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Journal of Molecular Catalysis A: Chemical 187 (2002) 129–134

JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL

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Liquid phase hydroformylation of 1,1-diarylethenes catalyzed by rhodium based heterogeneous catalysts

Maurizio Lenarda*, Renzo Ganzerla, Luca Riatto, Loretta Storaro

Dipartimento di Chimica, Università di Venezia Ca' Foscari, Via Torino 155/B, 30173 Mestre-Venezia, Italy

Received 28 January 2002; accepted 19 March 2002

Abstract

Heterogeneous rhodium based catalyst supported on inorganic oxides such as silica or silica–alumina and pillared clays, reduced with hydrogen or sodium borohydride, catalyze the hydroformylation of 1,1-diarylethenes and vinylnaphthalene. The reaction occurs with very good conversion and interesting chemio- and regio-selectivity values. Activity and selectivity resulted comparable or even better than those found using usual homogeneous rhodium based catalytic systems. No leaching of the active catalyst was observed under the reaction conditions.

Keywords: Hydroformylation; Diarylethenes; Aldehydes; Catalysis

1. Introduction

Several active principles of pharmaceutical products, with therapeutic activity ranging from spasmolithics, anti-spasmodics, neuroleptics, anti-hypertension, choleretics or antihistamines contain the 3,3-diaryl propylic or 3,3-diaryl butylic structural unit [1–3] in their molecule (Scheme 1).

The 3,3-diaryl propylic or butylic fragment can be introduced in the active molecule by various synthetic strategies. Recently, it was demonstrated that 3,3-diarylpropanals could be successfully used for this purpose [4–6]. The 3,3-diarylpropionic aldehydes can be prepared in homogeneous phase with good yields and selectivities by hydroformylation of the corresponding 1,1-diarylethenes [4–7].

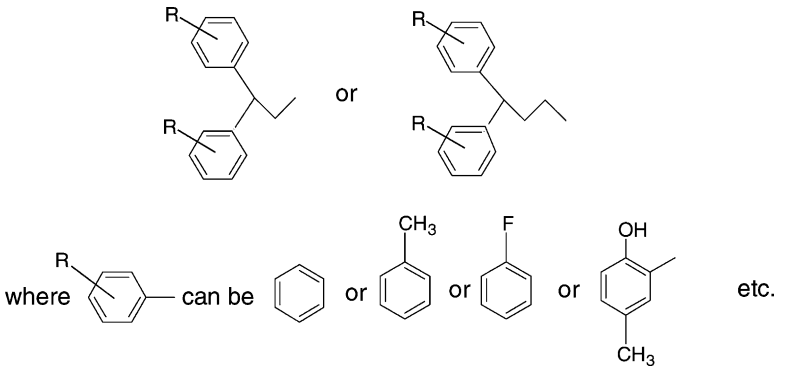
Heterogeneous catalysts are often preferred in industrial processes to the more active and selective homogeneous ones because of their good recoverability. Hydroformylation of simple olefins catalyzed by metals and clusters supported on unfunctionalized inorganic carriers was studied by several authors and the subject was reviewed some years ago [8].

The Rh/B, Rh–Co/B and Rh/Al systems supported on silica and alumina gave particularly interesting results in the vapor phase hydroformylation of ethylene and propylene [9–12].

The use of these catalysts was later extended to the liquid phase hydroformylation of ring substituted styrenes and the Rh–B and Rh–Zn–B systems supported on silica gave encouraging results with good yields and chemo-selectivities [13]. In this paper we present our studies on the liquid phase hydroformylation of some 1,1-diarylethenes and 2-vinylnaphthalene catalyzed by Rh based systems supported on silica, silica–alumina and aluminum pillared montmorillonite clay.

* Corresponding author. Tel.: +39-041-2346762; fax: +39-041-2346735.
E-mail address: lenarda@unive.it (M. Lenarda).

1381-1169/02/$ – see front matter
PII: S1381-1169(02)00175-9



Scheme 1.

2. Experimental

2.1. General methods and chemicals

Reagents and solvents were Aldrich products and when necessary were purified by conventional methods, while the 1,1-diphenylethylene was an Acros product.

Silica–alumina was a Strem Chemicals product with a surface area of 310 m^2/g and specific pore volume of 0.56 ml/g. Detercal P1™, obtained from C. Laviosa, S.p.A. (Leghorn, Italy), was a natural calcium rich bentonite (montmorillonite 97%), factory dried, ground and sieved. Silica was a 432(7) Grace silica catalyst support with a surface area of 320 m^2/g and specific pore volume of 1.65 ml/g. GC analyses were carried out on a Hewlett Packard 5890 gas chromatograph equipped with a FI detector, using a capillary column HP5 (30 m length, 0.53 mm OD). Flash chromatography was done on a silica gel (Merck 60) stationary phase.

Mass spectra were recorded on an HP 5971 instrument. FT-IR spectra were recorded on an FT-IR Nicolet Magna-IR™. ^{1}H NMR were done with a Brucker AC200 spectrometer, in $CDCl_3$ as solvent, at RT. X-ray diffraction (XRD) profiles were recorded on a Philips PW 1319 instrument.

2.2. Catalysts preparation

2.2.1. Rhodium supported on silica (Rh–B/SIL)

Rh–B/SIL was prepared as previously described [9]. Metal particle dimensions where evaluated by XRD using the line broadening method (Scherrer equation) and resulted $\langle D_{RX} \rangle$ (nm) = 4.

2.2.2. Rhodium supported on silica–alumina (Rh–H/SILAL)

The silica–alumina was previously activated at 823 K for 24 h. A suspension of 4 g of activated silica–alumina in 10 ml of anhydrous ethanol was slowly added, under argon, to a magnetically stirred solution of 0.26 g of $RhCl_3 \cdot 3H_2O$ found in the minimum quantity of anhydrous ethanol, contained in a three neck flask. The suspension was maintained at 310 K for 2 h and then the solvent was removed with a rotavapor. A total of 3 g of the resulting powder was placed in a glass U tube and heated in air flow (140 ml/min), increasing the temperature 0.5 °C/min up to 673 K. The sample was maintained at 673 K for 2 h, then cooled down in He flow. The powder was successively reduced in H_2 flow (30 ml/min) by heating the reactor at 8 °C/min up to 673 K, temperature at which it was maintained for 20 min. The rhodium content of the sample was determined by AA and resulted in 2.1% (w/w). Particle dimensions (XRD) $\langle D_{RX} \rangle$ (nm) = 2.

2.2.3. Rhodium supported on APA pillared clay (APARhS)

APA was an aluminum pillared clay prepared as before [14] from the commercial bentonite Detercal P1 (surface area of 312 m^2/g, specific pore volume of 0.24 ml/g, d_{001} = 1.8 nm). The CEC (cation exchange capacity) of the clay was determined as described [14]. The transition metal (Rh) was introduced by cation exchange of the ammonium form of the

pillared clay (APA–NH_4^+) which was previously prepared by treatment of the similarly prepared APA sample with ammonia vapors [14]. In order to obtain the theoretical complete substitution of the ammonium cations, APA–NH_4^+ (5 g) was added, under stirring, to a suitable amount of a diluted water solution of $[Rh(NH_3)_5Cl]Cl_2$, prepared as described in literature [15]. The suspension was stirred for 60 h at RT, centrifuged, washed with distilled water till all the Cl^- disappeared (was eliminated) (silver nitrate test), dried at 333 K, ground and sieved. The rhodium content of the sample was determined by AA and resulted in 1.9% (w/w). This sample is indicated as APARhS.

2.2.4. Reduction of APARhS with aqueous $NaBH_4$ (APARhBH)

A total of 50 ml of a 0.1 M $NaBH_4$ aqueous solution was added, under nitrogen, to a vigorously stirred suspension of 5 g of APARhS in water. When the effervescence subsided the powder was filtered under vacuum and washed, first with water, then with acetone and dried under nitrogen at 373 K. The rhodium content of the sample was determined by AA and resulted in 1.9% (w/w). Particle dimensions (XRD) $\langle D_{RX} \rangle$ (nm) = 2.

2.2.5. Reduction of APARhS in hydrogen flow (APARhSH)

A total of 2 g of APARhS, placed in a U tube, were treated as was the Rh–H/SILAL sample. The rhodium content of the sample was determined by AA and resulted in 1.9% (w/w). Particle dimensions (XRD) $\langle D_{RX} \rangle$ (nm) = 2.

2.3. Olefin synthesis

2.3.1. Preparation of 1-phenyl-1-(4-tolyl)ethylene

The olefin was synthesized from 4-methyl benzophenone as described in literature [4].

2.3.2. Preparation of 1,1-bis(p-fluorophenyl)ethylene

The olefin was prepared from 4,4′-difluoro benzophenone as described in literature [6].

2.3.3. Preparation of 1-[(2-hydroxy-5-methyl)-phenyl]-1-phenyl ethylene

The olefin was synthesized by *p*-cresol *ortho* alkenylation with phenyl acetylene catalyzed by alumina activated by calcination at 773 K for 5 h as previously described [16].

2.4. General hydroformylation procedure

2.4.1. Evaluation of the best operating conditions

The 1,1-diphenylethylene molecule and the Rh–B/SIL catalyst were used to evaluate the best reaction conditions. After several experiments the following conditions were selected for all the successive catalytic tests:

- substrate/catalyst (molar ratio) = 250/1;
- solvent = anhydrous toluene (10 ml), T = 373 K;
- $P_{CO} = P_{H_2} = 50$ bar, $P_{Tot} = 100$ bar, reaction time = 48 h.

An inert reaction atmosphere (argon) was chosen in order to avoid oxidative side reactions.

2.4.2. Leaching evaluation test

Leaching evaluation is very important when a heterogeneous catalytic system is used in condensed phase. The above described catalytic reaction, i.e., the hydroformylation of 1,1-diphenylethylene molecule with Rh–B/SIL as catalyst, was used to evaluate any leaching of the active phase during the reaction, in accordance with what suggested by Sheldon et al [17]. In particular, as described below, the catalytic activity was tested of the remaining solution, after reaction and after removal of the heterogeneous catalyst by centrifugation. The solution resulted totally inactive towards the olefin hydroformylation. The test was repeated with the same olefin and similar procedure, on the other catalytic systems.

2.4.2.1. Leaching evaluation procedure. A total of 8 ml of anhydrous toluene, 0.7 g (3.89 mmol) of 1,1-diphenylethylene and 2 ml of a solution obtained from a previous hydroformylation experiment and centrifuged to separate the solid catalyst was placed, under argon, in a 150 ml autoclave. The vessel was then charged with an equimolar CO/H_2 mixture up to 100 bar. The mixture was kept at 373 K under stirring for 48 h, then analyzed by GC and no hydroformylation products were detected.

3. Results and discussion

3.1. Catalytic tests

3.1.1. Hydroformylation of 1,1-diphenylethylene and 1-phenyl-1-(4-tolyl)ethylene

The 1,1-diarylethylenes have been actively studied in the recent past. Several studies [4,18,19] demonstrated that these substrates can be successfully transformed into the corresponding 3,3-diarylpropanals under oxo conditions with rhodium catalysts usually with good yields and selectivity. The linear aldehyde was formed in preference and an explanation of this behavior was recently proposed by Lazzaroni et al. [20].

A series of hydroformylation tests, under the conditions described in the experimental part Section 2.4.1, using as catalysts the materials described in Section 2.2 were performed on the 1,1-diphenylethylene and 1-phenyl-1-(4-tolyl)ethylene molecules. The results are reported in Tables 1 and 2.

Table 1
Product distribution for the hydroformylation of 1,1-diphenylethylene[a]

Catalyst	Conversion[b] (%)	S_{CHEM}[c] (%)	S_L[d] (%)	Alcohol (%)
Rh–B/SIL	97	100	100	0
Rh–H/SILAL	98	100	100	5
APARhSBH	99	100	100	0
APARhSH	99	100	100	2

[a] Substrate = 3.89 mmol.
[b] (Reacted olefin/starting olefin) × 100.
[c] (Total oxo products (moles)/reacted olefin) × 100.
[d] (Linear oxo products (moles)/total oxo products (moles)) × 100.

Table 2
Product distribution for the hydroformylation of 1-phenyl-1-(4-tolyl)ethylene[a]

Catalyst	Conversion[b] (%)	S_{CHEM}[c] (%)	S_L[d] (%)	Alcohol (%)
Rh–B/SIL	92	100	100	0
Rh–H/SILAL	99	100	100	0
APARhSBH	95	100	100	0
APARhSH	99	100	100	2

[a] Substrate = 1.56 mmol.
[b] (Reacted olefin/starting olefin) × 100.
[c] (Total oxo products (moles)/reacted olefin) × 100.
[d] (Linear oxo products (moles)/total oxo products (moles)) × 100.

Table 3
Product distribution for the hydroformylation of 1,1-bis(*p*-fluorophenyl)ethylene[a]

Catalyst	Conversion[b] (%)	S_{CHEM}[c] (%)	S_L[d] (%)	Alcohol (%)
Rh–B/SIL	91	84	100	0
Rh–H/SILAL	94	81	100	5
APARhSBH	95	83	100	1
APARhSH	92	84	100	1

[a] Substrate = 3.89 mmol.
[b] (Reacted olefin/starting olefin) × 100.
[c] (Total oxo products (moles)/reacted olefin) × 100.
[d] (Linear oxo products (moles)/total oxo products (moles)) × 100.

All the catalytic systems showed, in both cases, total selectivity to oxo products and linear derivatives. The conversion values were also very high, ranging from 92 to 99%. Moderate oxo alcohols formation was observed in some cases for the rhodium catalysts (RhH/SILAL and APARhSH) prepared by reduction with hydrogen with a maximum of 5% for the former. Slightly lower conversion values were observed in the case of 1-phenyl-1-(4-tolyl)ethylene when borohydride reduced catalysts (Rh–B/SIL and APARhSBH) were used.

Porosity and pores dimension appeared not to influence the products distribution.

Conversion and selectivity values were in general comparable to those found for the same substrates using homogeneous rhodium catalysts [4].

3.1.2. Hydroformylation of 1,1-bis(p-fluorophenyl)-ethylene

The 4,4-bis(*p*-fluorophenyl)butyl structural unit is present in the molecule of various pharmaceutical active principles [1–3]. The 4,4-bis(*p*-fluorophenyl)butanal molecule can be a very useful synthetic intermediate to introduce this unit in various pharmaceutical precursors. Recently the successful preparation of 4,4-bis(*p*-fluorophenyl)propanal by hydroformylation of 1,1-bis(*p*-fluorophenyl)ethylene with homogeneous rhodium catalysts and its conversion to 1,1-bis(*p*-fluorophenyl)butanal by homologation [5] was described. In Table 3 we report the results of the 1,1-bis(*p*-fluorophenyl)ethylene hydroformylation on the above described rhodium based heterogeneous catalysts.

Analogously to what found for the homogeneously catalyzed systems [5] the reaction rates are comparable to those of the related 1,1-diphenylethylene and 1-phenyl-1-(4-tolyl)ethylene molecules under similar reaction conditions. Regio-selectivity was still totally in favor of the desired linear oxo product but chemo-selectivity was lower, with a 15–20% of double bond hydrogenation. This finding can be tentatively attributed to the slightly higher stabilization of the metal–carbon bond caused by the fluorine *para* substitution in the aromatic ring. As observed for the preceding olefins the more acidic silica–alumina appeared to favor the oxo aldehyde hydrogenation.

3.1.3. Hydroformylation of 1-[(2-hydroxy-5-methyl)phenyl]-1-phenyl ethylene

The olefinic substrate 1-[(2-hydroxy-5-methyl)-phenyl]-1-phenyl ethylene, can be employed as useful precursor in the synthesis of (+)(R) tolterodine, an important drug, used as antidepressant and as controller of urinary incontinence [16].

The results of the hydroformylation tests carried on this substrate using the same series of heterogeneous rhodium catalysts are reported in Table 4.

The selectivity of all the four catalysts towards the linear oxo products is total as observed for the other 1,1-diphenyl olefins. A slight decrease in the overall conversion values was however observed. The phenomenon is particularly evident in the case of the two catalysts (Rh–B/SIL and APARhSBH) prepared by reduction with sodium borohydride and in these cases linked to a strong decrease of the chemo-selectivity. It was found that supported rhodium catalysts, prepared by metal salts reduction with sodium borohydride, contained variable amounts of oxidized boron species [11,12]. It is therefore possible to attribute the lower reactivity and chemo-selectivity of these systems to the bonding interaction of the oxydrilic group of the aromatic ring with surface boron species. The catalyst supported on silica–alumina confirmed its attitude to reduce the oxo aldehyde.

3.1.4. Hydroformylation of 2-vinylnaphthalene

The vinyl aromatic olefins can by utilized as good synthetic precursors for preparation of an interesting class of pharmaceutical principles, the aryl propanoic acids [21]. These compounds are in fact a highly active and commercially interesting class of NSAL, that can be prepared by the branched aldehyde obtained by hydroformylation of the corresponding vinyl olefin. One of the few commercially available vinyl olefins is the 2-vinylnaphthalene and therefore this substrate was chosen to test the behavior of the studied series of rhodium catalysts. The results of the catalytic tests are reported in Table 5.

All the systems are very active and totally selective towards the hydroformylation. All the catalysts show an interesting selectivity toward the formation of the branched oxo derivatives, with a peak of 90% in the case of Rh–H/SILAL. This is not surprising because vinylaromatic and heteroaromatic olefins usually give the branched derivative under oxo conditions. This behavior can be explained by the stabilization of the branched σ-alkyl rhodium intermediate by the aromatic ring. Nevertheless the rhodium heterogeneous systems appeared to be more active and selective than their homogeneous counterpart.

Table 4
Product distribution for the hydroformylation of 1-[(2-hydroxy-5-methyl) phenyl]-1-phenylethylene[a]

Catalyst	Conversion[b] (%)	S_{CHEM}[c] (%)	S_L[d] (%)	Alcohol (%)
Rh–B/SIL	80	53	100	0
Rh–H/SILAL	86	92	100	10
APARhSBH	87	68	100	0
APARhSH	82	95	100	0

[a] Substrate = 2 mmol.
[b] (Reacted olefin/starting olefin) × 100.
[c] (Total oxo products (moles)/reacted olefin) × 100.
[d] (Linear oxo products (moles)/total oxo products (moles)) × 100.

Table 5
Product distribution for the hydroformylation of 2-vinyl-naphthalene[a]

Catalyst	Conversion[b] (%)	S_{CHEM}[c] (%)	S_L[d] (%)	Alcohol (%)
Rh–B/SIL	100	100	76	0
Rh–H/SILAL	100	100	90	0
APARhSBH	100	100	78	0
APARhSH	100	100	74	0

[a] Substrate = 3.89 mmol.
[b] (Reacted olefin/starting olefin) × 100.
[c] (Total oxo products (moles)/reacted olefin) × 100.
[d] (Branched oxo products (moles)/total oxo products (moles)) × 100.

4. Conclusions

It possible to conclude, from the reported data, that heterogeneous rhodium based catalyst supported on inorganic oxides and pillared clays, can be successfully used to catalyze the hydroformylation of 1,1-diarylethenes and 2-vinylnaphthalene. The reaction occurs with conversion, chemio- and regio-selectivity values comparable or even better than the known homogeneous rhodium systems. Both the surface morphology and the porosity of the support did not appear to influence the activity and selectivity of the catalysts. Surface acidity (as observed in the case of silica–alumina) appears to slightly favor the reduction of the formed aldehydes to the corresponding alcohols. No leaching of the catalyst was observed under the reaction conditions.

Acknowledgements

This work was supported by funds of Ministero dell'Università e Ricerca Scientifica (MIUR). LR thanks S. Paganelli for the help in the olefin precursors synthesis. All the authors thank S. Paganelli, C. Botteghi and O. Piccolo for the helpful discussion.

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