Alkaloid Biosynthesis in *Croton flavens* L.

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WE report some radioisotopic studies on flavinantine (I; R^1 = Me, R^2 = H) and other morphinandienone alkaloids from *Croton flavens* L. Flavinantine could be formed from reticuline (II; R^1 = Me, R^2 = H) by first *para–para*-intramolecular oxidative coupling to give isosalutaridine (I; R^1 = H, R^2 = Me)[1] and then demethylation and re-methylation, in a manner analogous to the formation of crotonosine from coclaurine.[2] The intermediacy of the methylenedioxy-compound amurine (I; R^1, R^2 = CH_2) in such a scheme is also possible. Orientaline (II; R^1 = H, R^2 = Me) is a further possible precursor, with the subsequent formation of the bis-dienone (III) which would rearrange to give flavinantine directly. A bis-dienone of this type has been suggested as a precursor of the alkaloid acutumine.[3]

To test these theories, (±)-[*N-methyl*-^{14}C]reticuline (II; R^1 = Me, R^2 = H) and (±)-[*N-methyl*-14C]orientaline (II; R^1 = H, R^2 = Me) were synthesised,[4] and fed by the wick-feeding technique to *C. flavens*. (±)-[2-^{14}C]Phenylalanine was also fed in order to demonstrate, by degradation, that as with morphine biosynthesis, two units of this amino-acid were utilised.[5] The Table summarises the results of these experiments. The presence of sinoacutine (IV; R = Me) and norsinoacutine (IV; R = H) was a fortunate coincidence, as these alkaloids served as comparative indices of the biosynthesis of the more usual morphinandienone types.

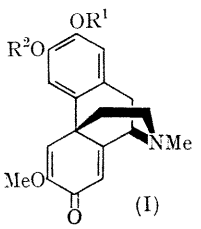
From these results it is clear that the biosynthetic scheme involving the use of reticuline was the favoured one, but the plant can utilise orientaline by some minor pathway.

% *Incorporation of precursors into* C. flavens *alkaloids*

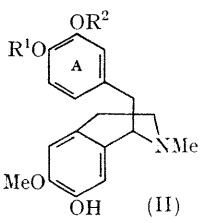
	(±)-Phenylalanine		(±)-Orientaline[a]	(±)-Reticuline[a]
Alkaloid	Expt. I[a]	II[b]		
Flavinantine	0·0012	0·0013	0·012	0·103
Sinoacutine	0·001	0·001	0·0002	0·0024
Norsinoacutine	0·003	0·005	0·00	0·00

[a] Reaped after 2 weeks; [b] reaped after 3 weeks.

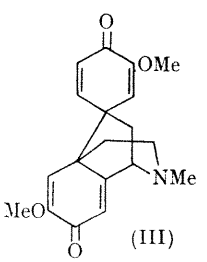
The poor incorporation of phenylalanine probably indicates a limited facility for the conversion of phenylalanine into tyrosine. It is known that several plants cannot convert phenylalanine into tyrosine.[6] By a degradation scheme similar to that carried out on amurine,[7] flavinantine [activity = 1·0] from the phenylalanine feeding experiments was converted into the phenanthrene (V), $C_{17}H_{17}O_4$,-$\frac{1}{2}H_2O$, m.p. 186—188° [activity = 0·47] and dimethylaminoethanol (trapped as the chloroaurate). This demonstrated that two units of phenylalanine were used to biosynthesise flavinantine. By a similar degradation scheme, it was shown that for flavinantine, there was no randomisation of the labelled *N*-methyl group for the (±)-orientaline and (±)-reticuline feeding experiments [phenanthrene activity = 0·0].



(I)



(II)



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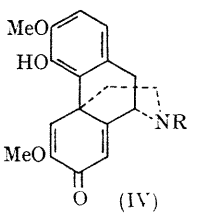

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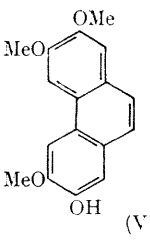

(V)

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