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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF WAYNE STATE UNIVERSITY]

Naturally Occurring Oxygen Heterocyclics. X.[1] 4-Phenyl-5,7-dihydroxy-6-isovaleryl-8-isopentenylcoumarin[2,3]

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The yellow toxic principle isolated from the peelings of the fruits of *Mammea americana L.* is shown to be 4-phenyl-5,7-dihydroxy-6-isovaleryl-8-isopentenylcoumarin(III).

In a recent report[6] from this laboratory, mammein, the insecticidal constituent isolated[7] from the seeds of *Mammea americana L.* (family *Guttiferae*) was shown to possess structure I. Through the generous cooperation of Dr. Murrell P. Morris of the U. S. Department of Agriculture Experiment Station of Mayaguez, Puerto Rico, we have obtained a supply of a yellow toxic[8] principle isolated from the peelings of the fruits of the same plant, and the present article is concerned with its structure elucidation.

Repeated chromatography and recrystallization of the yellow substance led to homogeneous samples with wide melting point ranges, apparently due to solvation. The analytical specimen had m.p. 98–109°, was optically inactive, gave a dark brown color with ferric chloride and was soluble in aqueous sodium hydroxide but insoluble in dilute hydrochloric acid.

The analytical results were consistent with the empirical formula $C_{25}H_{26}O_5$ which was confirmed by the preparation of a beautifully crystalline diacetate, m.p. 122–124° ($C_{29}H_{30}O_7$) and dimethyl ether, m.p. 86–89° ($C_{27}H_{30}O_5$). The ultraviolet and infrared spectral data (see Experimental) were reminiscent of a coumarin structure similar to that of mammein,[6] while the analytical data suggested the replacement of the *n*-propyl substituent in the latter by a phenyl substituent. Indeed, the presence of a mono-substituted phenyl group was indicated by infrared absorbtion bands at 776 and 698 cm.$^{-1}$ (carbon disulfide). Along with the spectral and analytical data, the recovery of the unchanged yellow compound after treatment with alkali under conditions previously[9] used to effect isomerization[10] of mammein (I) to isomammein (II) led us to consider structure III for this substance. All details of this structure (III) were verified by the experiments discussed below.

The presence of a double bond in the side chain was indicated by the facile uptake of one mole of hydrogen to yield a yellow dihydride, m.p. 99–103°, which was characterized as its diacetate derivative, m.p. 98–102°. The ultraviolet and infrared spectra of the dihydride IV were very similar to those of III, thus showing that the reactive olefinic link is not conjugated with the main chromophoric system. Ozonization of III, followed by reductive work up of the ozonide, led to the isolation of acetone (69% yield as the 2,4-dinitrophenylhydrazone) unaccompanied by formaldehyde, as well as the aldehydic moiety V, whose empirical formula substantiated its formation by simple fission of the double bond.

A more drastic, as well as more infomative, breach of the molecule was accomplished by prolonged refluxing of III with aqueous potassium hydroxide. Under these conditions, III was degraded to a mixture from which acetophenone (79% yield), isovaleric acid (57% yield), and two

(1) Paper IX, C. Djerassi, J. D. Gray, and F. A. Kincl, *J. Org. Chem.*, **25**, 2174 (1960).

(2) For preliminary communication, see R. A. Finnegan and C. Djerassi, *Tetrahedron Letters*, No. 13, 11 (1959).

(3) Financial support of this work by The National Heart Institute (grant No. H-2574) of the National Institutes of Health, U. S. Public Health Service, is gratefully acknowledged.

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(6) C. Djerassi, E. J. Eisenbraun, R. A. Finnegan, and B. Gilbert, *J. Org. Chem.*, **25**, 2164 (1960).

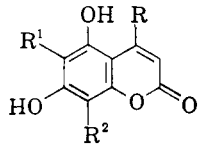
(7) M. P. Morris and C. Pagan, *J. Am. Chem. Soc.*, **75**, 1489 (1953).

(8) For a discussion of the toxicity of this fruit see M. P. Morris, C. Pagan, and J. Garcia, *Revista de Agricultura de Puerto Rico, Suplemento-Seccion, Alimentos Nutricion*, Vol. XLIII, No. 1, 288a (1952).

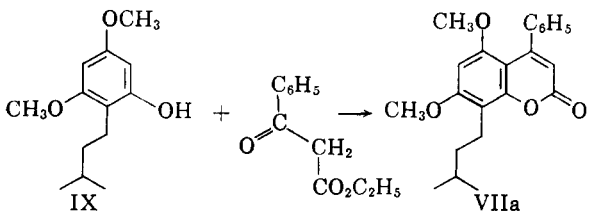
(9) C. Djerassi, E. J. Eisenbraun, B. Gilbert, A. J. Lemin, S. P. Marfey, and M. P. Morris, *J. Am. Chem. Soc.*, **80**, 3686 (1958).

(10) For discussion of the nature of this isomerization, see Ref. 6.

crystalline phenols: $C_{11}H_{14}O_3$, m.p. 102° (44% yield), and $C_{20}H_{18}O_4$, m.p. 214° (6% yield) could be isolated. The C_{11} phenol was shown to be isopentenylphloroglucinol (VIII) by its ultraviolet spectrum which is typical of monoalkyl phloroglucinols,[11] and by the formation of the known[6,12] isopentylphloroglucinol (VIIIa) upon hydrogenation. The structure of the C_{20} phenol VI followed from the conversion of its dimethyl ether VIa by hydrogenation to 4-phenyl-5,7-dimethoxy-8-isopentylcoumarin (VIIa), identical with an authentic specimen synthesized by the Pechmann condensation[13] of 2-isopentyl-3,5-dimethoxyphenol[14] (IX) with benzoylacetic ester.



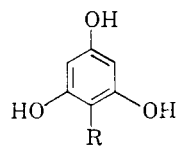
I.	R = $CH_3CH_2CH_2$—,	R^1 = $(CH_3)_2C$=$CHCH_2$—,	R^2 = $(CH_3)_2CHCH_2CO$—
II.	R = $CH_3CH_2CH_2$—,	R^1 = $(CH_3)_2CHCH_2CO$—,	R^2 = $(CH_3)_2C$=$CHCH_2$—
III.	R = C_6H_5—,	R^1 = $(CH_3)_2CHCH_2CO$—,	R^2 = $(CH_3)_2C$=$CHCH_2$—
IV.	R = C_6H_5—,	R^1 = $(CH_3)_2CHCH_2CO$—,	R^2 = $(CH_3)_2CHCH_2CH_2$—
V.	R = C_6H_5—,	R^1 = $(CH_3)_2CHCH_2CO$—,	R^2 = $OCHCH_2$—
VI.	R = C_6H_5—,	R^1 = H,	R^2 = $(CH_3)_2C$=$CHCH_2$—
VIa.	= VI with OH=OCH_3		
VII.	R = C_6H_5—,	R^1 = H,	R^2 = $(CH_3)_2CHCH_2CH_2$—
VIIa.	= VII with OH=OCH_3		
X.	R = C_6H_5—,	R^1 = $(CH_3)_2C$=$CHCH_2$—,	R^2 = $(CH_3)_2CHCH_2CO$—



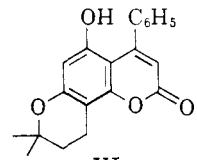
The results of the experiments described above are consistent only with structures III or its isomer X for the parent.[15]

In order to locate unambiguously the position of the isopentenyl substituent in III, use was made of the deacylation reaction conveniently brought about by 75% sulfuric acid. Discovered during synthetic studies,[14] this reaction found important application in the structure determination of mammein.[6] Accordingly, the dihydride IV was treated at room temperature with 75% aqueous sulfuric acid and the resultant phenolic coumarin VII converted to its dimethyl ether, VIIa. The product VIIa obtained in this sequence of reactions proved to be identical with the authentic sample of 4-phenyl-5,7-dimethoxy-8-isopentylcoumarin described above. The combination, then, of the alkaline and acidic degradations along with the hydrogenation and ozonolysis experiments, provides the necessary evidence for the assignment of structure III to the toxic principle.[16]

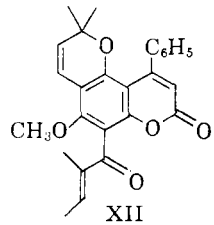
Although it does not bear directly on the structure proof, we wish to report one additional transformation of III. When the sulfuric acid–catalyzed deacylation reaction was applied to the parent III, there was readily obtained as the sole product (in addition to isovaleric acid), a phenol, m.p. 273–276°. Structure XI was assigned to this product on the basis of its microanalysis, infrared,



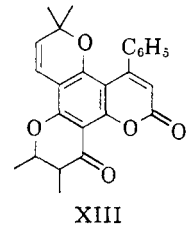
VIII. R = $(CH_3)_2C$=$CHCH_2$–
VIIIa. R = $(CH_3)_2CHCH_2CH_2$–



XI



XII



XIII

(11) T. W. Campbell and G. M. Coppinger, *J. Am. Chem. Soc.*, **73**, 2708 (1951).

(12) T. S. Kenny, A. Robertson, and S. W. George, *J. Chem. Soc.*, 1601 (1939).

(13) S. Sethna and R. Phadke, *Org. Reactions*, **7**, 1 (1953).

(14) R. A. Finnegan, B. Gilbert, E. J. Eisenbraun, and Carl Djerassi, *J. Org. Chem.*, **25**, 2169 (1960).

(15) The inference that the isopentenyl substituent which appears at position 8 in VI also occupies position 8 in III cannot be drawn from the alkaline degradation results, since the intermediate coumarinate salt may be cyclized in two directions upon acidification. For a discussion of the analogous situation with respect to mammein (I) and isomammein (II) see Ref. 6. Structure X may be ruled out, however, on the basis of its failure to isomerize to III on treatment with mild alkali. Ref. 6 contains a discussion of the mechanism and driving force operating during this isomerization.

(16) While it may be argued that the evidence cited does not rigorously place the isovaleryl substituent at position 6, we believe that its alternate location at position 3 is ruled out by the failure of the compound to isomerize during mild alkaline treatment (carbonyl group H-bonded with the C-5 hydroxyl group), by the failure to isolate either benzoic acid or methyl isopentyl ketone upon vigorous alkaline hydrolysis; and finally by the compelling biogenetic relationship to mammein.

and ultraviolet spectra, and the fact that it formed only a *monoacetate* and a *monomethyl* ether. It is apparent that cyclization of the 8-isopentenyl group with the 7-hydroxyl group has accompanied deacylation.

In conclusion, it may be noted that naturally occurring 4-substituted coumarins are very rare and that the isolation of mammein (I) and III from the same plant is of some biogenetic interest. Other 4-phenyl coumarins found in nature include dalbergin,[17] dalbergin methyl ether (4-phenyl-6,7-dimethoxycoumarin),[17] calophyllolide (XII)[18] and inophyllolide (XIII).[18,19] The close structural resemblance of the latter two to the presently described coumarin III is emphasized by the fact that both plant sources (*Calophyllum inophyllum L.* and *Mammea americana L.*) belong to closely related genera of the same family (*Guttiferae*).[20]

The authors are pleased to acknowledge many helpful conversations with Dr. E. J. Eisenbraun regarding this work.

EXPERIMENTS[21]

Isolation of III. The cylinder of a large Soxhlet extractor was filled with 900 g. of the dried peelings of the mamey fruit. The 3-l. receiver was filled with petroleum ether (b.p. 30–40°) and the extraction started and continued for 4 hr. The solvent in the receiver was then replaced by fresh solvent and the extraction continued for another 4 hr. The solvent was again changed and the extraction continued for 72 hr., the solvent being replaced every 24 hr. Each batch of solvent was evaporated to a small volume and allowed to stand at room temperature. The crystalline fractions which appeared at this point were combined into one main fraction. The yield of crude yellow solid was 5.2% based on the weight of dried peelings, or 1.5% if based on the weight of dried fruit minus seeds. (The latter figure is calculated from the fact that the dried unpeeled fruits minus seed contain 29% peel.) Seventy-five marketable fruit will yield 1 kg. of dried peel.[22]

The material thus obtained was a yellow powdery solid, m.p. 70–107°. It gave a dark brown ferric chloride test. It dissolved in 3*N* sodium hydroxide producing an orange solution, but did not dissolve in dilute hydrochloric acid. Its rotation in chloroform solution (21.3 mg./2 ml.) at 589 and 430 mμ was zero. Chromatography of the yellow solid (10 g.) on Merck acid-washed alumina (650 g.) did not effect resolution into more than one substance. Twenty-two fractions eluted in benzene-ether mixtures and in pure ether were separately crystallized from chloroform-hexane. Although the crystals were well formed needles, all fractions melted over the range 65–100°. Their infrared spectra were identical. After several recrystallizations from aqueous ethanol there was obtained material with m.p. 95–108° which was dried 48 hr. *in vacuo* to furnish the analytical sample, m.p. 98–109°; $\nu_{max}^{CHCl_3}$ 3436, 3289, 1730, 1621, 1587 cm.$^{-1}$; $\nu_{max}^{CS_2}$ 1745, 1620, 1597, 766, 698 cm.$^{-1}$; ν_{max}^{KBr} 1715 cm.$^{-1}$; $\lambda_{max}^{95\%\ ethanol-HCl}$ 281, 338 mμ, log ε 4.41, 4.00; $\lambda_{min}^{95\%\ ethanol-HCl}$ 249, 317 mμ, log ε 3.96, 3.94; $\lambda_{max}^{95\%\ ethanol-NaOH}$ 243, 301, 427 mμ, log ε 4.10, 4.15, 4.10; $\lambda_{max}^{95\%\ ethanol-NaOH}$ 256, 343 mμ, log ε 4.04, 3.43.

Anal. Calcd. for $C_{25}H_{26}O_5$: C, 73.86; H, 6.45; O, 19.68, mol. wt., 406. Found: C, 74.42; H, 6.47; O, 19.26; mol. wt., 350 (Rast). Material used in subsequent reactions was purified by passing it in ether solution through a column of Merck acid-washed alumina. (A grey-green band remained at the top of the column.). The residue remaining after evaporation of the eluate was crystallized from ether-hexane, m.p. 65–105°, then from aqueous ethanol, m.p. 97–109°.

Diacetate of III. When a solution of III (0.50 g.) in pyridine (12 ml.) was treated with acetic anhydride (3 ml.), the yellow color was almost immediately discharged. After a few minutes, the reaction mixture was diluted with water and extracted with ether. The ether extracts were washed with hydrochloric acid, then with water. These aqueous washings were extracted with ether and the combined ether extracts were washed with aqueous sodium bicarbonate, then with water. These washings were extracted with ether and the combined organic extracts dried and evaporated to give a pale yellow oil which was crystallized from ether-hexane, m.p. 76–87°, 0.48 g. Recrystallization from chloroform-hexane afforded material with m.p. 83–91°. One additional recrystallization caused the m.p. to rise abruptly to 122–124°, unchanged by further recrystallization. The product gave a negative ferric chloride test.

Anal. Calcd. for $C_{29}H_{30}O_7$: C, 71.00; H, 6.16; O, 22.83. Found: C, 71.00; H, 6.20; O, 22.99. $\nu_{max}^{CHCl_3}$ 1773, 1733, 1706 (shoulder), 1592, 1183 cm.$^{-1}$; $\nu_{max}^{CS_2}$ 1783, 1748, 1709, 1592, 1179 cm.$^{-1}$; ν_{max}^{KBr} 1815, 1795, 1742, 1704, 1179 (broad) cm.$^{-1}$; $\lambda_{max}^{95\%\ ethanol}$ 286 mμ, log ε 4.06; $\lambda_{min}^{95\%\ ethanol}$ 272 mμ, log ε 4.03.

Dimethyl ether of III. To a solution of III (0.30 g.) in 15 ml. acetone, 2 g. of potassium carbonate and 0.25 ml. of dimethyl sulfate were added. The mixture was allowed to reflux 4 hr. before it was cooled and filtered. The residue remaining after evaporation of the solvent was recrystallized three times from hexane to give the product, m.p. 86–89°, 79 mg., negative ferric chloride test.

Anal. Calcd. for $C_{27}H_{30}O_5$: C, 74.63; H, 6.96; O, 18.41; 2 OCH_3, 14.3; mol. wt., 434.5. Found: C, 74.61; H, 6.71; O, 18.26; OCH_3, 14.47; mol. wt., 401 (Rast). $\nu_{max}^{CHCl_3}$ 1727, 1582 cm.$^{-1}$; $\nu_{max}^{CS_2}$ 1742, 1706, 1592, 766, 699 cm.$^{-1}$; ν_{max}^{KBr} 1739, 1706, 1580, 766, 703 cm.$^{-1}$; $\lambda_{max}^{95\%\ ethanol}$ 299 mμ, log ε 4.08; $\lambda_{min}^{95\%\ ethanol}$ 272 mμ, log ε 3.94.

Treatment of III in ether with diazomethane afforded a substance identical with that described above.

The dihydride IV. An ethanol solution (100 ml.) of the parent substance III (3 g.) was hydrogenated at 28° in the presence of 300 mg. 10% palladium on charcoal. After three hours, 1.1 moles of hydrogen were absorbed. The mixture was filtered and concentrated to yield 1.41 g. of product IV, yellow needles, m.p. 96–101° from aqueous ethanol. A portion was recrystallized twice from 95% ethanol, m.p. 99–103°; $\nu_{max}^{CHCl_3}$ 1730, 1623, 1595 cm.$^{-1}$; $\nu_{max}^{CS_2}$ 1745, 1626, 1605 cm.$^{-1}$; $\lambda_{max}^{95\%\ ethanol-HCl}$ 282, 340 mμ, log ε 4.39, 3.98; $\lambda_{min}^{95\%\ ethanol-HCl}$ 248, 319 mμ, log ε 3.82, 3.91; $\lambda_{max}^{95\%\ ethanol-NaOH}$ 230 (very broad), 301, 429 mμ, log ε 4.18, 4.22, 4.05; $\lambda_{min}^{95\%\ ethanol-NaOH}$ 255, 346 mμ, log ε 4.13, 3.69.

Anal. Calcd. for $C_{25}H_{28}O_5$: C, 73.50; H, 6.91; O, 19.58. Found: C, 73.44; H, 6.94; O, 19.35.

Diacetate of IV. The dihydride IV (100 mg.) was dissolved in pyridine (5 ml.) with acetic anhydride (2 ml.). Within 1 min. the yellow color had disappeared and the reaction was worked up in the usual manner. The product was recrystallized four times from hexane, m.p. 98–102°, 34 mg.; $\nu_{max}^{CHCl_3}$ 1776, 1736, 1592, 1186 cm.$^{-1}$; $\nu_{max}^{CS_2}$ 1779, 1745, 1706, 1174 cm.$^{-1}$; $\lambda_{max}^{95\%\ ethanol}$ 247, 286, 325 mμ (shoulder), log ε 4.25, 4.11, 3.65; $\lambda_{min}^{95\%\ ethanol}$ 271.5 mμ, log ε 4.07.

Anal. Calcd. for $C_{29}H_{32}O_7$: C, 70.71; H, 6.55; O, 22.74. Found: C, 70.75; H, 6.36; O, 22.42.

(17) V. K. Ahluwalia and T. R. Seshadri, *J. Chem. Soc.*, 970 (1957).

(18) J. Polonsky, *Bull. Soc. chim. France*, 929 (1958).

(19) *Cf.* also calophyllic acid,[18] the *o*-hydroxycinnamic acid corresponding to XIII.

(20) The biogenetic relationship of 4-phenylcoumarins with flavonoids and benzophenones is briefly discussed by T. R. Seshadri, *Tetrahedron*, **6**, 172–173 (1959); also Ref. 17.

(21) All melting points were determined on a Kofler block. Microanalyses are by Dr. A. Bernhardt, Mulheim, Germany.

(22) The isolation procedure described is that of Dr. M. P. Morris, private communication.

Ozonolysis of III. (a) *Acetone.* A stream of ozonized oxygen was passed through a solution of III (1 g.) in glacial acetic acid (20 ml.) maintained at 15°. The exit gas gave a positive test for ozone with moist starch-iodide paper in less than 5 min. The reaction mixture was poured into a cooled (ice bath) aqueous solution of ferrous sulfate and the resulting mixture was stirred 45 min. Nitrogen was then passed through the gently warmed mixture for 20 hr. The exit gases were led in series through two bottles containing 2,4-dinitrophenylhydrazine in aqueous sulfuric acid. The precipitate was collected by extraction with benzene. The extract was dried, concentrated, and filtered through a column of Merck acid-washed alumina. The benzene eluate was evaporated to give 405 mg. (69% yield) acetone 2,4-dinitrophenylhydrazone m.p. 95–122°. The absence of the corresponding formaldehyde derivative was shown by chromatography of this product on Whatman number 7 filter paper, using a phenylcellosolve-heptane solvent system.[23]

Two recrystallizations of the product from chloroform-hexane raised the melting point to 123–124°, alone or admixed with an authentic sample of acetone 2,4-dinitrophenylhydrazone. The infrared spectra (chloroform) of the two samples were identical.

(*b*) *The aldehyde V.* The residue remaining after removal of the acetone (above) was extracted with ether. After the ether extracts were dried and concentrated, 0.60 g. of tan crystals were obtained, m.p. 156–174° from ether-hexane. These were recrystallized six times from chloroform-hexane to give pure V as pale yellow needles, m.p. 175–183°. The melting point did not change after two additional recrystallizations. ν_{max}^{KBr} 1721, 1621 (both broad), 768, 703, cm.$^{-1}$; $\nu_{max}^{CHCl_3}$ 1733 cm.$^{-1}$; $\lambda_{max}^{95\%\ ethanol\text{-}HCl}$ 279, 343 mμ, log ε 4.43, 4.04; $\lambda_{min}^{95\%\ ethanol\text{-}HCl}$ 247.5, 314 mμ, log ε 3.73, 3.38; $\lambda_{max}^{95\%\ ethanol\text{-}NaOH}$ 298, 415 mμ, log ε 4.32, 4.16; $\lambda_{min}^{95\%\ ethanol\text{-}NaOH}$ 343 mμ, log ε 3.92.

Anal. Calcd. for $C_{22}H_{20}O_6$: C, 69.46; H, 5.30; O, 25.24; Found: C, 69.28; H, 5.28; O, 25.14.

Attempted isomerization of III. A solution of III (300 mg.) in 50 ml. methanol containing 3 g. of potassium hydroxide was allowed to stand in a refrigerator for 8 hr. The reaction mixture was then diluted with water and extracted with ether (discarded). The aqueous layer was acidified and extracted with ether. These ether extracts, after being dried and evaporated, afforded 140 mg. yellow semisolid which was recrystallized from chloroform-hexane, m.p. 64–109°. The infrared spectrum of this substance was identical with that of the starting material III.

Alkaline degradation of III. (a) *Acetophenone.* The parent compound III (2.6 g.) was dissolved in 120 ml. of water with 18 g. of potassium hydroxide and the resulting orange solution was allowed to reflux for 67 hr. under a nitrogen atmosphere. The reaction mixture was then steam distilled. The distillate was collected in a solution of 2,4-dinitrophenylhydrazine (made up in the proportion: 1 g. of reagent, 20 ml. of sulfuric acid, 80 ml. of water) until no further precipitation was observed. The precipitate was collected on a filter, air dried, and passed in benzene solution through a column of Fisher (A-540) alumina. From the eluate was obtained, after evaporation of the solvent, 1.53 g. (79% yield) of acetophenone 2,4-dinitrophenylhydrazone, m.p. 243–245°. Recrystallization from chloroform-hexane afforded 1.1 g. of product, m.p. 245–246° alone or admixed with an authentic sample of acetophenone 2,4-dinitrophenylhydrazone. The infrared spectrum of the naturally derived material was identical to that of the authentic sample.

(b) *Isovaleric acid.* The aqueous residue remaining after removal of the acetophenone was acidified with 85% phosphoric acid and then steam distilled until the distillate no longer gave an acid reaction to litmus paper. The distillate was made basic, concentrated, reacidified, and extracted with ether. The ether extracts were dried and the solvent was removed through a Vigreux column. Upon distillation of the residue there was obtained 372 mg. (57%) of a colorless liquid whose infrared spectrum (carbon disulfide) was identical with that of an authentic sample of isovaleric acid. Confirmation of the identity of the naturally derived acid was obtained by vapor phase chromatography of its methyl ester and comparison of the elution curve with that of mixtures of authentic methyl esters. This study also indicated the presence in trace amount of methyl isobutyrate in the naturally derived ester.

(c) *4-Phenyl-5,7-dihydroxy-8-isopentenylcoumarin* (VI). The aqueous residue remaining after removal of the volatile acids (see above) was extracted with ethyl acetate. The extracts, after being dried and evaporated, afforded a brown resin which was chromatographed on 100 g. Merck acid-washed alumina. Elution was begun with 4:1 benzene-hexane and continued with benzene, benzene-ether mixtures, ether, ether–ethyl acetate mixtures, and ethyl acetate. From the 4:1 ether-benzene eluate through the 1:1 ether–ethyl acetate eluate was obtained a brown semisolid which crystallized from benzene, m.p. 182–213° subl., 130 mg. Two sublimations of a portion of this material afforded pale yellow crystals of 4-phenyl-5,7-dihydroxy-8-isopentenylcoumarin (VI), m.p. 208–214°; ν_{max}^{KBr} 3311, 1712, 1610, 1563, 747, 703 cm.$^{-1}$; $\lambda_{max}^{95\%\ ethanol}$ 266.5, 337 mμ, log ε 4.22, 4.06; $\lambda_{min}^{95\%\ ethanol}$ 244.5, 294 mμ, log ε 3.90, 3.66; $\lambda_{max}^{95\%\ ethanol\text{-}NaOH}$ 282, 405 mμ, log 4.15, 3.95; $\lambda_{min}^{95\%\ ethanol\text{-}NaOH}$ 275, 320 mμ, log ε 4.13, 3.35.

Anal. Calcd. for $C_{20}H_{18}O_4$: C, 74.52; H, 5.63; O, 19.85. Found: C, 74.45; H, 5.90; O, 18.68.

(d) *Isopentenylphloroglucinol* (VIII). After elution of coumarin VI from the column (see above), the main band was obtained by continued elution with 1:1 ether-ethyl acetate and pure ethyl acetate. Evaporation of the solvent afforded a solid which was recrystallized from hexane-chloroform, m.p. 96–100°, 0.55 g. (44% yield). Two additional recrystallizations from the same solvent furnished the analytical sample of isopentenylphloroglucinol (VIII), m.p. 101–102°; ν_{max}^{KBr} 3205, 1618 cm.$^{-1}$ (both broad); $\lambda_{max}^{methanol}$ 271, 274, 279 mμ, log ε 2.84, 2.82, 2.76; $\lambda_{min}^{methanol}$ 253 mμ log ε 2.49; $\lambda_{max}^{methanol\text{-}NaOH}$ 257, 279, 355 mμ, log ε 3.84, 3.76, 3.42; $\lambda_{min}^{methanol\text{-}NaOH}$ 245, 270, 315 mμ, log ε 3.79, 3.71, 2.94.

Anal. Calcd. for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27; O, 24.71; 1 C—CH_3, 7.73. Found: C, 67.97; H, 7.26; O, 25.06; C—CH_3, 5.60.

Hydrogenation of isopentenylphloroglucinol (VIII). *Formation of isopentylphloroglucinol* (VIIIa). Isopentenylphloroglucinol (VIII) (37 mg.) was stirred in ethanol solution with 10% palladium on carbon (10 mg.) in a hydrogen atmosphere for 2 hr. at 30°. The reaction mixture was filtered and evaporation of the filtrate afforded 33 mg. of tan crystals, m.p. 121–125° subl. Sublimation (110° at 0.1 mm.) raised the m.p. to 125–126.5°, undepressed upon admixture with an authentic sample[14] of isopentylphloroglucinol. The infrared spectra (potassium bromide) of the two samples were identical.

4-Phenyl-5,7-dimethoxy-8-isopentenylcoumarin (VIa). *Methylation of* VI. 4-Phenyl-5,7-dihydroxy-8-isopentenylcoumarin (VI) (100 mg. crude) obtained by alkaline degradation of the parent III (see above) was dissolved in 5 ml. of acetone with 0.3 ml. of dimethyl sulfate and the solution was allowed to reflux for 24 hr. over 1 g. of anhydrous potassium carbonate. After the mixture was cooled and filtered, the residue obtained by evaporation of the filtrate was chromatographed on 10 g. of Merck acid-washed alumina. The product dimethyl ether VIa was obtained in the benzene eluate and recrystallized twice from chloroform-hexane, m.p. 157–159°, 19 mg.; ν_{max}^{KBr} 1730, 1610, 1580, 763, 749, 707 cm.$^{-1}$

Anal. Calcd. for $C_{22}H_{22}O_4$: C, 75.41; H, 6.33. Found: C, 74.82; H, 6.38.

4-Phenyl-5,7-dihydroxy-8-isopentylcoumarin (VII). *Acid-*

(23) W. S. Lynn, L. A. Steele, E. Staple, *Anal. Chem.*, **28**, 132 (1956).