Stereocontrolled total synthesis of iminosugars and their lipophilic derivatives with potential therapeutic activity

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Iminosugars, or azasugars, are carbohydrate analogues belonging to the polyhydroxylated alkaloids family. They contain an endocyclic nitrogen instead of the oxygen characteristic of sugars 1. Thanks to their similarity with the sugars they are inhibitors of fundamental enzymes such as glycosidase and glycosyltransferase 2. Due to this activity these molecules are studied for their therapeutic potential in a vast array of diseases, 3 such as diabetes, glycosphingolipid storage disorders, and viral infections.

Our synthetic approach involves a stereocontrolled total synthesis starting from the inexpensive and commercially available cis-1,4-butanediol. Simply by suitably choosing of the chiral ligand in the two asymmetric reaction steps (asymmetric epoxidation and asymmetric dihydroxylation) and of the nucleophile in the epoxy ring opening, it is possible to access several iminosugar structures.

Moreover, according to several studies, the selectivity and power of these inhibitors significantly increase when lipophilic chains are introduced 4,5,6,7,8, allowing them to enter the cells’ lipophilic double layer, reaching the central nervous system. From this perspective, the functionalization of primary and secondary hydroxyl groups, introducing the alkyl chains in various steps of the synthetic pathway, allowed us to obtain several derivatives. These molecules could be tested for their biological activities and for their ability to immobilize on magnetic nanoparticles and silver nanoclusters for drug delivery applications.

References:

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