Synthesis of β-Carboline Derivatives Using *in situ* Transmetalation

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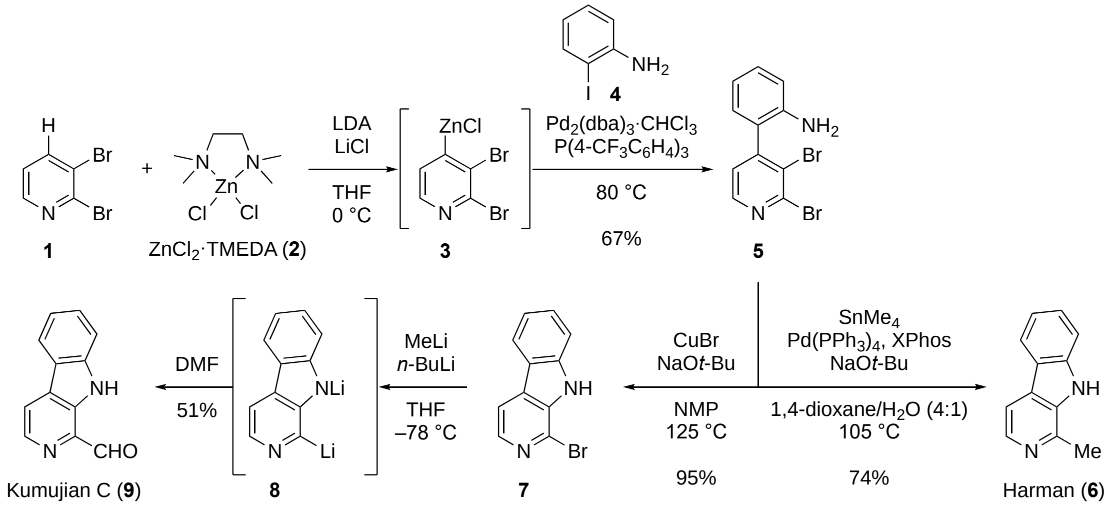
β-Carbolines bearing a substituent at the position 1 exhibit a wide range of biological activities. Although tryptamine derivatives undergo Pictet–Spengler reaction followed by oxidation to form β-carbolines,[1] an efficient synthetic method is still required. Herein, we report synthesis of functionalized β-carbolines by using *in situ* transmetalation of a pyridyllithium species generated from 2,3-dibromopyridine (**1**).

A THF solution of dibromopyridine **1** and $ZnCl_2$·TMEDA (**2**) was treated with LDA at 0 ℃ for 1 h to generate the corresponding organozinc **3** without the halogen dance reaction,[2] which was subjected to Negishi coupling with 2-iodoaniline (**4**) to provide 4-aryl-2,3-dibromopyridine **5** in 67% yield. The resultant biaryl compound **5** was converted to harman (**6**) in 74% yield in a single flask through Migita–Kosugi–Stille coupling and intramolecular Buchwald–Hartwig amination. Moreover, the intramolecular amination can be performed with the bromo group at the position 1 remained untouched. Thus, a combination of CuBr and NaO*t*-Bu was effective to form the β-carboline skeleton under heating conditions, providing 1-bromo-β-carboline (**7**) in 95% yield. This compound was treated with MeLi and *n*-BuLi to generate the dianion species **8**, which reacted with DMF to provide kumujian C (**9**) in 51% yield. In this presentation, details of the intramolecular amination will be discussed.



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