Journal of Molecular Catalysis A: Chemical 363–364 (2012) 49–57

Contents lists available at SciVerse ScienceDirect

Journal of Molecular Catalysis A: Chemical

journal homepage: www.elsevier.com/locate/molcata

Neutral η^6-arene ruthenium complexes with monodentate P-donor ligands Activation in the transfer hydrogenation reaction

Arnald Grabulosa[a], Alberto Mannu[a,b], Elisabetta Alberico[c], Stefania Denurra[b,d], Serafino Gladiali[b,d], Guillermo Muller[a,*]

[a] Departament de Química Inorgànica, Universitat de Barcelona, Martí i Franquès, 1-11, E-08028 Barcelona, Spain
[b] Dipartimento di Chimica, Università di Sassari, via Vienna, 2, 07100 Sassari, Italy
[c] Istituto di Chimica Biomolecolare, CNR, trav. La Crucca 3, 07100, Italy
[d] Leibinz Institut for Catalysis, Albert-Einstein Straße 29a, Rostock, Germany

ARTICLE INFO

Article history:
Received 16 April 2012
Received in revised form 21 May 2012
Accepted 23 May 2012
Available online 1 June 2012

Keywords:
Ruthenium arene complexes
Transfer hydrogenation
Acetophenone reduction
Induction period

ABSTRACT

Five Ru(II) neutral complexes **C** of the type [$RuCl_2(\eta^6$-arene)(**P**)] (**P** = monodentate phosphorus ligand) have been prepared: **C1** (arene = *p*-cymene, **P** = PPh_3); **C2** (arene = *p*-cymene, **P** = (*R*)-Monophos); **C3** (arene = *p*-cymene, **P** = (*S*)-Ph-Binepine); **C4** (arene = benzene, **P** = PPh_3); and **C5** (arene = benzene, **P** = (*S*)-Ph-Binepine). These complexes have been screened as catalytic precursors in the transfer hydrogenation of acetophenone with 2-propanol. Under optimised conditions at 82 °C complexes **C1** and **C4** provide full conversion in less than 20 min at a [Ru]:substrate ratio of 1:200. With the chiral complexes **C2** and **C3** good TOF values have been reached but with low enantioselectivities. The activation of the catalytic precursor has been studied. Based on NMR evidence, a mechanism in which the catalytically active species is a Ru monohydride complex arising from the reaction of the catalyst precursor **C** with 2-propanol in the presence of a base is suggested. The reaction shows different sensitivity towards excess of phosphine: whereas excess of PPh_3 slows down the reaction severely, excess of (*S*)-Ph-Binepine does not cause such a sharp effect. An excess of chloride ion affects the activation of the precursor **C**.

1. Introduction

Reduction of ketones to the parent alcohols is a classic transformation of organic chemistry, traditionally carried out by metallic hydrides or molecular hydrogen in the presence of heterogeneous catalysts [1]. Albeit effective, these strategies have severe disadvantages. The former involves the manipulation of pyrophoric hydrides and the generation of stoichiometric amounts of metallic salts as waste whereas the latter usually requires elevated temperatures and high pressures of hydrogen gas with the inherent risks associated with the manipulation of a highly flammable reagent. A much safer and simple alternative is the formal transfer of two H atoms from a hydrogen donor to the carbonyl group in the presence of a suitable homogeneous catalyst, a process known as transfer hydrogenation (TH) [2]. This process is a key transformation in homogenous catalysis, especially in the asymmetric version, because it frequently ensures quantitative conversions and high enantioselectivities in a short reaction time. Ruthenium precursors bearing chiral diamines and/or diphosphines such as BINAP, developed by Noyori and coworkers [3–5], "reverse tethered" precursors, described by Wills and coworkers [6], systems that contain cyclometallated terdentate ligands, described by Baratta et al. [7] and cycloruthenated complexes such as the ones recently reported by de Vries and coworkers [8] stand out within the most successful systems. In all these systems, the presence of at least one amine unit in the ligand structure seems to be pivotal for reaching very high TOF values and elevated enantioselectivities.

Ruthenium complexes of the type [$RuCl_2(\eta^6$-arene)(**P**)] with **P** as a monodentate phosphorus ligand [9] despite being stable and easy to prepare have seldom been used in TH. Rossell and coworkers [10] reported the use of [$RuCl_2(\eta^6$-*p*-cymene)(PPh_3)] and [$RuCl_2(\eta^6$-*p*-cymene)($PMePh_2$)] in the reduction of cyclohexanone, whereas Carriedo and coworkers [11] also used [$RuCl_2(\eta^6$-*p*-cymene)(PPh_3)] but in the reduction of acetophenone. Li and coworkers [12] have recently reported very good activities of [$RuCl_2(\eta^6$-benzene)(PAr_3)] complexes (Ar = Ph, *p*-An and *p*-CF_3Ph) in the reduction of the same substrate. Almost at the same time, some of us [13] reported the successful enantioselective reduction of acetophenone using several [$RuCl_2(\eta^6$-*p*-cymene)(**P***)] containing optically pure diarylic *P*-stereogenic phosphines **P***. Some of these complexes showed good activities and moderate enantioselectivities.

* Corresponding author. Tel.: +34 934039140; fax: +34 934907725.
E-mail address: guillermo.muller@qi.ub.es (G. Muller).

1381-1169/$ – see front matter © 2012 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.molcata.2012.05.015

In this paper the results obtained in H-transfer reduction of acetophenone by complexes of the same family with a broader selection of both chiral and achiral monophosphorus ligands are reported. A series of experiments have been carried out with precursors **C1** and **C3** in order to shed some light on the mechanism of the catalytic reaction promoted by such complexes.

2. Results and discussion

2.1. Synthesis of Ru complexes

Complexes **C1**–**C5** were easily prepared as air-stable solids following a known procedure [14–16], by treating one equivalent of the well-known dimers $[RuCl_2(\eta^6\text{-}p\text{-cymene})]_2$ (**D1**) or $[RuCl_2(\eta^6\text{-benzene})]_2$ (**D2**) with two equivalents of the monophosphorus ligand in dichloromethane (Scheme 1).

Synthesis of complexes **C1**–**C4** was achieved at room temperature whereas the preparation of **C5** required slightly higher temperature due to the poor solubility of **D2** in dichloromethane. All complexes were isolated in moderate to good yields as spectroscopically pure solids. Complexes **C1** [9,17], **C2** [18] and **C4** [12] are known compounds while (*S*)-Ph-Binepine [19,20] complexes **C3** and **C5** have not been reported previously. Complex **C3** is a dark orange solid featuring a singlet at 48.3 ppm in the ^{31}P NMR spectrum in CD_2Cl_2 with a coordination induced shift to lower field of almost 40 ppm compared to the free ligand (7.43 ppm). As a consequence of the coordination of the chiral Ph-Binepine ligand, the two methyl groups of the *i*-Pr moiety become diastereotopic and give rise to separate peaks in the ^1H NMR spectrum. For the same reason, all four arylic protons of the coordinated *p*-cymene substituent are distinguishable. In contrast, the six protons of the coordinated benzene of **C5** give rise to a single resonance at 5.40 ppm, indicative of a free rotation around the Ph–Ru axis.

2.2. Catalytic hydrogen transfer

2.2.1. Influence of the different parameters on the catalytic outcome

Optimisation of the reaction conditions for transfer hydrogenation of acetophenone was carried out using complex **C1**, already known to be active in TH (Scheme 2) [10,11].

In order to generate the catalytic active species, complex **C1** and potassium *tert*-butoxide were dissolved in 2-propanol and heated to reflux. After the allotted time (activation period), acetophenone was added. As shown in Table 1, the efficiency of the transfer hydrogenation reaction (yield and TOF value) turned out to be critically dependent on the activation period.

When catalytic precursor, base and substrate were mixed together, the conversion at 10 min (Table 1, entry 1) was much lower than when acetophenone was added later (Table 1, *cf.* entry 1 with entries 5 and 8). This suggests that some time is necessary in order to generate a steady concentration of the catalytically active species in solution. The activation process demands the presence of ^{t}BuOK since practically no conversion was observed without base (Table 1, entry 14). Further experiments at shorter activation times (not listed in the table) were carried out while sampling at every 5 min. Despite a very careful and quick sampling, erratic conversion values were obtained, suggesting that the process of formation of the active species is very sensitive. On the other hand, long induction periods (Table 1, entry 11) were detrimental for the conversion, probably due to catalyst decomposition in the absence of substrate. Therefore, an activation time of 15 min was judged to be optimal under the actual conditions, leading to the highest conversion possible (around 98%) in 20 min (Table 1, entry 6).

Table 1
Effect of the activation period on the TH of acetophenone using precursor **C1**.

Entry[a]	Activation period (min)	Time (min)[b]	Yield (%)[c] [TOF][d]
1	0	10	30.3[363]
2	0	20	48.2
3	0	30	66.7
4	0	40	81.2
5	15	10	93.1[1117]
6	15	20	97.7
7	15	30	98.1
8	30	10	84.6[1015]
9	30	20	95.3
10	30	30	97.6
11	60	10	67.5[810]
12	60	20	90.6
13	60	30	95.8
14[e]	15	0	1.3
15[e]	15	10	36.2[434]
16[e]	15	20	64.9
17[e]	15	30	83.9

[a] Conditions: 0.02 mmol of **C1** and 0.1 mmol of ^{t}BuOK were dissolved in 25 ml of ^{i}PrOH and heated to 82 °C. After the allotted time, 4 mmol of acetophenone were added [Ru/^{t}BuOK/acetophenone = 1:5:200].
[b] Time after addition of acetophenone.
[c] Yield in 1-phenylethanol, determined by GC.
[d] Turnover frequency, TOF = [mmol of 1-phenylethanol/mmol of **C1**]/time (h).
[e] The order of addition of ^{t}BuOK and acetophenone was reversed; the reaction time is counted after addition of ^{t}BuOK.

The next round of experiments was designed to analyse the effect of the amount of potassium *tert*-butoxide on the catalytic outcome (Table 2).

Although one equivalent of potassium *tert*-butoxide was sufficient to initiate the reaction, the latter did progress very slowly (Table 2, entries 1–3), 5 or more equivalents of base (Table 2, entries 4–9) instead ensured elevated conversions at shorter reaction times.

We next turned our attention to the effect of the temperature both on the activation time and catalysis efficiency (Table 3).

High temperatures were required for the catalytically active species to be formed since very low conversions at 10 min were recorded even in refluxing 2-propanol when the activation process was performed at room temperature (Table 3, entry 4). At 40 °C the catalyst apparently deactivates after about 10% of conversion (Table 3, entries 7–9). The reaction did not proceed at room temperature regardless of the activation temperature (Table 3, entries 10–12).

Having established the best conditions to generate the active catalytic species, other catalysts, either prepared *in situ* or

Table 2
Effect of the amount of ^{t}BuOK on the TH of acetophenone using precursor **C1**.

Entry[a]	Equivalents of ^{t}BuOK	Time (min)[b]	Yield (%)[c] [TOF][d]
1	1	10	9.0[108]
2	1	20	13.0
3	1	30	17.2
4	5	10	93.1[1117]
5	5	20	97.7
6	5	30	98.1
7	20	10	86.0[1032]
8	20	20	96.5
9	20	30	98.0

[a] Conditions: 0.02 mmol of **C1** and the allotted amount of ^{t}BuOK were dissolved in 25 ml of ^{i}PrOH and heated to 82 °C. After 15 min, 4 mmol of acetophenone were added [Ru/acetophenone = 1:200].
[b] Time after addition of acetophenone.
[c] Yield in 1-phenylethanol, determined by GC.
[d] Turnover frequency, TOF = [mmol of 1-phenylethanol/mmol of **C1**]/time (h).