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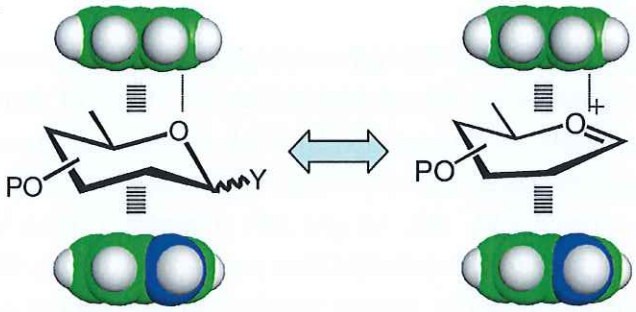
Grant Title: Aromatic Stacking in glycochemistry: Can glycosyil cations be tamed?

(a) Abstract

Central to carbohydrate chemistry is the *glycosylation reaction*, which implies the formation of a glycosidic bond between donor and acceptor molecules. It is commonly accepted that this process requires, in most cases, formation of transient ionic intermediates named glycosyl oxocarbenium and/or oxocarbenium-like transition states, whose stability and conformational properties determine to a large extent the reaction outcome. In principle, glycosyl cations can be partially stabilized by means of inter-molecular interactions. Indeed, this ability is key for the activity of glycosidases and glycosyl-transferases, and typically requires the participation of anionic functional groups such as carboxylates. The present project is based on the hypothesis that, similarly, stacking interactions involving electron-rich aromatic systems can be employed to stabilize glycosyl oxocarbenium intermediates and modulate the course of glycosidation reactions. In order to test this assumption, we have followed a bioorganic approach involving the following steps:



a) First, we have successfully designed and synthesized a variety of model compounds, all of them comprising a glycosidic donor fragment, which is involved in CH/π stacking interactions with an aromatic platform. Key structural parameters of the models, including the stacking geometry, the chemical nature of the anomeric leaving groups and the configuration at the different pyranose positions, have been systematically varied.

b) Second, selected models have been additionally prepared in its ^{13}C-labelled form in order to monitor glycosidation reactions by NMR, facilitating the detection of short-lived intermediates.

c) Third, the structural properties of the synthesized models have been dissected under the experimental conditions typically employed for glycosidation reactions, by low temperature NMR experiments. These studies confirmed the presence of CH/π bonds involving the glycosidic donor and the aromatic platform and allowed the determination of the preferred staking geometry.

d) As a final step, we have recently started a detailed reactivity study, considering a variety of acceptors and glycosidation conditions. This work is currently underway and the obtained results will be reported in due course.