The Application of Chiral Schiff Base in Asymmetric Catalysis

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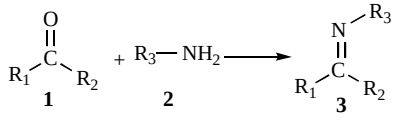
Abstract: This review will focus on the recent applications of chiral Schiff base in asymmetric catalysis. The developments in the preparation and use of chiral Schiff base in a variety of asymmetric transformations will be covered. Some remarkable characteristics and catalytic mechanisms of these reactions will be mentioned and the limitations of some asymmetric reactions will be also discussed.

Keywords: Schiff base, asymmetric catalysis, synthetic methods, enantioselectivity, mechanism, asymmetric transformation.

1. INTRODUCTION

Schiff base is a class of compound synthesized by the condensation of aldehydes or ketones **1** with primary amines **2** (Scheme **1**) [1]. It has been widely used as chemical intermediates in dyes, rubber accelerators, and liquid crystals for electronics. When stereogenic centers or other elements of chirality were introduced in the synthetic design by using chiral aldehydes or chiral amines, chiral Schiff bases were obtained. In recent years, the chiral Schiff base has attracted growing attention as a kind of economic and environmentally friendly catalyst for catalytic asymmetric reactions.



Scheme 1. Synthesis of Schiff base using aldehydes or ketones and primary amines.

Schiff bases have played a special role as chelating ligands in main group and transition metal coordination chemistry. Because they are stable under a variety of oxidative and reductive conditions [2], the complexes of metal/Schiff-base ligand were used in many kinds of reactions as catalysts, including addition, substitution, oxidation and hydrogenation [3]. In 2008, Gupta [4] made a review about the catalytic activities of Schiff base transition metal complexes. It focused on the catalytic activity of binaphthyl, binaphthol metal complexes combined with salen Schiff base, which have been used in the polymerization of ethylene and polymerization of ethylene and propylene, oxidation, allylic alkylations, hydrosilation, and so on. The synthesis of the Schiff base ligands and corresponding metal complexes as well as the mechanisms of those catalysts have also been discussed. Its purpose is not a review on asymmetric catalysis with Schiff base, and the enantioselectivities have only been shown in a few cases.

In fact, chiral Schiff base complexes have emerged as very effective catalysts for asymmetric reactions. Among them, the most prominent one is the Salen-type ligand that has been widely used in catalytic asymmetric epoxidation since 1980's [5, 6]. Katsuki [7-9] and Gilheany [10] have already reviewed the catalytic asymmetric epoxidation using optically active manganese- and chromium-salen and other metallosalen complexes as catalysts. Some others have also summarized this issue from different aspects, such as synthetic strategies and mechanism studies [11-14], the applications [15], and the homogeneous and heterogeneous chiral Salen catalysts [16, 17]. Therefore, in this article, we will have a review about chiral Schiff base catalysts much more than salens.

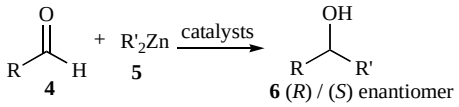
This review focuses on the history and development of chiral Schiff base catalysts which are used in a large variety of asymmetric reactions, and occasionally the mechanisms will be discussed. The reactions include Hetero-Diels-Alder reaction, Ene reaction, Mannich reaction, Aldol reaction, Strecker reaction, Baeyer–Villiger oxidation, asymmetric addition of timethylsilylcyanide to aldehydes, and so on. Moreover, besides the metal-Schiff base catalysis, some organocatalysts without metal atoms will also be mentioned.

The references cited in present review are mainly from 1990 to 2009, most of the chiral Schiff base catalysts mentioned have good enantioselectivities, stereoselectivities, and regioselectivities. Some chiral Schiff base catalysts are easily prepared with cheap materials, stable in the air, and have a broad application prospect in industrialization.

2. ASYMMETRIC CATALYSIS

2.1. Enantioselective Addition of Dialkylzincs to Aldehydes

An addition of organozinc reagents **5** to aldehydes **4** in the presence of catalytic amounts of chiral ligands is a successful catalytic reaction in the asymmetric synthesis (Scheme **2**). The chiral ligands utilized in this reaction often possess *α*, *β*-amino alcohol moiety which can bind zinc in a bidentate [18] or occasionally a tridentate manner [19].



Scheme 2. Enantioselective addition of dialkylzincs to aldehydes.

In 2000, Polt reported some tetracoordinate zinc complexes (Fig. (**1**)) formed from the amino acid-derived Schiff base ligand systems [20]. Those tetracoordinate zinc complexes worked quite well as the catalysts for the addition of alkylzincs to both the aromatic and aliphatic aldehydes.

In the presence of 3 mol% of the Zn(II)-*L*-Phe-*L*-Phe complex **7a**, Me_2Zn and Et_2Zn were added to several aldehydes, 97% yield and 96% ee can be obtained.

Further studies with the *L*-Ala-*L*-Ala **7b** and *L*-Val-*L*-Val **7c** complexes showed that increasing the bulk of the amino acid moiety on the catalyst caused an increase in selectivity for the aromatic as well as aliphatic aldehydes. When using the solid-phase ligand **8** as catalyst, which can be reused multiple times, the enantioselectivity was only slightly reduced.

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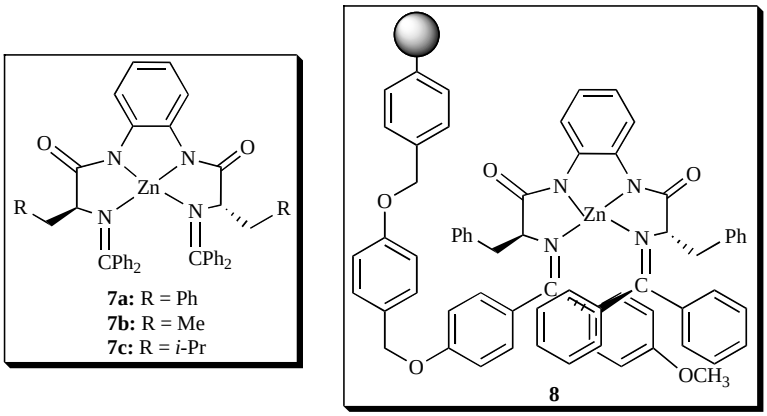


Fig. (1). The tetracoordinate zinc complexes.

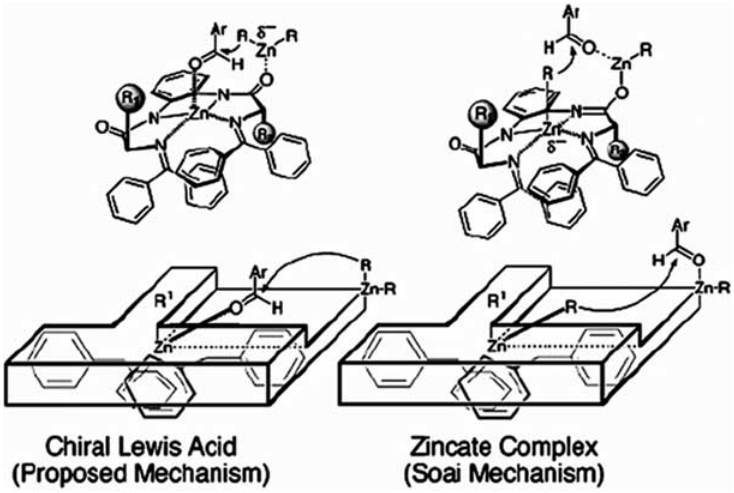


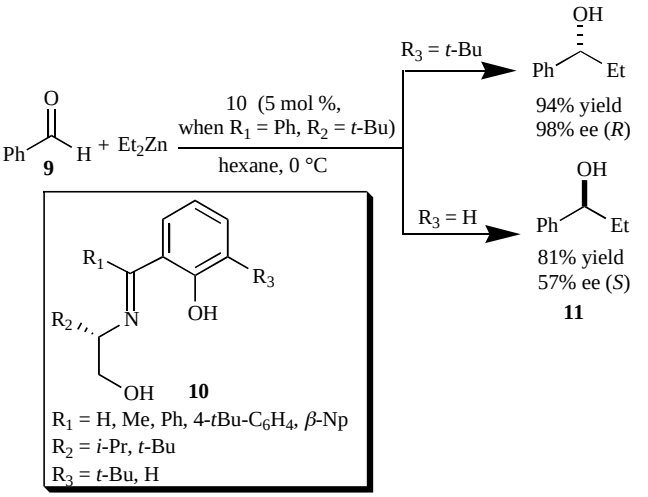
Fig. (2). Possible mechanism for the observed facial enantioselectivity of catalyst **7a-c**.

The possible mechanism of this kind of reaction is shown in Fig. (**2**). Two zinc atoms are involved in alkyl transfer, and the inner zinc is surrounded by electron-donating nitrogen, while the outer zinc is only solvated by exchangeable oxygen. Different roles were involved for the two zinc atoms, the "inner zinc" functioning as a chiral Lewis acid and the "outer zinc" functioning as the alkyl donor.

In 2006, Hayashi [21] developed new chiral Schiff base catalysts **10** for the enantioselective addition of diethylzinc reagents to aldehydes. The effect of different substituents at R_1, R_2 and R_3 in the Schiff base **10** has been investigated in the asymmetric addition to benzaldehyde, and the best optimized catalyst was the one with R_1 = Ph, R_2= *t*-Bu, R_3 = *t*-Bu or H in hexane (Scheme **3**). It gives the alkylated products high enantioselectivities (up to 96% ee). The effect of the *tert*-butyl group at the ortho position on the phenolic hydroxy group of the Schiff base catalyst is important. In the case of the use of 5 mol% of Schiff base without a *tert*-butyl group at the ortho position, the *S* enantiomer was obtained in 91% yield and 57% ee. While, with a *tert*-butyl group at the ortho position, the opposite enantiomer *R* was obtained in 94% yield and 96% ee (Scheme **3**). This zinc/Schiff base catalyst system is effective not only for aromatic aldehydes but also for aliphatic aldehydes.

They also examined the nonlinear effect in the zinc-Schiff base system (Fig. (**3**)). It can be ascertained that aggregation of the zinc species should participate in the catalytic cycle. But, the origin of the observed nonlinear effect in this reaction catalyzed by tridentate ligand was still unclear and under investigation.

They confirmed the reaction mechanism by ^{1}H NMR analysis, that, two of the ethyl groups in diethylzinc reacted with both hydroxy groups in Schiff base (phenolic and amino alcohol) resulting in the disappearance of the ethyl groups in diethylzinc. Therefore, the ethyl groups may add to aldehyde activated by the chiral zinc Schiff base as an ethyl transfer from diethylzinc.



Scheme 3. Effect of the *tert*-butyl group at the ortho position on the phenolic hydroxy group.

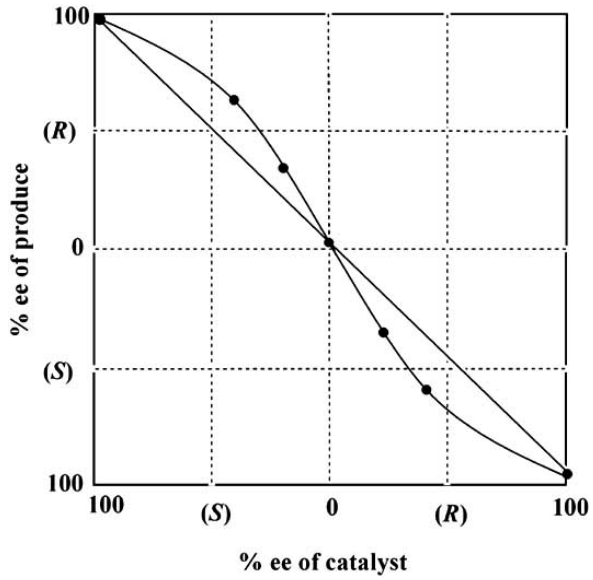


Fig. (3). The nonlinear effect in the catalytic enantioselective ethylation of benzaldehyde in the presence of catalyst **10** (R_1 = Ph, R_2= *t*-Bu). (Conditions: PhCHO/Et_2Zn/Schiff base = 1.0:2.0:0.01, 0° C, 24 h).

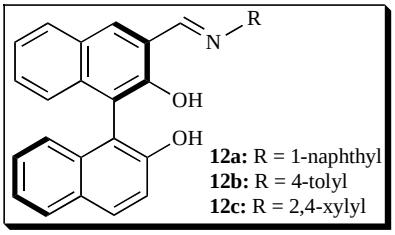
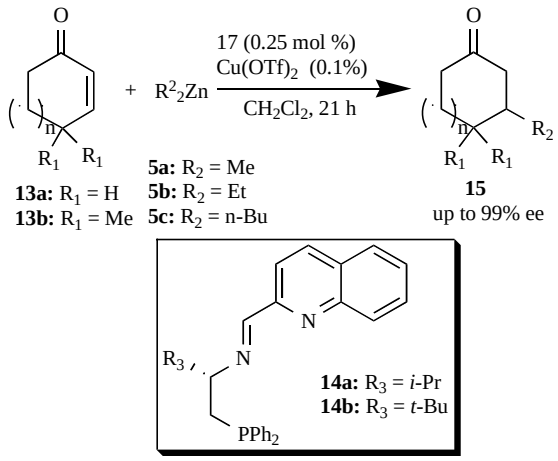


Fig. (4). The chiral 3-substituted BINOL Schiff base ligands **12a-c**.

In 2007, Li [22] has developed three new chiral 3-substituted BINOL Schiff base ligands **12a-c** (Fig. (**4**)) for the asymmetric diethylzinc addition to aldehydes in the presence of titanium tetraisopropoxide. The reaction provided optically active second alcohols in high yield and moderate enantioselectivity (67% ee).



Scheme 4. Enantioselective 1,4-addition of dialkylzinc to cyclic enones.

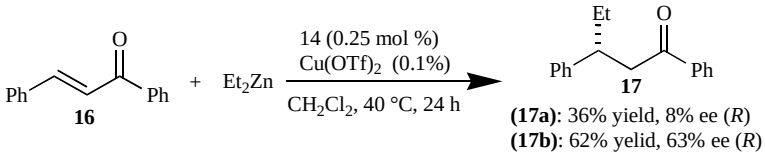
In 2008, Hayashi [23] found another novel *N*, *N*, *P*-tridentate ligands used in copper-catalyzed 1,4-addition of dialkylzincs to enones. Using 0.25 mol% of the *N*, *N*, *P*-tridentate ligand **14a, b** and 0.1 mol% of $Cu(OTf)_2$ enabled the enantioselective 1,4-addition of dialkylzincs to cyclic enones **13** to produce 1,4-adducts **15** in up to 99% ee at -40°C with **14a**, and up to 96% ee with **14b** (Scheme **4**).

The reaction of an acyclic enone and chalcone using 0.1 mol% of $Cu(OTf)_2$ and 0.25 mol% of *N*, *N*, *P*-ligands **14** gave the 1,4-adduct in 8% ee (36% yield) for **17a** and 63% ee (52% yield) for **17b**, as shown in Scheme **5**.

In 2008, Hoveyda [24] screened a series of chiral Schiff base ligands like **18** for catalytic asymmetric alkylation reactions of propargyl ketone with Et_2Zn. Up to 98% ee can be achieved in most cases, much better than the catalysts **19** and **20** (Fig. (**5**)), which were reported by his group in 2004 [25] and 2005 [26].

2.2. Hetero-Diels-Alder Reactions

The Hetero-Diels–Alder reaction (HDA) is a cycloaddition reaction of a conjugated diene with a double or triple bond (the dienophile) involving one or more heteroatom centers in one or



Scheme 5. Enantioselective 1,4-addition of dialkylzinc to acyclic enone and chalcone.

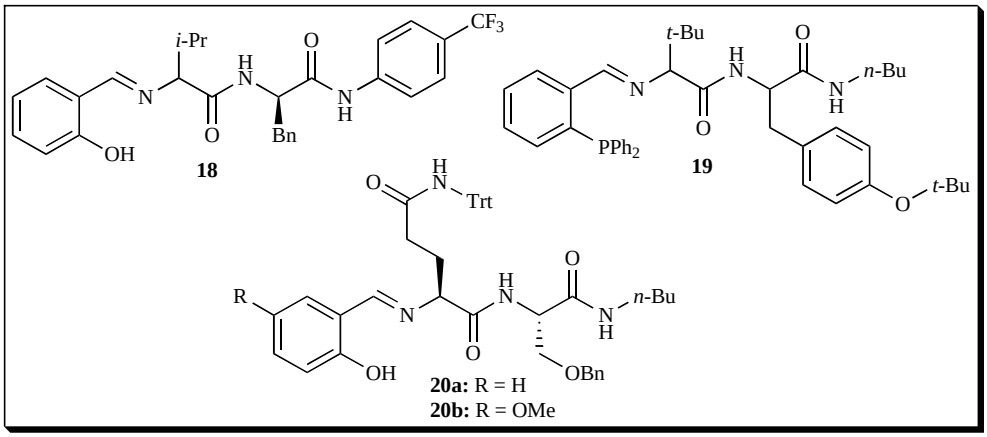
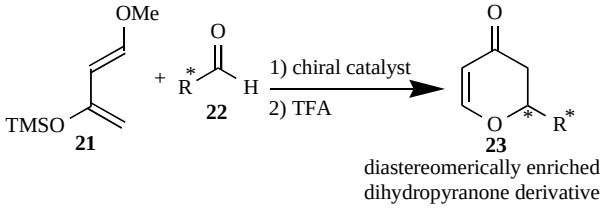


Fig. (5). Chiral Schiff base ligands reported by Hoveyda's group.

both substrates. It is one of the most important reactions in organic chemistry and can be used for the synthesis of six-membered heterocycles [27]. Great efforts have been put to control stereoselectivity in the Hetero-Diels-Alder reaction between Danishefsky's diene (**21**, 1-methoxy-3-[(trimethylsilyl)oxy]-1,3-butadiene) and aldehydes in the past few years. But most reports focused on the substrate-controlled diastereoselective reaction using chiral aldehydes **22** (Scheme **6**). Now the trend is to discover chiral catalysts that can catalyze enantioselective HDA reaction of either chiral or nonchiral aldehydes.



Scheme 6. Diastereoselective hetero-Diels-Alder reaction between Danishefsky's diene and chiral aldehydes.

In 1998 and 1999, Jacobsen [28, 29] has developed two catalyst systems for Hetero-Diels-Alder reactions. The (salen)Cr(III)-BF_4 complex **24** (Fig. (**6**)) [28] was found to be a reactive and on effective catalyst for asymmetric HDA reaction between **21** and chiral aldehydes **22** (Scheme **6**). Subsequently, the tridentate Schiff base-Cr(III) complexes **25a,b** [29] were identified as highly selective catalysts for enantioselective HDA reactions between less nucleophilic dienes and inactivated carbonyl compounds (Scheme **7**).

Being different from the reaction of electron-rich dienes such as Danishefsky's diene and electron-deficient dienophiles [30, 31], this new class of asymmetric HDA reaction would provide a direct route to enantiomerically enriched dihydropyran derivatives from simple achiral starting materials, setting up to three stereocenters in the cyclization and allowing ultimate access to tetrahydropyran derivatives with five defined stereocenters by elaboration of the resultant double bond.

Chiral Schiff bases **25a** and **25b** were testified to be good catalysts for HDA, which can also tolerate substrates like (2*Z*, 4*E*)-triethylsilyloxy-2,4-hexadiene **26** and different substituted aldehydes **27**. The product tetrahydropyranones **28** can be achieved with 95% de, up to 97% yield and 99% ee value (Scheme **8**).

Meng [32] has designed and synthesized a new type of dendritic 2-amino-2'-hydroxy-1,1'-binaphthyl (NOBIN)-derived Schiff base ligands **31a-c** (Fig. (**7**)) for the HDA reaction. Under optimized condition, the HDA reaction afforded the corresponding products in quantitative yields and excellent enantioselectivities (up to 97% ee).

In 2002, Jacobsen [33] tried to establish a catalyst system including chiral chromium-Schiff base complexes **24-25, 29-31** for the chiral-controlled diastereoselective HDA reactions (Scheme **6**). Such a strategy provides selective access to stereochemically elaborate dihydropyranone derivatives that are not readily accessible using substrate-controlled diastereoselective reactions or through simple enantioselective reactions of achiral substrates. It is the first successful example in the application of this approach.

The cycloaddition between diene **21** and lactaldehyde derivative and other chiral aldehydes was investigated in the model

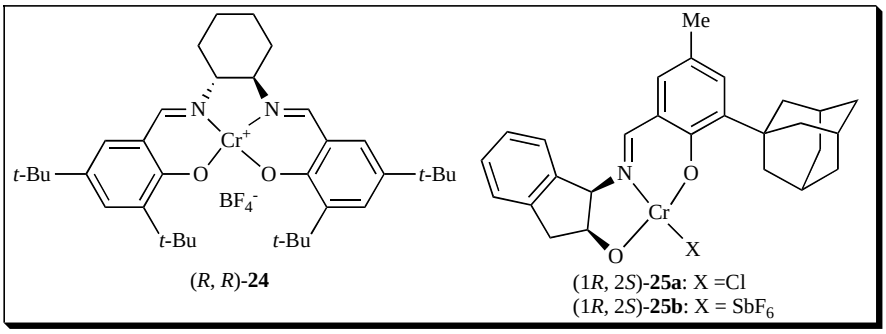
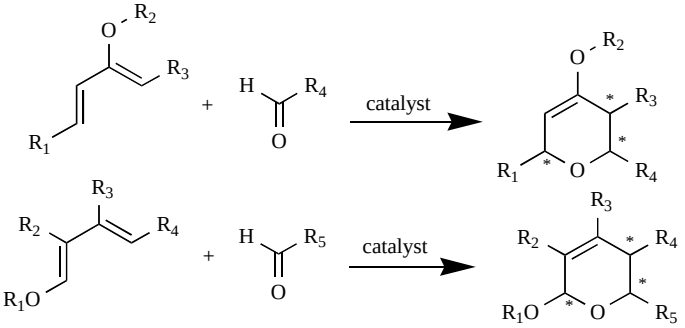
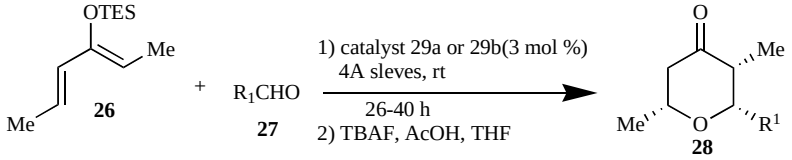


Fig. (6). Chiral Schiff base ligands reported by Jacobsen's group.



Scheme 7. Asymmetric HDA reactions between less nucleophilic dienes and unactivated carbonyl compounds.



Scheme 8. HDA reaction between substituted hexadienes **26** and aldehydes **27**.

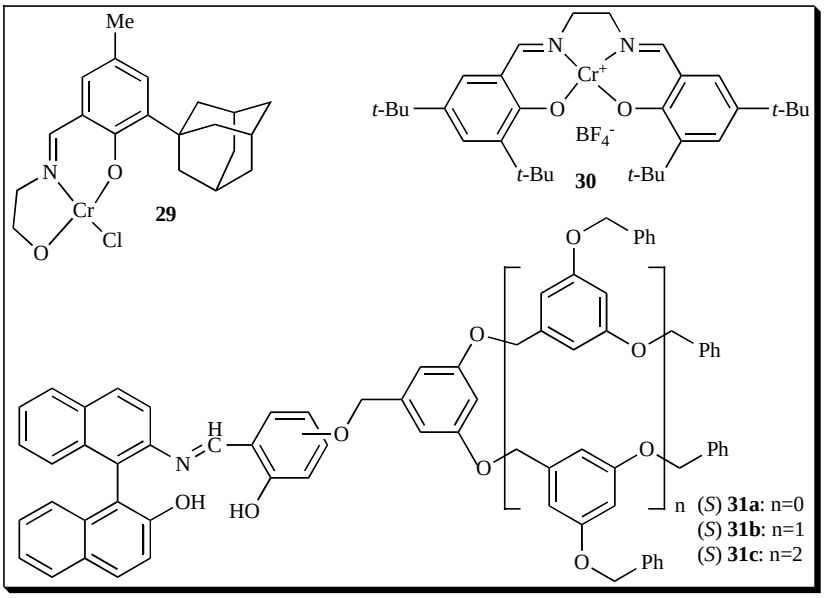


Fig. (7). Chiral Schiff base reported by Meng.

reaction (Scheme **6**). Catalysts (1*S*, 2*R*)-**25a,** (1*R*, 2*S*)-**25a** and **29** showed different activities to the substrates of hetero dienophile. Under the optimized conditions, a dihydropyranone product with diastereomeric ratio of 15:1, 97% yield and >99% ee could be obtained as the best result so far.

In addition, the (salen)Cr(III)-BF_4 catalyst **24** can improve the selectivities in cycloadditions between **21** and aldehyde **22d** or **22e** with better diastereomeric ratio 1:9.1 (Scheme **9**). In the presence of the achiral (salen)Cr(III)-BF_4 complex **29**, substrate **21** underwent cycloaddition with aldehyde (*R*)-**22e** on the Felkin face to provide **23e** with 1:5.6 dr. And with (*S*, *S*)-**24** reinforced the substrate bias, a high dr (up to 1:32) can be obtained.

When choosing the appropriate aldehyde and catalyst enantiomers in catalyst-controlled double diastereoselective HDA reactions between diene and chiral aldehydes, any of the four possible stereoisomers of the dihydropyranone products can be achieved.

2.3. Ene Reactions

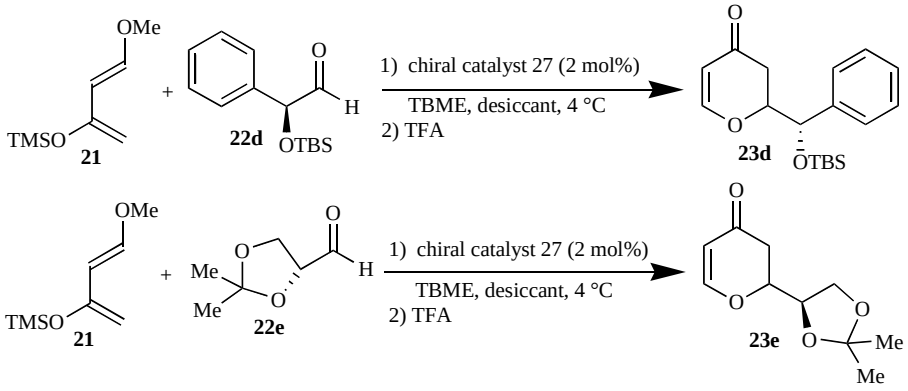
The Ene reaction is a valuable reaction particularly in the context of C-C bond forming process. There are many kinds of catalysts for this reaction, such as Lewis-acid catalyst [34], chiral palladium catalyst [35], and dicationic SEGPHOS-Pd complex [36].

In 2002, Jacobsen [37] described the highly selective Ene reaction between alkoxy- or silyloxyalkenes **33** and aromatic aldehydes **32** using tridentate Schiff base Cr(III) complex **34** (Scheme **10**).

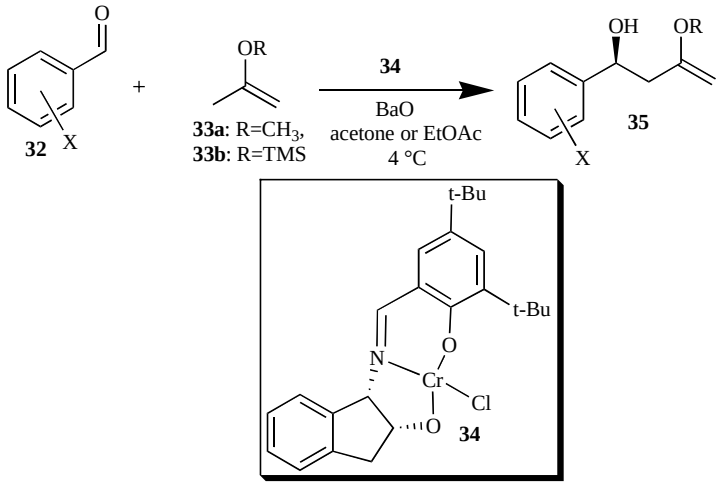
A variety of substituted benzaldehyde derivatives were examined with 2-methoxypropene at 4°C with 5-7.5 mol% catalyst. Under the optimized conditions, up to 97% yield and 96% ee were obtained. The products of *β*-hydroxyenol ether **35** formed in these reactions are valuable chiral building blocks, useful as nucleophilic partners in subsequent reactions or as direct precursors to *β*-hydroxyketone and *β*-hydroxyester derivatives.

A crystal structure of active catalyst **36** in the reaction was shown in Fig. (**8**). It displays slightly lower enantioselectivity than **34**, but can provide valuable information for mechanistic analysis of the Ene reaction. The X-ray data reveal a dimeric structure bearing two ligands and two Cr(III) centers bridged through the indane-bound oxygens. Each molecule of chromium is also bound to an axially positioned chloride ion and water molecule. They proposed that one molecule of bound water can be removed from the catalyst dimer by pre-stirring, thus providing an open coordination site for binding of aldehyde.

In 2007, Rawal [38] reported the enantioselective carbonyl-ene reactions of various 1,1-disubstituted and trisubstituted alkenes **38** with ethyl glyoxylate **37**. The reactions are catalyzed by a new



Scheme 9. Diastereoselective hetero-Diels-Alder reaction catalyzed by (salen)Cr(III) catalysts.



Scheme 10. Ene reaction of alkoxy- or silylopropene with aldehydes.

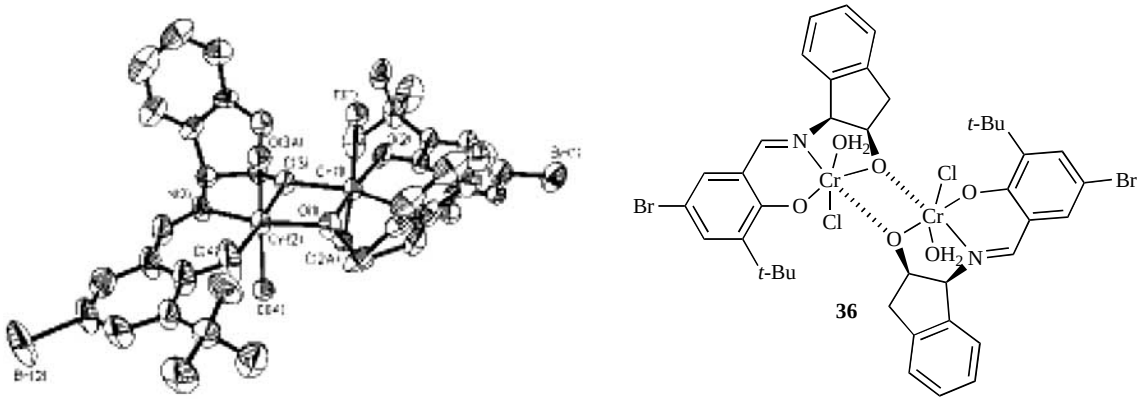


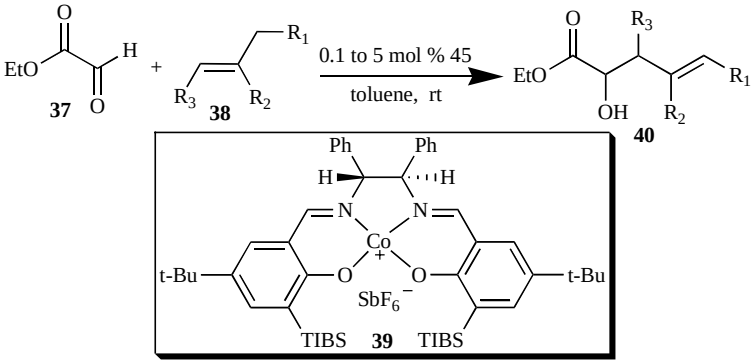
Fig. (8). X-ray crystal structure of catalyst **36**.

cobalt-salen complex **39**, in which bulky triisobutylsilyl (TIBS) substituents occupy the positions ortho to the phenolic oxygens. This complex catalyzed the reactions with loadings as low as 0.1 mol% at room temperature. The chiral, homoallylic alcohol products were gained in excellent yields (99%), enantioselectivities (98%), and diastereoselectivities (Scheme **11**). The *t*-butyl salen ligand used in the cobalt complex is commercially available, so there is a large potential for this efficient catalyst in asymmetric Ene reaction on an industrial level.

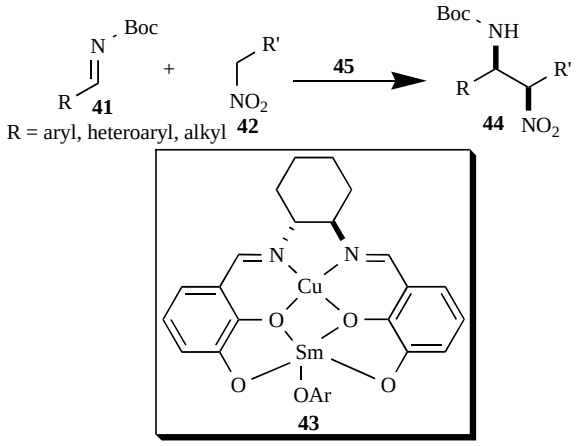
2.4. Mannich Reaction

The Mannich reaction is aminomethylation of CH-acidic substrates. It is the condensation reaction of a CH-acidic compound with aldehyde and amine, and the products of this reaction are called Mannich bases [39]. Catalytic asymmetric direct Mannich-type reaction is an efficient and straightforward method for producing chiral *α*, *β*-diamino acids [40] which are usually key structural components in many biologically active compounds.

The nitro-Mannich (aza-Henry) reaction provides synthetically versatile *β*-nitroamines that can be further converted to 1, 2-diamines and *γ*-aminocarbonyl compounds. Tremendous efforts have been devoted to develop catalytic enantioselective variants over the past decades. In 2007, Shibasaki [40] reported to have used a heterobimetallic Cu-Sm-Schiff base catalyst **43** to realize a *syn*-selective nitro-Mannich reaction (Scheme **12**). They found that both Cu and Sm metals were essential to realize high *syn*-selectivity. When the ratio of Cu/Sm/ligand **43** was 1:1:1, they got the best result with 96% yield and 80% ee. The achiral additives, 4-*t*-Bu-phenol can further improve the enantioselectivity. Under the



Scheme 11. Enantioselective carbonyl-Ene reactions catalyzed by Salen complex **39**.



Scheme 12. *Syn*-selective catalytic asymmetric nitro-Mannich reactions.

optimized conditions, with all kinds of *N*-Boc imines, an up to 98% ee and > 20:1 dr could be obtained.

The *β*-nitroamine product **44a** (R = Ph, R'= Me) can be successfully converted to *syn*-1,2-diamine **45** in 99% yield without epimerization using $NaBH_4$ and $NiCl_2$ (Scheme **13**).

In 2008, they [41] developed a new homodinuclear M_2-Schiff base **49** complex that promoted Mannich-type reactions of *N*-Boc imines **47** and *R*-substituted nitroacetates **48** to afford *α*-tetrasubstituted *anti-α, β*-diamino acid surrogates **50** in high ee (up to >99% ee when M = Ni) (Scheme **14**). The present bimetallic Ni_2-**49** complex was bench-stable and storable under air at room temperature for at least three months without loss of activity.

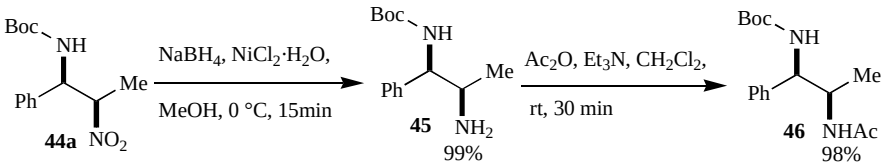
The utility of the *α*-tetrasubstituted *anti-α, β*-diamino acid surrogates **50** is shown in Scheme **15**. The corresponding 1,2-diamine could be obtained in 94% yield.

The use of Ni_2-**49** complex in Mannich-type reactions of other donors, such as malonates and *β*-keto ester is shown in Scheme **16**. High diastereo- and enantioselectivities (91-99% ee) were achieved at room temperature using 2.5 mol% of Ni_2-**49** in both cases.

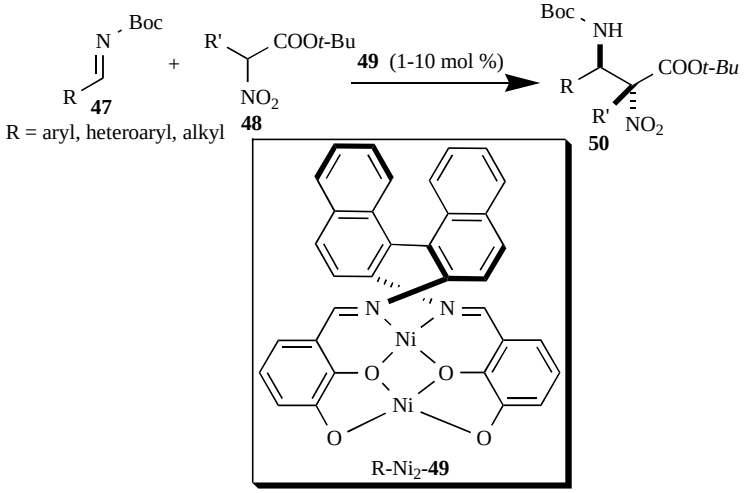
Control experiments indicated that neither a mononuclear Ni-**49**-H_2 complex nor Ni-salen complexes **56** with one single metal center were effective for the reaction in Scheme **14** (when R = Ph, R' = Me), resulting in a poor reactivity, diastereoselectivity and enantioselectivity. The cooperative functions of the two Ni metal centers in the Ni_2-**49** complex (Fig. (**9**)) is important for achieving high stereoselectivity as well as reactivity. But the mechanism to elucidate the precise role of the two Ni centers has not been known yet.

Asymmetric Mannich-type reactions of other substrates catalyzed by homodinuclear Ni_2-Schiff base complex **49** [42] were reported in 2008 (Scheme **17**). When promoted at 0°C, *β*-amino phosphonates **58** was prepared in 90% yield, 20:1 dr, and 99% ee. This complex also afforded good reactivity and enantioselectivity in other aryl and heteroaryl imines.

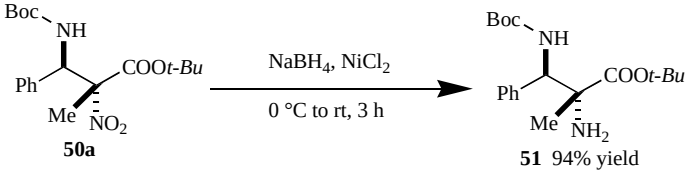
The result of the control experiments was just the same as in another article [41], two Ni metal centers in the complex Ni_2-**49** were both very important to the asymmetric reactions.



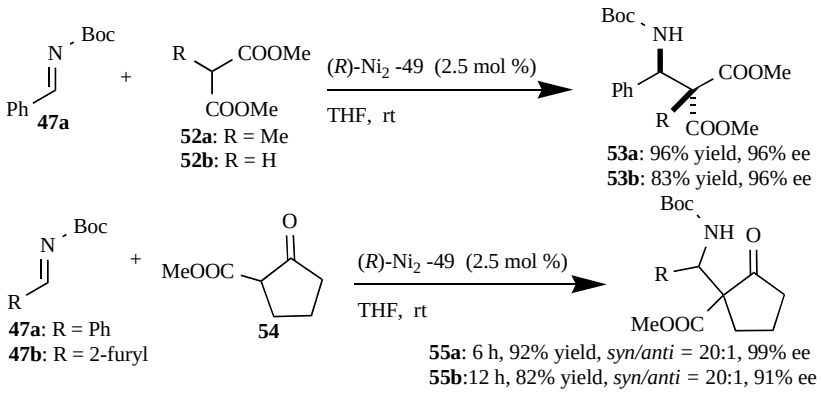
Scheme 13. Conversion of *β*-nitroamine to *syn*-1,2-Diamine.



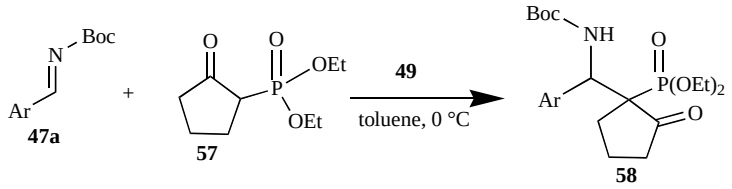
Scheme 14. Catalytic asymmetric Mannich-type reaction of nitroacetates **48** and *N*-Boc imines **47**.



Scheme 15. The utility of the *α*-tetrasubstituted *anti-α, β*-diamino acid.



Scheme 16. Ni_2-**49** complex is used in the Mannich-type reactions of malonates and *β*-keto ester.



Scheme 17. Mannich-Type Reaction of *N*-Boc Imines **47a** with *β*-Keto Phosphonates **57**.

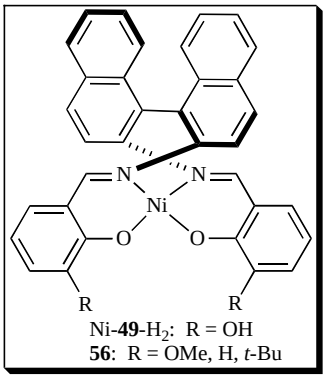


Fig. (9). The structure of Ni-**49**-H_2 complex and Ni-salen complexes **56.**

The postulated transition state model to afford *anti*-periplanar as a major adduct is shown in Fig. (**10**). They speculate that the Ni-aryloxide moiety in the Ni_2-**49** complex may function as a Brønsted base to generate a Ni-enolate from *β*-keto phosphonate **57**, which would react with *N*-Boc imines **47a** that are nicely fixed by the other Lewis acidic Ni metal center.

2.5. Enantioselective Addition of Terminal Alkynes to Aldehydes or Ketones

The asymmetric addition of terminal alkynes to carbonyl compounds was an important class of organic reactions, in which a new C-C bond was formed (Scheme **18**). But it is still a challenge to form optical tertiary propargylic alcohols by asymmetric alkynylation of ketones.

In 2003, Cozzi [43] first reported that a Zn/Schiff base complex **62 (**Fig. (**11**)), can promote alkylation of ketones with moderate enantioselectivities (typically 40-80% ee).

Then in 2006, Wang [44] reported a low catalyst loading, highly enantioselective addition of phenylacetylene to aromatic ketones catalyzed by Schiff-base-**63a,b** (Fig. (**11**)). When the loading of catalyst **63a** was 1 mol%, an ee value of up to 95% was obtained. High ee value of 85% was still achieved even in the loading of 0.1 mol%. Because of the reduced propensity of ketones to coordinate with Lewis acids, this system does not need to add any other stronger Lewis acid except zinc (**63**/Zn 0.01:1 ratio), and the alkynylzinc must be prepared in advance.

In 2007, You [45] prepared some novel *C*2-symmetric bis-Schiff base amino alcohols **64-65** (Fig. (**12**)), the structure of which is similar to Salens', for the enantioselective addition of phenylacetylene to aromatic aldehydes. Butyl lithium was chosen as

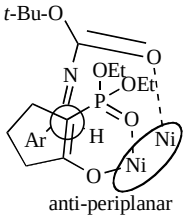
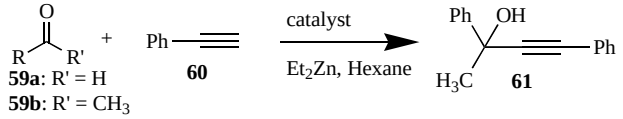


Fig. (10). Transition state model of direct Mannich-type reaction using Ni_2-**49** as the catalyst.



Scheme 18. Enantioselective addition of phenylacetylene to aldehydes or ketones.

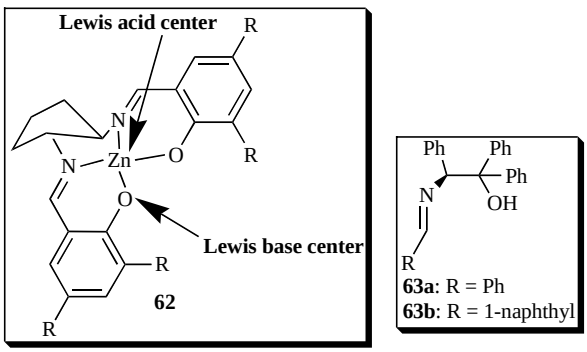


Fig. (11). The structure of Zn/Schiff base complex **62** and chiral Schiff bases **63a** and **63b**.

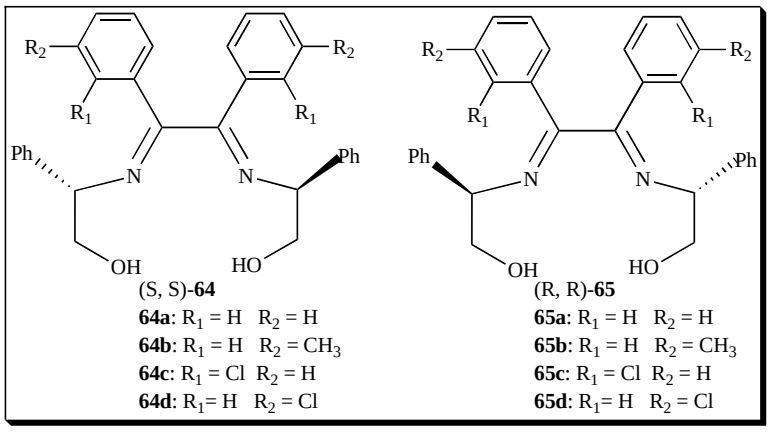


Fig. (12). *C*2-Symmetric bis-Schiff base amino alcohols **64** and **65**.

the base to generate nucleophilic reagent in the addition. As a result, only moderate enantioselectivity was observed, and the configuration of the product was influenced by the chirality of the ligand. Because of the stereospecific blockade, the ortho-substituted ligands provide better ee value. The ligand **64c** was the most effective catalyst in this reaction under the optimized condition. Various substituted benzaldehydes were used as substrates for the asymmetric addition under this reaction condition with **64c** as catalyst. The change of substituents of the benzene ring is proved to have an impact on the catalytic center and thus can provide different enantioselectivity in this reaction.

The possible transition state model for the alkynyl lithium addition using *C*2-symmetric bis-Schiff base amino alcohols **64c** and **65c** was shown in Fig. (**13**). It is helpful to explain the influence of the stereo center.

In 2007, Abdi [46] reported a recyclable polymeric Zn(salen) complex **66** (Fig. (**14**)) for the enantioselective phenylacetylene addition to aldehydes and ketones to produce corresponding chiral secondary propargylic alcohols with up to 96% yield and 72% ee. Tertiary propargylic alcohols can also be obtained in 79% yields and 68% ee at room temperature. Moreover, the polymeric complex kept the enantioselectivity after being reused four times.

2.6. The Asymmetric Strecker Reaction

The Strecker reaction was a reaction for preparing α-amino acids from aldehydes or ketones. The main purpose of the asymmetric Strecker reaction is to synthesize the enantiomerically enriched amino acids. It is also an important reaction to synthesize α-amino acids on an industrial scale.

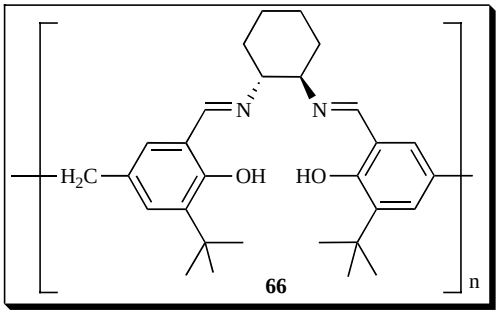


Fig. (14). The structure of recyclable polymeric Zn(salen) complex **66**.

In 1998, Jacobsen [47] reported to use the combinatorial chemistry approach to identify and optimize Schiff base catalysts for the asymmetric Strecker reaction (Scheme **19**).

They tried binaphthyl-based ligands, *C*2 symmetric phosphines, salen ligands, bisoxazolines, and tartrate- and *cinchona* alkaloid-derived compounds [48, 49], which are all the best known and are most effective chiral ligands. But only the tridentate Schiff base complexes were suitable to solid phase synthesis.

These catalyst systems **69** are typically comprised by three parts, a chiral amino alcohol, a salicylaldehyde derivative, and a metal (Fig. (**15**)). They use a diamine to replace the amino alcohol and the second nitrogen on the chiral backbone serving as the site for attachment to the solid support.

They founded three libraries to screen the best catalyst for this reaction. In the first library they selected different metal ions for it.

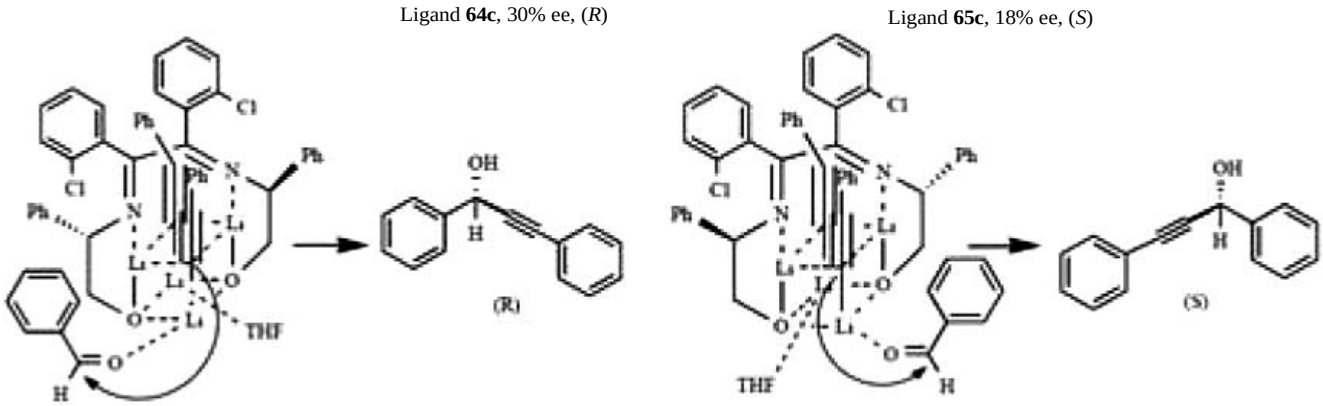
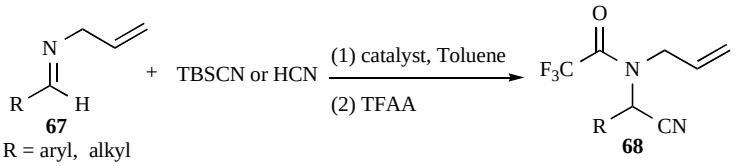


Fig. (13). Facial selectivity of phenylacetylene addition to benzaldehyde with ligand **64c** and **65c**.



Scheme 19. Asymmetric Strecker reaction.

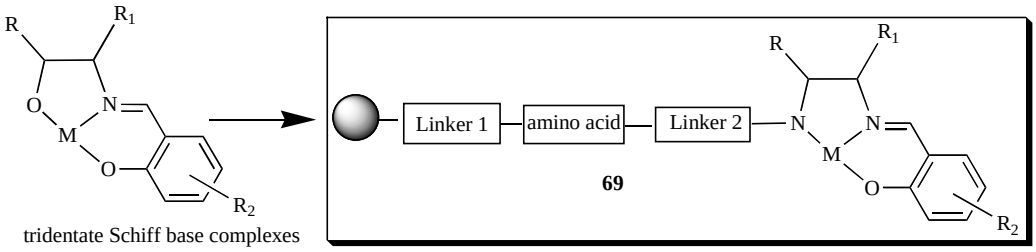


Fig. (15). Concept for the solid-phase synthesis of tridentate Schiff base complexes.

But the ligand in absence of any added metal ion has shown the best result (59% conv. and 19% ee). In library 2 the amino acid components have been selected, the (*R*, *R*)-diamine-derived catalysts coupled with *L*-leucine with 3-*tert*-butyl substituted on the salicylaldehyde were found to give the best result (32% ee). Further research in the third library showed that the *t*-Leu-CH-OMe **70a** (OMe denoting 3-*tert*-butyl-5-methoxysalicylaldehyde, Fig. (**16**)) afford the highest enantioselectivity (80% ee). Moreover, the polymer-supported catalysts **70a** could be reisolated readily by simple filtration and recycled repeatedly.

When the solution-phase catalyst **70b,** similar to **70a** was synthesized independently and tested in the asymmetric Strecker reaction shown in Scheme **19**, they found that **70b** catalyzed the formation of the Strecker adduct in 78% isolated yield and 91% ee at -78°C. And, for the first time, even the aliphatic imine derivatives have a good enantioselectivity (up to 80% ee). This study demonstrates that parallel synthetic libraries can afford the effective chiral Schiff bases catalysts for the Strecker reaction after further structure modifications.

In 2000, they [50] constructed a new optimization library of 70 compounds using seven amino acids with large α-substituents and ten new salicylaldehyde derivatives. Each compound was evaluated for enantioselectivity in the asymmetric Strecker reaction of aliphatic imine **67**. It was shown that **71b** (Fig. (**17**)) catalyzed the Strecker reaction of **67** with 75% isolated yield and 95% ee at -78°C. Benzaldimine **67** also underwent an improved enantioselectivity in hydrocyanation compared with other catalysts (95% ee with catalyst **71b** vs. 91% ee with **71a**).

In addition, the scope of the asymmetric Strecker reaction catalyzed by **71b** was remarkably broad. Both aryl imine substrates and aliphatic imine substrates with large groups afforded the high ee values (up to 97% ee).

Hydrolyzing the amino nitrile product of the Strecker reaction of **68a** required fairly harsh conditions (concentrated acid, >90°C) and resulted in considerable decomposition. To solve this problem, they protected the amino nitrile as the formamide, and 84% overall yield could be achieved after three steps of conversion (Scheme **20**).

Jacobsen [51] also developed a good method for enantioselective addition of HCN to ketoimines for the first time using the Schiff base catalyst **71b** (Scheme **21**). Essentially quantitative isolated yield and enantioselectivity of up to 95% ee were obtained. Furthermore, some of the Strecker adducts could be recrystallized in high recovery, yielding optically pure product. Conversion of the α-aminonitrile adducts to the corresponding α-quaternary α-amino acids was performed in high yield by a formylation/hydrolysis sequence. Afterwards, they improved the synthesis of **71b** in 5 steps from commercially available Boc-*tert*-leucine [52] in 80% overall yield. This practical procedure makes it possible to synthesize **71b** on a commercial scale.

In 2002, the same team [53] reported the structural and mechanistic studies on the Schiff base catalysts in the hydrocyanation of imines and laid the foundation for rational catalyst optimization.

The ground state conformation was determined through ROESY and NOESY NMR experiments in *d*8-THF and *d*8-dioxane solutions of **77** and found to be in full accord with the calculated energy-minimized geometry (Fig. (**18**)).

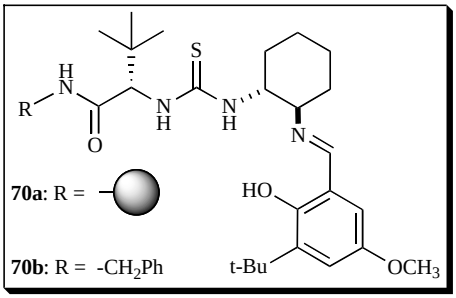


Fig. (16). The structure of chiral Schiff base **70a** and **70b**.

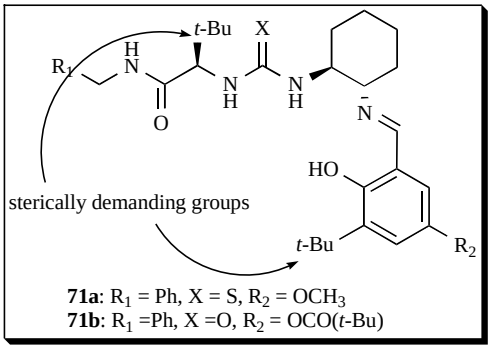
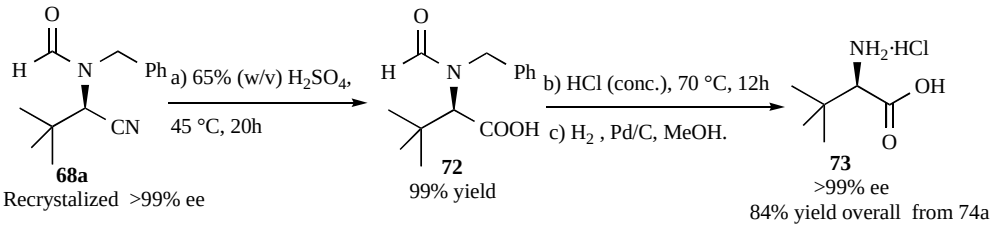
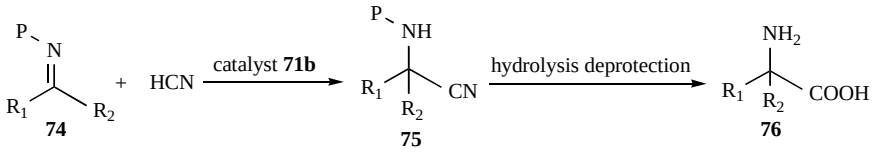


Fig. (17). The structure of chiral Schiff base **71a** and **71b**.



Scheme 20. Hydrolysis and deformylation of **68a**.



Scheme 21. Enantioselective addition of HCN to ketoimines and the conversion of the adducts.

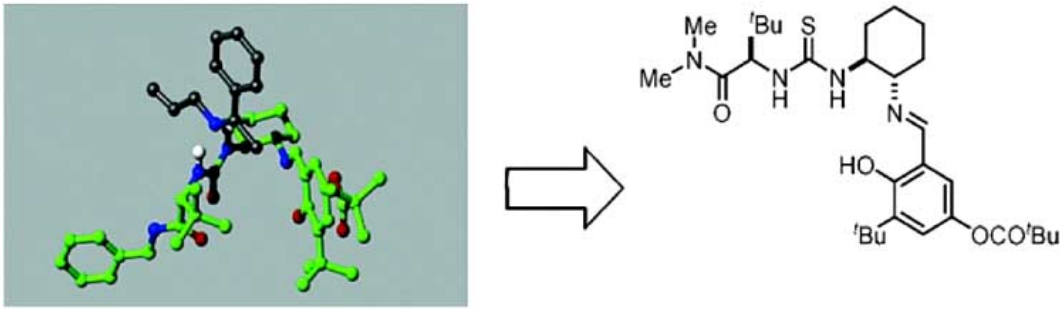


Fig. (18). The structure of catalyst **77**.

They also carried out kinetics research of the hydrocyanation of a model substrate (*N*-allyl-4-methoxybenzaldimine) to ascertain the precise role of **77** in this reaction. The rate studies showed the reversible formation of an imine-catalyst complex. It may form a hydrogen bond between the imine nitrogen and an acidic proton of the catalyst, which was proved to be the urea hydrogen. The data also provided the evidence that Strecker reactions using **77** involve binding of the imine substrate as the *Z*-isomer.

Based on the transition-state studies, several possible hypotheses about this reaction were set up to improve the enantioselectivity. A series of derivatives of **77** was prepared and tested as catalysts in the asymmetric Strecker reaction. According to the mechanism-driven optimization exercise, up to 99.3% ee value can be achieved with the optimized catalyst **78** (Fig. (**19**)).

In 2001, several different chiral Schiff base peptide ligands [54] were tested in the asymmetric Strecker reaction, and the conversion and enantioselectivities of Ti-catalyzed addition of cyanide to imines were measured (Scheme **22**). The ligand **80** got the best result with 99% ee and 85% conversion.

Molecular model involving imine **79** and Schiff base **80** suggested that association of substrate to one face of the distorted octahedral Ti-Schiff base complex is energetically more favorable (top *vs*. bottom face in Fig. (**20**)). It also suggested that chiral Schiff base peptide ligands can serve as bifunctional catalysts to deliver appreciable reactivity and high enantioselectivity.

There was a linear correlation between catalyst and enantioselectivity of the product (Fig. (**21**)). It is an evidence to suggest that the turnover-limiting step involves a highly ordered transition state. The activation parameters were measured for the asymmetric Ti-catalyzed cyanide addition to **79** through k_{obs} values measured at 5 °C intervals between -15 and +20°C. Calculations from an Eyring plot give $\triangle H^{\#}$= 8.98±1.3 kcal mol^{-1} and $\Delta S^{\#}$= -45.6±4.1 cal K^{-1} mol^{-1}.

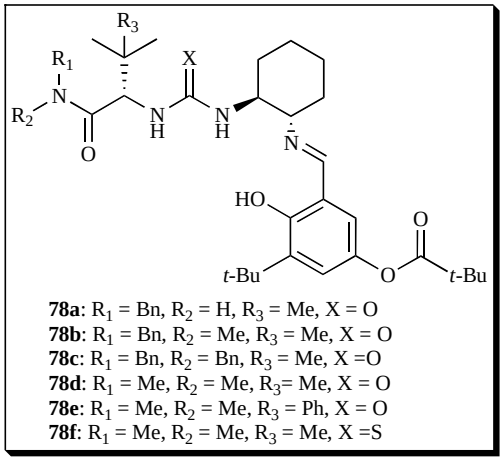
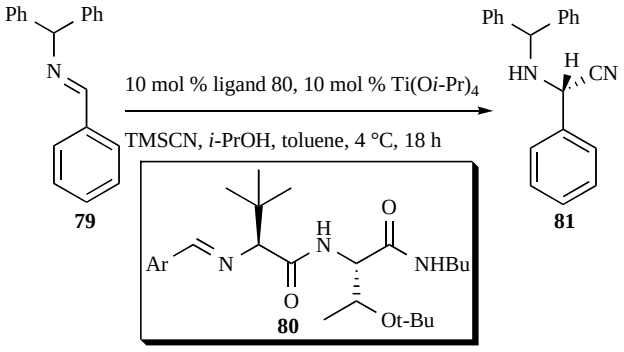


Fig. (19). The structure of chiral Schiff bases **78**.



Scheme 22. Addition of cyanide to imines catalyzed by Ti- Schiff base peptide complex.

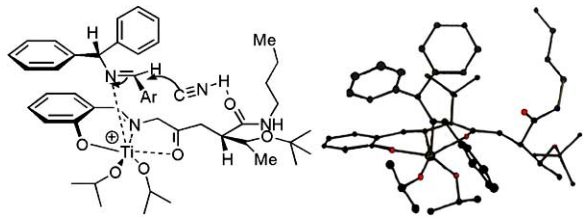


Fig. (20). Molecular model involving imine **79** and Schiff base **80**.

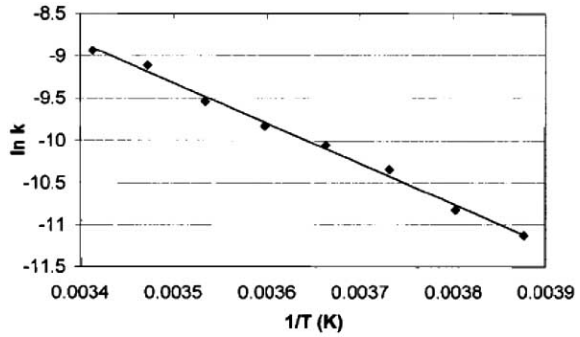


Fig. (21). Eyring plot for Ti-catalyzed cyanide addition to imine **79**.

Although the mechanistic hypotheses above were consistent with numerous features of the asymmetric Ti-catalyzed cyanide additions, they failed to explain the more subtle attributes of this class of transformations. It involves variations in the Schiff base moiety of the optimal chiral ligand as a function of the identity of different substrates.

2.7. Asymmetric Addition of Trimethylsilylcyanide to Aldehydes

The optically active cyanohydrins are versatile reagents in organic synthesis and good precursors to some important medications [55, 56], since the chiral cyanohydrins or cyanohydrin trimethylsilyl ethers can be readily converted to α-hydroxycarboxylic acids [57], α-hydroxyaldehydes [58], α-hydroxyketones [59], β-amino alcohols [60], and α-amino acid derivatives [61]. They can be mainly synthesized *via* asymmetric trimethylsilylcyanation of aldehydes catalyzed by chiral metal complexes, such as the complexes of titanium, magnesium, zinc, and lanthanum [62-64], or a chiral Lewis acid catalysts (Scheme **23**) [65].

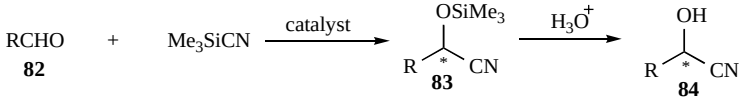
In 1999, Che [66] reported the titanium and ruthenium binaphthyl Schiff base complexes as catalysts for asymmetric trimethylsilylcyanation of aldehydes. They described an extensive study on the reaction as shown in Scheme **23** by using a series of Schiff base **85**-**86** (Fig. (**22**))**,** which are the binaphthyl derivatives of 2, 2'-bis(3-R_1-5-R_2-2-hydroxybenzylideneamino)-1,1'-binaphthyl. Excellent enantioselectivity (up to 96% ee) could be obtained by introducing bulky electron donating substituents on **85** (R_1 = R_2 = *t*-Bu). In addition, they used a ruthenium complex [Ru(II)(**85**-2H)(NO)Cl] in this reaction for the first time. It is also the first isolated ruthenium binaphthyl Schiff base complex. But the enantioselectivity using this new catalyst wasn't very good (43% ee, 57% yield).

Also in 1999, Belokon [67] discovered a series of titanium complexes **87** (Fig. (**23**)) derived from chiral salen ligand are highly active precatalysts for the asymmetric addition of trimethylsiyl cyanide to aldehydes and ketones (Scheme **23**). These precatalysts are easy to be prepared and be stable, and it made the reaction carry out in less than one hour at room temperature, with a low catalyst loading (substrate:catalyst = 1,000:1). The enantioselctivity of the cyanohydrin silyl ethers prepared in this way are 75-92% ee for products derived from aromatic aldehydes, 50% ee for aliphatic aldehydes, and 32-72% ee for ketones.

In 2000, Belokon [68] reported a mechanistic hypothesis according to the spectroscopic studies. The reaction cycle was shown in Scheme **24**. The key intermediate, binuclear complex **90** contains a dicyanide complex **88** and a mononuclear benzaldehyde adduct **89**. Intramolecular transfer of cyanide within complex **90** generates a complex **91** containing a titanium bound cyanohydrin. It would give the product and dinuclear dicyanide complex **92**. Complex **90** could be regenerated by displacement of one of the weak bound cyanide ligand of complex **92** by benzaldehyde. The results of the kinetics studies are consistent with the proposed catalytic cycle.

Kinetics experiments were carried out by monitoring the decrease in absorption (at 246 nm) as the benzaldehyde was consumed (Fig. (**24**)). The results indicate that the catalyst is a dinuclear complex in equilibrium with catalytically inactive mononuclear species.

When they investigated the transition state of the reaction between the aldehyde and trimethylsilyl cyanide catalyzed by complexes **87** (Fig. (**25**)), they found that the *re*-face of the aldehyde is exposed to intramolecular attack by the coordinated



Scheme 23. Asymmetric addition of trimethylsilylcyanide to aldehydes.

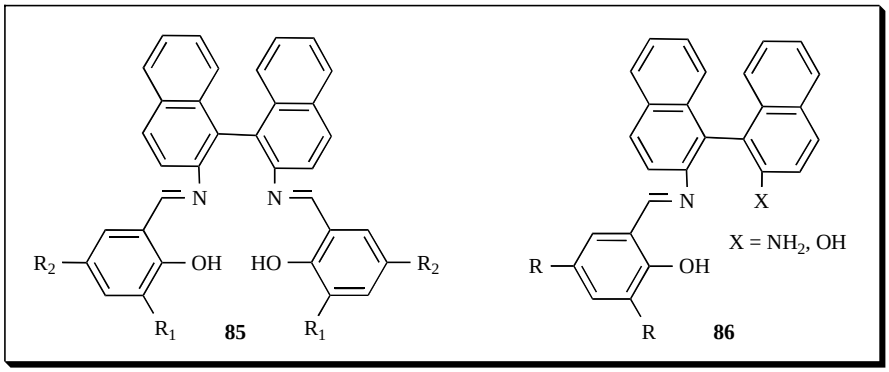


Fig. (22). The structure of chiral Schiff bases **85** and **86**.

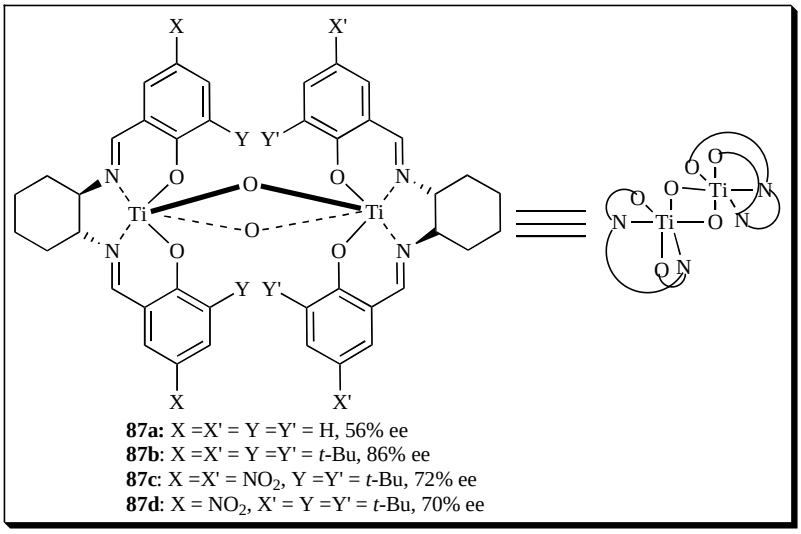
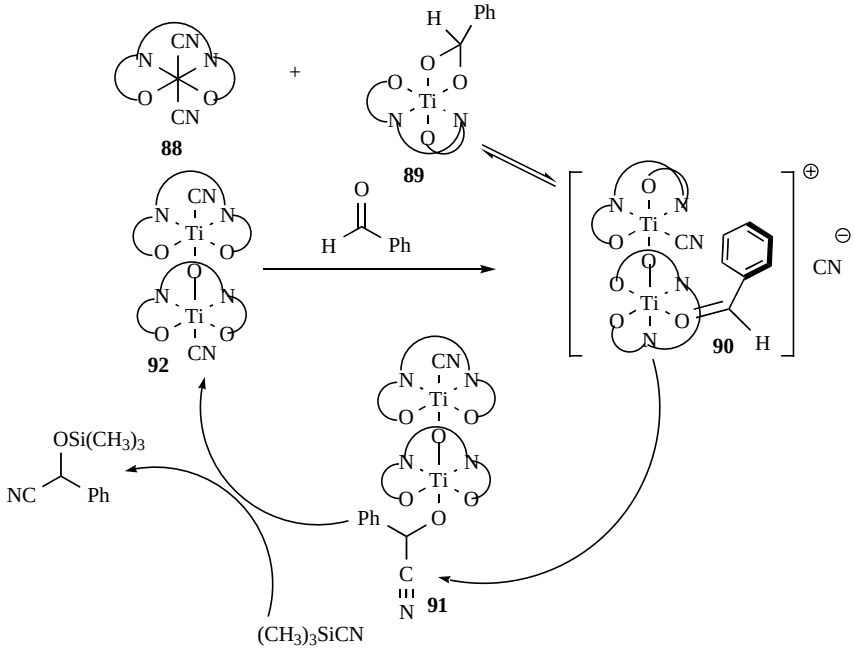


Fig. (23). The structure of chiral catalysts **87a-d**.



Scheme 24. The catalytic cycle of the asymmetric addition of trimethylsilyl cyanide to aldehydes.

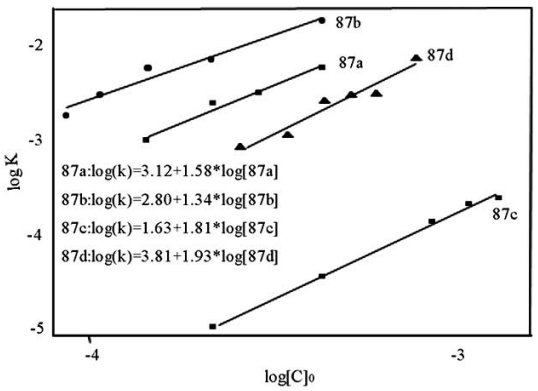


Fig. (24). Plots of log *k* versus log[C] for precatalysts **87a-d**.

cyanide, leading to the (*S*)-enantiomer of the cyanohydrin trimethylsilyl ether.

Walsh [69] has reported that, a titanium tetraisopropoxide, tridentate Schiff base ligand **88** was utilized in the asymmetric addition of trimethylsilylcyanide to benzaldehyde, which gave the cyanohydrins in 85% ee (Scheme **25**). They also found that the ligands derived from salicylaldehydes with bulky substituent in the 3-position can perform well to excellent enantioselectivity in the asymmetric addition reaction. However, with groups smaller than tert-butyl in the 3-position, a good amount (up to 73%) of the catalytically inactive L_2*Ti species are formed, resulting in large drop in the ee of the cyanohydrin. This study is interesting and valuable, because it gives a good explanation for the influence of the structure of ligands on the reactivity and enantioselectivity of the catalysts in this asymmetric C-C bond forming reaction.

Garcia [70] reported that single-wall carbon nanotube (SWNT) can be used as support for the preparation of a styryl functionalized vanadyl Schiff base catalyst **89**. They expanded the asymmetric version of the cyanosilylation using a chiral VOsalen derived from (1*R*, 2*R*)-(-)-cyclohexanediamine and a 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde instead of achiral VOsalen@SWNT (Fig.

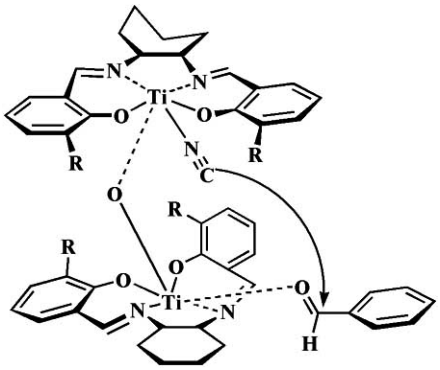


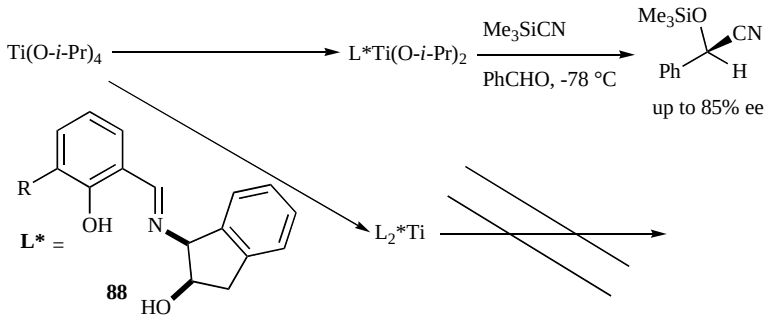
Fig. (25). The transition state of the reaction between aldehyde and trimethylsilyl cyanide catalyzed by complexes **87**.

(**26**)), thus obtaining 66% ee. Although the enantiomeric excess was lower than those reported for related homogeneous VOsalen complexes in solution (around 90% ee), they are encouraging and higher than those obtained for other supported metal salen complexes on inorganic oxides [71, 72].

2.8. Enantioselective Alkylations of Indoles

Indoles are ubiquitous in nature and utilized as building blocks for alkaloid synthesis, as well as development of potential therapeutic agents. It is an expedient route for the preparation of functionalized indoles *via* alkylation reactions catalyzed by Lewis acid-based catalysis, organocatalysis, late-transition metal catalysis and so on [73-75].

In 2007, Bandini [76] reported an update of the development of catalytic enantioselective alkylations of indoles using organocatalysts or organometallic catalysts. It focused on highly stereocontrolled Michael addition approaches, addition to carbonyl units, direct aromatic C-H activation/alkylation, and allylic alkylation. Several Schiff base catalysts were screened, as shown in Scheme **26**. For example, with **94** as catalyst an up to 99% ee can be obtained, and with **95** the enantiomeric excess is up to 98%.



Scheme 25. The asymmetric cyanohydration of benzaldehyde.

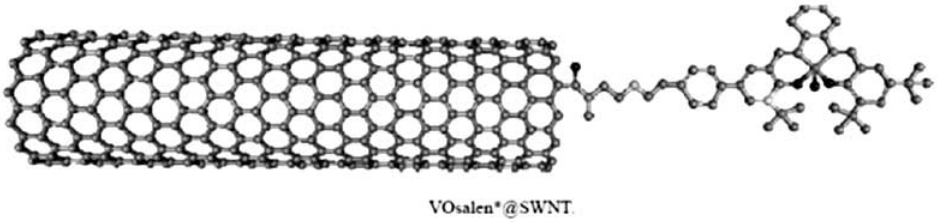
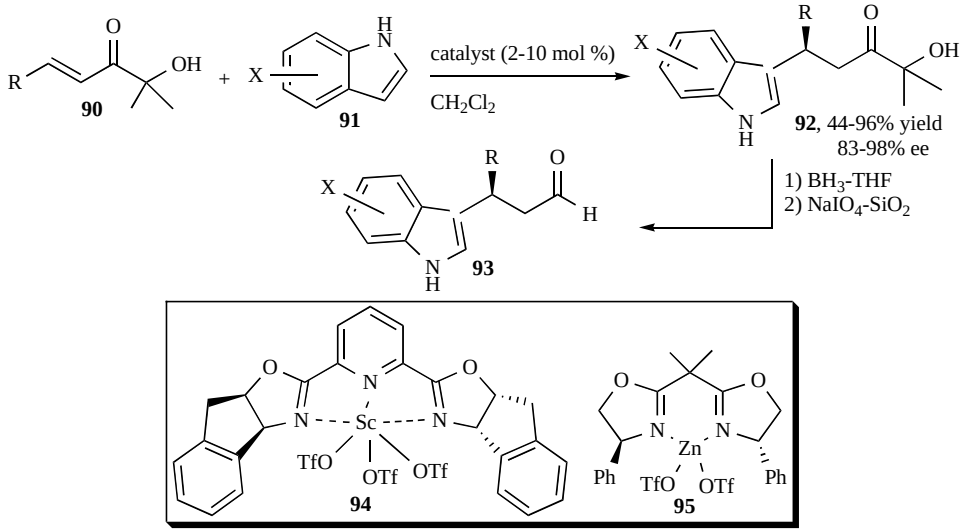
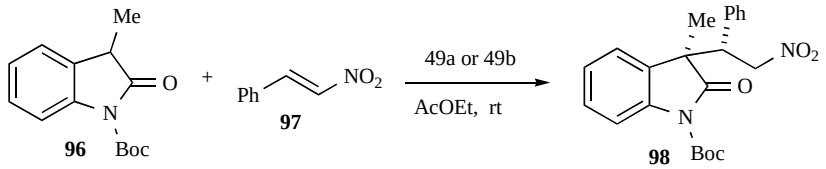


Fig. (26). The model of the chiral catalyst VOsalen@SWNT **89**.



Scheme 26. Catalytic enantioselective alkylations of indoles.



Scheme 27. Catalytic asymmetric 1, 4-additions of oxindoles **96** to nitroalkenes **97**.

In 2009, a homodinuclear $Mn(III)_2$-Schiff base complex **49** discovered by Shibasaki [77] has also been tested in the asymmetric Mannich reaction of oxindoles to nitroalkenes (Scheme **27**) [41]. Oxindoles with *β*-amino functionality are attractive and valuable synthetic targets. Catalytic asymmetric 1,4-addition of 3-substituted oxindoles **96** to nitroalkenes **97** provide a straightforward access to *β*-aminooxindoles **98** with vicinal quaternary/tertiary stereocenters. They got an up to 99% yield and 95% ee finally.

2.9. Direct Catalytic Asymmetric Aldol Reaction

The direct catalytic asymmetric aldol reaction is a powerful and atom-economical method for synthesizing chiral *β*-hydroxy carbonyl compounds.

In 2009, Shibasaki [78] reported direct catalytic asymmetric aldol reaction of *β*-keto esters with formaldehyde promoted by a dinuclear M-Schiff base complex **49** (M = Ni, Co, Mn, When using Co, Mn instead of Ni, only a lower ee value was obtained). Due to the high reactivity of formaldehyde, it is hard to control the reaction. So, the use of formaldehyde as a reagent in direct catalytic asymmetric Aldol reactions has been relatively limited. The homodinuclear Ni_2-Schiff base **49** complex (0.1-1 mol%) promoted the direct catalytic asymmetric Aldol reaction of *β*-keto esters with formaldehyde, giving hydroxymethylated adducts in 66-94% ee (Scheme **28**).

2.10. Asymmetric Henry Reaction

The Henry reaction (or Nitro-Aldol reaction in other words), is an important approach for the construction of carbon–carbon bond in synthetic chemistry (Scheme **29**). The corresponding chiral product from this asymmetric reaction can be easily transformed to chiral *β*-amino alcohols, *β*-hydroxy carboxylic acids, and so on. This reaction has been catalyzed by guanidine catalysis [79], *cinchona* alkaloids [80], metal-based chiral catalysts [81, 82], and so on. However, these reactions required harsh conditions, such as low temperature and anhydrous conditions, which limited the development of this reaction.

In 2009, Mao [83] developed a readily available, stable and low-cost bifunctional copper-based catalyst for asymmetric Henry reaction under mild conditions. A series of chiral ligands were evaluated, and ligand **105** was found to be the most effective one. The mechanism study found that the two hydroxyl and the imine functional groups were indispensable for the catalytic efficiency of **105** (Fig. (**27**)). But they have not been able to obtain crystals of the copper complexes suitable for X-ray analysis.

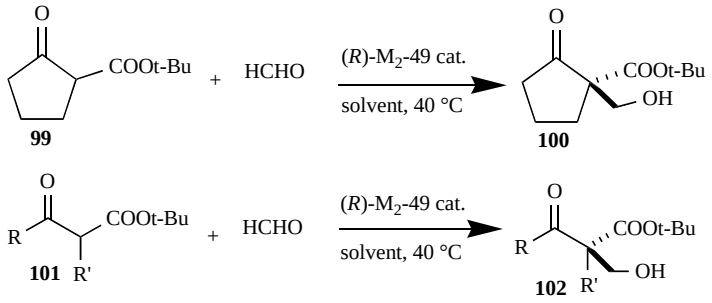
2.11. Catalytic Alkene Cyclopropanation

The catalytic enantioselective synthesis of cyclopropanes is of great interest to organic chemists, for the importance of the compounds in biological and medicinal chemistry [84]. The asymmetric addition of carbenes to electron rich alkenes was typical reaction to provide several products, for instance, styrenes with a diazoacetates in the presence of a chiral metal catalyst, giving a total of six organic products (Scheme **30**). Chemoselectivity, diastereoselectivity and enantioselectivity are all issues that should be considered.

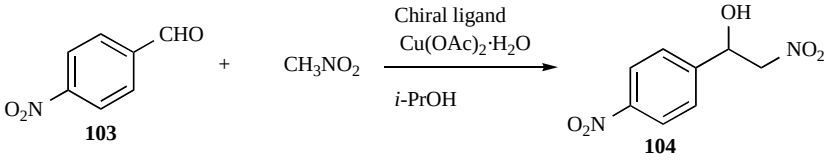
Chemoselectivity for cyclopropanes over carbene dimerization products is achieved by using an excess of alkene and slow addition of the carbene to the reaction mixture. For *trans*-selective catalysts, excellent enantiomeric excesses have been obtained, but most exhibit only moderate diastereoselectivity [84].

In 1999, Iyer [85] used six-coordinated chiral Ru(II)- Schiff base complexes $[RuLPPh_3(H_2O)_2]$ **109** (where L = terdentate chiral Schiff bases, Fig. (**28**)) as catalysts for asymmetric cyclopropanation of substituted styrene. Much better results were obtained with catalyst **109a** (47% ee) and **109b** (39% ee) with 4-nitrostyrene.

Scott [86] has applied the biaryldiimine complexes to enantioselective catalysis, and discovered the complex of **110a-c**



Scheme 28. Direct catalytic asymmetric Aldol reaction of *β*-keto esters with formaldehyde.



Scheme 29. Copper-chiral ligands catalyzed asymmetric Henry reactions.

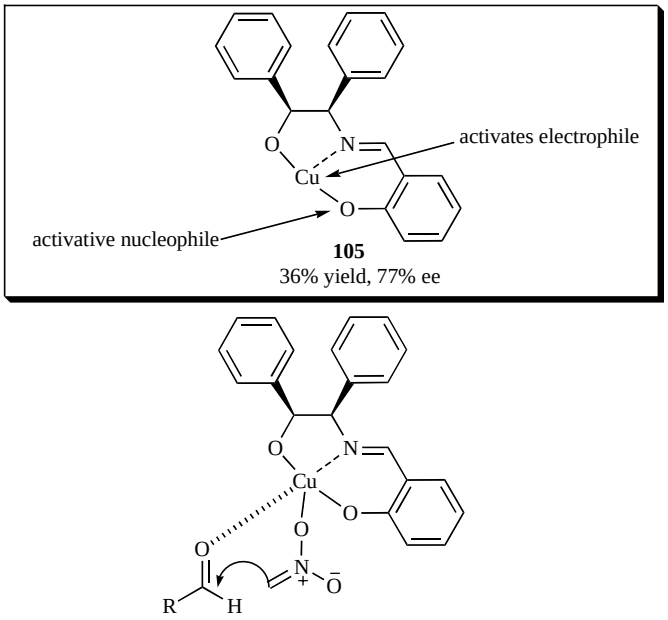
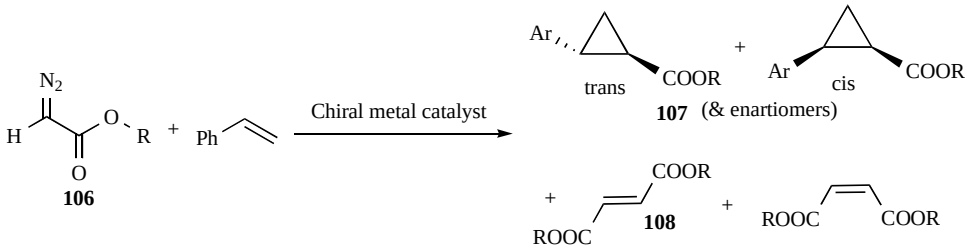


Fig. (27). Proposed transition state model for the enantioselective Henry reaction.



Scheme 30. Products typically formed in metal catalysed cyclopropanation *via* intermolecular carbene transfer to alkene.

(Fig. (**29**)) with the transition metal gives the *α-cis* topology I or occasionally the *β-cis* structure II; both arrangements dictate that the co-ligands X are placed in mutually *cis* coordination sites. It is significant to understand the process of alkene cyclopropanation by the complexes *α*/*β-cis*-[MLX_2] (M = Ru, L = **110a-c**).

When enantioselective cyclopropanation was catalyzed by (*R*)-*β-cis*-[$RuL(CH_3CN)_2$] (L = **110**), the ligand **110a** exhibited excellent diastereoselectivity and enantioselectivity (up to 99:1 dr and 98% ee) in the cyclopropanation of styrenes, compared with the bulky system **110b** and the electron withdrawing **110c**.

The removal of the CH_3CN groups and addition of the carbene derived from EDA (i.e.:$CH\text{-}CO_2Et$) led spontaneously to formation of a chelate, reminiscent of η^2- carboxylate, with both carbene carbon atom and carbonyl oxygen atom bound to Ru (Fig. (**30**)). This structure with the carbene C atom *trans* to phenolate is more stable than that with the carbene *trans* to imine. Up to 94% yield and 95% ee could be obtained in asymmetric cyclopropanation with styrene as substance.

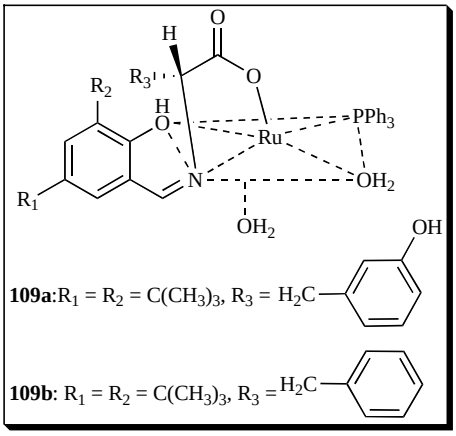


Fig. (28). The structure of chiral catalysts **109**.

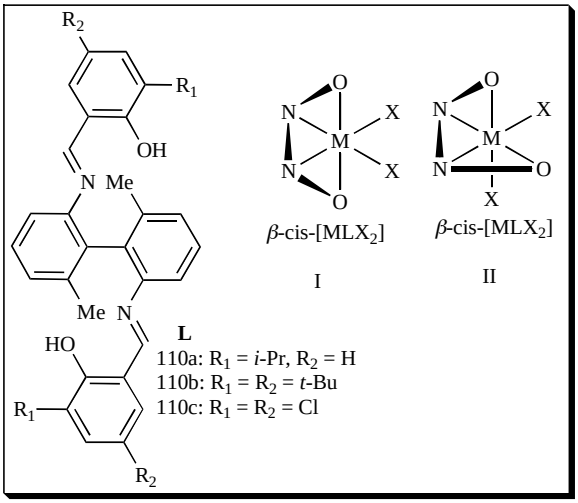


Fig. (29). The structure of chiral catalysts **110**.

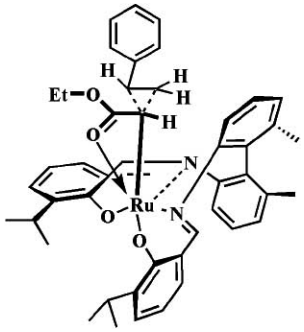


Fig. (30). The preferred orientation of approach of styrene to carbene catalyst [RuL(η^2-CHCO$_2$Et)] (L = **110a**).

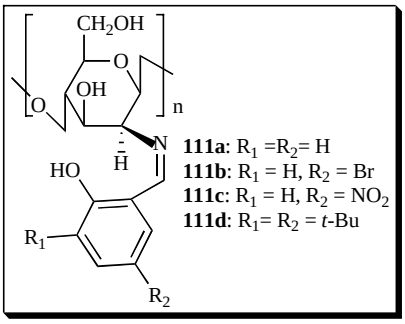


Fig. (31). The structure of chitosan-Schiff base **111**.

In 2002, Xia [87] reported an efficient heterogeneous solid chitosan-Schiff base copper(II) catalyst **111** (Fig. (**31**)) for the cyclopropanation of styrene with ethyl diazoacetate. High conversion in cyclopropanation was achieved, but with a low enantioselectivity (23% ee). For the chitosan-Schiff base copper(II) catalysts are insoluble in most solvents, it can be easily recovered and reused for further reactions without loss of activity during the fifth cycle.

2.12. Enantioselective Ring Opening of Aziridines

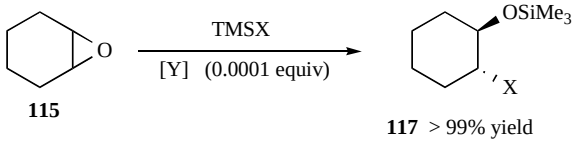
Aziridines and their ring-opened products are valuable intermediates in organic synthesis [88, 89]. A catalytic method for the enantioselective ring opening of meso aziridines by $TMSN_3$ was described by Jacobsen [90]. Tridentate Schiff base chromium complex **113** derived from 1-amino-2-indanol was identified as the optimal catalyst. *N*-Alkyl-substituted aziridines **112** with highly electron-deficient 2,4-dinitrobenzyl group was proved to be the effective substrates. Under the optimized conditions, 95% isolated yield and 94% ee were obtained (Scheme **31**).

Very recently, RajanBabu [91] reported the synthesis and application of readily available, discrete dimeric yttrium-salen complexes **116a-b** and **118a-c**, which catalyzed highly enantioselective desymmetrization of *meso*-aziridines with both $TMSN_3$ and TMSCN (Scheme **32**). Under the optimized conditions, with only 5 mol% catalyst, >99% isolated yield and 97% ee value can be obtained.

To explore the differences in the selectivity between mono- and dimeric catalysts, several different structures of the dissolvable salen-type catalysts were tested. The solid-state structure of the dimer **118b** proved to be best, and X-ray analysis was shown in Fig. (**32**). There is a well-defined chiral cavity which plays an important role in the asymmetric induction process. It also gave a good explanation that only from the opposite face the yttrium centers can be accessed.

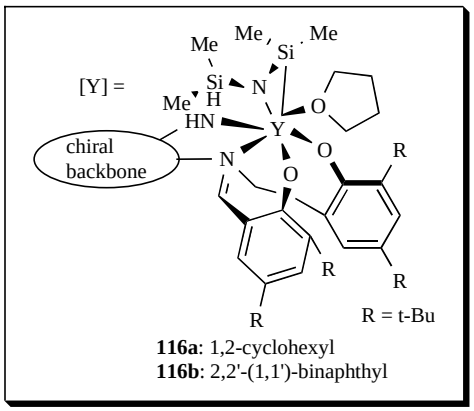
2.13. Asymmetric Baeyer–Villiger Oxidation

Baeyer–Villiger oxidation began with nucleophilic attack of an oxidant to the carbonyl group, and then formed the intermediate Criegee adduct with retention of its configuration, which giving the ester finally (Scheme **33**).



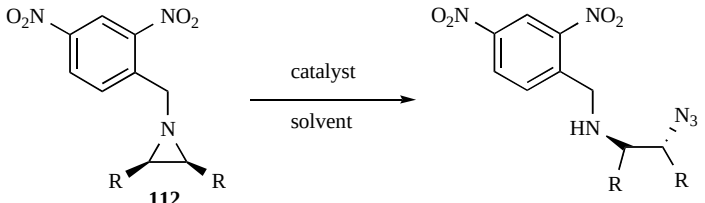
115

117 > 99% yield
with TMSCN ee up to 77%



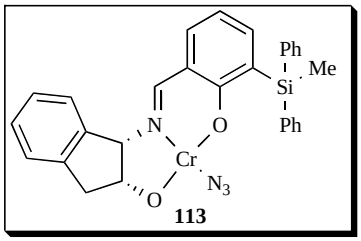
116a: 1,2-cyclohexyl
116b: 2,2'-(1,1')-binaphthyl

Scheme 32. The asymmetric ring opening of meso-aziridine with TMSCN and $TMSN_3$ using yttrium catalysts.



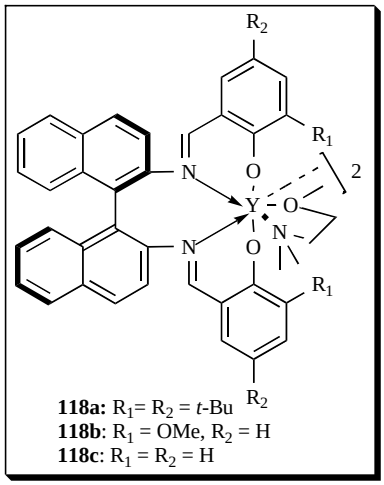
112

114:83-94% ee
80-95% yield



113

Scheme 31. Model reaction of enantioselective ring opening of meso aziridines.



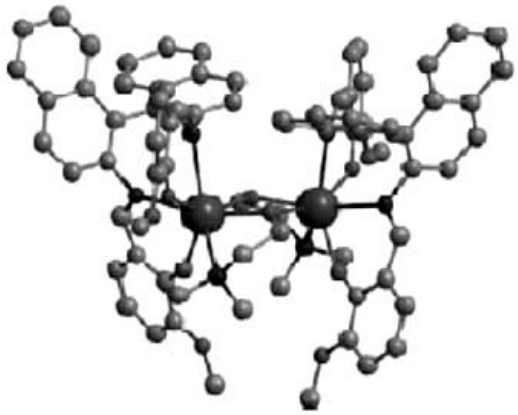
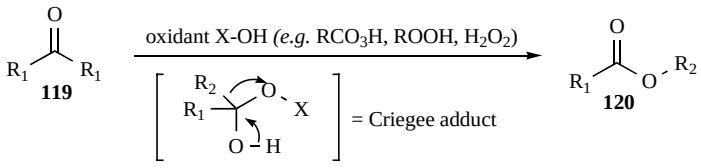


Fig. (32). Stereoview of the solid-state structure of **118b**.



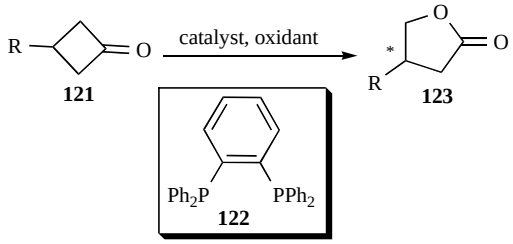
Scheme 33. Asymmetric Baeyer–Villiger oxidation.

In 1994, Bolm [92] reported the first enantiomer-differentiating reaction of racemic 2-substituted cycloalkanone by using a Cubis complex ([**122**Pt(CF_3)(CH_2Cl_2)]BF_4) as the catalyst under Mukaiyama conditions (a combination of molecular oxygen and aldehyde [93]), but only 58% ee was obtained even under the optimized reaction conditions.

Since then, various optically active metal complexes [94] have been used as catalysts for asymmetric Baeyer–Villiger oxidation, but few examples showed excellent enantioselectivities (Scheme **34**).

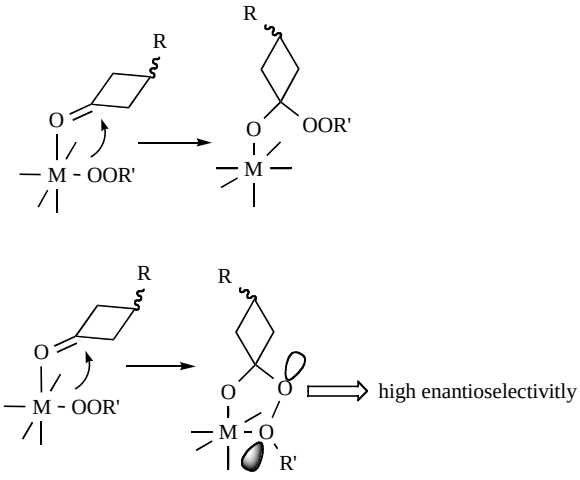
In 2001, Katsuki [95] proposed that two stereochemistries must be regulated in order to improve enantioselectivity in this reaction: (i) face selectivity in the formation of the Criegee adduct and (ii) enantioselectivity in C-C bond migration. The face selectivity could mainly be governed by the steric factor, and the conformation of the peroxy moiety of the adduct could influence the enantioselectivity (Scheme **35**). This consideration mentioned above suggested that the suitable catalyst for asymmetric Baeyer–Villiger oxidation should be a trigonal–bipyramidal or octahedral metal complex bearing two vacant *cis*-coordinating sites.

With this hypothesis in mind, they screened a lot of Co/*cis*-*β*-structure Schiff base complexes, and complex **124** (Fig. (**33**)) was the optimized catalyst for this reaction. Good enantioselectivity (up to 78% ee) was achieved when using 3-(*p*-methoxyphenyl)-cyclobutanones as the substance.



Scheme 34. Asymmetric Baeyer–Villiger oxidation of 3-phenylcyclobutanone using Co(salen) as the catalyst.

In 2002, Katsuki [96] delivered another report about asymmetric Baeyer–Villiger reaction. The attempt to modify complex **124** (77% ee, 72% yield) by introducing a chiral substituent at its 3- and 3'-carbons was tried. The complex **125** was found to be the best catalyst, with which 87% ee and 67% yield can be achieved. Baeyer–Villiger reaction of racemic bicyclo[4.2.0] octan-7-one was then examined in chlorobenzene. Both normal and abnormal rearrangement products (**A** and **B**) can be observed in this reaction. Enantiomeric excess of major normal product **A** was diminished as the reaction proceeded, while that of minor product **B** was constantly greater than 99% (Scheme **36**). The reaction of the fast isomer gave normal product **A** exclusively, while the ent-**A** and abnormal product (ent-**B**) in a ratio of 1:5.1 can be obtained in the reaction of the slow isomer. It indicated that the migratory attitude of the carbonyl substituent in Baeyer–Villiger reaction can be override by the topos selection of **125**.



Scheme 35. The selectivity in the migration influenced by the conformation of the peroxy moiety of the adduct.

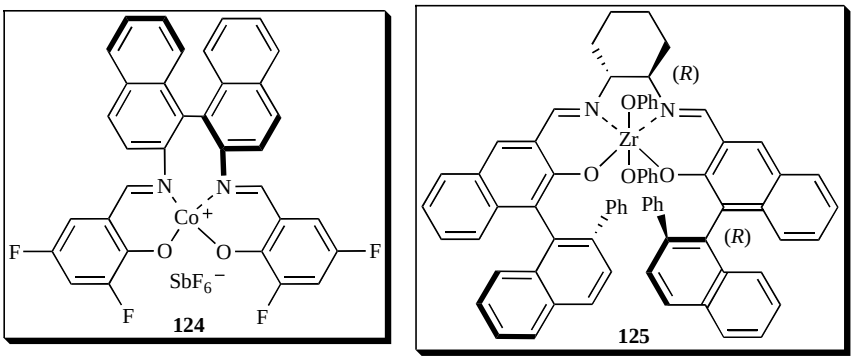
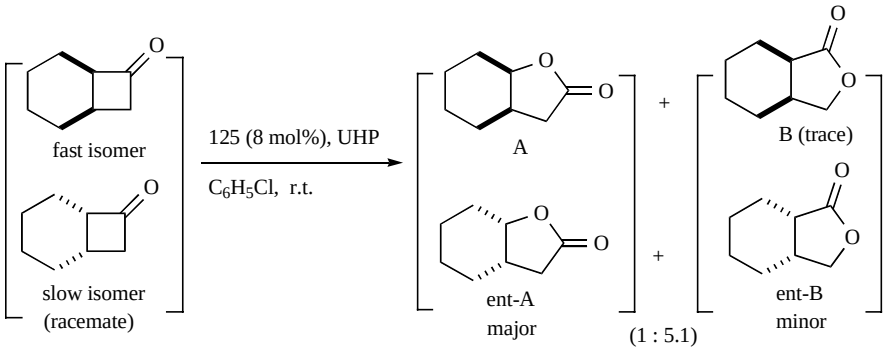


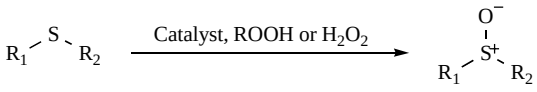
Fig. (33). The structure of chiral catalysts **124**-**125**.



Scheme 36. Baeyer–Villiger oxidation of racemic bicyclooctanone using Zr(IV)–salen complex **125** as catalyst.

2.14. Enantioselective Sulfoxidation

In the past, some efforts have been directed towards the development of enantioselective sulfoxidation for optically active sulfoxides in organic synthesis [97] (Scheme **37**).



Scheme 37. Enantioselective sulfoxidation.

Kagan [98] and Modena [99] have reported highly enantioselective sulfoxidation by using tartrate complexes, respectively. Various titanium-chiral diols complexes [100] have also been reported to serve as the catalyst for enantioselective sulfoxidation with hydrogen peroxide as the terminal oxidant. Jacobsen [101] has reported that asymmetric oxidation of sulfides using chloro(salen)manganese(III) complex **126** (Fig. **34**) with hydrogen peroxide, however only modest enantioselectivities were observed. In 1995 and 1998, Bolm [102, 103] reported that the vanadium- chiral Schiff base complexes **127a,b** can catalyze the asymmetric sulfoxidation, showing good enantioselectivity (94% yields and 70% ee). Berkessel [104] found **127c** to be a good

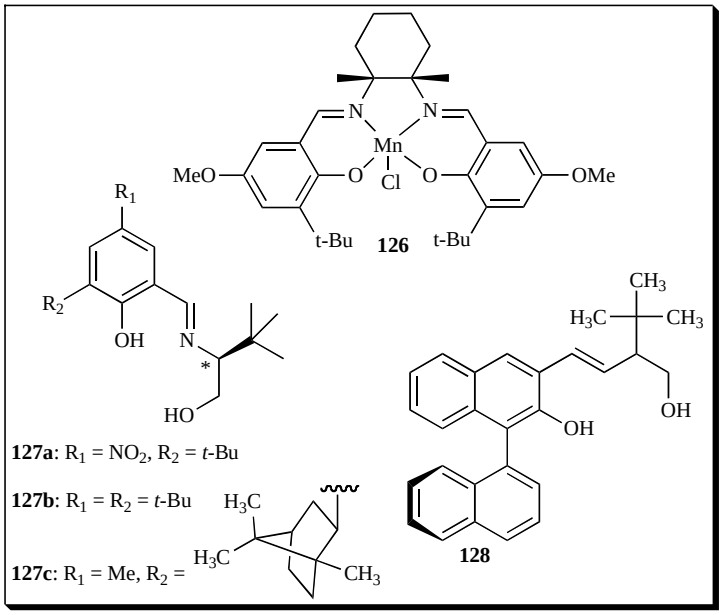


Fig. (34). The structure of chiral catalysts **126**-**128**.

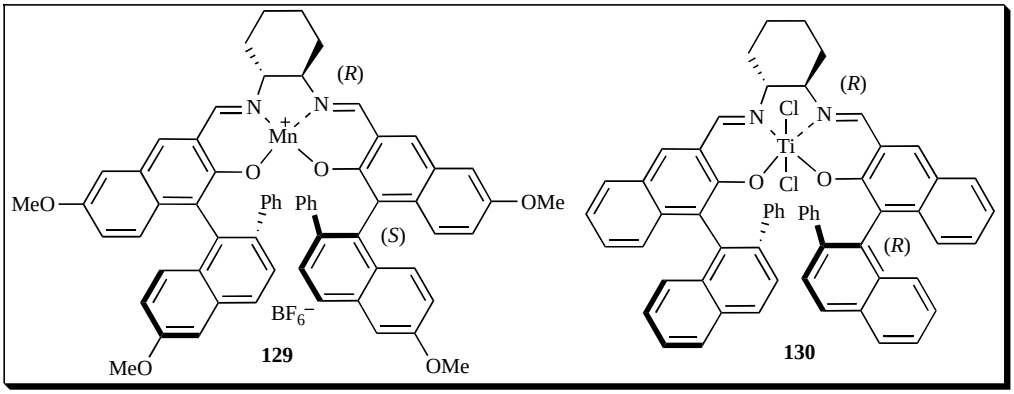


Fig. (35). The structure of chiral catalysts **129**-**130**.

catalyst for asymmetric sulfoxidation also, with 91% yield and 70% ee for thioanisole and 97% yield and 78% ee for *o*-bromothioanisole. The Schiff base **128** was also a good catalyst for asymmetric sulfoxidation of thioanisole (85% yield and 71% ee), but for *o*-bromothioanisolea only 41% yield and 19% ee can be obtained.

In 1996, Katsuki [105] reported that the second-generation (salen)manganese(III) complex **129** (Fig. (**35**)) was an efficient catalyst (94% ee) for the asymmetric oxidation of alkyl aryl sulfides with iodosylbenzene as the terminal oxidant instead of hydrogen peroxide. In 2001, they tried to use the (salen)titanium(IV) complex **130** as catalyst with hydrogen peroxide in methanol for the asymmetric oxidation of alkyl aryl sulfides. By treating complex **130** with water, triethylamine, dichloromethane, and a urea·H_2O_2 adduct (UHP) as oxidation, the corresponding di-μ-oxo (salen) titanium complex (FABMS analysis *m*/*z*=1778.55) was obtained and considerably good enantioselectivity was achieved (94% ee).

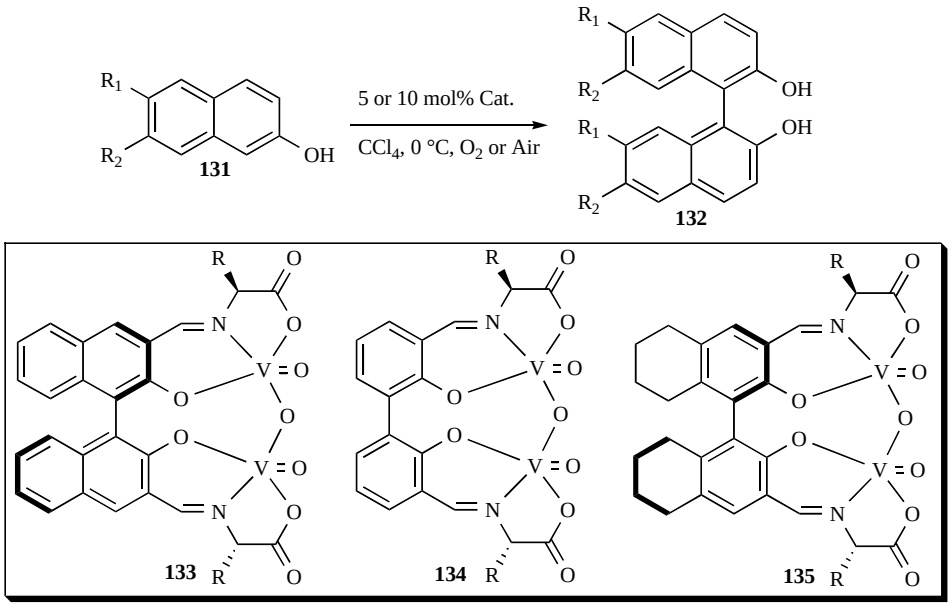
Then they examined oxidation of several substituted methyl phenyl sulfides. Not only methyl aryl sulfides, but also ethyl phenyl sulfide and benzyl methyl sulfide obtained a good enantioselectivity at 0°C (> 91% ee for all of them).

2.15. Enantioselective Oxidative Couplings of 2-Naphthols

In the history of asymmetric synthesis, binaphthol and its derivatives were important chiral auxiliaries and ligands in asymmetric transformations, which have a wide scope of application. A straightforward pathway to get the binaphthol is oxidative coupling of 2-naphthols with a large number of organocatalysts that have been discovered. As for the synthesis of optically active binaphthols, optical resolution of racemic binaphthols is a conventional method for the preparation of optically pure binaphthols [106, 107]. The resolution approach, however, suffers from the stoichiometric amounts of chiral sources as resolution agent.

The development of oxidative couplings of 2-naphthols in the presence of catalytic amounts of chiral catalyst has provided several promising results, and their applications to the synthesis of various chiral BINOL derivatives have been attempted. This methodology is easier to control, and may provide a possible low cost means. In 2007, Gong [108] designed the chiral bimetallic oxovanadium complexes **133-135** for the enantioselective oxidative coupling of 2-naphthols, which bearing various substituents at C6 and/or C7 (Scheme **38**).

When using the designed bimetallic oxovanadium complexes **133** as catalyst, an up to 98% ee was obtained in case of 7-substituted-2-naphthols. The biphenol-derived diastereomeric oxovanadium complexes **134** can also catalyze the oxidative coupling of 2-naphthols and its derivatives in excellent enantioselectivity (> 98% ee). The catalyst contains two *sec*-butyl substituents at R group. Then, a new chiral catalyst **135** was



Scheme 38. Oxidative coupling of 2-naphthol with bimetallic oxovanadium complexes.

discovered with improved catalytic performance (92% yield and 91% ee) compared with **133** (51% yield and 96% ee) and **134** (25% yield and 89% ee) with the same substrate 7-allyloxy-2-naphthol. It is interesting that the reaction got a faster speed and higher enantioselectivity in the presence of **135** under 1 atm air instead of 1 atm of oxygen. It's a very important discovery because the air is the most plentiful oxidant source and is safe and environmentally benign. The application of this finding is under going.

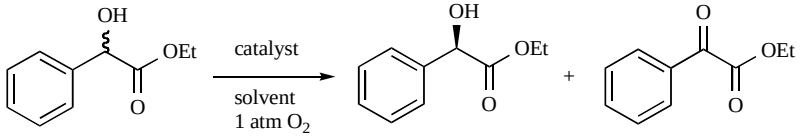
2.16. Asymmetric Oxidation of Ethyl Mandelate

Enantiomerically pure *α*-hydroxy esters are useful building blocks for chiral synthesis, which have significant interest in the pharmaceutical and fine chemical industries [109]. The recent years, a hard work has been devoted to get enantiomerically pure *α*-hydroxy esters or other secondary alcohols (Scheme **39**) [110].

Polymer and silica supported tridentate Schiff base vanadium catalysts derived from salicylaldehydes and *tert*-leucinol or *tert*-leucine are known to be excellent catalysts to meet this request [111]. They can be used for asymmetric oxidation of *α*-hydroxy esters such as ethyl mandelate.

Linear polystyrene supported catalysts **136a** and **136b** are partially soluble under the reaction conditions, and it is shown that the catalytic reactivity significantly influenced by the soluble species. Insoluble catalysts **137** supported by cross-linked polystyrene resin or mesoporous silica allow for catalyst recovery and recycle, showing equivalent selectivities over multiple reaction cycles at long times (16 h each circle) (Table **1**). The mesoporous silica supported catalyst **138** exhibits greater selectivity than the analogous homogeneous and polymer supported catalysts (Fig. (**36**)).

A comparison of the kinetic profiles of the *S*-enantiomer conversion in the first and fourth reaction cycles using catalyst **137** is given in Fig. (**37**). These results clearly suggest that there is a decrease in activity with each cycle even though the final



Scheme 39. Oxidative kinetic resolution of an *α*-hydroxy ester.

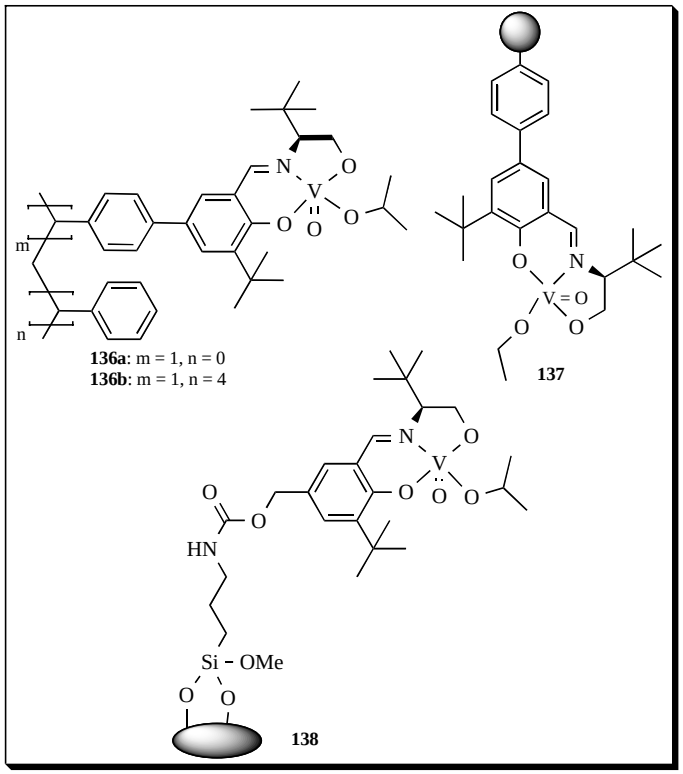


Fig. (36). The structure of chiral catalysts **136-138**.

Table 1. Recycle Data for the Oxidation of Ethyl Mandelate with Catalyst 137 after 16 h

Cycle	Loading (mol%)	Conversion of *S*-ethyl Mandelate [%]	ee [%] of *R*-ethyl Mandelate
1	5.5	99	96
2	5.5	99	96
3	5.5	> 99	> 99
4	5.5	> 99	> 99

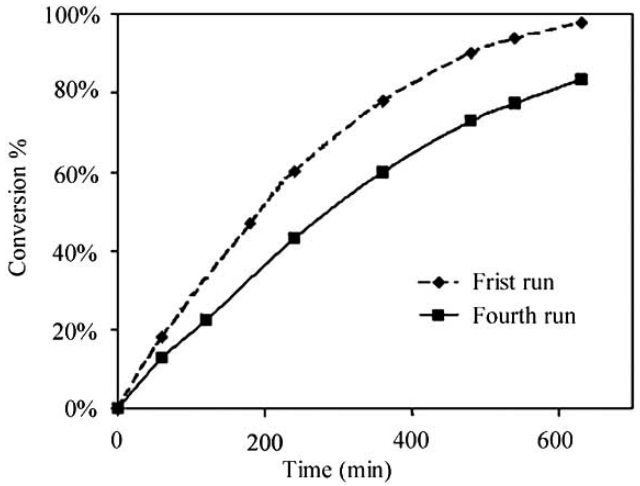
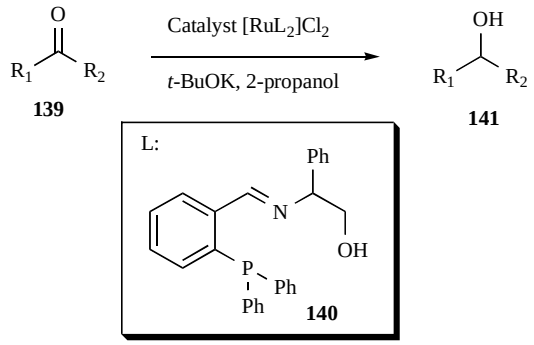


Fig. (37). Recycle experiments for the conversion of *S*-ethyl mandelate vs. time with catalyst **137**.

conversions are similar at long times. The loss of activity is attributed to the decomposition of some portion of the vanadyl complexes in each cycle.

2.17. Asymmetric Transfer Hydrogenation

Catalyzed asymmetric transfer hydrogenation of prochiral ketones is an alternative method for the preparation of chiral secondary alcohols [112, 113] (Scheme **40**). It is simple and does not require molecular hydrogen and high pressure equipment as the general catalytic hydrogenation.



Scheme 40. Catalyzed asymmetric transfer hydrogenation.

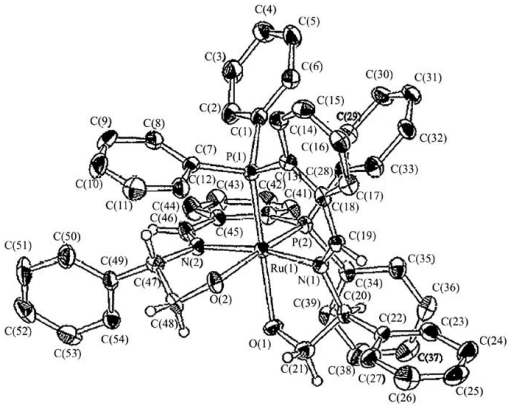


Fig. (38). X-ray crystallography of complex $[RuL_2]Cl_2$ (L= **140**).

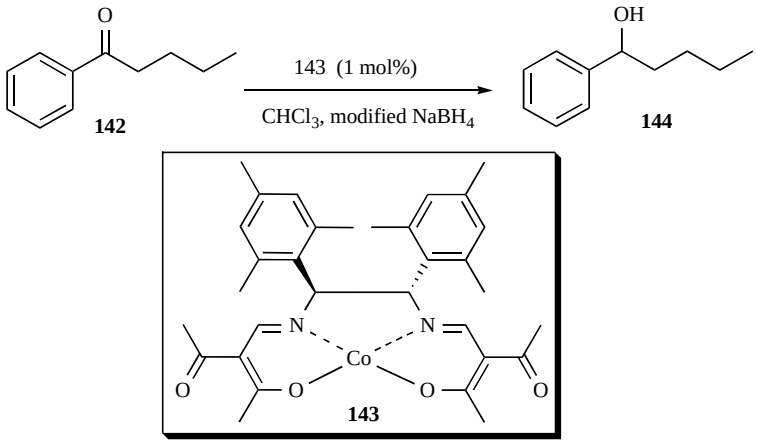
In 1999, Kwong [114] described a chiral ruthenium catalyst containing *P*, *N*, *O*-Schiff base ligand **140** for catalytic transfer hydrogenation. For most aryl methyl ketones, enantiomeric excess was obtained in the range of 50-80%. For isopropyl phenyl ketone, 81% ee could be achieved.

A ruthenium complex having the formula $[RuL_2]Cl_2$ (L = **140**) provided a good yield, and its structure was established by X-ray crystallography (Fig. (**38**)).

2.18. Borohydride Reduction

In 2006, Yamada [115] reported a Schiff base-cobalt complex for the enantioselective borohydride reduction in chloroform (Scheme **41**). Based on experimental and theoretical studies, the chloroform is not only the solvent but the reactant that activates the cobalt catalyst **143**. The substrate carbonyl compounds are fixed and activated by the alkali cation, and attacked by the hydride on the cobalt atom *via* a six-membered-like transition state to afford the corresponding alcohol. Up to 94% yield and 91% ee can be obtained.

They presumed the following three cobalt hydride models for the theoretical analysis (Fig. (**39**)): Model A: the simple cobalt hydride; Model B: the cobalt hydride with an axial ligand such as the dichloromethyl group; and Model C: the cobalt hydride with an axial ligand and a countercation, which is the alkali-metal cation from the borohydride. Based on the experimental observations, they assumed the key reactive intermediate was Model C. The theoretical analysis of the reaction pathway was performed for each of the presumed Models A–C. Based on those analyses, the mechanism of this reaction was proposed.



Scheme 41. Borohydride reduction catalyzed by the cobalt complex.

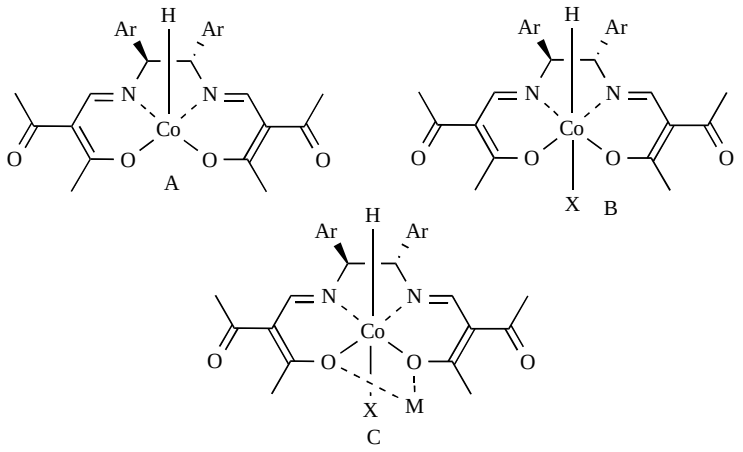


Fig. (39). Presumed models of the cobalt hydride intermediates.

As shown in Fig. (**40**), the original cobalt complex reacts with the hydride reducing agent to generate the corresponding dichloromethylcobalt hydride with the sodium cation intermediate, in the presence of chloroform. Ketone coordinates the sodium cation, which leads to the activation and stereochemical alignment of the carbonyl group. From the intermediate, the hydride on the cobalt atom attacks the carbonyl carbon to form a six-membered transition state. Coordination by both the chlorine and oxygen atoms of the ligand in the TS is essential. After the TS, the anionic character of the oxygen atom is delocalized to the cationic sodium ion.

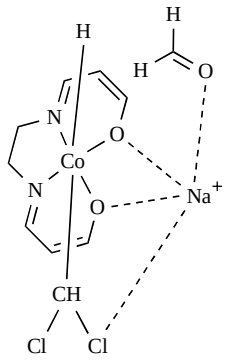


Fig. (40). Optimized transition state of cobalt hydride.

CONCLUSIONS

Asymmetric catalysis using chiral Schiff base catalysts has been recognized as a versatile methodology in asymmetric synthesis, featuring its simple experimental operations, mild reaction conditions, inexpensive and environmentally benign reagents and solvents. In the past two decades, those catalysts have seen significant advances and have been used in a large number of asymmetric catalytic reactions. The recent development of various asymmetric reactions delivers not only higher reactivity and enantioselectivity but also new synthetic opportunities, expanding the practical applicability of chiral Schiff base catalysts in modern organic synthesis. However, there are also some limitations in the catalytic process using chiral Schiff base. For example, the Schiff bases are usually not stable in water or acidic condition. A few metal-free Schiff base catalysts have been developed in this field. The mechanisms of some reactions are still not very clear.

Based on the recent practical aspects mentioned above, the study of chiral Schiff base catalysis is certainly one of the hottest research areas in asymmetric synthesis. Although some recently discovered catalysts show moderate enantioselectivity, the efficiency achieved in the chemical transformation has opened up a new perspective for catalytic asymmetric reactions. Continuous efforts should be made towards the understanding of the relationship between the structure of the catalyst and its activity and the studying of the mechanism in stereocontrolling process, which allows further rational catalyst design in the development of more efficient catalytic systems.

ACKNOWLEDGEMENT

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REFERENCES

[1] International Union of Pure and Applied Chemistry. "anils". *Compendium of Chemical Terminology* Internet edition.

[2] Garnovskii, A.D.; Nivorozhkin, A.L.; Minkin, V.I. Ligand environment and the structure of schiff base adducts and tetracoordinated metal-chelates. *Coord. Chem. Rev.*, **1993**, *126*, 1-69.

[3] Khan, N. H.; Agrawal, S.; Kureshy, R. I.; Abdi, S. H. R.; Mayani, V. J.; Jasra, R. V. Asymmetric addition of trimethylsilyl cyanide to aldehydes promoted by chiral polymeric vanadium(V) salen complex as an efficient and recyclable catalyst. *Tetrahedron Asymmetry*, **2006**, *17*, 2659-2666.

[4] Gupta, K. C.; Sutar, A. K. Catalytic activities of Schiff base transition metal complexes. *Coord. Chem. Rev.*, **2008**, *252*, 1420-1450.

[5] Jacobsen, E.N. *Catalytic Asymmetric Synthesis*. Ojima, I. Ed. VCH: New York, **1993**, p. 159.

[6] Samsel, E.G.; Srinivasan, K.; Kochi, J.K. Mechanism of the chromium-catalyzed epoxidation of olefins. Role of oxochromium(V) cations. *J. Am. Chem. Soc.*, **1985**, *107*, 7606-7617.

[7] Katsuki, T. Catalytic asymmetric oxidations using optically active (salen)manganese(III) complexes as catalysts. *Coord. Chem. Rev.*, **1995**, *140*, 189-214.

[8] Katsuki, T. Some recent advances in metallosalen chemistry. *Synlett*, **2003**, *3*, 281-297.

[9] Katsuki, T. Unique asymmetric catalysis of cis-*β* metal complexes of salen and its related Schiff-base ligands. *Chem. Soc. Rev.*, **2004**, *33*, 437-444.

[10] McGarrigle, E. M.; Gilheany, D. G. Chromium- and Manganese-salen promoted epoxidation of alkenes. *Chem. Rev.*, **2005**, *105*, 1563-1602.

[11] Venkataramanan, N. S.; Kuppuraj, G.; Rajagopal, S. Metal-salen complexes as efficient catalysts for the oxygenation of heteroatom containing organic compounds—synthetic and mechanistic aspects. *Coord. Chem. Rev.*, **2005**, *249*, 1249-1268.

[12] Barf, G. A.; Sheldon, R. A. Ruthenium catalyzed epoxidations: mechanistic and synthetic aspects. *J. Mol. Catal. A: Chem.*, **1995**, *102*, 23-39.

[13] Dalton, C. T.; Ryan, K. M.; Wall, V. M.; Bousquet, C.; Gilheany, D. G. Recent progress towards the understanding of metal-salen catalysed asymmetric alkene epoxidation. *Top. Catal.*, **1998**, *5*, 75-91.

[14] Cozzi, P. G. Metal-Salen Schiff base complexes in catalysis: practical aspects. *Chem. Soc. Rev.*, **2004**, *33*, 410-421.

[15] Kleij, A. W. Nonsymmetrical salen ligands and their complexes: synthesis and applications. *Eur. J. Inorg. Chem.* **2009**, 193-205.

[16] Xia, Q.-H.; Ge, H.-Q.; Ye, C.-P.; Liu, Z.-M.; Su, K.-X. Advances in homogeneous and heterogeneous catalytic asymmetric epoxidation. *Chem. Rev*., **2005**, *105*, 1603-1662.

[17] Baleiza, C.; Garcia, H. Chiral Salen Complexes: An overview to recoverable and reusable homogeneous and heterogeneous catalysts. *Chem. Rev*., **2006**, *106*, 3987-4043.

[18] Kitamura, M.; Okada, S.; Suga, S.; Noyori, R. Enantioselective addition of dialkylzincs to aldehydes promoted by chiral amino alcohols. Mechanism and nonlinear effect. *J. Am. Chem. Soc*., **1989**, *111*, 4028- 4036.

[19] Adams, H.; Bailey, N. A.; Fenton, D. E.; He, Q.Y. Zinc(II) complexes of tripodal ligands providing phenolate and pyridine donors: formation, structure and hydrolytic activity. *J. Chem. Soc., Dalton Trans.*, **1996**, 2857-2865.

[20] Dangel, D.; Polt, R. Catalysis by amino acid-derived tetracoordinate complexes: enantioselective addition of dialkylzincs to aliphatic and aromatic aldehydes. *Org. Lett.*, **2000**, *2*, 3003-3006.

[21] Tanaka, T.; Yasuda, Y.; Hayashi, M. New chiral Schiff base as a tridentate ligand for catalytic enantioselective addition of diethylzinc to aldehydes. *J. Org. Chem.*, **2006**, *71*, 7091-7093.

[22] Liu, B.; Fang, C.; Dong, Z. B.; Li, J. S. New BINOL Schiff Base as a tridentate ligand for catalytic asymmetric addition of diethylzinc to aldehydes in the presence of titanium tetraisopropoxide. *Lett. Org. Chem.*, **2007**, *4*, 172-174.

[23] Kawamura, K.; Fukuzawa, H.; Hayashi, M. Novel N,N,P-tridentate ligands for the highly enantioselective Copper-catalyzed 1,4-addition of dialkylzincs to enones. *Org. Lett.*, **2008**, *10*, 3509-3512.

[24] Friel, D. K.; Snapper, M. L.; Hoveyda, A. H. Aluminum-catalyzed asymmetric alkylations of pyridyl-substituted alkynyl ketones with dialkylzinc reagents. *J. Am. Chem. Soc*., **2008**, *130* (30), 9942-9951.

[25] Cesati, R. R.; Armas, J. D. III; Hoveyda, A. H. Enantioselective total synthesis of Erogorgiaene: applications of asymmetric Cu-catalyzed conjugate additions of alkylzincs to acyclic enones. *J. Am. Chem. Soc.*, **2004**, *126*, 96-101.

[26] Murphy, K. E.; Hoveyda, A. H. Preparation of *α, α'*-disubstituted *β,*γ-unsaturated esters through Cu-catalyzed asymmetric allylic alkylations. *Org. Lett.*, **2005**, *7*(7), 1255-1258.

[27] Jørgensen, K. A. Catalytic asymmetric hetero-Diels-Alder reactions of carbonyl compounds and imines. *Angew. Chem., Int. Ed*., **2000**, *39*, 3558-3588.

[28] Schaus, S. E.; Branalt, J.; Jacobsen, E. N. Asymmetric hetero-Diels−Alder reactions catalyzed by chiral (Salen)Chromium(III) complexes. *J. Org. Chem.*, **1998**, *63*, 403-405.

[29] Dossetter, A. G.; Jamison, T. F.; Jacobsen, E. N. Highly enantio- and diastereoselective hetero-Diels-Alder reactions catalyzed by new chiral Tridentate Chromium(III) catalysts. *Angew. Chem., Int. Ed*., **1999**, *38*, 2398-2400.

[30] Johannsen, M.; Jùrgensen, K. A.; Zheng, X.-F.; Hu, Q.-S.; Pu, L.A. Highly Enantioselective Hetero-Diels−Alder Reaction Catalyzed by Chiral Polybinaphthyl−Aluminum Complexes. *J. Org. Chem.*, **1999**, *64*, 299-301.

[31] Evans, D. A.; Olhava, E. J.; Johnson, J. S.; Janey, J. M. Chiral C_2-Symmetric Cu II complexes as catalysts for enantioselective Hetero-Diels-Alder reactions. *Angew. Chem. Int. Ed*., **1998**, *37*, 3372-3375.

[32] Ji, B.-M.; Yuan, Y.; Ding, K.-L.; Meng, J.-B. Assembled dendritic titanium catalysts for enantioselective Hetero-Diels-Alder reaction of aldehydes with Danishefsky's Diene. *Chem. Eur. J*., **2003**, *9*, 5989-5996.

[33] Joly, G. D.; Jacobsen, E. N. Catalyst-controlled diastereoselective Hetero-Diels-Alder reactions. *Org. Lett.*, **2002**, *4* (10), 1795-1798.

[34] Snider, B. B. Lewis-acid catalyzed ene reactions. *Acc. Chem. Res.*, **1980**, *13* (11), 426-432.

[35] Hao, J.; Hatano, M.; Mikami, K. Chiral Palladium(II)-Catalyzed asymmetric Glyoxylate−Ene Reaction:alternative approach to the enantioselective synthesis of *α*-Hydroxy Esters. *Org. Lett.*, **2000**, *2* (25), 4059-4062.

[36] Mikami, K.; Kawakami, Y.; Akiyama, K.; Aikawa, K. Enantioselective catalysis of Ketoester-ene reaction of silyl enol ether to construct quaternary carbons by chiral dicationic palladium(ii) complexes. *J. Am. Chem. Soc*., **2007**, *129* (43), 12950-12951.

[37] Ruck, R. T.; Jacobsen E. N. Asymmetric catalysis of Hetero-Ene reactions with Tridentate Schiff base Chromium(III) complexes. *J. Am. Chem. Soc*., **2002**, *124* (12), 2882-2883.

[38] Hutson, G. E.; Dave, A.H.; Rawal, V. H. Highly enantioselective Carbonyl-ene reactions catalyzed by a Hindered Silyl-Salen-Cobalt complex. *Org. Lett.*, **2007**, *9* (20), 3869-3872.

[39] Tramontini, M.; Angiolini, L. Further advances in the chemistry of mannich bases. *Tetrahedron*, **1990**, *46*, 1791-1837.

[40] Handa, S.; Gnanadesikan, V.; Matsunaga, S.; Shibasaki, M. *syn*-Selective catalytic asymmetric nitro-mannich reactions using a heterobimetallic Cu−Sm−Schiff base complex. *J. Am. Chem. Soc*., **2007**, *129* (16), 4900-4901.

[41] Chen, Z.-H.; Morimoto, H.; Matsunaga, S.; Shibasaki, M. A bench-stable homodinuclear Ni_2−Schiff base complex for catalytic asymmetric synthesis of *α*-Tetrasubstituted *anti-α,β*-Diamino acid surrogates. *J. Am. Chem. Soc*., **2008**, *130* (7), 2170-2171.

[42] Chen, Z.-H.; Yakura, K.; Matsunaga, S.; Shibasaki, M. Direct catalytic asymmetric Mannich-Type reaction of *β*-Keto phosphonate using a dinuclear Ni_2−Schiff base complex. *Org. Lett.*, **2008**, *10* (15), 3239-3242.

[43] Cozzi, P. G. Enantioselective alkynylation of ketones catalyzed by Zn(Salen) complexes. *Angew. Chem., Int. Ed*., **2003**, *42*, 2895-2897.

[44] Chen, C.; Hong, L.; Xu, Z.-Q.; Liu, L.; Wang, R. Low ligand loading, highly enantioselective addition of phenylacetylene to aromatic ketones catalyzed by Schiff-Base amino alcohols. *Org. Lett.*, **2006**, *8*, 2277-2280.

[45] Hong, M.; You, Q.-D. Enantioselective alkynylation of aromatic aldehydes catalyzed by new C_2-Symmetric Bis-Schiff base amino alcohol. *Lett. Org. Chem.*, **2007**, *4*, 571-575.

[46] Pathak, K.; Bhatt, A. P.; Abdi, S. H. R.; Kureshy, R. I.; Khan, N. H.; Ahmad, I.; Jasra, R. V. Enantioselective phenylacetylene addition to aldehydes and ketones catalyzed by recyclable polymeric Zn(salen) complex. *Chirality*, **2007**, *19*, 82-88.

[47] Sigman, M. S.; Jacobsen, E. N. Schiff base catalysts for the asymmetric strecker reaction identified and optimized from parallel synthetic libraries. *J. Am. Chem. Soc*., **1998**, *120*, 4901-4902.

[48] Burgess, K.; Lim, H.-J.; Porte, A. M.; Sulikowski, G. A. New catalysts and conditions for a C-H insertion reaction identified by high throughput catalyst screening. *Angew. Chem., Int. Ed. Engl*., **1996**, *35*, 220-222.

[49] Cole, B. M.; Shimizu, K. D.; Krueger, C. A.; Harrity, J. P. A.; Snapper, M. L.; Hoveyda, A. H. Discovery of chiral catalysts through ligand diversity: Ti-Catalyzed enantioselective addition of TMSCN to *meso* epoxides. *Angew. Chem., Int. Ed. Engl*., **1996**, *35*, 1668-1671.

[50] Sigman, M. S.; Vachal, P.; Jacobsen, E. N.; A General Catalyst for the Asymmetric strecker reaction. *Angew. Chem., Int. Ed*., **2000**, *39*, 1279-1281.

[51] Vachal, P.; Jacobsen, E. N. Enantioselective catalytic addition of HCN to ketoimines. Catalytic synthesis of quaternary amino acids. *Org. Lett.*, **2000**, *2*, 867-870.

[52] Su, J. T.; Vachal, P.; Jacobsen, E. N. Practical synthesis of a soluble Schiff Base catalyst for the asymmetric strecker reaction. *Adv. Synth. Catal.*, **2001**, *343*, 197-200.

[53] Vachal, P.; Jacobsen, E. N. Structure-based analysis and optimization of a highly enantioselective catalyst for the strecker reaction. *J. Am. Chem. Soc*., **2002**, *124*, 10012-10014.

[54] Josephsohn, N.S.; Kuntz, K. W.; Snapper, M. L.; Hoveyda, A. H. Mechanism of enantioselective Ti-Catalyzed strecker reaction: peptide-based metal complexes as bifunctional catalysts. *J. Am. Chem. Soc.*, **2001**, *123*, 11594-11599.

[55] Effenberger, F. Synthesis and reactions of optically active cyanohydrins. *Angew. Chem. Int. Ed. Engl*., **1994**, *33*, 1555-1564.

[56] North, M. Catalytic asymmetric cyanohydrin synthesis. *Synlett*, **1993**, 807-820.

[57] Ziegler, T.; Horsch, B.; Effenberger, F. Ein einfacher Zugang zu (*R*)-*α*-Hydroxycarbonsäuren und (*R*)- 1-Amino-2-alkoholen aus (*R*)-Cyanhydrinen. *Synthesis*, **1990**, 575-578.

[58] Jackson, W. R.; Jacobs, H. A.; Jayatilake, G. S.; Mathews, B. R.; Watson, K. G. Applications of optically active aryl cyanohydrins in the synthesis of *α*-hydroxy aldehydes, *α*-hydroxy ketones and *β*-hydroxy amines. *Aust. J. Chem.* **1990**, *43*, 2045-2062.

[59] Jackson, W. R.; Jacobs, H. A.; Mathew, B. R.; Jayatilake, G. S.; Watson, K. G. Stereoselective syntheses of ephedrine and related 2-aminoalcohols of high optical purity from protected cyanohydrins. *Tetrahedron Lett.* **1990**, *31*, 1447-1450.

[60] Effenberger, F.; Jager, J. J. Synthesis of the adrenergic bronchodilators (*R*)-terbutaline and (*R*)-salbutamol from (*R*)-cyanohydrins. *J. Org. Chem.* **1997**, *62*, 3867-3873.

[61] Zandbergen, P.; Brussee, J.; Vander Gen, A.; Kruse, C. G. Stereoselective synthesis of *β*-hydroxy-*α*-amino acids from chiral cyanohydrins. *Tetrahedron Asymmetry*, **1992**, *3*, 769-774.

[62] Jiang, Y.-Z; Zhou, X.-G.; Hu, W.-H.; Wu, L.-J.; Mi, A.-Q. Asymmetric synthesis XXII: asymmetric catalytic trimethylsilylcyanation of benzaldehyde by novel Ti(IV)-chiral schiff base complexes. *Tetrahedron Asymmetry*, **1995**, *6*, 405-408.

[63] Mori, M.; Imma, H.; Nakai, T. Asymmetric catalytic cyanosilylation of aldehydes using a chiral binaphthol-Titanium complex. *Tetrahedron Lett.*, **1997**, *38*, 6229-6232.

[64] Abiko, A.; Wang, G.-Q. A BMPD−Yttrium isopropoxide complex: highly efficient chiral Lewis acid catalyst for asymmetric silylcyanation. *J. Org. Chem.*, **1996**, *61*, 2264-2265.

[65] Evans, D. A.; Carrol, G. L.; Truesdale, C. K. Synthetic applications of trimethylsilyl cyanide. an efficient synthesis of *β*-aminomethyl alcohols. *J. Org. Chem.*, **1974**, *39*, 914-917.

[66] Zhou, X.-G.; Huang, J.-S.; Ko, P.-H.; Cheung K.-K.; Che, C.-M. Titanium and ruthenium binaphthyl Schiff base complexes as catalysts for asymmetric trimethylsilylcyanation of aldehydes. *J. Chem. Soc*., *Dalton Trans*., **1999**, 3303-3309.

[67] Belokon', Y. N.; Caveda-Cepas, S.; Green, B.; Ikonnikov, N. S.; Khrustalev, V. N.; Larichev, V. S.; Moscalenko, M. A.; North, M.; Orizu, C.; Tararov, V. I.; Tasinazzo, M.; Timofeeva, G. I.; Yashkina, L. V. The asymmetric addition of trimethylsilyl cyanide to aldehydes catalyzed by chiral (Salen)Titanium complexes. *J. Am. Chem. Soc.*, **1999**, *121*, 3968-3973.

[68] Belokon, Y. N.; Green, B.; Ikonnikov, N. S.; Larichev, V. S.; Lokshin, B. V.; Moscalenko, M. A.; North, M.; Orizu, C.; Peregudov, A. S.; Timofeeva, G. I. Mechanistic investigation of the asymmetric addition of trimethylsilyl cyanide to aldehydes catalysed by dinuclear chiral (Salen)titanium complexes. *Eur. J. Org. Chem.*, **2000**, 2655-2661.

[69] Flores-Lopz, L. Z.; Parra-Hake, M.; Somanathan, R.; Walsh, P. J. Structure/enantioselectivity study of the asymmetric addition of trimethylsilylcyanide to benzaldehyde catalyzed by Ti(IV)−Schiff base complexes. *Organometallics*, **2000**, *19*, 2153-2160.

[70] Baleizão, C.; Gigante, B.; Garcia, H.; Cormab, A. Vanadyl salen complexes covalently anchored to single-wall carbon nanotubes as heterogeneous catalysts for the cyanosilylation of aldehydes. *J. Catal.*, **2004**, *221*, 77-84.

[71] Belekon, Y.N.; North, M.; Parsons, T. Vanadium-catalyzed asymmetric cyanohydrin synthesis. *Org. Lett.*, **2000**, *2*, 1617-1619.

[72] Belekon, Y. N.; Green, B.; Ikonnikov, N. S.; North, M.; Parsons, T.; Tararov, V. I. Optimized catalysts for the asymmetric addition of trimethylsilyl cyanide to aldehydes and ketones. *Tetrahedron*, **2001**, *57*, 771-779.

[73] Jorgensen, K.A. Asymmetric Friedel-Crafts reactions: catalytic enantioselective addition of aromatic and heteroaromatic C-H bonds to activated alkenes, carbonyl compounds, and imines. *Synthesis*, **2003**, 1117-1125.

[74] Bandini, M.; Melloni, A.; Umani-Ronchi, A. New catalytic approaches in the stereoselective Friedel-Crafts alkylation reaction. *Angew. Chem. Int. Ed.*, **2004**, *43*, 550-556.

[75] Bandini, M.; Melloni, A.; Tommasi, S.; Umani-Ronchi, A. A journey across recent advances in catalytic and stereoselective alkylation of indoles. *Synlett*, **2005**, *8*, 1199-1222.

[76] Bandini, M.; Eichholzer A.; Umani-Ronchi, A. An update on catalytic enantioselective alkylations of indoles. *Mini Rev. Org. Chem.*, **2007**, *4*, 115-124.

[77] Kato, Y.; Furutachi, M.; Chen, Z.-H.; Mitsunuma, H.; Matsunaga, S.; Shibasaki, M. A homodinuclear $Mn(III)_2$-Schiff base complex for catalytic asymmetric 1,4-additions of oxindoles to nitroalkenes. *J. Am. Chem. Soc.*, **2009**, *131*, 9168-9169.

[78] Mouri, S.; Chen, Z.-H.; Matsunaga, S.; Shibasaki, M. Direct catalytic asymmetric aldol reaction of *β*-keto esters with formaldehyde promoted by a dinuclear Ni2-Schiff base complex. *Chem. Commun*., **2009**, 5138-5140.

[79] Marcelli, M.; Vander-Haas, R. N. S.; Van-Maarseveen, J.; Hiemstra, H. Asymmetric organocatalytic Henry reaction. *Angew. Chem. Int. Ed. Engl.*, **2006**, *45*, 929-931.

[80] Li, H.; Wang, B.; Deng, L. Enantioselective nitro-Aldol reaction of *α*-ketoesters catalyzed by cinchona alkaloids. *J. Am. Chem. Soc*., **2006**, *128*, 732-733.

[81] Liu, X. G.; Jiang, J. J.; Shi, M.; Development of axially chiral bis(arylthiourea)-based organocatalysts and their application in the enantioselective Henry reaction. *Tetrahedron Asymmetry*, **2007**, *18*, 2773-2781.

[82] Colak, M.; Aral, T.; Hosgoren, H.; Demirel, N. Synthesis of novel chiral Schiff-base ligands and their application in asymmetric nitro aldol (Henry) reaction. *Tetrahedron Asymmetry*, **2007**, *18*, 1129-1133.

[83] Guo, J.; Mao, J.-C. Asymmetric Henry reaction catalyzed by bifunctional Copper-based catalysts. *Chirality*, **2009**, *21*, 619-627.

[84] Salaün, J. Cyclopropane derivatives and their diverse biological. *Top. Curr. Chem.*, **2000**, *207*, 1-67.

[85] Kureshy, R. I.; Khan, N. H.; Abdi, S. H. R.; Patel, S. T.; Iyer, P. Chiral Ru(II) Schiff base complex-catalysed enantioselective epoxidation of styrene derivatives using iodosyl benzene as oxidant. *J. Mol. Catal. A Chem.*, **1999**, *150*, 175-183.

[86] Munslow, I. J.; Gillespie, K. M.; Deeth, R. J.; Scott, P. Bidentate carbenoid ester coordination in ruthenium(II) Schiff-base complexes leading to excellent levels of diastereo- and enantioselectivity in catalytic alkene cyclopropanation. *Chem. Commun.*, **2001**, 1638-1639.

[87] Sun, W.; Xia, C.-G.; Wang, H.-W. Efficient heterogeneous catalysts for the cyclopropanation of olefins. *New J. Chem.*, **2002**, *26*, 755-758.

[88] Tanner, D. Chiral aziridines - their synthesis and use in stereoselective transformations. *Angew. Chem., Int. Ed. Engl.*, **1994**, *33*, 599-619.

[89] Hodgson, D. M.; Gibbs, A. R.; Lee, G. P. Enantioselective desymmetrisation of achiral epoxides. *Tetrahedron*, **1996**, *52*, 14361-14384.

[90] Li, Z.; Fernndez, M.; Jacobsen, E. N. Enantioselective ring opening of meso aziridines catalyzed by tridentate Schiff base Chromium(III) complexes. *Org. Lett.*, **1999**, *1*, 1611-1613.

[91] Wu, B.; Gallucci, J. C.; Parquette, J. R.; RajanBabu, T. V. Enantioselective ring-opening enantioselective desymmetrization of meso-aziridines with $TMSN_3$ or TMSCN catalyzed by discrete Yttrium complexes. *Angew. Chem. Int. Ed.*, **2009**, *48*, 1126-1129.

[92] Bolm, C.; Schlingloff, G.; Weickhardt, K. Optically active lactones from a Baeyer-Villiger-type metal-catalyzed oxidation with molecular oxygen. *Angew. Chem., Int. Ed. Engl.*, **1994**, *33*, 1848-1849.

[93] Yamada, T.; Takahashi, K.; Kato, K.; Takai, T.; Inoki, S.; Mukaiyama, T. The Baeyer-Villiger oxidation of ketones catalyzed by Nickel(II) complexes with combined use of molecular oxygen and an aldehyde. *Chem. Lett.*, **1991**, 641-644.

[94] Gusso, A.; Baccin, C.; Pinna, F.; Strukul, G. Platinum-catalyzed oxidations with hydrogen peroxide: enantiospecific Baeyer-Villiger oxidation of cyclic ketones. *Organometallics*, **1994**, *13*, 3442-3451.

[95] Uchida, T.; Katsuki, T. Cationic Co(III)(salen)-catalyzed enantioselective Baeyer-Villiger oxidation of 3-arylcyclobutanones using hydrogen peroxide as a terminal oxidant. *Tetrahedron Lett.*, **2001**, *42*, 6911-6914.

[96] Watanabe, A.; Uchida, T.; Itob, K.; Katsuki, T. Highly enantioselective Baeyer-Villiger oxidation using Zr(salen) complex as catalyst. *Tetrahedron Lett.*, **2002**, *43*, 4481-4485.

[97] Kagan, H. B. In *Catalytic Asymmetric Synthesis*, 2nd ed.; Ojima, I., Ed.; Wiley-VCH: New York, **2000**; Chapter 6c.

[98] Pitchen, P.; Dunach, E.; Deshmukh, M. N.; Kagan, H. B. An efficient asymmetric oxidation of sulfides to sulfoxides. *J. Am. Chem. Soc*., **1984**, *106*, 8188-8193.

[99] Di Furia, F.; Modena, G.; Seraglia, R. Synthesis of chiral sulfoxides by metal-catalyzed oxidation with *t*-butyl hydroperoxide. *Synthesis*, **1984**, 325-326.

[100] Bolm, C.; Dabard, O. A. G. (*S*,*S*)-4,4′-Bis(3-hydroxy-estra-1,3,5(10),6,8-pentaene): an efficient ligand for the catalytic asymmetric oxidation of sulfides to sulfoxides. *Synlett*, **1999**, 360-362.

[101] Palucki, M.; Hanson, P.; Jacobsen, E. N. Asymmetric oxidation of sulfides with H_2O_2 catalyzed by (salen)Mn(III) complexes. *Tetrahedron Lett.*, **1992**, *33*, 7111-7114.

[102] Bolm, C.; Bienewald, F. Asymmetri sche sulfid-oxidation mit Vanadium-Katalysatoren und H_2O_2. *Angew. Chem.*, **1995**, *107*, 2883-2885.

[103] Bolm, C.; Bienewald, F. Asymmetric oxidation of dithioacetals and dithioketals catalyzed by a chiral Vanadium complex. *Synlett*, **1998**, 1327-1328.

[104] Vetter, A. H.; Berkessel, A. Schiff-base ligands carrying two elements of chirality: matched-mismatched effects in the Vanadium-catalyzed sulfoxidation of thioethers with hydrogen peroxide. *Tetrahedron Lett.*, **1998**, *39*, 1741-1744.

[105] Kokubo, C.; Katsuki, T. Highly enantioselective catalytic oxidation of alkyl aryl sulfides using Mn-Salen catalyst. *Tetrahedron*, **1996**, *52*, 13895-13900.

[106] Hon, S.-W.; Li, C.-H.; Kuo, J.-H.; Barhate, N. B.; Liu, Y.-H.; Wang, Y.; Chen, C.-T. Catalytic asymmetric coupling of 2-naphthols by chiral tridentate oxovanadium(IV) complexes. *Org. Lett.*, **2001**, *3*, 869-872.

[107] Chu, C.-Y.; Hwang, D.-R.; Wang, S.-K.; Uang, B.-J. Chiral oxovanadium complex catalyzed enantioselective oxidative coupling of 2-naphthols. *Chem. Commun*., **2001**, 980-981.

[108] Guo, Q.-X.; Wu, Z.-J.; Luo, Z.-B.; Liu, Q.-Z.; Ye, J.-L.; Luo, S.-W.; Cun, L.-F.; Gong, L.-Z.; Highly enantioselective oxidative couplings of 2-naphthols catalyzed by chiral bimetallic oxovanadium complexes with either oxygen or air as oxidant. *J. Am. Chem. Soc*., **2007**, *129*, 13927-13938.

[109] Coppola, G. M.; Schuster, H. F. *α-Hydroxy Acids in Enantioselective Synthesis VCH*, Weinheim: Germany, **1997**.

[110] Schultz, M. J.; Sigman, M. S.; Recent advances in homogeneous transition metal-catalyzed aerobic alcohol oxidations. *Tetrahedron*, **2006**, *62*, 8227-8241.

[111] Rebecca, A.; Shiels, K. V.; Christopher, W. J. Polymer and silica supported tridentate Schiff base Vanadium catalysts for the asymmetric oxidation of ethyl mandelate - activity, stability and recyclability. *Adv. Synth. Catal.* **2008**, *350*, 2823-2834.

[112] Alonso, D.A.; Gmjarro, D.; Pinho, P.; Temme, O.; Andersson, P.G. (1*S*, 3*R*, 4*R*)-2-Azanorbornylmethanol, an efficient ligand for Ruthenium-catalyzed asymmetric transfer hydrogenation of ketones. *J. Org. Chem.*, **1998**, *63*, 2749-2751.

[113] Matsumura, K.; Hashiguchi, S.; Ikariya, T.; Noyori, R. Asymmetric transfer hydrogenation of *α*,*β*-acetylenic ketones. *J. Am. Chem. Soc.*, **1997**, *119*, 8738-8739.

[114] Kwong, H.-L.; Lee, W.-S.; Lai, T.-S.; Wong, W.-T. Ruthenium catalyzed asymmetric transfer hydrogenation based on chiral P,N,O Schiff base ligands and crystal structure of a ruthenium (II) complex bearing chiral P,N,O Schiff base ligands. *Inorg. Chem. Commun*., **1999**, *2*, 66-69.

[115] Iwakura, I.; Hatanaka, M.; Kokura, A.; Teraoka, H.; Ikeno, T.; Nagata, T.; Yamada, T. The reactive intermediate of catalytic borohydride reduction by Schiff base-Cobalt complexes. *Chem. Asian J.* **2006**, *1*, 656-663.

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