Enzymes in Organic Chemistry: Transglycosilation

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Abstract

Therapeutic actions of a significant number of drugs today rely on the presence of carbohydrate moiety. Combinations of carbohydrates and other specific molecules, known as glycosides, comprise a wide range of drug types. To meet these aspects remarkable advances have been made in recent years in exploiting transglycosylation activity for oligosaccharide and glycoconjugate synthesis.

The relatively recent recognition of carbohydrates as a medically relevant class of biomolecules has led to the investigation or therapeutic agents based on glycan structure or mimics thereof. The development of carbohydrate-based therapies depends on the synthetic accessibility of novel glycoconjugates for study. Unfortunately, decades of synthetic research have yet to provide analogous methods for automated oligosaccharide synthesis. This is the result of carbohydrate structure, and is mainly due to the fact that even the simplest monosaccharides contain several hydroxyl groups of very similar chemical reactivity. When attempting to construct even a simple oligosaccharide, each hydroxyl group must be distinguished from the others in order to obtain the desired product, with correct regio- and stereochemistry. The hydroxyl differentiation process has generally been tedious, making arduous shuffling of protection group and lengthy synthetic routes that hallmark synthetic carbohydrate chemistry. Chemical synthesis of glycosidic moieties are mainly based on time-consuming protection and deprotection strategies, activation or metal catalysis, but are often accompanied by the formation of unwanted diastereomers and low yields. However, these difficulties can be overcome by the application of enzymatic syntheses. Both glycosyltransferases and glycosidases have been intensely studied for synthetic purposes [1]. Transglycosylation reactions are well known and widely used methods for glucoside syntheses [2]. In comparison with glycosyltransferase-catalyzed reaction that use complex sugar nucleotide as the donor and usually has very stringent substrate specificity, glucosidase-catalyzed transglycosylation has several advantages, including the use of readily available donor substrates and the relaxed substrate specificity for acceptors. Nevertheless, the use of glycosidases in synthesis is subject to two major limitations: the low transglycosylation yield and the product hydrolysis. Significant progresses have been made in recent years to overcome these problems. In the last few years some research groups reported transglycosylation reaction with very high glycosylation yield [3]. The other important discovery in the enzymatic synthesis of glucosides is the invention of glycosyntheses, a class of novel glycosidase mutants that can promote glycosidic bond formation when a suitable activated glycosyl donor is provided, but do not hydrolyze the newly formed glycosidic linkage [4].

The synthesis involving enzymatic transglycosylation has emerged as a powerful method for making complex oligosaccharides and glycoconjugates that are valuable for functional studies and for biomedical applications as well. The full potential of enzymatic transglycosilation is unfolding in front of us these days.

References


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Received September 25, 2012; Accepted September 27, 2012; Published September 29, 2012


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