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Review

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Ion Exchange Resins: Catalyst Recovery and Recycle

Pierluigi Barbaro* and Francesca Liguori

Istituto di Chimica dei Composti Organo Metallici - Consiglio Nazionale delle Ricerche, Area di Ricerca di Firenze, Via Madonna del Piano 10, 50019 Sesto Fiorentino, Firenze, Italy

Contents

1. Introduction

Chemical synthesis is greatly facilitated by catalysis and further on by catalyst recovery and recycle. Catalyst reuse increases the overall productivity and cost effectiveness of chemical transformations while minimizing their environmental impact, ultimately contributing considerably to the sustainability of chemical processes. Indeed, catalyst recycle fits most "principles of green chemistry"[1–4] and was included as a priority in several strategic research agendas both in the United States and in Europe.[5,6]

To date, catalytic technologies leading to fine-chemicals production, and particularly in selective, large-scale processes, are still largely dominated by homogeneous catalysts,[7–13] whose separation from the reaction products and reuse is a major concern.[14–16]

Due to the easier workup and integration in reactor equipments, the chemical industry has a strong preference for solid catalysts, which, however, usually do not provide selectivities (chemo, regio, or stereo) comparable to those observed in the homogeneous phase.[17,18]

There is therefore a clear need to develop new concepts bridging heterogeneous and homogeneous catalysis and to apply these to the engineering of catalytic devices for the industrial production of fine chemicals.[19–25]

In order to easily recover and recycle homogeneous catalysts, various techniques were developed over the last 20 years involving the immobilization of a catalyst precursor onto an insoluble support material, so that the catalyst can be quantitatively separated by filtration and recycled. This topic was extensively and excellently reviewed in the past.[26–39] A variety of solids, often highly sophisticated, have been exploited for this purpose, including inorganic (silica, clays, zeolites, metal oxides, heteropolyacids, etc.),[40–42] organic (carbon, dendrimers, polymeric ligands, polyelectrolytes, etc.),[43–45] and hybrid materials.[46–48] The active species can be immobilized on these supports by covalent or noncovalent binding, i.e. by adsorption, electrostatic interaction, or entrapment.[49–52]

Preformed, molecular homogeneous chemical catalysts (usually metal complexes or organometallic compounds) are most conveniently anchored to diverse materials through *noncovalent binding*. This approach, hereinafter referred to as *heterogenization of homogeneous catalysts*,[53–57] has several benefits:

-there is no need for the chemical modification, neither of the support nor of the catalyst, usually required using a covalent binding strategy,

-catalysts of known activity and selectivity are used,

-the anchoring procedures are simple,

-the problems arising from metal loading are minimized,

-the catalyst's active sites can be easily characterized,

-a systematic design of new, predictable catalysts is enabled.

The catalysts thus obtained can be classified into the more general family of *single-site catalysts* whose features were detailed by Thomas et al.[58] The catalytic performances of these heterogenized catalysts may vary enormously depending on the immobilization method and on the support, so that it is of outmost importance to get a systematic picture of favorable and unfavorable factors and to test different support materials.

This paper reviews the recent achievements in the field of the heterogenization of homogeneous chemical catalysts onto *ion-exchange resins*. The main focus will be on those applications for which the recycling of the catalyst has been demonstrated. This matter has been partially reviewed up to the end of 2004.[59–65] *The present manuscript covers the most significant papers that appeared in the literature from January 2005 to April 2008.* Some additional aspects are also taken into account, including reference to previous but unreviewed works. Applications will be described according to the reaction involved, irrespective of the nature of the supported metal or the type of the resin used.

The immobilization of biological catalysts,[66,67] the use of ion-exchange resins as Brönsted and/or Lewis solid acid catalysts (alone or in combination with metal ions),[68–71] or their use in simple extraction procedures (e.g., for metal

* To whom correspondence should be addressed. E-mail: pierluigi.barbaro@iccom.cnr.it.

Pierluigi Barbaro was born in Firenze in 1962. He obtained his Ph.D. in chemistry from the University of Florence and completed his postdoctoral work at ETH in Zurich, later becoming a permanent researcher at the Istituto di Chimica dei Composti Organo Metallici - Consiglio Nazionale delle Ricerche, Italy. He has been a member of the Network of Excellence IDECAT since 2005, and he is coordinator of the Initial Training Network NANO-HOST, funded by the European Commission under the VII° FP. In 1991 he was awarded with the national prize "Federchimica". He is the author of more than 70 research papers and 6 patents and is the editor of a book. His main research interest is in the field of homogeneous, heterogeneous, and asymmetric catalysis, with focus on homogeneous supported catalysts and nanostructured catalysts for sustainable production processes, microscopy, and nuclear magnetic resonance.

Francesca Liguori (born in 1971, Prato, Italy) received her degree in Organic Chemistry in 1999 at the University of Florence, Italy, with a thesis on the synthesis of heterocyclic alkaloids. After some postdegree research collaborations at the Department of Organic Chemistry of the University of Florence, she received her Ph.D. in Chemistry in 2005 with a thesis on the synthesis of gangliosides, mimetics of antitumor antigens. In 2006 she joined the Institute ISMAC-CNR (Milan, Italy) as a postdoctoral fellow, working on the synthesis of ethylene based copolymers with anti-oxidant activity. Since 2007 she has been a grant-holder at the Institute ICCOM-CNR (Florence, Italy), with a project funded by the Network of Excellence IDECAT on heterogeneous catalysts for asymmetric hydro-genation reactions. Her research interest extends over a wide range of organic product chemistry, heterocycles, carbohydrates, and organometallic complexes and, more recently, to the synthesis and reactivity studies of homogeneous catalysts heterogenized on diverse materials.

catalysts recovery),[72,73] as well as their use in the pyrolytic preparation of carbon-based catalysts,[74,75] will not be considered.

2. Ion-Exchange Resins and Homogeneous Catalysts Immobilization

A systematic description of ion-exchange resins is out of the scope of this paper. Comprehensive classifications and

Scheme 1
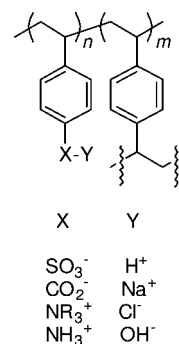
overviews of their properties were published elsewhere.[76-78] A short mention of the resin features which may affect the efficiency of the supported homogeneous catalysts and the viability of their recycle is provided here, aimed at a critical coverage of the cited literature.

Common uses of ion-exchange resins include water purification, metal recovery and separation, ion substitution, acid−base catalysis, as sensors or as solid electrolytes (e.g., in fuel cells, electrolyzers, electrodialysis devices), in chemical, food, and beverage industries, and in power, nuclear, semiconductor, and pharmaceutical industries.[79-81]

Most ion-exchange resins are based on cross-linked polystyrene−divinylbenzene copolymers bearing ion-exchanging functional groups (Scheme 1).[82,83] Classification of resins usually involves four main groups:

Cation exchanger (with anionic functionalities and positively charged mobile ions)
-strong acid exchange (e.g., containing sulfonic acid groups or the corresponding salts)
-weak acid exchange (e.g., containing carboxylic acid groups or the corresponding salts)
Anion exchanger (with cationic functionalities)
-strong base exchange (e.g., containing quaternary ammonium groups)
-weak base exchange (e.g., containing ammonium groups)

Other ion-exchanging materials include homopolystyrene and acrylic based resins and Nafion, a perfluorinated polymer containing sulfonic acid heads, whose structure and properties were previously carefully reviewed.[84-88]

Cross-linkage, typically from 0.5 to 20%, controls the resin porosity.[89] Low cross-linked resins have a gel (microporous) structure, whereas higher cross-linkage degrees result in macroreticular (macroporous) resins. Porosity affects some bulk properties of the resins which have consequences on their catalytic applications, i.e. swelling, capacity, equilibration rate, and selectivity. Usually, the lower the cross-linking percentage, the higher the moisture content, the equilibration rate, the loading capacity (typically from 1.5 to 10 mequiv/g on a dry basis), and the ability to accommodate larger ions. Non-cross-linked polymers are rarely used due to their lower stability (chemical, mechanical, thermal).

Swelling of the resins in the solvent of use is crucial for their behavior. Swelling volumes were carefully investigated, and increments up to 800% upon decreasing the cross-linking percentage were frequently found.[90-92] Hence, gel type resins are generally preferred over macroporous ones due to enhanced mass transfer inside the polymer beads, resulting in good active-sites accessibility to all soluble reactants.[93]

Ion-exchange resins are commercial products commonly available in the form of small beads (16 ÷ 400 mesh, 1180 ÷ 38 μm diameter) or as membranes. Shape and size allow

Scheme 2

Y = H, Na, Li   M = metal   L = ligand   Z = PF_6, BF_4
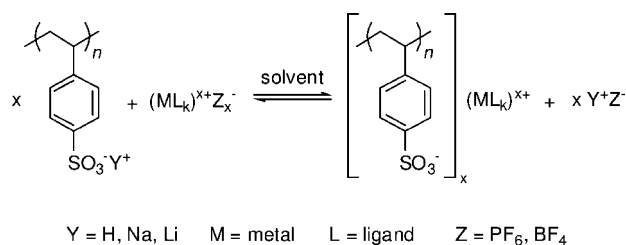
these materials to be easily and quantitatively recovered by simple filtration or decantation. This is not the case for other powdered materials often used as catalysts support (e.g., silica, zeolites, carbon, etc.). When the particle size is about 1 μm or less, they might not settle in the solution within a short time, and it would be very difficult to collect them for recycling. The separation of the catalyst thus requires centrifugation or ultrafiltration. Very fine powders may also clog or poison the reactors or the autoclaves employed in the catalytic experiments.

Immobilization of preformed, charged metal complexes onto ion-exchange resin is an equilibrium process driven by noncovalent electrostatic interactions (Scheme 2, strong cation exchanger example). The affinity and selectivity of resins varies with the ionic size and charge of the ions. Generally, the affinity is greatest for large ions with high valence.[94−96] Compared to other insoluble support materials, ion-exchange resins usually offer considerable advantages as catalysts carriers,[97] as summarized in Table 1.

The engineering of heterogenized catalyst should be accomplished with minimal chemical manipulations and energy consumption.[98] Ion-exchange resins are perfectly located in this setting: catalysts which are easy to use and to recover are readily obtainable through them. Reproducibility and ease of characterization is also ensured, which is not obvious for conventional heterogeneous catalysts. Performances, both activities and selectivities, comparable with those of the homogeneous counterparts are observable as well.

Batch or continuous flow operations with fixed beds of immobilized catalysts should be possible with minimum leaching of active species or metal impurities into the reaction solvent, particularly as far as the production of pharmaceutical precursors is concerned.[99,100] This can be an issue with noncovalently bound heterogenized catalysts, including ion-exchange resins. Nonetheless, ion-pair formation is sufficiently strong in exchange resins to allow for the uncommon advantage that the solvent in which the homogeneous catalysts is soluble can be used as the reaction medium. Viability of the use of water as solvent is also worthy to be
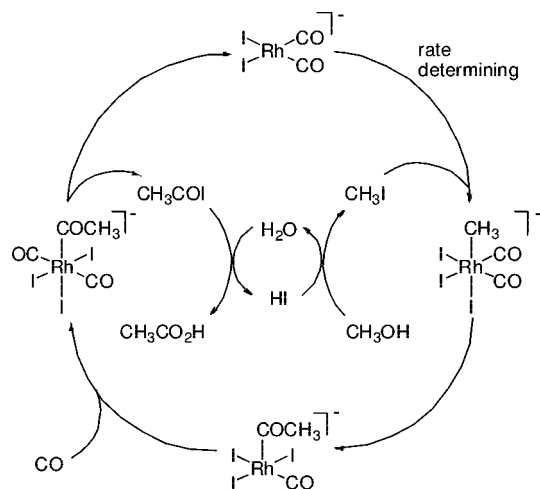
Figure 1. Proposed cycle for the rhodium catalyzed methanol carbonylation.

underlined due to its environmental implications.[101,102] The combination of the optimal resin swelling with the usual low-solubility of organometallic complexes in this medium may result in efficient catalysts and in reduced leaching.

3. Applications

3.1. Carbonylations

One of the most important examples of carbonylation reactions is the manufacture of acetic acid. More than 60% of the current industrial capacity of acetic acid is based on the so-called "Monsanto" methanol carbonylation process developed in the late 1960s.[103] The process is based on a well established homogeneous iodide/rhodium-catalyzed system operating under mild conditions (150−220 °C, 30−40 atm CO) and exhibiting high selectivity to acetic acid (99% yield from methanol).[104] Several mechanistic studies provided a detailed description of the catalytic cycle (Figure 1).[105]

The system requires a substantial quantity of water (14−15% w/w) to achieve high catalyst activity and maintain good catalyst stability because the hydration of acetyl iodide in the presence of excess water gives acetic acid and hydrogen iodide to complete the cycle. As a consequence, the homogeneous system is affected by some important drawbacks in relation to the solubility of the catalysts, the loss of the expensive rhodium metal due to precipitation in the purification steps, and the high corrosion rates caused by iodide.

Accordingly, several studies were reported, aimed at the heterogenization of rhodium catalysts for methanol carbo-

Table 1. Ion-Exchange Resins and Their Use as Support for Catalyst Immobilization

| advantages	disadvantages
commercially available in several varieties	
low-cost	
reasonably stable	
defined amounts of anchoring sites	
easy immobilization procedure	
ease of handling	
particle size allows quantitative recovery by simple filtration	
catalyst efficiency comparable to homogeneous reactions	
ease of catalyst recycle	reaction rates may decrease upon recycle
negligible to low metal leaching	leaching sometimes not acceptable for industrial applications
compatible with many reaction solvents, including water	
adaptable to the engineering of reactors	

Scheme 3

Scheme 4
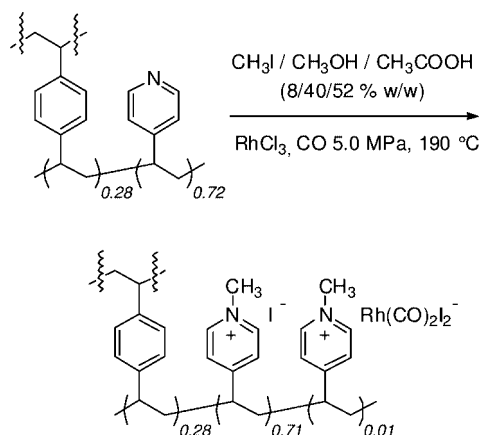
nylation on diverse solid supports.[106] The fact that all rhodium complexes involved in the catalytic cycle are anionic suggested this system to be an excellent candidate for noncovalent, ionic immobilization,[107] and, indeed, this was one of the earliest applications of molecular catalysts supported on ion exchange resins.[108,109] Most importantly, Chiyoda/UOP developed an industrial process, the Acetica Process, based on this technology.[110−112] The actual process employs beads of 33% w/w cross-linked 4-vinylpyridine/divinylbenzene copolymer resin (macroporous, Reillex 425, Reilly Corporation) as solid support.[113] Treatment of the resin with RhCl$_3$ and a methyl iodide/methanol/acetic acid mixture under reaction conditions (190 °C, 5.0 MPa carbon monoxide pressure, low water content) generates *in situ* both the *N*-methylpyridinium iodide ion-exchanger derivative and, subsequently, the immobilized catalyst, by substitution of iodide with the anionic rhodium(I) precursor [Rh(CO)$_2$I$_2$]$^−$, which forms under these conditions (Scheme 3).[114] The typical Rh loading observed for the heterogeneous catalyst is 0.8% w/w.

Investigations carried out using infrared spectroscopy and EXAFS measurements (extended X-ray absorption fine structure) indicated that the complex [Rh(CO)$_2$I$_2$]$^−$ supported on quaternized poly(4-vinylpyridine-*co*-styrene-*co*-divinyl-benzene) resins adopts an identical structure to that found in solution,[115] thus confirming the presence of the same active species in the homogeneous and heterogeneous processes.[108] This study also revealed that the immobilized [Rh(CO)$_2$I$_2$]$^−$ complex undergoes analogous reactivity and kinetics with CH$_3$I as in homogeneous phase, except for a subtle cation effect on the rate of the addition, being lower for the resin-supported complex and highest for soluble, monomeric *N*-methylpyridinium salts. However, close similarities in the rate constants suggested that the permeability of the resin to CH$_3$I is high and no mass-transfer limitations arise in the heterogeneous phase.

Recent studies on Reillex 425 showed that this resin markedly increased its swellability in water/methanol/acetic acid mixtures after iodomethylation.[116] The combination of SEM (scanning electron microscopy), ISEC (inverse steric exclusion chromatography), and ESR (electron spin resonance) techniques indicated this material develops a well defined nanoporosity and a good molecular accessibility in the swollen state that may help rationalize the catalytic efficiency of the ionically immobilized rhodium precursor.

The use of an heterogenized catalyst in the Acetica^{TM} Process displays several advantages over the conventional homogeneous-phase system:[117−119]
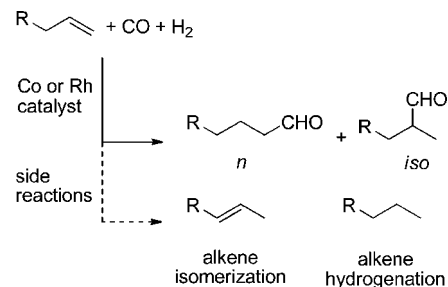
-high reactor productivity can be obtained because high catalyst concentrations are achievable without solubility limitations;
-rhodium loss is significantly reduced, as no catalyst separation from the reaction liquid is needed;
-the lower water content required (3−7%) minimizes byproduct formation (propionic acid and CO$_2$ *via* the water gas shift reaction) and corrosion, due to reduced hydrogen iodide content;
-tolerance of the resin to elevated temperatures and pressures provides very stable catalysts featuring no deactivation after prolonged continuous operations.

3.2. Hydroformylations

The catalytic homogeneous hydroformylation of alkenes to aldehydes is one of the largest industrial processes, accounting for a production of more than 6 × 10^6 tons per year as plasticizers, detergents, and fragrances (Scheme 4).[120]

Heterogenization of soluble hydroformylation catalyst, aimed at precious metals recovery and facile product separation, was attempted using a variety of materials,[121] including ion-exchange resins.[122] Hydroformylation of 1-hexene was recently accomplished using the known TPPTS-Rh(I) catalyst,[123] after immobilization onto macroporous Amberlite IRA-93 anion exchange resin (TPPTS = sodium triphenylphosphine trisulfonate).[124] The heterogeneous catalyst was prepared by derivatization of the resin with the phosphine ligand by anion exchange, followed by rhodium complexation (Scheme 5). The final rhodium content in the dry resin was ca. 0.2% (w/w).

The solvent used in the hydroformylation proved to be extremely important in determining the selectivity and the rate of the reaction. Several solvents were screened for conversion, hexene isomerization, selectivity to aldehyde, and *n/iso* ratio, with the former two being higher for benzene (99.3% conversion, 53.4% isomerization) and cyclohexene (99.0%, 58.7%), and the latter two for ethanol (71.4% selectivity, 2.31 *n/iso* ratio). Although no explanations were given for the observed solvent effect, a kinetic study carried out in ethanol revealed the reaction to be first order in hydrogen partial pressure and 1-hexene concentration with a maximum in the rate depending on the carbon monoxide partial pressure.

Interestingly, unlike the case of the homogeneous phase reaction, the *n/iso*-aldehyde ratio remained constant upon reaction progress. This behavior was explained in terms of hindered access of the isomerized olefin to the resin bound catalyst, which, thus, difficultly undergoes hydroformylation to the branched aldehyde. The performance of the heterogeneous catalyst was also checked on recycling. No major changes were observed in activity, selectivity, *n/iso* ratio, and rhodium leaching (below 0.1 ppm), over five catalysis

Scheme 5
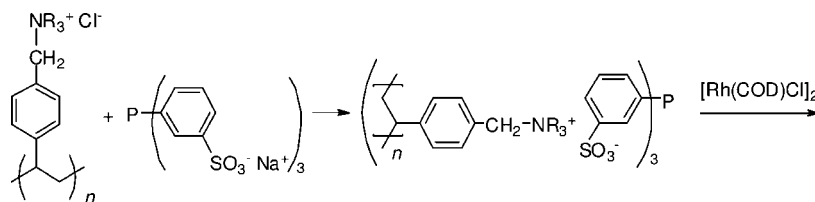
Scheme 6

Scheme 7
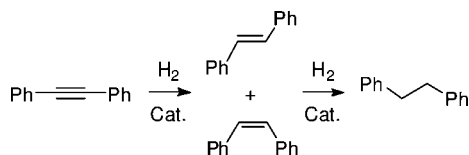
cycles. Turnover frequencies comparable to those found for comparable homogeneous systems were observed throughout (ca. 3000 h^{-1}).[121b]

3.3. Hydrogenations

The catalytic hydrogenation of C=C and C=O bonds is among the most useful tool for the production of fine chemicals, including pharmaceuticals, agrochemicals, and fragrances.[125−127] Lately, alkynes, cinnamaldehyde, and acetophenone were hydrogenated using the well-known water-soluble ruthenium(II) and rhodium(I) complexes [RuCl$_2$(*m*tppms)$_2$]$_2$ and RhCl(*m*tppms)$_3$,[128−130] after immobilization on commercially available anion-exchange resins (*m*tppms = [*m*-sulfonatopheny]diphenylphosphine sodium salt).[131] The DEAE-Molselect (strong, diethylaminoethyl groups), QAE-Sephadex (strong, diethyl(2-hydroxypropyl)aminoethyl groups), and Lewatit MonoPlus (strong, quaternary amine) exchangers were used as supports.

The ruthenium derivative showed to hydrogenate diphenylacetylene to *cis*-stilbene with good selectivity under mild reaction conditions (toluene/ethanol = 1/1, 30−80 °C, 30 bar H$_2$) (Scheme 6). The conversion increased by increasing the temperature, albeit with a decrease in selectivity. At the optimal temperature (50 °C), up to 83% selectivity was observed with an efficiency higher than that of the analogous water/toluene biphasic system (TOF = 25.1 h^{-1} heterogeneous, 1.96 h^{-1} biphasic).[132a] The catalyst was reused up to 20 times with only a slight decrease in activity and selectivity. No data were reported on possible metal leaching, however.

Consistently with the known full-hydrogenation attitude of rhodium, the Rh catalyst was less selective compared to ruthenium in diphenylacetylene reduction, providing 1,2-diphenylethane in 62% yield, at 87.5% total conversion (50 °C, 30 bar H$_2$).

As for the hydrogenation of α,β-unsaturated carbonyl compounds by molecular hydrogen, this can be efficiently accomplished using transition metal catalysts, although chemoselectivity may be an issue.[133] The hydrogenation of the C=C bond, in fact, generally competes favorably with that of the C=O group.[134]

[RuCl$_2$(*m*tppms)$_2$]$_2$ immobilized on Lewatit MonoPlus *selectively* hydrogenated *trans*-cinnamaldehyde (1) to 3-phenylpropanal (2), in low conversions (18% at 60 °C, 80 bar H$_2$, ethanol, TOF = 5.2 h^{-1}) (Scheme 7). Interestingly, this result compares positively with the selectivity provided by both parent homogeneous and biphasic systems.[132b] The
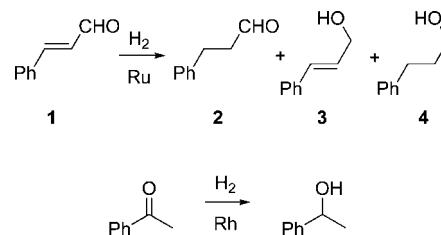
homogeneous phase RuCl$_2$(PPh$_3$)$_3$/toluene catalyst gave 3-phenyl-1-propanol (4) in 42% yield, with a selectivity to the saturated aldehyde of 23%, under comparable conditions (100 °C, 30 atm H$_2$, TOF (2) = 6.3 h^{-1}). By contrast, cinnamyl alcohol (3) was the major product (83%) using the 1/1 = water/toluene [RuCl$_2$(*m*tppms)$_2$]$_2$ two-phase system (100 °C, 30 atm H$_2$, TOF (2) = 1.2 h^{-1}), with a selectivity to 2 of 15%.[135]

Previous studies carried out on the analogous chlorobenzene/water−phosphate buffer biphasic system demonstrated the selectivity of the reaction to be ruled by the relative concentrations of the catalytically active species, either the monomeric [H$_2$Ru(*m*tppms)$_4$] or [HRuCl(*m*tppms)$_3$] complex.[132c−e] The former, which is the predominant ruthenium species at pH values greater than 6, led to the preferential production of alcohol 3 (up to 95% selectivity) *via* the classical Ru-assisted hydride transfer mechanism to the carbonyl group.[132e,f,136] The latter, which dominates below pH 5, gave aldehyde 2 as the main product (ca. 60%), *via* dissociation of a phosphine ligand followed by coordination and hydrogenation of the C=C bond (Figure 2).[132b,e,g,h]
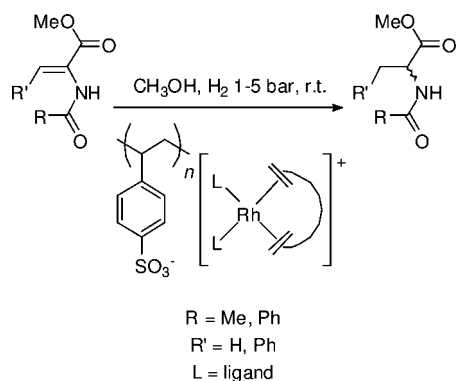
Although a rationale for the selectivity observed using ion-exchange supported tppms catalysis has not been provided, the above findings demonstrate a strong influence of the ionic solid support on the performance of the immobilized molecular catalysts and suggest that the effect on the selectivity can be attributed to the subtle role played by the support in the stabilization of intermediates similar to those sketched in Figure 2, maybe as a consequence of favorable dipolar interactions of the C=O group with the support or of the reduced steric hindrance of these intermediates.

It must be noted that the best catalysts to date, both in term of efficiency and (stereo) chemoselectivity, in the reduction of the C=O bond in α,β-unsaturated carbonyl compounds is the homogeneous, bifuctional system developed by Noyori based on [RuCl$_2$(phosphane)$_2$(1,2-diamine)] and an alkaline base, which produces cinnamyl alcohol from cinnamaldehyde in 99.9% selectivity.[137]
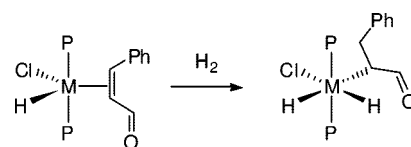
Figure 2. Proposed intermediates for the catalytic hydrogenation of the C=C bond in α,β-unsaturated aldehydes. See ref 132b.

Scheme 8

R = Me, Ph
R' = H, Ph
L = ligand

Figure 3. Typical ESEM image of a DOWEX 50WX2 resin bead containing the immobilized catalyst precursor [(−)-(TMBTP)Rh(N-BD)]$^+$ (TMBTP = 4,4′-bis[diphenylphosphino]-2,2′,5,5′-tetramethyl-3,3′-bithiophene, NBD = bicyclo[2.2.1]hepta-2,5-diene, back-scattered electrons, 1200 magnifications, 20 KeV, 1 Torr). Reproduced with permission from ref 59, page 5670. Copyright Wiley-VCH Verlag GmbH & Co. KGaA.
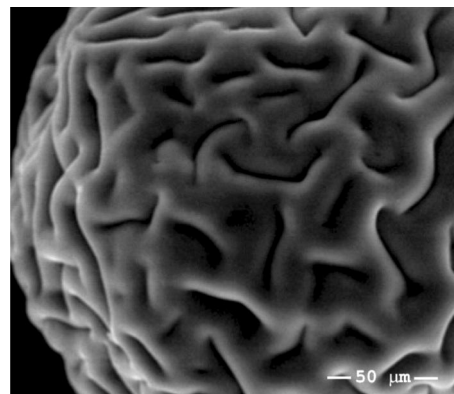
RhCl(*mt*ppms)$_3$ immobilized on DEAE-Molselect resin provided 1-phenylethanol from acetophenone in 15% yield (60 °C, 80 bar H$_2$, TOF = 11.2 h^{-1}, Scheme 7), which, however, cannot compare with the activity observed in other homogeneous catalyst systems.[134a,137e]

It is worth noticing that all reactions described in this section, involving immobilization onto ion-exchange resin, were carried out by packing the catalyst into a microfluidics-based flow system (H-Cube), thus showing this heterogenization technology to be suitable for the engineering of reactors and, eventually, for the scale-up to production processes.[138]

3.3.1. Asymmetric Hydrogenations

Asymmetric hydrogenation is likely the most investigated application of ion-exchange resin-supported molecular catalysts.[139−145] A survey of the literature on the topic was released in 2005.[59] Chiral homogeneous catalysts producing optically active chemicals, with exceptionally high enantioselectivities and yields, are well established compounds whose properties were widely described in the literature.[146−148] Typically, they consist of noble metal complexes bearing expensive, highly elaborated, single-enantiomer ligands. Their recovery and recycle is, therefore, a major economical need. The immobilization of these catalysts onto ion-exchange resins is usually attained efficiently under smooth conditions (metal loadings 0.3−1.5% w/w, using strong cation exchange resins).

The heterogenized rhodium catalysts so obtained show enantioselectivities comparable with those of the analogous homogeneous phase reactions in the asymmetric hydrogenation of prochiral activated olefins, though with slower reaction rates (Scheme 8). Representative literature examples are summarized in Table 2.

Easy, *in situ* catalyst recycling is possible, featuring negligible to very low rhodium leaching (0.3−2%), but with the common trend of a drop in the catalytic activity in the second and following cycles.

An in-depth investigation based on ESEM (environmental scanning electron microscopy), EDS (energy dispersive X-ray spectrometry), NMR (nuclear magnetic resonance), and GF-AAS (graphite furnace atomic absorption spectroscopy) analysis suggested that catalyst deactivation might be attributable to a binding interaction between the excess of noninnocent sulfonato groups from the resin and the rhodium centers after consumption of the substrate in the first hydrogenation step (Rh coverage of anionic sites ca. 3%).[149,150] However, the factors responsible for the activity decrease in these systems have not been completely clarified to date. Surface EDS microanalysis maps recorded on sections of the catalyst beads showed the rhodium to be evenly distributed within the solid support (see Figure 3 for an electron image of [(−)-(TMBTP)Rh(NBD)]$^+$ catalyst on strong cation exchange resin). This evidence indicated that the methanol, commonly used both for anchoring and catalysis due to effective swelling of the resin in this solvent, diffuses freely through the support, thus ensuring proper access of the reactants to the active sites. The metal loss was ascribed to catalyst decomposition due to fortuitous ligand oxidation on the basis of ^{31}P{^{1}H} NMR experiments.

The above hypotheses were recently partially confirmed by an asymmetric hydrogenation study carried out on methyl-2-acetamidoacrylate using [((*R*)-Monophos)Rh(COD)]$^+$ im-

Table 2. Asymmetric Hydrogenations Using Cationic Rh(I)−Chiral Diphosphine Ligand Catalysts Immobilized onto Ion-Exchange Resins[a]

chiral ligand	R/R′	resin	heterogeneous		homogeneous		ref
			TOF(h^{-1})	ee (%)	TOF (h^{-1})	ee (%)	
Ph-β-glup	Me/Ph	G-4-H$^+$	500^b	94.1	6^b	91.1	139
		G-2-H$^+$	135^b	94.9			139
		G-1-H$^+$	60^b	95.5			139
		G-0.5-H$^+$	38^b	95.3			139
	Me/H	Wofatit KP2	15^b	94.3	0.9^b	90.9	141
Propraphos	Me/Ph	G-0.5-Li$^+$	10^b	84.6	35^b	85.5	139
BDPP-(*p*NMe$_2$)$_4$	Ph/Ph	Nafion-NR-50	400	50	1200	57	142
DIOP	Me/H	DOWEX 50WX2	38	54.6	40	57.3	149
TMBTP	Me/H	DOWEX 50WX2	52	99.9	50	99.9	149

^{a} In methanol, room temperature, H$_2$ pressure 1−5 bar. Substrate/catalyst ratio 100/1. ^{b} Half-life time t/2 (min).

Scheme 9

Scheme 10

Y = axial ligand
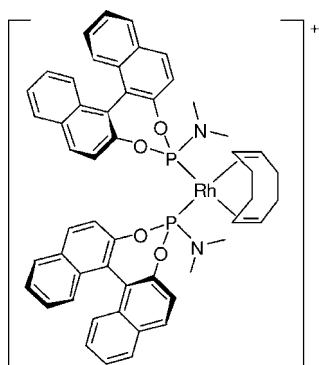
mobilized on Nafion (Scheme 9).[151] There, the activity and leaching of the supported catalyst were directly correlated to the swelling of Nafion and to the solubility of the molecular catalyst in the solvent used, respectively, by comparison with other insoluble anionic supports: the former was highest for water and methanol, while leaching was lowest for water. Phosphotungstic acid on alumina was shown to be the best support in this application, in terms of activity and leaching, whereas Nafion was the poorest. Negative effects due to immobilization by encapsulation rather than on ionic interactions in Nafion were hypothesized on these basis. Recycling was once again demonstrated with almost complete retention of selectivity and activity over four consecutive runs (water, 5 bar H_2, 20 °C, conversion 100%, TOF 17 h^{-1}, ee 90%, Rh loss 0.01 mg/L. Homogeneous: TOF 1700 h^{-1}, ee 97%, CH_2Cl_2. Data from ref 151).

3.4. Oxidations

Previous examples of oxidations of organic substrates by ion-exchange-supported homogeneous catalysts include the oxidation of dihydrogen;[152] the oxidation of hydrocarbons,[153,154] alcohols, ketones and thiols;[155−161] the hydroxylation of aromatics;[162,163] and the epoxidation of olefins, particularly by immobilized metalloporphyrins.[164−171] More recently, applications in the field concentrated on the epoxidation and dihydroxylation of alkenes, on photooxidation reactions, and on other few examples of miscellaneous oxidations. These are briefly discussed in the following sections.

3.4.1. Alkene Epoxidations

Dicationic Mn(III)-salen complexes immobilized on the macroporous strong cation exchange resins Dowex MSC-1 (exchange capacity 4.5 mequiv/g) and Amberlite IRA-200 were used as heterogeneous epoxidation catalysts of different alkenes by sodium periodate (Scheme 10).[172,173]

The ionic bonding between salen and the resins was so strong that neither common organic solvents nor acidic or electrolyte water solutions eluted the complex from the support. Catalysts with metal loading of 0.063 mmol/g (1.4% of exchange sites) proved to be quite efficient (TOF up to 50 h^{-1}) and selective (up to 100%) in the epoxidation of cyclic and linear alkenes, eventually bearing aromatic substituents, in aqueous acetonitrile (Table 3). Analogously to the parent homogeneous catalyst, a positive effect of a nitrogen base axial coligand was observed. Catalysts' reuse was achieved with ease, though with a significant loss of activity and leaching (<1%) in each run, which was ascribed to the degradation of the manganese complex.
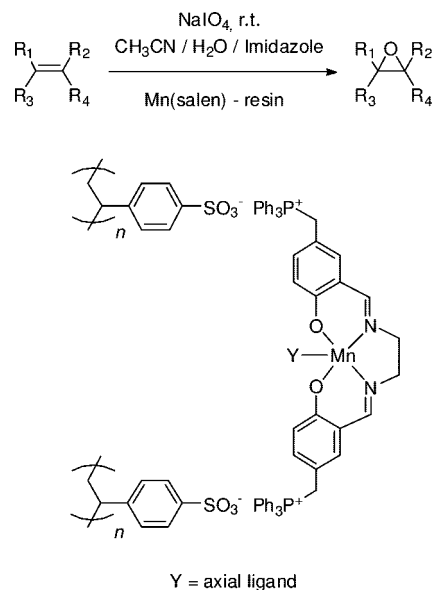
Questions may be raised on how the charge of a ionic reagent (e.g., periodate) influences its penetration into the interior of an ion-exchange resin. Indeed, at low ionic strength and neutral pH values, anion transport through Nafion membranes is known to be hindered by electrostatic repulsion forces between the anions and the sulfonate fixed-charge sites in the membrane.[174a] However, lowering the pH or increasing the ionic strength of a solution in contact with strong cation exchange membranes causes the suppression of electrostatic repulsions and a ready diffusion of anions through the membrane.[174b,c] Diffusion coefficients through Nafion were measured for Cl$^-$ and I$^-$ in the presence of their zinc salts,[174d] for bisulfate anion in 0.001−1 M sulfuric acid,[174a] and for bisulfate and Cr(VI) anions at high salt concentrations (0.05−1.3 M) and low pH values.[174e] Diffusivities comparable with those observed in large pore alumina ceramic diaphragms, with no negative fixed-charges, were obtained in this latter case (ca. 0.8−1.1 × 10^{-6} cm^2/s).

In the case at hand, i.e. periodate and fixed-charge sulfonate resin, we must assume that the ionic strength (NaIO$_4$ 0.13 M) is responsible for the smooth penetration of the anionic oxidant into the resin and, thus, for the remarkable activity observed. Replacement of the charged reactant with uncharged ones (H$_2$O$_2$, *tert*-BuOOH) led invariably to lower reaction rates, whereas addition of strongly basic amine cocatalysts did not significantly affect the catalyst's activity (rate enhancement was observed for strongly coordinating bases only).

The catalytic asymmetric epoxidation of unfunctionalized olefins by *meta*-chloroperbenzoic acid was accomplished using immobilized, sulfonato chiral salen Mn complex (Scheme 11).[175] A strong anion exchanger obtained from a commercial Merrifield resin after quaternization with tri-

Table 3. Examples of Alkene Epoxidations Using Mn(salen) on Dowex MSC-1 Based Catalysts[172]

alkene	TOF (h^{-1})	selectivity (%)
cyclooctene	50	
R-limonene	50	65 (1,2/8,9)
trans-stilbene	14	100 (*trans*)
cis-stilbene	15	55 (*cis/trans*)
1-heptene	21	

Scheme 11

resin-(R,R)-**1**

Scheme 12

	yield %	ee %
run 1	100	96
run 2	96	96
run 3	90	96
run 4	88	96

Conditions: m-CPBA, N-methylmorpholine oxide,
resin-(R,R)-**1** (1% mol), CH₃CN, - 20 °C, 5 min. Data
from ref. 175
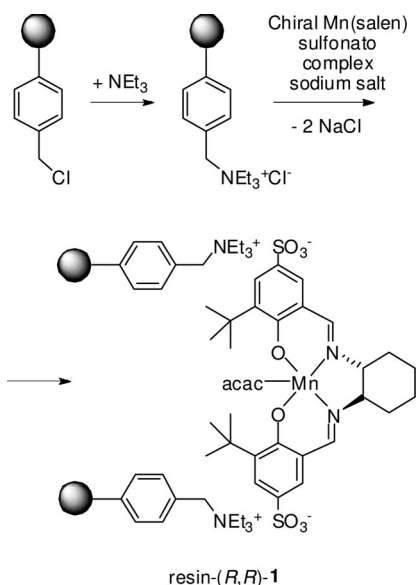
ethylamine was used as solid support (chloromethylated styrene−divinylbenzene copolymer, 2% cross-linkage, gel type).

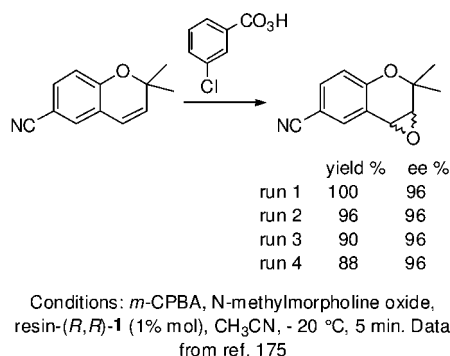The chiral epoxides were obtained faster, with higher enantioselectivities, lower catalyst deactivation, and metal leaching, compared both to the homogeneous catalyst and to other noncovalently supported heterogeneous systems using diverse porous materials (silica, Mg-Al-LDH). Selected figures are summarized in Table 4. No explanations for the observed behavior were given, however.

The resin-bound catalyst could be recovered by filtration and reused without loss in ee and only minor changes in activity. Data for 6-cyanochromene are reported in Scheme 12, as a representative example. Metal leaching was negligible in each run.
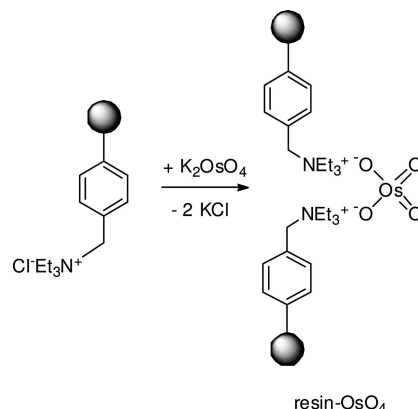
Table 4. Asymmetric Epoxidations of Olefins by m-CPBA Using Immobilized Chiral salen Mn Catalysts[175]

alkene	support	TOF (h⁻¹)	ee (%)
styrene		590	25
	silica	590	40
	LDH	1250	44
	resin	1250	48
trans-stilbene		100	18
	silica	50	42
	LDH	1250	29
	resin	1250	35

Scheme 13
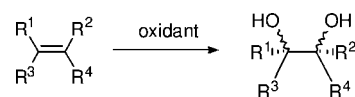
Scheme 14

resin-OsO₄

3.4.2. Asymmetric Dihydroxylations

Recent examples of dihydroxylation of alkenes by exchange-resin-supported catalysts are limited to the asymmetric version of this reaction (Scheme 13).[176]

Choudary et al. described an innovative system based on osmate anions immobilized by ion-exchange on a strong-base exchanger. The resin used was the quaternary ammonium Merrifield polymer mentioned in the previous section (Scheme 14).[177,178] The final polymeric material showed a metal content of 0.64 mmol Os/g and a BET surface area of 317 m²/g. Reuse of the catalyst was further motivated by the cost and toxicity of osmium in this case.

The heterogenized complex resin-OsO₄ was used in the osmium-assisted asymmetric dihydroxylation of olefins, using various co-oxidants, to give chiral vicinal diols after in situ complexation of the metal center with the chiral ligand (DHQD)₂PHAL ((DHQD)₂PHAL = dihydroquinidine 1,4-phthalazinediyl diether) (Figure 4).

The process involves the known Os(VIII)/Os(VI) redox cycle, in which the oxidation of resin-OsO₄ by the co-oxidant, followed by the interaction of the Os(VIII) oxo-complex with the olefin and the ligand, forms the osmium(VI) monoglycolate ester, whose hydrolysis provides the diol, with regeneration of the catalyst precursor.[179] It is interesting to note that neither OsO₄²⁻ nor Os(VIII) species are leached from the support during the catalytic reaction. This means that Os(VI) is held on the resin by strong interactions and that the Os(VIII) lifetime is too short to detach neutral OsO₄ from the support. The possibility that Os(VIII) is firmly anchored on the resin is ruled out by the fact that osmium leached into solution when the reaction was carried out in the absence of olefin.

Irrespective of the co-oxidant used (either N-methylmorpholine N-oxide (NMO), Fe(CN)₆³⁻, or O₂), the ion-exchanged catalyst showed superior efficiency, in terms of both activity and selectivity, compared to analogous silica and polymer bound recyclable systems (e.g., Kobayashi's ABS- and PEM-MC OsO₄ catalysts).[180] Data for the asymmetric dihydroxylation of methylstyrene are reported in Table 5 as a representative example.

This novel, favorable behavior was ascribed to proper swelling of the resin in the reaction medium (H₂O/t-BuOH),
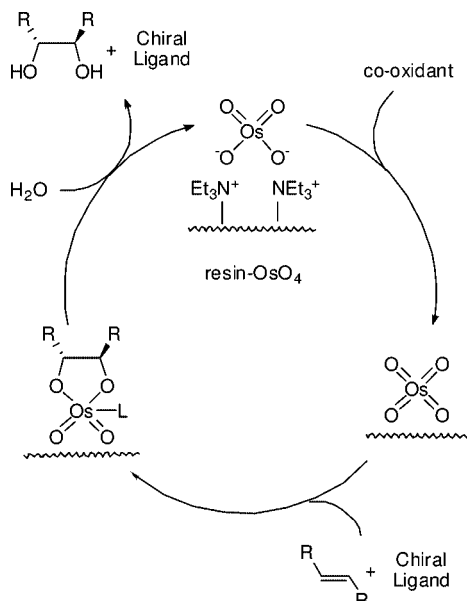
Figure 4. Proposed mechanism for the resin-OsO$_4$ catalyzed asymmetric dihydroxylation of olefins. Co-oxidant, NMO; solvent, t-BuOH/H$_2$O; rt; chiral ligand = (DHQD)$_2$PHAL. See ref 177.

which enables easy access of all reactants to the metal active sites inside the pores. Excellent yields and ee's were observed for acyclic, cyclic, and mono-, di-, and trisubstituted olefins. The catalyst could be quantitatively recovered and reused by simple filtration, showing consistently good and constant efficiency over five runs, independently from the nature of the co-oxidant and the solvent. Data for the asymmetric dihydroxylation of α-methylstyrene are reported in Scheme 15, as an example.

3.4.3. Various Oxidations

Cytochrome P450 biomimetic model compounds based on iron(III) porphyrins showed interesting nitric oxide synthase-like activity, i.e. the catalytic oxidation of L-arginine to nitric oxide and L-citrulline by hydrogen peroxide (Scheme 16), when supported on commercial ion exchange resins.[181] The strong cation exchanger Dowex 50WX8 (Na$^+$ form, gel type) was used to immobilize the cationic porphyrins FeTPAP (*meso*-tetrakis(N,N,N,-trimethylammoniumphenyl)porphyrin iron(III) chloride) and FeTMPyP (*meso*-tetrakis(1-methylpyridinium-4-yl)porphyrin iron(III) chloride). The anionic porphyrins FeTPPS (trisodiumdodecaaquatetrakis(p-sulfonatophenyl)porphyrinato iron(III)) and FeTCP (trisodium bisaquatetrakis(p-carboxyphenyl)porphyrinato iron(III)) were immobilized on the anion exchanger Dowex 1×8 (chloride form, gel type). Heterogenization of metalloporphyrin cata-

Table 5. Asymmetric, Os-Supported Catalytic Dihydroxylations of α-Methylstyrene[a]

support	TOF (h^{-1})	ee (%)	ref
resin[b]	7.8	91	177
LDH[b]	7.4	90	177
silica	7.5	90	177
PEM-MC[c]	3.4	76	180a
ABS-MC[b]	4.1	78	180b

[a] Chiral ligand (DHQD)$_2$PHAL. [b] Co-oxidant NMO. [c] Co-oxidant K$_3$Fe(CN)$_6$.

Scheme 15
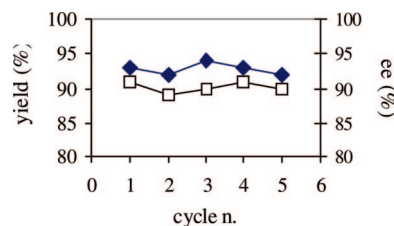
Conditions: NMO, resin-OsO$_4$ (1% mol), (DHQD)$_2$PHAL (1% mol), t-BuOH:H$_2$O, r.t.
◆ yield %, □ ee %.
Data from ref. 177

Scheme 16

L-arginine   L-citrulline
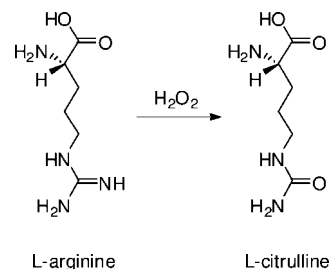
lysts was skillfully used to prevent catalyst deactivation by μ-oxo dimers formation.[182]
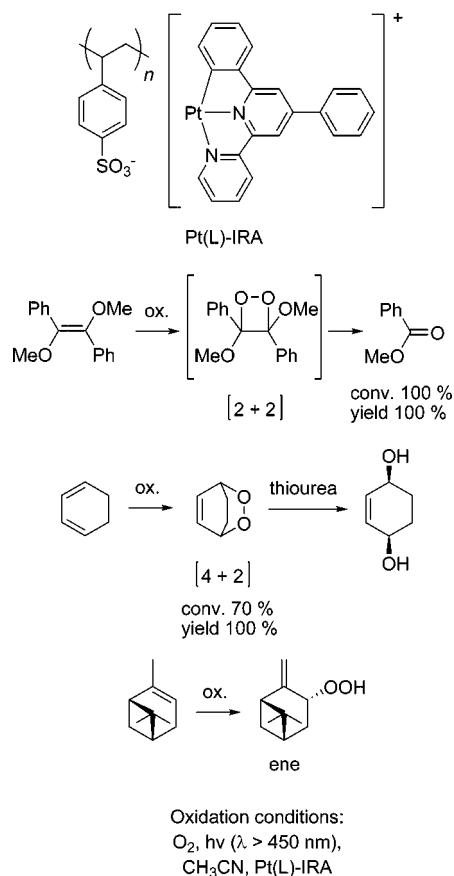
Indeed, compared to the corresponding homogeneous catalysts, the supported iron porphyrins are characterized by both higher activity and stability. Yields 30 to 50 times higher than those observed in the homogeneous phase were observed with negligible metal leaching (typical TOF 68−9 and 1−0.3 h^{-1}, for heterogeneous and homogeneous reactions, respectively). Contrarily, the soluble iron porphyrins were almost completely oxidized by H$_2$O$_2$ under the same reaction conditions (water, pH 7.8, 25 °C).

The photocatalyzed oxidation of alkanes and alkenes was recently achieved through resin-supported tungsten and platinum derivatives. Expensive platinum(II) bipyridine complexes loaded on IRA-200 exchanger were easily recovered by simple filtration and recycled in the O$_2$ oxidation of olefins, upon irradiation with visible light (Scheme 17).[183] The activity of the catalyst was very high, providing [2 + 2], [4 + 2] cycloaddition or ene reaction products, which were converted to the corresponding aldehydes, ester, or diols, depending on the substrate, in good yields. The oxidation rates were dependent on the Pt loading but decreased only slightly over ten consecutive runs.

Similarly, the known photooxidation catalyst decatungstate W$_{10}$O$_{32}$$^{4-}$, whose immobilization on silica and polymeric membranes was already explored,[184−186] was anchored onto anion exchange resins and used in the photocatalytic partial oxidation of cyclohexane with molecular oxygen (Scheme 18).[187]

Cross-linked poly(4-vinylpyridine) methyl chloride quaternary salts, poly(4-vinylpyridinium tribromide) and poly(4-vinylpyridinium p-toluenesulfonate), were used as solid support (Scheme 19). The most effective catalyst was that immobilized onto the cross-linked polymer (TON = 4.41 at catalyst concentration 407 μmol dm^{-3}, in acetonitrile), with no detectable amount of metal released into solution upon reuse, but with a decrease in the turnover number of ca. 20% in two subsequent 6 h reactions. Catalyst loading on the support affected the

Scheme 17

Scheme 18

Scheme 19

product selectivity but not the reaction rate. The lower loading promoted cyclohexanone production whereas the catalysts with high decatungstate content favored cyclohexyl hydroperoxide generation.

The degradative catalytic oxidation of 2,4-dichlorophenoxyacetic acid by H_2O_2 was accomplished with noticeable efficiency (93% conversion after 30 min), in the presence of ferrous ions immobilized on Amberlite IR-120 (sulfonic acid exchanger, 8% cross-linked, gel type, 26 mg Fe/g resin), UV light, and oxalate.[188] The heterogenized catalyst could be easily separated from the solution by filtration and recycled. Enhancement of the reaction rate with reused catalysts was attributed to massive Fe^{2+} leaching in solution upon irradiation, however.

Scheme 20

3.5. Polymerizations

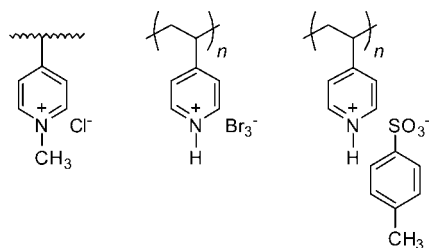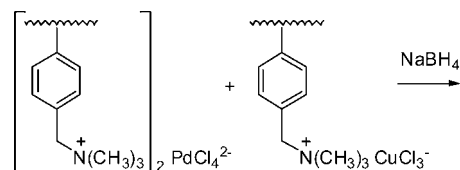The development of supported catalysts for olefin polymerization and copolymerization is mainly motivated by the cost and the environmental impact of products purification using homogeneous catalysts and by the need to reuse the expensive metal precursors, particularly in the scale-up to production processes.[189,190] A limited use of ion-exchange resin supports was reported in recent years.

A hybrid nickel−copper catalyst was described consisting of Ni^{2+} ions immobilized onto a macroporous, weak cation exchange resin (cross-linked polyacrylate, carboxylate derivative, Ni loading 1.04×10^{-4} mol/ g resin) and a Cu(II) complex (1 mol % CuCl2/tris[2-(dimethylamino)ethyl]amine), that was used in the controlled radical polymerization of methyl methacrylate.[191] The catalyst showed high activities, providing polymers with reasonable polydispersity (M_w/M_n = 1.26) at 90% conversion after 68 h (90 °C, m-xylene, MMA/Ni = 2000). The soluble copper cocatalyst was added with the aim to achieve a better polymerization control, due to its radical deactivator properties.[192] The heterogeneous nickel catalysts could be recovered by simple centrifugation and recycled with essentially the same activity, without any regeneration treatment. The metal residue in the product polymer was quite low (Ni 7 ppm, Cu 29 ppm).

The synthesis of polyketones by copolymerization of carbon monoxide and styrene was performed using a sulfonated-resin-supported palladium catalyst, and its recyclability was explored.[193] The immobilized catalyst showed activities noticeably lower than that of the corresponding homogeneous catalyst (143 g copolymer/g $Pd^{-1} \cdot h^{-1}$). Nonoptimized experiments proved that the catalyst can be reused, though with a decrease in efficiency and with significant metal leaching.

3.6. Miscellaneous

The selective, catalytic reduction of NO_3^- to N_2 with molecular hydrogen is an attractive way to purify low nitrate content water to drinking limits.[194] A bimetallic Pd−Cu system based on metal(II) anionic chloro complexes immobilized onto a strong anion exchanger (Dowex 1×4, gel type, tetraalkylammonium chloride) was used for this purpose and characterized by several techniques, including SEM, XRMA (X-ray microprobe analysis), XPRD (X-ray powder diffraction), and TEM (transmission electron microscopy).[195] The reduction of the immobilized complexes with NaBH4 in the liquid phase afforded the final catalyst in the form of very small or amorphous metallic palladium and copper nanodomains, evenly distributed within the resin beads (loadings Pd 4.10% w/w, Cu 0.95% w/w, Scheme 20). These were shown to be quite efficient (61% conversion after 135 min, 25 °C, water pH = 6) and selective (N_2 93.8%) in the reduction of nitrates, albeit less active than the corresponding alumina supported catalyst. Copper and palladium leaching in solution was below the detection limit.

The immobilized chiral salen Mn complex described previously in section 3.4.1 (Scheme 11) was successfully

Scheme 21

employed in the catalytic oxidative kinetic resolution of racemic secondary alcohols in water, using PhI(OAc)$_2$ as oxidant (Scheme 21).[196]

Conversions and enantiomeric excesses of the unreacted alcohols were only slightly lower than those obtained in the homogeneous phase catalysis, being highest for 1,2,3,4-tetrahydro-1-naphtol (TOF 134 h^{-1}, ee 96%). The selectivity factors were similar but modest in any case (ranging from 2.4 to 9.2). The heterogenized catalyst was filtered and reused with almost constant efficiency and without Mn leak into solution.

4. Conclusions

Previous and recent findings on the use of ion-exchange resins as support for the heterogenization of homogeneous chemical catalysts provide clear evidence of the effectiveness of this technology.

In one word, compared to other more sophisticated immobilization strategies and materials, this approach is characterized by its *simplicity*: easy to use and to recycle heterogeneous catalysts are readily obtained from low-cost, commercially available materials. The major benefits of the method include the following:

(1) versatility—in terms of variety of supported catalysts and reactions performed;

(2) efficiency—the activities and selectivities observed are comparable, and sometimes even better, with those of the free catalysts;

(3) quantitative recoverability;

(4) good stability—mechanical, thermal, and chemical;

(5) modularity—a proper combination of the resin type, supported catalysts, and immobilization strategy allows a systematic design of new heterogeneous catalysts.

Some broad conclusions concerning the activity and the selectivity of resin-supported catalysts may be gathered from literature examples. As a general rule, the activity of resin-supported catalysts is primarily governed by the swelling of the resin in the reaction solvent, that is, by its porosity at the microscale level and by its cross-linkage at the molecular level. Proper swelling of the resin ensures efficient mass transport throughout the support and faster reaction kinetics. Additionally, use of gel-type, low cross-linked resins usually provides good dispersions of the active species in the organic polymer, which result in an enhanced stability and performance of the supported catalysts. Site-isolation effects may also play an important role, especially in those processes (e.g oxidations) in which the formation of inactive dimers limits the catalyst functionality in solution. The interaction of the molecular catalyst with either the functional sites or the bulky polymer architecture of the resin may produce a favorable, confined nanoenvironment which is not found in the homogeneous phase.[35,58,197]

The effect of the ionic support on catalyst selectivity is evident but more difficult to predict. Hindered access of particular reaction intermediates to the catalysts' active site or stabilization of an unusual catalysts geometry, either by steric constraints or by electrostatic interaction, may be responsible for the selection of specific reaction pathways,

when high selectivities are observed. The anion influence on the enantioselectivity in catalytic asymmetric reactions was previously demonstrated in solution.[198] Further studies aimed at elucidating these relationships in ionically immobilized catalysts are awaited in the future.

Drawbacks of ion-exchange resin are occasional and limited to catalyst deactivation and/or metal leaching. Advances in the field should mainly address these critical issues. The functional groups bound to the polymer backbone seem to play a role in the catalytic activity decrease, at least in asymmetric hydrogenation reactions, where the catalytic efficiency drop was associated with the strong interaction between the sulfonato groups on the polymer and the metal center, after the first hydrogenation cycle. The effect of the counterion on the homogeneous phase reaction rates was highlighted in the past,[198,199] where the hydrogenation rate was shown to decrease across the series (Al[OC(CF$_3$)$_3$]$_4$)$^-$ > [B(C$_6$F$_5$)$_4$]$^-$ > PF$_6$$^-$ ≫ BF$_4$$^-$ > CF$_3$SO$_3$$^-$. This suggests that the introduction of "innocent", noncoordinating exchanger groups on the resin could be a useful strategy to successfully combat activity loss in resin-supported catalysts. The recent preparation of borate polystyrene colloids and fluoro-borate polyelectrolytes has to be considered with great interest in this regard.[200,201]

In order to gain high activities by resin-supported catalysts, further aspects of innovation are foreseen in relation to the materials shape and size. While the importance of obtaining precise information on the morphology, size, pore volume, and solvent mobility was already stressed before,[63,202] other macroscopic physical forms of porous ion-exchange resins may be of great relevance in order to overcome the diffusion limitations found with conventional beads, i.e. fibers[203−207] and (open-celled) monoliths.[208−212] A number of fibrous materials are available in the form of woven or nonwoven textiles, and some of them could be functionalized into ion-exchange fibers by grafting sulfonic or quaternary ammonium groups. With respect to powder and pellets, fibers have flexible structures and excellent mass transfer characteristics. They may find applications in liquid-phase operation, for their low diffusion resistance, and in three-phase operation for their low-pressure drop. Fibers may be used in several forms, and hence, they are expected to be easier and cheaper to install and disassemble than monolith-based reactors.

Porous monolith-type ion exchangers, either anion or cation exchangers, are three-dimensional open-cellular structures with 5−50-μm diameter pores and porous volumes of 8−10 mL/g, instead of 0.5−2 mL/g for usual resins. Compared with conventional exchangers, they have multiple advantages: they are easier to pack in a column, they have much higher ion exchange rates (faster equilibration), smaller ion exchange band lengths (higher ion selectivity), higher permeability, and remarkably improved mass transfer properties. Also, as the exchanger groups can be quantitatively introduced, ion-exchange capacity can be accurately tuned. These unique properties justify the many applications of resin monoliths, which include electrodeionization, production of ultrapure water, chromatography, and use as adsorbents. Use of these materials could be very promising as support for noncovalent catalyst immobilization: positive effects on activity and selectivity are presumable.

Although not exactly pertinent to the topic of the present review, it is worth noticing that catalytic systems based on supported palladium(0) nanoparticles obtained by the reduction of Pd^{2+} species immobilized onto ion-exchange resins,

which already have a number of precedents in the literature,[213] have now reached a high level of development thanks to the use of monolithic reactors based on polymer/glass composites.[214]

Finally, composite materials were shown to be helpful to reduce catalyst leaching; fine-tuning of their properties may contribute significantly to accomplish this goal.[215−218]

All the above considerations suggest that a new technology based on ion-exchange resin is nearly mature for the development of synthetic processes beyond the mere laboratory scale. A rational design of a new generation of (flow) reactors based on these materials is possible, including catalytic membrane reactors.[219−221] Examples in this review show that such immobilized catalysts are ideally suited for assembling into reactors and are already in operation for liquid-phase applications. Commercial processes based on heterogenized homogeneous catalyst are still rare: it is noteworthy that one of these, i.e., the Acetica process, involves the use of ion-exchange resins.

5. Acknowledgments

6. References

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