Pergamon

Tetrahedron Letters 43 (2002) 6625–6627

TETRAHEDRON
LETTERS

Highly enantioselective resolution of terminal epoxides using polymeric catalysts

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Received 7 May 2002; revised 3 July 2002; accepted 12 July 2002

Abstract—Poly-salen-Co(III) complexes were employed in the hydrolytic kinetic resolution (HKR) of terminal epoxides and ee's up to 98% were obtained. In the HKR of epichlorohydrin, the polymeric catalysts can be recovered and modified for recycling. The recovered polymer catalyst shows good activity and selectivity. © 2002 Elsevier Science Ltd. All rights reserved.

As the most powerful chiral catalyst for the hydrolytic kinetic resolution (HKR) of terminal epoxides to provide both optically active epoxides and diols, the Jacobsen's Salen-Co(III) complex (Fig. 1) has been used in the synthesis of libraries of important chiral intermediates.[1–7] The properties of the catalyst employed in the reaction have also been carefully studied and (a) the typical salen-Co(III) complex has proved to exhibit excellent efficiency in the HKR of terminal epoxides and to show good stability, and (b) the mechanism of the reaction has proved to involve cooperative bimetallic catalysis.[8,9] Because of these features, Jacobsen's and other groups have developed dimeric,[10,11] oligomeric,[12,13] polymeric,[14,15] dendrimeric framework[16] and inorganic-supported catalysts[17] in order to make the HKR of terminal epoxides more practical.

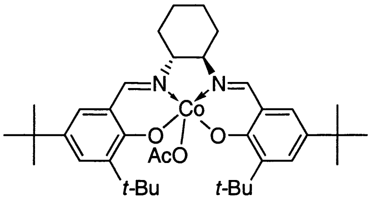
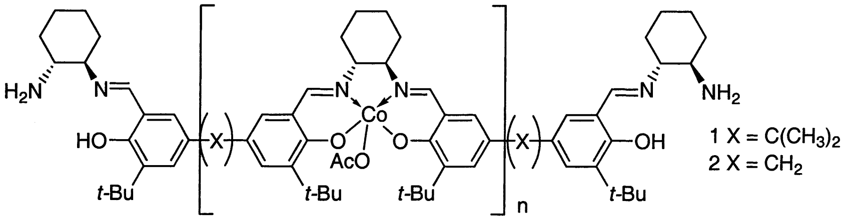


Figure 1. Jacobsen's catalyst.

In our previous reports, chiral poly-salen-Mn(III) complexes were employed for the catalysis of asymmetric epoxidation of unfunctionalized olefins and similar results to those olefins using the typical Jacobsen's catalyst were obtained. However, the polymeric catalysts partly decomposed during the experimental processes.[18,19] As a continuation of our research in developing highly efficient polymeric catalysts for asymmetric transformations, we report herein the HKR of terminal epoxides (Eq. (1)) using two of the abovementioned salen ligand cobalt complexes (Scheme 1) as catalysts. Both of the catalysts show good activities and enantioselectivities for the reaction; moreover, the -NH_2 groups, which exist at both ends of the polymeric catalyst molecules, can easily be modified in the HKR of epichlorohydrin making the catalysts water soluble.



Scheme 1. The polymeric catalysts.

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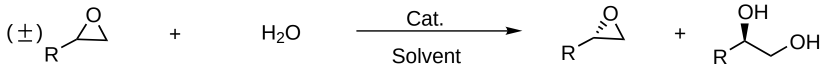
PII: S0040-4039(02)01446-6



(1)

There are two methods for preparing the polymeric catalysts (the syntheses of the polymeric ligands has been reported in our previous work).[18,19] (a) The cobalt atoms can be inserted into the polymeric ligands to obtain the polymeric catalysts according to the literature.[14] (b) The polymeric catalyst can be obtained using the reported Co(II) to Co(III) procedure.[20] However method (a) is much more suitable, because the catalysts are soluble in methanol/toluene solution during their preparation, thus the cobalt atoms can easily approach the center of the ligand.

The kinetic resolution of terminal epoxides was carried out by stirring the epoxide in the presence of 0.5 mol% catalyst (based on the catalytic unit), solvent and 0.55 equiv. of water at the indicated temperature. The results are summarized in Table 1.

As shown in Table 1, catalyst **1** shows excellent results for all three substrates and the ee's are 98, 97 and 98% for propylene oxide, epichlorohydrin and phenyl glycidyl ether, respectively (Table 1, entries 2, 5, and 8). When catalyst **2** is employed, slightly lower enantioselectivities were obtained. These results are in agreement with those obtained in the epoxidation reaction.[18,19]

In the HKR of epichlorohydrin, we observed an unusual phenomenon that was completely different from the HKR of propylene oxide.[21] Under our reaction conditions, with or without solvent, the reaction mixture became a single phase during the reaction. It is more interesting that the black polymeric catalysts can be easily dissolved in the aqueous phase but not in the organic phase. Therefore, the polymeric catalysts could be isolated easily from the reaction mixture by the following procedure. The unreacted epoxide is distilled off from the reaction mixture, diethyl ether is added to the residue and the catalyst can be precipitated and collected via filtration. This recovered catalyst **1** could be activated following the modified Jacobsen's procedure[20] before reusing. When the activated recovered catalyst **1** was used for the HKR of propylene oxide, excellent activity and enantioselectivity were obtained (entry 17 versus entry 1). In the HKR of phenyl glycidyl ether in CH_2Cl_2 or THF, the recovered catalyst **1** shows poor activity (entries 18 and 19),

Table 1. HKR of epoxides catalyzed by polymeric catalysts[a]

Entry	R	Cat.	Solvent	Temp. (°C)	Time (h)	Conv. (%)[b]	Ee (%)[c,d]	Conf.[e]
1	CH_3	**1**	None	rt	48	41	ND[f]/97	*R*
2	CH_3	**1**	THF	rt	48	48	ND[f]/98	*R*
3	CH_3	**1**	CH_2Cl_2	rt	48	49	ND[f]/95	*R*
4	CH_2Cl	**1**	None	10	12	47	90/92	*S*/*R*
5	CH_2Cl	**1**	THF	10	12	49	97/94	*S*/*R*
6	CH_2Cl	**1**	CH_2Cl_2	10	12	48	91/94	*S*/*R*
7	$PhOCH_2$	**1**	THF	rt	24	>47	94/89	*S*/*R*
8	$PhOCH_2$	**1**	CH_2Cl_2	rt	24	>49	98/87	*S*/*R*
9	CH_3	**2**	None	rt	48	51	ND[f]/93	*R*
10	CH_3	**2**	THF	rt	48	49	ND[f]/97	*R*
11	CH_3	**2**	CH_2Cl_2	rt	48	49	ND[f]/95	*R*
12	CH_2Cl	**2**	None	10	12	46	95/84	*S*/*R*
13	CH_2Cl	**2**	THF	10	12	49	97/91	*S*/*R*
14	CH_2Cl	**2**	CH_2Cl_2	10	12	47	97/83	*S*/*R*
15	$PhOCH_2$	**2**	THF	rt	24	>49	97/76	*S*/*R*
16	$PhOCH_2$	**2**	CH_2Cl_2	rt	24	>49	98/80	*S*/*R*
17	CH_3	Recovered **1**	None	rt	48	48	ND[f]/98	*R*
18	$PhOCH_2$	Recovered **1**	THF	rt	48	17	21/94	*S*/*R*
19	$PhOCH_2$	Recovered **1**	CH_2Cl_2	rt	48	31	45/95	*S*/*R*
20	$PhOCH_2$	Recovered **1**	H_2O	rt	30	>48	95/78	*S*/*R*
21	$PhOCH_2$	**1**	H_2O	rt	24	>48	95/57	*S*/*R*

[a] The reactions were carried using 10 mmol of epoxide, 0.5 mol% of catalyst (based on catalytic unit) and 0.55 equiv. of water at the indicated temperature.

[b] The conversion of the epoxide is based on the racemic epoxide added and the conversion of phenyl glycidyl ether is calculated according to the ee of the epoxide.

[c] The ee's of 1,2-propane diol and chloropropane diol were determined by GC analysis of the corresponding acetal using a chiral capillary column (cyclodex-β, 2,3,6-methylated, 30 m×0.25 mm (i.d.)); the ee's of epichlorohydrin were determined by GC analysis using a chiral capillary column (Gamma-225 30 m×0.25 mm (i.d.)); the ee's of phenyl glycidyl ether and 1-phenyl glycerol were determined by HPLC using a chiral OD column (90/10 hexanes/*i*-PrOH, 1 ml/min, 254 nm).

[d] The ee of epoxide/the ee of diol.

[e] Absolute configurations (epoxide/diol) were compared with the literature.[7]

[f] ND, not determined.

however, when water was used as both solvent and resolution reagent, very good activity and enantioselectivity were demonstrated (entry 20). It is worthwhile to note that the ee's of diols obtained by using the recovered catalyst **1** are better than those using the fresh catalyst **1** (entries 20 and 21). We suppose that the recovered catalyst **1** may be modified by the presence of hydrophilic groups at both ends of the polymer chain during the HKR of epichlorohydrin. Because an excessive amount of (*R*,*R*)-1,2-diaminocyclohexane is used for the synthesis of the polymeric ligand, two free -NH_2 might exist at both ends of the polymer ligand. When epichlorohydrin is employed as substrate, part of the epoxide reacts not only with H_2O, but also with these terminal -NH_2 groups, thus resulting in the water-soluble catalyst.

In summary, the kinetic resolution of terminal epoxides proceeds smoothly with poly-salen-Co(III) complexes to give excellent chemical yields and high ee's. It was found that the terminal groups of these polymeric catalysts can be modified to hydrophilic groups during the HKR of epichlorohydrin and the modified catalysts may promote the reaction with better enantioselectivities and provide a much easier isolation procedure.

Acknowledgements

This work was supported by the National Natural Science Foundation of China (29933050).

References

1. Li, L. S.; Wu, Y. L. *Chin. J. Org. Chem.* **2000**, *5*, 689–700 and references cited therein.
2. Kulig, K.; Holzgrabe, U.; Malawska, B. *Tetrahedron: Asymmetry* **2001**, *12*, 2533–2536.
3. Jin, C.; Ramirez, R. D.; Gopalan, A. S. *Tetrahedron Lett.* **2001**, *42*, 4747–4750.
4. Sharon, C.; William, K. *Chem. Commun.* **2001**, *11*, 1040–1041.
5. Rodriguez, A.; Nomen, M.; Spur, B. W.; Godfroid, J. J.; Lee, T. H. *Tetrahedron* **2001**, *57*, 25–37.
6. Gu, J.; Dirr, M. J.; Wang, Y.; Scoper, D. L.; De, B.; Wos, J. A.; Johnson, C. R. *Org. Lett.* **2001**, *3*, 791–794.
7. Schaus, S. E.; Brandes, B. D.; Larrow, J. F.; Tokunaga, M.; Hansen, K. B.; Gould, A. E.; Furrow, M. E.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 1307–1315.
8. Jacobsen, E. N.; Wu, M. H. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H., Eds.; Springer: New York, 1999; pp. 1309–1326.
9. Jacobsen, E. N. *Acc. Chem. Res.* **2000**, *33*, 421–431.
10. Konsler, R. G.; Karl, J.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1998**, *120*, 10780–10781.
11. Kureshy, R. I.; Khan, N. H.; Abdi, S. H. R.; Patel, S. T.; Jasra, R. V. *J. Mol. Chem. A: Chem.* **2002**, *179*, 1–2 and 73–77.
12. Joseph, M. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2001**, *123*, 2687–2688.
13. Joseph, M. R.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2002**, *41*, 1374–1377.
14. Annis, D. A.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1999**, *121*, 4147–4154.
15. Osburn, P. L.; Bergbreiter, D. E. *Prog. Polym. Sci.* **2001**, *26*, 2015–2081.
16. Breinbauer, R.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2000**, *39*, 3604–3607.
17. Kim, G.-J.; Park, D.-W. *Catal. Today* **2000**, *63*, 537–547.
18. Yao, X.; Chen, H.; Lü, W.; Pan, G.; Hu, X.; Zheng, Z. *Tetrahedron Lett.* **2000**, *41*, 10267.
19. Song, Y.; Yao, X.; Chen, H.; Pan, G.; Hu, X.; Zheng, Z. *J. Chem. Soc., Perkin. Trans. 1* **2002**, 870–873.
20. Tokunaga, M.; Larrow, J. F.; Kakiuchi, F.; Jacobsen, E. N. *Science* **1997**, *277*, 936–938 (activation of the recovered catalyst is achieved using a mixture of methanol:toluene (1:1)).
21. In the HKR of propene oxide, after stirring for 30 min, most of the catalyst is dissolved in the substrate, however, the mixture became cloudy and a red precipitate appeared after 0.55 equiv. of water was added. When epichlorohydrin is employed, the reaction mixture was a black solution 4 h after water was added.