

## The Synthesis of Tetrahydrosclerotioramine

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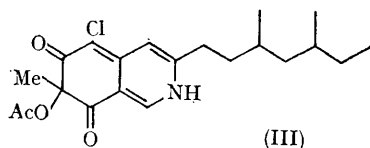
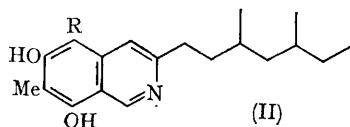
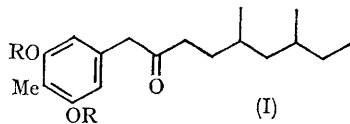
IN continuation of our investigations<sup>1</sup> into the sclerotiorin group of fungal metabolites, we report the application of a new isoquinoline synthesis to the synthesis of tetrahydrosclerotioramine.

Interaction of 3,5-dimethoxy-4-methylphenylacetyl chloride with the cadmium derivative of (+)-3,5(*S*)-dimethylheptyl bromide<sup>2</sup> gave the ketone (I; R = Me) which was demethylated to the dihydric phenol (I; R = H). When this was subjected to the Gattermann aldehyde synthesis

the intermediate aldimine cyclised spontaneously (probably at the isolation stage) to give dechlorotetrahydroapopsclerotioramine (II; R = H) identical with the product prepared from tetrahydroapopsclerotioramine<sup>3</sup> (II; R = Cl) by dehalogenation with boiling hydriodic/acetic acid. Chlorination of (II; R = H) with sulphuryl chloride in acetic acid regenerated tetrahydroapopsclerotioramine.

Acetoxylation of tetrahydroapopsclerotioramine

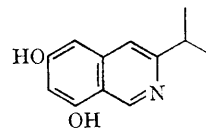
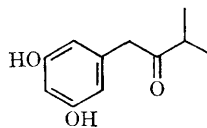
with lead tetra-acetate in acetic acid gave rise to a substance having the general properties of tetrahydro-sclerotioramine (III). Thus, although acetoxylation at C-7 would be non-specific the product had the requisite n.m.r., spectrum and was



indistinguishable on the basis of i.r., u.v., and t.l.c. from authentic tetrahydro-sclerotioramine.

Since (+)-4,6(S)-dimethyloctanoic acid, the precursor of (+)-3,5(S)-dimethylheptyl bromide has been synthesised<sup>4</sup> and since synthetic (III) will contain species of both configurations at C-7, our work constitutes a total synthesis of tetrahydro-sclerotioramine.

Application of this new isoquinoline synthesis to *e.g.*, 3,5-dihydroxyphenyl isopropyl ketone (IV) readily gave 6,8-dihydroxy-3-isopropylisoquinoline (V). The generality of this approach to 6,8-dihydroxyisoquinolines is being investigated.



All new compounds had the requisite spectral and analytical properties.

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<sup>1</sup> G. A. Ellestad and W. B. Whalley, *J. Chem. Soc.*, 1965, 7260.

<sup>2</sup> J. N. Chatterjea and W. B. Whalley, *J. Chem. Soc.*, 1965, 4127.

<sup>3</sup> H. C. Fielding, N. B. Graham, A. Robertson, R. B. Travers, and W. B. Whalley, *J. Chem. Soc.*, 1957, 4931.

<sup>4</sup> L. Crombie, M. Manzoor-i-Khuda, and R. J. D. Smith, *J. Chem. Soc.*, 1957, 479.