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SYNTHESIS OF (±)-O-METHYLAVERSIN

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The mould, Aspergillus versicolor (Vuillemin) Tiraboschi, produces a number of anthraquinonoid pigments[1-5] including aversin[1] and the versicolorins A, B, and C.[2] Analytical and spectroscopic investigations established structure (I, R = H) or (II) for aversin.[1] It was subsequently found that O-methylaversin is identical with tri-O-methylversicolorin B* for which structure (I, R = Me) has been proposed.[2] Considerable interest attaches to a confirmation of the structures of aversin and the versicolorins since anthraquinones of this type may well be the biogenetic precursors[6] of the carcinogenic aflatoxins (ex A. flavus) and the sterigmatocystins (ex A. versicolor and other species). We now describe a synthesis of a (±)-compound of structure (I, R = Me) and the establishment of its analytical, spectroscopic, and chromatographic identity with (-)-O-methylaversin (the methyl ether of natural aversin).

We envisaged the phenol (III)[7] as a useful intermediate in any attempted synthesis of O-methylaversin but we discounted an application of the classical method (involving a substituted phthalic anhydride) for converting phenols into hydroxy-anthraquinones because of the sensitivity of the tetrahydrofurofuran system to the rigorous acidic conditions which are necessarily involved in the final ring closure.

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* The identity of the two compounds was established by a comparison (m. p's, mixed m.p., and mass spectra) of O-methylaversin with a sample of tri-O-methylversicolorin B which had been kindly provided by Dr. Hamasaki, University of Tottori.

The conversion was, however, accomplished by the application of a new type of polyhydroxy-anthraquinone synthesis[8] in which the final ring closure is achieved in alkaline medium.

Reaction of the phenol (III) with oxalyl chloride in dry methylene chloride yielded the α-keto-lactone (IV)‡ which was cleaved by refluxing methanol to the ester (V). Methylation of ester (V) followed by hydrolysis and treatment of the phenylglyoxylic acid with thionyl chloride gave[9] the acyl chloride (VI). Friedel Crafts acylation of 3,5-dimethoxybenzyl cyanide[10] with the acyl chloride (VI) yielded the benzophenone (VII), base catalysed[8a] cyclisation of which led to a mixture (ca. 1:1) of the anthracenols (VIII and IX). These two isomers were separated by column chromatography on silica and compound (VIII) was characterised by its ^{1}H n.m.r. spectrum (hexadeutero-dimethylsulphoxide), signals for ArH occurring at τ 3.09 (s), 3.16 (d, J ca. 2 Hz), and 3.47 (d, J ca. 2 Hz). Treatment of the isomer (VIII) with alkaline hydrogen peroxide yielded a compound of structure (I, R = Me) which proved to be identical (in its ultraviolet, solution infrared, and ^{1}H n.m.r. spectra, and in its t.l.c. behaviour on silica) with a sample of (-)-O-methylaversin.

Aversin has, therefore, structure (I, R = H).

Acknowledgement

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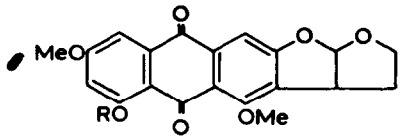
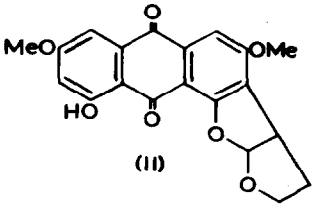
‡ Satisfactory analyses and/or spectra were obtained for all new compounds mentioned above.



(I)



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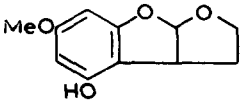

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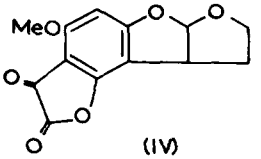

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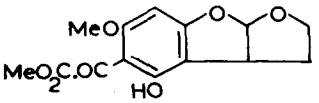

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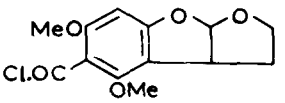

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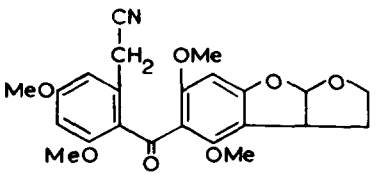

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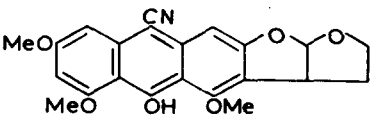

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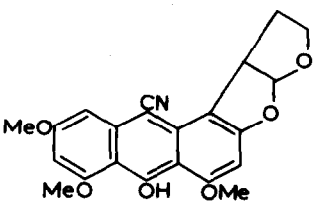

(IX)

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