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REVISED STRUCTURES OF DIPHYLLIN AND JUSTICIDIN A*

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Diphyllin, a phenolic lignan lactone, isolated from the roots of Diphylleia grayi, was assigned structure (Ia) by Murakami and Matsushima[1]. More recently, Munakata et al[2]. isolated from Justicia hayatai var. decumbens a compound called justicidin A and established its identity with the methyl ether of diphyllin. Based on the structure assigned earlier to diphyllin, structure (Ib) was proposed for justicidin A.

We have re-isolated diphyllin, along with other related compounds, from the leaves of Cleistanthus collinus (Roxb.) Benth. & Hook.f. (Family : Euphorbiaceae), a highly poisonous plant used as a fish poison and sometimes for committing suicide[3]. The methyl ether of our compound was found to be identical in all respects (mixed m.p., TLC and IR spectra) with an authentic sample of justicidin A. Since no degradative evidence had been reported in support of the structures assigned earlier to diphyllin and justicidin A, we decided to re-examine them. We now find that the structures of these two compounds have to be revised to (IIa) and (IIb) respectively.

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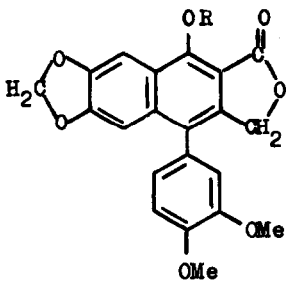
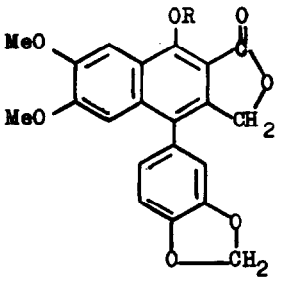


I



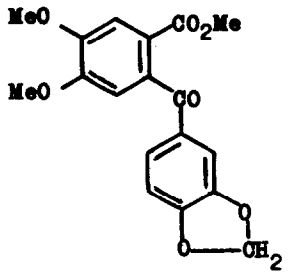
II

a : R = H

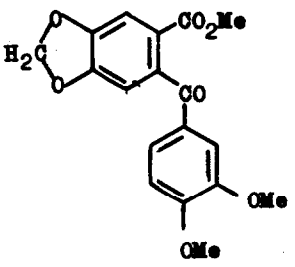
b : R = Me

Diphyllin, $C_{21}H_{16}O_7$ (molecular weight by mass spectrum 380), m.p. 291° (decomp.) (reported[1], 291°), has λ_{max}^{EtOH} 230, 268, 294, 312, 325 and 360 mμ (log ε 4.23, 4.60, 3.81, 3.78, 3.77 and 3.54), ν_{max}^{Nu} 3280 (hydroxyl), 1710 (hydrogen-bonded γ-lactone carbonyl), 1610 (aromatic) and 920 cm^{-1} (methylenedioxy group). It has two methoxyls (Zeisel determination, NMR spectrum), a methylenedioxy group (chromotropic acid test, NMR spectrum) and a phenolic hydroxyl. It forms an acetate, m.p. 234-235° (decomp.) (reported[1] 236~240°), a tosylate, m.p. 210-211° (decomp.) and a methyl ether, m.p. 263° (decomp.) (reported[1] 266~269°).

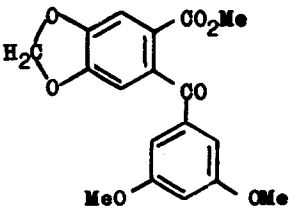
Controlled oxidation of diphyllin with acetone-potassium permanganate, followed by esterification of the acidic product with diazomethane, gave a keto-ester, $C_{18}H_{16}O_7$ (molecular weight by mass spectrum 344), m.p. 175°, ν_{max}^{KBr} 1705, 1655, 920 cm^{-1}, containing two methoxyl groups and a methylenedioxy group. The NMR spectrum of the ester showed peaks at δ 3.64 (3H, COOMe), 3.93 (3H, OMe), 3.99 (3H, OMe), 6.05 (2H, -O.CH_2.O-) and 6.72-7.55 p.p.m. (5H, aromatic protons). Three possible structures, (III), (IV), and (V), were synthesized by the method of Gensler and Samour[4] and the keto-ester obtained by degradation was found to be identical (mixed m.p., TLC, IR and NMR spectra) with compound (III).



III



IV



V

In agreement with this, more drastic oxidation of diphyllin with aqueous alkaline permanganate gave, albeit in low yield, 3,4-methylenedioxybenzoic acid identical with an authentic sample.

The results of these oxidation studies lead unambiguously to structures (IIa) and (IIb) for diphyllin and justicidin A respectively. Details of this work will be published elsewhere.

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