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CONSTITUENTS OF CALOPHYLLUM TOMENTOSUM AND CALOPHYLLUM APETALUM NUTS : STRUCTURE OF A NEW 4-ALKYL- AND OF TWO NEW 4-PHENYL-COUMARINS.

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In the course of our investigations of the structure (1,2) and biosynthesis (3) of the constituents of Calophyllum species (N.O. Guttiferae) we have isolated three new, optically inactive, compounds : tomentolide A (I) and tomentolide B (II) from C. tomentosum and apetalolide (III) from C. apetalum. Tomentolide B is a 4-propyl-coumarin while the two others are 4-phenyl-coumarins.

Tomentolide A (I)

On the basis of spectral investigation we propose structure (I) for tomentolide A [m.p. 201-205°, U.V. λ_{max} 237 mμ (log ε 4.63) 275-280 mμ (4.59) 350 mμ (3.9)], an isomer of the already known inophyllolide (IV) (1). Its mass spectrum shows a parent ion peak at m/e 402 (calculated for $C_{25}H_{22}O_5$: 402.1467 ; found: 402.1464) ; an intense peak at m/e 387 (M-15) is in agreement with the observed ready formation of stable benzopyrylium ions from 2,2-dimethylchromenes (4). Other important peaks are at m/e 331 (M-15-56) and m/e 303 (M-15-56-28) which arise from successive loss of butene and CO from the m/e 387 ion. A similar fragmentation is observed in the case of inophyllolide (IV) and seems to be characteristic of this series of compounds.

The I.R. spectrum of tomentolide A resembles that of inophyllolide and shows significant bands at 1740 cm^{-1} (lactone), 1690 cm^{-1} (CO) and at 753 and 699 cm^{-1} (monosubstituted phenyl).

The N.M.R. data (see TABLE I) provide substantial evidence for the structure (I) assigned to tomentolide A. The 4-phenyl substituent of the coumarin system causes strong shielding of the protons situated on the ring D. Thus, while in the case of inophyllolide (IV) the signals due to the methyl groups a and a' are at δ = 0.90 and δ = 0.96 ppm, the corresponding signals for tomentolide A are observed at δ = 1.49 and 1.52 ppm. In the same manner, the signals due to the methyl groups b and c and to the protons f and g in inophyllolide are shifted to higher field in tomentolide A.

TABLE I

N.M.R. data (60 Mc in $CDCl_3$; DMSO-d_6 for compound II a)

	a (3H) a' (3H)	b (3H)	c (3H)	e (1H)	e' (1H)	f (1H)	g (1H)	h (1H)
Tomentolide A (I)	1.49 s 1.52 s	0.71* d; J=6	1.00 d; J=6	5.58 d; J=10	6.78 d; J=10	2.18 m	3.78* m	5.85 s
Inophyllolide (IV)	0.90 s 0.96 s	1.58 d; J=6	1.21 d; J=6	5.32 d; J=10	6.50 d; J=10	2.46 m	4.59 m	5.78 s
Apetalolide (III)	1.38 s	1.92 d; J=7	1.95 s	5.67 d; J=10	6.50 d; J=10		6.60 m	6.05 s
Calophyllolide (V)	0.94 s	1.92 d; J=7	1.95 s	5.38 d; J=10	6.42 d; J=10		6.50 m	5.89 s
Tomentolide B (II)	1.51 s	1.53 d; J=7	1.15 d; J=7	5.58 d; J=10	6.85 d; J=10	2.42 m	4.22 m	5.79 s
Compound (II a)	1.30 s	1.78 d; J=6	1.88 s	5.76 d; J=10	6.79 d; J=10		6.45 m	5.95 s
Compound (II b)	1.38 s	1.88 d; J=7	1.95 s	5.72 d; J=10	6.15 d; J=10		6.50 m	6.03 s

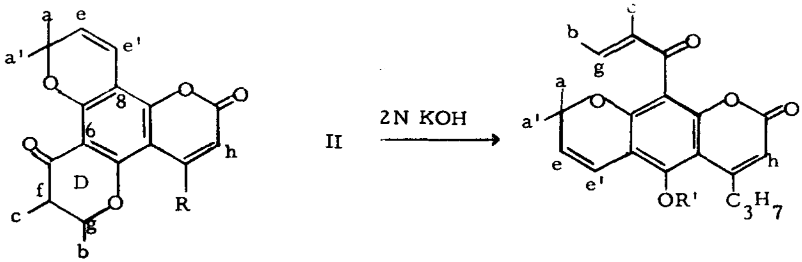
Values are expressed in δ units (ppm) and coupling constants in c/s). Symbols s, d, and m stand for singlet, doublet and multiplet, respectively.

* Double resonance shows that the methyl protons at 0.71 ppm are coupled with the proton at 3.78 ppm.

Tomentolide B (II)

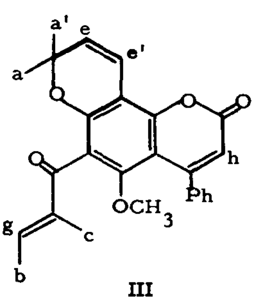
Tomentolide B [m.p. 158-160°, U.V.λ_{max} 231 mμ (log ε 3,59) 283 mμ (3,75) 346 mμ (3,25)] exhibits in its mass spectrum a molecular ion peak at m/e 368 (calculated for $C_{22}H_{24}O_5$: 368.1624 ; found: 368.1621) and a fragmentation pattern similar to that observed in the case of tomentolide A. The base peak is at m/e 353 (M-15) and the peaks corresponding to further loss of butene and then CO appear at m/e 297 and m/e 269.

The carbonyl frequencies of tomentolide B are the same as those of tomentolide A, but the bands characteristic for monosubstituted phenyl group are absent. The N.M.R. spectrum of tomentolide B does not reveal any benzenic protons and it indicates the presence of an n-propyl group at position 4 of the coumarin system (tripletsat δ = 1.00 ppm and δ = 2.81 ppm*). In the absence of a 4-aryl group, the N.M.R. spectrum does not permit a definite choice between a "6-acyl" and a "8-acyl" structure. Tomentolide B was therefore isomerised to the phenol (IIa) with 2N potassium hydroxide in methanol. The formation of phenol (IIa)** ($C_{22}H_{24}O_5$, M^+ 368, colourless needles, m.p. 190°, OH band at 3300 cm^{-1}) is only possible from a "6-acyl" structure. The N.M.R. spectrum of its more soluble acetate (IIb) ($C_{24}H_{26}O_6$, M^+410, m.p. 170-175°) shows clearly, along with the signals of the acetyl group and the almost unaltered 2,2-dimethylchromene ring, the transformation of the dimethyl dihydropyrone ring into a 2,3-dimethyl acryloyl side chain.

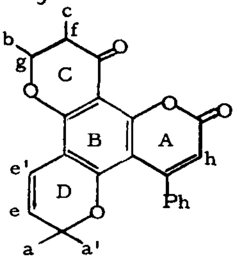


I : R = C_6H_5
II : R = $CH_2CH_2CH_3$

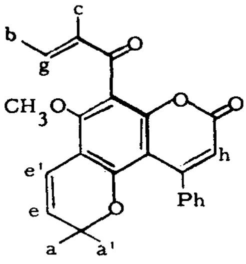
IIa : R' = H
IIb : R' = $COCH_3$



III



IV



V

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* The central CH_2 multiplet is masked by other signals.

** Negative ferric chloride test.

Apetalolide (III)

Apetalolide [m.p. 203-205°, U.V.λ_{max} 236 mμ (log ε 4,55) 275 mμ (4,40)] is the second natural 4-phenyl-coumarin which possesses a methoxyl group. It has a molecular weight of 416 corresponding to the formula $C_{25}H_{24}O_5$ (calculated : 416.1624 ; found:416.1624). Its U.V., I.R. and mass spectra are similar to those of calophyllolide (V) of known structure (1). The only noteworthy feature of the mass spectrum is the occurrence of an intense M-15 peak at m/e 401. A small peak at m/e 361 (M-55) corresponds to the loss of C_4H_7 from the 6-acyl substituent.

The shift of the OCH_3 signal from $\delta = 3.72$ ppm in calophyllolide (V) to $\delta = 3.03$ ppm in apetalolide (III), as well as the shift, in the opposite direction, of the signal due to the quarternary methyl groups (a and a') from $\delta = 0.94$ ppm in calophyllolide to $\delta = 1.38$ ppm in apetalolide, permit the assignment of structure (III) to apetalolide.

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