Construction of 1-Thio-β-Mannopyranosyl and 1-Thio-β-Rhamnopyranosyl Linkages via a Facile S_N2 Reaction

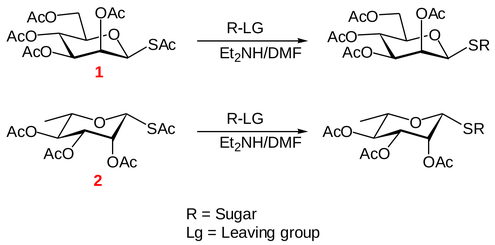
Henry N. Yu, Chang-chun Ling and David R. Bundle

Department of Chemistry, University of Alberta, Edmonton, Alberta, Canada,T6G 2G2

Abstract

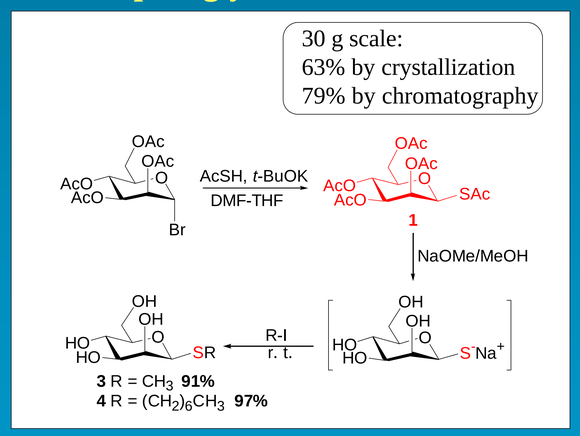
An efficient method for the synthesis of 1-thio-β-mannopyranosides[1] and 1-thio-β-rhamnopyranosides is reported.

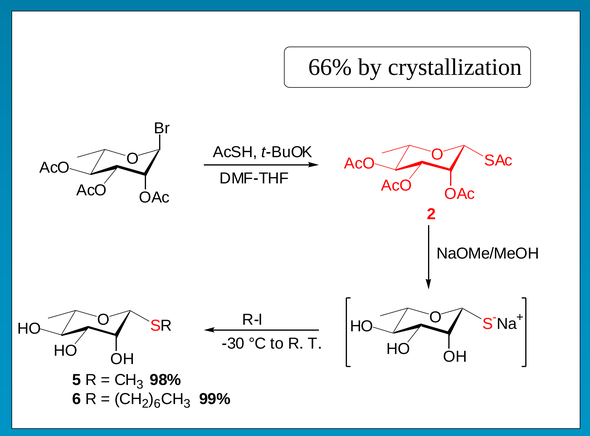
This method employs the simple, easy-to-make 2,3,4,6-tetra-*O*-acetyl-1-*S*-acetyl-1-thio-β-D-mannopyrannose **1** and 2,3,4-tri-*O*-acetyl-1-*S*-acetyl-1-thio-β-L-rhamnopyranose **2** as starting materials to conduct an *in situ* selective de-*S*-acetylation, and subsequent S_N2 reaction with an acceptor bearing a leaving group. The high nucleophilicity and slow anomerization of the intermediate thiol allowed the synthesis of 1,2-cis-β-thioglycosides in a simple and practical manner.



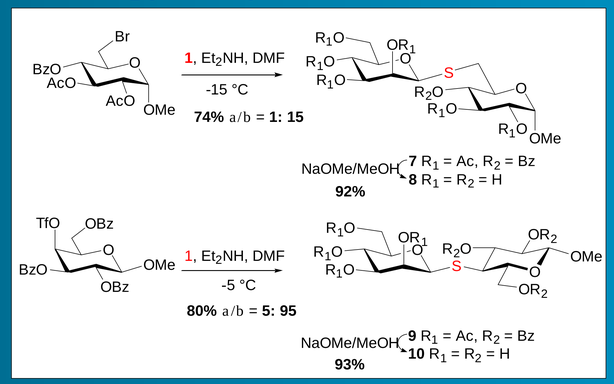
(1) H. N. Yu, C-C Ling, and D. R. Bundle, *J. Chem. Soc., Perkin Trans. 1*, (2001), 832-837.

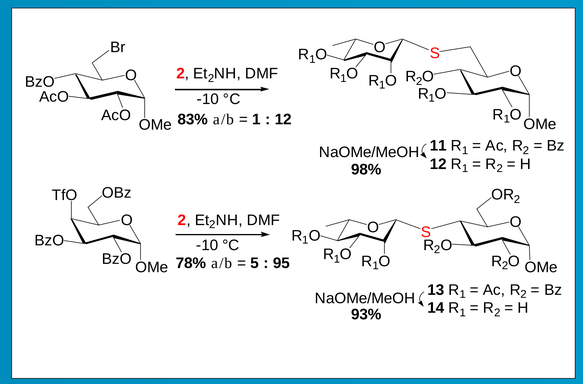
Synthesis of 1-thio-β-D-mannopyranoside and 1-thio-β-L-rhamnopyranoside with simple aglycones



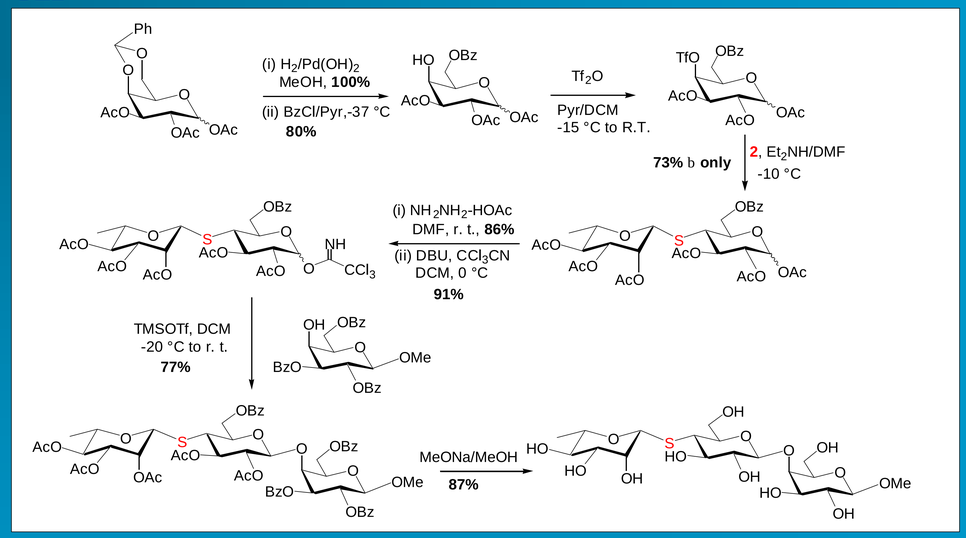


Synthesis of 1,6- and 1,4-linked 1-thio-β-mannopyranosyl and 1-thio-β-rhamnopyranosyl disaccharides





Assembly of a thio analog of a common fragment of the capsular polysaccharides of *S. pneumoniae* serotypes 2, 7F, 17F, 22F, 23F, 27, 32A and 32F



Conclusions:

- We have developed an efficient route for the preparation of 1-thio-β-mannopyranosides and 1-thio-β-rhamnopyranosides using the easily accessible compounds **1** and **2** as starting materials.
- Considering the significant difficulties in preparing *O*-linked 1,2-cis-β-glycosides, this route offers an alternative to the design and synthesis of carbohydrate analogs containing a β-mannoside and β-rhamnoside linkage.

Acknowledgements:

Financial support was provided by research grants from the National Science and Engineering Research Council of Canada (NSERC), the University of Alberta, and the Protein Engineering Network Centre of Excellence.