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Research Note

New approach toward the synthesis of asymmetric heterogeneous catalysts for hydrogenation reactions

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Abstract

A new type of asymmetric heterogeneous catalysts is presented, together with results obtained in the enantioselective hydrogenation of ethyl pyruvate and acetophenone. The catalysts are prepared by using techniques derived from the surface organometallic chemistry on metals (reaction between a supported and a reduced transition metal catalyst with an organometallic compound). In the hydrogenation of acetophenone employing Pt-based catalysts, the presence of the organotin promoter notably enhances the chemoselectivity to phenylethanol (the desired product) in all cases. The enantioselective hydrogenation of acetophenone afforded an excess of the (*S*)-phenylethanol, with an enantiomeric excess (ee%) value of around 20% and a selectivity over 97%. Reusing of the catalysts is possible, keeping the selectivity and the ee% values.

Keywords: Asymmetric catalysis; Hydrogenation; Acetophenone; Ethyl pyruvate; Supported organometallic catalysts; Enantiomeric excess

1. Introduction

The production of enantiopure compounds is becoming more and more important in the field of pharmaceuticals, flavors, fragrances, and agrochemical agents; thus, several industrial processes using asymmetric catalytic reactions have been developed [1]. Most of these processes comprise the use of homogeneous catalysts that have the disadvantage of difficult separation and reuse of the expensive catalysts employed.

Throughout the years, many methods have been introduced to develop heterogeneous or heterogenized chiral catalysts. For example, metal–ligand complexes can be immobilized by covalent or coordinative linkage or electrostatic attraction via functionalized ligands or by adsorption on porous supports to combine the good activities and selectivities of homogeneous catalysts and the simplicity of recovery and the possibility of reusing the heterogeneous ones [2]. Another approach, especially related to hydrogenation processes, is the one in which a chiral auxiliary in solution is contacted to a heterogeneous metal catalyst, in order to modify the enantioselectivity of the system. To this category belong the classical systems composed of Ni catalysts modified with tartrate/NaBr [3] and Pt(Pd) modified with cinchona alkaloids [4]. These kinds of systems are successfully employed nowadays for the hydrogenation of certain carbonyl compounds [1,5,6]. However, many of these heterogeneous and heterogenized chiral catalysts suffer from the leaching of the active metal or the chiral auxiliary into the solvent and from the decrease of enantioselectivity. In order to avoid these disadvantages, we are studying the development of a new type of asymmetric heterogeneous catalysts, prepared by using techniques derived from the surface organometallic chemistry on metals (SOMC/M). This well-proven methodology comprises the reaction between a supported and a reduced transition metal catalyst with an organometallic compound

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[7,8]. Previously published papers demonstrated that it was possible to anchor $Sn(C_4H_9)_4$ onto a monometallic catalyst and to generate an organometallic phase (retaining butyl groups on the surface) with very interesting properties in the selective hydrogenation of carbonyl compounds [9,10]. A somewhat similar approach has been developed by Smith et al., who published a method to deposit a chiral silyl ether moiety onto a Pd surface through Si–metal bonds. The so-modified catalysts were tested in the enantioselective hydrogenation of prochiral molecules containing C=C bonds [11].

In the present paper, we introduce the synthesis of a new kind of asymmetric heterogeneous catalysts, based on silica-supported Ni, Rh, and Pt, chemically modified with chiral organotin compounds. The systems were tested in the enantioselective hydrogenation of ethyl pyruvate and acetophenone, and the stability of these catalysts was also studied in order to verify if they could be reused.

2. Experimental

2.1. Synthesis and characterization of the chiral organotin compounds

Following the procedures described in the literature [12–14], the chiral organotin compounds, (−)-Men_3SnMe, (−)-$MenSnBu_3$, (−)-$MenPh_2SnMe$, and (−)-Men_3Sn–$SnMen_3$ (Men, menthyl; Bu, butyl; Me, methyl; Ph, phenyl), were very carefully synthesized, in order to obtain optically pure compounds having no epimerization of the carbon atom attached to the tin atom. In a typical preparation procedure to a solution of 10.3 g (0.040 mol) of $SnCl_4$ in 48 mL of dry C_6H_6, in an ice bath, 150 mL of a solution of 1.58 M (−)-menthylmagnesium chloride in dry tetrahydrofuran was added drop by drop (0.240 mol). Once the addition step was concluded, the reaction mixture was heated under reflux for 60 h and then it was allowed to cool down to room temperature under stirring. A 10% HCl solution was added (25 mL) and diluted with distilled water (25 mL). After the addition of ethyl ether (200 mL), the organic phase is separated and dried on anhydrous $MgSO_4$. The solvent was distilled under reduced pressure and the product was recrystallized in ethanol. These compounds were fully characterized by ^1H, ^{13}C, and ^{119}Sn NMR, using $CDCl_3$ with tetramethylsilane as the standard.

2.2. Catalyst preparation

Monometallic catalysts were prepared by ionic exchange starting from solutions of $[Pt(NH_3)_4]Cl_2$, $[Ni(NH_3)_6](NO_3)_2$, and $[Rh(NH_3)_5Cl]Cl_2$, in order to obtain 1 wt% Pt, 2.2 wt% Ni, and 1 wt% Rh in the resulting catalysts. In all cases, the support used was SiO_2 (Aerosil, 200 $m^2\ g^{-1}$). After the impregnation stage, solids were washed, dried, calcined, and finally reduced in H_2 flow (773 K for Pt/SiO_2, 923 K for Ni/SiO_2, and 676 K for Rh/SiO_2). The reduced monometallic catalyst is reacted in H_2 atmosphere with an adequate amount of the chiral organotin compound dissolved in n-heptane (catalysts based on Rh, reaction temperature 298 K) or n-decane (catalysts based on Pt and Ni, reaction temperature 393 and 423 K, respectively). Once the reaction is finished, the catalyst is washed with n-heptane portions in an Ar atmosphere. The preparation procedure is analogous to the one employed when $SnBu_4$ is the tin precursor compound, and it is described in detail in Ref. [15].

2.3. Catalyst characterization

Monometallic catalysts were characterized according to Ref. [15], by chemical composition, temperature-programmed reduction (TPR), hydrogen chemisorption by the volumetric method, and distribution of metallic particle sizes by transmission electron microscopy (TEM). The variation in the concentration of the organotin compound during the preparation of organometallic catalysts was analyzed by using a gas chromatograph Varian 3400 CX (column 10% OV-101, FID) and a GC/MS in a Shimadzu QP-5050A (capillary column SPB-%TM Supelco). The atomic ratio Sn/M (M = Rh, Pt, Ni) was determined based on the tin content in the catalysts, spectrophotometrically measured at 530 nm, after complexing the tin with phenylfluorone.

2.4. Catalytic reactions

A typical procedure is as follows. Hydrogenation reactions were carried out in a 100-mL stirred autoclave reactor. The amount of 0.25 g of the catalyst was placed in the reactor, and then a definite quantity of the substrate (2.65 mmol of ethyl pyruvate and 4.23 mmol of acetophenone) and 60 mL of 2-propanol (solvent) were introduced into the reactor under a hydrogen atmosphere. The reaction was carried out at 353 K at a pressure of 1.0 MPa of H_2, with continuous stirring at a rate of 800 rpm. Reactions were followed by analyzing a sufficient number of microsamples by gas chromatography, using a Varian 3400 CX, having a 30 m J&W DB-Wax capillary column and a FID detector. The enantiomeric excess (ee) was determined chromatographically on a CP-Chirasil DEX CB column (25 m, 0.25 mm i.d.), and calculated as $ee\% = 100(S-R)/(S+R)$. Reaction products were identified by GC/MS in a Shimadzu QP-5050A (capillary column SPB-%TM Supelco). In order to verify if the catalysts under study could be reused, a series of experiments were carried out. The procedure consisted in submitting the catalyst to a hydrogenation test (under the conditions previously noted). After finishing the reaction, the remaining liquid was separated, the catalyst was repeatedly 2-propanol, and then another hydrogenation test was performed.

3. Results and discussion

3.1. Synthesis, preparation, and characterization of catalysts

The attainment of the proposed catalytic systems is determined by the key stage of the synthesis of the chiral organotin compounds. An important aspect taken into account in the preparation of organotin compounds [(−)-MenSnMe$_3$, (−)-MenSnBu$_3$, (−)-MenPh$_2$SnMe] consisted in the fact that they were obtained optically pure, that is, without epimerization in the carbon atom of the menthyl group bonded to the tin atom. This was obtained with the addition of triphenylphosphine during the synthesis. Without the addition of this base, when Bu$_3$SnCl reacts with (−)-MenMgCl, a mixture with a 3:1 ratio of epimers is obtained. In the case of Ph$_3$SnCl with (−)-MenMgCl, a mixture of epimers with a 3:2 ratio is attained, and with the Me$_3$SnCl there exists no epimerization [16].

Monometallic catalysts employed as base catalysts for all preparations were characterized by the usual methods, such as TEM and H$_2$ chemisorption, and the metallic content was determined by atomic absorption. TEM results show that the preparation by ionic exchange allows systems with a quite homogeneous particle-size distribution to be obtained, with values of mean particle diameter around 2.9, 1.2, and 2.5 nm, for Ni/SiO$_2$, Rh/SiO$_2$, and Pt/SiO$_2$, respectively. Besides, the chemisorption runs reveal, for Rh/SiO$_2$ and Pt/SiO$_2$, a high metal dispersion ($\mathrm{H/Rh} = 0.65$ and $\mathrm{H/Pt} = 0.64$), and a relatively moderate dispersion for Ni/SiO$_2$ ($\mathrm{H/Ni} = 0.16$). These characteristics of surface homogeneity are essential for assuring the correct preparation of organometallic catalysts through techniques derived from SOMC/M.

The preparation of organometallic catalysts performed following the same procedure used to generate systems modified by SnBu$_4$ [15] can be represented by the following equation:

$$\mathrm{M/SiO_2} + y\mathrm{SnR_4} + (xy/2)\mathrm{H_2} \\ \rightarrow \mathrm{M[SnR_{4-x}]_y/SiO_2} + xy\mathrm{RH}.$$

The present tin amount was measured to determine the "y" value (Table 1). In order to study the specificity of the interaction between the monometallic catalysts and the organotin compounds, blank experiments were conducted in which the tin precursor was contacted with the SiO$_2$. No detectable tin amounts on the support were observed under the experimental conditions of this work. In the case of organotin compounds containing different organic fragments, one or more of the denominated with R that remain bonded to tin correspond to (−)-menthyl. It should be stressed, however, that no further characterization of the organometallic catalysts was performed, and hence the true nature of the superficial complexes is not yet really known.

Table 1
Composition, activity, selectivity, and enantioselectivity in the hydrogenation of acetophenone over different Pt- and Rh-based catalysts promoted with different chiral organotin compounds (PE, 1-phenylethanol; CMK, cyclohexylmethylketone; CHE, 1-cyclohexylethanol; EB, ethylbenzene; ECH, ethylcyclohexane)

Catalyst	Sn/M y	r[a]	S_{PE}	S_{CMK}	S_{CHE}	$S_{\mathrm{EB}}+S_{\mathrm{ECH}}$	ee%
Pt/SiO$_2$	0	460	31	43	15	11	0
Pt (−)-Men$_3$SnMe	0.4	332	99	0	1	0	24
Pt (−)-Men$_3$Sn–SnMen$_3$	0.4	358	98	0	2	0	17
Pt (−)-MenSnBu$_3$	0.4	171	97	0	0	3	20
Rh/SiO$_2$	0	208	0	15	55	30	0
Rh (−)-MenSnBu$_3$	0.3	374	0	8	48	44	–

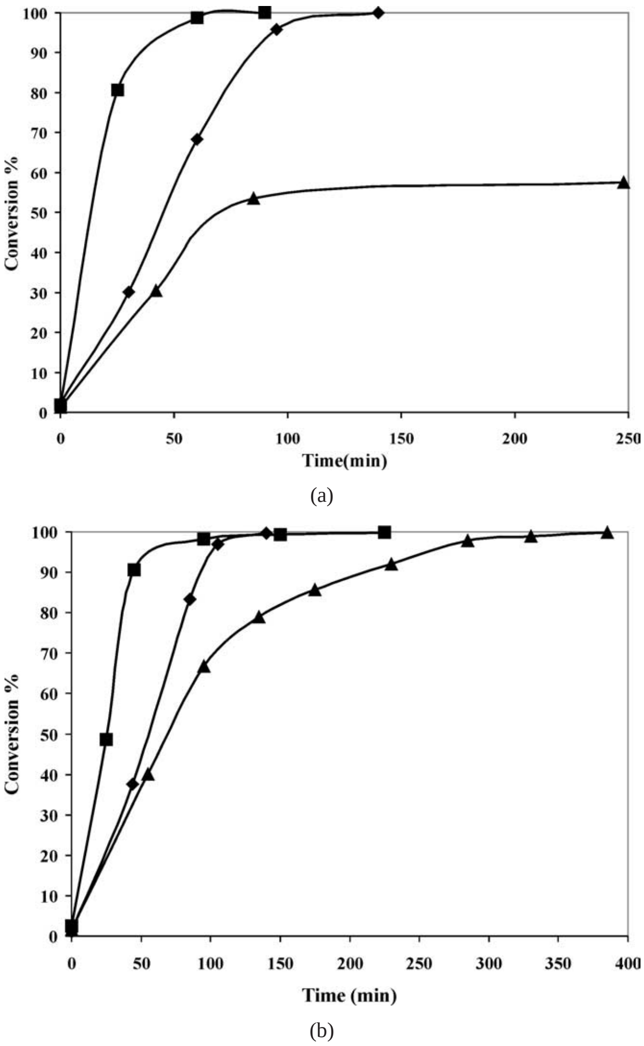
[a] Initial reaction rate (μmol $\mathrm{g_{M_s}^{-1}\,s^{-1}}$).

3.2. Hydrogenation of ethyl pyruvate

Chiral organometallic catalysts were studied in the hydrogenation of ethyl pyruvate, taking the respective monometallic as reference (Fig. 1a), and racemic mixtures were obtained. In the case of the systems based on Rh and Pt, the only products obtained were (R)-ethyl lactate and the (S)-ethyl lactate, while in the case of Ni/SiO$_2$ the appearance of certain additional light products was observed. The Ni/SiO$_2$ catalyst presented a certain level of deactivation probably due to the formation of dimers, oligomers, or hemiketals with the solvent.

In relation to the enantioselective hydrogenation of ethyl pyruvate, the system Ni(−)-MenSnBu$_3$ showed a hydrogenation rate similar to Ni/SiO$_2$ (363 and 331 μmol $\mathrm{g_{Ni_s}^{-1}\,s^{-1}}$, respectively), but it did not present deactivation, which could be attributed to the fact that tin poisons selectively the active sites that lead to reactions responsible for the deactivation of the monometallic catalyst. For the systems based on Rh and Pt modified by tin, a high hydrogenation rate and a behavior similar to the one observed with the respective monometallic catalysts were noted. The catalytic behavior of the tin-modified catalysts is presented in Fig. 1b.

With respect to the enantiomeric excess, for all the catalytic tests, the preferential formation of the (S) enantiomer of ethyl lactate was noted, contrary to what is observed when Pt/cinchonidine system are employed. However, the values of ee% obtained were very low (ca. 7%) for the three metals and all the studied chiral organotin compounds [17]. These results are in the same direction as those previously obtained by our research group with cinchonidine-modified PtSn/SiO$_2$ catalysts having a Sn/Pt atomic ratio greater than 0.04; these systems allowed us to obtain an ee% of the R enantiomer of ca. 10% [18]. In a paper of Margitfalvi et al. it is reported that the enantioselectivity of the Pt/Al$_2$O$_3$-dihydrocinchonidine catalyst is found to change only slightly upon promotion with tin, while the rate of ethyl pyruvate hydrogenation depends strongly on the amount of tin added. These authors also found that the hydrogenation activity is completely suppressed at relatively low tin coverage ($\mathrm{Sn/Pt_s} > 0.06$) [19].



(a)

(b)

Fig. 1. (a) Hydrogenation of ethyl pyruvate on monometallic catalysts. Conversion as a function of time for the following catalysts: (◆) Pt/SiO$_2$, (■) Rh/SiO$_2$, (▲) Ni/SiO$_2$. (For the experimental conditions see the text.) (b) Enantioselective hydrogenation of ethyl pyruvate on heterogeneous chiral catalysts. Conversion as a function of time for the following catalysts: (◆) Pt(−)-MenSnBu$_3$, (■) Rh(−)-MenSnBu$_3$, (◆) Ni(−)-MenSnBu$_3$. (For the experimental conditions see the text.)

3.3. Hydrogenation of acetophenone

In an attempt to demonstrate that this new type of asymmetric catalysts could be used for the enantioselective hydrogenation of different types of substrates, the acetophenone hydrogenation was also examined. The acetophenone hydrogenation can be produced at different points of the molecule: if the C–O bond is hydrogenated, 1-phenylethanol (PE) is obtained, a product of interest in the pharmaceutical and perfume industries. On the other hand, if the aromatic ring is hydrogenated, cyclohexyl methyl ketone (CMK) is obtained. Finally, subsequent hydrogenation of PE or CMK leads to 1-cyclohexylethanol (CHE), a product used to manufacture certain polymers. So, the selection of this substrate represents a higher challenge since the catalyst, besides presenting a enantiodifferentiating capacity, will have to be chemoselective up to the phenylethanol achievement.

Table 1 shows the results of activity and selectivity in the acetophenone hydrogenation for the different chiral catalysts based on the Rh and Pt studied, taking the respective monometallic systems as comparison. For this reaction, Rh/SiO$_2$ does not exhibit any selectivity to PE. The catalyst modification with the chiral compound (−)-MenSnBu$_3$ in an atomic ratio $\mathrm{Sn}/\mathrm{Rh} = 0.3$ produces an increment in the reaction rate, but the chemoselectivity remains the same. These results are different from those reported in the bibliography for the citral hydrogenation with organometallic catalysts of Rh containing butyl groups attached to the surface [10].

Systems based on Pt presented a very different behavior. Table 1 clearly shows that the monometallic catalyst produces a higher proportion of hydrogenation products of the ring, while the modification of such catalyst by addition of organotin compounds via SOMC/M notably enhances the chemoselectivity to phenylethanol (the desired product) in all cases. This result is in agreement with those previously obtained in the hydrogenation of α,β-unsaturated aldehydes, employing organobimetallic catalysts having butyl groups attached to the surface [9]. The origin of this catalytic effect is usually assigned to the fact that tin is found under the form of Sn(0) and Sn(II,IV), inducing important electronic effects, besides it can act as a site-blocking agent that changes the adsorption modes of the molecules. Besides, we suggest that the presence of the bulky menthyl groups is also responsible for the high selectivities obtained in the case of our catalytic systems.

The enantioselective hydrogenation of acetophenone afforded an excess of the (S)-phenylethanol isomer. An ee value of around 20% was obtained with all the chiral organotin compounds tested, which is a good result for acetophenone, a nonactivated ketone, and especially because of the high selectivity to PE (over 97%). Previously published results with the Pt/cinchonidine system showed an ee value of 17%, corresponding to a yield of 4.7% [20]. The similar ee obtained for the three rather different modifiers employed in this work seems to indicate that the chiral induction must be assigned to the presence of at least one menthyl group attached to the surface.

Finally, another important advantage of the catalytic systems presented here is their stability. As it is depicted in Fig. 2, taking Pt(−)-MenSnBu$_3$ as an example, there is a loss in neither the selectivity to PE nor in the ee% value obtained after using, washing, and reusing the catalysts. These findings are of special importance in the study of the catalysts presented here, because, if the detachment of organic fragments were produced during the reaction stage, this would provoke changes in the behavior of the system (conversion, selectivity to phenyl ethanol, enantioselectivity). These changes do not occur, so the stability of this type of supported chiral organobimetallic phases could be accepted, which is an important aspect facing their application in the field of asymmetric catalysis. Analogous results concerning

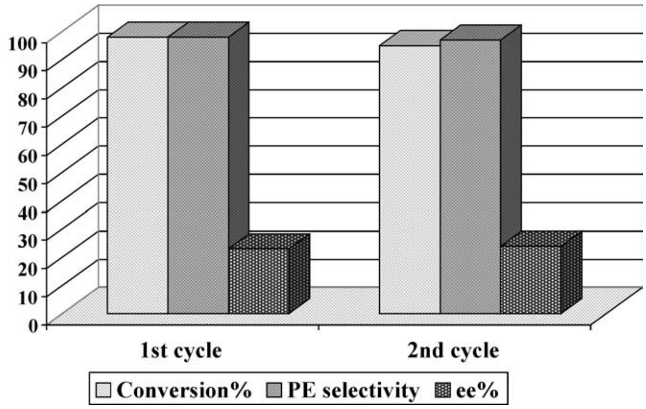


Fig. 2. Conversion, selectivity, and enantioselectivity (at 175 min of reaction) in the hydrogenation of acetophenone in two subsequent runs on Pt(−)-MenSnBu$_3$ catalyst. (For the experimental conditions see the text.)

the stability of organobimetallic phases have been reported by our research group in the case of organobimetallic PtSn catalysts for the selective hydrogenation of α,β-unsaturated aldehydes [9].

Summarizing, in this work we present a new type of asymmetric heterogeneous catalysts (tin-modified platinum-based catalysts) prepared by using techniques derived from the surface organometallic chemistry on metals. These catalysts were able to hydrogenate acetophenone to phenylethanol with a selectivity over 97%, giving an enantiomeric excess (ee%) value of around 20%. Reusing of the catalysts is possible, keeping the selectivity and the ee% values.

These interesting results encourage us to follow our research employing the concept of organometallic chiral catalysts, extending it to other asymmetric processes (i.e., other ketones, especially those involved in pharmaceutical processes, enamines, etc.).

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