MECHANISTIC AND SYNTHETIC STUDIES IN DEOXY SUGAR SYNTHESIS

Clay S Bennett

Department of Chemistry, Tufts University, 62 Talbot Ave., Medford, MA 02155, USA
clay.bennett@tufts.edu

The oligosaccharides found on many bioactive natural products and the O-antigens of Gram-negative bacteria are often composed of so-called rare sugars. Assembling these rare sugars into oligosaccharides presents a challenge as they often do not contain functionality at the C2 and C6 positions classically used to control the stereochemical outcome of glycosylation reactions. As a consequence, chemistries developed for the synthesis of C2 substituted sugars cannot be used for the construction of deoxy sugars. Our lab has demonstrated that activating hemiacetals with sulfonyl chlorides leads to the in situ formation of α-linked glycosyl sulfonates. When treated with a nucleophile, these latter species undergo highly selective glycosylation reactions to afford β-linked products, provided that the reactivity of the sulfonate is matched to the reactivity of the sugar donor. Primary kinetic isotope effect studies demonstrate that the selective reactions proceed through an S_N2-like manifold. Importantly, while different sugars require different sulfonate promoters, preliminary data form our lab is beginning to demonstrate that it should be possible to predict which sulfonate use for a particular reaction based off of the sugar donor's relative reactivity value (RRV). The scope of this reaction, mechanistic studies, and its application to synthesis will be discussed.