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Highly enantioselective resolution of terminal epoxides with cross-linked polymeric salen–Co(III) complexes

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Abstract—Crosslinked polymeric salen–Co(III) complexes derived from a novel dialdehyde and a trialdehyde were synthesized and employed in the hydrolytic kinetic resolution (HKR) of terminal epoxides. Up to 99% ee were obtained with only 0.16–0.02 mol% of catalyst (based on catalytic unit).

In the past decades, thousands of homogeneous chiral catalysts have been successfully developed, which exhibited high enantioselectivities and activities. However, separation and recovery of these expensive chiral catalysts are still non-trivial for industrial uses. To solve these problems, many heterogenized methods have been developed and the results with those heterogeneous catalysts have obtained much progress in recent years. It is noteworthy that some of them are even better than their homogeneous parent catalysts.[1,2] Typical salen–Co(III) complex, (Fig. 1) one of the most important chiral catalysts, shows excellent activities and enantioselectivities for the asymmetric hydrolytic kinetic resolution (HKR) of various terminal epoxides. The mechanism of the reaction has proven to involve cooperative bimetallic catalysis.[3–9] Many groups have devoted their efforts to developing heterogeneous analogs of the typical salen–Co(III) catalyst including organic or inorganic supported catalysts,[10–12] dimeric catalysts,[13] dendrimeric catalysts,[14] oligomeric catalysts,[15,16] FBS (Fluorous Biphase Systems)[17] and ionic liquid[18] for both academic and practical reasons. Among those reports mentioned above, Jacobsen's oligomeric catalysts (Fig. 2) exhibits exciting results, in which both the linkage length between metal centers and the counterions were carefully tuned to achieve an activity 100 times higher than that of the typical salen–Co(III) complex (Fig. 1) for the HKR of terminal epoxides. In this reaction, the cooperative effect has proven to be partly responsible for excellent results obtained with those oligomeric catalysts. Moreover, the same catalytic system could be extended to alcohols and phenols as nucleophiles for asymmetric ring-opening of terminal epoxides, while the typical salen catalyst (Fig. 1) has failed in this case.

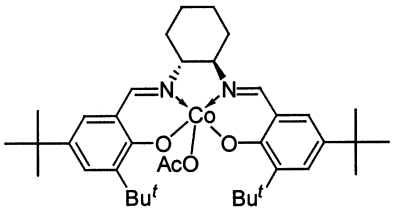

Figure 1. Jacobsen's catalyst.

On the basis of our research in developing polymeric chiral catalysts for asymmetric catalysis[19–21] and inspired by Jacobsen's work, we herein reported some novel salen–Co(III) complexes derived from an easily prepared dialdehyde and/or a trialdehyde with (*R*,*R*)-1,2-diaminocyclohexane for the asymmetric HKR of terminal epoxides. (Eq. (1)) We envisioned that the cooperative effect in the oligomeric catalysts can also be introduced to these new crosslinked polymeric chiral salen–Co(III) complexes by carefully tuning the unit structures. Furthermore, crosslinked polymeric chiral frameworks with different pore sizes could be constructed by using the trialdehyde and the dialdehyde in different proportions. It is foreseeable that excellent activities and enantioselectivities can be achieved with these kinds of crosslinked polymeric catalysts for the HKR of terminal epoxides.

The 3-*tert*-butyl-2,5-dihydroxybenzaldehyde **4** was prepared according to the literature with a slight modifica-

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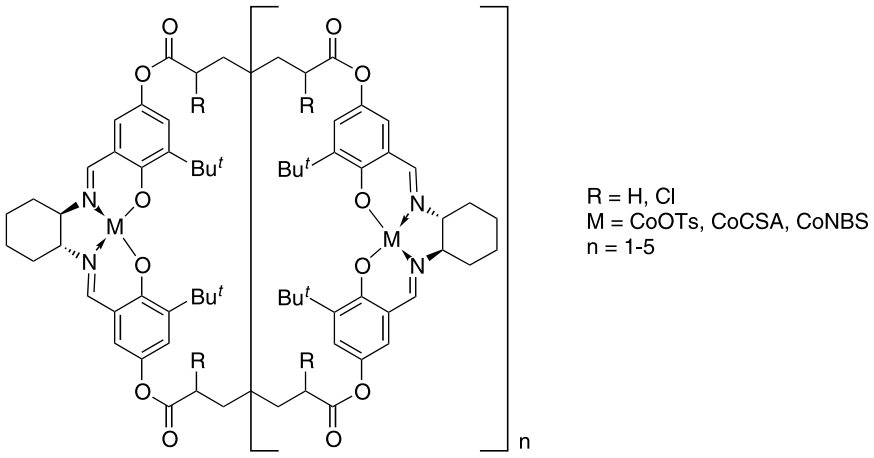
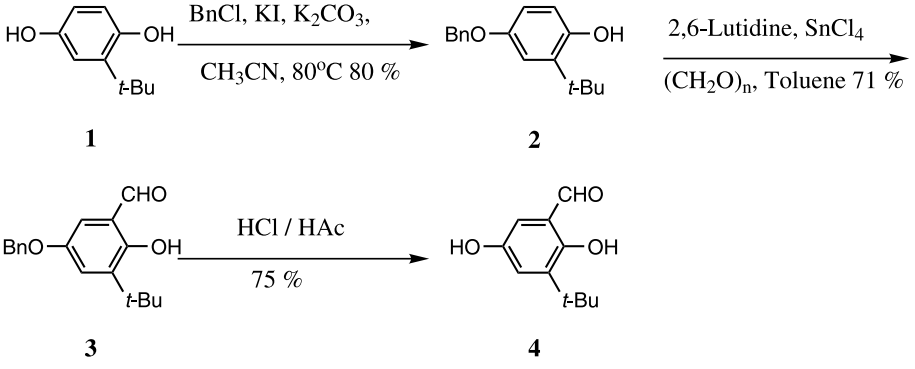


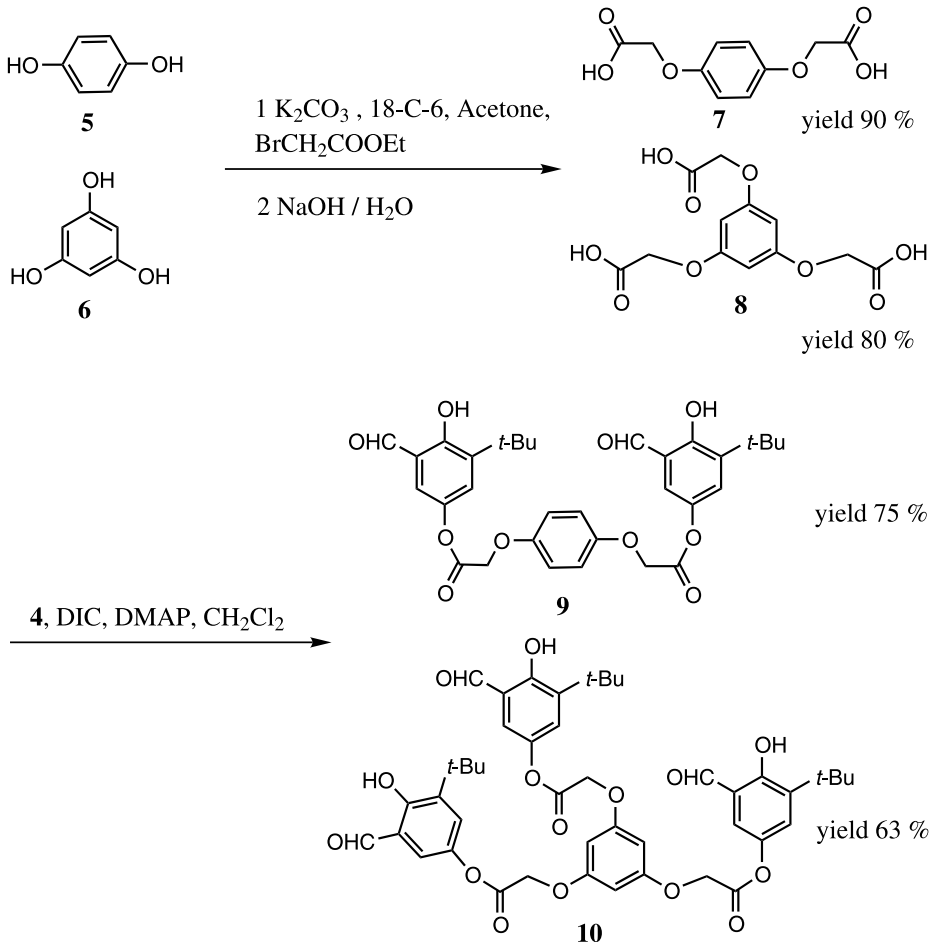
Figure 2. Jacobsen's oligomeric catalysts.

tion, the protective benzyl group was removed conveniently in a HCl/HOAc system.[22] (Scheme 1) The key dialdehyde **9** and trialdehyde **10** were synthesized through the condensation of 3-*tert*-butyl-2,5-dihydroxybenzaldehyde with diacid and triacid derived from hydroquinone and chloroglucinol (Scheme 2). The condensation of aldehyde and (*R*,*R*)-1,2-diaminocyclohexane stoichiometrically afforded the polymeric ligands. When only dialdehyde was employed, we obtained an oligomeric ligand. On the other hand, when different proportions of trialdehyde were mixed with the dialdehyde, the crosslinked polymeric ligand was obtained. In most cases, the polymeric ligands have an average molecular weight between only 4000 and 10000 (GPC). However, the complete crosslinked polymer ligand derived from trialdehyde and (*R*,*R*)-1,2-diaminocyclohexane exhibited as a gel polymer that was partially soluble in THF. Because of the ester groups in the polymer, other condensation conditions for synthesizing polymeric ligands with higher molecular weight were not evaluated. The polymeric catalysts were synthesized by simply mixing the chiral ligand, $Co(OAc)_2 \cdot 4H_2O$ and 2,6-lutidinium *p*-toluenesulfonate (LTPS) in toluene and methanol (3/1) with stirring in the air for 2 h (Scheme 3). When the proportion of trialdehyde/dialdehyde (tri/di) was lower than 20/100, most of the catalysts showed good solubility in CH_2Cl_2, and literature workup process to purify the catalysts were employed.[15] However, when that proportion was bigger than 25/100, most of the catalysts displayed poor solubility and the catalysts were collected through filtration and washing with CH_2Cl_2 and CH_3OH continuously.[23]

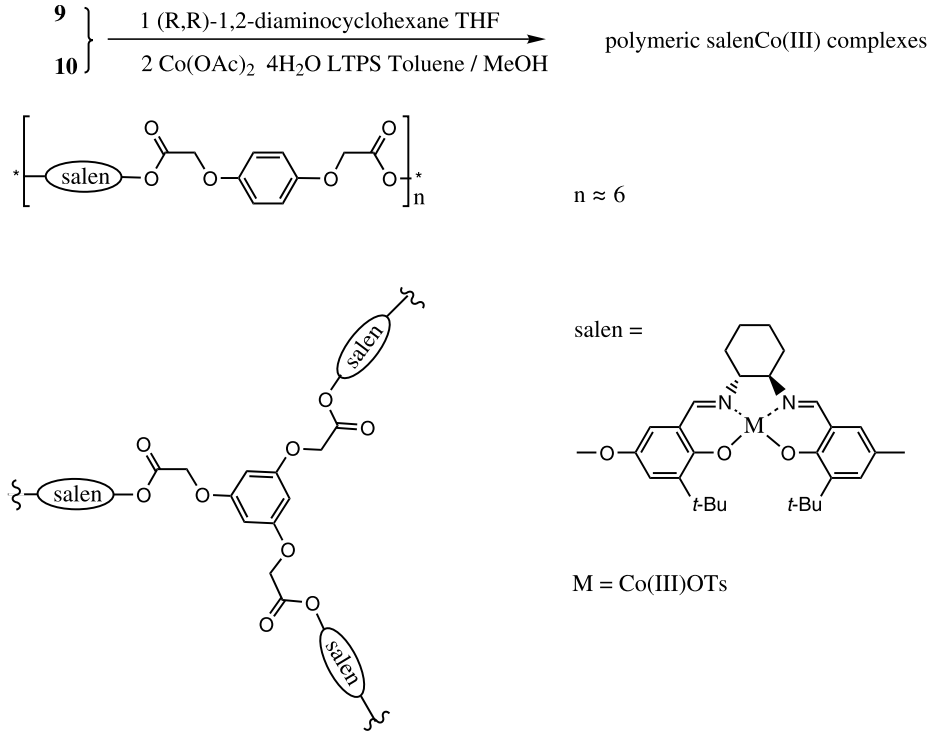
The HKR of terminal epoxides with the above-mentioned catalysts were performed following the typical procedure reported in the literature (Eq. (1)).[15,24] and the results are listed in Table 1. As shown in Table 1, all catalysts showed excellent activities and enantioselectivities for epichlorohydrin, styrene oxide and phenyl glycidyl ether. In a wide range of tri/di proportions, the crosslinked polymeric catalysts gave almost identical results. (entries 1–8) When the reaction was performed at lower temperature, a little longer time was needed and the enantioselectivities were the same (entries 9–12). Most of the crosslinked polymer catalysts showed better activities than those of the oligomeric one (tri/di = 0/100), which means the crosslinker we employed have some positive effects on the cooperation between metal centers (entries 1, 13, 17) The complete crosslinked polymeric catalyst showed slightly lower activities and enantioselectivities in the HKR of three substrates (entries 8, 12, 16, 20) we think that the poor solubility and some unknown reactive centers of the crosslinked polymeric catalyst ought to be responsible for this result. Using the recollected catalysts for another reaction has not been successful even with the



Scheme 1. Synthesis of 3-*tert*-butyl-2,5-dihydroxy benzaldehyde.



Scheme 2. Synthesis of the dialdehyde and the trialdehyde.



Scheme 3. Synthesis of the polymeric catalysts.

Table 1. HKR of epoxides catalyst by crosslinked polymer catalysts[a]

Entry	R	Tri/Di	Cat.	Time (h)	Temp. (°C)	Ee[b] (ep)	Ee[c] (diol)	Conv.[d,e]
1	CH_2Cl	0/100	0.02%	14	12	98%	97%	50%
2	CH_2Cl	2/100	0.02%	8	12	99%	96%	51%
3	CH_2Cl	6/100	0.02%	11	12	99%	96%	51%
4	CH_2Cl	10/100	0.02%	11	12	99%	95%	51%
5	CH_2Cl	14/100	0.02%	11	12	98%	96%	50%
6	CH_2Cl	25/100	0.02%	8	12	98%	95%	50%
7	CH_2Cl	50/100	0.02%	8	12	99%	91%	52%
8	CH_2Cl	100/0	0.02%	22	12	>99%	86%	53%
9	CH_2Cl	0/100	0.02%	27	2	97%	97%	50%
10	CH_2Cl	25/100	0.02%	16	2	97%	95%	51%
11	CH_2Cl	50/100	0.02%	16	2	98%	94%	51%
12	CH_2Cl	100/0	0.02%	27	2	93%	91%	47%
13	Ph	0/100	0.16%	14	20	98%	89%	52%
14	Ph	2/100	0.16%	14	20	97%	91%	52%
15	Ph	50/100	0.16%	21	20	97%	94%	51%
16	Ph	100/0	0.16%	21	20	95%	92%	48%
17	CH_2OPh	0/100	0.02%	15	20	96%	88%	48%
18	CH_2OPh	2/100	0.02%	15	20	97%	92%	51%
19	CH_2OPh	50/100	0.02%	15	20	97%	87%	53%
20	CH_2OPh	100/0	0.02%	15	20	85%	84%	43%

[a] The reactions were carried out on 28 mmol of epoxide, catalyst (based on catalytic unit) and 0.60 equiv. of water.
[b] The ee's of the epichlorohydrin and phenyl glycidyl ether were determined by GC analysis using a chiral capillary column (Gamma-225 30 m×0.25 mm (i.d.)); the ee of styrene oxide was determined by GC analysis using a chiral capillary column (cyclodex-β, 2,3,6-methylated, 30 m×0.25 mm (i.d.)).
[c] The ee's of the diols were determined by GC analysis of the corresponding acetals using a chiral capillary column (cyclodex-β, 2,3,6-methylated, 30 m×0.25 mm (i.d.)).
[d] Based on total racemic mixture.
[e] Estimated according to the ee's of the epoxides and diols, see Ref. 10.

complete crosslinked polymeric catalyst. We ascribe this to the fact that the oxygen adjacent to the carbonyl groups makes the ester linkages more sensitive to the reaction systems. The IR spectra showed the cleavage of the ester bonds in the recollected catalyst. A similar effect caused by chlorine substitutes has been reported in literature.[16]

In conclusion, crosslinked polymeric salen–Co(III) complexes were prepared with a novel dialdehyde and a trialdehyde. Excellent activities and enantioselectivities were achieved using these catalysts. The cooperative effects observed in Jacobsen's oligomeric catalysts have been successfully introduced into our crosslinked catalysts. The crosslinked catalysts exhibited slightly higher activity without obvious lose of enantioselectivities.

Acknowledgements

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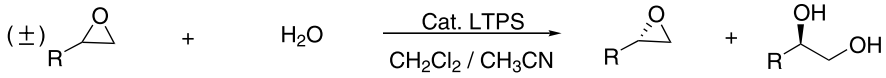
24. The representative procedure of asymmetric hydrolysis. A mixture of polymeric catalyst (0.02 mol% based on catalytic unit), LTPS 1.6 mg (0.04%), epichlorohydrin (28 mmol) and 0.1 mL of CH_2Cl_2/CH_3CN (1/1) was stirred at ambient temperature for 30 min, 0.3 mL of H_2O (0.6 equiv.) was added in one portion. The reaction mixture was stirred for 8–27 h, and the ee% values were determined by capillary GC. For the HKR of styrene oxide or phenyl glycidyl ether, more solvents are needed to dissolve the diols. Obviously the longer the reaction proceeded, the better the ee's of the epoxides. We could obtain up to 99% ee for all the substrates. The reported data in Table 1 keeps a balance between the ee's of epoxides and diols. The absolute configurations of the obtained epoxides and diols showed in Eq. (1) are compared with the literature.[15]



(1)