The Biogenesis, from Mevalonic Acid, of the Steroidal Antifungal Metabolite Viridin

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INSPECTION of the structure (II) of viridin, the highly active antifungal metabolic product of *Gliocladium virens*, strongly suggested[1] a steroidal biogenetic pathway from (*R*)-mevalonic acid lactone by way of farnesyl pyrophosphate, squalene epoxide, and lanosterol. Nevertheless, the aromatic ring C and the oxygenation pattern of ring A of viridin are unique among naturally occurring steroids and the possibility that the compound might be derived from mevalonic acid *via* geranyl geranyl pyrophosphate and a tricyclic diterpenoid skeleton (VII) of the cassaic acid type could not be excluded.

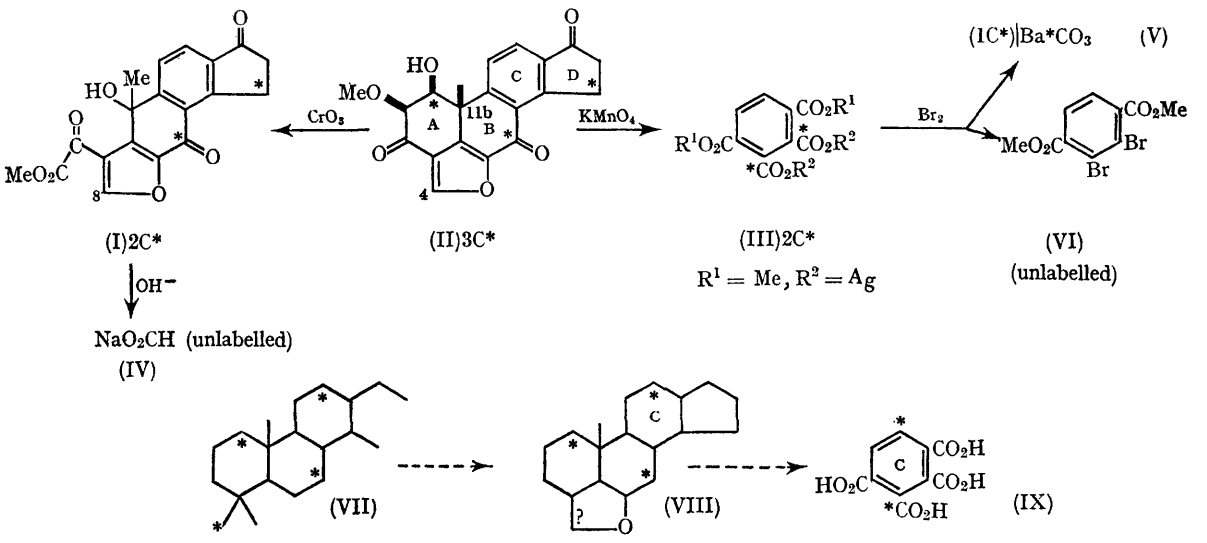
The carbon skeleton of viridin derived from [2-^{14}C]mevalonate by way of such a diterpenoid intermediate would be expected to have the labelling pattern (VIII) and to give benzene-1,2,3,4-tetracarboxylic acid (IX) labelled in the aromatic ring on oxidation with permanganate. On the other hand, [^{14}C]viridin derived from [2-^{14}C]mevalonate by tail-to-tail condensation of two farnesyl residues, to give a steroidal intermediate, would be expected to have the labelling pattern (II) and to yield benzene-1,2,3,4-tetracarboxylic acid (III; $R^1 = R^2 = H$) labelled only in the carboxy-groups. Position 4 in this [^{14}C]viridin may be labelled or unlabelled depending on which of the carbon atoms of the *gem*-dimethyl group of the hypothetical terpenoid precursor is retained.

The oxidation products (I) and (III; $R^1 = R^2 = Me$) of [2-^{14}C]mevalonate-labelled viridin were each found to have two-thirds, not three-quarters and one-half, respectively, of the total relative molar activity (r.m.a.) of viridin (see Table); the

TABLE

Radioactivity of degradation products of [2-^{14}C]*mevalonate-labelled viridin*

Compound	r.m.a. × 10^{-3}	C*
Viridin (II)	502	3
Keto-ester (I)	336	2·01
Sodium formate (IV)	0	0
Tetra-ester (III; $R^1=R^2=Me$)	320	1·92
Silver salt (III; $R^1=Me$, $R^2=Ag$)	336	2·01
Bromo-ester (VI)	0	0
Barium carbonate (V)	163	0·98



sodium formate (IV) derived, by alkaline hydrolysis, from position 8 in the keto-ester (I) was unlabelled, indicating that position 4 in viridin was unlabelled. The dibromo-ester (VI) obtained by subjection of the silver salt (III; R^1 = Me, R^2 = Ag) of the half-ester (III; R^1 = Me, R^2 = H) to the Hunsdiecker reaction was also unlabelled; the whole of the radioactivity present in the silver salt was found in the evolved carbon dioxide, isolated as barium carbonate (V).

These results are consistent only with the biogenesis of viridin by tail-to-tail condensation of two farnesyl residues. Position 4 in viridin appears to be derived from the methyl group of mevalonate, unless some more complex biogenetic scheme is involved.

With the steroidal nature of viridin firmly established the β-absolute configuration of the 11b-methyl group is indicated. Since the conformation and relative configuration of the substituents at positions 1 and 2 are known,[1] the absolute configuration (II) for viridin is deduced.

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[1] J. F. Grove, P. McCloskey, and J. S. Moffatt, *J. Chem. Soc.* (*C*), 1966, 743.