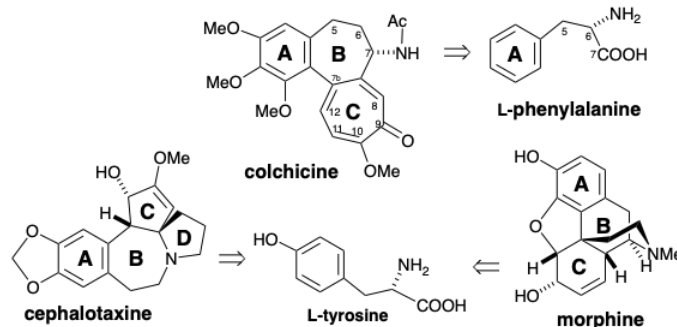


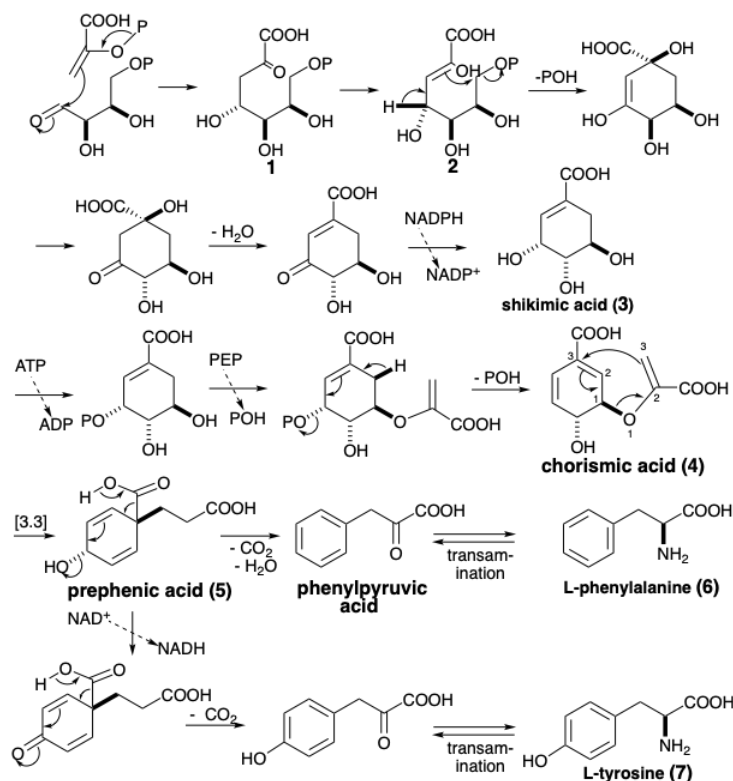
CHAPTER OVERVIEW

6: Amino Acids and Alkaloids

The alkaloids are a diverse family of nitrogen-containing natural products that generally are produced from amino acids in plants. Phenyl rings derived from aromatic amino acids may often be discerned embedded in the skeletons of some alkaloids. For example, the A ring of colchicine is derived from L-phenylalanine and the A rings of cephalotaxine and morphine are derived from L-tyrosine. Interestingly, the remaining carbons of the above mentioned alkaloids are also derived exclusively from L-phenylalanine or L-tyrosine. The loss of aromaticity that is common during such biosyntheses is an example of the unusual synthetic strategies that must be adopted in Nature owing to a limited selection of available starting materials.



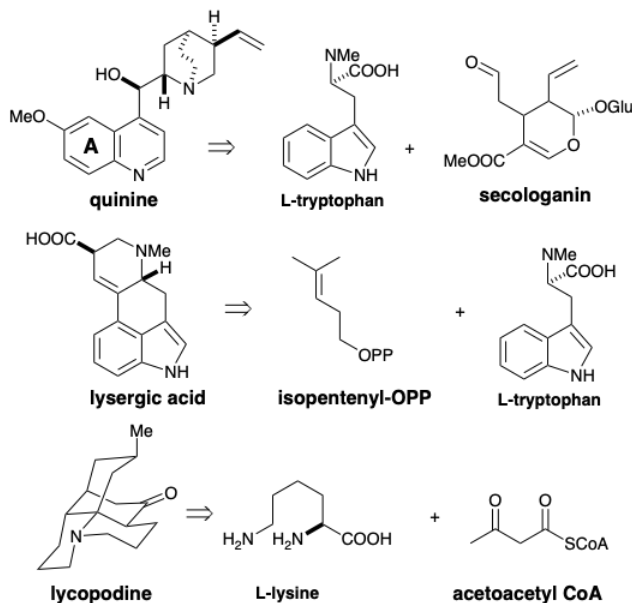
The aromatic rings of polyketides (see chapter 5) arise from acetyl-CoA by a *linear route* culminating in dehydrocyclization of intermediate poly- β -ketoalkanoic acids. In the biosynthesis of the aromatic amino acids L-phenylalanine, L-tyrosine, and L-tryptophan, the aromatic rings are assembled by a more *convergent route* starting with an aldol condensation of phosphoenolpyruvate (PEP) and erythrose 4-phosphate (E4P). These starting materials are available from glucose metabolism (see chapter 2).



Cyclization of the enol tautomer 2 of the resulting 3-deoxy-D-arabinoheptulosonic acid 7-phosphate (1) is reminiscent of the polyene cyclizations that are initiated by allylic pyrophosphates which are encountered in the biosynthesis of terpenes (see chapter 4). Dehydration and reduction then provide shikimic acid (3), the intermediate for which this biosynthetic pathway is named.

Phosphorylation of **3** and transesterification with a second molecule of PEP leads to a pivotal intermediate, chorismic acid (**4**). Appendage of the final three carbons of tyrosine and phenylalanine is achieved by a Claisen, i.e. [3,3] sigmatropic, rearrangement of **4** that produces prephenic acid (**5**). Decarboxylative elimination generates phenylpyruvic acid from **5** while oxidation and decarboxylation of the resulting vinylogous β -keto acid affords p- hydroxyphenylpyruvic acid. Transamination of the arylpyruvic acids (see **40** \rightarrow **43** on section 5.3) delivers the corresponding α -amino acids L-phenylalanine (**6**) and L-tyrosine (**7**).

Amino acids are not the only building blocks incorporated into alkaloids. Thus, for example, some alkaloids incorporate starting materials of terpenoid origin. Quinine is assembled in Nature by the union of L-tryptophan with secologanin, a monoterpene. Interestingly, neither the tryptophane origin of the aromatic portion of quinine nor the terpenoid biogenesis of secologanin are at all obvious.



Much more obvious is the presence of L-tryptophan and an isopentenyl group embedded in the skeleton of lysergic acid. Polyketide fragments and nonaromatic amino acids may also serve as building blocks for alkaloids. For example, lycopodine is derived in nature from two molecules of L-lysine and one of acetoacetyl CoA.

- [6.1: Colchicine](#)
- [6.2: Cephalotaxine](#)
- [6.3: Morphine](#)
- [6.4: Lysergic Acid](#)
- [6.5: Quinine](#)
- [6.6: Biosynthesis of Nonaromatic Amino Acids](#)
- [6.7: Lycopodine](#)
- [6.8: Terminology](#)
- [6.9: Study Questions](#)
- [6.10: References](#)