Synthetic study of keratan sulfate disaccharide library

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Abstract

Keratan sulfate (KS) is a sulfated polysaccharide belonging to glycosaminoglycan (GAG) superfamily. KS is mainly distributed in cornea, cartilage, bone, and brain as components of cell membrane or extracellular matrix. Recently, KS was found on the surface of iPS and ES cells, and a role of KS for the maintenance of cells has attracted attention.
KS chain is composed of repeating disaccharide consisting galactose (Gal) and *N*-acetylglucosamine (GlcNAc) and is sulfated heterogeneously owing to the multiple and random enzymatic modifications during the biosynthesis. The resultant microstructure of KS is related to the specific interaction with KS-binding proteins to regulate their activity. Therefore, the analysis of the structure-activity relations of KS with KS-binding protein at the molecular level is very important for clarifying their biofunction. In this study, we addressed systematic synthesis of KS disaccharide library to evaluate the binding property of KS against KS-binding proteins by surface plasmon resonance (SPR) bio-sensor.
Gal donor **1** and GlcNAc acceptor **2** were synthesized from D-galactose and D-glucosamine, respectively. The glycosylation of **2** with **1** gave the disaccharide intermediate **3,** which possesses orthogonally removable protecting group and can be converted to KS disaccharides with sulfation. The disaccharide **3** was then condensed with the glucose (Glc) moiety **4**, which works as a hydrophilic spacer at the immobilization on SPR sensor chip[1)] to prevent unexpected non-specific interaction. Currently selective deprotection and sulfation of trisaccharide intermediate **5** are on-going.

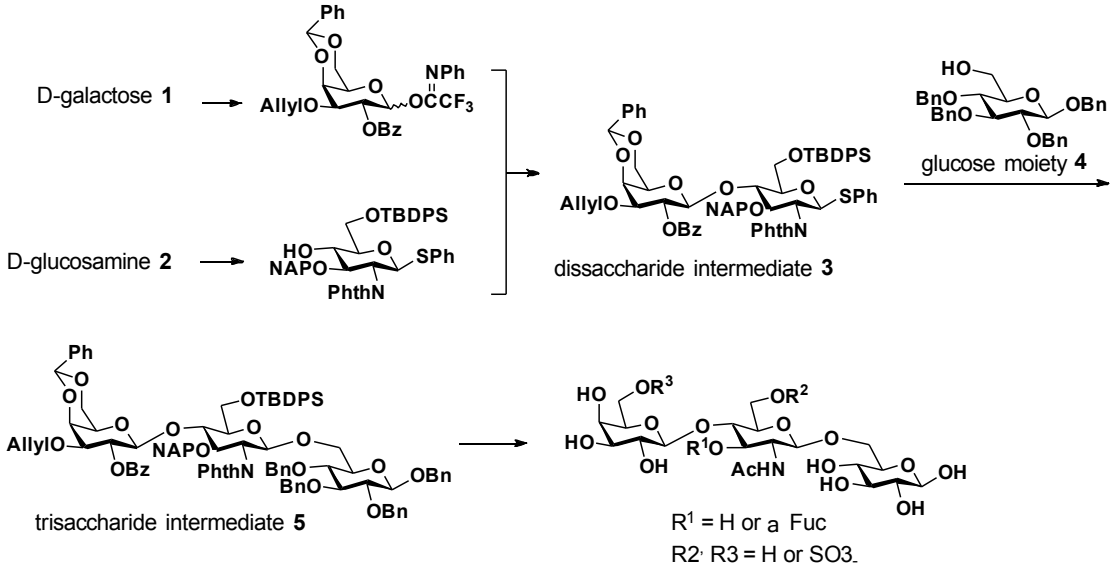

Fig. Schematic image of synthesis of KS disaccharide library.

Reference

1) Suda Y, Arano A, Fukui Y, Koshida S, Wakao M, Nishimura T, Kusumoto, S. Sobel, M. *Bioconj. Chem*. **2006**, *17*, 1125-1135.

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