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CHEMICAL CONSTITUENTS OF *CALOPHYLLUM APETALUM* WILLD.*

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A recent communication[1] on the isolation of three new coumarins from *Calophyllum tomentosum* and *Calophyllum apetalum* prompts us to record our own observations on the chemical constituents of *Calophyllum apetalum* Willd. (syn. *Calophyllum wightianum* T. Anders.). From the bark of the plant collected in Goa we obtained friedelin and a new acid named apetalic acid. The roots yielded friedelin, the stem gave friedelin and β-amyrin and the wood yielded β-sitosterol and mesoinositol.

We wish to present here evidence leading to structure (I) for apetalic acid.

Apetalic acid, m.p. 117°, $[\alpha]_D$ + 28.43° ($CHCl_3$, c 2.56), $C_{22}H_{28}O_6$ (molecular weight by mass spectrum 388), has λ_{max}^{EtOH} 227, 268, 276, 301, 315 and 368 mμ (log ϵ 3.99, 4.49, 4.53, 4.00, 4.03 and 3.37), $\lambda_{max}^{EtOH-NaOH}$ 398 mμ (log ϵ 3.73) $\nu_{max}^{CH_2Cl_2}$ 3500 (OH), 1700 (COOH), 1645 (hydrogen-bonded aryl ketone), 1620 and 1575 cm^{-1}. With ferric chloride, it gave a dark green colour. The UV and IR spectra of apetalic acid are very similar to those of blancoic acid for which structure (II) has been suggested by Stout *et al.*[2]

The NMR spectrum (Table 1) provides strong evidence in support of structure (I) for apetalic acid.

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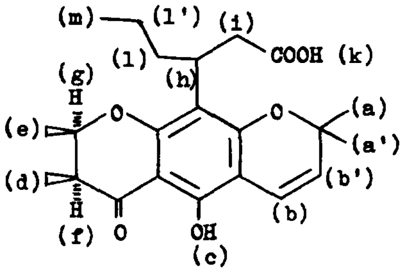
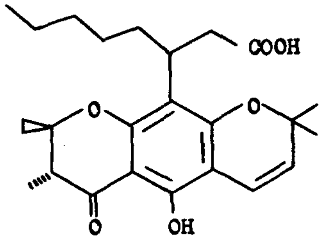
* Contribution No.111 from CIBA Research Centre



I



II

TABLE 1

NMR spectrum ($CDCl_3$, 100 mc) of apetalic acid (δ expressed in p.p.m., J in c.p.s. Symbols s, d, t and m stand for singlet, doublet, triplet and multiplet respectively).

δ	Number of protons	Multiplicity (J)	Assignment See Formula I
12.34	1	s	c
9.90	1	broad	k
6.54	1	d (10)	b
5.38	1	d (10)	b'
4.45	1	m (J_{H_f, H_g} 3*, J_{H_g, H_e} 7)	g
3.63	1	m	h
2.75	2	m	i
2.50	1	m (J_{H_f, H_g} 3*, J_{H_f, H_d} 7)	f
1.70	4	broad	l, l'
1.41	3	s	a
1.34	3	s	a'
1.31	3	d (7)	e
1.09	3	d (7)	d
0.82	3	t (6.5)	m

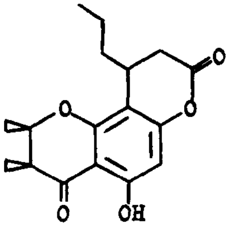
* Established by double resonance

The mass spectrum of apetalic acid shows a very intense peak at m/e 373 (M-CH_3) characteristic of the formation of stable benzopyrylium ions from 2,2-dimethylchromenes[3].

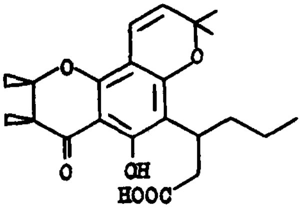
Apetalic acid reacts with diazomethane to give the methyl ester, b.p. 180-190°/0.3 mm., $[\alpha]_D$ + 30.36° ($CHCl_3$, c 2.64), $\nu_{max}^{CH_2Cl_2}$ 3620 (OH), 1730 (ester), 1640 (hydrogen-bonded aryl ketone), 1620, 1575 cm^{-1}. Its NMR spectrum showed a peak at δ 3.50 p.p.m. (COOMe). Refluxing the ester with dimethyl sulphate and potassium carbonate in acetone gives O-methylmethyl apetalate, b.p. 180-190°/ 0.4 mm., $\nu_{max}^{CH_2Cl_2}$ 1735 (ester), 1675 (aryl ketone), 1645, 1590 cm^{-1}. Its NMR spectrum shows peaks at δ 3.54 (COOMe) and 3.77 p.p.m. (OMe). The shift in the IR absorption band of the ketone carbonyl consequent to O-methylation shows that the keto group is strongly hydrogen-bonded to the phenolic hydroxyl in apetalic acid as well as its methyl ester.

The presence of a dimethylchromene ring in apetalic acid, indicated by the mass and NMR spectra, was confirmed by the identification of both acetone and acetaldehyde as their 2,4-dinitrophenylhydrazone derivatives following the degradation of apetalic acid with dilute base[4]. Catalytic hydrogenation of apetalic acid gave dihydroapetalic acid, yellow gum, λ_{max}^{EtOH} 217, 300, 348 mμ (log ε 4.34, 4.27, 3.49), λ_{sh} 232 mμ (log ε 4.17) which yielded, with diazomethane, methyl dihydroapetalate, b.p. 180°/0.5 mm. The NMR spectra of dihydroapetalic acid and its methyl ester lack the doublets due to the chromene ring hydrogens. Methyl apetalate, on refluxing with 2,4-dinitrophenylhydrazine in presence of acid, yielded a red <u>bis</u>-2,4-dinitrophenylhydrazone, dark red needles, m.p. 235° (decomp.), λ_{max}^{EtOH} 382 mμ (log ε 4.70). Besides reaction of the ketone present in methyl apetalate, the chromene ring has obviously been converted to the dinitrophenylhydrazone of the corresponding chromanone[5].

Treatment of apetalic acid with anhydrous aluminium chloride in benzene yielded 'lactone A' (III), m.p. 113-114°, $C_{17}H_{20}O_5$ (molecular weight by mass spectrum 304), $[\alpha]_D$ - 40.50° ($CHCl_3$, c 2.0), λ_{max}^{EtOH} 214, 284 and 344 mμ (log ϵ 4.49, 4.32, 3.58), λ_{sh} 229 mμ (log ϵ 4.30), $\lambda_{max}^{EtOH-NaOH}$ 254, 339 mμ (log ϵ 3.91, 4.56), ν_{max}^{KBr} 1785, 1655, 1650, 1625 cm^{-1}. The compound gave a purple colour with ferric chloride. Its NMR spectrum is entirely in accord with structure (III). On methylation with methyliodide-potassium carbonate in acetone, 'lactone A' yielded an O-methylether, m.p. 170°, ν_{max}^{KBr} 1775 (lactone) and 1680 cm^{-1} (ketone).



III



IV

The above results lead to structure (I) for apetalic acid. The alternate possibility (IV) is rejected since all attempts to lactonise apetalic acid were unsuccessful. Full details of this work will be published in Tetrahedron.

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REFERENCES

1. S.K. Nigam, C.R. Mitra, G. Kunesch, B.C. Das and J. Polonsky, Tetrahedron Letters, 2633 (1967).
2. G.H. Stout, K.D. Sears and G.L. Hickernell, Abstracts of papers presented at the 152nd meeting of the American Chemical Society, New York, September 11-16, 1966, S 078.

3. C.S. Barnes, J.L. Occolowitz, N.L. Dutta, P. Madhavan Nair, P.S. Phadke and K. Venkataraman, Tetrahedron Letters, 281 (1963).

4. G.H. Stout and K.L. Stevens, J. Org. Chem., **29**, 3604 (1964).

5. R. Livingstone and R.B. Watson, J. Chem. Soc., 1509 (1957).