Aerobic Cross-Dehydrogenative Coupling of Tertiary Amines and Carbon Nucleophiles using Dehydrogenative Catalysis of 1,10-Bridged Flavin

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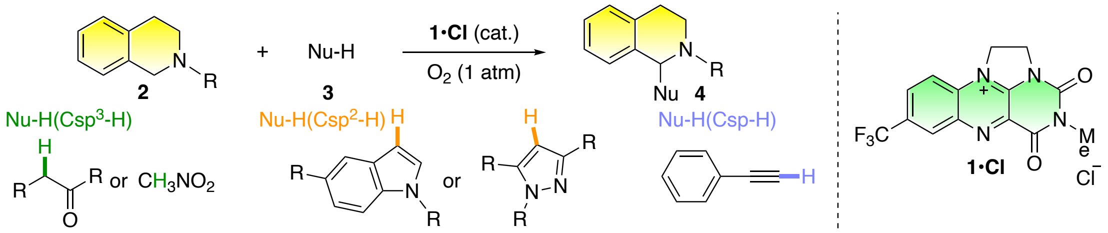
Flavin catalysts, developed by mimicking the enzymatic function of flavin monooxygenase, have attracted attention as biomimetic redox organocatalysts that enable efficient activation of oxygen molecules. Recently, we have applied the flavin catalysts to electrolysis, photoreactions, and a two-component catalyst system hybridized with an iodine catalyst.[1] Aerobic oxidation systems based on flavin catalysts have primarily been used for oxygen atom transfer reactions of various substrates, but their application to other oxidative transformations involving dehydrogenative oxidation is expected to provide environmentally friendly processes that meet the requirements of green chemistry. However, few successful examples of the dehydrogenative oxidation of substrates have been reported due to the low oxidative power of the commonly used flavin catalysts.

In this study, we focused on flavin catalysts with improved oxidation ability by designing the π-conjugated system with electron-withdrawing substituents. We anticipated that the catalyst would activate the α-C-H bond of tertiary amines by dehydrogenation, allowing cross-dehydrogenative coupling (CDC) with carbon nucleophiles to form a C-C bond. As a result, in the presence of a catalytic amount of 1,10-bridged cationic flavin catalyst **1・Cl**, the CDC reaction between tetrahydroisoquinolines **2** and sp^3, sp^2, and sp carbon nucleophiles **3** proceeded efficiently under molecular oxygen (1 atm) to give the corresponding product **4** in good yield.[2]



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