Self-supported solution synthesis of oligosaccharides using thioglycosides donors

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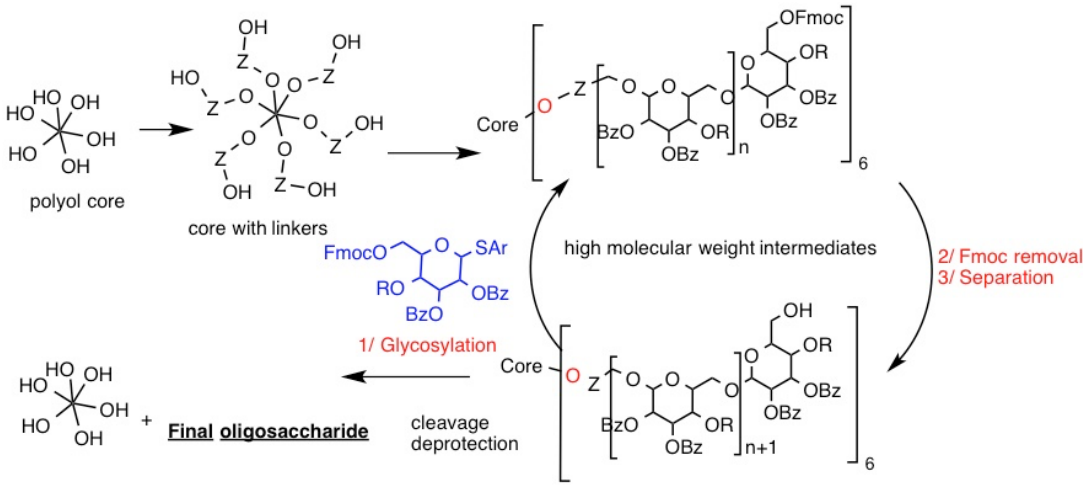
Phagocytosis of pathogens by macrophage is initiated by 3 activation pathways, antibody recognition, complement activation and the lectin pathway. In the latter case, pathogen-associated molecular patterns (PAMPs) present on the surface of the microbe bind to several macrophage lectins (mannose-binding lectin, dectins, Mincle, etc.) leading to the adhesion and internalization. In order to study this process, we recently developed glycosylated oil microdroplets as a microbial model using fluorescent mannolipids. (1). To further explore the specificity of sugars, small libraries of oligosaccharides should be prepared.

The chemical synthesis of oligosaccharides proceeds by repeating the sequence of glycosylation/deprotection steps and the solution synthesis of oligosaccharides generally requires separation and purification at each step, which is tedious and time-consuming. Solid phase alternatives have been successfully developed and are suitable for the rapid preparation of small amounts of oligosaccharides. In parallel, methods based on a soluble support have been proposed to overcome certain limitations of the solid phase approach (larger scale, use of less reactive donors, etc.). The most effective are the methods using fluorinated chains and ionic groups (2) We propose here a different strategy for the synthesis of oligosaccharides based on a multi-glycosylation of polyols. This method was exemplified by the successful preparation of a beta (1-6) tetraglucoside and a alpha(1-2) trimannoside using thioglycosyl donors. Compared to the reported syntheses, the separation here is not based on a specific marker (that transfers its solubility properties to whole molecules) but on the increase in molecular mass (from 1500 to 15000), allowing a simple separation on a steric exclusion column (Sephadex LH - 20). Moreover, the proposed protocol does not require any aqueous treatment and uses a yellow tracer to visually follow the separation without TLC or detector. (3)



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