

Design of Highly Active and Enantioselective Recyclable Oligomeric/Polymeric Co-Salen Catalysts for the Hydrolytic Kinetic Resolution of Epoxides

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Introduction

Chiral epoxides are among the most versatile building blocks for modern asymmetric synthesis due to the potential for the facile stereospecific attack of the strained three-membered ring unit by a wide spectrum of nucleophiles, radicals, and Lewis acids with the formation of new carbon-carbon, carbon-nitrogen, or carbon-oxygen bonds. [1] Among many available methods for the preparation of enantiomerically enriched epoxides, the catalytic asymmetric epoxidation and the kinetic resolution have been recognized as the most practical and eminent approaches. These reactions can be catalyzed by M-Salen complexes, with most epoxidations catalyzed by Mn-Salens and most epoxide ring-opening reactions catalyzed by Co or Cr-Salens. [2]

Both of these reactions can benefit from immobilization of the metal complex catalyst. In the case of epoxidation, isolation on a rigid support such as porous silica provides a useful catalyst, as it prevents catalyst deactivation via formation of μ -oxo-dimers. In contrast, a different immobilization strategy is required for epoxide ring-opening. This reaction is second order in salen complex, requiring two complexes in the transition state of the rate-limiting step. [1] Thus, in this case, catalyst tethering strategies must allow for complex-complex interactions, exactly the behavior that one sought to eliminate in the Mn-Salen case. Here we present two new strategies for the creation of heterogeneous Co-Salen catalysts that allow for cooperative interactions between the metal complexes, enhancing catalytic activity in enantioselective epoxide ring-opening reactions.

Materials and Methods

Two new tethering methods are presented here for the creation of supported Co-Salen catalysts for the hydrolytic kinetic resolution (HKR) of *rac*-epichlorohydrin. In the first case, cyclic oligomeric supports with Co-Salen complexes as side chains are prepared via a new methodology, ring-expanding olefin metathesis. [3] Cyclooctene monomers functionalized with pendant Co-Salen complexes are prepared and subsequently oligomerized using the third generation Grubbs' Ru metathesis catalyst. The resulting cyclic oligomeric catalyst, **1**, is shown in Figure 1. In the second approach, an unsymmetrically styryl-functionalized Co-Salen complex [4] is polymerized via atom transfer radical polymerization (ATRP) off various solid supports. Styrene copolymers containing pendant Co-Salen complexes are thereby constructed as polymer brushes emanating from the solid support [5]. The polymer brushes were grown off both nonporous silica and spinel ferrite superparamagnetic nanoparticle supports (Figure 1, catalysts **2** and **3** respectively).

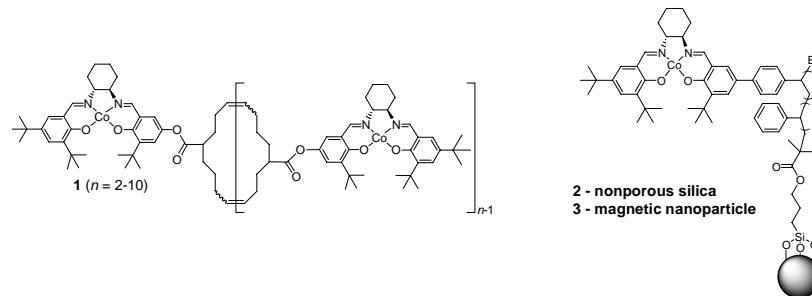


Figure 1. Cyclic oligomeric Co-Salen catalyst prepared by ring-expanding olefin metathesis (**1**), and styryl-Co-Salen based polymer brush catalysts grown off nonporous silica (**2**) or magnetic nanoparticles (**3**) via ATRP.

Results and Discussion

The hydrolytic kinetic resolution of *rac*-epichlorohydrin using the polymer brush catalyst **2**, effectively provides enantiomerically pure (>99% ee) in near theoretical yield (~45%) using 0.5 mol% catalyst in 90 minutes. The rate of reaction is similar to that of soluble styryl-Co-Salen polymer catalysts reported previously [4], and is faster than the homogeneous small molecule analogue under similar conditions. In addition, the catalyst can be easily recovered and reused with identical rates and selectivities.

Using the cyclic oligomeric catalyst, the reaction proceeds under extremely low catalyst concentrations of 0.01 mol% due to the enhanced complex-complex interactions imparted by the tethering strategy. [3] In this case, the catalysis is 40-50 times more active than the soluble styryl polymer case [4], and similar enantioselectivities and yields are obtained. The catalyst can be recovered by precipitation and reused with success, with the possibility of operation in continuous membrane processes considered as a potentially viable approach to commercial operation.

Significance

This study presents rare examples where properly supported metal complex catalysts can be more active than their homogeneous analogues. Owing to the bimolecular reaction mechanism, innovative supporting strategies can enhance complex-complex interactions, giving high reaction rates at low total catalyst concentrations. The cyclic oligomeric Co-Salen catalyst is among the most active HKR catalysts known, being the most active catalyst for some substrates and similar to the best catalysts for others.

References

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