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^{2}H Nuclear Magnetic Resonance Studies on Biosynthesis: Stereochemistry of the 5′-Hydrogen Atoms of Griseofulvin derived from Griseophenone B and 4-Demethyldehydrogriseofulvin *

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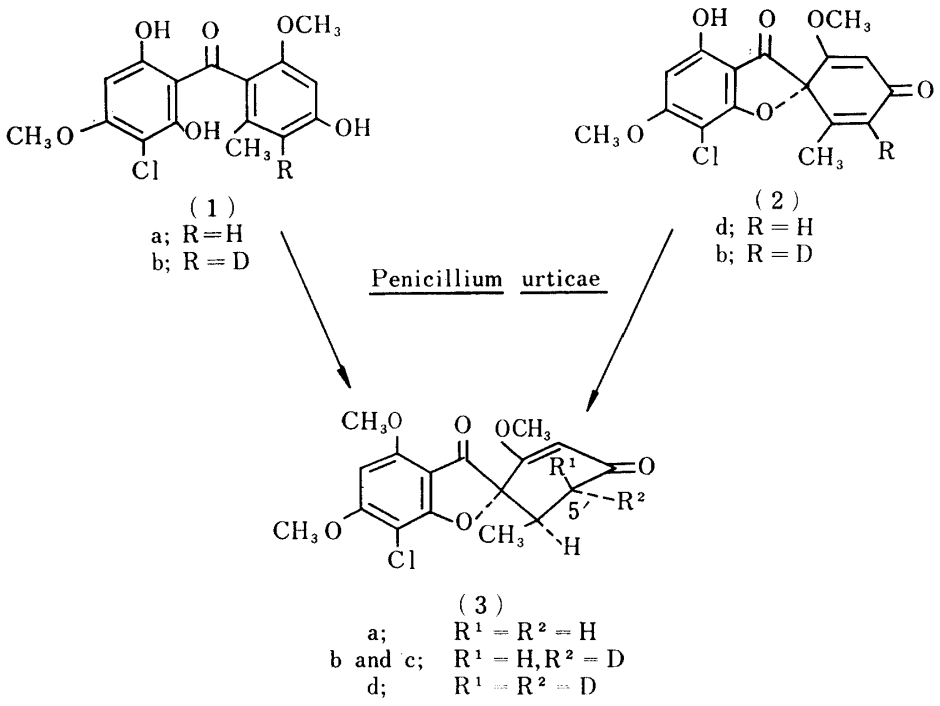
We report the stereochemical fate of the deuterium atom at C-5′ during the biosynthetic transformation of (1a) and (2a) by *Penicillium urticae* as studied by ^{2}H n.m.r. and mass spectrometry.

The two deuteriated tracer were synthesized as follows. Dehydrogenation of [5′-^{2}H] griseofulvin with selenium oxide followed by demethylation as previously described



SCHEME. R^1 and R^2 correspond to the β- and α-configuration, respectively.

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gave 4-demethyl[5′-^{2}H]dehydrogriseofulvin (2b). Tretment of (2b) with zinc-acetic acid afforded [5′-^{2}H]griseophenone B (1b).

To a suspension in medium 2 (15 40-ml flasks, 15 ml per flask) of the mycelium obtained from 7-day-old shaken cultures of *penicillium urticae* in medium 1 (15 40-ml flasks, 20 ml per flask), was administered 15mg of [5′-^{2}H]griseophenone B (1b). After a further 3 days griseofulvin (3b) was isolated from the broth. Similarly a tracer experiment with 4-demethyl[5′-^{2}H]dehydrogriseofulvin (2b) afforded another deuteriated griseofulvin (3c) (Scheme). Since the ^{2}H n.m.r. resonances of (3b) and (3c) are at the same position as that of the 5′α-signal of [5′α, 5′β-^{2}H]griseofulvin (3d), the configuration of the deuterium atoms was unequivocally ascribed as 5′α.

Accordingly, the present ^{2}H n.m.r. results confirm our previous conclusion that, in the feeding experiments involving [2-$^2H_3$]acetate, the 5′-deuterium atom in biosynthetically deuteriated griseofulvin has the α-configuration.

The isotopic dilutions of (3b) and (3c), as calculated from mass spectroscopy, were 13 and 8, respectively, consistent with the postulated biosynthetic sequence that (2b) is at a closer stage than (1b) to the final product. Furthermore, it is interesting that the stereochemical course of the 5′-hydrogen atoms is the same as that in the microbial hydrogenation of dehydrogriseofulvin to griseofulvin (3a) by *Streptomyces cinereocrocatus* NRRL 3443, suggesting the existence of similar enzyme systems in both microorganisms.