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CONSTITUENTS OF *MESUA FERREA L.*—II:

FERRUOL A, A NEW 4-ALKYLCOUMARIN

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Abstract Ferruol A, $C_{23}H_{30}O_5$, a new 4-alkylcoumarin isolated from the trunk bark of *Mesua ferrea* L., is shown to be I.

IN CONTINUATION of our study on the constituents of *Mesua Ferrea* L.,[1] the chemical investigation of the trunk bark of this tree is reported herein. Extraction of the bark with pet. ether afforded an apparently homogenous crystalline compound, m.p. 129–130°, which we have called ferruol. Ferruol is indeed a mixture of two structurally very similar homologous compounds, as revealed by mass spectral and TLC examination. In the order of their elution, they have been designated ferruol A and ferruol B. By extensive chromatography over silica gel only ferruol A could be isolated in the pure form.† In this paper we propose structure I for ferruol A, m.p. 126·5°, based mainly on the spectral and analytical data.

Analytical results and mass spectral mol wt determination (molecular ion peak at 386) established the molecular formula, $C_{23}H_{30}O_5$ for ferruol A. Its IR spectrum exhibits bands characteristic of OH (3370), coumarin carbonyl (1700), chelated acyl (1605) and aromatic (1585, 1550 cm^{-1}) groups. The UV spectrum (Table 1) in the

TABLE 1. UV DATA FOR I, II AND III

	$\lambda_{max}^{EtOH-HCl}$ mμ (log ε)	$\lambda_{max}^{EtOH-KOH}$ mμ (log ε)
Ferruol A (I)	296 (4·38)	256 (4·09)
	324 (4·21)	335 (4·50)
Mammea B BB (II)	222 (4·46)	225 (4·24)
	295 (4·37)	257 (4·05)
	320 (4·23)	333 (4·53)
Mammea C BB (III)	222 (4·50)	229 (4·20)
	294 (4·40)	257 (4·14)
	322 (4·25)	333 (4·54)

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† Dr. Crombie has kindly informed us that ferruol B is a slightly impure specimen of mammea B BA.

[1] Part I. T. R. Govindachari, B. R. Pai, P. S. Subramaniam, U. Ramdas Rao and N. Muthukumaraswamy, *Tetrahedron* **23**, 243 (1967).

presence of both acid and alkali shows a striking resemblance to those reported[2] for mammea B/BB (II) and mammea C/BB (III). At the outset, this evidence permits classification of ferruol A as a new alkylcoumarin structurally very close to II and III. Further information regarding the nature of the substituents and their location on a coumarin nucleus has been obtained from the NMR spectrum (Fig. 1). The chemical shifts and the most probable assignments are given in Table 2. In accordance with the observations of Crombie *et al.*,[2] the 8-acyl, 6-alkyl orientation follows both from the characteristic base-shifts in the UV and the peak positions of the OH protons in the NMR spectra. The downfield resonance at 14·6 δ must be ascribed to the strongly hydrogen bonded 7-OH and the one at 6·96 δ is due to the unchelated 5-OH proton. Corroborative chemical evidence has been obtained by the acid-catalysed deacylation[3,4] of ferruol A with 70% sulphuric acid which gives α-methyl-

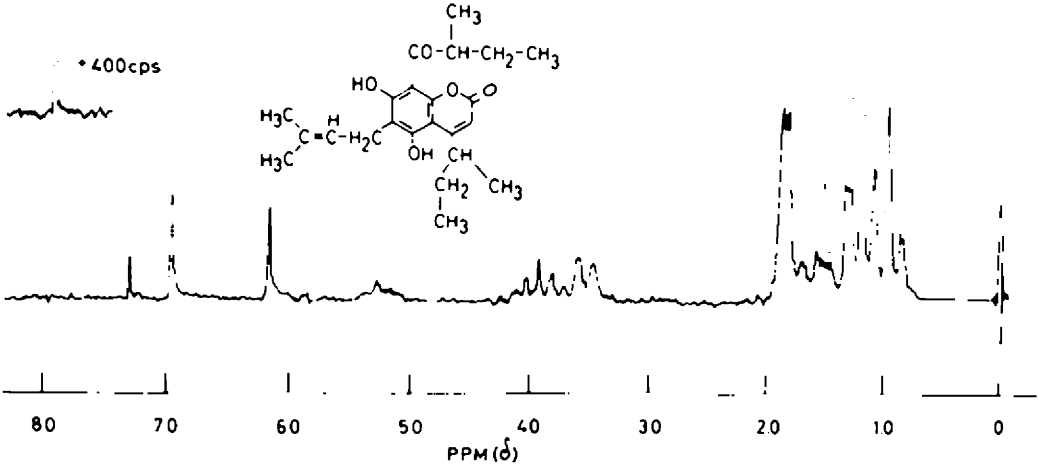

FIG. 1. NMR spectrum of ferruol A (I) in $CDCl_3$ at 60 Mc.

TABLE 2. NMR SPECTRUM OF I (60 Mc, $CDCl_3$)

Shift (δ)	Proton count	Assignment	Appearance
0·96	6	e, n	Triplet (J = 7 c/s)
1·18	3	c	Doublet
1·29	3	l	Doublet
1·57	4	d, m	Multiplet
1·83	6	i	Apparently doublet
3·51	2	g	Doublet (J = 7 c/s)
3·93	2	b, k	Symmetrical multiplet
5·26	1	h	Apparently triplet
6·16	1	a	Singlet
6·96	1	f	Singlet
14·6	1	j	Singlet

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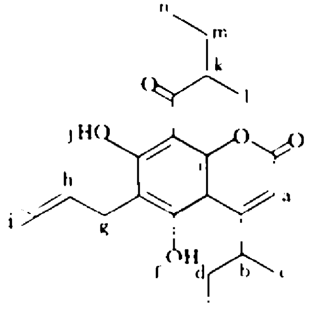
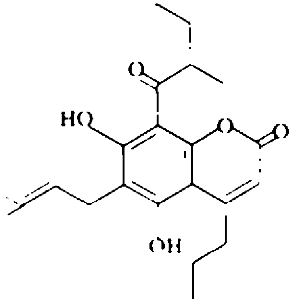
[2] L. Crombie, D. E. Games and A. McCormick, *Tetrahedron Letters* No. 2, 151 (1966)

[3] C. Djerassi, E. J. Eisenbraun, R. A. Finnegal and B. Gilbert, *J. Org. Chem.* **25**, 2164 (1960)

[4] R. A. Finnegal, M. P. Morris and C. Djerassi, *J. Org. Chem.* **26**, 1180 (1961).



I



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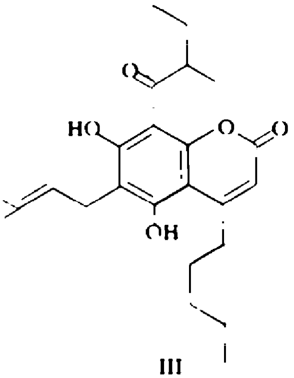

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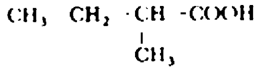

$\mathrm{CH_3{-}CH_2{-}\underset{\displaystyle CH_3}{CH}{-}COOH}$

IV

butyric acid (IV, identified through its anilide) and a chroman mixture (TLC two spots) presumably V (R = H), and VI. The isolation of α-methylbutyric acid unambigouously establishes the nature of the acyl residue in I. Separation of the chroman mixture by fractional crystallization followed by chromatography over alumina yielded two isomeric compounds $C_{18}H_{22}O_4$, V (R = H), m.p. 258–260°, being the major product and VI, m.p. 218–220°. Although both have virtually identical UV spectra (Table 3) in neutral medium characteristic of known 5,7-dioxygenated coumarins,[5] they undergo different base shifts thereby reflecting the different dispositions of the OH groups. Methylation of V (R = H) affords the monomethyl ether, $C_{19}H_{24}O_4$, m.p. 106°, (mol wt by mass spec 316) whose NMR spectrum (Fig. 2) is in complete accord with structure V ($R = CH_3$). The pair of triplets at 2·7 δ (2H, $J = 7$ c/s) and 1·81 δ (2H, $J = 7$ c/s) and the sharp singlet at 1·4 δ (6H) are typical of a 2,2-dimethyl-chroman system.[6] The substitution sequence $\mathrm{-\underset{\displaystyle CH_3}{CH}-CH_2-CH_3}$ at the position is clearly exhibited by the resonance 0·98 δ (triplet 3H, $J = 7$ c/s, primary γ-methyl), 1·23 δ (doublet 3H, $J = 7$ c/s, secondary α-methyl), 1·56 δ (broad unresolved multiplet 2H, β-methylene) and at ~3·91 δ (complex multiplet 1H,

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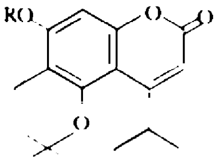
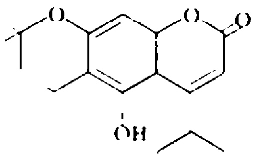
[5] R. A. Finnegan, B. Gilbert, E. J. Eisenbraun and C. Djerassi, *J. Org. Chem.* **25**, 2169 (1960).

[6] e.g. J. S. P. Schwarz, A. I. Cohen, W. D. Collis, E. A. Kaczka and L. M. Jackman, *Tetrahedron*, **20**, 1317 (1964).



V



VI

TABLE 3. UV DATA FOR V AND VI

	λ_{max}^{EtOH} mμ	(log ε)	$\lambda_{max}^{EtOH-KOH}$ mμ	(log ε)
V (R = H)	250 (sh)	(3·79)	240 (sh)	(4·23)
	260	(3·74)	270 (sh)	(3·88)
	332	(4·18)	385	(4·31)
VI	250 (sh)	(3·83)	275	(4·15)
	260	(3·77)	335	(4·03)
	330	(4·22)	400	(3·93)
V (R = CH_3)	257	(3·81)		
	325	(4·20)		

α-methine). The methoxyl protons appear at 3·9 δ as a sharp singlet (3H). The C-3 proton shows up as a singlet (1H) at 6·1 δ and the other singlet at 6·46 δ (1H) must be attributed to the lone aromatic proton at C-8.

The major and minor products in the deacylation have been assigned structures V (R = H) and VI respectively and not *vice versa* since only the minor product gives a positive Gibbs colour test.[7]

The sum of evidence above thus is in favour of structure I for ferruol A. Further degradative and synthetic experiments are on hand to establish unambiguously its structure.

EXPERIMENTAL

Isolation and separation of the ferruols. The milled trunk bark of *Mesua ferrea* L[9] (6 kg) was percolated in the cold with pet. ether. The brownish viscous oil obtained by distilling off the solvent, on being kept at room temp for 2 days, deposited ferruol as a colourless solid. It was collected, washed free from the oil with pet. ether, and dried (14 g). Two crystallizations from hexane gave colourless flakes, m.p. 128–130°. A mass spectrum of this specimen indicated it to be a mixture of 3 homologous compounds having mol wts 386, 372 and 358 with traces of a 400 mol wt compound. This was in agreement with TLC; after trying a variety of solvent systems, $CHCl_3$:pet ether:EtOAC 20:20:0·4 was found to be the most satisfactory system.

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[7] The validity of the Gibbs test has, however, been questioned by several authors; see for example, F. E. King, T. J. King and L. C. Manning, *J. Chem. Soc.* 563 (1957).

[8] M.ps are uncorrected. UV spectra were measured in 95% EtOH using a Beckmann model DU spectrophotometer. NMR spectra were taken in $CDCl_3$ on a 60 Mc Varian instrument with TMS as an internal standard. Kieselgel G and alumina G (E. Merck) were used for TLC. Petroleum ether refers to b.p. 40–60.

[9] The plant material was collected from the Western Ghats, Travancore.

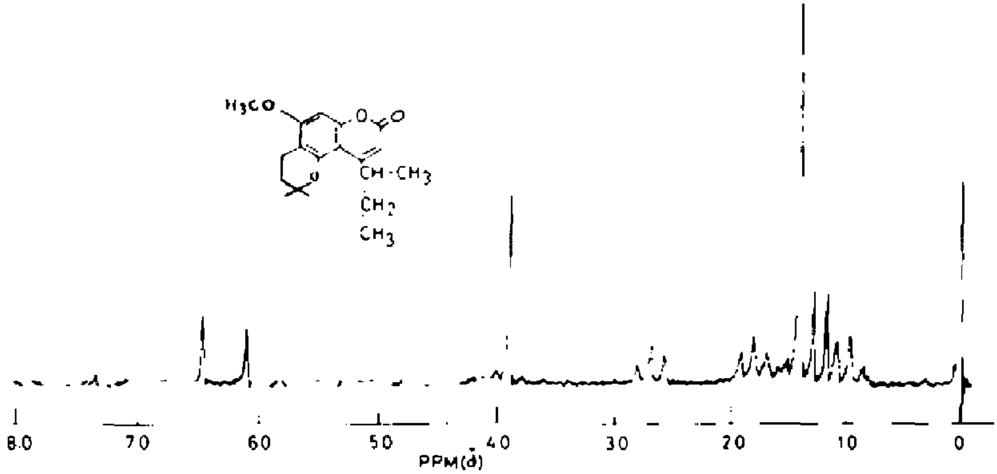

FIG. 2. NMR spectrum of compound V (R = CH_3) in $CDCl_3$ at 60 Mc.

For separation into its constituents, ferruol (0·5 g) was dissolved in the minimum amount of $CHCl_3$ pet ether and put on the top of a column of Silica gel (60 g, E. Merck, Kieselgel 0·05–0·20 mm for chromatography) in pet ether. Elution was carried out with a mixture of $CHCl_3$–pet ether–EtOAC 20:20:0·4, fractions (4 ml) were cut and analysed by TLC. Fractions 1–5 were combined and crystallized from hexane to give Ferruol A (65 mg). Fractions 25–35 were similarly worked up to get ferruol B. The mixed fractions were submitted for rechromatography.

Ferruol A (I). It crystallized from hexane as aggregates of short colourless needles m.p. 126·5° and gave a deep brown colour with alcoholic $FeCl_3$. (Found: C, 71·55; H, 8·08; Methoxyl nil. $C_{23}H_{30}O_5$ requires: C, 71·50; H, 7·77%.)

Acid-catalysed deacylation of I. A mixture of ferruol A (0·9 g) and 70% H_2SO_4 (10 ml) was stirred at room temp for 24 hr. The resulting brownish yellow viscous soln was then poured into ice water (~60 ml), kept in the ice-chest for several hr, filtered and the solid washed with a small amount of ice water and dried (0·56 g). The aqueous filtrate was saturated with Na_2SO_4, extracted exhaustively with ether, the ether soln washed with ice water, dried (Na_2SO_4) and ether distilled off. The residual pale yellow liquid was heated with $SOCl_2$ (0·5 ml) at 50° for 1 hr and the resulting acid chloride treated with aniline under strong cooling. After working up, the *anilide* crystallized from pet ether as colourless needles, m.p. 109–110° undepressed on admixture with an authentic specimen of *α-methylbutyranilide* (lit.[19], m.p. 109·5–110°).

TLC of the solid mixture of chromans above showed 2 spots. Repeated crystallization of the mixture from AcOEt afforded the *chroman* V (R = H) as colourless cubes (0·42 g) sparingly soluble in EtOAC, m.p. 258–260° (softening around 240°). (Found: C, 71·79; H, 7·24. $C_{18}H_{22}O_4$ requires: C, 71·53; H, 7·29%.) Chromatography of the mother liquors over alumina (elution with $CHCl_3$:benzene 3:1) afforded the *chroman* VI (20 mg) in the first few fractions, m.p. 218–220° (softening around 205°). Both V (R = H) and VI gave no colour with ferric chloride. In alkaline solution V (R = H) showed a bluish-violet fluorescence whereas VI turned yellow and showed no fluorescence.

Methylation of V (R = H). Chroman V (0·2 g), anhyd K_2CO_3 (2·5 g), MeI (5 ml) and dry acetone (80 ml) were refluxed for 18 hr. After working up in the usual manner, the methyl ether (V, R = CH_3) crystallized from pet. ether as colourless prisms (165 mg), m.p. 105–106° (Found: C, 72·02; H, 8·05. $C_{19}H_{24}O_4$ requires: C, 72·13; H, 7·65%.)

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[19] H. D. Schroeder, W. Bencze, O. Halpern and H. Schmid, *Chem. Ber.* **92**, 2338 (1959).