ABSTRACT

This thesis describes a new method for the synthesis of pseudodisaccharides containing a carbasugar analogue attached to a “true” sugar. The methodology is based on a Diels-Alder cycloaddition of vinyl sugars and appropriately substituted pyran-2-ones, followed by chemical manipulation of the resulting cycloadducts. The thesis also describes the synthesis of inhibitors of Golgi α-mannosidase II and glucokinase.

The first chapter is a comprehensive survey of the reported synthetic routes to pseudodisaccharides from the literature.

The results and discussions are presented in chapter 2. This chapter starts by discussion of the preparation of vinyl sugars and pyran-2-ones and the regio- and stereoselectivity of their cycloadditions. This is followed by reporting the chemical manipulations of these cycloadducts and the synthesis of a pseudodisaccharide. Cycloadducts are shown to lose carbon dioxide at elevated temperatures to afford dihydrobenzenes. The loss of the bridging carbon dioxide from the cycloadducts is experimentally and computationally investigated. The resulting dihydrobenzenes are shown to also be useful as precursors in the synthesis of pseudodisaccharides. The chemical manipulation of these dihydrobenzenes is used towards the synthesis of a pseudodisaccharide.

The third and fourth chapters focus on the synthesis of new inhibitors of Golgi α-mannosidase II and glucokinase respectively. A range of 6-aminoglucose and mannose derivatives were prepared and tested for the inhibition of Jack bean α-mannosidase, but were found to lack any inhibition. Similarly, a range of 6-triazologlucose derivatives were prepared but were found to lack any cytotoxicity.

The fifth chapter contains the details of the preparation, experimental procedures and spectroscopic characterisation of the synthesised chemical compounds.

Rate calculations are reported in Appendix I and the X-ray crystallographic data are presented in the Appendix II.

Key words: pseudodisaccharide, carbasugar, cycloaddition, Diels-Alder, synthesis

Supervisors: Dr. Kamyar Afarinkia and Proff. Laurence Patterson