Formal Total Synthesis of (±)-Cycloclavine

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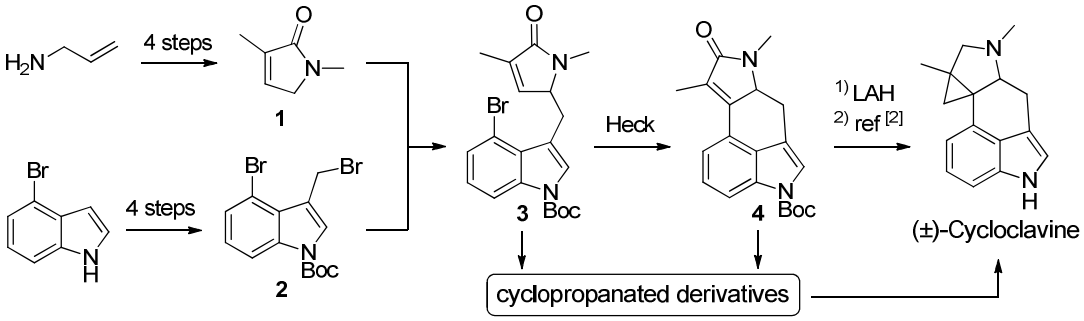
Among the ergot alkaloids, which are known for their various potent biological activities, the clavine-type alkaloid cycloclavine is noteworthy because of its unique pentacyclic structure.[1]

We here report a short convergent route to (±)-cycloclavine, which contains only eight linear steps and requires only four chromatographic purifications. The two building blocks **1** and **2** are synthesized in four linear steps from commercially available starting materials. They are linked by two consecutive coupling reactions, including a selective alkylation of a dienolate, which is the key step.



Compound **4** is easily reduced to complete the formal total synthesis of (±)-cycloclavine employing the cyclopropanation step by *Incze et al*.[2]. In order to improve the overall yield, we are currently working on the alternative cyclopropanation of amide precursors **3** and **4**, with a samarium-mediated process showing the most promising results so far.

References:

[1] D. Stauffacher *et al*., *Tetrahedron* **1969**, *25*, 5879-5887.

[2] M. Incze *et al*., *Tetrahedron* **2008**, *64*, 2924-2929.