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Heterogenization of Rh-MeDuPHOS by occlusion in polyvinyl alcohol films

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Abstract—A new recyclable chiral heterogeneous catalytic system was obtained by the occlusion of Rh-MeDuPHOS in polyvinyl alcohol film. Enantiomeric excess of up to 96% was achieved in the asymmetric hydrogenation of methyl 2-acetamidoacrylate in aqueous medium. © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

The use of immobilized homogeneous catalysts is of continuing interest. Polymer-supported chiral catalysts for high throughput synthesis such as dihydroxylation of olefins with microencapsulated osmium tetroxide,[1] allylic substitution and Suzuki coupling using microencapsulated palladium catalysts[2] have recently been developed. Efficient chiral heterogeneous catalysts were obtained by immobilization of transition-metal complexes through attachment to organic or inorganic supports or by entrapment in various polymer matrixes.[3–5] An alternative approach involved recycling of metal complexes using biphasic systems where the complex resides in a different phase from the substrate and/or product.[6,7]

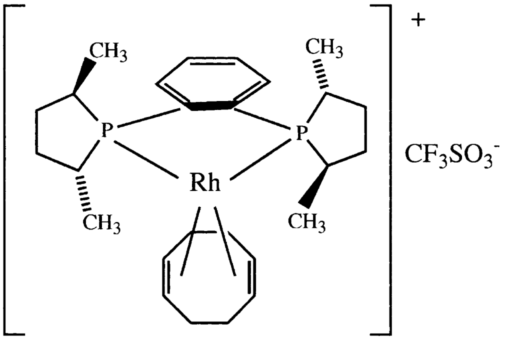
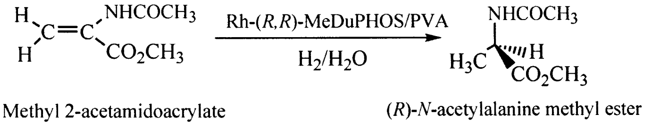


Figure 1. Rh-MeDuPHOS complex.

The Rh-MeDuPHOS complex (Fig. 1) has been found to be a very active and a most efficient enantioselective complex in the homogeneous asymmetric reduction of enamides to chiral amino acid derivatives.[8,9] In our ongoing study of the heterogenization of homogeneous chiral catalysts, we recently demonstrated that occluded Rh-MeDuPHOS in PDMS films could be used in the asymmetric hydrogenation of methyl 2-acetamidoacrylate in aqueous medium. In this case, the metal complex could be recycled without leaching.[10] The enantioselectivity was found to be comparable to that of the analogous homogeneous system.

We report herein on a new chiral heterogeneous catalytic system obtained by occlusion of Rh-MeDuPHOS in a polyvinyl alcohol (PVA) film as a representative hydrophilic film. The performance of the new heterogeneous system was compared with that of Rh-MeDuPHOS occluded in a hydrophobic PDMS film in the asymmetric hydrogenation of methyl 2-acetamidoacrylate to *N*-acetyl alanine methyl ester (Scheme 1) in aqueous medium.



Scheme 1. Asymmetric hydrogenation of methyl 2-acetamidoacrylate catalyzed by Rh-MeDuPHOS complex.

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Preparation of the film and incorporation of the metal complexes are straightforward processes and are described in Section 2. Since PVA crosslinks by itself in hydrophilic solvents such as water or ethylene glycol, by dissolving PVA in either solvent and then evaporating the solvent, PVA films physically crosslinked by hydrogen bonding are readily obtained.[11] However, PVA was dissolved in water rather than in ethylene glycol, since the latter demands the use of higher temperatures, which could harm the chiral complex. Addition of dialdehydes or dicarboxylic acids such as malic acid as crosslinker in the presence of an additional acid as catalyst yields covalently crosslinked PVA films.[12,13]

Homogeneous reactions were performed in the presence of various components used in the preparation of PVA films, such as water, acetic acid and malic acid (Table 1, entries 2–4). To help determine whether any of these components affect the activity and enantioselectivity of the chiral complex, a homogeneous reaction was also performed (entry 1). Water did not affect the enantioselectivity of the asymmetric hydrogenation of methyl 2-acetamidoacrylate (MAC) with Rh-MeDuPHOS but decreased the reaction rate. Likewise, addition of the crosslinker, malic acid, and addition of acetic acid, failed to alter either the activity or the enantioselectivity.

Table 1. Effect of additives on the performance of Rh-MeDuPHOS in the homogeneous asymmetric hydrogenation of methyl 2-acetamidoacrylate[a]

Entry	Additive	TOF (h^{-1})[b]	E.e. (%)
1	–	65	99
2	Water[c]	42	98
3	Acetic acid[d]	63	97
4	Malic acid[d]	65	97

[a] Reaction conditions: 25°C, H_2 (2 atm.), methanol (9 mL), MAC (0.1 g), $S/C=150$.

[b] After 10 min.

[c] Water (3 mL) and methanol (6 mL).

[d] Acid (16 μmol).

Thus, the PVA films containing Rh-MeDuPHOS complex were successfully crosslinked both physically and chemically. We then proceeded to examine the degree of leaching of complex from the films in different solvents (Table 2). For comparison, leaching of the complex from a hydrophobic PDMS film was also tested in the same solvents. ICP-MS was employed to detect very low metal concentrations (ppb).

As expected, high sorption of hydrophilic solvents was observed in the PVA films while the same solvents were poorly absorbed by the hydrophobic PDMS (Table 2). Chemically crosslinked PVA produced denser films than physically crosslinked PVA, with the swollen films displaying poorer sorption of all solvents, even good PVA solvents such as water. Leaching was only affected by the solubility of the metal complex in the solvent used and was not influenced by the degree of swelling of the film. In methanol, which dissolved the complex, high leaching of the complex was observed (entries 1–3). In xylene (entries 4–6) or water (entries 8–10), which are poor solvents for the complex, only limited complex leaching was observed. Addition of a small amount of methanol to xylene (entry 7) increased the degree of leaching as compared with xylene alone due to the higher solubility of the metal complex in the solvent mixture. In all solvents, use of the chemically crosslinked instead of physically crosslinked PVA film led to lower leaching, probably due to the increase in crosslinking density. A similar effect of crosslinking density on leaching was found for Rh-MeDuPHOS occluded in PDMS films.[10]

Examination of the behavior of PVA and PDMS films in different solvents revealed that leaching of the metal complex was higher when the solvent caused swelling of the polymer. In water, for example, leaching of Rh-MeDuPHOS from the hydrophilic PVA film (entries 8 and 9) was substantially higher than that from the hydrophobic PDMS film (entry 10). In xylene, the opposite pattern was observed (entries 4–6). The process of sorption seems to consist of two time-dependent

Table 2. Sorption of solvents and leaching experiments of Rh-MeDuPHOS occluded in PVA and PDMS films[a]

Entry	Solvent	Solubility of complex in the solvent	Polymer	Sorption of solvent in polymer (g/g)	Leaching of complex (%)
1	Methanol	High	PVA[b]	0.156	47
2	Methanol	High	PVA[c]	0.151	45
3	Methanol	High	PDMS[d]	0.049	31
4	Xylene	Low	PVA[b]	0.061	0.7
5	Xylene	Low	PVA[c]	0.061	0.7
6	Xylene	Low	PDMS[d]	1.177	2.9
7	Xylene/methanol (10:1 v/v)	High	PVA[c]	0.062	11
8	Water	Low	PVA[b]	0.884	5.2
9	Water	Low	PVA[c]	0.284	4.2
10	Water	Low	PDMS[d]	0.065	0.9

[a] Rh-MeDuPHOS (10 μmol), solvent (20 mL), 25°C, 1 atm, 24 h.

[b] Physical crosslinking.

[c] Chemical crosslinking with malic acid as crosslinker in the presence of acetic acid.

[d] PDMS dimethylvinyl terminated, average molecular weight of 5426 with 20 wt% silica.

steps: first, sorption of a particular solvent into the polymer takes place depending on the nature of both polymer and solvent; this is followed by dissolution of the chiral complex. Changing the nature of the film and the solvent influences the permeability of the reactants (substrate and hydrogen).

We tested the occluded complexes as catalysts in the asymmetric hydrogenation of methyl 2-acetamidoacrylate (MAC) in aqueous medium with Rh-MeDuPHOS occluded in PVA films, as illustrated in Table 3. The initial results obtained with Rh-MeDuPHOS occluded in PVA films (Table 3) showed that it was possible to perform the hydrogenation reaction in water and also to recycle the heterogeneous catalyst (entries 3 and 4) without any subsequent loss in activity or enantioselectivity. The reaction rate when physically crosslinked PVA film was used was slightly higher than that observed for chemically crosslinked film, probably due to the higher permeabilities of the physically crosslinked support. The PVA films tested were much denser than the PDMS film and the sorption of water to PVA film was higher. Although no complete comparison can be made between PVA and PDMS films, occlusion of the chiral metal complex in hydrophilic and hydrophobic films demonstrates the feasibility of working with different polymers and solvents.

In conclusion, for the first time a chiral transition-metal complex was successfully incorporated into polyvinyl alcohol films. The preparation of the heterogeneous system was very easy and did not involve modification of the metal complex. Leaching of Rh-MeDuPHOS from the PVA film was studied and compared to that from the PDMS system. It was found that using a poor solvent for the chiral complex prevents leaching. The heterogeneous catalytic system was successfully reused without loss of activity and enantioselectivity. Other substrates and complexes will have to be tested in order to determine the scope and limitations of this new catalytic system.

Table 3. Enantioselective hydrogenation of methyl 2-acetamidoacrylate with Rh-MeDuPHOS occluded in PVA and PDMS films[a]

Entry	Solvent	TOF (h^{-1})[b]	E.e. (%)
1	Water[c]	12.6	96.9
2	Water[d]	14.9	96.1
3	Water[e] (first cycle)	12.4	95.7
4	Water[e] (second cycle)	12.2	95.1

[a] Reaction conditions: 25°C, H_2 (2 atm), MAC (0.1 g), solvent (19 mL), catalyst (10 μmol).

[b] After 6 h.

[c] PDMS dimethylvinyl terminated, average molecular weight of 5426, with 20 wt% silica.

[d] Physically crosslinked PVA.

[e] Chemically crosslinked PVA.

2. Experimental

2.1. Preparation of the catalyst

The Rh-salt [bis(1,5-cyclooctadiene) rhodium(I)trifluoromethanesulfonate, 99%] and methyl-DuPHOS ligand [(−)-1,2-bis-(2*R*,5*R*)-2,5-dimethylphosphacyclopentyl)-benzene, 98%] were purchased from Strem. The Rh-MeDuPHOS catalyst was prepared in a glove box by dissolving the rhodium salt and the DuPHOS ligand separately in methanol (5 μmol salt in methanol (0.25 mL) and ligand (6 μmol) in methanol (0.2 mL), respectively) and stirring for 40 min. The ligand solution (5% excess) was added dropwise to the rhodium salt solution under constant stirring. After 30 minutes, the methanol was flushed out with nitrogen.

2.2. Preparation of films

Polyvinyl alcohol films were prepared using two crosslinking methods:[10] (a) physical crosslinking in water and (b) chemical crosslinking in water with the addition of malic acid as crosslinker and acetic acid or hydrochloric acid as catalyst. In both cases, an amount of 0.5 g PVA (99% hydrolyzed, $M_W = 50000$, purchased from Aldrich) was dissolved in distilled (5 g) water by warming to 50°C for 5 min (in some cases ethylene glycol was used instead of water, in which case the mixture was warmed to 120°C). The chiral complex was then dissolved in methanol (0.5 mL), added to the PVA solution and poured into a Petri dish. Water was evaporated in a vacuum oven at 80°C for 3 h. Evaporation was performed under a nitrogen atmosphere. After evaporation the film was easily removed from the Petri dish and added in pieces to the reaction mixture in the reactor. For the chemically crosslinked PVA film, 3 wt% each of malic acid and acetic acid (both purchased from Aldrich) were dissolved in water (5 mL) before the addition of PVA (0.5 g).

2.3. Leaching procedure

Leaching of the complex and solvent sorption were tested in various solvents (20 mL) for 24 h. The extent of leaching of the metal complex from the polymer matrices was measured by analyzing the liquid phase after separation with a PQ3/VG ICP-MS system. The sorption of the solvents was measured by weighing the polymer before and after sorption.

2.4. Typical hydrogenation procedure

A 25 mL reactor with magnetic stirring was used for both the homogeneous and the heterogeneous reactions. In the homogeneous reactions, the complex was dissolved in the reaction solvent. In the heterogeneous-catalyzed reactions the film was added in pieces to the reaction medium under a nitrogen atmosphere. A volume of solvent (18 mL) was added to the reactor together with the substrate (0.1 g). The reaction was performed at 25°C with high-purity hydrogen (99.995%) at a pressure of 2 bar. Samples were withdrawn periodically to determine the reaction rate and the enantiomeric excess as a function of time and were analyzed on a GC with an Astec Chirasil-Val capillary column. Reuse of the catalyst was tested by replacing the reaction liquid phase and washing the PVA film with the reaction solvent before addition of new reaction mixture.

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