The thesis entitled "**Divergent and stereoselective approach for the synthesis of some pyrrolidine, piperidine and pyrrolizidine iminosugars"** is divided into three chapters.

CHAPTER- I:

Section A: This section describes the introduction to the carbohydrate mimics or glycosidase inhibitors. Carbohydrates play an important role in many biological processes and in many disease progressions. A set of enzymes are involved in the breaking and making of the saccharide linkages of these carbohydrates. Inhibitors of these enzymes will have therapeutic potential. The compounds inhibit these enzymes are called as glycosidase inhibitors. Depending upon their modification, carbohydrate processing enzymes are of two types i.e. *glycosyltransferases* and *glycosidases.* These enzymes can be very specific with regard to the type of long-chain carbohydrate they work on.

Glycosidase inhibitors are classified into carbasugars, thiosugars and iminosugars depending on the replacement of ring oxygen by a methylene group, sulfur and nitrogen respectively (Figure 1). Some of the popular compounds belonging to this class are tamiflu, acarbose, and voglibose which are the aminocarbasugars and miglitol and miglustat which are iminosugars. These compounds are available in the market as drugs and some more are in the clinical trials at different phases.

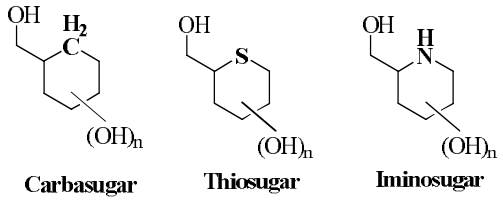


Figure 1

Iminosugars are of different types like polyhydroxy pyrrolidine, piperidine, pyrrolizidine, indolizidine, nortropanes and azepanes (Figure 2). Because of their prodigious biological activity against Gaucher disease, diabetes, hereditary lysosomal storage disorder, cancer metastasis, viral infections like HIV, dengue, influenza etc have attracted the attention of both chemists and biologists.

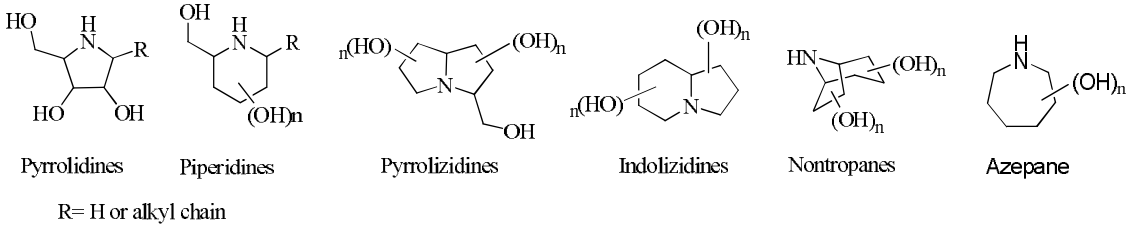


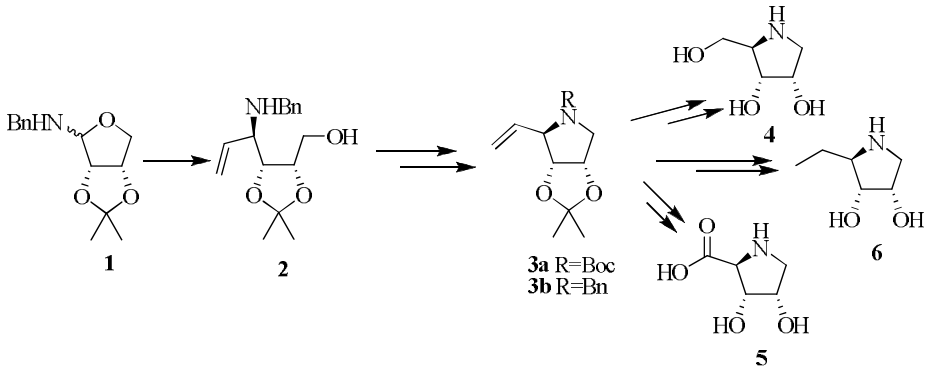
Figure 2

Statement of Problem

Section B: Stereoselective synthesis of 1,4-dideoxy-1,4-imino-derivatives of D-ribitol, ethyl-erythritol and (-)-2,3-*trans*-3-4-*cis*-dihydroxyproline.

Introduction: Naturally occurring compound 1,4-dideoxy-1,4-imino-D-ribitol **4** shows the strong specific inhibitory activity of eukaryotic polymerases and is a potent anti-HIV agent and also it acts as an anti-proliferative and anti-neoplastic agent. Extensive studies have shown that the methylamino and 5-*O*-alkyl and 5-*O*-aryl derivatives exhibit anti-cancer activity. (-)-2,3-*trans*-3-4-*cis*-dihydroxyproline **5**, a constituent of decapeptide Mefp1 and ethyl erythritol **6**, shows α-galactosidase, α-L-fucosidase, and β-D-glucosidase activity.

Methodology: There are some reports for the synthesis of compounds **4**, **5** and **6** with different strategies; here we synthesized all these compounds by highly stereoselective addition of Grignard reagent on lactamine prepared from D-ribose (Scheme 1).



Scheme 1

Results & discussion: Vinyl amino derivative **2** was prepared by stereoselective addition of vinyl magnesium bromide on lactamine **1.** All the target compounds **4**, **5** and **6** were obtained from vinyl pyrrolidine derivatives **3a** and **3b** which in turn obtained from the vinyl amino derivative **2**. Compound **2** was prepared from isopropylidene erythrose **1** which was prepared from D-ribose.

Conclusion: We have developed a short, common and stereoselective method for the synthesis of 1,4-dideoxy-1,4-imino-D-ribitol **4**, (-)-2,3-trans-3-4-*cis*-dihydroxyproline **5** and ethyl-erythritol **6**.

Statement of Problem

CHAPTER-II: Synthesis of some polyhydroxy pyrrolidine and piperidine iminosugars from ribosylamine

Introduction: This chapter describes the synthesis of some naturally occurring pyrrolidine and piperidine iminosugars. L-Lyxitol **7** is a α-mannosidase inhibitor and it is also a competitive inhibitor of α-D-galactosidase of the coffee bean while its *N*-benzyl derivative **8** is a strong competitive inhibitor α-L-rhamnosidase of naringinase. Trihydroxy-piperidine **9** shows the inhibition of β-glucosidase and α and β-galactosidase. *Epi*-isofagomine **10** and **11** are showing β-glucosidase and β-galactosidase inhibitory activity (Figure 3).

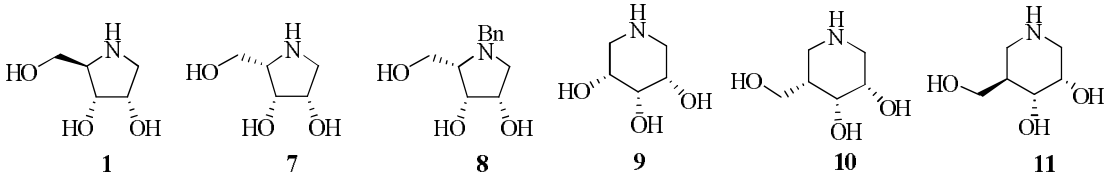
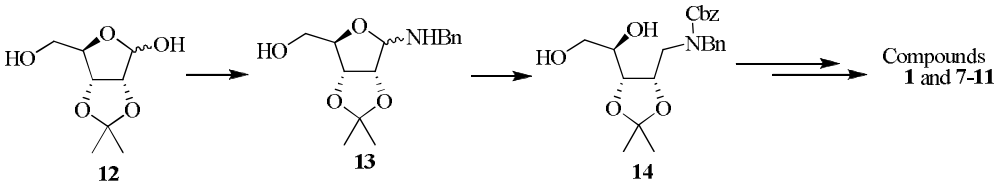


Figure 3

Methodology: The synthesis of compounds **1** and **7-11** are reported with different starting materials in the literature. The method developed by us is simple and could synthesize all these compounds within few steps from a common intermediate. Selective acylation, tosylation, cbz deprotection and the 5-*exo*-tet opening of epoxide are key steps in our common strategy for these compounds (Scheme 2).



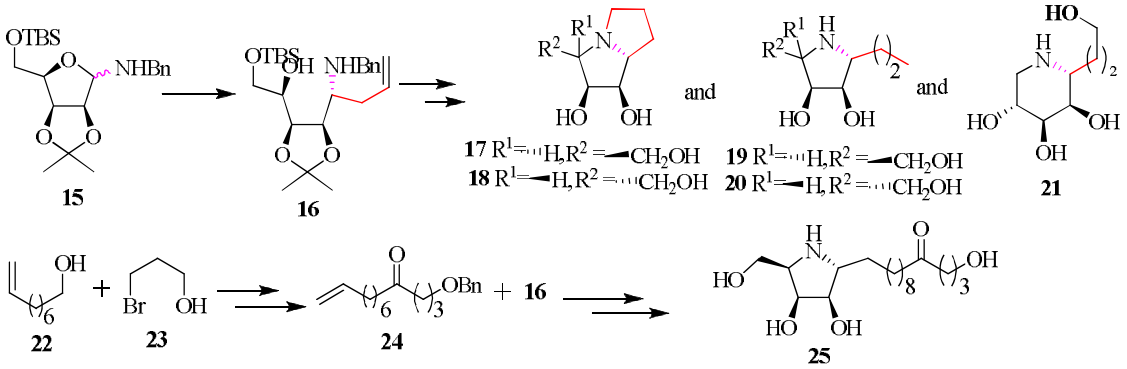
Scheme 2

Results & discussion: Compounds **1** and **7-11** were synthesized from the imperative intermediate **14** which was prepared from ribosylamine **13** which in turn prepared from acetonide protected D-ribose **12** (Scheme 2).

Conclusion: A divergent approach for the synthesis of some polyhydroxylated pyrrolidines and piperidine iminosugars was developed. This strategy is useful to make different iminosugars in short possible time to study their therapeutic activity.

Statement of Problem

CHAPTER-III: Stereoselective synthesis of polyhydroxy pyrrolidine, piperidine and pyrrolizidine iminosugars from lyxosylamine and efforts toward the total synthesis of broussonetinine A



Scheme 3

Introduction: This chapter deals with the synthesis of compounds **17-21** and **25**. Compound 2-*epi*-hyacinthacine A_2 **17** is a potent inhibitor of α-L-rhamnosidase while 2-*epi*-hyacinthacine A_2 **17** and (-)-7a-epi-hyacinthacine A_1 **18** shows activity against α-L-fucosidase. Pyrrolidines **19** and **20** are the moderate inhibitors of α-L-fucosidase and α-L-rhamnosidase and 1-deoxy-D-*altro*-homonojirimycin **21** which is a selective β-glucosidase inhibitor. Naturally occurring broussonetinine A **25** exhibit strong inhibition of α-glucosidase, β-glucosidase, β-galactosidase and β-mannosidase (Scheme 3).

Methodology: We have synthesized iminosugars **17-21** by highly stereoselective addition of allyl zinc on lyxosylamine. Pyrrolidine compound **19** is a truncated broussonetinine A **25**.

Results & discussion: Target compounds **17-21** were synthesized from a common intermediate **16** by the stereoselective addition of Zn and allyl bromide. Intermediate **16** was synthesized from commercially available D-lyxose. Some attempts for the synthesis of broussonetinine A **25** was also made from **16.**

Conclusion: We have developed a stereoselective approach for the synthesis of pyrrolizidines **17-18**, pyrrolidine **19-20** and piperidine iminosugars **21**.