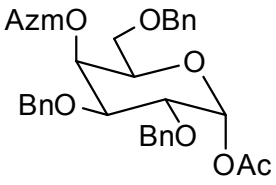
Chemistry 2302

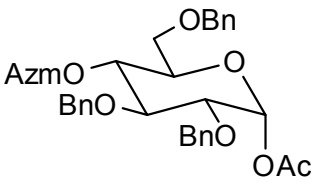
Workshop 22
Solid-Phase Synthesis of Oligosaccharides

In class, we talked about solid-phase organic synthesis of two classes of biopolymers—oligopeptides and oligonucleotides. Solid-phase syntheses of these molecules are successful because the reactions used are extremely high yielding. Solid-phase oligosaccharide synthesis, on the other hand, has been more difficult to achieve because the yields of glycoside coupling reactions are not so high. Nevertheless, there are a number of research groups around the world that are developing automated oligosaccharide synthesis machines that can do what similar machines already do for peptides and nucleic acids.

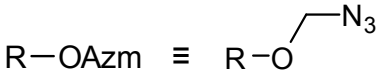
One big challenge for solid-phase sugar chemistry is engineering protecting groups. The Seeberger group at ETH-Zurich (Switzerland) has recently proposed synthetic schemes using the acid-stable azidomethyl (Azm) and benzyl (Bn) protecting groups:



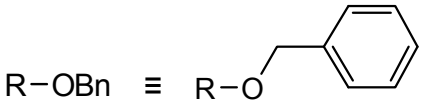
Azm-protected
D-galactose



Azm-protected
D-glucose



(deprotected by PR_3)



(deprotected by Pd, H_2)

1. The Azm protecting group can be selectively deprotected by a phosphine (e.g., PPh_3, PBu_3 or TCEP). What intermediate would be generated by the combination of the phosphine and the azide group? (*Hint:* Chapter 19.) How would this intermediate decompose to reveal an alcohol?

2. Using the two sugars on the previous page, and the polystyrene-based solid support on the right, design a solid-phase synthesis of the trisaccharide below: