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Synthesis of Polyhydroxy Azasugar via Chiral Epoxyaldehyde

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Abstract: Naturally occurring azasugar and homologous compounds have been the object of numerous synthetic efforts because these classes of compounds have interesting biological activities and the flexibility for the synthesis of chiral alkaloid comounds. As part of a program directed toward the preparation of glycosidase inhibitors, we prepared bicyclic perhydrooxazino- and oxazolopyridine from aminoalcohols and epoxyaldehyde as a common synthetic intermediate.

The piperidine and pyrrolidine nucleus can be frequently found in the structure of numerous naturally ocurring alkaloids and synthetic compounds with interesting biological and pharmacological properties. As a consequence, the development of general methods for the enantioselective synthesis of piperidine and pyrrolidine derivatives has been the subject of considerable synthetic efforts.

Among these alkaloid compounds, polyhydroxylated piperidines and pyrrolidines are of particular interest in the development of glycosidase inhibitor which interferes with the biosynthesis of glycoproteins. Glycoproteins located in the outer surface of cell play important roles in a variety of biological recognition events such as cell-cell communication, cancer metastasis, inflammation and viral infection. These glycoproteins are synthesized by a series of hydrolysis and glycosylation reaction in a common oligosaccharide unit to the nascent protein chain. Among all the types of enzymes that lead to the mature form of the glycoproteins, glycosidases, in particular, are key players. They are capable of cleaving glycosidic bond from the oligosaccharide already bound to the protein chain. For this reason, a number of inhibitors of glycosidases have been developed for obtaining the interesting biological responses such as antiviral, anti-HIV, anticancer, antifeedant and immunoregulatory

activities.

We describe our studies in the enatioselective preparation of diversly substituted piperidines and pyrrolidines from a common synthetic intermediate, epoxyaldehyde, and various aminoalcohols, and also show an efficient method to prepare substituted chiral pyrrolidines from (S)-phenylglycinol.