Gram-Scale Synthesis of Carbazomycin A–D

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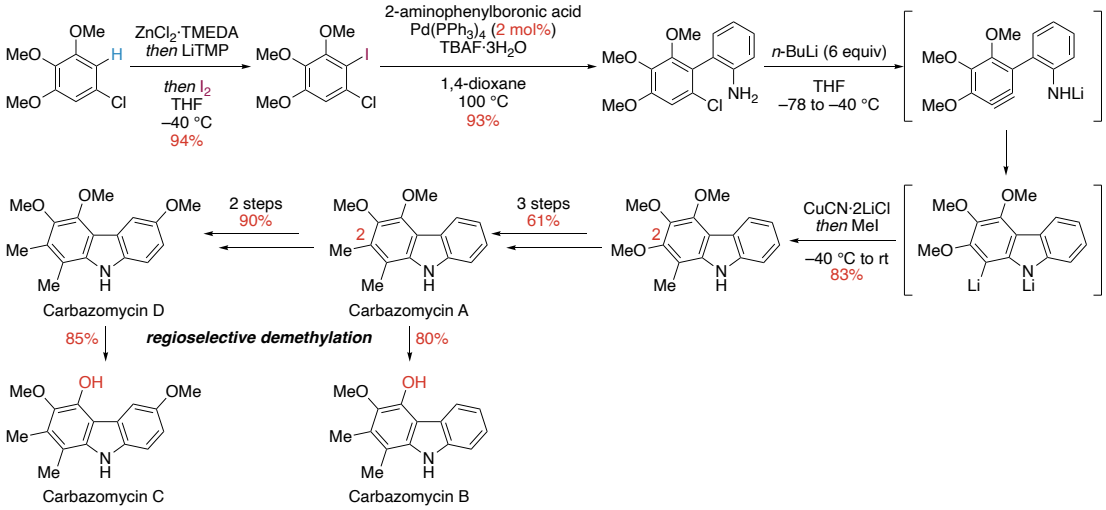
Carbazomycins A–D, isolated from *Streptoverticillium ehimense* by Nakamura and co-workers in the 1980s, are the first class of antibiotics containing a carbazole framework.[1] These compounds were characterized by a highly unsymmetrical structure, in which one of the benzene rings carries four electron-donating groups to form the fully substituted aromatic ring.

Herein, we achieved the total synthesis of carbazomycins A–D on gram scales. Iodination of the symmetrical trimethoxychlorobenzene and subsequent Suzuki–Miyaura coupling sequence gave the aminobiaryl bearing the chlorine atom. Treatment of this compound with six equivalents of *n*-BuLi led to the formation of the aryne, which underwent the intramolecular nucleophilic addition with the lithium amide tether to construct the carbazole framework. The use of the carbazole dianion enabled the synthesis of 1-methylcarbazole without protecting groups. Carbazomycin A was obtained by transforming the methoxy group at the C-2 position into the methyl group over three steps.[2] Subsequently, carbazomycin D was provided via the regioselective methoxylation from carbazomycin A over two steps. Finally, total synthesis of carbazomycins B and C was achieved through the regioselective demethylation of carbazomycins A and D, respectively.



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