

## **A Monoterpene Precursor in the Biosynthesis of Indole Alkaloids**

By P. LOEW, H. GOEGGEL, and D. ARIGONI

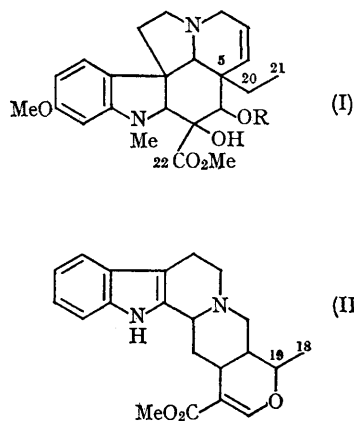
*(Organisch-chemisches Laboratorium, Eidg. Technische Hochschule, Zürich, Switzerland)*

RECENT studies<sup>1-3</sup> have established the mevalonoid nature of a number of indole alkaloids and

suggested that aliphatic monoterpenes are important intermediates in the biosynthesis of these

substances. We now report experimental evidence bearing on this latter point.

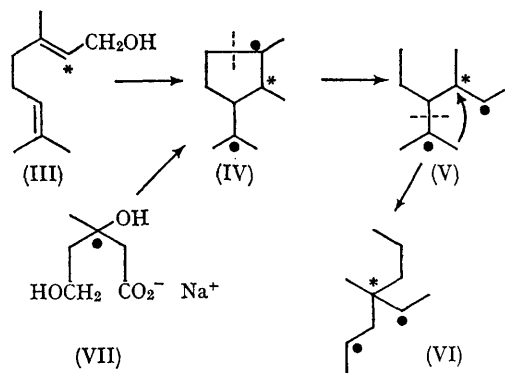
[2-<sup>14</sup>C]Geraniol (III), prepared from [2-<sup>14</sup>C]-bromoacetic ester and methylheptenone by standard methods, was made water-soluble by addition of Tween and administered to young shoots of



*Vinca rosea* L. All of the major alkaloid fractions isolated after seven days were radioactive. The labelled vindoline (I; R = Ac; ca. 0.1% incorporation) was hydrolysed to the *O*-desacetyl derivative (I; R = H), Kuhn-Roth oxidation of which gave a mixture of acetic and propionic acids carrying, respectively, <1% and 97% of the total activity. It follows that essentially all of the label is located at C-5, in keeping with the biogenetic scheme (III) → (IV) → (V) → (VI).<sup>4</sup>

The validity of this scheme was further corroborated by feeding sodium DL-[3-<sup>14</sup>C]mevalonate (VII) to the same plant. The ajmalicine thus

obtained (II; 0.06% incorporation) was degraded by the usual combination of Kuhn-Roth and Schmidt procedures: C-18 was found to be radioinactive, whereas C-19 carried 40% of the total activity. The vindoline from the same experiment (I; R = Ac; 0.5% incorporation) was degraded as



outlined in a previous paper<sup>1</sup> and shown to contain 47% of the label at C-20, with no detectable activity at C-5, C-21, C-22, and in the *O*- and *N*-methyl groups. This result is in excellent agreement with the recent findings of Battersby *et al.*<sup>3</sup> on the biosynthesis of the structurally related 1,2-dehydroaspidofermidine in *Rhazia stricta*.

Independent evidence for the intermediacy of geraniol in the biosynthesis of indole alkaloids has also been obtained by Battersby and by Scott with their co-workers and is reported in the accompanying Communications.

(Received, April 26th, 1966; Com. 283.)

<sup>1</sup> H. Goeggel and D. Arigoni, *Chem. Comm.*, 1965, 538.

<sup>2</sup> F. McCapra, T. Money, A. I. Scott, and I. G. Wright, *Chem. Comm.*, 1965, 537.

<sup>3</sup> A. R. Battersby, R. T. Brown, R. S. Kapil, A. O. Plunkett, and J. B. Taylor, *Chem. Comm.*, 1966, 46.

<sup>4</sup> R. Thomas, *Tetrahedron Letters*, 1961, 544; E. Wenkert, *J. Amer. Chem. Soc.*, 1962, 84, 98.