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BIOSYNTHESIS OF SCHELHAMMERIDINE: MODE OF SPECIFIC INCORPORATION OF [2-^{14}C]TYROSINE

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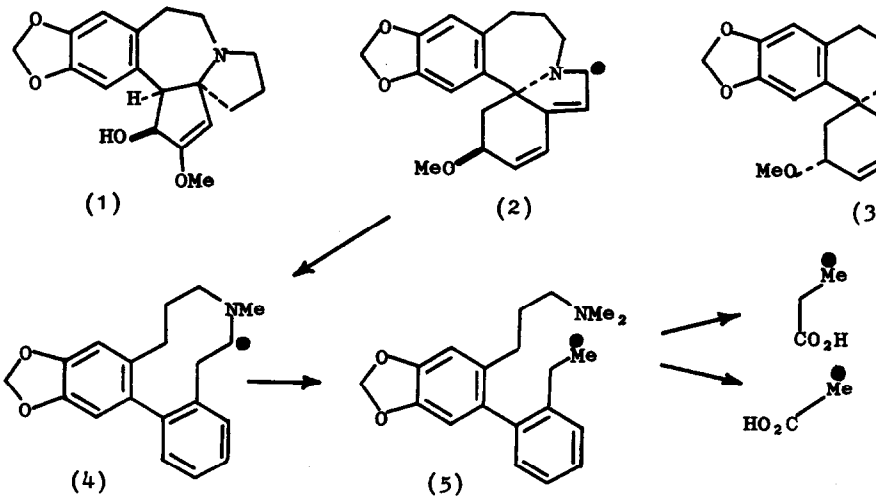
Cephalotaxine (1) and schelhammeridine (2) are the major alkaloids, respectively, of Cephalotaxus harringtonia[1] and Schelhammera pedunculata[2] and the occurrence of both structural types (as 1 and 2) together in C. wilsoniana[3] led to the suggestion that they are divergent products from an initially common biosynthetic pathway.[4]

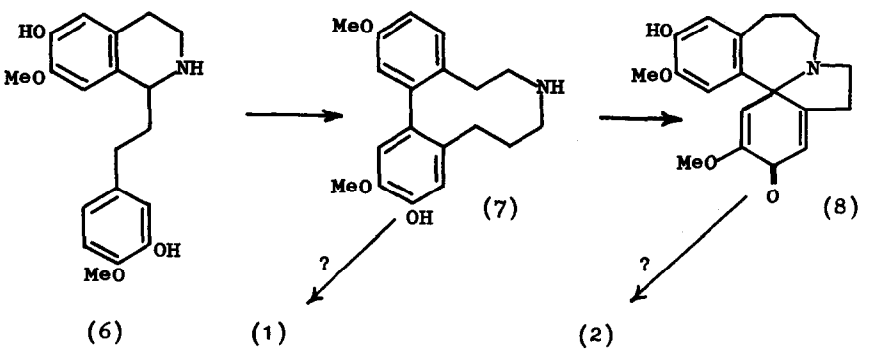
Schelhammeridine (2) is structurally related to erythraline (3) which is known[5] to be derived from a 1-benzylisoquinoline. It is thus reasonable to expect schelhammeridine to be biosynthesised (Scheme) from a 1-phenethylisoquinoline [(6) or a relative thereof], a system commonly produced by plants of the Liliaceae family of which Schelhammera is a member.

Knowledge of the biosynthesis of colchicine, a proven 1-phenethylisoquinoline derivative,[6] led us to test the precursors listed in the Table. Our findings lay the foundation for work on advanced precursors and also



are of interest in relation to a recent report[7] on the biosynthesis of cephalotaxine (1).

The labelled schelhammeridine (2) derived from [2-^{14}C]tyrosine was degraded[8] *via* (2) → (4) → (5), the last having the same molar activity as (2). Kuhn-Roth oxidation of (5) gave propionic and acetic acids which were isolated and purified as their *p*-bromophenacyl esters. Their molar activities corresponded, respectively, to 96% and 88% of that of the base (5). The result for propionic acid shows that tyrosine is incorporated specifically (and solely) into the C_6-C_2 residue of schelhammeridine (2) as illustrated.



Scheme

Initially, a lower molar radioactivity value was found for the above acetic acid derivative and it was only by the most rigorous precautions to exclude traces of C_2-units (especially from C_2-solvents) that the value was raised to that reported.

The results in the Table make it very probable (as proved for colchicine[6]) that the C_6-C_3 unit of schelhammeridine (2) is derived in Nature from phenylalanine *via* cinnamic acid and that dopamine follows tyrosine on the biosynthetic pathway. The lower incorporations (Table) and shortage of (2) itself has so far prevented demonstration of specific labelling from these precursors.

Possible late precursors (Scheme) of schelhammeridine (2) have been synthesised by standard methods and by a new route[9] and labelled forms are being tested in the living plants.

TABLE Tracer experiments on *Schelhammera pedunculata*

Precursor	% Incorporation into schelhammeridine (2)
(2RS)-[2-^{14}C]Tyrosine	0.008 - 0.18
(2RS)-[2-^{14}C]Phenylalanine	0.011
(2RS)-[1-^{14}C]Phenylalanine	0.006
Sodium[2-^{14}C]Cinnamate	0.017
[1-^{14}C]Dopamine	0.015

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