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COUMARINS OF *CLAUSENA DENTATA* (Willd.) R. and S.[1]

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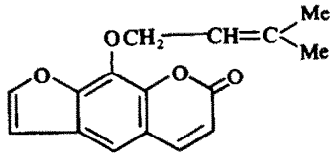
Abstract—Imperatorin (I) and two new coumarins, dentatin and nordentatin, have been isolated from the root bark of *Clausena dentata* (Willd.) R. and S. Based on spectral evidence and chemical correlations, dentatin is shown to be a new pyranocoumarin having structure IIa and nordentatin to be IIb.

Clausena dentata (Willd.) R. and S. (family Rutaceae) is a small tree found in South India. Rao and Subramaniam[2] isolated three compounds from the leaves which they named α-clausenan, di α-clausenan and β-clausenan. Later Rao[3] assigned a structure for α-clausenan.

In continuation of our work on the Indian Rutaceae we undertook the chemical investigation of the root bark of *Clausena dentata*. The hexane extract of the root bark gave a solid mixture of coumarins which on chromatography over silica yielded three crystalline compounds I, IIa and IIb melting at 102°, 95° and 182° respectively.

Compound I analysed for $C_{16}H_{14}O_4$. Its UV, IR and NMR spectra were reminiscent of imperatorin.[4, 5] This was confirmed by a direct comparison with an authentic sample.†



I

Dentatin (IIa), m.p. 95°, was obtained as colourless prisms from pet. ether. Analytical results and mass spectral mol wt determination (molecular ion peak at 326) established the molecular formula to be $C_{20}H_{22}O_4$. It gave no colour with ferric chloride. Its IR spectrum (in KBr) exhibited bands characteristic of coumarin carbonyl (1720 cm^{-1}) and aromatic (1590, 1610 cm^{-1}) groups. Its UV spectrum showed maxima at 230, 270 and 330 (sh) mμ (log ε 4·24, 4·36 and 3·96) indicative of the presence of a substituted coumarin. The NMR spectrum of dentatin showed a sharp singlet at 3·85 δ (3H) indicating the presence of a OMe group. The doublets at 6·15 δ (J = 10 c/s) and 7·9 δ (1H, J = 10 c/s) are characteristic of the 3 and 4 protons respectively of a coumarin ring system. The sharp singlet at 1·48 δ along with the doublets at 5·75 δ and 6·6 δ (J = 10 c/s) reveal the presence of a 2,2-dimethyl-

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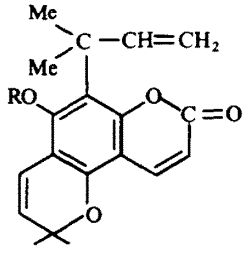
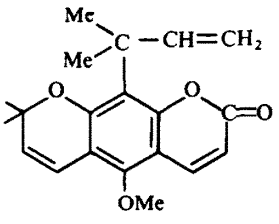
chromene ring.[6,7] This leaves out a C_5H_8 unit to be accounted for in the molecule which is seen clearly from the NMR spectrum as an α,α-dimethylallyl group. The sharp singlet at 1·69 δ (6H) with the multiplet at 4·98 δ (2H) and doublet at 6·15 δ (1H superimposed on coumarin 3 proton) are reminiscent of this side chain in macluraxanthone[8] and alvaxanthone.[9]

The mass spectrum exhibited a peak at *m/e* 311 (M-15) which is four times as intense as that of the parent ion with no other peaks of comparable intensity; this is characteristic of the ready formation of stable benzopyrylium ions from 2,2-dimethyl chromenes.[10a–e]

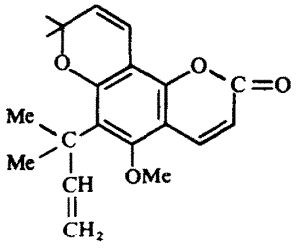
Thus, dentatin is a coumarin incorporating a OMe, a 2,2-dimethylchromene and an α,α-dimethylallyl system. On the biogenetic consideration that naturally occurring coumarins are predominantly 5,7 oxygenated,[11–13] the following three structures IIa, III and IV were considered as possibilities for dentatin:



IIa: R = Me
IIb: R = H



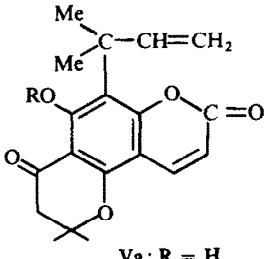
III



IV

Catalytic hydrogenation of dentatin gave the tetrahydro compound, m.p. 100°. Its NMR spectrum showed the complete absence of vinylic and olefinic protons (except the doublets at 6·2 and 7·9 δ, J = 10 c/s due to the C_3 and C_4 protons) and exhibited new triplets centred at 0·70 δ (primary Me) and 2·92 δ (2H benzylic).

In a recent publication[14] Joshi *et al.* reported the isolation of a new pyranocoumarin, clausenidin (Va) from the roots of a related plant. This report tempted us to consider structure IIa, as the most probable one for dentatin. To establish

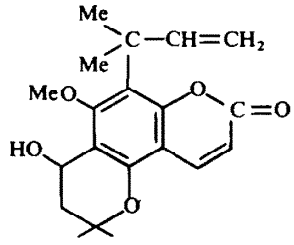


V

Va: R = H
Vb: R = Me

this unequivocally, clausenidinmonomethyl ether (Vb) was converted into dentatin by the following sequence of reactions: The methyl ether, m.p. 86–87°, gave on reduction a mixture of products one of which was identical in TLC with dentatin.

Chromatographic separation of the mixture on silica gel gave two compounds. One of these, m.p. 95°, was identical in all respects with dentatin. The other compound VI, m.p. 157–158°, showed the presence of a OH group (ν_{max}^{Nujol} 3560 cm^{-1}). Its mol wt by mass spectrum was 344. This compound dehydrated on passing through a long column of alumina in benzene–methanol (20:0·2) giving dentatin.



VI

This correlation establishes structure IIa for dentatin.

Nordentatin, m.p. 182°, has been isolated from the mother liquors of dentatin by chromatography over silica. It gave a green colour with ferric chloride. The molecular formula $C_{19}H_{20}O_4$ (mol wt by mass spectrum 312) is less by one CH_2 than that of dentatin. The characteristic base shift in the UV and the OH band at 3350 cm^{-1} (Nujol) in the IR spectrum show the presence of a phenolic OH group. This accounts for the presence of a sharp singlet at 7·28 δ (1H) in the NMR spectrum and the disappearance of the singlet at 3·85 δ (OMe, 3H) present in that of dentatin. The sum of evidence is thus in favour of structure IIb which has been confirmed by methylation of nordentatin to dentatin by means of methyl iodide, acetone and potassium carbonate.

EXPERIMENTAL*

Isolation of the coumarins. The powdered root bark† (1·4 kg) was percolated with cold hexane. The hexane extract was concentrated and the residual oil left in the refrigerator for several days. The colourless crystalline solid that separated was filtered, washed with hexane and dried (16 g). TLC examination of this on silica (benzene:EtOAc:MeOH—18:2:0·5) showed three spots. By fractional crystallization two of the compounds were separated in a fair state of purity.

The minor compound I (400 mg) was repeatedly crystallized from hexane and was found to be single by TLC, m.p. 102°. It was identical (m.p., m.m.p., TLC and IR) with an authentic specimen of imperatorin, λ_{max} 250, 300 mμ (log ε 4·24, 3·97). (Found: C, 70·9; H, 5·4. Calc. for $C_{16}H_{14}O_4$: C, 71·1; H, 5·2%.)

Dentatin. The major component of the hexane extract (12 g) contained an impurity which could not be removed by repeated crystallization. Chromatography of this compound (1 g) on silica (30 g) and elution with benzene:EtOAc:MeOH (18:2:0·5) afforded dentatin (800 mg) and nordentatin (10 mg) in the increasing order of polarity. Dentatin crystallized from pet. ether as colourless prisms, m.p. 95–96°. It gave no colour with $FeCl_3$; ν_{max}^{KBr} 1720, 1610, 1590 cm^{-1}, λ_{max} 230, 270, 330 (sh) mμ (log ε 4·24, 4·36, 3·96). (Found: C, 73·3; H, 7·1. $C_{20}H_{22}O_4$ requires: C, 73·6; H, 6·8%; mol. wt. by mass spectrum 326.)

Tetrahydrodentatin. Dentatin (400 mg) was shaken in an atmosphere of H_2 in methanolic soln (20 ml) in the presence of PtO_2 catalyst. When no more H_2 was absorbed it was filtered and the solvent removed.

* M.ps are uncorrected. UV spectra were taken in 95% EtOH using Beckmann model DU spectrophotometer. NMR spectra: $CDCl_3$ on a 60 m.c. Varian instrument with TMS as an internal standard. Silica refers to Kieselgel G. (E. Merck), alumina refers to M & B and petroleum ether refers to b.p. 40–60°. Kieselgel G. (E. Merck) was used for TLC.

† The plant material was collected from Rajbhavan Forests, Guindy, Madras.

The residue crystallized from pet ether as colourless prisms, (300 mg), m.p. 99–100°, ν_{max}^{Nujol} 1720, 1610 cm^{-1}, λ_{max} 260, 335 mμ (log ε 3·41, 4·12). (Found: C, 73·1; H, 8·0. $C_{20}H_{26}O_4$ requires: C, 72·7; H, 7·9%.)

Methylation of clausenidin. A mixture of clausenidin (500 mg), MeI (5 ml), ignited K_2CO_3 (4 g) and acetone (100 ml) was refluxed for 30 hr. The reaction mixture was filtered hot, the potassium salts washed with hot acetone and the solvent distilled. The product was purified by chromatography over silica followed by recrystallization from hexane (150 mg), m.p. 86–87°, undepressed with an authentic sample.*

$NaBH_4$ *Reduction of clausenidinmonomethylether.* $NaBH_4$ (0·15 g) was added to a soln of clausenidin monomethyl ether (0·15 g) in MeOH (7 ml) with stirring. The soln was stirred for 1 hr at 0° and the solvent removed *in vacuo*. The residue was poured on water and extracted with $CHCl_3$. The $CHCl_3$ layer was washed well with water, dried (Na_2SO_4) and evaporated. The product was chromatographed over silica and eluted with benzene and benzene–MeOH (20:0·2) respectively. The fraction eluted by benzene crystallized from hexane as colourless prisms (15 mg), m.p. 95°, alone or when mixed with an authentic specimen of dentatin. Their IR spectra, mass spectra and TLC behaviour were identical.

The fraction eluted by benzene–methanol crystallized from hexane as colourless prisms (30 mg; VI), m.p. 157–158°, ν_{max}^{Nujol} 3560, 1700, 1590 cm^{-1}, λ_{max} 265, 332·5 mμ (log ε 3·56, 4·08), mol wt by mass spectrum 344.

Dehydration of the alcohol VI *by alumina chromatography.* The above compound (20 mg) was dissolved in the minimum amount of benzene, adsorbed on alumina (20 g) in benzene and eluted with a mixture of benzene–MeOH (20:0·2). The product crystallized from hexane as colourless prisms (10 mg), m.p. 95°, and was identical with dentatin.

Nordentatin. Nordentatin crystallized from benzene as pale yellow *prisms*, m.p. 182°. It gave a green colour with $FeCl_3$. λ_{max}^{EtOH} 225, 275–280, 335 mμ (log ε 4·22, 4·24, 4·04). $\lambda_{max}^{EtOH-NaOH}$ 245, 310, 350, 400 mμ (log ε 4·07, 4·18, 3·90, 3·70). ν_{max}^{Nujol} 3350 (OH), 1750, 1675 cm^{-1}. (Found: C, 73·35; H, 6·50; mol wt by mass spectrum 312. $C_{19}H_{20}O_4$ requires: C, 73·07; H, 6·4%; mol wt 312.)

Methylation of nordentatin. A mixture of nordentatin (40 mg) MeI (2 ml) ignited K_2CO_3 (2 g) and acetone (30 ml) was refluxed for 30 hr. The methylated product crystallized from pet. ether as colourless prisms (20 mg), m.p. 95°, alone or when mixed with dentatin. Their IR spectra and TLC behaviour were identical. (Found: C, 73·6; H, 6·8; Calc. for $C_{20}H_{22}O_4$. C, 73·6; H, 7·04%.)

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