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Clausmarins A and B: Two Novel Spasmolytic Terpenoid Coumarins from *Clausena pentaphylla* (Roxb.) DC

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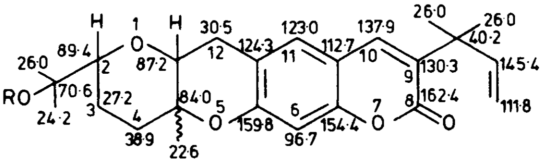
Summary The structures of two new isomeric terpenoid coumarins from *C. pentaphylla* have been shown to be 9-(1,1-dimethylallyl)-2-(1-hydroxy-1-methylethyl)-4a-methyl-2,3,4,4a,12,12a-hexahydrodipyrano[3,2-*b*][3′,2′-*g*]-[1]benzopyran-8-one (**1**) and its isomer (**5**), respectively on the basis of chemical and spectroscopic evidence.

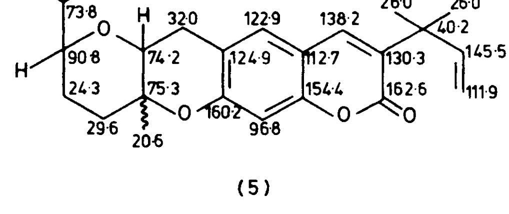
Clausmarins A and B, two isomeric coumarins from *C. pentaphylla* (Roxb.) DC. (Rutaceae), have been found to possess potent spasmolytic activity in experimental animals. The present communication gives the essential data which establish constitutions (**1**) and (**5**) respectively for clausmarins A and B. Significantly, the monoterpene part of these coumarins represents a new fundamental cyclization of geranyl pyrophosphate.

Clausmarin A, m.p. 131 °C, $[\alpha]_D^{18}$ +34° ($CHCl_3$), $C_{24}H_{30}O_5$ (M^+ 398·2066), showed u.v. absorptions at λ_{max} (EtOH) (log ϵ) 225 (4·12), 248 (3·59), 250 (3·49), 298 (3·89), and 332 nm (4·83) consistent with an oxygenated coumarin structure.[1] Its i.r. spectrum supported the above findings and showed bands at ν_{max} (KBr) 3500 (OH), 1710, 1630 (conjugated δ-lactone), and 1580 cm^{-1} (aromatic).

On catalytic hydrogenation, clausmarin A gave a dihydro-derivative, $C_{24}H_{32}O_5$ (M^+ 400), λ_{max} (EtOH) (log ϵ) 223 (4·21), 246 (3·58), 258 (3·48), 298 (3·88), and 333 nm (4·39), and a tetrahydro-derivative, $C_{24}H_{34}O_5$ (M^+ 402), λ_{max} (EtOH) 220 and 293 nm. Preservation of the parent chromophore in dihydroclausmarin A and the positive Lemieux Rudloff modified test[2] shown by clausmarin A confirmed the presence of a nonconjugated double bond in the latter. The presence of a prenyl unit containing the double bond and its point of attachment at C-9 were deduced by the appearance of (i) 10-H at τ 2·56 in the ^1H n.m.r. spectrum (90 MHz; $CDCl_3$) of clausmarin A and (ii) by the formation of 3,3-dimethyl-2-oxovaleric acid[3] as the product of potassium permanganate oxidation of dihydroclausmarin A.



(**1**) R = H
(**2**) R = Ac
(**3**) R = H; side chain reduced
(**4**) R = H; 9,10 double bond and side chain reduced



(**5**)

^{13}C N.m.r. data for (**1**) and (**5**); δ values in p.p.m. from Me_4Si.

Failure of Jones oxidation and the formation of a monoacetyl derivative, m.p. 85 °C, $[\alpha]_D^{18}$ + 21·8° (M^+ 440), (**2**) indicated the presence of a tertiary OH function in clausmarin A. The absence of any coupling between the two aromatic protons resonating at τ 2·87 and 3·36 necessitated the accommodation of the remaining C_{10} unit linearly in the molecule. This fragment consisted of a tertiary OH group (τ 7·98, s), 3 Me groups attached to carbon atoms bearing oxygen functions [τ 8·80 (6H, s) and 8·89 (3H, s)], 2 benzylic protons giving an octet (τ 6·89), 2 CH_2 groups (τ 8·13, m), and a pair of CH groups attached to carbon atoms bearing oxygen (τ 5·18, t and 6·14br, m). Two of the three methyl groups were identified as part of a 1-hydroxy-1-methylethyl fragment since they experienced a downfield shift in *O*-acetylclausmarin A. A similar shift of the methine group (τ 6·14) in this compound located it adjacent to the 1-hydroxy-1-methylethyl fragment on the one hand and the methylene groups (τ 8·13) on the other, as the multiplet of the latter was simplified by irradiating at the frequency of τ 6·14. Conversely, irradiation at τ 8·13 caused a collapse of the triplet at τ 6·14 to a sharp singlet. The proximity of the methine group at τ 5·18 to the benzylic protons was likewise confirmed.

Assuming the C-2 containing ring to have a distorted boat conformation, the coupling constant of 8·0 Hz attributed to the axial 2-H triplet (τ 6·14) is in agreement with its forming dihedral angles of <30 and 160°, respectively with two C-3 protons.

The non-equivalent benzylic protons (τ 6·89) in this isomer appear as slightly distorted combination of two sets of quartets, with J_{gem} 16·0 Hz, J_{vic} 8·0 Hz. Irradiation at τ 6·89 resulted in the collapse of the equatorial C-12a methine triplet (τ 5·18; *J* 8·0 Hz) into a singlet while irradiation at τ 5·18 transformed the benzylic octet into a double doublet with *J* 16 Hz. These observations are consistent with only a *cis*-conformation of the terpenoid ring junction.

On the basis of above evidence in conjunction with biogenetic considerations clausmarin A, dihydroclausmarin A, and tetrahydroclausmarin A can be assigned structures (**1**), (**3**), and (**4**), respectively.

Clausmarin B, m.p. 80 °C, $[\alpha]_D^{18}$ $-12{\cdot}1°$ ($CHCl_3$), $C_{24}H_{30}O_5$ (M^+ 398·2074) had u.v., i.r., and mass spectral characteristics similar to those of (**1**). Its ^{1}H n.m.r. spectrum revealed a striking resemblance with that of (**1**). 2-H in clausmarin B (τ 6·60) appeared as an undefined multiplet with narrower half-width, indicating equatorial placement. Its proximity with the C-3 protons was established by double-resonance experiments. A unique feature in this isomer was the observance of very close chemical shifts of both the benzylic protons (τ 6·85), the geminal coupling of which was not discernable on irradiation of the equatorial 12a-H (τ 5·36) which converted the former into a singlet. However, as both the benzylic protons are still magnetically non-equivalent, these split 12a-H into a double doublet (*J* 8·0 Hz). The terpenoid *cis* ring junction in this epimer was further substantiated by observing a nuclear Overhauser effect between 4a-Me (τ 8·85) and 12a-H which increased the intensity of the latter by 37%. With the C-2 containing ring again in a twisted boat form, clausmarin B could be formulated as (**5**).

The structures (**1**) and (**5**) for clausmarins A and B, respectively were corroborated by their ^{13}C n.m.r. spectra (25·05 MHz; $CDCl_3$), shown in the structural diagrams, which showed the presence of 24 carbon atoms with expected multiplicities. The higher chemical shifts of C-12a and C-4 in (**5**) as compared to those in (**1**) are in conformity with the stereochemical assignments of their respective C-2 substituents.

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