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BIOSYNTHESIS OF THE IBOGA ALKALOIDS : THE INCORPORATION OF TRYPTOPHAN-3-C^{14} INTO IBOGAINE[a]

Mikio Yamasaki and Edward Leete[b]

Department of Chemistry, University of Minnesota, Minneapolis.

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The biosynthesis of the Iboga alkaloids, of which ibogaine (II) is a typical example, has been discussed by several authors (1,2,3). The majority agree that tryptophan or tryptamine is the probable precursor of part of these alkaloids, and we have tested this hypothesis by tracer experiments in vivo.

DL-Tryptophan-3-C^{14} (I) (3.8 mg., 1.4 x 10^8 d.p.m.) was administered to six five-month-old Tabernanthe iboga plants[c] growing in soil by means of cotton wicks inserted into the stems. Three weeks later the plants were harvested (fresh wt. 83 g.) and extracted by previously described methods (4), affording ibogaine (132 mg.) having a specific activity of 2.2 x 10^7 d.p.m./mM. This represents an absolute incorporat-

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[b] Alfred P. Sloan Fellow, 1962-1965.

[c] We thank Dr. W. I. Taylor of Ciba Inc. for the viable Tabernanthe iboga seeds and for a generous supply of ibogaine. The plants were cultivated in a greenhouse by Robert C. McLeester of the Botany Department of the University of Minnesota.

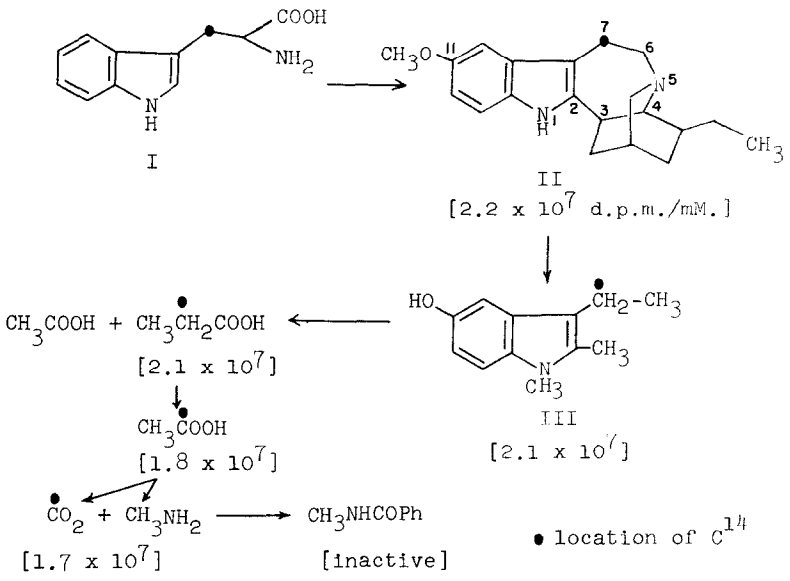

Figure 1. Degradation of the radioactive ibogaine

ion[a] of 6.7% . This is the highest incorporation of a labelled organic compound into an alkaloid that we have ever obtained with an intact higher plant. The location of activity in the radioactive ibogaine was determined as illustrated in Fig. 1. Fusion of the alkaloid with a mixture of sodium and potassium hydroxide at 310-360° yielded 1,2-dimethyl-3-ethyl-5-hydroxyindole (III) in 4.2% yield (5) . This indole derivative was oxidized with 30% chromium trioxide in water affording a mixture of propionic and acetic acid which were separated by partition chromatography on silicic acid (6).

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[a]Absolute incorporation is defined as the total activity found in the alkaloid divided by the total activity fed to the plant.

The propionic acid was oxidized with potassium dichromate in 18 N sulfuric acid (7) to acetic acid which was subjected to a Schmidt reaction affording carbon dioxide and methylamine which was assayed as N-methylbenzamide. The activities of the degradation products of ibogaine are recorded in Fig. 1. as d.p.m./mM. and it is apparent that most of the activity of the ibogaine was located at C-7 , indicating that tryptophan is indeed a direct precursor of the alkaloid.

Work is proceeding on the origin of the non-tryptophan derived portion of ibogaine, and attempts are also being made to determine at what stage hydroxylation at C-11 occurs.

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