (III) (R = R' = H), characterised as its monoacetate m.p. 292-294°, (R = H, R' = COCH$_3$) and as its dimethylether m.p. 206-209°, (III)(R = R' = Me).

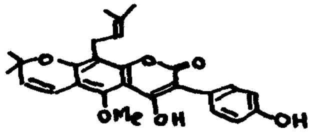


(III)

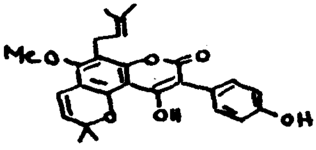
The presence of the two chroman rings was fully confirmed by the N.M.R. spectrum and the mass spectrum. The oxygenation pattern of ring A was proven by the synthesis of dimethyldihydroisonorscandenin. 4,5,7-Trihydroxy-4'-methoxy-3-phenylcoumarin was reacted with excess ββ-dimethylallyl bromide in the presence of boron trifluoride in diglyme. The product (III) (R = H, R' = Me) m.p. 290-292° was methylated to give (III) (R = R' = Me) identical in every respect with the product produced from scandenin. This leads to three possible formulae (IV), (V) and (VI) for scandenin.



(IV)



(V)



(VI)

On model 4-hydroxy-3-phenylcoumarins it has been shown that a 5-methoxyl group is shifted to slightly lower field in the N.M.R. spectrum than methoxyl groups attached to other relevant positions on the benzene rings, being seen at slightly over τ 6.0. On methylation of the 4-hydroxy group, the 5-methoxyl group moves to higher field by τ 0.11-0.14.

The methoxyl group of scandenin shows at τ 6.06 and on methylation the methoxyl groups appear at τ 6.19, 6.22 and 6.44. The band at τ 6.44 is due to the 4-methoxyl and so the methoxyl on ring A must have moved upfield in the N.M.R. spectrum by at least τ 0.13 on methylation. A 5-methoxy group is indicated and formula (VI) is contraindicated. Synthetic experiments to distinguish between formulæ(IV) and (V) are in progress.

Scandenin belongs to the class of 4-hydroxy-3-phenylcoumarins, a new type of natural product related to the isoflavones.

We are indebted to the Department of Scientific and Industrial Research for a Scholarship (to P.S.). We also thank Dr.M.Barber for running some mass spectra for us.