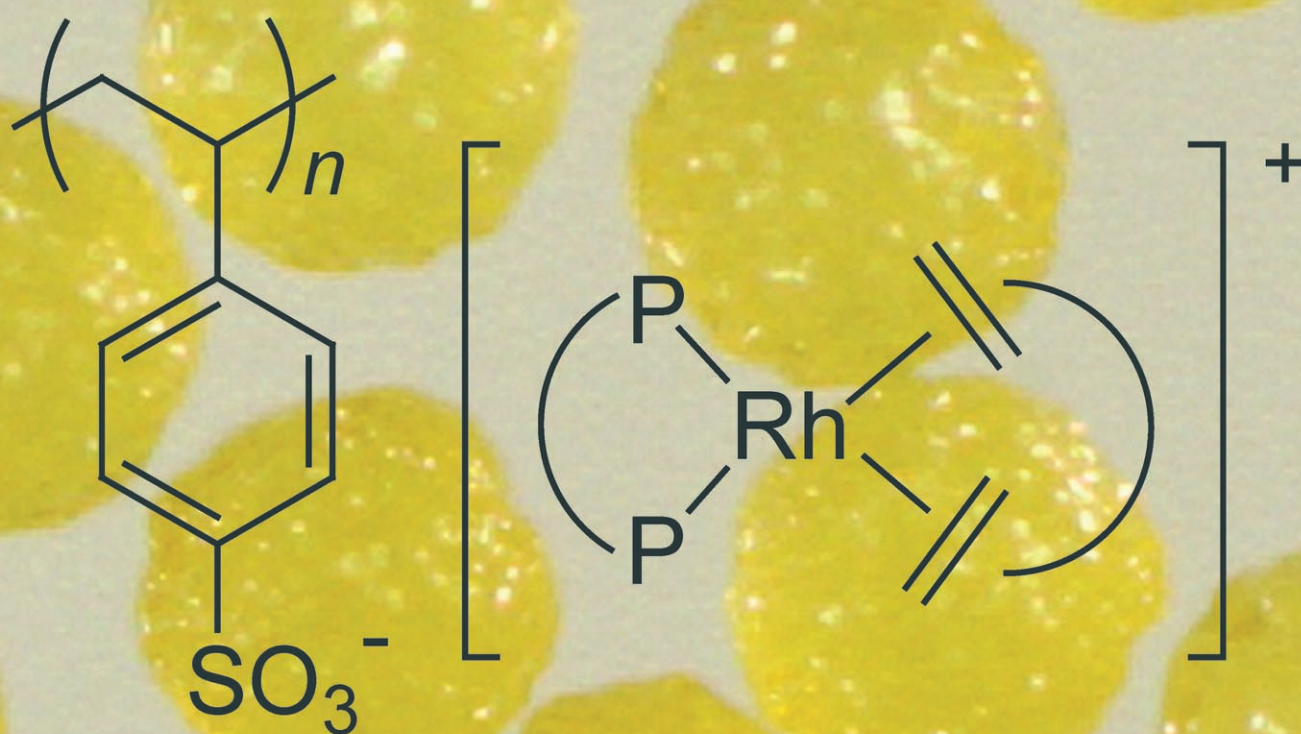


Asymmetric hydrogenation catalysts



on ion-exchange resins

Recycling Asymmetric Hydrogenation Catalysts by Their Immobilization onto Ion-Exchange Resins

Pierluigi Barbaro*^[a]

Abstract: Ion-exchange resins can be used as supports for the preparation of single-site, heterogenised asymmetric hydrogenation catalysts. The immobilised catalysts obtained can be efficiently and conveniently recovered and recycled. This article reviews the significant contributions in the field including the main concepts behind the design and the applications of this type of catalyst.

Keywords: asymmetric catalysis • heterogeneous catalysis • hydrogenation • immobilization • ion exchange • supported catalysts

Introduction

Catalyst recycling is currently one of the most important issues in sustainable, large-scale fine chemicals production, especially for those processes, like enantioselective synthesis, in which the cost of sophisticated ligands often exceed that of the noble metal employed.^[1–4] To easily recover and recycle asymmetric catalysts, various techniques and materials have been developed over the last twenty years involving the immobilisation of a chiral catalyst precursor, either onto a support material or into an appropriate phase system, so that the catalyst can be quantitatively separated from both product(s) and unreacted reagents by filtration or phase separation and, eventually, recycled.^[5–15] Three principal approaches were adopted in order to prepare immobilised enantioselective catalysts:^[16,17]

- Modification of a heterogeneous catalyst with a chiral auxiliary (e.g., modified metallic surfaces).
- Creation of the “heterogeneous counterparts” of a soluble chiral catalyst.
- Other techniques (e.g., gel entrapment, occlusion into membranes, immobilisation in fluoruous or ionic liquid phases).

The above methodologies generally lead to fundamentally different catalyst types. Particularly, single-site catalysts can be obtained by anchoring a complex formed by a metal ion and a chiral ligand to a solid support.^[18–24]

In general, immobilised single-site catalysts may be classified according to the nature of either the support material or the linkage between the support and the ligand. Alternatively, one can distinguish between preformed molecular complexes anchored to the support (either organic or inorganic) or complexes immobilised by reaction of a metal precursor with a preformed ligand matrix (usually a polymeric material with covalently bonded functionalised ligands or dendrimers). In the latter case one can talk of polymer-supported catalysts,^[25] whereas in the former the synthetic strategy is usually referred as “heterogenisation of a homogeneous catalyst”. This strategy offers some remarkable advantages:^[26–28]

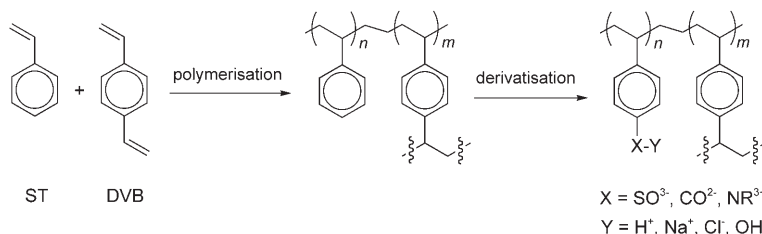
- The catalysts are easily prepared.
- The immobilised catalysts combine the high activity and selectivity of the homogeneous catalysts with a facile product separation, minimisation of waste production and use of environmentally friendly experimental conditions.
- The expenses and difficulties arising from complicated polymer ligand synthesis or chiral ligand functionalisation are avoided.
- The catalysts’ active sites are easily characterised.
- Catalyst loadings can be chosen and optimised.
- Problems arising from metal-loading processes are minimised.
- A systematic design of new catalysts is enabled.

[a] Dr. P. Barbaro
Istituto di Chimica dei Composti Organo Metallici—CNR
Area di Ricerca di Firenze, Via Madonna del Piano
50019 Sesto Fiorentino, Firenze (Italy)
Fax: (+39)055-522-5203
E-mail: pierluigi.barbaro@iccom.cnr.it

Successful examples in asymmetric hydrogenations include the immobilisation of transition metal complexes through anchoring to insoluble supports such as carbon,^[29] silica (SHB),^[30–32] clays,^[33–36] zeolites,^[37–39] heteropoly acids^[40–42] or ion-exchange resins.^[43–51] In all the above cases, a preformed optically active complex is anchored to the support through ion-pair formation or adsorption interactions.

Asymmetric hydrogenation of prochiral olefins is by far the most studied enantioselective organic transformation.^[52–54] Several soluble molecular catalysts with excellent selectivity and productivity have been described, and a number of industrial processes based on this technology are currently operational for pharmaceuticals and agrochemicals production.^[55–58] Transfer of this methodology to heterogeneous catalysis with the aim at catalyst reuse is highly desirable for its clear benefits both from an economical and environmental point of view.^[59,60]

This paper summarises the general concepts behind the use of ion-exchange resins as an insoluble support for heterogenised, single-site enantioselective hydrogenation catalysts, as well as examples of application and recent developments in the field.



Scheme 1.

Supported Catalysts Design and Characterisation

Many authors indicate that preformed, solid, insoluble supports for single-site heterogenisation of homogeneous catalysts should fulfil certain requirements:

- Be readily available in a number of varieties.
- Be inexpensive.
- Need the minimum amount of chemical manipulation before use.
- Be compatible with the solvent employed.
- Be thermally and mechanically stable.
- Be chemically resistant.
- Be easily filterable or decantable.
- Be of reliable quality.
- Be easily custom tailored.
- Have a defined amount of single anchoring sites.

Heterogenised catalysts for enantioselective hydrogenation reactions should:

- Not require synthetic modifications before attachment to the support.
- Be easily prepared and handled.
- Operate under smooth reaction conditions.
- Show turnover frequencies (TOF) and enantiomeric excesses (*ee*) comparable to those of the parent homogeneous catalyst.

- Be quantitatively and easily recoverable.
- Be recyclable (as many times as possible).
- Feature negligible catalyst leaching.

Resin types: In principle, ion-exchange resins meet all requirements defined for the catalysts supports. Nowadays, they are widely available from numerous commercial suppliers or simply synthesisable. They consist mainly of styrene–divinylbenzene cross-linked copolymers bearing a charged ion-exchanging group, that is, either strong or weak cationic (e.g., containing sulfonate or carboxylate groups) or strong and weak anionic (e.g., containing ammonium groups) (Scheme 1).^[61–63] Other ion-exchanging materials suitable as support include the perfluorinated polymer Nafion[®] resins containing sulfonic acid head groups.^[64,65]

The amount of cross-linking agent, typically ranging from 2 to 16%, controls the porosity of the resin particles (either with no discrete pores, referred to as gel resins or microporous resins, or with a porous, multichannelled structure, that is, macroporous or macroreticular resins) which, in turn, affects some of the bulk properties of the resin (e.g., swelling, capacity, equilibration rate, physical stability, selectivity, etc.). Usually, the lower the cross-linking percentage, the higher the moisture content, the equilibration rate, the capacity (ranging from 1.5 to 10 mequiv g⁻¹ on a dry volume basis), the fragility and the ability to accommodate larger ions. Additional characteristics relevant to catalytic purposes are the particle size (beads diameter 16–400 mesh, 1180–38 μm) and the ionic form (i.e., the counterion, usually H⁺, Na⁺, Cl⁻, OH⁻).

Ion-exchange resins used as support in enantioselective catalytic hydrogenations include the strong sulfonated cation-exchange resins listed in Table 1 as well as the Nafion-NR-50 polymer (pellets, H⁺ form, capacity 0.8 mequiv g⁻¹).^[49,51]

Limited use of weak carboxylate cation-exchange resins, namely SERDOLIT CW-18 (8% cross-linking, gel matrix, H⁺ form) and SERVACEL CM-32 (based on a cellulose matrix derivatised with carboxymethylchloride, capacity 1.0 mequiv g⁻¹), has also been reported.^[47] Most resins are commercially available (e.g., from Dow Chemical Company, DuPont, Bayer) and reasonably priced. The choice of resin type is fundamental in determining the efficiency of the immobilised catalysts (see later). To a first approximation,

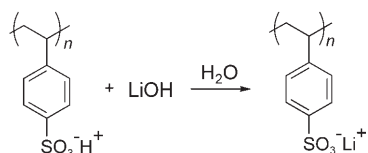
Table 1. Sulfonated ion-exchange resins used as support for heterogeneous asymmetric hydrogenations.

Resin name	Cross-link [%]	Matrix	Ionic form	Capacity [mequiv g ⁻¹]	Ref.
G-4-H ⁺	4		H ⁺	4.8	[44]
G-2-H ⁺	2		H ⁺	4.1	[44]
G-1-H ⁺	1		H ⁺	5.3	[44]
F-1-H ⁺	1		H ⁺	3.7	[44]
G-0.5-H ⁺	0.5		H ⁺	4.9	[44]
F-0.5-H ⁺	0.5		H ⁺	4.3	[44]
F-1-Li ⁺	1		Li ⁺		[44]
G-1-Li ⁺	1		Li ⁺		[44]
F-0.5-Li ⁺	0.5		Li ⁺		[44]
G-0.5-Li ⁺	0.5		Li ⁺		[44]
G-0.5-Na ⁺	0.5		Na ⁺		[44]
G-0.5 K ⁺	0.5		K ⁺		[44]
G-0.5-NH ₄ ⁺	0.5		NH ₄ ⁺		[44]
G-0.5-NMe ₄ ⁺	0.5		NMe ₄ ⁺		[44]
G-0.5-NBu ₄ ⁺	0.5		NBu ₄ ⁺		[44]
Wofatit KP2	2		H ⁺		[46]
DOWEX MSC-1		macroporous	Na ⁺	4.5	[47]
DOWEX HCR-S	8	gel	H ⁺	4.8	[47]
DOWEX 50WX2	2	gel	Li ⁺	4.8	[48]

four-coordinate, cationic, rhodium(I) complexes are among the most used homogeneous catalysts for enantioselective alkene reduction.^[53,68–70] The preformed, molecular complexes of the formula [Rh(PP)-(diolefin)]X were used for this purpose: PP is the bis-chelate chiral phosphine ligand Ph-β-glup,^[43–46] propraphos,^[43–46] norphos,^[47] DIOP^[47,48] or TMBTP^[48] depicted here; diolefin is NBD = bicyclo[2.2.1]hepta-2,5-diene or COD = 1,5 cyclooctadiene; and X is PF₆ or BF₄.

Anchoring of monocationic Rh^I complexes onto ion-ex-

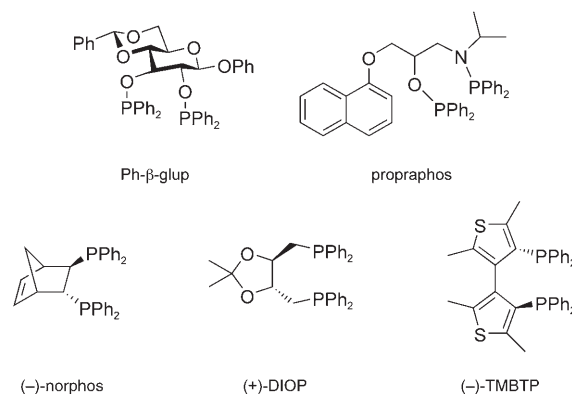
swelling of the resin in the adopted solvent is crucial for both catalyst anchoring and efficiency. For this reason, slightly cross-linked, gel-type resins are preferred over macroporous ones, owing to enhanced mass transport inside the polymer beads, hence giving a good active-site accessibility, as a consequence of swelling of the resin into methanol, which is commonly used as solvent. Swelling volumes have been carefully investigated by Selke using 0.5–4% cross-linked polymers and was found to increase up to 800% upon decreasing the cross-linking percentage.^[44] Because of the high solvation of lithium, swelling is also highest for Li⁺-derivatised resins (Scheme 2).^[44,48] Mechanical instability and difficulty of preparation prevented the use of very low cross-linked resins.



Scheme 2.

Beads size seems to play a secondary role, even if a residual acidity using large pellets of resins in the protonated form, due to incomplete exchange during the immobilisation process, may result in competitive esterification reactions when alcohols are used as solvent for hydrogenation.^[49]

Immobilised transition-metal complexes bearing underivatised chiral ligands: The immobilisation of transition-metal complexes onto ion-exchange resins is well documented and leads to both racemic^[66] and chiral^[67] efficient catalysts. Use of cation-exchange resins as insoluble supports for asymmetric hydrogenation catalysts is motivated by the fact that

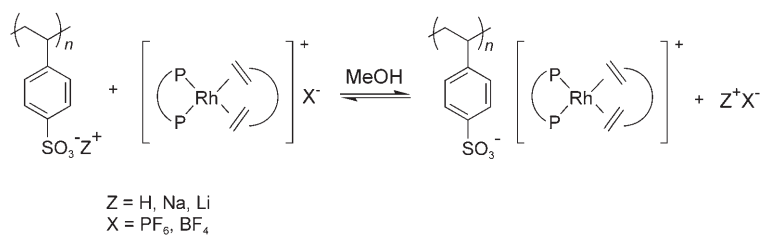


change resins is an equilibrium process that is usually attained after only few hours in methanol by using batch operations (i.e., stirring a solution of the complex in the presence of the support at room temperature, followed by filtration, washing and drying; Scheme 3).

Rhodium immobilisation proved to be effective under these conditions, even when a molecular complex/exchange capacity ratio of 0.5–5% (mmolmequiv⁻¹) is employed, due to the cost of the chiral precursors.^[46–48]

Indeed, catalyst loadings in the range 0.3–1.4% (Rh, w/w) were estimated by using various techniques, corresponding to a 17–99.9% of the total amount of complex used in the immobilisation process. Selected examples are reported in Table 2. As previously stated, catalyst loadings are highest for lower cross-linking percentages (Table 2, entries 1–4, see also Table 1) and for lithiated resins (Table 2, entries 5–8). The typical appearance of immobilised catalysts is shown in Figure 1, in which the colour of the resin is due to the presence of the attached rhodium(I) complex.^[71]

Recently, EDS analysis (energy dispersive X-ray spectrometry) coupled to ESEM microscopy (environmental



Scheme 3.

Table 2. Immobilisation of Rh^I chiral catalysts onto strong cation-exchange resins.

Anchored complex	Resin ^[c]	Rh loading (w/w) [%]	Rh immobilised [%]	Analysis method ^[d]	Ref.
1 [Rh(Ph-β-glupe)(cod)] ^{+[a]}	G-4-H ^{+(H)}	0.73	46	SP	[44]
2	G-2-H ^{+(H)}	1.41	99	SP	[44]
3	G-1-H ^{+(H)}	1.43	99.9	SP	[44]
4	G-0.5-H ^{+(H)}	1.43	99.9	SP	[44]
5 [Rh(propaphos)(cod)] ^{+[a]}	G-0.5-Li ^{+(Li)}	1.39	92	SP	[44]
6	G-0.5-Na ^{+(Na)}	0.44	28	SP	[44]
7	G-0.5 K ^{+(K)}	0.27	17	SP	[44]
8	G-0.5-NH ₄ ^{+(NH₄)}	1.18	84	SP	[44]
9 [Rh(diop)(nbd)] ^{+[b]}	DOWEX 50WX2 (Li)	1.04	68.7	ICP-AES	[48]
10 [Rh(tmbtp)(nbd)] ^{+[b]}	DOWEX 50WX2 (Li)	0.93	68.2	ICP-AES	[48]

[a] BF₄⁻ salt. [b] PF₆⁻ salt. [c] Ionic form in brackets. [d] SP = spectrophotometry, ICP-AES = inductively coupled plasma atomic emission spectroscopy.

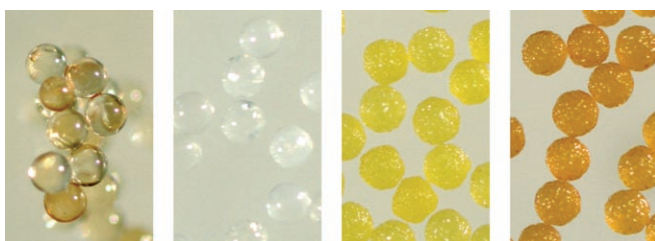


Figure 1. Conventional optical microscope images of DOWEX 50WX2 resin beads (200 magnifications). From the left: commercial resin, lithiated resin, resin with supported [Rh(diop)(nbd)]⁺ complex, and resin with supported [Rh(tmbtp)(nbd)]⁺ complex.^[71]

scanning electron microscopy) was used to characterise asymmetric hydrogenation catalysts immobilised onto ion-exchange resins.^[48] Examples of typical ESEM images and EDS spectra are reported in Figures 2 and 3, respectively.

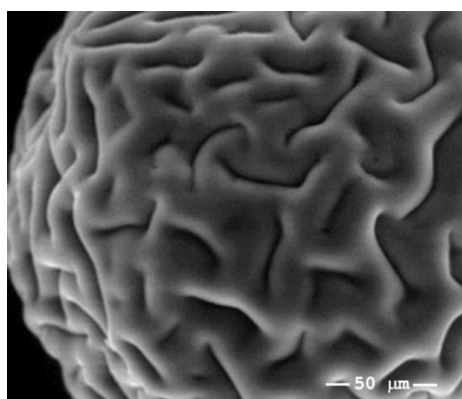


Figure 2. Typical ESEM images of [Rh(tmbtp)(nbd)]⁺ catalyst immobilised on DOWEX 50WX2 beads (backscattered electrons, 1200 magnifications, 20 KeV, 1 torr).^[72]

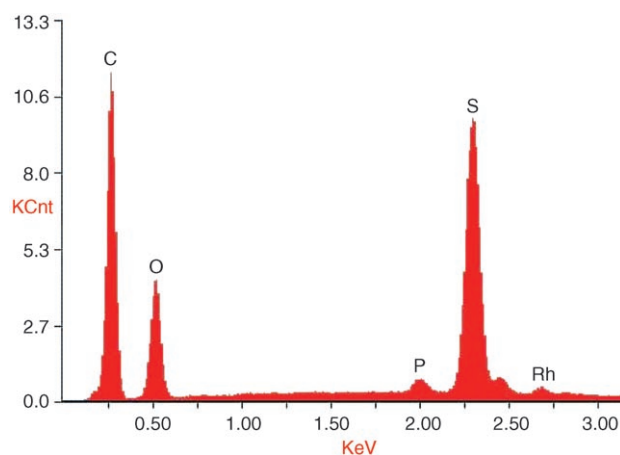


Figure 3. Typical EDS surface area spectrum of DOWEX 50WX2 beads containing the immobilised [Rh(tmbtp)(nbd)]⁺ complex. (1 torr, 20 KeV, 1600 magnifications). (See reference [48], supplementary material.)

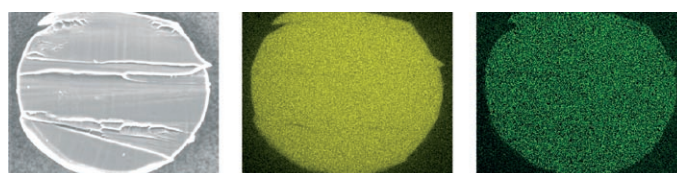
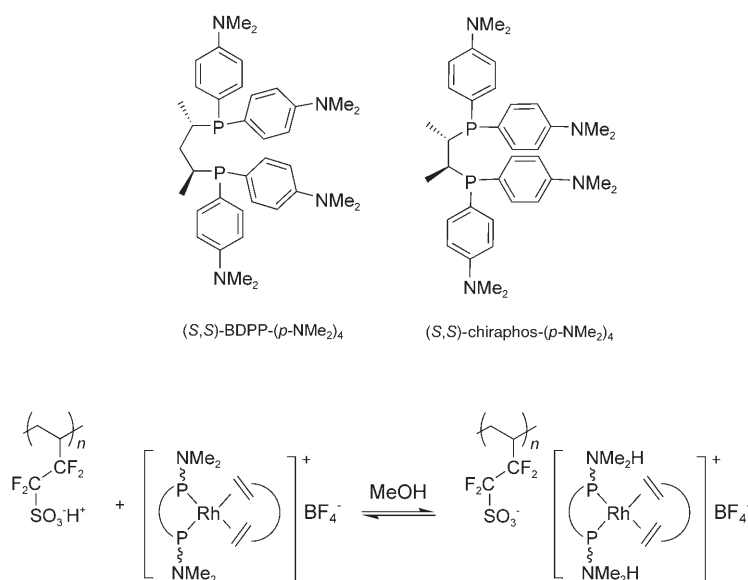


Figure 4. ESEM images of an equatorial section of DOWEX 50WX2/[Rh(tmbtp)(nbd)]⁺ supported catalyst beads (1 torr, 20 KeV, 890 magnifications). Left: secondary electrons; centre: sulfur X-ray EDS map (S_{Kα1}); right: rhodium EDS map (Rh_{Lα1}). (See reference [48], supplementary material.)

ly.^[48,72] Use of the above techniques proved to be particularly suited to investigate this kind of system, owing to the possibility to combine detailed analytical and morphological data at a nanometric level, without sample metallation and high-vacuum conditions.^[73] Metal loading estimates obtained by EDS analysis were comparable to those obtained through atomic emission spectroscopy.^[48]

In addition, EDS maps collected on sections of resin beads showed the metal to be evenly distributed within the solid support, thus proving that resin swelling in methanol allows solvent diffusion through all exchange sites during the immobilisation process (Figure 4).^[48]

Immobilised transition-metal complexes bearing derivatised chiral ligands: Immobilisation of rhodium(I) complexes containing derivatised chiral ligands was achieved as a consequence of simple acid-base exchange equilibria. Thus, protonation of the amino groups bounded to bis-P chelates, by using Nafion resins and the ligands (*S,S*)-BDPP-(*p*-NMe₂)₄ and (*S,S*)-chiraphos-(*p*-NMe₂)₄ depicted here, led to the quantitative removal of rhodium complexes dissolved in methanol under batch conditions (Scheme 4).^[49,51]

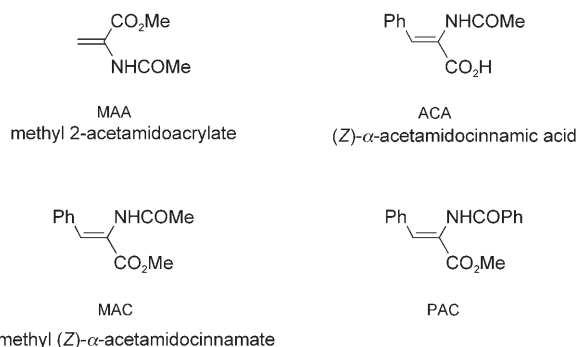


Scheme 4.

Catalysts immobilisation was possible thanks to the selective protonation of the amine nitrogen by the strong sulfonic acid groups on the resin.^[50] Typical loadings consumed 50% of the exchange capacity of Nafion (NR-50-H, 0.8 meq g⁻¹),^[74] corresponding to ca. 0.8% (w/w) metal content (Rh analysis by atomic absorption spectroscopy). The need to synthesise derivatised chiral ligands limits the applications of this methodology.^[75]

Catalyst Performance

The chiral rhodium(I) complexes described above and immobilised onto strong cation-exchange resins were tested as catalysts for the asymmetric hydrogenation of prochiral olefins. Probe substrates are depicted here.



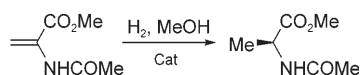
Standard experimental conditions adopted in the homogeneous phase were usually applied (methanol, room temperature, 1–5 bar hydrogen). Selected results are reported in Table 3. Results obtained in the homogeneous reactions are provided in the same table for comparison.

Yields and enantiomeric excesses (*ee*'s) are comparable to those obtained in the homogeneous phase in most cases. Particularly, appropriate selection of the support enables quantitative conversions and high *ee*'s under very mild reaction conditions, for example, Table 3 entries 4–6, 10 and 11. Reduced cross-linking percentages allow better resin swelling in methanol, which results in enhanced rates as a consequence of the kinetic reaction control through substrate diffusion to the active sites inside the polymer beads (Table 3, entries 1–4, see also Table 1).^[44] A drawback, with respect to the homogeneous reactions, is that lower reaction rates are usually observed. Complete conversion and stereoselectivity were recently obtained in the hydrogenation of MAA by using the TMBTP ligand and 2% cross-linked resins (Scheme 5).^[48]

Table 3. Examples of asymmetric hydrogenation reactions with catalysts immobilised onto ion-exchange resins.^[a]

Complex	Substrate	Resin	Heterogeneous			Homogeneous			Ref.
			<i>t</i> [min]	Yield [%]	<i>ee</i> [%]	<i>t</i> [min]	Yield [%]	<i>ee</i> [%]	
[Rh(Ph- β -glup)(cod)] ⁺	MAC	G-4-H ⁺	500 ^[b]		94.1	6 ^[b]		91.1	[44]
		G-2-H ⁺	135 ^[b]		94.9				[44]
		G-1-H ⁺	60 ^[b]		95.5				[44]
		G-0.5-H ⁺	38 ^[b]		95.3				[44]
		Wofatit KP2	15 ^[b]		94.3	0.9 ^[b]		90.9	[46]
[Rh(propraphos)(cod)] ⁺	MAC	G-0.5-Li ⁺	10 ^[b]		84.6	35 ^[b]		85.5	[44]
		DOWEX HCR-S	2460	100	67				[47]
[Rh(norphos)(cod)] ⁺ [c,d]	ACA	DOWEX MSC-1	1200	100	87				[47]
		Nafion-NR-50	15	100	50	5	100	57	[49]
[Rh(bdpp)(<i>p</i> -NMe ₂) ₄](nbd)] ⁺	PAC	Nafion-NR-50	15	100	50	5	100	57	[49]
[Rh(diop)(nbd)] ⁺	MAA	DOWEX 50WX2	150	99.9	54.6	150	99.9	57.3	[48]
[Rh(tmbtp)(nbd)] ⁺	MAA	DOWEX 50WX2	120	99.9	99.9	120	99.9	99.9	[48]

[a] In methanol, room temperature, H₂ pressure 1–5 bar. Substrate/catalyst ratio was 100:1 in all cases, except for ACA for which it was 90:1. [b] Half-life time *t*/2. [c] 50°C. [d] H₂ pressure 20 bar.



Scheme 5.

Evidence for truly heterogeneous reactions that use catalysts immobilised onto ion-exchange resins were given by the absence of any catalytic activity of the reaction solutions recovered after consumption of the substrate.^[48,51]

Conversely, the insoluble, anchored catalysts proved to be easily recovered and recycled in the vast majority of cases. Selected examples of catalyst reuse are reported in Table 4.

Recycling data analysis shows that asymmetric hydrogenation catalysts immobilised onto ion-exchange resins are featured by some common trends:

- Catalysts can be conveniently reused up to 5–15 times simply after decantation and washing with methanol.
- Enantiomeric excesses (*ee*'s) are almost constant in each hydrogenation cycle.
- Leaching of rhodium into solution is usually quite low in each cycle (0.1–6%).
- A significant decrease of the reaction rates in the second and following cycles is commonly observed.

Leaching of the metal can be quantified by means of spectrophotometric,^[44,46] atomic absorption^[49,51] or, more accurately, GF-AAS (graphite-furnace atomic absorption spectro-

copy) analysis^[48] of the methanol after each catalytic cycle. Rhodium loss is usually only slightly dependent on the cycle number and was ascribed to a chemical degradation of the catalytically active complex and, particularly, to phosphine oxidation on the basis of in situ NMR experiments.^[44,48] Negligible rhodium leaching was confirmed by EDS microanalysis, which showed that the rhodium content in the immobilised catalyst beads is essentially the same before and after catalysis and evenly distributed within the solid support.^[48]

A loss of catalytic activity after the first recycle is invariably displayed by the supported catalysts regardless from the resin type or the ligand nature. A typical kinetic behaviour is reported in Figure 5 for the reuse of [Rh(Ph-β-glup)(cod)]BF₄ on F-0.5-H⁺ resin in the enantioselective hydrogenation of MAC.^[44]

A possible explanation for this effect based on the degradation of the catalyst due to oxidation or solvolysis of the ligand is not completely convincing.^[44–46] To shed some light on the catalyst deactivation, a ³¹P high-pressure NMR study under catalytic conditions was recently carried out on the [Rh{(+)–diop}(nbd)]⁺/DOWEX 50WX2 system (Figure 6).^[48,71]

Actually, the only resonances detected at –40 °C in the hydrogenation of MAA in methanol were consistent with the formation of the catalyst–substrate adduct [Rh{(+)–diop}(maa)]⁺ together with a minor amount (2%) of phosphine oxide.^[76–78] A decrease in the reaction rate due to a stronger binding interaction between the sulfonate groups

from the resin and the rhodium centres, after NBD has been reduced and replaced by weaker ligands in the first hydrogenation step, was hypothesised on these basis. However, the absence of any other resonance prevented an unambiguous explanation for the decreased catalytic activity.

Taking into account the small loss of metal due to oxidation, the anchored catalysts can be usually quantitatively recovered after each recycling. Indeed, ESEM images of the catalyst beads, before and after catalysis, showed that the support material is not affected by breakage or cracking during the catalytic runs (Figure 7).^[48]

Conclusion

Recent examples of application of enantioselective hydrogenation catalysts supported onto

Table 4. Recycling of asymmetric hydrogenation catalysts immobilised onto ion-exchange resins.^[a]

Complex	Substrate	Resin	Cycle	<i>t</i> [min]	Yield [%]	<i>ee</i> [%]	Rh leach- ing [%]	Ref.
[Rh(Ph-β-glup)(cod)] ⁺	MAA	Wofatit KP2	1	14.9 ^[b]		94.0	0.3	[46]
			2	17.2 ^[b]		94.3	0.3	
			3	15.9 ^[b]		94.1	0.3	
			4	17.1 ^[b]		94.3	0.3	
			5	17.0 ^[b]		94.2	1.6	
			6	15.6 ^[b]		94.7	1.6	
			7	12.0 ^[b]		94.8	1.6	
			8	10.9 ^[b]		94.6	1.6	
			9	14.1 ^[b]		94.0	5.2	
			10	15.0 ^[b]		94.0	5.2	
[Rh(propaphos)(cod)] ⁺	MAC	G-0.5-Li ⁺	1	10 ^[b]		84.6	1.7	[44]
			2	12 ^[b]		84.3	1.7	
			3	16 ^[b]		83.0	1.7	
			4	30 ^[b]		81.2	1.3	
			5	33 ^[b]		78.5	1.3	
			6	50 ^[b]		71.3	1.3	
[Rh(norphos)(cod)] ⁺ ^[c,d]	ACA	DOWEX HCR-S	1	2460	100	67		[47]
			2	2760	93	64		
			3	3480	88	66		
			4	2880	75	60		
[Rh(bdpp(pNMe ₂) ₄)(nbd)] ⁺	PAC	Nafion-NR-50	1	15	100	50	1.2	[49]
			2	40	100	41	0.5	
			3	40	100	40	–	
			4	60	100	43	0.25	
[Rh(tmbtp)(nbd)] ⁺	MAA	DOWEX 50WX2	1	120	99.9	99.9	2.0	[48]
			2	600	99.9	99.9	2.0	
			3	720	99.9	99.9	1.8	

[a] In methanol, room temperature, H₂ pressure 1–5 bar. [b] Half-life time *t*/2. [c] 50 °C. [d] H₂ pressure 20 bar.

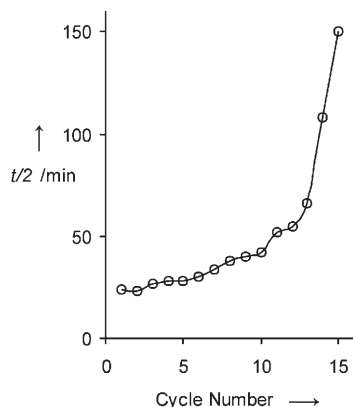


Figure 5. Plot of the catalytic activity versus the number of recycling of $[\text{Rh}(\text{Ph}-\beta\text{-glup})(\text{cod})]\text{BF}_4$ immobilised onto F-0.5- H^+ resin in the enantioselective hydrogenation of MAC. (Data from reference [44].)

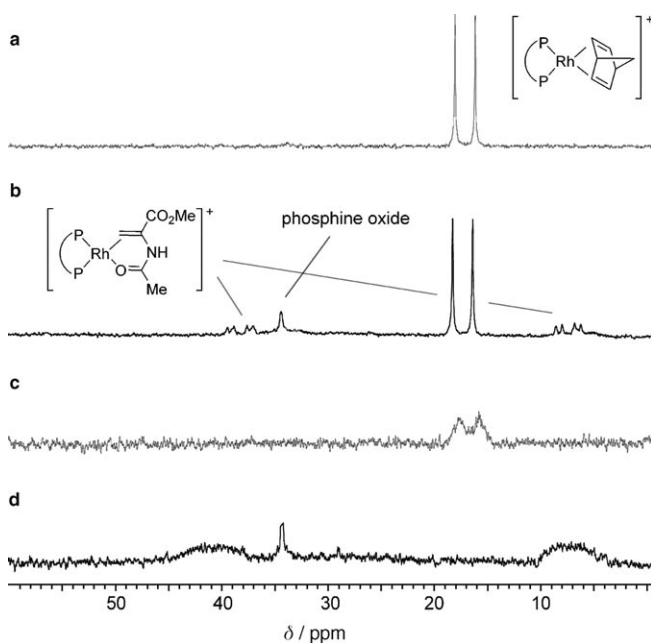


Figure 6. $^{31}\text{P}\{^1\text{H}\}$ H NMR spectra of the $[\text{Rh}(\text{diop})(\text{nbd})]^+/\text{DOWEX 50WX2}/\text{methanol}$ system in the presence of MAA. a) molecular catalyst (15 mg) and MAA (80 mg) under nitrogen at 294 K; b) molecular catalyst and MAA under 5 bar of hydrogen after 5 h at 294 K, spectrum recorded at 233 K; c) immobilised catalyst (120 mg, 1% Rh w/w) and MAA (80 mg) under nitrogen at 294 K; d) immobilised catalyst and MAA under 5 bar of hydrogen after 6 h at 294 K, spectrum recorded at 233 K.^[71]

ion-exchange resins show that an appropriate choice of both resin and molecular precursor provide several advantages for this immobilisation technique, in particular allowing for:

- 1) The use of inexpensive and commercially available supports.
- 2) No need for chiral ligand derivatisation.
- 3) Easy preparation and handling of the immobilised catalyst.

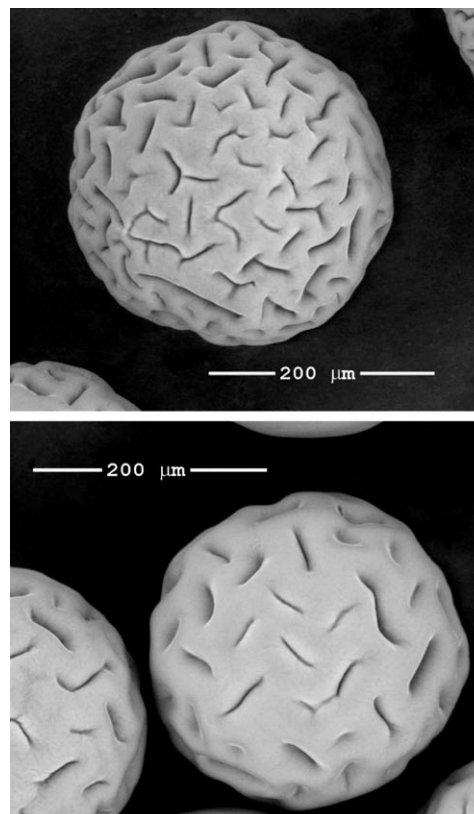


Figure 7. ESEM images of $\text{DOWEX 50WX2}/[\text{Rh}(\text{diop})(\text{nbd})]^+$ supported catalyst beads before (top) and after (bottom) use in the catalytic cycles (backscattered electrons, 600 magnifications, 20 KeV, 1 torr).^[48]

- 4) Catalyst efficiency comparable to that observed in homogeneous phase.
- 5) Very mild hydrogenation conditions.
- 6) Simple and quantitative catalyst recovery.
- 7) Negligible catalyst leaching.

All of the above features show that ion-exchange resins can be an ideal support for the development of single-site, heterogenised asymmetric catalysts suitable for easy and convenient recycling, with clear economical and environmental benefits. This is, of course, not a trivial matter and progress in the field is eagerly awaited.^[79] Improved ion-exchange supported systems aimed at minimising metal leaching and stabilising catalyst activity upon recycling are expected in the near future. Issues regarding the deactivation process have not been clarified to date and deserve further, in-depth studies.

Acknowledgements

The author thanks all colleagues at ICCOM—CNR for supporting this work. Thanks are also due to the IDECAT Network of Excellence, EC through FP6 and to Ente Cassa di Risparmio di Firenze for granting part of this work through project Hydrolab.

- [1] P. T. Anastas, J. C. Warner, *Green Chemistry: Theory and Practice*, Oxford University Press, Oxford, **1998**.
- [2] B. Horton, *Nature* **1999**, *400*, 797.
- [3] D. Macquarrie, *Green Chem.* **2001**, *3*, G11.
- [4] H. U. Blaser, C. Malan, B. Pugin, F. Spindler, H. Steiner, M. Studer, *Adv. Synth. Catal.* **2003**, *345*, 103.
- [5] C. Eui Song, S. G. Lee, *Chem. Rev.* **2002**, *102*, 3495.
- [6] K. Soai, S. Niwa, *Chem. Rev.* **1992**, *92*, 833.
- [7] H. U. Blaser, B. Pugin, in *Chiral Reactions in Heterogeneous Catalysis* (Eds.: G. J. James, V. Dubois), Plenum, New York, **1995**.
- [8] Q. H. Fan, Y. M. Li, A. S. C. Chan, *Chem. Rev.* **2002**, *102*, 3385.
- [9] H. U. Blaser, *Tetrahedron: Asymmetry* **1991**, *2*, 843.
- [10] K. Fodor, S. G. A. Kolmschot, R. A. Sheldon, *Enantiomer* **1999**, *4*, 497.
- [11] F. Fache, E. Schulz, M. L. Tommasino, M. Lemaire, *Chem. Rev.* **2000**, *100*, 2159.
- [12] D. Pini, A. Mandoli, A. Petri, P. Salvadori, *Chim. Ind.* **1999**, *81*, 189.
- [13] B. Pugin, H. U. Blaser, in: *Comprehensive Asymmetric Catalysis, Vol. 3* (Eds.: E. N. Jacobsen, A. Pfaltz, H. Yamamoto), Springer, Berlin, **1999**.
- [14] C. Bolm, A. Gerlach, *Eur. J. Org. Chem.* **1998**, 21.
- [15] C. Saluzzo, R. Halle, F. Touchard, F. Fache, E. Schulz, M. Lemaire, *J. Organomet. Chem.* **2000**, *603*, 30.
- [16] M. E. Davis, *Top. Catal.* **2003**, *25*, 3.
- [17] *Chiral Catalyst Immobilisation and Recycling* (Eds.: D. E. De Vos, I. F. J. Vankelecom, P. A. Jacobs), Wiley-VCH, Weinheim, **2000**.
- [18] Single-site heterogeneous catalysts are commonly defined as solid catalysts in which individual isolated atoms, ions, molecular complexes, including asymmetric organometallic species, are firmly and uniformly anchored to a support. See references [19–22].
- [19] For a comprehensive review on single-site heterogeneous catalysts see: J. M. Thomas, R. Raja, D. W. Lewis, *Angew. Chem.* **2005**, *117*, 6614; *Angew. Chem. Int. Ed.* **2005**, *44*, 6456; .
- [20] J. M. Thomas, R. Raja, *J. Organomet. Chem.* **2004**, *689*, 4110.
- [21] *Fine Chemicals Through Heterogeneous Catalysis* (Eds.: R. A. Sheldon, H. van Bekkum), Wiley-VCH, Weinheim, **2001**.
- [22] M. D. Jones, R. Raja, J. M. Thomas, B. F. G. Johnson, *Top. Catal.* **2003**, *25*, 71.
- [23] C. Bianchini, P. Barbaro, *Top. Catal.* **2002**, *19*, 17.
- [24] S. J. S. M. Shuttleworth, Allin; P. K. Sharma, *Synthesis* **1997**, 1217.
- [25] For recent examples of polymer supported asymmetric catalysts obtained either by polymerisation or covalent binding to modified silica, see: a) S. J. Bae, S. W. Kim, T. Hyeon, B. M. Kim, *Chem. Commun.* **2000**, 31; b) S. Abramson, M. Laspéras, A. Galarneau, D. Desplandier-Giscard, D. Brunel, *Chem. Commun.* **2000**, 1773; c) M. Laspéras, N. Belloq, D. Brunel, P. Moreau, *Tetrahedron: Asymmetry* **1998**, *9*, 3053; d) A. Heckel, D. Seebach, *Angew. Chem.* **2000**, *112*, 165; *Angew. Chem. Int. Ed.* **2000**, *39*, 163; ; e) K. Nozaki, Y. Itoi, F. Shibahara, E. Shirakawa, T. Ohta, H. Takaya, T. Hiyama, *J. Am. Chem. Soc.* **1998**, *120*, 4051; f) H. Sellner, D. Seebach, *Angew. Chem.* **1999**, *111*, 2039; *Angew. Chem. Int. Ed.* **1999**, *38*, 1918; ; g) D. J. Bayston, J. L. Fraser, M. R. Ashton, A. D. Baxter, M. E. C. Polywka, E. Moses, *J. Org. Chem.* **1998**, *63*, 3137; h) H. B. Yu, Q. S. Hu, L. Pu, *Tetrahedron Lett.* **2000**, *41*, 1681.
- [26] P. McMorn, G. J. Hutchings, *Chem. Soc. Rev.* **2004**, *33*, 108.
- [27] Q. H. Fan, C. Y. Ren, C. H. Yeung, W. H. Hu, A. S. C. Chan, *J. Am. Chem. Soc.* **1999**, *121*, 7407.
- [28] F. R. Hartley, *Supported Metal Complexes* (Eds.: R. Ugo, B. R. James), Reidel, New York, **1985**.
- [29] C. F. J. Barnard, J. Rouzaud, S. H. Stevenson, *Org. Process Res. Dev.* **2005**, *9*, 164.
- [30] R. Raja, J. M. Thomas, M. D. Jones, B. F. G. Johnson, D. E. W. Vaughan, *J. Am. Chem. Soc.* **2003**, *125*, 14982.
- [31] C. Bianchini, P. Barbaro, V. Dal Santo, R. Gobetto, A. Meli, W. Oberhauser, R. Psaro, F. Vizza, *Adv. Synth. Catal.* **2001**, *343*, 41.
- [32] F. M. de Rege, D. K. Morita, K. C. Ott, W. Tumas, R. D. Broene, *Chem. Commun.* **2000**, 1797.
- [33] W. P. Hems, P. McMorn, S. Riddell, S. Watson, F. E. Hancock, G. J. Hutchings, *Org. Biomol. Chem.* **2005**, *3*, 1547.
- [34] R. Margalef-Català, C. Claver, P. Salagre, E. Fernández, *Tetrahedron: Asymmetry* **2000**, *11*, 1469.
- [35] R. Margalef-Català, P. Salagre, E. Fernández, C. Claver, *Catal. Lett.* **1999**, *60*, 121.
- [36] M. Mazzel, W. Marconi, M. Riocci, *J. Mol. Catal.* **1980**, *9*, 381.
- [37] A. Corma, M. Iglesias, F. Mohino, F. Sánchez, *J. Organomet. Chem.* **1997**, *544*, 147.
- [38] C. Simons, U. Hanefeld, I. W. C. E. Arends, R. A. Sheldon, T. Maschmeyer, *Chem. Eur. J.* **2004**, *10*, 5829.
- [39] C. Simons, U. Hanefeld, I. W. C. E. Arends, A. J. Minnaard, T. Maschmeyer, R. A. Sheldon, *Chem. Commun.* **2004**, 2830.
- [40] R. L. Augustine, S. K. Tanielyan, S. Anderson, H. Yang, *Chem. Commun.* **1999**, 1257.
- [41] R. L. Augustine, S. K. Tanielyan, S. Anderson, H. Yang, *Conference Chira Tech.* **1998**.
- [42] R. L. Augustine, S. K. Tanielyan, US6025295.
- [43] R. Selke, M. Capka, *J. Mol. Catal.* **1990**, *63*, 319.
- [44] R. Selke, K. Häupke, W. Krause, *J. Mol. Catal.* **1989**, *56*, 315.
- [45] R. Selke, H. Pracejus, *J. Mol. Catal.* **1986**, *37*, 213.
- [46] R. Selke, *J. Mol. Catal.* **1986**, *37*, 227.
- [47] H. Brunner, E. Bielmeier, J. Wiehl, *J. Organomet. Chem.* **1990**, *384*, 223.
- [48] P. Barbaro, C. Bianchini, G. Giambastiani, W. Oberhauser, L. Morassi Bonzi, F. Rossi, V. Dal Santo, *Dalton Trans.* **2004**, 1783.
- [49] I. Tóth, B. E. Hanson, *J. Mol. Catal.* **1992**, *71*, 365.
- [50] I. Tóth, B. E. Hanson, M. E. Davis, *J. Organomet. Chem.* **1990**, *396*, 363.
- [51] I. Tóth, B. E. Hanson, M. E. Davis, *J. Organomet. Chem.* **1990**, *397*, 109.
- [52] *Asymmetric Synthesis, Vol. 5* (Ed.: J. D. Morrison), Academic Press, Orlando, FL, **1985**.
- [53] *Catalytic Asymmetric Synthesis*, 2nd ed. (Ed.: I. Ojima), Wiley-VCH, Weinheim, **2000**.
- [54] R. Noyori, *Asymmetric Catalysis in Organic Synthesis*, Wiley, New York, **1994**.
- [55] W. Tang, X. Zhang, *Chem. Rev.* **2003**, *103*, 3029.
- [56] R. M. Machado, K. R. Heier, R. R. Broekhuis, *Curr. Opin. Drug Discovery Dev.* **2001**, *4*, 745.
- [57] J. K. Whitesell, *Chem. Rev.* **1989**, *89*, 1581.
- [58] a) S. C. Stinson, *Chem. Eng. News* **2001**, *October 1*, 79; b) H. U. Blaser, E. Schmidt, *Asymmetric Catalysis on Industrial Scale*, Wiley-VCH, Weinheim, **2004**.
- [59] A. Thayer, *Chem. Eng. News* **2005**, *September 5*, 55.
- [60] C. Saluzzo, M. Lemaire, *Adv. Synth. Catal.* **2002**, *344*, 915.
- [61] F. C. Nachod, J. Schubert, *Ion Exchange Technology*, Academic Press, New York, NY, **1956**.
- [62] F. Helfferich, *Ion Exchange*, McGraw-Hill, New York, NY, **1962**.
- [63] Homopolystyrene- and acrylic-based ion-exchange resins are also available.
- [64] A. J. Seen, *J. Mol. Catal. A* **2001**, *177*, 105.
- [65] F. J. Waller, *Catal. Rev. Sci. Eng.* **1986**, *28*, 1.
- [66] See, for example: a) P. Ledgzdins, R. W. Mitchell, G. L. Rempel, J. D. Ruddick, G. Wilkinson, *J. Chem. Soc. A* **1970**, 3322; b) L. Yu, D. Chen, J. Li, P. G. Wang, *J. Org. Chem.* **1997**, *62*, 3575; c) C. Palazzi, F. Pinna, G. Strukul, *J. Mol. Catal. A* **2000**, *151*, 245; d) H. C. Sacco, Y. Iamamoto, J. R. Lindsay Smith, *J. Chem. Soc. Perkin Trans. 2* **2001**, 181; e) R. T. Smith, R. K. Ungar, M. C. Baird, *Transition Met. Chem.* **1982**, *7*, 288; f) M. M. Sharma, *React. Funct. Polym.* **1995**, *26*, 3; g) J. Balue, J. C. Bayon, *J. Mol. Catal. A* **1999**, *137*, 193; h) D. E. Bryant, M. Kilner, *J. Mol. Catal. A* **2003**, *193*, 83.
- [67] See, for example: a) B. M. Choudary, N. S. Chowdari, K. Jyothi, M. L. Kantam, *J. Am. Chem. Soc.* **2002**, *124*, 5341; b) B. M. Choudary, N. S. Chowdari, M. L. Kantam, K. V. Raghavan, *J. Am. Chem. Soc.* **2001**, *123*, 9220.
- [68] I. D. Gridnev, N. Higashi, T. Imamoto, *Organometallics* **2001**, *20*, 4542.

- [69] J. M. Brown, *Hydrogenation of Functionalized Carbon-Carbon Double Bonds, Vol. 1* (Eds.: E. N. Jacobsen, A. Pfaltz, H. Yamamoto), Springer, Berlin, **1999**, pp. 119–182.
- [70] M. G. Burk, *Acc. Chem. Res.* **2000**, *33*, 363.
- [71] P. Barbaro, *ISHHC XII International Symposium on Relations between Homogeneous and Heterogeneous Catalysis*, Firenze, July 18–22, **2005**.
- [72] P. Barbaro, unpublished results.
- [73] “Foundations of Environmental Scanning Electron Microscopy”: G. D. Danilatos, *Adv. Electron. Electron Phys.* **1988**, *71*, 109.
- [74] F. J. Waller, R. W. Scoyoc, *Chem. Tech.* **1987**, *17*, 438.
- [75] I. Tóth, B. E. Hanson, M. E. Davis, *Tetrahedron: Asymmetry* **1990**, *1*, 913.
- [76] J. M. Brown, P. A. Chaloner, *J. Chem. Soc. Chem. Commun.* **1978**, 321.
- [77] J. M. Brown, P. A. Chaloner, *J. Chem. Soc. Chem. Commun.* **1980**, 344.
- [78] J. Halpern, *Science* **1982**, *217*, 401.
- [79] S. Evans, *Chem. Sci.* **2004**, *1*, C51.

Published online: March 22, 2006