

SYNTHESIS OF POLYMER BRUSHES FROM SALEN LIGAND/SILICA AND ITS APPLICATION AS CATALYST FOR THE HYDROLYTIC KINETIC RESOLUTION OF EPICHLOROHYDRIN

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ABSTRACT

A new approach to polymer brushes based on the surface-initiated atom transfer radical polymerization (ATRP) of functionalized salen monomer and styrene on nonporous silica was demonstrated. The hybrid material was characterized using FT-IR, TGA, DSC, ²⁹Si and ¹³C CP-MAS NMR techniques. The corresponding cobalt complex of the polymer brushes was used as a highly efficient recyclable catalyst for the hydrolytic kinetic resolution of racemic mixture of epichlorohydrin. The reaction was carried out under solvent-free condition at room temperature in the presence of 0.5 mol% of cobalt, with enantiomeric excess (ee) of higher than 99% and a conversion of 55% being achieved after 1.5 hours. While formally heterogeneous, the hybrid cobalt(salen) catalyst could offer the high enantioselectivity and activity of homogeneous catalysts due to the soluble polymer chains, and the advantages of facile separation and recycling of heterogeneous catalysts.

I - INTRODUCTION

Grafting polymers onto solid surfaces to form a so-called "polymer brushes" has become progressively intriguing in numerous commercially important technologies, such as biotechnology and advanced micro-electronics [1]. The hybrid materials possess the combination of both the properties of the inorganic solids such as robustness, and those of the polymers, in particular solubility and chemical activity. Recently, surface-initiated atom transfer radical polymerization (ATRP) technique has been extensively employed to synthesize several polymer brushes from flat substrates, porous glass filters, carbon nanotubes, and nanoparticles including silica and gold nanoparticles, quantum dots, and magnetic nanoparticles [2-8]. To date the

exploitation of polymer-grafted silica for application in catalysis, however, is still very limited with the exception of a few examples of hybrid catalysts via ring-opening metathesis polymerization (ROMP) for C-C bond formation reactions by Buchmeiser et al [9, 10].

The Jacobsen hydrolytic kinetic resolution (HKR) of commercially available racemic terminal epoxides represents an attractive and powerful strategy for the synthesis of valuable enantiopure epoxides and the corresponding diols in a single step [11]. Whereas homogeneous HKR processes have been extensively investigated, the immobilization of salens to facilitate easy product separation and catalyst recycling still remains a challenge as lower enantioselectivities and efficiencies than the homogeneous counterparts are normally achieved. The development of dendrimer, silica,

oligomer, and polymer-supported salen-based catalysts for the HKR has been described in the literature [12-16]. Recently, we employed a soluble poly(styrene)-supported cobalt(salen) system as an efficient catalyst for the HKR of epichlorohydrin, though loss of catalyst during the precipitation workup still occurred to some extent [17].

We herein report the synthesis of polymer brushes using the surface-initiated ATRP of functionalized salen monomer and styrene on nonporous silica, and the high performance of the corresponding cobalt complex in the HKR of epichlorohydrin. The hybrid catalyst possesses active center that is essentially in homogeneous phase due to the soluble polymer chains, yet as the silica remains heterogeneous, it displays the beneficial properties of both. Indeed, the hybrid system exhibits comparable enantioselectivity and activity with the homogeneous Jacobsen catalyst, it also offers the facile catalyst separation and recycling and therefore holds practical significance over its soluble counterparts.

II - EXPERIMENTAL

1. Materials and instrumentation

Reagents were purchased from Sigma-Aldrich, Acros, or Alfa, and used as received unless noted below. Non-porous CAB-O-SIL M-5 fumed silica (B.E.T surface areas 200 m²/g, average particle length 0.2 - 0.3 μm) was purchased from Cabot Corporation (Tuscola, IL, USA), dried under vacuum at 200°C for 3 hours and stored in a nitrogen glove box prior to functionalization. 3-(Trimethoxysilyl)propyl 2-bromo-2-methylpropanoate was prepared according to previous procedures. (*R,R*)-*N*-(3,5-di-*tert*-butylsalicylidene)-*N'*-[3-*tert*-butyl-5-(4-vinylphenyl)salicylidene]cyclohexane-1,2-diamine were synthesized and characterized as previously reported [17].

¹H and ¹³C NMR spectra were acquired with a Varian Mercury 400 MHz spectrometer. Cross-polarization magic angle spinning (CP-MAS) *solid-state* NMR spectra were collected on a Bruker DSX 300-MHz instrument. Mass

spectra were recorded with a VG 7070 EQ-HF hybrid tandem mass spectrometer. GPC analysis was performed with American Polymer Standards columns equipped with a Waters 510 pump and a UV detector. Enantiomeric excesses (ee) were determined by GC analysis on a Shimadzu GC 14 A instrument equipped with a FID detector and a ChiralDEX G-TA column (30 m x 25 mm) with helium as a carrier gas.

A Netzsch Thermoanalyzer STA 409 was used for simultaneous thermal analysis combining thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC) with a heating rate of 10°C/min in air. FT-IR spectra were obtained on a Bruker IFS 66 V/S instrument with samples being dispersed in potassium bromide pellets. A low voltage Fischer Scientific FS60H was used to sonicate samples. Elemental analyses were performed by Desert Analytics Lab (Tucson, AZ, USA) and Atlantic MicroLab (Norcross, GA, USA).

2. ATRP of salen ligand and styrene from silica surface

A mixture of copper (I) bromide (0.144 g, 1 mmol), 1,1,4,7,10,10-hexamethyltriethylenetetramine (HMTETA) (0.460 g, 2 mmol) in toluene (30 mL) was stirred at room temperature for 1 week in a nitrogen glove box. The salen ligand (0.30 g, 0.506 mmol) was dissolved in toluene (5 mL) in a 50 mL flask under a nitrogen atmosphere. The flask was then charged with the immobilized bromoisobutyrate initiator (0.30 g), styrene (0.21g, 2 mmol), and 2.5 mL of the copper (I) bromide/ HMTETA solution in a nitrogen glove box. The mixture was sonicated for 15 minutes to suspend the silica in solution, and then heated at 110 °C for 96 hours under an argon atmosphere. The reaction mixture was cooled to room temperature, opened to air, sonicated for 30 minutes, and the solid was isolated by centrifugation. The particles were re-dispersed in toluene (40 mL), sonicated for 30 minutes, and allowed to stand overnight. The green precipitate was removed, and the polymer brushes were then recovered by centrifugation. The particles were re-dispersed in toluene (40 mL), sonicated until no particles were visually

observed (30 minutes), and the washing procedure was repeated 6 times. The polymer brushes were dried under vacuum at room temperature overnight. TGA of the polymer brushes shows an organic loading of 49%. ¹³C CP-MAS NMR: δ = 25 - 40 (aliphatic C), 73 (CH-N), 120 — 145 (aromatic C), 158 (C-O), 165 (C=N). ²⁹Si CP-MAS NMR: δ = -110, -105, -90; and -65, -60, -50. FT-IR: ν_{max} = 3430 (H₂O, O-H st), 3086 (aromatic C-H st), 3063 (aromatic C-H st), 3031 (aromatic C-H st), 2957 (aliphatic C-H st), 2934 (aliphatic C-H st), 2865 (aliphatic C-H st), 1727 (C=O st), 1630 (C=N st), 1456, 1102 (Si-O st), 815, 703 (aromatic C-H δ).

3. Metallation of the polymer brushes

A 100 mL flask was charged with the polymer brushes (400 mg), anhydrous DCM (10 mL) in a nitrogen glove box. A solution of anhydrous cobalt (II) acetate (80 mg) in anhydrous methanol (10 mL) was then added. A brick-red powder was observed immediately in the reaction mixture. The brick-red suspension was then sonicated for 30 minutes to disperse the particles in the solution. The reaction mixture was heated at reflux for 40 hours under an argon atmosphere. The suspension was then cooled to room temperature, and transferred to a centrifuge tube in a nitrogen glove box. The solid was recovered by centrifugation, and immediately transferred to the nitrogen glove box. Anhydrous methanol (40 mL) was then added, the suspension was sonicated for 30 minutes, and the solid was recovered by centrifugation. The washing procedure was repeated 6 times. The brick-red Co(II) pre-catalyst was dried under vacuum at room temperature overnight. Elemental analysis (ICP-MS) of the pre-catalyst showed a cobalt loading of 0.3 mmol/g.

4. General procedure for the hydrolytic kinetic resolution of (*rac*)-epichlorohydrin

The Co (II) pre-catalyst (19 mg, 5.7×10^{-3} mmol on the basis of cobalt) was suspended in DCM (1 mL) in a 5 mL pear-shaped flask with a half-round magnetic stirring bar. Glacial acetic acid (0.10 mL) was added and the reaction mixture was sonicated for 15 minutes to disperse the solid particles in the solution. The

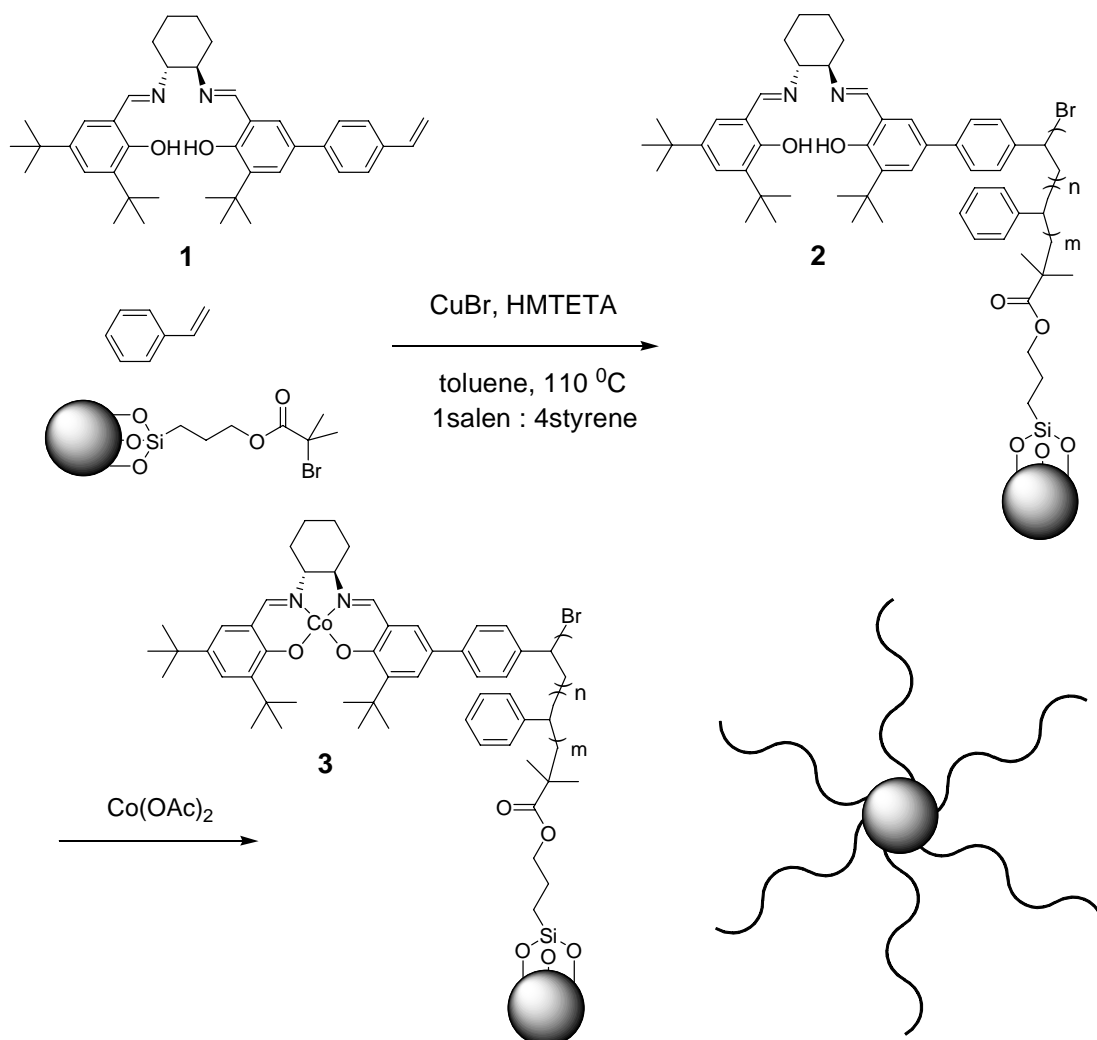
suspension was then stirred in the open air at room temperature for 30 minutes. The solvent and the excess acetic acid were roughly removed by a rotovap. The brown-black residue was dried under vacuum at room temperature for 30 min to give the Co (III) catalyst. Racemic epichlorohydrin (86 μ L, 1.1 mmol) and chlorobenzene (10 μ L, internal reference) were added to suspend the activated catalyst and the flask was immersed into a water bath at room temperature. Deionized water (0.7 equiv, 13 μ L, 0.7 mmol) was injected into the system to start the reaction. Samples (1 μ L) were taken from the reaction mixture with a micro-syringe at each designed time, diluted with anhydrous diethyl ether (2 mL), and passed through a plug of silica gel in a Pasteur pipette to remove the cobalt catalyst and water. The conversions (with reference to chlorobenzene) and enantiomeric excesses of epichlorohydrin were measured by GC.

III - RESULTS AND DISCUSSION

Mono-functionalized enantiopure unsymmetrical salen ligand **1** was synthesized according to a straightforward one-pot protocol using a 1:1:1 molar ratio of a hydrogen chloride-protected chiral diamine and two different salicylaldehydes [18]. The salen ligand possesses a styrene moiety which is ready for the surface-initiated ATRP. A bromoisobutyrate initiator was synthesized and immobilized onto a non-porous silica, Cab-O-Sil, as described in the literature [19]. Copper (I) mediated radical co-polymerization of the unsymmetrical salen ligand and styrene with the immobilized initiator was carried out at 110°C in toluene under an argon atmosphere using 1,1,4,7,10,10-hexamethyltriethylenetetramine (HMTETA) as a ligand in conjunction with copper (I) bromide (Scheme 1) [20]. Styrene was utilized (styrene:salen molar ratio of 4:1) to increase the flexibility of the polymer backbone on the silica surface and the solubility the polymer in solution, facilitating the homogeneous-like performance of the subsequent corresponding cobalt complex. The polymer brushes **2** were repeatedly dispersed in

toluene under sonication, isolated by centrifugation to remove any physically adsorbed un-reacted monomers, and

characterized by TGA, FT-IR, ^{29}Si and ^{13}C cross-polarization magic angle spinning (CP-MAS) solid-state NMR.



Scheme 1: Synthesis of the salen-based polymer brushes on non-porous silica

Thermogravimetric analysis of the polymer brushes **2** showed an organic loading of 49%, while an organic loading of 7% was observed for the immobilized initiator. Fourier transform infrared spectra of both the initiator and the polymer brushes (figure 1) exhibited the presence of an Si-O stretching vibration at 1102 cm^{-1} , a C=O stretching vibration at 1727 cm^{-1} , and an O-H stretching vibration at 3430 cm^{-1} due to physisorbed water and potentially surface

hydroxyls. The significant features observed for the polymer brushes were the appearance of several strong absorbance bands at $3086 - 3031\text{ cm}^{-1}$ (aromatic C-H stretching), $2957 - 2865\text{ cm}^{-1}$ (aliphatic C-H stretching), 1630 cm^{-1} (C=N stretching), and 703 cm^{-1} (aromatic C-H deformation). These features revealed the existence of the polymer structure on the silica, confirming that the polymer chains were successfully grown from the immobilized initiator.

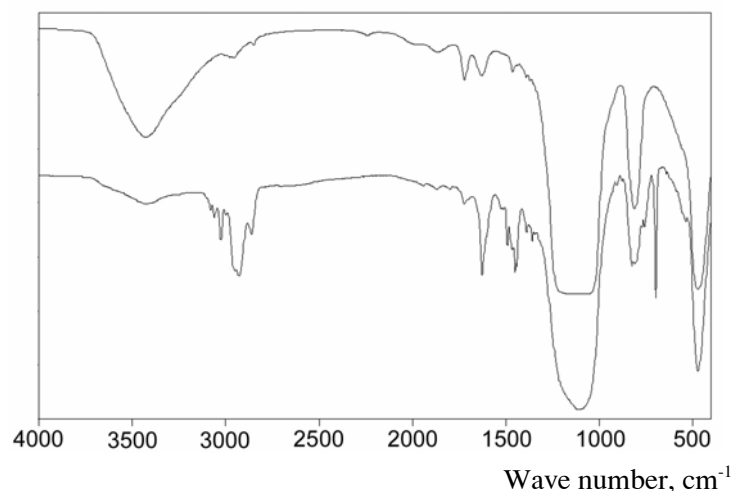


Figure 1: FT-IR spectra of the initiator (top) and the polymer brushes 2 (bottom)

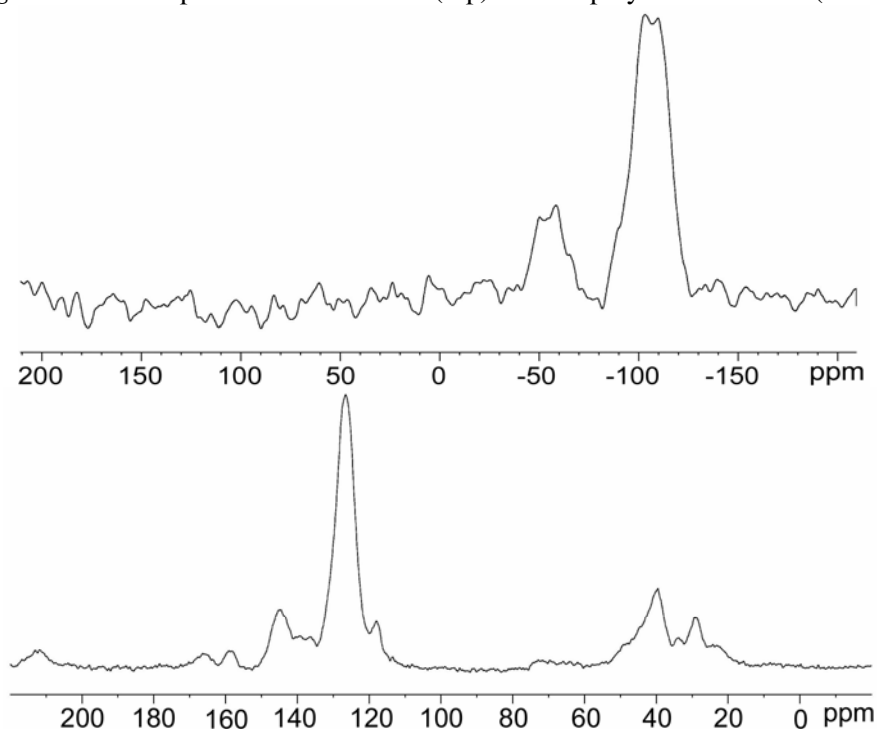


Figure 2: ^{29}Si (top) and ^{13}C (bottom) CP-MAS NMR spectra of the polymer brushes 2

The presence of the grafted polymer on the silica surface was also supported by ^{13}C and ^{29}Si CP-MAS solid-state NMR techniques (figure 2). The ^{29}Si NMR spectrum showed two sets of resonance in the ranges -90 to -110 and -50 to -65 ppm. The first group was characteristic of the silica framework, while second group corresponded to alkyl linkages to the silica

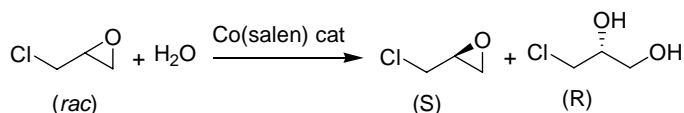
surface. The ^{13}C NMR exhibited the presence of aliphatic carbons at 25 - 40 ppm, and aromatic carbons at 120 - 145 ppm. There also existed the contribution of the C=N carbon at 165 ppm, the C-O carbon at 158 ppm, and the CH-N carbon at 73 ppm as expected. The ^{13}C and ^{29}Si CP-MAS solid-state NMR spectra, in combination with TGA and FT-IR results strongly indicated the

existence of the poly(styrene)-supported salens on the silica.

To determine the molecular weight and the molecular weight distribution of the grafted polymer, the polymer brushes **2** were destroyed with hydrofluoric acid (HF) to remove the silica [5]. The cleaved polymer was collected and characterized by $^1\text{H-NMR}$ and gel-permeation chromatography (GPC). According to GPC analysis using poly(styrene) as standard, the cleaved polymer had a number-average molecular weight (M_n) of 28700, with polydispersity indice (PDI) of 3.9. $^1\text{H NMR}$ spectrum of the cleaved polymer was in good agreement with that of the soluble poly(styrene)-supported salens as previously reported [17]. However, it was observed that HF had a slight effect on the salen structure during the silica removal. Approximately 7% ($^1\text{H NMR}$) of total the salen groups were hydrolyzed to the corresponding aldehydes. It should be noted that the hydrolysis of the salen structure was much more pronounced on long-time exposure to HF. It also observed that cleavage of the grafted polymer in aqueous sodium hydroxide solution resulted in the hydrolysis of the salen structure.

The polymer brushes **2** were converted to the corresponding brick-red cobalt (II) pre-catalyst **3** by refluxing them in the presence of anhydrous cobalt (II) acetate under the

protection of an argon atmosphere. The pre-catalyst **3** were repeatedly dispersed in methanol under sonication, isolated by centrifugation to remove any physically adsorbed cobalt (II) acetate. Elemental analysis with inductively coupled plasma mass spectroscopy (ICP-MS) showed a cobalt loading of 0.3 mmol/g of the pre-catalyst, indicating that approximately 88% of the salen centers were loaded with cobalt. The hybrid cobalt catalyst was examined for its enantioselectivity and activity in the HKR of racemic epichlorohydrin (Scheme 2). Prior to the catalytic reaction, the pre-catalyst **3** was oxidized to the corresponding Co (III).OAc active species with excess acetic acid in the open air. The oxidation process was evidenced by a dramatic color change from brick-red to dark brown as a character of cobalt (III)(salen) species [21]. The HKR was carried out under solvent-free condition at room temperature in the presence of 0.5 mol% of cobalt. Enantiomeric excess (ee) higher than 99% was achieved after 1.5 hour with a conversion of 55%. No reaction was detected for the unmetallated polymer brushes **2**. The reaction was also carried out using the commercially available homogeneous Jacobsen catalyst under the same conditions. It was observed that the hybrid catalyst showed almost the same enantioselectivity and activity with the homogeneous Jacobsen catalyst (figure 3).



Scheme 2: The hydrolytic kinetic resolution of epichlorohydrin

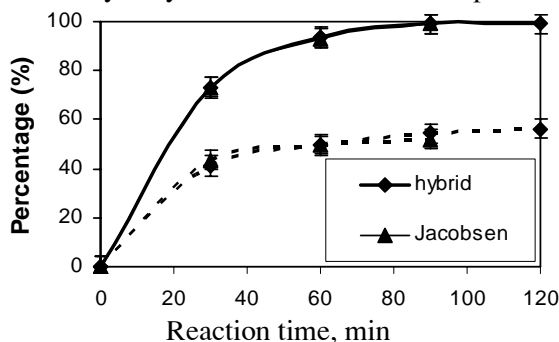


Figure 3: HKR reaction using the hybrid (diamonds), and homogeneous Jacobsen (triangles) catalysts. Broken lines show the reaction conversions

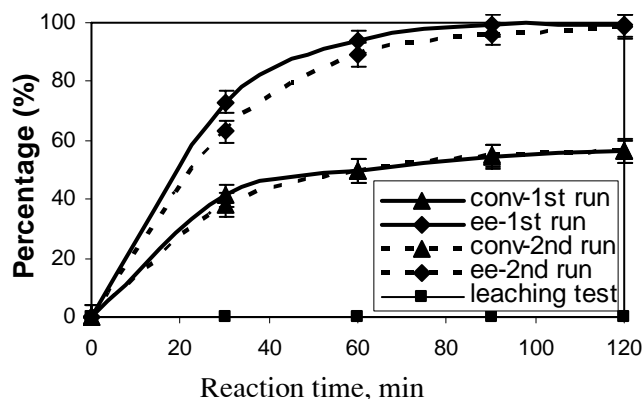


Figure 4: Catalyst recycling and leaching studies.

Broken lines show the kinetic data for the reaction with the recycled catalyst

A key motivation to develop immobilized metal complexes is their potentials for facile separation and reuse in subsequent reactions. The recycling of soluble polymer catalysts was normally achieved by precipitation upon adding suitable solvents [17, 22]. However, loss of catalysts during the precipitation workup is quite a common phenomenon for soluble polymer-supported catalyst and the problem still remains a challenge. The possibility of recycling soluble oligomer catalysts by precipitation method proved impossible due to their low molecular weight [14, 15]. Furthermore, recovery of cobalt(salen) catalyst by distillation of HKR products can lead to diminution of epoxide ee due to the chloride-catalyzed racemization of epichlorohydrin in the presence of Co (III)(salen) species [16]. Therefore, an improved method for the removal of the catalyst by simple filtration or centrifugation prior to the isolation of enantioenriched epoxides could hold practical significance. In this study, the hybrid cobalt(salen) catalyst was facilely recovered by centrifugation. The recovered catalyst was reactivated with acetic acid in the open air, and then reused under identical conditions to the first run. It was observed that the catalyst could be reused with only slight deactivation (Figure 4). Leaching test indicated that there was no contribution from leached active species. Although it was previously reported that no apparent loss of activity was observed for insoluble polymer and silica-supported cobalt(salen) catalysts in the HKR, no kinetic

data was provided, and only conversions and ee at the end of the experiment were mentioned [16]. Unfortunately, stable activity and selectivity cannot be proven by reporting only similar conversion and ee at long times. Kinetic studies are the true test of catalyst deactivation.

IV - CONCLUSIONS

In conclusion, we have demonstrated a new approach to polymer-supported cobalt(salen) catalysts based on the surface-initiated atom transfer radical polymerization (ATRP) of functionalized salen monomer and styrene on nonporous silica. While formally heterogeneous, the hybrid cobalt(salen) catalyst can offer the enantioselectivity and activity of homogeneous catalysts due to the soluble polymer chains, and the practicalities of heterogeneous catalysts. Though the hybrid catalyst exhibits comparable activity and selectivity with the homogeneous Jacobsen, the ease of separation and recycling of the hybrid system changes the picture dramatically. The successful use of the hybrid cobalt(salen) catalyst in the HKR provides an intriguing route to polymer-supported catalysts. By switching the metal center, the linkers to the polymer backbones, as well as the solid supports, a library of hybrid salen catalysts could thus be facilely generated and used in a variety of salen-catalyzed asymmetric organic transformations. Further exploration and optimization of the hybrid system appears warranted, and is the focus of on-going

investigation.

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