Komsan Imphanban 2009: Asymmetric Synthesis of (-)-*N*-Formylnornuciferine and (-)-*N*-Formylannonaine with Cardiotonic Activity. Master of Science (Chemistry), Major Field: Chemistry, Department of Chemistry. Thesis Advisor: Associate Professor Boonsong Kongkathip, Ph.D. 199 pages.

(-)-*N*-Formylnornuciferine and (-)-*N*-formylannonaine, two aporphine alkaloids isolated from stems of *Tinospora crispa* (Borapet in Thai), showed *in vitro* cardiotonic activity. They exhibited significant increase in force of contraction on atria of isolated rat heart with no change on the rate. Due to very limited amounts of these active compounds isolated from *T. crispa*, the cardiotonic activity evaluation of these compounds is hampered. One way to obtain enough quantities for pharmacological investigation is by chemical synthesis.

(±)-*N*-Formylnornuciferine and (±)-*N*-formylannonaine in racemic form were successfully synthesized by using palladium-catalyzed coupling reaction as a key step. (±)-*N*-Formylnornuciferine was synthesized in 6 steps from homoveratrylamine with an overall yield of 50%, whereas (±)-*N*-formylannonaine was also achieved in 9 steps from dopamine hydrochloride with an overall yield of 30%. Moreover, the enantiopures, (-)-*N*-formylnornuciferine and (-)-*N*-formylannonaine, were synthesized in 50% and 34% overall yield, respectively by asymmetric transfer hydrogenation method using chiral ruthenium complex as a catalyst.

For cardiotonic activity, it was found that the racemic mixture, (±)-*N*-formylnornuciferine and (±)-*N*-formylannonaine, showed the different activity from that of the natural ones, while the enantiopure of these two synthetic alkaloids showed quite similar results to the natural ones isolated from *T. crispa*. From our results, it may be possible to develop these active alkaloids to become a potential cardiotonic drug in the future.

_____ _____ ___ / ___ / ___

Student's signature Thesis Advisor's signature