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2-Pyrones, Stilbenes, Dihydrophenanthrenes, and Xanthones

INTRODUCTION

The enzymatic mechanisms for lengthening of the side chain of cinnamic acids by one or more C₂ units followed by cyclization are widespread in higher plants. Although by far the largest group of compounds formed by this route is the flavonoids, several other important structural entities are known to arise in this manner. Among these are the 2-pyrones, stilbenes, dihydrophenanthrenes, and xanthones.

2-Pyrones and Styrylpyrones

The bark of the plants *Nectandra coto* (syn. *Aniba coto*), *coto*, and *Ocotea pseudocoto* (*Aniba pseudocoto*), paracoto, (as well as other species of the Lauraceae) have long been known to contain biologically active secondary compounds (Geissman and Crout, 1969). The bark of these plants is used medicinally in South America.

Similar compounds are found in kava root, kavakava, kawakawa or yangona (*Piper methysticum*, *Piperaceae*), which is used to prepare a beverage widely consumed in the Pacific islands. The beverage is an integral part of the religious and social life and has tranquilizing and sleep-inducing properties (Lebot, 1991; Lewin, 1931; Schery, 1972).

The stem bark of *Goniothalmus giganteus* (*Annonaceae*) contains the related compounds, gonoiothalenone (alholactone) (1) and gonoiothalamin (2), in addition to a series of acetogenins (Fig. 10.1) (see Polyketides) (McLaughlin, 1991).

Biosynthesis

The mechanism for addition of two carbon units is like that of polyketide synthesis (Birch and Donovan, 1953). The starter unit is first converted to the CoA ester and C₂ units added from malonyl-CoA (Fig. 10.2). The chain then cyclizes in several ways which may be determined by the number of units added, the enzyme systems present, and other factors. Thus, one portion of the molecule is derived from shikimic acid and the other from acetate. In some cases, it is not possible to tell if a C₆-C₃ precursor is extended by two acetate units or if a C₆-C₁ precursor is extended by three units (Fig. 10.2). For example, paracotoin (3) [found in paracoto bark from *Aniba pseudocoto* (*Lauraceae*)] can be derived by either pathway (Fig. 10.3) (Manitto, 1981).

After the chain is extended to six carbon atoms, cyclization occurs to produce a 6-membered lactone ring.

Systematic Usefulness

The trunk woods of many species of *Aniba* (*Lauraceae*) contain phenylpropanoid compounds that serve as precursors to neolignans (see Chapters 8 and 11); other *Aniba* species contain pyrones and benzophenones, whereas yet others possess benzylisoquinoline alkaloids and benzyl benzoates. It is possible to divide *Aniba* species into those that contain pyrones and those that contain neolignans (Gottlieb, 1980).
Biological Activity

Both the beverage, kava or yangon, and the dried root of *Piper methysticum* are used as sources of a series of pyrones with biological activity. Kavalactones in this plant are diuretic, soporific, anticonvulsant, spasmolytic, local anesthetic, and antimycotic (Lebot, 1991). The dried root contains about 5–6% resin from which six related pyrones [yangonin (4), desmethoxyyangonin, kawain (5), dihydrokawain, methysticin (6), and dibydromethylsticin] have been isolated. All are more or less potent, centrally acting skeletal muscle relaxants that also possess antipyretic and local anesthetic properties (Tyler et al., 1981).

STILBENES

Stilbenes are a relatively small, but widely distributed, group of plant secondary metabolites found mostly as heartwood constituents in a heterogeneous assembly of plant species. Over 200 naturally occurring stilbenes and stilbene glycosides are known from higher plants and more than 80 from liverworts (Gorham, 1980, 1989). They are especially important in the heartwood of trees of the genera *Pinus* (Pinaceae), *Eucalyptus* (Myrtaceae), and *Maclura* (Moraceae) (Hart, 1981; Weiss and Edwards, 1980). Stilbenes are common by-products of paper manufacture (Kindl, 1985). Although stilbene aglycones are common in heartwood, living tissue often contains small amounts of stilbene glycosides (Hart, 1981). In several woody plants, stilbenes are accompanied by dihydrostilbenes or bibenzyl compounds, dihydrophenanthrenes, and phenanthrenes (Kindl, 1985).

The para-hydroxylated compound, resveratrol (7), is the most widespread stilbene in nature. This compound occurs in *Picea, Pinus*, the Fabaceae, Myrtaceae, and the Vitaceae among others (Kindl, 1985). Pinosylvin (8) and its derivatives are mostly restricted to the genus *Pinus*. The distribution of stilbenes in plants has been reviewed (Gorham, 1980, 1989) (Fig. 10.4).

Oxidative dimers of stilbenes called goetins occur in both of the unusual gymnosperms *Gnetum* and *Welwitschia* (Fig. 10.5) (Gottlieb and Kubitzki, 1988).