Tetrahedron Letters No. 13, pp.11-15, 1959. Pergamon Press Ltd. Printed in Great Britain.

NATURALLY OCCURRING OXYGEN HETEROCYCLICS

4-PHENYL-5,7-DIHYDROXY-6-ISOVALERYL-8-ISOPENTENYLCOUMARIN

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(Received 24 July 1959)

IN a recent communication[1] from this Laboratory it was shown that the insecticidal constituent[2] mammein from the seeds of Mammea americana L. possesses structure I. Through the kind co-operation of Dr. Murrell P. Morris of the U.S. Department of Agriculture Experiment Station in Mayaguez, Puerto Rico, we have obtained a supply of a yellow toxic principle derived from the pulp of the fruits of the same plant, and the present report is concerned with its structure elucidation.

Chromatographic purification of the yellow substance and repeated recrystallization from various solvents led to homogenous material with a wide melting point range, apparently due to solvation. The analytical

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[1] Paper V: C. Djerassi, E. J. Eisenbraun, R. A. Finnegan and B. Gilbert, Tetrahedron Letters No. 1, 10 (1959).

[2] M. P. Morris and C. Pagan, J. Amer. Chem. Soc. 75, 1489 (1953).

specimen (from aqueous ethanol) exhibited m.p. 98-109° (after drying at room temperature in vacuo), $\lambda_{max}^{EtOH-HCl}$ 282 and 339 mμ (log ϵ 4.49 and 4.13), λ_{min}^{EtOH} 249.5 and 320 mμ (log ϵ 4.09 and 4.07), $\lambda_{max}^{CHCl_3}$ 2.91, 3.04, 5.78, 6.17 and 6.30 μ, and gave a dark brown color with ferric chloride solution. The analytical results (Found: C, 74.42; H, 6.47; O, 19.26) were consistent with the empirical formula $C_{25}H_{26}O_5$ and this was confirmed by the preparation of the beautifully crystalline diacetate IIb (m.p. 122-124°; Found for $C_{29}H_{30}O_7$: C, 71.00; H, 6.20; O, 22.99) and dimethyl ether IIc (m.p. 86-89°; Found for $C_{27}H_{30}O_5$: C, 74.61; H, 6.71; O, 18.26; methoxyl, 14.47).

The analytical and spectral data suggested a coumarin skeleton, similar to that of mammein (I).[1] When the parent phenol IIa was heated under reflux for 67 hr with 15% potassium hydroxide solution, there were isolated isovaleric acid, acetophenone and isopentenylphloroglucinol (IIIa) (m.p. 101-102°; Found for $C_{11}H_{14}O_3$: C, 67.97; H, 7.26; O, 25.06). The structure of this phenol followed from its ultraviolet absorption spectrum (λ_{max}^{MeOH} 271, 274 and 279 mμ, log ϵ 2.84, 2182 and 2.76; $\lambda_{max}^{MeOH-NaOH}$ 257, 279 and 355 mμ), typical of monoalkyl phloroglucinols[3] and from the formation of isopentylphloroglucinol (IIIb)[4] upon hydrogenation. The precise location of the double bond was established by ozonolysis of the parent compound IIa, which yielded acetone (69% yield as 2,4-dinitrophenylhydrazone) unaccompanied by formaldehyde.

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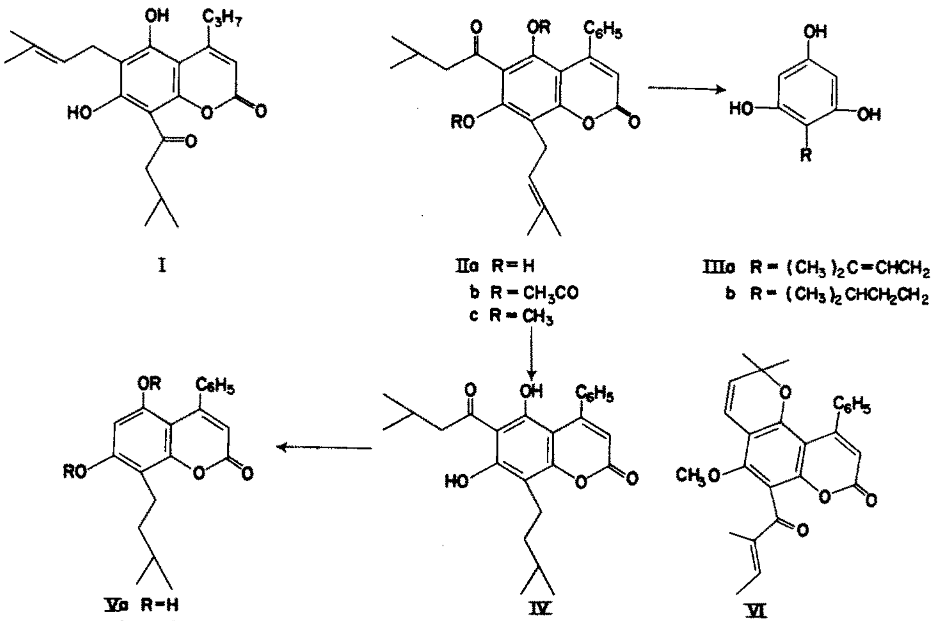
[3] T. W. Campbell and G. M. Coppinger, J. Amer. Chem. Soc. **73**, 2708 (1951).

[4] T. S. Kenny, A. Robertson and S. W. George, J. Chem. Soc. 1601 (1939).



I

IIa R=H
b $R=CH_3CO$
c $R=CH_3$

IIIa $R=(CH_3)_2C=CHCH_2$
b $R=(CH_3)_2CHCH_2CH_2$

Va R=H
b $R=CH_3$

IV

VI

The precise skeletal structure and the disposition of the substituents was demonstrated as follows. Hydrogenation of IIa with palladized charcoal resulted in the uptake of one equivalent of hydrogen with the production of a yellow dihydro derivative IV (m.p. 99 - 103°), whose relevant ultraviolet and infrared spectral bands coincided with those of IIa. Deacylation of the dihydro compound IV with 75% sulfuric acid[5] provided 4-phenyl-5,7-dihydroxy-8-isopentylcoumarin (Va) (m.p. 184-186°, λ_{max}^{EtOH} 266 and 338 mμ, log ϵ 4.08 and 4.04; Found for $C_{20}H_{20}O_4$: C, 74.15; H, 6.43; O, 19.69), which was methylated with dimethyl sulfate in acetone solution in the presence of potassium carbonate to give 4-phenyl-5,7-dimethoxy-8-isopentylcoumarin (Vb) (m.p. 131-132°; Found for $C_{22}H_{24}O_4$: C, 74.95; H, 6.63; O, 18.36; methoxyl, 17.24). Its constitution was proved by Pechmann condensation of 2-isopentyl-3,5-dimethoxyphenol (m.p. 56-57°)[6] with ethyl benzoylacetate which furnished the identical dimethyl ether (Vb).

The above results are only consistent with the structure of 4-phenyl-5,7-dihydroxy-6-isovaleryl-8-isopentenylcoumarin (IIa) for the toxic constituent of the pulp of the mamey fruit. Naturally occurring 4-substituted coumarins are very rare and the isolation of mammein (I) and IIa from the same plant is of some biogenetic interest. It is pertinent to mention that only three other substituted 4-phenylcoumarins have been encountered in nature, namely dalbergin,[7] dalbergin methyl ether (4-phenyl-6,7-dimethoxycoumarin)[7] and calophyllolide (VI).[8]

[5] Deacylation under these conditions does not cause any rearrangement, since the coumarin ring is not opened (see ref. 1).

[6] To be published.

[7] V. K. Ahluwalia and T. R. Seshadri, J. Chem. Soc. 970 (1957).

[8] J. Polonsky, Bull. Soc. Chim. Fr. 929 (1958).

The latter shows considerable structural resemblance to the presently described coumarin IIa and it should be noted that both plant sources (Calophyllum inophyllum L. and Mammea americana L.) belong to closely related genera of the same familiy (Guttiferae).

Financial assistance was generously provided by the National Heart Institute (grant No. H-2574) of the National Institutes of Health, U.S. Public Health Service.