FOUR OF A KIND: CHEMICAL SYNTHESIS AND GLYCOSYLATION OF BACTERIAL NONULOSONIC ACIDS

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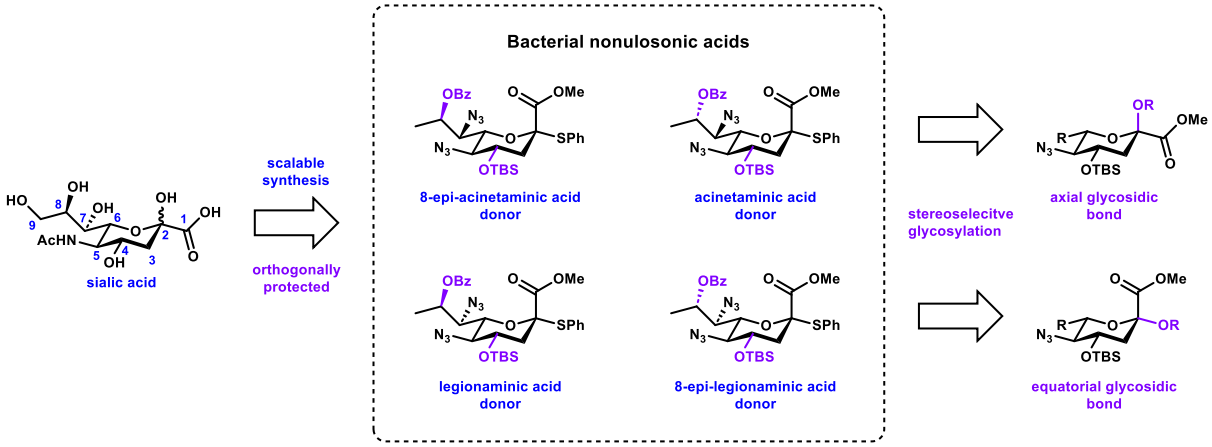
The development of novel antimicrobial therapies is increasingly aided by synthetic glycans, which can be used as probes to unravel biological interactions, as glycoconjugate vaccines, as diagnostics, and carbohydrate-based drugs. As attractive therapeutic targets, bacterial surface glycans, including capsular polysaccharides (CPS) and lipopolysaccharides (LPS), feature an incredible diversity of different monosaccharide types. A particularly intriguing class of monosaccharides, nonulosonic acids (NulOs), are nine-carbon sugars that consist of an α-keto acid pyranose ring connected to a three-carbon exocyclic side chain. In contrast to sialic acid, bacterial analogues are typically deoxygenated at the terminus of the side chain (C-9) and usually contain an additional amino group at C-7. Bacterial NulOs display a wide structural diversity, as five of the six stereocenters can vary in configuration, resulting in numerous possible stereochemical combinations. The structural complexity is further increased by the presence of various *O*/*N*-substituents, including acetyl, acetimidoyl, formyl, and 3-hydroxybutyryl groups. Additionally, these bacterial NulOs are both α- and β-linked to a wide variety of different sugar types within bacterial glycans.
The availability of bacterial NulOs has been hampered by difficulties in the synthesis of these structurally complex sugars [1]. Furthermore, directing NulO glycosylation is challenging due to facile elimination of reactive intermediates into a 2,3-glycal side product, the absence of neighboring group participation, and the deactivating effect of the C-1 carbonyl [2].
In this talk, a divergent gram-scale synthesis route to bacterial NulO donors will be presented, which provides these building blocks in sufficient amounts for mapping their glycosylation reactivity, as well as for synthesizing CPS fragments (K-Units) present on the surface of *Acinetobacter baumannii*.



References:
1. K. Pradhan, S.S. Kulkarni, *Eur. J. Org. Chem.* **2020**, *44,* 6819-6830.
2. A. M. Vibhute, N. Komura, H.-N. Tanaka, A. Imamura, H. Ando, *Chem. Rec.* **2021**, *21*, 3194-3223.