Synthetic study of sialoglycans found in capsular polysaccharide of *Neisseria meningitidis* W135

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Bacterial meningitis is a serious infection associated with high mortality and morbidity. Because of the serious and very rapid spread of infection, development of vaccine is important for its control. *Neisseria meningitidis* can be classified into different serogroups (eg. A, B, C, W135, X and Y) based on the chemical structures of their capsular polysaccharides. For the elucidation of their infection mechanism and the development of vaccines, pure and structurally well-defined capsular polysaccharides are highly demanded. In this study, we focused on the chemical synthesis of polysaccharides present in W135 serogroup, which consist of disaccharide repeating unit [-6)-Galα(1-4)Neu5Acα(2-] [1,2].

To approach the targeted polysaccharides, we envisioned a 2^n elongation through fully stereoselective α-sialylation [3] at the C6 hydroxyl group of the external Gal residue linked to Neu residue with an α(1-4)-glycosidic bond. First, a C4-hydroxy macrobicyclic sialyl acceptor was glycosylated with a 4,6-DTBS-protected galactosyl donor [4] to give a Galα(1-4)Neu derivative with perfect α-selectivity. Next, the disaccharide was converted into a phosphate donor and a 4,6-diol acceptor by the removal of DTBS group in the Gal moiety. Then, we performed a [2+2] coupling in the presence of TMSOTf in CH_2Cl_2 at −80 ˚C, providing a tetrasaccharide derivative in a high yield with complete α-stereoselectivity. Furthermore, [4+4] and subsequent [8+8] elongations were successfully carried out to produce a hexadecasaccharide for the first time. These results indicate the utility of the 2^n elongation strategy employing the fully stereoselective α-sialylation.

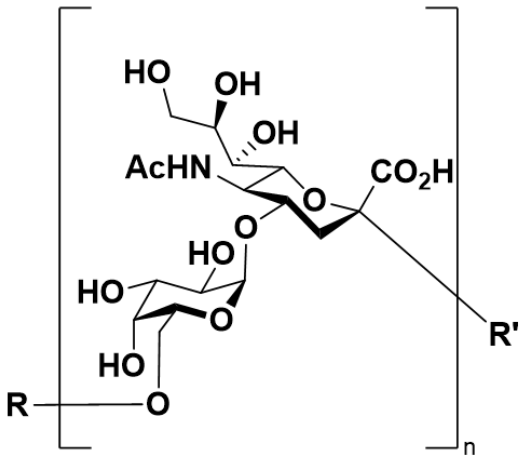

Fig 1. Structure of polysaccharides derived from Neisseria meningitidis W135

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