Total Synthesis of Lamellarins U and A3

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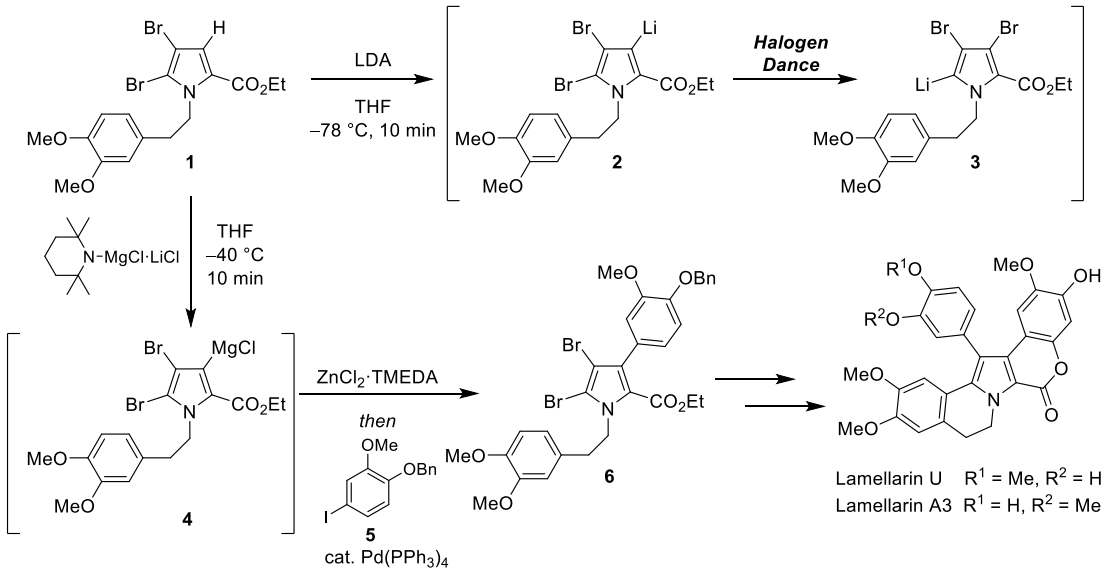
Lamellarins are marine natural products possessing a persubstituted pyrrole moiety.[1] We have recently reported a total synthesis of lamellarins through a halogen dance reaction of α,β-dibromopyrrole derivative **1**.[2] Treatment with LDA led to the formation of β-pyrrolyllithium **2**, which was transformed into a thermodynamically more stable α-pyrrolyllithium **3**. However, the two bromo groups at the two β positions have a similar reactivity, therefore the regioselective arylation was difficult.

Herein, we achieved a total synthesis of lamellarins U and A3 interrupting the halogen dance reaction.[3] Pyrrolylmagnesium reagent **4**, which was generated by deprotonative metalation of α,β-dibromopyrrole **1** using (TMP)MgCl·LiCl at –40 °C, was transmetalated into the corresponding organozinc species. Subsequent Negishi cross coupling with aryl iodide **5** furnished the desired monoarylated dibromopyrrole **6**. After lactonization, the lamellarin skeleton was constructed through a regioselective halogen–magnesium exchange at the α position followed by carboxylation and cyclization with stoichiometric palladium acetate. Lamellarin U and A3 were synthesized by the late-stage introduction of another aryl group.



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