

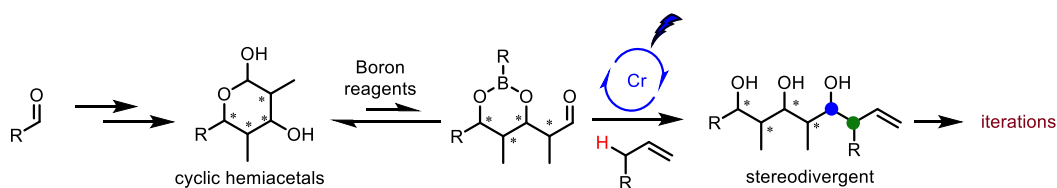
Catalytic Stereodivergent 1,3-Polyol Synthesis Using Cyclic Hemiacetal Aldols

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1,3-Polyols are valuable compounds that are found in many biologically active natural products.¹ Efficient synthesis of these scaffolds is highly essential for lead optimization of drug development. Nature does it smartly using polyketide synthetase enzymes, but stereoselective synthesis of 1,3-polyols is highly challenging. Due to tremendous utility of these polypropionate motifs, several strategies have been reported.² Among them, Evan's aldol reactions or Brown's crotylation methods are widely used strategies. However, these methods frequently depend on substrate-induced stereocontrol, which presents inherent limitations. Furthermore, these methodologies struggle with carbon elongation in the presence of hydroxy groups, necessitating protection steps during each elongation process, thereby rendering the synthesis inefficient. This issue arises not only from the protonolysis and deactivation of the carbon nucleophiles, but also due to the formation of cyclic hemiacetals from δ -hydroxyaldehydes, which halts further elongation.³

We have developed a strategy for stereoselective synthesis of 1,3-polyols using a hybrid catalyst system consisted by an acridinium photocatalyst, a chromium complex catalyst and a hydrogen atom transfer (HAT) catalyst through *in-situ* ring opening of cyclic hemiacetal double aldols by a boron reagent. We have found that depending on the chirality of the catalyst, diastereoselectivity can be controlled divergently. Several applications to short synthesis of potent intermediates of natural products were realized.



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