

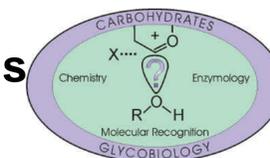


Thio-linked Oligosaccharides: Better Immunogens?

Synthesis and Binding Studies of S-linked Trisaccharides Related to *Shigella flexneri* Variant Y LPS Antigens

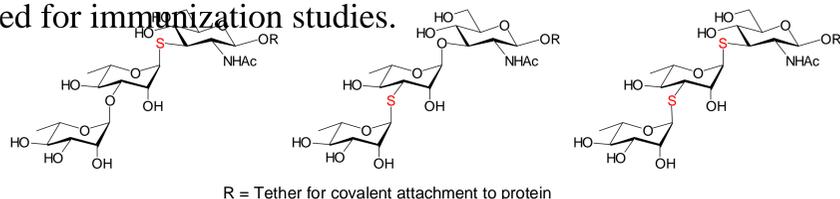
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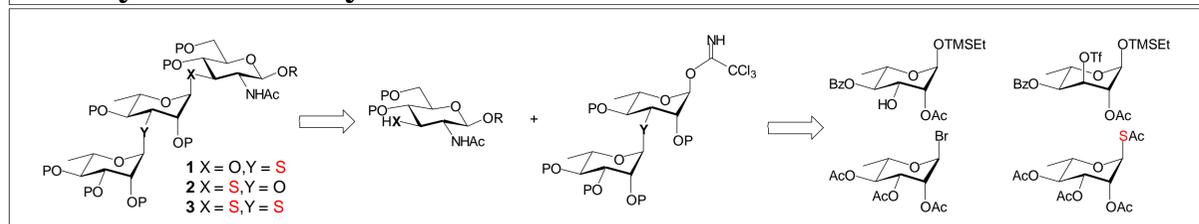


Abstract

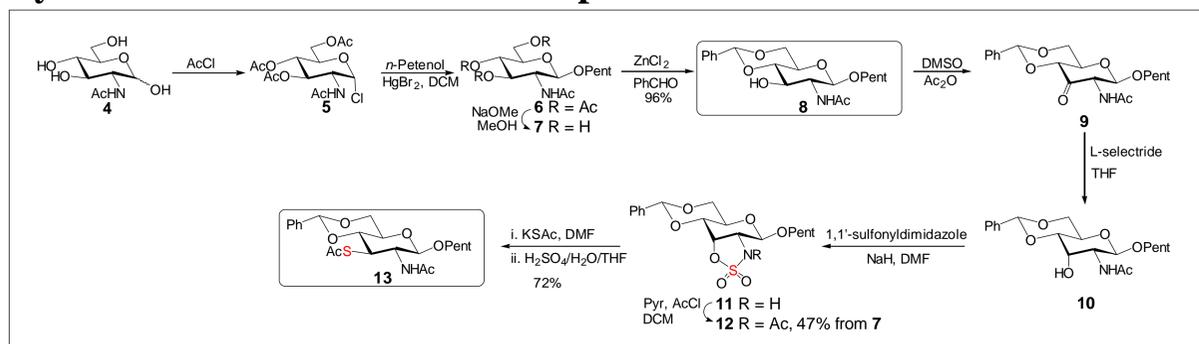
As synthetic vaccines assume greater importance, a key issue in their design is the extent to which unnatural but metabolically stable bonds might enhance the immune response to the antigenic determinant. Here our objective is to address two issues, firstly, using a crystallographically defined antibody, the inhibitory power of *S*-linked oligosaccharides is compared to *O*-linked analogs, and secondly, we address the question whether antibody produced against glycosidase resistant thio-analogs will bind to the natural *O*-linked oligosaccharides (Rha-Rha-GlcNAc). We have designed three analogs of the natural trisaccharide with sequential replacement of oxygen by sulfur at glycosidic linkages. The synthesis and initial inhibition studies of these new analogs will be reported. Three thio-analog protein conjugates have been synthesized for immunization studies.



Retrosynthetic Analysis



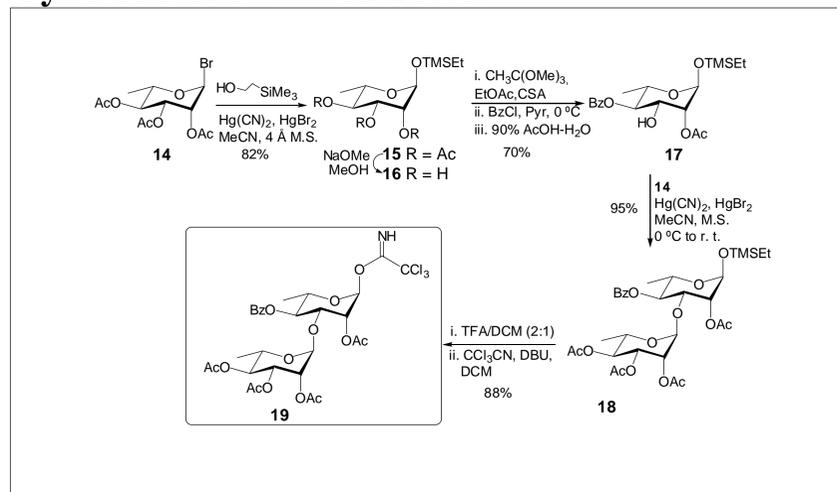
Synthesis of *O*- and *S*-linked Acceptors



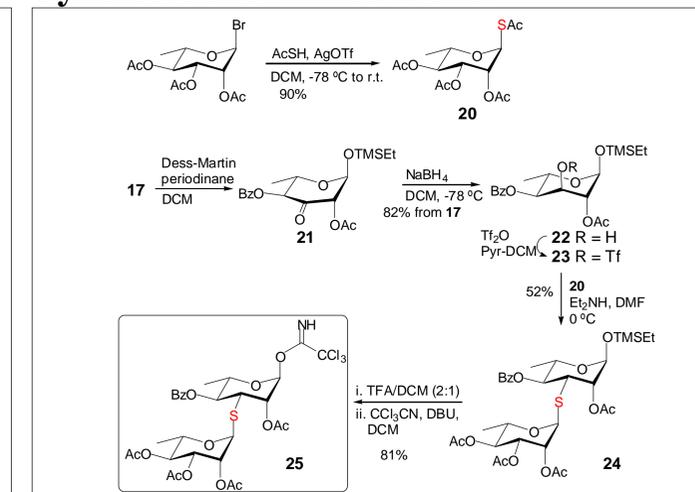
Acknowledgements:

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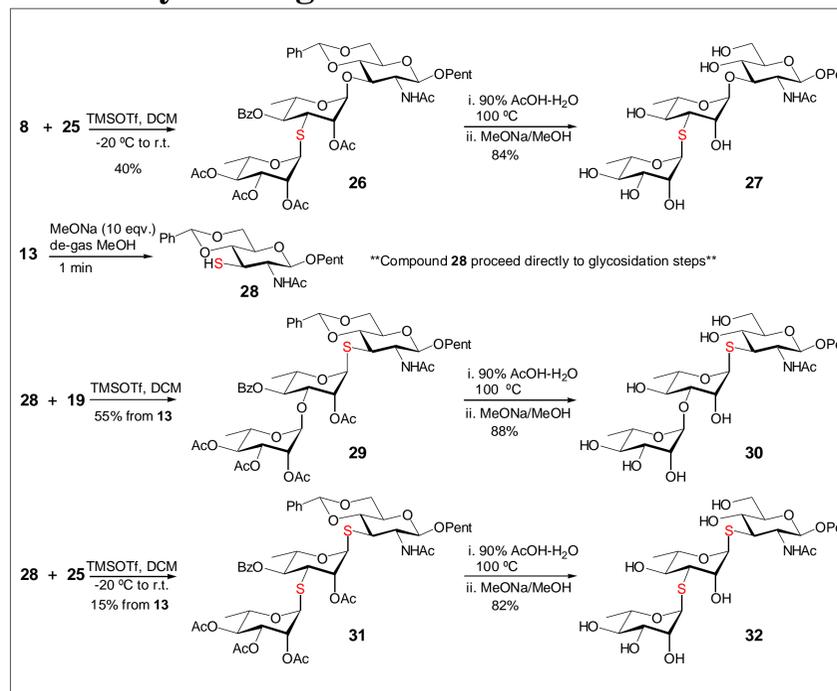
Synthesis of *O*-linked Donor



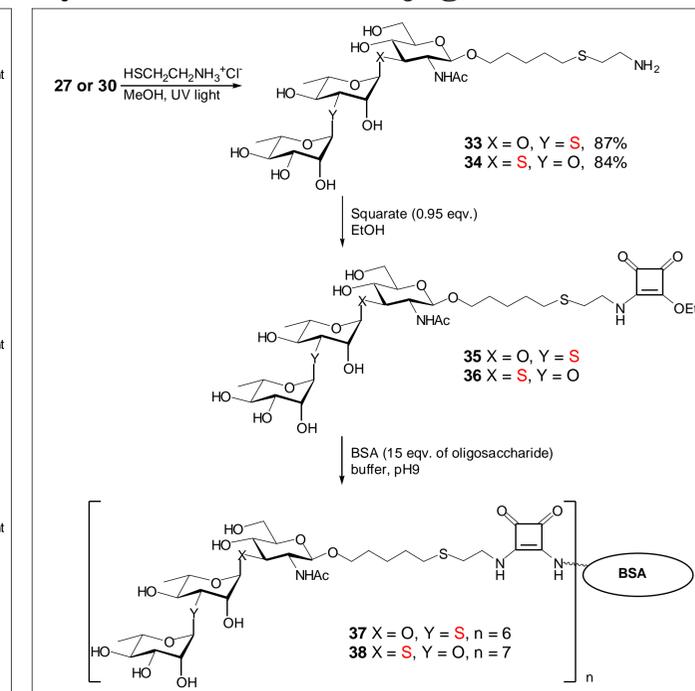
Synthesis of *S*-linked Donor



Assembly of Target Thio-linked Trisaccharides



Synthesis of BSA Conjugates



Result and Discussion:

- The thio-linked trisaccharides **27** & **30** have been evaluated in a competitive ELISA, and compared by their IC_{50} concentration. The IC_{50} for compound **27** is 0.9 mM, **30** is more than 10 mM by ELISA. In the same format, the natural *O*-linked trisaccharide has an IC_{50} of 17 μm . Compound **32** was not tested.
- BSA conjugates **37** and **38** are being used in immunization studies. Results will be reported in due course.