Total Synthesis of Lycoricidine Enabled by Dearomative Dihydroxylation with Arenophiles

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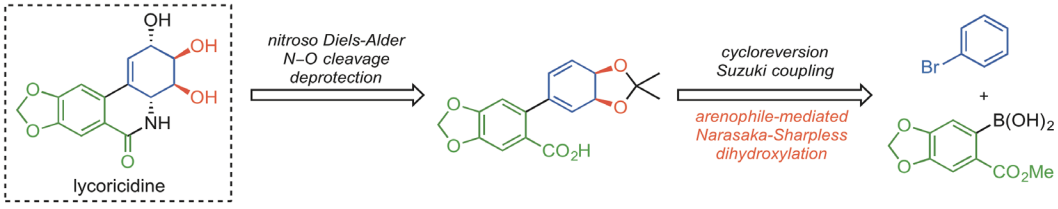
Dearomatization reactions represent an important class of transformations in the organic chemist's toolbox, having received significant attention and synthetic application in recent years. However, dearomative transformations for simple arenes that also introduce functionality are much less developed. We have recently disclosed a functionalization platform that uses small molecules, termed arenophiles, to facilitate dearomative dihydroxylation and diaminodihydroxylation of simple arenes. In the presented research, we have developed a unique Narasaka-Sharpless dihydroxylation/Suzuki coupling sequence that enables rapid access to dihydroxylated biphenyls. Moreover, this strategy has been applied to the expedient synthesis of the anti-cancer alkaloid lycoricidine, starting from feedstock bromobenzene and a simple arylboronic acid.



DNA-Catalyzed DNA Cleavage by a Radical Pathway with Well-Defined Products

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We report an unprecedented DNA-catalyzed DNA cleavage process in which a radical-based reaction pathway cleanly results in excision of most of a specific guanosine nucleoside. The deoxyribozymes generate hydrogen peroxide (H2O2) and lead to the same set of products as formed by the natural product bleomycin (3′-phosphoglycolate, 5′-phosphate, and base propenal), with product assignments by mass spectrometry and colorimetric assay. We infer the same mechanistic pathway, involving formation of the C4′ radical of the guanosine nucleoside that is subsequently excised. Consistent with a radical pathway, glutathione fully suppresses catalysis. Conversely, adding H2O2 from the outset strongly enhances catalysis. The deoxyribozymes do not require redox-active metal ions and function with a combination of Zn2+ and Mg2+, although including Mn2+ increases the activity, and Mn2+ alone also supports catalysis.