Synthetic Study of Acromelic Acid Derivatives

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Acromelic acid **1** was initially isolated from a Japanese poisonous mushroom that we called *Dokusasako* by Matsumoto and Shirahama at Hokkaido University in 1984 (Figure 1). Later, the same group reported the total synthesis and the most potent derivative, MFPA **3** (Figure 1). Since these amino acids exhibit neuroexcitatory activity derived from the agonistic effect on glutamate receptors, they could be useful probes for evaluating memory mechanisms. The recent progress in brain research reinforces the requirement of probe molecules targeting neurosystem. However, the scarcity of natural product had limited further biochemical study of **1**. In order to resolve this issue, we have started to develop an efficient synthetic method for acromelic acid derivatives with a view to a large scale production.

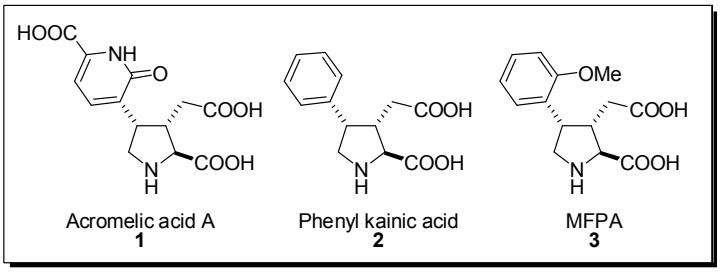
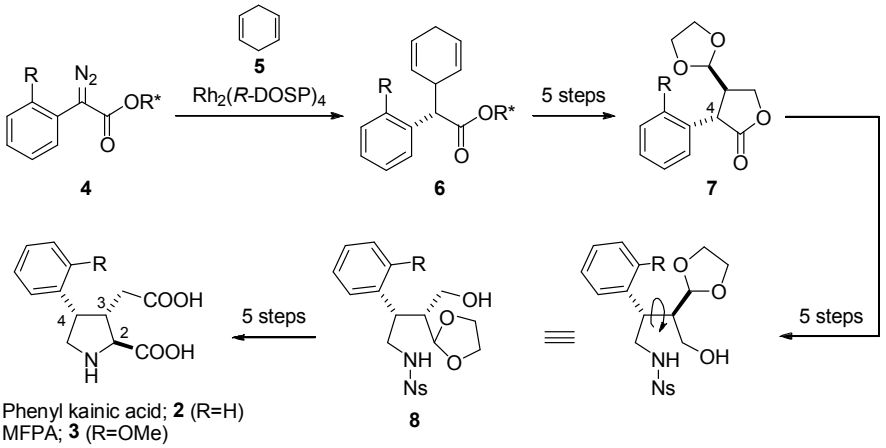


Figure 1. Acromelic acid derivatives.

Scheme 1. Synthetic method of acromelic acid derivatives.



First, employment of chiral rhodium catalyst, $Rh_2(R\text{-DOSP})_4$ for intermolecular C-H insertion reaction as a key step resulted in stereoselective construction of C4, one of the three contiguous chiral centers (Scheme 1). Other contiguous chiral centers were constructed based on the stereochemistry of C4.

This synthetic approach successfully afforded acromelic acid derivatives, phenyl kainic acid **2** and MFPA **3**.

Thus, we have succeeded in the synthesis of acromelic acid derivatives using the asymmetric intermolecular C-H insertion reaction as a key step.