Sol–gel entrapped chiral rhodium and ruthenium complexes as recyclable catalysts for the hydrogenation of itaconic acid

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Abstract

Chiral Ru–BINAP, Rh–DIOP and Rh–BPPM complexes have been physically entrapped in sol–gel matrices. The resulting materials are recyclable leach-proof catalysts for enantioselective hydrogenation of itaconic acid. Chiral methylsuccinic acid of o.p. up to 78% is obtained. The complexes, including the water insoluble Ru–BINAP derivatives, react both in organic and in aqueous media. © 1999 Elsevier Science B.V. All rights reserved.

Keywords: Enantioselective hydrogenation; Immobilized catalysts; Rhodium; Ruthenium; Sol–gel

1. Introduction

Entrapment of organic and organometallic compounds in sol–gel matrices has become an important technique for a wide spectrum of applications in the field of optics, chemical sensing, photochemistry and biochemistry [1]. Recently [2–4], we have found this technique applicable also to the conversion of soluble transition metal complexes into efficient, leach-proof and recyclable catalysts for double bond migration, hydroformylation, arene hydrogenation and disproportionation of dihydroaromatics. These immobilized catalysts were shown to have often superior catalytic properties than the corresponding non-entrapped analogs. The direct, physical entrapment of the catalysts in sol–gel matrices provides some advantages over the more traditional use of immobilization by covalent anchoring, e.g., with suitable trialkoxysilane derivatives [5]. Thus, lengthy synthetic procedures for the preparation of the suitable derivatized monomers is avoided, and the chemistry of the ligands remains untouched by such modification.

Two major interests of the pharmaceutical industry, are addressed in this report. The first one is chiral catalysis [6], and the other is the environmental-protection pressure of shifting the production processes from organic to aqueous solutions. Utilization of the sol–gel immobilization methodology is

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only in its infancy from these points of view. Thus, Shvo et al. [7] reported on the sol–gel entrapment of a catalytic peptide for hydrocyanation, and Shabat et al. [8] reported on the sol–gel entrapment of a chiral antibody for heterogeneous aqueous catalysis. Examples for trialkoxy-covalent entrapment include the work of Wieland and Panster [9] who reported on the stereoselective hydrogenation of a steroidal double bond with a (non-chiral) Rh complex, and the asymmetric hydrogen transfer study of Adima et al. [10], with a silylated diamine–Rh complex. In this paper we report the first examples for direct physical entrapment of chiral transition metal catalysts in sol–gel porous glasses and their utilization for the enantioselective hydrogenation of itaconic acid (Eq. (1)).

$$\text{(1)}$$
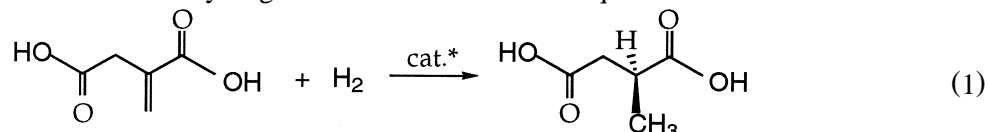
2. Experimental

2.1. General

[(*R*)-(+)- and [(*S*)-(−)-2,2′-bis(diphenylphosphino)-1,1′-binaphthyl]chloro(*p*-cymene)ruthenium chloride [(+)- and (−)-Ru–BINAP, respectively], (4*S*,5*S*)-(+)- and (4*R*,5*R*)-(−)-4,5-bis(diphenyl-phosphinomethyl)-2,2′-dimethyl-1,3-dioxolane [(+)- and (−)-DIOP, respectively], (2*S*,4*S*)-(−)-1-*tert*-butoxycarbonyl-4-diphenylphosphino-2-(diphenylphosphinomethyl)pyrrolidine [(−)-BPPM] and tetramethoxysilane were purchased from Sigma-Aldrich.

Ru-BINAP

DIOP

BPPM
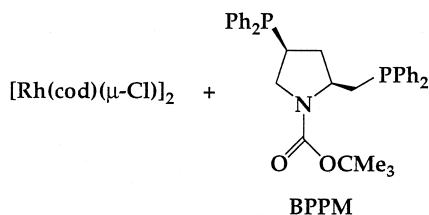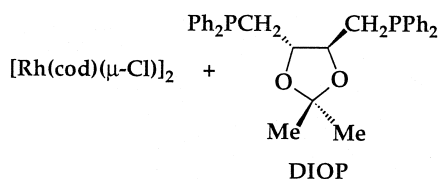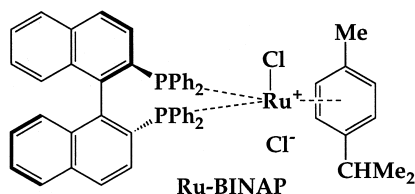
Optical rotation measurements were performed on a Perkin-Elmer polarimeter model 141. HPLC measurements were carried out with the aid of a Jasco Tri Roter-VI machine equipped with a Chiral-Pak AD column packed with amylose tris(3,5-dimethylphenylcarbamate) on 10 μm silica gel (Daicel Chemical Industries, Tokyo). NMR spectra were recorded on a Brucker AMX 300 instrument. MS analyses were carried out using a Hewlett-Packard Model 4989A mass spectrometer equipped with an HP gas chromatograph model 5890 series II. IR spectra were taken on a Perkin-Elmer Model 157 spectrophotometer. Atomic absorption measurements were carried out on a Perkin-Elmer instrument model 403 using Juniper rhodium and ruthenium cathode lamps.

2.2. Preparation of the immobilized catalyst

2.2.1. One step procedure

A 50-ml flask equipped with a magnetic bar, a rubber septum, and a gas inlet and outlet was charged, under nitrogen with 7.2×10^{-2} mmol of the appropriate homogeneous catalyst (or catalyst components) and 8 ml of peroxide-free THF. During the formation of entrapped (+)- and (−)-Ru–BINAP complexes (**1a** and **1b**, respectively), as well as during the encapsulation of the Rh–BPPM (catalyst **3**), 0.75–1.0 ml of NEt_3 was also added. After stirring for 15 min at room temperature 1.0 ml of degassed water was added and the stirring was continued for 5 min. Tetramethoxysilane (2.5 ml) was injected through the rubber septum and the stirring was continued for another 30 min. The reaction vessel was sealed under N_2 and left at room temperature until gelation was complete (4–5 days). The wet gel was dried at 0.5 Torr until constant weight was obtained. The xerogel was treated for 1 h with 20 ml of boiling CH_2Cl_2, sonicated, and dried at 0.5 mm. The CH_2Cl_2 washings were concentrated and the metal content in the residue (which proved to be < 1 ppm) was determined by atomic absorption analysis.

2.2.2. Two step procedure

A round bottomed flask was charged with 1.2 ml of HCl solution of pH 1.96 (prepared from 0.1 ml of 1.1 N hydrochloric acid and 9.9 ml H_2O), 2.5 ml (17 mmol) of $(MeO)_4Si$ and 3.5 ml of MeOH. The mixture was stirred magnetically for 15 min, and the pH was increased by addition at once of 0.44 ml of 0.1 N aqueous NH_4OH followed by a THF solution of the appropriate catalyst (prepared in situ by mixing of 2.2×10^{-2} mmol of $[Rh(cod)Cl]_n$ [11] and the equimolar quantity of the desired chiral ligand in 0.76 ml of THF). The mixture which gelled within a few minutes was dried, crushed, washed thoroughly with boiling CH_2Cl_2, sonicated for 30 min in the same solvent and dried at 0.5 Torr at room temperature until constant weight was obtained. The rhodium content of the washings proved by atomic absorption to be negligible.

2.2.3. Hydrogenation of itaconic and citraconic acids

To a preheated glass-lined mini autoclave (50–80°C as desired) was introduced a solution of 2.2 mmol of the unsaturated acid in 4 ml of the desired solvent. After addition of the immobilized catalyst the autoclave was sealed, flushed three times with H_2 and pressurized to 10–20 atm. The autoclave was heated with the aid of an oil bath thermostat for the desired length of time. The reaction vessel was cooled to 0–10°C, opened and the used catalyst filtered off, and the solvent evaporated. The residue was dissolved in 20 ml 0.5 N aqueous NaOH. The basic solution was treated (2 ×) with 5 ml Et_2O and the aqueous layer acidified with 1 N HCl to pH 1 and extracted (3 ×) with 15 ml Et_2O.

The organic layer was dried to give colorless methylsuccinic acid that was subjected to polarimetric and to HPLC analyses for determination of its optical purity. The recovered catalyst was washed ($2 \times$) with 20 ml of boiling CH_2Cl_2, sonicated and dried at 0.5 Torr for 3 h at room temperature. The CH_2Cl_2 washings were analyzed for leached metal by atomic absorption and the dried catalyst was used in a subsequent run.

3. Results and discussion

Entrapment of the commercially available ($+$)- and ($-$)-Ru–BINAP, respectively, in a silica sol–gel matrix in the presence of NEt_3 (catalyst: NEt_3 molar ratio of 1:100) by the general method described for the heterogenization of some other water insoluble complexes such as $RuCl_2(PPh_3)_3$ [3] gave the heterogenized catalysts **1a** and **1b**. One of the main motivations described in the literature for employing the lengthy trialkoxy route for covalent attachment of chiral catalysts to ceramic matrices is to avoid possible leaching of the catalyst [10]. It is therefore a significant observation that under our conditions no metal leaching could be detected (limit of detection, 1 ppm) and the used catalyst could be recycled after filtration, washing and drying at 0.5 Torr. Both **1a** and **1b** proved to promote smooth hydrogenation of aqueous itaconic acid (catalyst: substrate molar ratio of 1:30) at 80°C and 10 atm. H_2 to give methylsuccinic acids. In the presence of **1b**, e.g., quantitative yield of (R)-($+$)-methylsuccinic acid of 52% optical purity (deduced from both polarimetric measurements and HPLC analysis on a chiral column) was obtained under the conditions of Section 2 after 24 h. The o.p. was lower (24%) when the catalyst ratio was decreased to 1:100 and the pressure raised to 20 atm. Upon recycling of the catalyst (in the case of catalyst: substrate ratio 1:30) the yields in the first four runs were 100, 98, 95 and 90%, respectively, and the corresponding o.p. values 52, 50, 46 and 41%.

The catalysis by the entrapped (R)-($+$) complex, **1a**, yielded after 24 h at 70°C under the same conditions 66, 50, 42 and 33% of (S)-($-$)-methylsuccinic acid with 54, 49, 42 and 41% o.p., respectively, in the first four runs. Replacement of the water by THF (at 35°C), caused both the rate of hydrogenation and the enantioselectivity to increase (77.5% o.p. at full conversion), however, substantial metal-leaching prevented efficient catalyst recycling. The ability to employ the heterogenized complexes, **1a** and **1b**, in an aqueous medium is remarkable, since their water insoluble non-entrapped analogs are completely catalytically inactive under similar conditions in this medium [12].

The immobilized ($+$)- and ($-$)-Ru–BINAP–NEt_3 catalysts (**1a** and **1b**) were found to promote also the hydrogenation of the internal double bond of citraconic acid albeit with considerably lower selectivity than that observed in the reaction of itaconic acid. Thus, under similar conditions to those described in Section 2 (**1a**: substrate ratio 1:100; 20 atm H_2; 80°C, 24 h) aqueous citraconic acid gave quantitative yield of ($+$)-2-methylsuccinic acid of only 7–9% o.p. in the first three runs. Similar yield and o.p. of ($-$)-2-methylsuccinic acid were obtained when citraconic acid was hydrogenated in the presence of **1b**.

In analogy to the immobilization of ($+$)- and ($-$)-Ru–BINAP, we also entrapped the well known rhodium–DIOP complexes obtained from [Rh(cod)Cl]$_2$ and ($+$)-DIOP and ($-$)-DIOP [13] in a sol–gel matrix, resulting in materials **2a** and **2b**. While **1a** and **1b** were prepared by the direct, one step procedure in which the catalyst is added to the starting polymerizing system of $Si(OMe)_4$, it was essential to employ the so called 'two step' procedure (described in Section 2) [14] for the preparation of stable **2a** and **2b**. The immobilized rhodium catalysts formed by this manner, rather than by the

'one step' procedure, were shown to be leach-proof in EtOH and in other polar solvents, and could be recycled. Catalysts **2a** and **2b** so formed, resembled **1a** and **1b** in their ability to promote the hydrogenation of itaconic acid in water. Interestingly, in contrast to the entrapped ruthenium catalysts where the dextrorotatory complex **1a** gave (S)-$(-)$-methylsuccinic acid and vice versa levorotatory **1b**, **2a** promoted the formation of the (R)-$(+)$-acid and **2b** gave the (S)-$(-)$-product. In a typical set of experiments in which itaconic acid was hydrogenated in EtOH for 16 h in the presence of **2a** (catalyst: substrate ratio 1:50) at 75°C under 13 atm H_2, the conversions in the first three runs were 100, 55 and 39% and the respective o.p. values were 34, 32 and 25%. The decrease in activity has been assigned to partial blocking of the pore entrances in which the metal atoms exist. Indeed, upon treatment of the catalyst after the third cycle with boiling 2% aqueous $NaHCO_3$, that reopens blocked as well as new pores by cleavage of Si–O bonds, the conversion and optical purity rose in the following run again to 100 and 30%, respectively. Similar results were obtained when **2b** was used as catalyst. Hydrogenation by the non-encapsulated analog of **2a** afforded under the above conditions 100% of (R)-$(+)$-succinic acid of 41% o.p.

A third catalytic material, **3**, was obtained by the 'two step' entrapment of $(-)$-BPPM. The material proved to be leach-proof in a variety of organic solvents and gave (S)-$(-)$-methylsuccinic acid in good enantioselectivity. Thus, in an experiment in which the unsaturated acid and catalyst **3** in a 3:1 mixture of methanol and benzene (catalyst: substrate ratio 1:50) was treated with H_2 (13 atm) at 75°C for 16 h, quantitative yield of the saturated acid of 67% o.p. was obtained. In the subsequent runs the reaction rate decreased sharply (in the fourth run, e.g., the yield was only 27% after 29 h) but with only little changes in the o.p. of the product. However, a dramatic increase in reaction rate was observed when NEt_3 was added during the entrapment of the catalyst (catalyst: amine ratio 1:75). Quantitative yield of the product of 78% o.p. was formed already after less than 6 h. Thus, in this experiment the enantioselectivity reached the same value recorded in the hydrogenation of itaconic acid by the *non-immobilized* Rh–BPPM catalyst [15].

In conclusion, the two main observations made in this study are the ability to heterogenize chiral metal-complex catalysts without resorting to covalent bonding, and the ability of the sol–gel methodology to replace the organic solvent needed for the catalyst under homogeneous conditions with water in which the catalyst is insoluble. The replacement of organic solvents by water is environmentally beneficial.

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