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STRUCTURES OF CLAUSENIN, CLAUSENIDIN AND A SYNTHESIS OF CLAUSENIN AND XANTHOXYLETIN*

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From the roots of Clausena heptaphylla Wt. & Arn. (Rutaceae) two new pyranocoumarins have been isolated. The crystalline compounds were isolated by hexane extraction of the powdered roots and careful chromatographic separation on silica gel. Clausenin, m.p. 156-157°, $C_{14}H_{12}O_5$ (mol. wt. by mass spec. 260) and clausenidin, m.p. 136-137°, $C_{19}H_{20}O_5$ (mol. wt. by mass spec. 328) gave a deep violet ferric chloride colouration. They showed characteristic UV absorption spectrum of coumarins, resembling closely the spectrum of psoralen. Clausenin shows λ_{max}^{EtOH} 216, 279 and 320 mμ (log ϵ, 4.14, 4.44 and 4.08) and clausenidin λ_{max}^{EtOH} 222, 284 and 328 mμ (log ϵ, 4.23, 4.53 and 4.11). The two longer

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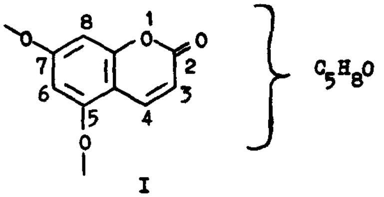
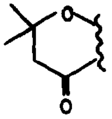
wavelength maxima show a bathochromic shift of about 17 mμ on addition of aluminium chloride to the alcohol solution (1). Both the compounds show IR bands at 1728 cm^{-1} (α,β-unsaturated ester or lactone) and 1639 cm^{-1} (chelated carbonyl). By the action of methanolic KOH, the δ-lactone ring opens in both the compounds providing the corresponding coumaric acids $C_{14}H_{14}O_6$, m.p. 214-215° (dec.) and $C_{19}H_{22}O_6$, m.p. 275-277° (dec.). The NMR spectrum of clausenin showed an AB quartet centred at δ 6.17 and 7.95 (J = 10 c/s) due to the C-3 and C-4 protons of the coumarin nucleus. Similarly clausenidin exhibits the C-3, C-4 proton quartet at δ 6.13 and 8.0 (J = 10 c/s). In the corresponding carboxylic acids, these protons appear at δ 6.38 and 8.0 (J = 16 c/s) and δ 6.66 and 7.8 (J = 16 c/s) respectively, showing the double bond protons of trans cinnamic acid. This shows therefore that both clausenin and clausenidin are coumarin derivatives in which the C-3 and C-4 positions of the coumarin nucleus are unsubstituted.

On fusion with KOH, clausenin gave phloroglucinol, thus leading to the partial formula (I). The NMR spectrum of clausenin exhibits a sharp singlet at δ 12.8, disappearing on deuteration which indicates the presence of a chelated phenolic hydroxyl group (2). One of the oxygens at C-5 or C-7 is phenolic and the other should be part of an ether linkage. The remaining three peaks in the NMR spectrum are a sharp singlet at δ 6.3 (1H), a two proton singlet at δ 2.83 due to a

-CH_2- group which does not have any neighbouring protons and a six proton singlet at δ1.53 due to gem-dimethyl groups.

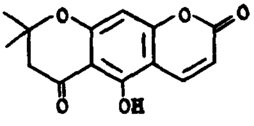


I



A

The NMR spectrum thus accounts for all the twelve protons of clausenin. Methylation with diazomethane gave a monomethylether, m.p. 149°, λ_{max}^{EtOH} 220, 262, 315 and 340 mμ (log ϵ, 4.16, 4.39, 4.11 and 4.04); ν_{max} 1729 cm^{-1} (δ-lactone), 1691 cm^{-1} (ketone) and 1611, 1599 cm^{-1} (aromatic). The methylether gave a crystalline 2,4-dinitrophenylhydrazone, m.p. 265-267°. This indicates that clausenin contains an α, α-dimethyl pyrone group (A) attached to the coumarin nucleus (I) in which the carbonyl group is strongly chelated to the phenolic hydroxyl. Only two such structures (II) and (III) could possibly be written for clausenin. The Gibbs test (3)



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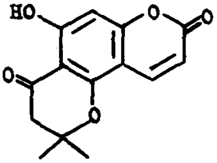
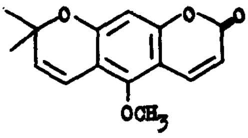


III

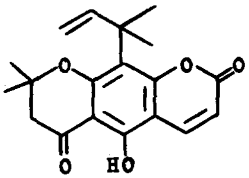


IV

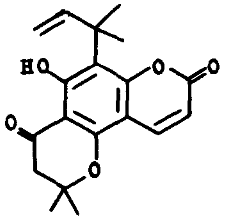
did not give a satisfactory answer to make a choice between the structures but an unambiguous synthesis proved that clausenin has the linear structure (II). 5,7-Dihydroxy-2,2-dimethyl chromanone (4) on condensation with ethylpropiolate (5) provided a mixture of two isomeric compounds, $C_{14}H_{12}O_5$ (a) m.p. 156-157° and (b) m.p. 220° which were separated by chromatography on silica gel. The UV, IR and NMR spectral evidence indicated that the compounds had the structures (II) and (III) but it was not possible to assign structures for (a) and (b). The monomethylether of (a), m.p. 148-149°, gave on reduction with sodium-borohydride, a mixture of products. Chromatographic separation gave the secondary alcohol $C_{15}H_{16}O_5$, m.p. 142°, which on dehydration with potassium bisulphate gave the corresponding chromene m.p. 130°. This was identical in its mixed m.p., IR and NMR spectra with an authentic sample of xanthoxyletin (IV) (6). The compound (a) and its methylether were found to be identical with clausenin and clausenin-monomethylether in their mixed m.p., TLC behaviour, UV, IR and NMR spectra. Clausenin and the product (a) should therefore, be constituted as (II) and the product (b) should have the angular structure (III).

Clausenidin possesses all the features of clausenin with an additional C_5H_8 unit. The NMR spectrum shows the chelated phenolic hydroxyl group at δ 13.1, the methylene singlet at δ 2.8 and the gem-dimethyl singlet at δ 1.52 as in clausenin. Clausenidin does not show any aromatic proton and the C_5H_8

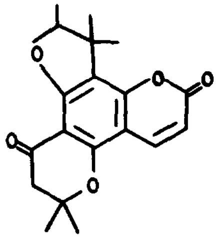
unit is clearly seen from the NMR spectrum as an α,α-dimethyl allyl group. The ABX spectrum with peaks at δ 6.13, 4.93 and 4.86 (Ja,x = 17 c/s; Jb,x = 10 c/s and Ja,b = 1.0 c/s) corresponding to a $-CH{=}CH_2$ group and a gem-dimethyl singlet at 1.68 δ (6H) are reminiscent of this side chain in macluraxanthone (7) and alvaxanthone (8). Clausenidin could therefore be represented by the structures (V) or (VI). In structure (V), there is no possibility of cyclisation of the side chain on the hydroxyl group; however, if clausenidin has the structure (VI) it should readily isomerize with acids to give the furan (VII) (9). Clausenidin when treated with conc. H_2SO_4 gave cycloclausenidin (VII), $C_{19}H_{20}O_5$, m.p. 152-153°. The NMR spectrum showed the disappearance of the hydroxyl and the ABX protons and the appearance of a secondary methyl doublet at 1.32 δ (J = 7 c/s) consistent with this structure. Clausenidin when refluxed with anhydrous aluminium chloride in benzene (10) gave the dealkylated product $C_{14}H_{12}O_5$, m.p. 220°, which was found to be identical in all respects



V



VI



VII

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