

A Hydrogen Shift in Tricothecane Biosynthesis

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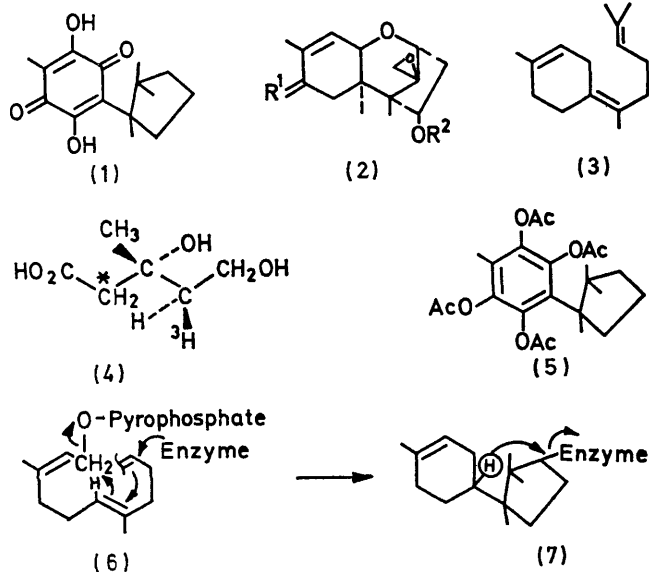
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Summary The retention of the central prenyl (4*R*)[4-³H]-mevalonoid hydrogen in the biosynthesis of helicobasidin and tricothecin is described.

THE fungal sesquiterpenoids helicobasidin (**1**), tricothecin (**2**; R¹ = O; R² = CO·CH=CHMe), and trichodermol (**2**;

R¹ = H₂; R² = H) bear a formal relationship in their biogenesis. Bisabolene intermediates [*e.g.* (**3**)] have been proposed¹ for both compounds. However, the demonstration that helicobasidin incorporates² two of the three possible *pro-R* hydrogen atoms from C-4 in mevalonic acid is in conflict with these ideas.

We have confirmed this by feeding (4*R*)-[4-³H,2-¹⁴C]-mevalonic acid (4) to *Helicobasidium mompa* and isolating the helicobasidin which was counted as its leucoacetate (5)



(mevalonate ³H:¹⁴C, 9.33:1; leucoacetate ³H:¹⁴C, 5.74:1). [2-³H,2-¹⁴C]Geranyl pyrophosphate (³H:¹⁴C, 7.06:1) was then fed to the fungus and again the helicobasidin was isolated and counted as its leucoacetate (³H:¹⁴C, 7.04:1). Consequently the label from the central prenyl unit of the farnesyl pyrophosphate has been retained.

We have previously shown³ that tricothecin (2; R¹ = O; R² = CO-CH=CHMe) and trichodermol (2; R¹ = H₂; R² = H) retain two of the three possible *pro-R* hydrogen atoms from C-4 of the mevalonate units and furthermore that one of these, located at C-10, comes from the terminal prenyl unit of farnesyl pyrophosphate. The second of the mevalonate labels was located at C-2. This did not define which prenyl fragment of the farnesyl pyrophosphate contributed the C-2 label. [2-³H,2-¹⁴C]Geranyl pyrophosphate was fed to *Tricothecium roseum*, *Trichoderma polysporum*, and *T. sporulosum* with the results in the Table.

TABLE

	³ H: ¹⁴ C		³ H: ¹⁴ C
Geranyl pyrophosphate	12.25:1	Tricothecin	12.6:1
" "	6.8:1	Trichodermol	5.45:1
			5.4:1

Thus both tricothecin and trichodermol retained the [2-³H]geranyl pyrophosphate label and hence it is the second (4*R*)-[4-³H] mevalonoid hydrogen that is retained in the final metabolites.

These results clearly preclude a bisabolene intermediate such as (3) in the biosynthesis. However these results may be accommodated in a concerted cyclization sequence involving (6) → (7) for example, in which a hydrogen transfer occurs in the enzyme displacement step. In the helicobasidin case an elimination may lead to a cuparene intermediate whilst in the tricothecane series the hydrogen transfer in (7) could act not only in the enzyme displacement step but also as the initiator for the methyl group rearrangements leading to a trichodiene or related intermediate.

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² S. Nozoe, M. Morisaki, and H. Matsumoto, *Chem. Comm.*, 1970, 926.

³ B. Achilladelis, P. M. Adams, and J. R. Hanson, *Chem. Comm.*, 1970, 511.