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Poly(styrene) Resin-Supported Cobalt(III) Salen Cyclic Oligomers as Active Heterogeneous HKR Catalysts

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Abstract: A cross-linked poly(styrene) support functionalized with cobalt(III) salen cyclic oligomers that can be used as a catalyst for the hydrolytic kinetic resolution (HKR) of terminal epoxides is reported. This catalyst is the most active heterogeneous catalyst to date for the HKR of terminal epoxides and can be recycled more than six times with excellent enantioselectivities for the HKR of epichlorohydrin. A 3-fold rate enhancement was observed when conducting the HKR reaction with 6 equivalents of water compared to 0.6 equivalents. We hypothesize that this rate enhancement is due to water sequestration of the diol product from the organic phase, thereby maintaining a high local concentration of epoxides and catalyst in the organic phase.

Keywords: bimetallic catalysis; heterogeneous catalysis; recycling; supported catalysis

Introduction

The production of pharmaceuticals, agro-chemicals, and natural products often requires compounds with defined stereochemistry. Enantiopure chiral epoxides, in particular, are attractive for these applications.[1] A wide range of reagents can open chiral epoxides without racemization making these epoxides very versatile compounds for the organic chemist.[1a,2] The hydrolytic kinetic resolution (HKR) of terminal epoxides using a cobalt(III) salen catalyst is one of these epoxide-opening reaction.[3] It serves on an industrial scale to prepare chiral epoxides and diols.[4] Cobalt(III) salen complexes have been supported on various materials with the aim of increasing the activity of the salen catalysts and/or to recover the metal species from the reaction mixture.[5]

Several research groups have designed homogeneous supports that facilitate the bimetallic mechanism of the HKR.[6] They were able to synthesize highly active catalysts by placing the metal centers in close proximity to each other.[7] Our group has reported the most active HKR catalyst composed of cyclic oligomers *via* ring-expanding olefin metathesis of cyclooctene salen monomers. The resultant structures have the salen units freely dangling off the macrocyclic backbone.[7b] We suggest that the high activity of this catalyst is due to the flexibility of these cyclic oligomeric supports.[8] A drawback of these soluble supported catalysts is their removal from the reaction mixture.[9] Products must be removed from the catalyst by precipitation, vacuum distillation or other energy-intensive processes that often create significant waste.

Heterogeneous-supported catalysis is focused on ease of recovery of a catalytic species from the reaction medium through filtration.[9] The Jacobsen group[5c] has synthesized heterogeneous cobalt salen catalysts grafted to poly(styrene) resins. A drawback was that higher loadings were required to obtain the performance of the molecular cobalt salen catalyst. One reason for the reduced performance is catalytic site isolation on the support, which does not facilitate the bimetallic interactions necessary for HKR. The Weck and Jones groups produced a more active heterogeneous HKR catalyst from copolymers composed of salen-functionalized styrene and styrene monomers grafted from silica.[10] The salen units being in close proximity by virtue of the polymer backbone allowed enhanced bimetallic cooperation. However, despite several attempts cited in the literature, heterogeneous-supported catalysts are in most cases not as active and selective as their homogeneous counterparts. Therefore it would be highly advantageous to obtain a HKR catalyst that is both highly active and easily recoverable. Herein we report such a system by im-

mobilizing the highly active cyclic oligomeric salen catalysts onto insoluble poly(styrene) resins. This strategy yields a highly active catalyst that can be easily recovered and recycled. Under our reaction conditions, we are able to separate the catalyst, the enantiopure epichlorohydrin, and the diol product from each other using filtration and decantation techniques. The resin-supported catalyst itself is easily synthesized and metallated with only simple filtration and washing procedures.

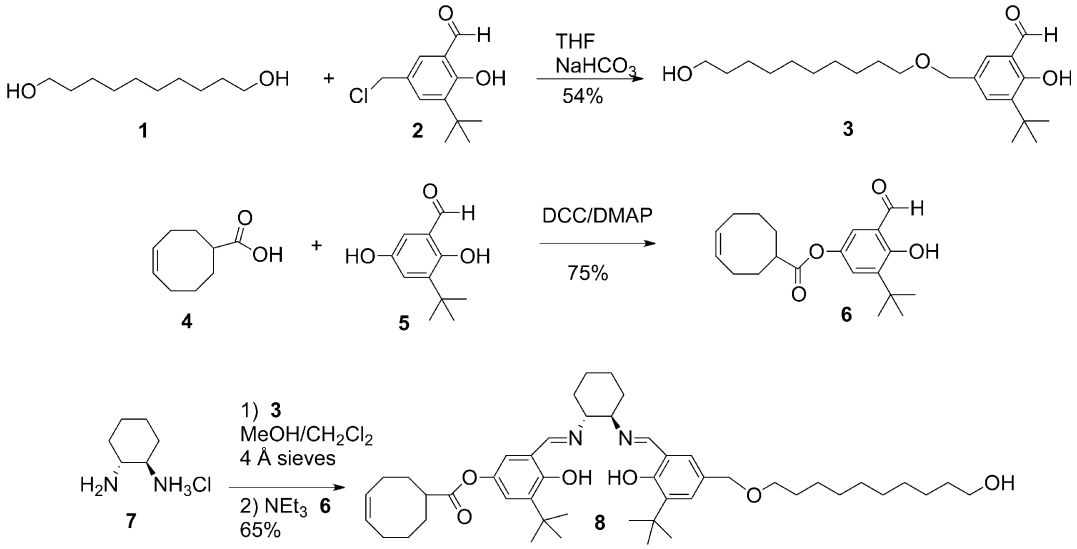
Results and Discussion

Aldehyde **3** was synthesized by Williamson ether synthesis from compounds **2** and **1**. Monomer **8** was synthesized by modification of a literature procedure (Scheme 1) and is bifunctional with a polymerizable cyclooctene group on one side and a C_{10} alkyl chain terminated with a hydroxy group for attachment to the resin on the other.[11]

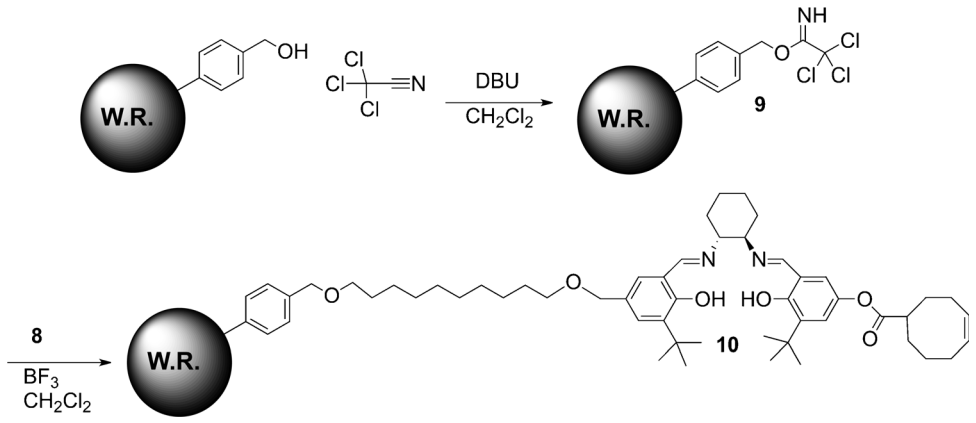
Initially, we investigated a grafting-to strategy for the functionalization of Merrifield resins with **8**. However, the grafting density was unacceptably low and we investigated the use of Wang resins instead. Following a literature procedure, we modified Wang resins to install trichloroimine leaving groups using DBU forming resin **9** (Scheme 2).[12] Using catalytic BF_3, a grafting density of 27% (based on 0.9 mmol g^{-1} initial resin functionalization) of **8** to the surface of the resin was achieved according to CHN analysis.

Compound **12**, the oligocyclooctene-functionalized Wang resin (Scheme 3), was then synthesized by swelling **10** in dichloromethane for one hour followed by the addition of Grubbs 3rd generation initiator and finally cyclooctene-salen **11** forming an oligomer containing units of **8** and **11**.[13]

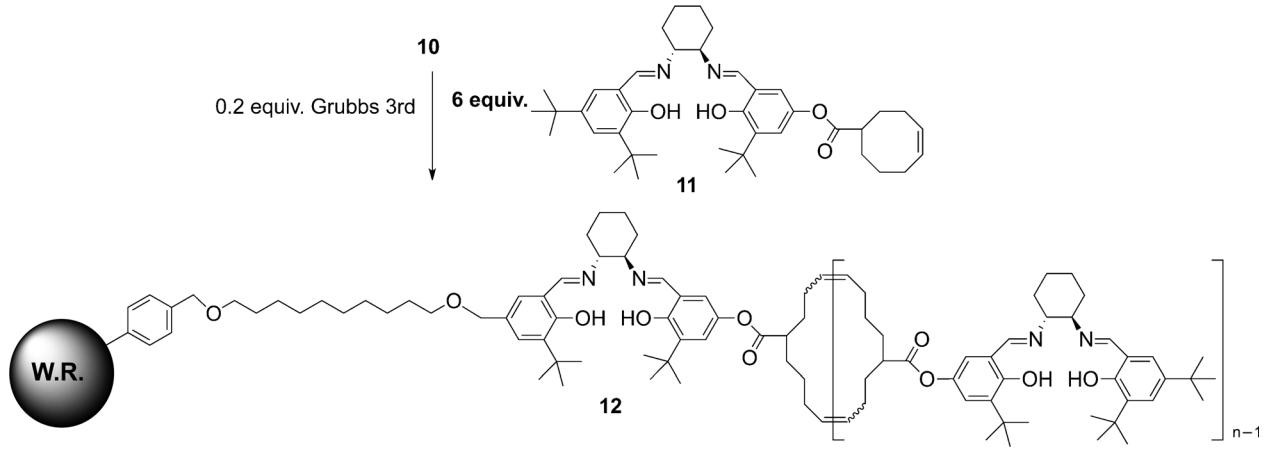
Proton NMR magic angle spinning spectroscopy experiments were conducted on functionalized resins **10** and **12** to examine for olefin resonances (Figure 1). We rationalized that the resins should only show resonances for the carbon-carbon double bonds due to



Scheme 1. Synthesis of monomer **8**.



Scheme 2. Functionalization of Wang resin (W.R.) with **8**.



Scheme 3. Polymerization on the resin surface.

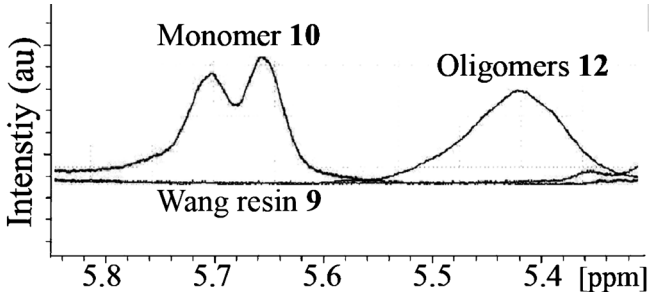


Figure 1. Partial magic angle spinning ^{1}H NMR spectrum of the olefin region of Wang resins **10** (5.7 ppm) and **12** (5.4 ppm) compared to trichloroimine Wang resin **9**.

either the cyclooctene monomers on **10** or the oligomeric cycles for **12**. Consistent with what we have observed before in solution using ^{1}H NMR spectroscopy, the olefin peaks after polymerization shift upfield from 5.7 ppm for the monomer to 5.4 ppm for the oligomers.[7b] This finding indicates the formation of ROMP products but does not give any details about the linear or cyclic structure of the polymers/oligomers that are formed.

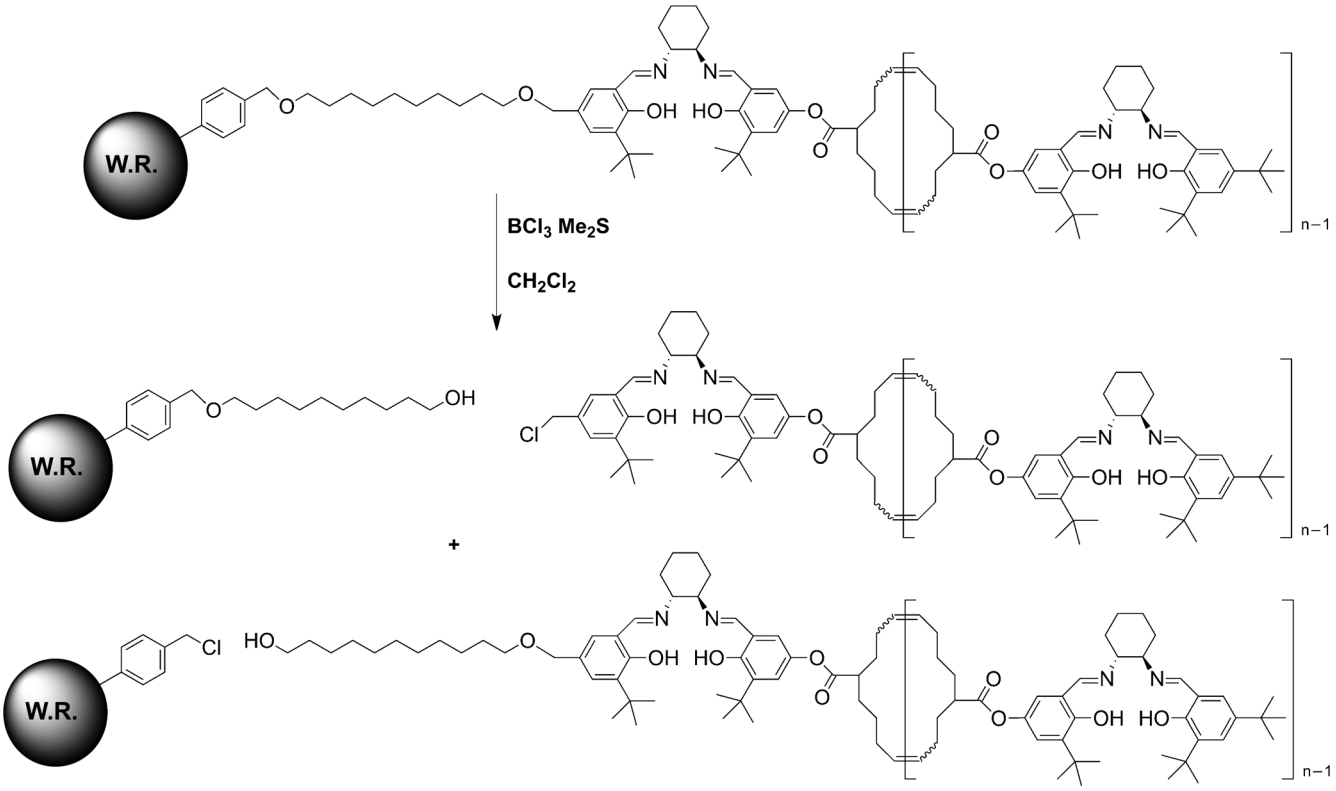
MALDI-TOF spectrometry can determine if the styrene group from the initiator and the vinyl group from the terminator are present, indicative of a linear polymer. To obtain a MALDI-TOF of the ROMP products on **12**, we cleaved them from the benzyl ether groups of the resin using a boron trichloride dimethyl sulfide complex.

The MALDI-TOF spectrum of the cleaved material (see Supporting Information) is consistent with the formation of cyclic oligomers with ring sizes ranging from dimers to pentamers. We observe the cleavage of benzyl ethers at different positions from the support as shown in Scheme 4.

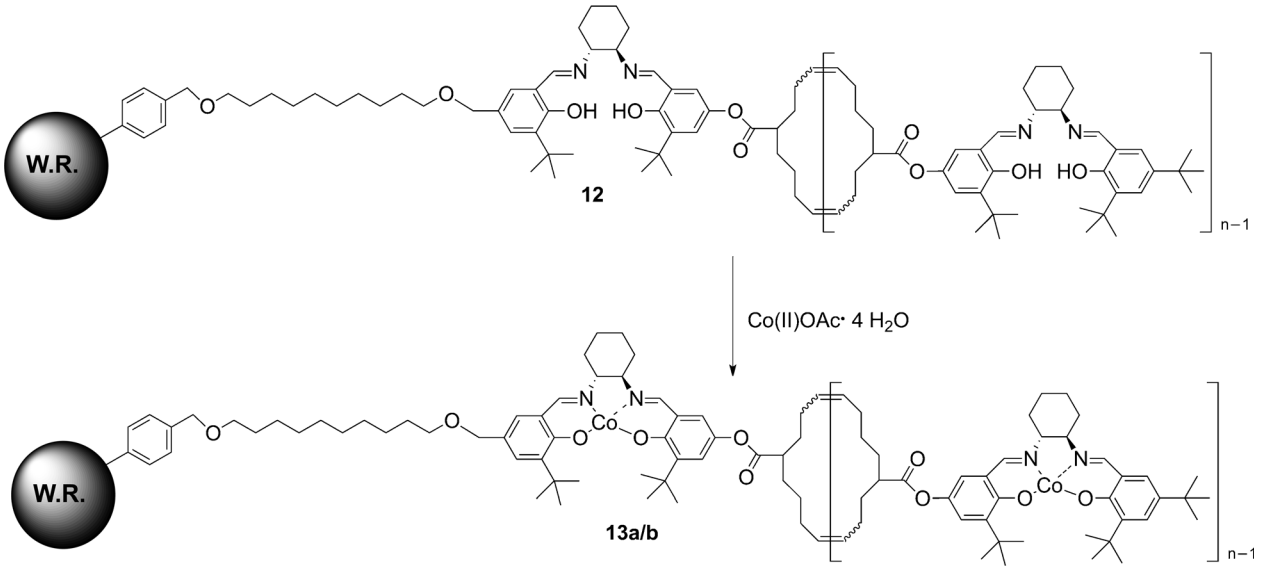
After verifying that we obtained cyclic ROMP-based oligomers containing supported salen ligands on **12**, the ligands were metallated using cobalt(II) acetate tetrahydrate. For this, the supported ligands were swelled in dichloromethane for one hour. Cobalt acetate was dissolved in methanol and added dropwise to the swollen resin under an inert atmosphere. The resin changed from a yellow to a brick-red color after several minutes and after an hour to a deep purple. The reaction mixture was stirred for four hours followed by washing three times with a 5:1 solution of dichloromethane and methanol. The resulting material was filtered and washed thoroughly with dichloromethane and dried under high vacuum to obtain pre-catalyst **13** (Scheme 5). Cobalt content was determined by ICP-MS to be 1.61% cobalt for **13a**. In repeating the synthesis of **13** the cobalt content was lower at 1.41%, denoted pre-catalyst **13b**. There was also a reduction in nitrogen according to CHN analysis indicating less ligand on the surface of the resin rather than an inefficient metallation. Differences in activity were observed between these catalysts where resins with higher cobalt content showed better activity. We hypothesize the correlation between activity and cobalt content is dependent on the local concentration of cobalt(III) salen units. Resins with higher cobalt content have more catalytic sites in closer proximity thereby enhancing the bimetallic cooperation necessary for HKR.[5g]

Pre-catalysts **13a** and **13b** were oxidized to Co(III)OAc by swelling them in dichloromethane for one hour followed by the addition of excessive acetic acid and stirring for 20 min under air. The liquids were decanted and the solids dried under high vacuum for one hour.

To investigate the catalytic activity of our heterogeneous catalysts, the catalyst-containing resins (0.01 mol% cobalt basis) were swollen in the epoxide of interest for 20 min with chlorobenzene as an internal standard. To initiate the reaction, 0.6 equivalents of water were added. Aliquots were removed at certain time intervals to determine when the reaction



Scheme 4. Oligomer fragments cleaved from surface of the resin for MALDI-TOF analysis.

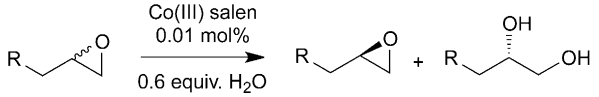


Scheme 5. Metallation of resin-supported cyclic oligomers.

reached an enantiomeric excess (*ee*) of 99%. Epichlorohydrin reached 99% *ee* in 4 h with conversions of 53%. This is more than an order of magnitude more active than the best heterogeneous HKR catalyst in the literature.[10] Hexene oxide was also tested as a substrate using **13a** reaching 99% *ee* in 240 min (Table 1).

We evaluated our supported catalysts under previously established conditions using epichlorohydrin, 0.1 mol% catalyst, 0.6 equiv. water, 25 °C, and acetate as the counterion.[14] Using catalyst **13a** 99% *ee* was reached in less than 20 min, which is comparable to the activity of the homogeneous cyclic oligomers.

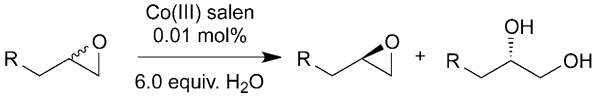
Table 1. HKR of epichlorohydrin and hexene oxide using 0.6 equiv. of water and catalyst **13a**.



R	Time [min][a]	% *ee*[b]	% Conversion[b,c]
Cl	240	99	53
n-propyl	240	99	52

[a] Time to reach 99% *ee*.
[b] Determined by chiral GC.
[c] Calculated relative to chlorobenzene as an internal standard.

Table 2. HKR of epichlorohydrin and hexene oxide using 6.0 equiv. of water and catalyst **13a**.



R	Time [min][a]	% *ee*[b]	% Conversion[b,c]
Cl	60	99	50.3
n-propyl	180	99	51

[a] Time to reach 99% *ee*.
[b] Determined by chiral GC.
[c] Calculated relative to chlorobenzene as an internal standard.

A significant rate enhancement was observed when conducting the HKR of epichlorohydrin and hexene oxide with a 10-fold excess of water (6 equiv.). The HKR was complete in one hour compared to four hours with the standard 0.6 equiv. of water. The HKR of hexene oxide reached 99% *ee* in 180 min using 6 equiv. of water (Table 2).

Our hypothesis to explain the significant rate enhancement with increased water concentration is based on solubility. When the reaction is carried out with 0.6 equivalents of water, an aqueous and an organic phase are seen initially. After approximately 10 min, an appreciable amount of diol product accumulates that acts as an intermediary between the phases. When the reaction is carried out using 6 equivalents of water, an unstable oil in water emulsion is formed over the entire course of the reaction. Figure 2 shows catalyst **13a** as brown spheres inside the colorless organic phase. The catalyst beads appear to accumulate at the interface of the two phases indicative of a Pickering emulsion. After stirring is stopped the epoxide droplets begin to coalesce. The diol product is more soluble in the aqueous phase, leaving the catalyst and epoxides in the organic phase[15] (*vide infra*).

A similar rate enhancement was observed when we conducted the HKR of epichlorohydrin using the homogeneous cyclic oligomers.[7b] This suggests that the rate enhancement it is not specific to **13**.

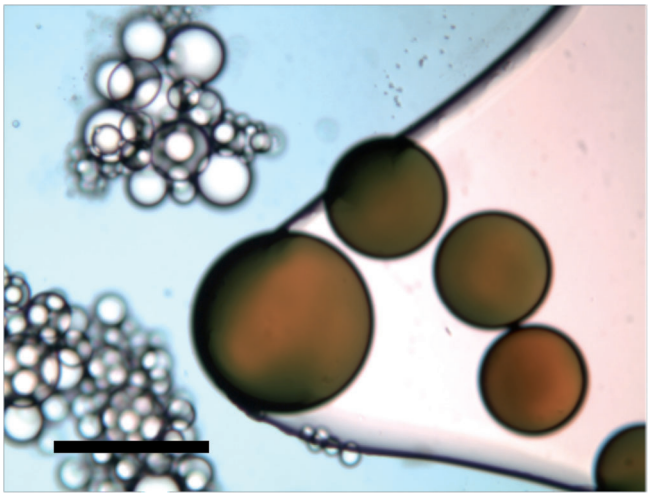


Figure 2. Optical microscopy image of the emulsion formed under HKR conditions using 6.0 equiv. of water. Scale bar is 200 μm. Water soluble blue dye used for contrast

To probe the origin of this rate enhancement, a series of experiments was conducted in which we gradually reduced the amount of water to investigate what effect this has on reaction rates. The rates remain generally the same using 6, 4, and 2 equivalents of water. Only when the reactions were run using 1 equivalent of water or less did we observe a single phase system. This resulted in as much as 3 times slower reaction rates (Table 3).

While the initial rates are similar for entries 1–5 (see Supporting Information), entries 4 and 5 have significantly reduced rates after 200 min. We hypothesized that this reduction in rate might be due to AcO^- counterion loss.[16] We theorized that reduced exposure of the catalyst to water would reduce counterion loss, thus maintaining the balance of Co–Ac and Co–OH species needed for high reaction rates.[6] Figure 3 shows two identical reactions at 0.6 equiv. of water. When 5 additional equivalents of water were added at 120 min (Figure 3, squares) we observed

Table 3. Water dependence of the reaction rate for the HKR of epichlorohydrin using **13b**.

Entry	Equiv. H_2O	Time [min][a]	% *ee*[b]
1	6	120	99
2	4	150	99
3	2	180	99
4	1	240	99
5	0.6	300	99

[a] Time to reach 99% *ee*.
[b] Determined by chiral GC.

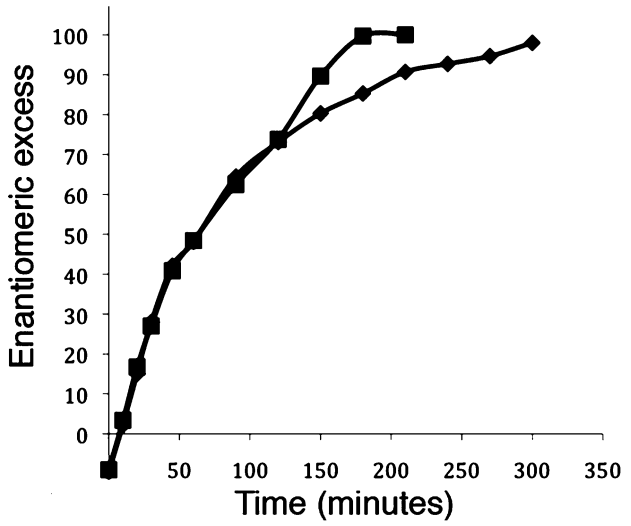


Figure 3. Kinetic plot of the HKR of epichlorohydrin. Diamonds; 0.01 mol% **13b**, 0.6 equiv. water. Squares; 0.01 mol% **13b**, 0.6 equiv. water, 5 additional equiv. added after 120 min.

a significant rate increase. This disproves the counterion loss theory since it is an irreversible process.[16]

Evidence of diol product sequestration into the aqueous phase was obtained by conducting the HKR of epichlorohydrin using D_2O. According to ^1H NMR spectroscopy experiments, we observe diol product accumulation in the aqueous phase contaminated with approximately 17% epichlorohydrin. The epichlorohydrin phase was contaminated with 3% diol product.

The fact that the products of the reaction self-separate under reaction conditions can be a very attractive feature to the industrial preperation of enantiopure epoxides as the energy intensive azeotropic distillation procedures and the use of solvents for extraction to separate components from the reaction mixure can be omitted.[4] We suggest that diffusion is the main reason behind this rate enhancement. Due to diol removal from the organic phase, where the supported catalyst resides, the concentration of the epoxides is maintained over the entire course of the reaction rather than being diluted by the diol product and water.

While we were able to demonstrate excellent catalytic activity of **13a** using our modified procedure, the other main goal of this work was being able to easily recover and reuse the catalyst. After each HKR cycle the catalyst was collected by filtration. Before the catalyst was used in the next cycle it was reactivated by stirring in a solution of dichloromethane and glacial acetic acid for 20 min.[17] We then decanted the liquids and any remaining volatiles were removed under vacuum yielding the reactivated catalytic species. We recycled **13a** 5 times with *ee* values above 99% while cycles 6 and 7 yielded *ee* values of 95%. Total turnover numbers (for all 7 cycles) for **13a** were calculated to be 37,480 (Table 4).

Table 4. Recycling studies for the HKR of epichlorohydrin with **13a** using 6.0 equiv. of water.

Cycle	Time [min][a]	% ee[b]	% Conversion[c]
1	75	99	50.6
2	90	99	53.8
3	135	99	52.1
4	150	99	55.9
5	180	99	49.8
6	210	95	57.4
7	240	95	55.2

[a] Time to reach 95–99% *ee*.
[b] Determined by chiral GC.
[c] Calculated relative to chlorobenzene as an internal standard.

Table 5. Elemental analysis of fresh and spent catalyst **13a** at 6.0 mol% water content.

	C[a]	H[a]	N[a]	O[b]	Co
Fresh	81.82	7.10	0.95	8.53	1.61[c]
Spent	77.41	8.02	0.94	12.63	1.00[c]

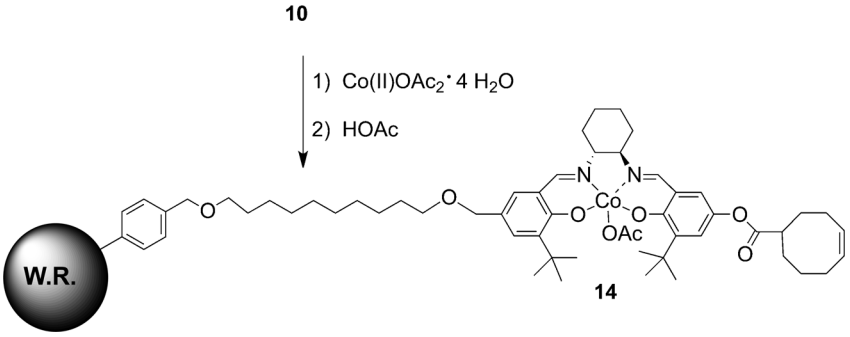
[a] Determined by CHN analysis.
[b] Calculated.
[c] Determined by ICP-MS.

While the *ee*s for each cycle are outstanding, the times required to obtain these yields increased for each cycle suggesting that some catalyst deactivates during each cycle. While there are many possible deactivation pathways, CHN elemental analysis of the spent catalyst shows a reduction in carbon relative to fresh catalyst, indicative of ligand hydrolysis (Table 5). Surprisingly the nitrogen content remains unchanged, contrary to what is seen in the literature,[10] as nitrogen reductions can be as high as 40–60%.

To investigate whether the macrocycles on the resin are a necessary feature of our catalytic system, a control experiment was conducted comparing the HKR activity of **13a** to **14** which is the metallated version of **10** (Scheme 6). The cobalt content of **14** is 1.1% Co.

Under our standard reaction conditions the HKR of epichlorohydrin using **14** reached 97% *ee* in 4 h using 6 equiv. water. This is an interesting result due to the fact that the small molecule analog, and similarly structured supported catalysts reported in the literature are significantly less active at loadings of 0.01 mol%.[5c,10] This suggests an increase in bimetallic cooperation between adjacent catalyst units grafted on the resin surface (Figure 4).

Perhaps the high grafting density can be attributed to the leaving group ability of trichloroimine com-



Scheme 6. Metallation of resin-supported monomer **10**.

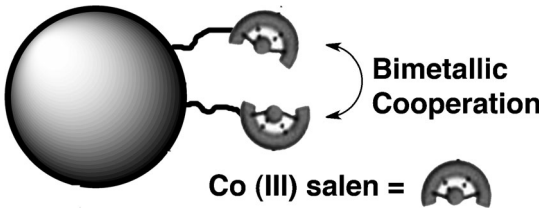


Figure 4. Schematic representation of the bimetallic cooperation between salen units on the resin surface of catalyst **14**.

pared to the benzyl chloride of the Merrifield resin. Additionally, the long, flexible C_{10} alkyl linker can have a significant effect on the activity as well.[18] The macrocyclic resin **13** is twice as active as **14** indicating the benefit of the cyclic structures for enhanced activities.

Conclusions

In conclusion, we report a highly active and selective heterogeneous Co(III) salen catalyst for the HKR of terminal epoxides. The supported catalyst is an order of magnitude more active than the best heterogeneously-supported HKR catalyst reported in the literature. A significant rate increase was observed when a 10-fold excess of water was added which we attribute to the diol product partitioning into the aqueous phase, maintaining a high concentration of the epoxides in the organic phase where the catalyst is located and active. This partitioning facilitates the separation of the reaction products increasing the utility of this process for potential industrial preparation of enantiomerically pure epoxides.

Experimental Section

General Remarks

Solution phase NMR spectra were recorded on a Bruker AV-400 (^{1}H: 400.1 MHz; ^{13}C: 100.6 MHz) spectrometer. Chemical shifts are reported in ppm and referenced to the corresponding residual nuclei in deuterated solvents. Solid-state NMR spectra were obtained using a 750 MHz wide bore Bruker magnet with a four channel Avance II Bruker console and a 4 mm HCND HRMAS probe. Spinning frequency was 6 kHz and the temperature 300 K. MALDI-TOF data were collected on a Bruker OmniFLEX spectrometer using anthracenediol as a matrix. Chiral gas chromatography data used to determine enantiomeric excesses were obtained on a Shimadzu 10 A instrument with a flame ionization detector using a β-Dex 120 column purchased from Supelco using helium as the carrier gas. Straight phase column chromatography was performed with silica gel 60 Å (230–400 mesh) from Sorbent Technologies. All solvents were passed over MBraun copper catalyst for drying and degassed by 3 freeze-pump-thaw cycles. Wang resin was purchased from Nova Biochem, 100–200 mesh, 0.9 mmol g^{-1} substitution. Other reagents were used as received from suppliers. Unless otherwise noted, all reactions were conducted under Schlenk conditions in a nitrogen atmosphere. All solid phase reactions were conducted in 15 mL poly(propylene) centrifuge tubes and stirred on a vortex mixer at 2000 rpm. Solid phase products were collected on 3 mL Supelco SPC filtration tubes. Grubbs' 3rd generation initiator was synthesized according to the literature.[13] Optical microscopy images were obtained on a Leitz Ergolux microscope at 10×.

Compound 3

Compound **2** was synthesized according to a literature procedure.[19] 1.62 g (9.3 mmol) of 1,10-decanediol were dissolved in 20 mL dry THF by gentle heating. 2.27 g (37.2 mmol) of $NaHCO_3$ were added and the solution was allowed to stir at room temperature for 1 hour. Compound **2**, 528 mg (2.33 mmol), was dissolved in 10 mL of THF and injected drop-wise through a septum into the reaction mixture. The solution was allowed to stir for 48 h at room temperature with an argon balloon to vent CO_2 generated during the reaction. The bulk of the THF was removed by rotary evaporation and the mixture was diluted in 200 mL diethyl ether and washed 2× with water and 1× with brine, dried over anhydrous magnesium sulfate, filtered, the solvent removed by rotary evaporation and dried under high vacuum. The crude mixture was purified by column chromatography using a 6:4 hexanes:ethyl acetate solvent system giving a viscous yellow oil; yield: 458 mg (1.52 mmol, 54%). ^{1}H NMR ($CDCl_3$): $\delta = 1.27$–1.39 (m, 13 H, alkyl), 1.41 (s, 9 H, CMe_3), 1.46–1.67 (m, 4 H, alkyl), 1.75 (s, 1 H, O*H*), 3.48

(t, $J=6.7$ Hz, 2H, OCH_2), 3.61 (t, $J=6.1$ Hz, 2H, HOCH_2), 4.44 (s, 2H, Bz), 7.38 (d, $J=2.1$ Hz, 2H, Ph), 9.86 (s, 1H, OH), 11.76 (s, 1H, O=CH); ^{13}C NMR ($CDCl_3$): $\delta=25.5$, 26.2, 29.1, 29.3, 29.4, 29.5, 29.6, 29.7, 32.7, 32.9, 35.0, 6 0.4, 62.9, 70.4, 70.9, 120.2, 125.9, 126.7, 129.3, 131.0, 134.0, 138.3, 160.7, 197.1; HR-MS (ESI): $m/z=387.2503$, calcd. for $C_{22}H_{36}O_4Na^+$: 387.16.

Compound 8

Compounds **6** and **7** were synthesized according to a literature procedure.[7b] Mono hydrochloride diamine **7**, 85.5 mg (0.57 mmol) was added to a round-bottom flask along with 200 mg 4 Å molecular sieves and purged with nitrogen. Compound **6**, 182 mg (0.57 mmol), was dissolved in 1 mL of methanol and 0.5 mL dichloromethane and injected through a septum into the reaction mixture and left to stir at room temperature for 4 h. Triethylamine, 627 mg (0.57 mmol) was added and stirred for 5 min. Then, compound **3**, 200 mg (0.57 mmol), was dissolved in 1 mL methanol and 0.5 mL dichloromethane and injected into the reaction mixture and the mixture was stirred for 16 h at room temperature. The reaction mixture was dissolved in 100 mL of methylene chloride and washed 2× with water and 1× brine, dried over anhydrous magnesium sulfate, filtered, and dried by rotary evaporation followed by drying on high vacuum giving a viscous yellow oil. Material was purified by column chromatography using 19:1 hexanes:ethyl acetate solvent system with 0.5% triethylamine giving a yellow foam; yield: 304 mg (0.39 mmol, 65%). ^{1}H NMR ($CDCl_3$): $\delta=1.27$–1.34 (m, 14H, alkyl), 1.37 (s, 9H, CMe_3), 1.39 (s, 9H, CMe_3), 1.42–2.72 (m, 25H, alkyl), 3.03 (m, 2H, alkyl), 3.38 (t, $J=7.3$ Hz, 2H, HOCH_2), 3.62 (t, $J=7.2$ Hz, 2H, HOCH_2), 4.33 (s, 2H, Bz), 5.65 (m, 2H, olefin), 6.71 (d, $J=2.9$ Hz, 1H, Ph) 6.88 (d, $J=2.9$ Hz, 1H, Ph), 6.96 (d, $J=2.6$ Hz, 1H, Ph), 7.21 (d, $J=2.6$ Hz, 1H, Ph), 8.21 (s, 1H, OH), 8.27 (s, 1H, OH), 13.77 (s, 1H, N=CH), 13.80 (s, 1H, N=CH); ^{13}C NMR ($CDCl_3$): $\delta=24.1$, 24.4, 25.7, 25.9, 26.2, 27.8, 29.1, 29.3, 29.4, 29.5, 29.6, 29.7, 31.4, 31.5, 32.8, 33.1, 43.7, 34.9, 43.2, 43.3, 63.1, 70.2, 72.2, 72.3, 72,7, 118.1, 121.3, 122.7, 127.6, 129.3, 129.4, 129.5, 130.6, 130.7, 132.3, 137.1, 138.5, 141.7, 157.9, 159.8, 164.7, 165.5, 176.4; HRMS (ESI): $m/z=773.5472$, calcd. for $C_{48}H_{72}O_6+H$: 773.10

Resin 9

Commercially available Wang resin (100–200 mesh, substitution 0.9 mmol g^{-1}, 140 mg) was swollen by vortex mixing in 2 mL dry dichloromethane for 60 min in a poly(propylene) centrifuge tube. 171 μL (1.7 mmol) of trichloroacetonitrile were added and the reaction mixture was cooled to 0 °C. DBU, 11 μL (0.076 mmol), was added and the reaction mixture was stirred for 1 hour maintaining 0 °C. The mixture was washed and decanted with dichloromethane 3× and then filtered using a peptide resin filter and washed with diethyl ether followed by drying under high vacuum giving an off white granular solid. IR (KBr): $\nu=3337$, 3062, 2847, 1948, 1804, 1662, 1602, 1510, 1444, 1374 cm^{-1}.

Resin 10

Trichloroimine functionalized Wang resin **9**, 500 mg, was swollen in 3 mL dichloromethane for 60 min. Compound **8**, 200 mg (0.25 mmol), was dissolved in 1 mL dichloromethane and added to the swollen resin. The mixture was stirred for 5 min then 5 μL (0.039 mmol) boron trifluoride etherate were added and the mixture was stirred for 1 hour. The reaction mixture was washed 4× with dichloromethane followed by decantation and filtered on a peptide resin filter giving a yellow granular solid; yield: 580 mg. CHN analysis found: C 83.08, H 7.64, N 0.84; IR (KBr): $\nu=3060$, 3025, 2849, 1945, 1874, 1716, 1602, 1505, 1444, 1368 cm^{-1}.

Resin 12

Compound **10**, 109 mg, was swollen in 1 mL dichloromethane for 60 min. Grubbs' 3rd generation initiator 2.98 mg (0.033 mmol) was dissolved in 100 μL dichloormethane and added to the reaction mixture. After 10 seconds, compound **11** was added and the mixture stirred for 30 min. The reaction was quenched with ethylvinyl ether and diluted and decanted with dichloromethane 3× and filtered using a peptide resin filter and washed with ether, and dried under high vacuum affording a dark yellow (slightly greenish) granular solid. CHN analysis found: C 80.92, H 7.88, N 0.92; IR (KBr): $\nu=3427$, 3059, 3025, 2849, 1944, 1874, 1804, 1749, 1716, 1600, 1506, 1443, 1364 cm^{-1}.

General Procedure for Precatalysts 13a/b, 14

In a glove box, 100 mg resin **12** was swollen in 2 mL dichloromethane for 60 min. Then 30 mg (0.12 mmol) of cobalt(II) acetate·4H_2O was dissolved in 200 μL methanol. The cobalt solution was added drop-wise into resin **12**. The color changed from yellow to red in 3 min followed by a deep purple after 20 min. The reaction was stirred for 4 h. The liquids were decanted and the resin was washed 4× with dichloromethane then filtered onto a peptide resin filter. The precatalyst was dried thoroughly under high vacuum before removal from the glove box.

13a CHN analysis found: C 81.82, H 7.10, N 0.95; ICP-MS cobalt analysis 1.61% Co.

13b CHN Analysis found: C 80.84, H7.22 N 0.93; ICP-MS cobalt analysis 1.41% Co.

An analogous procedure was used to produce pre-catalyst **14**. CHN analysis found: C 83.08, H 7.04, N 0.82; ICP-MS cobalt analysis 1.10% Co.

Cleavage of Cycles for MALDI-TOF Analysis

20 mg of supported ligand **12** were swollen in 0.5 mL dichloromethane for 60 min. Then 10 mg (0.056 mmol) of boron trichloride dimethyl sulfide complex were dissolved in 0.5 mL dichloromethane and added to swollen resin **10** and allowed to stir for 20 min. The solution turned from clear to yellow in color. The resin itself changed from a yellow to an off-white color, indicating the release of the ligand from the surface of resin. The solution was filtered and washed with a solution of saturated sodium bicarbonate, dried over $MgSO_4$, and the volatiles were removed by rotary evaporation.

Typical Procedure for HKR of Terminal Epoxides

In a typical experiment, 10 mg (0.00283 mmol Co basis) precatalyst **13a** were swollen in 2 mL dichloromethane and

stirred for 60 min. Then 20 μL of glacial acetic acid were added and stirred for 20 min open to the air. The liquids were decanted and the remaining volatiles were removed under high vacuum for 1 hour. 28.29 mmol terminal epoxide (epichlorohydrin or hexene oxide) were added to the activated catalyst with 200 μL of chlorobenzene as an internal standard. The mixture was stirred for 20 min, and then 305 mg (16.9 mmol) for 0.6 equiv. water or 3050 mg (169.0 mmol) for 6 equiv. water of water, were added to initiate the reaction. Aliquots of 5 μL were removed at certain time intervals and diluted in 300 μL of diethyl ether to monitor the progress of the reaction by chiral GC. For recycling experiments, the resin was collected on a peptide resin filter and washed with diethyl ether 3× and dried under high vacuum for 5 h. To reactivate the catalyst for the next cycle it was treated with acetic acid as outlined above.

13a spent catalyst (after 7 cycles) CHN analysis found: C 77.41, H 8.02, N 0.92; ICP-MS cobalt analysis 1.01% Co.

Epoxide-Diol Partitioning NMR Experiment

To determine how much of the diol product was diffusing into the aqueous phase; the HKR of epichlorohydrin was conducted using 6 equiv. D_2O. After the reaction was complete the catalyst was filtered on a peptide filter. The filtrate was centrifuged to separate the emulsion. The epichlorohydrin layer was separated, diluted in $CDCl_3$ and dried over Na_2SO_4. Integration of the spectra indicated that epichlorohydrin (peak used for integration = 3.2 ppm, 0.93 H) was contaminated with approximately 3% of the diol product (peak used for integration = 3.9 ppm, 0.03 H). The aqueous layer was diluted in D_2O for ^1H NMR spectroscopy measurements and showed that the diol product (peak used for integration = 3.9 ppm, 1.0 H) was contaminated with approximately 17% epichlorohydrin (peak used for integration = 2.9 ppm, 0.17 H, see Supporting Information for spectra).

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