Synthesis of Methyl-6-O-trityl-2,3,4-tri-O-benzyl-α-D-glucopyranoside in 1,6-Anhydrous Sugar Reaction Series

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Introduction

The synthesis of methyl-6-O-trityl-2,3,4-tri-O-benzyl-α-D-glucopyranoside is an important step in the reaction sequence to synthesize 1,6 anhydrous sugars. These sugars can be used in a variety of subsequent reaction processes such as creating glycosyl thiols[1]. This project involved exploring maximizing efficiency of this step.

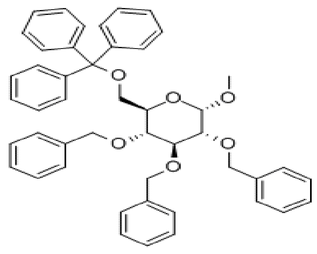
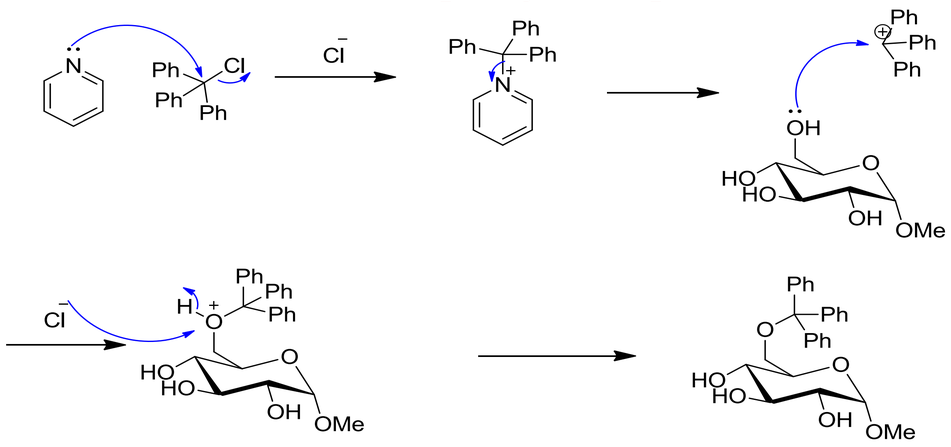


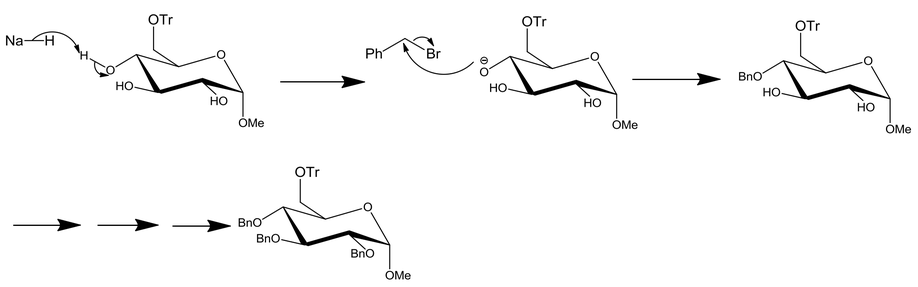
Figure 1: methyl-6-O-trityl-2,3,4-tri-O-benzyl-α-D-glucopyranoside[2]

Methods

Mechanism for Addition of Triphenyl Group



Mechanism for Benzylation



Laboratory Methods

Liquid-Liquid Extraction

This method is utilized to separate two different liquids based upon their solubility that are immiscible. Carried out in a separation funnel, the organic substance and an aqueous solution are combined, leading to two distinct layers of solution. The bottom aqueous layer is then drained from the funnel, leaving only the organic layer[3]. It was used to perform work up as part of the purification process with acid, base, and brine following the reaction.

Column Chromatography

Using silica gel as a stationary phase, and solvent as a mobile phase, column chromatography is able to purify products as components of the solution partition due to polarity and move through the silica at different rates. The eluent is then collected in fractions which are tested by thin layer chromatography in order to determine which fractions contain the final product[4].

Nuclear Magnetic Resonance (NMR)

^{1}H NMR uses a magnetic field to excite protons from one spin state to the opposite. The machine then reads the amount of radio frequency energy emitted by the protons in Megahertz, and are displayed in ppm

This produces a spectrum that can be interpreted by using a table of common chemical shifts based on the frequency of certain protons, which is influenced by factors such as the inductive effect, electron withdrawing groups, and adjacent, nonequivalent protons[5]. Analyzing a proton NMR spectrum allows one to determine if the product composition matches the desired product of the reaction, or if impurities remain.

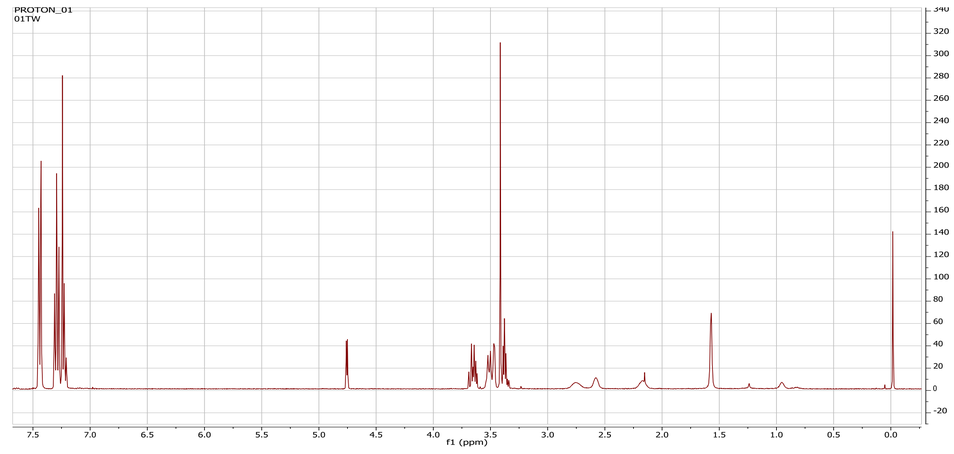
Results

Percent Yeild

The percent yield from the first reaction was 71.39%, while the percent yield from the final reaction was 29.69%.

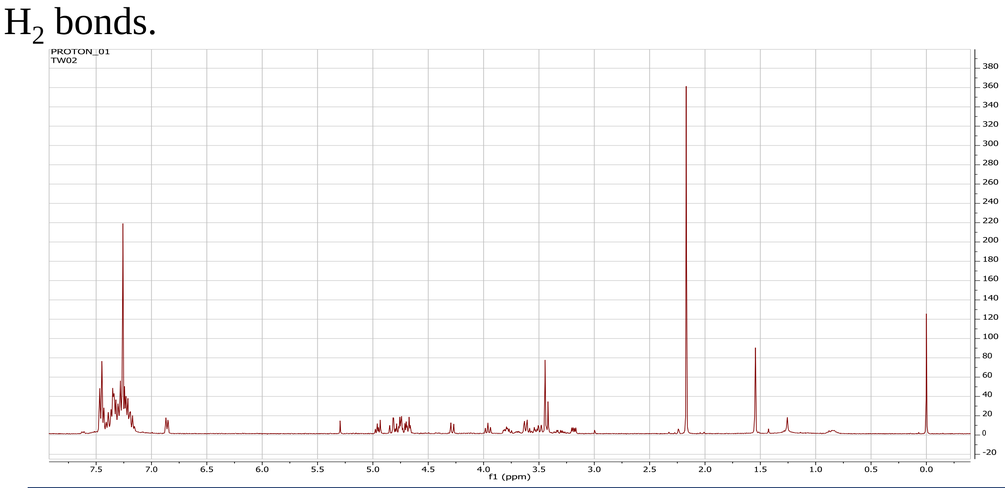
Proton NMR of Trytylated Product

^{1}H NMR analysis was performed on the specimen following the addition of the triphenyl group. The presence of the group was supported by evidence of aromatic protons, a multiplet located at 7.54-7.27 ppm.



Proton NMR of Benzylated Product

^{1}H NMR analysis following benzylation contained a multiplet at 7.61-7.39 ppm representing aromatic protons. Also, the increase in peaks between 4 and 3 ppm display the proper increase in C-H_2 bonds.



Conclusions

- Low percent yield following addition of triphenyl group due to human error and necessity for repetition of reaction.
- Reaction sequence effective in producing correct product based on product analysis.
- Efficient execution of synthesis useful for continuing sequence of producing 1,6-anhydrous sugars for the purpose of acting as chemical precursors.

References

1. Zhu, Xiangming et al., "Synthesis of α-Glycosyl Thiols by Stereospecific Ring-Opening of 1,6-Anhydrosugars", *The Journal of Organic Chemistry*, Vol. 76 (2011) p. 10187-10197
2. http://www.chemicalbook.com/ChemicalProductProperty_EN_CB5909988.htm
3. "Extraction", *Organic Chemistry at UC Boulder* http://orgchem.colorado.edu/Technique/Procedures/Extraction/Extraction.html, August 2013
4. Murphy, Tommy, "Column Chromatography", *Wake Forest Department of Chemistry , http://www.wfu.edu/chem/courses/organic/CC/index.htm*
5. Reusch, William. (2013, May 5th). NMR Spectroscopy. *Organic Chemistry Online*. Retrieved 7, November, 2013, from http://www2.chemistry.msu.edu/faculty/reusch/VirtTxtJml/Spectrpy/nmr/nmr1.htm.