Title: **STEREOSELECTIVE VINYLOGOUS ALDOL REACTIONS OF 3-ALKYLIDENE-2-OXINDOLES**

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Abstract

The thesis entitled "**Stereoselective Vinylogous Aldol Reactions of 3-Alkylidene-2-oxindoles**" deals with development of stereoselective vinylogous aldol reactions of 3-alkylidene-2-oxindole with activated carbonyl compounds and vinylogous nucleophilic addition of 3-alkenyl-2-silyloindole to reactive isobenzopyrolium intermediate for the synthesis of various highly functionalized scaffolds. The highlight of the work described in this thesis lies in the highly stereoselective reaction described that enables realization of challenging reaction yielding stereochemically pure compounds that are utmost importance for pharmaceutical application.

This thesis is mainly focused on the stereoselective synthesis of vinylogous adducts and has been divided into four chapters. The first chapter describes the importance of stereochemistry and methodology to develop the stereoselective molecule as well as the concept of vinylogy and different type of vinylogous nucleophile. This chapter emphasizes the organocatalytic approaches to obtain the stereoselective adduct.

Chapter 2 describes the reactivity of vinylogous 3-alkylidene-2-oxindole for methodology. In this chapter, we have established an enantioselective vinylogous aldol reaction of 3-alkylidene 2-oxindoles with α-ketoesters providing a chiral quaternary δ−hydroxy−3-alkylidene oxindoles catalyzed by bifunctional quinine derived thiourea. The activation of vinylogous nucleophile and electrophile through synchronized H-bond afforded aldol adduct in high yield (upto 92%) while obtaining high levels of regio- (100% γ-selective), diastereo (*E/Z* = >19:1) and enantio-control (upto 99% ee). A broad range of enantio-enriched tertiary alcohols have been synthesized. The regio, *E/Z* selectivity and absolute configuration of chiral centre of the aldol products were established by single crystal X-ray analysis of an analogue.

Chapter 3, deals with the asymmetric synthesis of chiral 4-hydroxy 4′-substituted pyrazolones by vinylogous aldol reaction of pyrazole-4,5-diones with 3-alkylidene-2-oxindoles. In this chapter we describe the enantioselective vinylogous aldol reaction of 3-alkylidene 2-oxindoles with pyrazole-4,5-diones providing a chiral 4-hydroxy 4′-subsituted pyrazolone catalyzed by bifunctional quinine derived amide catalyst. An extensive optimization of quinine catalysts has been performed. This reaction proceeds by the activation of vinylogous nucleophile and electrophile through formation of instantaneous H-

bond affording high yield (upto 98%) with high levels of regio- (100% γ-selective), diastereo (*E/Z* = >19:1) with moderate enantiocontrol (upto 86:14 *er*). With this reaction a broad range of 4-hydroxy 4′-substituted pyrazolone has been synthesized.

Chapter 4 describes the silver tetrafluoroborate catalyzed vinylogous addition to reactive isochromenylium intermediate generated *in situ* for the synthesis of functionalized 1*H*-isochromenes. A series of functionalized 1*H*-isochromenes comprising of oxindole core have been synthesized. The aliphatic, as well as aromatic substituted alkynes, of *ortho*-alkynyl arylaldehydes were successfully tested for the regioselective intramolecular 6-endo-*dig*-cyclization followed by vinylogous addition of substituted 3-alkenyl-2-silyloxindole leading to functionalized 1*H*-isochromene in high yield (upto 82%) and high levels of regio- (100% γ-selective), diastereo (*E/Z* = >19:1) control.