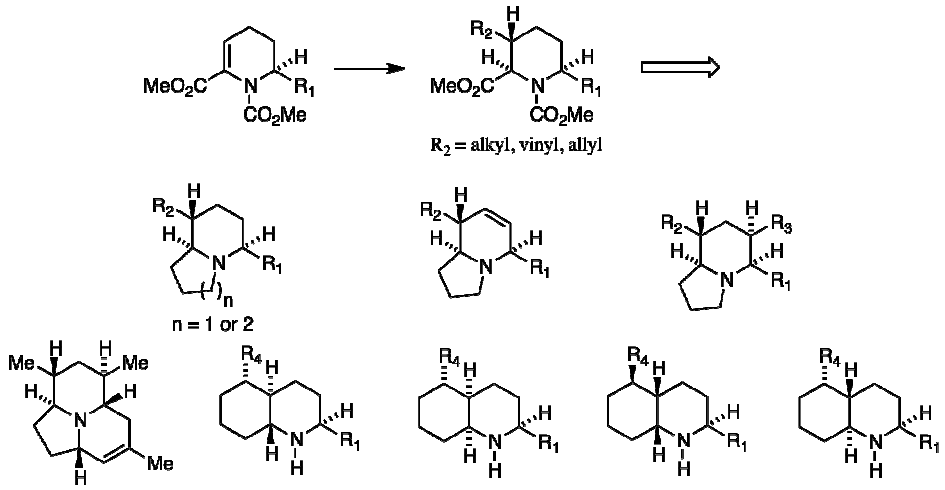
Synthesis of Poison-Frog Alkaloids

Naoki Toyooka

University of Toyama, Toyama, Japan

A variety of lipid-soluble alkaloids have been detected in amphibian skin, which contains over 20 structural classes and over 800 alkaloids. Many of these poison-frog alkaloids are expected to show interesting biological activities such as inhibitory effects on the neuronal nicotinic acetylcholine receptors (nAChRs).

We envisioned an efficient and flexible synthesis of 5,8-disubstituted, 6,7-dehydro-5,8-disubstituted, and 5,6,8-trisubstituted indolizidines, 1,4-disubstituted quinolizidines, decahydroquinoline-type poison-frog alkaloids using a Michael-type conjugate addition reaction of an enaminoester as the key step as shown below.



We will present our synthetic efforts toward the above alkaloids and the biological activity of the synthetic compounds on the nAChRs.