SYNTHESIS OF BENZOBOROXOLE DERIVATIVES AS RECEPTORS FOR SIALIC ACID

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Sialic acid is an important diagnostic biomarker, due to its presence as the terminal residue in the glycoproteins expressed by cancer cells. In a glycoprotein, it is linked to various other saccharides assuming its α anomeric conformation, which is characterised by the presence of the carboxyl group in the axial position [1]. Conversely, when unbound, the β anomeric conformation of sialic acid is present, with the carboxyl group in the equatorial position. Despite its relevance as a biomarker, sialic acid receptors are scarce and not without their own limitations. Sialic acid can be recognized by lectins, proteins able to bind sugars. The interactions involved between the sugar and the amino acid residues of lectins consist of H-bond, electrostatic and CH-π interactions [2]. However, lectins have many disadvantages including stability issues, low binding affinity and limited availability since they are difficult to purify from natural sources. Therefore, and in order to overcome current limitations, we have been developing small molecules as synthetic receptors for the recognition of sialic acid with high affinity and specificity. A series of benzoboroxole derivatives were designed and synthesised. Benzoboroxoles are able to covalently bind the sialic acid through formation of esters with the hydroxyl groups of the glycerol chain [3]. In order to increase the affinity, additional binding sites were incorporated in the benzoboroxole derivatives to specifically interact with the carboxylic group in the anomeric position. Our benzoboroxole derivatives are able to provide a dual interaction with sialic acid due to their functionalization with a positively charged group, providing an electrostatic interaction with the negatively charged carboxylate group. The binding affinity of the benzoboroxole receptors towards both anomers of sialic acid (α and β) was measured by isothermal titration calorimetry at 4 different pH values. These studies provide highly valuable information on how the affinity for the two anomers is influenced by tuning the design of the benzoboroxole-based receptor.

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