A Gram-Scale Total Synthesis of Carbazomycin A

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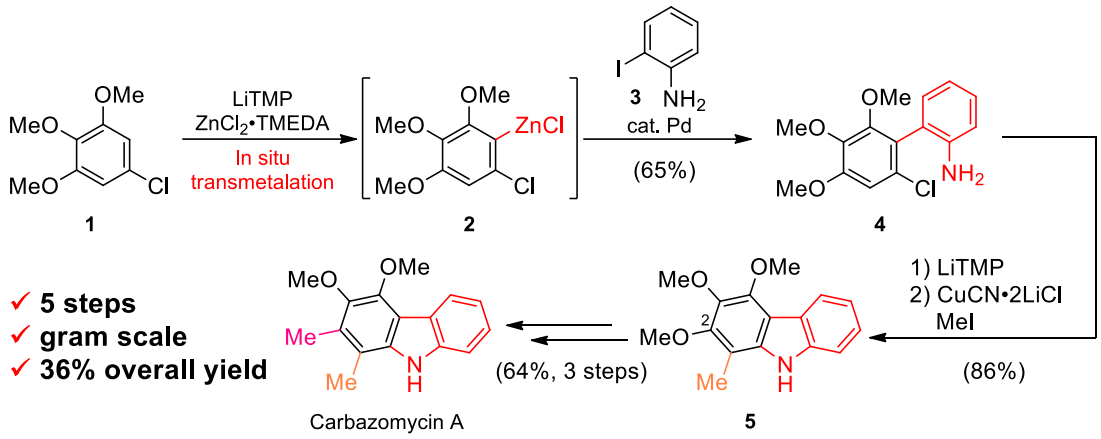
Carbazomycin A, isolated from *Streptomyces* strain H 1051-MY 10 by Nakamura and co-workers in 1980, is the first antibiotic containing a carbazole structure.[1] Knölker and Moody independently accomplished total synthesis of carbazomycin A in 1989.[2]

We report a new method to synthesize carbazomycin A on a gram scale which was realized by a $ZnCl_2$·TMEDA-mediated in situ transmetalation of a transient aryllithium. Our work commenced with the installation of a phenyl group onto the readily available chlorobenzene **1**. Treatment of **1** with LiTMP and $ZnCl_2$·TMEDA led to the smooth formation of the organozinc intermediate **2**, which was subjected to a palladium-catalyzed Negishi coupling reaction with iodoaniline **3** to yield the desired biaryl **4** as a precursor to carbazole. Without introducing a protecting group on nitrogen, biaryl **4** was converted to the trimethoxycarbazole **5** in a single flask utilizing a combination of LiTMP, CuCN·2LiCl complex, and MeI. A three-step transformation of the C2-methoxy group to the methyl group provided carbazomycin A in 5 steps in a 36% overall yield on a gram scale.



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