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Highly reactive and enantioselective kinetic resolution of terminal epoxides with H₂O and HCl catalyzed by new chiral (salen)Co complex linked with Al

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Abstract—The asymmetric hydrolytic kinetic resolution (HKR) of racemic terminal epoxides by new easily synthesized dimeric chiral (salen)Co bearing Al, provides a practical and straightforward method for the synthesis of enantiomerically enriched terminal epoxides (>99% ee) and diols. An inorganic acid, HCl is applied first time for the asymmetric ring opening reaction of terminal epoxides. Reactions are conveniently carried out at room temperature under an air atmosphere. © 2005 Elsevier Ltd. All rights reserved.

In the past decade asymmetric ring opening (ARO) of terminal epoxides by enantioselective hydrolytic kinetic resolution (HKR) has been one of the most intensively studied areas in the asymmetric catalysis.¹ Since the first application of chiral (salen)Co catalyst,² considerable effort has been made to broaden the application range of this catalyst system.^{3–7} An efficient strategy for achieving reasonable enantioselectivity of terminal epoxides from good to high ee values is still required using less complicated catalyst system. Despite more advances in asymmetric catalytic synthesis of epoxides, to date general methods for the direct preparation of highly enantioriched 1-oxiranes are still required, arguably the most valuable class of epoxides for organic synthesis⁸ chiral building blocks and target oriented synthesis.⁹

In continuation of multimeric chiral (salen)Co catalysts synthesis⁵ herein we report the synthesis of new easily synthesized dimeric chiral (salen)CoAlX₃ catalyst (**1b**–**5b**) where one oxygen of each salen unit is linked through Al atom. These dimeric catalysts exhibit not only remarkably enhanced reactivity, but also significantly higher enantioselectivity relative to monomeric chiral (salen)CoAlX₃ catalyst (**1a**–**4a**) for ARO of



(A) Monomers



Keywords: Chiral cobalt salen catalyst; Terminal epoxides; Asymmetric ring opening reactions; Kinetic resolution.

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terminal epoxides with H₂O and HCl. The general procedure for the ARO of epoxides was the same as shown in reported papers.^{2,5} The ee% values were determined by capillary GC using a chiral column (CHIRALDEX G-TA and A-TA, 20 m × 0.25 mm id (Astec).

The monomeric chiral (salen)Co and dimeric chiral (salen)Co catalysts were synthesized by mixing 1:1 and 1:2 mol ratios of chiral salen (R,R)-(-)-N,N'-bis (3,5di-tert-butylsalicylidene)-1,2-cyclohexane diamino cobalt(II) (structure 1; procured from Aldrich) and corresponding AlX₃ in methylene chloride (MC) at open atmosphere and at N₂ atmosphere in case of Al(CH₃)₃, respectively. Furthermore, the monomeric catalysts (1a-4a) and (1a'-3a') were synthesized after treated with 1 equiv of HCl (1.0 M HCl solution in ether) and 1 equiv of H₂O in tetrahydrofuran (THF) solvent. Dimeric catalysts (1b-4b) and (1b'-3b') were synthesized in the same manner as monomers except taking 2 equiv of each compound of HCl and H₂O. The treatment underwent in the aerobic condition for the sake of oxidation of Co(II) to Co(III) and enhancement of catalytic activity. Catalyst **5b** was prepared by reacting fully hydrolyzed monomer of 1a with another unhydrolyzed monomer (1a) in the presence of base triethylamine in tetrahydrfuran (THF) solvent after 6 h reaction time. The insertion and array of linkage of Al to Co salen unit can be evi-denced by ²⁷Al NMR. Monomeric catalyst (**1a**) shows ²⁷Al NMR on $\delta = 42.0$ ppm; line width = 22.8 Hz and dimeric catalysts (1b and 5b) $\delta = 32.7$ ppm; line width = 10.3 Hz and δ = 52.6, 59.05 ppm; line width = 77.4 Hz, respectively, taking $[Al(D_2O)_6]^{3+}$ as a reference at 0 ppm.

The presence of ionic species during synthesis of monomer and dimer catalysts were continuously monitored by conductometric measurements. For the monomeric and dimeric Co salen catalyst (1a–5b), the characteristic absorption band of Co(II)salen (1) at 420 nm disappeared and a new band at 360 nm was investigated on the UV-vis spectra. XRD patterns also support the existent of two distinct species, that is, monomers (1a-4a) and dimers (1b-5b). The oxidation of cobalt species was confirmed by ESCA analysis, showing the peak at the binding energy of 780 nm due to Co(III) (e.g., Co(II) at 783 nm). It is well known that oxygen atoms of the metal complexes of the Schiff bases are able to coordinate to metals.¹⁰ Taylor and Jacobsen has shown the dimeric structure of chiral (salen)Al complex linked through the oxygen atom.¹¹ Aoi et al. has already been reported the linkage of two phenolic oxygens of cobaltsalen to the metal atoms of Lewis acids such as AlH₃ and Al(i-Bu)₃.¹² On these basis possible structure of synthesized new chiral (salen)Co complex bearing AlX₃ is depicted in Figure 1.

The catalytic activity of the monomeric catalyst (1a) and dimeric catalyst (1b) for hydrolytic kinetic resolution of the racemic epichlorohydrine (ECH), epoxy butane (EB), glycidol and styrene oxide is shown in Figure 2. Other monomers (2a-4a) and dimers (2b-5b) show the similar trends. All the dimeric catalysts (1b-5b) show high enantioselectivity (95->99 ee%) and reactivity



Figure 1. Schematic drawing of the monomeric and dimeric chiral (salen)Co catalysts.



Figure 2. The catalytic activity of monomer and dimer for the asymmetric HKR of terminal epoxides using 0.5 mol % catalyst at ambient temp.

(within 6 h) even in low loading of catalyst (0.5 mol %). The order of reactivity of dimeric catalysts found to be $3b,3b' \sim 5b > 2b,2b' > 1b,1b' \sim 4b$. UV-vis spectroscopic studies under the reaction conditions reflect the absence of equilibrium between the monomeric and dimeric complexes.

These HKR reactions follow the cooperative bimetallic catalysis^{1a} where epoxide and nucleophile activate simultaneously by two different (salen)CoAl catalyst molecules (Scheme 1). Thus the linking of two (salen)Co



Scheme 1. (a) Proposed mechanism for a cooperative catalysis in the asymmetric ring opening (ARO) of terminal epoxides catalyzed by (salen)CoAlR₃; (b) cooperative catalytic ARO within a dimeric framework.

 Table 1. Kinetic data for the HKR of racemic ECH catalyzed by the monomeric and dimeric [Co(salen):AlCl₃] catalysts

Catalyst	No. of (salen)Co unit	$k_{\rm intra} (\min^{-1} \times 10^{-2})^{\rm a}$	$k_{\text{inter}} \ (M^{-1} \min^{-1})^{a}$
1a	1		1.0
1a′	1		1.1
1b	2	44.4	10.2
1b′	2	45.5	15.7
5b	2	48.9	17.7

^a Calculated from Figure 5 using Eq. 1 (see Supplementary data).

unit through the Al induce the cooperative mechanism, albeit through a far less enantiodiscriminating transition state than that attained with the monomeric (salen)CoAl catalysts. Kinetic studies (Table 1) of the HKR of ECH shows the two-term rate equation involving both intraand intermolecular components (Eq. 1),^{13,14}

rate
$$\propto k_{\text{intra}}[\text{catalyst}] + k_{\text{inter}}[\text{catalyst}]^2$$
 (1)

plots of rate/[catalyst] versus [catalyst] should be linear with slopes equal to k_{inter} and y-intercepts corresponding to k_{intra} . Analysis of such plots with rate data obtained with dimeric catalysts **1b**, **1b**' and **5b** revealed linear correlations with positive slopes and nonzero y-intercepts, consistent with participation of both interand intramolecular pathways in the HKR (Figure 5; see Supplementary data). Similar analysis of rate data obtained with monomeric catalysts **1a** and **1a**' revealed y-intercepts of zero, reflecting the absence of any firstorder pathway for these catalysts.

Thus, the dimer catalysts provide appropriate relative proximity and orientation, which eventually reinforces the reactivity and selectivity relative to monomeric complex. The relative reactivity of dimeric catalysts (1b–5b) could be explained by the ease of cooperativity of the two (salen)Co units. Nonlinearity of the HKR reactions is also consistent with cooperative reactivity between two (salen)Co centres.

The asymmetric ring opening of EP, ECH and EB with HCl are taken for the present study (Fig. 3 for 1,2epoxypropane, EP). To date no examples have been reported for the ARO of terminal epoxide with HCl. The nonlinear effect is more pronounced in HCl than H₂O. In contrast to HKR of the ECH and EB, it need high loading of the catalysts (5 mol %) and *tert*-butyl methyl ether (TBME) as solvent. The ee% of the ECH decreases with respect to time after attaining the maximal (79%). The ring-opened product of ECH shows the reversibility and it forms again ECH in the presence of catalyst after prolonged time. This problem can be overcome by stopping the reaction after getting high ee%. The asymmetric ring opening reaction of EP, ECH and EB may occur by the analogous cooperative bimetallic mechanisms (Scheme 1).

In conclusion, the easily synthesized dimeric chiral (salen)Co catalysts show several orders of magnitude times more reactive than monomeric analogues without loss in enantioselectivity. It provides high enantiomerically pure valuable terminal epoxides in one-step process.



Figure 3. Asymmetric ring opening of 1,2-epoxypropane EP with HCl catalyzed by monomer (i.e., **1a**) [Co^{III}(salen)(Cl)AlCl₃] and dimer (i.e., **1b**) [Co^{III}(salen)(Cl)AlCl₃Co^{III}(salen)(Cl)] catalysts.

The structural stability of catalysts in acidic medium makes possible asymmetric ring opening of terminal epoxides with HCl. It is hoped that these dimeric catalysts will shed light to ARO with HCl and allow their extension for other terminal epoxides. Further design, crystal structure and recyclability of the catalyst is currently under investigation for the generality of asymmetric ARO.

Supplementary data

Supplementary data associated with this article can be found, in the online version at doi:10.1016/j.tetlet. 2005.02.012.

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