INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

Name of the Student	:	Megha Balha
Roll Number	:	156122029
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Name of Thesis Supervisor(s)	:	Prof. Subhas Chandra Pan
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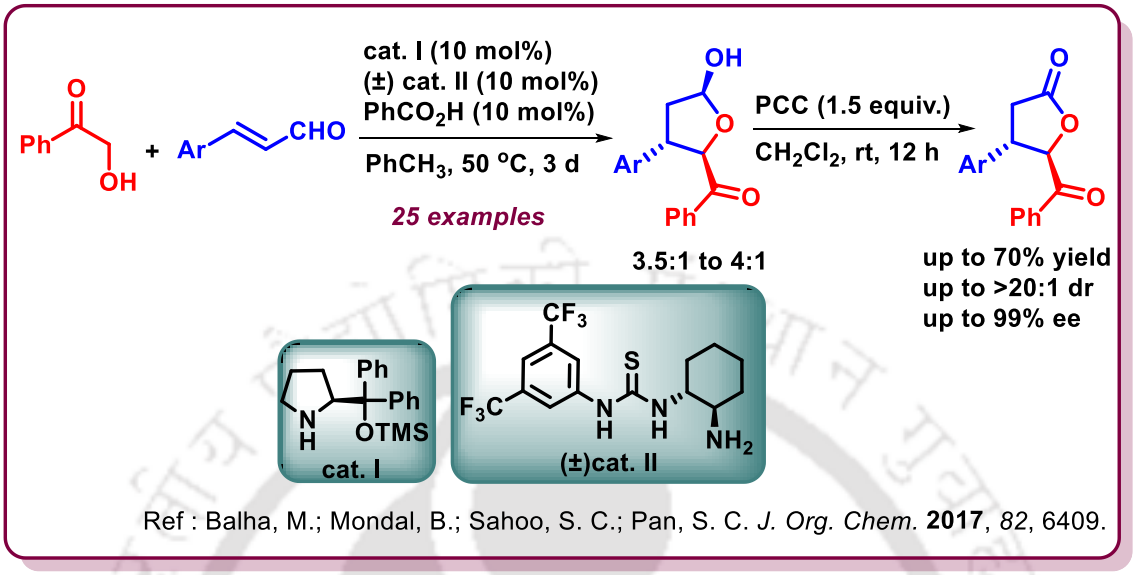
SHORT ABSTRACT

The present thesis, entitled as ***"Organocatalytic Asymmetric Reactions with Hydroxy Containing Carbon Nucleophiles"*** is divided into five chapters, based on the obtained results of experimental works performed during the complete course of the Ph.D. research period.

Chapter 1: Overview

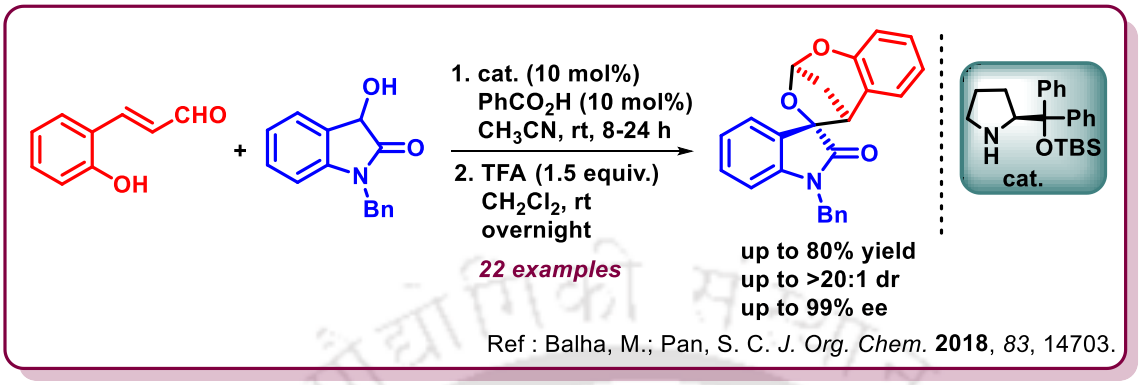
Chapter 1 contains a general overview of asymmetric organocatalysis with special emphasis on the generic modes of catalyst activation, induction, and reactivity. A brief description of the reactivity of α-hydroxy carbonyl compounds is also discussed here.

Chapter-II: Organocatalytic Asymmetric Michael-Hemiacetalization Reaction between 2-Hydroxyacetophenones and Enals: A Route to Chiral *β,γ*-Disubstituted *γ*-Butyrolactones



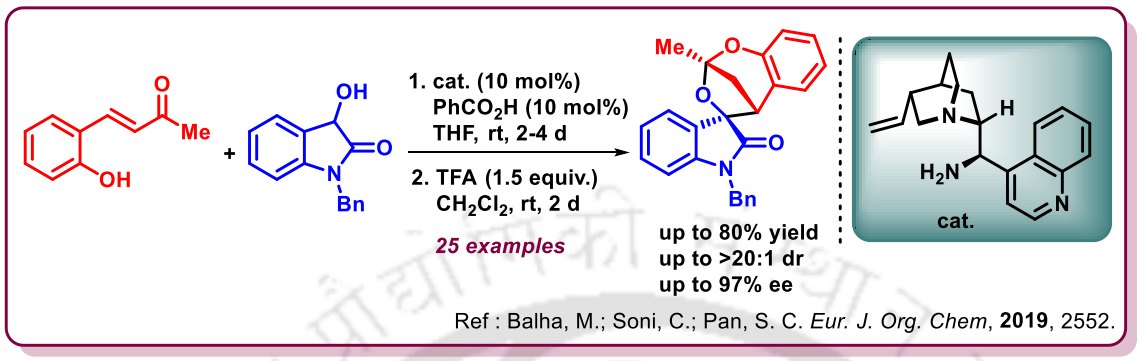
The nonracemic *γ*-butyrolactone motif is found to be present in a variety of biologically significant natural products, including antibiotic and antitumor agents. Further, it serves as an important building block in synthetic organic chemistry. However, the synthesis of chiral *β,γ*-disubstituted *γ*-butyrolactone derivatives have been less reported. In this chapter, we have reported a highly asymmetric synthesis of *β,γ*-disubstituted *γ*- butyrolactones from a Michael-hemiacetlization reaction between 2-hydroxyacetophenones and *α,β*-unsaturated aldehydes followed by pyridinium chlorochromate (PCC) oxidation. The combination of a primary amine and a secondary amine catalyst was found to be the best choice for this methodology. The desired products were obtained in high yields with excellent enantio- and diastereoselectivities. The utility of our method was then demonstrated by subjecting the hemiacetal to several useful organic transformations.

Chapter-III: Organocatalytic Asymmetric Synthesis of Bridged Acetals with Spirooxindole Skeleton



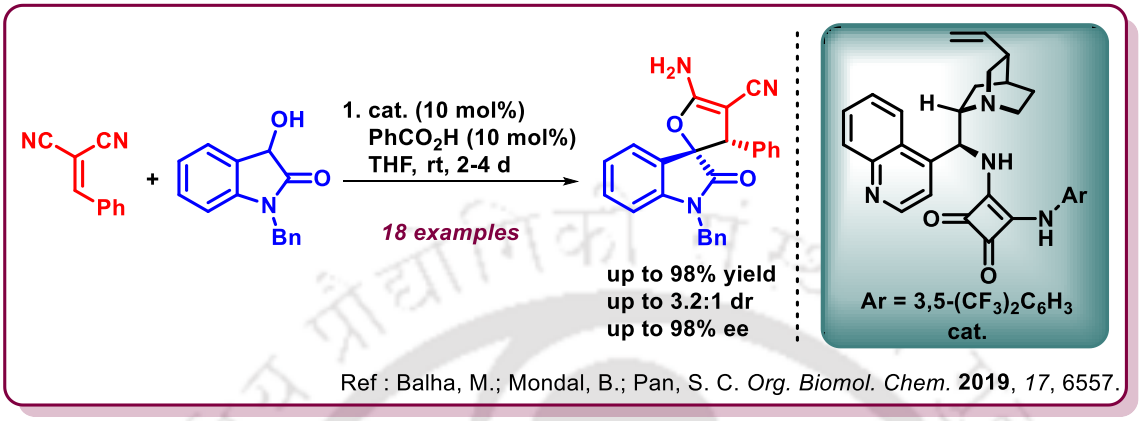
Chiral *O*,*O*-acetals are important structural motifs present in a range of natural products and pharmaceuticals and display a wide range of bioactivities. In recent years, considerable efforts have been devoted for the asymmetric synthesis of these compounds. However, catalytic asymmetric synthesis of spirooxindoles having bridged acetal structure is still not known despite the high medical importance of bridged acetals and spirooxindoles individually. In this chapter, we have discussed the first highly diastereo- and enantioselective synthesis of bridged *O*,*O*-acetals embedded with spirooxindoles. Dioxindoles and 2-hydroxy cinnamaldehydes were employed as the reaction partners in this method. The desired products were obtained via diaryl prolinol TBS ether catalyzed Michael reaction followed by acetal formation with TFA. The desired spirooxindole products were obtained in good to high yields with excellent enantio- and diastereoselectivities in operationally simple reaction conditions. Also, few products have been further functionalized via Suzuki coupling reaction.

Chapter-IV: Organocatalytic Asymmetric Synthesis of Bridged *O,O*-Ketals with Spirooxindole Motif



Chiral *O,O*-acetals and ketals are prevalent in many natural products and pharmaceuticals and a wide range of bioactivities are associated with them. Thus, a large number of synthetic research groups are engaged in the asymmetric synthesis of these compounds. Realizing the potential of chiral *O,O*-acetals, and ketals for medicinal chemistry, in this chapter, we embarked on the first organocatalytic enantioselective synthesis of bridged *O,O*-ketals embedded with spirooxindoles. Dioxindoles and *ortho*-hydroxy-benzylidene acetones were engaged as the reaction partners in this method. The methodology proceeds through primary amine catalyzed conjugate addition, followed by diastereoselective ketalization with TFA. The spirooxindole products were isolated in good to high yields with high diastereo- and enantioselectivities under mild and operationally simple reaction conditions. To exhibit the synthetic utility of our method, few derivatives were also prepared. Given the high pharmaceutical significance of spirooxindoles and bridged ketals, our products might be useful for drug discovery.

Chapter-V: Organocatalytic Asymmetric Synthesis of Dihydrofuran-Spirooxindoles from Benzylidene Malononitriles and Dioxindoles



Spirooxindoles are privileged structural motifs frequently found in a range of natural products and pharmaceutical molecules. Thus, significant interest has been observed over the years from a large number of chemists for the development of efficient and practical synthetic methods for this class of structural frameworks. In this chapter, we described the first organocatalytic enantioselective synthesis of dihydrofuran-spirooxindoles, having a linkage at the 2-position of the dihydrofuran motif. Dioxindoles and benzylidene malononitriles were employed in this method. The desired spirooxindole products were obtained *via* a Michael reaction followed by a Pinner reaction and isomerization, and good to high yields with moderate diastereo- and good to high enantioselectivities were observed. To demonstrate the synthetic potential of our method, a Suzuki coupling reaction was carried out on several spirooxindole products. Given the high medicinal importance of spirooxindoles and dihydrofurans, our products are expected to be useful in drug discovery.