A *Methyl Extension* for the Synthesis of Polyketide Derivatives *via* Diastereodivergent Reductive Ring-Opening of Epoxides

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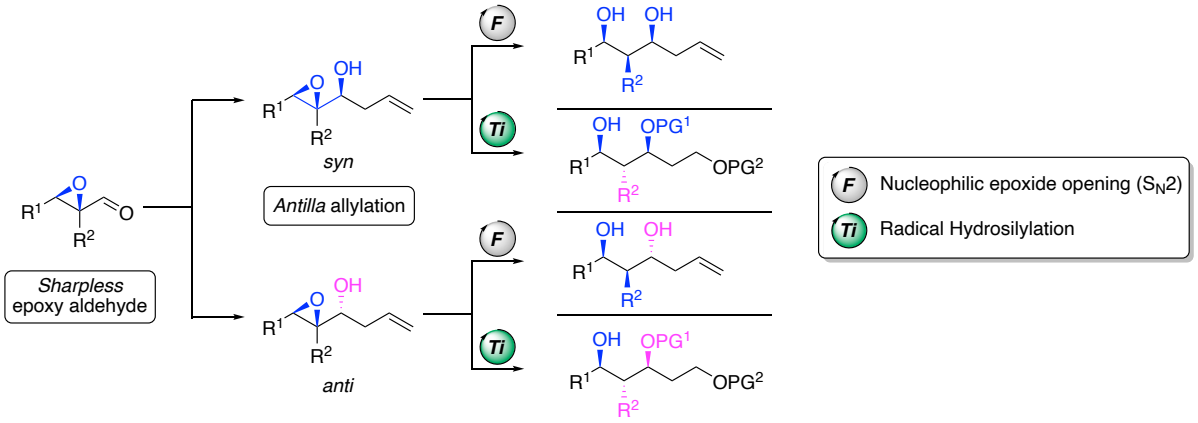
Polyketides constitute a class of natural products and are particularly valuable due to their diverse applications in medicine, including use as antibiotics, immunosuppressants, antiparasitics, cholesterol-lowering, and antitumoral agents.[1]

Building on our group's previous work regarding the flexible synthesis of polypropionates *via* diastereodivergent reductive ring-opening of trisubstituted secondary glycidols[1], my research focuses on exploring the applicability of the established system to substrates substituted with groups other than methyl at the tertiary C-atom of the epoxide ring.

Starting from the allyl alcohol, the epoxy aldehyde or its respective enantiomer can be synthesised *via Sharpless* asymmetric epoxidation and subsequent *Swern* oxidation. Followed by the mild and highly selective *Antilla* allylation, which is catalysed by a chiral phosphoric acid, either the *syn*- or *anti*-trisubstituted glycidol can be prepared. The opening of the epoxide at the more substituted C-atom through a formal hydride delivery from either the backside (fluoride-catalysed hydrosilylation *via* S_N2 mechanism) or the frontside (titanocene-catalysed radical hydrosilylation) enables the preparation of all possible stereoisomers from a single substrate.[2]



Scheme 1: Mechanism controlled stereodiversification of trisubstituted glycidols.[2]

References:

[1] C. Hertweck, *Angew Chem Int Ed* **2009**, *48*, 4688–4716.
[2] K. Pieper, R. Bleith, C. Köhler, R. Mika, A. Gansäuer, *Angew Chem Int Ed* **2024**, e202317525.