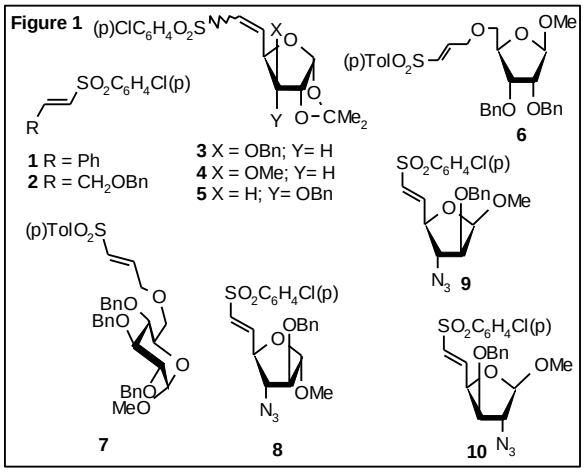
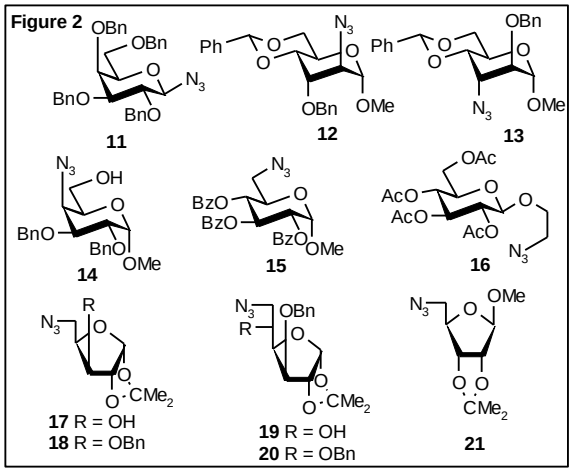
ABSTRACT

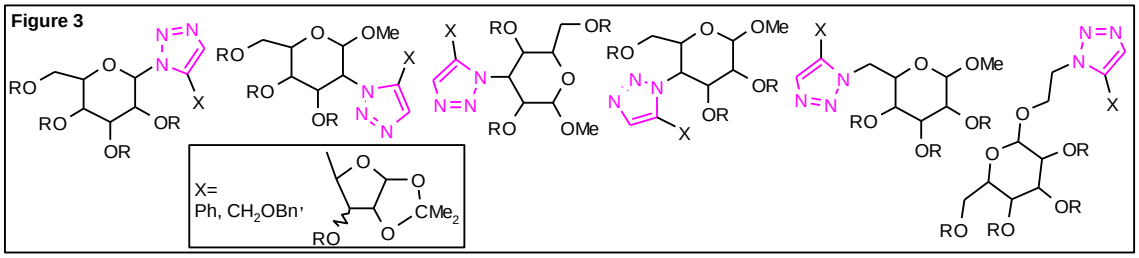
1,5-Disubstituted 1,2,3-Triazolylated Saccharides from Vinyl Sulfones: Syntheses and Applications

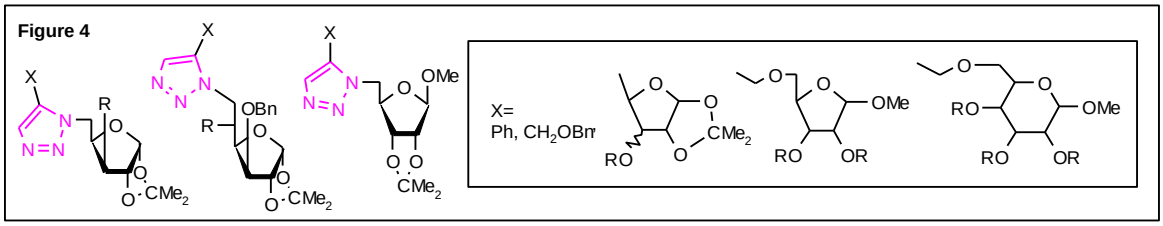
The copper (I)-catalyzed azide-alkyne cycloaddition (CuAAC) reaction constitutes a substantial improvement of the classical Huisgen thermal dipolar cycloaddition reaction affording only 1,4-disubstituted 1,2,3-triazoles (1,4-DTs). CuAAC has been widely used in the field of carbohydrate chemistry to afford a large number of 1,4-DT modified carbohydrates having interesting biological properties. The usefulness of 1,4-DTs generated interest to synthesize 1,5-DTs. There are only few scattered reports on the synthesis of 1,5-DT modified carbohydrates.

Vinyl sulfones carrying electron withdrawing fluoroalkyl groups reacted with azidosugar to afford only 1,4-DT modified carbohydrates. However, it was established from our laboratory that alkyl- and aryl-vinyl sulfones, more available than vinyl sulfoxides reacts efficiently with organic azides to afford only 1,5-DTs. Therefore, ten structurally varied vinyl sulfones (Figure 1), synthesized from easily available starting materials or commercially available reagents. The vinyl sulfones **1**-**7** were reacted with the azido-pyranosides **11**-**16** and azido-furanosides **17**-**21** (Figure 2) to afford triazolyl pyranosides (Figure 3) and triazolyl furanosides (Figure 4) respectively.



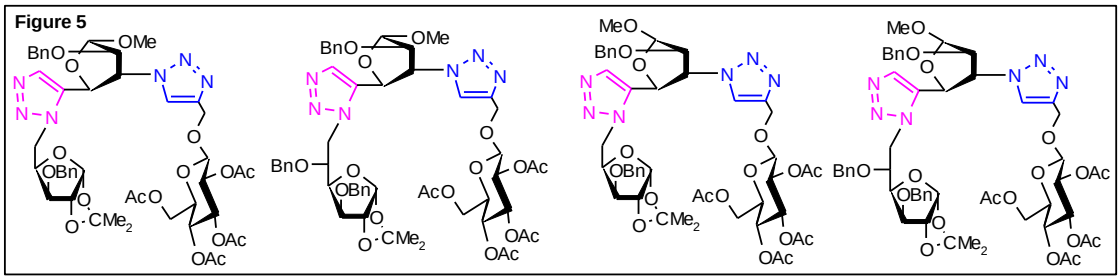






Some of the 1,5-DT linked disaccharides used as reducing as well as capping agents for the synthesis of silver nanoparticles (AgNPs). The AgNPs were formed in suspension having different shapes and sizes and unlike natural disaccharides, the triazolyl linked disaccharides were found to be stable under the conditions to produce AgNPs. The AgNPs showed high toxicity against bacterial strains *E. coli* and *S. aureus*. Some of the selected 1,5-DT linked disaccharides also emerged as potent RNase A inhibitors with inhibition constant (K_i) ranging from 284-50 μM. All the inhibitor molecules were competitive and reversible in nature.

The vinyl sulfone modified hex-5-eno-azidofuranosides **8** and **9** were reacted with the azidosugars **18** and **20** under refluxing conditions to afford the corresponding 1,5-DTs which were then coupled with 2-propynyl-2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside under CuAAC condition to afford the corresponding 1,5- and 1,4-DT linked heterotrisaccharides (Figure 5). However, the vinyl sulfone **10** was unstable and completely decomposed under the reaction condition and hence did not produce any 1,5-DTs.



In conclusion 1,5-DT modified monosaccharides and 1,5-DT linked disaccharides were synthesized for the first time using vinylsulfones and azidosugars. The general strategy presented in this thesis offers a practical route to simple as well as more complex structures. We avoided the use of expensive ruthenium based reagents and in most of the cases reactions were performed "on" water. The 1,5- and 1,4-DT linked trisaccharides were also synthesized for the first time.

Key words: 1,5-DT modified carbohydrates, cycloaddition, "on" water, vinyl sulfones, azido sugars, 1,5- and 1,4-DT linked trisaccharides.