The Absolute Configuration of Narciclasine: A Biosynthetic Approach

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Summary The absolute configuration of the lactam narciclasine represented in (4) is supported by feeding experiments which demonstrate its biological derivation from vittatine (2).

Narciclasine,[1] the lactam widespread among several *Amaryllidaceae* plants,[2] is formed biosynthetically, from *O*-methylnorbelladine (**1**) by phenol-coupling,[3] racemic crinine[4] being the most advanced intermediate in the degradation process.

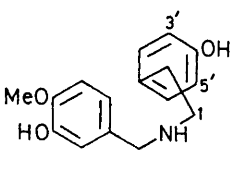
We now outline feeding experiments with optically active precursors which establish the biological derivation of narciclasine from vittatine (**2**).[5]

[3′,5′-$^3H_2$; 1-^{14}C]*O*-methylnorbelladine[6] was converted by *Nerine bowdenii* into crinine, and by *Pancratium maritimum* into its enantiomer vittatine (**2**) without tritium loss. The ^3H-labelling was expected at positions 2 and 4 in equal amounts. This was supported by oxidation to the ketone (**3**)[7] which by base-catalysed exchange with deuteriated water loses the tritium activity almost completely with uptake of three ^2H from the medium.[8]

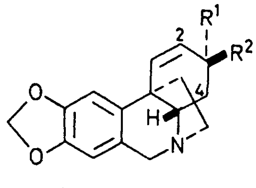
Thereafter, [2,4-$^3H_2$]crinine and [2,4-$^3H_2$]vittatine (**2**) of the required activity were obtained with a large feeding with [3′,5′-$^3H_2$]*O*-methylnorbelladine (**1**) in the two sets of plants.

"Twink" and "Texas" daffodil did not incorporate significantly labelled crinine into narciclasine (**4**), whereas in a parallel feeding with (±)-[3-^3H]crinine a 2·1% incorporation was observed.[4]

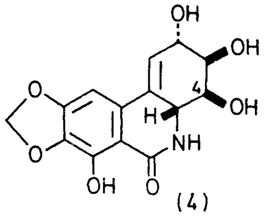
Instead, *Pancratium maritimum* converted labelled vittatine (**2**) into narciclasine (**4**) (0·8% incorporation) and into the alkaloid haemanthidine (2·3% incorporation). The labelling pattern of the radioactive narciclasine (**4**) was determined as before.[3] The relative activities for positions 2 and 4 of (**4**) are 2 : 1 (aromatisation to narciprimine caused 35% tritium loss), thus confirming that hydroxylation at C-4 of the intermediate leading to narciclasine (**4**) causes the loss of *ca.* half the tritium at that carbon.



(1)



(2) $R^1=H; R^2=OH$
(3) $R^1, R^2=O$



(4)

So far as experiments with different plants can be considered together, the evidence which establishes the intermediacy of vittatine (**2**), an alkaloid with the basic ring system of (+)-crinane, in the biosynthetic route to narciclasine (**4**), indicates for the lactam, in the light of the proposed relative stereochemistry,[1,9] the stereostructure (**4**).

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