Chemoenzymatic synthesis of an azidosugar that will enable targeting of *Helicobacter pylori* with therapeutics

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The pathogenic bacteria *Helicobacter pylori* colonizes the human gastrointestinal tract of 50% of the world’s population. As the source of ulcers or gastric cancer in afflicted persons, *H. pylori* have been extensively targeted with antibiotics and consequently have developed antibiotic resistance to such treatment. This antibiotic resistance necessitates an investigation of novel techniques for mitigating the effects of *H. pylori*.

One potential target for a new therapy is the sugar pseudaminic acid, which is located on *H. pylori*’s flagella and required for mobility, which enables colonization of the gastrointestinal tract and is therefore the cause of pathogenesis. However, pseudaminic acid is not present on human cells, and thus *H. pylori* can be selectively targeted. We are synthesizing an azide-modified pseudaminic acid precursor sugar that *H. pylori* can metabolize and incorporate into azido-pseudaminic acid residues on the surface of the bacteria. This process, known as Metabolic Oligosaccharide Engineering (MOE), employs the bacteria’s own biological system to process the chemically modified molecules. A bio-orthogonal reagent then reacts with the chemically-modified molecule without perturbing the biological system because of chemical selectivity. Our lab employs the Staudinger reagent, a molecule that has the corresponding substituent to react with the azide group, to target *H. pylori* with therapeutics. The Staudinger reagent can be modified with a variety of chemical warheads to render the *H. pylori* avirulent or non-viable.

Successful steps towards the synthesis of the pseudaminic acid precursor AltNAz include modification of UDP-GlcNAc through two enzymatic steps to UDP-AltNAc. Previous attempts have revealed that the chemical steps are most effective when the UDP-group is hydrolyzed prior to ligation. My current work is to perform the subsequent chemical modifications to hydrolyze the UDP-group and ligate on the azidoacetic acid substituent.
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