THE ORIGIN OF THE N-FORMYL GROUP IN NATURE AND THE BIOGENESIS OF CATHARINE AND CATHARININE

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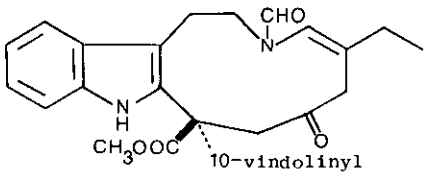
The presence of an N-formyl group in an alkaloid often points to an in vivo Baeyer-Villiger oxidative rearrangement of an iminium precursor. Vinblastine (3) is thus shown to be the most likely progenitor for the accompanying alkaloids catharine (1) and catharinine (2) in Catharanthus spp.

The importance of the Baeyer-Villiger type oxidative rearrangement of iminium salts in alkaloid biogenesis has only recently been recognized. The in vivo formation of the N-formyl groups in the benzylisoquinoline polycarpine[1] as well as in the benzophenanthridine derivatives iwamide, arnottianamide, and isoarnottianamide,[2] has been explained using such a process.[3]

The dimeric indole alkaloids catharine (1)[4] and catharinine (2)[5] have been found in a variety of Catharanthus species,[6] and are structurally related to the important and accompanying antitumor alkaloid vinblastine (3).



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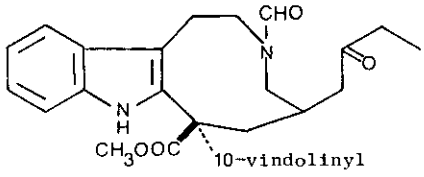

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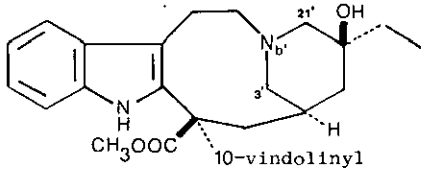

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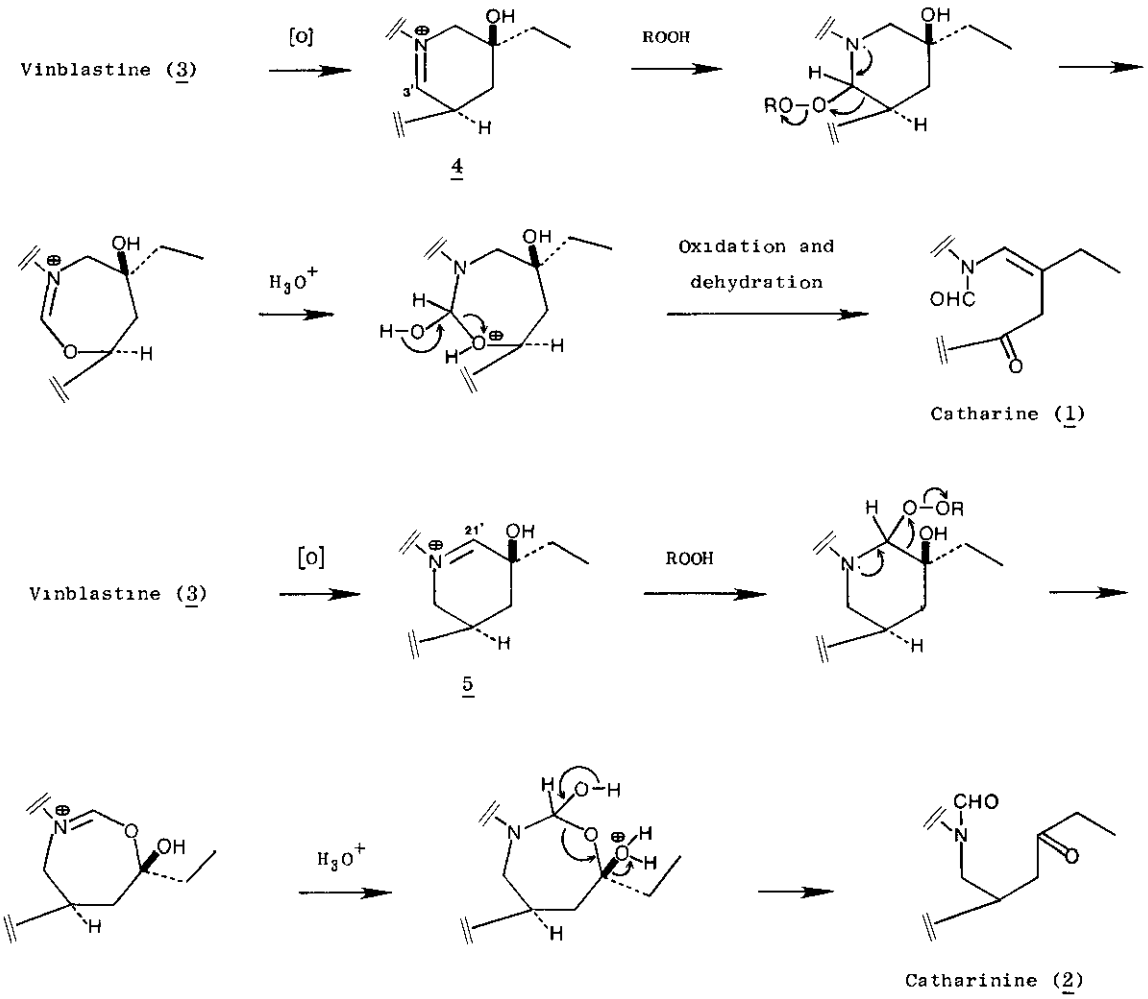
Alkaloids 1 and 2 bear an N-formyl group, and the problem of their biogenesis revolves essentially around the formation of this moiety. A variety of different precursors have been assumed, all proceeding to formaldiminium salts that can undergo an ill-defined oxidation to the corresponding formamides.[5,7]

Reconsideration of the biogenetic scheme for catharine (1) and catharamine (2) makes it clear that a common precursor must be the accompanying alkaloid vinblastine (3). This dimeric compound may readily lead to iminium species 4 and 5 which can suffer Baeyer-Villiger oxidative rearrangement as their key transformation in nature, to furnish eventually alkaloids 1 and 2, respectively (Scheme).[8,9]

Scheme



Although other routes to formylation in nature are known,[10] it is evident from the above that the Baeyer-Villiger type oxidative rearrangement of iminium salts must be borne in mind whenever the biogenesis of alkaloidal formamides is considered.

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References and Footnotes

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8. There is always a possibility that the true precursor of 1 and 2 may be a very close analog of 3, rather than 3 itself. Additionally, it is difficult to say specifically at which stage the dehydration step required for catharine formation occurs.
9. We favor iminium intermediates 4 and 5 in the biogenetic scheme, over alternate Baeyer-Villiger oxidation of formaldiminium salts ($\overset{\oplus}{N}=CH_2$) to obtain the formamides.
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