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Recycling asymmetric hydrogenation catalysts by their immobilisation onto ion-exchange resins[†]

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New systems based on cationic chiral phosphine–rhodium complexes anchored to a commercial cation-exchange geltype resin showed high efficiency and easy recycling in the asymmetric hydrogenation of prochiral olefins.

Catalyst recovery is of paramount importance in sustainable fine chemicals production, especially in large-scale asymmetric processes where the cost of the chiral ligands often exceeds that of the noble metal employed.¹ In order to easily recover and recycle asymmetric catalysts, various techniques and materials have been developed over the last twenty years.² The preparation of single-site recyclable catalysts can be achieved through the "heterogenisation of homogeneous catalysts", which involves the immobilisation of preformed molecular precursors onto various support materials.³ This strategy offers the advantage to combine the high activity and selectivity of the homogeneous catalysts with both a facile product separation and use of environmentally friendly experimental conditions. Successful examples in asymmetric hydrogenations include the immobilisation of transition metal complexes via anchoring to insoluble supports such as silica (SHB),4 clays,5 zeolites,6 heteropoly acids⁷ or ion-exchange resins.⁸⁻¹⁰ Herein, we report the preparation and characterization of new catalytic systems based on chiral Rh(1) complexes immobilized onto commercially available ion-exchange resins as well as a preliminary study of their catalytic potential for the stereoselective hydrogenation of prochiral substrates.

The [(PP*)Rh(NBD)]PF₆ complexes containing the chiral diphosphine (+)-DIOP and (–)-TMBTP (**1** and **2**, respectively) were used as molecular precursors (Scheme 1).[‡] The strong cation-exchange, sulfonated gel-type resin DOWEX 50WX2-100 was used as anchoring agent.§ After smooth lithiation of the commercial support, the immobilized catalysts were readily obtained by stirring the resin with a methanol solution of the appropriate Rh(1) complex (Scheme 2). Due to the cost of the chiral ligands, a catalyst (mmol)/resin (meq. ion exchange capacity) ratio of *ca*. 3% was used in each preparation. The amount of rhodium found in the tethered catalyst indicated an effective anchoring of the complex cation onto the resin. Table 1 summarises the metal uptake properties of the lithiated resin (**Li-D 50WX2**) as determined by ICP-AES spectroscopy.¹¹

The efficiency of the supported catalysts (Li-D 50WX2-1 and Li-D 50WX2-2) in the asymmetric hydrogenation of prochiral olefins was tested using MAA as a probe substrate (Scheme 3).¶All reactions were performed in methanol under 5 bar H_2 at room temperature. Catalyst recovery and recycling were straightforwardly

 \dagger Electronic supplementary information (ESI) available: Experimental section, $^{31}P\{^1H\}$ HP NMR spectra, typical EDS surface area spectrum and ESEM images. See http://www.rsc.org/suppdata/dt/b4/b406179a/

Table 1 Immobilisation of rhodium complexes on lithiated-DOWEX $50WX2 \text{ resin}^a$

Tethered catalyst	Rh loading $(w/w)^b$ (%)	Rh immobilised (%)
Li-D 50WX2-1	1.04(1)	68.7
Li-D 50WX2-2	0.93(1)	68.2

^{*a*} Experimental conditions: resin 300 mg (1.44 meq. ion exchange capacity), metal complex 37 mg (0.044 mmol), methanol 7.5 mL, 16 h, room temperature. ^{*b*} ICP-AES, average value over three samples.



performed by removing the reaction solution after the first catalysis cycle, washing of the solid catalyst with pure methanol, followed by addition of a second amount of substrate in methanol under hydrogen. Selected results are reported in Table 2. Results obtained in the homogeneous phase under analogous reaction conditions are provided in the same table for comparison.



Both catalysts gave conversions and enantiomeric excesses (ee's) in each catalytic cycle equal or comparable to those obtained in the homogeneous phase. Particularly, the immobilised Rh–TMBTP complex gave a complete conversion and stereoselectivity after 2, 10 and 12 h in the first, second and third hydrogenation cycle, respectively (Table 2, entry 2), with almost constant activity after the second recycle. A significant decrease of the reaction rates in the second and following cycles is commonly observed for ion-exchange resin-supported catalysts.^{8,10} In the present case, this

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Table 2 Asymmetric catalytic hydrogenation of MAA using Rh(1) complexes anchored on lithiated-DOWEX 50WX2 resin^a

Entry	Heterogeneous ^b												
		First cycle			Second cycle			Homogeneous ^c					
	Tethered catalyst	t/h	Yield ^d (%)	ee ^d (%)	Rh leaching ^e (%)	t/h	Yield ^d (%)	ee ^d (%)	Rh leaching ^e (%)	Catalyst	t/h	Yield ^d (%)	ee ^d (%)
1 2	Li-D 50WX2-1 Li-D 50WX2-2	2.5 2.0	99.9 [38] 99.9 [52]	54.6 99.9	1.8(1) 2.0(1)	12 10	98.2 [8] 99.9 [11]	49.6 99.9	1.5(1) 2.0(1)	1 2	2.5 2.0	99.9 [40] 99.9 [50]	57.3 99.9

^{*a*} Reaction conditions: solvent MeOH, room temperature, H₂ 5 bar. ^{*b*} Tethered catalyst (50 mg), *ca*. 1% Rh w/w, Rh (*ca*. 0.0048 mmol), solvent (6.5 ml), 500 rpm, substrate/Rh mol ratio 100: 1. ^{*c*} Rh (0.0034 mmol), solvent (4 ml), 400 rpm, substrate/Rh mol ratio 100: 1. ^{*d*} Reaction mixture, GC, turnover frequency h⁻¹ (mol product) (mol Rh h)⁻¹ in square brackets. ^{*e*} Reaction solution, GF-AAS, average value over three samples.

effect may be attributed 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.¹² Indeed, in situ high-pressure (HP) NMR spectroscopy showed that the hydrogenation of both 1 and Li-D 50WX2-1 in MeOH resulted in the formation of a species that does not contain hydride ligands and exhibits the same chemical shift of the bis-solvento complex $[((+)-DIOP)Rh(MeOH)_2]^+$ (see ESI[†]).¹² A ³¹P HP NMR study under catalytic conditions was carried out in both homogeneous (using 1) and heterogeneous phase (Li-D 50WX2-1). In either case, resonances were detected at -40 °C consistent with the formation of the catalyst–substrate complex [((+)-DIOP)Rh(MAA)]⁺ together with a minor amount (2%) of phosphine oxide.12 Taking into consideration this small loss of catalyst due to undesired oxidation, the tethered catalyst was quantitatively recovered after each run. Indeed, the ESEM images of the catalyst beads, before and after catalysis, showed that the support material was not affected by signs of breakage or cracking (Fig. 1).



Fig. 1 ESEM images of tethered catalyst Li-D 50WX2-1 beads before (left) and after (right) use in the catalytic cycles (backscattered electrons, 600 × magnification, 20 keV, 1 Torr).

Leaching of the metal into the reaction solution was directly quantified via GF-AAS analysis of the methanol solution after each catalytic cycle. The amount of leached rhodium was found to be negligible in each experiment (<2.0%). Consistently, and according with a truly heterogeneous reaction, no catalytic activity was shown by the solutions recovered after the first and second catalytic cycle. Therefore, the observed rhodium loss in each experiment can be safely ascribed to phosphine oxidation. Surface X-ray EDS microanalysis data supported the above results showing that the rhodium content in the tethered catalyst to be essentially the same before and after catalysis. Moreover, EDS maps recorded on sections of the catalyst beads before and after catalysis proved the metal to be evenly distributed within the solid support (see ESI⁺). This evidence indicates that the solvent diffuses freely into and out the support during both the anchoring and catalytic reactions, thus allowing good site accessibility to all soluble reactants. In conclusion, the present ion-exchange resin heterogenised asymmetric catalysts are featured by: (i) use of inexpensive and commercially available resin; (ii) no need of chemical modification of the chiral ligand; (iii) easy preparation and handling of the tethered catalyst; (iv) catalyst efficiency comparable to that observed in the homogeneous phase; (v) very mild hydrogenation conditions; (vi) facile and effective recovery and recycling; (vii) no catalyst leaching. Current studies in our laboratories with other chiral ligands (BINAP, JOSIPHOS), substrates (itaconates) and metals (ruthenium) confirm the validity and versatility of the heterogenisation protocol described in this work. Preliminary results show that the ruthenium(II) complex $[((-)-TMBTP)Ru(p-cymene)I]PF_6$ supported on **Li-D 50WX2** resin catalyses the hydrogenation of methyl aceto-acetate to methyl (*R*)-3-hydroxybutyrate in methanol with yields and ee's (68 and 73%, respectively) comparable to those obtained in the homogeneous phase and with very low Ru leaching.

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Notes and references

TMBTP = 4,4'-Bis(diphenylphosphino)-2,2',5,5'-tetramethyl-3,3'-bithiophene (P. Antognazza, T. Benincori, E. Brenna, E. Cesarotti, L. Trimarco and F. Sannicolò, *Eur. Pat.*, EP 0770085, 1996 (to Chemi SpA); DIOP = 2,3-O-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane; NBD = bicyclo[2.2.1]hepta-2,5-diene.

§ DOWEX 50WX2-100 strong cation-exchange resin, H⁺ form, gel-type is available from Aldrich (product n. 21,744-1).

¶ MAA = Methyl 2-acetamidoacrylate.

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