Advancements in *Trypanosoma cruzi* Mucins: Synthesis of a penthasaccharide constituent of core 2 mucins and derivatives

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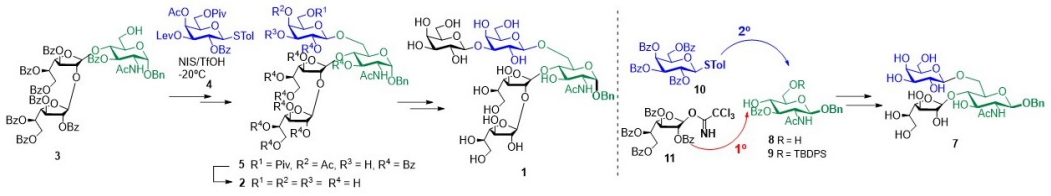
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Trypanosoma cruzi, the etiological agent of Chagas disease, is a protozoan parasite with a complex life cycle that alternates between hematophagous triatomine vectors and mammals, including humans. Mucin-like glycoproteins are major components of the *T. cruzi* surface. The oligosaccharides in the mucins are α-*O*-linked to the protein *via* GlcNAc and its composition is characteristic of each differentiation stage and strain.[1] In the internal cuticle of the rectal ampoule of the insect vector, epimastigotes are attached leading its differentiation into highly infectious forms as metacyclic trypomastigotes.

We have been developing synthesis methods for Gal*f*-containing oligosaccharide family (core 2) to explore their structure-activity relationship and biological implications through enzymatic studies and assays. We now present the synthesis of pentasaccharide β-D-Gal*f*-(1→2)-β-D-Gal*f*-(1→4)-[β-D-Gal*p*-(1→3)-β-D-Gal*p*-(1→6)]-α-D-GlcNAc (**1**) and tetrasaccharide **2** as benzyl glycosides. Previously, the synthesis of **1** was performed by a [3+2] convergent strategy with moderate yield. In this case, a sequential strategy was followed using trisaccharide **3** with an internal Gal*f* as acceptor and thiogalactopyranoside **4** as donor to give the corresponding tetrasaccharide with excellent yield. Deprotection of the orthogonal Lev group gave **5**. The differences of both strategies will be discussed.

Ex vivo binding assays in the presence of chemically synthesized oligosaccharides as α-benzyl glycosides by our group allowed the identification of the structure β-D-Gal*p*(1→6)-[β-D-Gal*f*(1→4)]-D-GlcNAcα-OBn (**6**) trisaccharide, as adhesion determinant. [3]

The β-benzyl glycoside of **6** was synthetized with the aim of studying the influence of the anomeric configuration of the GlcNAc unit on the adhesion process. Unlike the synthesis of trisaccharide α-analogue, the β-glycoside **7** was exclusively obtained by the introduction of the Gal*p* unit on secondary OH-4 followed by the Gal*f* unit on primary OH-6. Trisaccharide **7** inhibited the adhesion of epimastigotes to the inner lining hindgut, showing that the anomeric configuration is not relevant in the adhesion process providing more information about the involved receptor.



[1] G. A. Kashiwagi, V. M. Mendoza, R. M. Lederkremer, C. Gallo-Rodríguez,*Org. Biomol. Chem.* **2012**, *10*, 6322-6332 and references therein.
[2] Cámara, M. d. l. M.; Balouz, V.; Centeno Cameán, C.; Cori, C. R.; Kashiwagi, G. A.; Gil, S. A.; Macchiaverna, N. P.; Cardinal, M. V.; Guaimas, F.; Lobo, M. M.; de Lederkremer, R. M.; Gallo-Rodríguez, C.; Buscaglia, C. A. *PLoS Negl. Trop. Dis.* **2019**, 13, e0007418.