

THE ACYLOXYALLYLATION OF (UN)PROTECTED TETROSES REVEALING A PRONOUNCED DIASTEREODIVERGENCE AND A FUNDAMENTAL DIFFERENCE IN THE PERFORMANCE OF THE MEDIATING METAL

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The acyloxyallylation of unprotected aldoses was first demonstrated more than a decade ago as an elegant two-carbon homologation of reducing sugars (upon ozonolysis) [1], however, its application in real case syntheses remained scarce. Following up on such a successful show-case (short and scalable synthesis of the important bacterial sugar L-glycero-D-manno-heptose [2]) and to address several pending questions about this attractive transformation, we engaged in an in depth methodological re-investigation. The epimeric tetroses L-erythrose and D-threose in unprotected and protected aldehyde form were successfully applied to the indium and also zinc mediated acyloxyallylation, the latter being a first for an unprotected sugar. The investigation largely benefited from the choice of these more exotic starting materials as it allowed unambiguous identification of all hexose-products (authentic reference materials) as well as the reliable quantification of all diastereomers formed, even at very low proportions.

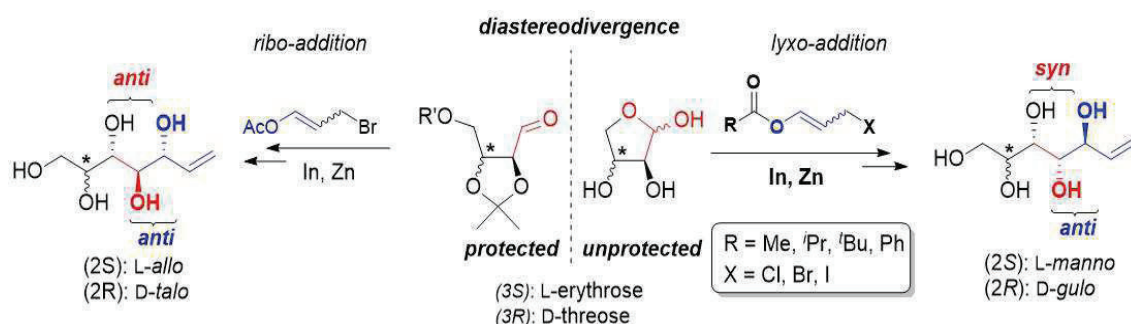


Fig. 1 – Diastereodivergence in the acyloxyallylation of protected and unprotected tetroses

The observed diastereoselectivities indicate a strong substrate control (stereochemistry at O2) and the influence of the reagent's structure on the selectivity was investigated in great detail based on a GC-based quantitative analysis. A strong facial diastereodivergence between related protected and unprotected structures was demonstrated (Fig. 1) and an unexpected, pronounced principle difference in performance between indium and zinc was revealed. This unexpected and rather rare difference in these two mediating metals supports our mechanistic hypotheses about the diastereodivergence as well as observed diastereoselectivities [3].

This consolidated knowledge allows for more refined predictions and we hope will inspire more people to consider acyloxyallylation as a synthetic tool, within and beyond the realm of carbohydrate chemistry. Applications based on acyloxyallylation towards further short synthetic solutions to currently rare and exotic sugars are currently being developed in our lab.

References

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