Biosynthesis of Peyote Alkaloids

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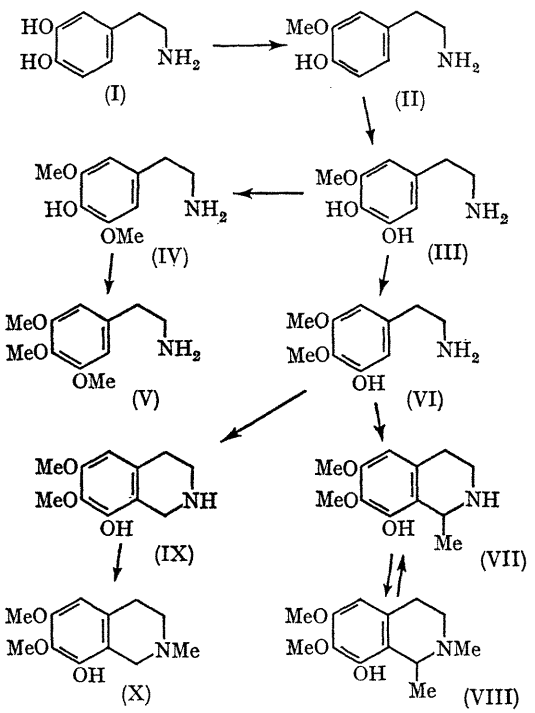
Summary A pathway of biosynthesis of mescaline and the phenolic tetrahydroisoquinoline alkaloids of peyote is suggested.

THE observed[1] low (0·028%) incorporation of 5-hydroxy-3,4-dimethoxyphenethylamine (VI) into pellotine (VIII), taken with the better (1·73%) incorporation of 3,4,5-trihydroxyphenethylamine[2] into anhalamine (IX), has led to



the suggestion[1] that cyclisation of 3,4,5-trihydroxyphenethylamine might precede *O*-methylation during the biosynthesis of peyote (*Lophophora williamsii*) alkaloids. The low percentage incorporation of (VI) and of 3,4,5-trihydroxyphenethylamine into mescaline (V) suggested to us that 4-hydroxy-3,5-dimethoxyphenethylamine (IV), formed from 3,4-dihydroxyphenethylamine (I) *via* *O*-methylation to 4-hydroxy-3-methoxyphenethylamine (II) and hydroxylation of (II) to 4,5-dihydroxy-3-methoxyphenethylamine (III), serves as the immediate precursor of (V).[3] Data presented here confirm this latter hypothesis and strongly support the suggestion that (VI) rather than 3,4,5-trihydroxyphenethylamine serves as the immediate precursor of the phenolic tetrahydroisoquinoline peyote alkaloids [anhalonidine (VII), anhalidine (X), (VIII), and (IX)].

Tracer experiments of *Lophophora williamsii* with [8-^{14}C]-labelled (II), (IV), (VI), and 3,4,5-trihydroxyphenethylamine were carried out in the manner previously described.[4,5] The alkaloids isolated were degraded in each instance to ensure that >99% of the radioactivity resided in the predicted carbon. The results showed that 15·42% of (IV) was incorporated directly into (V), supporting the hypothesis that (IV) is the immediate precursor of (V). Compound (VI) was incorporated to a significant extent into (VII) (6·24%) and into (IX) (5·96%). However, the relatively low incorporation of this precursor into (VIII) (0·26%) is in agreement with the results of Battersby *et al.*[1] While these data appear to be contradictory, the data of Battersby *et al.*[1] suggest that the conversion of (VIII) into (VII) is favoured. They report that 4·9% of (VIII) was converted into (VII) while only 1·5% of (VII) was converted into (VIII).

The incorporation of 3,4,5-trihydroxyphenethylamine into (VII) (0·12%) and (VIII) (0·06%) indicates that this compound is not an efficient precursor of these alkaloids. Unfortunately we were unable to isolate (IX) in this experiment. The percentages of incorporation of (II) into (VII) (2·2%), (VIII) (0·37%), and (IX) (0·72%) are in accord with the suggested pathway. Whether (III) is indeed a precursor of the alkaloids is under investigation.

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