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Asymmetric Total Synthesis of the Glycosidase Inhibitor, 1,4-dideoxy-1,4-imino-D-arabinitol(DAB1)

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Naturally occurring sugar mimics with a nitrogen in the ring are classified into five structural classes: polyhydroxylated pyrrolidines, piperidines, indolizidines. pyrrolizidine, and nortropanes. Glycosidase are involved in a wide range of important biological processes, such as intestinal digestion, post-translational processing of glycoproteins and the lysosomal catabolism of glycoconjugate. The realization that alkaloidal sugar mimics might have enormous therapeutic potential in many diseases such as viral infection, cancer and diabetes has led to increasing interest and demand for these compounds. Most of these effects can be shown to result from the direct or indrect inhibition of glycosidases.

Since glycosidase inhibitors(azasugars) proved to have the biological activity, we have held considerable interest in the context of the synthesis of nitrogen-containing natural products. In connection with previous work on the regioselective and stereoselective Chlorosulfonyl isocyanate(CSI) reaction with various benzyl ethers, we envisioned the synthesis of 1,4-dideoxy-1,4-imino-D-arabinitol(DAB1) from polybenzyl ethers, which were prepared from commercially available D-arabinose, by means of a regioselective and stereoselective amination of CSI as the key transformation. The efficient synthesis of DAB1 had been achieved in 9 steps in 21% overall yield.

This new synthetic strategy involving our regioselective and stereoselective CSI reaction as a key step can be widely applicable to the total synthesis of other alkaloidal sugar mimics.