THE BIOSYNTHESIS OF TROPIC ACID

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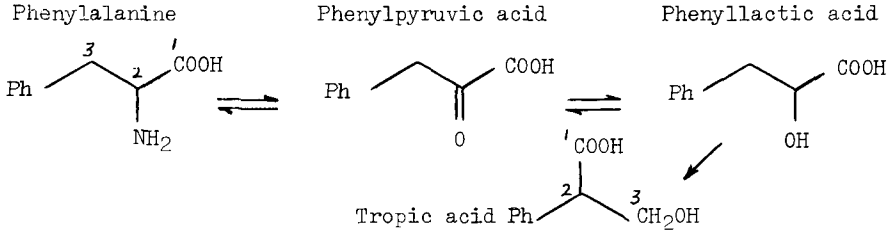
Tropic acid is the acid moiety of the medicinal alkaloids hyoscine and hyoscyamine. Leete and Louden (1962) have shown that the C6-C3 skeleton of tropic acid is formed from the amino acid phenylalanine. Carbons (1) (2) and (3) of the side-chain rearrange by a carboxyl migration, C(2) forming the hydroxymethyl group of tropic acid. The mechanism of this rearrangement is not understood and it is without parallel in nature.

The discovery of the alkaloid littorine, which is the phenyllactic acid ester of tropine (Cannon and others 1969, Evans and Major 1968), prompted an investigation into the role of this acid in the biosynthesis of tropic acid. It was shown that it could serve as a precursor at least as efficiently as phenylalanine (Evans and Woolley 1976). In similar experiments Liebisch and others (1972) have demonstrated that phenylpyruvic acid can also act as a precursor. Because of the facile interconversion of these three acids, it is difficult to decide which is the immediate precursor of tropic acid.

In an attempt to solve this problem phenyllactic acid-[1-^{14}C] was synthesised from phenylacetaldehyde and sodium cyanide-^{14}C and it was fed to Datura stramonium plants via cotton wicks sewn into the stems. The precursor was administered alone and in combination with phenylalanine and phenyllactic acid. In an identical manner, phenylalanine-[2-^{14}C] was fed singly and in competition with phenyllactic and phenylpyruvic acids. After 20 days the plants were collected and the alkaloids were separated by partition column chromatography on kieselguhr containing pH 6.8 buffer (Evans and Partridge 1952) and isolated as the picrates. It was found that the incorporation of phenylalanine-[2-^{14}C] was strongly inhibited by phenyllactic but, perhaps surprisingly, not by phenylpyruvic acid. By contrast phenylalanine did not depress the incorporation of phenyllactic-[1-^{14}C]. These results would suggest that the rearrangement takes place at the phenyllactic acid level.



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