Synthetic Studies on Illisimonin A

(*[1]Department of Chemistry, Hokkaido University, [2] Graduate School of Chemical Sciences and Engineering, Hokkaido University*) ○Muhammad Aiman bin Mohd Fariz[1], Takahiro Suzuki[1], Riko Nagahama[2], Yuki Yukutake[2], Keiji Tanino[1]

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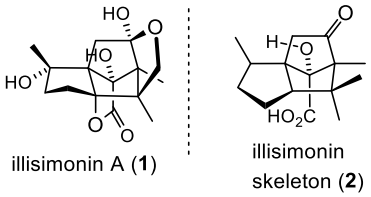
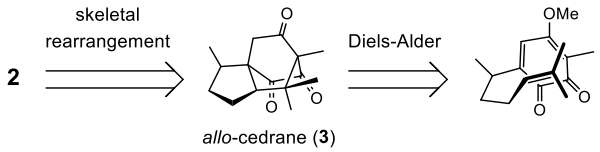
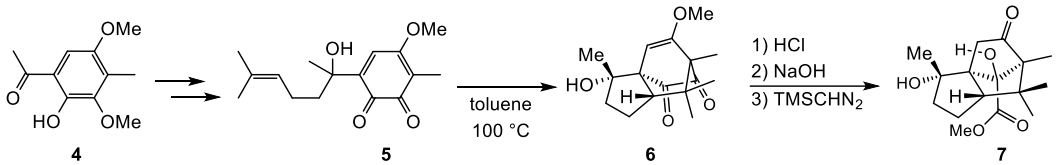
Illisimonin A (**1**), isolated from the fruits of *illicium simonsii* in 2017, is known for its neuroprotective effects against oxygen-glucose deprivation-induced cell injury.[1)] This promising bioactivity and its novel 5/5/5/5/5 pentacyclic skeleton make this compound a viable synthetic target.[2)] With the goal of developing an efficient method to construct the illisimonin skeleton (**2**), we achieved the synthetic strategy based on the intramolecular Diels-Alder (IMDA) reaction using *ortho*-benzoquinones and the biomimetic skeletal rearrangement of the resulting *allo*-cedrane skeleton.[3)]



We postulated that the biosynthesis of **1** occurs from the *allo*-cedrane skeleton that is common to the illicium sesquiterpenes. The highly oxidized *allo*-cedrane **3** can be transformed to **2** by benzylic acid rearrangement or retro-Claisen condensation/aldol reaction. *Allo*-cedrane **3** could be constructed by IMDA reaction with *ortho*-benzoquinone.



The IMDA reaction precursor **5** was prepared from the known ketone **4** as a starting material. Benzoquinone **5** was stirred in toluene at 100°C to give the tricyclic diketone **6** in moderate yield. The resulting **6** was first hydrolyzed to triketone under acidic conditions of hydrochloric acid, followed by skeletal rearrangement under basic conditions of NaOH and $TMSCHN_2$ to give methyl ester **7** in good yield. With the illisimonin skeleton in hand, we are now looking into the total synthesis of illisimonin A.



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