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Synthesis of the Tetrasaccharide Motif and Its Structural Analog Corresponding to the Lipopolysaccharide of Escherichia coli O75.

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Abstract

BACKGROUND: Extraintestinal pathogenic E. coli are mostly responsible for a diverse spectrum of invasive human and animal infections leading to the urinary tract infections. Bacterial lipopolysaccharides are responsible for their pathogenicity and their interactions with host immune responses. In spite of several breakthroughs in the development of therapeutics to combat urinary tract infections and related diseases, the emergence of multidrug-resistant bacterial strains is a serious concern. Lipopolysaccharides are attractive targets for the development of long-term therapeutic agents to eradicate the infections. Since the natural sources cannot provide the required amount of oligosaccharides, development of chemical synthetic strategies for their synthesis is relevant to gain access to a reservoir of oligosaccharides and their close analogs.

METHODOLOGY: Two tetrasaccharide derivatives were synthesized from a single disaccharide intermediate. β-d-mannoside moiety was prepared from β-d-glucoside moiety following oxidation-reduction methodology. A [2+2] stereoselective block glycosylation strategy has been adopted for the preparation of tetrasaccharide derivative. α-d-Glucosamine moiety was prepared from α-d-mannosidic moiety following triflate formation at C-2 and S(N) (2) substitution. A one-pot iterative glycosylation exploiting the orthogonal property of thioglycoside was carried out during the synthesis of tetrasaccharide analog.

RESULTS: Synthesis of the tetrasaccharide motif (1) and its structural analog (2) corresponding to the lipopolysaccharide of Escherichia coli O75 was successfully achieved in excellent yield. Most of the reactions are clean and high yielding. Both compounds 1 and 2 were synthesized as their 4-methoxyphenyl glycoside, which can act as a temporary anomeric protecting group for further use of these tetrasaccharides in the preparation of glycoconjugates.

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