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Chiral Cobalt Salen Complexes Containing Lewis Acid: A Highly Reactive and Enantioselective Catalyst for the Hydrolytic Kinetic Resolution of Terminal Epoxides[1]

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Abstract—A type of chiral salen complexes bearing Lewis acid, including $FeCl_3$, $AlCl_3$, $ZnCl_2$, and $SnCl_4$ has been synthesized. The prepared complexes proved to be reactive and enantioselective in the hydrolytic kinetic resolution of terminal epoxides. The catalysts could be recovered and reused several times with simple treatment after reaction, without loss of activity and enantioselectivity. (salen)Co(II) and Lewis acid in mol ratios of 1 : 1, 1 : 2, and 1 : 3 showed the same activity, enatioselectivity, and stability. The characterization of the complexes in-situ generated by the reaction of (salen)Co(II) and Lewis acid in mol ratios of 1 : 1, 1 : 2, and 1 : 3 in CH_2Cl_2 was performed by UV-Vis, which showed an identical spectrum and did not display any change along with the time prolonged. Thus, the present catalysts can be applicable for large scale processes for HKR reaction of racemic epoxides.

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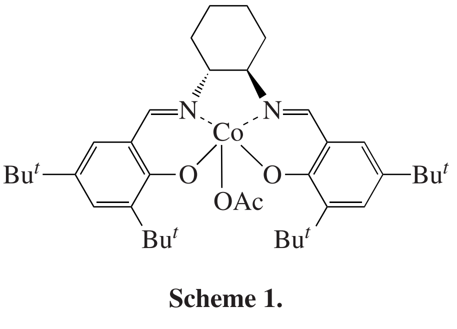
In the past decade, asymmetric ring opening (ARO) of terminal epoxides by enantioselective hydrolytic kinetic resolution (HKR) was one of the most intensively studied areas in asymmetric catalysis. The Hydrolytic Kinetic Resolution of terminal epoxides by the Jacobsen (Salen) Co complex (Scheme 1) became the standard method for the production of highly enantio-enriched terminal epoxide and 1,2-diols [1–4]. The reaction showed a high universality and functional group tolerance, as most of the evaluated epoxides (>50 types) were successfully resolved (ee > 99%). The catalyst in the reaction was the most important, which was studied by some researchers. Pozzi [5, 6] changed the tert-butyl in (salen)Co(II)(OAc) and get some better results. Jacobsen's group and others developed a dimeric [7, 8] oligomeric [9, 10], polymeric [4, 11], dendrimeric framework [12] and inorganic-supported catalysts [13] in order to make the HKR of terminal epoxides more practical. Kim et al. have recently developed a novel concept of heterometallic chiral salen catalysts formed by the addition to chiral salen Co(II) of the earth halide (BF_3 or GaX_3) in a molar ratio of 2 : 1 [14–19]. The bimetallic complexes bearing Lewis acids of B and Ga elements, especially chiral (Salen)$CoGaCl_3$ catalyst for HKR and enantioselective kinetic resolution of terminal epoxides turned out to have high catalytic activity.

Recently, Kim [20] presented the Lewis acid (MX_3)-promoted oxidation of chiral (salen) Co(II) complex, which proved neither the mononuclear nor dinuclear hetero-bimetallic chiral (salen)Co complexes such as $[(salen)Co(III)–X]\cdots MX_3$ or $[(salen)Co(III)–X]_2\cdots MX_3$ as reported in the literature, but rather the Jacobsen complexes, that is chiral (salen) Co(III)-X. However, Kim's chiral (Salen)$CoGaCl_3$ catalyst was not easy to prepare and the mechanism was indefinite. With the idea of the asymmetric ring opening of epoxides catalyzed by chiral (Salen) complexes and the reaction involving two separate chiral (Salen) metal species in the rate limiting step of the reaction, a simpler method could be used for synthesizing metallic complexes that would exhibit a faster reaction rate and higher enantioselectivity. The purpose of our own research was directed towards the design of chiral (Salen) Co catalysts bearing Lewis



Scheme 1.

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[1] This articles was submitted by the authors in English.

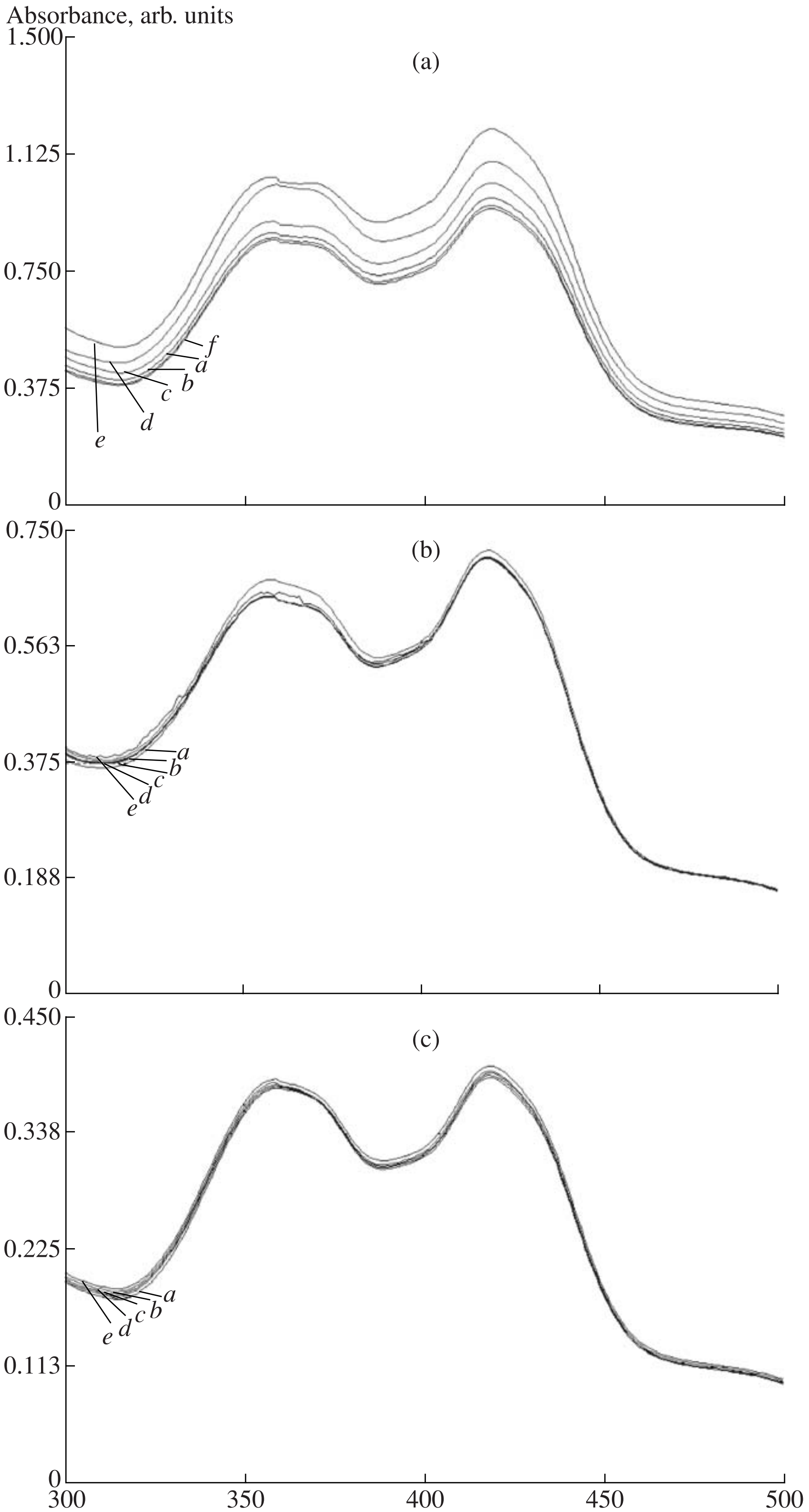
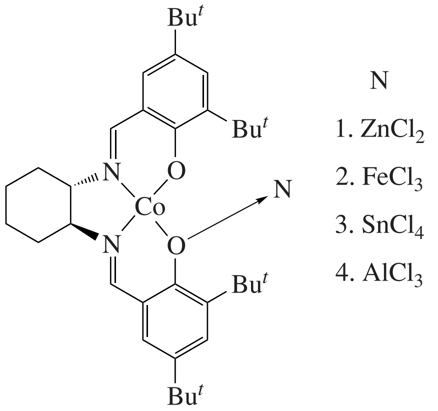


Fig. 1. (a) UV-vis absorption spectra of the (Salen) Co(II) and $ZnCl_2$ in a molar ratio of 1 : 1 which were continuously measured after mixing (*f,* (Salen) Co(II); *a*, UV spectrum after 1 min; *b*, after 30 min; *c*, after 60 min; *d*, after 240 min; *e*, after 1440 min); (b) UV-vis absorption spectra of the (Salen) Co(II) and $ZnCl_2$ in a molar ratio of 1 : 2 which were continuously measured after mixing (*a*, UV spectrum after 1 min; *b*, after 30 min; *c*, after 60 min; *d*, after 240 min; *e*, 1440 min); (c) UV-vis absorption spectra of the (Salen) Co(II) and $ZnCl_2$ in a molar ratio of 1 : 3 which were continuously measured after mixing (*a*, UV spectrum after 1 min; *b*, after 30 min; *c*, after 60 min; *d*, after 240 min; *e*, after 1440 min).

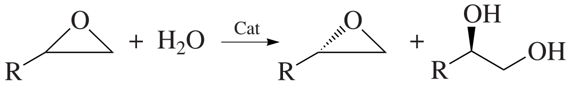


Scheme 2.

acid, including $FeCl_3$, $AlCl_3$, $ZnCl_2$, and $SnCl_4$ (Scheme 2) and the catalysts in-situ generated by reaction of (salen)Co(II) and Lewis acid in mol ratios of 1 : 1, 1 : 2, and 1 : 3 in CH_2Cl_2 performed by UV-Vis.

EXPERIMENTAL

The chiral (Salen) Co complexes catalysts were synthesized by mixing chiral Salen (R,R)–(–)–*N*,*N*'–bis(3,5-di-tert-butylsa-licyl-idene)–1,2-cyclohexane diamino cobalt(II) and Lewis acid in the open atmosphere for hours. For instance, the anhydrous $ZnCl_2$ (0.5 equiv) was added to a stirred solution of chiral (Salen) Co(II) in CH_2Cl_2 and the reaction mixture was analyzed directly by UV-Vis analysis. The mixture was stirred at room temperature for 1 day, then the CH_2Cl_2 was evaporated to obtained the resulting catalyst as a dark powder. The contents of metals were determined by Inductively Coupled Plasma Atomic Emission Spectrometry. The kinetic resolution of terminal epoxides (Eq. (I)) was carried out by stirring the epoxides in the presence of 0.25% catalyst (based on the catalytic unit), THF, and 0.55 equiv of water at the indicated temperature.



(I)

$R=CH_2Cl, CH_2CH_3, PhOCH_2$

RESULTS AND DISCUSSION

In the experiment, to our surprise, the (Salen) Co complexes bearing Lewis acid of $FeCl_3$, $AlCl_3$, $ZnCl_2$, and $SnCl_4$ (Scheme 2) could enhance reactivity and might be applied with substantially lower loading. As soon as the Lewis acid was added, the color of the solution was changed. UV-vis absorption spectra are shown in Fig. 1.

Figure 1 shows the characterization of the complexes in-situ generated by reaction of (salen) Co(II) and Lewis acid in mol ratios of 1 : 1, 1 : 2, and 1 : 3 in CH_2Cl_2; Fig. 1c (curve *a*) gives strong absorption bands at 360 and 420 nm because of the CT transition and *d*–*d* transition of (salen) Co(II), respectively. Figure 1 indicated the curves did not changed with the reaction processing and shifted with prolonged time. The phenomenon illustrated that the structure of (salen) Co(II)

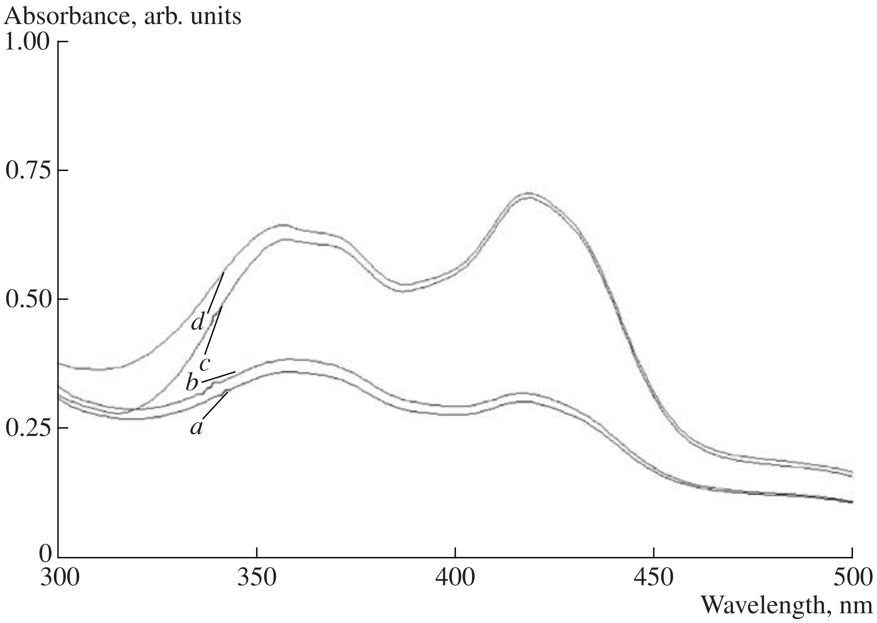


Fig. 2. UV-vis absorption spectra of the (Salen) Co(II) and *a*, $FeCl_3$, *b*, $SnCl_4$, *c*, $AlCl_3$, and *d*, $ZnCl_2$ in a molar ratio of 1 : 3 which were measured mixing after 1440 min.

HKR of epoxides catalyzed by chiral cobalt (Salen) complexes bearing Lewis acid catalysts

Entry	R	Cat.	Solvent	Temp. (°C)	Time, h	Epoxide		Diol	
						yield[a], %	ee(%)[b]	yield[a], %	ee(%)[c]
1	CH_2Cl	1	THF	20	25	44	99	43	96
2	CH_2Cl	2	THF	20	25	45	99	44	95
3	CH_2Cl	3	THF	20	10	45	>99	42	93
4	CH_2Cl	4	THF	20	10	44	>99	44	94
6	CH_2Cl	3	THF	30	25	43	97	44	95
7	CH_2Cl	3	THF	25	25	42	98	45	94
8	CH_2Cl	3	THF	15	25	44	94	43	95
9	CH_2Cl	3	CH_2Cl_2	20	10	40	89	42	96
10	CH_2Cl	3	None	20	25	39	90	41	93
11	CH_2Cl	3 (recycle 1)	THF	20	25	42	98	41	92
12	CH_2Cl	3 (recycle 2)	THF	20	25	42	99	41	91
13	CH_3	1	THF	20	10	43	98	45	93
14	CH_3	2	THF	20	10	44	99	42	92
15	CH_3	3	THF	20	10	45	>99	42	92
16	CH_3	4	THF	20	10	41	99	43	91
17	CH_3	4 (recycle 1)	THF	20	10	43	98	42	90
18	CH_3	4 (recycle 2)	THF	20	10	43	99	42	90
19	CH_3	3	CH_2Cl_2	20	10	42	89	43	95
20	CH_3	3	None	20	25	41	90	45	94
21	$PhOCH_2$	1	THF	20	25	44	99	43	91
22	$PhOCH_2$	2	THF	20	25	43	>99	42	95
23	$PhOCH_2$	3	THF	20	10	44	>99	43	96
24	$PhOCH_2$	4	THF	20	10	42	99	44	95
25	$PhOCH_2$	3	CH_2Cl_2	20	25	39	90	46	91
26	$PhOCH_2$	3	None	20	25	37	90	47	89
27	$PhOCH_2$	3 (recycle 1)	THF	20	10	43	99	45	97

[a] The isolated yield of the epoxide and diol is based on the racemic epoxide added.

[b] The ee's of propylene oxide were determined by GC analysis using a chiral capillary column (Y-cyclodextrin trifluoroacetyl, 40 m × 0.25 mm (i.d.)); the ee's of epichlorohydrine (ECH) 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 were determined by HPLC using a chiral OD-H column (90/10 hexanes/i-PrOH, 1 ml/min, 254 nm).

[c] Determined by capillary GC analysis of the isolated product on an HP Chira–20% permethylated β-cyclodextrin column.

Lewis acid complexes might be that shown in Scheme 2. The effects of $FeCl_3$, $SnCl_4$, and $AlCl_3$ as shown in Fig. 2 were similar to $ZnCl_2$.

The results of the kinetic resolution of terminal epoxides are summarized in the table.

As shown in the table, all catalysts showed excellent results for three substrates and the ee's were over 99.5% for ECH, propylene oxide, and phenyl glycidyl ether (table, entries 3, 4, 15, 22, and 23). When catalyst 1 or 2 was explored, slightly lower enantioselectivity was obtained.

Under the conditions of 0.5 mol% catalyst, THF, and 0.55 equiv of water at the temperature of 20°C, the ee's of ECH reached 99.5% in 6 to 10 h. It was significant that the catalysts could be hardly dissolved as the temperature was reduced. Therefore, the catalysts could be isolated easily from the reaction mixture by the following procedure listed below. The temperature of the mixture was reduced to –18°C, then most of the catalysts could be precipitated and collected via filtration. The recovered catalysts were not required to be activated before reusing. When the recovered catalysts were used for the HKR of ECH, excellent activity and enantioselectivity were achieved.

In summary, the kinetic resolution of terminal epoxides (propylene oxide, ECH, phenyl glycidyl ether) treated with these complexes could produce exciting chemical yields and high ee's, as well as provide much easier isolation procedure, which can be applicable for a large-scale process for HKR reaction of racemic epoxides.

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