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Review

Applications of controlled inversion strategies in carbohydrate synthesis

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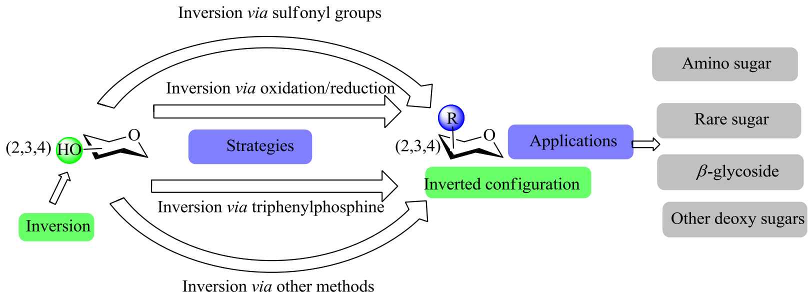
Graphical Abstract



Inversion strategies *via* sulfonyl groups, oxidation/selective reduction, *etc*. have been wildly used in introducing functionalities like amino group, abundantly synthesizing rare sugars and constructing the *β*-configurations in glycosylation.

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ABSTRACT

Carbohydrates play critical roles in mediating many biological processes, such as cell growth, migration, cell-cell adhesion, fertilization, signal transduction and immune response. The increasing demands for the study of these molecules greatly facilitate the development of carbohydrate synthesis. Inversion strategies *via* sulfonyl groups, selective reductions, *etc*. have been used to synthesize corresponding inverted configurations. This review focuses on the mechanisms of these inversion methods and their applications in constructing amino sugars, rare sugars and *β*-configurations in glycosylations.

1. Introduction

Carbohydrates not only serve as energy sources and structural elements but also play a very important role as signalling molecules in cells. Their biological significance includes cell proliferation, differentiation, migration, cell-cell adhesion, trafficking, and receptor binding and activation [1, 2]. Recently, intensive attention has been drawn to the synthesis of oligosaccharides, the main component of capsular polysaccharides (CPS) and lipopolysaccharides (LPS) on the bacterial cells related to immune responses [3-7]. For example, chemically synthesized polysaccharides have been employed in the development of carbohydrate-based vaccines [8-11].

Epimerization of secondary alcohols on carbohydrates towards the corresponding converted structures are ubiquitous in carbohydrate chemistry. For example, the synthesis of amino sugars, thio-sugars, halogen-sugars and rare sugars can be obtained by inversion methods from common saccharides. The "controlled inversion strategies" in carbohydrate synthesis [12], playing a key role in carbohydrate-related pharmaceutical research and development, are summarized in this review, including mechanisms and applications. Several different inversion strategies have been developed based on nucleophilic reactions of sulfonates, sequential oxidation/reduction routes, the Mitsunobu reaction with triphenylphosphine (PPh_3), enzymatic inversion methods and epimerization by non-classical acetalization.

2. Inversion *via* sulfonyl groups

The utilization of the sulfonyl groups for inverting a given hydroxyl group is a well-known method in carbohydrate chemistry, followed by S_N2 displacement with a variety of reagents, such as acetate, benzoate, thioacetate, a nucleophilic acetamido group, and others. The direct replacement of sulfonyl groups by nucleophilic reagents undergoes an S_N2 mechanism, which can be traced to the Richardson-Hough rules recently updated by Hale *et al.* [13, 14]. Among these epimerization reactions, the nitrite-mediated Lattrell-Dax

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