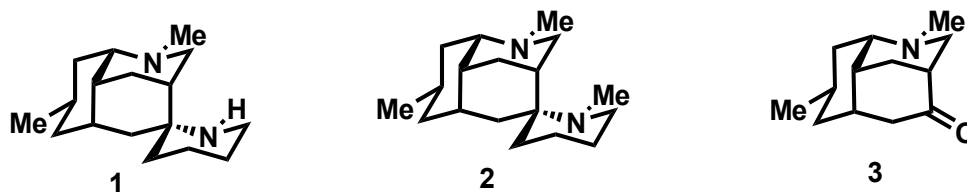


## Concise Total Syntheses of the *Lycopodium* Alkaloids (±)-Nankakurines A and B via Luciduline

### Abstract:



Studies on the extracts of *Lycopodium* club mosses continue to reveal a rich assortment of new alkaloid metabolites with interesting architectures and diverse biological activities. In 2006, Kobayashi and co-workers disclosed the structure of nankakurine B (**2**) and a revised assignment for nankakurine A (**1**), each isolated in minute quantities from *Lycopodium hamiltonii*. Low micromolar concentrations of nankakurine A (**1**) were found to induce the secretion of neurotrophic factors in a glial cell assay, which in turn promoted significant glial-cell-mediated morphological differentiation and neurite outgrowth in rat adrenal cells. Because the extent of neurodegeneration in disorders such as Alzheimer's and Parkinson's diseases can be correlated with diminished levels of neurotrophic support, there has been recent interest in small molecule nonpeptidyl agents capable of eliciting a neurotrophic response. The scarcity of nankakurine A (**1**) and nankakurine B (**2**), however, has not allowed for a more comprehensive evaluation of their neurobiological properties. The only previous total syntheses of nankakurines A (**1**) and B (**2**) by Overman and co-workers were achieved in 13 and 14 steps, respectively. In this presentation, total syntheses of the *Lycopodium* alkaloids nankakurines A (**1**) and B (**2**) have been accomplished in 6 and 7 steps, respectively, via a sequence that passes through a third *Lycopodium* alkaloid, luciduline (**3**), and forgoes the use of protecting groups on nitrogen. Key features include a short preparation of luciduline (**3**) followed by a concise and stereoselective aminoallylation/ring-closing metathesis protocol to fashion the spiro[3.3]heptane ring common to nankakurines A (**1**) and B (**2**). This novel synthetic sequence can potentially serve as an alternative and more efficient route to the two biologically active alkaloids and give access to sufficient quantities for more thorough and detailed biological assays.