Stereochemistry of Lignan Biosynthesis in *Wikstroemia sikokiana*\(^*1\)

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Lignan molecules are generally chiral and naturally occurring lignan specimens are mostly optically active. The sign of optical rotation of a particular lignan can vary with plant sources: \((-\) )-arctigenin was isolated from *Forsythia* plants,\(^1-3\) whereas the corresponding \((+\) )-enantiomer was from *Wikstroemia* plant\(^4\). Hence, stereochemical mechanisms involved in lignan biosynthesis can be different among various plants species.

Many reports have been published on enzyme systems involved in lignan biosynthesis with *Forsythia* plants as enzyme sources\(^5-18\). At present biosynthetic sequences of *Forsythia* lignans have been established, and the stereochemical mechanisms of each enzymatic conversion have been elucidated\(^5-18\).

On the other hand, little studies of the plans which produce opposite enantiomer to those of *Forsythia* lignans have been reported. Recently, Umezawa and Shimada\(^19\) reported isolation of \((−)\)-pinoresinol (74% e.e.), \((+\) )-matairesinol (optically pure) and \((+\) )-wikstromol (optically pure) from *Wikstroemia sikokiana*. These lignans are opposite enantiomer to those from *Forsythia* plants. Importantly, the enantiomeric composition of \((−)\)-pinoresinol isolated from *W. sikokiana* was only 74% e.e. This value was much smaller than that of \((+\) )-pinoresinol obtained from *Forsythia* plants (almost optically pure)\(^3\). They concluded that there are two differences in the stereochemical mechanisms of lignan biosynthesis between *W. sikokiana* and *Forsythia* spp.; one is that both plants produce (or accumulate) different enantiomers, and the other is that the step in the metabolic sequence to produce optically pure lignans are different between the plants. However, detailed mechanisms remained to be elucidated.

The present paper reports the further study of lignan biosynthesis in *W. sikokiana*.

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First, a survey of lignans, especially possible intermediates between pinoresinol and matairesinol, and determination of their enantiomeric compositions were carried out. Then feeding experiments with deuterium-labelled substrates were conducted to establish biosynthetic pathways of *W. sikokiana* lignans.

Six lignans, shown in Fig. 1, were isolated from MeOH extracts of *W. sikokiana* stems. The isolation of \((-\)-lariciresinol (39% e.e.), \((-\)-secoisolariciresinol (45% e.e.), and \((+\)-kusunokinin (optically pure) from this plant was reported for the first time in the present investigation. The predominant enantiomers of the *Wikstroemia* lignans are opposite to those isolated from *Forsythia* plants except for secoisolariciresinol.

Enantiomeric compositions of the lignans from *W. sikokiana* and those from *Forsythia* spp. are also different. Thus, pinosinol, lariciresinol, and secoisolariciresinol isolated from *W. sikokiana* were not optically pure, whereas those lignans from *Forsythia* spp. were optically pure (or almost optically pure)\(^3,7\). On the other hand, the present and previous investigations\(^3,7,12,19\) showed that all the dibenzylbutyrolactone lignans, e.g., matairesinol, isolated from both plants were optically pure.

Next, deuterium-labelled \([9,9-\text{H}_2, \text{OC}_2\text{H}_3]\) coniferyl alcohol as well as four lignans, \((\pm\)-\([9,9,9',9'\text{-H}_4]\) pinosinols, \((\pm\)-\([9,9,9',9'\text{-H}_4]\) lariciresinols, \((\pm\)-\([9,9,9',9'\text{-H}_4]\) secoisolariciresinols, and \((\pm\)-\([\text{aromatic-}2\text{H}]\) secoisolariciresinols, were administered to young shoots of the plant. Incorporation of \([9,9-\text{H}_2, \text{OC}_2\text{H}_3]\) coniferyl alcohol into pinosinol, lariciresinol, secoisolariciresinol, and matairesinol was observed. The values of % incorporation into the lignans except for matairesinol were pinosinol (0.81%), lariciresinol (0.32%), and secoisolariciresinol (0.09%). In addition, the following incorporation was demonstrated: \((\pm\)-\([9,9,9',9'\text{-H}_4]\) pinosinols to lariciresinol and
secoisolariciresinol, (±)-[9,9,9',9'-2H_4] lariciresinols to pinoresinol and secoisolarici-
resinol, and (±)-[9,9,9',9'-2H_4] secoisolariciresinols to pinoresinol and lariciresinol,
(±)-[aromatic-2H] secoisolariciresinols to matairesinol.

Feeding experiments with deuterium-labelled substrates suggested strongly the
pathway of lignan biosynthesis in the plant (Fig. 1). This pathway is similar with respect to
metabolic sequence to that in Forsythia spp., but there are two differences in the
stereochemical mechanisms. First, predominant enantiomers of the lignans occurring on
these plants are different. Second, there is a difference in the metabolic step to produce
optically pure lignans between W. sikokiana and Forsythia spp. The step is probably the
conversion of secoisolariciresinol to matairesinol in W. sikokiana, whereas the step is the
formation of pinoresinol from coniferyl alcohol in Forsythia spp.

In conclusion, a possible biosynthetic pathway for lignans in W. sikokiana was proposed.
This pathway is similar to that in Forsythia spp. The predominant enantiomers of the
lignans occurring in both plants were opposite each other, and the step in which an optically
pure lignan was produced is different in both plants.

References