Chiral Salen Complexes: An Overview to Recoverable and Reusable Homogeneous and Heterogeneous Catalysts

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1. Introduction and Scope

Enantioselective catalytic reactions in which the chirality of an asymmetric catalyst induces the preferred formation of a given product enantiomer have been one of the most important achievements in chemistry during the 20th century.[1] Initially the successful enantioselective reactions using homogeneous chiral catalysts were limited to stereospecific alkene hydrogenations using chiral binaphthylphosphine ligands[2] and to the Sharpless epoxidation of allylic alcohols using tartaric acid derivatives as ligands.[3,4]

After proof of the principle of enantioselective catalysis, there was an evident interest in expanding these results to virtually any substrate as well as for any reaction type. In this context, a limitation of the Sharpless enantioselective epoxidation was the failure to induce enantioselectivity in simple alkenes lacking allylic hydroxy groups. For this reason, the report by Jacobsen and Katsuki that chiral (salen)−Mn(III) complexes act as highly enantioselective catalysts for the asymmetric epoxidation of simple alkenes constituted a breakthrough in the field of asymmetric catalysis.[5−12]

Following the lead of alkene epoxidation, Jacobsen, Katsuki, and other groups expanded the scope of enantioselective catalysis to other reactions.[13−22] The outcome of this body of research is that metal complexes derived from chiral salen ligands are among the most powerful enantioselective catalysts. The importance of chiral salen ligands in enantioselective catalysis is due to the high enantiomeric excesses that can be achieved and their general applicability to many different reaction types. Apparently, chiral salen ligands with bulky substituents create a strongly stereogenic environment at the active metal center, producing a remarkable discrimination between the two transitions states leading to each enantiomer. The result is a very effective transmission of chirality to the reaction product for a broad range of substrates and reaction types.

One general trend in catalysis is to develop systems that allow the recovery and reuse of the catalyst.[23,24] Environmental concerns together with economic considerations make necessary and convenient this recovery. The high catalyst cost, usually considerably much higher than that of the products, can be affordable in commercial applications only when the productivity of the catalyst, measured as total kilograms of product produced per kilogram of catalyst, is sufficiently high to make the process economically viable. On the other hand, the principles of green chemistry require industry to make all necessary efforts to minimize wastes, particularly those of substances that contain noxious transition metals such as those typically present in metallic catalysts.[25−27] Following this general trend, the development

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Hermenegildo (Herme) García was born in Canals, Spain, in 1957 and studied chemistry at the Faculty of Science of the Universidad de Valencia, Spain, from which he graduated in 1979 with honors. He did his Ph.D. research on preparative organic photochmiestry under the guidance of Professor Miguel A. Miranda and was awarded that degree also with honors by the Universidad de Valenica in 1983. Then he moved to the Technical University of Valencia, where he initiated his career in 1983, first as assistant professor and becoming finally full professor in 1996. In 1991, he was appointed a member of the Institute of Chemical Technology, a joint center depending on the Spanish National Research Council (CSIC) amd the Technical University of Valencia that was founded in that year. He did a postdoctoral stay at the Chemistry Department of the University of Reading, United Kingdom, with Professor Andrew Gilbert in 1987 and later three successive sabbatical leaves in 1992–1993 (one year), 1995 (six months), and 2000 (three months) at the University of Ottawa, joining the laser flash photolysis group led by Professor J. C. (Tito) Scaiano. He has co-authored over 250 papers, most of them dealing with the application of zeolites as hosts of organic guests and as solid catalysts. He has held five international patents, one of them in commercial application. His main current interests are in supramolecular photochemistry and photocatalysis, development of photoactive nanoscopic materials, and heterogeneouos catalysis.

of reusable chiral salen−metal complexes appears to be of great interest.

In this review, we summarize the efforts aimed at setting up methodologies for recovering and reuse of chiral salen ligands. There have been published numerous reviews and accounts describing the use of salen−metal complexes as catalysts, including enantioselective reactions,[14,18,19,28−33] focusing mainly on the outcome of the reaction.[19,30,34−42] This information will not be covered here, and the reader is referred to these sources for an overview of the salen complex types,[43,44] their synthesis,[14,32,45] reaction types that can be catalyzed, suitable media, and their catalytic activity with respect to other alternative complexes or catalysts. To avoid duplicity with existing literature, herein we will focus on chiral salen−metal ligands and comment on those papers that have described methodologies and strategies that allow the recovery and eventually reuse of these complexes of high added value.

Most of these strategies to recover chiral salen complexes are of general applicability for other types of metal complexes or ligands. Thus, it can be assumed that most of the methodologies described in this review for chiral salen complexes have been already used or can be used for other complexes as well. However, there are notable differences in the synthetic routes depending on the actual structure of the ligand. Some of the peculiarities of salen ligands arise from the ease and mild conditions required for their synthesis, which, in the most frequent case when the two phenolic moieties are identical, is a single-step process.

This review covers the literature up to the beginning of 2006 with special emphasis on the most recent developments. After a preliminary section with some general comments about enantioselective reaction types catalyzed by chiral salen−metal complexes and general methodologies applicable to the development of recoverable catalytic systems (section 2), the core part of the review is organized in two sections, one devoted to strategies in homogeneous catalysis and the other commenting on methodologies of reusable and recoverable salen catalysts that act in a heterogeneous phase. Thus, section 3 is devoted to homogeneous systems in which the catalyst is in the same phase as reagents and products. In the simplest approach, the salen−metal complex can be exactly the same as that used in conventional organic solvents, without the need of functionalization that may require dedicated organic synthesis. In the case of homogeneous catalysis, separation of the reaction mixture from the catalyst after the reaction finishes has to be done on the basis of selective filtration, extraction, crystallization, etc., of the products while the catalyst is retained in the phase where the reaction has occurred. Homogeneous phase recoverable systems enjoy several advantages with respect to heterogeneous catalysts including (i) the maximum synthetic economy because no special salen functionalization is needed, (ii) higher reaction rates, and (iii) simpler kinetics because no interfacial mass transport is occurring. Most of the disadvantages of the homogeneous phase arise from the difficulty in designing continuous flow processes for this type of catalysis and catalyst recovery.

Sections 4−7 describe those systems in which the salen−metal complex is in a solid phase, being inorganic, carbonaceous, and polymeric or hybrid organic−inorganic. Catalysis is heterogeneous, and the solid can be immobilized in a fixed-bed reactor or can be suspended in the reaction medium using stirred tank reactors and recovered by filtration. Prototypical industrial catalysts are solids,[46] because this allows the design of continuous flow processes. However, preparation of

supported salen complexes requires indefinitely stable complexes, and a suitable funtionalization to bind the complex to a solid; otherwise, long-term leaching of the metal from the solid to the fluid phase and/or complex decomposition can occur. Also, kinetics in heterogeneous catalysis can be controlled by diffusion and mass transport through the interfacial surface. These aspects determine that, normally, heterogenization used to be considered as the last step in the evolution toward a reusable and recoverable catalyst.[46] However, as we will discuss, recent developments in homogeneous catalysis based on the use of novel "green" liquid media may lead to changes in the preference for heterogeneous versus homogeneous catalysis.

In the last section of this review (section 8) we will discuss some prospects about the future developments in the field covered by this review, giving special emphasis to those aspects that still require further research to be solved satisfactorily.

2. General Considerations

2.1. Chiral Salen Complexes

The word "salen" is an acronym widely used to denote a family of bisimine compounds having a structure derived from the *N,N'*-bis(salicylidine)ethylenediamine. The first salen−metal complex was probably reported by Pfeiffer et al. in 1933.[47] As indicated in Scheme 1, salen ligands are generally obtained by the uncatalyzed condensation of a salicylaldehyde with a 1,2-diamine. The numbering corresponding to the carbon of the phenolic moieties has been shown in Scheme 1. The imine functional group is generally known as a Schiff base.[48] Schiff bases are among the most general N ligands, because the basicity of the sp²-hybridized N lone pair, although lower than that of amines (sp³ hybridization), is well suited to form complexes with metal ions.[48] The salicylidene imine group is prone to undergo an acid-catalyzed hydrolysis, reverting to the corresponding salicylaldehyde and diamine in the presence of water. However, the stability of the Schiff base group increases considerably upon coordination with a metal ion and formation of the salen−metal complex. For this reason, in contrast to the salen ligand, the salen−metal complex can be used in wet solvents or even in aqueous media without undergoing hydrolysis.

Chiral salen ligands are easily synthesized starting from enantiomerically pure diamines. 1,2-Cyclohexadiamine and 1,2-diphenylethylene-1,2-diamine are the two chiral diamines most frequently used. Chiral salens together with 1,1'-binaphthyls and bisoxazolidines are the chiral ligands that have been used to develop the most powerful metallic complexes in asymmetric catalysis.[49]

For most of the transition metals, the corresponding metallic complex using salen as ligand has been reported. The list includes among other metals Mn, Cr, Co, V, Cu,
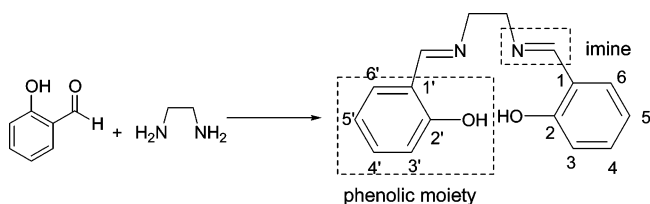
Ti, Ru, Pd, Au, Zn, and Al. Depending on the tetradentate N_2O_2 or pentadentate N_2O_2X coordination around the metal center, the complexes exhibit a distorted square planar or square pyramidal geometry.[8,50−52] Distorted octahedral $N_2O_2X_2$ coordination has been very frequently postulated for many intermediates involving salen−metal complex catalysts.

Chiral salen complexes have been found to act as catalysts of many different reaction types including alkene epoxidation, epoxide ring opening, cyclopropanations, aziridination, selective hydrogenations, carbonyl cyanosilylation, imine additions, and others. Table 1 provides a list of the reaction types reported using nonrecoverable chiral salen complexes, together with the enantiomeric excess (ee) achieved in each reaction and leading references. As commented above, the work that is going to be described in this review is the attempts and methodology developed to reuse the chiral salen catalysts for some of these reactions.

2.2. General Methodologies To Transform Homogeneous Salen−Metal Complexes into Recoverable and Reusable Catalysts

The trend toward the commercial production of optically pure compounds in the pharmaceutical and fine chemical industries has undoubtedly increased in recent years.[66−68] Among the various methods to selectively produce a single enantiomer, asymmetric catalysis is the most attractive method due to its synthetic economy and amplification of chirality. However, the contribution of asymmetric catalysis to the overall production of chiral chemicals is growing at a much slower rate than originally expected. The main reason for this slow industrial implementation is the need to have reusable chiral catalysts.

One of the major drawbacks of homogeneous enantioselective catalysis is the need for separation of the extremely expensive catalysts from the reaction mixture at the end of the process. Given the high value of the chiral catalysts, their recovery is a necessary condition to the development of a viable industrial process. Recoverable enantioselective catalysts with a high productivity are, therefore, necessary from the industrial point of view.

For these reasons, a general evolution in catalysis is the transformation of successful homogeneous catalysts into recoverable catalytic systems that can be easily separated from the reaction mixture and reused multiple times without the loss of the high activity and selectivity characteristic of the original catalyst.[23,24,46,69] In addition, to minimize the impact of the high cost of ligands and metals on the products, process design and waste minimization often require catalyst immobilization and catalyst recovery.[25−27] On the one hand, the conversion from a batchwise operation to a continuous flow process is facilitated by having the catalyst in a separate phase. On the other hand, complexes may have some noxious metal that have to be completely removed (even in trace quantities) from the reaction products and the disposal of which may be harmful for the environment and would require special handling.

Among the different strategies that have been used for the purpose of converting highly efficient homogeneous catalysts into recoverable and reusable catalytic systems, the simplest one consists of using the same complex, but changing the medium from conventional volatile organic solvents to novel "green" liquids. The necessary condition is that the catalyst has to remain in the novel liquid, whereas the products have

Scheme 1. Preparation of Salen Ligand and Numbering of Their Phenolic Moieties

phenolic moiety

to be separated by extraction, distillation, precipitation, membrane filtration, or other physical means. Given the relatively large molecular weight and structure of most catalysts, and specifically here those metal complexes based on salen ligands, the selective solubility requirement is often easily met when the liquid−liquid extraction is performed with an immiscible solvent with low solubility power such as an alkane or an ether. Organic products are commonly more soluble in such solvents than salen−metal complexes.

In this regard, the usual trend has been to combine the recovery of the catalyst with the use of an environmentally friendly novel medium. On the basis of the principles of green chemistry aimed at avoiding or reducing the use of volatile organic solvents,[25,26] for liquid substrates one option is to perform catalytic reactions under solvent-free conditions. However, in many cases solvents are still needed. Solventless conditions have as a general limitation the fact that the reaction products may act as quenchers or inhibitors of the catalyst. An important role of solvents in catalytic reactions is to assist desorbing products from the catalytic sites. Also, even though solventless conditions may be considered as ideal from the environmental point of view, this is true only when substrate conversion reaches very high percentages. Otherwise, product separation and catalyst recovery from unreacted starting material may be even more difficult, hazardous, or environmentally unfriendly than using conventional organic solvents.

Among the novel solvents that have been considered "green" as opposed to conventional volatile organic liquids, the most frequently used are water, perfluorinated liquids, supercritical fluids, and ionic liquids.[69] Given the importance of salen−metal complexes, examples of the use of salen−metal complexes as catalysts in any of these green solvents have been reported and reusability accomplished with a variable degree of catalyst activity decay.

In addition to the previous approach based on homogeneous catalysis in special liquid media, the next evolution for developing a recoverable and reusable catalytic system is transforming a homogeneous into a heterogeneous catalyst. Heterogeneous catalysts are easily separated from the reaction mixture and can be recovered and reused provided that they do not become deactivated during recycling. Also, if deactivation occurs, a suitable reactivation protocol can be devised to regain most of the initial activity, as, for instance, replenishing the depleted metal ions.

The simplest methodology to accomplish heterogenization is to support the active salen−metal complex onto or into an insoluble solid. The interaction between the complex and the support can range from physisorption to Coulombic forces and covalent anchoring. It is generally assumed that the latter approach, even though synthetically more demanding, gives the strongest complex-support binding, but, as we will show, this assumption should not be taken for granted and must be critically evaluated in each case. Concerning the support, it can be either organic polymers or inorganic oxides, each of them having advantages and limitations with respect to the other. The complex supported on a solid can be simply separated from the reaction mixture by filtration or placed in a continuous flow reactor.

A general condition for reusability in every recoverable system has to be the stability of the catalytic sites and maintenance of the catalytic activity. This point will be discussed in the next section.

2.3. Stability of Salen−Metal Complexes

Ideally for reusability, the complex has to be perfectly stable under the reaction conditions, a prerequisite that is difficult to meet. Although most of the salen−metal complexes have very high binding constants in the range of log $K > 20$,[70−72] demetalation of the complex can occur due to competitive complexation with reagents and products that can be favored by changes in the metal oxidation state during the catalytic cycle. Metal oxide formation is also common depending on the pH at which the reaction is performed and the presence of bases.

Besides demetalation, ligand degradation is also an important cause of complex instability, particularly when the catalytic reaction requires the presence of strong acids or oxidizing or reducing reagents. Acids can cause demetalation by protonation of the phenolate groups. This demetalation leads to the metal-free salen ligand that, as was stated earlier, is very prone to undergoing hydrolysis to salicylaldehyde and diamine.

Oxidation reactions require the presence of an oxidant in addition to certain acidic or basic conditions. Oxidizing reagents can attack the salen ligand at various sites including the imine and the phenolic ring. In general, Schiff bases can be easily oxidized. Reduction can also lead to complex degradation that is usually initiated by a reduction in the metal coordination number from penta- to tetra-coordinate.

In addition to advantages in terms of reaction mixture and engineering of the process, heterogenization can be also advantageous from the point of view of catalyst stability, as immobilization frequently improves catalyst stability compared to the homogeneous analogues. This stabilization can be attributed to steric constraints and site isolation that minimize complex degradation.

In general, it can be said that there is a paucity of studies dealing with salen−metal complex degradation even though these studies are necessary to assess the maximum theoretical productivity of the catalytic system. These stability studies should be performed prior to the determination of the most suitable immobilization procedure, because it may be useless to anchor a complex that will become degraded in a few catalytic cycles. Nevertheless, from the literature reports about reusability, it can be deduced that salen complex stability is significantly reduced in the presence of oxidizing reagents, as for instance in alkene epoxidation, and less problematic for epoxide ring opening and other nucleophilic additions.

Kim and co-workers have recently developed a novel concept of heterometallic chiral salen catalysts formed by the addition to chiral salen Co(II) of an alkali earth halide (BF$_3$, AlX$_3$, or GaX$_3$) in a molar ratio of 2:1.[73−78] Apparently the Lewis acid acts as bridge of two salen complexes forming a dimer that is more active and selective than the monomer for the asymmetric ring opening of terminal epoxides or hydrolytic kinetic resolution of terminal epoxides. Although the idea of obtaining dimeric and oligomeric salen units with enhanced catalytic activity by simple interaction with Lewis acid halides is certainly interesting and represents high synthetic economy, the stability of these entities is low and they are not sufficiently stable to be reused, due probably to hydrolysis of these entities under reaction conditions.

Table 1. Reaction Types and Enantiomeric Excesses Achieved Using Chiral Salen−Metal Complexes as Catalysts
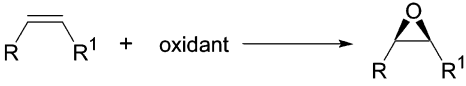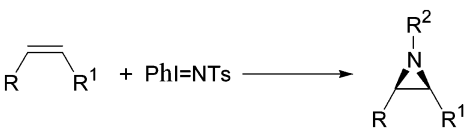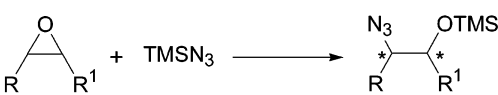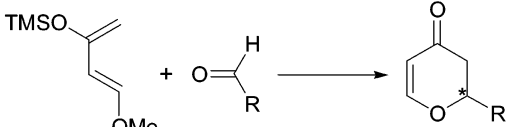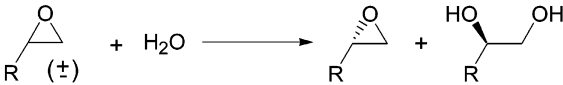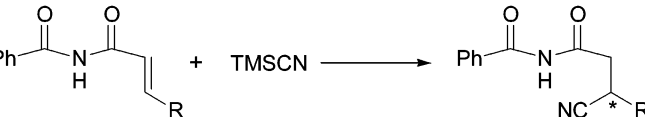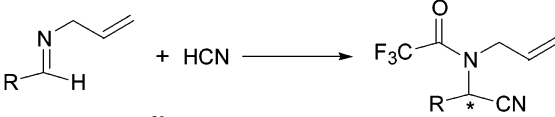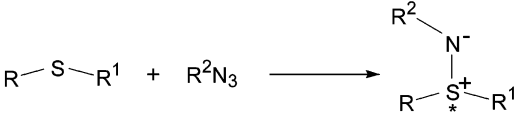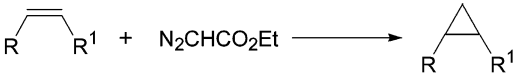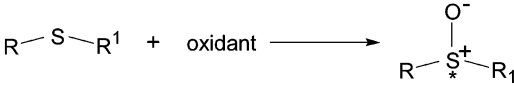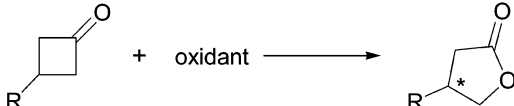
Metal	Reaction	e.e. (%)
Mn	alkene epoxidation [5]	89-92
Cu	alkene aziridination [53]	30-98
Cr	epoxide ring opening [54]	81-95
Cr	Hetero-Diels-Alder [55]	70-93
Co	epoxide kinetic resolution [56]	84-98
Al	conjugate addition of cyanide to α,β-unsaturated imides [57]	87-98
Al	addition of cyanhydric acid to imines − Strecker reaction [58]	37-95
Ru	sulfimidation [59]	8-99
Ru	cyclopropanation [60]	78-99
Ti	sulfoxidation [61]	92-96

Table 1 (Continued)

Metal	Reaction	e.e. (%)
Zn	addition of diethylzinc to aldehydes [62]	69-91
Zn	alkyne addition to ketones [63]	32-81
V	cyanosilylation of aldehydes – cyanohydrin synthesis [64]	68-95
Zr	Baeyer-Villiger [65]	45-99

On the negative side of supporting a chiral catalyst is the fact that the enantioselectivity of the heterogenized catalyst is commonly lower than that of the analogous salen—metal complex in solution. Although the origin of this lower asymmetric induction must be determined and addressed in each specific case, a general cause of negative influence on the asymmetric induction ability of supported chiral catalysts is the disturbance that the support imposes on the approach of the substrates to the metal center. For this reason, although not frequently the subject of detailed study, the tether or linker connecting the complex and the support has to be of sufficient length to allow the complex to move into the liquid phase far from the solid surface. In this way, there is a continuous effort to develop more efficient and practical immobilization methods for homogeneous chiral catalysts.

In the following sections we will summarize the main features of the recoverable systems using chiral salen metal complexes as catalysts in homogeneous and heterogeneous phase (Scheme 2), together with a critical overview based on currently available data of the reaction types reported, the actual metal—salen complexes used for them, and the advantages/limitations of the medium. For the purpose of organizing this review, we have classified the reports on heterogenization of chiral salen complexes into four main groups: inorganic oxides, carbonaceous materials, organic polymers, and hybrid organic—inorganic solids.

Scheme 2. Evolution from Nonrecoverable to Recoverable Homogeneous or Heterogeneous Catalysts
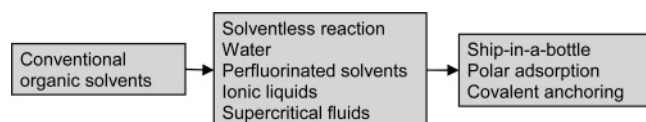
3. Reusable Chiral Salen Complexes Operating as Homogeneous Catalysts

In this section we will describe those catalytic systems operating in homogeneous phase that have been reported to allow the recovery of chiral salen—metal complexes. We will start with conventional solvents and will move toward novel liquids widely accepted as green media.

3.1. Salen—Metal Complexes Embedded in or Filtered by Membranes

Heterogenization of enantioselective salen—metal complexes is advantageous as it allows easy removal of the catalyst from the reaction mixture. However, it would be even more convenient to carry out the reaction in homogeneous phase in the appropriate solvent and then separate the catalyst from the reaction products by "simple filtration". This methodology seems at first sight impossible, because a filter able to discriminate between substrate, products, and catalyst is needed. However, pioneering work in the area of combining state-of-the-art nanofiltration membranes and catalytic reactions is pointing out that this possibility may become real soon, particularly considering that a metal—salen complex has a molecular mass of ≈600—800 Da, whereas most common reaction end products can weigh <100 Da. In addition, it is evident that bulkier chiral salen complexes can be easily synthesized by design with larger molecular size to increase the weight difference between catalyst and products or substrates.

A membrane is considered to be a nano- or microporous continuous film the main application of which is for filtration or for separation of two different phases. As the membrane technology has developed quickly,[79−82] it is possible to have membranes of a fairly uniform pore distribution in the sub-micrometric length scale.

Scheme 3. Preparation of Linear and Cross-linked PDMS Membranes

a) Non-crosslinked PDMS polymer

(linear PDMS)
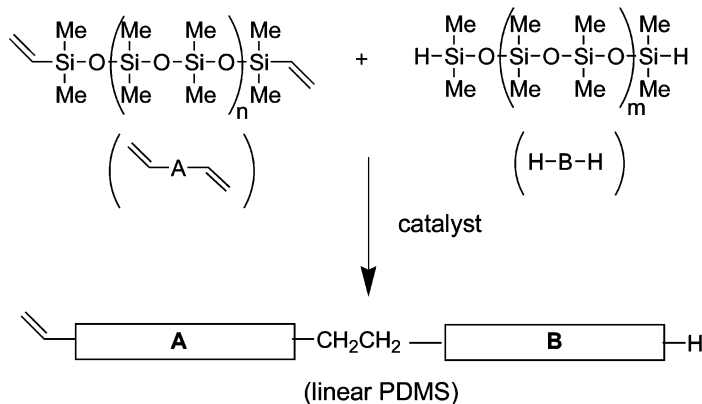
b) Crosslinked PDMS polymer

(crosslinked PDMS)
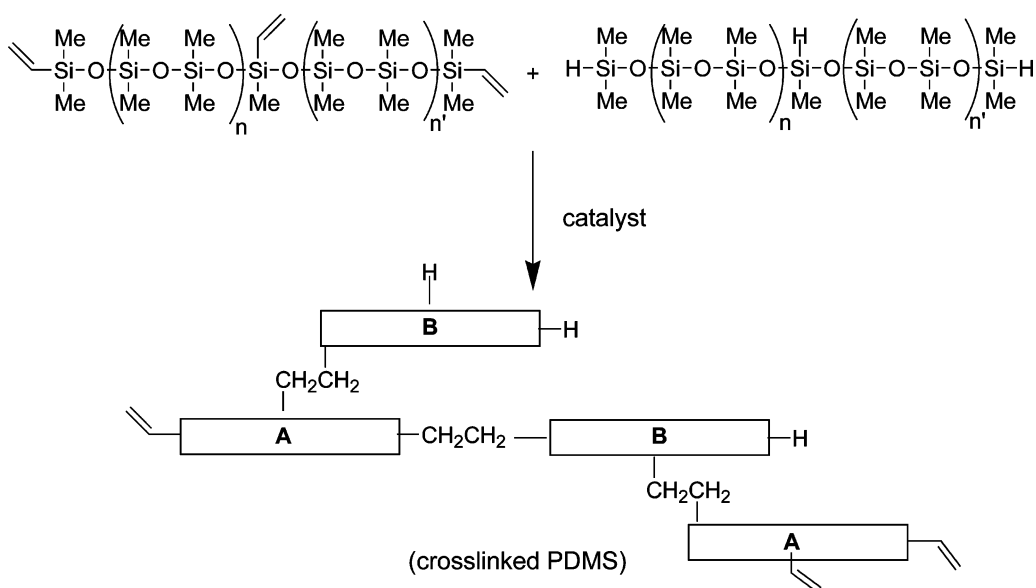
Jacobs's group has been working on catalyst immobilization in poly(dimethylsiloxane) (PDMS) membranes.[83–87] PDMS membranes can be easily obtained by cross-linking vinyl-substituted dimethylsiloxane prepolymeric chains through hydrosilylation (Scheme 3). Mechanical resistance, swelling, and porosity are some of the PDMS membrane properties that can be controlled in the polymerization process by selecting appropriately the substituted precursor chains that will end up in an adequate degree of cross-linking.

PDMS films can incorporate metal complex catalysts and in particular chiral salen−metal catalysts by physical occlusion and van der Waals forces. By using a PDMS membrane, Jacobs and co-workers have designed a catalytic system based on a membrane containing a metal phthalocyanine encapsulated inside zeolite that is able to promote efficiently the catalytic oxidation of cyclohexane by hydrogen peroxide in a biphasic hydrophobic−hydrophilic system separated by the PDMS membrane (Scheme 4).[88] The mode of action of PDMS-embedded zeolite-encapsulated metal phthalocyanine has a certain resemblance with the operating mechanisms of the cytochrome P-450 enzyme.

Whereas chemical binding of the catalyst to an organic or inorganic support leads very frequently to a decrease in

Scheme 4. Pictorial Illustration of a Zeolite-Encapsulated Catalyst Embedded in a PDMS Membrane That Is at the Interphase between an Aqueous Solution and a Hydrophobic Liquid and Is Able To Catalyze the Oxidation of the Organic Substrate (Based on Reference 88)
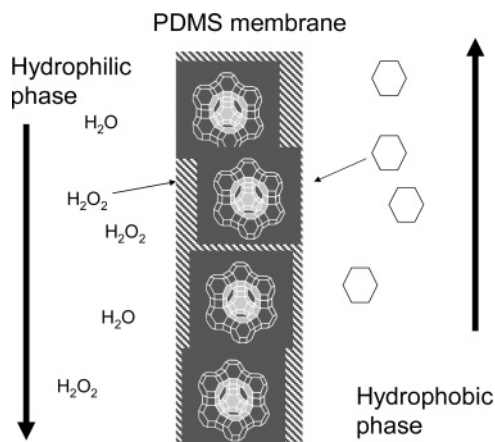
the enantioselectivity, it can be expected that *physical* entrapment should alter less the enantioselectivity of the metal complex with respect to that in solution. The reason

Scheme 5. Synthesis of Dimeric Mn−Salen Epoxidation Catalyst (Based on Reference 89)
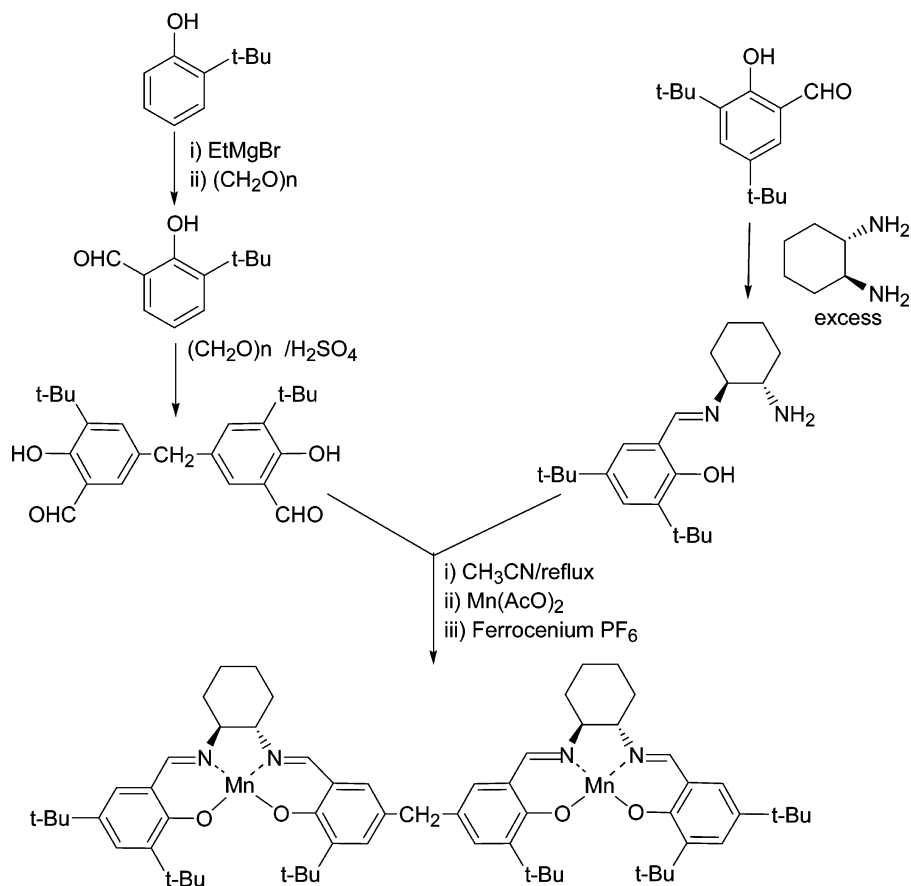
for this assumption is that the physical entrapment of the complex on a PDMS membrane occurs through van der Waals forces and mechanical (steric) immobilization. This assumption, however, would be worthwhile to be demonstrated because as the membrane pores are approaching molecular dimensions the steric hindrance in membrane holes can also result in a decrease in product enantioselectivity.

One general problem associated with physical occlusion in a membrane can be the leaching of the complex to the solution and losses associated with catalyst desorption. Therefore, before any methodology based on the combination of a membrane and a catalyst is feasible, it has to be demonstrated that the salen−metal complex will remain occluded in the membrane. This is particularly important in the case of PDMS membranes because the effect of swelling severely limits the types of solvents that can be used. In fact, it has been demonstrated that leaching of PDMS-entrapped Jacobsen's catalyst depends on complex solubility and swelling. Thus, leaching can be minimized by combining low complex solubility and minor swelling. These can be achieved by using the appropriate solvent, mainly alkanes.[89]

The chiral salen complex can be specially designed to be retained in the PDMS membrane. Thus, Jacobs and co-workers have reported that a monomeric[90] and a dimeric form[89] of the Jacobsen catalyst can be included in a PDMS membrane, with the dimeric form of the catalyst exhibiting an improved retention in PDMS membranes. The key steps in the preparation of the dimeric salen manganese complex are (i) the preparation of a monosubstituted (α-imine,β-amine)cyclohexane using an excess of 1,2-diaminecyclohexane and (ii) the use of a disalicylaldehyde methane (Scheme 5). It would be interesting to test such a dimeric

ligand for applications besides oxidation. However, the synthesis needs to be improved because it suffers from the low yields in the formation of the monosubstituted imine and the disalicylaldehyde.

Incorporation of the Jacobsen catalyst and its related dimer into the PDMS membrane was achieved at the PDMS polymerization stage by performing the process in a chloroform solution that, in addition to the PDMS comonomers, also contained the salen−Mn complex. The emphasis of the work was, however, that the solubility of the dimeric complex in most solvents (chlorobenzene, diethyl ether, dichloromethane, acetone, acetonitrile, and methanol) should be considerably lower than that of the corresponding monomer and, as result, leaching of the dimer out of the PDMS membrane should be reduced. It has to be said, however, that in heptane the solubility of both monomeric and dimeric salen complexes is very low but similar and, in contradiction with the aim of the work, leaching in this solvent is even higher for the dimer than for the monomer. Also, the enantiomeric excess of the dimeric manganese catalyst for alkene epoxidation is modestly diminished relative to the monomeric Jacobsen catalyst. This decreased asymmetric induction ability of the dimeric complex is most probably due to the lower steric encumbrance around the Mn center due to the lack of one *tert*-butyl group at the *para*-position of the phenolic ring. In any case, the enantiomeric excess (ee) values achieved are still unsatisfactorily low for any real application, and much improvement is needed to develop a highly enantioselective catalyst. Table 2 gives some relevant catalytic data comparing the activity of the dimeric and monomeric Jacobsen catalysts.[89]

Table 2. Results for the Catalytic Epoxidation of *t*-Methylstyrene in Solution or Embedded in PDMS Membranes (Adapted from Reference 89)

	Mn−(salen) monomeric		Mn−(salen) dimeric	
conditions	yield (%)	ee (%)	yield (%)	ee (%)
CH_2Cl_2 solution	17.0	24.5	10.5	28.5
PDMS	64.0	20.5	23.0	14.4
reused PDMS	27.6	10.6	17.0	15.8

A further evolution of PDMS membranes based on the use of an organic−inorganic composite containing zeolite Y has been more recently reported.[91−96] The zeolite-containing PDMS membrane is similar to that depicted in Scheme 4, and it has the additional advantage of being solvent-resistant. This composite PDMS-based membrane can retain the salen−Co(III) catalyst (MW 626 Da) using diethyl ether as reaction solvent, whereas reactants and products permeate through the membrane that is able to discriminate molecules in the nanometric scale. The system has been used for the hydrolytic kinetic resolution of epoxides, such as 1,2-epoxyhexane.[91] In an ideally enantioselective kinetic resolution, starting from a racemic mixture, one of the two enantiomers should remain unaltered, whereas the opposite enantiomer should undergo complete enantioselective ring opening to a single glycol enantiomer. Thus, in an ideal kinetic resolution, a racemic mixture of epoxides is transformed into a mixture of a single epoxide enantiomer and a single glycol enantiomer stereospecifically derived from the reacting epoxide enantiomer (Scheme 6). Needless to say, that many real epoxide kinetic resolutions are not ideal, and both epoxide enantiomers undergo a catalyzed ring opening, although at different reaction rates. Thus, in addition to ee values, an important parameter to characterize the efficiency of enantioselective ring opening of racemic epoxides is the ratio between the reaction rates for each enantiomer. In this way, in hydrolytic kinetic resolution there are four important catalytic parameters, namely, (i) conversion of the racemic mixture, 50% being the ideal value; (ii) the ee of the unreacted epoxide; (iii) the ee of the formed glycol; and (iv) the relative reaction rates for the enantiomeric epoxides.

The zeolite-containing PDMS system can work in diethyl ether and operates as a semicontinuous process using a dead-end filtration cell, which is used both as reactor and, when the reaction is finished, as filtration unit that becomes pressurized with N_2 to promote filtration. The membrane should retain the catalyst while the products should permeate through the membrane, thus allowing a conventional tetra-*tert*-butyl salen−cobalt(III) complex catalysis in solution

being recycled for the next batch. With the solvent-resistant PDMS membrane, a catalyst retention of 98% (30 bar pressure for filtration) with a permeability of 0.02 $g \cdot h^{-1} \cdot cm^{-2} \cdot bar^{-1}$ was obtained. These are the best values of a series of 11 membranes tested. A slow gradual decrease in the catalyst activity was partly due to the 2% losses in each run and also to some catalytic deactivation of the complex. Catalytic deactivation was assumed to be due to the change from Co(III) to Co(II), the latter oxidation state being inefficient to catalyze the reaction.[91]

Enantiospecific hydrolytic kinetic resolution of racemic mixtures of epichlorhydrin, 1,2-epoxybutane, styrene, and α-pinene oxides using the salen−Co(III) complex has also been accomplished using a ZSM-5/Anodisk membrane.[97] Anodisk is a trademark of Whatman that denotes anodized alumina membranes of controlled nanometric porosity. On one side of this membrane, a ZSM-5 zeolite film was prepared by synthesizing this medium-pore zeolite (0.54 nm pore diameter) directly on the Anodisk surface. The hydrothermal *on-substrate* synthesis of ZSM-5 zeolites produced a film that completely covered the Anodisk surface without pinholes or cracks, as observed by scanning electron microscopy. It could be even more interesting if the zeolite film could be synthesized with its channels oriented perpendicular to the Anodisk surface. Although this was not the case in the report of Choi and Kim, there are some precedents in the literature showing that this type of oriented film can be grown over certain substrates, such as quartz.[98−105] Maybe it could also be possible to grow such oriented films over Anodisk.

Commercial tetra-*tert*-butyl salen−Co(III) complexes were loaded into the macropore system of the Anodisk membrane from the surface free from ZSM-5 crystals by impregnation under vacuum (Scheme 7). Thus, if the fluid flow forces the complex to go through the ZSM-5 film, the salen−Co(III) complex should be immobilized on the ZSM-5/Anodisk interphase, simply because the tetra-*tert*-butyl salen complex (kinetic diameter > 1.5 nm) cannot enter the zeolite ZSM-5 micropores (0.54 nm). This catalytic system can be used in a biphasic membrane reactor where two phases exist separately.

Conversion and ee values (up to 99.8%) for the enantiospecific hydrolytic kinetic resolution using cationic Co(III) physically immobilized in the ZSM-5/Anodisk membrane were the same as those attained in homogeneous phase, showing that there are no negative effects on the catalytic performance by membrane incorporation of the complex. Three different salen−Co(III) complexes were tested, and

Scheme 6. Kinetic Resolution Using a Solvent-Resistant PDMS Containing Zeolite Y Filler (Based on Reference 91)
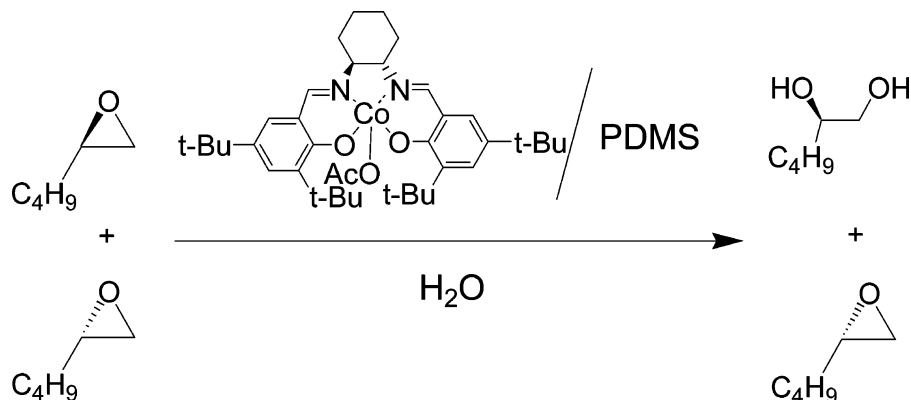
Scheme 7. Pictorial Representation of a ZSM-5/Anodisk Loaded with a Chiral Salen−Co(III) Complex[a]

Nanopores of Anodisk

ZSM-5 continuous film
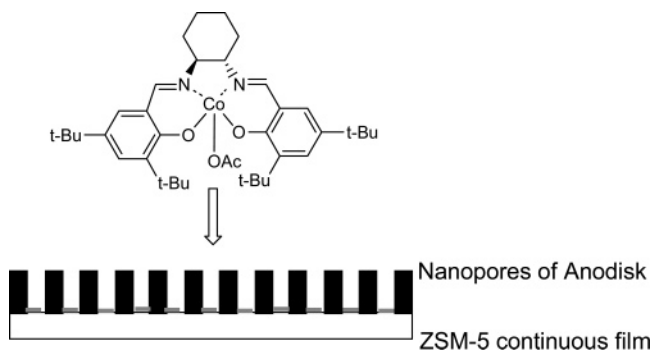
[a] The lines inside the Anodisk nanopores represent the location of the chiral salen complex on the ZSM-5 film (based on ref 97).

the one having an acetate ligand bonded to the cobalt atom undergoes deactivation upon reuse due to ligand dissociation. This explanation seems to be, however, contradictory with the fact that those complexes having a tetracoordinated cationic cobalt compensated by PF_6^- or BF_4^- were recyclable many times without observable loss in activity.[97] The Co(III) catalyst could not be detected in the liquid phases before and after the membrane, indicating that the retention of the complex in the system is perfect. The reaction time required for high conversions increases, however, upon reuse, indicating that some deactivation is occurring.

As a further development, a continuous reactor system in which the ZSM-5/Anodisk membrane loaded with cationic salen−Co(III) complex is placed on a tubular arrangement was reported.[97] The organic (containing the epoxides) and the aqueous (collecting the chiral diol) phases were circulated separately through the interior (organic) and exterior (aqueous) of the tubular reactor, respectively (Scheme 8). The key point of the membrane operation is that mass transfer of the diol from the organic to the aqueous phase occurs spontaneously while the reaction proceeds due to the polarity change from epoxide to diol. It would be useful to know more details about how this tubular membrane was prepared and characterized. It is clear that this type of continuous-flow, tubular reactor using commercial salen−metal complexes employed in solution and exhibiting the same enantioselectivity as in the homogeneous phase will be easily applicable to many other catalytic reactions besides epoxide kinetic resolution.

More recently, Nguyen, Hupp, and co-workers have supported a catechol-functionalized salen−manganese complex on mesoporous anodic aluminum oxide membranes to yield catalytic membranes that were highly active in the enantioselective epoxidation of 2,2-dimethyl-2*H*-chromene.[106] The heterogeneous enantioselective catalysts exhibit reaction rates and enantioselectivities similar to those obtained with the homogeneous catalyst in batch experiments. Recycling experiments show that the catalytic membrane exhibits a gradual decrease in activity (from 70% in the first cycle to 51% in the fourth cycle) and enantioselectivity (from 81% in the first cycle to 69% in the fourth cycle), with a small loss of Mn content (13−17% in the fourth cycle). The membrane was also used in a simple catalytic membrane reactor, with the catalyst being extremely active and its enantioselectivity similar to that under homogeneous conditions. When the catalyst was reused after one cycle in the membrane reactor, its activity and enantioselectivity remained intact.[106]

The authors attribute the high activity and selectivity obtained in the catalytic membrane reactor system to two effects of the Anodisk membrane: (i) the well-organized and unrestricted cylindrical pore structure of the membrane (all active catalyst sites readily accessible to reactant molecules) and (ii) the short catalyst contact time (more turnovers while maintaining high selectivity and minimizing overoxidation).[106]

3.2. Salen−Metal Complexes in CO_2-Containing Phases

Dense carbon dioxide phases (either compressed gas or liquid or in supercritical state) is an environmentally friendly, nontoxic, nonflammable, cheap, and readily available solvent. The supercritical state of CO_2 is easily achievable at moderate pressures (73.8 bar) and temperatures (31 °C) as compared to other gases (Scheme 9). The supercritical fluid state has interesting properties in catalysis including disappearance of the liquid−gas interphase, a fast gas-like molecular diffusion, and liquid-like solubility.[69,107−110] In general, the solubilities of compounds in supercritical fluids depend strongly on the pressure, temperature, and additives, particularly in the vicinity of the supercritical state conditions. Therefore, the reactants, products, and catalysts can be easily separated by pressure or temperature changes according to the phase diagram of a particular mixture. The reader is referred to previous reviews of reactions in supercritical fluids for a general view of the potential of this medium in catalysis.[69,111−115]

One specific property of supercritical CO_2 different from other supercritical fluids is, however, that its dielectric constant remains virtually unaffected over a wide range of pressure and, thus, solubility changes are better influenced

Scheme 8. Pictorial Illustration of a Two-Phase Continuous Reactor Based on a Tubular Anodisk Membrane Containing a Film of Zeolite and a Chiral Salen−Co(III) Catalyst (Based on Reference 97)
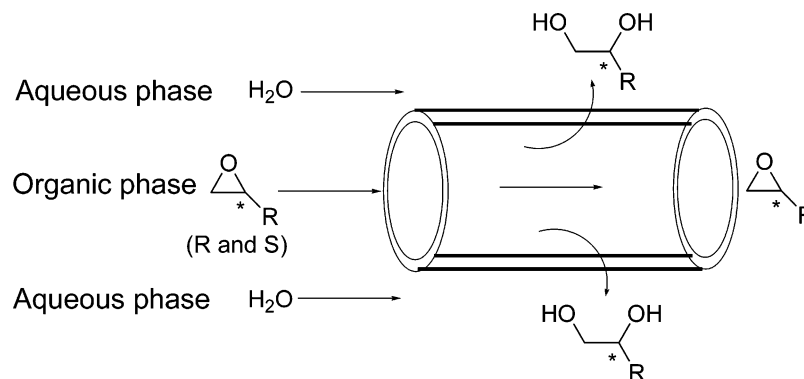
Scheme 9. Pictorial Description of Supercritical State

Supercritical conditions for CO_2

T= 31 °C, P=73.8 bars
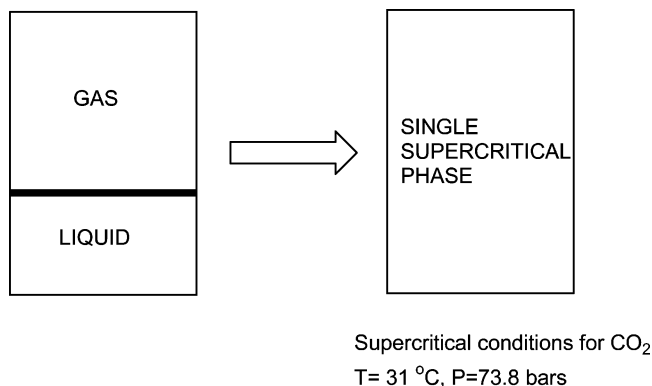
Scheme 10. Phenol Oxidation by Dioxygen in Supercritical CO_2 Catalyzed by Salen−Cobalt(II) (Based on Reference 17)

(predominant)
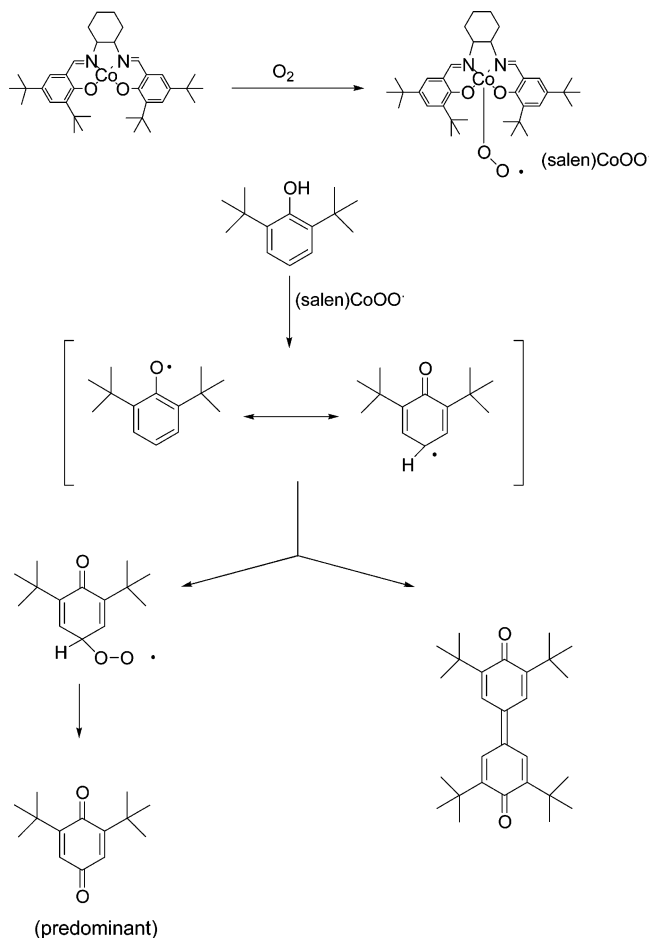
by additives. Alkanes are commonly added in small proportions to supercritical CO_2 to increase its otherwise poor solubility properties. In fact, a peculiarity of the CO_2 supercritical state is its low solubility, which may force the design of catalysts specifically to become dissolved in supercritical CO_2. For this reason, besides supercritical CO_2, other related media termed in general as "dense CO_2" with specific properties may derive from the mixture in different proportions of CO_2 and a cosolvent to improve the generally poor solubility of solutes in supercritical CO_2.

A concept opposite to dense CO_2 is that of "CO_2-expanded" solvent media, where relatively minor amounts of CO_2 are added to solvents having a significant solubility in CO_2. The main advantages of CO_2-expanded solvents are enhanced reaction rates, control of product distribution, and

Scheme 11. Vanadyl−Salen Catalyst Used for the Epoxidation of Allylic Alcohols in Supercritical CO_2 (Based on Reference 119)

acac: acetylacetonate
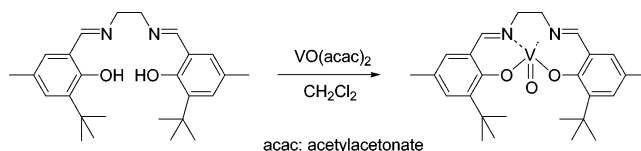
much lower operating pressures (tens of bars) as compared to processes utilizing supercritical CO_2 ($\approx$100 bars). As result of CO_2 addition, the solvent undergoes an apparent increase in volume ("expansion") while varying enormously the solubilities of the dissolved solutes, generally decreasing their solubility.[17,116−118] When CO_2-expanded solvents are used to replace conventional organic solvents, the catalyst solubility is frequently maintained but the solubility of gases (particularly O_2 and H_2) increases enormously.[17]

In this context it is worth mentioning that conventional organic solvents have a limited O_2 solubility that precludes, for instance, a detailed study of the influence of oxygen concentration on oxidation efficiency. Busch and co-workers have exploited the complete miscibility of oxygen in supercritical CO_2 to study the oxidation of phenols catalyzed by salen−cobalt(II) complexes.[17] This study strongly supports the formation of a Co(II) salen/O_2 intermediate, and this adduct would be the real reactant, activating dioxygen and attacking phenol (Scheme 10).

Vanadyl salen complexes (Scheme 11) can catalyze the stereoselective epoxidation of allylic alcohols with *tert*-butyl hydroperoxide in supercritical CO_2.[119] High diastereomeric excesses were obtained using achiral salen vanadyl complexes, indicating that the oxygen insertion occurs stereoselectively. Formation of an α,β-unsaturated ketone from oxidation of the hydroxy group instead of the C=C double bond also occurred, but in very low yield (Table 3). Visual observations of the reaction mixtures confirmed that at 40 °C the substrate, reagent, and catalyst were in a single phase, something that is unexpected considering the poor solubility power of CO_2. After the autoclave had been discharged, the catalyst was recovered and reused with similar activity. This catalytic system is specific for allylic alcohols because it failed to catalyze efficiently the epoxidation of nonallylic olefins.

Table 3. Some of the Results of the Stereoselective Epoxidation of Allylic Alcohols by *tert*-Butyl Hydroperoxide in Supercritical CO_2 Catalyzed by Salen−Vanadyl Complex (Reference 119)

R^1	R^2	R^3	R^4	yield (%)	diasteromeric excess (%)
H	H	H	H	40	>95
CH_3	H	H	H	76	69 (erythro)
n-C_5H_{11}	H	H	H	64	70 (erythro)
H	H	H	Ph	33	60
H	CH_3	Ph	H	86	90

3.2.1. Reusable Salen Complexes as Cocatalysts for CO_2 Insertion into Epoxides

In addition to being an inert green solvent, there is also an enormous interest in using CO_2 as a one-carbon feedstock.[120−123] Given the enormous stability of CO_2,

Scheme 12. Competition between CO_2 Insertion into Epoxides and Polycarbonate Formation
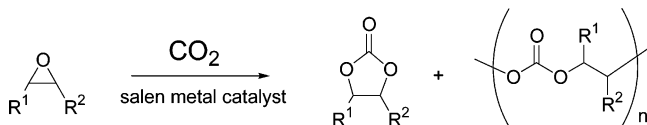
reaction types in which CO_2 intervenes as reactant are very few, and this topic remains one of the important challenges in current green chemistry focused on the use of renewable feedstock alternatives to fossil fuels.[120,121] In principle, CO_2 could replace methane in industrial processes leading to the synthesis of methanol or formaldehyde, as phosgene alternative, and other C1 bulk chemicals.

Insertion of CO_2 into epoxides to form cyclic carbonates is one of the most interesting CO_2 fixation reactions, because the products are valuable compounds as solvents, synthetic intermediates, and polymers (Scheme 12).[124−127] It can be anticipated that this reaction will grow in importance as some industrial processes develop.

Although there are many known catalysts for this CO_2/epoxide coupling, and in particular organozinc compounds and mixed-metal magnesium/aluminum oxides,[128−136] there has been a recent breakthrough in this area with the report by Paddock and Nguyen that salen−Cr(III) complexes in combination with *N,N*-dimethylaminopyridine (DMAP) can also catalyze this reaction using a large variety of terminal epoxides.[137] The fact that salen−Cr(III) complexes are active catalysts could be considered closely related on the one hand, to the precedents reporting the activity of porphyrin Cr(III) for CO_2 insertion[138,139] and, on the other hand, to the work of Jacobsen in the epoxide ring opening catalyzed by salen−Cr(III).[51,54]

The presence of DMAP or *N*-methylimidazole as cocatalyst is a prerequisite for the process, an optimum salen−Cr(III) to DMAP molar ratio being found at 0.5. In fact, the activity of the catalytic system decreases to zero at lower or higher ratios, although the inactivity of different mixtures of salen−Cr(III)/DMAP may be misleading because it would be apparent arising from only a lengthening of the induction period. Actually, the need of a bifunctional Lewis base/Lewis acid catalyst is very common in CO_2 activation.[132,140−145] It is generally assumed that CO_2 is better activated by a nucleophile, whereas the epoxide ring opening can be promoted by a Lewis acid. The coexistence in homogeneous phase of both acid and base requires a strict stoichiometry to be operative, because an inconvenient excess of acid or base can inhibit the activity of the complementary cocatalyst.

As indicated in Scheme 12, CO_2 insertion into epoxides is closely related to the CO_2 copolymerization leading to polycarbonates, and both processes can take place simultaneously in different proportions depending mainly on the epoxide, reaction temperature, and nature of the cocatalyst. In general, CO_2 insertion is predominant in epoxides of acyclic alkenes, whereas copolymerization becomes the prevalent process for epoxides of cyclic alkenes. Thus, cyclohexene epoxide tends to form copolymer due to the steric strain that would impose the cyclohexane ring on the cyclic carbonate. It is very easy to distinguish between a cyclic five-membered ring carbonate and any soluble oligo- or polycarbonate impurity by simply recording an infrared (IR) spectrum of the reaction mixture and observing the position of the C=O group either at ≈1820 cm^{-1} (cyclic carbonates) or at ≈1750 cm^{-1} (copolymer). It is very

common to observe both bands in the reaction mixture, indicating the simultaneous occurrence of these two parallel processes.[15]

Most of the studies dealing with CO_2 insertion use chromium complexes. However, as mentioned earlier, other salen−metal complexes are active as well. Apparently salen−aluminum(III) complexes can be more efficient than chromium catalysts, having the advantage of being environmentally benign when compared to chromium. He and co-workers have reported the formation of cyclic carbonate of ethylene oxide catalyzed by a series of salen−Al complexes in supercritical CO_2.[146] The supercritical state favors CO_2 insertion by increasing the miscibility of ethylene oxide and CO_2 and reactant diffusion.[146] In addition to Lewis bases, quaternary ammonium salts also increase markedly the catalytic activity of the salen−Al(III) complex. This fact could be possibly related to the phase transfer catalytic activity of the quaternary ammonium ion. Compared to aluminum, other metal−salen complexes show lower activity following the order Cr(III) > Co(II) > Ni > Mg, Cu, and Zn.

It was observed that a pressure increase beyond an optimal level has a dramatic negative influence on the catalytic activity. This effect is unprecedented and not well understood, although there is a possibility that according to Scheme 12 the amount of CO_2 controls the ratio between the formation of a cyclic carbonate and an epoxide/CO_2 copolymer. Polycarbonates are common impurities accompanying the intramolecular CO_2 insertion into epoxides, but due to analytical limitations when the mixture is analyzed by GC, its formation cannot be detected.

Temperature plays also a pronounced role on the ratio of CO_2 insertion versus copolymerization: a temperature increase favors the CO_2 insertion process versus copolymerization.[147] From the temperature dependence, the activation energies for the formation of cyclic carbonate and copolymerization for propylene oxide and cyclohexene oxide were estimated. It was found that for cyclohexene oxide, formation of the cyclic carbonate has an activation barrier of 80 kJ·mol^{-1}, which is a higher activation energy than that for copolymer production.[147] In contrast, the difference in activation energies between the formation of cyclic carbonate and copolymerization for propylene oxide is only 33 kJ·mol^{-1}, that is, considerably smaller than for the epoxide of the cyclohexene.[147] This remarkable difference has been attributed to the steric strain on the carbonate five-membered ring caused by the conformational requirements of the alicyclic cyclohexyl ring and explains the different product distributions attained with the cyclohexene and propylene oxides.[147]

The formation of cyclic carbonates by CO_2 insertion into a large series of monosubstituted terminal epoxides has also been catalyzed by salen−metal complexes derived from binaphthyldiamino Schiff bases in supercritical CO_2 using DMAP, triethylamine, pyridine, 1,4-diazabicyclo[2.2.2]octane (DABCO), or 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as cocatalysts (Scheme 13).[148] Table 4 lists some selected results. The presence of *tert*-butyl substituents on the salen phenolic moiety or the use of larger amounts of organic base cocatalyst lowers the yield of cyclic carbonate. Zn and Co complexes exhibit higher catalytic activity than those of Cu. Although the binaphthyl moiety introduces chirality to the salen complex, the study of the ee values of the cyclic carbonates obtained is still to be undertaken.

Scheme 13. Binaphthyl-Derived Salen−Metal Complexes as Cocatalysts for CO₂ Insertion into Epoxides (Based on Reference 148)
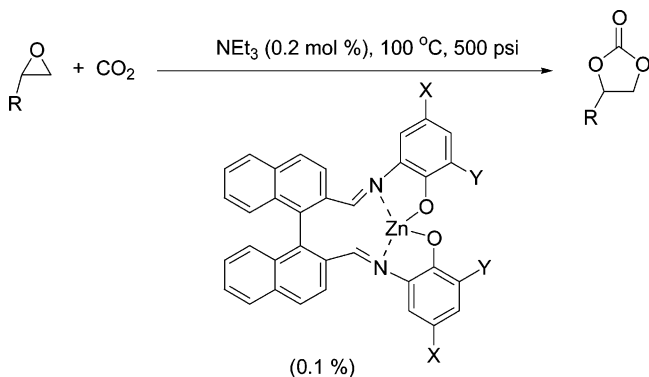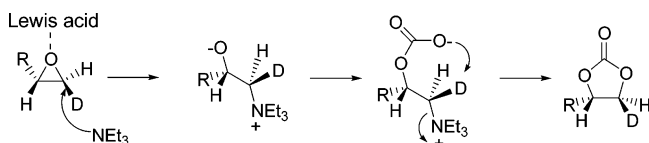

(0.1 %)

Table 4. Results of the CO₂ Insertion Catalyzed by Zn or Cu Binaphthyl-Derived Salen Complex (Reference 148)

metal complex	R	yield (%)
Zn	CH₃	100
	CH₂Cl₂	100
	Ph	90
	p-C₆H₄CH₂Cl	95
Cu	CH₃	99
	Ph	89
	p-C₆H₄CH₂Cl	89

Scheme 14. Proposed Mechanism To Explain the Retention of Epoxide Configuration in the Formation of Cyclic Carbonates (Based on Reference 148)

On the basis of the X-ray structure of the binaphthyl-diamine-derived salen complex, which is very far from planarity and makes impossible the close packing of two complexes, and also on deuterium labeling that shows retention of the epoxide configuration on the cyclic carbonate, a reaction mechanism in which the epoxide is simultaneously activated by the Lewis acid and base has been proposed (Scheme 14).[148] According to the current understanding, the retention of the epoxide configuration will be the result of a double inversion at the asymmetric carbon.

The group of Darensbourg has focused on the copolymerization of CO₂ and epoxides using salen−Cr(III) as catalyst and neutral organic bases as cocatalysts. They have shown that as occurs in related Cr(III) and Al(III) porphyrins,[149−152] the air- and moisture-stable salen−Cr(III) complex is an effective catalyst for the coupling of CO₂ and cyclohexene oxide to afford alternating copolymer poly(cyclohexenylene carbonate) with average molecular mass ≈11000 Da and a polydispersity index of 1.2.[147] A ¹³C nuclear magnetic resonance (NMR) study of the resulting polycarbonate indicates that the ring opening process lacks stereocontrol in contrast to the enantioselective epoxide ring opening observed by Jacobsen with chiral salen−Cr(III) catalysts.[54]

This has been interpreted as indicating the operation of a pathway unimolecular with respect to the salen−Cr(III) catalyst in contrast to the bimolecular process proposed by Jacobsen to explain the stereoselectivity of the salen−Cr(III) catalyst for the epoxide opening

The polymerization mechanism has been the subject of much interest to provide a conceptual framework to rationalize the nature of the salen complex and the role of cocatalysts. A detailed mechanistic proposal is shown in Scheme 15.[15] This mechanism has two parts: an induction period ("initiation") and the catalytic reaction ("propagation"). Initially, a fast equilibrium between two hexacoordinated salen−chromium complexes in which either the cocatalyst or the epoxide is bound to the chromium atom is established. When the concentration of the cocatalyst is increased or a stronger coordinating cocatalyst is used, the equilibrium concentration of the salen−chromium complex bound to the cocatalyst increases. Each of these two salen−chromium complexes generates differently the same key propagating intermediate that is common for the two pathways. When the hexacoordinated salen−chromium is bonded to the cocatalysts, the nucleophilicity of the chromium-ligated nucleophile is enhanced and formation of the intermediate requires only the attack of the epoxide. It is, therefore, first order with respect to the salen−chromium complex. When the propagating intermediate is formed from the salen−chromium bonded to the epoxide, a second salen complex containing the nucleophile is needed and the process is second order with respect to the salen−metal concentration (Scheme 15).[15] As a consequence of the coexistence of the two mechanistic pathways, the induction period can depend linearly, quadratically, or in a mixed order on the concentration of the salen−chromium complex.

Concerning the nature of the salen ligand, particularly under conditions in which the second-order process prevails, salen ligands less encumbered around the imino groups are more active for CO₂/epoxide copolymerization. For this reason, diaminocyclohexane is less suited than ethylenediamino-derived salen ligands.

Cyclohexene epoxide has been the favorite substrate to study the salen−Cr(III) copolymerization process (Scheme 15). However, applications of cyclohexene epoxide−CO₂ copolymer are considerably less important than those of the polycarbonate derived from bisphenol A, due to the better performance of the latter as an engineering plastic. For this reason, there have been studies aimed at performing the polymerization using other cyclic epoxides as substrates that could bring this reaction closer to commercial application. Thus, the copolymer of [2-(3,4-epoxycyclohexyl)ethyl] trimethoxy- or triethoxysilane and CO₂ (average MM 21000) was found to be of much interest because the resulting polycarbonate can later be cross-linked through the trialkoxysilyl groups to form an extremely hard resin (Scheme 16).[153] Compared to the parent cyclohexene epoxide, the trialkoxysilane group enhances remarkably the solubility in CO₂, and the reaction occurs in a single phase. The higher CO₂ miscibility due to the presence of silane groups has been claimed as the reason for a shorter induction period and can be used advantageously to effect the separation of the salen−metal catalyst (not CO₂ soluble) from the polymer (CO₂ soluble).

Structurally related to the cyclohexene epoxide is the epoxide derived from dihydronaphthalene (Scheme 17).[15] In this case, during the initial induction period the con-

Scheme 15. Mechanistic Proposal for the CO$_2$−Epoxide Copolymerization (Based on Reference 15)

a) initiation

CC: co-catalyst
Nu: Cl, N$_3$
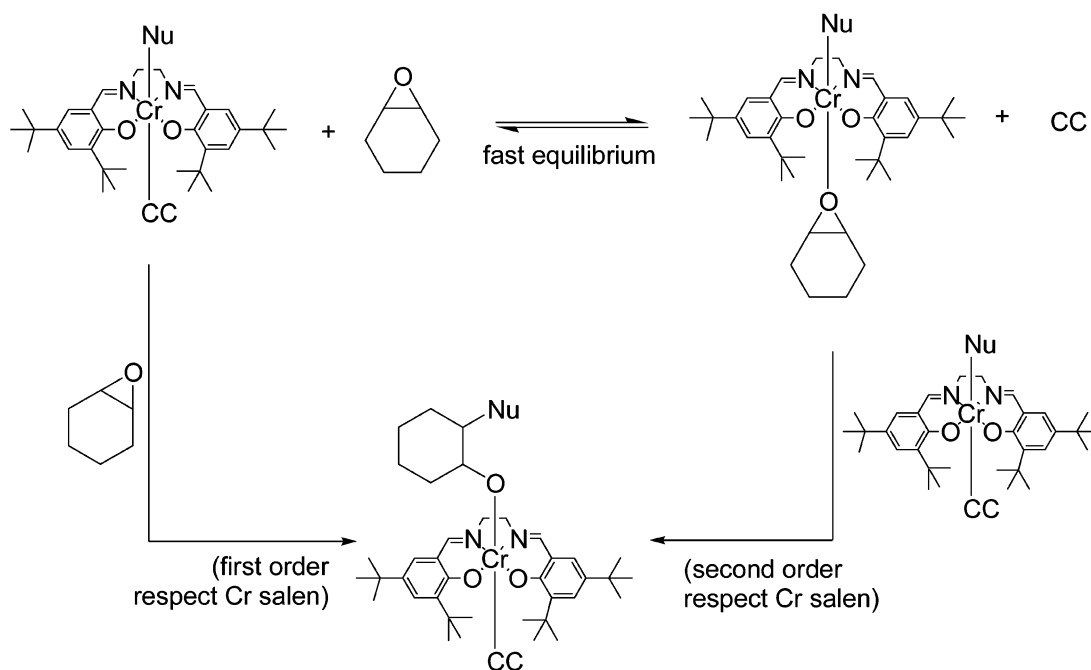
b) propagation

CO$_2$ insertion
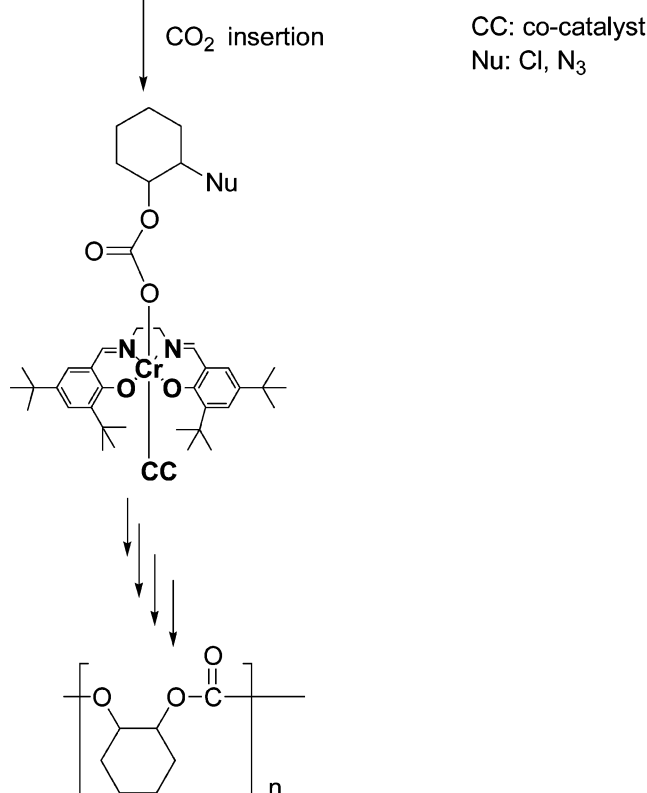
centration of the cyclic carbonate (predominantly cis) is higher than that of the copolymer, but at long reaction times only the copolymer is present, indicating that the cyclic carbonate is not stable under the reaction conditions and is transformed into the copolymer. Formation of the cis-configured copolymer is compatible with a double inversion as observed previously with deuterium labeling (Scheme 14).

Most of the studies on CO$_2$ insertion and CO$_2$ epoxide copolymerization have been carried out using chiral salen−

metal catalysts. In principle, the products, either the cyclic carbonates or the carbonate copolymers, are susceptible to having different stereoisomers. However, the issue of stereoselectivity has been largely ignored in most of these studies. It is unnecessary to use optically pure salen complexes when the target is not asymmetric catalysis. One simple explanation for this contradiction is the ready commercial availability of salen ligands derived from chiral 1,2-diamines.

On the other hand, the CO$_2$ insertion cannot be carried out at low temperatures, and for this reason the ee for this

Scheme 16. Copolymerization of a Trialkoxysilyl-Substituted Cyclohexene Epoxide and CO$_2$ (Based on Reference 153)

R: CH$_3$ or CH$_2$CH$_3$

Scheme 17. CO$_2$ Insertion versus Polymerization in the Reaction of Epoxide of Dihydronaphthalene Oxide (Based on Reference 15)
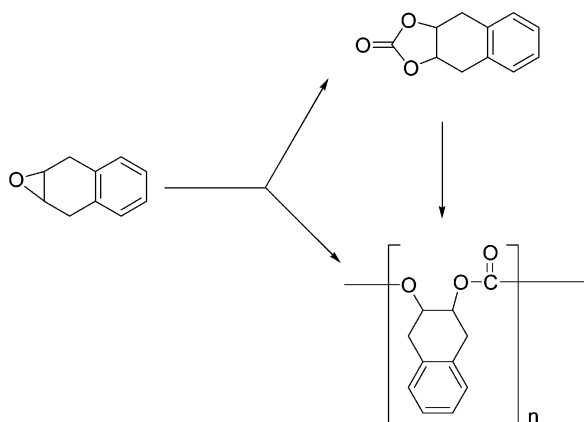
reaction using salen−Al as catalyst is expected to be low.[154] Nevertheless, it can be anticipated that soon there will be some work trying to accomplish the enantioselective CO$_2$ insertion and CO$_2$ epoxide copolymerization because these polymers can be highly promising in chiral recognition and in enantioselective catalysis.

3.3. Salen−Metal Complexes in Perfluorinated Solvents

In contrast to common chlorinated solvents, perfluorinated liquids are nontoxic, thermally and chemically inert, and they do not affect the ozone layer.[155−157] Given the high oxygen solubility and the lack of toxicity for humans, perfluorinated solvents can even be used in some circumstances as blood substitutes.[158,159] Also in sharp contrast to chlorinated liquids, perfluorinated hydrocarbons are very poor solvents for most organic compounds at room temperature. Their solubility, however, increases remarkably with the temperature, a phenomenon that has been reported as thermotropic solubility. In analogy to the word "aqueous", the term "fluorous" has been coined to denote the common properties and behavior of those compounds with a high fluorine content.[160−164] Thus, perfluorinated or highly fluorinated liquids are remarkably stable, have a low dielectic constant, and exhibit thermotropism.

This thermotropic solubility behavior can be used favorably to devise "fluorous biphasic systems" in catalysis (Scheme 18). In these systems, the substrate dissolved in a conventional organic solvent is contacted with a solution of the fluorous phase containing the catalyst. A number of reviews have described the principles and applications of fluorous biphasic systems.[69,165−167] The problem is, however, that given the low room temperature solubility power of perfluorinated liquids, the catalysts have to be conveniently
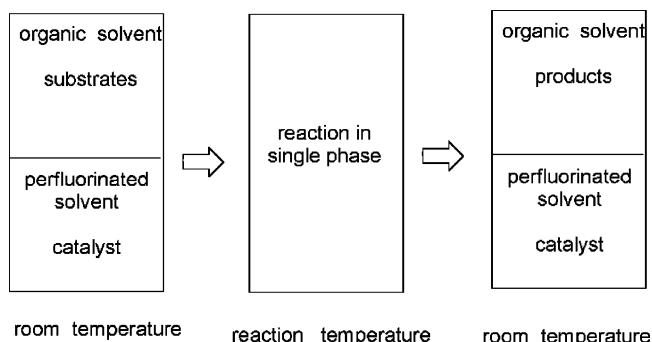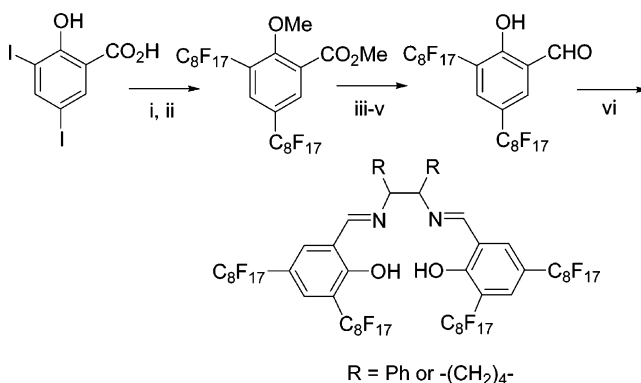
Scheme 18. Operation Procedure in a Fluorous Biphasic Systems (Based on Reference 69)

Scheme 19. Synthesis of Fluorous Salen Ligands As Described in Reference 169

R = Ph or -(CH$_2$)$_4$-

i) Me$_2$SO$_4$, K$_2$CO$_3$, CH$_3$COCH$_3$, reflux; ii) C$_8$F$_{17}$I, Cu, DMF, 125 °C;

iii) LiAlH$_4$, Et$_2$O, 0 °C; iv) aq. NaOCl, KBr, TEMPO, PhCF$_3$, 5 °C;

v) BBr$_3$, CH$_2$Cl$_2$, -78 °C to room temperature;

vi) 1,2-diamine, EtOH, reflux; vii) Mn(OAc)$_2$.H$_2$O (excess), EtOH, reflux

functionalized with fluorinated substituents to become soluble in the fluorous phase.

Pozzi and Shepperson have made most of the contributions on the use of salen complexes as catalysts in biphasic fluorous systems. These authors have recently reviewed the use of fluorous chiral catalysts.[168] As typically in any salen metal catalysis, the reactions that have been studied in fluorous media include asymmetric alkene epoxidation and asymmetric epoxide ring opening, but also interesting is the asymmetric Lewis acid-catalyzed Merweein−Ponndorf−Verley reduction of ketones to alcohols.

One of the major limitations of the biphasic fluorous strategy for homogeneous enantioselective catalysis is the position where the fluorinated tags are introduced in the chiral salen ligand without modifying drastically the catalytic activity and stereoselectivity of the catalyst. Thus, salen ligands derived from chiral cyclohexanediamine and from 1,2-diphenylethylene-1,2-diamine having perfluorooctyl substituents in the ortho- and para-positions of the phenolic moieties have been synthesized in six steps (Scheme 19). The corresponding manganese(III) complexes were soluble in cold perfluorohexanes [boiling point (bp) 56 °C], perfluoroctane (bp 100 °C), and perfluoro-*n*-butyltetrahydrofuran (bp 102 °C), but completely insoluble in common organic solvents.

Also as previously discussed in the case of dense CO$_2$ systems, it appears in principle that the need to heat the system above room temperature must be detrimental with respect to the asymmetric induction ability. It would be more

Table 5. Alkene Epoxidation Catalyzed by Fluorinated Chiral Manganese−Salen under Fluorous Biphasic Conditions (Reference 169)

| diamine of the salen−Mn catalyst	substrate[a]	oxidant	conversion (%)	yield (%)	ee (%)
1,2-cyclohexenediame	indene	O_2/pivalaldehyde	100	83	92
	1,2-dihydronaphthalene	O_2/pivalaldehyde	85	70	10
		PhIO[b]	85	65	6
		Bu_4NHSO_5	95	89	8
		m-ClC$_6$H$_4$CO$_3$H/NMO[c]	10	9	5
	styrene	O_2/pivalaldehyde	100	86	0
	t-β-methylstyrene	O_2/pivalaldehyde	100	75	0
	t-stilbene	O_2/pivalaldehyde	80	78	0
1,2-diphenyl-1,2-ethylenediamine	indene	O_2/pivalaldehyde	100	77	90
	1,2-dihydronaphthalene	O_2/pivalaldehyde	95	73	13

[a] Substrate dissolved in CH_2Cl_2 (0.33 M) unless indicated; substrate/catalyst molar ratio, 66; temperature, 20 °C. [b] MeCN was used as solvent for the substrate instead CH_2Cl_2. [c] NMO, N-methylmorpholine-N-oxide.

convenient to devise a fluorous system that could operate at or below room temperature.

These two chiral (salen)−manganese(III) acetates differing in the diamine moiety (R in Scheme 19) were tested as recoverable catalysts for the enantioselective epoxidation of alkenes under the so-called Mukaiyama conditions[169,170] using molecular oxygen as oxidizing reagent and pivalaldehyde as sacrificial relay. One of the main problems of this biphasic fluorous system for asymmetric catalysis is that the reactions have to be ideally conducted at low temperature (20 °C), and under these conditions the alkene dissolved in dichloromethane or toluene remains in a separate phase than the fluorous catalyst. Although the catalytic activity of the two chiral salen−manganese complexes indicated in Scheme 19 was high and a high substrate-to-catalyst molar ratio could be used, the enantiomeric excesses were very low or negligible except for the case of indene, for which the enantiomeric excess was >90%. The use of other oxidizing reagents instead of the O$_2$−pivalaldehyde couple did not lead to any improvement of the asymmetric induction ability. Some of the results reported are shown in Table 5. The catalyst was recovered at the end of the reaction by simple decantation and reused in a second run. It remains to be reported the maximum productivity and stability of these fluorous complexes in perfluorinated solvents.

The small ee values obtained with the fluorous (salen)−Mn(III)−OAc complexes were attributed to the low steric encumbrance of the perfluorinated octyl groups in the ortho- and para-positions of the phenolic moieties and to the negative electronic effect due to the strong electron-withdrawing character of the perfluorinated octyl chains.[170] To circumvent these two problems arising from the substituents, a second generation of fluorous (salen)−Mn(III) complexes were designed and synthesized (Scheme 20).[171,172] Bulky *tert*-butyl groups were placed in the ortho-positions of the salicylidene groups, and the perfluorinated tags were introduced in a satellite aromatic ring para to the salicylidene moiety through a biphenyl structure. In addition, chloride as apical ligand was replaced by C$_7$H$_{15}$COO$^-$, which even increases the fluorophilicity of the salen complexes. Not surprisingly, these salen complexes exhibit partition coefficients between n-perfluorooctane and acetonitrile of >1000.

Scheme 20. Fluorous Salen−Mn(III) Complexes Exhibiting High-Steric Encumbrance on the Metal Atom (Based on References 171 and 172)
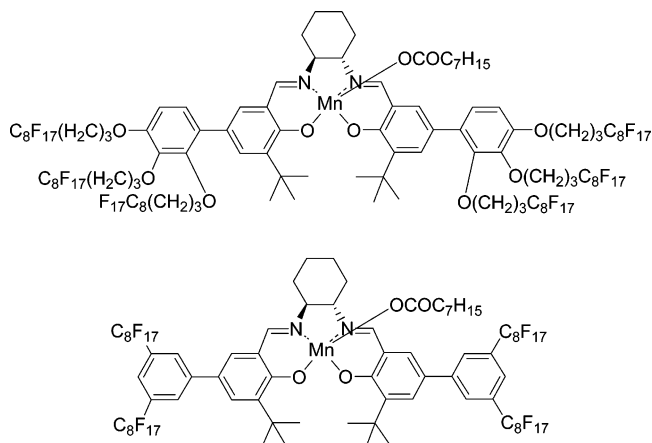
This second generation of "fluorophilic" salen−manganese complexes shows considerably higher asymmetric induction ability than those lacking ortho *tert*-butyl groups, and the ee values are comparable to those attained for conventional Jacobsen salen catalysts in acetonitrile. Interestingly, in contrast to what one would have predicted on the basis of a multitude of precedents about the negative influence of the temperature on the ee values, both yield and enantioselectivity rose with temperature under fluorous biphasic conditions, the best results being obtained at the boiling point of n-perfluorooctane (100 °C). These surprisingly excellent ee results at this high reaction temperature need, however, to be rationalized and expanded. Some selected results are contained in Table 6.

The main drawback of this methodology derives from the poor stability of the salen−manganese complex under oxidizing conditions at high temperatures as a consequence of complex degradation as evidenced by the progressive decrease of the ultraviolet−visible (UV−vis) absorption bands characteristic of (salen)−Mn(III) in the fluorous phase. Thus, upon reuse, the fluorous system containing the salen complexes shows a progressive diminution in its catalytic activity and asymmetric induction ability, which was more severe in the fourth use (see Table 6).

Table 6. Catalytic Performance of Chiral Fluorous Salen Manganese Catalysts for Alkene Epoxidation (References 171 and 172)

Catalyst	Substrate	Temperature (°C)	Yield (%)	e.e. (%)
(Mn salen complex with O(CH$_2$)$_3$C$_8$F$_{17}$ groups, C$_7$H$_{15}$OCO)	1,2-dihydronaphthalene	0	4.5	8
		20	46	26
		40	76	32
		70	74	42
		100	77	50
	Triphenylethylene 1st use	100	98	87
	4th use	100	80	71
	1-methylindene	100	98	77
(Mn salen complex with C$_8$F$_{17}$ groups, C$_7$H$_{15}$OCO)	1,2-dihydronaphthalene	100	68	50
	Triphenylethylene	100	98	80
	1-methylindene	100	96	70

Scheme 21. Ideal Enantioselective Kinetic Resolution of a Racemic Mixture of Epoxides
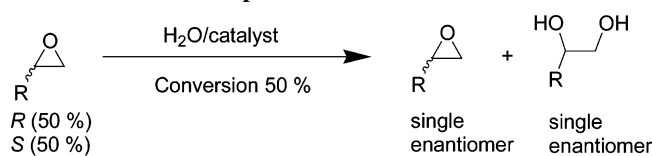
A reaction closely related to alkene epoxidation in most synthetic routes is hydrolytic epoxide ring opening. For this reason, hydrolytic kinetic resolution of a racemic mixture of epoxides can also be a viable synthetic procedure for the preparation of chiral epoxides and glycols that is alternative to the direct enantioselective alkene epoxidation and subsequent hydrolysis of a single enantiomer (Scheme 21). In an optimal epoxide kinetic resolution, at a conversion of 50%, only one of the epoxide enantiomers should be present and the other should have been converted quantitatively and stereospecifically into a single glycol enantiomer. One advantage of epoxide kinetic resolution over alkene epoxide is the higher stability of the chiral salen−metal catalyst under the mild conditions needed for the epoxide ring opening as compared to alkene epoxidation. This higher catalyst stability leads to a higher catalyst productivity and makes the enantioselective epoxide kinetic resolution more attractive than enantioselective epoxidation from the industrial point of view.

Pozzi et al. have also studied the asymmetric induction ability for epoxide kinetic resolution of three fluorous (salen)−Co(III) complexes having the same ligands as those previously used by this group for the enantioselective alkene epoxidation using (salen)−manganese(III) complexes.[173,174] As usual, the complex was formed by reacting Co(OAc)$_2$ and the fluorous salen ligand and performing a subsequent air oxidation of (salen)−Co(II) to (salen)−Co(III) in acetic

Table 7. Results of the Enantioselective Kinetic Resolution of Epoxides Using a Series of Recoverable Fluorous (Salen)−Co(III) Complexes (References 173 and 174)

catalyst	apical ligand, RH	substrate	conversion (%)	ee diol (%)	ee epoxide (%)
R^1 = R^2 = ^{t}Bu R^{3}R^3 = (CH$_2$)$_4$	AcOH	1-hexene oxide	50	98	98
R^1 = R^2 = C$_8$F$_{17}$ R^{3}R^3 = (CH$_2$)$_4$	AcOH	1-hexene oxide	10	81	10
R^1 = R^2 = ^{t}Bu R^3, R^3 = Ph	AcOH	1-hexene oxide	0		
R^1 = ^{t}Bu R^2 = C$_8$F$_{17}$ R^{3}R^3 = (CH$_2$)$_4$	AcOH	1-hexene oxide	43	97	72
R^1,R^2 = C$_8$F$_{17}$ R^{3}R^3 = (CH$_2$)$_4$	C$_8$F$_{17}$COOH	1-hexene oxide	29	85	33
R^1 = C$_8$F$_{17}$ R^2 = ^{t}Bu R^{3}R^3 = (CH$_2$)$_4$	C$_8$F$_{17}$COOH	1-hexene oxide	10	62	7
R^1 = ^{t}Bu R^2 = C$_8$F$_{17}$ R^{3}R^3 = (CH$_2$)$_4$	C$_8$F$_{17}$COOH	1-hexene oxide	46	≥99	91
R^1 = ^{t}Bu R^2 = C$_8$F$_{17}$ R^{3}R^3 = (CH$_2$)$_4$	C$_8$F$_{17}$COOH	1-hexene oxide	50	≥99	a, c
R^1 = ^{t}Bu R^2 = C$_8$F$_{17}$ R^{3}R^3 = (CH$_2$)$_4$	C$_8$F$_{17}$COOH	1-hexene oxide	36	≥99	b, c
R^1 = ^{t}Bu R^2 = C$_8$F$_{17}$ R^{3}R^3 = CH$_2$)$_4$	C$_8$F$_{17}$COOH	propylene oxide	≥49	75	c
R^1 = ^{t}Bu R^2 = C$_8$F$_{17}$ R^{3}R^3 = (CH$_2$)$_4$	C$_8$F$_{17}$COOH	1-octene oxide	≥47	≥99	≥99
R^1 = ^{t}Bu R^2 = C$_8$F$_{17}$ R^{3}R^3 = (CH$_2$)$_4$	C$_8$F$_{17}$COOH	styrene oxide	≥46	79	76

^{a} Reused catalyst after liquid−liquid extraction and with 16% cobalt leaching. ^{b} Reused catalyst after fluorous chromatography and with 50% cobalt leaching. ^{c} Data not available.

acid (AcOH). In addition to AcO$^-$, perfluorononanoic acid was also tested as apical ligand. Some of the cobalt catalysts, in particular those having 3,3′-di-*tert*-butyl groups, gave excellent enantiomeric excesses for the nonhydrolyzed epoxide and the resulting glycol. A selection of the results is listed in Table 7. The overall conclusion of this interesting comparison is that hydrolytic epoxide ring opening operates with the same or even higher enantioselectivity than the twin manganese complex for alkene epoxidation, but enjoying a higher service life of this catalyst.

In principle, it could have been anticipated that the presence of perfluorinated tags in the salen moiety with their strong electron-withdrawing effect should increase the Lewis acidity of the metal site by reducing the electron donor ability of the ligand. However, in contrast with these expectancies,

Scheme 22. Asymmetric Hydrogen Transfer Catalyzed by a Fluorous Schiff Base–Iridium Complex in Fluorous Medium (Based on Reference 175)

Scheme 23. Fluorous Chiral Diimine Ligands Used To Form Schiff–Metal Complexes Able To Act as Catalysts in Fluorous Media (Based on Reference 175)
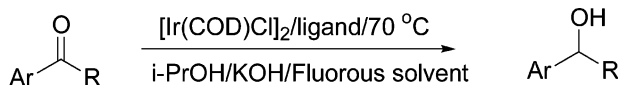
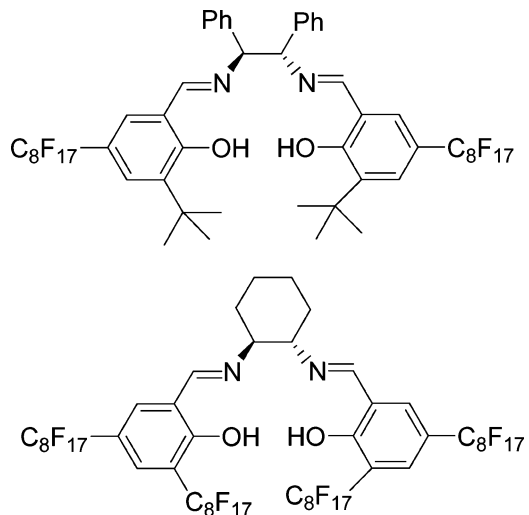fluorinated (salen)–Co(III) exhibited a lower activity than the original nonfluorinated Jacobsen catalyst (see Table 7). In this regard, it has to be mentioned that a systematic experimental study to determine the range of Lewis acid strength and the hardness/softness nature of salen complexes as a function of the nature of the substituents has not been undertaken. This information would be of interest to provide a conceptual framework to rationalize variations of the catalytic activity by substitution on the ligand.

The less fluorinated (F content < 50 wt %) (salen)–Co(III)C_7F_{15}COO complexes were not very soluble in perfluorinated solvents, but were sufficiently soluble in epoxides (in particular, the solubility in 1-hexene oxide was 1.66×10^{-2} M, equivalent to an epoxide/catalyst molar ratio of 500).[173] For this reason, recovery of the cobalt catalyst under the usual fluorous biphasic conditions was unsatisfactory. As a rule of thumb, the fluorine content has to be >70 wt % to ensure room temperature solubility of a compound in a perfluorinated solvent.[69]

Several options to overcome this limitation were tested, but none of them led to complete recovery of the fluorous complex. These recovery procedures included (i) liquid–liquid extraction with n-perfluorooctane after performance of the reaction in neat 1-hexene oxide and dilution with fluorophobic acetonitrile (84% recovery of the initial catalysts), (ii) conventional continuous liquid–liquid extraction of the acetonitrile-diluted reaction mixture with n-perfluorooctane (86% catalyst recovery), and (iii) use of fluorous chromatography to separate the catalyst (67% catalyst recovery). The problem in the latter procedure was the large affinity of the fluorinated (salen)–Co complex to the perfluoroalkyl-modified silica, resulting in a strong adsorption of the complex. Surprisingly, a last attempt to support by fluorophilic interaction the fluorinated (salen)–Co in fluorous reverse phase silica gel (a silica gel having covalently bonded perfluoroalkyl chains) and use the resulting solid as a heterogeneous catalyst also failed because it was found that the supported complex ($\approx$40 μmol of complex·g^{-1}) lost completely its catalytic activity.[174] This finding is rather surprising, and it was interpreted as arising from site isolation due to the low loading. It has been proposed that effective hydrolytic kinetic resolution requires the cooperation of two complexes in close proximity to activate the epoxide and the nucleophilic reagent, respectively. The outcome of this research is that a recoverable and reusable highly enantioselective salen catalyst based on the biphasic fluorous concept is still to be developed.

Catalytic asymmetric hydrogen transfer from simple alcohols to ketones has been reported to be catalyzed by perfluorosalen–iridium complexes in a mixture of perfluoroalkane/2-propanol as solvent (Scheme 22).[175,176] Enantiomeric excesses up to 60% were obtained with 3,3′-di-*tert*-butylsalicylidene or with 3,3′-diperfluorooctylbenzylidene ligands (Scheme 23) and the cyclooctadiene (COD) iridium chloride as metal source. To put these ee values into context, it has to be noted that the reaction in the fluorous biphasic systems is carried out at 45 °C or even higher temperature. The positive results obtained with the benzylidene cyclo-

hexadiimine ligand (structurally related to salen ligands but lacking phenolic OH groups) seem to point out that the presence of phenolic OH groups in the 2,2′-positions is not necessary to form the iridium complex. It would be, however, of interest to determine the coordination sphere and structure of the iridium complex derived from the bidentate N,N-diimine instead of the tetradentate N,N,O,O salen complex. Also, the stoichiometry of the benzylidene cyclohexadiimine (either 1:1 as assumed, 1:2 to have tetracoordinated Ir, or dimeric) was not determined. Structural resolution of the diimine iridium complex by single-crystal X-ray diffraction merits further investigation.

It was not possible to reuse the fluorinated iridium complexes due to several reasons, including their high solubility in 2-propanol and the occurrence of hydrolysis and decomplexation.[175] Although a higher partition coefficient to the fluorous phase can be simply achieved by adding sufficient fluorous tags to increase the fluorine content of the complex to values >70%, complex stability has a less straightforward solution that may severely hamper reusability. Concerning complex stability, one particular aspect that has not been sufficiently addressed, and it can be of much importance for the bidentate diimine ligand shown in Scheme 23, is the binding constant with different metals. Specifically, it would be of interest to know whether the perfluoroalkyl tags disfavor and, if so, how much, the otherwise high binding constant of salen ligands to di- and tripositive metal ions.

A way to overcome the problem of complex stability, increasing the reusability of the catalyst, has been to use diamine ligands obtained by metal hydride reduction of the aldimine function (Scheme 24). Amine lone electron pairs (sp^3) are more basic and bind more strongly to the metal than the imine (sp^2) lone electron pairs. It was observed that using as ligand of the iridium complex the diamine shown in Scheme 24 resulting from the imine reduction of dibenzylidene cyclohexanediimine, acetophenone was reduced with a ee value of 69%, and the complex could be reused with a minor metal leaching from the fluorous phase.[177] Some results are included in Table 8. It should be noted, however, that in the case reported none of these two secondary diamines contain bulky *tert*-butyl groups that could serve to create an optimal steric encumbrance around the metal atom

Scheme 24. Fluorous 1,2-Cyclohexadiamine Ligand Obtained by Diimine Reduction (Based on Reference 177)

R: OH or H
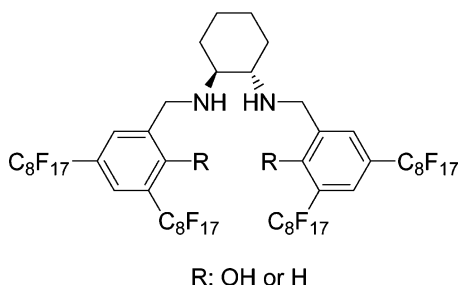
Table 8. Results of the Enantioselective Hydrogen Transfer from Isopropanol to Acetophenone Catalyzed by Recoverable Fluorous Chiral Metal Complexes Based on Any of the Ligands Indicated in Scheme 24 (Adapted from Reference 177)

| metal	ligand R	cycle	conversion (%)	ee (%)	metal leaching (%)
Ir	OH	1	95	23	51
Ir	OH	2	80	17	4
Ir	H	1	92	69	4
Ir	H	3	98	35	>5
Ir	H	4	96	53	>5
Ru	H	1	98	9	46
Ir	OH[a]	1	94	15	27
Ir	OH[a]	2	95	13	12

[a] Salen of cyclohexadiimine instead of diamine was used as ligand.

and that, on the other hand, reduction of the C=N bond introduces an undesirable conformational freedom around the resulting CH−NH single bond. Therefore, even though the reported ee value is encouraging, the synthesis of more rationally designed ligands to achieve higher ee is still pending. In the design of this ligand, the resolution of the crystal structure of the diamine iridium complex will be of much help.

The use of ruthenium instead of iridium led to lower ee values and poorer recyclability of the corresponding *N,N'*-dibenzylidenecyclohexadiamine−metal complex. In contrast to the latter bipodal diamine derived from benzaldehyde, the tetrapodal ligand derived from the aldimine reduction of the salen was less stable and non-reusable. Considerable iridium leaching was observed for this *N,N,O,O* tetrapodal ligand, a fact that was attributed by the authors to the negative influence of the phenolic hydroxy groups on the stability of the iridium complex. However, the reasons of this instability still need to be revisited to understand more clearly their structural origin, particularly with respect to salen stability. Overall, it seems that there is still room for further improvement in finding an appropriate reusable catalyst for enantioselective hydrogen transfer from alcohols to ketones, in terms of both asymmetric induction and stability and reusability.

3.4. Recoverable Salen−Metal Complexes in Ionic Liquids

Ionic liquids are those compounds constituted by anions and cations that are liquids at room temperature or near room temperature.[178,179] Ionic liquids and their use as alternative solvents in catalysis have become hot topics in chemistry.[180,181] Although ionic liquids, previously known as molten salts,[182] are certainly not a new class of compounds,[183] they have attracted recently considerable attention as green reaction media. The reason for this is the need to find suitable

Scheme 25. Synthesis and Structure of Common Nitrogen-Containing Ionic Liquids
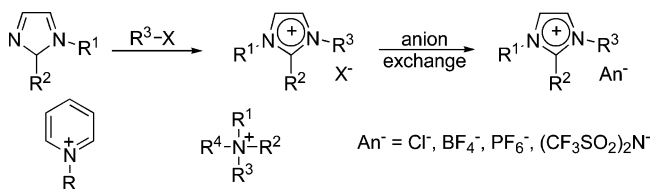
replacements for conventional volatile organic solvents, particularly chlorinated liquids that are harmful for the ozone layer. In this sense, ionic liquids having essentially zero vapor pressure and producing no atmospheric pollution are considered as green solvents because they comply with most of the principles of green chemistry.[181]

From the structural point of view, common ionic liquids are nitrogenated or phosphonated organic cations having inorganic counteranions. Because ionic liquids cannot be distilled and their purification is problematic, they have to be obtained in high purity directly by synthesis.[184,185] Nucleophilic substitution starting from a tertiary amine, nitrogen heterocycle, or phosphine with formation of the positive organic salt, followed by subsequent anion exchange, is the most general preparation procedure.[186−188]

The most widely used ionic liquids are derivatives of *N,N'*-dialkylimidazolium or *N*-alkylpyridinium with inorganic anions such as PF_6^-, BF_4^-, or even Cl^- (Scheme 25).[178,180] They combine a reasonable thermal stability, a sufficient solubility for most organic compounds, nonvolatility, and immiscibility with some organic solvents such as alkanes and ethers. One prerequisite for a liquid to be used as reaction media is to be inert under the reaction conditions. Special attention has to be paid to this point in some cases, because *N,N'*-dialkylimidazoliums or *N*-pyridiniums may not be completely stable and significant decomposition during reaction may occur. The topic of ionic liquid stability has recently been reviewed, and the reader is referred to published literature for further details.[189]

Using ionic liquids, the catalytic reactions are conducted in a single phase by dissolving in them reagents and catalyst. After completion of the reaction, the products are recovered by any physical means including precipitation, distillation, or liquid−liquid extraction. The condition for reusability is that the catalyst must remain dissolved in the ionic liquid during separation of the reaction mixture.

Given the viscosity of ionic liquids and the limited choice of immiscible organic solvents, complete recovery of the reaction products may be problematic. For this reason, mass balances indicating the percentage of the initial moles recovered either as unreacted substrate or converted products is an important value to be known, particularly for reaction data using fresh ionic liquid as solvent. When liquid−liquid extraction is used to separate the reaction mixture from the ionic liquid, the need of a volatile organic solvent for the extraction is one of the main drawbacks of the use of ionic liquids as green media This limitation can be overcome by using dense CO_2, particularly in its supercritical state, for the extraction. CO_2 is a good solvent due to its compatibility with ionic liquids, but it may have a limited solubility for some types of organic compounds.

Due to the high viscosity of most ionic liquids in which diffusion coefficients can be orders of magnitude smaller than in volatile organic solvents, the room temperature reaction rates using ionic liquids can be unsatisfactorily low.

In addition, many ionic liquids have melting points near ambient temperature and are frozen just below it. For these reasons, it is a common practice to conduct reactions in ionic liquids at temperatures higher than the ambient. As noted in the previous sections, 3.2. and 3.3., heating is expected to have a large negative influence on the enantioselectivity of the catalytic reaction, this fact being a general problem that still needs to be solved by developing less viscous, low melting point ionic liquids.

Room temperature ionic liquids can dissolve ionic or polar catalysts that remain in the ionic liquid phase upon the physical treatments to recover the reaction products. Apparently due to their polarity and viscosity, ionic liquids derived from N,N'-dialkylimidazolium dissolve most salen–metal complexes that, on the other hand, are fairly insoluble in alkanes and ethers. For this reason, ionic liquids as reaction media combined with subsequent liquid–liquid extraction is, by chance, a convenient experimental procedure that can serve to develop a suitable homogeneous reusable catalytic system. It has to be said, however, that the actual solubility of salen complexes in alkanes and the corresponding partition coefficient between imidazolium and alkane must be carefully surveyed in control experiments. The reason for this is the fact that the solubility of salen complexes depends evidently on the substituents and that the presence of four *tert*-butyl substitutents on the phenolic moiety increases considerably the solubility of salen complexes in alkanes.
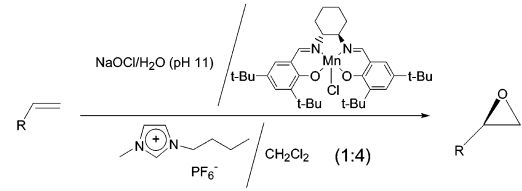
Song and co-workers were the first to exploit the high solubility of salen complexes in ionic liquids.[190] They have studied homogeneous enantioselective catalysis using chiral Schiff metal complexes in N,N'-dialkylimidazolium ionic liquids including the use of (salen)–Mn(III) chlorides.[190] The system has the advantage of employing as catalyst exactly the same salen–metal complex reported in conventional organic solvents without any modification of its structure.
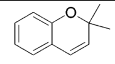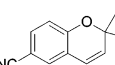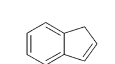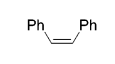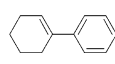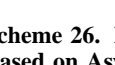
Thus, the asymmetric epoxidation of aromatic cyclic and acyclic alkenes has been carried out at 0 °C using buffered aqueous NaOCl (pH 11) as oxidant at a substrate-to-catalyst ratio of 3.8 mmol % using the R,R-configured salen complex.[190] Some of the reported results are shown in Table 9. Because at this temperature bmimPF$_6$ is solid, a 1:4 mixture of bmimPF$_6$–CH$_2$Cl$_2$ was used instead of pure imidazolium ionic liquid as solvent. At this point, this system can no longer be considered green. Apparently, the ionic liquid increases the reaction rate as compared to pure CH$_2$Cl$_2$ or conventional organic solvents. Thus, whereas chromene epoxidation in CH$_2$Cl$_2$ under certain conditions takes 6 h, the same conversion is achieved in 2 h using the 1:4 mixture of bmimPF$_6$–CH$_2$Cl$_2$. This fact was not fully explained and can reflect the positive influence of the polarity of the medium on the stabilization of the transition state. This reaction rate increase by imidazolium ionic liquids is very interesting and requires a better understanding of its origin.

The (salen)–MnCl–bmimPF$_6$ system was reused four times by washing the reaction mixture with water (hydrophobic PF$_6^-$ ionic liquids are generally not soluble in water) to remove the oxidizing reagent, concentrating the dichloromethane, and extracting the products with hexane. The system exhibits, however, a gradual decrease in activity and enantioselectivity upon reuse that was attributed to a progressive degradation of the salen complex.

More recently, Smith and co-workers have developed a salen–manganese catalyst based on binaphthyl units, which

Table 9. Results of the Enantioselective Epoxidation of Alkenes Using a Chiral Salen–Manganese Complex as Catalyst in N-Butyl-N'-methylimidazolium Hexafluorophosphate (bmimPF$_6$) (Adapted from Reference 190)

Substrate	Yield (%)	e.e. (%)	Configuration
	86 (1st use)	96	R,R
	53 (5th use)	88	R,R
	72	94	R,R
	72	84	R,S
	72	86	R,S
	77	84	S,S

Scheme 26. Enantioselective β-Amino Alcohol Synthesis Based on Asymmetric Ring Opening
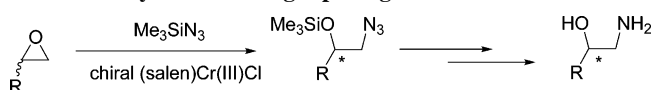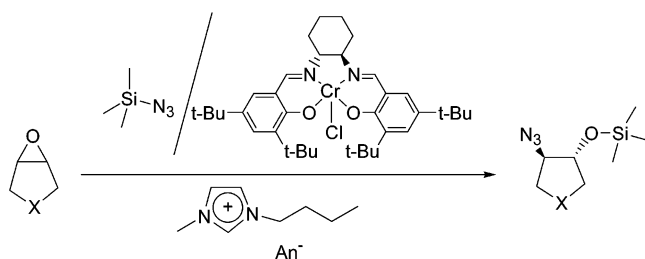
was used for the asymmetric epoxidation of 1,2-dihydronaphthalene using bmimPF$_6$ and bmimBF$_4$, in combination with CH$_2$Cl$_2$, as solvents. These systems show high conversions and enantioselectivities, similar to the results of the same catalyst in an organic solvent. However, the improvement was the reusability of the system during six consecutive runs, without an observed decrease in the enantioselectivity.[191]

Asymmetric ring opening of achiral epoxides is another important type of enantioselective reaction that can be catalyzed by chiral metal–salen complexes. Using trimethylsilyl azide as reagent, epoxide ring opening can yield chiral β-amino alcohols after reduction of the azide to the amino group and hydrolysis in mild acid conditions of the β-amino silyl ether initially obtained (Scheme 26). β-Amino alcohols are important building blocks for compounds with biological activity.

In contrast to the tendency of (salen)–Mn(III)Cl to undergo degradation under oxidizing conditions, Jacobsen and co-workers have demonstrated that (salen)–Cr(III)Cl is an indefinitely stable catalyst for the reaction of epoxides with trimethylsilyl azide, and, thus, the catalyst was reused a great number of times without decrease in conversion and β-amino alcohol enantiomeric excess.[19] The catalyst recovery in the absence of ionic liquids is unsatisfactory because the proposed procedure was based on the performance of the solventless epoxide opening and distillation of the reaction products. It has to be remembered, however, that due to safety reasons the hazardous distillation of azides is a limitation for large-scale industrial applications. However, for those kinetic resolutions in which products and reagents are volatile and nonexplosive, distillation of the reaction mixture can be a viable strategy to separate and recover the

Table 10. Influence of the Accompanying Anion on the Asymmetric Ring Opening by Trimethylsilyl Azide Catalyzed by Salen−Chromium Complex in Imidazolium Ionic Liquids (Adapted from Reference 193)

X	An⁻	yield (%)	ee (%)
−CH₂−	PF₆⁻	76 (first use)	94
		76 (fifth use)	93
−CH₂−	SbF₆⁻	75	87
−CH₂−	BF₄⁻	5	3
−CH₂−	CH₃SO₃⁻	traces	
−CH₂CH₂−	PF₆⁻	86	85
−O−	PF₆⁻	74	97

salen−metal complex.[192] In these cases distillation is performed safely at industrial scale.

A study by Song and co-workers has demonstrated that (salen)−Cr(III)Cl at 3 mol % dissolved in 1,3-dialkyl-imidazolium ionic liquids can also be a recoverable and reusable system for the homogeneous epoxide ring opening with trimethylsilyl azide.[193] In this case, the reaction products are separated from the catalysts by liquid−liquid extraction with hexane and the ionic liquid catalytic system (salen−chromium complex dissolved in ionic liquids) was reused four times without decay in conversion and enantioselectivity.

It was observed that the nature of the counteranion accompanying the imidiazolium cation has a strong influence on the catalytic activity and asymmetric induction ability of the chromium catalysts.[193] When the epoxide ring opening is performed in ionic liquids containing anions that render the imidazolium ionic liquid hydrophobic (such as PF₆⁻ and SbF₆⁻), the activity and enantioselectivity of (salen)−Cr(III)Cl are high and similar to those achieved by Jacobsen and co-workers in conventional organic solvents. In sharp contrast, the catalytic activity and enantioselectivity of (salen)−Cr(III)Cl decreases dramatically or even disappears when the reaction is carried out in hydrophilic imidazolium ionic liquids, that is, those in which the charge balancing anion is BF₄⁻ or CH₃SO₃⁻. It would be interesting to gain more insight into this effect in order to use the optimal ionic liquid. It could be that the influence of the anion on the catalytic activity is due to interaction with the salen catalyst such as complexation with the metal atom, or this effect could arise from tuning of polarity, viscosity, solubility, or other medium properties to the reaction mechanism. In fact, the (salen)−Cr(III)Cl complex is soluble in hydrophilic ionic liquids, but it is not fully soluble in hydrophobic imidazolium ionic liquids, where the catalyst remains mostly suspended. All of these facts deserve study in detail to clarify the reasons for this behavior and provide a conceptual framework that could be applied more generally to other enantioselective reactions.

A mixture of both types of hydrophobic and hydrophilic imidazolium ionic liquid combines solubility and activity and has been proposed as more adequate for this reaction.[193]

Enantioselective epoxidation of alkenes using (salen)−Mn(III) complexes to form chiral epoxides developed by

Table 11. Results of the Hydrolytic Kinetic Resolution of Epoxides in Imidazolium Ionic Liquids (Adapted from Reference 194)
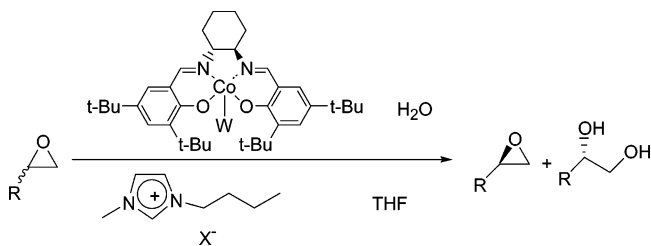
			substrate-to-catalyst molar ratio (mol/mol %)	conversion (%)	ee (%)	
R	W	X⁻			epoxide	diol
CH₂Cl	OAc	PF₆	0.5	52	>99	91.9
CH₂Cl	OAc	PF₆	0.1	52	>99	91.2
CH₂Cl	OAc	PF₆	0.025	55	>99	79.3
CH₂Cl		(Tf)₂Nᵃ	0.5	53	>99	86.0
CH₂Cl		(Tf)₂N	0.1	52	>99	91.2
CH₂Cl		(Tf)₂N	0.05	52	>99	90.3
Me	OAc	PF₆	0.5	51	>99	94.1
n-Bu	OAc	PF₆	0.5	54	>99	84.9
Ph	OAc	PF₆	1.0	53	97.5	86.3

ᵃ (Tf)₂N = bis(trifluoromethanosulfo)amidate.

Jacobsen and Katsuki constituted a major achievement in asymmetric catalysis.[5,9,11,12] An alternative to this process consists of the formation of racemic mixtures of epoxides and, then, to effect the kinetic resolution of this racemate, leaving unaltered a single enantiomer of the epoxide and forming the ring aperture products of the other. This approach may have practical advantages, particularly when the racemic mixture of epoxides is available in bulk scale due to the existence of an efficient industrial process using oxygen as oxidizing reagent. This is the case of propylene oxide and epichlorhydrin.

Related to the asymmetric ring opening is the kinetic resolution of epoxides. One of the most useful enantio-selective kinetic resolutions is the ring opening of terminal epoxides using water as nucleophile. As mentioned earlier, this hydrolytic kinetic resolution can be catalyzed in homo-geneous phase using Jacobsen's chiral (salen)−Co(III)(OAc) complex.[56,192] Although this cobalt Schiff base complex displays a high enantioselectivity, its turnover number is still unsatisfactory and there is a need for recovery and reuse of this catalyst. Following their earlier studies in enantioselec-tive (salen)−Mn(III) epoxidation, Song and co-workers have also shown that a convenient way to recycle (salen)−Co(III)(OAc) is to use 1-butyl-3-methylimidazolium ionic liquid as reaction medium.[194] The epoxides studied and some of the results obtained are summarized in Table 11.

An additional advantage of the use of imidazolium ionic liquids in this case is that the tendency of the (salen)−Co(III) complex to undergo reduction to catalytically inactive (salen)−Co(II) is suppressed in this medium, even upon extensive reuse of the system. The stability of the +III oxidation state avoids preactivation oxidative steps to form Co(III) from Co(II) that are necessary in other media. Moreover, if the reaction in imidazolium ionic liquid is conducted using the inactive form (salen)−Co(II) as catalyst, a spontaneous oxidation occurs in the ionic liquid and the resulting catalytically active (salen)−Co(III)⁺ is spontane-ously generated, remaining in this oxidized form. This effect is again poorly understood as well as the nature of the oxidant

when (salen)−Co(II) is employed. It would be of interest to perform further studies on this subject.

The experimental procedure uses a 4:1 mixture of tetrahydrofuran (THF) and imidazolium ionic liquid containing either PF_6 or bis(trifluoromethanosulfo)amidate as counterion.[194] At the end of the reaction, THF and the kinetically resolved epoxide are distilled from the ionic liquid. The diol derived from the hydrolytic opening of the epoxide is extracted with water. The system comprising the (salen)−Co(III)(OAc) was reused up to 10 times by employing a substrate-to-catalyst molar ratio of 0.5% without any decay in the enantiomeric excess that is in every case >99%.[194] Furthermore, the catalytic activity of the cobalt complex increases upon reuse, a fact that has been attributed to the gradual increase in the concentration of (salen)−Co(III)$^+$ when neutral (salen)−Co(II) was the initial oxidation state of the metal ion.[194]
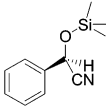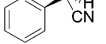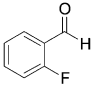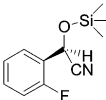
As a continuation of the pioneering studies by Song and co-workers, it has also been reported that chiral vanadyl Schiff bases dissolved in 1,3-dialkylimidazolium ionic liquid provide a reusable catalytic system to effect the enantioselective cyanosilylation of aldehydes.[195,196] After hydrolysis, the resulting trimethylsilyl ethers of α-cyanohydrins can be converted into chiral α-hydroxy acids, α-amino acids, or β-amino alcohols. Due to the importance of its derivatives in the pharmaceutical industry, mandelonitrile is a compound being produced enantiomerically pure in multihundred ton scale, and it is, therefore, one of the compounds being produced in the highest volume by asymmetric catalysis.[197,198]

The use of (salen)−V=O complexes as highly active and enantioselective catalysts in dichloromethane and other chlorinated solvents was reported by North and co-workers.[64,199] The use of dialkylimidazolium as solvent is environmentally greener and has the advantage of reusability without the performance of any synthetically demanding functionalization of the commercial tetra-*tert*-butyl salen ligand. As in the case of the epoxide ring opening by trimethylsilyl azide, a dramatic influence of the nature of the counteranion on the activity and enantioselectivity of the vanadyl complex was observed. As in the case of the (salen)−chromium(III) complex, hydrophilic Cl^- and BF_4^- were very inefficient, whereas the 1-butyl-3-methylimidazolium hexafluorophosphate gave activity and enantioselectivity values close to those found in dichloromethane for benzaldehyde. This influence of the counteranion still lacks rationalization.[195] Some of the results reported for the enantioselective addition of benzaldehyde and other aromatic and aliphatic aldehydes have been summarized in Table 12.[195,196]

The reaction products can be separated by hexane extraction and decantation from the ionic liquid containing the vanadyl salen complex. An issue that is necessary to address in every reaction in which phase separation occurs is the mass balance, that is, the percentage of the initial substrate that is being recovered and analyzed. Otherwise, analysis can be disguised by the preferent extraction of certain reaction products. Table 12 provides also the mass balance data of the enantioselective cyanosilylation performed in imidazolium ionic liquid. The catalytic system was reused four times without noticeable variation in the performance of the system or in the enantioselectivity of the products.

In the previous studies about the catalytic activity of salen−metal complexes dissolved in imidazolium ionic liquids, the same complex that was originally used in

Table 12. Enantioselective Cyanosilylation of Aldehyde Catalyzed by Tetra-*tert*-butyl Salen−Vandyl Complex in 1-Butyl-3-methylimidazolium Hexafluorophosphate (Adapted from Reference 195)

Substrate	Product	Mass balance (%)	Conversion (%)	e.e. (%)
(benzaldehyde)	(TMS O-protected cyanohydrin)	95 (1st use)	85	89
		95 (5th use)	83	89
(2-fluorobenzaldehyde)	(TMS O-protected cyanohydrin)	84	81	86
(cinnamaldehyde)	(TMS O-protected cyanohydrin)	87	76	98
(aliphatic aldehyde)	(TMS O-protected cyanohydrin)	94	97	83

conventional organic solvents was also employed without modifying the ligand to better adapt it to ionic liquids as a medium. A problem encountered in these cases is, however, that during the recovery of the reaction products from the ionic liquid, some catalyst even in trace quantities is also extracted, thus causing its gradual depletion from the ionic liquid while contaminating the reaction products. This problem arises from the fact that tetra-*tert*-butyl substitution increases substantially the catalyst solubility in hexane and other organic solvents that otherwise will be rather low in conventional volatile organic solvents.
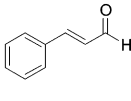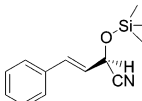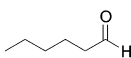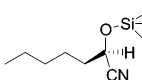
Further evolution in the transformation from nonrecoverable to recoverable catalysts requires synthetic modification of the catalyst to increase its coefficient partition in a given medium. As we have seen in the case of fluorous catalysts, increased affinity in a medium can be simply achieved by introducing tags peripheral to the catalytic site that have structural similarity with the new solvent. Yoshida and Itami have recently reviewed this methodology of catalyst modification.[51,200] In fluorous phase catalysis, the higher the weight percentage of this tag with respect to the rest of the catalyst, the higher would be the affinity for the new medium. As a rule of thumb, when the percentage of the solubilizing substituent is >70% of the total weight, the catalyst becomes indefinitely soluble in the novel medium and, very frequently, insoluble in conventional volatile organic solvents.

Mimicking the methodology used in fluorous media to increase the "fluoricity" of a homogeneous catalyst, vanadyl salen complexes have been modified by appending in peripheral positions of the ligand an *N*-methylimidazolium tag that should increase the "ionophilicity" of the salen catalyst.[201] The synthesis of the ionophilic complex has as a key step the radical-chain addition of mercapto groups to vinylic C=C double bonds, a process that is highly selective, takes place under mild conditions, and gives high product yields. Addition of mercapto groups to styryl groups is a reaction that has been widely used to effect the anchoring of organic components to inorganic supports.[202] The actual

Scheme 27. Synthetic Route for Preparation of an Ionophilic Salen−Vanadyl Complex (Based on Reference 201)

i) preparation of the asymmetric styryl substituted salen complex

Statistical
Ratio

R = R' = H   9
R = H, R' = $C_6H_4CH=CH_2$ 6
R = R' = $C_6H_4CH=CH_2$ 1
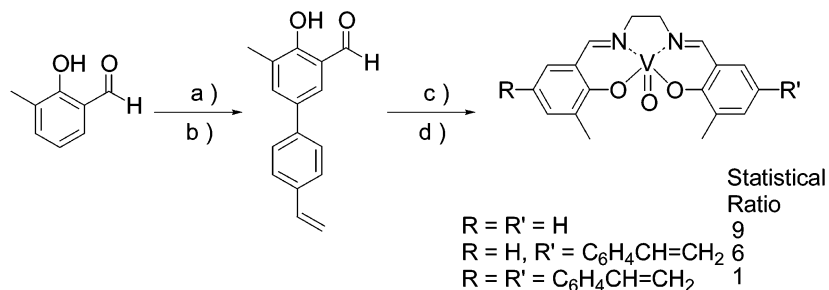
a) Br_2, CH_2Cl_2, 0° C, 1 h; b) 4-vinylphenylboronic acid, $[Pd(PPh_3)_4]$, 2 M Na_2CO_3, THF, 70° C, 3 h; c) 3-methylsalicylaldehyde, 1,2-ethanediamine, EtOH, relux, 1 h; d) VOacac, MeOH, r.t., overnight

ii) attachment of imidazolium tag
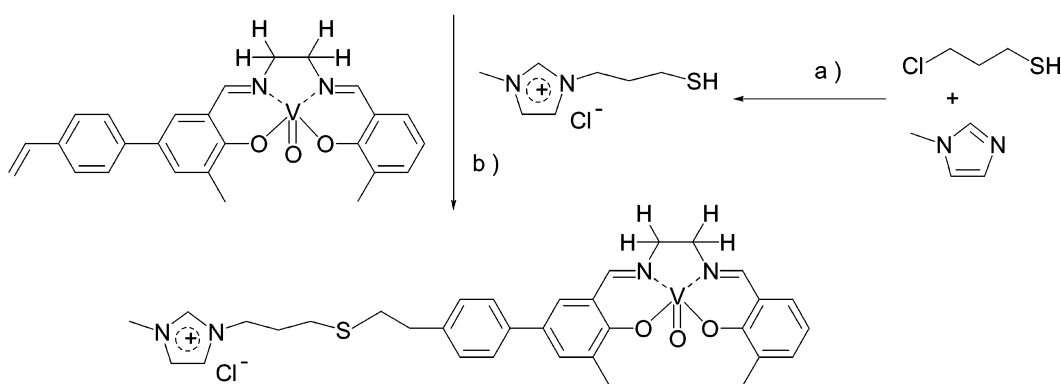
a) 80°C, 96 h; b) AIBN, $CHCl_3$, CH_3CN (degassed), 70° C, 20 h.

preparation route of the ionophilic vanadyl salen complex is presented in Scheme 27.

The synthesis shown in Scheme 27 requires an asymmetrically substituted salen ligand having a styryl unit in the para-position of one of the phenolic moieties. It is worth noting that what was used in the original study is a statistical mixture of vanadyl salen complexes.[201] The synthesis of asymmetrically substituted pure salen ligands is synthetically a highly demanding process, because the reaction of a diamine with aromatic aldehydes to give the monoimine/amine occurs only in low yield, bisimines being normally the products that can be obtained in high yields. The low yield of the monoimine/amine makes necessary a problematic isolation, something that may produce the extensive hydrolysis of the ligand. Clearly, a satisfactorily simple synthetic procedure of pure asymmetric salen ligands will be a step forward in this area.
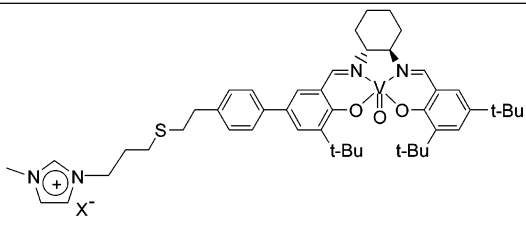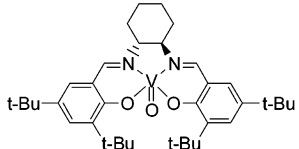
For this reason, a simple alternative to having pure asymmetrically substituted salen ligands is to make a statistical mixture of ligands by reacting a diamine with a mixture of two different aldehydes in appropriate proportion. In this way, the predominant symmetric ligand is not able to react with the 1-methyl-3-(3-mercaptopropyl)imidazolium chloride (step ii in Scheme 27) and would be easily separated from the appropriately functionalized metal−salen complex after the introduction of the imidazolium tag. On the other hand, the 6-fold less abundant symmetric ligand having two styryl units in the para-position of each phenolic moiety will be doubly functionalized by imidazoliums, but it will act as

catalyst similarly to the monoimidazolium-functionalized complex, therefore its presence not being a problem (step i in Scheme 27).

As expected, the ionophilic vanadyl salen was insoluble in hexane and fully soluble in 1-butyl-3-methylimidazolium hexafluorophosphate. A 2.6 wt % of ionophilic vanadyl salen was reused five times for the cyanosilylation of benzaldehyde at a substrate-to-catalyst molar ratio of 0.02 with high mass balances, conversion, and selectivity to the cyanohydrin trimethylsilyl ether.[201] Importantly, chemical analyses after extensive reuse have shown that the vanadium content of the ionic liquid is coincident to that of the fresh liquid.

The same methodology was applied to develop a chiral ionophilic vanadyl salen complex derived from (1R,2R)-(−)-diaminocyclohexane and 3,5-di-tert-butylsalicylaldehyde. As in other previous examples, it was observed that the conversion and enantioselectivity obtained with the chiral ionophilic salen vanadyl complex depends on the nature of the counteranion accompanying the 1-butyl-3-methylimidazolium cation. However, the enantiomeric excesses using this ionophilic salen vanadyl complex were very low as compared to those achieved using the symmetric tetra-tert-butyl salen−metal complex. Some of the reported results are listed in Table 13. Apparently, the steric encumbrance around the metal center in the ionophilic complex having only two tert-butyl substituents is not sufficient to introduce a strong stereogenicity around the metal atom as in the case of the tetra tert-butyl derivatives. Also, there is a possibility that an unfavorable interaction between the imidazolium tag or

Table 13. Results of the Enantioselective Salen−Vanadyl Catalyzed Cyanosilylation of Benzaldehyde in 1-Butyl-3-methylimidazolium Liquid (Based on Reference 201)

Catalyst	Counter anion	Conversion (%)	Enantiomeric excess (%)
	PF_6^-	88	57
	BF_4^-	16	20
	Cl^-	95	41
	CH_2Cl_2	95	90

the accompanying chloride with the vanadyl center effects a decrease on the asymmetric induction ability. Whatever the reason, the preparation of a chiral ionophilic vanadyl salen complex exhibiting high enantioselectivity is a task that will be worthwhile to be pursued until a highly stereoselective salen complex is obtained.

The activity and asymmetric induction ability of a tetra-*tert*-butyl salen vanadyl complex dissolved in 1-butyl-3-methylimidazolium hexafluorophosphate has been compared with those of a library of related recoverable vanadyl salen complexes including vanadyl covalently bonded to carbons and silicas.[195,196] It was concluded that tetra-*tert*-butyl salen vanadyl dissolved in imidazolium ionic liquids gives a good balance among economy in catalyst preparation, good ee values for the cyanosilylation, and recoverability of the catalytic system. In the following sections, we will describe in detail the preparation of these covalently anchored salen vanadyl complexes.

Inspired by the green chemistry principles[25−27] that promote a change from fossil to renewable feedstocks, there is a great current interest in developing processes that use CO_2 as reagent. As noted in section 3.2.1, development of large industrial processes that use CO_2 as raw material in substitution of current C1 feedstocks such as CO, $COCl_2$, CH_4, and CH_3OH will contribute also to meeting the requirements of the Kyoto agreement about the emission reduction of gases responsible for the greenhouse effect. For this reason, the recent reports that salen−chromium and cobalt can catalyze the CO_2 insertion into epoxides to form cyclic carbonates has attracted considerable attention.[137,203]

In view of the above precedents where metal−salen complexes have been used as recoverable catalytic systems in imidazolium ionic liquids, and also considering that CO_2 can be highly soluble in ionic liquids, it is of interest to study the activity of these complexes dissolved in ionic liquids as reusable and recoverable catalysts for the CO_2 insertion into epoxides. Working under supercritical CO_2 conditions (80 °C and 100 bar) and using 1-butyl-3-methylimidazolium ionic liquids, Garcia and co-workers have studied the influence of the presence of a substituent at the 2-position

Scheme 28. CO_2/Epoxide Insertion Catalyzed by Salen−Metal Complexes in Imidazolium Ionic Liquids

R: H or CH_3
An^-: PF_6^- or BF_4^-
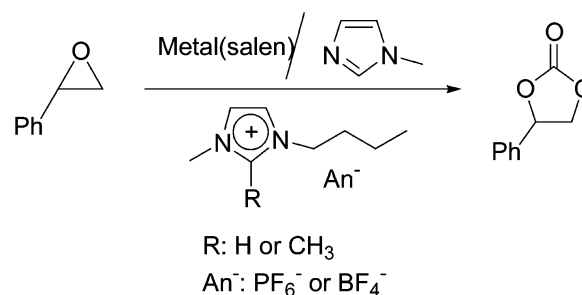
Table 14. Results of the CO_2 Insertion Catalyzed by Salen−Chromium Complex in Imidazolium Ionic Liquid (Adapted from Reference 204)

catalyst	substrate-to-catalyst molar ratio	cosolvent	conversion (%)	selectivity (%)	mass balance (%)
salen-Cr (not recoverable)	875	CH_2Cl_2	75	100	57
salen-Cr (first use)	875	bmimPF$_6$	25	79	80
salen-Cr (second use)	875	bmimPF$_6$	35	68	100
salen-Cr (third use)	875	bmimPF$_6$	37	67	100
salen-Cr (fourth use)	875	bmimPF$_6$	48	56	92
salen-Cr	292	bmimPF$_6$	50	100	54
salen-Cr/NH$_2$SiO$_2$[a]	875	CH_2Cl_2	66	89	100

[a] This catalyst corresponds to the salen−chromium catalyst supported on aminopropyl silica.

of the imidazolium ring and the nature of the corresponding counterion (hydrophilic or hydrophobic), as well as the influence of the salen complex metal atom and the base cocatalyst on the styrene oxide conversion to the corresponding cyclic carbonate (Scheme 28). Table 14 summarizes some of the results that have been published.[204]

Compared to dichloromethane, the CO_2 epoxide insertion in imidazolium under the same conditions in the presence of salen−chromium(III) chloride gave smaller epoxide conversions and the mass balances were not complete due to an inefficient pressurized reactor discharge. However, the system consisting of chromium salen dissolved in imidazo-

lium ionic liquid represents a step toward reusability after extraction of the products with hexane.[204] Thus, the activity of the (salen)−chromium(III) chloride complex was tested in four consecutive reuses, observing a gradual increase in epoxide conversion with a reduction in the cyclic carbonate yield. As discussed earlier, this evolution in the product distribution upon reuse seems to be a general trend when the initial activity of the Lewis acid catalyst decreases and some Brønsted acid sites develop. In contrast, the same (salen)−chromium(III) chloride complex adsorbed on aminopropyl-modified silica (last entry in Table 14) loses completely its activity due to the complete desorption of the complex under the reaction conditions and could not be reused at all.

4. Reusable Chiral Salen Complexes Supported on Inorganic Solids as Heterogeneous Catalysts

Inorganic solids have been widely used as supports of chiral salen complexes.[202,205] In the past decade there has been an enormous evolution in the strategies to immobilize salen complexes in inorganic supports, going from the encapsulation within the cavities of tridirectional large-pore zeolites of homogeneous salen complexes without any specific functionalization for this purpose[206] to synthetically more demanding methodologies whereby specific salen complexes with appropriate structures have been synthesized to effect covalent immobilization on the support.[16,20]

The use of inorganic solids has some advantages over other types of supports. The chemical and thermal stability of the inorganic supports makes them compatible with the widest range of reagents and experimental conditions. Also, mechanical resistance of the solids makes these inorganic particles less prone to attrition due to stirring and solvent attack during their use in a chemical reactor under continuous operation. One of the major problems in the design of an industrial process is the possible decrease of catalyst particle size due to mechanical abrasion, this issue being particularly important when polymer beads are used as supports.

For the purpose of organizing this review, we have grouped the reports on immobilized salen−metal complexes into/onto inorganic supports in three main categories depending on the support−complex interaction: (1) encapsulation within the cages of tridirectional large-pore zeolites using a methodology generally known as "ship in a bottle" (SIB) synthesis, the resulting salen complex becoming mechanically immobilized; (2) immobilization by weak dipolar or strong Coulombic interactions, where in the latter case the salen complex is adsorbed onto the support by ion-pairing with an anionic or cationic solid; and (3) connection by covalent bond of the salen ligand and the support, which requires the necessary functionalization of the complex to allow the immobilization. In the following sections we will describe and comment on each of these three strategies to develop heterogeneous chiral salen−metal complexes supported in/on inorganic solids.

4.1. SIB Occlusion of Salen Complexes Inside Porous Hosts

The SIB approach alludes to a methodology to immobilize homogeneous complexes in which the host−guest interaction is not chemical (neither ionic nor covalent bonding), but physical.[206] This situation can easily occur in tridirectional

Scheme 29. Molecular Model of the Best Docking of Copper Phthalocyanine Inside the Supercages of Zeolite Y (Based on Reference 222)
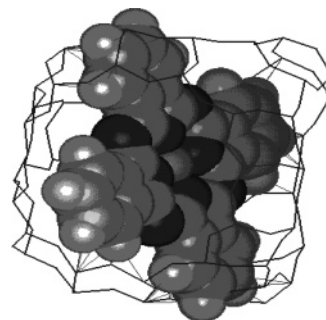
zeolites; their rigid structures define cages and cavities that are interconnected through smaller windows. Zeolites are aluminosilicates having crystal structure defined by empty channels and cavities of strictly regular diameter called micropores. These micropores allow mass transfer from the exterior to the interior of the zeolite particles, provided that the size of the diffusing molecules is smaller than the dimensions of the micropores. These micropores can be arranged in the three Cartesian axes (tridirectional zeolites) or in two directions (bidirectional zeolites) or can be ordered forming an array of parallel channels (monodirectional zeolites). The reader is referred to specialized monographs or reviews for a more detailed description of the structure, synthesis, and properties of zeolites as hosts.[207−213]

In the case of tridirectional zeolites having a pore geometry formed by large cavities interconnected by smaller windows, a situation can be envisioned in which a guest can be accommodated inside the zeolite cavity, but it is too large to diffuse outside the cavity through the smaller windows. The complex is retained in the interior of the zeolite cavity because it is too large to cross the corresponding cavity opening due to its bulkiness relative to the pore dimensions. The term *mechanical immobilization* has been coined by Stoddart to reflect a situation in which immobilization is not caused by a chemical bond between the host and the guest, but by the fact that the size impedes the guest from exiting through the host pores, like a large piece of furniture in a small room.[214−216]

The term SIB was probably coined by Herron, who reported the synthesis of several types of metallic complexes (including achiral salen−metal complex) encapsulated within zeolites.[217] The SIB concept refers to the similarity of the resulting complex imprisoned within the zeolite framework to the artistic bottles containing a ship larger than the bottleneck. However, even earlier than this term was used for the first time, other researchers had most probably already used this methodology. Thus, as an example, Schulz-Ekloff and Romanovskii synthesized independently metallic phthalocyanines inside faujasite X by reacting *o*-phthalodinitrile with a transition metal exchanged faujasite.[218−221] Scheme 29 shows a molecular model of a copper phthalocyanine encapsulated inside the supercages of zeolite Y.

The encapsulation of salen complexes within the cavity of a zeolite starts with the partial ion exchange by the desired metal of the charge-balancing cations (Na+ in faujasites) that are located inside the micropores. After this first step, the salicylaldehyde and the chiral diamine are added to the inorganic material to synthesize the complex formed from the complexation of the ligand and the metal (Scheme 30). To avoid formation of the salen ligand outside the zeolite

Scheme 30. Preparation of Zeolite-Encapsulated Chiral Salen−Metal Complex Using the SIB Methodology
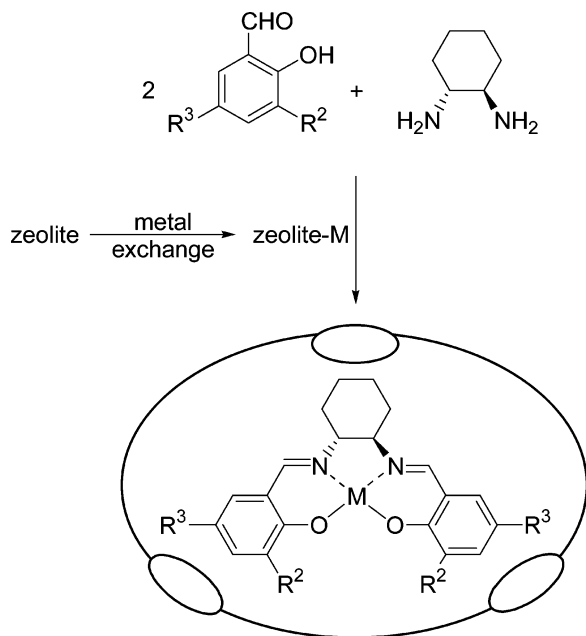
Table 15. Heterogeneous Chiral Salen−Metal Complexes That Have Been Imprisoned Inside Zeolites Using the SIB Methodology

zeolite	metal	asymmetric reaction	ref
Y	Mn(III)	epoxidation of alkenes	223
EMT	Mn(III)	epoxidation of alkenes	224
USY[a]	Co(III)	hydrogenation	225
Y or EMT	Cr(III)	epoxide ring opening	226
Y or X	Mn(III) and Co(III)	epoxidation of alkenes	227−229

[a] USY refers to a highly dealuminated (*u*ltra*s*table) zeolite *Y*.

micropores, the addition of salicyladehyde and diamine can be stepwise in such a way that during the synthesis they are not simultaneously present in the supernatant liquid phase.

One advantage of the use of a zeolite-encapsulated salen−metal complex as a heterogeneous catalyst is that the zeolitic host can introduce shape selectivity to the catalytic system; that is, only those substrates having a size that permits intracrystalline diffusion can reach the catalyst and react. On the other hand, encapsulation can have a positive effect on the stability of the encapsulated salen complex, prolonging the life of the salen catalysts. The increase in stability arises from the protection of the inert zeolite framework, making complex degradation more difficult by impeding sterically the attack to the more reactive parts of the ligand. Although shape selectivity and guest stabilization are effects generally observed in zeolite-based catalysts, more studies are still necessary in this area to fully exploit the potential of zeolite-imprisoned chiral salen−metal complexes. Tables 15 and 16 collect all of the available information that describes the encapsulation of chiral salen−metal complexes into the zeolite void space and their catalytic activity.

The first successful preparation of a chiral salen complex encapsulated into the *supercages* of a large pore zeolite was accomplished, approximately simultaneously, by Corma and Garcia using the Y zeolite[223] and by Ogunwumi and Bein using the EMT zeolite.[224] The pore structure of the Y zeolite consists of almost spherical 1.3 nm cavities interconnected tetrahedrally through smaller apertures of 0.74 nm diameter. EMT zeolite is a hexagonal form of the faujasite structure,

Table 16. Enantiomeric Excess and Performance of Encapsulated Salen−Metal Complexes Prepared by the SIB Methodology

catalyst	ee[a] (%)		leaching[b]	recycling[b]	ref
	homo	hetero			
Mn(III)/Y	8−74	5−58	N	na	223
Mn(III)/EMT	35−80	20−88	N	Y (deact second cycle)	224
Co(III)/Y	9−22	<3	N	na	225
Cr(III) or Cr(III)/EMT	18−68	3−16	N	na	226
Mn(III) or Co(III)/ zeolite X or Y	60−91	40−91	N	Y (three cycles)	227−229

[a] Comparison between the reported ee values for the homogeneous and heterogeneous catalysis under analogous reaction conditions. [b] N, no; Y, yes; na, data not available.

having cages larger than those of faujasites. For this reason, the EMT cavities are frequently called *hypercages* to emphasize their larger dimensions compared to faujasite supercages. The hypercages of EMT are accessible through three 12-ring windows with free dimensions of 0.69×0.74 nm and two 0.74 nm circular apertures. EMT contains also smaller cages denoted *hypocages* having only three windows, but the bulky salen−metal complex cannot be accommodated in these hypocages. In both papers dealing with chiral salen manganese encapsulated within zeolites, the complex prepared was derived from *trans*-1,2-diaminocyclohexane and the resulting encapsulated salen−Mn(III) complex used as heterogeneous catalyst for the asymmetric epoxidation of alkenes. The main difference between these two studies is that the use of EMT allows ortho *tert*-butyl substitution on the phenolic moieties of the salen complex, something that is impossible inside the somewhat smaller cavities of Y faujasite.

Using zeolite Y as host, the catalytic results in terms of reaction rate and ee are lower compared to the homogeneous counterpart.[223] The alkenes tested using chiral salen−Mn(III) were cyclohexene, styrene, *cis*- or *trans*-β-methylstyrene, and a cyclic indene. The lower reaction rates were attributed to the restrictions imposed on the diffusion of substrate and products through the micropores of the solid. The lower ee obtained by Corma and Garcia using the Y zeolite encapsulated salen−Mn(III) catalyst as compared to solution was initially attributed to a combination of two negative factors: (i) a noncatalyzed, unselective epoxidation route in the liquid phase and/or (ii) the existence of residual amounts of uncomplexed Mn^{2+} present in the zeolite that would act as a non-stereoselective catalytic species. The first option, however, was rejected because no leaching of Mn ions from the interior of the zeolite to the solution occurs, whereas the second was supported by electron paramagnetic resonance (EPR) observation of the presence of uncomplexed Mn^{2+} ions on the zeolite containing the salen−Mn(III) complex.[230,231]

Ogunwumi and Bein also observed lower reaction rates when comparing the EMT-encapsulated salen−Mn(III) catalyst with the homogeneous counterpart. However, the ee values attained for styrene and *cis*-β-methylstyrene as substrates with the heterogeneous EMT-encapsulated catalyst were similar to the ee values obtained using the homogeneous complex.[224] To determine if there was any leaching from the catalyst, half of the reaction mixture was filtered after some reaction time, and the reaction was allowed to progress under the same conditions but in the absence of any solid

catalyst. No further conversion was observed in the filtrate, whereas in the twin half in which the solid catalyst was present the reaction proceeded normally. Ogunwumi and Bein also addressed the activity of the catalyst upon reuse. However, in the recycling test the heterogeneous catalysts were observed to be completely deactivated after the first cycle.

Other salen–metal complexes, such as those of cobalt[225] and chromium,[226] have also been encapsulated inside the zeolite cages. A salen–cobalt complex has been entrapped inside the ultrastable zeolite Y (USY) and used as asymmetric heterogeneous catalyst for the transhydrogenation of acetophenone.[225] Zeolites Y and EMT have been used as hosts to immobilize salen–chromium complexes, which were employed for the asymmetric ring opening of epoxides (namely, cyclohexane oxide and cyclopentane oxide).[226] In both cases, lower reaction rates, caused most probably by diffusion restrictions inside the pores of the zeolite, were observed. In the case of the zeolite-encapsulated metal complexes, the substrates have to enter into the channels of the zeolite to approach the catalyst, and subsequently the products have to desorb from the zeolite micropores, and this intracrystalline diffusion may slow the reaction compared to solution. No leaching was observed when the chiral salen–metal complexes of Co and Cr encapsulated in zeolites were used. The ee values obtained with the two heterogeneous catalysts were lower compared with the homogeneous analogues. In the case of the chromium heterogeneous catalysts, three possible reasons were targeted by the authors for those results: (i) the presence of adventitious acid sites promoting unselective epoxide ring opening; (ii) the encapsulation of insufficiently stereogenic ligands (large substituents on the phenolic moiety cannot fit inside the zeolite cavities); and (iii) the occurrence of a change in the reaction mechanism from bimolecular in homogeneous catalysis with participation of two complexes to a unimolecular single-metal reaction mechanism in the heterogeneous phase, the unimolecular pathway having poorer asymmetric induction capability than the bimolecular one.[226]

Thus, in general, the transformation of a homogeneous chiral salen catalyst into a heterogeneous one by encapsulation of a chiral salen–metal complex within the cages of a zeolite leads to a decrease in the ee values. However, Hölderich and co-workers solved this problem of moderate enantiomeric excesses in the SIB strategy by introducing a postsynthetic zeolite modification prior to complex encapsulation to generate some mesoporosity in the zeolite particles.[232–234] Mesoporosity in zeolites can be created by controlled partial damage of the crystalline zeolite framework.[227–229] It has been proposed that the enlargement of some intrazeolitic cavities (those having a partially damaged framework) makes it possible for these mesopores to host chiral salen complexes with adequately large stereogenic substituents that enhance the asymmetric induction. The mesopores that are embedded in the undamaged zeolite micropore structure offer additional advantages in catalysis: (i) the metal complexes encapsulated have more conformational freedom behaving similarly to solution and (ii) they are more accessible during the catalytic reaction. The zeolites especially suited for this new methodology were zeolites X and Y characterized by a high aluminum content and, therefore, more adequate to create mesopores by dealumination. To effect the controlled attack on the zeolite framework, first the solids were submitted to severe de-

alumination by treatment with $SiCl_4$, and in a subsequent step the mesopores were formed by steaming. The chiral salen–metal complexes encapsulated in these new materials were those of cobalt and manganese, using *trans*-1,2-diphenylethylene-1,2-diamine as the chiral diamine to form the salen complex.[227–229] These heterogeneous salen–metal catalysts were used for the asymmetric epoxidation of olefins (limonene and α-pinene, respectively). Compared with the homogeneous analogues, the results showed that the zeolite-encapsulated chiral salen complexes provided higher reactions rates and ee values without loss of the chemoselectivity. Apparently this higher performance of dealuminated and steamed zeolites arises from the higher intrazeolitic space available for the diffusion of reactants and products, as well as for the accommodation of the transition states leading to the enantioselective discrimination. None of these heterogeneous catalysts suffer from leaching, and the heterogeneous manganese catalyst can be reused in three consecutive cycles without the loss of activity and selectivity. Thus, given the ease with which the SIB strategy can form heterogeneous catalysts containing chiral salen complexes of virtually any exchangeable metal, it would be of much interest to expand this approach of creating controlled mesoporosity in zeolites to reaction types other than alkene epoxidation.

4.2. Immobilization by Electrostatic Interaction

With the purpose of overcoming the moderate ee values that are generally obtained using the SIB methodology for chiral salen complex immobilization in commercially available zeolites, an alternative methodology that has been developed consists of complex immobilization on the external surface of inorganic nonporous solids or in the interior of porous solids with void dimensions larger than zeolites. In this methodology, one possibility to achieve the immobilization of the chiral salen complex on the support is by electrostatic interaction between the surface of the inorganic solid and an electrically charged homogeneous complex, either unmodified or suitably functionalized (as in the case of ionophilic complexes shown in Scheme 27). Advantages of electrostatic binding are the experimental simplicity of the procedure to support the complex on the solid and the fact that the purity of the immobilized complex can be better assessed. A conventional homogeneous complex or an appropriate derivative prepared in the liquid phase and characterized by routine analytical and spectroscopic techniques is simply stirred with the support, and the electrostatic binding occurs spontaneously even at low temperatures. Tables 17 and 18 collect the relevant information and catalytic results that have been reported with salen complexes supported by electrostatic binding.

The first report describing the heterogenization of a chiral salen complex by electrostatic interaction was published by Kosslick and co-workers, who immobilized a chiral salen–manganese complex in the pores of a mesoporous Al–MCM-41.[235] The complex was introduced inside the pores by impregnation, and the resulting supported salen complex was found to be strongly bound to the mesoporous aluminosilicate. It was proposed that immobilization arose from strong interactions between the aromatic rings of the complex and the internal surface silanol groups of the walls of the mesopores. In view of alternative data, it seems, however, that the interaction responsible for salen–manganese immobilization is more likely to occur between the surface silanol groups and the manganese ion of the complex.

Table 17. Supports, Metals, Interactions, and Catalytic Reactions of Heterogeneous Chiral Salen Metal Complexes Supported by Electrostatic Binding

support	metal	immobilization (interactions)	asymmetric reaction	ref
Al−MCM-41	Mn(III)	impregnation (support silanols/ phenyl salen groups)	epoxidation of alkenes	235
silica	Cr(III)	impregnation (support silanols/ phenyl salen groups)	ring opening and kinetic resolution of epoxides	236, 237
Al−MCM-41	Mn(III)	cation exchange (negative Al framework/ positive salen−metal complex)	epoxidation of alkenes	238−240
Al−MCM-41	Mn(III)	cationic metal coordination (negative Al framework/positive salen−metal complex)	epoxidation of alkenes	241, 242
K10, laponite, and bentonite	Mn(III)	cation exchange (cation exchange by positive salen−metal complex)	epoxidation of alkenes	243
Indian clay	Mn(III)	cation exchange (cation exchange by positive salen−metal complex)	epoxidation of alkenes	244, 245
Al pillared clays	Mn(III)	intercalation in the layers (in situ generation)	epoxidation of alkenes	246
Zn(II)−Al(III) LDH[a]	Mn(III)	intercalation in the layers (anion exchange by negative salen−metal complex)	epoxidation of alkenes	247

[a] LDH, layered double hydroxide.

Table 18. Relevant Catalytic Data of the Performance of Heterogeneous Chiral Salen−Metal Complexes Supported by Electrostatic Interactions

catalyst	ee[a,b] (%) homo	hetero	leaching[b]	recycling[b]	ref
Mn(III)/Al−MCM-41	60	55	N	na	235
Cr(III)/SiO2	na	45−99	Y (<2%)	Y (10 cycles)	236, 237
Mn(III)/Al−MCM-41	78	32−70	N	Y (deact second cycle)	238−240
Mn(III)/Al−MCM-41	18−78	27−86	N	Y (three cycles)	241, 242
Mn(III)/K-10	36−46	32−34	N	Y (deact second cycle)	243
Mn(III)/Indian clay	41−99	50−99	N	Y (four cycles)	244, 245
Mn(III)/Al pillared clay	6−58	1−14	N	Y (deact second cycle)	246
Mn(III)/Zn−Al−LDH	na	30−55	N	Y (three cycles)	247

[a] Comparison between the reported ee values for the homogeneous and heterogeneous catalysis under analogous reaction conditions. [b] N, no; Y, yes; na, data not available.
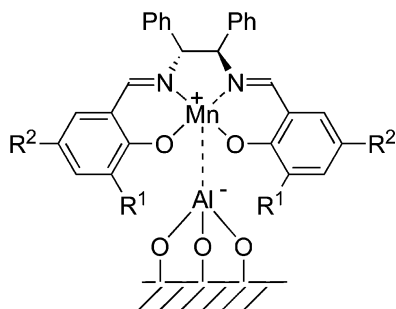
Whatever the origin of the interaction, what is important is that simple impregnation leads to an adsorption strong enough to avoid the complex leaching to the solution during the catalytic reactions. This heterogeneous catalyst was used for the asymmetric epoxidation of 1,2-dihydronaphthalene, exhibiting a high catalytic activity and having an ee value similar to that of the same complex in solution. On the basis of these good catalytic results, the authors suggested that the immobilized complex is probably aligned parallel to the walls of the mesopores and ready to interact with the reactants. No evidence for this proposed co-conformation of the salen complex with respect to the host pore was given.

Concerning the use of mesoporous silicas as support, one of the main advantages is their surface area, ranking these materials at the top of the list of high-surface area solids.[248] However, given the instability of mesoporous aluminosilicates that may undergo extensive collapse of their porous structure and their high price, it would be convenient not to take for granted their superior performance (especially upon extensive reuse of the solid catalyst) with respect to amorphous, nonporous silicas. Thus, more recently Jacobs et al. have also prepared a heterogeneous catalyst by impregnation, but using robust amorphous silica as support and a chiral salen−chromium complex as catalyst.[236] A thoughtful selection of solvents allowed them to use this heterogeneous catalyst for the asymmetric ring opening and kinetic resolution of epoxides, exhibiting good activity and a high enantioselectivity. The silica-supported chiral salen−chromium complex was recovered by filtration after each experiment and could be used for the asymmetric ring opening reaction of 1,2-epoxyhexane in more than 10

successive batch reactions, with limited leaching (<2%). This leaching can be minimized further if a less soluble dimeric chromium complex is supported on the silica.[237] This group used a simple fixed-bed, continuous-flow reactor containing the silica-supported dimeric salen−chromium complex. Although a concentration gradient for the chromium complex develops in the bed in the direction of the flow, leaching was avoided by periodically changing the flow direction in the reactor. Clearly, as the work of Jacobs has shown, impregnation of a conventional salen−metal complex on silica is surely the simplest and most straightforward procedure to accomplish immobilization, provided that care is taken to avoid leaching. Also, this work raises the need to justify adequately the use of sophisticated silica supports other than plain silica.

A more evolutional strategy to immobilize homogeneous chiral salen complexes on inorganic supports is by cation exchange into Al−MCM-41.[238−240] Hutchings et al. have prepared a manganese-exchanged Al−MCM-41 using the ion-exchange capacity introduced on the mesoporous silica by the presence of framework aluminum. Whereas all-silica MCM-41 does not contain charge-balancing cations, the isomorphic substitution of SiO_4^{4-} tetrahedra by AlO_4^{5-} introduces, as in the case of zeolites and other aluminosilicates, a net negative charge in the framework that needs the presence in close proximity of compensating cations.[248] Given the ionic nature of the bond between the mesoporous aluminosilicate framework and the charge-balancing cation, it is possible to exchange the cation without altering the structure of the solid. A positive salen−manganese complex can, therefore, be introduced in Al−MCM-41 by ion

Scheme 31. Proposed Immobilization by Cationic Metal Coordination between Positive Manganese and Framework Aluminum (Based on References 241 and 249)

Scheme 32. Strategies for Immobilization of Chiral Salen–Metal Complexes in Clays by Cationic Exchange Process[a]

[a] The positive charge can be at the metal or on the ligand (based on refs 243–245).
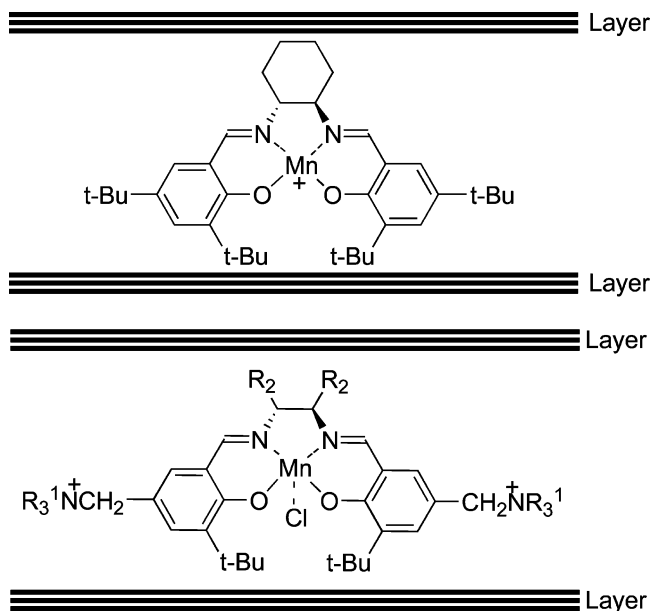
exchange, and it will remain strongly bound to the solid through Coulombic interactions. After ion exchange, the resulting solid containing a positively charged chiral salen complex was used as heterogeneous catalyst for the enantioselective epoxidation of *cis*- and *trans*-stilbene.[238–240] The results of activity and enantioselectivity of the heterogeneous catalyst were, however, less satisfactory than the results obtained with the homogeneous catalyst. In addition, although the catalyst was found to be completely heterogeneous, the chiral salen–Mn(III)/Al–MCM-41 catalysts deactivate in the second cycle. A regeneration process consisting of recalcination of the recovered material was considered, but following this procedure the activity and enantioselectivity of the deactivated samples compared to those of fresh samples were only partially restored.[238]

As in the previously discussed Hutchings's work, Kim et al. have also used Al–MCM-41 as support of a chiral salen–manganese complex. Kim proposed immobilization through cationic metal coordination between the aluminum of the solid framework and the metal center (Scheme 31).[241,242] However, the proposed interaction is not very convincing, because a Mn–Al bond seems very unlikely. It appears more reasonable that the negative charge of the AlO_4^{5-} tetrahedra interacts electrostatically with positive salen–Mn complexes. In the Kim paper, *trans*-1,2-diphenylethylene-1,2-diamine was used as chiral diamine. This salen–Mn(III)/Al–MCM-41 catalyst exhibits moderate activity for the asymmetric epoxidation of olefins (styrene and α-methylstyrene). The heterogeneous catalyst was stable during the reaction without undergoing any metal leaching. Kim et al. reported three uses without loss of activity and maintenance of a high enantioselectivity comparable to that of the same complex in homogeneous phase.

Silicas, mesoporous solids, and zeolites are the most common inorganic solids used for the immobilization of any metallic complex, but other inorganic solids, especially clays, were used for the same purpose.[243–245] Clays are layered aluminosilicates the sheets of which are constituted by two infinite two-dimensional layers of SiO_4 tetrahedra sandwiching a middle layer of AlO_6 octahedra.[250–255] The aluminosilicate layers are negatively charged depending on the chemical composition and the aluminum content of the clay. The required compensating cations (normally potassium or sodium) are located in the intergallery space. As in the case of zeolites, the initial charge-balancing cations can also be ion-exchanged for other different ones, either organic or inorganic. The interlayer space can vary depending on the size of the charge-balancing cations and the hydration degree. The interlayer distance in a clay can expand so much that the texture and volume of the solid can change macroscopi-

cally, this phenomenon being known as swelling.[254,256] Interlamellar spaces are highly polar and are normally not accessible to neutral or apolar organic molecules. For this reason, the surface area of clays measured by gas adsorption gives low values, because the gas can only access the external particle surface and not the intergallery spaces.

Due to their lamellar structure and cation-exchange capacity, clays can be utilized to support positively charged salen complexes that can be incorporated through ion exchange. Normally, the immobilization within the interlamellar space of these solids is achieved through Coulombic interactions between the negative layers and the positive salen complexes. The usual adsorption procedure is a simple ion-exchange process with cationic complexes, the positive charge being on the metal[243] or on the adequately functionalized ligand (Scheme 32).[244,245]

Mayoral et al. used several clays, namely, montmorillonite K10, laponite, and bentonite, in their studies on the incorporation a chiral salen–manganese(III) complex.[243] In this case, the cationic complex had the overall positive charge at the metal center and was incorporated by a Na^+-to-salen complex exchange process. The clay-containing chiral salen–manganese complex was tested for the asymmetric epoxidation of 1,2-dihydronaphthalene.[243] The activity of the clay reaches turnover numbers similar to or higher than those obtained in solution with related catalysts. Although the heterogeneous catalyst did not exhibit detectable leaching, the enantioselectivity was very poor and the catalyst deactivated in the first use. The author's studies on the deactivated samples revealed that deactivation was due partly to coke deposition and, above all, to the decomposition of the salen ligand. In fact, the instability of the salen ligand in strong oxidizing conditions must be the intrinsic limit to the maximum productivity of salen catalysts, regardless of whether they are or are not supported on a solid support or whether they are used in homogeneous conditions. However, a possible benefit of adsorption/encapsulation of salen–manganese complexes could be to increase their stability

under the reaction conditions and prolong the service life of the catalyst.

Another study reporting the use of clays for the immobilization of metal–salen complexes comes from the Kureshy group.[244,245] They synthesized an interesting dipositive salen–manganese complex that was prepared by introducing quaternary ammonium ion groups on the phenolic moieties. As chiral diamine either *trans*-1,2-diaminocyclohexane or *trans*-1,2-diphenylethylene-1,2-diamine was used. Incorporation of this dicationic salen complex into the lamellar space of a montmorillonite-type clay was accomplished by cation exchange.[244,245] These heterogeneous catalysts were tested for the asymmetric epoxidation of olefins (styrene, indene, and chromene), showing a significant enhancement in the ee values compared to those obtained in homogeneous systems. This good performance of the clay-bound manganese complex can be attributed to the unique spatial environment of the confined reaction medium in terms of polarity and co-conformational ordering of the complex with respect to the layers. In related compounds hosted inside clays,[257–259] X-ray diffraction has shown that the interlayer distance of the clay adapts to the dimensions of the guest that is perpendicular to or at a low tilt angle with respect to the clay layers. Excellent conversions and epoxide selectivity (>99%) were obtained with the three alkenes tested, namely, styrene, indene, and 6-nitro-2,2-dimethylchromene. The catalyst could be recycled efficiently four times without loss of activity, and no leaching was detected in all experiments. The authors attributed this good recycling behavior to the strong Coulombic interaction of the dicationic complex firmly immobilized between the negatively charged layers. More recently, Freire and co-workers have published the use of aluminum pillared clays, starting from the original Benavila and Wyoming clays, as supports for salen–Mn(III) complexes.[246] The encapsulation was obtained by in situ generation of the complexes inside the pillared clays. The ee values achieved with the heterogeneous catalysts in the asymmetric epoxidation of styrene are very poor when compared with those of the homogeneous counterpart. The catalysts deactivate after the first use, according to the authors, due to collapsing of the clay pillars.[246]

All of the previous examples describing immobilization through electrostatic binding between salen and support refer to neutral or positive complexes. For immobilization of a negative complex, a support having positive charges is required. One example of this type of support is layered double hydroxides (LDH). LDHs are layered solids in which the sheets contain simultaneously di- and trivalent cations coordinated with oxo and hydroxy groups. The presence of a certain percentage of the trivalent cation (up to one-third of the total number of cations) replacing the divalent cation introduces an excess of positive charge in the layer that is compensated by the presence of charge-balancing anions. Exchangeable, charge-compensating anions are located in the intergallery space.

The most common LDH contains Mg^{2+} and Al^{3+} in the layers and carbonate or nitrate in the interlamellar space.[260–263] Many other LDHs containing different combinations of divalent (Cu^{2+}, Zn^{2+}, Co^{2+}, Mn^{2+}) and trivalent (Fe^{3+}) cations of adequate ionic radius and inorganic or organic anions have also been prepared.[264,265] In many respects, LDHs are the negative analogues of clays. LDHs have also been used as supports to immobilize negatively charged transition metal complexes.[266,267] Thus, LDHs of Zn^{2+} and Al^{3+} have

Scheme 33. Immobilization in Zn^{2+}–Al^{3+} LDH by Anionic Exchange Process (Reprinted with Permission from Reference 247; Copyright 2004 Chemical Communications)
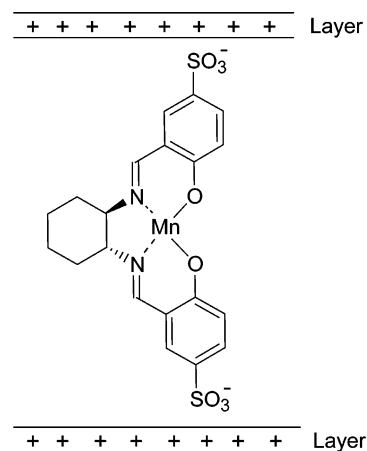
been used for intercalation of a dianionic form (sulfonic groups) of a salen–manganese complex by a simple anion-exchange process for the benzoate ion present initially in the solid (Scheme 33).[247] The complex incorporated in LDH exhibits high catalytic activity with excellent conversions (using 75 psi of oxygen pressure), but the enantioselectivities for the asymmetric epoxidation of limonene were only moderate. Spectroscopic analysis of the solution mixture after the catalytic reaction revealed that no leaching of manganese was occurring. The heterogeneous catalyst was used in three consecutive runs without decrease of the activities. More recently, the same group reported the use of this dianionic catalyst to perform the epoxidation of several alkenes (limonene, pinene, cyclohexene derivatives, and styrene derivatives) using molecular oxygen at atmospheric pressure as oxidant.[268–270]

Considered globally, the immobilization by electrostatic interactions is a very simple and appealing procedure that may allow the use of the same or very similar complexes as in the homogeneous phase with simple convenient supports such as amorphous silica. The ee values can be as high as those in solutions and with good activities. Leaching, however, is an issue that has to be always addressed and the system surveyed to determine migration of the complex to the solution. Also, the initial net (positive or negative) charge of the complex may be neutralized by some reagents or byproducts during the course of the reaction, which may lead to instability of the heterogeneous catalyst.

4.3. Immobilization by Formation of an Apical Coordinative Bond with the Metal

The previous papers have used unfunctionalized silicas and supports and, therefore, the simplest and less-sophisticated approach. However, the surface of the inorganic solids can be easily functionalized by introducing a variety of different organic functional groups that can enhance the interaction of the inorganic oxide with the salen complexes. A general procedure for surface functionalization is to effect the reaction of surface hydroxyl groups with organosilane coupling reagents, such as tri(alkoxy)organosilanes or trichloroorganosilanes. Most commonly, these organosilanes contain three leaving groups bonded to the silicon atom (trialkoxy or chloro groups) and one linear alkyl chain or aromatic ring having a terminal functional group (Scheme 34). Trialkoxy groups are normally preferred over chloro

Scheme 34. Surface Functionalization of Inorganic Solids
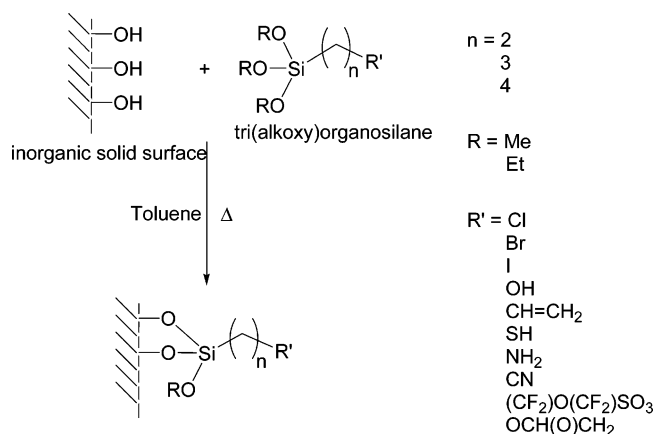
when the formation of hydrochloric acid is undesirable. Also, trimethoxy groups react very quickly with moisture and water traces, making the trimethoxyorganosilanes very difficult to store and handle. Ethoxy groups are significantly less reactive than methoxy and are usually preferred because surface modification can be performed in a more controllable way. The silane leaving group will condensate with the silanol groups of silica surfaces by refluxing a suspension of the solid and the silylating reagent in toluene in the absence of

moisture. One, two, or three covalent bonds between the surface and the silylating agent can be formed. Solid-state NMR showing the presence of residual alkoxy groups bonded to the silicon atoms as $(RO)(=)Si-R'$ indicates that mono- and bipodally anchored silane groups are mainly formed and that tripodally anchored silane groups are unlikely to be the predominant species. The reader is referred to recent reviews for an in-depth description of surface functionalization by silylation.[202]

Silylated silicas can be considered a hybrid material in which an inorganic solid has organic functionality covalently attached on its surface. These organic functional groups can be introduced to interact strongly with the salen complexes in the immobilization step, thus effecting a stronger adsorption than in the absence of organic modifier. However, the strength of this immobilization should not be taken for granted, and controls comparing adsorption of the salen–metal complex on the pristine solid lacking organic modifiers should be included for comparison.

The list of heterogeneous catalysts prepared following this strategy, the enantioselective reactions that have been tested, and the catalytic results achieved have been summarized in Tables 19 and 20.

In the case of pentacoordinated complex metals, one possibility to achieve immobilization is to use the apical ligand to bind with the support. Scheme 35 illustrates this

Table 19. Supports, Metals, Surface Functional Groups, and Catalytic Reactions of Heterogeneous Chiral Salen–Metal Complexes Immobilized by Apical Coordinative Binding of the Solid to the Metal

support	metal	surface functional groups (R')[a]	asymmetric reaction	ref
MCM-41	Ti(IV)	$-O^-$	cyanation of aldehydes	242
MCM-41	Ti(IV) dimer	$-O^-$	cyanation of aldehydes	271
MCM-41, SBA-15 and silica	Mn(III)	$-C_6H_4O^-$	epoxidation of alkenes	272, 273
MCM-41, ITQ-2 and ITQ-6	Mn(III)	$-(CH_2)_3S(CH_2)_nCOO^-$ or $-(CH_2)_3S(CH_2)_nCH_2O^-$	epoxidation of alkenes	274
MCM-41, SBA-15 and silica	Mn(III)	$-C_6H_4SO_3^-$	epoxidation of alkenes	275, 276
silica and ITQ-2	Cr(III)	$-(CH_2)_3NH_2$	epoxide ring opening	277
silica	Cr(III)	$-(CH_2)_3NH_2$	epoxide ring opening	278
MCM-41	Cr(III)	$-(CH_2)_3NH_2$	epoxidation of alkenes	279
SBA-15	Mn(III)	$-(CH_2)_3NH_2$	epoxidation of alkenes	280
MCM-41	Mn(III)	$-(CH_2)_3NHCOC_5H_4NO$	epoxidation of alkenes	281

[a] Corresponding to Scheme 35.

Table 20. Relevant Catalytic Data of the Performance of Heterogeneous Chiral Salen–Metal Complexes Supported by Apical Coordinative Binding[a]

	ee[b,c] (%)				
catalyst	homo	hetero	leaching[c]	recycling[c]	ref
Ti (monomer)/MCM41	66–90	67–94	na	na	242
Ti (dimer)/MCM41	67	43–60	N	Y	271
Mn(III)/MCM-41 Mn(III)/SBA-15 Mn(III)/silica	24–85	35–85	N	Y (three cycles)	272, 273
Mn(III)/MCM-41 Mn(III)/ITQ-2 Mn(III)/ITQ-6	na	46–86	na	Y (deact second cycle)	274
Mn(III)/MCM-41 Mn(III)/SBA-15 Mn(III)/silica	26–55	66–95	na	Y (five cycles)	275, 276
Cr(III)/SiO$_2$ Cr(III)/ITQ-2	59–84	52–70	Y (20–45%)	na	277
Cr(III)/SiO$_2$	85	65–77	Y (<1%)	Y (ten cycles)	278
Cr(III)/MCM-41	48–63	57–73	Y (<3%)	Y (deact third cycle)	279
Mn(III)/SBA-15	14–68	11–67	N	Y (five cycles)	280
Mn(III)/MCM-41	na	62–92	N	Y (four cycles)	281

[a] For the reaction type, see "asymmetric reaction" in Table 19. [b] Comparison between the reported ee values for the homogeneous and heterogeneous catalysis under analogous reaction conditions. [c] N, no; Y, yes; na, data not available.

Scheme 35. Immobilization of Salen Complexes on Inorganic Supports by Coordinative Binding through the Metal

Scheme 36. Immobilization of a Chiral Salen−Chromium(III) Complex on an Aminopropyl Modified Surface of Inorganic Supports through Apical Cationic Metal−Amino Group Coordination (Based on Reference 277)
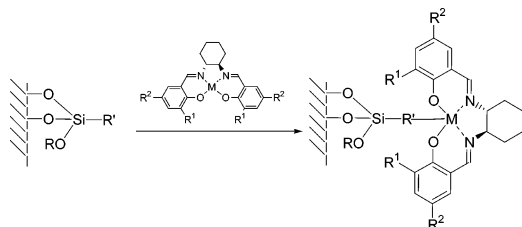
strategy. There are some reports of the heteroatom coordinated with the complex metal being a negatively charged oxygen atom. These negative oxygen atoms can be from the silanol groups on the surface of the solid[242,271] or from groups covalently attached to the surface of the inorganic solids as phenoxyl groups,[272,273] alkoxyl groups,[274] or phenylsulfonic groups.[275,276]

Salen−titanium complexes, either monomeric[242] or dimeric,[271] have been immobilized in all-silica MCM-41 by apical coordinative bond through the metal by means of the silanoxy groups present on the solid surface. These heterogeneous catalysts were tested for the asymmetric cyanohydrin formation of benzaldehydes using cyanotrimethylsilane as reagent, with contrasting results in terms of enantioselectivity. Although the monomeric Ti(IV) catalyst may exhibit higher enantiomeric excess than the homogeneous catalyst, the supported dimer shows somewhat lower enantioselectivities when compared with the homogeneous counterpart. No leaching was detected for the supported dimeric salen−titanium complex that was simply separated from the reaction mixture by filtration and was recycled two times with a decrease in the reaction rate. Over time, particularly in the presence of weak acids and moisture, silanoxy groups can be converted into silanols by protonation (pK_a of SiOH/SiO$^-$ $\sim$ 6), and this will weaken considerably the coordinative bond with the complex metal, leaching being more likely in this case.

The enantioselective epoxidation of alkenes was the test reaction for the chiral salen−manganese complexes immobilized through apical coordination to the metal by anionic alkoxide, phenoxide, or arylsulfonate groups covalently attached to the surface of MCM-41, SBA-15 and silica.[272,273,275,276]

In the case of phenoxyl groups[272,273] and phenylsulfonic groups,[275,276] the asymmetric epoxidation of α-methylstyrene, cis-β-methylstyrene, and 1-phenylcyclohexene may exhibit significantly higher enantioselectivities for the heterogeneous catalysts compared to the homogeneous complexes. In addition, the heterogeneous catalysts were recycled without losing any activity in several cycles (three and five, respectively). These results, in the opinion of the authors, can derive from the bulky axial group and the adequate confinement effect due to the correct mesopore dimensions of the MCM-41 and SBA-15.

In the case of the alkoxyl groups as apical covalent ligand,[274] the reaction rates and ee for the enantioselective epoxidation of alkenes (1-phenylcyclohexene, indene, and 1,2-dihydronaphthalene) were moderate to high and the catalysts deactivate in the second use. In this case, the alkoxyl group length and the silylation of the surface were found to have a significant influence on the catalyst activity. The results show that silylation of the surface improves the selectivity to the final products. This effect arises from a
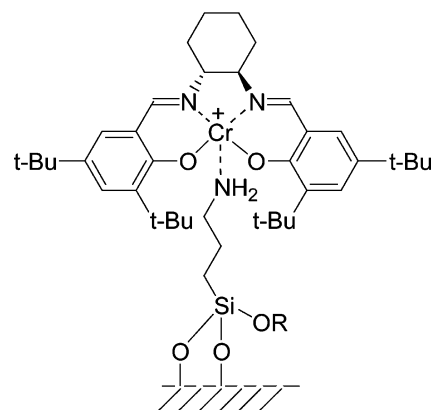
decrease of the secondary reactions caused by the adsorption of the reaction products on the hydrophilic surfaces. Silylation of the silanol groups transforms the hydrophilic surface of most as-synthesized mesoporous silicas into a hydrophobic surface, besides avoiding the characteristic reactions of −OH groups.[248,282] Silylation also reduces the effective pore size of the channels, depending on the bulkiness of the silyl groups.[248,283] We note, however, that a factor that has a negative influence should be the strong basicity of alkoxide anions. The presence of moisture or weak acids in the reaction mixture should neutralize these basic alkoxides ($pK_a \sim$ 18) and should weaken considerably the adsorption of the salen complex. Basicity of the alkoxide groups should also be responsible for the need of exhaustive silanol protection.

Anchoring of chiral salen complexes has also been accomplished using NH$_2$-modified inorganic solids. In this case the cationic metal atom of the salen−chromium complex establishes a strong apical coordination bond with the amino groups of the NH$_2$-modified silica and delaminated zeolite ITQ-2 (Scheme 36).[277,278] ITQ-2 is a delaminated zeolite formed by layers (2.5 nm depth) of crystalline material the surface of which defines cups (0.8 × 0.8 nm) as shown in Scheme 37. The main advantage of ITQ-2 as support is its large surface area ($\sim$700 m^2 × g^{-1}) that is all accessible and mostly external as compared to microporous zeolites.[284,285]

The heterogeneous catalysts prepared according to this method were used in the asymmetric ring opening of meso-epoxides. The heterogeneous catalysts prepared using silica and ITQ-2 as supports exhibit lower activity and enantioselectivity for the ring opening of cyclohexane oxide using trimethylsilyl azide as nucleophile than the same complex operating in homogeneous catalysis.[277] In addition, the supported catalysts on aminopropyl-functionalized solids were unstable, and a large extent of complex (20−45%) leached from the solid to the solution, catalyzing the reaction in the homogeneous phase. The authors suggested that this bleeding could be minimized using solvents with poorer solubility capability than the diethyl ether used as solvent in the reaction.[277]

Jacobs and co-workers have used an analogous strategy to immobilize chromium−salen complexes on silica.[278] Thus, the support was previously modified with terminal amino groups, and the resulting heterogeneous chromium catalyst

Scheme 37. Pictorial Representation of the Layered Structure of Delaminated ITQ-2 Zeolite Showing the Presence of Silanol Groups on the Upper and Lower Surface of the Layers (MR Corresponds to "Membered Ring") (Based on Reference 285)
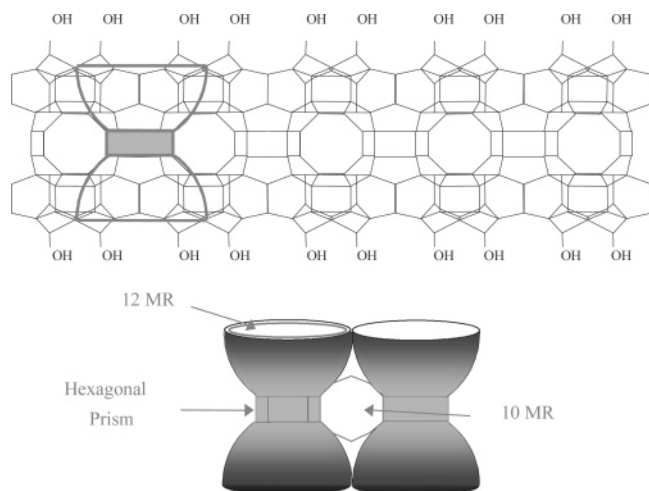
anchored to the silica was found to exhibit high activity for the asymmetric ring opening of cyclohexane oxide with trimethylsilyl azide. The enantioselectivity values obtained with the heterogeneous catalyst were somewhat lower than the ones achieved with the homogeneous counterpart. On the other hand, the supported catalyst was very stable and could be reused 10 times with low leaching levels (<1%). These good results were attributed in part to the choice of the appropriate solvent.[278] Toluene is apparently a more suitable solvent to avoid desorption of the salen−chromium complex than the diethyl ether used by Garcia and Corma.[277] On the other hand, Jacobs's work shows once again that plain amorphous silica, after being submitted to functionalization in this case, is a good alternative support combining a good balance between economy with respect to mesoporous silicas and catalyst efficiency.

As in the previous example, a chromium binaphthyl Schiff base complex has been immobilized by apical metal coordinative bond on aminopropyl-modified MCM-41 and used as enantioselective heterogeneous catalyst for the epoxidation of styrene derivatives.[279] The interest of this work is that the ee values obtained with the supported binaphthyl were significantly higher than those of the free complex and that the solid catalyst could be reused. The activity of the solid catalyst decreased considerably in the third cycle.[279]

Also, salen−manganese complexes were immobilized on SBA-15[280] and MCM-41[281] using the methodology of Scheme 36 with the apical coordination of the salen−metal to the amino group of a silylating agent anchored to the solid surface. The enantioselective heterogeneous catalysts were used for the epoxidation of styrene derivatives and bulkier alkenes (indene, 1,2-dihydronaphthalene, and 2,2-dimethyl-chromene). Both catalysts exhibit high ee, comparable with the results obtained in homogeneous phase. No detectable leaching was observed, and recycling experiments showed good levels of reusability with the catalysts remaining active for several cycles.

4.4. Immobilization by Covalent Binding of the Salen Ligand to the Support

In the first three methodologies described so far in sections 4.1, 4.2, and 4.3, the chiral salen complex to be immobilized

can be those used in homogeneous solution. In general, these approaches do not necessarily require special functionalization of the ligand in order for the complex to become supported. Some exceptions to the lack of specific functionalization are the use of electrically charged substituents in the salen complex to promote Coulombic interactions such as those shown in Schemes 32 (bottom part) and 33.[243−245] In the SIB methodology the complex is entrapped and imprisoned due to the relative dimensions of guest, cavity, and windows. In the electrostatic interaction, it is the complementarity of electrical charges and dipoles that maintains the complex supported on the solid surface. In the apical coordinative immobilization, the only prerequisite is to have a salen complex with pentacoordinated metal. To complete section 4, which is devoted to inorganic solids, the fourth general methodology deals with the immobilization of chiral salen complexes by covalent anchoring to the support through the ligand. This is accomplished by reacting complementary functional groups, one located in the solid and the other at the salen ligand.

As has been presented in Scheme 34, there is a large variety of functional groups that can be attached to the surface of inorganic solids. These terminal functional groups can react with suitable functionalized chiral salen complexes through the ligand in such a way that a new covalent bond connecting the solid and the complex is created. A chain or tether links the complex to the solid surface. Normally this approach has been considered to produce the strongest and safest immobilization of the complex on the support, but it has as major disadvantages including the need for extensive organic synthesis and a more elaborate anchoring procedure. Also, this highly costly methodology is acceptable only if the stability and reusability of the solid catalyst improve remarkably with respect to those of other simpler alternatives.

Several factors can influence the asymmetric induction capability of the supported complex. In the case of tethered complexes covalently bonded to a solid support, these factors include the nature of the support, the synthetic procedure used to bind the complex, the nature of the linker functional group, and the length of the linker connecting the complex to the support.

As can be seen in Schemes 38 and 39, there are several possibilities to immobilize covalently salen complexes: (i) stepwise formation of the complex by initial covalent anchoring of one of the components and consecutive solid-phase synthesis consisting of the condensation of the other components of the salen complex (Schemes 38 and 39A); (ii) ligand immobilization and subsequent complexation (Scheme 39B); and (iii) one-step complex immobilization by covalent binding through the ligand (Scheme 39C). Tables 21 and 22 contain a summary of reported immobilization through covalent binding.

The stepwise anchoring method consists of the solid-phase synthesis of the salen ligand and, then, the complex by performing consecutive reactions with salicylaldehydes and diamines to synthesize the ligand and eventually the complex starting from an appropriately functionalized inorganic support. A paradigmatic example of this methodology was reported by Kim and co-workers and is shown in Scheme 38. This stepwise solid-phase synthesis is based on the use, as key synthetic intermediate, of a dialdehyde, namely, 2,6-diformyl-4-*tert*-butylphenol.[249,286,287] Two main features of the anchoring strategy reported by Kim[249,286,287] are (i) the

Scheme 38. Immobilization of Salen Complexes by Covalent Binding through the Ortho Phenolic Position Using a Stepwise Solid-Phase Synthesis As Reported in References 249 and 286−288
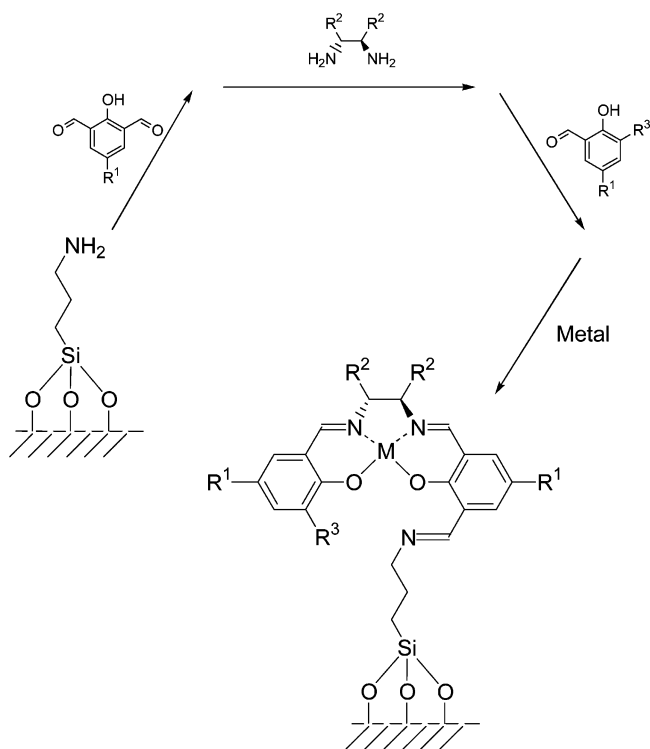
two phenolic moieties of the salen complex can be different, whereas commonly salen contains two identical phenolic moieties, and (ii) the complex is covalently attached to the solid surface through the carbon at the ortho phenolic position, a position that is very important for determining the asymmetric induction ability of the complex. In the examples shown in Scheme 38, siliceous MCM-41 modified with 3-aminopropyl groups was used as support and the salen complex was synthesized using *trans*-1,2-diphenylethylene-1,2-diamine.

Three optically active salen complexes immobilized using the strategy depicted in Scheme 38 have been reported so far: (i) a salen−manganese complex used for the asymmetric epoxidation of styrene derivatives;[286] (ii) a salen−cobalt(II) complex employed as catalyst for the enantioselective reduction of acetophenone and tetralone to the corresponding alcohols;[249] and (iii) a chiral cobalt(III) complex being active to effect the enantioselective hydrolysis of epoxides, including cyclohexane oxide, cyclopentane oxide, 1,2-hexane oxide, styrene oxide, and epichlorohydrin.[287] In the three chiral salen catalysts anchored by the stepwise solid-phase synthetic procedure, no leaching from the solid to the solutions was detected. The asymmetric induction capability of these anchored chiral salen ligands with respect to the analogous complexes in solution can be higher or lower, depending on the reaction (Table 22). Thus, although it was possible to recycle the heterogeneous catalyst five times while maintaining the initial activities, the heterogeneous manganese complex exhibited lower enantioselectivity for the asymmetric epoxidation of olefins when compared with the homogeneous complex in solution.[286] A more favorable situation is the case of the cobalt(II) heterogeneous catalyst, for which the ee values in the enantioselective reduction of ketones are similar to those obtained by the authors in homogeneous phase. The best performance of the anchored

salen catalysts was observed for the enantioselective hydrolysis of epoxides using the heterogeneous cobalt(III) complex as catalyst, for which the ee values were higher than those of the homogeneous phase.

A recent paper by Liu and co-workers describes the immobilization of a salen−Mn(III) complex on MCM-48 by stepwise anchoring using the key synthetic dialdehyde (2,6-diformyl-4-*tert*-butylphenol) depicted in Scheme 38.[288] The heterogeneous catalyst has been used for the asymmetric epoxidation of styrene and α-methylstyrene using *m*-chloroperbenzoic acid/*N*-methylmorpholine-*N*-oxide (NMO) as oxidant. The enantioselectivities achieved with the heterogeneous catalyst were higher than those in homogeneous phase. Recycling experiments show a good reusability of the catalysts with no decrease in the ee after three cycles. However, inductively coupled plasma−atomic emission spectrometry (ICP-AES) analyses detected the occurrence of leaching to some extent of the metal (∼1%).

The position of the tether connecting the complex and the support may play a role in the asymmetric induction of the resulting anchored complex due to the different contribution to the complex stereogenic ability of each substituent depending on its bulkiness. It is widely assumed that the general stereoselection of salen complexes arises from the steric encumbrance around the active metal atom. For this reason, the position where the complex is tethered to the support is not irrelevant. Covalent immobilization of chiral salen complexes through the ligand has also been reported through the *para* position of the ligand phenolic moiety (Scheme 39). There are three possibilities to accomplish this immobilization: (i) stepwise synthesis of the complex by solid-phase synthesis of the ligand, effecting the consecutive condensation of all of the components of the complex (Scheme 39A);[271,289−292] (ii) immobilization of the preformed ligand adequately functionalized followed by subsequent metal complexation (Scheme 39B);[293] and (iii) direct immobilization of a conveniently functionalized preformed complex (Scheme 39C).[277,294−299]

Kim and co-workers have prepared a heterogenized chiral salen−manganese catalyst anchored on a 3-mercaptopropyl-modified MCM-41 mesoporous silica.[289] The complex was synthesized stepwise (Scheme 39A), the first step being the radical-chain addition promoted by azobis(isobutyronitrile) (AIBN) as radical initiator of the support mercapto groups to the vinyl groups of a salicylaldehyde derivative. After a suite of condensations, the final step was complexation of the ligand. The heterogeneous catalyst was tested in the asymmetric epoxidation of styrene, obtaining only moderate ee. The heterogeneous catalyst, which was recovered by filtration, was reused in three cycles maintaining the initial activities. No leaching was detected. The same synthetic procedure was used to immobilize a salen−titanium complex on the surface of a MCM-41 support.[271] The enantioselectivity achieved with the heterogeneous titanium catalyst was higher compared with that of the homogeneous counterpart.

In addition to epoxidations, hydrolytic epoxide opening, carbonyl additions, cyclopropanations, and aziridations, chiral metal−salen complexes have also been used as hydrogenation catalysts. Hydrogenation of imines is an important synthetic reaction that transforms carbonylic compounds into primary and secondary amines and can serve to prepare chiral α- and β-amino acids.[48] Commonly, homogeneous imine hydrogenation catalysts are Ir and Rh complexes and require

Scheme 39. Strategies Reported for the Covalent Immobilization on Inorganic Supports of Chiral Salen Complexes through the *Para* Position of the Ligand Based on References 271, 277, and 289−299
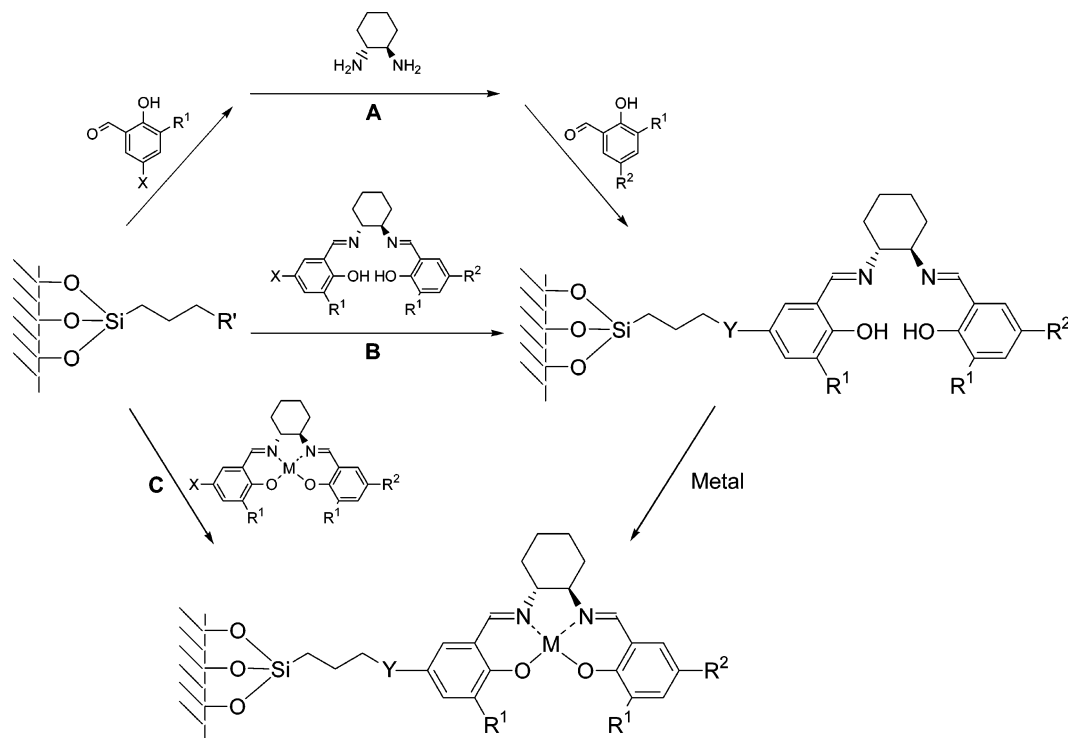
Table 21. Reported Heterogeneous Catalysts Prepared by Covalent Immobilization of Salen Complexes on Inorganic Solids and the Corresponding Asymmetric Reaction for Which They Were Used

solid	metal	immobilization method and reactive groups (support/complex)	asymmetric reaction	ref
MCM-41	Mn(III)	stepwise NH$_2$/o-CHO	epoxidation of alkenes	286
MCM-41	Co(II)	stepwise NH$_2$/o-CHO	reduction of ketones	249
MCM-41	Co(III)	stepwise NH$_2$/o-CHO	hydrolysis of epoxides	287
MCM-48	Mn(III)	stepwise NH$_2$/o-CHO	epoxidation of alkenes	288
MCM-41	Mn(III)	stepwise SH/p-CH=CH$_2$	epoxidation of alkenes	289
MCM-41	Ti(IV)	stepwise SH/p-CH=CH$_2$	cyanation of aldehydes	271
ITQ-2, MCM-41, and silica	Pd and Ni	stepwise OCN/p-CH$_2$NH$_2$	hydrogenation of imines	290
MCM-41 and silica	Mn (III), Cu (II)	stepwise OCN/p-CH$_2$NH$_2$	oxidation of sulfides	291
MCM-41 and silica	Mn (III)	stepwise triazine/p-OH	epoxidation of alkenes	292
silica	Mn (III)	anchoring of the ligand SH/p-CH=CH$_2$	epoxidation of alkenes	293
silica	Cr (III)	anchoring of the ligand SH/p-CH=CH$_2$	hetero Diels−Alder	293
silica	Mn (III)	anchoring of the complex SH/p-CH=CH$_2$	epoxidation of alkenes	294
MCM-41, ITQ-2, and silica	Cr (III)	anchoring of the complex NH$_2$/p-CH$_2$Cl	epoxide ring opening	277
MCM-41 and SBA-15	Mn (III)	anchoring of the complex NH$_2$/p-CH$_2$Cl	epoxidation of alkenes	295, 296
hexagonal mesoporous silica (HMS)	Mn (III)	anchoring of the complex NH$_2$/diamine COOH	epoxidation of alkenes	297, 298
HMS	Mn (III)	anchoring of the complex cyanuric chloride/ OH	epoxidation of alkenes	297, 298
MCM-41, ITQ-2 and silica	V(IV)	anchoring of the complex SH/p-CH=CH$_2$	cyanation of aldehydes	299

relatively high H$_2$ pressures. There is an incentive to develop heterogeneous highly active catalysts based on less expensive metals that work under lower hydrogen pressures. Corma,

Sanchez, and co-workers have reported chiral palladium− and nickel−salen complexes covalently anchored to a series of silica supports that are able to effect the hydrogenation

Table 22. Enantiomeric Excess Values, Leaching, and Reusability of the Heterogeneous Salen Catalysts Prepared by Covalent Binding between the Salen Complex and the Inorganic Support

catalyst	ee[a,b] (%)		leaching[b]	recycling[b]	ref
	homo	hetero			
Mn(III)/MCM-41	75−98	67−92	N	Y (five cycles)	286
Co(II)/MCM-41	17−65	23−73	N	Y	249
Co(III)/MCM-41	64−98	60−98	N	na	287
Mn(III)/MCM-48	44−48	32−99	Y (1%)	Y (three cycles)	288
Mn(III)/MCM-41	na	35−51	N	Y (four cycles)	289
Ti(IV)/MCM-41	67	87−93	N	Y	271
Pd(II) and Ni(II)/ITQ-2, MCM-41, SiO$_2$	80	10−15	N	Y (four cycles)	290
Mn (III) and Cu(II)/MCM-41, SiO$_2$	4−27	3−26	N	Y (five cycles)	291
Mn (III)/MCM-41 Mn(III)/SiO$_2$	89	26−84	N	Y (deact second cycle)	292
Mn(III)/SiO$_2$	75	75	N	Y (deact fourth cycle)	293
Cr(III)/SiO$_2$	80−83	74−84	N	Y (ten cycles)	293
Mn(III)/SiO$_2$	na	30−58	na	na	294
Cr(III)/MCM-41 Cr(III)/ITQ-2 Cr(III)/SiO$_2$	59−84	8−18	N	na	277
Mn (III)/MCM-41 Mn(III)/SBA-15	45−99	67−96	N	Y (four cycles)	295, 296
Mn(III)/HMS	4−17	1−28	N	Y (two cycles)	297,2 98
Mn(III)/HMS	26−51	1−22	N	Y (two cycles)	297, 298
V(IV)/MCM-41 V(IV)/ITQ-2 V(IV)/SiO$_2$	74−90	68−85	N	Y (deact fourth cycle)	299

^{a} Comparison between the reported ee values for the homogeneous and heterogeneous catalysis under analogous reaction conditions. ^{b} N, no; Y, yes; na, data not available.

of imines at 4 bar.[290] What is important in this work is that it has been established that the support can play a role in the catalysis, increasing the concentration of reactants near the catalytic site and, thus, contributing to the success of the hydrogenation. This idea is certainly original and points to the importance of the nature and properties of the support on the catalytic activity. Thus, the activity of identical salen complexes increases going from amorphous silica to mesoporous MCM-41, the highest using delaminated ITQ-2. ITQ-2 is a delaminated zeolite (Scheme 37). When the complex is anchored on ITQ-2, its activity is twice the activity of the unsupported complex in homogeneous phase. This has been interpreted as a preferent adsorption of hydrogen and reactants inside the cup-like holes of the ITQ-2 surface, because these cups create a potential well adsorbing guest molecules.[290]

Moreover, it is known that the presence of acids increases the hydrogenation activity of homogeneous catalysts.[48] Given the important role of the adsorption of reagents in mesoporous and delaminated zeolites, it was also observed that the use of acidic MCM-41 and ITQ-2 supports even increases the activity of the anchored complex due to the presence of Brønsted acid sites on the support. The stability of covalently anchored Pd− and Ni−salen complexes toward recycling was good, and no decrease in activity was observed after four reuses, the solids acting really as a heterogeneous catalyst because leaching was not observed.

The main drawback of these covalently anchored salen− Ni and −Pd catalysts is that despite their very high catalytic activity, they exhibit a low enantioselectivity (∼10−15%), far from the 80% obtained for the imine enantioselective hydrogenation with Ir complexes.[290] Also, the strategy followed for the preparation of the anchored complex, which is based on three consecutive reactions carried out on supported reactants and without possibility of purification (Scheme 40), may need to be revisited and improved.

Following a route analogous to that shown in Scheme 40, Corma et al. have also prepared several heterogeneous

catalysts with salen−manganese and −copper complexes as catalysts and MCM-41 or silica as supports.[291] This catalyst series was used for the chiral oxidation of phenyl sulfides. The ee values achieved with the heterogeneous catalysts were similar to the values obtained in homogeneous phase. After using the catalysts, the resultant solution exhibited no color and no metal was detected in the solution by atomic absorption spectroscopy. The catalysts were recovered by filtration and reused at least four times while retaining most of their initial catalytic activity.

The nature of the linker can also influence the enantioselectivity, stability, and performance of a supported catalyst. A salen−manganese complex has also been immobilized through the step-by-step strategy on the surface of silica and MCM-41 using an original approach consisting of employing a heterocyclic linker (Scheme 41).[292] The tethering of the complex to the support was accomplished by condensation using a s-triazine group attached to the solids and a salicylaldehyde derivative having a hydroxyl group. The supported chiral manganese complex was used for the asymmetric epoxidation of alkenes (1-phenylcyclohexene, styrene, indene, and 1,2-dihydronaphthalene).[292] Despite the originality of using s-triazine as linker, there were no advantages from the catalytic point of view because the catalysts prepared exhibit modest ee and low stability, with deactivation in the first reuse.

The stepwise synthetic procedure has many experimental advantages derived from the ease recovery of the solid from the reaction mixture. The main drawback is, however, the uncertainty in the complete characterization of the organic species attached to the solid as compared to performing the synthesis of the salen ligand and the complex in the liquid phase before they are anchored. The latter option permits chromatographic analyses and liquid NMR spectroscopy of the organic material that is not possible for species anchored on the solid support. As in solution the yield of each step is not 100%, it can be assumed that the solid contains in

Scheme 40. Preparation of Covalently Anchored Salen−Pd and −Ni Imine Hydrogenation Catalysts (Based on Reference 290)
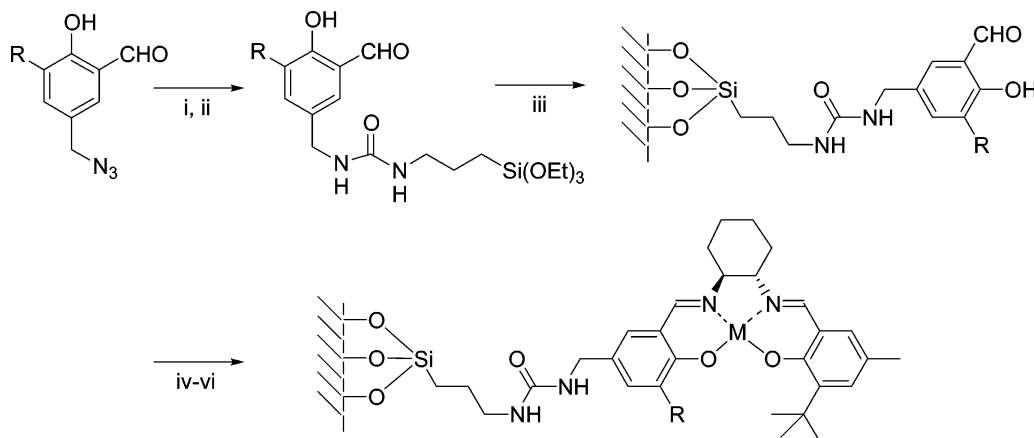
i) H_2, Pd/C; ii) OCN(CH$_2$)$_3$Si(OEt)$_3$; iii) support, toluene, 110 °C; iv) cyclohexanediamine;
v) 6-tert-butyl-4-methylsalicylaldehyde; vi) M(OAc)$_2$ (M= Pd, Ni)

Scheme 41. Covalent Immobilization of a Chiral Manganese Complex through a s-Triazine Linker (Based on Reference 292)
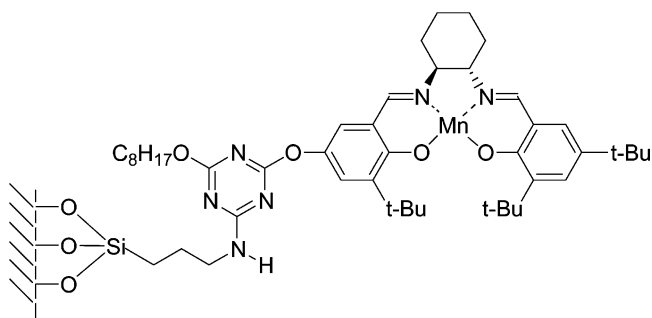
addition to the desired chiral salen complex a variable concentration of impurities.
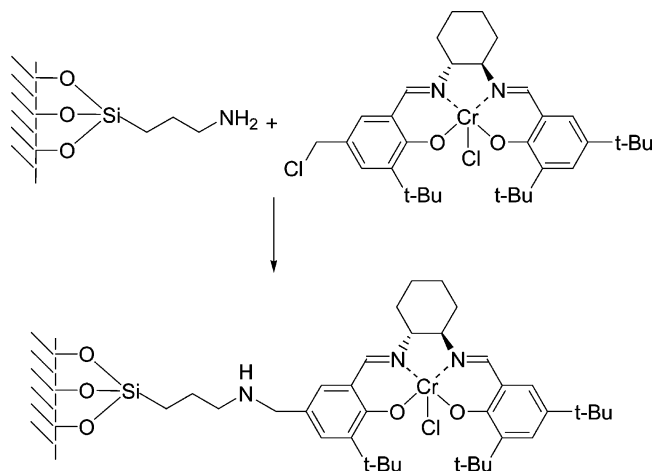
As we mentioned above, another possibility to immobilize covalent salen complexes through the ligand has two steps: initial covalent anchoring of a preformed salen ligand and further incorporation of the metal with final formation of the complex (Scheme 39B). An advantage with respect to the stepwise construction of the ligand is the economy of solid-phase reactions to obtain the final heterogeneous catalyst. In this way, Seebach et al. have anchored a preformed ligand to immobilize salen−manganese and −chromium complexes on the surface of a mercapto group modified silica.[293] The salen ligand having two identical phenolic moieties was designed with two vinyl groups forming part of styryl subunits, one in each phenyl ring. Using AIBN as radical initiator, it was possible to immobilize the salen ligand on the silica surface through a radical addition of mercapto groups onto the styryl moieties. The advantage of anchoring the ligand on the solid support instead of the preformed complex is its versatility to prepare a library of different complexes starting from the same salen ligand supported sample and introducing different metals. In this way, two types of salen−metal complexes were derived from a single sample of supported ligand. The manganese catalyst was used for the asymmetric epoxidation of alkenes (styrene and 1-phenylcyclohexene) and the chromium catalyst for the hetero Diels−Alder reaction of aldehydes (caproaldehyde and benzaldehyde) with Danishefsky's diene (Scheme 42).[293] The diamines used to build these libraries were *trans*-1,2-diaminocyclohexane and *trans*-1,2-diphenylethylene-1,2-di-

Scheme 42. Hetero Diels−Alder of Danishefsky's Diene and Aldehydes Catalyzed by Covalently Anchored Salen−Chromium Complex (Based on Reference 293)

amine. The enantioselectivities obtained with the heterogeneous anchored complexes were as good as with the soluble analogues and no leaching was observed. It was possible to reuse the supported complexes; however, the manganese catalyst deactivated in the fourth cycle, but the chromium catalyst was reused 10 times and the enantioselectivity even increased slightly in the first runs.

The direct immobilization of the salen−metal complexes by covalent binding through peripheral positions of the ligand is another possibility to anchor these complexes (Scheme 39C). Continuing with our comments on the differences among alternative strategies of covalent anchoring, tethering a preformed salen−metal complex to the support represents the maximum economy in solid-phase reactions as opposed to the step-by-step assembly of the ligand and then forming the complex on the solid. Step-by-step synthesis makes ample use of solid-phase reactions. The main advantage of minimization of the solid-phase reactions in the anchoring of the complex is the obtainment of convincing analytical and spectroscopic data firmly supporting the nature and purity of the chiral complex in the step before the final preparation of the heterogeneous catalyst. The strategy of covalent anchoring of the complex reduces the possibility of the existence of adventitious and undesirable populations of undefined (and probably unselective) catalytic sites such as free, uncomplexed metal ions and metal oxide clusters. On the other extreme, it is more likely that a solid catalyst prepared by stepwise assembly contains impurities difficult to be determined and quantified, although the experimental simplicity of solid-phase synthesis may counterbalance this drawback when the ee values of the catalyst prepared stepwise are sufficiently high.

A chiral salen−manganese complex was the first complex to be immobilized in inorganic solids (namely, silica) using the direct anchoring of the complex.[294] Salvadori et al. started

Scheme 43. Covalent Immobilization of a Chiral Salen−Manganese Complex by Direct Anchoring of Preformed Complex on a Mercapto-Functionalized Solid Support (Based on Reference 294)
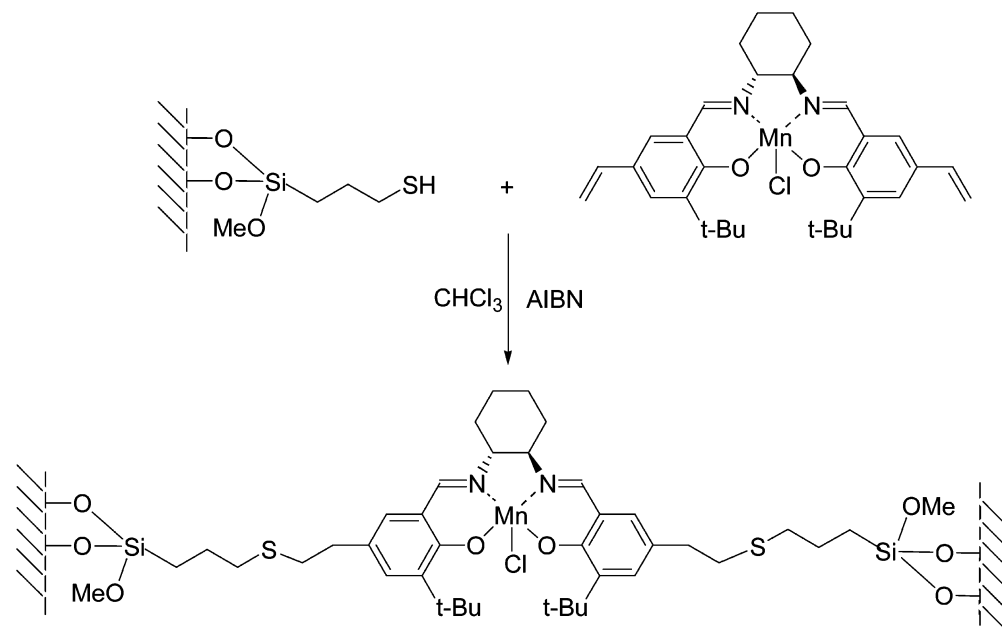
Scheme 44. Covalent Anchoring on Amino-Functionalized Silica of Chiral Salen−Chromium Having Two Different Phenolic Moieties (Based on Reference 277)

Scheme 45. Salen−Vanadyl Complex with Different ω-Alkenyl Chain Lengths on the Phenolic Rings That Have Been Anchored on a Mercapto-Functionalized Silica (Based on Reference 299)

with mercapto-functionalized silica and reacted it with a manganese complex with vinyl groups (Scheme 43).[294] The ee values obtained with these heterogeneous catalysts in the asymmetric epoxidation of several alkenes (1-phenylcyclohexene, indene, and 1,2-dihydronaphthalene) were, however, only moderate.

More recently and using this same strategy, Garcia and co-workers have anchored preformed salen−chromium[277] and −vanadyl[299] complexes on the surfaces of several solid silicates with different structures including mesoporous MCM-41, delaminated zeolite ITQ-2, and amorphous silica. In the case of the chromium complexes, the phenolic rings of the ligand were functionalized with methylene chloride groups and used complementary amino-modified supports (Scheme 44).[277] These heterogeneous salen−chromium catalysts were used for the asymmetric ring opening of epoxides (cyclohexane oxide). No metal leaching from the solid to the solutions was observed, but the ee values were modest compared to those obtained in homogeneous catalysis under comparable conditions. The authors attributed this poor performance to a change in the mechanism of the asymmetric

induction from bimolecular in solution to unimolecular for the supported chromium complex. Thus, although in solution there is cooperation between two chromium complexes, when the complex is immobilized on a solid surface, the reaction mechanism becomes most likely unimolecular. The mechanism involving a single complex is less efficient to induce asymmetry in the reaction products than the bimolecular mechanism.

Kureshy et al. have used the strategy depicted in Scheme 44 to immobilize covalently a chiral salen−manganese complex in the mesopores of SBA-15 and MCM-41.[295,296] The heterogeneous catalysts were tested for the asymmetric epoxidation of alkenes (styrene derivatives, indene, 1,2-dihydroxynaphthalene, and 2,2-dimethylchromene derivatives) with very high enantioselectivities (similar to those attained in homogeneous phase) and remarkable reusability (four cycles).[295,296]

Freire and co-workers have immobilized covalently two distinct salen−Mn(III) complexes onto an amine-functionalized hexagonal mesoporous silica (HMS).[297,298] The two complexes were immobilized through different points: (i) the first one was anchored by a hydroxyl group on the phenol ring of the ligand, as depicted in Scheme 39C, and (ii) the second one was anchored through a carboxylic group functionalized diimine bridge. The heterogeneous catalysts were tested for the asymmetric epoxidation of styrene and α-methylstyrene. The ee values achieved were different

Table 23. Chiral Salen Complexes That Have Been Supported on Carbonaceous Solids

support	metal	complex immobilization support/complex interaction	asymmetric reaction	ref
activated carbon	Mn(III)	electrostatic interaction O^-/complex metal	epoxidation of alkenes	305, 307
activated carbon	V=O (IV)	covalent anchoring of a preformed complex $SH/CH=CH_2$	cyanation of aldehydes	196
SWNT	V=O (IV)	covalent anchoring of a preformed complex $SH/CH=CH_2$	cyanation of aldehydes	306

depending on which catalyst was used. The catalyst immobilized through the diimine bridge displays an enantioselectivity higher than that in homogeneous phase. The inverse results are obtained with the catalysts immobilized through the phenol ring, for which ee values are lower than for the homogeneous counterpart. The catalyst was reused one time without any decrease in the activity, and no leaching was determined.[297,298]

In the case of chiral complexes that are active for the enantioselective cyanosilylation of aldehydes, including benzaldehyde derivatives and monoterpenoid citronellal, a series of salen−vanadyl complexes were prepared having terminal vinyl groups in pendent alkyl chains of various lengths (Scheme 45). The ω-alkenyl tether was connected to the para position of a salen ligand having two different phenolic moieties. The vanadyl complex was anchored by means of a radical-chain addition on high surface area silicas through mercapto groups.[299] Also in this study, in addition to the variation of the linker length, several other parameters such as silylation of the free silica silanol groups, the nature of the solvent, and the reaction temperature were studied.[299] The activity of the optimized enantioselective solid catalysts (silica with the largest linker in chloroform as solvent at the lowest reaction temperature) is very high, reaching 90% ee, close to that of the analogous complex in solution. The solid catalysts can be reused by simple filtration up to three times and retain a large part of the activity of the fresh catalyst without leaching of vanadyl into the solution being detected.

5. Reusable Chiral Salen Complexes Supported on Carbon as Heterogeneous Catalysts

In this section we will describe another type of support that has been used for the immobilization of chiral salen−metal complexes, representing a bridge between inorganic metal oxides and silicates and organic polymers.

Activated carbons are porous, readily available, and relatively inexpensive materials, extensively used as gas absorbers. Active carbons are among the materials exhibiting the largest specific surface area, easily reaching values of >1000 $m^2 \cdot g^{-1}$. In addition to their high porosity, active carbons also present the advantages of high thermal and chemical stabilities and very low cost. They have been used as supports for many noble metal catalyzed heterogeneous catalysts, particularly palladium on charcoal. The structure of active carbons, although not periodic and uniform, is being increasingly understood, and the presence of functional groups able to intervene in covalent anchoring, particularly hydroxyl and carboxyl groups, is recognized.[300−304] The population of these surface hydroxyl groups can be maximized by mild partial combustion and chemical oxidation processes.[302−304]

The use of carbonaceous materials, such as activated carbons and single-wall carbon nanotubes (SWNT), for the

Table 24. Enantiomeric Excess Values, Leaching, and Reusability of the Heterogeneous Salen Catalysts Supported on Carbons

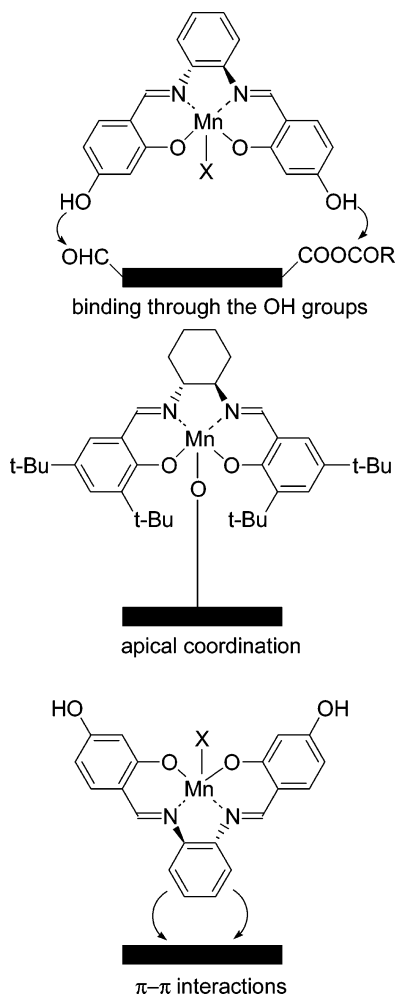| catalyst	ee^a (%) homo	ee^a (%) hetero	leaching[b]	recycling[b]	ref
Mn(III)/active carbon	12−60	12−57	N	Y (deact second cycle)	305, 307
VO(IV)/active carbon	90	48	N	na	196
VO(IV)/SWNT	90	66	N	Y (five cycles)	306

[a] Comparison between the reported ee values for the homogeneous and heterogeneous catalysis under analogous reaction conditions. [b] N, no; Y, yes; na, data not available.

immobilization of chiral salen−metal complexes has attracted much recent interest, and it is expected that the number of examples will increase soon.[196,305,306,307] Tables 23 and 24 list the chiral salen−metal complexes that have been anchored to carbonaceous supports.

Freire and co-workers have taken advantage of the presence of hydroxyl groups on the surface and have immobilized covalently a chiral salen−manganese on active carbons through the apical coordination to the metal (Scheme 46).[300,302,305,307,308] They have studied different pretreatments of the carbon supports using nitric acid and air oxidation to increase the population of surface OH groups.[309] The oxidizing treatment increases the surface area and the oxygen content of the original active carbon. It was found that particularly treatment with concentrated nitric acid increases notably the population of carboxylic acid functionalities as determined by measuring by mass spectrometry the CO_2 (carboxyl, anhydride, and lactone groups) and CO (phenolic hydroxy and ether groups) evolved upon thermal decomposition of the active carbons in the absence of oxygen.[308]

Adsorption of the salen−manganese(III) complexes was performed by heating dimethylformamide (DMF) and dichloromethane solutions in the presence of the active carbons, followed by exhaustive Soxhlet extraction. Complex adsorption can be monitored by UV−vis spectroscopy, which has also been used to assess leaching of adsorbed manganese complex contacted with organic solutions. The amount of salen−manganese complex adsorbed on each carbon depends on the oxidizing treatment and the substitution of the salen−manganese complex. Higher loadings are achieved with the air-oxidized activated carbon and with the hydroxy-substituted salen−manganese complex, for which a loading of 142 $\mu mol \cdot g^{-1}$ was obtained. It has been proposed that irreversible adsorption of the salen−manganese complex on the active carbons can occur by $\pi−\pi$ interactions with the salen ligand, by manganese complexation with the active carbon carboxy groups (for nitric oxidized active carbons), or by reaction of the salen ligand phenoxy groups with the aldehyde, ester, and anhydride groups of the active carbon (for those manganese complexes having OH substituents on the salen ligand).[300,302,305,307,308] This hypothesis is compatible with the effect of the oxidizing treatment on the active carbon (higher loading capacity for nitric oxidized active carbon)

Scheme 46. Possible Interactions between Salen–Manganese Complexes and Active Carbon Leading to Irreversible Adsorption (Based on Reference 308)

binding through the OH groups

apical coordination

π–π interactions

Scheme 47. Covalent Anchoring through the Ligand of a Salen–Vanadyl Complex on Active Carbon (Based on Reference 196)
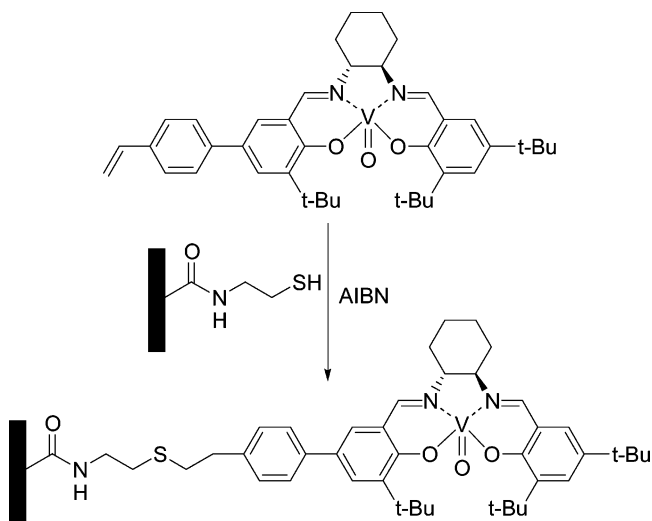

and with the influence of substitution on the salen–manganese complex.

The catalytic performance of these active carbon adsorbed manganese–salen complexes for the room temperature epoxidation of styrene using iodosylbenzene was, however, unsatisfactory. Thus, the selectivity of styrene toward epoxide was low, because noticeable amounts of benzaldehyde are formed. Part of this benzaldehyde arises from the undesired catalytic activity of active carbon. Also, the selectivity of the iodosylbenzene toward alkene epoxidation is low, because part of this oxidizing reagent oxidizes the active carbon. Thus, active carbon is not an innocent support in oxidation reactions and plays a negative role in the epoxidation catalysis. Also, deactivation of the salen–manganese complex by formation of the oxo dimer can occur when the complex is supported onto unoxidized active carbon. It was found that the best catalytic results were obtained by adsorbing the manganese complexes on air oxidized (11% burn off) for which the same chemoselectivity to the epoxide (~80%) as in homogeneous solution was obtained, but the active carbon supported catalyst could be reused for three consecutive runs without loss in conversion and chemoselectivity.

For the asymmetric epoxidation of styrene and α-methyl-styrene, the heterogeneous carbonaceous catalyst exhibits comparable ee values, conversions, and turnover numbers as the reaction carried out using homogeneous catalysis.[305,307]

Analysis by ICP-AES of manganese in the heterogeneous catalyst after its use showed no loss of metal during the catalytic reactions, indicating that no metal leaching occurred. However, in terms of reutilization, the catalyst deactivates after the first reuse.[305,307]

At the same time, Garcia et al. anchored covalently a chiral salen–vanadyl complex derivatized with vinyl groups on the porous structure of an activated carbon chemically modified by the presence of mercapto groups (Scheme 47). AIBN was used as radical initiator to promote the covalent anchoring. The active carbon supported catalyst showed lower ee for the enantioselective cyanosilylation of benzaldehyde. The ill-defined structure of the support, which contains probably other sulfur and oxygen functional groups, could be responsible for the low ee values obtained.[196]

Since their discovery by Iijima,[310–312] SWNTs have attracted increasing interest, mainly for their application in nanotechnology but also in catalysis. Whereas active carbons have an ill-defined structure consisting of lamellas connected by covalent bridges, SWNTs are a special carbon allotrope having a structure formed by tubes or bundles of tubes of micrometric length and nanometric diameters. Due to strong van der Waals forces, SWNT self-assemble in bundles of individual nanotubes. In catalysis, the periodic structure of ideal SWNTs can be used as insoluble solid support, alternative to active carbon. The main advantage of SWNT with respect to active carbon is the defined composition and structure. Purification of SWNT produces the partial oxidation of the tube tips and the formation of carboxylic acid functionalities. These carboxylic groups can be used for the covalent functionalization of SWNT. Functionalization of SWNT is also a topic of much current interest aimed at introducing response against external stimulii.[313–315]

Taking advantage of these structural and geometrical features of SWNT, Garcia and co-workers have covalently anchored a styryl-functionalized vanadyl Schiff base on a mercapto-modified SWNT using a radical-chain mechanism initiated by AIBN (Scheme 48).[306] The loading of a vanadyl–salen complex anchored to SWNT was quantified by combustion chemical analysis (S and N) and quantitative atomic absorption (V), resulting in 82 μmol·g^{-1}. The covalent bonding between the salen–vanadyl complex and the SWNT

Scheme 48. Chiral Salen−Vanadyl Complex Covalently Anchored to the Tips of SWNT (Based on References 196 and 306)
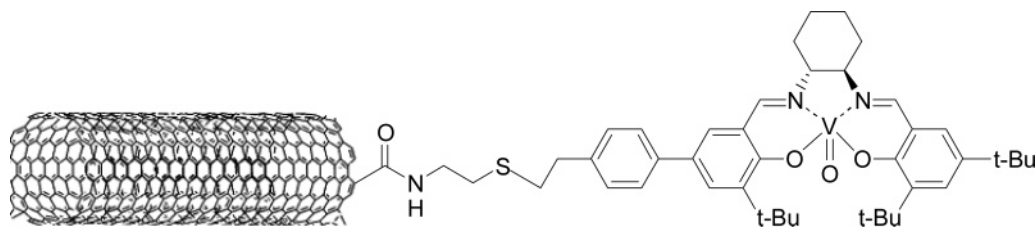
was inferred indirectly from two pieces of evidence: (i) a mechanical mixture of vanadyl−salen complex and SWNT was separated quantitatively by $CHCl_3$ extraction, and (ii) the IR spectrum of the resulting functionalized SWNT showed the disappearance of the S−H stretching vibration band at 2650 cm^{-1}, the maintenance of the amide band at 1726 cm^{-1}, and the appearance of the vanadyl− salen bands.

The salen−vanadyl covalently attached to SWNT exhibits high catalytic activity for the cyanosilylation of aromatic aldehydes with an almost complete conversion and selectivity toward the silylated cyanohydrin. This high catalytic activity is similar to that for an analogous complex in solution, but the solid was reused four times with the same conversion (>95%). Comparison of the performance of the salen− vanadyl complex anchored to SWNT with an analogous sample in which the vanadyl complex has been attached to activated carbon (Norit, surface area = 1400 m$^2 \cdot$g^{-1}) indicates that the activity is higher using SWNT as support.[306] An additional experimental advantage of having the complex attached to SWNT is that once the solid becomes suspended in halogenated solvents or DMF, the resulting suspensions are persistent and, even without stirring, the solid does not settle after prolonged time. The complex anchored to SWNT is truly heterogeneous (no leaching observed) and reusable (no decrease in activity) in five consecutive runs for the asymmetric cyanosilylation of benzaldehyde. The ee values obtained for the cyanosilylation of benzaldehyde were 66 at 67% conversion, still much lower than the homogeneous counterpart.[306] It has to be commented that the residual catalytic activity of activated carbon (five times higher than that of SWNT) makes this solid much less suited as support for enantioselective reaction.

Given that the chemistry of SWNT constitutes an emerging research front, it can be predicted that more studies will appear soon using SWNT as support of chiral salen−metal complexes. In the present examples, the salen complexes having been anchored to the tips of SWNT by functionalization of the carboxylic acids present at the termini of the tubes. It will be more interesting to develop a side wall functionalization strategy to anchor the complexes, because in this way, the potential loading of catalytically active sites will be increased by several orders of magnitude. On the other hand, sufficiently short SWNT can become soluble in conventional organic solvents. Up to now, long, insoluble SWNT have been used as supports for anchoring salen complexes, but it will be interesting to use also these soluble nanotubes.

Overall, it seems that the large adsorption capacity of active carbons and SWNT has been neglected in any of previous examples as a factor that can contribute to the increased efficiency of the enantioselective reaction. Thus, for instance, considering that SWNT are among the materials with the largest capacity to adsorb hydrogen,[316−318] it would be interesting to study enantioselective hydrogenations catalyzed by salen complexes using carbonaceous materials as supports.

6. Reusable Chiral Salen Complexes Anchored on Organic Polymers as Heterogeneous Catalysts

Since their early introduction in peptide and oligosaccharide solid-phase synthesis by Merrifield, insoluble polymers have been used to aid reaction workup, facilitate product purification, and, more recently, as supports for reagents, scavengers, and catalysts.[319−321] The use of organic polymers as supports to heterogenize active soluble catalysts has several important advantages, due to the unique microenvironment created for the reactants within the polymer matrix. The unique polarity, conformational, textural, and geometric factors may lead to an increase in the selectivity for catalytic reactions, an improved stability of the catalysts, and the possible enhancement of regioselectivity due to steric hindrance. There are a large number of reviews covering the use of polymers, either soluble or insoluble, derived from styrene or from other monomers, to develop recoverable and reusable catalytic systems.[202,322,323] The reader is referred to these sources for a broader view on this subject. Herein, we will limit specifically to those types of polymers used to anchor chiral salen complexes.

Compared to inorganic supports, the use of functionalized polymers can encounter some limitations: (i) the surface area of organic polymers is usually low compared to the inorganic supports, this being a limitation for the interfacial contact between the supported complex and the substrates; (ii) mechanical abrasion and chemical stability are important issues that can limit the use of organic polymers, although usually they do not play any negative role in inorganic supports; (iii) possible side reactions with the polymer backbone may occur during the reaction; and (iv) as in the case of sophisticated inorganic supports, the preparation of the functionalized polymer backbone can require dedicated organic synthesis. From the engineering point of view, depending on the reactor design, polymers can be fragile or mechanically too brittle. In these cases, upon recycling or extensive use the polymer beads can break down to smaller particles, then becoming suspended in the reaction mixture.

Another point that needs to be addressed is the polarity of the microenvironment where the complex is anchored. Common insoluble organic polymers can be highly hydrophobic. The hydrophobicity/hydrophilicity of the polymers is an issue of paramount importance. Solvation can be changed through the incorporation of various percentages and types of cross-linking agents, divinylbenzene (DVB) and ethylene glycol dimethylacrylate (EGDMA) being two of the most common. The latter monomer can introduce some polarity/hydrophilicity in the polymeric hydrocarbons.[324−326]

Of the several types of polymeric matrices that have been used as support of chiral catalysts in the past decade,

Scheme 49. Alternative Reported Strategies for the Immobilization of Chiral Salen Complexes on Polymers by Covalent Anchoring through the Ligand
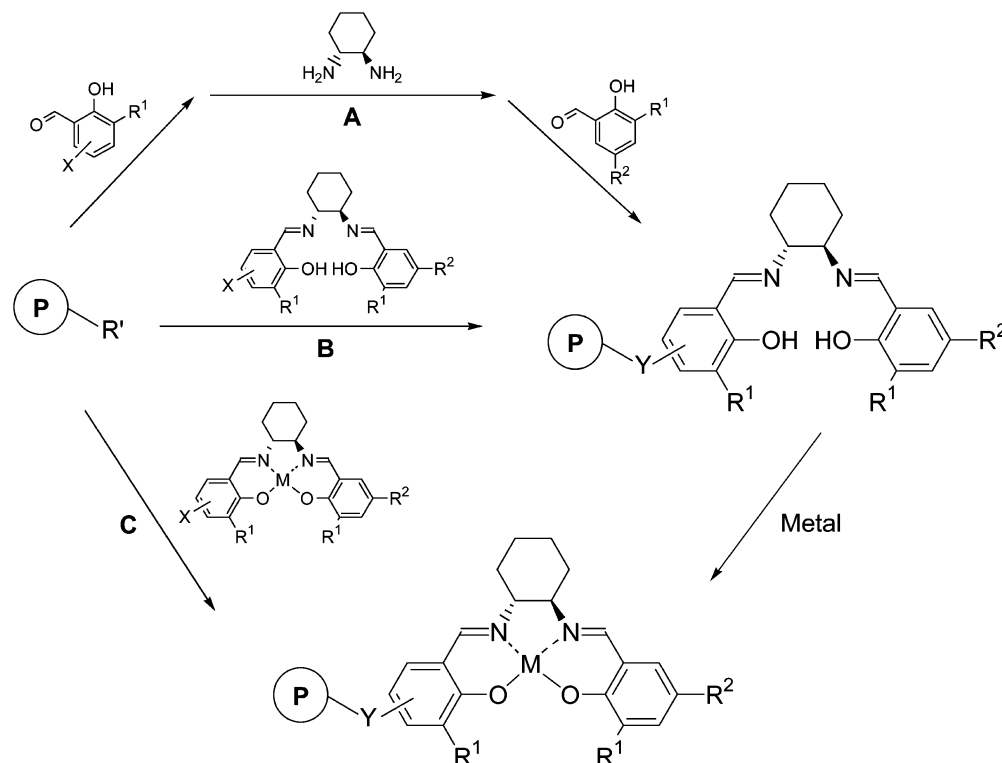
Scheme 50. Synthesis of a Chiral Salen–Manganese Complex Anchored to PS Polymer (Based on Reference 331)
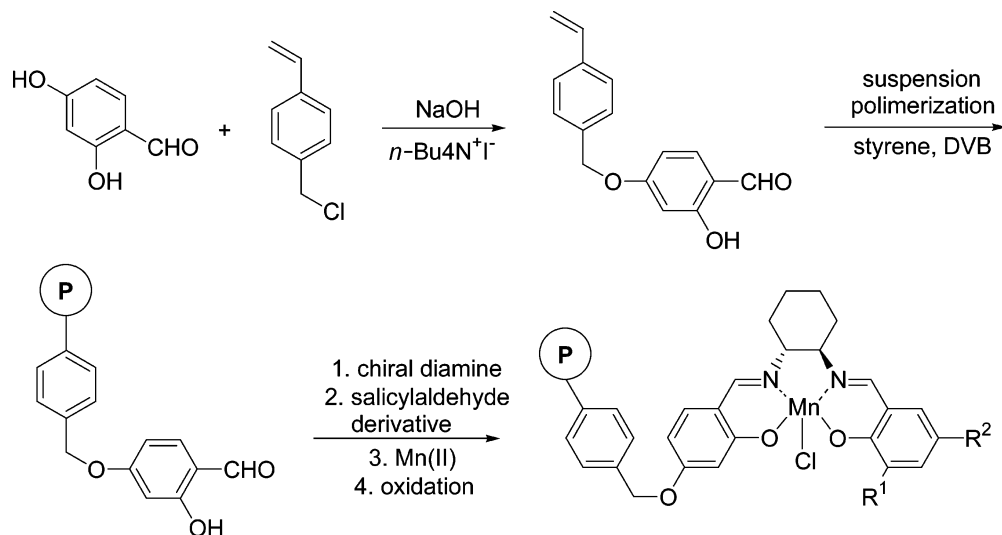
polystyrene (PS) is by far the most popular because of its unique properties, including high mechanical robustness and chemical inertness, ready availability, inexpensive preparation, and ease of functionalization and cross-linking.[323]

For the purpose of this review, we have classified the existing literature on immobilized chiral salen complexes anchored to functionalized polymers in two different methodologies, depending on whether the polymer is formed in the process: (i) use of solid-phase synthesis (SPS) methodology starting with a preformed functionalized polymer proceeding to anchor the complex by a direct reaction between a suitably substituted soluble complex or by synthesizing it through stepwise assembly of the components (Scheme 49); and (ii) forming the insoluble polymer containing the active complex through a suspension/copolymeriza-

tion technique (co-PT), the heterogeneous catalyst being prepared by copolymerization of styryl derivatives of the complex with styryl monomers (Schemes 54 and 55) or by self-polymerization of styryl–salen complex derivatives (Scheme 56).

6.1. Chiral Salen Complexes Anchored to Polymers Prepared by SPS

Analogously to the case of the inorganic supports discussed under section 4.4., in the SPS methodology the support has to be functionalized prior to anchoring of the salen complex. Fortunately, given the importance of functionalized polymers in SPS, there is a wide selection of commercially available functionalized polymers with a large variety of functional groups including chloromethylene, hydroxyl, amino, thiol, or pyridine rings.

Scheme 51. Anchoring of a Preformed Chiral Salen Ligand to a Suitably Derivatized PS and Consecutive Complexation of the Polymer-Bound Ligand (Based on Reference 332)
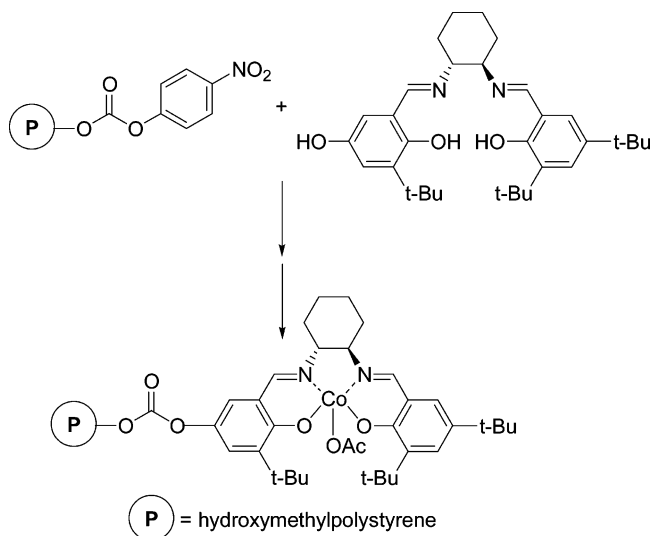
Scheme 52. Strategy for Anchoring Chiral Salen Complexes on Polymers by Connecting the Diamine Subunit Using a Glutaramide Spacer (Based on Reference 334)

Scheme 53. Chiral Salen–Manganese Complex Derived from *o*-Naphthylsalicylaldehyde Bonded to a Pyridine-Containing Polymer through Coordinative Bond to the Metal (Based on Reference 338)
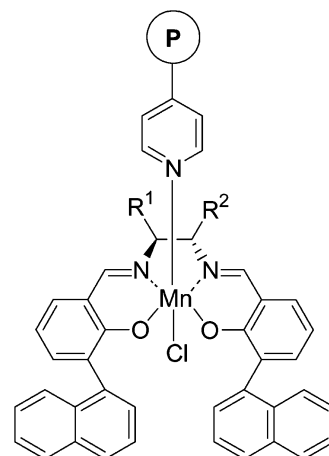
Scheme 54. Preparation of Polymeric Chiral Salen Catalysts Using the Co-PT Methodology and EGDMA as Comonomer (Based on Reference 340)

Three different strategies to immobilize by SPS chiral salen complexes on polymers have been reported. They are depicted in Scheme 49 and are parallel to those that have been used for covalent anchoring on inorganic solids (Scheme 39).

The first strategy makes extensive use of reactions in the solid phase and consists of the step-by-step synthesis of the complex by successive additions/condensations of the organic components. Starting with the functionalized polymer, this strategy requires at least four consecutive reactions performed in a stepwise manner to produce the desired chiral salen complex. This procedure enjoys the advantages of SPS in terms of ease of separation from the reagents needed in each step of the consecutive reactions and also the possibility to obtain salen complexes with two different phenolic moieties, by introducing two different salicylaldehydes (Scheme 49A). Another alternative is to immobilize a preformed ligand and proceed subsequently to metal complexation of the polymer-bound ligand (Scheme 49B). The possibility to prepare a library of polymer-bound salen complexes starting from a

single sample of polymer-supported ligand by adding different metals is the main attraction of this strategy.

The complex can also be immobilized in a single step by anchoring covalently to the polymer backbone a preformed salen–metal complex that contains a substituent in a peripheral position (Scheme 49C). Direct anchoring of the salen complex represents the maximum economy in solid-phase reactions, resulting in a purer and better characterized solid catalyst.

Tables 25 and 26 summarize the chiral salen–metal complexes anchored on polymers reported in the literature. In the tables we have indicated the complex immobilization methodology used, the asymmetric reaction for which they were tested, and the ee values obtained with the polymer-bound catalyst compared to the homogeneous phase analogues.

Scheme 55. Preparation of Polymeric Heterogeneous Salen Catalysts Using the Co-PT Methodology and Styrene and DVB as Monomers
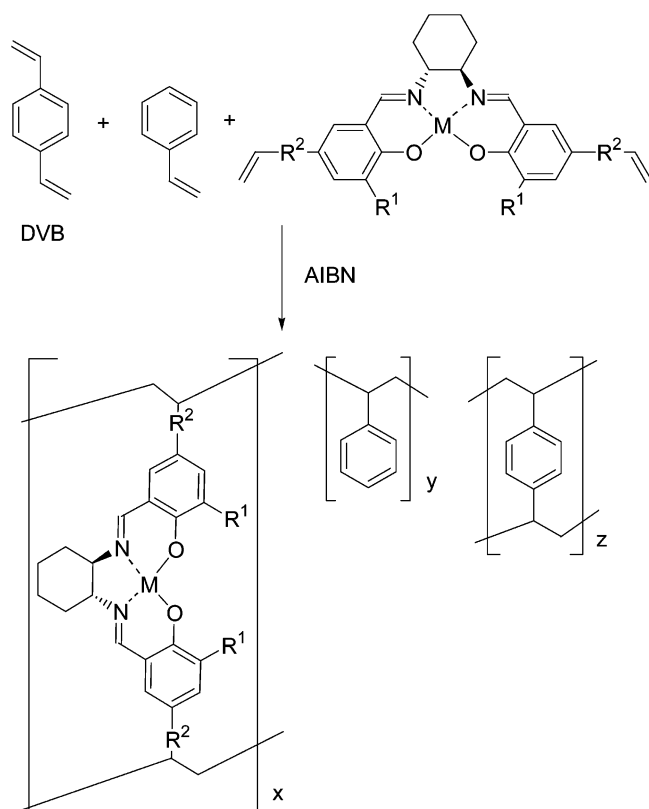
Scheme 56. Structures and Linking Motifs of the Poly-salen Catalysts That Have Been Obtained Using the Co-PT Methodology
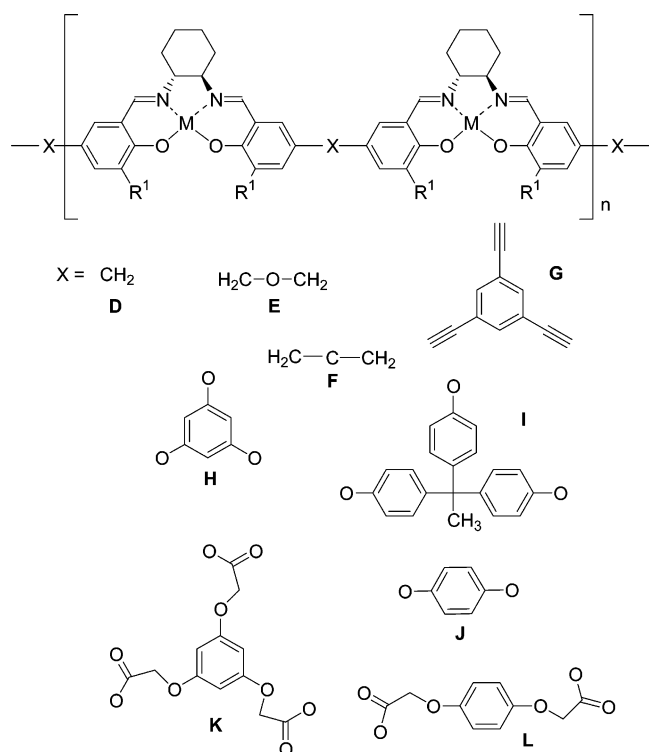
The Merrifield resin is one of the most used polymers for the purpose of immobilization of suitably derivatized homogeneous catalysts. In the case of chiral salen complexes, Laibinis et al. have immobilized a chiral salen−manganese

and −chromium complex to the Merrifield resin and tested the heterogeneous catalysts for the asymmetric epoxidation of alkenes (styrene and naphthalene derivatives) in the case of the manganese complex[327] and for the epoxide ring opening (hexene, propylene, and cyclohexene oxide) in the case of the chiral chromium catalyst.[328] The heterogeneous catalysts were prepared by the step-by-step strategy (Scheme 49A), the first reaction being the nuchleophilic attack of phenolic hydroxy groups of a salicylaldehyde derivative to the chloromethyl groups of the Merrifield polymer. Both polymer-bound salen catalysts, manganese and chromium, presented lower reaction rates when compared with the homogeneous counterpart, and the asymmetric induction of the complexes anchored on polymers were low[327] to moderate.[328] Recycling experiments were undertaken for both catalysts with contrasting results: whereas the manganese catalyst deactivates in the second cycle,[327] the polymer-bound salen−chromium catalyst could be reused in four consecutive cycles without decrease of activity.[328] These results are again in agreement with the higher stability of the salen complexes under hydrolytic conditions than under oxidative stress.

There are some authors who instead of using readily available commercial polymers as insoluble scaffolds to support salen complexes prefer to perform a copolymerization that effects simultaneously the formation of the polymer and complex anchoring. Sherrington and co-workers have immobilized a salen−manganese complex in a styrene- and methacrylate-based resin by adding a variety of cross-linker agents and comonomers such as p-divinylbenzene (DVB), ethane-1,2-diyl dimethacrylate, p-acetoxystyrene, N-(p-hydroxyphenyl)maleimide, and 3-methacryloyloxy-2-hydroxybenzaldehyde.[329,330] The series of heterogeneous catalysts prepared by copolymerization was tested for the asymmetric epoxidation of 1-phenylcyclohex-1-ene, for which lower reaction rates than the homogeneous counterpart, although in some cases with similar enantioselectivities, were observed. Recycling experiments have shown that the polymeric catalysts exhibit a very rapid deactivation with reduction of the activity and enantioselectivity already in the second cycle.[329,330]

Using a step-by-step strategy, the same group has developed a new type of polymeric chiral salen−manganese catalyst using a styrene comonomer having a salicylaldehyde derivative.[331] The synthesis starts from chloromethylstyrene that has been previously functionalized by reaction with 4-hydroxysalicylaldehyde. The resulting salicylaldehyde was used as comonomer together with styrene and DVB as cross-linker to obtain a cross-linked PS having pendent salicyldehyde units. This polymer was used to synthesize a chiral salen−manganese complex by means of consecutive solid-phase reactions (Scheme 50). Also for this new polymer, the ee values obtained for the asymmetric epoxidation of indene and 3,4-dihydronaphthalene were lower compared with the results achieved in homogeneous phase using the tetra-tert-butyl salen analogue.[331]

Jacobsen et al. have used hydroxymethyl-functionalized PS that was derivatized as the corresponding 4-nitrophenyl carbonate prior to immobilizing a salen ligand having a hydroxyl group at the para position of one phenolic ring.[332] 4-Nitrophenoxide is an excellent leaving group that renders the nucleophilic substitution easy. After the nucleophilic attack of the salen ligand hydroxyl group to the polymer 4-nitrophenyl carbonate (Scheme 51), the anchored ligand

Table 25. Polymer-Bound Chiral Salen Complexes, Corresponding Metals, Immobilization Strategy, and Asymmetric Reactions for Which They Were Used as Heterogeneous Catalysts

polymer[a]	metal	immobilization method[b]	asymmetric reaction	ref
Merrifield polymer	Mn(III)	A $R' = CH_2Cl$, $X = OH$	epoxidation of alkenes	327
Merrifield polymer	Cr (III)	A $R' = CH_2Cl$, $X = OH$	epoxide ring opening	328
styrene and methacrylate resin	Mn(III)	A	epoxidation of alkenes	329, 330
poly(styrene-co-DVB)	Mn(III)	A $R' = CH_2Cl$, $X = OH$	epoxidation of alkenes	331
polystyrene	Co(III)	B $R' =$ ester group, $X = OH$	hydrolytic kinetic resolution of epoxides	332
Merrifield resin, *JandaJel* resin	Mn(III)	B $R' = OH$, $X = COOH$	epoxidation of alkenes	333
amino oxazolidine resins	Mn(III)	B $R' = NH$, $X = COOH$	epoxidation of alkenes	334
Merrifield resin	Mn(III)	C $R' = CH_2Cl$, $X = OH$	epoxidation of alkenes	335
Polystyrene	Mn(III)	C $R' = C_6H_4COCl$, $X = OH$	epoxidation of alkenes	336
PAMAM dendrimer	Co(III)	C $R' = NH_2$, $X = CO_2C_6F_5$	hydrolytic kinetic resolution of epoxides	337
PVPD polymer	Mn(III)	through the metal $R' = N$	epoxidation of alkenes	338
polystyrene	Mn(III)	through the metal $R' = PhO$ or $PhSO_3$	epoxidation of alkenes	339

[a] *JandaJel*: copolymer of styrene, hydroxymethylstyrene, and styrene ether; PAMAM, polyamidoamine; PVPD, styrene−4-vinylpyridine−divinyl benzene polymer. [b] Codes corresponding to Scheme 49.

Table 26. Results Achieved Using the Polymer-Bound Chiral Salen Catalysts Prepared by the SPS Methodology

catalyst	ee[a,b] (%)		leaching[b]	recycling[b]	ref
	homo	hetero			
Mn(III)/Merrifield	na	7−79	N	Y (deact second cycle)	327
Cr(III)/Merrifield	na	6−36	N	Y (four cycles)	328
Mn(III)/PS	92	5−91	N	Y (deact second cycle)	329, 330
Mn(III)/methacrylate					
Mn(III)/PS	80−99	4−20	na	na	331
Co(III)/PS	na	>93[c]	N	Y (five cycles)	332
Mn(III)/Merrifield	57−88	35−90	N	Y (deact third cycle)	333
Mn(III)/*JandaJel*					
Mn(III)/	90−95	86−92	N	na	334
aminooxazolidine					
Mn(III)/Merrifield	94	90−94	N	Y (six cycles)	335
Mn(III)/polystyrene	94	90−94	N	Y (six cycles)	336
Co(III)/PAMAM	>98	>98[d]	na	na	337
Mn(III)/PVPD	na	16−46	N	Y (1ten cycles)	338
Mn(III)/polystyrene	24−93	34−92	N	Y (three cycles)	339

[a] Comparison between the reported ee values for the homogeneous and heterogeneous catalysis under analogous reaction conditions. [b] N, no; Y, yes; na, data not available. [c] Relative reaction rates for the enantiomeric epichlorhydrins ranged from 133 to 206 depending on the cycle. [d] Relative reaction rates for the enantiomeric 1,2-epoxyhexane were 24, 15, and 11 for the first, second, and third generation, respectively.

was submitted to complexation with cobalt, and the heterogeneous catalyst was tested for the hydrolytic kinetic resolution of terminal epoxides (epichlorohydrin, 4-hydroxy-1-butene, and epibromohydrin) showing excellent ee values. The catalytic kinetic resolution was found to be entirely heterogeneous with no leaching detected. The polymer-supported catalyst was used in five consecutive cycles without decrease of the activities.[332]

The same strategy (Scheme 49B) was used by Janda and co-workers to immobilize in several polymers, such as the Merrifield and *JandaJel* resins, a salen ligand derivatized with carboxylic groups.[333] *JandaJel* is a copolymer formed by polymerization of styrene, hydroxymethylstyrene, and styrene ethers. Ester groups formed by reaction of the ligand carboxylic acids and the polymer hydroxyl groups act as linkers anchoring the salen ligands to the polymer backbone. Manganese was added to the ligand, and the resulting in situ formed complex was used as catalyst for the asymmetric

epoxidation of alkenes (styrene, *cis*-β-methylstyrene, and dihydronaphthalene) with reaction rates and asymmetric ability similar to those of the homogeneous congener. No leaching was detected, and in the recycling experiments the polymeric catalyst showed deactivation in the third cycle.[333] It has to be noted that, due to the easy hydrolysis and the slightly basic conditions required in most oxidations, ester and carbonate groups (those groups linking the polymer backbone and the salen complex) may not be sufficiently robust under some oxidation reaction conditions.

A different type of covalent immobilization of salen complexes on polymers was reported by Song et al., who anchored the salen through the diamine moiety of the ligand.[334] The authors used pyrrolidine-3,4-diamine as chiral diamine, and after ligand synthesis, it was treated with glutaric anhydride, which acts as a spacer between the salen complex and the polymer. The glutaramide-derivatized salen ligand was immobilized on oxazolidine resins and then

Table 27. Polymeric Chiral Salen–Metal Complexes Prepared by the Co-PT Strategy and Enantioselective Reaction Types That Have Been Performed Using Them as Catalysts

monomer[a]	metal	asymmetric reaction	ref
EGDMA	Mn(III)	epoxidation of alkenes	340, 341
styrene and DVB	Mn(III)	epoxidation of alkenes	342, 343
styrene and DVB	Mn(III)	epoxidation of alkenes	344, 345
styrene and DVB	Cr(III)	hetero Diels–Alder	344
styrene and DVB	Ir(III)	reduction of ketones	346
styrene	Co(III)	hydrolytic kinetic resolution of epoxides	347
norbornene	Mn(III)	epoxidation of alkenes	348
norbornene	Co(III)	hydrolytic kinetic resolution of epoxides	348
poly-salen (D, E)	Mn(III)	epoxidation of alkenes	349
poly-salen (D, F)	Co(III)	hydrolytic kinetic resolution of epoxides	350
poly-salen (D)	Mn(III)	epoxidation of alkenes	351
poly-salen (F)	Mn(III)	epoxidation of alkenes	352
poly-salen (G)	Mn(III)	epoxidation of alkenes	353
poly-salen (D, H, I, J)	Co(III)	hydrolytic kinetic resolution of epoxides	354
poly-salen (K, L)	Co(III)	hydrolytic kinetic resolution of epoxides	355
poly-salen (K, L)	Ti(IV), V(V)	addition of KCN and Ac_2O to aldehydes	356, 357

[a] EGDMA, ethylene glycol dimethylacrylate; the letters from D–L refer to Scheme 56.

complexed with manganese to give a new heterogeneous catalyst (Scheme 52). This manganese-containing polymer was highly active and stable (no leaching) for the epoxidation of alkenes such as 2,2-dimethylchromene, 5-cyano-2,2-dimethylchromene, and 1-phenylcyclohexene, whereby similar enantioselectivities as found with the catalyst in homogeneous phase were obtained.[334]

Moving toward the maximum economy in solid-phase reactions, there are five examples using polymers as support in which the preformed salen–metal complex has been bound to the polymer. Three of these papers describe the binding of the catalyst by covalent anchoring through the ligand (Scheme 49C)[335–337] and two the binding by means of an apical coordinative bond to the metal following the strategy indicated in Scheme 35.[338,339] Thus, in the most straightforward methodology, a salen–manganese complex functionalized with peripheral hydroxyl groups was immobilized on a Merrifield resin[335] and polystyrenecarbonyl chloride[336] in a single step, and the resulting polymers were tested for the asymmetric epoxidation of 1,2-dihydronaphthalene. The polymer-bound catalyst exhibits lower reaction rates than the homogeneous counterpart but similar asymmetric ability.[335,336] Both catalysts were recycled six times without activity decrease and leaching.[335,336]

Using the same strategy, Jacobsen and co-workers have immobilized a salen–cobalt complex derivatized with esters groups on a highly pure polyamidoamine (PAMAM) dendrimer with free amino groups. Using this dendrimeric catalyst, higher reaction rates and enantioselectivities similar to those of the homogeneous system were obtained for the hydrolytic kinetic resolution of vinylcyclohexane epoxide and 1,2-epoxyhexane.[337]

Kureshy et al. have used three-component copolymer (PVPD)-containing styrene, 4-vinylpyridine, and divinylbenzene as comonomers to covalently immobilize salen–manganese complexes derived from *o*-naphthylsalicylaldehyde with different chiral diamines (diphenylethylenediamine, cyclohexanediamine, and diaminopropane). Binding of the complex to the polymers occurs through an apical coordinative bond between the manganese and the pyridine molecules of the polymer backbone (Scheme 53).[338] The series of catalysts exhibits moderate enantioselectivities for the asymmetric epoxidation of several styrene derivatives. The PVPD catalysts were reused nine times without activity decrease or leaching.[338]

More recently, Li and co-workers have immobilized a chiral salen–manganese complex with the two most used chiral diamines (diphenylethylenediamine and cyclohexanediamine), through an apical coordinative bond between the metal and a polystyrene resin derivatized with phenoxy or phenylsulfonic groups.[339] The catalysts were employed for the enantioselective epoxidation of styrene derivatives, exhibiting ee values similar to those of the homogeneous counterparts but with lower reaction rates. The catalysts were reused in two runs maintaining the activity and without detectable leaching.[339]

6.2. Chiral Salen Complexes Anchored to Polymers Formed in Situ by the Suspension Co-PT

The co-PT methodology is based on the synthesis of salen complex derivatives with terminal vinyl groups capable of copolymerizing with other vinylic monomers such as EGDMA (Scheme 54) or styrene and DVB (Scheme 55), in a radical-chain mechanism using AIBN or benzoyl peroxide as radical initiator. More recently, a variant of this strategy has been realized in which no monomer other than the salen complex is used (Scheme 56). The main difference between the co-PT and SPS strategies in which a suitable derivatized pure salen–metal complex is anchored on a polymeric backbone is whether a preformed polymer is one of the reagents (SPS strategy) or if the reaction takes place with a salen vinyl monomer that eventually will form the polymer (co-PT strategy). Other differences between co-PT and SPS arise from the fact that commercial polymers have special characteristics in terms of branching, average molecular weight, and polydispersity that can be difficult to achieve for inexperienced, non-polymer chemists. Relevant preparation and characterization data of these polymeric salen complexes prepared by co-PT and their catalytic activity are summarized in Tables 27 and 28.

As in the SPS variant in which a preformed complex is anchored to the polymer, the co-PT methodology has the initial advantage of having a well characterizable, pure complex prior to the formation of the polymer backbone. In this way, all of the synthetic steps needed for the preparation of the suitably derivatized chiral salen complex are performed with soluble compounds in homogeneous phase. This permits the possibility of effecting chromatographic purification of

Table 28. Relevant Catalytic Results and Enantiomeric Excess Values of the Polymeric Catalysts Prepared by the Co-PT Methodology

catalyst	ee[a,b] (%)		leaching[b]	recycling[b]	ref
	homo	hetero			
Mn(III)/EGDMA	na	2−30	na	na	340, 341
Mn(III)/styrene and Mn(III)/DVB	na	4−62	na	Y (five cycles)	342, 343
Mn(III)/styrene and Mn(III)/DVB	2−92	2−84	N	Y (ten cycles)	344, 345
Cr(III)/styrene and Cr(III)/DVB	na	50−72	N	Y (five cycles)	344
Ir(III)/styrene and Ir(III)/DVB	22	21−70	na	Y (deact second cycle)	346
Co(III)/styrene	93−99	81−99	Y (na)	Y (four cycles)	347
Mn(III)/norbornene	34−93	32−92	na	Y (deact second cycle)	348
Co(III)/norbornene	99	80−99	Y (na)	Y (three cycles)	348
Mn(III)/poly-salen (D, E)	na	25−92	na	Y (five cycles)	349
Co(III)/poly-salen (D, F)	na	45−98	na	Y (two cycles)	350
Mn(III)/poly-salen (D)	92	32−99	na	Y (deact third cycle)	351
Mn(III)/dimeric salen (F)	na	41−98	na	Y (three cycles)	352
Mn(III)/poly-salen (G)	na	12−64	na	Y (six cycles)	353
Co(III)/poly-salen (D, H, I, J)	na	>95	N	Y (seven cycles)	354
Co(III)/poly-salen (K, L)	na	84−99	na	Y (deact second cycle)	355
Ti (IV) and V(IV)/poly-salen (K, L)	44−89	74−88	na	Y (six cycles)	356, 357

[a] Comparison between the reported ee values for the homogeneous and heterogeneous catalysis under analogous reaction conditions. [b] N, no; Y, yes; na, data not available.

the intermediates as well as spectroscopy in solution and chemical analyses of the synthetic intermediates to fully characterize them. Thus, this methodology leaves less room for ill-defined spurious sites.

Dhal and co-workers were the first using the co-PT methodology to polymerize a vinylic chiral salen complex to form an insoluble polymer.[340,341] A salen−manganese complex with two peripheral vinyl groups in combination with EGDMA as the cross-linking monomer were copolymerized to obtain an insoluble polymeric chiral metal complex (Scheme 54), which is active for the asymmetric epoxidation of alkenes (styrene and naphthalene derivatives). The homogeneous system gave superior ee values compared to the heterogeneous polymeric system employed in the study. The author's speculate that this difference in the asymmetric induction ability of the polymeric complex may be attributable to steric reasons and/or certain microenvironmental effects associated with the macromolecular structure. In any case, the reasons for the decrease of the ee values deserve a deeper study to better understand their origin.

Styrene and DVB are the two most used comonomers in the co-PT methodology (Scheme 55). With these two monomers, there are examples using the co-PT methodology of the preparation of chiral salen manganese,[342−345] chromium,[344] and iridium[346] complexes immobilized in polymeric chains. Salvadori et al., first,[342,343] and Seebach and co-workers[344,345] more recently, have developed a poly(styrene-*co*-DVB) with a salen−manganese complex incorporated in the backbone. This polymer has been used as catalyst for the asymmetric epoxidation of styrene derivatives. The enantioselectivity achieved with these heterogeneous catalysts was lower than that of an analogous homogeneous reaction. In both cases, the catalysts could be recycled several times (5 and 10, in the cases of Salvadori and Seebach, respectively) maintaining the initial activity. The polymeric salen−chromium complex catalyst prepared by co-PT synthesis was tested for the hetero Diels−Alder reaction of Danishefsky's diene with aldehydes to give dihydropyranones in good enantioselectivities.[344] It was possible to use the catalyst in five consecutive cycles without detectable leaching or decrease in the catalytic activity. Heterogenized polymeric salen ligands complexed to iridium were tested for the asymmetric hydrogen exchange between 2-propanol as reductant and acetophenone.[346] Similar reaction rates and

higher ee values were obtained when compared to the homogeneous counterpart, but the recycling of the salen−iridium complex was unsatisfactory, catalyst deactivation occurring in the second cycle.

In a recent publication, Jones, Weck, and co-workers have published a polymeric chiral salen−cobalt complex prepared by co-PT synthesis using styrene as comonomer and a salen complex monovinyl derivative.[347] The heterogeneous catalyst was used for the hydrolytic kinetic resolution of epichlorohydrin, attaining ee values comparable to those obtained in homogeneous phase. The catalyst was reused three times maintaining the ee levels, but with a slight decrease in the reaction rate.[347]

The same group has also reported a new approach in the co-PT methodology using ring-opening metathesis to polymerize the monomers in a more controlled way.[348] In this case, two types of polymeric catalysts have been prepared: (i) a homopolymer, in which monofunctionalized salen−manganese or −cobalt complexes attached to a norbornene molecule were exclusively the only monomer used, or (ii) a copolymer with the monofunctionalized complex molecule being used in combination with norbornene as monomers. The polymeric manganese catalysts were used for the asymmetric epoxidation of styrene derivatives, whereas the polymeric cobalt complex was a suitable catalyst for the hydrolytic kinetic resolution of epichlorohydrin. Both polymeric salen−metal complexes have shown exceptional catalytic activities and selectivities comparable to those of the original catalysts.[348] Concerning recycling, whereas the activities of the salen−manganese catalysts drop immediately in the second cycle, the cobalt catalysts could be used in three consecutive cycles without decreases in the activities. The most relevant outcome of the results was, however, that the copolymeric catalysts are more active and selective than their homopolymer analogues. From these results the authors concluded that catalyst density and site isolation are the key issues in achieving extremely active and selective heterogeneous salen catalysts.[348]

The synthesis of polymeric salen catalysts connected through linkers different from vinylic monomers is one of the latest developments in the synthesis of heterogeneous salen catalysts. The use of nonvinylic linkers enables greater creativity and freedom in the synthetic steps, which can be simpler and less elaborate than some of the routes described

in the previous types of polymer-bound heterogeneous catalysts. In addition, the use of nonvinylic salen complexes leads to a high structural diversity of catalysts. The linking units used so far (X in Scheme 56) are mainly phenyl derivatives.

Poly-salen–manganese catalysts having methylene or methylene-oxy-methylene (X = D and E in Scheme 56) as linking motifs were developed by Zheng and co-workers.[349] The catalysts were tested for the asymmetric epoxidation of styrene and chromene derivatives with excellent enantioselectivities, and the catalysts could be recycled effectively four times. The same authors have published a poly-salen–cobalt catalysts with methylene and 2,2-propylene (X = D and F in Scheme 56) as linkers.[350] The heterogeneous catalysts were used in the hydrolytic kinetic resolution of epoxides with excellent results. Kureshy et al. also use D as linking unit for the synthesis of a chiral poly-salen–manganese catalyst, which exhibits higher enantioselectivities than the homogeneous system for the epoxidation of styrene and chromene derivatives.[351] The same group has synthesized a homochiral dimeric salen–Mn(III) complex using F as linker.[352] The polymeric catalysts were tested for the asymmetric epoxidation of alkenes (styrene, indene, and chromene derivatives), yielding excellent ee values and maintaining their activity upon reuse.[352] Another example of a poly-salen–manganese was described by Gothelf et al., who used a 1,3,5-benzenetriethynyl subunit (G in Scheme 56) as linker of the salen units to obtain a polymeric catalyst that exhibits moderate ee values for the epoxidation of cis-2-methyl-styrene.[353] The polymeric catalyst can be reused five times without reduced activity or decrease in the enantioselectivity. The reactivity of C≡C triple bonds may be a major drawback of this linker motif.

Polymeric chiral salen–cobalt complexes developed by Kim and co-workers using several linking agents (D, H, I, and J in Scheme 56) catalyze the hydrolytic kinetic resolution of epoxides (epichlorohydrin, styrene oxide, 1,2-epoxybutane, and 1,2-epoxyhexane) with very high enantioselectivities.[354] The polymeric catalysts were recovered and reused six times without any treatment after reaction, showing no decrease in activity and enantioselectivity. Analogously, Zheng et al. have used the same complex with different linkages (K and L in Scheme 56) to prepare highly enantioselective polymeric catalysts for the hydrolytic kinetic resolution of epoxides (epichlorohydrin, styrene oxide, and phenyl glycidyl ether).[355] However, the recycling experiments were not successful (deactivation occurred in the second cycle). The authors attributed this deactivation to the fact that the oxygen atoms adjacent to the carbonyl groups make the ester linkages more sensitive to the reaction systems. The same authors have prepared poly-salen–titanium and –vanadium catalysts (K and L as linking units in Scheme 56), which catalyze the enantioselective addition of KCN and Ac$_2$O to alkyl and aryl aldehydes.[356,357] Similar enantioselectivities were achieved with the polymeric catalysts when compared with the homogeneous congener, and it was possible to recycle the poly-salen complex five times while maintaining the initial activities.

Another approach to recover and reuse salen catalysts is by precipitation. In this case, the complex is recovered after precipitating it using a solvent in which the complex is poorly soluble. Hemmert and co-workers have synthesized macrocyclic salen–Mn(III) complexes with aliphatic polyether bridges (Scheme 57),[358] and the catalysts were used in the

Scheme 57. Macrocyclic Chiral Salen Complexes That Act as Homogeneous Catalysts and Can Be Reused after Precipitation (Based on Reference 358)
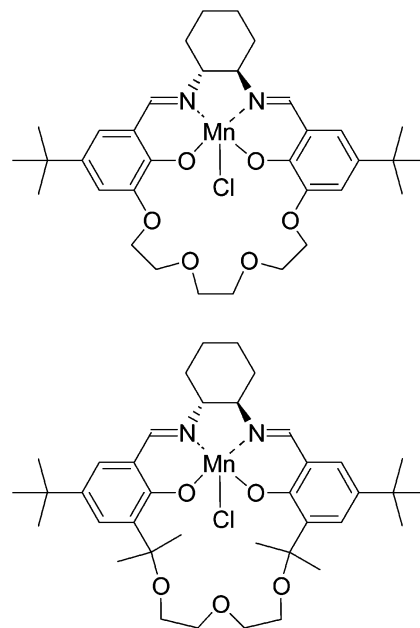
asymmetric epoxidation of cis-disubstituted olefins. After a reaction has been performed under homogeneous conditions and precipitation with hexane, the complexes can be reused two times, maintaining the original activities.[358]

A very interesting novel concept that has been recently developed by Kim and co-workers is that of dimeric and oligomeric chiral salen complexes formed by the addition of Lewis acids to monomeric chiral salen–metal complexes.[73–78] As an example, a poly-salen–cobalt(II) polymer analogous to those shown in Scheme 56 (the bridge X being a covalent bond) obtained by condensation of 4,4′-bis(2,2′di-tert-butylsalicylaldehyde) and (R,R)-1,2-diaminocyclohexane in boiling dioxane followed by the addition of cobalt(II) acetate is devoid of any catalytic activity for the hydrolytic kinetic resolution of epoxides. However, when this poly-salen was reacted with the adducts of a monomeric salen–cobalt(II) and BF$_3$ in either aqueous or etherous phase, the resulting polymer exhibits high activity and enatioselectivity for the hydrolytic kinetic resolution of terminal epoxides.[73] Evidence based on the behavior of monomeric salen–cobalt complexes suggests that a polymer with dimeric salen units connected by BF$_3$ bridges is formed (Scheme 58). Chemisorption of monomeric salen units to the polymer is compatible with the 34 wt % increase of the polymer upon addition of the salen/BF$_3$ adduct.[73] Although formation of these adducts is a very simple process that can be expanded to most chiral salen–metal and can serve to increase activity and enantioselectivity, the main problem of these adducts is the lability of the Lewis acid bridge and, therefore, this polymeric salen–cobalt(II) complex partially loses its activity in the first use due to the dissociation of the adducts from the polymer backbone under reactions conditions that require the presence of water.

7. Reusable Hybrid Chiral Metallosalen–Silica Materials as Heterogeneous Catalysts

There are some solid catalysts in which the salen complex forms part of a silica skeleton being grafted to the walls by

Scheme 58. Proposed Structures for the Poly-salen−Co(II)/Monomeric Co(II)/BF3 Adducts (Based on Reference 73)[a]
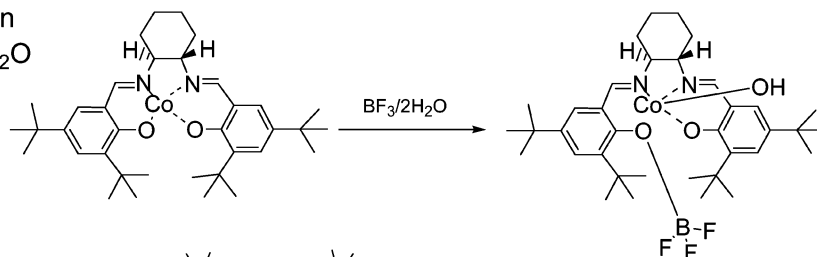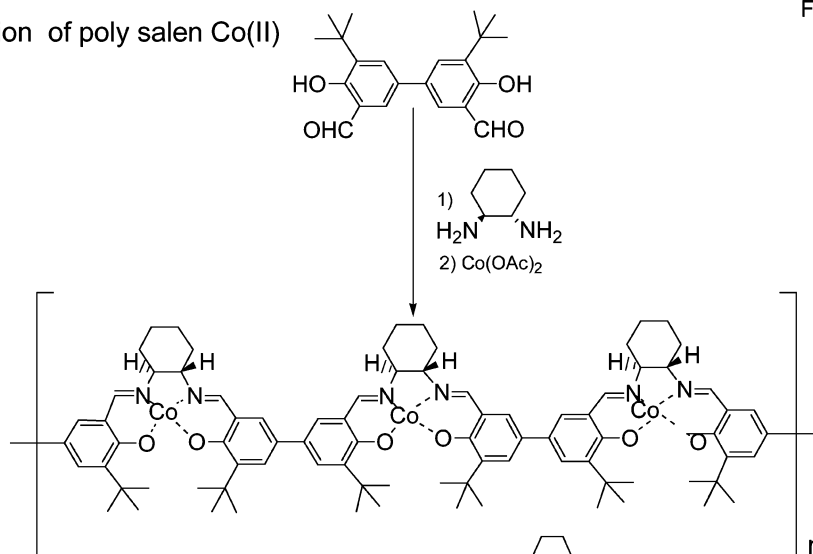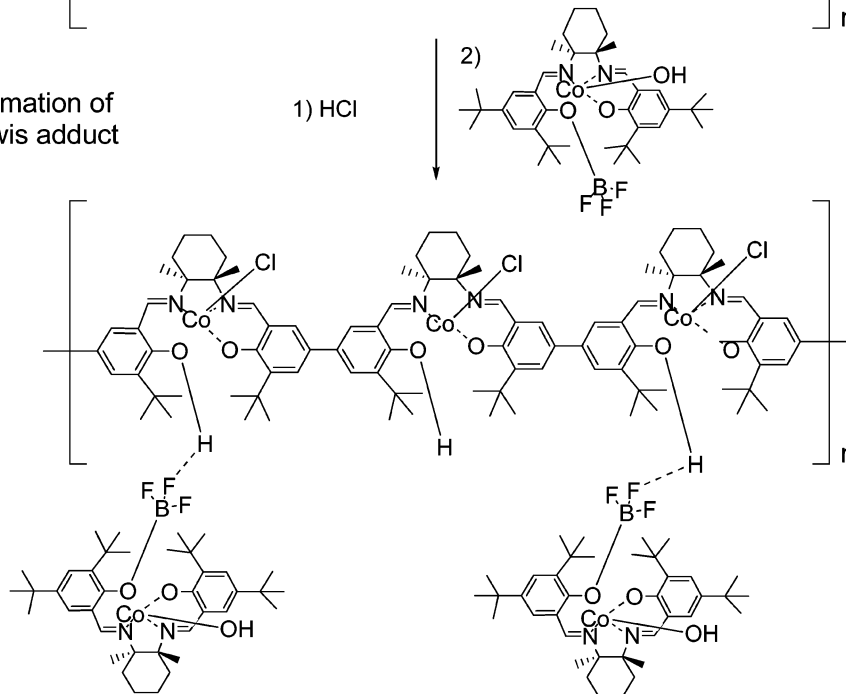
[a] Whereas polymeric salen−Co(II) is inert, the adduct shows remarkable activity and enantioselectivity for hydrolytic kinetic resolution.

two or more tethers.[359] The silicon oxide structure provides rigidity, insolubility, and ease of recovery, whereas the catalytic activity arises from the salen complex. Two types of these hybrid salen complex−silica materials have been reported, depending on whether the material is completely amorphous and the porosity of the material is randomly distributed (aerogels or xerogels) or if the solid has a periodic mesoporous organosilica (PMO) structure.

Baiker and co-workers have claimed to be the first reporting immobilization of a salen complex via a sol−gel procedure.[360] The actual complexes reported were the dimeric bis(salicylidenaminate) complexes of Co(III) and Cu(II).

These Schiff base ligands contain only a single imine group and lack the bridge connecting the two nitrogen atoms. Attempts to prepare the analogous manganese complex failed due to the formation of a precipitate during the hydrolysis step of the sol−gel procedure. One of the most appealing features of these Schiff base complexes reported by Baiker is that the formation of the imine ligand, metal complexation, and formation of the solid occur in one pot (Scheme 59).

This procedure suffers, however, from the problem of a poor complex characterization. Particularly, the crystal structure of the actual complex has not been reported, and it may be that the coordination sphere of the central metal atom

Scheme 59. Sol–Gel Synthesis of a Hybrid Metallo Salen–Silica Material Using a Triethoxysilane Schiff Base Complex as Precursor (Based on Reference 360)
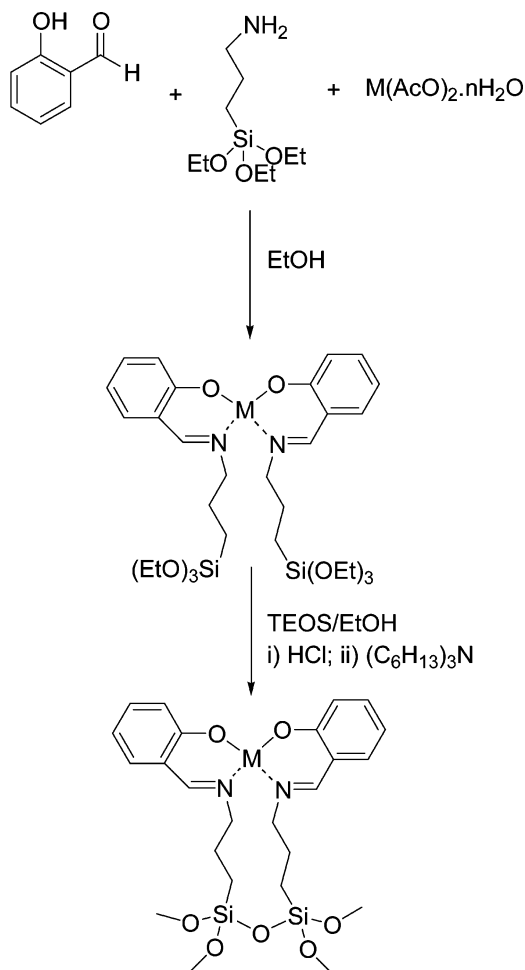
is different from N_2O_2. This is of particular interest in the case of Co atoms, where, depending on the oxidation state, the coordination of the metal atom can change from tetra- to pentacoordination.

The formation of the metal–Schiff base complex during the sol–gel synthesis of the hybrid material was supported in part by a control in which salicylaldehyde (the precursor of the imine synthesis) is observed in the absence of the metal acetate salt, but not in its presence. Imines are hydrolyzed more easily when they do not form a complex than when they are acting as metal ligands. Also, IR (shift of the C=N band from 1633 for the imine ligand to 1620–1625 cm^{-1} upon complexation) and UV–vis spectroscopy (absorption bands corresponding to the metal d–d transitions in the 362–400 nm range) are also compatible with complex formation.[360] It has to be noted, however, that it is known that the shifts of the IR C=N band in Schiff bases can be very small for pentacoordinated salen complexes, whereas this shift tends to be larger (~35 cm^{-1}) for tetracoordinated salen complexes.[361,362] This is a result of the differences in geometry and strength of the metal–nitrogen interaction depending on the position of the metal atom and its coordination number. Thus, IR spectroscopy may not be conclusive with regard to the formation of pentacoordinated salen complexes.

One point that was not clarified is whether acetate ions have been completely replaced from the coordination sphere of the metal atoms after formation of the metal–Schiff base

complexes. The observation that ethyl acetate (confirmed by MS and IR spectroscopies) is evolved in the thermal decomposition of the hybrid metal complex–silica solid, particularly for the cobalt complex, requires a deeper understanding, particularly in the context of the presence or absence of acetate in the solids, most probably coordinated to the metal ions.

The homogeneous distribution of the metal and, presumably also, the Schiff base complex in the solid was assessed by comparing the metal/Si ratio of different parts of the powder measured using laser ablation combined with inductively coupled plasma–mass spectrometry. Furthermore, these ratios fit well with the average metal/Si ratio of the bulk material obtained by chemical analysis.

Depending on the way in which the solid is dried after gelation, xerogels (conventional drying at 110 °C under vacuum for 24 h) and aerogels (supercrititcal CO_2 drying) were obtained. They differ in the porosity and surface area, aerogels showing a type IV isothermal N_2 adsorption profile characteristic of mesoporous materials and exhibiting 5–7 times higher pore volume than xerogels, which exhibit a typical behavior of microporous solids.

Leaching experiments performed by stirring the solids containing cobalt and copper in DMF, DMSO, and ethylbenzene at 110 °C in the presence of pyridine and K^{t}BuO showed that the solids were unaltered. Also, preliminary oxygen oxidation at 130 °C and 1 bar of neat ethylbenzene under continuous azeotropic distillation using the cobalt-containing hybrid aerogel material as catalyst renders acetophenone with 78% selectivity at conversions ≥99%. Chemical analysis showed the absence of cobalt in the solution (<0.1 wt %).

To develop hybrid metal salen–silica materials showing reversible binding ability toward dioxygen, Corriu, Reyé, and co-workers have immobilized covalently pentacoordinated bis(salicylidene)ethylenediamine Co(II) and bis(3-fluoro-salicylidene)ethylenediamine Co(II) complexes prepared also by the sol–gel process.[363,364] In addition, they prepared the analogous Cu(II) complexes, although the reversible O_2 binding ability of the Cu(II) complexes was not studied in the paper.[365]

Two strategies differing in the order in which metal complexation and gelation occur were tested.[363] In the preferred route, the salen–Co(III) and Cu(II) complexes having triethoxysilylphenylene units, as well as their corresponding ligands, were formed first and characterized by analytical and spectroscopic methods. Subsequently, gelation was performed under inert atmosphere by adding a certain proportion (between 9 and 19 equivalents) of tetraisopropyl orthosilicate and a stoichiometric water quantity and using tetrabutylammonium fluoride (1–10%) to promote hydrolysis (Scheme 60).[363] Different hydrolysis temperatures ranging from 30 to 80 °C and conditions were studied. An alternative procedure in which the salen ligand was gelled and the resulting solid was treated with metal acetylacetonate (acac) complex was found to be less effective in terms of dioxygen binding capacity. Given that di(3-aminopropyl)amine was used in the preparation of the salen ligands (see Scheme 60) and the salen–metal complexes were found to be penta-coordinated, one point that would have deserved further study is the crystal structure of the actual monometallic bis-silylated salen complexes that are the active components of the solids. On the basis of the study of the optical spectrum and the

Scheme 60. Sol−Gel Synthesis of Hybrid Pentacoordinated Salen Metal−Silica Material (Based on Reference 363)
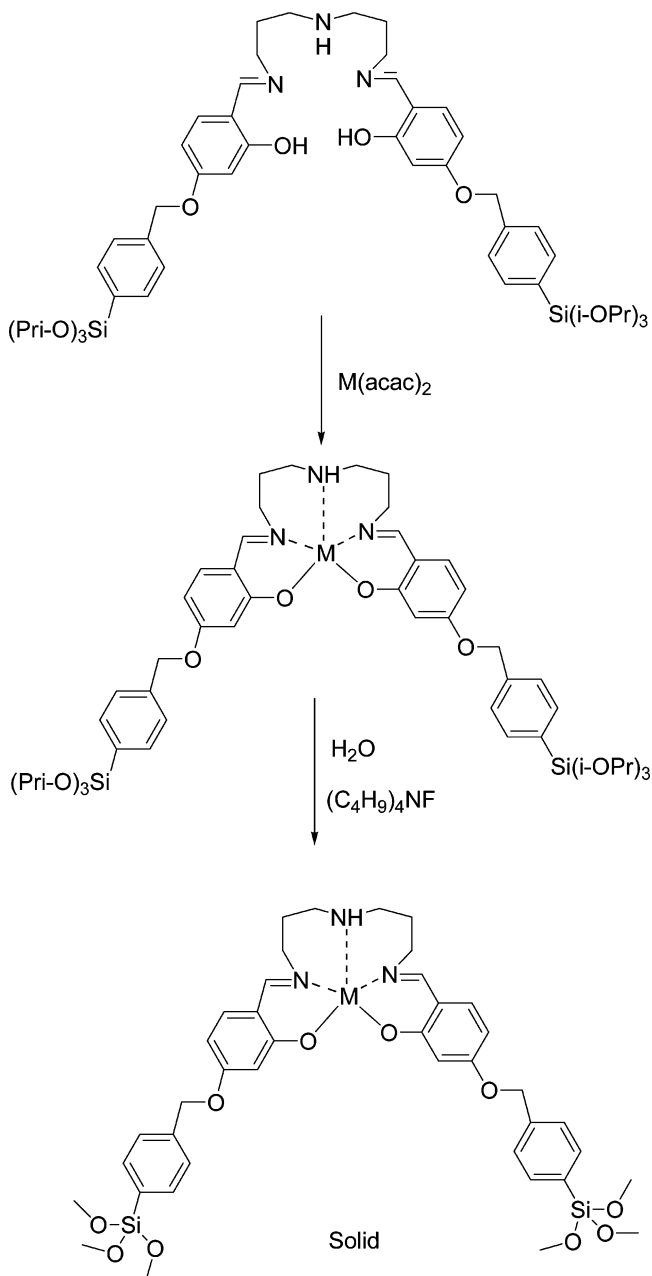
position of the d−d transitions, it was proposed that in the solids the complexes adopt a distorted trigonal bipyramid.

Despite the presence of Co(II) and Cu(II), solid-state ^{29}Si NMR spectra of the solids could be recorded and the observation of peaks at −76 and −70 ppm was attributed to T^3 and T^2 ≡Si-CH$_2$ atoms connected tri- or bipodally to the solid silica structure. The absence of peaks at −90 and −100 ppm, corresponding to Q^3 [**Si**(OSi≡)$_3$(OH)] and Q^4 [**Si**(OSi≡)$_4$] Si atoms, that is, those Si atoms not bonded to any carbon atom, indicates that the Si−CH$_2$ bonds have remained unaltered during the sol−gel process and that hydrolysis of the ≡Si−CH$_2$ has not occurred to a detectable extent.

Some of the solids exhibit a type IV isothermal N$_2$ gas adsorption with a remarkably narrow pore size distribution of ∼4 nm. When the ligand, instead of the actual metallic complex, was gelled, then the isothermal gas adsorption revealed a much broader pore size distribution centered at

10 nm. Dioxygen gas uptake of the cobalt materials was also studied and compared with the nitrogen adsorption, which was considered as a blank of the nonselective gas adsorption. Some of the results are shown in Table 29. These data show the advantage of treating the solids at 120 °C before O$_2$ adsorption.

In accordance with the selective binding of dioxygen to the cobalt atoms, it was found that the surface area of the solids was not the dominating factor, although the granulometry of the particles played a role, diffusion of oxygen being easier through fine powdered samples as compared to solid blocks. The stoichiometry of the Co:O$_2$ adsorption was 1:1, forming a Co(III)−superoxide adduct according to EPR measurements.[363] Dilution of the complex in the silica matrix by adding tetraisopropyl orthosilicate during the gelation gave solids with oxygen binding ability proportional to their cobalt content. In the best material, up to 41% of the total cobalt can intervene in the oxygen binding, this value comparing favorably with those of other cobalt complexes encapsulated inside zeolite Y, grafted on silica gel, or incorporated in organic polymers.[363] There was, however, some fatigue in the oxygen coordination, and ∼28% of the cobalt lose its ability to bind oxygen after three cycles. However, this fact needs further studies to be conveniently rationalized because it may indicate some irreversibility in the Co(II)/Co(III) adsorption/desorption or a partial destruction of the complex.

An analogous sol−gel strategy using salen−vanadyl complexes substituted with two trimethoxysilyl termini, but performed in the presence of cetyltrimethylammonium as structure-directing agent, has been reported by Gigante, Corma, and Garcia to develop periodic mesoporous organosilica (PMO) catalysts for the cyanosilylation of carbonyl compounds.[196,366,367] This strategy to prepare the (salen)−vanadyl∝PMO solid allowed the previous preparation and characterization of the molecular salen−vanadyl precursor. The synthesis of the trimethoxysilyl-substituted salen−vanadyl complex has as the key steps a palladium-catalyzed Suzuki coupling to form a *p*-styryl-substituted bis-salicylidene Schiff base and the radical addition of mercaptopropyl trimethoxysilane (Scheme 61). This route has also been used to obtain a chiral salen−vanadyl complex substituted with trimethoxysilyl groups that later can be used in the preparation of a chiral PMO (ChiMO).[366,367]

The synthesis of the PMO was performed under the typical MCM-41 conditions, but with the addition of some amount of ethanol as cosolvent to increase the solubility of the salen complex in the aqueous gel. After gelation and crystallization, the resulting vanadyl∝PMO solids exhibit a hexagonal pore structure of regular size (4.2 nm) that is maintained after removal of the structure-directing agent. The Ar and N$_2$ isothermal gas adsorption was of type IV typical for mesoporous solids, and the BET surface area was 900 m^2·g^{-1} with a wall thickness of 0.6 nm.

The fact that the salen−vanadyl complex has survived the experimental conditions needed for the synthesis of PMO was confirmed spectroscopically by the following facts: (i) the presence in the diffuse reflectance UV−vis spectroscopy of the characteristic complex visible absorption band at 400 nm; (ii) the presence in FT-IR spectroscopy of the imine and metallosalen vibration absoption bands at 1615 and 1535 cm^{-1}, respectively; and (iii) the presence in MAS ^{29}Si NMR of a T^3 peak at −90 ppm corresponding to Si atoms of −CH$_2$−**Si**(OSi≡)$_3$ overlapped with the Q^3 due to −**Si**(OH)(SiO≡)$_3$ of the PMO structure.

Table 29. Dioxygen and Nitrogen Adsorption Capacity of Hybrid (Salen)−Co−Silica Complexes (Reference 363)

sample preparation	cycle	V_{O_2} (cm^3·g^{-1})	V_{N_2} (cm^3·g^{-1})	% active Co
gelation at 30 °C of the (salen)Co[a]	1	11.0	0.4	41
	2	7.9		29
	3	8.0		29
ligand gelation and subsequent complexation with (acac)$_2$Co[a]	1	3.5	1.3	9
	2	3.0		7
gelation at 80 °C of the (salen)Co[b]	1	4.4	0.3	17
	4	1.6		5
gelation at 80 °C of the (salen)Co[a]	1	6.2	0.3	25
	3	6.8		27
co-gelation at 80 °C of (salen)Co and TEOS 1:9 mol ratio[a]	1	4.5	0.8	38
co-gelation at 80 °C of (salen)Co and TEOS 1:19 mol ratio[a]	1	2.3	0.4	23

[a] Materials treated at 120 °C under 10^{-3} Torr for 12 h before adsorbing the corresponding gas. [b] Material treated at 20 °C under 10^{-3} Torr for 12 h before adding the corresponding gas.

Scheme 61. Synthesis of a *p*-Styryl Salen−Vanadyl Complex That upon Reaction with 3-Mercaptopropyltriethoxysilane Can Be Used as a Precursor of a PMO (Based on Reference 366)
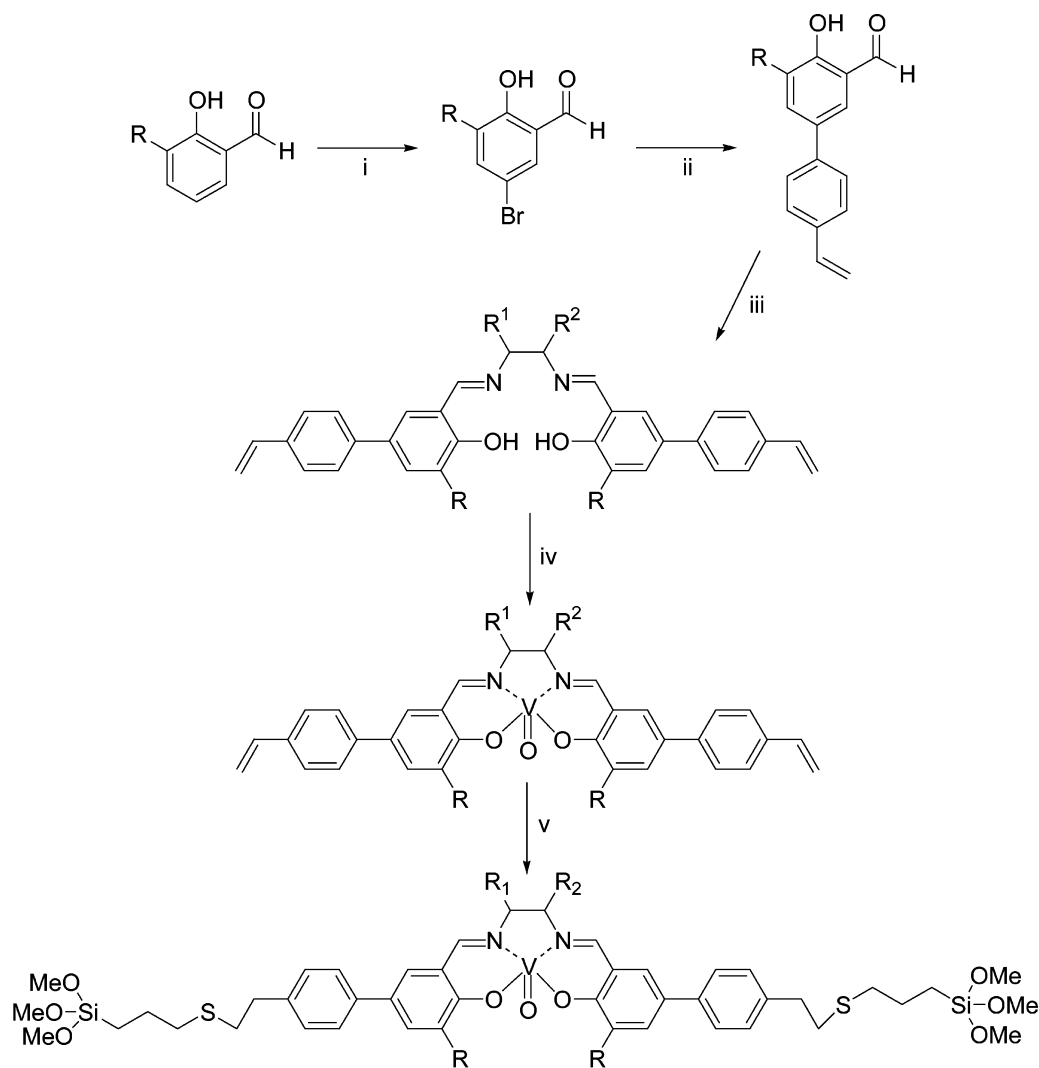
i) Br$_2$, CH$_2$Cl$_2$, 0 °C, 1h; ii) 4-vinylphenyboronic acid, [Pd(Ph)$_4$], 2 M Na$_2$CO$_3$, 70 °C, 3 h; iii) diamine, EtOH, 80 °C, 1h; iv) VOacac, MeOH, r.t., overnight; v) 3-mercaptopropyltrimethoxy silane, AIBN, CHCl$_3$ (degassed), 70 °C, 20 h.

The PMO solids containing salen−vanadyl complexes exhibit a high catalytic activity for the cyanosilylation of aromatic and aliphatic aldehydes (Table 30). The process was truly heterogeneous, and leaching experiments revealed that the reaction stops upon filtration of the catalyst. The solids were reused up to three times with a minor decrease in the final conversion.[366] The enantioselective version of

this PMO solid (ChiMO) using a chiral salen−vanadyl complex led only to a low ee when the reaction was performed at 0 °C.[366] These low ee values could not be increased upon silylation of the external surface to reduce the population of undesirable silanol groups. Interestingly, the chirality of the resulting solid could be assessed directly by measuring the optical activity of a suspension of the

Table 30. Results of the Aldehyde Cyanosilylation Using Excess of Trimethylsilylcyanide Catalyzed by Vanadyl–Salen PMO (Reference 366)

aldehyde (R)	run	conversion (%)
Ph	1	82
Ph	4	71
p-F$-C_6H_4$		86
p-MeO$-C_6H_4$		81
n-C$_6$H$_{11}$		79

ChiMO in 1,2-dichloroethane, a solvent with a refraction index similar to that of the solid.[366]

Given the novelty of this type of hybrid organic/inorganic mesoporous materials, it would be worthwhile to further develop this and other sol–gel strategies to expand the data about the activity, asymmetric induction ability, and de-activation of this family of materials. Compared to related silica-supported salen–metal catalysts, the main advantage of hybrid metallosalen solids is their large porosity and surface area.

8. Concluding Remarks and Future Prospects

Chiral salen complexes are among the most important catalysts for asymmetric synthesis, and this prevalence will be maintained in the future. It is also expected that new enantioselective processes using chiral salen complexes will be developed in solution in the years to come, with the consequent need to devise novel recoverable systems for them. Also, it can be expected that the preparation of heterometallic salens analogous to those recently reported using Lewis acids as bridge or with covalent linkers will serve to devise cascade processes in which several different chiral centers can be created in a single step. Whatever the new advances in solutions will be, reuse and recovery of the salen catalyst will continue to be an open issue.

With regard to reusability, an issue that must be definitely solved is the instability of certain chiral salen complexes, particularly in oxidation reactions. In the previous sections we have shown that although alkene epoxidation is the most important process catalyzed by salen complexes, the stability of the manganese complex is not complete; the intrinsic complex instability constitutes apparently the limit of reusability. The stability of the salen complex can be probably increased by selecting appropriate substituents and/or redesigning the salen ligand. Once the stability of the salen manganese complex is improved, the general methodologies described in this review can be applied to it. In contrast, it seems that other salen complexes, such as chromium and vanadyl, are indefinitely stable under mild reaction conditions.

Concerning the recovery methodology, it can be anticipated that the two alternatives, either homogeneous or heterogeneous, will continue to develop intensively in the future. In the case of dense CO_2, fluorous phase, and ionic liquids, fully satisfactory chiral salen catalysts have not yet been accomplished. In this case the negative influence of the reaction temperature required in these media should be recognized and probably accepted as a limitation impossible to overcome. The use of suitable porous membranes able to retain the chiral salen catalyst is a general and simple way

to recover the catalyst, but the problem is that this forces the process to operate batchwise.

Concerning supported chiral salen complexes, the use of polystyrene and silicas has been sufficiently exploited, and significant breakthroughs in this field are not expected. More efforts will be devoted to other supports such as soluble short single wall carbon nanotube derivatives, soluble polyethyleneglycols, etc. These soluble (but recoverable) scaffolds will be another link between homogeneous and heterogeneous recoverable catalytic systems.

With respect to the supporting methodology, comparative studies have to show the advantages and drawbacks of the covalent anchoring compared to the simple complex adsorption on the support by polar interactions or coordinative bonds. In the case of covalent anchoring, the emphasis should be placed in showing that the productivity of the system is sufficiently high to justify the extensive synthetic effort required for the preparation of the supported chiral salen catalyst.

The overall conclusion of the present review is that any catalytic process using chiral salen–metal complexes should take into account and deal with the recovery and reuse of the catalyst and that there is already a wide range of options going from homogeneous to heterogeneous for doing this. However, the influence on the ee values, particularly whether the ee values will decrease, cannot be anticipated or rationalized at the present stage.

9. List of Abbreviations

acac	acetylacetonate
AcOH	acetic acid
AIBN	azobis(isobutyronitrile)
An$^-$	anion
aq	aqueous
bp	boiling point
CC	cocatalyst
COD	cyclooctadiene
Conv	conversion
co-PT	copolymerization technique
DABCO	1,4-diazabicyclo[2.2.2]octane
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
deact	deactivated
DMAP	N,N-dimethylaminopyridine
DMF	dimethylformmide
DMSO	dimethyl sulfoxide
DVB	divinylbenzene
ee	enantiomeric excess
EGDMA	ethylene glycol dimethylacrylate
EPR	electronic paramagnetic resonance
Hetero	heterogeneous
HMS	hexagonal mesoporous silica
Homo	homogeneous
ICP-AES	inductively coupled plasma–atomic emission spectrometry
IR	infrared
K^{t}BuO	potassium $tert$-butoxide
LDH	layered double hydroxide
MCM-41	Mobil Corporate Material 41
MM	molecular mass
na	data not available
NMO	N-methylmorpholine-N-oxide
NMR	nuclear magnetic resonance
Nu	nucleophile
PAMAM	polyamidoamine
PDMS	poly(dimethylsiloxane)
PMO	periodic mesoporous organosilica
PS	polystyrene

PVPD	styrene−4-vinylpyridine−divinylbenzene polymer
refs	references
rt	room temperature
SBA-15	Santa Barbara Material 15
sc	supercritical
SIB	ship in a bottle
SPS	solid-phase synthesis
SWNT	single-walled nanotubes
TEOS	tetraethoxyorthosilicate
$(Tf)_2N$	bis(trifluoromethanosulfo)amidate
THF	tetrahydrofuran
UV−vis	ultraviolet or visible light
USY	ultrastable zeolite Y

10. Acknowledgments

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