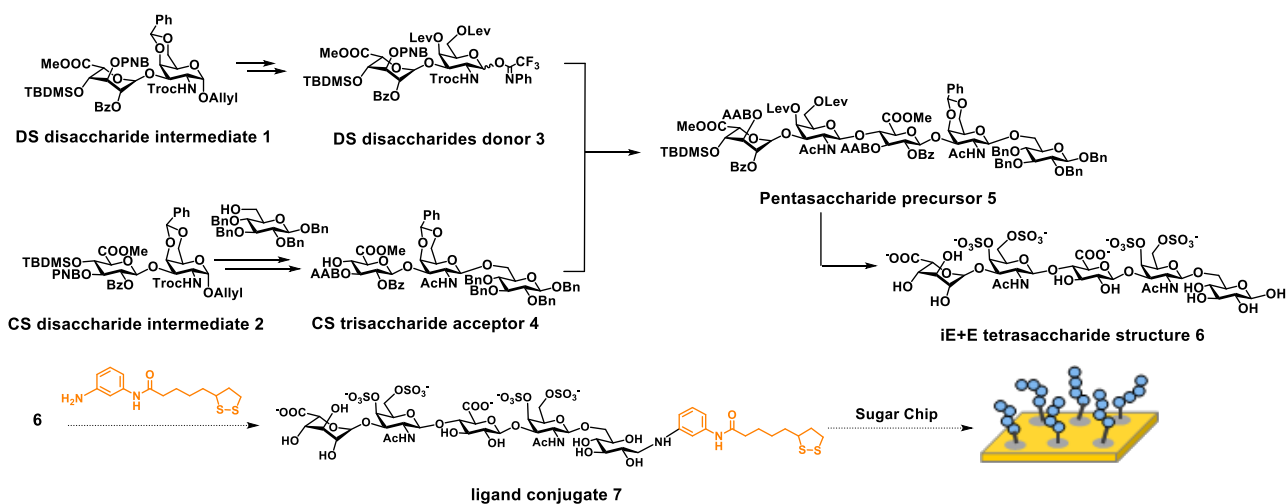


Synthetic study on dermatan sulfate/chondroitin sulfate hybrid tetrasaccharide structure

Takeru Oyama, Kyosuke Nishioka, Tatsuki Haranosono, Masahiro Wakao, Yasuo Suda

Dermatan sulfate (DS) and chondroitin sulfate (CS) belong to glycosaminoglycan (GAG) superfamily, and are linear sulfated polysaccharides. They are widely distributed in various tissues as components of cell membrane or extracellular matrix. DS and CS chains interact with bioactive proteins such as growth factors, cytokines, and matrix enzymes and regulate their functions. DS chain is biologically synthesized from chondroitin or CS chain by the random and imcompleted enzymatic modification such as C-5 epimerase and O-sulfotransferase, resulting the DS/CS versatile structure. Recently, a certain DS/CS structure is considered to be important for the specific interaction with bioactive proteins, and the elucidation of structure-activity relations at the molecular level is needed for understanding their biofunctions. In this study, we addressed chemical synthesis of DS/CS hybrid tetrasaccharide structure containing DS-E (iE) and CS-E (E) units.

The synthetic strategy for iE-E tetrasaccharide structure is shown in Scheme 1. DS and CS disaccharide intermediates **1** and **2** were prepared according to the previous method,^[1,2] and were transformed to DS disaccharide donor **3** and CS disaccharide acceptor **4**, respectively. Pentasaccharide precursor **5** was prepared by the glycosylation of donor **6** and acceptor **7**. iE-E tetrasaccharide structure **6** was obtained by the subsequent selective deprotection and sulfation, and the removal of the remaining protecting groups. As soon as the objective iE-E tetrasaccharide ligand conjugate **7** is obtained by the reductive amination with our original linker moiety, the molecular level analysis is performed using the Sugar Chip immobilized with conjugate **7**.



Scheme 1. Synthetic and experimental strategy for the tetrasaccharide structure containing tandem DS-E and CS-E disaccharide units.

References

- 1) K. Miyachi, *et al.*, *Bioorg. Med. Chem. Lett.*, **25**, 1552-1555 (2015).
- 2) Y. Kakitsubata, *et al.*, *Tetrahedron Lett.*, **57**, 1154-1157 (2016).