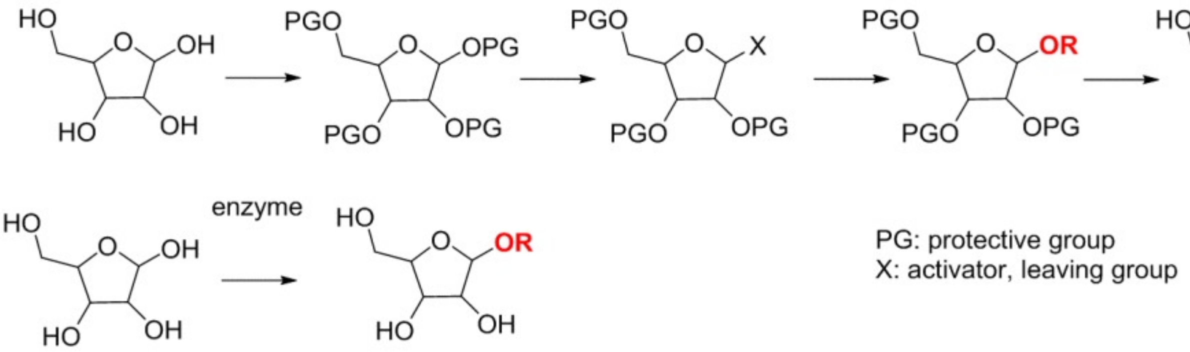
Operationally simple reactions with unprotected carbohydrates – an application of organocatalysis

Carbohydrates are ubiquitous in nature. They play an important role as an energy reservoir as well as they are the resource of countless biomaterials, such as cellulose or chitin. This importance has challenged chemists at all times to exploit or to imitate the natural metabolic transformations of carbohydrates (production of alcohol, paper industry, pharmaceutical industry etc.). In contrast to the ubiquitous occurrence of carbohydrates in biological systems there are but few examples that allow an easy and controlled handling of unprotected carbohydrates in academia and industry. Carbohydrates are characterized by a multitude of defined configured and even chemical different hydroxyl groups. For this reason, carbohydrates can create complex networks of hydrogen interactions between molecules or even in the same molecule under physiological conditions.

The successful differentiation of the hydroxyl groups is necessary to execute a reaction effectively. Enzymes can discriminate the different hydroxyl groups of carbohydrates on the base of the hydrogen bonds.



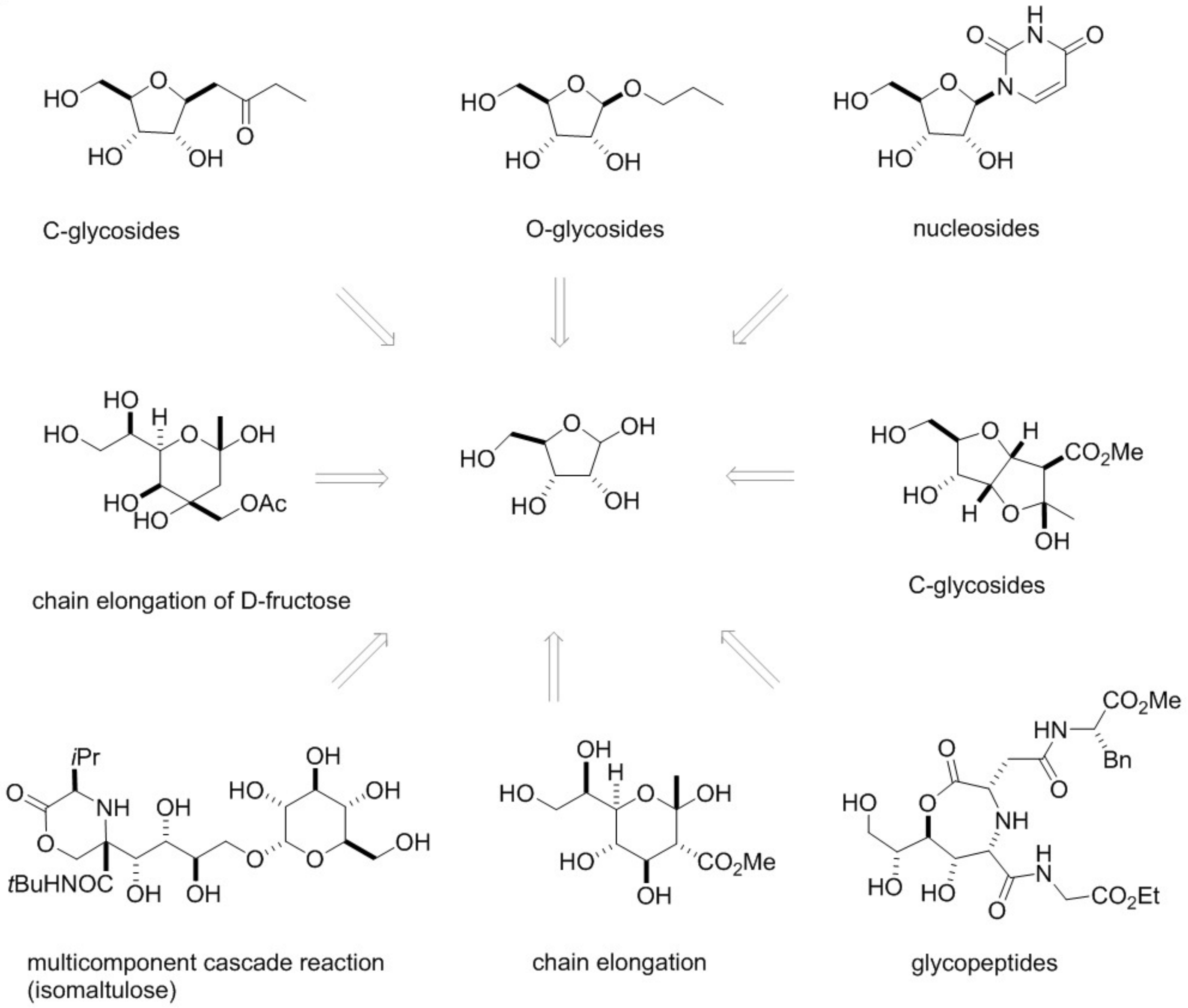
Scheme 1. Comparison of glycosylations by enzymes and by chemists

However, this easy differentiation of the extremely high number of different hydroxyl groups by enzymes poses a big challenge for a chemist. Many methods and concepts have been developed to overcome this issue. In general, chemists solve this problem by the extensive use of protective groups to shield and to deactivate the hydroxyl groups. This difference is illustrated by the O-glycosylation process of carbohydrates achieved by a chemists or by Nature (Scheme 1).

The full protection of all hydroxyl group is followed by the selective activation of the anomeric carbon atom. Subsequent glycosylation, followed by final deprotection, yields the corresponding glycoside. In contrast, the same glycoside can be selectively accessed by enzymatic glycosylation of unprotected carbohydrates. Nature works makes do without protective groups. A chemist needs four reaction steps where nature needs but a single reaction of unprotected carbohydrates in an enzyme-catalyzed glycosylation.

When used with protected carbohydrates the hydrogen bond network is affected. Thus, hydrogen bonds cannot be utilized for selective transformations. The valuable gift of nature – the hydrogen bond network - is completely destroyed when carbohydrates are protected.

Organic chemistry has a sub-discipline since 15 years now, called organocatalysis, which aims at all processes that are catalyzed by an organic compound. Most of these processes are based on the formation and utilization of hydrogen bonds. In this regard organocatalyzed reactions can imitate natural enzyme-catalyzed processes.



Scheme 2. Organocatalyzed reactions with unprotected carbohydrates

During our investigations in the field of organocatalysis we have developed several amine-catalyzed C-C bond formation processes with unprotected carbohydrates. In these reactions we have selectively exploited the carbonyl function of unprotected carbohydrates – the hemiacetal function at the anomeric carbon atom. Thus, we have successfully realized highly selective C-C bond formation processes with unprotected carbohydrates. An overview of this research is depicted in Scheme 2. These operationally simple processes give access to several important carbohydrates structures, namely O- and C-glycosides, nucleosides, novel glycopeptides, chain elongated higher carbohydrates and exceptionally branched carbohydrates. All these novel reactions offer extremely high stereo- and chemoselectivities.

Publication

The long underestimated carbonyl function of carbohydrates – an organocatalyzed shot into carbohydrate chemistry.
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