Single Donor Chemistry is sufficient for Full Length Arabinogalactan of Mycobacterium tuberculosis

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Mycobacterium tuberculosis is the etiological agent that causes tuberculosis, a disease that kills millions every year. Occurrence of tuberculosis in humans can be traced back to pre-mediaval times and in 1880s Robert Koch observed that M. Tuberculosis has a thick waxy cell wall which could be one of the factors for its survival in the presence of drugs. Indeed, some of the front line drugs that are used in the clinic actually inhibit the cell wall biosynthesis. Pioneering efforts from Brennan group resulted into the unravelling of the fine structure of mycobacterial cell wall. Importantly, MTb cell wall contains both arabinose, galactose in furanosyl form and there are two major parts viz. Lipoarabinomannan (LAM) and Arabinogalactan (AG). Additionally, the terminal residues of AG are esterified with cyclopropane containing mycolic acids. These unique and characteristic features and biological significance enticed many to develop strategies for the synthesis of them. However, synthesis of oligofuranosides is still a daunting task due to the absence of strong stereoelectronic effects. Our group discovered the use of gold(III) chemistry for the glycosidation using alkynalated Several glycopyranosyl donors had undergone gold-catalyzed sugars as glycosyl donors. glycosidation to synthesize glycomimetics, glycopolyacrylates, glycopolyacrylamides, glycopolypeptides etc. which are otherwise very difficult to synthesize.

Quite recently, we observed that 1,2-*trans* and 1,2-*cis* arabinofuranosides can be synthesized in a convenient manner using propargyl 1,2-orthoester strategy. 1,2-*trans* arabinofuranosides can be easily obtained from propargyl orthoesters in the presence of catalytic amount of gold(III) halides; whereas the 1,2-*cis* arabinofuranosides can be accessed in an indirect way similar to how mycobacteria synthesize. Initially, 1,2-*trans* ribofuranosides are synthesized by above mentioned orthoester strategy and subsequently, C-2 hydroxy group of rib*f* was oxidized and reduced to obtain 1,2-*c* arabinofuranosides in a fully diastereoselective fashion.

In this presentation, our efforts on the synthesis of full length arabinogalactan will be discussed.