Adventures around the anomeric centre towards glycomimetics

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The universal role of glycans in the vast majority of biological phenomena became a scientific commonplace during the past 2-3 decades. Glycans have been shown ubiquitous to all cells in nature and essential in all known forms of life. Due to the intrinsic complexity of such molecules and the difficulties in chemical syntheses of glycosides (such as variable ring size, necessity of complicated protection-deprotection strategies, issues of stereoselectivity in the formation of glycosidic linkages) it is still a challenge to get natural glycans by pure chemical means. In addition, the sensitivity of the glycosidic bond to acidic and especially enzymatic hydrolysis represents another obstacle to the wide use of glycans as biological probes. These problems raise an ever increasing demand toward glycomimetics, i. e. molecules that resemble natural glycans' structure and/or biological function. Such compounds may be obtained by simpler synthetic pathways, are stable to hydrolysis, offer several derivatization possibilities, and can be used as glycobiological tools as well as leads for drug design.

The presentation will give a brief overview of glycomimetic sugar derivatives and an outlook to marketed drugs based on glycomimetics as active ingredients. Design and syntheses of glycomimetics in the author's laboratory in the context of inhibition of glycogen phosphorylase as a potential antidiabetic therapy will be demonstrated by anomeric spirocycles and *C*-glycosyl heterocycles. The effect of modifications in the sugar part on the inhibition will also be discussed. Physiological studies with the prepared inhibitors showed hyperglycaemic effects, restoration of whole body insulin sensitivity, and improvement of pancreatic β-cell function. Synthesis and applications of anhydro-aldose tosylhydrazones, *exo*-glycals and 1-C-substituted glycals as well as the use of thiol-ene coupling reactions to result in a variety of glycomimetic structures will make the second part of the lecture.