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Communication

A five-component one-pot synthesis of phosphatidylinositol pentamannoside (PIM_5)

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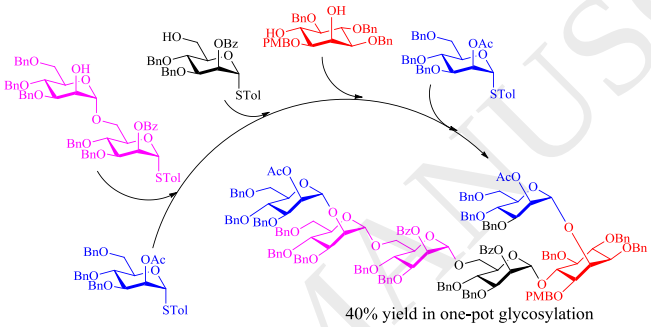
Graphical Abstract:



A practical and efficient synthesis of phosphatidylinositol pentamannoside (PIM_5) was achieved based on a five-component one-pot sequential glycosylation protocol with exclusive regio- and stereo-selectivity.

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ABSTRACT

A practical and efficient synthesis of phosphatidylinositol pentamannoside (PIM_5) was achieved based on a five-component one-pot sequential glycosylation protocol with exclusive regio- and stereo-selectivity. Two regioselective sequential glycosylations on inositol and *p*-tolyl thioglycosides as the sole type of building blocks made this protocol to avoid the tedious protective group manipulations. This synthetic strategy provides access to other important glycolipids with similar structures.

Tuberculosis (TB) is a major cause of mortality worldwide [1]. The thick glycolipid-containing cell envelope of *M. tuberculosis* is critical for bacterial survival and growth [2]. Among the glycolipids, phosphatidylinositol mannosides (PIMs) and their hypermannosylated structural relatives (lipomannans and lipoarabinomannans), noncovalently anchor to the plasma membrane and the outer capsule through palmitate, stearate and tuberculostearate lipid chains, as determinants for modulating the host immune system and dictating the fate of mycobacteria [3]. The isolation of homogeneous glycolipids from *M. tuberculosis* is challenging and does not give access to glycolipid derivatives or substructures. Therefore, chemical synthesis is employed to obtain these glycolipids with defined structures and high purity, which are suitable for biochemical assays and medical applications. PIMs are the biosynthetic precursors of lipomannan and lipoarabinomannan [4]. Especially, phosphatidylinositol pentamannoside (PIM_5) is similar to the