

STRUCTURE OF CALOPHYNIC ACID,
A NOVEL CONSTITUENT OF CALOPHYLLUM INOPHYLLUM

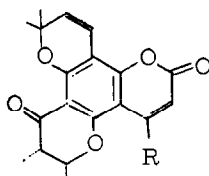
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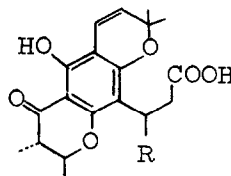
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The study of Calophyllum species (Guttiferae family) has led to the isolation of an increasing number of biogenetically related constituents :

4-phenyl and 4-alkylcoumarins of type I (examples : tomentolide A and B)¹ and hydroxy acids of type II (examples : isopetalic and chapelieric acid)².



I : R = phenyl : tomentolide A
R = alkyl : tomentolide B

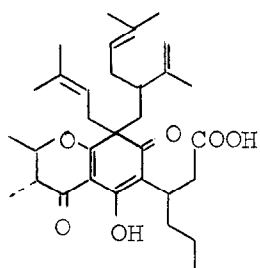


II : R = phenyl : chapelieric acid
R = alkyl : isopetalic acid

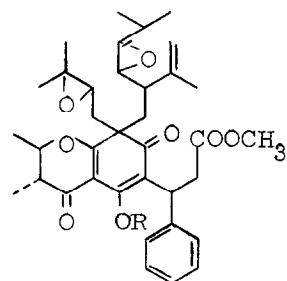
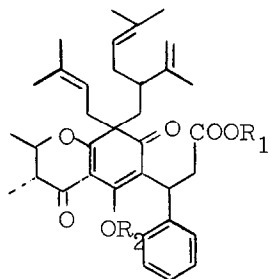
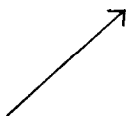
Cyclohexadienone derivatives (example : pseudobrasilic acid III) constitute the third type of characteristic Calophyllum constituents³. No phenyl analogue of (III) has been reported until now and the isolation and structure determination of such a compound is the object of the present paper.

Reinvestigation of the acid fraction of the chloroform extract of C.inophyllum seeds (origin : Madagascar) furnished along with calophyllic acid⁴ and pseudobrasilic acid (III)³ a new compound, named calophynic acid, C₃₅H₄₄O₆ ($\alpha_D = -266^\circ$) (M⁺ at m/e = 560) for which we propose structure (IVa) on the basis of the following evidence.

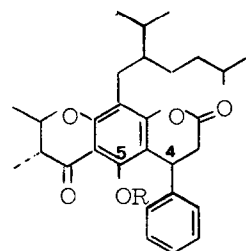
Its NMR spectrum shows a sharp singlet (1 H) at 12,2 ppm as well as a very broad signal (1 H) at about 9,3 ppm (both disappearing on deuteration), which can be attributed to an enol and a carboxyl group ($\nu_{C=O} = 1710 \text{ cm}^{-1}$) respectively. Treatment with CH₂N₂ in ether gives an ester C₃₆H₄₆O₆ (M⁺ at m/e = 574). No enol ether is obtained under these conditions due to the strong hydrogen bonding (positive Fe Cl₃ test) with the carbonyl group of a trans-2,3-dimethyl chromanone ring. The presence of this system is confirmed by its characteris-



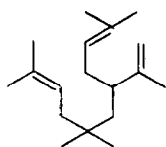
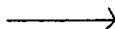
III

V R = CH₃

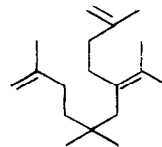
IV a : R₁ = R₂ = H
 b : R₁ = CH₃, R₂ = H
 c : R₁ = R₂ = CH₃



VI a : R = H
 b : R = CH₃



VII



VIII

tic spectral data ^{1,2}.

A group of 5 protons at 7,3 ppm in the NMR spectrum indicates the presence of a monosubstituted phenyl ring.

The most important fragments in the mass spectra of calophynic acid and its derivatives arise from a loss of $C_{10}H_{16}$ (2 unsaturations) due to a McLafferty rearrangement followed by a loss of C_4H_7 (1 unsaturation) and formation of a tropylium ion (base peak at $m/e = 369$). This fragmentation indicates a C_5 and a C_{10} chain attached to a single quaternary carbon.

The dihydro coumarin (VIa), $C_{30}H_{38}O_5$, ($\nu_{CO} = 1780\text{ cm}^{-1}$) (obtained by hydrogenation over Pt followed by p-TsOH catalysed lactonisation) furnished further useful information concerning the nature of the C_{10} side chain.

Its NMR at 100 MHz shows clearly a doublet ($J = 7\text{ Hz}$) for the two benzylic protons at $\delta = 2,59\text{ ppm}$ and (besides the two doublets of the trans-2,3 dimethyl chromanone) 4 secondary methyl groups between 0,70 and 1,00 ppm indicating the presence of a lavandulol side chain already encountered in Guttiferae constituents ^{3, 5}.

Its methyl ether (VIb) (obtained by treatment with dimethyl sulfate in acetone) shows a singlet of 3 protons (OCH_3) at $\delta = 3,50\text{ ppm}$. This chemical shift has to be compared with that of the corresponding derivatives of pseudobrasilic acid : $\delta = 3,85\text{ ppm}$. The shielding effect (although smaller than that observed in the case of 4-phenyl coumarins¹) determines the relative position of the phenyl and methoxyl groups at position 4 and 5 respectively.

The presence of 4 olefinic protons between 4,50 and 5,00 ppm in the NMR spectrum is complemented by that of 5 olefinic methyl groups. Although the facile McLafferty rearrangement in the mass spectrum necessitates a hydrogen atom in γ -position of the carbonyl function, another arrangement of the double bonds like (VIII) could not be totally excluded (especially since one would expect the olefinic protons of the dimethylallyl chains at about 5,1 ppm)⁵.

Chemical proof in favor of (VII) was obtained in the following manner : Ozonolysis followed by hydrolysis under reductive conditions furnished about twice as much acetone than formaldehyde. Furthermore, partial epoxidation of (IVc) (obtained by treatment of (IVa) with CH_2N_2 in MeOH) yielded a diepoxide (V) possessing 1 oxygen atom on each side chain (loss of $C_{10}H_{16}O$ followed by loss of C_4H_7O in the mass spectrum). In the NMR of the diepoxide (V), a broad signal (2 H) at 4,60 ppm ($= CH_2$) and the presence of only 1 olefinic methyl group (1,6 ppm) prove structure (IVa) for calophynic acid.

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