Addition of a Highly Oxygenated Side-chain to an Indole Derivative

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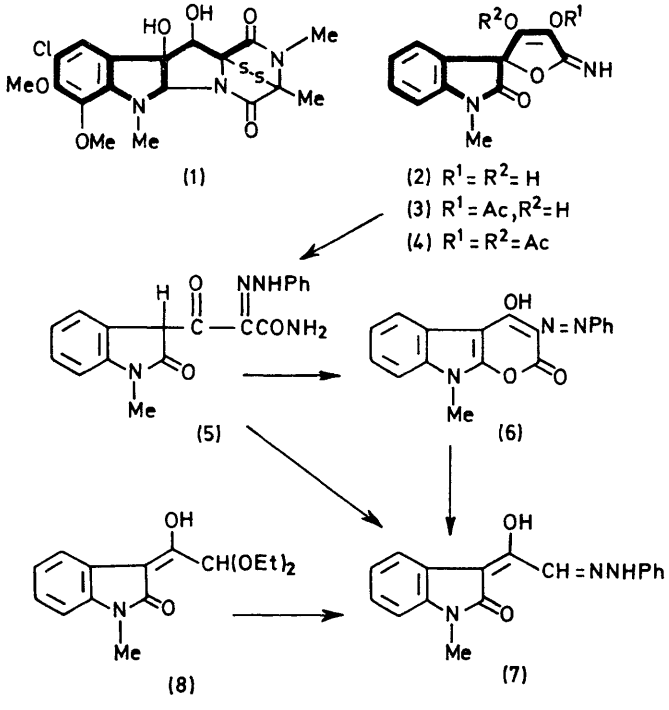
Summary 1-Methylindole-2(3*H*)-one-3-spiro-2′,3′,4′-dihydroxy-5′-imino-2′,5′-dihydrofuran (2) can be prepared in one step by reaction of 1-methylindole-2,3-dione with glyoxal bisulphite and sodium cyanide.

A GROUP of naturally-occurring toxins, having as their common feature the 3,6-epidithiopiperazine-2,5-dione system, has been described.[1] Sporidesmin (1) represents the parent compound of a large sub-group in which the structures also contain the reduced pyrroloindole ring system.



The oxidation level of the carbon skeleton, shown in bold in (1), is that of a 3-hydroxy-2-oxopropanoic acid side chain attached to the 3-position of a 2,3-dihydroxy-1-methylindoline. Such a structure poses a difficult problem of synthesis. We report a simple method for the preparation of an indole derivative (2) which, with the exception of the 2-position of the indole, has all the carbon atoms of the indole skeleton at the correct oxidation level.

Reaction of 1-methylindole-2,3-dione with glyoxal bisulphite and sodium cyanide in aqueous sodium carbonate solution, followed by neutralisation of the mixture with acetic acid, yielded a buff-coloured solid, m.p. 187°, $C_{12}H_{10}N_2O_4$.† The product, which was assigned structure (2) showed the acidity and the reducing properties characteristic of tetronimides and formed an acidic mono-acetate (3) and a di-acetate (4). The structure is thus established by comparison with the simpler tetronimides reported by Dahn and his co-workers.[2]

Treatment of the tetronimide (2) with phenylhydrazine in ethanolic hydrochloric acid yielded a phenylhydrazone $C_{18}H_{16}N_4O_3$, which crystallised as a solvate from ethanol, methanol, or benzene. Since aryltetronimides are known to be converted into 2,3-dioxopropanamide derivatives on acid hydrolysis,[3] the structure of the phenylhydrazone was formulated as (5). A resonance at δ 5·58 in the n.m.r. spectrum of (5) was assigned to the proton at the 3-position of the indole ring. On treatment of compound (5) with acetic anhydride, it lost the elements of ammonia and was converted into the pyranoindole (6). Alkaline hydrolysis of either compound (5) or (6) yielded, after acidification, the phenylhydrazone (7). Compounds (5), (6), and (7) were hydrolysed with boiling acid to yield 1-methylindol-2(3*H*)-one in each case, confirming the presence of the indole skeleton in compounds (2), (5), (6), and (7). Hydrolysis of (2) under the same conditions yielded only trace amounts of the same product. The overall conversion of 1-methylindole-2,3-dione into 1-methylindol-2-(3*H*)-one is in accordance with the intramolecular reduction of the indole ring in going from (2) to (5).

The structure of compound (7) was confirmed by its synthesis from the hydrolysis product of the acetal (8), which was prepared by condensing 1-methylindol-2(3*H*)-one with ethyl diethoxyacetate in the presence of sodium ethoxide. Of the three 3-acylindol-2(3*H*)-ones (5), (7), and (8), only the first exists in the keto-form.

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† Satisfactory analytical and spectroscopic data have been obtained for all the new compounds described.

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