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(54) Title: METHOD FOR PREPARING CHIRAL COMPOUND BY ASYMMETRIC RING OPENING REACTIONS OF EPOXIDES

(57) Abstract: The present invention relates to a method for preparing chiral compounds by asymmetric ring opening reactions of epoxides, more particularly, to a method for preparing chiral compounds by means of asymmetric ring opening reactions of epoxides with nucleophiles in the presence of ionic liquids as solvents and chiral salen metallic catalysts. Such a method facilitates recovery and reuse of the expensive catalyst in which the catalyst maintains its activity and enantioselectivity, such that chiral compounds can be prepared in a economic manner.



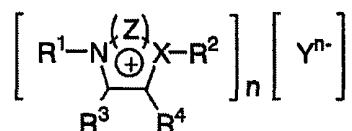
WO 02/12171 A1

**METHOD FOR PREPARING CHIRAL COMPOUND BY ASYMMETRIC RING
OPENING REACTIONS OF EPOXIDES**

TECHNICAL FIELD

5 The present invention relates to a method for preparing
chiral compounds by the asymmetric ring opening reactions of
epoxides, more particularly, to a method preparing chiral
compounds by means of asymmetric ring opening reactions of
epoxides with nucleophiles in the presence of a salt followed
10 formula 1 and chiral salen metallic catalysts. Such a method
facilitates recovery and reuse of the expensive catalyst in
which the catalyst maintains its activity and
enantioselectivity, such that chiral compounds can be prepared
in an economic manner.

15 (Formula 1)



wherein R¹, R², R³, R⁴, X, Z, n and Y are as defined in
the description.

20 **BACKGROUND OF THE INVENTION**

In recent years, there has been a sharp increase in the
demand for chiral compounds by the pharmaceutical industry,
the agricultural chemicals industry, and the perfumery

industry. Particularly, the demand for chiral compounds in the pharmaceutical industry is at an explosive level, taking advantage of the American Food and Drug Administration's (FDA) policy concerning chiral drugs. In detail, as for new drug
5 candidates, their optically active compounds, that is, chiral compounds are preferred rather than racemates. In the case of the products which have been sold in racemic mixtures, their enantiomers tend to receive approval as new drugs if they are proven to have more excellent medicinal effects or fewer side
10 effects than the racemic mixtures. Further, where new drug candidates have intramolecular stereogenic sites, the FDA stipulates that racemic mixtures and each enantiomer should be separated and tested for biological activity.

Production methods of chiral compounds in current use can
15 be classified into two groups: one taking advantage of chiral pools and the other using optical resolution.

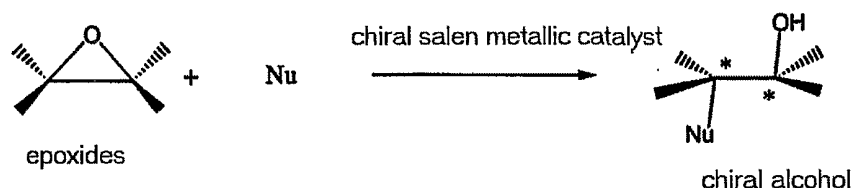
Typically, advantage is taken of chiral pools by traditional organic synthesis methods in which naturally occurring chiral compounds such as sugars and amino acids are
20 used as starting materials. However, such methods are disadvantageous in that kinds of naturally occurring chiral compounds are not versatile, and chiral compounds, though being available, have limited optical polarity, like D-sugars and L-amino acids.

25 Optical resolution methods take advantage of reagents in

optically resolving compounds. However, these methods are not suited to industrial application because as much as 50 % of the racemic mixture is wasted if the remaining stereoisomers do not find appropriate uses.

5 To circumvent these problems, much effort has been made, leading to the development of chiral catalysts that are useful for the production of chiral compounds. Particularly, the use of salen derivatives is one of the most successful methods when account is taken of technical aspects as well as the
10 industrial utility of the products. In the presence of such chiral catalysts, chiral compounds can be prepared through the asymmetric ring-opening reaction of racemic or meso epoxides (E. N. Jacobsen and M. H. Wu, *Ring Opening of Epoxides and Related Reactions, in Comprehensive Asymmetric Catalysis III*,
15 ed. E. N. Jacobsen, A. Pfaltz and H. Yamamoto, Springer Verlag, Berlin-Heidelberg-New York, **1999**, p. 1309).

(Reaction Scheme 1)



wherein *(asterisk) denote the positions at which the
20 absolute configuration of the carbon atoms means R or S.

The asymmetric ring opening of epoxides, as shown in the reaction scheme 1, are conducted with nucleophiles in the

presence of a chiral salen catalyst so as to produce chiral compounds with various functional groups. In this connection, examples of useful nucleophiles include N_3^- , NH_3 , H_2NR , HNR_2 , H_2O , ROH , PhOH , RSH , H^- , RCH_2^- , etc.

5 For such asymmetric ring opening reactions, a variety of chiral salen catalysts are usefully utilized[E. N. Jacobsen and M. H. Wu, *Ring Opening of Epoxides and Related Reactions*, in *Comprehensive Asymmetric Catalysis III*, ed. E. N. Jacobsen, A. Pfaltz and H. Yamamoto, Springer Verlag, Berlin-Heidelberg-
10 New York, **1999**, p1309; Jacoben et al., US 5,665,890 (1997); Jacobsen et al., US 5,929,232 (1999); Jacobsen et al., WO 9628402 (1996); Jacobsen et al., WO 0009463 (1999); Jacobsen et al., *Science*, **1997**, **277**, 936; Jacobsen et al., *J. Am. Chem Soc.*, **1996**, **118**, 7420; Jacobsen et al., *J. Org. Chem.*, **1998**,
15 **63**, 5252].

Aside from the asymmetric ring opening reactions, chiral salen catalysts are used to synthesize chiral epoxides through asymmetric epoxidation. Chiral salen catalysts, although being used for both asymmetric ring opening reactions and
20 epoxidation, can be distinguished from each other depending on the reactions for which they are used. For instance, chiral salen catalysts comprise Mn as a catalytically effective metal when they are used for epoxidation, while comprising Cr or Co as a catalytically effective metal for asymmetric ring opening
25 reactions[US 5,637,739 (1997), US 5,663,393 (1997), US

5,420,314 (1995), US 5,599,957 (1997), WO 93/03838 (1993) and WO 94/03271 (1994), US 5,352,814 (1994), US 5,639,889 (1997) and US 5,916,975 (1999)].

Taking advantage of the difference in reactivity to
5 nucleophiles from one enantiomer to another, kinetic resolution is to react a nucleophile with one enantiomer in the presence of a chiral catalyst to afford various chiral compounds. For instance, where water is used as a nucleophile for racemic epoxides, one enantiomer is opened by water to
10 produce chiral diols, which are very important intermediates that can find numerous applications in various fine chemical industries. On the other hand, the other epoxide enantiomer is not reacted with the nucleophile and thus remains as it is [Tokunaga, M.; Larrow, J. F.; Kakiuchi, F.; Jacobsen, E.,
15 *Science*, **1997**, **277**, 936].

The asymmetric ring opening reactions of epoxides using chiral salen catalysts can be broken down into the kinetic resolution of racemic epoxides and the enantioselective ring opening reaction of meso epoxides.

20 In spite of its strong ability to produce industrially useful chiral materials of high optical purity, the asymmetric ring opening of racemic or meso epoxides is difficult to apply to industrial fields because the chiral salen catalysts used are prepared under intricate reaction conditions by multi-step
25 processes, in addition to being very expensive. In order to

overcome the problems with the asymmetric ring opening methods of racemic or meso epoxides, extensive and intensive research has been directed to the recycling of the used chiral salen catalysts after the asymmetric ring opening reaction.

5 According to research reports made thus far, however, it is very difficult to recover used chiral salen catalysts after obtaining desired chiral compounds through the asymmetric ring opening reaction and virtually impossible to apply the catalysts to the industrial production of the desired chiral
10 compounds. Where trimethylsilyl azide is used as a nucleophile in the asymmetric ring opening reaction, the resulting azido alcohol is generally isolated by vacuum distillation, after which the remaining chiral salen metal catalyst is reused. In this case, it is practically impossible to apply the
15 asymmetric ring opening reaction for industrial production due to the danger of the explosion of produced azido compounds [L. E. Martinez, J. L. Leighton, D. H., Carsten, and E. N. Jacobsen, *J. Am. Chem. Soc.*, **1995**, **117**, 5897].

Additionally, various techniques for easy recovery,
20 repetitive use, and application to continuous process of chiral salen catalysts through immobilization on solid supports have been under active study. For instance, some modification of the chemical structures of chiral salen catalysts is made to chemically couple them with terminal
25 groups of solid supports, such as silica gel or polystyrene,

and the resulting solid forms of the catalysts are recovered by filtration after the asymmetric ring opening reaction [S. Peukert, E. N. Jacobsen, *Organic Letters*, **1999**, **1**, 1245; D. A. Annis and E. N. Jacobsen, *J. Am. Chem. Soc.*, **1999**, **121**, 4247-5 4154]. However, the modification in chemical structure of chiral salen catalysts and the need for immobilization on solid supports places an economic burden upon this technique.

Therefore, there remains a need for an improved chiral salen catalyst system that can be easily recovered and 10 repeatedly used after the asymmetric ring opening of epoxides without modifying the catalyst in chemical structure.

SUMMARY OF THE INVENTION

Leading to the present invention, the intensive and 15 thorough research on the asymmetric ring opening of epoxides by use of the chiral salen catalysts, conducted by the present inventors aiming to overcome the above problems encountered in prior arts, resulted in the finding that chiral salen catalysts are immobilized within certain salts such that, 20 after the asymmetric ring opening of epoxides in the salts or solvent systems containing the salts, the catalysts can be easily recovered in forms immobilized within the salts while the resulting products are separated by direct distillation or ordinary organic extraction. Also, the recovered chiral salen 25 catalysts were found to maintain their catalytic activity and

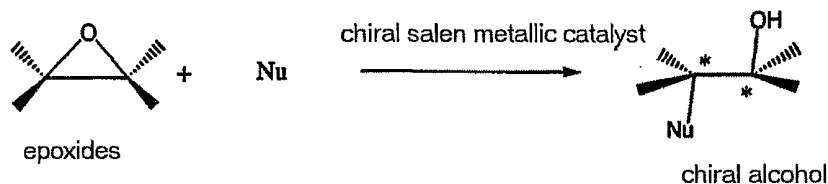
enantioselectivity as high as before use, and thus can be used repeatedly.

In the present invention, epoxides are reacted with nucleophiles in the presence of a chiral salen catalyst in a solvent containing only a salt represented by the following formula 1 alone or in combination with other solvent components, and the catalyst can be reused while remaining the solvent without a decrease in its catalytic activity and enantioselectivity.

DISCLOSURE OF THE INVENTION

The present invention relates to a method for preparing chiral compounds, more particularly to method for preparing chiral compound by means of asymmetric ring opening reactions that the chiral salen catalyst can be simply recovered and reused, comprising reacting epoxides with nucleophiles in the presence of a salt followed formula 1 or mixture with other solvents and chiral salen metallic catalysts.

(Reaction Scheme 1)

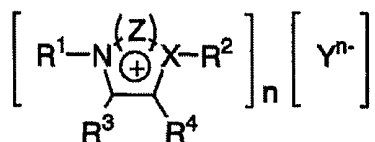


Examples of useful nucleophiles in this reaction include N_3^- , NH_3 , H_2NR , HNR_2 , H_2O , ROH , PhOH , RSH , H^- or RCH_2^- .

I. Salt

The present invention is concerned with the use of the salt represented by the following formula 1.

(Formula 1)



wherein,

if X is nitrogen atom,

Z is $-\text{C}(\text{R}^5)-$,

R^1 and R^2 are independently C_1 - C_{18} alkyl group,

R^3 , R^4 and R^5 are independently hydrogen or C_1 - C_{18} alkyl group; or

if X is carbon atom,

Z is $-\text{C}(\text{R}^5)-\text{C}(\text{R}^6)-$,

R^1 is C_1 - C_{18} alkyl group,

R^2 , R^3 , R^4 , R^5 and R^6 are independently hydrogen or C_1 - C_{18} alkyl group, and

n is an integer of 1-3, and

Y is an anion capable of forming salts and represents either a negatively charged halogen element, MX_k^- or R^7O^- ,

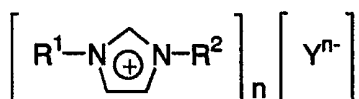
wherein M is selected from the group consisting of 1B, 2B, IIIA, IVA and VA elements in periodic table of elements(CAS version) and X is halogen atom, k is an integer of 2-6, R_7 is selected from the group consisting of alkyl sulfonyl,

haloalkyl sulfonyl, phosphoryl and alkylcarbonyl.

The term "C₁-C₁₈ alkyl group" as used herein is art-recognized and refers to primary, secondary or tertiary alkyls of C₁-C₁₈, exemplified by methyl, ethyl, propyl, isopropyl, butyl, isobutyl, t-butyl, pentyl, 2-methyl-butyl, 3-methyl-butyl, hexyl, heptyl or octyl.

Preferably, the salt is an imidazolium salt represented by the following formula 2:

(Formula 2)



wherein R¹, R², Y and n are the same as defined above.

Particular examples of the imidazolium salt include cations of 1-ethyl-3-methyl-imidazolium, 1-methyl-3-propyl-imidazolium, 1-butyl-3-methyl-imidazolium, 1-methyl-3-pentyl-imidazolium, 1-hexyl-3-methyl-imidazolium and 1-heptyl-3-methyl-imidazolium with anion such as hexafluoroantimonate (SbF₆), hexafluorophosphate (PF₆), tetrafluoroborate (BF₄), trifluoromethanesulfonate (OTf), acetate (OAc) and the like.

Of the salts represented by the formula 1, those that exist as liquid phases at 100 °C or lower are called ionic liquids. In the present invention, such an ionic liquid may be used as a sole solvent or in combination with other organic solvents. Applicable in the latter case are ordinary organic solvents exemplified by benzene, toluene, chlorobenzene,

diethyl ether, tetrahydrofuran, dioxane, dichloromethane, chloroform, ethyl acetate or acetonitrile.

The salts of the formula 1 have advantages of being highly stable to air and moisture, friendly to the environment and superior in thermal stability and exhibiting high solvation ability with no volatility and flammability. Also, the salts are well suited to catalytic reactions by virtue of their lack of the ability to form a coordinate bond to metals[P. Waaserscheid, W. Keim, *Angew. Chem. Int. Ed.* **2000**, **39**, 3772; T. Welton, *Chem. Rev.* **1999**, **99**, 2071; K.R. Seddon, *J. Chem. Tech. Biotechnol.* **1997**, **68**, 351; Y. Chauvin, H. Olivier, *CHEMTECH*, **1995**, **26**]. With these characteristic properties, the salts are able to make polar or ionic catalysts such as chiral salen catalysts immobilized in the ionic liquid or solvents and allow the products to be easily separated from the catalysts.

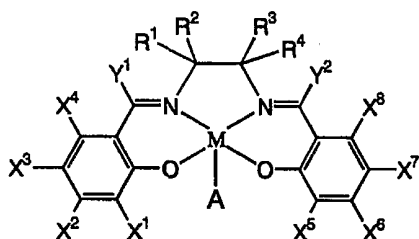
II. Chiral Salen Catalyst

Useful in the present invention are all the chiral salen catalysts that have been reported. Together with the salt represented by the formula 1, any chiral salen catalyst may be used in the production of chiral compounds through asymmetric ring opening of epoxides. Chiral salen catalysts used in the present invention may be classified into various groups according to chemical structure:

1. A preferred class of the chiral salen catalysts useful

in the present invention have the structure represented by the following formula 3:

(Formula 3)



5 wherein,

R^1 , R^2 , R^3 and R^4 are substituent groups to provide chirality to the structure, independently hydrogen, alkyl, carboxyl, aryl, substituted or non-substituted aryl group, wherein the substituent of aryl group is selected from the group consisting of halogen, alky, alkoxy, cyano or nitro group, R^1 , R^2 , R^3 and R^4 can be bonded each other to form a C_4-C_8 ring;

X^1 , X^2 , X^3 , X^4 , X^5 , X^6 , X^7 and X^8 are independently hydrogen, halogen, alkyl, silyl, silyoxy, alkenyl, alkynyl, hydroxy, alkoxy, amino, nitro, cyano, thiol, thioether, imino, amido, phosphoryl, carbonyl and sulfonyl group.

Y^1 and Y^2 are independently hydrogen or alkyl group.

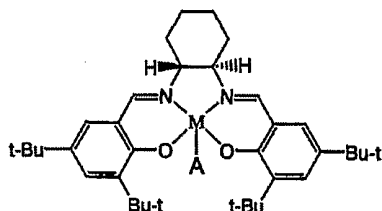
M represents metal, selected from the group consisting of Al, Mn, Cr, Fe, Co, Ti, V, Ru and Os, and preferably Cr or Co;

A^- represents an anion, preferably selected from the group consisting of Cl^- , N_3^- , CH_3OOO^- , BF_4^- , PF_6^- and SbF_6^- .

Wide variety of catalysts of formula 2 has been synthesized and utilized [Jacobsen et al., *J. Org. Chem.*, **1996**,

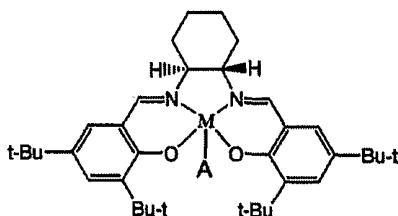
61 389; Jacobsen et al., *Tetrahedron Letters*, **1997**, **38**, 773; Jacobsen et al., US 5,665,890 (1997), Jacobsen et al., US 5,929,232 (1999)]. Representative of the chiral salen catalysts in the first example group are those represented by
5 the following formulas 3a, 3b, 3c and 3d with M-A being selected from the group consisting mainly of Cr-Cl, Co-OAc, Cr-N₃, Co-BF₄, Co-PF₆ and CoSbF₆.

(Formula 3a)

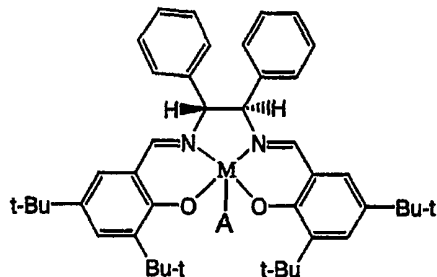


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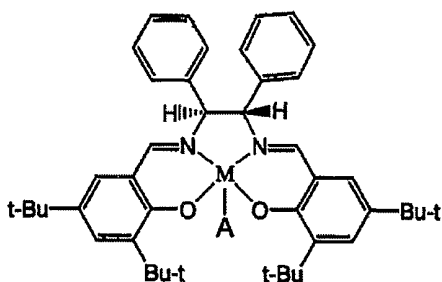
(Formula 3b)



(Formula 3c)

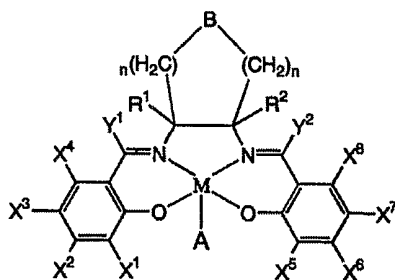


(Formula 3d)



2. Another class of the chiral salen catalysts useful in the present invention have the structure represented by the following formula 4:

5 (Formula 4)



wherein,

R^1 and R^2 are in trans-positions to each other, hydrogen, alkyl, carboxyl, substituted or non-substituted aryl group, wherein the substituent of aryl group is selected from the group consisting of halogen, alkyl, alkoxy, cyano and nitro group;

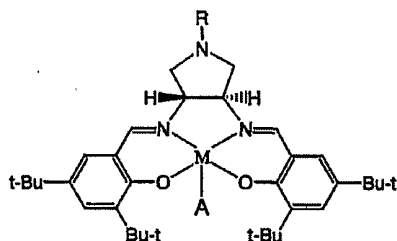
B represents oxygen, sulfur, sulfone, sulfoxide or NR wherein R is selected from the group consisting of alkyl, aryl, alkyl carbonyl ($-C(O)R$), aryl carbonyl ($-C(O)Ar$), alkyl carboxyl ($-C(O)OR$), aryl carboxyl ($-C(O)OAr$), alkyl sulfonyl ($-S(O)_2R$) and aryl sulfonyl group ($-S(O)_2Ar$);

n is an integer of 1-3,

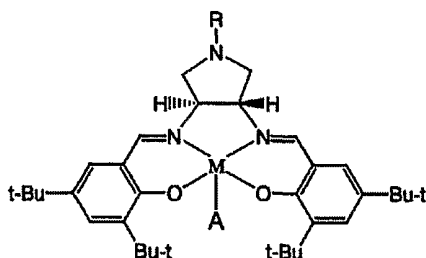
X^1 , X^2 , X^3 , X^4 , X^5 , X^6 , X^7 , X^8 , Y^1 , Y^2 , M and A^- are each the same as defined in the formula 3.

Preferable examples of the chiral salen catalysts of the formula 4 are represented by the following formula 4a and 4b [R. G. Konsler, J. Karl, E. N. Jacobsen, *J. Am. Chem. Soc.*, **1998**, **120**, 10780; C. E. Song et al., *Chem. Commun.* **2000**, 615].

(Formula 4a)

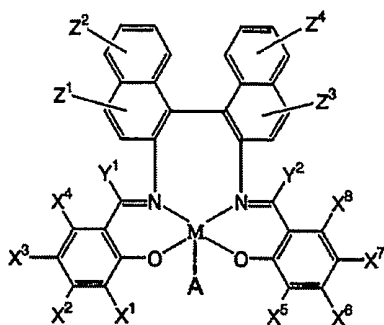


(Formula 4b)



3. In yet another preferred embodiment, the chiral salen catalysts useful in the present invention have the structure represented by the following formula 5 [Jacobsen et al., US 6,665,890 (1997) and Jacobsen et al., US 5,929,232 (1999)].

(Formula 5)



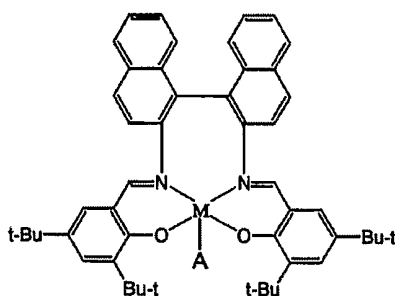
wherein,

Z^1 , Z^2 , Z^3 and Z^4 are independently hydrogen, alkyl, halogen, cyano or nitro group; and

5 X^1 , X^2 , X^3 , X^4 , X^5 , X^6 , X^7 , X^8 , Y^1 , Y^2 , M and A⁻ are each the same as defined in the formula 3.

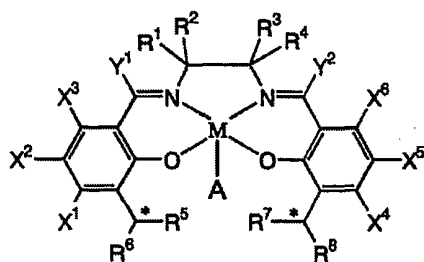
Preferable examples of the chiral salen catalysts of the formula 5 are represented by the following formula 5a [Jacobsen et al., US 5,665,890 (1997)].

10 (Formula 5a)



4. In still another class of the chiral salen catalysts useful in the present invention, there are those that have the structure represented by the following formula 6 [Jacobsen et al., US 5,665,890 (1997), Jacobsen et al., US 5,929,232 (1999), US 5,420,314 (1995), US 5,599,957 (1997), US 5,352,814 (1994), and US 5,639,889 (1997)].

(Formula 6)



wherein,

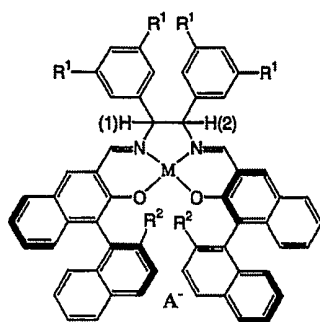
X^1 , X^2 , X^3 , X^4 , X^5 and X^6 are independently hydrogen,
 5 halogen, alkyl, silyl, silyloxy, alkenyl, alkynyl, hydroxyl,
 amino, nitro, thio, thioether, cyano, imino, amido, phosphryl,
 carbonyl or sulfonyl group; or X^1 and X^2 , X^4 and X^5 can be
 bonded each other to form a benzene ring;

R^5 , R^6 , R^7 and R^8 are independently alkyl, aryl,
 10 substituted or non-substituted aryl group, wherein the
 substituent of aryl group is selected from the group consisting
 of halogen, alkyl, alkoxy, cyano and nitro group; or R^5 and R^6 ,
 R^7 and R^8 can be bonded each other to form naphthyl group or
 alkyl- or aryl-substituted naphthyl group;

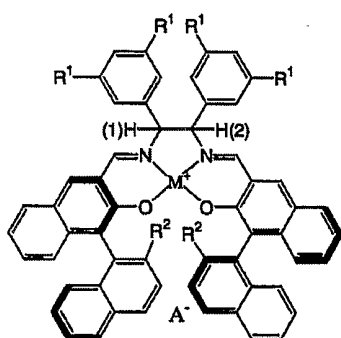
15 R^1 , R^2 , R^3 , R^4 , Y^1 , Y^2 , M and A each are the same as
 defined in the formula 3.

Of the chiral salen catalysts of the formula 6,
 preferable ones are represented by the following formula 6a,
 6b, 6c and 6d, which are collectively called "Katsuki's
 20 catalyst":

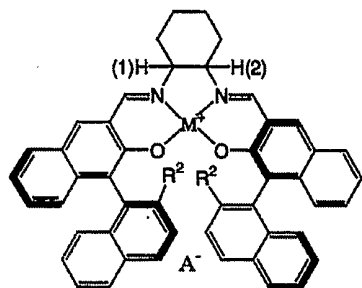
(Formula 6a)



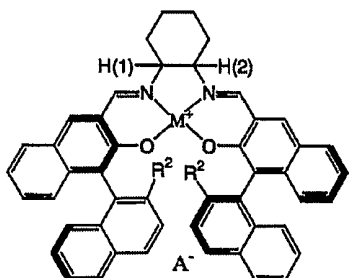
(Formula 6b)



(Formula 6c)



(Formula 6d)



wherein,

hydrogen atoms (1) and (2) together are in trans-

positions;

R^1 represents hydrogen or methyl group;

R^2 represents methyl or phenyl group, and preferably phenyl group;

5 M represents metal, and preferably Cr or Co; and

A^- represents an anion, and preferably selected from the group consisting of Cl^- , N_3^- and OAc^- .

Having been usually used for asymmetric epoxidation to produce chiral epoxides, the chiral salen catalysts
10 represented by the formula 6 can be applicable for the asymmetric ring opening reaction of the present invention.

III. Asymmetric Ring Opening of Epoxides

The asymmetric ring opening of epoxides by nucleophiles in the presence of the chiral salen catalysts may be carried
15 out in ordinary asymmetric ring opening conditions except that the salt of the formula 1 is used as a sole solvent or in combination with other organic solvent [US 5,665,890 (1997) and Jacobsen et al., US 5,929,232 (1999), Jacobsen et al., WO 9628402 (1996) and Jacobsen et al., WO 0009463 (1999; L. E.
20 Martinez, J. L. Leighton, D. H. Carsten, E. N. Jacobsen, *J. Am. Chem. Soc.* **1995**, **117**, 5897; M. Tokunaga, J. F. Larrow, F. Kakiuchi, E. N. Jacobsen, *Science*, **1997**, **277**, 936)]. Nucleophiles for use in the asymmetric ring opening of epoxides include neutral compounds such as alcohols, water,
25 amines, mercaptan and the like; anions such as alkoxides,

thiolates, carbanions, azides, cyanides, thiocyanides, acetates, formates, chloroformates, bisulfides and the like; organometallic reagents and hydrides such as organocuprates, organozinc compounds, organolithium compounds, Grignard
5 reagents, enolates, acetylides, and the like.

IV. Recovery of Chiral Salen Catalyst

After the production of chiral compounds through the asymmetric ring opening of epoxide using the chiral salen catalysts, their recovery can be achieved by adding an organic
10 solvent to the reaction mixture to separate the salt layer of the formula 1, in which the chiral salen catalysts exist.

Any organic solvent may be used in this solvent extraction if it dissolves target compounds, that is, chiral compounds, but does not mix with the salt of the formula 1.
15 Preferable examples of the organic solvents useful in the present invention include pentane, hexane, heptane, benzene, toluene, diethyl ether and isopropanol. For better solvent extraction, stirring is preferably conducted following the addition of the organic solvent. After the stirring, the
20 reaction mixture is divided into two phases. Because the salt of the formula 1 is high in density, it gathers in the lower portion of the reactor, while the upper portion, that is, the organic phase, contains the reaction product. After removal of the organic phase by an ordinary method, the product may be
25 separated from the organic phase by filtration, such as column

chromatography, distillation or recrystallization. Thereafter, the chiral salen catalyst can be recovered from the salt layer which remains in the lower portion.

Alternatively, products may be separated directly by
5 distillation. In this case, the catalyst can be reused without additional separation, that is, as it stands dissolved in or dispersed throughout the salt. With its catalytic activity and enantioselectivity unchanged, the recovered chiral salen catalyst is also effectively applied to the asymmetric ring
10 opening of epoxides.

A better understanding of the present invention may be obtained in light of the following examples which are set forth to illustrate, but are not to be construed to limit the present invention.

15 EXAMPLES

EXAMPLE 1: Preparation of chiral azido alcohol and recovery of chiral catalyst

In a 10 ml three-neck flask, to a solvent of 1 ml of PF₆ salt of 3-butyl-1-methylimidazolium, chiral salen catalyst
20 having formula 3a(Cr-Cl, 38 mg, 0.06 mmol) and cyclopentene oxide(0.175 ml, 2 mmol) were added, and stirred in a nitrogen atmosphere. To 0.28 ml(2.1 mmol) of trimethylsilyl azide was dropped to the imidazolium solution. The reaction solution was stirred while maintaining its internal temperature at 20 °C
25 for 28 hours in a nitrogen atmosphere. Subsequently, to the

reaction solution, hexane (10 ml) was added, and vigorously stirred for 30 min. The azido silyl ether of the hexane layer was measured for optical purity by gas chromatography using a Chrompack Chirasil- DEX CB column. In an isothermal condition of 95 °C, there was separated each enantiomer (24.7 min (1R, 2R), 26.9 min (1S, 2S)). The compound of the formula 3a was recovered as it remained fixed within the salt, and tested by IR spectra showing that the structure of the catalyst identified in which A was N₃. Separately, the hexane layer was concentrated, dissolved in methanol (5 ml) and added with camphorsulfonic acid (24 mg, 0.1034 mg), followed by incubation at room temperature for 30 min with stirring. After removal of the methanol in vacuo, the obtained residue was separated and purified with column chromatography (eluent; acetic acid ethyl ester:hexane=1:2), to give pure azido alcohol with 193.4 mg(76 % yield) and 94 % ee optical purity.

EXAMPLE 2: Preparation of chiral azido alcohol and recovery of chiral catalyst

Except that SbF₆ salt of 3-butyl-1-methyl imidazolium (1 ml) was used instead of PF₆ salt, the reaction was performed in the same manner as described in Example 1, to obtained the azido alcohol with 75 % yield and 87 % ee optical purity. The catalyst used was recovered as fixed in the salt.

EXAMPLE 3: Preparation of chiral azido alcohol and recovery of chiral catalyst

In a 10 ml three-neck flask, to a solvent of 1 ml of PF_6 salt of 3-butyl-1-methylimidazolium, chiral salen catalyst having formula 3a(Cr-Cl, 38 mg, 0.06 mmol) and cyclohexene oxide(0.20 ml, 2 mmol) were added, and stirred in nitrogen atmosphere. To 0.28 ml(2.1 mmol) of trimethylsilyl azidewas slowly added to the imidazolium solution. The reaction solution was stirred while maintaining its internal temperature at 20 °C for 18 hours in a nitrogen atmosphere. Subsequently, to the reaction solution, hexane(10 ml) was added, and vigorously stirred for 30 min. The azido silyl ether of the hexane layer was measured for optical purity by gas chromatography using the same column as in Example 1. In an isothermal condition of 110 °C, there was separated each enantiomer(24.3 min (1R, 2R), 27.1 min (1S, 2S)). The compound of the formula 3a was recovered as it remained fixed within the salt. The structure of the catalyst was identified to have N_3 at the position A as measured by IR spectra. Separately, the hexane layer was concentrated, dissolved in methanol(5 ml) and added with camphorsulfonic acid (24 mg, 0.1034 mg), after which the mixture was incubated at room temperature for 30 min with stirring. After removal of the methanol in vacuo, the obtained residue was separated and purified with column chromatography(eluen; acetic acid ethyl ester:hexane=1:2), to give pure azido alcohol with 242.7 mg(86 % yield), and 84 % ee optical purity.

EXAMPLE 4: Preparation of chiral azido alcohol and recovery of chiral catalyst

Except that SbF_6 salt of 3-butyl-1-methyl imidazolium (1 ml) was used instead of PF_6 salt, the reaction was performed in the same manner as described in Example 1, to obtained azido alcohol with 28 % yield and 72 % ee optical purity. The catalyst used was recovered as fixed in the salt.

EXAMPLE 5: Preparation of chiral azido alcohol and recovery of chiral catalyst

In a 10 ml three-neck flask, to a solvent of 1 ml of PF_6 salt of 3-butyl-1-methylimidazolium, chiral salen catalyst having formula $3a(\text{Cr}-\text{Cl}$, 38 mg, 0.06 mmol) and 3,4-epoxytetrahydrofuran(173.5 mg, 2 mmol) were added, and stirred in nitrogen atmosphere. To 0.28 ml(2.1 mmol) of trimethylsilyl azide was slowly added to the imidazolium solution. The reaction solution was stirred while maintaining its internal temperature at 20 °C for 28 hours in nitrogen atmosphere. Subsequently, to the reaction solution, hexane(10 ml) was added, and vigorously stirred for 30 min. The azido silyl ether of the hexane layer was measured for optical purity by gas chromatography using the same column as in Example 1. In the thermal condition of maintenance at an initiation temperature of 75 ° for 10 min, elevation at a rate of 2 °C per min, and maintenance at a final temperature of 200 °C for 5 min, there was separated each enantiomer (34.4 min (3R, 3R), 35.2

min (3S, 3S)). The compound of the formula 3a was recovered as it remained fixed within the salt. The structure of the catalyst was identified to have N₃ at the position A as measured by IR spectra. Separately, the hexane layer was concentrated, dissolved in methanol (5 ml) and added with camphorsulfonic acid (24 mg, 0.1034 mg), after which the mixture was incubated at room temperature for 30 min with stirring. After removal of the methanol in vacuo, the obtained residue was separated and purified with column chromatography (eluent; acetic acid ethyl ester:hexane=1:2), to give pure azido alcohol with 192.1 mg (74 % yield) and 97 % ee optical purity.

EXAMPLE 6: Preparation of chiral azido alcohol and recovery of chiral catalyst

Except that SbF₆ salt of 3-butyl-1-methyl imidazolium (1 ml) was used instead of PF₆ salt, the reaction was performed in the same manner as described in Example 1, to obtain azido alcohol with 45 % yield and 97 % ee optical purity. The catalyst used was recovered as fixed in the salt.

Yields, optical purities and preparation conditions of the azido alcohol compounds prepared in Examples 1 to 6 were summarized in Table 1, below.

(TABLE 1)

EXAM PLE	Catalyst	epoxides	Solvent ^a	Reaction time (hour)	Yield (%)	% ee ^b	Stero structure
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1	Catalyst of formula 3a (M-A=Cr-Cl)		[bmim] [PF ₆]	28	76	94	(1S,2S)
2	Catalyst of formula 3a (M-A=Cr-Cl)		[bmim] [SbF ₆]	28	75	87	(1S,2S)
3	Catalyst of formula 3a (M-A=Cr-Cl)		[bmim] [PF ₆]	18	86	84	(1S,2S)
4	Catalyst of formula 3a (M-A=Cr-Cl)		[bmim] [SbF ₆]	18	28	72	(1S,2S)
5	Catalyst of formula 3a (M-A=Cr-Cl)		[bmim] [PF ₆]	28	74	97	(3S,3S)
6	Catalyst of formula 3a (M-A=Cr-Cl)		[bmim] [SbF ₆]	28	45	97	(3S,3S)
a : [bmim] [PF ₆] is PF ₆ salt of 3-butyl-1-methylimidazolium [bmim] [SbF ₆] is SbF ₆ salt of 3-butyl-1-methylimidazolium b : Analysis by chiral gas chromatography							

EXAMPLE 7: Preparation of chiral azido alcohol and recovery of chiral catalyst

In a 10 ml three-neck flask, to a solvent of 1 ml of PF₆ salt of 3-butyl-1-methylimidazolium, chiral salen catalyst having formula 3b(Cr-Cl, 38 mg, 0.06 mmol) and 3-(1-naphthyloxy)propylene oxide(400 mg, 2 mmol) were added, and stirred under nitrogen atmosphere. To 0.13 ml(1 mmol) of trimethylsilyl azide was slowly added to the imidazolium solution. The reaction was stirred while maintaining its internal temperature at 0 °C for 48 hours in a nitrogen atmosphere. Subsequently, to the reaction solution, hexane(10 ml) was added, and vigorously stirred for 30 min. The azido

ether of the hexane layer was measured for optical purity by high performance liquid chromatography (HPLC) with a chiralpack AD column at UV 254 nm. In this regard, a developing solvent of 99/1 hexane/isopropanol was flowed at a rate of 1 ml/min through the column to separate enantiomers at 9.7 min (2R) and at 11.2 min (2S). The catalyst of the formula 3b was recovered as it remained fixed within the salt. IR spectra identified the structure of the catalyst in which A was N₃. Separately, the hexane layer was concentrated, dissolved in methanol (5 ml) and added with camphorsulfonic acid (24 mg, 0.1034 mg), followed by incubation at room temperature for 2 hours with stirring. After removal of the methanol in vacuo, the obtained residue was separated and purified with column chromatography (eluent; acetic acid ethyl ester:hexane=1:2), to give pure azido alcohol with 128.7 mg (26 % yield) and 37.9 % ee optical purity.

EXAMPLE 8: Preparation of chiral azido alcohol and recovery of chiral catalyst

Except that a solvent mixture of THF (1.5 ml) and a PF₆ salt of 3-butyl-1-methyl imidazolium (0.5 ml) were used, the reaction was performed in the same manner as described in Example 7, to obtained azido alcohol with 20 % yield and 68 % ee optical purity. The catalyst was recovered as it remained fixed with the salt.

EXAMPLE 9: Preparation of chiral azido alcohol and recovery of

chiral catalyst

Except that a solvent mixture of dichloromethane (1 ml) and a PF₆ salt of 3-butyl-1-methyl imidazolium (1 ml) were used, the reaction was performed in the same manner as described in Example 7, to obtained azido alcohol with 28 % yield and 65 % ee optical purity. The catalyst was recovered as it remained fixed with the salt.

EXAMPLE 10: Preparation of chiral azido alcohol and recovery of chiral catalyst

Except that a solvent mixture of dichloromethane (1 ml) and a PF₆ salt of 3-butyl-1-methyl imidazolium (0.5 ml) were used, the reaction was performed in the same manner as described in Example 7, to obtained azido alcohol with 28 % yield and 65 % ee optical purity. The catalyst was recovered as it remained fixed with the salt.

EXAMPLE 11: Preparation of chiral azido alcohol and recovery of chiral catalyst

Except that a solvent mixture of dichloromethane (1.5 ml) and a PF₆ salt of 3-butyl-1-methyl imidazolium (0.5 ml) were used, the reaction was performed in the same manner as described in Example 7, to obtained azido alcohol with 32 % yield and 78 % ee optical purity. The catalyst was recovered as it remained fixed with the salt.

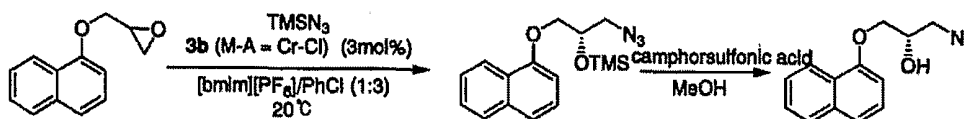
EXAMPLE 12: Preparation of chiral azido alcohol and recovery of chiral catalyst

Except that a solvent mixture of dichloromethane (2 ml) and a PF_6 salt of 3-butyl-1-methyl imidazolium (0.5 ml) were used, the reaction was performed in the same manner as described in Example 7, to obtained azido alcohol with 33 %
 5 yield and 85 % ee optical purity. The catalyst was recovered as it remained fixed with the salt.

EXAMPLE 13: Preparation of chiral azido alcohol and recovery of chiral catalyst

Except that a solvent mixture of chlorobenzene (1.5 ml)
 10 and a PF_6 salt of 3-butyl-1-methyl imidazolium (0.5 ml) were used, the reaction was performed in the same manner as described in Examp1 7, to obtained azido alcohol (see the following reaction scheme 2) with 23 % yield and 94 % ee optical purity. The catalyst was recovered as it remained
 15 fixed with the salt.

(Reaction scheme 2)



wherein PhCl denotes chlorobenzene.

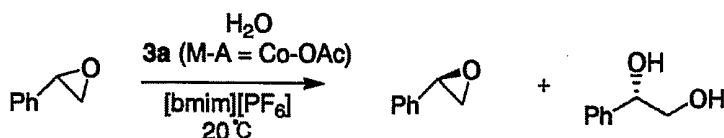
EXAMPLE 14: Preparation of chiral epoxide and chiral diol and
 20 recovery of chiral catalyst

In a 10 ml flask, to a solvent of 3 ml of PF_6 salt of 3-butyl-1-methylimidazolium, chiral salen catalyst having

formula 3a(Cr-OAc, 27.2 mg, 0.04 mmol) and styrene oxide (0.57 ml, 5 mmol) were added. To this reaction solution was slowly added water (0.063 ml, 3.5 mmol), followed by stirring at room temperature for 44 hours. Wubsequently, to the reaction
5 solution, hexane (10 ml) was added, and vigorously stirred for 30 min. After the upper layer (hexane layer) was removed, the lower layer containing the salt of the formula 1 was added with water (10 ml) and vigorously stirred, as shown in the following reaction scheme 3. After being removed, the aqueous
10 phase was added with diethyl ether to extract 1-phenyl-1,2-ethanediol. The styrene oxide of the hexane layer was measured for optical purity by gas chromatography using a Chrompack Chiral-DEX CB column. Under an isothermal condition of 80 °C, there was separated each enantiomer (7.8 min (R), 8.7 min (S)).
15 For the measurement of optical purity, the 1-phenyl-1,2-ethanediol of the diethyl ether layer was subjected to gas chromatography using a Chrompack Chiral-DEX CB column. Under a thermal condition of maintenance at an initiation temperature of 120 °C for 20 min, temperature elevation at a rate of 1
20 °C/min, and maintenance at a final temperature of 140 °C for 5 min, its enantiomers were separated (28 min (S), 29.3 min (R)). For purification, the fractions were deprived of solvents in vacuo and loaded onto a column by use of a 1 % triethylamine buffer, followed by eluting with a solvent mixture of 1:6
25 acetic acid ethyl ester : hexane to produce pure styrene oxide

252.3 mg (42 % yield, 96 % ee) and eluting with a solvent mixture of 1:1 acetic acid ethylester : hexane to produce pure 1-phenyl-1,2-ethanediol 262,5 mg (38 % yield, 96% ee).

(Reaction scheme 3)



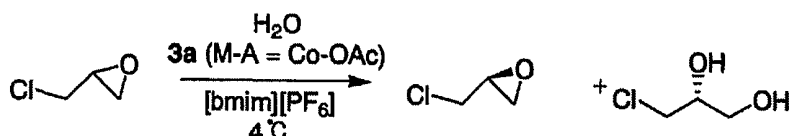
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EXAMPLE 15: Preparation of chiral epoxide and chiral diol and recovery of chiral catalyst

In a 10 ml flask, to a solvent of 3 ml of PF₆ salt of 3-butyl-1-methylimidazolium, chiral salen catalyst having
 10 formula 3a(Co-Oac, 27.2 mg, 0.04 mmol) and epichlorohydrin (0.39 ml, 5 mmol) were added, and stirred in nitrogen atmosphere. Following the slow addition of water (0.063 ml, 3.5 mmol), stirring was conducted at room temperature for 17 hours, as shown in the following reaction scheme 4. From this
 15 reaction mixture, epichlorohydrin and 3-chloro-1,2-propanediol were obtained by direct fractional distillation. The epichlorohydrin was measured for optical purity by gas chromatography using a Chiral-DEX γ-TA column. In an isothermal condition of 40 °C, there was separated each
 20 enantiomer (16.0 min (S), 20.6 min (R)). In the presence of a catalytic amount of p-toluene sulfonic acid, 3-chloro-1,2-propanediol was reacted with 2,2-dimethoxy propane to synthesize a ketal derivative, after which the optical purity

of 3-chloro-1,2-propanediol was determined by gas chromatography using a Chrompack Chiral-DEX CB column (11.2 min (S), 12.7 min (R)). Through the fractional distillation, (S)-epichlorohydrin was obtained at an amount of 200 mg (43 % yield, 96 % ee) and (R)-3-chloro-1,2-propanediol at an amount of 268 mg (48 % yield, 96 % ee).

(Reaction scheme 4)

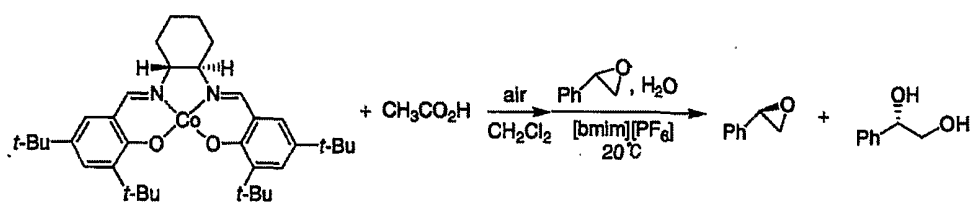


EXAMPLE 16: Preparation of chiral epoxide and chiral diol and recovery of chiral catalyst

In a 10 ml flask, (R, R)-(-)-N,N'-bis(3,5-di-tert-butylsalicylidene)-1,2-cyclohexanediamino cobalt (II) (24.1 mg, 0.04 mmol) was dissolved in dichloromethane (1.5 ml) and reacted with acetic acid (0.005 ml, 0.08 mmol) for 1 hour under the air with stirring to produce a catalyst represented by the formula 3a in which M-A was Co-OAc. This catalyst was directly used in the following reaction, as shown in the following reaction scheme 5. To the catalyst, a PF₆ salt of 3-butyl-1-methylimidazolium represented by the formula 1 (1.5 ml) and then styrene oxide (0.57 ml, 5 mmol) were added, and stirred together. Following the addition of water (0.063 ml, 3.5 mmol), stirring was conducted at room temperature for 44 hours. Subsequently, hexane (10 ml) was also added before the

reaction was vigorously stirred for 30 min. After the upper layer (hexane layer) was removed, the lower layer containing the salt of the formula 1 was added with water (10 ml) and vigorously stirred. After being removed, the aqueous phase was
5 added with diethyl ether to extract 1-phenyl-1,2-ethanediol. The styrene oxide of the hexane layer was measured for optical purity by gas chromatography using a Chrompack Chiral-DEX CB column. In an isothermal condition of 80 °C, there was separated each enantiomer (7.8 min (R), 8.7 min (S)). For the
10 measurement of optical purity, the 1-phenyl-1,2-ethanediol of the diethyl ether layer was subjected to gas chromatography using a Chrompack Chiral-DEX CB column. Under a thermal condition of maintenance at an initiation temperature of 120 °C for 20 min, temperature elevation at a rate of 1 °C/min, and
15 maintenance at a final temperature of 140 °C for 5 min, its enantiomers were separated (28 min (S), 29.3 min (R)). For purification, the fractions were deprived of solvents in vacuo and loaded onto a column by use of a 1 % triethylamine buffer, following eluting with a solvent mixture of 1:6 acetic acid
20 ethyl ester : hexane to produce pure styrene oxide 228.3 mg (38 % yield, 96 % ee) and eluting with a solvent mixture of 1:1 acetic acid ethylester : hexane to produce pure 1-phenyl-1,2-ethanediol 269.4 mg (39 % yield, 94% ee).

(Reaction scheme 5)



(TABLE 2)

EXAM PLE	Catalyst	Epoxides	solvent ^a	Reaction time (Hour)	Yield (%)	% ee
7	Catalyst of formula 3b (M-A=Cr-Cl)	3-(1-Naphtyl) propylene oxide	$[\text{bmim}][\text{PF}_6]$	0.5	26	37.9
8	Catalyst of formula 3b (M-A=Cr-Cl)	3-(1-Naphtyl) propylene oxide	$[\text{bmim}][\text{PF}_6]$ + THF 1.5ml	0.5	20	68
9	Catalyst of formula 3b (M-A=Cr-Cl)	3-(1-Naphtyl) propylene oxide	$[\text{bmim}][\text{PF}_6]$ 1ml+ CH_2Cl_2 1ml	0.5	28	65
10	Catalyst of formula 3b (M-A=Cr-Cl)	3-(1-Naphtyl) propylene oxide	$[\text{bmim}][\text{PF}_6]$ 1ml+ CH_2Cl_2 0.5ml	0.5	23	67
11	Catalyst of formula 3b (M-A=Cr-Cl)	3-(1-Naphtyl) propylene oxide	$[\text{bmim}][\text{PF}_6]$ 0.5ml+ CH_2Cl_2 1.5ml	0.5	32	78
12	Catalyst of formula 3b (M-A=Cr-Cl)	3-(1-Naphtyl) propylene oxide	$[\text{bmim}][\text{PF}_6]$ 0.5ml+ CH_2Cl_2 2ml	0.5	33	85
13	Catalyst of formula 3b (M-A=Cr-Cl)	3-(1-Naphtyl) propylene oxide	$[\text{bmim}][\text{PF}_6]$ 0.5ml+chlorob enzne 1.5ml	0.5	23	94
14	Catalyst of formula 3a (M-A=Co- OAc)	Stylene oxide	$[\text{bmim}][\text{PF}_6]$ 3ml	44	42	96 ^b
					33	96 ^c
15	Catalyst of formula 3a (M-A=Co- OAc)	Epichlorohydrin e	$[\text{bmim}][\text{PF}_6]$ 3ml	17	43	96 ^d
					48	96 ^e
16	Catalyst of formula 3a (M-A=Co- OAc)	Stylene oxide	$[\text{bmim}][\text{PF}_6]$ 1.5ml+ CH_2Cl_2 1.5ml	44	38	98 ^b
					39	94 ^c

a : $[\text{bmim}][\text{PF}_6]$ is PF_6 salt of 3-butyl-1-methylimidazolium
b : styrene oxide
c : 1-phenyl-1,2-ethyldiol
d : (s)-epichlorohydrine
e : (R)-3-chloro-1,2-propandiol

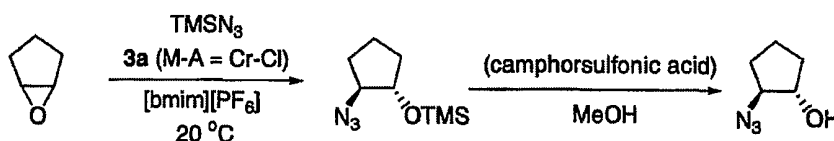
EXPERIMENTAL EXAMPLE 1: Reuse of chiral catalyst

To determine whether the chiral salen catalysts recovered
5 from a salt represented by the formula 1 which was used as a

solvent for the asymmetric ring opening of epoxides, could still maintain its catalytic activity and enantioselectivity, the following experiment was adopted.

In the same manner as in Example 1, cyclopentene oxide was reacted with trimethylsilyl azide in a solvent of a PF_6 salt of 3-butyl-1-methylimidazolium represented by the formula 1 in the presence of a chiral salen catalyst represented by the formula 3a in which M-A was Cr-Cl. After being recovered in the same manner as in Example 1, the catalyst was used for the asymmetric ring opening reaction while remaining fixed within the salt. Using the catalyst, the asymmetric ring opening reaction was performed five times in total. The catalyst was used at an amount of 3 mol % based on the total mole of the cyclopentene oxide. This process is illustrated in the following reaction 6.

(Reaction scheme 6)



wherein $[\text{bmim}][\text{PF}_6]$ represents a PF_6 salt of 3-butyl-1-methylimidazolium and TMSN_3 represents trimethylsilyl azide.

The azido alcohol obtained at each round of the asymmetric ring opening reaction was examined for yield and optical purity, and the results are given in Table 3, below.

(TABLE 3)

The number of reuse	Yield(%)	Optical purity(% ee)
1	76	94
2	74	90
3	78	93
4	76	93
5	78	93

As apparent from Table 3, the catalyst of the formula 3a can ensure a high production yield of 70 % or higher even when it is repeatedly used for the production of highly optically pure azido alcohols if its catalysis is conducted in a salt solvent of the formula 1.

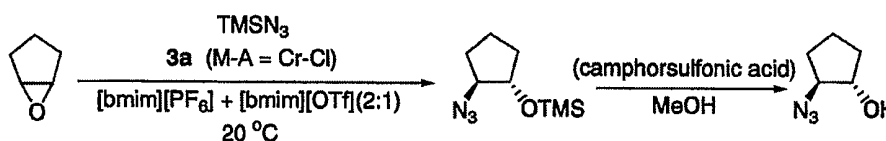
EXPERIMENTAL EXAMPLE 2: Reuse of chiral catalyst

In order to determine whether the chiral salen catalyst which was used and recovered from a solvent system consisting of various salts represented by the formula 1, could yet maintain its catalytic activity and enantioselectivity when it was reused, along with the solvent system, for use in the asymmetric ring opening of epoxides, the following experiment was performed.

In a 10 ml three-neck flask, a chiral salen catalyst (38 mg, 0.06 mmol) represented by the formula 3a in which M-A was Cr-Cl and a cyclopentene oxide (0.175 ml, 2 mmol) were added, along with a PF₆ salt (1 ml) and a trifluorosulfonate (CF₃SO₃⁻, hereinafter referred to as "OTf")(0.5 ml) of 3-butyl-1-methylimidazolium, both represented by the formula 1, and

stirred together under a nitrogen atmosphere. Following the slow addition of trimethylsilyl azide (0.28 ml, 2.1 mmol), stirring was conducted at 20 °C for 28 hours in a nitrogen atmosphere. Subsequently, hexane (10 ml) was also added before the reaction was vigorously stirred for 30 min. Then, azido ether was extracted from the supernatant formed after the stirring. The salt of the formula 1, contained in the lower layer, having therein the catalyst of the formula 3a in which A was N₃, was subsequently used for the same ring opening reaction as it was. Using this catalyst system, the asymmetric ring opening reaction was performed five times in total. The catalyst of the formula 3a in which M-A was Cr-Cl was used at an amount of 3 mol % based on the mole of the cyclopentene oxide. This process is illustrated in the following reaction scheme 7.

(Reaction scheme 7)



wherein [bmim][PF₆] represents a PF₆ salt of 3-butyl-1-methylimidazolium and TMSN₃ represents trimethylsilyl azide.

The azido alcohol obtained at each round of the asymmetric ring opening reaction was examined for yield and optical purity, and the results are given in Table 4, below.

(TABLE 4)

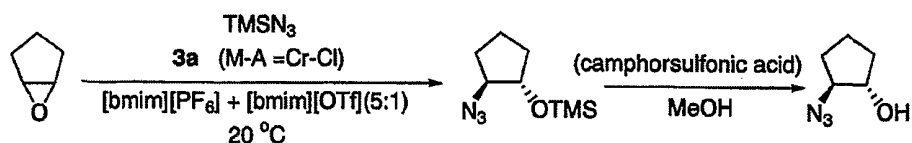
The number of reuse	Yield(%)	Optical purity(% ee)
1	51	85
2	71	93
3	36	70

EXPERIMENTAL EXAMPLE 3: Reuse of chiral catalyst

In order to determine whether the chiral salen catalyst which was used and recovered from a solvent system consisting of various salts represented by the formula 1, could yet
5 maintain its catalytic activity and enantioselectivity when it was reused, along with the solvent system, for use in the asymmetric ring opening of epoxides, the following experiment was performed.

In the presence of a catalyst of the formula 3a in which
10 M-A was Cr-Cl, cyclopentene oxide was subjected to asymmetric ring opening reaction in the same manner as in Example 18, except that a PF₆ salt (1 ml) and an OTf salt (0.2 ml) of 3-butyl-1-methylimidazolium, both represented by the formula 1, were used. After being recovered in the same manner as in
15 Example 8, the catalyst and solvent was used in its integrity for the next same ring opening reaction. Using this catalyst system, the asymmetric ring opening reaction was performed five times in total. The catalyst of the formula 3a in which M-A was Cr-Cl was used at an amount of 3 mol% based on the
20 mole of the cyclopentene oxide. This process is illustrated in the following reaction scheme 8.

(Reaction scheme 8)



The azido alcohol obtained at each round of the asymmetric ring opening reaction was examined for yield and optical purity, and the results are given in Table 5, below.

5 (TABLE 5)

The number of reuse	Yield(%)	Optical purity(% ee)
1	58	94
2	72	92
3	85	93
4	75	94
5	76	94

As apparent from the data of Table 5, the adoption of a mixture of a PF_6 salt and an OTf salt of 3-butyl-1-methylimidazolium in the volume ratio of 5:1, both represented by the formula 1, allows the (R,R)-catalyst represented by the formula 3a in which M-A is Cr-Cl to be reused many times for the production of azido alcohol at high yield and high optical purity.

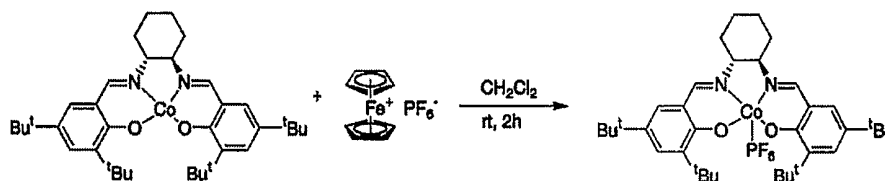
EXAMPLE 17: Preparation of chiral epoxide and chiral diol and recovery of chiral catalyst

15 In a 10 ml flask, (R, R)-(-)-N,N'-bis(3,5-di-tert-butylsalicylidene)-1,2-cyclohexanediamino cobalt (II) (30.2 mg, 0.05 mmol) was dissolved in dichloromethane (1.5 ml) and reacted with ferrocenium hexafluorophosphate (16.5 mg, 0.05 mmol) at room temperature for 2 hours with stirring to produce

a catalyst represented by the formula 3a in which M-A was Co-PF₆. This catalyst was directly used in the following reaction, as shown in the following reaction scheme 9. To the catalyst, a PF₆ salt of 3-butyl-1-methylimidazolium represented by the
5 formula 1 (0.5 ml) was added and then stirred together. Following the removal of dichloromethane in vacuo, epichlorohydrin (0.78 ml, 10 mmol) and water (0.126 ml, 7 mmol) were added and reacted at 20 °C for 24 hours with stirring. From the reaction mixture was extracted
10 epichlorohydrin by fractional distillation under reduced pressure. 3-chloro-1,2-propanol was extracted from the distillation residue with water (10 ml). Also, fractional distillation isolated epichlorohydrin from the dichloromethane layer. After being concentrated, the aqueous phase was added
15 with diethyl ether to extract 3-chloro-1,2-propanediol. The epichlorohydrin obtained through distillation was measured for optical purity by gas chromatography using a chirasil-DEX γ-TA column. Its enantiomers were separated into an S-form at 10.1 min and an R-form at 13.2 min under the isothermal condition
20 of 40 °C. In the presence of a catalytically effective amount of p-toluene sulfonic acid, 3-chloro-1,2-propanediol was reacted with 2,2-dimethoxy propane to synthesize a ketal derivative, after which the optical purity of 3-chloro-1,2-propanediol was determined by gas chromatography using a
25 Chrompack Chirasil-DEX CB column. In this regard, there was

separated each enantiomer (11.8 min (S), 13.4 min (R)) under the isothermal condition of 60 °C. Through fractional distillation, (S)-epichlorohydrin was obtained at an amount of 36.8 mg (39.8 % yield, >99 % ee) and (R)-3-chloro-1,2-propanediol at an amount of 55.7 mg (50.4 % yield).

Reaction scheme 9



EXAMPLE 18: Preparation of chiral epoxide and chiral diol and recovery of chiral catalyst

In a 10 ml flask, a catalyst (37.4 mg, 0.05 mmol) represented by the formula 3a in which M-A was Co- PF_6 was dissolved in tetrahydrofuran (1.5 ml) and a PF_6 salt of 3-butyl-1-methylimidazolium (0.5 ml) represented by the formula 1 and reacted with epichlorohydrin (0.78 ml, 10 mmol) and water (0.126 ml, 7 mmol) at 20 °C for 24 hours with stirring. From the reaction mixture was extracted epichlorohydrin by fractional distillation under reduced pressure. 3-chloro-1,2-propanol was extracted from the distillation residue with water (10 ml). After being concentrated, the aqueous phase was added with diethyl ether to extract 3-chloro-1,2-propanediol. The epichlorohydrin obtained through distillation was measured for optical purity by gas chromatography using a Chirasil-DEX

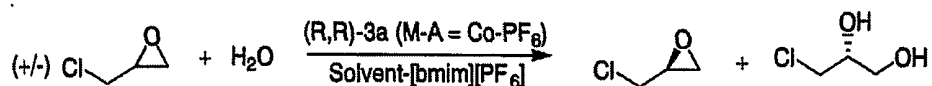
γ-TA column. Its enantiomers were separated into an S-form at 10.1 min and an R-form at 13.2 min under the isothermal condition of 40 °C. In the presence of a catalytically effective amount of p-toluene sulfonic acid, (R)-3-chloro-1,2-propanediol was reacted with 2,2-dimethoxy propane to synthesize a ketal derivative, after which the optical purity of 3-chloro-1,2-propanediol was determined by gas chromatography using a Chrompack Chirasil-DEX CB column. In this regard, there was separated each enantiomer (11.8 min (S), 13.4 min (R)) under the isothermal condition of 60 °C. Through fractional distillation, (S)-epichlorohydrin was obtained at an amount of 34.1 mg (36.8 % yield, >99 % ee) and (R)-3-chloro-1,2-propanediol at an amount of 52.0 mg (47.1 % yield, 92 % ee).

15 EXAMPLE 19: Preparation of chiral epoxide and chiral diol and
recovery of chiral catalyst

In a 10 ml flask, a catalyst (37.4 mg, 0.05 mmol) represented by the formula 3a in which M-A was Co-PF₆ was dissolved in a PF₆ salt of 3-butyl-1-methylimidazolium (1 ml) represented by the formula 1 and stirred. This reaction mixture was reacted with epichlorohydrin (0.78 ml, 10 mmol) and water (0.126 ml, 7 mmol) at 20 °C for 24 hours with stirring. From the reaction mixture, (S)-epichlorohydrin was extracted by fractional distillation at reduced pressure. For the extraction of 3-chloro-1,2-propanol, water (10 ml) was

added to the distillation residue. After being concentrated, the aqueous phase was added with diethyl ether to extract 3-chloro-1,2-propanediol. The epichlorohydrin obtained through distillation was measured for optical purity by gas chromatography using a Chiral-DEX γ -TA column. Its enantiomers were separated into an S-form at 10.1 min and an R-form at 13.2 min under the isothermal condition of 40 °C. As for the optical purity of 3-chloro-1,2-propandiol, its determination was achieved by gas chromatography using a Chrompack Chiral-DEX CB column after (R)-3-chloro-1,2-propanediol was reacted with 2,2-dimethoxy propane in the presence of a catalytically effective amount of p-toluene sulfonic acid to synthesize a ketal derivative. In this regard, there was separated each enantiomer (11.8 min (S), 13.4 min (R)) under the isothermal condition of 60 °C. Through fractional distillation, (S)-epichlorohydrin was obtained at an amount of 35.6 mg (38.5 % yield, >99 % ee) and (R)-3-chloro-1,2-propanediol at an amount of 57.0 mg (51.6 % yield, 90 % ee).

(Reaction scheme 10)



20

EXAMPLE 20: Preparation of chiral epoxide and chiral diol and recovery of chiral catalyst

In a 10 ml flask, a catalyst (37.4 mg, 0.05 mmol)

represented by the formula 3a in which M-A was Co-PF₆ was dissolved in a PF₆ salt of 3-butyl-1-methylimidazolium (0.5 ml) represented by the formula 1 and stirred. Following the addition of epichlorohydrin (0.78 ml, 10 mmol) and water (0.126 ml, 7 mmol), stirring was conducted at 20 °C for 24 hours. Fractional distillation of the reaction mixture at reduced pressure resulted in an extraction of (S)-epichlorohydrin. For the extraction of 3-chloro-1,2-propanol, water (10 ml) was added to the distillation residue. The (S)-epichlorohydrin contained in the dichloromethane layer was also extracted by distillation. After being concentrated, the aqueous phase was added with diethyl ether to extract 3-chloro-1,2-propanediol. Using gas chromatography with a Chiral-DEX γ-TA column, a measurement was made of the optical purity of the (S)-epichlorohydrin obtained through distillation. Its enantiomers were separated into an S-form at 10.1 min and an R-form at 13.2 min under the isothermal condition of 40 °C. As for the optical purity of 3-chloro-1,2-propandiol, its determination was achieved by gas chromatography using a Chrompack Chiral-DEX CB column after (R)-3-chloro-1,2-propanediol was reacted with 2,2-dimethoxy propane in the presence of a catalytically effective amount of p-toluene sulfonic acid to synthesize a ketal derivative. In this regard, there was separated each enantiomer (11.8 min (S), 13.4 min (R)) under the isothermal condition of 60 °C. Through

fractional distillation, (S)-epichlorohydrin was obtained at an amount of 35.8 mg (38.7 % yield, >99 % ee) and (R)-3-chloro-1,2-propanediol at an amount of 45.9 mg (41.5 % yield, 92 % ee).

5 EXAMPLE 21: Preparation of chiral epoxide and chiral diol and recovery of chiral catalyst

In a 10 ml flask, a catalyst (18.7 mg, 0.025 mmol) represented by the formula 3a in which M-A was Co-PF₆ was dissolved in a mixture of tetrahydrofuran (1.5 ml) and a PF₆ salt of 3-butyl-1-methylimidazolium (0.5 ml) represented by the formula 1 and reacted with epichlorohydrin (0.78 ml, 10 mmol) and water (0.126 ml, 7 mmol) at 20 °C for 24 hours with stirring. From the reaction mixture was extracted (S)-epichlorohydrin by fractional distillation under reduced pressure. 3-chloro-1,2-propanol was extracted from the distillation residue with water (10 ml). After being concentrated, the aqueous phase was added with diethyl ether to extract 3-chloro-1,2-propanediol. The (S)-epichlorohydrin obtained through distillation was measured for optical purity by gas chromatography using a Chiral-DEX γ-TA column. Its enantiomers were separated into an S-form at 10.1 min and an R-form at 13.2 min under the isothermal condition of 40 °C. In the presence of a catalytically effective amount of p-toluene sulfonic acid, (R)-3-chloro-1,2-propanediol was reacted with 2,2-dimethoxy propane to synthesize a ketal derivative, after

which the optical purity of 3-chloro-1,2-propanediol was determined by gas chromatography using a Chrompack Chiral-DEX CB column. In this regard, there was separated each enantiomer (11.8 min (S), 13.4 min (R)) under the isothermal condition of 5 60 °C. Through fractional distillation, epichlorohydrin was obtained at an amount of 35.1 mg (37.9 % yield, 75.6% ee) and 3-chloro-1,2-propanediol at an amount of 50.0 mg (45.2 % yield, 89 % ee).

EXAMPLE 22: Preparation of chiral epoxide and chiral diol and
10 recovery of chiral catalyst

In a 10 ml flask, a catalyst (13.7 mg, 0.025 mmol) represented by the formula 3a in which M-A was Co-BF₄ was dissolved in a mixture of THF (1.5 ml) and a PF₆ salt of 3-butyl-1-methylimidazolium (0.5 ml) represented by the formula 15 1, added with epichlorohydrin (0.78 ml, 10 mmol) and water (0.126 ml, 7 mmol), and stirred at 20 °C for 24 hours. From the reaction mixture, (S)-epichlorohydrin was extracted by fractional distillation at reduced pressure. For the extraction of 3-chloro-1,2-propanol, water (10 ml) was added 20 to the distillation residue. Distillation also extracted (S)-epichlorohydrin from the tetrahydrofuran layer. After being concentrated, the aqueous phase was added with diethyl ether to extract 3-chloro-1,2-propanediol. The (S)-epichlorohydrin obtained through distillation was measured for optical purity 25 by gas chromatography using a Chiral-DEX γ-TA column. Its

enantiomers were separated into an S-form at 10.1 min and an R-form at 13.2 min under the isothermal condition of 40 °C. As for the optical purity of 3-chloro-1,2-propandiol, it was determined by gas chromatography using a Chrompack Chiral-DEX
5 CB column after (R)-3-chloro-1,2-propanediol was reacted with 2,2-dimethoxy propane in the presence of a catalytically effective amount of p-toluene sulfonic acid to synthesize a ketal derivative. In this regard, there was separated each enantiomer (11.8 min (S), 13.4 min (R)) under the isothermal
10 condition of 60 °C. Through fractional distillation, (S)-epichlorohydrin was obtained at an amount of 36.3 mg (39.2 % yield, 97.2 % ee) and (R)-3-chloro-1,2-propanediol at an amount of 51.3 mg (46.4 % yield, 91 % ee).

EXAMPLE 23: Preparation of chiral epoxide and chiral diol and
15 recovery of chiral catalyst

In a 10 ml flask, a catalyst (21.0 mg, 0.025 mmol) represented by the formula 3a in which M-A was Co-SbF₆ was dissolved in a PF₆ salt of 3-butyl-1-methylimidazolium (0.5 ml) represented by the formula 1. Following the addition of (S)-
20 epichlorohydrin (0.78 ml, 10 mmol) and water (0.126 ml, 7 mmol), stirring was conducted at 20 °C for 24 hours. Fractional distillation of the reaction mixture at reduced pressure resulted in an extraction of (S)-epichlorohydrin. For the extraction of 3-chloro-1,2-propanol, water (10 ml) was
25 added to the distillation residue. The (S)-epichlorohydrin

contained in the tetrahydrofuran layer was also extracted by distillation. After being concentrated, the aqueous phase was added with diethyl ether to extract 3-chloro-1,2-propanediol. Using gas chromatography with a Chiral-DEX γ -TA column, a measurement was made of the optical purity of the (S)-epichlorohydrin obtained through distillation. Its enantiomers were separated into an S-form at 10.1 min and an R-form at 13.2 min under the isothermal condition of 40 °C. As for the optical purity of 3-chloro-1,2-propandiol, it was determined by gas chromatography using a Chrompack Chiral-DEX CB column after 3-chloro-1,2-propanediol was reacted with 2,2-dimethoxy propane in the presence of a catalytically effective amount of p-toluene sulfonic acid to synthesize a ketal derivative. In this regard, there was separated each enantiomer (11.8 min (S), 13.4 min (R)) under the isothermal condition of 60 °C. Through fractional distillation, (S)-epichlorohydrin was obtained at an amount of 37.5 mg (40.5 % yield, >99 % ee) and (R)-3-chloro-1,2-propanediol at an amount of 54.3 mg (49.1 % yield, 94 % ee).

(TABLE 6)

EXAM PLE	Catalyst	Epoxides	solvent ^a	Reaction time (Hour)	Yield (%)	% ee
20	Catalyst of formula 3a (M-A=Co-PF ₆)	Epichlorohydrine	[bmim] [PF ₆] 0.5ml + CH ₂ Cl ₂ 1.5 ml	24	39.8	>99 ^a
					50.4	^b
21	Catalyst of formula 3a	Epichlorohydrine	[bmim] [PF ₆] 0.5ml + THF 1.5 ml	24	36.8	>99 ^a

	(M-A=Co-PF ₆)		1.5 ml		47.1	92 ^b
22	Catalyst of formula 3a (M-A=Co-PF ₆)	Epichlorohydrine	[bmim] [PF ₆] 1.5 ml	24	38.5	>99 ^a
					51.6	95 ^b
23	Catalyst of formula 3a (M-A=Co-PF ₆)	Epichlorohydrine	[bmim] [PF ₆] 0.5ml	24	38.7	>99 ^a
					41.5	92 ^b
24	Catalyst of formula 3a (M-A=Co-PF ₆)	Epichlorohydrine	[bmim] [PF ₆] 0.5ml + THF 1.5 ml	24	37.9	75.6 _a
					45.2	89 ^b
25	Catalyst of formula 3b (M-A=Co-BF ₄)	Epichlorohydrine	[bmim] [PF ₆] 0.5ml + THF 1.5 ml	24	39.2	97.2 _a
					46.4	91 ^b
26	Catalyst of formula 3b (M-A=Co-Sb ₆)	Epichlorohydrine	[bmim] [PF ₆] 0.5ml + THF 1.5 ml	24	40.5	>99 ^a
					49.1	94 ^b

[bmim] [PF₆] is a salt of 3-butyl-1-methylimidazolium.

a : (s)-epichlorohydrine

b : (R)-3-chloro-1,2-propandiol

EXPERIMENTAL EXAMPLE 4: Reuse of chiral catalyst

To determine whether the chiral salen catalysts recovered from a salt represented by the formula 1 which was used as a solvent for the asymmetric ring opening of epoxides, could still maintain its catalytic activity and enantioselectivity, the following experiment was conducted.

In the same manner as in Example 18, epichlorohydrin was subjected to asymmetric ring opening through the reaction with water in a mixture of THF and a PF₆ salt of 3-butyl-1-methylimidazolium represented by the formula 1 in the presence of a chiral salen catalyst represented by the formula 3a in which M-A was Co-PF₆. After being recovered in the same manner

as in Example 21, the catalyst was used for the asymmetric ring opening reaction while remaining in the salt. Using the catalyst, the asymmetric ring opening reaction was performed five times in total. The catalyst was used at an amount of 0.5 mol % based on the total mole of the epichlorohydrin.

The (S)-epichlorohydrin thus obtained at each round of the asymmetric ring opening reaction was examined for yield and optical purity, and the results are given in Table 7, below.

(TABLE 7)

The number of reuse	Yield(%)	Optical purity(% ee)
1	37	>99
2	37	>99
3	38	>99
4	36	>99
5	38	94.2

As apparent from Table 7, the (R, R)-catalyst of the formula 3a in which M-A is Co-PF₆ can ensure a high production yield, even when it is repeatedly used for the production of highly optically pure (S)-epichlorohydrin, if the reaction is conducted in a solvent mixture of tetrahydrofuran and a PF₆ salt of 3-butyl-1-methylimidazolium represented by the formula 1.

EXPERIMENTAL EXAMPLE 5: Reuse of chiral catalyst

In order to determine whether the chiral salen catalyst which was used in and recovered from a solvent of a salt

represented by the formula 1, could yet maintain its catalytic activity and enantioselectivity when it was reused, along with the solvent, for the asymmetric ring opening of epoxides, the following experiment was performed.

5 In the same manner as in Example 18, epichlorohydrin was reacted with water in a solvent of a PF_6 salt of 3-butyl-1-methylimidazolium represented by the formula 1 in the presence of a chiral salen catalyst represented by the formula 3a in which M-A was Co-PF_6 . After being recovered in the same manner
10 as in Example 21, the catalyst was used for the same asymmetric ring opening reaction while remaining in the salt. Using the catalyst, the asymmetric ring opening reaction was performed three times in total. The catalyst was used at an amount of 0.5 mol % based on the total mole of the
15 epichlorohydrin.

The (S)-epichlorohydrin thus obtained at each round of the asymmetric ring opening reaction was examined for yield and optical purity, and the results are given in Table 8, below.

20 (TABLE 8)

The number of reuse	Yield(%)	Optical purity(% ee)
1	39	>99
2	38	>99
3	38	89.9

As apparent from Table 8, the (R, R)-catalyst of the formula 3a in which M-A is Co-PF_6 can ensure a high production

yield even when it is repeatedly used for the production of highly optically pure (S)-epichlorohydrin if its catalysis is conducted in a solvent of a PF_6 salt of 3-butyl-1-methylimidazolium represented by the formula 1.

5 EXPERIMENTAL EXAMPLE 6: Reuse of chiral catalyst

For the determination of the catalytic activity and enantioselectivity of the chiral salen catalyst, which was used in and recovered from a solvent of a salt represented by the formula 1, when it was reused, along with the solvent, for
10 the asymmetric ring opening of epoxides, the following experiment was performed.

In the presence of a chiral salen catalyst of the formula 3a in which M-A was Co-PF_6 , epichlorohydrin was subjected to asymmetric ring opening reaction through the reaction with
15 water in a solvent system consisting of dichloromethane and a PF_6 salt of 3-butyl-1-methylimidazolium represented by the formula 1 in the same manner as in Example 18. After being recovered while remaining in the solvent, the catalyst solution was used as its for the next same ring opening
20 reaction in the same manner as in Example 31. Using this catalyst system, the asymmetric ring opening reaction was performed three times in total. The catalyst was used at an amount of 0.25 mol% based on the mole of the epichlorohydrin.

The (S)-epichlorohydrin thus separated at each round of
25 the asymmetric ring opening reaction was examined for yield

and optical purity, and the results are given in Table 9, below.

(TABLE 9)

The number of reuse	Yield(%)	Optical purity(% ee)
1	41	>99
2	40	92.5
3	42	92.1

As apparent from the data of Table 9, the adoption of a solvent mixture of dichloromethane and a PF₆ salt of 3-butyl-1-methylimidazolium allows the (R,R)-catalyst represented by the formula 3a in which M-A is Co-SbF₆ to be reused many times for the production of (S)-epichlorohydrin at high yield and high optical purity.

INDUSTRIAL APPLICABILITY

As described hereinbefore, salts represented by the formula 1 or solvent systems containing the salts allow chiral salen catalysts to perform its catalytic activity with high enantioselectivity and efficiency in the asymmetric ring opening of epoxides, as well as ensuring the easy recovery of the catalysts without deteriorating the activity and enantioselectivity thereof nor changing their structures. Thus, the method for preparing chiral compounds according to the present invention is very useful industrially.

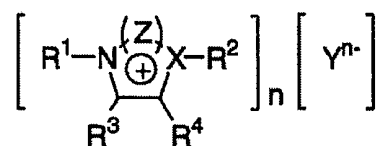
The present invention has been described in an illustrative manner, and it is to be understood that the

terminology used is intended to be in the nature of description rather than of limitation. Many modifications and variations of the present invention are possible in light of the above teachings. Therefore, it is to be understood that
5 within the scope of the appended claims, the invention may be practiced otherwise than as specifically described.

WHAT IS CLAIMED IS:

1. A method for preparing chiral compounds by the asymmetric ring opening of epoxides in the presence of a chiral salen metallic catalyst and one or more salts having
 5 formula 1 or mixture thereof with other organic solvents.

(Formula 1)



wherein,

if X is nitrogen atom,

10 Z is $-\text{C}(\text{R}^5)-$,

R^1 and R^2 are independently C_1 - C_{18} alkyl group,

R^3 , R^4 and R^5 are independently hydrogen or C_1 - C_{18} alkyl group; or

if X is carbon atom,

15 Z is $-\text{C}(\text{R}^5)-\text{C}(\text{R}^6)-$,

R^1 is C_1 - C_{18} alkyl group,

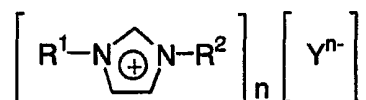
R^2 , R^3 , R^4 , R^5 and R^6 are independently hydrogen or C_1 - C_{18} alkyl group, and

n is an integer of 1-3, and

20 Y is an anion capable of forming salts.

2. The method according to claim 1, wherein the salts have formula 2:

(Formula 2)



wherein,

R^1 and R^2 is independently $\text{C}_1\text{-C}_{18}$ alkyl group,

n is an integer of 1-3, and

5 Y is an anion capable of forming salts.

3. The method according to claim 2, wherein,

R^1 and R^2 are independently $\text{C}_1\text{-C}_8$ alkyl group,

Y is halogen element, MX_k^- or R^7O^- , wherein M is selected from the group consisting of 1B, 2B, IIIA, IVA and VA elements in periodic table of elements(CAS version) and X is halogen atom, k is an integer of 2-6 and R^7 is selected from the group consisting of alkyl sulfonyl, haloalkyl sulfonyl, phosphoryl and alkylcarbonyl.

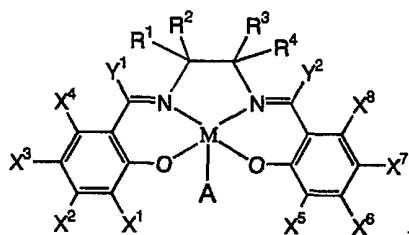
4. The method according to claim 3, wherein X is fluoride.

5. The method according to claim 2, wherein R^1 is methyl, R^2 is ethyl, propyl, butyl, isobutyl, pentyl, 2-methylbutyl, 3-methylbutyl, hexyl, 2-methylpentyl, 3-methylpentyl, 4-methylpentyl, heptyl or octyl, and Y^- is CH_3COO^- , PF_6^- , BF_4^- , SbF_6^- or CF_3SO_3^- .

6. The method according to claim 5, wherein R^1 is methyl, R^2 is butyl and Y^- is PF_6^- , SbF_6^- , BF_4^- or CF_3SO_3^- .

7. The method according to claim 1, wherein the chiral salen metallic catalyst has formula 3:

(Formula 3)



wherein,

R^1 , R^2 , R^3 and R^4 are substituent groups to provide
 5 chirality to the structure, independently hydrogen, alkyl,
 carboxyl, substituted or non-substituted aryl group, wherein
 the substituent of aryl group is selected from the group
 consisting halogen, alkyl, alkoxy, cyano and nitro group, R^1 ,
 R^2 , R^3 and R^4 can be bonded each other to form a C_4 - C_8 ring;

10 X^1 , X^2 , X^3 , X^4 , X^5 , X^6 , X^7 and X^8 are independently hydrogen,
 halogen, alkyl, silyl, silyoxy, alkenyl, alkynyl, hydroxy,
 alkoxy, amino, nitro, cyano, thiol, thioether, imino, amido,
 phosphoryl, carbonyl or sulfonyl group;

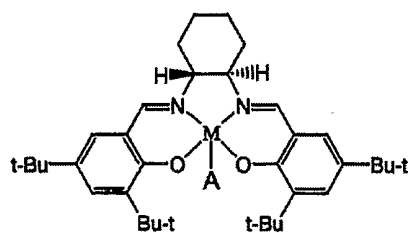
Y^1 and Y^2 are independently hydrogen or alkyl group;

15 M represents metal; and

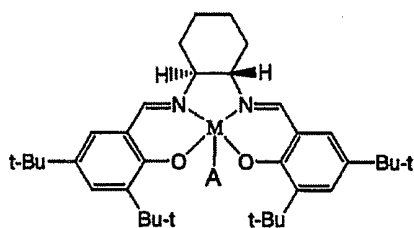
A^- represents an anion.

8. The method according to claim 7, wherein the chiral
 salen metallic catalyst has formula 3a, 3b, 3c or 3d.

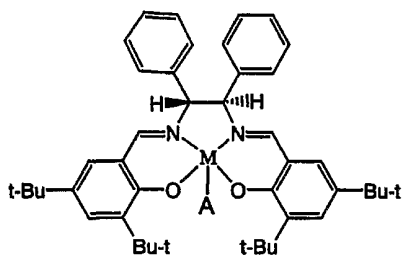
(Formula 3a)



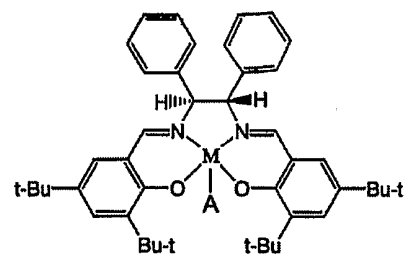
(Formula 3b)



(Formula 3c)



(Formula 3d)



wherein,

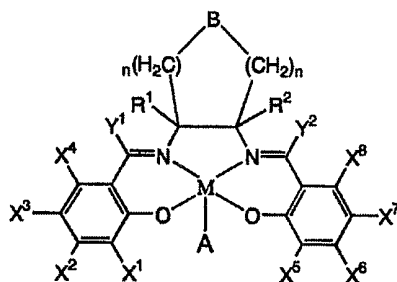
M represents Al, Mn, Fe, Ti, V, Ru, Co or Os,

A⁻ represents Cl⁻, N₃⁻, CH₃COO⁻, BF₄⁻, PF₆⁻ or SbF₆⁻.

9. The method according to claim 8, wherein the M-A represents Cr-Cl, Cr-N₃, Co-OAc, Co-BF₄, Co-PF₆ or Co-SbF₆.

10. The method according to claim 1, wherein the chiral metallic salen catalyst has formula 4.

(Formula 4)



5 wherein,

R^1 and R^2 are in trans-positions to each other, hydrogen, alkyl, carboxyl, substituted or non-substituted aryl group, wherein the substituent of aryl group is selected from the group consisting of halogen, alkyl, alkoxy, cyano and nitro group;

10

B represents oxygen, sulfur, sulfone, sulfoxide or NR wherein R is selected from the group consisting of alkyl, aryl, alkyl carbonyl(-C(O)R), aryl carbonyl(-C(O)Ar), alkyl carboxyl(-C(O)OR), aryl carboxyl(-C(O)OAr), alkyl sulfonyl(-S(O)₂R) and aryl sulfonyl group (-S(O)₂Ar);

15

n is an integer of 1-3,

X^1 , X^2 , X^3 , X^4 , X^5 , X^6 , X^7 and X^8 are independently hydrogen, halogen, alkyl, silyl, silyoxy, alkenyl, alkynyl, hydroxy, alkoxy, amino, nitro, cyano, thiol, thioether, imino, amido, phosphoryl, carbonyl or sulfonyl group;

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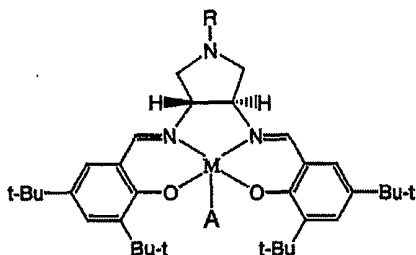
Y^1 and Y^2 are independently hydrogen or alkyl group;

M represents metal,

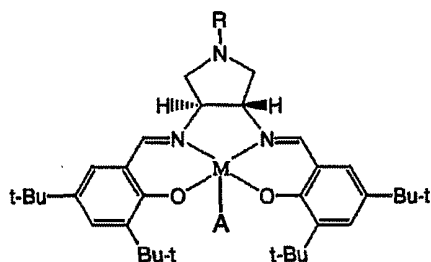
A^- represents anion.

11. The method according to claim 10, wherein the chiral
5 salen metallic catalyst has formula 4a or 4b.

(Formula 4a)



(Formula 4b)



10 wherein,

R is selected from the group consisting of alkyl, aryl, alkyl carbonyl($-C(O)R$), aryl carbonyl($-C(O)Ar$), alkyl carboxyl($-C(O)OR$), aryl carboxyl($-C(O)OAr$), alkyl sulfonyl($-S(O)_2R$) and aryl sulfonyl group ($-S(O)_2Ar$);

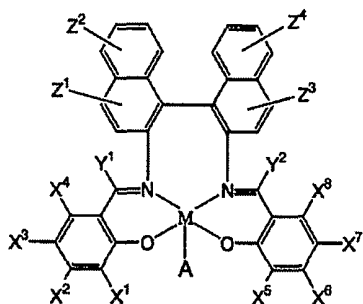
15 M represents Al, Mn, Cr, Fe, Ti, Ru, Co or Os; and

A^- represents Cl^- , N_3^- , CH_3COO^- , BF_4^- , PF_6^- or SbF_6^- .

12. The method according to claim 11, wherein the M-A represents Cr-Cl, Cr- N_3 , Co-OAc, Co- BF_4 , Co- PF_6 or Co- SbF_6 .

13. The method according to claim 1, wherein the chiral salen metallic catalyst has formula 5:

(Formula 5)



5 wherein,

X^1 , X^2 , X^3 , X^4 , X^5 , X^6 , X^7 and X^8 are independently hydrogen, halogen, alkyl, silyl, silyoxy, alkenyl, alkynyl, hydroxy, alkoxy, amino, nitro, cyano, thiol, thioether, imino, amido, phosphoryl, carbonyl or sulfonyl group;

10 Y^1 and Y^2 are independently hydrogen or alkyl group;

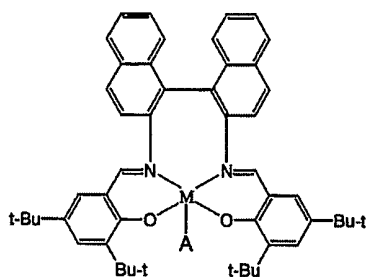
Z^1 , Z^2 , Z^3 and Z^4 are independently hydrogen, alkyl, halogen, cyano or nitro group;

M represents metal; and

A^- represents anion.

15 14. The method according to claim 13, wherein the chiral salen metallic catalyst has formula 5a.

(Formula 5a)



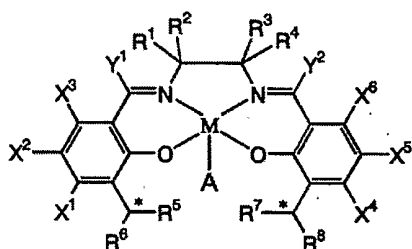
wherein,

M represents Al, Mn, Cr, Fe, Ti, Ru, Co or Os and,

A⁻ represents Cl⁻, N₃⁻, CH₃COO⁻, BF₄⁻, PF₆⁻ or SbF₆⁻.

- 5 15. The method according to claim 1, wherein the chiral salen metallic catalyst has formula 6:

(Formula 6)



wherein,

- 10 R¹, R², R³ and R⁴ are independently hydrogen, alkyl, carboxyl, substituted or non-substituted aryl group, wherein the substituent of aryl group is halogen, alkyl, alkoxy, cyano or nitro group, R¹, R², R³ and R⁴ can be bonded each other to form a C₄-C₈ ring;

- 15 X¹, X², X³, X⁴, X⁵ and X⁶ are independently hydrogen, halogen, alkyl, silyl, silyloxy, alkenyl, alkynyl, hydroxyl, amino, nitro, thio, thioether, cyano, imino, amido, phosphryl,

carbonyl or sulfonyl group, or X^1 and X^2 , X^4 and X^5 can be bonded each other to form a benzene ring;

R^5 , R^6 , R^7 and R^8 are independently alkyl, substituted or non-substituted aryl group, wherein the substituent of aryl group is selected from the group consisting of halogen, alkyl, alkoxy, cyano and nitro group; or R^5 and R^6 , R^7 and R^8 can be bonded each other to each other to form naphthyl group or alkyl- or aryl-substituted naphthyl group;

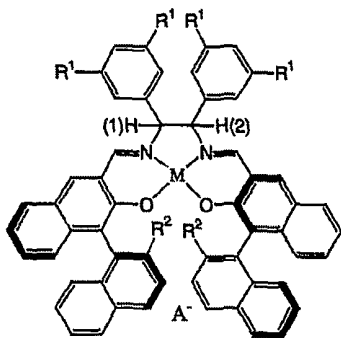
Y^1 and Y^2 are independently hydrogen or alkyl group;

M represents metal; and,

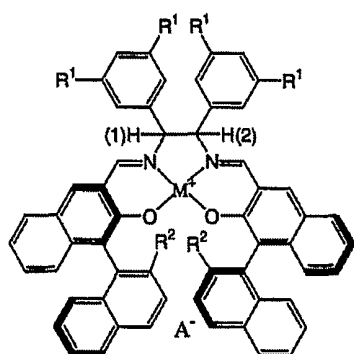
A^- represents anion.

16. The method according to claim 15, wherein the chiral salen metallic catalyst has formula 6a, 6b, 6c and 6d.

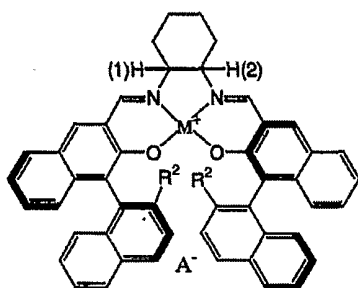
(Formula 6a)



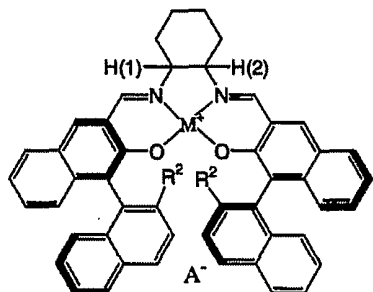
(Formula 6b)



(Formula 6c)



(Formula 6d)



5

wherein,

hydrogen atoms (1) and (2) together are in trans positions;

R^1 represents hydrogen or methyl group;

10 R^2 represents methyl or phenyl group, and preferably phenyl group;

M represents metal, and preferably Cr or Co; and

A^- represents anion, and preferably selected from the group consisting of Cl^- , N_3^- and OAc^- .

INTERNATIONAL SEARCH REPORT

International application No.
PCT/KR01/00597

A. CLASSIFICATION OF SUBJECT MATTER**IPC7 C07C 247/04**

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07D, C07C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

JP, KR

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

STN(REGISTRY, CA), CA-on CD, Dictionary of Organic Chemistry Compound on CD

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US-A-5929232(99.7.27) see the whole document	1-16
A	Ionic Liquid for Clean Technology, Kenneth R. Seddon, Journal of chemical technology and biotechnology, 1997, 68-4, page 351-356 see the whole document	1-6
A	US-A-4469875(84.9.4) see the whole document -----	1-6

☐ Further documents are listed in the continuation of Box C.☒ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

09 JULY 2001 (09.07.2001)

Date of mailing of the international search report

10 JULY 2001 (10.07.2001)

Name and mailing address of the ISA/KR

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Telephone No. 82-42-481-5536



INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/KR01/00597

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-----End of Documents-----			