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ISOPAVINE ALKALOIDS: SYNTHESIS AND BIOSYNTHETIC SPECULATIONS

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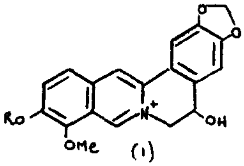
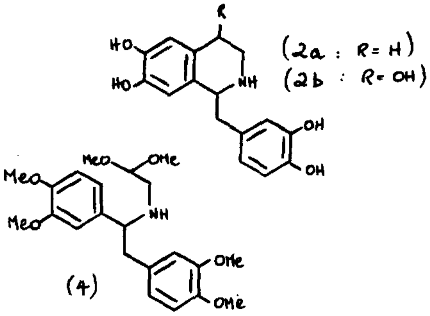
Considerable interest has been aroused by the recent isolation of the first two 5-hydroxyberberine alkaloids, berbastine (1, R = Me) from[1] Hydrastis canadensis L. and thalidastine (1, R = H) from[2] Thalictrum fendleri. Both plants also contain berberine, among other alkaloids, and it has been found[1b] that noradrenaline is an efficient precursor of berberastine, but not of berberine, in H. canadensis. The conclusion that berberine is not a precursor of berberastine has led to the postulate[1b] that 4-hydroxynorlaudanosoline (2b) may be involved in the biosynthesis of berberastine. It is feasible that (2b), like norlaudanosoline (2a), is the precursor of a diverse group of alkaloids, one such substance, 5-hydroxytetrahydroberberine, has recently been detected[1b] in H. canadensis.

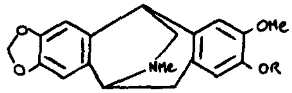


(1)



(2a : R = H)
(2b : R = OH)

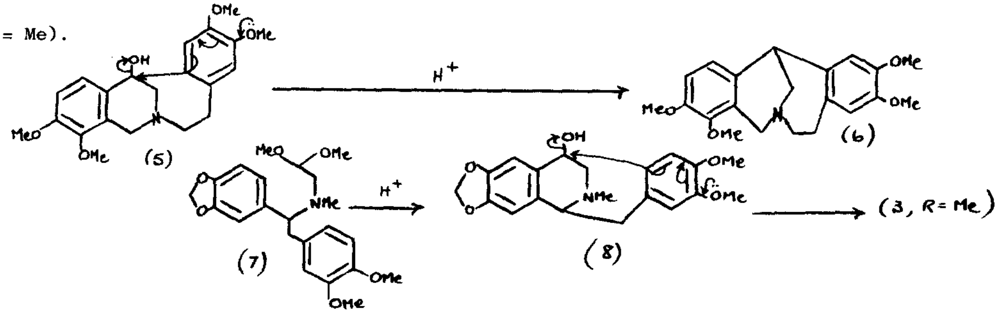
(4)



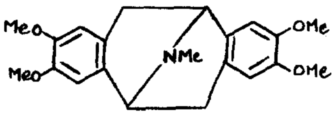
(3)

We recently observed[3] that when the 4-hydroxytetrahydroisoquinoline (5) was treated with acids the product obtained was (6), and we rationalised this result as shown. It is possible that isopavine[4] alkaloids e.g. amurensine (3:R = H), or amurensinine (3:R = Me) are formed in vivo from (2b) by a similar displacement of the hydroxyl group by the 1-benzyl substituent. In the laboratory the aminoacetal (7) when treated with conc. HCl at R.T. for five days gave amurensinine[5] (24%), and it is known[3,6] that 4-hydoxy-1,2,3,4-tetrahydroisoquinolines are formed when benzylacetaldehyde aminoacetals are treated with mineral acid.

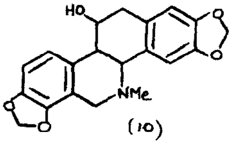
So far, however, we have been unable to isolate (8) in the pure state; it rapidly cyclises to (3:R = Me).



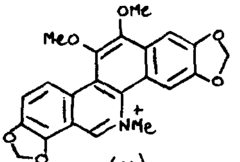
It has been suggested[7] that pavine alkaloids, for example arge monine (9) are derived in Nature from norlaudanosoline (2a) but it is tempting to suggest that 4-hydroxynorlaudanosoline is involved. A dehydration reaction, which is known[3] to occur readily, would yield the 1,2-dihydroisoquinoline from which the formation of the pavine skeleton is straightforward[8].



(9)



(10)



(11)

It is now well established that the benzo[c]phenanthridine alkaloids, such as chelidonine (10) are derived in the plant from berberine, and it is possible that mecarpine (11) is formed via a 5-hydroxyberberine precursor.

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