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THE BIOSYNTHESIS OF THE ERGOT ALKALOIDS

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TRYPTOPHAN[1,2] has been implicated as a precursor in the biosynthesis of the ergot alkaloids including lysergic acid (I), agroclavine (II; R=H), and elymoclavine (II; R=OH). We[3] recently suggested that the remaining five carbon atoms [cf.(I)] in this group of substances arise from **mevalonic** acid. **Others**[1] have expressed similar views.

We have now grown a Claviceps purpurea species[4] on media containing, in turn, (2-^{14}C)-mevalonic lactone, $CH_3{}^{14}CO_2Na$ and $^{14}CH_3CO_2Na$, and have found radioactivity to be incorporated in each case into the resulting agroclavine and elymoclavine. Kuhn - Roth oxidation of the labelled agroclavine gave acetic acid derived from the 8- and 17-positions of the alkaloid. Reduction of the labelled **elymoclavine** with sodium in boiling isopropyl

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1 K. Mothes, F. Weygand, D. Groger and H. Grisebach, Z.Naturf.136, 41 (1958).

2 W.A. Taber and L.C. Vining, Chem. & Ind. 1218 (1959).

3 A.J. Birch and Herchel Smith, CIBA Foundation Symposium on Amino Acids and Peptides with Antimetabolic Activity (Edited by Wolstenholme and O'Connor) p. 247. J. and A. Churchill, London (1958).

4 A. Hofmann, R. Brunner, H. Kobel and A. Brack, Helv.Chim.Acta 40, 1358 (1957).

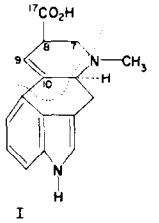
alcohol, and Kuhn - Roth oxidation of the product, gave acetic acid, presumably derived from the same two positions. Degradation of the acetic acid has in each case given the labelling on the individual carbon atoms. Radiochemical incorporations and the relative molar activities of the alkaloid and the samples of barium carbonate derived from the 8- and 17-positions are tabulated below.

Substrate	Agroclavine	Incorporation (%)	$BaCO_3(C_{17})$	$BaCO_3(C_8)$
(2-^{14}C)-mevalonic lactone	16,300	1.0	5060	0
$CH_3{}^{14}CO_2Na$	30,200	0.43	0	16,570
$^{14}CH_3CO_2Na$	59,850	0.83	5750	470

Substrate	Elymoclavine	Incorporation (%)	$BaCO_3(C_{17})$	$BaCO_3(C_8)$
(2-^{14}C)-mevalonic lactone	91,070	1.4	80,020	0
$CH_3{}^{14}CO_2Na$	82,950	1.0	0	37,980
$^{14}CH_3CO_2Na$	80,650	2.1	22,000	1780

Assuming the normal mode of incorporation of the substrates into terpenoid substances, we would expect radioactivity from (2-^{14}C)-mevalonic lactone to be incorporated only into the 7- or 17-positions, or possibly both. Likewise, we would expect radioactivity to be incorporated from $CH_3{}^{14}CO_2Na$ into the 8- and 10-positions, and from $^{14}CH_3CO_2Na$ mainly, if not solely, into the 9-, 16-, and 17-positions in the C_5-unit. The results above are fully

consistent with, although they do not prove, the presence of a terpenoid fragment in the two alkaloids.



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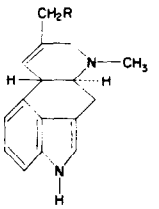

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