

STUDIES IN THE BIOCHEMISTRY OF MICROORGANISMS

Part XVI.—Interconversion of Yasimin and Nornidulin, Metabolic Products of *Aspergillus unguis* Emile-Weil and Gaudin

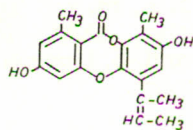
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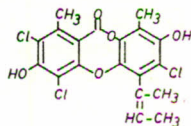
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The structural relationship of yasimin and nornidulin has been established through chlorination of yasimin into nornidulin and dechlorination of nornidulin to obtain yasimin.

In earlier communications we described the isolation, structure¹ and biogenesis² of the very interesting metabolite of *Aspergillus unguis* yasimin. The structure of yasimin (I) was established as that of nornidulin (II) without its three chlorine atoms.



(I)



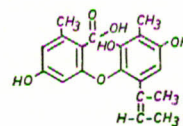
(II)

During a recent synthesis of amudol³ we carried out chlorination of the intermediate diacetyl derivative: 2,5-diacetoxytoluene successfully in presence of triethylamine as catalyst under irradiation with a 1000W lamp. It was felt that chlorination under similar conditions, if successful, could give nornidulin, the trichloro derivative of yasimin. This had to be under controlled conditions to reduce the possibility of chlorine substitution on the butyl side chain. Conversely, if nornidulin (II) could be dechlorinated it would give yasimin (I).

For obtaining nornidulin, a solution of yasimin in a mixture of chloroform and tetrahydrofuran containing triethylamine as catalyst was employed. The solution was saturated with chlorine gas in the cold and exposed to a 1000 W lamp. The chlorinated product was found to be a mixture of three products, one of which was nornidulin. It was separated through radiodilution method by the isolation of tritiated nornidulin (r.m.a. 3500) mixed with authentic sample of cold nornidulin.

For getting yasimin from nornidulin it was dechlorinated with the nickel-aluminium alloy in aqueous sodium hydroxide. This not only resulted in dechlorination, but also, as expected,

in the opening of the ring B, yielding the hydroxy acid (III).



(III)

This was cyclised back by heating in alcohol containing a few drops of hydrochloric acid, to yield yasimin, confirmed through its UV and IR spectra, which were identical to that of the authentic specimen of the material.

Experimental

IR spectra were taken on a Perkin-Elmer 137 spectrophotometer and the UV spectra were measured in methanol on a Beckman D.K. 2. Radioactivity is described in relative molar activity. Petroleum ether employed had b.p. 65–85°C.

Chlorination of Yasimin (I).—Yasimin (20 mg) was dissolved in chlorine-saturated mixture of tetrahydrofuran (1 ml), chloroform (10 ml) and triethylamine (0.2 ml). The solution was exposed (4 hr) to the light of a 1000 W lamp. The product was taken up in ethyl acetate, washed with a few drops of dil HCl followed by water, dried and the solvent removed. The isolated material was transferred to a 6 in × 0.5 in (dia) tube and dissolved in triethylamine (0.5 ml). To this solution tritium oxide (1 drop, 5 curies) was added. The tube was sealed under vacuum and heated (2 hr) in a water bath. The product was taken up in ethyl alcohol and the solvent removed under reduced pressure. The residue was taken up in ethyl acetate, successively washed with 0.1N HCl and water and dried (Na₂SO₄). The solution, on removal of the solvent, gave the hot semisolid

material (12 mg). It showed four spots on a silica gel TLC plate (petroleum ether-ether 3:1) one of them identical to that of normidulin (R_f 0.5). In order to isolate normidulin cold normidulin (20 mg) was added and the mixture was crystallized four times from ether-petroleum ether. Pure, hot normidulin (r.m.a. 3500, 10 mg) was obtained.

Dechlorination of Normidulin.—Normidulin (100 mg) was taken up in aqueous NaOH (10%, 5 ml) and nickel-aluminium alloy (50% 150 mg) was added in small portions, with heating over a period of 2 hr. The cold solution was acidified with dil HCl, extracted with ethyl acetate, charcoaled and dried (Na_2SO_4). The extract, on removal of the solvent, gave the hydroxy acid of yasimin(III). Heating the hydroxy acid (2 hr) in alcohol (3 ml) containing concd HCl (1 ml) cyclised it to give pure yasimin. It was crystallized from hexane, 32 mg, m.p. 201°C, undepressed with an authentic sample of the material. It had identical IR and

UV spectra and the same R_f value (0.5, ether: petroleum ether 1:1) as that of yasimin.

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References

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