

Metal–Salen Schiff base complexes in catalysis: practical aspects

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Schiff base ligands are considered “privileged ligands”¹ because they are easily prepared by the condensation between aldehydes and imines. Stereogenic centres or other elements of chirality (planes, axes) can be introduced in the synthetic design. Schiff base ligands are able to coordinate many different metals, and to stabilize them in various oxidation states, enabling the use of Schiff base metal complexes for a large variety of useful catalytic transformations. Practical guidelines for the preparation and use of different Schiff base metal complexes in the field of catalytic transformations are discussed in this *tutorial review*.

1 Introduction

Hugo Schiff described the condensation between an aldehyde and an amine leading to a Schiff base in 1864.² Schiff base ligands are able to coordinate metals through imine nitrogen and another group, usually linked to the aldehyde. Modern chemists still prepare Schiff bases, and nowadays active and well-designed Schiff base ligands are considered “privileged ligands”. In fact, Schiff bases are able to stabilize many different metals in various oxidation states, controlling the performance of metals in a large variety of useful catalytic transformations. In this article we show that Schiff bases are also able to transmit chiral information to produce non-racemic products through a catalytic process; chiral aldehydes or chiral amines can be used. From a practical point of view, the aspects involved in the preparation of Schiff base metal complexes are spread out in the literature. We wish to summarize and introduce some practical guidelines for the preparation and use of Schiff base metal complexes in catalysis. The present review will focus on the different ways of preparing metal complexes and their use in catalytic processes. Generally,

active catalytic Schiff base metal complexes are obtained *in situ*, and are not well characterized. However, the appropriate choice of metal precursor and the reaction conditions are crucial for catalytic properties. Finally, a particular class of Schiff bases will also be discussed. When two equivalents of salicylaldehyde are combined with a diamine, a particular chelating Schiff base is produced. The so-called Salen ligands, with four coordinating sites and two axial sites open to ancillary ligands, are very much like porphyrins, but more easily prepared. Although the term Salen was used originally only to describe the tetradentate Schiff bases derived from ethylenediamine, the more general term Salen-type is used in the literature to describe the class of [O,N,N,O] tetradentate bis-Schiff base ligands (Fig. 1). Basic guidelines for the design,

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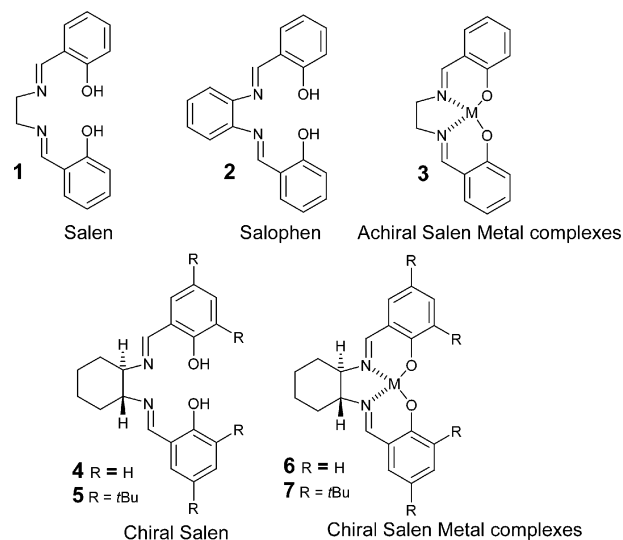


Fig. 1 Different Salen ligands and M(Salen) complexes.

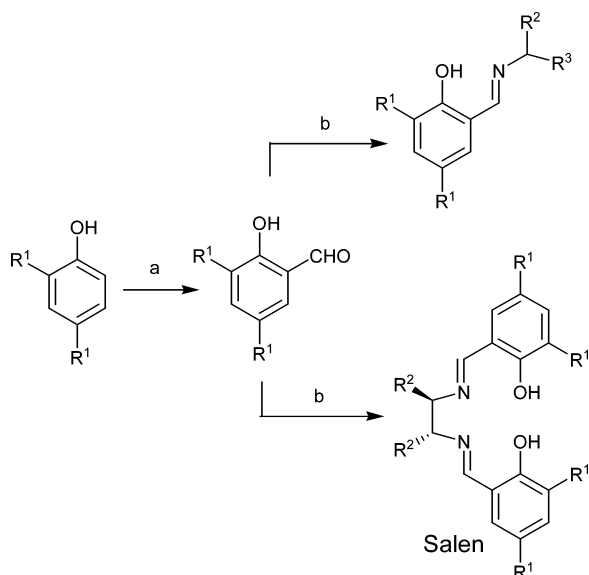
synthesis and application of metal Schiff base complexes in catalysis will thus be surveyed with the emphasis on the relevant problems in producing active and useful complexes.

Preparation of Schiff bases

Condensation between aldehydes and amines is realized in different reaction conditions, and in different solvents. The presence of dehydrating agents normally favours the formation

of Schiff bases. MgSO_4 is commonly employed as a dehydrating agent.

The water produced in the reaction can also be removed from the equilibrium using a Dean Stark apparatus, when conducting the synthesis in toluene or benzene. Finally, ethanol, at room temperature or in refluxing conditions, is also a valuable solvent for the preparation of Schiff bases. Degradation of the Schiff bases can occur during the purification step. Chromatography of Schiff bases on silica gel can cause some degree of decomposition of the Schiff bases, through hydrolysis. In this case, it is better to purify the Schiff base by crystallization. If the Schiff bases are insoluble in hexane or cyclohexane, they can be purified by stirring the crude reaction mixture in these solvents, sometimes adding a small portion of a more polar solvent (Et_2O , CH_2Cl_2), in order to eliminate impurities. In general, Schiff bases are stable solids and can be stored without precautions. Condensation of salicylaldehydes or salicylaldehyde derivatives with 1,2-diamines leads to the formation of one extremely important class of ligands, generally known as ‘‘Salens’’ (Fig. 1). Salicylaldehydes bearing different substituents are obtained by the introduction of a formyl group, using a simple and well-established reaction, into the corresponding phenol derivatives (Scheme 1, a). The combinatorial approach to the discovery of



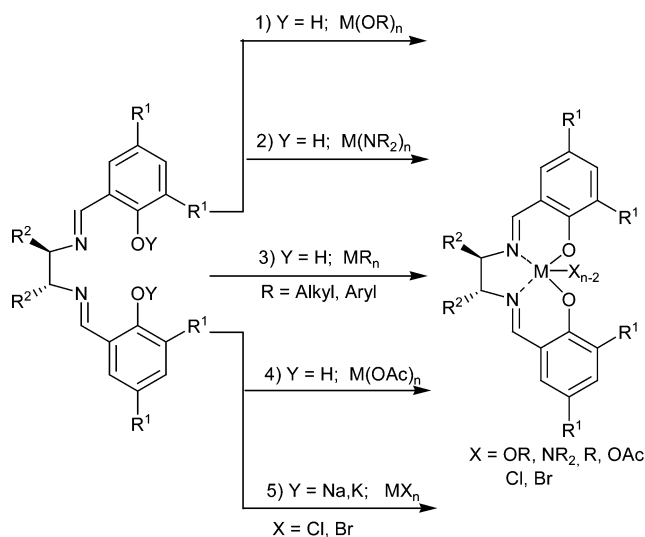
Scheme 1 Preparation of Schiff bases.

new catalysts is an innovative and exciting area of research.³ Schiff bases are suitable ligands for the preparation of libraries due to the easy reaction conditions and the variety of chiral amines and aldehydes used as precursors. Amino acids and peptides are particularly suitable for the creation of effective catalysts, as indicated in the research of Hoveyda and Snapper.⁴ The condensation of aldehyde-bearing coordinating groups with amino acids and peptides provides interesting Schiff bases, used to make a combinatorial library of ligands.³

The complexation steps: different routes

In many catalytic applications Schiff base metal complexes are prepared *in situ* by producing a reaction between the Schiff base and available and well-defined metal complexes. This approach is clearly simple and suitable for catalytic applications. Essentially, five different synthetic routes can be identified for the preparation of Schiff base metal complexes (Scheme 2).

Route 1 involves the use of metal alkoxides ($\text{M}(\text{OR})_n$). For early transition metals ($\text{M} = \text{Ti}, \text{Zr}$), alkoxide derivatives are



Scheme 2 Preparation of Schiff base complexes.

commercially available and easy to handle, while the use of other alkoxide derivatives is more problematic, particularly in the case of highly moisture-sensitive derivatives of lanthanides. The reaction of a Schiff base with a metal alkoxide is an equilibrium reaction and the identity of the species generated is sometimes difficult to predict. Different complexes can be present in different concentrations, as a function of the equilibrium constant. However, the introduction of a bulky group in the Schiff bases can control the identity and homogeneity of the complex, by shifting the equilibrium towards the formation of a single species. The stability of the complexes is regulated by the equilibrium constant, and a disproportionation between Schiff base metal complexes and the metal alkoxides can occur. The disproportionation between the metal Schiff bases and metal alkoxides is also affected by the substitution pattern of the Schiff base, but bulky groups normally prevent the Schiff base complex from undergoing disproportionation. Metal alkoxides are sensitive to hydrolysis and the presence of adventitious water can result in the formation of μ -oxo species. Additionally, metal Schiff bases bearing alkoxide groups as ligands, are sensitive to traces of water, producing various μ -oxo species. The presence of adventitious water is difficult to control, especially when the reaction between the Schiff bases and the metal alkoxide is performed *in situ*. The formation of μ -oxo species can cause difficulties in reproducing the results of catalytic reactions. Metal amides $\text{M}(\text{NMe}_2)_4$ ($\text{M} = \text{Ti}, \text{Zr}$) are also highly suitable precursors for the preparation of Schiff base metal complexes of early transition metals. The reaction occurs *via* the elimination of the acidic phenolic proton of the Schiff bases, occurring at the same time as the formation of volatile NHMe_2 . The reaction of $\text{Ti}(\text{NMe}_2)_4$ or $\text{Zr}(\text{NMe}_2)_4$ with Salen gives a Schiff base metal complex bearing two bisamido groups that can be reacted further. The reaction of the bis-amido Salen complex with Me_3SiCl transforms the bis-amido into the bis-chloride complex. A Schiff base metal complex can be prepared in a clean and effective way using metal alkyl complexes as precursors (route 3). Various metal alkyls in the main group of metals (AlMe_3 , GaMe_3 , InMe_3) are commercially available and can be used in the preparation of Schiff bases by a direct exchange reaction. In this context, particularly suitable for the synthesis of iron, manganese, vanadium and copper Schiff bases are the corresponding $\text{M}(\text{Mesityl})_n$ ($\text{M} = \text{Fe}, \text{Mn}, \text{V}, \text{Cu}$, Mesityl = 2,4,6-trimethylbenzene) compounds. They are obtained from the reaction of the corresponding metal halides with a mesityl Grignard reagent. This reaction only liberates a by-product, 3,5,6-trimethylbenzene (mesitylene). Although the synthesis of mesityl metal complex

precursors can be difficult due to their sensitivity, their use can avoid the presence of an uncharacterized impurity or the formation of binuclear complexes. Alkyl titanium and zirconium tetrabenzyl alkyl complexes are used in the preparation of Schiff base metal complexes, that are active as polymerization catalysts. These alkyl reagents are obtained from titanium and zirconium halides by the reaction of a benzyl Grignard reagent. As indicated in route 4, many Schiff base metal complexes can be obtained through the treatment of the Schiff base with the corresponding metal acetate, normally by heating the Schiff base in the presence of the metal salt under reflux conditions. Copper, cobalt and nickel Schiff bases are prepared using the corresponding acetate $M(\text{OAc})_2$ ($M = \text{Ni}, \text{Cu}, \text{Co}$). Instead of using acetate, a direct exchange with metal halides is also possible. In fact, early transition Schiff bases are sometimes prepared by direct reaction with TiCl_4 or ZrCl_4 . All the methods presented (routes 1–4) are used for Schiff bases or Salen metal complexes. The synthetic scheme presented in route 5 is quite effective in obtaining Salen metal complexes. It consists of a two-step reaction involving the deprotonation of the Schiff bases and a successive reaction with metal halides. Deprotonation of the acidic phenolic hydrogen can be realized using lithium bases (MeLi , BuLi). However, since lithium alkyls can attack the imine group of the Schiff base, it is advisable to perform the deprotonation step with NaH or KH in coordinating solvents. The deprotonation step is normally rapid at room temperature, but heating the reaction mixture to reflux does not cause decomposition. Use of excess NaH and KH is recommended, when the Na and K Salen obtained are soluble in the reaction solvent. THF is the solvent generally used for this type of preparation, and the sodium or potassium hydride used in excess can be eliminated by filtration, when the formation of the $\text{Na}_2(\text{Salen})$ or $\text{K}_2(\text{Salen})$ is complete. The reaction scheme is quite general, and metal halides other than titanium and lanthanides could be used. Instead of adding the metal halides to the reaction mixture, the use of available tetrahydrofuran adducts, such as $\text{TiCl}_4(\text{THF})_2$, $\text{ZrCl}_4(\text{THF})_2$, or $\text{VCl}_3(\text{THF})_3$, is more effective. When not commercially available, the tetrahydrofuran adducts of metal halides are easily prepared by the addition of THF to metal halides in a different solvent, normally CH_2Cl_2 . Tetrahydrofuran adducts are moderately sensitive salts, and can rapidly be handled freely in air. However, in the case of the more sensitive $\text{VCl}_3(\text{THF})_3$ and $\text{TiCl}_3(\text{THF})_3$ this procedure is not recommended. When large amounts of Salens are available, performing the synthesis on a large scale could be recommended using route 5. However, this synthetic strategy can create problems in the purification steps, during the isolation of the Schiff base metal complex. The reaction of $\text{Na}_2(\text{Salen})$ or $\text{K}_2(\text{Salen})$ with metal halides generates sodium or potassium salts as by-products. Generally, the formation of the Salen metal complex *via* route 5 is performed in THF and the insoluble sodium or potassium halides obtained as by-products can be eliminated by filtration. However, as the oxygens of the $M(\text{Salen})$ are Lewis basic centers, coordination of sodium or potassium halides could result, leading to many problems in the purification of the Schiff base metal complexes. For catalytic purposes, when synthesis is performed *in situ* by route 5, the presence of coordinated salts can alter the catalytic performance of the Schiff base metal complexes.

Substitution and conformational effects in Schiff bases

Coordination of the metal with bi- or tridentate Schiff bases can produce dimeric, or a saturated metal complex. Particularly with early transition metals, which have a tendency to coordinate ligands in an octahedral manner, the complexation step realized *in situ* can produce a saturated octahedral complex. When chiral Schiff bases are used in the catalytic process,

the formation of a saturated inactive complex is detrimental to catalysis. The formation of stable or saturated complexes is, of course, a factor of lack of efficiency in the catalytic process. The introduction of bulky substituents near the coordination sites can eliminate this problem and enhance the catalytic performance of the Schiff base metal complex, thus preventing the early transition Schiff base complexes from forming stable and catalytically inert octahedral complexes. Metals coordinated to Schiff bases can transmit chiral information *via* the coordination of the electrophile to the Lewis acidic center, or *via* an activation of the nucleophile. Metal Salen complexes have the unusual characteristic of activating, in certain reactions, both the nucleophile and the electrophile. In the transfer of carbene, nitrene or oxene (Fig. 2), the structure of Salen influences the

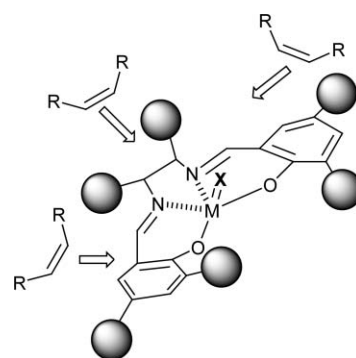


Fig. 2 Different approaches of a substrate to the Salen complex.

incoming trajectory of the substrate and its orientation. Although stereogenic centres are normally placed in the diamine moiety, subtle conformational effects transfer the chiral information. $M(\text{Salen})$ can adopt different conformations, as shown by crystallographic studies.

While a few $M(\text{Salen})$ complexes show planar conformations, most of the examples reported in the literature show a bowl (or umbrella, Fig. 3A) conformation, and a stepped



Fig. 3 Different shapes of Salen complexes.

non-planar conformation is also assumed by the complex in the solid state (Fig. 3B). In the stepped conformation, the degree of folding is correlated to the size of the metal, its oxidation state, the absence or presence of apical ligands, and the nature of the substituent. $\text{Cr}(\text{v})(\text{Salen})$ is folded, while the corresponding $\text{Cr}(\text{III})(\text{Salen})$ is near planar.⁵ The conformation of Salen in the particular oxidation state influences the trajectory of approach of the incoming substrate. Therefore, bulky groups on the aromatic aldehyde do not block the approach but regulate the orientation of the incoming substrates, determining a high diastereofacial preference.

When different elements of chirality are present in the same ligand, the conformational effects are more pronounced. This is the case for the Salen described by Katsuki⁵ (Fig. 4).

$M(\text{Salen})$ like **8** and **9**, with a chiral binaphthyl or similar structure, belong to the second generation of $M(\text{Salen})$. $M(\text{Salen})$, when different chiral elements are not combined, belongs to the first generation. The ligand conformation in Fig. 4, where a binaphthyl unit is combined with diamine containing stereogenic centers, is dictated by at least two factors. The combination of stereogenic elements controls the folding. The binaphthyl ligands bring an aryl group close to the metal.

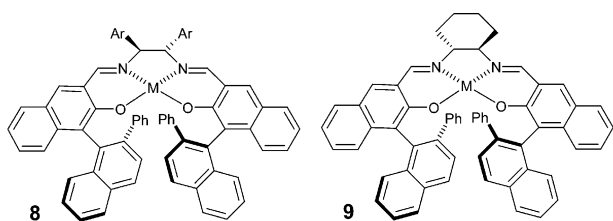


Fig. 4 The second generation of Salen.

The polar π -interactions occurring between the aryl group and an apical ligand, usually water, can act synergistically with a folding effect, usually water, can act synergistically with a folding effect. The folding effect, deriving from the conformation imposed by the chelating diamine moiety, is thus enhanced in these Salens, compared to other Salen metal complexes. On the other hand, these effects can act conversely, reducing the folding. In general, the fact of the absence of an axial coordinating ligand can either reduce or enhance the folding of the metal complex. This is important for the transmission of chiral information. Theoretical calculations have shown that axial donor ligands, which change the conformation of the catalyst, bring the metal closer to the substrate in rate-determining stereoselective processes, enhancing the enantioselectivity (Fig. 5).

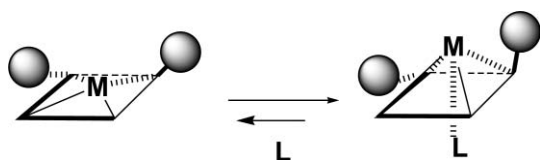


Fig. 5 Effect of an axial ligand on the Salen complex.

2 Chiral Schiff bases of early transition metals

The Ziegler–Natta catalyst was originally based on the combination of TiCl_4 with alkylaluminum, and it was soon discovered that MgCl_2 -supported titanium was more stable and more active. The breakthrough, due to the introduction of group 4-metallocene as a well-defined metal complex, in combination with partially hydrolyzed trimethylaluminum (methylalumoxane, MAO), has made the industrial application of these catalysts possible. Soon it was realized that a system able to mimic the coordination properties of metallocene would be able to perform polymerization as well. In this context Schiff bases were widely used, because they can control the coordination properties of the metal and form a coordination environment, similar to a metallocene (Fig. 6). In fact, Schiff bases

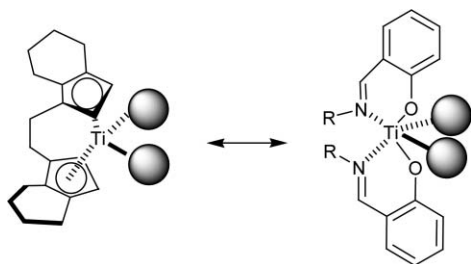


Fig. 6 Formal equivalence between indenyl complexes and Schiff bases.

possess many interesting characteristics. They are moderate electron donors, with a chelating structure and a low electron counting number. In addition, a large library of Schiff bases can easily be generated, with structural diversity, both sterically

and electronically. Schiff base complexes of early transition metals are active catalysts for polymerization, provided that some simple criteria in the synthetic design are met.⁶

The coordination of phenoxy-imine to zirconium and titanium displays a distorted octahedral structure, with two nitrogen atoms and two chlorine atoms in *cis* position. It is important to realize that several isomers are possible, and the stability and reactivity are functions of the substituents of the Schiff bases. The introduction of bulky groups in the phenoxy ring near to the oxygen is important, in order to stabilize these Schiff bases and make them synthetically useful for polymerization. Interestingly, the octahedral and C_2 -symmetric Ti- and Zr-bis(phenoxyimine) complexes are chiral at the metal, with the titanium assuming a fluxional Λ or Δ configuration (Fig. 7).

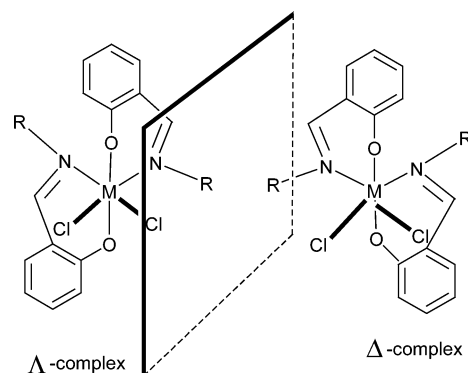


Fig. 7 A fluxional octahedral Schiff base complex.

Although the rapid exchange in the polymerization process is beneficial to stereocontrol, the formation of different diastereoisomers can cause low stereocontrol in other reactions, especially if stereogenic centers are inserted in the ligands. For this reason, the chiral Schiff bases employed in catalysis with early transition metals have been designed specifically to avoid the problem. Two solutions have been indicated by various authors in the course of their studies on the use of Schiff base early transition metal complexes: a) the use of tridentate or tetradentate Schiff bases; b) the use of Salen as a rigid tetradentate coordinating framework. Tridentate Schiff base ligands have been used successfully in several asymmetric catalytic reactions. In this type of catalysis, the size of the substituents on the periphery of the ligand plays a key role in determining the enantiomeric excess of the product. The reaction with $\text{Ti}(\text{O}i\text{Pr})_4$ and Schiff base ligands is clean only if the R^1 group is bulky (Scheme 1). When R^1 is not bulky, two ligands can coordinate titanium, even if it is present in stoichiometric amounts. Thus, the reaction between a tridentate ligand and $\text{Ti}(\text{O}i\text{Pr})_4$ can give three different isomers. A *t*-butyl group is normally sufficient to control the formation of an active monomeric species, while groups such as hydrogen, bromine or methoxy result in significant amounts of diastereoisomeric titanium species. The octahedral titanium species containing two ligands are inactive because of this kind of reaction, and, in general, this can be assumed in other reactions, if a Lewis acidic titanium centre is needed. Most importantly, the formation of the diastereoisomeric $L^*_2\text{Ti}$ species reduces the number of catalytically active species and, when the percentage of $L^*_2\text{Ti}$ is greater, the concentration of free titanium isopropoxide able to catalyze processes resulting in no stereoselection is higher. These considerations have a practical importance in the design of proper, successful Schiff bases in catalytic processes. Chiral tridentate Schiff bases are used with vanadium to promote the asymmetric oxidation of

sulfides, disulfides, and thioacetal. The importance of these results stems from the simple preparation of the vanadium Schiff base metal complexes and from the importance of the enantioenriched products obtained.⁷ Also, in the case of Ti(Salen) complexes different species are formed by the reaction of Ti(OiPr)₄ and chiral Salen. Traces of water are responsible for the formation of oxo species. Oxo titanium species (Fig. 1, 7, M = Ti(O)) are clearly shown to be effective catalysts by Belokon and North for the enantioselective addition of Me₃SiCN to aldehydes and ketones.⁸ Also, the corresponding chiral VO(Salen) **10** (Fig. 1, 7, M = V(O)) is an effective catalyst. Metal Salen oxo species are stable to moisture and can be used for catalytic reactions in environmentally-friendly catalytic conditions. Detailed mechanistic studies have shown that the active species in this reaction is a bimetallic titanium complex.⁹ The reaction shows one of the peculiar characteristics of the Salen metal complexes: the ability of a Salen metal complex to act cooperatively (Fig. 8). This unique

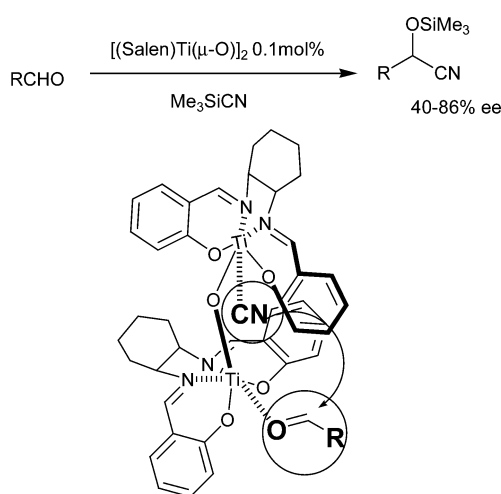
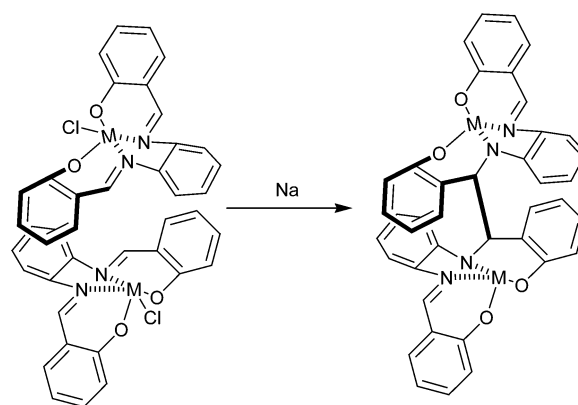


Fig. 8 Ti(Salen) catalysed addition of Me₃SiCN to aldehydes *via* activation of both electrophile and nucleophile.

behaviour, which is more pronounced in other M(Salen) (Cr, Co) mediated processes, is highly advantageous for designing processes in which activation of nucleophile and electrophile is necessary.

The advantages of working with VO(Salen) are the high stability of the complex and simple synthesis from commercially available VOSO₄. However, it is necessary to perform the synthesis under nitrogen or argon, to avoid the formation of cationic V(v)O(Salen). Various titanium Salen Schiff bases can also be prepared by direct exchange with TiX₄, or by reaction with a sodium or potassium salt of the Schiff bases.⁷ These Ti(Salen)X₂ complexes contain two reactive sites, but attempts to alkylate TiLX₂ could result in decomposition, reduction or the migration of the alkyl group to the imino group of the Schiff base. The redox chemistry mediated by vanadium or titanium Schiff bases can involve variations in the oxidation state of the metal or the ligand. In fact, with some Schiff bases, chosen specifically because they have highly delocalized π electrons, as in Salophen or [*N,N*-phenylenebis(salicyleneimine)] (Fig. 1, 2), the reduction of the metal becomes extremely difficult. This is an important aspect to evaluate when working with Schiff bases. Oxidation or reduction can occur exclusively to the ligand. The consequent reductive coupling of the imino group across two monomeric units of Schiff bases leads to the formation of a C–C bond (Scheme 3).

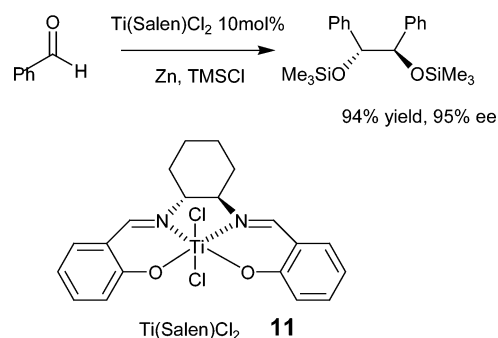
Although the electrons received by the system are stored in a C–C bond, reduced vanadium and titanium Salophen are able



Scheme 3 Coupling of a metal Schiff base promoted by a reductant.

to react with oxygen and organic molecules. A key point in the development of redox chemistry, particularly catalytic redox chemistry with Schiff bases, is the control of the deactivation of the system and possible dimerization *via* coupling of the imino group. Redox transformations, based on titanium and vanadium, are well known.¹⁰ In fact, titanium in a low oxidation state was reported to perform useful C–C bond-forming reactions by McMurry.¹¹ Different methods employing various titanium salts have successfully been introduced. For all of these, titanium is used in stoichiometric amounts. Recently, Fürstner introduced a catalytic variant of these methods.¹² Catalytic redox reaction is based on two concepts: the use of a metal able to reduce the titanium complex in the active form, although not interfering with the C–C bond-forming reaction, and the use of an oxophilic additive as a mediator of the catalytic cycle. Chlorosilanes and silicon hydrides appear to be suitable additives.

Schiff base complexes are able to stabilize titanium in a low oxidation state and enable the control of simple diastereoselection in the pinacol coupling of aromatic aldehydes.¹³ The reactions are performed using the protocol developed by Fürstner. The presence of the oxophilic additive Me₃SiCl does not decompose the Schiff base titanium complexes. Low valent chiral titanium Schiff bases mediate the enantioselective pinacol coupling of aromatic aldehydes (Scheme 4).¹⁴ The



Scheme 4 Enantioselective pinacol coupling promoted by Ti(Salen).

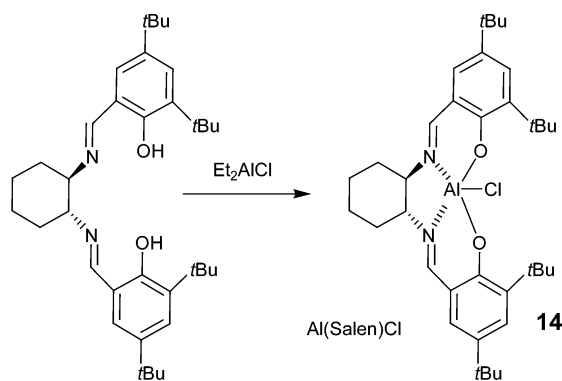
unsubstituted Salen gives the highest enantiomeric excess. On the other hand, bulky groups need to be introduced with tridentate Schiff bases in order to stabilize the Ti(III) Schiff base.¹³ In the enantioselective pinacol coupling reported by Joshi,¹⁴ the author describes an interesting synthetic approach towards Ti(Salen)Cl₂ **11** (Fig. 1, 6, M = TiCl₂) avoiding the use of TiCl₄ or NaH, or KH.

The Ti(Salen)Cl₂ **11** is formed by treating the corresponding Ti(Salen)(OiPr)₂ with Me₃SiCl. Hoveyda, Snapper and coworkers have used peptide Schiff base ligand libraries in

the presence of $\text{Ti}(\text{O}i\text{Pr})_4$ to promote the addition of Me_3SiCN to epoxides and imines.¹⁵ In a mechanistic analysis of the reaction, the cooperative role of the Schiff base peptide ligand was disclosed. These Schiff base peptide ligands are modular ligands consisting of three assembled fragments. All three fragments of the peptide catalyst work together in delivering the nucleophile (CN^-) to the substrate, coordinated to the titanium.¹⁶ This is another example of the cooperative mechanism acting in asymmetric catalysis. Modular ligands assembled with different parts can be advantageously exploited whenever activation of both nucleophile and electrophile is necessary. Zirconium Schiff bases are well known, easily prepared by exchange with $\text{Zr}(i\text{OPr})_4$ or by the addition of $\text{ZrX}_4(\text{THF})_2$ to the sodium or potassium salt of the Schiff bases. Although chiral zirconium Salens are rarely used in catalysis, an interesting chiral transformation mediated by $\text{Zr}(\text{Salen})\text{Cl}_2$ has been reported. Chiral $\text{Zr}(\text{Salen})\text{Cl}_2$ **12** (Fig. 4, **9**, $\text{M} = \text{ZrCl}_2$) was described as catalyzing a Baeyer–Villiger oxidation for particular substrates in a highly enantioselective way.¹⁷ On the other hand, zirconium is more electrophilic, and the imine of the Schiff bases coordinated to the zirconium is highly activated. Zirconium Schiff bases can be unstable in the presence of nucleophiles or hydrides. In a recent study, Hoveyda reported that zirconium peptide Schiff bases are able to catalyze the addition of zinc reagents to imines.¹⁸ However, under reaction conditions, a reduction of the imine of Schiff base to the corresponding amine took place.¹⁸ Imine bonds of the Schiff bases are quite susceptible to reduction or nucleophilic attack, especially when zirconium is coordinated to the imino bond. Reduction or alkylation always needs to be taken into account as a possible pathway for the deactivation of the catalyst, whenever a Schiff base is employed as a ligand.

3 Chiral Schiff bases of main group metals

Group 13 Salen metal complexes are easily obtained from the reaction of a Schiff base with a group 13 alkyl (Scheme 5).¹⁹

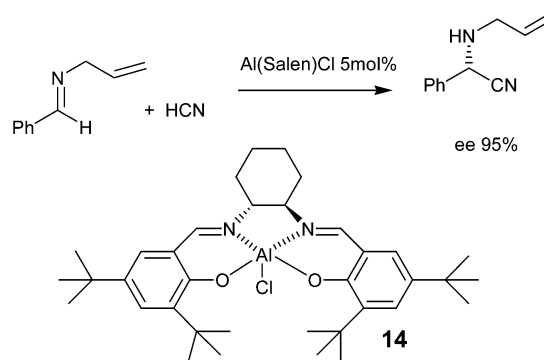


Scheme 5 Preparation of $\text{Al}(\text{Salen})$ metal complexes.

Gallium, aluminium and indium Salen metal complexes¹⁹ can be prepared using this protocol. Generally speaking, the reaction is performed in toluene by adding the alkyl derivatives at a low temperature and warming the solution up to room temperature. Although the complexes are quite stable, care needs to be taken in the synthesis. In fact, it has been reported that, with achiral Schiff bases, harsh conditions, such as refluxing in high boiling solvents, caused alkylation in the imine of the Schiff bases. In the synthesis of metallic complexes, oxygen-containing solvents are normally avoided. The Schiff base metal complex is insoluble, and is recovered by filtration. If the synthesis is performed using a Salen ligand, five-coordinate metal complexes are generally obtained.

The group 13 metal Salen complexes containing halide (Cl,

Br, I), $\text{M}(\text{Salen})\text{X}$ are prepared using the alkyl reagents R_2MX ($\text{X} = \text{Cl}, \text{Br}, \text{I}$). Difficulties in the isolation and characterization of the complexes can arise from the low solubility of the complexes. It is worth noting that Schiff base complexes can also combine and, sometimes, the oxygen atom of a Schiff base can become the sixth ligand donor. In order to facilitate the isolation and characterization of Schiff base complexes, the introduction of a *t*butyl group in an *ortho* or *para* position, on the aromatic aldehyde, makes the complex soluble even in hydrocarbon solvents. The structural characterization of the compounds shows five-coordinate complexes that can be trigonal bipyramidal, or square pyramidal, depending on the nature of the backbone to which the two nitrogen atoms are connected. The greater the flexibility of the backbone, the more frequently a trigonal bipyramidal geometry is obtained. An important aspect of the coordination chemistry of Schiff base complexes is how the metal is displaced out of the plane of the ligand core. This distance is important in catalysis as it allows the transmission of chiral information, and is crucial to the catalytic step. In group 13 Salen complexes this distance is the function of the metal radii, and in $\text{In}(\text{Salen})$ complexes higher displacement normally occurs. Note that the alkyl groups are displaced more than the corresponding halides. Alkyl and chloride Salen complexes are quite robust, and can be handled in the open air without decomposition. This is an important aspect of $\text{Al}(\text{Salen})$ complexes, which can be advantageously used for catalytic applications. The complete displacement of one coordinate ligand from the Schiff base complex causes the formation of the cationic complex. For example, the dissolution of the achiral Salen $\text{Al}(\text{Salen})\text{Cl}$ **13** (Fig. 1, **3**, $\text{M} = \text{AlCl}$) in protic bases (H_2O , MeOH), or in the presence of aprotic ligands (THF , HMPA), leads to the formation of cationic hexacoordinate $\text{Al}(\text{Salen})\text{L}_2$. Interestingly, cationic $\text{Al}(\text{Salen})$ complexes seem to be quite stable, and can also be generated in water. Cationic complexes of Al are involved in the polymerization of oxiranes and the polymerization of ethylene.¹⁹ Additional reactions were examined, among them Meerwein–Ponndorf–Meerwein reduction, Friedel–Crafts reactions, Oppenauer oxidation, phospho aldol reaction, Diels–Alder reactions and Claisen rearrangements.¹⁹ Amido, alkoxy, oxo, hydroxy, $\text{Al}(\text{Salen})$ compounds can easily be prepared by exchange reactions, using $\text{Al}(\text{Salen})\text{R}$ alkyl derivatives ($\text{R} = \text{Me}, \text{Et}$). The rapid formation of pentacoordinate compounds combined with their Lewis acidic properties, make $\text{Al}(\text{Salen})$ a good candidate for catalysis. In this context, Jacobsen reported the use of chiral $\text{Al}(\text{Salen})\text{Cl}$ complex **14** in the addition of HCN to imines (Scheme 6).²⁰



Scheme 6 Catalytic enantioselective addition of hydrogen cyanide to imines catalysed by $\text{Al}(\text{Salen})\text{Cl}$.

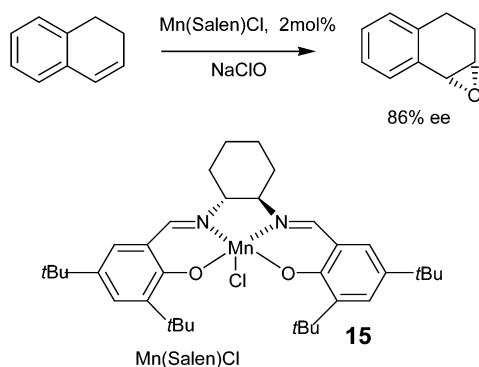
The reaction probably takes place *via* a double activation process, in which one molecule of $\text{Al}(\text{Salen})$ delivers the nucleophile and one activates the substrate. This double activation is a general feature in $\text{Al}(\text{Salen})$ chemistry and the

Michael catalyzed addition of CN^- , CNCH_2COOR and N_3^- to amides takes place in this way.²¹ The formation of the activated catalytic complex is obtained by the exchange reaction *in situ* and commercially available $\text{Al}(\text{Salen})\text{Cl}$ **14** is used. The tendency to exchange the fifth apical coordination site in the $\text{Al}(\text{Salen})$ complex can be attributed to the relatively weak bond between the group 13 element and the group occupying the apical position. This type of bond can be described more appropriately as electrostatic. The particular substrates used in the Michael reaction are determined by the propensity of the Salen to coordinate a carbonyl in the axial position *via* a monodentate coordination. α,β -Unsaturated oxazolidinone, or other Michael acceptors, are not suitable for this chemistry.

4 Manganese and chromium Schiff bases

In 1985 Kochi described the first application of the achiral chromium Salen complex in catalysis.²² Careful synthetic and mechanistic investigations have prompted further exciting developments in this field.²³

Chiral manganese Salen complexes were described by Jacobsen and Katsuki. The chiral ligand **5** developed by Jacobsen is easily prepared by using accessible methods and reactions.²⁴ The manganese complex **15** (Fig. 1, $\text{M} = \text{MnCl}$) is normally prepared using $\text{Mn}(\text{OAc})_2$ and subsequent oxidation of the intermediate $\text{Mn}(\text{II})(\text{Salen})$ by exposure to air. Complexes containing chloride ions are obtained by an exchange reaction performed during work-up, through treatment with chloride-containing aqueous solution. On the other hand, chiral and achiral $\text{Mn}(\text{II})(\text{Salen})$ are more difficult to obtain, and much more sensitive. Chiral $\text{Mn}(\text{III})(\text{Salen})$ complexes are quite efficient catalysts for the asymmetric epoxidation of *cis* olefins. Oxidation takes place with $\text{PhI}=\text{O}$, or derivatives, but other oxidants, such as NaClO , H_2O_2 , NaIO_4 , and peracid have also been used (Scheme 7).

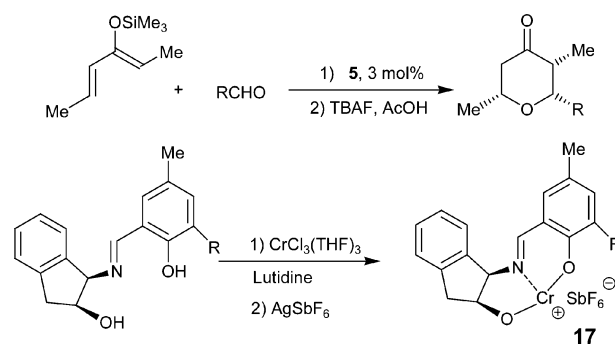


Scheme 7 Enantioselective epoxidation promoted by $\text{Mn}(\text{Salen})\text{Cl}$.

The key intermediate is an $\text{Mn}(\text{O})(\text{Salen})$, studied using spectroscopic and theoretical calculations. An analysis of the mechanism of the reactions suggests that a stepped conformation of the Salen is crucial in transmitting chiral information. The ligand introduced by Jacobsen is now commercially available, or can easily be prepared, while the ligand described by Katsuki is obtained from Binol (Binol = 1,1'-bi-2-naphthol) following several synthetic steps. Katsuki's $\text{Mn}(\text{Salen})$ complex **16** (Fig. 4, **8**, $\text{M} = \text{MnCl}$, $\text{Ar} = \text{Ph}$) gave higher turnover numbers with respect to Jacobsen's ligand, but its application in catalytic enantioselective reactions has only been reported on a small scale. It is quite important to note that, in the application of Jacobsen–Katsuki asymmetric epoxidation, olefins bearing aromatic substituents, or bearing double or triple bonds, are normally used. This could be determined by the possible orientation of the alkene when it is approaching the $\text{Mn}(\text{oxo})$ derivatives. Theoretical calculations have also

underlined the stepwise mechanism of epoxidation, which, to some extent, leads to the formation of a variable amount of *trans* epoxide, when the radical intermediate is stabilized by polar substituents on the alkene. The admittance of co-ligands to the reaction mixture, particularly pyridine *N*-oxides, is of practical importance. The ligand has multiple roles. As discussed earlier, the ligands force the manganese oxo to come closer to incoming olefins. More importantly, the $\text{Mn}(\text{O})(\text{Salen})$ is in equilibrium in different forms, while the oxo ligand can coordinate another $\text{Mn}(\text{Salen})$. Regarding epoxidation, the dimer is considered inactive. Axial ligands are able to stabilize the monomer form of the complex. Easy catalyst deactivation and irreversible ligand oxidation have prompted recent efforts to stabilize the active form of the catalyst. This concept is realized by isolating the $\text{Mn}(\text{Salen})$ catalyst through the use of cross-linked polymer supports, and immobilization in polysiloxane, zeolites or supramolecular multimetallic architectures.²⁵

Chromium Schiff bases have found some interesting applications in catalysis. Tridentate and tetradentate achiral Schiff bases provide stabilizing ligands for polymerization catalysis and, due to their accessibility, libraries of ligands are easily prepared. The introduction of bulky groups in an *ortho* position to the phenoxy group is the key action in preparing highly active complexes for polymerization, using late transition metals. The methodology employed for the synthesis of the complex chromium Schiff bases is interesting. The soluble organometallic precursor (*p*-tolyl) $\text{CrCl}_2(\text{THF})_3$, obtained from the addition of Grignard reagents to $\text{CrCl}_3(\text{THF})_3$, is added to the Schiff base. Metalation, with the formation of the chromium Schiff bases, occurs by the elimination of toluene.²⁶ The use of organometallic precursors avoids the route *via* potassium or sodium salts of the Schiff base and eliminates the tedious problem of the purification of NaCl or KCl byproducts. Chiral tridentate Schiff bases are prepared by a different route. Jacobsen reported the Cr Schiff base metal complex **17** as a catalyst for highly diastereoselective and enantioselective hetero Diels–Alder, inverse electron demand hetero Diels–Alder (Scheme 8), and hetero-ene reactions.²⁷ Catalysis is

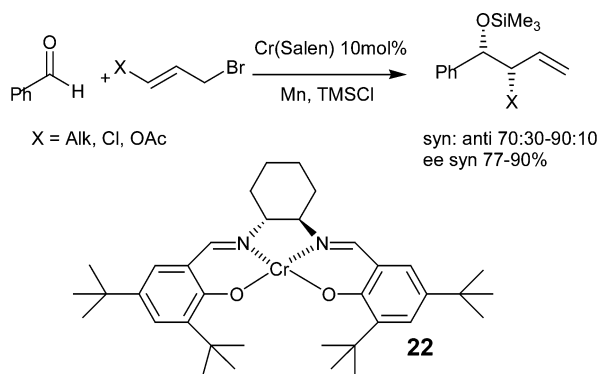


Scheme 8 Enantioselective hetero Diels–Alder reaction promoted by a chiral tridentate chromium Schiff base.

sometimes performed in the presence of a dehydrating agent as the structure of the catalyst is dimeric, and the octahedral chromium coordinates water.

The new methodology for the preparation of the catalyst is shown in Scheme 8. The coordination of the chromium complex takes place by means of $\text{CrCl}_3(\text{THF})_3$ in the presence of a base, such as lutidine. The method for the preparation of achiral and chiral $\text{Cr}(\text{Salen})\text{X}$ metal complexes is interesting. Chiral $\text{Cr}(\text{Salen})\text{Cl}$ **18** (Fig. 1, **7**, $\text{M} = \text{CrCl}$) is normally obtained by using $\text{Cr}(\text{II})\text{Cl}_2$, which is commercially available, and operating under a strictly nitrogen atmosphere. When complexation of the Salen has occurred, producing a brown

solution, the flask is exposed to the air and stirred. Complexation between CrCl_3 and Salen does not take place, and the use of $\text{Na}_2(\text{Salen})$ or $\text{K}_2(\text{Salen})$ in combination with $\text{CrCl}_3(\text{THF})_3$ is essential. Synthesis with CrCl_2 is sometimes difficult, since this salt is highly sensitive to the air. Moreover, this route is not recommended for certain applications, because CrCl_2 contains a variable amount of water, which can modify the coordination and properties of the $\text{Cr}(\text{Salen})$ obtained. However, water coordinated to $\text{Cr}(\text{Salen})$ is essential to promote a catalytic cycle. In the addition of Me_3SiN_3 to epoxides described by Jacobsen,²⁸ the formation of active $\text{Cr}(\text{N}_3)(\text{Salen})$ complex **19** (Fig. 1, 7, $\text{M} = \text{Cr}(\text{N}_3)$) is determined by the water present in the reaction mixture. The difficulties in obtaining chiral $\text{Cr}(\text{III})(\text{Salen})\text{Cl}$ for epoxidation reaction have prompted Gilheany to explore a different route. The reduction of purified $\text{Cr}(\text{III})$ performed with $\text{Na}(\text{Hg})$ has proven to be an efficient strategy to prepare the $\text{Cr}(\text{II})$ *in situ*, while allowing the preparation of chiral $\text{Cr}(\text{Salen})\text{X}$ complexes.²⁹ Kochi's work on the epoxidation reaction with achiral $\text{Cr}(\text{Salen})$ ²² **20** (Fig. 1, 3, $\text{M} = \text{CrCl}$) did not follow in an efficient enantioselective methodology until Gilheany discovered that the epoxidation of *trans* olefins can be carried out in the presence of stoichiometric and catalytic amounts of stable oxo $\text{Cr}(\text{Salen})$ **21**, (Fig. 1, 7, $\text{M} = \text{Cr}(\text{O})$) with iodosylbenzene as an oxygen source.³⁰ An interesting mechanistic analysis of the reaction by DFT calculation has shown the intriguing way in which Salen is able to transmit stereochemical information during the epoxidation reaction.²⁹ We have presented a different route for a chiral $\text{Cr}(\text{Salen})$ **22** (Fig. 1, 7, $\text{M} = \text{Cr}$) for a specific application, by reducing the insoluble CrCl_3 in THF or in CH_3CN with solid Mn .³¹ Other research groups have adopted this methodology for the preparation of optically active chromium complexes. $\text{Cr}(\text{Salen})\text{Cl}$ **18** has remarkable properties, and should be regarded as a privileged complex, as it can be used for many different applications. Jacobsen has described catalytic reactions and has discovered an interesting feature of $\text{M}(\text{Salen})$ metal complexes: namely, that there is a cooperative mechanism enabling $\text{Cr}(\text{Salen})$ to activate the nucleophile and the electrophile and assemble them in a well organized transition state. $\text{Cr}(\text{Salen})\text{Cl}$ **18** is treated with a silver salt (AgOTf , AgPF_6 , AgBF_4) to promote the formation of cationic chromium complexes. Chiral cationic $\text{Cr}(\text{III})(\text{Salen})$ is able to promote catalytic enantioselective reactions in which the Cr complex behaves like a chiral Lewis acid, as also reported by Katsuki.⁵ Catalytic redox reaction can also be performed by $\text{Cr}(\text{Salen})$ s. The enantioselective version of the Nozaki–Hiyama reaction (Scheme 9) was described using a catalytic



Scheme 9 Catalytic enantioselective and diastereoselective redox reactions promoted by $\text{Cr}(\text{Salen})$.

amount of $\text{Cr}(\text{Salen})$ **22**.³¹ The mechanistic analysis of the reaction shows that the aggregation between different molecules of $\text{Cr}(\text{Salen})$ is responsible for the enantioselectivity obtained. The simple general *syn* diastereoselection obtained

by the $\text{Cr}(\text{Salen})$ mediated addition of stereogenic allyl halides to aldehydes, is of considerable interest.³¹

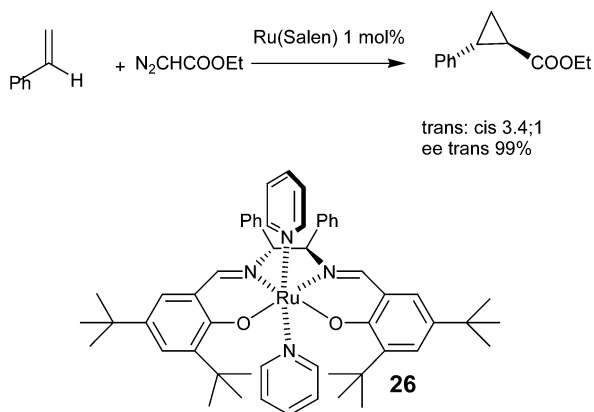
5 Iron and ruthenium Schiff base complexes. A useful source of carbene

A variety of enzymes are able to catalyze different reactions such as oxidation, reduction and isomerization, containing iron bound to porphyrin (Heme). Given the similarity between Salen and porphyrins, recent work has been directed towards exploiting iron Schiff bases in order to promote different catalytic reactions. Preparation of $\text{Fe}(\text{Salen})\text{Cl}$ **23** (Fig. 1, 3, $\text{M} = \text{FeCl}$) seems quite straightforward, since FeCl_3 hydrated in refluxing ethanol is used, but the material can be contaminated by iron μ -oxo species. Dimeric chiral and achiral $\text{Fe}(\text{Salen})$ μ -oxo species are prepared by Nguyen and used in catalytic transformations.³² An interesting approach to the synthesis of quite sensitive $\text{Fe}(\text{II})(\text{Salen})$ considers the use of an organometallic reagent. Fe_2Mes_4 is prepared from $\text{FeCl}_2(\text{THF})_{1.5}$ using standard mesityl Grignard.³³ Fe_2Mes_4 is a rather sensitive compound, but can react with the acidic phenolic oxygens of the Salen to produce the formation of the desired $\text{Fe}(\text{II})(\text{Salen})$ in pure forms. $\text{Fe}(\text{II})(\text{Salen})$ is sensitive to oxygen and moisture, and difficult to handle. The easy oxidation of $\text{Fe}(\text{Salen})$ has hampered its use in catalysis. Different approaches to the synthesis of Schiff base complexes using stable precursors have also been considered. Bolm reported the preparation of a tridentate Schiff base iron catalyst, prepared *in situ* from $\text{Fe}(\text{acac})_3$, which is able to promote the enantioselective oxidation of sulfide to sulfoxides.³⁴ Although the enantiomeric excesses obtained were inferior to the excesses using the same process catalyzed by vanadium, the possibility of preparing libraries of Schiff bases will certainly increase enantiomeric excess. The dimeric μ -oxo $\text{Fe}(\text{Salen})$ s prepared by Nguyen have found an interesting use as stable precursors for the generation of iron carbene complexes, able to catalyze the enantioselective cyclopropanation of olefins with ethyl diazoacetate.³⁵

The synthesis of $\text{Ru}(\text{Salen})$ was realized using a nitrosyl as precursor.⁵ Many ruthenium complexes can serve as catalysts for various oxidation reactions. Asymmetric epoxidation can be exploited by ruthenium complexes to reach moderate levels of enantioselectivity. Nitrosyl chloro(Salen) ruthenium complexes **24** and **25** (Fig. 4, 8 and 9, $\text{M} = \text{Ru}(\text{NO})\text{Cl}$) are described by Katsuki⁵ in interesting reactions mediated by visible light. The complex is, in fact, coordinatively saturated so that irradiation by visible light makes it active, leading to the dissociation of the apical nitrosyl ligand. An electron transfer mechanism seems to be involved in these transformations. The scope of ruthenium Salen epoxidation is quite interesting, since *cis* and *trans* olefins can be epoxidated. Chiral $\text{Ru}(\text{Salen})$ **24** is also used to promote cyclopropanation of olefins. The intermediate carbene is approached by the olefin, and the highly-stepped second generation of Katsuki's Salen complexes have an ideal structure for exhibiting high diastereo- and enantioselectivity. The synthesis of $\text{Ru}(\text{Salen})$ without the nitrosyl group was difficult to realize, until Nguyen reported that ruthenium(II) Salen complexes were a very efficient catalyst for the cyclopropanation of olefins.³⁵ The key discovery of the synthesis was the stabilization of the intermediate $\text{Ru}(\text{II})\text{Salen}$ by pyridine, as shown in **26** (Scheme 10).

6 Co(Salen). Useful catalyst for opening epoxides

Achiral $\text{Co}(\text{Salen})$ **27** (Fig. 1, 3, $\text{M} = \text{Co}$) has a well-established ability to bind oxygen.³⁶ The square pyramidal coordination geometry, imposed by the Salen framework, is necessary for $\text{Co}(\text{II})$ complexes to obtain the correct electronic configuration



Scheme 10 Catalytic enantioselective and diastereoselective cyclopropanation catalyzed by Ru(Salen).

for O_2 binding. This property has stimulated research into selective binding of O_2 with reversible carriers,³⁷ able to perform the catalytic oxidation of organic substrates.³⁸ In particular Co(Salen) **27** has been used for the preparative oxidation of phenols, indoles, flavonols and amines. The electrochemistry and ligand exchange were investigated in different solvents. The complexation with a stronger donor molecule makes Co(Salen) a stronger reducing agent. The binding ability of O_2 to Co(Salen)-type complexes depends on the basicity of the axial ligand. More importantly, oxidation takes place *via* the coordination of the substrate to the cobalt. Organic substrates containing donor atoms (phenols, indoles, and amines) are more easily oxidized.³⁹ As in Nature, Schiff base metal complexes were designed to include a cavity, in order to accommodate dioxygen or some small ligands.⁴⁰ However, as already presented in this review, non-covalent secondary interactions are essential in order to obtain selective and efficient catalysts with Salen metal complexes. The tailored design of a Salen cobalt complex with the introduction of non-covalent secondary interactions was recently reported by Crego-Calama and Reinhoudt.⁴¹ Coordination of the donor atom to the cobalt metal center was used in order to insert the Co(Salen) into an insoluble matrix. Polyaniline appears to be a suitable supporting reagent for Co(Salen), since the presence of nitrogen atoms enables the stabilization of the complexes by axial coordination.⁴² Copolymerization of particular Co(Salen) complexes into porous material provides a reversible oxygen carrier, suitable for the storage/release of gases.⁴³

MetalloSalen cobalt complexes are useful for the transfer of carbene and for opening epoxides. The cobalt(II) Salen complexes are readily prepared by using Co(OAc)_2 . The oxidation from Co(II) to Co(III) can be realized by treating Co(II) with air and acetic acid, or using various acids in the presence of air. Other counter ions can be introduced by oxidation performed with the cationic ferrocenium Cp_2FeX , where X is PF_6 , BF_4 . Oxidation conducted with ferrocenium gives the soluble Cp_2Fe that can be purified by extraction. Reduction of the Co(Salen) **27** complex to a formal Co(I) and re-oxidation to Co(III) *via* oxidative addition, could be another route for the catalytically active Co(III)Salen. Co(I)(Salen) **28**, an extremely air-sensitive compound, is able to activate small and inert molecules, such as CO_2 .⁴⁴ Reduced Co(I)(Salen) is prepared by treatment of the Co(II) complex with Na or K sand. An important feature of M(Salen) complexes is shown by these cobalt(I) complexes. The Salen is a bifunctional molecule with a Lewis acid (metal center) and Lewis basic center (oxygen of the Schiff bases). Coordination of the Na or K molecules takes place through the oxygen of the Salen. Activation of the inert CO_2 takes place through the two metals.⁴⁴ Addition of carbene by Co(Salen) is described by different groups with different Salen-type

molecules. Interestingly, Schiff bases are described and then used to promote carbene addition, as well as other transformations. Chiral Co(III)(Salen) **29** (Fig. 1, 7, M = Co) has been used for the kinetic resolution of epoxides promoted by water.⁴⁵ The mechanism of the reaction involves double activation, which is a feature of the Salen complexes. Water coordinated to Co(Salen) is delivered to an epoxide coordinated to another molecule of Co(Salen). The special spatial arrangement in which the transmission of the chiral information is maximized was defined by Jacobsen as “head to tail” (Fig. 9).

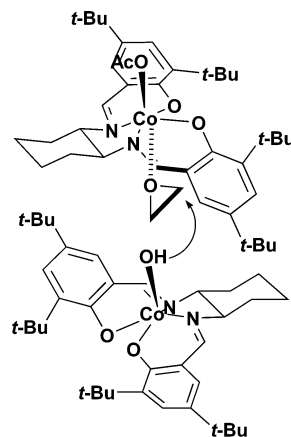


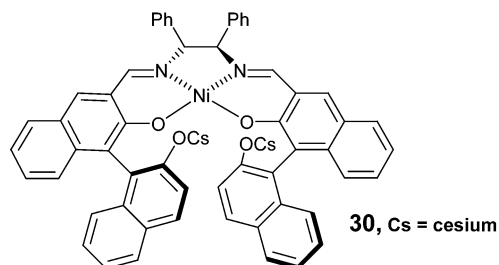
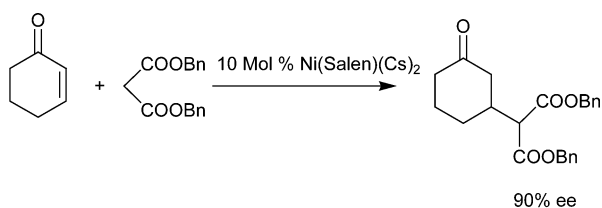
Fig. 9 Supramolecular arrangements “head to tail” between two Salen units.

This particular arrangement is found in many dimeric structures of Salens, and can derive from minimizing steric hindrance between the two Salen molecules. The feature has been proven by careful kinetic analysis and by the synthesis of different models. This feature is also important in improving the catalytic performance of the system, based on Salen. In fact, several oligomeric and dendritic Co(Salen) prepared on the basis of trial and error, have been used for the kinetic resolution of epoxides,⁴⁵ showing an increased activity. The new frontier in these studies is to build up an innovative geometry for a dimeric transition state, in which two molecules of Salen are involved, using different reactions and different metals.

7 Nickel and copper transition metal Schiff bases

Schiff bases have an important role to perform as polymerization catalysts, and are able to stabilize a reactive cationic nickel complex. In order to stabilize cationic intermediate nickel complexes, the Schiff bases are prepared using the reaction of hindered aromatic amines (2,6-diisopropylaniline) with diketones. Although Ni(Salen) complexes have not found many applications in catalysis, their planar coordination geometry constitutes an interesting platform to coordinate other metals. The Schiff bases are able to act as a metalla crown, and an interesting structure containing different metals can result. Ni(Salen) **30** bearing another metal can behave as a bifunctional catalyst, as prepared by Kozłowski (Scheme 11).⁴⁶

Copper Schiff bases have found a more extensive use, since copper(I) can be stabilized by Schiff bases and used in nitrene transfer.⁴⁷ Schiff bases derived from two types of diamine have also been described.⁴⁷ The preparation of the complexes generally uses copper(I), but copper(II) sources have also been considered. Similar results obtained in nitrene transfer are probably due to the fact that a reduction of copper(II) to copper(I) takes place, determined by the nitrene source. Due to the particular geometry and properties of the Schiff base, Cu(Salen) **31** (Fig. 1, 6, M = Cu) is able to coordinate ions, *via* the interaction with the oxygen of the Schiff base.⁴⁸ The



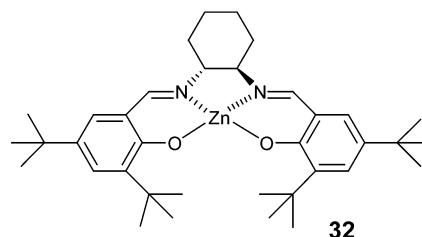
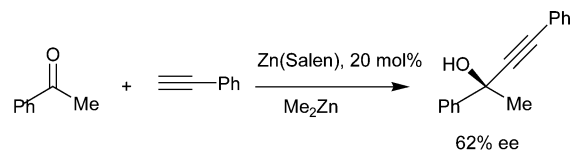
Scheme 11 Michael catalyzed addition by a bimetallic Ni(Salen) complex.

complexes are prepared by the reaction of Salen with copper acetate in ethanol. The Cu(Salen) is stable when exposed to air and moisture, and it is possible to perform enantioselective alkylation in phase transfer conditions.

8 Zn(Salen): catalytic addition of organometallic reagents

Several reports describe the synthesis of zinc(II) Salen complexes from either Zn(OAc)₂ or ZnCl₂/Et₃N. However, these routes can create some difficulties in isolating a pure metalated product. In some cases a mixture between the complex and the free Salen is isolated. A more direct route is the treatment of Schiff bases with the reactive alkyl derivatives ZnMe₂ or ZnEt₂. This strategy is an advantage compared to the use of Zn salts, since both alkyls are commercially available in toluene solution or hexane solution. Isolation of Zn(Salen), and its characterization by X-ray analysis, are facilitated by the use of pyridine. On the other hand, without pyridine the complex can be isolated in polymeric form, where the oxygen of the Schiff base coordinates the zinc of another molecule of Salen. Another possible Zn derivative for the synthesis of Zn Schiff bases is Zn[N(SiMe₃)₂]₂. The use of this reagent is particularly recommended for bidentate Schiff bases, because it is possible to avoid the formation of fully coordinated Zn Schiff base complexes. The intermediate Zn(Schiff base)hexamethylsilamide can be used as a starting material for the preparation of three mixed coordinated unsaturated (salicylaldiminato)-Zn(OR) complexes (where R = Me, Ph, or OCOMe), which are useful for catalytic applications. As in the case of Al(Salen), chiral Zn(Salen) **32** (Fig. 1, 7, M = Zn) shows interesting photophysical properties, and the luminescence of the complex is well recognized during its preparation.⁴⁹ Due to their stability in aqueous systems Schiff bases can be suitable for carrying active metals and investigating photophysical properties in biological systems. One of the reasons why it is difficult to crystallize anhydrous Zn(II) Salen complexes can be ascribed to the ability of Salen oxygen to coordinate metal and salts, even after chelation. This property can be used advantageously to develop new catalytic reactions. Zn(Salen) **32** can catalyze the addition of ZnEt₂ to aldehydes. We have reported the use of Salen in this “privileged” reaction,⁵⁰ and Kozłowski⁵¹ has modified the structure of Salen, using the same concepts and enhancing the reactivity of the system. Salen can act as a bifunctional catalyst, mimicking the common aminoalcohols widely used in Zn-mediated additions of Et₂Zn to aldehydes. Zn(Salen) **32** has the ability to promote the

addition of other organometallic reagents as well. Alkynylation has attracted considerable interest in recent years, as propargylic alcohols are valuable synthetic precursors. The undeveloped addition of alkynyl zinc reagents to ketones can be realized using Zn(Salen) as a catalyst, leading to new perspectives in the formation of quaternary stereocenters (Scheme 12).⁵²

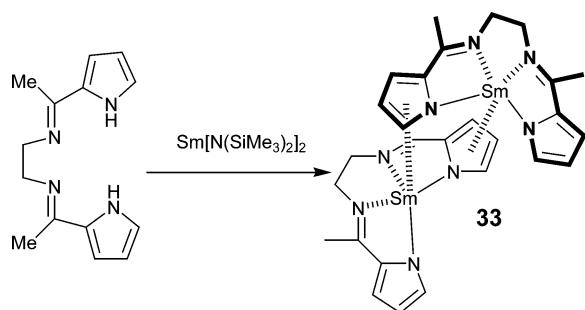


Scheme 12 Catalytic enantioselective alkylation of ketones promoted by Zn(Salen).

9 Lanthanide metal Schiff bases

Ligands able to coordinate lanthanides exhibiting a low coordination number can be considered a primary topic in modern f-element chemistry. Schiff bases, because of their simple synthesis, are a valuable alternative to the widely-employed and studied cyclopentadienyl framework. One of the great problems in coordinating lanthanide with Schiff bases derives from the small charge to the radius of the ions. In fact, lanthanides prefer to use higher coordination numbers. Lanthanides coordinated to Schiff bases have the propensity to yield dinuclear or polymeric species. Dianionic tetradentate ketoiminato Schiff base complexes can be prepared with low coordination number by the introduction of a bulky imido or aryloxo group. The starting material for the preparation of lanthanide Schiff base complexes is crucial, as well as the consideration of the ionic radii of the lanthanides employed. Higher coordination numbers are obtained by producing a reaction between the larger La or Nd and the Schiff bases. The choice between coordinating and uncoordinating solvents is also important. To isolate a mononuclear lanthanide complex from a reaction of a Schiff base with a larger lanthanide, it is necessary to perform the synthesis in coordinating solvents, *i.e.* THF. The coordinating solvent can bind to the metal ion, and is capable of preventing the formation of dimers or polymers. The synthesis of lanthanide Schiff bases is realized by the employment of suitable precursors. Anhydrous lanthanide trichloride is accessible by different synthetic methods. If the lanthanide Schiff base is prepared by route 5, purification of the complex is quite difficult as the Schiff base tends to bind sodium or potassium chloride. An alternative preparation uses alkyl lanthanides. These are usually quite difficult to obtain, and only a few reports concerning the synthesis of these species have been published to date. Another possible synthetic route for lanthanide Schiff bases involves special silylamide Ln[N(SiHMe₂)₂]₃. The use of other silylamides is problematic, and can lead to insoluble oligomeric complexes. The use of a special silylamide enables the coordination of the silicon atom to the lanthanide center. The imido complexes of lanthanide, resulting from this synthetic route, are interesting reactive intermediates for catalytic chemistry. In fact, an interesting

application of lanthanide Schiff base complexes in catalysis has been recently reported. RajanBabu⁵³ described an interesting yttrium complex surrounded by chiral Salen **5** in the catalytic kinetic resolution of alcohols. The complex is prepared by the silylamide route. X-ray analysis shows that the large yttrium ion is placed above the N₂O₂ plane, and two *cis* oriented coordination sites are probably involved in the catalytic reaction. Morken describes another active yttrium complex, prepared by a different route in the enantioselective variant of a Tishchenko reaction.⁵⁴ The combination between yttrium and the chiral Salen **5** was found in a combinatorial approach, in which several other ligands and metals were examined. The complex prepared using Y₅O(O*i*Pr)₁₃ is seven-coordinated and bridged by two hydroxide ions to a second yttrium atom. The structure is considerably folded. Lanthanides in a low oxidation state are important, and are used in organic chemistry. Low valent samarium iodide (SmI₂) introduced by Kagan, has found extensive use in redox chemistry, in the formation of organosamarium(III).⁵⁵ Chiral samarium complexes are still rarely developed, and Schiff bases provide an advantageous use of ligands, available on a large scale for stoichiometric enantioselective reactions. Unfortunately, Schiff bases are quite sensitive to samarium(II) reagents. In fact, the direct route to Sm(II) Schiff bases results in the formation of a dimeric Salen Sm, *via* the coupling of the imine (see Scheme 3). On the other hand, the reduction of Sm(III)(Salen) with a strong reducing agent causes the dimerization of the Schiff base. Recently the Sm(II) Schiff base **33** obtained directly by the combination of Sm(II)[N(SiMe₃)₂]₂ and the Schiff base ligand has been described. Stability of the Schiff bases, in the presence of an Sm(II) reagent, is determined by the introduction of a pyrrole ring able to coordinate η⁵ to samarium ion (Scheme 13).



Scheme 13 Stabilizing Sm(II) with pyrrole Schiff bases.

This strategy will be developed further in the future. The employment of Sm(II)[N(SiMe₃)₂]₂ requires Schlenk techniques and the reagent is quite moisture- and air-sensitive.⁵⁶

10 Conclusions

This overview of Schiff bases has been neither comprehensive nor exhaustive, and omissions of important contributions are regretted. We hope to have introduced some useful guidelines for preparing, handling, and designing new catalytic processes performed by Schiff base metal complexes.

As a challenging transformation, the formation of quaternary stereocenters requires the use of the rather unreactive ketones, so catalytic transformation which can enhance the reactivity of both nucleophiles and electrophiles will become increasingly more important in the future. Schiff base metal complexes can act cooperatively, and could be used with such difficult substrates. The introduction of chiral and achiral Schiff base metal complexes in proteins, or other biologically active molecules, can also be used to control different types of

substrate activation. Molecular recognition, supramolecular interaction and host-guest chemistry will almost certainly be used to design the next generation of chiral Schiff bases.

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