Full stereocontrol of alpha-glycosidations of sialic acid and Kdo by macrobicyclic glycosyl donors

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Sialic acid and Kdo (3-deoxy-D-*manno*-2-octulosonic acid) belong to the class of 3-deoxy-2-ketoaldonic acid and share common structural features, which make their stereoselective glycosidation difficult. The oxocarbenium ion intermediates of the both are unstable owing to the anomeric carboxyl group and vulnerable to decomposition via 1,2-elimination, which is enhanced by the 3-deoxy structure. The absence of a hydroxyl group at the position adjacent to the anomeric center prevents neighboring participation in the stereocontrol. Recently, we reported that macrobicyclic sialyl donors, which were tethered at the anomeric carboxyl group and the C5 amino group, enabled the fully alpha-selective sialylation that was unaffected by substrate structures and reaction conditions.[1] This method ensured the direct sialylation of oligosaccharides and glycolipids in high yields,[2] suggesting the potential of this method to rewrite the synthetic scheme of sialoglycans. Very recently, we demonstrated that macrobicyclic Kdo donors with alpha-configuration allowed for the full stereocontrol in the alpha-glycosidation.[3] This method facilitated the stereoselective synthesis of the dimeric and trimeric Kdos found in lipopolysaccharide of pathogenic bacteria.

In this presentation, I will share our recent results on the alpha-glycosidations of sialic acid and Kdo using bicyclic donors and their application to the synthesis of highly complex glycans and functionalized probes.

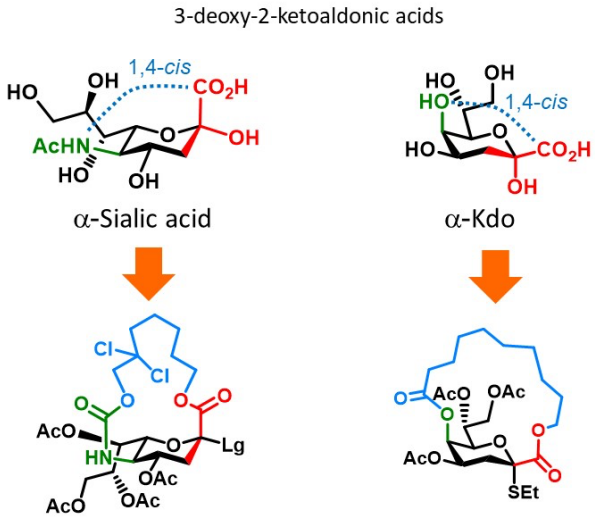

Fig. Macrobicyclic glycosyl donors of sialic acid and Kdo

Bibliographic references:

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