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Mechanistic Aspects of Metal Valence Change in SalenCo(III)OAc-Catalyzed Hydrolytic Kinetic Resolution of Racemic Epoxides

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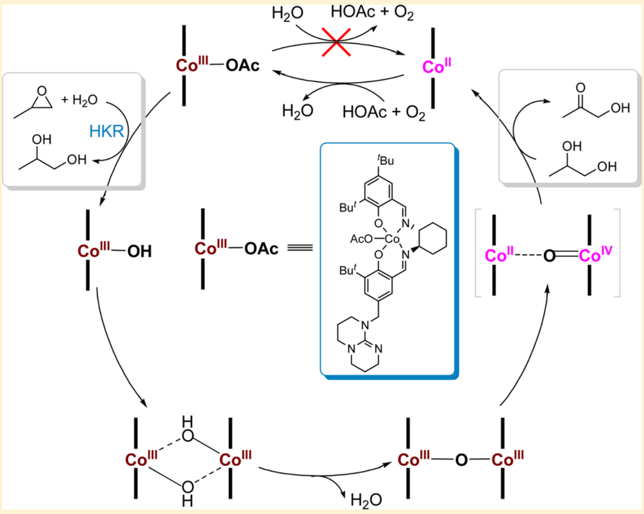
Supporting Information



ABSTRACT: The chiral SalenCo(III)OAc-catalyzed hydrolytic kinetic resolution (HKR) of racemic terminal epoxides to afford both enantioenriched epoxides and diols presents one of the most important achievements in asymmetric synthesis chemistry. Previous studies mainly focused on the development of highly efficient catalysts, while rare reports concerned the mechanistic understanding of metal valence change, associated with the formation of inactive Co(II)-Salen complex. Herein, we report the mechanistic aspects of catalyst deactivation regarding the transformation of Co(III) to Co(II) derivative in the HKR of racemic epoxides catalyzed by SalenCo(III)OAc complexes with an appended 1,5,7-triazabicyclo[4.4.0]dec-5-ene on the ligand framework by means of electrospray ionization mass spectrometry (ESI-MS). Continuous determination of transient cationic species in ESI-MS positive mode in conjunction with UV−vis spectroscopic studies at various time points provides evidence that a certain amount of SalenCo(III)OAc molecules were reduced to the corresponding Co(II) derivatives in the HKR of racemic propylene oxide or styrene oxide. To be accompanied by the reduction of Co(III) to Co(II), the resultant diols were oxidized to α-hydroxy ketones. These analyses along with some control experiments gave a mechanistic understanding of catalyst deactivation of SalenCo(III)OAc-catalyzed HKR of racemic epoxides regarding an unveiled redox reaction between Co(III)-Salen and diol, the hydrolyzed product.

■ INTRODUCTION

Hydrolytic kinetic resolution (HKR) of racemic terminal epoxides using chiral Co(III)-Salen catalysts is one of the most powerful methods for the preparation of both enantiomerically pure epoxides and diols as a direct result of its remarkable practical appeal, high selectivity, and broad substrate scope.[1] These enantiopure epoxides are important intermediates for synthesizing a wide variety of biologically and pharmaceutically target compounds.[2] Detailed mechanistic investigations of the HKR and related epoxide ring-opening reactions have revealed a second-order kinetic dependence on the catalyst concentration,[3] supporting a cooperative bimetallic mechanism for epoxide ring opening (Scheme 1).[4] In the catalytic cycle, one cobalt center is proposed to serve as Lewis acid for epoxide activation and another as counterion for binding to the hydroxide ion. This mechanistic insight propelled the development of different approaches to build various cooperative cobalt-Salen structures, including dimeric,[5] oligomeric,[6] dendrimeric,[7] polymeric,[8] self-assembly,[9] encapsuled[10] and nanoporous complexes based on a metal−organic framework.[11] These catalysts all exhibited an intramolecular {SalenCo(III)X}−{SalenCo(III)X} interaction, evidenced by higher catalytic activity and enantioselectivity, in comparison with their monomeric counterparts. Notably, they were proven to be efficient in a very dilute solution.

In contrast to the high activity of SalenCo(III)X in catalyzing the HKR of racemic terminal epoxides, the corresponding Co(II) derivatives proved to be inactive. We were interested to note that in the initial reports Jacobsen and co-workers observed the formation of salenCo(II) as brick red solid precipitation during the HKR of racemic epoxides using SalenCo(III)OAc complex **1** as catalyst.[1c] A similar change of metal valence was found in the supported Co(III)-Salen catalyst system by Kim and co-workers.[12] However, explicit spectroscopic studies focusing on how to produce the brick red solid are scarce. Although some elegant mechanistic studies on the HKR process have been reported,[3,13] none of them provided insight into the oxidation−reduction reaction mechanism regarding the change of Co(III) to Co(II).

Inspired by the ground-breaking work of Jacobsen and co-workers, our group reported the synthesis of optically active organic carbonates by a catalytic kinetic resolution process of

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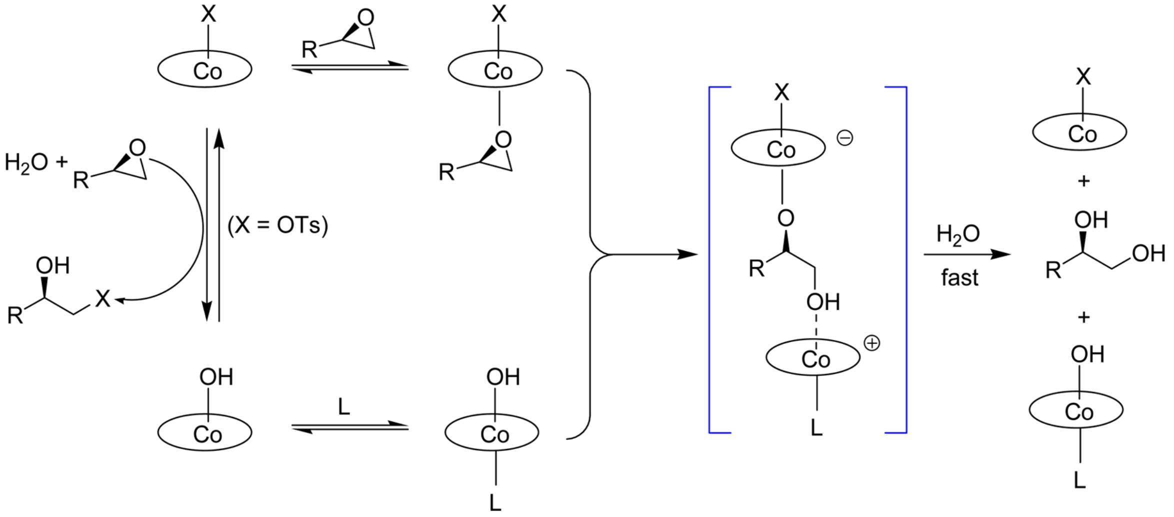
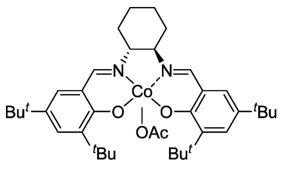
Scheme 1. Cooperative Bimetallic Mechanism Involved in the HKR of Racemic Epoxides Proposed by Jacobsen et al.[3]



racemic epoxides using CO_2 as reagent.[14,15] The process involves the simple use of a chiral SalenCo(III)X in conjunction with a nucleophilic cocatalyst such as quaternary ammonium halide or sterically hindered organic base under mild conditions. The addition of a nucleophilic cocatalyst is essential to perform this coupling reaction smoothly and has a significant effect on the catalytic performance of SalenCo(III)X. On the contrary, no or very low activity was observed in the systems with SalenCo(III)X alone as catalyst, and in the meantime SalenCo(II) was produced as a brick red solid precipitate, particularly in the presence of a certain amount of water, or/and at elevated temperatures.[16,17] The unexpected results prompted us to think what compound was being oxidized in this process. Jacobsen and co-workers have suggested an equilibrium (eq 1) existing in the HKR of racemic epoxides, which seems to imply that the SalenCo(III)OAc can oxidize the water affording the corresponding Co(II) derivatives and oxygen.[1c] However, such an oxidation is difficult to achieve in the coupling of CO_2 and epoxides, because the trace quantities of water in the reaction mixture more easily take part in the chain transfer reaction.[18] These results stimulate us to reconsider whether the SalenCo(III)X complexes were indeed reduced to Co(II) derivatives during the HKR of racemic epoxides. Moreover, if the reduction of Co(III) to Co(II) is really a fact, another question raised is which compound is being oxidized in this process. What oxidation−reduction reaction mechanism does make SalenCo(III)X complexes change into the corresponding Co(II) derivatives?

$$\text{SalenCo(II)} + \text{HOAc} + \frac{1}{4}\text{O}_2 \rightleftharpoons \text{SalenCo(III)OAc} + \frac{1}{2}\text{H}_2\text{O} \qquad (1)$$

Herein, we applied electrospray ionization mass spectrometry (ESI-MS) to track the reduction process of Co(III) to Co(II) during the HKR of racemic epoxides, using the Co(III)-Salen complexes **2** and **3** with an appended 1,5,7-triazabicyclo[4.4.0]-dec-5-ene (designated as TBD, a sterically hindered organic base) on the ligand framework as catalyst. Furthermore, efforts have been made to gain a greater insight into the mechanistic aspects of metal valence change by combining ESI-MS, UV−vis, GC−MS, and HPLC−MS methods.



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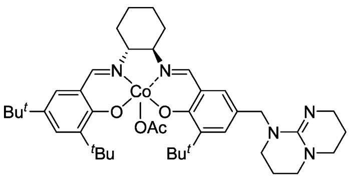

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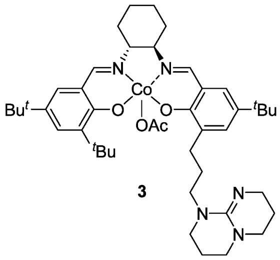

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RESULTS AND DISCUSSION

Electrospray ionization (ESI) is a soft ionization method that can keep any weakly bound ligand intact in a complex ion.[19] This property has enabled ESI to become increasingly popular as an analytical tool in inorganic/organometallic chemistry.[20] ESI, in combination with tandem mass spectrometry (MS/MS), has been employed to study mechanistic aspects of biochemistry process,[21] organic reaction,[22] and homogeneous polymerization catalysis.[23] Recently, we reported a cobalt-Salen complex with an appended TBD on the ligand framework for investigating the mechanism of the copolymerization of CO_2 and epoxides by means of ESI-MS.[24] The cobalt-Salen catalyst **3** containing a TBD group could be easily detected by ESI-MS. In the present paper, we also performed ESI-MS in positive mode for continuous determination of transient cationic species associated with the catalyst at various time points during the HKR reaction catalyzed by TBD-appended cobalt-Salen complex **2** or **3**.

Initially, when complex **2** was applied to catalyze the HKR of racemic propylene oxide at a [epoxide]/[catalyst] ratio of 1000 under ambient temperature, three species of m/z^+ 698.4, 757.4, and 832.4 were detected in the ESI-MS spectra in the positive ion mode (Figure 1A).[25] The species of m/z^+ 698.4 was ascribed to complex **2** with the dissociation of the counterion according to our previous studies.[24] Since the nucleophilic attack of the appended TBD of complex **2** at the coordinated propylene oxide

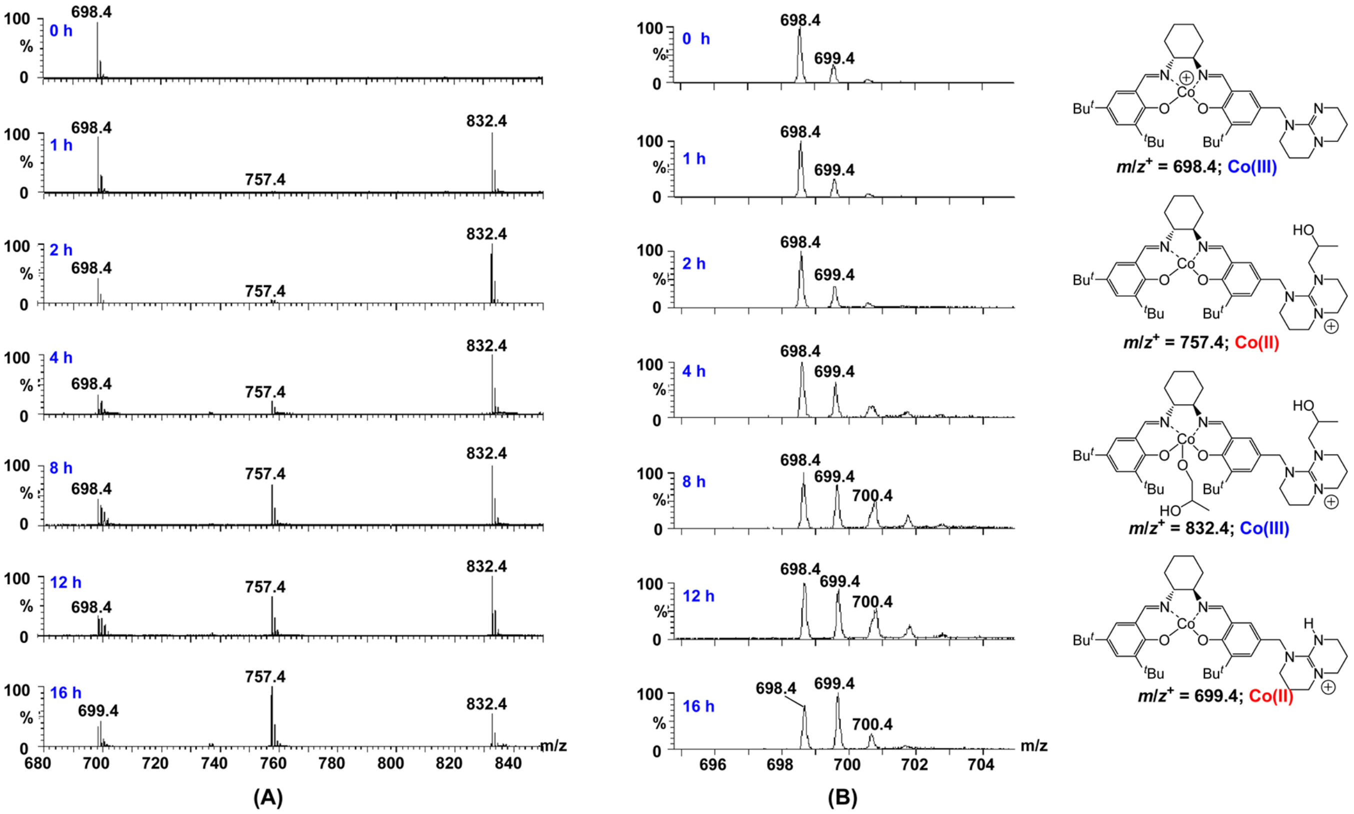


Figure 1. (A) ESI-MS spectra of the reaction mixture of the HKR of racemic propylene oxide catalyzed by complex **2** (the molar ratio of epoxide to complex **2** is 1000) at ambient temperature with various time points and (B) detailed spectra of the isotope ratio of the species of m/z^+ 698.4 and 699.4.

on the metal center occurs easily, the species of m/z^+ 757.4 and 832.4 are ascribed to the corresponding Co(II) and Co(III) derivatives, respectively. Furthermore, with time the intensity of the species of m/z^+ 757.4 increases gradually. It is worth noting that an increasing intensity at the species of m/z^+ 699.4, which is also ascribed to Co(II) derivative, was observed with time by comparing the isotope ratio of the species of m/z^+ 698.4 (Figure 1B). To further investigate the reduction of the Co(III)-Salen complex, we performed the HKR of racemic propylene oxide catalyzed by complex **2** in the presence of oxygen and 10 equiv of acetic acid. As anticipated, the species of m/z^+ 698.4 and 832.4 were observed in the initial reaction stage, while only a very small amount of the species of m/z^+ 699.4 and 757.4 were detected even with a reaction time up to 16 h (See Supporting Information, Figure S1). This is derived from the excess of acetic acid and O_2 to inhibit the formation of Co(II) species.

In 2007, Davis and co-workers reported the mechanistic aspects of catalyst deactivation in the HKR of epichlorohydrin catalyzed by complex **1**.[13a] They found a very small amount of Co(III) was reduced to Co(II) by means of a UV−vis spectroscopic study. In the present paper, we also applied UV−vis spectroscopy to investigate the reduction of Co(III) to Co(II). As shown in Figure 2A and 2B, the Co(III)-Salen complex presents an absorption band at ∼400 nm, whereas the Co(II)-Salen complex shows two absorption bands at ∼360 and 420 nm. When the complex **2**-catalyzed HKR of racemic propylene oxide was performed for 16 h, we observed a discernible absorption band at ∼360 nm, indicating the reduction of Co(III) to Co(II) (Figure 2C). Interestingly, when epichlorohydrin was used as the substrate to investigate the metal valence change, only a very small feature at ∼360 nm was detected at the same condition (Figure 3C), in consistence with the Davis results.[13a] Similarly, in the ESI-MS spectra of the HKR of epichlorohydrin, only a weak signal of m/z^+ 699.4 ascribed to Co(II) derivative was observed (see Supporting Information, Figure S2). It is worthwhile noting here parenthetically that a byproduct, 1,3-dichloro-2-propanol, was unexpectedly detected in the HKR of epichlorohydrin by GC analysis (see Supporting Information, Figure S3). The compound 1,3-dichloro-2-propanol should originate from the reaction of epichlorohydrin and HCl.[26] To further examine the effect of the epoxide substrate on the reduction of Co(III) to Co(II), we performed the HKR of styrene oxide catalyzed by complex **2**, and a similar result with propylene oxide as substrate was obtained (Figure 4C).

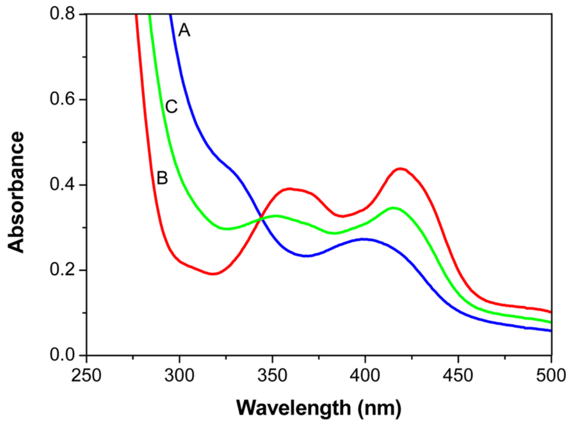


Figure 2. UV−vis spectra of (A) complex **2**, (B) the corresponding Co(II) derivatives of complex **2**, and (C) the reaction mixture from the HKR of racemic propylene oxide catalyzed by complex **2** (the molar ratio of epoxide to complex **2** is 1000) at ambient temperature after 16 h.

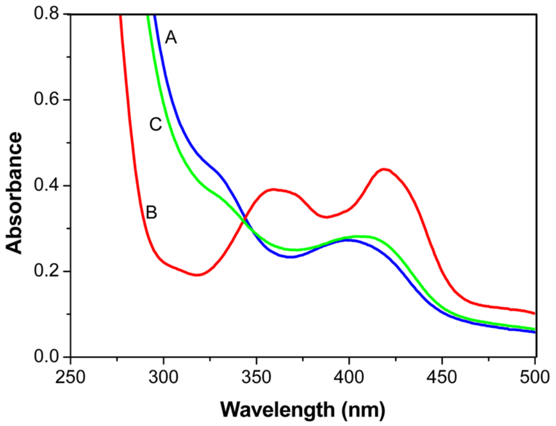


Figure 3. UV−vis spectra of (A) complex **2**, (B) the corresponding Co(II) derivatives of complex **2**, and (C) the reaction mixture from the HKR of racemic epichlorohydrin catalyzed by complex **2** (the molar ratio of epoxide to complex **2** is 100) at ambient temperature after 16 h.

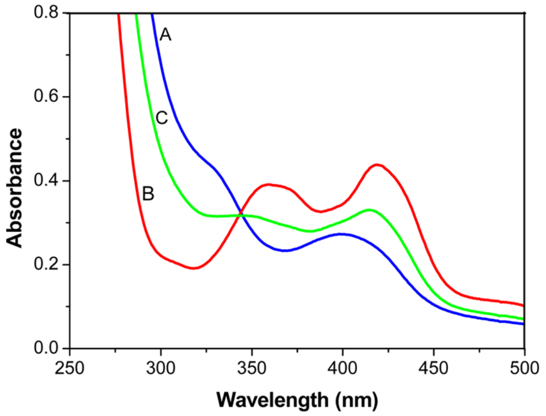


Figure 4. UV−vis spectra of (A) complex **2**, (B) the Co(II) corresponding derivatives of complex **2**, and (C) the reaction mixture from the HKR of racemic styrene oxide catalyzed by complex **2** (the molar ratio of epoxide to complex **2** is 500) at ambient temperature after 16 h.

In previous mechanistic investigation concerning CO_2/epoxide copolymerization catalyzed by SalenCo(III)X complexes with an appended TBD on the ligand framework, we had detected the Co(II) derivatives using an ESI-MS method.[24] It is generally known that the reduction process must be accompanied by an oxidation reaction. Indeed, the question of what compound is oxidized in the reaction system has puzzled us for several years. The same question also exists in the HKR process. Jacobsen and co-workers proposed that SalenCo(III)OAc could oxidize water, affording the corresponding Co(II) derivatives and oxygen.[1c] We applied the Clark-type oxygen electrode to monitor the generation of O_2 in the HKR of various racemic epoxides catalyzed by complex **1** or **2**. The instrument is very sensitive to O_2 and its detection limit is about 1 ppb. Unfortunately, no oxygen was detected in the system, while the formation of the Co(II) derivatives had been confirmed by ESI-MS.

Recently, much attention has been focused on the aerobic catalytic oxidation of alcohols to the corresponding ketones or aldehydes using cobalt catalysts.[27] This fact inspired us to consider whether the resultant diols were oxidized in the HKR reaction. First, the complex **1**-catalyzed HKR of racemic propylene oxide was chosen as a model reaction to explore the feasibility, and the reaction process was monitored by GC. Fortunately, a product with the same retention time as 1-hydroxy-2-propanone was detected (see Supporting Information, Figure S4). The GC−MS analysis of this product showed a molecular weight of 74.0, which is consistent with that of 1-hydroxy-2-propanone. Moreover, we monitored the relationship between the formation of Co(II) and 1-hydroxy-2-propanone during the HKR of racemic propylene oxide. As shown in Figure 5A, the complex **1** exhibits a similar feature as complex **2** and has no obvious absorption band near 360 nm in the UV−vis spectroscopy. The absorption intensity of the band at ~360 nm is dramatically enhanced as the reaction proceeds, indicating the production of the corresponding Co(II) species. Simultaneously, the GC analyses of the reaction mixture at various time points were performed to track the formation of 1-hydroxy-2-propanone (Figure 5B). The results showed that the amount of 1-hydroxy-2-propanone increased with time. In fact, the cobalt(III)-complex-catalyzed oxidation of alcohols to ketones or aldehydes is an aerobic transformation. However, when the HKR of racemic propylene oxide was performed in the absence of O_2, the Co(II) derivatives and 1-hydroxy-2-propanone were also detected by UV−vis and GC spectroscopies (see Supporting Information, Figures S5 and S6). Notably, we can calculate the amount of the resultant Co(II) based on the epoxide conversion and the molar ratio of hydroxyl ketone to diol (Figure 6). These

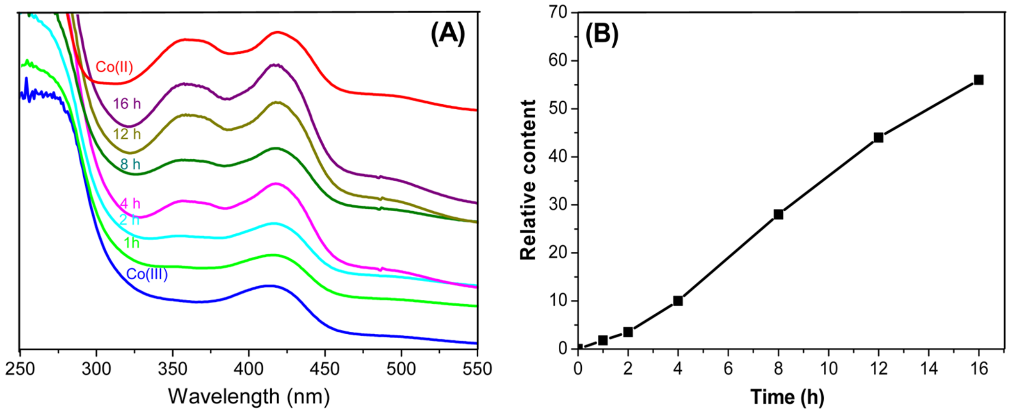


Figure 5. (A) UV−vis spectra of complex **1** and its Co(II) derivatives and the reaction mixture of the HKR of racemic propylene oxide catalyzed by complex **1** (the molar ratio of epoxide to complex **1** is 1000) at ambient temperature with various time points. (B) Time profile of the formation of 1-hydroxy-2-propanone determined by GC with 1,2-dimethoxyethane as internal standard.

results provide evidence that a certain amount of SalenCo(III)-OAc molecules were reduced to the corresponding Co(II) derivatives in the HKR of racemic propylene oxide.

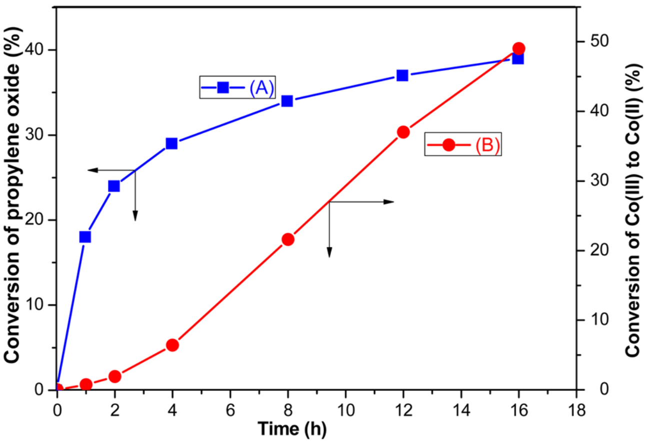


Figure 6. Time profiles of (A) the conversion of propylene oxide and (B) the conversion of Co(III) to Co(II) during the HKR of racemic propylene oxide catalyzed by complex **1** with a [epoxides]/[catalyst] ratio of 1000 at ambient temperature.

In order to further confirm the oxidation of diols to α-hydroxy ketones, the HKR of racemic styrene oxide was carried out at a [epoxide]/[catalyst] ratio of 100 and ambient temperature. This process was likewise monitored by HPLC. As expected, the oxidized product, 2-hydroxy-1-phenylethanone, was detected and further identified by UV−vis spectroscopy (see Supporting Information, Figures S7 and S8). In the meantime, HPLC−MS analysis also demonstrated the formation of 2-hydroxy-1-phenylethanone (Supporting Information, Figure S9). Furthermore, we succeeded in isolating the oxidized product by column chromatography, and the structure of the resultant 2-hydroxy-1-phenylethanone was confirmed by NMR spectroscopy (Figure 7). This analysis in combination with chromatographic and spectral studies indicate that the reduction of SalenCo(III)OAc to the corresponding Co(II) derivatives is accompanied by an oxidation of the produced diols to the corresponding α-hydroxy ketones in the HKR of racemic epoxides.

For clarifying the mechanistic aspects in the oxidation of diols to α-hydroxy ketones, we studied the reaction of complex **2** with propane-1,2-diol by GC and ESI-MS spectroscopies. No Co(II) species such as m/z^+ of 699.4, as well as the peak of 1-hydroxy-2-propanone was detected. This result indicated SalenCo(III)OAc cannot directly oxidize diols to the corresponding α-hydroxy ketones (Scheme 2). On the contrary, when propane-1,2-diol was added into the SalenCo(III)OAc/H_2O/styrene oxide system, both 1-hydroxy-2-propanone and 2-hydroxy-1-phenylethanone were produced, together with the formation of SalenCo(II) (*vide infra*).

Pedro and co-workers applied square-planar cobalt(III) complexes to catalyze the selective oxidation of a wide range of secondary alcohols to the corresponding ketones in the presence of dioxygen and pivalaldehyde.[28] They proposed that the high-valent oxocobalt(IV) is the actual oxidant, which would be derived by oxygen atom transfer from the acyl peroxyl radical (generated by metal-mediated free-radical autoxidation of the aldehyde with O_2) to the lower valent cobalt(II) complex. These studies promoted us consider whether the oxidation of diols to α-hydroxy ketones was performed by an oxocobalt species.

In our previous publication, complex **3** was chosen as a model catalyst for studying the mechanistic aspects in the CO_2/epoxide copolymerization by means of ESI-MS method.[24] Herein, we likewise applied this complex to explore the oxidation process of diols to α-hydroxy ketones during the HKR process. In the ESI-MS spectrum of the complex **3**/H_2O/propylene oxide (1/100/5000, molar ratio) system, we observed two monocharged species of m/z^+ 727.4 and 758.4 and one doubly charged species of m/z^{2+} 744.4.[29] The latter species is ascribed to a dimeric cobalt-Salen complex with OH^- counterion (Figure 8B). The species of m/z^{2+} 744.4 was further characterized by collision-induced dissociation (CID). Two scission species were produced, one of them appearing at m/z^{2+} 735.5 under a low CID voltage of 3 V (Figure 9). These two species are ascribed to complex **3** without the axial anion and the dimeric cobalt-Salen complex as a $\{Co^{III}{-}O{-}Co^{III}\}$ structure, respectively. Increasing the CID voltage to 7 V resulted in the formation of two new species of m/z^+ 727.4 and 743.4, which are tentatively ascribed to the Co(II) and Co(IV) derivatives, respectively. Indeed, it is possible that a mixed valence at the excited state exists in the neutral redox active dinuclear complexes with a bridge.[30] More recently, Ray et al. synthesized and characterized a coordinated oxocobalt(IV) complex.[31] The realization of isolation of the highly reactive Co(IV)=O complex was attributed to the interaction with a Lewis acid Sc^{3+} ion for generating a $\{Co^{IV}{=}O\cdots Sc^{3+}\}$ core, which was characterized by ESI-MS. Therefore, the present Co(IV) derivatives of m/z^+ 743.4 was also suggested to be stabilized by the Co(II) species of m/z^+ 757.4 to form a $\{Co^{IV}{=}O\cdots Co^{II}\}$ core, similar as described by Ray and co-workers. Thus, we can deduce that the produced diols were oxidized by an oxocobalt(IV) species to afford the corresponding α-hydroxy ketones. In order to support this hypothesis, we added 1,2-propanediol to the reaction mixture of the HKR of styrene oxide catalyzed by complex **1** (Scheme 2) and monitored the production of α-hydroxy ketones by GC (Supporting Information, Figure S10). As expected, the peak of 1-hydroxy-2-propanone was detected when the brick red solid was observed in the reaction mixture. Similarly, when 1-phenyl-1,2-ethanediol was added to the reaction mixture of the HKR of propylene oxide, 2-hydroxy-1-phenylethanone was also found in the system on the basis of HPLC analysis (see Supporting Information, Figure S11).

On the basis of the facts described above, a reaction mechanism is proposed and shown in Scheme 3, in which a Co(IV) intermediate is suggested to oxidize the resultant diols to α-hydroxy ketones. In the initial stage, the nucleophilic counterion (such as OAc) of one Co(III)-Salen molecule attacks the epoxide coordinated on the metal center of another Co(III)-Salen to form a ring-opened product (**A**). This process followed by the addition of water to produce SalenCo(III)OH (**B**). SalenCo(III)OH easily forms a dimer (**C**), which further undergoes a dehydration to afford the intermediate (**D**) containing the $\{Co^{III}{-}O{-}Co^{III}\}$ unit. Then, disproportionation of the intermediate $\{Co^{III}{-}O{-}Co^{III}\}$ produces a Co(II) species (**E**) and a Co(IV) species (**F**), in which the highly active Co(IV) species is stabilized by the Co(II) species *via* formation of $\{Co^{IV}{=}O\cdots Co^{II}\}$ core. Finally, the oxocobalt complex can easily oxidize the diols to the corresponding α-hydroxy ketones following a typical oxidation mechanism of high-valent metal oxide.

It is worth noting that the transformation of SalenCo(III)X (X $\neq$ OH) to SalenCo(III)OH is another reason accounting for the catalyst deactivation during the HKR process, which was

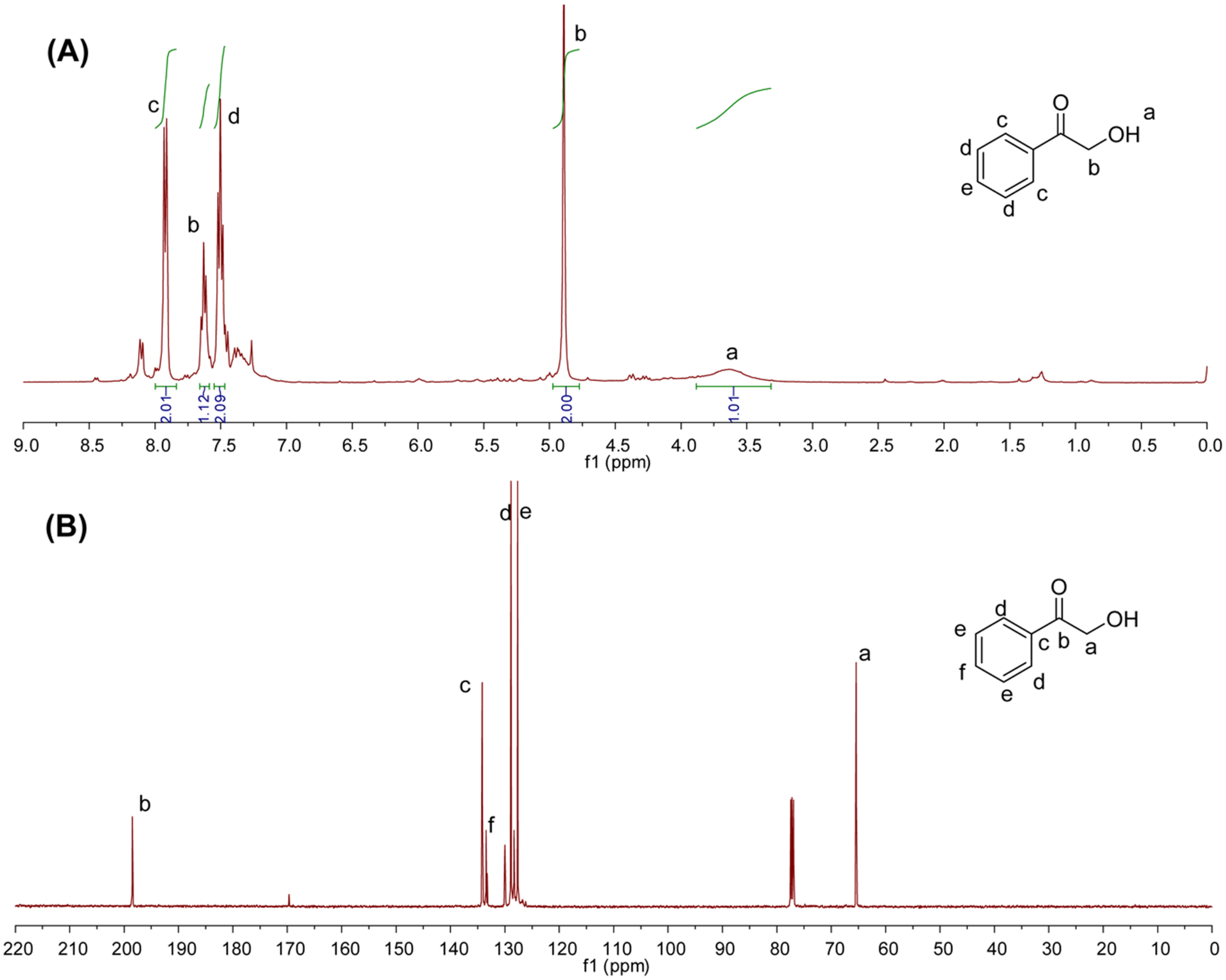
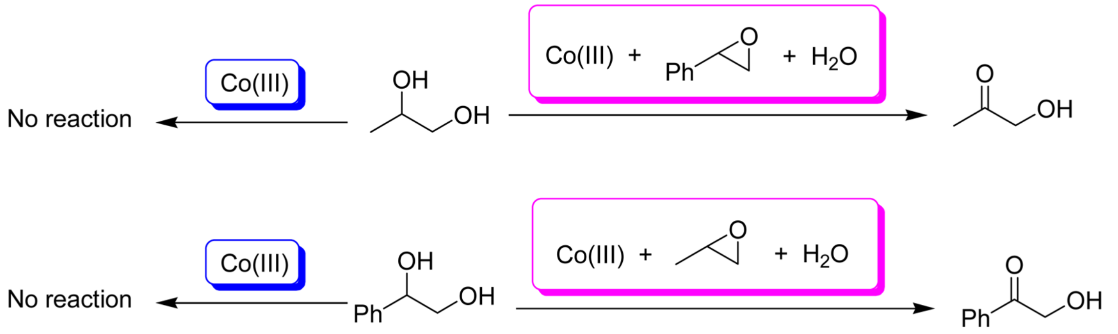


Figure 7. (A) ^{1}H NMR and (B) ^{13}C NMR spectra of α-hydroxy ketone isolated from the reaction mixture of the HKR of racemic styrene oxide catalyzed by complex **1** at ambient temperature for 12 h (molar ratio of styrene oxide to complex **1** is 100).

Scheme 2. Oxidation of Diols at Various Conditions



proposed by Jacobsen and co-workers according to the detailed kinetic studies involving the reaction calorimetry.[3] They found that a maximum rate of epoxide ring opening is achieved by a mixed cobalt-Salen catalyst system in which 50% of the catalyst has an OH^{-} counterion. For commonly used SalenCo(III)OAc complex, both forms of the Co-Salen (OH and OAc) were present at the initial stage of the HKR, which leads to a faster reaction. This suggested that nearly all SalenCo(III)OAc molecules were transferred into weakly Lewis acidic SalenCo(III)OH after complete and irreversible counterion addition to epoxide in the late stages of the HKR. As a result, the HKR rate significantly decreased with time, due to the inefficiency of SalenCo(III)OH for epoxide activation.[32] Davis and co-workers also suggested that addition of the Co-Salen counterions to epoxide forming Co−OH is the chief factor for the catalyst deactivation during the HKR of racemic epichlorohydrin.[13a] As to the HKR of racemic propylene oxide in the present system, however, a dimeric [SalenCo(III)OH]$_2$ structure was detected, which was supposed to play an important role in catalyst deactivation. It is suggested that the dimeric [SalenCo(III)OH]$_2$

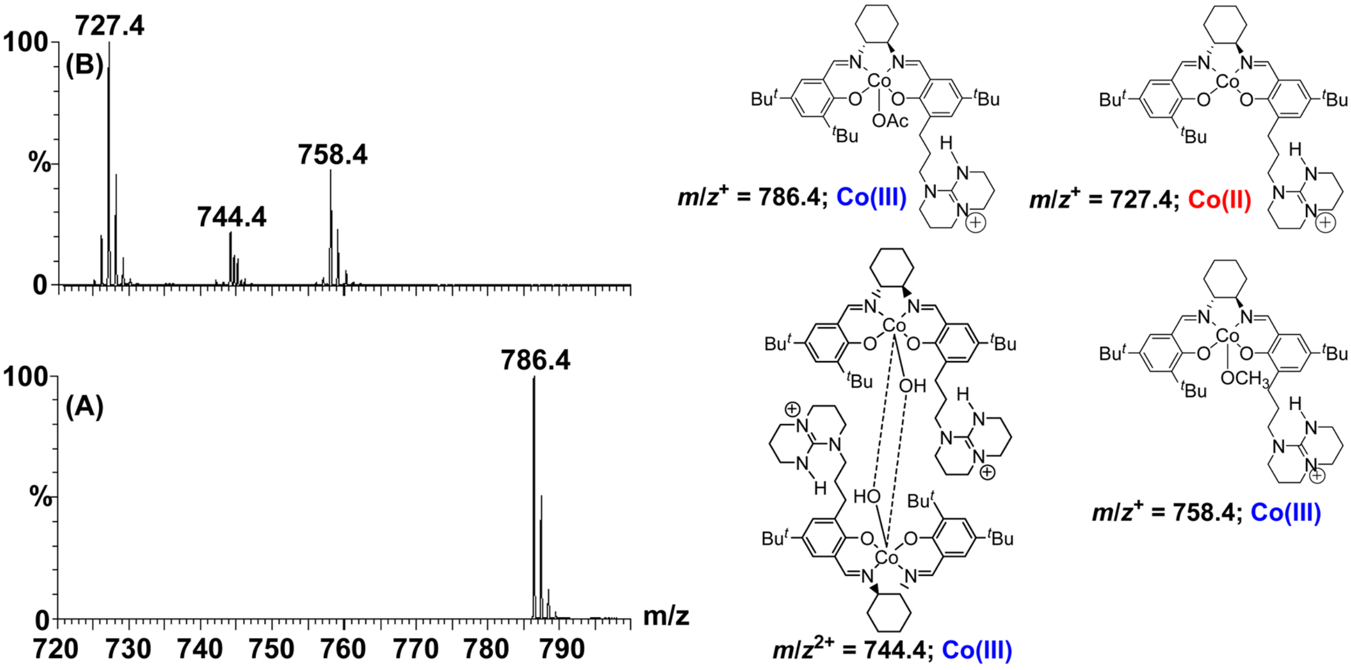


Figure 8. ESI-MS spectra of (A) complex **3** in CH_2Cl_2 and (B) the reaction mixture of complex **3**/H_2O/propylene oxide ([complex **3**]/[H_2O]/[epoxide] = 1/100/5000, molar ratio).

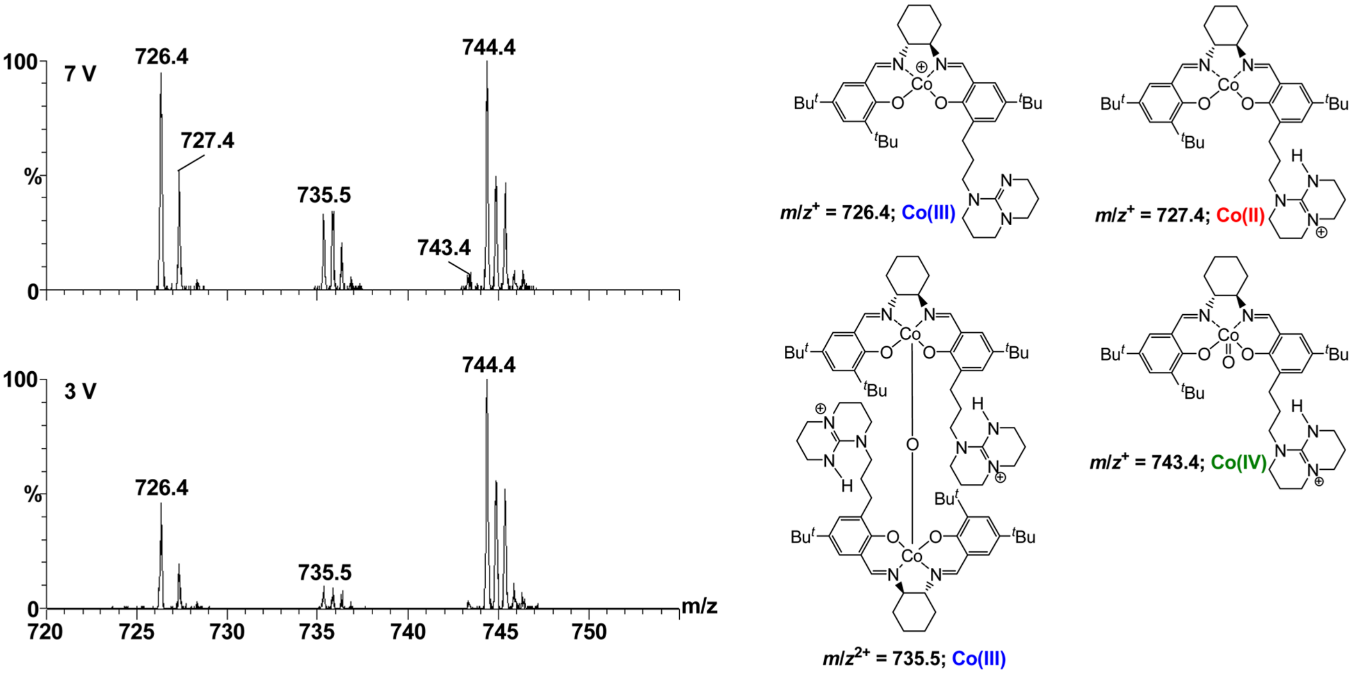


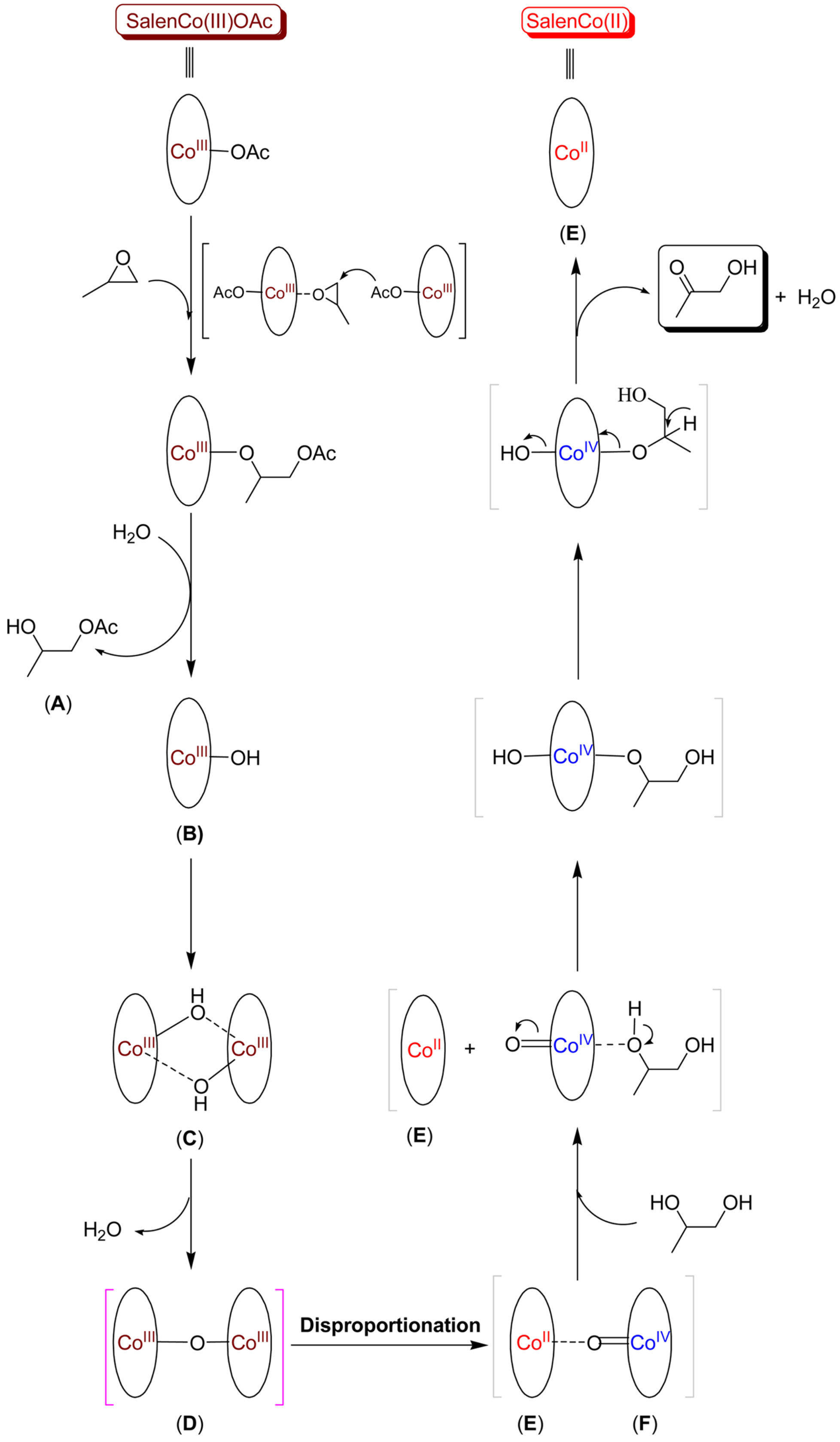
Figure 9. Collision-induced dissociation (CID) of the species of m/z^{2+} 744.4 resulted from the system of complex **3**/H_2O/propylene oxide with various voltages.

complex benefits the formation of the inactive Co(II) derivatives by disproportionation. On the other hand, the dimerization of the resultant SalenCo(III)OH significantly retards the ring opening of epoxide, which may be another reason for the inactivity of SalenCo(III)OH except for the weak Lewis acidity. For clarifying this hypothesis, we investigated the relationship between the formation of the dimeric $[\text{SalenCo(III)OH}]_2$ (species of m/z^{2+} 744.4) and the catalytic activity during the HKR of racemic propylene oxide catalyzed by complex **3**. The results showed that the HKR rate gradually reduced with the formation of the dimeric $[\text{SalenCo(III)OH}]_2$, as well as the production of Co(II) species (Figure 10). These results indicated that the dimerization of the resultant SalenCo(III)OH contributes to the catalyst deactivation.

■ CONCLUSION

In summary, we propose a new mechanistic understanding of metal valence change in the SalenCo(III)X-catalyzed HKR of racemic propylene oxide or styrene oxide, concerning a redox reaction between Co(III)-Salen and diol, the hydrolyzed

Scheme 3. Possible Mechanism for the Reduction of SalenCo(III)OAc to SalenCo(II) and Oxidation of the Diols to α-Hydroxy Ketones



product. The mechanism is based on two important facts: one is the direct observation of the formation of Co(II) derivatives in the TBD-appended SalenCo(III)OAc-catalyzed HKR process by ESI-MS and UV−vis studies, and another is the isolation of the

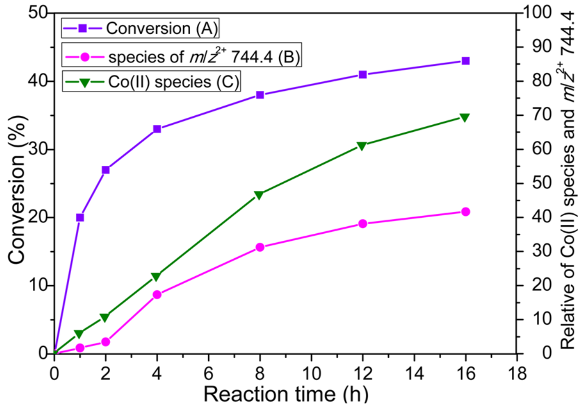


Figure 10. (A) Time profile of the conversion of propylene oxide resulted from the HKR of racemic propylene oxide catalyzed by complex **3** (complex **3**/H_2O/epoxide = 1/550/1000, molar ratio) and plots of the relative intensity of (B) the species of m/z^{2+} 744.4 and (C) Co(II) species versus reaction time from ESI-MS spectra.

oxidation product, 2-hydroxy-1-phenylethanone, from the SalenCo(III)OAc/H_2O/styrene oxide system, affording direct evidence involving the oxidation of the produced diols. The intermediate Salen(III)OH plays an important role in the HKR process concerning the formation of a dimer (**C**) in Scheme 3. Highly reactive oxocobalt(IV) is suggested to be formed by dehydration and disproportionation of the dimer on the basis of ESI-MS investigation and is responsible for the oxidation of diols to afford α-hydroxy ketones.

EXPERIMENTAL SECTION

Synthesis of Ligand of Complex 2. A flask was charged with (1*R*,2*R*)-diaminocyclohexane mono(hydrogen chloride) (0.15 g, 1.0 mmol), activated 5 Å molecular sieves (1.00 g), and anhydrous methanol (10 mL). 3,5-Di-*tert*-butyl-2-hydroxybenzaldehyde (0.28 g, 1.2 mmol) was added in one portion, and the reaction mixture was stirred at room temperature for 2 h. A solution of 7-(5-*tert*-butyl-4-hydroxy-2-formylphenyl)methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene[24] (0.33 g, 1.0 mmol) in anhydrous ethanol (10 mL) was then added to the reaction system, followed by the slow addition of triethylamine (0.27 mL, 2.0 mmol). After stirring at room temperature for an additional 4 h, the reaction mixture was filtered through a short pad of dry silica gel. Then all solvents and the excess triethylamine were removed *in vacuo*. The residue was purified by column chromatography on silica gel using petrol ether/ethyl acetate (5:1, 1% Et_3N) as the mobile phase to give the afforded compound as a bright yellow solid (0.42 g, 67%). ^1H NMR (400 MHz, $CDCl_3$): δ 13.7 (s, 1H), 13.5 (s, 1H), 8.36 (s, 1H), 8.32 (s, 1H), 7.32 (s, 1H), 7.12 (m, 2H), 7.03 (s, 1H), 4.91−4.95 (m, 1H), 4.65−4.69 (m, 1H), 3.52−3.58 (m, 2H), 3.18−3.37 (m, 8H), 1.54−2.05 (m, 12H), 1.41 (s, 9H), 1.40 (s, 9H), 1.24 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.6, 164.9, 160.4, 157.9, 150.8, 139.9, 137.6, 136.3, 129.7, 129.4, 126.7, 126.0, 123.6, 118.6, 117.8, 72.5, 72.0, 53.5, 48.2, 47.4, 44.9, 38.5, 34.9, 34.7, 34.0, 33.3, 33.1, 31.3, 29.3, 29.2, 24.2, 21.1, 20.8. HRMS (m/z) calcd for $[C_{40}H_{60}N_5O_2]^+$ 642.4747, found 642.4786. $[\alpha]^{20}_D$ −289.2 (c 1.0, $CHCl_3$).

Synthesis of Complex 2. Cobalt(II) acetate (0.089 g, 0.6 mmol) and the ligand (0.32 g, 0.5 mmol) were dissolved in methanol (10 mL). After stirring for 12 h at room temperature, LiCl (0.11 g, 2.5 mmol) was added, and the mixture was further stirred for 12 h. The solvent was removed *in vacuo*, and the residue was extracted with CH_2Cl_2. The organic layer was washed with saturated aq. $NaHCO_3$ and brine, then dried over anhydrous sodium sulfate. The mixture was filtered, and the filtrate was concentrated under vacuum. After removal of the solvent, the residue was dissolved in CH_2Cl_2 (10 mL) in a 40 mL Schlenk, and AgOAc (0.1 g, 0.6 mmol) was added. The mixture was stirred for 24 h and then filtered to remove the Ag byproduct. After the solvent was removed *in vacuo*, the resultant solid was further treated with the methylene chloride/hexane mixture to afford complex **2** as a brown solid (0.35 g, 86%). ^1H NMR (400 MHz, DMSO-d_6): δ 8.05 (s, 1H), 7.94 (s, 1H), 7.63 (s, 1H), 7.43 (s, 1H), 7.38 (s, 1H), 7.21 (s, 1H), 4.65 (m, 2H), 3.54−3.59 (m, 2H), 3.36−3.42 (m, 4H), 3.24−3.30 (m, 4H), 2.97−3.08 (m, 2H), 1.54−1.99 (m, 10H), 1.73 (s, 9H), 1.71 (s, 9H), 1.57 (s, 3H), 1.30 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 164.7, 164.6, 161.7, 161.2, 150.6, 141.4, 137.2, 135.8, 130.4, 129.5, 129.0, 128.6, 127.1, 119.3, 118.0, 70.1, 69.8, 48.2, 47.7, 46.7, 45.3, 38.6, 35.3, 33.4, 31.3, 29.4, 29.3, 24,3, 24.2, 22.9, 20.8, 20.5. HRMS (m/z) calcd for $[C_{42}H_{61}N_5O_4Co]^+$ 758.4056, found 758.4013.

Representative Procedure for the HKR of Racemic Epoxides. A 50 mL flask equipped with a stir bar was charged with (*R*,*R*)-**2** (76 mg, 0.1 mmol). The catalyst was treated with propylene oxide (7.0 mL, 100 mmol) and 2 mL of THF. The reaction flask was cooled to 0 °C, and H_2O (1.0 mL, 55 mmol, 0.55 equiv) was added slowly. The reaction mixture was allowed to warm to room temperature and sampled at certain intervals for ESI-MS and GC analysis.

ASSOCIATED CONTENT

Ⓢ Supporting Information

General experimental procedures; NMR spectra of complex **2** and its ligand; HPLC−MS, GC−MS, and UV−vis studies for α-hydroxy ketones. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(26) Probably, HCl originates from the preparation of epichlorohydrin. Another possibility for HCl production is the intramolecularly ring-closing of the hydrolytic product, 3-chloro-1,2-propanediol. Of importance, in the presence of HCl, O_2 can reoxidize the resulting SalenCo(II) to the active Co(III)-Salen complex with a Cl^- counterion, which was detected in the ESI-MS (the species of m/z 734.4; see Supporting Information, Figure S2). These results give us a reasonable explanation on the formation of very limited amount of Co(II) species during the HKR of epichlorohydrin.

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