INDIUM(III) CHLORIDE CATALYZED TRANSFORMATIONS ON CARBOHYDRATES: STEREOSELECTIVE SYNTHESIS OF UNSATURATED GLYCOSIDES, DISACCHARIDES AND AZASUGARS

by

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DEPARTMENT OF CHEMISTRY

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Dedicated to my beloved parents and sisters

Mr. K. Paramathevar

Mrs. P. Parvathyammal

Mrs. Vasantha Rajendran

Mrs. Selvi selvam

Mrs. Yogamani Balamurugan

CERTIFICATE

This is to certify that the thesis entitled "**INDIUM(III) CHLORIDE CATALYZED TRANSFORMATIONS ON CARBOHYDRATES: STEREOSELECTIVE SYNTHESIS OF UNSATURATED GLYCOSIDES, DISACCHARIDES AND AZASUGARS** ", being submitted by **Mr. P. Nagaraj** to Indian Institute of Technology, Delhi, for the award of the degree of **Doctor of Philosophy**, is a record of bonafide research work carried out by him. Mr. P. Nagaraj has worked under my supervision and guidance and has fulfilled all the requirements for the submission of a Ph.D. thesis, which to my knowledge has reached the requisite standard and is worthy of consideration for the award of Ph.D. degree.

The work embodied in this thesis has not been submitted, in part or full, to other University or Institute for the award of any degree or diploma.

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(P. Nagaraj)

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ABSTRACT

The thesis titled "**Indium(III) Chloride Catalyzed Transformations on Carbohydrates: Stereoselective Synthesis of Unsaturated Glycosides, Disaccharides and Azasugars**" presents the research work carried out on the utilization of glycals for the synthesis of unsaturated glycosides, disaccharides, Perlin aldehydes and novel unsaturated azasugars.

Glycals and glycal derived chiral intermediates are important class of precursors that serve as versatile building blocks for the syntheses of many biologically important compounds.

Chapter I: This chapter highlights the literature reports on the use of $InCl_3$ as an efficient Lewis acid catalyst for various transformations in the area of carbohydrate chemistry.

Chapter II: This chapter describes the efficiency of $InCl_3$ in effecting the Ferrier rearrangement of glycals possessing a free hydroxyl group at *C*-3 position in presence of a wide array of alcohols including monosaccharides and phenols.

Anhydrous $InCl_3$ (5 mol%) has been shown to efficiently catalyze the Ferrier rearrangement of glycals possessing a free hydroxyl group at *C*-3 position with a variety of oxygenated nucleophiles to afford the corresponding 2,3-unsaturated glycosides in high yields at ambient temperature. This methodology obviates the need for protecting the *C*-3 hydroxyl group of glycals. The reaction works in equal ease with both 4,6-di-*O*-benzyl-D-glucal and 4,6-di-*O*-benzyl-D-galactal. The mildness of $InCl_3$ makes this approach compatible for glycosyl acceptors with acid labile groups. A significant observation was that in the case of 4,6-di-*O*-benzyl-D-galactal, the otherwise usually formed side product, namely 2-deoxy galactosides, were not obtained in the present case.

Chapter III discusses a new approach to the synthesis of 2-*C*-methylene-α-*O*-glycosides via $InCl_3$ catalyzed rapid and a highly stereoselective [1,3]-alkoxy migration of glycal ethers. A

possible explanation for the exclusive formation of α-glycosides has been provided based on some preliminary calculations.

Chapter III also reports a direct allylic substitution reaction of the hydroxyl group of 2-*C*-hydroxymethyl glycals with oxygenated nucleophiles to afford a variety of 2-*C*-methylene alkyl and aryl glycosides as well as disaccharides in high yields. This protocol surpasses the existing methods for the synthesis of 2-*C*-methylene glycosides as it obviates the need for functionalizing the allylic hydroxy group of glycals. The interest of this methodology relies on the extremely mild conditions required even with a free hydroxyl group at the allylic position of the glycals and that too only with a catalytic amount of $InCl_3$.

A direct synthesis of an α,α-(1→1)-linked disaccharide derivative via $InCl_3$ catalyzed domino reaction of 2-*C*-hydroxymethyl galactal has also been reported in chapter III. A detailed mechanistic investigation on its formation reveals that the reaction proceeds through a self Ferrier rearrangement followed by a stereoselective 1,3-alkoxy migration.

Chapter IV discusses about the use of $InCl_3$-CH_3CN-H_2O as an efficient catalyst-solvent combination for the synthesis of Perlin aldehydes and related systems from glycals. An interesting observation was that the product distribution was found to be dependent on the nature of the protecting groups. While acetylated glycals afforded the Perlin aldehydes directly with $InCl_3$ and water, benzylated glycals on the other hand provided the hemiacetals under identical condition. The methodology reports a non-mercurial approach to Perlin aldehydes. Noteworthy is that this reaction is more facile as well as highly selective with glycals possessing a hydroxyl as a leaving group than with a benzyloxy group. Extension of this reaction to 2-*C*-hydroxymethyl glycals resulted in the formation of the corresponding hemiacetals, which were further transformed in to unsaturated azasugars with an *exo*-methylene group at *C*-2 position.

Glycosidase inhibition studies reveal that these compounds display selectivity in inhibiting glucosidases rather than galactosidases.

TABLE OF CONTENTS