Poster Presentation
Inter-Disciplinary Explorations in Chemistry (I-DEC 2018)

"A Cooperative Catalyzed Enantioselective A^3 Coupling Reaction using Chiral Cu^{I}-*i*PrpyboxdiPh and *N*-Boc-(*L*)-Proline Complex: Application in the synthesis of (indol-2-yl)methanamines"

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Abstract: Indol-2-yl-methanamines are important structural motif found in many natural products and biologically active molecules (Figure 1, **1a-c**). Their diverse range of biological activities is evident from observed antihypertensive, antiviral antimalarial, anticancer, inhibitors of HIV protease, $5HT_{2B}$ receptor antagonists activities. For instance, calindol **1a** is a well known calcium sensing receptor, whereas chiral (indol-2-yl)methanamine sulfonamide **1b** act as endothelial differentiation gene 1 receptor antagonist for treatment of cancer. Tetrahydro-*β*-carbolines (Figure 1, **2a-c**) and Pyrazino[1,2-a]indoles (Figure 1, **3a-b**) are two significant classes of compound omnipresent in many alkaloids and pharmacophores. The core structure of these two classes is comprised of indol-2-yl-methanamines. Hence the development of efficient process to synthesis of indol-2-yl-methanamines has received much attention to the organic chemistry.

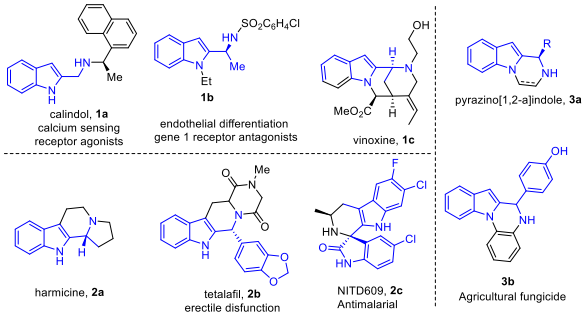
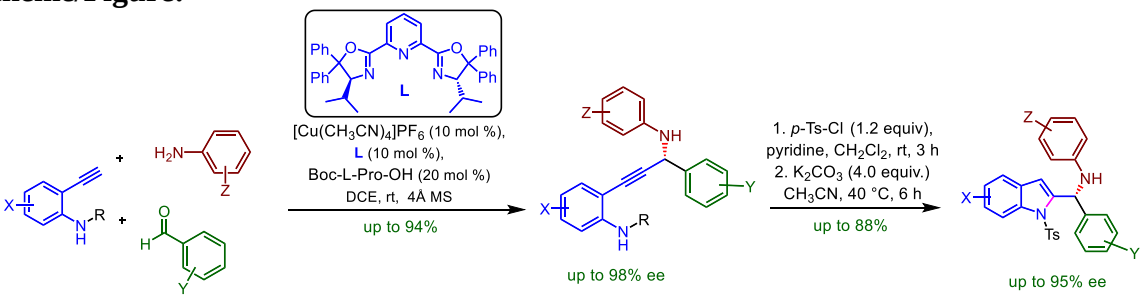


Figure 1. Selected biologically active Indol-2-yl-methanamines and related analogues

Catalytic enantioselective synthesis of biologically important indol-2-yl-methanamines has been less explored. Herein we demonstrated enantioselective synthesis of 2-aminopheyl propargylamines through one-pot three-component alkynylation reaction *via* cooperative catalysis using Cu^{I}-*i*PrpyboxdiPh complex with *N*-Boc-(*L*)-proline at ambient condition. Structurally diverse functionalized amines, aldehydes and 2-ethynyl anilines reacted smoothly and afforded the corresponding products in synthetically viable yields (up to 94%) with excellent enantioselectivities (up to 98%). Finally, propargylamines were efficiently converted in to indol-2-yl-methanamines in good to excellent yields with enantioselectivities (up to 95%) over two steps.

Scheme/Figure:



Scheme 1: Synthesis of Chiral propargylamines and indol-2-yl-methanamines

References and Notes:

1. (a) Bisai, A.; Singh, V. K. Org. Lett. **2006,** *8,* 2405**.** (b) Lu, Y.; Johnstone, T. C.; Arndtsen, B. A. J. Am. Chem. Soc. **2009**, *131*, 11284.