Biosynthesis of a β-Carboline Alkaloid from 1-Methyl-1,2,3,4-tetrahydro-β-carbolin-1-carboxylic Acid

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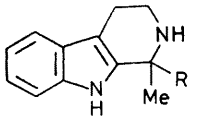
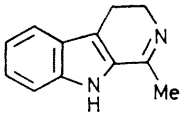
Summary 1-Methyl-1,2,3,4-tetrahydro-β-carbolin-1-carboxylic acid (**2**) is shown to be an intact and very efficient precursor for harman (**4**).

THE biosynthesis of the simple β-carboline alkaloids, *e.g.* harman (**4**) and eleagnine (**1**), has been shown to be simply from tryptamine (**5**).[1] The nature of the first intermediate containing all the β-carboline carbon atoms is, however,

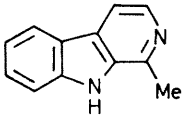
uncertain *N*-Acetyltryptamine (**6**) is apparently clearly implicated in harman (**4**) formation, *via* (**3**), in *Passiflora edulis*,[1] whereas it is not a precursor for eleagnine (**1**) in *Eleagnus angustifolia*, nor is it a natural constituent of this plant [2]



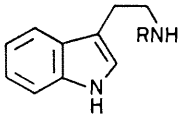
(1) R = H
(2) R = CO_2H



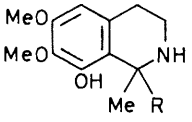
(3)



(4)



(5) R = H
(6) R = Ac



(7) R = H
(8) R = CO_2H

N-Acetyl-compounds corresponding to (**6**) are proved not to be involved in the formation of simple isoquinoline alkaloids, *e g* anhalonidine (**7**) [3] Instead, the amino-acid (**8**) is an intermediate in the formation of (**7**),[4] as are similar compounds in the biosynthesis of related isoquinoline alkaloids [3] By analogy with this, 1-methyl-1,2,3,4-tetrahydro-β-carbolin-1-carboxylic acid (**2**) is a plausible intermediate in the formation of β-carboline alkaloids We have tested the amino-acid (**2**) as a precursor for harman (**4**) in *P edulis*, the precursor was prepared[5] with suitable double labelling [*Ar*-^{3}H, *methyl*-^{14}C] in order to monitor any fragmentation prior to utilization in β-carboline formation

TABLE Incorporation of [*Ar*-^{3}H, *methyl*-^{14}C]-1-methyl 1,2 3 4-tetrahydro-β-carbolin-1-carboxylic acid [as (**2**)] into harman (**4**), in whole plants of *P edulis*

Experiment	^3H . ^{14}C (**2**)	^3H ^{14}C (**4**)	Incorporation (%)
1 (Winter)	4 7	4 3	0 47
2 (Spring)	6 8	6·6	1 5

We find (**2**) to be an intact and very efficient precursor for harman (**4**) (Table), which strongly indicates that it is normally used in biosynthesis, logically *via* the known[1] harman precursor (**3**) (*cf* isoquinoline biosynthesis) [3,4] Harmalan (**3**) is also a precursor for eleagnine (**1**)[2] and may again be derived from (**2**) It should be noted that our results do not prove that (**2**) is an obligatory intermediate in β carboline biosynthesis Experiments designed to do so are in hand

Note added in proof The amino-acid (**2**) has now been isolated in a radioactive form from *P edulis* after feeding radioactive tryptophan, thus strongly indicating that (**2**) is a normal intermediate in harman (**4**) formation

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[4] G J Kapadia, G S Rao, E Leete, M B E Fayez, Y N Vaishnav, and H M Fales, *J Am Chem Soc*, 1970, **92**, 6943
[5] G Hahn, L Barwald, D Schales, and H Werner, *Justus Liebig's Ann Chem*, 1935, **520**, 107.