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Recent progress in asymmetric heterogeneous catalysis: use of polymer-supported catalysts

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Abstract

The asymmetric heterogeneous catalytic reduction of carbonyl bonds by hydrogen transfer reduction or hydrogenation by means of molecular hydrogen as well as the asymmetric allylic substitution of allylic acetates are reported. In order to perform these reactions, new polymer-supported catalysts were employed. These polymers are either a Merrifield resin with a chiral pendent ligand or a chiral main chain polymer with ureas, thioureas and a diphosphine as functional groups. Comparison of the results obtained in these heterogeneous asymmetric reactions was made with those obtained in the homogeneous ones.

Keywords: Heterogeneous catalysis; Asymmetric catalysis; Polymers

1. Introduction

Over the past three decades, homogeneous asymmetric catalysis was subjected to a successful development. Nevertheless, only few examples have been developed to an industrial scale. Pharmaceuticals, agrochemicals, flavors and flagrances [1] are the principal areas which require the synthesis of optically pure chiral compounds. Most of them are still synthesized starting from the chiral pool or in their racemic form, followed by resolution.

The lack of employment of the homogeneous asymmetric catalysis is probably and essentially due to problems of separation and recycling of the expensive chiral catalyst. To overcome these drawbacks, very early after the discovery of homogeneous asymmetric catalysis, heterogeneous catalysis has been employed, particularly polymer-supported homogeneous catalysis. This methodology was brought out by Kagan et al. [2] and Stille et al. [3], in the 1970s and was used for reactions like hydroformylation [3c,4], dihydroxylation [5], epoxidation [6] and hydrogenation [7]. This method consists of the 'heterogenization' of an homogeneous catalyst by anchoring the catalyst on a solid support, i.e. an inorganic material [8] or an organic polymer [9], in order to perform the separation of the catalyst from the reaction mixture, by filtration. However, lower activities and selectivities are mostly observed. In all cases, the choice of the polymer is crucial: a large swelling with the reaction solvent is necessary. Moreover, the active sites must be at the proper location [10]. Most of the existing systems involves crosslinked polystyrene, polyacrylate or polypeptide supported reagents [11]. In order to combine the advantages of homogeneous (mobility, accessibility of the active sites) and heterogeneous catalysis (easy separation), soluble polymer-supported catalysts could be employed [6a,12]. Then, by precipitation upon addition of an appropriate solvent followed by filtration, the catalyst is recovered.

We herein report our efforts to develop new reusable, partly soluble or non-soluble polymer-supported catalysts for allylic substitution of allylic acetates and asymmetric reduction by means of hydrogen transfer or molecular hydrogen. Different kinds of polymers were involved in these reactions. Asymmetric allylic substitu-

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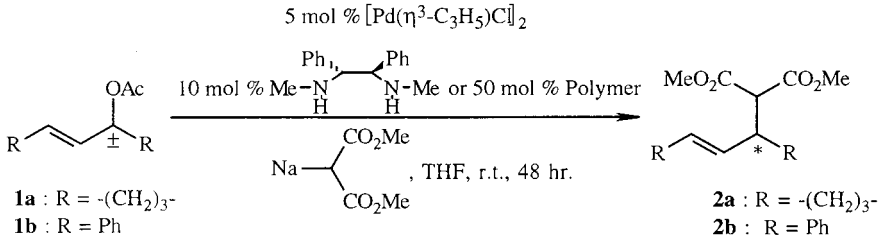


Scheme 1.

tion was performed with polyamides and polyureas with main chain chirality presenting a pseudo C_2 symmetry. Hydrogen transfer reductions were thus performed with catalysts synthesized from a sulfonamide-supported Merrifield resin, from polyureas and polythioureas. Finally, hydrogenation with molecular hydrogen was tested with a polyurea containing in its main chain the BINAP structure.

2. Enantioselective allylic substitution

Palladium catalyzed allylic substitution has received considerable attention because it is a very useful method for carbon–carbon bond formation. Numerous soluble, non-polymeric phosphine-containing ligands were tested in order to effect highly enantioselective reactions [13]. On the opposite, only a few nitrogen-ligands with σ-donor character have been used [14].

In 1995, we showed that the use of *N*,*N*′-dimethyl-1,2-diphenylethylene diamine as ligand for the homogeneous allylic substitution of allylic acetates (**1**) led to interesting results (Scheme 1, Table 1) [15].

Indeed, the transformation of acetates **1a** and **1b** into compounds **2a** and **2b** yields to high conversions (up to 85%) and 16% and 95% ee, respectively (runs 1 and 2, Table 1). Then, we decided to develop a new strategy which consists of using polymeric nitrogen-ligands like polyamide **4a** and polyureas **5a** and **5b**, in order to study the catalytic asymmetric allylic substitution by means of a polymer-supported catalyst [15,16]. These polymers were easily obtained in good yield by copolymerization of C_2 symmetric chiral diamines with a diarylchloride or various diisocyanates respectively (Scheme 2, Table 2).

Polyamide **4a** shows the highest enantioselectivity but the lowest catalytic activity (run 2) compared to the polyureas **5a** and **5b** (runs 1 and 3). It is noteworthy that contrary to what was generally observed, better results were obtained with the heterogeneous system (run 1, Table 2) compared to the homogeneous one for the allylic substitution of acetate **1a** with (1*S*,2*S*) *N*,*N*′-dimethyl-1,2-diphenylethylenediamine (Table 1, run 1).

A difference in solubility was observed between polyamide and polyureas. Polyureas **5a** and **5b** are soluble in THF whereas polyamide **4a** is insoluble in organic solvents. Unfortunately, attempts to recover and reuse the catalytic systems were ineffective.

To our knowledge, it was the first time that such polyamide and polyurea ligands were employed to afford enantioselective alkylations. Actually, much attention was focused on the nature of this kind of polymer in order to stabilize the Pd°. It should be noted that one of the best ligands so far tested is the ligand developed by Trost et al. which possesses two phosphine and two amide functional groups in order to form a 'chiral pocket' [17].

3. Reduction

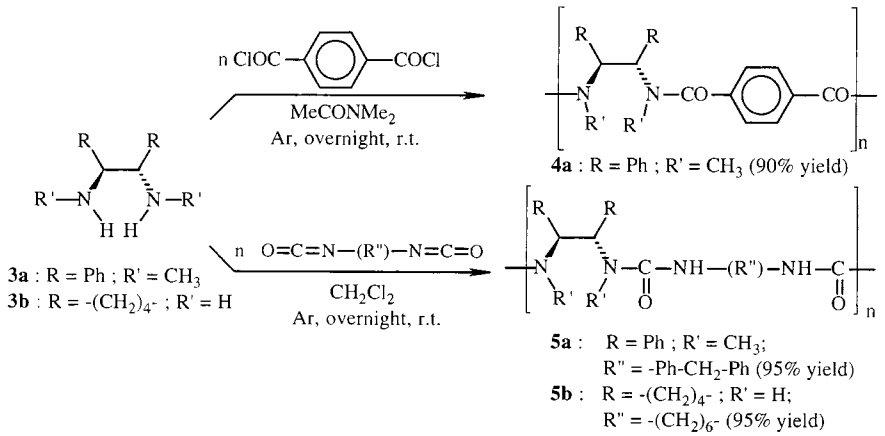
3.1. Reduction by hydrogen transfer catalysis

The hydrogen transfer reduction (HTR) is an attractive method because it avoids the use of hydrogen pressure which requires specific equipment. Several different substrates have been successfully reduced by transfer hydrogenation in the presence of both heterogeneous [18] and homogeneous catalysts [19]. This reaction includes generally as hydrogen acceptors, ketones, α,β-unsaturated carbonyl compounds, α,β-unsaturated acids and esters, imines and nitro compounds and as hydrogen donors, alcohols (mainly *i*-PrOH) and the formic acid/triethylamine system. Chiral ligands first employed in this asymmetric reaction were chiral phosphines (DIOP, CHIRAPHOS, NORPHOS, BINAP), then, since the beginning of the 1990s, chiral bidentate nitrogen ones have been mainly used.

Encouraging results were obtained in homogeneous asymmetric catalysis when we used diamine ligands in the reduction of prochiral ketones by means of hydrogen transfer reduction [20] (Scheme 3).

Table 1
Homogeneous alkylation of allylic acetates

Run	Acetate	Product	Conversion (%)	ee (%) (configuration)
1	**1a**	**2a**	85	16 (*S*)
2	**1b**	**2b**	90	95 (*S*)



Scheme 2.

Table 2
Pd-catalyzed allylic substitution with polyamide and polyureas as ligands

Run	Acetate	Ligand	Product	Conversion (%)	ee (%) (configuration)
1	**1a**	**5b**	**2a**	80	25 (*R*)
2	**1b**	**4a**	**2b**	38	80 (*R*)
3	**1b**	**5a**	**2b**	72	38 (*R*)

Then, two types of ligands derived from diamines had been used with success; the first one having a C_2 symmetry like diureas and dithioureas, the second one without such symmetry like an amino sulfonamide. We have synthesized heterogeneous catalysts by means of organic polymers. In the case of the ligand without C_2 axial symmetry, we prepared materials presenting the ligand moiety as a pendent group on a polystyren matrix. With other polymeric ligands, chirality and ligand were included in the main chain of the polymer. This last type of structure allows the conservation of a pseudo C_2 axis along the polymer chain.

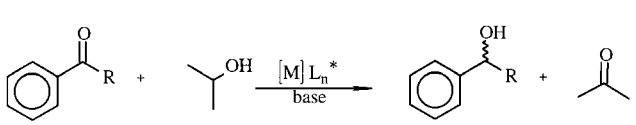
3.1.1. Aminosulfonamide as a pendent group on Merrifield-type materials

In 1995, Noyori et al. reported the use of (1*S*,2*S*)-*N*-(toluene-*p*-sulfonyl)-1,2-diphenylethylene diamine with very high ee [21] in the Ru-catalyzed hydrogen transfer reduction of ketones (97% ee for acetophenone). On the other hand, Knochel et al. obtained ee up to 92% with *N*-monotosylated 1,2-diaminocyclohexane derivatives [22]. We considered the synthesis of chiral polymers containing Noyori's monomer in a polymeric matrix (Scheme 4). These polymers were subsequently tested as ligands for the Ir^{I} and Ru^{II} catalyzed hydrogen transfer reduction of acetophenone [23].

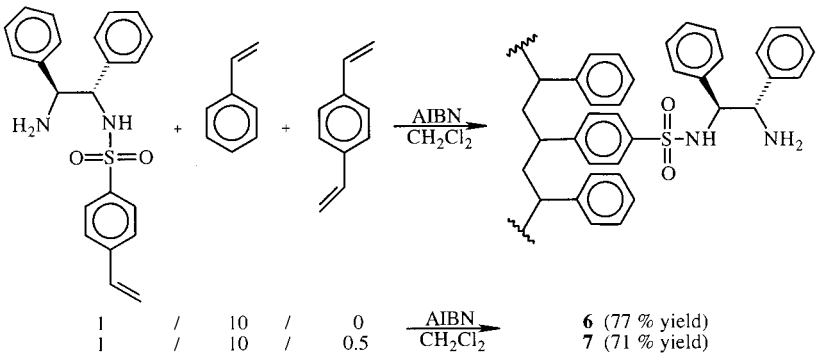
Table 3 summarizes the data of the asymmetric hydrogen transfer reduction of acetophenone carried out in the presence of polymers **6** and **7**.

Both polymers were used for the catalytic transfer hydrogenation of acetophenone in the presence of 0.025 equivalents of metal precursor and *i*-PrOH–KOH for Ir or *i*-PrOH–Et_3N for Ru, at 70°C for 2 days.

When the chiral non-crosslinked polymer **6** was used with Ru as metal, we have observed that conversion and ee were dependent on the nature of the precursor employed (runs 2 and 3). Similar observations (runs 5 and 6) were made with crosslinked polymer **7**. However, a different behavior between polymers **6** and **7** was pointed out. In the case of polymer **6**, with $[Ru(benzene)Cl_2]_2$ better ee and lower conversion than $[Ru(p\text{-cym})Cl_2]_2$ were obtained (runs 2 and 3) contrary to polymer **7** which presented with $[Ru(p\text{-cym})Cl_2]_2$ better conversion but lower ee than $[Ru(benzene)Cl_2]_2$ (runs 5 and 6). This difference of behavior remains unexplained. However, when the chiral polysulfonamides **6** and **7** were used with Ir as metal, excellent conversions and enantioselectivities were obtained (runs 1 and 4). Moreover, heterogeneous Ir catalysts showed higher enantioselectivities compared to the homogeneous analog for which only 75% of conversion and 89% of enantiomeric excess were obtained. This difference could be explained by the formation of chiral microenvironments upon polymerization.



Scheme 3.



Scheme 4.

Table 3
Reduction of acetophenone with polymers **6** and **7** and $[Ir(COD)Cl]_2$ or $[Ru(benzene)Cl_2]_2$ as metal precursors

Run	Ligand	Metal precursor	Time (days)	Conversion (%)	ee (%) (configuration)
1	**6**	$[Ir(COD)Cl]_2$	3	94	92 (*S*)
2	**6**	$[Ru(benzene)Cl_2]_2$	2	20	64 (*S*)
3	**6**	$[Ru(p\text{-cym})Cl_2]_2$	2	72	40 (*S*)
4	**7**	$[Ir(COD)Cl]_2$	3	96	94 (*S*)
5	**7**	$[Ru(benzene)Cl_2]_2$	2	96	31 (*S*)
6	**7**	$[Ru(p\text{-cym})Cl_2]_2$	2	23	84 (*S*)

Attempts to reuse the catalysts showed that the Ru-containing one, although less selective, is more stable upon reuse than the Ir derivative.

More recently, Bayston et al. [24], with a similar objective have prepared the polymer **8** (Scheme 5) starting from the aminostyrene Merrifield-type polymer. They used ruthenium precursors and obtained 91% ee with 88% conversion. Compared to ligand **7** with ruthenium catalyst (run 3) this ligand showed better conversion and selectivity. Nevertheless, conversion and selectivity were comparable with Ir catalyst (runs 1 and 4, Table 3).

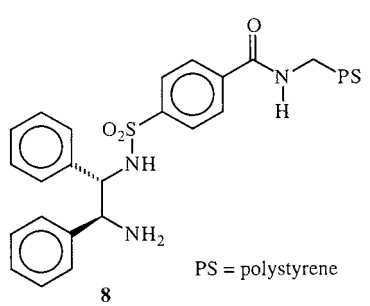
3.1.2. Asymmetric ligands in main chain polymer

3.1.2.1. Polyureas, new materials for polymer supported catalysis. Diureas were tested as ligands for asymmetric hydrogen transfer. The best results were obtained with phenylisocyanides as precursors (for propiophenone, 87% conversion and 80% ee were observed) (Scheme 6) [25].

We have heterogenized chiral diamines (1,2-cyclohexyldiamine, 1,2-diphenylethylene diamine and *N*,*N*′-dimethyl-1,2-diphenylethylene diamine) by their incorporation into polymer backbones by polycondensation with diisocyanates (as shown in Scheme 1). Thus pseudo C_2 symmetric polyurea ligands were obtained (Scheme 4) [15,26]. Their molecular weight was about 2000 g mol^{-1} (determined by NMR spectroscopy).

The study of the hydrogen transfer reduction was performed at 70°C, with acetophenone in the presence of $[Rh(COD)Cl]_2$ with a diamine polymer unit/Rh ratio of 10, *i*-PrOH as hydrogen donor and KOH. The results are summarized in Table 4.

It is noteworthy that the pseudo C_2 symmetry seems to be important. When using the dissymmetric polyurea **9a**, synthesized with the dissymmetrical 2,4-toluene diisocyanate, no ee was observed (run 2) contrary to its analog **9b** (13% ee) (run 3) obtained with the symmetri-



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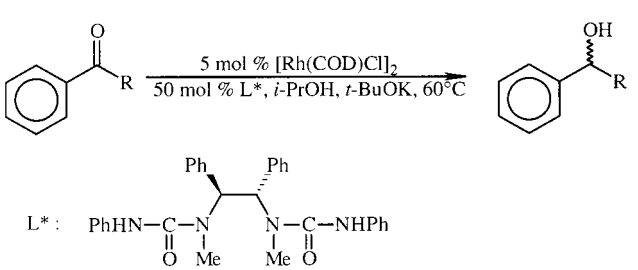
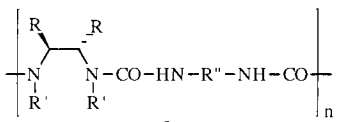
Scheme 5.



Scheme 6.

Table 4
Hydrogen transfer reduction of acetophenone with polyamide **4a** and polyureas

Run	Chiral polymer–rhodium catalyst	Conversion	Time (days)	ee (%) (configuration)
1	Polyamide **4a**	22	7	28 (*R*)
2	Polyurea **9a**	80	4	0
3	Polyurea **9b**	50	4	13 (*S*)
4	Polyurea **9c**	97	3	39 (*R*)
5	Crosslinked polyurea **9c**	100	1	60 (*R*)



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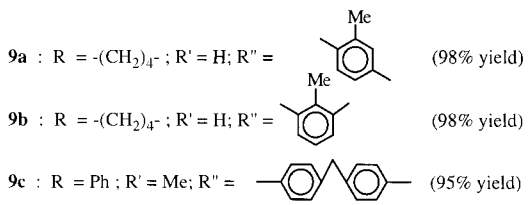


Scheme 7.

cal 2,6-toluene diisocyanate (Scheme 7). Rigidity of the polymer appeared to be another important parameter. Polyurea **9c** (run 5), crosslinked by a mixture of 70% of diisocyanate and 30% of different triisocyanates, showed higher catalytic activity as well as higher enantioselectivity than the polyamide **4a** or other polyureas. Moreover, this chiral crosslinked polyurea presents a slightly increased enantioselectivity over the amine monomer analog (55% ee and 94% conversion in similar conditions). These results could be explained by the rigidity of the active site which is crucial for the selectivity and the stability of the catalytic system. On the other hand, this crosslinked polyurea **9c** was recovered by filtration and reused twice with no loss of either catalytic activity or enantioselectivity.

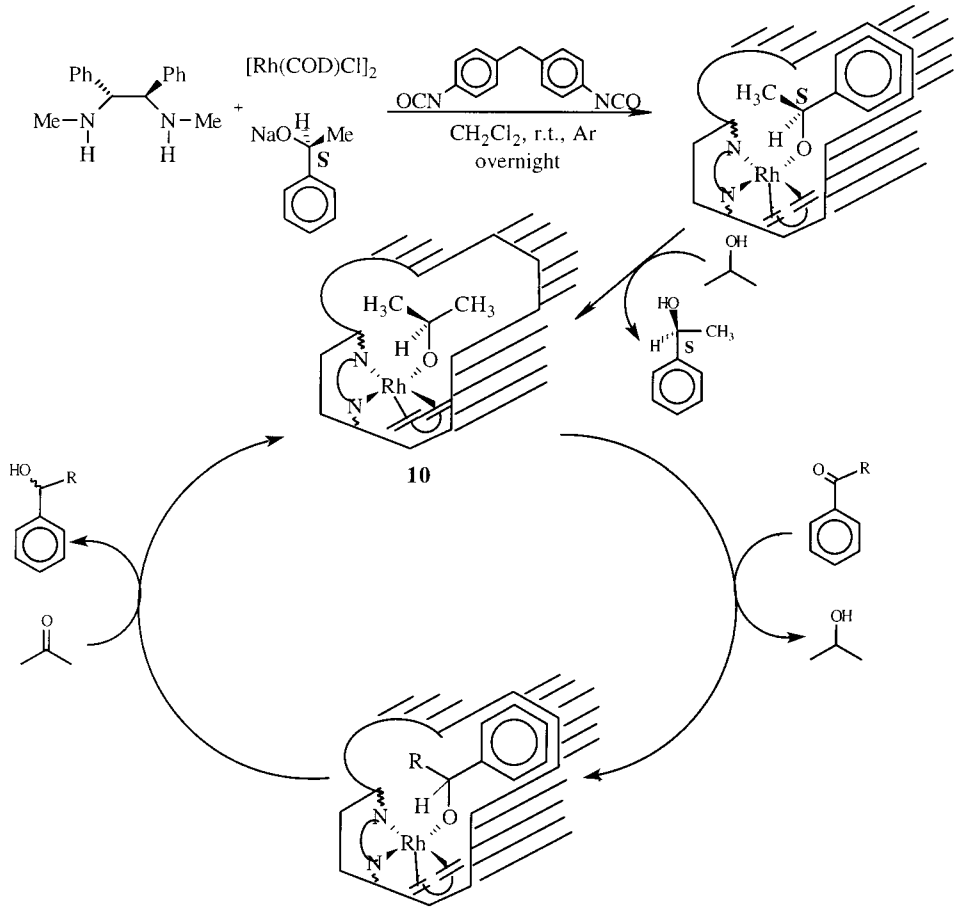
The importance of the rigidity of the material led us to be interested in the molecular imprinting technique for which crosslinking is required. The principle of molecular imprinting consists of copolymerization and cross-coupling of a polymer in the presence of a chiral molecule used as a printed molecule (PM). The latter, included into the polymer by means of a covalent or a non-covalent bond, can be removed in order to let its chiral imprint in the polymeric matrix. This chiral cavity is then able to act as a center of molecular recognition [27]. This methodology has intensively been used in the chromatography area especially for resolution of racemates by HPLC [28]. Catalysis has also been investigated but on a smaller scale and has shown an increase of activity compared to the corresponding homogeneous catalytic reaction [29]. The molecular imprinting effect seems to be an interesting tool in order to reach high enantioselectivity. We have prepared a new catalyst by polymerization of the chiral rhodium ([(*N*,*N*′-dimethyl-1,2-diphenylethylene diamine, COD) rhodium]) complex in the presence of sodium 1-(*S*)-phenylethanolate (template) with di- and triisocyanates [30] (Scheme 8).

The hydrogen transfer using non-templated or templated polymer was performed in the presence of 5 mol% of Rh-polymer with a KOH/[Rh] ratio of 4, at 60°C. Results are presented in Table 5.

The molecular imprinting effect was noted by an increasing ee in the case of the acetophenone reduction (runs 1 and 2). The best results are obtained in the case of the propiophenone reduction; the ee increased from 47% with non-templated polymerized complex (run 3) to 67% with the templated polymerized complex (run 4). Optimization of the crosslinking ratio led to the best compromise between activity and selectivity (70% ee) [30c]. One of the main advantages of this method is that, in most cases, it allows an increase of the obtained ee compared to the homogeneous phase. Nevertheless, it is noteworthy that in the case of sterically demanding substrates such as *tert*-butyl phenyl ketone, little or no reduction was observed, indicating a substrate specificity different from that observed in homogeneous catalysis.

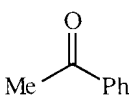
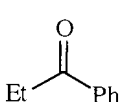
Finally, in most cases, for the reduction of ketones by hydrogen transfer, we have shown that the chiral supported-polymer catalysis, involving polymers such as aminosulfonamide Merrifield-type materials or chiral main chain polyureas and polythioureas, led to similar or better results, compared to those of homogeneous catalysis. The imprinting effect is obvious for molecules similar to the structure of the template and is not efficient if the substrate structure is very different from the template one.

3.1.2.2. Polythioureas as material for asymmetric catalysis. Conversely, for oxygen-containing functional groups, the sulfur-containing molecules are more or less considered as poison for transition metal catalysis. On the other hand, stronger interactions with 'soft' transition metals could be expected with the sulfur atom compared to the oxygen donor.



Scheme 8.

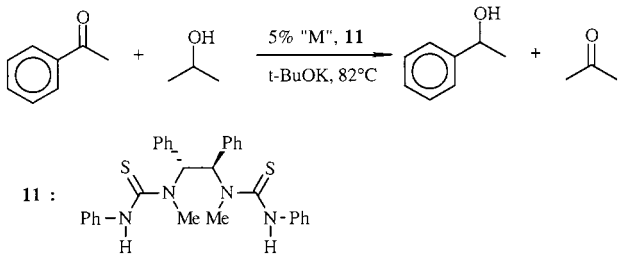
Table 5
Molecular imprinting effect in reduction by using Rh catalyst with templated and non-templated polymer **10**

Run	Substrate	Catalyst	Inductor configuration	Conversion	Time (days)	ee (%) (configuration)
1		Polymerized	(*S*,*S*)	98	1	25 (*R*)
2		(*R*) templated	(*S*,*S*)	98	1	43 (*R*)
3		Polymerized	(*S*,*S*)	96	6	47 (*R*)
4		(*R*) templated	(*S*,*S*)	91	9	66 (*R*)

We were also interested in the hydrogen transfer reduction of prochiral ketones with thioureas [31] as ligand in homogeneous catalysis (Scheme 9). Encouraging results obtained with acetophenone in the presence of Rh and Ru catalysts (Rh catalyst gives 98% conversion and 66% ee instead of 98% conversion and 89% ee for the Ru analog) led us to synthesize and test polythioureas for heterogeneous catalysis.

Polythioureas were easily obtained by polyaddition of *N*,*N*′-dimethyl-1,2-diphenylethylene diamine with isothiocyanates (Scheme 10). In such cases, the best results were obtained when using rigid diisothiocyanate although crosslinking does not increase selectivity of the reduction.

Elemental analysis provides an evaluation of the DP of polymer **12** which is about 13 and of the molecular weight of ca. 7700 g mol^{-1}. The reduction of acetophenone was carried out at 70°C in the presence of a *t*-BuOK/metal ratio of 4 and 5 mol% of metal.



Scheme 9.

The polymer **12** was tested with different catalyst precursors. The ratio L/M (ligand/metal) was increased until the ee reaches its highest value. Only the best results are reported in Table 6.

The results presented in Table 6 show that rhodium led to weaker selectivities (run 1). The nature of ruthenium-containing catalyst precursors, [Ru(*p*-cymene)Cl_2]$_2$ or [Ru(benzene)Cl_2]$_2$, did not furthermore influence the selectivity (63% ee in both cases) (runs 2 and 3). Then, further reduction of acetophenone was carried out with [Ru(benzene)Cl_2]$_2$ as metallic precursor after 1 day at 70°C with an L/M ratio of 1.5; 92% of conversion and 70% ee was obtained.

This polymer was recovered by filtration and from the first to the fourth recycled polymer, no loss of catalytic activity was observed contrary to selectivity which decreased slightly from 70% to 61% ee.

The use of polymer **12** in hydrogen transfer reduction of other aryl ketones was also studied (reaction conditions: L/M = 1.5, Ru/substrate = 4, *t*-BuOK = 4, 70°C) (Table 7). For all ketones tested, conversions up to 85% and ee up to 70% were observed.

Table 7
Aryl-alkyl ketones (RCOR′) reduced with polymer **12** in the presence of [Ru(benzene)Cl_2]$_2$

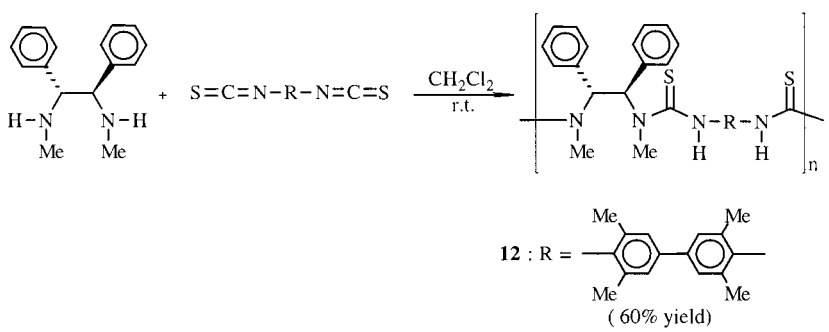
Run	R	R′	Time (days)	Conversion (%)	ee (%)
1	Ph	Me	1	92	70
2	Ph	Et	1	95	80
3	Ph	*i*-Pr	1	87	84

4. Reduction with molecular hydrogen

Hydrogen transfer presents several distinct advantages as a reducing process, nevertheless, it requires basic or acidic conditions not always compatible with useful substrates. On the contrary, the use of molecular hydrogen as a reducing agent could be performed in neutral conditions. Thus, hydrogenation using molecular hydrogen is of more general industrial application [32].

Asymmetric hydrogenation reactions catalyzed by rhodium or ruthenium complexes containing chiral phosphines have been successfully performed and constitute examples of well established catalytic methodologies. Among them, BINAP metal complexes were extensively studied and applied from both academic and industrial points of view [33]. Heterogenization of such asymmetric catalytic systems containing phosphorus ligands has received an increasing interest in recent years.

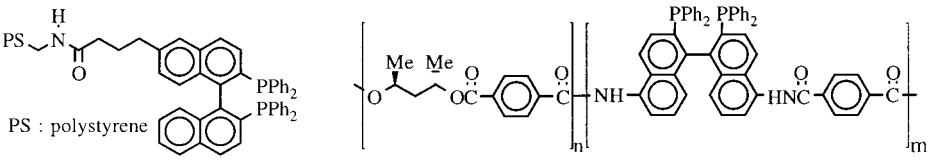
Recently Bayston et al. have succesfully performed the heterogenization of BINAP by anchoring it onto an



Scheme 10.

Table 6
Influence of the catalyst precursor on the enantioselectivity of the reduction of acetophenone

Run	Precursor	L/M	Time (h)	Conversion (%)	ee (%)
1	[Rh(COD)Cl]$_2$	3	15	96	47
2	[Ru(*p*-cymene)Cl_2]$_2$	2	15	93	63
3	[Ru(benzene)Cl_2]$_2$	2	15	98	63



Bayston's heterogenized BINAP Chan's heterogenized BINAP

Scheme 11.

existing polymer (Merrifield resin type) (Scheme 11) [34]. This ligand was used in the hydrogenation of carbonyl compounds as β-ketoesters with conversions of about 80–100% using a substrate/catalyst ratio of 500/1 and ee values up to 90%. Acrylic acid was also hydrogenated; conversion up to 90% and ee about 60% were observed. On the other hand, Chan et al. [35] have chosen the strategy which includes the BINAP in the main chain of a polymer (Scheme 11), in order to study the hydrogenation of acrylic acid derivatives (conversion from 65% to 100% with a ratio substrate/catalyst of 200, and ee values from 88 to 95% were obtained).

At the same time, we have chosen this second possibility, i.e. the inclusion of BINAP in the backbone of the polymer. We have synthesized *diam*-BINAP (6,6′-dimethylamino-2,2′-diphosphino-1,1′-binaphtalene) (Scheme 12) as a precursor of heterogenized BINAP. *diam*-BINAP was obtained from enantiopur binol in five steps in about 20% overall yield [36]. Then, by polyaddition with 2,6-diisocyanatotoluene, *diam*-BINAP was transformed into *poly*-NAP, a polyurea which presents a pseudo C_2 symmetry (Scheme 13) and which is soluble in polar aprotic solvents (DMF, DMSO) [36].

We have used *poly*-NAP as a ruthenium ligand in asymmetric hydrogenation of C=O and C=C bonds. The results are summarized in Tables 8 and 9. Comparative results with BINAP are presented.

In the case of the β-keto-ester (runs 1 and 2, Table 8), similar activity and selectivity (99%) were observed. An attempt to reuse the *poly*-NAP–$RuBr_2$ was performed with this substrate and after four times, no loss of either selectivity or activity was observed.

In 1995, Noyori et al. [38] reported the use of both BINAP–Ru catalyst and a chiral diamine (mainly diphenylethylene diamine: DPEDA) as an additional ligand allowing reduction of various prochiral ketones. They have shown a synergetic effect of the amine, as BINAP–Ru catalyst alone was unable to reduce unfunctionalized ketones. Then, we carried out the reduction of acetophenone in the presence of DPEDA. The reaction conditions employed with *poly*-NAP (run 4), even though different from Noyori's conditions (run 3), yielded total conversion (100%) and an interesting enantioselectivity (68%). For this reaction, the catalytic system was filtered and reused four times. We have observed only a slight loss of enantioselectivity (from 68% to 61%).

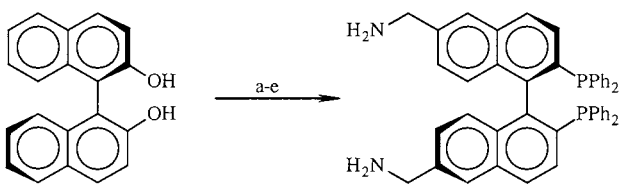
The hydrogenation reaction in the presence of *poly*-NAP–ruthenium as catalyst was extended to ethylenic substrates (Table 9). Comparable results, concerning activity and enantioselectivity, were obtained for *poly*-NAP and BINAP for the reduction of α-acetamido acrylic acid. Conversions are about 95% and ee up to 70% which is close to that observed in similar conditions with BINAP itself.

Poly-NAP proved to be an efficient ligand for hydrogenation of β-ketoesters, ketones and ethylenic substrates.

5. Conclusion

The renewed interest for homogeneous supported catalysis is partly due to the development of nitrogen-containing ligands. The chemistry of this functional group is much more adapted to the formation of polymers than their phosphorus counterparts. Even in the case of phosphine-containing ligands, the introduction of an amine group onto the homogeneous ligand allows the formation of efficient and selective materials.

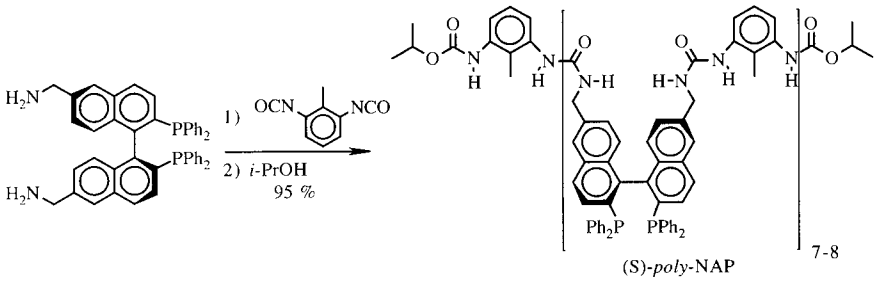
We have shown that polymer-supported analogs such as polysulfonamide Merrifield resins and chiral main chain polymers, such as polyureas or polythioureas presenting a pseudo C_2 symmetry were suitable for different types of asymmetric heterogeneous catalytic reactions: allylic substitution and hydrogen transfer reduction of ketones. Moreover, the heterogenization of



diam-BINAP

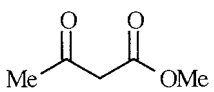
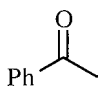
a) Br_2, CH_2Cl_2, -75°C (82%); b) Tf_2O / pyr., CH_2Cl_2, 0°C (92%);
c) CuCN, NMP, 180°C (62%); d) $HPPh_2$ / DABCO, $NiCl_2$dppe, DMF, 100°C (47%)
e) $LiAlH_4$, THF / toluene (100%)

Scheme 12.



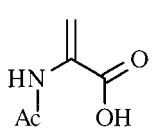
Scheme 13.

Table 8
Reduction of carbonyl compounds with H_2, at 50°C under 40 bar

Run	Substrate	Catalyst	Solvent	Time (h)	S/C	Conversion (%)	ee (%)
1		BINAP-$RuBr_2$	MeOH	14	1000	100	99 (*S*) [37]
2		*Poly*-NAP–$RuBr_2$	MeOH	14	1000	100	99 (*S*)
3		(*S*) BINAP–$RuCl_2$·dmf[a]+(*S*,*S*) DPEDA	*i*-PrOH–KOH	18	500	99	87 (*R*) [38]
4		(*S*) *Poly*-NAP–$RuBr_2$+(*S*,*S*) DPEDA	*i*-PrOH–*t*-BuOK	18	1000	100	68 (*S*)

[a] Hydrogen pressure: 4 bar.

Table 9
Hydrogenation of olefinic substrates at 50°C under 10 bar

Run	Substrate	Catalyst	Solvent	Time (h)	S/C	Conversion (%)	ee (%)
1		BINAP–$RuCl_2$·dmf	MeOH	14	100	95	78
2		(*S*) *Poly*-NAP–$RuCl_2$·dmf	MeOH	14	100	95	70

BINAP into *poly*-NAP (polyurea) was successful and allowed the efficient hydrogenation of carbonyl and ethylenic compounds.

From the synthetic point of view, in most cases, the use of polymer-supported ligands in these reactions is interesting because high conversions and enantioselectivities were obtained. On the other hand, they offer easy separation of the catalyst from the reaction products and their reuse is mostly effective without any loss either of conversion or enantioselectivity.

6. Experimental

6.1. Example of polymer synthesis

6.1.1. Synthesis of polymer **12**

Typically, 2.06 mmol of 2,6,2′,6′-tetramethylbiphenyl-4,4′-diisothiocyanate (synthesized according to Kim and Yi [39]) are dissolved in a minimal volume of CH_2Cl_2 and 2.09 mmol of diamine in 1 ml of CH_2Cl_2 are then added. The reaction mixture is stirred for 12 h under argon, then 50 ml of *i*-PrOH is added and the solution is stirred for 12 h again. The polymer then precipitates. It is washed twice with 50 ml of *i*-PrOH and dried for 2 days under vacuum (20 mmHg) at room temperature (r.t.) in the presence of P_2O_5.

Yield: 56%, $[\alpha]_D = -200.2$ ($c = 0.52$, DMSO); Fp = 215°C; ^{1}H-RMN ($(CD_3)_2SO$): 2.23; 2.42; 3.13; 7.2–7.6; 8.07; 9.01. Elemental analysis: Anal. Found: C, 72.06; H, 6.36; N, 9.87; S, 11.71. Calc.: C, 72.11; H, 6.33; N, 9.76; S, 11.8%.

6.2. Example of hydride transfer reduction

The catalyst precursor (6×10^{-3} mmol of metal) and the appropriate quantity of ligand are mixed in 2 ml of a 0.012 M solution of *t*-BuOk. After 1 h of stirring

under argon, the ketone is added (6×10^{-2} M). After 12 h of stirring at r.t., the system is heated at 70°C. The conversion is followed by GC (cydex β SGE 25 m × 0.25 mm).

The catalysts *poly*-NAP–$RuBr_2$ and *poly*-NAP–$RuCl_2$·dmf were respectively prepared according to Genet et al. [37] and Noyori et al. [40].

6.3. Example of reduction with hydrogen

To the prepared *poly*-NAP catalyst was added the substrate (β-Ketoester or unsaturated acid substrate) in 2 ml of methanol. The resulting suspension was stirred for 14 h at 50°C under 40 bar of hydrogen pressure. After centrifugation of the suspension, the liquid part was removed by a syringe and analyzed by GC (lipodex A 25 m × 0.25 mm for ketoesters or Supelco β-DEX™ 225, 30 m × 0.25 mm for unsaturated compound after transformation of the acid into their corresponding methyl esters).

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