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Grant Title: New Methods for the Synthesis of O-glycosides

Abstract:

The stereoselective synthesis of 2-deoxyglycosides remains one of the most challenging problems in carbohydrate chemistry. Traditionally, glycosyl donors are activated to form oxocarbenium intermediates, which are engaged by glycosyl acceptors to form the new glycosidic bond. 2-Deoxyglycosides lack a substituent at C2, arguably the most versatile position to induce selectivity in the glycosylation step, which renders glycosylations for these substrates extremely challenging. By reductively lithiating 2-deoxythioglycosides, we are able to generate anomeric anions, which can be precisely controlled to form either the α-anion or the β-anion, and can then engage methyltetrahydropyranyl peroxide electrophiles to generate 2-deoxy *O*-glycosides. These reactions typically proceed in >70% yields and >50:1 diastereoselectivities for the desired anomer. As an added benefit, an inconsequential mixture of starting thioglycosides can be used. This strategy is amenable to the syntheses of oligosaccharides, 2-deoxyaminoglycosides, and unprotected 2-deoxyglycosides.

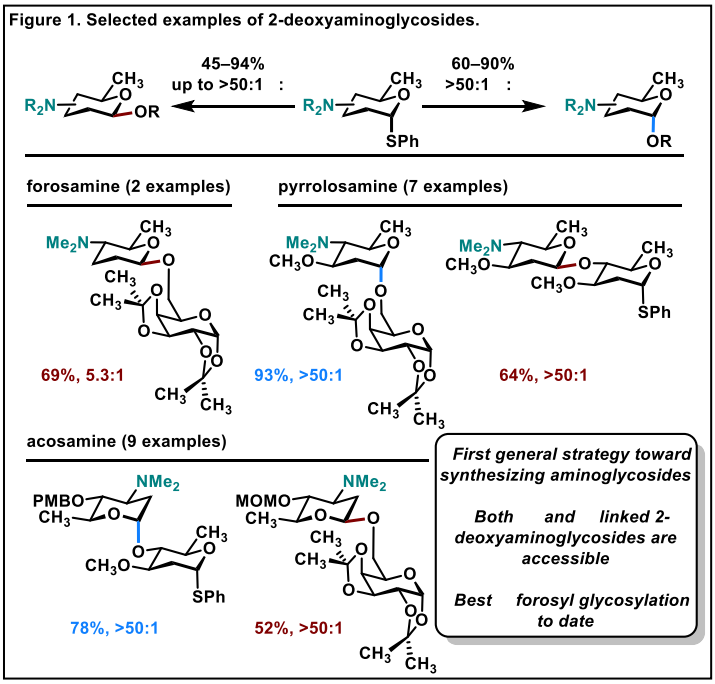

Figure 1. Selected examples of 2-deoxyaminoglycosides.