

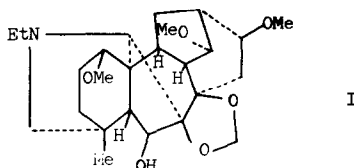
MEVALONIC ACID AND DELPHELINE BIOSYNTHESIS

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The biosynthetic incorporation of mevalonic acid into a natural product is frequently used to test whether the substance is of terpenoid origin. Our recent results on the biosynthesis of the diterpenoid alkaloid delpheline<sup>(1)</sup> (I) emphasise the need for caution in interpreting experiments with mevalonic acid.



Young plants of *Delphinium elatum* were fed with DL-[2-<sup>14</sup>C]mevalonic acid through the cut ends of leaf stalks. After four days, extraction with light petrol and hydrolysis of the extract gave a non-saponifiable fraction which was radioactive (1.3% incorporation). Chromatography on alumina increased the specific activity of this fraction threefold. That one component of the mixture was  $\beta$ -sitosterol was shown by dilution with inactive material. Crystallisation gave radiochemically pure  $\beta$ -sitosterol (0.02% incorporation) which retained its activity when converted into the corresponding acetate.

Surprisingly, the delpheline isolated from the same experiment had no detectable activity, its specific activity being less than  $10^{-4}$  that of the plant sterols. Moreover it was possible to show that delpheline

biosynthesis was proceeding in plants at the same stage of growth. The delpheline content of young plants was assayed from time to time and a rapid increase was observed (dry wt. of plant then ca. 0.4 g.) coinciding with vigorous growth of the plant. Feeding experiments were all performed during this phase of active alkaloid synthesis. Also, L-[methyl- $^{14}\text{C}$ ]-methionine was incorporated (0.025%) into delpheline under the conditions used in the mevalonic acid experiment. De-alkylation with hydrogen iodide revealed activity in the methoxyl (88% of total) and N-ethyl (11%; some contamination by methoxyl was possible) groups. However, the activity of the methylenedioxy group, determined by hydrolysis to formaldehyde, was very low (4.5%). The last result is interesting in that delpheline provides one of the rare examples of a methylenedioxy group attached to saturated carbon. In contrast to this methionine is an efficient precursor for aromatic methylenedioxy groups<sup>(2)</sup>, which are known to be derived from O-methoxy phenols<sup>(3)</sup>.

Accepting that delpheline is a true terpenoid<sup>(1)</sup> the lack of incorporation of mevalonic acid is most easily explained by assuming that this precursor is converted into the non-basic plant terpenoids before it reaches the site of alkaloid synthesis.

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