42
Immobilization Techniques

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42.1
Introduction

The immobilization of homogeneous catalysts remains an intensively developing research area, despite some doubts about its universal value for industrial application. Many books and reviews have been devoted to this topic over the past 40 years [1–13]. Hydrogenation with homogeneous catalysts is an important synthetic tool because of its regio- and enantioselectivity and its tolerance of functional groups. Therefore, homogeneous hydrogenation catalysts are among the most frequently targeted systems for immobilization. The majority of efforts for the immobilization of homogeneous hydrogenation catalysts are directed towards asymmetric hydrogenation. This is understandable, as enantioselective hydrogenation utilizes expensive precious metals and chiral ligands. Immobilization offers the possibility of ready separation and re-use of these catalysts. In this way – especially when a relatively cheap substrate is hydrogenated – a significant saving can be made in catalyst costs, making enantioselective hydrogenation eventually competitive with other routes such as optical resolution, chiral pool, biological approach, and so forth. As discussed below, various methods and support materials are used for immobilization. In truly ideal cases, some additional benefits are obtained by the immobilization, such as synergetic effects with the support giving enhanced activity and/or selectivity for the supported catalyst. Immobilization can also increase the stability of the supported complex against dimerization or cluster formation, which otherwise can be reasons for deactivation. Naturally, immobilization requires additional synthetic routes and procedures for making the complexes and supports suitable for immobilization, and this can increase the catalyst costs significantly. For this reason, an immobilized catalyst generally should possess several times higher turnover number (TON) or higher activity than its homogeneous counterpart. Blaser and coworkers [14] have recommended minimal turnover frequencies (TOFs) of 500 and $10\,000\,h^{-1}$, or minimal TONs of 1000 and 50 000 for small- and large-scale production of fine chemicals, respectively. These conditions are

not easily met in practice because of eventual deactivation or degradation of the catalyst.

Catalyst loss during separation of the homogeneous catalyst from the product can be an important issue, especially when using precious metal complexes, not only for economical but also for toxicological (environmental) reasons. The former is more characteristic for large-scale production, while the latter is seen more for small-scale fine chemicals or pharmaceuticals. Immobilization offers a solution not only for easy catalyst recovery, but also for the problems of product contamination. However, the development of an active and stable immobilized analogue of a homogeneous catalyst, which does not leach the metal component, is quite a laborious task. Too often, the time frame given to develop a synthetic route is so tight that an industrial research team can barely deal with these challenges. It is perhaps due to the latter issue – together with the relatively few homogeneous applications – that has so far prevented the broad spread of supported homogeneous hydrogenation catalysts within the chemical industry.

42.2
Engineering and Experimental Aspects

Heterogeneously catalyzed hydrogenation is a three-phase gas–liquid–solid reaction. Hydrogen from the gas phase dissolves in the liquid phase and reacts with the substrate on the external and internal surfaces of the solid catalyst. Mass transfer can influence the observed reaction rate, depending on the rate of the surface reaction [15]. Three mass transfer resistances may be present in this system (Fig. 42.1):

- at the gas–liquid interface for hydrogen;
- at the liquid–solid interface;
- by diffusion in the pore system of the catalyst.

Mass transfer can disguise the intrinsic kinetics severely [15]. For example, suppose the intrinsic kinetics is given by a power rate law:

$$r = k_0 \exp(-E_a/RT)[S]^m[H_2]^n[\mathrm{cat}] \quad (M\,s^{-1})$$

The observed rate in the pore diffusion regime would then be (hydrogen diffusion limiting):

$$r_{obs} = k_0 \exp(-\tfrac{1}{2}E_a/RT)[S]^m[H_2]^{(n+1)/2}[\mathrm{cat}] \quad (M\,s^{-1})$$

Hydrogen transfer from the gas phase to the liquid phase becomes rate limiting with very fast hydrogenations (or with insufficient agitation). The observed reaction rate is then equal to the rate of gas–liquid mass transfer of hydrogen and becomes first order in hydrogen and independent of substrate concentration. The activation energy decreases to that of a diffusion process.
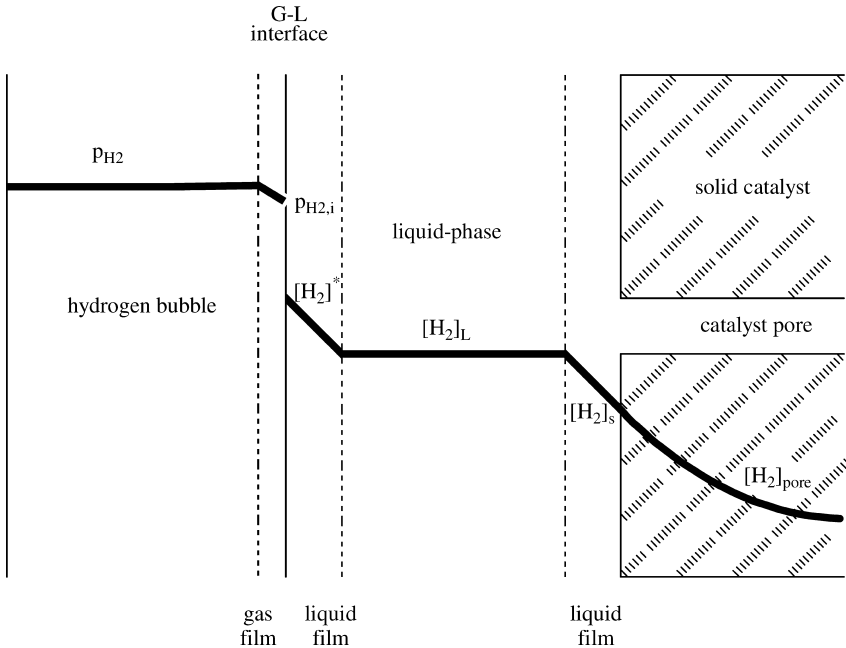
Fig. 42.1 Mass transfer resistances for hydrogen in heterogeneous catalytic hydrogenation.

$$r_{obs} = k_{GL}[H_2]^* = k_{GL}He\, p_{H2}[cat] \quad (M\,s^{-1})$$

In this formula, $[H_2]^*$ is the concentration of hydrogen in the liquid in equilibrium with the gas phase, related by the Henry coefficient.

It is clear from above that it is by no means easy to obtain intrinsic kinetics. However, comparison of different catalysts makes no sense when mass transfer effects disguise the intrinsic kinetics. Kinetic data are also hardly available from the TOF values, which are typically used for the characterization of the catalysts. These values are very convenient for a fast comparison of catalyst activities by measuring under the same reaction conditions (reaction temperature and time; catalyst, substrate and hydrogen concentration, etc.). However, different research groups seldom use the same reaction conditions, making comparison in activity difficult solely on the basis of TOF. Some notion of the intrinsic kinetics, either in the form of a power rate law or more sophisticated Langmuir-Hinshelwood type expressions, would help the chemical engineer greatly in scale-up and reactor design.

One could even think of taking advantage of pore diffusion limitation in enantioselective hydrogenation. The enantiomeric excess (ee) is in many homogeneously catalyzed cases dependent on the hydrogen concentration in solution, and increases with decreasing hydrogen pressure in some cases. The origin of this effect was explained by Landis and Halpern [16] in terms of the different

responses of the major and minor catalyst–substrate diastereomers to the hydrogen pressure. Blackmond and coworkers [17] showed later the importance of gas–liquid hydrogen transfer in this respect, and emphasized the role of the actual hydrogen concentration in solution, which was the decisive factor in determining the enantioselectivity. Anchoring of the catalyst in small pores would offer the opportunity to reduce the hydrogen concentration in the pore system below that of the bulk liquid phase and might help to increase enantioselectivity. Perhaps this mechanism is playing a role in the enantioselective hydrogenations using mesoporous silica supports. The difference with conventional silica supports may not stem from enhanced confinement in the mesoporous environment as was proposed [18], but from different diffusional regimes instead.

The reader should also be aware of some experimental pitfalls, which were not fully recognized in the early days of immobilization.

1. The leached metal can be catalytically active, either in the homogeneous phase or in the form of small metallic particles, suspended in the solution or deposited on the reactor wall or internals.
2. When no traces of metal are observed in the products of a batch experiment, one cannot exclude the possibility that metal went into solution under reaction conditions. Then, the dissolved metal could catalyze the reaction homogeneously with re-adsorption on cooling down at the end of the experiment.
3. The metal may be reduced to its zerovalent state and form small metallic particles on the support. These metal particles may take part in the reaction, especially in catalytic hydrogenation.

Therefore, it is advised to perform a "filtrate test" by taking a sample of the reaction solution under reaction conditions by hot filtering, and testing this solution for catalytic activity immediately, before any leached species can transform into an inactive one [19]. Furthermore, used catalysts should be checked on the presence of metallic particles. These are certainly not easily detected in small amounts and/or when they are of nanometer size. However, peculiar selectivity changes in time could give an indication of metal formation. Hydrogenation activity for aromatic rings is especially suspicious, because unlike most metals of Groups 8 to 10 of the Periodic Table, homogeneous catalysts are generally inactive for this reaction.

42.3
Immobilization Methods

Homogeneous catalysts can be immobilized on solid inorganic supports, such as silica, alumina and active carbon, or on solid polymers, often in the form of cross-linked polystyrene [1–5]. The inorganic supports have the advantages of a dimensionally stable pore system, generally better transport of reactants, higher mechanical strength and higher temperature stability. The polymeric supports

on the other hand are chemically more stable and offer more possibilities for fine-tuning of their structure during synthesis.

One can distinguish between physical and chemical methods of immobilization (Fig. 42.2). The former makes use of weak interactions between the metal
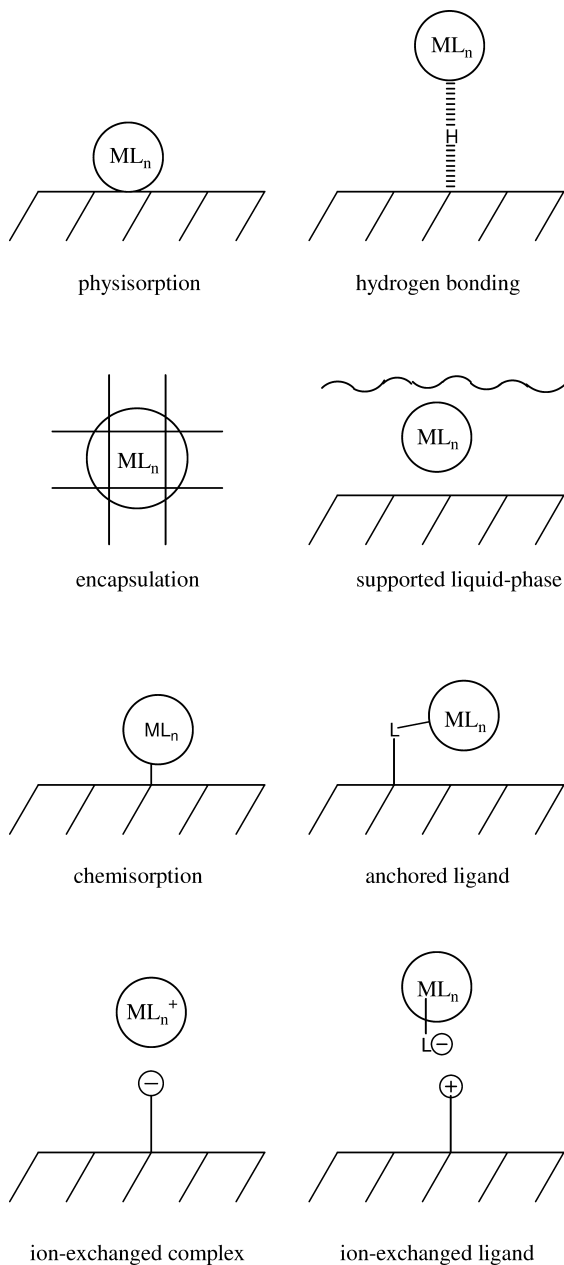

physisorption

hydrogen bonding

encapsulation

supported liquid-phase

chemisorption

anchored ligand

ion-exchanged complex

ion-exchanged ligand

Fig. 42.2 Immobilization methods.

complex and the support: van der Waals forces, dipole–dipole interaction, π-π-stacking, and hydrogen bonding. Examples are physical adsorption, encapsulation of metal complexes in zeolites or entanglement in a polymer matrix, supported liquid phase catalysts, and hydrogen-bonded catalysts. The latter leads to the formation of a covalent or ionic chemical bond between the complex and the support. Examples are chemisorption of the metal complex on the support (usually through a metal–surface bond), covalent bonding of the ligand to the support, ionic bonding of the complex to the support (where the charge may reside on the metal or on a functional group of the ligand).

Immobilization on a soluble support is a special case with the clear advantage of avoiding mass transfer resistances inherent to a heterogeneous catalyst. However, separation of the catalyst from the products being in the same phase is less straightforward. Separation can be done by precipitation of the catalyst by changing the solvent polarity, but a more favored method is membrane filtration. The latter method is possible when the homogeneous catalyst is attached to a polymeric chain or to a dendrimer; its size becomes then large enough for a feasible ultrafiltration. Catalysis in two immiscible liquid phases, with the homogeneous catalyst being dissolved (immobilized) in a separate liquid phase, is discussed in Chapters 38 and 40.
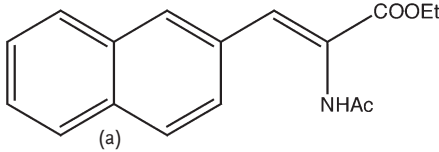
42.3.1
Physical Methods of Immobilization

The simplest method of immobilization is physical adsorption of the metal complex onto a porous inorganic support material. However, the catalytic complexes are easily re-dissolved in the reaction medium because of the relatively weak interaction of the metal complex with the support by only physical forces. Therefore, application of this type of physisorbed homogeneous catalysts is limited to gas-phase reactions or to reactions in liquid media, in which the complexes are insoluble [2, 20]. Although physisorption is only a weak interaction, the catalytic properties may change, as the relative energies of the species in the catalytic cycle may have different degrees of interaction with the surface. One cannot define a sharp borderline between physisorption and chemisorption of the metal complex, because supports will always contain surface groups, which can form a coordinative bond with the metal atom (see Section 42.3.5) or which can form hydrogen bonds to a part of the metal complex (Section 42.3.1.2).

Another physical method of immobilization is occlusion of the homogeneous catalyst into the voids of an inorganic or organic matrix, which contain pore systems small enough to prevent escaping of the metal complex [1]. Occluded metal complexes in the cages of zeolites are most appealing in this respect because of their well-defined structure. The entanglement of metal complexes in a cross-linked inorganic or organic polymer is also a powerful method.

Table 42.1 Enantioselective hydrogenations using (*R*)-RuCl$_2$(*p*-cymene)(BINAP) adsorbed on zeolite Beta [22].

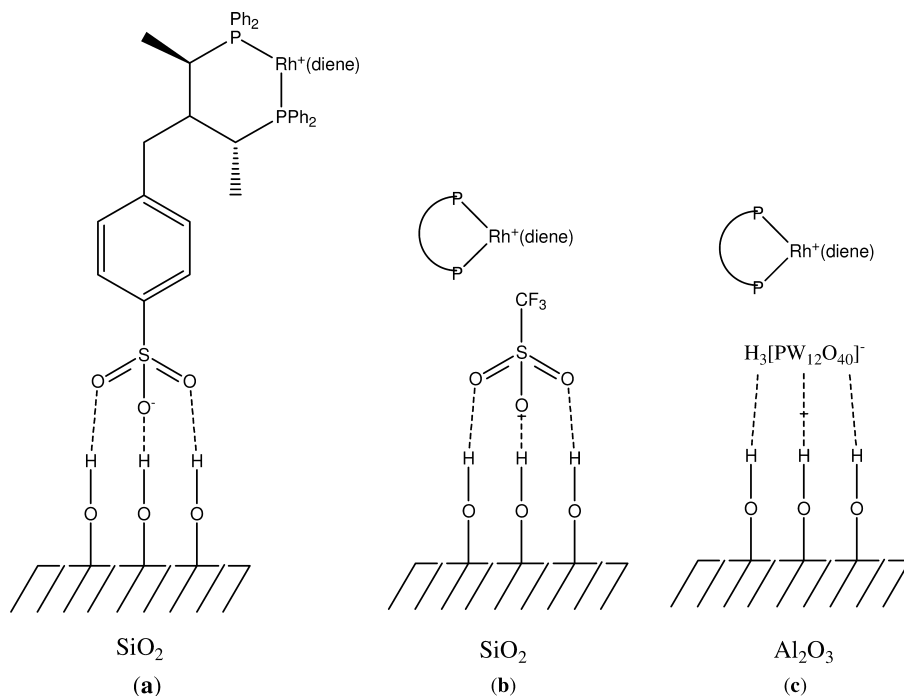| Substrate	Substrate: Ru ratio	Temp. [K]	P$_{H_2}$ [MPa]	Time [h]	Conversion [%]	TOF [h^{-1}]	ee [%]
(a)	100	293	0.69	3	100	60	82.3
	100	293	0.69	22	99	6	80

Reactions carried out in methanol or ethylene glycol solvent. (a) Homogeneous catalyst.

42.3.1.1 Physisorption of Metal Complexes

Liquid-phase application of rhodium complexes adsorbed on zeolite VPI-5 proved to be possible for hydrogenation of sodium 4-styrenesulfonate in aqueous solution. The catalytic complexes are hardly soluble in water, and these immobilized catalysts could be recycled with low loss of rhodium and reactivity [20]. Adsorption of chiral rhodium and ruthenium complexes in hexagonal mesoporous silica, with a pore size of 26 Å for a tight fit, yielded catalysts with low leaching by using water or aqueous methanol as solvent. However, only moderate enantioselectivities (11–62% ee) were obtained [21]. More success was achieved with the adsorption of BINAP complexes on zeolite BETA. The chloro-Ru–BINAP catalyst system was adsorbed strongly on the acid form of zeolite BETA. The adsorbed catalyst system provided significantly higher activities and enantioselectivities in the enantiomeric hydrogenation of prochiral dehydroamino acids than the homogeneous analogue (Table 42.1). [22]. Furthermore, the heterogenized catalyst showed no leaching. Clearly, the heterogeneous system proved to be superior to the homogeneous counterpart. The exact nature of binding of the chiral chloro-Ru–BINAP system is not known. However, among a variety of zeolites and silicas tested, only the acid form of zeolite BETA proved to be a suitable support material. This led to the conclusion that the chiral Ru complex is immobilized by another means than ion exchange and/or hydrogen bonding. Molecular modeling studies indicated a very good fitting of the π-electron-rich aryl groups of the chiral ligand in the surface pores of zeolite BETA. Thus, a "key–lock" effect might be responsible for the success of this particular system.

42.3.1.2 Weak Chemisorption: Supported Hydrogen-Bonded (SHB) Catalysts

Most immobilization methods require modification of the ligands for anchoring to the support by introducing functional groups such as vinyl, trialkoxysilyl, sulfonic acid, and amino groups. The consequence is often a more elaborate synthesis of the ligand, which adds to the costs of an immobilized catalyst. However, two interesting approaches were developed in recent years, when unmodi-

diene: norbornadiene, cyclooctadiene
P-P: bidentate (chiral) phosphorus ligand

Fig. 42.3 Hydrogen bonding in the adsorption of metal complexes [25, 32].

fied homogeneous catalysts were immobilized, using hydrogen-bonding interactions with the support.

The first example is a Rh complex of a tripodal sulfonated phosphine, where the sulfonic acid group forms hydrogen bonds to the silanol groups of the silica support (Fig. 42.3a). Because of hydrogen bonding, the catalyst resembles supported aqueous-phase catalysts (these are discussed in Section 42.3.4). The adsorption strength of the complex is highly dependent on the coverage with silanol groups, which depends on the temperature pretreatment of the silica. The adsorbed catalyst was tested in the hydrogenation of styrene in liquid phase showing no loss of activity and Rh-leaching during recycle runs [23].

Analogous to the attachment of sulfonate groups in the previous example, other highly polar anionic groups such as non-coordinating trifluoromethylsulfonate (triflate) anions will also bind to silica or zeolites. Thus, it is possible to attach the anions of a positively charged metal complex by hydrogen bonding to the silica. In this way, cationic Ru or Rh complexes containing an achiral or a chiral bisphosphine, respectively, were successfully immobilized to silicas for hydrogenation reactions [24–28]. The triflate anions are thought to be hydrogen-bonded to the surface silanol groups of silica, immobilizing the metal complex by electrostatic forces (Fig. 42.3b). In both cases, the heterogenized catalysts

provided higher selectivity than the homogeneous counterparts (Table 42.2). In an attempt to rationalize the high selectivity of the SHB catalyst, various model studies were carried out in different phases with the Ru system. The obtained results led to the conclusion that, in contrast to the homogeneous system in solution, no heterolytic splitting of H_2 at Ru occurs in the heterogeneous phase. Another possible explanation for the enhanced selectivity with the SHB systems is that of site isolation. Both systems showed no metal leaching upon several consecutive uses, and the activity of the chiral SHB Rh system was even higher than that of the homogeneous analogue.

Augustine [29–31] has discovered an anchoring method for cationic complexes by using heteropoly acids (HPA: $H_xAB_{12}O_{40}$, A = P, Si; B = Mo, W, V) modified oxidic supports. The heteropoly acid probably binds through hydrogen bonds to the support and acts as a linker to the metal complex. Thus, these systems are probably analogous to the SHB catalysts, which are described above. The nature of the binding of the complex to the HPA is not yet clear; it could be a weak coordinate bonding of the HPA oxygen atoms to the metal or an ionic bond between a cationic metal complex and a negatively charged HPA (Fig. 42.3 c). Researchers at Engelhard Corporation have actively investigated this new type of immobilized catalysts in cooperation with Chirotech Technology Ltd. [32–35], while Johnson Matthey – another catalyst producer – has obtained a license for this Cataxa technology from Seton Hall University [36].

The preparation of this type of catalyst is quite simple. HPAs such as phosphotungstic acid were adsorbed onto inorganic supports such as clays, alumina, and active carbon. Subsequently, the metal complex was added to form the immobilized catalyst. If necessary, the catalyst can be pre-reduced. These types of catalysts were developed mainly for enantioselective hydrogenations. For instance, a supported chiral catalyst that was based on a cationic Rh(DIPAMP) complex, phosphotungstic acid and alumina showed an ee-value of 93% with a TOF of about 100 h^{-1} in the hydrogenation of 2-acetamidoacrylic acid methyl ester (Fig. 42.4; Table 42.2).

As shown in Table 42.2, the immobilized catalysts showed higher activity than their homogeneous counterparts. Furthermore, the enantioselectivity of the supported Rh–dipamp system was also higher than that of the homogeneous analogue. Leaching was hardly observed, and the catalysts could be recycled many times, when appropriate reaction conditions and solvent polarity were chosen. Because of the negative charge of heteropoly acids, this immobilization method is also suited for supporting other cationic hydrogenation catalysts.
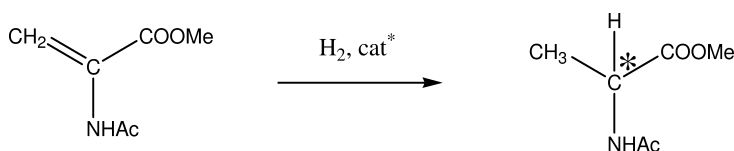

Fig. 42.4 Enantioselective hydrogenation of 2-acetamidoacrylic acid methyl ester.

Table 42.2 Enantioselective hydrogenation of methyl-2-acetamidoacrylate with [RhL*{COD}]$^+$ SHB catalyst at 298 K in ethanol.

Ligand	Anion	Support	Substrate: Rh ratio	P$_{H_2}$ [MPa]	Cycle number	TOF [h^{-1}]	ee [%]	Reference
dipamp	BF$_4$	None	40		homog.	15	76	31
	PTA	Al$_2$O$_3$		0.1	1	19	90	31
	PTA	Al$_2$O$_3$			3	100	95	31
Me-Duphos		None	40		homog.	198	96	31
	PTA	Al$_2$O$_3$		0.1	3	264	95	31
	OTf	None[a]		0.055	homog.	x>99%	87	27
	OTf	MCM-41[a]			4	x>99%	99	27

PTA = phosphotungstic acid; x = conversion.
a) Solvent = hexane.

The latter and above-described SHB catalysts represent some of the few examples when an immobilized system is superior to its homogeneous counterpart. Naturally, the use of these catalyst systems is limited to reactions, where the metal keeps its positive charges in all intermediates of the catalytic cycle (see further in Section 42.3.7).

The studies of Thomas and Raja [28] showed a remarkable effect of pore size on enantioselectivity (Table 42.3). The immobilized catalysts were more active than the homogeneous ones, but their enantioselectivity increased dramatically on supports which had smaller-diameter pores. This effect was ascribed to more steric confinement of the catalyst–substrate complex in the narrower pores. This confinement will lead to a larger influence of the chiral directing group on the orientation of the substrate. Although pore diffusion limitation can lead to lower hydrogen concentrations in narrow pores with a possible effect on enantioselectivity (see Section 42.2), this seems not to be the case here, because the immobilized catalyst with the smallest pores is the most active one.
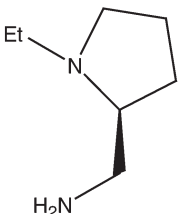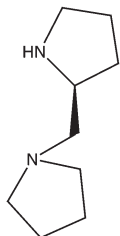
Some of these catalysts with non-chiral ligands showed interesting regioselectivity in the hydrogenation of the carbon–carbon double bond of unsaturated ketones [24] and of the aldehyde group of 4-nitro-benzaldehyde (the nitro group was not affected). Furthermore, a remarkable tolerance was observed to sulfur in the hydrogenation of sulfur-containing aldehydes [32, 33].

42.3.2
Encapsulated Homogeneous Catalysts

Zeolites are crystalline porous solids with pore dimensions at the molecular level. Some zeolite types, such as the faujasites (zeolite X and Y or their hexagonal isomer EMT), possess large supercages with an internal diameter of approximately 1.2 nm, connected by pores with a diameter of approximately 0.75 nm. A metal complex will be confined in the supercage, when its size exceeds 0.8 nm.

Table 42.3 Enantioselective hydrogenation of methyl benzoyl-formate using [Rh(COD)(L-L)][OTf] SHB catalysts supported on Davison silicas of different pore sizes [28].

Ligand	Pore diameter [nm]	Conversion [%]	TOF [h^{-1}]	ee [%]
	Homogeneous	62	46	0
	3.8	93.3	153	77
	6	93.9	154	61
	25	86.1	141	0
	Homogeneous	46.2	145	53
	3.8	95.8	166	94
	6	91.5	159	78
	25	86.9	151	59

Reaction conditions: Substrate = 0.5 g; solvent = 30 mL; H$_2$ pressure = 2 MPa; temperature = 313 K; reaction time = 2 h.

Although zeolite-encapsulated metal complexes were known for some time, the principle that such complexes could act as a new type of immobilized homogeneous catalysts was probably first demonstrated only in 1985 [37]. This achievement opened a new and fruitful area of research in immobilizing homogeneous catalysts. These catalysts are named appropriately ship-in-the-bottle (SIB) catalysts (see Fig. 42.5). General overviews of zeolite-encapsulated metal complexes were given [38, 39].

42.3.2.1 Synthesis of SIB Catalysts

Three methods can be followed for the synthesis of a SIB catalyst: (i) zeolite synthesis around the metal complex; (ii) template synthesis; and (iii) the flexible ligand method.

Zeolite synthesis around a metal complex was introduced by Balkus [40]. The metal complex is added to the zeolite synthesis mixture and is incorporated into the zeolite structure during the zeolite synthesis. Of course, this procedure is only applicable when the metal complex is soluble in the synthesis mixture and can withstand the hydrothermal synthesis conditions. Another requirement is that the zeolite structure-directing agent added must be removable by a milder
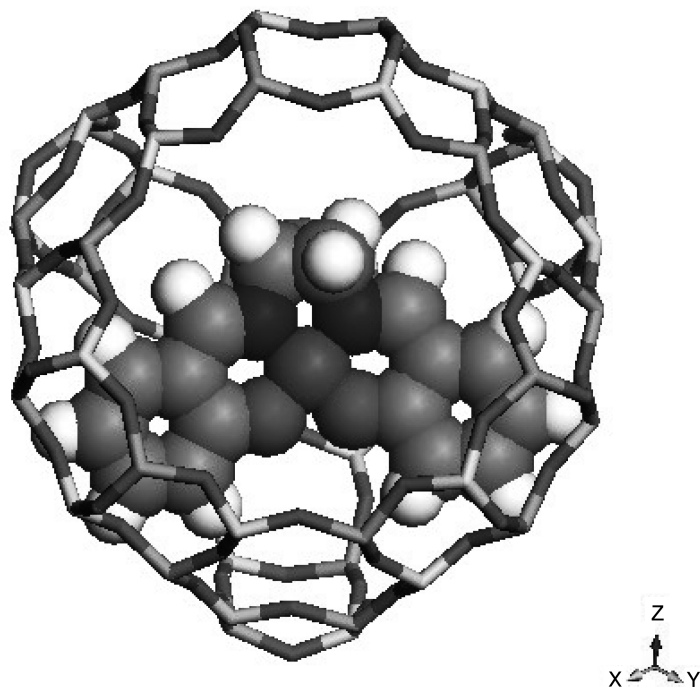
Fig. 42.5 Schematic view of Pd–salen complex in the supercage of faujasites.

procedure than calcination, which would also destroy the occluded metal complexes.

Metal ions are introduced first in the zeolite by ion exchange in the other two methods. These metal ions act as a template for small, coordinating molecules in the template method. Finally, these small ligands react with each other to form a large multidentate ligand around the metal atom. In this way, the metal complex becomes too large for escaping from the zeolite cage. Fine examples are the formation of metal phthalocyanine complexes from 1,2-dicyanobenzene and the formation of salen complexes from salicylaldehyde and diamines.

Subsequent to an exchange with metal ions, the zeolite is treated with a solution or a melt of the ligand in the flexible ligand method. It is required that the ligand can diffuse through the zeolite pores in a stretched conformation. When the ligand encounters a metal ion, it will form a metal complex by folding itself around the metal ion. The final complex is then confined to the zeolite cage. An example is the synthesis of salen-type complexes in faujasites. This method works quite well with nitrogen ligands, when they are not too bulky. In all three methods, any excess ligand or metal complexes adsorbed on the exterior surface of the zeolite must be removed by thorough extraction procedures to obtain the final catalyst.

Phosphine ligands cause problems in SIB catalyst synthesis because of their size and of their chemical reactivity. The commonly used bidentate phosphine

ligands are too bulky to pass the window of the faujasite supercage. It is difficult to obtain well-defined products, even with small monodentate phosphines such as PMe$_3$, PMe$_2$Ph or PMePh$_2$ as shown with [Rh(CO)$_2$Cl]$_2$ inside dealuminated zeolite Y [41].

The diffusion of reactants inside zeolite pores is slow (Knudsen diffusion). Access to the catalytic species would become even more difficult, when the zeolite has a too-high loading with metal complexes. Too many occupied supercages would block the zeolite pore system and make most of the metal complexes inaccessible for reactants. An unrestricted diffusion through the zeolite crystal is only guaranteed when an occupied supercage is surrounded by empty ones; a rule of thumb is to aim at a loading of one metal complex per every 10 supercages. In that case, real SIB catalytic systems are obtained, as was shown by the work of Jacobs and many others.

42.3.2.2 Application of SIB Catalysts

The zeolite types that can be used as a host for SIB catalysts are rather limited. They must possess large cages that are accessible through at least 10-ring windows for the ligands or the precursors to pass. Obvious choices are the faujasite zeolites X and Y and their hexagonal isomer, zeolite EMT (diameter supercage approximately 1.2 nm and window 0.74×0.65 nm), or the more recently discovered cloverite [42] that possesses far larger cages (3 nm diameter). A new approach by Hölderich and coworkers [43] enlarges the void space in the zeolite structure by dealumination and steaming. This method allows the introduction of larger ligands than the original faujasite supercage.

The metal complexes in an SIB catalyst are confined to separate supercages. Consequently, the formation of inactive dimers is no longer possible. Shape-selectivity is another feature of SIB catalysts that follows from the restricted space inside the zeolite pore system. This can be simply due to discrimination in size of the reactant molecules (a large reactant molecule is excluded from the zeolite) or to a constrained orientation of the reactant at the catalytic site (transition state selectivity).

The few examples of SIB hydrogenation catalysts consist mainly of encapsulated Group 8 to 10 metal complexes of the salen ligand (Fig. 42.5). Pd(salen) complex encaged in zeolite Y is a more selective catalyst than PdY or Pd/carbon in the hydrogenation of octene-1 and cyclooctadiene at 333 K under 1.5 MPa of H$_2$ pressure [44]. Salen-type complexes with other metals such as Ru, Ni, and Rh were also effective catalysts for alkene hydrogenation [45–47]. These SIB catalysts were more active than the homogeneous catalysts due to the prevention of dimer formation, and showed shape-selective behavior in some studies. More bulky alkenes were hydrogenated less rapidly. There are very few examples of asymmetric hydrogenations with SIB catalysts; enantioselectivities are comparable with or lower than those of the homogeneous catalysts [46, 48].

42.3.3
Catalysts Entangled in a Polymer

Free motion of organic molecules in a polymer gel becomes impossible when their size is too large with respect to the pore dimensions of the polymer network. Thus, a large homogeneous metal complex catalyst can be entrapped in a polymer network, which is the amorphous equivalent of encaging the catalytic complex in the crystalline structure of a zeolite. Flexibility in the polymer network can be advantageous in order to keep the conformation of the metal complex similar to that in the liquid phase. On the other hand, too much flexibility leads to swelling in certain solvents with leaching of the complex as a consequence.

The same entrapment can be obtained in a silica matrix by sol–gel polymerization of tetramethoxysilane (for more detail, see Section 42.3.6.2) in the presence of dissolved metal complex [49]. A number of phosphine complexes of Ru, Rh, and Ir were immobilized by this method and tested for the isomerization of allylbenzene. It turned out that a good solubility of the complexes in the aqueous sol–gel mixture is important to achieve a high loading. The water-soluble TPPTS complexes are therefore more suitable precursors than the lipophilic triphenylphosphine complexes. Avnir and Blum [50,51] used the same method to obtain leach-proof, recyclable catalysts for hydrodehalogenation and alkene hydrogenation, respectively. Enantioselectivities of these catalysts were comparable to those of the corresponding homogeneous catalysts in the hydrogenation of itaconic acid (Table 42.4). Metal leaching was below the detection limit of 1 ppm. Some deactivation occurred, probably because of pore blocking by the product. The catalyst could be fully regenerated by washing with dichloromethane.

Table 42.4 Enantioselective hydrogenation of itaconic acid using sol–gel-entrapped Rh complexes [51].

Catalyst	Cycle number	Yield [%]	ee [%]
Ru(BINAP)Cl$_2$(p-cymene)/SiO$_2$ [a]	1	100	52
	2	98	50
	3	95	46
	4	90	41
Rh(diop)(COD)Cl/SiO$_2$ [b]	1	100	34
	2	55	32
	3	39	25
	4 [c]	100	30
Rh(diop)(COD)Cl [b] homogeneous	n.a.	100	41

a) Substrate : Ru ratio = 30; solvent = water; reaction time = 24 h; temperature = 353 K; H$_2$ pressure = 1.01 MPa.
b) Substrate : Ru ratio = 50; solvent = ethanol; reaction time = 16 h; temperature = 348 K; H$_2$ pressure = 1.32 MPa.
c) After washing with CH$_2$Cl$_2$.

Table 42.5 Enantioselective hydrogenation of methyl-2-aceta-midoacrylate with [Rh(MeDuphos)(COD)][CF$_3$SO$_3$] entangled in a polymer network.

Matrix	Solvent	T [K]	P$_{H_2}$ [MPa]	Time [h]	TOF [h^{-1}]	ee [%]	Reference
Homogeneous	MeOH	333	4	2	482	99	55a
PDMS	MeOH	333	4	24	28	90	55a
PDMS	Water	298	0.2	6	12.6	96.9	55b
PVA-1	Water	298	0.2	6	12.9	96.1	55b
PVA-2	Water	298	0.2	6	12.4	95.7	55b

Patchornik and coworkers [52] have introduced [Rh(norbornadiene)(dppe)][PF$_6$] inside the polymer matrix of a cross-linked polystyrene gel using tetrahydrofuran (THF) as a solvent. This medium resulted in a high degree of swelling of the polymer. Shrinkage of the gel occurred after evaporation of THF, and the complex remained encapsulated in the polymer matrix. This catalyst hydrogenated hexene-1 in methanol as solvent, which caused no swelling of the polymer. The catalyst was stable upon repeated use and no indication of homogeneous catalytic activity was found. These findings show that the metal complex is confined in the polymer matrix as long as no swelling of the polymer occurs.

A metal complex can also be incorporated in a polymer matrix by creating the polymer network *in situ*. A fine example of this is the cross-linking of polydimethylsiloxane (PDMS) pre-polymer in the presence of the dissolved metal complex and a cross-linker. The metal complex becomes entangled in the polymer network, giving no leaching into solution unless swelling of the polymer occurs. FePc, Ru–BINAP and Jacobsen's catalyst were each immobilized in this way [53]. Chiral hydrogenation with Ru–BINAP/PDMS showed catalytic activity and enantioselectivity approaching those of the homogeneous catalyst. The PDMS is more than a carrier for the complex. It also plays an active role in the transport of reactants to the catalytic site. This field was reviewed in 2000 [54], though some more recent investigations have described the encapsulation of [Rh(MeDuPHOS)(COD)][CF$_3$SO$_3$] in PDMS and cross-linked polyvinylalcohol (PVA) for the asymmetric hydrogenation of methyl-2-acetamidoacrylate [55]. Excellent enantioselectivities were obtained, but the catalytic activity was significantly lower than that of the homogeneous catalyst (Table 42.5).

42.3.4
Catalyst Dissolved in a Supported Liquid-Phase

As mentioned in Section 42.2, mass transfer can be rate-limiting in the case of very active homogeneous systems. Since mass transfer from gas to liquid or from liquid to liquid is dependent on the contacting area, this problem can be circumvented by adsorbing the catalyst solution onto an inert porous support

(e.g., silica, alumina, kieselguhr) which has a very large (inert) surface area. The supported liquid-phase catalyst (SLPC) system obtained is also advantageous for eliminating corrosion problems, as most of the supported solution is not in direct contact with the reactor material. Since the liquid phase containing the catalyst must remain supported throughout the reaction, the term SLPC also refers to stationary liquid-phase catalysis. It follows that by the original concept, SLP catalysts are most suited for gas-phase processes, as soluble liquid reactants or products would cause dilution or leaching of the catalyst. However, gas-phase hydrogenation is not sensible due to the readily available choice of reliable heterogeneous catalysts and to the low volatility of the most interesting substrates. Thus, understandably, most of the studies on conventional SLP system were performed for other reactions, such as hydration of ethylene or hydroformylation of small olefins by using concentrated acids or Rh-compounds in molten PPh$_3$, respectively, as supported catalysts.

42.3.4.1 **Supported Aqueous-Phase Catalysis**

Parallel with the development of two-(liquid)-phase catalysis, the concept of SLPC has been extended to liquid-phase processes. For this purpose, also two immiscible solutions are required. One of these contains the catalyst and is supported on an appropriate porous carrier, while the other serves as a mobile phase for the transport of substrate and products. Arhancet et al. have demonstrated the concept first by adsorbing an aqueous solution of the highly water-soluble Rh-complex of trisulfonated triphenylphosphine, TPPTS, on a hydrophilic support (controlled-pore silicate glass) [56]. The supported aqueous-phase catalyst (SAPC) obtained showed no Rh-leaching in continuous hydroformylation of olefins in apolar solvents [19a]. By the most likely model (except when the pores are completely flooded with the aqueous solution or not too-water-soluble substrates are used), the highly hydrophilic substituents on the ligands of SAPC are strongly associated with the adsorbed water and surface hydroxyl groups. Meanwhile, the metal center (M), which is in a relatively hydrophobic local environment, is pushed into the non-aqueous phase (see Fig. 42.6) [12, 57]. In this manner, SAPC resembles analogous silica-anchored, SHB or ion-exchanged catalyst.

By the development of two-phase catalysis a large number of water-soluble ligands including chiral ligands have been synthesized, which could make an excellent basis for SAPC. Unfortunately, this opportunity is not yet fully exploited for hydrogenation, perhaps partly due to some problems in the continuous use or recycling of these catalysts. For example, Ru-TPPTS catalysts showed excellent results in the first use for the selective hydrogenation of some α,β-unsaturated aldehydes [58]. Hydrogenation of 3-methyl-2-butenal to 3-methyl-butenol was carried out at 323 K under 100 bar H$_2$ pressure with 88.5% selectivity and 100% conversion (TON $\sim$490). However, upon recycling the activity of the catalyst decreased dramatically without losses of metal or selectivity. The catalysts showed the same characteristic for other aldehydes. Based on infra-red measurements and by the increased carbon content on the silica after use, it was reasoned that adsorption
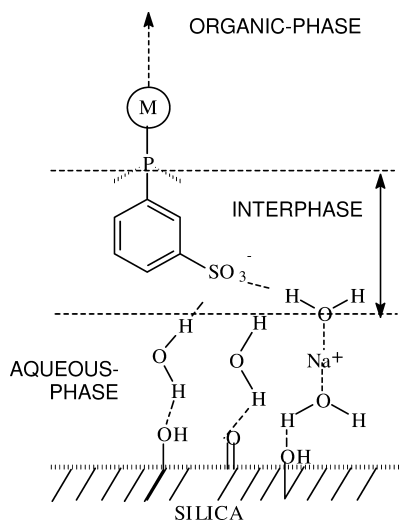
Fig. 42.6 Working model for SAP Rh-TPPTS catalyst.

of the substrate and products was the primary cause of deactivation. Several water-soluble ligands such as BDPP and Chiraphos derivatives were also tested in SAP for the hydrogenation of dehydroamino acids [57]. These catalysts also showed deactivation upon reuse, without detectable metal leaching. Because the enantioselectivity of these catalysts was lower than that of the homogeneous analogues (organic or two-phase), these catalysts were not investigated further.

42.3.4.2 Hybrid SLP Systems

Clearly, a two-phase system can also be created between two organic phases. Many water-soluble (polar) ligands are also soluble in a polar organic solvent directly or after further functionalization. The obtained polar phase with the catalysts can be supported on the silica, analogous to SLPC above. When the reaction product is (partly) soluble in a second immiscible apolar organic solvent (and the catalyst is not), an anhydrous analogue of SAPC is created. The elimination of water content can be advantageous for the selectivity, as proven by Davis and Wan by using chiral Ru-sulfonated BINAP systems for enantioselective hydrogenation of double bonds using glycols as solvents for the supported phase [59]. The use of this hybrid catalyst is also advantageous for the minimization of supported-liquid loss, which is a typical problem of SAP or SLP catalysts. Another successful hybrid SLPC system was reported by Horváth using $PtCl_2(CH_3CN)_2$ dissolved in $BF_3 \cdot H_2O$ as stationary phase [60]. The solution was supported on silica-glass and used in a trickle-bed reactor for the continuous hydrogenation of aromatic hydrocarbons at room temperature under 27–55 bar H_2 pressure. It was shown that no metal leaching took place upon a one-day test, but the catalyst showed a slight deactivation after 48 h, possibly due to loss of
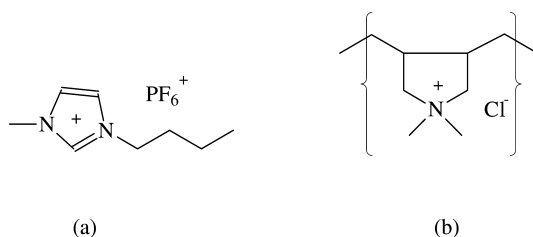
Fig. 42.7 Ionic liquid and its support used for making SILP catalyst [63].

the $BF_3 \cdot H_2O$ (acid) component. Some metallic particles were also found, indicating that heterogeneous contribution could not be excluded.

Until now, SLPC catalysts have remained difficult to control in the plant due to loss of supported liquids, adsorption of substrates/products, or changes in the pore structure [61]. Some recent developments to overcome these problems have included chemical bonding of the stationary phase by the analogy of gas chromatography (GC) practice. For example, polyglycols can be bound to the silica after appropriate functionalization [62]. Another interesting approach has been developed by Vankelecom and coworkers, by supporting transition-metal complexes in ionic liquid solvents on poly(diallyldimethylammonium) chloride (Fig. 42.7) [63]. The supported ionic-liquid phase (SILP) Wilkinson catalyst obtained showed similar performance to its homogeneous counterpart in the hydrogenation of alkenes. The SILP variant of Ru-BINAP catalyst was somewhat slower (TOF 29 h^{-1}, at 333 K, under 40 bar H_2 pressure) in the hydrogenation of methylacetoacetate to the monoalcohol derivative than its homogeneous variant giving yet similarly high (97% ee) enantioselectivity. However, none of these SILP catalysts contained traces of metals in the mobile phases (toluene, ether, methanol, isopropanol).

42.3.5
Covalently Bound Metal Centers

Here, only chemisorbed metal complexes with a direct bond between the metal and the surface will be discussed. Immobilized complexes, where the organic ligand forms a covalent bond with the support, are treated separately in Section 42.3.6. Reactions of organometallic compounds with the surface of carriers have evolved into a new branch of chemistry, frequently termed Surface Organometallic Chemistry. The reaction of organometallic species with surface hydroxyls produces isolated alkyl- or hydrido-metal species that are grafted to the surface and show very interesting catalytic properties. Usually, the proton reacts with the organic ligand or an anionic ligand under elimination of a hydrocarbon or HX. For example, neopentyl (Np) complexes of Ti, Zr, Hf and Ta were immobilized and the catalytic properties of these new materials were explored [64–66]. The surface bound tris(isopropyloxy) species of Zr, Hf and Nd (Table 42.6) are among the best heterogeneous catalysts for the Meerwein-Ponndorf-Verley hydrogen transfer reduction of ketones (Fig. 42.8) [67, 68].

Table 42.6 Transfer hydrogenation using grafted metal alkoxide catalysts.

Substrate	Catalyst	Support	S:M	T [K]	Time [h]	Conversion [%]	*trans/cis*	Reference
4-*t*-Butyl-cyclo-hexanone	Al(O*i*Pr)$_3$	–	20	298	5	<1	7	68
	Nd(O*t*Bu)$_3$	–	7	298	5	95	2.7	68
	=Nd(O*i*Pr)	MCM-41	52	298	5	90	3.3	68
	=Nd(O*t*Bu)	MCM-41	59	298	5	96	3.3	68
Cyclohexanone	-Zr(O*i*Pr)$_3$	Silica	77	353	23	73		67
	-Hf(O*i*Pr)$_3$	Silica	77	353	23	50		67

S:M = substrate:metal ratio.
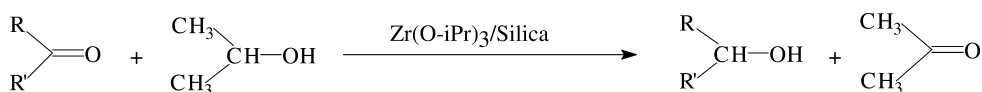
Fig. 42.8 Meerwein-Ponndorf-Verley reaction.

42.3.6
Covalent Attachment of Ligands

Anchoring of one or more ligands of a homogeneous catalyst to the support is preferred over chemisorption of the metal, because the coordination shell around the metal is kept as close as possible to the homogeneous case. In fact, the distance between the complex and the surface can be controlled by choosing an appropriate spacer, which links the ligand to the support. Covalent anchoring of the ligand is by far the most intensively investigated method, despite the laborious synthetic efforts involved. Some general remarks about this method are:

1. When using monodentate ligands, it is better to anchor the complex instead of the ligand to preserve the conformation of the catalyst.
2. The metal is usually stronger bound by anchored bi- or multidentate ligands than by monodentate ones.
3. Higher loading should lead to more active catalysts. However, complexes on neighboring sites frequently form inactive dimers. Site isolation is therefore desirable, which can be performed by several methods: (i) decreasing the density of hydroxyl groups on the support; (ii) dilution of the reactive ligand with another reagent for hydroxyl groups; or (iii) incorporation of the functionalized ligand during synthesis of the support.
4. Degradation of the ligand or the linker to the support must be avoided, as this results in metal leaching and catalyst deactivation. For example, phosphorus ligands are sensitive to oxidizing impurities in the feed (peroxides).
5. Recovery of the metal from a spent catalyst is possible, but the recovery of the ligand is not.

42.3.6.1 **Grafting to Oxide Supports**

Functionalized trialkoxysilanes are most widely used for grafting of ligands to inorganic supports. They have been used for a long time in other areas such as the preparation of stationary phases for chromatography and the improvement of adhesion between polymers and metal surfaces [69–72]. Trialkoxysilanes react with the surface hydroxyl groups to form from one to three Si–O bridges to the surface. Silica is the preferred oxide because of its high temperature stability and chemical resistance except under alkaline conditions. Today, ordered mesoporous silicas of the MCM-41 type are quite popular, because they have tunable uniform cylindrical pores in the range of 2 to 10 nm.

The surface density of hydroxyl groups depends on the thermal pretreatment of the silica [73, 74]. Drying at 473 K results in a high density (ca. 4–5 OH nm^{-2}), while a pretreatment temperature of 973 K is recommended to obtain isolated silanol groups (1.5 OH nm^{-2}) [75].

Solid-state NMR studies have provided important information on the grafting process and the mobility of anchored metal complexes; in this respect, reference is made to investigations by the groups of Fyfe [76], Blümel [77], Lindner [78], and others [79].

Some examples will illustrate the versatility of the covalent anchoring of catalytic complexes to silica. At Solvias/Ciba-Geigy [80–84], Pugin and Blaser and coworkers grafted many chiral ligands to silica through amide and carbamate bonds (Fig. 42.9). Commercially available 3-amino and 3-isocyanatopropyltrialkoxysilanes proved very useful for anchoring a range of carboxylic acid, sulfonic acid, and amino- and hydroxy-substituted ligands. The immobilized catalysts retained high activity and enantioselectivity in the asymmetric hydrogenation of dehydroamino acid derivatives without leaching of metal.

The immobilized catalysts attained similar enantioselectivities as the homogeneous catalysts, but the latter were still more active (Table 42.7). An astonishing high turnover frequency was obtained with the immobilized xyliphos catalyst (Fig. 42.9c) on silica for the hydrogenation of the so-called MEA-imine, a precursor of the herbicide *S*-metolachlor [83]. The polystyrene-supported variant was significantly slower, most likely due to slower mass transport. Variation in ligand loading had only a small effect on catalytic activity of cationic metal complexes, whereas activity was decreased substantially on increased loading of neutral complexes. This effect was ascribed to the formation of inactive dimers in the latter case, while electrostatic repulsion effectively inhibited dimer formation from cationic complexes [81, 82].

The cyclopentadienyl group is another interesting ligand for immobilization. Its titanium complexes can be transformed by reduction with butyl lithium into highly active alkene hydrogenation catalysts having a TOF of about 7000 h^{-1} at 60 °C [85]. Similar metallocene catalysts have also been extensively studied on polymer supports, as shown in the following section.

Alcohols react with surface hydroxyl group to form C–O–Si bonds. Because this type of bond is not very stable, trialkoxysilanes are preferred for anchoring. Exceptions to this rule are polyhydric alcohols, such as tris(hydroxymethyl)phosphine [86], which forms multiple bonds with the surface.
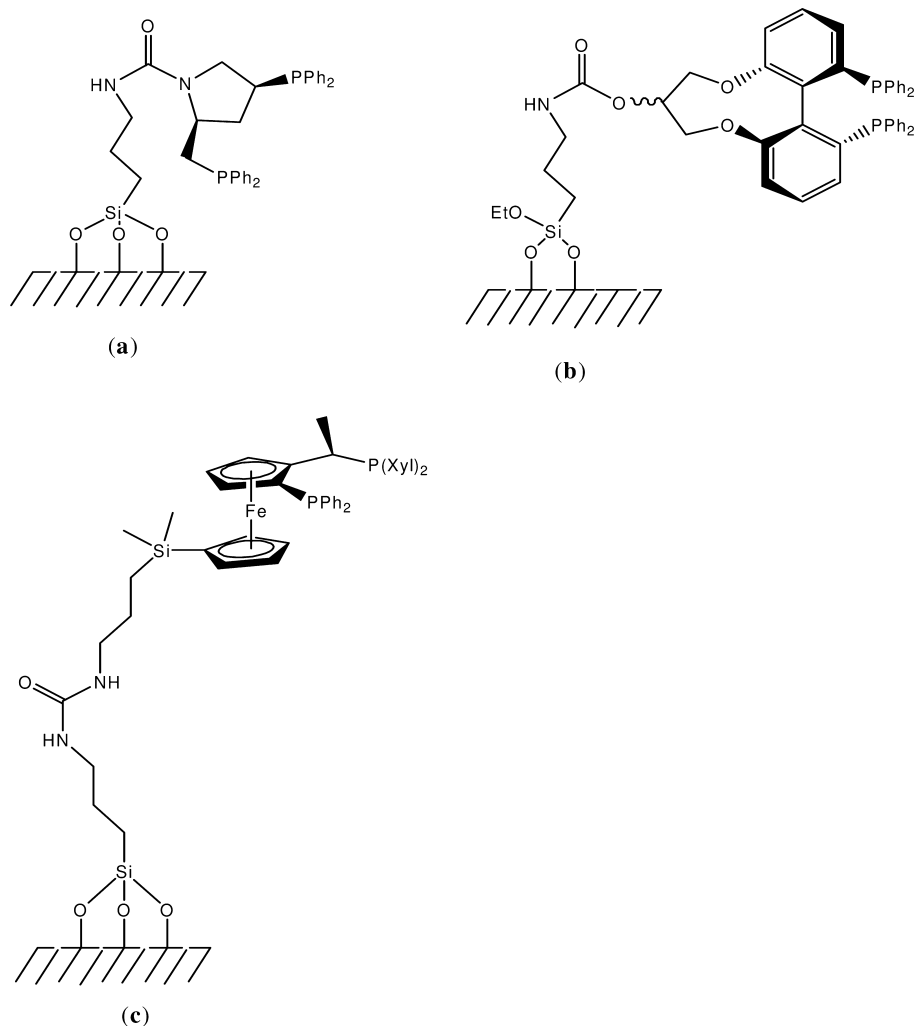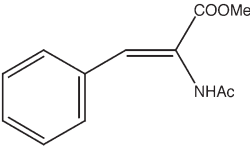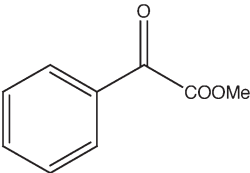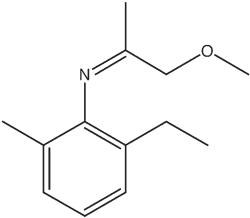
(**a**)

(**b**)

(**c**)

Fig. 42.9 Examples of covalently bound ligands on silica.

42.3.6.2 Sol–Gel Method

An alternative approach to using a preformed support material is the sol–gel method, which utilizes trialkoxysilyl-modified ligands or metal complexes in co-condensation with tetraethoxysilane (tetraethoxy orthosilicate, TEOS) under hydrolytic conditions. Multinuclear solid-state NMR studies showed that a more homogeneous dispersion was obtained in the final silica structure than by using preformed supports [87]. Furthermore, the ligand is bound more strongly through more Si–O–Si bonds and a higher loading can be achieved. It is also claimed that less metal leaching occurs with these sol–gel catalysts than is ob-

Table 42.7 Examples of enantioselective hydrogenations with silica-grafted catalysts.

| Substrate	Ligand	Metal precursor	Substrate: Rh ratio	T [K]	P_{H_2} [MPa]	TOF [h^{-1}]	ee [%]	Reference
	bppm (Fig. 42.9a)	[Rh(COD)$_2$] [BF$_4$]	200 200	298 298	0.1 0.1	1080 780	94.8 93.5	82
	MeO-bi-phep (Fig. 42.9b)	[Rh(COD)$_2$] [BF$_4$]		313 313	8 8	32 21	90 82	84
	Xyliphos (Fig. 42.9c)	[Ir(COD)Cl]$_2$	120 000 120 000	298–303 298–303	8 8	55 400 12 000	80 78	83

tainable by attachments to a silica surface. On the other hand, part of the active material may not be accessible to reactants, as was shown for a sol–gel-immobilized cyclopentadienyl titanium hydrogenation catalyst [88]. The activity of the immobilized catalyst depends on the purity of the TEOS used; more active catalysts are obtained using commercial TEOS than with freshly distilled TEOS. The commercial TEOS contained more condensed silicates by ageing and led to a product with six times more titanium species in the surface layer. Fine-tuning of the pore system of the silica structure can also be carried out by using organic cross-linkers, such as 1,4-bis(triethoxysilyl)benzene. The sol–gel method was used by Degussa to manufacture commercially available immobilized homogeneous catalysts, known under their trade name Deloxan (Table 42.8) [89].

42.3.6.3 Anchoring with Organic Phosphonates

Organic phosphonates represent another class of anchoring agents, which react with zirconium hydroxide to form pillared structures. These are also referred to as molecularly engineered layered structures (MELS). Layered compounds of organic phosphonates of zirconium with the formula of Zr(RPO$_3$)$_2$ have been rec-

Table 42.8 Deloxan hydrogenation catalysts.

Catalyst code	Immobilized functionality	Particle size [mm]	BET [m^2 g^{-1}]
HK I/Rh	RhCl [PhP[(CH$_2$)$_3$-SiO$_{3/2}$]$_2$]$_3$	0.4–1.8 0.1–0.4	550–750
AP II/PM	PdCl$_2$ [N[(CH$_2$)$_3$-SiO$_{3/2}$]$_3$]$_2$	0.3–2.0 0.02–0.2	400–800
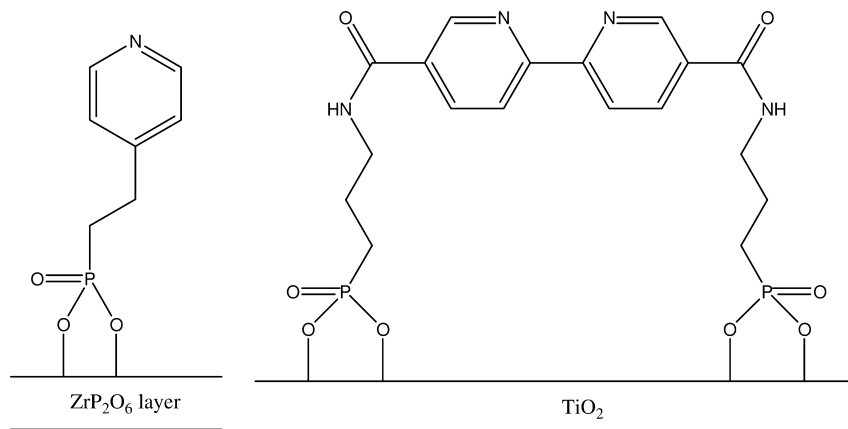
Fig. 42.10 Ligands anchored to zirconium phosphonate-layered structures or titanium dioxide particles.

ognized for 30 years. The size of the organic R group determines the spacing between the ZrP$_2$O$_6$ layers, while the presence of a functional group in R may give acidic or basic properties to the material, or it may serve as a ligand for the immobilization of homogeneous catalysts. This field was pioneered by DiGiacomo, and Dines and Callahan at Occidental Research Corporation [90], who developed (among others) supported catalysts for hydrogenation. These catalysts were attached through pyridine ligands (Fig. 42.10). Pillaring with bisphosphonic acids, which have a large rigid spacer between the two phosphonic acid functions, can further optimize the pore system of the layered material.

A selective hydrogenation catalyst for alkynes was obtained with the PdCl$_2$ complex of such immobilized pyridine. Diphenylacetylene was hydrogenated under 0.44 MPa H$_2$ in ethanolic solution. At full conversion, the following selectivities were observed: *cis*-stilbene 80.7%, *trans*-stilbene 16.1%, and only 3.2% 1,2-diphenylethane [90].

A similar type of immobilization was obtained by reacting the phosphonylated 2,2′-bipyridine ligand depicted in Figure 42.10 with excess titanium alkoxide. Rhodium and iridium complexes of this immobilized ligand showed activity for

the hydrogenation of olefinic double and triple bonds and for the hydrogenation of ketones. This catalyst showed very little leaching, and could be recycled at least for four times with no loss of activity [91].

42.3.6.4 Attachment to Polymer Supports

Merrifield was the first to use polymer supports, such as functionalized polystyrenes, in a reaction other than simple acid–base catalysis. His group has synthesized polypeptides by the stepwise addition of amino acids to a growing peptide chain, which was covalently bound to the resin [92]. Because Merrifield's discovery coincided with the rapid development of homogeneous catalysis, the idea was quickly and extensively adapted for polymer-supported transition metal catalysis. Today, virtually all homogeneous catalytic reactions have been tested on polymer supports, and a large variety of functional groups have been introduced to polymers. Furthermore, various polymeric composites – including natural products and enzymes – have been employed as carrier. Here, because of the limited space, only a few examples will be provided, but for a broad overview of the subject the reader is referred to references [1–5]. Covalently bound polymer-supported catalysts are synthesized using either of the three following methods: (i) by attachment to functionalized polymers; (ii) by attachment to a functionalized monomer unit followed by polymerization; or (iii) by grafting to another polymer after introduction of the ligands.

42.3.6.4.1 Functionalized Polymers as Supports

Grubbs, Collman, and Pittman, Jr. have developed methods for the phosphination and subsequent catalytic use of Merrifield and other styrene–divinylbenzene resins [1–5]. For example, the $P(C_6H_5)_2$-group was attached to Merrifield resins by reaction with $LiP(C_6H_5)_2$. The phosphine functionality can be introduced to polystyrenes by alternative approaches, such as lithiation (e.g., with butyllithium) followed by a reaction with $ClP(C_6H_5)_2$. Lithiation offers also an alternative route to the introduction of other functional groups. It was found that the distribution of relatively bulky phosphine groups in the resin was strongly affected by the degree of cross-linking. In spite of this, the phosphinated resins obtained provided active polymer-supported Wilkinson catalysts after treatment with Rh-precursors [93]. It was shown that by using solvents, which caused swelling, Rh–phosphine complexes were formed inside the resin. Subsequently, after removing the solvent, only the surface species could be destroyed by oxidative treatment. By re-swelling the beads, the locked catalytic sites inside the micro channels became active, while the catalyst could be readily separated after each use by simple filtration. Furthermore, the supported Wilkinson catalyst showed shape selectivity for the hydrogenation of small olefins. Encouraged by this success, various phosphines were immobilized on Merrifield and other resins and tested for other systems as homogeneous catalysis evolved [1–5]. Today, phosphinated styrene–divinylbenzene resins are commercially available with varying amounts of cross-links. One disadvantage

with regard to the use of phosphinated Merrifield resins is their low thermal stability due to ready quaternization of the supported phosphine groups by neighboring residual benzyl chloride groups above 353 K. Another potential problem, which is generally associated wtih monodentate ligands (see also other sections), is to control the coordination chemistry in reactions with metal complexes. For example, six different supported Rh–phosphine complexes were identified using NMR spectroscopy in the reaction of phosphinated polystyrene with an Rh-precursor [94]. In order to achieve a regular distribution of two or more monodentate ligands in the supported complex, it is preferable to immobilize the ligands after complexation. This can be achieved by using alternative polymerization methods, as discussed in the following two sections.

Alternatively, bi- or multidentate ligands can also be used for support. As an additional benefit, the latter offer greater stability for the coordinatively bound metal center against leaching through ligand dissociation and substitution reactions. The first, somewhat remarkable, approach to this is shown in Figure 42.11, based on numerous examples of the support of bidentate phosphines on polymers [1–5].

The supported DIOP derivative above represents one of the first attempts for supported enantioselective catalysis [95]. The immobilized ligand was used in the presence of Rh-precursors for asymmetric hydrogenation of prochiral olefins. Dehydroamino acids require polar solvents for dissolution, which cause shrinking of the polystyrene resins. For this reason, the supported Rh–DIOP complex gave no activity for such substrates. By using apolar systems such as a-ethylstyrene in benzene some activity could be detected, albeit with very low enantioselectivity (1.5% ee). The resin-supported DIOP catalyst proved to be a much better suited catalyst for the enantioselective hydrosilylation of ketones in apolar solvents, giving up to 58% ee to the appropriate chiral alcohols, and similar to that obtained with the homogeneous analogue.

Another interesting example is the supportation of Noyori's catalyst family containing Ru-chiral BINAP and chiral 1,2-diphenylethylenediamine [96]. These catalysts are suitable for the enantioselective hydrogenation of a variety of sub-
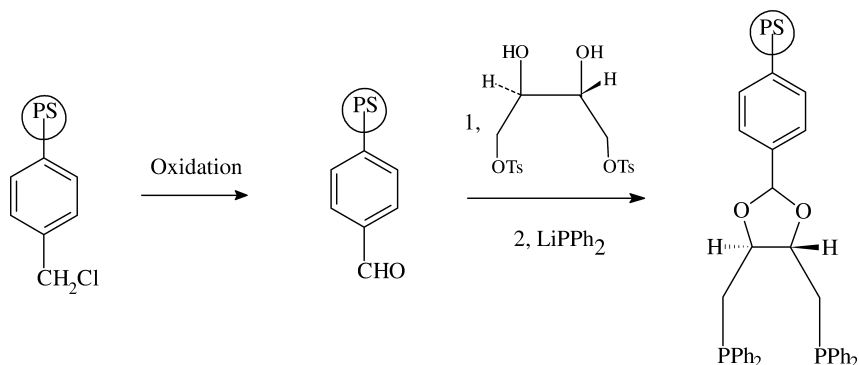

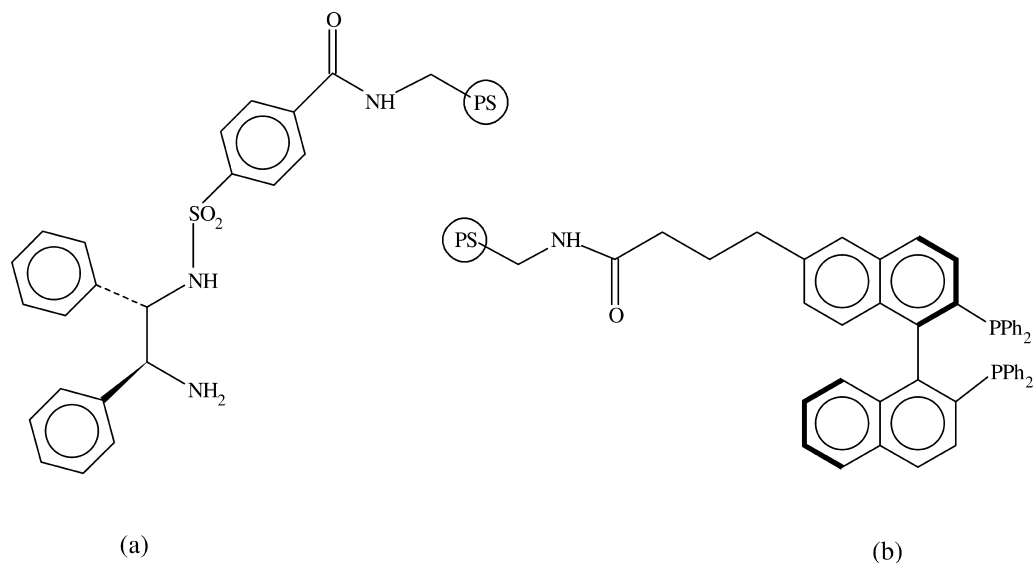**Fig. 42.11** Immobilization of chiral DIOP to Merrifield resin.

(a) (b)

Fig. 42.12 Immobilization of Noyori's catalyst components on functionalized polystyrene.

strates and for chiral transfer hydrogenation of ketones. By using two different approaches, either the chiral amine component (Fig. 42.12 a) [97] or the chiral diphosphine component (Fig. 42.12 b) [98, 99] was supported on aminomethylated polystyrenes. After adding the Ru-precursor and the other component, the obtained catalysts were used in enantioselective transfer or direct hydrogenation of various ketones at 303 K, 1 bar or 298–323 K under 8–40 bar H_2 (including also itaconic acid derivatives as substrates), respectively. Most of these catalysts gave >95% ee, albeit with relatively low rates (the homogeneous system also gives relatively low activity). Nevertheless, because of the very slight extent of deactivation, up to 33 000 TON could be achieved upon repeated recycling [99]. These catalyst systems were also immobilized to other resins, including poly-ethylene glycol (PEG), and yielding similarly good results [100, 101].

In addition to phosphine ligands, a variety of other monodentate and chelating ligands have been introduced to functionalized polymers [1–5]. For example, cyclo-pentadiene was immobilized to Merrifield resins to obtain titanocene complexes (Fig. 42.13) [102]. The immobilization of anionic cyclopentadiene ligands repre-sents a transition between chemisorption and the presently discussed coordinative attachment of ligands. The depicted immobilization method can also be adopted for other metallocenes. The titanocene derivatives are mostly known for their high hydrogenation and isomerization activity (see also Section 42.3.6.1) [103].
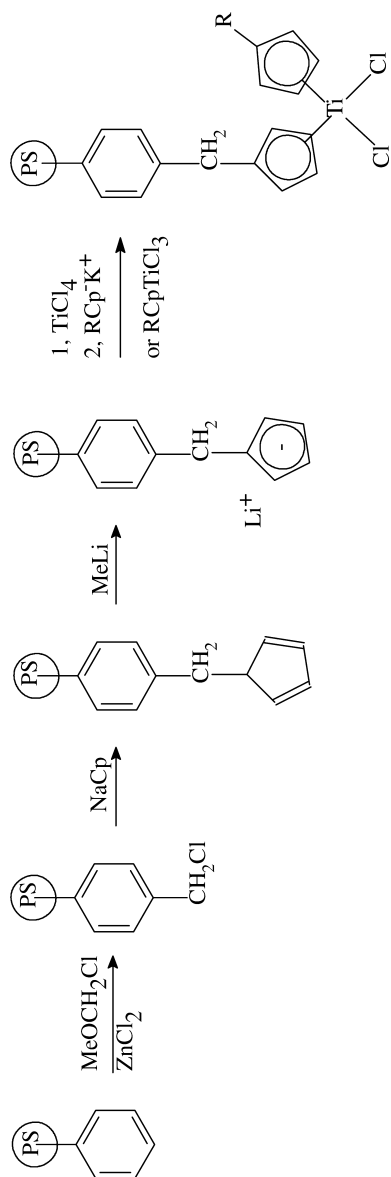
Fig. 42.13 Immobilization of cyclopentadiene for the preparation of polymer-supported titanocene complex.

42.3.6.4.2 **Enzymes as Support**

Natural polymers can also be used as carriers for immobilized catalyst. Enzymes can be immobilized to polymers or to other supports and, interestingly, can also be used to support homogeneous catalysts to provide real biomimetic systems [104]. It was reasoned that enzymes such as avidin have asymmetric sites, and this could induce chirality. Thus, in principle, the immobilization of an achiral complex into a chiral enzyme could give an asymmetric catalyst. Biotin as a substrate was known to bind strongly with the enzyme avidin, and it was for this reason that biotin was selected as spacer between an achiral bidentate aminophosphine and the active site of the enzyme (Fig. 42.14). The biotin-functionalized phosphine was coordinated to a Rh(I)-precursor and attached to the enzyme; the enzyme-supported catalyst gave optical induction in the hydrogenation of a dehydroamino acid derivative. A maximum of 41% ee was achieved, which indicated significant chiral induction by the enzyme support. A similar effect was noted by supporting the achiral Wilkinson complex to optically active cellulose for similar reactions [105].

42.3.6.4.3 **Functionalized Monomers**

Polystyrene or other polymer carriers are tunable in terms of properties such as swelling and pore size by varying the degree of cross-linking, or by introducing copolymer units. However, pre-made polymers provide an intrinsically inhomogeneous structure due to the limited accessibility of the polymer-pores for functionalization. This problem can be circumvented by attaching the ligand or catalyst complex to a monomer unit. Subsequently, the functionalized monomer can be polymerized or copolymerized with an appropriate choice of other units to obtain the desired supported catalyst. One potential disadvantage of this method is that the physical properties of the designed polymer are not always known beforehand, and this might lead to laborious fine-tuning. In copolymerization of the ligand-substituted monomer, it is also important to match the activity of different monomer units for a random polymerization.

For example, a proline-based chiral ligand was attached to a vinyl-substituted monomer (Fig. 42.15) by reacting vinylbenzoyl chloride with the amine functionality of the ligand [106]. As mentioned previously, the apolar Merrifield resin as a support is not swollen in polar solvents. Hence, in order to match the polarity of the resin with that of the typically used substrates in enantioselective hydrogenation, the functionalized monomer was copolymerized with polar units of methacrylic acid 2-hydroxyethyl ester.

The polymer-supported chiral phosphine obtained (Fig. 42.15) was treated with an Rh precursor and used for the enantioselective hydrogenation of dehydroamino acid derivatives. The obtained catalyst gave up to 82% ee, albeit with still low activity. Stille has developed this immobilization technique further by even more careful tuning of the polarity of the support with that of the reaction medium. For example, he introduced DIOP to a monomer vinylbenzaldehyde in reactions analogous to those shown for the polymer in Figure 42.11.
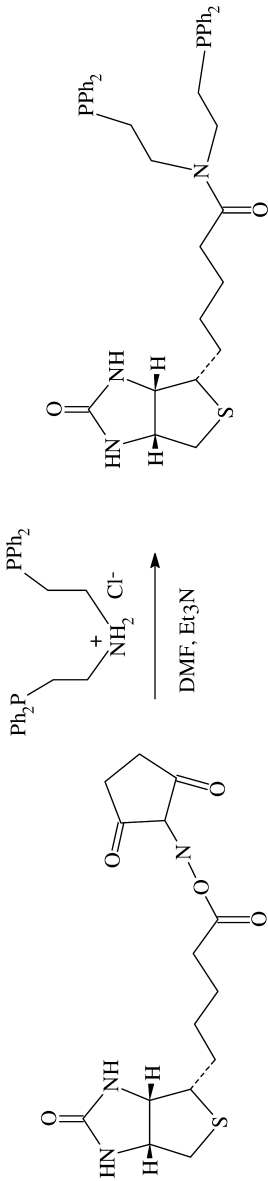
Fig. 42.14 Immobilization of an achiral phosphine derivative via enzyme-bound biotin.
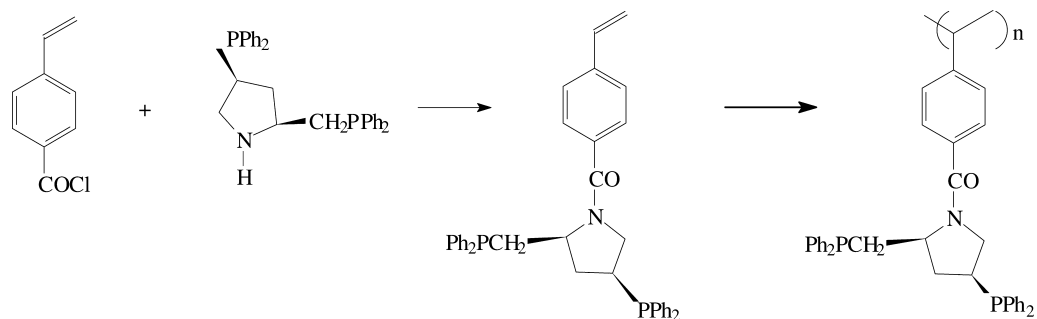
Fig. 42.15 Immobilization via functionalization of the monomer unit.

The monomer was copolymerized with methacrylates to obtain various composites with the supported ligand [107]. The obtained catalysts showed similar enantioselectivities in the hydrogenation of dehydroamino acids to their homogeneous counterparts, but with reduced rates. Nevertheless, the immobilized catalysts could be recycled by simple filtration without loss of Rh or enantioselectivity. By using an interesting approach, the styrene derivative of the DIOP ditosylate precursor was copolymerized with methylvinyl ketone. The carbonyl groups of the polymer-supported chiral ditosylate obtained were then hydrogenated enantioselectively by using homogeneous DIOP complexes [108]. Thus, supported chiral alcohol functionalities were obtained on the polymer. Subsequently, the supported ditosylate groups, which remained intact upon hydrogenation, were converted into supported chiral Rh–DIOP complexes. By using this approach, the role of chiral supports could be studied in asymmetric induction.

Using another interesting approach, the attachment of chiral BINAP was carried out by polycondensation of an amino-BINAP derivative with terephthaloyl chloride in the presence of optically pure 2,4-pentanediol (Fig. 42.16), which resulted in the formation of a chiral polyamide–polyester composite [109]. In fact, a similar material was obtained to that described above by Stille in an elegant and simple manner. The chiral polymer-bound ligand was then used in Ru-catalyzed hydrogenation of the Naproxen® precursor, with excellent optical purities. Because BINAP as a chiral ligand is so effective in similar reactions, it is difficult to estimate whether the chiral support contributed to the improvement in enantioselectivity. However, the support had a positive effect on the rates, which were significantly higher with the immobilized catalyst than with the homogeneous Ru–BINAP. The concept of this immobilization method can clearly be adopted for other enantioselective catalytic reactions.

Ultimately, the ligand itself can be polymerized and used as both ligand and support in one [110]. Pu and coworkers have prepared the rigid chiral poly-BINAP ligand below (Fig. 42.17) and used it after treatment with Rh and Ru in asymmetric hydrogenations. The supported catalysts showed similar activities and enantioselectivities to their homogeneous analogues, with the benefit of
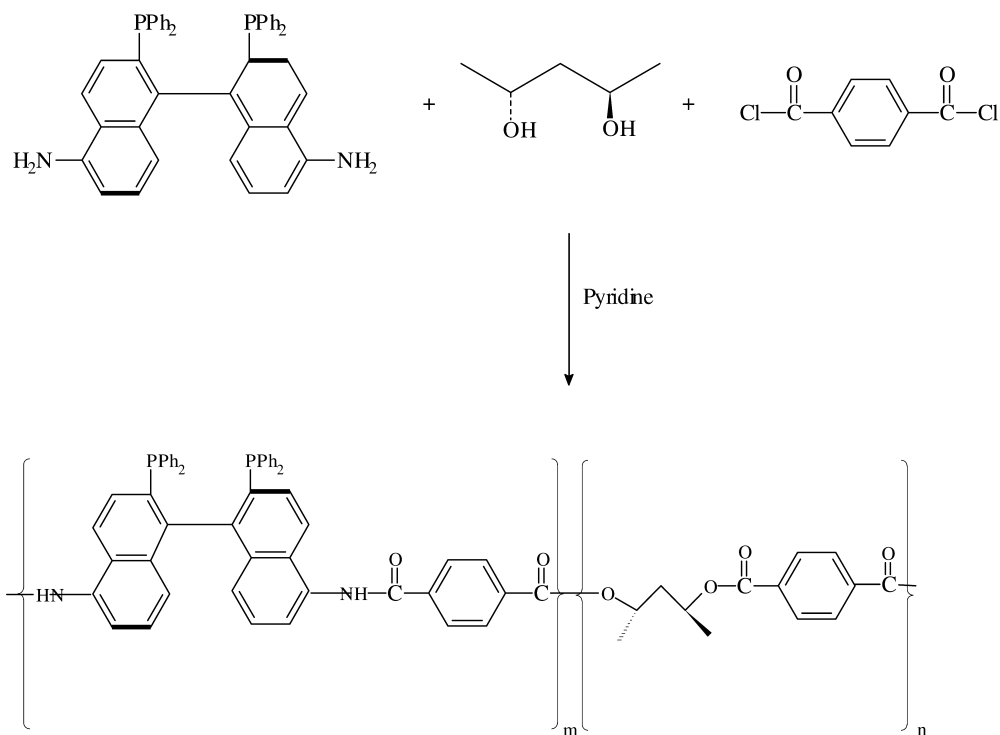
Fig. 42.16 Chiral polyester–polyamide composite containing supported BINAP.

easy separation by simple filtration. The recovered catalyst showed identical rate and ee upon re-use.

Chiral catalysts remain primary targets for immobilization by using similar methods. Since the steric arrangement of bulky aromatic groups of chiral ligands is the primary source of optical induction, most approaches use the chelate backbone of ligands for functionalization in order to minimize interference with the chelate (aryl) conformation.

Instead of monomers, the ligands and catalyst can also be attached to organic, fluorocarbon-, or water-soluble oligomers. Bergbreiter has pioneered the synthesis and use of these systems [111]. Thus, by varying the properties of the oligomeric chain, supported catalysts can be designed, which dissolve at high temperature and separate at lower temperature, thereby facilitating catalyst–product separation. Alternatively, oligomeric supports are also available which have reverse solubility parameters, separating at high temperatures.
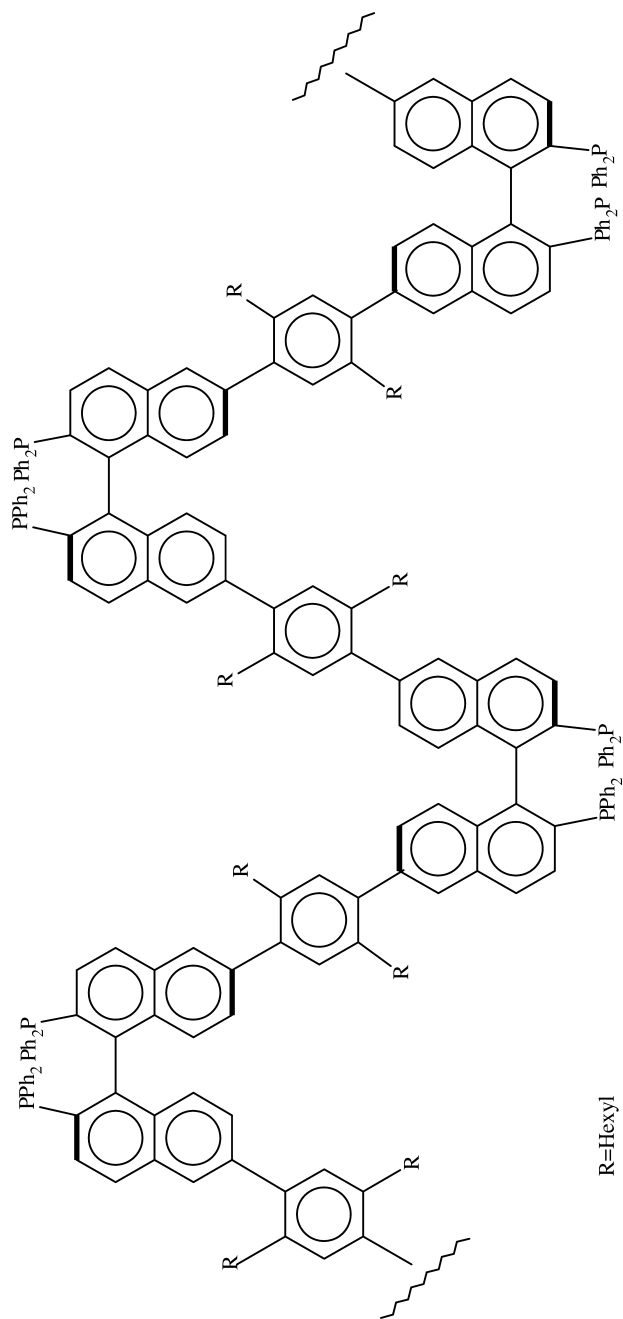
R=Hexyl
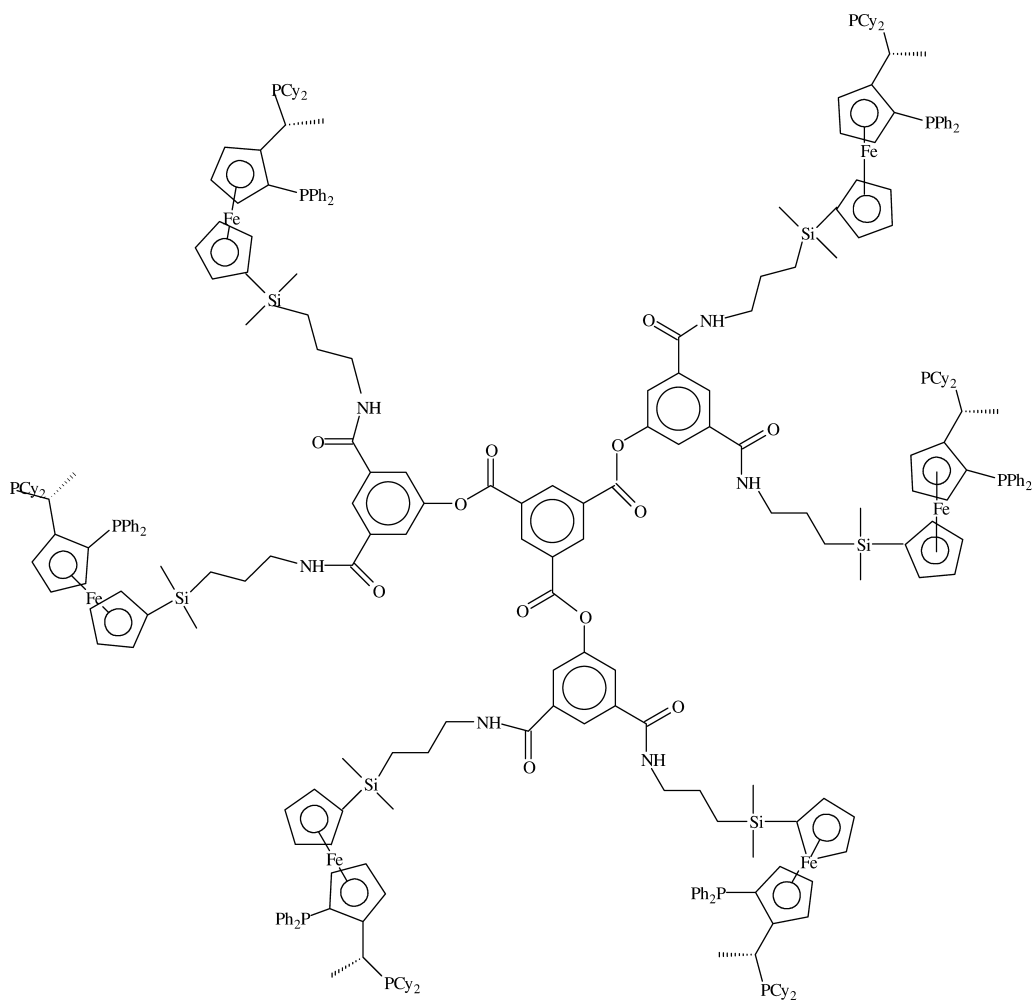
Fig. 42.17 Rigid poly-BINAP ligand.

Fig. 42.18 Dendrimer-supported Josiphos.

42.3.6.4.4 **Dendrimers as Supports: Membrane Filtration**

By using a somewhat analogous approach, the catalysts can also be attached to soluble dendrimers, long fluorocarbons, cyclodextrins or crown ethers and used conveniently in membrane filtration for catalyst-product separation. For example, a chiral ferrocenyl ligand, Josiphos, was attached to some different dendrimers containing benzene-1,3,5-tricarboxylic acid (three arms) (Fig. 42.18) and adamantane-1,3,5,7-tetracarboxylic acid cores (four arms) [112]. After treating with Rh-precursors, the soluble dendrimer-supported catalyst obtained showed similar activity and enantioselectivity (>98% ee) in the hydrogenation of dimethyl itaconate as their homogeneous analogue, albeit with a slight decrease

in ee-value due to an increase in dendrimer size. All of the dendrimers were retained by a commercial nanofiltration membrane [112].

Membrane filtration can also be achieved by attaching carbosilane dendrimers to a single bidentate ligand [113]. In this case, the ligand itself serves as core for the dendrimer, and the size and polarity can be tuned as desired. Another way of performing membrane filtration is to introduce long fluorous ponytails to phosphine ligands [114]. The subsequently obtained Rh-complex is then soluble in supercritical CO_2 and can be used, amongst other things, for the hydrogenation of 1-butene at 353 K, 200 bar. The catalyst can be used with slight deactivation in either batch or continuous mode by using a simple microporous silica membrane for filtration.

42.3.6.4.5 Grafting to Polymers

The internal space of polymers is generally not accessible to molecules of unmatched polarity. Furthermore, the attachment of very large catalyst complexes might even be sterically hindered at the surface. By using functionalized monomers as support (see Section 42.3.6.4.3), the attached ligand (catalyst) might be locked in the formed copolymer. An alternative solution to this problem is to graft the functionalized monomer or oligomer to a carrier polymer. One advantage of this approach is that the properties of the core are irrelevant and the desired monomer/oligomer structure can be introduced as a surfactant and spacer. The grafting can be carried out by using either irradiation, electrochemical or/and chemical methods [12]. In addition to silica carriers, the grafting of phosphine-substituted styrene on phosphinated Merrifield resins was also studied [115].

Grafted catalysts are commercially available on fibrous polyethylene supports; for example, Johnson Matthey has developed the FibreCat^{TM} catalyst family for a variety of reactions [116]. By using this approach, diphenylphosphino groups could be grafted to the fiber via phenyl or benzyl linkers, followed by complexation to transition-metal compounds. For example, the Rh FibreCat catalysts obtained (Fig. 42.19) showed similar selectivity to their homogeneous counterparts in reactions such as hydrogenation of geraniol to citronellol or carvone to 7,8-dihydrocarvone. Because hydrogenation of the least-hindered double bond in these substrates occurs more rapidly with homogeneous and FibreCat catalysts than with other double bonds in the molecule, selective hydrogenation can be achieved [116]. However, this is generally not the case when using conventional heterogeneous catalyst.

In conclusion, the covalent attachment of ligands to a support material is a widely investigated and still expanding field, and includes many examples of recyclable catalysts with activity and (enantio-) selectivity which is comparable to that of the corresponding homogeneous catalyst. However, this method requires the inclusion of extra synthetic steps in order to attach the ligand to the support, while stability of the ligand/linker combination is a prerequisite to prevent metal leaching.
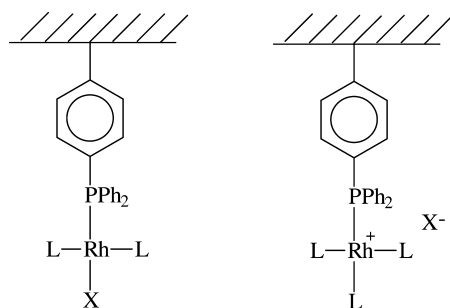
Fig. 42.19 Rh-FibreCat™ family.

42.3.7
Ionic Bonding of Metals to Supports

As an alternative to covalent attachment, the metal centers of catalyst complexes can also be supported by ion exchange. Clearly, a condition of this approach is that both the metal complex and the support are appropriate ionic compounds. By using multiply charged metal complexes, multiply bound supported complexes can be obtained, and this can minimize the chance of leaching. Furthermore, it should be considered that most homogeneous catalytic reactions proceed through changes in the oxidation state of the metal. Thus, before starting immobilization, it is important to consider whether the metal center retains at least one of its charges in each of the possible intermediates of the whole catalytic cycle.

As described below, ionic catalyst complexes can be supported to both inorganic and polymer (dendrimer) carriers. The efficiency of the support is determined by the general rules of ion exchange and, for this reason, in order to achieve a successful approach it is important to exclude the formation or presence of other ionic compounds, which might compete for (liberate) the catalyst ion from the support.

42.3.7.1 Ionically Bound Metal Centers on Inorganic Supports

The most significant class of inorganic supports, which is used for the direct ion exchange of positively charged transition-metal complexes, are smectite clays. Pinnavaia has introduced the use of these swelling, layered silicate clays for catalysis. Other clays include montmorillonite, bentonite, and laponite. As shown by Pinnavaia, cationic transition-metal complexes can be readily exchanged (intercalated) into the solvated interlayers of these silicates (Eq. (1)) [117]:

$$\overline{Na^+(solv)} + ML_n^+ \xrightarrow{\text{solvent}} \overline{ML_n^+(solv)} + Na^+ \tag{1}$$
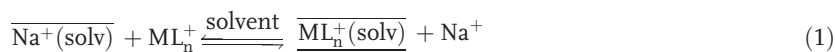
When using appropriate solvents for swelling of the interlayers, the intercalated metal ions are accessible to both substrates and catalysis. One of the first such demonstrations was also carried out with the Wilkinson complex for hydrogena-

tion reactions [118]. The intercalated Rh–PPh$_3$ complexes showed similar activities in the hydrogenation of several olefins and alkynes (298 K, 1 bar H$_2$) to their homogeneous counterparts, albeit with some extent of deactivation. The deactivation was attributed to the formation of the monohydrido compound, which is in equilibrium with the cationic dihydrido species (Eq. (2)) [119]. (The formation of monohydride is especially favored in the presence of bases).

$$H_2Rh^+(PPh_3)_3 \xrightleftharpoons{\qquad} H^+ + HRh(PPh_3)_3 \qquad\qquad (2)$$
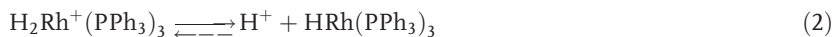
Other than catalyst stability, shape selectivity is an additional important aspect that is associated with the use of intercalated complexes. For this reason, many studies have concentrated on demonstrating shape- and size-selective catalysis by influencing the interlayer space with swelling solvents rather than carrying out leaching tests. Some of these attempts were successful, and with several types of intercalated catalyst, including the Wilkinson analogues. For example, it has been shown that a chiral Rh$^+$–DIOP complex, when intercalated into sodium hectorite, is highly sensitive to the size of the ester group in terms of activity and enantioselectivity in the enantioselective hydrogenation of itaconic ester derivatives [120].

Naturally, other inorganic supports were also studied, one example being the immobilization of the Wilkinson complex on bentonite [121]. In this case, only surface-supported complexes were obtained, which were significantly faster than the homogeneous analogues (at 308 K, 1 bar) for several different alkenes such as 1-octene, cyclohexene, norbornadiene, and cyclohexen-1-one. This effect was explained by site isolation which prevented dimer formation. These complexes also showed some deactivation, most likely for the same reason as outlined above (see Eq. (2)). Other silicates such as mesoporous MCM-41 can also be used as supports for ionic complexes. Hölderich et al. immobilized cationic Rh-complexes of chiral ligands in the pores of this support [122] and, by using Me-Duphos complexes, were able to achieve TON values exceeding 4000 and 92% ee in the hydrogenation of itaconate by maintaining the catalyst configuration. The activity of the complexes was less high, most likely due to the limited accessibility of the intercalated catalysts.

42.3.7.2 Ionically Bound Metal Centers on Polymer Supports

Ion-exchange resins are the most obvious choices for supporting ionic complexes on polymer carriers. Cation-exchange resins are synthesized by introducing strong or weak acid groups, most frequently -SO$_3$H or -COOH, to polymer supports. Anion-exchange resins contain quaternary and/or tertiary amines as functional groups. Because of the easy functionalization, polystyrene–divinylbenzene and (meth)acrylic acid–divinylbenzene polymers are the dominant materials for used ion-exchange resins. Most commercially available ion-exchange resins are designed to function in aqueous media, and are usually gel-type polymers with a low degree of cross-linking and high polarity in the functional

groups. These resins are hygroscopic materials, and can barely tolerate organic solvents. Macroreticular forms with a lower degree of functional groups are better suited for use in organic media, and several of the latter type are available commercially. The traditional polystyrene- or acrylate-based ion-exchange resins have relatively low thermal stability, with a maximum recommended reaction temperatures of 80 to 100 °C. Several new resins offer some improvement in thermal stability; these include Nafion (DuPont) as cation and polyvinylpyridine (and other cyclic nitrogen base) derivatives as anion exchange resins. The structure of Nafion, which consists of a perfluorinated polymeric backbone with side chains containing $CF_2CF_2SO_3H$ groups, can be considered as particularly unique. The sulfonate groups are clustered together to give the resin an inverse micellar structure. Nafion can be used in either protic or polar solvents and, since the H-form is a very strong heterogeneous acid (superacid), the resin has found use in a variety of synthetic applications. Nafion resins are also available in solutions, as membrane foils, and as layers supported on silica.

Cation-exchange resins have been exploited mainly for the immobilization of monocationic Rh-phosphine complexes for hydrogenation reactions. According to Eq. (2), formation of the monohydride can be suppressed by using an excess of acidic resin. However, the presence of an acid can catalyze undesirable side reactions in the case of sensitive alkenes. Bidentate phosphines are somewhat less sensitive for the formation of monohydrido complexes, especially in the absence of strong bases. It has been shown that supported cationic Rh complexes of several chiral bisphosphinites on sulfonated polystyrenes maintained their high enantioselectivity over 15 consecutive uses in the enantioselective hydrogenation of dehydroamino acids [123]. However, the activity of the supported complexes slowly decreased, and some Rh-leaching occurred. This was ascribed to a slow decomposition through oxidation of the ligand rather than to monohydride formation. It was also shown that free acid functionality gave a higher supportation efficiency than either Li- or ammonium salts, though the latter gave a higher activity in the reaction. The use of the salt form was required with one phosphinite ligand, which was sensitive to acid-catalyzed hydrolysis. The swelling properties of the resins had only a slight effect on the enantioselectivity, but greatly influenced the hydrogenation rates.

42.3.8
Attachment of Ligands via Ion Exchange

As described in Section 42.3.7, ion-exchanged metal ions are often vulnerable to leaching through the formation of a neutral or zerovalent species. In similar manner to the situation in Section 42.3.6, this problem can be circumvented by ion exchanging the metal complexes via the ligands rather than the metal itself. As in covalent immobilization in general, two approaches can be followed: the ligands can be exchanged either prior to or after complexation to the metal centers. In particular, when the presence of several coordinated monodentate ligands is required, the latter method is advised as it provides better control on

the coordination chemistry and immobilization efficiency. As discussed earlier, many homogeneous catalyst complexes contain electronic charges at the metal center. However, when ion exchange of the metal center is not desirable, it can be avoided by choosing the opposite electronic charge for the functional groups of the ligand. As with the support, the same materials can be used as described in Section 42.3.6. However, to date predominantly ion-exchange resins (see Section 42.3.7.2) have been used, as the ion exchange of large ligands into the restricted interlayer space of smectite clays or other silicates (see Section 42.3.7.1) is a much more difficult task.

The first attempts at immobilizing ligands onto ion-exchange resins were also carried out by using Wilkinson analogues. For example, acid forms of macroporous cation-exchange resins were treated with a *p*-amino-substituted triphenylphosphine derivative $P[(4-C_6H_4)N(CH_3)_2]_3$ [124]. Tang and coworkers found that the phosphine functionality was protonated more easily by the resin than the amino group and, in this manner, in subsequent treatments with Co, Rh, or precursors, predominantly amine complexes were obtained. Presumably, because of the relatively weak coordinative binding of amine ligands, these catalyst systems showed leaching in the hydroformylation test reaction. Protonation or quaternization of the phosphorus groups of similar aminophosphines can be avoided by protecting them. Since the phosphorus atoms of these aminophosphines coordinate much more strongly than the amino groups, the phosphorus atoms can be most conveniently protected by coordination to the desired metal precursor before immobilization. This was demonstrated by using similar amino derivatives of several chiral bidentate phosphines such as Chiraphos and BDPP in the Rh-catalyzed enantioselective hydrogenation of dehydroamino acid derivatives [125]. For example, the reaction of *S,S*-Chiraphos-*p*-$(N(CH_3)_2)_4$ with Rh^+-precursors resulted in the formation of bidentate phosphine complexes, which could subsequently be protonated at the free amine functionalities with acid forms of ion-exchange resins. Thus the complex, including the charge at Rh, could be bound with five ion pairs to the resin (Fig. 42.20). Presumably due to this strong bonding, the catalysts showed no leaching in subsequent catalytic tests. Furthermore, it was found that the addition of amines stronger than *N,N*-dimethylaniline removed the complex completely from the resin by simple acid–base chemistry. Such easy liberation of the catalyst would be very useful in the regeneration of fouled (spent) catalyst, which is a clear advance compared to covalently bound catalysts.

The size and swelling of the resin beads was found to have a dramatic influence on the reaction rate and enantioselectivity. When using large beads of gel-type resins – which swell well – the rates with ion-exchange catalysts were several orders of magnitude less than those of the homogeneous counterpart. However, by using finely dispersed gel-type resins (with an increased surface area), and Nafion-based resins in particular (Fig. 42.20), the rates were significantly improved and approached those of the homogeneous analogues [125].

In general, the reaction rates can be increased by introducing longer spacer groups to the (covalently or ionically) bound ligands, by detaching the metal
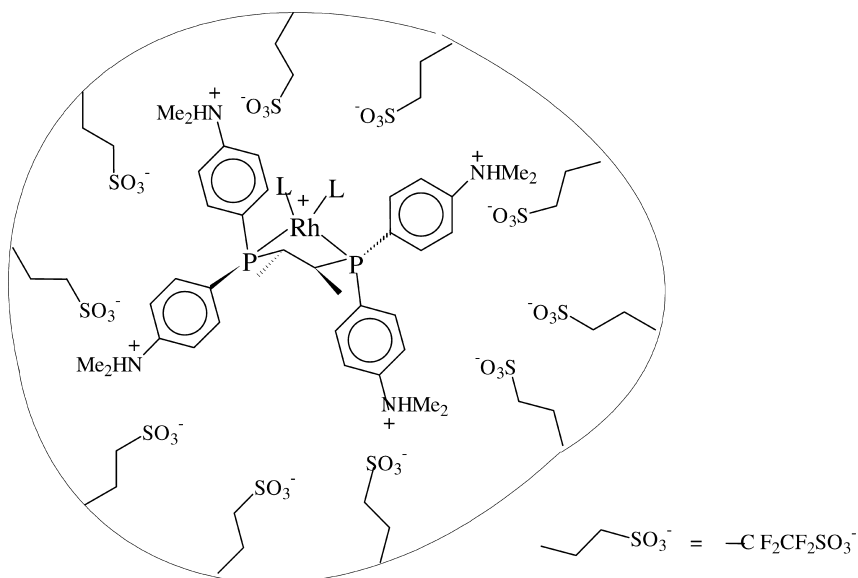
Fig. 42.20 Nafion-supported [Rh$^+$-(S,S)-Chiraphos-(p-N(CH$_3$)$_2$)$_4$].

center from the proximity of the surface. For example, it was shown that by using Rh$^+$(NBD)[Ph$_2$P(CH$_2$)$_n$PMe$_3^+$]$_2$ complexes, which were supported on cation-exchange resins in hydrogenation reactions, the rates generally increased by increasing the alkyl chain from n=2 to n=10 [126]. However, the effect was not shared by each alkene tested. One possible reason for this might be that Rh as a monocation is also exchanged to the resin, thus disturbing the trend. As mentioned above, ion exchange with the metal can be avoided by choosing the opposite charge for the ionic groups of the ligands. For this goal, and by assuming a typically cationic metal center as example, negatively charged ligands should be used with anion-exchange resins. Most water-soluble ligands developed for two-phase catalysis contain anionic sulfonate (SO$_3^-$) groups (see Chapter 39), and these could be readily used for immobilization by ion exchange. Despite the large number of available sulfonated ligands and the convenience of immobilization, this option has not yet been fully exploited. However, several examples are known which utilize sulfonated chiral BINAP on layered double hydroxides and sulfonated triphenylphosphine on anion-exchange resin in hydrogenation reactions [127, 128].

One special case is the combination of immobilization by entanglement and ionic bonding. A negatively charged phosphonated BINAP ruthenium complex and a phosphonic acid spacer reacted with a positively charged polymer to give a polymer network, which is held together by ionic bonding [129]; the structure of this is depicted in Figure 42.21.

This catalyst showed high enantioselectivity in the hydrogenation of dimethyl itaconate. The best enantioselectivities (83–89% ee) were obtained in ethanol as
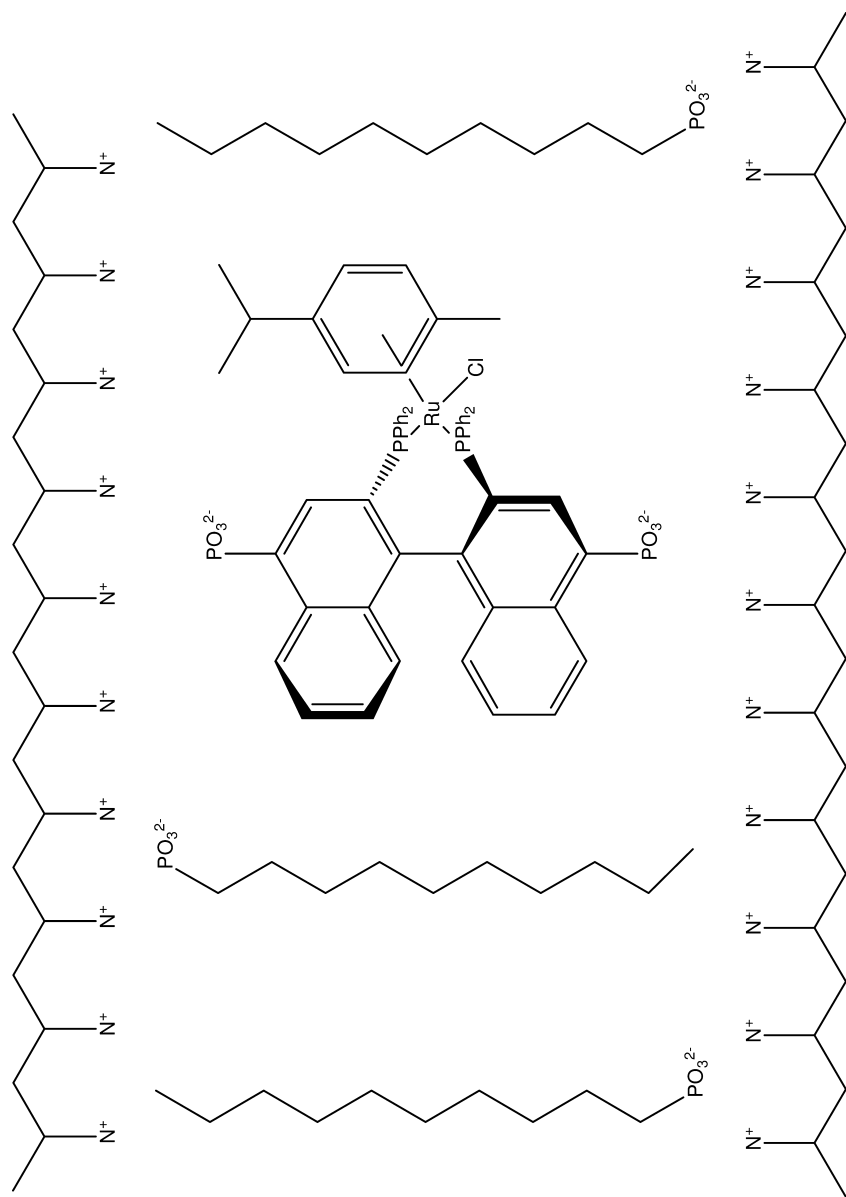
N$^+$: quaternary ammonium or N-methylpyridinium ion

Fig. 42.21 Schematic drawing of the polyelectrolyte-entrapped ruthenium complex.

solvent, and approached the value obtained with a homogeneous Ru–BINAP catalyst (91% ee). The partial dissolution or swelling of these catalysts in ethanol may be responsible for the observed high enantioselectivities. Remarkably, much lower – and even opposite – enantioselectivities were found in less-polar solvents, such as toluene. It appears that the conformation of the network – and probably also the structure of the complex – depend heavily on the solvent used.

42.4
Catalyst Deactivation

Every catalyst is susceptible to catalyst deactivation, and immobilized catalysts form no exception to this rule. A number of observed deactivation mechanisms are listed below (see also Chapter 44):

- Loss of metal by ligand degradation. The oxidation of phosphorus ligands by peroxide impurities in the feed is an example. Purification of the feed is an obvious remedy. It is much more difficult to find a solution when ligand degradation is inherent to the catalytic reaction mechanism (e.g., phosphonium salt formation).
- Loss of metal by ligand substitution. Reactants or products can form soluble complexes with the metal by replacing the original ligands. In particular, weakly coordinating ligands such as amines, imines and O-based ligands are susceptible for replacement.
- Loss of catalytic complex by dissolution from the support. This can either occur to physically bound catalysts (physisorbed, entangled in a polymer, hydrogen-bonded), when the reaction medium has too-good solvent properties. The catalyst complex can also be dissolved from ionically bound species by ion exchange with electrolytes in the reaction mixture, or when the covalent bond to the support is broken (e.g., by hydrolysis). In the case of SIB catalysts, a good solvent such as ethanol can displace a salen-type ligand from the metal.
- Formation of inactive dimeric species. Site isolation is the solution to this problem, which is not possible using homogeneous catalyst.
- Reaction of the active species with functional groups (hydroxyls) on the support. Protection (end-capping) of the functional groups is the proposed remedy, but it is difficult to protect them all, for steric reasons.
- Deposition of insoluble material in the pores of the catalyst by polymerization or condensation reactions, for instance. Sometimes a washing procedure regenerates the catalyst.
- Deactivation may also be inherent to the catalytic system and similar to deactivation of the homogeneous catalyst. An example is the formation of a stable *ortho*-metalated species.
- Deactivation or loss of selectivity can also occur when the ligands are not able to protect the metal against reduction to metallic particles. In this case, one must avoid high hydrogen pressures.

The regeneration of deactivated immobilized catalysts is not as easy as with conventional supported metal catalysts, where combustion of the deposited material is frequently used. Because such a procedure would destroy the organic ligands, one must resort to washing procedures. However, when this method fails, attempts must be made to recover the metal and the ligand, and to prepare a fresh catalyst. In principle, it is possible to recover the metal complexes from physically and ionically immobilized catalysts. This can also be done from covalently bound catalysts by using an easily hydrolyzable linker.

42.5
Conclusions

The selectivity of homogeneous hydrogenation catalysts often surpasses that of conventional heterogeneous catalysts. The application of homogeneous hydrogenation catalysts in the fine chemical industry is steadily increasing, though process economics dictate the recovery and re-use of the catalyst in order to arrive at acceptable catalyst costs, unless the catalyst is extremely active. Since the separation and recovery of a homogeneous catalyst from a product mixture is not always possible without destroying the catalyst, homogeneous catalysts were modified to alleviate the separation problem. One direction of research is to immobilize homogeneous catalysts on a solid support in order to obtain a heterogeneous catalyst with at least similar catalytic activity and selectivity as the original homogeneous catalyst. However, the application of such an immobilized catalyst always introduces the possibility of mass-transfer limitations from the liquid phase to the exterior catalyst surface, or within the catalyst pore system. More detailed knowledge of the reaction kinetics is needed to evaluate the performance of this type of catalyst, and for scale-up and reactor design.

42.6
Outlook

The most promising immobilization methods are in our view:
- Physical entrapment in a polymer matrix.
- Surface hydrogen-bonding.
- Ionic bonding of the ligand to an ion exchanger.
- Covalent bonding of the ligand to the support.

The first two methods have the advantage that no modification of the homogeneous catalyst is needed. Surface hydrogen-bonded catalysts are limited to cationic complexes, while physical entrapment is more widely applicable. However, both methods are very sensitive to the solvent properties of the reaction medium. The chemical methods of immobilization require modification of the ligand, and this may be quite laborious. In the case of irreversible catalyst deacti-

vation, recovery of the metal is possible for all four types of immobilized catalysts. Recovery of the ligand or the entire complex is possible in all cases, except for the covalently bound ligands. Attachment of the homogeneous catalyst to a soluble polymer or dendrimer permits its use as a homogeneous catalyst with a size which is large enough for separation by membrane filtration. However, although this approach is very popular nowadays in academia, it is likely that industrial applications will have to wait until the stability of membranes has been proven.

Abbreviations

HPA	heteropoly acid
MELS	molecularly engineered layered structures
PDMS	polydimethylsiloxane
PVA	polyvinylalcohol
SAPC	supported aqueous-phase catalysis
SHB	supported hydrogen-bonded
SIB	ship-in-the-bottle
SILP	supported ionic-liquid phase
SLPC	supported liquid-phase catalyst
TEOS	tetraethoxy orthosilicate
THF	tetrahydrofuran
TOF	turnover frequency
TON	turnover number
TPPTS	trisulfonated triphenylphosphine

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