Synthetic Study of the *Kopsia lapidilecta* Alkaloid Lapidilectam

Jun Maruyama, Takeshi Watanabe, Hiromichi Yamashita, Shigeru Arai and Atsushi Nishida
(Graduate School of Pharmaceutical Sciences, Chiba university)

The genus *Kopsia* (*Apocynaceae*, subfamily *Plumerioideae*) is comprised of about 30 species that grow in South and Southeast Asia. Lapidilectam (1) is one of several pyrroloazocinoindoles that have been isolated from this genus of plants. It was isolated by Awang, et al. from the stems and bark of the tree *Kopsia lapidilecta* in 1993. Although there are no reports on the pharmacological effects of *Kopsia lapidilecta* alkaloids, various medicinal uses of other *Kopsia* alkaloids have been reported. No synthetic studies on Lapidilectam (1) have been reported. We report herein our synthetic study of *Kopsia lapidilecta* alkaloid, namely Lapidilectam (1).

Pyrroloazocine derivative 2, prepared from known pyrrolidinone derivative in 10 steps, was condensed with 2-iodoaniline. The resulting enamine 3 was converted to tetracyclic key intermediate 4 containing ABCE-ring using new type of Heck reaction via selective isomerization of double bond. The relative configuration, however, was unnatural syn-isomer. Therefore, the stereochemistry at 3-position was inverted by conversion to exo-olefin 5 followed by stereoselective hydroboration. Next, regio- and stereoselective C7-acylation via magnesium salt of indole was accomplished (7→8). Final D-ring formation is now in progress.