INVITED LECTURE

New approaches to the synthesis of hyaluronic acid and chondroitin sulfate oligosaccharides

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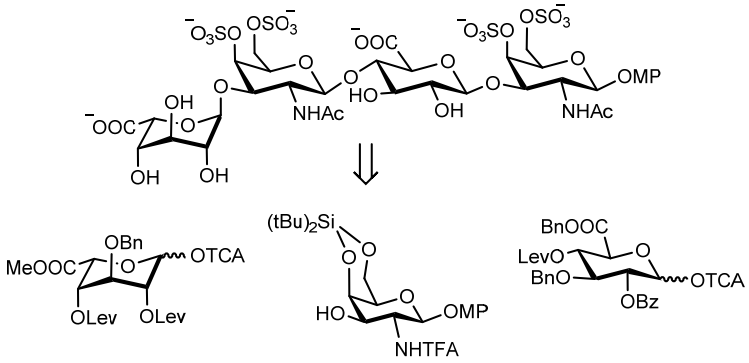
Glycosaminoglycans (GAGs), such as hyaluronic acid, chondroitin sulfate and heparin, modulate important biological processes by their interactions with different protein receptors. Synthetic oligosaccharides are crucial for the study of GAG-protein interactions and the establishment of structure-activity relationships, improving our understanding of the role that these complex polisaccharides play in nature. Despite the recent advances in GAG oligosaccharide synthesis, the preparation of these compounds is still challenging. For example, glycosylation of poorly reactive uronic acids often leads to moderate yields. Final deprotection/sulfation steps are also associated with experimental problems such as long reaction times and low isolated yields.

In this lecture, we present our contributions to the synthesis of hyaluronic acid and chondroitin sulfate oligosaccharides. We have explored the use of perfluorated tags to facilitate the purification of the protected intermediates in a hyaluronic acid synthetic sequence. We have also developed a novel strategy for the preparation of chondroitin/dermatan sulfate oligosaccharides that is based on the use of *N*-trifluoroacetyl-protected galactosamine building blocks.[1] Glycosylation reactions proceeded in high yields using our protecting group design. Following this approach, several tetrasaccharides, bearing different uronic acid compositions and sulfation patterns, were successfully synthesized. On the other hand, we have employed a fluorescence polarization assay to evaluate the interactions between the synthesized oligosaccharides and FGF-2, a model GAG-binding protein. Our results show that this method is an excellent platform for the rapid analysis of GAG-protein interactions in solution.



References

[1] Maza, S.; Kayser, M. M.; Macchione, G.; López-Prados, J.; Angulo, J.; de Paz, J. L.; Nieto, P. M.; *Org. Biomol. Chem.* **2013**, *11*, 3510.