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# MORELLIC, ISOMORELLIC AND GAMBOGIC ACIDS[a,b]

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On the basis of X-ray crystallography, NMR spectra and chemical evidence the structure of morellin, a pigment occurring in the seeds of *Garcinia morella*, was established as I.[1] A scheme of biogenesis was suggested, which has found support in the isolation of desoxymorellin (III) and dihydroisomorellin (II; single bond at *a*).[2] It was also shown that morellin and isomorellin (II) are *cis*-*trans* isomers, the methyl and methylene groups of the aldehyde side-chain having the *trans* configuration around the double bond in morellin and the *cis* configuration in isomorellin.[3]

α-Gambogic acid was isolated by Furrer[4] in the form of its *O*-acetyl derivative from the dry latex of *G. morella*. Yates *et al.*[5] obtained acetyl-α-gambogic acid from the same source and suggested structure IV on the basis of the structure for morellin. This has now been confirmed by Ollis *et al.*,[6] mainly as the result of the acid-catalysed cyclization of the side-chain R of IV with the chromene ring to form gamboginic acid; their source of gambogic acid was *G. hanburryi*, formerly regarded as a variety of *G. morella*.

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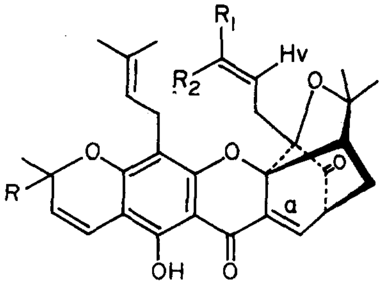
[a] The colouring matters of *G. morella*. Part VI. For Part V see H. B. Bhat, P. Madhavan Nair and K. Venkataraman, *Indian J. Chem.* 2, 405 (1964).

[b] Communication No. 868 from the National Chem. Lab., Poona.



I $R = R_1 = Me$; $R_2 = CHO$.
II $R = R_2 = Me$; $R_1 = CHO$.
III $R = R_1 = R_2 = Me$.
IV $R = CH_2\text{-}CH_2\text{-}CH{=}CMe_2$; $R_1$ or $R_2$ = Me or COOH
V $R = R_1 = Me$; $R_2 = COOH$.
VI $R = R_2 = Me$; $R_1 = COOH$

As part of our study of the pigments of G. morella, we examined the latex obtained from Mangalore in South India, and were unable to isolate gambogic acid from it. We found instead that it contained two acids, morellic and isomorellic acids, which were separated from the carbonate-soluble fraction. Morellic acid was nearly insoluble in hexane and isomorellic acid much more soluble. They were both amorphous, but on heating with acetic anhydride and sodium acetate gave acetyl derivatives which crystallized from methanol in yellow plates, m.p. 240° and 174° respectively. Elemental analyses and mass spectral molecular weights led to the same molecular formula, $C_{35}H_{38}O_9$, for both the acetates, and the acetyl values showed that they were monoacetates. The presence of a carboxyl group, indicated by the carbonate solubility, was confirmed by the iodide-iodate test and the IR spectrum, although neither of the acids (as well as gambogic acid) responded to the hydroxamic acid test. With diazomethane the two acids gave monomethyl esters. Morellin can be isomerized to isomorellin by running a hexane solution through a column of silica gel or fullers earth or by treatment at room temperature with hydrochloric acid in acetone. By the same procedure morellic acid was converted to isomorellic acid, showing that morellic and isomorellic acids were probably related to each other in the same way as morellin and isomorellin. The NMR spectra of the acetates of morellic and isomorellic acids in comparison with those of morellin and isomorellin readily showed that morellic and isomorellic acids are carboxylic acids (V and VI) corresponding to morellin and isomorellin. In the spectra of the two acids the aldehyde signals of morellin and isomorellin were replaced by broad hydroxyl signals at 1.35 and 1.42 $\tau$; except in the C-methyl region, in which there were differences to be discussed in detail elsewhere, the correspondence between the two pairs of spectra was very close. Seven *C*-methyl groups, a 2,2-dimethylchromene system, a prenyl side-chain attached to an aromatic ring, and the bicyclooctenone part of the morellin skeleton were all readily recognizable. The vinyl proton ($H_v$) of the $\alpha,\beta$-unsaturated carboxylic acid side-chain of morellic acid acetate appeared at 3.85 $\tau$ and the corresponding absorption of isomorellic acid acetate was at 3.25 $\tau$, the downfield shift indicating the isomerization of the carboxyl group from a *trans* to a *cis* configuration, as discussed earlier in connection with morellin and isomorellin.[3]

Ollis *et al.*[6] have stated that "the stereochemistry of the side-chain" carrying the carboxyl group "is probably as shown (IV; $R_1$=Me; $R_2$=COOH), but the NMR results are not conclusive." Yates *et al.*[5] have not presented the NMR spectrum of acetyl-α-gambogic acid and have made no reference in their discussion to the chemical shift of the vinyl proton ($H_v$). Ollis *et al.* did not examine acetyl-α-gambogic acid, but they recorded the NMR spectra of the pyridine salt of gambogic acid, dimethyl gambogate (the ether-ester), and monomethyl gamboginate; $H_v$ appeared at 3.88, 4.03, and 4.12 τ respectively in the three compounds. We have examined the NMR spectrum of gambogic acid kindly supplied by Professor H. Auterhoff who prepared it through the pyridine salt from a commercial 'Harzdrog' which was believed to originate from *G. morella*. In the spectrum of gambogic acid $H_v$ appeared at 3.88 τ and in the light of the data cited for the morellins and the morellic acids it may be concluded that the carboxyl (or carbomethoxyl) group and $H_v$ have the *trans* configuration in gambogic acid, dimethyl gambogate and methyl gamboginate; gambogic acid therefore corresponds to morellic acid. In the NMR spectrum of acetyl-α-gambogic acid, which we prepared from the gamboge of *G. hanburryi* procured from Bangkok, $H_v$ appeared at 3.35 τ, from which it follows that the acetate is derived from isogambogic acid corresponding to isomorellic acid. Isomerization from the unstable angelic acid to the more stable tiglic acid configuration takes place during the treatment with sodium acetate and acetic anhydride.

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