Asymmetric Total Synthesis of (+)-Streptoverticillin

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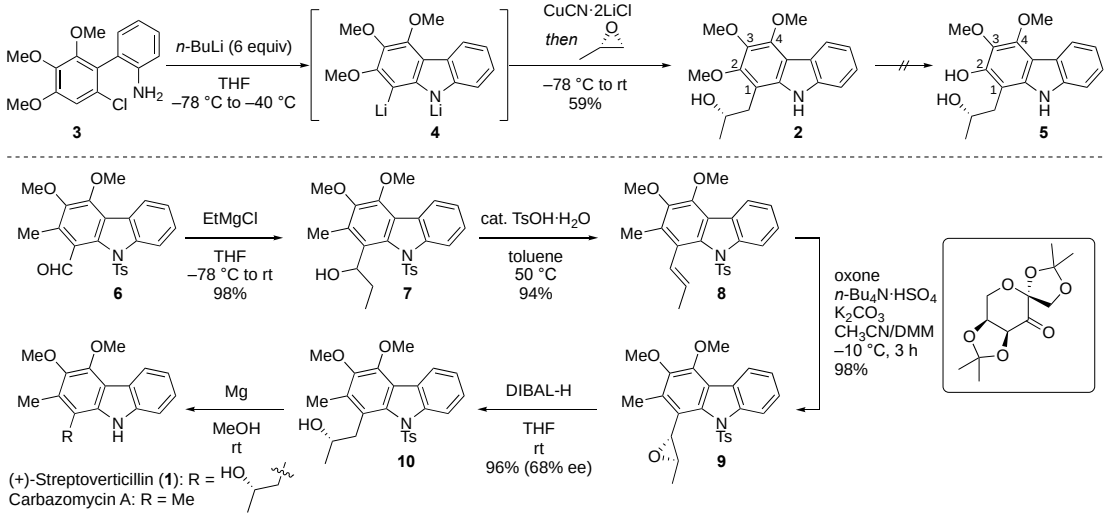
(+)-Streptoverticillin (**1**), isolated from *Streptoverticillium morookaense* by Wei and co-workers in 2007,[1] has a fully substituted benzene bearing a 2-hydroxypropyl group at the C-1 position. Recently we reported a total synthesis of structurally similar carbazomycins A−F using our original method to form carbazole via the aryne intermediate.[2] Herein, we report the asymmetric total synthesis of (+)-streptoverticillin.

The synthesis began with preparation of (2-hydroxypropyl)carbazole **2**. Treatment of the aminobiphenyl **3** with six equivalents of *n*-BuLi generated carbazole dianion **4** through aryne formation and subsequent nucleophilic addition of the tethered nitrogen, which reacted with (*S*)-propylene oxide in the presence of CuCN·2LiCl to give desired carbazole **2**. We attempted a regioselective demethylation of the methoxy group at the C-2 position,[2a,2c] but the desired product **5** was not detected. We next focused on an alternative approach using 1-formyl-2-methylcarbazole **6**, which we reported in the total synthesis of carbazomycins E and F.[2b] The ethyl group was incorporated to synthesize benzyl alcohol **7**. We then dehydrated the secondary alcohol under acidic conditions to yield alkene **8**. This alkene was subjected to Shi asymmetric epoxidation to provide epoxide **9**. Regioselective cleavage of the epoxide was performed with DIBAL-H to give the corresponding alcohol **10** in 68% ee. Finally, we achieved the asymmetric total synthesis of (+)-streptoverticillin (**1**) by removal of the tosyl group.



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