AL06 Design, Synthesis and Application of Nitrogen-Containing Useful Molecules

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Nitrogen-containing compounds are very important in organic, medicinal and synthetic chemistry due to their biological activities, so that their scalable preparation by chemical synthesis has been important issue in synthetic community. The author focused on 2 different topics to achieve efficient multi-step and single step synthesis of these molecules, the former is alkaloid synthesis and the latter is transition metal-catalyzed cyanation of non-activated C-C multiple bonds. This abstract summarizes above 2 projects briefly.

1) Total synthesis of kopsia alkaloids

Lundurine A-D have been attractive synthetic targets due to their unique indoline-cyclopropane core structure and biological activities, however their synthetic study have not been well-investigated past over 20 years since their discovery. The author planned to focus on spiro structure that can be observed in all lundurine family. Simple and symmetric structure has advantages for its preparation as an optically active form. Asymmetric deprotonation-cyclopropanation sequence was effective to access the optically active structure lundurine. This intermediate was also effective to complete the total synthesis of other alkaloids (Fig. 1).

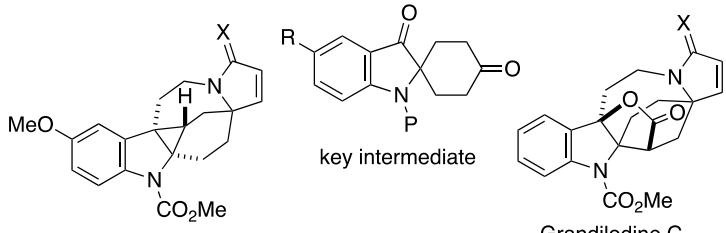

Fig. 1 Kopsia alkaloids & key intermediate

2) Transition metal-catalyzed cyanation

A cyano group is a key functionality for the transformation to aminomethyl and carboxylic groups as well as nitrogen heterocycles, so its install into organic molecules particularly with regio- and stereoselective manner has been important issue in synthetic chemistry. Transition metal complexes such as Ni, Pd and Co are effective catalysts in these chemical transformations using simple alkynes and alkenes. The unexpected discovery of 1,2-dicyanation under Pd catalysis was the trigger to develop this cyanation chemistry and herein the major topic is focused on Ni-catalyzed hydrocyanation. To control regio- and stereochemistry in Ni-catalyzed cyanation of CC multiple bonds, cyclizative hydrocyanation was investigated to discriminate unsaturated C-C bonds in enyne and allen-yne substrates (Fig. 2). Further application for cyclopropane cleavage, chirality transfer and alkaloid synthesis will be discussed.

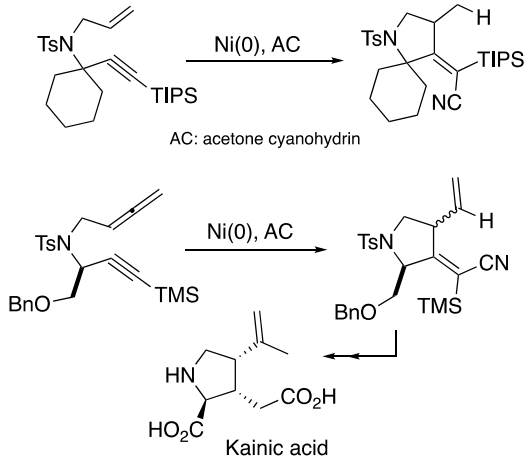

Fig. 2 Ni-catalyzed cyanation and its application