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BIOSYNTHESIS OF DUCLAUXIN

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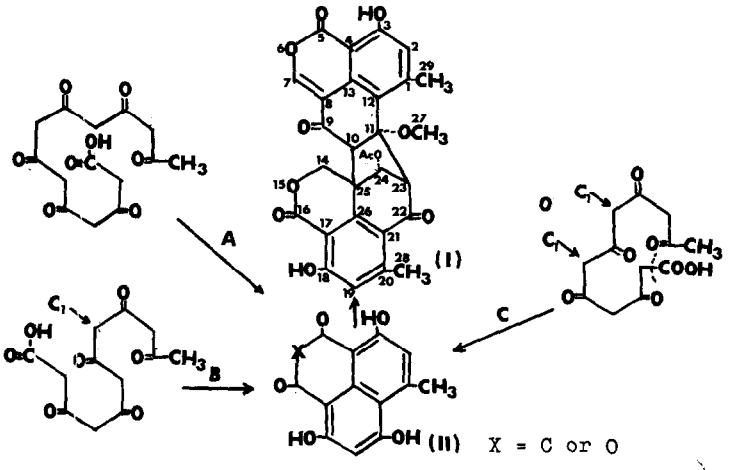
Penicillium duclauxi DELACROIX produces several dimeric derivatives of modified phenalenone (1,2,3), whose structures reveal a close biogenetical correlation.

Duclauxin, a main metabolite of the fungus, has now been studied biosynthetically. In regard to the established structure (I) of duclauxin, it would not be unreasonable to assume that duclauxin arises by the aldol condensation and the oxidative coupling of a hypothetical intermediate (II).

The intermediate (II) would be derived by one out of three biosynthetical schemes, A, B, and C, in which acetate and malonate participate to form the main skeleton, while in the case of B and C the C_1-unit incorporation would be expected to complete the skeletal ring system. In every case, another C_1-unit should be introduced to form a tertiary methoxyl.

In the present experiments, sodium formate-^{14}C, sodium acetate-1^{14}C or -2^{14}C was administered on the 3 rd day of cultivation of Penicillium duclauxi on the Czapek-Dox medium.

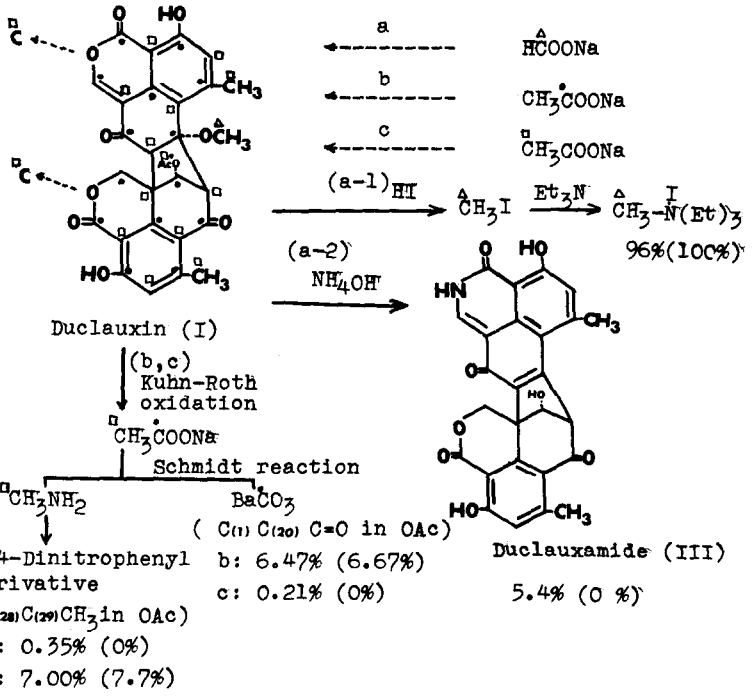


Duclauxin which was isolated from the fungus harvested on the 6th day of cultivation after administration of the tracer showed the incorporation ratios 2.5%, 2.1% and 0.65% for sodium formate-^{14}C, sodium acetate-1^{14}C and sodium acetate-2^{14}C, respectively. The ^{14}C-labelled duclauxin diluted with non-labelled duclauxin was degraded as outlined below.

The radioactivity was localized into the methoxyl of duclauxin, when formate-^{14}C was administered. It agrees with the theoretical value (100%) of the incorporation of ^{14}C into methoxyl calculated on the basis of the scheme A, otherwise the calculated values by the scheme B and C are 33.3% and 20%, respectively.

Duclauxamide (III) derived from duclauxin (3) should give the incorporation ratios, 0%, 66.7% and 80%, calculated on the basis of the schemes A,B, and C, respectively, and the

experimental value, 5.4%, also proved the formation of duclauxin by the route A.



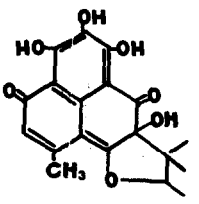
§ The figures in the parentheses are the theoretical values of incorporation.

As shown in the chart, the results of the Kuhn-Roth and the Schmidt degradations of duclauxin which was labelled with sodium-1^{14}C and -2^{14}C showed a good agreement with the calculated values by the scheme A.

Barton et al.(4) suggested the polyketide pathway for the biosynthesis of the skeleton of fungal phenalenones, atrovenetin, herqueinone and norherqueinone. The biosynthetic

study of norherqueinone (IV) was carried out by Thomas (5) to show the incorporation of acetate in the skeleton.

The hypothetical intermediate (II X=C) of duclauxin has now been proved to be derived by the biosynthetical pathway which is common with that of the above fungal phenalenones.



(IV)

However, it is partly modified by the elimination of one ring carbon on oxidation to form an isocoumarin ring system. Corresponding to the peri-naphthalic anhydride derivative derived from norherqueinone by oxidation (4), xenoclauxin* and cryptoclauxin** would be arisen by the biological oxidation of the intermediate (II X=C) eliminating one carbon atom.

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* See formulas(XII) and ** (XIV) in the preceding paper (3).