
Synthesis of constrained C-glycosidic analogues of Tn antigen

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Résumé

Tumor associated carbohydrate antigens (TACAs) are highly present on cancer cells, but almost no detectable on normal cells. Therefore, these components are of great interest as therapeutics targets, particularly in anticancer vaccines. By incorporating such structures into this kind of vaccine, the immune system should produce a more efficient response against cancer cells. However, the chemical instability of the *O*-glycosidic link in biological system towards glycosidases presents a major downside of their use in this purpose.(1) The replacement of the glycosidic bond is well known to afford more stable analogues such as *C*-glycosidic ones. Furthermore, constrained analogues of Tn antigen in vaccine could improve the anticancer immune response.(2)

Very recently we focus our attention on the synthesis of original constrained *C*-glycosidic analogues of the Tn antigen. For that, a synthetic strategy based on a (3+2) cycloaddition between a *C*-vinylGalNAc **1** and a chiral cyclic nitrone **2** has been developed (scheme 1). This key step provided access to constrained *C*-glycosidic analogues stereoselectively and regioselectively controlled(3). Moreover, the cleavage of N-O bond of the isoxasoline ring and the post-functionnalization will allow the access to several original C-glycosides analogues of Tn antigen. Conformational study of constrained analogues, using DFT calculations and NMR experiences, has been performed. The global synthesis will be presented as well as the conformational study.

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*Intervenant