SYNLETT
Spotlight 5

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Polyamino acids

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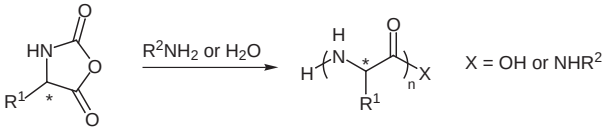
Introduction: Enzymes are among the most versatile catalysts for asymmetric synthesis concerning enantio- and substrate-selectivity. Polymers of simple amino acids are a first step towards the application of more complex synthetic polypeptide structures. Due to their insolubility, these catalysts can be efficiently removed and reused.

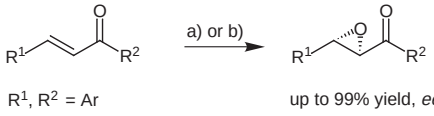
The Juliá-Colonna epoxidation provided the first highly enantioselective catalytic reaction using a polyamino acid as source of chirality.[1] Recently, Roberts et al. replaced the original three-phase system comprising alkaline aqueous hydrogen peroxide by a non-aqueous two-phase system.[2]

Preparation: Polyamino acids are obtained by simple polymerisation of amino acid *N*-carboxyanhydrides (NCA) using an amine or a humidity tank.[3]
Amine-loaded cross-linked polystyrenes or PEG-polystyrenes also initiate the polymerisation of NCA's, leading to polymer-supported polyamino acids with increased stability.[2b, 4]



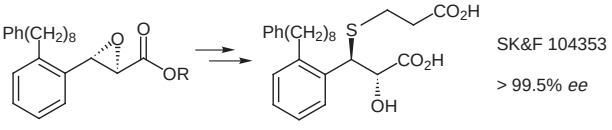
Abstracts

A) The polyamino acid catalysed asymmetric epoxidation of chalcones, discovered by Juliá and Colonna et al., provides the epoxides in excellent yields and enantioselectivities, but the long reaction times lead to degradation of the polymer.[1, 3]

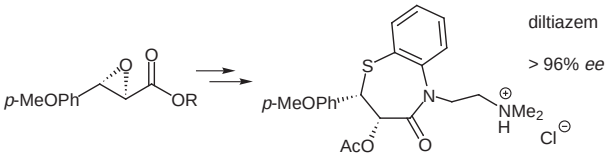


a) Poly-(*L*)-Leucin, NaOH, H_2O, H_2O_2, THF or ^{t}BuOMe, 48h [1]
b) Poly-(*L*)-Leucin, urea/H_2O_2, DBU, toluene, 15-120 min [2]

B) Lantos et al. used the triphasic polyamino acid catalysed epoxidation for the synthesis of the leukotriene antagonist SK&F 104353 in 82% yield and 95% *ee*. After Baeyer-Villiger oxidation, recrystallisation and highly regioselective opening of the epoxide with methyl 3-mercaptopropionate, the target molecule was obtained in >99.5% ee. [5]



C) Roberts et al. described the preparation of diltiazem, a blood pressure lowering agent starting from a simple enone precursor via a similar epoxidation/Baeyer-Villiger oxidation/epoxide opening protocol. [6]



References

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